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THE MEAN GEOMETRY OF THE PEPTIDE UNIT FROM CRYSTAL STRUCTURE DATA*

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SUMMARY

The average dimensions of the peptide unit have been obtained from the data reported in recent crystal structure analyses of di- and tripeptides. The bond lengths and bond angles agree with those in common use, except for the bond angle C–N–H, which is about 4° less than the accepted value, and the angle C_2^α–N–H which is about 4° more. The angle τ (C^α) has a mean value of 114° for glycyl residues and 110° for non-glycyl residues. Attention is directed to these mean values as observed in crystal structures, as they are relevant for model building of peptide chain structures.

It has been the common practice in the literatures of peptide and protein conformation to use the dimensions of the peptide unit as given by Corey and Pauling (PC) [1]. For instance, these are given in reviews by Ramachandran and Sasisekharan [2] and Scheraga [3] and have been widely used, in spite of the fact that the analyses made by Marsh and Donohue [4] indicated slight differences from the PC values. During the last two or three years, a number of very accurate crystal structures of di- and tripeptides, determined using X-ray diffractometer data, have appeared. Neutron diffraction measurements, which give hydrogen atom positions very accurately, have also appeared. Therefore, an analysis was made of the bond lengths and bond angles of the peptide unit, $-(C_1^\alpha\text{–CO–NH–}C_2^\alpha)-$, which occurs in these examples. The values of bond lengths occurring in the peptide unit, along with their standard deviations, are given in Table I. The bond angles in the peptide unit, along with their standard deviations, are given in Table II. For the bond angles τ(C–N–H) and τ(H–N–C_2^α), in which one of the atoms involved is a hydrogen, the neutron diffraction data in the first two rows are much more accurate than the rest, namely, X-ray diffraction data. Consequently, the mean of the ten X-ray data are given within square brackets in the last row of the table. It will be noticed that they agree well with the mean of the two neutron data. The result is shown in Fig. 1, where the numbers shown are the weighted averages of the various quantities with their standard deviations given in brackets.

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TABLE I

THE BOND LENGTHS IN THE PEPTIDE UNIT, ALONG WITH THEIR STANDARD DEVIATIONS, FROM CRYSTAL DATA

	C_1^α–C	C–O	C–N	N–H	N–C_2^α	Technique* and ref. No.
Gly–Gly, HCl, water	1.515 (3)	1.233 (3)	1.329 (3)	1.034 (6)**	1.440 (3)	N, 5
α-Gly–Gly	1.515 (2)	1.238 (3)	1.326 (2)	1.021 (2)**	1.446 (2)	N, 6
Gly–L-Leu	1.502 (6)	1.231 (4)	1.334 (5)	0.898 (40)	1.463 (6)	X, Venkatesan, K., personal communication
L-Ala–Gly	1.524 (3)	1.216 (2)	1.335 (3)	0.948 (31)	1.443 (3)	X, 7
L-Ala–Ala	1.531 (7)	1.225 (6)	1.346 (3)	0.943 (47)	1.456 (6)	X, 8
Glutathione	1.493 (7)	1.218 (6)	1.350 (6)	0.786 (40)	1.452 (6)	X, Cole, F. E., personal communication
	1.516 (7)	1.214 (6)	1.308 (5)	0.881 (43)	1.425 (6)	
DL-*N*-Chloroacetyl-Ala	1.509 (3)	1.236 (3)	1.317 (3)	0.859 (26)	1.453 (3)	X, 9
Gly–Gly-phosphate	1.512 (3)	1.211 (4)	1.333 (4)	0.927 (55)	1.447 (6)	X, 10
N-Methyldiprolyl acetamide	1.510 (5)	1.241 (5)	1.320 (6)	0.894 (61)	1.445 (5)	X, 11
Gly–Gly, nitrate	1.514 (2)	1.222 (2)	1.330 (2)	0.760 (20)	1.453 (2)	X, 12
N-Acetyl-L-Phe-L-Tyr	1.507 (3)	1.231 (3)	1.335 (3)	0.870 (20)	1.442 (3)	X, 13
Weighted mean	1.516 (10)	1.227 (9)	1.331 (11)	0.86 (29)	1.449 (9)	

* N = neutron diffraction, X = X-ray diffraction.

