

# Tuning the C–H $\cdots\pi$ Interaction by Different Substitutions in Benzene–Acetylene Complexes

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## S Supporting Information

**ABSTRACT:** The influence of substitutions in aromatic moieties on the binding strength of their complexes is a subject of broad importance. Using a set of various substituted benzenes, Sherrill and co-workers (*J. Am. Chem. Soc.* **2011**, *133*, 13244; *J. Phys. Chem. A* **2003**, *107*, 8377) recently showed that the strength of a stacking interaction ( $\pi\cdots\pi$  interaction) is enhanced by adding substituents regardless of their nature. Although the binding strength of an activated C–H $\cdots\pi$  interaction is comparable to that of a stacking interaction, a similar systematic study is hitherto unknown in the literature. We have computed the stabilization energies of the C–H $\cdots\pi$  complex of acetylene and multiple fluoro-/methyl-substituted benzenes at the coupled-cluster single and double (triple) excitation [CCSD(T)]/complete basis set (CBS) limit. The trend for interaction energies was found to be hexafluorobenzene–acetylene < *sym*-tetrafluorobenzene–acetylene < *sym*-trifluorobenzene–acetylene < *sym*-difluorobenzene–acetylene < benzene–acetylene < *sym*-dimethylbenzene–acetylene < *sym*-trimethylbenzene–acetylene < *sym*-tetramethylbenzene–acetylene < hexamethylbenzene–acetylene. Therefore, contrary to the case of stacking interaction (Hohenstein et al. *J. Am. Chem. Soc.* **2011**, *133*, 13244), we show here that electron-withdrawing groups weaken the dimer while electron-donating groups strengthen the interaction energy of the dimer. Various recently developed density functional theoretic (DFT) methods were assessed for their performance and the M05-2X, M06-2X, and  $\omega$ B97X-D methods were found to be the best performers. These best DFT performers were employed in determining the influence of other representative substituents (–NO<sub>2</sub>, –CN, –COOH, –Br, –Cl, –OH, and –NH<sub>2</sub>) as an extension to the above work. The results for the complex of acetylene and various para-disubstituted benzenes revealed a trend in binding energies that is in accordance with the ring-activating/deactivating capacity of each of these groups. The stabilization energy was partitioned via the DFT symmetry-adapted perturbation theory (SAPT) method, and both dispersion and electrostatic interactions were seen to be major driving forces for the complex stabilization. Interestingly, the sum of the energy contributors such as dispersion, exchange, induction, etc., is close to zero and the total energy follows the trend of the electrostatic energy. We observe an excellent linear correlation between the optimized intermolecular separation of the different complexes and the exchange/dispersion interaction.

## ■ INTRODUCTION

Complexes having stacking interactions (also known as  $\pi\cdots\pi$  interactions) or C–H $\cdots\pi$  interactions have gained a lot of attention in recent years. These interactions are usually weaker than a typical hydrogen bond and it is debatable whether the C–H $\cdots\pi$  interactions should be categorized as hydrogen bonds. Despite being among the weakest interactions, they play diverse, critical, and significant roles in nature; for example, they influence the crystal packing of molecules having aromatic moieties,<sup>1–4</sup> molecular aggregates,<sup>5</sup> molecular recognition processes,<sup>6,7</sup> supramolecular chemistry,<sup>7,8</sup> stabilizing three-dimensional structures of biomolecules and proteins,<sup>9–12</sup> and rational drug design.<sup>13,14</sup> One of the first significant reports on stacking interactions appeared in 1985, where it was shown that 60% of the aromatic side chains in the proteins participate in aromatic–aromatic interactions.<sup>15</sup> A crystal structure database study showed that C–H $\cdots\pi$  interactions were present in more than 35% of the organic crystals.<sup>16</sup>

In the past decade, several reports addressing the influence of substituents of an aromatic ring on the stacking interaction have appeared. The conventional understanding regarding the

role of substituents was based on the electrostatic interaction or on the change in the quadrupole moment of the aromatic molecule.<sup>17,18</sup> Accordingly, an electron-withdrawing group would enhance the binding strength of the stacked dimer, while an electron-donating group would reduce the binding strength. This model was refuted by Sherrill and co-workers,<sup>19–22</sup> who performed highly accurate estimated coupled-cluster single, and perturbative triple excitation [CCSD(T)]/complete basis set (CBS) computations and found an increase in the binding strength of the mono/multiple-substituted benzene dimer, regardless of the nature of the substituent. For monosubstituted cofacial benzene dimers, a good correlation is found between the relative interaction energy and the Hammett parameter ( $\sigma_m$ ),<sup>23,24</sup> although this correlation breaks down for multiple substitution.<sup>19,20</sup> Watt et al.<sup>25</sup> calculated the interaction energy for several benzene and substituted benzene complexes in the stacked geometry and found an excellent correlation between the interaction energy and a combination

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of electrostatic ( $\sum\sigma_m$ ) and polarizability ( $\sum M_r$ ) substituent constants. Recently, Wheeler<sup>26</sup> has examined a set of 25 monosubstituted pyridines and mono- and disubstituted benzenes with a large set of substituents using the CCSD(T) and the B97-D methods. It was shown that the stacking interaction between the two aromatic rings is enhanced by through-space interaction of the substituent on one ring with the other stacked ring.<sup>26</sup>

