JOC *Article*

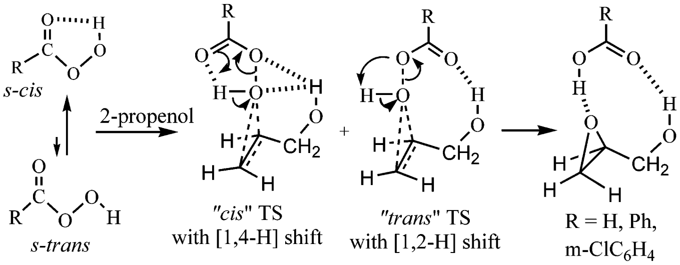
Peroxy Acid Epoxidation of Acyclic Allylic Alcohols. Competition between s-trans and s-cis Peroxy Acid Conformers

Mauro Freccero,† Remo Gandolfi,*,† Mirko Sarzi-Amadè,† and Augusto Rastelli‡

Dipartimento di Chimica Organica, Università di Pavia, V.le Taramelli 10, 27100 Pavia, Italy and Dipartimento di Chimica, Università di Modena, Via Campi 183, 41100 Modena, Italy

remo.gandolfi@unipv.it

Received July 30, 2005



RB3LYP calculations, reported here, indicate that peroxy acid s-cis conformer is more stable than its s-trans counterpart, in agreement with experimental data. Difference in stability is the highest in the gas phase, but it falls considerably on going from the gas phase to moderately polar solvent. In the case of peroxy formic acid, the enthalpy (free energy) difference is about 3.4 (2.5) kcal/mol, respectively, in the gas phase but decreases to 1.2 (0.6) kcal/mol in dichloromethane solution. Introduction of an alkyl or aryl substituent on the peroxy acid, that is, on passing to peroxy acetic, peroxy benzoic (PBA), and *m*-chloroperoxy benzoic acid (MCPBA), adds a further significant (1.0−1.5 kcal/mol) favor to the s-cis isomer. RB3LYP/6-31+G(2d,p) calculations on the epoxidation of 2-propenol with peroxy formic and peroxy benzoic acids, respectively, suggest that the less stable peroxy acid s-trans conformer can compete with the more stable s-cis form in epoxidation reaction of these substrates. Transition structures arising from s-trans peroxy acids ("trans" TSs) retain both the well-established, for "cis" TS, perpendicular orientation of the O−H peroxy acid bond relative to the C═C bond and the one-step oxirane ring formation. These TSs collapse to the final epoxide via a 1,2-H shift at variance with the 1,4-H transfer of the classical Bartlett's "cis" mechanism. The "trans" reaction pathways have a higher barrier in the gas phase than the "cis" reaction channels, but in moderately polar solvents they become competitive. In fact, the "trans" TSs are always significantly more stabilized than their "cis" counterparts by solvation effects. Calculations also suggest that going from peroxy formic to peroxy benzoic acid should slightly disfavor the "trans" route relative to the "cis" one, reflecting, in an attenuated way, the decrease in the peroxy acid s-trans/s-cis conformer ratio. The predicted behavior for MCPBA parallels that of PBA acid.

Introduction

Epoxidation with peroxy acids still represents a very important tool for introduction of oxygen functionality in organic molecules.[1] The classical Bartlett's "butterfly" mechanism, which suggests concerted formation of the oxirane ring with concomitant 1,4-transfer of the proton of the peroxy acid to the carbonyl oxygen,[2] has been substantially supported during the years by experimental data and, more recently, by high level computational investigations. Obviously, it has also been significantly refined, and major points in this context are represented by:

(i) The computational demonstration that "spiro" TSs (in which the peroxy acid plane has a perpendicular orientation with respect to the C═C bond) are, as a rule,

---

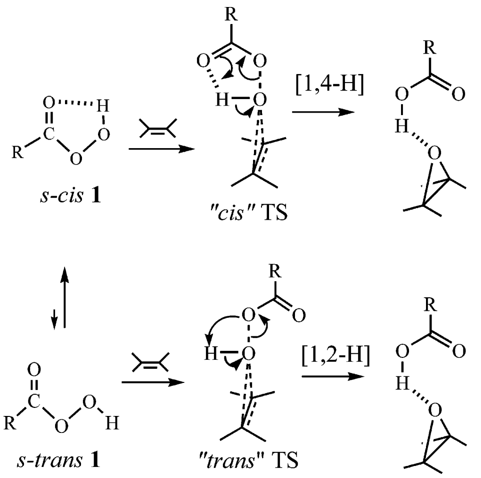
* Corresponding author. Phone: +39-382-987668. Fax: +39-382-987323.
† Università di Pavia.
‡ Università di Modena.

[1] (a) *Methods of Organic Chemistry (Houben-Weyl)*, 4th ed.; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; G. Thieme: Stuttgart, New York, 1995; Vol. E, 21e. (b) For a review on substrate directable reactions, see: Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307. (c) For a review on hydroxy group directivity in the epoxidation of allylic alcohols, see: Adam, W.; Wirth, T. *Acc. Chem. Res.* **1999**, *32*, 703.

[2] Bartlett, P. D. *Rec. Chem. Prog.* **1950**, *11*, 47; **1957**, *18*, 111.

10.1021/jo0515982 CCC: $30.25

SCHEME 1

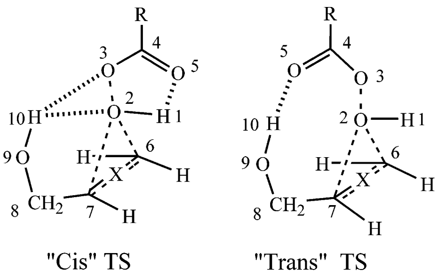


preferred over "planar" TSs (in which the peroxy acid plane contains the C=C moiety);[3–5] planar-like TSs are operative only in the case of sterically congested systems, which cannot accommodate spiro-like TSs, and exhibit a very high asynchronicity in C- - -O bond formation.[5e]

(ii) The experimental[6] and computational[3–5] evidence that breaking of the peroxy acid OH bond is not heavily involved in the first part of the epoxidation process, namely, at TS elongation of this bond, is very small, demonstrating that H transfer has not started yet.

The latter observation makes it clear that operation of the 1,4-mechanism for the hydrogen shift is not an essential requisite to make the epoxidation process viable. Actually, the O−H bond plays, at the "cis" TS, the very same role it plays in the starting s-cis peroxy acid (i.e., it stabilizes the system through an efficient intramolecular hydrogen bonding (HB) interaction; see Scheme 1). Thus, one can reasonably argue that the less stable s-trans peroxy acid conformer can enter epoxidation reactions through a "trans" TS that will collapse to the final epoxide via a 1,2-H shift (Scheme 1). It is quite evident that the presence of the intramolecular HB interaction in "cis" TSs will make these TSs highly favored over "trans" TSs in the epoxidation of alkenes (Scheme 1). Consistently, we have previously demonstrated that peroxy acid epoxidation of simple alkenes has lower barriers for "cis" TSs than for "trans" TSs irrespective of solvent influence[7] and have concluded that one can reasonably exclude a role of s-trans conformers in epoxidation of alkenes at least in the absence of specific interaction of peroxy acids with solvent or catalysts. However, in allylic alcohol epoxidation intermolecular HB interaction can provide "trans" TSs (Scheme 2) with an additional efficient stabilization that counterbalances intramolecular HB in "cis" TSs, making competition between the two routes less easily predictable.

SCHEME 2



X is a dummy atom

Very recently we have demonstrated, by B3LYP calculations, that in the epoxidation of cyclic allylic alcohols (e.g., 2-cyclobutenol) not only that the "trans" route represents a viable pathway but also that this alternative reaction channel has a slightly lower activation free energy than that of the classical mechanism in moderately polar solvents (B3LYP/6-311+G(d,p) data for PFA epoxidation in dichloromethane solution).[7] To substantiate this conclusion and to assess how general it is, we extended our study to acyclic alcohols. We report here a careful DFT study (i) of the "s-cis"/"s-trans" conformational equilibrium of the starting peroxy acid in both gas phase and solution (benzene and dichloromethane) and (ii) of the 2-propenol epoxidation with peroxy formic acid (PFA), peroxy benzoic acid (PBA), and *m*-chloroperoxy benzoic acid (MCPBA) in both the gas phase and solution. Acyclic allylic alcohols lack the inherent conformational constraint of cyclic ones, and this observation is particularly true for the parent 2-propenol in which also 1,3-allylic strains[1c] are almost absent so that the OH group can easily adjust its conformation to maximize HB interactions with the attacking peroxy acid. Our study is focused on the competition between "trans" and "cis" TSs.

