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Microwave-Assistant Synthesis, Crystal Structure and Fungicidal Activity of 3-Chloro-2-hydrazinylpyridine

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A pyridine derivative *i.e.*, 3-chloro-2-hydrazinylpyridine ($C_5H_6N_3Cl$) was synthesized under microwave irradiation and its structure was studied by X-ray diffraction and ^{1}H NMR. The crystals are monoclinic, space group $p2_1/c$ with a = 11.6276 (14), b = 3.8924 (5), c = 13.9558 (17) Å, α = 90.00, β = 103.447 (6), γ = 90.00º, V = 614.31(13)Å^3, Z = 4, $F_{(000)}$ = 296, D_c = 1.552g/cm^3, μ = 0.52 cm^{-1}, the final R = 0.0623 and wR = 0.1897. A total of 7008 reflections were collected, of which 1406 were independent (R_{int} = 0.0544). The fungicidal activity of this compound was also studied.

Key Words: Microwave assistant synthesis, Crystal structure, Biological activity.

INTRODUCTION

In recent years, heterocyclic compounds had received considerable attentions because of their important biological activity[1]. So the synthesis of broader spectrum and highly bioactive compounds becomes the mainstream in the medicinal and agriculture chemistry field[2]. Pyridine derivatives also exhibited excellent property, such as nicotinate mononucleotide adenylyltransferase inhibitor[3], antifungal activity[4], antiinflammatory activity[5], antimicrobial activities[6], anticancer activity[7], antiviral activity[8], cholesterol absorption inhibitors[9]. Microwave technique has been widely used for a variety of organic reactions, such as Claisen, heterocyclic synthesis, oxidation, hydrolysis, esterification, etherification, *etc*.

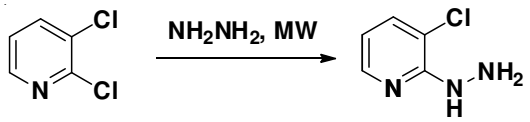
In order to search for new compounds with good biological activity, a pyridine compound was synthesized under microwave irradiation. Their structures are confirmed by ^{1}H NMR and single crystal. The preliminary biological tests show that these compounds had moderate fungicidal activity.

EXPERIMENTAL

Melting points determined by a Yanaco MP-241 apparatus and uncorrected. Infrared spectra were recorded on a Bruker Equinox55 spectrophotometer as KBr tablets. ^{1}H NMR spectra were measured on a Bruker AC-P500 instrument (300 MHz) using TMS as internal standard and $CDCl_3$ as solvent. Crystallographic data of the compound collected on a BRUCKER CCD SMART diffractometer. All chemicals were of AR grade.

Crystal structure determination: The crystal of 3-chloro-2-hydrazinylpyridine with dimensions of 0.12 mm × 0.08 mm × 0.06 mm was mounted on a Rigaku Saturn CCD area-detector diffractometer with a graphite-monochromated MoK_α radiation (λ = 0.71073 Å) by using a phi and scan modes at 294(2) K in the range of 3.1º ≤ θ ≤ 27.7º. The crystal belongs to monoclinic system with space group $P2_1/C$ and crystal parameters of a = 11.6276(14) Å, b = 3.8924(5) Å, c = 13.9558(17) Å, α = 90º β = 103.447(6)º, γ = 90º, V = 614.31(13) A^3 D_c = 1.552 g/cm^3. The absorption coefficient μ = 0.520 mm^{-1} and Z = 4. The structure was solved by direct methods with SHELXS-97 and refined by the full-matrix least squares method on F^2 data using SHELXL-97. The empirical absorption corrections were applied to all intensity data. H atom of N-H was initially located in a difference Fourier map and were refined with the restraint Uiso(H) = 1.2Ueq(N). Other H atoms were positioned geometrically and refined using a riding model, with d(C-H) = 0.93-0.97 Å and Uiso(H) = 1.2 Ueq(C) or 1.5 Ueq(Cmethyl). The final full-matrix least squares refinement gave R = 0.0623 and wR = 0.1897.

Synthesis: A modified two-phase procedure was applied. 2,3-Dichloropyridine (0.2 mol), hydrazine hydrate (85 %, 1 mol) were put in a sealed vial, then refluxed at 100 ºC for 0.5 h under microwave irradiation. The product was obtained after filtrated. ^{1}H NMR ($CDCl_3$, 400 MHz): 3.97 (br. s, 2H, NH_2), 6.21 (br. s, 1H, NH), 6.64 (m, 1H, pyridyl-H), 7.47 (d, 1H, *J* = 7.6 Hz, pyridyl-H), 8.09 (d, 1H, *J* = 4.9 Hz, pyridyl-H).



