Supramolecular Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713649759

Supramolecular Polyglycine II-Type Structure of Glycylglycine Bolaamphiphile

Masaki Kogiso[a]; Mitsutoshi Masuda[a]; Toshimi Shimizu[a]
[a] Department of Organic Materials, National Institute of Materials and Chemical Research, Ibaraki, Japan

To cite this Article Kogiso, Masaki , Masuda, Mitsutoshi and Shimizu, Toshimi(1998) 'Supramolecular Polyglycine II-Type Structure of Glycylglycine Bolaamphiphile', Supramolecular Chemistry, 9: 3, 183 — 189

To link to this Article: DOI: 10.1080/10610279808034985

URL: http://dx.doi.org/10.1080/10610279808034985

SUPRAMOLECULAR CHEMISTRY, Vol. 9, pp. 183–189
Reprints available directly from the publisher
Photocopying permitted by license only

Published by license under
the Harwood Academic Publishers imprint,
part of The Gordon and Breach Publishing Group.
Printed in India.

Supramolecular Polyglycine II-Type Structure of Glycylglycine Bolaamphiphile

MASAKI KOGISO*, MITSUTOSHI MASUDA and TOSHIMI SHIMIZU

Department of Organic Materials, National Institute of Materials and Chemical Research, 1-1 Higashi, Tsukuba, Ibaraki 305, Japan

(Received 9 September 1997; In final form 3 November 1997)

Bolaamphiphile with a glycylglycine unit at each end, *N,N′*-bis(carboxymethylcarbamoylmethyl)decane-1, 10-dicarboxamide, has been synthesized. The crystal structure was determined by single-crystal X-ray analysis. The space group is $P2_1/a$ with unit cell parameters: $a = 8.678(3)$, $b = 4.873(4)$, $c = 27.161(3)$ Å, $\beta = 92.68(2)°$, $Z = 2$, $Dc = 1.33 g/cm^3$, and $R = 0.051$ for 2095 data. The two halves of the molecule are related by a center of symmetry and have a folded —CH_2—CH_2—CO— conformation ($T\bar{G}S$ or $TG\bar{S}$). The molecules are arranged in a layered structure along the *c*-axis, forming a linear polymolecular chain stabilized by acid-acid dimerization at each end. Each chain is arranged in a pseudo-hexagonal lattice stabilized by three-dimensional hydrogen-bond networks between amide groups. This supramolecular crystal structure provides the first example of polyglycine II-type structure made of noncovalent polymolecular chains.

Keywords: Dipeptide, amphiphile, crystal structure

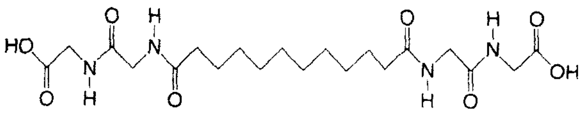
INTRODUCTION

Construction of supramolecular assemblies via noncovalent bonds is becoming an important area of research [1]. Directional, complementary, and cooperative hydrogen bonds have been frequently utilized as a binding force [2]. Two-dimensional structures of polypeptides are strongly influenced by the nature of the constituent amino acids and hydrogen-bond motifs [3]. In particular, the conformation of the glycine residue differs according to identities of the preceeding and following amino acid residues. Poly(L-alanylglycine) assumes a β-sheet structure [4], whereas poly(L-prolyl-L-prolyl-L-glycine) adopts a three-standard collagen-type structure [5]. On the other hand, aliphatic polyamides (nylons) always form sheet-like structures. In contrast, copolyamides of glycine and ϵ-amino acid (nylons $2/n$) form helical structures [6]. Thus, incorporation of the glycine residue into synthetic polyamides tends to induce a helical structure.

We have recently reported that oligoglycine-based bolaamphiphiles self-assemble to form vesicle-encapsulated tubes [7]. By tuning the hydrogen-bond motifs between the terminal carboxyl groups, we succesfully obtained thin-platelet crystals from water [8]. Our synthetic strategy for the construction of well-defined supramolecular structures is based on the

---

* Corresponding author.



