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Role of Hydrogen Bonding in Determining the Crystal Structures of the Adducts between Acetone and Urea Derivatives[†]

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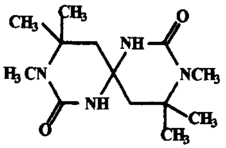
The adducts obtained by the reaction between three molecules of acetone and two molecules of urea or 1-methylurea form different hydrogen bonding patterns in the solid. The patterns are determined by the number of proton donors and proton acceptors available for the hydrogen bond formation. The adduct between acetone and urea crystallizes with different solvent molecules. When crystallized from water, it forms a three-dimensional network, where the water molecules are arranged in an infinite sheet made up of hydrogen bonded four-, six-, and eight-membered rings that link layers of the organic compound by hydrogen bonds. When crystallized from dimethyl sulfoxide (DMSO) both water and DMSO molecules participate in an infinite two-dimensional hydrogen bonding network.

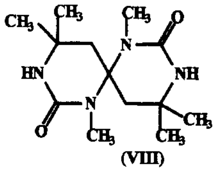
Introduction

Hydrogen bonds are the second to covalent bonds in their importance. The existence of stable molecules depends on the strength of the covalent bonds between atoms. Hydrogen bonds play a similar role in determining the stability and the existence of an assembly of molecules. The understanding of the relative strength of hydrogen bonds and their role in determining the structure of these assemblies is of great importance in planning "syntheses" of assemblies of molecules that are needed as advanced materials. The interest in the compounds discussed in this paper started because of their high melting points, and continued because of their structures that provided beautiful examples of the role of hydrogen bonds in determining their structures in the solid.

The reaction between acetone (I) and urea (II) is a special case in the chemistry of urea, because it has been examined several times in the past and different structures (III–VI) having the same chemical analysis have been proposed for the reaction product. Weinschenk[1] in 1901, suggested the structure of III, while Harvey[2] proposed IV. On the basis of spectral data, Hatt and Triffett[3] in 1965 and later Zigeuner et al.[4] in 1966 proposed the structure of hydropyrimidine V. At the same time Inoi et al.[5] proposed the structure shown in VI. Butler et al.[6] in 1980 have repeated the reaction between acetone and urea and confirmed its molecular formula. On the basis of ^{1}H NMR spectroscopy it was concluded that V is the correct structure. Under similar experimental conditions the analogous product from the reaction between acetone and 1-methylurea was prepared and the analogous structure proposed (VII). Butler and co-workers have pointed out that the ^{1}H and ^{13}C NMR spectra can be rationalized by two different structures, VII and VIII. The two structures differ by the positions of the methyl groups and could not be unambiguously distinguished. On the basis of the proposed mechanism of the reaction between urea and acetone and on the assumption that NMe is the more nucleophilic part of the molecule, the structure of VII was proposed as the correct one. However, the structure of the reaction product of a similar system, between 1-methylurea and mesityl oxide, was not found to be the one proposed[6] based on the same mechanism. A revised mechanism was suggested by Kaftory et al.[7] Since the difference between the proposed structure and the correct one was determined by the relative positions of the NMe groups and since there were four possible structures, it prompted us to determine the crystal structures of the products of the reactions between acetone and urea or 1-methylurea. The crystal structures of three compounds will be described here, emphasizing the special packing imposed by the presence of solvent molecules such as water and dimethyl sulfoxide (DMSO).



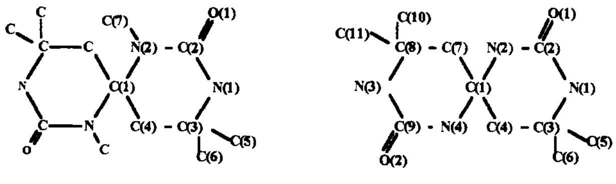
(VII)



(VIII)

Results and Discussions

Crystal Structure Comments. For ACMU (the adduct between acetone and 1-methylurea), the 2-fold axis of the molecule (running through C(1), see notation given in IX) coincides with the crystallographic 2-fold axis. The



ACMU

ACURW (or ACURD)

(IX)

[†] Dedicated to the memory of Professor Margaret Etter.

[⊗] Abstract published in *Advance ACS Abstracts,* August 15, 1994.

(1) Weinschenk, A. *Ber.* **1901,** *34,* 2185.

