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Molecular Pair Analysis: C–H···F Interactions in the Crystal Structure of Fluorobenzene? And Related Matters

Jack. D. Dunitz* **and W. Bernd Schweizer***[a]

Abstract: The crystal structure of fluorobenzene is compared with isomorphous crystal structures of molecules of roughly similar shape. The lowest-energy fluorobenzene dimers are identified by theoretical calculations. Molecular pair analysis of the crystal structure of fluorobenzene and of an isomorphous virtual low-energy polymorph of benzene suggests that the important intermolecular interactions in the two structures are closely similar. In particular, the intermolecular C–H···F interactions in the fluorobenzene crystal have approximately the same structure-directing ability and influence on the intermolecular energy as the corresponding C–H···H interactions in benzene. Molecular pair analysis of the isomorphous crystal structures of benzonitrile, alloxan, and cyclopentene-1,2,3-trione indicates that essentially the same crystal structure can be adopted with quite different patterns of pair energies and atom–atom interactions. The question as to whether the packing radius of organic fluorine is larger or smaller than that of hydrogen, is addressed, but not answered.

Keywords: ab initio calculations · fluorobenzene · solid-state structures · through-space interactions

Introduction

Interest in the question of how good organic fluorine is as a hydrogen-bond acceptor seems to have no end.[1,2] One hesitates before adding yet another paper on the subject, especially when we have no new experimental data, merely some reinterpretations of data already published by other authors. Our present contribution consists mainly of new quantum-mechanical calculations at several theoretical levels on various fluorobenzene dimer structures, together with observations about the close relationship between the crystal structures of fluorobenzene and other molecules with similar shapes, including benzene. Most of the current wisdom about the hydrogen-bond acceptor properties of organic fluorine rests on the recognition of X–H···F contacts in crystal structures of fluorinated organic molecules and the interpretation of such contacts as significant contributors to the cohesive energy of the crystal, sometimes backed by computational results. From such studies it has become clear that organic fluorine acts only rarely as an acceptor with strong O–H and N–H hydrogen-bond donors;[2a] much of the discussion has therefore involved C–H···F interactions. These are obviously very common, indeed they are almost unavoidable wherever a fluorinated organic molecule comes into contact with other molecules, whether in crystals, host–guest complexes, or as fluorinated substrates in enzymatic complexes, and are recognized to be "weak". Nevertheless, they are often regarded as playing an important role in controlling the structure and energetics of such systems. In the present work, we show that the C–H···F interaction in crystalline fluorobenzene has about the same structure-directing ability and influence on the intermolecular energy as a typical C–H···H interaction in crystalline benzene. Finally, although the fluorine atom is generally considered to be "larger" than hydrogen (e.g., it is assigned a larger van der Waals radius), we raise the possibility that this picture may not always be quite correct and may require modification.

Results and Discussion

Molecular pair energies: It seemed to us that something useful might be learned from a thorough analysis of molecular pair energies of a suitable simple aromatic fluorocarbon, particularly a fluorinated benzene, since the crystal structures of many fluorinated benzenes are available[1d] for comparison with computational results. Our earlier calcula-

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[a] Prof. Dr. J. D. Dunitz, Dr. W. B. Schweizer
Organic Chemistry Laboratory
ETH-Zurich, 8093 Zurich (Switzerland)
Fax: (+41) 446-321-109
E-mail: dunitz@org.chem.ethz.ch
schweizer@org.chem.ethz.ch

tions[2b,3] for hexane and perfluorohexane homodimers using the Pixel method[4] led to low-energy pairs that were closely similar to the arrangements of neighboring pairs in the respective crystal structures.[5,6] For the heterodimer of hexane and perfluorohexane, no co-crystal structure is available for comparison (and, judging from the behavior of the corresponding liquid mixtures,[7] it is unlikely that a co-crystal will ever be obtained). The calculated binding energy of the best heterodimer is less than the binding energy of the hexane homodimer (Table 1). This behavior differs from that in the aromatic series where the benzene–perfluorobenzene parallel-stacked heterodimer is calculated to be appreciably more stable than either of the corresponding homodimers, in accord with the existence of a 1:1 co-crystal with a melting point higher than that of either component.[8] According to the Pixel energy partitioning scheme, dispersion provides a nearly equal major contribution to the stability of all three aromatic dimers; the extra stability of the heterodimer stems from its coulombic energy, which may not come entirely as a surprise. It is perhaps more surprising that in the "nonpolar" aliphatic series, coulombic interactions make a significant contribution to the greater stability of the hexane homodimer although they yield hardly anything to the stabilization of the perfluorohexane homodimer or the heterodimer, the only one for which any C–H···F interactions are present.[9] Thus, for these systems, molecular pair analysis has led to considerable insight into the actual behavior of the compounds.

Table 1. Stabilization energies $E\,[\mathrm{kJ\,mol^{-1}}]$ of homodimers and heterodimers as estimated by the Pixel energy-partitioning method for aromatic and aliphatic molecules. For the former, the aromatic rings are stacked parallel at a fixed distance of 3.4 Å; for the latter, the molecular chains are parallel at optimal distances (in parentheses). For details, see reference [3].

Dimer	E_{coul}	E_{pol}	E_{disp}	E_{rep}	E
benzene	−0.8	−4.0	−32.3	23.5	−13.6
perfluorobenzene	−0.8	−4.2	−36.0	19.4	−19.9
mixed	−12.7	−4.7	−33.8	21.6	−29.7
hexane (3.8 Å)	−8.5	−3.8	−37.4	27.8	−22.0
perfluorohexane (5.1 Å)	−0.8	−0.1	−12.2	3.9	−9.1
mixed (4.9 Å)	−1.0	−0.4	−11.9	4.7	−8.5

For benzene itself, the calculation of pairing energies of parallel-displaced (PD) and perpendicular (T-shaped) gas-phase dimers has been a popular topic in computational chemistry for many years. The reliability of the results has presumably improved with time up to the present, although still subject to uncertainties of a few $\mathrm{kJ\,mol^{-1}}$, depending on various factors, such as choice of basis set orbitals, treatment of electron correlation, and allowance for the basis-set superposition error (BSSE). The main problems in calculating the cohesive energy of supramolecular aggregates by quantum-mechanical methods are the underestimation of the binding energy at the Hartree–Fock level (no allowance for electron correlation) and its overestimation at the level of second-order perturbation theory (MP2). This overestimation is due to the fact that the basis set for the molecular aggregate is larger than the basis set of the separate constituent molecule. An approximate method of correcting for the BSSE is known as counterpoise correction. For benzene, where dispersion energy is important, the correction reduces the calculated energy of the parallel-displaced (PD) dimer from 20.7 to 11.6 $\mathrm{kJ\,mol^{-1}}$ and that of the T-shaped dimer from 15.2 to 11.5 $\mathrm{kJ\,mol^{-1}}$.[10] From these calculations it also appears that the energy hypersurface is relatively flat with no pronounced preference for either parallel or perpendicular structures. Analogous calculations do not seem to have been published for fluorobenzenes. In the absence of theoretical calculations, intermolecular close contacts that occur in crystal structures of these compounds have served as the basis for qualitative arguments about C–H···F interactions.[1d] Do C–H···F interactions contribute significantly to the lattice energy? Are they structure-directing? Or even controlling? These are the questions we address here.

