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Geometry of the N–H···O=C Hydrogen Bond. 1. Lone-Pair Directionality

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Abstract: A survey of 1509 N—H···O=C hydrogen bonds, observed by X-ray or neutron diffraction in 889 organic crystal structures, gave the following results. There is a statistically significant tendency for hydrogen bonding to occur in the directions of the conventionally viewed oxygen sp^2 lone pairs. This is partly due to steric factors, but may also reflect an inherent preference for hydrogen bonding in the lone-pair directions. The "directional influence" of the lone pairs becomes more pronounced as the H···O distance is decreased. There are appreciable differences between the geometries of intramolecular and intermolecular bonds. The geometry of the hydrogen bond also depends on the nature of the acceptor species: bonds involving ionized carboxylate acceptors are different from those involving un-ionized carbonyl acceptors.

Introduction

The N—H···O=C hydrogen bond plays a major role in biological chemistry and has therefore been studied extensively by crystallographic techniques.[1-5] However, many aspects of its geometry and structure are, as yet, imperfectly understood. We have undertaken a statistical analysis of approximately 1500 N—H···O=C hydrogen bonds, the geometries of which have been determined by X-ray or neutron diffraction. We intend to report the results of the survey in a short series of papers.[6] In this, the first, we examine the controversial topic of lone-pair directionality.[5,7,8] Specifically, we seek to answer the following questions: (1) Is there a distinct preference for hydrogen bonding in the directions of the conventionally viewed oxygen sp^2 lone pairs? (2) If so, what is the reason for this preference?

The present survey differs from earlier studies in two respects. Firstly, it is based on a very large data set. Secondly, systematic errors in the X-ray hydrogen-bond geometries have been corrected by "normalization".[9] This involves moving the hydrogen atom position along the observed N–H bond direction until the N–H distance is equal to a standard value (1.030 Å). A comparison of X-ray and neutron diffraction results for 57 N—H···O=C hydrogen bonds determined by both methods showed that there was excellent agreement between the majority of neutron and "normalized" X-ray hydrogen-bond geometries.[10]

Methodology

Crystallographic Data. All crystallographic data were retrieved from the Cambridge Structural Database (1982 release).[11] The survey was based on 1509 N—H···O=C hydrogen bonds (deuterium bonds were excluded) in which the acceptor oxygen atom is part of a carbonyl group or a carboxylate ion.[12] The hydrogen bonds were taken from 889 organic crystal structures with *R* factors less than 0.08. Disordered structures were not used. Most of the structures (852, containing 1426 of the hydrogen bonds) were determined by X-ray diffraction, the remainder by neutron diffraction. All of the X-ray hydrogen bond geometries were normalized, as described above.

Geometrical Parameters. The hydrogen bond geometries were described by the spherical polar coordinates shown in Figure 1a. The z axis in this figure is normal to the least-squares mean plane of O, C, A, and B (except when A or B is a hydrogen atom,[13] in which case z is normal to the plane containing the three nonhydrogen atoms). The y axis lies along the C=O bond direction, and the x axis completes a right-handed set with its origin at O. For the purposes of the study, differences between A and B were neglected; i.e., the acceptor moiety was assumed to have C_{2v} symmetry. Thus, the proton position could be reflected into the quadrant with $x \geq 0$, $z \geq 0$. The parameter θ_H was then defined as the angle between the z axis and the O···H vector ($90 \geq \theta_H \geq 0°$), and ϕ_H was defined as the angle between the x axis and the projection of the O···H vector on the xy plane ($90 \geq \phi_H \geq -90°$; ϕ_H = negative if y = negative). In addition, $\Delta\phi_H$ was defined as:

$$\Delta\phi_H = |\phi_H - 30|°$$

i.e., the modulus of the difference between ϕ_H and the ϕ value of an idealized oxygen sp^2 lone pair (for which $\theta = 90°$, $\phi = 30°$).[14] The position of the nitrogen atom was defined by the analogous parameters θ_N, ϕ_N, and $\Delta\phi_N$ (Figure 1b).

Statistical Techniques. Whenever possible, nonparametric statistical techniques were used.[15] Although generally less powerful than parametric methods, they have two advantages. Firstly, they are relatively resistant to outliers; i.e., they are unlikely to be affected by the presence of a few very inaccurate hydrogen bond geometries. Secondly, they are distribution-free; i.e., it is unnecessary to assume that the parameter being studied is normally distributed. This is important because many of the parameters used to describe hydrogen bond geometries have very skew distributions.

Throughout the study, results obtained from the complete sample of hydrogen bonds were checked by examining the 83 neutron hydrogen-bond geometries. In no case were the neutron geometries inconsistent with the results obtained from the complete sample.

Results and Discussion

Preliminary Results. Preliminary results were obtained as follows. The surface of the quadrant shown in Figure 1c was divided into a 9 × 18 grid. The (θ, ϕ) coordinates of the grid points

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[1] Ramakrishnan, C.; Prasad, N. *Int. J. Protein Res.* **1971**, *3*, 209–231.

