

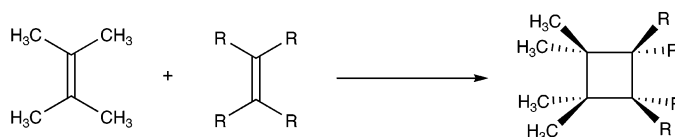
Progressive Systematic Underestimation of Reaction Energies by the B3LYP Model as the Number of C–C Bonds Increases: Why Organic Chemists Should Use Multiple DFT Models for Calculations Involving Polycarbon Hydrocarbons

Catherine E. Check and Thomas M. Gilbert*

Department of Chemistry and Biochemistry, Northern Illinois University, DeKalb, Illinois 60115

tgilbert@niu.edu

Received July 25, 2005



Computational studies of three different reaction types involving hydrocarbons (homolytic C–C bond breaking of alkanes, progressive insertions of triplet methylene into C–H bonds of ethane, and [2+2] cyclizations of methyl-substituted alkenes to form polymethylcyclobutanes) show that the B3LYP model consistently underestimates the reaction energy, even when extremely large basis sets are employed. The error is systematic and cumulative, such that the reaction energies of reactions involving hydrocarbons with more than 4–6 C–C bonds are predicted quite poorly. Energies are underestimated for slightly and highly methyl-substituted cyclic and acyclic hydrocarbons, so the errors do not arise from structural issues such as steric repulsion or ring strain energy. We trace the error associated with the B3LYP approach to its consistent underestimation of the C–C bond energy. Other DFT models show this problem to lesser extents, while the MP2 method avoids it. As a consequence, we discourage the use of the B3LYP model for reaction energy calculations for organic compounds containing more than four carbon atoms. We advocate use of a collection of pure and hybrid DFT models (and *ab initio* models where possible) to provide computational “error bars”.

Introduction

Density functional theory (DFT) has opened computational chemistry to problems far too resource-intensive to be attacked by perturbation theory, allowing study of the physical properties and reaction energetics of compounds containing up to 100 or so heavy atoms.¹ The computational efficiency of DFT has motivated the development of numerous functionals and their implementation into available programs that run on desktop computers or small workstations, thereby allowing non-experts to examine systems of interest computationally without requiring collaboration with experts.

Unfortunately, this ease of use (and the generally good agreement found between DFT methods and experimental results) has allowed too many workers to employ computational methods without a clear understanding of the pitfalls and limitations, and how one should deal

with them. Unlike perturbation theory approaches, DFT models are not currently improved by adding more terms/more electronic configurations to the overall molecular description; they are not iterative. As a result, there is no “best” DFT model.² Thus users of DFT approaches should view their results critically, and test them by comparison either to experimental data or to high-level perturbation theory results.

Though no “best” model exists, the B3LYP model is by far the most popular DFT approach, particularly for those chemists using computational chemistry to support synthetic/mechanistic concepts rather than perform method tests. This stems from B3LYP being the first hybrid model coded into the popular Gaussian suite, and to its early recognition for good agreement with structural data and with the G2 test set of data.³ A perusal of the journals oriented toward organic chemists demonstrates

* Address correspondence to this author.

(1) Koch, W.; Holthausen, M. C. *A Chemist's Guide to Density Functional Theory*; Wiley-VCH: New York, 2000.

(2) Interesting lists of functionals developed appear in: (a) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2005**, *109*, 5656–5667. (b) Boese, A. D.; Martin, J. M. L.; Handy, N. C. *J. Chem. Phys.* **2003**, *119*, 3005–3014.

their belief that systems of interest to them (i.e., covalently bonded compounds containing main group elements from the first and second rows) are accurately described by the B3LYP approach, in that it is rare to find another DFT model used.

For very small molecules, such as most of those in the G2 test set, this confidence in the B3LYP model may be justified. However, over the past decade, definite shortcomings of the B3LYP approach have been uncovered. Its inability to properly model dispersion forces (true of all current DFT methods to some extent) leads to poor descriptions of the energetics of van der Waals molecules and hydrogen bonded systems.^{2a,4} Situations in inorganic chemistry where B3LYP performs poorly include determining spin states for first-row transition metal compounds,⁵ electric field gradients of CuCl,⁶ structures of unusual main-group compounds,⁷ and dative B–N bond dissociation energies of R₃B–NR₃ complexes.⁸

Organic chemistry has seen its share of DFT/B3LYP “failures” as well. Schreiner and co-workers noted that several DFT methods, including B3LYP, incorrectly evaluated the energy difference between allene and propyne, and energies of other cumulenes as well.⁹ They suggested this stemmed from the unexpected behavior of the Becke exchange term when applied to a cumulene. They have more recently shown that B3LYP and other hybrid DFT models perform badly when applied to diradicals as part of the Bergman cyclization.¹⁰ Bachrach and Gilbert,¹¹ and Houk and co-workers,¹² have reported cyclizations where B3LYP predictions are inconsistent with those of higher level methods.

