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Application of Dispersion-Corrected Density Functional Theory

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A newly developed dispersion-corrected density functional theory (B3LYP-DCP) was tested against the S22 benchmark set containing noncovalently bound complexes, resulting in a mean absolute deviation of 0.77 kcal mol^{-1}. It is found that B3LYP-DCP is capable of describing a multitude of weak interactions, including hydrogen bonds. The method was applied to study the toluene dimer, where it is found to describe the dissociation energy ($D_0 = 3.57$ kcal mol^{-1}) in excellent agreement with experimental ($D_0 = 3.46 \pm 0.23$ kcal mol^{-1}) and recent CCSD(T) counterpoise-corrected ($D_0 = 3.36$ kcal mol^{-1}) values. A large number of slipped, stacked isomers are found to be almost isoenergetic. A slipped stack, cross-type isomer is found to be the most stable, and sandwiched and T-shaped dimers appears not to be stationary states on the potential energy surface.

1. Introduction

In recent years, a main focus within the development of density functional theory (DFT) has been toward the accurate treatment of dispersive interactions between noncovalently bonded molecules. One of the more successful approaches has been presented by Grimme and co-workers, who have added an empirical van der Waals correction term to existing DFT functionals (in general terms called DFT-D) which can then accurately treat dispersion forces.[1−3] The Truhlar group, on the other hand, has developed new functionals (M06 and M06-2X) that clearly have an improved ability to treat these weak interactions, as compared to standard DFT functionals.[4] An alternative way of handling systems interacting via dispersion forces has been presented by Röthlisberger and co-workers. They use nonlocal pseudopotentials as implemented in plane-wave codes with existing DFT methods to simulate dispersion binding.[5] The group of DiLabio recently developed atom-centered, local dispersion-correcting potentials (DCPs) for use with a variety of common functionals and basis sets. The DCP approach is very attractive, since it is applicable in many computational chemistry programs (for example Gaussian, Gamess, Molpro).[6,7] The DCPs were optimized to reproduce the dispersion binding in a training set consisting of noncovalently bound dimers of hydrocarbons and of heteroatom-containing molecules. The approach has been applied to study dispersion binding in a number of diverse systems outside the training set, including cyclic aromatic hydrocarbons,[6,7] benzothiophenes,[8] and small hydrocarbons and pentacene on hydrogen-terminated silicon surfaces.[9,10] However, since the method itself is new, information about its general utility is unavailable. For example, DiLabio et al. did develop DCP for B3LYP but have not used them in subsequent studies.[7] Of special interest to us is the evaluation of dispersion corrections to the B3LYP functional, particularly because this is the most commonly used functional today and because it shows generally excellent performance for thermochemistry.[11,12] However, due to its repulsive long-range behavior,[6] B3LYP poorly describes weakly interacting systems.[12] If the most applied DFT functional, however, in its dispersion-corrected form is applicable on challenging systems, such as weakly interacting systems, it can be a method to be used more or less as a standard for a broad range of chemical problems, rather than using specialized functionals and large basis sets. Therefore, in this study, we evaluate B3LYP with DCPs to predict binding energies of the 22 noncovalently bonded dimers that comprise the S22 benchmark set.[13] The set covers systems in which the interactions are dominated by hydrogen bonding, dispersive interactions, and a mix of the two. The method was then applied to the toluene dimer, for which dispersive interactions dictate the orientation of the two aromatic rings and, thus, the energetics of the toluene dimer. A comparison with other methodologies aimed at modeling dispersion interactions is also presented.

2. Computational Methods

All compounds were optimized using B3LYP[14−16]/6-31+G(d,p)[17−19] with Gaussian03[20] in combination with the DCPs (B3LYP/6-31+G(d,p)-DCP) taken from Mackie and DiLabio's study.[7] The modifying dispersion-correcting potential is added in the form of two Gaussian functions, of which one is attractive and the second, repulsive. This was necessary to avoid overbinding for larger systems.[6,7] The coefficients for the two functions were optimized by DiLabio et al. to minimize the deviation between calculated and literature values for interaction energies in a set of noncovalently bound dimers. It was found that binding energies could be predicted within 15%, and monomer separations within 0.1 Å, of high-level ab initio data.[6,7] The best balance between performance and computing time among different basis sets was found to be for the 6-31+G(d,p) basis set.[7] It is important to keep in mind that different functionals and different basis sets have slightly different coefficients for the Gaussian functions, and thus, these need to be changed in the input when another method is used. Examples of input for performing this type of calculation using Gaussian can be found in the Supporting Information.

