STUDIES IN THE ORGANIC SOLID STATE

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ABSTRACT

This paper describes an approach to crystal engineering based on designing and analyzing hierarchical levels of crystalline architecture. The system under study consists of 1:1 co-crystals of melamines and barbituric acids that self-assemble into crystallographically infinite hydrogen-bonded tapes. The formation of structural elements can be rationalized and controlled using familiar molecular concepts such as steric repulsion.

INTRODUCTION AND BACKGROUND

Controlling the packing of organic molecules in crystals presents a major design challenge for molecular engineering.[1-3] The ultimate goal of patterned, functional arrays of organic molecules is of potentially great interest and reward. Fundamental investigations of the physical-organic chemistry of the solid state should find application throughout materials science.

Design of Our System.[4-6] Our approach attempts to simplify the packing of molecules by constraining them to adopt only a handful of orientations. The problem of rationally studying (let alone designing) molecular crystals would be intractable without some kind of control of this sort: the number of possible three-dimensional orientations of molecules in a crystal could be very large. Competing packing arrangements might have similar energies, and although progress is being made,[7-9] computational routines to predict the most energetically favorable arrangements are in their infancy. The geometries that result from our constraints simplify comparison of packing motifs and render the overall crystal structures analyzable in terms of successive levels of organization.

The particular system that we used as a conceptual guide is the 1:1 complex between cyanuric acid and melamine (Fig. 1).[10,11] The planar molecules in this structure are proposed to hydrogen bond with each other to give infinite hydrogen-bonded sheets. We hypothesized that by appending substituents to certain positions of these molecules, we could prevent hydrogen bonding in some directions and obtain structural elements that would be responsive to physical-organic-type investigations.

Hydrogen bonds possess several properties that recommend them as structural linkage units in molecular solids: they are directional, their formation is reversible at room temperature, and they can be incorporated into many different organic structures. Non-directional, dispersion-type interactions such as the stacking of van der Waals surfaces could lead to numerous options for the geometries of adducts. The three-fold hydrogen bonding of these planar molecules (or analogues of them) permits, by contrast, only two intermolecular orientations, which are related by rotation around the central NH---N contact. The planar, rigid

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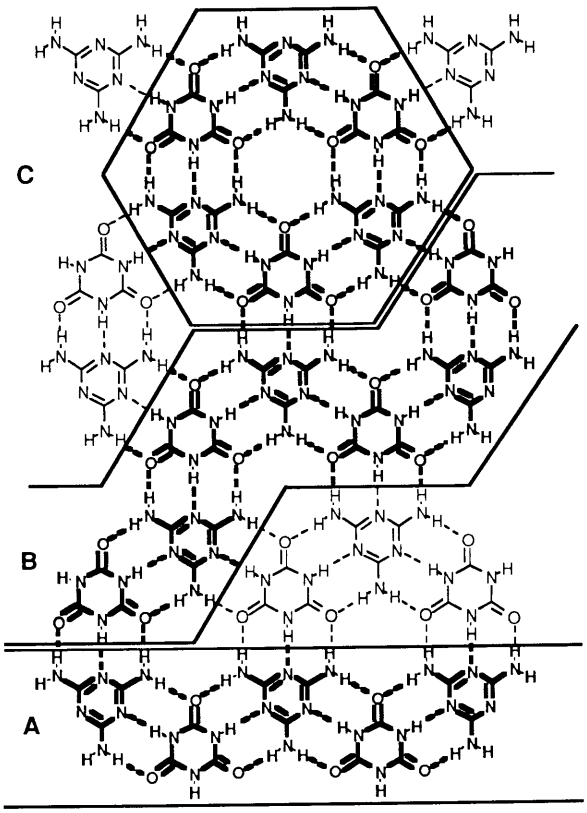

Figure 1. Postulated sheet structure of the complex between cyanuric acid and melamine. Hydrogen bonding continues from the molecules at the periphery to give an infinite two-dimensional network. The lines indicate substructures, or motifs, that could be obtained if hydrogen-bonding were prevented by substituents: A = linear tape, B = crinkled tape, C = rosette.

character of these molecules is also beneficial in generating simple structures. Hydrogen-bonding moieties connected by flexible chains (for example, an aliphatic dicarboxylic acid) would again weaken our chances to predict intermolecular geometry.