Tsuzuki and co-workers<sup>27–30,32</sup> have made a significant contribution in the area of C–H $\cdots\pi$  interactions. The C–H $\cdots\pi$  interaction between benzene and methane, ethylene, and acetylene was studied theoretically as well as experimentally, and the experimental binding energies were observed to be in good agreement with those predicted at the CCSD(T)/CBS level of theory.<sup>28</sup> The C–H $\cdots\pi$  interaction between methane and certain aromatic molecules (benzene, toluene, *p*-xylene, mesitylene, and naphthalene) was studied by Morita et al.<sup>30</sup> and the binding energies were shown to have the following trend: C<sub>6</sub>H<sub>6</sub>–CH<sub>4</sub> < C<sub>6</sub>H<sub>5</sub>Me–CH<sub>4</sub> < C<sub>6</sub>H<sub>4</sub>Me<sub>2</sub>–CH<sub>4</sub> < C<sub>6</sub>H<sub>3</sub>Me<sub>3</sub>–CH<sub>4</sub> < C<sub>10</sub>H<sub>8</sub>–CH<sub>4</sub>. It was found that the electrostatic component was close to zero and the dispersion energy was the primary source for strengthening the C–H $\cdots\pi$  interaction. However, Ringer et al.<sup>31</sup> reported that both dispersion and electrostatic components play significant roles in stabilizing the C<sub>6</sub>H<sub>6</sub>–CH<sub>4</sub> complex. The interaction energies for various mono-, di-, and trisubstituted alkanes with benzene were computed, and the weakest complex was found to be C<sub>6</sub>H<sub>6</sub>–CH<sub>4</sub> (interaction energy = –1.45 kcal/mol), while the most strongly bound complex was found to be C<sub>6</sub>H<sub>6</sub>–CHCl<sub>3</sub> (binding energy = –5.64 kcal/mol) at the CCSD(T) level of theory.<sup>32</sup> Raju et al.<sup>33</sup> reported the stabilization energies of the C<sub>6</sub>H<sub>6</sub>–CH<sub>4</sub> and C<sub>6</sub>F<sub>6</sub>–CH<sub>4</sub> dimers at the CCSD(T) level and, interestingly, they turned out to be very similar.

The second-order Møller–Plesset (MP2) method has been widely used in literature, mainly due to its reasonable computational cost. It is well-known that the MP2 method overestimates the binding energy of the complexes having C–H $\cdots\pi$  interaction and that the error can be as large as 100%.<sup>34–36</sup> Therefore, it has become a standard practice to perform computations via the CCSD(T) method to estimate the energy at the CCSD(T)/CBS limit. This energy can be obtained by using the two-points extrapolation scheme, proposed by Helgaker et al.,<sup>37</sup> or by adding the correction term  $E[\text{CCSD(T)}] - E(\text{MP2})$  to  $E(\text{MP2}/\text{CBS})$ , as shown by Sinnokrot and Sherrill.<sup>20</sup>

It is also well-established that popular density functional theory (DFT) methods, such as B3LYP, fail to predict the correct binding energy for  $\pi\cdots\pi$  stacked and C–H $\cdots\pi$  complexes. The B97-D method has been shown to perform well for substituted stacked dimers as well as for C–H $\cdots\pi$  interactions.<sup>26,38</sup> Chai and Head-Gordon<sup>39</sup> found that the performance of the  $\omega$ B97X-D functional is superior to that of several other functionals (such as B3LYP-D, BLYP-D, B97-D, and  $\omega$ B97X) when used across several training sets including noncovalent interactions. Also, the M05-2X and M06-2X functionals, developed by Zhao and Truhlar,<sup>40,41</sup> were found to be promising, especially for stacking interactions and other noncovalent interactions. The double-hybrid density functional B2PLYP and its counterpart with long-range dispersion correction, B2PLYP-D, have gained attraction in recent times.<sup>42,43</sup> Burns et al.<sup>44</sup> performed a systematic study of the hydrogen-bonding and noncovalent interaction test sets using various dispersion-corrected DFT methods in conjunction with

aug-cc-pVDZ and aug-cc-pVTZ basis sets. Among the various DFT methods used therein, B3LYP-D3, B97-D3,  $\omega$ B97X-D, and B2PLYP-D3 turned out to be better performers with the aug-cc-pVTZ basis set, while M05-2X, B97-D3, and B970-D2 were found to be better performers with the aug-cc-pVDZ basis set.

To the best of our knowledge no systematic study has been reported to account the substituent's influence on a C–H $\cdots\pi$  interaction. In the present work, the benzene–acetylene (bz–ac) dimer was chosen as a reference dimer. Fluorine and methyl substituents were appropriately selected for analyzing their influence on the C–H $\cdots\pi$  interaction. While the fluorine atom is an electron-withdrawing group (being the most electronegative atom in the periodic table), the methyl substituent is an electron-donating group. The substitutions were made in a manner that the total dipole moment of the aromatic molecule remains zero. The following aromatic moieties were chosen: *sym*-difluorobenzene (2F-bz), *sym*-trifluorobenzene (3F-bz), *sym*-tetrafluorobenzene (4F-bz), and hexafluorobenzene (6F-bz). The methyl substitutions were also made in similar fashion. The calculations were performed at the CCSD(T)/aug-cc-pVDZ level and employed the MP2 method in conjunction with the aug-cc-pVXZ (where X = D, T, and Q) basis sets. Several recently developed DFT methods (B97-D,  $\omega$ B97X-D, M05-2X, M06-2X, and B2PLYP-D) were used and their performance in predicting the stabilization energy was assessed. The best DFT performers were further used to study the influence of certain other substituents (NO<sub>2</sub>, CN, COOH, Br, Cl, OH, and NH<sub>2</sub>).