Many organic chemists might view these as pathological systems, containing strained rings, cumulated multiple bonds, and unpaired electrons—“different” from much organic chemistry. Recent studies on simpler systems provide more cause for concern and critical examination. Two papers^{13,14} showed that B3LYP performs poorly in predicting the C–C bond energies for several short-chain hydrocarbons. Others from Curtiss et al.^{15,16} showed that the errors in B3LYP-predicted

enthalpies of formation for chain hydrocarbons rose rapidly and asymptotically with carbon number to approximately 0.62 kcal/mol *per bond* at C16 (i.e., an error of ca. 30.4 kcal/mol), with the asymptotic value at ca. 0.67 kcal/mol per bond.¹⁷ (In our view, workers should read these papers and thoroughly absorb their points prior to performing DFT calculations on many-carbon molecules.) Curtiss et al. proposed a homodesmotic correction approach for large systems.¹⁵ They suggested that the large number of conformers available to large-chain molecules might account for some portion of the error. They did not, however, expand on this, or investigate whether errors in C–H or C–C bond energies contributed more, or whether cyclic systems, with inherently fewer conformers available, showed similar behavior. It has since been suggested that the inability of DFT approaches to model dispersion effects is the root cause for this. Truhlar’s finding that hybrid meta DFT methods designed to accurately model noncovalent interactions also tend to model thermochemistry well¹⁸ supports this view.

We report here DFT energy studies of three types of hydrocarbon reactions, involving C–C bond dissociation energies of alkanes based on the ethane template, the insertion of triplet methylene into C–C bonds to form higher alkanes, and [2+2] cyclizations of substituted alkenes (Scheme 1). We find that the B3LYP approach fails here because it underestimates the C–C bond energy. This effect is cumulative, so that total C–C bond energies of large hydrocarbons are grossly underestimated. While other DFT methods perform better, none perform at the level of composite ab initio approaches. We therefore recommend that energetic calculations be performed with several DFT approaches (and perturbational approaches when possible), and that the results be viewed as computational “error bars” by analogy to experimental value determination.

Computational Methods

All calculations were performed with the Gaussian98 suite of programs.¹⁹ Most molecules were fully optimized without constraints with use of the Hartree–Fock/6-31+G(d) approach. The substituted cyclobutanes were optimized in the highest available symmetries consistent with their puckered rings and substitution patterns (for example, *c*-C(CH₃)₂C(CH₃)₂CH₂CH₂ was optimized under C₂ symmetry, while *c*-C(CH₃)₂C(CH₃)₂C(CH₃)₂C(CH₃)₂ was optimized under D_{2d} symmetry). Scans of the poten-

(3) Foresman, J. B.; Frisch, A. *Exploring Chemistry with Electronic Structure Methods*, 2nd ed.; Gaussian, Inc.: Pittsburgh, PA, 1996; Chapter 7.

(4) (a) Tao, J.; Perdew, J. P. *J. Chem. Phys.* **2005**, *122*, 114102. (b) Zhao, Y.; Truhlar, D. G. *J. Chem. Theory Comput.* **2005**, *1*, 415–432. (c) Tsuzuki, S.; Lüthi, H. P. *J. Chem. Phys.* **2001**, *114*, 3949–3957. (d) Tuma, C.; Boese, A. D.; Handy, N. C. *Phys. Chem. Chem. Phys.* **1999**, *1*, 3939–3947.

(5) Harvey, J. N. *Struct. Bonding (Berlin, Ger.)* **2004**, *112*, 151–183.

(6) Schwerdtfeger, P.; Pernpointner, M.; Laerdahl, J. K. *J. Chem. Phys.* **1999**, *111*, 3357–3364.

(7) Mire, L. W.; Wheeler, S. D.; Wagenseller, E.; Marynick, D. S. *Inorg. Chem.* **1998**, *37*, 3099–3106.

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

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

(10) (a) Schreiner, P. R.; Navarro-Vasquez, A.; Prall, M. *Acc. Chem. Res.* **2005**, *38*, 29–37. (b) Prall, M.; Wittkopp, A.; Schreiner, P. R. *J. Phys. Chem. A* **2001**, *105*, 9265–9274.

(11) Bachrach, S. M.; Gilbert, J. C. *J. Org. Chem.* **2004**, *69*, 6357–6364.

(12) Leach, A. G.; Goldstein, E.; Houk, K. N. *J. Am. Chem. Soc.* **2003**, *125*, 8330–8339.

(13) Feng, Y.; Liu, L.; Wang, J.-T.; Huang, H.; Guo, Q.-X. *J. Chem. Inf. Comput. Sci.* **2003**, *43*, 2005–2013.

(14) Yao, X.-Q.; Hou, X.-J.; Jiao, H.; Xiang, H.-W.; Li, Y.-W. *J. Phys. Chem. A* **2003**, *107*, 9991–9996.

