Attractions and Repulsions in Molecular Crystals: What Can Be Learned from the Crystal Structures of Condensed Ring Aromatic Hydrocarbons?

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Received September 25, 1998

Introduction

It is a matter of common observation that compounds consisting of large molecules tend to have higher melting points, higher boiling points, and lower solubility than compounds consisting of small molecules. Large molecules have a greater cohesive energy than small ones. This is obvious from Figure 1 where standard vaporization enthalpies $\Delta H°$(vap) of normal alkanes C_nH_{2n+2} are plotted against the number N of carbon atoms.[1] There is an almost perfect linear dependence; $\Delta H°$(vap) increases by 4.9 kJ mol^{-1} for each additional methylene group in the alkane chain.[2,3] This effect is largely attributable to sheer size. To break free from a condensed phase, a large molecule has to overcome more attractive interactions with its neighbors than a small one.[4] Less obvious is perhaps the notion that repulsions also influence the stability of condensed phases. Using a series of rigid aromatic hydrocarbons as an example, this Account analyzes the balance of forces in a crystal structure.

Correlations such as the one in Figure 1 are typical of homologous series of liquid and solid compounds. In general, vaporization enthalpies of liquids and sublimation enthalpies of crystals show smoother behavior than do fusion enthalpies of solids. The solid−liquid transition is more complicated because of the possibility and frequent occurrence of premelting phase transitions in the solid. Unfortunately, however, the relevant experimental thermodynamic data are not always available, and in particular, sublimation enthalpies of solids have been measured for only a few hundred[3] of the almost 200 000 known organic crystal structures.[5] In their absence we are forced to resort to calculated estimates of the missing information. For crystals, estimates of lattice energy can be made from a knowledge of the crystal structure with the help of empirical atom−atom pair potential functions. Thus, lattice packing energies are calculated simply as PE = $\sum A \exp(-BR) - CR^{-6}$, where A, B, and C are empirical parameters for each atom pair type and R is any intermolecular interatomic distance from an atom in a reference molecule. When these parameters are suitably calibrated, calculated lattice energies should be directly comparable with sublimation enthalpies at 300 K, since these quantities are used in the energy scaling. Even when the crystal structure is unknown, empirical correlations allow sublimation enthalpies $\Delta H°$(sub) to be estimated roughly from size-dependent molecular parameters such as the number of valence electrons (Z) or van der Waals surface area (S): for example, in non-hydrogen-bonded oxohydrocarbons[6]

$$\Delta H(\text{sub}) = 0.841Z + 39.3 \quad \text{kJ mol}^{-1}$$

$$\Delta H(\text{sub}) = 0.322S\ (\text{Å}^2) + 37.2 \quad \text{kJ mol}^{-1}$$

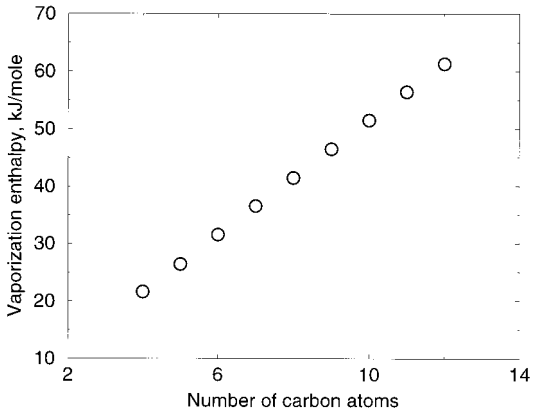

FIGURE 1. Standard vaporization enthalpies, $\Delta H°$(vap), of normal alkanes C_nH_{2n+2}.

Condensed Ring Aromatic Hydrocarbons

It seems useful to try to extend and improve such correlations for other groups of crystal structures. One can expect them to work best for groups of compounds that are "chemically similar", that is, containing the same elements and the same kinds of chemical bonds. With the help of the Cambridge Structural Database[5] (CSD) we have collected a sample of 24 crystal structures of planar, condensed-ring, aromatic hydrocarbons[7] and estimated various physical properties for them with the help of a reasonably reliable set of atom−atom pair potentials. For consistency, and because X-ray hydrogen atom positions

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10.1021/ar980007+ CCC: $18.00
Published on Web 05/05/1999

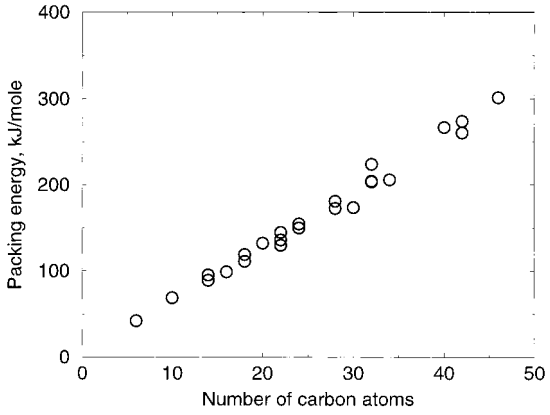

FIGURE 2. Calculated estimates of packing energy ($-E = \Delta H°$(sub)) for 24 aromatic hydrocarbon crystals[7] with known crystal structure. The increase is 6.4 kJ/mol per carbon atom.

