

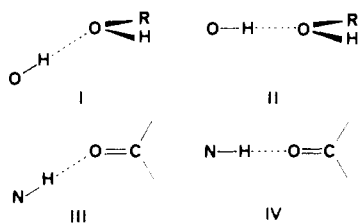
# Hydrogen-Bond Geometry in Organic Crystals<sup>†</sup>

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In 1920 Latimer and Rodebush suggested that "a free pair of electrons on one water molecule might be able to exert sufficient force on a hydrogen held by a pair of electrons on another water molecule to bind the two molecules together".<sup>1</sup> This speculation (greeted with some scepticism at the time) initiated two generations of research into the hydrogen bond, the output of which has been prodigious. As long ago as 1960, Pimentel and McClellan were able to list over 2000 references dealing specifically with hydrogen bonding.<sup>2</sup> We hesitate to guess what the figure would be now, but it must surely run into the tens of thousands. It is surprising, then, that many aspects of hydrogen bonding are still contentious. For example, do hydrogen bonds tend to form along lone-pair directions (i.e., I rather than II, III rather than IV)? Is the C-H group capable of par-



ticipating in hydrogen bonds? Are amides better acceptors than ketones, or the unsubstituted ammonium ion a better donor than substituted ammonium ions? In this Account, we review some recent crystallographic results that shed light on these and other questions relating to hydrogen-bond geometry and structure. In particular, we concentrate on the factors influencing hydrogen-bond distances, angles, and lone-pair directionality.

These apparently esoteric details of hydrogen-bond geometry are of more than academic interest. Hydrogen bonding is responsible for holding together many organic crystals; it also plays a major role in determining the conformations of nucleic acids, proteins, and polysaccharides. Consequently, a thorough understanding of hydrogen-bond geometry should assist us in modelling the structures of large biological molecules. We are a long way from achieving this goal. Even so, some steps have been taken along the way, and in this Account we discuss a few representative examples.

Robin Taylor was born in Birmingham, England, in 1951. Having obtained a B.A. from Oxford and a Ph.D. in chemical crystallography from Cambridge, he held postdoctoral positions in York and Pittsburgh before joining the Cambridge Crystallographic Data Centre in 1980. His research interests include the structure and geometry of hydrogen-bonded systems and the application of statistical methods to crystallographic data.

Olga Kennard was born in Hungary and is a naturalized British citizen. After graduating from Cambridge University, she worked at the Cavendish Laboratory and subsequently joined the Medical Research Council in London. She returned to Cambridge in 1961, as a member of the M.R.C. External Staff, to build up an X-ray crystallographic unit in the University Chemical Laboratory. Her research is concerned with biological structures, particularly oligonucleotides. She was awarded an Sc.D. (Cantab) in 1971 and the Structural Chemistry Prize of the Chemical Society in 1980.

**Table I**  
Comparison of Neutron and X-ray Hydrogen-Bond Geometries<sup>4</sup>

parameter	neutron		unnormalized X-ray		normalized X-ray	
	mean <sup>a</sup>	SD <sup>b</sup>	mean <sup>a</sup>	SD <sup>b</sup>	mean <sup>a</sup>	SD <sup>b</sup>
N-H, Å	1.030	0.015	0.938	0.075	1.030	
H...O, Å	1.865	0.122	1.956	0.119	1.869	0.108
N...O, Å	2.849	0.090	2.850	0.089	2.850	0.089
N-H...O, deg	161.5	11.2	162.2	11.4	161.3	11.6
O...N-H, deg	12.0	7.6	12.2	7.8	12.2	7.8

<sup>a</sup> Unweighted mean of 57 observations. <sup>b</sup> Sample standard deviation of 57 observations.

## Experimental Considerations: X-ray vs. Neutron Diffraction<sup>3</sup>

Many crystal structures are determined with the specific intention of studying the hydrogen-bond arrangement. It is therefore a source of exasperation to crystallographers that the hydrogen atom is a weak X-ray scatterer and can be difficult to locate by X-ray diffraction. Proof of this is the large number of crystal-structure communications with missing or incomplete tables of hydrogen-atom coordinates. The problem is particularly acute for exactly those hydrogen atoms that are of the most interest: (O-)H and (N-)H atoms in largish structures of biological importance. Even if the hydrogen atoms are found, the precision with which they are located is comparatively poor. Typical random errors in X-ray N-H or O-H bond lengths are 0.05-0.1 Å;<sup>4</sup> by way of comparison, random errors in C-C or N-O distances are usually an order of magnitude smaller. Moreover, X-rays are scattered primarily by electrons, and the electron density around a bonded hydrogen atom is distorted along the Don-H direction toward the Don atom (throughout the text, "Don" signifies a hydrogen-bond donor atom and "Acc" a hydrogen-bond acceptor atom). Thus, X-ray Don-H distances tend to be about 0.1 Å shorter than the true mean internuclear separation.<sup>4</sup>

One way of avoiding these problems is to use neutron rather than X-ray diffraction. Neutrons are scattered primarily by atomic nuclei, and Don-H distances are therefore measured without serious systematic error. Furthermore, the neutron scattering powers of hydrogen, carbon, oxygen, and nitrogen are all of comparable magnitude. Consequently, N-H and O-H distances are measured almost as precisely as, e.g., C-C or N-O distances (typical random errors would be  $\approx 0.005$  Å).

