Why the Standard B3LYP/6-31G* Model Chemistry Should Not Be Used in DFT Calculations of Molecular Thermochemistry: Understanding and Correcting the Problem

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S *Supporting Information*

ABSTRACT: We analyze the error compensations that are responsible for the relatively good performance of the popular B3LYP/6-31G* model chemistry for molecular thermochemistry. We present the B3LYP-gCP-D3/6-31G* scheme, which corrects for missing London dispersion and basis set superposition error (BSSE) in a physically sound manner. Benchmark results for the general main group thermochemistry, kinetics, and noncovalent interactions set (GMTKN30) are presented. A detailed look is cast on organic reactions of several arenes with C_{60}, Diels−Alder reactions, and barriers to [4 + 3] cycloadditions. We demonstrate the practical advantages of the new B3LYP-gCP-D3/6-31G* scheme and show its higher robustness over standard B3LYP/6-31G*. B3LYP-gCP-D3/6-31G* is meant to fully substitute standard B3LYP/6-31G* calculations in the same black-box sense at essentially no increase in computational cost. The energy corrections are made available by a Web service (http://www.thch.uni-bonn.de/tc/gcpd3) and by freely available software.
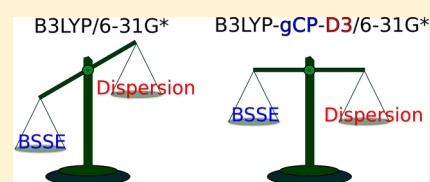
1. INTRODUCTION

Kohn−Sham density functional theory (DFT) methods[1] have evolved to be a standard tool in quantum chemistry to better understand chemical reactions. The number of collaborative experimental and theoretical publications has grown immensely, and DFT has emerged as the theory of choice in many applications. Selection of an appropriate and feasible ("cost-effective") level of theory for a specific problem is a nontrivial task, particularly because the number of newly proposed density functionals is huge. It comes as no surprise that often methods are selected by nonexperts purely because of their popularity but deemed outdated in the theoretical community.[2,3] The combination ("model chemistry") of B3LYP[4,5] with the 6-31G*[6] Gaussian AO basis set (or other slightly varied, double-ζ basis sets) is such an example. Famous for, at its time, unprecedented accuracy,[7] theoretical and practical limitations of this approach grew more obvious over the years, and serious doubts about its usefulness were raised, especially if noncovalent interactions were involved.[2,8−11]

Many empirical observations such as qualitatively correct reaction energies (or barriers) support the B3LYP/6-31G* approach and its disappearance is not expected soon. However, in this context it should not be forgotten that often two different quantities are compared: The energy differences (ΔE, often the gas phase) and the (free) enthalpy differences (often in solution). Strong influences on thermochemical properties are to be expected from zero point vibrations, finite temperature, entropy, and solvation effects. Nonetheless, relative energies often give a good first approximation to the problem. If the need arises for a more detailed answer and if solvation effects should be taken into account, it is clear that each energy component (gas-phase energy, (free) enthalpy corrections from nuclear motions, solvation energy) must be calculated as accurately as possible. For recent discussions of the influence of solvation effects and Gibbs free enthalpy calculations on reaction and binding energies, see refs 12−15.

For DFT, the statistical evaluation (i.e., benchmarking) of density functionals (DFs) is an important procedure to elucidate the performance of the different DFs and helps to select appropriate DFs from the growing "zoo" of functionals. The first benchmarking studies were already undertaken by Pople and co-workers (G1 set[16]) and later prominently extended to a broader chemical spectrum by Truhlar.[17−20] In a successful effort, a large benchmark database was developed by some of us that covers general main group thermochemistry, kinetics, and noncovalent interactions (GMTKN) and consists of 30 individual data sets.[21,22] These sets were either compiled from existing ones or newly developed. From a statistical analysis over all results for the GMTKN30 benchmark suite, well-founded recommendations for the selection of density functionals were given.[3]

Table 1. Overview of the GMTKN30 Benchmark Set and Its Subsets along with the Classification of Basic Properties, Reaction Energies, and Noncovalent Interactions as in the Original Publications[21,22]

benchmark set	description	classification
MB08-165	Decomposition energies of artificial molecules	
W4-08	Atomization energies of small molecules	
G21IP	Adiabatic ionization potentials	
G21EA[a]	Adiabatic electron affinities	
PA	Adiabatic proton affinities	
SIE11	Self-interaction error related problems	basic properties
BHPERI	Barrier heights of pericyclic reactions	
BH76	Barrier heights of hydrogen transfer, heavy atom transfer, nucleophilic substitution, unimolecular and association reactions	
BH76RC	Reaction energies of the BH76 set	
RSE43	Radical stabilization energies	
O3ADD6	Reaction energies, barrier heights, association energies for addition of O_3 to C_2H_4 and C_2H_2	
G2RC	Reaction energies of selected G2/97 systems	
AL2X	Dimerization energies of AlX_3 compounds	
NBPRC	Oligomerizations and H_2 fragmentations of NH_3/BH_3 and H_2 activation with PR_3/BR_3 systems	reaction energies
ISO34	Isomerization energies of small and medium-sized organic molecules	
ISOL22	Isomerization energies of large organic molecules	
DC9	Nine difficult cases for DFT	
DARC	Reaction energies of Diels-Alder reactions	
ALK6	Fragmentation and dissociation reactions of alkaline and alkaline-cation-benzene complexes	
BSR36	Bond separation reactions of saturated hydrocarbons	
IDISP	Intramolecular dispersion interactions	
WATER27[a]	Binding energies of water, $H^+(H_2O)_n$ and $OH^-(H_2O)_n$ clusters	
S22	Binding energies of noncovalently bound dimers	
ADIM6	Interaction energies of n-alkane dimers	
RG6[b]	Interaction energies of rare gas dimers	
HEAVY28[b]	Noncovalent interaction energies between heavy element hydrides	noncovalent interactions
PCONF	Relative energies of phenylalanyl-glycyl-glycine tripeptide conformers	
ACONF	Relative energies of alkane conformers	
SCONF	Relative energies of sugar conformers	
CYCONF	Relative energies of cysteine conformers	

[a]Left out, because the 6-31G* basis set is a too unrealistic choice. [b]No basis functions for all elements in the set for 6-31G*.

The above-mentioned benchmark studies were mostly conducted with large basis sets (at least def2-QVZP) to minimize basis set errors. Thorough studies with smaller basis sets were also carried out, however, without correcting for the so-called basis set superposition error (BSSE). It is known that applying small basis sets in the calculation of interaction energies leads to an unbalanced description of the reactant and complex wave functions. The latter is energetically too low because in the complex each (former) reactant will use each other's basis functions. This "borrowing" of basis functions from the neighbor molecules is termed (intermolecular) BSSE.

