Superstructure Topologies and Host−Guest Interactions in Commensurate Inclusion Compounds of Urea with Bis(methyl ketone)s

M. E. Brown,† J. D. Chaney,†
B. D. Santarsiero,‡ and M. D. Hollingsworth*,†

Department of Chemistry, Indiana University
Bloomington, Indiana 47405
Department of Chemistry, University of California
Berkeley, California 94720-1460

Received May 6, 1996
Revised Manuscript Received July 3, 1996

Although the topological features of networks of hydrogen bonds in a crystal can be described in terms of graph sets[1,2] or connectivity patterns, prediction of these topological features is often confounded by subtle factors such as packing efficiency,[3] strain, and long-range Coulombic interactions. For supramolecular assemblies containing more than one type of molecule, the opportunity for different stoichiometries and sequential patterns represents extra degrees of freedom for the crystal packing arrangement and requires the crystal engineer to remove other degrees of freedom from the system by judicious choice of complementary and directional intermolecular contacts. In systems containing flexible groups and several hydrogen-bond donors and acceptors, the multitude of energetically feasible packing arrangements is a sobering fact that keeps the field of crystal engineering in the empirical stage. Success is most often met when one recognizes or discovers an existing motif and exploits it in a logical manner.[1,4] Here we show that the reliable set of local structural motifs present in urea inclusion compounds (UICs) of bis(methyl ketone)s allows one to construct simple models that can be used to predict the gross features of stable crystal packing arrangements for the hosts and guests. Because certain UICs are ferroelastic,[5] this method constitutes an important step toward designing and synthesizing new ferroelastic inclusion compounds. It should also help identify guest molecules that are good candidates for chiral resolution with UICs.[6]

With relatively few exceptions,[7] UICs share a common packing arrangement in which urea molecules are connected by hydrogen bonds to form helical ribbons, which repeat every six urea molecules (11.0 Å) to form a series of linear, hexagonal tunnels (Figure 1).[8,9]

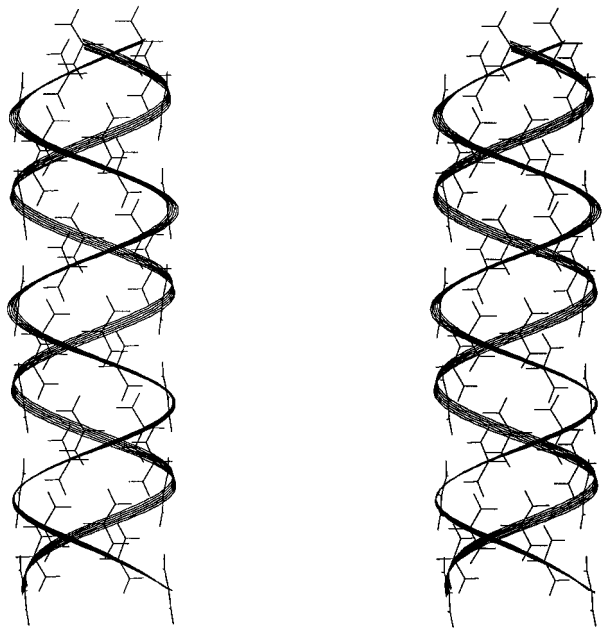

Figure 1. Stereodiagram showing the helix structure of one host channel of a UIC. (A stereoviewer is recommended.) The chiral ribbons, which are defined by the *anti* N−H- - -O hydrogen bonds, run antiparallel to each other along the *c* axis. These hexagonal channels are linked by their edges to form a solid-state honeycomb structure. Note that at each *z* coordinate, the two urea molecules from separate helixes are related by a *C*2 axis perpendicular to the channel axis. (Coordinates for this left-handed helical system were taken from ref 9.)

