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Structure and Molecular Interactions Analysis of (*E*)-N′-(3,4,5-trimethoxybenzylidene) isonicotinohydrazide dihydrate

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Abstract: *The compound (E)-N′-(3,4,5-trimethoxybenzylidene)isonicotinohydrazide dihydrate crystallizes in the monoclinic space group $P2_1/n$ with unit cell parameters a = 9.1136(9) Å, b = 16.3007(13) Å, c = 11.7446(10) Å, β = 91.425(9)º and number of molecules per unit cell (Z) = 4. The crystal structure was solved by direct methods and refined by full matrix least squares procedures to a final R value of 0.070 for 1809 observed reflections. The Schiff base molecule exists in E conformation with respect to the C=N double bond. The structure exhibits inter-molecular H-bonds of the type O-H…N, O-H…O, N-H…O and C-H…O.*

Keywords: *Crystal Structure; Direct Methods; Isonicotinohydrazide; Intermolecular interaction.*

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I. Introduction

The crystallographic and pharmaceutical importance of isoniazid and some of its derivatives is well known.[1-3] Most of such derivatives have been found to possess potential tuberculostatic activity.[4-6]. The compounds which contain an azomethine group (-HC=N-) have gained increasing attention due to their broad spectrum of biological activities.[7,8] Some of these compounds showed moderate to good antimycobacterial activity at micro molar concentrations.[9] The ease of synthesis and high pharmacological value of such compounds lead to much experimentation by varying substitution on carbonyl compounds and using a variety of compounds containing an amine group. In view of the fascinating results that accrue from such like molecules, we report here the molecular interaction analysis of the structure of (*E*)-N′-(3,4,5-trimethoxybenzylidene) isonicotinohydrazide dihydrate.

II. Experimental

Procedure for the synthesis of (*E*)-N′-(3,4,5-trimethoxybenzylidene)isonicotinohydrazide dihydrate:

A mixture of isoniazid (0.138 g, 1 mmol), 3,4,5-trimethoxybenzaldehyde (0.196 g, 1 mmol) and catalytic amount of ceric ammonium nitrate (2 mol %) in 5 ml of H_2O was sonicated at 60 W for 10 minutes. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was filtered and washed with distilled water. The pure product was obtained by further recrystallization using alcohol, and crystals of the purified compound are produced from alcohol by a slow evaporation method (M.P.: 455-457 K). The reaction scheme is represented in Figure 1.

X-Ray Intensity Data Collection:

X-ray intensity data of the crystal of dimensions (0.30 X 0.20 X 0.20 mm) having well-defined crystal morphology were collected at 293(2) K on *X'calibur* CCD area-detector X-ray Diffractometer[10] equipped with Mo*Kα* radiation (λ=0.710Å). The intensities were measured by employing ω-scan mode for the diffraction angle ranging from 4.186 to 27.645º. A total number of 7225 reflections were measured of which 3417 were found to be unique. The criterion *($I > 2\sigma(I)$)* was employed to the unique data set and hence 1809 reflections were treated as observed. Data were corrected for Lorentz and Polarization factors. The structure was solved by direct methods using SHELXS97.[11] All non-hydrogen atoms of the molecule were located in the best E-map and Full-matrix least-squares refinement was carried out using SHELXL97.[11] The final refinement cycles converged to R = 0.070 and $wR(F^2)$ = 0.173 for 1809 observed reflections. The residual electron density ranges from -0.23 to

0.39 eÅ^{-3}. Atomic scattering factors were taken from International Tables for X-ray Crystallography (1992, Vol. C, Tables- 4.2.6.8 and 6.1.1.4). The crystallographic data are summarized in Table 1. Bond distances, bond angles and torsion angles which play an important role in collating the structural properties of this molecule with the related structures are presented in Table 2. An ORTEP[12] view of the molecule with atomic labeling is shown in Figure 2. The geometry of the molecule was calculated using the PLATON[13] and PARST[14] software. **CCDC**-1871490 contains the supplementary crystallographic data for the structure.