Crystal structure of fluorobenzene: Thalladi et al.[1d] determined the crystal structure analysis of seven of the twelve possible fluorobenzenes (mono-, 1,2-di and 1,4-di, 1,3,5-tri, 1,2,3,4- [two polymorphs] and 1,2,4,5-tetra, and pentafluorobenzene). The stated objective of the work was to rigorously evaluate the role of C–H···F interactions in the crystal structures of these compounds, which are obviously of special relevance because they contain only C, H, and F atoms. Fluorobenzene itself crystallizes in the tetragonal space group $P4_32_12$ (or equivalently $P4_12_12$) with cell dimensions (at 123 K, m.p. 231 K) $a = b = 5.799(2)$ Å, $c = 14.503(7)$ Å. With $Z = 4$, the molecules are constrained to lie on the twofold rotation axes of the space group. The crystal structure is illustrated in Figure 1. Thalladi et al. noted that the symmetry-related *ortho*-H atoms are involved in C–H···F interactions (2.47 Å), the *meta*-H atoms in so-called C–H···π interactions. In addition, they observed that the fluorobenzene crystal structure shows close similarities with the crystal structures of pyridinium fluoride (PyHF),[11] pyridine-1-oxide (PyNO),[12] and benzonitrile (PhCN),[13] and concluded that "the nature and character of the structure-determining intermolecular interactions in these four structures *are iden-*

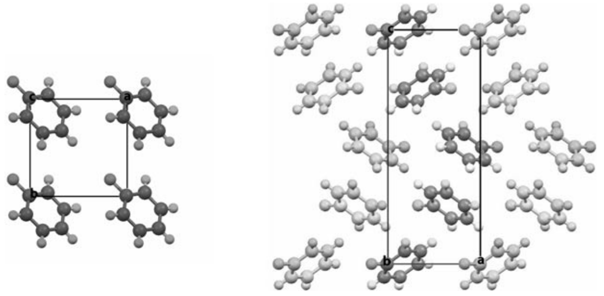

Figure 1. Crystal structure of fluorobenzene, showing helical chains of molecules along the c axis (right) and the square array of molecules in the plane at $z = 0$.[1d]

tical" (emphasis in original text). Thus, since the N−H···F$^-$ interaction in PyHF was taken to be a significant hydrogen bond, and since the C−H···O and C−H···N hydrogen bonds in PyNO and PhCN are regarded as examples of well-known types of interaction that control and direct crystal packing, Thalladi et al. concluded "that the C−H···F interaction, albeit probably weaker, in **1** (fluorobenzene) is likewise important in the adoption of the observed crystal structure."[14] It is interesting that the fluorobenzene crystal is also isostructural with one of the low-energy virtual crystal structures of benzene itself. This tetragonal structure appears as N5 in a listing of hypothetical structures for low-pressure benzene, with a calculated lattice energy only 1.1 kJ mol^{-1} above that of the known stable polymorph, and as H2 in the listing of hypothetical structures at 30 kbar pressure, with a calculated enthalpy only 0.4 kJ mol^{-1} above that of the most stable high-pressure polymorph.[15] The calculated powder pattern of H2 was described as having a reasonable resemblance to that observed experimentally at 31 kbar. Thus the fluorobenzene crystal structure is closely similar not only to the crystal structures of the polar molecules mentioned by Thalladi et al. listed in Table 2, but also to a low-energy virtual crystal structure of nonpolar benzene that may occur under high-pressure conditions. To this listing of similar crystal structures might be appended those of two other cyclic molecules with quite different types of functional group and intermolecular interaction, namely alloxan[16] and cyclopentene-1,2,3-trione,[17] with their strongly polar carbonyl groups. As seen from Table 2, they have the same space group and similar unit-cell dimensions as fluorobenzene, in spite of the obvious differences in molecular structure.

Table 2. Unit cell dimensions of fluorobenzene and some isostructural crystals with space group $P4_32_12$ (or equivalently $P4_12_12$).

	$a = b$[Å]	c[Å]
fluorobenzene[1d]	5.799	14.503
pyridinium fluoride[11]	6.059	14.280
pyridine-*N*-oxide[12]	5.816	13.747
benzonitrile[13]	6.361	14.240
alloxan[16]	5.841	13.853
cyclopentene-1,2,3-trione[17]	5.701	14.113
benzene (virtual structure N5)[15]	5.54	15.32
benzene (virtual structure H2)[15]	5.29	14.29

Fluorobenzene dimers: The interaction energy of a pair of fluorobenzene molecules is a function of structure in six-dimensional hyperspace, even when the molecules are held rigid. As the molecules interact, dimer formation can be expected to change the nuclear positions and electron density distributions of the separate molecules to a slight extent. For a full energy minimization of the molecular pair, consisting of 24 atomic nuclei, allowing all geometrical variables to change, there are thus $(3\times24)-6 = 66$ variables, too many for the full space to be explored conveniently by highest level quantum-mechanical calculations, and far too many to depict. It cannot be stressed too strongly that the intermolecular binding energies of fluorobenzene dimers are minuscule in relation to the total binding energy of the systems involved and are hence acutely sensitive to the level of theory employed in the quantum-mechanical calculation, besides their dependence on details of the structural model.

We have explored several regions of the energy hypersurface by imposing suitable constraints on the mutual molecular orientation—in-plane orientation, parallel-stack orientation, perpendicular (T-shaped) orientation—and have searched for local energy minima under these constraints with allowance for the molecular structures to adjust. Figure 2 shows a selection of the locally constrained minimum-energy fluorobenzene dimer structures **A**–**G**. Table 3

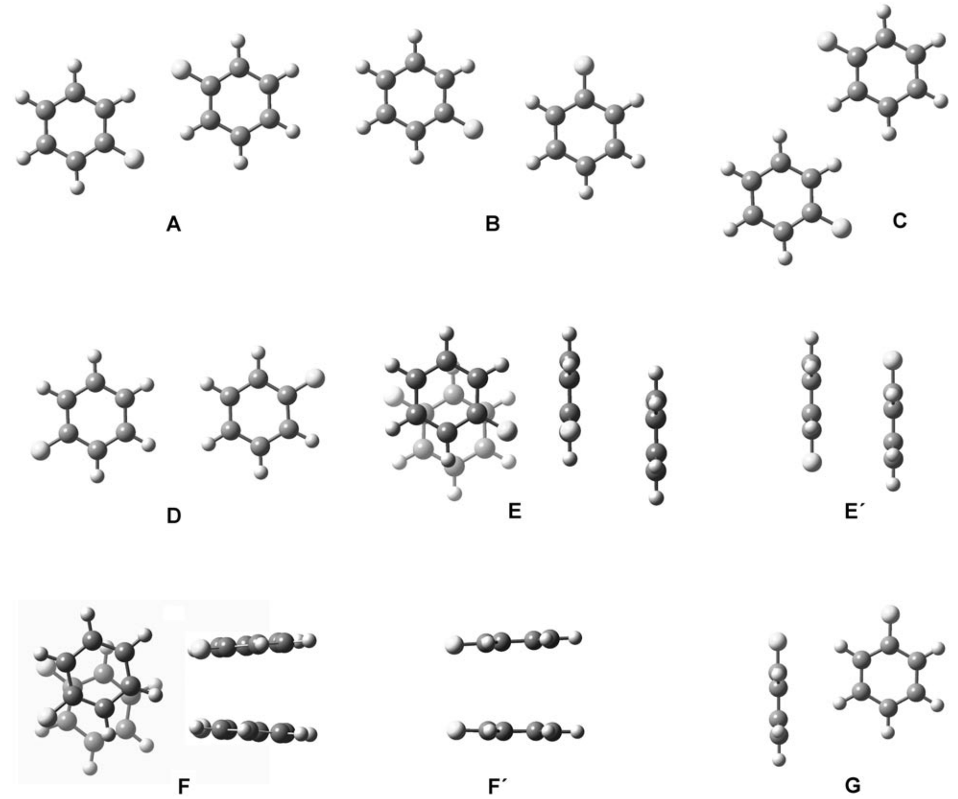

Figure 2. Selected local minimum-energy fluorobenzene dimers **A**, **B**, **C**, **D**, **E**, **F**, **G**.

