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Generation of Possible Crystal Structures from the Molecular Structure for Low-Polarity Organic Compounds

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Abstract: This paper describes a new method for searching the potential energy hypersurface of organic crystals. Clusters made of 2–4 molecules are built with the most common symmetry elements: the inversion center, the screw axis, and the glide plane. The relative importance of these elements, as well as of lattice translation, in building the cohesive energy of the crystal, is assessed by using a statistical analysis of known hydrocarbon structures. A full-crystal structure is then built by translation of these clusters, yielding the most frequent space groups for organic compounds. Cluster and lattice energies are calculated by using empirical potentials; use is also made of statistical correlations between molecular and crystal properties to guide the search. Tests on known crystal structures of hydrocarbons show that in some favorable cases the method can predict the crystal structure from molecular structure only; for one compound, a prediction of the unknown crystal structure is given. The results demonstrate quantitatively that many crystal structures with small energy differences are possible for moderately polar organic molecules.

1. Introduction

Several authors[1-3] have underlined the lack of a predictive theory of organic crystal structure. There is no need to further emphasize the relevance of such a theory to many branches of theoretical and applied chemistry. The physical nature of the forces acting between organic molecules (here meaning recognizable units made of C, H, N, O, S, and halogen atoms) in crystals is rather well understood; what is difficult to grasp is the complex spatial pattern of such forces, reflecting the articulate nature of the entity that initiates them—mainly, the valence electron distribution. The problem of organic crystal structure prediction is therefore a tight tangle of a "force" and a "geometry" component.

At present, a vast amount of raw information on packing modes is available through the thousands of crystal structures collected in the Cambridge Structural Database[4] (CSD). Attempts, sometimes successful, to organize this essentially geometrical information into meaningful solid-state chemistry have been made;[5,6] they rely on a structure correlation approach, where molecular parameters are tentatively correlated to crystal parameters. But at the same time simple and effective potentials which accurately simulate the intermolecular field are available,[7,8] and computing power is becoming so large that extensive searches of the crystal potential hypersurface are possible. Efficient computer programs for packing energy optimization have been prepared;[9] not surprisingly, however, they only function when at a reasonable distance from the minimum.

This paper proposes and illustrates an intermediate and synergistic approach, in which the most common symmetry operators are used to build plurimolecular clusters (nuclei), which, when translated in three directions in space, provide a number of trial crystal structures in the most frequent space groups.[10] In a genuinely chemical way of thinking the method focuses on molecular units, sorting out and exploiting the symmetry and energy relationships among them, and taking advantage of the combined use of statistics on geometrical and energetic parameters and of energy calculations. In favorable cases, this leads to a completely ab initio prediction of crystal structure from molecular structure. But even if this ambitious goal is not always reached, no other packing analysis procedure has such a broad scope in searching the energy hypersurfaces of organic crystals.

2. The Molecular Nuclei Concept

The number of independent structural determinants in a crystal is usually very small, namely, it equals the number of symmetry operators in the space group plus three translational interactions (e.g., 3 in $P1$, 4 in $P\bar{1}$, 6 in $P2_1/c$ or $P2_12_12_1$; we do not consider cases with more than one molecule in the asymmetric unit, and we consider the appropriate subgroup when the asymmetric unit is only part of the molecule). The number of relevant interactions may be even smaller; it is well-known[11,12] that most of the cohesion energy comes from interactions with a few molecules in the first coordination sphere. We call T a translation operator, I an inversion center, S a screw, and G a glide operator; their combinations produce all of the most frequent space groups for organic crystals[13] (more than 80% of all observed crystal structures in the CSD).

We propose therefore to build couples of molecules related by S, G, or I operators as an intermediate step in building a crystal structure. The stability of such couples has to be judged by their intermolecular potential energy; it is understood that what is calculated in this case is not the true attraction potential of the isolated dimer but the potential the dimer would have in the solid, since the empirical formulations used in the calculation were calibrated for crystals. This is just what is needed for the present purposes, but it should be remembered that a strong interaction does not mean in itself that the couple is in fact likely to appear

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(1) A provocative statement to this effect has been made by Maddox: Maddox, J. *Nature*, **1988**, *335*, 201.

(2) Curtin, D. Y.; Paul, I. C. *Chem. Revs.* **1981**, *81*, 525.

(3) Leiserowitz, L.; Hagler, A. T. *Proc. R. Soc. London, A* **1983**, *388*, 133. These authors however, were able to rationalize the packing patterns of hydrogen-bonded amides.

(4) Allen, F. H.; Kennard, O.; Taylor, R. *Acc. Chem. Res.* **1983**, *16*, 146.

(5) (a) Gavezzotti, A. *J. Am. Chem. Soc.* **1989**, *111*, 1835. (b) Gavezzotti, A. *J. Phys. Chem.* **1990**, *94*, 4319. (c) Gavezzotti, A. *Acta Crystallogr.* **1990**, *B46*, 275.

(6) (a) Taylor, R.; Kennard, O. *Acc. Chem. Res.* **1984**, *17*, 320. (b) Nyburg, S. C.; Faerman, C. H. *Acta Crystallogr.* **1985**, *B41*, 274. (c) Ramasubbu, N.; Parthasarathy, R.; Murray-Rust, P. *J. Am. Chem. Soc.* **1986**, *108*, 4308. (d) Buergi, H.-B.; Dunitz, J. D. *Acc. Chem. Res.* **1983**, *16*, 153.

(7) Mirsky, K. V. *Acta Crystallogr.* **1976**, *A32*, 199.

(8) Williams, D. E.; Starr, T. L. *Comput. Chem.* **1977**, *1*, 173. See, for a review: Pertsin, A. J.; Kitaigorodski, A. I. *The Atom-Atom Potential Method*; Springer-Verlag: Berlin, 1987.

(9) Williams, D. J. PCK83, Program 548, Quantum Chemistry Program Exchange, Indiana University, Bloomington, Indiana.

(10) We learned at an advanced stage of development that a similar treatment has been proposed for two-dimensional systems: Scaringe, R. P. Personal communication. See also: Scaringe, R. P.; Perez, S. *J. Phys. Chem.* **1987**, *91*, 2394.

(11) Kitaigorodski, A. I. *Molecular Crystals and Molecules*; Academic Press: New York, 1973.

(12) Gavezzotti, A.; Desiraju, G. R. *Acta Crystallogr.* **1988**, *B44*, 427.

