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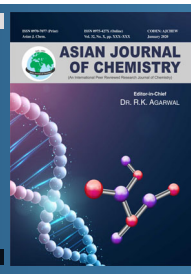

Synthesis, Characterization and Crystal Structure of 2-Pyridinecarboxamide

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2-Pyridinecarboxamide was synthesized from 2-picoline through two-steps reaction. Initially, 2-picoline was converted into 2-cyanopyridine by ammoxidation in a stainless-steel fixed-bed reactor at 370 ºC with V_2O_5 loaded on TiO_2 as catalyst. The 2-cyanopyridine was transformed into 2-pyridinecarboxamide through oxidation hydrolysis in basic solution using MnO_2 as oxidant at 70 ºC. The final product was characterized by FT-IR, NMR and UV-visible analysis, and 2-pyridinecarboxamide in the final product was determined using HPLC. The crystal structure of 2-pyridinecarboxamide was investigated using X-ray diffraction and SHELX 2018/3 (sh) software and the result indicated that 2-pyridinecarboxamide crystallized in the monoclinic system, space group P21/n with a = 5.207(2), b = 7.097(3), c = 16.243(6) Å, V = 595.7 (4) Å^3; Z = 4.

Keywords: 2-Picoline, 2-Pyridinecarboxamide, Crystal structure.

INTRODUCTION

The importance of pyridinecarboxamide as pharmaceutical and agricultural intermediates has been well established. For example, 2-pyridinecarboxamide could be used for synthesis of antipsychotic drugs [1], glucokinase activators [2] and as ligand in the formation of La(III) and Ce(III) complexes [3]. 3-Pyridinecarboxamide is the key intermediate for preparing imidazo[4,5-*c*]pyridinecarboxamide derivatives that could be utilized as PARP-1 inhibitors [4]. There are several methods could be utilized for preparing pyridinecarboxamide, such as aminification reaction of pyridinecarboxylic acid or its derivatives with ammonia [5], controlled hydrolysis of cyanopyridine [6] and conversion of pyridinecarboxaldehyde with hydroxylamine [7], *etc*. Herein, we report the synthesis of 2-pyridinecarboxamide from 2-picoline through two-steps, which includes ammoxidation and oxidation hydrolysis. The crystal structure of 2-pyridinecarboxamide also was investigated.

EXPERIMENTAL

2-Picoline, vanadium pentoxide (V_2O_5) , titanium dioxide (TiO_2) and manganese dioxide (MnO_2) were purchased from Sinopharm Chemical Reagent Co. Ltd. (Shanghai, P.R. China). All chemicals were of reagent grade and used without further purification as received.

Fourier transform infrared (FT-IR) spectrum was recorded with KBr pellets on a Nicolet Nexux FT-IR 670 spectrometer, sixteen scans at a resolution of 4 cm^{-1} were averaged and referenced against air. ^{1}H NMR spectrum was obtained with Bruker AV-500 spectrometer at 500.13 MHz and measured in D_2O solution at 30 ± 0.5 ºC and the sample was dissolved in a 5 mm diameter tube at a concentration of about 20 mg mL^{-1}. UV-visible spectrum was obtained with TU-1810 ultraviolet-visible spectrophotometer with scan interval was 400~190 nm and water as solvent. The contents of final product was determinated by L600 high performance liquid (HPLC) chromatography and X-ray diffraction was performed on a Bruker APEXII CCD diffractometer.

Preparation of catalyst: The catalyst of V_2O_5 loaded on TiO_2 was prepared according to reported method [8] with some modification. Briefly, 150 g of TiO_2 and 20 g of NH_4VO_3 were added to 50 mL deionized water. The mixture was formed into a cylindrical catalyst of 5~7 mm length and 2~4 mm diameter. The cylindrical catalyst was dried for 1.0 h at 60 ºC, then calcined for 2.0 h at 250 ºC and for 5.0 h at 750 ºC in muffle furnace. The content of V_2O_5 loading in catalyst was 8.3 mol %.

