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Molecular Orbital Study of Crystalline 1,3-Cyclohexanedione. 2. Aggregates in Two and Three Dimensions

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Semiempirical (AM1) molecular orbital calculations on two- and three-dimensional aggregates of the anti-enol form of 1,3-cyclohexanedione containing up to 16 molecules as models of the nucleating crystal are presented. The interaction energies between linear chains to form layers and between layers are evaluated and discussed. The attraction between chains in a layer is primarily due to C–H···O H-bonding between a nonactivated C–H bond on C_5 to a C=O in the adjacent chain. The interaction energies between chains are found to be cooperative with a significant nonadditive component to this cooperativity. The total interaction energy is more than the sum of the pairwise interactions between chains. The intermolecular distances decrease upon augmenting the number of chains in a layer. The interactions between layers are weaker than those between chains. As only two layers were studied, no energetic component to the cooperativity between layers could be evaluated. However, interdimensional cooperativity seems to be operative as the intermolecular distances between individual molecules in the chains decrease upon the stacking of layers.

Crystal engineering, the ability to apply the principle of rational synthesis to the design of crystalline materials with desired properties and structures, was pioneered by Margaret Etter and her collaborators.[1] To better understand the nature of the intermolecular interactions that are important in the processes of crystal nucleation and formation, we have applied the techniques of molecular orbital (MO) theory to determining the energetics and structures of various aggregates of molecules leading to crystals. In a previous paper, we have presented the results of MO calculations on one-dimensional aggregates of 1,3-cyclohexanedione (CHD).[2] Etter has shown that this molecule can crystallize in a linear form as its anti-enol, or form a 6:1 cocrystal with benzene[3] when crystallized under appropriate conditions. Our previous calculations provided an energetic rationale for both of these observations. Nevertheless, complete understanding of the crystal structure requires study of the intermolecular interactions in the other directions, as well. In this paper, we present the results of MO calculations on the interactions between linear aggregates of CHD to form sheets of molecules.

In the crystal structure,[3] adjacent chains of CHD molecules in their anti head to tail (AHT) form are held together by C–H···O H-bonding interactions between alkyl C–H's and the C=O bonds of a molecule in an adjacent chain. C–H···O H-bonding interactions are quite common in crystals.[4] They tend to be weaker than O–H···O and N–H···O interactions (there are exceptions).[5] Typical C–H···O interactions are predicted to be stabilizing by about 1 kcal/mol.[6] Although several C–H···O interactions have been documented in the gas phase[7–11] and in inert matrices,[12] one would expect these interactions to be most important in crystal structures, where the almost infinite repetition can make even a weak interaction structurally determinant. A particularly dramatic example is the case of crystalline acetic acid,[13] where the normally characteristic carboxylic acid dimer, present in both the gas and liquid phases (and characteristic of most carboxylic acid crystal structures),[14] is replaced by a three-dimensional pattern where each acetic acid molecule participates in one O–H···O, two normal C–H···O and one very weak C–H···O interactions.[15,16]

Methods

The sizes of the aggregates discussed in this paper are too large to be studied by ab initio MO methods. We have previously shown that the AM1 approximation to MO theory is reasonably reliable for H-bonding[17] and crystal aggregation[15,16,18] and particularly so for C–H···O H-bonding interactions.[6]

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We used the AM1 MO method[19] for all the calculations discussed in this paper. We have used this method with success in several hydrogen-bonding studies,[20] including modeling of the H-bonding between molecules of various nitroanilines in the crystalline state.[14,21]

The geometries of the individual molecules were completely optimized within the following constraints: The aggregates were optimized completely with the constraints that the geometry of all molecules in each aggregate be the same and that the three carbons and two oxygens involved in the enolic fragment be coplanar with the corresponding atoms in the other molecules. In addition, the translational vectors characteristic of the crystal structure were optimized and kept parallel. These geometric constraints allow one to calculate one or more parameters of the unit cell and compare them to the experimentally determined values. All calculations were performed using the AMPAC 2.1 program[22] on IBM RS/6000 workstations.