(2) Harvey, M. T. U.S. Patent 2592565.

(3) Hatt, H. H.; Trifett, A. C. K. *Chem. Commun.* **1965,** 439.

(4) Zigeuner, G.; Fuchs, E.; Brunnetti, H.; Sterk, H. *Monatsh* **1966,** *97,* 36.

(5) Inoi, T.; Okamoto, T.; Koizumi, Y. *J. Org. Chem.* **1966,** *31,* 2700.

(6) Butler, A. R.; Hussain, I. *J. Chem. Soc., Perkin Trans. 2* **1980,** 232.

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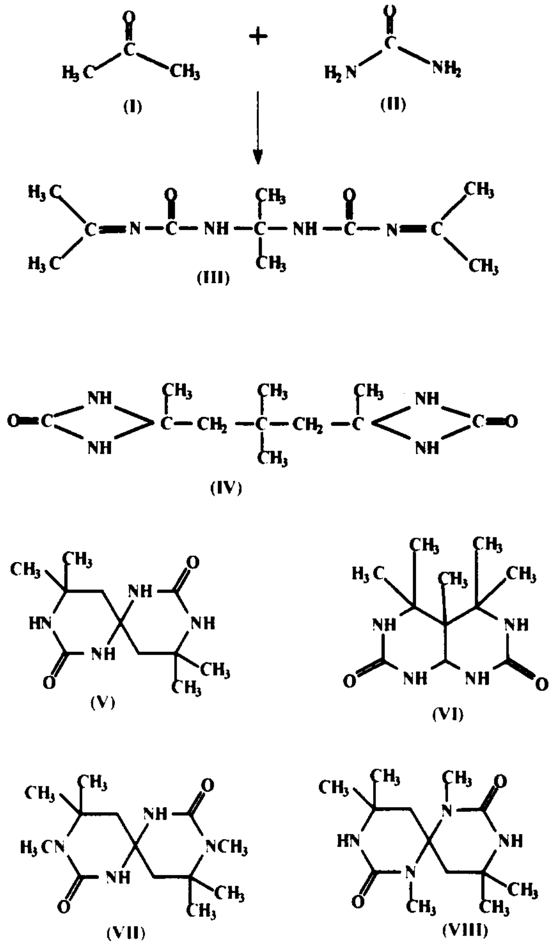
Scheme 1

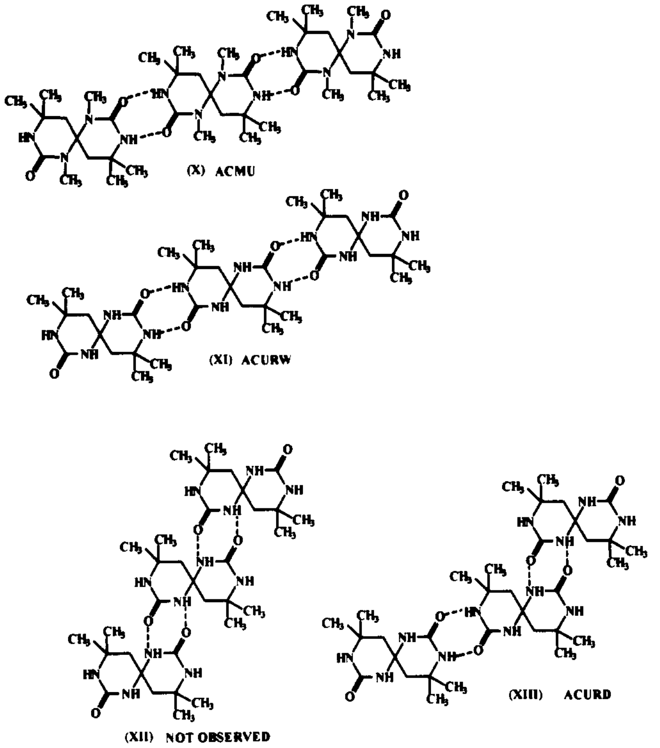


molecules are arranged in arrays and held by hydrogen bonds between amide groups related by inversion centers. This arrangement indicates that all carbonyl oxygen atoms and all the NH groups are occupied in hydrogen bonding. The packing of the molecules is shown in Figure 1.

