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The relationship between indentation hardness of organic solids and their molecular structure

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A model has been developed relating the indentation hardness of organic molecular solids to their cohesive energy density, the length of the Burgers vector, the weakest plane from the crystal structure and crystal structural parameters. Whilst the described model is pragmatic, calculated indentation values for a variety of materials based on the weakest plane using specific Burgers vectors agree well with those from literature data.

1. Introduction

The use of the solubility parameter δ, or cohesive energy density (CED) to predict properties and interactions in materials has long been recognized. Hildebrand and Scott [1, 2] were the first to discuss the universality of the concept, by the establishment of correlations with surface tension and other critical properties. The cohesive energy density has similarly been correlated with Youngs modulus for simple molecular solids, Ne, Ar and N_2 [3], for polymers by plotting the dynamic Youngs modulus at a temperature of $(T_g - 50)$ °C [4] and for organic pharmaceutical solids [5]. Furthermore, in the last paper [5] it was shown that cohesive energy density (calculated from the chemical structure) could be used to estimate the Youngs modulus of powders using a simple relationship.

In this paper the concept has been extended by examining the role of the cohesive interactions on the indentation hardness and therefore the yield properties of molecular organic solids.

2. Theoretical considerations

The indentation hardness H is a measure of the resistance of a solid to local deformation [6] and the hardness of a ductile material is essentially a measure of its plastic flow or yield stress, σ_y (and $H/\sigma_y = 3.0$ for a plastic rigid solid [7]). It is well recognized that yield (plastic flow) in all crystalline solids is due to the motion of defects such as vacancies and edge or screw dislocations within the crystal lattices, and to the intermolecular energy between the molecular crystal planes. The extent that a material will plastically deform is dependent both on the width of the dislocation (materials which have wider dislocations are soft [8]) and the strength of the intermolecular bond that is successively broken and connected in the process.

In molecular crystals plastic flow occurs via a slip mechanism through the migration of edge dislocations (Fig. 1) along specific directions in the crystal [9]. It is interesting to note that for molecular solids at high temperatures and low stresses, e.g. during creep, the mechanism for the deformation is dislocation climb. Similarly for plastic crystals (disordered molecular crystals of very high plasticity) at low temperatures and high stresses the mechanism of plastic deformation is by the movement of an edge dislocation via slip [9]. Since the mechanism of plastic flow in organic solids used in the pharmaceutical industry is primarily by slip via motion of edge dislocations, these types of solids will be considered in developing a predictive approach to the yield properties of molecular solids.

The prediction of indentation properties is complex and difficult but two workers have had notable successes – Balta-Calleja [10] with polymers and Gilman [11, 12] with borides and carbides. For crystalline polymers Balta-Calleja [10] derived the ideal shear strength of a van der Waals solid from the lateral surface free energy using the Thomas–Stavely relation [13]. Although the values of the calculated ideal shear

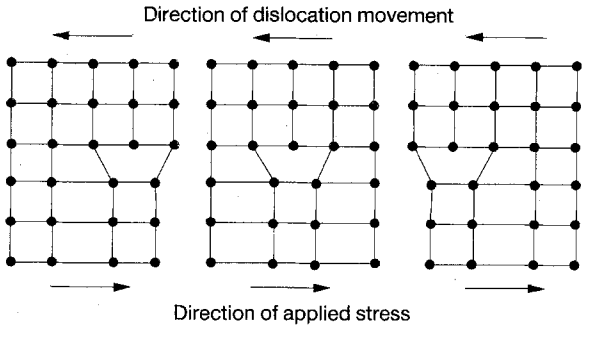

Figure 1 Movement of an edge dislocation during the application of a shear stress.

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strength and measured Vickers hardness were in good agreement, the calculation requires a knowledge of the crystalline polymer chain cross-section and a displacement factor for the movement of molecules to give sufficient lattice destruction. Hence the method is of little use as a predictive technique.