The pairwise interactions between chains were obtained by performing MO calculations on the individual pairs of chains in the orientations and optimized geometries of the larger aggregate, then subtracting the energies of the individual optimized chains. These pairwise interactions consist of the interaction between the chains in the (distorted) geometry they take in the aggregate plus the distortion energy of each chain. The nonadditive part of the interactions is the stabilization of the supermolecule minus the sum of the pairwise interactions corrected for the different quantity of distortions in each. For the special case of n units, where each unit is constrained to the same geometry (thus, the distortion energies are the same for each) it can be

$$\Delta E_{\text{nonadd}} \cong \Delta E_{\text{supermolecule}} - \Sigma \Delta E_{\text{pairwise}} + (n^2 - 2n)\,\Delta E_{\text{distort}} \quad (1)$$

shown that this correction is $(n^2 - 2n)$ times the distortion energy (eq 1).[23] A similar equation can be written for the enthalpies at 298 K, which are calculated by AM1, or any other state function.

Results and Discussion

We performed calculations on from two to four interacting chains of trimers and tetramers in two-dimensional layers, as well as on structures of two interacting layers each consisting of two trimer or tetramer chains. In the following discussion, we designate the structures as $l/c/m$, where l denotes the number of layers, c, the number of chains per layer and m, the number of monomers per layer.

Figure 1 presents the largest layer, 1/4/4 (four tetramers interacting, approximating the structure of the crystal). The layer is held together primarily by C–H···O H-bonding interactions between unactivated C—H bonds and C═O's in adjacent chains. The C–H bond is in the equatorial 5-position. Thus, it is not expected to be significantly acidic as it is not vinylic, allylic, or adjacent to an electron-withdrawing group. Each monomer participates in two such interactions: its carbonyl group is the H-bond acceptor to one of two neighboring chains, while its C_5 is the H donor toward the other chain.

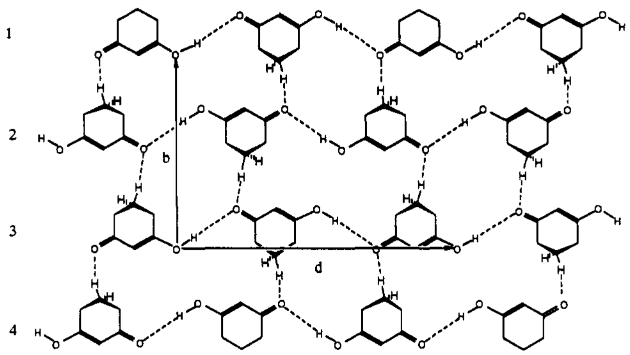

Figure 1. Layer containing four interacting tetramers.

Table 1. AM1 Incremental Interaction Enthalpies (kcal/mol) between Interacting Trimers and Tetramers (m = 3, 4 in c/m Aggregates)[a]

	no. of interacting chains		
chains	$c = 2$	$c = 3$	$c = 4$
$m = 3$	−5.76	−5.50	−5.86
$m = 4$	−9.34 (−4.93)	−4.56	−9.75

[a] Number in parentheses corresponds to a different H-bonding pattern. See text for more explanation.

Table 2. Geometrical Characteristics of AM1 Optimized Two- and Three-Dimensional Structures (Distances in angstroms)

aggregates	O···O	O···H(O)	O···C	O···H(C)	*d*	*a*	*b*	*c*	*β*
				Trimers					
1/1/3	3.033	2.066			13.983				
1/2/3	3.025	2.055	3.483	2.362	13.989				
1/3/3	3.023	2.052	3.464	2.342	14.011		12.006		
1/4/3	3.022	2.051	3.457	2.335	14.015		12.010		
2/2/3	3.022	2.049	3.438	2.320	14.046	9.073		8.664	104.70
				Tetramers					
1/1/4	3.028	2.061			13.973				
1/2/4	3.014	2.044	3.478	2.356	13.976				
$1/2/4_a$	3.022	2.051	3.501	2.380	13.992				
1/3/4	3.019	2.048	3.478	2.356	13.995		12.006		
1/4/4	3.016	2.044	3.461	2.339	13.996		12.001		
2/2/4	3.020	2.048	3.466	2.344	14.006	8.875		8.869	104.25
exptl[3]	2.561	1.63			11.007	8.193	11.712	6.128	99.44

