Table III. GC/MS-CI Identification of Oxidation Products

compd	MW	m/z^a
1a	267	128, 268, 114, 252
1e	168	169, 141, 197, 209
1f	166	167, 139, 195, 123
1b	124	125, 97, 153, 165
1k	230	231, 259, 127, 203
1m	96	97, 111, 125, 137
2a	161	162, 128, 114, 89
2b	320	321, 160, 114, 128, 193
2f	110	111, 139
2g	209	210, 238, 250
3b	117	102, 116, 118
3e	131	132, 116, 72, 100, 263
4b	290	291, 331
4c	157	158, 141, 198
4d	151	152, 122, 180, 192

[a] In decreasing intensities.

sample of *N*-isopropylhydroxylamine oxalate (**3d**; Fluka Chemical, >98% pure) was dissolved in a 50 vol % *tert*-butyl alcohol solution, and the ^{13}C NMR spectrum was run to obtain reference chemical shift values (see Table IIB). An equal molar amount of *m*-CPBA was added to the solution. The nitrogen was oxidized immediately to the hydroxylamine *N*-oxide (**3f**). Consistent with the previous results, this caused the α carbon to shift downfield ca. 10 ppm (see Table IIB). Decomposition of **3f** occurred almost immediately; after a few hours, only $(CH_3)_2CH$-N=O (^{13}C NMR: δ 18.0 and 60.3) and $(CH_3)_2C$=NOH (^{13}C NMR: δ 15.0, 21.3, and 157.1) were observed in solution.

C. Procedure for Kinetic Studies by ^{31}P NMR. A weighed amount of the substrate (**1a**, **1e**, or **1h**) was placed into a new 5-mm-o.d. Pyrex NMR tube. The appropriate amount of oxidant was weighed into a separate glass vial and dissolved in the appropriate solvent. An aliquot of the oxidizing solution was then pipeted into the NMR tube; the tube was quickly capped, wrapped with Parafilm, and shaken to ensure complete mixing of the reactants. The NMR tube was placed in the spectrometer, and spectra were recorded periodically. The substrate concentrations were typically 0.01-0.05 M. The estimated error in the rate determinations is ±3-5%.

D. Procedure for the Rate Determination in Dilute Solutions by ^1H NMR. Observed first-order rates were determined for VX and **1e** in the presence of excess Oxone (0.1 or 0.17 M [O]) in D_2O by ^1H NMR. The substrate concentration was 0.0005 M, and the spectrum was recorded periodically using the VXR-400S FT NMR at 18.5 °C. The sweep width was narrowed to 1.6 ppm to observe only the methyl region. Sixty-four transients were accumulated for each spectrum by using a 90° pulse width and a repetition rate of 3.74 s. The progress of the reaction was monitored by following the disappearance of the CH_3P doublet of the reactant and the appearance of the CH_3P resonances from the phosphonic acid product **1b**. The resonances were expanded and digitally integrated to obtain the peak areas.

3. Gas Chromatography/Mass Spectrometry Identification. Gas chromatography/mass spectrometry (GC/MS) and direct exposure probe (DEP) mass spectrometry were used to assist and confirm the NMR identification of the oxidation products. Spectra were obtained on a Finnigan Model 5100 GC/MS in the chemical ionization mode. Methane (0.6 Torr internal source pressure) was used as the reagent gas. The source temperature was 100 °C. Both phosphonic and sulfonic acids and other ionic products could be detected with the DEP, which was ramped from 0 to 1 A at 200 mA/s. The identification of volatile organic products was made by extracting these products from the aqueous reaction mixtures into methylene chloride and characterizing the extract by GC/MS.

The instrument was equipped with a 25 m × 0.25 mm i.d. fused-silica GB-1 capillary column (Foxboro/Analabs, North Haven, CT). The injection port temperature was 210 °C, and the oven was programmed from 60 to 270 °C at 10 °C/min. A 0.01-μL aliquot of sample was injected with a split ratio of 50:1. The mass range was scanned from 60 to 450 amu at a rate of 1 scan/s. Spectral assignments were obtained by comparison to reference spectra in an existing in-house library and on the basis of characteristic fragmentation patterns. The CI mass spectra of the major products are listed in Table III.

Acknowledgment. We are grateful to Prof. Clifford A. Bunton of the University of California at Santa Barbara for helpful discussions and for recommending Oxone to detoxify VX; to Mr. Leonard J. Szafraniec of CRDEC for the syntheses **1e**, **1h**, and **3c**; and to Dr. Franklin A. Davis of Drexel University for a sample of **4a**.

An Approach to the Design of Molecular Solids. The Ureylenedicarboxylic Acids

Xinqi Zhao, Yuh-Loo Chang, Frank W. Fowler,* and Joseph W. Lauher*

Contribution from the Department of Chemistry, State University of New York at Stony Brook, Stony Brook, New York, 11794. *Received October 26, 1989. Revised Manuscript Received May 11, 1990*

Abstract: The crystal structures of a series of ureylenedicarboxylic acids have been determined as part of a project directed toward the design of molecular solids. The ureylenedicarboxylic acids were chosen for study because they were predicted to form a two-dimensional hydrogen-bonded network. This two-dimensional network is the result of two orthogonal linear arrays of self-complementary hydrogen-bonded functionalities, the dicarboxylic acids and N,N'-disubstituted ureas, being present in the same molecule. The simplest molecules of the series, 2,2'-ureylenediacetic acid (**1**), 3,3'-ureylenedipropionic acid (**2**), and 4,4'-ureylenedibutyric acid (**3**) as well as the simplest ureylene derived from a dipeptide, *N,N'*-carbonylbisglycylglycine (**4**) were synthesized and studied by using X-ray crystallographic techniques. Each molecule was found to crystallize to give the predicted solid-state structure. Two compounds, related to compound **3**, were also studied. the methyl ester of **3**, dimethyl 4,4'-ureylenedibutyrate (**5**), crystallizes to give a one dimensional network based only upon hydrogen bonds between the urea functionalities. The thiourea analogue of **3**, 4,4'-thioureylenedibutyric acid (**6**) forms a network based upon carboxylic acid hydrogen bonds, but there is no linear alignment of the thiourea functionality presumably due to the lower energy of hydrogen bonds to sulfur.

The design of molecular solids is a worthy but elusive goal.[1] In order for a molecular solid to exibit a particular solid-state phenomena, such as electrical conductivity, nonlinear optical behavior, or solid state polymerization, the composite molecules must possess both the requisite molecular structure *and* molecular orientation in the solid state. Chemical synthesis is employed for the preparation of a given molecular structure. However, the ability to control or even predict solid-state structure is a very difficult problem with few useful solutions.

Dipolar interactions play an important role organizing molecules in the solid state. Among these dipolar interactions, the hydrogen

(1) The number of reports in both the scientific and popular literature are an indication of the awareness that is developing with respect to new materials. For example, a recent issue of *Science* was entirely devoted to this subject (*Science* **1990**, *247*, 608).

