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# Elementary Patterns in Protein–Nucleic Acid Interactions. VI. Structure of 3-(7-Adeninyl)propionamide Monohydrate, $C_8H_{10}N_6O.H_2O$

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**Abstract.** $M_r = 224.2$, monoclinic, $P2_1/c$, $a = 9.850\,(1)$, $b = 28.326\,(1)$, $c = 7.261\,(1)$ Å, $\beta = 96.63\,(1)°$, $V = 2012.4$ Å$^3$, $D_m = 1.48$, $D_x = 1.480$ Mg m$^{-3}$, $Z = 8$, $\lambda(\text{Cu } K\alpha) = 1.54184$ Å; $R = 0.057$ for 3079 diffractometer-measured intensities. The two independent molecules in the asymmetric unit form a dimer, with hydrogen bonds between the carbamoyl group of one molecule and the adenine N(1) of another. This NH···N hydrogen bond may suggest a strong affinity of the carbamoyl group for adenine N(1).

**Introduction.** As part of a study on elementary patterns of interaction between amino acid residues and purine–pyrimidine bases, the title compound was prepared by esterification followed by ammonolysis of 3-(7-adeninyl)propionic acid which is obtained together with 3-(9-adeninyl)propionic acid and 3-(7-adeninyl)-propionic acid lactam in the reaction reported by Kondo, Sato & Takemoto (1973).

**Experimental.** Prismatic crystals (from a methanol–water solution), 0·5 × 0·25 × 0·05 mm, $D_m$ by flotation in a mixture of cyclohexane and carbon tetrachloride, Weissenberg photographs showed systematic absences ($h0l$ $l$ odd, $0k0$ $k$ odd) of $P2_1/c$; Rigaku automated four-circle diffractometer, Ni-filtered Cu $K\alpha$ radiation ($\lambda = 1.54184$ Å); unit-cell dimensions determined by least squares with the $2\theta$ values of 48 high-angle reflexions; intensity data in the range $5° < 2\theta < 122°$ collected by means of $\omega/2\theta$ scanning, scan speed 8° ($2\theta$) min$^{-1}$, scan width 0·8° ($\omega$) plus $\alpha_1$–$\alpha_2$ divergence; five reference reflexions monitored periodically showed no significant intensity deterioration; no absorption correction; 3079 measured independent reflexions, 231 with no net intensities; observational threshold value $F_{\text{lim}} = 1.03$; standard deviations estimated by $\sigma^2(F_o) = \sigma_p^2(F_o) + qF_o^2$ with $\sigma_p(F_o)$ evaluated from counting statistics and $q$ ($1.99 \times 10^{-5}$) from variations of monitored reflexions (McCandlish & Stout, 1975); structure solved by direct methods, anisotropic block-diagonal least-squares, $\sum w(|F_o| - |F_c|)^2$ minimized, $w = 1/\sigma^2(F_o)$; H (from difference map) isotropic; zero reflexions (with $|F_c| > F_{\text{lim}}$) included in least-squares calculation by assuming $F_o = F_{\text{lim}}$ and $w = \sigma(F_{\text{lim}})$; final $R = 0.057$ for 3079 measured reflexions ($wR = 0.054$), maximum shift of parameters in the last cycle $0.1\sigma$; atomic scattering factors from *International Tables for X-ray Crystallography* (1974); $F(000) = 944$.

**Discussion.** Atomic parameters are listed in Table 1.* Bond distances and angles in molecules *A* and *B* are shown in Fig. 1. The values in the two adenine moieties are similar to each other and, in general, to those found in 7-substituted purine derivatives (Takenaka, Nakano & Sasada, 1979; Watson, Sweet & Marsh, 1965). The purine moieties are planar with maximum shifts of 0·029 Å at C(5*A*) and 0·016 Å at N(1*B*). N(6*A*) and N(6*B*) deviate by 0·058 and 0·037 Å, respectively, from their purine planes. The conformation of the ethyl chain with the carbamoyl group is similar to that found in the complex 3-(9-adeninyl)propionamide–1-methylthymine dihydrate (Takimoto, Takenaka & Sasada, 1982), but different from that of 3-(9-adeninyl)propionamide (Takimoto, Takenaka & Sasada, 1981). In the present crystal, the torsion angles N(7)—C(11)—C(12)—C(13) and C(11)—C(12)—C(13)—N(13) are 39·6 (3) and −134·6 (3)°, respectively, in *A*; the corresponding values in *B* are −47·2 (3) and 122·5 (3)°. The dimensions of the carbamoyl group are similar to those of 3-(9-adeninyl)propionamide.