In the same sense, for example, one part of the molecule can (like a functional group) use the basis functions from another, nearby molecular part. This leads to the concept of *intra*molecular BSSE (IBSSE).[10,23,24] The standard approach to circumvent the *inter*molecular BSSE is the widely used counterpoise correction (CP) scheme by Boys and Bernadi[25] (BB). A similar popular approach to correct IBSSE is missing, albeit various possible approaches are suggested.[26] Herein, we suggest using the recently developed *geometrical counterpoise correction* (gCP)[27] that is able to treat inter- and intramolecular BSSE on the same footing at practically vanishing computa-

tional costs (see section 2). It is thus widely applicable to relative energies such as, for example, reaction/binding energies or barrier heights, conformational energies, and (intramolecular) rearrangement reactions, the latter two being not well-defined in the BB-CP approach (an arbitrary breaking of covalent bonds would be needed).

For the treatment of all but the smallest systems, noncovalent interactions[28,29] play an important role for both structures and energetics.[30−32] A crucial drawback of DFT approximations (using common semilocal and conventional hybrid functionals) is their inability to provide the correct $-C_6/R^6$ dependence of the London dispersion interaction energy on the interatomic/molecular distance R. There exist several approaches to tackle this problem (see, for example, ref 32 for a recent review). Herein, we will use the widely accepted DFT-D3[33]-denoted scheme of dispersion-corrected DFT in its latest variant,[34] which already proved successful in many practical applications.[9,35−38]

Friesner and co-workers recently addressed known shortcomings of B3LYP, suggesting the B3LYP-MM method[11] that employs an 11-parameter force-field type function and models explicitly each of the following effects: London dispersion,

hydrogen bonding, and cation−π interaction. Basis set effects are implicitly corrected through a basis set specific parametrization. Especially for the small LACVP basis set, large improvements were reported. While presenting impressive results it is noted by the authors themselves that the high accuracy is deemed to decrease if a broader range of chemical interactions is considered, which does not hold true for the expectations of a *robust* methodology. In the same direction goes the recently presented B3LYP-DCP approach of DiLabio and co-workers,[39] who refitted their dispersion correction (dispersion core-potentials, DCP) for the elements H, C, N, O to be used with B3LYP and "small basis sets" (6-31+G(2d,2p) performs best).

In general, a dispersion potential (from any dispersion correction) is unsuitable to model basis set effects such as BSSE because dispersion interactions decay asymptotically with R^{-6}, and BSSE is expected to decay roughly exponentially because of a strong dependence on the decay of the basis functions (usually contracted Gaussian-functions) themselves. Thus, it is only to a very limited extent possible to model dispersion interactions and BSSE with the same potential.

In a first step, we will discuss the two major shortcomings of B3LYP/6-31G*, namely basis set size and missing dispersion. We will then compare the proposed B3LYP-gCP-D3/6-31G* model chemistry with reference calculations near the basis set limit (with the quadruple-ζ basis set "def2-QZVP"[40]) and with B3LYP/6-31G*. This comparison is carried out on the GMTKN30 benchmark sets (see Table 1). The contributions from dispersion interaction and BSSE will be analyzed. Some thermochemical examples finally illustrate the benefits of using our B3LYP-gCP-D3/6-31G* model chemistry. We propose it as a substitute to B3LYP/6-31G* for everyday organic chemistry applications.

2. RESULTS AND DISCUSSION

We will start with a discussion about the shortcomings of small basis set Hartree−Fock (HF) and DFT calculations that were already indicated in the introduction. The first one is the basis set error. The basis set error can be split into the BSSE and the basis set incompleteness error (BSIE).[41] The BSIE is an inherent basis set problem and leads to an insufficient description of physical effects such as electrostatics or induction (polarization). In practice, BSSE and BSIE are seldom strictly distinguishable, and only the BSSE will be subject herein. The most commonly known approach is to remove the additional binding energy using the counterpoise correction of Boys and Bernadi (BB-CP). The BB-CP-corrected interaction energy ΔE_{CP} for a dimer complex is the following:

$$\Delta E_{CP} = [E(A)_a - E(A)_{ab}] + [E(B)_b - E(B)_{ab}] > 0$$

where a and b denote the basis set belonging to the monomer A and B (in their frozen complex geometries). The corrected binding energy (BE, normally <0) is then obtained by simple addition:

$$\Delta E_{BE}^{CP} = \Delta E_{BE} + \Delta E_{CP}$$

Although not free of criticism,[41−43] the BB-CP is widely used and, at least for HF and DFT, found to be a robust approximation of the intermolecular BSSE. Recently, some of us[27] proposed a semiempirical scheme that allows calculation of the BSSE solely from the geometrical structure at practically no computational costs. This geometrical counterpoise correction

(gCP) is parametrized to give the BB-CP in the case of intermolecular BSSE and accounts additionally for intramolecular BSSE (IBSSE) effects, e.g., for conformational questions. Although the IBSSE misses a rigorous, uniform definition, its importance is meanwhile widely recognized.[10,23,24,44,45] IBSSE influences both structures and energetics of molecular systems. The gCP correction can be added to the BE just the same way:

$$\Delta E_{BE}^{gCP} = \Delta E_{BE} + \Delta E_{gCP}$$

The second major shortcoming is missing London dispersion interactions.[46] The inability of many DFT functionals to treat dispersion sufficiently is meanwhile well-known, and several approaches exist to overcome this problem (see ref 32). Herein, we use the latest DFT-D3[33] version in the updated Becke−Johnson damping variant.[34] DFT-D3 evaluates the missing dispersion energy through an atom-pairwise potential based on first principles data.

In practice, both corrections (gCP, D3) can be directly added to the electronic DFT (or HF) energy. To compute the binding/reaction energy of the complex AB from A and B, first the DFT ground-state energy is obtained and then the corrections are added, i.e., for molecule X (= A, B, AB), as follows:

$$E(X)_{gCP-D3} = E(X)_{DFT} + E(X)_{gCP} + E(X)_{D3}$$

Then the corrected binding/reaction energy $\Delta E(AB)$ is computed the usual (supermolecular) way,

$$\Delta E(AB)_{gCP-D3} = E(AB)_{gCP-D3} - E(A)_{gCP-D3} - E(B)_{gCP-D3}$$

to yield directly the gCP-corrected result from dispersion-corrected DFT (e.g., B3LYP-gCP-D3/6-31G*). The methods DFT-D3 and gCP are implemented in separate, freely available programs.[47] A future release of the ORCA[48] quantum chemistry software will also contain the gCP correction, in addition to the already available DFT-D3 implementation.