A number of workers have described regularities in the packing of hydrogen-bonded molecular solids. Etter and her colleagues have performed pathfinding work on systematic categorization of the patterns that hydrogen-bonding moieties are likely to adopt in solids.[12,13] This work has been critical in suggesting tools for use in crystal engineering. Leiserowitz and coworkers have comprehensively catalogued packing features found in carboxylic acids and amides.[14] Others have ingeniously employed hydrogen-bonding molecules in a

variety of solid-phase systems. Lehn has used three-fold hydrogen bonding in mesogenic compounds.[15] Kunitake has made microassemblies in the form of discs of controlled sizes.[16] Researchers at the Weizmann Institute have explored recognition properties at surfaces of crystals.[17,18] Lauher and Fowler have begun systematic work toward constructing crystalline arrays with the potential for solid-state reactivity.[19]

RESULTS

General Structural Features. The structural motifs that we have repeatedly obtained are those that are suggested by the sheet structure of Fig. 1, or "tapes" that are crystallographically infinite in one dimension and are held together by hydrogen bonds. These motifs provide starting points for an approach to crystal engineering based on hierarchies of crystalline architecture (Fig. 2). We label these

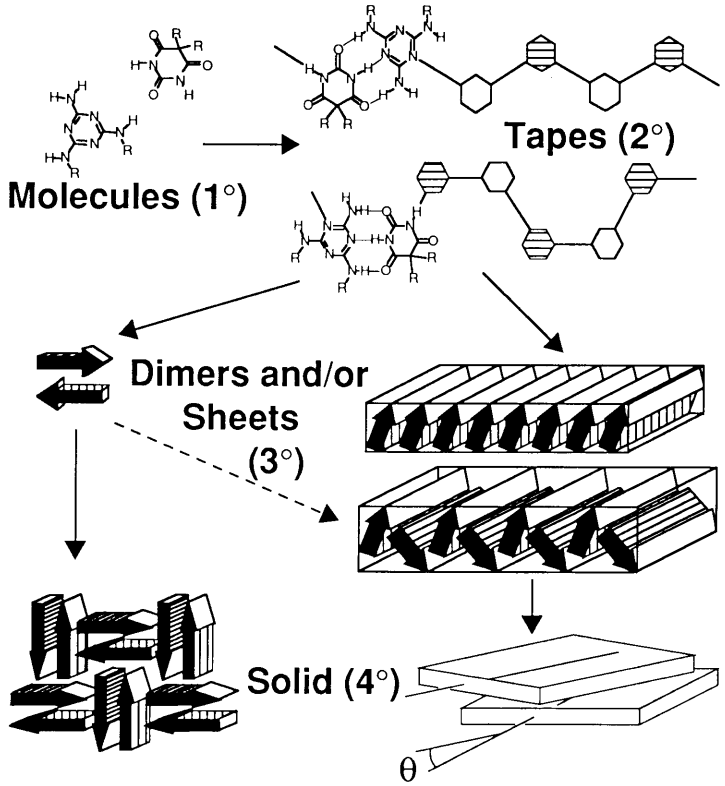

Figure 2. Schematic view of hierarchies of crystalline architecture that we observe in 1:1 co-crystals of melamines and barbituric acids.

successive levels of aggregation by analogy with the nomenclature that is already in use for describing protein structure. *Primary* structure is simply the molecular composition and/or sequence of a molecular crystal, which can be built from a single component or from a complex of varying stoichiometry, in the order ABAB, AABB, etc. The *secondary* level of architecure consists of the initial motif of aggregation of molecules into linear tapes, crinkled tapes, or rosettes (see Fig. 1). *Tertiary* structure refers to aggregates of secondary elements (e.g. "sheets" or dimers). Finally, *quaternary* structure is built up from aggregates of tertiary elements, giving the final three-dimensional solid.