In light of the fact that the dispersion correction explicitly covers the basis set superposition error, no further correction was employed. Both default settings and optimizations with a more strict convergence criterion and with a very tight grid for the numerical integration were evaluated in this study. In the

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TABLE 1: Calculated Interaction Energies (in kcal mol^{-1})

entry	system	B3LYP-DCP[a]	S22 benchmark[b]	absolute deviation	updated benchmark	absolute deviation	B3LYP	absolute deviation
1	ammonia dimer	−3.12	−3.17	0.05	−3.14[c]	0.02	−3.12	0.02
2	water dimer	−6.04	−5.02	1.02	−4.98[c]	1.06	−6.04	1.06
3	formic acid dimer	−17.21	−18.61	1.40	−16.15[d]	1.06	−15.85	0.30
4	formamide dimer	−14.47	−15.96	1.49	−14.94[d]	0.47	−13.59	1.35
5	uracil dimer h-bonded	−18.90	−20.65	1.75	−20.50[e]	1.60	−17.40	3.10
6	2-pyridoxine 2-aminopyridine	−15.06	−16.71	1.65	−16.71	1.65	13.70	3.01
7	adenine thymine Watson−Crick type	−14.38	−16.37	1.99	−15.43[f]	1.05	−12.74	2.69
mean: 1−7				1.34		0.99		1.65
8	methane dimer	0.02	−0.53	0.55	−0.51[d]	0.53	0.00[j]	0.51
9	ethene dimer	−0.75	−1.51	0.76	−1.42[d]	0.67	+0.03[j]	1.45
10	benzene-methane complex	−0.69	−1.50	0.81	−1.23[g]	0.54	−0.05[j]	1.18
11	benzene dimer parallel displaced	−2.58	−2.73	0.15	−2.61[h]	0.03	−0.27[j]	2.34
12	pyrazine dimer	−3.63	−4.42	0.79	−4.42	0.79	−0.40[j]	4.02
13	uracil dimer stack	−8.57	−10.12	1.55	−9.68[e]	1.11	−10.21[k]	0.53
14	indole benzene complex stack	−4.85	−5.22	0.37	−5.22	0.37	−2.14[l]	3.08
15	adenine thymine complex stack	−10.01	−12.23	2.22	−12.23	2.22	−2.48	9.75
mean: 8−15				0.90		0.78		2.86
16	ethene ethyne complex	−1.47	−1.53	0.06	−1.53	0.06	−0.94	0.59
17	benzene water complex	−3.21	−3.28	0.07	−3.17[i]	0.04	−2.11	1.05
18	benzene ammonia complex	−1.56	−2.35	0.79	−2.35	0.79	−0.95	1.40
19	benzene HCN complex	−4.31	−4.46	0.15	−4.46	0.15	−2.59	1.87
20	benzene dimer T-shaped	−1.88	−2.74	0.86	−2.74	0.86	−0.48	2.26
21	indole benzene T-shaped	−4.10	−5.73	1.63	−5.73	1.63	−2.15	3.58
22	phenole dimer	−6.72	−7.05	0.33	−7.05	0.33	−5.42	1.63
mean: 16−22				0.56		0.55		1.77
mean: 1−22				0.93		0.77		2.13

[a] Dispersion corrected B3LYP/6-31+G(d,p)-DCP, this work. [b] Ref 13. [c] Ref 40. [d] Ref 41. [e] Ref 24. [f] Ref 13. [g] Ref 42. [h] Ref 43. [i] Ref 44. [j] No bonding complex. [k] Minimizes to a hydrogen bonded complex where the H(N3) atom rather than H(N1) is the donor. [l] Minimizes to a T-shaped complex.

