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Reliability of assigning O–H ··· O hydrogen bonds to short intermolecular O ··· O separations in cyclodextrin and oligosaccharide crystal structures *

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Abstract

The statistical relation between intermolecular O ··· O separations and the occurrence of hydrogen bonding is described for six high-resolution neutron crystal structures of cyclomalto-oligosaccharide (cyclodextrin) complexes. All O ··· O contacts shorter than 3.0 Å are actually associated with hydrogen bonds. Van der Waals O ··· O contacts without a hydrogen bond occur beyond 3.0 Å; in the interval 3.1 to 3.2 Å, they comprise 15%, and in the interval 3.2 to 3.3 Å over 30%, of the contacts. For O ··· O separations > 3.6 Å, no hydrogen bonds are observed. A procedure is suggested as to how hydrogen bonds can be assigned to intermolecular O ··· O contacts in cyclodextrin crystal structures with a low risk of error; this includes the identification of certain patterns of three-center hydrogen bonds. The results are also valid for linear malto-oligosaccharides.

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1. Introduction

In crystal structures of inclusion complexes of cyclomalto-oligosaccharides (cyclodextrins, CDs), which are usually hydrated, complex patterns of O–H ··· O hydrogen bonds are observed because of the abundance of hydroxyl groups, glycosidic O atoms, and water molecules. The best method for studying these hydrogen bonds is neutron diffraction since neutrons are scattered by nuclei and permit the location of H as reliably as C and O. In X-ray diffraction, scattering occurs at the electron shells of the atoms, and H is consequently less well defined

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* Topography of Cyclodextrin Inclusion Complexes, Part 32. For Part 31, see K. Geßler, Th. Steiner, G. Koellner and W. Saenger, *Carbohydr. Res.*, 249 (1993) 327–344.

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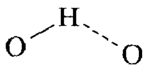
in electron density maps than the heavier atoms. If, as is frequently found for cyclodextrin inclusion compounds, guest and water molecules are disordered, H atoms may virtually become invisible and, consequently, hydrogen bond networks cannot be defined. For this reason, hydrogen bonds are assigned on the basis of short O · · · O separations in most X-ray diffraction studies of cyclodextrin complexes. For this assignment, presently most authors use distance cut-off limits of 3.0 or 3.2 Å for O · · · O.

However, O · · · O contacts can be interpreted as hydrogen bonds with only a certain reliability. In the present study, we quantify this reliability for the special case of intermolecular contacts in cyclodextrin inclusion complexes on the basis of six neutron crystal structures. The results will also be valid for the structurally related linear malto-oligosaccharides.

2. Method and data sample

Much work has been published on hydrogen bond geometries in carbohydrates [1–4]. Since the main cohesive force in hydrogen bonds is electrostatic, this interaction only slowly diminishes with increasing H · · · O distance, and is operative even at distances beyond the van der Waals separation of H and the acceptor atom. Consequently, distance cut-off definitions of hydrogen bonds should be avoided because they interrupt a smoothly decreasing force at a distance that is arbitrary. In practice, however, cut-off criteria often cannot be completely avoided; for the present study, a hydrogen bond is defined as an O–H · · · O interaction with H · · · O distances shorter than 3.0 Å and angles at H larger than 90°. The problems of such cut-off criteria are discussed in greater detail elsewhere [3–5]. To distinguish interactions of the types



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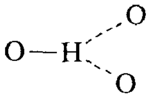

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the terms *two-center* (**1**) and *three-center* hydrogen bonds (**2**) are used [3]. In three-center bonds, the shorter H · · · O contact is called the '*major component*', whereas the longer one is called the '*minor component*'. *Four-center* bonds are defined analogously; for simplicity, they are combined with the three-center bonds throughout the text, and are not treated separately.

Six high-resolution neutron-diffraction studies of cyclodextrin complexes are presently available: α-CD · $6H_2O$ at room temperature (RT) [6], β-CD ~ $11D_2O$ at RT [7], β-CD · $11.6D_2O$ at 120 K [8], β-CD–ethanol · $8D_2O$ at 15 K [9] and at RT [10], and γ-CD ~ $16D_2O$ at 110 K [11] (for a number of related experiments, only preliminary results have been published [12–14]). All six structures exhibit some degree of disorder, and the geometries of the disordered groups are only determined with reduced accuracies. For this reason, the guest molecules in the cavities of β-CD hydrate at RT and of γ-CD hydrate at 110 K were excluded from the analysis. In the other four crystal structures, major sites of disordered atoms were used in the analysis, whereas sites with occupancy factors < 0.5 were excluded. In the original publications, estimated standard deviations given for O $\cdots$ O distances are below 0.01 Å, and for H $\cdots$ O distances around or below 0.01 Å.

