Synthesis and Crystal Structure of 4-[2-(Methyl-pyridin-2-ylamino)ethoxy]-benzaloxime

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The title compound, C₁₅H₁₇N₃O₂, was synthesized, and the structure was characterised spectroscopically by ¹H NMR and ¹³C NMR methods, and finally confirmed by an X-ray diffraction study. The compound crystallizes in the triclinic crystal class in the space group *P* $\bar{1}$ with the following cell parameters: *a* = 7.3332(8) Å, *b* = 8.6358(7) Å, *c* = 11.7675 Å, α = 75.306(8)°, β = 73.835(9)°, γ = 89.698(8)°, *Z* = 2 and *V* = 690.63(11) Å³.

(Received September 20, 2011; Accepted January 11, 2012; Published on web April 10, 2012)

Functionalized nitrogen-heterocycles play a predominant role in medicinal chemistry. Pyridine derivatives represent a peculiar class of antiviral compounds that qualify as promising novel drugs for exploration as potential anti-HIV agents.¹ Pyridine derivatives are used in the treatment of Alzheimer's disease,² and Mycobacterium tuberculosis H37Rv,³ and as agonists at 5-HT_{1A} receptors.⁴ The pyridine nucleus is prevalent in numerous natural products, and is extremely important in the chemistry of biological systems.⁵ The title compound, 4-[2-(methyl-pyridin-2-ylamino)ethoxy]benzaloxime, is a very useful intermediate for the synthesis of many biologically active isoxazolines and isoxazoles.⁶

A microwave irradiation technique was used for synthesis of the title compound using a CEM Discover microwave apparatus. A mixture of 2-chloropyridine and 2-(*N*-methylamino)ethanol was introduced into a CEM Discover microwave vessel equipped with a magnetic stirrer. The vessel was sealed and the reaction mixture was irradiated by 300 W microwaves for 10 min at 140°C, twice successively. The resultant product was treated with 4-fluorobenzaldehyde, KOH powder and TBAHS and microwave irradiated for 20 min at 80–85°C. The aldehyde

Fig. 1 Schematic diagram of the molecule.

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Table 1 Crystal data and structure refinement

Empirical formula	C ₁₅ H ₁₇ N ₃ O ₂
Formula weight	271.32
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	<i>P</i> $\bar{1}$
Cell dimensions	<i>a</i> = 7.3332(8) Å <i>b</i> = 8.6358(7) Å <i>c</i> = 11.7675(10) Å α = 75.306(8)° β = 73.835(9)° γ = 89.698(8)°
Volume	690.63(11) Å ³
<i>Z</i>	2
Density (calculated)	1.305 Mg/m ³
Absorption coefficient	0.089 mm ⁻¹
<i>F</i> ₀₀₀	288
Crystal size	0.30 × 0.20 × 0.10 mm
Theta range for data collection	3.44° to 25.99°
Index ranges	−8 ≤ <i>h</i> ≤ 9 −10 ≤ <i>k</i> ≤ 10 −14 ≤ <i>l</i> ≤ 12
Reflections collected/Unique	5744/2697 [<i>R</i> _{int} = 0.0340]
Absorption correction	None
Refinement method	Full-matrix least-squares on <i>F</i> ²
Data/restraints/parameters	2697/0/249
Goodness-of-fit on <i>F</i> ²	0.978
Final <i>R</i> indices	<i>R</i> ₁ = 0.0539, <i>wR</i> ₂ = 0.1080
<i>R</i> indices (all data)	<i>R</i> ₁ = 0.1105, <i>wR</i> ₂ = 0.1314
Extinction coefficient	0.0141(17)
Largest diff. peak and hole	0.139 and −0.152 e Å ⁻³
Measurement	Xcalibur, Sapphire3 System
Structure Determination	SHELXS-97
Refinement	SHELXL-97
CCDC deposition number	844631

Fig. 2 ORTEP drawing of the molecule with thermal ellipsoids drawn at 50% probability.

formed was further treated with hydroxylamine hydrochloride and sodium acetate, and then microwave irradiated for 10 min at 60 – 65°C to give 4-[2-(methyl-pyridin-2-ylamino)ethoxy]-benzaldehyde. Yield = 85%. Oxime was recrystallized from ethyl acetate. Figure 1 is a schematic diagram of the molecule. The spectral data and synthetic scheme are deposited at the journal web site.

A single crystal of the title compound with dimensions of 0.30 × 0.20 × 0.10 mm was chosen for an X-ray diffraction study. The data were collected on a Xcalibur, Sapphire3 system equipped with a normal focus and a sealed X-ray source of graphite monochromated MoK α radiation. The structure was solved by direct methods using SHELXS-97.⁷ All non-hydrogen atoms were revealed in the first Fourier map, itself. A least-squares refinement using SHELXL-97 with isotropic temperature factors was performed for all non-hydrogen atoms. Subsequent refinements were carried out with anisotropic thermal parameters for non-hydrogen atoms. After a refinement, the residuals converged to 0.0539. Details of the crystal data and refinement are given in Table 1. The crystallographic data have been deposited in Cambridge Crystallographic data Center, under reference CCDC number 844631. Figure 2 is an ORTEP⁸ diagram of the molecule with thermal ellipsoids drawn at 50% probability.

The position of the N7 atom is indistorted trigonal planar geometry, as indicated by angles C8-N7-C11 = 117.5(2)°, C2-N7-C8 = 122.1(2)° and C2-N7-C11 = 120.4(2)°. The sum of three angles around atom N7 is 360°. The bond angles O14-N13-C12 = 111.6(2)°, N13-C12-C4' = 120.5(2)° are comparable with the values C7-N1-O1 = 111.47(16)°, N1-C7-C6 = 120.37(18)°, respectively, reported earlier.⁹ Also, bond angle of C9-O10-C1' = 116.2(2)° is slightly less than the corresponding value, C8-O1-C9 = 119.1(2)°, for the compound reported earlier.¹⁰ The methyl group substituted at the N7 position is in a +antiperiplanar conformation, as indicated by the dihedral angle value of 175.4(2)° for atoms C11-N7-C2-N1, which is similar to the dihedral angle value of C6-N2-C5-N1 = 176.6(6)° for a previously reported compound.¹⁰ The structure exhibits intermolecular H-bonds of the type O-H...N and C-H...O. The intermolecular hydrogen bonds are O14-H14...N1⁽ⁱ⁾, C12-H7...O14⁽ⁱⁱ⁾, and C9-H92...N13⁽ⁱⁱⁱ⁾, having lengths of 2.783(3)Å, 3.471(3)Å, 3.450(4)Å and angles 159(3)°, 175(2)°, 146.9(18)° with symmetry codes (1-x, 1-y, -z)⁽ⁱ⁾, (2-x,

Fig. 3 Packing of the molecules when viewed along the *b* axis. The dashed lines represent the hydrogen bonds.

-y, -z)⁽ⁱⁱ⁾ and (1-z, 1-y, -z)⁽ⁱⁱⁱ⁾, respectively. The stability of the crystal structure can be accounted for by these hydrogen bonds. Figure 3 shows the packing of the molecule when viewed down the *b*-axis. The dotted line represents an intermolecular hydrogen bond. The selected bond lengths and bond angles are given in Table 2S.

Acknowledgements

One of the authors, S. L. Gaonkar, thanks the Japan Society for the Promotion Of Science for Postdoctoral fellowships for Foreign Researchers-Standard.

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