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A Statistical Study of Density and Packing Variations among Crystalline Isomers

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Abstract—Crystal structures of groups of isomeric hydrocarbons, oxahydrocarbons and azahydrocarbons have been retrieved from the Cambridge Structural Database. Correlations among crystal and molecular descriptors were sought, with particular attention to factors affecting crystal density. Packing coefficients do not differ much from 0.74, so organic molecules have roughly the same packing efficiency as a close packed assembly of spheres. Molecular shape factors associated with high crystal density are difficult to identify. However, crystal density is higher for compact polycyclic molecules, since they have smaller molecular volumes. Also, flat, rigid molecules pack better than flexible, twisted ones. On the other hand, substituents such as alkyl or nitrile groups tend to lower the packing efficiency. High crystal density does not necessarily lead to high lattice energy, and, in particular, hydrogen bonding seems to have no immediate effect on crystal density. Results of bivariate statistics were confirmed by principal component analysis. These results may be of interest for practical applications in crystal chemistry and crystal physics. © 2000 Elsevier Science Ltd. All rights reserved.

Introduction

Potential applications of organic crystalline materials in many fields of crystal chemistry and physics are often hampered by low mechanical strength and thermal conductivity, leading to low resistance to external stress or to the effects of electromagnetic radiation, and therefore to unstable and quickly deteriorating devices. These undesirable properties arise to some extent from the relatively low compactness of organic, as compared with inorganic, mineral or metal crystals. It would therefore be of great interest to be able to predict how organic molecules could be designed so as to pack into more compact crystals.

Crystal density is one easily accessible property connected with packing strength and thermal conductivity. Since crystal density depends on molecular mass, meaningful comparisons of the effect of molecular shape and chemical constitution must be conducted among groups of crystals of identical stoichiometry. We have therefore considered crystals containing isomeric molecules. Differences in intramolecular energy may be large but they are irrelevant to our purpose, since we are not interested in absolute crystal energies; rather, we expect to compare intermolecular energies, together with densities, hoping to probe the relative ability of different shapes and of different functional groups to form compact crystalline aggregates. While the general problem of shape versus packing efficiency had already been hinted at in previous work,[1,2,3] the matter has not yet been taken up systematically. The present study is a venture in that direction; it is thus a continuation of our earlier searches for traces of a systematic of crystal packing, where we have analyzed space group distributions,[4] packing modes and energies of different chemical classes of compounds, such as those with the same elemental ingredients (e.g. oxahydrocarbons[5]), racemates and their homochiral counterparts,[6] condensed aromatic hydrocarbons,[7,8] and ordinary polymorphs.[9,10]

Computational details

Crystal structures of isomers were retrieved from the Cambridge Structural Database (CSD).[11] Crystal packing and molecular geometries were checked by visual examination, and hydrogen atoms positions were reset as described in previous papers (1.08 Å for C–H, 1.00 Å for O–H and N–H bonds, bond angles adjusted as previously described[5]). In the clean-up stage, many structures with suspicious features (disorder, wrong densities, wrong intermolecular contacts) were discarded; it was noted especially that published X-ray proton positions of O–H groups are often completely arbitrary. Only room temperature structures with full atomic coordinates were retained. Entries so retrieved are listed in Table 1.

Keywords: isomeric hydrocarbons; crystal density; molecular shape.

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Table 1. Number of entries retrieved from the Cambridge Structural Database for each group of isomers (a full list of refcodes is available from the authors upon request)

