

A Theoretical Investigation of the Geometries and Binding Energies of Molecular Tweezer and Clip Host–Guest Systems

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Abstract: A quantum chemical study of host–guest systems with dimethylene-bridged clips and tetramethylene-bridged tweezers as host molecules and six different aliphatic and aromatic substrates as guests is presented. The geometries and binding energies of the complexes are investigated using the recently developed density functional theory with empirical corrections for dispersion interactions (DFT-D) in combination with the BLYP functional and basis sets of TZVP quality. It is found that the DFT-D method provides accurate geometries for the host–guest complexes that compare very favorably to experimental X-ray data. Without the dispersion correction, all host–guest complexes are unbound at the pure DFT level. Calculations of the clip complexes show that the DFT-D binding energies of the guests agree well with those from a more sophisticated SCS-MP2/aug-cc-pVTZ treatment. By a partitioning of the host into molecular fragments it is shown that the binding energy is clearly dominated by the aromatic units of the clip. An energy decomposition analysis of the interaction energies of some tweezer complexes revealed the decisive role of the electrostatic and dispersion contributions for relative stabilities. The calculations on the tweezer complexes show that the benzene spaced tweezer is a better receptor for aliphatic substrates than its naphthalene analogue that has a better topology for the binding of aromatic substrates. The tweezer with a OAc substituent in the central spacer unit is found to favor complex formation with both aliphatic and aromatic substrates. The theoretical results are qualitatively in very good agreement with previous experimental findings although direct comparison with experimental binding energies which include solvent effects is not possible. The good results obtained with the DFT-D-BLYP method suggest this approach as a standard tool in supramolecular chemistry and as the method of choice for theoretical structure determinations of large complexes where both electrostatic and dispersive interactions are crucial.

1. Introduction

The noncovalent interactions between atoms and molecules play an important role in structural biology and supra-

molecular chemistry. They control the structures of proteins and DNA, host–guest systems, enzyme–substrate binding, antigen–antibody recognition, or the orientation of molecules on surfaces or in molecular films.^{1,2} Because of their ubiquitous role in diverse fields the investigation and understanding of these weak interactions has become one of the major goals of modern chemistry. Besides the relatively strong hydrogen bonding,^{3–5} ion pairing,^{6–8} and

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cation- π interactions,⁸ the nonspecific van der Waals (vdW, dispersive) interactions seem much more important than first expected.^{9,10}

Molecular tweezers and molecular clips as synthesized and investigated in the group of Klärner^{11–18} are simple hydrocarbons containing only nonconjugated benzene and/or naphthalene rings arranged in a convex-concave molecular topology. Experimentally, it was observed that the molecular tweezers and clips serve as selective receptors for electron deficient aromatic and aliphatic substrates.^{11,13–18} Computational methods at different levels of theory (e.g. AM1, HF/6-31G*, and standard density functional theory, DFT) have been used to generate electrostatic potential surfaces on the convex and concave side of the hosts.¹² The results show considerably larger negative potential within the tweezers and clips interior than at the exterior which could explain binding of electron-deficient aromatic and aliphatic substrates into the host cavity.

Despite the growing interest in host–guest complexation processes relatively few quantum chemical computations on tweezer and clip systems have been reported so far.^{12,19–21} Studies that employ reliable quantum chemical methods and perform complete geometry optimizations of the complexes are still lacking, and thus, important structural information is often missing. From the computational point of view, ab initio methods that accurately account for the important dispersive interactions [e.g. CCSD(T)] suffer from very demanding computation times even for small- to medium-sized systems. On the other hand, the cheaper second-order Møller–Plesset perturbation theory (MP2)^{22,23} systematically overestimates the binding energies for dispersive π - π interactions (see, e.g. refs 24–26 and references therein). Another drawback for the application of correlated ab initio methods to weakly bound systems is the usually large basis set superposition error (BSSE). When dispersion is dominant for the interaction, the BSSE is often several times larger than with mean-field methods such as Hartree–Fock or DFT. Thus, additional calculations of the so-called counterpoise correction (CP²⁷) are mandatory.

Recently one of us introduced an empirical correction scheme for density functional theory calculations (termed DFT-D²⁸) that accounts for vdW interactions by pairwise additive C_6/R^6 potentials. Calculations with this very efficient method have shown promising results for a wide variety of weakly bonded systems^{28–30} (for related methods see e.g. refs 31–33, for other recent attempts to the DFT/vdW problem see refs 34–37). Standard DFT with current functionals of GGA or hybrid-type must strictly be avoided for vdW complexes because it fails completely not providing any binding at all (this also holds for recently proposed functionals such as e.g. X3LYP, see ref 38).

