

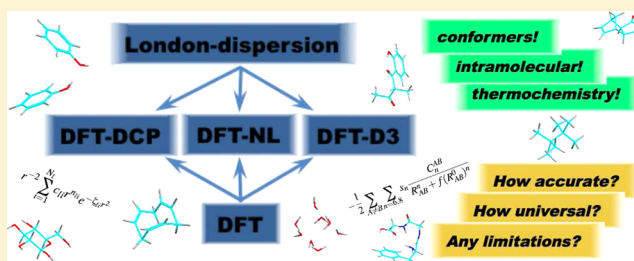
# How Do DFT-DCP, DFT-NL, and DFT-D3 Compare for the Description of London-Dispersion Effects in Conformers and General Thermochemistry?

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## S Supporting Information

**ABSTRACT:** The dispersion-core-potential corrected B3LYP-DCP method (Torres and DiLabio *J. Phys. Chem. Lett.* **2012**, *3*, 1738) is for the first time thoroughly assessed and compared with the B3LYP-NL (Hujo and Grimme *J. Chem. Theory Comput.* **2011**, *7*, 3866) and B3LYP-D3 (Grimme et al. *J. Comput. Chem.* **2011**, *32*, 1456) methods for a broad range of chemical problems that particularly shed light on intramolecular London-dispersion effects in conformers and general thermochemistry. The analysis is based on a compilation of 473 reference cases, the majority of which are taken from the GMTKN30 database (Goerigk and Grimme *J. Chem. Theory Comput.* **2010**, *6*, 107; **2011**, *7*, 291). The results confirm previous findings that B3LYP-DCP indeed predicts very good binding energies for noncovalently bound complexes, particularly with small basis sets. However, problems are identified for the description of intramolecular effects in some conformers and chemical reactions, for which B3LYP-DCP sometimes gives results similar or worse than uncorrected B3LYP. Surprisingly large errors for total atomization energies reveal an unwanted influence of the DCPs on the short-range electronic structure of the investigated systems. However, a recently modified carbon potential for B3LYP-DCP (DiLabio et al. *Theor. Chem. Acc.* **2013**, *132*, 1389) was additionally tested that seems to solve most of those problems and provides improved results. An overall comparison between all tested methods shows that B3LYP-NL is the most robust and accurate approach, closely followed by B3LYP-D3. This is also true when small basis sets of double- $\zeta$  quality are applied for which those methods have not been parametrized. However, binding energies of noncovalently bound complexes can be more strongly influenced by basis-set superposition-error effects than for B3LYP-DCP. Finally, it is noted that the DFT-D3 and DFT-NL schemes are readily applicable to a large range of chemical elements and they are therefore particularly recommended for more general applications.



## 1. INTRODUCTION

London-dispersion<sup>1</sup> is a ubiquitous, attractive, many-electron correlation effect that is crucial not only for the structural stability of biomolecules<sup>2–6</sup> or other large molecular aggregates<sup>7,8</sup> but also for various thermochemical properties of medium-sized systems, such as reaction energies or barrier heights.<sup>9–11</sup> Because of its universality, a proper description of London-dispersion is a prerequisite in any accurate computational treatment. Kohn–Sham density functional theory<sup>12,13</sup> (DFT) has become the major methodology in computational quantum chemistry, and although it is in principle an exact theory, it is now well-established that current approximations to the “true functional” cannot describe London dispersion in a physically sound way.<sup>14–18</sup> The past 10 years have seen great effort to overcome this problem, and various strategies for the treatment of London dispersion with DFT have been developed that can be classified into four categories:<sup>19,20</sup>

(1) Density functionals parametrized against noncovalent interaction energies, such as methods using reparametrized forms of the Perdew–Wang<sup>21</sup> exchange functional, e.g., the mPW exchange or the mPW1PW hybrid functionals.<sup>22</sup> Also very popular are Zhao’s and Truhlar’s highly parametrized

M05<sup>23</sup> and M06<sup>24</sup> classes of density functionals and subsequent developments.<sup>25–28</sup>

(2) Density functionals that directly include a nonlocal portion allowing for the description of London-dispersion. The van-der-Waals density functional<sup>29</sup> (vdw-DF) combines a standard exchange-correlation functional with an additional nonlocal energy term. Either this nonlocal term is added in a post-SCF fashion to the converged result of the underlying (semi)local density functional, or it is already included in the SCF itself, allowing the electron density to adjust to London-dispersion effects. Subsequent developments such as vdw-DF2,<sup>30</sup> VV09,<sup>31</sup> and VV10<sup>32</sup> use different forms of the nonlocal term. Hujo and Grimme have adjusted the VV10 nonlocal functional contribution for combinations with various standard density functionals (DFT-NL).<sup>33</sup> A different way of directly taking London-dispersion effects into account is to include information from virtual orbitals, as done for instance in the active research field of the random phase approximation (RPA) methods.<sup>34–38</sup> Note that double-hybrid density functionals,

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such as B2PLYP,<sup>39</sup> also include a term depending on virtual orbitals but that London-dispersion effects are not completely incorporated and that additional dispersion corrections have to be applied to them.<sup>40,41</sup>

(3) Additive dispersion corrections that can be combined with standard density functionals ensuring the correct asymptotic behavior of the dispersion energy per construction. These corrections can be divided into two subcategories:

(a) To this category belong Grimme's density-independent, atomic pairwise corrections DFT-D1,<sup>42</sup> DFT-D2,<sup>43</sup> and DFT-D3.<sup>9,44</sup> Note that the latter is additionally dependent on the geometry of the investigated system and therefore more system-specific than the two older corrections.

(b) Density-dependent corrections, such as the dipole exchange-hole model by Becke and Johnson (XDM),<sup>45–49</sup> the DFT+vdw/vdW approach by Tkatchenko and Scheffler,<sup>50</sup> and the dDsC correction by Steinmann and Corminboeuf.<sup>51</sup>

(4) Effective one-electron potentials designed to mimic many-electron London-dispersion effects. This approach is inspired by the idea of effective-core-potentials (ECPs),<sup>52</sup> normally used to describe the core electrons of heavier elements. In the context of London dispersion, these potentials are also applied to light elements and specifically adjusted for each element to reproduce interaction energies of benchmarks of noncovalently bound dimers. They can be adjusted for any standard functional and influence the SCF step itself. R  thlisberger and co-workers developed the dispersion-corrected atom-centered potentials (DCACPs) containing local and nonlocal contributions.<sup>53–56</sup> Recently, a second version of this approach (DCACP2) has been proposed by Jordan and co-workers.<sup>57</sup> In addition to DCACP, local potentials were introduced by Sun et al. (local atomic potentials; LAPs)<sup>58</sup> and by DiLabio and co-workers (dispersion-corrected potentials; DCPs).<sup>59–62</sup> The latest version of the latter approach (“third generation DCPs”) is based on the popular B3LYP<sup>63,64</sup> functional and contains both local and semilocal terms.<sup>65</sup>

The methods belonging to the first three categories have been thoroughly tested and compared with each other in applications to inter- and intramolecular London-dispersion effects influencing for instance interaction energies, geometries, and also general thermochemistry.<sup>9–11,66–78</sup>

Of the methods belonging to the third category, in particular Grimme's DFT-D3 correction has received a lot of attention and has been used successfully in various studies proving its universality, including studies on general main group thermochemistry,<sup>9,10</sup> geometries,<sup>79,80</sup> relative energies in conformers of organic-chemical or biological relevance,<sup>9,10,80–83</sup> or noncovalently bound dimers in nonequilibrium geometries,<sup>84</sup> to only name a few examples (for applications of other additive dispersion corrections, see e.g. refs 6, 69–71, 73–78). Recently, DFT-D3 has been compared to other methods belonging to the first three categories for interaction energies in very large complexes, and it has been shown that it reproduces the important long-range dispersion contributions very well.<sup>8</sup>

Density functionals belonging to the first category have also received a lot of attention, in particular the M05 and M06 classes of functionals. There is no doubt that they belong to the most accurate DFT methods for thermochemistry,<sup>10,24</sup> but when it comes to the description of noncovalent interaction energies, it is important to distinguish whether the investigated systems are in their equilibrium geometry or not. Due to the way their parameters have been determined, these methods can

still describe short- and medium-range effects, but it has been established that the asymptotic region of the dispersion energy is still not correct and that also these functionals do benefit from additional dispersion corrections such as DFT-D3.<sup>10,84</sup>

The methods belonging to the second category (vdw-DF and VV10/DFT-NL) have been tested for noncovalent interactions, thermochemistry, and geometries, and it has been shown that they can treat specific difficult situations better than DFT-D3.<sup>33,66,85</sup> However, they have mostly been applied with larger basis sets, and for instance results for double- $\zeta$  basis sets are still rare.

