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Quantitative Ranking of Crystal Packing Modes by Systematic Calculations on Potential Energies and Vibrational Amplitudes of Molecular Dimers

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Abstract: Quantum chemical calculations including electron correlation and calculations with the density sums (Pixel) method have been performed on a variety of molecular dimers representing some frequently observed recognition modes in molecular condensed phases. Notwithstanding some individual fluctuations when different computational methods are used, there is a general agreement for the relative orders of magnitude. The results have been collected in a table that ranks the interaction energies and amplitudes of the energy wells for the recognition between molecular fragments, providing a quantitative guideline to assess the relative importance of hydrogen bonding, aromatic ring stacking, antiparallel arrangements of polar moieties, weak Coulombic C−H···X interactions, and dispersive interactions between nonpolar groups. Since the Pixel method naturally allows for a separation between Coulombic, dispersion, polarization, and repulsion energy contributions, their relative importance can be analyzed with respect to the chemical constitution of the interacting partners. The relevance of these results to the current ideas and methods of "crystal engineering" is discussed.

1. Introduction

Qualitative concepts, related to intuitive permanent polarizations of functional groups and recognizing selected contacts between atom spheres or molecular fragments of supposed relevance, are often used for the analysis, prediction, and control of the architecture of organic crystals. The identification of these "synthons" usually relies on contact distance criteria; a cursory, random search through the latest issues of some major journals found several reports of accurate crystallographic structural results, interpreted in terms of short atom−atom distances.[1] These analyses are seldom, if ever, accompanied by a quantitative calculation of the implied energies. In fact, when one takes into proper account the physical foundations of the intermolecular potential field in organic crystals, the problem reveals its complexity,[2] because packing forces are weak and scarcely selective, so that many different structures of nearly equal energy are possible. A quantitative calculation of the intermolecular potentials becomes, then, indispensable; even that may not be sufficient to resolve all ambiguities, but a scale of orders of magnitude of involved energies would be a great help in setting at least a reproducible background to packing analysis. The nature of the problem is the same when the same molecular recognition concepts are applied to the analysis of the structure of biological macromolecules or of interactions within the biological world in general, such as drug−receptor or enzyme−DNA binding and the like.

The idea that the key interactions between complex molecular systems can be modeled by choosing appropriate molecular dimers with a confrontation of selected interaction units goes back to the times when the first reliable, all-electron quantum chemical calculations became possible.[3] In the past years, electron correlation gradually became tractable for molecular dimers, and the number of calculations of that kind that have appeared in the literature is very large and ever increasing; systems of interest here that have

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Quantitative Ranking of Crystal Packing Modes

J. Chem. Theory Comput., Vol. 1, No. 5, 2005 **835**

been treated by high-level quantum chemical methods include the water dimer;[4,5] small alcohols;[6,7] fluoromethanes with water, alcohols, and formaldehyde[8] or with ammonia and small amines;[9] water and other hydrides with small hydrocarbons, acetylene, ethylene, methane, ethane,[10] or their fluorinated derivatives;[11] ethylene and benzene π systems against first row hydrides[12] or other hydrocarbons;[13] formic acid hydrogen bonds;[14] benzene[15,16] and its fluorinated dimers;[17,18] pyrimidine−benzoquinone;[19] pyrimidine− water;[20] and the hydrogen bond between small amides,[21] this being a sample and by no means exhaustive list. Because of computational limitations, such studies usually consider rather small systems, but one can also find essays in the calculation of dimerization energies for large molecules such as naphthalenes.[22] In this paper, we show that the results of the recently proposed density sums (Pixel) method[23−25] match very well those of accurate quantum chemical calculations that require a 100-fold larger computing effort. We thus have systematically applied the Pixel method to the calculation of potential energy profiles for the production of a quantitative compendium of the interaction energies for typical molecular recognition modes. Perhaps even more important than the total binding energy is the width of the corresponding energy well, a measure of the expected vibrational amplitudes and, hence, of the reliability of the corresponding approach mode as a true packing binder. In addition, the relative importance of Coulombic-polarization contributions against dispersive-repulsion effects can be analyzed and discussed.[2,25]

