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Empirical Corrections to Density Functional Theory Highlight the Importance of Nonbonded Intramolecular Interactions in Alkanes

Matthew D. Wodrich,[†] Daniel F. Jana,[†] Paul von Ragué Schleyer,[‡] and Clémence Corminboeuf*,[†]

Laboratory for Computational Molecular Design, Institut des Sciences et Ingénierie Chimiques, Ecole Polytechnique Fédérale de Lausanne, CH-1015 Lausanne, Switzerland, and Center for Computational Chemistry and Department of Chemistry, University of Georgia, Athens, Georgia 30602

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Energies of alkanes computed with many popular and even newer density functionals are flawed by systematic errors, which become considerable with larger molecules. The same energies, however, are well described by post-Hartree–Fock methods. Similar DFT shortcomings are well documented for cases involving descriptions of *inter*molecular van der Waals complexes. One solution to the density functional problem is the addition of an empirical correction term, which more accurately models the known R^{-6} dependence of van der Waals energies. Here, we present the first empirical correction to DFT parametrized to reproduce experimental energies associated with *intra*molecular interactions in alkanes. Our training set used only three reactions involving simple linear and branched alkanes and provides a remarkable improvement over conventional DFT methods and empirical corrections optimized for *inter*molecular interactions. In contrast to many standard density functionals, the *intra*molecular empirical correction correctly predicts the lowest energy alkane isomer in addition to performing satisfactorily for describing the interaction energies of *inter*molecular complexes.

Introduction

The quest for an exchange-correlation density functional that accurately describes van der Waals (dispersive) interactions remains a challenge for practical computations. Despite active developments in the field,[1−8] the exchange and correlation functionals within the standard Kohn–Sham approach are local in nature and thus fail to reproduce the well-known R^{-6} dependence of van der Waals (vdW) energies. Dispersion forces, originating from the interaction between instantaneous fluctuating dipoles, are important in systems involving neutral, nonpolar, and weakly polar interactions, including those in DNA base pairs, proteins, dimers of polyaromatic hydrocarbons, and packing of molecular crystals, to name only a few. While it has long been realized that density functional theory (DFT) poorly describes intermolecular bindings of vdW complexes (e.g., benzene dimer or rare-gas diatomic molecules),[9−12] recent studies also have highlighted DFT difficulties for treating seemingly simple intramolecular interactions and dissociation energies of small saturated organic molecules.[13−20] As an example, the intramolecular 1,3-alkyl–alkyl interaction present in all alkanes larger than ethane, termed protobranching by Schleyer et al.,[21] is poorly described by a wide variety of popular density functionals.[14] Similarly, the DFT description of alkane isomerization energies shows unusual errors.[20,22] While the physical origin of (proto)branching is still unclear, correlated post-Hartree–Fock methods, which accurately account for medium/long-range vdW interactions, perform well for the energies of these systems.[14,21] In fact, Pitzer and Catalano in 1956 first pointed to the greater number of intramolecular vdW interactions as being responsible for the enhanced stability of branched over linear alkanes.[23]On the other hand, Grimme postulated that shortcomings in alkane isomerization energies using DFT result to a greater extent from inaccurate descriptions of medium-range electron correlation rather than from intramolecular vdW-type interactions.[22] More recently, Yang et al.,[24−28] as well as Perdew and Scuseria et al.,[29] emphasized that the many-electron self-interaction error (also termed delocalization error) is a major source of DFT failures. While the underlying physics of the correlation problem is not the scope of this paper, we aim to provide an empirical correction that accurately models DFT reaction energies and stereoelectronic effects for various alkane systems containing nonbonded intramolecular interactions. In addition, since a robust potential is desirable, the applicability of our correction has also been tested on representative intermolecular complexes.

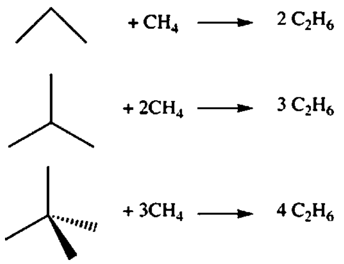

Figure 1. Training set used for the intramolecular parametrization of *a*, *b*, and *c*.

TABLE 1: *a*, *b*, and *c* Parameters Fit for the Inter- and Intramolecular Training Sets[a]

	a	*b*	*c*
intramolecular	14.6371	0.7141	0.7780
intermolecular	8.906	0.9343	0.6496

[a] Intermolecular parameters taken from ref 40.

