Investigations into the Robustness of Secondary and Tertiary Architecture of Hydrogen-Bonded Crystalline Tapes

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Five crystal structures of hydrogen-bonded complexes (N-phenyl-p-iodophenyl)-N'-phenyl-p-cyanophenylmelamine-barbital, N,N'-diphenylmelamine-5,5-dimethylbarbituric acid, 2-amino-4-((m-bromophenylamino)-6-chloro-1,3,5-triazine-barbital, melamine-5,5-dibromobarbituric acid, and melamine-barbituric acid) are presented. These particular components represent perturbations on the molecules that were previously used to construct crystallographic hydrogen-bonded tapes (Zerkowski, J. A.; MacDonald, J. C.; Seto, C. T.; Wierda, D. A.; Whitesides, G. M. J. Am. Chem. Soc. 1994, 116, 2382). Four of the complexes pack in the solid state as linear tapes, while the diphenylmelamine-dimethylbarbituric acid complex packs as a crinkled tape due to the closer stacking of tapes permitted by the small methyl substituents. The triad of hydrogen bonds that forms tapes is apparently robust to this sort of variation, even though some of the substituents introduce noncovalent intertape interactions, such as halogen-nitrogen contacts, ionic forces, and other hydrogen bonds. The potential of such intertape interactions for designing crystalline architecture is discussed.

Introduction

To probe the modifiability and robustness of hydrogen-bonded cocrystalline "tapes", we have begun investigating the effects that major structural changes have on the formation and packing of tapes. We have shown that crystalline architecture1 could be constructed and rationalized from complexes of 1 and 2. In particular, by varying the steric properties of the substituents R of 1, we have obtained three structural motifs. When R was a phenyl ring substituted in the para position with CF3 or a smaller group, we obtained linear tapes.2 When the para substituent on the phenyl group was CO2Me,3 the meta substituent was Cl or Br,4 or when R was tert-butyl,5 crinkled tapes were obtained. When the para substituent was tert-butyl, a pseudo-C3 cyclic structure (a "rosette") was obtained.3 Barb(Et)2 (barbital) has been the barbiturate that we used most frequently, although other substituents on the barbiturate have also generated crystalline tapes.5

In the research presented in this paper, we examined the influence of larger variations in the structures of both components on the structure of the 1:1 cocrystals. With an unsymmetrically substituted melamine (3, R1 = p-iodophenyl, R2 = p-cyanophenyl), a non-melamine (4), unsubstituted melamine (5), or significantly truncated substituents on the barbiturate (R' = Br (6) or H (7)), linear tapes are still obtained. With the seemingly minor perturbation of shortening the ethyl groups of Barb(Et)2 to methyl groups (8), the secondary architecture switched from a linear to a crinkled motif. We were also interested in surveying how substitution patterns of these kinds might be used to control intertape orientation, or tertiary crystalline architecture.

Results

Figures 1-5 are conglomerate pictures of the sort we introduced in previous work. These pictures show several
different views of the packing of the complexes. Table 1 lists crystallographic data and some geometric parameters describing the packing of tapes.

