There is no other hydrogen bonding in the structure. Instead the molecules are held together largely by van der Waal's forces between the methyl and *t*-butyl parts of the azetidinium ions, and by similar forces between the methyl groups of the methanesulfonate ions.

The S–O distances in the methanesulfonate group are 1.438 and 1.439 Å, identical within experimental error. Cesium methanesulfonate[38] has two different S–O distances, 1.434 and 1.485 Å, but Brandon and Brown[38] suggest that an average of these may be as realistic. Since their error must therefore be about ±0.03 Å, a more reliable S–O distance is probably given by the present study.

The S–C distance of 1.73 Å is on the short end of the range reported for S–C bond lengths[39] although a bond length of 1.79 Å is reported for the case of dimethyl sulfone.[40] The bond lengths and angles in the *t*-butyl group appear normal.

The azetidinium ring geometry is similar to that of azetidinecarboxylic acid:[4] the ring is not planar, the bond angles are remarkably close to 90°, and the bond lengths are almost the same. The C–N distances, 1.525 Å, are not significantly different from the C–C ring distances of 1.528 Å, although these are not so close in azetidinecarboxylic acid. The average ring distance in HAM is 1.527 Å compared with 1.523 Å in azetidinecarboxylic acid, which leads us to conclude that the ring bond lengths are identical within experimental error.

The degree of puckering of the ring is not large compared to some cyclobutane compounds. The out-of-plane bending in this structure is 14 ± 1°, quite similar to the 11 ± 1° puckering found for the case of azetidinecarboxylic acid. While small, these values are still consistent with the assumption made by Gaertner[41] in his interpretations of steric and entropic effects on ring-opening alkylations of azetidinium cations. We would anticipate, however, that planar azetidinium derivatives will be found. Thus, the results of the present study should not be taken to suggest that azetidines or azetidinium compounds will necessarily be nonplanar, but that steric effects due to specific ring substituents bring about a nonplanar ring conformation in the present case.

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The Crystal and Molecular Structure of L-Azetidine-2-carboxylic Acid. A Naturally Occurring Homolog of Proline[1,2]

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Abstract: The crystal structure of L-azetidine-2-carboxylic acid (AzCOOH) has been determined by application of superposition methods using an E^2-1 Patterson synthesis. The data were collected on a four-angle Picker automatic diffractometer using θ–2θ scan. The space group is $P2_12_12_1$, with four molecules in a unit cell of dimensions $a = 7.457$, $b = 9.810$, and $c = 6.328$ Å. The molecule is in the zwitterionic form. Both hydrogen atoms on the nitrogen atom act as hydrogen-bonding donors to the oxygen atoms in neighboring molecules. The single hydrogen atom attached to the α carbon atom is a hydrogen-bond donor to a nearby carboxylate oxygen atom. The azetidine ring is buckled by 11° from a plane so that the carboxylate group lies farther from C(4), the distal ring carbon, than would be the case for a planar ring. The conformation of AzCOOH resembles those of proline and hydroxyproline, but its substitution for either of these amino acids in a polypeptide could bring about conformation changes sufficient to significantly alter the tertiary structure of the polypeptide.

L-Azetidine-2-carboxylic acid (AzCOOH) is a naturally occurring amino acid homologous with proline from which it differs by the loss of one methylene group from the ring.[5] From 11 to 76% of the total amino and imino acid nitrogen present in ethanolic extracts of certain plants may be due to AzCOOH; so far this imino

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(4) Recipient of Public Health Service Research Career Development Award No. K4 GM 17,620-01 from the National Institute of General Medical Sciences.
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acid has been identified in 16 species of plants.[5] At least in the case of *Convallaria majalis* (lily of the valley), it has been demonstrated that the four-carbon chain of methionine can serve as a very efficient precursor for AzCOOH.[6]

The growth of cultures of *Escherichia coli*[7] and the biosynthesis of a cyclic polypeptide antibiotic by *Trichoderma viride*[8] are inhibited by addition of AzCOOH to the culture medium. The induction of an enzymatically active nitrate reductase in certain plant tissues was found to be strongly inhibited by AzCOOH.[9] Fowden has established that the inhibitory action of AzCOOH on the growth of various seedlings depends upon its incorporation into plant proteins, where it replaced an equivalent amount of proline.[10]