The reason why B3LYP/6-31G* sometimes performs surprisingly well can be explained by looking at the two largest errors that are made in B3LYP calculations. The first error, the neglect of attractive London dispersion interactions, will result in binding energies of complexes (underbinding) that are too low (positive). As noted above, the BSSE is also an attractive energy component and the removal of BSSE, e.g., by the BB-CP or gCP correction or some other suitable scheme, will destabilize the complexes. In this sense, dispersion- and BSSE-corrections are opposing (counteracting) "energy components". To yield good results with plain B3LYP/6-31G*, it is thus required that the missing dispersion interaction is compensated by BSSE. The prerequisite that dispersion and BSSE are of equal (or very similar) magnitude is, however, generally not given as we will see below.

The influence of both corrections is demonstrated in Figure 1, which shows the relaxed, potential energy surface of the Diels−Alder reaction between tetrachlorocyclopentadiene and maleimide. The reaction coordinate (RC) is defined as follows: Starting from the fully relaxed transition structure, one reactant is displaced along the newly forming C−C bonds. To avoid both reactants from tilting toward each other during the relaxed potential surface scan, an additional constraint at the opposing site is introduced (see Supporting Information). The RC coordinate is varied by 0.1 Å (plus additional points near each extremum), and at each point the geometry is relaxed under the
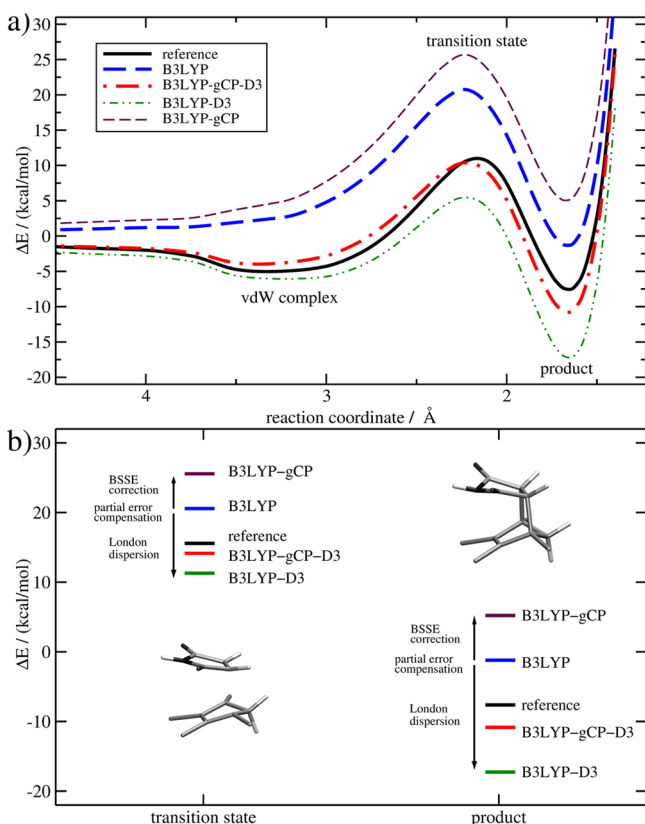
Figure 1. Relaxed potential energy surface (a) of a Diels–Alder reaction between tetrachlorocyclopentadiene and maleimide using the 6-31G* basis set for all but the "reference" calculation that employs def2-QZVP. Close up of two selected points (transition state and product) (b) on the surface.

constraint of the frozen coordinates. The reference point ($\Delta E = 0$) refers to both reactants at infinite separation.

For this and all following examples, we will employ B3LYP-D3/def2-QZVP as the reference method. The large def2-QZVP basis set yields results practically near the basis set limit for B3LYP-D3. Therefore, genuine B3LYP-D3 results, which are unaffected by basis set errors, are obtained. All other values, except the reference calculations, are obtained with the 6-31G* basis set. Therefore, the basis set is omitted while denoting the level of theory from now on. Qualitatively our conclusions should also hold for functionals other than B3LYP except that the dispersion effects are mostly weaker.[3]

In the reaction curve (Figure 1a) the contributions to B3LYP-gCP-D3 are plotted separately to demonstrate the energetic effects of the corrections. Starting from plain B3LYP, the dispersion correction D3 lowers the energies at each data point (B3LYP-D3 curve). The magnitude of the dispersion stabilization is larger than the effect of the BSSE-correction gCP (B3LYP-gCP curve) so that B3LYP-gCP lies closer to plain B3LYP, while B3LYP-D3 lies already quite close to the reference curve with the large basis set. The comparably small gCP correction then shifts the curve (B3LYP-gCP-D3) mostly on top of the reference curve. We also note that a particular problem for plain B3LYP is the inability to compute the stable van der Waals (vdW) complex before the transition state.

Next, we take a more detailed look at the two extrema of the reaction curve, the transition state, and the product in Figure 1b, aiming to illustrate the effects of the BSSE and dispersion interactions in more detail. The opposing effects, the BSSE-

removal (*de*stabilization) and the adding of dispersion interaction (stabilization), are highlighted for the activated complex (transition state) and the final product. The plain B3LYP result stems from a partial error compensation that is, however, still considerably off from the reference (B3LYP-D3/def2-QZVP). This picture of opposing effects is essential and explains many of the results exemplified below.

For a statistical evaluation, we look at the GMTKN30 benchmark set that enables us to test the methods under scrutiny against more than 800 high-quality reference data points stemming from accurate wave function methods. However, four sets had to be left out of the GMTKN30 superset that is briefly described in Table 1: For the heavy element hydride dimer (HEAVY28) and rare gas dimer (RG6) sets, no 6-31G* basis set is available for most of the elements included in these sets. The WATER27 and G21EA sets are not reported because small basis sets such as 6-31G* yield very large errors for the water cluster interaction (WATER27) and electron affinity set (G21EA). An in-depth description of all individual sets of the GMTKN30 can be found in refs 21 and 22.

The (signed) mean deviations (MDs) for B3LYP, B3LYP-D3, and B3LYP-gCP-D3 (Figure 2) on the GMTKN30
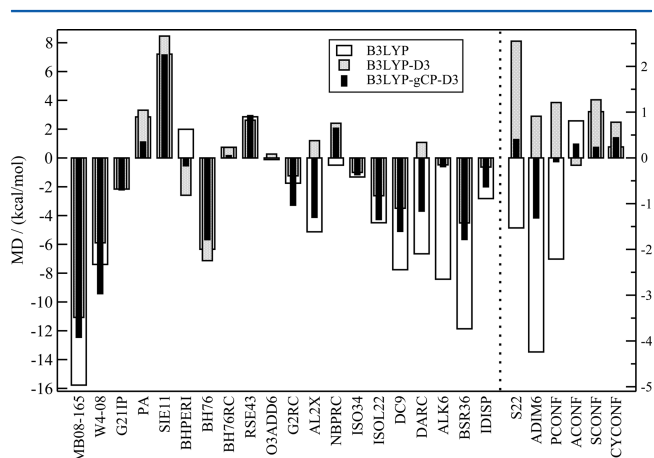

Figure 2. Mean deviations (MDs) for 26 sets of the GMTKN30 benchmark suite in kcal/mol. The basis set 6-31G* is used for all calculations. The values for the sets S22, ADIM6, PCONF, ACONF, SCONF, and CYCONF are displayed on a separated (smaller) scale for better visualization.

benchmark with 6-31G* are taken to discuss the notions presented above. The benchmarking is done against the original GMTKN30 ab initio reference data. We concentrate foremost on the performance for reaction barriers, reaction energies, and noncovalent interactions.