<table>
<thead>
<tr>
<th>complex</th>
<th>space group</th>
<th>a (Å)</th>
<th>b (Å)</th>
<th>c (Å)</th>
<th>α (deg)</th>
<th>β (deg)</th>
<th>γ (deg)</th>
<th>R²</th>
<th>C₄⁺⁺</th>
<th>density (g/cm³)</th>
<th>crystallization solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mel(p-i-Ph)(p-CN-Ph)-Bar(Et)₂</td>
<td>P62d</td>
<td>30.603</td>
<td>35.760</td>
<td>9.711</td>
<td>97.34</td>
<td>91.25</td>
<td>95.41</td>
<td>0.052</td>
<td>0.68</td>
<td>1.534</td>
<td>EtOH</td>
</tr>
<tr>
<td>4Bar(Et)₂</td>
<td>P1</td>
<td>7.424</td>
<td>9.944</td>
<td>13.599</td>
<td>97.34</td>
<td>91.25</td>
<td>95.41</td>
<td>0.059</td>
<td>0.72</td>
<td>1.625</td>
<td>MeOH</td>
</tr>
<tr>
<td>Mel-Bar(Br)₂</td>
<td>Cm2₁</td>
<td>7.207</td>
<td>9.740</td>
<td>17.072</td>
<td>97.34</td>
<td>91.25</td>
<td>95.41</td>
<td>0.035</td>
<td>0.81</td>
<td>2.284</td>
<td>H₂O</td>
</tr>
<tr>
<td>MelH⁺-BarH⁻</td>
<td>Cc2</td>
<td>5.052</td>
<td>12.221</td>
<td>15.742</td>
<td>97.34</td>
<td>91.25</td>
<td>95.41</td>
<td>0.045</td>
<td>0.79</td>
<td>1.737</td>
<td>H₂O</td>
</tr>
<tr>
<td>Mel(PhH)-Bar(Me)₂</td>
<td>P2₁/a</td>
<td>9.295</td>
<td>16.911</td>
<td>13.520</td>
<td>96.16</td>
<td></td>
<td></td>
<td>0.058</td>
<td>0.70</td>
<td>1.366</td>
<td>MeOH</td>
</tr>
</tbody>
</table>

⁶ The underlined cell dimensions represent the repeat distance in a linear tape. ⁷ A blank indicates that the angle is constrained to be 90°. ⁸ This value is the crystallographic reliability index, R = \(|F_{o}| - |F_{c}||/|F_{o}|. ⁹ This value is the packing coefficient based on molecular volumes calculated using MacroModel (see Results). For a comparison of our modified, MacroModel-derived C₄⁺⁺ values to “classical” C₄ values, see ref 2. ¹⁰ Calculated.

Although we assumed that the replacement of ethyl with methyl groups would have no effect on the secondary architecture, the complex packs as a crinkled tape, rather than the linear tape observed for Mel(Ph)₂-Bar(Et)₂. One of the phenyl groups is almost coplanar with the melamine ring, while the other is more twisted out of the plane (torsion angles 11° and 28°, respectively). With no substituents extending very far out of the hydrogen-bonded plane of the tape (relative to tapes with ethyl groups or phenyl groups with larger torsion angles), these crinkled tapes appear “flat” (see the end-on view in Figure 2) and can stack closely on top of each other. Conversely, there are no contacts between adjacent stacks of tapes (e.g., between tapes B and C in Figure 2). There are two intratape CH-·-O contacts under the sum of the van der Waals radii (~2.7 Å). One involves an ortho proton on the nearly in-plane phenyl ring and the neighboring barbituric acid. The other contact involves a meta proton on the other, more twisted phenyl ring and the barbituric acid three units away in the tape (see the top of Figure 2). Both H-·-O distances are ~2.55 Å.

2-Amino-4-((m-bromophenyl)amino)-6-chloro-1,3,5-triazine-Barbital, 4-Bar(Et)₃ (Figure 3). This melamine analogue (a triazine) was chosen primarily because it has only two amine groups. Chlorine is one of many substituents that might go in the remaining ring position, and the m-bromophenyl ring fortuitously gave good crystals; neither of these substituents was chosen to test a specific hypothesis. The linear tape motif is preserved, even though one hydrogen bond has been deleted relative to complexes constructed from melamines. The chlorine and oxygen that occupy the space of the former hydrogen bond are just at van der Waals contact (distance = 3.3 Å, \(\Sigma_{d} = 3.3 \text{ Å}\)). With the removal of one of the NHR groups, the phenyl group of the remaining NHR has room to lie almost coplanar with the triazine ring: the mean planes of the two rings differ by only approximately 3°. Due to this orientation of the phenyl ring, one ortho-hydrogen is positioned close to a barbital oxygen at 2.5 Å.