1

strategic use of multiple hydrogen-bonds [9–12]. In this paper, we describe a supramolecular crystal structure that provides the first example of a polyglycine II-type structure made of glycylglycine bolaamphiphile 1.

EXPERIMENTAL

Synthesis of *N,N'*-bis(carboxymethylcarbamoylmethyl)decane-1,10-dicarboxamide (1)

To a solution of 1,10-decanedicarboxylic acid (0.50 g, 2.17 mmol) and 1-hydroxybenzotriazole (0.65 g, 4.77 mmol) in DMF (10 Ml), a solution of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (0.92 g, 4.77 mmol) in $CHCl_3$ (10 Ml) was added with stirring at −5°C. After 1 h, a solution of glycylglycine benzyl ester hydrochloride (1.24 g, 4.77 mmol) in MeOH (10 Ml) and triethylamine (0.67 Ml, 4.77 mmol) were added to the reaction mixture. It was stirred for 24 h at 0°C and allowed to gradually warm to room temperature. Evaporation of the solvent gave a white powder, which was then washed with 10% citric acid, water, 4% sodium hydrogencarbonate, and water. Recrystallization from DMF gave the benzyl ester of **1** as a white powder (1.15g). To a solution of the powder (1.15 g, 1.80 mmol) in DMF (50 Ml), 0.1N NaOH (40 Ml, 4 mmol) was added at 50°C. After stirring for 3 h, the solution was acidified with 1N HCl (ca. 5 Ml, ca. 5 mmol). The solvent was evaporated under reduced pressure to leave a white solid residue. The product was thoroughly washed with water and acetone to give a white powder (0.83 g, yield 83%) mp > 230°C. ^1H NMR (DMSO-d_6) δ: 1.25 (m, 12H, $CH_2(CH_2)_6CH_2$); 1.49 (m, 4H, $CH_2(CH_2)_6CH_2$); 2.09 (t, J = 5.4Hz, 4H, $COCH_2(CH_2)_8CH_2CO$); 3.70 (d, J = 5.4Hz, 4H, $CONHCH_2CO$ × 2); 3.75 (d, J = 5.4Hz, 4H, CH_2COO × 2); 7.96 (t × 2, J = 5.4Hz, 4H, NH). Anal. Calcd. for $C_{20}H_{34}O_8N_4$: C, 52.28; H, 7.47; N, 12.22%. Found: C, 52.40; H, 7.47; N. 12.11%.

X-Ray Single Crystal Analysis

When the weakly alkaline aqueous solution of **1** (10 mM, $8 < pH < 9$) was gradually acidified by vapor diffusion of 1% acetic acid into water, thin platelets were obtained as a single crystal. A colorless prismatic crystal having approximate dimensions of 0.3 × 0.5 × 0.02 mm was used for data collection. All measurements were made on Rigaku AFC7R diffractometer with graphite monochromated Cu-Kα radiation ($\lambda = 1.54178$ Å) and a 12 kW rotating anode generator at room temperature. The unit cell dimensions were obtained from a least-square refinement using the setting angles of 20 centered reflections in the range of $52.72 < 2\theta < 57.78°$. The data were collected using the ω-2θ scan technique to a maximum 2θ value of 120.0°. The corrected 1952 reflections out of 2095 were unique. The intensities of the crystal were checked by the three representative reflections measuring after every 150 reflections. Crystal data and a summary of the experimental details are given in Table I.

The structure was solved by the direct method (SAPI91) and refined by Fourier techniques (DIRDIF92). All the non-hydrogen atoms were refined anisotropically. All the hydrogen atoms were placed at calculated positions [d(C–H)=0.97 Å]. All the located hydrogen atoms were included in the full-matrix, least-squares refinement. All the calculations were carried out using the teXsan crystallographic software package (Molecular Structure Corp). The refinement converged at $R = 0.051$, $R_w = 0.055$. The atomic coordinates of the non-hydrogen atoms are listed in Table II.