Formation of this tunnel structure requires the presence of guest molecules, which are typically straight-chain hydrocarbons and substituted analogues that pack within van der Waals contact of each other within a channel. Although UICs have served as prototypical inclusion compounds, they have been remarkably resistant to full structure solution by conventional X-ray crystallography.[10] In large part, the difficulty arises because these inclusion compounds are typically non-stoichiometric (incommensurate) solids in which the repeat distances of host and guest along the channel axis (c_h and c_g) do not satisfy the relation $n|c_h| = m|c_g|$ for reasonably small integers m and n. This problem is compounded by the dynamic nature of the guests, which typically undergo substantial motions, including translations and diffusive motions or jumps about the channel axis.[11]

Although they are tethered by hydrogen bonds with other host molecules, urea molecules are known to undergo rapid 180° flips about their 2-fold axes.[12] Our recent crystallographic work[5,13] has revealed that this dynamic process has a static counterpart in certain bis(methyl ketone)/UICs, in which urea molecules near

† Indiana University.
‡ University of California.
* To whom correspondence should be addressed.

(1) Etter, M. C. *Acc. Chem. Res.* **1990**, *23*, 120−6.
(2) Etter, M. C.; MacDonald, J. C.; Bernstein, J. *Acta Crystallogr., Sect. B: Struct. Sci.* **1990**, *B46*, 256−62. Bernstein, J.; Davis, R. E.; Shimoni, L.; Chang, N.-L. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1555−1573.
(3) Hollingsworth, M. D.; Brown, M. E.; Santarsiero, B. D.; Huffman, J. C.; Goss, C. R. *Chem. Mater.* **1994**, *6*, 1227−1244.
(4) Desiraju, G. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2311−2327.
(5) Brown, M. E.; Hollingsworth, M. D. *Nature (London)* **1995**, *376*, 323−327.
(6) Schlenk, W., Jr. *Justus Liebigs Ann. Chem.* **1973**, *7*, 1195−1209, 1156−1178, 1179−1194, 1145−55.
(7) For example, see: Hollingsworth, M. D.; Santarsiero, B. D.; Harris, K. D. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 649−652.
(8) Smith, A. E. *Acta Crystallogr.* **1952**, *5*, 224−235.
(9) Harris, K. D. M.; Thomas, J. M. *J. Chem. Soc., Faraday Trans.* **1990**, *86*, 2985−96.
(10) Takemoto, K.; Sonoda, N. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Eds.; Academic Press: London, 1984; Vol. 2, pp 47−67.
(11) Greenfield, M. S.; Vold, R. L.; Vold, R. R. *J. Chem. Phys.* **1985**, *83*, 1440−3. Greenfield, M. S.; Vold, R. L.; Vold, R. R. *Mol. Phys.* **1989**, *66*, 269−98. Harris, K. D. M. *J. Solid State Chem.* **1993**, *106*, 83−98.
(12) Heaton, N. J.; Vold, R. L.; Vold, R. R. *J. Am. Chem. Soc.* **1989**, *111*, 3211−17. Heaton, N. J.; Vold, R. L.; Vold, R. R. *J. Magn. Reson.* **1989**, *84*, 333−43. Bell, K. A.; Hoatson, G. L.; Vold, R. L. *J. Magn. Reson., Ser. A* **1994**, *108*, 238−243.
(13) Hollingsworth, M. D.; Brown, M. E.; Hillier, A. C.; Santarsiero, B. D.; Chaney, J. D. *Science*, in press.

S0897-4756(96)00264-5 CCC: $12.00

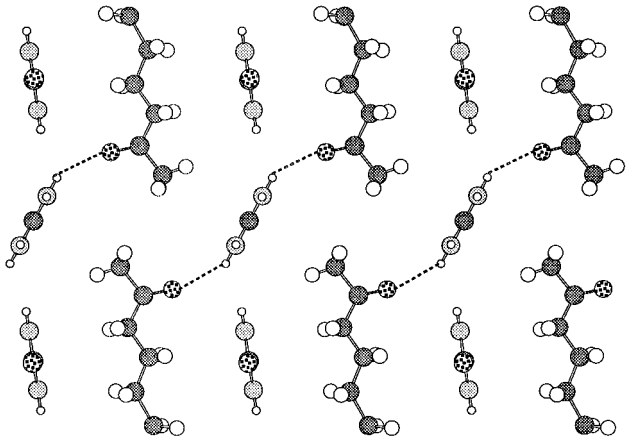

Figure 2. Cutaway view showing characteristic host−guest hydrogen bonding motif found in bis(methyl ketone)/UICs (channel axis (*c* axis) vertical). In this motif, urea molecules turn about their 2-fold axes by 30−40° to form hydrogen bonds with guest molecules with different *z* coordinates in adjacent channels.