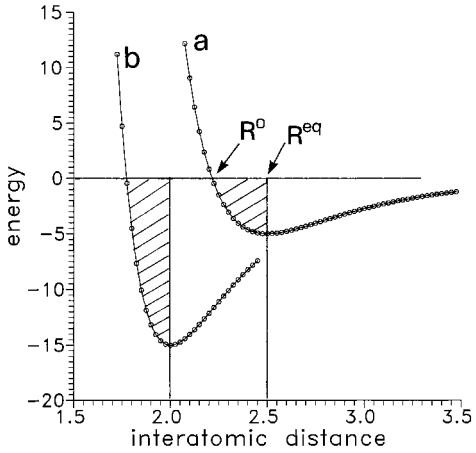

FIGURE 3. Typical nonbonded atom−atom curves (distances and energies in arbitrary units): (a) shallow minimum, small curvature; (b) deeper minimum, sharper curvature. $R < R^{eq}$, repulsive, $R > R^{eq}$, attractive, $E < 0$, stabilizing, $E > 0$, destabilizing. Hatching denotes regions of repulsion (force) and stabilization (energy). In molecular crystals, repulsive stabilizing contacts are common.

are unreliable, H atoms were placed on the bisector of the relevant C−C−C angle with a C−H distance of 1.08 Å, resulting in slight discrepancies with published H positions. Where comparison is possible with experimental sublimation enthalpies, the agreement is good.[8] Figure 2 shows calculated lattice energies E plotted against N, the number of carbon atoms in the molecule. We note that E varies from about 40 kJ mol^{-1} (roughly the energy of two hydrogen bonds and nearly the same as the vaporization enthalpy of water) for benzene to almost 300 kJ mol^{-1} (roughly the energy of a typical covalent bond) for the largest molecules.

The crystal correlation is not as perfect as for the vaporization enthalpies of aliphatic hydrocarbon liquids. It cannot be, because, even for molecules of similar size and shape, crystal packing arrangements can be very different, in contrast to the more similar averaged molecular environments in liquids. The differences E(naphthalene) − E(benzene) and E(anthracene) − E(naphthalene) are identical, a little less than the lattice energy of benzene. Of course, structural variability is greater here than in the normal alkanes; for example, E(anthracene) > E(phenanthrene). Nevertheless, the size effect is clearly at work, and the trend is clear. Linear regression of the data in Figure 2 leads to an estimated increase in packing energy of 6.4 kJ mol^{-1} per additional C atom. It may come as a surprise that this increase per additional C atom is less than the corresponding estimate of 8.8 kJ mol^{-1} (see ref 2) for n-alkanes. We merely note that the molecular polarizability of n-hexane (11.9×10^{-24} cm^3) is larger than that of benzene (10.3×10^{-24} cm^3),[9] a fact that seems at variance with popular theories of molecular interaction invoking highly polarizable π-electrons in benzene rings. The nomenclature of such special features of the crystal packing of aromatic hydrocarbons, such as $\pi-\pi$ or T-type interactions, is as varied as it is ill-defined. In any case, these effects do not seem to contribute much to packing energy.

Atom−Atom Pair Potentials

Much money, time, and effort are currently invested in computer modeling exercises, mostly using atom−atom pair potentials, as pioneered by Kitaigorodskii.[10] Various types of potential are in use, some based on attempts to imitate the underlying physics of the interactions (and therefore including terms designed to represent specifically charge, induction, dispersion interactions, exchange repulsion, charge transfer, etc.), others on parametrization of standard potential functions. Of these, the most popular are $E(R) = A \exp(-BR) - CR^{-6}$ and $E(R) = AR^{-12} - BR^{-6}$, where A, B, and C are simply treated as empirical constants for each type of atom−atom interaction and R is the internuclear distance. Coulombic (i.e., R^{-1}) terms may also be added, if regarded as necessary. Since there is no rigorous way of factorizing the total interaction energy into separate terms, and since we are interested in functions that are readily transferable from one system to another and are as far as possible characteristic of the atom−atom pairs, regardless of their chemical environment, we admit to a preference for the purely empirical approach,[8] whenever practicable. Omission of charge parameters, and of the troublesome R^{-1} terms, is an additional bonus. Indeed, for the complex interactions involved in condensed phases, this is the only feasible approach. What we lose in rigor, we gain in utility.

All atom−atom pair potential curves share some characteristic common features (Figure 3): (1) The deeper the energy minimum, the sharper the curvature at the turning point. (2) The anharmonicity of the function is such that the cubic term in a power series expansion about the minimum is always negative; that is, when the interatomic distance is increased, energy rises less sharply from its minimum value than when it is decreased. While these features are indeed common to all interatomic interactions, we note that in a valence bonding potential the system spends most of its time in a nearly or completely harmonic environment, whereas this is not so for the much shallower intermolecular potentials. While a covalent bond is kept together by a resisting force which is nearly equally strong on both sides of the minimum, molecules in the bulk of a crystal are held together by their

Table 1. Atom−Atom Potentials and Interatomic Distance (Å)

type	depth (J mol^{-1})	R^{eq}	R^0	R^{vdW}
H···H	42	3.36	2.98	2.4
H···C	205	3.29	2.92	2.9
H···O	506	2.80	2.48	2.6
C···C	389	3.89	3.45	3.4
N···N	628	3.70	3.28	3.0
O···O	335	3.61	3.20	2.8
F···F	293	3.20	2.84	2.7
S···S	1862	3.83	3.39	3.7
Cl···Cl	1004	3.83	3.39	3.6

mutual attraction, but are clamped in their places—in contrast to molecules in a liquid—mainly by resistance to compression, in other words, by repulsions that oppose the disentanglement of interlocking molecules and thus hinder any displacement from their equilibrium positions and orientations.