(15) Redfern, P. C.; Zapol, P.; Curtiss, L. A.; Raghavachari, K. *J. Phys. Chem. A* **2000**, *104*, 5850–5854.

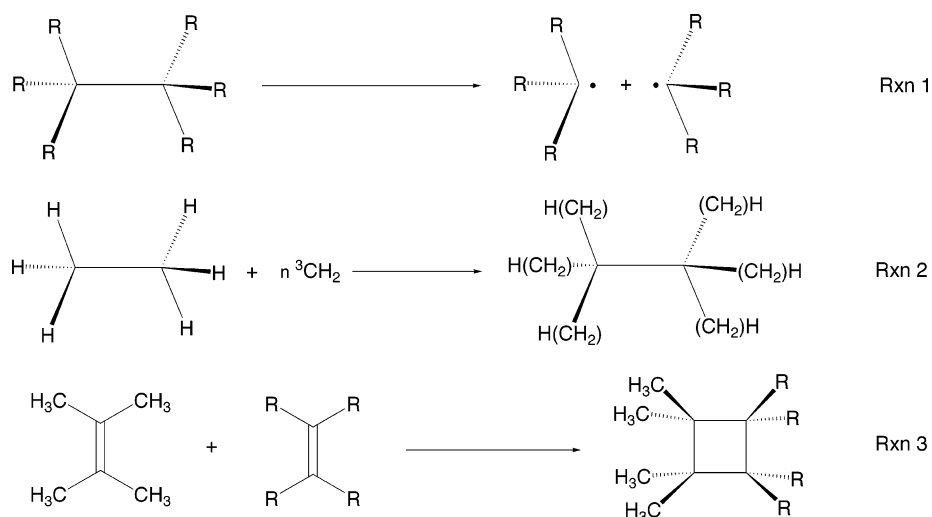
(16) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Pople, J. A. *J. Chem. Phys.* **2000**, *112*, 7374–7383.

(17) No distinction is made between C–H and C–C bonds in this analysis.

(18) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2004**, *108*, 6908–6918.

(19) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, A. D.; Rabuck, K. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; 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.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, Revision A.11; Gaussian, Inc.: Pittsburgh, PA, 1998.

SCHEME 1



tial energy surfaces were performed for conformationally disymmetric molecules so as to ascertain conformational minima. All stationary point structures were shown to be minima by analytical frequency analysis (no imaginary frequencies), which also provided zero-point energies (ZPEs). ZPEs were scaled by 0.9153 when used to correct the raw energy values.²⁰ The structures were then re-optimized at the levels given in Tables 1–4, and the results used to calculate the relative energies given. Except as noted, all calculations reported employed the 6-311++G(d,p) basis set, which we believe combines superior efficiency with acceptable accuracy. The 6-311++G(d,p), 6-311++G(3df,3pd), and aug-cc-pVTZ basis sets were those coded into the G98 program. The “polarization-consistent” pc-3 basis set was taken from Jensen’s work.²¹ This basis set has been shown to be superior to the correlation-consistent cc-pVTZ basis set for DFT calculations. The “single energy” MP2,²² B3LYP,²³ B3PW91,²⁴ mPW1PW91 and mPWPW91,²⁵ and PBEPBE²⁶ models, and the composite²⁷ G3²⁸ and G3MP2²⁹ approaches were used as coded in the program; the MPW1k model was employed, using the IOp procedure reported.³⁰

The structural data for the species studied are unexceptional. Therefore only optimized Cartesian coordinates predicted by either MP2/6-311++G(d,p) or MP2-(full)/6-31G(d) methods for the compounds investigated

are supplied as Supporting Information. Absolute energies for the structures at all computational levels examined are also available as Supporting Information.

Results

Carbon–Carbon Bond Dissociation Energies (BDEs) of Alkanes Based on an Ethane Template (Reaction 1). Experimental and predicted energies required to break the internal C–C bond in the series of alkanes created by progressive substitution of methyl groups on the ethane template appear in Table 1. The experimental values decrease erratically as methyl substitution increases, but tend toward an average decrease of ca. 2 kcal/mol per added CH₃. This statement is slightly misleading, since the change over the first four substitutions is only ca. 4 kcal/mol, whereas the change over the final two substitutions is 7 kcal/mol. This argues that the increasing steric repulsions between vicinal methyl groups do not affect the BDE substantially until so many exist that they cannot be compensated for through conformational or other structural changes.

The composite G3 and G3MP2 values agree reasonably with the experimental values, although the root-mean-square deviation lies above the desired 1 kcal/mol limit. The two models provide similar energies for the cases where both were obtained, suggesting that the G3MP2 approach can be used in place of the more resource-intensive G3 approach for the systems here and below. Owing to this combination of efficiency and accuracy, we have adopted the G3MP2 model as our standard for comparisons throughout this work. The G3MP2 energies show intriguing behavior with respect to experiment: the model underestimates the BDEs for low levels of substitution, reaches a crossover point when four methyl groups have been added, and thereafter overestimates the BDEs. Another way to view this is to note that the BDEs remain essentially constant with increasing methyl substitution until four methyls have been added, whereupon they drop slightly, for an overall decrease from ethane to 2,2,3,3-tetramethylbutane of only 6.1 kcal/mol, as compared with 13.1 kcal/mol experimentally. Since the MP2 approach shows this behavior as well, to a greater extent (see below), and since the G3 composite model appears to as

(20) Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502–16513.

