International Journal of Recent Research and Review, Vol. XIII, Issue 2, June 2020
ISSN 2277 – 8322

A Facile Synthesis and Characterization of Some Novel Naphthyridinic Acids

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***Abstract*- In this work, some naphthyridinic acids were synthesized by the adoption of Dohbner reaction. The method involves the reaction of benzaldehde and derivatives either the 2-amino pyridine or 3-amino pyridine, the ring closure followed by the addition of pyruvic acid to give 2-phenyl -4-carboxy -1,8-naphthyridine or 1,5-naphthyridine derivatives respectively. The synthesis of 2-morpholino-4-carboxy-1,8-naphthyrine has also been achieved.The synthesized mono and bis- hydrazones were characterized on the bases of their physical properties and spectroscopic data.**

***Keywords*-1,8-naphthyridine,1,5-naphthyridineDohbner reaction,amino pyridine**

I. INTRODUCTION

Naphthyridine compounds are a class of aromatic heterocyclic chemical compounds that have the formula C8H6N2. They consist of a naphthalene double ring in which two of the carbon atoms have been replaced with nitrogen atoms. There are ten positional isomers, which differ by the locations of the nitrogen atoms .1,8-naphthyridine derivatives have received the most study in the last 30 years [1] and have gained special attention of researchers on account of their demonstrating avariety of interesting biological activities. A wide range of biol. properties establishes them as potent scaffolds in therapeuticand medicinal research. The broad spectrum of activities primarily includes antimicrobial, antiviral, anticancer, anti-inflammatory and analgesic activities [2].The 1,8-naphthyridine deriv. approved as the drug with antibacterial activity [3]. The effect of some substituted 1,8-naphthyridine derivatives has been investigated for their antimicrobial activity [4]and as antitumor agents[5].Substituted 2-aminopyridines, in particular, 2-amino-3-for-mylpyridine and its derivatives, possess much higher synthetic potential 1,8–naphthyridinecompounds [6-8]. While, some of 1,5-naphthyridine derivatives are potent and selective inhibitors of the transforming growth factor[9],also Substituted 1,5-naphthyridine derivatives as novel antileishmanial agents[10]

II. EXPERIMENTAL

Melting points were determined usingelectro thermal 9300 melting point apparatus and are uncorrected. Infrared (FT-IR) spectra were recorded as (KBr) disc using a Bruker, FT-IR, and Spectrophotometer Tensor 27. Ultra-Violet (U.V) spectra were performed on Shimadzu UV-Visible Spectrophotometer UV-1650 PCusing ethanol as a solvent. NMR spectra were recorded using (AS 100MHz) with TMS as internal standard, and DMSO-d_6 as solvents; [(s) singlet; ((m) multiplet],

General method for synthesis of 2-substitutedphenyl -4-carboxy-1,8-naphthyrdine(2a-h):[11,12]

Heating of (0.025 mole) substituted benzaldehyde in (10 ml) of absolute ethanol to 30˚C,to this solution of substituted 2-amino pyridine (0.025mole) in (5ml) absolute ethanol was added with stirring and heating at (30 - 35˚C) ,then (0,025 mole) of pyruvic acid was added drop by drop with vigorous stirring. Then refluxed for (12hrs.) with stirring and kept overnight at room temperature. The contents were coolingand the precipitate was filtered off and recrystallized from suitable solvent to obtain the desired products **(2a-h)** , the physical and spectral data were listed in Tables(I and II).

Synthesis of 2-morpholino-4-carboxy-1,8-naphthyrdine(2i):

By using the above general method and using 2-amino pyridine and 4-morpholine carbaldehyde. The

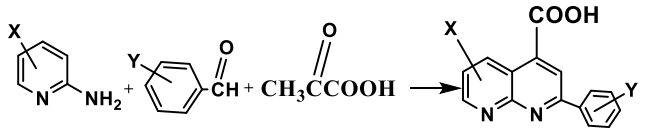
excess solvent was distilled off, cooled and the solid product was filtered off, washed with cold water and then recrystallized from ethanol. To obtained a solid product as brown color (yield 27%,m.p.112-114).

General method for synthesis of 2-substitutedphenyl -4-carboxy-1,8-naphthyrdine(3a,b):

By using the above general method and using 3-amino pyridine and benzaldehyde or 3,4 –dimethoxy benzaldehyde and refluxed at about (14hrs.) and kept overnight at room temperature .The excess solvent was distilled off, cooled and the solid product was filtered off, then recrystallized from petroleum ether(40-60) yielded (3a and 3b) respectively .