Table 1. Commensurate Relations, Host−Guest Stoichiometries, and Infrared Spectral Data for Guest Carbonyl Groups in Bis(methyl ketone)/UICs

no. of carbons in guest	$n\,c_g' = m\,c_h'$ host−guest stoichiometry				guest C═O band	
	n	m	no. of guest mols	no. of host mols	$\bar{\nu}$ (cm^{-1})	fwhh (cm^{-1})[a]
8	6	7	1	7	1714	9
9	4	5	2	15	1723	15 ←
10	3	4	1	8	1717	9
11	2	3	1	9	1717	11
12	12	19	2	19	1723	15 ←
13	3	5	1	10	1716	11
14	6	11	1	11	1719	12
15[b]	12	23	2	23	1721	16 ←
16	1	2	1	12	1717	10

[a] Arrows on right denote superstructures requiring more than one hydrogen bonding environment for the guest. [b] The superstructure listed here is consistent with the observed repeat for the guest ($c_g' = 21.084(6)$ versus 21.1 Å predicted for 12 $c_g' = 23\ c_h'$), but the weakness of the diffraction pattern lends considerable uncertainty to this assignment.

the ends of the guest chains turn about their 2-fold axes to make hydrogen bonds with guest carbonyl groups in adjacent channels (Figure 2). In addition to the known structures of 2,10-undecanedione/urea (**1**)[5] and 2,9-decanedione/urea (**2**),[13] several other members of the same series exhibit prominent X-ray diffraction patterns for commensurate structures, as described in Table 1.[14] When these relations are compared with the frequencies and bandwidths in the IR spectra of guest carbonyl groups (Figure 3 and Table 1), it becomes clear that for host−guest systems in which one guest molecule is matched with an integral number of urea molecules (C_8, C_{10}, C_{11}, C_{13}, C_{14}, C_{16}), an ordered system containing host−guest hydrogen bonding is possible. With each of these systems, it is possible to fulfill the symmetry and stoichiometry requirements of the inclusion system with just one type of binding site for guest carbonyls. For other chain lengths (C_9, C_{12}, C_{15}), there is no simple match between the repeat of one guest and that of an integral number of urea molecules along the channel, so the C═O stretching bands of the guests are broadened and shifted to higher average frequencies relative to their counterparts in the more ordered systems (see arrows in Table 1). Although crystal structures are not available for the C_9, C_{12}, or C_{15} bis(methyl ketone)/UICs, the IR spectra and metric properties of these UICs suggest that there are two different host environments for these guest carbonyls, one with host−guest hydrogen bonding and one without it.

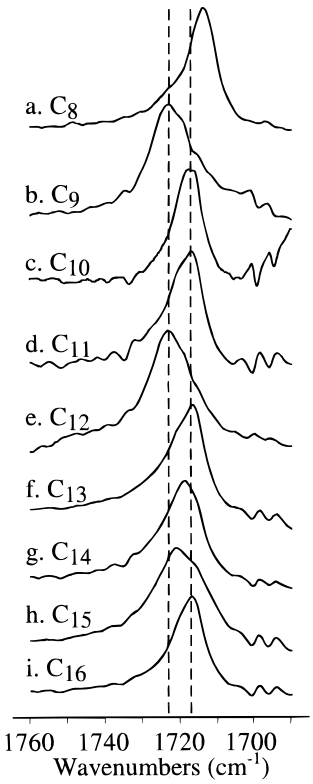

Figure 3. Infrared absorption spectra (2 cm^{-1} resolution, Nujol) of the C═O stretching region for guests in a series of bis(methyl ketone)/UICs. Each IR spectrum was obtained by subtracting a scaled absorbance spectrum of decane/urea from the spectrum of the bis(methyl ketone)/UIC. For superstructures requiring more than one host environment for the guest (C_9, C_{12}, C_{15}), the C═O stretching bands occur at higher frequency and have low frequency shoulders.

