

06-Crystallography of Organic Compounds

06.03 – Molecular Recognition, Chirality

PS-06.03.01 DEHYDRATION OF β -CYCLODEXTRIN-HYDRATE AT DIFFERENT AMBIENT HUMIDITIES.

G. Koellner*, Th. Steiner & W. Saenger.

Institut für Kristallographie, Freie Universität Berlin,
Takustr. 6, W-1000 Berlin 33, Germany

Crystalline β -cyclodextrin hydrate is an important model system to explore structural and dynamic properties of inclusion complexes and of hydrogen bond networks. Even though it was early known that the substance suffers some dehydration at ambient conditions, this was never quantitatively described. Only recently, an X-ray crystal structure analysis showed that the dehydration does not affect the crystalline order, and that it is completely reversible (Steiner, Th., Koellner, G., Ali, S., Zakim, D. & Saenger, W. *Biochem. Biophys. Res. Commun.*, 1992, **188**, 1060-1066).

To quantify these observations, crystal structural analyses were performed on β -CD hydrate at five atmospheric humidities between 15% and 100%. To obtain defined and constant humidities, crystals were sealed in capillaries together with various saturated aqueous salt solutions. The unit cell volume *continuously* decreases with decreasing humidity, with no sign of a phase transition. Preliminary results of the structure analyses indicate that the water content continuously reduces from $\sim \beta$ -CD \cdot 12 H₂O to $\sim \beta$ -CD \cdot 10 H₂O in the observed humidity range. The location of the water sites does not change upon the dehydration, but the occupancies gradually lower. This mainly affects the water molecules that are enclosed in the β -CD cavity.

PS-06.03.02 CRYSTAL AND MOLECULAR STRUCTURES OF TWO DIASTEREOISOMERIC 2-BENZENESULFONYLAMINO-N, O³-ISOPROPYLIDENE-1(2-FURYL)BUTANE-1,3-DIOLES.

By Z. Gaidecki* and A. Fruziński, Institute of General and Ecological Chemistry, Technical University of Łódź, ul. Żwirki 36, 90-924 Łódź, Poland

The structures and configurations of two diastereoisomers of the title compound were determined. The compounds are synthesized by O. Achmatowicz and B. Szechner at the Pharmaceutical Research Institute in Warszawa and crystallize in the orthorhombic space group P2₁2₁2₁ with Z = 4. The lattice constants are:

compound	a[Å]	b[Å]	c[Å]	used
I	7.864(2)	11.394(2)	19.550(4)	CuK α
II	7.721(2)	11.587(2)	19.636(4)	MoK α

X-ray data were collected on a KM-4 diffractometer for compound I and on a P3 SIEMENS diffractometer for compound II. The structures were solved by direct methods and refined by full-matrix least-squares using SHELXTL-PC. The final R factors were:

compound	R	R _w	GOOF	Obs. reflections with F > 4 σ (F)
I	0.0354	0.0423	1.56	1686
II	0.0429	0.0458	1.61	1623

The configuration of (I) is (R)C1, (S)C2, (R)C3 and for compound (II) (S)C1, (S)C2, (R)C3

There are the following intramolecular hydrogen bonds (including weak interactions) in crystals of I and II:

(I) O1 - H ... O3	=	2.307(3)Å,	143.6(3)°
(I) O1 - H ... N	=	2.672(3)Å,	99.1(3)°
(II) O1 - H ... O(S)	=	1.947(5)Å,	171.6(4)°
(II) O1 - H ... N	=	2.495(5)Å,	107.5(4)°
(II) O1 - H ... S	=	2.723(4)Å,	143.0(4)°

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Cyclodextrin Hydrates Continue to Give Insight into O-H...O and C-H...O Hydrogen Bonding.

Th. Steiner and W. Saenger.

Institut für Kristallographie, Freie Universität Berlin, W-1000 Berlin 33, Germany.

