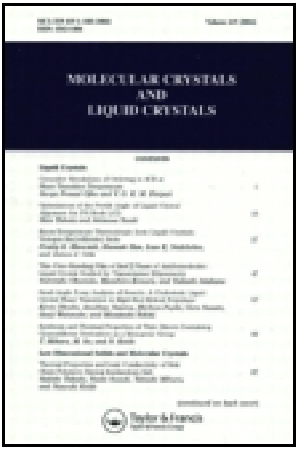

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A Modelling Approach to Organic Solid-State Chemistry

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A MODELLING APPROACH TO ORGANIC SOLID-STATE CHEMISTRY

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Abstract A method is described for the analysis of non-bonded forces in crystalline organic compounds. It is developed by reference to the photoreactive compound 2-benzyl-5-benzylidene-cyclopentanone (BBCP) and its derivatives, but it is of general validity. The approach is valuable for predicting the structural consequences of substitution at different positions in a given molecule; this ability is of importance in predicting the reactivity of organic solids.

INTRODUCTION

It is now generally accepted that the solid-state mechanisms of organic chemical reactions are characterised by a minimum of atomic and molecular movement. A consequence of this is that, for a given reaction, the structures of the intermediate and product molecules are largely constrained by the molecular and crystal structures of the reactants.

A major drawback, however, to the widespread adoption of organic synthesis in the solid state is that the crystal structure of a given reactant molecule often cannot be predicted with confidence. Although ab initio methods have progressed considerably for hydrogen-bonded systems[1], such methods cannot be applied easily to hydrocarbons, which are stabilised largely by dispersive non-bonded interactions. Semi-empirical pairwise potentials are useful in testing the feasibility of trial structures, but they cannot be relied upon to discriminate between alternative crystal structures which lie close in energy to one another.

A partial solution to the problem of predicting the crystal structures of reactant molecules is described in this paper. The method is developed by referring to the 2-benzyl-5-benzylidene-cyclopentanone (BBCP) system of compounds (Figure 1), of which a wide variety of crystal structures are known[2,3,4,5,6,7] Not all of the predictions made by this approach have been tested, but it is self-consistent when applied to all the BBCP derivatives whose structures have been determined experimentally.

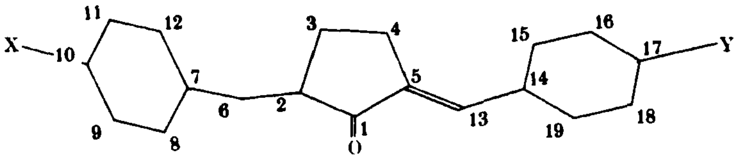

FIGURE 1. Atomic numbering in BBCP

METHOD

A summary of the crystallographic data of some of the BBCP derivatives is given in Table 1.

TABLE 1. Crystallographic data for some BBCP derivatives

Compound	X	Y	Space Group	Z	Cell constants	React-ive?	Type
BBCP	H	H	Pbca	8	a=31.29Å b=10.78Å c=8.69Å	Yes	1
pCl BBCP	Cl	H	$P2_1/c$	4	a=17.18Å b=10.59Å c=8.80Å β=103.7°	Yes	1
B pCl BCP	H	Cl	Pbca	8	a=31.05Å b=8.52Å c=11.64Å	No	2
pBr BBCP	Br	H	$P2_1/c$	4	a=17.46Å b=10.56Å c=8.85Å β=104.1°	Yes	1
B pBr BCP	H	Br	Pbca	8	a=34.22Å b=10.92Å c=8.43Å	Yes	1
pMe BBCP	Me	H	$P2_1/c$	4	a=17.34Å b=10.68Å c=8.74Å β=102.6°	Yes	1
B pMe BCP	H	Me	Pbca	8	a=31.17Å b=8.46Å c=11.70Å	No	2
pMe B pBr BCP	Me	Br	$P2_1/c$	4	a=18.38Å b=11.21Å c=8.29Å β=94.5°	Yes	1
pBr B pMe BCP	Br	Me	Pbca	8	a=34.18Å b=8.41Å c=11.77Å	No	2

The compounds in the table cover two common structural types, one of which is photo-reactive and the other photo-stable. The reactive 'Type 1' structural motif is illustrated in Figure 2(a), with the 'Type 2' photostable structural motif given in Figure 2(b).

