

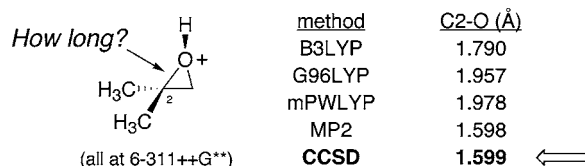
Protonated 2-Methyl-1,2-epoxypropane: A Challenging Problem for Density Functional Theory

Paul R. Carlier,* Nipa Deora, and T. Daniel Crawford

Department of Chemistry, Virginia Tech, Blacksburg, Virginia 24061

pcarlier@vt.edu

Received November 7, 2005



Protonated epoxides feature prominently in organic chemistry as reactive intermediates. Herein, we describe 10 protonated epoxides using B3LYP, MP2, and CCSD/6-311++G** calculations. Relative to CCSD, B3LYP consistently overestimates the C2–O bond length. Protonated 2-methyl-1,2-epoxypropane is the most problematic species studied, where B3LYP overestimates the C2–O bond length by 0.191 Å. Seventeen other density functional methods were applied to this protonated epoxide; on average, they overestimated the CCSD bond length by 0.2 Å. We present a range of data that suggest the difficulty for DFT methods in modeling the structure of the titled protonated epoxide lies in the extremely weak C2–O bond, which is reflected in the highly asymmetric charge distribution between the two ring carbons. Protonated epoxides featuring more symmetrical charge distribution and cyclic homologues featuring less ring strain are treated with greater accuracy by B3LYP. Finally, MP2 performed very well against CCSD, deviating in the C2–O bond length at most by 0.009 Å; it is, therefore, recommended when computational resources prove insufficient for coupled cluster methods.

Introduction

Epoxides are important functional groups in natural products,^{1–4} in medicinal,^{5,6} polymer,^{7,8} and supramolecular⁹ chemistry and are extremely useful intermediates in organic syntheses.^{10,11}

Nucleophilic ring opening generally proceeds stereoselectively, and reactions under neutral and acidic conditions provide complementary regioselectivities.^{10–12} Consequently, numerous computational studies of neutral and protonated epoxides,^{13–16} their ring-opening reactions,^{17–22} and their rearrangement via a 1,2-hydride shift^{23–25} have been published.

* Corresponding author. Fax: (425) 984-8099.

- Rossiter, B. E.; Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 464–465.
- Schmidt, U.; Schmidt, J. *J. Chem. Soc., Chem. Commun.* **1992**, 529–530.
- Balog, A.; Meng, D. F.; Kamenecka, T.; Bertinato, P.; Su, D. S.; Sorensen, E. J.; Danishefsky, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2801–2803.
- Ghosh, A. K.; Wang, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11027–11028.
- Wilson, S. C.; Howard, P. W.; Forrow, S. M.; Hartley, J. A.; Adams, L. J.; Jenkins, T. C.; Kelland, L. R.; Thurston, D. E. *J. Med. Chem.* **1999**, *42*, 4028–4041.
- James, K. E.; Asgian, J. L.; Li, Z. Z.; Ekici, O. D.; Rubin, J. R.; Mikolajczyk, J.; Salvesen, G. S.; Powers, J. C. *J. Med. Chem.* **2004**, *47*, 1553–1574.
- Cheng, Z. P.; Zhu, X. L.; Fu, G. D.; Kang, E. T.; Neoh, K. G. *Macromolecules* **2005**, *38*, 7187–7192.
- Bulut, U.; Crivello, J. V. *Macromolecules* **2005**, *38*, 3584–3595.
- Carlier, P. R. *Angew. Chem., Int. Ed.* **2004**, *43*, 2602–2605.
- Behrens, C. H.; Sharpless, K. B. *Aldrichimica Acta* **1983**, *16*, 67–79.
- Smith, J. G. *Synthesis* **1984**, 629–656.