(21) Jensen, F. *J. Chem. Phys.* **2002**, *116*, 7372–7379.

(22) Moller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618–622.

(23) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98* (11), 623–627.

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

(25) Adamo, C.; Barone, V. *J. Chem. Phys.* **1998**, *108*, 664–675. It should be noted that this functional was coded incorrectly into Gaussian 98, leading to a slight error. Commentary on this may be found on the World Wide Web at <http://comp.chem.umn.edu/info/mpw1k.pdf>.

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

(27) The G3 and G3MP2 approaches approximate very large QCISD-(T)/G3Large calculations by summing the energies from a series of smaller calculations and correction factors.

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

(29) Curtiss, L. A.; Redfern, P. C.; Raghavachari, K.; Rassolov, V.; Pople, J. A. *J. Chem. Phys.* **1999**, *110*, 4703–4709.

(30) Lynch, B. J.; Truhlar, D. G. *J. Phys. Chem. A* **2001**, *105*, 2936–2941.

TABLE 1. Experimental^a and Predicted^b Bond Dissociation Energies (kcal/mol) for the Internal C–C Bond in Progressively Methyl-Substituted Alkanes [6-311++G(d,p) Basis Set for the MP2 and B3LYP Models]

reaction	expt ^a	G3	G3MP2	MP2	B3LYP
CH ₃ –CH ₃ → CH ₃ + CH ₃	90.2 ± 0.2	85.8(4.4)	85.9(4.3)	86.6(3.6)	81.5(8.7)
CH ₃ CH ₂ –CH ₃ → CH ₃ CH ₂ + CH ₃	88.5 ± 0.5	85.7(2.8)	85.9(2.6)	87.3(1.2)	79.1(9.4)
(CH ₃) ₂ HC–CH ₃ → (CH ₃) ₂ HC + CH ₃	88.2 ± 0.9	85.6(2.6)	85.7(2.5)	87.8(0.4)	76.5(11.7)
CH ₃ CH ₂ –CH ₂ CH ₃ → CH ₃ CH ₂ + CH ₂ CH ₃	86.8 ± 0.6		86.0(0.8)	88.1(–1.3)	76.7(10.1)
(CH ₃) ₃ C–CH ₃ → (CH ₃) ₃ C + CH ₃	86.9 ± 0.7	85.4(1.5)	85.6(1.3)	88.2(–1.3)	73.7(13.2)
(CH ₃) ₂ HC–CH ₂ CH ₃ → (CH ₃) ₂ HC + CH ₂ CH ₃	86.1 ± 0.9		85.4(0.7)	88.1(–2.0)	73.0(13.1)
(CH ₃) ₃ C–CH ₂ CH ₃ → (CH ₃) ₃ C + CH ₂ CH ₃	84.5 ± 0.9		84.7(–0.2)	87.9(–3.4)	69.2(15.3)
(CH ₃) ₂ HC–CH(CH ₃) ₂ → (CH ₃) ₂ HC + CH(CH ₃) ₂	84.5 ± 1.1		84.1(0.4)	87.3(–2.8)	68.2(16.3)
(CH ₃) ₃ C–CH(CH ₃) ₂ → (CH ₃) ₃ C + CH(CH ₃) ₂	81.5 ± 1.1		82.6(–1.1)	86.3(–5.2)	63.2(18.3)
(CH ₃) ₃ C–C(CH ₃) ₃ → (CH ₃) ₃ C + C(CH ₃) ₃	77.1 ± 1.0		79.8(–2.7)	84.1(–7.0)	56.0(21.1)
rms deviation from expt			2.2	3.5	15.0

^a Luo, Y.-R. *Handbook of Bond Dissociation Energies in Organic Compounds*; CRC Press: New York, 2003; Chapter 4. ^b Values in parentheses are deviations from experiment, calculated as BDE_{expt} – BDE_{calc}.