$C_{12}H_{10}$	4	$C_{18}H_{14}O_1$	6	$C_8N_2H_4$	4
$C_{12}H_{12}$	6	$C_{18}H_{14}O_2$	12	$C_8N_2H_6$	9
$C_{12}H_{16}$	3	$C_{18}H_{16}O_4$	5	$C_8N_4H_{12}$	4
$C_{12}H_{18}$	3	$C_{18}H_{20}O_2$	15	$C_8N_5H_5$	3
$C_{14}H_{10}$	7	$C_{18}H_{20}O_4$	7	$C_8N_6H_8$	3
$C_{14}H_{12}$	6	$C_{18}H_{24}O_2$	16	$C_9N_3H_9$	5
$C_{14}H_{14}$	3	$C_{18}H_{24}O_4$	5	$C_{10}N_4H_8$	4
$C_{14}H_{16}$	4	$C_{20}H_{18}O_5$	5	$C_{10}N_4H_{10}$	4
$C_{14}H_{18}$	3	$C_{20}H_{20}O_6$	8	$C_{11}N_4H_8$	4
$C_{14}H_{24}$	2	$C_{20}H_{22}O_4$	21	$C_{11}N_6H_6$	3
$C_{15}H_{12}$	5			$C_{12}N_2H_8$	6
$C_{15}H_{14}$	3			$C_{12}N_2H_{10}$	11
$C_{15}H_{18}$	4			$C_{12}N_2H_{16}$	7
$C_{16}H_{10}$	7			$C_{12}N_4H_8$	5
$C_{16}H_{12}$	11			$C_{13}N_2H_{14}$	4
$C_{16}H_{14}$	9			$C_{14}N_2H_{12}$	4
$C_{16}H_{16}$	13			$C_{14}N_2H_{14}$	10
$C_{16}H_{20}$	7			$C_{14}N_2H_{16}$	8
$C_{16}H_{26}$	3			$C_{14}N_2H_{20}$	4
$C_{18}H_{12}$	10			$C_{14}N_2H_{22}$	3
$C_{18}H_{14}$	6			$C_{14}N_2H_{24}$	5
$C_{18}H_{16}$	16			$C_{14}N_4H_{12}$	6
$C_{18}H_{18}$	11				
$C_{18}H_{20}$	12				
$C_{18}H_{30}$	5				

For each crystal, the density, D_c, is regarded as the leading parameter ($D_c = M_{mol}Z/V_{cell}$, where M_{mol} is the molecular mass ($=M_W 1.66\times10^{-24}$), and Z is the number of molecules in the crystal unit cell). Other quantities were then calculated.

1. Molecular volume, V_{mol} (Å^3; the volume of a single molecule). Molecular volumes were estimated by assigning a radius to each atomic sphere centered at the X-ray position (C=1.75, H=1.17, O=1.40, N=1.50 Å), and calculating the volume of the resulting object by summation of small volume elements.[12] Except for highly strained cyclic structures, these volumes are practically identical to those obtained by the spheres-and-caps method described by Kitaigorodski.[13] For clarity, note that the molecular volume is sometimes defined (e.g. in the CSD) as the cell volume per molecule, V_{cell}/Z, in other words, the space occupied by a molecule in a particular crystal structure. The two volumes are related by the Kitaigorodski packing coefficient $C_k=ZV_{mol}/V_{cell}$. We may also speak of the molecular density, $D_{mol}=M_{mol}/V_{mol}$ and molecular surface, S_{mol} (in Å^2).[12]

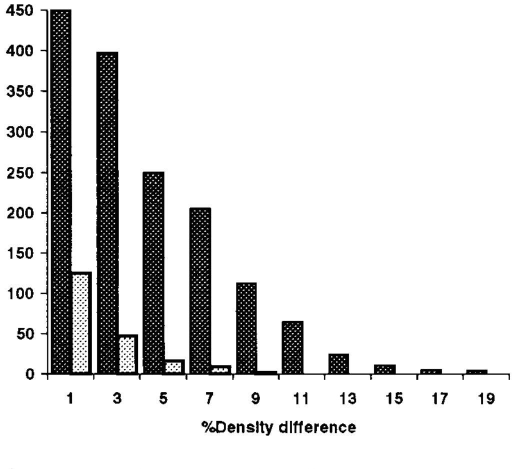


Figure 1. Histogram of percent density differences over pairs of isomeric crystals structures in the sample of Table 1 (darker bars) and over pairs of polymorphs (lighter bars, from Ref. 9, where Fig. 1a and b are interchanged).

