

The Deuteration Effect on the Hydrogen Bond Length of the α -helix of Polypeptides

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Synopsis

The calculations of computational model building of the α -helix of polypeptides were carried out, by the use of only the helical parameters taking into considerations the non-planarity of the peptide groups in order to clarify the effect of deuteration on the hydrogen bond length of NH—O system. The results indicate the increment by about 0.02 Å or less, if any, of hydrogen bond length on deuteration.

Introduction

It is reported that in N-deuterated polymers of γ -benzyl-L-glutamate and β -benzyl-L-aspartate, the hydrogen bond lengths are increased by about 0.025 Å than in the normal forms of the α -helix, as it is shown in table 2(a)(1). The change in the spacing of the 5.4 Å layer in the X-ray diffraction patterns upon deuteration is an increment of 0.027 ± 0.008 Å in both cases. However, this conclusion is derived on the assumption that the hydrogen bonds in the α -helix are virtually oriented parallel to the helix axis and the radius of the helix does not change on deuteration.

Actually, as it is shown in this work, the direction of the hydrogen bonds in the α -helix is not parallel but N-H bonds make an angle of 12-15° to the helix axis (table 1(d)). And it is not reasonable to neglect the change of the helix radius in spite of the slight expansion (1%) of lattice constant for the deuterated forms (1).

The purpose of this note is to report the molecular geometry of the α -helix with the standard bond lengths and angles (2), which were

calculated only by using the helical parameters observed in the X-ray diffraction pattern, in order to make clear the effect of deuteration on the hydrogen bond lengths of NH—O system. Structural models with the non-planar peptide groups were also considered and their potential energy was estimated to compare the relative stability.

Methods

The computer programmes applied for the model building of polypeptide structures were made by using the equations of reference (3), which give the relations between the three internal rotational angles (ϕ , ψ , ω) and the helical parameters (p , θ) (4). Here, p is the residue translation along the helix axis and θ is the rotation angle around the same axis, of which values are accurately determined from the layer line distribution in the X-ray diffraction pattern (12). Bond lengths and bond angles must conform with the standard (2). For comparison of the stability of α -helix with planar peptide and with nonplanar peptide, potential energy for mainchain structures with methyl group as sidechain (poly-L-alanine) was calculated by Scheragas method, except that hydrogen bond energy was estimated by using Lippincott-Schroeder model (5-6). As the potential barrier height around the peptide bonds, the value of 12.7 kcal/mol. residue was used, which was deduced from the force constant (0.20 md.A) of amide VII vibration by subtracting the effect of non-bonded and electrostatic interactions of N-methyl acetamide (7).

Results

When the torsion angle around the peptide bonds (ω -angle) is smaller than or equal to 178.0° ($p=1.47-1.53 \text{ \AA}$, $\theta=100.0^\circ$), or larger than or equal to 181.0° ($p=1.47-1.51 \text{ \AA}$, $\theta=100.0^\circ$), there is no exact models for a right-handed α -helix with an axial translation per residue of about 1.50 \AA and a rotation angles per residue of 100.0° . Some values on the molecular geometry of the α -helix of a planar ($\omega=$

180.0°) and a non-planar ($\omega=179.0^\circ$) peptide model is shown in table 1. Their detailed atomic coordinates would be published elsewhere.

Table 1

Some values on the molecular geometry of the right-handed α -helix

	ψ°	ϕ°	(a)	(b)	(c)	(d)	(e)
planar peptide model ($\omega=180.0^\circ$)	-46.79	-58.06	2.91	14.8	3.24	15.0	-12.41
non-planar peptide model ($\omega=179.0^\circ$)	-54.25	-49.71	2.86	8.3	3.08	12.6	-12.71
Pauling's model ($\omega=180.0^\circ$)	-57.63	-46.21	2.84	7.9	2.97	12.1	—

(a) hydrogen bond length (\AA) (N—O)

(b) hydrogen bond angle ($^\circ$) ($\angle\text{HNO}$)

(c) distance between C_β and O atom three residues away (\AA)

(d) N—H bond orientation to the helix axis ($^\circ$)

(e) estimated potential energy (kcal/mol. residue)

The hydrogen bond length is longer by 0.07 \AA in the computed model and its angle is as large as twice in the physical wire model. The distance between β -carbon and carbonyl oxygen three residue away in the wire model is shorter by about 0.3 \AA , which is considered to have a important role in the stability of mainchain structure.