At high enough temperature, increased kinetic energy enables the molecules to slide past one another, and the crystal then transforms to a liquid with a sudden increase in intermolecular distances. For molecules on the crystal surface, the situation is different. Such molecules can escape from the crystal in the direction normal to the surface without undergoing compression. They are held in their place in the crystal by attractive forces and may escape if they have sufficient kinetic energy to overcome these forces. The relevant quantity here is the surface attachment energy, which is less than the lattice energy and different for different crystal faces.[11] We also note some elementary but essential points. At distances greater than R^{eq} the interaction term is stabilizing and attractive, at R^{eq} the interatomic force is zero by definition, and at distances smaller than R^{eq} the force becomes repulsive (Figure 3). Thus, for distances smaller than R^{eq} and larger than R^0 the interaction term is stabilizing and repulsive, and for distances smaller than R^0 it is destabilizing and repulsive. We refer to interactions at distances less than R^{eq} as "contacts". Contacts are then the subset of the totality of pairwise interactions that are repulsive, although they will often correspond to stabilizing terms in the energy. We need to be careful in distinguishing between "attraction" meaning attractive force and "attraction" meaning stabilizing energy contribution. To avoid confusion, we shall use the term attraction to refer only to force and the term stabilization to refer to energy. Similarly we distinguish between repulsion (force) and destabilization (energy): we may refer to these as the virial and energetic aspects of the interaction, respectively.

In interactions involving contacts between pairs of atoms on the peripheries of different molecules, the force is repulsive. The associated energy terms may be stabilizing or slightly destabilizing. In terms of an atom−atom potential curve (Figure 3), we are climbing a little from the energy minimum at R^{eq} up the repulsive slope, which is usually very steep, so we cannot climb far. Table 1 shows the interatomic distances R^0 at which the interaction energy is zero for several typical atom−atom potential curves. Distances longer than R^0 correspond to stabilization, shorter ones to destabilization. For the deeper atom−atom potentials (e.g., Cl···Cl or S···S), the van der Waals distance R^{vdW} is shorter than R^{eq} but longer than R^0; i.e., the van der Waals distance corresponds to a repulsive force but to an energy stabilization. For the shallow potentials (e.g., H···H), R^{vdW} is shorter than both R^{eq} and R^0; here the van der Waals distance is repulsive and destabilizing. Different potential sets may differ in detail, but this interpretation is broadly consistent with the physics of the interaction.

Repulsive Force Must Balance Attractive Force

Along a given homologous series of molecules, the attractive forces arising from the atom−atom interaction potentials should be of essentially constant type and strength. Indeed, this is the justification for using the same C···C, C···H, and H···H potential functions throughout the series. Insofar as these forces are additive, molecules along a given series should experience an increasing intermolecular pull with increasing size; for example, in the atom−atom approximation, two N-atom molecules share N^2 attractive terms. We have seen that large molecules of a given structural type indeed have a stronger mutual attraction than small molecules of the same type, as reflected in the heats of sublimation. In an equilibrium situation, stronger attraction must be balanced by stronger repulsion. In a crystal, it is not just a matter of balancing forces from individual atom−atom interactions; the force on a given atom does not arise solely from its interaction with its closest nonbonded neighbor but is the result of forces arising from its interactions with many other atoms. Most of these interactions are attractive, for attractive forces extend over longer distances, while repulsive forces operate only at short range, and then only between atoms on molecular boundaries, that is, between atoms in different molecules that are in contact. For each such contact pair interaction, there must be many noncontact pairs at longer distances in the attractive range.

Since overall attraction between molecules increases with molecular size, it follows that, for equilibrium in the crystalline state, overall repulsion must also increase with molecular size. Short intermolecular contact distances should therefore tend to become even shorter—an expectation that runs contrary to the simplistic view that atoms can be assigned characteristic van der Waals radii, or at least makes atoms more compressible than usually thought. In aromatic hydrocarbon crystals, the shortest intermolecular distances are always between hydrogen atoms. Figure 4 shows that there is indeed a correlation between the shortest H···H distance in the crystal and molecular size. Apart from one outlier at 2.03 Å (pyrene, $C_{16}H_{10}$),[12] the three shortest distances, 2.11, 2.15, and 2.16 Å, occur in the crystals of the three largest molecules, kekulene, $C_{46}H_{24}$, dibenzonaphthopyranthrene, $C_{42}H_{20}$, and hexabenzocoronene, $C_{42}H_{18}$. For comparison, the shortest H···H distance in crystalline benzene is about 2.6 Å and the van der Waals diameter of hydrogen is usually taken as 2.4 Å. A recent survey of intermolecular distances in organic crystal structures[13] shows that only a tiny fraction

