J. Am. Chem. Soc. **1994,** *116,* 10336–10337

Density Functional Theory Isotope Effects and Activation Energies for the Cope and Claisen Rearrangements

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Received August 2, 1994

Density functional theory (DFT)[1] has given promising results in a wide variety of chemical applications,[2] including the calculation of transition structures for a few typical pericyclic reactions.[3] For these reactions, DFT with nonlocal corrections for exchange and correlation energies gave results which closely matched those calculated at the MP2/6-31G* level.[4] However, the cases reported are ones treated similarly by *ab initio* and semiempirical methods. A much more challenging issue involves the nature of the transition states of [3,3]-sigmatropic shifts.[5-8] Here we report the excellent results obtained using DFT with large basis sets.

The mechanisms of the Cope and Claisen reactions remain a source of controversy in spite of having been probed repeatedly by experimental[5] and theoretical inquiry.[6,7] Which of the three species shown in Figure 1 corresponds to the lowest energy transition structure?[8]

Computational predictions have been equivocal because of the relative flatness of the potential energy surface connecting the competing, possible transition structures (e.g., 0.6 kcal/mol at the CASSCF/6-31G* level).[6c] Fortunately, a very sensitive probe of transition state structure is available in the experimental kinetic isotope effects (KIEs).[9] Transition state geometries determine vibrational frequencies, which then dictate isotope effects.[10] We report here transition state structures, energetics, and theoretical kinetic isotope effects for both the Cope and Claisen rearrangements calculated using DFT methods.

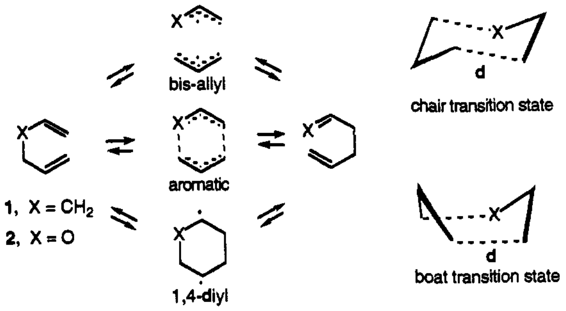

Figure 1. Possible [3,3]-shift mechanisms and two transition state conformations.

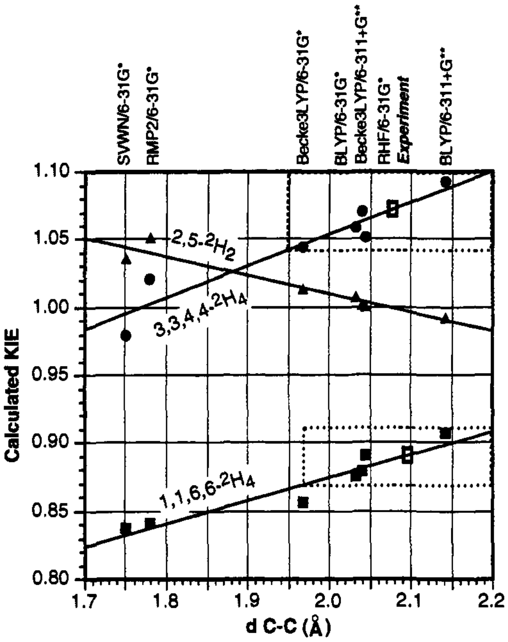

Figure 2. Calculated kinetic isotope effects versus interallylic distance, *d*. Rectangular dashed boxes represent the experimental error limits (see text).

