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Saturated Hydrocarbon−Benzene Complexes: Theoretical Study of Cooperative CH/π Interactions

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High-level ab initio calculations at the CCSD(T)/aug-cc-pVTZ//MP2/aug(d,p)-6-311G(d,p) level were employed to investigate the cooperative CH/π effects between the π face of benzene and several modeled saturated hydrocarbons, propane, isobutane, cyclopropane, cyclobutane, cyclopentane, cyclohexane, cyclopentane, cyclooctane, and bicyclo[2.2.2]octane. In all cases, multiple C−H groups (2−4) are found to interact with the π face of benzene, with one C−H group pointing close to the center of the benzene ring. The geometries of these complexes are governed predominantly by electrostatic interaction between the interacting systems. The calculated interaction energies (10−14 kJ mol^{-1}) are 2−3 times larger than that of the prototypical methane−benzene complex. The trends of geometries, interaction energies, binding properties, as well as electron-density topological properties were analyzed. The calculated interaction energies correlate well with the polarizabilities of the hydrocarbons. AIM analysis confirms the hydrogen-bonded nature of the CH/π interactions. Significant changes in proton chemical shift and stretching frequency (blue shift) are predicted for the ring C−H bond in these complexes.

Introduction

CH/π interaction, an attractive interaction between a C−H bond and an aromatic π system, has attracted much recent interest.[1−4] This type of intermolecular force is almost ubiquitous in many fields of organic, inorganic, biochemical, and material chemistry.[1,4] The CH/π interaction was first proposed by Nishio and co-workers to explain the preference of conformations in which bulky and phenyl groups are in close contact.[5] It is important to note that the acceptor of the CH/π interaction is not limited to an aromatic π system. Other unsaturated functional groups, such as C═C, C═O, etc., are also good candidates as CH/π acceptors.[1−4] During the last two decades, numerous experimental studies which support the existence of this noncovalent attraction have been reported.[4] In particular, the short contact between a C−H bond and a π system is observed in a very large number of crystals of organic molecules,[6,7] peptides,[8] and proteins.[9] It is believed that the CH/π interaction is important in understanding many chemical phenomena such as conformational preference, crystal packing, host−guest complexation, and self-organization processes.[4] The importance of CH/π interaction for structures and properties of biological systems has also been reported.[1,8,9]

In recent years, several theoretical studies of simple benzene complexes have been carried out to evaluate the interaction energy of the CH/π interaction and gain insight into the nature of the interaction.[10−15] The best calculation of the methane−benzene complex suggests that the CH/π bond strength is about 6 kJ mol^{-1}.[10b] In many organic molecules there are several C−H protons oriented in such a way that multiple CH/π interactions can occur simultaneously with the π face of an aromatic system. Thus, it is intriguing to ask whether multiple CH/π interactions can interact in a cooperative manner. Recent elegant 2D solid-state NMR study has revealed that multiple CH/π interactions can cooperatively stabilize nanostructures entrapped as guests in channels formed by an aromatic host.[16] To better understand the role of multiple CH/π interactions, we systematically investigated the benzene complexes of propane, isobutane, and several saturated cyclic compounds, namely, cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, cyclooctane, and bicyclo[2.2.2]octane, using high-level ab initio calculations. These chosen hydrocarbon models are characterized by several "axial" hydrogens in close proximity. In particular, isobutane and cyclohexane have three axial C−H bonds parallel to each other, which readily interact with the π cloud of benzene. Methane− and ethane−benzene complexes have been examined previously,[10−15] but these systems were included in this study for the purpose of comparison. The geometrical features, interaction energies, binding properties, and topological properties will be examined to gain further insight into the nature of CH/π interactions in this series of hydrocarbon−benzene complexes.

Computational Methods

Dispersion interaction is important in the proper description of both the geometries and the binding energies of CH/π complexes.[2,3,10b,11a,15b] As a consequence, both the Hartree−Fock (HF) and density functional theory (DFT) methods grossly underestimate the binding energies of the complexes examined here. For instance, the HF and B3LYP interaction energies, corrected for basis set superposition error (BSSE), of isobutane−benzene complex (+0.3 and +1.0 kJ mol^{-1}, respectively) are considerably smaller the MP2 and CCSD(T) values (−4.1 and −2.1 kJ mol^{-1}, respectively) [Table S1, Supporting Information]. In addition, a large basis set is required for proper description of the weak intermolecular CH/π complexes. Hence, geometry optimizations of the hydrocarbon−benzene CH/π complexes (**1**−**11**) were carried out at the MP2/aug(d,p)-6-311G(d,p) level (without BSSE correction). The aug(d,p)-6-311G(d,p) basis set, proposed by Tsuzuki et al.,[10b,17] corresponds

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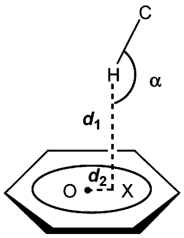
CHART 1