Preparation of 2-cyanopyridine: Ammoxidation for synthesizing 2-cyanopyridine was carried out in a stainless-steel fixed-bed reactor filled with the catalyst of V_2O_5 loaded on TiO_2, and the height of catalyst bed was 40 cm. The reactor was surrounded by a heating jacket to control the temperature of fixed bed at 370 ºC. The reactants were fed from the top of reactor and three calibrated flow meters were used for ammonia, air, and the mixture of 2-picoline and water, respectively. The product of ammoxidation was cooled using a condenser and 2-cyanopyridine was obtained by vaccum distillation. When the molar ratio of 2-picoline versus ammonia was 1.0:6.0 and that of 2-picoline *versus* water was 1.0:3.3, yield of 2-cyanopyridine was found to be 86.40 %.

Synthesis of 2-pyridinecarboxamide: 2-Cyanopyridine (5.20 g, 0.050 mol), 32 mL of acetone, 32 mL of 5 % aqueous solution of NaOH and 4.35 g of MnO_2 (0.050 mol) were added into reaction bottle and reacted for 3.5 h at 70 ºC with continuous stirring. The reactant was distilled under 60 ºC for removing the acetone and then filtrated to separate the remaining MnO_2 and its conversion product. The filtrate was cooled to ambient temperature for forming the crystal of 2-pyridinecarboxamide before filtration. The wet filter residue was dried at 60 ºC using vacuum drying oven and 5.14 g of 2-pyridinecarboxamide was obtained (**Scheme-I**).

X-ray crystallography: A colourless block-like crystal of 2-pyridinecarboxamide grown in acetone-H_2O ($V_{acetone}$:V_{H2O} = 1.0:1.0) with dimensions of 0.18 mm × 0.16 mm × 0.11 mm was used for structural determination. Diffraction data were collected on a Bruker APEXII CCD diffractometer by using graphite mono chromated MoKα radiation (λ = 0.71073 Å). The structure was solved by direct methods with SHELXL-97 and refined on F^2 by extinction method with SHELXL-2018/3 (sh). All the non-hydrogen atoms were refined anisotropically.

RESULTS AND DISCUSSION

FT-IR analysis: In the FT-IR spectrum of synthesized compound, the absorption bands at 3418.34 cm^{-1} was assigned to ν(N-H) of free amide, 3276.05 and 3177.21 cm^{-1} were assigned to ν(N-H) of associated amide. The peaks at 1662.77, 1602 and 1389.83 cm^{-1} were ascribed to ν(C=O), δ(N-H) and ν(C-N) of primary amide, respectively. Similarly, a band at 756.57 cm^{-1} was ascribed to γ(C-H) of monosubstituted pyridine ring and 630.41 cm^{-1} was ascribed to γ(N-H) of primary amide (Fig. 1).

NMR analysis: In ^{1}H NMR of the synthesized compound, the peaks at 8.47 and 7.50 ppm were ascribed to the proton of C4 and C5 of pyridine ring, respectively. Similarly, a peak at 7.87~7.88 ppm were ascribed to the proton of C3 and C6 of pyridine ring, whiel the peak at 4.70 ppm was ascribed to the H of primary amide and residual proton of D_2O (Fig. 2).

UV-visible analysis: In the UV-visible spectrum of 2-pyridinecarboxamide, the presence of absorbing peaks at 217 and 265 nm indicated the existence of conjugate structure in its molecule (Fig. 3).

