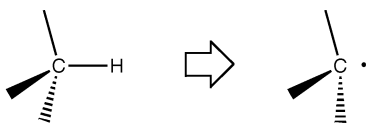# JOC *Notes*

Evidence that Alkyl Substitution Provides Little Stabilization to Radicals: The C−C Bond Test and the Nonbonded Interaction Contradiction

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ΔBDE = Radical Stabilization Energy **?**

Although the C−H bond dissociation energies of alkanes have been widely employed as measures of radical stability, it is shown here that the assumptions needed for that conclusion are incompatible with experimental and computational data related to C−C bond dissociation energies. Calculations at the QCISD(T)/6-311+G(d,p) level on model systems show that 1,3 nonbonded interactions in alkanes are repulsive, whereas the conventional radical stabilization analysis of bond dissociation energies requires that they become more attractive with increasing steric bulk. This result puts a severe limit on the role that radical stabilization can play and indicates that another factor must be responsible for the observed variation in the C−H bond dissociation energies of alkanes.

Introduction

The conventional interpretation of the variation in C−H bond strengths in alkanes focuses on the stability of the resulting radicals. In this argument, the weakening seen in going from 1° to 2° to 3° C−H bonds is caused by greater hyperconjugative stabilization of the more highly substituted radicals. This conclusion has been widely accepted, but it relies on a highly restrictive set of assumptions, which may not have been fully appreciated. Recently we challenged the radical stabilization model and suggested that the variation of C−H bond strengths in alkanes is driven by the release of greater steric strain in the more highly substituted alkanes.[1] We have used the term "geminal repulsion" to identify this type of strain. We were not the first to make such an argument. In 1932, Eyring suggested that steric strain may control C−H bond strengths.[2]

(1) Gronert, S. *J. Org. Chem.* **2006**, *71*, 1209.
(2) Eyring, H. *J. Am. Chem. Soc.* **1932**, *54*, 3191.

SCHEME 1. Nonbonded, 1,3-Interactions (NB) that Are Lost in Alkanes during C−H Bond Cleavage
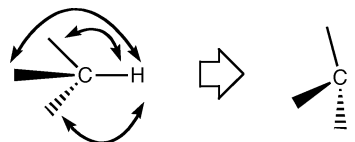
In a series of papers starting in the 1970s, Rüchardt has presented compelling evidence that nonbonded interactions are a key to describing C−C and C−H bond strengths and radical reactivity.[3,4] Here we use patterns in C−C bond strengths to show that the critical assumptions of the conventional interpretation of C−H bond dissociation energies are not supported by experimental or computational data.

Arguments in favor of the radical stability model have focused on the ability of adjacent carbon groups to provide stabilization to a radical through hyperconjugation. Rarely have proponents of this interpretation focused on the other side of the equation, namely, the effect of substitution on the stability of the alkane. Because bond dissociation energies (BDEs) are energy differences, observed substituent effects can result from their impact on the reactant, the product, or both. If one believes that radical stability controls the C−H bond strengths, the implied assumption is that alkyl substitution has no impact on the C−H bonding interaction in the alkane (i.e., all C−H bonds provide the same total bonding energy to an alkane). This is illustrated in eq 1 where the BDE is broken into 3 components: the intrinsic bond energy (BE),[5] the radical stabilization energy (RS), and terms for the three nonbonded, 1,3-interactions in the alkane (NB) that are lost when the bond breaks (Scheme 1). In this context,

$$BDE[C–H] = BE[C–H] − RS[C(CH_3)_m H_{3−m} − mNB[H–C–CH_3] − (3 − m)NB[H–C–H] \quad (1)$$

CH_3 could be generalized to be any carbon-centered group. The sign conventions used in eq 1 are such that a positive RS stabilizes the radical (weakens bond) and a positive NB destabilizes the alkane (weakens bond).

In the conventional interpretation, the assumption is that BE is constant for all alkanes, NB[H−C−CH₃] = NB[H−C−H] so that the nonbonded interaction terms are a constant for all C−H bonds, and RS varies with the substitution pattern on the radical center, having its largest value for $m = 3$ (i.e., a tertiary radical). These assumptions are outlined in Scheme 2.