All calculations were carried out using GAUSSIAN92/DFT[11] with standard basis sets. Slater[12] (S) or Becke[13] (B and Becke3) functionals were used for exchange energies. Vosko, Wilk, and Nussair[14] (VWN) or the gradient corrected Lee, Yang, and Parr[15] (LYP) functionals were used for the correlation energy. All structures reported have been characterized by analytical frequency analysis. Kinetic isotope effects were calculated using QUIVER.[16] Frequencies were left unscaled for DFT results.[17]

Results for the Cope reaction are summarized in Table 1. DFT using a local spin density approximation (S-VWN/6-31G*) gives a poor estimate of the activation energy and predicts a diyl-like geometry ($d = 1.753$ Å). The resulting KIEs are in accord with that "tight" transition structure but differ significantly from

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(1) (a) Labanowski, J. W.; Andzelm, J. *Density Functional Methods in Chemistry*; Springer: New York, 1991. (b) Parr, R. G.; Yang, W. *Density Functional Theory of Atoms and Molecules*; Oxford University Press: New York, 1989. (c) Jones, R. O. In *Ab Initio Methods in Quantum Chemistry, Vol. I*; Lawley, K. P., Ed.; Wiley & Sons: New York, 1987.

(2) (a) Johnson, B. G.; Gill, P. M. W.; Pople, J. A. *J. Chem. Phys.* **1993**, *98*, 5612. (b) Andzelm, J.; Wimmer, E. *J. Chem. Phys.* **1992**, *96*, 1280. (c) Ziegler, T. *Chem. Rev.* **1991**, *91*, 651.

(3) (a) Stanton, R. V.; Merz, K. *J. Chem. Phys.* **1994**, *100*, 434. (b) Sosa, C.; Andzelm, J.; Lee, C.; Blake, J. F.; Chenard, B. L.; Butler, T. W. *Int. J. Quantum Chem.* **1994**, *49*, 511. (c) Carpenter, J. E.; Sosa, C. *J. Mol. Struct. (THEOCHEM.)*, in press.

(4) Houk, K. N.; Li, Y.; Evanseck, J. D. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 682.

(5) (a) Cope, A. C.; Hardy, E. M. *J. Am. Chem. Soc.* **1940**, *62*, 441. (b) Doering, W. von E.; Toscano, V. G.; Beasley, G. H. *Tetrahedron* **1971**, *27*, 5299. (c) Gajewski, J. J. *Hydrocarbon Thermal Isomerizations*; Academic Press: New York, 1981; p 166.

(6) (a) Borden, W. T.; Loncharich, R. J.; Houk, K. N. *Annu. Rev. Phys. Chem.* **1988**, *39*, 213. (b) Dewar, M. J. S.; Jie, C. *Acc. Chem. Res.* **1992**, *25*, 537. (c) Dupuis, M.; Murray, C.; Davidson, E. R. *J. Am. Chem. Soc.* **1991**, *113*, 9756. (d) Hrovat, D. A.; Morokuma, K.; Borden, W. T. *J. Am. Chem. Soc.* **1994**, *116*, 1072. (e) The aromaticity of the loose transition structure has been confirmed by calculations of the exaltation of magnetic susceptibility: Jiao, H.; Schleyer, P. v. R. *Angew. Chem. Int. Ed. Engl.* in press.

(7) (a) Vance, R. L.; Rondan, N. G.; Houk, K. N.; Jensen, F.; Borden, W. T.; Komornicki, A.; Wimmer, E. *J. Am. Chem. Soc.* **1988**, *110*, 2315. (b) Dewar, M. J. S.; Jie, C. *J. Am. Chem. Soc.* **1989**, *111*, 511.

(8) (a) Doering, W. von E. *Proc. Natl. Acad. Sci. U.S.A.* **1981**, *78*, 5279. (b) Roth, W. R.; Bauer, F.; Beitat, A. Ebbrecht, T.; Wustefeld, M. *Chem. Ber.* **1991**, *124*, 1453.

(9) Gajewski, J. J.; Conrad, N. D. *J. Am. Chem. Soc.* **1979**, *101*, 6693.

(10) (a) Houk, K. N.; Gustafson, S. M.; Black, K. A. *J. Am. Chem. Soc.* **1992**, *114*, 8565. (b) Houk, K. N.; Yoo, H. Y. *J. Am. Chem. Soc.*, in press. (c) Storer, J. W.; Raimondi, L.; Houk, K. N. *J. Am. Chem. Soc.*, in press. (d) Houk, K. N.; Li, Y.; Storer, J. W.; Raimondi, L.; Beno, B. *J. Chem. Soc., Faraday Trans.* **1994**, *90*, 1599.