- Parker, R. E.; Isaacs, N. S. *Chem. Rev.* **1959**, *59*, 737–799.
- Cremer, D.; Kraka, E. *J. Am. Chem. Soc.* **1985**, *107*, 3800–3810.
- Nobes, R. H.; Rodwell, W. R.; Bouma, W. J.; Radom, L. *J. Am. Chem. Soc.* **1981**, *103*, 1913–1922.
- Liang, C.; Allen, L. C. *J. Am. Chem. Soc.* **1991**, *113*, 1878–1884.
- Vila, A.; Mosquera, R. A. *Chem. Phys. Lett.* **2003**, *371*, 540–547.
- Ford, G. P.; Smith, C. T. *J. Am. Chem. Soc.* **1987**, *109*, 1325–1331.
- Na, J.; Houk, K. N.; Shevlin, C. G.; Janda, K. D.; Lerner, R. A. *J. Am. Chem. Soc.* **1993**, *115*, 8453–8454.
- Laitinen, T.; Rouvinen, J.; Peräkylä, M. *J. Org. Chem.* **1998**, *63*, 8157–8162.
- Lau, E. Y.; Newby, Z. E.; Bruice, T. C. *J. Am. Chem. Soc.* **2001**, *123*, 3350–3357.
- Helten, H.; Schirmeister, T.; Engels, B. *J. Phys. Chem. A* **2004**, *108*, 7691–7701.
- Helten, H.; Schirmeister, T.; Engels, B. *J. Org. Chem.* **2005**, *70*, 233–237.
- George, P.; Bock, C. W.; Glusker, J. P. *J. Phys. Chem.* **1992**, *96*, 3702–3708.

Walden inversion is the normal stereochemical outcome of nucleophilic ring opening, even under acidic conditions.^{10,12} Racemization, when it occurs, signals the operation of an S_N1 pathway; however, this mechanism intervenes only when the epoxide bears a functional group that can stabilize the incipient carbocation via resonance.¹⁰ Thus, ring opening under acidic conditions is generally assumed to occur via a nucleophilic attack on a protonated epoxide intermediate.¹²

A number of previous studies have addressed the structure of protonated epoxides and their energies relative to the corresponding ring-opened hydroxy-carbocations. Radom and co-workers studied protonated ethylene oxide **1**-H⁺ at MP2/6-31G**//HF/4-31G;¹⁴ both the protonated epoxide and the ring-opened hydroxy-carbocation **2** were found as minima, and **2** was estimated to be 24.8 kcal/mol higher in energy than the protonated epoxide **1**-H⁺. As is typical for these systems, the protonated aldehyde (resulting from a 1,2-hydride shift in **1**-H⁺, not shown) was found to be the lowest energy structure on the potential surface. Subsequent studies at a higher level geometry (MP2/6-31G**//HF/6-31G*), including a zero-point vibrational energy (ZPVE) correction, found the open hydroxy-carbocation **2** to be 24.6 kcal/mol higher in energy than the protonated epoxide.¹⁷

