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Branched Alkanes Have Contrasting Stabilities

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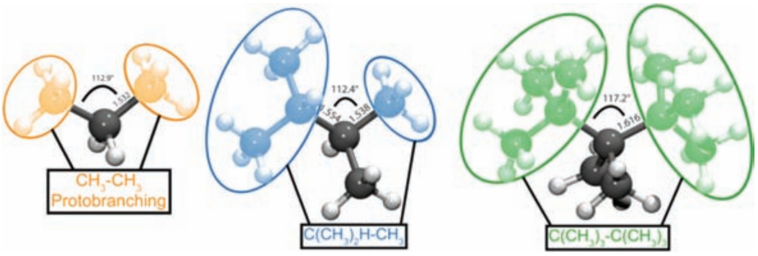
ABSTRACT



Bond separation reactions of highly branched alkanes are used to assess (de)stabilizing interactions associated with various 1,3-nonbonded substituent patterns. While *n*- and singly methylated alkanes show positive bond separation energies (BSEs), which increase systematically along the series, permethylated alkanes are characterized by decreasing BSEs. Analysis shows that singly methylated alkanes are more stabilized than linear alkane chains and that the unique destabilizing feature of permethylated alkanes arises from the close proximity of bulky methyl groups causing highly distorted geometries along the carbon backbone.

Detailed knowledge of fundamental processes and interactions within simple hydrocarbons has profound implications for all aspects of organic chemistry. Within this context, significant advancements have been made in the understanding of hydrocarbon thermochemistry since the pioneering works of Rossini and Nenitzescu in the 1930s.[1] A recently developed concept, protobranching,[2] proposes that linear *n*-alkanes are stabilized through similar (although fewer) 1,3-alkyl−alkyl interactions than those present in their more stable branched counterparts. This concept has shown to be useful in reconciling previously inconsistent values for quantifying energies of organic phenomenon (e.g., the resonance energy of benzene); nonetheless, the relevance and interpretation of protobranching interactions remains heavily debated.[3] The energies associated with protobranching (and other 1,3-nonbonded alkyl−alkyl interactions) provide significant insight into the understanding of alkane stability and behavior. Despite the notion that branched species are more stable than linear alkanes, too much branching can destabilize molecules,[4] manifested in weaker C−C bond energies.[5] Presumably, the close proximity of bulky methyl groups in highly branched alkanes is responsible for much of this destabilization. This paper proceeds along three lines: (i) establishing a reliable and inexpensive computational technique for predicting accurate heats of formation of highly branched alkanes, (ii) probing the

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[1] (a) Rossini, J. *J. Res. Natl. Bur. Stand.* **1934**, *13*, 21. (b) Nenitzescu, C. D.; Chicos, I. *Ber. Dtsch. Chem. Ges.* **1935**, *68B*, 1584.

[2] (a) Wodrich, M. D.; Wannere, C. S.; Mo, Y.; Jarowski, P. D.; Houk, K. N.; Schleyer, P. v. R. *Chem.—Eur. J.* **2007**, *13*, 7731. (b) Wodrich, M. D.; Schleyer, P. v. R. *Org. Lett.* **2006**, *8*, 2135.

[3] (a) Gronert, S. *J. Org. Chem.* **2006**, *71*, 1209. (b) Zavitsas, A. A.; Matsunaga, N.; Rogers, D. W. *J. Phys. Chem. A* **2008**, *112*, 5734. (c) Gronert, S. *Chem.—Eur. J.* **2009**, *15*, 5372. (d) Fishtik, I. *J. Phys. Chem. A* **2010**, *114*, 3731. (e) Schleyer, P. v. R.; McKee, W. C. *J. Phys. Chem. A* **2010**, *114*, 3737. (f) Kemnitz, C. R.; Mackey, J. L.; Loewen, M. J.; Hargrove, J. L.; Lewis, J. L.; Hawkins, W. E.; Nielsen, A. F. *Chem.—Eur. J.* Earlyview, DOI: 10.1002/chem.200902550.

[4] For example, the heat of formation of *n*-tridecane (−74.5 kcal/mol) is lower than its highly branched isomer tri-*tert*-butylmethane (−56.2 kcal/mol). Values taken from NIST thermochemical database; see ref 10.

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(de)stabilizing effects of various branching patterns, and (iii) identifying the pattern causing the destabilization of highly branched alkanes.