(13) (a) Mighell, A. D.; Himes, V. L.; Rodgers, J. R. *Acta Crystallogr.* **1983**, *A39*, 737. (b) Wilson, A. J. C. *Acta Crystallogr.* **1988**, *A44*, 715. (c) Padmaja, N.; Ramakumar, S.; Viswamitra, H. A. *Acta Crystallogr.* **1990**, *A46*, 725.

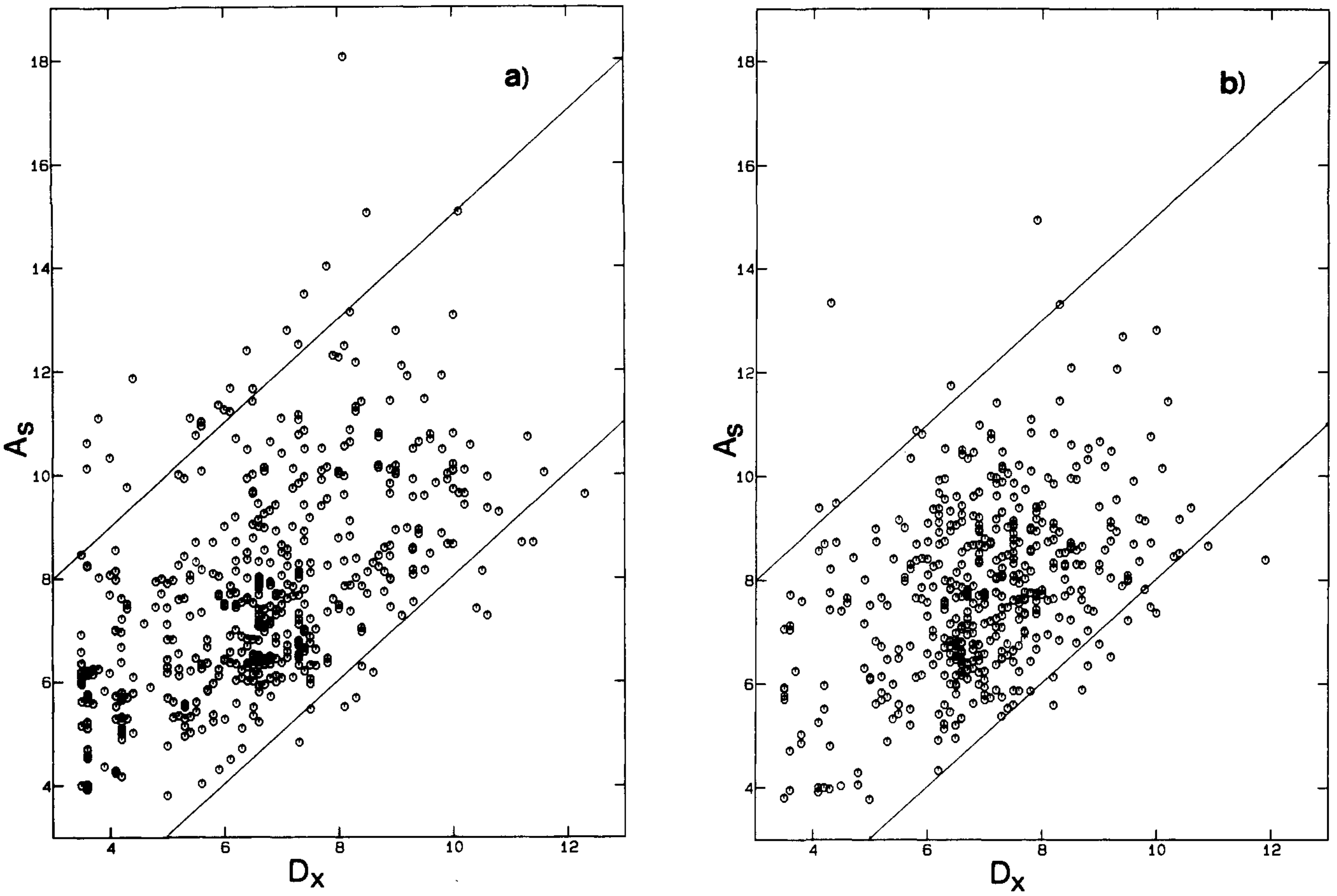

Figure 1. Plots of the length of the shortest cell axis against the shortest molecular dimension: (a) 484 crystal structures of hydrocarbons or molecules with one C═O or C≡N group; (b) 460 structures of molecules containing C, H, and O atoms.

in the crystal—whose stability can only be judged by a full lattice energy calculation. One cannot use here the usual "strong" assumption of potential energy minimization; rather, the "weak" assumption is made that at least one of the S, I, or G nuclei appearing in the real crystal must have a substantial interaction energy within itself and must lie in an energy valley, so that its lifetime at the moment of crystal formation is long enough for it to survive in the solid. Therefore, rather than looking for the most stable nucleus, many nuclei must be considered promising for crystal formation.

3. Generation of the Nuclei

A molecular model has to be supplied first, in which internal degrees of freedom are frozen. Either the molecule is rigid or an intramolecular energy optimization has to be performed (coupling of the intra- and intermolecular energies is planned in future developments). Then, nuclei are built as follows:

(a) For the I nucleus, an inversion center is located at each point of a grid in the surroundings of the molecule, and the interaction energy between the original and the inversion-related molecule is computed. A map with the nucleus energy at each point of the grid is obtained.

(b) For the S nucleus, a screw axis is located at a variable distance from the molecular center of mass, and the molecular orientation is varied by three eulerian angles. The screw pitch is also varied. In the resulting distance/pitch map, each point has the energy for the most favorable molecular orientation.

(c) The G nucleus is built the same as the S nucleus, but the variables are the distance from the glide plane to the center of mass and the glide translation. Appendix I, supplementary material, has the algebra for the calculation of the Cartesian coordinates of all atoms in the nuclei and some detail on the search.

The molecular couple optimized under the action of a first operator can be subjected to a second operator, thus yielding product symmetries and already some translational periods of the final structure. Of course, the reciprocal orientation of the two operators and the origin of the reference frame must be properly chosen to produce acceptable space groups.[14] The combinations so far considered are collected in Table I, but it is an easy task to include other operators, like the centering, the 2-fold axis or the mirror plane, and more combinations of operators, giving access to other, although less populated, space groups.