From the total stabilization energy data, one could only speculate on the physical origin of the interaction relying on chemical intuition. For an objective understanding of the actual driving forces of the interaction, decomposition of the total energy into various components has been a favored choice in the literature. There are several energy decomposition schemes available. An accurate partitioning of the total interaction energy data is particularly important in the area of force-field parametrization development, where the individual components of the total interaction energy are parametrized. In the frequently used symmetry-adapted perturbation theory (SAPT),<sup>45,46</sup> the total interaction energy ( $E_{\text{tot}}$ ) is naturally partitioned into electrostatic ( $E_{\text{elec}}$ ), effective induction ( $E_{\text{ind}}$ ), effective dispersion ( $E_{\text{disp}}$ ), and effective exchange-repulsion ( $E_{\text{exch}}$ ) energies. The DFT-SAPT method has been preferred over the SAPT method, owing to its modest computational cost. The use of this method has given satisfactory results in our earlier works<sup>47,48</sup> and also in those reported by others.<sup>49,50</sup> Tekin and Jansen<sup>51</sup> employed the DFT-SAPT method to compute the stabilization energy for the benzene–acetylene complex in various conformers and the results were found to be in excellent agreement with the CCSD(T) values. Therefore, we have chosen the DFT-SAPT method in this study.

## ■ COMPUTATIONAL DETAILS

MP2, CCSD(T), B97-D,  $\omega$ B97X-D, M05-2X, M06-2X, and B2PLYP-D computations were performed with the Gaussian09 suite of programs.<sup>52</sup> The geometry of the monomers and 1:1 clusters were optimized at the MP2/aug-cc-pVDZ level. We have also tested the geometry optimization at the MP2/aug-cc-pVTZ level for the case of the 2F-bz–ac dimer (the smallest complex in our data set). The difference in stabilization energies at “MP2/aug-cc-pVTZ + opt” and MP2/aug-cc-pVTZ//MP2/aug-cc-pDZ levels was found to be only 0.03

**Table 1.** BSSE-Corrected MP2 and CCSD(T) Interaction Energy Values for Fluoro- and Methyl-Substituted Benzene–Acetylene Complexes

complex	$\Delta E$ (kcal/mol)					
	MP2/aVDZ	MP2/aVTZ	MP2/aVQZ	CCSD(T)/aVDZ	MP2/CBS	est CCSD(T)/CBS
6F-bz-ac	−0.64	−1.11	−1.23	0.10	−1.31	−0.58
4F-bz-ac	−1.15	−1.67	−1.76	−0.37	−1.83	−1.05
3F-bz-ac	−1.48	−1.99	−2.09	−0.70	−2.16	−1.38
2F-bz-ac	−1.90	−2.40	−2.48	−1.12	−2.54	−1.76
bz-ac	−2.81	−3.29	−3.40	−2.02	−3.49	−2.70
2Me-bz-ac	−3.47	−4.00	−4.12	−2.48	−4.21	−3.22
3Me-bz-ac	−3.83	−4.38	−4.52	−2.74	−4.62	−3.53
4Me-bz-ac	−4.57	−4.66	−4.80	−3.38	−4.90	−3.71
6Me-bz-ac	−4.78	−5.36	−5.71	−3.32	−5.96	−4.51

kcal/mol. Therefore, we believe that reasonably good geometries were obtained by use of the aug-cc-pVDZ basis set. The optimized geometries were used in subsequent single-point energy calculations at MP2/aug-cc-pVTZ, MP2/aug-cc-pVQZ, and CCSD(T)/aug-cc-pVDZ level. The core electrons were kept frozen in all the calculations. Computations with DFT methods were also performed with the frozen geometries to avoid any influence from the geometric parameters. The aug-cc-pVTZ basis set was used in conjunction with DFT methods. Interaction energies ( $\Delta E$ ) for the clusters were computed by the supermolecule approach:

$$\Delta E(X\text{-bz-ac}) = E(X\text{-bz-ac}) - E(X\text{-bz}) - E(\text{ac}) \quad (1)$$

where  $E(X\text{-bz-ac})$ ,  $E(X\text{-bz})$ , and  $E(\text{ac})$  are the energies of the complex, substituted benzene, and acetylene, respectively. All the interaction energies were corrected for the basis-set superposition error (BSSE) by the counterpoise correction (CP) method.<sup>53</sup>

The MP2/CBS energy values were obtained via the two-point extrapolation scheme proposed by Helgaker et al.,<sup>37</sup> which exploits the fact that the correlation energy is proportional to  $X^{-3}$  for the aug-cc-pVXZ basis set. Energy values were determined at the MP2/CBS ( $\Delta E_{\text{MP2/CBS}}$ ) limit by extrapolating the  $\Delta E_{\text{MP2/aug-cc-pVQZ}}$  and  $\Delta E_{\text{MP2/aug-cc-pVTZ}}$  energy values by use of the following equation:

$$\Delta E_{\text{MP2/CBS}} = \frac{(64\Delta E_{\text{MP2/aug-cc-pVQZ}} - 27\Delta E_{\text{MP2/aug-cc-pVTZ}})}{37} \quad (2)$$

The estimated CCSD(T)/CBS energy was computed with the following formula:

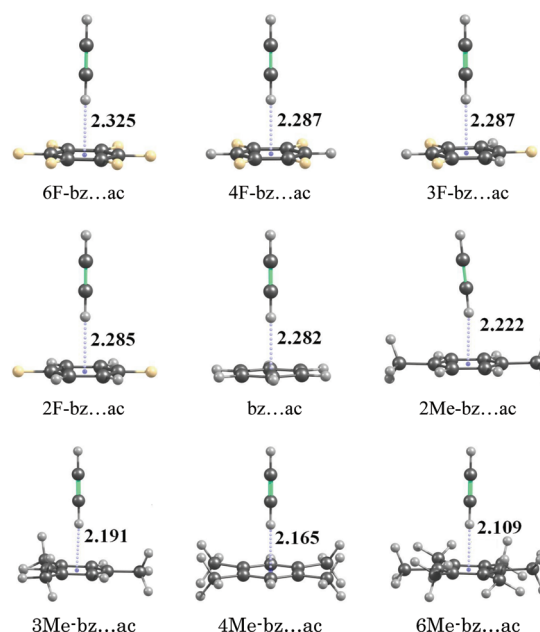
$$\begin{aligned} \text{est } \Delta E_{\text{CCSD(T)/CBS}} &= \Delta E_{\text{MP2/CBS}} + [\Delta E_{\text{CCSD(T)/aug-cc-pVDZ}} \\ &\quad - \Delta E_{\text{MP2/aug-cc-pVDZ}}] \end{aligned} \quad (3)$$

The DFT-SAPT(PBE0) calculations were performed with the MOLPRO suite.<sup>54</sup> The PBE0 functional<sup>55</sup> with aug-cc-pVDZ basis set was used. The coupled Hartree–Fock response term ( $d_{\text{HF}}$ ) was computed and added to  $E_{\text{tot}}$ . It is worth mentioning here that the  $E_{\text{exch-ind}}$  and  $E_{\text{exch-disp}}$  interaction terms were summed in  $E_{\text{ind}}$  and  $E_{\text{disp}}$ , respectively.

## RESULTS AND DISCUSSION

The energy values (BSSE-corrected) obtained at the MP2 and CCSD(T) levels for fluoro- and methyl-substituted bz-ac complexes are listed in Table 1, and the corresponding

geometries are depicted in Figure 1. From the stabilization energy values it is obvious that, by introducing fluorine atoms

**Figure 1.** Optimized geometry (MP2/aug-cc-pVDZ) of multiple fluoro- and methyl-substituted benzene–acetylene complexes. Intermolecular separations are given in angstroms.

as substituents, the interaction strength of C–H... $\pi$  is reduced significantly, while by introducing methyl groups as substituents, the interaction strength is amplified. The least and most stable complexes are found to be 6F-bz-ac and 6Me-bz-ac, with stabilization energies of −0.58 and −4.51 kcal/mol, respectively. Therefore, the interaction strength can be tuned up to ~4 kcal/mol by multiple substitutions. The stabilization energy of the reference bz-ac complex falls in the middle. Similar inference can be drawn from the intermolecular separation data shown in Figure 1. The separation between the hydrogen atom of acetylene and the center of the aromatic moieties decreases from 2.325 to 2.109 Å upon moving from the least stable complex (6F-bz-ac) to the most stable complex (6Me-bz-ac). Clearly, the results are quite contrary to the ones observed for the aromatic stacked dimers, where the various substitutions always enhanced the binding energy.<sup>19</sup> The stabilization energy linearly increases upon going from 6F-bz-ac to 6Me-bz-c (Figure S1, Supporting Information). The energy values computed at the MP2/aug-cc-pVDZ level are

found to be close to the estimated CCSD(T)/CBS values, which is clearly due to the cancelation of errors. The MP2/aug-cc-pVTZ and MP2/aug-cc-pVQZ methods considerably overestimate the stabilization energy (Figure S1, Supporting Information).

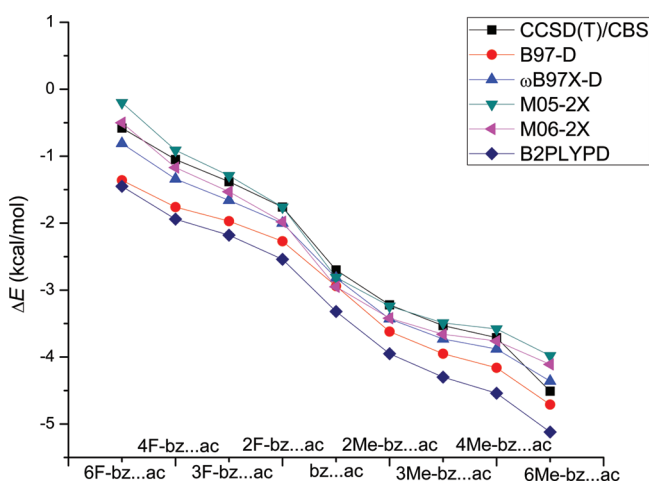
The relative stabilization energies from various DFT methods with respect to the estimated CCSD(T)/CBS energy values and the corresponding mean absolute deviation (MAD) values are listed in Table 2. The energy values obtained from