to the 6-311G(d,p) basis set augmented with diffuse *d* functions on carbon and diffuse *p* functions on hydrogen atoms ($\alpha_d(C) = 0.1565$ and $\alpha_p(H) = 0.1875$). Frequency analysis was performed at the MP2/6-31G(d) level to evaluate zero-point energy (ZPE) correction and to determine the C−H frequency shift in the complex. Previous theoretical studies have established undoubtedly that a large basis set including multiple polarization functions and appropriate electron correlation are necessary to accurately evaluate the interaction energies of CH/π complexes.[2,3,10b,11a,15e] Thus, more reliable prediction of interaction (binding) energies were obtained via higher-level single-point calculations at the CCSD(T)[18] level in conjugation with a larger aug-cc-pVTZ basis set, obtained via additivity approximation at the MP2 level. Correction for basis set superposition error (BSSE), based on the counterpoise method,[19] was included in the final calculated interaction energy. Unless otherwise noted, the interaction energies reported in the text correspond to the CCSD(T)/aug-cc-pVTZ level including zero-point energy (MP2/6-31G(d), scaled by 0.967)[20] and BSSE corrections. NMR chemical shift calculations were performed using the gauge-independent atomic orbital (GIAO) method.[21] Atomic charges were obtained using the natural bond orbital (NBO) approach, based on the MP2/aug(d,p)-6-311G(d,p) wave function.[22] Charge density analysis, based on Bader's theory of atoms in molecules (AIM),[23] was carried out using the MORPHY98 program,[24] and the electrostatic potential map was generated using the MOLDEN program.[25] All other calculations were performed using the Molpro 2002,[26] Gaussian 98,[27] and Gaussian 03[28] programs.

Results and Discussion

1. Complex Geometries. There are several important structural parameters which characterize a CH/π interaction, namely, d_1, d_2, and α (see Chart 1). O is the center (centroid) of the benzene ring, while X represents the projection point of a C−H hydrogen on the molecular plane of benzene. Thus, d_1 corresponds to the nonbonded intermolecular distance, d_2 represents the distance of the projection point away from the benzene center (O), and α is the CHX angle. On the basis of previous experimental and theoretical studies[1−4] the characteristic properties of a typical CH/π interaction are as follows: (1) the intermolecular distance d_1 is in the range 2.6−3.0 Å, (2) the C−H bond points close to the center of an aromatic ring, (3) the CHX angle (α) is close to linearity, and (4) the C−H bond length is shortened upon complexation, which leads to a higher C−H stretching frequency.

The optimized geometries of all the hydrocarbon−benzene complexes (**1**−**11**) are shown in Figure 1. Selected structural parameters, d_1, d_2, and α, are listed in Table 1. The most stable conformation of each complex favors multiple (2−4) CH/π contacts (except for methane and ethane complexes). This clearly demonstrates that several C−H groups of the hydrocarbon can interact with the π face of benzene in a cooperative manner. Let us consider in detail the various possible conformations of the cyclohexane−benzene complex. There are two types of C−H bonds in the chair form of cyclohexane: axial and equatorial. The three axial C−H bonds are parallel to each other. Furthermore, the dimension of these three axial hydrogens is similar to the size of the benzene ring. In other words, multiple CH/π contacts are feasible for benzene to interact with the axial hydrogens. Therefore, one would expect two possible modes of interaction between the cyclohexane and benzene: face-to-face and T-shaped. In the first model, both molecules are oriented parallel to each other with all three axial hydrogens directed toward the face of benzene. In the second model, only one equatorial C−H group is directed toward the center of the benzene ring. Two different conformations were obtained for the face-to-face model of interaction: symmetrical (C_{3v}, **13**, Figure 2) and asymmetrical (C_1, **8**, Figure 1). In the symmetrical structure, the three axial C−H bonds lie exactly perpendicular to three carbon atoms of benzene (**13**, Figure 2). On the other hand, the asymmetrical structure (**8**), which has one C−H group, directs toward the center of the benzene ring, and the other two C−H groups lie outside the benzene ring. The asymmetrical conformation is slightly more stable than the symmetrical form by 1.0 kJ mol^{-1}. Interaction of an equatorial C−H group of cyclohexane with benzene leads to a T-shaped structure with one CH/π interaction ($d_1 = 2.346$ Å, $d_2 = 0.094$ Å, and $\alpha = 159.2°$) close to the center of benzene (C_1, **12**, Figure 2). This T-shaped structure is 2.2 kJ mol^{-1} less stable than the most stable form of the complex (**8**). For the isobutane−benzene complex there exists a similar high-symmetry conformation (C_{3v}, **14**). However, all three C−H groups point perpendicular to the middle of three C−C π bonds of benzene in this case (**14**, Figure 2). This conformation is predicted to lie very close in energy (0.1 kJ mol^{-1}) to the asymmetrical structure (**4**). Since the intermolecular potential of this system is very flat, it is likely that both the symmetrical and asymmetrical conformations can coexist. In summary, the conformation with multiple CH/π contacts is energetically more favored in the series of hydrocarbon−benzene complexes.

Each CH/π contact of all the hydrocarbon−benzene complexes (**1**−**11**) is characterized by a short contact distance $d_1 <$ 3.0 Å and a bond critical point (see section 4). The intermolecular distances (d_1) lie in the range 2.31−2.82 Å (Table 1). This in good agreement with the statistical analysis, based on CSD analysis for the crystal structures with a saturated type of C−H bonds (∼2.7 Å).[6,7,29,30] In all cases (**1**−**11**) the complex geometry has one C−H group directed toward the center of the benzene ring (we shall designate this hydrogen as "ring" hydrogen). The other CH/π contacts lie outside the benzene ring and are located in specific regions defined by the C−C and C−H bonds. In general, the ring C−H hydrogen has the shortest contact distance (d_1) among all the C−H groups facing the π face of benzene (Table 1). Accordingly, the CHX angle (α) associated with the ring hydrogen is larger. For the isobutane (**4**) and cyclohexane (**8**) complexes the α values are very close to 180°. Interestingly, all the ring hydrogens lie somewhat offset the center of the benzene ring, $d_2 = 0.08−0.23$ Å, except for the cyclooctane complex. Our finding on the preference of an offset is consistent with the frequency distribution study of hydrogen-bond trajectories for the CH···Ph interactions by Cjunik and Desiragu.[31] These authors found that CH···Ph interaction generally favors an offset from the benzene centroid with 0.3−0.6 being the maximum. For methane−benzene complex (**1**) we found that an asymmetric geometry (**1**) lies almost identical in energy (0.1 kJ mol^{-1}) to the symmetrical C_{3v} geometry (**15**, $d_1 = 2.472$ Å, $d_2 = 0.0$ Å, and $\alpha = 179.3°$, Figure 2) previously reported.[10b] Since the intermolecular

