($CDCl_3$) δ 2.61 (s, 3 H), 4.63 (bs, 1 H), 4.73 (s, 2 H), 7.33 (s, 1 H); MS, *m/e* 129 (m^+).

2-Methyl-5-(chloromethyl)thiazole (9a).[12b] This compound was prepared according to the literature procedure. Starting with 1.8 g (13.95 mmol) of **8a**, we obtained 1.62 g (78.7%) of **9a** as a colorless solid on sublimation: mp 43–45 °C; IR (CH_2Cl_2) 2965, 1528, 1462, 1160, 965, 860 cm^{-1}; NMR ($CDCl_3$) δ 2.70 (s, 3 H), 4.75 (s, 2 H), 7.55 (s, 1 H).

Trimethyl(2-methyl-5-thiazolyl)ammonium Chloride (10a). This was prepared as described for **3**. Thus chloride **9a** (1.2 g, 8.13 mmol) afforded, after drying in vacuo, 1.5 g (89.3%) of **10a** as a crystalline hygroscopic solid: mp 176–183 °C dec; NMR (Me_2SO-d_6) δ 2.70 (s, 3 H), 3.46 (s, 9 H), 5.50 (s, 2 H), 8.05 (s, 1 H).

***anti-anti-* and *anti-syn*-[2.2](2,5)Thiazolophane (13a and 13b).** The chloride salt **10a** (1.35 g, 6.54 mmol) was converted with Ag_2O (1.1 g, 8.88 mmol) to the corresponding hydroxide **11a** and pyrolyzed as described for **6a** and **6b**. After removal of the solvent, the crude residue (435 mg) was chromatographed on silica gel (20 g). Elution with 10% methanol in $CHCl_3$ afforded a solid, which was found to be a mixture (1:1) of **13a** and **13b** by HPLC analysis. The two compounds were separated by preparative high-pressure liquid chromatography (Waters Prep LC, reverse phase, Partisil M9 10/50 ODS-3 column, acetonitrile solvent system), which afforded **13a** (123 mg, 17%) and **13b** (118 mg, 16.3%). An analytical sample of **13a**, was obtained by crystallization from hexane–chloroform: mp 240–245 °C dec; UV λ_{max} (95% EtOH) (log ε) 275 (3.84), 243.5 (3.95) nm; IR (KBr) 3050, 2960, 1500, 1420, 1270, 1110, 1090, 1076, 975, 842 cm^{-1}; NMR ($CDCl_3$) δ 3.33 (m, 8 H), 7.55 (s, 2 H); MS, *m/e* 222 (m^+), 111. Anal. Calcd for $C_{10}H_{10}N_2S_2$: C, 54.05; H, 4.50; N, 12.52; S, 28.82. Found: C, 53.89; H, 4.64; N, 12.45; S, 29.03.

An analytical sample of **13b** was prepared by crystallization from ethyl acetate: mp 222–225 °C dec; λ_{max} (95% EtOH) (log ε) 263.4 (3.97), 230 (3.82) nm; IR (KBr) 3050, 2910, 1590, 1500, 1430, 1285, 1110, 1160, 853, 825 cm^{-1}; NMR ($CDCl_3$) δ 3.23 (m, 4 H) 3.55 (s, 4 H), 7.52 (s, 2 H); MS *m/e* 222 (m^+), 111.

2-Methyl-5-(hydroxymethyl-d_2)thiazole (8b). Ester **7** (4.1 g, 23.97 mmol) was reduced with lithium aluminum deuteride[23] (1.0 g, 23.81 mmol) in dry tetrahydrofuran as described for the preparation of **8a**. After Kugelrohr distillation (bp 85–95 °C (2mm)) carbinol **8b** was obtained (2.4 g, 76.5%) as a light yellow oil: IR (CH_2Cl_2) 3595, 3260, 2914, 1535, 1460, 1300, 1180, 1162, 1086, 1047, 960, 868, 820 cm^{-1}; NMR ($CDCl_3$) δ 2.64 (s, 3 H), 3.83 (bs, 1 H), 7.35 (s, 1 H); MS; *m/e* 131 (m^+).

2-Methyl-5-(chloromethyl-d_2)thiazole (9b). Carbinol **8b** (2.3 g, 17.55 mmol) was converted to the corresponding deuterated chloro derivative **9b** as described.[12b] A colorless oil (2.47 g, 93%, bp 85–95 °C (10 mm)) was obtained. The oil solidified on standing for a day: mp 43–45 °C; IR (CH_2Cl_2) 2985, 1530, 1460, 1402, 1375, 1182, 1165, 1052, 964, 870 cm^{-1}; NMR ($CDCl_3$) δ 2.64 (s, 3 H), 7.51 (s, 1 H).

Trimethyl(2-(methyl-d_2)-5-thiazolyl)ammonium Chloride (10b). This was prepared as described for **3**. Thus, starting with 2.25 g (15.05 mmol) of chloride **9b**, we obtained 2.7 g (86%) of the crystalline hygroscopic salt **10b** mp 181–184 °C dec; NMR (M_2SO-d_6) δ 2.73 (s, 3 H), 3.40 (s, 9 H), 7.90 (s, 1 H).