2. Computation Methods

Besides standard MP2 and DFT techniques,[26] we use a method based on numerical integration over the whole molecular charge density, the Pixel-SCDS (semiclassical density sums) method.[23−25] In the latter approach, a molecule is a rigid object and no intramolecular energies are calculated. For the evaluation of intermolecular interactions, the valence molecular charge density is calculated[26] from the MP2/6-31G** wave function on a grid with a step of 0.08 Å. These original charge pixels, typically around 10^6 in number, are then condensed so that each condensed pixel contains the sum of an $n \times n \times n$ block from the original charge density. On the basis of previous experience,[25] n, called the condensation level, is taken as equal to 4 for crystal calculations and equal to 3 for dimer calculations, and those pixels whose charges are below the threshold of 10^{-6} electrons are screened out. Each molecule is, thus, eventually represented by atomic nuclear locations and charges and by 5000−20 000 condensed electron charge pixels.

Both the original and the condensed charge pixels are assigned to atomic basins by a new procedure, as follows. Let p be the number of atoms for which the nucleus−pixel distance is smaller than the atomic radius. If $p = 1$, the charge pixel is within one atomic sphere only, and it is assigned to that atom. If $p > 1$, the pixel is assigned to the atom from which the distance is the smallest fraction of the atomic radius. If $p = 0$, the pixel is assigned to the atom whose atomic surface is nearest. Atomic polarizabilities α_{atom} are reassigned in a consistent manner (H, 0.39; aliphatic C, 1.05;

aromatic C, 1.35; N, 0.95; O, 0.75; F, 0.50 Å^3), and the local polarizability at a pixel of charge q_i belonging to the basin of an atom with a number of valence electrons equal to Z_{atom} is calculated as before:[24]

$$\alpha_i = (q_i/Z_{atom})\alpha_{atom}$$

Intermolecular Coulombic energies, E_{coul}, are calculated as sums over pixel−pixel, pixel−nucleus, and nucleus− nucleus charges, without any empirical parameterization. By definition, these Coulombic energies include penetration energies. Accuracy here is inversely proportional to the condensation level, but with $n = 3$, the numbers thus obtained are in good agreement with those obtained by accurate integration or by other energy partitioning schemes.[2]

The electric field, ϵ_i, generated by the pixel distribution in all surrounding molecules at any pixel of the molecule under consideration is then calculated, and the total polarization energy, E_{pol}, of that molecule is evaluated as a sum over pixel contributions, $E_{POL,i}$, each of which is calculated by a damped linear polarization formula (damping parameter $\epsilon_0 = 150 \times 10^{10}$ V m^{-1}):

$$E_{POL,i} = -\tfrac{1}{2}\alpha_i(\epsilon_i \, d_i)^2 \text{ with } d_i =$$
$$\exp -[\epsilon_i/(\epsilon_0 - \epsilon_i)] \text{ for } \epsilon < \epsilon_0$$
$$E_{POL,i} = 0 \text{ for } \epsilon > \epsilon_0$$

The Pixel polarization energy is, thus, a many-body, non-pairwise additive energy.

Dispersion energies, E_{disp}, are evaluated as sums of pixel− pixel dispersion contributions, $E_{i,j}$, by a London-type formula, also damped to avoid divergence at short intermolecular distances between overlapping electron densities (damping parameter $D = 3.5$ Å):

$$E_{i,j} = -\tfrac{3}{4}f(R) \, \omega\alpha_i\alpha_j/[(4\pi\epsilon°)^2(R_{ij})^6] \text{ with } f(R) =$$
$$\exp[-(D/R_{ij}-1)^2] \text{ for } R_{ij} < D \text{ and } f(R) = 1 \text{ for } R_{ij} > D$$

The "oscillator strength" ω is taken here as the molecular first ionization potential, in turn taken as its Koopmans' theorem equivalent, the energy of the highest occupied molecular orbital. This is an acceptable approximation whenever the HOMO is indeed populated by the electrons involved in the intermolecular contact but might fail when the dispersion effect concerns inner electrons. A refinement of the method, using a variable ω for each intermolecular contact on the basis of a weighted average of atomic ionization potentials is presently being considered.