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* Address correspondence to this author. E-mail: clemence.corminboeuf@epfl.ch.

[†] Ecole Polytechnique Fédérale de Lausanne.

[‡] University of Georgia.

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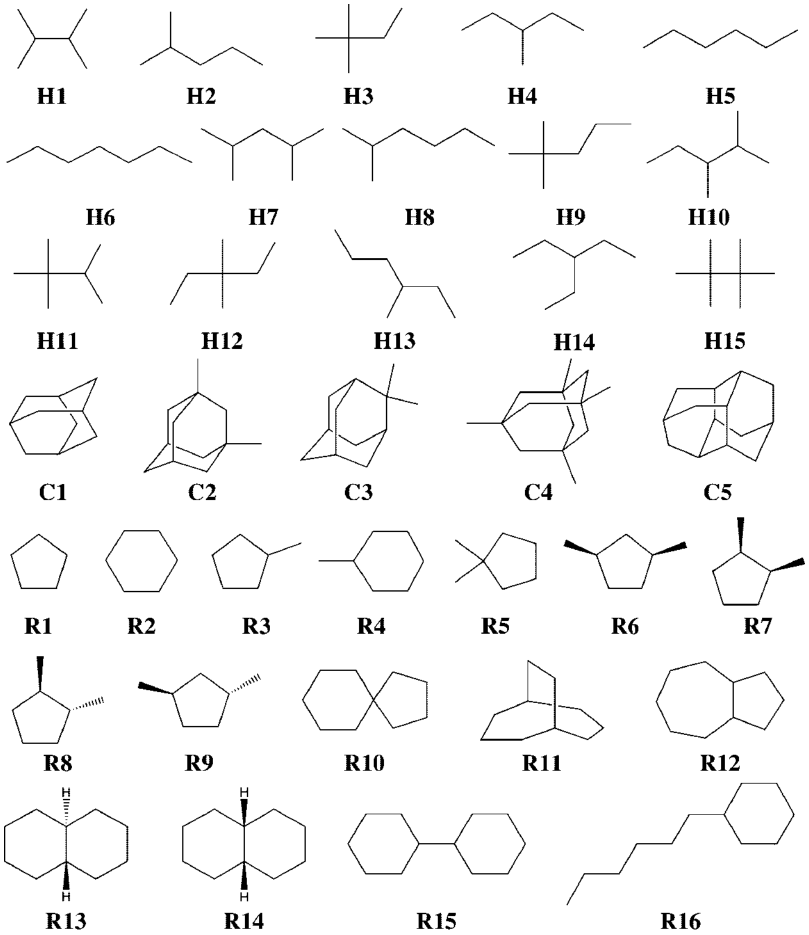
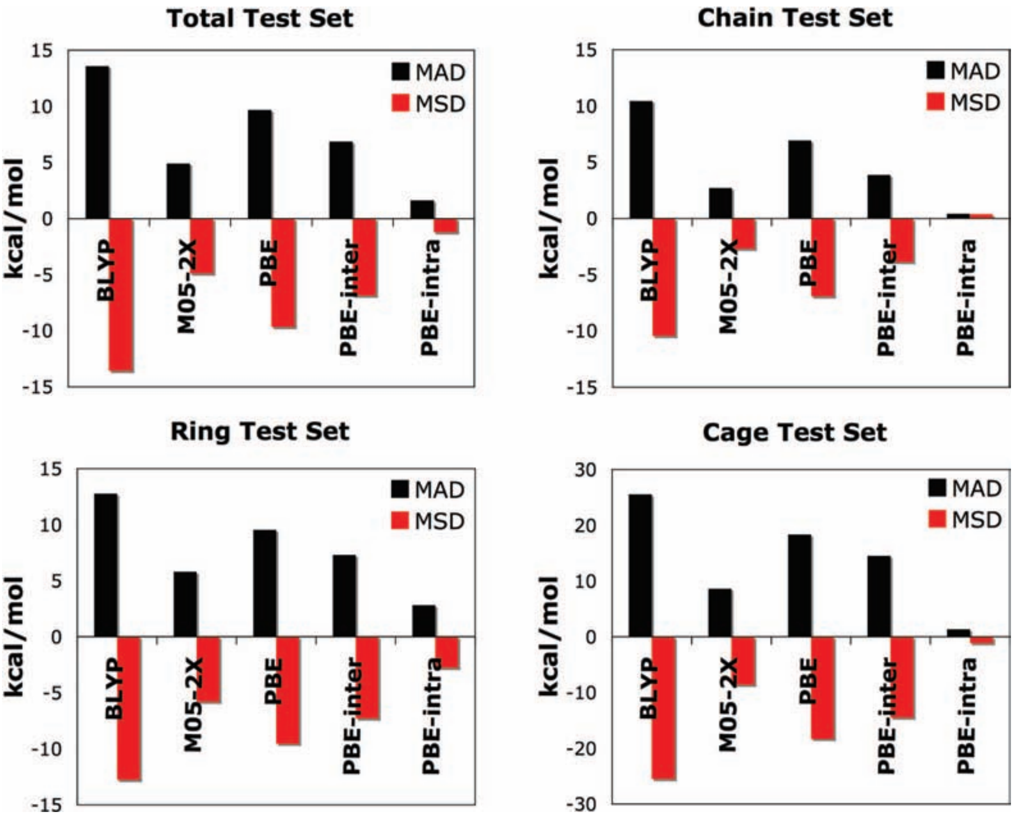