From these neutron data, it can be determined how many (and which percentage) of the O $\cdots$ O contacts in any distance interval actually represent hydrogen bonds, providing a statistical description of the relation between O $\cdots$ O contacts and hydrogen bonding. To avoid effects due to intramolecular steric constraints, this study will be restricted to intermolecular hydrogen bonds only.

The data sample contains crystal structures determined at different temperatures. In principle, one could form subsets of room temperature and low temperature data, which must reflect the shortening of hydrogen bonds with reduction in temperature, and yield somewhat different statistical results. In the present context, however, this does not seem to be justified because the temperature effect on hydrogen bond distances (some 0.01 Å [10]) is small compared to the step-width of O $\cdots$ O distances, 0.1 Å, used in this analysis.

3. Results

First, the relations between intermolecular O $\cdots$ O contacts and hydrogen bonding in the six neutron crystal structures will be statistically described. The implications for the assignment of hydrogen bonds to O $\cdots$ O contacts will be discussed later.

Distribution of O $\cdots$ O distances.—Of the 474 intermolecular O $\cdots$ O contacts < 4.0 Å in the data set, 193 are associated with two-center hydrogen bonds or major components of three-center bonds, 56 with minor components of three-center hydrogen bonds, and 225 are not associated with a hydrogen bond. In Fig. 1A, the distribution of O $\cdots$ O distances is shown in a histogram; Fig. 1B shows the percentages of the specified types of O $\cdots$ O contacts in each distance interval with a step-width of 0.1 Å. O $\cdots$ O distances shorter than 2.9 Å exclusively represent two-center bonds and major components of three-center bonds. Starting with the interval 2.9–3.0 Å, an increasing fraction of the O $\cdots$ O contacts is associated only with minor components of three-center bonds; beyond the van der Waals separation of ~ 3.0 Å [15], there are O $\cdots$ O contacts which are not associated with a hydrogen bond at all. The fraction of the latter increases with increasing O $\cdots$ O distance, and for O $\cdots$ O > 3.6 Å, no more hydrogen bonds with H $\cdots$ O < 3.0 Å are observed in the data sample (the numerical values are given in Table 1).

Short O $\cdots$ O contacts without a hydrogen bond.—Three different types of short intermolecular O $\cdots$ O contacts without a hydrogen bond are observed in the data set: (*1*) If donors hydrogen bond to the same acceptor, their O atoms may approach so closely that a triangular arrangement with all O $\cdots$ O separations < 3.2 Å is formed; an example is shown in Fig. 2A. These arrangements always contain very short repulsive O–H $\cdots$ H–O contacts [16]. (*2*) In three-center

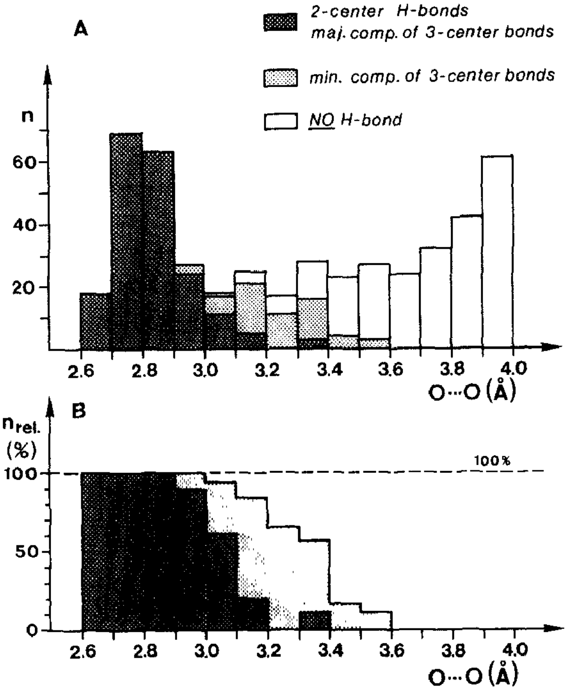


Fig. 1. (A) Histogram of all intermolecular O ··· O separations (6 cyclodextrin neutron crystal structures). Dark shading: O ··· O contacts associated with a two-center hydrogen bond or the major component of a three-center bond. Light shading: O ··· O contacts associated with the minor component of a three-center bond (H ··· O < 3.0 Å). Unshaded region: O ··· O contacts without a hydrogen bond. (B) Percentages of O ··· O contacts in each distance interval associated with two-center (and major components of three-center) bonds, with minor components of three-center bonds, and with no hydrogen bond.

