

## Experimental Geometry of the Epoxidation Transition State

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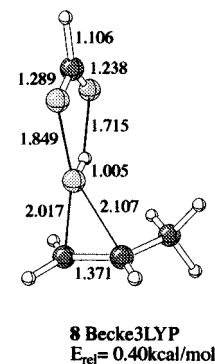
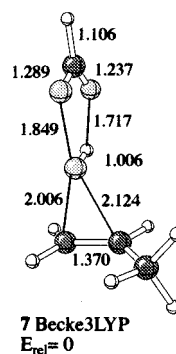
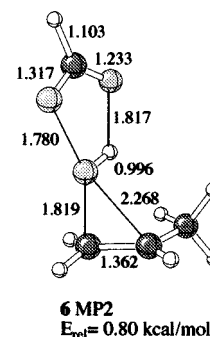
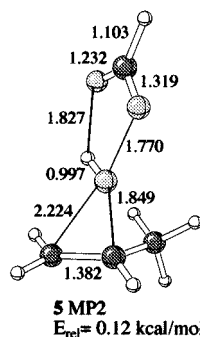
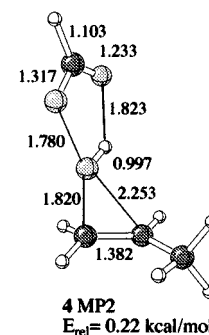
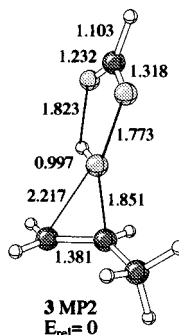
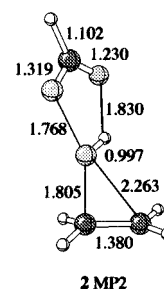
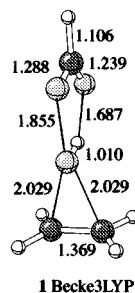
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The epoxidation of alkenes with peracids is a general synthetic method,<sup>1</sup> and has had a hallowed place in the annals of physical organic chemistry since Bartlett proposed that the reaction occurs through the “butterfly” mechanism.<sup>2</sup> For the most part the concerted nature of the mechanism has been accepted, but there have been many contrasting suggestions about the timing of formation of the two CO bonds and the sequence of events involved in CO bond formation and the requisite hydrogen transfer.<sup>3–8</sup> Classical studies of substituent effects suggested nearly synchronous formation of the two CO bonds.<sup>7</sup> For example, 2-butene and isobutene are epoxidized at nearly identical rates.<sup>7b</sup> In contrast, <sup>2</sup>H kinetic isotope effects (KIEs) for epoxidation of 4-vinylbiphenyl were interpreted as implicating a very asynchronous transition state.<sup>3</sup> This view has recently been supported by ab initio calculations at the MP2/6-31G\* level which predict highly unsymmetrical and asynchronous transition structures.<sup>5,6</sup>

We have recently used the comparison of a large set of high-precision experimental KIEs with high-level transition structure/KIE calculations to explicitly define the geometry of a Diels–Alder transition state.<sup>9</sup> Here we apply this methodology to epoxidation. The results provide a detailed, experimentally based picture of the epoxidation transition state consistent with nearly synchronous formation of the CO bonds and confirm predictions made about epoxidation transition states in general.<sup>8</sup>

For the reaction of ethylene with performic acid, the Becke3-LYP/6-31G\* (B3LYP)<sup>10</sup> transition structure (**1**) differs dramatically from that obtained previously in MP2/6-31G\* (MP2) calculations (**2**).<sup>5,6</sup> They are both spiro, but while **1** has *C<sub>s</sub>* symmetry, the two new CO bonds in **2** have formed to very different extents and the rough plane of the performic acid is skewed at ≈50° to the CC axis of the ethylene. The activation barrier predicted for **1** at the Becke3-LYP/6-31G\* + ZPE level



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(1) Epoxidation reviews: Jacobsen, E. N. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Chapter 4.2.

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

(3) Hanzlik, R. P.; Shearer, G. O. *J. Am. Chem. Soc.* **1975**, *97*, 5231.

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(7) (a) Lynch, B. M.; Pausacker, K. H. *J. Chem. Soc.* **1955**, 1525. (b) Boeseken, J.; Stuurman, J. *Rec. Trav. Chim.* **1937**, *56*, 1034.