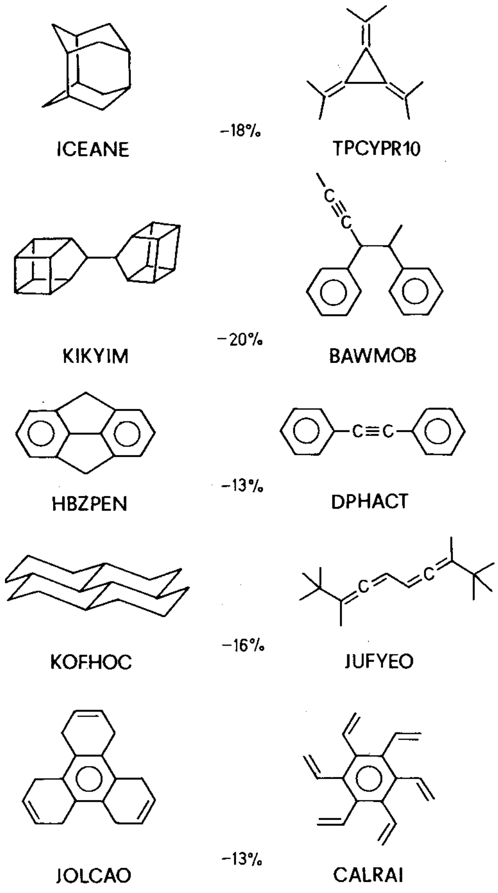


Figure 2. Extreme cases of crystal density differences between hydrocarbon isomers: left, denser; right, less dense crystal. In between is the percent density difference.

2. The packing energy E (in kJ/mol), calculated by pairwise additive atom–atom potentials calibrated for organic crystals;[14] lattice sums were cut at 10 Å, and the energy was corrected for convergence by dividing by 0.95, in accordance with previous experience, to compare directly with the heat of sublimation.
3. E_{HB}, or the percent of E which pertains to hydrogen-bonding intermolecular interactions; the calculation of E_{HB} is immediate in an atom–atom approximation;
4. N_B, the number of links (a link being a single, double or triple bond) between non-hydrogen atoms in the molecule; this indicator has to do with molecular shape, to the extent that a high number of links means a more compact molecule. As an alternative indicator one could consider the ring number, defined as the number of cuts needed to convert the molecule into a linear or branched chain (e.g. ring number of *n*-hexane 0, benzene 1, cubane 5): for a hydrocarbon C_xH_y, this number is obtained by subtracting $x-1$ from N_B.
5. D_{av}, or the average coordination distance: this quantity is the average of the distances from the center of mass of a reference molecule to the centers of mass of the nearest

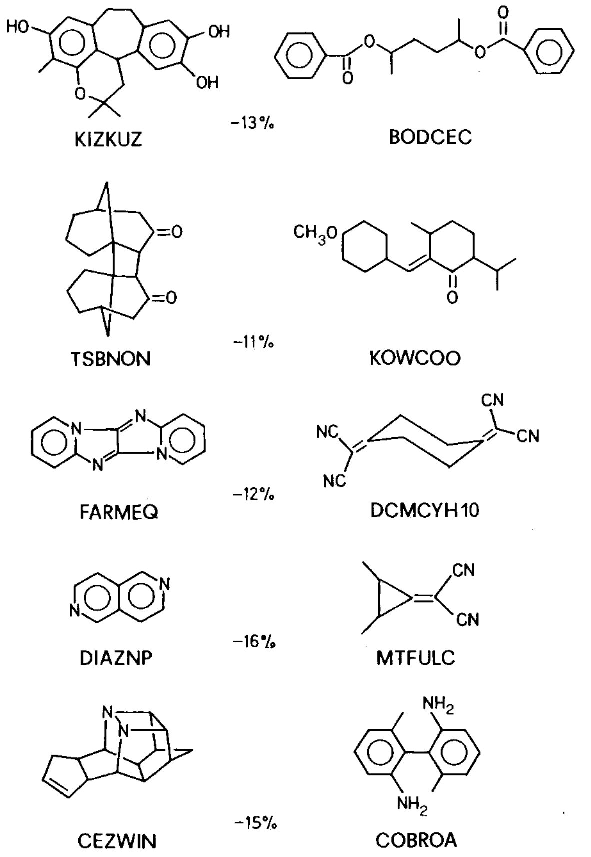


Figure 3. Extreme cases of crystal density differences: left, denser; right, less dense crystal. In between is the percent density difference.

neighbors in the crystal, these being defined as those neighbors which provide more than 5% of the total cohesive energy in the crystal (all these energy dissections are immediate in the atom–atom approximation).