[2] Koetzle, T. F.; Lehmann, M. S. In "The Hydrogen Bond"; Schuster, P., Zundel, G., Sandorfy, C., Eds.; North-Holland: Amsterdam, 1976; Vol. II, Chapter 9.

[3] Leiserowitz, L.; Tuval, M. *Acta Crystallogr., Sect. B* **1978**, *34*, 1230–1247.

[4] Jeffrey, G. A.; Maluszynska, H. *Int. J. Biol. Macromol.* **1982**, *4*, 173–185.

[5] Olovsson, I.; Jönsson, P.-G. In ref 2, Chapter 8.

[6] It is intended that subsequent papers in the series will cover (a) bifurcated and trifurcated bonds and (b) the N—H, H···O, N···O, C=O, and N—H···O distributions.

[7] Donohue, J. In "Structural Chemistry and Molecular Biology"; Rich, A., Davidson, N., Eds.; W. H. Freeman: San Francisco, 1968, pp 443–449.

[8] Millen, D. J. *Croat. Chem. Acta* **1982**, *55*, 133–145.

[9] Jeffrey, G. A.; Lewis, L. *Carbohydr. Res.* **1978**, *60*, 179–182.

[10] Taylor, R.; Kennard, O. *Acta Crystallogr., Sect. B* **1983**, *39*, 133–138.

[11] (a) Allen, F. H.; Bellard, S.; Brice, M. D.; Cartwright, B. A.; Doubleday, A.; Higgs, H.; Hummelink, T.; Hummelink-Peters, B. G.; Kennard, O.; Motherwell, W. D. S.; Rodgers, J. R.; Watson, D. G. *Acta Crystallogr., Sect. B* **1979**, *35*, 2331–2339. (b) Kennard, O.; Watson, D. G.; Town, W. G. *J. Chem. Doc.* **1972**, *12*, 14–19.

[12] Throughout the text, we use the symbol "N—H···O=C" to refer to a hydrogen bond in which the acceptor is a carbonyl *or* a carboxylate ($-CO_2^-$) group.

[13] Only 30 hydrogen bonds fell into this category.

[14] The direction of an "idealized" oxygen sp^2 lone pair (i.e., $\theta = 90°$, $\phi = 30°$) is used here as a convenient reference vector. A referee has pointed out that the true lone-pair directions in any given hydrogen bond are unknown.

[15] Nonparametric techniques are described in many statistical texts, e.g., (a) Siegel, S. "Nonparametric Statistics for the Behavioral Sciences", International Student Edition; McGraw-Hill Kogakusha: Tokyo, 1956. (b) Snedecor, G. W.; Cochran, W. G. "Statistical Methods", 7th ed.; Iowa State University Press: Ames, Iowa, 1980.

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Table I. Bivariate (θ_H, ϕ_H) Distribution for All Hydrogen Bonds in Sample[a]

θ_H, deg	ϕ_H, deg −20 to −10	−10 to 0	0 to 10	10 to 20	20 to 30	30 to 40	40 to 50	50 to 60	60 to 70	70 to 80	80 to 90
0 to 27.27	0	1	0	2	5	1	2	1	4	6	3
27.27 to 38.94	0	2	3	2	3	7	10	11	7	12	8
38.94 to 48.19	0	0	3	3	7	12	12	21	11	17	12
48.19 to 56.25	0	0	2	4	7	12	23	16	20	18	8
56.25 to 63.61	1	0	3	8	23	28	28	27	21	15	12
63.61 to 70.53	1	3	2	7	20	33	32	25	24	11	7
70.53 to 77.16	2	4	4	11	30	46	27	27	16	15	12
77.16 to 83.62	0	13	8	27	35	75	39	30	21	16	18
83.62 to 90	0	11	8	47	56	102	56	33	37	27	27

[a] Table gives number of hydrogen bonds falling in each grid square. There are no bonds with $\phi_H < -20°$.

Table II. Bivariate (θ_H, ϕ_H) Distribution for All Intramolecular Bonds[a]

θ_H, deg	ϕ_H, deg −20 to −10	−10 to 0	0 to 10	10 to 20	20 to 30	30 to 40	40 to 50	50 to 60	60 to 70	70 to 80	80 to 90
0 to 27.27	0	0	0	0	0	0	0	0	1	2	0
27.27 to 38.94	0	1	3	1	0	0	0	1	3	2	0
38.94 to 48.19	0	0	3	2	1	0	0	1	0	0	0
48.19 to 56.25	0	0	0	0	0	0	0	0	2	3	0
56.25 to 63.61	1	0	2	2	2	1	1	0	2	2	0
63.61 to 70.53	1	3	0	4	0	0	1	0	1	0	0
70.53 to 77.16	2	3	0	4	1	3	0	0	0	0	0
77.16 to 83.62	0	13	6	18	2	0	1	0	0	0	0
83.62 to 90	0	10	6	30	1	1	1	0	0	1	0

[a] Table gives number of hydrogen bonds falling in each grid square. There are no bonds with $\phi_H < -20°$.