Computational Methods

A reliable prediction for the mechanism of peroxy acid epoxidation of allylic alcohols is a challenging task for computational methods. It is well-known that it is difficult to correctly evaluate HB interactions[8] as well as to properly describe the properties of peroxidic systems,[9] while also asynchronicity of developing C- - -O bonds is a delicate point. We have chosen the hybrid B3LYP functional[10] since high-level computational investigations, performed very recently by Bach et al., demonstrated that this variant of DFT is a useful and reasonably accurate method of choice for the study of

---

(3) (a) Bach, R. D.; Estevez, C. M.; Winter, J. E.; Glukhovtsev, M. N. *J. Am. Chem. Soc.* **1998**, *120*, 680. (b) Bach, R. D.; Glukhovtsev, M. N.; Gonzales, C. *J. Am. Chem. Soc.* **1998**, *120*, 9902. (c) Adam, W.; Bach, R. D.; Dimitrenko, O.; Saha-Moller, C. R. *J. Org. Chem.* **2000**, *65*, 6715. (d) Bach, R. D.; Dimitrenko, O.; Adam, W.; Schambony, S.; Gonzales, C. *J. Am. Chem. Soc.* **2003**, *125*, 924. (e) Bach, R. D.; Dimitrenko, O. *J. Phys. Chem. A* **2003**, *107*, 4300.

(4) (a) Houk, K. N.; Liu, J.; DeMello, N. C.; Condroski, K. R. *J. Am. Chem. Soc.* **1997**, *119*, 10147. (b) Houk, K. N.; Washington, I. *Angew. Chem., Int. Ed.* **2001**, *40*, 4485. (c) Washington, I.; Houk, K. N. *Org. Lett.* **2002**, *4*, 2661.

(5) (a) Freccero, M.; Gandolfi, R.; Sarzi-Amadè, M. *Tetrahedron* **1999**, *55*, 11309. (b) Freccero, M.; Gandolfi, R.; Sarzi-Amadè, M.; Rastelli, A. *J. Org. Chem.* **1999**, *64*, 3853. (c) Freccero, M.; Gandolfi, R.; Sarzi-Amadè, M.; Rastelli, A. *J. Org. Chem.* **2000**, *65*, 2030. (d) Freccero, M.; Gandolfi, R.; Sarzi-Amadè, M.; Rastelli, A. *J. Org. Chem.* **2000**, *65*, 8948. (e) Freccero, M.; Gandolfi, R.; Sarzi-Amadè, M.; Rastelli, A. *J. Org. Chem.* **2002**, *67*, 8519.

(6) (a) Hanzlik, R. P.; Shearer, G. O. *J. Am. Chem. Soc.* **1975**, *97*, 5231. (b) Koerner, T.; Sleboka-Tilk, H.; Brown, R. S. *J. Org. Chem.* **1999**, *64*, 196.

(7) Freccero, M.; Gandolfi, R.; Sarzi-Amadè, M.; Rastelli, A. *J. Org. Chem.* **2004**, *69*, 7479.

(8) Staroverov, V. N.; Scuseria, G. E.; Tao, J.; Perdew, J. P. *J. Chem. Phys.* **2003**, *119*, 12129.

(9) Wu, A.; Cremer, D.; Plesnicar, B. *J. Am. Chem. Soc.* **2003**, *125*, 9395.

peroxy acid epoxidation.[3e] The 6-311++G(3df,2pd) basis set is certainly large enough and well-balanced[8,9] to fulfill all the stringent requirements of our problem. We used the B3LYP/6-311++G(3df,2pd) method to evaluate the conformational equilibrium of PFA (in the gas phase and solution) as well as to locate all the TSs of 2-propenol epoxidation with this peroxy acid in the gas phase. The results of these calculations were used as benchmark to determine how well lower level methods perform. We found that the B3LYP/6-31+G(2d,p) method nicely reproduces the relative stability of PFA conformers as well as that of PFA epoxidation TSs (in particular the relative energy of "trans" and "cis" TSs) found at the B3LYP/6-311++G(3df,2pd) level. In contrast, not only the standard B3LYP/6-31G(d) method but also, somewhat surprisingly, the popular B3LYP/6-311+G(d,p) method are significantly worse. The TSs for the gas-phase epoxidation with peroxy benzoic acid as well as with MCPBA were located with the B3LYP functional and 6-31G(d), 6-31+G(2d,p), and 6-311+G(d,p) basis sets, but only the reliable B3LYP/6-31+G(2d,p) results will be here reported.

The search for TSs was limited to concerted transition structures (i.e., only restricted B3LYP methods were used). All gas-phase TSs reported in this article gave a positive answer to the stability test (i.e., all TSs were found stable with the keyword Stable = Opt). All TSs were characterized as genuine transition structures by vibrational analysis (one imaginary frequency). Vibrational frequencies, calculated under the rigid-rotor harmonic approximation, were used unscaled[11] to compute zero-point energies, thermal corrections to enthalpy, entropy, and Gibbs free energy. Activation parameters (at 298.15 K) for all of the TSs are referred, for sake of homogeneity and clarity, to the more stable s-cis form of the starting peroxy acid and to the most stable propenol conformer (the "out" conformer). The standard state of the molar concentration scale (gas in ideal mixture at 1 mol/L, $P = 1$ atm) was used. For conversion from 1 atm standard state to 1 mol/L standard state (both for gas-phase reactions), the following contributions were added to standard enthalpy, entropy, and Gibbs free energy: $-RT$, $-R \ln R'T - R$, and $RT \ln R'T$, where R' is the value of R constant given in (L atm)/(mol K). For a reaction with A + B = C stoichiometry, the corrections for $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta G^{\ddagger}$ are RT, $R \ln R'T + R$, and $-RT \ln R'T$, respectively (0.592 kcal/mol, 8.34 eu, and −1.893 kcal/mol, respectively, at 298.15 K).[11]

Bulk solvent effects on TS geometries and energies were calculated with the self-consistent reaction field (SCRF) theory using the PCM-united atom topological model (UAHF) model, as implemented in the C.02 version of Gaussian 2003.[10] The solvent cavity is composed of interlocking spheres centered on non hydrogen atoms (and hydrogen atom are enclosed on the sphere of the atom) with radii obtained by the Barone's HF parametrization known as UAHF. The keyword RADII = UAHF was used, and the number of tesserae per atom sphere was set to 100 (TSNUM = 100). It is worth emphasizing also that the choice of the solvation model is a problematic point as far as competition between "trans" and "cis" TSs is concerned. Our choice was dictated by the observation that the PCM-UAHF method gives results that are consistent with those obtained with the PCM-UFF (radii from the UFF force field and spheres also on hydrogen atoms) as well as with those from the PCM-UA0 (radii from the UFF force field and hydrogen atom enclosed on the sphere of the atom) with spheres on the two acidic hydrogens (H−O). The default PCM-UA0 (radii from the UFF force field and hydrogen atom enclosed on the sphere of the atom) model tends to overestimate the stability of "trans" structures for both peroxy acids and epoxidation TSs. For example, it predicts, in contrast with experimental data,[12] that the s-trans peroxy acid form should be more stable than the s-cis one in dichloromethane solution.

B3LYP/6-31+G(2d,p) full geometry optimizations and frequency calculations were performed also for TSs of PFA epoxidations in benzene and dichloromethane,[13] while solvation effects for the PBA and MCPBA reactions were evaluated by single-point B3LYP/6-31+G(2d,p) calculations on gas-phase optimized geometry at the same theory level. The enthalpy and free energy data for benzene and dichloromethane solutions of PBA and MCPBA epoxidation reaction were obtained by adding the gas phase thermal corrections (to enthalpy and free energy, respectively) to the "total free energy in solution" (that includes, in addition to electrostatic effects, also cavitation, dispersion, and repulsion energy).[14]

IRC calculations were performed with the B3LYP/6-31G(d) method in the gas phase.

Results and Discussion

Conformational Equilibrium of Peroxy Acids. A computational investigation on the relative stability in the gas phase of s-cis and s-trans conformers of peroxy acids (Scheme 3) has recently been carried out by Plesnicar et al. by using the B3LYP/6-311++G(d,p) method.[12] The very similar B3LYP/6-311+G(d,p) method has been routinely used for peroxy acid epoxidations[3,5] as well as for hydrogen bonding[15] problems since it has a moderately large and a reasonably balanced basis set. However, these basis sets are not fully adequate to study the peroxy acid s-cis/s-trans conformational problem since they probably overestimate the stability of the s-trans form. This conclusion is suggested by the data reported in Tables 1 and S1 and is based on the presumption that the accuracy of the B3LYP/6-311++G(3df,2pd) method is highest. In fact, inspection of Tables 1 and S1 clearly shows that the B3LYP/6-311+G(d,p) method, of triple-ζ quality, systematically overestimates the relative stability of the s-trans form by about 1 kcal/mol in the case of peroxy formic acid and slightly less in the case of peroxy acetic and peroxy benzoic acids both in the gas phase and in solution. By contrast, and somewhat surprisingly, the B3LYP/6-31+G(2d,p) method, of double-ζ quality but

---

(10) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision C.02; Gaussian, Inc.: Wallingford, CT, 2004.

(11) Rastelli, A.; Bagatti, M.; Gandolfi, R. *J. Am. Chem. Soc.* **1995**, *117*, 4965

(12) Erzen, E.; Koller, J.; Plesnicar, B. *J. Org. Chem.* **2001**, *66*, 5155 and references therein.

