Evidence for O–H···C and N–H···C Hydrogen Bonding in Crystalline Alkynes, Alkenes, and Aromatics

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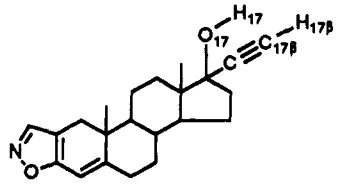
Abstract: Attempts have been made to understand the nature and significance of hydrogen bonds of the type X–H···C (X = O, N). These unusual interactions have been discussed recently. Crystallographic studies on 17α-ethynylandrosta-2,4-dieno[2,3-*d*]dihydroxazol-17β-ol (donazole) provide direct evidence of such an O–H···C interaction. Ab initio computations, IR spectroscopy, and database studies show that these hydrogen bonds, while uncommon, are energetically and structurally significant.

Unusual hydrogen bonds of the type X–H···C (X = O, N) have been discussed recently.[1-7] While C–H···O hydrogen bonds are widespread,[8-10] the complementary O–H···C interaction is rare because C is not as electronegative as O and also because C atoms are not often situated in sterically-unhindered positions (unlike carbonyl and ethereal O atoms which permit easy access by C–H groups to form C–H···O bonds). This report shows that, in spite of these limitations, a sufficiently electron-rich C atom (alkyne, alkene, aromatic) has a propensity to form a hydrogen-bond-like interaction with X–H groups (X = O, N) thus contributing to crystal stability. This interaction has been referred to as a π-hydrogen bond.[3]



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A striking example of such an O–H···C hydrogen bond is found in the crystal structure of 17α-ethynylandrosta-2,4-dieno[2,3-*d*]dihydroxazol-17β-ol (donazole, **1**) (Figure 1: $P2_12_12_1$, $Z = 4$; $a = 6.595$, $b = 10.519$, $c = 26.166$ Å; $R = 0.036$, $R_w = 0.034$; 1500 observed reflections; C, N, O anisotropic; all H-atoms located from difference maps and refined isotropically). The 17β-hydroxyl H atom is directed toward the C≡C bond of a neighboring 2_1-related molecule (O(17)···C(17β) = 3.25 Å; H(17)···C(17β) = 2.45 Å; O(17)–H(17)···C(17β) = 144°). This intermolecular interaction therefore has all the geometrical attributes of a hydrogen bond.[8,11] Additionally, the alkyne C–H forms a conventional C–H···O hydrogen bond to the 17-hydroxyl group of another 2_1-screw related molecule (C(17β)···O(17) = 3.19 Å; H(17β)···O(17) = 2.45 Å; C(17β)–H(17β)···O(17) = 145°). These O–H···C and C–H···O hydrogen bonds assist each other cooperatively and constitute the dominant motif in the crystal packing. Evidence for the O–H···C interaction in **1** is also available from IR data. While the O–H and C–H (alkyne) stretches appear at 3565 and 3290 cm^{-1} (CH_2Cl_2), these values are red shifted by 75 and 50 cm^{-1} in the solid state (KBr).

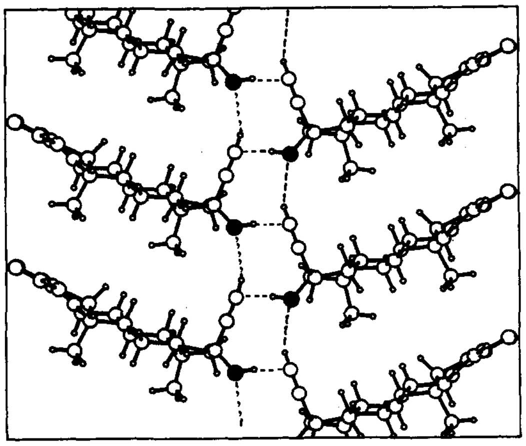

Figure 1. Crystal structure of donazole (**1**) down [010] to show the O–H···C and C–H···O bonds between the 17β-hydroxyl and ethynyl groups. Notice the cooperative network of hydrogen bonds. The *a*-axis is vertical in the plane of the paper. O atoms are shaded.

