First-Principles Modeling of Non-Covalent Interactions in Supramolecular Systems: The Role of Many-Body Effects

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ABSTRACT: Supramolecular host−guest systems play an important role for a wide range of applications in chemistry and biology. The prediction of the stability of host−guest complexes represents a great challenge to first-principles calculations due to an interplay of a wide variety of covalent and noncovalent interactions in these systems. In particular, van der Waals (vdW) dispersion interactions frequently play a prominent role in determining the structure, stability, and function of supramolecular systems. On the basis of the widely used benchmark case of the *buckyball catcher* complex ($C_{60}@C_{60}H_{28}$), we assess the feasibility of computing the binding energy of supramolecular host−guest complexes from first principles. Large-scale diffusion Monte Carlo (DMC) calculations are carried out to accurately determine the binding energy for the $C_{60}@C_{60}H_{28}$ complex (26 ± 2 kcal/mol). On the basis of the DMC reference, we assess the accuracy of widely used and efficient density-functional theory (DFT) methods with dispersion interactions. The inclusion of vdW dispersion interactions in DFT leads to a large stabilization of the $C_{60}@C_{60}H_{28}$ complex. However, DFT methods including pairwise vdW interactions overestimate the stability of this complex by 9−17 kcal/mol compared to the DMC reference and the extrapolated experimental data. A significant part of this overestimation (9 kcal/mol) stems from the lack of dynamical dielectric screening effects in the description of the molecular polarizability in pairwise dispersion energy approaches. The remaining overstabilization arises from the isotropic treatment of atomic polarizability tensors and the lack of many-body dispersion interactions. A further assessment of a different supramolecular system − glycine anhydride interacting with an amide macrocycle − demonstrates that both the dynamical screening and the many-body dispersion energy are complex contributions that are very sensitive to the underlying molecular geometry and type of bonding. We discuss the required improvements in theoretical methods for achieving "chemical accuracy" in the first-principles modeling of supramolecular systems.

1. INTRODUCTION

Supramolecular host−guest complexes play an important role in natural and artificially engineered chemical and biological systems. In such complexes, a guest molecule modifies the structure of the host moiety, frequently leading to novel concerted effects in the host−guest complex, when compared to isolated molecules. Here we focus on one prototypical example from a wide variety of possible host−guest systems— the so-called buckyball catcher complex.[1] We concentrate on the ability of different electronic structure methods to fully capture the wide spectrum of noncovalent interactions present in this prototypical $\pi-\pi$ stacking system.

Many encouraging methods have been developed for describing vdW interactions within density-functional theory (see, e.g., refs 2−7 and references therein), and the best asymptotically correct methods perform better than the so-called *chemical accuracy* of 1 kcal/mol for intermolecular and intramolecular energies for small molecules, such as for the prototypical S22 database.[8] Also, important developments have recently been done to extend the validity of methods for calculating the dispersion energy to extended systems, such as solids and inorganic/organic interfaces.[9−12] In contrast, much less is known about the performance of dispersion-inclusive DFT methods for intermediate systems between small molecules and extended solids, simply because there are no trusted reference binding energy data for systems beyond several dozens of light atoms. Supramolecular host−guest complexes belong to this class of challenging systems lying between small molecules and periodic solids.

For small systems, up to a few dozen atoms, the "gold standard" method for determining intermolecular binding energies is coupled cluster with single, double, and perturbative triple excitations, CCSD(T). Its rather steep $O(N^7)$ scaling with system size N prohibits using the CCSD(T) approach for larger systems. An alternative to coupled-cluster theory are the different variants of Quantum Monte Carlo (QMC) methods, which explicitly solve the full electronic structure problem assuming a flexible ansatz for the many-electron wave function. In particular, diffusion Monte Carlo (DMC) is a very promising tool for computing binding energies of large systems with chemical accuracy. The QMC methods (see, e.g., ref 13) have been shown to be very accurate to describe the energetics of covalently bound molecules,[14] hydrogen-bonded systems,[15,16] weakly interacting systems,[17,18] including complexes involving hydrocarbons[19,20] and graphene.[21,22]

Here, we apply DMC to calculate an accurate reference binding energy for the buckyball catcher complex ($C_{60}@C_{60}H_{28}$). This complex has been recently synthesized, and studied using a variety of theoretical methods. It can be