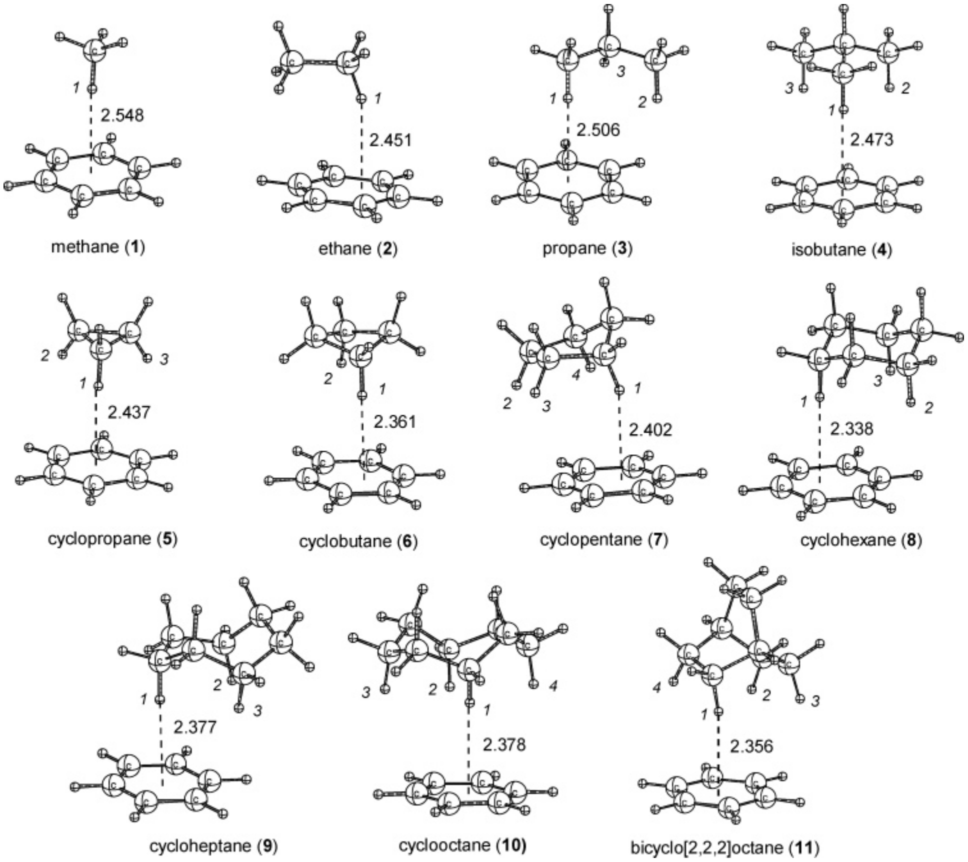


Figure 1. Optimized [MP2/aug(d,p)-6-311G(d,p)] geometries of various hydrocarbon−benzene CH/π complexes. The dotted line represents the projection line of the ring C−H hydrogen of the hydrocarbon perpendicular to the molecular plane of benzene.

potential of this CH/π complex is very flat, it is difficult to determine the preferred geometry with certainty. As with **1**, ethane−benzene complex (**2**, Figure 1) favors an asymmetrical structure with the CH/π contact slightly away from the benzene centroid (d_2 = 0.110 Å and α = 157.2°). Interestingly, the propane−benzene complex (**3**, Figure 1) has three sets of CH hydrogens in close contact with the π face of benzene.

How do we account for the structural features of these CH/π complexes? In particular, why does the ring hydrogen point away from the benzene centroid? Inspection of the electrostatic potential map of benzene (Figure 3) indicates that the maximum negative potential is located approximately 0.5 Å from the center of the ring. Thus, it is not surprising that the ring hydrogen of each complex favors a molecular geometry outside the center of the benzene ring. Strong negative potentials are also found in regions outside the ring, in the six regions defined by the C−C and C−H bonds (see Figure 3). Figure 3 also plots the projection points (X, see Chart 1) of all the CH/π hydrogens for complexes **1**−**11**. It is immediately obvious that all the projection points fall in the regions of strong negative electrostatic potential. It thus appears that the most stable geometry of each CH/π complex favors a maximum overlap of the electropositive C−H hydrogens with the electron-rich regions of benzene. In other words, the geometries and directionalities of interaction of the hydrocarbon−benzene complexes are determined mainly by the electrostatic interaction between the interacting molecules.

Our theoretical finding here is supported by analyses of data collected in the Cambridge Structural Database and Brookhaven Protein Data Bank.[9b,29,30] In particular, Cjunik et al.[30] showed close intermolecular contacts between alicyclic (such as cyclohexane and cyclopentane) and aromatic rings in a number of crystal structures. Most importantly, multiple CH/π contacts are frequently observed.