Melamine-5,5-Dibromobarbituric Acid, Mel-Bar(Br)₂ (Figure 4). This substituted barbituric acid (and barbituric acid itself, Figure 5) was examined to determine the influence of replacing the ethyl groups of barbital by smaller but more polarizable and/or reactive substituents. The bromine atoms of Bar(Br)₂ are involved in several intratape contacts with nitrogen atoms of melamine at 2.7 and 2.8 Å (\(\Sigma_{d} = 3.4 \text{ Å}\), see Figure 7 for a closeup view). These intratape interactions are reflected in the high value of C₄⁺⁺ (Table 1).

Melamine-Barbituric Acid, MelH⁺-BarH⁻ (Figure 5). Proton transfer from the CH₂ of barbituric acid to a ring nitrogen of melamine has occurred. This complex
also has a high value of $C_6^*$. The crystallographically infinite hydrogen-bonded axes of the tapes are parallel within a stack of tapes, but adjacent stacks are twisted by 78° with respect to each other. This structure is the first in which we have observed nonparallel tapes.

**Packing Fractions.** The values of $C_6^*$ for the complexes incorporating Bar(Br)$_2$ and BarH are higher than normal for organic molecular crystals. The value for Mel·Bar(Br)$_2$ is the highest we have observed in any tape. This increase in the efficiency of space filling is probably due to two factors. The first is the presence of

\[ C_6^* = NV_{\text{mol}}/V_{\text{cell}}, \]

where $N$ is the number of molecules in a unit cell, $V_{\text{mol}}$ is the molecular volume, and $V_{\text{cell}}$ is the volume of the unit cell. Kitaigorodsky, A. I. Organic Chemical Crystallography; Consultants Bureau: New York, 1961. For a discussion of the relationship between our modified $C_6^*$ values and traditionally calculated $C_6$ values, see ref 2.

(11) Values of $C_6$ usually range from roughly 0.85 to 0.77: Desiraju, G. R. Crystal Engineering: The Design of Organic Solids; Elsevier: New York, 1989; Chapter 2. Some of the highest values listed by Kitaigorodsky are 0.785 (p-querterphenyl), 0.781 (1,2-anthraquinone), and 0.805 (perylene). The value for graphite is 0.887, which can probably be considered an effective upper limit.
strong electrostatic intertape forces such as those between bromine and nitrogen atoms in Mel-Br and the ionic interactions in Mel\(\cdot\)Bar. Ionic interactions in crystals of the latter compound cause them to have a high density (1.737 g/cm\(^3\)) for a material containing only C, H, O, and N. The second factor is geometric: the individual molecules are flatter than melamines and barbiturates substituted with phenyl or ethyl groups; this shape allows the tapes to stack with little empty space between them.

**Discussion**

The complex of Mel(\(p\)-Ph)(\(p\)-CN-Ph) with Bar(Et)\(_2\) was investigated because it represented a preliminary experiment in the control of tertiary architecture. We hypothesized that this complex might pack analogously to the Mel(\(p\)-Ph)\(_2\)Bar(Et)\(_2\) complex (Figure 8). There were extensive I - - - I contacts between tapes in that complex; we thought that replacing one iodine with a nitrile group would allow for virtually isostructural packing and
the introduction of I- -CN interactions. Instead, a different kind of packing arrangement occurred, namely, the head-to-tail dimeric orientation of tapes that we have observed in many complexes. In this structure, an iodine- -nitrogen interaction different from the one we expected was formed (Figure 6). This contact, which is only about 0.1 Å under the sum of van der Waals radii, is probably weak, but it may help to stabilize the perpendicular orientation of tapes. The intended packing arrangement shown at the bottom of Figure 8 may have

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(14) We have previously observed an iodine-nitrile interaction in the $N,N'$-bis(m-iodophenyl)melamine-barbital-acetonitrile crystalline solvate.

(15) Since the iodine atoms in the $\text{Mel(p-I-Ph)}_2 \cdot \text{Bar(Et)}_2$ complex were involved in interactions among themselves, they did not engage in short contacts with nitrogen in that complex.