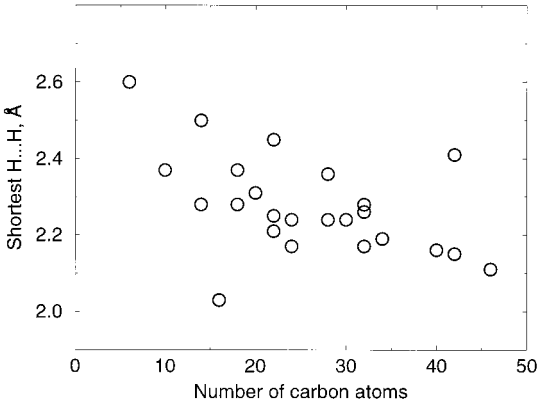

FIGURE 4. Aromatic hydrocarbon crystals:[7] shortest intermolecular H···H distance, R(H···H), versus number N of carbon atoms in the molecule. The regression line is $R(\mathrm{HH}) = 2.43 - 0.0061N$.

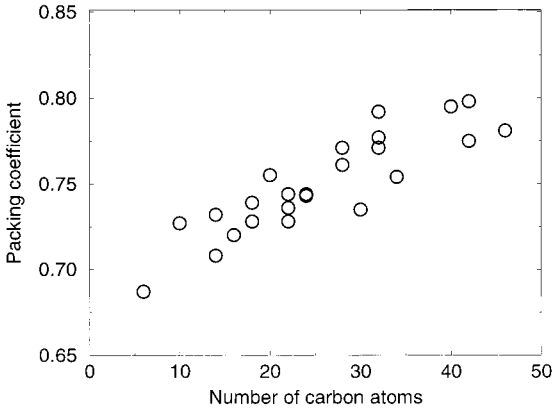

FIGURE 5. Aromatic hydrocarbon crystals:[7] packing coefficient k versus number N of carbon atoms in the molecule. The regression line is $k = 0.69 + 0.002N$.

of intermolecular H···H distances are shorter than 2.2 Å. Of course, the equilibrium balance of forces not only involves the shortest H···H distance in each crystal structure, but embraces many intermolecular interactions. More detailed analysis shows that, as the molecules become larger, the whole pattern of H···H, C···H, and C···C contact distances moves toward closer mutual approach of the molecules. Stronger intermolecular attraction is seen to go with tighter crystal packing, and both effects are correlated with molecular size, at least in the sample considered here.

The fact that the closest H···H contact distances in our sample cover a range from 2.6 to 2.1 Å should be a warning that conclusions based on the hard sphere approximation for atoms in condensed phases need to be treated with reserve. In particular, any attempt to derive "improved" sets of van der Waals radii to predict or interpret intermolecular contact distances in condensed phases seems a waste of effort.

We have been assuming that intermolecular interactions can safely be broken down into atom−atom pairwise additive terms. This will not always be valid, but it should be a reasonable approximation for atom−atom potentials calibrated explicitly against the observed atom−atom distance distributions in organic crystals. There should be nothing disturbing about the concept of repulsive destabilizing contacts, especially if one abandons the simplistic view of a crystal as a static architecture. The atomic "positions" in a crystal are time- and space-averaged positions, and at elevated temperatures (such as room temperature), the atoms undergo sizable displacements from these averaged positions in the course of molecular translational and especially rotational vibrations. Thus, even for a structure with normal contact distances, peripheral atoms may be instantaneously displaced quite a long way up the repulsive branch of the interaction potential curves in the course of a molecular vibration. The energy barriers resisting molecular motions in crystals arise mainly from peripheral atoms bumping together rather than being pulled apart.

The above discussion shows that any attempt to interpret short specific contact distances (as, for example, in postulated weak C−H···O hydrogen bonds) must consider both energetic and virial aspects of the problem—a requirement that is not always followed. The tendency to identify short contact distances exclusively or mainly with specific attractive forces between the atoms concerned fails this condition. To preserve equilibrium, short intermolecular distances in crystals are *always* associated with repulsive forces. The very concept of structure-defining interactions may need reconsideration.

Close Packing

A widely accepted figure for assessing tightness of packing is the packing coefficient k, the ratio of the molecular volume V_{mol} to the volume available in the particular condensed phase we are interested in.[14] For close packing of spheres, $k = 0.74$, for close packing of circular disks or cylinders, $k = 0.907$, and for close packing of ellipsoids, k lies between these values. For molecular crystals, $k = ZV_{\mathrm{mol}}/V_{\mathrm{cell}}$, where Z is the number of molecules in the unit cell. Although there is no rigorous definition of V_{mol}, it can be estimated once "sizes" are assigned to the constituent atoms. Different estimation methods give similar results. Here we have used the most straightforward, known as Kitaigorodski's spheres and caps method.[10] For molecular crystals k usually lies in the range 0.65−0.77.[10] For our sample, it increases from 0.68 for benzene to 0.80 for hexabenzocoronene.

