

Physical Nature of Substituent Effects in XH/ π Interactions

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S Supporting Information

ABSTRACT: XH/ π interactions (e.g.: CH/ π , OH/ π , etc.) are ubiquitous in chemical and biochemical contexts. Although there have been many studies of substituent effects in XH/ π interactions, there have been only limited systematic studies covering a broad range of substituents. We provide a comprehensive and systematic study aimed at unraveling the nature of aryl substituent effects on model BH/ π , CH/ π , NH/ π , OH/ π , and F/ π interactions (e.g.: BH₃...C₆H₅Y, CH₄...C₆H₅Y, etc.) based on estimated CCSD(T)/aug-cc-pVTZ interaction energies as well as symmetry-adapted perturbation theory (SAPT) results. We show that the impact of substituents on XH/ π interactions depends strongly on the identity of the XH group, and the strength of these effects increases with increasing polarization of the XH bond. Overall, the results are in accord with previous work and follow expected trends from basic physical principles. That is, electrostatic effects dominate the substituent effects for the polar XH/ π interactions (NH/ π , OH/ π , and FH/ π), while dispersion effects are more important for the nonpolar BH/ π and CH/ π interactions. The electrostatic component of these interactions is shown to correlate well with Hammett constants (σ_m), while accounting for the dispersion component requires consideration of molar refractivities (MR) and interaction distances concurrently. The correlation of the dispersion component of these interactions with MR values alone is rather weak.

I. INTRODUCTION

XH/ π interactions (i.e.: CH/ π , OH/ π , NH/ π , etc. See Figure 1), in which an XH bond points toward the face of an aromatic

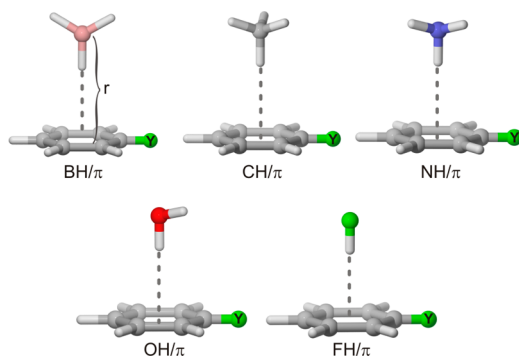


Figure 1. Model XH/ π interactions between BH₃, CH₄, NH₃, OH₂, and FH and monosubstituted benzenes. In all cases, a single XH bond is directed toward the centroid of the phenyl ring and the interaction distance (r) is defined as the distance between the heavy atom of the XH group and the ring centroid.

ring, have proven vital in numerous chemical and biochemical contexts including the tertiary structures of proteins,^{1–6} crystal packing,^{7–11} and molecular recognition.^{12–26} There have been many reviews covering these interactions,^{22,27–30} with the bulk of previous work focusing on CH/ π and OH/ π interactions. As with other noncovalent interactions involving aromatic rings,^{31,32} there is widespread interest in developing ways of tuning XH/ π interactions through substituent effects. By understanding how simple substituents change the strength of these interactions, we can further unravel the physical nature of these interactions while also providing a potentially powerful tool for supramolecular chemistry.

There have been numerous computational studies of XH/ π interactions, including many studies of the impact of substituents. We recently reviewed³² computational studies of substituent effects in noncovalent interactions involving aromatic rings, including CH/ π , OH/ π , and NH/ π interactions; we provide merely a summary here. Kodama et al.³³ introduced the concept of CH/ π interactions to explain the favorable interactions between alkyl groups and phenyl rings. Subsequently, CH/ π interactions, which are driven by dispersion interactions,^{27,34} have been the focus of multitudinous experimental and theoretical studies, in part because of the important role that these interactions play in the recognition of carbohydrates by proteins.³⁵ Tsuzuki and co-workers^{36,37} studied CH/ π complexes of benzene with methane, ethane, ethylene, and acetylene at the coupled-cluster with single and double and perturbative triple excitations [CCSD(T)] level, showing that the nature of the alkyl group affects the interaction energy. In particular, they showed that the interaction becomes considerably stronger as the hybridization of the carbon in the CH bond changes from sp³ to sp² to sp. For example, the CH/ π interaction of acetylene with benzene is an order of magnitude stronger than that of ethane with benzene.³⁷ This can be understood in terms of the increasing polarity of the CH bond with increasing s -character of the carbon.