***anti-anti-* and *anti-syn*-[2.2](2,5)Thiazolophane-d_4 (14a and 14b).** Chloride **10b** (2.3 g, 11.03 mmol) was treated with Ag_2O (2.2 g, 17.76 mmol) to generate the corresponding hydroxide **11b**, which was pyrolyzed as detailed for **6a** and **6b**. Purification of the crude reaction mixture was effected as described for **13a** and **13b** and afforded **14a** (193 mg, 15.5%) and **14b** (164 mg, 13.3%). **13a**: mp 239–244 °C dec (hexane–chloroform); IR (KBr) 2930, 1500, 1428, 1285, 1215, 1155, 994, 955, 840, 742, 719 cm^{-1}; NMR ($CDCl_3$) δ 3.33 (AB, q, 4 H, J = 15 Hz), 7.55 (s, 2 H); MS; *m/e* 226 (m^+), 113. **14b**: mp 222–225 °C dec (ethyl acetate); IR (KBr) 2925, 1500, 1430, 1315, 1270, 1145, 1108, 1062, 880, 847, 750, 715 cm^{-1}; NMR ($CDCl_3$) δ 3.55 (s, 4 H), 7.52 (s, 2 H); MS, *m/e* 226 (m^+), 113.

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Registry No. 1, 39755-31-2; **2**, 82190-68-9; **3**, 82190-69-0; **4**, 82190-70-3; **6a**, 82190-71-4; **6b**, 82190-72-5; **7**, 79836-78-5; **8a**, 56012-38-5; **8b**, 82190-73-6; **9a**, 63140-11-4; **9b**, 82190-74-7; **10a**, 82190-75-8; **10b**, 82190-76-9; **11a**, 82190-77-0; **11b**, 82190-78-1; **13a**, 82190-79-2; **13b**, 82190-80-5; **14a**, 82190-81-6; **14b**, 82190-82-7; diazomethane, 334-88-3; bromoacetyl bromide, 598-21-0; acetonitrile, 75-05-8; ethyl α-chloro-α-formylacetate, 33142-21-1; thioacetamide, 62-55-5.

(23) Supplied by Aldrich Chemical Co., 98% deuterium.

Crystal Structure of *cyclo*-(Gly-L-Pro-L-Pro-Gly-L-Pro-L-Pro) Trihydrate. Unusual Conformational Characteristics of a Cyclic Hexapeptide

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Abstract: The crystal structure of *cyclo*-(Gly-L-Pro-L-Pro-Gly-L-Pro-L-Pro) trihydrate, $C_{24}H_{34}O_6N_6 \cdot 3H_2O$, has been determined from single-crystal X-ray diffraction data. The phase problem was solved by direct methods. The space group is $P2_12_12_1$ with the dimensions a = 9.237 (4) Å, b = 13.972 (3) Å, c = 20.851 (3) Å, and Z = 4. The synthetic hexapeptide contains one transannular intramolecular C=O···NH hydrogen bond. In combination with three molecules of water, a coherent system of hydrogen bonds is formed in which also an intermolecular bifurcated hydrogen bond is present. Thus in the lattice parallel to the b axis, linear molecular chains are formed. The peptide backbone contains one cis Gly–Pro and one cis Pro–Pro linkage in consecutive positions. The most striking feature of the asymmetric conformation is, however, the occurrence of a hydrogen-bonded type I β-turn encompassing two trans-configured proline residues in the other half of the molecule. Concerning these linkages, the conformation of the cyclic hexapeptide in the present crystal differs from that in its Mg^{2+} complex.

As a part of systematic investigations into the biological activity, conformation, and complexing ability of antamanid analogues, Wieland and Hollósi have synthesized a series of cyclic peptides consisting of glycine and two pairs of L-proline only.[2] One of these model peptides, *cyclo*-(Gly-Pro-Pro-Gly-Pro-Pro) (thereafter GPPGPP), proved to be of particular interest for its CD spectrum does not show solvent dependence. The high selectivity of the cyclic hexapeptide for alkaline earth ions over alkali metal ions

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0002-7863/82/1504-4465$01.25/0

Table I. Crystallographic Data for *cyclo*-(Gly-L-Pro-L-Pro-Gly-L-Pro-L-Pro) Trihydrate

formula	$C_{24}H_{34}O_6N_6 \cdot 3H_2O$
formula wt	556.615
color	colorless transparent
habit	stubby prismatic
space group	$P2_12_12_1$
a, Å	9.237 (4)
b, Å	13.972 (3)
c, Å	20.851 (3)
V, Å^3	2691.02
Z	4
d(calcd), g/cm^3	1.373
radiation	Mo Kα
wavelength, Å	0.71073
no. of reflctns	2988

is also unique within the above series.[3]

By ^{1}H and ^{13}C NMR observations aided by the use of specifically ^{2}H-, ^{13}C-, and ^{15}N-labeled isotopomers,[4] GPPGPP was shown to preferentially assume asymmetric conformations in solution with one or two cis X–Pro bonds both in free and complexed form.[5] In the asymmetric conformer prevailing in Me_2SO-d_6 and D_2O solutions, the peptide skeleton is characterized by a two-cis–two-trans X–Pro geometry. ^{1}H NMR data and variable temperature and solvent titration experiments indicate the presence of only one intramolecular H bond between one of the glycine carbonyl O atoms and the NH of the other glycine residue. These data, however, did not determine unambiguously the place of the cis peptide linkages with respect to the intramolecular H bond.