**Table 2. Relative Stabilization Energies for Fluoro- and Methyl-Substituted Benzene–Acetylene Complexes**

complex	$\Delta\Delta^*E = \Delta E(\text{DFT/aVTZ}) - \Delta E [\text{CCSD(T)/CBS}]$ (kcal/mol)				
	B97D	wB97XD	M05-2X	M06-2X	B2PLYP-D
6F-bz-ac	-0.78	-0.23	0.38	0.08	-0.87
4F-bz-ac	-0.71	-0.29	0.14	-0.12	-0.89
3F-bz-ac	-0.59	-0.28	0.09	-0.15	-0.80
2F-bz-ac	-0.51	-0.24	0.00	-0.22	-0.78
bz-ac	-0.24	-0.12	-0.11	-0.25	-0.62
2Me-bz-ac	-0.40	-0.21	-0.02	-0.20	-0.73
3Me-bz-ac	-0.42	-0.20	0.04	-0.13	-0.77
4Me-bz-ac	-0.45	-0.17	0.13	-0.05	-0.83
6Me-bz-ac	-0.20	0.15	0.53	0.40	-0.61
MAD <sup>a</sup>	0.48	0.21	0.16	0.18	0.77

<sup>a</sup>Mean absolute deviation.

the DFT methods are listed in Table S4 in Supporting Information. The trend in stabilization energies of the complexes for various methods is depicted in Figure 2. The



**Figure 2.** Energy profiles obtained by various DFT methods and CCSD(T) for multiple fluoro- and methyl-substituted benzene–acetylene complexes.

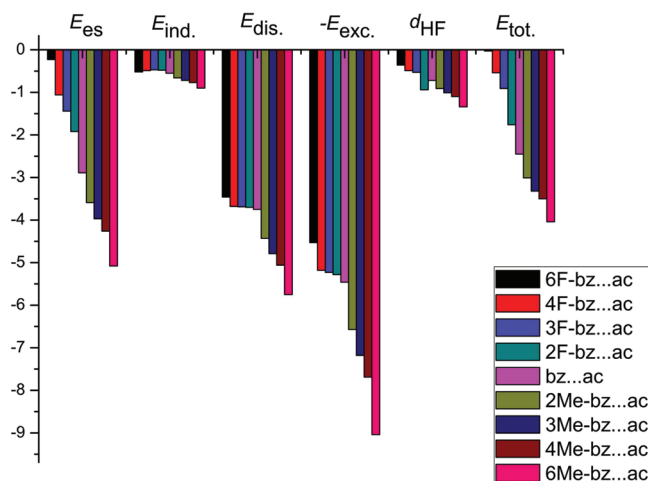
three best performers were found to be M05-2X, M06-2X, and  $\omega$ B97X-D, with MAD values of 0.16, 0.18, and 0.21 kcal/mol, respectively. The B97-D method, which has been frequently used in the literature to study the influence of substituents, produced a MAD of 0.48 kcal/mol. The  $\omega$ B97X-D method clearly turns out to be superior to the B97-D method. The M05-2X and M06-2X methods predicted excellent stabilization energy values, except for the case of 6Me-bz-ac, where the errors are relatively large. Surprisingly, the computationally

more expensive method B2PLYP-D produced a large MAD value of 0.77 kcal/mol.

As previously mentioned, partitioning the total stabilization energy into its various components helps in understanding the major driving force of the interaction. Results obtained via the DFT-SAPT(PBE0) method are reported in Table 3, with a

**Table 3. Energy Decomposition Results for Fluoro- and Methyl-Substituted Benzene–Acetylene Complexes**

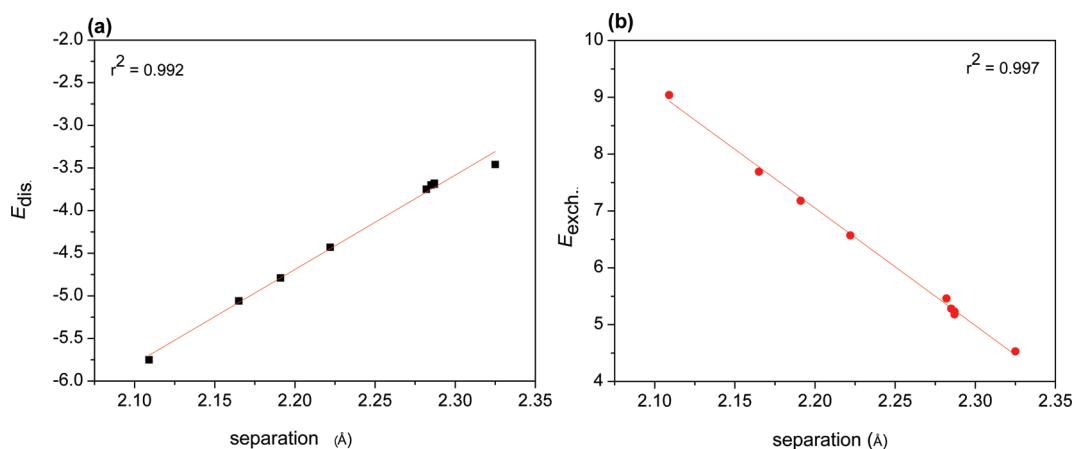
complex	DFT-SAPT (PBE0) results (kcal/mol)						$\Delta E_{\text{CCSD(T)/CBS}}$
	$E_{\text{es}}$	$E_{\text{ind}}$	$E_{\text{dis}}$	$E_{\text{exch}}$	$d_{\text{HF}}$	$E_{\text{tot}}$	
6F-bz-ac	-0.23	-0.52	-3.46	4.53	-0.36	-0.03	-0.58
4F-bz-ac	-1.06	-0.49	-3.68	5.18	-0.49	-0.54	-1.05
3F-bz-ac	-1.44	-0.47	-3.69	5.23	-0.53	-0.91	-1.38
2F-bz-ac	-1.92	-0.48	-3.70	5.28	-0.94	-1.76	-1.76
bz-ac	-2.89	-0.55	-3.75	5.46	-0.72	-2.45	-2.70
2Me-bz-ac	-3.59	-0.66	-4.43	6.57	-0.91	-3.01	-3.22
3Me-bz-ac	-3.97	-0.72	-4.79	7.18	-1.01	-3.32	-3.53
4Me-bz-ac	-4.26	-0.77	-5.06	7.69	-1.10	-3.50	-3.71
6Me-bz-ac	-5.08	-0.90	-5.75	9.04	-1.34	-4.04	-4.51