(13) These TSs, in benzene and dichloromethane, were located also at the B3LYP/6-3G(d) and B3LYP/6-311+G(d,p) levels, but these results will not be reported here. We also have carried out some C-PCM calculations on these reactions that gave results similar to those obtained with the PCM ones.

(14) The energies obtained from PCM calculations have the status of free energies since they take implicitly into account thermal and entropic contribution of the solvent; however, they do not include the thermal contribution of molecular motions of the solute.

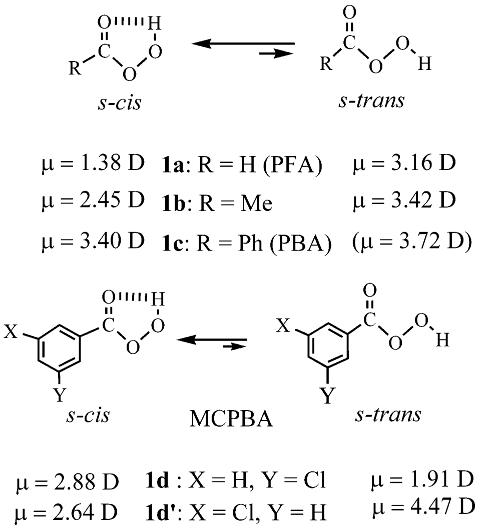
(15) (a) Alabugin, I. V.; Manoharan, M.; Peabody, S.; Weinhold, F. *J. Am. Chem. Soc.* **2003**, *125*, 5973. (b) Chen, X.; Walthall, D. A.; Brauman, J. I. *J. Am. Chem. Soc.* **2004,** *126*, 12614.

TABLE 1. Enthalpy ($\Delta H = H_{s-trans} - H_{s-cis}$) and Free Energy ($\Delta G = G_{s-trans} - G_{s-cis}$) Differences (kcal/mol) between the s-cis and s-trans Conformer of Peroxy Acids in Gas Phase and Solution (Benzene and Dichloromethane) Calculated with the RB3LYP Method and Different Basis Sets[a]

basis set	ΔH_{gas}	$\Delta H_{C_6H_6}$	$\Delta H_{CH_2Cl_2}$	ΔG_{gas}	$\Delta G_{C_6H_6}$	$\Delta G_{CH_2Cl_2}$
			peroxy formic acid **1a**			
6-31G(d)	3.51	2.67	1.37	2.39	1.65	0.71
6-311+G(d,p)	2.42	1.56	0.23	1.22	0.59	−0.29
6-31+G(2d,p)	3.43	2.50	1.09	2.36	1.73	0.53
6-311++G(3df,2pd)	3.40	2.51	1.16	2.46	1.77	0.62
Aug-cc-pVTZ	3.46			2.52		
			peroxy benzoic acid **1c**			
6-31G(d)	5.70	4.48	3.14	2.13	3.47	2.13
6-311+G(d,p)	(4.72)^b	(3.60)^b	2.04	–	–	1.07
6-31+G(2d,p)	(5.52)^b	(4.45)^b	2.76	–	–	1.71
6-311++G(3df,2pd)	(5.47)^b	(4.46)^b	(2.87)^b	–	–	–

[a] For peroxy formic acid with the CBS-QB3 (G3B3) method: ΔH_{gas} = 3.76 (3.68) kcal/mol and ΔG_{gas} = 2.99 (2.68) kcal/mol. [b] ΔE evaluated by single-point calculations on 6-31G(d) geometries.

SCHEME 3



Dipole moment values (μ) from B3LYP/6-31+G(2d,p) calculations (gas phase)

with one more polarization function on heavy atoms, nicely reproduces the data of the largest basis set method.

As for the relative stability of the two conformers, the data of Tables 1 and S1 demonstrate that dominance of the s-cis form predicted for PFA is further enhanced on going to peroxy acetic acid and to aromatic peroxy acid (PBA and MCPBA). In fact, introduction of a methyl or an aryl group on the parent peroxy acid significantly favors the s-cis isomer, that is, by ~1.5 kcal/mol in the case of the peroxy acetic acid and by ~2.1 kcal/mol in the case of peroxy benzoic acid (in the gas phase, Table 1 and S1). A strengthening of the intramolecular HB interaction in the s-cis conformer, induced by the substituent, with a resultant stabilization of this isomer can be held responsible of this observation. In fact, inspection of peroxy acid geometry (Figure 1) reveals that introduction of the methyl or phenyl group brings about a relevant reduction in the OH- - -OC distance in the s-cis conformer while, consistently, the O−H stretching frequency in peroxy acetic and peroxy benzoic acid decreases by ~40 and 60 cm,^{1} respectively, in comparison with that of peroxy formic acid (Figure 1).

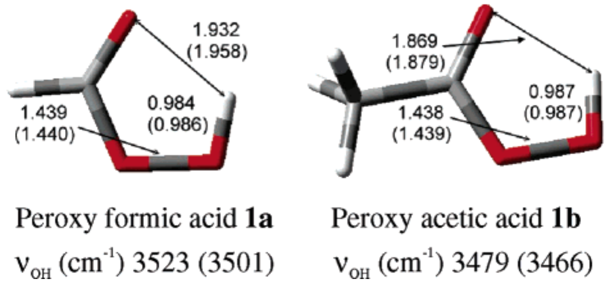


FIGURE 1. B3LYP/6-31+G(2d,p) O−O, O−H bond lengths (Å), C=O- - -HO distance (Å), and O−H stretching frequency (ν, cm^{-1}) for the cis conformers of peroxy formic and peroxy acetic acid in the gas phase and (in parentheses) dichloromethane solution. The corresponding values for peroxy benzoic acid are: 1.435 (1.435), 1.843 (1.851), 0.988 (0.988), and 3461 (3.446).

The s-trans/s-cis energy gap for PFA is strongly attenuated on going from the gas phase to solution. The preferential stabilization of the s-trans isomer by solvation effects reduces the energy difference between the two conformers by about 1 kcal/mol in benzene and 2 kcal/mol in dichloromethane. A very similar solvent effect was observed for the substituted derivatives. Since the difference in dipole moment values between the two conformers strongly decreases along the series peroxy formic acid, peroxy acetic acid, and peroxy benzoic acid (Scheme 3), whereas their differential stabilization by solvation remains substantially unaltered, we conclude that this effect is inherently related to the trans/cis geometry difference more than to the trans/cis dipole moment difference. That is, the s-trans form experiences a much higher solvation stabilization even when its dipole moment is similar to that of the s-cis form.[16]

At this point it is worth emphasizing that the stationary point corresponding to the local minimum of the

---

[16] The observation that the dipole moment difference is not, in the case under study, a good indicator of differential solvent effect is supported by the observation that the enthalpy difference between s-*cis*-**1d** (μ = 2.88 D) and s-*trans*-**1d** (μ = 1.91 D) is reduced by 2.61 kcal/mol on passing from gas phase to dichloromethane solution (Table S1) notwithstanding a decrease in dipole moment value while a very similar decrease in the enthalpy gap (2.72 kcal/mol) was calculated for the s-*cis*-**1d′** (μ = 2.64 D)/s-*trans*-**1d′** (μ = 4.47 D) pair in the presence of a sizable enhancement of the dipole moment.