Tables 1 and 2 contain the most important energetic and geometric data calculated for the layers. The incremental interaction energies between the chains for adding a new chain to a layer to form 1/2/3, 1/3/3, and 1/4/3 structure are −5.76, −5.50, and −5.86 kcal/mol, respectively. Adding a chain to a 1/2/3 (to form a layer with three chains) creates another interaction between adjacent chains (1–2 interaction), plus a new interaction (1–3) between nonadjacent chains. As adding the third chain is less stabilizing than combining two independent chains (formation of 1/2/3), the interaction between the first and third chains appears to be repulsive. The stabilization of adding the fourth chain is 0.36 kcal/mol greater than for adding the third chain. Upon addition of a fourth chain, three new pairwise (between chains) interactions are created: a 1–2 attractive interaction, a repulsive 1–3 interaction and a new attraction between the first and fourth chains (1–4 interaction). If one subtracts the new small (−0.09 kcal/mol) 1–4 pairwise interaction, the difference (0.25 kcal/mol) can be attributed to cooperat-

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Table 3. Pairwise Interactions (kcal/mol) between C–H···O H-Bonded Chains in 1/4/3 Aggregate

	pairwise interaction[a]					
aggregate	1–2	1–3	1–4	sum of pairwise interactions[b]	calcd interaction energy	non-additivity
1/4/3	−5.73 (−5.95)	+0.58 (+0.36)	−0.09 (−0.31)	−17.00	−17.12	−0.12

[a] Pairwise interactions include the distortion energies of the individual trimer chains upon forming the aggregate. Values in parentheses are the interactions between the distorted trimer chains (the distortion energies have been subtracted). [b] The sum of the pairwise interactions is corrected for the four ($n^2 - 3n$) extra distortions in the simple sum of the interactions.

ivity in the interaction of chains to form layers.

Calculations of all possible pairs of chains, frozen in their optimized geometries for the 1/4/3 layer allow us to independently evaluate the 1–2, 1–3, and 1–4 pairwise interactions. These data are collected in Table 3. The 1–2 (and the equivalent 2–3, 3–4) interactions are attractive by −5.73 kcal/mol. The 1–3 (and 2–4) interactions are repulsive by 0.58 kcal/mol, the 1–4 pairwise interaction is slightly attractive (−0.09 kcal/mol). The sum of the pairwise interactions after correction for distortions (see eq 1) for the 1/4/3 complex, −17.00 kcal/mol, is 0.12 kcal/mol less than the total interchain stabilization calculated from the supermolecule containing all four chains (−17.12 kcal/mol) indicative of the presence of a nonadditive contribution.[24] We have observed similar nonadditive cooperative effects in calculations on other crystal structures.[15,16] However, the nonadditivity here is particularly significant since the primary interactions in forming the layers are C–H···O H bonds involving carbons that are not conjugated to the π-system.

The shortening of the distances in the O–H···O H-bonding within the chains as more chains are added to a layer (Table 2) are consistent with the suggestion that cooperative effects in this second dimension influence the strength of the H-bonds within the individual chains. The C···O and (C)H···O interchain distances are relatively short, 3.45–3.48 and 2.33–2.36 Å, respectively. These C–H···O H-bonding distances are similar to those we calculated for other C–H···O interactions.[6,18]