<sup>†</sup> Dedicated to Professor J. D. Dunitz on the occasion of his 60th birthday.

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(2) Pimentel, G. C.; McClellan, A. L. "The Hydrogen Bond"; Freeman: San Francisco, 1960.

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Table II  
Mean H...O Distances of N-H...O=C Bonds<sup>10</sup>

donor		acceptor				row mean
		carboxyl	ketone	amide	carboxylate	
>N-H	N <sup>a</sup>	117	38	597	74	1.959
	$\mu^b$	2.002 (12)	1.970 (22)	1.934 (5)	1.928 (19)	
>N <sup>+</sup> -H	N	11	2	12	36	1.888
	$\mu$	1.983 (55)	1.844 (126)	1.858 (43)	1.869 (28)	
NH <sub>4</sub> <sup>+</sup>	N	13	2	4	56	1.946
	$\mu$	1.916 (41)	1.995 (110)	1.988 (75)	1.886 (18)	
RNH <sub>3</sub> <sup>+</sup>	N	68	8	15	226	1.885
	$\mu$	1.936 (14)	1.872 (60)	1.891 (34)	1.841 (8)	
R <sub>2</sub> NH <sub>2</sub> <sup>+</sup>	N	6	3	3	47	1.860
	$\mu$	1.887 (47)	1.966 (178)	1.793 (70)	1.796 (14)	
R <sub>3</sub> NH <sup>+</sup>	N	0	1	2	11	1.835
	$\mu$		1.938 (-)	1.845 (14)	1.722 (25)	
column	mean	1.945	1.931	1.885	1.840	

<sup>a</sup> Number of observations. <sup>b</sup> Mean H...O distance in angstroms. Number in parentheses is standard error of mean, in units of 10<sup>-3</sup> Å.

Unfortunately, neutron diffraction is an expensive and relatively difficult technique; for one thing, it requires access to a nuclear reactor. It is not surprising, then, that X-ray determinations outnumber neutron studies by about a hundred to one.<sup>4</sup> Obviously, it is highly desirable to make use of this extensive X-ray data if possible.

The simplest and perhaps most effective way of doing this is to "normalize" the X-ray hydrogen-bond geometries.<sup>5</sup> In this procedure, the hydrogen atom is moved along the observed Don-H bond direction until the Don-H distance is equal to a "standard" value (typically taken as the average neutron Don-H distance, e.g., 1.03 Å for N-H,<sup>4</sup> 0.97 Å for O-H<sup>5</sup>). The consequences of normalization were investigated in a recent comparison of the X-ray and neutron diffraction geometries of 57 N-H...O=C bonds that have been determined by both methods.<sup>4</sup> It was found that the majority of neutron and "normalized X-ray" geometries were in reasonably good agreement (Table I, Figure 1). Furthermore, the average values of the H...O distance and N-H...O angle calculated from the normalized X-ray data were virtually identical with the corresponding values derived from the neutron data (Table I). It therefore appears that mean values of hydrogen-bond distances and angles can be estimated almost as well from normalized X-ray data as from neutron data. The reason for this lies in the extreme sensitivity of the hydrogen bond to its chemical environment. In the above example, the 57 hydrogen bonds are found in a wide variety of crystal-field environments, and the geometries of the bonds are *genuinely* different from one another. This is the major factor limiting the precision with which the average values of H...O and N-H...O can be determined.<sup>4,6</sup> The fact that the random *experimental* errors in the normalized X-ray geometries are larger than those in the neutron geometries is only of secondary importance.

### Hydrogen-Bond Distances

The hydrogen bond is largely an electrostatic phenomenon (i.e., due to Coulombic attraction between Don-H<sup>δ+</sup> and Acc<sup>δ-</sup>).<sup>7</sup> Consequently, the length of a hydrogen bond is highly dependent on the nature of the

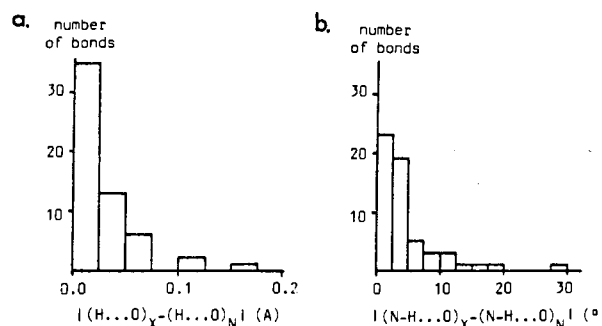
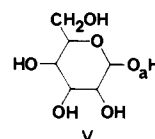