There have been a variety of studies of aryl substituent effects on CH/ π interactions.^{20,38,39} Tsuzuki and co-workers³⁸ presented extrapolated CCSD(T) interaction energies for the interaction of methane with toluene, *p*-xylene, mesitylene, and naphthalene. Their data showed a correlation between the interaction energies and the polarizabilities of the arenes, highlighting the importance of dispersion effects for these

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interactions. Raju et al.²⁰ analyzed the effect of aryl perfluorination on the benzene methane interaction. They showed that the effect is negligible; methane has only a slightly more favorable interaction with benzene than it has with hexafluorobenzene.

Earlier this year, Mishra et al.³⁹ analyzed the interaction of acetylene with the face of substituted benzenes using CCSD(T), several density functional theory (DFT) functionals, and symmetry adapted perturbation theory (SAPT). This was the first systematic study of substituent effects in CH/ π interactions spanning a broad range of substituents. Overall, they found that the main driver of substituent effects in these interactions was electrostatic effects, and that electron donors enhance the interaction while electron acceptors hinder the interaction. They also noted a strong correlation between the dispersion and exchange-repulsion components of these interactions, although no explanation for this finding was provided.

Several studies have examined the impact of halogen substituents on the CH-bearing group. For example, Fujii et al.⁴⁰ showed that although electrostatic interactions increase with the number of chlorine atoms, dispersion interactions remain the primary component of the overall interaction energies. Tsuzuki et al. expanded upon this with the inclusion of fluorine.^{38,41} They found that both fluorine and chlorine substituted methanes interact with benzene more strongly because of enhanced electrostatic and dispersion interactions. Ugozzoli et al.⁴² performed a more thorough DFT study of the effect of substituents on methane, considering substitution with F, Cl, Br, I, CN, and NO₂. They found that computed interaction energies increased with increasing electron withdrawing capability of the substituent.

Several groups have also examined substituent effects in aromatic CH/ π interactions, as exemplified by the T-shaped and edge-to-face configurations of the benzene dimer.^{31,43–46} These include high-accuracy studies of Sherrill and co-workers^{43,44} and Kim et al.,^{45,47} as well as work by Riley and Merz⁴⁶ and Wheeler and Houk.³¹ For substituents on the edge or axial ring, electron donors hinder the interaction while electron acceptors promote the interaction.

In addition to CH/ π interactions, prototypical OH/ π interactions (e.g., H₂O...C₆H₆ complexes) have been reported in both experimental and theoretical works.^{48–56} More complex systems featuring both CH/ π and OH/ π interactions have also been studied. For example, Raju et al.^{20,21,57,58} examined interactions between several types of carbohydrates and substituted benzenes, while Kumari et al.⁵⁹ studied simple carbohydrates paired with tryptophan.

NH/ π interactions are less well studied. It has been shown that dispersion interactions constitute a large part of the overall interaction energy for these interactions while electrostatic effects impact the orientation of NH/ π interactions.³⁷ The strength of the NH/ π interaction falls between that of CH/ π and OH/ π interactions.⁶⁰ Kim and co-workers⁶¹ studied dimers of several substituted benzenes with ammonia, finding a competition between an NH/ π configuration and a complex in which the ammonia interacted with the edge of the arene. The latter complexes were preferred in benzenes with electron-withdrawing substituents.

There have been previous computational studies examining a broad range of XH/ π interactions with both substituted and unsubstituted benzenes. For example, Mishra and Sathyamurthy⁶² examined dimers of CH₄, NH₃, OH₂, and FH with