In our laboratory, cyclodextrin complexes are used as a biologically relevant model system for general studies of hydrogen bonding. In particular, a series of neutron diffraction studies was performed over a period of over 10 years (1 and references therein). As an ensemble, these neutron studies supply accurate structure data for analysis of various hydrogen bond properties, which were not considered in the original publications. Some of the recent results, which also show the unique power of high resolution neutron diffraction, are briefly summarized (further related studies are in progress):

Due to the high density of O-H, C-O-C and H₂O donor and acceptor groups, the cyclodextrins hydrates exhibit an exceptionally high number of three-center hydrogen bonds and also of short O-H...H-O contacts. The numerous three-center bonds give the possibility to observe a lengthening of the covalent O-H bond due to long-distance H...O interactions? (H...O > 2.2 Å. This is not possible with 'normal' two-center bonds, which are rarely longer than 2.1 Å). From the O-H...H-O contacts, the shortest possible H...H approach (van der Waals distance) in cooperative hydrogen bonds could be determined³.

Only recently, it became clear that the cyclodextrins (and also the carbohydrates in general) abound with C-H...O hydrogen bonds⁴. In cyclodextrins, no less than 70% of all C-H groups form such interactions with H...O < 2.7 Å; the shortest H...O separations are slightly below 2.3 Å. Numerous types of intra- and intermolecular C-H...O hydrogen bonds could be specified; of particular interest are host-guest C-H...O interactions.

(1) Ding, J., Steiner, Th., Zabel, V., Hingerty, B. E., Mason, S. A., Saenger, W. *J. Am. Chem. Soc.* **113** (1991) 8081-8089.(2) Steiner, Th., Saenger, W. *J. Am. Chem. Soc.* **114** (1992) 7123-7126.(3) Steiner, Th., Saenger, W. *Acta Cryst.* **B47** (1991) 1022-1023; **B48** (1992) 551-552.(4) Steiner, Th., Saenger, W. *J. Am. Chem. Soc.* **114** (1992) 10146-10154.

PS-06.03.04 RESONANCE ASSISTED HYDROGEN BONDS BETWEEN OXIME AND CARBOXYL GROUP. THE COMPARISON OF TETRAMERIC STRUCTURES OF 4-METHYL-2-OXOPENTANOIC ACID OXIME AND LEVULINIC ACID OXIME. By Jan K. Maurin*, Institute of Atomic Energy, Świerk, Małgorzata Winnicka-Maurin, Institute of General Chemistry, Warsaw Agricultural University and Andrzej Leś, Department of Chemistry, Warsaw University, Poland.

Several structures of compounds containing both carboxyl and oxime groups have been studied (Padmanabhan, Paul, Curtin, 1989; Maurin, Paul, Curtin, 1992a,b, 1993). All of them consist of infinite polar chains of molecules bonded together by pairs of strong intermolecular hydrogen bonds O-H...O and N...H-O between carboxyl and oxime groups. This head to tail arrangement of molecules suggested the strong preference of oxime-carboxyl interaction comparing to the usual centrosymmetric oxime-oxime or carboxyl-carboxyl hydrogen bonds, what was also proved by the studies on the reaction between benzoic acid and acetophenone oxime in solid state and solutions

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(Maurin, Winnicka-Maurin, Paul, Curtin, 1992).

The two title compounds (Figure 1 and 2, respectively), unlike any other mentioned before, form cyclic tetrameric units in crystalline state. The molecules are bonded together by pairs of hydrogen bonds between oxime and carboxyl groups. Seemingly similar

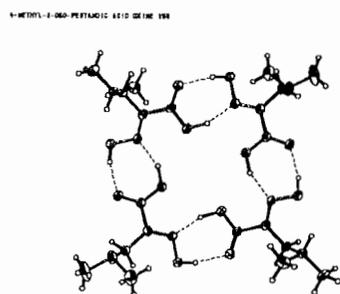


Figure 1

LOWA-1111 ACID OXIME

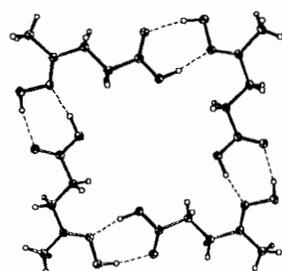


Figure 2

structures differ significantly both in molecular geometries and hydrogen bond dimensions. The dramatic changes in C=N and N-O bond lengths as well as in O...O and O...N hydrogen bond lengths in 4-methyl-2-oxopentanoic acid oxime comparing to levulinic acid oxime and other compounds could be interpreted as the result of resonance interaction between oxime and carboxyl group in the first compound. This reasoning is strongly supported by quantum mechanic calculations done for both title compounds.

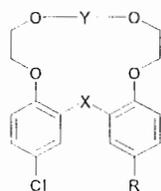
References.