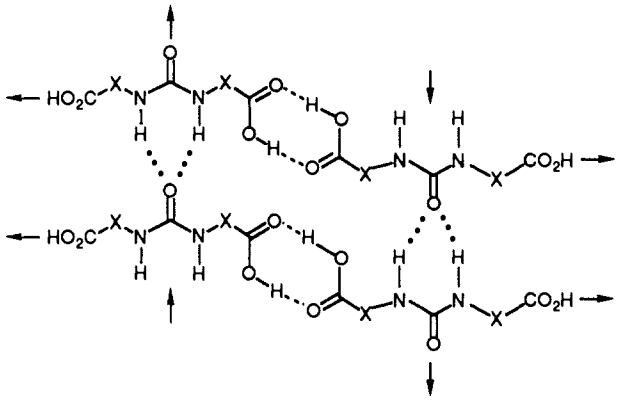
0002-7863/90/1512-6627$02.50/0

bond has long been noted as a powerful organizing force in molecular crystals[2] and biopolymers.[3,4] For example, complementary hydrogen bonding systems, such as the Watson–Crick base pairs, are particularly important for the proper function of the nucleic acids. Therefore, a logical approach to the design of molecular solids would be the use of persistent complementary intermolecular hydrogen bonding for molecular organization.

As a realistic and useful goal we sought a family of molecules that would form predictable two-dimensional planar arrays in the crystalline state. We sought to design this two-dimensional network by choosing molecules that would form two dependable independent sets of one-dimensional self-complementary hydrogen-bonded arrays oriented in orthogonal directions.

Two self-complementary hydrogen-bonding functionalities that form one-dimensional hydrogen-bonded polymeric structures in the solid state are the dicarboxylic acids[5] and N,N′-disubstituted ureas.[6] If these two functionalities are present in the same molecule and if the self-complementary hydrogen patterns persist then a two-dimensional hydrogen-bonded molecular network will result.

This preliminary analysis and subsequent model building led us to the ureylenedicarboxylic acids. The carboxylic acid groups at each end of a ureylenedicarboxylic acid molecule should form a hydrogen bonded array in a direction orthogonal to the linear hydrogen-bonded array formed by the urea functionality. The predicted molecular array is shown below.

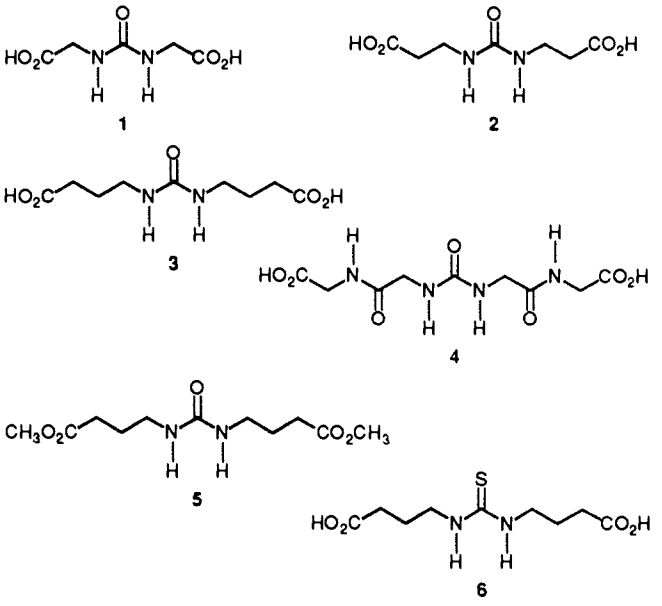


We will call this two-dimensional array of self-complementary hydrogen-bonded molecules a β-network since it is based upon two independent, self-complementary, one-dimensional hydrogen-bonded arrays designated α-networks.

In this paper, we wish to report the results of our initial studies. We have prepared and determined the structures of the three simplest symmetrical ureylenedicarboxylic acids all expected to form β-networks. Included are the compounds with one, two, and three methylene carbons in the carboxylic acid chains (compounds **1**, **2**, and **3**, respectively; Chart I) as well as the extended ureylenedicarboxylic acid **4** derived from the simplest dipeptide, glycylglycine.

To further test the approach we also prepared and determined structures of two compounds related to compound **3** that were expected to form one dimensional hydrogen bonded α-networks. We anticipated that compound **5** the methyl ester of **3**, would form an α-network with hydrogen bonds only along the urea direction. Sulfur forms weaker hydrogen bonds than oxygen thus compound

Chart I



6, the thiourea analogue of **3**, was not expected to form the β-network, but only a one-dimensional α-network of carboxylic acid chains.

Experimental Section[7]

Compounds **2**[8] (H_2O), **3**[9] (H_2O), **5**[9] (CH_3OH), and **6**[9] (H_2O) were prepared as previously described and crystals suitable for crystallographic analysis were obtained from the solvent indicated.

2,2′-Ureylenediacetic Acid (1). Diethyl 2,2′-ureylenediacetate[10] (0.242 g) was treated with 2.7 mL of 1 M NaOH, and the reaction mixture was heated on the steam bath for 1 h. The reaction mixture was neutralized to about pH 3 with 5% HCl and the solvent removed in vacuo to dryness. The residue was heated in ethanol and filtered. Removal of the solvent in vacuo followed by recrystallization from H_2O gave **1** (48%) as colorless needles, mp 202–4 °C (lit.[11] mp 204–6 °C). Samples suitable for crystallographic analysis were obtained by slow recrystallization from H_2O/CH_3CO_2H.

***N,N′*-Carbonylbisglycylglycine (4).** To 2.89 g (2.2 mmol) of glycylglycine and 3.65 g of potassium carbonate (2.2 mmol) in a three-neck flask equipped with a magnetic stirrer and two addition funnels was added 10 mL of H_2O. The flask was cooled in an ice bath, and, simultaneously, 0.694 g of triphosgene (trichloromethyl carbonate, 3.7 mmol) in 2 mL of toluene and 4.1 g of $K_2CO_3 \cdot {}^1/_2H_2O$ (2.5 mmol) in 10 mL of H_2O were added to the vigorously stirred solution over 30 min. The pH of the reaction mixture was maintained below 10. The toluene layer was then separated, and the aqueous layer was extracted twice with ether. The aqueous solution was acidified with concentrated HCl to approximately pH 2 and a crystalline precipitate formed on cooling. The precipitate was filtered, washed with small portions of cold H_2O, and air dried. A pure sample was obtained by recrystallization from H_2O: mp 237–239 °C (lit.[12] mp 232 °C); NMR (DMSO-d_6/$CDCl_3$, 5/1) δ 3.68 (2 H, d, 6 Hz), 3.74 (2 H, d, 6 Hz), 6.46 (1 H, t, 6 Hz), 8.02 (1 H, t, 6 Hz); IR (KBr) 3342, 3283, 1701, 1660, 1625, 1590, 1554 cm^{-1}. Samples suitable for crystallographic analysis were obtained by recrystallization from H_2O.