TABLE 2. Predicted Energies (kcal/mol) for the Progressive Insertion of Triplet CH₂ Molecules into the C–H Bonds of Ethane To Form Progressively Methyl-Substituted Alkanes [6-311++G(d,p) Basis Set]

reaction	G3MP2	MP2	B3LYP	mPW1 PW91	PBEPBE
CH ₃ CH ₃ + CH ₂ → CH ₃ CH ₂ CH ₃	–95.5	–94.2	–92.3	–93.1	–96.4
CH ₃ CH ₃ + 2CH ₂ → (CH ₃) ₂ CHCH ₃	–193.2	–190.7	–185.5	–187.2	–194.0
CH ₃ CH ₃ + 2CH ₂ → CH ₃ CH ₂ CH ₂ CH ₃	–191.3	–188.5	–184.7	–186.2	–192.9
CH ₃ CH ₃ + 3CH ₂ → (CH ₃) ₃ CCH ₃	–292.2	–288.8	–278.6	–281.5	–291.7
CH ₃ CH ₃ + 3CH ₂ → (CH ₃) ₂ CHCH ₂ CH ₃	–288.5	–284.5	–276.8	–279.4	–289.6
CH ₃ CH ₃ + 4CH ₂ → (CH ₃) ₃ CCH ₂ CH ₃	–386.9	–381.9	–368.9	–372.8	–386.4
CH ₃ CH ₃ + 4CH ₂ → (CH ₃) ₂ CHCH(CH ₃) ₂	–385.0	–379.6	–367.8	–371.6	–385.3
CH ₃ CH ₃ + 5CH ₂ → (CH ₃) ₃ CCH(CH ₃) ₂	–482.6	–476.4	–458.7	–463.9	–481.0
CH ₃ CH ₃ + 6CH ₂ → (CH ₃) ₃ CC(CH ₃) ₃	–578.9	–571.9	–547.4	–554.2	–574.8
average energy per CH ₂	–96.4 ± 0.6	–95.1 ± 0.7	–92.2 ± 0.5	–93.1 ± 0.4	–96.5 ± 0.4
rms deviation of total energy from G3MP2		4.8	18.1	14.1	1.8

well, we suspect the result reflects some neglect of correlation in the MP2 model, which manifests itself in the MP2 components of the G3x approaches.

Overall, the MP2 BDE values agree well with experiment, with a root-mean-square deviation only 1.3 kcal/mol above that of the G3MP2 model. However, the MP2 values deviate from the experimental trend, as mentioned above, for an overall decrease from ethane to 2,2,3,3-tetramethylbutane of only 2.5 kcal/mol, less than half that of the G3MP2 model and 20% of the experimental change. However, the biggest discrepancies between the MP2 values and experiment occur for the extremes of substitution, so generally this model chemistry predicts the BDEs well.

By contrast, the B3LYP model performs very poorly. While the predicted BDEs decrease fairly smoothly, as per the experimental values, they drop by an average of 4 kcal/mol with each additional methyl group, for a total drop from ethane to 2,2,3,3-tetramethylbutane of 25.5 kcal/mol (approximately twice the experimental drop). Moreover, the B3LYP approach suggests a BDE for ethane almost 9 kcal/mol lower than the experimental value. Combining this with the exaggerated drop per methyl group results in an expected BDE for 2,2,3,3-tetramethylbutane of only 56 kcal/mol, some 21 kcal/mol below the experimental value. Overall, the root-mean-square deviation for the B3LYP model is 15 kcal/mol, 4–7 times greater than that for the other approaches. Clearly this model provides untrustworthy results here.

Progressive Insertion of Triplet CH₂ Molecules into the C–H Bonds of Ethane To Form Progressively Methyl-Substituted Alkanes (Reaction 2). Given the behavior of the various models with progres-

sive methyl substitution, we felt it worthy to examine reactions that progressively increase the number of methyl groups. Data for insertion of triplet methylene into the C–H bonds of ethane to form larger alkanes appear in Table 2.

As above, we use the G3MP2 level as a standard. At this level, the first insertion evolves an energy of 95.5 kcal/mol, and each subsequent insertion evolves a similar amount (the average energy per CH₂ unit is 96.4 ± 0.6 kcal/mol). This correlates with chemical intuition since each insertion should be approximately independent as computed this way; steric effects are not incorporated into the calculation since the starting materials are identical throughout and only the stoichiometry changes.

The MP2 model predicts per-unit energies slightly smaller than those from the composite model (95.1 ± 0.7 kcal/mol). Again this suggests that the model chemistry does not account for all the correlation energy. We note that, since the per-unit deviation is cumulative, the 1.3 kcal/mol difference translates to a 7 kcal/mol difference in the predicted energy for the reaction between ethane and six methylene units to form 2,2,3,3-tetramethylbutane, and a sizable root-mean-square deviation from the G3MP2 values of 4.8 kcal/mol.