Due to the difficulties arising from the asymmetry of the steric structures of GPPGPP, notwithstanding the constitutional symmetry of the molecule, the relationship between the conformations of the cyclic peptide in solution and in the solid state seemed to be of considerable interest. Recently, the crystal structure of the 2:1 complex of GPPGPP and Mg^{2+} has been reported by Karle and Karle.[6] In this paper we report the crystal structure and conformation of the uncomplexed cyclic hexapeptide.

Experimental Section

The cyclic hexapeptide GPPGPP crystallized from water was found to be stable in air. X-ray diffraction data were collected on an automatic four-circle diffractometer (Nonius CAD-4) with graphite monochromated Mo Kα radiation (λ = 0.71073 Å). Cell parameters were obtained from the setting angles of 25 reflections by a least-squares fit. The cell parameters and other pertinent data are listed in Table I. In the course of intensity measurement, the intensities of three standard reflections were monitored after every 0.5 h of exposure time. These did not show loss of intensity during the data collection. A total of 2988 independent reflections were measured, from which 545 were considered as unobserved ($I \leq 2\sigma(I)$). After Lorentz and polarization corrections, the normalized structure factors were derived with aid of the Wilson plot.

The phase problem was solved by direct methods using the program MULTAN[7] and applying 208 reflections of the highest E values ($E \geq 1.70$). The E map computed from a phase set with the best consistency gave a 24-atom fragment of the molecule. Remaining non-hydrogen atoms of the skeleton were subsequently found in Fourier syntheses. After three cycles of isotropic least-squares refinement ($R = 0.26$), the following difference electron density synthesis clearly indicated the presence of three additional solvent molecules in the lattice. Near the conclusion of the anisotropic refinement of the non-hydrogen atoms, all but the hydrogens of the >NH groups and water molecules were generated. The latter were taken from difference Fourier calculations. To yield better coordinates for all these hydrogen atoms, we refined their positional parameters against 1424 observations with $\sin\theta/\lambda \leq 0.49$. The final unweighted R factor is 0.034 for 2298 reflections ($I \geq 2.5\sigma(I)$). The labeling of atoms is given in an orthogonal projection of the unit cell on plane (100) (Figure 1). The final atomic parameters are listed in Tables II and III. Bond lengths and angles are listed in Table IV. The conformational angles of the hexapeptide molecule are in Table V.

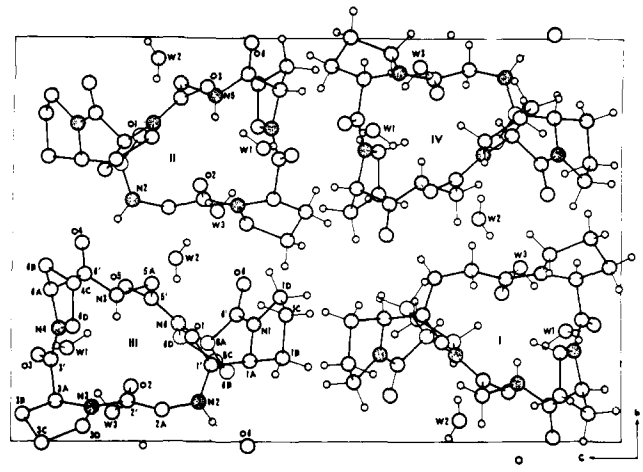

Figure 1. Orthogonal projection of the unit cell on plane (100) with labeling of atoms of the molecule in the third symmetry-related position. Intra- and intermolecular hydrogen bonds are assigned by dotted lines. Greek letters are replaced by Roman ones.