On the basis of our understanding of the geometrical features of the series of hydrocarbon−benzene complexes examined here, we envisage a system with five CH/π interactions being feasible. *cis*-1,3-Dimethylcyclohexane provides one such simple example. In this case, the hydrocarbon has five parallel axial C−H bonds and the appropriate dimension to match the negative electrostatic potential of the benzene molecule. Indeed, geometry optimization [MP2/aug(d,p)-6-311G(d,p)] of such a complex (**16**) yields the predicted geometry with one C−H bond pointing close to the center of benzene (d_2 = 2.497 Å, d_2 = 0.092 Å, and α = 179.7°) and the other four C−H bonds lying on the four regions outside the ring where electrostatic potential are strong. At the CCSD(T)/aug-cc-pVTZ+ZPE+BSSE level the computed stabilization energy of **16** is −15.8 kJ mol^{-1}, 3.2 kJ mol^{-1} larger than that of cyclohexane−benzene complex (**8**). Remarkably, analysis of the Cambridge Crystal Database (CSD) revealed a crystal structure (Figure S1, Supporting Information)[32] with such a geometrical feature. As seen in Figure S1, the substituted phenyl moiety interacts favorably with the dimethylcyclohexane unit via five sets of CH/π interactions.

In general, the geometry of the hydrocarbon is hardly changed upon complexation with benzene. Cyclooctane (**10**) and bicyclo[2.2.2]octane (**11**) complexes are the only two exceptions. In **10** the cyclooctane ring is slightly distorted with one torsion angle increasing from 84° to 114°, while the six-membered ring of the hydrocarbon is distorted by 17° in **11**. In both cases, the change allows a maximum electrostatic fit between the four C−H groups of the cyclic alkane with benzene. As with previous theoretical findings, there is a slight contraction of all C−H

TABLE 1: Calculated Structural Parameters (d_1, d_2, and α)[a] and Topological Properties[b] (ρ, $\nabla_2\rho$, and ϵ, in Au) at the Bond Critical Point of Various Hydrocarbon−Benzene Complexes (1−11), Evaluated at the MP2/aug(d,p)-6-311G(d,p) Level

hydrocarbon	label[c]	d_1	d_2	α	ρ	$\nabla_2\rho$	ϵ
methane (**1**)	1	2.548	0.205	145.5	0.0066	0.0205	7.09
ethane (**2**)	1	2.451	0.110	157.2	0.0074	0.0234	6.51
propane (**3**)	1	2.506	0.150	146.2	0.0070	0.0219	11.8
	2	2.557	2.499	145.8	0.0061	0.0176	2.94
	3	2.629	2.353	140.9	0.0056	0.0163	0.97
isobutane (**4**)	1	2.473	0.170	178.4	0.0075	0.0232	3.73
	2	2.602	2.414	176.2	0.0066	0.0195	1.83
	3	2.602	2.415	176.2	0.0066	0.0195	1.83
cyclopropane (**5**)	1	2.437	0.189	152.8	0.0077	0.0239	4.46
	2	2.618	2.339	145.4	0.0062	0.0176	0.89
	3	2.618	2.339	145.6	0.0062	0.0176	0.89
cyclobutane (**6**)	1	2.361	0.123	165.5	0.0091	0.0285	7.36
	2	2.374	2.575	165.0	0.0076	0.0215	1.70
cyclopentane (**7**)	1	2.402	0.231	161.8	0.0088	0.0269	3.90
	2	2.309	2.945	155.1	0.0059	0.0174	0.91
	3	2.737	2.299	133.5	0.0056	0.0170	0.81
	4	2.512	2.490	153.1	0.0070	0.0200	1.21
cyclohexane (**8**)	1	2.338	0.121	176.1	0.0092	0.0288	4.68
	2	2.567	2.484	172.9	0.0066	0.0182	1.21
	3	2.571	2.481	172.9	0.0066	0.0182	1.21
cycloheptane (**9**)	1	2.377	0.148	162.8	0.0088	0.0275	4.18
	2	2.404	2.580	150.2	0.0073	0.0205	1.63
	3	2.684	2.174	175.4	0.0067	0.0183	0.88
cyclooctane (**10**)	1	2.376	0.000	150.0	0.0084	0.0257	12.04
	2	2.490	2.401	158.1	0.0078	0.0203	1.09
	3	2.504	2.628	167.5	0.0061	0.0158	0.79
	4	2.815	2.293	165.7	0.0054	0.0136	0.43
bicyclo[2.2.2]octane (**11**)	1	2.356	0.079	167.9	0.0089	0.0278	5.26
	2	2.348	2.711	162.1	0.0074	0.0209	1.53
	3	2.578	2.464	152.7	0.0059	0.0165	0.61
	4	2.779	2.256	147.5	0.0050	0.0147	0.53

[a] Bond lengths in Ångstroms and angles in degrees. [b] On the basis of AIM analysis. [c] See Figure 1 for hydrogen labeling.

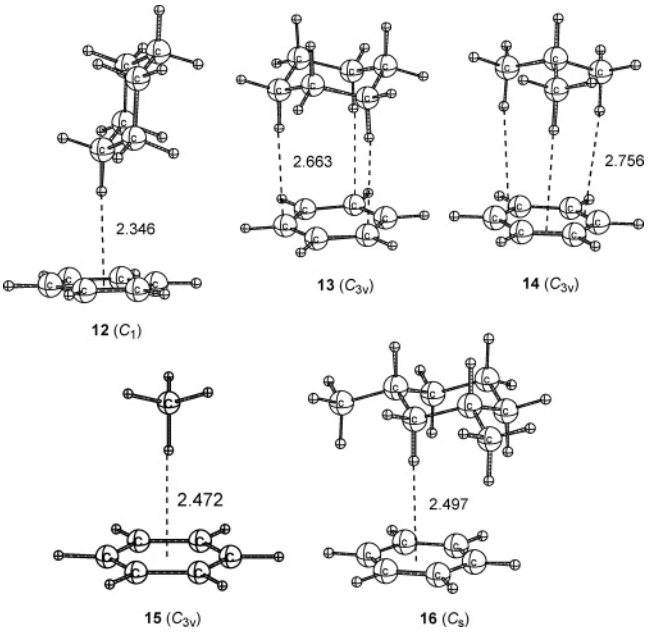


Figure 2. Conformations of methane−, isobutane−, cyclohexane−, and 1,3-dimethylcyclohexane−benzene complexes.

bonds in contact with the π face of benzene. The possible origin of this bond shortening will be discussed in section 4.