Statistical results are presented either in the form of plots seeking a correlation between two given properties, or in the form of plots of differences in properties. In this last case, the abscissa is always the difference in density between a pair of isomer crystal structures, positive by construction, while the ordinate is the corresponding difference in a second property. For each group of N isomers listed in Table 1, there are $N(n-1)/2$ such pairs of differences.

Results

Early analyses of crystal data based on geometrical parameters of crystal packing, such as the distribution of atom–atom intermolecular distances or the quest for unusual atom–atom contact distances have not led to useful generalizations and were not pursued further here.

Fig. 1 shows the distribution of density differences among isomers in organic crystals and among polymorphs.[9] It shows that different crystal packings of the same molecule give a somewhat smaller spread in density than among isomers with different constitution and molecular shape. The range of crystal density variation for a given molecular mass is less than 15% and compares with the percent density difference between solids and liquids. A crystal is by definition a compact entity, and even a large difference in chemical constitution may not lead to a large decrease in density.

A chemical flavor for the origin of density differences among crystalline isomers can be had from Figs. 2 and 3, which collect molecular diagrams for isomer pairs with top density differences within our data set. Flat, rigid molecules (typically, condensed aromatics) give higher densities than flexible and twisted molecules, an effect attributable to the easier arrangement in space of objects of more regular shape (although any shape factor is as evident to the eye as it is difficult to quantify).

Polycyclic cage molecules have small molecular volumes and therefore give high crystal density. In contrast, nitriles, alkynes and heavily methylated compounds have low densities; methyl groups shield the molecule from attractive intermolecular contacts, and share with triple bonds the ability to decrease the number of intramolecular links among carbon atoms.

Molecular constitution has been analyzed in search of a relationship between hydrogen bonding donor–acceptor capability and crystal density. One might imagine that

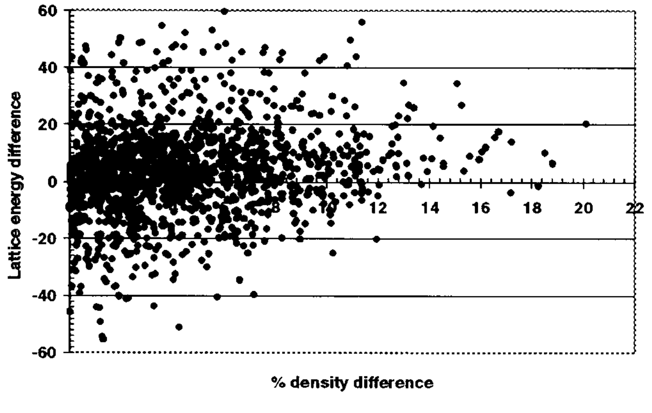


Figure 4. Scatterplot of lattice energy difference (kJ/mol) as a function of percent density difference between pairs of isomeric crystal structures. Data from all isomer pairs generated by the structures in Table 1 (1521 data points).

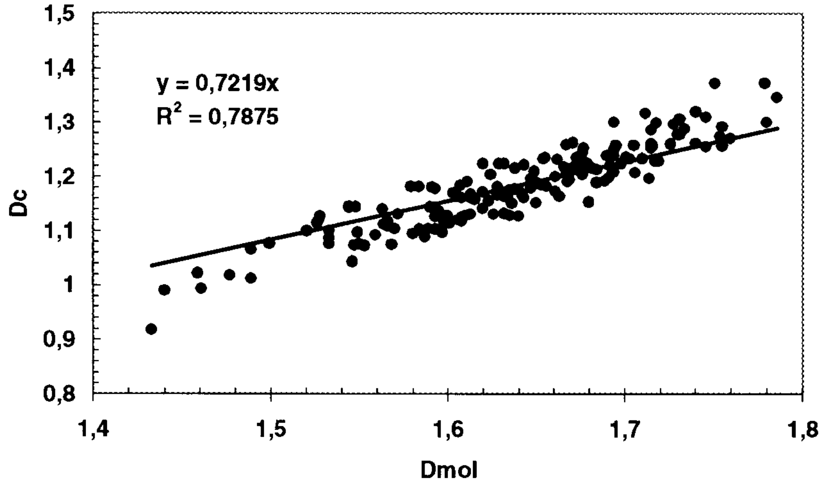


Figure 5. Crystal density versus molecular density (see text for definition) for hydrocarbon crystals.