Isodesmic bond separation energy (BSE)[6] evaluations are commonly used to determine the total sum of (de)stabilizing interactions within a molecule of interest. In the BSE procedure, all bonds between heavy (non-hydrogen) atoms are split into their simplest (or parent) molecular fragments preserving the heavy atom bond types. Reactions are balanced by inclusion of the necessary number of simple hydrides (methane, ammonia, water, etc.). Positive bond separation energies reflect a stabilizing phenomenon, while negative energies correspond to destabilization. The BSE of propane (eq 1) has been used to quantify the 1,3-methyl−methyl protobranching stabilizing interaction, 2.83 kcal/mol.[2] Here, we employ the BSE as a tool to probe the (de)stabilizating interactions in highly branched alkanes.

 + CH_4 ⟶ 2 C_2H_6 2.83 kcal/mol   (1)

Determination of Heats of Formation of Branched Alkanes. Because experimental data is unavailable for many highly branched alkanes, it is desirable to employ an accurate, yet inexpensive, scheme for computing heats of formation. Note that these heats of formation may be computed from any reaction when well-established experimental values for all reactants and products, other than the molecule of interest, are known.[7] Within this context, Wheeler et al.[8] demonstrated the remarkable error-canceling ability of hyperhomodesmotic equations (e.g., eq 2),[9] which provide good experimental agreement using inexpensive standard DFT methods. In contrast, isodesmic reactions, including bond separation equations, generally require computationally expensive, correlated methods to achieve reasonable experimental agreement. To gauge overall accuracy, two techniques (direct and indirect) for computing bond separation reaction energies have been tested on a set of 16 branched alkanes with experimental data (see the Supporting Information).[10a,b] Note that these gas-phase enthalpies of formation are nearly identical to those in the classic text of Stull, Westrum, and Sinke[10c] (errors ranging from 0.0 to 0.2 kcal/mol for available compounds smaller than $C_{10}H_{22}$). The computations are based on lowest energy conformer searches as assessed by the procedure described in ref 12.

In the *direct* procedure, computed enthalpies are used to determine the isodesmic bond separation reaction energy of the alkane of interest. The *indirect* alternative uses hyperhomodesmotic equations[11] to determine the theoretical heat of formation. The BSE is then computed on the basis of this value along with the experimental heats of formation of methane and ethane. Figure 1 illustrates average and maximum deviations of various theoretical levels[12] between computed and experimental bond separation energies using both the direct and indirect procedures.

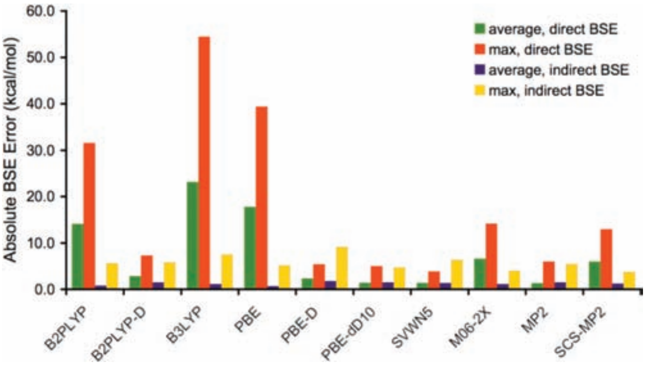
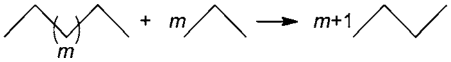


Figure 1. Absolute errors of computed bond separation energies from experimental data (in kcal/mol). Indirect BSE uses both experimental and computed heats of formation from hyperhomodesmotic reactions, while direct uses only DFT energies.



(2)

As previously reported, standard density functionals give inaccurate BSEs for hydrocarbons.[13] The average error from experiment for the popular B3LYP[14] and PBE[15] functionals

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(6) (a) Hehre, W. J.; Ditchfield, R.; Radom, L.; Pople, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 4796. (b) Radom, L.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 289. (c) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; John Wiley & Sons: New York, 1986.

(7) For instance, the theoretical heat of formation for propane could be computed from eq 1, so long as the experimental heats of formation of both methane and ethane are known.

(8) Wheeler, S. E.; Houk, K. N.; Schleyer, P. v. R.; Allen, W. D. *J. Am. Chem. Soc.* **2009**, *131*, 2547.