** These values were not considered in calculating the weighted mean of the N–H bond length.

The geometry of the peptide unit

The bond lengths obtained in this analysis are only slightly different from the values already being used. The only exception is the distance between N and H which has a value (0.86 ± 0.06) Å, which is less than the standard value of 1.0 Å by 0.1 Å. The average quoted here is from X-ray data. The two neutron diffraction measurements give values 1.02 Å to 1.03 Å for the N–H distance. Since the neutron diffraction data fix the nuclear positions and since they are much more accurate, a value of 1.0 Å is recommended for the N–H bond length, as shown in Fig. 1a in square brackets. The bond angles at the C atom do not deviate by more than 2° from the accepted values. On the other hand, the direction of the N–H bond, relative to the other atoms, differs by as much as 4° from the one which is currently in use. The average values calculated from the data for the angles C–N–H and H–N–C_2^α are 119.5° and 118.2° as marked in Fig. 1b. However, most of the data are for structures at which there is a non-planarity of the three bonds meeting at nitrogen. Since the angle C–N–C_2^α does not change appreciably with changes in non-planarity, the value of 121.9° for this is also suggested for a planar peptide unit. In order to make the sum of the three angles at N equal to 360°, it is recommended that the value of 119.7° and 118.4° may be used for the other two angles C–N–H and H–N–C_2^α at nitrogen, respectively. The way in which these two angles vary for a non-planar peptide unit is mentioned in the next paragraph.

TABLE II

THE BOND ANGLES OF THE PEPTIDE UNIT AND THE ANGLE AT C_2^α ATOM ALONG WITH THEIR STANDARD DEVIATIONS FROM CRYSTAL DATA, AS OBSERVED IN SIMPLE PEPTIDES AND AMIDES

	C_1^α–C–O	C_1^α–C–N	O–C–N	C–N–H	C–N–C_2^α	H–N–C_2^α	(C_2^α)	Residue at C_2^α
Gly–Gly, HCl, water	120.46 (20)	114.38 (17)	125.12 (20)	118.15 (33)	123.09 (16)	118.68 (32)	114.2 (2)	Gly
α-Gly–Gly	120.27 (16)	116.68 (13)	122.97 (16)	119.89 (16)	121.59 (12)	118.03 (16)	113.3 (2)	Gly
Gly–L-Leu	122.59 (34)	114.02 (32)	123.39 (32)	121.5 (2.6)	120.64 (32)	113.7 (2.6)	111.4 (4)	Leu
L-Ala–Gly	121.63 (8)	114.34 (17)	124.0 (19)	121.0 (2.0)	120.22 (18)	118.8 (2.0)	114.2 (2)	Gly
L-Ala–Ala	120.89 (36)	113.16 (33)	125.93 (37)	119.2 (2.6)	122.38 (31)	117.8 (2.6)	109.2 (2)	Ala
Glutathione	122.00 (44)	117.01 (40)	120.93 (44)	119.0 (2.9)	120.74 (38)	118.8 (2.9)	115.7 (2)	Glu
	118.51 (43)	117.69 (39)	123.78 (44)	117.8 (2.9)	123.85 (37)	118.5 (2.9)	117.5 (3)	Gly
DL-*N*-Chloroacetyl-Ala	118.28 (24)	118.89 (22)	122.83 (24)	117.1 (1.8)	123.06 (21)	119.3 (1.8)	106.7 (2)	Ala
Gly–Gly-phosphate	121.33 (23)	114.56 (22)	124.11 (25)	115.8 (2.7)	122.50 (23)	120.9 (2.7)	113.9 (3)	Gly
N-Methyl-diprolyl acetamide	121.30 (37)	117.41 (36)	121.29 (38)	115.8 (3.3)	122.38 (37)	120.0 (3.3)	—	—
Gly–Gly, nitrate	121.20 (10)	115.4 (1)	123.4 (1)	118.6 (1.7)	121.6 (1)	119.6 (1.7)	109.8 (1)	Gly
N-Acetyl-L-Phe	121.83 (21)	116.07 (20)	122.10 (20)	119.7 (1.7)	123.29 (19)	116.9 (1.7)	111.8 (2)	Phe
L-Tyr	122.57 (19)	115.31 (16)	121.81 (15)	120.3 (1.7)	121.02 (17)	117.7 (1.7)	111.1 (2)	Tyr
Weighted mean	121.1 (1.3)	115.6 (1.6)	123.2 (1.4)	119.5 (1.7) [119.0 (1.8)]	121.9 (1.1)	118.2 (1.7) [118.3 (1.8)]	111.6 (2.9)	