Gaussian03 input, the following keywords were then used for the latter case: scf = novaracc, Opt = (tight, newton), int = (grid = −96032). The use of the Newton−Raphson step during the optimization was found necessary due to the extremely flat potential energy surface. Default RFO step or opt = (tight, gdiis) did not converge. In a few cases, the keywords opt = (calcfc,tight,newton) were needed for optimization convergence. Comparisons were also made with calculations using M06-2X[4]/6-31+G(d,p) with option iacc = 2 as implemented in Jaguar,[21] or with B3LYP-D[1,3]/6-31+G(d,p) in combination with settings "VeryTightSCF Grid6 finalgrid 6 tightopt" as implemented in ORCA.[22] It should be remembered that B3LYP-D uses an empirical atom pair specific potential of C_6/R^6 type added to the DFT energy, whereas B3LYP-DCP uses a local atom-centered potential. All geometries were characterized as minima or saddle points on the potential energy surface by using the sign of the eigenvalues of the force constant matrix obtained from a frequency calculation.

3. Results and Discussion

Benchmarking. An evaluation of the S22 benchmark test set using B3LYP/6-31+G(d,p)-DCP is presented in Table 1. Similar to the original S22 paper,[13] the benchmark systems were divided into three categories: Entries 1−7 represent hydrogen bonded complexes, entries 8−15 represent complexes with mainly dispersive interactions, and entries 16−22 represent mixed complexes. When comparing B3LYP-DCP and the original S22 data set interaction energies, the mean absolute deviation (MAD) for entries 1−7 was found to be 1.34 kcal mol^{-1}. However, some of the entries have more recently been updated by W1, W2,[23] or CCSD(T)/CBS calculations and are, therefore, considered to be more reliable, on the basis of earlier studies by Martin et al.[23] The updated benchmark values are also presented in Table 1 for an easy comparison to those in the original S22 database. It is now observed that the agreement is improved with a MAD of only 0.99 kcal mol^{-1}. As a comparison, non-dispersion-corrected B3LYP/6-31+G(d,p) was found to result in a MAD of 1.65 kcal mol^{-1} (Table 1). For the second subset (entries 8−15) in this study, application of B3LYP/6-31+G(d,p)-DCP resulted in a MAD of 0.90 kcal mol^{-1}, but with some of the entries updated (Table 1), the MAD is reduced to 0.78 kcal mol^{-1}. The corresponding value for non-dispersion-corrected B3LYP is 2.86 kcal mol^{-1}, although for most of these, no stable, stacked complexes could be found. For the third category, entries 16−22, a MAD of 0.55 kcal mol^{-1} (0.56 kcal mol^{-1} compared to the original S22 data set) was calculated, whereas non-dispersion-corrected B3LYP gives 1.77 kcal mol^{-1}. Clearly, B3LYP-DCP gives a significant improvement and outperforms non-dispersion-corrected B3LYP in all three categories. This is especially satisfying and shows that B3LYP-DCP is able to handle a multitude of weak interactions, including hydrogen bonds. The overall MAD for all 22 complexes was found to be 0.93 and 0.77 kcal mol^{-1} when compared with the original S22 and updated benchmarks, respectively (see Table 1). When inspecting the individual deviations, it becomes clear that B3LYP-DCP underestimates the interaction energies. However, as has been noted by Hobza and co-workers,[24] the S22 benchmark might represent the upper limit of the interaction energy for stacked complexes. If this is true, the agreement for B3LYP-DCP will be improved. As a comparison, the overall MAD for M06-2X/6-31+G(d,p) was reported by Zhao and Truhlar[4] to be 0.47 kcal mol^{-1}, but non-dispersion-corrected B3LYP/6-31+G(d,p) is in this study found to result in a MAD of 2.13 kcal mol^{-1}. Additional comparisons worth mentioning here are Grimme's B97-D/TZV(2df, 2pd)[25] calculations with an overall MAD of 0.35 kcal mol^{-1} and DFT-LAP[26] with a MAD of 0.51 kcal mol^{-1}. Thus, B3LYP-DCP gives a MAD for interaction energies well within 1 kcal mol^{-1} of current benchmark values and therefore seems to complement existing methodologies capable of handling weakly interacting systems, although not reaching their full accuracy. With the information on the performance of B3LYP-DCP now in hand, a challenging system was sought which could be investigated. In the following section, an investigation of the toluene dimer using the above evaluated B3LYP/6-31+G(d,p)-DCP method is presented.