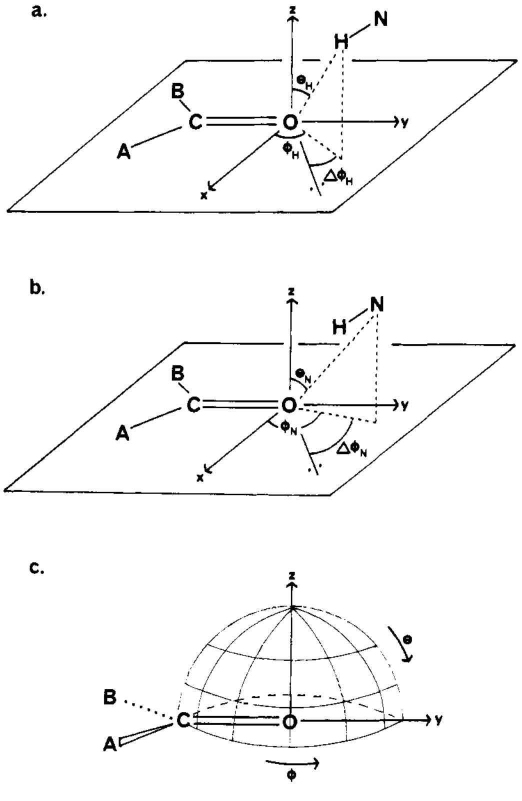

Figure 1. (a) Parameters θ_H, ϕ_H, and $\Delta\phi_H$. Positive ϕ_H values correspond to hydrogen bonds in the octant with $y > 0$ (i.e., C═O···H > 90°); negative ϕ_H corresponds to $y < 0$ (i.e., C═O···H < 90°). (b) Parameters θ_N, ϕ_N, and $\Delta\phi_N$. Positive ϕ_N corresponds to C═O···N > 90°; negative ϕ_N corresponds to C═O···N < 90°. (c) Schematic drawing of grid system used in statistical analysis. Every third grid line is shown.

were chosen so that all grid squares were of equal area.[16] Thus, if the distribution of hydrogen-bond geometries were random, we would expect an equal number of hydrogen bonds in each grid square. The observed (θ_H, ϕ_H) distribution for the complete sample of 1509 hydrogen bonds is given in Table I; the cumulative distributions of θ_H and ϕ_H are shown as histograms in Figure 2.[17] The mean values of θ_H and ϕ_H are 70.3 and 45.0°, respectively. The paucity of hydrogen bonds in the octant with $\phi < 0°$ is presumably due to steric effects, i.e., repulsion between the N—H and >C═O groups. The (θ_H, ϕ_H) distribution in the octant with $\phi > 0°$ is obviously not uniform. This was confirmed at the 99.9% significance level by a χ^2 goodness-of-fit test. Binomial tests showed the following results to be statistically significant at the 99.9% level. (1) The number of hydrogen bonds lying within 12.84° of the lone-pair plane (i.e., $\theta_H > 77.16°$; $\cos\theta_H < {}^2/_9$) is

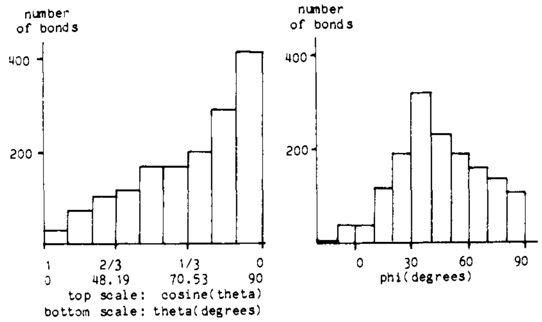

Figure 2. Cumulative distributions of θ_H and ϕ_H for all hydrogen bonds in sample.

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(16) Great circles (i.e., lines of longitude) were separated by equal ϕ intervals of 10°. Small circles (i.e., lines of latitude) were separated by equal intervals of $\cos\theta$; i.e., the equatorial line of latitude corresponded to $\cos\theta = 0$, and the lines above it to $\cos\theta = {}^1/_9, {}^2/_9, {}^3/_9, \ldots$, etc.

(17) In order to make visual comparisons easier, all θ_H histograms in the paper have been normalized to approximately the same area; similarly, the areas of the ϕ_H histograms are all approximately equal. The horizontal scales of histograms showing θ_H (or θ_N) distributions are nonlinear in θ_H (or θ_N) but linear in $\cos\theta_H$ (or $\cos\theta_N$). Thus, a θ_H histogram in which all bars are of equal height would suggest that the energy of the hydrogen bond is independent of θ_H.