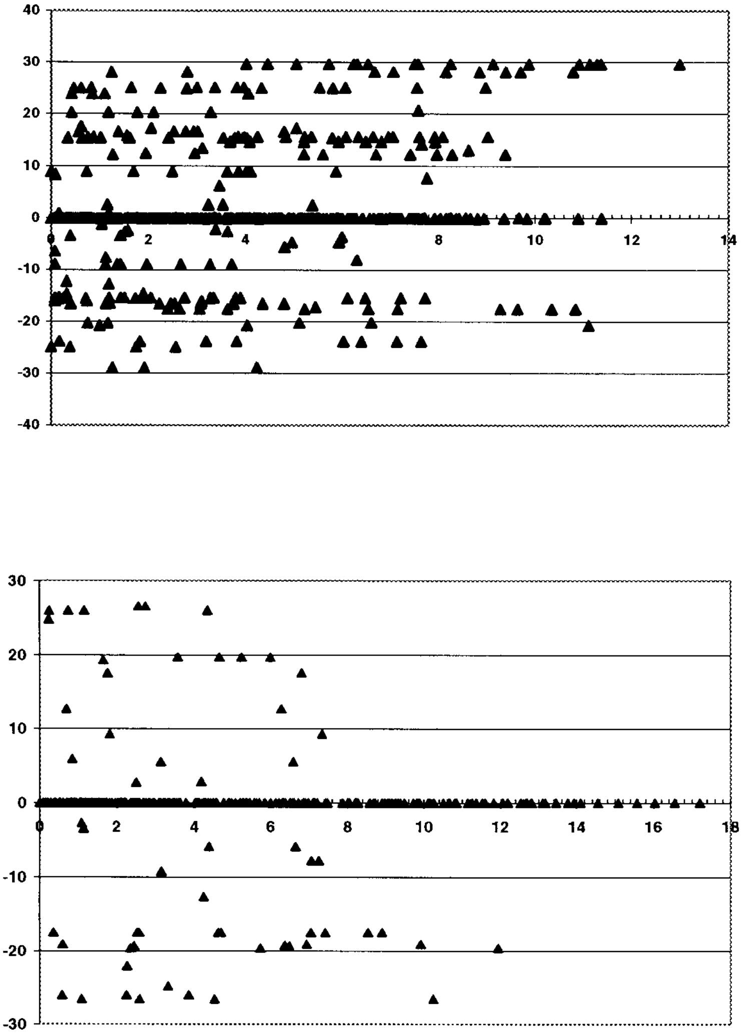
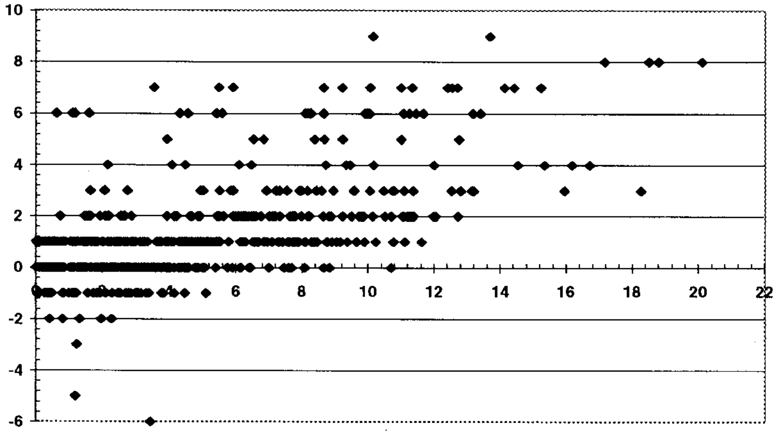


Figure 6. Differences in hydrogen bonding energy (kJ/mol) as a function of percent density difference. Top: oxahydrocarbons; bottom: azahydrocarbons. The layer structure is due to the fact that many structures have zero H-bonding energies and hence many differences are equal.