(16) We have not searched for polymorphs of this complex (nor of any of the structures presented in this paper); other packing arrangements, perhaps even the proposed one shown in Figure 8, could of course occur for this complex.
failed to form because the strong dipoles of the nitriles would have been too close to each other in an unfavorable head-to-head orientation.17

The difference between hypothesized and observed structures emphasizes that it is still difficult to predict solid-state structures, even when the prediction is based on a relatively modest change to a known structure.

The hypothesis motivating our study of the Mel(Ph)2-Bar(Me)2 complex was that small alkyl substituents on the barbiturate component would permit close stacking of tapes. The Mel(Ph)2-Bar(Et)2 complex packs as linear tapes, its tertiary architecture consisting of dimers of tapes arranged in a herringbone pattern.2 We suspected that replacement of ethyl groups with methyl groups might alter this dimer-based packing to a sheetlike arrangement, similar to that observed in 4-Bar(Et)2 (Figure 3) or Mel-Bar(Br)2 (Figure 4), where all the tape backbones in a given stack are parallel.

While the crinkled tape that resulted does display some of the close-stacking features that small barbiturate substituents should allow, the crossover to a crinkled motif was entirely unexpected. On closer examination, however, the factors that favor adoption of a crinkled motif become clearer. One of the phenyl rings of Mel(Ph)2 is nearly coplanar to the triazine ring. It thus protrudes into the region of space that phenyl groups on a neighboring melamine in a linear tape would need to occupy. The flat, in-plane orientation of this phenyl group is favored by stacking interactions between two tapes (e.g., C and D in Figure 2) involving both the heterocyclic, hydrogen-bonded backbone rings and the aromatic substituents. The intended close stacking of tapes arising from a reduction in the ratio of alkyl to aryl surface area has therefore occurred, but maximal close packing of flat, aromatic and heterocyclic surfaces at the tertiary level is apparently energetically favorable enough to dictate the motif of secondary architecture that is adopted.

The 4-Bar(Et)2 complex was investigated to see if 3-fold hydrogen bonding is essential to the construction of cocrystalline tapes between barbiturates and derivatives of triazines. Evidently, it is not. We do not know if the approach of the chlorine to the oxygen atom is energetically favorable or repulsive. If repulsive, it is apparently not strong enough to overwhelm the favorable tape-forming

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Figure 6. Closeup of the iodine-nitrogen interaction between two perpendicular melamines in Mel(p-1-Ph)(p-CN-Ph)-Bar(Et)₂. The melamine on the left belongs to tape A in Figure 1; the melamine on the right belongs to tape B. The number adjacent to the dashed line that indicates this interaction represents the value of the distance of the contact minus the sum of the van der Waals radii (in angstroms).

Figure 7. Closeup of the intermolecular interactions involving bromines in Mel-Bar(Br)₂. The letters indicate to which tape in Figure 4 the molecules belong. The numbers adjacent to the dashed lines that indicate these interactions represent the value of the distance of the contact minus the sum of the van der Waals radii (in angstroms). The hydrogen atoms were placed in calculated positions for crystallographic refinement, with a N–H bond length of 0.9 Å.

Figure 8. Back-to-back orientations of two tapes linked by noncovalent interactions between substituents in the para positions of the diphenylmelamines. At the top is the observed structure of the Mel(p-1-Ph)₂-Bar(Et)₂ complex. At the bottom is the hypothetical structure that we predicted (incorrectly) might result by replacing one iodine with a nitrile group. The observed structure is given in Figure 1.

hydrogen bonds. In a structural sense, we have "muted" the symmetrically substituted melamine component that we have usually employed for constructing tapes into this kind of chlorotriazine by replacing one NHR group (R = alkyl or aryl) with a chlorine atom. As a result, an indentation or hole has been generated along the periphery of the linear motif (see Figure 3). Note that a nearly coplanar orientation of the bromophenyl and triazine groups can be accommodated by the linear motif when the other substituent on the triazine ring is small (chlorine in 4 compared to NHPh in Mel(Ph)₂).