Specific Families of Complexes. We chose initially to restrict the scope of our investigations to a closely related series of complexes, in particular those constructed from 5,5-diethylbarbituric acid and N,N'-diphenylmelamines substituted in the *para*-positions.[4] This family will be referred to as the *para*-series, where the substituents are -H, -F, -Cl, -Br, -I, $-CH_3$, and $-CF_3$. The structural perturbations that we made were therefore at only two points of one molecule of the complex, distant from the common hydrogen-bonding core. As it turned out, all of these complexes crystallized as linear tapes. All the *para*-substituents of the melamines are lined up along one edge of the tape, and the only chemical differences between these molecules (there are slight torsional variations) are along that edge. Any changes to tertiary packing upon a change of substituent are therefore due to these relatively small perturbations on one side of the tape.

Figure 3 shows packing diagrams of two of the complexes. These views are looking down the crystallographically infinite axes of the tapes, which project into and out of the plane of the paper. The views illustrate two common arrangements of tertiary architecture. The first, in the *para*-methyl tape, is constructed from tapes that are stacked into sheets. The second, in the *para*-chloro tape, consists of head-to-tail dimers of tapes.

Polymorphism. At this point, we need to mention a feature of crystals that introduces potential drawbacks as well as interesting opportunities. Any study purporting to offer a systematic view of molecular solids must take the possiblity of polymorphism into account.[1] In the *para*-series, we have searched for polymorphism by crystallizing the complexes from different solvents. The *para*-bromo complex does crystallize as two polymorphs. The first is isomorphous to the *para*-chloro complex, while the second is closely related to the *para*-methyl complex. Molecular modelling studies indicate that the first polymorph has a more favorable packing energy (D. Chin, unpublished), which is consistent with that polymorph's closer packing.[1] Figure 4 shows comparisons between calculated x-ray powder diffraction patterns (based on the single-crystal structure) and experimental patterns for both polymorphs. Comparisons of this type suggest that the other members of the *para*-series, except for X = CF_3, do not crystallize in polymorphic forms, at least not from the common crystallization solvents we employed at room temperature.

Crinkled Tapes. Since all the *para*-substituents are adjacent to each other on one side of a linear tape, it seemed reasonable to expect that, if these substituents could be made to interfere with each other, linear tapes would be disfavored. We achieved such interference simply by increasing the size of the substituents to X = COOMe.[20] To avoid steric repulsion, the molecules adopt a different motif of secondary architecture, the "crinkled" tape. *Para*-substituents are then on alternate