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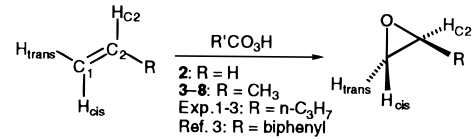
(10) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785. For reviews of density-functional methods see: (c) Ziegler, T. *Chem. Rev.* **1991**, *91*, 651. (d) *Density Functional Methods in Chemistry*; Labanowski, J., Andzelm, J., Eds.; Springer: Berlin, 1991. (e) Parr, R. G.; Yang, Y. *Density-Functional Theory of Atoms and Molecules*; Oxford University Press: New York, 1989.

is 14.7 kcal/mol, and the barrier determined for **2** at the MP4/6-31G\*/MP2/6-31G\* + ZPE level is 16.3 kcal/mol;<sup>5</sup> both are in reasonable agreement with experimental values.<sup>11</sup>

In order to distinguish experimentally with KIEs whether peracid epoxidations intrinsically favor a synchronous transition state as in **1** or highly asynchronous CO bond formation as in **2**, it was necessary to study “moderately unsymmetrical”<sup>12</sup> alkenes. We chose the reaction of *meta*-chloroperbenzoic acid (mCPBA) with 1-pentene for experimental study and the reaction of performic acid with 1-propene as the calculational model. Four transition structures were found in MP2

(11) Dryuk, V. G. *Tetrahedron* **1976**, *32*, 2855–66.

(12) Symmetrical alkenes would show symmetrical KIEs whether the transition state was synchronous or highly asynchronous due to averaging. On the other hand, with the <sup>2</sup>H KIEs observed previously in 4-vinylbiphenyl epoxidation, there was some question of whether the implied asynchrony was simply a consequence of the biphenyl substituent.<sup>3</sup>

**Table 1.** Calculated and Experimental KIEs ( $k_H/k_D$ ) for Epoxidations (25 °C)


	calculated <sup>a</sup>			experimental <sup>b</sup>			
	2	3–6 MP2	7–8 B3LYP	exp 1	exp 2	exp 3	ref 3
C <sub>1</sub>		1.015	1.012	1.013(4)	1.012(3)	1.010(3)	
C <sub>2</sub>		1.023	1.009	1.009(4)	1.009(2)	1.006(3)	
H <sub>trans</sub>	0.915 <sup>c</sup>	0.975	0.934	<i>d</i>	0.931(4)	0.929(8)	0.91 <sup>c</sup>
H <sub>cis</sub>	0.915 <sup>c</sup>	0.965	0.927	<i>d</i>	0.935(7)	0.931(6)	0.91 <sup>c</sup>
H <sub>C2</sub>	1.077	0.928	0.949	<i>d</i>	0.963(7)	0.98(2)	0.99

<sup>a</sup> The KIEs for **2** are based on ref 6. The other KIEs are calculated as described in ref 15. <sup>b</sup> Experiments 1, 2, and 3 are reactions carried to 90.0(8), 89.4(8), and 81(1.4)% completion, respectively. Standard deviations shown in parentheses. See Supporting Information for further details. <sup>c</sup> Estimated as the square root of the reported value for  $k_{H2}/k_{D2}$ . <sup>d</sup> <sup>2</sup>H KIEs not determined.

calculations—two regioisomerically asynchronous sets with the OH either *anti* (**3** and **4**) or *syn* (**5** and **6**) to the methyl group—while only two transition structures were found in B3LYP calculations—*anti* (**7**) and *syn* (**8**). Just as in **2**, the MP2 structures are highly asynchronous, while the B3LYP calculations predict that the methyl substituent induces a small amount of asynchrony (the forming CO bonds differ by  $\approx 0.05$  Å from the average).

Experimental KIEs for the reaction of mCPBA with 1-pentene were determined by recently reported methodology for the combinatorial high-precision determination of <sup>13</sup>C and <sup>2</sup>H KIEs at natural abundance.<sup>13</sup> Reactions of natural abundance 1-pentene on a 1–3 mol scale with mCPBA in chlorobenzene were taken to 90, 89.4, and 81% completion. The remaining 1-pentene was recovered by distillation and brominated. The resulting 1,2-dibromopentane was analyzed by <sup>13</sup>C and <sup>2</sup>H NMR compared to a standard sample of dibromopentane derived from the original 1-pentene.<sup>14</sup> The changes in <sup>13</sup>C and <sup>2</sup>H isotopic composition were calculated using the methyl group of the pentene as an “internal standard” with the assumption that its isotopic composition does not change. From the changes in isotopic composition the KIEs were calculated in a standard fashion.<sup>13</sup> The resulting KIEs are summarized in Table 1, along with KIEs predicted for **3–6** and **7–8** using the method of Bigeleisen and Mayer<sup>15</sup> (weighting the contribution of each transition structure based on a Boltzmann distribution<sup>16</sup>). Also shown are comparable KIEs based on Yamabe’s predictions with **2**,<sup>6</sup> and previous KIEs observed with 4-vinylbiphenyl.<sup>3</sup>

(13) Singleton, D. A.; Thomas, A. A. *J. Am. Chem. Soc.* **1995**, *117*, 9357.

