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THEORETICAL STUDIES OF THE SUPRAMOLECULAR SYNTHON BENZENE · · · HEXAFLUOROBENZENE

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The benzene · · · hexafluorobenzene stacking interaction was evaluated at several levels of theory. At the MP2/6–31G level, it is estimated that the interaction is stabilizing by approximately 3.7 kcal mol^{-1}. Lower levels of theory perform poorly on this system. This is a fairly strong non-covalent interaction, suggesting this motif may be a valuable supramolecular synthon. © 1997 by John Wiley & Sons, Ltd.**

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INTRODUCTION

Non-covalent interactions play a critical role across a broad range of disciplines, from materials chemistry to molecular biology. In the materials field, one of the most challenging areas is 'crystal engineering'–the rational design and manipulation of solid-state structures. In an effort to develop a unifying design principle for such efforts, Desiraju[1] coined the phrase 'supramolecular synthon' to describe a set of supramolecular interactions that form and modulate recognition patterns in the solid state.

It has been known for some time that benzene and hexafluorobenzene undergo a favorable interaction (Figure 1), the most spectacular manifestation being the higher melting point of the 1:1 co-crystal of the two compared with either pure compound.[2] Recently, we have demonstrated the potential generality of this novel supramolecular synthon.[3] Face-to-face stacking has been seen in several phenyl- · · · pentafluorophenyl systems, suggesting this is a reliable force for designing co-crystals and crystals of pure substances.

The benzene · · ·hexafluorobenzene interaction is also of interest with regard to the general role of aromatic rings in supramolecular chemistry. Williams' detailed analysis of the benzene · · ·hexafluorobenzene crystal structure emphasizes the important role of the large, permanent quadrupole moments of the two molecules, which are comparable in magnitude but of opposite sign.[2] The stacking of benzene and hexafluorobenzene is seen to be consistent with expectations based on maximizing the favorable quadrupole–quadrupole interaction. The importance of the quadrupole moment for understanding intermolecular interactions of aromatics in general has been cogently discussed by Luhmer *et al*.[4] The quadrupole has been invoked in rationalizing the T-shaped geometry of the benzene · · ·benzene complex (and hexafluorobenzene · · ·hexafluorobenzene),[5–8] and electrostatic interactions involving the quadrupole have been shown to be significant contributors to the cation–π interaction,[9–11] another important non-covalent interaction involving aromatics.

In the present work we evaluated the applicability of modern theoretical methods in quantifying the benzene- · · · hexafluorobenzene interaction. Our goals were twofold. First, we hoped to provide a quantitative estimate of the energetic stabilization associated with the basic benzene- · · · hexafluorobenzene interaction. Second, anticipating efforts to model such interactions in crystals or other supramolecular systems, we hoped to determine a minimal level of theory that can be reliably applied to the benzene · · ·hexafluorobenzene interaction. Our results suggest that only fairly high levels of theory will be applicable; making the benzene · · ·hexafluorobenzene interaction a challenge for future modeling efforts.

RESULTS AND DISCUSSION

We began with Hartree–Fock (HF) calculations using the 6–31G** basis set. Early calculations showed that the eclipsed forms of benzene · · ·hexafluorobenzene differed from the staggered by $<0{\cdot}1$ kcal mol^{-1} (1 kcal = 4·184 kJ). Similarly, offset geometries are not significantly different in energy than the perfectly stacked geometry. Full geometry optimization of the eclipsed complex at HF/6–31G** gave

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an interplane separation, defined as the distance between the centroids of the two rings (r) of 4·08 Å and a binding energy (ΔE) of $-1{\cdot}52$ kcal mol^{-1}. We were surprised by the small magnitude of the binding energy, but the value of r was much more distressing. Our own recent results[3] and a survey of existing crystal structures suggested that more typically r is in the range 3·4–3·6 Å. In the parent benzene · · ·hexafluorobenzene co-crystal,[2] the interplane separation is 3·4 Å. In the crystal, the rings are offset, so the centroid–centroid distance, r, is 3·77 Å^2; only for the perfectly stacked (C_{6V}) complexes of the sort calculated here is r equivalent to the interplane separation.

While the solid state is different from the gas-phase environment of the calculations, the discrepancy in r between theory and experiment seemed too large to be attributed to a phase change. HF theory is well known to have considerable weaknesses in evaluating non-covalent molecular complexes, and the benzene · · ·hexafluorobenzene system might be expected to be an especially pathological case. The large surface contact involving relatively polarizable C and H atoms should make dispersion forces very important in this system, and HF theory is inadequate for dispersion interactions.

We therefore turned to the second-order Møller–Plesset (MP2) level of theory in an attempt to include such dispersion interactions. At the HF geometry (r = 4·08 Å), the MP2/6–31G** binding energy was $-4{\cdot}00$ kcal mol^{-1}, an increase by more than a factor of 2 over the HF value. In addition, it was clear that the MP2 level would lead to a shorter optimal value of r.