Coxon and co-workers studied *cis*- and *trans*-protonated 1,2-epoxypropane (*trans*-**3**-H⁺ and *cis*-**3**-H⁺) at MP2/6-31G* and found the C2–O bond lengths to be somewhat extended relative to that of **1**-H⁺ (cf. 1.562 Å for *trans*-**3**-H⁺ and 1.498 Å for **1**-H⁺).²⁴ This increase in bond length relative to **1**-H⁺ can be interpreted as evidence of the stabilization of the developing charge at C2 by the methyl group. Consistent with this proposal, a decreased endothermicity for ring opening to **4a** and **4b** is also seen relative to ethylene oxide (now only 12.7 and 9.3 kcal/mol relative to *trans*-**3**-H⁺). Subsequently, protonated 2-methyl-1,2-epoxypropane **5**-H⁺ was studied at B3LYP/6-31G*; even though a different theoretical method was used, the results follow the expected trend.²⁵ Ring opening of **5**-H⁺ to the hydroxy-carbocation **6** is less endothermic than that of *trans*-**3**-H⁺, as expected from the increased positive charge stabilization imparted by the additional methyl group. Consistent with this charge stabilization model, the C2–O bond increases from 1.562 Å in *trans*-**3**-H⁺ (MP2/6-31G*) to 1.691 Å in **5**-H⁺ (B3LYP/6-31G*). Mosquera et al. subsequently published a study of protonated epoxides at B3LYP/6-311++G** and concluded that 1,2-epoxypropane **3** and 2-methyl-1,2-epoxypropane **5** underwent ring opening upon protonation. Although the C–O distances were not disclosed, *trans*-**3**-H⁺ and **5**-H⁺ were considered to be substantially carbocationic, instead of adopting the oxonium ion structures depicted in Scheme 1.¹⁶ The same phenomenon was noted for *cis*- and *trans*-**7**-H⁺ (Scheme 1). These findings prompted us to repeat B3LYP/6-311++G** calculations on the putative protonated epoxides **1**-H⁺, *cis*- and *trans*-**3**-H⁺, **5**-H⁺, and *cis*- and *trans*-**7**-H⁺. Our studies demonstrate an unusually long C2–O bond for **5**-H⁺ at B3LYP/6-311++G**; yet, this structure is distinct from its open ring conformer, hydroxy-carbocation **6**. In addition, we also find that the popular B3LYP method fails to adequately model the structures of asymmetrically substituted protonated epoxides. This failure is exacerbated by an unsymmetrical charge distribu-

tion among the ring carbons and is most dramatic for protonated 2-methyl-1,2-epoxypropane **5**-H⁺.

Computational Methods

Hartree–Fock, DFT,²⁶ MP2,²⁷ CCSD,^{28,29} G2,³⁰ G3,³¹ G3B3,³² and CBS-Q³³ calculations were performed using Gaussian 03.³⁴ DFT investigations employed a variety of exchange (B3,³⁵ mPW and mPW1,³⁶ G96,³⁷ PBE³⁸) and correlation (LYP,³⁹ P86,⁴⁰ PW91,⁴¹ PBE³⁸) functionals. CCSD(T)⁴² single-point calculations at the 6-311++G**⁴³ and aug-cc-pVDZ⁴⁴ basis sets were performed using Gaussian 03. CCSD(T)/aug-cc-pVTZ single points and CCSD(T) and MP2 geometry optimizations using correlation consistent basis sets were calculated using PSI3.⁴⁵ All MP2, CCSD, and CCSD(T) calculations were performed “frozen core” to exclude inner-shell electrons from the correlation calculation. All stationary points were characterized as minima by vibrational frequency analysis, except in the case of CCSD, where cost considerations limited us to the study of **1**-H⁺. Because MP2 geometries were shown to closely approximate the CCSD geometries of all 10 protonated epoxides studied and because the CCSD/6-311++G** ZPVE of **1**-H⁺ differed from the corresponding MP2 ZPVE by only 0.08 kJ/mol

(26) Parr, R. G.; Yang, W. T. *Density Functional Theory of Atoms and Molecules*; Oxford University Press: New York, 1989.

(27) Head-Gordon, M.; Pople, J. A.; Frisch, M. J. *Chem. Phys. Lett.* **1988**, *153*, 503–506.

(28) Bartlett, R. J. In *Modern Electronic Structure Theory*; Yarkony, D. R., Ed.; World Scientific: Singapore, 1995; pp 1047–1131.

(29) Crawford, T. D.; Schaefer, H. F. *Rev. Comput. Chem.* **2000**, *14*, 33–136.

(30) Curtiss, L. A.; Raghavachari, K.; Trucks, G. W.; Pople, J. A. *J. Chem. Phys.* **1991**, *94*, 7221–7230.

(31) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Rassolov, V.; Pople, J. A. *J. Chem. Phys.* **1998**, *109*, 7764–7776.

(32) Baboul, A. G.; Curtis, L. A.; Redfern, P. C.; Raghavachari, K. *J. Chem. Phys.* **1999**, *110*, 7650–7657.