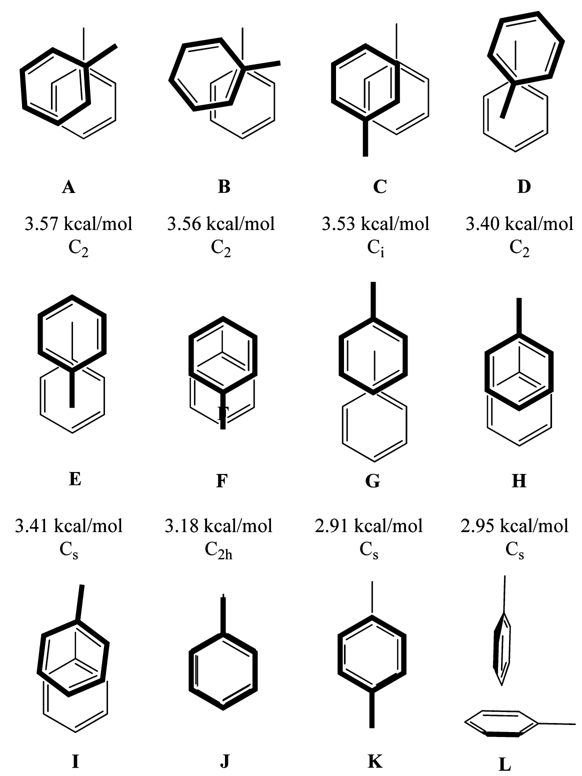

Figure 1. B3LYP/6-31+G(d,p)-DCP calculated dissociation energies (D_0) for different isomers of the toluene dimer. See Table 1 for values for isomers **J**−**L**.

The Toluene Dimer. A few computational studies of the toluene dimer have recently been presented, but these do not agree on which isomer of the dimer is the most stable. Rogers et al. showed in a study of the toluene dimer based on counterpoise-corrected CCSD(T)/6-311++G(d,p)//MP2/6-311++G(d,p) energies that an antiparallel isomer was slightly more stable than a cross structure.[27] The dissociation energies (D_e) for these two isomers were reported as 3.47 and 3.24 kcal mol^{-1}, respectively. A parallel structure was also optimized and found to have a dissociation energy of 2.71 kcal mol^{-1}. The authors did not explicitly calculate the zero-point energy (ZPE); instead, they used the ZPE from a study by Tsuzuki and co-workers.[28] By adding the ZPE-correction term (0.11 kcal mol^{-1}), the D_0 values for the isomers in Rogers' study are 3.36, 3.12, and 2.60 kcal mol^{-1}, respectively. This is in excellent comparison to the experimental D_0 value of 3.46 ± 0.23 kcal mol^{-1}.[29] A saving clause concerning their reported energies is that the toluene monomer geometry was taken from the respective complex. Thus, if using a fully relaxed monomer of toluene, the dissociation energies will be slightly reduced but still within the error bars of the experimental value. In contrast to Rogers' study, Tsuzuki and co-workers found, using CCSD(T) energies extrapolated to the basis set limit, a cross structure to be the most stable isomer ($D_0 = 3.97$ kcal mol^{-1}), and an antiparallel and parallel structure were 0.31 and 0.67 kcal mol^{-1}, respectively, less stable.[28] An explanation of why the final resulting most stable isomer of Tsuzuki is different from that in Rogers' study, except for different computational approaches being used, might be that the antiparallel structure in Tsuzuki's investigation has C_{2h} symmetry, whereas in Rogers' study, no symmetry was used. Similarly, Gervasio and co-workers found that an antiparallel stucture was ~1 kcal mol^{-1} more stable than a parallel structure.[30] However, closer examination of their antiparallel structure indicates this to have C_2 symmetry, with the two methyl groups positioned above each phenyl ring. All of these recent studies, however, are in agreement with experiments which suggest that (at least) two isomers of the toluene dimer are almost isoenergetic.[31,32] Although the calculated dissociation energy in Rogers' study is close to the experimental value, Tsuzuki's value is slightly outside the error bars. In addition, Grimme, using his new functional B97-D, calculated the D_e value to be 5.07 kcal mol^{-1}, which is considerably larger than both experimental and ab initio values.[3] Thus, there are discrepancies and uncertainties concerning details of the toluene dimer that are yet to be solved.