Figure 1. Distributions of (a)  $|(H...O)_X - (H...O)_N|$  and (b)  $|(N-H...O)_X - (N-H...O)_N|$ , observed in a survey of 57 N-H...O hydrogen bonds whose geometries have been determined both by X-ray and neutron diffraction.<sup>4</sup> The subscript "N" denotes a value determined by neutron diffraction, while "X" denotes a normalized X-ray value.

donor and acceptor atoms; even small changes in their properties may produce significant alterations in the H...Acc distance. For example, theoretical calculations suggest that the hemiacetal ("anomeric") oxygen atom in pyranoses (O<sub>a</sub> in V) is electron deficient compared



with the other oxygen atoms in the molecule.<sup>8</sup> Thus, we would expect the O<sub>a</sub> atom to be an exceptionally good proton donor in hydrogen bonds. This was confirmed by a survey of carbohydrate crystal structures, which showed that O<sub>a</sub>-H...O bonds tend to be shorter than other O-H...O bonds.<sup>9</sup>

The dependence of hydrogen-bond distances on the nature of the donor and acceptor atoms was recently investigated in a study of 1352 intermolecular N-H...O=C bonds.<sup>10</sup> Donor groups were divided into six categories: uncharged donors, >N-H; charged trigonal donors, >N<sup>+</sup>-H; unsubstituted ammonium ions, NH<sub>4</sub><sup>+</sup>; and mono-, di-, and trisubstituted ammonium ions (RNH<sub>3</sub><sup>+</sup>, R<sub>2</sub>NH<sub>2</sub><sup>+</sup>, R<sub>3</sub>NH<sup>+</sup>). Acceptor groups were categorized as carboxylate anions (O=C O<sup>-</sup>); henceforth termed "carboxylates", amides, ketones, and

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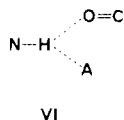
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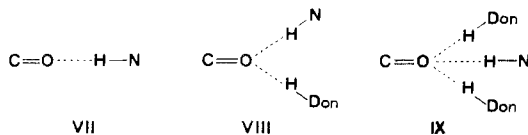
(10) Taylor, R.; Kennard, O.; Versichel, W. *Acta Crystallogr., Sect. B* 1984, B40, 280-288.

unionized carboxylic acids and esters (henceforth termed "carboxyls"). The mean H...O distances for the various donor-acceptor combinations are given in Table II. Marginal figures in this table are row and column means (e.g., the figure at the end of the first row is  $[2.002 + 1.970 + 1.934 + 1.928]/4$ ). Although some "cells" of the table contain only a few observations, it is fairly clear that the mean H...O distances tend to increase along the series: carboxylate < amide < ketone < carboxyl. They also tend to increase along the approximate series  $R_3NH^+ < R_2NH_2^+ < RNH_3^+ < >N^+-H < NH_4^+ < >N-H$ , so the strongest type of bond seems to be  $R_3NH^+ \cdots$ carboxylate while the weakest is  $>N-H \cdots$ carboxyl. Electrostatic effects may well be important in explaining these results: donor groups that carry a formal positive charge tend to form shorter bonds than uncharged  $>N-H$  groups, and the negatively charged carboxylate ion is a stronger acceptor than the uncharged amides, ketones, and carboxyls. Steric effects may also be relevant. For example, the  $R_3NH^+$  ion has only one "active" proton and therefore forms only one hydrogen bond. In contrast, the  $NH_4^+$  ion invariably donates all four protons in hydrogen bonds. Steric interactions between the four acceptor species surrounding the  $NH_4^+$  ion may tend to lengthen  $H_3N^+-H \cdots O$  bonds relative to  $R_3N^+-H \cdots O$  bonds.

Although hydrogen-bond lengths are clearly influenced by the nature of the donor and acceptor atoms, there is little doubt that *most* of the observed variation in H...O distances is due to crystal-packing effects.<sup>10</sup> Indeed, some clear correlations have been discovered between hydrogen-bond distances and crystal-field environments. A simple example is provided by three-center ("bifurcated") bonds such as VI, where the