benzene, hexafluorobenzene, and 1,3,5-trifluorobenzene, finding that for fluorinated rings the complexes adopt structures in which the interaction is with the edge of the ring rather than the center. Similarly, Kim and co-workers⁶³ showed that for complexes of HF and HCl with benzene, the XH bond is directed toward the edge of the benzene rather than its center. They extended this work a few years later⁶⁴ to complexes of BH₃, CH₄, NH₃, OH₂, and FH with benzene and ethylene, showing that differences in computed binding energies among these systems were due to electrostatic effects and induction. Overall, they found that CH₄, NH₃, OH₂, and FH complexes exhibit an XH/ π interaction toward the bonds and atoms of the benzene, while for the BH₃...C₆H₆ complex the plane of BH₃ is roughly parallel to that of the benzene. In fact, BH₃ and AlH₃ both exhibit this parallel structure as the global minimum energy configuration.^{65,66} Kim and co-workers⁴⁵ subsequently examined complexes of HF, HCl, OH₂, H₂, with a range of substituted benzenes, finding that for the strongly polar species (e.g.: H₂O, HCl, HF) the impact of substituents on the interaction energy could be substantial because of dipole-driven electrostatic effects. These effects, along with those in substituted T-shaped benzene dimers, were captured by a Hammett-like substituent constant. Ultimately, Kim et al.⁴⁵ highlighted the need for future studies to elucidate the physical origin of these interactions to aid the rational design of supramolecular systems and novel molecular devices.

Although a myriad of studies have examined XH/ π interactions involving substituted arenes,^{20,21,38,39,57,58,62–64} there has been only one systematic study³⁹ of the impact of aryl substituents on these interactions covering a broad range of substituents. Moreover, there has been no comprehensive study of substituent effects across the full range of XH/ π interactions. Below we present such a systematic study quantifying the effect of aryl substituents on model XH/ π interactions (X = BH₂, CH₃, NH₂, OH, and F). The physical origins of these substituent effects have been unveiled through SAPT computations and correlations with substituent constants.

II. THEORETICAL METHODS

Constrained optimizations were executed at the B97-D/TZV(2d,2p)^{67,68} level of theory using Gaussian09⁶⁹ by fixing the XH bond over the centroid of the substituted phenyl ring, constraining this bond to remain orthogonal to the ring plane, and fixing the coordinates of all the ring atoms. All other coordinates were permitted to optimize. It should be noted that these geometries are in general not energy minima on the full potential energy surface. Instead, these model dimers are intended to permit an investigation of the impact of substituents on the strength of XH/ π interactions in the absence of complicating factors from geometric changes. Throughout this work, the interaction distance (r) is defined as the optimized distance from the heavy atom of the XH group to the centroid of the arene.

CCSD(T)/AVTZ interaction energies, evaluated at the B97-D optimized geometries, were estimated by appending a basis set correction computed at the second-order Møller–Plesset perturbation theory (MP2) level to CCSD(T)/AVDZ energies, where AVXZ denotes the aug-cc-pVXZ basis set.^{70–72} That is, the CCSD(T)/AVTZ interaction energies were estimated via

$$\begin{aligned} \Delta E(\text{CCSD(T)}/\text{AVTZ}) \\ \approx \Delta E(\text{CCSD(T)}/\text{AVDZ}) + \Delta E(\text{MP2}/\text{AVTZ}) \\ - \Delta E(\text{MP2}/\text{AVDZ}) \end{aligned}$$

To provide insight into the physical nature of substituent effects in these interactions, SAPT0/AVDZ energies⁷³ were computed at these same geometries using SAPT2008⁷⁴ paired with Molpro.⁷⁵ Both the B97-D and the SAPT0 interaction energies are in good agreement with the CCSD(T) data (see Supporting Information, Tables S1 and S2). The CCSD(T) and MP2 energies were computed using Molpro.⁷⁵ To further analyze substituent effects in XH/ π interactions, multidimensional linear regression analyses were carried out comparing individual components of the interaction energies with substituent constants⁷⁶ as well as the optimized interaction distance, r .

III. RESULTS AND DISCUSSION

The prototypical XH/ π interactions depicted in Figure 1 were studied primarily at the estimated CCSD(T)/AVTZ and SAPT0/AVDZ levels of theory. We first consider the effect of substituents on the total interaction energies for these model systems before examining the individual energy components and correlations with substituent constants. Overall, the SAPT0 interaction energies closely follow the CCSD(T)/AVTZ data, supporting the use of SAPT0 to study individual components of these interactions. Similarly, the good performance of B97-D relative to CCSD(T)/AVTZ lends credence to the use of B97-D optimized geometries.