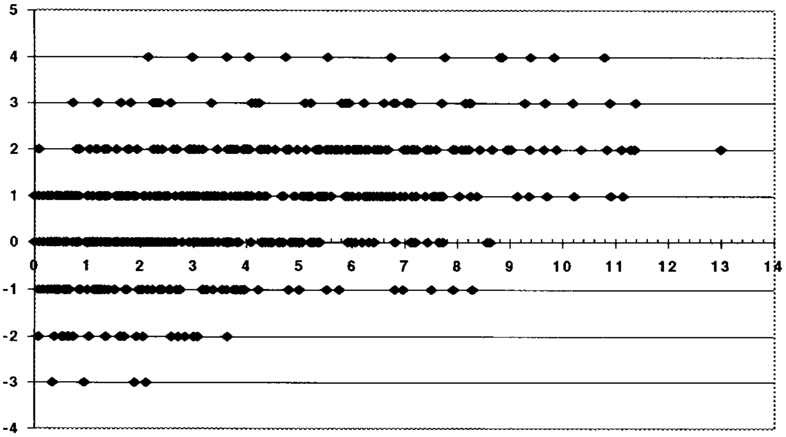


Figure 7. Scatterplots of differences in number of non-C–H links as a function of percent density difference. The upward trends means that a higher density goes with a higher number of links. Top: hydrocarbons; bottom: oxahydrocarbons.

strong intermolecular hydrogen bonding should lead to greater compactness, but, on the other hand, its strongly directional properties can produce open, non-compact crystal structures (as in ice). Judging from spot checks, as well as on more quantitative results (see below), neither tendency is operative.

One might also guess that a denser crystal should have a higher lattice energy. That this is not the case in general is shown by Fig. 4, which shows that for a density difference ΔD lower than 10%, that is, for the vast majority of cases, a positive ΔD may equally well correspond to a negative or a positive lattice energy difference. There is indeed a weak correlation between density and lattice energy for $\Delta D > 10\%$. To be sure, this result is sensitive to the quality of the potentials, but differences between energies based on different parametric potential schemes are around 10%, and unlikely to change the main picture.

Indeed, it is difficult to see any property that shows a strong correlation with lattice energy in all the isomer groups. While molecular surface S_{mol} correlates well with lattice energy within a given class of molecules, e.g. condensed aromatic hydrocarbons,[12] it does no better than density D_{c} or molecular volume V_{mol} for isomers of different structure and shape.

We find that crystal density D_{c} correlates best with molecular density D_{mol} (Fig. 5) or molecular volume, V_{mol}. Since the relationship between D_{c} and D_{mol} goes through the packing coefficient C_{k}, this correlation implies that C_{k} does not vary much throughout the entire collection of crystal structures. Indeed, for the hydrocarbon subset of 164 structures the mean value of C_{k} is 0.721 with standard deviation 0.022. Thus, although the molecules are of very different shape and size, their crystal packing efficiency does not vary much and is only slightly less than in cubic closest packing of spheres. Values for the oxahydrocarbon and azahydrocarbon subsets are quite similar, with a somewhat greater scatter. Although the variation in packing coefficient is small, it does show a discernible dependence on molecular shape. Isomers with compact shape and small V_{mol} (e.g. polycyclic hydrocarbons) tend to pack more efficiently than isomers with larger V_{mol}, e.g. those with alkyl or other substituents.

For hydrocarbons, we find that V_{mol} can be approximated by

Table 2. Factor loadings (×100) of the top factor (principal component) in the multivariate analysis over several sets of isomer structures

Set	Variance %	D_c	E	C_k	E_{HB}	S_{mol}	V_{mol}	N_b	D_{av}
$C_{16}H_{16}$	60	97	14	69	–	−91	−83	94	−63
$C_{18}H_{16}$	55	96	51	−30	–	−80	−98	98	1
$C_{18}H_{20}$	45	51	−38	−61	–	−50	−97	97	51
$C_{18}H_{20}O_2$	50	97	43	35	60	−91	−83	83	–44
$C_{18}H_{24}O_2$	53	96	−15	59	−41	−95	−92	91	−40
$C_{20}H_{22}O_4$	48	70	16	24	68	−92	−91	90	−54
$C_{12}N_2H_{10}$	47	25	54	−43	84	−91	−94	90	2

the formula:

$$V_{mol} \sim 8.85 + 9.95n(\mathrm{C}) + 2.72\ n(\mathrm{H})\ \text{Å}^3$$

Crystal density can therefore be estimated quite well from the molecular formula:

$$D_c = 0.72M_{mol}/V_{mol}\ \mathrm{gm/cm^3}$$

Fig. 6 indicates that a positive density difference may correspond equally well to a positive or negative hydrogen bonding energy difference, so that hydrogen bonding has practically no effect on density, as discussed in the previous section on a more qualitative basis. This is another aspect of the absence of a necessary correlation between lattice energy and crystal density. There is also no correlation between density and D_{av}, the average coordination sphere radius; a crystal can have a high density with or without hydrogen bonds, or with a compact or scattered coordination sphere, as noted earlier.[9]

