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ECO-FRIENDLY SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF 6-ARYL-9-METHYL-10H-[1,2,4]TRIAZINO[4,3-a][1,8]NAPHTHYRIDIN-10-ONES UNDER MICROWAVE IRRADIATION

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Abstract

A straight forward and highly efficient procedure has been described efficient for the synthesis of 6-aryl-9-methyl-10H-[1,2,4]triazino[4,3-a][1,8]naphthyridin-10-ones 3 by the reaction of 8-naphthyridines 1, 3-aryl-2-hydrazino-1with ethyl pyruvate 2 in the presence of a catalytic amount of DMF in solvent-free conditions under microwave irradiation. The items are acquired in great yields and in a condition of high immaculateness. The auxiliary assignments of compounds 3 depended on their elemental investigation and spectral (IR, 1H NMR and MS) information. The compounds 3 have been screened for their antibacterial action.

***Key Words*:** 1,8-Naphthyridine, 1,2,4 triazine, antibacterial activity, microwave irradiation.

1 Introduction

1,8-Naphthyridines constitute an imperative class of compounds possessing differing biologicalactivities1-3. The triazine moiety is an important pharmacophoric element in medicinal chemistry4,5. In this way, it was visualized that chemical substances with both 1,8-naphthyridine, and triazine may result in compounds with interesting biological activity.

Microwave (MW) actuation as nonconventional energy source has turned into an exceptionally famous and valuable innovation in synthetic organic chemistry6-8. The utilizations of microwave (MW) heating under solvent-free response conditions is promising other option to polluting responses and has been a present field of interest. Inspired by the above perceptions, we now portrayed a proficient strategy for the synthesis of 6-aryl-9-methyl-10H-[1,2,4] triazino[4,3-a][1,8]naphthyridin-10-ones in solvent-free conditions beneath MW illumination.

2 RESULTS AND DISCUSSION

Chemistry

Treatment of 3-aryl-2-hydrazino-1,8-naphthyridines 1 with ethyl pyruvate 2 in the existence of catalytic amount of DMF without any solvent under microwave irradiation furnished 6-aryl-9-methyl-10H-[1,2,4]triazino[4,3-a][1,8] naphthyridin-10-ones 3 (Scheme-1) in very good yields. 91-95% with short reaction time (3.0-3.5 min) the experimental procedure is very simple and purity of the products is excellent. The process is environmentally friendly.

In an average trial technique, a mixture of 2-hydrazino-3-phenyl-1, 8-naphthyridine 1a, ethyl pyruvate 2 and DMF (5 drops) was presented to MW light at 400 watts intermittently at 30sec intervals for 3.0 min. The response mixture was cooled to RT, processed with cold water and filtered off. After usual work-up 6-phenyl-9-methyl-10H-[1,2,4]triazino[4,3-a][1,8]naphthyridin-10-one 3a was obtained in 92% yield. The reaction is of general applicability and the different triazino [4,3-a][1,8]naphthyridin-10-ones 3 synthesized are presented in Table-1. Intergesting, the reaction proceeds only to a minor extent (7-12% in 3.5-4.0 min) at the point when directed under customary conditions in an oil-bath preheated to 120oC (tempera-

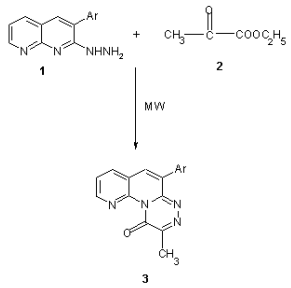
ture estimated at end of the presentation during MW experiment), which affirms the rate enlargement during MW heating.

The structures of the compounds 3 were affirmed by their basic investigations and spectral (IR, 1H NMR and MS) information. The critical focal points of this methodology are the short response times, great yields, high purity of the products and simple operation. **Antibacterial activity**

The title compounds 3 were screened for their antibacterial activity against Gram negative Escherichia coli and Gram positive Bacillus subtilis using channel paper circle system of Vincent and Vincent9 at 250 and 500 g/plate focuses. Gentamycin was utilized as a standard medication for examination. The results are given in Table-2. Compounds 3e, 3h and 3j exhibited significant antibacterial activity.

3 EXPERIMENTAL

Melting points areidentified on a Cintex melting point mechanical get together and are uncorrected. Flawlessness of the compound has been checked by making use of precoated TLC plates (Merck, 60F-254). IR spectra (KBr) has been recorded on a Perkin-Elmer FT-IR spectrophotometer, 1H NMR spectra on a Varian Gemini 400 MHz spectrometer utilizing TMS as internal standard and mass spectra on a VG 170708H spectrometer. Microanalyses were executed on a Perkin-Elmer 240 CHN fundamental analyser. Microwave lights were finished using nearby microwave stove (LG MG 556P, 2450 MHz). The ethyl pyruvate 2 was procured from Aldrich Chemical Company. **Synthesis of 6-aryl-9-methyl-10H-[1,2,4] triazino[4,3-a][1,8]naphthyridin-10-ones 3: General procedure** A mixture of 3-aryl-2-hydrazino-1,8-naphthyridines 1 (0.01mol), ethyl pyruvate 2 (0.01 mol) and DMF (5 drops) was subjected to MW illumination at 400 watts intermittently at 30 sec intervals for indicated time (Table-1). After finishing the reaction as specified by TLC, the reaction mixture was cooled and treated with cold water. The resulting thing strong was filtered, washed with water and cleaned by recrystallization from ethanol to afford 3 (Table-1).