A. Substituent Effects on Total Interaction Energies.

Computed interaction energies for the five model XH/ π interactions (see Figure 1) are plotted in Figure 2 versus Hammett constants (σ_m) for 22 monosubstituted benzenes. The corresponding data are listed in Table 1. For unsubstituted benzenes ($Y = \text{H}$), the interaction energies increase monotonically progressing from BH to CH, NH, OH, and FH. The mean interaction energies across all 22 substituents follow this same trend. This enhanced interaction with increasing polarization of

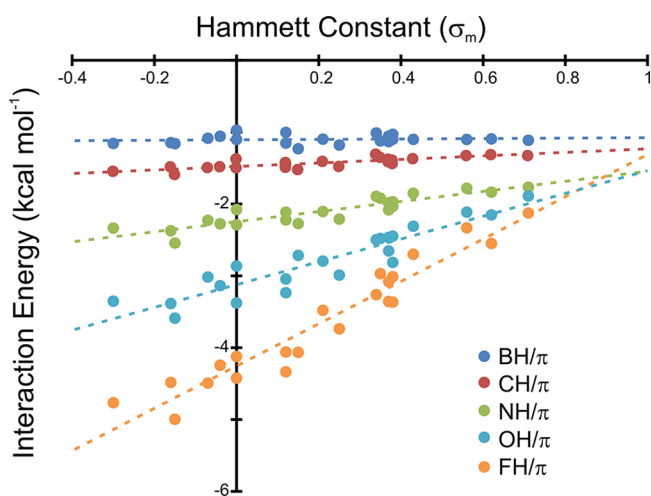


Figure 2. Estimated CCSD(T)/AVTZ interaction energies (kcal mol^{-1}) for prototypical XH/ π interactions (See Figure 1) for 22 substituted benzenes versus Hammett constants (σ_m). Dashed lines are the results of linear least-squares fits to the corresponding XH/ π data.

Table 1. Estimated CCSD(T)/AVTZ Interaction Energies (kcal mol^{-1}) for Prototypical XH/ π Interactions for 22 Substituted Benzenes

Y	σ_m	BH ₃	CH ₄	NH ₃	OH ₂	FH
H	0.00	-0.97	-1.38	-2.08	-2.86	-4.12
CCH	0.21	-1.10	-1.41	-2.11	-2.80	-3.48
CF ₃	0.43	-1.10	-1.38	-1.85	-2.31	-2.70
CH ₂ OH	0.00	-1.10	-1.50	-2.29	-3.38	-4.42
CH ₃	-0.07	-1.09	-1.50	-2.23	-3.02	-4.49
CHO	0.35	-1.12	-1.36	-1.92	-2.48	-2.97
CN	0.56	-1.10	-1.33	-1.78	-2.11	-2.33
COCH ₃	0.38	-1.03	-1.44	-2.03	-2.81	-3.37
COOCH ₃	0.37	-1.13	-1.42	-2.08	-2.65	-3.36
COOH	0.37	-1.06	-1.38	-1.98	-2.47	-3.08
F	0.34	-1.01	-1.31	-1.89	-2.50	-3.26
N(CH ₃) ₂	-0.15	-1.16	-1.60	-2.54	-3.59	-5.00
NH ₂	-0.16	-1.15	-1.49	-2.37	-3.39	-4.48
NHCH ₃	-0.30	-1.16	-1.55	-2.34	-3.35	-4.77
NHOH	-0.04	-1.06	-1.49	-2.28	-3.14	-4.24
NO ₂	0.71	-1.11	-1.33	-1.77	-1.89	-2.13
NO	0.62	-1.10	-1.32	-1.84	-2.15	-2.55
OCF ₃	0.38	-1.10	-1.40	-1.97	-2.45	-3.01
OH	0.12	-1.00	-1.43	-2.11	-3.04	-4.06
OCH ₃	0.12	-1.15	-1.50	-2.22	-3.24	-4.34
SCH ₃	0.15	-1.23	-1.53	-2.27	-2.72	-4.07
SH	0.25	-1.18	-1.48	-2.21	-2.99	-3.74
min.		-0.97	-1.31	-1.77	-1.89	-2.13
max.		-1.23	-1.60	-2.54	-3.59	-5.00
mean		-1.10	-1.43	-2.10	-2.79	-3.63
std. dev.		0.06	0.08	0.21	0.47	0.84