Table III. Bivariate (θ_H, ϕ_H) Distribution for All Intermolecular Bonds[a]

	ϕ_H, deg										
θ_H, deg	−20 to −10	−10 to 0	0 to 10	10 to 20	20 to 30	30 to 40	40 to 50	50 to 60	60 to 70	70 to 80	80 to 90
0 to 27.27	0	1	0	2	5	1	2	1	3	4	3
27.27 to 38.94	0	1	0	1	3	7	10	10	4	10	8
38.94 to 48.19	0	0	0	1	6	12	12	20	11	17	12
48.19 to 56.25	0	0	2	4	7	12	23	16	18	15	8
56.25 to 63.61	0	0	1	6	21	27	27	27	19	13	12
63.61 to 70.53	0	0	2	3	20	33	31	25	23	11	7
70.53 to 77.16	0	1	4	7	29	43	27	27	16	15	12
77.16 to 83.62	0	0	2	9	33	75	38	30	21	16	18
83.62 to 90	0	1	2	17	55	101	55	33	37	26	27

[a] Table gives number of hydrogen bonds falling in each grid square. There are no bonds with $\phi_H < -20°$.

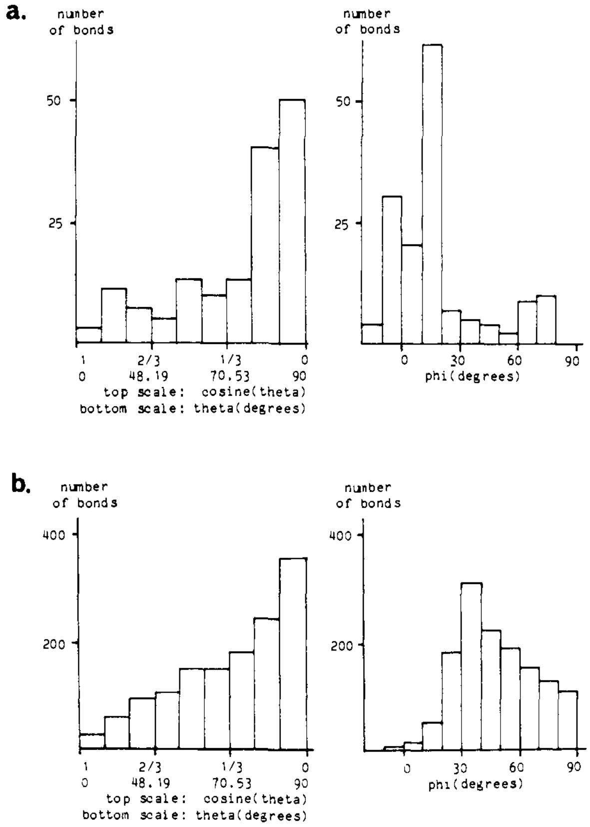
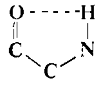


Figure 3. Cumulative distributions of θ_H and ϕ_H for (a) all intramolecular bonds, and (b) all intermolecular bonds.

larger than would be expected from purely geometrical considerations (if the energy of the hydrogen bond were independent of θ_H, the number of bonds in the range $\theta_H \pm \delta\theta_H$ would be expected to be proportional to sin θ_H). (2) The number of hydrogen bonds lying within 10° of the idealized lone-pair direction (i.e., $20 < \phi_H < 40°$) is larger than would be expected if the underlying distribution of ϕ_H were uniform (the maximum in the ϕ_H distribution actually occurs at 36–38°, i.e., 6 to 8° away from the direction of an idealized sp^2 lone pair). Thus, the answer to question 1 of the Introduction is established beyond reasonable doubt. *In the crystalline state, there is a distinct preference for N—H···O═C hydrogen bonds to form in, or near to, the directions of the conventionally viewed oxygen sp^2 lone pairs.* In the remainder of the paper, we consider possible reasons for this.

Comparison of Intermolecular and Intramolecular Bonds. The (θ_H, ϕ_H) distribution for the 152 intramolecular bonds in our sample is shown in Table II and Figure 3a. The distribution for the 1357 intermolecular bonds is given in Table III and Figure 3b. The results show that intramolecular bonds tend to have larger θ_H values and smaller ϕ_H values than intermolecular bonds. Almost all of the hydrogen bonds with $\phi_H < 0°$ (i.e., with C═O···H < 90°) are intramolecular, suggesting that this geometry rarely occurs unless it is imposed on the system by intramolecular geometrical constraints. The difference between the intermolecular and intramolecular distributions is probably due to the prevalence of the intramolecular hydrogen-bonding arrangement **1**. Intramolecular bonds were excluded from the remainder of the study. The conclusions given in the preceding section are unchanged if the statistical tests are performed on the sample of 1357 intermolecular bonds rather than the complete sample of 1509 bonds.