The assumption that the intrinsic BE is roughly constant is reasonable and Schleyer has shown that computed bond critical

(3) Rüchardt, C. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 830.
(4) Rüchardt, C.; Beckhaus, H.-D. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 429.
(5) The conventional argument requires the assumption of an intrinsic, constant C−H bond energy for all alkanes. From this assumption, it follows that measured bond strengths differ from this value (BE) because the resulting radicals are stabilized by substituent groups. The intrinsic C−H bond energy in alkanes is effectively defined as the bond strength in methane. The corresponding definition for an intrinsic C−C bond energy would be that in ethane.

SCHEME 2.   Assumptions Required to Link C−H BDEs to Radical Stabilization Energies

1.   BE is constant.

2.   NB[H-C-CH$_3$] = NB[H-C-H].

3.   RS varies with substitution pattern.

∴   ΔBDE[C-H] = ΔRS

point electron densities support this conclusion.[6] The assumption that NB[H−C−CH$_3$] = NB[H−C−H], however, has little theoretical support. Nonetheless, eq 1 has been widely used in this way to obtain the following, familiar radical stabilization energies (relative to methyl): 1° = 3.9 kcal/mol; 2° = 6.4 kcal/mol; and 3° = 8.5 kcal/mol.[7,8] An analogous equation can be applied to C−CH$_3$ bonds (eq 2). If one assumes that BE is

$$BDE[C-CH_3] = BE[C-C] - RS[C(CH_3)_mH_{3-m}] - mNB[CH_3-C-CH_3] - (3-m)NB[CH_3-C-H] \quad (2)$$

constant for C−H bonds, then one must also assume the same is true for C−C bonds (here, there is essentially no electronegativity difference in the bond). Moreover, Schleyer's bond critical point analysis also indicates that BE[C−C] is roughly a constant.[6,9] The same radicals are formed in the process, so one must use the RS values obtained in eq 1. The C−CH$_3$ BDEs follow a different pattern than C−H BDEs, and in fact, are much less sensitive to changes in the substitution pattern. The R−CH$_3$ BDEs are 89.8, 88.8, 88.3, and 87.2 kcal/mol for R = CH$_3$, CH$_3$CH$_2$, (CH$_3$)$_2$C, and (CH$_3$)$_3$C, respectively.[7] This issue was raised many years ago by Rüchardt[3] and Nicholas[10] and has been discussed in detail recently by Zavitsas[11,12] and Radom.[13]

Given the necessary assumption that BE is constant, the only way to explain the difference in the patterns for C−H and C−CH$_3$ bonds is to allow for variations in the nonbonded terms in eq 2.[14] If one fits eq 2 using experimental C−CH$_3$ BDEs and the RS values from eq 1, one is left with the requirement that NB[CH$_3$−C−CH$_3$] ≈ NB[CH$_3$−C−H] − 2 kcal/mol. A positive NB indicates destabilization of the alkane, so this result requires that the CH$_3$−C−CH$_3$ nonbonded interaction must be 2 kcal/mol *more* favorable than a CH$_3$−C−H interaction. To probe the validity of this requirement, the first important question is whether the nonbonded interaction terms are stabilizing or destabilizing. It is true that Pitzer and Catalano[15] suggested in the 1950s that 1,3-interactions between nonbonded groups are attractive, but this conclusion was based on the

SCHEME 3.   Tetrahedral Arrangement of Pyramidal BH$_3$ Groups Representing the Methyl Groups in Neopentane[a]
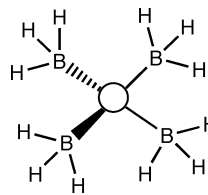
[a] The circle at center is the location of the central carbon that was deleted.

questionable assumption that for intramolecular interactions, one could ignore the repulsive component of a Lennard-Jones potential.[16] Recently, Schleyer[17] also has suggested that these interactions are attractive. In contrast, there is a significant amount of evidence, including alkane geometries and vibrational spectra, that indicates that these nonbonded interactions are, at the very least, on the repulsive face of the interaction potential.[1,18−29]

Although it is difficult to definitively extract 1,3-interaction energies from molecular energies, it is possible to investigate them with simple model systems. For example, the methyl/methyl interactions in neopentane can be probed by deleting the central carbon and replacing the remaining carbons with boron (i.e., four BH$_3$ groups placed at the corners of a tetrahedron and locked into the same geometry and orientation as the methyl groups in neopentane, Scheme 3).