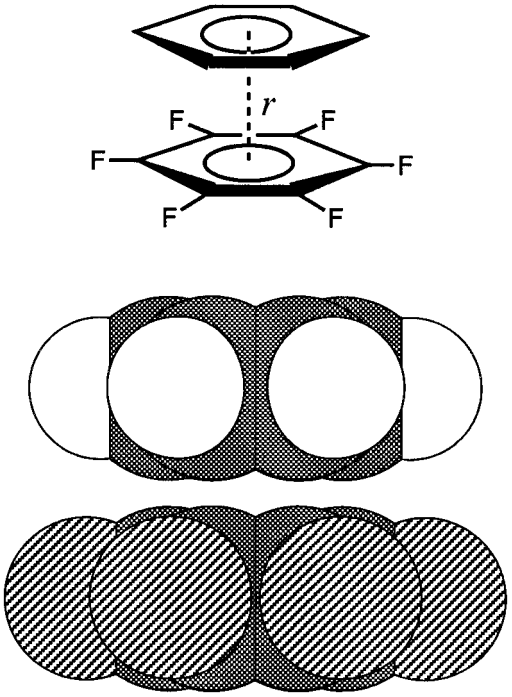

Figure 1. Top: the benzene · · ·hexafluorobenzene interaction, showing the defintiion of r. Bottom: space-filling model of the complex at the MP2 geometry (r = 3.35 Å).

Full geometry optimization at the MP2/6–31G** level indeed gave a much shorter value of 3·37 Å for r (Figure 1), in excellent agreement with the interplane separation seen in the crystal. The binding energy was $-6{\cdot}89$ kcol mol^{-1}. The staggered complex gave $\Delta E = -6{\cdot}72$ kcal mol^{-1} (r = 3.35 Å), thus confirming our initial findings. At a slipped geometry similar to that found in the crystal, $\Delta E = -6{\cdot}78$ kcal mol^{-1}, indicating the relative flatness of the surface in this region. At the MP2 eclipsed geometry, HF/6–31G** theory predicts the complex to be repulsive by $+3{\cdot}09$ kcal mol^{-1}. Thus, the MP2 results for benzene- · · · hexafluorobenzene are substantially different than the HF results, in contrast to the results from a comparable study of a simple cation–π interaction.[12]

Given the evident importance of correlation effects in the benzene · · ·hexafluorobenzene interaction, it seemed possible that density functional theory (DFT)[13] would be valuable here. We therefore evaluated the complex at the B3LYP/6–31G** level.[14] As a first test, we optimized the Na^+ · · · benzene cation–π complex. This level of DFT gave $\Delta E = -28{\cdot}4$ kcal mol^{-1} and a value of 2·38 Å for r, in acceptable agreement with experiment and other calculations.[10] For example, MP2/6–31G** gives r = 2·38 Å and $\Delta E = -29{\cdot}93$ kcal mol^{-1}.

However, for the benzene · · ·hexafluorobenzene complex, B3LYP/6–31G** gave results similar to HF theory: r = 3·96 Å and a ΔE of only -1.05 kcal mol^{-1}. The DFT methods have not yet been as extensively evaluated on a wide variety of structures as the more conventional methods such as MP2, and there is some indication that the methodology is not well suited to weak, non-covalent interactions.[14, 15] At present, we conclude that the MP2 results are more reliable, and we will focus on them here.

A serious concern for calculations of this type is basis set superposition error (BSSE). Studies of molecular complexes at this level overestimate the stabilities of the complexes, fundamentally because the complex has a larger basis set than the reference monomers, creating a bias in favor of the complex. The binding energies given above have not been corrected for BSSE. We have addressed this issue using the counterpoise method (CP) of Boys and Bernardi.[16] This method is believed to correct accurately for BSSE at the HF level. It is probably also reliable at higher, correlated levels of theory such as MP2, although there is still disagreement as to whether overcorrection occurs in these cases.[17]

At the HF geometry, the HF CP correction amounts to $+0{\cdot}98$ kcal mol^{-1}, further weakening the HF binding energy to $-0{\cdot}54$ kcal mol^{-1}. (At the more compact MP2 geometry, the HF CP correction amounts $+2{\cdot}22$ kcal mol^{-1}. If we apply this correction to the MP2 value for ΔE, the corrected binding energy is $-4{\cdot}67$ kcal mol^{-1}). We have also performed a CP calculation using the MP2 method at

the MP2 geometry. This gives a larger correction of $+4{\cdot}21$ kcal mol^{-1}, thus reducing the binding energy to $-2{\cdot}69$ kcal mol^{-1}.