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considered as a prototype for large vdW-bound systems because of its rather large $\pi-\pi$ interacting area (see Figure 1). Using DMC as a reference method, we assess the accuracy
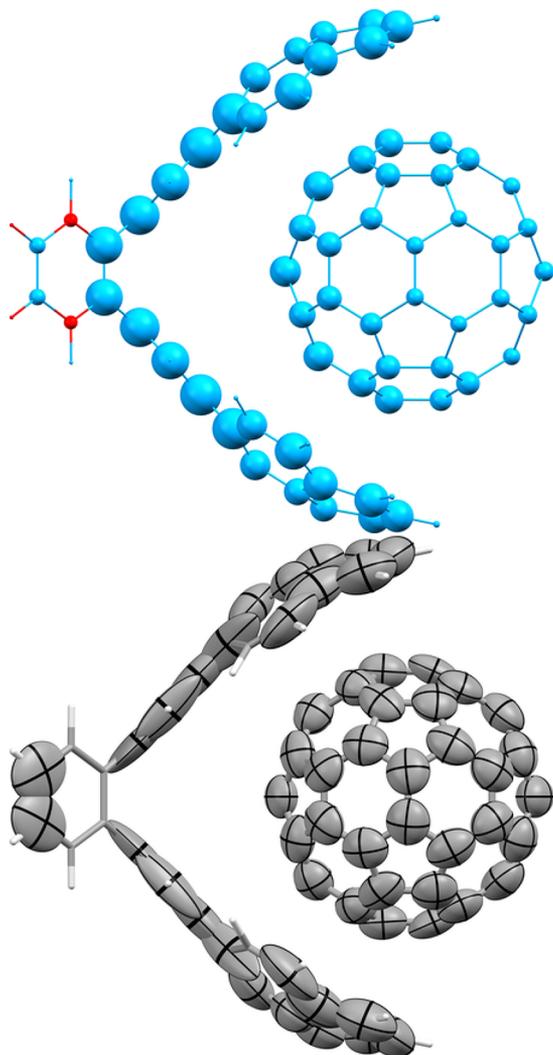

Figure 1. (Color online) Top: The change in the isotropic TS-vdW +SCS C_6 coefficients [eq 2] of the whole $C_{60}@C_{60}H_{28}$ complex with respect to the sum of C_6 coefficients for the isolated C_{60} and $C_{60}H_{28}$ molecules, having the same geometry as the full complex. Blue color indicates a decrease in the C_6 coefficient of a given atom in the complex, while red color indicates increase. Bottom: Illustration of the anisotropy in the atomic TS-vdW+SCS polarizabilities of the $C_{60}@$ $C_{60}H_{28}$ complex. The polarizability tensors are visualized as ellipsoids.[25].

of widely used and efficient density-functional theory (DFT) approaches that include dispersion interactions. As expected, we find that vdW dispersion interactions lead to a large stabilization of the $C_{60}@C_{60}H_{28}$ complex. However, pairwise long-range corrected DFT methods overestimate the stability of this complex by 9–17 kcal/mol compared to the DMC reference and extrapolated experimental data. A significant part of this overestimation (9 kcal/mol) is attributed to the lack of dynamic dielectric screening effects in the description of the molecular polarizability in pairwise dispersion energy methods. The remaining overstabilization arises from the isotropic treatment of the atomic polarizability tensors and the lack of

nonadditive many-body dispersion interactions in pairwise energy expressions.

We find that dynamical screening effects, polarizability anisotropy, and nonadditive many-body dispersion interactions could affect the binding of any sufficiently large molecule to a significant degree.[23,24] Therefore, we conclude that next-generation methods for the dispersion energy should aim to accurately model these important physical contributions.

2. REFERENCE BINDING ENERGY FOR THE BUCKYBALL CATCHER

Diffusion Monte Carlo calculations have been performed with the CASINO code,[26] using trial wave functions of the Slater–Jastrow type:

$$\psi_T(\mathbf{R}) = D^{\uparrow}D^{\downarrow}e^J \tag{1}$$

where $D^{\uparrow}$ and $D^{\downarrow}$ are Slater determinants of up- and down-spin single-electron orbitals, and e^J is the so-called Jastrow factor, which is the exponential of a sum of one-body (electron–nucleus), two-body (electron–electron), and three body (electron–electron–nucleus) terms. Imaginary time evolution of the Schrödinger equation has been performed with the usual short time approximation and the locality approximation.[27] To investigate convergence of the binding energy with respect to time step, we repeated the calculations using time steps of 0.0125, 0.005, and 0.002 au. With the shortest time step the acceptance rate was 99.96%.