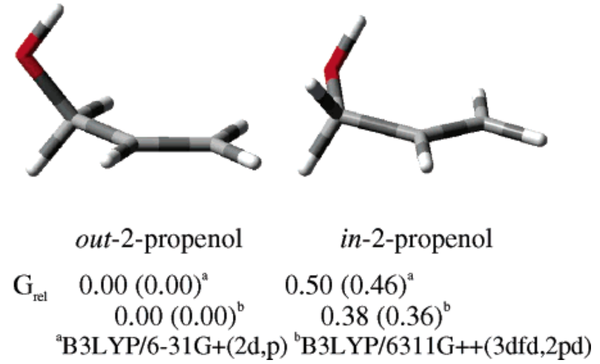
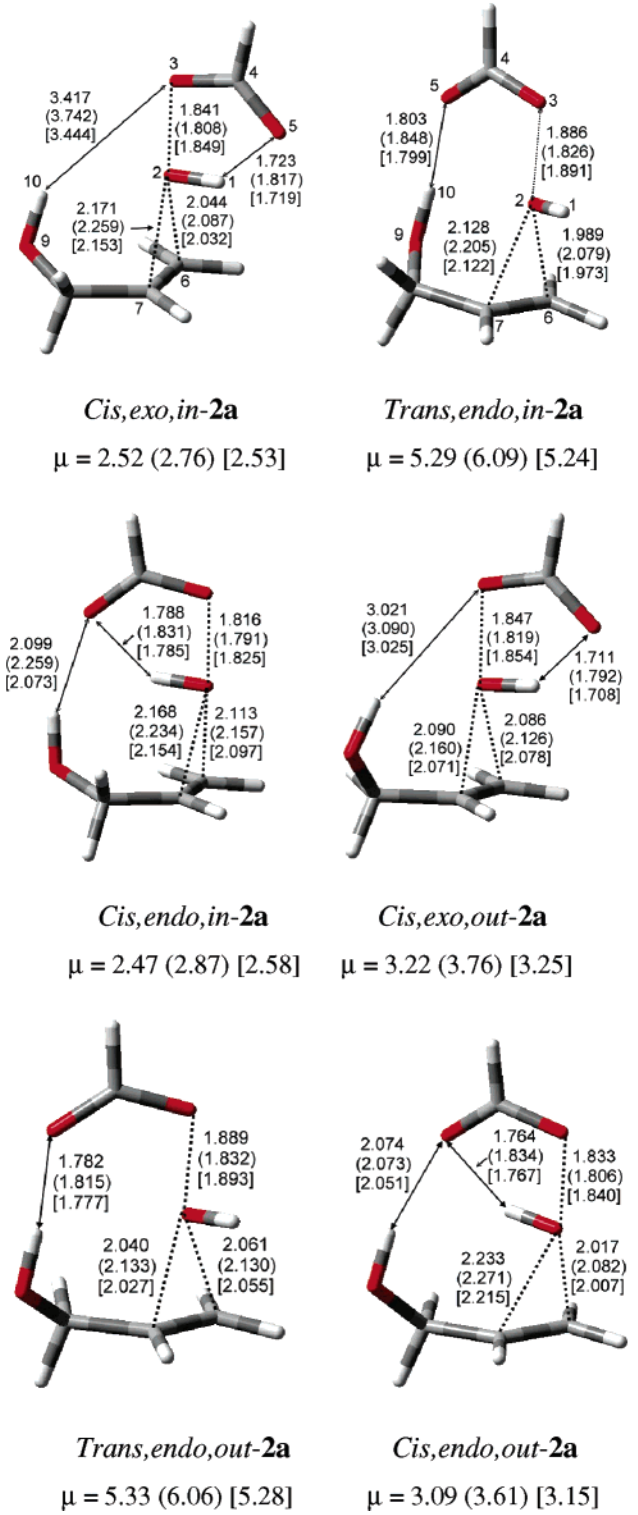


FIGURE 2. Relative free energies (kcal/mol) of the most stable 2-propenol conformers in the gas phase and in dichloromethane solution (in parentheses).

s-trans conformer has been located at all theory levels in both gas phase and solution for both peroxy formic acid and peroxy acetic acid. However, the potential energy well of the s-trans conformer is very shallow, as testified by the very low frequency (as a rule less than 100 cm^{-1}) of the vibration connected with rotation of the OH bond, around the O−O bond, that transforms the s-trans into the s-cis isomer. The potential energy surface surrounding the s-trans conformer is particularly flat in the case of peroxy benzoic acid and MCPBA. Actually, in the gas phase and in benzene solution we were able to locate the s-trans conformer of peroxy benzoic acid only at the lower theory level [B3LYP/6-31G(d)], whereas with the B3LYP/6-31+G(2d,p) and B3LYP/6-311+G(d,p) methods the s-trans structure either did not converge or collapsed to the s-cis conformer. The s-trans isomer could be located at all three theory levels in dichloromethane solution certainly as a result of solvent stabilization that deepens the energy well of this conformer. The s-trans isomers of MCPBA (s-*trans*-**1d** and s-*trans*-**1d′**) were characterized at the B3LYP/6-31G(d) and B3LYP/6-31+G(2d,p) theory levels in both the gas phase and dichloromethane solution, but gas-phase B3LYP/6-311+G(d,p) calculations on these isomers did not converge.

To summarize, the calculation data reported above predict that the fast equilibrium between the s-trans/s-cis peroxy acid conformers always lies on the side of the s-cis isomer, in accord with experimental observations,[12] and that the conformer energy gap in solution (dichloromethane) is not very large. This difference increases on passing from the parent peroxy formic acid to substituted (Me or Ar) peroxy acids so that some caution is in order in inferring the role played by the s-trans isomer, in reactions with the substituted peroxy acids, on the basis of calculations performed with the parent derivative. In other words, s-trans/s-cis competition in epoxidations with substituted peroxy acids deserves a specific computational investigation.

B3LYP Study of Epoxidation of 2-Propenol with Peroxy Formic Acid. In the two dominant 2-propenol conformers (Figure 2), the OH group occupies an inside (in) and outside (out) position, respectively, with the OH group involved in a weak H-bonding interaction with the π-bond. In both conformers, which have similar energy (Figure 2), the OH bond is ideally oriented to assist the attack of s-cis or s-trans peroxy acid by an intermolecular HB interaction.



Cis,exo,in-**2a** μ = 2.52 (2.76) [2.53]

Trans,endo,in-**2a** μ = 5.29 (6.09) [5.24]

Cis,endo,in-**2a** μ = 2.47 (2.87) [2.58]

Cis,exo,out-**2a** μ = 3.22 (3.76) [3.25]

Trans,endo,out-**2a** μ = 5.33 (6.06) [5.28]

Cis,endo,out-**2a** μ = 3.09 (3.61) [3.15]

FIGURE 3. Geometries (bond lengths and distances in Å) and dipole moments (μ, Debye) for B3LYP/6-31+G(2d,p) transition structures of the peroxy formic acid epoxidation of 2-propenol in the gas phase and (in parentheses) dichloromethane solution. Data in brackets are from gas-phase B3LYP/6-311++G-(3df,2pd) calculations.

Choice of Basis Set. Figure 3 displays six TSs,[17a] originating from the reaction of the s-cis and s-trans peroxy formic acid conformers with both the in and out propenol conformers. We have considered only TSs

TABLE 2. Relative Gas-Phase Activation Energy ($\Delta E^{\ddagger}$, kcal/mol with Respect to $\Delta E^{\ddagger}$ of TS *cis,exo,in*-2a) for TSs of Competing Pathways of Peroxy Formic Acid Epoxidation of 2-Propenol with the B3LYP Method and Different Basis Sets

TS	6-31G(d) $\Delta E^{\ddagger}$	6-311+G(d,p) $\Delta E^{\ddagger}$	6-31+G(2d,p) $\Delta E^{\ddagger}$	6-311++G(3df,2pd) $\Delta E^{\ddagger}$	Aug-cc-pVTZ[b] $\Delta E^{\ddagger}$
cis,exo,in-**2a**	0.00 (9.49)[a]	0.00 (11.17)[a]	0.00 (11.93)[a]	0.00 (13.64)[a]	0.00 (14.03)[a]
trans,endo,in-**2a**	0.34	−0.42	0.45	0.37	0.50
cis,endo,in-**2a**	−1.76	−0.19	−0.44	−0.65	−0.64
cis,exo,out-**2a**	0.24	0.20	0.12	0.20	0.23
trans,endo,out-**2a**	1.58	0.57	1.28	1.16	1.28
cis,endo,out-**2a**	0.34	1.20	0.86	0.76	0.73

[a] Absolute activation energy of *cis,exo,in*-**2a**. [b] Single-point calculation on cc-pVTZ geometry.

TABLE 3. Orientation of the O_2-H_1 Bond Relative to the C=C Bond (Dihedral Angle $H_1O_2XC_6$),[a] Planarity of the Peroxy Acid Moiety (Dihedral Angle $H_1O_2O_3C_4$), and Stretching Vibration Frequencies of the O_2-H_1 (ν_{O2H1}) and O_9-H_{10} (ν_{O9H10}) Bonds in TSs of the Propenol Epoxidation with Peroxy Formic (TSs 2a) and Peroxy Benzoic (TSs 2c) Acids (B3LYP/6-31+G(2d,p) Calculations in the Gas Phase)

TS	$H_1O_2XC_6$[a] (deg)	$H_1O_2O_3C_4$ (deg)	$\nu_{O_2H_1}$ (cm^{-1})	$\nu_{O_9H_{10}}$ (cm^{-1})	TS	$H_1O_2XC_6$[a] (deg)	$H_1O_2O_3C_4$ (deg)	$\nu_{O_2H_1}$ (cm^{-1})	$\nu_{O_9H_{10}}$ (cm^{-1})
cis,exo,in-**2a**	−95.9	0.2	3221	3789	*cis,exo,in*-**2c**	−94.3	0.6	3048	3786
trans,endo,in-**2a**	−89.1	−165.3	3761	3429	*trans,endo,in*-**2c**	−89.4	−165.8	3761	3389
cis,endo,in-**2a**	90.2	10.3	3441	3711	*cis,endo,in*-**2c**	90.4	8.4	3313	3697
cis,exo,out-**2a**	−86.1	1.0	3183	3775	*cis,exo,out*-**2c**	−87.1	1.0	3001	3771
trans,endo,out-**2a**	−83.7	−132.7	3787	3446	*trans,endo,out*-**2c**	−85.2	−132.9	3789	3408
cis,endo,out-**2a**	117.1	11.2	3403	3691	*cis,endo,out*-**2c**	115.9	10.2	3269	3677