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(10) (a) Afeefy, H. Y.; Liebman, J. F.; Stein, S. E. Neutral Thermochemical Data. In *NIST Chemistry WebBook, NIST Standard Reference Database Number 69*; Linstrom, P. J., Mallard, W. G., Eds.; National Institute of Standards and Technology: Gaithersburg, MD; 2010; http://webbook.nist.gov. (b) Cox, R. D.; Pilcher, G. *Thermochemistry of Organic and Organomettalic Compounds*; Academic Press: New York, 1970. (c) Stull, D. R.; Westrum, E. F.; Sinke, G. C. *The Chemical Thermodynamics of Organic Compounds*; John Wiley & Sons, Inc.: New York, 1969.

(11) Hyperhomodesmotic equations used are derived from the highest rung of Wheeler's hierarchy of homodesmotic equations. See ref 8.

(12) Only the lowest energy conformers were considered in our computations as Boltzmann averaging was found to be negligible compared to the DFT errors (see Table S3, Supporting Information). Conformational searches were performed using a random atomic search with molecular topology imposed by a MM force field (Dreiding). At least 1000 random conformers per structure were generated, classically optimized, and then refined at the B3LYP/6-31G* level. Single-point energies were computed on the global minima using the cc-pVTZ basis set together with SVWN5, B3LYP, M06-2X, PBE, PBE-D, PBE-dD10, B2PLYP, B2PLYP-D, density-fitted MP2, and spin component scaled df-MP2. Gaussian09 (Frisch, M. J. et al. *Gaussian 09, Revision A.02*; Gaussian, Inc.: Wallingford, CT, 2009), MOLPRO (Werner, H.-J. et al. *MOLPRO*, version 2009.1) and deMon-2K (Köster, A. M. et al. *deMon-2K*; 2006) were used for computations. See the Supporting Information for full citations.

(13) (a) Grimme, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 4460. (b) Wodrich, M. D.; Corminboeuf, C.; Schleyer, P. v. R. *Org. Lett.* **2006**, *8*, 3631. (c) Schreiner, P. R.; Fokin, A. A.; Pascal, R. A., Jr.; de Meijere, A. *Org. Lett.* **2006**, *8*, 3635. (d) Wodrich, M. D.; Corminboeuf, C.; Schreiner, P. R.; Fokin, A. A.; Schleyer, P. v. R. *Org. Lett.* **2007**, *9*, 1851. (e) Schreiner, P. R. *Angew. Chem., Int. Ed.* **2007**, *46*, 4217. (f) Wodrich, M. D.; Jana, D. F.; Schleyer, P. v. R.; Corminboeuf, C. *J. Phys. Chem. A* **2008**, *112*, 11495. (g) Wodrich, M. D.; Corminboeuf, C. *J. Phys. Chem. A* **2009**, *113*, 3285.

(14) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

using the direct method are 23.2 and 17.7 kcal/mol, respectively. Specifically parametrized functionals, such as M06-2X,[16] and those supplemented with an empirical dispersion term (B2PLYP-D,[17,18] PBE-D,[19] PBE-dD10[20]) reduce this value to under 10 kcal/mol. The correlated MP2[21] method outperforms all functionals for the direct computations, including SCS-MP2.[22] Using hyperhomodesmotic equations to determine heats of formation significantly reduces the deviation from experiment for BSE reactions (the indirect method). The 23.2 kcal/mol average B3LYP error using the direct method is reduced to a mere 1.1 kcal/mol with the *indirect* method. Other functionals, both with and without dispersion corrections, peform remarkably well in the indirect procedure. The PBE functional gives the lowest average error from experiment (0.70 kcal/mol) and, therefore, is used to derive the heats of formation of the highly branched alkanes investigated throughout the remainder of this work. Thus, the indirect procedure allows for determination of remarkably accurate heats of formation of complex molecules using computationally inexpensive DFT methods.

Quantifying Nonbonded Group Interactions in Branched Alkanes. Having validated a reliable method for computing the heats of formation of highly branched alkanes, we employ bond separation reaction energies to delineate the extent of their destabilization and identify its origin. The BSE of *n*-alkanes (eq 3) show positive values, which increase linearly as the alkane is elongated. Starting from propane, the addition of each methylene group increases the overall stabilization by 2.81 kcal/mol on average (orange set, Figure 2). This procedure and quantitative value were previously used to define the energy of a single protobranching interaction.[2] The substitution by a methyl group of one hydrogen atom on each methylene leads to the singly methylated alkane series (eq 4). Similar to the *n*-alkanes, the BSEs of the singly methylated species are positive and increase linearly with parent chain lengthening (blue set, Figure 2). Despite the introduction of energetically unfavorable skew interactions,[23a] singly methylated alkanes show a ~4.8 kcal/mol BSE increase per $CH(CH_3)$ moiety added, nearly twice the value of *n*-alkanes (2.81 kcal/mol).