TABLE I Crystal data and summary of experimental details for 1

Molecular formula	$C_{20}H_{34}O_8N_4$
Molecular weight	458.51
Crystal type	Monoclinic
Space group	$P2_1/$ a
Z value	2
Lattice parameters	
a (Å)	8.678(3)
b (Å)	4.873(4)
c(Å)	27.161(3)
β(Å)	92.68(2)
Cell volume (Å^3)	1422.3(6)
Crystal dimension (mm)	0.30 × 0.50 × 0.02
Dcalc (g/cm^3)	1.327
Radiation	CuKα(λ = 1.54178Å) Graphite monochromated
Number of reflections measured	2095
Number of unique reflections	1952
Number of observations	1240[$F > 3\sigma(F)$]
Scan mode	ω scan
2θ range	$18 < 2\theta < 120$
R-factor	0.051
R_W	0.055

TABLE II Fractional atomic coordinates and equivalent isotropic thermal parameters

atom	x/a	y/b	z/c	B(eq)
O1	0.3687(4)	−0.2824(7)	0.9804(1)	6.14(9)
O2	0.5249(3)	−0.0068(6)	0.94065(10)	5.05(7)
O3	0.2548(3)	−0.0008(5)	0.83621(9)	4.17(7)
O4	0.3075(3)	−0.3059(5)	0.72283(9)	6.18(7)
N1	0.4598(3)	−0.2752(7)	0.8528(1)	3.72(7)
N2	0.3662(3)	−0.1255(6)	0.7442(1)	3.25(7)
C1	0.4387(5)	−0.2030(9)	0.9413(1)	4.05(10)
C2	0.4013(4)	−0.3822(9)	0.8975(1)	4.34(10)
C3	0.3837(4)	−0.0790(8)	0.8266(1)	3.17(8)
C4	0.4698(4)	−0.0362(8)	0.7842(1)	3.47(8)
C5	0.2869(4)	−0.0578(7)	0.7169(1)	2.95(8)
C6	0.1715(4)	−0.0491(7)	0.6787(1)	3.31(8)
C7	0.1955(4)	−0.0623(7)	0.6275(1)	3.27(8)
C8	0.3362(4)	−0.0465(7)	0.6037(1)	3.21(8)
C9	0.3560(4)	−0.0619(8)	0.5521(1)	3.33(8)
C10	0.4908(4)	−0.0576(8)	0.5258(1)	3.36(8)

RESULTS AND DISCUSSION

Molecular Structure

The molecular structure (ORTEP drawing) with atomic numbering is given in Figure 1. Bond lengths and angles are also shown in Figure 2. Each molecule is centrosymmetric about the midpoint. Therefore, the torsion angles of the half molecule are the same but have opposite signs. The torsion angles around the backbone of **1** are given in Figure 3. The molecule adopts a *trans-gauche-staggered* ($T\bar{G}S$) folded conformation at the C5 —C6 —C7 —C8 sequence. This ($T\bar{G}S$) conformation is different from the extended zig-zag conformation commonly observed in linear amides [13]. We have demonstrated that the conformation of the connecting hydrocarbon links varies widely depending on the head group of the bolaamphiphiles or the chain length [9–12]. Hydrogen-bond motifs between the head groups and van der Waals interactions of the alkylene chains are responsible for these conformational differences in the connecting links [14].

The glycylglycine moiety does not adopt an extended conformation, but forms a helical structure. The torsion angles (ϕ, ψ, ω) around the glycine residue through the N2 —C4 —C3 —N1 sequence are summarized in Table III and compared to those of related compounds. The angles $\phi = -70.0°$, $\psi = 149.7°$, and $\omega = 172.8°$ are unusual in comparison to those in the α-form [15], the β-form [16] of glycylglycine, and in glycylglycine 2,6-naphthalene sulfonate [17]. The dihedral angle of two amide C = O bonds in **1** is 114° (O3 —C3 —C5 —O4) (Fig. 3). Up to now, two typical structures, β-sheet-like structure (polyglycine I-type) and a helical structure (polyglycine II-type), have been observed for the polyglycine [18]. The torsion angles of the glycine residue (ϕ, ψ, ω) and the rotation of the two C = O bonds in **1** are in good agreement with a polyglycine II-type structure (Tab. III) [18].