hydrogen bonds, the two acceptors A_1 and A_2 may approach closely, leading to triangular arrangements with all O ··· O separations < 3.2 Å, Fig. 2B. One can argue that, in such arrangements, the two acceptor atoms are in fact indirectly linked by a 'hydrogen bond' $A_1 \cdots H \cdots A_2$, although neither of them contributes the H atom as a donor. (*3*) There are short O ··· O contacts, in which the O atoms are engaged neither in hydrogen bonds with a common donor nor with a common acceptor. An example is the square arrangement of O-6^2, O-2^7, O-3^1, and W-4 in Fig. 2C, which would almost certainly be interpreted as a four-membered ring of cooperative hydrogen bonds if the H atom positions were not known.

Long O ··· O distances associated with hydrogen bonds.—The longest O ··· O distances observed for two-center hydrogen bonds, 3.3 to 3.4 Å (Fig. 1A), originate from O_W–H ··· O-4 interactions within the cyclodextrin cavities and will be discussed in the next section. Even longer O ··· O separations of 3.4 to 3.6 Å are

Table 1
O ··· O contacts that are associated with hydrogen bonds in the neutron diffraction data sample. No distinction is made between major and minor components of three-center hydrogen bonds. Compare Fig. 1

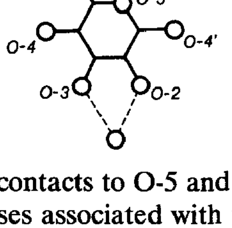
O ··· O (Å)	$n_{O \cdots O}$ [a]	$n_{H\text{-bond}}$ [b]	Percentage of H-bonds [c]
$2.6 \le d < 3.0$	177	177	100 (–)
$3.0 \le d < 3.1$	18	17	94 (5)
$3.1 \le d < 3.2$	25	21	84 (7)
$3.2 \le d < 3.3$	17	11	65 (12)
$3.3 \le d < 3.4$	28	16	57 (9)
$3.4 \le d < 3.5$	23	4	17 (8)
$3.5 \le d < 3.6$	27	3	11 (6)
$3.6 \le d < 3.7$	24	0	0 (–)

[a] Number of intermolecular O ··· O contacts in the given distance range. [b] Number of O ··· O contacts associated with hydrogen bonds (H ··· O < 3.0 Å and angle at H > 90°). [c] Percentage p of the O ··· O contacts that represent hydrogen bonds. $p = n_{H-\text{bond}} / n_{O \cdots O}$. The standard error of the percentage is roughly estimated by $[p(1-p)/n]^{1/2}$ and given in parentheses (reflecting *only* the statistical uncertainty due to the limited number of data).

only observed for minor components of three-center hydrogen bonds; two typical examples are shown in Fig. 3.

Intermolecular hydrogen bonds to the glycosidic O-4 atoms.—The glycosidic O-4 atoms linking the glucose residues are accessible for intermolecular contacts only from inside the cyclodextrin cavities, and flanking H-3 and H-5 atoms hinder close approach of possible hydrogen-bond donors. If an O–H ··· O-4 hydrogen bond is formed, it is always associated with short O–H ··· H–C van der Waals contacts (Fig. 4). The distribution of O ··· O-4 separations shown in Fig. 5 differs from Fig. 1A. There are only very few O ··· O contacts < 3.1 Å, all of which represent hydrogen bonds. Longer contacts ≤ 3.5 Å are more frequently associated with hydrogen bonds as in Fig. 1A (with reservations due to the small number of data).

Simultaneous contacts to O-5 and O-6, and to O-2 and O-3 of the same glucose residue.—In cyclodextrin crystal structures, hydroxyl groups and water molecules frequently form simultaneous intermolecular contacts to O-5 and O-6, or to O-2 and O-3 of the same glucose residue, as in **3**.



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If in contacts to O-5 and O-6, both O ··· O separations are < 3.5 Å, they are in most cases associated with three-center hydrogen bonds of the types **4–6** [10].