III. Results and Discussion

The molecule consists of a pyridine and benzene ring. The structural parameters, including bond distances and angles show a normal geometry[15] and are in agreement with the values observed for some related structures.[3,16] Rings A and B are essentially planar, with atom C1 and C11 displaced out of their mean ring planes by 0.011 Å and 0.014 Å, respectively. The O2 atom attached with the carbon atom C11 is coplanar with the ring B and it is indicated by the magnitude of torsion angles O2-C11-C10-C9 = -178.2(3)˚ and O2-C11-C12-C13 = 178.2(3)˚. This feature can also be seen in a related structure.[17] The dihedral angle between the pyridine and benzene ring is 175.0(8)˚.

In the crystal structure, most of the intermolecular hydrogen interactions occur due to the oxygen atoms of water of hydration, viz. N2-H2A…O6, O5-H5A…O1, O5-H5A…O2, O6-H6A…N1, O5-H5C…N3, C1-H1…O6, C7-H7…O6, O5-H5C…O4 and O6-H6B…O5. The C-H…O, N-H…O and O-H…O type of hydrogen bonds are typical of happening in a small molecule of this kind. The geometry of hydrogen bonding is presented in Table 3 and strong intermolecular hydrogen bond in Figure 4 (Mercury).[18] No significant C-H…π contacts are observed in the molecular packing of title compound. The molecular packing in the unit cell as viewed down the *a*-axis is shown in Figure 3 (PLATON).[13] The crystal structure is further stabilized by a π-π interaction (Figure 5) and the details are given in Table 4.

IV. Figures and Tables

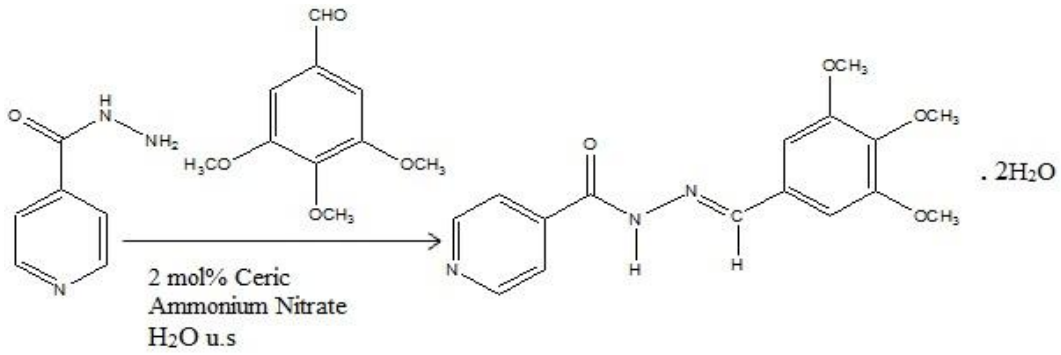

Figure 1: Reaction Scheme.

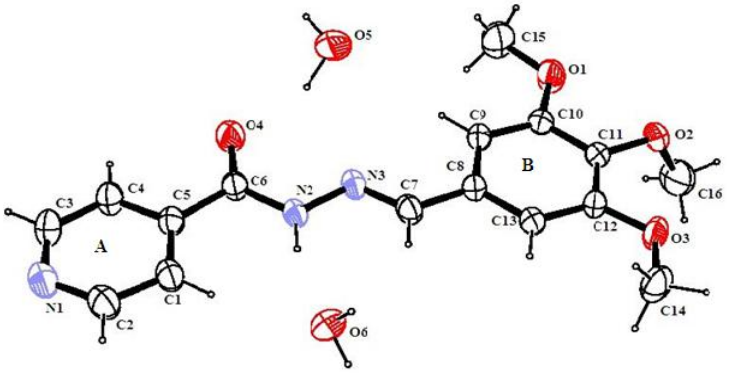

Figure 2: ORTEP view of the molecules with displacement ellipsoids at the 40% probability level. H atoms shown as small spheres of arbitary radii.

