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Hydrogen-Bond Distances and Angles in the Structures of Amino Acids and Peptides

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Abstract

Intermolecular hydrogen-bond parameters for amino acids and the corresponding peptides in the solid state are presented. Crystallographic data were retrieved from the Cambridge Structural Database. The interactions investigated include hydrogen bonds between the main chains as well as hydrogen-bonding side chains. The tendency for peptides to line up 'head to tail' in crystal structures is demonstrated. The mean hydrogen-bond angles in C^α–COO$^-$···$^+$H$_3$N–C$^\alpha$ and $>$C=O···H–N$<$ interactions are not significantly different, but there are higher relative frequencies of bonds with angles in the intervals 180–170° and 150–110° for the former. The amino-acid histidine shows an exceptional ability to form short hydrogen bonds. In the protonated state, it is donor of two types of bonds with significantly different mean N···O distances [2·644 (17) and 2·730 (17) Å]. A side-chain aspartyl– or glutamyl–COO$^-$ group on average accepts 4·00 H atoms. These groups are better acceptors than main-chain carboxylate groups.

Introduction

Most researchers in the field of crystallography will have a fairly good idea which hydrogen-bond lengths to expect for different interactions. However, despite the rapidly increasing number of published structures and also papers on hydrogen bonds, a peptide chemist may well have difficulties telling whether an N···O distance of 2·80 Å should be classified as long or short in a specific amino-acid or peptide structure. The present paper deals with this group of compounds and supplies acceptor···donor [r(Acc···Don)] and H···acceptor [r(H···Acc)] distances and donor–H···acceptor angles [α(Don–H···Acc)] for most interactions likely to be encountered in crystals.

Methodology

The Cambridge Structural Database (CSD) presently (May 1988 release; Allen et al., 1979) contains information on more than 67 000 organic compounds. A subfile of crystallographic data for 749 amino-acid and peptide structures (chemical class 48) was generated from the database.* Only entries with diffractometer-measured intensity data, R factors < 0·075 and experimentally determined H-atom positions were accepted. The subfile was then searched for interactions between hydrogen-bond donors and acceptors of the main chain. Finally, amino-acid residues with a donor and/or acceptor group in the side chain (all unsubstituted) were treated one by one in order to obtain parameters for different types of hydrogen

Table 1. *Hydrogen-bonding residues in the database*

N_{sto} = total number of structures containing residue in database, N_{sus} = number of X-ray structures used with $R < 0.075$, N_{res} = number of hits for residue in the N_{sus} structures. N_{res} may be larger than N_{sus} as some structures contain two molecules in the asymmetric unit.

	Arg	Asn	Asp	Gln	Glu	His	Lys	Ser	Thr	Trp	Tyr
N_{sto}	17	20	25	5	28	29	10	23	17	18	44
N_{sus}	8	9	12	1	16	16	2	10	4	8	19
N_{res}	9	9	13 (6)*	1	17 (12)*	18 (8)*	2	11	4	9	20

* Number of protonated residues in parentheses.

bonds. An upper limit for $r(H \cdots Acc)$ was set at 2·4 Å and $\alpha(Don-H \cdots Acc)$ was confined to the interval 110·0–180·0°. No special measures were taken to handle three-center (bifurcated) bonds. Duplicate structures were rejected. Unweighted means are used throughout this analysis (Taylor & Kennard, 1983a).

H atoms are weak X-ray scatterers and their positions are not accurately determined by X-ray diffraction (XR); nevertheless, XR determinations only are used for hydrogen bonds in this paper. This is because estimates for the donor–H bond length are different for XR and neutron diffraction (Taylor & Kennard, 1983b), and neutron studies constitute only about 1% of the structure determinations in the CSD. However, lists of donor–acceptor distances are supplemented with values obtained from high-precision neutron-diffraction studies.

Three-letter abbreviations for amino-acid names are used in this paper and all nomenclature follows recommendations of the IUPAC–IUB Joint Commission on Nomenclature (1984). Table 1 summarizes the relevant content of the database. The two amino acids in the pairs Asp-Glu, Asn-Gln and Ser-Thr have been merged in Tables 2–5 as they were found to have equal properties as acceptor and donor.

