The Crystal and Molecular Structure of *N*-Carboxy Anhydride of Glycine

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The crystal and molecular structure of *N*-carboxy anhydride(NCA) of glycine was determined from three-dimensional X-ray diffraction data. The crystals of glycine-NCA are monoclinic with space group C2/c and $Z=8$; the cell dimensions are $a=9.298(2)$, $b=5.156(2)$, $c=16.900(4)$ Å and $\beta=107.88(2)°$. A pair of molecules forms the dimer structure around a center of symmetry, with two N(1)–H(1)···O(1′) hydrogen bonds in the crystals.

Amino acid-NCA's are very often used for synthesis of polypeptides. The polymerization has been carried out not only in homogeneous system but also in heterogeneous system and crystalline state.[1-3]

Generally, it might be expected that polymers with unique structures may be produced in the crystalline state polymerization, the crystal structure of monomer affecting that of the resulted polymer.[4] There have been several studies about the crystalline state polymerization of amino acid-NCA's. Miller and his co-workers reported that *N*-benzyloxycarbonyl L-lysine-NCA could be polymerized by allowing it to stand in air.[5] Morawetz and his co-workers reported on the polymerization of some amino acid-NCA's by heating.[6] In both cases, however, the complete crystal structures of the NCA's were not determined and therefore, the investigation on the polymerization mechanism could not be done in detail.

We found that high-molecular-weight polypeptides were produced when the crystals of amino acid-NCA's were immersed in hexane (the non-solvent of both the monomer and polymer crystals) and triethylamine or *n*-butylamine was added into the system as the initiator.[7] It becomes necessary to know the crystal structures of the amino acid-NCA's to discuss their polymerizability.

In this paper, we shall report the crystal structure of the simplest amino acid-NCA, glycine-NCA.

Experimental

Powdered glycine (10 g : 0.132 mol) was dispersed in about 700 ml of purified tetrahydrofuran in a round-flask, and 9 ml (0.075 mol) of trichloromethyl chloroformate was added into it. The reaction mixture was allowed to stand at about 50 °C with stirring. After about 6 h the system changed to be clear, and subsequently the sovlent was evaporated up to about 50 ml at reduced pressure and room temperature. Hexane (about 100 ml) was added to the resultant mixture, and then crude crystalline material appeared. The crude crystals were dissovled in ethyl acetate up to saturated state at about 40 °C, and this solution was cooled down to −20 °C to obtain the purified crystals. After several times of this purification process, well-shaped crystals suitable for X-ray work were selected.

Oscillation and Weissenberg photographs taken with nickel-filtered Cu$K\alpha$ radiation indicated the crystals to be monoclinic and the possible space group C2/c or Cc (systematic absences: $h\,k\,l$, $h+k$ odd; $0\,0\,l$, l odd). The former was chosen on the basis of the E(normalized structure factor) statistics and confirmed by the structure analysis.

The density of the crystal was measured by a flotation mothod using the mixture of bromoform and hexane.

Table 1. CRYSTAL DATA OF GLYCINE-NCA

$C_3NO_3H_3$	$U=771.6(4)$ Å^3
M. W. : 101.06	Space group : C2/c
monoclinic	$Z=8$
$a=9.298(2)$ Å	$D_c=1.74$ g·cm^{-3}
$b=5.156(2)$	$D_m=1.74$ g·cm^{-3}
$c=16.900(4)$	μ(Mo$K\alpha$) $=1.940$ cm^{-1}
$\beta=107.88(2)°$	

All diffraction experiments were done within a few days after the crystallization, because the auto-polymerization took place conspicuously in two or three days, which was visible as white turbidity on the crystals.

A colorless prismatic crystal with approximate dimensions $0.4\times0.5\times0.7$ mm was mounted on a Rigaku automated four-circle diffractometer with the b axis nearly parallel to the ϕ-axis of the goniometer. Accurate cell parameters were obtained by the least-squares refinements with 29 high angle reflections. Crystal data are given in Table 1. The intensity data with 2θ less than 55° were collected by usual ω-2θ scans using Zr-filtered Mo$K\alpha$($\lambda=0.7107$ Å) radiation. A total of 887 independent reflections (783 of them were non-zero) were obtained.