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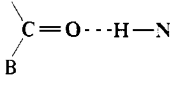
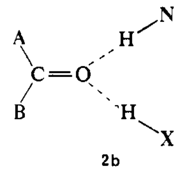
Steric Effects. Figure 4a–c shows the cumulative distributions of θ_H and ϕ_H for intermolecular N—H···O═C bonds in which the C═O group accepts a total of (a) one, (b) two, and (c) three hydrogen bonds (**2a–c**). In this context, a hydrogen bond is defined as a C═O···H—X contact (X = O, N, S, halogen) with H···O < 2.4 Å and C═O···H ≥ 90°. The results suggest that steric effects are partly responsible for the phenomenon of lone-pair directionality. Thus, the peak centered at $\phi_H \simeq 37°$ is more pronounced for bonds of type **2b** than for bonds of type **2a**. Presumably, this is because nonbonded repulsions in **2b** are minimized when the hydrogen bonds lie along the lone-pair directions. Small values of θ_H seem to be particularly common when the C═O group accepts three hydrogen bonds. This suggests that steric repulsions in **2c** tend to force one of the hydrogen bonds out of the lone-pair plane. However, the result may be due to statistical chance because only 34 bonds contribute to the histograms in Figure 4c.



2a



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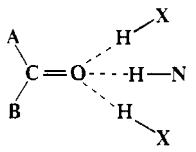

2c

Although the peak centered at $\phi_H \simeq 37°$ is less pronounced in Figure 4a than in Figure 4b, it is still present. This suggests that the phenomenon of lone-pair directionality is not entirely due to steric effects of the type referred to above. In order to confirm this, we determined the (θ_H, ϕ_H) distribution for intermolecular N—H···O═C bonds in which the C═O group forms no other C═O···H—X contacts (X = O, N, S, halogen) with H···O < 2.8 Å and C═O···H ≥ 80°. C═O groups coordinated to alkali metal ions were also excluded. The results are shown in Table IV and Figure 5. A χ^2 test confirmed that the (θ_H, ϕ_H) distribution is significantly (99.9% level) nonuniform. Binomial tests showed that there is still a significant (>99.9%) tendency for hydrogen bonding to occur within 12.84° of the lone-pair plane (i.e., $\theta_H > 77.16°$) and within 10° of the conventionally viewed lone-pair direction (i.e., $20 < \phi_H < 40°$). There are two possible explanations for these results. Firstly, they may be due to some sys-

Table IV. Bivariate (θ_H, ϕ_H) Distribution for Intermolecular Bonds in Which the C=O Group Forms No Other C=O···H–X Contacts (X = O,N,S, Halogen) with H···O < 2.8 Å, C=O···H ⩾ 80°[a]

	ϕ_H, deg										
θ_H, deg	−20 to −10	−10 to 0	0 to 10	10 to 20	20 to 30	30 to 40	40 to 50	50 to 60	60 to 70	70 to 80	80 to 90
0 to 27.27	0	0	0	0	0	0	0	0	1	0	0
27.27 to 38.94	0	0	0	0	0	1	4	4	1	2	2
38.94 to 48.19	0	0	0	0	1	2	0	8	3	3	3
48.19 to 56.25	0	0	0	1	2	3	2	5	6	10	5
56.25 to 63.61	0	0	0	1	1	8	11	8	7	5	11
63.61 to 70.53	0	0	0	0	4	8	11	9	11	6	4
70.53 to 77.16	0	0	0	1	9	19	9	8	7	6	10
77.16 to 83.62	0	0	1	3	19	35	15	14	9	8	12
83.62 to 90	0	0	0	6	25	53	27	18	25	18	20

[a] Table gives number of hydrogen bonds falling in each grid square. There are no bonds with $\phi_H < -20°$.

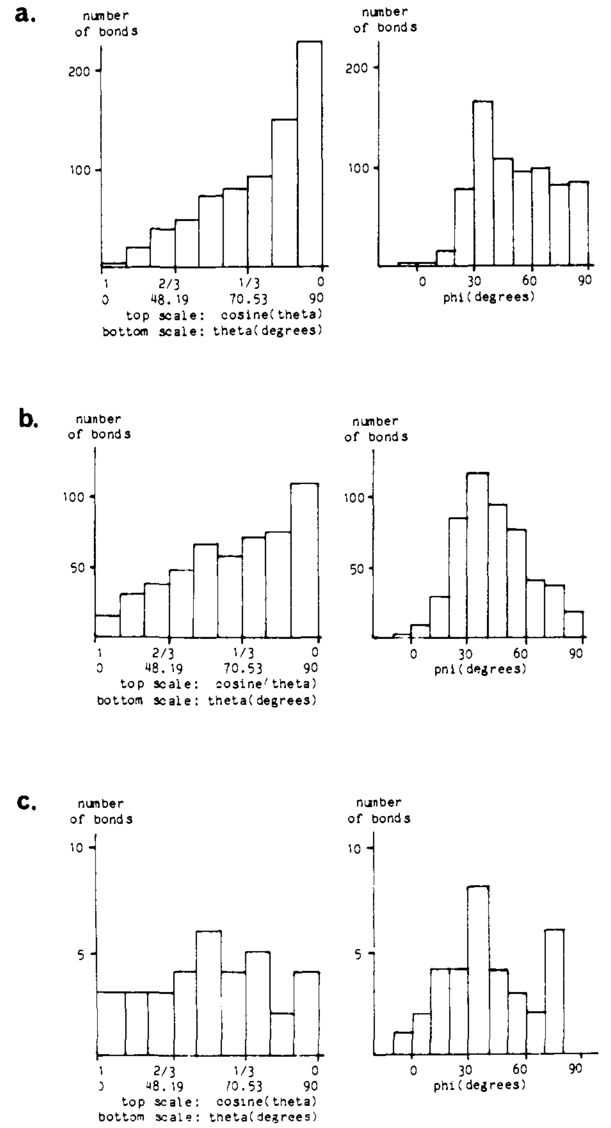

Figure 4. Cumulative distributions of θ_H and ϕ_H for intermolecular bonds in which the C=O group accepts a total of (a) one, (b) two, and (c) three hydrogen bonds (**2a**, **2b**, **2c**, respectively).