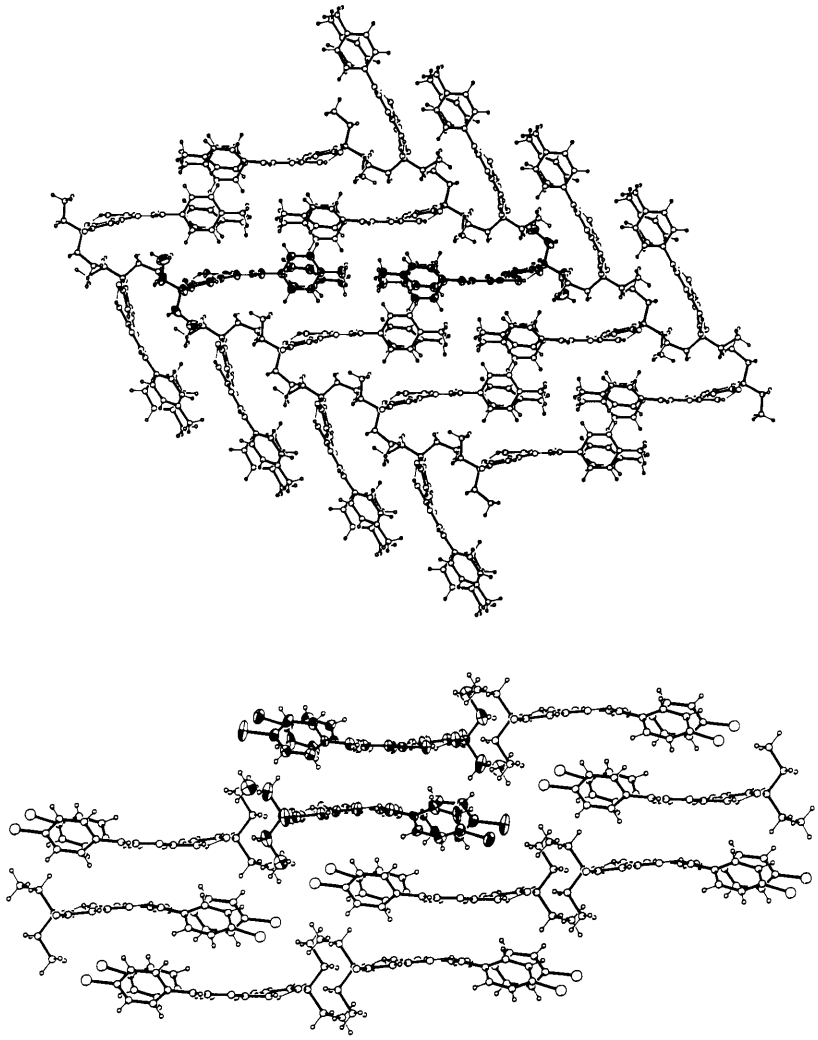

Figure 3. End-on packing views, looking down the long axes of linear tapes, of two complexes. Top: N,N'-bis(4-methylphenyl)melamine•5,5-diethylbarbituric acid, with a back-to-back pair of tapes in two adjacent sheets highlighted. Bottom: N,N'-bis(4-chlorophenyl)melamine•5,5-diethylbarbituric acid, with a head-to-tail dimer of tapes highlighted.