Main-chain interactions

Hydrogen bonds were divided into four categories (Fig. 1). The interaction between the two ionized moieties is the strongest, which is a natural result of the predominantly electrostatic nature of the bond. The low occurrence of type 3 and type 4 interactions clearly reflects the tendency for peptides to line up 'head to tail' in crystal structures (Suresh & Vijayan, 1985). This feature has been investigated further by locating the four different hydrogen bonds in a subfile of unsubstituted, linear peptides; 33 dipeptides, 11 tripeptides and 3 tetrapeptides. The frequencies were: type 1, 56; type 2, 22; type 3, 5; type 4, 13. Thus, even if $-NH_3^+ \cdots {}^-OOC-$ and $>N-H \cdots O=C<$ interactions dominate, there is still a significant contribution from the other two considered.

The distribution patterns of $r(N \cdots O)$ and $r(H \cdots O)$ are shown in Fig. 2 for type 1 and 2 hydrogen bonds. Some of the uncertainty in the determination of H-atom

positions is seen from the much larger sample standard deviation for $r(H \cdots O)$ as compared with that for $r(N \cdots O)$. The distribution for $\alpha(N-H \cdots O)$ is shown in Fig. 3 for type 1 and 2 interactions. Olovsson & Jönsson (1976) have noted that $N-H \cdots O$ bonds with $=NH$ or NH_2 as donor groups were, on average, more closely linear than those with $-NH_3^+$ or NH_4^+ as donor groups. This is not indicated by the data in Fig. 1; it can be seen from Fig. 3 that there is a higher relative frequency of bonds with $\alpha(N-H \cdots O) < 150°$ for type 1 than for type 2, but the most pronounced difference between the two distributions is the higher occurrence of bonds in the interval 170–180° for type 1. Consequently, the type 1 α-value also has a larger sample standard deviation. While the mean values for most types of hydrogen-bond angle are close to 160°, type 3 interactions seem to deviate more from linearity. All results compare favorably with an analysis of the $N-H \cdots O=C$ hydrogen bond by Taylor, Kennard & Versichel (1984).

Type 1 (237)
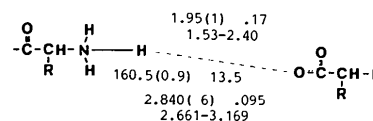
Type 2 (118)
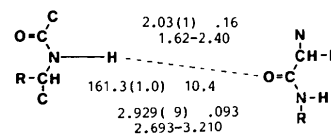
Type 3 (9)
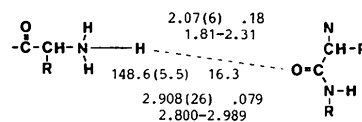
Type 4 (23)

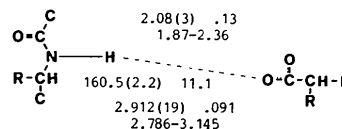Fig. 1. The four categories of hydrogen bonds between the main chains; each with the number of observations in parentheses. Parameters for each bond are: $r(H \cdots O)$ (Å), $\alpha(N-H \cdots O)$ (°) and $r(N \cdots O)$ (Å) with the standard deviation of each mean in parentheses. The standard deviation for the observations in the sample is also given. For bond lengths, the range of observations is indicated.

Side-chain donors

The results are given in Tables 2 and 3. Three acceptors are of general importance; solvent water, the carboxylate group and the O atom of the main-chain amide group. Only the acceptor atom is given in Table 2; the nature of the acceptor group is described in Table 3. In Table 3 a strong tendency is demonstrated for Asp/Glu, together with the charged hydrogen-bond donors Lys, Arg and protonated His (HisH$^+$), to associate with carboxylate, whereas amide—C=O is not a very frequent acceptor. On the other hand, the remaining neutral residues use H_2O and particularly amide—C=O to a much larger extent.

Donor\Acceptor	—COO$^-$	Amide—C=O	H_2O
Asp/Glu, Arg, Lys, HisH$^+$	54	8	9
Tyr, Ser/Thr, Asn/Gln, Trp, His	20	27	10