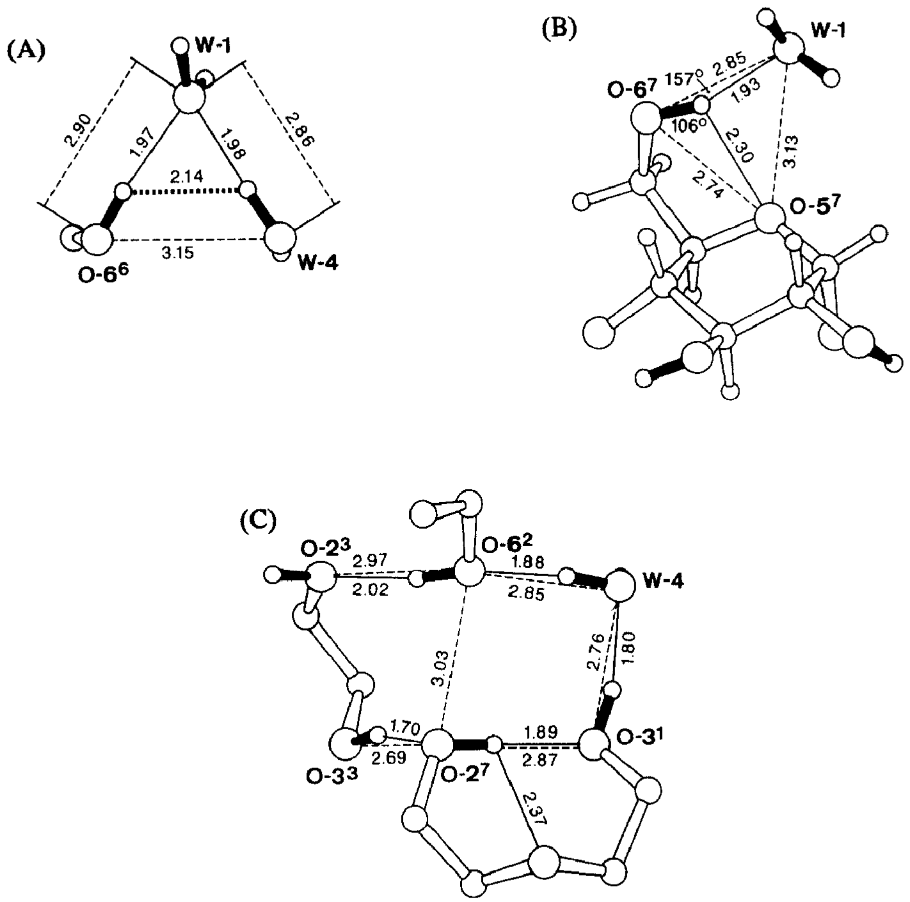
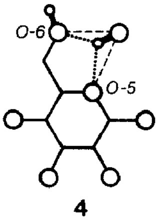


Fig. 2. Examples of very short O $\cdots$ O contacts that are not associated with a hydrogen bond between the O atoms. (A) A hydroxyl group and a water molecule donating hydrogen bonds to the same acceptor (note the short H $\cdots$ H contact). In α-CD·$6H_2O$ [6]. (B) A three-center bond with a short intermolecular contact between the two acceptor atoms. W-1 is oriented such that it donates no hydrogen bond to O-5. In β-CD–ethanol·$8D_2O$ at 15 K [9]. (C) Two hydroxyl groups with no common hydrogen-bond partner, but a very short separation of 3.03 Å. Note the square arrangement O-6^2, O-2^7, O-3^1, and W-4, which would be interpreted as a four-membered ring of cooperative hydrogen bonds if the H atom positions were unknown. In β-CD–ethanol·$8D_2O$ at 15 K [9].



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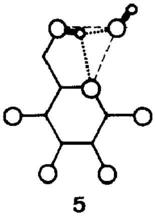

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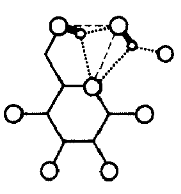

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If the contacting group acts as the donor (4), the major component of this '*chelated*' [3] three-center bond may be directed towards O-6 or to O-5, and if O-6