Although the length of one guest molecule matches the length of an integral number of host molecules in the C_8, C_{10}, C_{11}, C_{13}, C_{14}, C_{16} bismethyl ketone/UICs, generation of a crystallographically repeating unit requires the application of further symmetry operators, such as 2-fold, 3-fold, or 6-fold screw axes.[15] This is highlighted quite dramatically in the structure of 2,7-octanedione/urea (**3**), which is a commensurate structure with a long axis of 77 Å in which 6 $c_g' = 7\ c_h'$ (Figure 4).[16,17] In this structure, the guest repeat is exactly 7/6 the unit cell repeat of a normal UIC (11.0 Å). Each guest molecule repeat therefore coincides with the repeat of seven urea molecules in the host channel, so adjacent guest molecules within a given channel are rotated by 60° (about the channel axis) relative to each other. The space group for this 77 Å structure ($P6_122$)

(14) For chain lengths C_9 through C_{16} (Table 1), the progression of denominators in the host/guest ratios (1,2,1,1,2,1,1,2,1) arises from a near coincidence in the channel axis repeat of two urea molecules (3.67 Å) with that of three methylene groups in the guest (3.78 Å).

(15) For 2,15-hexadecanedione/urea (C_{16}), translation operations are sufficient to generate the crystal structure from the unit containing 12 hosts and one guest.

(16) For incommensurate UICs, the typical host repeat along the channel axis (c_h) of 11.0 Å comprises six urea molecules. With commensurate UICs, c_h may be some other value (e.g., 33.0 Å), so for these systems we use the terms c_g' and c_h' to denote the average molecular repeat distance for the guest and the 11.0 Å repeat for six urea molecules.

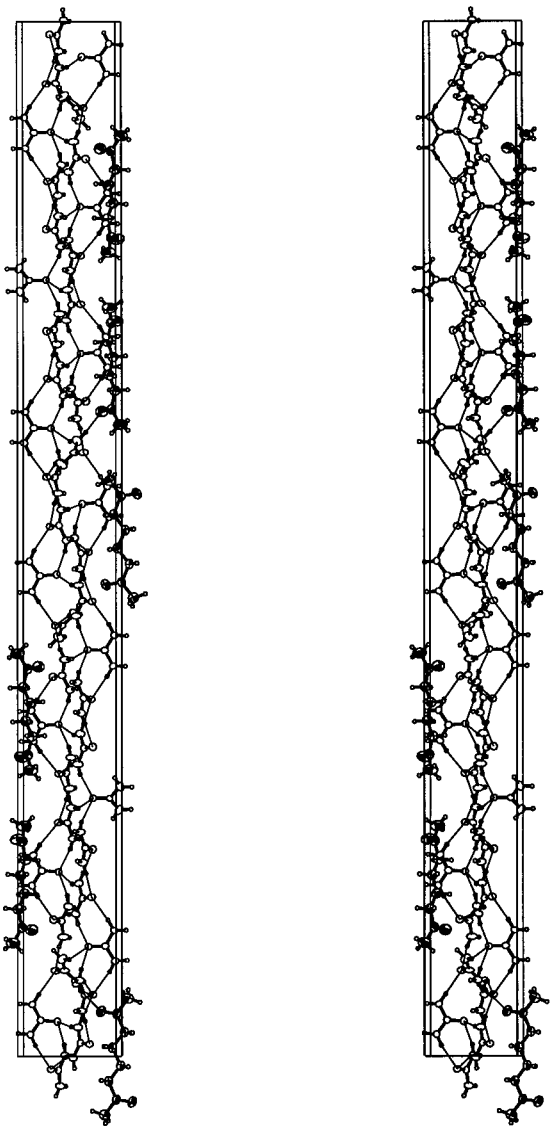

Figure 4. ORTEP stereodiagram showing one unit cell of 2,7-octanedione/urea (view down [100]). Distances (d, Å) and angles ($\angle$, deg) for these hydrogen bonds are as follows (H_s = *syn* hydrogen of urea): d(O- - -H_s) = 2.262(4) Å, d(N−H_s) = 0.90 Å, d(C−O) = 1.201(7), d(O- - -N) = 3.038(7) Å, $\angle$(O- - -H_s−N) = 144.1(2), $\angle$(C−O- - -H_s) = 144.3(3). The least-squares planes of the turned urea molecules lie 38.5° from the channel axis.