The toxic effects of AzCOOH are reversed by the simultaneous administration of proline.[7,9] It appears that AzCOOH does not poison its natural plant sources because such species have amino acid activating enzymes capable of discriminating between proline and AzCOOH with the result that, in the presence of both AzCOOH and proline, only the latter amino acid will be transformed into the biosynthetically active transfer RNA molecule.[11] However, even the amino acid activating enzymes of rat liver require a larger concentration of AzCOOH than of proline in order to reach an equivalent degree of saturation.[12]

AzCOOH has also been shown to produce abnormal development in the tail-tube proteins of T-even bacteriophage,[13] in the eggs of the sea urchin, *Paracentrotus lividus*,[14] and in chick embryos.[15] Introduction of the amino acid was shown, in the latter case, to result in a deformation of the limbs. This observation is consistent with the assumption that the amino acid is incorporated into collagen by the growing embryo.

The structural basis for the toxic effect of AzCOOH is not known but presumably involves the effect of changes in the conformation of proteins when the four-membered ring homolog is incorporated in place of the natural proline. It has been estimated that the AzCOOH residue would cause an α helix to turn through an angle approximately 15° smaller than would proline, but no experimental or theoretical basis for this estimate was given.[7] One of the objects of the present study is to estimate from the structure of the free amino acid how the conformation of a peptide might be affected by the incorporation of AzCOOH in place of proline. Moreover, until the presentation of a preliminary communication of this work[2] there were no reported crystallographic studies of the structure of simple, non-fused-ring azetidinium compounds.[16,17]

Experimental Section

Crystalline L-azetidine-2-carboxylic acid obtained from Calbiochem (lot no. 40003) was recrystallized from 50% (v/v) EtOH–H_2O to give well-formed prismatic crystals displaying [111] and [011] faces. One of these was selected having approximate dimensions 0.3 × 0.2 × 0.2 mm. The crystal was mounted on the tip of a 50-μ glass fiber using Ambroid cement thinned with nitrobenzene. Precession photographs were taken with Mo Kα radiation and 447 reflections were measured with Cu Kα radiation using a Picker automatic four-circle diffractometer and a variable width scan. Of the 447 reflections, 14 were unobserved. Due to the shape of the crystal and the low absorption coefficient, absorption corrections were considered unnecessary and were not applied; crystal data are given in Table I.

Table I. Crystal Data for L-Azetidine-2-carboxylic Acid

$C_4H_7NO_2$	$a = 7.457 \pm 0.007$ Å
Mol wt 101.1	$b = 9.810 \pm 0.009$ Å
Space group $P2_12_12_1$	$c = 6.328 \pm 0.006$ Å
$z = 4$	$D_m = 1.463 \pm 0.002$
Orthorhombic	$D_x = 1.451$
	$\mu_{Cu\ K\alpha} = 11.2$

Structure Determination and Refinement. The structure was determined by application of superposition methods[18] on an E^2-1 Patterson synthesis. A peak at 0.033, 0.075, and 0.200 was selected for calculation of a two-atom symmetry minimum function and the atomic positions thus derived were used in a four-atom multiple minimum function. The resulting map contained a recognizable structure for which the agreement index was 0.30. The structure was refined with Shiono's version[19] of the Busing, Martin, and Levy least-squares program[20] using a weighting scheme suggested by Hughes.[21]

The 200 reflection was omitted from the refinement as its value was obviously low due to extinction. Atomic scattering factors were taken from the International Tables for X-Ray Crystallography.[22] After several cycles of isotropic and then anisotropic refinement a difference Fourier synthesis was calculated. The seven hydrogen atoms were located unambiguously and were assigned positions at the observed peaks. The hydrogen atom positions were then adjusted by 0.1 Å or less to make all C–H distances 1.08 Å and the N–H distance 1.04 Å. The positional and anisotropic thermal parameters of the heavier atoms and the isotropic thermal parameters of the hydrogen atoms were refined, keeping hydrogen atom positions constant, to a final agreement index of 0.052. The final atomic parameters are listed in Table II, and the rms atomic displacements due to thermal motion are shown in Table III. The structure factors from the final refinement are available from the authors.