The tendency for k to increase with molecular size (Figure 5) is due to a combination of two factors: one is the tendency of molecules to be pulled into closer mutual contact by the greater attractive forces; the other is that, as the number of condensed rings increases, the molecules become more graphite-like.[15] One may note that pyrene is no longer an outlier. Its k value fits nicely into the general trend. One must remember that thermal expansion coefficients of molecular crystals may be quite large and that therefore k may change considerably with temperature (and pressure). For benzene it changes by about 10%, from 0.73 at 0 K to 0.66 close to the melting point.[16] In benzene II, the high-pressure form, k is around 0.82 at 294 K and 25 kbar,[17] so one can extrapolate to an estimated k of around 0.9 at 0 K and 25 kbar. This is close

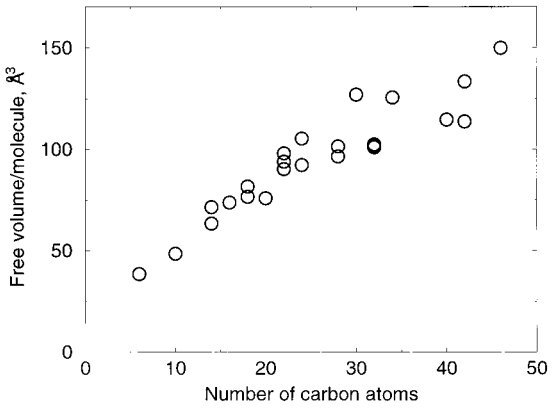

FIGURE 6. Aromatic hydrocarbon crystals:[7] free volume per molecule, $V_{cell} - ZV_{mol}$, versus the number of carbon atoms in the molecule.

to the value for close packing of circular disks. Benzene may be an extreme example, but it typifies the general tendency.

The packing coefficient k is a fraction, a dimensionless number. For a given k, as V_{mol} rises, so does the volume of empty space, $V_{cell} - ZV_{mol}$. Thus, with increasing molecular size, although the fraction of free space tends to decrease, the absolute volume of empty space per molecule tends to increase (Figure 6). As far as the packing energy is concerned, empty space is wasted space. Moreover, dispersive interactions are always stabilizing and additive in the atom−atom pair approximation. According to the empirical atom−atom potentials we and others have used,[8] C···C interactions still yield small stabilization contributions at separations as large as 5−6 Å.[18] Figure 7 shows the convergence of lattice sums as a function of cutoff for two representative compounds. As molecular size increases, these additional contributions to intermolecular atom−atom stabilization energy clearly outweigh the energy deficit due to wasted space, in agreement with the regular increase in molar sublimation enthalpies for aromatic hydrocarbon crystals with their more or less disk-shaped molecules.

Packing coefficients as high as those for disk-shaped aromatic hydrocarbons may not be possible for other molecular types. If the molecules are less tightly packed in the crystal, they will be subject to weaker restoring forces and hence to larger displacement amplitudes from their equilibrium positions and orientations, at a given temperature. Such crystals will have higher entropy than tightly packed ones,[18] and hence rotationally or translationally disordered phases may become thermodynamically stable as temperature is raised and entropic effects become more important. Increase the temperature, lower the packing further, and the crystal melts with a characteristic drop of 10% or more in density.[10,20] Viewed from the other direction, crystallization requires that molecules condense into a close-packed pattern. When crystals are grown from solution, a more dense packing may sometimes be achieved if large intermolecular cavities are occupied by solvent molecules to form "inclusion compounds". For this to occur, the extra stabilization energy due to host−guest interactions should normally be greater

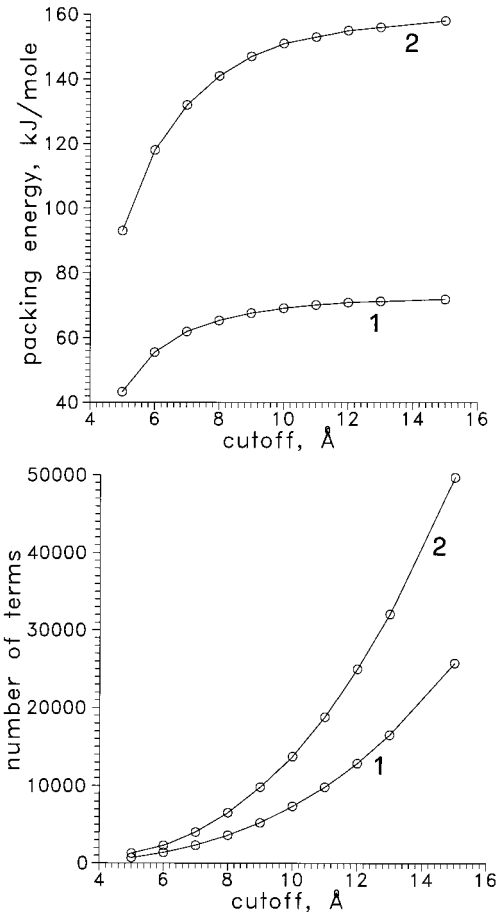

FIGURE 7. (a, top) Calculated packing energy as a function of the cutoff applied to lattice summations. (b, bottom) Number of terms in the lattice summation in each case: (1) naphthalene, (2) coronene.

than the cohesive energy of the solvent by at least $T\Delta S$, where ΔS is the entropic cost of transferring a solvent molecule from the liquid to a site in the crystal where it is relatively immobile.[21] Depending on the amount of stabilization associated with the host−guest interaction, the solvent molecules will tend to escape as the temperature is raised. [22] Of course, condensed-ring aromatic hydrocarbons may not form solvates or clathrates since they are practically insoluble in any solvent.