In the present study we have investigated a series of typical host–guest complexes with the DFT-D method. Our systems consist of dimethylene-bridged clips and tetramethylene-bridged tweezers as host molecules and six different aliphatic and aromatic substrates as guest molecules. The “real” systems investigated experimentally are considered without any modification. The DFT-D binding energies and structures as obtained from full geometry optimizations will be

presented. Although we are aware that solvent effects are important to interpret and understand the experimental condensed phase data (for a force-field approach to this problem see ref 19), we think that it is also important to investigate the intrinsic properties of the systems in the gas phase. Note, that the present DFT-D approach represents the first attempt to model both the electrostatic and dispersive interactions in such large complexes at a similar level of accuracy (for a CCSD(T) study of this aspect for smaller benzene model complexes see ref 39). Force-field methods that are usually applied for such complexes suffer from an oversimplified description (often of point-charge type) of the electrostatic interactions.

After consideration of some technical details in section 2, the accuracy of the DFT-D method for binding energies and geometries is considered in section 3.1. In the following sections (3.2 and 3.3) the complexes are grouped according to their host structure. The dimethylene-bridged clips (named CLIP1 and CLIP2 in Figure 1) and tetramethylene-bridged tweezers (named TWEEZER1–TWEEZER3 in Figure 1) as the host molecules and the following substrates as guest molecules are considered: cyanomethane (1), dicyanomethane (2), benzene (3), 1,4-dicyanobenzene (4), 1,4-benzene-carbaldehyde (5), and quinone (6). The detailed analysis of the host–guest interactions in the framework of an energy decomposition scheme^{40,41} will be discussed in section 3.4.

2. Technical Details

All density functional theory (DFT)^{42,43} and second-order Møller–Plesset perturbation theory (MP2)^{22,23} calculations have been performed with the TURBOMOLE package of programs.⁴⁴ The optimum geometries and binding energies were obtained using the DFT-D method²⁸ together with the B-LYP^{45,46} functional. Additionally, the spin-component-scaled MP2 approach (termed SCS-MP2²⁶) which improves in general the accuracy of MP2 has been employed. In all DFT-D, MP2, and SCS-MP2 calculations the resolution of identity (RI) approximation for the two-electron integrals^{47,48} is used. The RI auxiliary basis sets^{49,50} are taken from the TURBOMOLE library.⁵¹

All geometries have been fully optimized without any symmetry restrictions. Gaussian valence-triple- ζ AO basis set augmented with polarization functions on all atoms (TZVP⁵²) have been used in the DFT-D calculations. For all MP2 and SCS-MP2 calculations Dunning's aug-cc-pVTZ basis set⁵³ has been employed. Diffuse basis functions that are necessary in MP2 calculations to accurately describe the fragment polarizabilities do not necessarily improve the description of weak complexes when DFT approaches are applied.²⁸ As long as larger monomers (with more than 4–6 atoms) are considered and AO basis sets of at least TZVP quality are used, BSSE effects are quite small ($<10\%$ of ΔE) at the DFT level, and the laborious calculation of the counterpoise-correction (CP)²⁷ can be avoided (these small BSSE effects have been absorbed into the dispersion potential, for details see ref 28). The CP correction is mandatory when correlated wave function methods are used, and thus all MP2 and SCS-MP2 calculations have been CP corrected and only these values are reported.