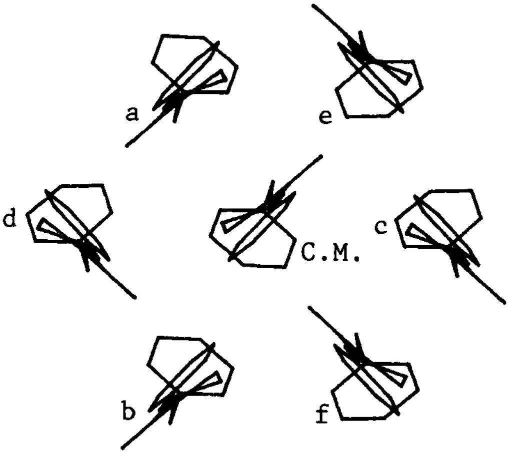

FIGURE 2(a). The 'Type 1' structural motif (for pCl BBCP). The central molecule is labelled C.M., with coordinating molecules labelled a,b,c...f.

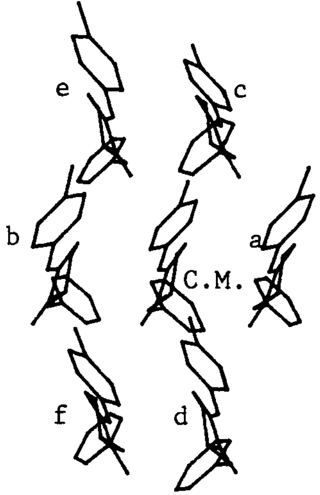

FIGURE 2(b). The 'Type 2' structural motif (for B p Cl BCP). Labelling is as in Figure 2(a). Molecules g and h lie above and below the plane of the motifs shown.

The reactivity of the 'Type 1' motif is explained by the parallelism of two olefinic bonds, separated by a distance which varies between 3.8 and 4.2Å among photoreactive BBCP derivatives. Upon irradiation with u-v light, a (2+2)-cycloaddition takes place, to form dimers.

The classification into structural types is performed most easily by looking at the potential energies of interaction of a molecule (designated the 'central molecule') with its successively neighbouring molecules in the crystal. For this purpose, it is sufficient to use semi-empirical pair potentials of the form $u = -A/r^6 + B \exp(-Cr)$, where the constants A,B and C are available from the literature.[8] The results of these calculations for the crystal structures in Table 1 are given in Table 2.

TABLE 2. Potential energies of interaction (in kJ/mole) of the central molecule with successively neighbouring molecules, a,b,c....h

Compound	a	b	c	d	e	f	g	h
BBCP	49.97	32.45	30.54	30.54	29.86	29.86	6.57	6.57
*p*Cl BBCP	50.76	35.19	33.71	33.71	31.31	31.31	15.42	4.50
B *p*Cl BCP	46.39	46.39	31.07	31.07	28.90	28.90	9.13	9.13
*p*Br BBCP	49.63	33.82	33.82	33.08	31.48	31.48	15.94	5.32
B *p*Br BCP	63.19	32.82	32.32	32.32	29.71	29.71	8.95	8.95
*p*Me BBCP	49.03	31.72	31.72	31.20	29.31	29.31	14.34	4.11
B *p*Me BCP	48.85	48.85	30.88	30.88	29.12	29.12	9.60	9.60
*p*Me B *p*Br BCP	65.21	36.89	32.20	32.20	28.64	28.64	19.87	5.65
*p*Br B *p*Me BCP	49.93	49.93	31.05	31.05	27.84	27.84	11.62	11.62

Three of these energy-profiles are shown graphically in Figure 3: those of BBCP, *p*Cl BBCP and B *p*Cl BCP. 'Type 1' structures (BBCP and *p*Cl BBCP) have a large drop in energy between coordinating molecules a and b, whereas 'Type 2' structures do not. Further, the magnitudes of these energies suggest that, in all derivatives, the central molecule is coordinated most strongly by six molecules (a-f), with molecules g and h contributing much less to the total binding energy of the central molecule. Further structural types of other BBCP derivatives have been identified by this method[7,9] but they need not be considered in the present discussion.

