

A SIMPLE AND CONVENIENT PREPARATION OF 2-CHLORO-5-METHYLPYRIDINE-3-CARBALDEHYDE IMINES[†]

B.Gangadasu, B.China Raju* and V.Jayathirtha Rao*

Organic Chemistry Division -II
Indian Institute of Chemical Technology
Hyderabad-500 007, India.

Abstract: A series of new 2-chloro-5-methylpyridine-3-carbaldehyde imines **3a-o** were prepared conveniently by the reaction of 2-chloro-5-methylpyridine carbaldehyde **1** and amines **2a-o** in excellent yields.

Introduction

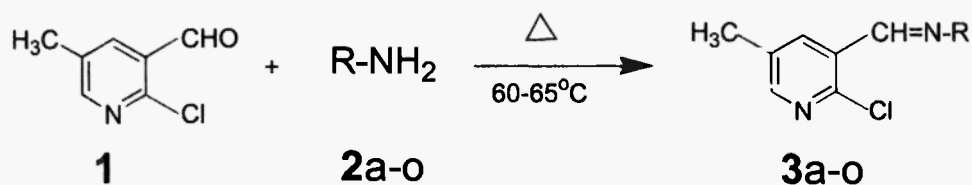
The imines¹ are an important synthetic organic compounds in that they have been reported as potential herbicides², fungicides³, neoplasm inhibitors⁴, antiviral⁵, anti convulsants⁶, anti microbial⁷, anti cancer & tubercular⁸, as plant growth regulators⁹, and also have role in biology (vision and ATP synthesis).¹⁰⁻¹¹ Pyridine Schiff bases are very good synthons for the preparation of α -nornicotin derivatives¹² and as pesticides¹³. The most of the Schiff base reactions are acid catalyzed and are generally carried out by refluxing the carbonyl compounds and amines^{1b} in a suitable solvent. Imine formation between aliphatic aldehydes & amines requires mild conditions like low temperatures¹⁴. Some Schiff base preparations were carried out using titanium chloride catalyst¹⁵, Lewis acids¹⁶, alumina¹⁷ catalysts and the liberated water removal was achieved by azeotropic means, using KOH/NaOH base and also molecular sieves¹⁸.

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Results and Discussion

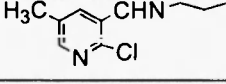
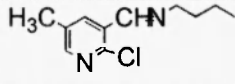
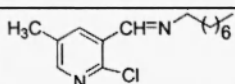
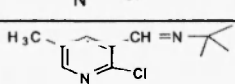
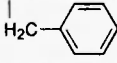
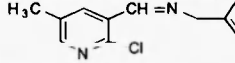
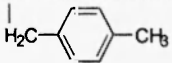
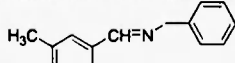
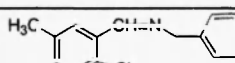
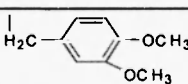
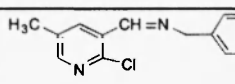
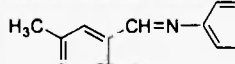
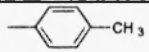
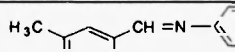
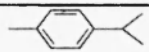
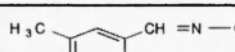
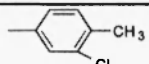
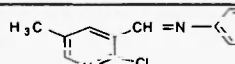
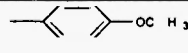
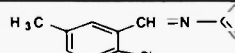
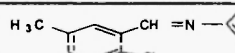
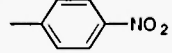
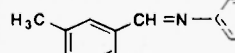
In continuation of our work on biologically active molecules¹⁹, and on pesticidal compounds²⁰, makes us here to report a simple and convenient preparation of a series of new 2-Chloro-5-methylpyridine-3-carbaldehyde derived imines. 2-Chloro-5-methylpyridine-3-carbaldehyde was prepared by acetylating the propionaldehyde/benzylamine Schiff base and the resulting enamide was cyclized under Villsmeyer formylation conditions to give the corresponding aldehyde²¹. Thus prepared 2-Chloro-5-methylpyridine-3-carbaldehyde²² was used to synthesize a series of new imines (Schiff bases) in excellent yields. The results of these studies are arranged in Table. The general synthetic reaction is depicted in Scheme. The synthesized imines were characterized by spectral means and the spectral data is provided in experimental section.

Scheme



Experimental section

¹H NMR spectra were recorded on a Gemini (200MHz) Spectrometer in CDCl₃ using TMS as internal standard. IR spectra were recorded on a Nicolet 740 FTIR Spectrometer and Mass spectra on a VG Micro Mass 7070H. The melting points were determined in open glass capillaries on Toshniwal melting point apparatus and are uncorrected.