We used Dirac–Fock pseudopotentials (PP) for C and H.[28,29] The C PP has a frozen He core and a core radius of 0.58 Å. The H PP has a core radius of 0.26 Å. The single particle orbitals have been obtained by DFT plane-wave (PW) calculations using the local density approximation and a PW cutoff of 300 Ry (4082 eV), using the PWSCF package,[30] and re-expanded in terms of B-splines,[31] using the natural B-spline grid spacing given by $a = \pi/G_{max}$, where G_{max} is the length of the largest vector employed in the PW calculations. The B-spline basis set shares the properties of plane-waves of being unbiased and systematically improvable (by reducing the grid spacing, equal to ~0.1 Å in the present case), and therefore convergence of the trial wavefuctions with respect to basis set representation is obtained. Therefore, there is no basis set superposition error (BSSE) in the DMC calculations. The PW calculations were performed by putting the systems in cubic boxes with 26.46 Å sides, which ensured that periodic images were separated by at least 12 Å. The DMC calculations were then performed with no periodic boundary conditions.

The relaxed geometry of the buckyball catcher complex and the isolated monomers were obtained from ref 32 and used for both the DMC calculations here and DFT calculations in the next section. Using the above computational settings with the converged time step of 0.005 au, the obtained DMC binding energy for the $C_{60}@C_{60}H_{28}$ complex is 25.8 ± 1.5 kcal/mol.

Recently, Grimme has presented a database of a few supramolecular complexes,[32] and he estimated their binding energies by empirically computing the free energy of binding and "removing" enthalpic and entropic contributions from the experimentally measured binding affinities.[1] Given that the calculated free energies are larger in magnitude than the experimental one, the value of 28 kcal/mol obtained by Grimme for the binding energy of the buckyball catcher complex represents an upper limit.[32] This value is in good

agreement with the binding energy computed from first principles using DMC.

On the basis of our DMC calculations and the extrapolated experimental data, we conclude that the binding energy of the $C_{60}@C_{60}H_{28}$ complex is 26 ± 2 kcal/mol. We will now use this value as a reference for assessing the performance of approximate, albeit more efficient, DFT methods.

3. PERFORMANCE OF DFT FUNCTIONALS FOR THE BUCKYBALL CATCHER

The stability of the buckyball catcher complex has been studied using a combination of DFT functionals and methods for the dispersion energy. Grimme and co-workers used the B97-D method and obtained a binding energy of 43.1 kcal/mol for $C_{60}@C_{60}H_{28}$.[33] The most recent study by Grimme using the pairwise DFT-D3 method[34] reported interaction energies from 37.5 kcal/mol for TPSS-D3 to 41.2 kcal/mol for B97-D3.[35] In ref 32, it was estimated that the three-atom Axilrod−Teller term could reduce the binding energy by ∼3 kcal/mol. A binding energy of 36.1 kcal/mol was reported by Podeszwa and co-workers using a pairwise dispersion energy expression with the so-called dlDF functional.[36] Unfortunately, the def2-SVP basis set used by Podeszwa et al. is far from being converged. The authors also reported an interaction energy of 30.9 kcal/mol when the dispersion energy was computed with a coupled Kohn−Sham (CKS) approach, instead of the pairwise dispersion approximation. However, they remark that the computed CKS dispersion energy is not converged with respect to the basis set, and the converged binding energy is likely to be significantly larger. In fact, a full SAPT calculation with a converged basis set would be required to benchmark the results of Podeszwa et al. To our knowledge, such calculations have not yet been carried out. Zhao and Truhlar used the empirical Minnesota-type (M05 and M06) functionals, and obtained binding energies from 20.7 to 26.4 kcal/mol.[37] These meta-GGA functionals were trained on a set of small molecules, and by construction they are not designed to describe the long-range dispersion interactions[38,39] that are significant for such large systems as the $C_{60}@C_{60}H_{28}$ complex. Below, we show that the M06-L functional considerably overestimates the binding energy of the buckyball catcher complex after explicitly including the long-range dispersion interactions.