Similar assessments of the methods belonging to category 4 and comparisons with other popular approaches are scarce. Most applications of these effective one-electron potentials concentrate on weakly bound complexes,<sup>86–90</sup> and only a very small number of reactions involving intramolecular London dispersion have been assessed with earlier versions of DFT-DCP,<sup>60,91</sup> for instance, in a study on rate constants and activation energies of six radical-clock reactions, it was observed that the DCP corrections increased the activation energies by about 1 kcal mol<sup>−1</sup> (see Supporting Information of that specific study),<sup>91</sup> while other dispersion corrections did not significantly influence the results for the same reactions. The meaning of this remained unclear, and those numbers make it worthwhile to inspect the DCP approach for a broader range of systems and reactions.

To the best of our knowledge and at the time of submission of this study, there has not been a thorough assessment carried out for the application of dispersion-corrected potentials—and related approaches—for intramolecular dispersion in conformers and general thermochemistry. Given the interest of the community in modern approaches to treat London dispersion, this study closes this gap and aims to provide a fair overview of the applicability of such methods. The focus herein lies on a recent B3LYP-DCP development that is currently applicable to systems containing H, C, N, and O. It has been shown to give good interaction energies of noncovalently bound dimers in the S66,<sup>92</sup> S22,<sup>93</sup> and HSG-A<sup>65</sup> benchmark sets, even with small basis sets. Herein, B3LYP-DCP is briefly assessed for interaction energies in weakly bound complexes before focusing on relative energies of conformers and basic thermochemical properties, such as total atomization energies, reaction energies, and barrier heights. Most test cases are taken from the large GMTKN30 database for general main group thermochemistry, kinetics, and noncovalent interactions,<sup>41,94</sup> for which results for more than 50 dispersion-corrected DFT methods have been published,<sup>10,33</sup> but also additional test sets<sup>81,82,95</sup> will be analyzed.

B3LYP-DCP is compared with B3LYP-NL, which is of particular interest because both methods influence the electron density. However, a direct comparison of these approaches with each other has not been undertaken before, and this study provides first insights into this aspect. Second, B3LYP-NL has only been benchmarked for the large def2-QZVP basis set, whereas in this study also basis set effects and results for a smaller double- $\zeta$  basis are discussed. Additionally, B3LYP-D3 in its latest version, including Becke-Johnson damping,<sup>9</sup> is evaluated for the same systems.

In the following section, the theoretical foundations of the three evaluated methods are shortly explained. In section 3, information on all computational details are given, while in section 4 all results are presented and analyzed.

## 2. THEORETICAL BACKGROUND OF THE THREE DISPERSION CORRECTIONS

**2.1. The DFT-D3 Correction.** DFT-D3<sup>44</sup> is an atomic pairwise correction that is added to the result of a converged standard DFT calculation. This correction comes at no computational cost, making it easily applicable to large systems. Currently, DFT-D3 allows treatment of the first 94 elements of the periodic table and provides therefore the means to treat London-dispersion effects in a broad range of chemical systems. It is implemented in many major quantum chemistry codes and also available for free as a stand-alone program.<sup>96</sup> About a year after its first publication, the original DFT-D3 method was modified<sup>9</sup> by including a damping function originally defined by Becke and Johnson.<sup>46–48</sup> This modified DFT-D3 is sometimes called DFT-D3(BJ), but because only DFT-D3(BJ) is used in this study, the suffix in parentheses is skipped in the following. The energy contribution from this latest DFT-D3 variant reads:<sup>9</sup>

$$E_{\text{disp}}^{\text{DFT-D3}} = -\frac{1}{2} \sum_{A \neq B} \sum_{n=6,8} s_n \frac{C_n^{AB}}{R_{AB}^n + f(R_{AB}^0)^n} \quad (1)$$

where the sum is over all atom pairs  $AB$  in the system.  $n$  equals 6 and 8, introducing an  $R_{AB}^{-6}$  long-range and an  $R_{AB}^{-8}$  medium-range behavior of the atomic-pair contribution to the dispersion energy, where  $R_{AB}$  is the internuclear distance. The  $C_n^{AB}$ 's are the averaged (isotropic)  $n$ th-order dispersion coefficients for atom pair  $AB$ . In contrast to the more empirical DFT-D1 and DFT-D2 versions, DFT-D3 calculates these atomic-pair dispersion coefficients on the fly from atomic dispersion coefficients that have been derived from first principles and that additionally depend on the geometrical environment of each atom (see the original DFT-D3 reference for more details).<sup>44</sup> The  $s_n$ 's are global scaling factors, and for common density functionals,  $s_6$  is set to unity to ensure the correct asymptotic behavior of the dispersion energy, while  $s_8$  is adjusted for each functional.  $f(R_{AB}^0)$  is a damping function according to Becke and Johnson:<sup>46–48</sup>

$$f(R_{AB}^0) = a_1 R_{AB}^0 + a_2 \quad (2)$$

with

$$R_{AB}^0 = \sqrt{\frac{C_8^{AB}}{C_6^{AB}}} \quad (3)$$

$a_1$  and  $a_2$  are free fit parameters. As seen in eq 2, this damping function leads to a constant contribution of the dispersion energy to the total correlation energy from each spatially close pair of atoms, which is in accordance with the finding that even at the unified-atom limit there is an attractive dispersion contribution.<sup>97</sup> Thus, DFT-D3 in its latest version ensures a physically correct description of the dispersion energy in the short-range and long-range regions.

The parameters  $s_8$ ,  $a_1$ , and  $a_2$  control the connection between the DFT-D3 and the short-range DFT potentials, and they are the only empirically adjusted parameters in this approach, fitted for each functional by a least-squares fit to a set comprising 130 benchmark values, including the S22 and S22+<sup>44</sup> benchmark sets, and various other benchmark sets for noncovalent interaction energies of dimers and for relative energies of conformers. The parameters were determined with the large def2-QZVP quadruple- $\zeta$  basis set. In subsequent studies by others,<sup>65,67</sup> it has been argued that consequently DFT-D3

should be a suitable correction only when large basis sets are applied but that these parameters should be refitted for applications with smaller basis sets. However, it has also been shown that this is at least not true for applications with triple- $\zeta$  basis sets.<sup>10</sup> When using smaller basis sets, it is of course expected that the basis-set superposition error (BSSE) influences the results; however, it has been discouraged from trying to fit BSSE effects into the DFT-D3 dispersion correction, as BSSE is expected to decay faster than the dispersion energy, and thus two entirely different potentials should be used to describe two different problems.<sup>98,99</sup> In fact, Kruse and Grimme showed that DFT-D3 does not need to be refitted for small basis sets when their new gCP correction for inter- and intramolecular BSSE is applied.<sup>98</sup> This new gCP correction in combination with DFT-D3, B3LYP, and the 6-31G\* basis set has also been shown to be more robust and reliable for thermochemistry than the corresponding standard B3LYP/6-31G\* model chemistry.<sup>99</sup>

**2.2. The B3LYP-DCP Approach.** In the DFT-DCP approach, atom-centered potentials  $U(r)$  are applied during the SCF of the form:

$$U_l(r) = r^{-2} \sum_{i=1}^{N_l} c_{li} r^{n_{li}} e^{-\zeta_{li} r^2} \quad (4)$$

where  $l$  stands for the angular momenta (the maximum  $l$  for H is p, and for C, N, O it is f),  $N_l$  is the number of Gaussian functions for each  $l$ ,  $n_{li}$  is the power of  $r$ , and  $c_{li}$  and  $\zeta_{li}$  are the coefficients and exponents for the Gaussian functions, respectively. For B3LYP-DCP,<sup>65</sup> all  $n_{li}$  are fixed to a value of 2, while the coefficients and exponents have been fitted to interaction energies of 17 noncovalently bound dimers, with each dimer being represented by four to six different distances between its monomers. So far, DCPs have been determined for the elements H, C, N, and O. The parameters have been fitted using the 6-31+G(2d,p) basis set, and two sets of DCPs have been developed. The first set has been obtained by fitting the parameters without applying any BSSE corrections, thus attempting to correct for BSSE within the DCP, in contrast to the argumentation outlined in the previous section on DFT-D3. The second set has been determined while applying the Boys and Bernardi<sup>100</sup> counterpoise (CP) corrections, and it has been recommended to use them in combination with CP corrections. Although fitted to a specific double- $\zeta$  basis set, both sets of DCPs were recommended for use with a large range of basis sets. Studies on the S66 and S22 databases and on a benchmark set containing dimers taken from an HIV-II protease crystal structure found that the optimal basis set for B3LYP-DCP is 6-31+G(2d,2p).

The advantage of DCP and related approaches is that dispersion effects are included on the electronic-structure level, allowing the electron density to adjust to these effects. Also, DCPs can be used with any quantum chemistry code that supports ECPs. A practical disadvantage is that for each element enough reliable reference data have to be found, which can be difficult when extending these methods to heavier elements. In its current form, B3LYP-DCP is only applicable to standard organic compounds.