Table 3. Calculated ab initio energies E_{QM} [kJ mol^{-1}] at the MP2/6-31++g(d,p) level with counterpoise correction for basis-set superposition error (BSSE) for the fluorobenzene pairs **A**–**G** (Figure 2). For comparison, E_{PIX} energies, calculated by the Pixel method, based on the same charge density distribution as the monomers, are also shown with corresponding energy partitioning.

Molecular pair	$D^{[a]}$ [Å]	E_{QM}	E_{PIX}	E_{COUL}	E_{POL}	E_{DISP}	E_{REP}
A	6.8	−8.3	−8.9	−8.9	−1.5	−4.9	6.4
B	7.14	−5.3	−5.9	−3.8	−0.8	−3.8	2.6
C	6.77	−2.0	−3.8	0.9	−0.7	−5.9	1.9
D	6.82	−0.7	−1.6	2.0	−0.5	−4.3	1.2
E	3.54	−15.2	−12.5	−10.7	−4.6	−26.8	29.6
E′	3.72	−12.6	−10.2	−5.5	−2.8	−23.2	21.3
F	3.76	−15.1	−9.4	−9.0	−3.7	−4.8	8.2
F′	3.89	−8.0	−7.8	1.4	−1.2	−16.8	8.8
G	5.11	−10.5	−11.6	−5.6	−2.2	−14.9	11.2

[a] Distance between ring centers.

gives the corresponding calculated interaction energies E_{QM} as obtained by ab initio calculations at the MP2/6-31++g(d,p) level[18] with counterpoise correction for basis-set superposition error (BSSE).[19] In most of these searches, we started from a symmetrical pair structure and allow the symmetry to relax. Energy-minimized structures at one level of theory may not correspond exactly to those at a different level. To save time, the preliminary searches for local energy-minimum structures were done at the MP2 level without counterpoise correction, which was then applied to the MP2-level energy-optimized dimer in a further calculation.

We had initially hoped that the introduction of the counterpoise correction would leave the *location* of the energy minimum in the energy hyperspace essentially unaltered, changing only the energy value. However, when we found that there were suspicious structural features (unusually short intermolecular distances) in the energy-optimized nonplanar dimers **F** and **G** at the MP2 level, we decided to reoptimize the structures of these dimers at the counterpoise-corrected level. This led to more realistic structures involving molecular displacements of more than 0.2 Å from the previously determined structures, with slightly improved dimer binding energies. This shift in the *location* of the energy minima in the energy hyperspace shows that the change in binding energy on applying counterpoise corrections is neither constant with respect to small structural changes nor proportional to the MP2-level energy, but has instead a different dependence on the nuclear coordinates. Of course, the binding energies of the dimers are tiny compared to the total binding energy. The difference between the total energy of the dimer and twice the energy of the monomer is only of the order of a few mH compared with the total binding energy of around 660 H. Since the dimer-binding energies are so small, the energy hypersurface in the neighborhood of any local energy minimum can be expected to be quite flat with only small slopes and curvatures, especially when the monomers are moved apart. The detection and location of such local energy minima must then be sensitive to all sorts of minor changes in the details of the calculation.

We then decided to reoptimize the structures of all the remaining dimers in our collection at the counterpoise-corrected level. This resulted in various adjustments to their structures, but only a negligible change in their binding energies. The relevant regions of the energy hypersurface are so flat and featureless that the energy changes associated with finite mutual displacements of the monomers in the dimer are insignificant. For example, Figure 3 shows the change in binding energy of dimer **E** as the interplanar distance is altered; as the latter increases by almost 0.3 Å (from 3.32 Å to 3.60 Å) the binding energy stays constant within 0.5 kJ mol^{-1}, an insignificant amount. Under such circumstances, the exact *location* of the minimum-energy structure becomes meaningless. It is possible that higher-level calculations could still lead to small changes in the structures of our collection of local energy-minimum dimers, but we do not think they would change the general pattern of interaction energies.

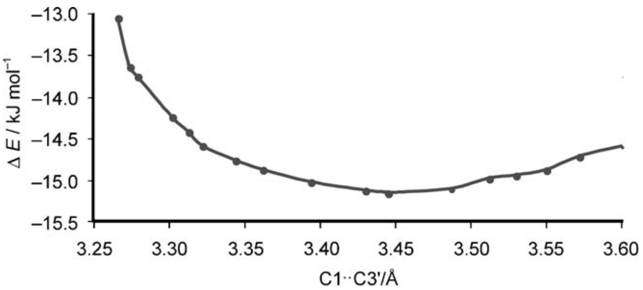

Figure 3. Dependence of ab initio energy E_{QM} (in kJ mol^{-1}) on the distance (in Å) between the closest pair of C atoms for dimer **E** at the MP2/6-31++g(d,p) level with counterpoise correction for basis-set superposition error (BSSE). The energy does not vary by more than 0.5 kJ mol^{-1} over a range of more than 0.3 Å.

It might seem desirable to calculate the vibrational frequencies for each dimer in order to ensure that they are all real (i.e., that the matrix of second derivatives of the energy with respect to the coordinates has only positive eigenvalues). However, when the energy hypersurface in the neighborhood of the minima is so flat as that depicted in Figure 3, such an exercise would be not only computationally expensive, but also futile. Following some long-drawn-out calculations for dimer **F′**, we decided that the effort involved in such a task was not worthwhile. Similar problems are likely to arise for many other dimer species, such as benzene dimers, where major structural changes can occur with only a minimal change in the binding energy.[10]

The energies of the dimers **A**–**G** calculated at the MP2/6-31++g(d,p) level with counterpoise correction for basis-set superposition error (BSSE) agree well with the corresponding energies E_{PIX}, calculated by the semiclassical density sums (SCDS) or Pixel method[4] for these pair structures with the same dimer geometry (Table 3). In the Pixel calculations, the electron density of the fluorobenzene molecules was calculated at the MP2++g(d,p) level. The Pixel method may not be so fundamental as the ab initio methods, but its partitioning of the intermolecular interaction energy into coulombic, polarization, dispersion, and repulsion terms, although not rigorous, can provide useful comparisons at a certain level of insight. While the polarization and dispersion terms are always negative and the repulsion term is always positive, the coulombic term can have either sign and it is sometimes decisive in determining the relative stabilities of rival structures. Some comments on the structures and binding energies of the individual dimers are needed.

A: in-plane dimer, C_{2h} local symmetry, two linear C–H···F interactions, d(F···H) = 2.43 Å, $E_{QM} = -8.3$ kJ mol^{-1}, $E_{PIX} = -8.9$ kJ mol^{-1}. The same local energy-minimum structure is reached from several starting points, suggesting that it corresponds to a genuine feature of the energy hypersurface.