Table II. Fractional Coordinates and Isotropic Thermal Parameters (Å^2) with Standard Deviations in Parentheses

atom	x	y	z	B(eq)[a]
N_1	0.0749 (2)	0.2133 (1)	0.3969 (1)	3.4 (1)
C^{α}_1	0.1540 (3)	0.3040 (2)	0.3905 (1)	3.1 (1)
C'_1	0.2289 (3)	0.3141 (2)	0.3261 (1)	2.8 (1)
O_1	0.2724 (2)	0.2449 (1)	0.2949 (1)	3.7 (1)
C^{β}_1	0.2678 (3)	0.2967 (2)	0.4440 (1)	4.5 (1)
C^{γ}_1	0.2958 (4)	0.1900 (3)	0.4493 (2)	5.6 (2)
C^{δ}_1	0.1473 (4)	0.1457 (2)	0.4409 (1)	4.9 (1)
N_2	0.2511 (2)	0.4045 (1)	0.3065 (1)	3.0 (1)
C^{α}_2	0.3233 (3)	0.4246 (2)	0.2465 (1)	3.3 (1)
C'_2	0.2289 (3)	0.4020 (2)	0.1895 (1)	2.7 (1)
O_2	0.1067 (2)	0.3670 (1)	0.1953 (1)	3.3 (1)
N_3	0.2873 (2)	0.4164 (1)	0.1315 (1)	2.6 (1)
C^{α}_3	0.2011 (3)	0.4006 (2)	0.0732 (1)	2.8 (1)
C'_3	0.1440 (3)	0.3000 (2)	0.0646 (1)	2.5 (1)
O_3	0.0194 (2)	0.2897 (1)	0.0441 (1)	3.3 (1)
C^{β}_3	0.3029 (3)	0.4324 (2)	0.0191 (1)	3.6 (1)
C^{γ}_3	0.4037 (3)	0.5039 (2)	0.0506 (1)	4.0 (1)
C^{δ}_3	0.4272 (3)	0.4637 (2)	0.1178 (1)	3.7 (1)
N_4	0.2269 (2)	0.2232 (1)	0.0778 (1)	2.5 (1)
C^{α}_4	0.1699 (3)	0.1272 (2)	0.0645 (1)	2.9 (1)
C'_4	0.0755 (3)	0.0885 (2)	0.1186 (1)	2.8 (1)
O_4	0.0169 (2)	0.0104 (1)	0.1130 (1)	4.0 (1)
C^{β}_4	0.3070 (3)	0.0684 (2)	0.0544 (1)	3.6 (1)
C^{γ}_4	0.4144 (3)	0.1124 (2)	0.1008 (1)	3.9 (1)
C^{δ}_4	0.3792 (3)	0.2193 (2)	0.0998 (1)	3.0 (1)
N_5	0.0677 (2)	0.1426 (1)	0.1713 (1)	3.0 (1)
C^{α}_5	−0.0086 (3)	0.1139 (2)	0.2288 (1)	3.2 (1)
C'_5	−0.1628 (3)	0.1508 (2)	0.2280 (1)	3.2 (1)
O_5	−0.2469 (2)	0.1218 (1)	0.1858 (1)	4.1 (1)
N_6	−0.2054 (2)	0.2124 (2)	0.2727 (1)	3.3 (1)
C^{α}_6	−0.1125 (3)	0.2600 (2)	0.3207 (1)	3.4 (1)
C'_6	−0.0503 (3)	0.1890 (2)	0.3684 (1)	3.4 (1)
O_6	−0.1130 (3)	0.1141 (1)	0.3806 (1)	5.3 (1)
C^{β}_6	−0.2165 (4)	0.3296 (3)	0.3525 (2)	6.8 (1)
C^{γ}_6	−0.3585 (4)	0.3043 (4)	0.3338 (2)	7.5 (1)
C^{δ}_6	−0.3561 (3)	0.2468 (2)	0.2756 (2)	4.3 (1)
OW_1	−0.2647 (2)	0.2724 (2)	0.0903 (1)	5.1 (1)
OW_2	0.3591 (2)	0.0524 (2)	0.2664 (1)	6.0 (1)
OW_3	−0.1805 (3)	0.4310 (2)	0.1656 (1)	7.2 (1)

[a] B(eq) is a value derived from the six anisotropic temperature coefficients associated with each atom. It is defined by the following: $B(\text{eq}) = {}^4/_3 \Sigma_i \Sigma_j \beta_{ij} \vec{a}_i \vec{a}_j$.

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Table III. Fractional Coordinates of the Relevant Hydrogen Atoms

atom	x	y	z
HN_2	0.217 (4)	0.453 (2)	0.330 (1)
HN_5	0.101 (4)	0.195 (2)	0.171 (2)
H_1W_1	−0.264 (4)	0.236 (2)	0.124 (1)
H_2W_1	−0.190 (3)	0.267 (2)	0.074 (1)
H_1W_2	0.317 (4)	0.103 (2)	0.270 (2)
H_2W_2	0.298 (3)	0.011 (2)	0.285 (1)
H_1W_3	−0.091 (4)	0.411 (2)	0.180 (1)
H_2W_3	−0.201 (4)	0.384 (2)	0.142 (1)

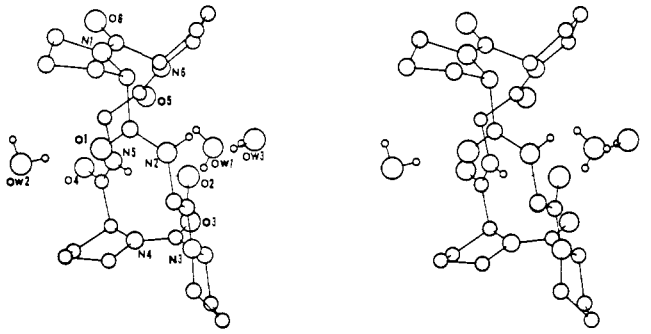
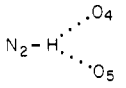


Figure 2. Stereodrawing of the molecule with the related three water molecules.

