*Available online at*www.scholarsresearchlibrary.com

Scholars Research Library

Archives of Applied Science Research, 2015, 7 (7):8-11
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-508X
CODEN (USA) AASRC9

A base mediated synthesis and characterization of some pyridine-3-carbohydrazides

B. Lourdu Rani and B. Hari Babu*

Department of Chemistry, Acharya Nagarjuna University, Guntur, AP-India

---

ABSTRACT

A base mediated synthetic method was developed for the synthesis of series of pyridine-3-carbohydrazide (Schiff base) derivatives from ethylnicotinate. The nicotinichydrazide required was obtained from ethylnicotinate on treatment with hydrazine monohydrate in eco-friendly conditions. Nicotinichydrazide reacted with various aromatic aldehydes in ethanol in presence of base to give the Schiff base derivatives ***(3a-3k).*** *The reactions were monitored by TLC. The structure of all synthesized compounds ware established on the basis of their spectral (IR, H^1&C^{13} NMR and Mass) and analytical data.*

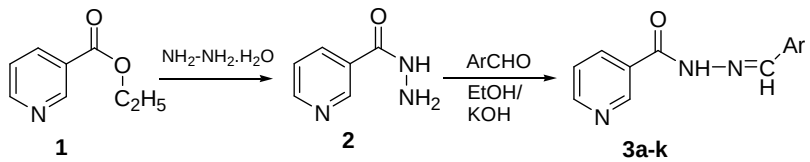
Keywords: Ethylnicotinate, nicotinichydrazide, Schiff base, pyridin-3-carbohydrazides.

INTRODUCTION

Generally Schiff bases are formed by the condensation of a primary amine with a carbonyl compound by heating or in presence of either acid or base. Moreover, the Schiff bases formed from aromatic aldehydes, having an extended conjugation, are more stable [4-7] and those of aliphatic systems are relatively less stable and may readily undergo polymerization [1-3]. The formation of a Schiff base from an aldehydes or ketones is a reversible reaction. Many Schiff bases can be hydrolysed back to their aldehydes or ketones and amines by aqueous acid or base.

Further, Schiff bases were found in number of enzymatic reactions concerning interaction of an enzyme [8] with an amine group or a carbonyl group of the substrate. One of the most widespread types of catalytic mechanisms in biochemical processes involves condensation of a primary amine, usually that of a lysine residue, with a carbonyl group of a substrate [9] to form Schiff base. A rapid development in this field resulted in the synthesis of many biologically important Schiff bases; having antibacterial [10-14], antifungal [15-17], antioxidant [18], anticonvulsant [19], anti HIV[20], anti-inflammatory[21] and anti tumor[22 - 23] activity.

Recently the author reported [24] a acetic acid-ethanol mediated method for the synthesis of novel Schiff bases from nicotinic hydrazide which was prepared by refluxing ethyl nicotinate with hydrazine hydrate in presence of ethanol medium for 16hrs. In further development of this methodology an attempt was made to develop a base mediated method for the synthesis of titled compounds and the intermediate nicotinic hydrazide was obtained by a neat reaction between ethyl nicotinate and hydrazine monohydrate (scheme 1).



1 **2** **3a-k**

Scheme 1: Synthesis and Characterization of Some Pyridine-3-Carbohydrazides

MATERIALS AND METHODS

The melting points were determined by open capillaries on Meltemp made melting point apparatus and are uncorrected. The progress of the reaction was monitored by pre coated silica gel plates (0.25mm, 60 F254, MERCK) using hexane and ethylacetate (6:4) mobile phase. The IR Spectra were recorded on Bruker FTIR Spectrophotometer; ^{1}H and ^{13}C Spectra were recorded on Bruker AMX, 400MHz/100 MHz (TMS is used as an internal standard) spectophotometers. The mass spectra were recorded on agilent 1100 ESI-MASS (Turbospray) spectrometer. All the chemicals and solvents used were of AR grade, ethylnicotinate and hydrazine monohydrate were obtained from Sigma Aldrich.

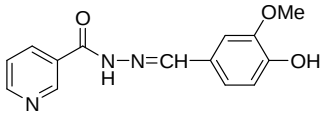
2.1 Synthesis of Nicotinichydrazide

A mixture of 15.1gm (0.1mol) of ethylnicotinate and 10gm (0.2mol) of hydrazine monohydrate was taken in round bottom flask and then stirred continuously for overnight. After completion of the reaction which was monitored by TLC using Hexane/Ethylacetate 6:4 mobile phase the reaction mixture was poured into crushed ice. The white precipitate obtained in the aqueous medium was separated and recrystallised from ethanol. Finally it was confirmed by its spectral data IR, NMR, mass by comparing with the literature data.

