

- LOUDON, G. M. (1984). *Organic Chemistry*, p. 835. Reading, MA: Addison-Wesley.
- MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCO, J.-P. & WOOLFSON, M. M. (1980). *MULTAN80. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
- MOTHERWELL, W. D. S. (1978). *PLUTO*. Plotting program for molecular crystal packing diagrams. Univ. of Cambridge, England.
- SHELDRIK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.
- STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

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Structures of Some *N*-Acetylamides of Amino Acids

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Abstract. *N*-Acetylglycinamide (NAGA), C₄H₈N₂O₂, *M_r* = 116.12, monoclinic, *P*₂₁/*n*, *a* = 5.341 (1), *b* = 8.041 (2), *c* = 13.638 (2) Å, β = 93.24 (2)°, *V* = 584.8 (3) Å³, *Z* = 4, *D_x* = 1.319 Mg m⁻³, λ(Mo *Kα*) = 0.71073 Å, μ = 0.099 mm⁻¹, *F*(000) = 248, room temperature, final *R* = 0.042 for 1018 observed reflexions. *N*-Acetyl-L-alaninamide (L-NAAA), C₅H₁₀N₂O₂, *M_r* = 130.15, monoclinic, *P*₂₁, *a* = 5.942 (1), *b* = 7.480 (2), *c* = 8.414 (1) Å, β = 106.07 (3)°, *V* = 359.3 (2) Å³, *Z* = 2, *D_x* = 1.203 Mg m⁻³, λ(Cu *Kα*) = 1.54178 Å, μ = 0.75 mm⁻¹, *F*(000) = 140, room temperature, final *R* = 0.035 for 662 observed reflexions. *N*-Acetyl-L-leucinamide (L-NALA), C₈H₁₆N₂O₂, *M_r* = 172.23, orthorhombic, *P*₂₁2₁2₁, *a* = 5.776 (1), *b* = 10.205 (4), *c* = 17.256 (4) Å, *V* = 1017.0 (8) Å³, *Z* = 4, *D_x* = 1.125 Mg m⁻³, λ(Cu *Kα*) = 1.54178 Å, μ = 0.63 mm⁻¹, *F*(000) = 376, room temperature, final *R* = 0.047 for 694 observed reflexions. In the three crystals the molecular packing is ruled by the intermolecular hydrogen bonds which involve all the polar groups. However, in L-NALA the necessity to accommodate increasingly bulky alkyl side chains does not allow the maximum number of possible hydrogen bonds. Besides, the packing density and cohesiveness decrease with increasing molecular weight, from NAGA to L-NAAA to L-NALA. The crystallographic results can explain qualitatively the trend of the enthalpies of melting and sublimation recently determined.

Introduction. In this paper we present the results of X-ray studies on some *N*-acetylamides of amino

acids, of general formula: CH₃-CO-NH-CHR-CO-NH₂. These uncharged molecules have been proposed (Blackburn, Lilley & Walmsley, 1980) as models, better than amino acids, for thermodynamic and theoretical studies on polypeptides. The crystallographic study of the uncharged peptidomides and their derivatives is part of a research program on the physico-chemical properties of these substances. In fact, accurate knowledge of the crystal structure gives an insight of the factors controlling the interactions between groups of the same or different polarity. Moreover, the geometrical parameters obtained by X-ray analysis can be used, together with spectroscopic data, dipolar moments and sublimation energies, for deriving the parameters for semiempirical potential relations and for conformational analysis. The knowledge of intermolecular interactions in the solid state can give a simple explanation for the trends of enthalpies of melting and sublimation recently determined (Ferro, Della Gatta & Barone, 1988) and will be used as support for theoretical calculations concerning the weak non-bonding interactions in solution which have recently been the subject of extensive experimental studies (Barone, Castronuovo, Elia & Giancola, 1985; Blackburn, Lilley & Millburn, 1986; Barone, Castronuovo, Del Vecchio, Elia & Giancola, 1987).