Others have questioned if a many-electron correlation effect like London dispersion can actually be described by one-electron potentials.<sup>19</sup> Given that DCP, LAP, or DCACP rely on Gaussian functions, it was also argued that these potentials decay too quickly and do not show the correct asymptotic  $R^{-6}$



long-range behavior.<sup>19,88,90</sup> B3LYP-DCP has been fitted to nonequilibrium geometries, and consequently it appears that its long-range behavior has improved, as can be seen from tests conducted by DiLabio and co-workers.<sup>101</sup> Therefore, this topic is of no relevance to this study. Note that the long-range behavior of DCAPs has also been recently discussed.<sup>57</sup>

A second interesting issue is the short-range behavior of DCPs. The Gaussian exponents are relatively small compared to standard ECPs,<sup>65</sup> and therefore it has been outlined that these diffuse functions should not influence the short-range regime.<sup>61</sup> The test cases discussed herein allow us to further analyze this point.<sup>102</sup>

**2.3. The DFT-NL Approach.** DFT-NL<sup>33</sup> is a slightly modified variant of the VV10 functional,<sup>32</sup> which belongs to the class of van-der-Waals density functionals.<sup>29</sup>

In this approach, a standard exchange-correlation functional  $E_{XC}^{DFT}$  is combined with a nonlocal (NL) correlation contribution  $E_C^{NL}$  that allows the description of London-dispersion effects:

$$E_{XC}^{DFT-NL} = E_{XC}^{DFT} + E_C^{NL} \quad (5)$$

In VV10 and DFT-NL, the nonlocal term has the general form:

$$E_C^{NL} = \int dr \rho(r) \left[ \frac{1}{32} \left[ \frac{3}{b^2} \right]^{3/4} + \frac{1}{2} \int dr' \rho(r') \phi(r, r') \right] \quad (6)$$

Equation 6 describes a double integral evaluating the electron density  $\rho$  over two different points in space,  $r$  and  $r'$ . The correlation of the densities at those two points is described by the kernel  $\phi(r, r')$ . The specific form of  $\phi(r, r')$  can be found in ref 32; in the present context, it suffices to know that it contains the same short-range attenuation parameter  $b$  that is also present in eq 6 and which is adjusted to the interaction energies of the S22<sup>93</sup> set—in the case of DFT-NL by using the large def2-QZVP basis set.

The original VV10 method uses the rPW86PBE<sup>103,104</sup> GGA functional for  $E_{XC}^{DFT}$ , whereas Hujo and Grimme, who introduced the more general name DFT-NL,<sup>33</sup> fitted eq 6 to two different GGA functionals and additionally to three hybrid functionals. In all of these cases, the parameter  $b$  was readjusted to best reproduce the S22 interaction energies. Herein, only the B3LYP-NL method is considered.

In DFT-NL the nonlocal term can either be evaluated in a post-SCF fashion based on the converged density of the underlying exchange-correlation functional or it is fully included in the SCF procedure. The first approach was shown to be a valid approximation if the electron density itself is not changed significantly by dispersion effects. However, to allow a better comparison with the DCP approach, which also allows a variation of the density compared to its underlying functional, the second approach is chosen in this work.

### 3. COMPUTATIONAL DETAILS

All calculations discussed herein were carried out with ORCA 2.9.1.<sup>105,106</sup> In some cases, additional double-checks were carried out with Gaussian 09<sup>107</sup> to ensure transferability of the DCPs and to check that outliers in the results were not artifacts but also reproducible with a second program. The B3LYP version in the original form<sup>63,64</sup> with VWN-5<sup>108</sup> LDA

correlation was used, in contrast to the default version in Gaussian with VWN-3 and to which the DCPs had been fitted. However, tests showed that the differences in the relative energies discussed in this paper are only marginal and that the DCPs can be easily transferred to the B3LYP version with VWN-5. The SCF energy convergence criterion was set to  $10^{-8}$   $E_h$  (ORCA keyword *tightscf*), and the largest ORCA quadrature grid of size 7 was applied. For all calculations, extended-Hueckel initial guesses for the orbitals were carried out. All systems were analyzed with the 6-31+G(2d,2p)<sup>109,110</sup> double- $\zeta$  and the def2-QZVP<sup>111</sup> quadruple- $\zeta$  basis sets; where possible B3LYP/def2-QZVP single-point energies were taken from previous studies on the GMTKN30 database,<sup>9</sup> and double-checks ensured that these results are practically identical with the ORCA values based on slightly different technical settings. Benchmark sets involving negatively charged species (the G21EA and WATER27 test sets) were additionally treated with diffuse s and p functions for non-hydrogen atoms that were taken from Dunning's aug-cc-pVQZ<sup>112</sup> basis; the resulting basis set is called aug'-def2QZVP. While def2-QZVP calculations converged without any problems, convergence problems were frequently observed for larger delocalized systems in the 6-31+G(2d,2p) calculations. The diffuse functions were identified to cause this technical problem, which could be solved by changing the convergence technique to Newton–Raphson SCF (ORCA keyword *nrsf*), sometimes additionally augmented with a Hessian step (ORCA keyword *ahsf*). The DFT-D3 correction with Becke-Johnson damping<sup>9,44</sup> was applied to both B3LYP/6-31+G(2d,2p) and B3LYP/def2-QZVP levels of theory with the originally published parameters.<sup>9</sup> In the case of B3LYP-DCP/6-31+G(2d,2p), the DCP parameters were applied that had been fitted without counterpoise corrections.<sup>65</sup> A large basis set like def2-QZVP, however, is almost BSSE free, which is why it seemed more appropriate to apply the DCPs fitted to CP-corrected results in B3LYP-DCP/def2-QZVP calculations. This choice was verified by additional calculations with the other set of DCPs for the S22 test set, which showed larger deviations (see Table S1). All B3LYP-NL<sup>33</sup>/6-31G+(2d,2p) calculations were carried out by applying the nonlocal correction self-consistently (ORCA keyword *scnl*) with a special integration grid of size 4 (ORCA keyword *vdwgrid 4*).

### 4. RESULTS AND DISCUSSION

Most test sets in this study are taken from the GMTKN30<sup>41,94</sup> database for general main group thermochemistry, kinetics, and noncovalent interactions, comprising 841 data points that are organized into 30 benchmark sets and based on accurate high-level quantum chemical or experimental reference values. Due to the limitation of the B3LYP-DCP approach to H, C, N, and O, some of the original GMTKN30 test sets have to be discarded or their size is reduced. In a few cases, this reduction is significant, and consequently the entire test sets are discarded as well. Also, test sets that are considered as irrelevant in this context, because B3LYP itself has been shown to be problematic, are left out. The remaining test cases are extended by three additional sets. The entire compilation comprises 473 entries organized into 21 benchmark sets and is listed in Table 1. Note that the original name of all benchmark sets is maintained to ensure consistency, even if some of them are smaller than in the original GMTKN30 publications. In the present study, this compilation of benchmark sets is divided into four categories, and each category is discussed separately: *noncovalently bound complexes*, *relative energies of conformers*,

**Table 1. Overview of the Benchmark Sets According to Their Categories Discussed in This Study<sup>a</sup>**

benchmark set	description	# of entries <sup>b</sup>
noncovalently bound complexes		
S22	binding energies of noncovalently bound dimers	22
ADIM6	interaction energies of <i>n</i> -alkane dimers	6
WATER27	binding energies of water, H <sub>3</sub> O <sup>+</sup> (H <sub>2</sub> O) <sub><i>n</i></sub> and OH <sup>−</sup> (H <sub>2</sub> O) <sub><i>n</i></sub> clusters	27
relative energies of conformers		
ACONF	relative energies of alkane conformers	15
SCONF	relative energies of sugar conformers	17
PCONF	relative energies of phenylalanyl-glycyl-glycine tripeptide conformers	10
TPCONF*	relative energies of biologically relevant tetrapeptide conformers of the form ACE-ALA-X-ALA-NME, with X being GLY or SER	8
MCONF*	relative energies of melatonin conformers	51
basic properties		
W4-08	total atomization energies of small molecules	41 (99)
W4-11*	extended version of W4-08 with additional larger organic molecules	70 (140)
G21EA	adiabatic electron affinities	11 (25)
G21IP	adiabatic ionization potentials	13 (36)
PA	adiabatic proton affinities	8 (12)
BH76	barrier heights of hydrogen transfer, heavy atom transfer, nucleophilic substitution, unimolecular and association reactions	38 (76)
BHPERI	barrier heights of pericyclic reactions	22 (26)
reaction energies		
BH76RC	reaction energies of the BH76 set	17 (30)
G2RC	reaction energies of selected G2/97 systems	12 (25)
RSE43	radical stabilization energies	28 (43)
DARC	reaction energies of Diels–Alder reactions	14
BSR36	bond separation reactions of saturated hydrocarbons	36
ISO34	isomerization energies of small and medium-sized organic molecules	34
ISOL22	isomerization energies of large organic molecules	14 (22)

<sup>a</sup>Most benchmark sets are part of the GMTKN30 database,<sup>41,94</sup> while some were taken from other studies and are marked with an asterisk.<sup>81,82,95</sup> <sup>b</sup>The numbers in parentheses show the size of the original benchmark set including systems with elements other than H, C, N, or O.