2. Interaction Energies. To determine a suitable level of theory for reliable prediction of the interaction energies of the weakly bonded systems studied here, we initially performed a benchmark study of the interaction energy of the isobutane−benzene complex (**4**) at various levels of theory. In general, the Hartree−Fock and density functional methods cannot describe this long-range CH/π interaction properly. As a consequence, HF and most DFT methods substantially underestimate the binding energy (Table S1). The only notable exception is the modified PW91 method (mPW1PW91) proposed by Adamo and Barone,[33] which yields results close to those of the higher levels of theory. As dispersion interaction is the main source of attraction in these complexes, MP2 theory gives a much improved result. However, the MP2 value is somewhat overestimated compared to the QCISD(T) and CCSD(T) values (Table S1). We note that the effect of triple excitations is particularly important. For instance, on going from CCSD to CCSD(T) (or MP3 to MP4) there is a significant increase of the binding energy by 1.5 kJ mol^{-1}. Not surprisingly, the choice of basis set has a very strong influence on the computed stabilization energy. Previous studies[10b,11a,15c,e] have shown that a fairly flexible basis set with multiple polarization functions is required for reliable prediction of the binding energy of the weak CH/π complex. Tsuzuki and co-workers have shown that the basis set including diffuse polarization functions on both carbon and hydrogen atoms yields a result close to that of the complete basis set limit. Here, we confirmed that the aug(d,p)-6-311G(d,p) basis set gives an interaction energy close to those obtained with the larger 6-311++G(3df,2p) and cc-pVQZ basis sets (Table S1). Thus, the aug(d,p)-6-311G(d,p) basis set is a practical choice for calculating the interaction energies for large systems.

As evidenced in Table S1, the MP2 interaction energies are very sensitive to the effect of BSSE correction. As expected, the BSSE correction is smaller for the larger basis set. On the basis of benchmark calculations on the methane−benzene complex we found that the BSSE correction at the CCSD(T) level is similar to that at the MP2 level for a range of basis sets. A similar finding has been reported by Tsuzuki et al.[10b]

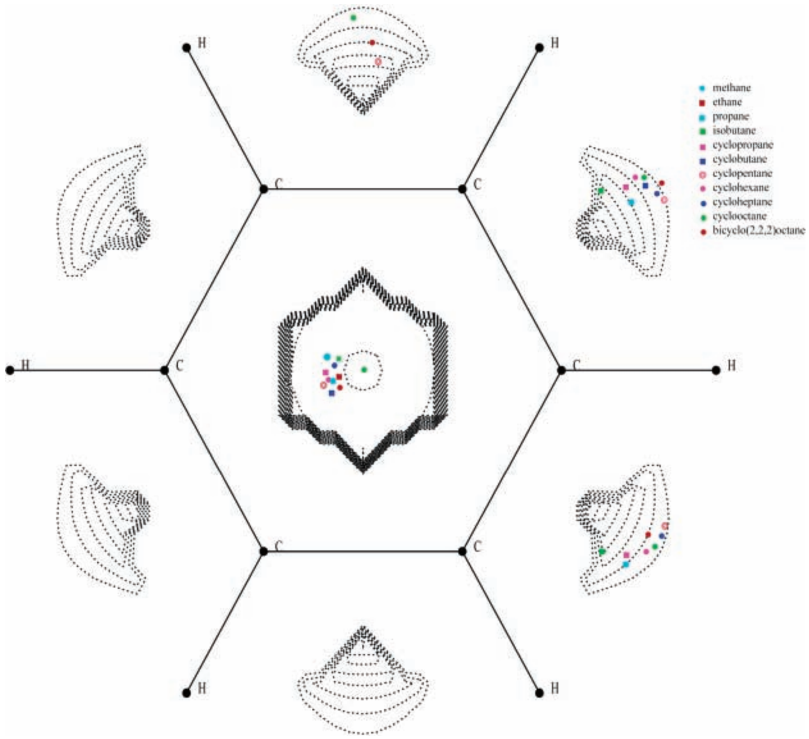


Figure 3. Negative electron potential map of benzene in the molecular plane. The data points represent the projection points of the C−H hydrogens of various hydrocarbon−benzene complexes.

TABLE 2: Calculated Structural Parameters (d_1, d_2, and α) and Interaction Energies[a] (Δ*E*, kJ mol^{-1}) of Cyclopropane−Benzene Complex (5) Evaluated at Various Levels of Geometry Optimization

level	d_1	d_2	α	Δ*E*
MP2/6-31G(d)	2.654	0.277	151.1	−9.0
MP2/aug(d,p)-6-311G(d,p)	2.437	0.189	152.8	−7.9
MP2/6-311+G(2df,p)	2.521	0.145	152.1	−8.8
MP2/cc-pVTZ	2.532	0.159	151.8	−8.7
CP-MP2/6-31G(d)[b]	3.026	0.535	149.5	−10.7

[a] CCSD(T)/aug(d,p)-6-311G(d,p) level including ZPE (MP2/6-31G(d)) and BSSE corrections. [b] Counterpoise-corrected gradient optimization.