Crystal Structure

The crystal structure of **1** is depicted in Figures 4a and 4b. The bolaamphiphile **1** forms a layered structure, in which the alkylene chains are arranged in a parallel sheet. The sub-cell dimensions indicate that their packing is ortho-

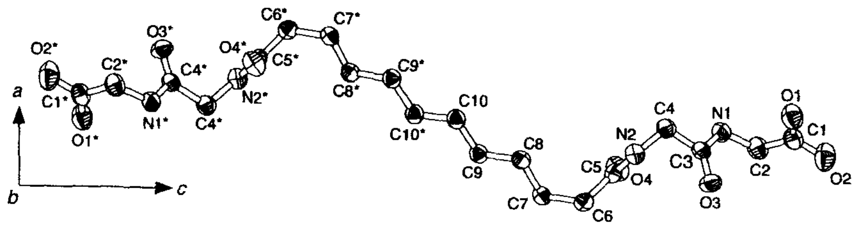


FIGURE 1 Molecular structure (ORTEP drawing) with atomic numbering. Thermal ellipsoids are drawn at 50% probability.

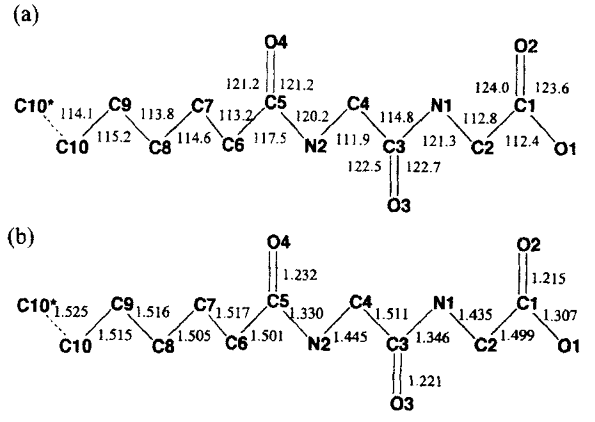


FIGURE 2 (a) Bond angles (°) and (b)bond lengths (Å) in 1. Half of the molecule is drawn.

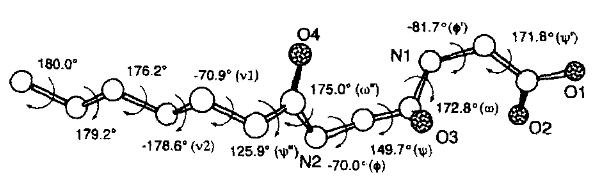


FIGURE 3 The torsion angles around the backbone of 1.

TABLE III Selected torsion angles (°) in glycine residues

Compound	ϕ	ψ	ω
Bolaamphiphile 1	−70.0	149.7	172.8
α-Gly-Gly [a]	154.6	152.3	174.5
β-Gly-Gly [b]	177.7	156.2	178.7
Gly-Gly2,6-naphthalenesulfonate [c]	121.0	−172.8	−178.7
Glycine dicarboxamide [d]	−68.1	154.4	180.0
Polyglycine II [e]	−80.0	150.0	180.0

[a] glycylglycine (α-form) [15].
[b] glycylglycine (β-form) [16].
[c] glycylglycine 2,6-naphthalenesulfonate [17].
[d] *N, N'*-bis(propylcarbamoylmethyl)adipamide [24].
[e] polyglycine (form II) [18].

rhombic ($O_\perp$)[19]: $a_s = 8.68$, $b_s = 4.87$, $c_s = 2.55$ Å, $\beta_s = 124.1$.

The carboxylic acid at each terminus is linked to form a cyclic dimer by an intermolecular hydrogen bond, as shown in Figure 4c. The torsion angles around the C = O,C —O, and O···O bonds indicate that the dimer adopts a chair-type conformation (Fig. 5). This distorted conformation is quite different from the planar one normally found in carboxylic acids [20]. The one-dimensional hydrogen-bond network of the dimer extends infinitely along the backbone chain. Thus, bolaamphiphile **1** forms a linear polymolecular chain along the *c*-axis [8].