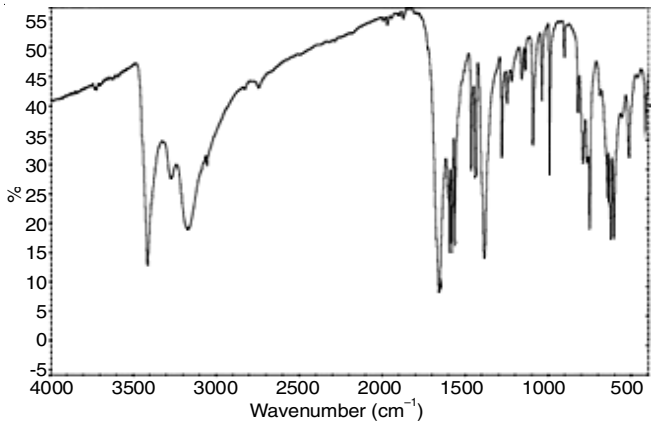


Fig. 1. FT-IR spectrum of final product

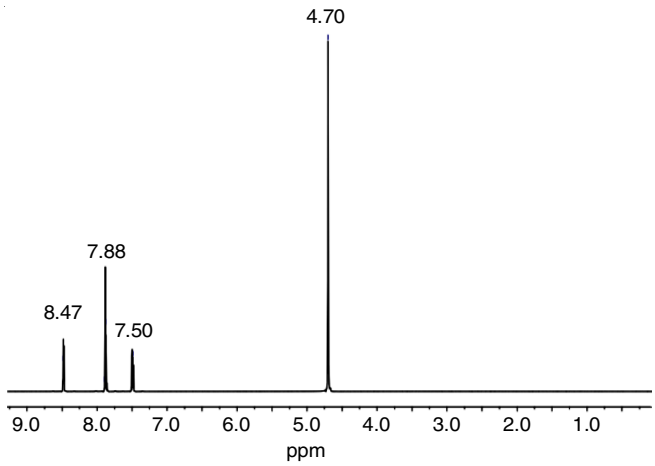


Fig. 2. ^{1}H NMR spectrum of final product

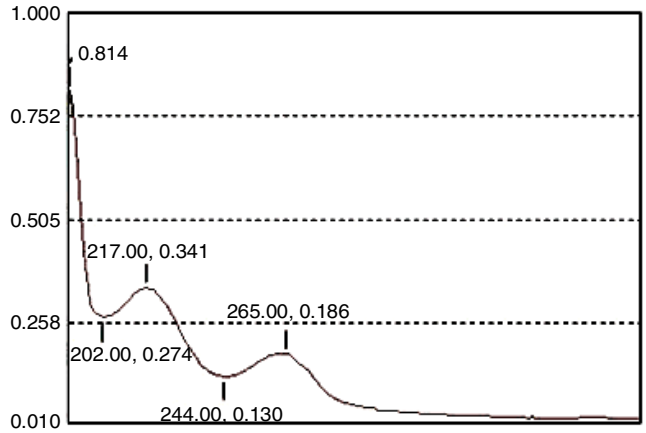
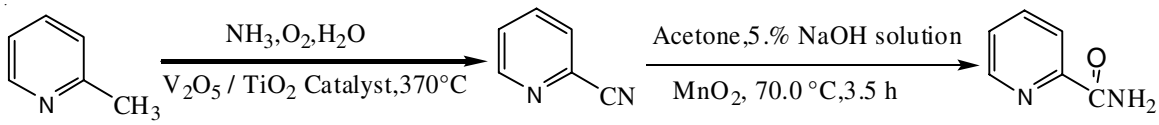


Fig. 3. UV-visible spectrum of final product

HPLC analysis: It could be seen from the HPLC spectrum that the main component in the final product was much high, and the result of area normalization indicated that the content of 2-pyridinecarboxamide in the final product was 99.87 % (Fig. 4). Thus, from the analysis of the characterization data, the synthesized product is confirmed as 2-pyridinecarboxamide.



Scheme-I: Route for preparing 2-pyridinecarboxamide

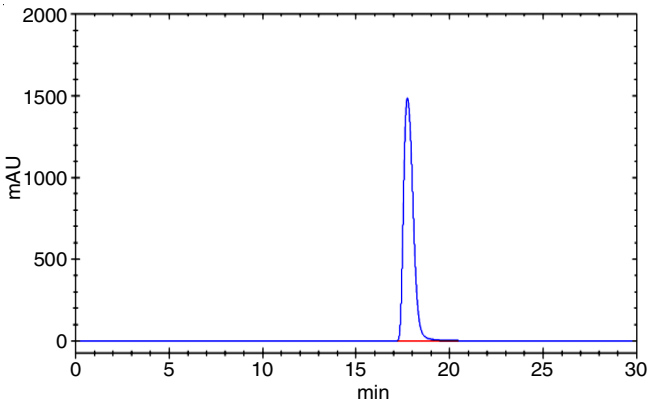


Fig. 4. HPLC spectrum of final product

Crystal structure: The crystal configuration of 2-pyridinecarboxamide was confirmed by X-ray structural analysis. The X-ray data collection is presented in Table-1 and the geometric parameters for 2-pyridinecarboxamide are listed in Table-2. The molecular structure and packing plot of 2-pyridinecarboxamide are shown in Figs. 5 and Fig. 6, respectively.

