Some Remarks About Potential Energy Calculations in Crystals

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The method of calculating the potential energy in crystals to determine the molecular packing has rarely been used. Since this approach is likely to be employed more frequently to solve the phase problem and for theoretical calculation of physical properties, it is believed to be useful both to clarify the strategy used in applying the packing analysis and to emphasize some misconceptions about its real power and limits on the basis of our experience. As an example the paper of Kawaguchi, Takashina, Tanaka & Watanabé on the crystal structure of bromoform is discussed.

Introduction

Some successful attempts to solve the phase problem in crystals of unknown structure have recently been made by using semi-empirical potential functions describing van der Waals and electrostatic interactions between non-bonded atoms and ions and the formation of hydrogen bonds (among the most recent papers: Ahmed, Kitaigorodsky & Mirskaya, 1971; Williams, 1969; Coiro, Giacomello & Giglio, 1971; Capaccio, Giacomello & Giglio, 1971).

The calculation of the potential energy, as a function of the rotational and translational degrees of freedom of the asymmetric unit, is justified by the equivalence of one of its minima, very often the deepest one, with the crystal free-energy minimum. Of course, once the unit-cell dimensions and the space group have been experimentally determined, this statement is valid if the entropy and the vibration energy changes between states characterized by different values of rotational and translational parameters are negligible. Fortunately this is in general true.

In principle to apply this method we must know:

(*a*) The approximate geometry of the asymmetric unit, the knowledge of the molecular conformation being often unnecessary.

(*b*) The unit-cell parameters and the possible space groups.

(*c*) The semi-empirical potentials allowing the computation of, at least, the most important inter- and intramolecular interactions.

In the following we shall briefly discuss the above-mentioned requirements.

General considerations

(*a*) Many bond lengths and angles are available from the literature with an accuracy adequate for this procedure. Furthermore, even if unfavourable molecular geometries are adopted, as for 5α-androstan-3,17-

dione (Damiani, Giglio, Liquori & Mazzarella, 1967), diketopiperazine (Giacomello & Giglio, 1970) and *N,N'*-dicyclohexylurea (Coiro, Giacomello & Giglio, 1971), the crystal structures may still be determined.

The conformation of a molecule may be established by means of intramolecular potential energy calculations, as for spermine (Liquori, Costantino, Crescenzi, Elia, Giglio, Puliti, De Santis Savino & Vitagliano, 1967; Giglio, Liquori, Puliti & Ripamonti, 1966; Iitaka & Huse, 1965) and *N,N'*-dicyclohexylurea. The appearance of more than one minimum in the intramolecular energy map necessitates taking into account several conformations (as a rule two or three at most) which may increase the computing time, in the worst case, by a factor of two or three. Therefore the possibility of undertaking the packing analysis in two stages, by evaluating first the intramolecular energy surface and then the intermolecular one, markedly simplifies the energy search.

(*b*) The unit-cell parameters and space-group determination is a matter of standard routine. The frequent uncertainty in the choice of the space group, mainly concerning the presence of a centre of symmetry, can be bypassed sometimes by means of intramolecular energy calculations, determining the molecular geometry as for *N,N'*-dicyclohexylurea. Otherwise the packing analysis must be carried out in the two space groups. Obviously, if a noticeably better packing energy is achieved with one of two possible space groups, it is reasonable to discard the one less energetically stable.

(*c*) The potential energy consists of many terms such as van der Waals, torsional, coulombic, dipole–dipole, ion–dipole, hydrogen bonding and charge transfer energies, to mention only the most important. There can be no doubt that, among them, the van der Waals energy, arising from dispersion and exchange repulsive terms, nearly always plays the leading role, especially in organic crystals. Considerable effort is being devoted to determining the coefficients of the poten-

tials describing non-bonded interactions, by different approaches. However, it is our opinion that, at present, all the available semi-empirical potentials may be handled as a crude approximation to reach only qualitative agreement. Even in the very simple cases of the noble gases, the various potentials at our disposal witness the failure to reproduce at the same time all the measured molecular properties such as, for example, heats of sublimation, second virial and viscosity coefficients and crystal properties. The poor quantitative agreement generally obtained indicates that some assumptions of the theory are inadequate.