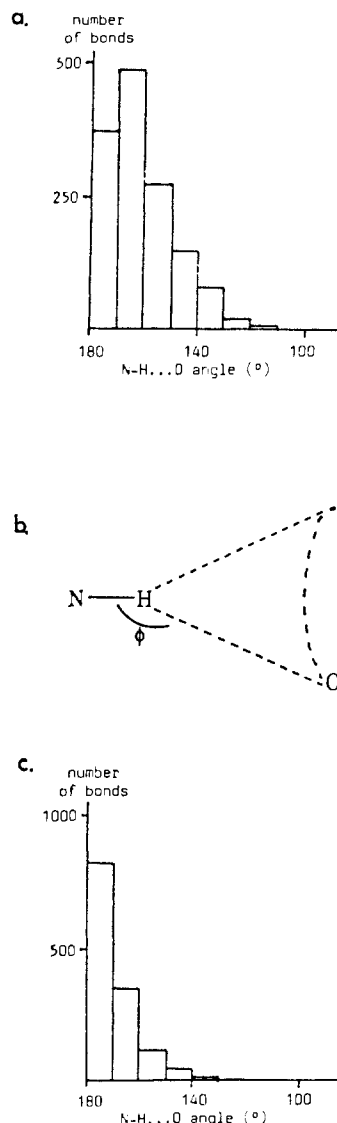


presence of the second hydrogen-bond acceptor atom, A, tends to lengthen the primary H...O contact. Thus, the mean H...O distance of 304 three-center bonds of type VI was 2.004 (9) Å, compared with a mean distance of 1.899 (4) Å for 1199 two-center ("linear") N-H...O bonds.<sup>11</sup> Presumably, this is due to steric interactions between N, O, and A in VI. Hydrogen-bond distances can also be correlated with the number of hydrogen bonds in which the acceptor group is involved. A survey of N-H...O=C bonds showed that, in general, bonds involving "single acceptors" (i.e., C=O groups that only accept one hydrogen bond, VII) are shorter than those involving "multiple acceptors" (VIII, IX).<sup>10</sup> Again, this is probably due to steric effects, i.e., repulsions between the two (or three) donor species in VIII (or IX).



A further example of the relationship between hydrogen-bond distances and crystal-field environments is provided by the "cooperative effect".<sup>5,12</sup> Theoretical

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**Figure 2.** (a) Distribution of N-H...O angles observed in a survey of 1357 intermolecular N-H...O=C bonds.<sup>10</sup> (b) Geometrical factor affecting N-H...O distribution. (c) Distribution of N-H...O angles corrected for geometrical factor.

calculations suggest that the formation of an O-H...O bond polarizes the electron density at the donor group so as to increase the partial negative charge at the oxygen atom.<sup>13,14</sup> This atom therefore becomes a better hydrogen-bond acceptor. Consequently, long chains of "cooperative" bonds ( $\cdots O-H \cdots O-H \cdots$ ) should be stronger than isolated, "noncooperative" bonds (O-H...O). This was confirmed by an analysis of 24 neutron-diffraction crystal structures, where the mean H...O distance of cooperative bonds [1.805 (9) Å] was significantly shorter than the mean H...O distance of noncooperative bonds [1.869 (23) Å].<sup>15</sup>

### Linearity of Hydrogen Bonds

Figure 2a shows the distribution of N-H...O angles observed in a survey of 1357 intermolecular N-H...

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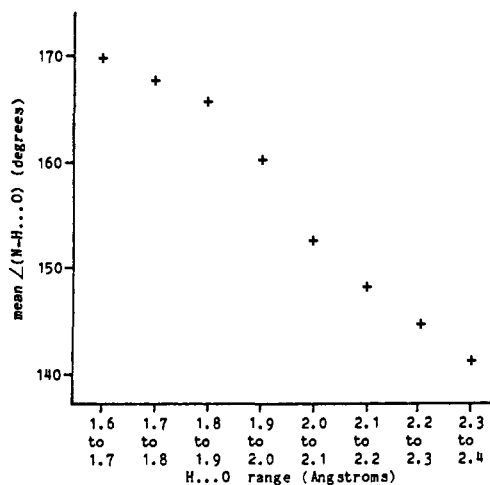
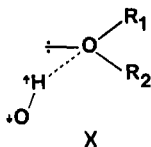


Figure 3. Plot of mean N-H...O angle against H...O range, based on a sample of 1357 intermolecular N-H...O=C bonds.<sup>10</sup>

O=C bonds.<sup>10</sup> The mean of the distribution is 161.2 (3)° (intramolecular bonds were found to be appreciably less linear: mean = 132.5 (15)°, based on 152 bonds<sup>10</sup>). Studies of O-H...O and C-H...O bonds produced rather similar distributions. O-H...O bonds seem to be slightly more linear (mean = 163.1°, based on 99 inter- and intramolecular neutron bonds<sup>15</sup>) and C-H...O bonds are considerably less linear (mean = 152.7°, based on 41 intermolecular neutron bonds<sup>16</sup>). Although Don-H...Acc angles of 180° are rare, the distribution in Figure 2a is not inconsistent with an energetic preference for linearity, because the number of possible spatial configurations with Don-H...Acc =  $\phi \pm \delta\phi$  is proportional to  $\sin \phi$  (Figure 2b).<sup>17,18</sup> Figure 2a can be approximately corrected for this geometric factor by multiplying each bar of the histogram by  $N/\sin \bar{\phi}$ , where  $\bar{\phi}$  is the average of the upper and lower limits of the bar and  $N$  is a normalization constant. The "corrected" histogram (Figure 2c) is obviously consistent with an energetic preference for linearity or near-linearity. In fact, more detailed analysis shows that small deviations from linearity may be energetically favorable in some circumstances (a result consistent with theoretical calculations<sup>7</sup>). For example, a study of 196 O-H...O< bonds (X-ray data) suggested that, in cases where the donor group lies outside the acceptor lone-pair plane (i.e., the plane bisecting the R<sub>1</sub>-O-R<sub>2</sub> angle in X), the proton tends to be drawn toward this plane while the donor oxygen is repelled away from it.<sup>18</sup> This result was later substantiated by an analysis of neutron data.<sup>15</sup>