Table I. Some Combinations of Symmetry Operators and the Resulting Space Groups

first operator[a]	second operator	space group	lattice periodicities[b]
T	none	$P1$	
I	none	$P\bar{1}$	
S	none	$P2_1$	$b = 2y_0$
G	none	Pc	$c = 2z_0$
S	I	$P2_1/c$	$b = 2y_0$ $c = 4R_0$
I	S	$P2_1/c$	$b = 2y_0$ $c = 4R_0$
S	S[c]	$P2_12_12_1$	$a = 4R_0$ $b = 2y_0$ $c = 2z_0$

[a] S along y, G perpendicular to y with translation on z, b unique axis in monoclinic. [b] Resulting from the combinations; y_0, z_0, optimized screw or glide translations; R_0, optimized distance between the two operators. [c] Along z.

4. Procedures for the Translational Search

Three translation vectors for the generation of a full crystal structure starting from the nuclei are generated, when necessary, by systematic variation of the polar coordinates of each vector

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(14) *International Tables for X-ray Crystallography*; Birmingham: Kynoch Press, 1952; Vol. I.

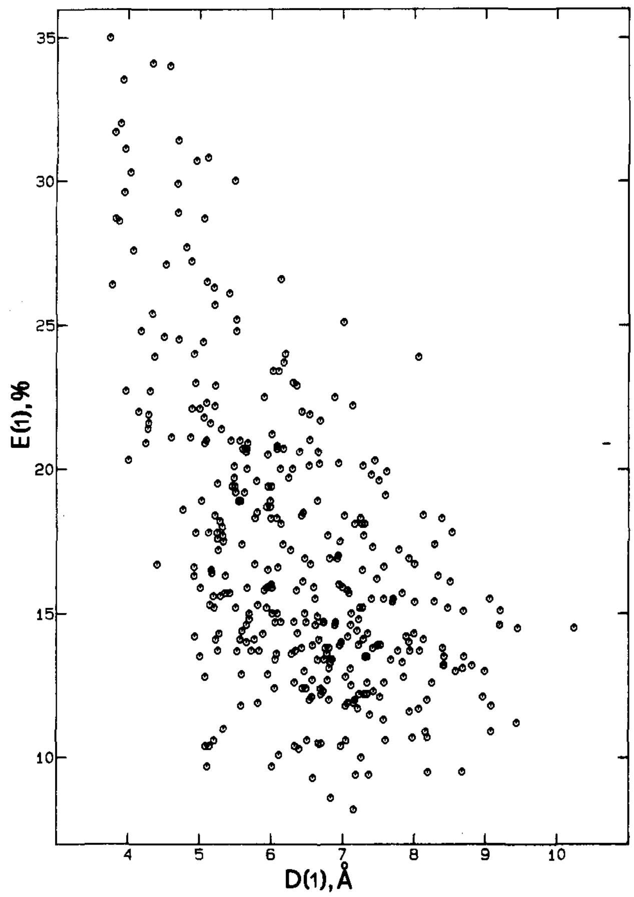


Figure 2. Percent of packing energy due to the top-ranking symmetry operator ($E(1)$) versus the distance between centers of mass ($D(1)$)—358 hydrocarbon crystal structures, no cases with two molecules in the asymmetric unit.

(see Appendix II, supplementary material). Some restrictions to the ranges of cell vector lengths can be imposed by using the results of Figure 1. Calling D_x the distance between extreme points of the molecule along the axis of maximum inertia (a sort of "shortest" molecular dimension), one can see that the shortest cell vector ranges between $D_x - 2$ and $D_x + 5$ Å. A similar graph shows that the longest cell vector cannot be shorter than $D_z - 3$ Å, where D_z is the longest molecular dimension.

The translational search is performed in a sequential way, by building first a string along one direction, next a layer in two directions, and then the three-dimensional structure. Each successive stage is accessed only if the previous one gave an increase in cohesive energy (that is, if no repulsions due to mismatch were found). Whenever a new structure is within a preset range of packing coefficient and packing energy, a first rough optimization by steepest descent is performed. Up to this stage all energies are calculated by sums of atom–atom Lennard-Jones (6-exp) potentials with parameters as in ref 7, and a 7 Å cutoff in the summations (this set will be called Mirsky-7, or M7). In the final refinement stages, use is made of the program PCK83,[9] which provides the best set of potential energy parameters, including forced convergence of lattice sums and explicit electrostatic terms (this set will be called Convergent-Coulomb-Williams, or CCW), and a very efficient optimization algorithm (see Appendix III, supplementary material, for the use of this program).

5. Statistics on Known Crystal Structures

Statistics on known crystal structures available from the CSD are very helpful in guiding the structure search. The packing potential energy (PPE) of a molecule in an organic crystal can be computed by sums of empirical atom–atom potentials. The packing energy, related to the sublimation energy, is PE = PPE/2. The sums can be divided into parts due to each atom i, E_i (the sum of all interactions between atom i of a reference molecule and the surroundings[5a]), or to each molecule–molecule interaction, $E(j)$ (the sum of the interactions between all atoms of a reference molecule and all atoms in the neighbor molecule j[5c]); the appropriate subgroup is considered when the asymmetric unit is a fraction of a molecule. The $E(j)$'s can be ranked in order of magnitude; the associated distances between molecular centers of mass, $D(j)$, usually rank in the reverse order. Since each molecule is related to the reference one by a symmetry operator $O(j)$, the relative importance of each operator within the crystalline edifice can be measured by the rank of the respective $E(j)$. For comparisons among different crystal structures, $E(j)$ is better expressed as a percent of PE. Figure 2 shows a plot of this quantity for the top-ranking neighbor ($E(1)$), against $D(1)$, in a sample of hydrocarbon crystals.[5a] Points in the upper part of the graph are for crystals in which most of the cohesion is localized over one or few molecule–molecule interactions (a compact coordination sphere (c.c.s.); points in the lower part have a scattered coordination sphere (s.c.s.). The variety of motifs adopted by organic crystals between these two extremes is impressive.

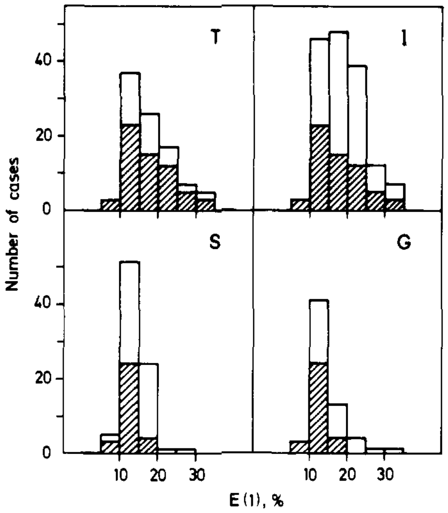


Figure 3. Histograms of the occurrence of each operator as top-ranking. Shaded areas are for molecules on a center of symmetry (S = G or T = I; see text).