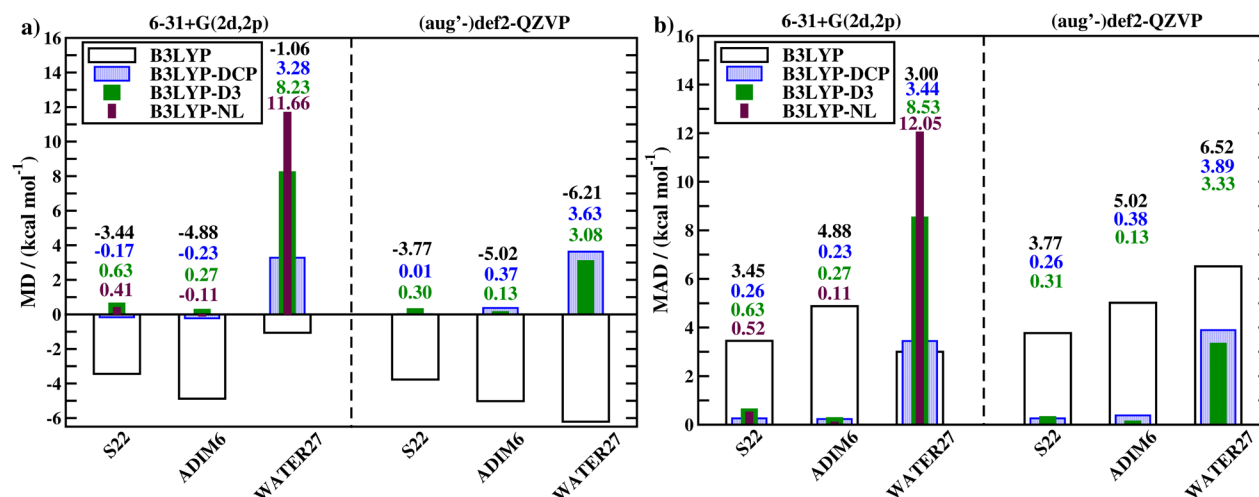
*basic properties*, and *reaction energies*. All results are shown in the SI in Tables S1–S21.

**4.1. Noncovalently Bound Complexes.** First, three benchmark sets for noncovalently bound complexes are discussed, all taken from GMTKN30. Figure 1 shows all mean deviations (MDs)—with deviations calculated as differences between the results for an evaluated method and the reference values—and mean absolute deviations (MADs). We start our discussion with Hobza's S22<sup>93</sup> set of noncovalently bound dimers combined with Sherrill's improved reference values.<sup>113</sup> As expected, pure B3LYP used with the 6-31+G(2d,2p) and def2-QZVP basis sets underbinds the complexes, resulting in highly negative MDs of around −3.4 kcal mol<sup>−1</sup> and −3.8 kcal mol<sup>−1</sup>, respectively, and MADs of the same absolute magnitude. B3LYP-DCP shows significant improvements with MDs being close to zero (−0.17 kcal mol<sup>−1</sup> and 0.01 kcal mol<sup>−1</sup>) and with MADs of 0.26 kcal mol<sup>−1</sup> in both cases, confirming previous findings that already at the double- $\zeta$  level, B3LYP-DCP can provide results of quadruple- $\zeta$  quality.<sup>65</sup> In the original B3LYP-DCP study, an MAD of 0.23

kcal mol<sup>−1</sup> has been reported for S22, and this difference can be explained with the fact that different S22 reference values and Gaussian's version of B3LYP have been used. Note that such low MADs for S22 are usually only achieved with dispersion-corrected double-hybrid density functionals that are one rung above B3LYP in Perdew's Jacob's Ladder<sup>114</sup> classification.<sup>10,41</sup> Combined with the def2-QZVP basis set, B3LYP-D3 gives an MAD of 0.31 kcal mol<sup>−1</sup> that is doubled when 6-31+G(2d,2p) is used. The MDs in both cases are positive, indicating an overbinding tendency of DFT-D3 for the dimers in S22. B3LYP-NL/6-31+G(2d,2p) shows a similar overbinding tendency as B3LYP-D3, but it has slightly smaller MDs and MADs (0.41 and 0.52 kcal mol<sup>−1</sup>, respectively). A value of 0.5 kcal mol<sup>−1</sup> has been reported for B3LYP-NL/def2-QZVP.<sup>33</sup> It appears that for this test set, B3LYP-NL shows a smaller basis set dependence than B3LYP-D3.

The ADIM6<sup>44</sup> set contains six alkane dimers—from the ethane to the heptane dimers—at their equilibrium distances. The MDs in Figure 1 show that B3LYP-DCP slightly underbinds with −0.23 kcal mol<sup>−1</sup>, whereas for the bigger basis set it overbinds with an MD of 0.37 kcal mol<sup>−1</sup>. The MD for B3LYP-D3 improves from 0.27 kcal mol<sup>−1</sup> for the smaller basis set to 0.13 kcal mol<sup>−1</sup> for the larger basis. Comparing the MADs of both approaches with each other reveals a different trend than observed for the S22 set, with both methods now being statistically very close to each other even for the smaller basis set (MAD = 0.23 kcal mol<sup>−1</sup> for B3LYP-DCP and 0.27 kcal mol<sup>−1</sup> for B3LYP-D3). For the def2-QZVP set, the MAD for B3LYP-DCP increases to 0.38 kcal mol<sup>−1</sup>, whereas B3LYP-D3 gives a value of only 0.13 kcal mol<sup>−1</sup>, thus lying within the accuracy of the CCSD(T)/CBS reference values of this test set. B3LYP-NL reaches this accuracy already at the double- $\zeta$  level with an MAD of 0.11 kcal mol<sup>−1</sup> (Figure 1), and a slightly higher value of 0.2 kcal mol<sup>−1</sup> has been published for the def2-QZVP basis set.<sup>33</sup>

The third set discussed in this section is the WATER27<sup>115</sup> set containing neutral water clusters and charged complexes of the form H<sub>3</sub>O<sup>+</sup>(H<sub>2</sub>O)<sub>*n*</sub> and OH<sup>−</sup>(H<sub>2</sub>O)<sub>*n*</sub>. For this test set, it has been reported that a strong basis-set superposition error (BSSE) was observed for double- $\zeta$  basis sets,<sup>10</sup> as indicated by the MDs for B3LYP that are much closer to zero for the smaller basis set (MD = −1.06 kcal mol<sup>−1</sup>) than for the more complete aug'-def2-QZVP basis (MD = −6.21 kcal mol<sup>−1</sup>). All dispersion corrections additionally stabilize the systems, and combined with the BSSE effects for 6-31+G(2d,2p) the clusters are overbound; however the magnitudes of the MDs differ significantly, with B3LYP-DCP yielding the better result with 3.28 kcal mol<sup>−1</sup>. In accordance with previous findings for the aug'-def2-SV(P) basis,<sup>10</sup> the MD for B3LYP-D3 is very large with 8.23 kcal mol<sup>−1</sup>. The same behavior can be observed for B3LYP-NL. In the double- $\zeta$  case, the results seem to benefit from the fact that B3LYP-DCP has been fitted to BSSE-uncorrected results. However, the BSSE effects are not fully taken into account, resulting in a slightly higher MAD of 3.44 kcal mol<sup>−1</sup> for B3LYP-DCP than for pure B3LYP (3.00 kcal mol<sup>−1</sup>). B3LYP-D3 has an MAD of 8.53 kcal mol<sup>−1</sup> and B3LYP-NL an MAD of 12.05 kcal mol<sup>−1</sup>. At this stage, it is not possible to improve this value by including a BSSE correction such as gCP,<sup>98</sup> as it has not been adjusted to this particular basis set. This picture changes when going to practically BSSE-free aug'-def2-QZVP results with MADs of 6.52 kcal mol<sup>−1</sup> for B3LYP, 3.89 kcal mol<sup>−1</sup> for B3LYP-DCP, and 3.33 kcal mol<sup>−1</sup>



**Figure 1.** Statistical results (kcal mol<sup>-1</sup>) for B3LYP, B3LYP-DCP, B3LYP-D3, and B3LYP-NL for the S22, ADIM6, and WATER27 test sets. Part a shows mean (MD) and part b shows mean absolute deviates (MAD). Results are shown for the 6-31+G(2d,2p) and (aug'-)def2-QZVP basis sets, except for B3LYP-NL, for which only values for 6-31+G(2d,2p) are shown. B3LYP-NL/(aug'-)def2-QZVP results are discussed in detail in ref 33.