In this study, a large number of different isomers of the toluene dimer could be examined due to the use of density functional theory rather than high-level ab initio methods (Figure 1). In comparison to CCSD(T), which formally scales as N^7, DFT scales as N^3, which gives a major increase in computational speed. In addition, at this level of theory, it is possible to perform frequency calculations for the ZPE and to verify if the structure is a minimum or a saddle point. A fully relaxed monomer with a mirror plane perpendicular to the ring plane of toluene was used as the reference for calculation of the dissociation energies. This equilibrium structure is in accordance with neutron powder diffraction data.[33]

During the optimization of the toluene dimer, it became obvious that a multitude of structures (Figure 1) were very close in energy, within 0.5 kcal mol^{-1}, and that there does not appear to be a clear-cut answer to the final structure of the toluene dimer. In light of the small energy and structural differences, all isomers were therefore the subject for optimization with a more strict convergence criterion and with a very tight grid for the numerical integration (cf. Computational Methods and Table 2). In addition, Martin et al. and Johnson et al have pointed out that for systems with very flat potential energy surfaces, default optimization settings and grids are not adequate.[34,35] ZPE

TABLE 2: Dissociation Energies (D_0) in kcal mol^{-1} of Different Isomers of the Toluene Dimer Using B3LYP/6-31+G(d,p)-DCP and Two Different Optimization and Grid Settings[a,b]

isomer	default	strict[c]
A	3.38 (0)	3.57 (0)
B	3.25 (0)	3.56 (0)
C	3.36 (0)	3.53 (0)
D	3.30 (0)	3.40 (0)
E	3.30 (2)	3.41 (2)
F	3.01 (1)	3.18 (2)
G	2.85 (0)	2.91 (0)
H	2.92 (2)	2.95 (1)
I	2.84 (0)	2.92 (0)
J	1.35 (3)	isomer **H**
K	1.63 (2)	isomer **F**
L	1.66 (3)	isomer **H**

[a] Number of imaginary frequencies in parentheses. [b] Due to the large magnitude of possible combinations of conformations for the two methyl groups for isomers **A**−**I** of the toluene dimer, not all possible minima were investigated. For the monomer of toluene, the relative energy for a second isomer with the methyl group rotated 30° was only 0.13 kcal mol^{-1} higher. Our conclusion that the toluene dimer prefers a slipped, stacked orientation is most likely not affected by this simplification. [c] See Section 2, Computational methods.

corrections were found to alter the energy ordering of the different isomers, and keeping in mind the use of the harmonic approximation for evaluation of thermodynamic corrections, it seems valid to ask the question if the toluene dimer should be described by a single structure or, rather, as an ensemble of degenerate structures. This parallels the findings for the very fluxional CH_5^+ molecule, which has a particularly complex IR spectrum and several almost isoenergetic states.[36,37] Nevertheless, it is instructive to report on the different optimized structures and energies of the toluene dimer as a comparison to previous studies and also to highlight the energetics between different stacked, sandwiched, and T-shaped isomers. In Table 2, calculated dissociation energies using default settings in Gaussian03 are presented, together with those using more strict settings, as described above. Only results for the more strict settings will be discussed in the text.