Crystallographic Analysis. All three of the urelyenedicarboxylic acids, **1–3**, readily form highly crystalline solids, but in each case difficulty was encountered in obtaining a suitable crystal for single crystal X-ray

(2) For recent references on the use of hydrogen bonds to assemble molecules in the solid state, see: (a) Etter, M. C.; Frankenbach, G. M. *Chem. Mater.* **1989**, *1*, 10. (b) Ducharme, Y.; Wuest, J. D. *J. Org. Chem.* **1988**, *53*, 5787. (c) Panunto, T. W.; Urbanczyk-lipkowska, Z.; Johnson, R.; Etter, M. C. *J. Am. Chem. Soc.* **1987**, *109*, 7786 and references cited therein.

(3) (a) Schultz, G. E.; Schirmer, R. H. *Principles of Protein Structure*; Springer-Verlag: New York, 1979; pp 66–107. (b) Saenger, W. *Principles of Nucleic Acid Structure*; Springer-Verlag: New York, 1984; pp 116–131. (c) Dickerson, R. E.; Geis, I. *The Structure and Action of Proteins*; Benjamin/Cummings: Menlo Park, CA, 1969, 24–43.

(4) Arnott, S.; Dover, D. S.; Elloitt, A. *J. Mol. Biol.* **1967**, *30*, 201.

(5) Leiserowitz, L. *Acta Crystallogr.* **1976**, *B32*, 775.

(6) (a) Deshapande, S. V.; Meredith, C. C.; Pasternak, R. A. *Acta Crystallogr.* **1968**, *B24*, 1396. (b) Caron, A.; Donohue, J. *Ibid.* **1969**, *B25*, 404.

(7) Melting points were recorded on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer FTIR 1600. The absorption intensities are described as strong (s), medium (m), or weak (w) and the absorption of polystyrene at 1601 or 1944 cm^{-1} was used as a reference. Proton and C^{13} NMR spectra were recorded on a General Electric QE-300 spectrometer. All chemical shifts were reported in ppm from tetramethylsilane as an internal standard and are described as singlet (s), doublet (d), triplet (t), quartet (q), quintet (q′), or multiplet (m).

(8) Tarlton, E. J.; McKay, A. F. *Can. J. Chem.* **1958**, *36*, 496.

(9) McKay, A. F.; Tarlton, E. J.; Petri, S. I.; Steyermark, P. R.; Mosley, M. A. *J. Am. Chem. Soc.* **1958**, *80*, 1510.

(10) Kondo, K.; Murata, K.; Miyoshi, N.; Murai, S.; Sonoda, N. *Synthesis* **1979**, 735.

(11) *Beilsteins Handbuch Org. Chem., 4th ed.* **1950**, *359*, II 792.

(12) Fischer, E. *Chem. Ber.* **1902**, *35*, 1102.

Table I. Crystal and Data Collection Parameters[a]

	1	2	3	4	5	6
empirical formula	$C_5H_8N_2O_5$	$C_7H_{12}N_2O_5$	$C_9H_{16}N_2O_5$	$C_9H_{14}N_4O_7$	$C_{11}H_{20}N_2O_5$	$C_9H_{16}N_2O_4S$
formula weight	176.13	204.18	232.24	290.23	260.29	248.30
crystal system	monoclinic	monoclinic	monoclinic	triclinic	monoclinic	monoclinic
lattice parameters						
a (Å)	9.175 (3)	19.863 (8)	10.529 (6)	4.896 (2)	10.858 (4)	25.592 (8)
b (Å)	4.569 (2)	9.180 (3)	4.666 (3)	31.546 (6)	4.629 (2)	5.213 (2)
c (Å)	17.462 (3)	20.83 (1)	22.255 (9)	4.636 (2)	26.449 (9)	8.921 (3)
α (deg)	–	–	–	94.10 (3)	–	–
β (deg)	93.1 (2)	100.94 (6)	91.25	118.23 (4)	93.2 (1)	92.50
γ (deg)	–	–	–	89.56 (3)	–	–
vol (Å^3)	730.9 (8)	3729. (5)	1093. (2)	629. (1)	1327. (2)	1189. (1)
space group	$C2/c$ (#15)	$C2/c$ (#15)	$C2/c$ (#15)	$P\bar{1}$ (#2)	$C2/c$ (#15)	$P2_1/c$ (#14)
Z value	4	16	4	2	4	4
D_{calc} (g/cm^3)	1.60	1.45	1.41	1.53	1.30	1.39
$F000$	368	1728	496	304	560	528
μ (Mo Kα) cm^{-1}	1.55	1.34	1.24	1.43	1.10	2.73
$2-\theta$ (max)	63.9	49.9	40.4	44.0	44.0	39.9
no. of observations $I > 3.00\sigma$	746	1057	316	921	388	827
no. variables	57	256	74	181	83	145
residuals: R; R_w	0.061; 0.072	0.083; 0.116	0.052; 0.064	0.053; 0.066	0.064; 0.072	0.045; 0.062
goodness of fit	1.99	3.17	1.99	2.03	2.07	1.94
largest peak in final difference map	0.49	0.37	0.22	0.34	0.28	0.22

[a] All data collected on an Enraf-Nonius CAD4 diffractometer at room temperature with use of Mo Kα radiation (λ = 0.71069 Å) and a graphite monochromator.

analysis. The compounds **1** and **3** grew as long flat needles, often with a small cross section. The crytal of compound **1** used for data collection had a cross section of only 0.05 mm × 0.50 mm. The subsequent analysis revealed a common crystal morphology for the two compounds. In each case, the end faces of the needles were of the form {010} indicating that the most favorable growth direction was along the b axis, the direction of the urea hydrogen bond network. The flat most exposed faces of the long flat crystals were of the form {001}. The edge faces were of the form {100}, parallel to the β-network. The crystals of the two compounds, particularly those of **1**, all readily cleaved to form new faces of the form {100}. This is consistent with the fact that there are no hydrogen bonds between the β-networks, the β-networks appear to be held together by weaker van der Waals forces. Compound **2** also crystallized as needles parallel to the b axis and the urea repeate axis corresponds to the needle axis. The crystals had a more uniform cross section with side faces of the forms {101} and {10$\bar{1}$}. The ester **5** grew high quality crystals as elongated plates. The crystal morphology was identical with that of the corresponding acid **3**. Subsequent analysis revealed that the two structures had similar unit cell dimensions, both with $C2/c$ symmetry and a similar molecular packing. The crystals of the triclinic compound **4** grew as plates with the principal exposed faces of the form {010} corresponding to the long b axis of the unit cell and the hydrogen-bonded carboxylic acid chains. Compound **6** grew with roughly uniform dimensions with no unusual morphology.