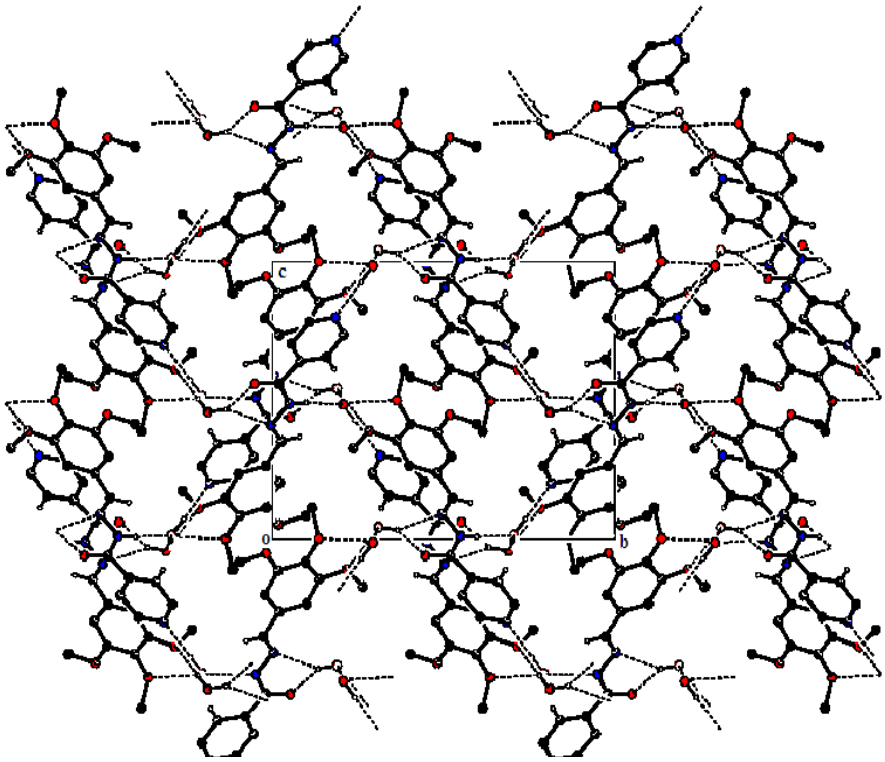

Figure 3: Packing of the molecules viewed down the a-axis.

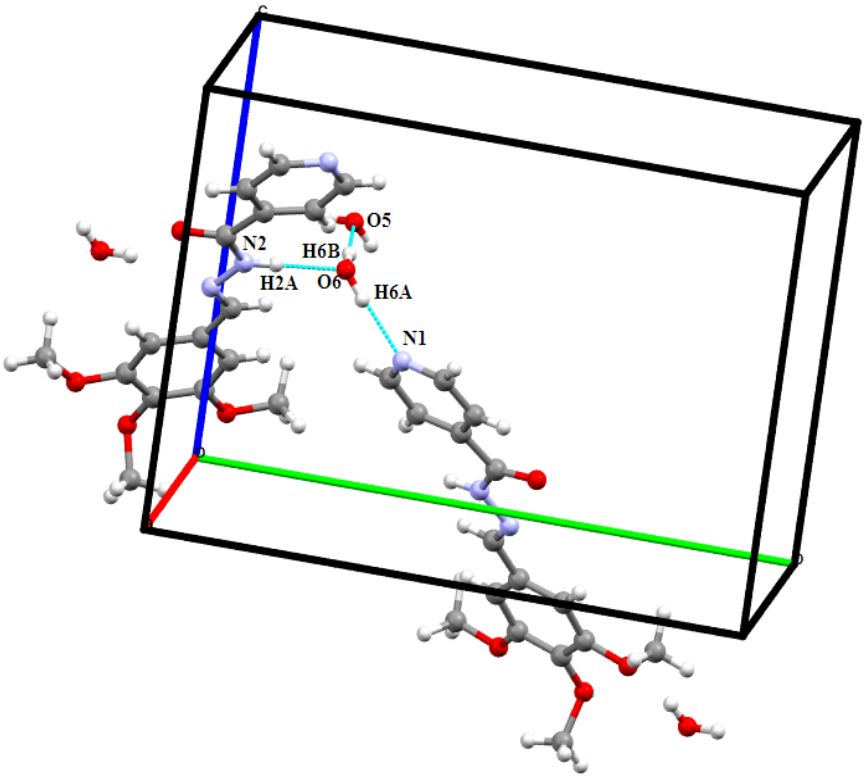

Figure 4: Strong Intermolecular hydrogen bonding.