Experimental. The present compounds (NAGA, L-NAAA and L-NALA) were prepared in our laboratory using the method described by Blackburn, Lilley & Walmsley (1980). Single crystals were grown as colourless prisms by slow evaporation from

ethanol and diethyl ether mixtures for NAGA and L-NAAA, and from chloroform for L-NALA.

Enraf-Nonius CAD-4F diffractometer, room temperature, cell dimensions from 25 reflections at medium θ , ω scan as suggested by peak-shape analysis. Three monitoring reflections for each data collection, intensity variation $\leq 5\%$. Lp correction, absorption ignored. The structures were solved by *MULTAN80* (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). Anisotropic full-matrix least squares minimized $\sum w(\Delta F)^2$, $w = 1/\sigma^2(F)$, $\sigma(F)$ from counting statistics and a fudge factor of 0.045. H-atom positional parameters from ΔF synthesis and geometrical considerations, refined in NAGA and L-NAAA, not refined in L-NALA because of the significantly lower ratio of observed reflections per parameter. Thermal parameters of H atoms set equal to the B_{eq} of the parent atoms and not refined. A correction for secondary extinction was refined in NAGA and L-NAAA, not applied in L-NALA. The most significant structural refinement parameters and the crystal data for each structure are summarized in Table 1. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974). Enraf-Nonius (1979) *SDP* software and PDP11/34 computer of the 'Centro di Metodologie Chimico-fisiche dell'Università di Napoli'. Final atomic parameters for the three structures are listed in Table 2.*

Discussion. Views of the NAGA, L-NAAA and L-NALA molecules are given in Fig. 1 (*a*, *b* and *c* respectively) together with the atomic numbering schemes used. The geometrical parameters, reported in Table 3, on average compare well with the values generally found for similar compounds (Benedetti, 1982, and references therein). In the crystal structures, the conformation (see torsion angles in Table 3) of NAGA is very similar to that of L-NALA and both agree with the conformation adopted by the second amino acid residue in a β bend type I ($\varphi = -70^\circ$; $\psi = -30^\circ$). On the other hand, the conformation of L-NAAA is close to that of a residue in the β sheet regions ($\varphi = -120^\circ$; $\psi = 110^\circ$).

The molecular arrangements in the three crystals are shown in Figs. 2 (NAGA), 3 (L-NAAA) and 4 (L-NALA). The most remarkable feature of these structures is the presence of characteristic patterns of hydrogen bonds, whose geometry is reported in Table 4. In the NAGA crystal, pairs of centrosymmetrically related molecules are held by the double

Table 1. *X-ray data collection and structural refinement parameters*

	NAGA	L-NAAA	L-NALA
Crystal size (mm)	0.08 × 0.32 × 0.65	0.05 × 0.19 × 0.34	0.06 × 0.23 × 0.58
θ_{max} (°)	30	72	65
Range of <i>h, k, l</i>	-7,0,0 to 7,11,19	-7,0,0, to 7,9,10	0,0,0 to 6,12,20
No. of independent reflections	1710	830	1034
No. of observed reflections [$I \geq 3\sigma(I)$]	1018	662	694
No. of parameters refined	98	112	109
Extinction coefficient	$7.0(1) \times 10^{-6}$	$5.2(1) \times 10^{-5}$	—
Final <i>R</i>	0.042	0.035	0.047
Final <i>wR</i>	0.059	0.050	0.068
Max. final Δ/σ	0.07	0.04	0.09
<i>S</i>	2.05	2.05	1.85
Max. and min. $\Delta\rho$ (e Å ⁻³)	+0.20, -0.18	±0.16	±0.18

Table 2. *Positional parameters ($\times 10^4$) and equivalent isotropic thermal parameters (Å²) with e.s.d.'s in parentheses for non-H atoms*

