ISSN 1063-7745, Crystallography Reports, 2017, Vol. 62, No. 7, pp. 1144–1147. © Pleiades Publishing, Inc., 2017.

STRUCTURE OF ORGANIC COMPOUNDS

Single Crystal X-ray Study of 6-Phenyl-4-(*p*-tolyl)pyridin-2(1*H*)-one[1]

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Received June 28, 2016

Abstract—The title compound 6-phenyl-4-(*p*-tolyl)pyridin-2(1*H*)-one was synthesized *via* one-pot, three component reaction of (*E*)-1-phenyl-3-(*p*-tolyl)-2-propen-1-one, ethyl 2-nitroacetate and ammonium acetate in refluxing ethanol, as a shiny green crystalline solid in 83% yield. Its structure was characterized by spectral studies and unambiguously corroborated by X-ray diffraction crystallography. The crystals of title compound are monoclinic, sp. gr. $P2_1/n$, a = 11.8346(7) Å, b = 13.4413(9) Å, c = 17.7626(10) Å, β = 99.479(5)°, and Z = 8. All the rings in molecule of the title compound are planar. Hydrogen interactions play significant role in stabilizing the crystal structure and the supramolecular aggregate of molecules is facilitated by strong N–H···O and C–H···O type of hydrogen interactions.

DOI: 10.1134/S1063774517070227

INTRODUCTION

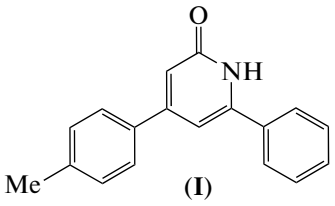
Pyridin-2(1*H*)-ones represent a "privileged" class of six-membered aza heterocyclic compounds, having significant interest in current medicinal chemistry and emerge in many biologically active natural products, therapeutics and synthetic compounds [1, 2]. Due to the dual properties of an aromatic ring and an amide, pyridin-2(1*H*)-ones show many useful interactions with biological molecules. Pyridin-2(1*H*)-ones display a variety of interesting biological properties including anti-cancer [3], cardiotonic [4], cardiovascular [5], anti-viral [6], anti-hypertensive [7], anti-anaphylactic [8], anti-allergenic [9], anti-inflammatory [10], anti-oxidant [11], and anti-microbial [12] ones. Pyridin-2(1*H*)-ones have also been used as lead compounds for the preparation of several drugs such as selective anti-cancer agents [13], anti-viral agents [14], potent anti-hepatitis B [15], subtype selective GABA receptor agonists [16], MEK-1 inhibitors [17], receptor tyrosine kinase c-Kit inhibitors [18], anaplastic lymphoma kinase inhibitors [19], pim-1 kinase inhibitors and inhibitors of amyloid-β peptide aggregation, an important character in amyloid formation in Alzheimer's disease [20]. Owing to the significance of pyridin-2(1*H*)-ones as bioactive molecules, we reported an expedient metal/base-free, one-pot method of preparation of pyridin-2(1*H*)-one core bearing 4,6-diarylpyridin-2(1*H*)-ones [21]. In this paper, we report the structural elucidation of the title compound 6-phenyl-4-(*p*-tolyl)pyridin-2(1*H*)-one (**I**) by X-ray crystallographic study along with other analytical and spectral data.

EXPERIMENTAL

Synthesis. In an oven-dried round bottomed flask, a mixture of (*E*)-1-phenyl-3-(*p*-tolyl)-2-propen-1-one (0.222 g, 1.0 mmol), ethyl 2-nitroacetate (0.133 g, 1.0 mmol) and ammonium acetate (0.462 g, 6.0 mmol) in ethanol (5.0 mL) was refluxed with vigorous stirring for 6 h [21]. On completion of the reaction (TLC using petroleum ether:ethylacetate 7 : 3 v/v as eluent), the reaction mixture was cooled to room temperature and the solid obtained was filtered off and washed with ethanol to obtain the crude product. The crude product was purified just by recrystallization from ethanol without carrying out column chromatography to obtain the pure 6-phenyl-4-(*p*-tolyl)pyridin-2(1*H*)-one as a shiny green crystalline solid in 83% yield. The structure of I was elucidated by analytical as well as spectral studies viz. ^{1}H NMR, ^{13}C NMR, FT-IR, and HRMS, and unambiguously authenticated by single crystal X-ray diffraction study.