2.2 Synthesis of compounds (3a-3k):

The above synthesised compound i.e. nicotinichydrazide 137mg, (1 mmol.) and substituted aldehyde (1 mmol.) were dissolved in absolute ethanol (5 mL), added KOH base (4 mmol) and stirred for 3 hrs. The reaction was monitored by TLC using hexane: ethylacetate (6:4) as mobile phase (R_f = 0.5-0.7). After the completion of the reaction, the mixture was poured into ice cold water and filtered for final product. Finally, the compounds were purified recrystalization from ethanol. The spectral data and physical constants of the known compounds **3a-j** were compared with the literature data.

2.3. Spectral data of N^1-(3^1-methoxy &4^1-hydroxy benzilidine)-pyridin-3-yl–carbohydrazide(3k).



m.p: 182-184 ºC; yield (%): 94; Rf: 0.62; Molecular formula: $C_{14}H_{13}N_3O_3$; Molecular weight: 271; **IR (cm^{-1}):** 3352 (N-H Str), 3070 (=C-H str), 1653 (C=O Str), 1596 (C=C Str), 1510 (C=N Str), 1275 (C-O-C Str). **H^1 NMR (d6, DMSO, 400MHz):** δ 12.36 (1H, s, N-H), 9.31 (1H, s, H-2), 8.94 (1H, d, *J* = 4.0Hz, H-6), 8.72 (1H, d, *J* = 4.0Hz, H-4), 8.47 (1H, s, =CH), 7.92 (1H, t, *J* = 6.0Hz, H-5), 7.33 (1H, s, H-2'), 7.12 (1H, d, *J* = 8.0Hz, H-6'), 6.88 (1H, d, *J* = 8.0Hz, H-5'). **^{13}C NMR (D6, DMSO, 100MHz)**: δ 159.7, 149.6, 149.4, 148.0, 147.9, 144.9, 140.0, 130.8, 125.4, 122.3, 115.5, 109.4, 55.6.

RESULTS AND DISCUSSION

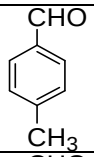
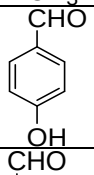
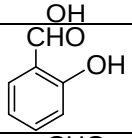
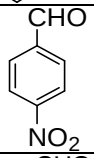
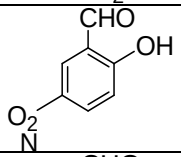
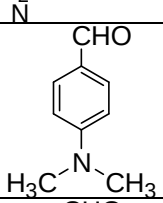
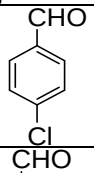
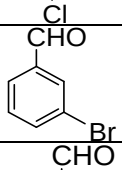
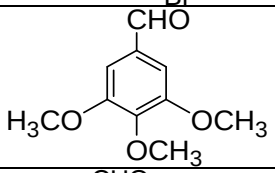
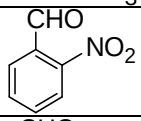
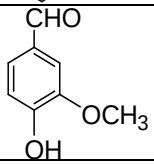
3.1. Synthesis of Schiff base derivatives

The Schiff base derivatives (**3a-3k**) were synthesized by treating of nicotinichydrazide with various aldehydes in presence of base followed by continuous stirring for 3 hours and the reaction was monitored by TLC using hexane/ethylacetate (6:4) as mobile pahse, followed by pouring it in to ice cold water and filtered off. These compounds were purified recrystalization from ethanol. The details of the yields and melting points of the compounds were presented in Table 1. These compounds were further conformed by their spectral data like IR, NMR and mass spectral data.

3.2. Analysis of Spectral data

For the compounds (**3a-3k**), the N-H stretching values are in the range of 3568-3303 cm^{-1}, double bonded C-H stretching frequency is observed in the range of 3052-3256 cm^{-1}. Among the synthesized compounds **3a**, **3d**, **3g**, **3h, 3j** & **3k** showed C=O stretching frequency approximately same value (1653-1668 cm^{-1}) as observed for nicotinichydrazide (1661cm^{-1}). It is noticed that for **3c**,**3e**,**3f** and **3i** compounds the C=O frequency is decreased (1601-1646 cm^{-1}) which is due to weakening of C=O bond. High C=O frequency stretching observed for compound **3a** (1671 cm^{-1}). Synthesized compounds showed C=N stretching frequency in the range of 1552-1601 cm^{-1}.

Table 1: Synthesis of pyridin-3-carbohydrazides

Entry	ArCHO	Product	mp's (°C)	Yield
1		**3a**	90-92	97.7%
2		**3b**	230-232	92.5%
3		**3c**	172-174	90.9%
4		**3d**	250-252	89.0%
5		**3e**	260-262	98.5%
6		**3f**	140-144	94.0%
7		**3g**	230-232	91.5%
8		**3h**	100-102	92%
9		**3i**	150-152	85%
10		**3j**	150-160	88%
11		**3k**	182-184	94%

The chemical shift values of N-H, =C-H protons are deshielded in presence of electron withdrawing groups on ring 'B' indicating the values are little bit higher than normal values. In case electron releasing groups on ring B the protons are shielded which means the chemical shift values are going up field hence the values decrease.

