Asian Journal of Chemistry Vol. 19, No. 4 (2007), 2801-2805

Synthesis and Characterization of 1,8-Naphthridine Derivatives

May S. Saeed†, Alaa E. Ayoub‡, Mohamed N. Ibrahim
and Marei M. El-Ajaily*
Department of Chemistry, Faculty of Science, Garyounis University, Benghazi, Libya
E-mail: mni46uk@yahoo.com

1,8-Naphthridine derivatives were obtained by treatment of the condensation products of the aromatic aldehyde derivatives with 2-aminopyridine derivatives in presence of pyruvic acid.

Key Words: Synthesis, 1,8-Naphthridine derivatives.

INTRODUCTION

Naphthridines are the heterocyclic analogue of naphthalene contains two N-hetero atoms at positions 1 and 8. These compounds can exist in six possible isomers with different names and since 1936 have been known in literature as Naphthridines[1]. The synthetic methods of these compounds are similar to those of the synthesis of quinolines.

The first successful synthesis was achieved by Bobrenski and Sucharda[2] and then many researchers have attempted to synthesis 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 of quinolines[6,7]. The importance of these compounds lies in their uses in drug industries and have 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

---

†Department of Chemistry, Darna University, Libya.
‡Department of Chemistry, Masrata University, Libya.

them to other substances readily[12]. Naphthridinic acids have been prepared by many authors an from a wide variety of compounds[13]. In this paper, 1,8-Naphthridine derivatives have been syntheiszed *via* applying Doebner reaction[14].

EXPERIMENTAL

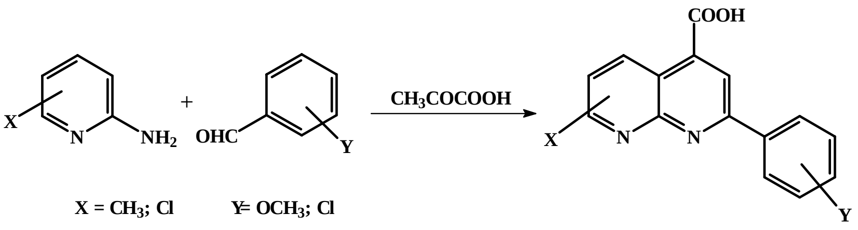
Melting points were measured by Gallenkamp apparatus and are uncorrected. IR spectra were recorded by Perkin-Elmer 580 B spectrophotometer. ^{1}H NMR were recorded by Hitashi Perkin-Elmer 90 MHz spectrometer in $CDCl_3$ with TMS as internal standard. Chemical shifts (δ) were given in ppm. Elemental analysis were performed on Carlo Erba type 1106 analyzer.

The purities of the obtained substances and the composition of the reaction mixtures were monitored by TLC on silica gel sheets. Solvents and chemicals used were of reagent grade and obtained from Fluka and Aldrich.

General preparation of 2-phenyl-4-carboxy-1,8-naphthridine[16]

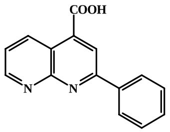
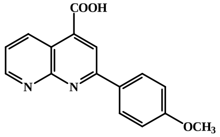
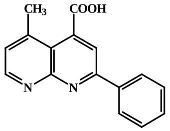
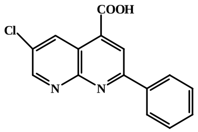
Benzaldehyde (0.025 mol) kept in a round bottomed flask provided with reflux condenser protected with $CaCl_2$ tube. Absolute ethanol (10 mL) was added and the mixture was heated in water bath for 0.5 h. 2-Aminopyridine (0.025 mol) in absolute ethanol (5 mL) was added in one portion followed by drop wise addition of pyruvic acid (0.025 mol) with vigorous stirring and maintaining the temperature at 30-50°C, the addition lasts 1 h. Then the reaction mixture was refluxed in the water bath for further 12 h the reaction mixture then left to stand overnight. The solvent was removed under vacuum and the oily residue was treated with water to give solid material which after crystallization from ethanol gave a yellow crystals.

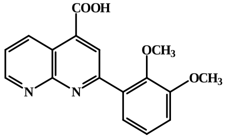
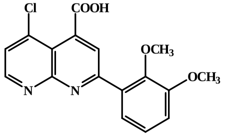
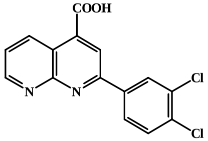
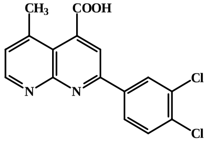
The physical and spectral data are given in the Table-1. Other derivatives were also prepared by the same procedure using the corresponding aldehydes.