The X-ray diffraction data were collected using an Enraf-Nonius CAD4A diffractometer with a Mo source equipped with a graphite monochromator. Unit cell parameters were determined by a least squares analysis of 25 automatically centered reflections in the range $20° < 2\theta < 30°$. Data were collected using the $\omega/2\theta$ method with full details presented in Table I.

The data analysis and refinement was carried out with use of the programs of the TEXAN software package. The structures were solved by using direct methods and refined with anisotropic thermal parameters assigned to the non-hydrogen atoms. The carboxylate hydrogen atoms of compounds **1**, **3**, **4**, and **6** were located in electron density difference maps. The positions of all other hydrogens and all six compounds were calculated. All hydrogens were included as fixed isotropic contributors in the final refinements. The figures were drawn by using a locally developed program CHARON.

Results

Molecular Structures. The *molecular* structures of the five compounds show no unusual features. Compounds **1**, **3**, and **5** each have a crystallographic 2-fold axis passing through the urea carbonyl group. The unit cell of compound **2** contains three unique molecules, two of them have a 2-fold axis, the third does not. The glycylglycine derivative **4** and the thiourea **6** have no crystallographically imposed symmetry but each has a pseudo-2-fold molecular axis. Selected bond distances and angles for the compounds are listed in Table II. Due to crystal quality problems, the intramolecular distances and angles of compound **2** were not very accurately determined. Within the error limits, the molecular geometries are in good agreement with each other and those of similar compounds.

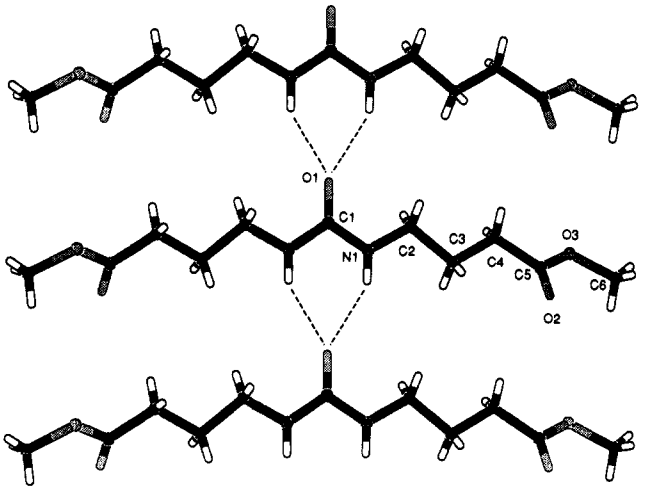


Figure 1. A portion of the crystal structure of the ester **5**. The vertical central carbonyl groups form an α-network of self-complementary hydrogen bonds along a 2-fold axis of the $C2/c$ unit cell parallel to the short, 4.629 (2) Å, b axis. In this and subsequent figures the dotted lines indicate hydrogen bonds.

The carboxyl hydrogen atoms of compounds **1**, **3**, **4**, and **6** were located in electron density difference maps. In each case the position was adjacent to the oxygen with the longer carboxyl carbon to oxygen bond distance as expected. In the case of compound **2**, the carboxyl hydrogen atoms of the three independent molecules could not be located in difference maps and the hydrogen atoms were thus placed in calculated positions adjacent to the oxygen atom with the longer carbon to oxygen bond distance.

Crystal Structures. Each of the six compounds studied has a crystal structure dominated by hydrogen bonds. We will discuss each compound in turn starting with compounds **5** and **6**, each expected to only form strong hydrogen bonds in one direction.

Dimethyl 4,4′-Ureylenedibutyrate (5). The molecular structure of this molecule is almost ideal with a nearly perfect staggering of the methylene groups (Figure 1). The molecule has a 2-fold

Table II. Selected Bond Distances (Å) and Angles (deg) for Disubstituted Urea Molecules

	1	2	3	4	5	6
			Urea Functionality			
C=O	1.24 (4)	1.28 (2) 1.23 (1) 1.28 (2)	1.25 (1)	1.233 (5)	1.23 (1)	1.687 (5) (S)
C—N	1.348 (3)	1.33 (1) 1.29 (1) 1.35 (1) 1.34 (1)	1.33 (1)	1.343 (7) 1.349 (7)	1.344 (7)	1.319 (6) 1.343 (6)
N—R	1.440 (3)	1.45 (1) 1.46 (1) 1.47 (1) 1.51 (2)	1.429 (9)	1.425 (7) 1.436 (7)	1.436 (7)	1.442 (6) 1.433 (7)
O=C—N	121.6 (1)	120.9 (8) 121.6 (8) 124 (1) 122 (1)	120.8 (4)	122.6 (5) 121.8 (5)	122.2 (5)	122.3 (4) (S) 122.3 (4)
N—C—N	116.8 (3)	117 (2) 118 (2) 114 (1)	118.4 (9)	115.6 (4)	116 (1)	115.4 (4)
			Carboxyl Functionality			
C=O	1.242 (3)	1.24 (1) 1.21 (1) 1.23 (1) 1.24 (1)	1.237 (8)	1.219 (7) 1.196 (6)	1.186 (8)	1.229 (6) 1.203 (6)
C—O	1.266 (3)	1.29 (1) 1.25 (1) 1.30 (1) 1.26 (1)	1.277 (7)	1.290 (7) 1.269 (7)	1.316 (8)	1.229 (6) 1.305 (6)
R—C	1.505 (5)	1.50 (2) 1.49 (2) 1.46 (2) 1.64 (2)	1.474 (8)	1.490 (8) 1.487 (8)	1.489 (9)	1.484 (7) 1.491 (7)
O=C—O	124.2 (3)	126 (1) 125 (1) 122 (1) 120 (1)	122.4 (6)	123.5 (6) 123.6 (6)	123.3 (7)	123.0 (5) 122.0 (5)
R—C=O	119.7 (2)	117 (1) 119 (1) 124 (1) 116 (1)	121.7 (6)	123.5 (6) 124.4 (6)	124.8 (7)	122.1 (5) 124.1 (5)
R—C=O	116.1 (2)	117 (1) 116 (1) 115 (1) 123 (2)	115.9 (6)	112.9 (6) 112.0 (5)	111.8 (7)	114.9 (5) 113.9 (5)

Table III. Space Group and Unit Cell Parameters of Representative Disubstituted Urea Compounds[a]

compd	space group	*a*	*b*	*c*	α	β	γ	ref
urea	$P42_1m$	5.66	5.66	*4.72*	–	–	–	*b*
N,N-dicyclohexylurea	$P2/c$	11.54	*4.69*	12.03	–	95.47	–	*c*
diphenylurea	$Pna2_1$	*9.09*	10.53	11.76	–	–	–	*d*
1	$C2/c$	9.175 (3)	*4.549 (2)*	17.462 (3)	–	93.1 (2)	–	*e*
2	$C2/c$	19.863 (8)	*9.180 (3)*	20.83 (1)	–	100.94 (6)	–	*e*
3	$C2/c$	10.529 (6)	*4.66 (3)*	22.255 (9)	–	91.25 (7)	–	*e*
4	$P\bar{1}$	4.896 (2)	31.546 (6)	*4.636 (2)*	94.10 (3)	118.23 (4)	89.56 (3)	*e*
5	$C2/c$	10.858 (4)	*4.629 (2)*	26.449 (4)	–	93.2 (1)	–	*e*