Asp/Glu, Tyr, Ser/Thr

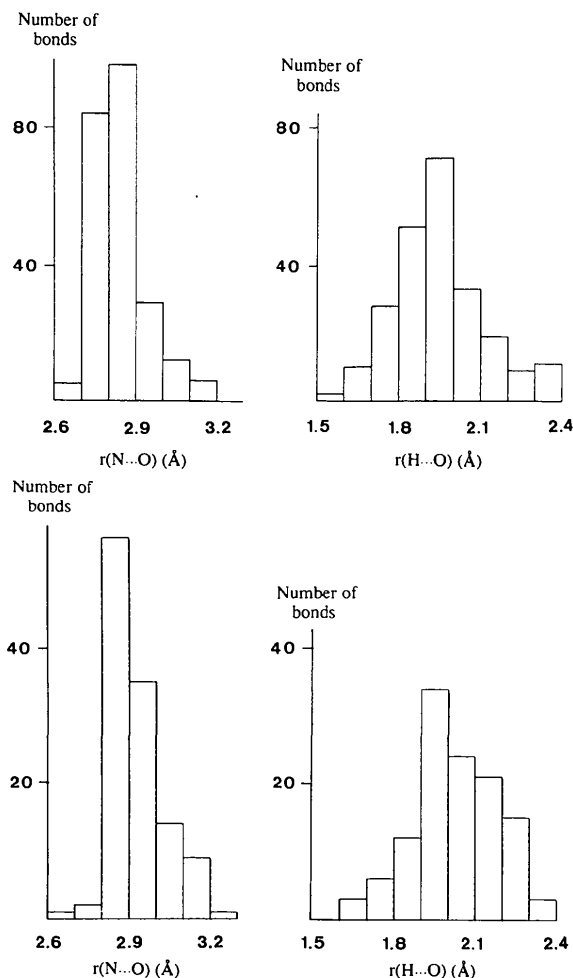The mean $r(H \cdots Acc)$ and $r(O \cdots Acc)$ distances (Tables 2, 3) increase along the series: Asp/Glu < Tyr

< Ser/Thr. Clearly, this sequence parallels a reduction of partial positive charge at the H atom. All hydroxylic protons normally form hydrogen bonds and there is only one example of an 'unused' proton, involving a Tyr residue.

Asn/Gln, Arg, Lys, Trp

The standard deviations for this group are rather large, and the only reasonably safe conclusion to be drawn is that Asn/Gln is a less potent hydrogen-bond donor than the other residues. The mean value for $\alpha(N-H \cdots O)$ involving tryptophane is 171 (2)°, indicating a strong preference for linear hydrogen bonds. Also for Asn/Gln, Arg and Trp a few incidents of 'unused' protons occur.

His

Hydrogen bonds involving His are well known in globins (Phillips & Schoenborn, 1981) and in the active site of several enzymes. At physiological pH, the side imidazole ring can exist in either a neutral basic or a protonated state. Protonation has been shown to influence the stability of β turns in model peptides (Boussard, Marraud & Aubry, 1986; Aubry, Vlassi & Marraud, 1986).

Neutral side chain. In the neutral state, histidine is known to exist in Nπ—H and Nτ—H tautomeric forms (Fig. 4). Both are encountered in the liquid phase (Tanokura, 1983; Ashikawa & Itoh, 1978), but the latter is favored and is observed in all crystal structures in accordance with theoretical studies (Ramani & Boyd, 1981). The observed Nτ—H$\cdots$O hydrogen bonds are rather short; the mean value is just 2·824 Å.

Protonated side chain. Protonation of the histidine residue (to give HisH$^+$) further increases the strength of the Nτ—H$\cdots$O hydrogen bond. A Wilcoxon rank-sum test (Bhattacharyya & Johnson, 1977) for $r(N \cdots O)$ indicates that Nτ(HisH$^+$)—H$\cdots$O is significantly (>99%) shorter than Nτ(His)—H$\cdots$O. More

Fig. 2. Distribution of $r(N \cdots O)$ and $r(H \cdots O)$ for type 1 (top) and type 2 interactions (bottom).

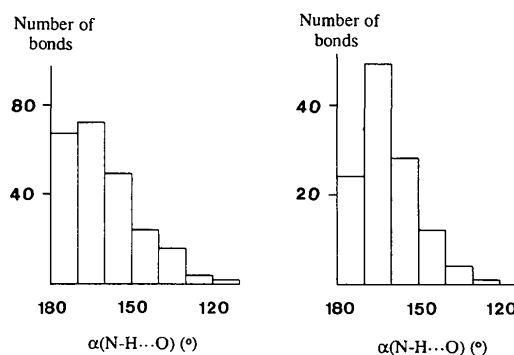Fig. 3. Distribution of $\alpha(N-H \cdots O)$ for type 1 (left) and type 2 interactions (right).