(33) Ochterski, J. W.; Petersson, G. A.; Montgomery, J. A. *J. Chem. Phys.* **1996**, *104*, 2598–2619.

(34) 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 B.05; Gaussian, Inc.: Wallingford, CT, 2004.

(35) Becke, A. J. *J. Chem. Phys.* **1993**, *98*, 5648–5652.

(36) Adamo, C.; Barone, V. *J. Chem. Phys.* **1998**, *108*, 664–675.

(37) Gill, P. M. W. *Mol. Phys.* **1996**, *89*, 443–445.

(38) Perdew, J.; Burke, K.; Ernzerhof, M. *Phys. Rev. Lett.* **1996**, *77*, 3865–3868.

(39) Lee, C. T.; Yang, W. T.; Parr, R. G. *Phys. Rev. B: Condensed Matter* **1988**, *37*, 785–789.

(40) Perdew, J. P. *Phys. Rev. B: Condensed Matter* **1986**, *33*, 8822–8824.

(41) Perdew, J. P.; Burke, K.; Wang, Y. *Phys. Rev. B: Condensed Matter* **1996**, *54*, 16533–16539.

(42) Pople, J. A.; Head-Gordon, M.; Raghavachari, K. *J. Chem. Phys.* **1987**, *87*, 5968–5975.

(43) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650–654.

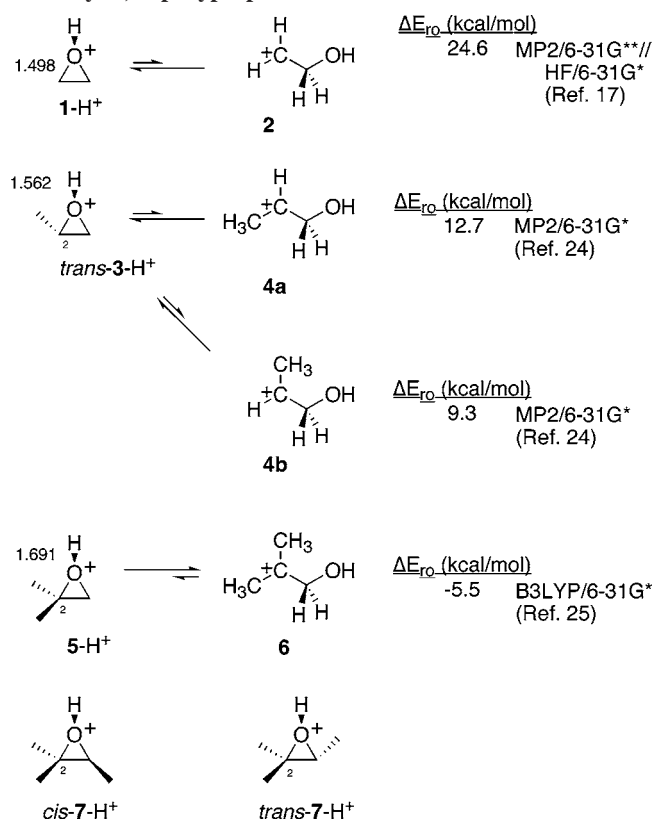
(44) Kendall, R. A.; Dunning, T. H.; Harrison, R. J. *J. Chem. Phys.* **1992**, *96*, 6796–6806.

(45) Crawford, T. D.; Sherrill, C. D.; Valeev, E. F.; Fermann, J. T.; King, R. A.; Leininger, M. T.; Brown, S. T.; Janssen, C. L.; Seidl, E. T.; Kenny, J. P.; Allen, W. D. *PSI 3.2*; 2003.

(24) Coxon, J. M.; Maclagan, R. G. A. R.; Rauk, A.; Thorpe, A. J.; Whalen, D. J. *Am. Chem. Soc.* **1997**, *119*, 4712–4718.

(25) Coxon, J. M.; Thorpe, A. J.; Smith, W. B. *J. Org. Chem.* **1999**, *64*, 9575–9586.