No.	Amine R =	Temp. °C	Time hr	Product	Mp °C	% Yield
1	$-(CH_2)_2-CH_3$	65	1	 3a	liquid	98
2	$-(CH_2)_3-CH_3$	65	1	 3b	liquid	99
3	$-(CH_2)_7-CH_3$	65	1	 3c	42	98
4	$-C-(CH_3)_3$	65	1	 3d	liquid	98
5		65	1	 3e	liquid	98
6		65	1	 3f	liquid	98
7		72	2	 3g	80	92
8		80	3	 3h	liquid	65
9		65	1	 3i	liquid	98
10		65	1	 3j	58	96
11		65	1	 3k	liquid	94
12		65	3	 3l	123	85
13		65	1	 3m	84	90
14		90	3	 3n	106	75
15		110	4	 3o	144	60

Preparation of 3a-o; General procedure:

2-Chloro-5-methylpyridine-3-carbaldehyde **1** (0.2 g, 0.00129 moles) and n-prop amine **2a** (0.076 g, 0.00129 moles) was heated to 60-65°C in an oil bath for one hour. The reaction mixture was cooled and extracted with dichloromethane. The organic layer was

separated, dried over sodium sulfate. The solvent was removed under reduced pressure to give the liquid 3a in 98% (0.247 g) Yield.

Spectral Data:

3a. $^1\text{H-NMR}$ (200 MHz, CDCl_3): δ 0.98 (t, 3H, CH_3), 1.70 (m, 2H, CH_2), 2.37 (s, 3H, CH_3), 3.62 (t, 2H, N-CH_2), 8.12 (s, 1H, hetero aromatic), 8.22 (s, 1H, hetero aromatic), 8.58 (s, 1H, -N=CH); IR (Neat CHCl_3): 2960, 1640, 1480, 1080 cm^{-1} ; MS: M^+ , m/z 195.

3b. $^1\text{H-NMR}$ (200 MHz, CDCl_3): δ 0.88 (t, 3H, CH_3), 1.24 (m, 2H, CH_2), 1.68 (p, 2H, CH_2), 2.38 (s, 3H, CH_3), 3.64 (t, 2H, -N-CH_2), 8.14 (s, 1H, hetero aromatic), 8.20 (s, 1H, hetero aromatic), 8.58 (s, 1H, -N=CH); IR (Neat CHCl_3): 2960, 1640, 1480, 1080 cm^{-1} ; MS: M^+ , m/z 210.

3c. $^1\text{H-NMR}$ (200 MHz, CDCl_3): δ 0.92 (t, 3H, CH_3), 1.35 (m, 10H, 5CH_2), 1.68 (m, 2H, CH_2), 2.38 (s, 3H, CH_3), 3.62 (t, 2H, -N-CH_2), 8.14 (s, 1H, hetero aromatic), 8.20 (s, 1H, hetero aromatic), 8.58 (s, 1H, -N=CH); IR (Neat CHCl_3): 2980, 1650, 1480, 1080 cm^{-1} ; MS: M^+ , m/z 266.

3d. $^1\text{H-NMR}$ (200 MHz, CDCl_3): δ 1.30 (s, 9H, 3CH_3), 2.38 (s, 1H, CH_3), 8.14 (s, 1H, hetero aromatic), 8.20 (s, 1H, hetero aromatic), 8.56 (s, 1H, -N=CH); IR (Neat CHCl_3): 2960, 1650, 1470, 1070 cm^{-1} ; MS: M^+ , m/z 210.

3e. $^1\text{H-NMR}$ (200 MHz, CDCl_3): δ 2.38 (s, 3H, CH_3), 4.88 (s, 2H, N-CH_2), 7.38 (m, 5H, aromatic), 8.24 (s, 1H, hetero aromatic), 8.30 (s, 1H, hetero aromatic), 8.78 (s, 1H, -N=CH); IR (Neat CHCl_3): 3030, 2940, 1650, 1440, 1360, 1080 cm^{-1} ; MS: M^+ , m/z 244.

3f. $^1\text{H-NMR}$ (200 MHz, CDCl_3): δ 2.38 (s, 6H, 2CH_3), 4.82 (s, 2H, -N-CH_2), 7.10-7.25 (m, 4H, aromatic), 8.24 (s, 1H, hetero aromatic), 8.28 (s, 1H, hetero aromatic), 8.72 (s, 1H, -N=CH); IR (Neat CHCl_3): 3040, 2950, 1640, 1460, 1070 cm^{-1} ; MS: M^+ , m/z 258.