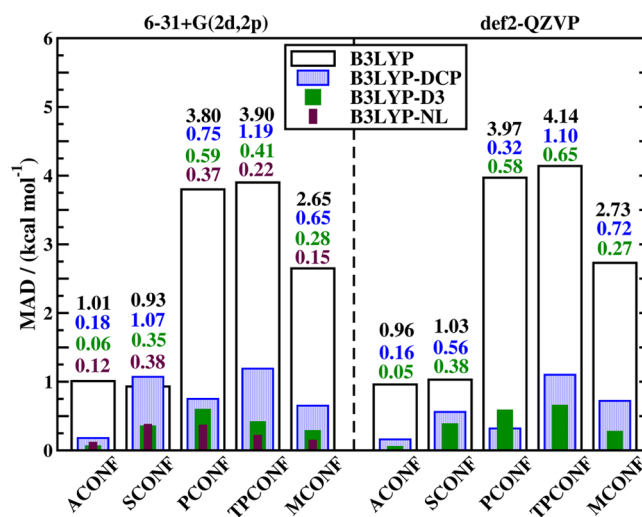
for B3LYP-D3. For B3LYP-NL/aug'-def2-QZVP, a higher value of 6.9 kcal mol<sup>-1</sup> has been published.<sup>33</sup>

In summary, the B3LYP-DCP approach combined with 6-31+G(2d,2p) is a valuable approach for the description of noncovalently bound complexes, whereas at the quadruple- $\zeta$  level B3LYP-D3 is similar or more accurate, thus confirming previous findings.<sup>65</sup> B3LYP-NL is a competitive approach, but particularly prone to BSSE effects in water clusters. In the next sections, intramolecular London-dispersion effects are discussed.

**4.2. Relative Energies of Conformers.** An accurate description of the relative energies of conformers is of particular importance in many applications. It has been established that benchmark sets like S22 or S66 can give important insights into a method's performance for intermolecular noncovalent interactions, but that they do not allow to draw conclusions about the same method's behavior for intramolecular interactions in conformers, which is why special benchmark sets for these cases have to be evaluated.<sup>84</sup>

Herein, five test sets for conformations of various organic and biologically relevant compounds are tested, three of which are part of the GMTKN30 database. MADs for all benchmark sets and methods are shown in Figure 2. The ACONF<sup>116</sup> set contains *n*-butane, *n*-pentane, and *n*-hexane conformers, and the results are contrary to the intermolecular cases discussed in the previous section. While both B3LYP-D3 and B3LYP-DCP capture parts of the important dispersion effects and although they significantly improve over B3LYP, the MAD for B3LYP-D3 is already at the double- $\zeta$  level, only a third of that of B3LYP-DCP (0.06 vs 0.18 kcal mol<sup>-1</sup>), and moreover, these values do not change for the larger def2-QZVP basis set. B3LYP-NL/6-31+G(2d,2p) is slightly better than B3LYP-DCP/6-31+G(2d,2p) with an MAD of 0.12 kcal mol<sup>-1</sup>.

For the SCONF<sup>94,117</sup> set of sugar conformers, it is observed that B3LYP-DCP/6-31+G(2d,2p) with an MAD of 1.07 kcal mol<sup>-1</sup> is no improvement over B3LYP with an MAD of 0.93 kcal mol<sup>-1</sup>, while B3LYP-DCP/def2-QZVP nearly halves the MAD of B3LYP/def2-QZVP to 0.56 kcal mol<sup>-1</sup>. B3LYP-D3 yields MADs of 0.35 kcal mol<sup>-1</sup> for 6-31+G(2d,2p) and 0.38 kcal mol<sup>-1</sup> for def2-QZVP. B3LYP-NL/6-31+G(2d,2p) is very similar to B3LYP-D3 (MAD = 0.38 kcal mol<sup>-1</sup>). Note that for ACONF and SCONF, similar values have been reported for



**Figure 2.** Mean absolute deviations (MADs) in kcal mol<sup>-1</sup> for B3LYP, B3LYP-DCP, B3LYP-D3, and B3LYP-NL for the five conformer test sets. Results are shown for the 6-31+G(2d,2p) and def2-QZVP basis sets, except for B3LYP-NL for which only values for 6-31+G(2d,2p) are shown. B3LYP-NL/def2-QZVP results are discussed in detail in ref 33.

B3LYP-NL and the larger def2-QZVP basis set,<sup>33</sup> meaning that in this cases basis set effects can be ignored, probably due to fortuitous error compensation.

The next two test sets allow assessing peptide conformations. The PCONF<sup>118</sup> set for conformers of the PHE-GLY-GLY tripeptide is part of GMTKN30, and all dispersion-corrected approaches improve significantly over B3LYP, which incorrectly predicts unfolded conformers to be more stable than folded ones. When the 6-31+G(2d,2p) basis set is used, B3LYP-D3 (MAD = 0.59 kcal mol<sup>-1</sup>) describes the conformers statistically better than B3LYP-DCP (MAD = 0.75 kcal mol<sup>-1</sup>). This picture is reversed for def2-QZVP, with B3LYP-DCP improving to an MAD of 0.32 kcal mol<sup>-1</sup>, while the MAD of B3LYP-D3 is 0.58 kcal mol<sup>-1</sup>. Note, that it has been observed that these specific tripeptides are a challenging case for B3LYP-D3 with Becke-Johnson damping, but that the DFT-NL approach is a valuable alternative to this problem.<sup>33</sup> Indeed,



Table 2. Mean Absolute Deviations (MADs) in kcal mol<sup>-1</sup> for the Basic Properties Test Sets

benchmark set	6-31+G(2d,2p)				(aug'-)def2-QZVP		
	B3LYP	B3LYP-D3	B3LYP-DCP	B3LYP-NL	B3LYP	B3LYP-D3	B3LYP-DCP
W4-08	4.4	4.6	20.5	5.4	3.1	3.4	21.7
W4-11(new systems)	3.6	2.4	36.2	4.0	3.4	2.2	40.2
W4-11(complete)	4.0	3.7	27.0	4.8	3.3	2.9	29.4
G21EA	2.0	2.0	3.2	3.1	1.4	1.4	3.0
G21IP	5.4	5.4	5.0	5.3	4.5	4.5	5.2
PA	3.8	4.0	1.6	3.4	3.0	3.2	1.3
BH76	4.3	5.2	5.6	5.6	3.8	4.6	4.9
BHPERI	3.6	1.7	3.2	2.0	4.9	1.8	2.5

additional B3LYP-NL/6-31+G(2d,2p) calculations give an MAD of 0.37 kcal mol<sup>-1</sup>.

The recently published TPCONF set contains biologically relevant conformers of tetrapeptides of the form ACE-ALA-X-ALA-NME, where X is GLY or SER, and it has been shown that particularly the helical conformers in this set are prone to intramolecular BSSE effects.<sup>81</sup> All three dispersion-corrected approaches improve compared to B3LYP, but only B3LYP-D3 and B3LYP-NL yield MADs below 1 kcal mol<sup>-1</sup>. In fact, B3LYP-NL/6-31+G(2d,2p) has an MAD of 0.22 kcal mol<sup>-1</sup>, which is even lower than the previously reported best values for this benchmark set based on double-hybrid density functional calculations at the quadruple- $\zeta$  level.<sup>81</sup>

The final benchmark set of this section is a recently introduced test set for more than 50 melatonin conformers (MCONF).<sup>82</sup> B3LYP-NL yields a very low MAD of 0.15 kcal mol<sup>-1</sup> at the double- $\zeta$  level. The MADs for the other two methods are very similar for both basis sets, with B3LYP-D3 yielding MADs of about 0.3 kcal mol<sup>-1</sup> and B3LYP-DCP about 0.7 kcal mol<sup>-1</sup>.

**4.3. Basic Properties.** GMTKN30 includes a category called “basic properties” containing chemical problems that provide valuable insights into a method’s general applicability. It is desired for a generally applicable dispersion-corrected method that it automatically captures London-dispersion effects when they are present, but that it gives the results of the underlying density functional when those effects are negligible. An ideal test case for this is total atomization energies (TAEs). Although it has been outlined that chemically motivated evaluations of computational methods should not be based solely on them,<sup>10</sup> TAEs are a tough test case, and errors in their description help reveal underlying methodological problems. The GMTKN30 database includes the W4-08<sup>19</sup> benchmark set of highly accurate TAEs of small molecular systems for which London-dispersion effects only play a marginal role. In 2011, W4-08 has been extended to the W4-11 set by including larger, mostly organic molecules, for which dispersion effects are expected to play a more significant role.<sup>95</sup> Table 2 separately lists MADs for the W4-08 set, the subset of additional W4-11 systems, and the complete W4-11 set. The MADs for pure B3LYP are 4.4 kcal mol<sup>-1</sup> for 6-31+G(2d,2p) and 3.1 kcal mol<sup>-1</sup> for def2-QZVP, respectively. For B3LYP-D3, a marginal increase to 4.6 kcal mol<sup>-1</sup> and 3.4 kcal mol<sup>-1</sup> is observed, but overall one can conclude that the B3LYP-D3 results confirm the intuitive assumption that London-dispersion effects are not important in these systems. The second assumption that dispersion effects are important for larger organic molecules is confirmed by analyzing only the additional 29 systems of W4-11, as B3LYP-D3 lowers the MADs by 1.2 kcal mol<sup>-1</sup> compared to B3LYP for both basis sets. For the combined W4-11 set, a

slight reduction of about 0.3 to 0.4 kcal mol<sup>-1</sup> in the MADs is observed.