The relative importance of each operator has been analyzed by studying its occurrence as top-ranking in hydrocarbon crystals. Out of 391 crystal structures,[5a] 26 with two molecules in the asymmetric unit and 15 with crystal symmetry higher than orthorhombic were excluded. Of the remaining, 218 had molecules in general positions; in six cases, O(1) was a 2-fold axis, and in one instance O(1) was the centering operator. Also, 93 structures had centrosymmetric molecules lying on a crystallographic center of symmetry, so that T is equivalent to I and S to G. For 39 structures, the nature of O(1) was not clear-cut, owing to more complex interaction between crystal and molecular symmetry; these were not considered in this analysis. Figure 3 shows histograms of the energetic relevance, $E(1)$, for each operator, when top-ranking; the spectrum is rather wide for T or I (5–35% of PE), while S and G contribute between 10 and 20% of PE, although the I interaction is unique, while T, S, and G interactions involve two equivalent neighbor molecules (in fact, a chain), so that their relevance is at least twice $E(1)$.

While I is by far the most frequently occurring top-ranking operator, the frequency of translation (either pure or as a disguised center of symmetry) is surprising. S and G follow in order of importance. There is no strict relationship between O(1) and space group symmetry (for example, I need not be top-ranking in $P\bar{1}$). The results in Figure 3 provide the range of $E(1)$ to be observed by each operator as a further guide in the acceptance of promising nuclei (see below). The interpretation of these results with respect to space group frequencies[13b] deserves more space than is allowed in this context.

Table II. Results of the Calculations for **1** (CSD refcode BADAMN)

space group	Z	a	b	c	α	β	γ	C_K[d]	D[e]	$-PE$[f]		coord sphere[g]		
										M7	CCW	1,2	3,4	5,6
$P\bar{1}$														
obs[a]	1	6.531	6.577	10.457	87.5	104.6	119.9	0.735	1.196	25.6		12	12	11
opt[b]	1	6.54	6.55	10.52	87.8	105.4	120.0	0.749	1.219		30.7			
calc[c]	1	6.40	6.59	9.76	91.2	100.1	114.8	0.753	1.225	25.5	29.4	13	12	11
$P2_1$	2	11.00	6.55	12.17	90	60.9	90	0.720	1.172	24.1	29.2	13	13	12

[a] From the X-ray structure, without optimization. Cell parameters in Å and deg. [b] Optimized from footnote *a*. [c] Found in the present work; Niggli reduced cell (computed as in: Nardelli, M. *Comput. Chem.* **1983**, *7*, 95). [d] Kitaigorodski packing coefficient (molecular volume/cell volume). [e] Crystal density, g/cm³. [f] kcal·mol⁻¹. [g] Percent of PE provided by the *j*th neighbor molecule, $E(j)$ (see text).

Table III. Results of the Calculations for **3** (CSD refcode DITDEP)[a]

space group	Z	a	b	c	α	β	γ	C_K	D	$-PE$	
										M7	CCW
$P\bar{1}$											
obs	2	7.519	10.689	10.830	100.76	108.67	104.92	0.703	1.135	23.6	
opt	2	7.39	10.33	11.02	100.5	107.1	105.6	0.721	1.164		31.2
calc	2	7.36	10.88	10.92	111.7	65.5	106.8	0.734	1.185	25.3	32.4
$P2_1$	2	8.93	7.56	11.90	90	70.0	90	0.710	1.145	23.2	28.8
$P2_1/c$	4	10.54	12.91	13.95	90	50.6	90	0.730	1.177	24.8	31.3
$P2_12_12_1$	4	11.51	7.60	17.41	90	90	90	0.703	1.134	22.5	27.7

[a] For symbols and units, see footnotes to Table II.

Empirical correlations, based on M7 calculations, are available to predict the PPE of organic compounds without hydrogen bonds, from the size and shape of the molecule. For hydrocarbons[5c]

$$\mathrm{PPE} = 0.114S_m + 13.8\ \mathrm{kcal/mol}$$

and for oxygen-containing compounds[15]

$$\mathrm{PPE} = 0.109S_m + 12.7\ \mathrm{kcal/mol}$$

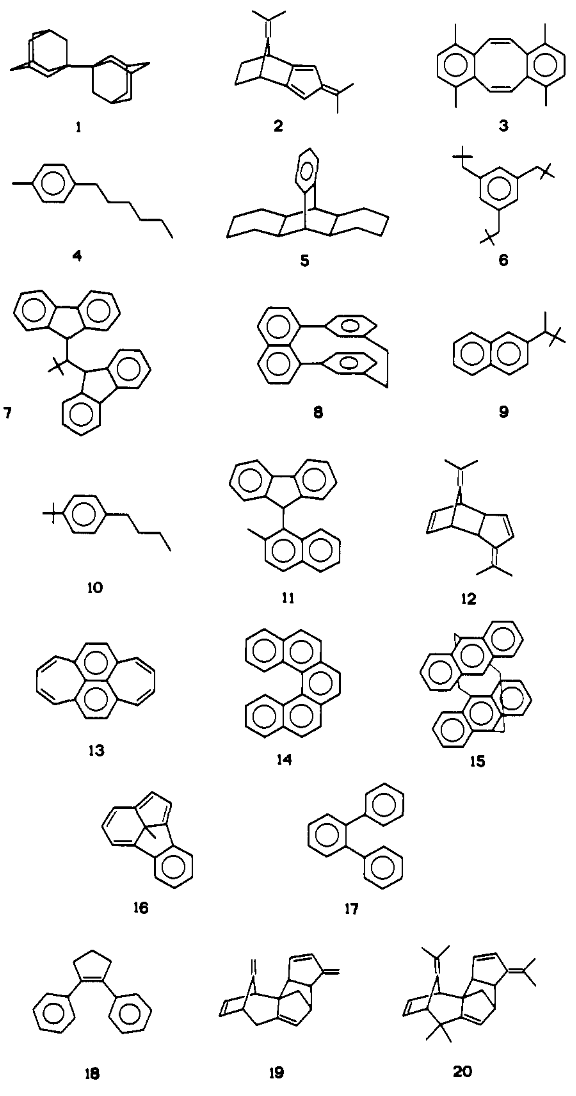
where S_m is the molecular surface. Otherwise the PPE can be predicted as a sum of the average atomic increments.[5a] Therefore, the PPE to be expected for a given molecule is approximately known, and, calling $E(n)$ the molecule–molecule interaction energy calculated for a nucleus, the ratio of $E(n)$ to PPE must be, as a first guess, within the limits fixed in Figures 2 and 3. The E_i's, or atomic relevances, fall within narrow ranges for each atomic species or type;[5a] this provides another criterion for acceptance of a calculated structure.

