Synthesis Of 1, 8-Naphthridine Under Microwave Induction And Microwave Irradiation

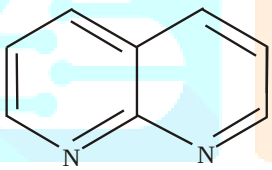
Shiv Kumar Rai* & Shailendra Kumar Sinha (supervisor/guide) **
*Research Scholar, Department of Chemistry, L.S.College, Muzaffarpur – 842001(Bihar)
**Department of Chemistry, L.S.College, Muzaffarpur – 842001(Bihar)

Abstract: - Microwave induction method, a super fast method is used to synthesise 1, 8- Naphthridine derivatives. 1, 8- Naphthridine derivatives have been synthesised by reaction of the condensation products of the aromatic aldehyde derivatives and pyruvic acid with 2 – aminopyridine. In fact a mixture of aromatic aldehyde, pyruvic acid and 2- aminopyridine was achieved in few minutes.

Keywords: - Naphthridines, microwave irradiation, solvent free conditions, 2 – aminopyridine.

INTRODUCTION

Naphthridines (pyridopyridines) are the heterocyclic analogues of naphthalene containing two N-atoms ; one in each ring. These compounds can exist in six possible isomers with different names and have been known in literature as naphthridines[1].



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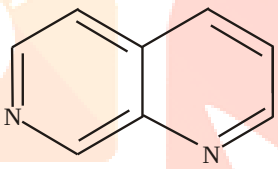

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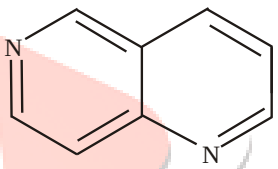

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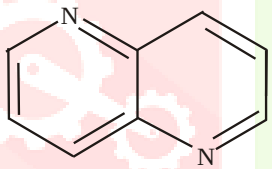
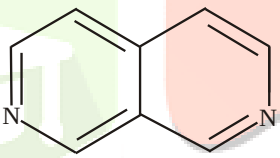


1, 5



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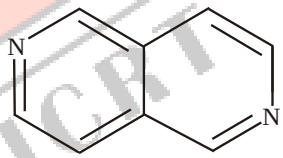


2, 6

The synthetic methods of these compounds are similar to those of synthesis of quinolines.

The first successful synthesis was achieved by Bobrenski and Sucharda[2] and then many researchers have attempted to synthesise these compounds, some of them through modification of skraup method[3-5].

Many studies were also concerned with the reactions of these compounds and found to be similar to those quinolines[6-7]. The importance of these compounds lies in their uses in drug industries and has biological activities in many aspects[8-9]. These findings encourage many scientists to concentrate on modifying these compounds for the purpose of using them in treatment of many different diseases[10-11].

Naphthridinic acids are the most important derivatives of naphthridine series. They have many applications through the possibility of converting them to other substances readily[12].

Some naphthridinic acids[13] have been prepared in two steps by traditional heating of 12 hours. In this chapter, the same has been achieved in one step with the help of microwave irradiation only in few minutes. Here, use of solvent (ethanol) has been eliminated. Reactions leading to the formation of target (1, 8-naphthridine derivatives) have been depicted in Scheme-1.

Microwave irradiation is an efficient and environmentally benign method to activate various organic transformations to afford products in higher yields and in shorter reactions periods. It also results in an incrase in the purity of the products and involves very small amount of solvent or no solvent. Further, the use of microwave acceleration eliminates the need for heating baths, reaction flasks, and reflux condensers with ground glass joints[14].

EXPERIMENTAL

All melting points were determined in open capillary tubes and are uncorrected. TLC was used for monitoring the reaction and to check the purity. Reactions were carried out under microwave irradiation in a Kenstar OM-20ESP (800W), unmodified domestic oven operating at 2450 MHz for the time indicated in Table-1.

To synthesise 2-phenyl-1, 8-naphthridine-4-carboxylic acid (2a), a mixture of benzaldehyde (0.025 mol), 2-aminopyridine (0.025 mol) and pyruvic acid (0.025 mol) was irradiated by microwaves at 40% (320W) level in a Kenstar OM-20ESP (800W), unmodified domestic oven operating at 2450 MHz for the time indicated in Table-1. The reaction mixture was poured into cold water, whereupon a solid mass product. It was filtered, dried and finally recrystallised from ethanol.Other derivatives were also prepared by the same method using corresponding 2-aminopyridine.

2-Phenyl-1, 8-naphthridine-4-carboxylic acid (2a) :

IR (υ_{max} , cm^{-1}) ; 3300 - 2700 (O-H), 1700 (C = O), 1650 (C = N), 1600 (C = C). ^{1}H NMR (δ ppm) ; 7.3 - 8.6 (m, 8H) Ar - H, 8.7 (s, IH) H_3, 11.0 (s, 1H) O-H.

5-Methyl-2-phenyl-1, 8-naphthridine-4-carboxylic acid (2b) :

IR (υ_{max} , cm^{-1}) ; 3300 - 2700 (O-H), 1700 (C = O), 1625 (C = N), 1600 (C = C).

^{1}H NMR (δ ppm) ; 2.7 (s, 3H) CH_3, 7.1 - 8.6 (m, 8H) Ar - H, 11.0 (s, 1H) O-H.