Table 2. *Statistics of hydrogen-bond parameters for side-chain donors (distances in Å, angles in °)*

Donor		Don···Acc O···O	H···Acc H···O	α(Don—H···Acc) OH···O
Asp/Glu—COOH···O	μ*	2·603 (13)	1·67 (3)	167·0 (1·7)
	σ	0·054	0·14	7·2
	r	2·536–2·714	1·49–1·93	149·8–176·0
	N	18	18	18
Tyr—OH···O	μ	2·677 (16)	1·79 (3)	165·2 (2·8)
	σ	0·064	0·11	11·4
	r	2·562–2·813	1·62–1·99	139·4–179·7
	N	16	16	16
Ser/Thr—OH···O	μ	2·758 (25)	1·91 (3)	164·3 (2·5)
	σ	0·103	0·12	9·6
	r	2·618–3·055	1·75–2·13	145·3–176·3
	N	17	15	15
		N···O	H···O	NH···O
Asn/Gln—CONH₂···O	μ	2·984 (24)	2·12 (3)	153·2 (4·1)
	σ	0·103	0·14	17·0
	r	2·862–3·247	1·93–2·35	123·0–177·4
	N	19	17	17
Arg—NH—C⁺ NHH / NH—H···O	μ	2·892 (16)	2·08 (3)	159·0 (2·3)
	σ	0·086	0·15	11·7
	r	2·734–3·102	1·85–2·36	124·5–175·4
	N	30	26	26
Arg—N—C⁺ O···H NHH / NHH	μ	2·920 (46)	2·05 (6)	166·8 (4·0)
	σ	0·137	0·18	12·0
	r	2·762–3·197	1·82–2·39	143·1–178·2
	N	9	9	9
Lys—NH₃⁺···O	μ	2·875 (32)	1·99 (7)	160·9 (6·9)
	σ	0·091	0·16	17·0
	r	2·762–2·998	1·80–2·22	133·2–176·5
	N	8	6	6
Trp—NH···O	μ	2·917 (49)	2·00 (5)	170·8 (2·0)
	σ	0·120	0·13	4·8
	r	2·751–3·064	1·75–2·11	162·5–177·6
	N	6	6	6
His—N(τ)H···O†	μ	2·824 (24)	1·89 (4)	162·8 (5·0)
	σ	0·073	0·13	14·9
	r	2·691–2·933	1·70–2·12	128·7–178·5
	N	9	9	9
HisH⁺—N(τ)H···O	μ	2·730 (17)	1·81 (3)	162·3 (3·5)
	σ	0·049	0·08	9·9
	r	2·664–2·828	1·68–1·96	149·9–177·2
	N	8	8	8
HisH⁺—N(π)H···O	μ	2·644 (17)	1·68 (4)	166·1 (3·2)
	σ	0·041	0·10	7·8
	r	2·568–2·688	1·53–1·79	159·0–176·9
	N	6	6	6

* Definitions for Tables 2–5: μ = sample mean with standard deviation in parentheses, σ = sample standard deviation, r = range of observations, N = number of observations in sample.

† For explanation of N(τ) and N(π), see Fig. 4.

Table 3. *Side-chain donors: dependence of r(Don···Acc) on the nature of the acceptor (distances in Å)*

Donor		Acceptor —COO⁻	Amide—C=O	H₂O	Others
Asp/Glu—COOH	μ	2·592 (13)	2·630 (42)	2·569 (1)	
	σ	0·043	0·073	0·002	
	N	12	3	2	1*
Tyr—OH	μ	2·662 (9)	2·715 (25)	2·653 (34)	
	σ	0·020	0·066	0·060	
	N	5	7	3	1
Ser/Thr—OH	μ	2·765 (55)	2·727 (25)	2·741 (6)	
	σ	0·145	0·056	0·007	
	N	7	5	2	3
Asn/Gln—CONH₂	μ	2·946 (30)	2·968 (29)	2·917	
	σ	0·067	0·087	—	
	N	5	9	1	4
Arg—NH—C⁺ NHH / NH—H	μ	2·882 (23)	2·954 (37)	2·918 (24)	
	σ	0·097	0·053	0·059	
	N	20	2	6	2
Arg—N—C⁺ H NHH / NHH	μ	2·885 (39)	2·982	—	
	σ	0·103	—	—	
	N	7	1	0	1
Lys—NH₃⁺	μ	2·884 (48)	—	—	
	σ	0·108	—	—	
	N	5	0	0	3
Trp—NH	μ	2·751	2·894 (47)	—	
	σ	—	0·082	—	
	N	1	3	0	2
His—N(τ)H	μ	2·736 (44)	2·859 (37)	2·841 (29)	
	σ	0·063	0·064	0·058	
	N	2	3	4	0
HisH⁺—N(τ)H	μ	2·736 (35)	2·731 (24)	2·699	
	σ	0·069	0·033	—	
	N	4†	2	1	1
HisH⁺—N(π)H	μ	2·644 (17)	—	—	
	σ	0·041	—	—	
	N	6‡	0	0	0