- Maurin, J.K., Paul, I.C. & Curtin, D.Y. (1992a). *Acta Cryst.*, **C48**, 0000-0000.
 Maurin, J.K., Paul, I.C. & Curtin, D.Y. (1992b). *Acta Cryst.*, **C48**, 0000-0000.
 Maurin, J.K., Paul, I.C. & Curtin, D.Y. (1993). *Acta Cryst.*, **C49**, (submitted).
 Maurin, J.K., Winnicka-Maurin, M., Paul, I.C. & Curtin, D.Y. (1992). *Acta Cryst.*, **B48**, 0000-0000.
 Padmanabhan, K., Paul, I.C. & Curtin, D.Y. (1989). *Acta Cryst.*, **B45**, 411-416.

PS-06.03.05 X-RAY STUDY OF DIPHENYLAMINE

CONTAINING CROWNS. By Zs. Böcskei¹, V. Németh², B. Ágai², K. Simon¹, ¹Chinoin Pharmaceutical and Chemical Works Ltd, Budapest, POB 110, H-1325, Hungary, ²Department of Organic Chemical Technology, Technical University Budapest, H-1521, Hungary.

Three crowns, **1** (R=H, X=NH, Y=CH₂-CH₂), **2** (R=H, X=NH, Y=CH₂-CH₂-O-CH₂-CH₂), **3** (R=Cl, X=S, Y=CH₂-CH₂-O-CH₂-CH₂) have been analyzed by X-ray crystallography. A water molecule is situated in the middle of crown **2** H-bonded to the N-H group and two oxygen atoms. The conformation of the three macrocycles will be compared.



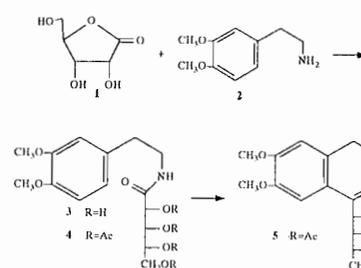
Compound	1	2	3
Formula	C ₁₈ H ₂₀ ClNO ₄	C ₂₀ H ₂₄ ClNO ₅ ·H ₂ O	C ₂₀ H ₂₂ Cl ₂ O ₅
a, Å	11.147	12.463	12.741
b, Å	12.356	12.619	13.516
c, Å	13.743	13.422	12.992
β, °	107.81	102.86	98.10
V, Å ³	1802	2058	2215
Z	4	4	4
S.G.	P2 ₁ /c	P2 ₁ /c	P2 ₁
N _{refl}	2753	1668	1736
R	0.08	0.10	in progress

PS-06.03.06 ENANTIOSELECTIVE SYNTHESIS OF ISOQUINOLINE ALKALOIDS FROM SIMPLE SUGAR. by Z. Czarnocki^{*}, *Department of Chemistry, Warsaw University, Pasteura 1, 02-093 Warsaw, Poland*, J.K. Maurin and K. Wieteska, *Institute of Atomic Energy, Solid State Physics Department, 05-400 Otwock-Świerk, Poland*.

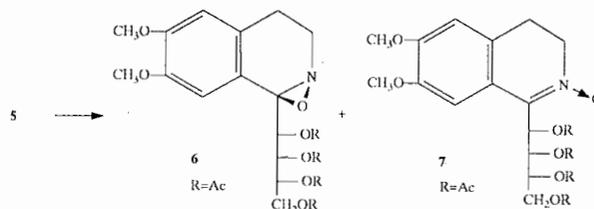
In the course of our study on enantioselective synthesis of isoquinoline alkaloids from various naturally occurring chiral substrates, we launched a project of using a simple sugar - D-ribose as a chiral building block. The synthetic sequence started with a condensation of **1** with 3,4-(dimethoxyphenyl)ethylamine **2** to give an amide **3**, which after acetylation to **4** and Bischler-Napieralski cyclization gave a very unstable imine **5** (Czarnocki 1992).

When **5** was subjected to m-chloroperbenzoic acid (MCPBA) oxidation, compounds **6** and **7** were formed in a relative ratio depending on the temperature (Czarnocki, 1992). The synthetic utility of nitron **7** was further elucidated by its transformation, in several steps, into two isoquinoline alkaloids

Scheme 1



Scheme 2



(R)-calycotomine, and (S)-xylopinine. Both compounds, **6** and **7**, were characterized by spectral means (¹H and ¹³C-NMR) as well as by X-ray structural analysis.