Don-H...Acc angles are undoubtedly affected by many other factors. For example, the H...O distances and N-H...O angles of 1357 intermolecular N-H...O=C bonds were found to have a rank correlation coeffi-

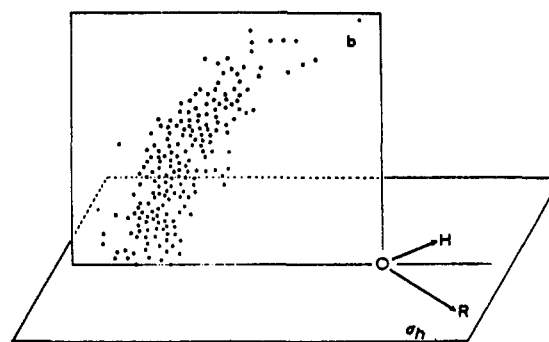
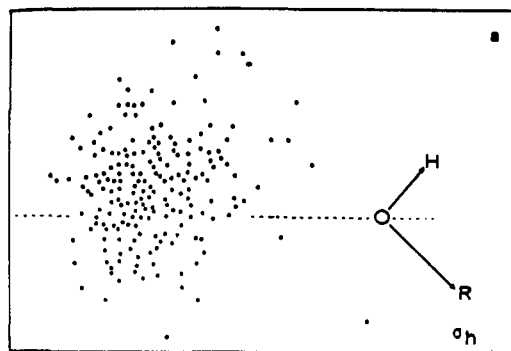


Figure 4. (a) Projections of observed hydrogen-atom positions on plane of R-O-H acceptor group. (b) Projections of observed hydrogen-atom positions on lone-pair plane of acceptor group. These plots are based on a survey of 196 O-H...O< bonds and are reprinted with permission from ref 18. Copyright Elsevier Science Publishers, B.V., 1975.

cient<sup>19</sup> of -0.521.<sup>10</sup> This is significantly different from zero at the 99.9% confidence level, showing that short hydrogen bonds tend to be more linear than long bonds. Figure 3<sup>10</sup> illustrates this correlation: the first (left-most) point represents the mean N-H...O angle of bonds with 1.6 < H...O < 1.7 Å, the next point represents the mean angle for bonds with 1.7 < H...O < 1.8 Å, and so on. A simple explanation<sup>7,20</sup> of the correlation is that, for any given N-H...O angle, the N...O non-bonded interaction becomes more unfavorable as H...O is decreased. Thus, short bonds tend to "straighten out" so as to increase the N...O distance.

### Lone-Pair Directionality

One of the most controversial questions about hydrogen-bond geometries is: do hydrogen bonds tend to form along lone-pair directions (i.e., are I and III more stable than II and IV, respectively)? A study of 196 O-H...O< bonds (X-ray data) suggested that the answer is "no".<sup>18</sup> The hydrogen bonds certainly showed a pronounced tendency to lie in the lone-pair plane of the acceptor atom, but no preference could be discerned for the sp<sup>3</sup> (i.e., tetrahedral) lone-pair directions within that plane. This result is illustrated by Figure 4,<sup>18</sup> where the observed distribution of hydrogen-bond directions is projected on (a) the plane of the acceptor (R-O-H) group and (b) the acceptor lone-pair plane. A later analysis of neutron-diffraction O-H...O< bonds produced similar results.<sup>15</sup> Unfortunately, this crystallographic evidence is contradicted by spectroscopic results; for example, microwave studies of the gas-phase

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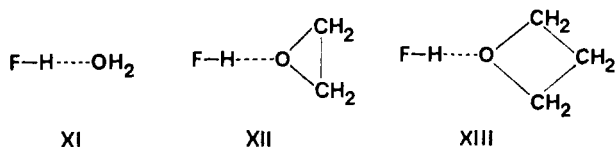
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Table III  
Distribution of Hydrogen Bonds on Surface of Quadrant Shown in Figure 5b (Ref 23)<sup>a</sup>

$\theta$ , deg	$\phi$ , deg									
	-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	1	0	2	5	1	2	1	3	4	3
27.27 to 38.94	1	0	1	3	7	10	10	4	10	8
38.94 to 48.19	0	0	1	6	12	12	20	11	17	12
48.19 to 56.25	0	2	4	7	12	23	16	18	15	8
56.25 to 63.61	0	1	6	21	27	27	27	19	13	12
63.61 to 70.53	0	2	3	20	33	31	25	23	11	7
70.53 to 77.16	1	4	7	29	43	27	27	16	15	12
77.16 to 83.62	0	2	9	33	75	38	30	21	16	18
83.62 to 90	1	2	17	55	* 101	55	33	37	26	27