At first glance, this might seem like a drastic manipulation of the system, but the calculated atomic charges (NPA) of BH$_3$ and CH$_3$ constrained to this geometry have nearly the same magnitude (−0.118 vs +0.135 on the hydrogens). In addition, the dipole moments of BH$_3$ and CH$_3$ in this geometry are not so different (1.00 vs 0.69 D), though in the opposite direction. As a result, BH$_3$ constrained in this geometry provides a rough model for CH$_3$ in terms of size, polarizability, and polar

(6) Exner, K.; Schleyer, P. v. R. *J. Phys. Chem. A* **2000**, *105*, 3407.

(7) Blanksby, S. J.; Ellison, G. B. *Acc. Chem. Res.* **2003**, *36*, 255.

(8) Afeefy, H. Y.; Liebman, J. F.; Stein, S. E. Neutral Thermochemical Data. In *NIST Chemistry WebBook*; Mallard, W. G., Linstrom, P. J., Eds.; NIST Standard Reference Database Number 69 (http://webbook.nist.gov), National Institute of Standards and Technology: Gaithersburg, MD, 2005.

(9) Specifically, Schleyer found that there was only a 0.7 kcal/mol difference between his estimates of BE(C−C) for ethane and cyclohexane.

(10) Nicholas, A. M. d. P.; Arnold, D. R. *Can. J. Chem.* **1984**, *62*, 1850.

(11) Matsunaga, N.; Rogers, D. W.; Zavitsas, A. A. *J. Org. Chem.* **2003**, *68*, 3158.

(12) Zavitsas, A. A. *J. Chem. Educ.* **2001**, *78*, 417.

(13) Coote, M. L.; Pross, A.; Radom, L. *Org. Lett.* **2003**, *5*, 4689.

(14) It is true that the difference in the C−CH$_3$ vs C−H BDEs can simply be attributed to differences in the heats of formation of the parent alkanes; however, any attempt to link BDEs to radical stabilization energies requires separately assessing the effect of alkyl substitution on the stability of the alkane and radical (i.e., analyzing the BE and NB terms in eqs 1 and 2).

(15) Pitzer, K. S.; Catalano, E. *J. Am. Chem. Soc.* **1956**, *78*, 4844.
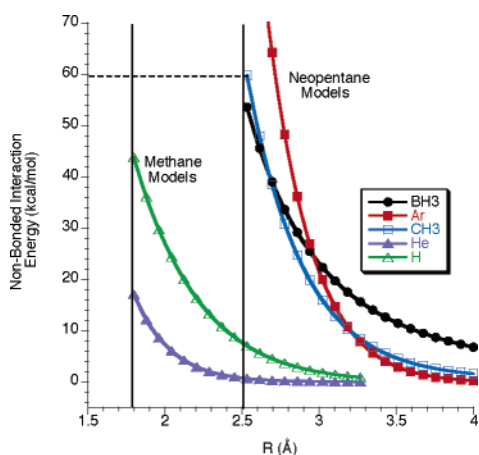
(16) Because all intramolecular interactions are treated as stabilizing, this assumption leads to the prediction that *gauche*-butane is more stable than *anti*-butane. Pitzer and Catalano realized this contradiction and suggested that a steric term be used to correct the overestimation of stabilization in *gauche*-butane. However, it does not seem logical that hydrogens with a 1,5 relationship (i.e., those on the methyl groups of propane) would have a stabilizing effect, whereas those with a 1,6 relationship (i.e., those on the methyl groups of *gauche*-butane) would have a sharply destabilizing effect, despite the fact that the distances are fairly similar. Further evidence of problems with this assumption can be seen in its predictions about the methane/methane van der Waals complex. At the C−C distance (3.35 Å) where MP2/6-311+G(2df, 2pd) calculations predict the onset of repulsion (i.e., interaction energy = 0), Pitzer's and Catalano's interaction potential predicts over 1.5 kcal/mol of attraction (>3 times the known complexation energy) because no repulsive terms are included to balance the attraction. See Rowley, R. L.; Pakkanen, T. *J. Chem. Phys.* **1999**, *110*, 3368.