B: in-plane dimer, C_s symmetry, two C-F···H interactions, (bifurcated fluorine bonds or bridges?), one linear, d(F···H) = 2.83 Å, the other bent, d(F···H) = 2.68 Å, $E_{QM} = -5.3$ kJ mol^{-1}, $E_{PIX} = -5.9$ kJ mol^{-1}. Note that this dimer has one F atom engaged with two H atoms, and not one H atom engaged with two F atoms (conventional bifurcated-donor hydrogen bond[1g]).

C: in-plane dimer, C_{2h} local symmetry, molecular dipoles opposed and slightly inclined to the perpendicular of the molecular separation axis; $E_{QM} = -2.0$ kJ mol^{-1}, $E_{PIX} = -3.8$ kJ mol^{-1}. This dimer is only very weakly bound. In the Pixel partitioning, E_{COUL} is slightly positive, despite the favorable orientation of the molecular dipoles. The only important attractive contribution to E_{PIX} comes from the dispersion energy.

D: in-plane dimer, C_{2h} local symmetry, molecular dipoles opposed at an angle of about 30° to the molecular separation axis: $E_{QM} = -0.7$ kJ mol^{-1}, $E_{PIX} = -1.6$ kJ mol^{-1}. Both calculations agree that the dimer is practically unbound in this orientation; E_{COUL} is more positive than for dimer **C**, and the only attractive contribution comes from the dispersion energy.

E, **F**: parallel (nearly parallel?) displaced (PD) dimers. These are found to be the most stable fluorobenzene dimers. As for benzene itself, there is a range of PD structures on a rather flat energy surface at around −10 to −15 kJ mol^{-1}, representing stronger binding than for any of the in-plane dimers. The interplanar distances are 3.5–3.9 Å, similar to, but slightly greater than those in benzene dimers, 3.4–3.6 Å, according to recent high-level calculations.[10] However, unlike the benzene dimers, the fluorobenzene dimers **F** and **F′** deviate from strictly parallel orientation of the molecular planes. The highest possible symmetries of fluorobenzene dimers are C_{2h} (molecular dipoles opposed, structure **E′**) and C_{2v} (molecular dipoles parallel, structure **F′**). Relaxation of these symmetries leads to extra stabilizations of 2.6 kJ mol^{-1} for dimer **F** and 7.1 kJ mol^{-1} for dimer **E**. In the former case, the C_{2h} dimer **E′** relaxes into a centrosymmetric structure (structure **E**, symmetry C_i, interplanar distance 3.54 Å) with $E_{QM} = -15.2$ kJ mol^{-1}, $E_{PIX} = -12.5$ kJ mol^{-1}, in which the molecular dipoles are still opposed. As already mentioned, the dependence of the binding energy on the inter-ring distance is very small (see Figure 3). The minimum-energy dimer **F′** with imposed C_{2v} symmetry ($E_{QM} = -8.0$ kJ mol^{-1}, $E_{PIX} = -7.8$ kJ mol^{-1}) has a feature that came as a surprise to us (Figure 2): the ring planes are not quite parallel, but are mutually inclined such that the distance between the eclipsed F atoms at one end of the molecule is markedly shorter than the distance between the eclipsed H atoms at the opposite end (3.70 Å against 4.06 Å—the corresponding distances in the structure optimized at the MP2 level were both around 0.3 Å shorter than these values!). When the imposed C_{2v} symmetry is relaxed, structure **F′** falls into a C_2-symmetric structure (structure **F**) with $E_{QM} = -15.1$ kJ mol^{-1}, $E_{PIX} = -9.4$ kJ mol^{-1}, in which the molecular dipoles are inclined at an angle of 78° to one another. Since fluorobenzene has quite a sizeable electric dipole moment of 1.58 D,[20] the close similarity of the binding energies of dimers **E** and **F** with very different molecular dipole orientations can be construed as a warning against the use of simple electrostatic arguments to estimate intermolecular interaction energies at short intermolecular distances. In dimer **F**, like dimer **F′**, the deviation from perfectly parallel molecular planes is also appreciable (see Figure 2); the two C atoms bearing the F substituents are 3.37 Å apart (F···F, 3.81 Å), whereas the distance between the almost superposed β-C atoms is 3.70 Å (H···H, 3.84 Å). As for the **E** dimers, the corresponding distances in the dimer optimized at the MP2 were about 0.2 Å shorter than these. In the Pixel calculations for dimers **E** and **F**, the destabilizing repulsion contributions E_{REP} slightly outweigh the stabilizing dispersion energy contributions E_{disp}. For both these dimers, the E_{COUL} contribution is decisive in the energy balance and has nearly the same value, despite the difference in mutual orientation of the molecular dipole moments. Indeed, the coulombic energy of these dimers is similar to that of the best in-plane dimer **A**, with its two linear C–H···F interactions. It is only in the **F′** structure with exactly parallel dipoles that the E_{COUL} contribution is slightly destabilizing.

G: perpendicular (T-shaped) dimers. As with the PD structures, there is a range of structures with slightly different inter-ring orientations on a rather flat energy surface. The most stable structure found (with approximate mirror symmetry) is shown in Figure 2, with the *meta*-H atom of one molecule 2.70 Å from the ring center of the other and almost equidistant from its six C atoms. The binding energy is calculated to be $E_{QM} = -10.5$ kJ mol^{-1}, $E_{PIX} = -11.6$ kJ mol^{-1}. When counterpoise corrections were not included in the energy minimization steps but only in the energy minimized structure, the resulting dimer was considerably more compact, with the rings displaced by more than 0.2 Å towards one another, but it was only marginally less stable ($E_{QM} = -8.6$ kJ mol^{-1}, $E_{PIX} = -11.1$ kJ mol^{-1}). Changes in the mutual orientation of the two molecules in the dimer lead to only small changes in the binding energy. Again, according to Pixel, even for the T-shaped dimer, the dispersion energy is the main contributor to the binding energy, although the coulombic energy also plays a part.

The ab initio and Pixel calculations agree that dimer **A** with two C–H···F interactions is the most strongly bound of the in-plane dimers. Dimer **A** also stands out as one in which the coulombic energy is larger than the dispersion energy and thus provides the dominant stabilization contribution. These results would seem to provide some justification for regarding the C–H···F interactions as weak-to-very-weak hydrogen bonds. However, dimer **A** with its two C–H···F interactions is not markedly more stable than dimer **B** with its bifurcated C-F···H interactions, and it does not play any part in the experimental crystal structure (see below).

Fluorobenzene crystal structure pairs: Figure 1 depicts the crystal structure of fluorobenzene, as seen in projection down the [100] and [001] axial directions. The structures **H**–**J** in Figure 4 represent pairs of neighboring fluorobenzene molecules related by the symmetry operations of the crystal: 4_1 and $(4_1)^3$ screw axis relationships, and the symmetry-equivalent **a** and **b** translations. In the crystal, these pairs do not occur in isolation; each pair is part of an infinite repeating pattern. Thus, these pairs, unlike the dimers **A**–**G**, cannot be expected to correspond to local minima in the energy landscape. They represent compromises, each pair being influenced by the pushes and pulls of neighboring molecules in the crystal. However, for comparison with the calculated energies of the dimers **A**–**G**, we have calculated the energies of the crystal pairs **H**–**J** at the same computational level.