Results

The macro ring of the molecule is fairly distorted (Figure 2) and adopts a shape where the adjoining hydrophilic atoms point outward from the ring with the exception of N_5 and O_2 atoms. This arrangement differs from the widely recognized form of other ionophore oligopeptides[8] where the hydrophilic entities are generally directed toward the center, thus supporting CH_2 groups to form a lipophilic skin on the surface of these molecules.

In the cyclic hexapeptide molecule, there is one 4→1 transannular $C'_2{=}O_2{\cdots}HN_5$ hydrogen bond encompassing Pro_3 and Pro_4 residues (Figure 1). There is also an intermolecular bifurcated hydrogen bond maintained by



Both are rather weak. The molecule is accompanied by three molecules of solvation, which together with the two mentioned hydrogen bonds form a coherent system of hydrogen bonds (Figure 3 and Table VI). With the aid of these bonds, linear molecular chains are built up parallel to the *b* axis and may play an important role in forming the crystal lattice. The conformation of the cyclic hexapeptide molecule differs from that of *cyclo*-(Gly-L-Pro-L-Pro-Gly-L-Pro-L-Pro)$_2Mg^{2+}$ complex (thereafter $(GPPGPP)_2Mg$), which has been reported recently.[6] In the crystal structure of the complex, the molecule has two cis Pro–Pro linkages while in the present uncomplexed form there is one cis Gly_5–Pro_6 and one cis Pro_6–Pro_1 peptide linkage. All other peptide units have trans configuration with essentially planar amide linkages (Table V).

Upon comparison of the conformational angles with the corresponding ones in the crystal structure of $(GPPGPP)_2Mg$, there is no essential difference for the $\phi_i(N_i{-}C^{\alpha}_i)$ angles, but the $\psi_i(C^{\alpha}_i{-}C'_i)$ angles differ for both the Gly_2-Pro_3 and the Pro_3-Pro_4 sequences. Similar differences are found for some of the $\omega_i(C'_i{-}N_{i+1})$ angles, which originate from the fact that one of the cis Pro–Pro linkages in the $(GPPGPP)_2Mg$ complex is in the present uncomplexed hexapeptide replaced by the cis peptide linkage of the Gly_5-Pro_6 sequence (Table V and Figure 4).

The conformational angles ϕ and ψ of Pro_3 and Pro_4 (Table V) compare well with those given by Venkatachalam, as approximate values for a bend type I (−60°, −90° and −30°, 0°, respectively).[9] In *N*-acetyl-*N'*-methylamides of trans-configured

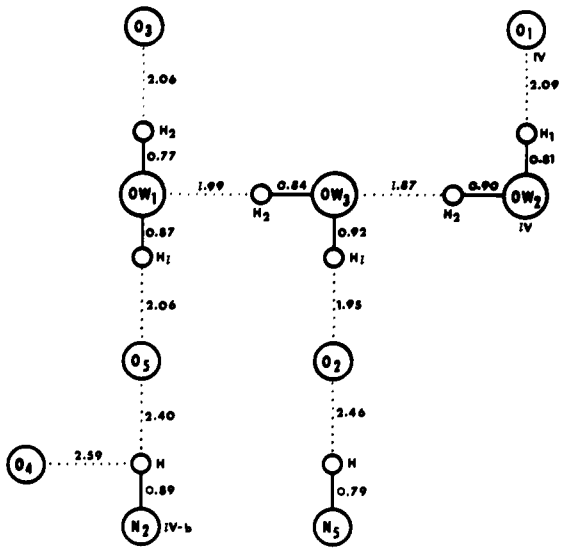


Figure 3. Scheme of the coherent system of hydrogen bond in the crystal lattice.

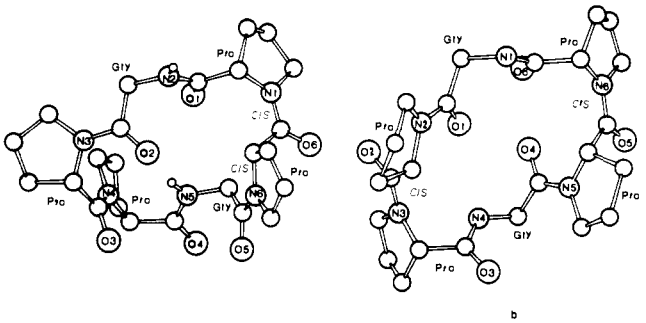


Figure 4. The two conformations of the cyclic hexapeptide *cyclo*-(Gly-L-Pro-L-Pro-Gly-L-Pro-L-pro) molecule: (a) in the title crystal; (b) in the Mg^{2+} complex crystal.[6]