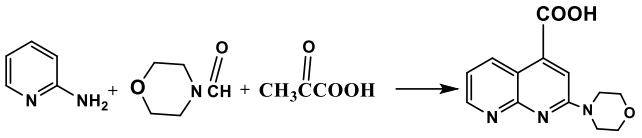
III. RESULTS AND DISSCUSION

2-Aminopyridine and 3-aminopyridine are used as good essential group to give the required product represented by compounds substituted 1,8-naphthyridine and 1,5-naphthyridine respectively by reaction with substituted benzaldehyd in the presence of pyruvic acid. On treatment of substituted 2-amino pyridine with substituted benazldehyde and pyruvic acid gave the target 2-substitutedphenyl -4-carboxy-1,8-naphthyrdine(2a-h) as shown below scheme 1.



Scheme 1

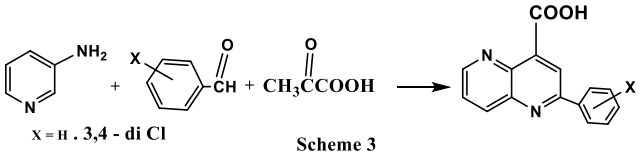
The structure of these compounds were confirmed by (C.H.N microanalysis) and spectroscopicanalysis, FT-IR and U.V and ^{1}HNMR, Table (1) in IR spectra these compounds showed the following stretching bands; at the range (3300-3500cm^{-1}) due to the (OH) bond, (1700-1730 cm^{-1}) for the (C=O) of carboxylic bond. (1645-1650 cm^{-1}) stretching for (C=N)group and (1470-1600cm^{-1}) due to (C=C) group,while The ^{1}H-NMR spectra for compounds (2a-h) in (DMSO-d_6)as shown in table III, showed singlet bands in therange(10.4-11-7ppm) due to OH group also singletbands at the range (8.4-8.8) due to H_3in these compounds,in addition the multiplet peaks for aromatic parts in the rang (6.9-8.7ppm).Also 2-morpholino-4-carboxy-1,8- naphthyridine(2i) was formed by the same reaction scheme 2 .



Scheme 2

The compound (2i) in IR spectra showed the following stretching bands; at the range (3300-3700cm^{-1}) due to (OH) bond, (1710 cm^{-1}) for the(C=O) of carboxylic bond. (1650cm^{-1}) stretching for (C=N) group and (1600cm^{-1}) due to (C=C) group, while The ^{1}H-NMR spectra for compounds (2a-h) in (DMSO-d_6) as shown in table III showed singlet bands in (11ppm) due to OH group also singlet bands at the range (8.4ppm) due to H_3 in these compounds, in addition the multiplet peaks for aromatic parts in the rang (6.9-8.1ppm),also triplet band at (3.25ppm)due to (NCH_2) and another triplet band at (3.55pp) for (OCH_2) in compound (2i).

3-aminopyridine was used as a good essential group to give the required product represented by compounds substituted 1, 5-naphthyridinewhich showed Scheme (3)



Scheme 3

The structure of the compounds (3a and 3b) were confirmed by spectroscopic analysis, FT-IR and U.V and ^{1}HNMR Actually, in IR spectra these compounds showed the following stretching bands; at the range (3300-3500cm^{-1}) due to the (OH) bond, (1700-1713 cm^{-1}) for the(C=O) of carboxylic bond. (1630 cm^{-1})stretching for (C=N) group and (1600cm^{-1}) due to (C=C) group, while The ^{1}H-NMR spectra for compounds (3b) in (DMSO-d_6) the appearance of a singlet band in (11.2 ppm)due to OH group and a singlet band at (8.6 ppm for H3 in this compound.

IV. REFERENCES

[1] V P Litvinov, (2004), *Russian Chemical Reviews 73 (7) 637 -669* .

[2] Madaan, Alka; Verma, Ritu; Kumar, Vivek; Singh, Anu T.; Jain, Swatantra K.; Jaggi, Manu(2015),der Pharmazie (Weinheim, Germany) , 348(12), 837-860.