Structure Determination

The position of the oxygen atom O(1) was obtained from an analysis of the Harker section (u 0 w) and the interatomic vector resulting from a center of symmetry on a three-dimensional sharpened Patterson function. Subsequently, Buerger's minimum function was calculated using the O–O vectors between four symmetry related atoms, and seven non-hydrogen atoms were located in this map, where the carbon and nitrogen atoms could not be distinguished clearly. Successive Fourier synthesis with the phases based on these seven atoms showed the position of the nitrogen atom.

Refinement by a block-diagonal least-squares method (HBLS V Program[8]) using anisotropic temperature factors was continued until the R-value ($R=\sum||F_o|-|F_c||/\sum|F_o|$) dropped to 0.0683. At this stage, a difference Fourier synthesis map revealed the position of all hydrogen atoms. Finally, all the positional parameters together with the anisotropic temperature factors for the non-hydrogen atoms and the isotropic temperature factors for the hydrogen atoms are refined, and the R-value was reduced to 0.0428. A list of observed and calculated structure factors has

Table 2. Final atomic coordinates and thermal parameters for glycine-NCA with their estimated standard deviations

The anisotropic thermal parameters ($\times 10^5$) are expressed in the form:
$\exp\{-(B_{11}h^2+B_{22}k^2+B_{33}l^2+B_{12}hk+B_{13}hl+B_{23}kl)\}$
The isotropic thermal parameters of the H atoms are B/Å^2.

Atom	x	y	z	B_{11}(or B)	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
C(1)	0.4166 (1)	0.2198 (4)	0.4327 (2)	214(6)	2009(66)	895(23)	− 23(35)	242(20)	−397(66)
C(2)	0.3222 (1)	0.0768 (4)	0.2181 (2)	234(7)	2129(68)	789(23)	− 75(35)	264(20)	−237(65)
C(3)	0.3605 (1)	0.3195 (4)	0.1796 (2)	291(8)	2449(74)	749(22)	−367(40)	213(21)	−100(69)
N(1)	0.4180 (1)	0.3877 (4)	0.3255 (2)	283(6)	2231(61)	830(20)	−427(34)	183(19)	−205(59)
O(1)	0.4542 (1)	0.2176 (3)	0.5667 (2)	320(6)	3238(63)	808(17)	−263(33)	135(16)	−137(56)
O(2)	0.3603 (1)	0.0226 (3)	0.3690 (1)	262(5)	1976(48)	792(16)	−215(27)	14(15)	112(48)
O(3)	0.2690 (1)	−0.0579 (3)	0.1413 (2)	336(6)	3063(61)	955(19)	−733(33)	165(17)	−514(58)
H(1)	0.4507(14)	0.5336(50)	0.3436(26)	2.1(5)					
H(2)	0.3178(14)	0.4538(48)	0.1338(25)	1.7(5)					
H(3)	0.3919(14)	0.2692(48)	0.1105(25)	1.6(5)					

been deposited with the Chemical Society of Japan (Document No. 7613).

Results and Discussion

The final atomic coordinates and the thermal parameters are shown in Table 2. The perspective view of glycine-NCA molecule is shown in Fig. 1 together with the numbering of the atoms, the bond lengths and angles. The bond length C(1)–O(1) is 1.212(3) Å, slightly longer than the usual value. This might be caused by the hydrogen bond formed between N(1)–H(1) and O(1′) as will be discussed later. The bond length C(1)–N(1) (1.326 Å) is shorter than C(3)–N(1) (1.449 Å), probably due to the resonance effect between the double bond of C(1)–O(1) and the lone-pair electrons of the N(1) atom.

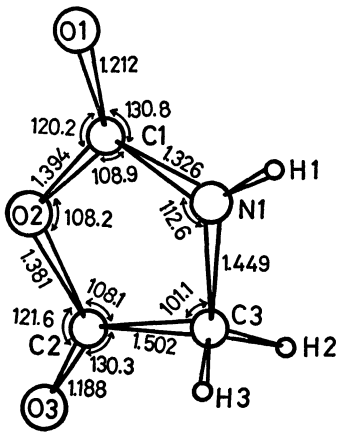

Fig. 1. A perspective view of glycine-NCA seen along the a axis with the numbering of the atoms, the bond lengths (l/Å) and angles (ϕ/°). The estimated standard deviations are 0.002—0.003Å in distances and 0.02° in angles.
The bond lengths involving hydrogen atoms are N(1)–H(1) 0.919(26), C(3)–H(2) 0.996(25) and C(3)–H(3) 0.986(25) Å.
The bond angles involving hydrogen atoms are C(1)–N(1)–H(1) 123.2(16), C(3)–N(1)–H(1) 124.2(16), N(1)–C(3)–H(3) 109.5(15), C(2)–C(3)–H(3) 107.0 (15) and H(2)–C(3)–H(3) 111.7(20)°.