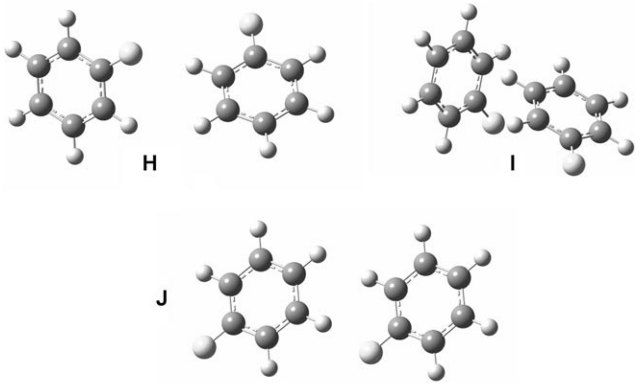

Figure 4. Fluorobenzene molecular pairs (**H**, **I**, **J**) that occur in the crystal structure. The **H** and **I** pairs are related by the operations of the fourfold screw axes (4_1 and $4_1{}^3$), the **J** pair by the operations of the *a* and *b* translations.

As mentioned earlier, Thalladi et al.[1d] noted that the symmetry-related *ortho*-H atoms are involved in C–H···F interactions (2.48 Å), the *meta*-H atoms in so-called C–H···π interactions. The C–H···F interaction in question occurs in crystal pair **H**, which has a calculated pairing energy $E_{\mathrm{QM}} = 5.1\,\mathrm{kJ\,mol^{-1}}$, $E_{\mathrm{PIX}} = 5.5\,\mathrm{kJ\,mol^{-1}}$. The calculated energy of the crystal pair **I** is about twice this value, $E_{\mathrm{QM}} = 10.1\,\mathrm{kJ\,mol^{-1}}$, $E_{\mathrm{PIX}} = 9.1\,\mathrm{kJ\,mol^{-1}}$. As in dimer **G**, the *meta*-hydrogen atom of one molecule is poised roughly over the ring center of the other molecule, with H···C distances 3.02–3.24 Å. The calculated pairing energy is seen to be about the same as that of the T-interaction in the "optimized" dimer **G** (Table 3, $E_{\mathrm{QM}} = 9.5\,\mathrm{kJ\,mol^{-1}}$, $E_{\mathrm{PIX}} = 9.6\,\mathrm{kJ\,mol^{-1}}$) although in the crystal pair the distance of the hydrogen atom to the other ring center is about 0.3 Å longer than in the "optimized" structure and the orientation of the two molecules in the pairs is different, although the ring planes are nearly perpendicular to one another in both pairs. Despite these structural differences, the calculated pairing energies are very close, a further expression of the flatness of the energy hypersurface over a wide range of T-type molecular pairs. Clearly, the crystal pair is affected by the presence of other neighboring molecules and the requirement of periodicity; factors that do not operate in the ideal dimer **G**. In any case, crystal pair **I** is seen to be the major contributor to the stabilization of the crystal. Besides the **H** and **I** pairs, there is the translation pair **J**. Here the molecules are necessarily parallel but, as can be inferred from Figure 1, they do not overlap at all when viewed down the plane normal; the interplane distance is less than 2.8 Å, while the distance between centers of mass is 5.80 Å. There is no obvious description in terms of atom–atom interactions; however, with $E_{\mathrm{QM}} = 6.3\,\mathrm{kJ\,mol^{-1}}$, $E_{\mathrm{PIX}} = 4.9\,\mathrm{kJ\,mol^{-1}}$, this pair contributes significantly to the cohesive energy of the crystal. For the crystal pairs, the overall agreement between ab initio and Pixel energies is as good as can be expected; however, one should not place too much reliance in the actual numbers since they are highly sensitive to small changes in the details of the calculations.

The lattice energy of fluorobenzene is not known. The crystal has a lower melting point (240–242 K) than benzene (278 K) and is unlikely to have a larger lattice energy. We may take the lattice energy of benzene, 40–45 kJ mol^{-1},[21] as an upper limit. The calculated energies of the three types of symmetry pairs **H**, **I**, and **J** allow us to make a theoretical estimate of the lattice energy. A given reference molecule is involved in four interactions of each type, representing its twelve nearest neighbors. The corresponding interaction energy, the packing potential energy (PPE),[22] is then $4\times(5.1 + 10.1 + 6.3) = 86.0\,\mathrm{kJ\,mol^{-1}}$, and the lattice energy is half this amount, namely around 43 kJ mol^{-1} (Table 4)[23]

Table 4. Interaction energies [kJ mol^{-1}] for molecular pairs in the crystal structure of fluorobenzene (FB) and benzene (B, virtual structure N5) as calculated by quantum mechanics (QM) at the MP2/6-31++g(d,p) level with counterpoise correction for basis-set superposition error (BSSE) together with estimated lattice energy E(L). The energies estimated by the Pixel method are also listed for comparison. See Figure 4 for pictorial images.

Molecular pair	Symmetry operation	Multiplicity	FB (QM)	FB (PIX)	B (QM)	B (PIX)
H	4_1	4	−5.1	−5.5	−3.03	−5.2
I	$(4_1)^3$	4	−10.1	−9.1	−7.75	−8.0
J	*a*/*b* translation	4	−6.3	−4.9	−5.82	−6.6
E(L)			43.0	39.0	33.2	39.6

The Pixel calculations lead to a closely similar value of 39 kJ mol^{-1}. The major contribution to the packing energy of crystalline fluorobenzene is seen to stem from the interactions of type **I** between molecules related by the fourfold screw axes. As in the optimized T-shaped dimer **G**, it is not the *para*-H atom but the *meta*-H atom that "points" towards the center of the other molecule in the pairing, which, of course, in the periodic structure, continues the chain of interacting molecules along each 4_1 axis.

As mentioned earlier, the fluorobenzene crystal structure is closely similar to one of the low-energy virtual structures of benzene itself (N5 structure, Table 2). We have analyzed this virtual benzene structure in the same manner as that of fluorobenzene and calculated the interaction energies for the three analogous symmetry pairings of benzene molecules at the same computational level as for the fluorobenzene pairings **H**, **I**, and **J** (Table 3). There is not a great difference between corresponding molecular pairs in the two structures, and their calculated energies are found to be similar—indeed, they are practically identical as far as the Pixel calculation is concerned. For the N5 structure, the E_{QM} lattice energy, estimated from the energy contributions of twelve nearest neighbors is 33.2 kJ mol^{-1}, slightly less than that of the fluorobenzene crystal structure. The Pixel value ($E_{PIX} = -39.6$ kJ mol^{-1}) is practically the same as for the fluorobenzene crystal structure. In any case, a better agreement can hardly be expected, considering that different levels of theory yield energies that differ by as much as 4–5 kJ mol^{-1} for a given type of benzene dimer.[10] In the absence of any experimental values for the fluorobenzene and benzene N5 lattice energies, we may note that the experimental lattice energy of the *Pbca* crystal structure of benzene is about 44 kJ mol^{-1}.[23] Our recent analysis of this structure in terms of crystal pairs led to just this value according to the Pixel calculation and to a somewhat higher value, 52 kJ mol^{-1}, according to the best ab initio estimate.[24]

Table 5. Interaction energies [kJ mol^{-1}] for molecular pairs in several closely related crystal structures with the same space group $P4_32_12$ (or equivalently $P4_12_12$) and similar unit cell dimensions (listed in Table 2) and as estimated by the Pixel method together with estimated lattice energies *E*(L).[a]