For ACURD, the adduct between acetone and urea crystallizes with one molecule of water and one molecule of DMSO when left in DMSO for a long period of time. It was found that the DMSO molecule is disordered so that the sulfur atom occupies two positions, of equal weight. Description and discussion of the hydrogen bonding scheme is given below. The molecular packing is shown in Figure 2. The two parts of the molecule (joined through the spiro C(1) atom) adopt the same conformation, but they are related by a mirror plane and not by a 2-fold rotation axis.

For ACURW, the adduct between acetone and urea can be crystallized with three molecules of water either from water or from a DMSO solution that contains traces of water. The transparent crystals are unstable and turn opaque within an hour. A crystal was therefore placed in a capillary and the intensity data were collected at low temperature (200 K). There are two molecules in the asymmetric unit which adopt the same conformation (as also found in ACMU) and both have a pseudo-2-fold rotation symmetry through C(1). Since the packing of the molecules is very complicated, we prefer to explain it first and then to draw it by parts. (see Figures 3–5).

Chart 1



Hydrogen-Bonding Patterns. The packing of the molecules in the unit cell and the content of solvent molecules are determined by the hydrogen-bonding patterns. The ability to form these patterns is determined by the presence of acceptor and donor groups of protons. The two adducts are very rigid (spiro shape), and consist of two perpendicular six-membered rings that are flattened as in lactam systems. This molecular shape provides sites for three-dimensional hydrogen bonding patterns which will be shown and discussed below.

The complexity of a hydrogen-bond pattern within a crystal structure is dependent on the number of unique hydrogen-bond donors and acceptors. In the adduct formed between acetone and 1-methylurea, there are only two proton donor (NH) and two proton acceptor groups (C=O). In the adduct molecules between acetone and urea, there are four proton donor (NH) and two proton acceptor groups (C=O). Moreover, since molecular and crystallographic symmetry coincide in the ACMU adduct, the number of unique hydrogen-bond donors and acceptors is reduced by one half. Therefore, the possibility for the formation of hydrogen bonding patterns is expected to be more complex in the later than in the first.

In all three structures, the skeleton of the hydrogen bonding pattern is made up by infinite strips consisting of molecules adopting the ideal alignment for close hydrogen bonded dimer.[8] In ACMU, there is only one way for the molecules to be packed so that the requirement for a close hydrogen bonded dimer will be met. Two molecules that are related by inversion center are hydrogen bonded with NH···O distance of 2.164 Å and N–H···O bond angle of 161.3° (see X, Chart 1). In ACURD and ACURW an additional proton donor (NH) in each six-membered ring, is available for the formation of hydrogen-bonded

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(7) Kaftory, M.; Butler, A. R.; Hussain, I. *J. Chem. Res.* **1981**, (S) 183, (M) 2401.

(8) (a) Leiserowitz, L.; Schmidt, G. M. J. *J. Chem. Soc. A*, **1969**, 2372. (b) Leiserowitz, L.; Tuval, M. *Acta Crystallogr.* **1978**, *B34*, 1230. (c) Berkovitch-Yellin, Z.; Leiserowitz, L. *J. Am. Chem. Soc.* **1980**, *102*, 7677.

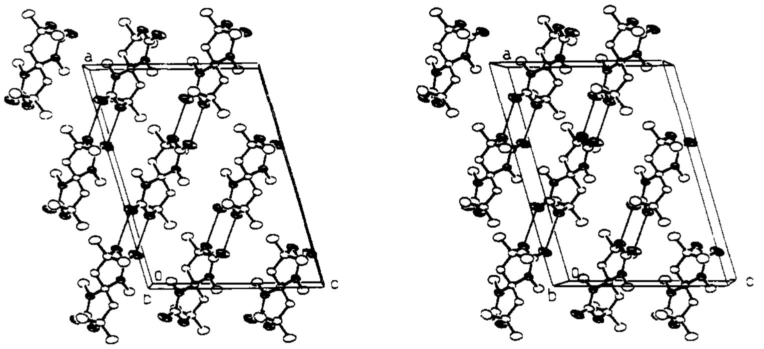


Figure 1. Stereoscopic drawing of ACMU (clear ellipses, C atoms; enveloping ellipses with principal axes, O atoms; enveloping ellipses with principal axes and octant shading, N atoms.