tematic crystal-packing effect. Secondly, they may reflect an inherent preference for hydrogen bonding along the lone-pair directions *in the isolated N—H···O=C bond.* We cannot positively establish which of these explanations is correct, but the second seems more likely. The distribution in Table IV is based on 551 hydrogen bonds in 456 crystal structures, and crystal-packing effects may well average out over such a large number of structures. The 456 structures cover a wide range of chemical types.[18]

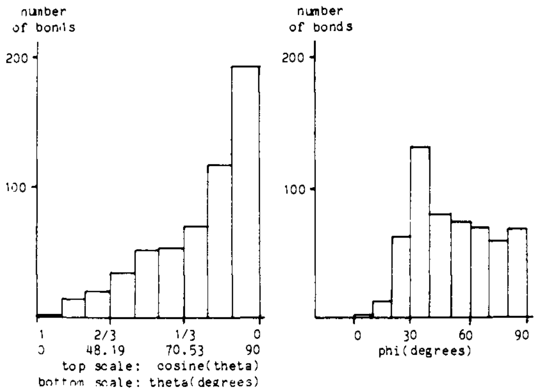

Figure 5. Cumulative distributions of θ_H and ϕ_H for intermolecular bonds in which the C=O group forms no other C=O···H—X contacts (X = O,N,S, halogen) with H···O < 2.8 Å, C=O···H ≥ 80°.

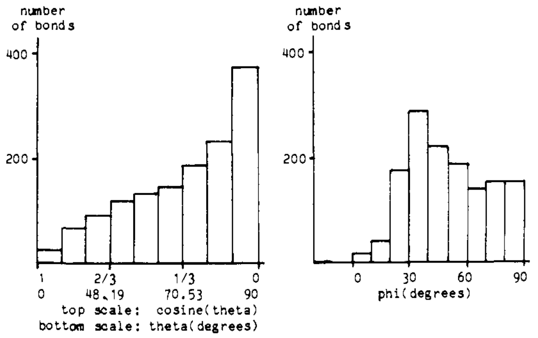

Figure 6. Cumulative distribution of θ_N and ϕ_N for all intermolecular bonds.

θ_N and ϕ_N Distributions. Figure 6 shows the cumulative distributions of θ_N and ϕ_N for the 1357 intermolecular bonds. The distributions have the same general features as those of θ_H and ϕ_H (Figure 3b), although the peak at $30 < \phi_N < 40°$ is somewhat smaller than that at $30 < \phi_H < 40°$. The mean values of the quantities ($\theta_H - \theta_N$) and ($\Delta\phi_H - \Delta\phi_N$) are −0.05 (13)° and −1.70 (16)°, respectively. A paired Wilcoxon test showed that the first of these values is not significantly different from zero. However, the second one is significant at the 99.9% level. Thus $\Delta\phi_H$ tends to be smaller than $\Delta\phi_N$; i.e., the N—H group prefers to point

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(18) Each structure in the Cambridge Structural Database is assigned to a basic chemical class.[11] The distribution of classes for the 456 structures contributing to Table IV is as follows: 113 amino acids and peptides; 39 heterocyclic nitrogen compounds (three-, four-, and five-membered monocycles); 35 heterocyclic nitrogen compounds (two fused rings); 28 heterocyclic nitrogen compounds (six-membered monocycles); 26 aliphatic carboxylic acid derivatives; 22 pyrimidines and purines; 15 heterocyclic nitrogen compounds (more than two fused rings); 13 nucleosides and nucleotides; 12 benzoic acid derivatives; 12 heterocyclic oxygen compounds; 12 heterocyclic (oxygen and nitrogen) compounds; 12 barbiturates; and 117 structures in 25 other classes.

"toward" the idealized lone-pair direction rather than "away" from it. This may be due to electrostatic or steric effects.

Variation of Lone-Pair Directionality with H···O Distance. The $\Delta\phi_H$ angles and H···O distances of the 1357 intermolecular bonds have a Spearman rank correlation coefficient of +0.22. This is significantly different from zero at the 99.9% level. Thus, as the H···O distance decreases, there is a small but significant tendency for the proton to move toward the conventionally viewed lone-pair direction (i.e., $\Delta\phi_H$ decreases). The θ_H angles and H···O distances have a correlation coefficient of −0.09. Although small, this too is significantly different from zero at the 99.9% confidence level. We therefore conclude that there is a *very slight* tendency for the proton to move toward the lone-pair plane as the H···O distance is decreased.