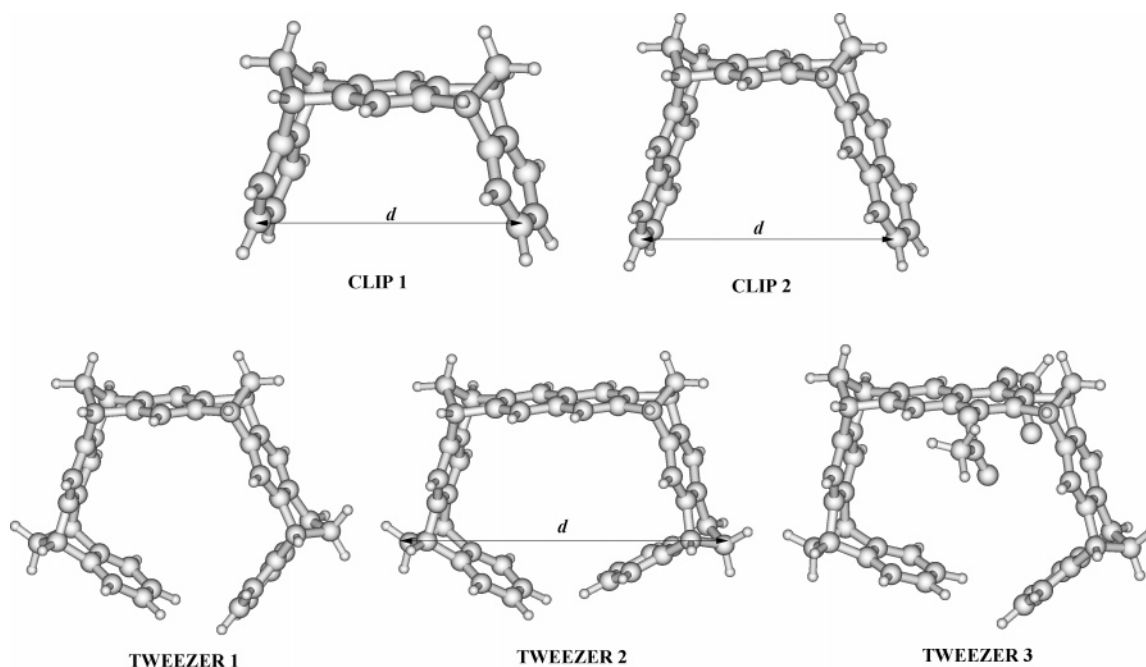


Figure 1. Optimized structures (DFT-D-BLYP) of the host molecules CLIP1, CLIP2, TWEEZER1, TWEEZER2, and TWEEZER3.

Table 1. Comparison of Selected Calculated and Experimental Geometric Parameters (r in Å, Angles in Degree) for the Tetramethylene-Bridged Tweezer as Host and 1,4-Dicyanobenzene as Guest (4@TWEEZER2)

geometric parameter	DFT-D	exp
r_{C2-C6}	3.59	3.61
r_{C3-C7}	3.49	3.59
r_{C9-C10}	12.50	12.62
$r_{C11-C12}$	3.91	4.16
angle C2–C6–C5	86.7	82.8
dihedral angle C1–C4–C5–C8	93.4	95.7

3. Results and Discussion

3.1. Accuracy of the DFT-D Method. In this section we compare the DFT-D-BLYP binding energies for the smallest system to those from MP2 and SCS-MP2 calculations. A comparison of calculated and experimental X-ray¹¹ parameters for some important geometrical variables of the tetramethylene-bridged TWEEZER2 as host and 1,4-dicyanobenzene as guest molecule are also presented (see Table 1, the atom numbering scheme is given in Figure 4). A graphical overlay of calculated and experimental structures is given in Figure 2. Both comparisons should provide some impression what accuracy can be expected from the DFT-D-BLYP method for the most important properties.

In the 4@TWEEZER2 complex, the guest molecule is placed almost parallel to the central naphthalene spacer unit with calculated distances of 3.59 Å (C2–C6) and 3.49 Å (C3–C7), respectively. This is in good agreement with the experimentally found values of 3.61 and 3.59 Å, respectively. Note, that for typical van der Waals complexes differences between theory and experiment for intermolecular distances are often about 0.1–0.2 Å even for very sophisticated theoretical treatments due to the flatness of the corresponding potentials.²⁸ The distance C9–C10 describes the width of the host cavity and is calculated to be 12.50 Å which is only

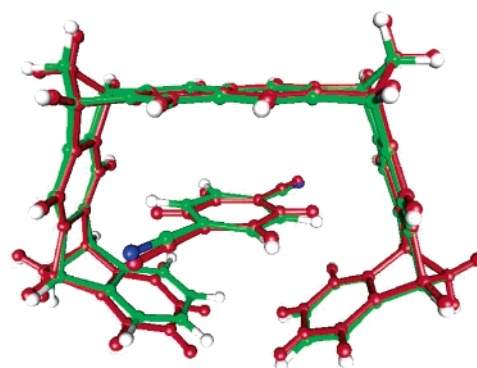


Figure 2. Comparison of DFT-D-BLYP (green) and experimental (red) structures for the host–guest complex 4@TWEEZER2.

0.12 Å shorter than found experimentally (12.62 Å). The distance C11–C12 is the shortest nonbonded contact within the host cavity, and the calculated value of 3.91 Å agrees again well with the experimental value of 4.16 Å. The position of the guest molecule within the cavity can be described by the angle C2–C6–C5 and the dihedral angle C1–C4–C5–C8. The calculated and experimental values differ by only about 4 and 1.3 degrees, respectively. This can be considered as very satisfactory especially if one keeps in mind that the potential energy surface of the host–guest interactions are very flat (which, unfortunately, results in many necessary geometry optimization cycles).

In a successful theoretical investigation^{20,21} of the NMR chemical shifts of the same host–guest complex, the structure has been optimized at the Hartree–Fock level. However, in this work it was necessary to employ constraints in the geometry optimization in order to preserve the shape of the complex as observed in the X-ray structure. This underlines the importance of the dispersive interactions that are not accounted for in standard HF or DFT calculations. With DFT-D, full geometry optimizations resulting in force-free