X-Pro dipeptides, this type of β turn was shown by Scheraga et al. to be of rather high energy due to the conformational limitations imposed by the pyrrolidine ring on the Pro residue itself and the residue that precedes it.[10] In agreement with the above results, proline residue has been observed to occur in the second corner position of a β turn in crystalline cyclic peptides only once so far. A β turn of type II' encompassing a Gly-L-Pro sequence was found in the conformation of the cyclic pentapeptide *cyclo*-(Gly-L-Pro-L-Ser-D-Ala-L-Pro).[11] More unexpectedly, both corner positions of a *β-turn type I* are occupied by proline residues in the title compound. This is the first observation in a crystal of a Pro-Pro sequence in a β turn even if with a weak hydrogen bond (Table VI). The other unique feature of the conformation is the location of the cis X–Pro bonds in the other half of the asymmetric peptide backbone. The ϕ and ψ values of consecutive cis-configured Pro residues are rather close to those reported for poly(proline I).[12]

In the crystal structure of GPPGPP, the β-turn type I conformation seems to be stabilized by the coherent system of hydrogen bonds (especially by the water-promoted hydrogen bridges formed between the carbonyls of Pro_3 and Pro_6) rather than by the weak 4→1 transannular hydrogen bond. The question is whether the same type of intramolecular hydrogen bond is involved in stabilizing the predominant asymmetric conformation of the cyclic hexapeptide in polar solvents or whether the solution conformation is fixed by other possible types of hydrogen bonding (type VI bend with a cis peptide bond between two proline residues). In the latter case, however, the crystallization should be

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Table IV. Bond Lengths (Å) and Angles (Deg) with Standard Deviations in Parentheses

	Pro_1	Gly_2	Pro_3	Pro_4	Gly_5	Pro_6
			Bonds			
N_i–$C^{\alpha}{}_i$	1.469 (3)	1.445 (3)	1.470 (3)	1.467 (3)	1.447 (3)	1.477 (3)
$C^{\alpha}{}_i$–C'_i	1.517 (3)	1.508 (3)	1.512 (3)	1.525 (3)	1.515 (4)	1.518 (4)
C'_i–O_i	1.233 (3)	1.236 (3)	1.236 (3)	1.224 (3)	1.242 (3)	1.223 (3)
C'_i–N_{i+1}	1.343 (3)	1.339 (3)	1.347 (3)	1.336 (3)	1.328 (3)	1.344 (3)
$C^{\alpha}{}_i$–$C^{\beta}{}_i$	1.536 (3)		1.534 (3)	1.524 (4)		1.519 (4)
$C^{\beta}{}_i$–$C^{\gamma}{}_i$	1.517 (5)		1.515 (4)	1.516 (4)		1.413 (5)
$C^{\gamma}{}_i$–$C^{\delta}{}_i$	1.515 (5)		1.525 (3)	1.529 (4)		1.456 (6)
$C^{\delta}{}_i$–N_i	1.477 (3)		1.479 (3)	1.481 (3)		1.474 (3)
			Angles			
C'_{i-1}–N_i–$C^{\alpha}{}_i$	127.3 (3)	121.1 (3)	120.4 (3)	119.1 (3)	123.4 (3)	126.5 (3)
N_i–$C^{\alpha}{}_i$–C'_i	112.8 (4)	112.0 (4)	115.3 (4)	112.9 (4)	110.8 (4)	111.7 (4)
$C^{\alpha}{}_i$–C'_i–N_{i+1}	115.2 (4)	116.6 (4)	121.2 (4)	116.0 (4)	119.4 (4)	116.8 (4)
$C^{\alpha}{}_i$–C'_i–O_i	122.9 (4)	122.3 (4)	118.3 (4)	119.9 (4)	119.0 (4)	121.1 (4)
N_{i+1}–C'_i–O_i	121.8 (4)	121.0 (4)	120.5 (4)	124.0 (4)	121.6 (4)	122.1 (4)
C'_i–$C^{\alpha}{}_i$–$C^{\beta}{}_i$	109.7 (4)		113.3 (4)	112.7 (4)		111.8 (4)
N_i–$C^{\alpha}{}_i$–$C^{\beta}{}_i$	102.5 (3)		103.4 (3)	102.7 (3)		102.5 (4)
$C^{\alpha}{}_i$–$C^{\beta}{}_i$–$C^{\gamma}{}_i$	103.6 (4)		104.4 (4)	103.7 (4)		107.8 (5)
$C^{\beta}{}_i$–$C^{\gamma}{}_i$–$C^{\delta}{}_i$	103.8 (4)		104.1 (4)	104.4 (4)		110.7 (6)
$C^{\gamma}{}_i$–$C^{\delta}{}_i$–N_i	102.7 (4)		102.6 (3)	104.0 (3)		103.2 (5)
$C^{\delta}{}_i$–N_i–$C^{\alpha}{}_i$	112.5 (3)		112.4 (3)	111.5 (3)		112.0 (3)
$C^{\delta}{}_i$–N_i–C'_{i-1}	120.2 (4)		126.4 (3)	129.3 (3)		121.3 (4)