[a] The unit cell axis shown in italics corresponds to the direction of the urea hydrogen bond network within each structure. [b] Vaughan, P.; Donohue, J. *Acta Crystallogr.* **1952**, *5*, 530. [c] Coiro, V.; Giacomello, P.; Giglio, E. *Acta Crystallogr.* **1971**, *B27*, 2112. [d] Dannecker, W.; Kopf, J.; Rust, H. *Cryst. Struct. Commun.* **1979**, *8*, 429. [e] This work.

axis with the carbonyl group aligned with the short *b* axis, 4.629 (2) Å, of the unit cell. This short axis is characteristic of ureas and was first recognized 20 years ago.[13] Table III gives a representative, but not comprehensive list of urea structures, most showing a similar short unit cell axis (4.5–4.8 Å), corresponding to aligned urea molecules. In the remaining compounds this distance is doubled to the 9.0–9.2 Å range. In these doubled structures two urea molecules are aligned along the axis and related to one another by either a crystallographic screw axis or a glide plane.

The linear alignment and characteristic repeat distance of the α-network of urea functionalities is due to the hydrogen bonds between the N–H donors of one molecule and the carbonyl lone pair acceptors of the molecule below. Table IV shows derived geometric values for this hydrogen-bond network. The 2.916 (7) Å N to O distance is somewhat longer than the average value of 2.85 Å reported by Taylor.[14] However, there are two such hydrogen bonds in this case, and the overall structure would appear to be quite stable.

(13) Jadžyn, J.; Stockhausen, M.; Żywucki, B. *J. Phys. Chem.* **1987**, *91*, 754.

(14) (a) Taylor, R.; Kennard, O. *Acc. Chem. Res.* **1984**, *17*, 320. (b) Taylor, R.; Kennard, O.; Versichel, W. *Acta Crystallogr.* **1984**, *B40*, 280.

Table IV. Selected Intermolecular Distances (Å) for Disubstituted Urea Molecules

	1	2	3	4	5	6
			Urea Functionality			
N—H	0.95[a]	0.95[a]	0.95[a]	0.95[a]	0.95[a]	0.95[a]
=O···H	2.032	1.941	2.102	2.061	2.058	2.486 (*S*)
		2.051		2.064		2.706 (*S*)
=O···N	2.861 (3)	2.81 (1)	2.960 (7)	2.916 (5)	2.916 (7)	3.419 (4) (*S*)
		2.90 (1)		2.918 (5)		3.587 (4) (*S*)
		2.88 (1)				
		2.89 (1)				
			Carboxylic Acid Functionality			
—O—H	1.034	0.95	1.227	0.965		1.025
				0.966		
=O···H	1.637	1.621	1.435			1.590
		1.734				
		1.722				
		1.735				
=O···O—	2.662 (7)	2.57 (1)	2.623 (6)	2.691950		2.613
		2.67 (1)		2.695 (1)		
		2.67 (1)				
		2.68 (1)				
			Amide Functionality			
N—H					0.95	
=O···H					1.884	
					1.850	
=O···N					2.831 (6)	
					2.793	

[a] These distances were used to calculate the position of the indicated hydrogen atom.

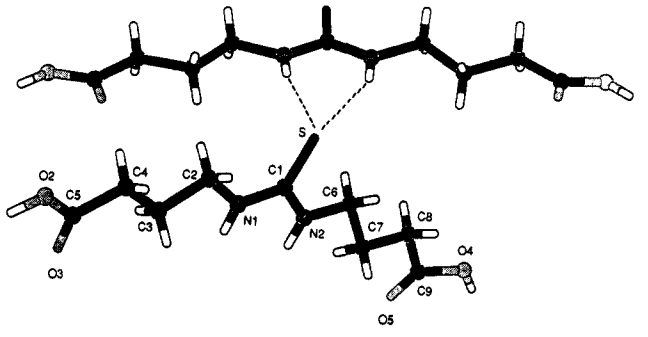


Figure 2. A portion of the crystal structure of the thiourea **6**. The thiourea sulfur atom has a close approach to the urea hydrogens of a second molecule from below. Unlike the analogous urea, compound **3**, there is no forced linear alignment of the thiourea functionalities.

4,4′-(Thioureylene)dibutyric Acid (6). This molecule forms a linear, hydrogen-bond α-network via its carboxylic acid groups. The chains in this thiourea compound have a close approach as they cross to form hydrogen bonds between the sulfur atom and the N-H groups of a second molecule, Figure 2, but the forces apparently are insufficient to line up the thiourea groups in a manner found for the urea compounds. The molecular planes of the two thiourea groups are nearly orthogonal to each other with the N-H groups approaching the side of the thiocarbonyl group. The interaction is asymmetric in this case with one S to N distance shorter than the other, 3.419 (4) Å versus 3.587 (4) Å.

4,4′-Ureylenedibutyric Acid (3). This urea is the direct analogue of the thiourea **6** discussed above. The two molecules have similar molecular structures with the trimethylene side chains arranged in nearly perfect anti conformations.

In the absence of hydrogen bonds, a simple oxygen containing organic molecule will have a density less than its thio analogue. In this case, the density of the urea **3** is 1.41 g/cm^3 while the density of the thiourea **6** is actually less, 1.39 g/cm^3, despite its higher molecular weight. The greater density for the urea is good indicator of a tighter lattice presumably due to the increased strength of the hydrogen bonds.

As discussed above, the thiourea **6** a forms linear α-network through its two carboxylic acid functionalities. The urea **3** also forms this network, but in addition forms a second α-network via

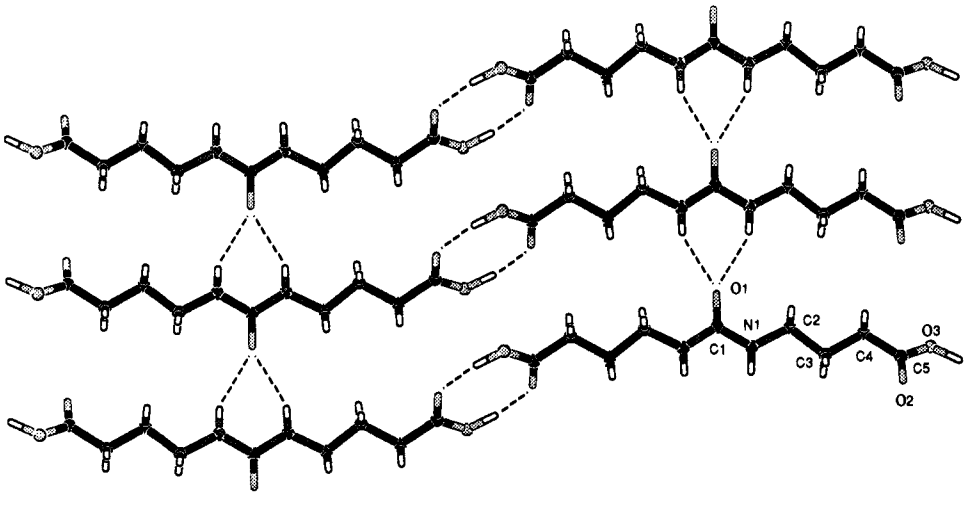


Figure 3. A portion of the crystal structure of the trimethylene compound, **3**. The vertical central carbonyl groups forms a linear α-network along a 2-fold axis of the *C*2/*c* unit cell parallel to the short, 4.66 (3) Å, *b* axis. A second perpendicular α-network is formed via carboxylic acid hydrogen bonds. The two perpendicular one-dimensional α-networks combine to give the predicted planar β-network.