is the same as that for a normal 11 Å structure of the host in a typical UIC. In this case, however, the asymmetric unit of the crystal consists of 3.5 urea molecules and 0.5 guests. Application of the 2-fold axes gives seven ureas for each guest, then further application of the 6_1 screw axis generates the unit cell, which contains six guests and 42 urea molecules.

In 2,7-octanedione/urea, as in **1** and **2**, both of the guest C═O groups are hydrogen bonded to the urea molecules in the motif depicted in Figure 2. From the above discussion, one might expect that in other commensurate UICs, the guests would be constrained in the same way, so it would be useful to develop simple tools that can be used to predict the host−guest connectivities and hydrogen-bonding topologies of these structures. Because the positions of the urea molecules are relatively invariant from structure to structure, it is possible to concentrate on the metric and symmetry properties of the guest molecules to see how best the host and guest can fit together to form a commensurate structure. At issue is whether the extended form of the guest is too long or too short to match the commensurate repeat, whether the guest is an odd- or even-chain diketone and whether one or both of the helixes shown in Figure 1 are used to tether a given guest.

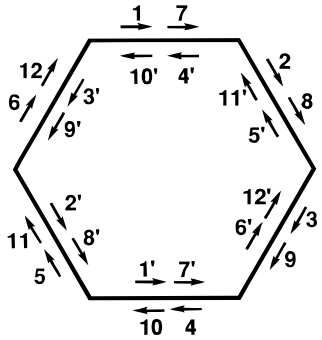

Figure 5. General helical wheel diagram representing two full turns of the helixes for a UIC containing right handed channels. Arrows show the C−O directions of the urea carbonyl groups. Note that urea molecules with the same z coordinates are related by $C2$ axes in the plane of the page. By convention, the lowest numbers for each helix (1,1′) represent the ureas closest to the viewer, and higher numbers represent ureas that are further down the channel. An analogous, left-handed wheel diagram can also be drawn for systems containing left-handed channels.

We have employed a simple construct akin to the helical wheel diagrams that biochemists use to display the amino acid sequences found in α helixes of proteins.[18] In the general helical wheel diagram shown in Figure 5, the two sets of numbers, N (helix 1) and N' (helix 2), denote the sequences of host molecules in the two urea helixes that make up a given channel. Much like DNA,[19] UICs are chiral objects in which the two intertwined helixes are of the same handedness and are related by a C2 axis perpendicular to the channel. Each urea in helix 1 has a counterpart directly across the channel (at the same z coordinate) in helix 2 (e.g., 1 and 1′, 2, and 2′). These two molecules are parallel to each other and are related by a $C2$ axis. As shown by the arrows, which denote the C−O directions of the urea carbonyl groups (and the projections of the N−H_s groups on the channel wall), helix 1 moves down the channel (1- - -2- - -3- - -4···) by leading with its carbonyl group, whereas helix 2 (1′- - -2′- - -3′- - -4′···) does the same by leading with its N−H_a bond. In the present example, the channel is composed of two right-handed helixes, but with achiral guests, the occurrence of the enantiomorphic (left handed) crystal form is equally probable.

