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MICROWAVE ASSISTED SYNTHESIS OF 3,4-DIHYDRO-3-PYRIDYL-2*H*-NAPHTHO[2,1-*E*][1,3]OXAZINE DERIVATIVES

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ABSTRACT
A simple and efficient method was developed to synthesis several 3,4-dihydro-3-pyridyl-2*H*-naphtho[2,1-*e*][1,3]oxazine derivatives from 1-naphthol, various pyridines and formalin solution by microwave method.

INTRODUCTION
In recent decades, a large number of reports on synthesis of heterocycles compounds containing N, O and S have been published due to their wide range of biological activity. Numerous data concerning synthesis of heterocycles under microwave conditions have been published.[i-iii] Pyridinium salts belong to the category of cationic surfactants consisting of a hydrophilic part, such as a quaternary nitrogen moiety which is able to interact in polar chemical milieu, and a hydrophobic part which can penetrate into non-polar molecular agglomerates. These are unsaturated heterocyclic compounds with different functional groups present either on pyridine ring or on nitrogen atom. A great deal of pyridinium derivatives have been investigated concerning their biological and pharmacological activities. Their importance lies in their effective antimicrobial,[iv-ix] antiviral,[x-xii] antihypertensive and immunostimulating activities.[xiii] Some of pyridinium aldoxime derivatives are potential antidotes against organophosphate poisoning.[xiv-xvii] The advantages of microwave heating compared to conventional synthesis are: a shorter reaction time (from hours or days to minutes), better utilization and decrease in by-product production.[xviii].
Several methods for the preparation of 1,3-oxazine derivatives have previously been reported,[xix-xxi] few have been focused on the multicomponent reactions method. The present method is beneficial over previous reports due to its solvent-free condition.

EXPERIMENTAL

All the Chemical and reagents used were purchased from Aldrich. All the solvents were of analytical grade. Thin-layer chromatography (TLC) was checked by Merck AL silica gel 60 F_{254} plates and visualized under UV light. IR spectra were recorded in KBr pellet with a shimazu spectrum gx FTIR instrument and all the diagnostic, intense peaks are reported. ^{1}H NMR spectra were recorded in $CDCl_3$, and DMSO- d_6 with a Varian Mercury plus 400 MHz instrument. All the chemical shifts were reported in δ (ppm) using TMS as an internal standard. The ^{1}H NMR chemical shifts and coupling constants were determined assuming first-order behaviour. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad); the list of coupling constants (*J*) corresponds to the order of multiplicity assignment. Mass spectra were recorded on a Shimadzu mass spectrometer. All the reactions were performed under inert atmosphere.

GENERAL PROCEDURE FOR THE SYNTHESIS OF COMPOUNDS (4A-G):

A mixture of formalin (2.0 mmol), aromatic pyridine (1.0 mmol), 1-naphthol (1.0 mmol) and was made as paste and irradiated under microwave for 2-3min. The reaction was monitored by TLC. After completion of reaction, reaction mixture was extracted with methylene dichloride (3×50 mL). The organic layer was washed with water (2×10 mL) and brine (2×20 mL) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The obtained product was purified by column chromatography on silica gel by hexane: ethyl acetate as eluent.

3,4-dihydro-3-(pyridin-4-yl)-2H-naphtho[2,1-e][1,3]oxazine (4a):
IR: 1050 (C-O-C), 1198 (C-O-C);
^{1}H NMR 4.79 (s, 2H, -Ar-CH_2-N-), 5.43 (s, 2H,-0-CH_2-N-), 6.85-7.58(m.9H), 8.42(d, 1H); MS: m/z 263 (m+1);

3,4-dihydro-3-(pyridin-3-yl)-2H-naphtho[2,1-e][1,3]oxazine (4b):
^{1}H NMR 4.78 (s, 2H, -Ar- CH_2-N-), 5.42(s,2H,-0-CH_2-N-) 6.84-7.56 (m, 8H),8.40(m, 2H); MS: m/z 263 (m+1);

3,4-dihydro-3-(pyridin-2-yl)-2H-naphtho[2,1-e][1,3]oxazine (4c).
^{1}H NMR 4.78 (s, 2H, -Ar- CH_2-N-), 5.41(s, 2H,-0-CH_2-N-), 6.85-7.57 (m, 9H), 8.41(d, 1H); MS: m/z 263 (m+1);

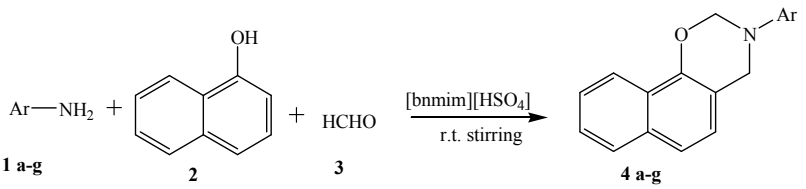
3,4-dihydro-3-(6-methylpyridin-2-yl)-2H-naphtho[2,1-e][1,3]oxazine (4d).
^{1}H NMR 2.42(s, 3H), 4.79 (s, 2H, -Ar- CH_2-N-), 5.42 (s, 2H,-0-CH_2-N-) 6.86-7.58 (m, 9H); MS: m/z 277 (m+1);

3,4-dihydro-3-(5-methylpyridin-2-yl)-2H-naphtho[2,1-e][1,3]oxazine (4e).
^{1}H NMR 2.39(s, 3H), 4.77 (s, 2H, -Ar- CH_2-N-), 5.41 (s, 2H, -0-cH_2-N-), 6.85-7.58 (m, 8H), 8.40 (d, 1H); MS: m/z 277 (m+1);