In sharp contrast with both *n*- and singly methylated alkanes, the BSE profile of permethylated alkanes (eq 5) shows an average *destabilization* of 8.2 kcal/mol (green set, Figure 2) per motif added. The total bond separation reaction energy even crosses over from positive (representative of stabilization) to negative values (destabilizing) for compounds with a parent chain length larger than seven. This permethylated alkane BSE trend, which opposes *n*- and singly methylated alkanes, is indicative of a dramatically different type of interaction.

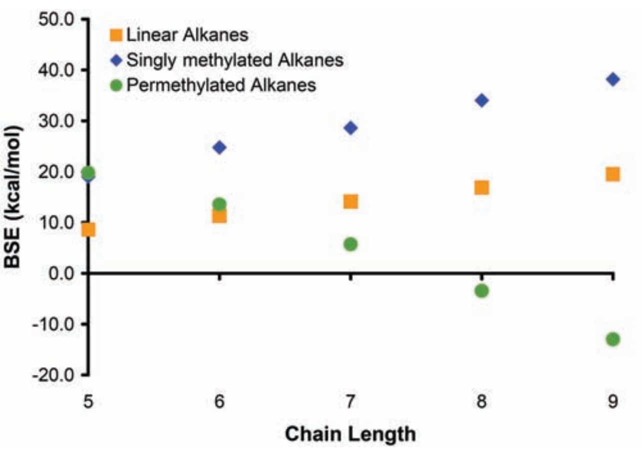
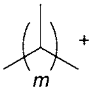


Figure 2. Bond separation reaction energies of *n*-, singly methylated, and permethylated alkanes (in kcal/mol).

As the degree of branching increases, additional 1,3-topologies, not present in simple *n*-alkanes, are introduced (Abstract graphic). The monomethylation of the methylene groups in *n*-alkane not only results in protobranching-type interactions (between methyl and/or methylene groups) but also gives rise to topological motifs featuring tertiary and primary carbons [$CH_3\cdots CH(CH_3)R$ and $R(CH_3)CH\cdots CH(CH_3)R$, R = alkyl] as well as 1,4-skew interactions.[23a]

Similarly, permethylated species, which have widely spaced conformational energy levels and thus one dominant conformation,[24] contain unique 1,3-motifs between primary and quaternary carbon groups [$CH_3\cdots C(CH_3)_2R$ and $R(CH_3)_2C\cdots C(CH_3)_2R$, R = alkyl]. To determine the energetic quantities associated with these various 1,3-alkyl−alkyl substituent patterns (i.e., the number of hydrogen and methyl groups attached to 1,3-disposed carbon atoms) and identify the origin of destabilization of highly branched alkanes, we dissect the total bond separation energies (eqs 3−5) into individual motif contributions by using a combination of previously established values and data-fitting procedures.

$$+ \, m\, CH_4 \longrightarrow m{+}1\, C_2H_6 \qquad (3)$$



$$+ \, 2m\, CH_4 \longrightarrow 2m{+}1\, C_2H_6 \qquad (4)$$

$$+ \, 3m\, CH_4 \longrightarrow 3m{+}1\, C_2H_6 \qquad (5)$$

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(22) Grimme, S. *J. Chem. Phys.* **2003**, *118*, 9095.

(23) (a) The destabilization arising from the 1,4-methyl−methyl interaction when the groups are separated by a ±60° torsion angle also known at gauche interaction. This destabilization is absent in the anti (180°) conformation. (b) Quantity estimated from gauche (skew) vs *n*-butane computed using a CCSD(T)-F12 cc-pVDZ-F12/cc-pVTZ-F12 extrapolation. See: Hill, J. G.; Peterson, K. A.; Knizia, G.; Werner, H.-J. *J. Chem. Phys.* **2009**, *131*, 194105. (c) Previous estimates place this value between 0.6 and 0.9 kcal/mol; see: Pitzer, K. S. *Chem. Rev.* **1940**, *27*, 39. Pitzer, K. S. *J. Chem. Phys.* **1944**, *12*, 310. Murcko, M. A.; Castejon, H.; Wiberg, K. B. *J. Phys. Chem.* **1996**, *100*, 16162. Smith, G. D.; Jaffe, R. L. *J. Phys. Chem.* **1996**, *100*, 18718.