**Figure 3.** Trend for various energy components (in kilocalories per mole, via DFT-SAPT) for multiple fluoro- and methyl-substituted benzene–acetylene complexes.

corresponding histogram illustrated in Figure 3. From the values we can see that the DFT-SAPT(PBE0) performs very well for the methyl-substituted complexes but gives large deviations for the fluoro-substituted complexes when compared to the estimated CCSD(T)/CBS values. One of the reasons for the large deviations could be use of the aug-cc-pVDZ basis set. Recently, Řezáč and Hobza<sup>56</sup> found a root-mean-square error of 0.68 kcal/mol for a set of 31 noncovalent bound complexes when aug-cc-pVDZ basis set was used. Therefore, the various energy components listed here can be considered in a qualitative manner. For both fluoro- and methyl-substituted complexes, the major contributors are found to be  $E_{\text{es}}$ ,  $E_{\text{dis}}$ , and





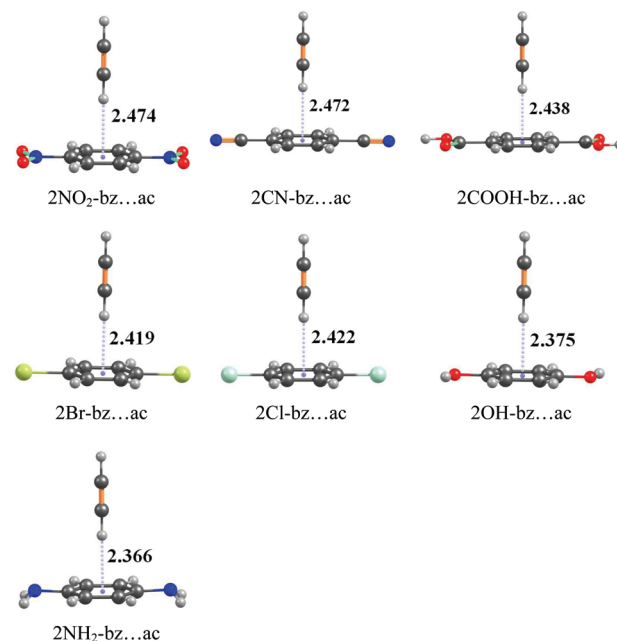
**Figure 4.** Correlation diagrams between (a)  $E_{\text{dis}}$  and (b)  $E_{\text{exch}}$  (in kilocalories per mole) and optimized intermolecular separation (angstroms) for multiple fluoro- and methyl-substituted benzene–acetylene complexes.

$E_{\text{exch}}$ , where the former two are attractive in nature and the latter is repulsive (Figure 3). It is quite obvious that the total energy has a trend that very closely resembles that of the electrostatic energy. This leads to the inference that, in an activated C–H $\cdots\pi$  interaction, the electrostatic term is the major contributor in stabilizing the complex. An excellent correlation ( $r^2 = 0.99$ ) was observed between the total energy and the electrostatic energy, as depicted in Figure S3 in Supporting Information. The  $E_{\text{dis}}$  and  $E_{\text{exch}}$  values, although comparable, are of opposite nature; therefore, they tend to counterbalance each other. In order to gain further insight, we looked at the correlation diagrams for  $E_{\text{dis}}$  and  $E_{\text{exch}}$  with respect to the separation between the H atom of acetylene and center of the substituted-benzene ring. Interestingly, an excellent correlation ( $r^2 = 0.99$ ), with opposite slopes for  $E_{\text{dis}}$  and  $E_{\text{exch}}$  (as illustrated in Figure 4), can be seen. Curiously,  $E_{\text{dis}}$  and  $E_{\text{exch}}$  values for the 3F-bz-ac, 4F-bz-ac, and 6F-bz-ac complexes lie very close to each other. This can be explained in the following manner: Since, by addition of more fluorine atoms, the intermolecular separation remains constant, the dispersion and exchange energies are almost constant. The influence of additional fluorine atoms is seen primarily on the electrostatic interaction. On the other hand, by introducing increasingly more methyl groups, the intermolecular separation decreases, leading to a linear increase in the magnitude of each term ( $E_{\text{es}}$ ,  $E_{\text{dis}}$ , and  $E_{\text{exch}}$ ).