TABLE 3: Calculated Interaction Energies[a] (Δ*E*, kJ mol^{-1}) and Bond Characteristics (Δd_1, Δν, and Δδ) of the Ring C−H Bonds of Various Hydrocarbon−Benzene Complexes

hydrocarbon	Δ*E*	Δd_1[b,c]	Δν[c,d]	Δδ[e]
methane (**1**)	−4.4	−0.0011	8.5	2.291
ethane (**2**)	−7.4	−0.0007	11.7	2.673
propane (**3**)	−9.6	−0.0003	10.4	2.534
isobutane (**4**)	−10.2	−0.0010	7.9	2.426
cyclopropane (**5**)	−9.7	−0.0000	4.2	2.749
cyclobutane (**6**)	−11.2	−0.0023	12.7	2.885
cyclopentane (**7**)	−12.7	−0.0021	14.7	2.785
cyclohexane (**8**)	−12.6	−0.0033	15.2	2.919
cycloheptane (**9**)	−13.3	−0.0026	20.3	2.878
cyclooctane (**10**)	14.2	−0.0043	30.9	2.736
bicyclo[2.2.2]octane (**11**)	14.7	−0.0015	15.7	2.985

[a] CCSD(T)/aug-CC-PVTZ//MP2/aug(d,p)-6-311G(d,p) level including BSSE and ZPE corrections. [b] Bond distance shortening (Δd_1, Å) upon complex formation. [c] MP2/aug-(d,p)-6-311G(d,p) level. [d] C−H stretching frequency shift (Δν, cm^{-1}) upon complex formation. [e] Change in ^{1}H NMR chemical shift (Δδ, ppm) upon complex formation, evaluated by the GIAO method at the MP2/6-31G(d) level.

This justifies our use of the basis set additivity approximation in calculating the CCSD(T) interaction energies.

To investigate the influence of the basis set on the geometries of the CH/π complexes, we examined the geometry of the cyclopropane−benzene complex (**5**) with several basis sets including aug(d,p)-6-311G(d,p), 6-311+G(2df,p), and cc-pVTZ at the MP2 level. In addition, optimization including BSSE effect, using the counterpoise-corrected gradient optimization technique,[34] was performed. As seen in Table 2, the d_2 and α values vary very little with the size of basis set. The predicted intermolecular distance d_1 is slightly smaller with a larger basis set. On the other hand, counterpoise-corrected optimization leads to a significantly longer d_1 value of 3.026 Å. Previous theoretical studies have shown that the intermolecular potential energy surface is rather flat for the CH/π complexes. Thus, it is not surprising that the calculated interaction energies of **5** employing different basis set are fairly close (Table 2). However, the stabilization energy obtained is significantly larger than (by 1.7 kJ mol^{-1}) that derived from the BSSE-uncorrected optimized geometry. Our result suggests that the MP2/aug(d,p)-6-311G-(d,p) level employed for geometry optimization is sufficiently reliable.

The calculated interaction energies of all the hydrocarbon−benzene complexes are summarized in Table 3. At the CCSD(T)/aug-cc-pVTZ+ZPE+BSSE level the computed binding energy for the methane−benzene complex (**1**), a prototypical system with a single CH/π interaction, is −4.5 kJ mol^{-1} (−5.9 kJ mol^{-1} without ZPE correction), in good agreement with the best theoretical estimate of −6.0 kJ mol^{-1} (without ZPE correction).[10b] As evidenced in Table 3, all the larger hydrocarbons form a stronger complex with benzene with an interaction energy 2−3 times larger than that of the methane complex. The largest binding energies (−15 kJ mol^{-1}) correspond to systems with four CH/π interaction contributions, namely, cyclooctane (**10**) and bicyclo[2.2.2]octane (**11**) complexes. This indicates that the additional CH/π contacts provide further stabilization to the intermolecular complexes. However, the magnitude of the interaction energy is not directly proportional to the number of CH/π interactions. This is perhaps not unexpected as the ring CH/π interaction has greater stabilization energy than those CH/π contacts outside the benzene ring. The

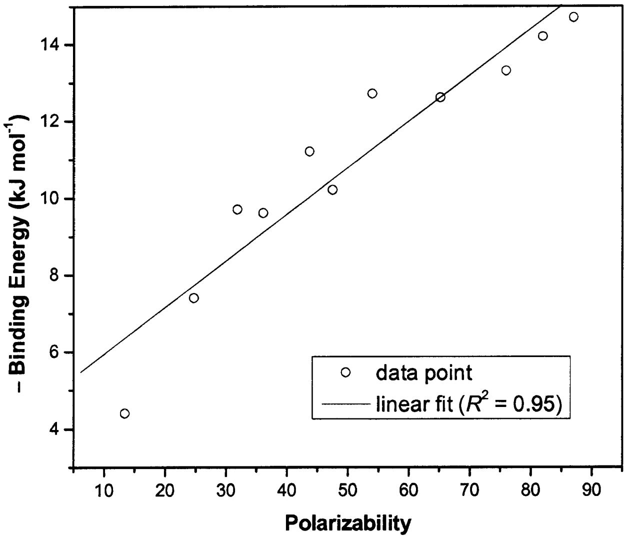


Figure 4. Plot of binding energy against polarizability.

CH/π interactions outside the ring are expected to be weaker due to the lower π density. Since isopropyl, long-chain alkyl groups, and cyclic rings are commonly found in organic and biological systems, the cooperative CH/π interactions should play an essential role in understanding many aspects of organic and biological chemistry. As seen in Table 3, there is a gradual increase in the binding energy with the size of the hydrocarbon. Thus, one may expect the stabilization energy to depend on the polarizability of the hydrocarbon. Indeed, a strong correlation ($R^2 = 0.95$) is found between the interaction energies and calculated polarizabilities [MP2/aug(d,p)-6-311G(d,p)] for the series of hydrocarbon−benzene complexes (Figure 4). As the magnitude of dispersion energy depends on polarizability, the correlation found here confirms that dispersion is the major source of stabilization of the CH/π complexes examined in this paper. The importance of polarizability is also reflected in the T-shaped cyclohexane−benzene complex (**12**), which has one CH/π interaction. Its interaction energy is twice that of the methane−benzene complex (**1**). Although the scope of this study is limited only to the saturated hydrocarbons, it is important to note also that the strength of the CH/π interaction depends on the carbon hybridization of the C−H bond.[10b,11a,13c,14] The unsaturated C−H bond forms a stronger CH/π bond with an aromatic system.