The energy associated with the methyl(ene)···methyl(ene) interaction, taken as 2.81 kcal/mol, is derived from the average BSE of *n*-alkanes.[25] Similarly, a value of −0.67 kcal/mol is derived for the skew interaction.[23b,c] Using these predetermined values, best-fit parameters to the Figure 2 BSE curves have been established for the interactions associated with the two additional patterns present in singly methylated and permethylated alkanes (see details in the Supporting Information).

Table 1. Quantities, kcal/mol, Associated with Specific Types of 1,3 and Skew (1,4) Patterns

interaction	value (kcal/mol)
$CH_3 \cdots CH_3$ (*n*-alkane like)[a]	2.81
$CH_3 \cdots CH(CH_3)R$[b]	2.53
$CH_3 \cdots C(CH_3)_2R$[b]	2.74
$R(CH_3)CH \cdots CH(CH_3)R$[b]	1.72
$R(CH_3)_2C \cdots C(CH_3)_2R$[b]	−18.00
skew	−0.67

[a] Values of $CH_3 \cdots CH_2$ and $CH_2 \cdots CH_2$ interactions are taken to be identical with $CH_3 \cdots CH_3$ interactions. [b] R = alkyl.

Table 1 provides a summary of the energetic quantities associated with each interaction type. Singly methylated alkanes have two new types of 1,3-alkyl−alkyl interactions absent in *n*-alkanes: $CH_3 \cdots CH(CH_3)R$ and $R(CH_3)CH \cdots CH(CH_3)R$ (R = alkyl), which contribute positively to the BSE by 2.53 and 1.72 kcal/mol, respectively. Although slightly smaller, note that both values are comparable to the original protobranching energy in *n*-alkanes (2.81 kcal/mol). Permethylated alkanes also add two additional 1,3-nonbonded motifs, $CH_3 \cdots C(CH_3)_2R$ and $R(CH_3)_2C \cdots C(CH_3)_2R$. While the value for $CH_3 \cdots C(CH_3)_2R$ (2.74 kcal/mol) remains close to the protobranching value, the quantity associated with the $R(CH_3)_2C \cdots C(CH_3)_2R$ substitution pattern is dramatically destabilizing (−18.00 kcal/mol). Given the negative slope associated with the BSEs of permethylated alkanes (Figure 2), it is clear that a large destabilization is needed to overcome the numerous other stabilizing 1,3-alkyl−alkyl interactions dominating the BSE of singly methylated chains. This destabilization, existing only in highly branched alkanes, is caused by the steric hindrance between 1,5-methyl groups, which manifests itself in highly distorted bond lengths and angles (Abstract graphic).[26] The central CCC bond angle opens by over 4° and is accompanied by a C−C bond lengthening of nearly 0.1 Å as compared to propane. Similarly, the carbon−carbon geminal distance has increased by 8%, from 2.554 Å in propane to 2.759 Å in 2,2,3,3,4,4-hexamethylpentane.

In this paper, we have shown an efficient scheme for computing heats of formation of large branched alkanes using computationally inexpensive methods and employed bond separation evaluations to probe the destabilizing interactions associated with branched alkanes. Moreover, we have provided information regarding the magnitude and sign of specific 1,3-alkyl−alkyl interactions arising from various branching patterns. Singly methylated alkanes are characterized by unfavorable skew interactions absent in *n*-alkanes; however, that destabilization is overwhelmed by the greater number of energetically favorable 1,3-interactions. All 1,3-nonbonded alkyl−alkyl patterns, except those involving two quaternary carbon atoms, result in a stabilization between 1.7 and 2.8 kcal/mol. However, the presence of $R(CH_3)_2C \cdots C(CH_3)_2R$ bulky motifs destabilizes the permethylated alkanes dramatically (−18.00 kcal/mol). Thus, despite the simplified picture of branched alkane stability presented in many organic chemistry textbooks,[27] these species show widely varying stability trends based on number and location of added methyl groups.

Acknowledgment. The Sandoz Family Foundation, Swiss NSF Grant 200021_121577/1, and EPFL are acknowledged for financial support.

Supporting Information Available: Experimental and computed enthalpies and energies of relevant species, a detailed description of the best-fit procedure, test set of compounds, and full citation for ref 10 are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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[24] Alder, R. W.; Manunder, C. M.; Orpen, A. G. *Tetrahedron Lett.* **1990**, *31*, 6717.

[25] Note that using the attenuated values of protobranching for singly methylated (2.58 kcal/mol estimated from isobutane) and permethylated alkanes (2.28 kcal/mol estimated from neopentane), respectively, have no effect on general trends.

[26] Relationships between elongated C−C bonds and molecular strain have previously been established. See ref 5.

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