TABLE-1
CRYSTALLOGRAPHIC DATA FOR COMPOUND **II**

Item	Data or description
Formula	$C_6H_6N_2O$
Formula weight	122.13
Temperature (K)	296 (2)
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	P21/n
a (Å)	5.207(2)
b (Å)	7.097(3)
c (Å)	16.243(6)
Volume (Å^3)	595.7(4)
Z	4
Calculated density (g/cm^3)	1.362
Absorption coefficient (mm^{-1})	0.097
F(000)	256
Crystal size (mm)	0.18 × 0.16 × 0.11
Theta range for data collection (°)	2.53 to 25.00
Reflections collected/unique	3206/1039 [R(int) = 0.0304]
Completeness to theta = 25.00 (%)	99.3
Max. and min. transmission	0.989 and 0.983
Refinement method	SHELXL-2018/3 (sh)
Data/restraints/parameters	1039/0/83
Goodness-of-fit on F^2	1.048
Final R indices [I>2σ(I)]	R1 = 0.0377, wR2 = 0.0952
R indices (all data)	R1 = 0.0331, wR2 = 0.0899
Largest diff. peak and hole (e. Å^{-3})	0.127 and -0.120

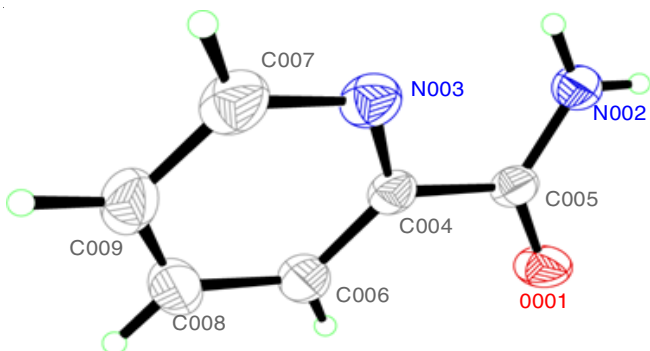


Fig. 5. Molecular structure of 2-pyridinecarboxamide

TABLE-2
GEOMETRIC PARAMETERS FOR COMPOUND **II**

Bond	Dist. (Å)	Bond	Dist. (Å)
O1–C5	1.2321 (16)	N2–C5	1.3211 (16)
N3–C4	1.3360 (16)	N3–C7	1.3380 (19)
N2-HB	0.8598	N2-HA	0.8600
C4–C6	1.3762 (19)	C4–C5	1.5018 (18)
C6–C8	1.383 (2)	C7–C9	1.368 (2)
C8–C9	1.369 (2)	C6–H6	0.9300
C7–H7	0.9299	C8–H8	0.9300
C9–H9	0.9300		
Angle	**Data (°)**	**Angle**	**Data (°)**
C4–N3–C7	116.68 (12)	C5–N2–HA	119.98
C5–N2–HB	120.00	HA–N2–HB	120.02
N3–C4–C5	116.67(10)	N3–C4–C6	123.45(12)
C5–C4–C6	119.88(10)	N2–C5–C4	116.57(10)
N3–C4–C6	123.45(12)	C5–C4–C6	119.88(10)
O1–C5–N2	123.69(12)	O1–C5–C4	119.74(10)
C4–C6–C8	118.49(13)	N3–C7–C9	123.66(14)
C6–C8–C9	118.71(14)	C7–C9–C8	118.98(14)
C4–C6–H6	120.75	C8–C6–H6	120.75
N3–C7–H7	118.19	C9–C7–H7	118.16
C6–C8–H8	120.65	C9–C8–H8	120.64
C7–C9–H9	120.51	C8–C9–H9	120.51
C7–N3–C4–C6	1.08(18)	C7–N3–C4–C5	-178.82(11)
N3–C4–C5–N2	-18.82(16)	C4–N3–C7–C9	-1.6(2)
C6–C4–C5–N2	161.28(12)	N3–C4–C5–O1	161.73(12)
C6–C4–C5–O1	-18.17(18)	N3–C4–C6–C8	0.5(2)
C4–C6–C8–C9	-1.6(2)	C5–C4–C6–C8	-179.62(12)
C6–C8–C9–C7	1.1(2)	N3–C7–C9–C8	0.5(2)