The molecular structure of the title compound **I** is shown in Fig. 1. The crystallographic data for the compound **I** are given in Table 1.

[1] The article is published in the original.



(I)

Fig. 1. Chemical structure of 6-phenyl-4-(*p*-tolyl)pyridin-2(1*H*)-one (**I**).

Characterization. ^{1}H and ^{13}C NMR spectra in DMSO-d_6 were recorded on a Bruker Avance III-400 MHz, using $(CH_3)_4Si$ as an internal standard at 400 and 100 MHz, respectively. Infrared spectrum was recorded on a Shimadzu (FT-IR 8400S) FT-IR spectrophotometer using KBr disc. For the HRMS measurement, a Q-TOF Micro mass spectrometer was used. The melting point was recorded on a Chemiline CL-725 melting point apparatus and was uncorrected. The progress of the reaction and purity of the synthesized compound was monitored by TLC using silica gel 60 F254 aluminum plates. Visualization was accomplished by UV light, exposure to iodine vapours and by treating the plates with dragendorff reagent followed by heating.

A shiny green solid. Yield: 83% (0.217 g). Mp: 233–234°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.68 (br s, 1H, exchangeable with D_2O), 7.89 (d, J = 6.3 Hz, 2H), 7.72 (d, J = 7.9 Hz, 2H), 7.50 (d, J = 6.2 Hz, 3H), 7.32 (d, J = 7.9 Hz, 2H), 6.97 (s, 1H), 6.64 (s, 1H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 152.1, 139.5, 134.9, 130.0, 129.1, 127.4, 127.2, 112.5, 104.8, 21.2. IR (KBr, cm^{-1}): 3235.62, 1613.47. HRMS (ESI): Calcd. for $C_{18}H_{15}NO$ $[M + H]^+$ 262.1226; Found: 262.1228. Elemental analysis: Calcd. for $C_{18}H_{15}NO$, %: C, 82.73; H, 5.79; N, 5.36; Found: C, 82.77; H, 5.73; N, 5.43.

Table 1. Crystallographic characteristics, X-ray data collection and structure refinement parameters for the title compound **I**

Crystallographic data	Compound ($C_{18}H_{15}NO$)
System, sp. gr., Z	Monoclinic, $P2_1/n$, 8
a, b, c, Å	11.8346(7), 13.4413(9), 17.7626(10)
α, β, γ, deg	90.00, 99.479(5), 90.00
V, Å^3	2787.0(3)
D_x, g cm^{-3}	1.25
Radiation, λ, Å	MoK_α, 0.71073
μ, mm^{-1}	0.077
T, K	293(2)
Sample size, mm	0.30 × 0.20 × 0.20
Diffractometer	X'calibur
Scan mode	ω
Absorption correction, T_{min}, T_{max}	Multi-scan, 0.78416, 1.00000
θ_{max}, deg	28.30
h, k, l ranges	$-14 \le h \le 14$, $-16 \le k \le 13$, $-21 \le l \le 21$
Number of reflections: measured/unique ($N1$), R_{int}/with $I > 2\sigma(I)$ ($N2$)	11389/5458, 0.0382/2917
Refinement method	Full-matrix least-squares on F^2
Number of refined parameters	371
R_1/wR_2 relative to $N1$	0.1113/ 0.1656
R_1/wR_2 relative to $N2$	0.0572/0.1313
S	0.975
$\Delta\rho_{max}/\Delta\rho_{min}$, e/Å^3	0.304/–0.173
Programs	SHELXS97 [22], SHELXL97 [22]

Crystal structure determination and refinement. The structure was solved by direct methods using SHELXS97 [22]. Multisolution tangent refinement was used. All non-hydrogen atoms of the molecule were located in the best E-map and refined in anisotropic approximation.

H atom associated with N atom was located from Fourier difference map. All other H atoms were geometrically fixed and allowed to ride on their parent atoms with C–H = 0.93–0.96 Å, and $U_{iso}(H) = 1.5U_{eq}$ of the attached C atoms for methyl groups and $1.2U_{eq}$(N, C) for other H atoms.

Full-matrix least-squares refinement was carried out using SHELXL97 [22]. The crystallographic data of the title compound are summarized in Table 1. The geometry of the molecule was calculated using the WinGX [23], PARST [24], and PLATON [25] softwares.

CCDC no. 1487796 contains crystallographic data. The data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif by e-mailing data request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallography Data Centre, 12 Union Road, Cambridge, CB2 IEZ, UK. Fax: +44(0) 1223-336033.