]]>

TABLE-1
PHYSICAL AND SPECTROSCOPIC DATA OF 2-PHENYL-4-CARBOXYL-1,8-NAPHTHRIDINE

No.	Structure/(m.f.)	m.p.(ºC)/ Yield (%)	IR (cm^{-1})				^{1}H NMR (ppm)	Microanal. (%) Found (calcd.)		
			ν(OH)	ν(C=O)	ν(C=N)	ν(C=C)		C	H	N
I	 ($C_{15}H_{10}N_2O_2$)	142d/ (36)	3300- 2700	1700	1650	1600	7.3-8.6 (m, 8H) Ar-H 8.7 (s, 1H) H_3 11.0 (s, m, 1H) OH	72.3 (72.0)	3.9 (4.0)	11.2 (11.2)
II	 ($C_{16}H_{12}N_2O_3$)	147d/ (33)	3500- 2700	1705	1650	1600	3.9 (s, 3H) OCH_3 7.2-8.7 (m, 7H) Ar-H 8.8 (s, 1H) H_3 11.6 (s, 1H) OH	69.0 (68.5)	4.4 (4.2)	10.1 (10.0)
III	 ($C_{16}H_{12}N_2O_2$)	140d/ (42)	3300- 2700	1700	1625	1600	2.7 (s, 3H) CH_3 7.1-8.6 (m, 8H) Ar-H 11.0 (s, 1H) OH	72.8 (72.7)	4.6 (4.5)	11.0 (10.6)
IV	 ($C_{15}H_9N_2O_2Cl$)	187-189/ (57)	3000- 2500	1730	1650	1600	7-8.6 (m, 8H) Ar-H 11.5 (s, 1H) OH	61.9 (63.2)	3.0 (3.1)	9.7 (9.8)

No.	Structure/m.f.	m.p. (°C)/ Yield (%)	IR (cm^{-1})				^{1}H NMR (ppm)	Microanal. (%) Found (calcd.)		
			ν(OH)	ν(C=O)	ν(C=N)	ν(C=C)		C	H	N
V	 ($C_{17}H_{14}N_2O_4$)	108d/ (42)	3500- 2700	1713	1650	1600	3.7 (s, 6H) 2OCH_3 7.15-8.0 (m, 6H) Ar-H 8.4 (s, 1H) H_3 10.4 (s, 1H) OH	66.0 (65.8)	4.6 (4.5)	8.8 (9.0)
VI	 ($C_{17}H_{13}N_2O_4Cl$)	191/ (53)	3500- 2500	1710	1650	1600	3.8 (S, 6H) 2OCH_3 7.2-8.5 (m, 5H) Ar-H 11.0 (s, 1H) OH	60.0 (59.2)	4.1 (3.7)	8.3 (8.1)
VII	 ($C_{15}H_8N_2O_2Cl_2$)	127d/ (38)	3330- 2700	1710	1650	1600	6.9-8.1 (m, 6H) Ar-H 8.4 (s, 1H) H_3 11.7 (s, 1H) OH	56.1 (56.4)	3.2 (2.5)	9.0 (8.7)
VIII	 ($C_{16}H_{10}N_2O_2Cl_2$)	151-153/ (46)	3500- 2500	1710	1650	1600	2.6 (s, 3H) CH_3 7.1-8.6 (m, 6H) Ar-H 10.4 (s, 1H) OH	58.0 (57.6)	3.1 (3.0)	8.2 (8.4)

REFERENCES

1. A.R. Katritzky and C.V. Rees, Comprehensive Heterocyclic Chemistry, Bergamm (Oxford), Vol. 2, Part 4A (1984).
2. E.P. Hart, *J. Chem. Soc.*, 1879 (1954).
3. Y. Hemada and I. Takeuchi, *Chem. Farm. Bull.*, **19**, 1857 (1971).
4. W. Panlder and T.J. Kress, *J. Org. Chem.*, **32**, 832 (1967).
5. Y. Hemada, I. Takeuchi and M. Sato, *Yakugaku Zasshi*, **94**, 1328 (1974); *Chem. Abstr.*, **82**, 43211e (1975).
6. J.T. Adams, C.K. Bradsher, D.S. Breslow, S.T. Amore and C.R. Hanser, *J. Am. Chem. Soc.*, **68**, 1317 (1946).
7. W.W. Paulder, D.J. Pokorny and S.J. Cornrich, *J. Heterocycl. Chem.*, **7**, 291 (1970).
8. R.M. Titokova, A.S. Elina, E.N. Padeskaya and L.M. Polukhine, *Khim. Farm. Zh.*, **9**, 10 (1975).
9. G.C. Crumplin, J. Midgley and J.T. Smith, *Top. Antipiot Chem.*, **3**, 9 (1980); *Chem. Abstr.*, 19673b (1980).
10. R.K. Rajendar, K. Mogilaiah and B. Sreenivasulu, *J. Indian Chem. Soc.*, **64**, 193 (1987).
11. E.M. Hawes, D.G. Wibberley, *J. Chem. Soc. (C)*, 1564 (1967).
12. W.W. Paulder and T.J. Kress, *Adv. Heterocycl. Chem.*, **11**, 123 (1970).
13. V. Burckhardt, H. Suter and W. Kundig, German Patent, 829894 (1952); *Chem. Abstr.*, **52**, 11127d (1958).
14. A.I. Vogel, Practical Organic Chemistry, Longmans, London, edn. 3 (1991).

(*Received*: 3 April 2006; *Accepted*: 12 January 2007) AJC-5324