6. Results

The potential maps for the nuclei usually show several promising zones, so that several nuclei are candidates for the translational search. Compact nuclei will have a higher interaction energy, with a close contact between the two molecules; their stability is more recognizable and they are more frequently considered as promising, so that the method works better for c.c.s. structures.

The search for possible I nuclei takes a few minutes of computing time (all times given as solar times for a Gould-NP1 minisupercomputer, not using vectorialization). The search for S and G nuclei may take a few hours, since also the molecular orientation has to be scanned. These searches are however done only once, and they serve for the analysis of several space groups. The translational search is long (a few hours) for triclinic structures, while for monoclinic and orthorhombic some or all of the cell parameters are already determined (Table I) after the nuclei search, and the structure is ready to enter the final optimization stage with a limited or no translational search. On average, one space group can be completely analyzed in 1 day, including the interpretation of the results. The procedure is not yet automatic, and a number of decisions are still to be made by the user, according to his or her subjective judgment; it is, however, a substantial improvement with respect to a blind search over space groups, cell parameters, and molecular location and orientation, and even when it fails to predict the true crystal structure, it still is useful in many solid-state problems, as described in the following sections.

Chart I



Some hydrocarbon molecules whose crystal structure is known were used as tests. The molecular structure was taken from the X-ray analysis and kept fixed. To allow meaningful comparisons, the experimental crystal structures were optimized by the program PCK83.

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(15) Gavezzotti, A. Unpublished results.

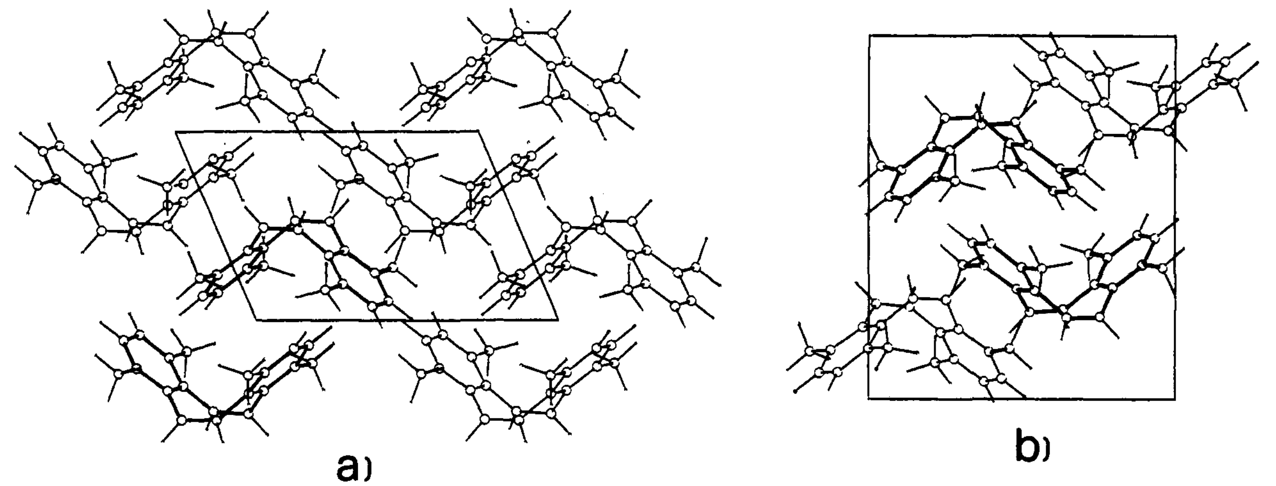

Figure 4. (a) The X-ray crystal structure of **3** ($P\bar{1}$ space group; projected along *b*) and (b) the calculated $P2_1/c$ crystal structure of **3** (projected along *a*). The centrosymmetric couples are highlighted.

(a) 1,1′-Biadamantane (1; $P\bar{1}$, $Z = 1$). The molecule is centrosymmetric and lies on a crystallographic inversion center, so that the space group considered is $P1$. The results are shown in Table II; the correct structure was found in a few minutes by the translational search. There is good agreement between observed and calculated PE, cell parameters, and composition of the coordination sphere. The $P2_1$ structure is in fact a repetition of the $P1$ structure, since molecules lie parallel along the elongation axis, and the effect of the screw axis is indistinguishable from pure translation.

(b) 1,4,7,10-Tetramethyldibenzocyclooctene (3; $P\bar{1}$, $Z = 2$). The molecule has a pronounced butterfly shape and approximate *mm*2 symmetry. The observed crystal structure was reproduced quite satisfactorily (Table III). A $P2_1/c$ crystal structure was also found, with the same PE as the observed $P\bar{1}$ structure. Given the molecular symmetry, the packing pattern of this structure is quite similar to that of the $P\bar{1}$ structure; the main molecular plane is parallel to the crystal glide plane, so that the effect of I is the same as that of G. This structural similarity is clear from Table IV, where glide operators in $P2_1/c$ are seen to take the place of I operators in $P\bar{1}$. Figure 4 shows the two structures: the similarity of the centrosymmetric couples is evident. Nevertheless, the two structures are different, and our results predict the existence of an unknown $P2_1/c$ polymorph.

The two noncentrosymmetric structures for **3** stem from the same S nucleus, reflected in the common *b* cell parameter and in the similar composition of the coordination sphere (Tables III and IV). They have lower PE's due to the lack of the center of symmetry, which appears to be crucial for the self-recognition of this molecule. In this case, success in crystal structure prediction can be claimed, since the observed structure was found to be the lowest energy one.

(c) Other $P\bar{1}$ Structures. A few other hydrocarbons crystallizing in $P\bar{1}$ were considered, but only in the observed space group. As can be seen in Table V, and also by comparison of the structure of the centrosymmetric dimer and of the coordination sphere, the observed structure was reproduced satisfactorily for **2** and **4**, and rather well for **5**. For **6**, **7**, and **8** the observed structure could not be found. These judgments are based on a weighted combination of the discrepancies in cell parameters, CCW packing energies, and especially $D(1)$ and $E(1)$ (see also the Discussion).