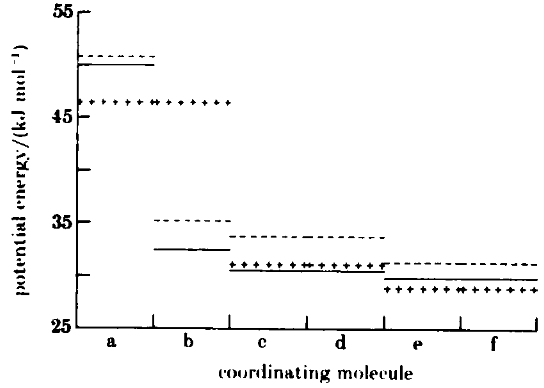

FIGURE 3. Profiles of non-bonded energy for three of the derivatives (—— : BBCP; - - - : *p*Cl BBCP; +++++ : B *p*ClBCP)

These energy-distributions lead naturally to the idea of a 'molecular cluster', consisting of the central molecule and the six coordinating molecules that interact most strongly with it. About 80 per cent of the bulk stabilisation of the central molecule comes from interactions with molecules within the appropriate cluster; so a given molecular cluster may be thought of as the basic structural motif of a crystal structure.

Having classified the structures, our aim is to understand the relationship between the positions of substituents and structural type. A simple approach is to assign a van der Waals radius to each atom (C: 1.70Å; H: 1.20Å; O: 1.40Å; Cl: 1.80Å; Br: 1.95Å), and calculate a local packing density for each hydrogen atom in the central BBCP molecule.

Let us denote a hydrogen atom in the central molecule as atom i, and let atoms j represent non-bonded atoms belonging to other molecules <u>within the cluster</u>. The local packing density at atom i is then defined as:

$$n(i) = \sum_{j=1,6} 1/r_{ij}^2 \qquad (1)$$

In this equation, r_{ij} is the shortest distance from the centre of hydrogen atom i to the surface of the van der Waals sphere about atom j. The summation is performed over the six shortest non-bonded distances only, as longer distances would correspond to atoms outside the first coordination shell of the hydrogen atom i. Thus we have assumed a maximum coordination of six non-bonded atoms around a given H-atom of the central molecule. n(i) coefficients give an indication of the amount of space surrounding a hydrogen atom in the crystal: the higher the value of n(i), the less likely it is that atom i can be substituted by a larger group such as Cl, Me or Br. Note that coordinating atoms j which belong to molecules outside the cluster are excluded from the summation; this is because the way in which these molecules coordinate the central molecule does not affect the basic structural type.

Values of n(i) for the 18 hydrogen atoms of BBCP are quoted in Table 3.

TABLE 3. Local packing densities, n(i), for the 18 hydrogen atoms in BBCP

Atom	n(i)	Atom	n(i)	Atom	n(i)	Atom	n(i)
H-2	2.188	H-31	2.847	H-32	2.723	H-41	2.111
H-42	3.059	H-61	2.883	H-62	2.623	H-8	2.517
H-9	1.510	H-10	0.720	H-11	1.672	H-12	2.441
H-13	2.000	H-15	2.169	H-16	2.619	H-17	1.852
H-18	2.490	H-19	2.597				

i gives the position of the C to which H is bonded. If i<19 there are two H's. First digit gives the position.