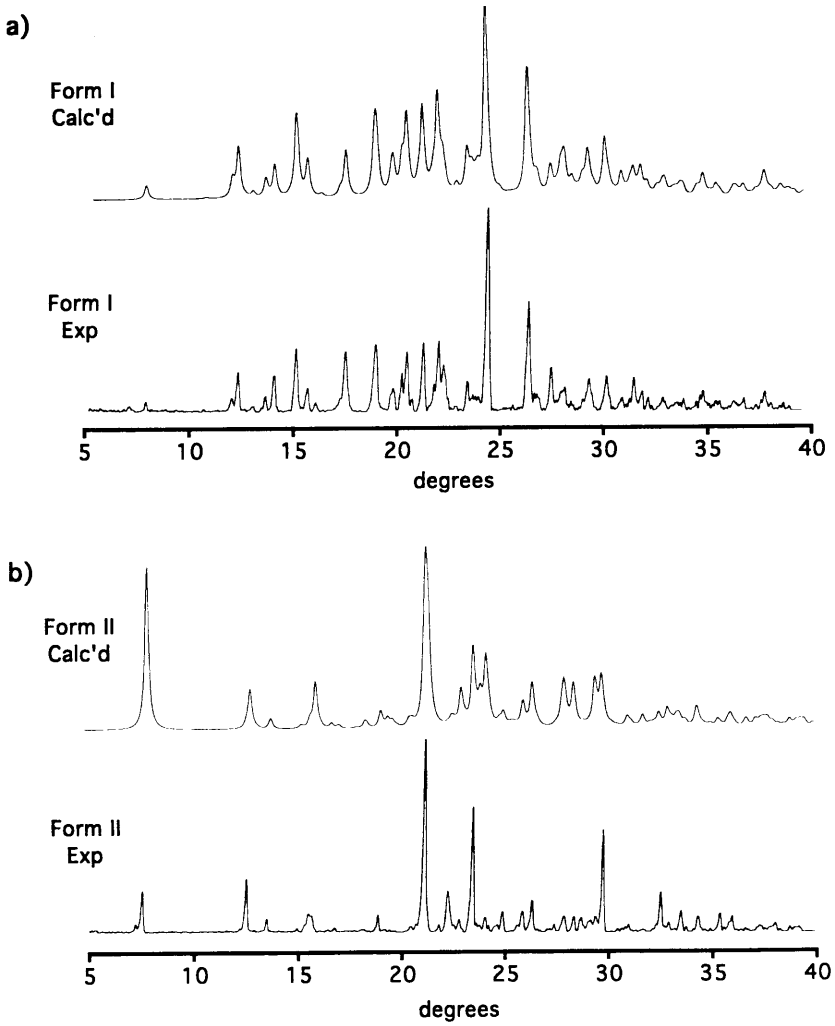

Figure 4. Calculated and experimental x-ray powder diffraction traces for two polymorphs of N,N'-bis(4-bromophenyl)melamine•5,5-diethylbarbituric acid. a) The polymorph isomorphous to the *para*-chloro complex; b) the polymorph related to the *para*-methyl complex. Agreement between the positions of the calculated and experimental peaks of the second form is good, but the relative intensities agree less well.

sides of this new kind of tape. Figure 5 also shows that these substituents could experience further steric hindrance. If the crinkled tape motif cannot be formed, a crystallographically finite motif, the "rosette" (also shown schematically in Fig. 1), can occur.[20]

This observation led to investigations of a different family, that constructed from N,N'-di-(*tert*-butyl)melamine with a variety of barbituric acids.[5] Although the "spacer" (a *para*-phenyl group) between the sterically hindered region (*tert*-butyl groups) and the hydrogen-bonding core (melamine) has been removed, the

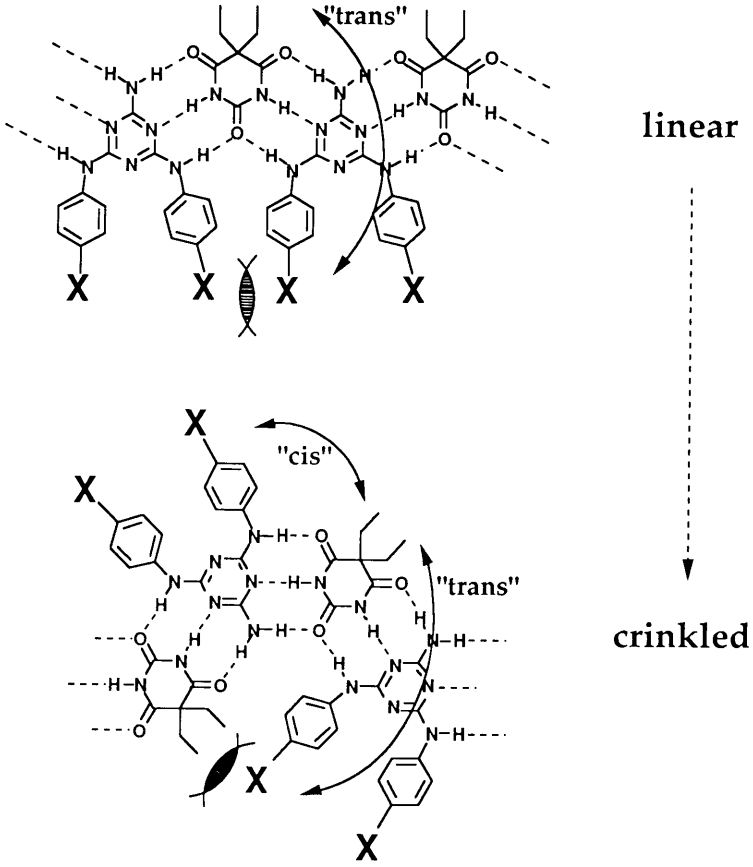

Figure 5. Steric pressures on secondary architecture generated by interactions between neighboring phenyl substituents in a developing linear tape can force adoption of a crinkled motif. Further steric clashes, now with barbituric acid substituents, could lead to the all-"cis" cyclic hexamer or "rosette".[20]

same principle applies with the same result (Fig. 6). All four examples of tapes in this family are crinkled. Using N,N'-di-(*tert*-butyl)melamine, we feel that we have a reliable route to molecular solids built from crinkled secondary architecture.