The second approach of Gilman [11, 12] involves a calculation based on interatomic interactions and the motion of dislocations by use of a simple relationship (Equation 1 below) between the free energy of formation ΔF and the molar volume V of carbides [12]. For both carbides and borides there was reasonable agreement between calculated and experimental hardnesses.

$$H \simeq 2\frac{\Delta F}{V}(\text{MPa}) \tag{1}$$

This simple relationship was derived from Equation 2 [11] which relates the free energy of formation to the Burgers vector **b**, shear stress S and the co-ordination number C:

$$\frac{\Delta F}{C} = \frac{S\mathbf{b}^3}{4} \tag{2}$$

This approach can be modified for organic solids, where the interactions are between molecules rather than between atoms as in the borides [12], by replacing ΔF with ΔE_{coh}, i.e. the cohesive energy which is equivalent to the heat of vaporization. Furthermore the shear stress can be replaced by the indentation hardness since $H = 6S$ [14]. Thus rearranging Equation 2 gives

$$H = \frac{24\Delta E_{coh}}{C\mathbf{b}^3} \tag{3}$$

The term in Equation 3 in which the cohesive energy is divided by a volume term $\mathbf{b}^3$ is clearly analogous to the cohesive energy density and $\Delta E_{coh}/V$, where V is the molar volume.

In order that a simple model can be developed further, the parameter C (co-ordination number) needs to be estimated. The co-ordination number and the close packing of molecular crystals has been discussed by Kitaigorodsky [15] who observed that the packing coefficient of molecular crystals (ratio of the volume occupied by the molecules to the unit cell volume) is generally quite high (0.65–0.75), i.e. similar to that obtainable by close packing of spheres and ellipsoids. A prerequisite for high packing efficiency is that the co-ordination number is high, and for the majority of molecular solids it can be taken as 12 [15] with less efficient packing for co-ordination numbers of 10 and 14. Similarly Gavezzotti [16] showed that for hydrocarbon crystals the percentage of the total packing energy due to the first twelve neighbouring molecules was about 96% of the total packing energy, thus confirming the general findings that molecular solids have co-ordination numbers of 12. By using $C = 12$ Equation 3 can be rearranged further:

$$H = \frac{2\Delta E_{coh}}{\mathbf{b}^3} \tag{4}$$

In order that indentation hardness can be predicted, the value of the Burgers vector of organic solids requires estimation. Much work has been carried out to determine the lengths of Burgers vectors in elements and inorganic materials [17]. However, for organic crystals limited data are available [9]. Data for unit cell length a, versus the Burgers vector **b**, for many materials are shown in Fig. 2. The majority of materials fall into two groups with a ratio of $\mathbf{b}/a$ of 0.7070 and 1, representing slip via (1 1 0) **1**/2 [$\bar{1}$ 1 0] (in face-centred cubic for example) and slip along a unit cell vector (any crystal system). It is interesting to note that only one material, the element chromium, has a large Burgers vector in relation to a (i.e. $\mathbf{b}/a = 1.615$).

It is proposed that for all crystal classes the ratio of the Burgers vector to the unit cell vector R_c, whether a, b or c is used to estimate the hardness, is called the slip ratio S_r (which can have values of 0.7070 and 1) and is as follows:

$$S_r = \frac{\mathbf{b}}{R_c} \tag{5}$$

This relationship can be incorporated into Equation 4 to give

$$H = \frac{2\Delta E_{coh}}{S_r^3 R_c^3} \tag{6}$$

In order that the cohesive energy density can be used in the expression it is necessary to replace the term R_c^3 with the molar volume V, by use of the relationship between unit cell volume V_c and unit cell constants, i.e. in the general case for any crystal class

$$V_c = R_c C_1 C_2 F_a \tag{7}$$

where R_c is the reference unit cell vector in Equation 5, C_1 and C_2 are the other two unit cell constants and F_a is an angular function related to α, β and γ depending on the crystal class, e.g. for monoclinic systems $F_a = \sin\beta$; if $R_c = a$ then $C_1 = b$ and $C_2 = c$ and therefore $V_c = abc\sin\beta$.