3.3. Yields of the products

An examination of the yields of the condensation products (**3a-k**), the presence of strong withdrawing and strong releasing groups in *ortho*- and *para*- positions the yields are low when compared to the electron withdrawing group present in meta- position and weak electron releasing groups present in *ortho* and *para*- position. i.e. why the entry '1' and '5' showed impressive yields.

CONCLUSION

A base mediated method was developed for the synthesis of pyridine-3-carbohydrazide schiff's bases. The synthesized new compounds are characterized by spectral data. These spectral values depends on the substituents which are present on the phenyl ring. Activating groups present on the phenyl ring showed high stretching frequency. Withdrawing groups decreases the electron density and resulted into high desheilding. So highly desheilding nuclei show high chemical shift values. The electron withdrawing group present in meta- position and weak electron releasing groups present in ortho and para- positions increased the yields.

Acknowledgments

The design of synthetic work, calculations of melting point and R_f values of research work was completely performed at Chemistry Laboratory of Acharaya Nagarjuna university. The analysis work of this designed compounds characterized by ^{1}H NMR , ^{13}C NMR and Mass spectroscopy at Laila Impex Laboratory , vijayawada.

REFERENCES

[1] Young, D.W.; *Heterocyclic Chemistry*., 1st Ed, London: Longman group Ltd., **1975**.
[2] MC Naught, A.D.; Wilkinson, A.; *IUPAC*, compendium of chemical terminology., 1st Ed, Oxford: Blackwell Scientific Publications, **1997.**
[3] C.M. Brewster, *J. Am. Chem. Soc*., **1924**, 46(11), 2463.
[4] A.M. Awadallah, El-Halabi, *J. Islamic University of Gazo*, **2010**,13(2), 85.
[5] F.A. Carey, R.A. Sundberg, *Advanced Orgnic Chemistry*., 5th Ed, New York: Springer**; 2007**.
[6] J. Hine, C.Y. Yeh, *J. Am. Chem. Soc*., **1967,** 89, 2669.
[7] I. A. Savich,; A. K. Pikaev,; I.A. Lebedev,; V. I. Spitsyn,; *Vestnik. Moskov. Univ*., **1956,** II, 225.
[8] G. M. Loudon,; *Organic Chemistry*, Addison-Wesley, California, 4thEd, **2002**, 874.
[9] A.L. Lehlinger, *Biocemistry*, Wort publisher, 2nd Ed , **1975**, 84,85,220,563.
[10] P. Paneerselvem,; R.R. Nair, G. Vijayalakshmi,; E.H. Subramanian,; S.K. Sridhar, *Eur. J. Med. Chem.*, **2005**,40(2), 225.
[11] S.K. Sridhar, M. Saravan, A. Ramesh, *Eur. J. Med. Chem.*, **2001**, 36,6, 15-25.
[12] S. V. More, D. V. Dongarkhadekar, R. N. Chavan, W. N. Jadhav, S. R. Bhusare, R. P. Pawar, *J. Indian Chem. Soc.*, **2002**, 79, 768-769**.**
[13] S. K. Sridhar, M. Saravanan, A. Ramesh, *European Journal of Medicinal Chemistry*, **2001**, 36, 7, 615–625.
[14] A.S. Rathod, B.N. Berad, A.G. Dhoshi, *Oriental J. Chem*, **1997**,13, 3, 269-272.
[15] S.P. Rajendran, R. Karvembu, *Indian Journal of Chemistry*, **2002,** 41B, 222-224.
[16] U. Calis, M. Yarim, M. Koksal, M. Koksal, M. Ozalp, *Arzneimittel for schung*, **2002**, 52,10, 778-81.
[17] K.A. Sheikh, M.A. Baseer, N.A. Mote, *Asian J.Chem.*, **2001,**13,496.
[18] M.D. Deshmuk, A.G. Doshi, *Orient. J. Chem.*, **1995,** 11, 1, 85.
[19] S.K. Sridhar, S.N. Pandeya, J.P. Stables, A. Ramesh, *Eur. J. Parm. Soc*., **2002,** 16, 3, 129.
[20] S.K. Sridhar, S.N. Pandeya, E. De Clereq, *BollettinoChimico Farmaceutic*, **2001,** 140, 5, 302.
[21] S. Sridhar, A. Ramesh, *Indian Drugs*, **2001,** 38, 4, 174.
[22] S.B. Desai, P.B. Desai, K.R. Desai, *Heterocyclic Communications*, **2001,** 7(1), 83.
[23] P. Pathak, V.S. Jolly, K.P. Sharma, *Oriental. J. Chem.*, **2000,** 16, 161.
[24] B.Lourdu Rani, N. Madhavi, *Int. J Pharm. Res. Dev.*, **2013**, 5(7), 7.