(14) As described in the Supporting Information, a number of precautions were taken to minimize both random and systematic errors in the NMR analysis, see: Rabenstein, D. L.; Keire, D. A. In *Modern NMR Techniques and Their Application in Chemistry*; Popov, A. I., Hallenga, K., Eds.; Marcel Dekker: New York, 1991; pp 323–369. Samples from recovered and standard material were prepared identically and a T<sub>1</sub> determination was carried out for each sample. <sup>13</sup>C spectra were obtained with inverse-gated <sup>1</sup>H decoupling and a 120-s delay between calibrated 2 $\pi$ /9 pulses.

(15) (a) Bigeleisen, J.; Mayer, M. G. *J. Chem. Phys.* **1947**, *15*, 261. (b) Wolfsberg, M. *Acc. Chem. Res.* **1972**, *5*, 225. The calculations used the program QUIVER (Saunders, M.; Laidig, K. E.; Wolfsberg, M. *J. Am. Chem. Soc.* **1989**, *111*, 8989) with frequencies scaled by 0.963 for Becke3LYP calculations and 0.9427 for MP2 calculations. (Rauhut, G.; Pulay, P. *J. Phys. Chem.* **1995**, *99*, 3093. Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502.) Tunneling corrections were applied using the one-dimensional infinite parabolic barrier model (Bell, R. P. *The Tunnel Effect in Chemistry*; Chapman & Hall: London, 1980; pp 60–63).

(16) See the Supporting Information for details. Although the predicted KIEs vary with the calculated energies of the contributing transition states, almost any mixture of contribution from **7** and **8** will closely approximate the observed KIEs, while no combination of **3–6** can do so.

The C<sub>1</sub>, C<sub>2</sub>, and H<sub>trans</sub> KIEs predicted from the B3LYP structures are well within experimental error of the observed values,<sup>17</sup> and the predicted KIE for H<sub>cis</sub> is very close to experiment. Only the experimental values for H<sub>C2</sub> are perhaps significantly greater than predicted for **7/8**. This may suggest a slightly greater asynchrony in the experimental reaction, though such would not explain the excellent agreement of the <sup>13</sup>C KIEs. Considering the differences between the experiment and theoretical model—mCPBA versus performic acid, solution versus gas phase, 1-pentene versus propene—the agreement between experimental and predicted KIEs is outstanding. It appears that **7** and **8** are excellent representations of the solution chemistry. In contrast, the KIEs predicted from the MP2 structures **3–6** do not match up well with experiment.<sup>16</sup>

It would appear that classical substituent effect studies provided the best view of the epoxidation transition state involving synchronous or nearly synchronous CO bond formation. In retrospect, the previous KIE studies on vinylbiphenyl do not imply as much asynchrony as thought at the time. The low KIE for H<sub>C2</sub> (0.99) was interpreted as implying negligible bond formation to C<sub>2</sub> at the transition state, but, as indicated by the calculated KIEs for **2** and recent observations in the literature,<sup>18</sup> if there were no bond formation to C<sub>2</sub>,  $k_H/k_D$  for H<sub>C2</sub> would be  $\gg 1$ .

The results here and in our previous observations with the Diels–Alder reaction establish that Becke3LYP DFT calculations provide superior predictions of transition state geometry and isotope effects. We plan to continue to use these calculations in concert with high-precision KIE determinations to gain detailed, experimentally based knowledge of organic transition states.

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**Supporting Information Available:** Procedures for reactions, NMR measurements, and calculations, and energies and coordinates of all structures reported (12 pages). See any current masthead page for ordering and Internet access instructions.

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(17) The relatively small magnitudes of the <sup>13</sup>C KIEs may be related to the observation that the “equilibrium” <sup>13</sup>C isotope effect for epoxidation of ethylene is calculated to be fairly inverse (0.987) in RHF/6-31G\* calculations.

(18) Olson, L. P.; Niwayama, S.; Yoo, H. Y.; Houk, K. N.; Harris, N. J.; Gajewski, J. J. *J. Am. Chem. Soc.* **1996**, *118*, 886–892.