Therefore efforts to fashion the potentials in order to fit, for instance, the experimental data of one or more crystalline compounds do not deserve to be taken into account as they lack any heuristic value. In fact this procedure becomes a mere mathematical game allowing us to get potentials which cannot reproduce the same physical property even in crystals of similar compounds.

For this reason we have chosen the potentials we use in solving the phase problem (Giglio, 1970, and references quoted therein) simply by testing their validity in known crystal structures as a function of the unit-cell edges and angles and of some degrees of freedom of the asymmetric unit. We have regarded the potentials as reliable when the experimental structure is the one corresponding reasonably well to the deepest minimum in the energy surface, computed by leaving unchanged the crystal symmetries and considering the molecules as rigid bodies. Some potential functions, relative to interactions involving the more common atoms in organic crystals, such as hydrogen, carbon, nitrogen, oxygen, sulphur, chlorine, bromine, iodine and the methyl group, have been verified in real crystals. The crystals have been selected in such a way that only one potential controls to a large extent the molecular packing. More sophisticated approaches have not been considered justified.

For the qualitative purpose of the crystal-structure determination, the potentials must primarily possess proper positions of the van der Waals minima, the other parameters of the energy curve playing a minor role. This assertion is demonstrated by the good results obtained by using potentials of the rare gases, argon, krypton and xenon, to represent the interactions sulphur–sulphur, chlorine–chlorine, bromine–bromine and iodine–iodine (Giglio, Liquori & Mazzarella, 1968; Di Nola & Giglio, 1970; Giglio, 1970). Furthermore, a straightforward method of building up new potentials for other atoms is proposed (Giglio, 1970).

Some potentials accounting for the formation of hydrogen bonds (Giglio, 1969; Giacomello & Giglio, 1970; Coiro, Giacomello & Giglio, 1971) and describing electrostatic interactions between oxygen and sodium, potassium, rubidium and caesium (Capaccio, Giacomello & Giglio, 1971) have given satisfactory results. In this connexion the difficulty, at present

insurmountable, of putting on the same scale the numerical values of different terms contributing to the total energy should be emphasized. In this case the energy values are still less reliable quantitatively.

Outline of the method

The procedure followed in carrying out the packing analysis may be explained by describing a standard computer program. Since a large computing time may be a considerable handicap in searching for the energy minima, we have so far written programe in Fortran IV and V for special cases. The framework of the programs is always the same so that it is easy to modify the program of any crystal structure in such a way as to adapt it to another compound.

Looking at the energy as a continuous function, calculation on net points in a multi-dimensional parametric space can be accomplished to find the regions in which the energy reaches its minima.

The most important input data are:

I.   The unit-cell parameters.
II.   The angular and translational values, defining the regions to be scanned in the multi-dimensional space, together with the relative increments.
III. The coefficients of the potentials to be used.
IV.   The atomic coordinates of the first asymmetric unit.
V.   Nine elements of a rotation matrix and three components of a translational vector for each asymmetric unit to be generated from the first one.

The potential energy is estimated on the basis of all the interactions between the first asymmetric unit and the nearest neighbours, usually ranging from two to thirteen, obtained by space-group symmetry and considered with the proper multiplicity.

The first asymmetric unit is rotated and translated in a right-handed orthogonal framework $Oxyz$ orientated with respect to the triclinic crystallographic system $Oabc$ in such a way that, for example, Oz and Oc coincide, Ob lies in the yz plane and the positive Ox and Oa semi-axes are on the same side of the yz plane. In addition intramolecular rotations are performed, if required, together with independent rotations and translations of parts of the first asymmetric unit.