If values of n(i) for H-10 and H-17 (denoted n(10) and n(17)) are compared, for example, it is seen that atom H-10 is less closely coordinated than H-17 by atoms within the cluster. This ties in with the observation that pCl BBCP and pMe BBCP adopt a Type 1 cluster, whereas B pCl BCP and B pMe BCP pack in a Type 2 manner: i.e. substitution of Cl or Me for H-10 does not disrupt the Type 1 cluster, whereas substitution of Cl or Me for H-17 causes a change of cluster from Type 1 to Type 2. We may therefore identify a critical value of n(i) in the range $n(10) < n(i) < n(17)$, i.e. $0.720 < n(i) < 1.852$, at which substitution of a chloro or methyl group for a hydrogen atom begins to disrupt the Type 1 cluster. Most of the hydrogen atoms in BBCP have n(i) values greater than 1.852; hence it can be predicted that substitution at these positions will break up the Type 1 cluster adopted by BBCP. So derivatives with substituents at positions with $n(i) > 1.852$ are likely to be photo-stable.

Note that substitution of Cl and Me for H-17 does cause a change in packing, whereas substitution of the larger Br-group for H-17 does not. It appears, therefore, that arguments based on volume alone do not account for the observed behaviour, and the propensity of the bromo group to coordinate itself closely with the carbon atoms of a phenyl group must be taken into account.[10]

A consideration of all the known structures of BBCP derivatives gives the following 'critical values' of n(i), which are empirically derived:

$0.934 < n(i) < 1.852$ for Cl & Me substitution

$2.217 < n(i) < 2.490$ for Br substitution.

When a given hydrogen atom has an n(i) value within these ranges, substitution of that hydrogen atom may well cause a change in structural type; and as more structures are examined, the uncertainty in these 'critical values' will be reduced. Where local packing densities lie outside the above critical ranges, the method gives unequivocal predictions.

We may use this method to predict the structural types of di-substituted derivatives as well. For example, to predict the structural type of pBr B pCl BCP, n(i) values for both pBr BBCP and B pCl BCP can be considered; this is because the di-substituted derivative can be regarded either as a Cl-substituted derivative of pBr BBCP or as a Br-substituted derivative of B pCl BCP. The method predicts, incidentally, that pBr B pCl BCP will adopt a photo-stable 'Type 2' structure.[9]

Having seen that this simple method is successful for BBCP derivatives, it remains to be seen whether it is applicable to other systems in which the dominant stabilisation comes from dispersive forces. A suitable test-system needs to be fairly rigid, or, at least, the molecular conformation should be largely invariant between crystal structures of different derivatives. An obvious system to consider is the anthracene and anthraquinone set of derivatives; these crystal structures can be obtained from the Cambridge Crystallographic Database. The molecular cluster for anthracene is shown in Figure 4, with the atomic numbering and corresponding n(i) coefficients given in Figures 5(a) and (b).