***Meta*-substituted complexes**. We have also placed the substituents that were employed in the *para*-series at the *meta*-position of diphenylmelamines.[6] The *meta*-family is somewhat more complicated in its packing arrangements than the

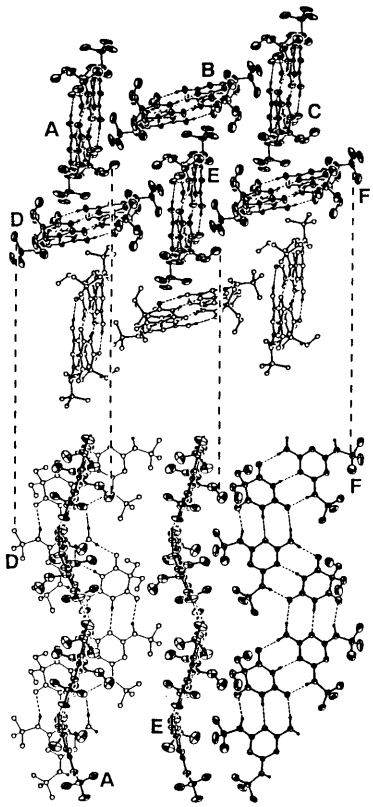

Figure 6. Composite view of the packing of the N,N'-di(*tert*-butyl)melamine• 5,5-diethylbarbituric acid complex. The view at top, looking down the long axes of the crinkled tapes, shows their herringbone packing; the bottom view (at 90° to the first) shows the waviness of the hydrogen-bonded backbones in the edge-on perspectives of tapes A and E. Dotted lines connect identical tapes in the two views.

para-family. This complexity seems reasonable in light of the greater number of isomers that the *meta*-family can access through rotation around the NH-phenyl bond. In particular, both linear and crinkled motifs are adopted. The *meta*-chloro and *meta*-bromo complexes, which pack very similarly, possess a short CH---O intratape contact that may stablize the crinkled motif.[21] The chloro, bromo, iodo, and trifluoromethyl complexes pack with solvent molecules in the lattice. In the *meta*-trifluoro complex, the manner of inclusion of solvent is interesting: channels of acetonitrile molecules exist between the linear tapes.

Attempts To Control Tertiary Architecture. Once molecules have self-assembled into infinite tapes, they can pack into tertiary structural elements in a number of fashions. While we have had some success at identifying forces responsible for determining secondary architecture, and at rationalizing and controlling these linear and crinkled motifs, tertiary structure is more difficult to predict. Nonetheless, it is at this level of organization (as well at the quaternary level) that packing needs to be effectively controlled in order to attain a desired three-dimensional orientation of molecules (such as an acentric material).

We therefore attempted to construct tapes bearing substituents capable of intertape interactions. We had no success growing crystals with polar substituents in the *para*-positions of diphenylmelamines: COOH, $CONH_2$, and CN groups may have strong directional packing requirements themselves that are incompatible with close packing of tapes. Instead we took the radically different approach of trimming off all the substituents from the melamine and barbituric acid cores. Our expectation was that the extra hydrogen-bonding sites at the backsides of the tapes (that is, hydrogen-bonding moieties that were not engaged in holding together the tapes) would be free for making intertape contacts. We did not expect proton transfer from barbituric acid to melamine to occur as it did (Fig. 7).