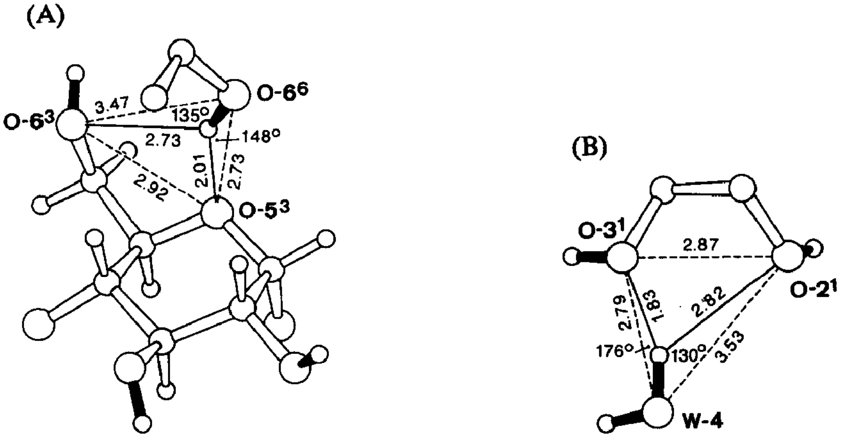


Fig. 3. Examples for long O ··· O contacts that are associated with minor components of three-center hydrogen bonds. Most intermolecular contacts with similar O ··· O separations do *not* represent hydrogen bonds (compare Fig. 1). (A) A hydroxyl group donating a three-center bond to O-5 and O-6 of the same glucose residue. In β-CD–ethanol·$8D_2O$ at 15 K [9]. (B) A water molecule donating a three-center bond to O-2 and O-3 of the same glucose residue. In β-CD·$11.6D_2O$ at 120 K [8].

acts as the donor (**5** and **6**), the contacting group may or may not donate to O-5 an additional minor component of a three-center bond; examples are shown in Figs. 2B and 3A.

All simultaneous contacts to O-5 and O-6 in the data set with both O ··· O separations < 3.7 Å are shown in Fig. 6A; 28 of the 30 contacts with both O ··· O distances < 3.5 Å exhibit three-center bonds as shown above, whereas the contacts with the longer O ··· O separation exceeding 3.5 Å do not. In particular, common

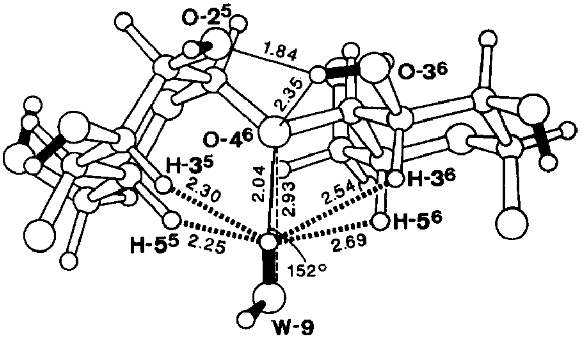


Fig. 4. The shortest hydrogen bond accepted by an O-4 atom in the data sample. This atom type can accept intermolecular hydrogen bonds only from inside the cyclodextrin cavity. Intermolecular O–H ··· O-4 interactions are always associated with short O–H ··· H–C contacts. In β-CD·$11.6D_2O$ at 120 K [8].

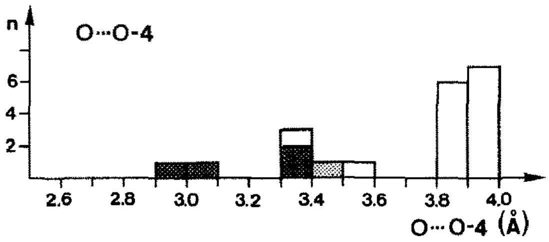


Fig. 5. Histogram of intermolecular O · · · O-4 distances in the data sample. Symbols as in Fig. 1.

contacts to O-5 and O-6 with both O · · · O separations < 3.3 Å are in *all* cases associated with three-center bonding.

Simultaneous contacts to O-2 and O-3 are less frequent than those to O-5/O-6, and the differences between shorter and longer O · · · O separations are larger on the average (Fig. 6B and 7–9). Some of them are in fact associated with three-center bonds having configurations analogous to those at O-5/O-6

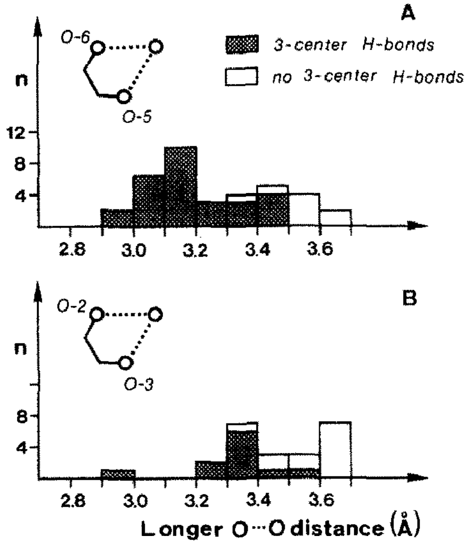


Fig. 6. Histograms of (A) simultaneous contacts to O-5 and O-6 of the same glucose residue, and (B) simultaneous contacts to O-2 and O-3 of the same glucose residue. On the horizontal axis, the *longer* O · · · O distance is drawn. Shading: three-center hydrogen bonds. No shading: contacts with two-center or with no hydrogen bonds. Note that simultaneous contacts to O-5 and O-6 are more frequent than those to O-2 and O-3, and that they have shorter O · · · O separations on the average.