* Each row can be summed to give the number N in the first column of Table 2.

† Three main chain, one side chain.

‡ Four main chain, two side chain.

surprisingly, Nπ—H···⁻OOC— is shorter than Nτ—H···⁻OOC— for HisH⁺. The mean values are 2·644 and 2·736 Å, respectively. The difference is significant (Wilcoxon test, >99%) and is not a result of the different natures of the receptors (see Tables 2 and 3). The value 2·644 Å is extraordinarily low compared with any other type of N—H···O interaction in this study.

Side-chain acceptors

The results are given in Tables 4 and 5. Again, the former shows only the nature of the donor atom, the latter gives the nature of the donor group in more detail. As can be seen from Table 5, the three donors

considered were solvent water, R—NH₃⁺ and main chain >N—H. For all acceptors except histidine, hydrogen bonds are more linear with a donor O atom than an N atom as described by Olovsson & Jönsson (1976).

Asp/Glu

A total of six different combinations of donor and acceptor atoms have been investigated. The hydroxyl group proved to be of limited interest as an acceptor, only two Asp/Glu—HO···H—X (X = O, N) were observed.

Interestingly, the Asp/Glu—COO⁻···⁺H₃N—R interaction is shorter than the main-chain—COO⁻···⁺H₃N—R (type 1) interaction; r(O···N) is 2·796 (11) and 2·840 (6) Å, respectively. Having two groups with mean values μ_1 and μ_2, and testing $\mu_1 = \mu_2$, one finds that the test statistic $Z = (\mu_1 - \mu_2)/(\sigma_1^2/n_1 + \sigma_2^2/n_2)^{1/2}$ is approximately $N(0,1)$ (normal distribution with sample mean 0 and standard deviation 1, where σ_i is the sample standard deviation and n_i is the number of objects in the sample) (Bhattacharyya & Johnson, 1977). Applying the central-limit theorem and compar-

ing the two groups above, one finds that they are significantly different (>99%).

The only other possibility of studying a similar effect in this material is in the interaction Arg$\cdots$carboxylate. Of the 20 Arg–NH–N(NH$_2$)$_2$$\cdots$$^-$OOC– hydrogen bonds given in Table 3, seven carboxylate groups are from Asp/Glu, the remaining originate from the main chain. The first category, with a mean r(N$\cdots$O) of 2·824 (23) Å, is significantly shorter than the second, 2·914 (28) Å, above the 97% level (Wilcoxon test). Thus, the deviation seems to be of about the same magnitude for this interaction.

In total, 12 Asp and Glu carboxylates accept 36 H atoms giving 1·50 hydrogen bonds for each O atom. Excluding atoms which interact with metal ions and a group close to a disordered water molecule, the figure rises to 2·00, or 4·00 for a carboxylate group. These values are unique in the present study. It is noteworthy that neither carboxyl nor carboxylate groups ever accept hydrogen bonds from the main chain $>$N–H.

Asn/Gln

Other authors have noted that amides tend to be involved in shorter hydrogen bonds when acting as acceptors as compared with unionized carboxylic acids (Berkovitch-Yellin, Ariel & Leiserowitz, 1983). This is probably a result of different partial charges on the O atoms involved, as the magnitudes of charges are important for hydrogen-bond lengths (Umeyama & Morokuma, 1977). A slight, but not significant difference between R–NH$_3^+$$\cdots$carboxyl and R–NH$_3^+$$\cdots$ amide is seen in Table 5.

Ser/Thr, Tyr

Only about a half of these residues act as acceptors in hydrogen bonds. The observed bonds are longer than those found for the carboxyl, carboxylate and amide groups discussed above.

His

Neutral histidine is also a very efficient H-atom acceptor on Nπ. All available N atoms are involved in

hydrogen bonds, and adjusting for the larger covalent radius of N compared with O, these bonds are all of considerable strength.