Reaction barriers are found in the sets BHPERI,[49−53] BH76,[18,19] and (in parts) O3ADD6,[20] which describe pericyclic reactions, various atom transfers, and ozonolysis reactions, respectively. The BHPERI set shows overestimation (positive MD values) of the barrier heights for plain B3LYP (MD = 2.0 kcal/mol), meaning that the transition state is insufficiently stabilized relative to the reactants. Adding the dispersion energy (B3LYP-D3) then leads to an overstabilization and yields barriers (MD = −2.6 kcal/mol) that are too low. This, in turn, is mostly compensated by the gCP correction to yield a final MD of −0.5 kcal/mol. The situation is slightly different for the BH76 set, where B3LYP already yields barriers (MD = −6.3 kcal/mol) that are much too low. Correcting for BSSE and

dispersion raises the barrier only slightly toward the correct values (MD = −5.7 kcal/mol). Because O3ADD6 includes both barriers and reactions, the signs of errors are opposite and partially cancel each other out, which leads to MDs that are close to zero. Alternatively, taking a look at the MAD for O3ADD6 (see Figure 3) shows that gCP-D3-corrected B3LYP yields an MAD that is better, by 1 kcal/mol, than the MAD of plain B3LYP.
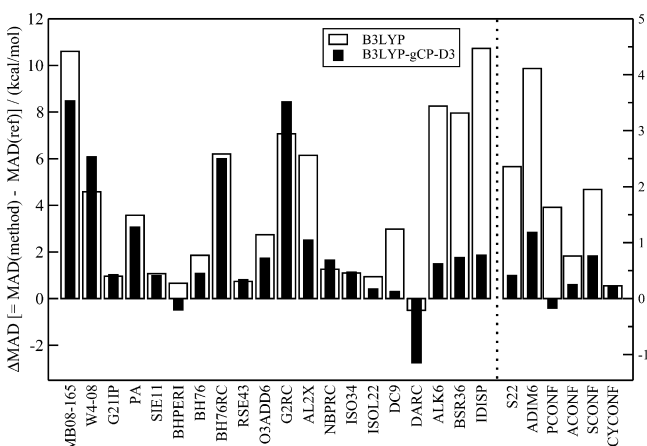

Figure 3. Mean absolute deviation differences (ΔMAD) to the B3LYP-D3/def2-QZVP reference (ref) in kcal/mol for B3LYP/6-31G* and B3LYP-gCP-D3/6-31G* (method). The values for the sets S22, ADIM6, PCONF, ACONF, SCONF, and CYCONF are displayed on a separated (smaller) scale for better visualization.

Interesting examples for reaction energies are found in the sets AL2X,[54] DARC,[54] and ALK6,[33] which describe dimers of the AlX$_3$ type, Diels−Alder reactions, and reactions involving alkaline atoms or ions. The MD of AL2X shows that uncorrected B3LYP strongly underestimates the reaction energies (MD = −5.1 kcal/mol). The AL2X set shows slight overbinding with B3LYP-D3, which is mainly caused by the dimerization reaction AlF$_3$ → Al$_2$F$_6$. This reaction yields a rather large BSSE of about −19 kcal/mol calculated by gCP, which fits reasonably well to the (approximate) BB-CP of −16 kcal/mol for this system (fragmentation at the newly formed covalent bond). Generally, gCP overshoots in all reactions but still improves over B3LYP by 1 kcal/mol (MD = −4.1 kcal/mol). The Diels−Alder reaction set DARC gives a similar picture, but the overall improvement of B3LYP-gCP-D3 over B3LYP is significantly better and lowers the MD by about 3 kcal/mol. Good results for the gCP correction are also obtained for the ALK6 set, where the (catastrophic) MD of −8.4 kcal/mol for B3LYP improves to −0.6 kcal/mol for B3LYP-gCP-D3.

The interaction energy trends for the noncovalently bound dimer complexes (S22,[55,56] ADIM6[33]) are similar to those of the reaction energies, but because the dispersion energy and BSSE have larger relative impacts, the effect of overbinding for B3LYP-D3 is more pronounced. Similar overestimations of B3LYP-D3 with small basis sets were already observed by Friesner[11] and ourselves.[27] However, it is very clear that the BSSE cannot fully compensate for the missing dispersion interaction, and basically all complexes are underbound at plain B3LYP (see also ref 27).

The XCONF sets (X = P, A, S, CY for (tri)peptide,[57] alkanes,[58] sugars,[21,59] cysteine[60]) comprise relative energies of conformers. They are not only important tests for intra-

molecular dispersion interactions but also for intramolecular BSSE. Among the XCONF sets, the largest errors for B3LYP are found for PCONF (MD of −4.2 kcal/mol) and SCONF (MD of −2.2 kcal/mol). Both sets benefit strongly from the gCP-D3 correction (MDs are −1.3 and 0.1 kcal/mol, respectively). The exact order of those conformational energies, e.g., in the PCONF set (contains single-molecule conformers of phenylalanyl-glycyl-glycine), is extremely difficult to accurately determine but is, in general, acceptable with DFT-D3/"large basis" calculations.[3,34] Plain B3LYP, however, fails to get even a rough idea of the correct order. The benchmark reference predicts, for example, the two most stable conformers 0.14 kcal/mol apart from each other. B3LYP predicts a 3 kcal/mol difference between those two, which turns the formerly most stable conformer into the least stable. In fact, B3LYP favors unfolded conformers over folded ones. The order is much better for B3LYP-gCP-D3, which correctly yields the two lowest conformers and a reasonable general trend. Such conformer studies are highly important for the computation of theoretical spectra (ECD, VCD, UV/Vis, IR, etc.), for which the spectra of several conformers are often Boltzmann weighted within a 1.5 kcal/mol range (at room temperature) to yield a final spectrum. If the general trend is not predicted at all, and the most stable conformer misses completely, such as for plain B3LYP, all successive (and usually more expensive) calculations for the spectra are deemed to give wrong results.