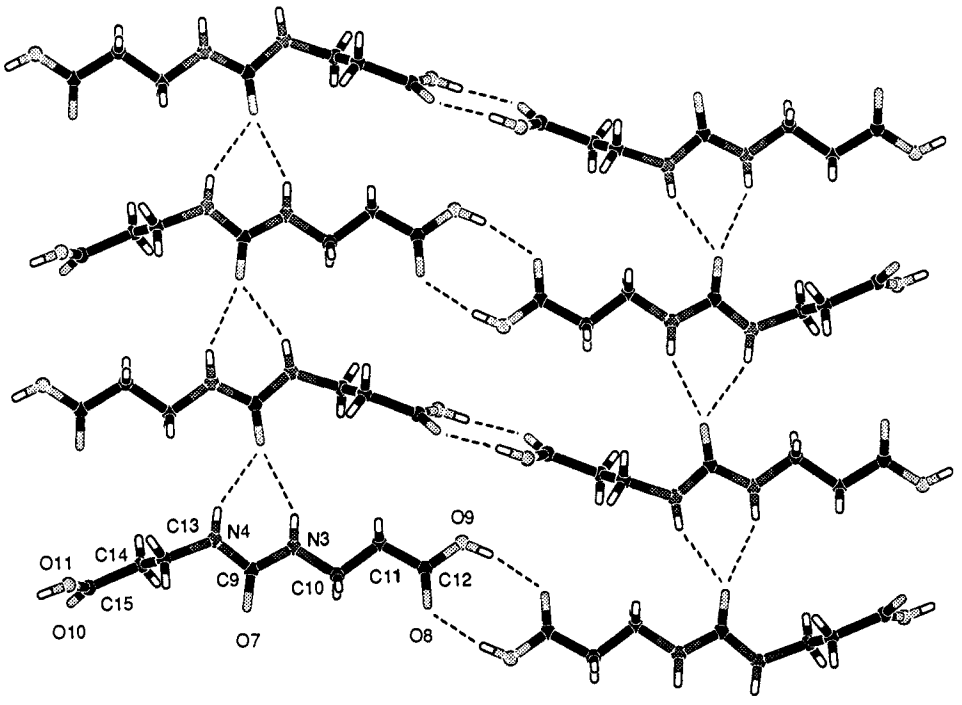
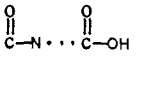


Figure 4. The sheet I β-network of the dimethylene compound, **2**. The molecule sits on a general position in the $C2/c$ unit cell. Subsequent molecules are related in the vertical direction by a 2-fold screw axis parallel to the b axis. The sheet I β-network alternates with the sheet II β-network pictured in Figure 5.

Table V. Selected Dihedral Angles for Ureylenedicarboxylic Acids[a]

					
1	10.2 (2)	−23.5 (3)	158.1 (2)	65.9 (3)	78.2 (5)
2					
sheet I, C4 molecule	7 (1)	−10 (1)	169 (1)	152 (1)	21 (1)
sheet I, C8 molecule	2 (1)	179 (1)	−2 (1)	97 (1)	80 (1)
sheet II, C12 end	8 (1)	−5 (1)	175 (1)	180 (1)	16 (1)
sheet II, C15 end	10 (1)	163 (1)	−20 (1)	−97 (1)	74 (1)
3	6.7 (6)	150.7 (6)	−30 (1)	172.3 (4)	45 (1)

[a] X = C or N.

urea hydrogen bonds. These two orthogonal α-networks result in a planar sheet of molecules held together by intrasheet hydrogen bonds, Figure 3. This is the molecular array predicted from our model building studies, a structure we have termed the β-network.

The urea carbonyl groups are aligned with the b axis of the $C2/c$ unit cell. This b axis is short, 4.666 (3) Å and corresponds to the characteristic urea repeat distance found in other urea compounds. The individual sheets are nearly planar, with all carbon and nitrogen atoms within 0.21 Å of the best least-squares plane of all non-hydrogen atoms. The carboxylic acid functionality is turned 45 (1)° out of the plane (Table V); thus oxygen atoms deviate 0.83 and 0.70 Å from the plane. Intersheet interactions would seem to be limited to van der Waals and long range dipole–dipole forces. The nearly planar sheets are arranged such that the carboxylic acid groups of one sheet are closest to the methylene units of the two neighboring sheets. This is presumably a steric effect since the carboxylic acid groups turning out of the plane require more room.

3,3′-Ureylenedipropionic Acid (2). This urea also crystallizes in the space group $C2/c$, but its structure is more complicated. There are 16 molecules in the unit cell, with one entire and two half molecules in the asymmetric unit. There are two independent β-networks that alternate to make up the overall crystal structure.

One molecule is at general position in the cell and forms a β-network sheet (sheet I, Figure 4) with neighboring symmetry-related molecules. Each molecule forms urea hydrogen bonds to two others related by a 2-fold screw axis along the b axis. Since this is not a real 2-fold axis, there is no forced alignment of the urea hydrogen bonds; it is thus not surprising to find a tilting of the ureas. However the hydrogen bonded N to O distances, 2.88 (1) and 2.89 (1) Å, are still essentially equivalent, Table IV.

In sheet I the carboxylic acid groups at the two ends of the molecule are turned in very different configurations, with dihedral angles of 16 (1)° and 74 (1)° with respect to the plane of the central urea functionality. Each carboxylic acid group is hydrogen bonded to a similar group of neighboring molecule through a center of symmetry forming the expected dicarboxylic acid chains.

Sheet II, Figure 5, is formed by the two unique half molecules, each located on a real 2-fold axis of the $C2/c$ unit cell. Along the b axis the two molecules alternate to form the characteristic self-complementary urea hydrogen bond structure. The length of the b axis, 9.180 (3) Å, is twice the characteristic urea repeat distance. The two unique molecules making up sheet II have different orientations of their carboxylic acid functionalities, with dihedral angles of 20.8 (1)° and 80.4 (1)° with respect to the central urea functionalities.