3. Spectroscopic Properties. Next, we examined the influence of the cooperative CH/π interactions on the structures, vibrational spectra, and proton NMR chemical shifts on the hydrocarbon monomers. Only the bond properties of the ring C−H hydrogen are considered. As evidenced in Table 3, a significant C−H bond shortening is observed in all cases with the largest (0.0043 Å) predicted for cyclooctane complex and the smallest (0.0003 Å) computed for cyclopropane complex. In general, bond contraction is more pronounced for the larger complexes. This bond shortening may be attributed to charge polarization (see next section) upon complex formation. In accord with the bond contraction, the C−H stretching vibration undergoes a significant blue shift upon complexation with benzene. For this reason, Hobza called the CH/π interaction a "blue-shift" hydrogen bond.[2,35] The blue shift in C−H stretching frequencies of CH/π systems has been studied by Hirota et al.[36] The calculated frequency shifts for complexes **1**−**11** range from 4 to 31 cm^{-1} (Table 3). Not surprisingly, the extent of the blue shift correlates well with the magnitude of the bond shortening ($R^2 = 0.94$). A rather large blue shift of 31 cm^{-1} is predicted for the cyclooctane complex (**10**), which represents a potential candidate for future experimental characterization of the CH/π interaction. It is worth noting that correction of anharmonicity and use of CP-corrected geometry are likely to yield better results for these weak complexes.[12,35] Nevertheless, our predicted frequency shifts may serve as a useful guide for future experimental characterization of these complexes in matrix experiments.

Apart from the fact that the new intermolecular modes appear in the vibrational spectra of the complex, formation of a CH/π interaction is also accompanied by a significant upfield shift of the NMR chemical shift of the reference hydrogen (δ_H) in the hydrocarbon. This shift is due to the effect of the diamagnetic field induced by the benzene ring and becomes prominent when the CH hydrogen is close to the center of benzene. This is essentially the so-called deshielding effect due to the ring current of benzene. Hence, ^{1}H NMR spectroscopy was employed in early experimental studies of intermolecular CH/π interaction.[4,37] Here, we examined the shielding tensor using the gauge-including atomic orbital (GIAO)[21] method at the MP2/6-31G-(d) level. $\Delta\delta$ represents the change of proton chemical shift (δ_H) on going from the free CH donor to the CH/π interacting system. As most of these ring protons have a similar distance from the center of the ring (i.e., similar d_1 and d_2 values, see Table 1), their deshielding effects are expected to be comparable. Indeed, the calculated upfield shifts ($\Delta\delta$) are fairly uniform (2.3−3.0) except for the isobutane complex (**4**) (Table 3). Our computed NMR shifts suggest that the NMR spectroscopic method is a potential tool to probe the presence of CH/π interactions in the hydrocarbon−benzene complexes.

4. Topological Properties and Charge Distributions. To gain a better understanding on the nature of the cooperative CH/π interactions of the hydrocarbon−benzene complexes (**1**−**11**), we examined the topological properties of the electron density using Bader's theory of atoms in molecules (AIM)[23] at the MP2/aug(d,p)-6-311G(d,p) level. Previously, a theoretical study by Novoa and Mota showed that the CH/π interaction can be characterized by a bond path and its associated bond critical point (bcp).[14] For each of the multiple CH/π contacts of the various complexes examined here there exists a bond path linking the hydrogen atom with one or more carbon atoms of benzene. The calculated topological properties at the bond critical points, namely, electron density (ρ), Laplacian of electron density ($\nabla_2\rho$), and ellipicity (ϵ), are summarized in Table 1. The positive sign of $\nabla_2\rho$ indicates the closed-shell nature of interaction, e.g., hydrogen bond.[38] For all the CH/π contacts, the small ρ and positive $\nabla_2\rho$ values are similar to the characteristic topological properties of a weak hydrogen bond, such as CH···O and OH···π interactions.[14] Significant bond ellipticity (ϵ) is calculated for the ring C−H bond (Table 1). This readily confirms the stronger π interaction in the ring C−H bond compared to the other CH/π interactions outside the benzene ring. The stronger CH/π interaction of the ring C−H group for each complex is also reflected in the larger ρ and $\nabla_2\rho$ values compared to those CH/π bonds outside the ring.