Scheme-I: Synthesis route of 3-chloro-2-hydrazinylpyridine

RESULTS AND DISCUSSION

Synthesis and spectroscopic properties: The title compound was synthesized under conventional and microwave irradiation condition. If the title compound was synthesized under refluxing, it should react with ethanolic solution of NH_2NH_2 for 72 h. Surprisingly, it was synthesized for 0.5 h under microwave irradiation. ^{1}H NMR spectrum of the title compound tested shows 3.97 and 6.21 is the peak of NH_2 and NH, respectively. The 6.647.478.09 can be assigned to the three CH of pyridine. The melting point is according to the reference.

Structure of the title compound: Crystallographic and refinement parameters are given in Table-1. The selected bond lengths and bond angles listed in Tables 2-4, respectively. The structure was solved by direct methods. Anisotropic displacement parameters were applied to all nonhydrogen atoms in full-matrix least-square refinements based on F^2. The hydrogen atoms were set in calculated positions with a common fixed isotropic thermal parameter.

TABLE-1
CRYSTAL DATA AND STRUCTURE REFINEMENT FOR THE TITLE COMPOUND

Items	Values
Empirical formula	$C_5H_6N_3Cl$
Formula weight	143.58
Crystal system	monoclinic
Space group	$p2_1/c$
Unit cell dimensions	
a (Å)	11.6276(14)
b (Å)	3.8924(5)
c (Å)	13.9558(17)
Unit cell angles (º)	
α	90
β	103.447(6)
γ	90
Volume (Å^3)	614.31(13)
Z	4
Temperature (K)	296(2)
Wavelength (Å)	0.71073
Calculated density (g/cm^3)	1.552
Absorption coefficient (mm^{-1})	0.520
$F_{(000)}$	296
Theta range for data collection (º)	1.80-27.72
Reflections collected	7008
Independent reflections	1406 [$R_{(int)}$ = 0.0544]
Final R indices [I > 2σ(I)]	R_1 = 0.0623, wR_2 = 0.1897

The molecular structure and atom labels are shown in Fig. 1. The one-dimensional linework of hydrogen bonds (dashed lines) is illustrated in Fig. 2, respectively.

In Table-3, the results indicate that the lengths of three C-N bond C5-N3, C1-N2 and N3-C1 are 1.348(5), 1.365(4) and 1.335(4) Å, respectively, which are all longer than those in the single heterocycle ring. However, the C5-N3, C1-N2

TABLE-2
SELECTED BOND LENGTHS [Å] FOR THE TITLE COMPOUND

Bond lengths	X-Ray crystal	Bond lengths	X-Ray crystal
Cl(1)-C(2)	1.740(3)	N(2)-H(2A)	0.86
N(3)-C(1)	1.335(4)	C(2)-C(3)	1.357(5)
N(3)-C(5)	1.348(5)	C(4)-C(5)	1.369(6)
N(1)-N(2)	1.403(4)	C(4)-C(3)	1.389(6)
N(1)-H(1A)	0.86	C(4)-H(4A)	0.93
N(1)-H(1B)	0.86	C(5)-H(5A)	0.93
C(1)-N(2)	1.365(4)	C(3)-H(3A)	0.93
C(1)-C(2)	1.412(4)	–	–

TABLE-3
SELECTED BOND ANGLES [º] FOR THE TITLE COMPOUND

Bond angles	X-Ray crystal	Bond angles	X-Ray crystal
C(1)-N(3)-C(5)	118.1(3)	C(3)-C(2)-Cl(1)	120.9(3)
N(2)-N(1)-H(1A)	120	C(1)-C(2)-Cl(1)	118.6(2)
N(2)-N(1)-H(1B)	120	C(5)-C(4)-C(3)	118.4(3)
H(1A)-N(1)-H(1B)	120	C(5)-C(4)-H(4A)	120.8
N(3)-C(1)-N(2)	118.4(3)	C(3)-C(4)-H(4A)	120.8
N(3)-C(1)-C(2)	120.7(3)	N(3)-C(5)-C(4)	123.8(3)
N(2)-C(1)-C(2)	121.0(3)	N(3)-C(5)-H(5A)	118.1
C(1)-N(2)-N(1)	121.5(3)	C(4)-C(5)-H(5A)	118.1
C(1)-N(2)-H(2A)	119.3	C(2)-C(3)-C(4)	118.6(3)
N(1)-N(2)-H(2A)	119.3	C(2)-C(3)-H(3A)	120.7
C(3)-C(2)-C(1)	120.5(3)	C(4)-C(3)-H(3A)	120.7