Furthermore the unit cell volume V_c is also related to the molar volume V by the relationship

$$V_c = \frac{VZ}{N_A} \tag{8}$$

where Z is the number of molecules in a unit cell and

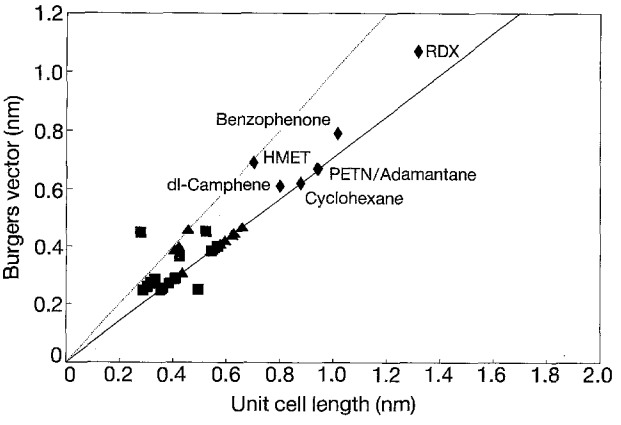


Figure 2 The Burgers vector versus the unit cell length a for a series of materials: (■) elements, (▲) inorganic crystals, (◆) organic crystals (individually identified). (——) $S_r = 0.7070$, (. . .) $S_r = 1$.

$N_A = 0.6$ (Avogadros number reduced to take account of the molar volume being in units of $cm^3\ mol^{-1}$).

These two equations can be combined to give

$$R_c C_1 C_2 = \frac{VZ}{N_A F_a} \tag{9}$$

This gives an equation which relates $R_c C_1 C_2$ to molar volume. However, the terms C_1 and C_2 must be eliminated from Equation 9 to allow this equation to be substituted into Equation 6 for R_c^3. The ratio between the reference unit cell vector R_c and that of the other two unit cell constants C_1 and C_2 is simply given by the two following expressions:

$$R_1 = R_c/C_1 \tag{10}$$

$$R_2 = R_c/C_2 \tag{11}$$

Using these expressions in Equation 9 gives the relationship between R_c^3 and molar volume:

$$R_c^3 = \frac{VZR_1R_2}{N_A F_a} \tag{12}$$

Substituting this equation into Equation 6 gives

$$H = \left(\frac{2F_a N_A}{R_1 R_2 S_r^3 Z}\right)\frac{\Delta E_{coh}}{V} \tag{13}$$

Substituting Equations 9 and 10 into Equation 13 and taking account of the fact that cohesive energy density $CED = \Delta E_{coh}/V$, then

$$H = \left(\frac{C_1 C_2 F_a 2N_A}{R_c^2 S_r^3 Z}\right) CED \tag{14}$$

This general equation can be used for any crystal class. However, we need not concern ourselves with all crystal systems, since over half of organic solids crystallize into space groups which are in the monoclinic class. In fact the percentages that are monoclinic, orthorhombic, triclinic, tetragonal, trigonal/hexagonal and cubic are 53.7, 25.8, 14.8, 2.9, 2.3 and 0.5%, respectively (data adapted from Mighell *et al.* [18]). Therefore the equations for only the top three crystal classes will be given, since they represent 94.3% of all the crystal classes for organic crystals.

For instance if the reference unit cell vector $R_c = a$ (and therefore $C_1 = b$ and $C_2 = c$) then for the three most common crystal classes Equation 14 can be modified to give Equations 15, 16 and 17 below for monoclinic, orthorhombic and triclinic, respectively:

(a) Monoclinic, where $F_a = \sin\beta$ in Equation 14:

$$H = \left(\frac{bc\sin\beta 2N_A}{a^2 S_r^3 Z}\right) CED \tag{15}$$

(b) Orthorhombic, where $F_a = 1$ in Equation 14:

$$H = \left(\frac{bc2N_A}{a^2 S_r^3 Z}\right) CED \tag{16}$$

(c) Triclinic, where $F_a = (1 - \cos^2\alpha - \cos^2\beta - \cos^2\gamma + 2\cos\alpha\cos\beta\cos\gamma)^{1/2}$ in Equation 14:

$$H = \left(\frac{bc(1 - \cos^2\alpha - \cos^2\beta - \cos^2\gamma + 2\cos\alpha\cos\beta\cos\gamma)^{1/2}2N_A}{\alpha^2 S_r^3 Z}\right) CED \tag{17}$$

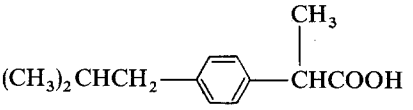
For the reference unit cell vector to be identified, the crystal structure needs to be examined since deformation via slip will always occur along a specific crystal plane and in a specific direction [19]. This plane and direction will be dependent on the crystal structure. Since the primary slip system will be a slip plane and slip direction in which dislocations can move easily and multiply, this is likely to be the plane that has the lowest Peierls stress [19]. It is proposed that the plane and direction in which primary slip occurs is that of the weakest plane, e.g. in terms of lowest energy and/or widest spacing or other structural features–the formation of hydrogen bonding networks (see below). With this information available, likely slip planes can be identified and used to determine the most likely unit cell vector, R_c, for a number of monoclinic crystals. Thus Equation 14 can then be utilized to enable predictions of indentation hardness from cohesive energy density using two slip ratios, S_r, of 0.7070 and 1.

The only other assumption that has to be made is that the cohesive energy, which is related to the lattice energy, may not be representative of the energy of the weakest slip plane since it is an average for the crystal structure. Whilst this may not universally be the situation, the use of the CED will be explored since it is relatively easy to calculate from chemical structure.

3. Results

3.1. Calculation of molar volume, solubility parameter and cohesive energy density

The molar volume V was primarily evaluated from the true density determined by air comparison pycnometry (Beckmann model 930) and the molecular weight. In some instances, molar volume was determined by a group contribution method of Fedors [20]. The technique is illustrated in Table I for ibuprofen and it can be seen that the agreement between the two methods is reasonable. Fedors [21, 22] demonstrated that this method of calculation by group contributions was less than 10% in error.



Ibuprofen

Where literature CED data were not available they were calculated from total and partial solubility parameters using the Hansen [23] approach from tables of group molar attraction contributions (dispersion, polar and hydrogen-bonding components [24]). The technique is illustrated in Table I for ibuprofen where the notation is the same as used by Hansen [23] and where the dispersion, polar and hydrogen-bonding contributions are calculated by use of Equations 18, 19 and 20, respectively:

$$\delta_d = \frac{\sum_z^z F_d}{V} \tag{18}$$

TABLE I Calculation of the solubility parameters for ibuprofen[a]

Group	No. (z)	V ($cm^3 mol^{-1}$)	${}^zF_d$ ($J^{1/2} cm^{3/2} mol^{-1}$)	${}^zF_p^2$ ($J cm^3 mol^{-2}$)	${}^zU_h$ ($J mol^{-1}$)
	1	52.4	1270	12100	0
CH	2	− 2.0	160	0	0
CH_2	1	16.1	270	0	0
CH_3	3	100.5	1260	0	0
COOH	1	20.8	530	176400	10000
$\sum$		187.8	3490	188500	10000
$\delta = 20.36\ MPa^{1/2}$			$\delta_d = 18.84\ MPa^{1/2}$	$\delta_p = 2.34\ MPa^{1/2}$	$\delta_h = 7.35\ MPa^{1/2}$

[a] Molecular weight = $206.3\ g\ mol^{-1}$, true density = $1.11\ g\ cm^{-3}$, molar volume $V = 185.2\ cm^3\ mol^{-1}$.