All DFT calculations in this work employed FHI-aims,[40] an all-electron electronic structure code which uses numerical atom-centered orbitals (NAO) as a basis set. The tier2 NAO basis set has been used throughout. This basis set yields results that are similar in accuracy to those of the aug-cc-pVQZ Gaussian basis set for the S22 database[39] and has been explicitly tested for convergence by selected comparisons with computations using the higher level, tier3 NAO basis set. The tier3 basis set yields results essentially at complete basis set limit, therefore the reported binding energies in this work are converged to within a fraction of a kcal/mol.

We started by calculating the binding energy of the $C_{60}@C_{60}H_{28}$ complex using the local-density approximation (LDA) for the exchange-correlation functional. It is well-known that the electronic kinetic energy resulting from an LDA calculation[41] is overly attractive and the resulting artificial binding helps when studying small vdW-bonded compounds. As the size of the system is increased, the lack of long-range vdW interactions in LDA typically leads to an underestimation of the binding energy. Our calculated LDA value of 21.2 kcal/mol is indeed smaller by 4.6 kcal/mol compared to the DMC

reference energy. In contrast to LDA, PBE predicts an unstable complex with a negative binding energy of −12.5 kcal/mol. Similarly, upon inclusion of 25% of Hartree−Fock exchange in the PBE0 functional, the $C_{60}@C_{60}H_{28}$ complex turns out to be unstable with a binding energy of −9.7 kcal/mol. When using the M06-family of functionals, a rather flexible empirical functional form for the exchange and correlation allows them to capture middle-range vdW interactions.[39,42,43] The M06-L functional yields a binding energy of 25.8 kcal/mol, in seemingly excellent agreement with the DMC calculations. However, as mentioned above, the M06 functionals lack the long-range dispersion interactions, similar to LDA or GGA functionals. Upon including the dispersion energy using the M06-L+TS-vdW method,[39] the binding energy is increased to 46.5 kcal/mol—a significant overestimation compared to the DMC reference.

Finally, we used the TS-vdW method[44] coupled with nonempirical PBE[45] and PBE0[46,47] functionals to study the binding of the buckyball catcher. In the TS-vdW method, the vdW parameters (C_6 coefficients and vdW radii) are determined from first-principles using the electron density of the molecular system and reference values for the isolated atoms. As expected, the dispersion energy is important for the buckyball catcher complex. When using the PBE+TS-vdW approach, the resulting binding energy is 43.0 kcal/mol (43.2 kcal/mol for PBE0+TS-vdW).

We conclude that irrespective of the employed generalized gradient approximation (PBE), hybrid (PBE0), or meta-GGA (M06-L) DFT functionals, the addition of the pairwise dispersion energy leads to an overestimation of 9−17 kcal/mol for the binding energy of the $C_{60}@C_{60}H_{28}$ complex with respect to the DMC reference. We now proceed to analyze the reasons for this overestimation.

4. DYNAMICAL SCREENING AND ANISOTROPY OF THE DISPERSION ENERGY

The analysis of the performance of different DFT methods in the previous section shows that upon including the long-range dispersion interactions, *all* of these methods overestimate the binding energy of the buckyball catcher complex compared to the DMC reference calculated in this work. We also note that widely different DFT functionals (e.g., PBE, PBE0, or M06-L) yield consistent binding energy within a few kcal/mol when including dispersion interactions using the TS-vdW method. This is a clear indication that pairwise models for the dispersion energy strongly overestimate the binding of the C_{60} molecule with the $C_{60}H_{28}$ moiety.

One of the strongest approximations of pairwise models for the dispersion energy is the additivity of polarizabilities and C_6 coefficients for atoms in molecules. This is a good approximation for small molecules, but it fails dramatically as the size of the molecule increases. For example, in large semiconductor clusters and solids, such as diamond and silicon, the long-range dynamical screening reduces the atom−atom C_6 coefficients by a factor of 1.6 to 1.8.[11] The screening effects stem from the dynamic electric field that every atom in a molecule or material experiences from all the surrounding atoms. Therefore, screening is by definition a many-atom phenomenon. In the static field approximation, the influence of screening has been studied for almost a century.[48,49] The Dyson-like equation provides a natural formalism to include the effects of dynamical screening. We have recently introduced an efficient first-principles model to accurately compute the fully

screened polarizability tensor for molecules and solids, based on the dipole approximation to the Dyson-like screening equation.[23]