The three DFT models examined showed strikingly different behavior with respect to each other. The PBEPBE “pure” DFT approach predicts per-methylene-unit energies essentially identical with the G3MP2 results, but this is somewhat misleading because these energies appear to track the degree of substitution. This contrasts with the composite model. As a result, the predicted energy for the reaction between ethane and six methylene units to form 2,2,3,3-tetramethylbutane differs from the

TABLE 3. Predicted Energies (kcal/mol) for the [2+2] Cyclization of Tetramethylethene and Various Alkenes To Form Methyl-Substituted Cyclobutanes [6-311++G(d,p) Basis Set]

reaction	G3MP2	G3MP2B3	MP2	B3LYP	B3PW91
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{CH}_2\text{CH}_2 \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{CH}_2\text{CH}_2$	-19.3	-19.4	-27.2	-7.2	-15.0
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{CH}_2\text{CH}(\text{CH}_3) \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{CH}_2\text{CH}(\text{CH}_3)$	-17.4	-17.4	-26.9	-4.4	-12.2
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{C}(\text{CH}_3)_2\text{CH}_2 \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2\text{CH}_2$	-15.7	-15.7	-23.4	2.2	-5.4
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{cis-CH}(\text{CH}_3)\text{CH}(\text{CH}_3) \rightarrow \text{cis-}c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)$	-18.0	-18.3	-25.8	-0.1	-7.8
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{trans-CH}(\text{CH}_3)\text{CH}(\text{CH}_3) \rightarrow \text{trans-}c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)$	-16.7	-16.7	-27.7	-2.0	-9.8
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{C}(\text{CH}_3)_2\text{CH}(\text{CH}_3) \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2\text{CH}(\text{CH}_3)$	-15.5	-15.7	-25.0	4.1	-3.6
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + (\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2$	-15.8	-16.1	-23.3	9.4	1.6
rms deviation from G3MP2			9.5	19.1	11.2

reaction	mPW1K	mPW1 PW91	PBEPBE	mPW PW91
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{CH}_2\text{CH}_2 \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{CH}_2\text{CH}_2$	-23.6	-19.0	-15.8	-12.6
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{CH}_2\text{CH}(\text{CH}_3) \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{CH}_2\text{CH}(\text{CH}_3)$	-21.2	-16.4	-13.1	-9.7
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{C}(\text{CH}_3)_2\text{CH}_2 \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2\text{CH}_2$	-14.9	-9.9	-6.9	-3.2
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{cis-CH}(\text{CH}_3)\text{CH}(\text{CH}_3) \rightarrow \text{cis-}c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)$	-17.4	-12.3	-8.9	-5.3
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{trans-CH}(\text{CH}_3)\text{CH}(\text{CH}_3) \rightarrow \text{trans-}c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)$	-19.4	-14.3	-10.9	-7.3
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{C}(\text{CH}_3)_2\text{CH}(\text{CH}_3) \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2\text{CH}(\text{CH}_3)$	-13.7	-8.4	-5.1	-1.1
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + (\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2$	-9.4	-3.7	-0.2	4.1
rms deviation from G3MP2	3.8	6.7	9.8	13.6

G3MP2 value by 4 kcal/mol. Again, this represents an extreme case; the root-mean-square deviation of the total energies between the PBEPBE and G3MP2 models is only 1.8 kcal/mol.

The hybrid density functional mPW1PW91 and B3LYP models perform poorly for these reactions, with the latter marginally worse. Both show average energies per CH_2 unit 3–4 kcal/mol below that for the G3MP2 model, translating to differences for the reaction forming hexamethylethane of 24 kcal/mol for the former and 31 kcal/mol for the latter. The root-mean-square deviations of these hybrid DFT models from the G3MP2 results are unacceptably large, some 3–5 times that of the MP2 model.

[2+2] Cyclizations of Tetramethylethene and Methyl-Substituted Ethenes To Form Substituted Cyclobutanes (Reaction 3). Owing to our interest in [2+2] cyclizations,³¹ we performed extensive calculations on [2+2] cyclizations of alkenes. Results appear in Table 3.

The G3MP2 results are consistent with chemical intuition. All the reaction energies are similar, although the reactions forming the most crowded cyclobutanes exhibit slightly lower exothermicities. All the reactions are exothermic, indicating enhanced stability for the singly bonded ring systems over the doubly bonded monomers. We note that data employing the G3MP2B3 model also appear. This approach is a composite model employing identical calculations to the G3MP2 model, save that the structure used for the single point energy calculations is optimized at the B3LYP/6-31G(d) level rather than at the MP2(full)/6-31G(d) level used in G3MP2, and the zero point energy (ZPE) correction is derived from this as well. The goal was to determine whether B3LYP-derived structures would differ sufficiently from MP2-derived structures to affect the com-

posite energies, thus providing some explanation for the poor performance of the B3LYP model in all these calculations. Comparing the results from the two approaches shows that the differently optimized structures and the differing ZPE corrections nonetheless provide identical predictions of reaction energetics. Thus the poor predictions of the B3LYP model cannot be ascribed to its predictions of structural parameters.

Inspection of the data for the other models shows one typical trend: the MP2 model tends to overbind the cyclobutanes, while all DFT methods tend to underbind them. Interestingly, the mPW1PW91 model, which performed so poorly in predicting reaction energies above, performs quite well here. The related MPW1k model, which differs from mPW1PW91 only in the amount of exact exchange employed in the functional, gives the best agreement with the G3MP2 results of all. By contrast, the PBEPBE model, which performed exceptionally in predicting the methylene addition energies, fares badly here. Its most glaring flaw is its prediction that the dimerization of tetramethylethene is essentially thermoneutral. The MP2 model, while exhibiting a root-mean-square deviation almost identical with that of PBEPBE, at least predicts the thermodynamically proper result that two single σ bonds in a cyclobutane are stronger than two π bonds in the alkenes.