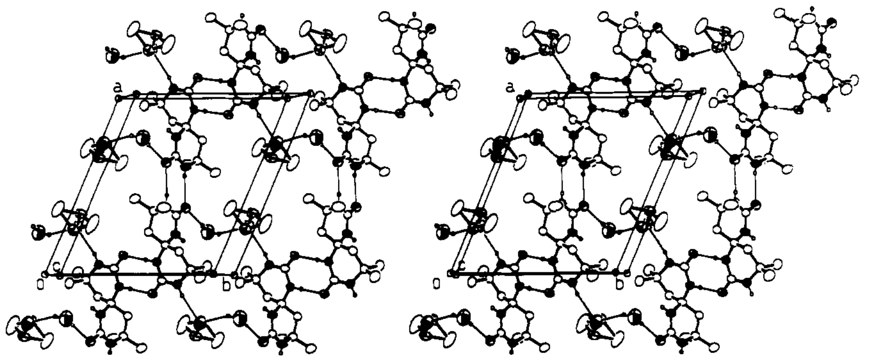


Figure 2. Stereoscopic drawing of ACURD (clear ellipses, C atoms; enveloping ellipses with principal axes, S atoms; enveloping ellipses with principal axes and octant shading, O atoms; ellipses with principal axes, N atoms.

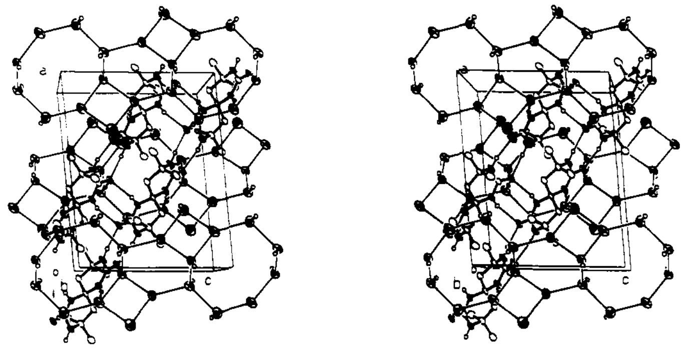
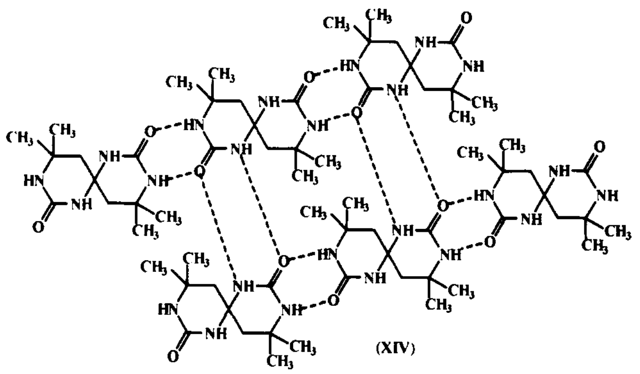


Figure 3. Stereoscopic drawing of ACURW (clear ellipses, C atoms; enveloping ellipses with principal axes, N atoms; enveloping ellipses with principal axes and octant shading, O atoms.

dimers. The three possible infinite hydrogen-bond patterns of these adducts are shown in XI–XIII). The first one (XI) was found in the structure of ACURW, between molecules related by *n*-glide plane symmetry (NH···O distances are 1.987, 1.983 Å and 1.954, 2.014 Å in each of the dimers). The second pattern (XII) was not observed, and the third pattern (XIII) was found in ACURD where inversion center symmetry was found in each of the two different hydrogen bonded dimers (N–H···O distances of 2.009 and 2.284 Å).

All proton acceptors and proton donors in ACMU (X) are participants in the infinite hydrogen-bond pattern discussed above. Therefore, the three-dimensional structure consists of infinite chains held together by weaker intermolecular interactions. The infinite chains shown in XI and XIII, however, have unused proton donors that can be used to link neighboring chains. In ACURW (shown schematically in XIV and stereoscopically in Figure 3), the additional proton donor (NH) is used in an hydrogen bond which links neighboring chains. This link occurs in dimers of hydrogen bonds (between two crystallographic non equivalent molecules) between the NH groups and the second lone-pair electrons of a carbonyl oxygen (NH···O distances are 2.171 and 2.201 Å, N–H···O bond angles are 141.5° and 154.2°). The links between chains in ACURW are available because they are running in parallel and therefore close contacts are possible. Since there are two different types of hydrogen bonds it forms a zigzag chain (see XIII) rather then a straight line chain. Therefore