The screening effects are treated microscopically by modeling the environment as a dipole field and solving the resulting classical electrodynamics self-consistent screening (SCS) equation,[49−51]

$$\alpha^{SCS}(\mathbf{r};\, i\omega) = \alpha^{TS}(\mathbf{r};\, i\omega) + \alpha^{TS}(\mathbf{r};\, i\omega)$$
$$\times \int d\mathbf{r}'\mathcal{T}(\mathbf{r} - \mathbf{r}')\alpha^{SCS}(\mathbf{r}';\, i\omega) \qquad (2)$$

where $\alpha^{TS}(\mathbf{r};\, i\omega)$ is the sum of the TS-vdW effective atomic polarizabilities,[44] and $\mathcal{T}(\mathbf{r} - \mathbf{r}')$ is the dipole−dipole interaction tensor. Equation 2 is discretized in the basis of atomic positions and then solved directly and exactly by inverting the tensor corresponding to the coupled dipoles (quantum harmonic oscillators (QHO)). The QHO parameters are defined using the TS-vdW polarizability.[23] The solution yields the nonlocal molecular polarizability tensor $\alpha^{SCS}_{pq}(i\omega)$. The contraction of the molecular tensor for every atom p yields the atomic polarizability tensors $\alpha^{SCS}_{pq}(i\omega)$. These tensors now include both the short-range hybridization effects from the TS-vdW method and the long-range Coulomb screening from the solution of the SCS equation.

Upon including the dynamical screening contributions in the atomic polarizabilities, one can now use these parameters to compute the two-body vdW energy corresponding to the fully screened system. One of the necessary approximations in this case is the assumption of isotropic vdW parameters (C_6 and vdW radius) obtained after taking the trace of the atomic polarizability tensors.

The inclusion of screening in the atomic polarizabilities leads to minor effects for small molecules in the S22 database of intermolecular interactions. The mean absolute error and the mean absolute relative error with respect to the CCSD(T) reference[52] are the same for TS-vdW and TS-vdW+SCS methods within 0.1 kcal/mol and 1%, respectively. A very different situation is found for larger molecules and solids. We have recently developed a method to calculate the screened vdW energy for ionic and semiconductor crystals[11] and hybrid inorganic/organic interfaces.[12] In extended systems, screening plays an essential role in the obtained vdW energies, and here we assess its importance for a large supramolecular complex. Using the screened vdW parameters in the PBE+TS-vdW method (see refs 11 and 23 for details), we obtain a binding energy of 34 kcal/mol for the $C_{60}@C_{60}H_{28}$ complex, a reduction of 9 kcal/mol compared to the pairwise PBE+TS-vdW method. Clearly, screening effects are very significant not only in extended systems, but also for molecules larger than the simple small molecules such as those found in typical benchmark databases.

The significant reduction of 9 kcal/mol due to dynamical screening can be understood upon analyzing the polarizabilities and C_6 coefficients of the isolated C_{60} and $C_{60}H_{28}$ moieties and the full $C_{60}@C_{60}H_{28}$ complex. Every carbon atom in the isolated C_{60} molecule is equivalent by symmetry with the isotropic carbon−carbon C_6 coefficient being 24.6 hartree bohr[6]. The symmetry is broken upon the formation of the $C_{60}@C_{60}H_{28}$ complex, and in this case the polarizability of all the carbon atoms in the C_{60} molecule is decreased. This effect is displayed in Figure 1, which shows the *change* of the carbon−carbon C_6 coefficients of the complex as compared to the sum

of the C_6 coefficients of the isolated C_{60} and $C_{60}H_{28}$ molecules. The C_{60} carbon atoms closest to the corannulene molecule possess the smallest C_6 coefficient of 18.6 hartree bohr[6], while the farthest carbon atoms in the C_{60} molecule have the C_6 coefficient of 22.9 hartree bohr[6]. Similar phenomenon can be observed in the corannulene molecule—overall depolarization of all of the atoms except in the linker moiety located outside of the bonding region.