Description of the Structure

A stereo view of the molecule produced by the Oak Ridge Plotting Program[23] is shown in Figure 1, and Table IV lists the interatomic distances and bond angles. The lack of hydrogen atoms bonded to either of the two oxygen atoms and the presence of the two hydrogen atoms near the nitrogen atom confirm the expected zwitterionic structure. This is consistent with the observed C(1)–O(1) and C(1)–O(2) distances which are equal within experimental error.

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Table II. Atomic Positional and Anisotropic Temperature Parameters in AzCOOH[a]

Atom	x	y	z	β_{11} or B_{iso}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N	0.0948 (3)	0.5476 (2)	0.5084 (3)	0.0135 (5)	0.0035 (3)	0.0123 (7)	−0.0017 (3)	−0.0006 (5)	0.0005 (3)
C(1)	0.0137 (3)	0.3251 (3)	0.3177 (5)	0.0081 (4)	0.0054 (3)	0.0131 (7)	0.0010 (3)	0.0012 (5)	−0.0012 (4)
C(2)	0.0430 (4)	0.3994 (2)	0.5267 (5)	0.0098 (4)	0.0034 (3)	0.0111 (7)	−0.0000 (3)	−0.0009 (5)	−0.0003 (3)
C(3)	−0.1222 (4)	0.4380 (3)	0.6598 (5)	0.0142 (5)	0.0074 (4)	0.0148 (7)	−0.0012 (4)	0.0013 (5)	0.0000 (4)
C(4)	−0.0493 (4)	0.5835 (3)	0.6688 (5)	0.0199 (6)	0.0053 (3)	0.0147 (7)	0.0008 (4)	−0.0000 (7)	−0.0030 (4)
O(1)	−0.0635 (3)	0.2127 (2)	0.3405 (4)	0.0175 (4)	0.0056 (3)	0.0186 (7)	−0.0037 (3)	0.0038 (5)	−0.0028 (3)
O(2)	0.0720 (3)	0.3763 (2)	0.1526 (3)	0.0171 (5)	0.0085 (3)	0.0128 (6)	−0.0032 (3)	−0.0003 (4)	0.0006 (3)
Coordinates not refined									
H(N)	0.076	0.588	0.358	3.84					
H(N)′	0.225	0.573	0.550	7.64					
H(C2)	0.141	0.338	0.609	5.76					
H(C3)	−0.161	0.388	0.805	3.84					
H(C3)	−0.246	0.440	0.573	5.76					
H(C4)	0.005	0.610	0.822	4.96					
H(C4)	−0.126	0.666	0.603	5.76					

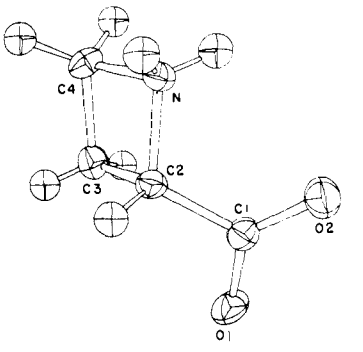
[a] Estimated standard deviations in parentheses refer to the last decimal positions of respective values. The temperature factor expression used was exp $-(h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{33} + 2hk\beta_{12} + 2lh\beta_{13} + 2kl\beta_{23})$.