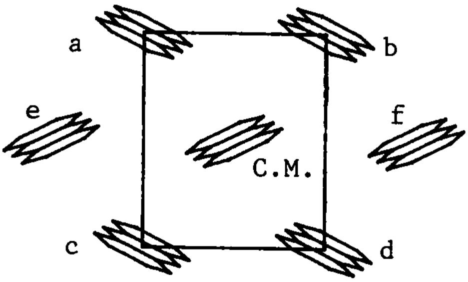

FIGURE 4. The molecular cluster of anthracene

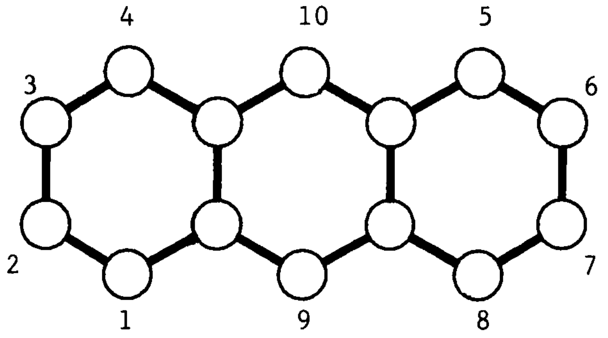

FIGURE 5(a). Atomic Numbering in anthracene

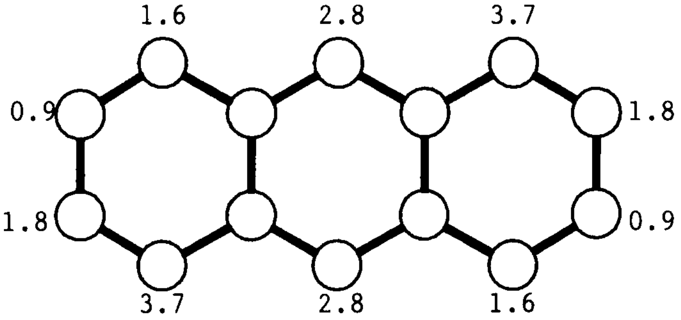

FIGURE 5(b). Local packing densities, n(i), for anthracene

It is seen that the 9 and 10 positions, as well as the 1 and 5 positions have very high n(i) values, such that no substituents may be accommodated without breaking up the herring-bone type of cluster shown in Figure 4. By contrast, we expect that the 3 and 7 positions can accommodate large substituents, whilst still maintaining the herring-bone motif. Owing to the symmetry of the molecule, positions 1,4,5 and 8 are chemically equivalent, as are positions 2,3,6 and 7; hence mono-substitution in the end phenyl rings is unlikely to break up the anthracene motif, at least for bromo-substitution. By contrast, substitution at positions 9 and 10 in the middle phenyl ring will break up the motif. This is observed in practice, as almost all of the 9,10-substituted derivatives adopt an alternative structural motif of parallel stacks of anthracene units; this structural type is widely identified as the β-type structure.[11] The prevalence of the β-structural type is, in part, interpretable by the n(i) coefficients one obtains for compounds which crystallise in this motif. Consider, for example, anthraquinone, as shown in Figure 6.

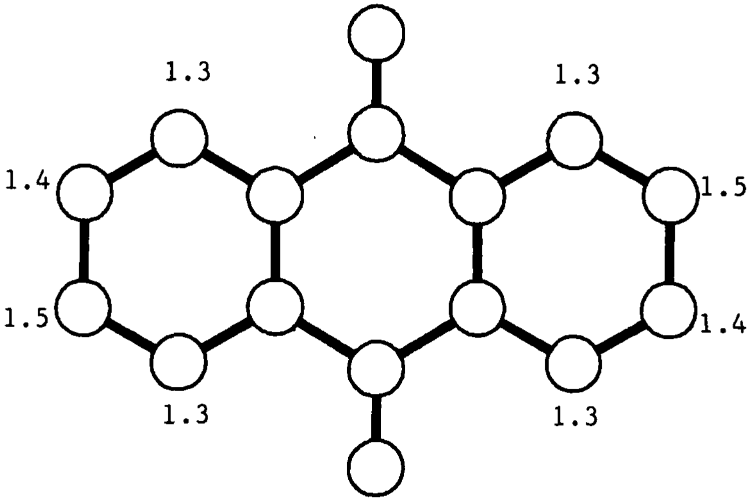

FIGURE 6. Local packing densities, n(i), for anthraquinone

If one takes the molecular cluster as the central anthraquinone molecule coordinated by two other molecules, one above and the other below that central molecule in the β-stack, n(i) coefficients are obtained as given in Figure 6. These are all low values, hence it is predicted that substituted anthraquinones will maintain the β-structural motif.

DISCUSSION

The approach described is intended to complement the experimental results of a crystallographer working on a particular family of compounds. It relies, in the first instance, upon the crystal data of the parent compound in a given series of derivatives. Whereas it can identify patterns of substitution that will lead to different structural motifs, it cannot predict the structures of these motifs. Predictions of this kind require either a highly developed intuition or powerful *ab initio* methods; these have not yet been developed.

Perhaps the greatest strength of this approach is its simplicity; a similar simple approach, based on calculation of molecular volumes, has already been applied successfully to a study of steric factors influencing organic solid-state reactivity.[12] It is hoped that workers in this field will wish to make use of the method, and the computer-programmes are available for distribution from NWT.

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