The approximation of isotropic C_6 coefficients becomes exact as the distance between the atoms is increased. However, at shorter interatomic distances the anisotropy could play a non-negligible role.[53] In fact, the atomic polarizability tensors of the $C_{60}@C_{60}H_{28}$ complex are highly anisotropic, as shown in the lower part of Figure 1. Currently, there is no efficient method that accurately calculates the fully anisotropic dispersion energy at close interatomic distances, since the damping function has to become anisotropic as well. This statement applies to the widely employed interatomic dispersion methods, as well as nonlocal density functionals (e.g., different variants of the vdW-DF method[5]). Work is in progress to seamlessly include anisotropy in dispersion energy expressions.[53,54] The anisotropy in the atomic polarizabilities will change the vdW energy contribution in different directions. In the case of the $C_{60}@C_{60}H_{28}$ complex, the polarizability of the $C_{60}H_{28}$ molecule is highly anisotropic as shown in Figure 1. In the isotropic approximation, the dispersion energy between the C_{60} molecule and the corannulene moieties is overestimated, because the polarization is artificially extended toward the C_{60} molecule. The fully anisotropic treatment of the dispersion energy is therefore expected to bring the binding energy closer to the DMC reference value.

We further note that large molecules with delocalized π electrons tend to have small HOMO−LUMO gaps that lead to rather high polarizabilities for low frequencies of the electric field. These effects are in principle not fully treated by the SCS equation [eq 2] that relies on modeling the coupling between localized dipoles. We have already shown in ref 23 that the SCS equation is able to accurately describe the polarizability and C_6 coefficients of hydrogen-saturated silicon clusters where the HOMO−LUMO gap changes by almost an order of magnitude with increasing cluster size. This clearly shows that the SCS equation is able to correctly describe the polarizability for systems with widely varying HOMO−LUMO gaps. In the limit of widely delocalized electrons, such as found, e.g., in low-dimensional carbon-based systems, the SCS model will not describe fully the coupling between the localized and the delocalized electrons. However, we expect these coupling effects to have a rather small contribution to the vdW dispersion energy. In fact, the coupling between localized and delocalized electrons is significant only at rather low frequencies of the electric field, leading to an effectively negligible energy contribution for the interlayer binding between graphene layers.[55]

5. MANY-BODY DISPERSION ENERGY

The dispersion energy includes many-body effects beyond the screening discussed in the last section. For example, the well-known Axilrod−Teller−Muto term[56] corresponds to the dispersion interaction between three atoms. These many-body interactions are not included in the screened polar-izabilities obtained after solving eq 2. We have recently developed the MBD method, that includes the many-body energy to infinite order.[23,24] The MBD method is based on the

so-called coupled fluctuating dipole model (CFDM), extensively used before for model systems, such as chains, layers, cubes, and rare-gas liquids.[57−64] The MBD method is a significant extension of the CFDM model that allows us to accurately and efficiently determine the dispersion energy of complex molecular and condensed matter systems with a finite HOMO−LUMO gap. The MBD energy, containing many-body contributions to infinite order, is calculated as the difference between coupled and uncoupled zero-point energies, where the former are obtained upon exact diagonalization of the CFDM Hamiltonian,[58]

$$H = -\frac{1}{2}\sum_{p=1}^{N} \nabla_{\chi_p}^2 + \frac{1}{2}\sum_{p=1}^{N} \omega_p^2 \chi_p^2 + \sum_{p>q}^{N} \omega_p \omega_q \sqrt{\alpha_p \alpha_q} \chi_p \mathcal{T}_{pq} \chi_q$$

(3)

where $\chi_p = (m_p \mu_p)^2$, with μ_p being the displacement of an atom p from equilibrium and $m_p = (\alpha_p \omega_p^2)^{-1}$. We note that the input to the MBD Hamiltonian are the TS-vdW+SCS polarizabilities from eq 2. These polarizabilities are already screened, and can be considered as coming from a nonlocal exchange-correlation kernel in the adiabatic connection fluctuation−dissipation theorem framework. See refs 23 and 54 for a detailed discussion.

