

Crystal Structure of 2-(4-Hydroxy-3-Methoxyphenyl)-6-(4-Hydroxy-3-Methoxystyryl)-1-Methyl-2, 3-Dihydropyridine-4 (1H)-One by X-Ray Powder Diffraction

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Abstract: Problem statement: The studied dihydropyridone was synthesized for the first time via the microwave assisted reaction of curcumin and methylamine and it is important to support the mechanism by the crystal structure. **Approach:** The crystal structure of the title compound was determined using high resolution x-ray diffraction. PowderSolve program was used to solve the structure while the refinement was done in material studio Reflex module. **Results:** The findings obtained with high-resolution x-ray powder diffraction and molecular location methods based on simulated annealing algorithm after Rietveld refinement showed that the monoclinic unit cell was $a = 13.4925 \text{ \AA}$, $b = 12.8162 \text{ \AA}$, $c = 11.5231 \text{ \AA}$, $\alpha = 90.000^\circ$, $\beta = 99.0401^\circ$, $\gamma = 90.000^\circ$; cell volume = 1967.85 \AA^3 and space group P 21/a with 4 molecules in a unit cell. **Conclusion/Recommendations:** Powder diffractometry could be a powerful tool for determining crystal structures for organic molecules.

Key words: Dihydropyridone, x-ray powder diffraction, rietveld refinement, PowderSolve, treor

INTRODUCTION

Dihydropyridones are important intermediates for synthesis of natural products, particularly alkaloids and many approaches to their synthesis have been developed (Donohoe *et al.*, 2009; Comins and Ollinger, 2001; Song *et al.*, 2007; Saito *et al.*, 2009; Dieter and Guo, 2009; MacDonald and Burnell, 2009). Sugiyama *et al.* (1970) were synthesized the dihydropyridone 2, 3-dihydro-1, 2-diphenyl-6-(2-phenylethenyl)-4-pyridone from the reaction of 6-methyl-1, 2-diphenyl-2, 3-dihydro-4-pyridone with benzaldehyde. In a previous study (Elias *et al.*, 2008) we reported the synthesis of a series of dihydropyridones that structurally related to that synthesized by Sugiyama *et al.* (1970), by the reaction of curcumin and amines or amine acetates under microwave irradiation in an approach that seems unexpected.

In this study we report the crystal structure of the compound 2-(4-hydroxy-3-methoxyphenyl)-6-(4-hydroxy-3-methoxystyryl)-1-methyl-2, 3-dihydropyridine-4(1H)-one (Fig. 1).

The compound is yellow powder and difficult to crystallize. Powder x-ray diffraction is the method of choice for characterizing the structures if solids are not available as suitable single crystals. Over past decade, Structure Determination from Powder Diffraction (SDPD) has matured into a technique that is widely and successfully used in the context of organic, inorganic and organometallic compounds (David and Shankland, 2008; Bail, 2005).

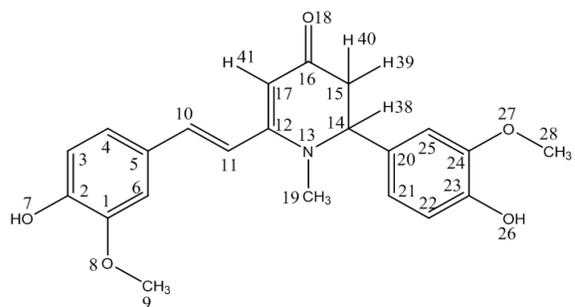


Fig. 1: Molecular structure of the studied compound

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MATERIALS AND METHODS

The compound was synthesized according to previously described procedure (Elias *et al.*, 2008). High resolution x-ray powder diffraction data was collected on an MXPI8A-HF (MAC science, Japan) diffractometer with Cu-K α (1.540593 Å) radiation at room temperature. The tube voltage and the tube current were 50 kV and 200 MA respectively. The 2 θ scan range was from 3 to 80° with a step size of 0.02° and counting time of 3 sec per step. The powder diffraction pattern was auto indexed using Treor 90 with Powder X software (Dong, 1999). PowdeSolve software (Engel *et al.*, 1999) was used to solve the structure using simulated annealing method. The refinement was done in material studio Reflex module.

RESULTS

The crystallographic details are summarized in Table 1.

The final positional parameters are listed in Table 2.