[a] X is a dummy atom located at the center of the $C_6=C_7$ bond.

stabilized by intermolecular hydrogen bonding between the peroxy acid and propenol since they are significantly more stable than TSs that lack this interaction.[5c−e,7] Moreover, we have previously demonstrated that competition between the peroxy acid conformers (the problem under study) comes into play only in the presence of this interaction.[7] TSs have been located by using the hybrid B3LYP functional first with the small standard 6-31G(d) basis set and then progressively larger basis sets to eventually reach the relatively large cc-pVTZ and 6-311++G(3df,2pd) levels. The TS relative potential energies, for some representative basis sets of the series investigated by us, are gathered in Table 2. Once again the B3LYP/6-31+G(2d,p) data nicely reproduce the TS ranking obtained with the highest theory methods, while the B3LYP/6-311+G(d,p) ones are definitely worse since they overestimate the stability of "trans" TSs relative to the corresponding "cis" TSs (by about 0.6−0.9 kcal/mol) and underestimate that of "cis,endo" TSs in comparison with the corresponding "cis,exo" TSs (by about 0.4 kcal/mol). As for absolute values of activation energy, B3LYP/6-31+G(2d,p) calculations continue to perform better than B3LYP/6-311+G(d,p) ones even if for this property they compare less satisfactorily with the highest theory level. Since we are primarily interested in relative "cis"/"trans" TS stability, we feel that the B3LYP/6-31+G(2d,p) method can be considered "validated" by these calculations, and from now on we will report and discuss only the data obtained with this method.

TS Geometries. Geometries of "cis" TSs as well as those of "trans" TSs are displayed in Figure 3 (see also Table 3). Enlargement of the basis set leads to slightly later TSs while solvation effects make TSs slightly earlier, but all the important characteristic features remain unaltered. All six TSs are concerted but slightly asynchronous TSs. Here again, it is worth noticing the perpendicular-like[17b] orientation of the peroxy acid O_2-H_1 (see Scheme 2 and Figure 3 for numbering) bond relative to the C=C bond (in both "cis" and "trans" TSs) that, along with concertedness, is the most characteristic feature of peroxy acid epoxidation transition structures. Remarkably, the angle between the peroxy acid O_2-H_1 bond and the $C_6=C_7$ bond (as described by the $H_1O_2XC_6$ torsional angle, in which X is a dummy atom located at the center of the C=C bond, Scheme 2) is within a few degrees (less than seven) of the 90.0° value for five of the six TSs, in particular for both the "trans" TSs (Table 3). It is also interesting to notice that deviation from perpendicularity entails a parallel increase in asynchronicity in C---O bond development: *cis,endo,out*-**2a** is the most asynchronous (the difference in incipient bond length is about 0.2 Å) as well as the least perpendicular ($H_1O_2XC_6 = 117.1°$) TS.

As for the former peroxy acid moiety, it is planar ($H_1O_2O_3C_4 \approx 0°$) in cis,exo,in and cis,exo,out TSs, while a small (~10°) (Table 3) out-of-plane distortion of this moiety is present in cis,endo,in and cis,endo,out TSs. The latter distortion is promoted by proximity of the hydroxyl proton (H_{10}) that competes with the peroxy acid proton (H_1) in hydrogen bonding to the carbonyl oxygen, with a consequent electrostatic repulsion between them. In "trans" TSs, the $H_1O_2O_3C_4$ dihedral angle is always sizably different from 180° as a result of rotation of the

---

(17) (a) The meaning of the descriptors used are as follows: cis and trans indicate that the TS formally originates from s-cis and s-trans, respectively, conformer of peroxy formic acid; endo and exo TSs exhibit the formate moiety on the same side and on the opposite side, respectively, relative to the CH_2OH moiety; in and out TSs derive from in and out, respectively, conformers of 2-propenol. (b) The descriptor "perpendicular" (synonymous with "spiro" in the case of "cis" TSs) indicates a TS in which the O_2-H_1 bond of the peroxy acid adopts a perpendicular orientation relative to the $C_6=C_7$ bond [the torsion angle $C_6XO_2H_1$ (X is a dummy atom at the center of the $C_6=C_7$ bond, see Scheme 2) is close to 90° (that is, larger than 45°)], while in a "planar" TS this angle is close to 0° (smaller than 45°) and the O_2-H_1 and $C_6=C_7$ bonds lie in the same (or almost the same) plane.

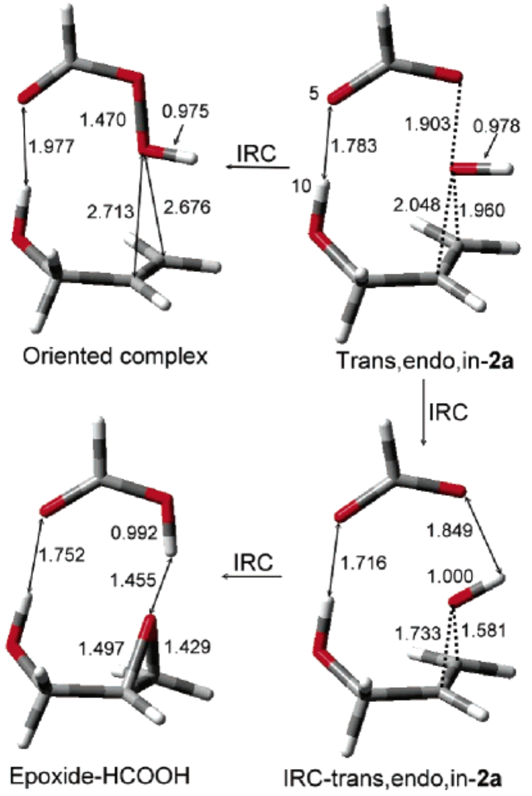


FIGURE 4. IRC following [B3LYP/6-31G(d)] from TS *trans,endo,in*-**2a**. Bond lengths in Å.

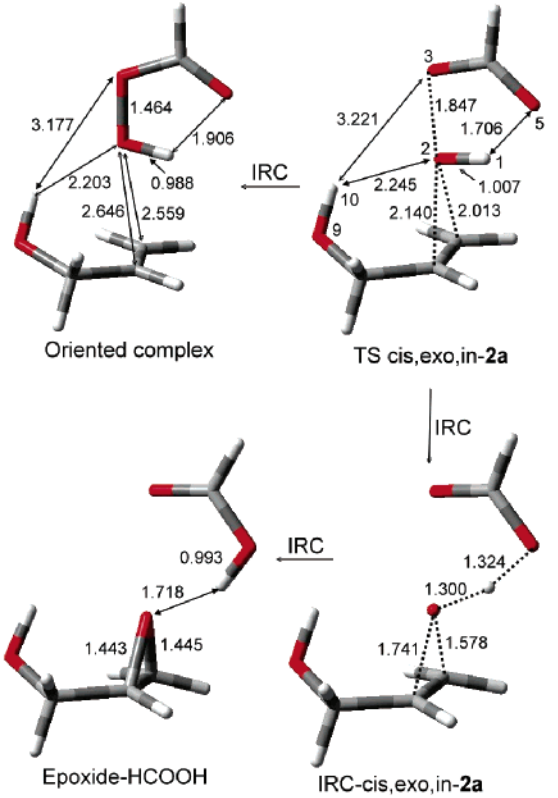


FIGURE 5. IRC following [B3LYP/6-31G(d)] from TS *cis,exo,in*-**2a**. Bond lengths in Å.

formate moiety around the breaking O_2- - -O_3 bond in order to bring the carbonyl oxygen as close as possible to the O_9H_{10} bond. The strong hydrogen-bonding interaction in the almost linear O_5- - -$H_{10}O_9$ system of "trans" TSs benefits from the partial negative charge, which develops on the formate moiety on going from educts to TS, and from the inherently high basicity of the carbonyl oxygen.[18] This intermolecular HB interaction efficiently drives the approach of the peroxy acid to propenol from the very beginning of the reaction and plays an important role along all the reaction coordinate as suggested by the O_5- - -H_{10} distance that decreases for most of the pathway (see the forward and reverse IRC analysis for TS *trans,endo,in*-**2a**, Figure 4). Also the attack by the s-cis peroxy acid to propenol is favored by an intermolecular HB interaction between the hydroxylic O_9H_{10} group and the O_2-O_3 peroxy system (or carbonyl oxygen) in the cis,exo (cis,endo) TSs, but this interaction is certainly weak and fades away along the reaction coordinate (see IRC of TS *cis,exo,in*-**2a**, Figure 5). The higher strength of intermolecular HB in "trans" TSs relative to "cis" TSs is nicely reflected in the lower O_9-H_{10} stretching vibration in the former (~3440 cm^{-1}) than in the latter TSs (~3780 cm^{-1} in cis,exo TSs and ~3700 cm^{-1} in cis,endo TSs) (Table 3). In the case of the reaction of the s-cis peroxy acid, the only strong HB interaction is the intramolecular one (O_2-H_1- - -O_5) in the peroxy acid moiety that, beyond TS, facilitates the 1,4-H shift in concert with oxirane ring formation (Figure 5). Figure 4 clearly documents (for TS *trans,endo,in*-**2a**) that a 1,2-H transfer takes place in the descent from "trans" TSs to the final epoxide. No intermediate could be located even if the first part of the descent is dominated by protonated oxirane ring formation that subsequently releases proton to the formate moiety.[19]

In short, calculations reported here fully confirm, for the peroxy acid epoxidation of acyclic allylic alcohols, our previous observation for cyclic allylic alcohols, namely, the viability of "trans" reaction channels, with the 1,2-H transfer, in competition with the classical "s-cis" pathways.