the XH bond is accompanied by an increased sensitivity to substituent effects, as indicated by the increased slope of the best-fit lines in Figure 2. This is in agreement with the previous findings of Kim et al.⁴⁵ in their study of complexes of H₂O, HF, etc. with substituted benzenes. This leads to stark differences in substituent effects between the nonpolar (BH and CH) and polar (NH, OH, and FH) groups. For example, the standard deviations across the set of 22 substituents for the interactions involving NH₃, OH₂, and FH range from 0.2 to 0.8 kcal mol^{-1} . For BH₃ and CH₄, computed interaction energies are essentially constant across the full range of substituted benzenes.

A consequence of the increase in slope with the polarity of the XH group is that for electron-withdrawing substituents (e.g. NO₂, CN, etc.) there is a relatively small difference in interaction energies across the different XH/ π interactions. For example, for NO₂ substituted benzene ($\sigma_m = 0.71$) the interaction with BH₃ and FH differ by only 1.0 kcal mol^{-1} , although this does represent a doubling of the BH₃ interaction energy. This can be contrasted with NHCH₃ ($\sigma_m = -0.30$) substituted benzene, for which the interaction is enhanced by more than a factor of 4 going from BH/ π to FH/ π . This suggests that greater differentiation between different XH/ π interactions can be achieved with aryl rings bearing electron-donating groups.

Overall, electron-donating groups enhance XH/ π interactions while electron-withdrawing groups hinder these interactions, as noted for acetylene-benzene dimers by Mishra et al.³⁹ This behavior, along with the SAPT0 results discussed below, indicates the importance of electrostatic interactions for

Table 2. Mean Values and Standard Deviations for the Interaction Distance (in Å) and the Electrostatic (Elec), Exchange-Repulsion (Exch), Induction (Ind), and Dispersion (Disp) Components of the SAPT0 Energies (kcal mol⁻¹) As Well As Correlation Coefficients between These Individual Components and the Total SAPT0 Interaction Energies for XH/ π Interactions

X	<i>r</i>	Elec	Exch	Ind	Disp
Mean \pm Standard Deviation					
BH ₂	3.90 \pm 0.02	-0.81 \pm 0.06	2.50 \pm 0.13	-0.28 \pm 0.05	-2.77 \pm 0.10
CH ₃	3.69 \pm 0.02	-1.05 \pm 0.07	2.72 \pm 0.13	-0.30 \pm 0.05	-3.18 \pm 0.12
NH ₂	3.45 \pm 0.02	-1.97 \pm 0.24	3.54 \pm 0.19	-0.59 \pm 0.07	-3.53 \pm 0.12
OH	3.30 \pm 0.01	-2.66 \pm 0.52	3.75 \pm 0.15	-1.02 \pm 0.08	-3.29 \pm 0.09
F	3.16 \pm 0.01	-3.13 \pm 0.93	3.65 \pm 0.20	-1.84 \pm 0.11	-2.74 \pm 0.09
Correlation Coefficients with Total Interaction Energies					
BH ₂		0.63	-0.38	0.37	0.63
CH ₃		0.88	-0.79	0.91	0.84
NH ₂		0.97	-0.87	0.94	0.85
OH		0.99	-0.92	0.97	0.77
F		1.00	-0.95	0.98	0.87

Table 3. Mean Values and Standard Deviations for Various Sums of Electrostatic (Elec), Exchange-Repulsion (Exch), Induction (Ind), and Dispersion (Disp) Components of the SAPT0 Energies (kcal mol⁻¹) As Well As Correlations between These Triply-Additive Energies and the Total SAPT0 Interaction Energy for XH/ π Interactions