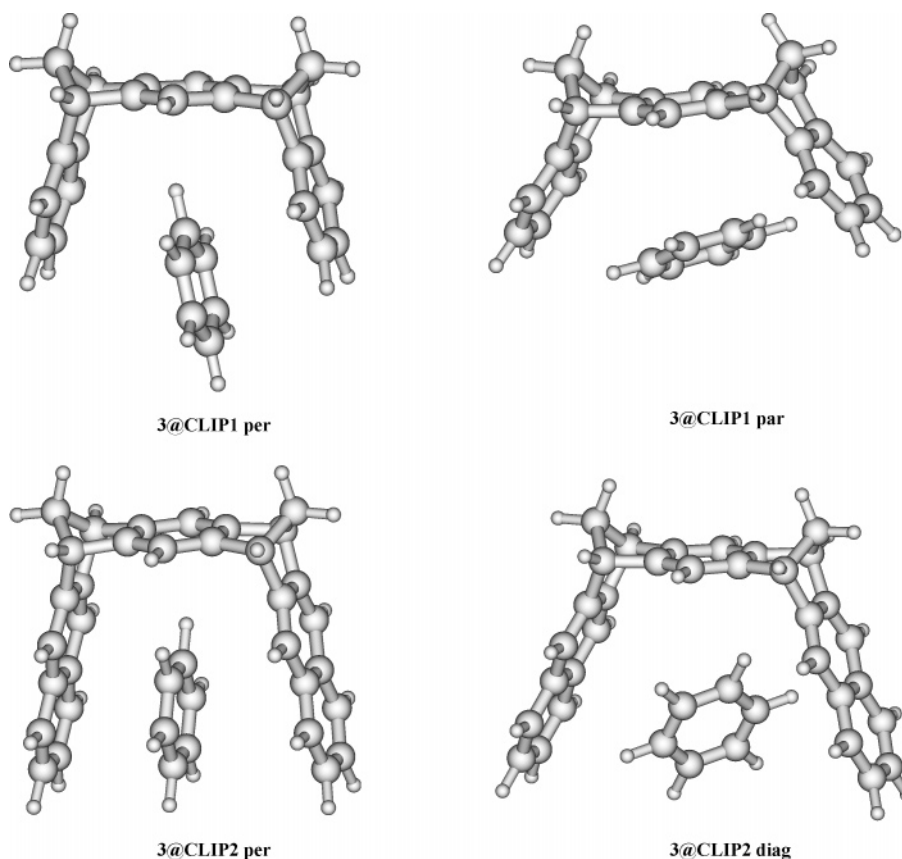


Figure 3. Optimized structures (DFT-D-BLYP) of the host–guest complexes 3@CLIP1PAR, 3@CLIP1PER, 3@CLIP2DIAG, and 3@CLIP2PER.

structures are possible that compare favorably with experimental data.

The 3@CLIP1PER complex is relatively small compared to the other systems that will be discussed further, and, therefore, computationally more demanding treatments such as MP2 and SCS-MP2 can be performed. The MP2 and SCS-MP2 binding energies have been obtained by rigid monomer calculations on the DFT-D-BLYP optimized structures. Opposed to a previous MP2 treatment of 4@TWEezer1,²¹ we employed the large aug-cc-pVTZ AO basis in these benchmark calculations that should provide a quite realistic account of the dispersive host–guest interactions. Note that as mentioned above, the BSSE is much larger for the MP2 type methods, and thus these data include the counterpoise correction. The MP2 and SCS-MP2 binding energies in the 3@CLIP1PER complex are computed to be -12.1 kcal/mol and -7.8 kcal/mol, respectively. As found previously^{26,30,54} the SCS-MP2 results for systems with π – π interactions (e.g. benzene dimers) are much better and more consistent compared to standard MP2 which tends to overbind considerably. In our calculations, the SCS-MP2 values compare favorably with DFT-D results with differences of about 1.2 kcal/mol. This also holds for the 3@CLIP1PER complex where DFT-D and SCS-MP2 agree to within 1.8 kcal/mol, while MP2 is off by almost a factor of 2. In conclusion one can be quite certain that the DFT-D absolute interaction energies are accurate to about 10–20% of the true values (slightly underbinding), while the errors on a relative scale (i.e. when comparing different guests and/or hosts) may be even smaller.

3.2. Clip Complexes. First, complexes of benzene with the dimethylene-bridged clip (named CLIP1 in Figure 1) are discussed.

The geometry optimizations lead to two different structures 3@CLIP1PER and 3@CLIP1PAR (see Figure 3). In the 3@CLIP1PER complex the guest molecule benzene is oriented parallel to the sidewalls and almost perpendicular to the central benzene unit of the host molecule. The DFT-D-BLYP binding energy of this complex is computed to be -6.6 kcal/mol (see Table 2).

The binding energy of the 3@CLIP1PAR complex, where the substrate molecular plane is nearly parallel to the central unit, is computed to be lower by 1.4 kcal/mol. This relatively small energy difference between the 3@CLIP1PER and 3@CLIP1PAR complexes indicates that the associated potential energy surface (PES) is quite flat. In the complexes 3@CLIP1PER and 3@CLIP1PAR the distances between the benzene sidewalls (named d in Figure 1) are computed to be 7.43 and 9.35 Å, respectively, while without any substrates bound it is computed to be 7.98 Å. The increase in steric strain resulting from an expansion of the cavity in 3@CLIP1PAR (that has more CH- π s than π – π interactions) is certainly the main reason that the complex 3@CLIP1PER with a parallel arrangement of the substrate is more stable.