Compound/Refcode	Pair	E_{TOT}	E_{COUL}	E_{POL}	E_{DISP}	E_{REP}	D[b] [Å]
fluorobenzene	**H**	−5.5	−3.6	−1.3	−5.9	+5.2	6.57
FACFAQ	**I**	−9.1	−6.3	−3.0	−17.3	+17.5	4.79
	J	−4.9	−3.6	−1.4	−8.9	+8.9	5.80
	E(L)	39.0					
N5 benzene	**H**	−5.2	−0.8	−0.8	−7.8	+4.1	6.38
	I	−8.0	−4.7	−2.3	−14.1	+13.0	4.89
	J	−6.6	−6.5	−1.9	−11.1	+12.9	5.54
	E(L)	39.6					
benzonitrile	**H**	−4.3	−2.5	−2.2	−5.9	+6.3	7.29
BZONTR	**I**	−7.2	−3.9	−2.6	−11.3	+10.6	4.85
	J	−11.3	−5.9	−2.8	−19.6	+17.0	6.36
	E(L)	45.6					
cyclopentene-1,2,3-trione	**H**	−8.9	−10.8	−4.1	−6.8	+12.8	6.54
CIMHUH	**I**	−18.5	−20.0	−7.1	−22.1	+30.7	4.64
	J	−7.2	−1.8	−2.5	−10.2	+7.3	5.70
	E(L)	69.2					
alloxan	**H**	−23.1	−29.1	−10.0	−15.2	+31.2	6.29
ALOXAN11	**I**	−24.3	−34.9	−10.9	−29.4	+50.9	4.76
	J	−6.1	−8.3	−3.0	−13.9	+19.1	5.84
	E(L)	107.0					

[a] Atomic coordinates and cell dimensions were taken from the Cambridge Structural Database[26] (refcodes listed), except for the virtual N5 benzene structure, for which the atomic coordinates were kindly provided by Dr. B. P. van Eijck.[15] [b] Distance between the molecular centers.

The comparison shows that any contribution of the putative C−H···F interaction to the cohesive energy of the fluorobenzene crystal is not substantially different from that of a typical C−H···H interaction in the benzene structure. If it comes as a surprise that nonpolar benzene can pack in virtually the same molecular arrangement as polar fluorobenzene, which has an electric dipole moment of 1.58 D,[21] the reason may be simply that the two molecules have nearly the same hexagonal shape.

Crystal structure pairs in crystals isostructural with fluorobenzene: As seen in Table 2, several other molecules besides fluorobenzene crystallize in the same space group $P4_32_12$ (or equivalently $P4_12_12$) with similar unit cell dimensions. We have analyzed three of these structures, benzonitrile, alloxan, and cyclopentene-1,2,3-trione, by the Pixel method[4] to see what, if anything, they have in common with one another and with fluorobenzene.[25] The molecular pairs in these crystal structures have the same symmetry relationships as the **H**, **I**, and **J** pairs shown in Figure 4 for fluorobenzene, but they differ in important respects. The pair energies and especially the partitioning of these energies can be very different since the molecules have new functionalities that lead to different patterns of intermolecular interactions. Results of the calculation are shown in Table 5, together with the corresponding energy partitionings for fluorobenzene and virtual N5 benzene.

According to the Pixel calculations shown in Table 5, the lattice energy of benzonitrile is greater than that of fluorobenzene. This result stems partly from the larger contribution of the **J** translation pairing in benzonitrile, although the intermolecular separation (translation distance) is greater here because the molecules are less steeply inclined with respect to the (001) plane. From an atom–atom interaction viewpoint, it is not obvious why the **J** pairing should be best here. Perhaps it has to do with the greater "overlap" of the benzene ring of one molecule with the cyano group of its partner, compared with the fluoro group, thus leading to a C–H···N interaction (H···N, 2.81 Å, C–H···N, 122°). The **H** pairing also has a C–H···N interaction (H···N, 2.76 Å, C–H···N, 149°) that could be interpreted as a weak hydrogen bond; however, this bond must be very weak indeed because the total binding energy is a mere 4.3 $kJ\,mol^{-1}$. In the **I** pair, with a binding energy of 7.2 $kJ\,mol^{-1}$, the *meta*-H atom of one benzonitrile molecule is located nearly over the ring center of its partner, with H···C distances of 3.20–3.25 Å, a narrower spread than in the corresponding fluorobenzene pair with approximately the same energy. Until now we have not considered the crystal pair related by translation along the dyad axis (the base diagonal) of the tetragonal unit cell. In the benzonitrile crystal, the molecular separation in this pair is $\sqrt{2}\times 6.36$ Å = 8.99 Å; however, the greater length of the benzonitrile molecule along the diagonal leads to an intermolecular C–H···N distance of 2.59 Å in this crystal pair, the shortest such distance in the crystal. The Pixel energy for this diagonal translation pair is calculated to be as much as $-11.4\,kJ\,mol^{-1}$ for benzonitrile, as opposed to $-0.4\,kJ\,mol^{-1}$ and $-0.9\,kJ\,mol^{-1}$ for the analogous pairs in fluorobenzene (C–H···F, 3.02 Å) and N5 benzene (C–H···H, 2.99 Å), respectively. Of all the molecular pair interactions we have mentioned here, the binding energy of this pair stands out as the only one clearly describable in terms of a specific atom–atom interaction, an intermolecular C–H···N hydrogen bond—perhaps one of the best examples of such. The Pixel energy partitioning shows that the stabilization here comes almost entirely from E_{COUL} ($-10.9\,kJ\,mol^{-1)}$. Inclusion of the contribution of this crystal pair increases the value of the estimated lattice energy to 56.9 $kJ\,mol^{-1}$. As far as we are aware, an experimental value of the sublimation enthalpy of benzonitrile is not known. The melting point of benzonitrile is higher than that of fluorobenzene (260 K versus 231 K), and so is the boiling point (464 K versus 358 K). Indeed, benzonitrile stands out as having a remarkably large liquid temperature range of more than 200 K, attributable in part to the large electric dipole moment of the molecule, namely 4.18 D.[20] If we use Trouton's Rule to estimate the vaporization enthalpy of the liquids, we obtain values of about 30 $kJ\,mol^{-1}$ for fluorobenzene and about 40 $kJ\,mol^{-1}$ for benzonitrile, values that seem quite compatible with our lattice energy estimates.