The hydrogen-bond distances and angles are given in Table 2. Molecules *A* and *B* in the asymmetric unit form a pair through hydrogen bonds between carbamoyl N(13)H and adenine N(1) and are related by the pseudo inversion centre. The dihedral angle between the purine plane of *A* and the carbamoyl plane of *B* is 63·2 (1)° [the torsion angle C(13*A*)—N(13*A*)···

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* Lists of structure factors, anisotropic thermal parameters of C, N and O atoms, atomic parameters of H atoms, bond angles involving H atoms, the least-squares planes of the purine ring and the carbamoyl group and hydrogen-bond distances and angles involving H atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38082 (19 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. *Fractional coordinates and equivalent isotropic temperature factors*

*B* values are the equivalent isotropic temperature factors calculated from the anisotropic thermal parameters using the equation $B = 8\pi^2(U_1 + U_2 + U_3)/3$, where $U_1$, $U_2$, and $U_3$ are principal components of the mean-square displacement matrix **U**. Values in angle brackets are the anisotropicity defined by $[\sum(B - 8\pi^2U_i)^2/3]^{1/2}$. The e.s.d.'s in parentheses refer to the last decimal places.

| | *x* | *y* | *z* | *B* (Å²) |
|---|---|---|---|---|
| N(1*A*) | 0·5968 (2) | 0·09308 (7) | 0·7890 (3) | 2·4 ⟨7⟩ |
| C(2*A*) | 0·6473 (3) | 0·0496 (1) | 0·8301 (4) | 2·7 ⟨6⟩ |
| N(3*A*) | 0·5882 (2) | 0·00803 (8) | 0·7994 (3) | 2·6 ⟨7⟩ |
| C(4*A*) | 0·4582 (3) | 0·01219 (9) | 0·7158 (4) | 2·2 ⟨4⟩ |
| C(5*A*) | 0·3942 (2) | 0·05494 (9) | 0·6695 (3) | 1·9 ⟨3⟩ |
| C(6*A*) | 0·4675 (3) | 0·09720 (9) | 0·7059 (4) | 2·0 ⟨3⟩ |
| N(6*A*) | 0·4206 (2) | 0·14048 (7) | 0·6616 (3) | 2·6 ⟨11⟩ |
| N(7*A*) | 0·2651 (2) | 0·04286 (7) | 0·5834 (3) | 2·04 ⟨53⟩ |
| C(8*A*) | 0·2605 (3) | −0·00514 (9) | 0·5848 (4) | 2·5 ⟨8⟩ |
| N(9*A*) | 0·3733 (2) | −0·02518 (7) | 0·6611 (3) | 2·6 ⟨10⟩ |
| C(11*A*) | 0·1466 (3) | 0·07283 (9) | 0·5245 (4) | 2·2 ⟨6⟩ |
| C(12*A*) | 0·0839 (3) | 0·09297 (9) | 0·6893 (4) | 2·3 ⟨5⟩ |
| C(13*A*) | 0·0455 (3) | 0·0542 (1) | 0·8189 (4) | 4·2 ⟨6⟩ |
| N(13*A*) | 0·0815 (3) | 0·06178 (8) | 1·0000 (3) | 3·3 ⟨17⟩ |
| O(13*A*) | −0·0162 (2) | 0·01817 (7) | 0·7567 (3) | 3·42 ⟨202⟩ |
| N(1*B*) | 0·2709 (2) | 0·14821 (8) | 1·0730 (3) | 2·4 ⟨6⟩ |
| C(2*B*) | 0·2368 (3) | 0·1932 (1) | 1·0251 (4) | 2·8 ⟨6⟩ |
| N(3*B*) | 0·3087 (2) | 0·23207 (8) | 1·0601 (3) | 2·6 ⟨6⟩ |
| C(4*B*) | 0·4337 (3) | 0·22403 (9) | 1·1551 (4) | 2·1 ⟨5⟩ |
| C(5*B*) | 0·4806 (3) | 0·17933 (9) | 1·2081 (4) | 2·0 ⟨2⟩ |
| C(6*B*) | 0·3952 (3) | 0·14021 (9) | 1·1653 (4) | 2·1 ⟨3⟩ |
| N(6*B*) | 0·4271 (2) | 0·09543 (8) | 1·2135 (4) | 3·1 ⟨15⟩ |
| N(7*B*) | 0·6102 (2) | 0·18626 (7) | 1·3002 (3) | 2·06 ⟨34⟩ |
| C(8*B*) | 0·6310 (3) | 0·2337 (1) | 1·2970 (4) | 2·6 ⟨8⟩ |
| N(9*B*) | 0·5292 (2) | 0·25790 (8) | 1·2127 (3) | 2·6 ⟨8⟩ |
| C(11*B*) | 0·7113 (3) | 0·1513 (1) | 1·3777 (4) | 2·4 ⟨5⟩ |
| C(12*B*) | 0·7757 (3) | 0·12551 (9) | 1·2259 (4) | 2·6 ⟨7⟩ |
| C(13*B*) | 0·8530 (3) | 0·15911 (9) | 1·1135 (4) | 2·4 ⟨7⟩ |
| N(13*B*) | 0·8153 (2) | 0·16053 (8) | 0·9327 (3) | 2·8 ⟨7⟩ |
| O(13*B*) | 0·9457 (2) | 0·18377 (7) | 1·1917 (3) | 3·5 ⟨13⟩ |
| O(*W*1) | 1·1626 (2) | 0·18635 (6) | 0·4879 (3) | 3·15 ⟨114⟩ |
| O(*W*2) | 0·9451 (2) | 0·21785 (8) | 0·6772 (3) | 4·2 ⟨13⟩ |