For a variety of guest molecules, this helical wheel diagram provides a simple way of either predicting or rationalizing the topological features of the host−guest hydrogen-bonding scheme. As an example, 2,7-oc-

(17) $C_8H_{14}O_2$·$7CH_4N_2O$, mp 126−7 °C (dec), hexagonal, $P6_122$ (No. 178), $a = b = 8.211(4)$, $c = 76.91(5)$ Å, $V = 4490(3)$ Å^3, $D_{calc} = 1.25$ g cm^{-3}, $Z = 6$, (Mo Kα, graphite monochromator) $\lambda = 0.710\ 69$ Å, 16 115 reflections ($2\theta \leq 61°$) at 18 °C, (MSC R-AXIS IIC area detector) were averaged over 622 symmetry to give 3724 averaged observations ($R_{merge} = 0.069$), of which 1638 reflections with $I > 4\sigma(I)$ were used in the final cycles of refinement. Non-hydrogen atoms were refined with anisotropic Gaussian displacement parameters, whereas hydrogen atoms were constrained with a riding model to give a structure with $R_F = 0.068$, $R_{WF} = 0.049$, and GOF = 2.82.

(18) Schiffer, M.; Edmundson, A. B. *Biophys. J.* **1967**, *7*, 121−135.

(19) Watson, J. D.; Crick, F. H. C. *Nature* **1953**, *171*, 737−738; Franklin, R. E.; Gosling, R. G. *Nature* **1953**, *171*, 740−741. See also: Crick, F. H. C. *Acta Crystallogr.* **1953**, *6*, 689−697.

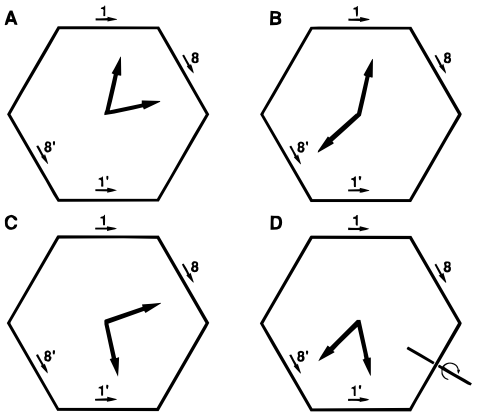

Figure 6. Right-handed helical wheel diagram showing four possible arrangements for host−guest hydrogen bonding in 2,7-octanedione/urea. The *C*2 axis shared by A and D is shown in D. Long arrows in the center of each diagram denote the orientations of the two carbonyls in one guest molecule. This simple model correctly predicts topology B.

tanedione/urea (**3**) is considered here. The urea:guest stoichiometry of this inclusion compound is 7:1, so the hydrogen-bonding motif depicted in Figure 2 requires that the two C═O groups of a given guest molecule are tethered to urea molecules at positions 1 (1′) and 8 (8′) in the channel.[20] Using Figure 5 as a guide, it is first necessary to write down the wheel diagrams that represent the four possible combinations of host−guest connectivities (1- -8, 1- -8′, 1′- -8, 1′- -8′; see Figure 6). (For chiral guests, an enantiomorphic set of diagrams is also required.) In Figure 6A, for example, the carbonyls of the guest (represented by large arrows) form hydrogen bonds with the $N-H_s$ groups of ureas 1 and 8 from the same helix. In other topologies, the guest can form hydrogen bonds to ureas in different helixes (Figure 6B,C). Because they are related by a *C*2 axis (noted in Figure 6D), the topologies represented in Figure 6A and D are isoenergetic.

The diagrams shown in Figure 6 represent the three possible O═C···C═O torsion angles that the guest must adopt to form a commensurate structure containing a periodic hydrogen-bonded network with urea.[21] To choose among the different topologies, it is necessary only to compare the "natural" length of the guest (in its extended form) with the repeat distance that is required for a commensurate relation with the host structure. Such idealized lengths are available either from molecular mechanics or from X-ray diffraction studies of similar inclusion compounds[13] and in particular from the exhaustive studies of Lenné,[22] who measured repeat lengths for 32 classes of guests in UICs. Because the molecular lengths of alkanes, alkanones, and alkanediones are almost identical,[13] Lenné's repeat for octane in urea (12.40 Å) and his extrapolated value for *n*-octanones (12.39 Å) allow us to predict that the extended form of 2,7-octanedione is shorter than the commensurate repeat of ∼12.85 Å (1.836 Å/urea × 7 urea molecules)[9] required for this structure. Thus, for this even-chain diketone, diagram 6B gives the most reasonable structure because it maximizes the O−C···C−O torsion angle for the two carbonyls in the guest. This pattern, which is observed in the crystal structure of **3** (Figure 7), tethers the guest to two different urea helixes.