In Figure 3 the difference between the MAD of the B3LYP-D3 reference calculation and the MAD of the investigated methods (B3LYP-gCP-D3 or B3LYP with 6-31G* basis set) is shown, i.e., the MAD value of the reference-B3LYP-D3 calculation is subtracted from the MAD value of the B3LYP or B3LYP-gCP-D3 calculation, respectively. Thus, positive values mean that the investigated method gives larger errors than a B3LYP-D3 calculation near the basis set limit, and negative values show that the performance is better than it should be and error compensation fixes even shortcomings of the functional itself. B3LYP-gCP-D3 gives for the majority of sets a superior performance over B3LYP. Especially for the cases where dispersion energy becomes more important, the improvements for B3LYP-gCP-D3 reach several kcal/mol. The well-known noncovalent interactions test set S22 is improved by almost 2 kcal/mol, and also the intramolecular test sets gain accuracy as seen for the IDISP[22,61−63] set (specifically designed for intramolecular dispersion interactions) where the ΔMAD is reduced by 8 kcal/mol (almost one-fifth of the original value!). For the sets W4-08[49] (atomization energies) and G2RC[64] (reaction energies of small closed-shell molecules), B3LYP shows better results, which means either that in these cases the BSIE is also "corrected" by error compensation or that D3-gCP is problematic with these test sets that comprise rather small molecules. However, even if B3LYP/6-31G* shows a statistical superiority in these two cases, a better choice is clearly the larger basis set in the reference B3LYP-D3 calculation that is easily affordable for these test molecules. For a few sets, there is little statistical difference (for a ΔMAD of >2, everything within a range of 0.5 kcal/mol is rather similar) between B3LYP and gCP-D3, but these often contain rather small molecules.

The statistical absolute performance of B3LYP-gCP-D3 is shown in Figure 4, where the mean absolute deviations (MADs) in kcal/mol for the GMTKN30 benchmark are presented along with the optimal B3LYP reference (B3LYP-D3/def2-QZVP). Both methods are benchmarked against the GMTKN30 high-level reference data. The performance of
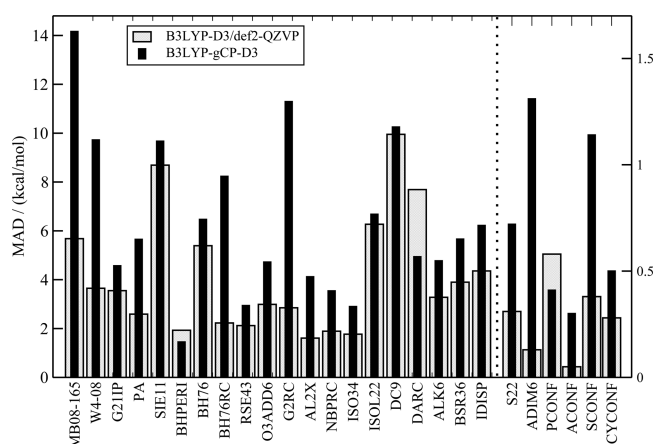
Figure 4. Mean absolute deviations (MADs) for B3LYP-D3/def2-QZVP and B3LYP-gCP-D3/6-31G* on the GMTKN30 benchmark set in kcal/mol. The reference values are taken from the original publications. The values for the sets S22, ADIM6, PCONF, ACONF, SCONF, and CYCONF are displayed on a separated (smaller) scale for better visualization.

B3LYP-gCP-D3 is compared to the reference-type B3LYP-D3 calculations and demonstrates a reasonable trade-off between cost and accuracy for many cases. The accuracy is somewhat limited, (mostly) because of the BSIE of the small 6-31G* basis and only second because of gCP errors. The plot thus also shows limitations of BSSE-corrected computations using small basis sets in general. Our experience shows basis sets such as def2-TZVP[40] or 6-311G(2df,2p)[65] or a similar size should be used to avoid large BSIE. In our laboratory, large basis sets such as def2-QZVP are nowadays routinely employed. The choice of functionals is not in the scope of this paper and has been extensively addressed previously.[3] It can be, however, argued that B3LYP, while widely popular, is not the best choice for general applicability even if it is corrected for London dispersion and large basis sets are used (see refs 3 and 35 and references therein).

In the GMTKN benchmark studies, a single-number measurement, the weighted mean absolute deviation (WTMAD), is calculated to express the performance of a method across the complete set.[3,21] The MADs are weighted according to a factor that accounts (a) for the number of systems within a set and (b) for the (estimated) difficulty of the set (for exact definition and weighting factors, see refs 3 and 21). For the reduced GMTKN30 database used herein, the WTMADs for B3LYP, B3LYP-D3, and B3LYP-gCP-D3 are 8.75, 7.00, and 6.87 kcal/mol, respectively. For comparison, the WTMAD of B3LYP-gCP-D3/def2-QZVP is 3.3 kcal/mol. By using the ΔMAD values from Figure 3 to obtain a global performance for B3LYP/6-31G* and B3LYP-gCP-D3/6-31G* against the B3LYP-D3 reference, we obtain a WTΔMAD of 4.3 kcal/mol for B3LYP and of 2.8 kcal/mol for B3LYP-gCP-D3. Both values, WTMAD and WTΔMAD, show a clear statistical improvement of the proposed B3LYP-gCP-D3 scheme over plain B3LYP.

3. EFFECTS OF LONDON DISPERSION AND BSSE IN ORGANIC CHEMISTRY APPLICATIONS

Three typical examples for applications of DFT to organic chemical reactions will be discussed in the following. The emphasis will be put on the effect of the small basis set and the lack of a proper description of London dispersion effects in mere B3LYP/6-31G* calculations. We will discuss these effects for reaction energies and barrier heights and compare again against the B3LYP-D3/def2-QZVP calculations that yield results close to the basis set limit for DFT. Note again that even at this level of theory, B3LYP was shown to be a rather moderately performing functional in terms of accuracy and robustness.[3] However, overall robustness and accuracy is not the main point of this discussion, and a thorough discussion of this point would be beyond the scope of this study. We refer the reader to previous studies, e.g., ref 3, about the reliability of B3LYP and other DFT methods.