Table III. Principal Axes of Thermal Ellipsoids[a]

Atom	i	U_i Å	$U_i \cos\theta_{ia}$, Å	$U_i \cos\theta_{ib}$, Å	$U_i \cos\theta_{ic}$, Å
N	1	0.124 (5)	0.032	0.119	−0.013
	2	0.158 (4)	−0.022	−0.012	−0.156
	3	0.200 (4)	0.191	−0.054	−0.023
C(1)	1	0.135 (5)	0.095	−0.071	−0.064
	2	0.165 (5)	−0.116	−0.069	−0.095
	3	0.174 (5)	0.018	0.129	−0.116
C(2)	1	0.128 (5)	0.009	0.125	0.026
	2	0.148 (5)	−0.050	0.032	−0.136
	3	0.168 (4)	0.158	0.001	−0.058
C(3)	1	0.170 (4)	−0.057	−0.037	0.155
	2	0.184 (5)	−0.076	−0.154	−0.065
	3	0.207 (4)	0.175	−0.104	0.042
C(4)	1	0.134 (6)	−0.007	0.104	0.083
	2	0.193 (5)	0.019	−0.119	0.151
	3	0.237 (4)	0.236	0.025	−0.010
O(1)	1	0.140 (4)	0.046	0.126	0.039
	2	0.181 (4)	0.096	0.013	−0.154
	3	0.249 (3)	0.195	−0.105	0.113
O(2)	1	0.160 (4)	−0.009	−0.027	0.157
	2	0.180 (4)	−0.109	−0.141	−0.030
	3	0.180 (4)	0.191	−0.144	−0.014

[a] The root mean square displacement U_i corresponds to the ith principal axis of the ellipsoid and $U_i \cos\theta_{ia}$, $U_i \cos\theta_{ib}$, $U_i \cos\theta_{ic}$ are rms components of thermal displacement along principal axis i projected on crystallographic axes a, b, c.

Table IV. Intramolecular Distances and Angles in AzCOOH



	Distance, Å		Angle, deg
C(1)–C(2)	1.525 (4)	C(2)–C(1)–O(1)	112.7 (2)
C(2)–C(3)	1.539 (4)	C(2)–C(1)–O(2)	119.1 (2)
C(3)–C(4)	1.528 (4)	O(2)–C(1)–O(1)	128.0 (2)
		C(1)–C(2)–C(3)	118.4 (2)
C(4)–N	1.519 (4)	N–C(2)–C(1)	115.5 (2)
N–C(2)	1.507 (3)	N–C(2)–C(3)	90.5 (2)
		C(2)–C(3)–C(4)	88.0 (2)
C(1)–O(1)	1.252 (4)	C(3)–C(4)–N	90.5 (2)
C(1)–O(2)	1.238 (4)	C(4)–N–C(2)	89.5 (2)

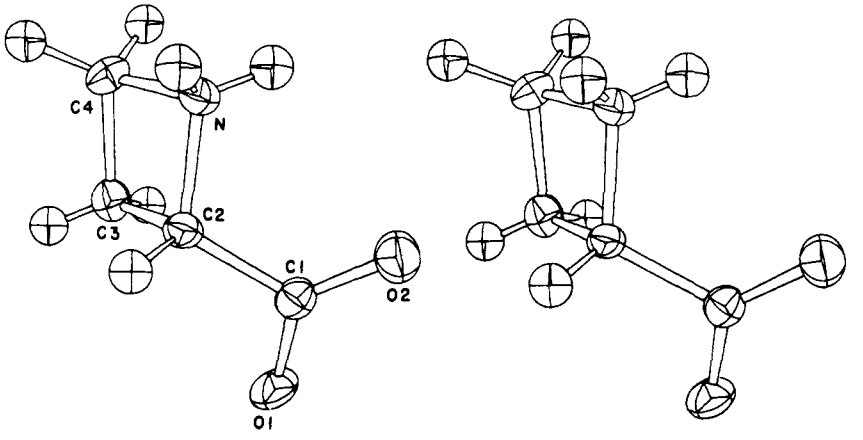


Figure 1. Stereo pair showing the AzCOOH molecule.