The repulsion energy, E_{rep}, is modeled as proportional to intermolecular overlap. The total overlap integral between the charge densities of any two molecules is calculated by numerical integration over the original uncondensed densities and is then subdivided into contributions from pairs of atomic species, S_{mn}, using the assignment of pixels to atomic basins. For each $m-n$ pair, the repulsion energy is evaluated as

$$E_{REP,mn} = (K_1 - K_2\Delta\chi_{mn})S_{mn}$$

where $\Delta\chi_{mn}$ is the corresponding difference in Pauling electronegativity (C, 2.5; N, 3.0; O, 3.5; H, 2.1; Cl, 3.0). The values of K_1 and K_2 were optimized at 4800 and 1200,
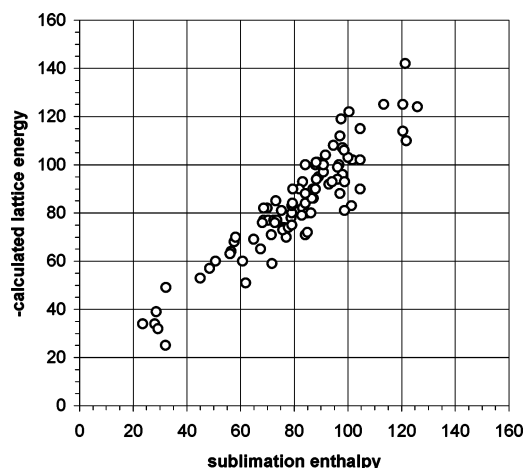
Figure 1. Negative of Pixel-calculated lattice energies versus experimental heats of sublimation for 91 organic crystals (kJ mol^{-1}). The least-squares line is $y = 1.03x$; $R^2 = 0.84$.

respectively (for energies in kJ mol^{-1} with electron densities in electrons Å^{-3}). The rationale behind this approach is that when atoms of different electronegativity meet, a larger reorganization of the electron density occurs and the overlap repulsion must be smaller. The total repulsion energy is then the sum over all $m-n$ pairs.

The total Pixel energy is then the sum of the various contributions:

$$E_{Pixel} = E_{coul} + E_{pol} + E_{disp} + E_{rep}$$

The present form of the Pixel method differs from previous applications[23-25] in the new assignment of pixels to atomic basins and in the new form of the repulsion energy. As an overall check of performance, lattice energies calculated for 91 crystal structures retrieved from the Cambridge Structural Database[27] for molecules containing C, H, N, O, and Cl atoms, including most of the common chemical functions with or without hydrogen-bonding capability, were compared with measured enthalpies of sublimation.[28] As seen in Figure 1, the overall agreement between calculated lattice energies and sublimation enthalpies is acceptable. Some discrepancies, some of which are systematic over certain chemical functionalities, do however remain. The difficulties in the comparison between calculated lattice energies and experimental heats of sublimation have been discussed previously;[29-31] they stem from the temperature dependence of the experimental value versus the theoretically "no-temperature" nature of the calculation, in comparison also with the temperature at which the crystal structure determination (from which the starting data for the calculation were taken) has been carried out; from the intrinsic awkwardness of the experimental determinations, which require the evaluation of extremely low vapor pressures, witness the spread of values often reported for the same compound, quite often spanning as much as 5−10 kJ mol^{-1}, and from other less-predictable factors. For a perhaps extreme example, the sublimation enthalpy entry for anthracene in ref 28 has 24 different values in the range 84−105 kJ mol^{-1}. Another measure of the reliability of a computational method can be drawn from a comparison of its performance with the performance of other

well-established methods for the same calculation; the results of the present Pixel calculations are slightly better than those obtained on a more restricted set of crystal structures with the previous formulation of the Pixel method and are also slightly better than those obtained by computing lattice energies with a heavily parameterized atom−atom force field[29,30] calibrated using the same thermodynamic database. In addition, it should be recalled that these discrepancies are the result of an accumulation of errors over many molecular dimers in the crystal. The adverse effects of the remaining deficiencies of the Pixel formulation are expected to be less relevant for single dimer calculations.