For molecular shapes that contain "bumps" and "hollows", a popular, if somewhat reductive, interpretation of the close-packing principle requires that bumps in one molecule must be fitted into the hollows of another to attain complementarity of molecular surfaces, as emphasized by Pauling and Delbrueck many years ago.[23] Molecules that pack well together must then be self-complementary in that sense. For a given molecule, we can therefore expect a good correlation between packing coefficient and lattice energy, as confirmed by the results of computational[24] and experimental[25] studies. Nevertheless, for a given molecular size and shape, several almost equidense and hence almost equienergetic arrangements are often possible. Thus, important as the close-packing principle may be, its predictive power is limited. From this point of view, the frequent occurrence of polymorphism comes as no surprise. Moreover, since less dense struc-

tures are likely to have higher vibrational entropy, there is no guarantee that the most tightly packed polymorph, even if it has the largest packing energy, will have the lowest free energy at ambient temperature.

Implications for Molecular Recognition and Crystal Nucleation

The association of large molecules in solution is favored by entropic factors (partial liberation of bound solvation shell to bulk solvent), but intermediate- to long-range dispersion interactions may be important too. In contrast to Coulomb interactions, which may be attractive or repulsive and hence tend to cancel out at long distances, all terms in the dispersive interaction are attractive, and since there are very many of them, they may sum up to a considerable attractive force.[26] To a first approximation, intervening solvent molecules will not weaken this attraction (compared with vacuum); indeed, they may add to it, by acting as further attraction centers between surrounding solute molecules. Differences in medium polarizability and density may also play a role. At a given temperature, translational (equipartition) kinetic energy is the same for small or for large molecules, while the attractive force is larger for the latter; in this simplified model, therefore, large molecules should meet more frequently than would be expected on the basis of random diffusion, and once in contact, they should stick together more strongly (longer) than for small-molecule association. Thus, in addition to any specific short-range molecular recognition factors (hydrogen-bonding, donor–acceptor interactions, etc.) there is a generalized, nonspecific mutual attraction that is greater for large molecules and supramolecular systems than for small ones.[27] Such factors may play a role in the aggregation of biomolecules and in crystal nucleation.

Summary and Conclusions

The additive nature of dispersive interactions means that the mutual attraction between large molecules should be stronger than between small molecules. Therefore, in an equilibrium situation, as in a crystal, intermolecular repulsion must also increase with molecular size. A survey of crystal structures of 24 condensed-ring aromatic hydrocarbons shows that the larger molecules indeed tend to pack more tightly than the smaller ones, with intermolecular distances up to 0.3 Å shorter than accepted van der Waals distances. It is essential to distinguish here between attractive and repulsive *forces*, and stabilizing and destabilizing *energies*. The equilibrium crystal structure corresponds to a balance between attractive and repulsive forces. The anharmonic shape of dispersion–repulsion potential curves implies that a crystal is held in this structure mainly by resistance to compression, that is, by repulsions that prevent the disentanglement of interlocking molecular surfaces.

Correlations among molecular size, packing energy, and other crystal properties make it possible to predict the sublimation enthalpy and density of unknown aromatic hydrocarbons with considerable confidence. However, they cannot be expected to apply without modification to other groups of compounds. For example, extrapolation of the linear regression shown in Figure 2 would lead one to predict a sublimation enthalpy of about 380 kJ mol^{-1} for C_{60}, roughly double the experimental value of 182 kJ mol^{-1}.[28] The free molecular surface is a good indicator of the extent of availability of a given molecule to intermolecular interactions, and the free surface of C_{60} is about half (only one side) of the available surface of a flat, unwrapped aromatic hydrocarbon.

Long-range periodicity, the characteristic property of the crystalline state, is produced by short-range interactions, resulting in optimal space filling. We are not aware of any formal proof that the requirement of optimal space filling of a collection of identical (or enantiomorphic) molecules necessarily leads to a periodicity, but it seems to us almost intuitively to be true;[29] imagine the effect of any deviation from strict periodicity in the periodically symmetric two-dimensional patterns produced by the late Maurits Escher.[30]

References

(1) Majer, V.; Svoboda, V. *IUPAC Chemical Data Series No. 32*; Blackwell Scientific Publications: Boston, MA, 1985.

(2) The corresponding sublimation enthalpies show an even–odd alternation arising from the existence of two types of crystal structures. They are also much less reliable than the vaporization enthalpies of the liquids, partly because they are influenced by phase transitions in the solid state and partly because of intrinsic inaccuracies due to experimental difficulties in measuring $\Delta H°$(sub). Nevertheless, the size effect is clearly present. From data provided in ref 3, $\Delta H°$(sub) at 298 K increases in the higher *n*-alkanes by about 8.8 kJ mol^{-1} for each additional methylene group. See also: Filippini, G.; Gavezzotti, A.; Simonetta, M.; Mason, R. Lattice Energies of Crystals of n.Alkanes: Molecular Motions, Defects and Phase Transitions. *Nouv. J. Chim*. **1981**, *5*, 211–217.