In stark contrast to that, the DCP approach does not reproduce these findings and significantly overestimates the TAEs with MADs ranging between 20 and 40 kcal mol<sup>-1</sup> for the three (sub)sets and both basis sets, errors that are comparable to local density approximation (LDA) functionals.<sup>10</sup>

These findings allow one to make an important conclusion: although the Gaussian functions in the B3LYP-DCP approach are diffuse—due to small exponents—they seem to interfere with the short-range electronic regions of the systems, thus leading to double-counting effects that influence the systems’ electronic structures even if no dispersion effects are expected. TAEs are of course very difficult cases, and the absolute errors naturally depend on the number of atoms. The error for the TAE of ethane for example is 67 kcal mol<sup>-1</sup>, which is increased to 101 kcal mol<sup>-1</sup> for propane (Table S9). The errors also increase when going from propyne (86 kcal mol<sup>-1</sup>), to propene (94 kcal mol<sup>-1</sup>), to propane. All of these errors are surprisingly large and were not foreseeable, as can be seen for propane, whose dimer in the ADIM6 set is well described by B3LYP-DCP/6-31+G(2d,2p) with an error of only 0.12 kcal mol<sup>-1</sup> (Table S1); see also section 4.5 for a further discussion of this problem.

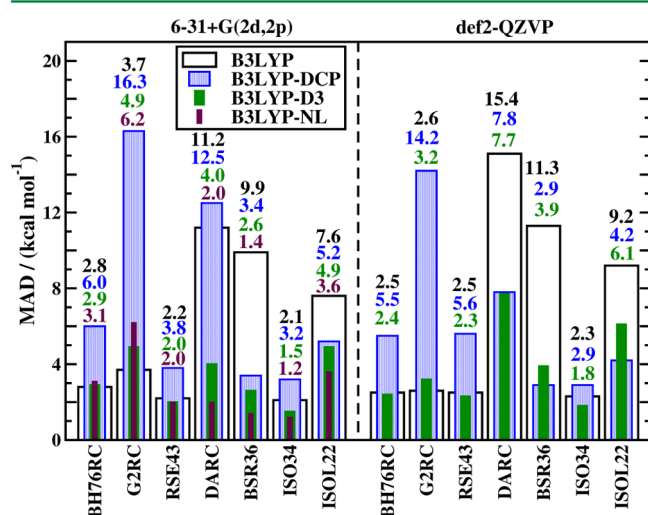
The basic-properties category of GMTKN30 also includes adiabatic electron affinities (G21EA<sup>120</sup>) and ionization potentials (G21IP<sup>120</sup>) of atoms and small molecules and proton affinities (PA<sup>121,122</sup>) of small molecules and linear polyenes. The electron affinities and ionization potentials are not affected at all by B3LYP-D3, as it does not influence the electronic structure but is based on the geometries only, which do not change or only change marginally by subtraction or addition of an electron; the MADs for B3LYP-DCP, however, increase by up to 1.5 kcal mol<sup>-1</sup> (Table 2). In the case of the PA set, particularly the description of the proton affinities of the polyenes is improved by the DCP approach for which the MADs are more than halved compared to B3LYP, e.g., 1.6 kcal mol<sup>-1</sup> vs 3.8 kcal mol<sup>-1</sup> for 6-31+G(2d,2p), while B3LYP-D3 gives an MAD similar to B3LYP.

The BH76 set is a combination of Truhlar’s HTBH38<sup>123</sup> and NHTBH38<sup>124</sup> test sets for barrier heights of hydrogen transfer, heavy atom transfer, nucleophilic substitution, and unimolecular and association reactions, and BHPERI<sup>119,125–128</sup> considers barrier heights of pericyclic reactions. MADs for both test sets are shown in Table 2. In the BH76 case, it is observed that both dispersion-corrected approaches lower the barriers, as they stabilize transition states relatively to the reactants/products, which however leads to an increase in the MADs of around 0.9 kcal mol<sup>-1</sup> for B3LYP-D3 and between 1.1

to 1.3 kcal mol<sup>-1</sup> for the DCP method compared with B3LYP. For BHPERI, it has already been outlined elsewhere that London dispersion plays an important role,<sup>10,94</sup> and B3LYP-D3 more than halves the absolute averaged errors of B3LYP, resulting in MADs of 1.7 and 1.8 kcal mol<sup>-1</sup> for the small and the large basis sets, respectively. B3LYP-DCP/6-31+G(2d,2p) shows no significant improvement over B3LYP, whereas B3LYP-DCP/def2-QZVP reduces the errors but still has a higher MAD than B3LYP-D3 (2.5 kcal mol<sup>-1</sup>).

DFT-NL also corrects for London dispersion on the electronic level. As can be seen from the statistical values for B3LYP-NL/6-31G+(2d,2p) for the basic properties in Table 2 and from the results shown in Tables S9–S14, this approach gives sometimes higher MADs (also for W4-11) than pure B3LYP or B3LYP-D3, but its errors are not as large as for B3LYP-DCP. This means that the NL correction does not have a very strong influence in the short-range regime and that double-counting effects in the covalent-bond regions are smaller.

**4.4. Reaction Energies.** GMTKN30 includes a variety of benchmark sets for reaction energies comprising chemical problems that are either affected by London dispersion, that are difficult to treat with dispersion corrections, or that remain unaffected by them. Figure 3 shows all relevant MADs for the



**Figure 3.** Mean absolute deviations (MADs) in kcal mol<sup>-1</sup> for B3LYP, B3LYP-DCP, B3LYP-D3, and B3LYP-NL for the seven reaction energies test sets. Results are shown for the 6-31+G(2d,2p) and def2-QZVP basis sets, except for B3LYP-NL, for which only values for 6-31+G(2d,2p) are shown. B3LYP-NL/def2-QZVP results are discussed in detail in ref 33.

seven benchmark sets analyzed in this study. The BH76RC and G2RC sets contain reactions between small molecules and are based on values published for the BH76 and G2/97 test sets.<sup>123,124,129</sup> Compared with B3LYP, B3LYP-D3 gives very similar MADs for BH76RC for both basis sets, but worse MADs (increased by 0.6 and 1.2 kcal mol<sup>-1</sup>) for G2RC. The averaged errors of the DCP approach are more than doubled for BH76RC for both basis sets, and B3LYP-DCP shows significantly high MADs for G2RC (16.3 kcal mol<sup>-1</sup> for 6-31+G(2d,2p) and 14.2 kcal mol<sup>-1</sup> for def2-QZVP). These errors are not evenly distributed over all reactions in these test sets. In fact, error cancellation is observed in cases where reactants and products are electronically similar to each other.

For instance, in BH76RC the hydrogen abstraction from ammonia with a hydroxyl radical forms water and the amidogen radical (NH<sub>2</sub>), for which B3LYP/6-31+G(2d,2p) gives an error of 0.3 kcal mol<sup>-1</sup> and B3LYP-DCP of -0.1 kcal mol<sup>-1</sup> (Table S15). A second example is the reaction between CO<sub>2</sub> and dihydrogen to formic acid in G2RC, for which both B3LYP and B3LYP-DCP show similar absolute errors between 1.2 and 1.7 kcal mol<sup>-1</sup> (Table S16). An example for failed error compensation in G2RC is the decomposition energy of benzene into three equivalents of ethyne that is overestimated by almost 50 kcal mol<sup>-1</sup> for B3LYP-DCP/6-31+G(2d,2p) (Table S16). Interestingly, the benzene dimer and the ethane–ethyne complex are both parts of the S22 set, and the very good description of both complexes with B3LYP-DCP does not indicate any particular problem with these systems (Table S1). In fact, if the absolute single-point energies of the respective S22 monomers are taken, whose structures had been optimized at a different level of theory than for G2RC, the same decomposition energy of about 200 kcal mol<sup>-1</sup> is obtained for this reaction, thus conforming that these errors are not specific to the structures used in the G2RC set but to the underlying method.

The B3LYP-NL approach is very similar to B3LYP-D3 for BH76RC, but its MAD is about 1 kcal mol<sup>-1</sup> larger for the G2RC set.