We have selected 55 molecular dimers that, in our opinion, represent the most common recognition modes in organic crystals as well as the effects of electron-withdrawing substituents in increasing the "acidity" of C−H groups. Pixel total energies were then calculated as a function of intermolecular separation, along the most obvious approach coordinates (interplanar distance for aromatic ring dimers, X···H separation for hydrogen bonds) using rigid, standardized monomer geometries.[32] Equilibrium intermolecular distances and binding energies calculated by the Pixel method were compared with literature ones, when a high quality quantum chemical calculation was available; otherwise, potential-energy curves were recalculated at the MP2 or DFT 6-31G** level. The results are obviously very sensitive to basis set superposition error (BSSE), which depends on the chemical constitution of the interacting moieties at short range, so that its entity may be different even for two different orientations of the same dimer. Although the most frequent procedure is to consider both corrected and uncorrected energies, attaching more physical significance to the latter, sometimes the attitude of the quantum chemical community toward the counterpoise correction oscillates and uncorrected energies are considered for some purposes,[8,9] whereas it has also been suggested that the full counterpoise correction may, in some cases, overestimate the error[12] and that the use of 50% counterpoise correction may be advisable.[33] We have applied the standard counterpoise correction procedure ("counterpoise = 2" option[26]), and we report both uncorrected and corrected interaction energies. The width of the potential-energy well was estimated as corresponding to an energy increase of 5 kJ mol^{-1}, about $1.5RT$ at 400 K, an average melting temperature for an organic crystal, or about $2RT$ at room conditions.

3. Results and Discussion

For hydrogen-bonded dimers (see Table 1), the Pixel results are in very good agreement with the results of high-level quantum mechanical calculations as well as with the experimental results available for the water dimer.[34] In addition, the Pixel-calculated dimerization energies are in good agreement with the results of counterpoise-corrected MP2 ab initio calculations. For the $\pi-\pi$ interactions between parallel aromatic rings, the Pixel results are more similar to those obtained by MP2 calculations without counterpoise correction (see Table 2). This may suggest that the Pixel dimerization energies are overestimated, but the comparison with very high quality calculations for the benzene dimer[15]

Quantitative Ranking of Crystal Packing Modes

J. Chem. Theory Comput., Vol. 1, No. 5, 2005 **837**

Table 1. Equilibrium Distances, Binding Energies, and Widths of the Potential-Energy Well for Hydrogen Bonds

dimer	$R^{\circ a}$	ΔE^b	width^c	literature R° and ΔE
benzoic acid, cyclic O−H···O=C	1.75	67	1.65−1.95	
formic acid, cyclic O−H···O=C	1.75	67	1.65−1.95	1.68, 68[14]
formic acid, single O−H···O=C	1.75	38	1.55−2.05	1.76, 40[14]
pyridone, cyclic N−H···O=C	2.05	48	1.85−2.35	2.05, 42; 1.90, 68^d
formamide, cyclic N−H···O=C	2.0	52	1.85−2.2	2.0, 55[21]
formamide, single N−H···O=C	2.05	25	1.8−2.45	
methanol O−H···O−H	1.95	23	1.7−2.3	2.1, 22; 1.95, 28^d; 1.9, 23[6]
methanol-acetone O−H···O=C	2.0	19	1.7−2.5	
formamide-acetone N−H···O=C	2.0	19	1.75−2.45	
formamide-acetonitrile N−H···N	2.1	22	1.8−2.5	
formic acid-acetone O−H···O=C	1.8	31	1.55−2.1	1.9, 28; 1.9, 36^d
water	2.0	23	1.85−2.2	1.96, 22.6 exptl[34]

^{a} O···H or N···H hydrogen-bonding distance, Å. ^{b} Binding energy, kJ mol^{-1}. ^{c} Range of the distance coordinate for an energy increase of 5 kJ mol^{-1} from the minimum. ^{d} MP2/6-31G** with and without counterpoise correction.

shows that the best estimate of the interaction energy is even larger than the uncorrected MP2 estimate and is close to the Pixel value. A more serious difficulty is encountered for the interaction between the π system of benzene and highly polar

OH or NH bonds in water and ammonia; the strength of these interactions is clearly overestimated by Pixel. On the other hand, the C−H···π dimerization energies are well-represented by the Pixel formulation, the results being similar to those of high-level quantum chemical calculations and being between those of counterpoise-corrected and -uncorrected MP2 calculations.

The dimerization energies calculated by the Pixel method for dimers constructed over C−H···O and C−H···N contacts are in good agreement with quantum mechanical results (see Table 3), being always between counterpoise-corrected and -uncorrected MP2 energies, and as such, they are presumably slightly overestimated. Table 4 shows that the repulsion between approaching hydrogen-rich molecular rims is disfavored, as expected. This table also shows that the interaction between parallel aliphatic chains is too attractive in the Pixel representation. This effect is visible also in the calculated lattice energies of saturated hydrocarbon crystals, which systematically exceed the corresponding sublimation enthalpies.

All considered, one can see a consistent agreement between Pixel and quantum mechanics results for a wide variety of chemical environments, although the computational cost of Pixel calculations is a very small fraction of that of quantum chemical calculations.