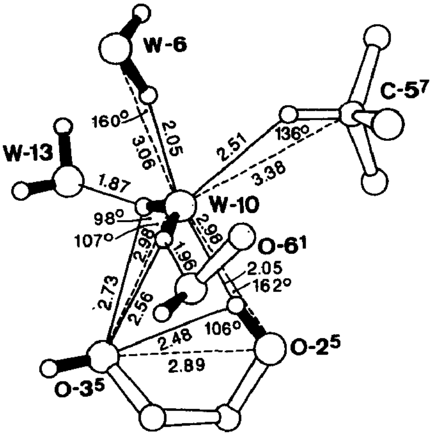
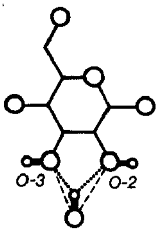


Fig. 7. One of the most remarkable hydrogen-bond configurations in the data set: W-10 in β-CD · $11.6D_2O$ at 120 K [8]. O-W-10 has the same distance to the hydroxyl O atoms O-2^5 and O-3^5 (2.98 Å), but it accepts the major component of a three-center bond from the former, whereas it donates only minor components of three-center bonds to the latter. Note that the two-center bond W-6-H · · · W-10 has a longer O · · · O separation than the minor hydrogen-bond components donated from W-10 to O-3^5. Also note the intramolecular minor component of the hydrogen bond donated by O-2^5. W-10 also accepts a C–H · · · O_W interaction from the wall of the β-CD cavity [5]. Donor–acceptor distances that are not indicated: W-10 · · · W-13 = 2.75 Å ($\theta = 165°$), W-10 · · · O-6^1 = 2.81 Å ($\theta = 147°$).



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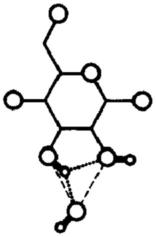

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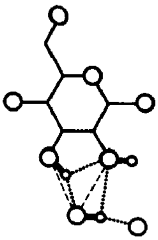

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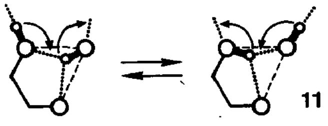
(in all cases, the roles of O-2 and O-3 may be reversed), but also two-center bonds are not uncommon. For the longer O · · · O distance exceeding 3.4 Å, two-center bonds are more frequent than three-center bonds, although the latter are observed to O · · · O separations longer than 3.5 Å (examples are shown in Figs. 3B and 7).

The *orientation* of the three-center bonds cannot be recognized from the O · · · O separations. This becomes immediately clear from the existence of 'flip-flop'-type [17] disorder both at O-2/O-3 and O-5/O-6 [7,10], shown in **10** and **11**, in which the H atom positions and hydrogen bond orientations flip dynamically, whereas the O · · · O distances do not change.



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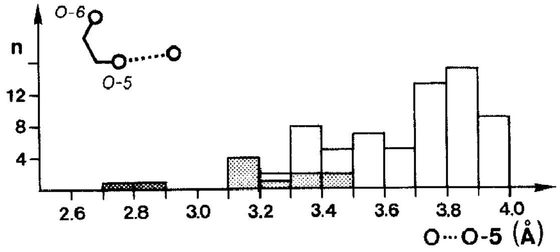

Fig. 8. Histogram of intermolecular O · · · O-5 distances in the data sample, which are *not* associated with a contact to O-6 shorter than 3.5 Å. Symbols as in Fig. 1.

Intermolecular contact to O-5, but not to O-6.—A short contact to O-5 is not necessarily associated with one to O-6: Fig. 8 shows the distribution of O · · · O-5 contacts for which the O · · · O-6 separation is > 3.5 Å. Pure two-center bonds directed towards O-5 are rare, but they occasionally do occur. In some instances, O-5 accepts minor hydrogen-bond components with the major component accepted by another atom than O-6.