Table V. Conformational Angles (Deg)[a]

angle	Pro_1	Gly_2	Pro_3	Pro_4	Gly_5	Pro_6
$\phi_i(N_i$–$C^{\alpha}{}_i)$	−73.3 (4)	72.5 (4)	−60.1 (4)	−84.3 (4)	−92.9 (4)	−66.6 (4)
$\psi_i(C^{\alpha}{}_i$–$C'_i)$	154.0 (4)	−178.7 (4)	−41.6 (4)	−5.1 (3)	−117.2 (4)	154.2 (4)
$\omega_i(C'_i$–$N_{i+1})$	179.1 (5)	−177.1 (5)	−175.9 (5)	−175.6 (5)	8.0 (4)	4.5 (4)
χ_{i1}	30.1 (3)		−25.8 (3)	34.8 (3)		13.0 (5)
χ_{i2}	−39.1 (4)		36.5 (3)	−36.1 (3)		−20.3 (5)
χ_{i3}	32.0 (3)		−32.3 (3)	23.1 (3)		18.3 (5)
χ_{i4}	−13.3 (3)		16.7 (3)	−1.1 (3)		−9.5 (4)
$C^{\delta}{}_iN_iC^{\alpha}{}_iC^{\beta}{}_i$	−10.5 (3)		5.5 (3)	−21.0 (3)		−1.8 (4)
θ''_i=$C^{\delta}{}_iN_iC^{\alpha}{}_iC'_i$	107.4 (4)		129.7 (4)	100.7 (4)		118.1 (4)
$\theta''_i - \phi_i$	180.7		189.8	185.0		184.7
			Cremer and Pople Puckering Parameters[13]			
Q, Å	0.376		0.354	0.360		0.178
φ(m), deg	88		262	105		259

angle	Pro_6	Gly_1	Pro_2	Pro_3	Gly_4	Pro_5
ω_i, deg[b]	178	−176	11	−178	−174	−1
	177	178	15	179	−174	−2

[a] The convention followed for labeling conformation angles is that proposed by the IUPAC-IUB Commission on Biochemical Nomenclature, *Biochemistry*, **1970**, *9*, 3471. [b] The corresponding $\omega_i(C'_i$–$N_{i+1})$ values of the two independent Mg^{2+} complexed molecules.[6] Consider that serial numbers are shifted by one relative to those in the title crystal.

Table VI. Hydrogen Bonds[a,b]

A–H···B	A–H, Å	H···B, Å	A–B, Å	∠A–H···B, deg
N_5–HN_5···O_2	0.79	2.46	3.195	155.3
N_2–HN_2···O_5(IV)	0.89	2.40	3.041	129.1
N_2–HN_2···O_4(IV)	0.89	2.59	3.337	141.2
OW_1–H_1W_1···O_5	0.87	2.06	2.902	164.3
OW_1–H_2W_1···O_3	0.77	2.06	2.806	163.3
OW_2–H_1W_2···O_1	0.81	2.09	2.869	160.9
OW_2–H_2W_2···OW_3(IV − *b*)	0.90	1.87	2.758	172.2
OW_3–H_1W_3···O_2	0.92	1.95	2.867	170.4
OW_3–H_2W_3···OW_1	0.84	1.99	2.825	175.3

[a] Standard deviations are of the order of 0.03 Å for distances and 2.3° for angles. [b] Symmetry-related positions: I, *x*, *y*, *z*; II, $^1/_2 - x$, $-y$, $^1/_2 + z$; III, $^1/_2 + x$, $^1/_2 - y$, $-z$; IV, $-x$, $^1/_2 + y$, $^1/_2 - z$; the letter with the sign after the Roman numeral means the shift of the atom parallel to the corresponding crystallographic axis.

accompanied by a conformational transition requiring the isomerization of the two peptide bonds. Therefore, though energetically unfavorable in small linear peptides with two Pro residues in consecutive corner positions, the bend type I stabilized by both an intramolecular hydrogen bond and specific solvent interactions is likely to occur also in the solution conformation of GPPGPP.