Results of Pixel calculations for alloxan and cyclopentene-1,2,3-trione are included in Table 5 for comparison with those of the substituted benzene derivatives. Again, we do not know the sublimation enthalpies; however, the lattice energy of alloxan has been estimated from an atom–atom force-field calculation, by means of distributed multipoles associated with the atom centers, to be about 115 $kJ\,mol^{-1}$,[27] close to the Pixel value. Because of the changes in the molecular structure, the parallelism between the crystal pairs **H**, **I**, and **J** from crystal to crystal is not as clear as in the benzene derivatives, but it still has some significance. In both **I** pairs it is the carbonyl O atom of the trione system that sits above the ring plane of the other molecule, providing examples of the much discussed O···C=O type of interaction[28] with d(C···O) = 2.72 Å (alloxan) and 2.92 Å (cyclopentene-1,2,3-trione) with pair binding energies 24.3 and 18.5 $kJ\,mol^{-1}$ respectively. The **H** pair is characterized by two N–H···O interactions (hydrogen bonds?) with d(H···O) = 2.31 and 2.34 Å that link each such pair via their ureido groups. The geometry of this hydrogen-bonded (?) system with N–H···O angles of about 140° is so far from optimal that in a recent careful study the alloxan crystal structure[29] was described as "unusual in that it contains no hydrogen bonds". Nevertheless, the calculated **H** pair energy is 23.1 $kJ\,mol^{-1}$, practically the same as for the **I** pair. In the above-mentioned study,[29] these unusual features are described as illustrating "the limitations of the functional group approach to predicting molecular crystal structures." In the analogous cyclopentene-1,2,3-trione **H** pair, the ureido groups are replaced by an ethene group, and the pair of N–H···O hydrogen bonds is replaced by a single C–H···O interaction with d(H···O) = 2.35 Å with a corresponding reduction of the binding energy from 23.1 $kJ\,mol^{-1}$ to 8.9 $kJ\,mol^{-1}$. There is not much to say about the **J** translation pairs, which have approximately the same binding energies as the analogous fluorobenzene pair.

Although alloxan and cyclopentene-1,2,3-trione have very similar crystal structures to that of fluorobenzene, the distribution of binding energy among the important crystal pairings is quite different, as indeed is to be expected from their very different functional groups. Closely similar crystal structures are thus not necessarily directed by the same kinds of intermolecular interaction. In the aromatic compounds listed in Table 5, the **H** pairings might be invoked as examples of C–F···H, C–H···H, and C–CN···H interactions, although none of them seem in any way to be structure-determining. In alloxan, the **H** pair involves two N–H···O interactions which, depending on the criteria applied, may or may not be taken as hydrogen bonds but which in any case contribute significantly to the large lattice energy of this crystal. While the **I** pair contributes to the lattice energy of all five crystals, it represents a quite different type of intermolecular interaction in the aromatic compounds and in the other two. In the former it involves what can be described as a C–H···π interaction, while the other two are textbook examples of O···C=O interactions. The benzonitrile structure achieves extra stabilization through the chains of parallel molecules along the unit cell diagonals, involving C–H···N interactions between successive molecules in a chain; there is no analogous interaction in the others. Although the five crystal structures can be classed from their similar unit cell dimensions and common space group as isostructural and share the same general pattern of molecular pairings, they do not share any common structure-directing or -controlling features. Molecular pair analysis indicates that crystal structures result from a complicated balance of intermolecular pushes and pulls. Interpretations of even quite simple crystal structures solely in terms of particular atom–atom interaction patterns thus underestimate the complexity of the pattern of forces that determine the molecular arrangement in a periodic crystal.

A comment on pixel energy partitioning: We cannot agree with Hunter's opinion, expressed in a recent review[30] that "Since repulsion, induction, and dispersion contribute only negligibly to intermolecular interactions, this leaves us with the prospect of using only electrostatics to explain everything." Inspection of Table 5 shows that in the Pixel partitioning scheme dispersive and repulsive contributions to the interaction energy of molecular pairs are quite comparable with, and sometimes more important than, the coulombic energy terms. This holds even when the latter are large, as in the alloxan and cyclopentene-1,2,3-trione crystals, where the large coulombic energies are accompanied by smaller but not negligible polarization energies. Of course, dispersive and repulsive contributions necessarily have opposite signs so that the magnitude of their sum is less than the separate terms; however, it is incorrect to describe them as contributing only negligibly to intermolecular interactions. They are often the largest terms. Insofar as we find it useful to partition the total intermolecular interaction energy into coulombic, polarization, dispersion, and repulsion terms, we cannot afford to regard any of them as negligible.

To be sure, if the *exact* distribution of electrons and nuclei in the system could be established, then, according to the Hellmann–Feynman theorem,[31] only coulombic interactions need be taken into account. In that limit, however, repulsion, induction, and dispersion do not become negligible; they simply disappear from the stage and play no role whatsoever in the calculation of the energy of the system. Nevertheless, we are still far from that limit for systems as large as molecular pairs and clusters. The Pixel energy calculation is based not on the exact charge distribution of a multimolecular system but on the unperturbed charge distributions of the separated molecules in that system. In the Pixel energy partitioning scheme, the polarization, dispersion, and repulsion terms arise from the interactions among these unperturbed charge distributions. As can be seen from Table 3, Pixel energies for fluorobenzene molecular pairs agree well with results of high-level quantum-mechanical calculations and also provide the breakdown into energy terms that have meaningful interpretations at our current level of chemical and physical understanding.

Is fluorine larger or smaller than hydrogen?: The question is meaningless, yet Pauling ascribed a larger van der Waals radius to fluorine than to hydrogen (1.35 Å versus 1.2 Å)[32] and so did Bondi (1.47 Å versus 1.2 Å)[33] and Kitaigorodsky (1.42 Å versus 1.17 Å).[34] These allocations were intended to describe general intermolecular packing trends and distances in molecular crystals and may still have a certain utility for such purposes. However, the structures of the calculated fluorobenzene dimers **F** and **F′** (Figure 2) do not fit into this scheme. In the C_{2v} symmetric dimer **F′**, the distance between the F atoms at one end of the molecule is 3.70 Å, the distance between the H atoms at the opposite end is 4.06 Å. Similarly, in the C_2 symmetric dimer **F**, the intermolecular C···C distance is significantly smaller for the fluorinated C atoms than for the C atoms at the opposite side of the dimer. Of course, one can dismiss these features as mere fluctuations in a theoretical calculation that has passed its level of serviceability; however, on the other hand, the calculations of the other stable dimers at the same level of theory lead to results that seem eminently reasonable.

Since the electron density falls off rapidly on proceeding outwards from a molecule, one measure of an atomic or molecular boundary is the contour surface at a particular limiting electron density, sometimes chosen in the region 0.001 to 0.002 a.u.[35] (1 a.u. = 6.76 e Å^{-3}). Figure 5 shows the fluorobenzene molecule with bounding surfaces corresponding to electron densities of 0.01, 0.001, and 0.0001 a.u., calculated at the MP2/6-31++g(d,p) level. At first sight, the molecule might appear to have sixfold symmetry but, on closer inspection, the contours around the F atom are seen to differ from those around the H atoms, mainly because the C–F bond length (1.38 Å) is longer than the C–H bond length (1.08 Å). The bounding surfaces give an impression of the effective "nonbonding" sizes and shapes of the atoms. The van der Waals envelope would correspond roughly to the middle bounding surface. There is an interesting difference between the relative atom sizes as judged from the inner and outer bounding surfaces. According to the inner and middle bounding surfaces, the F atom is larger than H in all directions; however, according to the outer 0.0001 a.u. bounding surface the F atom is smaller in the direction normal to the molecular plane. At this outer surface, the electron density may appear to be vanishingly small but it is far from negligible as far as the overlap of the molecular electron densities is concerned. In the Pixel calculation, 4×4×4 superpixels containing more than 10^{-6} electrons are retained, the others are rejected. The electron density at the outer bounding surface (0.0001 a.u ≈ 0.00068 e Å^{-3}) is thus almost 700 times greater than this limiting density and will thus be significantly involved in "penetration effects"[4b] caused by partial overlapping of molecular densities. In the directions along the chemical bonds, this outer bounding surface is about 1.98 Å from the F atom and about 1.88 Å