Comparison of Carbonyl and Carboxylate Acceptors. Some 450 of the 1357 intermolecular N—H···O=C bonds involve carboxylate ($-CO_2^-$) acceptors (**3**). There are at least three reasons why these bonds might be expected to differ from the 907 intermolecular bonds involving carbonyl acceptors. Firstly, the electron density distributions around the oxygen atoms may be different in carbonyl and carboxylate groups. Secondly, the mean H···O distance of the bonds involving carboxylate acceptors [1.855 (6) Å] is significantly shorter than the corresponding value for bonds involving carbonyl acceptors [1.942 (4) Å], and it was shown above that lone-pair directionality is correlated with hydrogen-bond distance. Thirdly, oxygen atoms belonging to carboxylate ions tend to accept more hydrogen bonds than oxygen atoms belonging to carbonyl groups. Thus, in 316 of the 450 bonds involving carboxylate ions, the oxygen atom accepts at least one other hydrogen bond (defined as a C=O···H—X contact with X = O, N, S, or halogen, H···O < 2.4 Å and C=O···H ≥ 90°). The corresponding figure for bonds involving carbonyl groups is 238 out of 907.[19]

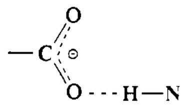

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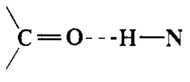
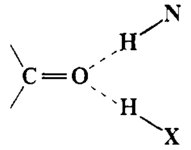
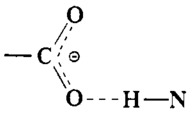
Figure 7a–d shows the cumulative distributions of θ_H and ϕ_H for (a) bonds involving carbonyl groups, in which the oxygen atom accepts no other hydrogen bonds (**4a**); (b) bonds involving carbonyl groups, in which the oxygen atom accepts one other hydrogen bond (**4b**); (c) bonds involving carboxylate ions, in which the oxygen atom accepts no other hydrogen bonds (**4c**); (d) bonds involving carboxylate ions, in which the oxygen atom accepts one other hydrogen bond (**4d**). Binomial tests confirmed that the ϕ_H distributions are all consistent with an energetic preference for hydrogen bonding in, or near to, the idealized lone-pair directions. However, there are appreciable differences between the θ_H distributions: the tendency for hydrogen bonds to form in, or near to, the lone-pair plane is less pronounced for carboxylate acceptors than for carbonyl acceptors. This is especially true for bonds of type **4d**; a binomial test on the θ_H distribution in Figure 7d showed that the number of bonds with θ_H > 77.16° is not significantly greater than the number expected on purely geometrical grounds. We suggest two reasons for this. Firstly, it may reflect a difference