Even though the local symmetries are different, the two independent sheets, I and II, are quite similar. In both cases there is an alternation of the orientation of the carboxylic acid functionality as one goes from one molecule to the next along the b axis direction. One half of the molecule in the general position making up sheet I has a side chain conformation similar to one of the molecules of sheet II; the other half of the molecule has a conformation similar the second molecule of sheet II.

2,2′-Ureylenediacetic Acid (1). This urea, derived from two glycine molecules, is the simplest member of the series. Like the previous two compounds, it crystallizes in the space group $C2/c$. The 2-fold axis of the unit cell again passes through the carbonyl group of the urea functionality orienting the urea hydrogen bonds with the short, 4.569 (2) Å, b axis. The carboxylic acid functionalities once again dimerize about a center of symmetry yielding the expected dicarboxylic acid chains (Figure 6).

Thus, the crystal structure of **1** would seem to be very similar to the crystal structure of **3**. The space group is the same, the molecular symmetry is the same, and the intermolecular interactions are similar. There is, however, a significant difference between the two structures. The β-network of compound **3** (Figure

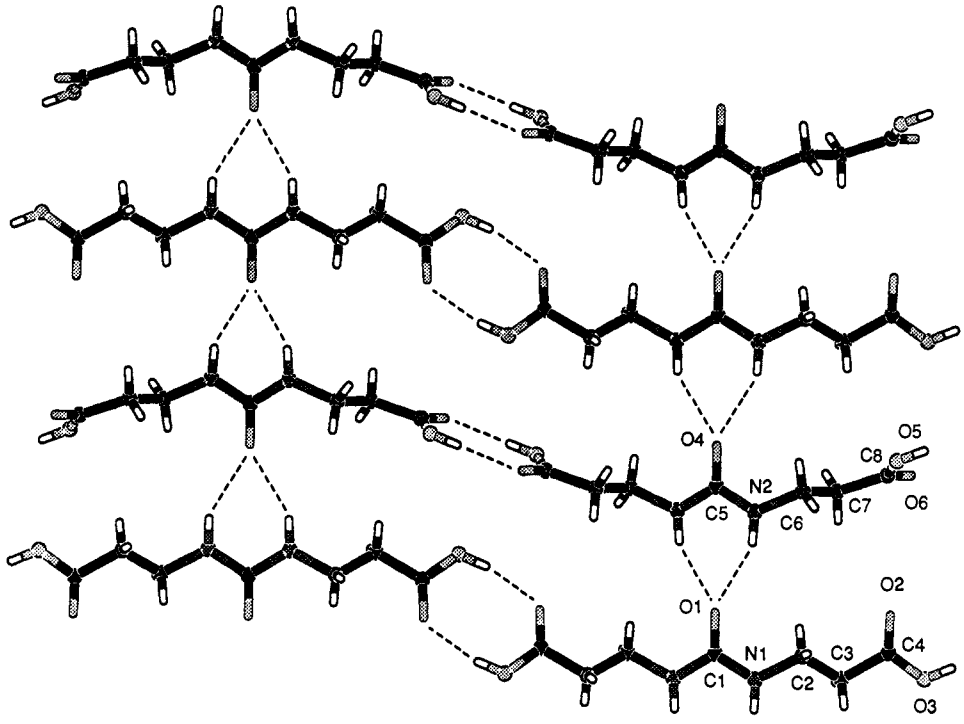


Figure 5. The sheet II β-network of the dimethylene compound, **2**. The two independent molecules sit on a 2-fold axis of the $C2/c$ unit cell parallel to the b axis. The sheet **II** β-network alternates with the sheet I β-network pictured in Figure 4.

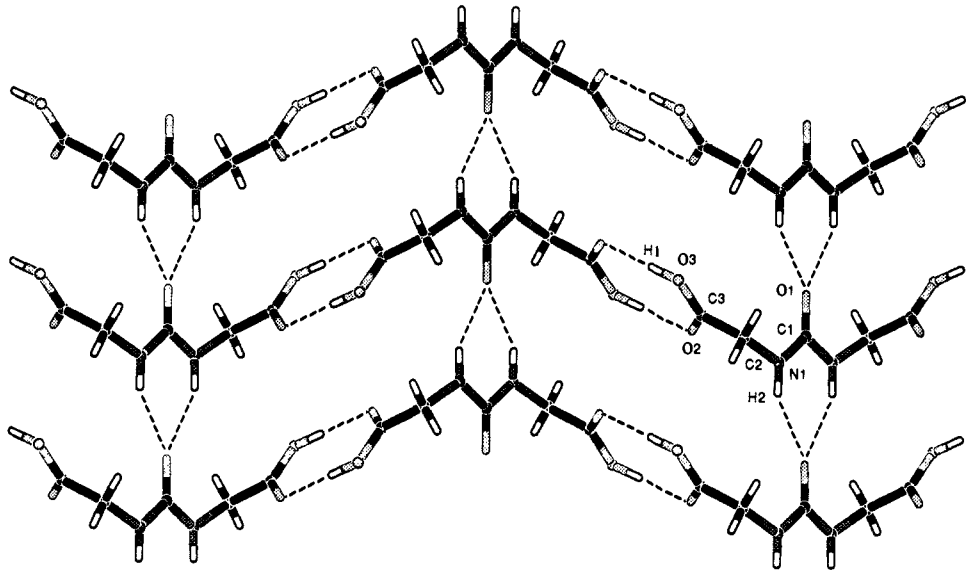


Figure 6. The β-network of the monomethylene compound, **1**. The molecules sit on a 2-fold axis of the $C2/c$ unit cell parallel to the short, 4.549 (2) Å, b axis. The carboxylic acid groups form hydrogen bonds about centers of symmetry.

7a) is nearly planar, but the β-network of compound **1** is pleated with significant deviations from planarity (Figure 7b).

The pleating of the β-network of compound **1** is very reminiscent of the pleating found in a protein β-sheet. The α-carbon of the amino acid is at the edge of the pleat in both cases with the sites for potential substituents of alternate α-carbons pointing up and down.

The Urea Derived from Glycylglycine. The urea from the simplest dipeptide, glycylglycine, forms the β-network shown in Figure 8. The compound crystallizes in the triclinic space group, $P\bar{1}$, with the urea hydrogen bonds aligned with the 4.636 (2) Å c axis and the carboxylic acid hydrogen-bonded chains aligned with the long 31.546 (6) Å b axis with the usual center of symmetry between neighboring molecules of the chain. These molecules have a set of amide groups in the side arms, and these functionalities form additional hydrogen bonds in the third dimension to the next β-network layer. Each molecule forms amide hydrogen bonds to two molecules in the layer above and two molecules in the layer below. These interplane hydrogen bonds are parallel to a second short axis, the 4.896 (2) Å a axis of the unit cell. Each molecule is hydrogen bonded to a total of eight neighbors, two through carboxylic acid hydrogen bonds, two through urea hydrogen bonds and four through the amide groups of the side chains. With hydrogen bonds in three directions the structure should be considered a γ-network, although the two-dimension β-network sheets are still a readily identifiable structural feature.