The azetidine ring is not planar. For example, the planes defined by the atoms N–C(2)–C(3) and N–C(1)–C(3) meet with a dihedral angle of 169 ± 1°. Viewed along N–C(3) or along C(2)–C(4) (see Figure 2) the 11° deviation from planarity can be clearly seen. The two possible dihedral angles are only 0.1° different, an order

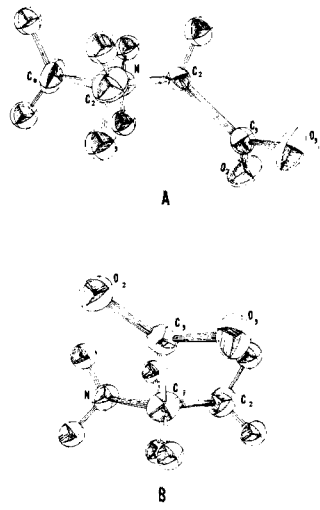


Figure 2. (a) View along the N–C(3) direction, and (b) view along the C(2)–C(4) direction of the AzCOOH molecule, showing the dihedral angle of 169° or the "buckling" of 11° in the ring.

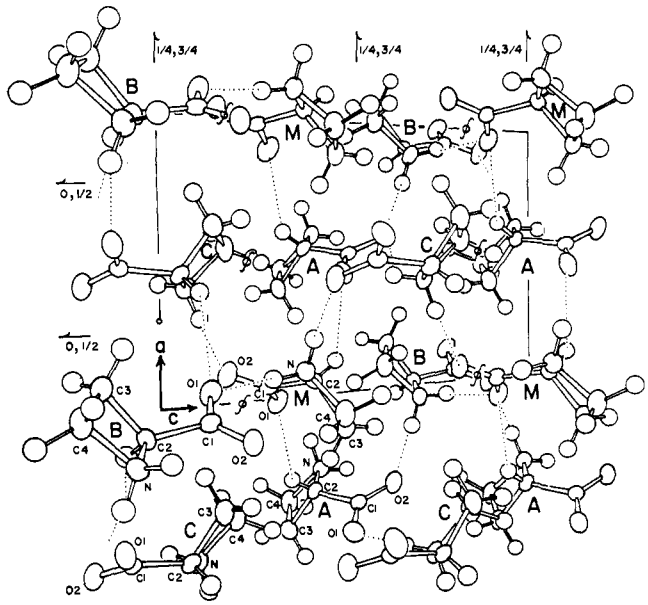


Figure 3. Molecular packing diagram with perspective, viewed 10° off the *b* axis, and showing hydrogen-bonding schemes. The symmetry code for the molecules is M = x, y, z; A = $1/2 + x, 1/2 - y, -z$; B = $-x, 1/2 + y, 1/2 - z$; C = $1/2 - x, -y, 1/2 + z$.

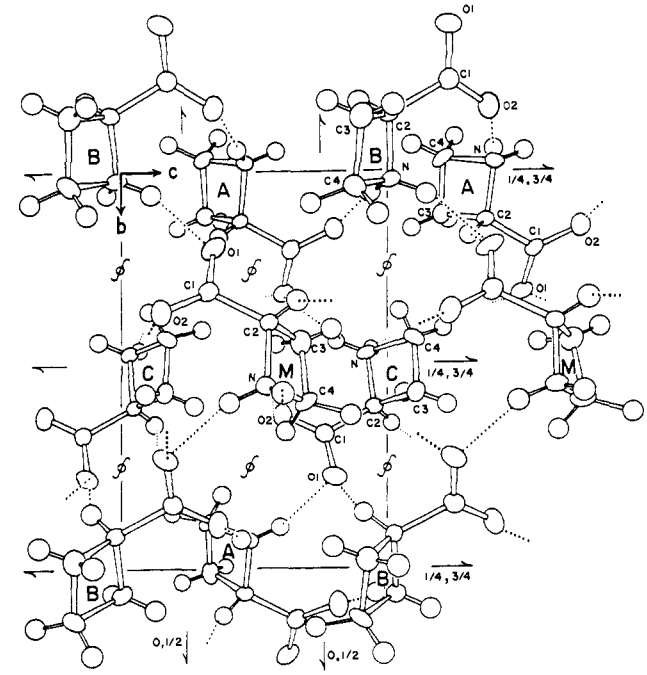


Figure 4. Molecular packing diagram with perspective, viewed down the *a* axis, and showing hydrogen-bonding schemes. Molecular symmetry code is the same as in Figure 3.