Formation of a CH/π bond normally results in shifts of electron density. Although these shifts are relatively small in magnitude, they are useful in providing further insight into the nature of such bonds. Here, we examined the charge distributions of complexes **1**−**11** using NBO analysis based on the MP2/aug(d,p)-6-311G(d,p) wave function. NBO atomic charges of small molecules have recently been demonstrated to agree well with experimental values obtained from X-ray diffraction data.[39] The calculated atomic charges of the carbon and hydrogen of

TABLE 4: Calculated Atomic Charges (q),[a] Charge Transfer (CT),[a] and Dipole Moments (μ, D) of Various Hydrocarbon−Benzene Complexes[b]

hydrocarbon	q(H)[c]	Δq(H)[c,d]	q(C)[c]	Δq(C)[c,d]	CT[e]	μ[b]
methane (**1**)	0.1950	0.0038	−0.7648	−0.0008	−0.0039	0.27
ethane (**2**)	0.1867	0.0060	−0.5432	−0.0011	−0.0044	0.33
propane (**3**)	0.1877	0.0075	−0.5523	−0.0047	−0.0041	0.38
isobutane (**4**)	0.1878	0.0072	−0.5556	−0.0039	−0.0075	0.40
cyclopropane (**5**)	0.1986	0.0058	−0.3868	−0.0011	−0.0060	0.43
cyclobutane (**6**)	0.1852	0.0070	−0.3639	−0.0031	−0.0081	0.49
cyclopentane (**7**)	0.1838	0.0079	−0.3733	−0.0051	−0.0072	0.49
cyclohexane (**8**)	0.1822	0.0070	−0.3712	−0.0074	−0.0106	0.59
cycloheptane (**9**)	0.1822	0.0081	−0.3666	−0.0086	−0.0099	0.57
cyclooctane (**10**)	0.1871	0.0092	−0.3879	−0.0238	-0.0126	0.61
bicyclo[2.2.2]octane (**11**)	0.1916	0.0038	−0.3823	−0.0082	−0.0110	0.59
dimethylcyclohexane (**12**)	0.1878	0.0099	−0.3876	−0.0080	−0.0105	0.44

[a] On the basis of NBO analysis. [b] MP2/aug(d,p)-6-311G(d,p) level. [c] The "ring" C−H bond of the complex. [d] Change in atomic charge on going from the monomer to the complex. [e] Charge transfer from benzene to hydrocarbon in the complex.

the ring C−H bond and the magnitude of charge transfer from benzene to the hydrocarbon monomer are given in Table 4. In all cases, there is a small amount of charge transfer from benzene to the hydrocarbon in the intermolecular CH/π complexes. This confirms the nature of the soft acid (hydrocarbon)−soft base (benzene) interaction. Interestingly, the trend of charge transfer follows that of the stabilization energy. Both the carbon and hydrogen atoms of the ring C−H bond display strong charges (Table 4). Unexpectedly, the ring C−H hydrogen becomes more positive and the adjacent carbon more negative (Table 4). In other words, there is a larger degree of charge separation of the C−H bond upon complexation with benzene, which results in an increase in the Coulomb attraction in the C−H bond. As evidenced in Table 4, the degree of charge separation parallels to magnitude of bond shortening (Table 3). Perhaps this increase in charge polarization, i.e., charge separation, of the C−H bond is one of the main reasons for the C−H bond shortening in the CH/π complexes. Although all complexes exhibit a small amount of charge transfer, there is an obvious trend in the series: the degree of charge transfer increases with the size of the hydrocarbon (Table 3). In addition, we note that the calculated binding energy correlates well with the magnitude of charge transfer. Although the dispersion interaction is the main source of stabilization energy for the CH/π complexes examined here, the charge density analysis suggests that the electrostatic and charge-transfer interactions also contribute to the stabilization energies.

As mentioned in the previous section, the geometries of the various hydrocarbon−benzene complexes can be explained by the electrostatic interaction between the interacting molecules. Our argument is further supported by point charge calculations. In these model calculations the carbon and hydrogen atoms of the benzene molecule are replaced by point charges, which were obtained from NBO analysis. Full geometry optimizations of the hydrocarbons were then carried out in the presence of the set of point charges. The optimizations readily reproduce the bond contraction of C−H bonds.

Conclusions

In summary, we investigated the cooperative behavior of CH/π interactions in several hydrocarbon−benzene complexes using high-level ab initio calculations. On the basis of the computed interaction energies, structural features, binding properties, and bond critical point analysis it is clear that the multiple CH/π interactions play a complementary role in stabilizing the intermolecular complexes. The CH/π interaction involving the "ring" C−H group is the dominant source of stabilization, while the CH/π interactions outside the benzene ring play a lesser but significant role. Dispersion is confirmed to be the major source of stabilization. The calculated interaction energy correlates with the polarizability of the hydrocarbon. As the size of the hydrocarbon increases, the electrostatic and charge-transfer effects play a more prominent role in governing the structures and binding properties of the complexes. To assist further experimental characterization of the CH/π interaction, spectroscopically observable features relative to the unperturbed hydrocarbons are predicted. Given the nonnegligible interaction energy (10−15 kJ mol^{-1}) of the multiple CH/π interactions and the fact that cycloalkyl, long-chain alkyl, and aromatic functional groups are almost ubiquitous in organic compounds and biomolecules, we believe that the CH/π interaction is even more important than one may have anticipated in our understanding of the conformational behavior of organic molecules, molecular recognition, crystal engineering, protein structures, and hydrophobic effect. Since benzene is a common solvent for organic molecules, one might also expect the CH/π interaction to be an important source of solvent−solute interaction. For instance, we have shown recently a reverse of the *gauche/trans* equilibrium of 2,2′-dimethyl-2,2′-bi-1,3-dithiolanyl on going from carbon tetrachloride to benzene, which could be explained in terms of the specific benzene−solute interaction via cooperative CH/π interactions.[40] Last, we note that the cooperative CH/π interactions should also be prevalent in nonpolar and aprotic polar media based on SCRF[41] solvent effect calculations (mPW1PW91/6-31G(d) level) of several representative systems. The geometries and binding energies of the hydrocarbon−benzene complexes are relatively unperturbed on going from the gas phase to a dielectric medium.

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Supporting Information Available: X-ray structure, computed binding energies of cyclopropane−benzene complex at various levels of theory, Cartesian coordinates and absolute energies of all calculated compounds, and complete references for refs 26−28. This material is available free of charge via the Internet at http://pubs.acs.org.

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