X	Exch+Ind+Disp	Elec+Ind+Disp	Elec+Exch+Disp	Elec+Exch+Ind
Mean \pm Standard Deviation				
BH ₂	-0.55 \pm 0.06	-3.86 \pm 0.17	-1.08 \pm 0.07	1.41 \pm 0.08
CH ₃	-0.77 \pm 0.05	-4.54 \pm 0.22	-1.52 \pm 0.06	1.36 \pm 0.06
NH ₂	-0.58 \pm 0.06	-6.09 \pm 0.42	-1.97 \pm 0.18	0.98 \pm 0.16
OH	-0.56 \pm 0.06	-6.97 \pm 0.67	-2.20 \pm 0.45	0.07 \pm 0.46
F	-0.93 \pm 0.06	-7.70 \pm 1.12	-2.22 \pm 0.81	-1.32 \pm 0.85
Correlation Coefficients with Total Interaction Energies				
BH ₂	0.35	0.53	0.61	0.01
CH ₃	0.60	0.87	0.88	0.02
NH ₂	0.02	0.95	0.98	0.83
OH	0.00	0.99	1.00	0.98
F	0.02	1.00	1.00	1.00

each of the XH/ π interaction types. However, a closer examination of the individual components of the interaction energies reveals more subtle behavior (vide infra). In general, the observed substituent effects in all of these XH/ π interactions are consistent with popular models of substituent effects in π -stacking interactions: the π -resonance-based model of Hunter and Sanders,^{77–80} the polar/ π model of Cozzi and Siegel,^{81,82} as well as the local, direct interaction model proposed by Wheeler^{83–85} based on through-space effects of the substituents (i.e.: field effects).

B. Components of Interaction Energies. Insight into the physical nature of these substituent effects is provided by SAPT0 results, which enable the decomposition of the total interaction energies into contributions from electrostatic (Elec), exchange-repulsion (Exch), induction (Ind), and dispersion (Disp) effects. Part of our analysis of these SAPT0 data is based on a scheme recently used by Watt et al.⁸⁶ in their work on the benzene sandwich dimer. For example, to analyze the impact of electrostatic effects on a given XH/ π interaction, we add the exchange, induction, and dispersion energies together and examine the correlation of this “triply additive energy” with the total energy for each of the substituted dimers. A lack of correlation in this case indicates a balancing of the dispersion and induction energies with the exchange energy. This, in combination with a strong correlation between the electrostatic component and total energy, can indicate that

electrostatic effects are the main cause of substituent effects. Such analyses have been performed for each of the four components of the total interaction energy for all five XH/ π interactions.

First, however, we examine individual components of the interaction energy as well as the correlation of these individual components with the total interaction energies. Mean values and standard deviations across the set of 22 substituents are provided in Table 2 for the individual components of the interaction energy for each of the XH/ π interactions. Mean interaction distances are also provided. On average, the electrostatic and induction components increase with increased polarity of the XH group, as expected. These enhanced electrostatic and induction effects most likely drive the concurrent decrease in interaction distances (see Table 2). The mean dispersion component, on the other hand, increases going from BH to CH to NH, but then peaks and decreases going from NH to OH to FH. This can be explained in terms of competing effects of decreasing interaction distance and the decreasing polarizability of the XH group going from CH₄ to HF. The exchange-repulsion component increases with the decreasing interaction distance, as expected.

All four energy components are strongly correlated with the total interaction energy, providing surprisingly little physical insight. Examining the standard deviations of these energy components across the set of 22 substituents does indicate that

some components contribute more than others to the overall substituent effect. Moreover, the component exhibiting the greatest change across the set of substituents varies among the XH groups. In general, increases in the electrostatic component of these interactions are accompanied by increases in its variation across the set of substituents. For example, for the FH/ π interactions the standard deviation in the electrostatic component of the interactions is 0.9 kcal mol⁻¹, while the other three components have standard deviations less than 0.2 kcal mol⁻¹.

One difficulty with analyzing individual energy components is that they are coupled, in part, through the interaction distance. This is particularly true of the dispersion and exchange-repulsion terms. Evidence for the relative importance of the electrostatic energies in driving substituent effects for some XH/ π interactions can be garnered by considering the triply additive energies discussed above and listed in Table 3. For the triply additive energies that exclude electrostatic effects, there is very little variation across the set of substituents, as indicated by the uniformly small standard deviations for Exch+Ind+Disp in Table 3. The other sums, which include electrostatic contributions, vary more considerably across the set of substituents, and this variation increases with increasing polarity of the XH group. The correlations of these triply additive energies with the total SAPT0 interaction energies tell a similar story: for NH, OH, and FH/ π interactions there is no correlation between Exch+Ind+Disp and the total interaction energy, indicating that the electrostatic component is vital to describe the substituent effects. On the other hand, for the BH and CH/ π interactions the triply additive energy with a low correlation is Elec+Exch+Ind. This suggests that for these two XH/ π interactions the dispersion contribution is the most important.