(XIV)

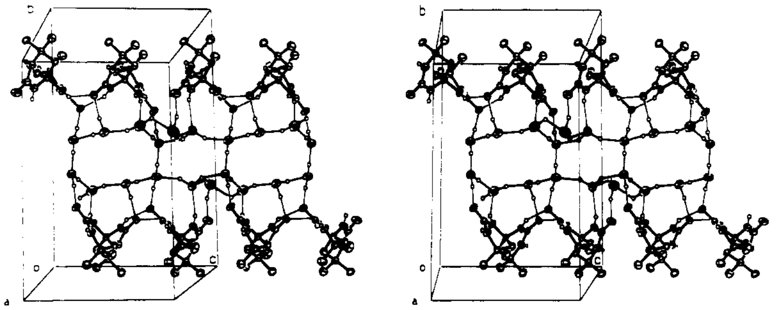


Figure 4. Stereoscopic drawing of ACURW showing the hydrogen bonding between the organic moiety and the sheet of water molecules (clear ellipses, C atoms; enveloping ellipses with principal axes, N atoms; enveloping ellipses with principal axes and octant shading, O atoms.

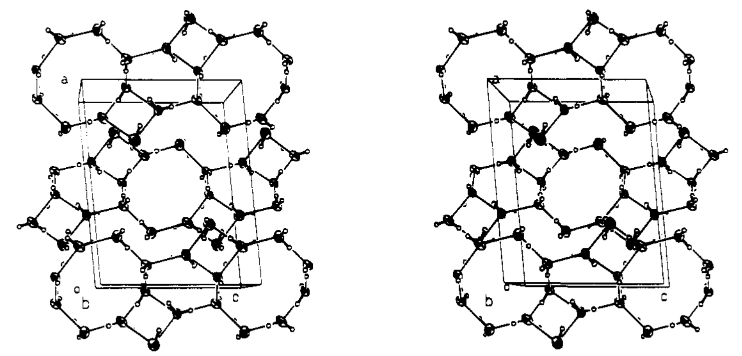
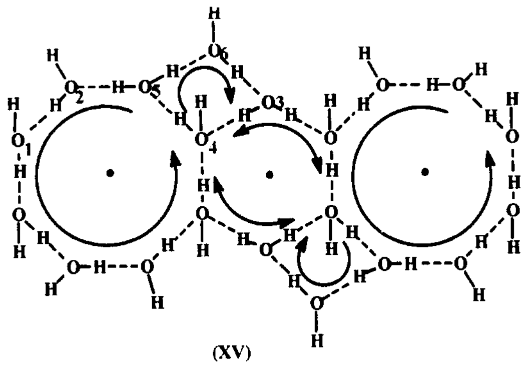


Figure 5. Stereoscopic drawing of sheets of hydrogen-bonded water molecules in ACURW.

one of the NH groups is right next to two geminal methyl groups and therefore is sterically blocked (see Figure 2). The links between strips are formed by water and DMSO molecules (see Figure 2). The NH group is hydrogen bonded to the oxygen atom of a DMSO molecule. The DMSO molecule hydrogen bonded to a water molecule which is hydrogen bonded to a carbonyl oxygen atom. Thus, in ACURD, an infinite two-dimensional pattern is formed. In ACURW, a three-dimensional pattern is formed by the molecules. The two-dimensional parallel ribbons made up by the adduct between acetone and urea are surrounded by infinite two-dimensional sheets of hydrogen bonded water molecules. It is interesting to note that all of the hydrophilic groups are pointing toward the water sheet, while all the hydrophobic groups (mainly methyls) are pointing away from it (see Figures 3 and 4). The sheet is made up of water molecules forming, by hydrogen bonds, four-, six-, and eight-membered rings sharing edges with each other as shown in XV. The six- and the eight-membered rings occupy crystallographic inversion centers. The hydrogen atoms were located from a difference Fourier map and each of them is involved in building up the hydrogen bonding pattern. There are three "circular" hydrogen bond patterns[9] involving the water molecules, the four- and the eight-membered ring patterns are *homodromic*, the six-membered ring pattern is *antidromic* (see XV and Figure 5.). This sheet forms hydrogen bonds with the organic matrix. Harlow[11] observed a similar arrangement in the crystal structure of RGD peptide. These water molecules form an "ordered" array containing four-, five-, and seven-membered rings in channels formed by the peptide molecules. The arrangement was stable at low temperatures (below 0 °C), but above 0 °C, the crystal undergoes a phase transition which involves "melting" of water. Bertagnolli[10] suggested that the structure of water may consist of a mixture of cubes and planar four-membered rings.