Three-dimensional hydrogen-bond networks involving two amide groups are shown in Figure 6. The hydrogen bond distances and angles between the amide groups are summarized in Table IV along with those for related compounds. The Bolaamphiphile **1** links to six closest neighbors *via* eight hydrogen bonds in a pseudo-hexagonal lattice. The O4 = C5 —N2 and O4* = C5* —N2* amide groups adjacent to the alkylene chain from intermolecular hydrogen bonds with the neighboring two molecules (Fig. 6c). The angle of C5 = O4···N2' is 175.5°, indicating that this network is almost planar and can be designated as a translation motif [21]. The distances and the angles of the N—H···O hydrogen bond geometry are similar to those of *N*-propyldipropylacetamide [22]. On the other hand, the O3 = C3 —N1 and O3* = C3* — N1* amide groups of the glycylglycine link to the neighboring four molecules (Fig. 6d). The angle of C3 = O3···N1' (139°) indicates non-planar network of the hydrogen-bond chain

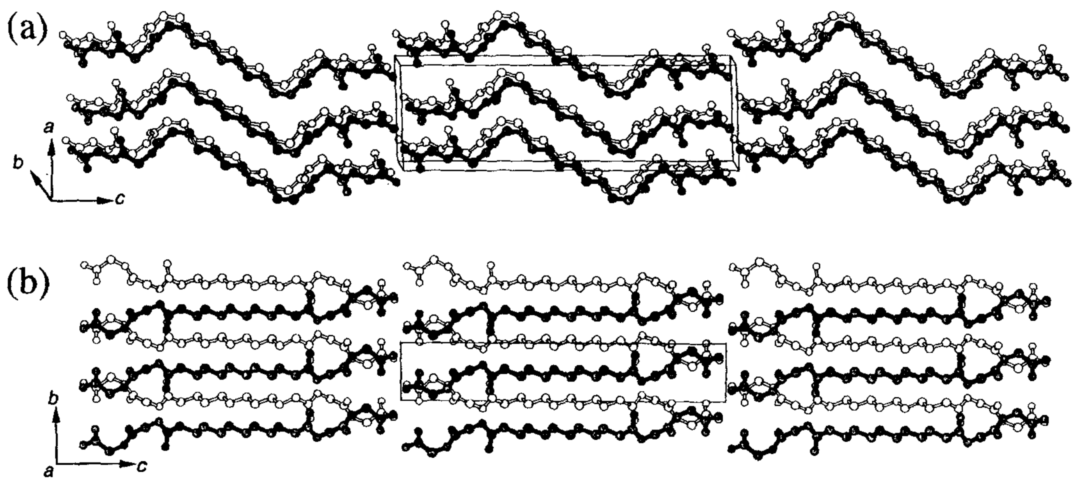


FIGURE 4 Layered structure of 1; (a) viewed along the *b*-axis, (b) the *a*-axis, and (c) hydrogen-bond scheme around the terminal glycylglycine moieties. Hydrogen bonds are drawn by dashed line.

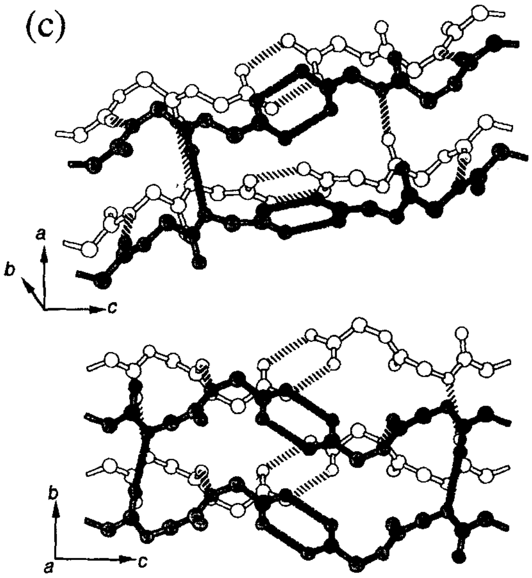


FIGURE 4 (Continued).