Intramolecular London dispersion effects usually begin to play a noticeable role when around 10 or more non-hydrogen atoms are present. This is the case for most standard organic chemical applications. In fact, dispersion interactions have been shown to be influential on reaction energies,[3] and they can stabilize a system by 60 to 100 kcal/mol or more for big systems.[37,66,67] Among others, this was also shown for fullerenes.[68] Hence, our first example will discuss six model reactions of C$_{60}$ fullerene with ethene, benzene, naphthalene, or triphenylene. The formed products are either benzene,
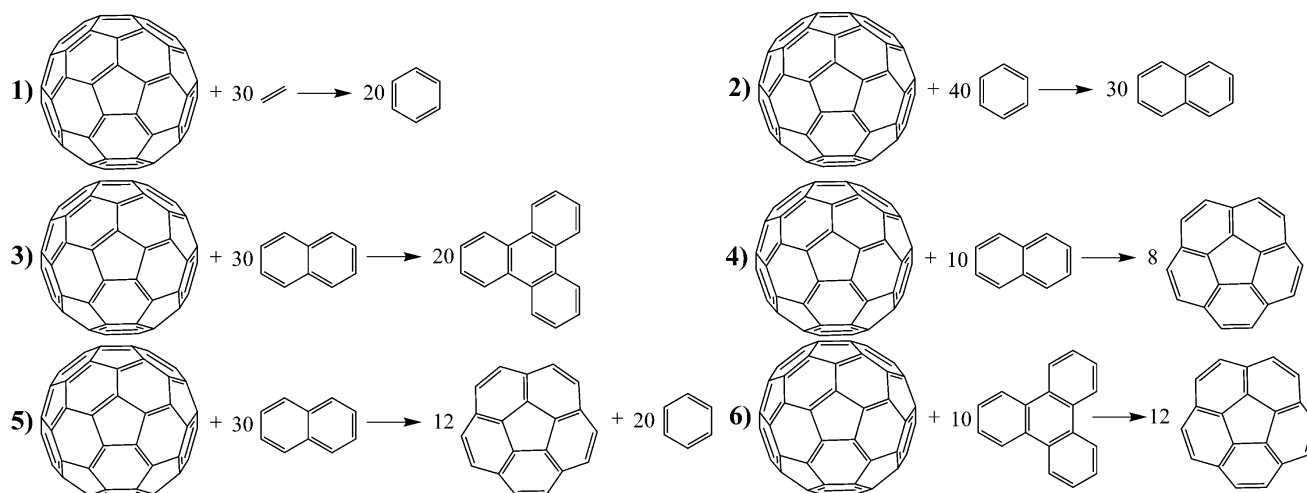

Figure 5. Lewis structures of six model reactions involving C$_{60}$ fullerene.

naphthalene, triphenylene, or corannulene (see Figure 5). Those fullerene reactions are challenging because the strain and special conjugation of the fullerenes compared to the other annulenes makes methodological error compensation unlikely, and the reaction energy range of several hundred kcal/mol is rather large.

Table 2 shows the results for the B3LYP-D3/def2-QZVP "reference" and the various approaches based on calculations

Table 2. Reaction Energies for the Fullerene Reactions 1−6 (see Figure 5)[a]

| no. | "reference" | B3LYP | deviation | | |
			B3LYP-D3	B3LYP-gCP	B3LYP-gCP-D3
1	−691.8	−43.1	−8.4	−32.1	2.6
2	−396.6	−15.2	−30.2	−4.6	−19.6
3	−442.8	29.0	−24.9	58.2	4.2
4	−42.7	−13.1	−3.8	−14.1	−4.7
5	134.3	−12.1	9.4	−18.8	2.8
6	157.4	−34.2	6.8	−50.2	−9.2
MD		−14.8	−8.5	−10.3	−4.0
MAD		24.5	13.9	29.7	7.2
MIN		−43.1	−30.2	−50.2	−19.6
MAX		29.0	9.4	58.2	4.2
error range		72.1	39.6	108.4	23.9

[a]"Reference" values in kcal/mol are based on B3LYP-D3/def2-QZVP calculations. Deviations from those reference values are shown for calculations with the 6-31G* basis set for plain B3LYP, B3LYP-D3, B3LYP-gCP, and B3LYP-gCP-D3. The deviations were computed as differences between those values and the reference method. Mean deviations (MDs), mean absolute deviations (MADs), minimum (MIN) and maximum (MAX) errors, and the error range for the set of those six reactions are given below.

with the 6-31G* basis. Like in the discussion above, we will skip the basis set name 6-31G* whenever it is clear in the text.

The first four reactions are very exothermic with reaction energies ranging between −690 and −40 kcal/mol, and the last

two reactions are endothermic with reaction energies around 135 to 160 kcal/mol. Statistical values averaged over these six reactions are also given in Table 2. The mean deviation (MD) for B3LYP is −14.8 kcal/mol, which is lowered by almost 11 kcal/mol by taking into account dispersion and BSSE effects in B3LYP-gCP-D3. The remaining MD of −4.0 kcal/mol for B3LYP-gCP-D3 can be attributed to the incompleteness of the basis. The effect of BSSE on the results can be further seen for the mean absolute deviations (MADs) and error ranges. Plain B3LYP yields an MAD of 24.5 kcal/mol and an error range of 72.1 kcal/mol. When BSSE-corrected, these values increase significantly to 29.7 and 108.4 kcal/mol, respectively. This indicates that a partial error compensation in B3LYP with a small basis set can give lower statistical deviations. The data also show that taking into account London dispersion effects is crucial, and only for B3LYP-gCP-D3, the MAD and error-range drop to 7.2 and 23.9 kcal/mol, respectively. To reduce the remaining errors due to basis set incompleteness, we recommend using at least a triple-ζ basis set whenever possible, which is nowadays a feasible task using efficient DFT codes.

The next two examples are applications discussed in 2010[69] and 2011[70] by Houk and co-workers, which were recently reviewed by the same group.[71] The authors discussed the importance of aromatic interactions on the stereoselectivity of cycloadditions. The reaction shown in Figure 6 describes a [4 + 3]-cycladdition between furan derivatives (substituted at position 2) with an oxoallylic system.[70] This oxoallylic system is formed in situ by ring-opening of a cyclopropanone. Depending on the orientation of the substituent of furan toward the oxoallyl and on the side at which the latter is attacked, four different endo-products can be formed. Experimentally it was shown that the ratio of these products depends on the type of substituent and whether ZnCl$_2$ is added as catalyst. Herein, we will only discuss the reaction of 2-methylfuran without any catalyst in the gas phase. The transition states are depicted in Figure 6 and called *syn*-I, *anti*-I, *syn*-II, or *anti*-II. The products are called *syn−endo*-I, *anti−endo*-I, *syn−endo*-II, and *anti−endo*-II in Figure 6, but they will not be considered further. The barrier heights are
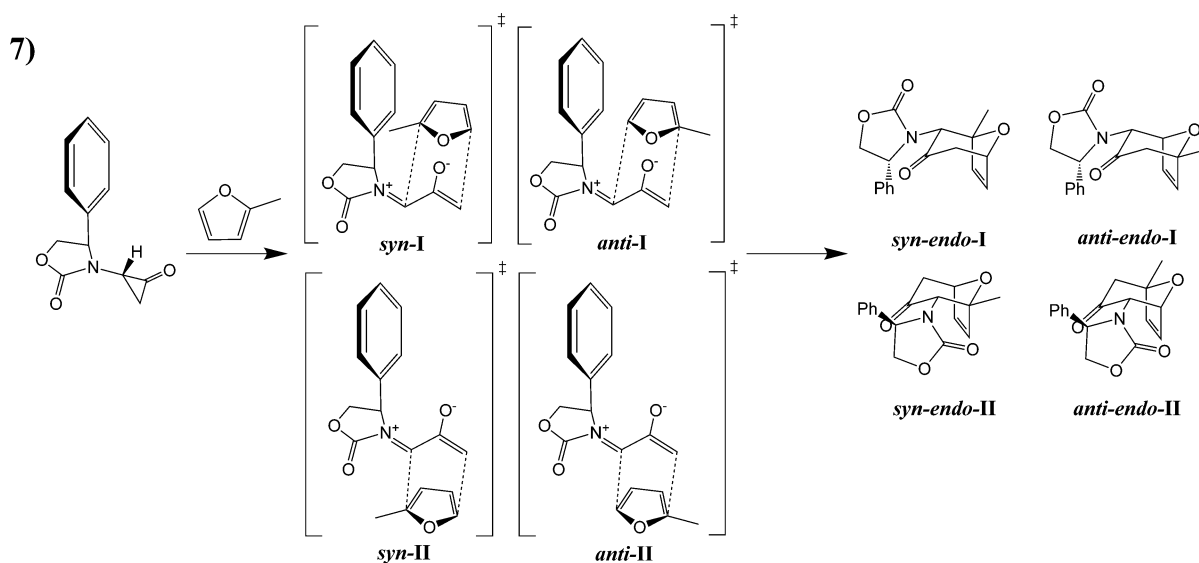