3,4-dihydro-3-(4-methylpyridin-2-yl)-2H-naphtho[2,1-e][1,3]oxazine (4f).
^{1}H NMR 2.38 (s, 3H), 4.78 (s, 2H, -Ar- CH_2-N-), 5.42 (s, 2H,-0-VCH_2-N-) 6.86-7.59 (m, 8H), 8.41 (d, 1H); MS: m/z 277 (m+1);

3-(5-chloropyridin-2-yl)-3,4-dihydro-2H-naphtho[2,1-e][1,3]oxazine (4g).
^{1}H NMR 4.78 (s, 2H, -Ar- CH_2-N-), 5.42 (s, 2H,-0-CH_2-N-) 6.85-7.58 (m, 8H), 8.40 (d, 1H); MS: m/z 298 (m+1);

SCHEME 1



1 a-g **2** **3** **4 a-g**

Ar = 4-pyridyl, 3-pyridyl, 2-pyridyl, 2-(6-methylpyridyl), 2-(5-methylpyridyl), 2-(4-methylpyridyl), 2-(5-chloropyridyl)

TABLE 1

S. No.	Compound	Ar	Yield (%)	M. P. (°C)
1	4a	4-pyridyl	63	68
2	4b	3-pyridyl	75	72
3	4c	2-pyridyl	74	76
4	4d	2-(6-methylpyridyl)	72	80
5	4e	2-(5-methylpyridyl)	68	86
6	4f	2-(4-methylpyridyl)	69	88
7	4g	2-(5-chloropyridyl)	76	91

RESULTS AND DISCUSSION

We wish to report the synthesis of 3,4-dihydro-3-pyridyl-2*H*-naphtho[2,1-*e*][1,3]oxazine derivatives promoted by microwave process (Scheme 1). We have considered the reaction of pyridine (1 mmol), 1-naphthol (1 mmol) and formalin (2 mmol) at room temperature stirring condition as the model reaction.

REFERENCES

i. S. Sharma, S. Gangal, A. R. Rauf, J. Chem. 2008, 1, 693.

ii. P. Lidström, È. Jason, J. Tierney, B. Watheyand, J. Westman, Tetrahedron 2001, 57, 9225. N R' R X 3. Oxidation 2. Penetration 3. Hole formation Bacterial Cell Membrane Target Figure 2. Proposed mode of antimicrobial action for pyridinium compounds. V. BUŠIĆ et al.: Microwave-assisted Quaternization of Pyridine Derivatives … 433 DOI: 10.5562/cca2937 Croat. Chem. Acta 2017, 90(3), 425–433

iii. C. O. Kappe, Angew. Chem. 2004, 43, 6250.

iv. T. Thorsteinsson, M. Masson, K. G. Kristinsson, M. A. Hjalmarsdottir, H. Hilmarsson, E. J. Poziomek, J. B. E. Hackley, G. E. Steinberg, J. Org. Chem. 1958, 23, 714.

v. Z. A. Vnutskikh, Y. V. Shklyaev, T. F. Odegova, Y. S. Chekryshkin, A. G. Tolstikov, N. V. Elchishcheva, Khim-Farm. 2006, 40, 19.

vi. I. G. Ovchinnikova, O. V.Fedorova, G. L. Rusinov, M. N. Zueva, G. G. Mordovskoi, Khim-Farm. 2003, 37, 17.

vii. J. R. Burke, P. A. Frey, J. Org. Chem. 1996, 61, 530.

viii. P. Madaan, V. K. Tyagi, J. Oleo. Sci. 2008, 57, 197.

ix. A. A. Altaf, A. Shahzad, Z. Gul, N. Rasool, A. Badshah, B. Lal, E. Khan, JDDMC. 2015, 1, 1.

x. S. Mavel, J. L. Renou, C. Galtier, R. Snoeck, G. Andrei, J. Balzarini, E. De Clercq, A.

Gueiffier, Arzneimittelforschung 2001, 51, 304.
xi. D. H. Jones, R. Slack, S. Squires, K. R. H. Wooldridge, J. Med. Chem. 1965, 8, 676.
xii. A. M. R. Bernardino, L. C. S. Pinheiro, V. F. Ferreira, A. R. Azevedo, Heterocycl. Commun. 2004, 10, 407.
xiii. A. Saleh, S. A. Bahshwan, A. M. Amer, A. A. Fayed, J. Am. Sci. 2010, 6, 151.
xiv. M. P. Stojiljković, M. Jokanović, Arh. Hig. Rada. Toksikol. 2006, 57, 435.
xv. J. Kassa, K. Musilek, J. Z. Karasova, K. Kuča, J. Bajgar, Mini- Rev. Med. Chem. 2012, 12, 24.
xvi. R. T. Delfino, T. S. Ribeiro, J. D. Figueroa-Villar, J. Braz. Chem. Soc. 2009, 20, 407.
xvii. D. Gašo-Sokač, M. Katalinić, Z. Kovarik, V. Bušić, S. Kovač, Chem-Biol. Interact. 2010, 187, 234.
xviii. I. Zrinski, M. Eckert-Maksić, Kem. Ind. 2005, 54, 469.
xix. J. Agag, App. Poly. Sci., 100, 3769, (2006).
xx. W. J. Burke K. C. Murdock, G. Ec, J. Am. Chem. Soc., 76, 1677, (1954).
xxi. B. P. Mathew, M. Nath, J. Heterocyclic Chem., 46, 1003, (2009).

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