SCHEME 1. Previously Calculated C2–O Bond Lengths (Å) and ZPVE-Corrected Energies for the Ring Opening of Protonated Ethylene Oxide, 1,2-Epoxypropane, and 2-Methyl-1,2-epoxypropane



(0.04%), MP2 ZPVE were used to correct the CCSD electronic energies. As a result of the wide range of methods and basis sets employed in this study, ZPVE were calculated from unscaled frequencies.

Results and Discussion

Because bond lengths were not disclosed in Mosquera's study, we compared B3LYP/6-311++G** electronic energies and ZPVE for $1-H^+$, cis - and $trans$ - $3-H^+$, $5-H^+$, and cis - and $trans$ - $7-H^+$. A perfect correspondence was found (see Supporting Information), and we thus began our examination of the structural features of these species (Figure 1).

As can be seen in Figure 1, all of the protonated epoxides retain a clear cyclic framework, although the 1.79 Å C2–O bond length in $5-H^+$ is quite unusual and is nearly 0.1 Å longer than previously found with the smaller 6-31G* basis set.²⁵ This lengthening prompted us to explore the basis set dependence of C2–O bond lengths and ring-opening energetics for $5-H^+$ at B3LYP (Table 1).

As can be seen in Table 1, at B3LYP the C2–O bond progressively lengthens as diffuse functions are added to heavy atoms and as polarization functions are added to hydrogen. However, the use of a valence triple-zeta basis set appears to cause the largest lengthening (cf. 6-31+G** and 6-311+G**, 6-31++G** and 6-311++G**).⁴⁶ We then explored the use of other methods with the 6-311++G** basis set to see whether

(46) The standard Gaussian 03 STABLE analysis of $5-H^+$ at B3LYP/6-311++G** indicated that the Kohn–Sham orbitals were stable under the perturbations considered.

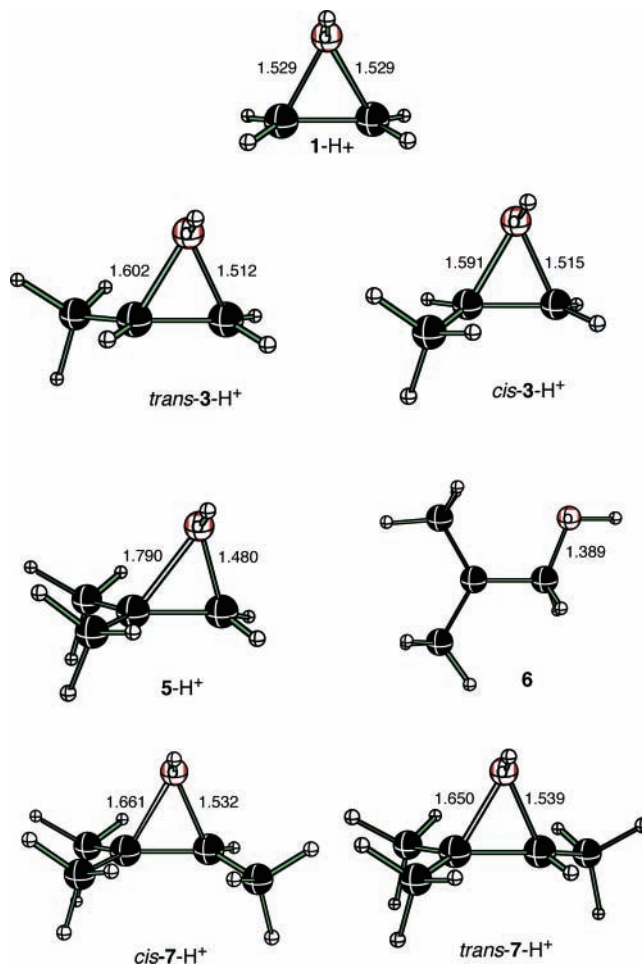


FIGURE 1. B3LYP/6-311++G** geometries of $1-H^+$, cis - and $trans$ - $3-H^+$, $5-H^+$, cis - and $trans$ - $7-H^+$, and **6**; C–O bond lengths are shown in Å.