Figure 2 shows a plot of the refined diffraction pattern. The agreement factors were $R_{wp} = 13.04\%$ and $R_p = 9.97\%$.

The representation of the crystal system with four molecules in the unit cell is shown in Fig. 3.

Table 1: Summary of crystallographic data

Molecular formula	C ₂₁ H ₂₄ NO ₅
Formula weight	381
Crystal system	Monoclinic
Space group	P2 ₁ /a
Cell constants (Å)	
a	13.4925
b	12.8162
c	11.5231
α	90.000
β	99.040
γ	90.0000
Volume (Å³)	1967.8
Z	4
R_{wp}	13.04%
R_p	9.97%

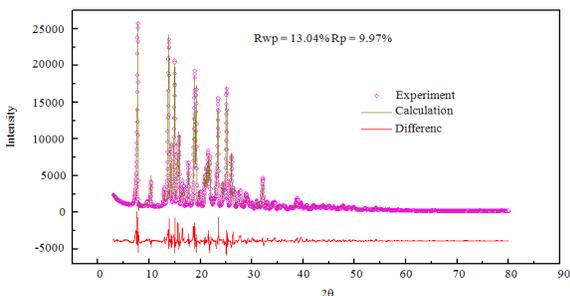


Fig. 2: Plot of the refined diffraction pattern

The overall shape of the molecule is illustrated in Fig. 4.

Torsion angles, bond lengths and bond angles are gathered in Table 3-5 respectively.

Table 2: Functional atomic coordinates of non-hydrogen atoms

Atom	X	Y	Z
C1	-0.55377	-0.13412	0.16650
C2	-0.64498	-0.16366	0.09690
C3	-0.70239	-0.08781	0.03068
C4	-0.67379	0.01524	0.03495
C5	-0.58729	0.04622	0.10928
C6	-0.25736	-0.02958	0.17332
C7	-0.68199	-0.26311	0.08840
C8	-0.49599	-0.21276	0.22790
C9	-0.39298	-0.18870	0.26630
C10	-0.56729	0.16135	0.12066
C11	-0.47592	0.20379	0.16299
C12	-0.45838	0.30932	0.17574
C13	-0.36050	0.34609	0.20154
C14	-0.33865	0.45664	0.22994
C15	-0.41887	0.52733	0.16621
C16	-0.52393	0.49013	0.16143
C17	-0.53706	0.37745	0.16322
C18	-0.59087	0.55483	0.14951
C19	-0.27878	0.27299	0.24327
C20	-0.32223	0.47437	0.36207
C21	-0.38855	0.44208	0.43548
C22	-0.36653	0.45667	0.55566
C23	-0.27750	0.50485	0.60629
C24	-0.21031	0.53984	0.53293
C25	-0.23438	0.52347	0.41282
C26	-0.25958	0.51576	0.72579
C27	-0.12137	0.58725	0.58368
C28	-0.07361	0.65267	0.50887

Table 3: Torsion angles (°)

Torsion angle	Angle
C6-C1-C2-C3	4.50
C6-C1-C2-O7	-176.00
O8-C1-C2O-C3	-177.40
O8-C1-C2-O7	2.00
C2-C1-C6-C5	-2.50
O8-C1-C6-C5	179.50
C2-C1-O8-C9	160.90
C6-C1-O8-C9	-21.10
C1-C2-C3-C4	-2.30
O7-C2-C3-C4	178.20
C3-C4-C5-C6	3.90
C3-C4-C5-C10	-172.70
C10-C5-C6-C1	174.70
C4-C5-C10-C11	-161.80
C6-C5-C10-C11	21.70
C5-C10-C11-C12	-178.50
C10-C11-C12-N13	-169.70

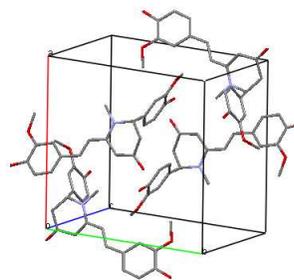


Fig. 3: Representation of the unit cell of the studied compound

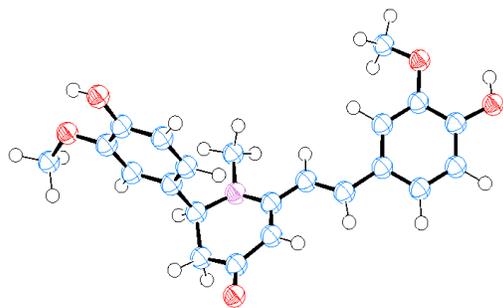


Fig. 4: The refined structure of the studied compound

Table 4: Bond lengths (Å)