Figure 2. Schematic representation of the 36 saturated hydrocarbons used to test the empirical corrections.


Total Test Set

Chain Test Set

Ring Test Set

Cage Test Set

Figure 3. Mean absolute deviations (MAD) and mean signed deviations (MSD) for the total intramolecular test set, chain set, cage set, and ring set, using the standard BLYP, PBE, and M05-2X functionals, as well as inter- and intramolecular empirically corrected PBE (denoted PBE-Inter and PBE-Intra).

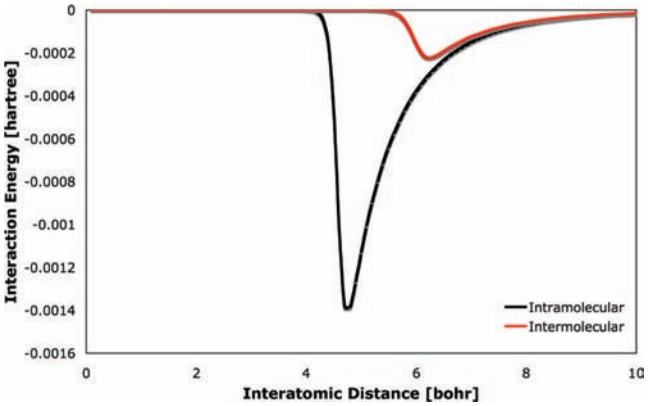


Figure 4. Empirical correction plot for C−C distance for intramolecular and intermolecular parametrizations.

Various methods have emerged as solutions to the known problems for describing weak interactions. These include (i) the introduction of (double-hybrid) exchange correlation functionals incorporating an improved asymptotic form of the interaction potential,[1,2,4,5] (ii) the optimization of effective atom-centered potentials,[30] (iii) the model developed by Becke and Johnson based on the position-dependent dipole moment of the exchange hole,[31−37] and (iv) an empirical (Lennard-Jones type) atom−atom correction term.[38−44] To date, these developments have been benchmarked and applied predominantly to typical weakly bound molecular complexes (intermolecular). In this paper we present the first empirical correction term specifically tailored for reproducing experimental intramolecular interaction energies of (proto)branched hydrocarbons. In addition, we demonstrate that parametrization based on a three-reaction training set provides excellent agreement with experimental and high-level computational results across chemical systems possessing intramolecular interactions.

Methods

The empirical correction is of the established form of eq 1.

$$E_{\mathrm{disp}} = -\sum_{i=1}^{N_{\mathrm{at}-1}} \sum_{j=i+1}^{N_{\mathrm{at}}} f_{\mathrm{d}}(R_{ij}) \frac{C_6^{\,ij}}{R_{ij}^{\;6}} \qquad (1)$$

where E_{disp} is the sum of diatomic ij contributions, and $f_{\mathrm{d}}(R_{ij})$ is a function that damps the R^{-6} term at short distances (where the density functional performs satisfactorily). Ducéré and Cavallo's[40] sigmoid damping function was employed (eq 2), as implemented in both ADF[45−47] and deMon-2K:[48]

$$f_d(R_{ij}) = \frac{c}{1 + \exp[-a(R_{ij} - bR_0)]} \qquad (2)$$

where a, b, and c are parameters optimized for our training sets (see Figure 1), R_{ij} is the interatomic distance, and R_0 the sum of the Bondi radii.[49] The C_6 parameters were derived by using the Slater−Kirkwood[50,51] approximation of eq 3 with Miller's atomic polarizabilites (α_i) and Halgren's effective number of electrons (N_i).