the extremely long C2–O bond would be retained (Table 2). Hartree Fock predicts a dramatically shorter bond (1.623 Å), as do methods based on ab initio treatments of electron correlation (MP2, CCSD). Unlike B3LYP, the MP2 C2–O bond lengths of $5-H^+$ changed little as the basis set size was increased from 6-31G* (1.598 Å) to 6-311++G** (1.598 Å). The CCSD/6-311++G** C2–O bond length is nearly 0.2 Å shorter than that predicted by B3LYP; note that the MP2 and CCSD/6-311++G** C2–O bond lengths agree quite well (within 0.001 Å).

To confirm the adequacy of the CCSD/6-311++G** geometry for higher level single-point calculations, we examined the effects of correlation consistent basis sets and triples excitation. MP2 geometry optimizations using the cc-pVDZ, cc-pVTZ, and aug-cc-pVDZ basis sets gave C2–O bond lengths of 1.605, 1.595, and 1.626 Å, respectively, demonstrating that the use of a valence triple-zeta basis set and diffuse functions cause small opposing changes. Thus, we project that the MP2/aug-cc-pVTZ C2–O bond length (if available) would be very close to the MP2/6-311++G** C2–O bond length (1.598 Å). To assess the effect of triples excitation, a mixed cc-pVTZ(C,O)/cc-pVDZ-(H) basis set was chosen for the computationally expensive CCSD(T) optimization, because it includes f-type functions on the heavy atoms, which are often critical for accurate predictions of molecular structures. Because only a minimal (+0.01 Å) change in the C2–O bond length is observed versus CCSD/6-

TABLE 1. Calculated C2–O Bond Lengths for 5–H⁺, and the Energetics of Ring Opening to 6

method	basis set	C2–O (Å)	ΔE_{ro}^a (kcal/mol)
B3LYP	6-31G*	1.692	–5.6
	6-31+G*	1.714	–7.4
	6-31+G**	1.725	–8.1
	6-31++G**	1.726	–8.0
	6-311+G**	1.792	–8.7
	6-311++G**	1.790	–8.7
HF	6-311++G**	1.623	–11.8
MP2	6-311++G**	1.598	–1.5
CCSD	6-311++G**	1.599	–4.4
CCSD(T) ^b	6-311++G**	1.599 ^b	–3.1
CCSD(T) ^b	aug-cc-pVDZ	1.599 ^b	–3.9
CCSD(T) ^b	aug-cc-pVTZ	1.599 ^b	–3.5
G2		1.597 ^c	–2.1
G3		1.596 ^c	–2.6
CBS-Q		1.591 ^c	–2.2

^a Energy of ring opening, defined as $E_0(\mathbf{6}) - E_0(\mathbf{5-H}^+)$, where E_0 is the unscaled ZPVE-corrected electronic energy. Scaling of the MP2/6-311++G** ZPVE by 0.98 reduced ΔE_{ro} only slightly (–1.5 to –1.4 kcal/mol). MP2/6-311++G** ZPVE values were used to correct CCSD and CCSD(T) electronic energies. ^b The single-point energy calculation is at the CCSD/6-311++G** geometry; depicted bond lengths are from the CCSD/6-311++G** geometry optimization. ^c The G2 and G3 methods are based on MP2(full)/6-31G* geometries; CBS-Q is based on an MP2/6-31G⁺ geometry.