Furthermore, complexes of benzene with dimethylene-bridged clips including naphthalene sidewalls (CLIP2 in Figure 1) are discussed. Two different structures are obtained: 3@CLIP2PER, with the substrate molecular plane oriented parallel to the receptor sidewalls, and 3@CLIP2DIAG, where the substrate molecule is placed parallel to the

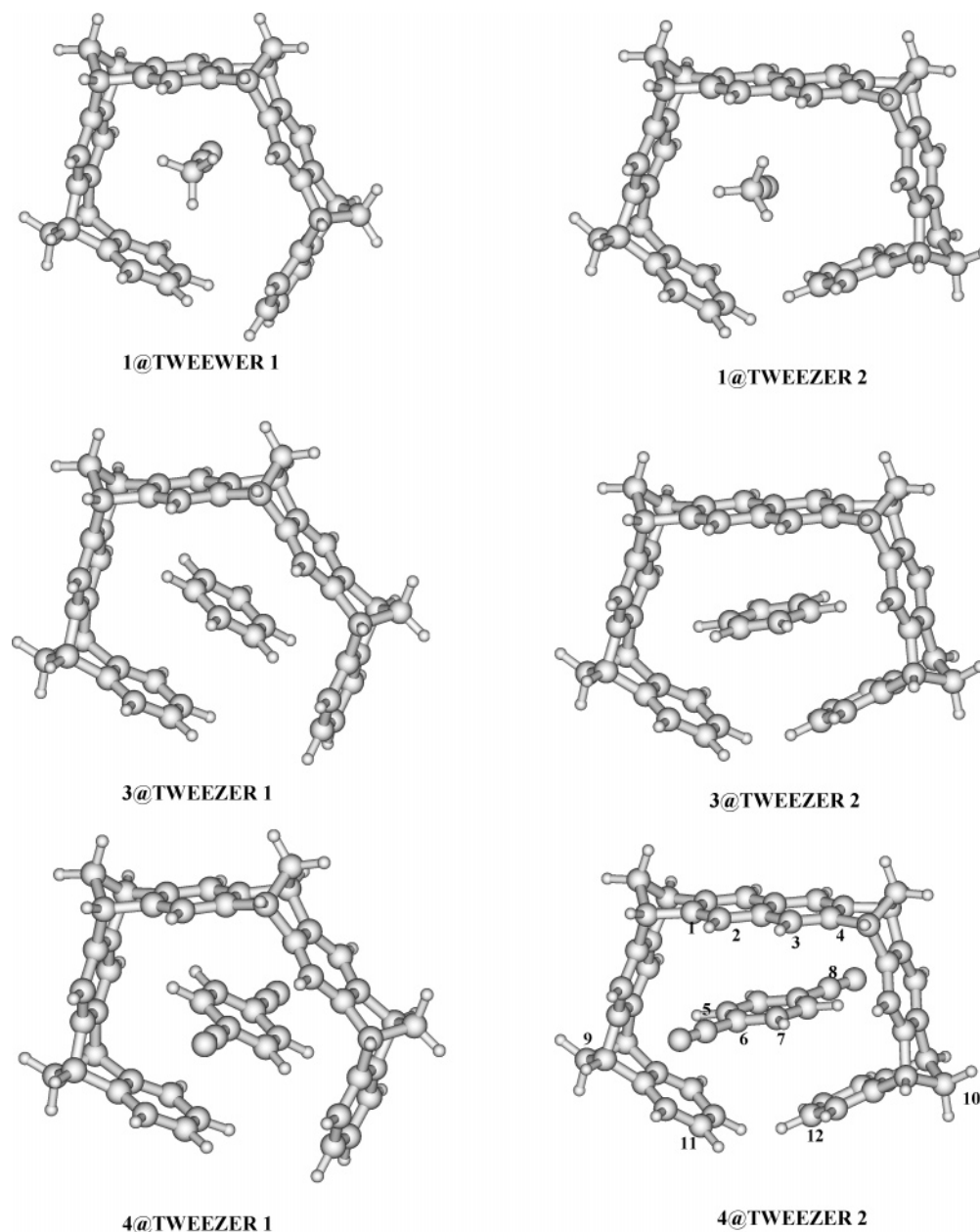


Figure 4. Optimized structures (DFT-D-BLYP) of the host–guest complexes 1@TWEezer1, 1@TWEezer2, 3@TWEezer1, 3@TWEezer2, 4@TWEezer1, and 4@TWEezer2.