Energetics. The activation enthalpies, entropies, and free energies for the six TSs **2a** (Figure 3) calculated with the B3LYP/6-31+G(2d,p) method are listed in Table 4 and Figure 6. Table 4 makes it clear that we are in the presence of an intricate and delicate competition since differences in TS enthalpies as well as in TS free energies never exceed 3.3 kcal/mol. The TSs with the hydroxylic OH group in the inside position (TSs *in*-**2a**) are always more stable, in both gas phase and in solution, than the corresponding TSs with this group oriented outside (TS

---

[18] Electron transfer from 2-propenol to peroxy acid is similar in "cis" and "trans" TS [e.g., −0.30 (CHELPG) and −0.380 (NPA) for TS *cis,exo,in*-**2a**; −0.38e (CHELPG) and −0.42e (NPA) for TS *trans,endo,in*-**2a** in the gas phase with B3LYP/6-31+G(2d,p) calculations]. The highest negative charge on the formate moiety is associated with the carbonyl oxygen (O_5) [for example, TS *cis,exo,in*-**2a**: −0.438e on O_3 and −0.605e on O_5 (CHELPG charges), −0.450e on O_3 and −0.680e on O_5 (NPA charges); TS *trans,endo,in*-**2a**: −0.537e on O_3 and −0.690e on O_5 (CHELPG charges), −0.496e on O_3 and −0.677e on O_5 (NPA charges)].

[19] A 1,2-H pericyclic shift to an adjacent lone pair (as, for example, in H_2O_2) is formally forbidden and should have a very high barrier. However, IRC analysis of "trans" routes clearly shows that in the case under study we are not in the presence of a pericyclic transfer, but the mechanism looks like a proton transfer from a cation to an anion.

TABLE 4. Relative Activation Parameters ($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, $\Delta G^{\ddagger}$ with Respect to Those of TS *cis,exo,in*-2a)[a] for TSs of 2-Propenol Epoxidation with Peroxy Formic Acid in the Gas Phase and Solution (Benzene and Dichloromethane)[b] at the B3LYP/6-31+G(2d,p) Level

TS	$\Delta H^{\ddagger}_{gas}$	$\Delta H^{\ddagger}_{C_6H_6}$	$\Delta H^{\ddagger}_{CH_2Cl_2}$	$\Delta S^{\ddagger}_{gas}$	$\Delta S^{\ddagger}_{C_6H_6}$	$\Delta S^{\ddagger}_{CH_2Cl_2}$	$\Delta G^{\ddagger}_{gas}$	$\Delta G^{\ddagger}_{C_6H_6}$	$\Delta G^{\ddagger}_{CH_2Cl_2}$
cis,exo,in-**2a**	0.00 (12.29)[c]	0.00 (12.69)[c]	0.00 (13.05)[c]	0.00 (−29.65)[c]	0.00 (−29.06)[c]	0.00 (−28.35)[c]	0.00 (21.13)[c]	0.00 (21.37)[c]	0.00 (21.50)[c]
trans,endo,in-**2a**	0.18	−0.68	−1.46	−2.80	−3.44	−4.43	1.02	0.36	−0.14
cis,endo,in-**2a**	−0.24	0.31	0.86	−2.18	−2.37	−3.01	0.40	1.03	1.75
cis,exo,out-**2a**	0.17	0.40	0.65	−0.64	−0.93	−1.48	0.36	0.69	1.09
trans,endo,out-**2a**	1.10	0.13	−0.72	−1.98	−2.67	−3.79	1.69	0.94	0.41
cis,endo,out-**2a**	1.01	1.39	1.79	−2.07	−2.41	−3.18	1.63	2.12	2.74

[a] The rigid rotor-harmonic oscillator approximation has been assumed for evaluation of the thermodynamic properties; energies in kcal/mol, entropy in cal/(mol K); $\Delta H^{\ddagger}$, $\Delta G^{\ddagger}$ are the molar activation enthalpy and Gibbs free energy; $\Delta S^{\ddagger}$ is the molar activation entropy; all these parameters are referred to the s-cis peroxy formic acid (s-cis **1a**), to the most stable 2-propenol conformer (the "out" conformer), and to the standard state (298.15 K) of the molar concentration scale (gas in ideal mixture at 1 mol/L, $P = 1$ atm). [b] Solution data were evaluated from full geometry optimization and frequency calculations in solution. [c] Absolute activation parameters for TS *cis,exo,in*-**2a**.

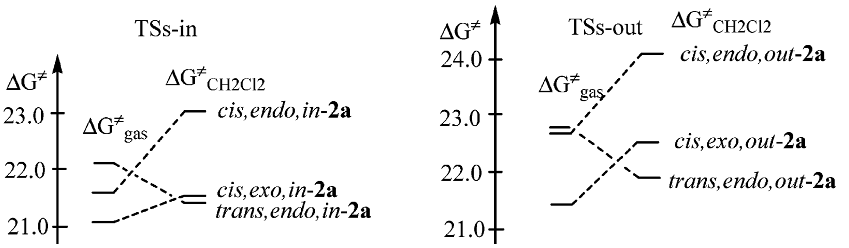


FIGURE 6. Activation free energies for TSs of 2-propenol epoxidation with peroxy formic acid in the gas phase ($\Delta G^{\ddagger}_{gas}$) and dichloromethane solution ($\Delta G^{\ddagger}_{CH_2Cl_2}$).

out-**2a**). The inside OH group does not suffer from sizable 1,3-allylic strain, and the stereoelectronic withdrawal of electron density from the $\pi_{C=C}$ orbital by σ^*_{C-O} of an inside OH is slightly smaller than that of an outside OH. This stereoelectronic effect is detrimental for the peroxy acid electrophilic attack to the π double bond, thus preferentially disfavoring the outside TSs.[20]

Our concern in evaluating energetics was focused on competition of trans,endo TSs versus their cis,exo (and cis,endo) counterparts. As for enthalpy in the gas phase, TS *cis,endo,in*-**2a** resides at the lowest level while *trans,endo,out*-**2a** is the least stable TS and, what mostly matters in this context, both trans,endo TSs (in and out) are less stable than the related cis,exo TSs. Intermolecular hydrogen bonding in "trans" TSs is certainly strong with respect to that one in "cis" TSs, as judged from the small H_{10}- - -O_5 distance and the relevant reduction in hydroxylic O−H vibration frequency, but enthalpy data tell us that it is not efficient enough to fully compensate for the absence of intramolecular HB that stabilizes only "cis" TSs. However, one can anticipate that the cis/trans enthalpic stability ranking could be deeply changed on going from the gas phase to condensed phase. In fact, dichloromethane stabilization of trans,endo TSs relative to corresponding cis,exo and cis,endo TSs is quite remarkable, spanning the range of 1.6−2.7 kcal/mol, while the relative effect evaluated for benzene solvation is about half this value. As a result, in the gas phase the TS enthalpy ranking is as follows: *cis,endo,in*-**2a** < *cis,exo,in*-**2a** < *cis,exo,out*-**2a** ≈ *trans,endo,in*-**2a** < *cis,endo,out*-**2a** < *trans,endo,out*-**2a**, whereas in dichloromethane solution it becomes *trans,endo,in*-**2a** < *trans,endo,out*-**2a** < *cis,exo,in*-**2a** < *cis,exo,out*-**2a** < *cis,endo,in*-**2a** < *cis,endo,out*-**2a**. *It is noteworthy that in the latter solvent both "trans" TSs exhibit a lower enthalpy than all of the "cis" TSs.* In particular, trans,endo,in and trans,endo,out TSs reside at lower enthalpy than their cis,exo,in and cis,exo,out counterparts, respectively, by ~1.4 kcal/mol.

Kinetic competition is governed by relative activation free energies, and consequently, it is mandatory to compare reaction pathways on the basis of this parameter.[21,22] In the case of peroxy acid s-cis/s-trans conformational equilibria entropic factors significantly favor the s-trans conformer. This observation does not hold for epoxidation TSs. In fact, cis,exo TSs have activation entropies less negative by ~2−4 entropy units than those of the corresponding trans,endo TSs. Trans,endo and cis,endo TSs exhibit similar entropies, suggesting that endo orientation of the formate moiety and the strong HB interaction between the C=O bond and the hydroxilic OH enhances structural rigidity of TSs, thus decreasing their vibrational entropy. As a result, at the free energy level, cis,exo reaction channels become slightly more favored than they are on the basis of enthalpy. Actually, they prevail over their trans,endo competitors by 1.0−1.3 kcal/mol in the gas phase, but this favor falls to ~0.3−0.4 kcal/mol in benzene. In dichloromethane solution, the trans,-

---

[20] This observation is reminiscent of Houk's *inside alkoxy effect* well-documented for 1,3-dipolar cycloaddition. For a review, see: Raimondi, L. *Gazz. Chim. Ital.* **1997**, *127*, 167.