(d) 1,2-Diphenylcyclopentene (18; $P2_1$, $Z = 2$). This molecule is conformationally flexible in solution but chooses to crystallize in a chiral space group, thus achieving spontaneous resolution. The search in $P2_1$ was unsuccessful (Table VI) since the true crystal has a scattered coordination sphere while the S nucleus search yielded a strongly bound dimer ($E(1) = 19\%$). The calculated centrosymmetric structures are both less stable than the observed one, but the energy differences are rather small, so that a slight adjustment in molecular conformation could conceivably compensate for them, yielding a racemic crystal as stable as the chiral one. This example shows how subtle the discriminating factors (in terms of free energy, or even more likely, in kinetic terms) must be.

Table IV. Composition of the Coordination Sphere for Crystal Structures of **3**

space group	*Z*	$O(j)$, $D(j)$,[a] $E(j)$[b] 1	2	3	4
$P\bar{1}$ obs	2	I	I	I	I
		5.4	7.1	7.7	8.6
		26.1	15.5	14.8	7.4
$P\bar{1}$ calc	2	I	I	I	I
		5.4	7.6	7.1	8.5
		25.0	15.1	14.7	7.1
$P2_1/c$	4	I	G	G	G
		5.4	7.4	7.4	8.5
		25.2	14.7	14.7	6.9
$P2_1$	2	S	S	S	S
		6.5	6.5	7.7	7.7
		19.6	19.6	10.8	10.8
$P2_12_12_1$	4	S	S	S	S
		6.4	6.4	7.8	7.8
		20.7	20.7	9.8	9.8

[a] Angstrom units. [b] Percent of total PE.

For **9**, another $P2_1$ crystal structure, the search was conducted in the observed space group only. As seen in Table V, it was partially successful, but a rather substantial difference in cell parameters remains.

(e) 1-*tert*-Butyl-4-*n*-butylbenzene (10; *Pc*, $Z = 2$). There is only one *Pc* crystal structure in the whole sample of known hydrocarbon structures;[5a] this is in agreement with our analysis of top-ranking operators and discourages the construction of G nuclei in our searches. Table V shows however the complete success achieved in finding the true crystal structure, although the observed space group was imposed and not predicted.

(f) $P2_1/c$ Crystal Structures (Table V). For **11**, a structure similar in some respects to the observed one was found in $P2_1/c$; there is a 10% difference in the *c*-axis length, and the parameters of the top-ranking operator are substantially different (especially $D(1)$). No better success can be claimed for **14**, where the calculated length of the unique axis is different from the observed one. For **15**, the calculated structure is similar to the observed one in many respects, but there is a 10% difference in the length of *a*. For this molecule, the space group considered is in fact $P2_1$ since it lies on a center of symmetry. For these last three molecules, only the observed space group was analyzed.

Table VII shows the results for **13**. Here the true crystal structure was traced and optimized by the search and was found to be the most stable of the three space groups that were tried (the two $P2_1$ structures are very nearly, but not quite, the same).

Table V. Results for Some Test Structures[a]

compd no.	CSD refcode	space group	cell parameters[b]							-PE				
			a	*b*	*c*	*α*	*β*	*γ*	C_K	M7[c]	CCW[d]		*D*(1), Å	*E*(1), %
2	DEPYAY	*P*$\bar{1}$	6.341	8.078	14.003	106.6	90.6	110.8	0.697	21.6	25.8	I	6.09	20.6
			6.27	8.05	13.41	83.9	81.6	69.4	0.710		25.7	I	5.97	21.8
4	MHXBEN[e]	*P*$\bar{1}$	5.658	7.807	13.810	82.2	85.5	70.4	0.702	21.2		I	3.90	22.6
			5.67	7.60	13.53	99.3	91.7	105.3	0.722	19.4		I	3.77	25.6
5	DHTRYP10	*P*$\bar{1}$	6.696	10.077	11.101	95.04	93.81	93.91	0.732	25.9	30.7	I	6.56	16.6
			6.64	9.45	12.41	84.1	89.7	76.2	0.723		29.6	I	6.49	15.1
6	FAGHAW	*P*$\bar{1}$	10.406	10.458	11.149	62.8	72.5	63.1	0.696	26.7	31.1	I	4.71	24.4
			9.48	10.65	11.51	117.3	95.4	90.1	0.649		27.0	I	4.69	28.2
7	BUFLFN	*P*$\bar{1}$	9.624	11.187	11.259	78.6	71.0	71.0	0.705	27.1	39.6	I	6.14	26.6
			9.42	9.96	13.94	79.6	70.8	62.4	0.694		37.8	I	6.94	25.2
8	BONJUJ	*P*$\bar{1}$	7.848	10.278	11.163	99.73	112.79	78.43	0.730	24.9	35.1	I	5.63	19.2
			8.23	9.28	12.95	89.0	89.5	56.4	0.718		30.8	I	6.87	20.1
9	CARRAO	$P2_1$	7.87	6.07	13.70		91.0		0.698	19.8	27.8	S	6.47	12.8
			6.71	6.94	14.60		94.5		0.674		25.2	S	7.04	14.4
10	TBNBBZ	*Pc*	10.17	6.146	10.51		103.8		0.679	19.4	23.9	G	5.26	19.6
			10.22	5.89	10.39		104.0		0.715		23.9	G	5.20	19.0
11	COTYUF	$P2_1/n$	9.264	8.621	21.08		91.5		0.704	24.7	35.7	I	5.51	24.7
			8.83	8.21	23.20		93.0		0.707		33.0	I	6.96	20.3
14	DBPHEN02	$P2_1/c$	5.815	14.178	17.498		94.41		0.728	25.3	35.7	T	5.82	18.3
			8.67	7.88	22.69		112.0		0.730		32.2	I	6.46	19.2
15	ANTMEU	$P2_1/c$	10.28	12.79	8.47		112.9		0.762	29.7	43.9	S	7.67	13.3
		($Z = 2$)	9.19	12.98	8.92		101.9		0.750		41.2	S	7.95	12.8
16	BITTED10	$P2_12_12_1$	6.887	9.297	17.673				0.688	17.8	26.5	S	5.51	15.2
			11.48	5.59	16.71				0.726		25.9	S	6.14	13.7
17	TERPHO02	$P2_12_12_1$	18.58	6.02	11.73				0.698	20.5	29.4	T	6.02	15.8
			12.10	5.96	19.59				0.648		26.1	T	5.96	18.3

[a] For each entry: first line, X-ray; second line, calculated results. For some symbols and units, see footnotes to Table II. [b] Niggli reduced cells for triclinic structures. [c] Without structure optimization. [d] After PCK83 optimization. [e] PCK83 optimization not necessary.