The RSE43 benchmark set contains radical stabilization energies, defined as the reaction energies of methyl-radical mediated hydrogen abstractions from organic molecules.<sup>130</sup> Given that DFT-D3 is no electronic correction, B3LYP-D3 only shows a minor improvement of 0.2 kcal mol<sup>-1</sup> compared to B3LYP, due to the structural similarity of the reactants and products, while the MADs of B3LYP-DCP are by 50% larger than B3LYP for 6-31+G(2d,2p) and by more than a factor of 2 larger for def2-QZVP. B3LYP-NL does not seem to have problems with the open-shell species discussed in this set and gives the same MAD as B3LYP. Similar findings have been reported for B3LYP-NL/def2-QZVP.<sup>33</sup>

The final four benchmark sets in this section contain systems that are stabilized by intramolecular London dispersion. For the DARC<sup>131</sup> test set of Diels–Alder reactions, B3LYP has a large MAD of about 11 kcal mol<sup>-1</sup> for 6-31+G(2d,2p) and of about 15 kcal mol<sup>-1</sup> for def2-QZVP. Compared to the high-level reference values, B3LYP correctly predicts that all reactions are exothermic, but overall it underestimates their absolute reaction energies, due to the inability of describing London-dispersion effects contributing to the stability of the products. As all deviations in this study are calculated as differences between tested method and reference values, this leads to positive MDs of the same size as the MADs. Thus, a significant basis-set effect is observed, and in the double- $\zeta$  case the products seem to be more stable than for the larger basis set, demonstrating the influence of intramolecular BSSE on these reactions, as also outlined elsewhere.<sup>99</sup>

The DCP approach is able to describe these London-dispersion effects in DARC, and the products are more stable than they are for dispersion-uncorrected B3LYP; however, in the double- $\zeta$  case B3LYP-DCP strongly overestimates this stabilizing effect, leading to an MD of -12.5 kcal mol<sup>-1</sup> (see Table S18) and an MAD of a similar absolute magnitude to that of B3LYP (Figure 3). The B3LYP-D3 approach provides a more balanced description of London dispersion with an MD of 3.5 kcal mol<sup>-1</sup> and an MAD of 4.0 kcal mol<sup>-1</sup>. This result, however, is also affected by BSSE, and the MAD for B3LYP-



D3/def2-QZVP increases to 7.7 kcal mol<sup>-1</sup>, which is still about half of the result for pure B3LYP. B3LYP-NL yields the lowest MAD at the double- $\zeta$  level with 2.0 kcal mol<sup>-1</sup>. B3LYP-DCP gives almost the same MAD for def2-QZVP as B3LYP-D3, the MDs of both approaches however have opposite signs, indicating again that the DCP approach overestimates the specific dispersion effects while B3LYP-D3 underestimates them. For B3LYP-NL/def2-QZVP, an MAD of 4.0 kcal mol<sup>-1</sup> has been reported for the complete DARC test set,<sup>33</sup> also containing elements that had to be left out of this study due to the limitations to H, C, N, and O. Nevertheless, this value indicates that also the good value for B3LYP-NL/6-31+G-(2d,2p) benefits from BSSE effects.

The BSR36 test set contains 36 bond-separation reactions of saturated hydrocarbons.<sup>132</sup> No problems are observed for these reactions, and all three dispersion-corrected approaches are significant improvements over standard B3LYP with error reductions of factors of 3 or more. B3LYP-NL outperforms B3LYP-D3 and B3LYP-DCP for the 6-31G+(2d,2p) basis (MAD = 1.4 kcal mol<sup>-1</sup> vs MAD = 2.6 kcal mol<sup>-1</sup> vs MAD = 3.4 kcal mol<sup>-1</sup>), whereas for def2-QZVP, B3LYP-DCP (MAD = 2.9 kcal mol<sup>-1</sup>) is better than B3LYP-D3 (MAD = 3.9 kcal mol<sup>-1</sup>; Figure 3). A value of 2.7 kcal mol<sup>-1</sup> has been reported for B3LYP-NL/def2-QZVP.<sup>33</sup>

Figure 3 also shows the results for the ISO34<sup>133</sup> and ISOL22<sup>134</sup> benchmark sets for isomerization reactions of medium-sized and large systems. Here, basis-set effects are either negligible (ISO34) or they are much smaller than for the DARC test set (ISOL22). Compared to pure B3LYP, B3LYP-D3 improves the results by about 0.5 to 0.6 kcal mol<sup>-1</sup> for both basis sets for ISO34, while B3LYP-DCP shows larger errors (between 0.6 and 1.1 kcal mol<sup>-1</sup> compared to B3LYP). For ISOL22, both approaches describe dispersion effects adequately, and their MADs are between 2.7 and 5 kcal mol<sup>-1</sup> lower than for B3LYP. For 6-31+G(2d,2p), both approaches give similar MADs, while B3LYP-DCP/def2-QZVP is on average by 2 kcal mol<sup>-1</sup> better than B3LYP-D3/def2-QZVP. B3LYP-NL yields the best MADs at the double- $\zeta$  level with 1.2 kcal mol<sup>-1</sup> for ISO34 and 3.6 kcal mol<sup>-1</sup> for ISOL22.

In previous studies with GMTKN30, so-called weighted total mean absolute deviations (WTMADs) have been introduced, providing averaged estimates over a method's performance. Herein, the original WTMAD formula for the Reaction Energies section is adjusted to changes compared with the original GMTKN30 set, see the SI for more information. WTMADs averaged over the seven reaction-energy test sets are shown in Table 3. For the 6-31+G(2d,2p) basis set, B3LYP-NL is the best approach, with a WTMAD of 2.1 kcal mol<sup>-1</sup>, followed by B3LYP-D3 (2.8 kcal mol<sup>-1</sup>). B3LYP-DCP follows with a higher WTMAD (5.7 kcal mol<sup>-1</sup>) that is close to that of B3LYP (6.6 kcal mol<sup>-1</sup>). Also for def2-QZVP, B3LYP-D3 yields a lower WTMAD (3.8 kcal mol<sup>-1</sup>) than B3LYP-DCP (4.9 kcal

mol<sup>-1</sup>) and B3LYP (7.7 kcal mol<sup>-1</sup>). For the complete section of reaction energies of GMTKN30, it has been reported elsewhere that B3LYP-NL has a lower WTMAD than B3LYP-D3 for def2-QZVP,<sup>33</sup> which parallels the findings for the smaller basis set.

#### 4.5. Analysis of a Recently Modified Carbon Potential.

The previous results have shown that B3LYP-DCP describes dispersion effects particularly well in noncovalently bound dimers, but that problems can occur for reaction energies and barrier heights. While this manuscript was undergoing the peer-review process and subsequent revision, DiLabio and co-workers—inspired by the findings reported herein<sup>135</sup> and by their own findings on the  $\beta$ -scission of the cumoxyl radical—have suggested the use of a modified carbon potential with coefficients smaller by factors of 5 to 10 than the originally developed C-DCP,<sup>136</sup> thus becoming more diffuse. This was done to ensure that the potential does not affect the electron density of covalent carbon–carbon bonds. This modified potential was fitted to the 6-31+G(2d,2p) basis set and combined with the already existing potentials for H, N, and O. In an analysis of four benchmark sets for noncovalent interactions and of 10 test sets of GMTKN30—four conformers and five reaction-energy test sets that are also assessed in this study—it was shown that the new potential (herein dubbed DCP\*) does improve on the original one.

Herein, this modified B3LYP-DCP\* is applied to all 21 benchmark sets and is thus as thoroughly assessed as the previously discussed methods. A comparison of those results with the previously discussed values for B3LYP-DCP is done in Table 4. Note that only results for 6-31+G(2d,2p) without CP corrections are discussed, as the new potential was fitted to this basis set. In 13 cases, we note that B3LYP-DCP\* does indeed yield lower MADs than B3LYP-DCP, for instance, ADIM6 and the five conformer test sets. In particular, the new carbon potential positively influences barrier heights—the MAD for BHPERI is lowered by 0.6 kcal mol<sup>-1</sup>—and reaction energies involving larger compounds. For instance, the MADs for BSR36 and the two isomerization energy test sets are more than halved. The new potential does also improve the description of Diels–Alder reactions (MAD = 3.9 kcal mol<sup>-1</sup>) and solves most of the problems in the atomization-energy test set, although the final MAD for W4-11 is still higher than for the other tested methods (6.5 kcal mol<sup>-1</sup>). The description of the open-shell species in the RSE43 test set is also improved by 1.3 kcal mol<sup>-1</sup>, and the final MAD of 2.3 kcal mol<sup>-1</sup> is close to those of B3LYP-D3 and B3LYP-NL.

Contrary to that, not much change compared with the original DCP is found for electron affinities and ionization potentials. The description of small-molecule reactions in G2RC is improved, but the final MAD of 7.3 kcal mol<sup>-1</sup> is still higher than for the other tested methods.