$$C_6^{\,ij} = \frac{3}{2} \frac{\alpha_i \alpha_j}{(\alpha_i/N_i)^{1/2} + (\alpha_j/N_j)^{1/2}} \qquad (3)$$

The damping function parameters, a, b, and c, were fit to correct intramolecular energies by using the Perdew−Burke−Ernzerhof (PBE) functional[52] (which simulates medium range dispersion partially but which performs poorly for this set of compounds) with triple-ζ quality basis sets[53] (TZP in ADF). Our training set employed NIST experimental data[54] for the three bond separation reactions involving alkanes, shown in Figure 1. The results of the least-squares fitting for the a, b, and c parameters in eq 2 are given in Table 1. Computations employing the empirical corrections, along with ZPE and thermal corrections for computed data to 298 K, provide the computed enthalpies used to determine the Pople bond separation energies (BSE)[55−57] for a set of 36 representative saturated hydrocarbons (Figure 2). Structural features include the following: chains (H1−H15), cages (C1−C5), and rings (R1−R16). Results were compared with the standard PBE functional,[52] the M05-2X hybrid meta-GGA of Truhlar[2,58] (a functional designed for reproducing energies of nonbonded systems), BLYP[59,60] (a "repulsive" functional known to represent nonbonded interactions poorly), and empirically corrected-PBE (denoted PBE-Inter) whose parameters were fit to reproduce energies of weakly bound intermolecular complexes (i.e., the benzene dimer). Note that only the performance of "commonly available" functionals, as opposed to those available to specialists and implemented in development versions of codes, are considered.[61,62]

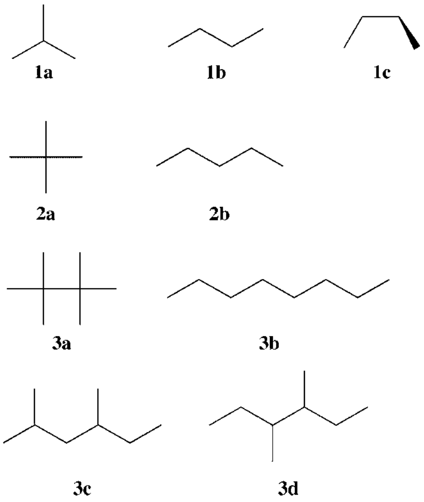


Figure 5. Test set of illustrative alkane isomers.

TABLE 2: Calculated Relative Energies (in kcal/mol) for Alkane Isomerization Reactions

reaction	MP2	BLYP	PBE	PBE-Inter	PBE-Intra
1a → **1b**	1.8[a]	0.8	1.2	1.5	1.9
1a → **1c**	2.4[a]	1.7	2.0	2.1	2.4
1b → **1c**	0.6[a]	0.9	0.8	0.6	0.5
2a → **2b**	3.6[b]	1.5	2.4	3.5	4.8
3a → **3b**	4.6[b]	−6.7	−3.1	−0.3	5.8
3a → **3c**	1.6[b]	−4.9	−2.8	−1.5	2.5
3a → **3d**	3.8[b]	−1.3	0.5	1.7	3.8
3b → **3c**	−3.0[b]	1.8	0.4	−1.2	−3.3
3b → **3d**	−0.8[b]	5.4	3.6	2.0	−2.0
3c → **3d**	2.2[b]	3.6	3.2	3.2	1.3

[a] Computed at MP2/cc-pVTZ. [b] Derived from ref 22.