Tables 1−4 can be used as working tables for the estimation and ranking of packing forces. The largest potential-energy gain is for the acid O−H···O=C hydrogen bond (30−40 kJ mol^{-1}), followed by the stacking of condensed aromatic rings or benzenes with polar substituents (20−30 kJ mol^{-1}) and by the hydrogen bond in amides (15−25 kJ mol^{-1}) or alcohols (20−25 kJ mol^{-1}). Contrary to

Table 2. Equilibrium Distances, Binding Energies, and Widths of the Potential-Energy Well for Recognition Modes Involving Aromatic $\pi-\pi$ or H···π Interactions

dimer	$R^{\circ a}$	ΔE^b	width^c	quantum mechanical results for R° and ΔE
		Parallel^d		
$C_6H_6-C_6F_6$	3.5	23	3.25−4.0	3.7, 15; 3.4, 28^e
1,3,5-$C_6H_3F_3$	3.6	20	3.3−4.0	3.7, 12; 3.5, 23^e
pyrimidine-benzoquinone	3.45	22	3.2−3.85	ΔE = 23 at 50% BSSE[19]
chlorobenzene	3.6	18	3.35−4.0	3.9, 7; 3.6, 17^e
C_6F_6	3.55	17	3.28−4.0	
C_6H_6	3.70	10	3.4−4.4	4.1, 3; 3.8, 10;^{e} 3.75, 13[15]
nitrobenzene	3.45	29	3.15−3.8	3.5, 20; 3.3, 41^e
		Offset Parallel^f		
benzene	3.6	12	3.3−4.25	3.4, 18[15]
naphthalene	3.6	26	3.35−3.9	≈3.7, ≈25[22]
benzoquinone	3.35	18	3.15−3.85	3.6, 9; 3.2, 23^e
		H···π Interactions		
benzene π−water^g	2.65	17	1.4−2.35	3.3, 12[12]
benzene π−ammonia^g	3.05	10	1.6−2.7	3.4, 8[12]
C−H···π acetylene−acetylene^h	2.6	8	2.15−3.5	2.7, 5; 2.7, 9^e
C−H···π benzene−benzene^i	2.65	11	2.25−3.5	2.4, 15; 2.7, 7;^{e} 2.45, 14[15]
C−H···π acetylene−benzene^i	2.6	12	2.1−3.4	2.9, 8; 2.7, 16;^{e} ΔE =13[13]
CH_3···π ethane−benzene^j	3.2	7	2.75−4.3	3.45, 2; 3.2, 7;^{e} ΔE = 6[13]

^{a} Equilibrium distance, Å. ^{b} Binding energy, kJ mol^{-1}. ^{c} Range of the distance coordinate for an energy increase of 5 kJ mol^{-1} from the minimum, Å. ^{d} Two rings on top of one another; R is the distance between ring planes. ^{e} MP2−6-31G** with and without counterpoise correction. ^{f} Two parallel rings, offset by half a ring length; R is the distance between ring planes. ^{g} O−H or N−H bond pointing to the center of the benzene ring; R is the O···ring or N···ring distance. ^{h} C−H of one acetylene pointing to the midpoint of the triple bond of the other; R is the H···midpoint distance. ^{i} C−H bond pointing to the center of the benzene ring; R is the H···center distance. ^{j} Ethane C−C bond perpendicular to the center of the benzene ring; R is the distance between the plane of methyl hydrogens and that of the ring.

Table 3. Equilibrium Distances, Binding Energies, and Widths of the Potential-Energy Well for Recognition Modes Involving C–H···N or C–H···O Contacts

