Visualising intermolecular interactions in crystals: naphthalene *vs*. terephthalic acid

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A recently-devised scheme for partitioning crystal space into smooth molecular volumes is used to visualise intermolecular interactions in the crystal structures of naphthalene and terephthalic acid.

The detailed description and classification of intermolecular interactions in molecular crystals is of considerable current interest in crystal engineering,[1] *ab initio* crystal structure prediction,[2] and studies of polymorphism.[3] We have recently described[4] a remarkable new way of exploring molecular crystals by isosurface rendering of smooth, non-overlapping molecular surfaces arising from a partitioning of crystal space based on Hirshfeld's stockholder scheme.[5] These molecular Hirshfeld surfaces partition space in the crystal into regions where the contribution from the sum of spherically-symmetric electron distributions for atoms in the molecule (the promolecule) exceeds the contribution from the corresponding sum over the crystal (the procrystal). Following Hirshfeld, a weighting function $w(\mathbf{r})$ is defined by eqn. (1).

$$w(\mathbf{r}) = \sum_{a \in molecule} \rho_a(\mathbf{r}) \Big/ \sum_{a \in crystal} \rho_a(\mathbf{r}) = \rho_{promolecule}(\mathbf{r}) / \rho_{procrystal}(\mathbf{r}) \tag{1}$$

The Hirshfeld surface for the particular molecule is defined by $w(\mathbf{r}) = 0.5$, and the volume occupied by the molecule in the crystal is that region where $w(\mathbf{r}) \geqslant 0.5$. For a given crystal structure and set of spherical atomic electron densities, the isosurface defined by $w(\mathbf{r}) = 0.5$ is unique. The first quantitative applications of this partitioning scheme, including measures of molecular size and shape as well as 3D isosurface pictures of these Hirshfeld surfaces, have recently been reported[6] for a variety of van der Waals and hydrogen-bonded crystals.

In a recent article[1a] Desiraju highlighted the way in which crystal engineering is presently at 'an exciting intersection of structural and supramolecular chemistry' and outlined three broad areas in which progress is needed if designer crystals are to become a reality. One of these is the visualisation of a crystal structure in its entirety, rather than focusing on assumed important interactions. This objective recognises the increasingly evident one-upmanship of nature in thwarting attempts to engineer structures for specific purposes,[7] and points to a compelling need for new tools to explore and analyse molecular crystals, taking into account all manner of forces and interactions, strong and directional as well as weak and isotropic. Desiraju gave an example of such a tool, NIPMAT,[8] an interaction display program which produces a pictorial grey-scale matrix from the deviation between all close intermolecular atom-atom contacts in the crystal and the sum of their van der Waals radii, thereby summarising all of the intermolecular interactions simultaneously. In that work, Desiraju demonstrated the application of NIPMAT to two dissimilar molecular crystals: naphthalene and terephthalic acid [see Fig. 6 of ref. 1(*d*)]. Inspired by this example, we decided to apply our Hirshfeld surface partitioning to the same molecular crystals, in the process demonstrating the potential for Hirshfeld surfaces to provide detailed information on all intermolecular interactions at the same time, as well as the relationship between Hirshfeld surfaces in crystals and more conventional representations of molecular surfaces: fused van der Waals spheres and surfaces of constant electron density.

Fig. 1 shows Hirshfeld surfaces for the two molecules, and close examination of them confirms how elegantly and beautifully these surfaces summarise the utter difference between intermolecular packing patterns in these two crystals.‡ The Hirshfeld surface for naphthalene reflects the weak and largely non-directional forces in the crystal, with smoothly varying curvature over the entire surface, and the edge-to-face C–H··π interaction evident as a broad depression above the plane of one ring, in much the same way as seen for benzene.[6] In contrast to this, the Hirshfeld surface of terephthalic acid is characterised by abrupt changes of curvature, especially in the vicinity of the O–H···O hydrogen bonds where the surface is extremely flat, and above and below the molecular plane, where the surface is essentially flat, but with subtle undulations which echo the packing of neighbouring molecules. From Fig. 1 it is evident that naphthalene does not pack in a planar arrangement, while terephthalic acid utilises hydrogen-bonded ribbons which pack slightly offset to, and on top of, one-another.

Fig. 2 illustrates the relationship between the Hirshfeld surfaces in the crystal (mesh in this case) and space-filling representations of the isolated molecules as fused van der Waals spheres. The van der Waals representation of naphthalene fits snugly within the Hirshfeld surface, leaving ample room within this volume in all directions. The same pattern is also seen for terephthalic acid in the vicinity of the phenyl C–H bonds, but the regions around the carboxy groups are dramatically different. Here, as expected, the van der Waals spheres for O and H clearly protrude well beyond the Hirshfeld mesh surface at the ends of the molecule. More subtle is the way in which the oxygen spheres and one H sphere just protrude beyond the Hirshfeld surface on the side of the molecule, corresponding to close C–H···O contacts in the crystal.

Fig. 3 superimposes the Hirshfeld surfaces of these two molecules (mesh) on surfaces of constant electron density on which the molecular electrostatic potential has been colour

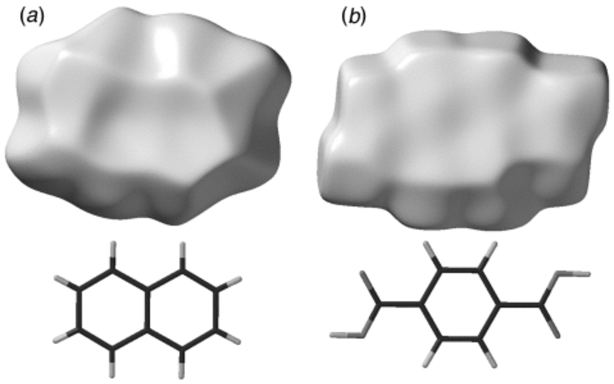

Fig. 1 Hirshfeld surfaces for (*a*) naphthalene and (*b*) terephthalic acid beside stick molecular models. Models and surfaces are all drawn to the same scale.