311++G**, we conclude that this latter geometry was sufficiently accurate and suitable for higher-level single-point calculations.⁴⁷

Regarding the energetics of the ring opening of 5–H⁺ to 6, it is worth noting that the CCSD level of theory indicates the reaction is exothermic by only 4 kcal/mol. CCSD(T) single-point energies at the CCSD/6-311++G** geometries converge well here, giving ΔE_{ro} of –3.1, –3.9, and –3.5 kcal/mol at the 6-311++G**, aug-cc-pVDZ, and aug-cc-pVTZ basis sets, respectively. As a final point of comparison, we calculated 5–H⁺ and 6 with the G2, G3, and CBS-Q methods to get an accurate estimate of ΔE_{ro} ; these values (–2.1 to –2.6 kcal/

mol)⁴⁸ diverge sharply from the B3LYP/6-311++G** value of ΔE_{ro} and approach that obtained at CCSD(T)/aug-cc-pVTZ//CCSD/6-311++G**.

The B3LYP density functional, therefore, appears poorly suited for the description of the protonated epoxide 5–H⁺. To ascertain to what degree this failure stemmed from the charge and to determine whether other functionals fared poorly, we studied 5–H⁺, neutral epoxide 5, and hydroxycarbocation 6 using 17 other functionals (all at 6-311++G**). Deviations from the CCSD/6-311++G** bond length and ΔE_{ro} are shown in Table 2.

As can be seen in Table 2, DFT methods consistently overestimate the length of the C2–O bond in protonated epoxide 5–H⁺, on average, 0.19 Å longer than CCSD. DFT methods also consistently overestimate the exothermicity of the ring opening of 5–H⁺ by approximately 4 kcal/mol. Interestingly, for each of the five exchange functionals examined (B3, mPW, mPW1, G96, PBE), the LYP correlation functional gives the longest C2–O bond. In particular, the mPWLYP, G96LYP, and PBELYP methods gave C2–O bonds 0.379, 0.358, and 0.371 Å longer than those predicted by CCSD. Only two functionals (mPW1PW91 and mPW1PBE) gave C2–O bond lengths within 0.05 Å of those predicted by CCSD. Finally, as mentioned previously, HF and MP2 both perform very well to estimate the C2–O bond length in 5–H⁺. These deviations from the CCSD C2–O bond length are shown graphically in Figure 2.

In contrast, all 18 of the functionals chosen performed well in estimating the C2–O bond length of the neutral epoxide 5 (average deviation from CCSD is 0.017 Å; RMS difference is 0.020 Å). These contrasting results for the protonated and neutral epoxides suggest that the difficulty in modeling 5–H⁺ with DFT methods stems from the C2–O bond, which is disproportionately weakened by hyperconjugative stabilization of the incipient carbocation at C2. The weakness of the C2–O bond in 5–H⁺ is underscored by the calculated energetics of the ring opening; at B3LYP/6-311++G**, hydroxy-carbocation 6 is 8.7 kcal/mol lower in energy than protonated epoxide 5–H⁺.

TABLE 2. Differences in C2–O Bond Lengths and Ring-Opening Energetics for 5–H⁺ and 5 Using ab Initio Methods and Density Functionals vs CCSD (6-311++G**)

ab initio method	exchange functional	correlation functional	$\Delta(\text{C2–O})$ in 5–H ⁺ (Å)	$\Delta(\text{C2–O})$ in 5 (Å)	$\Delta\Delta E_{ro}^a$ (kcal/mol)
HF			0.024	–0.026	–7.4
MP2			–0.001	0.009	+2.9
	B3	LYP	0.191	0.01	–4.3
		P86	0.069	0.001	–3.8
		PW91	0.072	0.001	–3.7
	mPW	LYP	0.379	0.034	–3.0
		P86	0.215	0.024	–3.2
		PW91	0.202	0.022	–3.1
	mPW1	PBE	0.188	0.022	–3.1
		LYP	0.165	0.008	–4.5
		PW91	0.045	–0.003	–3.6
	G96	PBE	0.043	–0.005	–3.5
		LYP	0.358	0.032	–2.9
		P86	0.200	0.022	–3.0
	PBE	PW91	0.189	0.021	–2.9
		PBE	0.175	0.019	–2.9
		LYP	0.371	0.033	–3.2
		P86	0.199	0.022	–3.4
		PW91	0.188	0.021	–3.3
		PBE	0.174	0.02	–3.3
		avg DFT deviation from CCSD ^b	+0.190	+0.017	–3.7