On the other hand, Fig. 7 shows the good correlation between differences in density and in the number of non-C–H links. On average, one additional link is worth about 5% increase in density. Exceptions are fewer in hydrocarbon than in oxahydrocarbon crystals.

Scatterplots drawn on differences in crystal density against differences in molecular volume or molecular surface confirm the above. Among isomer pairs, a smaller molecular volume or surface generally leads to a higher crystal density. Very roughly, the percent difference in molecular volume in a given isomer pair equals the percent difference in crystal density. This is a further confirmation that a leading factor in producing high crystal density is the ability of the molecule, by its shape and functionalization, to compress the molecular mass into a small molecular volume (a high molecular density, see Fig. 5).

A standard principal component analysis was carried out, as previously described,[12] on the quantities density, lattice energy, packing coefficient, hydrogen bond energy (where applicable), molecular surface, molecular volume, number of links and average coordination distance. This amounts to a variance of seven for hydrocarbons and of eight for non-hydrocarbons. The analysis was carried out, using a normalized covariance matrix, on selected sets of isomers for which the number of members of the set was higher than the variance.

The results are summarized in Table 2, which shows the top principal component (the one corresponding to the highest eigenvalue) and its factor scores. The top PC typically is responsible for about 50% of the total variance, while the top three are responsible for about 90%. The factor scores, judging from their signs, show the strong correlation between molecular surface, molecular volume and number of bonds, and the very consistent correlation of the factor composed by surface, volume and intramolecular links to crystal density. As previously discussed, factor scores for density, energy, packing coefficient and average coordination distance can equally well appear with the same or with opposite sign in the top principal component.

Conclusions

Crystals of isomers show differences in density up to 20% in extreme cases, and double the range observed among polymorphs. Even very large differences in shape or chemical constitution do not seriously violate the drive towards close packing, and none of the crystals in our study has a packing coefficient very different from 0.74, the value for close-packed spheres. Flat, regular molecules do, however, pack better than twisted ones, and methyl groups are always detrimental to compactness. However, the main factor in promoting high crystal density is the compression of heavier atoms (carbon, oxygen, nitrogen in organic compounds) into a small volume; this results from an increase in the number of links between these atoms, as in polycyclic molecules. Multiple bonds, especially in acetylenes and allenes, produce the opposite effect and are therefore detrimental to crystal density. These conclusions are summarized in the very sharp correlation found (Fig. 5) between crystal and molecular density. Since the molecular volume is easily predictable, at least for hydrocarbons, from the number of carbon and hydrogen atoms, a quick estimate of the crystal density, as D_c=0.72M_{mol}/V_{mol}, is possible.

Among isomeric structures a denser crystal may not always have a higher lattice energy. The ways in which matter is more efficiently packed into a small space are not always the same as those in which a larger number of attractive intermolecular contacts are produced. Hydrogen-bonded crystals are more cohesive than non-hydrogen bonded isomers, but they are not always more dense. In summary, the correlation of lattice energy with molecular shape and functionalization is far from clear.

Our analysis refers here to idealized crystals containing motionless molecules. The ways in which molecular shape or constitution may influence the dynamic properties of the crystal can be studied at different levels. For example, a lattice-dynamical treatment of external modes yields an estimate of vibrational entropy contributions to free energy differences among crystalline isomers. A full molecular dynamics treatment, nowadays quite feasible for the systems considered here, would in principle allow an evaluation of the different temperature behavior of isomer pairs and an estimate of melting temperatures, to be compared with experimental ones. Eventually, studies could be conducted on computer-generated isomeric or polymorphic 'virtual' crystal structures to probe selected molecular shape or constitution effects. All these developments are being considered for future work.

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