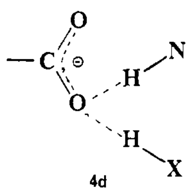
4a



4b



4c



4d

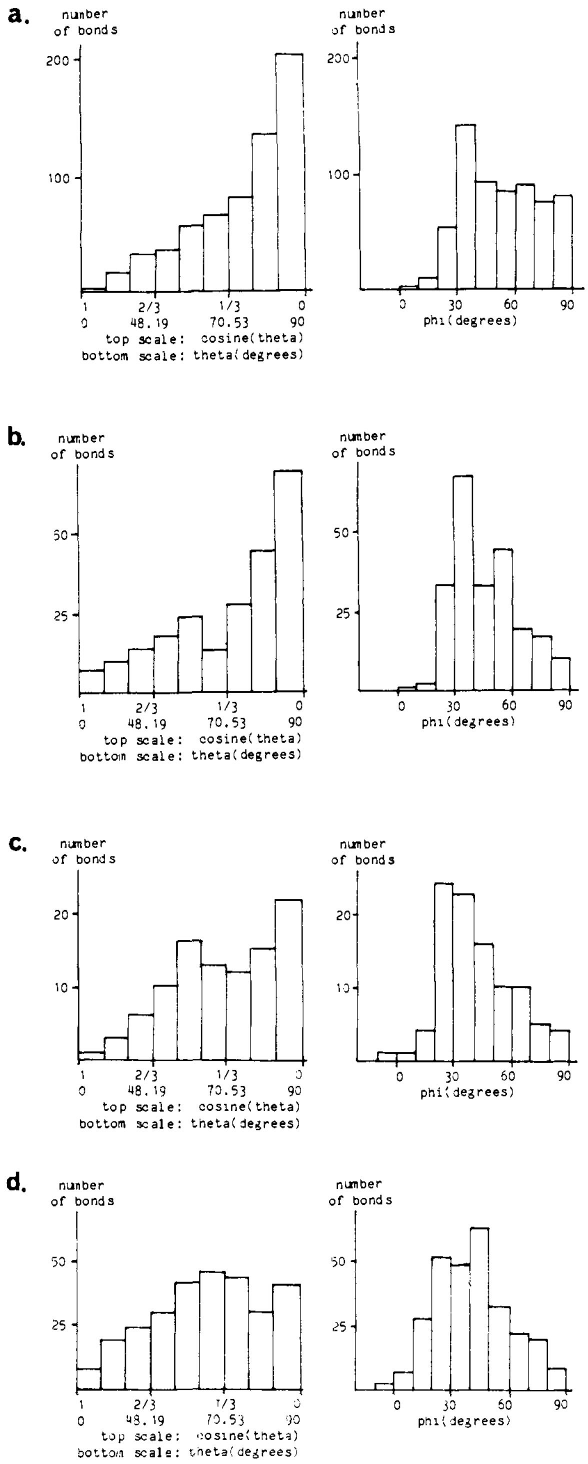


Figure 7. Cumulative distributions of θ_H and ϕ_H for (a) bonds involving carbonyl groups, in which the oxygen atom accepts no other hydrogen bonds (**4a**); (b) bonds involving carbonyl groups, in which the oxygen atom accepts one other hydrogen bond (**4b**); (c) bonds involving carboxylate ions, in which the oxygen atom accepts no other hydrogen bonds (**4c**); (d) bonds involving carboxylate ions, in which the oxygen atom accepts one other hydrogen bond (**4d**).

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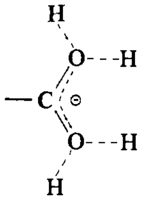
[19] This observation, together with the preceding one concerning the H···O distances, suggests that carboxylate oxygen atoms form stronger hydrogen bonds than carbonyl oxygen atoms. This can be rationalized on electrostatic grounds.

in the electron density distributions around carbonyl and carboxylate oxygen atoms. Secondly, it may be due to the prevalence of the hydrogen bond pattern **5** (note that the majority of carboxylate oxygen atoms accept *two* hydrogen bonds). It seems likely that nonbonded repulsions in **5** will force at least one of the hydrogen bonds out of the lone-pair plane.



5

Conclusions

The survey shows that N—H···O=C hydrogen bonds in the crystalline state tend to form in approximately the directions of the conventionally viewed oxygen sp^2 lone pairs. The "directional influence" of the lone pairs is dependent on several factors, e.g., the hydrogen bond distance, the nature of the acceptor species, and whether or not the hydrogen bond is intramolecular. Lone-pair directionality in the crystalline state is partly due to steric factors. However, there may be a small *electrostatic* preference for hydrogen bonding in the lone-pair directions. This preference, if it exists, is not necessarily due to a simple Coulombic attraction between the proton and the lone-pair electron density. The optimum hydrogen-bond geometry will depend on the *whole* of the electrostatic interaction between the donor and acceptor moieties.[20,21]

Charge density studies show that the lone-pair deformation density in carbonyl groups is usually resolved into two distinct maxima, in approximately the directions expected for sp^2 hybridization.[22] In contrast, the lone-pair deformation density in water molecules and hydroxy groups is generally found as one broad peak extending over a large part of the lone-pair region.[22] Thus, it is possible that the "directional influence" of sp^3 lone pairs is less important than that of sp^2 lone pairs. This is consistent with recent surveys of O—H···O< bonds in carbohydrate crystal structures,[23,24] which failed to find a significant correlation between the hydrogen-bond geometries and the directions of the oxygen sp^3 lone pairs. However, spectroscopic studies of the gas-phase dimers between hydrogen fluoride and oxirane, oxetane, and water suggest that the O···H—F bonds form in approximately the lone-pair directions.[8] A reexamination of the crystallographic data would therefore be worthwhile. Presumably, it would be necessary to use a much larger sample of hydrogen bonds than those studied previously, in order to establish whether sp^3 lone pairs have a significant "directional influence" in the crystalline state.

Acknowledgment. Olga Kennard is a member of the external staff of the Medical Research Council.

Supplementary Material Available: Table V, listing references for the 889 crystal structures used in the survey (38 pages). Ordering information is given on any current masthead page.

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(20) Politzer, P., Truhlar, D. G., Eds. "Chemical Applications of Atomic and Molecular Electrostatic Potentials"; Plenum: New York, 1981.

(21) The present study does not establish whether the electrostatic interaction between the N—H and C=O groups favors hydrogen bond formation in *exactly* the directions of the conventionally viewed lone pairs (i.e., $\phi_H = 30°$). The most common value of ϕ_H is 36–38°, but this may be partly due to steric effects. Nonbonded repulsions between the proton-donor group and the atoms bonded to the C=O group may tend to favor ϕ_H values in the range 30–40° rather than 20–30°.

(22) Olovsson, I. *Croat. Chem. Acta* **1982**, *55*, 171–190.

(23) Kroon, J.; Kanters, J. A.; Van Duijneveldt-Van de Rijdt, J. G. C. M.; Van Duijneveldt, F. B.; Vleigenthart, J. A. *J. Mol. Struct.* **1975**, *24*, 109–129.

(24) Ceccarelli, C.; Jeffrey, G. A.; Taylor, R. *J. Mol. Struct.* **1981**, *70*, 255–271.