Acceptor directionality of sterically unhindered C–H···O=C hydrogen bonds donated by acidic C–H groups

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Crystal correlation study of acidic and sterically unhindered C–H groups (chloroform, dichloromethane and terminal alkynes) forming short contacts with carbonyl acceptors, reveals a soft but significant preference for the conventional carbonyl lone-pair direction.

C–H···O interactions are currently one of the main topics of hydrogen-bond research.[1] However, the directionality properties of these interactions are not yet well understood. For the donor directionality, it has been shown that short C–H···O contacts (H···O < 2.4 Å) have a similar preference for approximate linearity as O–H···O hydrogen bonds.[2] With increasing H···O distance, this preference rapidly becomes softer, leading to a continuous transition to more or less isotropic behaviour.[3] The *acceptors* of hydrogen bonds generally exhibit a more complex directionality, which depends on their chemical nature. This was studied in detail for O/N–H···O bonding: for carbonyl acceptors, X–H vectors tend to point in the direction of the oxygen 'lone-pair lobes', which are in the carbonyl plane, theoretically forming angles of 120° with the C=O bond.[4] This directionality, however, is weaker than is often assumed, and is easily disobeyed. For ether, hydroxy and water acceptors, the directionality is even softer with accepted hydrogen bonds being weakly clustered in the bisecting plane of R^1–O–R^2 ('lone-pair plane').[5]

In the context of weak hydrogen bonding, acceptor directionality has as yet been discussed only for C–H···O=C interactions. For this system, acceptor directionality was allusively shown in crystal correlation studies,[2,6] but these earlier results are persistently questioned. Since the discussed effects are subtle and affected by bias of different kinds, it seems necessary to investigate the anticipated acceptor directionality in a structural data set with largely reduced conceptual bias.

When selecting a suitable data sample, it is necessary to avoid effects that can smear a possibly existing acceptor directionality, and it is equally necessary to avoid effects that can feign a fictitious correlation. Therefore, the study was restricted to C–H···O=C pairs with the following properties. (*a*) C–H groups with high and comparable 'donor strength' (*i.e.* acidity[7]), ensuring that C–H···O interactions of appreciable strengths are analysed. (*b*) No steric hindrance at the C–H and at the O=C sides. (*c*) No O=C accepting additional hydrogen bonds from O/N–H or from other acidic C–H donors, or being involved in other intermolecular contacts shorter than (C)H···O; this is to ensure that the C–H···O=C hydrogen bond under question is the dominant intermolecular interaction formed by O=C. (*d*) Little tendency to form *specific patterns* that are associated with specific hydrogen-bond geometries. Unfortunately, these necessary restrictions exclude the vast majority of C–H groups; the obtained small data set, however, has superior predictive power compared to large but inhomogeneous data sets used in earlier studies. The analysed acidic C–H donors are $CHCl_3$, CH_2Cl_2, and the ethynyl residue, –C≡C–H. The details of data retrieval are given in a footnote.†

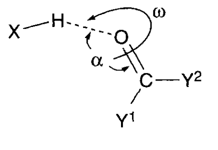
The approach of X–H to O=C is here characterized by the angle α = H···O=C and the torsion angle ω = H···O=C–Y; **I**. No distinction is made between the two atoms to which C=O is bonded; therefore, all ω values can be transformed to the quadrant $0 \leqslant \omega \leqslant 90°$. In this notation, the theoretical lone-pair orientation is α = 120°; ω = 0°.

For the present data set, histograms of angles α and ω are shown in Fig. 1. For α, values of *ca.* 130° are slightly favoured over the more linear angles. The distribution of torsion angles ω shows clear preference of in-plane contacts with small ω values, but out-of-plane contacts with ω close to 90° are also observed. The acceptor directionality is further quantified in a polar scatterplot of ω *vs.* α, Fig. 2. The scaling of this plot is such that equal areas of the plot correspond to equal solid angles around O,‡ so that clustering in the plot actually represents clustering in the spherical α,ω-space. Despite the small data quantity, the general properties are obvious: the population density is largest for α between 120 and 150° and small ω, and smallest in the polar region and for $\omega \approx 90°$. The clustering, though significant, is not very pronounced; this shows that the preferences can easily be disobeyed.

The data in Figs. 1, 2 carry two important implications.

(*a*) C–H···O=C contacts are favourably directed roughly at the carbonyl lone-pair lobes, *i.e.* C–H···O acceptor directionality *per se* exists (at least for acidic C–H).

(*b*) The broad shapes of the distributions show that the acceptor directionality is very soft. Even close to linear H···O=C contacts and contacts perpendicular to the carbonyl plane occur with considerable frequency. Due to this softness, individual C–H···O=C contacts with very distorted geometry can not be regarded as 'anomalous', but just as somewhat less favourable cases. *Therefore, acceptor directionalities have very limited predictive power for individual crystal structures or other supramolecular arrangements* (*i.e.* it is not possible to predict reasonably, whether for an unknown structure, acceptor directionality is obeyed or not). This softness will be even more



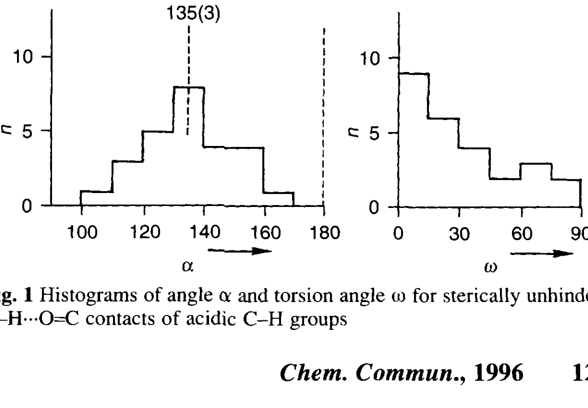


Fig. 1 Histograms of angle α and torsion angle ω for sterically unhindered C–H···O=C contacts of acidic C–H groups

pronounced for less acidic C–H donors than those under study, or if steric hindrance or competition with stronger donors come into play.