TABLE-4
SELECTED BOND ANGLES [º] TORSIONAL ANGELS (º) FOR THE TITLE COMPOUND

Bond angles	X-Ray crystal
C(5)-N(3)-C(1)-N(2)	-177.6(3)
C(5)-N(3)-C(1)-C(2)	0.4(5)
N(3)-C(1)-N(2)-N(1)	-9.2(5)
C(2)-C(1)-N(2)-N(1)	172.8(3)
N(3)-C(1)-C(2)-C(3)	-0.3(5)
N(2)-C(1)-C(2)-C(3)	177.7(3)
N(3)-C(1)-C(2)-Cl(1)	178.4(3)
N(2)-C(1)-C(2)-Cl(1)	-3.6(5)
C(1)-N(3)-C(5)-C(4)	-0.1(5)
C(3)-C(4)-C(5)-N(3)	-0.3(6)
C(1)-C(2)-C(3)-C(4)	-0.2(6)
Cl(1)-C(2)-C(3)-C(4)	-178.8(3)
C(5)-C(4)-C(3)-C(2)	0.5(6)

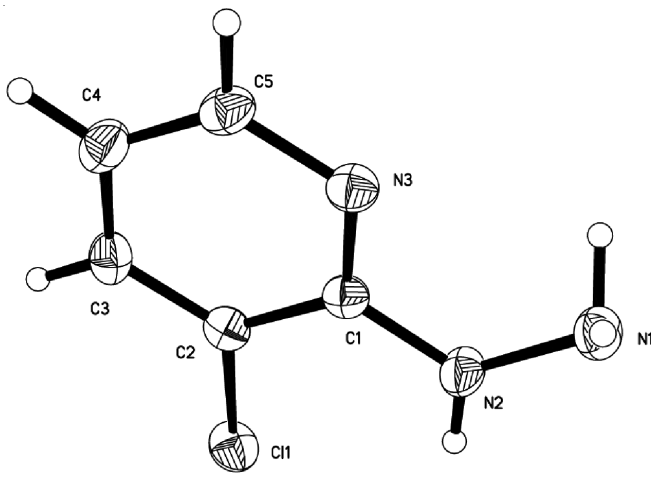


Fig. 1. Molecular structure of 3-chloro-2-hydrazinylpyridine

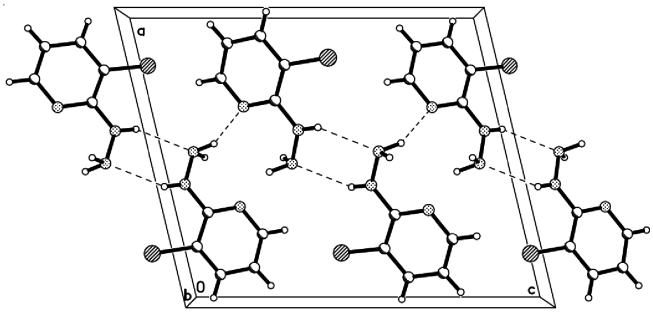


Fig. 2. The two-dimensional network of hydrogen bonds (dashed lines)

and N3-C1 are longer than the general C=N double bond length of 1.27 Å. The N1-N2 bond lengths is 1.403(4) Å. The bond angles of pyridine ring vary from 118.4(3) to 121.5(3)º with the average of 120º.

The title compound has an extensive network of hydrogen bonding involving the two acceptor atoms N. In the ac plane, they are linked together by N(1)-H(1C)···N(2)# 2, N(1)-H(1B)···N(3)# 2 hydrogen bonds. This hydrogen-bonding sequence is repeated to form a ring. The ring has two N atoms at the vertices, leading to a hydrogen-bond network defining cyclic motifs denoted $R_2^2(6)$. The vertices are shared with neighbouring decagon to form an infinite two-dimensional network of hydrogen bonds in the ac plane.

Bioassay of fungicidal activities: Fungicidal activity of title compounds against *Gibberella zeae (*Schwein.) Petch., *Alternaria solani* (Ellis et Martin) Jones et Grout., *Cercospora arachidicola, Botryosphaeria berengeriana* f.sp. *piricola* (Nose) koganezawa et Sakuma, *Fusarium oxysporum* f.sp. *cucumerinum,* were determined according the reference. At the dose of 50 μg/mL, the title compounds display moderate fungicidal activity against *Gibberella zeae (*Schwein.) Petch. (32 %), *Alternaria solani* (Ellis et Martin) Jones et Grout. (44 %), *Cercospora arachidicola* (18 %)*, Botryosphaeria berengeriana* f.sp. *piricola* (Nose) koganezawa et Sakuma (51 %), *Fusarium oxysporum* f.sp. *cucumerinum* (21 %), respectively.

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