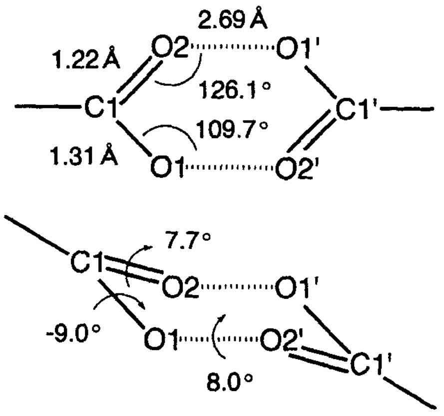


FIGURE 5 Bond distances (Å), bond angles (°), and torsion angles (°) of the cyclic dimer made of two carboxyl groups in 1.

designated as a glide motif [21]. Similar hydrogen bonding can be observed for *N*-bromoacetamide [23]. These amide hydrogen bonds out of the carbonyl plane are responsible for the formation of the pseudo-hexagonal lattice. It is well-known that polyglycine II can adopt a hexagonal array where hydrogen bonds are formed in three directions at angles of 120° [18]. Navarro *et al.* has recently reported that the dicarboxamide derivatives having a glycine residue also adopt a polyglycine II-type lattice that is not based on the polymolecular chain [24]. Thus, the present supramolecular crystal structure can provide the first example of a polyglycine II-type structure made of noncovalent polymolecular chains.

It is well documented that the oxalamide and urea derivatives of glycylglycine also adopt a