(17) Wodrich, M. D.; Schleyer, P. v. R. *Org. Lett.* **2006**, *8*, 2135.

(18) Bartell, L. S. *J. Am. Chem. Soc.* **1959**, *81*, 3497.

(19) Bartell, L. S. *J. Chem. Phys.* **1960**, *32*, 827.

(20) Bartell, L. S.; Kuchitsu, K. *J. Chem. Phys.* **1962**, *37*, 691.

(21) Fitzwater, S.; Bartell, L. S. *J. Am. Chem. Soc.* **1976**, *98*, 5107.

(22) Bauld, N. L.; Cessac, J.; Holloway, R. L. *J. Am. Chem. Soc.* **1977**, *99*, 8140.

(23) Wiberg, K. B. *Angew. Chem.* **1986**, *98*, 312.

(24) Gronert, S.; Azizian, K.; Friedman, M. *J. Am. Chem. Soc.* **1998**, *120*, 3220.

(25) Gronert, S.; Lee, J. M. *J. Org. Chem.* **1995**, *60*, 6731.

(26) Gillespie, R. J.; Robinson, E. A. *C. R. Chim.* **2005**, *8*, 1631.

(27) Gillespie, R. J.; Robinson, E. A. *Chem. Soc. Rev.* **2005**, *34*, 396.

(28) McKean, D. C. *Chem Soc. Rev.* **1978**, *7*, 399.

(29) Brocks, J.; Beckhaus, H.-D.; Beckwith, A. L. J.; Rüchardt, C. *J. Org. Chem.* **1998**, *63*, 1935.

FIGURE 1. Interaction energies for a tetrahedral arrangement of four BH₃ groups (circles), four argon atoms (squares), four methyl radicals in a quintet state (open squares), four helium atoms (triangles), and four hydrogen atoms in a quintet state (open triangles) at the QCISD-(T)/6-311+G(d,p) level.[32] Vertical lines represent the approximate methyl/methyl distance in neopentane (2.5 Å) and the hydrogen/hydrogen distance in methane (1.78 Å). The horizontal dashed line is the energy of four methyl radicals in a quintet state at the separation found in neopentane. Energies are relative to four, infinitely separated groups.

SCHEME 4. Nonbonded Interaction Energy Relationships Required to Satisfy Equations 1 and 2 as Well as the Assumptions of a Radical Stabilization Model

$$NB[CH_3\text{-}C\text{-}CH_3] < NB[H\text{-}C\text{-}CH_3] = NB[H\text{-}C\text{-}H].$$

interactions. Interaction energies for the tetrahedral arrangement of four BH₃ groups, relative to isolated BH₃ groups in the same geometry, are shown in Figure 1. The surface is wholly repulsive and reaches a value of about +50 kcal/mol when the interatomic distance matches that found in neopentane.[30] *The magnitude of this repulsive interaction is sufficient to overwhelm any concerns related to the appropriateness of the model.* Other models can be considered. The van der Waals radius of an argon atom (1.9 Å) is near that of a methyl group (2.0 Å), but slightly larger than that of carbon (1.7 Å), so one could imagine a model based on four argon atoms in a tetrahedral arrangement.[31] This is illustrated in Figure 1. Not surprisingly, the less polarizable argon atoms lead to a larger repulsive interaction at short distances. Finally, one could employ a tetrahedral arrangement of four methyl radicals constrained to the geometry they adopt in neopentane. Here, a quintet state must be employed to limit direct bonding between the radical centers. This model is not ideal, but also gives a fully repulsive interaction potential (Figure 1). Clearly, the nonbonded 1,3-interactions create significant steric strain and are not attractive in nature.