The PBE+MBD binding energy for the $C_{60}@C_{60}H_{28}$ complex is determined to be 36 kcal/mol, which is 7 kcal/mol closer to the DMC reference than with PBE+TS-vdW, but 2 kcal/mol larger than with the fully screened PBE+TS-vdW method. This result stems from the importance of polarizability anisotropy at shorter distances where the many-body dispersion interactions are in fact dominant. We expect the full treatment of anisotropy to play a larger role in the MBD method than in effective pairwise methods for the dispersion energy. Work is in progress to develop a fully anisotropic MBD method.[54] We conclude that the many-body dispersion energy contributes significantly to the stability of supramolecular systems, reinforcing our conclusions in ref.[24]

6. APPLICATION TO AN ADDITIONAL SUPRAMOLECULAR COMPLEX: GLH@MCYCLE

To assess the validity of our conclusions regarding the effect of dispersion energy contributions beyond effective pairwise methods, we analyze the binding in a different supramolecular system: glycine anhydride (GLH) interacting with an amide macrocycle (mcycle). In this case, there is a hydrogen bonding contribution to the binding between the molecules as shown in Figure 2, yet dispersion interactions clearly play a prominent role.[32] More importantly, DFT with empirical pairwise dispersion interactions appears to *underestimate* the binding energy, in contrast to the buckyball catcher complex.[32] Using the same level of DMC calculations as for the buckyball catcher complex, we obtain a binding energy of 33.4 ± 1.0 kcal/mol for GLH@mcycle. The DMC binding energy agrees rather well with an estimate of 34.8 kcal/mol in ref 32.

In contrast to the buckyball catcher complex, the PBE+TS-vdW method leads to good agreement with our DMC calculations, yielding a binding energy of 35.7 kcal/mol. The inclusion of screening effects using the TS-vdW+SCS method affects the binding energy by less than 0.1 kcal/mol. Similarly, the inclusion of many-body dispersion energy using the PBE+MBD method[23] yields a binding energy of 36.2 kcal/mol. We rationalize these findings by the fact that the screened polarizability of the full GLH@mcycle system is roughly
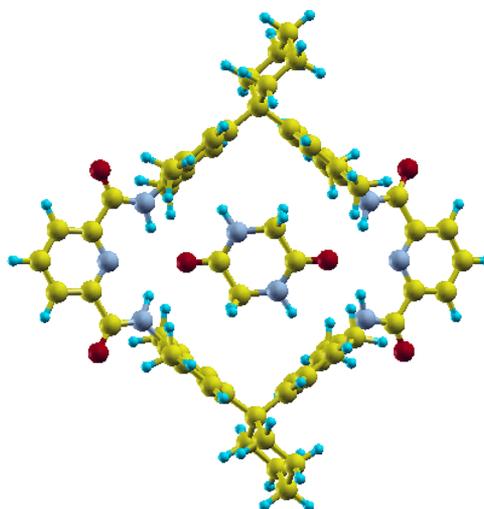

Figure 2. The structure of glycine anhydride (GLH) interacting with an amide macrocycle (mcycle).

equal to the sum of the polarizabilities of the isolated GLH and mcyle molecules. Although the screening does have an effect on the overall distribution of the polarizability, its effect on the energy is negligible in this case. These results demonstrate that both screening and many-body dispersion energy are complex contributions that are very sensitive to the underlying molecular geometry and type of bonding. The GLH@mcycle complex illustrates that effective pairwise methods for the dispersion energy can rather successfully mimic the binding of selected systems, but they are not guaranteed to be accurate in general, as clearly illustrated above for the buckyball catcher complex.

7. OUTLOOK

We calculated an accurate reference binding energy for the buckyball catcher $C_{60}@C_{60}H_{28}$ complex and the GLH@mcycle complex using a wave function-based DMC method. The reference binding energies have been used to assess the performance of approximate DFT methods. We find that the recently developed methods for the dispersion energy that include dynamical dielectric screening and many-body dispersion energy can significantly improve the binding energy, in particular for the $C_{60}@C_{60}H_{28}$ complex. The issue that remains to be addressed is the full treatment of anisotropy in the molecular polarizability, and its influence in the computation of the dispersion energy.

Our conclusion that the existing methods for the dispersion energy can lead to large errors of a few kcal/mol when it comes to larger supramolecular systems is in marked contrast with the fact that the best asymptotically correct methods are able to compute the dispersion energy to 0.2 − 0.3 kcal/mol for small benchmark systems in several existing databases. We expect to see significant improvements in methods for computing the dispersion energy in the next few years that should be able to consistently achieve chemical accuracy for small, medium, and large molecules and solids.

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Notes
The authors declare no competing financial interest.

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