Ab initio calculations (GAUSSIAN80, 3-21G) on the model system, methylacetylene–methanol, show that the O–H···C interaction is attractive in nature. The computed total energies for CH_3—C≡C—H and CH_3—OH respectively are −115.224 962 1 and −114.397 187 1 au. For an optimized H···C distance of 2.66 Å, the energy of the complex was found to be −229.625 004 3 au. The attractive force between the two species is therefore equivalent to −0.002 855 1 au or −1.79 kcal/mol. The calculation also shows that the H···C≡C angle lies ideally between

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(1) Ueji, S.; Nakatsu, K.; Yoshioka, H.; Kinoshita, K. *Tetrahedron Lett.* **1982**, *23*, 1173–1176.

(2) Jorgensen, W. L.; Severance, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 4768–4774.

(3) Atwood, J. L.; Hamada, F.; Robinson, K. D.; Orr, G. W.; Vincent, R. L. *Nature* **1991**, *349*, 683–684.

(4) Al-Juaid, S. S.; Al-Nasr, A. K. A.; Eaborn, C.; Hitchcock, P. B. *J. Chem. Soc., Chem. Commun.* **1991**, 1482–1483.

(5) Mootz, D.; Deeg, A. *J. Am. Chem. Soc.* **1992**, *114*, 5887–5888.

(6) Suzuki, S.; Green, P. G.; Bumgarner, R. E.; Dasgupta, S.; Goddard, W. A.; Blake, G. A. *Science* **1992**, *257*, 942–945.

(7) Hanton, L. R.; Hunter, C. A.; Purvis, D. H. *J. Chem. Soc., Chem. Commun.* **1992**, 1134–1136.

(8) Taylor, R.; Kennard, O. *J. Am. Chem. Soc.* **1982**, *104*, 5063–5070.

(9) Desiraju, G. R. *Acc. Chem. Res.* **1991**, *24*, 290–296.

(10) Desiraju, G. R. *Crystal Engineering. The Design of Organic Solids*; Elsevier: Amsterdam, 1989; pp 142–165.

(11) Jeffrey, G. A.; Saenger, W. *Hydrogen Bonding in Biological Structures*; Springer-Verlag: Berlin, 1991.

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Table I. Results of Database Analysis of Intermolecular X-H···C Hydrogen Bonds

X-H···C	no. of entries with X-H and π-groups	no. of X-H···C bonds[a]	mean X···C (Å)	mean H···C (Å)	mean X-H···C (deg)
O—H···C≡C	154	5[c]	3.33	2.69	127
N—H···C≡C	68	5[d]	3.30	2.61	129
O—H···C=C	4393	20[e]	3.26	2.77	113
N—H···C=C	3217	5[f]	3.31	2.82	111
O—H···phenyl[b]	2823	5[g]	3.29	2.43	150
N—H···phenyl[b]	3057	12[h]	3.31	2.47	148

[a] Intramolecular bonds are excluded. [b] For the X–H···phenyl bonds, the shorter of the distances between X/H to the centroid of the six-membered ring and X/H to the nearest edge C atom was chosen to compute the mean. [c] Refcodes BETXAZ, CERYED, DAXWOO, DOJHEP, MNPREY. [d] Refcodes GERYEH (2), GICPIR, TEYNBH (2). [e] Refcodes BACXAE10 (2), BIWDEQ, BIWSOP (2), CAFVEK, CIMTEX, CYTOCH10, DULHUN, FADWOW, FENZED, FUPXUJ, GEZPUW, GIMZIL, LUTOSK, MOXCTS10, OHDLST, PROSTE, RTRSIN, RUGULA. [f] Refcodes ANTMYCO1, BPURMN, DEFMUW, FIWRAE, URPOAD10. [g] Refcodes APALTY, BHPHOL, DOZMIO, GEYZAL, MTBCHO. [h] Refcodes ABHYTZ, AMPHOM02, BAGFIY, BARKIO10, BIRKUI, FAJVIV, GEYXUD, KARHUG, MAMPOL, MXTRYP, TRYPTB, VUXYUI.

60 and 120°, presumably due to steric hindrance in other alternative positions. In steroid **1**, this angle is 93°.