<sup>a</sup> Table gives number of hydrogen bonds in each grid square (there are no bonds with  $\phi < -10^\circ$ ). The intervals of  $\phi$  and  $\theta$  are chosen so that all grid squares are of equal surface area. Thus, lines of longitude are separated by equal  $\phi$  intervals of  $10^\circ$ ; lines of latitude are separated by equal intervals of  $\cos \theta$ . The asterisk indicates idealized lone-pair direction ( $\theta = 90^\circ$ ,  $\phi = 30^\circ$ ).

dimers XI-XIII show that the F-H...O bonds lie in approximately the lone-pair directions.<sup>21</sup> Probably,



there is an energetic preference for hydrogen bonding in the directions of  $sp^3$  lone pairs. However, this preference may be small enough to be of little importance in determining hydrogen-bond geometries in the crystalline state.

Charge density studies show that the lone-pair deformation density in water molecules and hydroxy groups is usually found as one broad peak extending over a large part of the lone-pair region.<sup>22</sup> In contrast, the lone-pair deformation density in C=O groups is generally resolved into two distinct lobes, in approximately the directions expected for  $sp^2$  hybridization.<sup>22</sup> Thus, lone-pair directionality may be more important for  $sp^2$  lone pairs than for  $sp^3$  lone pairs. A recent survey of 1357 intermolecular N-H...O=C bonds supports this prediction.<sup>23</sup> The hydrogen-bond geometries were described by the spherical polar coordinates  $\theta$  and  $\phi$  in Figure 5a. Differences between A and B (see Figure 5a) were neglected; i.e., the acceptor moiety was assumed to have  $C_{2v}$  symmetry. Thus, the proton position in any hydrogen bond could be reflected into the quadrant with  $x \geq 0$ ,  $z \geq 0$  (i.e.,  $90^\circ \geq \theta \geq 0^\circ$ ;  $90^\circ \geq \phi \geq -90^\circ$ ; see caption to Figure 5a). The surface of this quadrant was then divided into a  $9 \times 18$  grid (Figure 5b), the  $(\theta, \phi)$  coordinates of the grid points being chosen so that all grid squares were of equal surface area. If the distribution of hydrogen-bond geometries was random, we would expect an equal number of hydrogen bonds in each grid square. The observed  $(\theta, \phi)$  distribution (Table III) shows quite clearly that this is not the case; there is a statistically significant tendency for hydrogen bonds to occur within about  $13^\circ$  of the lone-pair plane and  $10^\circ$  of the idealized  $sp^2$  lone-pair direction (i.e.,  $\theta = 90^\circ$ ,  $\phi = 30^\circ$ ).<sup>23</sup> Thus, there is a distinct preference for N-H...O=C hydrogen bonds to form in, or near to, the directions of the  $sp^2$  lone pairs.

It is interesting to speculate on the reasons for this. In bonds involving "double acceptors" (VIII), steric

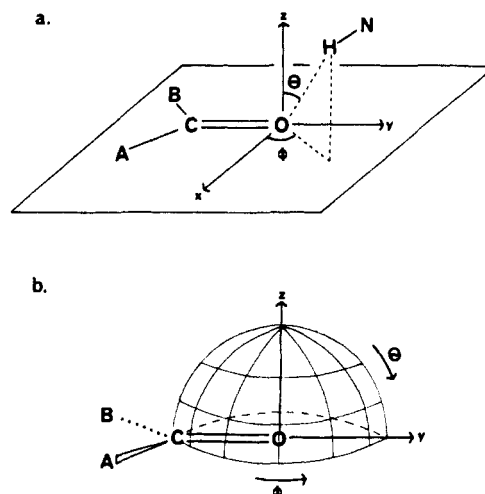


Figure 5. (a) Spherical polar coordinates used in study of lone-pair directionality in N-H...O=C bonds.<sup>23</sup> Positive  $\phi$  corresponds to hydrogen bonding in the octant with  $y > 0$  (i.e., C=O...H  $> 90^\circ$ ), and vice versa. (b) Schematic drawing of grid system used in statistical analysis. Every third grid line is shown.

effects may be partly responsible. However, a subset of bonds involving "single acceptors" still showed a statistically significant tendency for hydrogen bonding in the lone-pair directions (in fact, the tendency for hydrogen bonds to occur in the lone-pair plane was even more pronounced for this subset than for the complete data set).<sup>23</sup> Thus, there may be a small electrostatic preference for the lone-pair directions.