The most stable isomer (**A**) using B3LYP/6-31+G(d,p)-DCP was found to be a slipped, stacked structure with C_2 symmetry. In this structure, the two monomeric units are aligned neither parallel nor antiparallel. The two rings are, rather, slipped in such a manner that a portion of the rings is overlaid. One of the rings is rotated so that the dihedral angle between C(Me)−C−C−C(Me) is ∼58°. This gives the features of a cross-type structure similar to that optimized by Tsuzuki,[28] but different from that sketched in Rogers' study in which one of the methyl groups is positioned above the plane of the aromatic ring.[27] Rotation of one of the methyl groups leads to isomer **B** (C−C−C−C dihedral angle = 77°), with smaller ring overlap due to ring rotation. Isomer **A** is only 0.01 kcal mol^{-1} more stable than isomer **B**, indicating a very flat potential energy surface (PES) for the interaction of the two rings and for methyl group rotation. The dissociation energy (D_0) for isomer **A** is found to be 3.57 kcal mol^{-1}; thus, in very good agreement with the experimental value of 3.46 ± 0.23 kcal mol^{-1} and within the error bars reported. In addition to isomers **A** and **B**, several other slipped, stacked isomers (**C**−**I**) were optimized and analyzed. Among these, it can be observed that an antiparallel orientation (isomers **C**, **E**, or **F**) of the two rings is slightly more favorable than a parallel orientation (isomers **G** and **H**). However, isomers **E**, **F**, and **H** were found to be saddle points and not minima on the PES (Table 1). Interestingly, for isomer **G** with the methyl groups oriented parallel, the two phenyl rings are oriented tilted at an angle of 20° to each other. Due to the inherent flatness of the PES for the toluene dimer, a distinction as to which structure is *the* most stable does not seem possible due to the small energy differences calculated. For example, isomers **C** and **D** are only 0.04 and 0.17 kcal mol^{-1} less stable than isomer **A**. In contrast, the sandwiched structures **J** and **K** are ∼1.5 kcal mol^{-1} less stable than isomer **A**, independent of having a parallel or antiparallel alignment. These isomers rearrange to isomers **H** and **F**, respectively, when employing the stricter convergence criteria and do not seem to be true stationary points on the PES. A similar behavior is found for the T-shaped structure **L**, which rearranges to a structure similar to isomer **H** when using the stricter optimization settings (Figure 1). Considering the small energy difference (0.04 kcal mol^{-1}) among isomers **A**, **B**, and **C**, which is well below the MAD observed for B3LYP-DCP for the S22 data set, one may question the definitive ordering of the isomers. However, it may be argued that the accuracy for relative energies between different isomers is higher than the accuracy for the dissociation energies. This was therefore verified by performing CCSD(T)/6-311++G(d,p)//B3LYP/6-31+G(d,p)-DCP calculations. The relative energies calculated were 0, 0.09, and 0.11 kcal mol^{-1}, for **A**, **B** and **C**, respectively. Thus, the energy ordering is conserved from that observed from the B3LYP/6-31+G(d,p)-DCP calculations.

From these energy values, it can be concluded that the toluene dimer prefers to have the two rings in a slipped, stacked orientation, whereas the exact position of the two rings seems to be very fluxional. Most of the isomers **A**−**I** would be populated even at low temperatures and, thus, make a spectroscopic assignment of the toluene dimer more complex.

Employing B3LYP/6-31+G(d,p) without dispersion correction on isomer **A** led immediately to a complex with only a fraction of stabilization between the two monomers, −0.05 kcal mol^{-1}, and with no interaction of a stacking type (closest C−C distance: 4.4 Å). Adding the DCP and reoptimizing led again to a slipped, stacked isomer (**B**) with a closest C−C distance of 3.3 Å. This control analysis was made both to ensure that the starting structure used would not result in another, so far not found, more stable minimum structure and also to show that the interaction leading to the final structure also works on a longer distance between the rings. The reoptimization is added as a link to the manuscript to visualize the result.