All the interatomic distances are calculated and stored, but a point on the energy surface is skipped as soon as one contact is found to be less than a cut-off distance, previously fixed, for every pair of chemical species in each energy term. The cut-off distances are established mainly on the basis of the van der Waals radii. Usually they are assumed to be about 20% less than the sum of the van der Waals radii of the atoms involved and depend on the increments of the rotational and translational movements. Then the potential energy is evaluated by simple grid-point calculations and the more significant parameters of the deepest minima may be preserved. The first run is performed

with large angular and translational increments, normally 20° and 0·5 Å respectively, and minimization techniques may be successively employed to locate the point of lowest energy in a minimum region. At present we tend to use the simple and fast method of steepest descent, even if we cannot draw any decisive conclusion because of our limited experience.

At this stage the atomic coordinates of a minimum may be compared with the X-ray observed data by structure-factor calculations. The agreement index R is computed as a function of small changes in the rotational and translational degrees of freedom near a minimum of the energy surface. As a rule only the reflexions with $\sin \theta/\lambda \leq 0·3$ Å^{-1} are utilized to increase the speed of the procedure. An average temperature factor, derived by a Wilson plot, is assumed. Subsequently the atomic coordinates corresponding to a promising R are refined by least squares to establish if the solution is correct.

The time required by a computer to carry out a full search increases very quickly with the number both of the degrees of freedom and of the independent parts of the asymmetric unit. To save computing time various expedients are available. The main considerations in this regard are the following:

(i) The scanning of the multi-dimensional parametric space can be accomplished in the 'Cheshire cell' (Hirshfeld, 1968), so being reduced by taking into account the space group and the molecular symmetry.

(ii) The range of every degree of freedom to be explored may be limited if there are present such symmetry elements as rotation axes, mirror planes and inversion centres. Furthermore, very strong reflexions may indicate the approximate position of the asymmetric unit, making the packing analysis easier and much faster.

(iii) Often many atoms of the asymmetric unit can be left out in the packing analysis when they are screened by outer atoms and cannot produce short interatomic distances. In connexion with the possibility of reducing the number of atoms, the determination of simple intermolecular potentials (Berne & Pechukas, 1972) derived from a Gaussian overlap model is worthy of note. These potentials, useful in describing interactions between two molecules or chemical groups, will be tested in our laboratory in order to solve the phase problem in crystals.

(iv) The sequence of the parameter changes may be planned in such a way as to vary more rapidly those entailing less calculation and giving rise to a larger number of points of the energy surface which can be discarded for some short contacts. A similar criterion may also be applied in structure-factor calculations because, for instance, a translation modifies a structure factor through a modulation with a proper phase factor. Usually it is suitable to vary the translational parameters more frequently than the rotational ones, both in the energy and in agreement index routines.

(v) The potential energy is estimated only after all

the interatomic contacts become longer than the relative cut-off distances. The values of the energy curves, generated with an appropriate increment and stored at the beginning of the program, are associated with the corresponding distances through an index allowing us to by-pass the energy computation *via* semi-empirical formulae.

As an example we report the case of a crystal, space group $P\bar{1}$, with 52 atoms in the asymmetric unit. All the interactions between the central asymmetric unit, and the thirteen nearest ones (multiplicity 2) have been considered. There are five rotational degrees of freedom, two being intramolecular. The first two range from 0 to 360°, the third from 0 to 90° and the last two from 0 to 180°. The full scanning of the energy surface with angular increment of 20° and the subsequent steps, up to the R value analysis for the three lowest minima, requires about fifty-five minutes on a UNIVAC 1108 computer.

The computing time may be considerably reduced if a reliable minimization procedure is available. Many techniques can be employed (Wilde, 1964) but all are unsatisfactory when several variables are present and the starting position of the asymmetric unit is very different from the experimental one. In this case the convergence to the experimental arrangement generally fails. Besides finding many false minima it is doubtful if it is always possible to jump out of a valley once its position has been reached. On the other hand the difficulty of determining all the minima in order to discard the highest ones makes the analysis of the energy surface very uncertain.

The crystal structure of bromoform

The crystal structure of bromoform has been determined (Kawaguchi, Takashina, Tanaka & Watanabé, 1972) by X-ray diffraction. The space group is $P6_3$, $Z=2$. Because the molecules are statistically disordered and oriented up and down along the c axis with nearly equal weight, the space group becomes approximately $P6_3/m$.