The three best methods (M05-2X, M06-2X, and  $\omega$ B97X-D) were applied to investigate the interaction between the acetylene and various disubstituted benzenes. The stabilization energy values are listed in Table 4, and the corresponding geometries are illustrated in Figure 5. The chosen substituents can be classified in three categories: strong deactivators ( $\text{NO}_2$ , CN, and COOH); weak deactivators (Br, Cl, and F); and activators (OH,  $\text{NH}_2$ , and Me). It is well-known that the  $\text{NO}_2$  group is a strong electron-withdrawing group through both negative induction effect ( $-I$ ) and negative resonance effect ( $-R$ ). Indeed, the complex  $2\text{NO}_2\text{-bz-ac}$  is found to be the least stable among all. It is worth noticing here that the electron-withdrawing power of the two nitro groups is comparable to that of 4–6 fluorine atoms. This could possibly be explained by the fact that the  $\text{NO}_2$  group exerts a  $-R$  effect on the ring, contrary to the F atom, which has a  $+R$  effect on the ring, although both the groups are electron-withdrawing, owing it to the  $-I$  effect. The second least stable complex is

**Table 4.** Stabilization Energy Obtained by Three Methods in Conjunction with aug-cc-pVTZ Basis Set for Various Para-Disubstituted Benzene–Acetylene Complexes

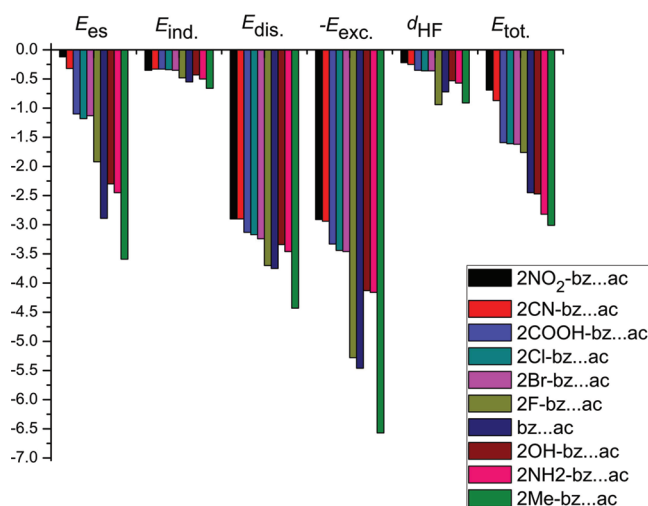
complex	$\Delta E$ (kcal/mol)		
	$\omega$ B97XD	M05-2X	M06-2X
$2\text{NO}_2\text{-bz-ac}$	−1.43	−0.78	−0.92
$2\text{CN-bz-ac}$	−1.55	−0.99	−1.14
$2\text{COOH-bz-ac}$	−2.29	−1.67	−1.85
$2\text{Cl-bz-ac}$	−2.3	−1.89	−2.02
$2\text{Br-bz-ac}$	−2.39	−1.87	−2.04
$2\text{F-bz-ac}$	−2.37	−1.93	−2.08
$2\text{OH-bz-ac}$	−3.15	−2.76	−2.92
$\text{bz-ac}$	−3.11	−2.87	−2.99
$2\text{NH}_2\text{-bz-ac}$	−3.46	−3.10	−3.22
$2\text{Me-bz-ac}$	−3.74	−3.38	−3.49



**Figure 5.** Optimized geometry (MP2/aug-cc-pVDZ) of various disubstituted benzene–acetylene complexes. Intermolecular separations are shown in angstroms.

found to be 2CN-bz-ac; this is not surprising, since the CN group is also an electron-withdrawing group, due to the negative inductive (−I) and negative resonance (−R) effects. It is worth mentioning here that the trend in the stabilization energies,  $2\text{NO}_2\text{-bz-ac} < 2\text{CN-bz-ac} < 2\text{COOH-bz-ac}$ , is in accordance with the extent of resonance (−R),  $\text{NO}_2 > \text{CN} > \text{COOH}$ . Hence, the higher the negative resonance (−R), the lower the stabilization energy. The three halogen substituents are known to be weakly deactivating groups. Expectedly, their stabilization energy values fall in the middle. The  $\text{NH}_2$  and OH groups are known to be strong activators through positive resonance (+R), and consequently their complexes have much higher stabilization energy. Finally, the methyl group is considered strongly electron-donating by having both positive induction effect (+I) and hyperconjugation effect, thus stabilizing the complex to a much greater extent. The correlation diagrams between  $E_{\text{dis}}/E_{\text{exch}}$  and intermolecular separation for these substituents (shown in Figure S2 in Supporting Information) indicate a linear trend almost comparable to the one observed with methyl and fluoro substitutions.

The results obtained via DFT-SAPT(PBE0) are summarized in Figure 6 and Table 5. Once again we see that the major



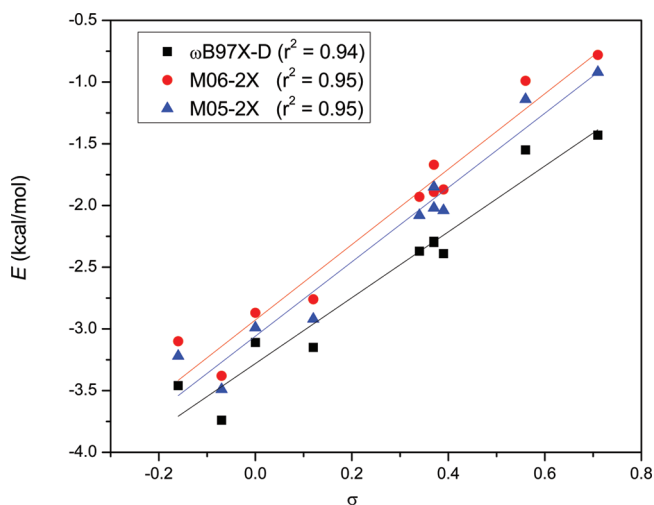
**Figure 6.** Trend for different energy components (in kilocalories per mole, via DFT-SAPT) for various disubstituted benzene-acetylene complexes.