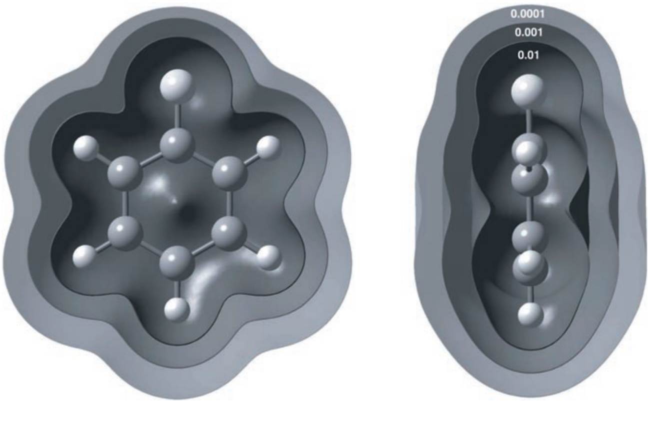

Figure 5. Fluorobenzene molecule with bounding surfaces corresponding to electron densities of 0.01, 0.001, and 0.0001 a.u. (1 a.u. = 6.76 e Å^{-3}).

from each H atom; in the direction normal to the molecular plane, the corresponding distances are 2.17 Å for the F and 2.40 Å for the H atom. If we retain the unperturbed molecular charge distributions of Figure 5, then, for the approach of two fluorobenzene molecules as in dimer **F** (Figure 2, Table 3), the electron densities of the H atoms will begin to overlap significantly at interplanar distances where the overlap of the F atoms is still negligible. In other words, the H atoms would appear to be larger than the F atoms. This could be the reason for what we regarded as an "unusual" feature of the calculated dimer **F**: the ring planes are not quite parallel, but are inclined such that the distance between the eclipsed F atoms at one end of the dimer is shorter than the distance between the eclipsed H atoms at the other end. Of course, this is merely a suggestion based on theoretical results for which there is no experimental evidence whatsoever. It is also interesting that, judging from the outer 0.0001 a.u. bounding surface of the molecule, the F atom appears to be more isotropic than the H atoms. The H atoms appear to be slightly smaller along the C–H bond direction than perpendicular to that direction, while the F atom would appear to be more isotropic. This may again seem to run counter to expectation, but there is at least one kind of experimental evidence in its favor: the typical displacement of the centroid of H-atom electron density in an X–H bond towards the bonded X atom in X-ray crystallographic studies, which leads to apparent X–H distances 0.1–0.2 Å shorter than the corresponding internuclear distances. If we wish to speak of atomic sizes and shapes in molecules, then we should not be surprised if different theoretical and conceptual models sometimes lead to apparently contradictory results.

Conclusion

An analysis of the geometry and energy of neighboring molecular pairs in the crystal structure of fluorobenzene shows that although short intermolecular C–H···F distances (2.47 Å) occur in this crystal structure,[1d] the interaction in question makes only a minor contribution to the cohesive energy of the crystal. The most important contribution to the cohesive energy comes from the molecular pair **G** (Figure 2) in which the *meta*-H atom of one molecule sits 2.8 Å above the approximate center of the other molecule (T-shaped dimer), with a binding energy of around 10.0 $\mathrm{kJ\,mol^{-1}}$, according to high-level quantum mechanical and Pixel calculations. Almost the same binding energy was calculated for a whole range of other T-shaped dimers and displaced parallel-stack dimers (with molecular dipoles parallel and antiparallel). It may seem surprising that such large structural differences are associated with what might seem to be only small changes in the binding energy, but, after all, the *total* binding energy of these weakly bonded dimers is small and any change in it must be even smaller. That is why the entire energy hypersurface for a whole range of more or less stable dimers is so flat. Considering that the zero energy corresponds to a completely separated pair of molecules and that the depth of the energy minima is, at most 10 $\mathrm{kJ\,mol^{-1}}$ below zero energy, energy barriers separating these minima must be less than 10 $\mathrm{kJ\,mol^{-1}}$, and presumably much less, The in-plane dimers **A**–**D** (Figure 2) have calculated binding energies ranging from nearly zero to nearly 10 $\mathrm{kJ\,mol^{-1}}$. The crystal structure of fluorobenzene has been analyzed in terms of the molecular pairs that occur in it. This crystal structure is isostructural with those of several other molecules of similar size and shape (Table 1), indicating that similar intermolecular interactions are at work. In particular, there is a very close similarity between the crystal structure of fluorobenzene and one of the virtual crystal structures (N5, H2) of benzene.[15] The two molecules have nearly the same size and shape, and the calculated energies of the corresponding molecular pairs in the two crystal structures are also very similar. These results suggest that the replacement of an H atom of benzene by an F atom in fluorobenzene has only a very minor effect on the pattern and strength of the intermolecular interactions. We conclude that C–H···F interactions in the fluorobenzene crystal have about the same structure-directing ability and influence on the intermolecular energy as a typical C–H···H interaction in crystalline benzene. Both structures depend on a balance of weak intermolecular forces and energies that happen to be similar. With only slight modifications, the same kinds of molecular pair occur in crystals of isostructural benzonitrile. For quantitative descriptions, we need interactions between molecular charge distributions and not between point atoms.[36] Although the alloxan and cyclopentene-1,2,3-trione molecules are of a quite different type to fluorobenzene, their crystal structures are also isostructural. Finally, the question of whether the packing radius of the F atom is larger or smaller than that of H is raised, but not satisfactorily answered. On the whole, we believe that weak intermolecular binding energies estimated by the Pixel method are just about as reliable (or unreliable) as those obtained by ab initio calculations at the MP2/6-31++g(d,p) level with counterpoise corrections. For most of the dimer structures, the two methods lead to very similar binding energies. Where they differ, we suspect that the Pixel structure and energy are to be preferred.[37]

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[37] **Note Added in Proof** (July 5, 2006): An observant reviewer has pointed out that we have not included borazine, $B_3H_6N_3$, ("inorganic benzene") in our list of crystals isostructural with fluorobenzene (Table 2) nor in the comparisons of molecular pair interactions in these crystals (Table 5). Indeed the crystal structure of borazine as determined by R. Boese et al.[38] at 115 and 160 K is closely similar to that of fluorobenzene (space group $P4_32_12$, $a = b = 5.428$ Å, $c = 16.279$ Å at 115 K). Unfortunately, when we carried out the work described in this paper we were unable to include Pixel energy calculations for borazine molecular pairs for comparison with those of Table 5 because essential parameters for boron atoms were not available in the Pixel calculation scheme. This deficiency has now been remedied.[39] Pixel energies for the H, I, and J pairs (Figure 4) in the borazine crystal structure are -5.6, -8.8, and $-6.3\ \mathrm{kJ\,mol^{-1}}$, respectively, closely similar to the values calculated for fluorobenzene and N5 benzene (Table 5). The estimated lattice energy E(L) of borazine is then $-41.4\ \mathrm{kJ\,mol^{-1}}$. Although no experimental value of the borazine lattice energy is available, we expect it to be about the same magnitude as that of benzene, 40–45 $\mathrm{kJ\,mol^{-1}}$,[40] so the Pixel estimate agrees well with this. On the other hand, G. Raabe[41]

has estimated from semiempirical quantum-mechanical calculations that the lattice energy of borazine is around 5 kcal mol^{-1} (about 21 kJ mol^{-1}) less negative than that of normal *Pbca* benzene.

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