The lattice energies of bromoform and iodoform, probably isomorphous with bromoform, have been calculated in the two space groups $P6_3$ and $P6_3/m$, taking into account the van der Waals and dipole-dipole interactions as well as the induced effects. Similar calculations have been carried out for chloroform, space group $Pnma$, in the actual space group and in the hypothetical ones $P6_3$ and $P6_3/m$, in an attempt to explain energetically why its crystal system is orthorhombic and not hexagonal like that of bromoform and iodoform.

Kawaguchi, Takashina, Tanaka & Watanabé (hereinafter referred to as KTTW) report energy data in Table 5 of their paper. The comparison of the lattice energies of bromoform or iodoform in the space groups $P6_3$ and $P6_3/m$ is hazardous because the numerical values depend on the potentials employed and no criteria are

available for preferring one set of potentials. KTTW find quite small differences, less than 0·15 kcal/mole, between the two molecular arrangements by using potentials almost as soft as those of Scott & Scheraga (1965), which rapidly rise from relatively deep minima and show short van der Waals minimum distances. Therefore the potentials proposed by Scheraga and co-workers and tested in known crystal structures produce a considerable decrease of the unit-cell volume (Liquori, Giglio & Mazzarella, 1968; Giglio, Liquori & Mazzarella, 1969; Di Nola & Giglio, 1970).

The situation is much more critical for chloroform. The unit-cell parameters of the hypothetical space groups $P6_3$ and $P6_3/m$ have been assumed to be $a = 6·03$ and $c = 7·10$ Å without reasonable grounds. In fact the molecular volumes do not agree in the hexagonal (111·8 Å^3) and orthorhombic (103·8 Å^3) space groups. Furthermore, the decreasing trend of the unit-cell edges and the volume in the series iodoform, bromoform and chloroform is quantitatively different from the behaviour observed in boron triiodide, tribromide and trichloride, to which KTTW refer.

Thus the comparison of the energy values of chloroform in the space groups $P6_3$ (or $P6_3/m$) and $Pnma$ is meaningless, mainly for the following reasons:

1. KTTW have adopted potentials giving the lowest energy values for smaller unit-cell volumes.

2. The hypothetical hexagonal structures have been assumed with a molecular volume larger than the orthorhombic one and this automatically ensures a better van der Waals energy for $Pnma$.

3. KTTW have taken into account for the dispersion term all the pairwise interactions within a range of 20 Å. In such a sphere there are about 300 and 323 molecules in the hexagonal and orthorhombic crystals respectively. The closer contacts and the larger number of interactions decrease the dispersion energy for $Pnma$. The same situation occurs for the dipole–dipole term.

4. The dipole–dipole and van der Waals energies have been computed by means of semi-empirical potential functions, which may provide qualitative results, but show serious deficiencies in quantitative treatments. These potentials have usually been derived by parametrization *ad hoc* for a class of compounds. Each extension to a new set of compounds is almost always unsuccessful (see, for example, Williams, 1966, 1967).

5. The different energy terms must be put on the same scale before they can be summed.

6. The entropic contributions to the free energy may be rather dissimilar for two different space groups, especially when one of them is statistically disordered. Of course this remark also holds for bromoform and iodoform.

With respect to points 2 and 3 it should be noticed that the van der Waals energy is improved by rather more than 1 kcal/mole in the space group $P6_3$ with the potentials adopted by KTTW if a and c are changed in

such a way as to give the same molecular volume as in $Pnma$. Then the two crystal phases show nearly the same van der Waals energy, that of $Pnma$ being 0·3 kcal/mole less. A similar reasoning may be developed for the dipole–dipole energy.

These calculations have been performed by assuming the following bond distances and bond angles for chloroform: $C–H = 1·08$ Å; $C–Cl = 1·75$ Å; $H–\hat{C}–Cl = Cl–\hat{C}–Cl = 109°28'$.