TABLE II True densities, molar volumes, solubility parameters and cohesive energy densities of various molecular crystals

Material	True density ($g\ cm^{-3}$)	V ($cm^3\ mol^{-1}$)	δ ($MPa^{1/2}$)	CED (MPa)	Reference
Ibuprofen	1.11	185.2[a]	20.4	416.2	Calculated (Table I)
Aspirin	1.40	128.4	24.5	600.3	[5]
Adipic acid	1.36	107.5[a]	24.8	615.0	Calculated
Salicylamide	–	92.4[b]	31.3	979.7	Calculated
Sucrose	1.56	219.4[a]	32.8	1075.8	Calculated
α-lactose monohydrate	–	236.8	39.9	1592.0	[25]

[a] Molar volume calculated from true densities and molecular weight.
[b] Molar volume calculated by the method of Fedors [20, 21].

$$\delta_p = \frac{\left(\sum_z^z F_p^2\right)^{1/2}}{V} \quad (19)$$

$$\delta_h = \left(\frac{-\sum_z^z U_h}{V}\right)^{1/2} \quad (20)$$

The total solubility parameter δ is calculated from Equation 21 and the cohesive energy density *CED* by Equation 22:

$$\delta^2 = \delta_d^2 + \delta_p^2 + \delta_h^2 \quad (21)$$

where δ_d = solubility parameter due to dispersion forces, δ_p = solubility parameter due to dipole interactions and δ_h = solubility parameter due to hydrogen bonding (or in general due to donor–acceptor interactions); and

$$CED = \delta^2 \quad (22)$$

All the data for cohesive energy density from sources used in this paper are presented in Table II.

3.2. Indentation hardness data

Indentation data for the various molecular crystals were taken from a number of sources as indicated in Table III. The majority of the indentation hardness values are on single crystals using a Vickers indenter, and as indicated by Ichikawa *et al.* [27] were performed on the crystal face possessing the largest area. Since this face is the dominant face it will dominate the subsequent properties of the material. This is particularly important when considering the compaction properties of these materials. The exception is ibuprofen where measurements were carried out on porous specimens using a Brinell impact tester, the values in Table III being zero porosity values. The values of indentation hardness taken from the literature are considered by the authors to be representative of the material and the values used are essentially from crack-free indents.

TABLE III Indentation hardness of some molecular crystals with their respective literature reference

Material	Indentation hardness (MPa)	Reference
Ibuprofen (lot A)	35	[26]
Ibuprofen (lot B)	99	[26]
Ibuprofen (lot C)	161	[26]
Aspirin	96	[27]
Adipic acid	123	[28]
Salicylamide	123	[27]
Salicylamide	151	[29]
Sucrose	636	[29]
α-lactose monohydrate	523	[27]

3.3. Crystal structural parameters

Literature values from single-crystal data of lattice cell constants a, b, c, β and Z (number of molecules in the unit cell) are given in Table IV.

3.4. Indentification of slip planes and directions

The whole basis for the prediction of indentation hardness is reliant on the identification of slip planes in organic crystals. The primary slip plane in such materials is assumed to be the weakest plane on the basis that, energetically, slip is preferred along this plane. Three methods have been used to identify such planes: (a) from attachment energy data, (b) from cleavage planes and (c) inference from hydrogen bonding patterns.

TABLE IV Crystal structural data for various materials

Material	a (nm)	b (nm)	c (nm)	β	Z	Space group	Reference
Ibuprofen	1.4667	0.7886	1.0730	99.36	4	$P2_1/c$	[30]
Aspirin	1.143	0.6591	1.1395	95.68	4	$P2_1/c$	[31]
Adipic acid	1.001	0.515	1.006	136.75	2	$P2_1/c$	[32]
Salicylamide	1.292	0.498	2.104	91.8	8	$P2_1/a$	[33]
Sucrose	1.086	0.871	0.778	102.4	2	$P2_1$	[34]
α-lactose monohydrate	0.7982	2.1562	0.4824	109.57	2	$P2_1$	[35]

3.4.1. Attachment energies

The attachment energy E_{ATT} is calculated from intermolecular force fields and represents the energy released per mole when a new layer of structure is added to each face. It is related to the sublimation energy E_{SB} by the equation

$$E_{SB} = \frac{E_L}{2} + E_{ATT} \quad (23)$$

where E_L is the layer or slice energy and is the bond energy per molecule of a two-dimensional slice with thickness d_{hkl}.