	$B_{eq} = \frac{1}{3} \sum_i \sum_j \beta_{ij} a_i \cdot a_j$			
	<i>x</i>	<i>y</i>	<i>z</i>	B_{eq}
NAGA				
O(1)	2625 (3)	451 (2)	4076 (1)	3.78 (2)
O(2)	6288 (3)	784 (2)	1793 (1)	4.16 (3)
N(1)	4267 (3)	-1638 (2)	1881 (1)	2.82 (2)
N(2)	5719 (3)	-1402 (2)	3910 (1)	3.52 (3)
C(1)	2556 (3)	-1010 (2)	2572 (1)	2.88 (3)
C(2)	3689 (3)	-595 (2)	3583 (1)	2.76 (3)
C(3)	5959 (3)	-652 (2)	1499 (1)	2.87 (3)
C(4)	7549 (4)	-1410 (1)	714 (1)	4.48 (4)
L-NAAA				
O(1)	5290 (4)	6879*	5013 (3)	5.45 (4)
O(2)	8754 (4)	4530 (4)	10374 (2)	6.22 (5)
N(1)	7047 (4)	4384 (3)	7648 (2)	4.41 (4)
N(2)	7379 (4)	8871 (3)	6816 (3)	4.93 (5)
C(1)	8471 (4)	5767 (4)	7217 (3)	4.25 (5)
C(2)	6896 (4)	7220 (3)	6264 (3)	3.83 (5)
C(3)	7305 (5)	3827 (4)	9188 (3)	4.49 (5)
C(4)	5748 (6)	2357 (5)	9416 (4)	6.00 (7)
C(5)	9990 (6)	5051 (6)	6196 (5)	7.05 (9)
L-NALA				
O(1)	7229 (5)	-761 (3)	3739 (2)	6.04 (7)
O(2)	3848 (5)	2046 (3)	2885 (2)	5.73 (7)
N(1)	1621 (5)	674 (3)	3565 (2)	4.26 (7)
N(2)	4221 (5)	-1285 (3)	3012 (2)	4.20 (7)
C(1)	3559 (6)	197 (3)	4028 (2)	3.89 (8)
C(2)	5196 (7)	-645 (4)	3565 (2)	4.25 (8)
C(3)	1916 (7)	1535 (4)	2992 (2)	4.44 (9)
C(4)	-107 (9)	1840 (6)	2500 (3)	6.50 (9)
C(5)	2634 (8)	-550 (4)	4726 (2)	4.71 (9)
C(6)	1241 (9)	273 (4)	5307 (3)	5.6 (1)
C(7)	26 (13)	-597 (6)	5887 (3)	8.2 (1)
C(8)	2748 (12)	1266 (6)	5716 (3)	8.9 (1)

* Fixed to define the origin.

bridge N(2)—H(1)···O(1) between the facing amide groups. In addition the molecules related by glide symmetry are connected through two hydrogen bonds N(2)—H(2)···O(2) and N(1)—H···O(1). Hence, the overall packing is stabilized by a three-dimensional network of intermolecular hydrogen bonds.

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters for each structure have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51948 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Instead, in the two chiral substances, the hydrogen-bond patterns are two-dimensional. In L-NAAA the polar groups of molecules, related by the screw axis along *b*, are assembled in layers extending approximately parallel to the *b*, *a*-*c* plane. These layers separate apolar regions, comprising the methyl groups C(4) and C(5) at distances close to the van der Waals separation [C(4)—C(4) = 4.028 (2), C(5)—C(5) = 4.249 (4) Å]. In this structure, as in NAGA, the peptide and amide hydrogens are each engaged in a hydrogen bond and the oxygen O(1) behaves as a double acceptor of hydrogen bonds. On the contrary, in L-NALA, there are only two hydrogen bonds which link together molecules translated along *a* and molecules related by the screw axis parallel to *b* [N(1)—H...O(1) and N(2)—H₂...O(2) respectively]. The molecules of L-NALA form wrinkled polar sheets which extend perpendicular to *c* and make concavities, similar to those of a half egg box, in which the twisted side chains settle. Therefore, the polar layers are intercalated with apolar regions containing the side chains.