Table 3. The equation of the least-squares plane through the atoms in glycine-NCA

Equation	Atom	Deviation
$-0.8136X+0.5433Y+0.2071Z+3.3117=0$	C(1)	−0.002 Å
	C(2)	0.002
$X=ax+cz\cos\beta$	C(3)	−0.003
$Y=by$	N(1)	0.004
$Z=cz\sin\beta$	*O(1)	0.031
	*O(2)	−0.047
	*O(3)	0.037
	*H(1)	0.037
	*H(2)	0.770
	*H(3)	−0.864

* Atoms not included in the least-squares calculation.

Other bond lengths are normal and well agree with the corresponding values of maleic anhydride and succinic anhydride, respectively.[9,10]

The equation of the best plane through four atoms C(1), C(2), C(3) and N(1) in the five-membered ring of glycine-NCA was calculated and is shown in Table 3, together with the deviations of the atoms from the plane. The atoms C(1), C(2), C(3), and N(1) can be regarded to be coplanar, their maximum deviation from the plane being 0.004 Å. Both the exocyclic atoms O(1) and O(3) are slightly displaced out of the plane on the same side.

The packing of the molecules in the crystal viewed along the b axis are shown in Fig. 2. One can see a dimer joined together in a pair around a center of symmetry, by two N–H···O hydrogen bonds with a distance of 2.915(2) Å and the angle of N(1)–H(1)–O(1′) 162(2)°.

Other intermolecular distances can be explained in terms of the packing of van der Waals type.

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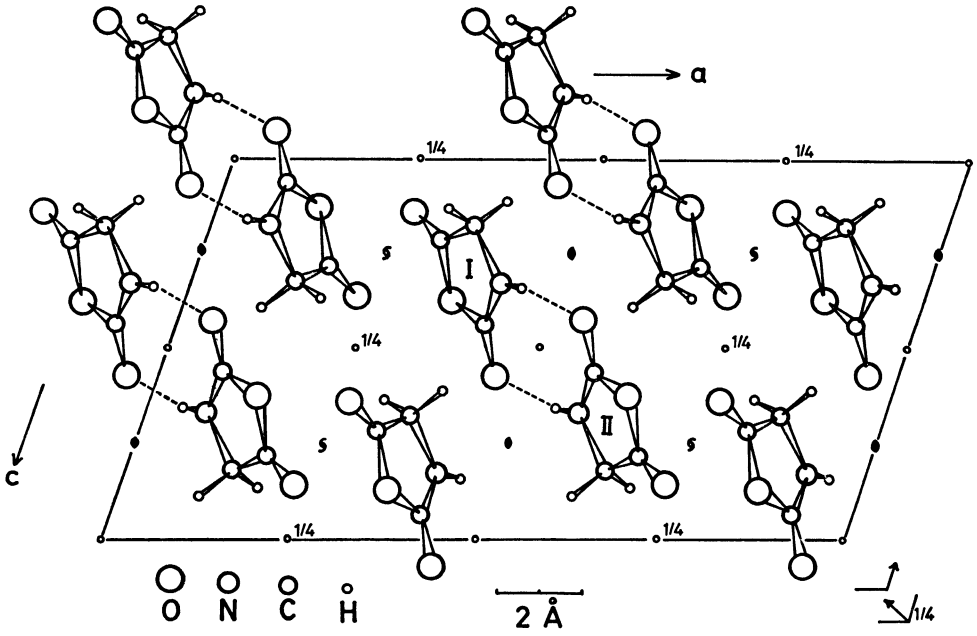

Fig. 2. Projection of the crystal structure of glycine-NCA along the b axis.
General coordinates: I, (x,y,z); II, $(1-x, 1-y, 1-z)$.
Hydrogen bonds are shown by broken lines.

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