Discussion

The symmetrical ureylenedicarboxylic acids studied in this paper form crystal structures based upon predictable arrays of hydrogen bonds. The hydrogen bonds within each array are segregated into two self-complementary sets, urea α-networks and dicarboxylic acid α-networks. Individually the α-networks are well known, having been seen in many previously reported structures. The ureylenedicarboxylic acid crystal structures are unique with these

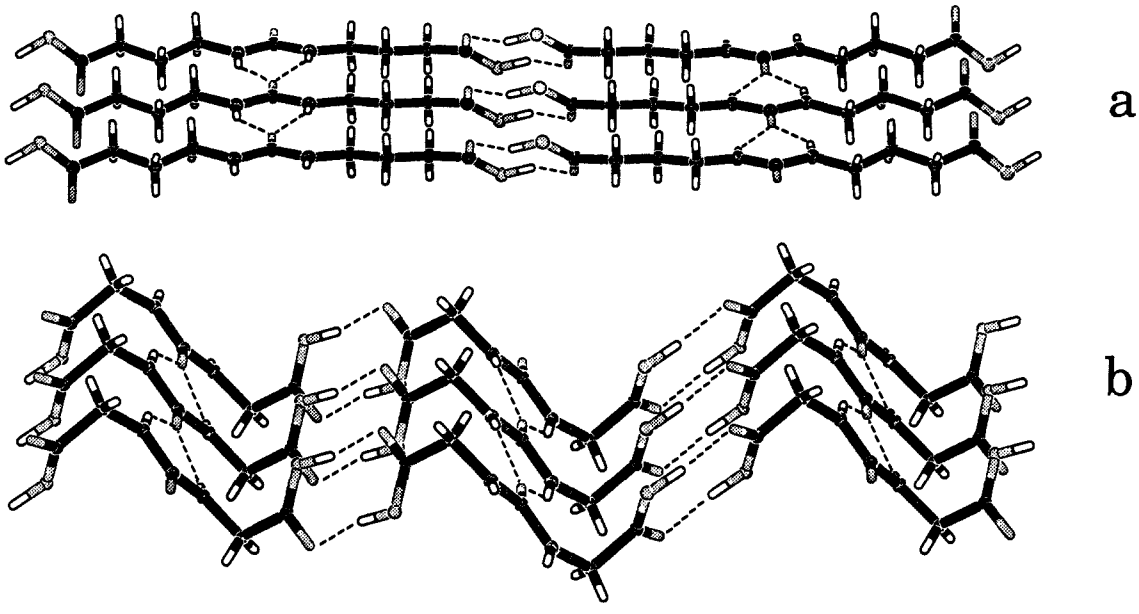


Figure 7. An edge on view of β-networks formed by compounds **1** and **3**. In a the β-network of **3** is shown to be nearly planar, while in b the β-network of **1** is shown to be significantly puckered.

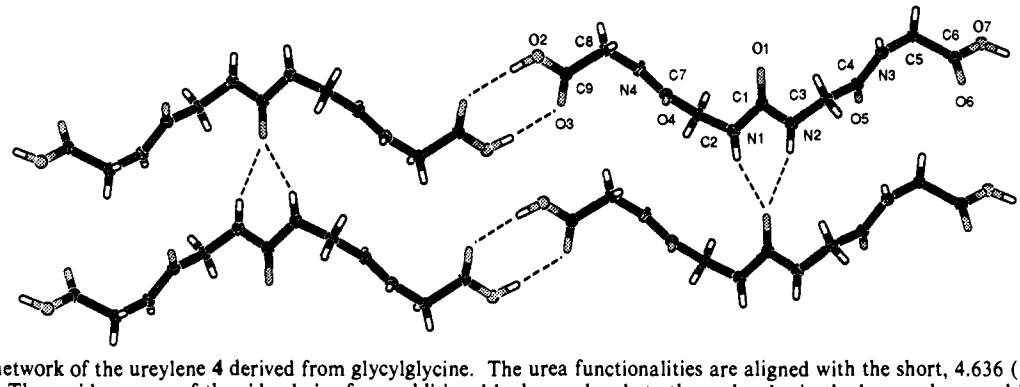


Figure 8. The β-network of the ureylene **4** derived from glycylglycine. The urea functionalities are aligned with the short, 4.636 (2) Å, *c* axis of the triclinic unit cell. The amide groups of the side chains form additional hydrogen bonds to the molecules in the layers above and below. This third self-complementary hydrogen-bonded α-network converts the overall structure into a three-dimensional γ-network, although the two-dimensional β-network is still the most characteristic feature of the structure.

two different α-networks coexisting and combining to give a planar two dimensional β-network.

The formation of self-complementary intermolecular hydrogen bonds is a characteristic of many urea compounds (see Table III), although there are examples of disubstituted ureas that do not form such structures.[15-17] The enthalpies of the urea hydrogen bonds have been measured in solution[13] and can be estimated to be about 5 kcal/mol.

The vast majority of carboxylic acids form cyclic hydrogen-bonded dimers in the solid state.[5] Such hydrogen bonds are known to be relatively strong with various enthalpy estimates available in the range of about 7-7.5 kcal/mol.[18]

In the simple ureylenedicarboxylic structures each molecule forms a total of four strong carboxylic acid hydrogen bonds plus four urea hydrogen bonds with an enthalpy total as high as 50 kcal/mol, presumably giving considerable strength to the resulting β-network. In some cases, alternate crystal structures might be possible with similar favorable enthalpies, but the inherent self-complementarity of the hydrogen bonds as found appear to make the observed structures particularly preferable.

In this preliminary study, our attempts to design a molecular solid have been successful. The molecules that we have chosen crystallize in predictable two-dimensional β-networks. Extensions of the work to ureylenes derived from other amino acids and small polypeptides will be of interest and will no doubt exhibit considerable structural diversity.

Acknowledgment. Support for this research was provided by a grant from the donors of the Petroleum Research Fund, administered by the American Chemical Society.

Supplementary Material Available: Tables of atom coordinates and thermal parameters, intramolecular bond distances and angles for compounds **1-6** (30 pages); tables of observed and calculated structural factor amplitudes for compounds **1-6** (35 pages). Ordering information is given on any current masthead page.

(15) Hart, H.; Lin, L.-T. W.; Goldberg, I. *Mol. Cryst. Liq. Cryst.* **1986**, *137*, 277.
(16) Etter, M. C.; Panunto, T. W. *J. Am. Chem. Soc.* **1988**, *110*, 5896.
(17) Chang, Yuh-Loo; Fowler, Frank W.; Lauher, Joseph W. Unpublished work.
(18) Curtis, L. A.; Blander, M. *Chem. Rev.* **1988**, *88*, 827.