(3) Chickos, J. S. Heats of Sublimation. In *Molecular Structure and Energetics*; Liebman, J. F., Greenberg, A., Eds.; Verlag Chemie: Weinheim, 1987; Vol. 2.

(4) Since the molecular weight (MW) of alkanes also depends linearly on the number *N* of carbon atoms, it follows that enthalpies of vaporization and sublimation per gram of substance, $\Delta H°$(vap)/MW and $\Delta H°$(sub)/MW, remain essentially constant throughout the series.

(5) The Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, England, produces and distributes the Cambridge Structural Database (CSD), which contains, in computer-readable form, unit cell dimensions, space groups, atomic coordinates, and bibliographic data for organic and organometallic crystals of known structure, plus software for retrieval, visualization, and statistical analysis of the results. The CSD contains almost 200 000 entries and is expanding by about 20 000 entries annually.

(6) Gavezzotti, A. Are Crystal Structures Predictable? *Acc. Chem. Res.* **1994**, *27*, 309–314.

(7) Since we are interested in comparing intermolecular distances, which are temperature-dependent quantities, we chose results of structure determinations at room temperature or as close as possible. Structures showing pronounced disorder effects were excluded. The CSD refcodes are BENZEN, NAPHTA10, PHENAN12, ANTCEN07, PYRENE02, CRYSEN01, BZPHAN, BNPYRE10, DBNTHR01, DBNTHR10, ZZZOYC01, CORONE02, TEBNAP10, DBPERY, TBZPYR, DNAPAN, OVALEN01, CORXAI10, DBZCOR, TBZPER, QUATER10, HBZCOR01, DUPHAX, and KEKULN10.

(8) Filippini, G.; Gavezzotti, A. Empirical Intermolecular Potentials for Organic Crystals: The '6-exp' Approximation Revisited. *Acta Crystallogr.* **1993**, *B49*, 868−880. Ideally, calculated lattice energies should be scaled to sublimation enthalpies at 0 K, but experimental estimates of the latter quantity are practically nonexistent. Sublimation enthalpies at 300 K are available for several hundred organic crystals (ref 3), but this is only a tiny fraction of those of known structure.

(9) *CRC Handbook of Chemistry and Physics*, 73rd ed.; Lide, D. R., Ed.; CRC Press: Boca Raton, FL, 1992.

(10) Kitaigorodskii, A. I. *Molecular Crystals and Molecules;* Academic Press: New York, 1973.

(11) Despite the introduction of techniques such as scanning tunneling microscopy (STM), atomic force microscopy (AFM), and low-energy electron diffraction (LEED), the structure of molecular crystal surfaces is not known in sufficient detail to enable the accurate determination of intermolecular contact distances between and within surface layers. However, it seems clear that crystal surfaces tend to have low packing density and often exhibit a high degree of mobility approaching that of a liquid: Somorjai, G. A. *Introduction to Surface Chemistry and Catalysis;* Wiley: Interscience: New York, 1994; p 42.

(12) The crystal structure of pyrene (pyrene I) has been the subject of several investigations by both X-ray and neutron diffraction, and there seems no doubt that it contains an anomalously short intermolecular H···H contact distance (2.03−2.07 Å). The exact value depends on which analysis one chooses and how the hydrogen positions are estimated. The structure is built from pairs of pyrene molecules associated into well-defined dimers across inversion centers. On cooling below about 100 K, pyrene I undergoes a first-order transition to a closely related structure in which very similar dimeric units alter their relative orientation in such a way as to alleviate the anomalously short H···H distance, which is actually longer in the low-temperature structure than at room temperature. See: Knight, K. S.; Shankland, K.; David, W. I. F.; Shankland, N.; Love, S. W. The Crystal Structure of Perdeuterated Pyrene II at 4.2 K. *Chem. Phys. Lett.* **1996**, *258*, 490−494.

(13) Rowland, R. S.; Taylor, R. Intermolecular Nonbonded Contact Distances in Organic Crystal Structures: Comparison with Distances Expected from van der Waals Radii. *J. Phys. Chem.* **1996**, 100, 7384−7391.

(14) Kitaigorodskii, A. I. *Organic Chemical Crystallography;* Consultants Bureau: New York, 1961.

(15) The packing coefficient of graphite can be taken as equal to or slightly less than 1, depending on the value adopted for the "thickness" of a carbon atom in a graphite layer.

(16) Estimated from results by Jeffrey et al. (Jeffrey, G. A.; Ruble, J. R.; McMullan, R. K.; Pople, J. A. The Crystal Structure of Deuterated Benzene. *Proc. R. Soc. London* **1987**, *A414*, 47−57) (hexadeuteriobenzene at 15 K) and by Cox et al. (Cox, E. G.; Cruickshank, D. W. G.; Smith, J. A. S. The Crystal Structure of Benzene at −3 °C. *Proc. R. Soc. London* **1958**, *A247*, 1−21) (benzene at 270 K). The value 0.68 in our compilation (Figure 5) is based on a study at 218 K by Bacon et al. (Bacon, G. E.; Curry, N. A.; Wilson, S. A. A Crystallographic Study of Solid Benzene by Neutron Diffraction. *Proc. R. Soc. London* **1964**, *A279*, 98−110).