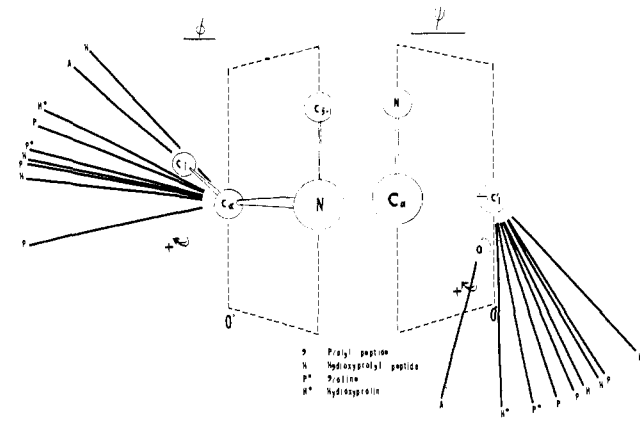


Figure 5. Conformation angles, ϕ and ψ, for AzCOOH, proline, and some prolyl peptides. Positive direction and zero datum are indicated by the arrows and figures. The atoms are drawn to correspond to AzCOOH (A), but projection lines indicate the positions which would be taken up in other cases.

of magnitude less than experimental error. The azetidine ring is only slightly buckled, and the ring angles are nearly 90°, although their sum, as it must be from geometric considerations, is less than 360°. Ring buckling is such as to bring the HC(4) atom farther from the carboxyl group connected to the C(2) atom across the ring (see Figure 2a). The conformation of the azetidine ring, just as in the case of the cyclobutane ring, is greatly affected by cross-ring, or 1,3 steric interactions.[16]

The C–C bond lengths are normal at 1.530 Å, and there is no distinction between the cyclic and exocyclic bond distances. The C_α–N and N–C_{ring} bond lengths of 1.507 and 1.519 Å are somewhat longer than those found in L-leucyl-L-prolylglycine[24] (1.45 and 1.46 Å), but equal within experimental error to those found in tosyl-L-proly-L-hydroxyproline[25] (1.49 and 1.50 Å) and in free proline[26] (1.53 and 1.48 Å). While it is not possible to state conclusively from these observations that the C–N distances in AzCOOH are always greater than in proline, it is not surprising that this is true in some cases, and may be attributable to strain in the azetidine ring. The C–O bonds are equal within experimental error (1.252 and 1.238 Å) and correspond well to the values usually found for carboxylic acid anions.

Hydrogen Bonding

The crystal structure consists of layers of molecules perpendicular to the *a* axis with their mean planes at $x = 0$ and $x = 1/2$. The hydrogen bonds can therefore

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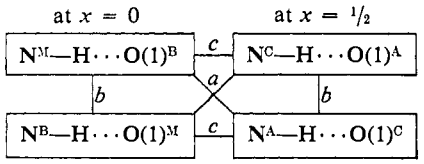
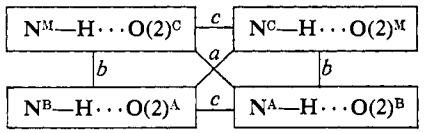
Table V. Types and Symmetry Properties of Hydrogen Bonds and Infinite Chains[a]

1. Intralayer Hydrogen Bonds N—H···O



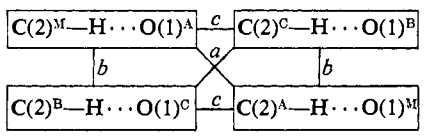
N—H = 1.04 Å ∠N—H···O(1) = 158.7°
H—O(1) = 1.754 Å H displacement from straight line, 0.25 Å
N—O(1) = 2.748 Å

2. Interlayer Hydrogen Bonds N—H···O(2)



between $x = 0$ and $x = 1/2$: N—H = 1.043 Å; ∠N—H···O(2) = 171.8°
H—O(2) = 1.713 Å; H displacement from straight line, 0.16 Å
between $x = 1/2$ and $x = 1$: N—O(2) = 2.750 Å

