Internal Rotation in Amino Acids

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Introduction

Several models of proteins have been presented[1-4]. They cannot differ much from one another in bond lengths and bond angles. The essential point in their difference lies in the manner of the chain-folding due to the internal rotation about single bonds contained in the polypeptide chain.

With regard to the equilibrium angles of internal rotation in amides and related compounds we have published many papers[5,6,7]. The work has been extended to the study of equilibrium angles in amino acids based on the data of the X-ray structure analysis. The references for these data are as follows:

DL-Norleucine (α-form); A. M. Mathieson, *Acta Cryst.*, **6**, 399 (1953).

DL-Methionine (α-form); A. M. Mathieson, *Acta Cryst.*, **5**, 332 (1952).

DL-Methionine (β-form); A. M. Mathieson, *Acta Cryst.*, **5**, 332 (1952).

Hydroxy-L-proline; J. Donohue, *Acta Cryst.*, **5**, 419 (1952).

DL-Serine: D. P. Shoemaker, R. E. Barieau, J. Donohue and Chia-Si Lu; *Acta Cryst.*, **6**, 241 (1953).

Glycyl-L-tyrosin hydrochloride; D.W. Smits and E. H. Wiebenga; *Acta Cryst.*, **6**, 531 (1953).

α-Glycine; G. Albrecht and R. B. Corey, *J. Am. Chem. Soc.*, **61**, 1087 (1939).

α-DL-Alanine; H. A. Levy and R. B. Corey, *J. Am. Chem. Soc.* **63**, 2095 (1941), J. Donohue, *J. Am. Chem. Soc.*, **72**, 949 (1950).

β-Glycylglycine; E. W. Hughes and W. J. Moore, *J. Am. Chem. Soc.*, **71**, 2618 (1949).

N-Acetylglycine; G. B. Carpenter and S. Donohue, *J. Am. Chem. Soc.* **72**, 2315 (1950).

L$_S$-Threonine; D. P. Shoemaker, J. Donohue, V. Shoemaker and R. B. Corey, *J. Am. Chem. Soc.*, **72**, 2328 (1950).

DL-Glutamic acid hydrochloride; B. Dawson, *Acta Cryst.*, **6**, 81 (1953).

Glycyl-L-asparagine; R. A. Pasternak, L. Katz and R. Corey: *Acta Cryst.*, **7**, 225 (1954).

NN'-Diglycyl-L-cystine dihydrate; H. L. Yakel and E. W. Hughes, *Acta Cryst.*, **7**, 29 (1954).

D(−)-Isoleucine hydrochloride; J. Trommel and J. M. Bijvoet; *Acta Cryst.*, **7**, 703 (1954).

D(−)-Isoleucine hydrobromide: J. Trommel and J. M. Bijvoet; *Acta Cryst.*, **7**, 703 (1954).

L-Glutamine; W. Cochran and B. P. Penfold, *Acta Cryst.*, **5**, 644 (1952).

1) T. Shimanouchi and S. Mizushima, *Kagaku*, **17**, 24, 52 (1947); *Bull. Chem. Soc. Japan*, **21**, 1 (1948); S. Mizushima, Advances in Protein Chemistry IX.

2) H. Zahn, *Z. Naturforschung*, **2B**, 104 (1947).

3) E. J. Ambrose and W.E. Hanby, *Nature*, **163**, 483 (1949).

4) L. Pauling, R.B. Corey and H.R. Branson. *Proc. Natl. Acad. Sci. U.S.*, **37**, 205 (1951).

5) For the summary, see S. Mizushima, Structure of Molecules and Internal Rotation, Academic Press, New York (1954). See also ref. 1.

6) S. Mizushima, T. Shimanouchi, M. Tsuboi, et al., *J. Am. Chem. Soc.*, **72**, 3490 (1950); **73**, 1330 (1951); **74**, 270, 4639, 5550 (1952); **75**, 1863 (1953); **76**, 2479, 6003 (1954).

7) T. Shimanouchi and S. Mizushima, *J. Chem. Phys.*, **23**, 707 (1955).

L-Glutamic acid; S. Hirokawa, *Acta Cryst.*, 8, 637 (1955)*.

The Method of Calculation

In order to obtain equilibrium angles of internal rotation from the X-ray data, it is convenient to express the positions of atoms in rectangular coordinate systems.