The resulting linear tapes thus have one negatively charged edge (the malonyl fragment of barbituric acid) and one positively charged edge (the protonated triazine ring of melamine), further increasing the likelihood of strong tape-tape contacts. Apparently the disposition of charged hydrogen-bonding moieties is such that the most favorable intertape arrangement is a skewed one, where the long tape axes in the crystal are not all parallel (θ in Fig. 2 $\neq 90°$). This is the only structure that we have observed with this arrangement of tapes. Crystals of this complex are dense (1.72 g/cm^3), indicating the presence of extensive intermolecular forces.

CONCLUSIONS AND PROSPECTS

This work demonstrates that partial control of molecular packing in crystals can be attained by choosing the right system. Our approach is to use rigid molecules that can co-crystallize in only a few orientations that are determined by the multiple hydrogen bonding between the molecules. Substituents on these molecules limit hydrogen bonding to give crystallographically infinite tapes. Tapes pack into arrays that occur recognizably across families of complexes. The overall crystal structure is composed of levels of architecture that can be considered individually.

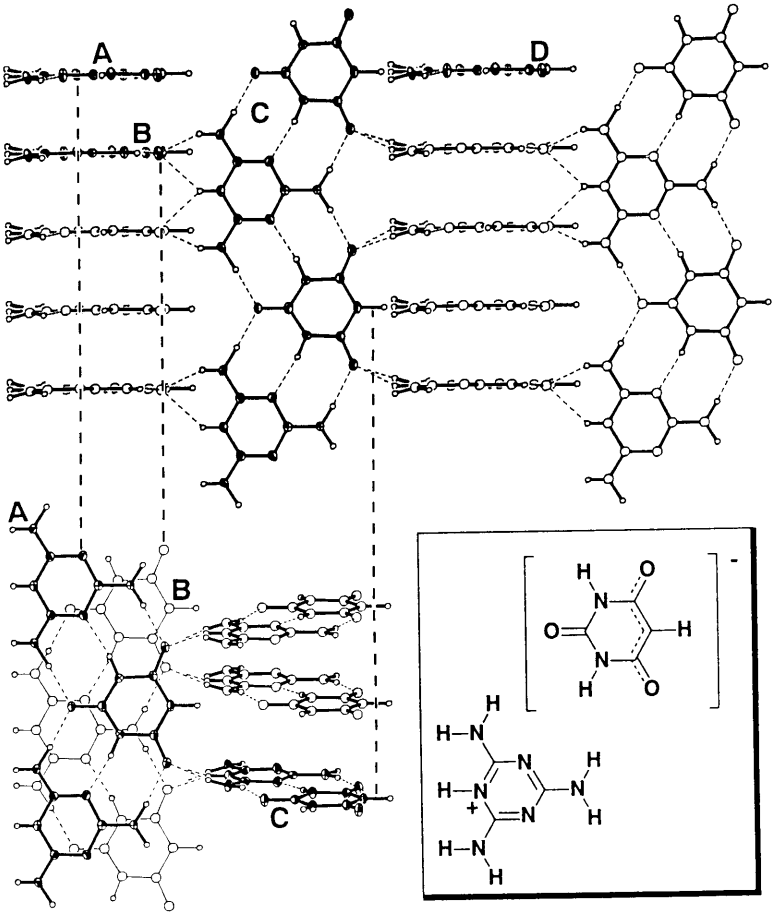

Figure 7. Composite view of the packing of the melamine•barbituric acid complex. Tapes A and B are perpendicular to tape C.

While we have made some inroads into rationalizing and controlling secondary structure, doing the same for tertiary architecture is still in its early stages. The above systems do suggest further experiments, however. Polymorphism makes it difficult to be certain that a given packing arrangement is thermodynamically favored, but as a consequence, different polymorphs can be compared to identify common or contrasting architectural features. One avenue that is being pursued is computational: since secondary building blocks (tapes) are comparatively reliably formed, calculating energetically favorable tertiary arrangements might augment our admittedly slender predictive capabilities. We remain optimistic that this sort of approach to crystal engineering, based on designing and analyzing hierarchical levels of crystalline architecture, will make useful contributions to the physical-organic chemistry of the solid state and ultimately to materials science.

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