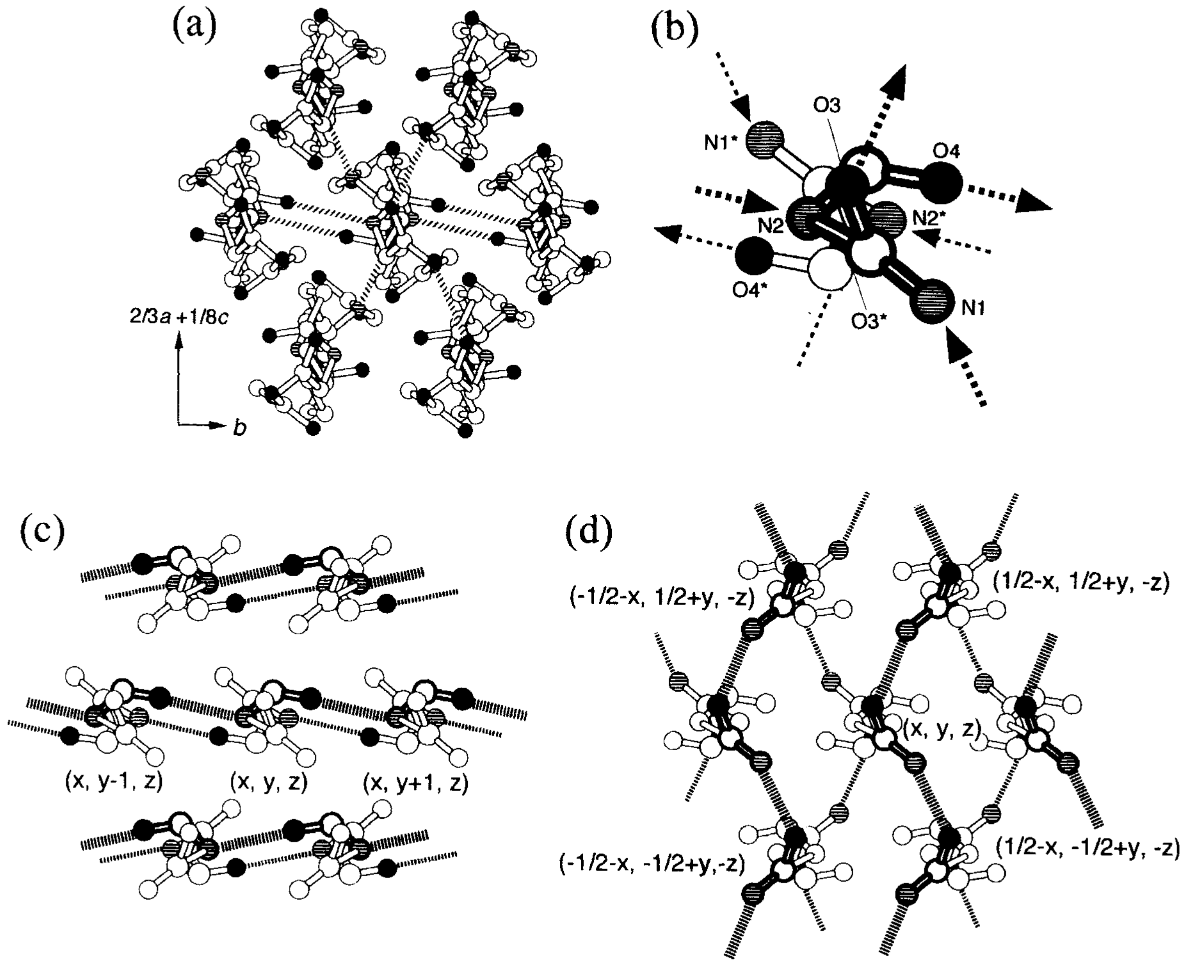


FIGURE 6 (a) Polyglycine II-type structure of **1** stabilized by three-dimensional hydrogen-bonded networks. (b) Eight hydrogen-bonds formed between the central molecule and its six neighbors. (c) Hydrogen-bond chain in the translation motif, formed between the amide goups adjacent to the alkylene chain. (d) Hydrogen-bond chain out of the carbonyl plane in the glide motif formed between the amide groups of the glycylglycine moieties. Only four amide groups are drawn for clarity in Figures 7(b), 7(c), and 7(d).

TABLE IV Hydrogen-bond distances (Å) and angles (°) with symmetry code[a]

Compound	Hydrogen-bond motif	Distance (Å) N···O	Angles (°) C=O···N	C—N···O
Bolaamphiphile 1				
$\mathrm{N1-H\cdots O3'}$(*i*)	glide	2.834(4)	139.1	127.8
$\mathrm{N2-H\cdots O4'}$(*ii*)	translation	2.871(4)	175.5	117.0
$\mathrm{C1=O2\cdots O1'}$	translation	2.693 [b]	126.1 [c]	109.7 [d]
N-Bromoacetamide [25]				
$\mathrm{N-H\cdots O'}$	glide	2.784	149.2	121.7
N-propyldipropylacetamide [26]				
$\mathrm{N-H\cdots O'}$	translation	2.865	177.0	118.4
Oxalamide of GlyGly [30]				
$\mathrm{N-H\cdots O\cdots O'}$	translation	2.762	174.7	116.9
$\mathrm{N-H\cdots O'}$	translation	2.854	167.8	134.4

[a] (*i*) (−1/2−x, 1/2+y, −z), (−1/2+x, −1/2−y, −z), (1/2−x, 1/2+y, −z), and (1/2−x,−1/2+y, −z). (*ii*) (x, y − 1, z) and (x, y+1, z).
[b] The $\mathrm{O2\cdots O1'}$ distance.
[c] The $\mathrm{C1=O2\cdots O1'}$ angle.
[d] The $\mathrm{C1-O1\cdots O2'}$ angle.

pseudo-hexagonal lattice [25–28]. The oxalamide and urea of glycylglycine forms hydrogen-bonds with four of six neighbouring molecules *via* amide groups. The observed hydrogen-bond motif is translational and planar. Therefore, it is quite intersting that glycylglycine bolaamphiphile **1** forms hydrogen-bonded networks by using both the translation (planar) and the glide (non-planar) motifs. This is why the bolaamphiphile **1** constructs a polyglycine II-type structure.

Acknowledgments

This work was partly supported by the New Energy and Industrial Technology Development Organization (Advanced Industrial Technology Research, "Synthesis of Polymer Objects").