The pyrrolidine rings are to some extent twisted and approximate the C_2 symmetry (half-chair) in Pro_1 and Pro_3 and the C_s symmetry (envelope) in Pro_4 and Pro_6, with the symmetry elements passing through N_1, N_3 and $C^{\beta}{}_4$, $C^{\gamma}{}_6$, respectively. The extent of puckering of the ring is very similar in Pro_1, Pro_3, and Pro_4 but more reduced in Pro_6 (Table V). A similar puckering of the pyrrolidine rings has been found in the $(GPPGPP)_2Mg$ crystal. The C′ and O atoms of the proline moieties are out of the best planes of the pyrrolidine rings with deviations greater than 1.33 and 1.95 Å, respectively, with the exception of Pro_3, occupying the $i + 1$ position of the β turn, for which these deviations are extremely low (0.81 and 0.37 Å, respectively). Similarly low deviation can be found in the corresponding Pro residue of both independent molecules in the $(GPPGPP)_2Mg$ crystal but interestingly only for the C′ atoms. According to the classification proposed by Ashida and Kakudo,[14] the pyrrolidine ring of Pro_3

(13) Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354–1358.

with negative χ_1 torsion angle adopts the B form, and the other three rings with positive χ_1 values adopt the A form (Table V). In the $(GPPGPP)_2Mg$ crystal, however, instead of one, there are two pyrrolidine rings of each independent molecule that adopt the B form.

The pyramidality of the N atoms of the proline moieties of the molecule is negligible as their deviations from the planes formed by their immediate three neighbor atoms are less than 0.08 Å. Moreover the difference of the two torsion angles $(\theta''_i - \phi_i)$, which gives a measure of the coplanarity of the bonds connected to the N atom, approximates 180° for each proline unit with a maximum deviation of 9.8° (Table V).

C–C bond lengths in the pyrrolidine rings vary between 1.515 and 1.536 Å with the exception of $C^{\beta}_6 - C^{\gamma}_6$ and $C^{\gamma}_6 - C^{\delta}_6$, which have been found to be as short as 1.413 and 1.456 Å, respectively (Table IV). These extraordinarily short bond lengths may be partly attributed to the high thermal vibration or unresolved positional disorder of C^{β}_6 and C^{γ}_6. It is noteworthy to mention that for the same pyrrolidine ring in both independent molecules of the $(GPPGPP)_2Mg$ complex these two bonds show similar deviations with values of 1.449 and 1.499 Å, respectively. The N–C^{α} bond lengths in the two glycine units 1.445 and 1.447 Å are shorter than those in the pyrrolidine rings, for which the average N–C^{α} bond length is 1.471 Å with a maximum deviation of 0.006 Å. This difference of N–C^{α} bonds in glycine and proline units is not so firmly expressed in the crystal structure of $(GPPGPP)_2Mg$ complex whereas the individual values show some deviations.

Similar to the bond lengths, the corresponding bond angles of the different peptide units also show smaller deviations in the uncomplexed hexapeptide than in the complexed one, but when the average values of the same angles are taken, they are nearly the same in both structures.

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Supplementary Material Available: Listing of observed and calculated structure factors as well as tables of anisotropic thermal parameters of non-hydrogen atoms, coordinates of hydrogen atoms, best planes of the pyrrolidine rings and glycine moieties of the molecule together with their dihedral angles, pyramidality of the N atoms of the proline moieties, and intermolecular contact distances other than hydrogen bonds (26 pages). Ordering information is given on any current masthead page.

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Kinetic Studies on the Formation of Two Intramolecular Excimers in Substituted Dinaphthylpropanes

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Abstract: The emission properties of 1,3-bis(4-methoxy-1-naphthyl)propane (BMNP) and 1,3-bis(4-hydroxy-1-naphthyl)propane (BHNP) have been investigated in fluid solution. They exhibit, in addition to the monomer fluorescence, two structureless emissions derived from two different types of excimer: a normal excimer and a second excimer, the latter having a partially overlapping structure of aromatic rings. The kinetic analysis of transient decay curves for the fluorescence of BMNP showed that the second excimer is not formed from or converted to the normal excimer and that the two are formed independently from the excited monomer. Some activation energies and rate constants were determined. The activation energy for the second excimer formation was found to be smaller than that of the normal excimer formation.

Numerous investigations of a so-called second excimer in poly(*N*-vinylcarbazole) (PVCz) and its derivatives in fluid solution have been reported.[1-7] While the stable "normal excimer" configuration is reported to be a symmetrical sandwich arrangement,[8] the second excimer may have a partially overlapped sandwich structure of two aromatic rings.[3,4] The emission characteristics of such excimers must be sensitive to the structure and conformation of polymers, and actually there exists a significant difference in emission between isotactic-rich PVCz derivatives and ones rich in syndiotactic structure.[3,4,6,7] However, the elucidation of the second excimer formation and its application to investigate the conformation of polymers should be clearly distinguished, because of the possible occurrence of energy migration and other complicating phenomena in polymers.

A useful approach for studying the intramolecular excimer formation in vinyl polymers, which is inherently complex due to a large number of possible configurations, is to consider first simpler model systems in which two chromophores are attached to 1,3-positions of a propane chain. Investigations of such dimer models corresponding to the "$n = 3$ rule", first studied by Hirayama for diphenyl- and triphenylalkanes,[9] have been carried out for dinaphthylalkanes by Chandross and Dempster,[8] for 1,3-bis(*N*-carbazoyl)propane by Klöpffer[10] and Johnson,[11] and for dipyrenylalkanes by Zachariasse.[12] However, the dimer models

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