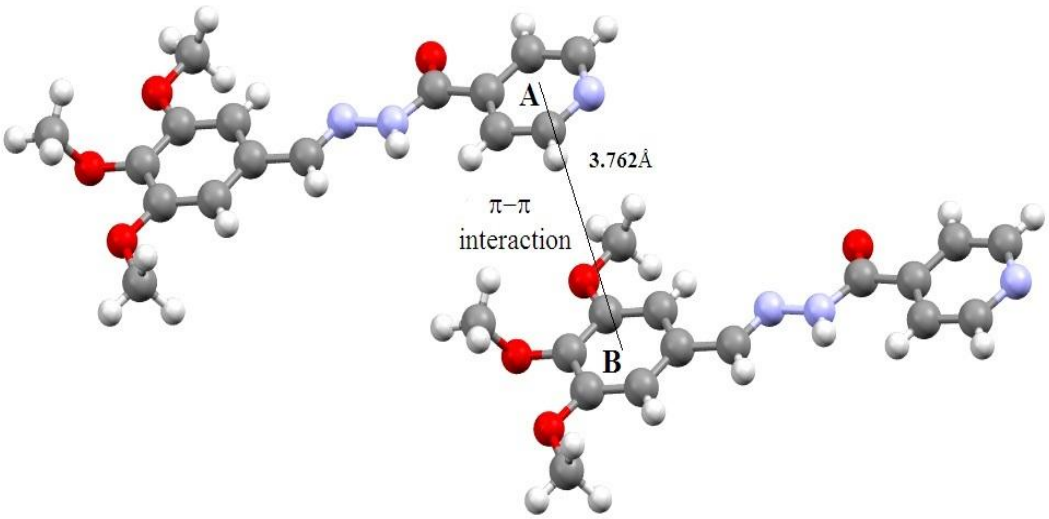

Figure 5 : π–π interaction.

Table 1: Crystal data and other experimental details

CCDC Number*	1871490
Crystal description	Block
Crystal size	0.30 x 0.20 x 0.20 mm^3
Empirical formula	$C_{16}H_{17}N_3O_4.2H_2O$
Formula weight	351.36
Radiation, Wavelength	Mo *Kα*, 0.71073 Å
Unit cell dimensions	a = 9.1136(9) Å , b = 16.3007(13) Å, c = 11.7446(10) Å β = 91.425(9)°
Crystal system, Space group	Monoclinic, P $2_1/n$
Unit cell volume	1744.2(3)$Å^3$
No. of molecules per unit cell, Z	4
Absorption coefficient	0.103 mm^{-1}
F(000)	744
θ range for entire data collection	4.19< θ < 27.65º
Reflections collected / unique	7225/3417
Reflections observed I > 2σ(I))	1809
Range of indices	h= -11 to 9, k= -19 to 20, l= -13 to 14
No. of parameters refined	267
Final R-factor	0.0700
wR(F^2)	0.1738
Rint	0.0465
Rsigma	0.0849
Goodness-of-fit	1.034
Final residual electron density	-0.225< Δρ >0.389 e$Å^{-3}$
Measurement	*X'calibur system – Oxford diffraction make, U.K.*
Software for structure solution:	SHELXS97[11]
Software for refinement	SHELXL97[11]
Software for molecular plotting	ORTEP-3[12] PLATON[13] PARST[14] MERCURY[18]