Dependence of hydrogen-bond length on acid strength

In trying to explain the differences in mean hydrogen-bond lengths for the pairs of interactions involving HisH$^+$, NH$_3^+$$\cdots$$^-$OOC– and Arg–H$\cdots$$^-$OOC–, the most notable deviation within each pair is a change in pK_a value for either the donor or the acceptor. This is illustrated by the following observations for r(N$\cdots$O) and r(H$\cdots$O) (approximate pK_a values as superscripts, main and side-chain carboxylate groups indicated by m and s, respectively):

$$N\pi^{6\cdot0}\text{–H}\cdots^-\text{OOC–}^{2\cdot1}m < N\tau^{6\cdot6}\text{–H}\cdots^-\text{OOC–}^{2\cdot1}m$$
$$\text{for HisH}^+$$

$$N^{9\cdot5}H_3^+\cdots^-\text{OOC–}^{4\cdot0}s < N^{9\cdot5}H_3^+\cdots^-\text{OOC–}^{2\cdot1}m$$

$$N^{12\cdot5}H_2\cdots^-\text{OOC–}^{4\cdot0}s < N^{12\cdot5}H_2\cdots^-\text{OOC–}^{2\cdot1}m$$
$$\text{for Arg.}$$

The pK_a values for HisH$^+$ were taken from Boschcov, Seidel, Muradian, Tominaga, Paiva & Juliano (1983).

Although pK_a values refer to aqueous solutions, it may seem that they are still indicative for hydrogen-bond lengths in the solid phase. It is not straightforward to justify this observation. Hydrogen-bond lengths depend on a wide range of parameters and energies for each bond can only be computed by sophisticated calculations with ab $initio$ methods (Umeyama & Morokuma, 1977). Nevertheless, some general remarks may be given. In a simple model described by Olovsson & Jönsson (1976), a minimum bond length for an X–H$\cdots$$Y$ hydrogen bond would be expected when X and Y are equally good hydrogen-atom acceptors (or XH and YH are equally good hydrogen-bond donors). Such a situation is obtained if X and Y are chemically similar, which often also implies that they have comparable pK_a's. Indeed, the short hydrogen bonds in the interval 2·4–2·5 Å are most frequently observed in acid salts between groups of comparable pK_a's (Speakman, 1972). Tentatively, a
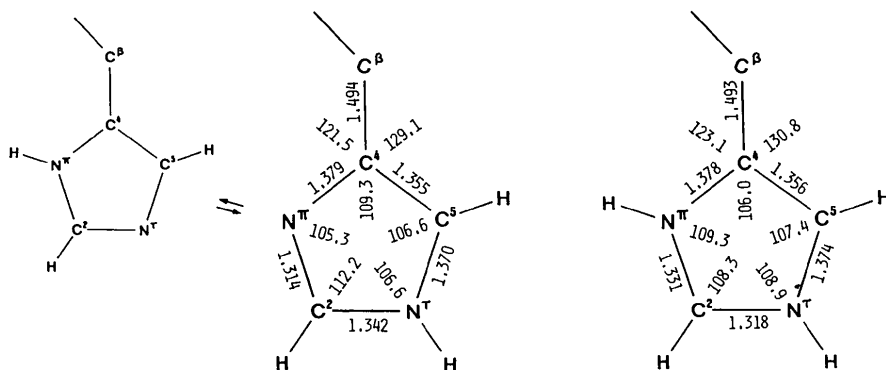

Fig. 4. Left: tautomerism of the neutral imidazole ring in histidine. Right: structure of HisH$^+$. Average bond lengths (Å) and bond angles (°) from the present study are given for the stable form of His (Nτ–H tautomer) and HisH$^+$. Standard deviations are 0·002–0·004 Å and 0·1–0·3°, respectively.