Table 2. Calculated Binding Energies (in kcal/mol) for the Investigated Clip Complexes^b

molecule	ΔE		
	DFT-D-BLYP	MP2 ^a	SCS-MP2 ^a
3@CLIP1PER	−6.6 (7.0)	−12.1	−7.8
3@CLIP1PAR	−5.2 (7.6)		
3@CLIP2PER	−9.5 (11.2)	−17.8	−11.3
3@CLIP2DIAG	−7.9 (6.4)		

^a aug-cc-pVTZ AO basis. ^b Values in parentheses refer to a pure DFT-BLYP treatment, i.e. without the dispersion correction.

methylene bridged groups and diagonal to the sidewalls and central unit (see Figure 3). A structure with benzene orientated parallel to the central benzene unit similar to those obtained with CLIP1 could not be found and instead converged to 3@CLIP2DIAG structure. The results for the binding energies in Table 2 show that the 3@CLIP2PER

complex is more stable than 3@CLIP2DIAG, and the binding energies are −9.5 kcal/mol and −7.9 kcal/mol, respectively. The characteristic distances d are computed to be 7.62 Å for 3@CLIP2PER, 10.24 Å for 3@CLIP2DIAG, and 9.67 Å for the host molecule without the substrate.

Inspection of Table 2 also reveals that CLIP2 with naphthalene sidewalls forms more stable complexes with benzene than CLIP1 with benzene sidewalls. This can be explained by more favorable van der Waals contacts with the naphthalene sidewalls. Similar effects for hosts with naphthalene and anthracene sidewalls are discussed in ref 16.

3.3. Tweezer Complexes. In the following we discuss the structures and binding energies of the complexes with the tetramethylene-bridged molecular tweezer (TWEezer1 in Figure 1) as receptor. It was found that the bond angle distortions in molecular tweezer systems require little energy

Table 3. DFT-D-BLYP Binding Energies (in kcal/mol) of the Investigated Tweezer Complexes^a

guest	ΔE		
	@TWEezer1	@TWEezer2	@TWEezer3
1	−13.7 (1.5)	−12.0 (1.6)	−15.0 (0.4)
2	−19.0 (1.8)	−16.6 (1.1)	−20.4 (0.2)
3	−9.5 (12.2)	−12.7 (13.5)	−15.2 (13.5)
4	−18.3 (8.7)	−26.7 (8.2)	−29.3 (8.0)
5	−20.2 (11.4)	−23.5 (11.6)	−27.7 (10.3)
6	−17.2 (9.6)	−22.2 (8.3)	−23.7 (9.6)

^a Values in parentheses refer to a pure DFT-BLYP treatment, i.e. without the dispersion correction.

meaning that these systems are flexible enough to allow the receptor sidewalls to adjust their geometry specifically for different substrate binding.¹⁶ This should be investigated in this study by consideration of the six substrates.

The binding energies (see Table 3) for small aliphatic substrates such as acetonitrile (**1**) in the 1@TWEezer1 complex and malononitrile (**2**) in the 2@TWEezer1 complex are already for these small guests quite large, i.e., −13.7 kcal/mol and −19.0 kcal/mol, respectively. For the complexes with the naphthalene-spaced analogue (TWEezer2) with the same aliphatic substrates (1@TWEezer2 and 2@TWEezer2) the corresponding values are slightly smaller, i.e., −12.0 kcal/mol and −16.6 kcal/mol, respectively (for the optimized structures see Figure 4).

In the experimental study^{11,16} it was shown that aliphatic substrates will be bound only inside the benzene-spaced host. Evidently, our calculations agree with this observation and show that the benzene-spaced tweezer is indeed a better receptor for aliphatic substrates than its naphthalene-spaced analogue. The differences $\Delta\Delta E$ between TWEezer1 and TWEezer2 are 1.7–2.4 kcal/mol which is large enough to explain the observed selectivity in solution (in the gas phase, of course, most reasonably sized molecules will have negative binding energies, and so the absolute values cannot be directly compared with experimental findings).

The binding energies of the aromatic substrates **3–6** with TWEezer1 are calculated to be −9.5 kcal/mol, −18.3 kcal/mol, −20.2 kcal/mol, and −17.2 kcal/mol, respectively. This underlines the importance of ES interactions because benzene as a substrate is bound by about 10 kcal/mol less strongly than the other guests. Inspection of the complex structures shows that the distances between the methylene groups of the sidewalls in the receptor molecule (named *d* in Figure 1) are expanded from 11.47 Å in the empty TWEezer1 to 12.1 Å, 12.0, 11.9, and 12.4 Å in the host–guest complexes, respectively. According to these results the binding of aromatic substrates in the benzene-spaced tweezer requires a substantial distortion of the receptor geometry which is only partly compensated by the attractive substrate–receptor interactions. Moreover, we find that all aromatic substrates bound into TWEezer1 have the molecular plane aligned parallel to the sidewalls of the complex, which is not the case for the naphthalene-spaced TWEezer2 as the host molecule.