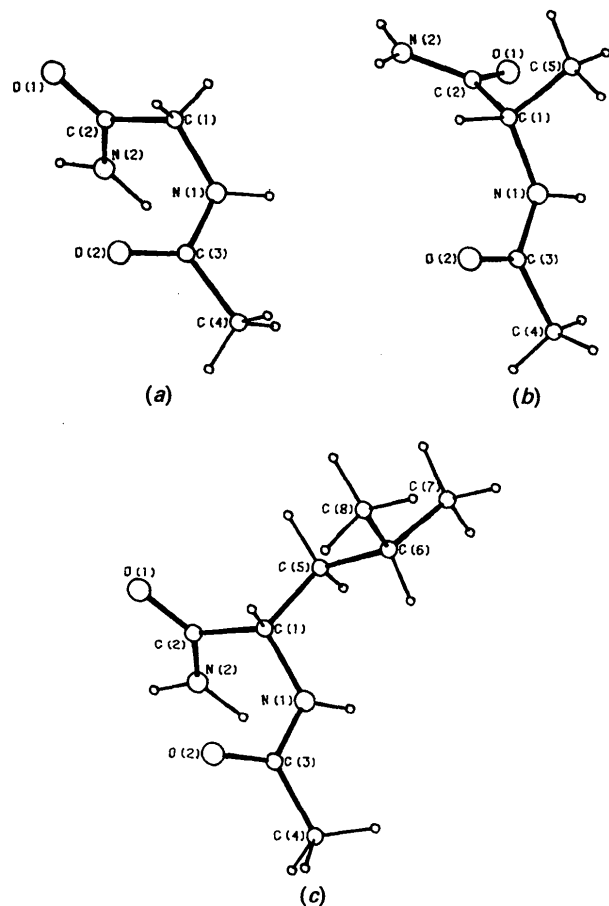


Fig. 1. Views of the molecules with the atomic numbering schemes: (a) NAGA, (b) L-NAAA, (c) L-NALA.

Table 3. Bond lengths (Å), bond angles (°) and some torsion angles (°) with *e.s.d.*'s in parentheses

	NAGA	L-NAAA	L-NALA
O(1)—C(2)	1.235 (2)	1.236 (2)	1.217 (4)
O(2)—C(3)	1.231 (2)	1.240 (2)	1.246 (4)
N(1)—C(1)	1.441 (2)	1.445 (3)	1.458 (4)
N(1)—C(3)	1.331 (2)	1.329 (3)	1.333 (4)
N(2)—C(2)	1.319 (2)	1.323 (2)	1.286 (4)
C(1)—C(2)	1.512 (2)	1.512 (3)	1.508 (5)
C(1)—C(5)	—	1.506 (4)	1.523 (5)
C(3)—C(4)	1.495 (2)	1.483 (4)	1.478 (5)
C(5)—C(6)	—	—	1.537 (5)
C(6)—C(7)	—	—	1.511 (5)
C(6)—C(8)	—	—	1.511 (6)
C(1)—N(1)—C(3)	121.2 (1)	123.5 (2)	121.9 (3)
N(1)—C(1)—C(2)	116.0 (1)	109.2 (1)	112.4 (3)
N(1)—C(1)—C(5)	—	111.9 (2)	109.3 (3)
C(2)—C(1)—C(5)	—	109.5 (2)	110.7 (2)
O(1)—C(2)—N(2)	123.1 (1)	122.2 (2)	123.8 (4)
O(1)—C(2)—C(1)	118.3 (1)	121.4 (2)	121.9 (4)
N(2)—C(2)—C(1)	118.6 (1)	116.3 (2)	114.1 (3)
O(2)—C(3)—N(1)	121.2 (1)	121.2 (2)	120.0 (3)
O(2)—C(3)—C(4)	122.9 (1)	122.0 (2)	122.4 (3)
N(1)—C(3)—C(4)	115.8 (1)	116.8 (2)	117.6 (3)
C(1)—C(5)—C(6)	—	—	115.2 (3)
C(5)—C(6)—C(7)	—	—	110.7 (3)
C(5)—C(6)—C(8)	—	—	111.7 (3)
C(7)—C(6)—C(8)	—	—	110.6 (3)
N(1)—C(1)—C(2)—N(2)	-27.5 (2)	127.9 (4)	-30.3 (6)
C(1)—N(1)—C(3)—O(2)	7.3 (3)	2.9 (4)	-6.7 (6)
C(2)—C(1)—N(1)—C(3)	-71.3 (3)	-124.7 (4)	-67.6 (7)
C(1)—N(1)—C(3)—C(4)	-173.9 (3)	-178.2 (5)	173.1 (8)
O(1)—C(2)—C(1)—C(5)	—	68.9 (4)	-83.3 (6)
N(1)—C(1)—C(5)—C(6)	—	—	-64.4 (6)
C(1)—C(5)—C(6)—C(7)	—	—	169.0 (8)
C(1)—C(5)—C(6)—C(8)	—	—	-67.2 (7)