The B3LYP model again shows by far the worst performance of any. The prediction for the cyclization between tetramethylethene and ethene is underestimated by 12 kcal/mol; the rapid decrease with further methyl substitution means that the dimerization of tetramethylethene is underestimated by 25 kcal/mol and is predicted to be sizably endothermic (9.4 kcal/mol). Indeed, 5 of the 7 reactions are predicted by this model to be essentially thermoneutral or endothermic, completely inconsistent with known chemical behavior.

To probe whether the poor B3LYP predictions (and generally erratic DFT results) stem from basis set incompleteness, we examined the first and last reactions in Table 3 using larger basis sets. The results appear in Table 4. Markedly little difference arises between these calculations and those from the smaller 6-311++G(d,p)

(31) (a) Check, C. E.; Gilbert, T. M. Presented at the 229th National Meeting of the American Chemical Society, San Diego, CA, March 2005; paper INOR 582. (b) Gilbert, T. M.; Bailey, J. M. Presented at the 229th National Meeting of the American Chemical Society, San Diego, CA, March 2005; paper COMP 242. (c) Bissett, K. M.; Gilbert, T. M. *Organometallics* **2004**, *23*, 5048–5053. (d) Bissett, K. M.; Gilbert, T. M. *Organometallics* **2004**, *23*, 850–854. (e) Gilbert, T. M. *Organometallics* **2003**, *22*, 3748–3752.

TABLE 4. Predicted Energies (kcal/mol) for the [2+2] Cyclization of Tetramethylethene and Various Alkenes To Form Methyl-Substituted Cyclobutanes with Use of Varied DFT Models and Basis Sets

	B3LYP	mPW1 PW91	PBEPBE
6-311++G(3df,3pd) basis set			
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{CH}_2\text{CH}_2 \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{CH}_2\text{CH}_2$	-5.8	-17.7	-14.6
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + (\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2$	11.6	-1.5	1.8
Aug-cc-pVTZ basis set			
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{CH}_2\text{CH}_2 \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{CH}_2\text{CH}_2$	-5.2	-16.7	-14.0
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + (\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2$	12.4	-0.1	2.7
pc-3 basis set			
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + \text{CH}_2\text{CH}_2 \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{CH}_2\text{CH}_2$	-5.2	-16.6	-13.9
$(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 + (\text{CH}_3)_2\text{CC}(\text{CH}_3)_2 \rightarrow c\text{-}(\text{CH}_3)_2\text{CC}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2\text{C}(\text{CH}_3)_2$	12.6	0.2	3.0

basis set; they confirm that the inadequacies of the B3LYP model do not arise from basis set incompleteness.

Discussion

The data provided in this work show that the B3LYP model consistently underestimates the energy of each hydrocarbon reaction type investigated. The combined results from the reactions, particularly reactions 1 and 3, allow us to distinguish between the model's ability to accurately predict C–H vs C–C bond energies. Clearly, the B3LYP approach specifically underestimates the C–C bond energy sizably and systematically. The degree of underestimation varies with the size of the molecule and the reaction of interest, but values of 4–10 kcal/mol per C–C bond can be derived. These lie well in excess of the 2 kcal/mol per CH_2 group (enthalpy) values suggested by Curtiss et al.,¹⁵ but are consistent with the (bond energy) values from Liu and Guo.¹³ The Liu and Guo data further support the error being associated with C–C bond energies, in that they find errors in C–H bond energies of only 2–3 kcal/mol.³²

As a result, as the number of C–C bonds in a molecule of interest increases, the less likely it is that the B3LYP prediction of a reaction energy involving the molecule will be correct. So we discourage the use of the B3LYP model unless a compelling reason exists to believe it will provide accurate results for a particular system.

We wish to make it clear that this work is not a call to discard the B3LYP approach entirely. The model has proven itself in predicting, for example, vibrational,²⁰ absorption,³³ EPR,³⁴ and NMR³⁵ spectra. However, its limitations should be recognized, particularly by those new to the field of computational chemistry. The limitation delineated here is the decay of the accuracy of the model as it is applied to larger molecules containing many C–C bonds.