acceptor[a] C–H donor	$R°$	ΔE[b]	width[c]	quantum mechanical results for $R°$ and ΔE
water acetylene	2.1	14	1.85–2.75	2.2, 12; 2.2, 17;[d] 2.2, 11[10]
water benzene	2.4	7	2.05–3.6	
water CF$_3$H	2.35	14	2.0–3.0	2.2, 21, no counterpoise correction[11]
water methane	2.6	3		2.7, 4, no counterpoise correction[11]
acetone acetylene	2.2	11	1.85–3.0	
acetone benzene	2.45	6	2.05–4.0	2.5, 5; 2.4, 9[d]
acetone CF$_3$H	2.4	12	2.0–3.2	
acetone methane	2.6	2.5		
ammonia acetylene	2.15	20	1.8–2.65	2.3, 15; 2.2, 22;[d] 2.3, 14[10]
ammonia benzene	2.45	9	2.15–4.2	
ammonia CF$_3$H	2.35	18	2.0–3.2	2.3, 24, no counterpoise correction[11]
ammonia methane	2.6	4		2.7, 3, no counterpoise correction[11]
acetonitrile acetylene	2.25	13	1.9–2.9	
acetonitrile benzene	2.5	6.5	2.15–4.2	2.7, 5; 2.6, 8[d]
acetonitrile CF$_3$H	2.4	14	2.0–3.1	
acetonitrile methane	2.6	2.5		
benzoquinone C=O···H–C[e]	2.35	15	2.1–3.0	
pyridimide-benzoquinone[f]	2.5	15	2.2–3.0	2.7, 11; 2.5,21;[d] $\Delta E = 19$ at 50% BSSE[19]

[a] A C–H bond points at the O or N atom of the acceptor molecule; R is the O···H or N···H distance, Å. [b] Binding energy, kJ mol^{-1}. [c] Range of the distance coordinate for an energy increase of 5 kJ mol^{-1} from the minimum, Å. [d] MP2–6-31G** with and without counterpoise correction. [e] Parallel coplanar rings, O···H cyclic double contact; R is the O···H distance, Å. [f] Parallel coplanar aromatic rings, C–H···O and C–H···N interaction; R is the O···H and N···H distance, Å.

Table 4. Analysis of Contacts between Nonpolar Atoms or Moieties

dimer	$R°$[a]	ΔE[b]	quantum mechanical results for $R°$ and ΔE
H$_3$C–H···H–CCH	broad	≈1	2.9, 2[13]
CH$_2$···H$_2$C ethylene	broad	≈2	
C–H···H–C coplanar benzene	2.5	3	2.4, 1; 2.4, 3[c]
Ar$_2$	3.9	1.2	
parallel ethane	2.7	5	3.0, 1.5; 2.8, 3[c]
parallel chain butane	2.5	9	2.7, 3; 2.5, 6[c]
parallel chain hexane	2.6	14	
CH$_3$–Cl···Cl–CH$_3$	no minimum		no minimum[c]
CH$_3$–Cl···CH$_3$Cl	3.2[d]	5.5	3.3, 3; 3.3, 4[c]

[a] H···H, Ar···Ar, or Cl···Cl distance, Å. Equilibrium distances are only approximate because the minima are always very broad. [b] Binding energy, kJ mol^{-1}. [c] MP2–6-31G** with and without counterpoirse correction. [d] Distance between Cl and the plane of methyl hydrogens, Å.

widespread conceptions, the hydrogen bond is not always the strongest intermolecular interaction. Nonpolar interactions among benzene rings are at a lower level in the hierarchy (10–15 kJ mol^{-1}), the three modes for pure benzene—on-top parallel, offset parallel, and perpendicular—being almost isoenergetic, a result that does not support simple-minded H(+)···π(−) or quadrupole–quadrupole interaction models. In the same energy range, one finds many interactions among C–H···X moieties (X = O, N, or a π system), but only when the donor hydrogen is highly acidic (acetylene, trifluoromethane). Lateral interactions between aliphatic chains are worth about 1.5 kJ mol^{-1} for each carbon atom, so that a hexane chain has about the same cohesive energy as a benzene ring. At a still lower level (<10 kJ mol^{-1}), one finds interactions between benzene C–H groups and O or N atoms, and the experimental results concur, if the total interaction energy between an oxyrane and a trifluoromethane molecule including three C–H···O or C–H···F short contacts is worth

about 6.7 kJ mol^{-1}.[35] Interactions between aliphatic C–H groups and all kinds of polar acceptors involve less than 5 kJ mol^{-1}, whereas Cl···Cl interactions are hardly cohesive at all, as already recognized.[36] The use of these last interactions to categorize intermolecular recognition leads to the oxymoron of a zero-energy bond.