References

[1] For example, see; (a)Lehn, J.-M. (1990). *Angew. Chem. Int. Ed. Engl.*, **29**, 1304. (b)Whitesides, G. M., Mathias, J. P. andSeto, C. T. (1991). *Science*, **254**, 1312. (c)Philp, D. andStoddart, J. F. (1996). *Angew. Chem. Int. Ed. Engl.*, **35**, 1154.
[2] For example, see; (a)Geib, S. J., Vicent, C., Fan, E. and Hamilton, A. D. (1993). *Angew. Chem. Int. Ed. Engl.*, **32**, 119. (b)Ghadiri, M. R., Granja, J. R., Milligan, R. A., McRee, D. E. and Khazanovich, N. (1993). *Nature*, **366**, 324. (c)Kimizuka, N., Kawasaki, T., Hirata, K. and Kunitake, T. (1995). *J. Am. Chem. Soc.*, **117**, 6360.
[3] Miyazawa, T. (1962). in *Polyamino Acids, Polypeptides and Proteins*, Wisconsin Univ. Press, Madison.
[4] Lotz, B., Brack, A. and Spach, G. (1974). *G. J. Mol Biol.*, **87**, 193.
[5] Traub, W. and Yonath, A. (1966). *J. Mol. Biol.*, **16**, 404.
[6] (a)Puiggalí, J., Muñoz-Guerra, S. and Lotz, B. (1986). *Macromolecules*, **19**, 1119; (b) Puiggalí, J., Muñoz-Guerra, S. andSubirana, J. A. (1987). *Polymer*, **28**, 209; (c) Bella, J. andPuiggalí, J., Subirana, J. A. (1994). *Polymer*, **35**, 1291.
[7] Shimizu, T., Masuda, M. and Kogiso, M. (1996). *Nature*, **383**, 487.
[8] Shimizu, T., Masuda, M. andKogiso, M. (1997). *J. Am. Chem. Soc.*, **119**, 6209.
[9] Masuda, M. andShimizu, T. (1996). *Chem. Commun.*, 1057.
[10] Masuda, M. andShimizu, T. (1997). *Carbohydr. Res.*, **302**, 139.
[11] Shimizu, T. andMasuda, M. (1997). *J. Am. Chem. Soc.*, **119**, 2812.
[12] Shimizu, T., Masuda, M. andShibakami, M. (1997). *Chem. Lett.*, No. 3, 267.
[13] Harkema, S., Gaymans, R. J. andVan Hummel, G. J. (1983). *Acta Crystallogr. Sect. Cryst. Struct. Commun.*, **39**, 385.
[14] Valiyaveettil, S., Enkelmann, V., Moebner, G. andMüllen, K. (1996). *Macromol. Symp.*, **102**, 165.
[15] Biswas, A. B., Hughes, E. W., Sharma, B. D. and Wilson, J. N. (1968). *Acta Crystallogr.*, **B24**, 40.
[16] Hughes, E. W. and Moore, W. J. (1949). *J. Am. Chem. Soc.*, **71**, 2618.
[17] Sudbeck, E. A., Etter, M. C. and Gleason, W. B. (1994). *Chem. Mater.*, **6**, 1192.
[18] Crick, F. H. C. and Rich, A. (1955). *Nature*, **176**, 780.
[19] Vand, V. (1951). *Acta Cryst.*, **4**, 104.
[20] Leiserowitz, L. (1976). *Acta Cryst.*, **B32**, 775.
[21] Leiserowitz, L. and Tuval, M. (1978). *Acta Cryst.*, **B34**, 1230.
[22] Dubey, R. J. (1971). *Acta Cryst.*, **B27**, 23.
[23] Cohen, C.-A. and Grand, A. (1974). *Acta Cryst.*, **B30**, 186.
[24] Navarro, E., Tereshko, V., Subirana, J. A. andPuiggalí, J. (1995). *Biopolymer*, **36**, 711.
[25] Zhao, X., Chang, Y. L., Fowler, F. W. andLauher, J. W. (1990). *J. Am. Chem. Soc.*, **112**, 6627.
[26] Chang, Y. L., West, M. A., Fowler, F. W. and Lauher, J. W. (1993). *J. Am. Chem. Soc.*, **115**, 5991.
[27] Kane, J. J., Liao, R.-F., Lauher, J. W. and Fowler, F. W. (1995). *J. Am. Chem. Soc.*, **117**, 12003.
[28] Coe, S., Kane, J. J., Nguyen, T. L., Toledo, L. M., Wininger, E., Fowler, F. W. and Lauher, J. W. (1997). *J. Am. Chem. Soc.*, **119**, 86.