Given that the NB terms are destabilizing, eq 2 and the assumptions related to eq 1 (i.e., Scheme 2) require that NB-[H−C−CH₃] and NB[H−C−H] be equal and both be 2 kcal/mol *more destabilizing* than the NB[CH₃−C−CH₃] interaction (Scheme 4). This requirement is counter-intuitive and implies that methane suffers from greater steric crowding at the central

carbon than neopentane! The implausibility of this outcome can be illustrated with a model where the hydrogens in methane are represented by helium atoms. Helium has approximately the same van der Waals radius (1.4 Å) as hydrogen,[33] but Figure 1 clearly shows that this model causes significantly less repulsion than the models for the methyl/methyl interactions in neopentane. One also could use a tetrahedral arrangement of four hydrogen atoms in a quintet state to model the nonbonded interactions in methane. The need to restrict this system to a high spin state again makes it a less desirable model (it leads to an exaggeration of the hydrogen van der Waals radius[34]), but nonetheless, the data in Figure 1 also indicate that the hydrogen/hydrogen interaction is less destabilizing than those found in the models for methyl/methyl interactions in neopentane.

The models used for the interactions in methane may not be optimum, but alkane geometries provide very compelling evidence on this issue and clearly indicate that methyl/methyl 1,3-interactions are more repulsive than hydrogen/hydrogen 1,3-interactions. For example, CH₃−C−CH₃ angles are always expanded at the expense of H−C−H angles in alkanes. In propane, the angles at the central carbon are ∠C−C−C = 112.4°, ∠H−C−C = 109.5°, and ∠H−C−H = 106.1°.[35] Geometry is one of the "gold standards" in interpreting intramolecular interactions so these data cannot be taken lightly. All of these results indicate that NB[H−C−H] must be less than, not greater than, NB[CH₃−C−CH₃].[36] The relationship in Scheme 4 is not consistent with the data in Figure 1 or the geometries of alkanes.

Although it has been widely accepted that C−H bond dissociation energies are controlled by the stability of the resulting radicals, the models presented here provide evidence that the basic assumptions in this argument are flawed and as a result fail when extended to C−C bonds. The small variation in the experimental C−C BDEs puts a severe constraint on radical stabilization by alkyl substitution, limiting it to being at most a very minor contributor to the observed reduction in C−H BDEs caused by substitution. For example, if one lets NB[H−C−CH₃] = NB[CH₃−C−CH₃], the C−C BDEs only allow about 2.5 kcal/mol of radical stabilization in the *tert*-butyl radical (less than ¹/₃ the observed reduction in bond strength in isobutane). Because NB[CH₃−C−CH₃] is undoubtedly larger than NB[H−C−CH₃], the true radical stabilization must be much smaller than this limit. On the other hand, we recently showed that a model based on allowing the NB terms to vary in the expected way, while keeping BE and RS as constants, can fit experimental data to eqs 1 and 2 very well.[1] The empirical values derived in those fits for the 1,3-interactions (geminal

(30) An electrostatic analysis of the system based on the NPA charges indicates that electrostatic repulsion is only a minor contributor to the repulsion observed in Figure 1. Neopentane itself would also suffer to some extent from electrostatic repulsion.
(31) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441.