RESULTS AND DISCUSSION

An ORTEP view [26] of the title compound with atomic labeling is shown in Fig. 2. The packing view of molecules within the unit cell is shown in Fig. 3. The asymmetric unit cell comprises of two independent molecules of title compound. All the rings are essentially planar in both the molecules. The relative orientations of mean planes of rings in both molecules vary slightly from each other as reflected by dihedral angles

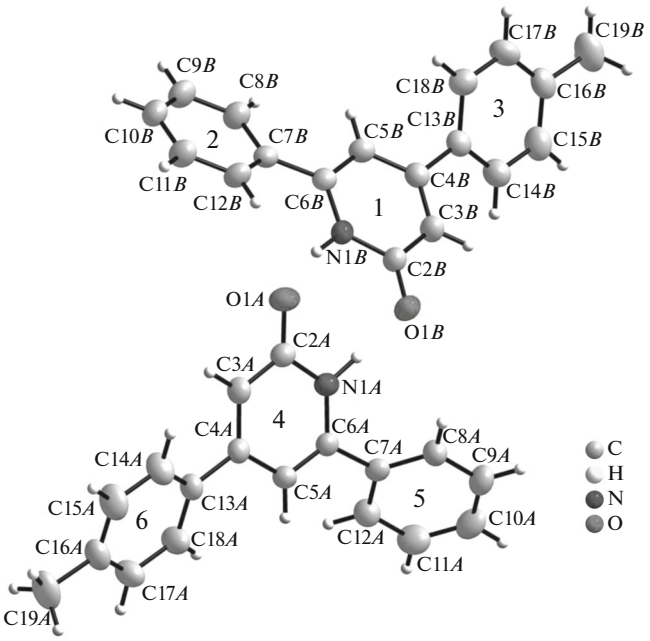


Fig. 2. An ORTEP diagram of the title compound **I** with displacement ellipsoids drawn at 50% probability level.

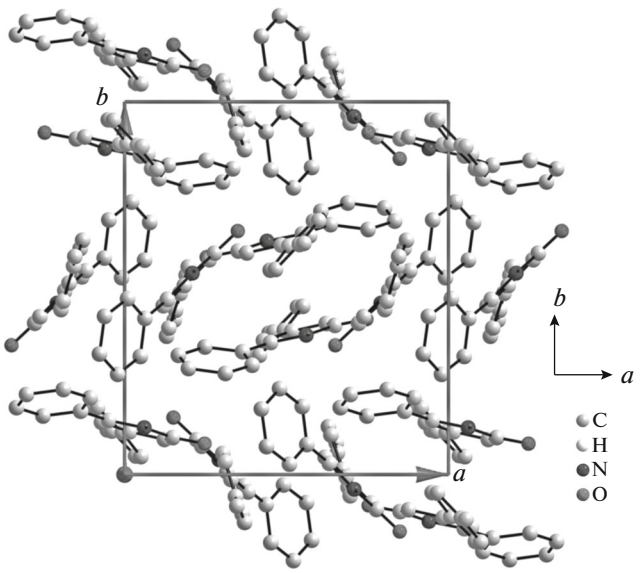


Fig. 3. A view of the packing of the title compound **I** along the *b* axis.

viz. 1–2 = 47.77(8)°, 1–3 = 27.28(8)°, 2–3 = 37.58(8)°, 4–5 = 22.20(8)°, 4–6 = 33.82(7)°, and 5–6 = 51.92(7)° (Fig. 2). The oxygen atoms O1*A* and O1*B* attached to pyridine rings in both molecules lie above the mean plane of attached rings by 0.066(2) Å and 0.011(2) Å, respectively. The bond distances C2*A*–

Table 2. Selected bond lengths *d* (Å) of the title compound **I** for non-hydrogen atoms