### The Future: Rationalization of Hydrogen-Bonding Patterns

Hydrogen bonding is the major cohesive force in many organic crystal structures, and it would be helpful if we could use the results outlined above to devise "rules" for rationalizing, or even predicting, crystal-structure hydrogen-bonding patterns. At a simple level, such rules have been used by crystallographers for many years.<sup>24</sup> For example, it is unusual for an O-H or N-H group *not* to be hydrogen bonded if an acceptor atom is available in the crystal structure (presumably because hydrogen bonding is a very strong interaction compared with other nonbonded forces). Thus, crystallographers would view such an unbonded O-H or N-H group with suspicion. Recently, evidence has emerged that C-H groups also tend to form short contacts to electroneg-

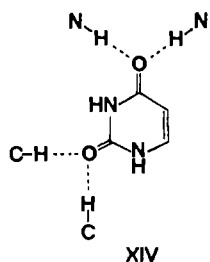
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ative atoms—this is particularly true of relatively electropositive groups such as  $N^+-C-H$ .<sup>16</sup> The energy of a  $C-H\cdots Acc$  interaction is probably small but may occasionally play a role in stabilizing organic crystal structures. For example, uracil forms a structure in which one of the carbonyl groups accepts two  $N-H\cdots O$  hydrogen bonds and the other makes short contacts to two  $C-H$  groups (XIV).<sup>25</sup> A more homogeneous hydrogen-bond pattern can be envisaged,<sup>26</sup> in which both carbonyl groups participate in  $N-H\cdots O$  bonds (as in 5-fluorouracil<sup>27</sup> and 6-azauracil<sup>28</sup>). Thus, the short  $C-H\cdots O$  interactions may be instrumental in stabilizing the observed uracil structure.<sup>26</sup>



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Recently, it was suggested that crystal structures also tend to form so as to involve the maximum number of acceptors in the hydrogen-bonding scheme.<sup>29</sup> This conclusion was based on the packing arrangements of about 50 structures and can be explained by the observation that hydrogen bonds involving "single acceptors" (e.g., VII) are usually more stable than bonds involving "multiple acceptors" (e.g., VIII, IX; see section on hydrogen-bond distances). However, Berkovitch-Yellin et al. pointed out that the rule is broken in the crystal structures of some *N*-acylated amino acids ( $R\cdot CO\cdot NH\cdot CHR'\cdot CO_2H$ ), in which the amide oxygen atom accepts two hydrogen bonds and the carboxyl  $C=O$  group none.<sup>30</sup> Presumably, this is because amides are better acceptors than carboxyls (again, see section on hydrogen-bond distances). Thus, we see that the observed hydrogen-bonding arrangements are the results of compromises between two conflicting factors: a preference for including as many acceptors as possible in the hydrogen-bonding scheme and a preference for strong acceptors to form hydrogen bonds at the expense of weak acceptors.

This situation is quite general: crystal-structure hydrogen-bonding patterns are the products of compromise, and this is why they are so difficult to predict. The compromises involve not only hydrogen bonding but also other nonbonded interactions.<sup>31</sup> For example, many secondary amides adopt the packing arrangement XV, which we would expect to be favorable because the  $N-H\cdots O$  bonds are approximately linear and in the directions of the oxygen  $sp^2$  lone pairs.<sup>32</sup> However, the alternative arrangement XVI is favored for secondary amides containing hydrocarbon chains, such as *N*-methylsorbamide<sup>32</sup> and *N*-methyldipropylacetamide.<sup>33</sup>

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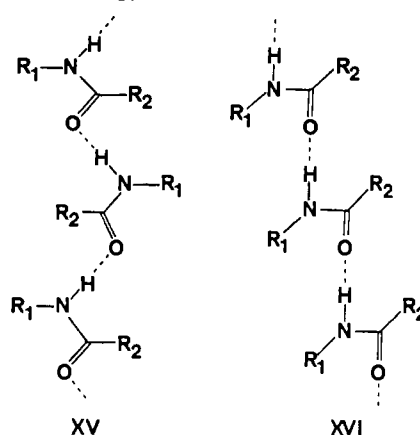
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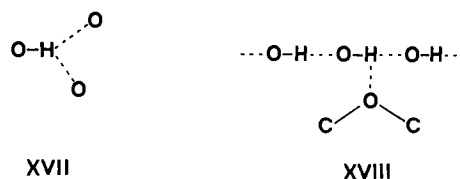
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The hydrogen-bonding geometry is less favorable in this arrangement, but the hydrocarbon chains are closely packed. In XV, the chains would be separated from each other, resulting in a lack of intermolecular contacts along the hydrogen-bonding axis and a consequent loss of dispersion energy.<sup>32</sup>