However, overall, it can be concluded that the modified carbon potential improves the original B3LYP-DCP approach. Particularly, reaction energies are much better described, as can be seen in a WTMAD of 2.4 kcal mol<sup>-1</sup>, which is about half of that for the original B3LYP-DCP version.

**4.6. Overall Comparison.** In total, five methods have been investigated at the double- $\zeta$  level for 21 benchmark sets, and it is worthwhile to conclude with a discussion about how many times a certain method yields the best MAD for a specific test case (see the last column of Table 4). First of all, it is seen that uncorrected B3LYP still has the best MAD in five cases: WATER27, G21EA, BH76, BH76RC, and G2RC. These are

**Table 3. Weighted Total Mean Absolute Deviations (WTMADs) in kcal mol<sup>-1</sup> for the Reaction-Energies Category**

method	6-31+G(2d,2p)	def2-QZVP
B3LYP	6.6	7.8
B3LYP-DCP	5.7	4.9
B3LYP-D3	2.8	3.8
B3LYP-NL	2.1	

**Table 4. Mean Absolute Deviations for the Subsets of the Truncated GMTKN30 Database for B3LYP-DCP and B3LYP-DCP\* with Modified Carbon Potentials in kcal mol<sup>-1</sup><sup>a</sup>**

benchmark set	DCP	DCP*	best method <sup>b</sup>
noncovalently bound complexes			
S22	0.26	0.33	B3LYP-DCP (0.26)
ADIM6	0.23	0.17	B3LYP-NL (0.11)
WATER27	3.44 <sup>c</sup>	3.44 <sup>b</sup>	B3LYP (3.00)
relative energies of conformers			
ACONF	0.18	0.05	B3LYP-DCP* (0.05)
			B3LYP-D3 (0.06)
SCONF	1.07	0.68	B3LYP-D3 (0.35)
PCONF	0.75	0.65	B3LYP-NL (0.37)
TPCONF	1.19	0.96	B3LYP-NL (0.22)
MCONF	0.65	0.48	B3LYP-NL (0.15)
basic properties			
W4-11	27.0	6.5	B3LYP-D3 (3.7)
G21EA	3.2	2.5	B3LYP (2.0)
			B3LYP-D3 (2.0)
G21IP	5.0	4.9	B3LYP-DCP (5.0)
			B3LYP-DCP* (4.9)
PA	1.6	3.4	B3LYP-DCP
BH76	5.6	4.9	B3LYP (4.3)
BHPERI	3.2	2.4	B3LYP-D3 (1.7)
reaction energies			
BH76RC	6.0	3.2	B3LYP (2.8)
G2RC	16.3	7.3	B3LYP (3.7)
RSE43	3.8	2.3	B3LYP-D3 (2.0)
			B3LYP-NL (2.0)
DARC	12.5	3.9	B3LYP-NL (2.0)
BSR36	3.4	1.2	B3LYP-DCP* (1.2)
ISO34	3.2	1.5	B3LYP-NL (1.2)
ISOL22	5.2	2.7	B3LYP-DCP* (2.7)
WTMAD <sup>d</sup>	5.7	2.4	B3LYP-NL (2.1)

<sup>a</sup>The results were obtained with the 6-31+G(2d,2p) basis set. The last column shows the best of all tested methods on the same basis set level. <sup>b</sup>The numbers in parentheses show the MADs of the respective best method. <sup>c</sup>The same as B3LYP-DCP due to the lack of carbon atoms. <sup>d</sup>Weighted total mean absolute deviation for the reaction-energy subsets.

mostly small-molecule test sets, except for WATER27, for which the BSSE is the prime source of error, which leads to an overbinding of hydrogen-bond strengths when dispersion corrections are applied.

B3LYP-D3 yields the best MADs in six cases: ACONF, SCONF, W4-11, G21EA, BHPERI, and RSE43. The original B3LYP-DCP is the best method for the S22 and PA test sets, whereas the modified B3LYP-DCP\* competes with B3LYP-D3 for ACONF, and it is the best approach for ionization potentials, bond separation reactions (BSR36) and isomerization reactions of large systems (ISOL22).

However, the overall best approach is B3LYP-NL (seven cases). B3LYP-NL also yields the lowest WTMAD for reaction energies with 2.1 kcal mol<sup>-1</sup>.

## 5. SUMMARY AND CONCLUSIONS

Three versions of dispersion-corrected density functional theory have been compared for the treatment of inter- and intramolecular London-dispersion effects influencing binding energies of noncovalently bound complexes, relative stabilities

of conformers, and general thermochemistry. The focus lay on dispersion-core-potential corrected density functional theory based on the B3LYP functional (B3LYP-DCP)<sup>65</sup> and on the nonlocal B3LYP-NL approach,<sup>33</sup> both of which allow the electron density to respond to London-dispersion effects. Those two methods were compared with the B3LYP-D3 method in its latest version, including Becke-Johnson damping,<sup>9,44</sup> which is known for its general applicability and accuracy. Furthermore, this study concentrated on the use of the 6-31G+(2d,2p) double- $\zeta$  basis set—recommended for B3LYP-DCP—and assessed the basis set dependence of those methods compared to the large def2-QZVP quadruple- $\zeta$  basis set, which had been originally used in the parametrization of the B3LYP-D3 and B3LYP-NL approaches.

In total, 473 accurate reference energies, taken from the large GMTKN30<sup>41,94</sup> benchmark database and a few additional studies, allowed scrutinization of the tested approaches for general applicability and robustness.

Studying three benchmark sets for noncovalently bound dimers, and neutral and charged water clusters, confirms previous findings<sup>65</sup> that B3LYP-DCP/6-31G+G(2d,2p) yields indeed very good results of nearly quadruple- $\zeta$  quality in these cases. However, as also outlined elsewhere,<sup>84</sup> this study reveals that results for noncovalently bound complexes generally do not allow conclusions about a method's behavior for intramolecular London-dispersion effects. Indeed, it is found that B3LYP-D3 and B3LYP-NL outperform B3LYP-DCP for both applied basis sets for the prediction of relative energies of organic and biologically inspired conformers. B3LYP-NL turns out to be particularly useful in the description of relative energies of tri- and tetrapeptide conformers. It is also demonstrated that the specific parameters of the D3 and NL corrections can be used with smaller basis sets, although they have been obtained with a larger basis.

London-dispersion effects influencing reaction energies, for instance in Diels–Alder reactions or isomerization reactions, and barrier heights—particularly of pericyclic reactions—are better described by B3LYP-D3 and B3LYP-NL than by B3LYP-DCP. In cases in which London-dispersion effects do not play a role, it is observed that B3LYP-DCP is sometimes worse than pure B3LYP. Surprisingly large errors are found for total atomization energies but also for other reactions in which the electronic structures of reactants and products differ significantly from each other. These findings give rise to the conclusion that DCPs, although designed to mimic long-range interactions, also influence the short-range electronic regions of atoms and molecules. However, during the peer-review and revision process, a new carbon-DCP was introduced by DiLabio and co-workers—partially inspired by a private communication relating the results of the present study.<sup>136</sup> This modified DCP was designed to have a smaller effect on the electron density of carbon–carbon bonds, and indeed it improves the difficult cases and outliers found for the original DCP approach. It also provides very good results at the double- $\zeta$  level for bond-separation and isomerization reactions of large systems.

An overall comparison between all tested methods reveals that B3LYP-NL provides a means to describe a range of properties with high accuracy, closely followed by B3LYP-D3. Regarding DCPs, the new carbon potentials should be favored over the first B3LYP-DCP version. DCPs are found to be able to obtain accurate binding energies of noncovalently bound molecular aggregates containing H, C, N, and O. Moreover,

they are less influenced by basis-set superposition-error effects in small basis sets than B3LYP-NL and B3LYP-D3 due to the fitting procedure with which its parameters have been obtained. For the latter two methods, schemes like the geometrical counter-poise correction can be recommended, as published elsewhere in the case of B3LYP-D3.<sup>98,99</sup>

Finally, if hitherto unknown problems are explored, for which the importance of London-dispersion effects is not always predictable, and for intramolecular dispersion effects influencing conformers and reactions, it is recommended to use the B3LYP-NL or B3LYP-D3 schemes. Note that they are readily applicable to a broad range of elements for which DCPs have not been fitted yet or for which such a fitting procedure would be very difficult. Particular DFT-D3 has been thoroughly compared with other contemporary approaches in the past, and therefore the results of this study also allow comparisons between those methods and B3LYP-NL and B3LYP-DCP. All in all, these findings help complement the general picture about the advantages and limitations of the various dispersion-corrected DFT methods.

## ■ ASSOCIATED CONTENT

### ■ Supporting Information

All results for the tested approaches and benchmark sets and the formula calculating the weighted total mean absolute deviation for the Reaction Energies 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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