Table VI. Results of the Calculations for **18** (CSD refcode DPCYPE)[a]

space group	*Z*	*a*	*b*	*c*	*α*	*β*	*γ*	C_K	*D*	-PE		coord sphere			
										M7	CCW	1	2	3	4
$P2_1$															
obs	2	9.025	9.516	8.036	90	112.4	90	0.697	1.146	20.2		10	10	9	9
opt	2	8.98	9.54	7.99	90	113.2	90	0.707	1.162		27.9				
calc	2	7.97	8.83	9.95	90	71.7	90	0.668	1.099	18.7	22.6	19	19	9	9
P$\bar{1}$	2	6.42	9.80	14.78	64.9	58.8	56.0	0.687	1.129	19.4	25.3	14	14	14	11
$P2_1/c$	4	8.36	13.85	11.24	90	80.9	90	0.693	1.139	19.7	25.7	15	15	13	9

[a] For symbols and units, see footnotes to Table II.

A crystal structure prediction, as discussed earlier, has thus been accomplished for this compound.

(g) $P2_12_12_1$ Structures. For **16** and **17** (Table V) only the observed space group was considered. Remarkably, for **16** a crystal structure is found which is quite different from the observed one, but it has very nearly the same PE. A good agreement between calculated and observed cell parameters was found for **17**, although the PE's are rather different.

For **12**, three space groups were considered (Table VIII). The observed structure was reproduced after some false starts; it is calculated to be the most stable one, but a *P*$\bar{1}$ structure has almost the same PE as the chiral one. The comment on the problem of spontaneous resolution already made for **18** applies here.

(h) Ab Initio Crystal Structure Prediction. A test compound of unknown crystal structure, **20**, was constructed by deleting six methyl groups from **19** (CSD refcode BEDFAR). The M7 PE expected for crystals of **20** from a sum of average atomic increments[5a] is 19.9 kcal/mol, quite close to those obtained by our procedure (Table IX) for the *P*$\bar{1}$ and $P2_1$ calculated structures. The top-ranking operator O(1) for the *P*$\bar{1}$ structure is I, and the associate *E*(1) is only 11%, at the lower edge of the allowed values in the histogram of Figure 3. On the contrary, O(1) for the $P2_1$ structure is S and *E*(1) is 11%, quite close to the average value for S operators. All considered, the $P2_1$ structure is favored, although the calculated structures are all within 8% of the PE of the most stable one. It would be interesting to match the above results with an X-ray crystal structure determination for **20**.

7. Mention of Previous Work

Many years ago, crystal structure determination by PPE minimization was considered a possible "real space" solution of the phase problem in X-ray crystallography,[16] but it became less and less attractive after the advent of direct methods.[17] New efforts in the same direction are nowadays made for the study of biological macromolecules,[18] where crystal structure solution and refinement is still a formidable task. PPE calculations have been employed in the prediction of crystal morphology.[19] Other attempts to generate trial crystal structures for hydrogen-bonded molecules have been reviewed.[20] Crystal structure prediction and control is important for the design of organic solids with desired physical properties, and the subject has been reviewed.[21]

8. Discussion

The PPE optimization with CCW potential parameters, starting from the X-ray structures, never led to large deviations from observed cell parameters, even if the molecules here considered are quite different from those for which the empirical potential was optimized. The CCW set is therefore reliable. The M7 set, with a few exceptions, gave the same energy ordering as the CCW one for the various structures found for each molecule. M7 energies are 70 to 85% of the CCW ones, the difference depending on the cutoff distance (7 Å) and the lack of explicit electrostatic terms in M7. Optimized structures are always more densely packed than the observed ones (the PPE parameters do not take

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Table VII. Results of the Calculations for **13** (CSD refcode DIHDON)[a]

space group	Z	a	b	c	α	β	γ	C_K	D	-PE M7	-PE CCW	coord sphere 1	coord sphere 2	coord sphere 3
$P2_1/c$														
obs	4	8.245	10.516	13.668	90	90.85	90	0.738	1.279	22.5		30	10	10
opt	4		7.91	10.80	13.58	90	95.7	90	0.758	1.313	33.2			
calc	4	7.93	10.58	13.93	90	93.9	90	0.749	1.299	22.8	32.2	29	10	10
$P2_1$	2	10.03	6.90	9.17	90	68.7	90	0.740	1.282	21.6	31.7	12	12	11
$P2_1$	2	10.62	6.53	10.33	90	56.9	90	0.729	1.263	21.3	31.6	14	14	12
$P\bar{1}$	2	9.90	7.00	12.25	57.0	75.5	61.6	0.698	1.209	20.3	28.6	23	23	14

[a] For symbols and units, see footnotes to Table II.

Table VIII. Results of the Calculations for **12** (CSD refcode BIRLUJ)[a]

space group	Z	a	b	c	α	β	γ	C_K	D	-PE M7	-PE CCW
$P2_12_12_1$											
obs	4	7.385	10.080	16.714	90	90	90	0.716	1.131	21.4	
opt	4	7.39	10.11	16.48	90	90	90	0.725	1.145		25.9
calc	4	7.39	10.09	16.45	90	90	90	0.726	1.147	21.8	25.9
$P\bar{1}$	2	10.42	9.96	13.79	70.9	120.5	58.7	0.712	1.125	21.1	25.1
$P2_1/c$	4	11.95	7.34	15.63	90	69.9	90	0.692	1.093	19.8	23.5

[a] For symbols and units, see footnotes to Table II.

Table IX. Crystal Structure Prediction for **19**[a]

space group	Z	a	b	c	α	β	γ	C_K	D	-PE M7	-PE CCW	coord sphere[b]
$P2_1$	2	7.40	6.72	13.28	90	88.9	90	0.698	1.177	19.3	25.2	11 (T), 11 (S), 11 (T)
$P\bar{1}$	2	7.16	8.79	13.33	106.9	59.4	113.8	0.702	1.183	19.0	24.5	11 (I), 10 (I), 10 (I)
$P2_1/c$	4	7.44	7.12	25.96	90	98.3	90	0.678	1.144	17.8	23.6	11 (T), 11 (T), 11 (I)
$P2_12_12_1$	4	14.17	6.79	14.22	90	90	90	0.674	1.136	17.8	22.4	12 (S), 11 (S), 11 (T)

[a] For symbols and units, see footnotes to Table II. [b] Percent of PPE due to the operator in parentheses.

lattice expansion into account).