Much effort has been put into rationalizing the crystal-structure hydrogen-bonding arrangements of pyranoses and pyranosides. A survey of hydrogen bonding in 24 monosaccharide and related crystal structures showed that three-center bonds (XVII) are more common in these structures than had been supposed previously.<sup>15</sup> One possible reason for this is that



three-center bonding allows the ring oxygen atom (see V) to participate in the hydrogen-bonding scheme without breaking up favorable, cooperative  $\cdots O-H\cdots O-H\cdots$  chains (i.e., XVIII; since the ring oxygen can be a hydrogen-bond acceptor but not a donor, it must necessarily terminate such a chain). This possibility provoked a more detailed analysis<sup>34</sup> in which it was concluded that pyranoside hydrogen-bonding arrangements are governed by three rules. Firstly, the energy of the hydrogen-bond scheme is maximized by including all of the hydroxyl groups and as many as possible of the ring and glycosidic oxygen atoms. Secondly, the formation of  $\cdots O-H\cdots O-H\cdots$  chains or loops is favored because of the cooperative effect (see above); long, or infinite, chains are preferred over short ones. Thirdly, hydrogen bonds involving the anomeric oxygen atom as a donor are favored, but bonds involving anomeric acceptors are disfavored (see section on hydrogen-bond distances). These three rules are mutually incompatible and compromises between them produce four basic types of hydrogen-bond arrangement (one of which is XVIII).<sup>34</sup>

### Concluding Remarks

Systematic analyses of X-ray and neutron-diffraction crystal structures provide detailed information about the basic factors governing hydrogen-bond geometry.

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For example, H...Acc distances can be correlated with the nature and environment of the donor and acceptor groups; Don-H...Acc angles have an energetic preference for linearity or near-linearity; and there is a slight tendency for hydrogen bonds to form in the directions of the acceptor-atom lone pairs. The importance of these results is that they may be used to devise "rules" for rationalizing, or even predicting, crystal-structure hydrogen-bonding arrangements. Recent studies on simple molecules such as amides and monosaccharides

suggest that this is already a profitable area of research. In fairness, though, we must quote from a reviewer's report on this paper: "There have been some heroic attempts and a few minor advances ... but [rationalization of crystal-structure hydrogen-bonding patterns] ... is still at the foot of the rainbow". The truth of this remark cannot be denied: we have come a long way, but there is much further to go. Still, it is encouraging to recall the conventional wisdom about rainbows: pots of gold are to be found at their ends!

## New Synthetic Chemistry of Transition-Metal Trialkylsilane Complexes

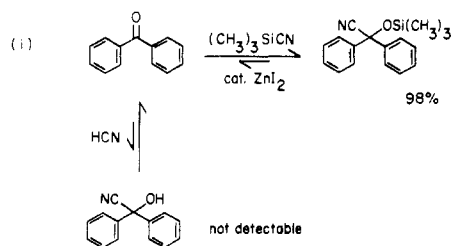
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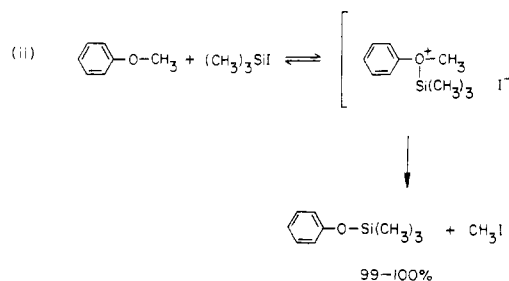
Many useful transformations, such as the Wittig reaction, are thermodynamically driven by the formation of strong heteroatom-oxygen or metal-oxygen bonds. Silicon makes an exceptionally strong single bond to oxygen (106-127 kcal/mol),<sup>1</sup> and this provides the basis for many of the applications of silicon reagents in organic synthesis.<sup>2</sup>

Our attention was drawn to trimethylsilyl (pseudo)-halogen compounds,  $(\text{CH}_3)_3\text{SiX}$ ,<sup>2-4</sup> by the elegant research of three Southern California colleagues: Evans, Jung, and Olah. These reagents are capable of effecting types of organic transformation (particularly with oxygen-containing substrates) which otherwise require harsh conditions or are impossible with the corresponding protic acids HX. A striking example is provided by the 1,2-addition of  $(\text{CH}_3)_3\text{SiCN}$  to benzophenone to give a silylated cyanohydrin (eq i).<sup>3a</sup> No cyanohydrin is obtained when benzophenone is treated with HCN. Another example is the cleavage of ethers by  $(\text{CH}_3)_3\text{SiI}$  (eq ii).<sup>4b,d</sup> This reaction is believed to involve the initial formation of an oxonium salt ion pair.



We sought to determine if reactivity patterns similar to eq i and ii might be exhibited by *transition-metal*

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trialkylsilanes,  $L_n\text{MSiR}_3$ .<sup>5</sup> In other words, can the -CN and -I in eq i and ii be replaced by metals? If so, it might be possible to achieve (1) conceptually new syntheses of organometallic complexes, (2) heretofore difficult or unprecedented organic transformations by elaboration of these organometallic complexes, and (3) stoichiometric analogues of postulated but yet unobserved steps in the catalytic hydrosilylation of unsaturated organic molecules. As precedent, we noted Ellis' observation that  $L_nM^-$  moieties often exhibit halide-like ( $X^-$ ) reactivity.<sup>6</sup>

Examples of readily available transition-metal trialkylsilanes include  $(\text{CO})_4\text{CoSi}(\text{CH}_3)_3$ ,<sup>7</sup>  $(\text{CO})_5\text{MnSi}(\text{C}-$

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