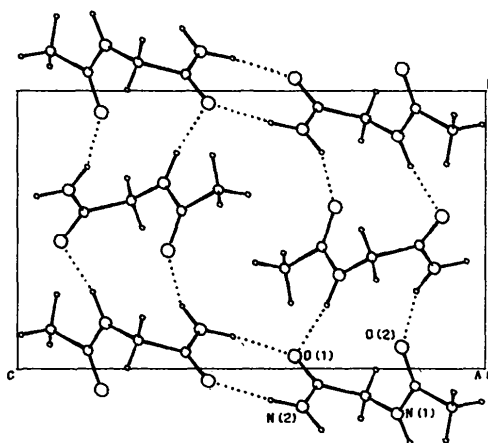


Fig. 2. Crystal packing of NAGA along the *a* direction. Hydrogen bonds are indicated by dotted lines; the symmetry of atoms hydrogen bonded is reported in Table 4.

Altogether the crystal packings of these three molecules are the result of compromises between the tendency to maximize the number of hydrogen bonds and the necessity to accommodate the increasingly bulky alkyl substituents. Because of these contrasting effects, the crystal density of NAGA is 10% higher

than that of L-NAAA and about 18% higher than that of L-NALA (1.32, 1.20, 1.12 g cm⁻³ respectively).

The crystallographic results can explain qualitatively the trend of the enthalpies of melting and sublimation which decrease with increasing molecular weight and side-chain dimensions (Ferro, Della Gatta & Barone, 1988). The values of the $\Delta H_{\text{fus}}^\circ$ are 25.6 (4), 21.7 (2) and 20.2 (3) kJ mol⁻¹, at 408, 431 and 404 K respectively, for NAGA, L-NAAA and D-NALA; the corresponding values of $\Delta H_{\text{subl}}^\circ$ are

Table 4. *Hydrogen-bonding geometry* (Å and °)

D—H...A	D...A	H...A	D—H...A	Code
NAGA				
N(1)—H...O(1)	2.838 (1)	1.92 (2)	158 (1)	(i)
N(2)—H1...O(1)	2.939 (2)	1.95 (2)	174 (1)	(ii)
N(2)—H2...O(2)	2.961 (1)	2.03 (2)	158 (1)	(iii)
L-NAAA				
N(1)—H...O(1)	2.955 (2)	2.00 (2)	167 (2)	(iv)
N(2)—H1...O(1)	2.931 (2)	1.99 (3)	173 (2)	(v)
N(2)—H2...O(2)	2.847 (2)	1.94 (2)	170 (2)	(vi)
L-NALA				
N(1)—H...O(1)	2.945 (3)	1.96*	177*	(vii)
N(2)—H2...O(2)	2.558 (3)	1.56*	171*	(viii)

Symmetry of acceptor: (i) $-x + \frac{1}{2}, y - \frac{1}{2}, -z + \frac{1}{2}$; (ii) $-x + 1, -y, -z + 1$; (iii) $-x + \frac{3}{2}, y - \frac{1}{2}, -z + \frac{1}{2}$; (iv) $-x + 1, y - \frac{1}{2}, -z + 1$; (v) $-x + 1, y + \frac{1}{2}, -z + 1$; (vi) $-x + 2, y + \frac{1}{2}, -z + 2$; (vii) $x - 1, y, z$; (viii) $-x + 1, y - \frac{1}{2}, -z + \frac{1}{2}$.