(XV)

Hydrogen-Bond Geometry. It is interesting to compare the geometry of the hydrogen bonds among the various patterns. The N–H···O bond tends to be linear, as pointed out by Leiserowitz and Tuval,[8a,b] with an angle range between 141.5 and 179.5°. Some of the oxygen atoms are involved in either one or two hydrogen bonds. However there are no remarkable differences between the C═O··H(N) bond angles. They range between 108.8 and 122.9°, where the smallest value (108.8°) and the largest value (122.9°) were observed in ACURW on the same oxygen atom that is involved in a very strained hydrogen bond between the two strips. The NH···O═(C) bond lengths range between 1.98 and 2.28 Å (the range of the N···O nonbonded distances is between 2.831 and 3.005 Å, which is within the range found for primary and secondary amides[8a,b]). The sulfoxide oxygen forms weaker hydrogen bond with NH group (S═O···HN distance being 2.31 Å) than with the water molecule (S═O···HOH distance being

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(9) (a) Saenger, W. *Nature (London)* **1979**, *279*, 343. (b) Saenger, W.; Lindner, K. *Angew. Chem.* **1980**, *92*, 404. (c) Chacko, K. K.; Saenger, W. *J. Am. Chem. Soc.* **1981**, *103*, 1713.

(10) Bertagnolli, H. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1577.

(11) Harlow, R. XVI Congress and General Assembly, International Union of Crystallography, Beijing, China, p 142, and private communication.

2.09 Å). The hydrogen bonding of the organic sheet to the water sheet provides data for comparison of the strength of the hydrogen bonding of water molecule to a carbonyl group, water molecule to an urea NH group and between water molecules. The first is the strongest, with a range of C=O···H distances between 1.67 and 1.74 Å (the corresponding O···O distances are 2.741–2.803 Å). The next strongest is of the hydrogen bond between water molecules, with a range of H···O distances between 1.73 and 1.87 Å (O···O distances between 2.79 and 2.89 Å). The weaker one is between water molecules and the NH group, with the two NH···O distances of 2.21 and 2.26 Å (N···O distances 3.008 and 3.075 Å).

Graph Sets. Margaret C. Etter together with others[12] in a series of papers suggested a systematic use of graph-sets assignments to define the morphology of hydrogen-bonded arrays. The three structures presented here are examples of increasing complexity of assigning graph sets to their hydrogen-bonding networks.

ACMU: There is only one type of hydrogen bond (the second one is symmetry related), and the whole pattern is made up of a chain of rings. The first-order network is $N_1 = C(8)[R_2^2(8)]$.

ACURW: This pattern is very complicated, and therefore we ignore the bonding between the organic moiety and the water molecules. Although the hydrogen patterns of chain of rings is similar to that described above, it is different in many aspects. Here, there are two different chains of rings (made up of the two different molecules (A and B) in the asymmetric unit. Also, within a ring there are two different hydrogen bonds (they are not related by symmetry), and in each molecule there are four donors and two acceptors. Each of the molecules form a first-order network that can be written as $N_1 = C(8)C(8)$. In each there is also a ring and therefore $N_2 = R_2^2(8)$. The combination of the two different molecules should therefore be $N_1 = C(8)C(8)C(8)C(8)$ (unitary) and $N_2 = R_2^2(8)$-$R_2^2(8)$ (binary). The two infinite chains are connected to each other by two different hydrogen bonds and at the unitary level they should be assigned DD, at the binary level it is $R_2^2(8)$.

ACURD: Here there are two different N–H···O hydrogen bonds; each one forms a dimer through inversion center. In the unitary level the network is $N_1 = R_2^2(8)R_2^2(8)$, and in the binary level the network is $C_2^2(14)[2R_2^2(8)]$. The solvent molecules add three additional hydrogen bonds (three additional motifs) in the unitary graph set, these will be designated (1) N—H···O=S:D; (2) O(H_2O)—H···O=S:D; (3) O(H_2O)—H···O=C:D. The binary graphs set of these (1)–(2) is $D_2^2(3)$ and (2)–(3) is $D_2^2(5)$.