The analysis of interactions between tetramer chains is somewhat more complex. Figure 1 indicates that, while each adjacent pair of chains form four C–H···O interactions, two different patterns exist for adjacent chains. In the first kind (those between the first and the second, or third and fourth chains), the two end C–H···O interactions *between the chains* are to C=O's that are not H-bonded to another molecule *within the chains*. As these C=O's are only interacting with the C–H's of the adjacent chain, one might expect these C–H···O interactions to be stronger than the two central C–H···O interactions, where the C=O's are interacting with O–H's, as well as C–H's. The second kind of interaction is illustrated by that between the second and third chains. In this interaction, all four C–H···O interactions are to fully H-bonded carbonyl groups. In the first kind of interaction, the terminal C–H···O interactions to non-hydrogen-bonding carbonyl groups result from artificial end effects inherent in a finite model. On the other hand, the C–H···O H-bonds between the second and third chains are free of these effects. Thus they are more characteristic of the interactions found in crystals. Accounting for the two different H-bonding patterns between chains, two 1/2/4 aggregates are possible: 1/2/4 (with interactions as between chains 1 and 2 in Figure 1) and $1/2/4_{\mathrm{a}}$ (with interactions as between chains 2 and 3).

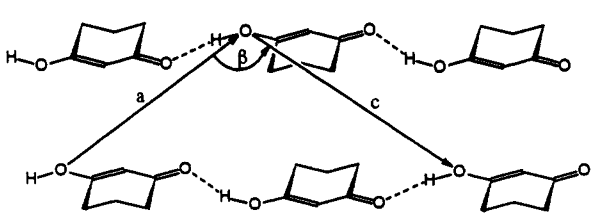

Figure 2. Illustration of the unit-cell parameters *a*, *c*, and *β*.

The interaction energies are listed in Table 1 (in parentheses for $1/2/4_{\mathrm{a}}$). The large difference in the two types of interaction energies for the 1/*c*/4 layers suggests that they are less appropriate models then 1/*c*/3 layers for evaluating cooperative effects. Examination of Figure 1 will show that 1/*c*/3 layers have two C–H···O interlayer interactions to fully H-bonded C=O's and one two a C=O showing the end effect discussed above for all interactions of adjacent chains. The incremental interaction energies between the chains for the formation of the 1/4/4 structure of Figure 1 are −9.34, −4.56, and −9.75 while those for the formation of a 1/4/3 layer are −5.76, −5.50, and −5.86 kcal/mol (Table 1).

The $1/2/4_{\mathrm{a}}$ aggregate contains only C–H···O interactions to fully H-bonded C=O's. It typifies the interactions in an infinite layer except that (since it contains only two chains) it lacks the cooperative part of the interchain interactions. Thus, we can estimate a lower limit to the strength of the individual C–H···O bonds from this structure. As the interaction is due to the four (roughly) equivalent C–H···O H-bonds, we estimate the stabilization due to a single C–H···O H-bond as one fourth of the interchain stabilization (−4.93 kcal/mol from Table 1) or −1.23 kcal/mol, in good agreement with previous work.[6]

Other geometric features of the layers are also illustrated in Table 2. Upon application of appropriate restrictions during the geometry optimization, one can obtain geometric parameters that are characteristic of the crystal, such as the unit-cell parameters. These results provide additional tests of the reliability of AM1 for modeling this crystal structure. A translation vector connecting every second monomeric unit within the chains corresponds to the diagonal (*d*) of a parallelogram defined by *a*, *c*, and *β* of the unit cell. Another translation vector between every second chain in a layer corresponds to *b* (see Figures 1 and 2). The calculated value of *b* agrees well with the experimental data, suggesting that description of the interactions between the chains is good. On the other hand, the diagonal is too long by 27%. This error is mainly due to the underestimation of the strength (and corresponding overestimation of the interaction distances) of O–H···O H-bonds by AM1. the overestimated diagonal causes *a*, *b*, and perhaps *β* also to be overestimated (though to a lesser extent).