The attachment energy has been primarily used to predict the habit of organic crystals with notable successes (e.g. see for instance Berkovitch-Yellin [36]). Where the face with the lowest attachment energy represents the slowest-growing face it will be the major habit face of the crystal. Furthermore this plane will coincide with the major cleavage plane [37] and will exhibit twinning. It is therefore the weakest plane and is assumed to be the primary slip plane of the crystal. It is thus relatively straightforward to identify slip planes from attachment energies of organic crystals (Table V).

TABLE V Lowest-energy planes (hkl) as determined from attachment energies

Material	Lowest-energy plane (hkl)[a]	Reference
Ibuprofen	(100)	[37]
Aspirin	(100)	[37]
Adipic acid	(011)	[38]
Sucrose	(100)	[39]
α-lactose monohydrate	(010) and (0$\bar{1}$0) centre	[40]

[a] From attachment energies.

TABLE VI Literature information on the cleavage planes of various organic crystals

Material	Cleavage plane (hkl)	Reference
Aspirin	(100)	[41]
Adipic acid	(011)	[32]
Salicylamide	(001)	[33]
Sucrose	(100)	[42]
α-lactose monohydrate	No cleavage	[35]

3.4.2. Cleavage planes

Cleavage planes in crystals provide direct evidence for the weakest plane. They also are the twinning planes indicative of plastic deformation. Information on cleavage planes is often given in structural papers, and published data for the materials used in this study are given in Table VI. For aspirin, adipic acid and sucrose there is good agreement between the weakest plane from attachment energies (Table V) with that from cleavage planes (Table VI).

3.4.3. Inference from hydrogen-bonding patterns

The crystal structure can also be utilized on the weakest planes to gain an understanding by consideration of the hydrogen-bonding patterns that are formed by molecules. These structures, whether they be chains, ribbons, sheets or dimers, etc., are separated from each other by van der Waals forces, which despite their weakness contribute greatly to the packing energy of a crystal. The identification of such planes can be illustrated by examining the crystal structures of adipic acid, salicylamide, sucrose and α-lactose monohydrate.

Adipic acid forms infinite chains of molecules which are strongly hydrogen-bonded and these lie parallel to the a axis and therefore it might be expected that slip will proceed either along the direction of the chain ([100] direction) or at right angles to the chain direction ([011] or [001] direction). It might be expected purely from geometrical and therefore energetic considerations that slip will be preferred via the latter direction, and this is in agreement with that found from attachment energies.

Salicylamide and its derivatives are capable of forming both intramolecular and intermolecular hydrogen bonds, the competing interaction between proton donors and acceptors being responsible for the resulting hydrogen bonding patterns [43]. For salicylamide its two proton donors (NH_2 and OH) and one acceptor (C = O) are responsible for the hydrogen-bonded pattern, the molecules being connected by NH–O hydrogen bonds, the first set forming a dimer across the centre of symmetry and the second set joining the dimers into an endless ribbon extending along the a axis. There is also an intramolecular H-bond formed via OH and C = O. It is clear that slip can either occur along this axis ([100] direction) or along a direction

which is at right-angles to the H-bonded ribbon structure ([0 1 0] direction). The plane formed by these two slip directions is in agreement with the (0 0 1) cleavage plane data.

The sucrose crystal structure is dominated by hydrogen bonds (O–H . . . O), of which there are seven per asymmetric unit including two intramolecular bonds forming a complicated mesh across a number of planes. However, only one of these hydrogen bonds extends across the (1 0 0) plane and therefore this is likely to be the weakest plane. This plane has the lowest attachment energy (Table V) and is the observed cleavage plane (Table VI). It is interesting to note that on a freshly cleaved (1 0 0) face the cleavage direction is [0 1 0]. Observations of alignment of each pit indicates that the movement of dislocations takes place along the [0 1 0] direction [42].