6-Chloro-2-phenyl-1, 8-naphthridine-4-carboxylic acid (2c) :

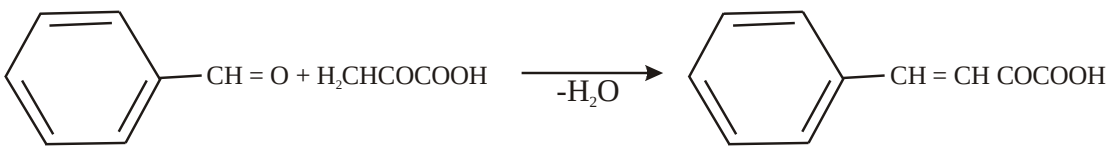
IR (υ_{max} , cm^{-1}) ; 3300 - 2500 (O-H), 1730 (C = O), 1650 (C = N), 1600 (C = C).

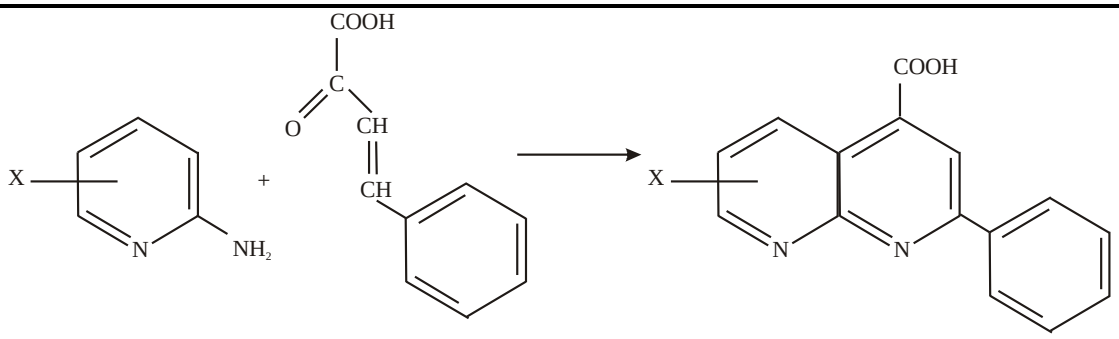
^{1}H NMR (δ ppm) ; 7 - 8.6 (m, 8H) Ar - H, 11.5 (s, 1H) O-H.

RESULT AND DISCUSSION

The reaction was attempted first with microwaves at 20% (160 W) level in a Kenstar OM-20ESP (800W) for few minutes, whereupon no action was observed. The reaction was successfully attempted with microwaves at 40% (320W) level of full power, 800W of the oven used. The time taken for completion of reaction was decided by hit and trial method. The time required for completion of reaction by traditional heating[13] is about 12 hours and it is only 7-9 minutes by microwave that we have done. Here use of solvent has been ignored, due to which cost of the product may be lowered.

Reactions were carried out under atmospheric pressure in an open vessel adapted to a microwave oven. Purity of the compounds were checked by TLC. Melting points were taken in an open glass capillary using Elico Melting Point apparatus and are uncorrected. The compounds (2a-c) are all known compounds and have been characterised on the basis of their melting points, IR and NMR.





1a : X = Hydrogen
1b : X = 4 - Methyl
1c : X = 5 - Chloro

2a : X = Hydrogen
2b : X = 5 - Methyl
2c : X = 6 - Chloro

(Scheme - 1)

Table - 1

Results of naphthridine derivatives synthesised under microwave irradiation in solvent free condition

Compound	Experimental			Literature[13]	
	Time (Min)	Yield (%)	m.p.(^{0}C)	Yield %	m.p. (^{0}C)
2a	70	80	141	16	142d
2b	85	75	139	12	140d
2c	90	70	188	17	187-189

REFERENCES

1. V.K.Ahluwalia and Renu Aggarwal, *Organic Synthesis*, Special Techniques, . . Second Edition (2006).
2. May S. Saeed, Alaa E. Ayoub, Mohamed N. Ibrahim and Marei M. El-Ajily, .. . *Asian Journal of Chemistry*, vol. **19**, No.**4**, pp.2801-2805 (2007).
3. W.W.Paulder and T.J.Kress, *Adv. Heterocycl. Chem.*, **11** 123 (1970).
4. E.M.Hawes, D.G.Wibberley, *J.Chem. Soc.* (C), 1564 (1967)
5. R.K.Rajendar, K. Mogilaiah and B.Sreenivasulu, *J.Indian Chem. Soc.*, **64**, 193 . (1987).
6. G.C.Crumplin, J.Midgley and J.T.Smith, *Top Antipiot Chem.*, **3**, 9(1980) ; *Chem Abstr.*, 19673b (1980).
7. R.M.Titokova, A.S.Elina, E.N.Padeskaya and L.M.Polukhine, *Khim.Farm Zh.*, **9**,10(1975).
8. W.W.Paulder, D.J. Pokorny and S.J.Cornrich, *J.Heterocycl. Chem.*, **7**, 291 (1970).
9. J.T.Adams, C.K. Bradsher, D.S.Breslow, S.T.Amore and C.R.Hanser, *J.Am. Chem. Soc.*, **68**, 1317 (1946).
10. Y.Hemada, I. Takeuchi and M. Sato, *Yakugaku Zasshi*, **94**, 1328 (1974) ; *Chem. Abstr.*, **82**, 43211e(1975).
11. W.Panlder and T.J.Kress, *J.Org. Chem.*, **32**, 832 (1967).
12. Y.Hemada and I. Takeuchi, *Chem. Farm. Bull.*, **19**, 1857 (1971).
13. E.P.Hart, *J.Chem. Soc.* 1879 (1954).
14. A.R.Katritzky and C.V.Rees, *Comprehensive Heterocyclic chemistry*, Bergamm (Oxford), Vol.**2**, Part 4A (1984).