Results and Discussion

1. Intramolecular Interactions. The intramolecular damping function parametrized in this work (PBE-Intra) reduces the mean absolute deviation (MADs) dramatically from those of the intermolecular parametrization, as well as the BLYP, M05-2X, and standard PBE functionals (Figure 3). The errors are even ameliorated over MP2 (see Figure 1 in the Supporting Informa-

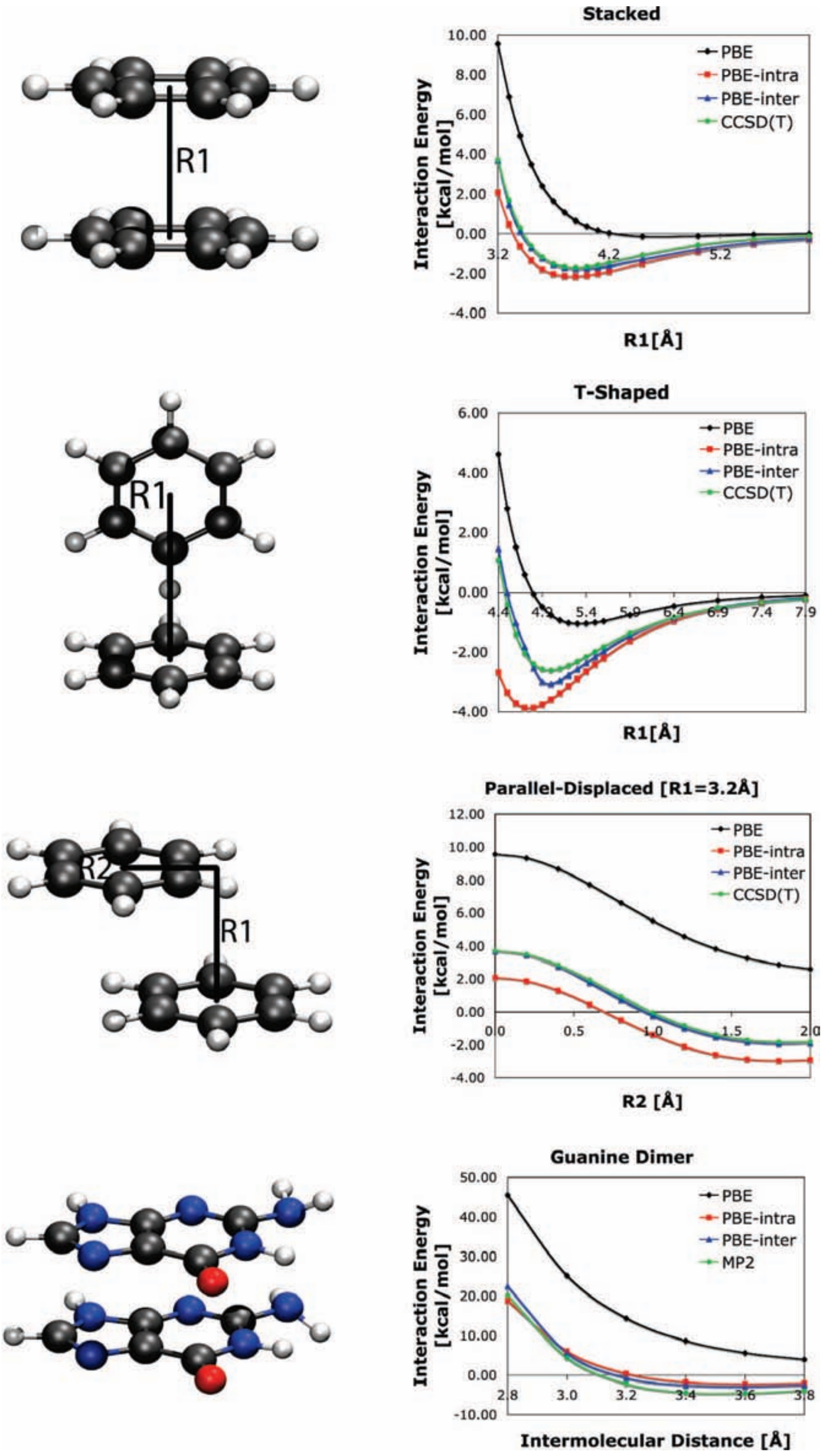


Figure 6. Benzene and guanine dimer structures and potential energy curves computed at PBE, PBE-Inter, PBE-Intra, and either CCSD(T) or MP2. CCSD(T) data taken from ref 63.

tion). As expected, the resulting energy corrections for the intramolecular interactions are much larger and occur at shorter interatomic distances than those from the intermolecular fit, suggesting that they are not primarily due to long-range dispersion (Figure 4). Furthermore, the remarkable transferability of protobranching interactions is reflected by the excellent energetic assessment obtained for a series of 36 saturated hydrocarbons, using a correction, based on a training set of only three bond separation reactions (Figure 1). These results confirm that protobranching-like interactions, similar to those present in propane, are prevalent in a variety of larger saturated hydrocarbon chains, rings, and cages (Figure 2).

