Distinction between the weak hydrogen bond and the van der Waals interaction

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The angular distributions of C–H··O interactions for different types of C–H groups show that the directionality decreases with decreasing C–H polarisation, but that it is still clearly recognisable for methyl groups; for C–H··H–C van der Waals contacts, in contrast, isotropic angular characteristics are observed.

It is by now well-recognised that C–H groups can act as weak hydrogen bond donors.[1,2] While vibrational spectroscopy shows that the C–H donor strength depends on the carbon hybridisation as C(sp)–H > $C(sp^2)$–H > $C(sp^3)$–H,[3] early crystallographic data suggests some donor potential even for the weakly polarised methyl groups.[4] Statistical database surveys demonstrate that mean C···O distances in C–H···O contacts correlate convincingly with conventional C–H acidities,[5] and even for methyl groups $R–CH_3$, mean H···O distances have been found to depend on the nature of the R group.[6] All these experimental studies indicate that most kinds of C–H groups can donate weak hydrogen bonds. While the bonds formed by acidic C–H groups (alkynes, haloforms) are moderately strong, those that involve weakly polarised C–H groups are much weaker. Many studies have concentrated on the stronger of the C–H···O hydrogen bonds, possibly because they are associated with more dramatic structural and spectroscopic effects, and this has meant that experimental information on weakly polarised C–H donors is relatively scarce. Still, theoretical calculations have been published for weakly polarised C–H groups,[7] estimating C–H···O hydrogen bond energies to be around 0.5 to 1 kcal mol^{-1}.

Despite this wealth of experimental and theoretical work, the concept of the C–H···O hydrogen bond, and that of the weak hydrogen bond in general, has been persistently questioned. The strong disapproval that was published[8] in the 1960s has, over the years,been steadily diluted into oral objections that may best be described as stationary. It is therefore of some interest that a recent paper in this journal states that the typical C–H···O/N hydrogen bond represents 'nothing more than a classical van der Waals interaction.[9] Here this claim will be directly falsified.

A fundamental difference between hydrogen bonds and the van der Waals interaction lies in their different directionality characteristics. Hydrogen bonds are inherently *directional*, with linear or close to linear geometries favoured energetically over bent ones. In contrast, van der Waals contacts are *isotropic*, with interaction energies independent of the contact angle θ. This difference allows one, in principle, to distinguish between hydrogen bonds and the van der Waals interaction. However, hydrogen bond directionality is soft,[10] and even for moderately strong bonds it cannot be characterised from single examples or small data samples. A proper description of angular preferences, or lack thereof, requires statistical analysis of large quantities of structural data, such as may be retrieved from the Cambridge Structural Database (CSD).[11] Database analysis is complicated by factors such as steric hindrance and chemical inhomogeneity, which in adverse situations can completely smear structural trends.‡ However, one can plan and perform CSD analyses so as to minimise these complicating factors.

The angular characteristics of the weakest kinds of C–H···O hydrogen bonds have not yet been described. Therefore, we report here a CSD study of these characteristics in conjunction with those for van der Waals contacts of the type C–H···H–C. Structural data were retrieved§ for C–H···O contacts involving the prototypes of the C(sp)–H, $C(sp^2)$–H and $C(sp^3)$–H groups, that is ethynyl, vinyl and ethyl groups. For comparison, data for conventional hydrogen bonds from hydroxy donors is also presented. To reduce chemical inhomogeneity, only organic carbonyl acceptors were considered. For the H···O distance cutoff, a long value of 3.0 Å was selected; this is greater than the van der Waals sum by 0.3 Å.[12] Initial tests showed that this cutoff value is not critical for the subsequent analysis. Data for C–H···H–C van der Waals contacts were also retrieved to the distance limit of the van der Waals sum plus 0.3 Å (= 2.7 Å). Numerical data giving mean hydrogen bond distances and angles are listed in Table 1. To examine the degree to which linear contact geometries are preferred, histograms of angular C–H···O distributions were generated (Fig. 1). Since the solid angle covered by an angular interval $\Delta\theta$ is smaller for nearly linear angles θ than for bent ones (Fig. 2), the angular distribution must be weighted by a correction factor of $1/\sin\theta$ to properly reflect angular preferences. This is termed the 'cone correction'.[13]

The histogram for hydroxy donors shows the well-known directional behaviour of conventional hydrogen bonds [mean θ = 154.0(4)°].[10,13] For the acidic ethynyl donors C≡C–H, the mean C–H···O angle θ is only slightly smaller, 152(2)°, and the angular distribution is only slightly broader. For vinyl donors, the mean angle θ falls to 143(1)° and the angular distribution widens considerably. For the very weakly polarised methyl donor of the ethyl group, the mean angle θ falls further to 137.1(7)° and the angular distribution is correspondingly softened, *but it still shows directional behaviour with linear contact geometries being favoured*. Finally, the mean C–H···H angle for C–H···H–C contacts of methyl groups is 128.6(3)°. Here, however, the angular distribution is almost ideally isotropic in the range 120 to 180°, while for θ < 120°, the frequencies fall because side-on contacts are sterically disfavoured [Fig. 1(*e*)]. This is exactly the picture that is expected for the non-directional van der Waals interaction.