C. Correlations with Substituent Constants. To provide additional physical insight into these interactions, we also examined correlations of the individual SAPT0 components with Hammett constants (σ_m) and molar refractivities (MR). Hammett constants are frequently used in the literature, and are intended to capture effects due to a substituent's electrostatic properties. Molar refractivities, on the other hand, are commonly used as a measure of polarizabilities.⁸⁷ We also consider correlations involving the interaction distance (r), which can be considered a property of the substituted benzene when making comparisons across different substituents for a given XH monomer. This distance is used, in part, because these noncovalent interaction energies are all dependent upon electron cloud overlap at close range (e.g.: penetration effects). There is the obvious issue of using the interaction distance in linear correlations, because the components of these interaction energies should not depend linearly on r . However, this linear approximation should be acceptable given the narrow range of distances considered. Linear regression analyses were conducted for each of the SAPT0 energy components with the individual substituent constants as well as all pairwise combinations of these constants and the three constants together.

Before considering the correlations of interaction energies with substituent constants, we must first discern whether σ_m , MR, and r are independent of one another across the set of substituents (see Supporting Information, Table S3). For these 22 substituents, the MR and σ_m values are uncorrelated, indicating a diverse sample of substituents. However, there is a strong correlation between σ_m and r , with the strength of the

correlation increasing with increasing polarity of the XH bond. MR and r are only weakly correlated, and the strength of this correlation decreases with increasing XH bond polarity. These trends arise because the correlation of r with the other two parameters follows the extent to which those parameters describe the overall interaction (vide infra). Consequently, care must be exercised before conclusions are drawn regarding the correlation with any individual substituent constant.

As shown in Table 4, the electrostatic components of all of the XH/ π interactions except BH/ π are fairly well described by

Table 4. Correlation Coefficients for the Electrostatic, Exchange-Repulsions, Induction, And Dispersion Components of XH/ π Interactions with Hammett Constants (σ_m), Molar Refractivity (MR), Interaction Distance (r), and Combinations of These Constants^a

X	σ_m	r	MR	($\sigma_m r$)	(MR r)	(σ_m MR)	(σ_m MR r)
Electrostatic							
BH ₂	0.04	0.18	0.20	0.48	0.25	0.28	0.51
CH ₃	0.68	0.77	0.15	0.94	0.79	0.75	0.94
NH ₂	0.86	0.81	0.07	0.96	0.82	0.88	0.96
OH	0.84	0.86	0.03	0.92	0.89	0.84	0.93
F	0.92	0.91	0.03	0.96	0.92	0.92	0.97
Exchange-Repulsion							
BH ₂	0.27	0.98	0.29	0.98	0.98	0.48	0.98
CH ₃	0.38	0.97	0.31	0.98	0.97	0.60	0.98
NH ₂	0.66	0.96	0.12	0.98	0.97	0.72	0.98
OH	0.80	0.95	0.07	0.96	0.95	0.82	0.96
F	0.82	0.99	0.04	0.99	0.99	0.83	0.99
Induction							
BH ₂	0.89	0.53	0.10	0.95	0.53	0.93	0.95
CH ₃	0.88	0.55	0.10	0.96	0.57	0.92	0.96
NH ₂	0.88	0.81	0.09	0.97	0.81	0.91	0.97
OH	0.90	0.87	0.09	0.96	0.87	0.93	0.96
F	0.87	0.96	0.10	0.97	0.96	0.91	0.98
Dispersion							
BH ₂	0.24	0.84	0.61	0.84	0.98	0.76	0.98
CH ₃	0.25	0.86	0.62	0.86	0.96	0.78	0.97
NH ₂	0.39	0.81	0.51	0.82	0.96	0.78	0.96
OH	0.44	0.78	0.48	0.81	0.95	0.81	0.95
F	0.65	0.86	0.32	0.87	0.98	0.86	0.98

^aThe columns in bold indicate the constants or simplest combination of constants providing the best correlation across all five XH/ π interactions.

the Hammett constants alone. However, the strength of the correlations becomes weaker with decreased polarity of the XH group. Once the Hammett constants and the interaction distances are used in concert, the correlations become very good, again with the exception of boron. The fact that inclusion of r is necessary for strong correlations is possibly due to the importance of charge penetration.