Bond	*d*	Bond	*d*
N1*A*–C6*A*	1.367(3)	C16*B*–C15*B*	1.375(4)
N1*A*–C2*A*	1.378(3)	C16*B*–C17*B*	1.384(4)
N1*B*–C6*B*	1.371(3)	C16*B*–C19*B*	1.498(3)
N1*B*–C2*B*	1.378(3)	C7*B*–C12*B*	1.387(3)
C7*A*–C8*A*	1.383(3)	C7*B*–C8*B*	1.392(3)
C7*A*–C12*A*	1.385(3)	C13*B*–C14*B*	1.381(3)
C7*A*–C6*A*	1.480(3)	C13*B*–C18*B*	1.392(3)
O1*A*–C2*A*	1.254(3)	C8*A*–C9*A*	1.377(3)
C6*A*–C5*A*	1.348(3)	C18*B*–C17*B*	1.392(3)
O1*B*–C2*B*	1.256(3)	C8*B*–C9*B*	1.379(3)
C5*A*–C4*A*	1.421(3)	C10*A*–C9*A*	1.373(4)
C3*A*–C4*A*	1.373(3)	C10*A*–C11*A*	1.381(4)
C3*A*–C2*A*	1.421(3)	C14*B*–C15*B*	1.381(3)
C4*A*–C13*A*	1.475(3)	C12*A*–C11*A*	1.386(4)
C4*B*–C3*B*	1.366(3)	C12*B*–C11*B*	1.379(3)
C4*B*–C5*B*	1.415(3)	C10*B*–C9*B*	1.367(3)
C4*B*–C13*B*	1.486(3)	C10*B*–C11*B*	1.370(3)
C5*B*–C6*B*	1.367(3)	C16*A*–C17*A*	1.376(4)
C6*B*–C7*B*	1.479(3)	C16*A*–C15*A*	1.380(4)
C13*A*–C14*A*	1.379(3)	C16*A*–C19*A*	1.508(3)
C13*A*–C18*A*	1.387(3)	C17*A*–C18*A*	1.379(3)
C3*B*–C2*B*	1.408(3)	C15*A*–C14*A*	1.388(3)

Table 3. Selected bond angles ω (deg) of title compound **I** for non-hydrogen atoms

Angle	ω	Angle	ω
C6*A*–N1*A*–C2*A*	123.2(2)	C15*B*–C16*B*–C17*B*	117.8(3)
C6*B*–N1*B*–C2*B*	124.4(2)	C15*B*–C16*B*–C19*B*	120.8(3)
C8*A*–C7*A*–C12*A*	119.0(2)	C17*B*–C16*B*–C19*B*	121.4(3)
C8*A*–C7*A*–C6*A*	121.5(2)	C12*B*–C7*B*–C8*B*	117.2(2)
C12*A*–C7*A*–C6*A*	119.5(2)	C12*B*–C7*B*–C6*B*	122.4(2)
C5*A*–C6*A*–N1*A*	119.6(2)	C8*B*–C7*B*–C6*B*	120.4(2)
C5*A*–C6*A*–C7*A*	123.4(2)	C14*B*–C13*B*–C18*B*	117.3(2)
N1*A*–C6*A*–C7*A*	116.9(2)	C14*B*–C13*B*–C4*B*	121.3(2)
C6*A*–C5*A*–C4*A*	121.2(2)	C18*B*–C13*B*–C4*B*	121.3(2)
C4*A*–C3*A*–C2*A*	122.2(2)	C9*A*–C8*A*–C7*A*	120.7(3)
C3*A*–C4*A*–C5*A*	117.5(2)	C17*B*–C18*B*–C13*B*	120.9(3)
C3*A*–C4*A*–C13*A*	121.7(2)	C9*B*–C8*B*–C7*B*	121.2(2)
C5*A*–C4*A*–C13*A*	120.7(2)	C9*A*–C10*A*–C11*A*	120.1(3)
C3*B*–C4*B*–C5*B*	118.7(2)	C16*B*–C17*B*–C18*B*	121.1(2)
C3*B*–C4*B*–C13*B*	120.2(2)	C13*B*–C14*B*–C15*B*	121.6(3)
C5*B*–C4*B*–C13*B*	121.0(2)	C10*A*–C9*A*–C8*A*	120.1(3)
C6*B*–C5*B*–C4*B*	120.9(2)	C7*A*–C12*A*–C11*A*	120.3(3)
O1*A*–C2*A*–N1*A*	118.8(2)	C11*B*–C12*B*–C7*B*	121.1(2)
O1*A*–C2*A*–C3*A*	125.1(2)	C9*B*–C10*B*–C11*B*	119.3(3)
N1*A*–C2*A*–C3*A*	116.1(2)	C17*A*–C16*A*–C15*A*	117.6(3)
C5*B*–C6*B*–N1*B*	118.0(2)	C17*A*–C16*A*–C19*A*	120.9(3)
C5*B*–C6*B*–C7*B*	124.0(2)	C15*A*–C16*A*–C19*A*	121.5(3)
N1*B*–C6*B*–C7*B*	118.0(2)	C10*B*–C11*B*–C12*B*	120.6(2)
C14*A*–C13*A*–C18*A*	116.9(2)	C16*A*–C17*A*–C18*A*	121.1(3)
C14*A*–C13*A*–C4*A*	122.3(2)	C16*B*–C15*B*–C14*B*	121.4(3)
C18*A*–C13*A*–C4*A*	120.8(2)	C17*A*–C18*A*–C13*A*	121.8(3)
C4*B*–C3*B*–C2*B*	122.0(2)	C10*B*–C9*B*–C8*B*	120.5(2)
O1*B*–C2*B*–N1*B*	119.8(2)	C16*A*–C15*A*–C14*A*	121.2(3)
O1*B*–C2*B*–C3*B*	124.1(2)	C13*A*–C14*A*–C15*A*	121.3(3)
N1*B*–C2*B*–C3*B*	116.0(2)	C10*A*–C11*A*–C12*A*	119.8(3)