[3] Surylo, Piotr; Kowalski, Piotr; Holda, Magdalena (2003),Wiadomosci Chemiczne , 57(3-4), 247-266.
[4] Laxminarayana, E.; Karunakar, T.; Shiva Shankar, S.; Thirumala Chary, M. (2012), Journal of Advances in Drug Research , 2(2), 6-11.
[5] Farrell, Nicholas , (1997), US patent 5624919 A 19970429
[6] K R Reddy, K Mogilaiah, B Sreenivasulu(1984). J. Indian Chem. Soc.61 888.
[7] R G Rama,K Mogilaiah, B Sreenivasulu (1989) ,Collect. Czech. Chem.Commun. 54 1716.
[8] D H Lorne, R G Gedir, E M Hawes, D G Wibberley, (1985).Eur. J.Med. Chem. 20 381 .
[9] Françoise Gellibert , James Woolven, Helen Goodland, Victoria Lovegrove, Alain Laroze,, David Hartley (2004)J Med Chem 26;47(18):4494-506
[10] AnaTejería,YolandaPérez-Pertejo,RosaM.Reguera, RafaelBalaña-Fouce, (2018),European Journal of Medicinal Chemistry ,Volume 152, Pages 137-147
[11] F.P.Mazza and C.Migliaridi,(1940)Attiaccad Sci.Fis.Mat.Nat.,75,438.
[12] V.Burckhardt,H.Suter and W.Kudig (1952);German Ptent ,829,894Jan.31(C112P,10)

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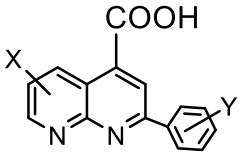
Table I

The physical data for compounds (2a-h)



Comp. No.	X	Y	M.P (˚C)	Yield (%)	Chemical formula	C.H.N C% H% N% Calculate (Measured)	Crystalline Solvent
2a	H	H	142 dec.	36	$C_{15}H_{10}N_2O_2$	72.0 4.0 11.2 (72.32 3.93 11.21)	Ethanol
2b	H	4-OCH_3	147 dec.	33	$C_{16}H_{12}N_2O_3$	68.57 4.28 10.01 (69.02 4.44 10.18)	Ethanol
2c	4-CH_3	3,4-diCl -	151-153	46	$C_{16}H_{10}N_2O_2Cl_2$	57.65 3.0 8.4 (58.07 3.11 8,22)	CCl_4
2d	4-CH3	H	140dec.	42	$C_{16}H_{12}N_2O_2$	72.27 4.54 10.60 (70.88 4.66 11.09)	Acetone
2e	H	2.3-dioMe	108dec.	42	$C_{17}H_{14}N_2O_4$	65.8 4.51 9.03 (66.03 4.66 8.85)	Ethanol
2f	H	3,4-diCl -	127 dec.	38	$C_{15}H_8N_2O_2Cl_2$	56.42 2.50 8.77 (56.11 3.22 9.03)	Ethanol
2g	5- Cl	H	187-189	57	$C_{15}H_9N_2O_2Cl$	43.26 3.16 9.84 (61.99 3.01 9.77)	Methanol
2h	5- Cl	3.4 - dioMe	191-193	53	$C_{17}H_{13}N_2O_4Cl$	59.21 3.77 8.12 (60.08 4.12 8.33)	Methanol

Table II

The IR and U.V. Spectra of compounds (2a-h)

Comp. No.	(MeOH) λmax (nm)	FT-IR νcm^{-1} (KBr)				
		C=O	C=C	C=N	OH	Others
2a	288,342	1700	1600,1580	1650	3300-2700	
2b	245,344	1705	1600,1540	1645	3500-2700	C-O-C asym. 1432, sym. 1340
2c	276,352	1710	1600,1535	1650	3500-2500	C-Cl 737
2d	229,333	1700	1600,1500	1645	3300-2700	C-Cl 742
2e	254,344	1713	1600,1545	1650	3500-2700	C-O-C asym. 1426, sym. 1338
2f	256,358	1710	1600,1500	1650	3330-2700	C-Cl 745
2h	239,319	1730	1600,1470	1650	3500-2700	C-Cl 751

Table III

The ^{1}H-NMR spectral data for compounds (2a-e)

Compd. No.	^{1}H-NMR (δ,ppm, DMSO-d_6)
2a	δ8.7 (s,1H,H_3), δ7.34-8.6(m, ,8H aromatic), δ 11.0(s,1H,OH)
2b	δ 3.9 (s,3H,OCH_3), δ7.2-8.7(m, ,7H aromatic), δ8.8 (s,1H, H_3), δ 11.6(s,1H,OH)
2c	δ 2.6 (s,3H,C-CH_3), δ7.1-8.4(m, ,6H aromatic), δ8.8 (s,1H, H_3), δ 10.4(s,1H,OH)
2d	δ 2.58 (s,3H,C-CH_3), δ7.2-8.5(m, ,6H aromatic), δ8.7 (s,1H, H_3), δ 10.6(s,1H,OH))
2e	δ 3.8 (s,3H,OCH_3), δ7.1-8.7(m, ,7H aromatic), δ8.7 (s,1H, H_3), δ 11.2(s,1H,OH)