[21] Unfortunately, free energies can be flawed by the fact that small errors in very low TS frequencies can lead to very large errors in entropies[22] that, probably, are only partially compensated in TS comparison. Thus, it is good practice to be somewhat cautious in using free energy data, calculated by standard procedures as implemented in Gaussian and other program packages, for discussion on reactivity, and this explains why some authors prefer not to discuss free energy and to restrict themselves to enthalpy. Actually, there are several very low frequencies, lower than 100 cm^{-1} in TS structures under study, and "cis" TSs exhibit the lowest frequencies. Thus the entropy effect can be, at least in part, a result of an artifact of calculations.

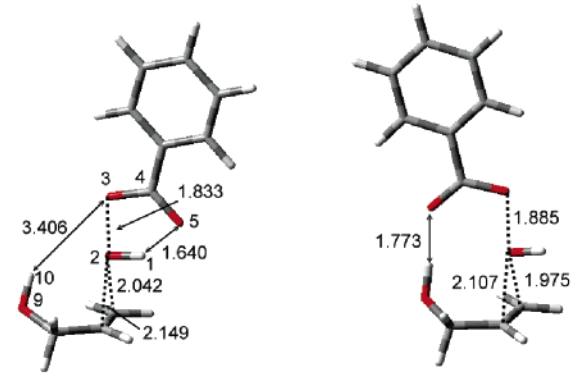
[22] Cramer, C. J. *Essentials of Computational Chemistry*; Wiley: Hoboken, NJ, 2004; p 375.

endo routes tend to have a slightly lower activation free energy than the corresponding cis,exo pathways (Table 4 and Figure 6). As for the two cis,endo TSs, calculations predict that in condensed phase they always are, on a free energy basis, the two least stable TSs so that, for example, they should play a marginal role in propenol epoxidation by peroxy formic acid performed in dichloromethane solution (Figure 6).

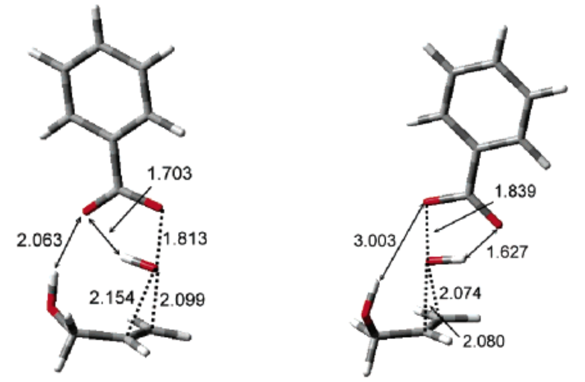
To summarize, the above data reveal that the mechanism of peroxy formic epoxidation of allylic alcohol actually is a very complex one, featuring competition among six TSs. Moreover, these TSs not only span a surprisingly small range of relative activation free energy (~1.6 kcal/mol in the gas phase, ~2.0 kcal/mol in benzene, and ~3.0 in dichloromethane) but also their stability ranking is changed by solvation effects (Figure 6). It is quite evident that one could have suggested operation of such an intricate reaction scheme on the basis of qualitative reasoning, but a reliable assessment of the relative stability of these TSs, in the different media investigated, could have hardly been anticipated intuitively. Our good level computational investigations throw light on TS ranking and allow us to safely conclude that, in the case of peroxy formic acid epoxidation of acyclic allylic alcohols in condensed phase, we must complement the classical Bartlett's mechanism, via "perpendicular"[17] "cis" TSs with 1,4-H shift, by considering also competing pathways via "perpendicular" "trans" TSs with 1,2-H transfer.

Epoxidation of 2-Propenol with Peroxy Benzoic and MCPBA. The free energy gap between the more stable s-cis form and the s-trans conformer increases on going from the parent peroxy formic acid to peroxy benzoic acid by ~2.1 kcal/mol and ~1.2 kcal/mol, respectively, in the gas phase and in dichloromethane solution (see Table 1). A similar observation ($\sim\Delta\Delta G^{\ddagger} \approx 1.7$ kcal/mol in the gas phase and ~0.5 kcal/mol in dichloromethane) holds for MCPBA in which the substituent effect is slightly reduced (Table S1). This substituent effect, which influences the relative stability of s-cis versus s-trans peroxy acid isomers, is certainly operative also in determining the "cis"/"trans" TS competition of epoxidation reactions, but it is necessary to assess whether it is substantially emphasized or attenuated. Calculations offer the opportunity to unravel also this fine mechanistic detail.

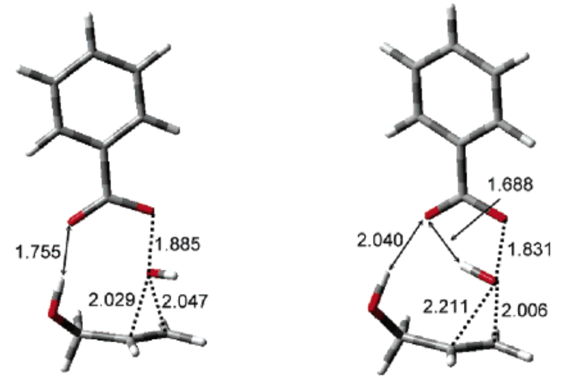
We located six TSs for peroxy benzoic epoxidation of 2-propenol, and the optimized B3LYP/6-31+G(2d,p) structures are reported in Figure 7. As expected, these TSs resemble peroxy formic acid TSs in particular as far as lengths of incipient C- - -O and breaking O- - -O bonds as well as perpendicularity between peroxy acid O_2-H_1 and $C_6=C_7$ bonds are concerned. A remarkable difference is represented by the shorter (~0.08 Å) O_5- - -H_1 distance exhibited by TSs *cis*-**2c** relative to TSs *cis*-**2a** that is consistently reflected in a lower (~130−180 cm^{-1}) O_2-H_1 stretching vibration in the former than in the latter TSs (see Table 3). That is, the stronger intramolecular HB interaction present in s-cis peroxy benzoic acid, with respect to that in s-cis peroxy formic acid, is carried over to the corresponding TSs. The introduction of the Ph group strengthens also the intermolecular HB interaction in TSs *trans*-**2c** as documented by the shorter (~0.03 Å) H_{10}- - -O_5 distance and the lower (~130−180 cm^{-1}) O_9-H_{10} stretching vibration (Table 3) relative to TSs *trans*-**2a**.



Cis,exo,in-**2c** (1.52 D) *Trans,endo,in*-**2c** (4.79 D)



Cis,endo,in-**2c** (1.45 D) *Cis,exo,out*-**2c** (2.08 D)



Trans,endo,out-**2c** (4.74 D) *Cis,endo,out*-**2c** (1.90 D)

FIGURE 7. Gas-phase optimized geometries and (in parentheses) dipole moments for transition structures of the peroxy benzoic epoxidation of 2-propenol. Bond lengths in Å. Dipole moments in Debye.

As for energetics, in the gas phase *all the "cis" TSs of peroxy benzoic acid epoxidation of 2-propenol are definitely more stable than the two "trans" TSs on the basis of both enthalpy and free energy* (Table 5, and Figure 8). However, in condensed phase things become less clear-cut and dominance of "cis" over "trans" TSs is progressively reduced in parallel with increasing solvent polarity.

TABLE 5. Relative Activation Parameters ($\Delta H^{\ddagger}$ and $\Delta G^{\ddagger}$ with Respect to Those of TS *cis,exo,in*-2c)[a] for TSs of 2-Propenol Epoxidation with Peroxy Benzoic Acid in the Gas Phase and Solution (Benzene and Dichloromethane)[b] at the B3LYP/6-31+G(2d,p) Level

TS	$\Delta H^{\ddagger}_{gas}$	$\Delta H^{\ddagger}_{C_6H_6}$	$\Delta H^{\ddagger}_{CH_2Cl_2}$	$\Delta G^{\ddagger}_{gas}$	$\Delta G^{\ddagger}_{C_6H_6}$	$\Delta G^{\ddagger}_{CH_2Cl_2}$
cis,exo,in-**2c**	0.00	0.00	0.00	0.00	0.00	0.00
	(14.11)[c]	(14.68)[c]	(14.98)[c]	(23.12)[c]	(23.69)[c]	(23.99)[c]
trans,endo,in-**2c**	1.60	0.49	−0.73	2.20	1.09	−0.13
cis,endo,in-**2c**	−0.48	0.05	0.40	0.14	0.68	1.03
cis,exo,out-**2c**	0.06	0.28	0.43	0.34	0.57	0.71
trans,endo,out-**2c**	2.45	1.34	0.10	2.73	1.63	0.39
cis,endo,out-**2c**	0.77	1.12	1.33	1.46	1.81	2.02

[a] See footnote a in Table 4. [b] Solution data were evaluated with single-point calculations on gas-phase optimized geometries. Molecular motion contributions from gas-phase data. [c] Absolute activation parameters for TS *cis,exo,in*-**2c** are referred to s-cis peroxy benzoic acid conformer (s-cis **1c**) and out-2-propenol conformer.