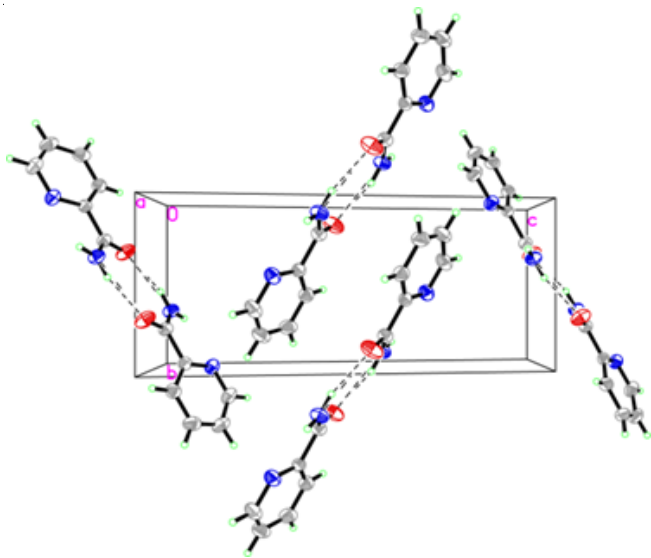


Fig. 6. Packing plot of 2-pyridinecarboxamide

According to X-ray crystallographic data, 2-pyridinecarboxamide crystallized in a P 21/n space group of the monoclinic system. The strong intramolecular N-H···N and N-H···O contacts were observed and hydrogen-bond geometry for 2-pyridinecarboxamide are listed in Table-3. And the unit cell parameters having space group P21/n with a = 5.207(2), b = 7.097(3), c = 16.243(6) Å, V = 595.7 (4) Å^3 ; Z = 4 were found.

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TABLE-3
HYDROGEN-BOND GEOMETRY FOR COMPOUND **II**

D	H	A	Dist. of D-H (Å)	Dist. of H...A (Å)	Dist. of D...A (Å)	Angle of D-H...A (°)
N2	HA	O1	0.8600	2.0900	2.933(2)	167.00
N2	HB	O1	0.8600	2.4400	3.0524(19)	129.00
N2	HB	N3	0.8600	2.3800	2.7204(19)	104.00

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. M.S. Xu, Y. Wang, F.P. Yang, C.H. Wu, Z.Wang, B. Ye, X.R. Jiang, Q.J. Zhao, J.F. Li, Y.J. Liu, J.C Zhang, G.H. Tian, Y. He, J.S. Shen and H.L. Jiang, *Bioorg. Med. Chem. Letts.,***28**, 606 (2018); https://doi.org/10.1016/j.bmcl.2018.01.038.
2. M. Mitsuya, K. Kamata, M. Bamba, H. Watanabe, Y. Sasaki, K. Sasaki, S. Ohyama, H. Hosaka, Y. Nagata, J. Eiki and T. Nishimura, *Bioorg. Med. Chem. Letts.,***19**, 2718 (2009); https://doi.org/10.1016/j.bmcl.2009.03.137.
3. X.Q. He, Q.Y. Lin, R.D. Hu and X.H. Lu, *Spectrochim. Acta A Mol. Biomol. Spectrosc.*, **68**, 184 (2007); https://doi.org/10.1016/j.saa.2006.11.012.
4. Q.H. Zhu, X.Y. Wang, Z.X. Chu, G.W. He, G.P. Dong and Y.G. Xu, *Bioorg. Med. Chem. Lett*., **23**, 1993 (2013); https://doi.org/10.1016/j.bmcl.2013.02.032.
5. K.N. Ali, A. Parhami, M.N.S. Rad and A. Zarea, *Tetrahedron Lett*., **46**, 6879 (2005); https://doi.org/10.1016/j.tetlet.2005.08.021.
6. M. Tamura, T. Tonomura, K. Shimizu and A. Satsuma, *Appl. Catal. A: Gen*., **417-418**, 6 (2012); https://doi.org/10.1016/j.apcata.2011.12.004.
7. W. Wang, X.M. Zhao, J.L. Wang, X. Geng, J.F. Gong, X.Q. Hao and M.P. Song, *Tetrahedron Lett.*, **55**, 3192 (2014); https://doi.org/10.1016/j.tetlet.2014.04.020.
8. J.B. Pan, J.M. Huang, J.X. Li, Z.Y. Jiang, J.L. Lan, C. Qian and X.Z. Chen, *Monatsh. Chem*., **145**,1365 (2014); https://doi.org/10.1007/s00706-014-1196-7.