The exchange-repulsion components of these interactions are strongly correlated with the interaction distance alone. This is where considering a range of XH/ π interactions proves highly useful, because r and σ_m are correlated to a different extent for the different XH groups. For example, consideration of only OH and FH/ π interactions, for which σ_m and r are strongly correlated, would lead to the false conclusion that the Hammett constants provide a sound predictor of the exchange-repulsion component of XH/ π interactions. This misleading correlation arises when electrostatic interactions are significant, the

Hammett parameters indirectly capture the exchange-repulsion trends because electrostatic effects impact the overall energies and interaction distances.

The induction energy is captured mostly in the Hammett constants of the substituents. There is essentially no correlation between the induction energies and the MR values, indicating that the substituent effects on the induction component arise primarily from changes in the electrostatic properties of the substituents, not changes in their polarizabilities. That is, the changes in the induction energy arise from the different substituents polarizing the XH group. This could indicate a variety of possibilities, including that the changes in the electrostatic properties of the substituents are effectively larger than the changes in their polarizabilities. Alternatively, this could arise because the electric multipoles of the XH group are small enough that changes in the polarizabilities of the substituents result in negligible changes in the total induction energy. That the correlations of MR values with the induction energy are uniform across the different XH groups supports the former possibility. The correlation of the induction energies is significantly improved by inclusion of the interaction distance, as was observed for the electrostatic component of these interactions.

Finally, the dispersion component of these interactions is best described by a combination of r and MR values. Again, the correlation between the σ_m and r for the polar cases provides an artifactual correlation between the dispersion energies and Hammett constants for the more polar XH groups because of the correlation between σ_m and r for these interactions.

IV. SUMMARY AND CONCLUDING REMARKS

We have presented a comprehensive, systematic study of substituent effects in model XH/ π interactions ($X = \text{BH}_3, \text{CH}_4, \text{NH}_3, \text{OH}_2$, and FH) based primarily on estimated CCSD(T)/AVTZ interaction energies. Insight into the physical nature of these substituent effects was gleaned from SAPT0 computations as well as correlations with Hammett constants (σ_m), molar refractivities (MR), and the optimized interaction distances, r .

Substituents can have a dramatic impact on XH/ π interactions, but the magnitude of these effects as well as their physical origin depends strongly on the nature of the X group. In particular, increased polarity of the XH bond is accompanied by a substantial increase in the magnitude of substituent effects. On the basis of the above data, we can draw the following main conclusions:

(1) The electrostatic and induction components of XH/ π interactions (except BH/π) are strongly correlated with σ_m and r . For BH/π interactions these components do not change upon substitution, so no correlation is observed.

(2) Exchange-repulsion is correlated most strongly with the interaction distance, and no individual substituent constant can capture the effect of substituents on exchange-repulsion effects without explicitly accounting for the changes in interaction distance.

(3) The dispersion component of the interactions is correlated with both MR and r . The correlation of the dispersion component with MR values alone is relatively weak.

(4) The strength of XH/ π interactions increases with increasing electron-donating character of the substituents, as do the differences among the different XH/ π interactions.

(5) The primary driver of substituent effects for the polar XH groups ($\text{NH}_3, \text{OH}_2, \text{FH}$) is the electrostatic energy, while

dispersion effects dictate substituent effects for the nonpolar monomers (BH_3, CH_4).

Overall, substituent effects in XH/ π interactions are in general accord with previous work,^{39,45} and follow expected trends based on simple physical models. Examining the full range of XH/ π interactions has provided a comprehensive and unified view of the physical origin of substituent effects in these interactions. Although these results are based on idealized model dimers in which the X–H bond is perpendicular to the aryl ring and directed toward the ring centroid (see Figure 1), they should provide a qualitative guide to XH/ π interactions in more realistic supramolecular complexes.

■ ASSOCIATED CONTENT

Supporting Information

Electronic energies, Cartesian coordinates. 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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