As mentioned above, the benzene-spaced TWEezer1 is a better receptor for aliphatic substrates than its naphthalene-

spaced analogue TWEezer2, and experimentally it was found that the TWEezer2 has an almost ideal topology for the binding of aromatic derivatives.^{14,16} The binding energies for the aromatic substrates **3–6** are calculated to be −12.7 kcal/mol, −26.7 kcal/mol, −23.5 kcal/mol, and −22.2 kcal/mol, respectively. These values are 3.1–8.1 kcal/mol lower than for TWEezer1. Inspection of the complex geometries shows that the distances between the sidewalls in the aromatic TWEezer2 complexes (named *d* in the Figure 1) has to expand only very slightly, i.e., from 12.4 to 12.6 Å, 12.5, 12.4, and 12.5 Å, respectively. This smaller increase in steric strain compared to the analogue TWEezer1 complexes where the distance between sidewalls change up to 0.9 Å clearly leads to an additional stabilization of the TWEezer2 complexes. Opposed to the TWEezer1 complexes, in all investigated complexes of TWEezer2 with aromatic substrates the plane of the guest molecule is aligned parallel to the central spacer unit. The optimized structures of the 1@TWEezer1, 1@TWEezer2, 3@TWEezer1, 3@TWEezer2, 4@TWEezer1, and 4@TWEezer2 complexes are shown in Figure 4. Previous MP2/SVP calculations of 4@TWEezer1²¹ reported a binding energy of −38.8 kcal/mol. However, this study suffers from the small AO basis set employed, and the important BSSE effects that have not been considered seem to be responsible for the large difference to our DFT-D result (−18.3 kcal/mol).

We extend our study to the molecular tweezer (named TWEezer3 in Figure 1) substituted with OAc groups in the central space unit. Our discussion focuses on the effect of the substituent on the stability of the complexes with aliphatic and aromatic substrates. Although, the OAc groups can have several different conformations in TWEezer3, we only investigated the conformation in which both OAc groups point toward the molecular cavity. This conformation is expected to allow more favorable ES interactions between the negatively charged carbonyl oxygen atoms and the electron deficient substrate molecules.

The binding energies of the aliphatic substrates such as acetonitrile (**1**) in 1@TWEezer3 and malononitrile (**2**) in the 2@TWEezer3 complex are calculated to be −15.0 kcal/mol and −20.4 kcal/mol, respectively. The comparison of these binding energies with the corresponding values of the parent complexes 1@TWEezer2 and 2@TWEezer2 shows that the OAc substituent favors complex formation with aliphatic substrates. The complex formation with the aromatic substrates is also favored due to presence of the OAc groups. The calculated binding energies for **3–6** are −15.2 kcal/mol, −29.3 kcal/mol, −27.7 kcal/mol, and −23.7 kcal/mol, respectively, and are in the range of 1.4–4.2 kcal/mol more negative than for TWEezer2. This is in line with the results of recent experimental work¹⁸ where the effect of the several substituents in the molecular tweezers on the complex formation was examined.

3.4. Analysis of the Host–Guest Interactions. To obtain more detailed information about which parts of a molecular host system are involved in binding a substrate, the host in the 3@CLIPER complex is portioned into three different parts: the central benzene unit and the two benzene rings forming the sidewalls. The relative orientation of the guest

Table 4. Energy Decomposition Analysis for the Binding Energies (in kcal/mol) of Some of the Investigated Tweezer Complexes

	ΔE_{Pauli}	ΔE_{ES}	ΔE_{POCT}	ΔE_{DFT}	ΔE_{disp}	$\Delta E_{\text{DFT-D}}$
1@TWEezer1	13.5	-9.0	-4.1	0.4	-14.5	-14.1
1@TWEezer2	11.5	-7.7	-3.5	0.2	-12.6	-12.4
1@TWEezer3	16.2	-12.0	-5.2	-1.0	-14.9	-16.0
3@TWEezer1	25.0	-8.0	-5.0	12.0	-24.0	-12.0
3@TWEezer2	26.8	-8.2	-5.3	13.3	-26.3	-13.0
3@TWEezer3	29.0	-10.3	-6.0	12.7	-28.9	-16.2

with respect to the host fragments is kept constant and dangling bonds are saturated with hydrogens. The interaction energies with the substrate molecule are computed to be -2.1 kcal/mol, -2.1 kcal/mol, and -1.9 kcal/mol for the three parts, respectively. This sums up to a total binding energy of -6.1 kcal/mol which is only slightly less than from the full calculation that yielded -6.6 kcal/mol. This indicates that the interactions influencing the binding energies are clearly dominated by the aromatic units of the clip and that the bridging units only place the aromatic rings into some more or less fixed position with respect to the guest. In the same spirit it was shown that individual aromatic units dominate the NMR chemical shifts of the 1,4-dicyanobenzene guest in the tetramethylene-bridged tweezer host.^{20,21}