3g. $^1\text{H-NMR}$ (200 MHz, CDCl_3): δ 2.38 (s, 3H, CH_3), 4.80 (s, 2H, N-CH_2), 7.18 - 7.38 (m, 4H, aromatic), 8.20 (s, 1H, hetero aromatic), 8.26 (s, 1H, hetero aromatic), 8.72 (s, 1H, -N=CH); IR (Neat CHCl_3): 3400, 1640, 1240, 1040 cm^{-1} ; MS: M^+ , m/z 279.

3h. $^1\text{H-NMR}$ (200 MHz, CDCl_3): δ 2.37 (s, 3H, CH_3), 3.82 (s, 3H, -OCH_3), 3.84 (s, 3H, -OCH_3), 4.78 (s, 2H, -N-CH_2), 6.80 (m, 3H, aromatic), 8.20 (s, 1H, hetero aromatic), 8.24 (s, 1H, hetero aromatic), 8.70 (s, 1H, -N=CH); IR (Neat CHCl_3): 2940, 2840, 1655, 1490, 1250 cm^{-1} ; MS: M^+ , m/z 304.

3i. $^1\text{H-NMR}$ (200 MHz, CDCl_3): δ 2.40 (s, 3H, CH_3), 7.18-7.32 (m, 3H, aromatic), 7.38-7.42 (m, 2H, aromatic), 8.30 (s, 1H, hetero aromatic), 8.38 (s, 1H, hetero aromatic), 8.80

(s, 1H, -N=CH); IR (Neat CHCl₃): 2940, 1640, 1450, 1380, 1080 cm⁻¹; MS: M⁺, m/z 230.

3j. ¹H-NMR (200 MHz, CDCl₃): δ 2.40 (s, 3H, CH₃), 2.42 (s, 3H, CH₃), 7.12 - 7.20 (m, 4H, aromatic), 8.30 (s, 1H, hetero aromatic), 8.40 (s, 1H, hetero aromatic), 8.82 (s, 1H, -N=CH); IR (Neat CHCl₃): 2950, 1650, 1480, 1360, 1080 cm⁻¹; MS: M⁺, m/z 244.

3k. ¹H-NMR (200 MHz, CDCl₃): δ 1.30 (d, 6H, 2CH₃), 2.40 (s, 3H, CH₃), 2.98 (m, 1H, -CH), 7.18 (m, 2H, aromatic), 7.26 (m, 2H, aromatic), 8.30 (s, 1H, hetero aromatic), 8.38 (s, 1H, hetero aromatic), 8.80 (s, 1H, -N=CH); IR (Neat CHCl₃): 2960, 1640, 1480, 1090 cm⁻¹; MS: M⁺, m/z 272.

3l. ¹H-NMR (200 MHz, CDCl₃): δ 2.42 (s, 6H, 2CH₃), 7.20 - 7.26 (m, 3H, aromatic), 8.30 (s, 1H, hetero aromatic), 8.36 (s, 1H, hetero aromatic), 8.80 (s, 1H, -N=CH); IR (Neat CHCl₃): 2950, 1640, 1480, 1410, 1360 cm⁻¹; MS: M⁺, m/z 278.

3m. ¹H-NMR (200 MHz, CDCl₃): δ 2.42 (s, 3H, CH₃), 3.82 (s, 3H, OCH₃), 6.82 - 6.88 (m, 2H, aromatic), 7.20 - 7.32 (m, 2H, aromatic), 8.24 (s, 1H, hetero aromatic), 8.36 (s, 1H, hetero aromatic), 8.80 (s, 1H, -N=CH); IR (Neat CHCl₃): 2940, 1640, 1470, 1240, 1080 cm⁻¹; MS: M⁺, m/z 260.

3n. ¹H-NMR (200 MHz, CDCl₃): δ 2.42 (s, 3H, CH₃), 7.02 - 7.18 (m, 2H, aromatic), 7.24 - 7.40 (m, 2H, aromatic), 8.38 (s, 1H, hetero aromatic), 8.42 (s, 1H, hetero aromatic), 8.76 (s, 1H, -N=CH); IR (Neat CHCl₃): 2960, 1640, 1480, 1340, 1080 cm⁻¹; MS: M⁺, m/z 309.

3o. ¹H-NMR (200 MHz, CDCl₃): δ 2.42 (s, 3H, CH₃), 7.28 (m, 2H, aromatic), 7.32 (m, 2H, aromatic), 8.30 (s, 1H, hetero aromatic), 8.34 (s, 1H, hetero aromatic), 8.80 (s, 1H, -N=CH); IR (Neat CHCl₃): 3480, 3340, 2960, 1640, 1480, 1100 cm⁻¹; MS: M⁺, m/z 275.

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