To verify the calculated dissociation energies for isomer **A**, two other approaches were also applied: (a) the M06-2X[4]/6-31+G(d,p) as implemented in Jaguar,[21] and (b) B3LYP-D/6-31+G(d,p),[1,3] as implemented in ORCA.[22] Counterpoise (CP) corrections[38] were added to the D_0 values for the M06-2X calculations.

TABLE 3: Experimental and Calculated Dissociation Energies (in kcal mol^{-1})

	exptl[29]	B3LYP/ 6-31+G(d,p)-DCP	M06-2X/ 6-31+G(d,p)[a]	B3LYP-D/ 6-31+G(d,p)
dissociation energy	3.46 ± 0.23	3.57	3.24 (4.00)	5.44

[a] Non-counterpoise-corrected values in parentheses.

As can be seen in Table 3, M06-2X gives a D_0 value similar to that using B3LYP-DCP (3.24 and 3.57 kcal mol^{-1}, respectively), and this is also within the experimental error bars, but only after employing the CP correction for the basis set superposition error. In contrast, B3LYP-D overestimates the dissociation energy (5.44 kcal mol^{-1}) similar to how B97-D did.[3] This artifact[39] of the DFT-D method has been reported to have its origin in the double counting of correlation effects by the introduction of the dispersion correction term but is, in general, effectively reduced by the introduction of a damping function.[3,25]

3. Conclusions

A recent literature study showed that more than 80% of all DFT investigations utilize the B3LYP functional, and as such, it is the most widely used DFT method of today.[12] B3LYP is still one of the best density functionals when it comes to thermochemistry, but similar to most density functionals, it is not able to accurately treat non-covalently bonded molecules; for example, interacting via dispersion interactions. The group of DiLabio recently developed atom-centered, local dispersion-correcting potentials (DCPs) to be combined with a variety of common functionals and basis sets. An evaluation of dispersion-corrected B3LYP in the form of B3LYP-DCP has been performed in this study by comparing to the benchmark S22 data set. It is observed that the overall MAD of interaction energies is smaller than 1 kcal mol^{-1}, and gratifyingly, the method gives good results for a variety of weak interactions, including hydrogen bonds for which non-dispersion-corrected DFT is known to give poor results.

B3LYP/6-31+G(d,p)-DCP was then used for an investigation of the toluene dimer, for which it was found that a large number of slipped, stacked isomers are almost isoenergetic. The three most stable isomers are found to differ by only 0.04 kcal mol^{-1}. Therefore, the energy ordering for these was verified also with CCSD(T)/6-311++G(d,p)/B3LYP/6-31+G(d,p)-DCP calculations, which nicely confirmed the energy ordering observed from the B3LYP/6-31+G(d,p)-DCP calculations. Sandwiched and T-shaped isomers are not stable minima on the potential energy surface and rearrange to stacked isomers. Estimated energies using default optimization and grid settings indicate that these are ~2 kcal mol^{-1} less stable in energy than slipped, stacked isomers. The calculated dissociation energy (D_0) for the most stable slipped, stacked, cross-type isomer of 3.57 kcal mol^{-1} is within the error bars of the experimentally determined value and differs by only 0.2−0.3 kcal mol^{-1} from high-level ab initio and M06-2X calculated energies.

Thus, it appears that B3LYP-DCP is able to accurately predict weak interactions. It will therefore be a useful approach in studies of biological systems in which hydrogen bonds, non-covalent $\pi-\pi$-, CH-π interactions, and other dispersive interactions are thought to play an important role. More specifically, it will aid in studies about how amino acids orient and interact, not only with each other but also with drugs having aromatic functionalities.

Bearing in mind the vast amount of chemistry that has been handled by B3LYP calculations, it will now be useful to apply B3LYP-DCP to some systems, both where B3LYP has been successful and also where it has failed, to see the influence of dispersion correction in chemical terms. Such studies are currently in progress.

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Supporting Information Available: Cartesian coordinates and total energies for isomers **A**−**I** are given. An example of a Gaussian input for performing a B3LYP/6-31+G(d,p)-DCP calculation is given. This material is available free of charge via the Internet at http://pubs.acs.org.

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