Such a large value for the BSSE, comparable in magnitude to the total binding energy, raises a concern. One would expect the BSSE (and hence the CP correction) to increase with decreasing *r*. As such, it seemed possible that adding a CP correction to the MP2 results could lead to a larger optimum value of *r*. Such an effect was seen in an *ab initio* study of the benzene dimer.[6] To study this effect, we optimized *r* using CP-corrected MP2 energies (CP-MP2/6–31G**//CP-MP2/6–31G**, with the understanding that the CP calculations were involved only in the optimization of *r*, with all other geometrical parameters fixed at the MP2/6–31G** monomer values). This approach indeed led to a longer value of 3·6 Å for *r*, still within the range typically seen for this type of interaction in the solid state. The new value of ΔE was $-3{\cdot}7$ kcal mol^{-1}, a significant increase over that for the MP2 geometry. We consider this our best estimate of the geometry and binding energy for the benzene · · ·hexafluorobenzene complex.

This is a relatively large energy for the interaction of two neutral, 'non-polar' molecules. For comparison, the T-shaped benzene dimer interaction, which also involves quadrupoles, is generally considered to be worth -2 kcal mol^{-1} or less.[5–8] A prototypical cation–π interaction for an organic cation with benzene, the benzene · · ·tetramethylammonium interaction, is worth *ca* -9 kcal mol^{-1}, a larger value, but the interaction involves one ionic species.[18] The value for benzene · · ·hexafluorobenzene reported here is compatible with other attempts to quantify the interaction. For example, Williams' detailed analysis of the crystal structure of the complex led to an estimate of *ca* $-3{\cdot}5$ kcal mol^{-1} for the electrostatic component of the interaction, which is supplemented by a dispersion interaction that is of the same order of magnitude.[2]

It is perhaps surprising that at the HF level, the anticipated stabilizing electrostatic interactions between the quadrupoles are not apparent, given the success of this level of theory in studies of other interactions where comparable electrostatic terms are important.[10] To pursue this point further, we evaluated a complex that is expected to have a much smaller electrostatic interaction. In 1,3,5-trifluorobenzene the quadrupole moment is near zero.[2,10] The dimer of this structure should have comparable dispersion interactions to the benzene · · ·hexafluorobenzene complex–in fact the comparison between the two complexes is an isodesmic reaction–but little or no electrostatic interaction. We find that, at the HF/6–31G** level, the benzene · · ·hexafluorobenzene complex is more stable than the 1,3,5-trifluorobenzene dimer (D_{3d} geometry) by 1·9 kcal mol^{-1} when $r = 3{\cdot}35$ Å. The optimized 1,3,5-trifluorobenzene dimer has $r = 4{\cdot}22$ Å and $\Delta E = -0{\cdot}39$ kcal mol^{-1}, again much less attractive than the benzene · · ·hexafluorobenzene complex at the same level of theory. We conclude from this result that there is a significant electrostatic interaction in the benzene · · ·hexafluorobenzene complex, but in the HF calculations it is overwhelmed by the known tendency of this level of theory to be inadequate for dispersion interactions. Consistent with Williams' analysis,[2] the results suggest that terms other than electrostatics, such as dispersion and charge transfer, are also important in the benzene · · ·hexafluorobenzene complex.

Our results indicate that only a fairly high level of *ab initio* theory can adequately treat the benzene · · ·hexafluorobenzene interaction. It would thus be especially useful if semi-empirical methods performed better, but, perhaps not surprisingly, Hartree–Fock theory at this level is also inadequate. The AM1 method gives $r = 4{\cdot}67$ Å and an interaction energy of $-{\cdot}47$ kcal mol^{-1}; PM3 gives $r = 4{\cdot}52$ Å and $\Delta E = -0{\cdot}54$ kcal mol^{-1}.

CONCLUSIONS

The benzene · · ·hexafluorobenzene interaction holds considerable promise as a general supramolecular synthon for crystal engineering and related efforts.[3] We have attempted to obtain a quantitative measure of the stabilization involved in such an interaction. Our best estimate (CP-MP2/6–31G**//CP-MP2/6–31G**) produces a stabilization energy of *ca* 3.7 kcal mol^{-1} and an interplane separation of 3·6 Å. Only a fairly high level of theory, one that includes some estimate of correlation energy, gives an acceptable treatment. Clearly, Hartree–Fock *ab initio* and semi-empirical methods are not reliable for the benzene · · ·hexafluorobenzene interaction. Given the complexity of the calculations performed here, and the possible ambiguities introduced by the counterpoise methodology, we would hope that these results will prompt further studies of this interesting system at still higher levels of theory. The 3.7 kcal mol^{-1} value for ΔE represents a fairly large interaction energy, and it suggests that the benzene · · ·hexafluorobenzene interaction might provide a powerful and general supramolecular synthon.

METHODS

All calculations were performed using either Gaussian 92/DFT,[19] Gaussian 94[20] or Spartan version 4.1.1.[21] MP2 calculations included all electrons (i.e. no 'frozen' core approximation).

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