**Cambridge Crystallographic Data Deposition number*

Table 2: Selected Bond Lengths, Bond angles and Torsion angles

Bond Distances (Å)		**Bond Distances (Å)**	
C1-C2	1.380 (4)	C12-C13	1.384 (4)
C3-C4	1.374 (4)	N1-C2	1.319 (4)
C5-C1	1.374 (4)	N1-C3	1.327 (5)
C5-C4	1.372 (4)	N3-C7	1.265 (4)
C5-C6	1.498 (4)	N3-N2	1.377 (3)
C6-N2	1.343 (4)	O1-C10	1.365 (3)
C8-C7	1.458 (4)	O1-C15	1.413 (5)
C8-C9	1.396 (4)	O2-C11	1.365 (3)
C8-C13	1.387 (4)	O2-C16	1.415 (4)
C10-C9	1.389 (4)	O3-C12	1.358 (3)
C10-C11	1.385 (4)	O3-C14	1.412 (4)
C11-C12	1.388 (4)	O4-C6	1.221 (3)
Bond Angles(˚)		**Bond Angles(˚)**	
C5-C1C2	118.1 (3)	O1-C10-C9	124.2 (3)
N1-C2-C1	125.2 (3)	O1-C10-C11	114.5 (3)
N1-C3-C4	123.3 (3)	C10-C11-C12	120.0 (2)
C5-C4-C3	120.0 (3)	O2-C11-C10	119.2 (3)
C1-C5-C6	125.1 (3)	O2-C11-C12	120.7 (3)
C4-C5-C1	117.5 (3)	C13-C12-C11	119.2 (3)
C4-C5-C6	117.4 (3)	O3-C12-C11	115.8 (2)
N2-C6-C5	116.2 (3)	O3-C12-C13	125.0 (3)
O4-C6-C5	120.7 (3)	C12-C13-C8	120.8 (3)
O4-C6-N2	123.1 (3)	C2-N1-C3	115.9 (3)
N3-C7-C8	123.4 (3)	C6-N2-N3	119.1 (3)
C9-C8-C7	122.0 (3)	C7-N3-N2	115.6 (3)
C13-C8-C7	117.6 (3)	C10-O1-C15	118.1 (3)
C13-C8-C9	120.4 (3)	C11-O2-C16	114.5 (3)
C10-C9-C8	118.3 (3)	C12-O3-C14	117.3 (3)
C11-C10-C9	121.3 (3)		
Torsion Angles (º)		**Torsion Angles (º)**	
C5-C1-C2-N1	1.9(6)	C9-C10-C11-C12	-2.5 (5)
N1-C3-C4-C5	-0.1(5)	C9-C10-C11-O2	-178.2 (3)
C4-C5-C1-C2	-2.1(5)	O1-C10-C11-C12	177.8 (3)
C6-C5-C1-C2	177.4(3)	O1-C10-C11-O2	2.1 (4)
C1-C5-C4-C3	1.3(5)	C10-C11-C12-C13	2.6 (5)
C6-C5-C4-C3	-178.2(3)	C10-C11-C12-O3	-177.6 (3)
C1-C5-C6-N2	7.7(5)	O2-C11-C12-C13	178.2 (3)
C1-C5-C6-O4	-172.1(3)	O2-C11-C12-O3	-2.0 (4)
C4-C5-C6-N2	-172.9 (3)	C11-C12-C13-C8	-1.1 (5)
C4-C5-C6-O4	7.4(5)	O3-C12-C13-C8	179.1 (3)
C5-C6-N2-N3	178.2(2)	C3-N1-C2-C1	-0.8 (6)
O4-C6-N2-N3	-2.1(5)	C2-N1-C3-C4	-0.1 (6)
C9-C8-C7-N3	1.5(5)	N2-N3-C7-C8	177.5 (3)
C13-C8-C7-N3	-177.2(3)	C7-N3-N2-C6	174.5 (3)
C7-C8-C9-C10	-178.0(3)	C15-O1-C10-C9	3.1 (5)
C13-C8-C9-C10	0.7(5)	C15-O1-C10-C11	-177.2 (4)
C7-C8-C13-C12	178.2(3)	C16-O2-C11-C10	-103.1 (4)
C9-C8-C13-C12	0.5(5)	C16-O2-C11-C12	81.3 (4)
C11-C10-C9-C8	0.9(5)	C14-O3-C12-C11	176.4 (3)
O1-C10-C9-C8	-179.5(3)	C14-O3-C12-C13	-3.8 (5)

Table 3: Geometry of Intra and Inter molecular Hydrogen bonds

D–H…A	D–H(Å)	H…A(Å)	D…A(Å)	D–H…A(o)
N2-H2A…O6^{iii}	0.86	2.06	2.898(4)	164
O5-H5A…O1^{ii}	0.82	2.44	3.185(4)	153
O5-H5A…O2^{ii}	0.82	2.36	2.903(4)	125
O6-H6A…N1^{i}	0.88	1.99	2.851(4)	164
O6-H6B…O5^{iv}	0.86	1.90	2.764(5)	177
C1-H1…O6^{iii}	0.93	2.33	3.245(5)	168
C7-H7…O6^{iii}	0.93	2.53	3.334(4)	145
O5-H5C…O4^{v}	1.02	1.92	2.871(4)	154
O5-H5C…N3^{v}	1.02	2.48	3.115(4)	120