α-lactose monohydrate molecules are held together by hydrogen bonds involving connections both between lactose molecules and between lactose and water molecules, forming a three dimensional network. Two molecules are related by a translation along the *a* axis, these being strung together in sheets by three hydrogen bonds, two involving glucose residues and one involving galactose [35]. A fourth hydrogen bond links the sheets of molecules parallel to the *a* axis in such a way that they form infinite zigzagging chains of hydrogen bonds parallel to the *c* axis. The hydrogen bonds involving water molecules lie across the centre of the unit cell parallel to the *a* and *c* axes. The slip plane is therefore likely to involve breakage of hydrogen bonds across the centre of the unit cell parallel to the (0 1 0) plane, since this would appear to be the weakest plane based on the geometry of the crystal lattice. This agrees with the weakest plane predicted from attachment energies (Table V).

These four examples demonstrate the influence that hydrogen-bonding patterns have on directing molecular slip. In adipic acid and salicylamide, this essentially takes place between networks of hydrogen bonds and in sucrose and α-lactose monohydrate it involves breaking of the weakest hydrogen bonds.

From the data presented in Tables V and VI two possible slip directions for each plane can be postulated. These are shown in Table VII. By reference to all this information (Tables II–VII) and Equation 14, the indentation hardness can be calculated for two slip ratios (Table VIII).

TABLE VII The weakest planes (*hkl*) and their corresponding two slip directions [*uvw*]

Material	Weakest planes (*hkl*)	Slip directions [*uvw*]
Ibuprofen	(1 0 0)	[0 1 0], [0 0 1]
Aspirin	(1 0 0)	[0 1 0], [0 0 1]
Adipic acid	(0 1 1)	[0 1 1], [1 0 0]
Salicylamide	(0 0 1)	[1 0 0], [0 1 0]
Sucrose	(1 0 0)	[0 1 0], [0 0 1]
α-lactose monohydrate	(0 1 0)	[1 0 0], [0 0 1]

4. Discussion

From Equation 14 it might be expected that as the cohesive energy density increases then the indentation hardness increases. This in general terms is true (see Tables II and III) but use of this simple approach is obviously not suitable for accurate predictions since it does not take account of the obvious differences in crystal packing. These differences are quite often reflected in the dimensions of the unit cell and are essentially the factors enabling this aspect to be taken into account in Equation 14.

The predictions of indentation hardness of a number of organic solids (Table VIII) show that in all cases when $S_r = 0.7070$ the values are much too high when compared with experimental values and therefore are unlikely. The most likely slip ratio for these solids is therefore unity. However, for all the organic solids there are at least two possible slip systems, the problem being how to decide which system is the more

TABLE VIII Comparison of the predicted and literature indentation hardness data for the various organic crystals for the various slip systems

Material	Indentation hardness (MPa)			Slip system (*hkl*) [*uvw*]	R_c
	Literature	$S_r = 0.7070$	$S_r = 1$		
Ibuprofen	35, 99, 166	882	312	(1 0 0) [0 1 0]	*b*
		350	124	(1 0 0) [0 0 1]	*c*
Aspirin	96	1520	537	(1 0 0) [0 1 0]	*b*
		294	104	(0 1 1) [0 1 1]	*c*
Adipic acid	123	2715	960	(0 1 1) [0 1 1]	*b*
		364	129	(0 1 1) [0 1 1]	*c*
		370	131	(0 1 1) [1 0 0]	*a*
Salicylamide	123, 151	261	92	(0 0 1) [1 0 0]	*a*
		4554	1610	(0 0 1) [0 1 0]	*b*
Sucrose	636	1974	698	(1 0 0) [0 1 0]	*b*
		2793	987	(1 0 0) [0 0 1]	*c*
α-lactose monohydrate	523	4156	1469	(0 1 0) [1 0 0]	*a*
		18828	6656	(0 1 0) [0 0 1]	*c*

likely. This can be done on energetic grounds since it is unlikely that slip will take place in the direction which gives the higher hardness values, i.e. the weakest direction will be energetically favoured providing that this is not blocked (influence of dislocation entanglement). In all cases (Table VIII) there are large differences in the indentation hardness between the alternative slip directions for a particular slip plane, e.g. in the case of aspirin the hardness values are 537 and 104 MPa for the two slip directions [0 1 0] and [0 0 1], respectively; the latter is therefore favoured.