The sequence of histograms in Fig. 1 clearly shows a gradual decrease of directionality for C–H···O interactions with decreasing C–H polarisation. For alkyne donors, the directionality

Table 1 Numerical data for X–H···Y contacts with H···Y< 3.0 Å (2.7 Å for H···H contacts). Data for normalised H-atom positions

Contact type	Number	Mean H···Y (Å)	Mean X···Y (Å)	Mean X–H···Y (°)
$C(sp^3)$–O–H···O=C	3330	1.974(6)	2.837(4)	154.0(4)
C≡C–H···O=C	44	2.36(4)	3.31(2)	152(2)
$C{=}CH_2$···O=C	124	2.67(1)	3.56(2)	143(1)
$CH_2–CH_3$···O=C	767	2.761(6)	3.590(7)	137.1(7)
$CH_2–CH_3$···H–C	3975	2.500(2)	3.246(4)	128.6(3)

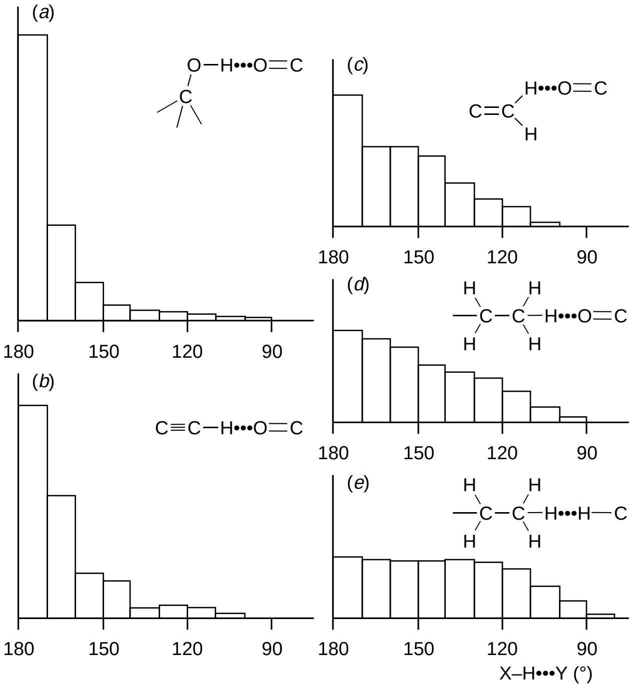

Fig. 1 CSD results. Histograms with angular frequencies of X–H···O=C contacts for different donor types, and of C–H···H–C van der Waals contacts: (*a*) hydroxy, (*b*) ethynyl, (*c*) vinyl and (*d*) ethyl donors and (*e*) van der Waals contacts. The distributions are 'cone-corrected' (ref. 13) (*i.e.* weighted by $1/\sin\theta$) and scaled in such a way that they cover the same area.

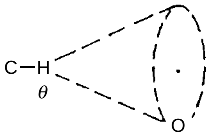

Fig. 2

behaviour is that of conventional hydrogen bonds such as those formed by hydroxy groups. For vinyl donors, the directionality is weaker, but is still clearly pronounced. For methyl groups, the directionality is the weakest, but is still clearly different from the perfectly isotropic behaviour for C–H···H–C contacts. Since C–H···O interactions of alkyl groups are *not* isotropic (even at the long distance cutoff of 3.0 Å), they should definitely not be classified as mere van der Waals contacts. The observed differences in directionality behaviour between any kind of C–H···O hydrogen bond and the van der Waals interaction is a consequence of the fundamentally different distance and angle fall-off characteristics of these interactions.

It is important to note that weak hydrogen bonds encompass a wide scale of strengths just as do carbon acidities. It is therefore misleading to consider all kinds of C–H···O hydrogen bonds as being exactly alike, even as it is misleading to assign hydrogen bond character only to a certain class of C–H···O contacts and consider the rest as nothing more than classical van der Waals interactions. *A C–H···O hydrogen bond does not become a van der Waals contact just because the H···O distance crosses an arbitrary threshold.* It is pointed out, however, that this does not mean that every C–H···O contact of a methyl group is 'automatically' a hydrogen bond: it has been shown theoretically and also experimentally that some C–H···O geometries formed by methyl groups have zero or possibly even positive interaction energies.[7,14]

In this light, the more interesting question is the nature of the interface between the weak hydrogen bond and the van der Waals interaction. Recent experiments indicate that this grey area is shrinking.[15] Investigating such matters will undoubtedly be difficult, but given the continuous spectrum of these structural phenomena, it is not hard to conceive of a domain wherein the distance falloff characteristics of an interaction X–H···A varies between those expected for a hydrogen bond and for a van der Waals interaction. Exploration of this region will surely yield new insights.

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Notes and References

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‡ When studying the correlation of carbon acidity with mean C···O distances in C–C–H···O interactions, it was observed that this correlation is clearcut for sterically unhindered donor types, but completely smeared for sterically hindered groups (ref. 5). The finer effect of acceptor basicity on mean distances could subsequently be shown *only* in chemically homogeneous sets of sterically unhindered C–H···O hydrogen bonds (ref. 6).

§ Database analysis: Cambridge Structural Database, June 1997 update with 167 797 entries, ordered and error-free organic crystal structures with R values < 0.05 (for alkynes: $R < 0.07$), H-atom positions normalised. Distance cutoff values: H···O < 3.0 Å for hydrogen bonds, H···H < 2.7 Å for van der Waals contacts. No angle restriction.

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