One must ask why the B3LYP approach underestimates reaction energies so significantly. As mentioned above, one likely problem is the inability of any “first generation”³⁶ DFT model to correctly describe dispersion

forces. The results above support this in that the DFT models vary significantly in their ability to predict energies, and that no one method appears best in every case. It is noteworthy that the PBEPBE approach performs superbly in dealing with reaction 2, while only fairly in dealing with reaction 3, while the mPW1PW91 model shows the reverse behavior. The literature is filled with similar results. Another known problem with first generation models is their lack of a term describing the kinetic energy density.³⁷ Specific to B3LYP are indications that the relative amounts of Becke exchange¹⁰ and Hartree–Fock exchange^{5,38} in the hybrid functional may have been unwisely chosen, at least in terms of predicting the energetics of large molecules. The values determined for exchange contributions were determined (as is true for most hybrid functionals) by minimization of differences between predicted and experimental data from the G2 database. The database contains small molecules with few bonds, and thus may provide spurious indications of the utility of a contribution (or indeed a functional) when applied to large molecules. This apparently holds for the B3LYP approach. Whatever the crucial factors are, the message for organic chemists is that B3LYP energy calculations, by themselves, cannot be trusted to be accurate.

Given this, what solutions or alternatives exist? As mentioned above, Curtiss et al. showed that atomization energies of large molecules could be more accurately predicted by using homodesmotic B3LYP calculations.¹⁶ This approach is sound, but requires careful selection of the homodesmotic reaction components. Bachrach has commented on the utility of the group equivalent approach in this regard.³⁹

For those systems amenable to them, the use of high-level perturbational models such as MP2, CCSD, or any of the Gx approaches, even if only for comparison, seems warranted. Though computationally intensive, they provide trustworthy checks on the accuracy of DFT computations. Even the minimalist G3MP2 composite model provides values sufficiently close to experiment to allow them to act as standards when experimental data are unavailable.

Second and third generation DFT models represent another option, although few of these have been tested broadly and on large molecules. However, several important examples are available in the Gaussian03 pro-

(32) We note in passing a worrying point from the Liu/Guo data: the mean errors of the C–H and C–C bond energies *increase* as the basis set size increases. One expects the errors to decrease as the basis set size increases.

(33) Rosa, A.; Ricciardi, G.; Gritsenko, O.; Baerends, E. J. *Struct. Bonding (Berlin, Ger.)* **2004**, *112*, 49–116.

(34) Munzarová, M.; Kaupp, M. *J. Phys. Chem. A* **1999**, *103*, 9966–9983.

(35) Magyarfalvi, G.; Pulay, P. *J. Chem. Phys.* **2003**, *119*, 1350–1357.

(36) Zhao, Y.; Pu, J.; Lynch, B.; Truhlar, D. G. *Phys. Chem. Chem. Phys.* **2004**, *6*, 673–676.

(37) Boese, A. D.; Handy, N. C. *J. Chem. Phys.* **2002**, *116*, 9559–9569.

(38) Salomon, O.; Reiher, M.; Hess, B. A. *J. Chem. Phys.* **2002**, *117*, 4729–4737.

(39) Bachrach, S. M. *J. Chem. Educ.* **1990**, *67*, 907–908.

gram, including the HCTH approaches of Handy et al.,⁴⁰ the TPSS model from Perdew et al.,⁴¹ and standard functionals that Truhlar and co-workers have mixed and modified^{2a} into a host of new DFT approaches. While none of these can yet be considered “best” for predicting physical parameters and reaction energies, they all represent substantial improvements over B3LYP. Users will need to learn about the strengths and weaknesses of each approach (and for the Truhlar methods, how to modify the program to run them), but the benefits of increased reliability of the results outweigh the necessary effort over time.

Our current “solution”, which we recommend for those using DFT models of *any* generation, is to employ several models for each reaction studied, comparing them with perturbational approaches if possible. The combined results from multiple calculations of the same system represent a computational “error bar”. While this cannot be viewed as an error bar in the conventional sense, because generally DFT predictions are not randomly distributed around a central value,⁴² the varied results at least give a sense of the range of the possible error.

(40) Boese, A. D.; Handy, N. C. *J. Chem. Phys.* **2001**, *114*, 5497–5503.

(41) Tao, J.; Perdew, J. P.; Staroverov, V. N.; Scuseria, G. E. *Phys. Rev. Lett.* **2003**, *91*, 146401.

By way of example, it is computationally honest to indicate to a reader that the predictions of the energy for the first reaction in Table 3 range from -7.2 to -27.2 kcal/mol, with the most likely value being the G3MP2 value of -19.4 kcal/mol. The range appears uncomfortably wide considering that chemists view chemical accuracy as ± 1 kcal/mol, but just as experimentalists must be forthcoming about the errors in their numbers, computationalists must do likewise. Just as an experimentalist examining reaction kinetics would never trust a one-point rate or a line drawn between only two points, a computational chemist cannot trust a one-type DFT calculation.

Supporting Information Available: Optimized structures (Cartesian coordinates) at either the MP2/6-311++G-(d,p) or MP2(full)/6-31G(d) levels and absolute energies (hartrees, corrected for ZPE) of all compounds examined at all levels employed. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO051545K

(42) It is well-known that nearly all DFT models systematically underbind transition states and van der Waals molecules, while they systematically overbind two center, three-electron systems such as X_2^+ (X = halogen).