Table 2. *Hydrogen-bond distances* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

*A* and *B* refer to molecules *A* and *B*.

| | | | |
|---|---|---|---|
| N(1*A*)···N(13*B*) | 2·975 (3) | N(13*A*)···N(1*B*) | 3·086 (3) |
| N(3*A*)···N(6$B^{vi}$) | 2·936 (3) | N(3*B*)···O($W1^{ii}$) | 2·741 (3) |
| N(6*A*)···O($W1^{vii}$) | 3·000 (3) | N(13*B*)···O(*W*2) | 2·874 (3) |
| N(6*A*)···N(9$B^{ix}$) | 3·078 (3) | O(13*B*)···O($W1^{iii}$) | 2·852 (3) |
| N(9*A*)···N(6$B^{iii}$) | 2·870 (3) | O(13*B*)···O($W2^{iv}$) | 2·789 (3) |
| N(13*A*)···O(13$A^{viii}$) | 2·988 (3) | O(*W*1)···O(*W*2) | 2·820 (3) |
| C(2*A*)—N(1*A*)···N(13*B*) | 106·0 (2) | C(2*B*)—N(3*B*)···O($W1^{ii}$) | 114·1 (2) |
| C(6*A*)—N(1*A*)···N(13*B*) | 135·1 (2) | C(4*B*)—N(3*B*)···O($W1^{ii}$) | 131·6 (2) |
| C(2*A*)—N(3*A*)···N(6$B^{vi}$) | 156·3 (2) | C(6*B*)—N(6*B*)···N(3$A^{iii}$) | 157·6 (2) |
| C(4*A*)—N(3*A*)···N(6$B^{vi}$) | 91·7 (2) | C(6*B*)—N(6*B*)···N(9$A^{iii}$) | 150·3 (2) |
| C(6*A*)—N(6*A*)···O($W1^{vii}$) | 138·7 (2) | C(4*B*)—N(9*B*)···N(6$A^{iv}$) | 113·6 (2) |
| C(6*A*)—N(6*A*)···N(9$B^{ix}$) | 136·4 (2) | C(8*B*)—N(9*B*)···N(6$A^{iv}$) | 141·6 (2) |
| C(4*A*)—N(9*A*)···N(6$B^{iii}$) | 94·0 (2) | C(13*B*)—N(13*B*)···O(*W*2) | 124·3 (2) |
| C(8*A*)—N(9*A*)···N(6$B^{iii}$) | 161·7 (2) | C(13*B*)—N(13*B*)···N(1*A*) | 115·9 (2) |
| C(13*A*)—N(13*A*)···O(13$A^{viii}$) | 114·1 (2) | C(13*B*)—O(13*B*)···O($W2^{iv}$) | 123·3 (2) |
| C(13*A*)—N(13*A*)···N(1*B*) | 112·5 (2) | C(13*B*)—O(13*B*)···O($W1^{v}$) | 144·2 (2) |
| C(6*B*)—N(1*B*)···N(13*A*) | 116·7 (2) | C(13*A*)—O(13$A^{viii}$)···N(13*A*) | 122·4 (2) |
| C(2*B*)—N(1*B*)···N(13*A*) | 125·2 (2) | | |
| N(13)···O(*W*2)···O(13$B^{ix}$) | 122·7 (1) | O(*W*2)···O(*W*1)···N(3$B^{x}$) | 93·0 (1) |
| O(13$B^{ix}$)···O(*W*2)···O(*W*1) | 109·6 (1) | N(3$B^{x}$)···O(*W*1)···O(13$B^{i}$) | 119·8 (1) |
| O(*W*1)···O(*W*2)···N(13*B*) | 123·7 (1) | O(*W*2)···O(*W*1)···O(13$B^{i}$) | 80·3 (1) |