Table 4. Geometry of intermolecular hydrogen bonds and π–π interactions in the title compound **I**

D–H···*A*	*D*–H, Å	H···*A*, Å	*D*···*A*, Å	*D*–H···*A*, deg
N1*B*–H1*A*···O1*A*^{i}	0.90(2)	2.02(2)	2.882(3)	161
N1*A*–H1*B*···O1*B*^{i}	1.02(3)	1.74(3)	2.761(3)	178
C12*A*–H12*A*···O1*A*^{ii}	0.93	2.47	3.377(3)	166
C12*B*–H12*B*···O1*A*^{ii}	0.93	2.34	3.188(3)	151

Symmetry codes: (i) $-x+1,-y+1,-z+1$; (ii) $-x+1/2, y-1/2, -z+1/2$.

O1*A* and C2*B*–O1*B* are 1.254(3) Å and 1.256(3) Å, respectively, and they are slightly longer than the literature values [27]. The endocyclic bond angles C2*A*–N1*A*–C6*A* and C2*B*–N1*B*–C6*B* about heteroatom in pyridine rings are 123.2(2)° and 124.4(2)°, slightly higher than ideal values. Selected bond distances and angles are tabulated in Table 2 and Table 3, respectively. Methyl groups are coplanar to respective attached phenyl rings as reflected by torsion angles C14*A*–C15*A*–C16*A*–C19*A* = 178.3(3)° and C14*B*–C15*B*–C16*B*–C19*B* = 178.2(2)°. The geometry of hydrogen interactions is given in Table 4. The hydrogen bonding interactions play an important role in stabilizing supramolecular aggregates, in which the oxygen atoms of carbonyl groups in both molecules act as bifurcated acceptors to the pair of donors as shown in Fig. 4.

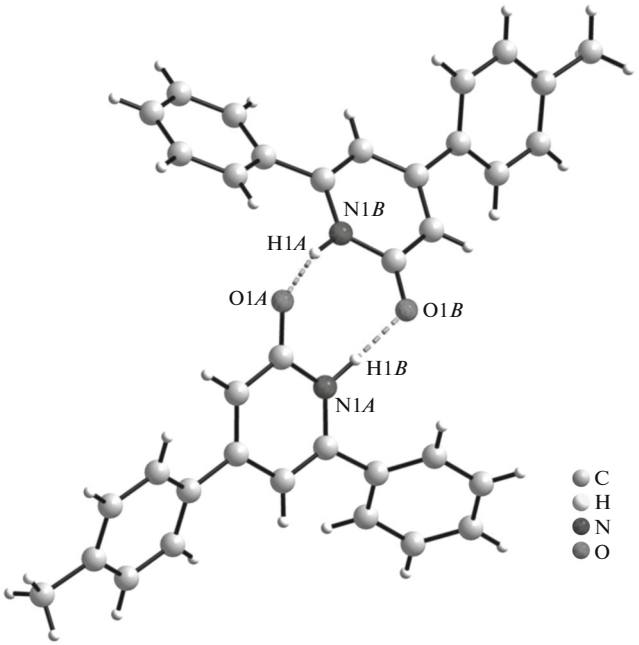


Fig. 4. H-bonded dimer in the structure of the title compound **I**.

ACKNOWLEDGMENTS

Rajni Khajuria is thankful to University Grants Commission, New Delhi for awarding her a Senior Research Fellowship.

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