Figure 3 also illustrates deviations for experiment for the BSE of chain, cage, and ring hydrocarbons. Because they most closely resemble the training set compounds, energies of the chain set are closest to experiment (average error of less than 0.5 kcal/mol). The assessment of hydrocarbon cages is notably improved over standard PBE. For instance, the error for 1,3,5,7-tetramethyladamantane (C4) is reduced from 21.53 (noncorrected PBE) to 0.43 kcal/mol (PBE-Intra). The description of ring hydrocarbons is complicated by the numerous possible conformations, especially when methyl groups are present. Nonetheless, the PBE-Intramolecular values show a marked improvement over standard-PBE and M05-2X even for large compounds.

2. Alkane Isomerization Energies. DFT computed alkane isomerization energies also are known to be inaccurate.[22] Illustrative examples based in Figure 5 compounds showing the results of the BLYP and standard PBE functionals are included in Table 2. Other commonly used density functionals also perform poorly quantitatively, and in about half the cases even assign the lowest energy isomer incorrectly. The empirically corrected PBE-Inter[40] results are only somewhat better. However, the addition of the intramolecular empirical correction gives accurate qualitative agreement (see the PBE-Intra data in Table 2) and also results in an average deviation less than 0.6 kcal/mol from MP2 computations.

3. Intermolecular Test Set. Although robustness is a highly valued characteristic, potentials for modeling nonbonded intramolecular systems are not widely applicable. Consequently, we tested the performance of PBE, PBE-Inter, and PBE-Intra in computing the interaction energies of several representative intermolecular complexes (see Figure 6, also SI Figures 2−4). The interaction energies of various benzene dimer orientations serve as a well-investigated computational benchmark[63−69] as do the energetic description of stacking interactions in biological systems (e.g., the guanine dimer).[38,40,70−72]

The standard PBE functional performs poorly in describing all four intermolecular nonbonded interactions. Both the stacked and the parallel-displaced benzene dimers, as well as the guanine dimer, are predicted to be unbound. Dramatic improvement is achieved by adding empirical corrections (parametrized either for intermolecular or for intramolecular interactions). It is not surprising that the intermolecular empirical correction does well in reproducing CCSD(T) interaction energies, since it was parametrized to reproduce the potential energy curves of the benzene dimer. Remarkably, PBE-Intra, despite being parametrized to reproduce intramolecular alkane interaction energies, also performs quite well in the examples in Figure 6 (also see SI Figures 2−4). The PBE-Intra association curve for the parallel stacked benzene dimer matches the reference data very well. While this intramolecular correction does result in slight intermolecular overbinding in the parallel-displaced and particularly in the "T-shaped" benzene dimer cases, the overall performance is satisfactory.

The guanine dimer example also is noteworthy. Although one expects better performance for this intermolecular bound complex from the "intermolecular" empirical correction (PBE-Inter), PBE-Intra does even better in reproducing the MP2 interaction energies (Figure 6, bottom). Despite being parametrized on the simple bond separation reactions of small alkanes, our "intramolecular" empirical correction (PBE-Intra) is robust and describes the energies of both inter- and intramolecular complexes well.

Conclusions

We have devised an empirical correction to density functional by parametrizing a damping function (PBE-Intra) that describes the energies of nonbonded intramolecular interactions in saturated hydrocarbons accurately. Compared to the standard PBE and BLYP functional, the newer M05-2X as well as to an intermolecular empirical correction (PBE-Inter), the PBE-Intra parametrization (based only on propane, isobutane, and neopentane as prototype molecules) improves saturated hydrocarbon bond separation and isomerization energies dramatically. These results emphasize the importance of propane-like protobranching interactions in the analyses of organic molecule energies. The PBE-Inter empirical corrections (optimized for reproducing intermolecular energies, e.g., for the benzene dimer) only slightly improve the description of intramolecular interactions. The *PBE-Intra* corrections perform satisfactorily for *intermolecular* interactions. The advantage of this approach is that it is practical, easy to implement, and readily accessible unlike the many recent "theoretically pure" alternatives that are available only to functional developers.

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Supporting Information Available: Bond separation reactions and energies used to create Figure 3, and computed energies of relevant compounds for Figure 3, Table 2, and Figure 6 are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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