The transformation from oblique coordinates to rectangular coordinates can be expressed as:

$$X = AU, \tag{1}$$

where X and U are unit vectors in the rectangular and oblique coordinates, respectively and A is a matrix:

$$A = \begin{pmatrix} a, & b\cos\gamma, & c\cos\beta \\ 0, & b\sin\gamma, & \frac{c}{\sin\gamma}(\cos\alpha - \cos\beta\cos\gamma) \\ 0, & 0, & \frac{c}{\sin\gamma}(\sin^2\gamma - \cos^2\alpha - \cos^2\beta + 2\cos\alpha\cos\beta\cos\gamma) \end{pmatrix} \tag{2}$$

Here a, b, c are the lengths and α, β, γ, the angles of the unit cell in the oblique coordinate system.

The equilibrium angle θ of internal rotation about X_2–X_3 axis of the part X_1–X_2–X_3–X_4 is calculated as:

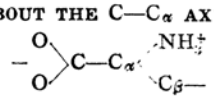
$$\cos\theta = \pm(\lambda\lambda' + \mu\mu' + \nu\nu'), \tag{3}$$

where λ, μ, ν and λ', μ', ν' are the direction cosines of the normals to the X_1–X_2–X_3 and X_2–X_3–X_4 planes, respectively.

The results of the calculation are listed in Tables I–VI. Table I refers to the

TABLE I

θ ABOUT THE C—C_α AXIS IN



Compound	NH_3^+	C_β
α-DL-Norleucine	12.5°	− 71.5°
α-DL-Methionine	33.5	− 90
β-DL-Methionine	29.5	− 89
Hydroxy-L-proline	3	−114
DL-Serine	4	−126
α-Glycine	13	—
α-DL-Alanine	17	−104.5
L_S-Threonine	25	− 95
DL-Glutamic acid hydrochloride	37	− 90
D(−)-Isoleucine hydrochloride	6.5	138
D(−)-Isoleucine hydrobromide	14	−121
L-Glutamine	51	−113
L-Glutamic acid	43	77
L-Glutamic acid hydrochloride	18	100

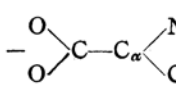
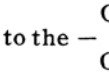
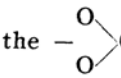
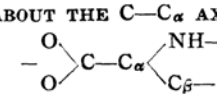
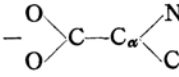
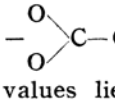
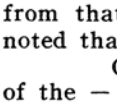
internal rotation about the C—C_α axis in  . The θ values of the NH_3^+ group lie in the range 0 to 37° and those of the C_β atom in the range −126° to −90° referred to the  plane. An exception is made for D(−)-isoleucine hydrochloride with the θ value of 138°. By some reason the C_β atom and the NH_3^+ group are on the same side of the  plane.

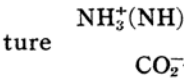
TABLE II

θ ABOUT THE C—C_α AXIS IN



Compound	NH	C_β
β-Glycylglycine	0°	—
N-Acetylglycine	2.5	—
Glycyl-L-tyrosine hydrochloride	37	174.5
Glycyl-L-asparagine	63	173.5
NN′-Diglycyl-L-cystine dihydrate	73.5	175

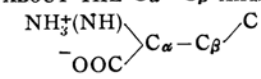
Table II lists the θ values for the structure  . Those for the stable positions of the —NH— group fall into two groups. One has the θ values almost equal to zero: i.e. the N atom lies close to the  plane. In the other group the θ values lie in the range ca. 40° to 70°. This difference is due to the presence of the C_β atom in the latter group which makes the steric relation in the molecule quite different from that of the former group. It is to be noted that the C_β atom lies on the other side of the  plane with respect to the N atom.

The θ values of the C_γ atom of the structure  are shown in Table III. In some cases we have the OH group or S atom in place of the C_γ atom. The values lie in the three ranges, 50° to 80°, 180° to 160° and −80° to −60°. These correspond, respectively, to the *gauche*, *trans* and *gauche* positions with respect to C_α—CO_2^- and to the *gauche*, *gauche* and *trans* positions with respect to C_α—$NH_3^+(NH)$. In other words, the stable positions are almost the same as those found in simple molecules such as ClH_2C—CH_2Cl.

* The author has calculated the equilibrium angles of internal rotation.