Symmetry code: (i) –x, 1-y, -z (ii) -½+x, ½-y, -½+z (iii) ½-x, ½+y, ½-z
(iv) -½+x, ½-y, ½+z (v) x, y, z

Table 4: Geometry of π–π interaction*

CgI…CgJ	CgI…CgJ (Å)	CgI…P(Å)	α(°)	β(°)	Δ(Å)
Cg(1)…Cg(2)	3.7618	3.5111	4.95	25.95	1.3505

Symmetry code: (i) -x, -y, 1-z

* Cg1 and Cg2 represent the centre of gravity of pyridine (A) and phenyl (B) rings, respectively.

V. Conclusions

The molecular structure has been determined by using X-ray diffraction techniques. The structure of compound (E)-N′-(3,4,5-trimethoxybenzylidene)isonicotinohydrazide dihydrate consists of a pyridine and benzene ring. The dihedral angle between the pyridine and benzene ring is 175.0(8)˚. In the crystal structure, most of the intermolecular hydrogen interactions occur due to the oxygen atoms of water of hydration. The oxygen atoms participate extensively as donor and acceptors. There exists C-H…O, N-H…O and O-H…O type of intermolecular hydrogen bond, besides a π–π interaction.

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References

[1]. H. S. Naveenkumar, A. Sadikun, P. Ibrahim, C. S. Yeap and H.-K. Fun, *Acta Cryst*. E, **66**, o1918-o1919 (2010).
[2]. S.-K. Chen, *Acta Cryst.* E, **62**, o5352-o5353 (2006).
[3]. H.-K. Fun, W.-S. Loh, D. N. Shetty, B. Narayana and B. K. Sarojini, *Acta Cryst.* E, **68,** o2303-o2304 (2012).
[4]. Y. L. Janin, *Bioorg. Med. Chem*., **15**, 2479–2513 (2007).
[5]. R. Maccari, R. Ottana and M. G. Vigorita, *Bioorg. Med. Chem. Lett*., **15**, 2509-2513 (2005).
[6]. R. A. Slayden and C. E. Barry, *Microbes infect.*, **2**, 659-669 (2000).
[7]. C. M. da Silva, D. L. da Silva, L. V. Modolo, R. B. Alves, M. A. de Resende, C. V. B. Martins and A. de Fatima, *J. Adv. Res.*, **2,** 1-8 (2011).
[8]. P. P. Kumar and B. L. Rani1, *Int. J. ChemTech Res.*, **3,** 155-160 (2011).
[9]. H. S. Naveen Kumar, T. Parumasivam, F. Jumaat, P. Ibrahim, M.Z. Asmawi and A. Sadikun, *Med Chem Res.*, **23**, 269–279 (2014).
[10]. Oxford Diffraction. *CrysAlis PRO* and *CrysAlis RED*. Oxford Diffraction Ltd, Yarnton, England (2010).
[11]. G. M. Sheldrick, *Acta Cryst*. A, ***64***, 112 (2008).
[12]. L. J. Farrugia, *J. Appl. Cryst.*, **32**, 837 (1999).
[13]. A. L. Spek, *Acta Cryst.* D, **65**, 148 (2009).
[14]. M. Nardelli, *J. Appl. Cryst.*, **28**, 659 (1995).
[15]. F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen and R. Taylor, *J. Chem. Soc*., *Perkin Trans-II.*, **S1,** 19 (1987).
[16]. H.-K. Fun, C. K. Quah, P. C. Shyma , B. Kalluraya and J. H. S. Vidyashree, *Acta Cryst.* E, **68,** o2122-o2130 (2012).
[17]. H. S. Naveen Kumar, A. Sadikun, P. Ibrahim, C. S. Yeap and H.-K. Fun, *Acta Cryst.* E, **66,** o1235-o1236 (2010).
[18]. C. F. Macrae, P. R. Edgington, McCabe, E. Pidcock, G. P. Shields, R. Taylor, M. Towler, J. Van de Streek and P. A.Wood, *J. Appl. Cryst.*, **41**, 466-470 (2008).

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