Reliability of assigning O–H · · · O hydrogen bonds to intermolecular O · · · O contacts.—If, in cyclodextrin X-ray crystal structures, hydrogen bonds are assigned to intermolecular O · · · O distances without using any further information, the data shown in Fig. 1B can serve as a rough estimate for the reliability of such an assignment; the relevant numeric values are given in Table 1. For a contact between 3.1 and 3.2 Å, for example, there is an ~ 16% probability that it is *not* associated with a hydrogen bond, but with an arrangement of the types shown in Fig. 2. Also, in this distance interval, the majority (but not all) of the hydrogen bonds should be minor components of three-center bonds (Fig. 1B). For O · · · O contacts around 3.5 Å, an assignment with a hydrogen bond is already very doubtful (although it may be true), as the risk of error is ~ 90% (Fig. 1b).

Risk of O · · · O cut-off limits.—Fig. 1B shows the problem of defining a reasonable O · · · O cut-off limit for hydrogen bonds. The transition between (almost) certainty for hydrogen bonding (O · · · O < 3.0 Å) and (almost) certainty for no hydrogen bonding (O · · · O > 3.6 Å) smoothly takes place over a distance region of ~ 0.6 Å. A cut-off limit at 3.0 Å inevitably neglects even two-center hydrogen bonds, whereas the other extreme at 3.6 Å includes a large number of contacts that do not represent hydrogen bonds. Any cut-off value between 3.0 and 3.6 Å will neglect some hydrogen bonds and at the same time include pure van der Waals contacts. The frequently used cut-off value of 3.2 Å is to some degree justified: it omits almost no two-center hydrogen bonds and major components of three-center bonds, whereas only few van der Waals contacts are unintentionally included. In the next interval, 3.2 to 3.3 Å, already ~ 1/3 of the O · · · O contacts are not associated with a hydrogen bond.

Recognizing three-center bonds at O-5 and O-6, and at O-2 and O-3.—Assigning minor components of three-center hydrogen bonds to relatively long O · · · O contacts is hazardous: in the distance interval 3.2 to 3.3 Å, the risk of error is already ~30%, and it increases rapidly for larger O · · · O separations, Fig. 1B. However, triangular patterns formed by O atoms with O-5 and O-6 of the same glucose are almost invariably associated with three-center bonds (of unknown orientation), Fig. 6A. Even if the longer O · · · O separation is between 3.3 and 3.5 Å, this assignment can be made with a bearable risk of error (neutron data: 9 three-center bonds for 11 contacts in this distance range). The data shown in Fig. 6A suggest the use of a cut-off limit of 3.5 Å to identify three-center bonding for this pattern.

To recognize three-center bonding in simultaneous contacts to O-2 and O-3 of the same glucose residue only from O · · · O separations, cut-off limits can only be used with great reservation; the most reasonable value might be 3.4 Å, Fig. 6B.

A strategy to assign hydrogen bonds to intermolecular O · · · O contacts.—On the basis of these results, it is possible to elaborate procedures for assignment of hydrogen bonds to intermolecular O · · · O contacts in cyclodextrin X-ray crystal structures that are superior to the simple use of a 3.2-Å (or any other) cut-off limit. A relatively conservative procedure consisting of several steps is: (*1*) All intermolecular O · · · O contacts shorter than ~3.7 Å are determined. (*2*) Simultaneous contacts to O-5 and O-6 of the same glucose residue are sorted out, and assigned as three-center bonds if the longer O · · · O separation is <3.5 Å. The probability of error is almost zero if the longer contact is <3.3 Å, and ca. 20% if the longer contact is between 3.3 and 3.5 Å (Fig. 6A). The neutron data set contains no three-center bond *outside* this cut-off. (*3*) Simultaneous contacts to O-2 and O-3 of the same glucose residue are sorted out, and assigned as three-center bonds if the longer O · · · O separation is <3.4 Å. The probability of error is presumably small if the longer contact is <3.3 Å, and ca. 20% if the longer contact is between 3.3 and 3.4 Å (Fig. 6B). If the longer distance is between 3.4 and 3.6 Å, the occurrence of a three-center bond is possible, but cannot be predicted with reliability (Fig. 6B). (*4*) O · · · O-4 contacts of guest molecules within the cyclodextrin cavity with glycosidic O-4 atoms are assigned as hydrogen bonds if the O · · · O separation is <3.4 Å, Fig. 5. The probability of error can hardly be estimated from the low quantity of neutron data. (*5*) For the remaining bulk of intermolecular O · · · O contacts, separations >3.2 Å can be associated with hydrogen bonding only with unacceptable probabilities of error, Fig. 1B. Here, a distance cut-off at 3.2 Å represents an appropriate compromise value: it excludes (almost) only minor components of three-center bonds (the very long two-center bonds in Fig. 1 correspond to O–H · · · O-4 interactions, which have already been recognized in step *4*), whereas it includes only few van der Waals contacts of the types shown in Fig. 2. For the distance interval 3.0 to 3.2 Å, the probability of error is roughly estimated to be 10%.