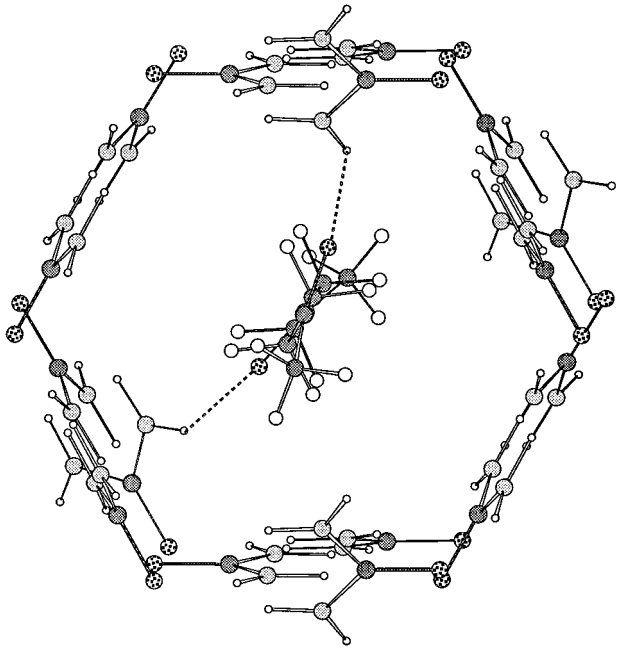

Figure 7. Channel axis view of **3** showing a single guest molecule hydrogen bonded to urea molecules in two different helixes (ureas 1 and 8′ in Figure 6B). The O═C···C═O torsion angle for the guest is 160.0°.

This simple model has allowed us to correctly predict the topological features of a number of UICs containing bis(methyl ketone)s and bis(acetate ester)s, including several systems exhibiting ferroelasticity, which should be intimately related to the topological features of the hydrogen bonded network.[5,23] In a few cases, the difference in O═C···C═O torsion angles for the most likely topologies is so small (104° vs 120° for 2,9-decanedione/urea)[13,24] that it is impossible to choose between the models without resort to calculations.[25] For such large systems containing cooperative hydrogen-bonded arrays, reliable calculations are quite difficult, so this method provides a viable alternative for predicting the qualitative features of the structures.

Acknowledgment. We thank the NSF (CHE-9423726), the donors of the Petroleum Research Fund, administered by the American Chemical Society (24396-AC4 and 29932-AC4), for financial support.

Supporting Information Available: Sample preparation and characterization, X-ray data collection and structure solution procedures, AGDPs, bond distances and angles, selected least squares planes and plots (17 pages) and tables of observed and calculated structure factors (17 pages) for 2,7-octanedione/urea. See any current masthead page for ordering information.

CM960264D

(20) Each end of the guest is tethered to half a urea molecule (as in Figure 2), so the first and the eighth ureas are used, not the first and the seventh. It follows that for a UIC with 8:1 host:guest stoichiometry (e.g., 2,9-decanedione/urea), the guest will be tethered to the first and the ninth ureas, and so on.

(21) Because the first and eighth urea positions are spatially separated, they may be treated as independent. As a consequence, this problem can be reduced to one concerning intratunnel interactions alone. Thus, for guests of sufficient length, each of the four topologies generates a periodic three-dimensional structure by application of appropriate symmetry operators. For extremely short guest molecules, interactions between tethered urea molecules must also be considered.

(22) Lenné, H. U.; Mez, H. C.; Schlenk, W., Jr. *Justus Liebigs Ann. Chem.* **1970**, *732*, 70−96.

(23) Brown, M. E.; Chaney, J. D.; Still, E. J.; Hollingsworth, M. D., manuscript in preparation.

(24) Because the natural length of 2,9-decanedione is significantly longer than the required commensurate repeat,[13] one must choose between coiled configurations with similar torsion angles. If the guest is shorter than the commensurate repeat, the topology that most closely matches the extended form of the guest is chosen.

(25) These models can obviously serve as starting points for calculations.