(11) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Wong, M. W.; Foresman, J. B.; Robb, M. A.; Head-Gordon, M.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez C.; Martin, R. L.; Fox, D. J., Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. GAUSSIAN92/DFT, Revision G.1; Gaussian, Inc.: Pittsburgh, PA, 1993.

(12) Slater, J. C. *Quantum Theory of Molecules and Solids, Vol. 4*: *The Self Consistent Field of Molecules and Solids*; McGraw-Hill: New York, 1974.

(13) (a) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372.

(14) Vosko, S. H.; Wilk, L.; Nussair, M. *Can. J. Chem.* **1980**, *58*, 1200.

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

(16) Saunders, M.; Laidig, K. E.; Wolfsberg, M. *J. Am. Chem. Soc.* **1989**, *111*, 8989.

(17) Preliminary results indicate that the frequencies from DFT calculations tend to be slightly too low: ref 2a,b.

0002-7863/94/1516-10336$04.50/0

Table 1. Energies (E + ZPE) and Geometries of the Cope Transition Structure and KIE Values (248 °C)

method	**1** (C_i)	C_{2h} chair		C_{2v} boat		KIE	
	E (hartree)	ΔE (kcal/mol)	d (Å)	ΔE (kcal/mol)	d (Å)	1,1,6,6-$^2H_4$	3,3,4,4-$^2H_4$
experiment[a]		33.5 ± 0.5		44.7 ± 2.0		0.89 ± 0.02	1.07 ± 0.03
SVWN/6-31G*	−233.125 65	19.8	1.753	33.2	1.966	0.837	0.979
BLYP/6-31G*	−234.328 79	29.7	2.034	36.0	2.289	0.875	1.058
BLYP/6-311+G**	−234.407 33	30.0	2.145	35.0	2.376	0.906	1.092
Becke3LYP/6-31G*	−234.469 25	34.2	1.971	42.0	2.208	0.855	1.044
Becke3LYP/6-311+G**	−234.541 39	34.8	2.043	41.2	2.279	0.878	1.070
RHF/6-31G*[b]		56.6	2.046			0.89	1.05
RMP2/6-31G*[b]		31.4	1.783			0.84	1.02

[a] Experimental KIEs are for the 3-methyl and the 1-methyl derivatives, ref 9. [b] Reference 10a.

Table 2. Energies (E + ZPE) and Geometries of the Claisen Chair Transition Structure and KIE Values (160 °C)

method	**2**	chair TS			KIE				SKIE	
	E (hartree)	ΔE (kcal/mol)	d_{C-O} (Å)	d_{C-C} (Å)	3-^{18}O	2-^{14}C	4-^{14}C	6-^{14}C	4,4-$^2H_2$	6,6-$^2H_2$
experiment[9,19,20]		30.6			1.050 ± 0.0007	1.027 ± 0.0007	1.072 ± 0.0008	1.0178 ± 0.0007	1.092 ± 0.005	0.976 ± 0.005
SVWN/6-31G*	−268.908 09	20.8	1.696	2.094	1.025	1.003	1.040	1.028	1.022	0.948
BLYP/6-31G*	−270.268 84	21.1	1.959	2.428	1.024	1.002	1.039	1.023	1.059	0.969
Becke3LYP/6-31G*	−270.386 67	26.8	1.902	2.312	1.027	1.003	1.042	1.024	1.058	0.953
Becke3LYP/6-311+G**	−270.471 88	26.1	1.954	2.384	1.026	1.002	1.041	1.023	1.070	0.960
RHF/6-31G*[10b]	−268.667 46	47.7	1.918	2.266	1.032	1.005	1.053	1.028	1.053	0.932
CASSCF/6-31G* (6e/6o)[10b]	−268.875 04	42.5	2.100	2.564	1.043	1.024	1.069	1.030	1.144	1.005

experimental values. The nonlocal methods (B-LYP and Becke3-LYP) yield looser "aromatic" chair transition structures (d = 1.98–2.15 Å) and much better estimates of the activation energies. Becke3-LYP, using 6-31G* and 6-311+G** basis sets, provides estimates of the activation energy within 1 kcal/mol of the experimental value.[10a]