The estimated potential energy of the α -helix with the non-planar peptides ($\omega=179.0^\circ$) is lower than that with the planar peptides ($\omega=180.0^\circ$) by 0.03 kcal/mol. residue as it is shown in table 1 (e). This energy difference is obtained only when the energy is minimized, allowing the rotation of sidechain methyl group ($\chi=54^\circ$ and 48° respectively). So, the peptide groups in the α -helix could be non-planar, which is expected from a geometrical consideration of the hydrogen bonds as it is shown in table 1 (a) and 1 (b). In this respect, the refinement of X-ray diffraction analysis of α -poly-L-alanine structure shows the appreciably small distorsion of ω -angle to the opposite

direction ($\omega = -179.8^\circ$) (8). By the similar method described above, hydrogen bond lengths and angles in the deuterated and normal forms of PBLG and PBLA were calculated using the values of the helical parameters observed in the X-ray diffraction patterns, which appeared in reference (1).

Table 2

Hydrogen bond lengths in the normal and deuterated forms

	p(Å)	(a)	(b)	(c)	(d)	(e)
PBLG* ¹	1.494±0.002	0.025 Å	2.910 Å	16.75°	2.843 Å	8.627°
d-PBLG	1.501±0.002		2.911 Å	14.60°	2.860 Å	8.256°
PBLA* ²	1.496±0.001	0.029 Å	2.910 Å	16.10°	2.848 Å	8.502°
d-PBLA	1.504±0.002		2.914 Å	13.86°	2.868 Å	8.207°

- (a) increased values of the hydrogen bond distance (N—O) given by reference (1).
 (b) hydrogen bond length calculated by using a planar peptide model ($\omega = 180.0^\circ$)
 (c) hydrogen bond angles ($\angle HNO$) calculated by using a planar peptide model
 (d) hydrogen bond length calculated by using a non-planar peptide model ($\omega = 179.0^\circ$ for PBLG and $\omega = 181.0^\circ$ for PBLA)
 (e) hydrogen bond angles calculated by using a non-planar peptide model

*¹ PBLG : poly- γ -benzyl-L-glutamate (right-handed helix)

*² PBLA : poly- β -benzyl-L-aspartate (left-handed helix)

In the model used for these calculations, only the ϕ , ψ , ω angles and N—H bond length are allowed to vary. Therefore, the change of the N—O distance naturally results in the slight change of ψ and ϕ angles, of which values are -2.00° and 2.40° respectively in the planar peptide model and -1.20° and 1.43° respectively in the non-planar peptide model of PBLG as it is shown in table 3.

Table 3

Internal rotational angles of normal and deuterated forms

	(a)		(b)	
	ψ°	ϕ°	ψ°	ϕ°
PBLG* ¹	-45.02	-60.18	-53.24	-50.92
d-PBLG	-47.02	-57.78	-54.44	-49.49
PBLA* ²	45.61	59.47	53.55	50.54
d-PBLA	47.76	56.89	54.87	48.96

(a) planar peptide models ($\omega=180.0^\circ$)(b) non-planar peptide models ($\omega=179.0^\circ$ for PBLG and $\omega=181.0^\circ$ for PBLA)*¹ PBLG : poly- γ -benzyl-L-glutamate (right-handed helix)*² PBLA : poly- β -benzyl-L-aspartate (left-handed helix)

The change of ω -angle on deuteration could be negligible because of its higher barrier constant of 14 kcal/mol..

Although the appreciable change of spacing in the 1.5 Å and 5.4 Å reflections upon deuteration were observed, the increment of the hydrogen bond length in the former case (table 2 (b)) is less than the errors of the observed spacing. Consequently, it is more probable to consider that the hydrogen bond lengths were altered by the order of about 0.020 Å or less, if any, as it is shown in table 2 (c).

The results of ammonium oxalate by neutron diffraction analysis showed only very small expansion (0.004 Å on average) on deuteration (11). However, such an effect has not yet been confirmed on the hydrogen bonded system of peptides.

Discussion

The expansion of hydrogen bond length upon deuteration is generally explained by the anharmonicity of the potential energy curve for the motion of hydrogen atom in the N-H—O hydrogen bond system, where the maxima of the probability distribution curve is

displaced to the right (dissociation part) of potential minimum, the more so the greater the zero point energy (9).

On this basis, the lower zero point energy of deuterium compared with hydrogen would result in a decrease in the N-H distance on average, and produce an increase in N—O distance on substituting D for H in hydrogen bonds, as it is shown in Lippincott-Schroeder model of hydrogen bond (6, 10).

In stead of that, the present results of computations of $\angle\text{HNO}$ angles in H-forms show the decrease on deuteration by 0.30° - 2.20° , if any, as it is shown in table 2 (c) and 2 (e). A detailed explanation for this result would be considered at a later date.

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