(17) Piermarini, G. J.; Mighell, A. D.; Weir, C. E.; Bloch, S. Crystal Structure of Benzene II at 25 kilobars. *Science* **1969**, *165*, 1250−1255.

(18) For what the numbers are worth, the C···C potential we have used, $E(R) = 226145 \exp(-3.47R) - 2418R^{-6}$ (E in kJ mol^{-1}, R in Å), with a minimum at $E(3.89) = -385$ J mol^{-1}, has $E(5) = -146$ J mol^{-1} and $E(6) = -50$ J mol^{-1}.

(19) It has indeed been shown (Gavezzotti, A.; Filippini, G. Polymorphic Forms of Organic Crystals at Room Conditions: Thermodynamic and Structural Implications. *J. Am. Chem. Soc.* **1995**, *117*, 12299−12305) that, in polymorph pairs, the crystal with higher density mostly has a lower lattice vibrational entropy.

(20) Despite the remarkable ice/water transition, we are not aware of a single organic compound that contracts on melting.

(21) For water, this entropic cost lies in a range up to about 30 J mol^{-1} K^{-1}, corresponding to a free enthalpy cost of up to 9 kJ mol^{-1} at 300 K. See: Dunitz, J. D. The Entropic Cost of Bound Water in Crystals and Biomolecules. *Science* **1994**, *264*, 670.

(22) As H. M. Powell pointed out many years ago (The Structure of Molecular Compounds. Part IV. Clathrate Compounds. *J. Chem. Soc.* **1948**, 61−73) the formation of inclusion compounds is also possible even in the absence of attractive forces between host and guest. The guest molecule may simply be caught during crystal formation and held in an intermolecular cavity by repulsive forces: "...When this molecule approaches a possible hole of exit its outward passage will be opposed by the repulsive forces that arise when any two atoms approach closely...". Powell introduced the term "clathrate" compound to describe this situation, and it seems a pity that the term is often applied indiscriminately for inclusion compounds in general. Powell's emphasis on the importance of repulsive forces in mantaining crystal structures comes close to views expressed in this Account.

(23) Pauling, L.; Delbrueck, M. The Nature of the Intermolecular Forces Operative in Biological Processes. *Science* **1940**, *92*, 77−79.

(24) (a) van Eijck, B. P.; Spek, A. L.; Mooij, W. T. M.; Kroon, J. Hypothetical Crystal Structures of Benzene at 0 and 30 kbar. *Acta Crystallogr.* **1998**, *B54*, 291−299. (b) Gavezzotti, A. Polymorphism of 7-Dimethylaminocyclopenta[c]coumarin: Packing Analysis and Generation of Trial Crystal Structures. *Acta Crystallogr.* **1996**, *B52*, 201−208.

(25) Richardson, M. F.; Yang, Q.-C.; Novotny-Bregger, E.; Dunitz, J. D. Conformational Polymorphism of Dimethyl-3,6-Dichloro-2,5-Dihydroxyterephthalate. II. Structural, Thermodynamic, Kinetic and Mechanistic Aspects of Phase Transformations Among the Three Crystal Forms. *Acta Crystallogr.* **1990**, *B46*, 653−660.

(26) See also Stone, A. J.; Tsuzuki, S. Intermolecular Interactions in Strongly Polar Crystals with Layer Structures. *J. Phys. Chem*. **1997**, *B101*, 10178−10183.
(27) See for example: Israelachvili, J. *Intermolecular and Surface Forces*, 2nd ed.; Academic Press: New York, 1991; p 155 ff. Hobza, P.; Zahradnik, R. *Intermolecular Complexes. The Role of van der Waals Systems in Physical Chemistry and in the Biodisciplines*; Academia: Prague, 1988; p 215 ff. Gavezzotti, A. Molecular Aggregation of Acetic Acid in a Carbon Tetrachloride Solution: a Molecular Dynamics Study with a View to Crystal Nucleation. *Chem. Eur. J.* **1999**, *5*, 567−576 and references therein.
(28) Mathews, C. K.; Baba, M. S.; Narasimham, T. S. L.; Balasubramanian, R.; Sivaraman, N.; Srinivasan, T. G.; Rao, P. R. V. Vaporization Studies of Buckminsterfullerene. *J. Phys. Chem*. **1992**, *96*, 3566−3568.
(29) A formal proof that the hexagonal and cubic close packing of spheres is more dense than any irregular, i.e., nonperiodic, packing has been achieved only recently by Wu-yi Hsiang (*Sphere Packings and Spherical Geometry—Kepler's Conjecture and Beyond;* Center of Pure and Applied Mathematics, University of California: Berkeley, 1991). An extended discussion of the problem can be found in an article by N. Max (*Nature* **1992**, *355*, 115−116). Added in proof: But see Sloane, N. J. A. Kepler's Conjecture Confirmed. *Nature* **1998**, *395*, 435−436 for recent criticism of Hsiang's proof and description of a new proof by T. C. Hales.
(30) Macgillavry, C. H. *Symmetry Aspects of M. C. Escher's Periodic Drawings;* A. Oosthoeks Uitgeversmaatschappij N.V.: Utrecht, The Netherlands, 1965.

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