TABLE 6. Dipole Moments (μ) and Relative Activation Parameters ($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, $\Delta G^{\ddagger}$ with Respect to Those of TS *cis,exo,in*-2d)[a] for cis,exo,in and trans,endo,in TSs of 2-Propenol Epoxidation with *m*-Chloroperoxy Benzoic Acid in Gas Phase and Solution (Dichloromethane)[b] at the B3LYP/6-31+G(2d,p) Level

TS	μ_{gas} (D)	$\Delta H^{\ddagger}_{gas}$	$\Delta H^{\ddagger}_{CH_2Cl_2}$	$\Delta S^{\ddagger}_{gas}$	$\Delta G^{\ddagger}_{gas}$	$\Delta G^{\ddagger}_{CH_2Cl_2}$
cis,exo,in-**2d**	3.40	0.00	0.00	0.00	0.00	0.00
		(13.29)[c]	(14.20)[c]	(−28.8)[c]	(21.88)[c]	(22.79)[c]
cis,exo,in-**2d′**	2.24	−0.04	−0.06	−1.35	0.36	0.34
trans,endo,in-**2d**	4.75	1.18	−0.94	−4.15	2.41	0.30
trans,endo,in-**2d′**	6.62	1.34	−0.91	−3.64	2.43	0.17

[a] See footnote a in Table 4. [b] Solution data were evaluated with single-point calculations on gas-phase optimized geometries. [c] Absolute activation parameters for TS *cis,exo,in*-**2d** relative to s-cis MCPBA conformer (s-cis **1d**) and out-2-propenol conformer.

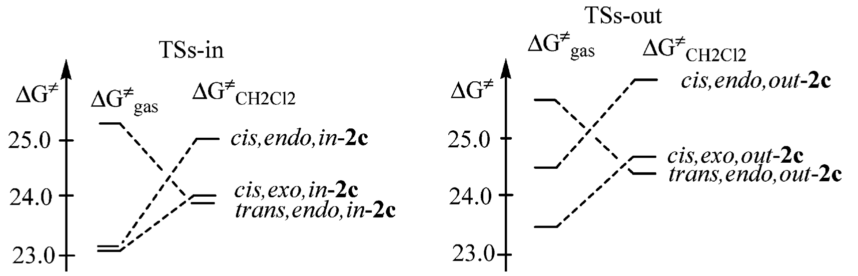


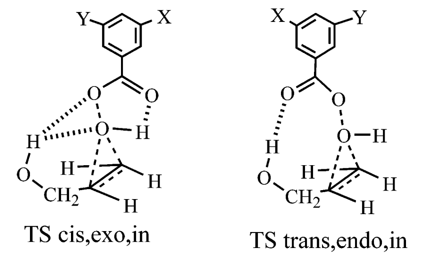
FIGURE 8. Activation free energies for TSs of 2-propenol epoxidation with peroxy benzoic acid in the gas phase ($\Delta G^{\ddagger}_{gas}$) and dichloromethane solution ($\Delta G^{\ddagger}_{CH_2Cl_2}$).

In fact, in dichloromethane solution *trans,endo,in*-**2c** shows the lowest activation enthalpy and the *cis,endo,out*-**2c** the highest one, but it is only 2.1 kcal/mol higher than the former TS, while the other four TSs reside about midway between these two TSs (Table 5).

Moreover, in dichloromethane solution a close contest is expected between cis,exo TSs and trans,endo TSs, on the basis of activation free energy, while cis,endo TSs although disfavored are not completely out of competition (Table 5 and Figure 8).

In the case of MCPBA reactions one may wonder whether the two TS conformers, i.e., **2d** and **2d′**, arising by rotation of the aryl group, differ from each other in energy and whether this conformational isomerism influences competition between the "cis" and "trans" reaction channels (Figure 9).

The data reported in Table 6 for a pair of cis,exo,in as well as trans,endo,in TSs clearly demonstrate that there should not be any relevant difference in energy between these TS conformers not only in the gas phase but also in solution notwithstanding the significant difference in dipole moment. Moreover, Table 6 strongly suggests that the "cis"/"trans" TS stability trends observed for peroxy benzoic acid should hold also for MCPBA. Thus, here again we observe that prevalence of cis,exo over trans,endo TSs in the gas phase is more clear-cut on the ground of free energy than of enthalpy, while in dichloromethane trans,endo TSs lie slightly lower in enthalpy than cis,exo TSs and have a very similar activation free energy.



2d: X = H and Y = Cl **2d'**: X = Cl and Y = H

FIGURE 9.

Conclusion

Our careful computational study (RB3LYP with several basis sets) of s-cis/s-trans equilibrium for peroxy acids (performic, peroxy benzoic, and *m*-chloroperoxy benzoic acids) predicts, in accord with experimental data, that the s-cis form is sizably more stable than the s-trans conformer and that difference in stability is the highest in the gas phase but falls considerably on going from the gas phase to moderately polar solvent. Thus, in the case of peroxy formic acid, the enthalpy (free energy) difference is about 3.4 (2.5) kcal/mol in the gas phase but decreases to 1.2 (0.6) kcal/mol in dichloromethane solution. The reported calculations indicate that the s-cis/s-trans stability gap increases (by ~1.0−1.5 kcal/mol) in the case of peroxy acetic, peroxy benzoic, and *m*-chloroperoxy benzoic acid but also confirm that the s-trans isomer benefits from an inherent stronger solvent stabilization, with respect to the s-cis isomer, that is not strictly related to the difference in dipole moment values between the two conformers.

The study of the epoxidation reaction of 2-propenol with peroxy formic acid, peroxy benzoic acid, and MCPBA was performed at the B3LYP/6-31+G(2d,p) theory level since this method nicely reproduces TS relative stability evaluated with the large basis set B3LYP/6-311++G(3df,2pd) method. For the reaction of peroxy formic and peroxy benzoic acids, we have located six TSs in which the propenol OH group is engaged, as hydrogen bond donor, in hydrogen-bonding interaction with the peroxy acid. Three of them originate from the "in" propenol conformer, while the other three derive from the "out" propenol conformer. The TSs of the former set are slightly more stable than those of the latter one. One TS, in each one of the TS sets, arises from the peroxy acid s-trans conformer ("trans" TS) and the other two TSs from the s-cis peroxy acid ("cis" TSs). "Trans" TSs exhibit, likewise "cis" TSs, a perpendicular orientation of the O−H peroxy acid bond relative to the C=C bond and a one-step oxirane ring formation. These TSs collapse to the final epoxide via a 1,2-H shift at variance with the 1,4-H transfer operative for the classical "cis" TSs. "Trans" TSs take advantage of strong hydrogen bonding between the hydroxylic OH and the peroxy acid carbonyl oxygen, but they lack the intramolecular hydrogen bonding present in peroxy acid moiety of "cis" TSs. In the reaction of peroxy formic acid with 2-propenol the "trans" reaction pathways have a higher barrier in the gas phase than the corresponding "cis" reaction routes, but in moderately polar solvents (dichloromethane) they become competitive (slightly favored). Actually the "trans" TSs are always more stabilized than their "cis" counterparts by solvation effects. The "trans" route is less important for the reaction of peroxy benzoic acid as well as MCPBA relative to that of peroxy formic acid, and this observation parallels, in an attenuated way, the fact that the s-trans/s-cis conformer ratio is smaller for the former than for the latter peroxy acids. In fact, in the reaction of aromatic peroxy acid the classical "s-cis" mechanism clearly prevails both in gas phase and in benzene solution, while in dichloromethane solution the difference in activation free energy between the two competing pathways is very small. Calculations in progress strongly suggest that these conclusions hold also for the reactions of peroxy formic acid and peroxy benzoic acid with chiral allylic alcohols (such as (*Z*)-3-penten-2-ol, 3-methyl-3-buten-2-ol, and (*Z*)-3-methyl-3-penten-2-ol).

Acknowledgment. Support of this work by MURST (National Project: Efficient and Environment Friendly Processes for Selective Oxidation of Organic "Target" Compounds) (Rome, Italy) is gratefully acknowledged. We also thank CICAIA (University of Modena) and CINECA (University of Bologna) for computing facilities.

Supporting Information Available: Energy and Cartesian coordinates of all TSs and reactants at the B3LYP/6-31+G(2d,p) level (gas phase and CH_2Cl_2 solution). Imaginary frequency for all TSs. Cartesian coordinates of the IRC points at the B3LYP/6-31G(d) level. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0515982