TABLE III

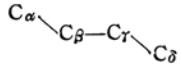
θ ABOUT THE $C_\alpha - C_\beta$ AXIS IN



Compound	C_γ	Note
DL-Norleucine	178.5	
α-DL-Methionine	177	
β-DL-Methionine	179	
L$_S$-Threonine	177.5	OH in place of C_γ
DL-Glutamic acid hydrochloride	157	
Glycyl-L-asparagine	173.5	
D(-)-Isoleucine hydrochloride	160	
DL-Serine	53	OH in place of C_γ
D(−)-Isoleucine hydrochloride	79	
D(−)-Isoleucine hydrobromide	65	
L-Glutamine	54	
Glycyl-L-tyrosine hydrochloride	−80	
L$_S$-Threonine	−63	
NN′-Diglycyl-L-cystine dihydrate	−77.5	S in place of C_γ
D(−)-Isoleucine hydrobromide	−60	
L-Glutamic acid	180	

TABLE IV

θ ABOUT THE $C_\beta - C_\gamma$ AXIS IN



Compound	C_δ	Note
DL-Norleucine	179°	
α-DL-Methionine	177	S in place of C_δ
β-DL-Methionine	176.5	S in place of C_δ
D(−)-Isoleucine hydrochloride	172	
D(−)-Isoleucine hydrobromide	−69	
L-Glutamine	176	
L-Glutamic acid	90	
DL-Glutamic acid hydrochloride	180	

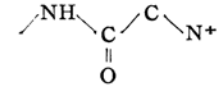
Table IV refers to the structure of $C_\alpha - C_\beta - C_\gamma - C_\delta$ which is similar to that of a segment of a normal paraffin molecule. This has been shown to be in the *trans* form (or the extended form) in the solid state[8]. As shown in this table, the C_δ atom is almost in the *trans* position with respect to the C_α atom except for D(−)-isoleucine hydrobromide.

Table V shows structure of NH—C—C—N^+, including the similar structures with C in place of NH and with C or N in place of N^+. NH (or C) is in the *trans* position with respect to N^+ (or C or N).

Table VI refers to the structure of C—NH—C—C. C=O is in the *trans* or the *gauche* position with respect to the C atom.

TABLE V

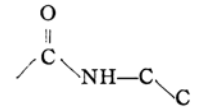
θ ABOUT THE C—C AXIS IN

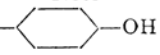


Compound	N(C)	Note
β-Glycylglycine	−146°	
Glycyl-L-asparagine	−172	
Glycyl-L-asparagine	−171	C in place of N^+
NN′-Diglycyl-L-cystine	−170.5	
L-Glutamine	−165	C in place of N^+

TABLE VI

θ ABOUT THE N—C AXIS IN



Compound	C	Note
Glycyl-L-tyrosine hydrochloride	177.5°	
β-Glycylglycine	177.5	
N-Acetylglycine	180	
NN′-Diglycyl-L-cystine	154	CO_2^-
Glycyl-L-tyrosine hydrochloride	85	CO_2^-
NN′-Diglycyl-L-cystine dihydrate	62.5	CH_2

In addition to the axes of internal rotation mentioned above we have the C—S axis in the structure of C—C—S—C and the S—S axis in the structure of C—S—S—C. The θ values in the former in α and β forms of DL-Methionine are 80° and 170°, respectively and that of the latter in NN′-diglycyl-L-cystine dihydrate is 101°. It is to be noted that in the S—S axis the dominant factor in determining the θ value is the electronic clouds on the S atoms which are unsymmetrical about the S—S axis[9]. In other cases where the hindering of internal rotation mainly arises from the interaction between the rotating groups, the results obtained above for amino acids are compatible with our conclusion of the *trans* and *gauche* stable positions derived from the structure determination of many molecules containing the C—C, C—O and C—N axes[5,7]. The result obtained in the present work provides us with further information which would permit the reliable prediction of the structure of polypeptide chain.

Summary

Equibrium angles of internal rotation about single bonds in amino acids have been calculated based on the data of the X-ray structure analysis. The result was similar to that obtained so far for many molecules containing similar bonds

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8) S. Mizushima and T. Shimanouchi, *J. Am. Chem. Soc.*, **71**, 1320 (1949).

9) Y. Morino and S. Mizushima, *Sci. Pap. Inst. Phys. Chem. Res., Tokyo*, **32**, 220 (1937).