Table 4. *Statistics of hydrogen-bond parameters for side-chain acceptors (distances in Å, angles in °)*

Acceptor		Acc···Don O···O	Acc···H O···H	α(Acc···H—Don) O···HO
OH	μ	2·753 (26)	1·93 (12)	173·3 (3·6)
Asp/Glu—C=O···H—O	σ	0·051	0·24	7·2
	r	2·711–2·828	1·65–2·21	163·0–179·4
	N	4	4	4
Asp/Glu—COO⁻···H—O	μ	2·801 (22)	1·96 (4)	167·8 (1·4)
	σ	0·079	0·13	5·1
	r	2·694–2·915	1·77–2·28	157·5–175·6
	N	13	13	13
HNH	μ	2·590	1·82	175·5
Asn/Gln—C=O···H—O	σ	—	—	—
	r	—	—	—
	N	1	1	1
H	μ	2·901 (60)	1·94 (10)	165·2 (7·9)
Ser/Thr—O···H—O	σ	0·120	0·17	13·7
	r	2·759–3·049	1·76–2·11	152·8–179·8
	N	4	3	3
H	μ	2·871	1·80	166·9
Tyr—O···H—O	σ	—	—	—
	r	—	—	—
	N	1	1	1
		N···O	N···H	N···HO
His—N(π)···H—O	μ	2·827 (64)	1·94 (10)	165·5 (3·7)
	σ	0·110	0·18	6·4
	r	2·712–2·932	1·78–2·13	160·2–172·6
	N	3	3	3
		O···N	O···H	O···HN
OH	μ	2·852 (15)	2·07 (6)	147·4 (6·1)
Asp/Glu—C=O···H—N	σ	0·049	0·19	20·2
	r	2·777–2·911	1·73–2·33	114·8–172·6
	N	11	11	11
Asp/Glu—COO⁻···H—N	μ	2·807 (12)	1·91 (3)	165·9 (1·8)
	σ	0·058	0·12	8·7
	r	2·649–2·902	1·66–2·12	145·7–176·9
	N	23	23	23
HNH	μ	2·870 (31)	1·90 (4)	162·6 (5·2)
Asn/Gln—C=O···H—N	σ	0·087	0·09	12·7
	r	2·745–2·994	1·74–2·01	137·3–170·2
	N	8	6	6
H	μ	2·954 (48)	2·08 (5)	155·6 (1·3)
Ser/Thr—O···H—N	σ	0·116	0·12	3·0
	r	2·773–3·124	1·88–2·17	152·2–159·0
	N	6	5	5
H	μ	2·921 (21)	2·12 (5)	151·7 (4·9)
Tyr—O···H—N	σ	0·062	0·14	14·6
	r	2·849–3·037	1·87–2·31	133·3–177·1
	N	9	9	9
		N···N	N···H	N···HN
His—N(π)···H—N	μ	2·960 (24)	2·01 (7)	170·2 (2·5)
	σ	0·060	0·17	6·2
	r	2·886–3·045	1·73–2·15	161·3–177·5
	N	6	6	6

longer hydrogen bond might be expected when the pK_a difference is larger.

Concluding remarks

An assessment has been made of mean hydrogen-bond parameters in the solid state of amino acids and peptides for a wide range of interactions. There are significant variations depending on the nature of the acceptor as well as the donor. The data presented can support conclusions as to whether a feature of a particular hydrogen bond is unique or not. The results might also be an aid in protein crystallography for the

Table 5. *Side-chain acceptors: dependence of $r(Acc\cdots Don)$ on the nature of the donor (distances in Å)*

Acceptor		Donor				
		H_2O	Other —OH	$R{>}N{-}H$ / $R{>}N{-}H$	$R{-}NH_3^+$	Other —NH
OH	μ	2·767 (30)	—		2·847 (15)	
Asp/Glu—C=O	σ	0·053			0·048	
	N	3*	1*	0†	10†	1†
Asp/Glu—COO⁻	μ	2·801 (22)	—		2·796 (11)	
	σ	0·079			0·036	
	N	13	0	0	11	12‡
HNH	μ	—		2·914 (40)	2·820 (44)	
Asn/Gln—C=O	σ	—		0·070	0·089	
	N	0	1	3	4	0
H	μ	2·895 (84)		2·977 (11)	2·930 (103)	
Ser/Thr—O	σ	0·146		0·019	0·178	
	N	3	1	3	3	0
H	μ	2·871		2·957 (46)	2·904 (21)	
Tyr—O	σ	—		0·079	0·051	
	N	1	1	3	6	1
His—N(π)	μ	2·827 (64)		2·975 (12)	2·886	
	σ	0·110		0·020	—	
	N	3	0	3	1	2

* Numbers add to give the N values in the top part of Table 4.
† Equivalent for bottom part.
‡ Of these, 11 are arginine residues.

optimization of hydrogen-bond parameters within a structure.

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