To get even more insight into the host-guest interactions in the tweezers, an energy decomposition analysis (EDA) of the binding energies has been performed for the tweezer complexes. The EDA has proven to give detailed information about the nature of chemical bonding⁴¹ as well as for the interactions in hydrogen bonded systems.⁵⁵ The method has been described in detail before and is only briefly described here. The formation of bonding between two fragments (guest and host in our case) is divided into three physically plausible steps. In the first step, the fragment electronic densities (in the frozen geometry of the supermolecule) are superimposed which yields the quasiclassical electrostatic interaction energy ΔE_{ES} . Renormalization and orthogonalization of the product of monomer wave functions yield a repulsive energy term that is usually called Pauli (exchange) repulsion (ΔE_{Pauli}). In the final step, the molecular orbitals are allowed to relax to their final form which yields the (usually stabilizing) polarization, orbital and charge-transfer interaction energy ΔE_{POCT} . The sum $\Delta E = \Delta E_{\text{ES}} + \Delta E_{\text{Pauli}} + \Delta E_{\text{POCT}} + \Delta E_{\text{disp}}$, that also includes the dispersion energy term from the DFT-D approach, differs from the true interaction energy by the energy necessary to bring the optimum monomer geometries into the form they have in the supermolecule (ΔE_{prep}). The latter term is very small (<1.5 kcal/mol) in our case and not discussed further. Preliminary investigations of the EDA/DFT-D scheme for weakly bonded complexes have shown that the individual terms compare very well to those from a more sophisticated SAPT analysis.^{56,57}

As can be seen from Table 4, the guests acetonitrile (1) and benzene (3) behave very differently, while the hosts TWEezer1-TWEezer3 are more similar. With acetonitrile, the uncorrected DFT interaction energies are close to zero meaning that repulsive Pauli and attractive electrostatic/

CT/orbital interactions almost cancel. Thus, the total binding energy (and also the differences between the three hosts) are entirely given by the dispersion correction. For benzene as a guest the situation is completely different: here, the repulsive Pauli contribution is about a factor of 2 larger and overcompensates the other terms that are similar to the guest (1). However, in this case also the dispersion correction is much larger leading overall to very similar interaction energies for acetonitrile and benzene. In conclusion one can thus say that the binding of acetonitrile is dominated by the electrostatics while it is mostly dispersion for benzene. Turning now to the different hosts it is clearly seen that all individual terms are (absolutely) larger for the TWEezer3 with OAc groups which leads in summary to a lower total binding energy. This can be explained by considering ΔE_{ES} as the driving force that yields short intermolecular contacts and thus larger (absolute) Pauli and dispersion terms for TWEezer3 compared to TWEezer1 and TWEezer2 (similar arguments have been put forward to deconvolute the role of potential and kinetic energy in the formation of a chemical bond, see e.g. ref 58). Note, however, that the ordering of the binding energies for TWEezer1-TWEezer3 ($3 > 1 > 2$ and $3 > 2 > 1$ for acetonitrile and benzene, respectively) is not correctly described at the pure DFT level and entirely dominated by the small differences in the vdW terms.

4. Conclusion

The recently developed DFT-D method with empirical corrections for long-range dispersion effects has been used to predict the structures and binding energies of host-guest systems consisting of dimethylene-bridged clips and tetramethylene-bridged tweezers as receptors and six aliphatic and aromatic guest molecules. On the basis of the presented results a number of useful conclusions considering the strength of π - π and π -H interactions in the host-guest complexes with molecular tweezers and clips and the applicability of the DFT-D-BLYP method can be drawn. This study has shown that the DFT-D-BLYP method provides accurate geometries of the investigated complexes compared to the experimental X-ray data. It can therefore serve as a reliable method for fully geometry optimization of the large host-guest complexes.

For two structures of the 3@CLIP2 complex we have demonstrated that the DFT-D method provides accurate binding energies compared to computationally more demanding SCS-MP2 calculations. By an energy partitioning into different parts of the host we have shown that the binding in the 3@CLIP2 complex is clearly dominated by the aromatic units of the clip and that the bridging units only place the aromatic rings into the right position with respect to the guest. The calculations for CLIP2 with naphthalene sidewalls revealed that more stable complexes with benzene are formed compared to CLIP1 which can be explained by better van der Waals contacts in CLIP2.

The calculations on the tweezer complexes have shown that the benzene-spaced TWEezer1 is a better receptor for aliphatic substrates than its naphthalene-spaced analogue TWEezer2. On the other hand, TWEezer2 has an almost

ideal topology for the binding of aromatic substrates. Moreover, our calculations have shown that all aromatic substrates bound into TWEEZER2 have the molecular plane aligned parallel to the central spacer unit, whereas in the TWEEZER1 they are aligned parallel to the molecular sidewalls. The calculations on TWEEZER3 with a OAc substituent in the central spacer demonstrate that the polar OAc group favors complex formation with aliphatic and aromatic substrates. The conclusions discussed above are in very good qualitative agreement with previous experimental findings. We thus finally conclude that the DFT-D method represents an important tool for large scale applications in supramolecular chemistry where the complex geometries are not known and where both electrostatic and dispersive interactions are important.

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