The structure of a three-dimensional microcrystal is shown in Figure 3. The structure depicts a 2/2/4 AM1 optimized aggregate. Note that this aggregate consists of two different layers, 1/2/4 and $1/2/4_{\mathrm{a}}$, which differ in their H-bonding pattern. There is no corresponding difference

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(24) A referee has pointed out that the interlayer separation in graphite had been shown to involve cooperativity (Girifalco, L. A.; Lad, R. A. *J. Chem. Phys.* **1956**, *25*, 693). These authors considered only pairwise Leonard-Jones potentials which do not include the nonadditive part of the cooperativity.

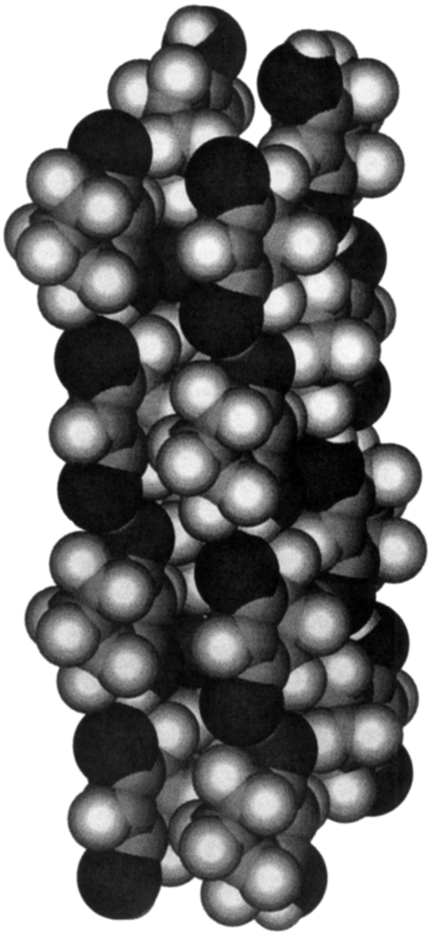

Figure 3. A 2/2/4 microcrystal (AM1 optimized structure).

between the interacting layers the 2/2/3 complex as both layers are equivalent. The calculated structures (Table 2) of these two three-dimensional structures (2/2/3 and 2/2/4) confirm the earlier conclusions based upon the energetic and geometric data.

The interaction energy is small between layers which lack strong H-bonds between them, as expected. The layers are shifted relative to each other (Figure 2). The oxygens of the upper layer appear to be weakly attracted to the axial hydrogens on the rings of the layer beneath. The nearest H···O interlayer distances are in the range 4.0–5.0 Å. These distances are somewhat longer than those characteristic of C–H···O H-bonding, suggesting that the interactions between the layers might be due to weaker interactions. The stabilizations between two layers are –0.50 and –0.90 kcal/mol for 2/2/3 and 2/2/4 structures, respectively.

The decrease of the O···O (within a chain), and O···C (within a layer) distances upon increasing aggregate size in the third direction manifests the existence of three-dimensional cooperative effects (Table 2). In the presence of the second layer, both these distances decrease. For example, (a) the C···O distance between the chains (Table 2) decreases from 3.483 Å (in 1/2/3) to 3.438 Å (in 2/2/3), and (b) while the O···O distance decreases from 3.043 to 3.033 Å as one goes from single dimer (1/1/2) to trimer (1/1/3), the aggregation of trimers into layers and microcrystals further decreases this distance to 3.025 Å in the 1/2/3 and 3.022 Å in the 2/2/3 aggregates. As shorter O···O H-bonding distances generally indicate stronger H-bonding interactions, these observations confirm interdimensional cooperativity.

Conclusions

AM1 molecular orbital calculations allow us to understand the interactions between chains and layers, as well as, between molecules in a chain as previously reported. C–H···O H-bonding between the unactivated C–H bond on C_5 and the C=O of a molecule in an adjacent chain is the most important component of the interactions between chains. The interaction between layers is weaker than that between chains. While the axial C–H bonds on C_4 and C_6 point in the direction of the two O's of a molecule in the adjacent layer, the H···O distances are greater than normal for C–H···O H-bonds. Cooperativity is evident in the formation of layers from chains, as well as between aggregation in the three different directions of growth.

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