Figure 6. Four different transition states of a reaction between 2-methylfuran and a substituted cyclopropanone.[70] The cyclopropanone undergoes ring-opening to an oxyallyl, which reacts in a [4 + 3]-cycloaddition. Depending on the side of the attack and the orientation of the methyl group of 2-methylfuran, the four transition states are dubbed *syn*-I, *anti*-I, *syn*-II, and *anti*-II.

calculated with respect to the closed cyclopropanone. This is basically done to make our study consistent with previous ones. In general, however, one could also calculate barriers with respect to the opened species, a likely formed reactant-complex, but this is beyond the scope of this manuscript. To discuss the effects of dispersion and BSSE on the electronic activation energies it is again sufficient to compare the results with B3LYP-D3/def2-QZVP results.

The qualitative difference between B3LYP-D3 at the quadruple-ζ and at the 6-31G* level becomes very obvious for all four reaction barriers (see Table 3). While B3LYP/6-

Table 3. Electronic Activation Energies $\Delta E^{\ddagger}$ in kcal/mol for Four Different Reaction Paths of Reaction 7 (see Figure 6)[a]

method	$\Delta E^{\ddagger}$ (anti-I)	$\Delta E^{\ddagger}$ (syn-I)	$\Delta E^{\ddagger}$ (anti-II)	$\Delta E^{\ddagger}$ (syn-II)
B3LYP-D3/def-QZVP	−3.4	−4.6	−1.4	−1.9
B3LYP	6.8	5.5	7.2	6.1
B3LYP-D3	−6.0	−7.3	−4.0	−4.2
B3LYP-gCP	12.0	10.5	12.3	10.9
B3LYP-gCP-D3	−0.8	−2.2	1.1	0.5

[a]Values are shown for B3LYP-D3/def2-QZVP and for various B3LYP variants at the 6-31G* level.

31G* predicts positive barriers between 5.5 and 7.2 kcal/mol, the higher level of theory predicts all barriers to be negative (see below). The BSSE in this reaction is rather pronounced and shows that B3LYP/6-31G* artificially lowers the barriers by 5 kcal/mol. Adding a dispersion-correction lowers the barriers further such that B3LYP-D3 underestimates them by about 3 kcal/mol. Only in combination with the BSSE-correction gCP are the barriers in best agreement with the quadruple-ζ results; B3LYP-gCP-D3 overestimates them by 2.5 kcal/mol on average. The relative energies between the various transition states do not change significantly when comparing the different theoretical approaches with each other, an indication that the barriers are merely energetically shifted. This is also true when including enthalpic and entropic effects. Additional calculations performed by us show that the final Gibbs free energy barrier heights are between 10.5 and 13.5 kcal/mol, which is reasonable for a reaction at room temperature. Herein, we will not compare these results directly with experimental findings. First of all, it was seen in the previous publication on this reaction that only a qualitative assessment of the reaction pathways was possible and that the product ratios could not be explained by the differences in the activation barriers.[70] As mentioned in the Introduction, additional factors must be taken into account when comparing directly with experiment, and not all effects can be adequately addressed theoretically with reasonable computational effort. An agreement for B3LYP/6-31G* methods with experiment could be rather considered as a lucky hit, and we note in passing that this discussion is beyond the scope of the present work.

Therefore, also the last example will again consist of an analysis of dispersion and BSSE effects with reference to B3LYP-D3/def2-QZVP electronic energies. The Diels−Alder reaction between anthracene and a maleic anhydride derivative was taken from a study by Houk and co-workers.[69] For the reaction shown in Figure 7 only one product is expected. In their original publication, Houk and co-workers also investigated substituted compounds yielding two diastereomers. We
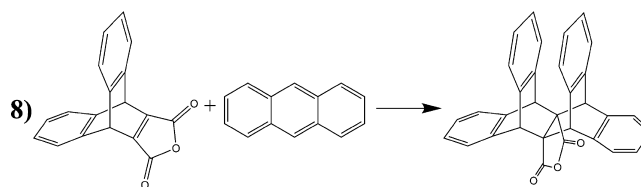

Figure 7. Diels−Alder reaction of a maleic anhydride derivative with anthracene.

also examined effects in those compounds, but as the conclusions were basically all the same, we will only discuss the unsubstituted case for the sake of simplicity. Table 4 shows reaction energies and barrier heights for the forward and backward barriers at the various levels of theories that were also discussed for the previous examples.

Table 4. Electronic Reaction Energies ΔE and Forward and Backward Barriers $\Delta E^{\ddagger}$ in kcal/mol for the Diels−Alder Reaction 8 (see Figure 7)[a]

method	ΔE	$\Delta E^{\ddagger}_{forward}$	$\Delta E^{\ddagger}_{backward}$
B3LYP-D3/def-QZVP	−26.3	14.2	40.5
B3LYP	−12.0	32.3	44.3
B3LYP-D3	−37.0	6.7	43.6
B3LYP-gCP	−5.1	37.7	42.7
B3LYP-gCP-D3	−30.0	12.1	42.1

[a]Values are shown for B3LYP-D3/def2-QZVP and for various B3LYP variants at the 6-31G* level.