3. Interlayer Aliphatic Hydrogen Bonds C(2)—H···O(1)



between $x = 0$ and $x = 1/2$: C—H = 1.084 Å; ∠C—H···O(1) = 147.5°
H—O(1) = 2.277 Å; H displacement from straight line, 0.40 Å
between $x = 1/2$ and $x = 1$: C—O(1) = 3.245 Å

4. Sequences of Helices and Chain, in Positive x Direction or y Direction

Eight atom helix parallel to a (12 atoms including H)

(O(2)—C(1)—O(1))^B···H—N^M—H···(O(2)—C(1)—O(1))^C···H—N^A—H···repeat

(O(1)—C(1)—C(2))^M···H—N^C—H···(O(1)—C(1)—O(2))^A···H—N^B—H···repeat

Six atom helix parallel to a (8 atoms including H)

(O(1)—C(1)—C(2))^M—H···(O(1)—C(1)—C(2))^A—H···repeat

(C(2)—C(1)—O(1))^C···H—(C(2)—C(1)—O(1))^B···H—repeat

Eight atom chain parallel to b (10 atoms including H)

(O(1)—C(1)—C(2)—N)^B—H···(O(1)—C(1)—C(2)—N)^M—H···repeat

(O(1)—C(1)—C(2)—N)^A—H···(O(1)—C(1)—C(2)—N)^C—H··· repeat

[a] Structural layers are perpendicular to the a axis. Atoms N, C, or O are superscripted with the molecular symmetry code (see Figure 3). The lower case letters between the boxes indicate the screw symmetry operator relating the two hydrogen bonds to each other. For instance, in section 1 the nitrogen atom in molecule M is hydrogen bonded to O(1) in molecule B, both in the layer at $x = 0$. This hydrogen bond is related by a, b, and c screw symmetry operators to identical hydrogen bonds in the same and in different layers. Lengths and angles of bonds are based on observed peak locations in the difference map.

be described as inter- and intralayer (see Figures 3 and 4).

The types of hydrogen bonds found, their lengths, and the angles subtended at the hydrogen atoms are listed in Table V. The first two types of hydrogen bond are normal with over-all donor–acceptor distances less than 2.8 Å. These alone form a reasonable network of inter- and intralayer connections and may indeed be the only true hydrogen bonds in the structure. A third type of hydrogen bond apparently occurs between the aliphatic C(2) atom and the O(1) atom. The hydrogen atom was unambiguously located on the difference map at a point 0.40 Å from the line of centers between C(2) and O(1). While the C(2)–O(1) distance is rather long (3.24 Å), the angles H(C2)–C(2)–N and H(C2)–C(2)–C(3) are such that less strain would result if the H(C2) atom were further away from the O(1) atom, from which it is inferred that the C(2)–H–O(1) grouping represents a bonding interaction.

Biological Implications

Conformation diagrams are given in Figure 5 and the angles in Table VI for AzCOOH, proline,[26] hydroxyproline,[27] L-leucyl-L-prolylglycine,[24] tosy-L-prolyl-L-hydroxyproline,[25] poly-L-proline, and poly-L-hydroxyproline.[28,29] The angles were calculated in all cases from atomic coordinates as published (with correction of some obvious errors) and expressed as ϕ and ψ angles.[30]

Table VI. Conformation Angles in Peptides and Amino Acids[31]

Structure	ϕ, deg	ψ, deg
L-Azetidine-2-carboxylic acid	131	14
Proline in		
L-Proline[26]	105	−10
L-Leucyl-L-prolylglycine[24]	112	−18
Tosyl-L-prolyl-L-hydroxyproline[25]	78	−23
Poly-L-proline[28]	101	−32
Hydroxyproline in		
Hydroxy-L-proline[27]	117	−1
Tosyl-L-prolyl-L-hydroxyproline[25]	137	−43
Poly-L-hydroxyproline[29,a]	98	−26

[a] These numbers are the result of model building, and the backbone of poly-L-hydroxyproline is almost identical with that of poly-L-proline.