^a Defined as $\Delta E_{ro}(\text{method}) - \Delta E_{ro}(\text{CCSD})$. ^b Root mean square DFT deviations from CCSD are 0.203 Å, 0.020 Å, and 3.4 kcal/mol, respectively.

and the C2–O WBIs for the twelve compounds in Table 3. Protonated epoxide **5**–H⁺, with the longest C2–O bond (1.79 Å), features the lowest WBI (0.47); the C1–O bond in this species is considerably shorter (1.480 Å) and has a much larger WBI (0.83). A reasonable inverse correlation ($R^2 = 0.88$) is evident between the C2–O WBIs and the B3LYP–CCSD deviation in the C2–O bond lengths. Therefore, as we had inferred previously (based on C2–O bond lengths and Mulliken charges), as the C2–O bond weakens, B3LYP performance deteriorates. An examination of WBI values also allows the effect of protonation on the epoxide C–O bond strength to be assessed. Neutral epoxide **5** features a C2–O WBI of 0.88; the corresponding WBI value of 0.47 in **5**–H⁺ represents a near 50% reduction in bond order. WBIs at MP2 and CCSD/6-311++G** are slightly higher (0.58), as expected from the 0.19 Å shorter C2–O bond length. Therefore, significant bonding still exists between C2 and O, and we do not consider **5**–H⁺ to be a ring-opened species.

Finally, since CCSD may be prohibitive for the study of larger molecules, we examined the protonated cyclic ethers listed in Figure 3 at MP2/6-311++G**. As expected, MP2 provides a much better approximation of the CCSD structures than B3LYP; an average deviation in the C2–O bond length of +0.005 Å was observed. Here the largest deviation was observed not for **5**–H⁺ (–0.001 Å) but for symmetrically substituted **10**–H⁺ (0.009 Å). Therefore, for larger systems, MP2 could be recommended as an acceptable approximation of the CCSD structures. It is interesting to note that the dichotomy seen between MP2 and B3LYP in modeling protonated epoxides mirrors similar behavior in amine–borane complexes.⁴⁹ The C2–O bonds of **5**–H⁺, **3**–H⁺, and **7**–H⁺ are weak and are

expected to have dative character like the B–N bonds in amine–boranes; in both systems, MP2 outperforms B3LYP for the estimation of the dative bond length. In addition, as was found for B–N dative bonds, mPW1PW91 is superior to B3LYP for estimating the length of the C2–O bond in **5**–H⁺.⁵⁰ Most importantly, this study joins a growing body of work to provide a cautionary tale. Organic chemists have a tendency to uncritically accept computational studies on the basis of a single popular computational method (e.g., B3LYP);⁵¹ this practice is not prudent, and members of the community would do well to concurrently explore the use of multiple density functionals and perturbation methods.^{49,52,53}

Acknowledgment. We thank Professor Diego Troya for helpful discussions. We thank the National Science Foundation (CHE-0213535) and the Department of Chemistry, Virginia Tech, for financial support of this work.

Supporting Information Available: Optimized structures (CCSD/6-311++G**), electronic and zero-point energies at all levels, selected bond lengths, selected mulliken charges, and selected WBIs for all calculated species. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO052303N

(49) Gilbert, T. M. *J. Phys. Chem. A* **2004**, *108*, 2550–2554.

(50) Note, however, that the mPW1PW91 method is not significantly different from B3LYP for modeling ΔE_{ro} (Table 2), which provides an indirect measure of the strength of the dative C2–O bond in **5**–H⁺.

(51) Gill, P. M. W. *Australian J. Chem.* **2001**, *54*, 661–662.

(52) Woodcock, H. L.; Schaefer, H. F., III; Schreiner, P. R. *J. Phys. Chem. A* **2002**, *106*, 11923–11931.

(53) Check, C. E.; Gilbert, T. M. *J. Org. Chem.* **2005**, *70*, 9828–9834.