Experimental Section

The adducts between acetone and urea or 1-methylurea were prepared by Butler and Hussain[6] and recrystallized from water or from DMSO.

4,4′-Spirobi-3,6,6-trimethyl-3,4,5,6-trihydropyridin-2(1H)-one (ACMU), $C_{13}H_{24}N_4O_2$, $M_r = 268.36$, mp 328 °C, space group $C2/c$, $a = 16.103(9)$, $b = 7.894(4)$, $c = 12.055(6)$ Å, $\beta = 105.51(2)°$, $U = 1476.6$ Å^3, $Z = 4$, $D_x = 1.206$ g cm^{-3}, Cu Kα, $\lambda = 1.5418$ Å. $R = 0.072$ for 1183 observed reflexions [$F_o > 0.0$] out of 1203 measured reflections ($R_w = 0.095$).

4,4′-Spirobi-6,6-dimethyl-3,4,5,6-trihydropyridin-2(1H)-one dimethyl sulfoxide monohydrate (ACURD), $C_{11}H_{20}N_4O_2{\cdot}H_2O$, C_2H_6SO, $M_r = 336.44$, mp 265 °C, space group $P\bar{1}$, $a = 13.500(7)$, $b = 11.889(6)$, $c = 6.217(3)$ Å, $\alpha = 104.89(3)$, $\beta = 95.91(3)$, $\gamma = 67.07(3)°$, $U = 888.1$ Å^3, $Z = 2$, $D_x = 1.259$ g cm^{-3}, Mo Kα, $\lambda = 0.710\,69$ Å. $R = 0.058$ for 2204 observed reflexions [$F_o > 3\sigma(F_o)$] out of 3029 measured reflections ($R_w = 0.063$).

4,4′-Spirobi-6,6-dimethyl-3,4,5,6-trihydropyridin-2(1H)-one trihydrate (ACURW), $C_{11}H_{20}N_4O_2{\cdot}3H_2O$, $M_r = 294.36$, mp 265 °C, space group $P2_1/n$, $a = 14.621(7)$, $b = 18.703(9)$, $c = 11.350(6)$ Å, $\beta = 95.51(2)°$, $U = 3089.4$ Å^3, $Z = 8$, $D_x = 1.266$ g cm^{-3}, Mo Kα, $\lambda = 0.710\,69$ Å. $R = 0.066$ for 3507 observed reflections [$F_o > 3.0\sigma(F_o)$] out of 5255 measured reflexions at 200 K ($R_w = 0.058$).

The intensity data were measured by a Philips PW 1100 computer-controlled four-circle diffractometer with graphite-monochromated radiation. Lattice parameters were calculated using 25 reflections for each compound. Three standard reflections (for each) were monitored during the data collections and did not show variations greater than 3%. Absorption corrections were not applied. The structures of ACMU and ACURW were solved by MULTAN 77[13] and ACURD with SHELX76.[14] The structures were refined by SHELX76,[14] with anisotropic thermal parameters for the non-hydrogen atoms and isotropic for the H atoms.

Supplementary Material Available: Tables of fractional coordinates, atomic displacement parameters, bond lengths and bond angles, and drawings showing the hydrogen bonds geometry (12 pages); tables of observed and calculated structure factors (40 pages). Ordering information is given on any current masthead page.

Acknowledgment. We would like to express our thanks to Professor A. R. Butler for providing samples of the adducts and to Professor J. Bernstein for his help in assigning the graph sets. The research was partially supported by "The center for Absorption in Science, Ministry of Immigrant Absorption, State of Israel".

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[12] (a) Etter, M. C. *Acc. Chem. Res.* **1990**, *23*, 120. (b) Etter, M. C.; MacDonald, J. C.; Bernstein, J. *Acta Crystallogr.* **1990**, *B46*, 256. (c) Etter, M. *J. Phys. Chem.* **1991**, *95*, 4601.

[13] Main, P.; Woolfson, M. M.; Lessinger, G.; Germain, G.; Declercq, J. P. "Multan 77, a System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data", 1977, University of York and Louvain.

[14] Sheldrick, G. M. SHELX, "Program for crystal Structure Determination", University of Cambridge, 1976.