The key feature of both complexes incorporating melamine is that some of the hydrogen-bonding sites of the melamine remain unutilized by the formation of linear tapes. That is, one edge of the planar melamine molecule, representing a donor–acceptor–donor triad (HN–N–NH), is uncomplexed. It is therefore free to engage in intertape interactions that can direct tertiary architecture. The occurrence of several close contacts involving bromine and nitrogen atoms in the Bar(Br)₂ complex (Figure 7) is due to the availability of these melamine sites for participation in electrostatic interactions.

In the Mel⁺ Bar⁻ complex, the uncomplexed state of one ring nitrogen of melamine permits proton transfer from the CH₂ group of barbituric acid. Protonation creates ionic interactions between Mel⁺ and Bar⁻ both within and between tapes, and the hydrogen-bonding network throughout the crystal is three-dimensional. To maximize the influence that these strong forces can provide and thereby minimize the lattice energy, stacks of the tapes twist with respect to each other. This crystal structure is the only one in which we have observed tapes with nonparallel axes. We hypothesize that in the absence of such strong intertape forces, the arrangement of tapes that permits the closest possible packing (reflected in a high C₄⁺) is one in which the hydrogen-bonded axes of all tapes are parallel.

Conclusions

The crystal structures presented in this paper demonstrate that hydrogen-bonded co-crystalline tapes are robust to a wide range of structural variations. Even variations that preclude formation of the full triad of hydrogen bonds, such as replacement of a melamine by a chlorotriazine, do...
not disrupt the tape motif. Interactions between tapes involving bromine–nitrogen contacts, ionic forces, or hydrogen bonds can lead to close packing of tapes and to high densities. Intertape stacking interactions appear to be able to cause a switch from a linear to a crinkled motif. This phenomenon runs counter to our previous hypothesis that intratape steric effects are most likely to force adoption of a crinkled motif. On the other hand, we have also noted that electrostatic interactions (e.g., CH\_\_\_-O contacts) or the packing of tapes around trapped solvent molecules may play a role in crinkling. The Mel-(Ph)\_2-Bar(Me)\_2 complex can be viewed as combining these two effects: the immediate cause leading to crinkling is intratape (secondary) steric repulsion involving flat phenyl groups, but the underlying cause is favorable intertape (tertiary) stacking of these groups and the heterocyclic tape backbones. These initial forays into controlling tertiary architecture show that moieties that are capable of engaging in noncovalent interactions can be appended to the peripheries of tapes. Directing those interactions in a specific manner, however, remains a challenge.

**Experimental Section**

**General Methods.** N-(p-Iodophenyl)-N'-(p-cyanophenyl)melamine (Mel(p-I-Ph)(p-CN-Ph)), 2-amino-4-((m-bromophenyl)amino)-6-chloro-1,3,5-triazine (4), N,N'-diphenylmelamine (Mel(Ph)\_2), and 5,5-dimethylbarbituric acid (Bar(Me)\_2) were prepared according to previously published procedures. The supplementary material contains spectroscopic details and elemental analyses (see paragraph at end of paper). Melamine and dibromobarbituric acid were obtained from Aldrich Chemicals, barbital from Fisher Scientific, and barbituric acid from Alfa Products. Solvents were reagent grade and were used as received without purification.

**Crystallizations.** Mel(p-I-Ph)(p-CN-Ph)-Bar(Et)\_2, 4-Bar(Et)\_2, and Mel(Ph)\_2-Bar(Me)\_2. These 1:1 complexes were prepared according to procedures described previously. Crystals of the first two complexes were obtained by room-

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**Supplementary Material Available:** Experimental details for Mel(p-I-Ph)(p-CN-Ph) and 4 and crystallographic details including tables of atomic positional parameters and bond lengths and angles (56 pages); tables of observed and calculated structure factors (36 pages). Ordering information is given on any current masthead page.