Bond	Bond length
C1-O8	1.390
C2-O7	1.367
C5-C6	1.398
C5-C10	1.502
O8-C9	1.425
C10-C11	1.366
C11-C12	1.377
C12-N13	1.390
C12-C17	1.365
N13-C14	1.473
N13-C19	1.469
C14-C15	1.511
C14-C20	1.521
C15-C16	1.488
C16-C17	1.456
C16-O18	1.218
C23-C24	1.407
C23-O26	1.367
C24-C25	1.387
C24-O27	1.390
O27-C28	1.427

Table 5: Bond angles (°)

Bond angle	Angle
C2-C1-O8	118.1
C6-C1-O8	123.3
C1-C2-O8	124.2
C3-C2-O7	116.5
C4-C5-C10	117.1
C6-C5-C10	123.7
C1-O8-C9	116.4
C5-C10-C11	124.2
C10-C11-C12	124.0
C11-C12-N13	119.8
C11-C12-C17	120.0
N13-C12-C17	120.2
C12-N13-C14	121.6
C12-N13-C19	119.5
C14-N13-C19	115.3
N13-C14-C15	111.5
N13-C14-C20	111.0
C12-C14-C20	112.2
C14-C15-C16	115.6
C15-C16-C17	115.8
C15-C16-O18	118.1
C17-C16-O18	126.0
C12-C17-C16	122.8

DISCUSSION

The molecule is twisted about the bond C14-C20, the value of the torsion angle C15-C14-C20-C25 is -108.2° . The phenyl rings are essentially planar (Table 3).

The six-membered central ring twisted about C12-N13-C14 and adopts half chair conformation. The angles of the torsion bonds C16-C15-C14-N13 and C17-C12-N13-C14 are 29.1 and 7.4 respectively. The phenyl group at C14 (Fig. 4) is oriented axially with respect to the pyridone ring; accordingly the torsion angle C16-C15-C14-C20 has the value 93.8° . On the other hand the styryl group at C-12 oriented equatorially and adopts a roughly coplanar conformation with the conjugated system of the pyridone ring through the system C10-C11-C12-C17-C16-O18. The values of the torsion angles within this system namely; O18-C16-C17-C12, C16-C17-C12-C11, C17-C12-C11-C10 and C12-C11-C10-C5 are 179.3 , 172.4 , 10.4 and 185.5° respectively. This coplanarity which support effective conjugation is confirmed by the observed bond lengths C16-C17 and C10-C11 (1.455 and 1.377Å respectively) which are decreased compared to C15-C16 and C14-C15 (1.488 and 1.511Å respectively) as could be shown in Table 4.

Meanwhile the double bonds C12-C17 and C10-C11 (1.365 and 1.366Å respectively) become longer compared to the C=C bond in ethylene which is 1.334 - 1.339Å (Choi, 1997). The bond length of C12-C17 is comparable to the value of the corresponding bond in 1, 3-cyclohexendione in its crystalline enol form measured by inelastic incoherent neutron scattering spectra (Hudson *et al.*, 2004), which is 1.361Å . To less degree of agreement (but of reasonable similarity) are other bonds on this compound corresponding to the bonds C14-C15, C15-C16, C16-C17 and C16-O18 which are 1.448 , 1.531 , 1.532 and 1.241Å respectively. The torsion angles between geminal protons H39 and H40 and the proton H38 are 40.1 and -81.9° . This supports the assignment of the two peaks that appear in ^1H NMR spectrum of the studied compound which appear as two doublets of doublets at 2.42 ppm ($J = 16$ and 4 Hz) and at 2.84 ppm ($J = 16$ and 7 Hz) (Elias *et al.*, 2008). The distortion of the pyridone ring forces the protons H39 and H40 to adopt two different torsion angles with the O18 atom. The observed values of these torsion angles are -82.1 and 30.3° respectively. The measured angles are gathered in Table 5.

CONCLUSION

The study demonstrates that structure determining from powder diffractometry could be a powerful tool

for determining crystal structures for organic molecules.

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