(32) The CH₃ system is at the QCISD(T)/6-31+(d, p) level.
(33) Values from 1.2 Å (see ref 31) to 1.45 Å have been reported: Allinger, N. L.; Hirsch, J. A.; Miller, M. A.; Tyminski, I. J.; Van Catledge, F. A. *J. Am. Chem. Soc.* **1968**, *90*, 5773.
(34) The high spin state appears to exaggerate the repulsive nature of the hydrogen/hydrogen interaction. Using this potential energy surface, a van der Waals radius of over 1.6 Å is indicated for the hydrogen atom. In contrast, the geometries of methane/methane van der Waals complexes suggest a more conventional van der Waals radius for the hydrogen atom. The model of neopentane employing four methyl groups in a quintet state did not suffer to a great extent from this problem, and the potential energy surface predicts a van der Waals radius of about 2 Å for the methyl group.
(35) Hellwege, K. H.; Hellwege, A. M. *Atomic and Molecular Physics, Structure Data of Free Polyatomic Molecules*; Springer-Verlag: Berlin, 1976; Vol. 7.
(36) Rüchardt has made related arguments based on geometries: Rüchardt, C.; Beckhaus, H.-D. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 529.

repulsion) are of the same general magnitude as the values suggested in the present model systems. In addition, we showed that radical geometries and pyramidalization energies do not fit the pattern expected for hyperconjugative stabilization of radicals by alkyl groups. The present data suggest that radical stabilization of any kind is limited in these systems.

In summary, this study shows that the assumptions built into the conclusion that C−H BDEs are a measure of radical stabilities are incompatible with experimental C−C BDEs and the available data on nonbonded interactions. The BDEs in these systems simply offer no evidence that alkyl substitution provides stabilization to radicals because experimental data do not allow the BE and NB terms in eqs 1 and 2 to be treated as constants.[37] Although there is no doubt that hyperconjugation to adjacent alkyl groups can provide some stabilization to a radical center, the key question is whether it is sufficient to explain the variation observed in alkane C−H BDEs. Stabilization energies, by their very nature, cannot be determined definitively because they are based on relative energies from an arbitrary reference reaction and generally require some assumptions with respect to whether the substituent stabilizes the product or destabilizes the reactant in the reference reaction. It is possible, however, to test the required assumptions of a stabilization model and determine whether they are likely or unlikely given the available data. Equating the variation in C−H BDEs with radical stabilization energies requires a set of assumptions (Scheme 2) that lead to a highly unlikely prediction about nonbonded interaction energies (Scheme 4). Therefore, the available data indicate that a factor other than radical stabilization (e.g., geminal repulsion)

must be responsible for the majority of the energetic variation in alkane C−H BDEs. To make a radical stabilization model viable, proponents must show how it can simultaneously satisfy eqs 1 and 2 while producing rational, testable patterns in BE and NB. As it stands, the conventional model fails a clear test of the validity of its assumptions.

Methods

All calculations were completed with Gaussian 03.[38] Neopentane was optimized at the MP2/6-31+G(d) level. Energy calculations were completed at the QCISD(T)/6-311+G(d,p) level for all species except the CH_3 system, which was calculated at the QCISD(T)/6-31+G(d,p) level. The standard counterpoise correction in Gaussian 03 was used in the model systems. In generating the plots in Figure 1, a Z-matrix was employed using the scan option in Gaussian 03 to vary the distance to the dummy, central atom of the tetrahedral arrangement. For the models involving CH_3 and BH_3, the B−H and C−H distances were set to 1.097 Å (the computed C−H distance in neopentane) and the X−C−H and X−B−H angles (X is a dummy atom representing the central carbon of neopentane) were set to 110.9 Å (H−C−C angle computed for neopentane). The electronic properties of constrained CH_3 and BH_3 (dipole and charges) were calculated at the MP2/6-311+G(d,p) level.

Supporting Information Available: The complete citation for ref 38 as well as tables including the geometries and energies from the computational work. This material is available free of charge via the Internet at http://pubs.acs.org.

JO060797Y

(37) One could fit the equations by allowing BE to be a variable (while setting the NB terms to a single, constant value), but the available data would require that BE balance the changes in RS (i.e., alkyl substitution would provide nearly equal stabilization to the radical and parent alkane and, therefore, have only a minor effect on the dissociation energy). In any case, allowing BE to be a variable eliminates any possibility of equating BDEs with radical stabilization energies.

(38) Frisch, M. J.; et al. *Gaussian 03*, revision B04; Gaussian, Inc.: Pittsburgh, PA, 2003.