The widths of the corresponding energy wells are even more revealing than the binding energies. These results are quite similar in the Pixel calculations and in all sorts of corresponding quantum chemical calculations. The expected vibrational amplitude for the stronger hydrogen bond in average thermal conditions is 0.3–0.5 Å, increasing to 0.5–0.7 Å for the weaker hydrogen bond or for aromatic ring stacking. These data are still compatible with a definite bonding interaction (the corresponding quantity for an average intramolecular single bond in organic compounds is 0.2–0.3 Å). On the contrary, the vibrational amplitudes of even the strongest C–H···O, C–H···N, or C–H···π "bonds", those formed by acetylenic protons, already exceed 1 Å, and those involving benzene or aliphatic hydrogens put these interactions at the limit of spontaneous dissociation. Unless a careful analysis is conducted to ensure that other contributions are even less relevant or are constant over all possible structural variations, the description and prediction (let alone control) of the crystal structures of complex and multifunctional organic compounds as depending on these weaker interactions is not to be encouraged.

4. Orientation Dependence

The results shown in the previous section concern binding curves for molecular dimers as a function of separation between centers of mass. The Pixel method also gives a clear picture of the angular dependence on the interaction, thanks to its partitioning into recognizable Coulombic-polarization and dispersion terms (Table 5). The benzene stacked dimer

Quantitative Ranking of Crystal Packing Modes

J. Chem. Theory Comput., Vol. 1, No. 5, 2005 **839**

Table 5. Angular Dependence of Some Typical Interactions between Aromatic Ring Systems[a]

	E_{coul}	E_{pol}	E_{disp}	E_{rep}	E_{tot}
		Benzene			
$\theta = 0$	3.7	−1.5	−20.6	8.8	−9.6
$\theta = 15$	3.7	−1.5	−20.6	9.1	−9.4
$\theta = 30$	3.7	−1.5	−20.6	9.1	−9.4
		1,3,5-TFB			
$\theta = 0$	−0.6	−0.7	−26.9	11.5	−16.7
$\theta = 20$	−1.4	−0.7	−26.8	12.0	−16.9
$\theta = 40$	−3.0	−0.7	−26.8	11.9	−18.6
$\theta = 60$	−3.8	−0.7	−26.9	11.9	−19.4
		1,4-Dinitrobenzene			
$\theta = 0$	5.0	−1.5	−37.4	18.9	−15.0
$\theta = 180$	−7.9	−1.7	−33.3	13.5	−29.5

[a] θ is the in plane rotation angle at fixed inter-ring distance equal to the equilibrium value in Table 1. $\theta = 0$ corresponds to exact on-top parallel stacking, with eclipsed substituents. Binding energy = $-E_{tot}$.

is quite insensitive to the reciprocal orientation of the two rings. The 1,3,5-trifluorobenzene stacked dimer is, instead, sensitive to orientation, because the Coulombic term is unfavorable when fluorine atoms are on top of fluorine atoms and becomes favorable when fluorine atoms are on top of hydrogen atoms. The effect is obviously magnified in the case of the more strongly polar nitrobenzene molecule; in the dimer, an antiparallel orientation of the nitro substituents is largely favored on a purely Coulombic basis, as expected.

5. Conclusions

Our results reveal that, even for strongly bound dimers, like stacked polar aromatic rings or hydrogen-bonded species, many different interaction modes ensure very similar binding energies, and identifying the leading cohesion energy contributions may be difficult. When dimerization energies fall below 20 kJ mol^{-1}, a large pool of different interaction modes, many of which are bound to appear in nearly all crystal packings of ordinary organic molecules, have approximately equal energies and are highly "stretchable" at ordinary temperatures. In this light, special caution should be exerted in the structural analysis of organic crystals in terms of the structure-defining power of localized interactions between certain groups. In particular, the role of the so-called "weak hydrogen bonds" has been greatly overemphasized, as already suggested in critical examinations.[37]

A necessary (although maybe not sufficient) condition for consistent predictions is a careful evaluation of small differences in cohesion energies arising from interactions between delocalized electron densities. Also important must be an even more careful consideration of cooperative effects in the propagation of long-range order in determining the amount of stretch from the free dimer minimum energy structure (a planned extension of the present work is the analysis of destabilizing options, or "antirecognition" interaction modes, that packing molecules cannot take). Besides, crystallization out of this near continuum of structural possibilities has a good chance of being dictated by kinetics rather than by thermodynamics.

Absolute values in our tables do change by a few kJ mol^{-1} upon different theoretical treatments, but the agreement between the different methods, some of which are of indisputable maturity, gives confidence in the Pixel results and strongly suggests that relative orders of magnitude must not change significantly, so that the above conclusions may be refined but not substantially changed.

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