Symmetry code: (i) $x,y,-1+z$; (ii) $-1+x,\frac{1}{2}-y,\frac{1}{2}+z$; (iii) $1-x,-y,2-z$; (iv) $x,\frac{1}{2}-y,\frac{1}{2}+z$; (v) $x,y,1+z$; (vi) $1-x,-y,1-z$; (vii) $-1+x,y,z$; (viii) $-x,-y,2-z$; (ix) $x,\frac{1}{2}-y,-\frac{1}{2}+z$; (x) $1+x,\frac{1}{2}-y,-\frac{1}{2}+z$.

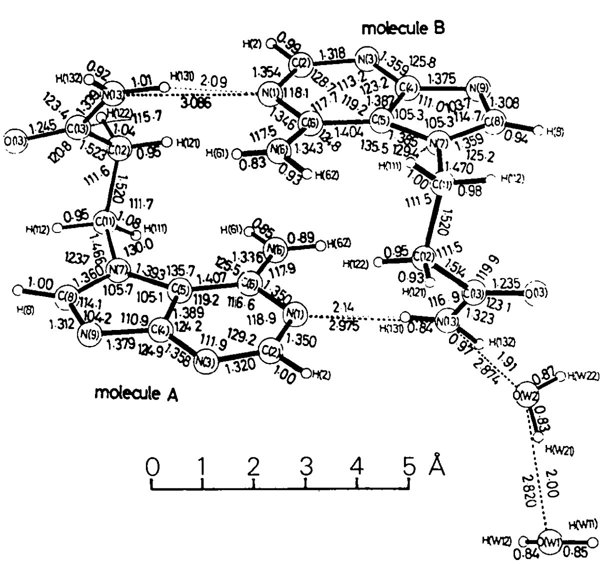

Fig. 1. Atomic numbering, bond distances (Å) and bond angles (°).

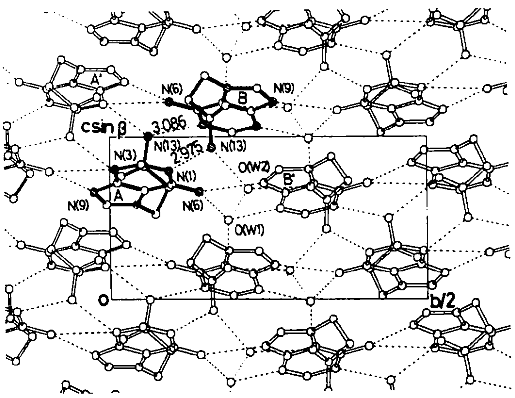

Fig. 2. The crystal structure projected along the *a* axis.

N(1*B*)—C(2*B*) is 62·4 (3)°], and that between *B* and *A* is 57·2 (1)° [the torsion angle C(13*B*)—N(13*B*)···N(1*A*)—C(2*A*) is −60·8 (3)°]. The purine planes of *A* and *B* are almost parallel to each other with a dihedral angle of 4·9 (1)°.

The crystal structure viewed down the *a* axis is shown in Fig. 2. Two molecules around a crystallographic inversion centre are paired by the N(13*A*)H···O(13*A*′) hydrogen bond between the carbamoyl groups. Molecule *A*′ related by the inversion centre at (0, 0, 1) is connected to *B* through the N(6*B*)H···N(3*A*′) and N(6*B*)H···N(9*A*′) hydrogen bonds. The molecule *B*′ related by the *c* glide at $y = \frac{1}{4}$ is hydrogen bonded to molecule *A* and one water molecule through N(9*B*′)···N(6*A*) and

N(3*B*′)···O(*W*1), respectively. The remaining H atom of the carbamoyl group in *B* participates in a hydrogen bond with the water oxygen O(*W*2). Furthermore, additional hydrogen bonds with the water molecules link molecules *A* and *B* in the three-dimensional network.