The values of the conformation angle ϕ (Table VI) show that AzCOOH has a much higher value than those of either free proline or the prolyl peptides.[31] The angle ψ is also 20° or more higher than that of any other peptide or amino acid considered in Table VI with the exception of hydroxyl-L-proline. The angle ϕ for proline peptides seems to remain within experimental error of that of free proline itself, except for the low value of tosyl-L-prolyl-L-hydroxyproline.[25,31] Using data published by Ramachandran[32] it is possible to estimate that

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(31) The average of the ϕ values reported in Table VI is 99° for proline, 117° for hydroxyproline, and 107° for both groups together.
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the height h of the repeating unit in a helical polymer of AzCOOH would be smaller by an amount approaching 1 Å than that of a corresponding polymer of proline. Azetidinecarboxylic acid, having a comparatively rigid four-membered ring and a value of ϕ some 20° to 30° higher than that of the average proline residue, must transmit most of this difference to any peptide into which it is incorporated. This implies that the growth-inhibitory properties of AzCOOH must result from its conformational differences with proline and that significant changes in tertiary structure are thus caused when AzCOOH is incorporated in place of proline in a polypeptide having a biological function. To confirm this, a model was constructed at a scale of 1.25 cm/Å using foam balls for the azetidine ring and gluing standard Corey–Pauling–Koltun model components[33] to the ring at C(1), O(1), and O(2), and substituting an amide carbon atom for the two hydrogen atoms on nitrogen. This model was compared with one of proline by alternately inserting them one residue short of the N-terminal residue in a model of an α helix. AzCOOH caused a change in direction at the N-terminal amide bond of 16° and an alteration of position of the succeeding amide carbons of 0.7 Å. However, the altered conformation resulted largely from features not expressible as ϕ or ψ angles; the square ring of AzCOOH differs from the pentagon of proline by about 18° in the direction of adjacent ring-to-out-of-ring bonds. Thus it was no surprise that the directions of successive amide bonds in the helix were changed by 16°.

We therefore conclude that the conformation of AzCOOH is sufficiently different from that of proline to cause the growth-modifying effects observed when it replaces proline in functional polypeptides.[34] Furthermore, the conformational features of AzCOOH and other amino acids cannot be fully described by reference to ϕ and ψ angles, even though the bond lengths have close to average values. We suggest that an examination of the detailed physical and chemical properties of polypeptides and proteins having azetidinecarboxylic acid in place of proline could be a fruitful line of investigation.

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The Synthesis and Certain Pharmacological Properties of Deamino-oxytocinoic Acid Methylamide and Deamino-oxytocinoic Acid Dimethylamide[1,2]

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Abstract: Deamino-oxytocinoic acid methylamide and deamino-oxytocinoic acid dimethylamide, analogs in which methyl groups have replaced one or both hydrogens, respectively, on the nitrogen of the 9-carboxamide group of deamino-oxytocin, have been synthesized by the Merrifield solid phase method and their oxytocic and avian vasodepressor potencies have been determined. Deamino-oxytocinoic acid methylamide possessed approximately 29 units/mg of oxytocic activity and the dimethylamide analog possessed approximately 16 units/mg. Neither analog exhibited any detectable amounts of avian vasodepressor activity. Deamino-oxytocin possesses 803 ± 36 units/mg of oxytocic activity and 975 ± 24 units/mg of avian vasodepressor activity.

In earlier investigations[4–6] it was found that oxytocinoic acid (9-deamido-oxytocin) possessed extremely low levels of oxytocic and avian vasodepressor activities in contrast to the high levels characteristic of oxytocin. Thus the amide group of the glycinamide residue at position 9 of oxytocin (Figure 1) is highly important for the manifestation of these activities. It has likewise been found that deamino-oxytocinoic acid[6] possesses an extremely low level of avian vasodepressor activity and no detectable oxytocic activity, in contrast to deamino-oxytocin[7–10] which is even more potent than oxytocin with respect to these activities. Deamino-oxy-

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(2) All optically active amino acid residues are of the L variety.

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