The generality of this novel X–H···C interaction was probed with the 1990 version of the Cambridge Structural Database[12] (82 129 entries). Error-free, nondisordered structures with $R < 0.100$ and refined H-atom positions were accepted. The intermolecular contacts were stringently evaluated with the program GSTAT90: the X···C distance was specified to lie between 2.9 and 3.4 Å, even though C···O distances up to 3.75 Å have been considered viable for C–H···O hydrogen bonds;[9] the X–H···C angle was constrained to lie between 100 and 180°; the hits were always scrutinized manually; and in several cases we referred to the original literature, and obviously inappropriate compounds were eliminated. With these stipulations, five unambiguous O—H···C≡C contacts were found. We obtained similar results for N—H···C≡C (5 bonds), O—H···C=C (20 bonds), N—H···C=C (5 bonds), O-H···phenyl (5 bonds), and N—H···phenyl (12 bonds). The results are summarized in Table I and, when considered along with Figure 1 and the details of the individual structures, provide compelling evidence that X–H···C hydrogen bonds, though rare and weak, are structurally significant when they do occur.

Table I shows that the more acidic hydrogens and the more basic π-systems are more likely to form better X–H···C hydrogen bonds. Further, contacts involving weaker acids (N–H) and weaker π-bases (alkene, phenyl) are more likely to be intramolecular and/or accompanied by bifurcation to stronger hydrogen bond acceptors (O, N). The O—H···C≡C contacts are distinctive and seem able to control crystal packing in a decisive manner as in steroid **1**.

The database analysis also reveals that, for X–H···phenyl contacts, the hydrogen atom is directed into the middle of the aromatic ring system (centroid type).[3] There is also the occurrence of a second type of interaction, where the X–H group makes a close approach to only two adjacent carbons of a particular phenyl group (edge type). This is observed in crystalline 2,6-diphenylphenol[13] and 4-nitro-2,6-diphenylphenol[1] though the contacts are intramolecular and as such not readily accessible via GSTAT90. Interestingly this edge-type X–H···phenyl contact has not been studied theoretically. The distinction, if any, between the centroid type and the edge type of X–H···phenyl contact is still elusive and warrants further study. Very little is known about N–H···C interactions, barring an ab initio calculation on the ammonia–benzene system[2] and a recent structural report,[7] and we believe that the present work may be the first to systematically study these interactions. To continue this line of reasoning, can a sufficiently acidic C–H group form a hydrogen-bond-like C–H···C interaction? Or is such a geometry merely an extreme manifestation of the C–H(δ+)···C(δ–) herringbone interaction?[14] The crystal structures of propiolic and butynoic acids[15] are of some relevance in this context.

Table I includes biologically significant substances such as nucleic acid model compounds, steroids, and amino acids. Additionally, it is expected that this X–H···C hydrogen bond occurs not only in crystals but also in other environments such as aqueous media, either alone or in conjunction with other interactions.

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Supplementary Material Available: Tables of crystal data, positional parameters, general displacement parameter expressions, and distances and angles and a list of bibliographic references for the compounds in this study (15 pages); tables of structure factors (4 pages). Ordering information is given on any current masthead page.

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(12) Allen, F. H.; Taylor, R.; Kennard, O. *Acc. Chem. Res.* **1983**, *16*, 146–152. Typical questions (for O—H···C≡C contacts) were framed as follows. Search question: save 2; prin 1; t1 *conn; at1 c 1 0,1; at2 c 1 0,1; bo 1 2 3; end; quest t1. This generated 1074 hits out of 82 128 entries. Geometry analysis question: brief; nod; nerr; hnorm; calc inter from o 1.70 to c 1.70 ext; frag; at1 o 2; at2 h 1; at3 c 2; at4 c 1; bo 1 2 0.9 1.1; bo 1 3 2.9 3.4; bo 3 4 1.1 1.2; test ang 1 2 3 100.0 180.0; end; def *rfact; def dis 1 3; def dis1 2 3; def dis2 3 4; def ang 1 2 3; def ang1 2 3 4.

(13) Nakatsu, K.; Yoshioka, H.; Kunimoto, K.; Kinugasa, T.; Ueji, S. *Acta Crystallogr.* **1978**, *B34*, 2357.

(14) Desiraju, G. R.; Gavezzotti, A. *J. Chem. Soc., Chem. Commun.* **1989**, 621–623. Desiraju, G. R.; Gavezzotti, A. *Acta Crystallogr., Sect. B* **1989**, *45*, 473–482.

(15) Leiserowitz, L. *Acta Crystallogr., Sect. B* **1976**, *32*, 775–802.