The NH···N hydrogen bond between the carbamoyl group and adenine N(1) mentioned above is similar to that found in the complex 3-(9-adeninyl)propionamide–1-methylthymine dihydrate, in spite of the different crystal fields. This may suggest a strong affinity of the carbamoyl group in glutamine or asparagine residues for the adenine N(1) site.

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# Conformation and Structure of α-L-Leucyl-L-glutamic Acid, $C_{11}H_{20}N_2O_5$

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**Abstract.** $M_r = 260{\cdot}3$, orthorhombic, $P2_12_12_1$, $a = 15{\cdot}042\,(4)$, $b = 15{\cdot}993\,(5)$, $c = 5{\cdot}517\,(2)$ Å, $V = 1327{\cdot}03$ Å$^3$, $Z = 4$, $D_x = 1{\cdot}303$, $D_m$ (flotation in methylene chloride/1,2-dichloroethane) $= 1{\cdot}28\,(2)$ Mg m$^{-3}$, Mo $K\alpha$ radiation ($\lambda K\alpha_1 = 0{\cdot}70926$, $\lambda K\alpha_2 = 0{\cdot}71354$ Å), $\mu = 0{\cdot}11$ mm$^{-1}$, $T = 292$K, $R = 0{\cdot}066$, $wR = 0{\cdot}041$ for 1181 observations. The dipeptide crystallizes as a zwitterion with the main-chain carboxyl ionized and the amino terminus protonated. The dipeptide adopts a *trans* configuration with an $\omega$ torsion angle of 172°. The side chains adopt fully extended conformations on opposite sides of the peptide linkage. There is intermolecular, and possibly intramolecular, hydrogen bonding in the structure. Neither the peptide carbonyl O nor the amide N atoms are involved in the intermolecular hydrogen-bonding network.

**Introduction.** The conformational and structural properties of peptides containing the acidic residues glutamic acid (Glu), aspartic acid (Asp) or γ-carboxyglutamic acid (Gla) are of considerable interest, partly because of the importance of these residues in calcium-binding proteins (Kretsinger & Nelson, 1976). Recently, we have undertaken a systematic structural study of peptides containing acidic residues and have reported the structures of several of these molecules (Valente, Hiskey & Hodgson, 1979; Eggleston, Valente & Hodgson, 1981*a*,*b*; Eggleston & Hodgson, 1982*a*,*b*,*c*). In extending this study, we here report the structure of α-L-Leu-L-Glu. This peptide sequence, with Glu replaced by Gla, occurs three times in the γ-carboxyglutamic-acid-rich fragment of prothrombin (Davie & Hanahan, 1977).

**Experimental.** Colorless rods from Vega Biochemicals, Inc., grown by slow cooling of an aqueous solution, crystal 0·40 × 0·60 × 1·0 mm; Enraf–Nonius CAD-4 diffractometer; systematic absences *h*00 for *h* odd, 0*k*0 for *k* odd, and 00*l* for *l* odd, cell constants from a least-squares analysis of 25 reflections with $30° \le 2\theta(\text{Mo}) \le 38°$ measured on the diffractometer; $F(000) = 560{\cdot}0$; intensity data collected in a θ–ω scan mode, as suggested by examination of the shapes of several peaks; 1778 independent reflections, $2\theta \le 55°$, $0 \le h \le 19$, $0 \le k \le 20$, $0 \le l \le 7$; Lorentz–polarization correction, no absorption correction; no systematic fluctuations in reflections $\bar{4}50$, $1\bar{6}\bar{1}$, and $\bar{2}74$ monitored at the beginning and each 3 h during data collection (17 times); maximum deviations in *F* 2·2, 1·6, and 3·3%, respectively; mean values of *F* 63·5 (7), 83·0 (7), and 52·1 (8), respectively. Programs in the CAD-4 structure determination package; the structure determined using *MULTAN* (Germain, Main & Woolfson, 1971); *E* map revealed positions of all non-hydrogen atoms; anisotropic least-squares refinement (on *F*) of these positions led to *wR* 0·094; weights $4F_o^2/\sigma^2(I)$; subsequent difference Fourier maps revealed

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