* H atoms are not refined.

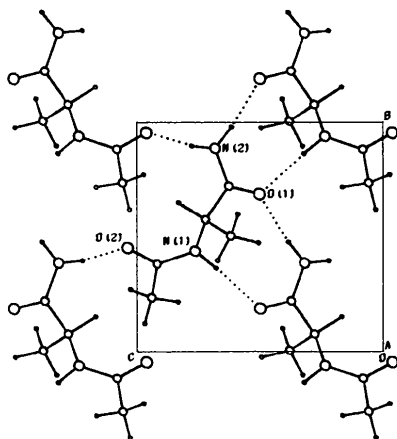


Fig. 3. Molecular assemblage of L-NAAA projected on the *bc* plane; hydrogen bonds are indicated by dotted lines.

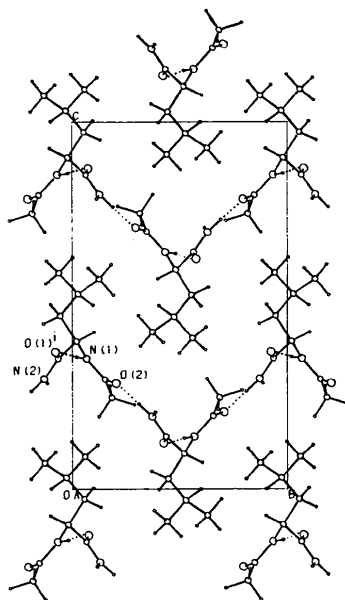


Fig. 4. Crystal packing of L-NALA along the *a* direction: dotted lines indicate the intermolecular hydrogen bonds; symmetry code (i) $x - 1, y, z$.

153 (3), 115 (3) and 101 (3) kJ mol⁻¹, determined in a small range of temperature very near to the melting points. Indeed, in both the NAGA and L-NAAA crystals, each molecule shares six hydrogen bonds with its nearest neighbours, but in the first structure this is attained through a more dense packing and shorter intermolecular contacts, the cohesiveness therefore being higher. In the L-NALA crystal, each molecule is involved in only four intermolecular hydrogen bonds, the cohesive forces are weaker and the density and sublimation energy are the lowest in the series.

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References

- BARONE, G., CASTRONUOVO, G., DEL VECCHIO, P., ELIA, V. & GIANCOLA, C. (1987). *Thermochim. Acta*, **122**, 105–115.
- BARONE, G., CASTRONUOVO, G., ELIA, V. & GIANCOLA, C. (1985). *J. Thermal Anal.* **30**, 1367–1374.
- BENEDETTI, E. (1982). In *Chemistry and Biochemistry of Amino Acids, Peptides and Proteins*, Vol. VI, edited by B. WEINSTEIN, pp. 105–184. New York: Marcel Dekker.
- BLACKBURN, G. M., LILLEY, T. H. & MILLBURN, P. J. (1986). *J. Chem. Soc. Faraday Trans. 1*, **82**, 2965–2976.
- BLACKBURN, G. M., LILLEY, T. H. & WALMSLEY, E. (1980). *J. Chem. Soc. Faraday Trans. 1*, **76**, 915–922.
- Enraf-Nonius (1979). *Structure Determination Package*. Enraf-Nonius, Delft, The Netherlands.
- FERRO, D., DELLA GATTA, G. & BARONE, G. (1988). *J. Thermal Anal.* **34**, 835–841.
- International Tables for X-ray Crystallography* (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)
- MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCO, J.-P. & WOOLFSON, M. M. (1980). *MULTAN80. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.