Using these guidelines, the values of predicted indentation hardness (when $S_r = 1.00$) compare very well with those from experiment using the designated slip directions, with the exception of α-lactose monohydrate. For this material the lowest predicted value is three times larger than that found by experiment. This could be due to a number of factors:

(a) As discussed above, the crystal structure of α-lactose monohydrate is a significantly hydrogen-bond dominated structure and this could lead to co-ordination number differences between that assumed (the co-ordination number was taken to be 12) and that found in practice. For instance, the co-ordination number would have to be of the order of 34 for the slip system (0 1 0) [1 0 0] (back-calculating a value of C from Equation 14, using an indentation hardness of 523 MPa–see Table III), and this is unlikely to be the case.

(b) Another possibility is that the Burgers vector is much larger than that taken. If it is assumed to be an unstable dislocation with a slip ratio $S_r = 1.4142$ (e.g. equivalent to (1 1 0) [1 1 0] in an f.c.c structure) then for the slip system (0 1 0) [1 0 0] the predicted indentation hardness would be 520 MPa. Since this is remarkably close to the experimental value this situation is a realistic possibility, but difficult to prove without an examination of actual Burgers vectors in α-lactose monohydrate crystals.

Finally, it is interesting to note that ibuprofen has a literature value of 35 MPa for the indentation hardness (Table III), much lower than predicted. This suggests that the slip plane as assigned using attachment energies, although being the weakest plane, may not be the slip direction with the lowest energy. In fact Bunyan et al. [37] found anomalies for ibuprofen between the predicted crystal habit and experimental habits, notably when comparing crystals produced from low-polarity and high-polarity solvents. The (0 0 1) plane is the major habit face (when recrystallized from hexane, toluene, ethyl acetate, acetonitrile and propan-2-ol) but has the second lowest attachment energy, whereas the (1 0 0) face predominates when crystallization is performed in ethanol and methanol. This seems to suggest that the energetics of the crystal lattice in terms of the directional properties (slip) is very important, more so than the energetics of a plane. When the calculations are performed using the (0 0 1) face, which gives the slip directions [1 0 0], and [0 1 0], the indentation hardnesses are 48 and 312 MPa, respectively (assuming $S_r = 1$) and therefore the [1 0 0] direction is likely to be the more favourable. The lower value is in good agreement with the lower value of 35 MPa found in the literature (Table III).

It should be noted that the ibuprofen was recrystallized at various rates and gave indentation hardnesses of 35, 99 and 161 MPa for lots A, B and C respectively (Table III [26]). This may be indicative of a change in slip direction, e.g. the more slowly grown material of lot A is probably more perfect than the other two lots which may have the [1 0 0] direction blocked due to the influence of impurities and/or dislocation interactions (note that all the lots had the same powder X-ray diffraction pattern and therefore are the same polymorph).

5. Conclusions

A pragmatic model has been developed to enable predictions of the indentation hardness of organic crystals. It has been demonstrated that for the majority of materials the predictions agree well with literature data. For α-lactose monohydrate, which has a structure dominated by a complicated hydrogen-bonding network, the agreement is poor.

A prerequisite for the prediction is the solution of the crystal structure. With this information the slip plane and direction can be identified either by calculation of attachment energies and/or determination of cleavage planes and/or an inference from hydrogen-bonding patterns. The latter approach demonstrates the importance of the directional behaviour of hydrogen bonding and formation of subsequent networks and its influence on the subsequent physical properties of organic crystals.

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