The results for the reaction energies resemble those discussed for the fullerene reactions. The systems, particularly the product, are strongly stabilized by intramolecular dispersion effects, but also the BSSE has a sizable contribution of 7 kcal/mol. Only the B3LYP-gCP-D3 results come closest to the "reference" with −30.0 kcal/mol, which is an underestimation of almost 4 kcal/mol. The forward barrier is affected by the same effects as discussed for the previous example, and again only B3LYP-gCP-D3 comes closest to the reference with an underestimation of about 2 kcal/mol. The dispersion effects for the forward reaction are again significant with almost 26 kcal/mol. The results for the backward barrier show that a systematic (sometimes partial) error compensation, in which the missing dispersion effects and the BSSE have opposite signs, cannot always be expected. Because the dispersion effects of the product and the transition state are very similar, the barrier is only lowered by 0.7 kcal/mol by the DFT-D3 correction, and the missing dispersion effects in B3LYP/6-31G* do not play such a major role. The difference between B3LYP/6-31G* and the reference is about 4 kcal/mol.

The BSSE correction, on the other hand, lowers the barrier further by a significant amount of 1.6 kcal/mol. The difference to the reference is lowered for B3LYP-gCP-D3 to about 2 kcal/mol. These results again show the benefit of including corrections for dispersion and BSSE effects. They also show that users should not rely on error compensation effects, as it cannot be foreseen which signs those errors have. Under certain circumstances, the fortuitous error compensation can yield acceptable results, but as the last example shows, sometimes these errors point in the same direction, leading to larger deviations from more reliable reference values. Therefore, we have to warn about B3LYP/6-31G* as a standard black-box tool due to its unsystematic errors. Without additional costs,

one can easily take into account dispersion and BSSE effects through the D3 and gCP corrections, and the resulting method becomes, thus, more robust and controllable in terms of its inherent errors.

4. CONCLUSIONS

Our study unraveled the error compensations in the often criticized B3LYP/6-31G* model chemistry for thermochemical problems, and we propose B3LYP-gCP-D3/6-31G* as a more robust and physically sound substitute. The new scheme retains the features of B3LYP/6-31G*, a well-known hybrid density functional approximation combined with a small basis set (i.e., low computational costs) but at the same time removes the two major deficiencies: missing London dispersion effects and basis set superposition error.

Benchmark results on the GMTKN30 database show a statistical improvement (e.g., WTMAD decreases from 8.75 to 6.87 kcal/mol) of B3LYP-gCP-D3/6-31G* over plain B3LYP/6-31G*. Compared to highly accurate reference data, B3LYP-D3/6-31G* typically exhibits significant overbinding that could be attributed to BSSE due to the small basis set. This could effectively be removed by using the new BSSE-correction method gCP. It was statistically shown that the partial error compensation effects in the plain B3LYP/6-31G* model chemistry are unsystematic and strongly depend on the chemical nature of the test set. The improvement of the gCP-D3 scheme over plain B3LYP is largest for systems with noncovalent interactions, but also the performance for reaction energies, barrier heights, or isomerization reaction is enhanced significantly.

This was further analyzed in three applications to reactions of C_{60} with arenes, a Diels−Alder reaction, and barrier heights of a [4 + 3] cycloaddition. We could show that plain B3LYP with small basis sets can benefit from error compensation if the amount of missing dispersion effects and intramolecular BSSE are of similar size. However, it was also shown that this compensation is unsystematic even for one reaction regarding forward and backward reaction energy, respectively, and therefore it is, in general, not foreseeable. B3LYP-gCP-D3/6-31G*, on the other hand, offers a much more reliable and robust description of these reactions. In comparison to results with the large def2-QZVP basis, its superior performance over B3LYP/6-31G* was clearly demonstrated.

In summary, the direct comparison between B3LYP-D3/def2-QZVP and B3LYP-gCP-D3/6-31G* showed that although major deficiencies are removed, the small basis set is limiting the accuracy; the largest remaining error is expected to be the basis set incompleteness error. In general, we thus recommend using at least basis sets of triple-ζ quality (such as def2-TZVP, 6-311G(2df,2p)) in standard applications. However, if, because of a lack of computer resources or the size of the system, only a double-ζ basis is feasible, we strongly recommend the gCP-D3 approach. It can readily be used with all DFT functionals and a selection of small basis sets (see ref 27 for details). If an inexpensive and "qualitative-level" DFT black-box method is sought, we strongly urge the use of B3LYP-gCP-D3/6-31G* over B3LYP/6-31G* because of a better physical foundation and robustness. Note finally that we have unraveled here the error compensations in B3LYP/6-31G* calculations for isolated molecules (gas phase) without any account for vibrational and/or entropic contributions. If comparisons to experimental data obtained in solution are made, one should compute these additional thermodynamic terms as accurately as possible and not rely on other nonphysical compensation effects (see ref 72 for further discussion on a practical example).

5. COMPUTATIONAL DETAILS

All GMTKN30 calculations were carried out with Turbomole[73,74] 6.3. The 6-31G*[6] basis set and the B3LYP functional[4,5] were employed as implemented in Turbomole. For the def2-QZVP basis set calculations, the resolution of the identity (RI-J) approximation for the Coulomb part[75] is used. All auxiliary basis functions were taken from the Turbomole basis set library.[76,77] If not noted otherwise, the Turbomole grid $m5$[77] was used and the wave function was converged to an energy error below 10^{-8} E_h.

The DFT-D3 correction[33,34] was applied with our group's program *dftd3*. Becke−Johnson (BJ) damping[34,78,79] is the default damping function used, i.e., DFT-D3 always corresponds to DFT-D3(BJ). The three damping and short-range parameters in the D3 method were used as originally determined[34] for all B3LYP-D3 variants. The gCP correction[27] was also applied with our group's program *gcp*. Both programs are freely available from the author's Web site.[47] Additionally, the gCP-D3 energy correction can be directly obtained by a Web service to be found on the author's Web site.

The structures for the potential energy curve in Figure 1 were optimized at the B3LYP-D3/def2-TZVP[40] level of theory with ORCA 2.9.1[48] using the RIJCOSX approximation.[80−82] Subsequent single-point calculations on these structures were also performed with ORCA, and the internal DFT-D3 correction was used. The same B3LYP functional as in Turbomole was used. The convergence criteria for the wave function and the gradient were requested according to the keywords TightOpt and TightSCF.

The structures for the fullerene reactions 1−6 were optimized at the B3LYP-D3/def2-TZVP level of theory. All structures for the two cycloaddition reactions were taken from the literature.[69,70] For the fullerene reactions, Turbomole was used, and for the cycloadditions, a modified version of ORCA 2.9[48] was used.

■ ASSOCIATED CONTENT

ⓢ Supporting Information

The definition of the frozen coordinates for Figure 1, numerical data for Figures 2−4, structural data for the fullerene reactions, and single-point energies for the application section. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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