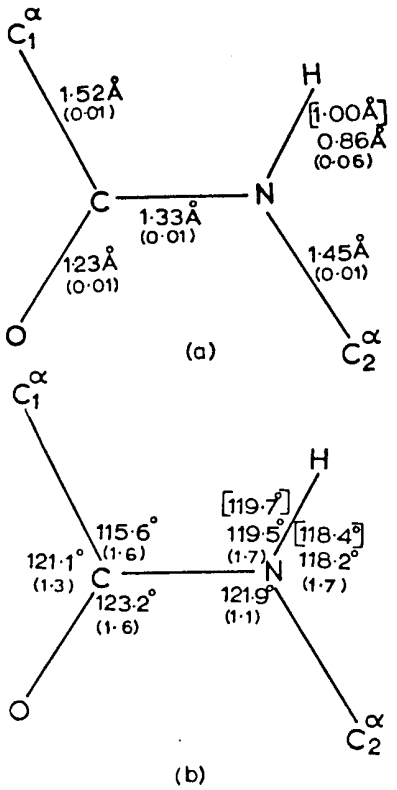

Fig. 1. (a) Bond lengths for the *trans* peptide unit, with their standard deviations given in brackets. The N–H bond length given is that determined by X-rays. Recommended value of 1.0 Å for this parameter is given in square brackets (see text). (b) Bond angles, along with their standard deviations given in brackets. Suggested values for bond angles C–N–H and H–N–C_2^α for a perfectly planar peptide unit are shown in square brackets.

It must be pointed out, that in spite of the fact that the observed peptide unit in various crystal structures is not exactly planar and has non-planar distortions at the N atom, the data reported in Fig. 1 pertain to the planar structure for the peptide unit. The non-planarity observed in the peptide unit in various crystal structures was discussed earlier in a paper from this laboratory [14] and a thorough analysis of this, including neutron diffraction data, is in preparation. As mentioned in ref. 14, this non-planarity can be represented by two dihedral angles ω and θ_N, between which a correlated variation denoted approximately by $\theta_N = -2\Delta\omega$ exists. Therefore, it is suggested that, if a non-planar peptide unit is needed, then the planar unit shown in Fig. 1 is given the rotations ω and θ_N about the bond C–N, keeping the atoms C_1^α, C, O and N fixed. During this process, the angles C–N–C_2^α and C–N–H are kept constant. The resulting variation (say $\Delta\tau$) in the angle C_2^α–N–H is calculated. Then the angles C–N–H and C_2^α–N–H are made equal by changing both by $\Delta\tau/2$. The process is suggested here on the basis of an empirical analysis of the observed structures.

Angle at C^α in the backbone of the dipeptide unit

A value of 110° is normally used for this angle, both for the glycyl and non-glycyl α-carbon atom. It is well-known that the allowed domain of the contact map of the dipeptide unit increases when $\tau(C^\alpha)$ is increased from 110° to 115° [15]. If an overall average is taken of the observed crystal structure data given in Table II for glycyl and

non-glycyl α-carbon atoms, then a mean value of 111.6° is obtained. However, the number of data, separately for the glycyl and non-glycyl α-carbon atom is rather small in Table II, and therefore they are not calculated separately. However this angle does not involve a hydrogen atom and is therefore reasonably accurate, even in older data. A set of 35 structures of peptides and amides were taken for which the average value for the glycyl α-carbon atom is 114.0° and for non-glycyl cases the average is 110.3°, which is very close to the currently used value of 110°.

It is particularly noteworthy that the backbone angle $\tau(C^{\alpha})$ for a glycyl residue is appreciably larger than 110°. This should be considered in building theoretical polypeptide and protein chains.

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