**Table 5. Energy Decomposition Results for Various Disubstituted Benzene-Acetylene Complexes**

complex	DFT-SAPT(PBE0) results (kcal/mol)					
	$E_{\text{es}}$	$E_{\text{ind}}$	$E_{\text{dis}}$	$E_{\text{exch}}$	$d_{\text{HF}}$	$E_{\text{tot}}$
2NO <sub>2</sub> -bz-ac	−0.12	−0.35	−2.90	2.91	−0.22	−0.69
2CN-bz-ac	−0.32	−0.33	−2.90	2.94	−0.25	−0.87
2COOH-bz-ac	−1.10	−0.33	−3.13	3.33	−0.35	−1.59
2Cl-bz-ac	−1.18	−0.34	−3.17	3.44	−0.36	−1.61
2Br-bz-ac	−1.13	−0.35	−3.24	3.46	−0.36	−1.62
2F-bz-ac	−1.92	−0.48	−3.70	5.28	−0.94	−1.76
bz-ac	−2.89	−0.55	−3.75	5.46	−0.72	−2.45
2OH-bz-ac	−2.30	−0.43	−3.34	4.13	−0.53	−2.47
2NH <sub>2</sub> -bz-ac	−2.45	−0.50	−3.46	4.16	−0.57	−2.82
2Me-bz-ac	−3.59	−0.66	−4.43	6.57	−0.91	−3.01

contributors in the total energy are the  $E_{\text{es}}$ ,  $E_{\text{dis}}$ , and  $E_{\text{exch}}$  terms. These results further reinforce our finding that the C–H $\cdots\pi$  interaction is majorly governed by the electrostatic term. The trend in the distribution of the different energy components is consistent with the explanation given above regarding the electron-withdrawing and resonance effects of the individual substituents. This effect can be clearly seen in the case of the activating groups (OH,  $\text{NH}_2$ , and Me). Hydroxyl and amine, being +R and −I groups, show correspondingly similar energy values (in all the energy components), whereas the methyl group shows a markedly higher value for all energies. This deviation could be possibly due to the methyl being a +R and +I group, which is different from the OH and  $\text{NH}_2$  groups. Similarly, for the  $\text{NO}_2$  and CN groups,  $E_{\text{dis}}$  and  $E_{\text{exch}}$  cancel out and small attractive contributions from  $E_{\text{es}}$ ,  $E_{\text{ind}}$  and  $d_{\text{HF}}$  lead to small total stabilization energy.

There have been several attempts in the literature to correlate the binding energy to the substituents' Hammett  $\sigma$  constants ( $\sigma_m$ ) for stacked aromatic dimers, and the general consensus is that  $\sigma_m$  alone cannot describe the substituents' influence. Since activated C–H $\cdots\pi$  complexes are mainly guided by electrostatic interaction, one would expect a correlation between  $\sigma_m$  and the stabilization energy, due to  $\sigma_m$  being a measure of electron-withdrawing/electron-donating capacity of a substituent. Congruent with this expectation, the stabilization energies for the various disubstituted benzenes and acetylene complex correlate appreciably well with  $\sigma_m$ , as shown in Figure 7.  $\omega\text{B97X-D}$ , M05-2X, and M06-2X gave correlation values of 0.94, 0.95, and 0.95, respectively.



**Figure 7.** Correlation diagrams between total energy and Hammett constant ( $\sigma$ ) of various groups.

## CONCLUSION

Contrary to the case of aromatic stacked dimers, where the stabilization energy was enhanced irrespective of the nature of the substituents, we have shown, using state-of-the-art computational techniques, that the C–H $\cdots\pi$  interaction behaves in a tunable way. The binding energy is enhanced/reduced by using methyl/fluoro groups as substituents, and the trend is  $6\text{F-bz-ac} < 4\text{F-bz-ac} < 3\text{F-bz-ac} < 2\text{F-bz-ac} < \text{bz-ac} < 2\text{Me-bz-ac} < 3\text{Me-bz-ac} < 4\text{Me-bz-ac} < 6\text{Me-bz-ac}$ . The performance of several DFT methods was investigated in determining the stabilization energy, and the three best

performers were found to be the M05-2X, M06-2X, and  $\omega$ B97X-D methods, when compared to the estimated CCSD-(T)/CBS results. The influence of several other substituents on the C–H $\cdots\pi$  interaction strength was also found to be in accordance with chemical intuition based on the resonance and induction effects of the group. By partitioning the stabilization energies for the different fluoro, methyl, and other representative electron-withdrawing and electron-donating substituents in benzene, we conclude that this C–H $\cdots\pi$  interaction is majorly governed by the electrostatic term. The large dispersion energy values also participate in stabilizing the complexes but are outnumbered by repulsive exchange energy values. The excellent linear correlation of the dispersion and exchange energies of all these complexes with intermolecular separation is an interesting finding. Some of the systems that we have explored here have a significant binding energy, which is well amenable by experiments, and hence the binding energies that we predict can be subjected to verification by a cleverly designed experiment.

## ■ ASSOCIATED CONTENT

### ■ Supporting Information

Three figures showing stabilization energies of multiple fluoro- and methyl-substituted benzene–acetylene complexes computed at the MP2 and CCSD(T) levels of theory, correlation plots between  $E_{\text{dis}}/E_{\text{exch}}$  and intermolecular separation for various disubstituted benzene–acetylene complexes, and correlation plot between electrostatic and total energy; and one table listing stabilization energy values for various DFT methods used. 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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