Theoretical deuterium secondary KIEs are plotted as a function of the calculated interallylic distance (d) for Cope transition structures obtained from several computational methods (Figure 2). The calculated KIEs are found to depend on d, but they are quite independent of the method of calculation. This correlation, combined with experimental KIE values, predicts a σ bond distance of 2.085 Å. This value is in reasonable agreement with the RHF and nonlocal DFT geometries but differs markedly from the transition structure estimated on the basis of CASPT2 calculations (1.885 Å at the CASPT2/6-311(2d,2p) level).[6d]

The boat transition structure is calculated by DFT at all levels to be a looser transition structure by about 0.25 Å and to be about 5–6 kcal/mol higher in energy than the chair structure. Basis set expansion from 6-31G* to 6-311+G** yields a loosening of both the chair and boat structures (≈0.1 Å) with modest changes in energies (<1 kcal/mol).

The results for the Claisen rearrangement of **2** (Table 2) are similar to those for the Cope rearrangement. While the local spin density approximation does not describe the transition state properly, the nonlocal methods tested provide a much better picture and indicate an aromatic-type transition state with bond lengths of 1.90–1.96 Å for the breaking C–O and 2.31–2.43 Å for the forming C–C bond. The computed activation energies are too low, but the values using the Becke3-LYP functional are in better agreement with the experimental data than RHF or CASSCF values.[18]

The calculated deuterium secondary KIEs show the same trends as found for the Cope rearrangement (see supplementary material). The nonlocal DFT secondary KIE values are in better agreement with the experimental data than those obtained by other methods.

The calculated heavy atom primary KIEs are less sensitive to changes in the bond lengths than the secondary KIEs. The primary KIEs for the breaking C–O bond (3-^{18}O and 4-^{14}C) are essentially constant for the different DFT methods used and somewhat too small as compared to the experimental values, whereas values calculated for the forming C–C bond (6-^{14}C) are too large. The primary KIE at 2-C (Table 2) is described poorly, perhaps due to an inadequate description of the radicaloid character at this center.

These DFT energy and KIE results, combined with previous calculations of energies in pericyclic reactions, make clear that the S-VWN local density functional is not appropriate for the description of these transition states. However, the nonlocal B-LYP and hybrid Becke3-LYP methods both provide transition state energies on a par with correlated molecular orbital theory.[3] At the same time, these DFT methods also provide very good estimates of the transition state geometries, as validated through comparison of theoretical and experimental kinetic isotope effects.

Acknowledgment. We are grateful to the National Science Foundation for financial support of this research and the Office of Academic Computing at UCLA for computer time and facilities. O.W. thanks the Alexander von Humboldt Foundation for a Feodor Lynen Fellowship. K.A.B. acknowledges support from the W. M. Keck Foundation and The Research Corporation.

Supplementary Material Available: Geometries, energies, and zero-point energy corrections for all structures reported in this study, and a plot of calculated isotope effects versus bond distances for the Claisen rearrangement (9 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(18) On the basis of the RHF/6-31G* and MP2/6-31G* activation energies (47.7 and 24.6 kcal/mol), we estimate the CASPT2/6-31G* value will be about 19.4 kcal/mol.

(19) Kupczyk-Subotkowska, L.; Saunders, W. H., Jr.; Shine, H. J.; Sobotkowski, W. *J. Am. Chem. Soc.* **1993**, *115*, 5957.

(20) Schuler, F. W.; Murphy, G. W. *J. Am. Chem. Soc.* **1950**, *72*, 3155.