Linear malto-oligosaccharides.—Malto-oligosaccharides have the same hydrogen-bonding functional groups as the cyclodextrins. No neutron diffraction studies are available for these molecules, but it is reasonable to expect that they have intermolecular hydrogen-bond properties similar to cyclodextrins, and that the results shown above are qualitatively valid for hydrated oligosaccharides in general.

Actually, in an X-ray study of a hydrated *p*-nitrophenyl *α*-maltohexaoside, hydrogen bond patterns were observed that very closely resemble those found in cyclodextrin hydrates [18]. In particular, numerous simultaneous ('chelated') intermolecular contacts to O-5 and O-6 or to O-2 and O-3 of the same glucose residue are observed, which should be interpreted as three-center interactions as discussed above.

Note added in proof. Occasionally, roughly tetrahedral coordination angles around O atoms are regarded as a requirement for O–H · · · O hydrogen bonds. In the present study, such criteria were avoided due to the extreme softness of these angles: in the data set, two-center bonds with C–O · · · O angles up to ~ 150° are observed, whereas, for example, the short van der Waals contact O-6^6 · · · W-4 in Fig. 2A is associated with an almost ideal C–O · · · O angle of 106.5°. A brief *addendum* to this study is in preparation, where these circumstances will be discussed.

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References

[1] G.A. Jeffrey and S. Takagi, *Acc. Chem. Res.*, 11 (1978) 264–270.

[2] C. Ceccarelli, G.A. Jeffrey, and R. Taylor, *J. Mol. Struct.*, 70 (1981) 255–271.

[3] G.A. Jeffrey and W. Saenger, *Hydrogen Bonding in Biological Structures*, Springer Verlag, Berlin, 1991.

[4] Th. Steiner and W. Saenger, *Acta Crystallogr., Sect. B*, 48 (1992) 819–827.

[5] Th. Steiner and W. Saenger, *J. Am. Chem. Soc.*, 115 (1993) 4540–4547.

[6] B. Klar, B.E. Hingerty, and W. Saenger, *Acta Crystallogr., Sect. B*, 36 (1980) 1154–1165.

[7] Ch. Betzel, W. Saenger, B.E. Hingery, and G.M. Brown, *J. Am. Chem. Soc.*, 106 (1984) 7545–7557.

[8] V. Zabel, W. Saenger, and S.A. Mason, *J. Am. Chem. Soc.*, 108 (1986) 3664–3673.

[9] Th. Steiner, S.A. Mason, and W. Saenger, *J. Am. Chem. Soc.*, 112 (1990) 6184–6190.

[10] Th. Steiner, S.A. Mason, and W. Saenger, *J. Am. Chem. Soc.*, 113 (1991) 5767–5687.

[11] J. Ding, Th. Steiner, V. Zabel, B.E. Hingerty, S.A. Mason, and W. Saenger, *J. Am. Chem. Soc.*, 113 (1991) 8081–8089.

[12] M. Czugler, G. Geiger, and J.J. Stezowski, *Z. Kristallogr.*, 162 (1983) 54–55.

[13] G. Le Bas, S.A. Mason, N. Rysanek, and G. Tsoucaris, in D. Huber and J. Szejtli (Eds.), *Proc. 4th Int. Symp. Cyclodextrins*, Kluwer, Dordrecht, 1988, pp 243–246.

[14] Th. Steiner, V. Zabel, B.E. Hingerty, S.A. Mason, and W. Saenger, *Z. Kristallogr., Suppl. 5*, (1992) 239.

[15] A. Bondi, *J. Phys. Chem.*, 68 (1964) 441–451.

[16] Th. Steiner and W. Saenger, *Acta Crystallogr., Sect. B*, 47 (1991) 1022–1023; addendum: *ibid.*, (1992) 551–552.

[17] W. Saenger, Ch. Betzel, B.E. Hingerty, and G.M. Brown, *Nature* (*London*), 296 (1982) 581–583.

[18] W. Hinrichs and W. Saenger, *J. Am. Chem. Soc.*, 112 (1990) 2789–2796.