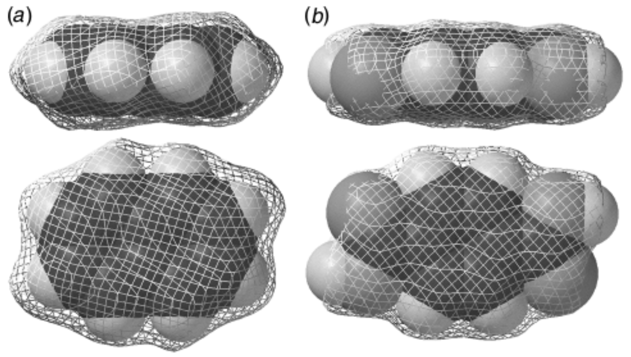

Fig. 2 Front and side views of Hirshfeld surfaces (mesh) for (*a*) naphthalene and (*b*) terephthalic acid superimposed on fused van der Waals sphere representations [van der Waals radii: 1.40 (H), 1.70 (C) and 1.50 Å (O)]

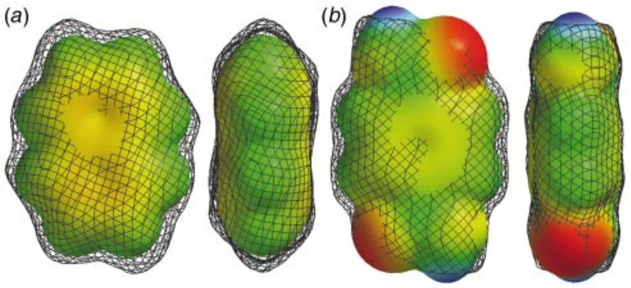

Fig. 3 Front and side views of Hirshfeld surfaces (mesh) for (*a*) naphthalene and (*b*) terephthalic acid superimposed on surfaces of constant electron density (0.002 au) for the isolated molecules, upon which the molecular electrostatic potential has been colour-coded. Colours range from red (–190 kJ mol^{-1} for a unit charge) to blue (+370 kJ mol^{-1}); the same colour range has been used for both molecules.

coded.§ The slightly polar nature of naphthalene (green around the C–H bonds, yellow above the rings) contrasts with the highly localised nature of polarity in the carboxy group of terephthalic acid, and the protrusion of O and H atoms in the latter is evident. A new feature seen in Fig. 3 is the way in which the Hirshfeld surface dips below the surface of constant electron density above the benzene rings for the isolated molecules, just perceptibly in the case of terephthalic acid, but far more so for naphthalene, where it is strikingly evident that, whereas the two rings are essentially equivalent in the electron density surface for the isolated molecule, there is a much closer C–H$\cdots\pi$ contact to one ring than the other in the crystal structure. The C–H$\cdots$O contacts on the edge of the terephthalic acid molecule are also more obvious here than in Fig. 2

We believe that the information on intermolecular interactions which is implicitly contained in an accurate crystal structure analysis is reliably encoded on these Hirshfeld surfaces. The illustrations in this article show how, in a very qualitative manner, this appears to be the case, while at the same time highlighting how the Hirshfeld surfaces, defined as they are for molecules in the crystal, differ fundamentally from representations of isolated molecules. Curvature of the Hirshfeld surface seems to be intimately related to the nature and strength of intermolecular interactions for all examples we have investigated so far, and our future lines of inquiry with these intriguing surfaces will explore this connection further.

Notes and References

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‡ Our calculations used the same crystal structures as Desiraju (CSD: NAPHTA10, TEPHTH) with details of the computational method given in ref. 6. Global descriptors of size indicate that the Hirshfeld surfaces of these two molecules are surprisingly similar, with similar volumes (V_H = 172.3 and 169.3 Å^3 for naphthalene and terephthalic acid, respectively), surface areas (S_H = 176.0 and 179.3 Å^2) and packing ratios (P_H = 0.970 and 0.969). As for shape, results for globularity (G = 0.851 and 0.825), a measure of the degree to which the surface area differs from that of a sphere of the same volume, suggest that naphthalene is marginally more spherical than terephthalic acid, while anisotropy ($\sqrt{\Omega}$ = 0.354 and 0.435) confirms that the surface for naphthalene is markedly more isotropic than that for terephthalic acid.

§ These results obtained with the SPARTAN package (see ref. 9); electron density surfaces are at $\rho(\mathrm{r})$ = 0.002 au, from a Hartree–Fock SCF calculation on the isolated molecule with a 6-31G* basis set, at the same geometry as the molecule in the crystal; electrostatic potentials for both molecules utilise the same gradation of colour, with red electronegative and blue electropositive.

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7 See, for example: F. H. Allen, V. J. Hoy, J. A. K. Howard, V. R. Thalladi, G. R. Desiraju, C. C. Wilson, and G. J. McIntyre, *J. Am. Chem. Soc.*, 1997, **119**, 3477; J. A. Swift, R. Pal and J. M. McBride, *J. Am. Chem. Soc.*, 1998, **120**, 96. In the latter work the authors remark that 'This work demonstrates again the current superiority of molecules over chemists in discovering stable crystal packing patterns'.

8 R. S. Rowland, *Am. Crystallgr. Assoc. Abstr.*, 1995, **23**, 63. See also the description and use of NIPMAT in ref. 2(*c*).

9 SPARTAN version 4.0, Wavefunction Inc., 18401 Von Karman Ave., #370, Irvine, CA 92715, USA.

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