A moderate success was achieved in reproducing the observed crystal structures of test compounds. There are however unavoidable difficulties in comparing two crystal structures determined by different methods. Cell parameters can be similar for different structures, and different for similar structures; the cell choice is always arbitrary, and, for triclinic structures, even cell reduction algorithms may be inconclusive, due to the large expected uncertainty in calculated cell parameters. Cell angles are particularly critical, since it is often unclear which set of angle supplements is more convenient (the possibility of enantiomorph structures further complicates the matter). PE alone is also an unreliable indicator of structure similarity (see below, about its precision); packing coefficients and crystal density also can be fortuitously coincident for different structures or slightly different for similar structures. Graphic methods are deceiving.

Safer parameters for the match are the orientation of distinguishable molecular features (e.g., aromatic planes) in the crystal and the nature of $O(j)$, $E(j)$ and $D(j)$, that is, the composition of the coordination sphere. Such overall parameters identify a crystal structure chemically, albeit much more roughly than the overdetailed X-ray picture. On the whole, it can be said that the comparison of two crystal structures obtained by methods of widely different precision is the most difficult step in assessing the performance of the method. The criteria we use are by no means unique or fully objective.

The present work demonstrates that, as generally felt by organic solid-state chemists, it is possible to construct a large number of crystal structures for a given molecule, whose PE's differ by less than 10%. We may go as far as saying that it is possible to construct an acceptable (in the above sense) crystal structure from almost any nucleus with a reasonable cohesion energy E_n; these hypothetical structures do not have repulsive contacts, the lower PE resulting from lower contributions from all atoms in the molecule, as seen by comparing the E_i's; a less stable crystal is less attractive, not more repulsive. Still, their densities are well within the expected ranges.[5c] This implies that a large part of the potential in crystals of low-polarity molecules is scarcely directional, but it depends mainly on molecular size. The directional part of the potential, not unexpectedly, is rather small.

This raises the question of the intrinsic precision of PPE calculations, especially when one is dealing with molecules that are very different from those on which the potential parameters were optimized. Accurate energy differences between phases have been calculated for benzene and anthracene,[22] and the CCW set has been successfully employed to the same purpose for naphthalene, anthracene, and biphenyl;[23] but all these molecules are among the staples of organic crystal chemistry. Another source of uncertainty is the location of hydrogen atoms, done by a procedure which is sometimes arbitrary for unusual bond connectivities, for highly strained molecules, and even for methyl groups. Finally, in our experience, the converged PE from PCK83 may vary by as much as 3% depending on the starting point and the parameters of the optimization procedure; the reasons for this apparent malfunction could conceivably be technical, and disappear if time were spent in a thorough search of the best optimization. One cannot however exclude that minor interactions lock the search into false minima, since potential energy valleys may not be smooth in the surroundings of the true minimum. All these arguments concur to place PE uncertainties in the same order of magnitude as the differences between phases.

In spite of these difficulties, it is encouraging to see that the method is able in some cases to give a correct crystal structure prediction. This is appreciable in a field where anything above zero is considered a good percentage of success. In any case, a simple and relatively inexpensive method for the systematic generation of possible crystal structures, using only (readily available) information on molecular geometry, is a great help in many crystal chemistry problems. In the study of polymorphism, when one phase is known experimentally, then the packing coefficient, the PE, and the crystal density cannot be too different for the other polymorphs, so that the search is made easier and

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its success can be readily judged. For families of similar compounds (like the acenes, the polyphenyls, etc.), the method can easily predict crystal structures in which the space group is the same as that of the parent compound, and some cell parameters are changed. This task has been accomplished for a number of thiophene oligomers.[24] In general, the approach outlined here can be useful whenever partial structural or spectroscopic information is available; then, trial structures can be generated, and the calculated crystal properties can be matched to the experimental ones.

The procedure should become more and more selective, and therefore efficient, with increasing molecular polarity and when stronger directional pointers are present, as is the case for hydrogen bonding. Of course, the empirical potentials must be appropriately updated to deal with such systems.[25] Generalization of the method to include more complex interaction potentials and to take into account any combination of symmetry operators is being considered for future work.

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Supplementary Material Available: Table X, with C-atom coordinates for all the calculated structures, and Appendix I, Cartesian coordinate model of the nuclei, Appendix II, Generation of translation vectors, and Appendix III, Use of the PCK83 program (16 pages). Ordering information is given in any current masthead.

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One-Electron Reduction of *N*-Bromosuccinimide. Rapid Expulsion of a Bromine Atom[†]

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Abstract: By means of pulse radiolysis *N*-bromosuccinimide, SBr, was reduced to its radical anion, SBr$^{\bullet-}$. Evidence is presented that SBr$^{\bullet-}$ rapidly fragments into the succinimide anion, S$^-$, and a free bromine atom, Br$^\bullet$, which is converted into Br$_2^{\bullet-}$ by reacting with Br$^-$ present. The rate constant of hydrogen abstraction by Br$^\bullet$ from 2-propanol and methanol have been determined. The carbon-centered radical of *tert*-butyl alcohol was also found to react with SBr yielding Br$_2^{\bullet-}$ in the presence of Br$^-$.

Introduction

Succinimidyl radical chemistry has long been dominated by a lively discussion[1-4] about the possible existence of two-electron isomeric succinimidyl radicals, to which were assigned the π and σ states.[1e] This suggestion was eventually abandoned,[1a] but in the system *N*-bromosuccinimide(SBr)/bromine/substrate quantification of the end products appears to demand the existence of a third chain carrier.[1a,3] Attempts to generate succinimidyl radical from SBr via a one-electron reductive pathway initially looked promising,[5,6] but later it turned out that the reactions observed could be better explained by a polar mechanism.[7,8] Lasting facts from these studies were provided by the isolation and X-ray structural elucidation of SBr$\cdots$Br$^-$ complexes[9,10] which seem to play an important role in the chemistry of SBr, as, for example, indicated by a catalytic effect of bromide ion upon the electron-transfer oxidative properties of SBr toward ferrocene,[11] in the formation of tribromide ion in the thermal decomposition of SBr/bromide solutions in acetonitrile[12] and in halogen heteroexchange reactions between *N*-halosuccinimide and halide ion.[13] The existence and stability of SBr/Br$^-$ complexes lend credibility

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