Inspecting the recent literature, we gain the impression that in the context of C–H···O interactions, most chemists either under- or over-estimate the importance of acceptor directionalities. One view is to consider C–H···O contacts as isotropic interactions. The other view is to point at the (proven) hydrogen-bond nature of C–H···O interactions and to conclude that the interaction *must* be pronouncedly directional. Our results indicate a situation between these extremes.

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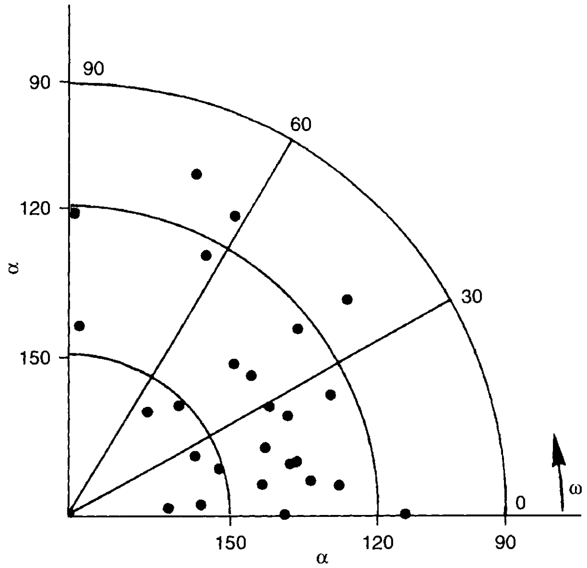

Fig. 2 Polar scatterplot of ω *vs.* α. The scaling is such that equal areas in the plot correspond to equal solid angles around O (see footnote‡).

Footnotes

† *Data retrieval.* First step: Cambridge Structural Database[8] (CSD), ordered and error-free organic crystal structures (R < 0.07) containing $CHCl_3$, CH_2Cl_2 or R–C≡C–H forming C–H···O=C< contacts with H···O < 2.8 Å. Nature of >C=O not restricted. C–H bond lengths normalized to 1.083 Å. This yielded 48 contacts in 39 X-ray crystal structures. Second step: C=O acceptors were filtered out that accept additional hydrogen bonds from stronger or equally strong donors, or that form other inter- or intramolecular contacts shorter than the C–H···O=C contact. In the second step, the correlations in Fig. 2 were appreciably sharpened. Final data set: 26 C–H···O contacts in 22 crystal structures (9 from $CHCl_3$, 5 from CH_2Cl_2, 12 from –C≡C–H). The H···O separations range from 2.03 to 2.45 Å, mean value 2.19 Å, showing that the 'strong end' of C–H···O hydrogen bonding is analysed here.

‡ In a cartesian plot of ω against α, or in a polar plot with a linear scale of α, equal areas do not in the general case correspond to equal solid angles in the spherical ω–α-space. A plot where equal areas actually correspond to equal solid angles is given in a polar plot of ω *vs.* α, with a non-linear scale of α: $\alpha_{\text{scale}} = (1 + \cos \alpha)^{1/2}$.

References

1 G. A. Jeffrey and W. Saenger, *Hydrogen Bonding in Biological Structures*, Springer, Berlin, 1991; J. Bernstein, M. C. Etter and L. Leiserowitz, in *Structure Correlation*, ed. H.-B. Bürgi and J. D. Dunitz, VCH, Weinheim, 1994, vol. 2, pp. 431–507; G. R. Desiraju, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2311.

2 R. Taylor and O. Kennard, *J. Am. Chem. Soc.*, 1982, **104**, 5063.

3 Th. Steiner and W. Saenger, *J. Am. Chem. Soc.*, 1992, **114**, 10 146.

4 R. Taylor, O. Kennard and W. Versichel, *J. Am. Chem. Soc.*, 1983, **105**, 5761; P. Murray-Rust and J. P. Glusker, *J. Am. Chem. Soc.*, 1984, **106**, 1018.

5 J. Kroon, J. A. Kanters, J. G. C. M. van Duijneveldt-van de Rijdt, F. B. van Duijneveldt and J. A. Vliegenthart, *J. Mol. Struct.*, 1975, **24**, 109.

6 D. Braga, F. Grepioni, K. Biradha, V. R. Pedireddi and G. R. Desiraju, *J. Am. Chem. Soc.*, 1995, **117**, 3156.

7 V. R. Pedireddi and G. R. Desiraju, *J. Chem. Soc., Chem. Commun.*, 1992, 988.

8 F. H. Allen, J. E. Davies, J. J. Galloy, O. Johnson, O. Kennard, C. F. Macrae, E. M. Mitchell, G. F. Mitchell, J. M. Smith and D. G. Watson, *J. Chem. Inf. Comput. Sci.*, 1991, **31**, 187.

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