The molecule is oriented almost exactly as bromoform and its arrangement has been verified energetically by rotating about the 6_3 screw axis parallel to c. The van der Waals energy, evaluated as a function of a and c, shows the lowest minimum ($-12·8$ kcal/mole) at $a = 5·6$ and $c = 6·5$ Å.

Conclusions

On the basis of the above considerations the predictive reliability of potential energy calculations in solving the phase problem at least in crystals of average complexity is apparent. It should not be assumed that semi-empirical potentials provide a quantitative model for physical properties of crystals or for the intra-molecular energy in the conformational analysis of molecules and of synthetic and biological polymers. With regard to the conformational analysis it has to be mentioned that very short interatomic distances are frequently present in a macromolecule and the corresponding energy values are certainly inaccurate to a large extent. In fact, the calibration of the potentials by using such crystal properties as the unit-cell parameters and the heats of sublimation gives rise to dispersion terms, useful for qualitative purposes, and to unreliable repulsive terms, since the intermolecular contacts in a crystal lie, normally, on the attractive part of the potential curve and influence only slightly the repulsive one. Thus the use of the Lennard-Jones and Buckingham equations, for instance, is at best a rough approximation.

It is hoped that in the future the theory will be re-examined in order to obtain quantitative results and that at present potential energy calculations are applied with caution.

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Constrained Refinement of Orthorhombic Sulphur

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Constrained refinement shows there is considerable distortion of the molecules of sulphur S_8 on forming a crystal. The diffraction data are fitted very well by a rigid-body motion model for the thermal motion. It is shown however that a deduction that the motion is in reality of rigid-body type would be erroneous as the rigid-body motion model includes most of the effects of the internal modes.

Introduction

The structure of orthorhombic sulphur has not received attention for many years. We are at present (see Pawley, Rinaldi & Windsor, 1971) making measurements of the phonon dispersion curves ,and in order to analyse the results a model for the dynamics is required. For this it is necessary to know the crystal structure as accurately as possible, and this has prompted us to do the constrained refinements reported here.

The data used in the present paper are those of Abrahams (1955). The structure is orthorhombic, Fddd,

$$a = 10.437 \ (10), \ b = 12.845 \ (10), \ c = 24.369 \ (10) \ \text{Å} .$$

Refinement with an overall isotropic temperature factor reached an R value (see Table 2) of 0·162, but this cannot be compared directly with the present result as there are differences in the models used, one minor difference being that we used the neutral atom scattering factor of Doyle & Turner (1968). In all our refinements an empirical weighting scheme was used, following Cruickshank (1965). The weight for the ith observation was

$$[2F_{min} + F_i^{obs} + 2(F_i^{obs})^2/F_{max}]^{-1} ,$$

with $F_{min} = 40$ and $F_{max} = 250$. Only those 669 observations not including the 'less-thans' were used, following Abrahams.

Although the structure is composed of molecules it is most likely that these are distorted and do not move as rigid bodies. This follows from the fact (see Cyvin, 1970) that the frequency of the lowest internal mode of the free molecule is 86 cm^{-1}, which is lower than the expected frequency of some lattice modes. The extent of molecular distortion and internal mode motion is here investigated through constrained refinements.

Refinements

(i) Molecular symmetry

In the free state the molecules of S_8 have the symmetry $\bar{8}m$. The shape can be completely determined by two parameters as in Fig. 1. Atoms 1, 2, 3' and 4' lie on a square in the plane $X = -x$, while the other four atoms lie on a similar square at $X = x$. The radial distance perpendicular to the X axis for all atoms is r.

Refinements of the crystal structure were performed using the techniques described by Pawley (1971), in such a way that all the molecules in the crystal maintained the free state symmetry. The parameters x and r were varied, reaching optimum values

$$x = 0.4920 \pm 0.0024 \ \text{Å}$$
$$r = 2.3368 \pm 0.0020 \ \text{Å} .$$

From these values the S–S bond length and S–S–S bond angle are 2·041 ± 0·005 Å and 108° 5' ± 11'. These