	Ar		Ar
a	: C_6H_5	**f**	: 2-F C_6H_4
b	: 4-$CH_3OC_6H_4$	**g**	: 3-F C_6H_4
c	: 2-ClC_6H_4	**h**	: 4-F C_6H_4
d	:3-ClC_6H_4	**i**	:3-CF_3 C_6H_4
e	:4-ClC_6H_4	**j**	:4-CF_3 C_6H_4

Scheme-1

TABLE I Physical data of compounds 3

Compd	Ar	Reaction time (min)	M.P (°C)	Yield (%)
3a	C_6H_5	3.0	225	92
3b	4-$CH_3OC_6H_4$	3.5	232	94
3c	2-ClC_6H_4	3.0	256	92
3d	3-ClC_6H_4	3.0	260	91
3e	4-ClC_6H_4	3.5	252	95
3f	2-FC_6H_4	3.0	223	92
3g	3-FC_6H_4	3.5	240	90
3h	4-FC_6H_4	3.0	262	94
3i	3-$CF_3C_6H_4$	3.0	254	91
3j	4-$CF_3C_6H_4$	3.5	268	93

All the compounds gave satisfactory C, H, N elemental analyses.

TABLE II Antibacterial activity data of compounds 3

Compd	Inhibition zone (in mm)			
	E. coli at		*B. subtilis* at	
	250 µg/disc	500 µg/disc	250 µg/disc	500 µg/disc
3a	8.5	12.5	6.5	10.5
3b	9.5	17.0	6.0	9.5
3c	9.0	16.5	6.5	11.0
3d	8.5	12.5	6.0	10.0
3e	11.0	20.5	7.0	13.5
3f	8.5	13.0	6.5	11.5
3g	8.0	11.0	6.0	10.0
3h	10.5	20.0	7.0	13.0
3i	8.5	12.0	6.5	11.0
3j	10.0	19.5	7.0	12.5
Gentamycin	12.0	22.0	8.0	15.0

4 SPECTRAL DATA

3a: IR(KBr): 1675(C=O),1605(C=N); 1H NMR(CDCl3): 2.52(s,3H,CH3), 7.85 (m, 2H, C3-H, C5-H), 8.03 (m, 1H, C4-H), 8.68 (m, 1H, C2-H), 7.10-7.40 (m, 5H, Ar-H); MS(ESI):m/z 289 $[M+H]^+$
3b: IR(KBr): 1672(C=O), 1603(C=N); 1H NMR (CDCl3): 2.60(s,3H,CH3) 3.84(s,3H,OCH3), 7.82 (m, 2H, C3-H, C5-H), 8.10 (m, 1H, C4-H), 8.62 (m, 1H, C2-H), 7.08-7.25 (m, 4H, Ar-H); MS(ESI):m/z 319$[M+H]^+$
3c: IR(KBr): 1670 (C=O), 1604 (C=N); 1H NMR(CDCl3): 2.54(s,3H,CH3), 7.80 (m, 2H, C3-H, C5-H), 8.08 (m, 1H, C4-H), 8.58 (m, 1H, C2-H), 7.12-7.40 (m, 4H, Ar-H); MS(ESI):m/z 323$[M+H]^+$
3d: IR(KBr): 1674 (C=O), 1603 (C=N); 1H NMR(CDCl3): 2.70(s,3H,CH3), 7.84 (m, 2H, C3-H, C5-H), 8.18 (m, 1H, C4-H), 8.64 (m, 1H, C2-H), 7.09-7.30 (m, 4H, Ar-H); MS(ESI):m/z 323$[M+H]^+$
3e: IR(KBr): 1676 (C=O), 1605 (C=N); 1H NMR(CDCl3): 2.62(s,3H,CH3), 7.85 (m, 2H, C3-H, C5-H), 8.15 (m, 1H, C4-H), 8.68 (m, 1H, C2-H), 7.18-7.43 (m, 4H, Ar-H); MS(ESI):m/z 323$[M+H]^+$
3f: IR(KBr): 1672 (C=O), 1604 (C=N); 1H NMR(CDCl3): 2.70(s,3H,CH3), 7.83 (m, 2H, C3-H, C5-H), 8.10 (m, 1H, C4-H), 8.60 (m, 1H, C2-H), 7.12-7.35 (m, 4H, Ar-H); MS(ESI):m/z 307$[M+H]^+$
3g: IR(KBr): 1670 (C=O), 1607 (C=N); 1H NMR(CDCl3): 2.56 (s,3H,CH3), 7.88 (m, 2H, C3-H, C5-H), 8.02 (m, 1H, C4-H), 8.68 (m, 1H, C2-H), 7.15-7.46 (m, 4H, Ar-H); MS(ESI):m/z 307$[M+H]^+$

3h: IR(KBr): 1674 (C=O), 1606 (C=N); 1H NMR(CDCl3): 2.72(s,3H,CH3), 7.85 (m, 2H, C3-H, C5-H), 7.98 (m, 1H, C4-H), 8.64 (m, 1H, C2-H), 7.10-7.28 (m, 4H, Ar-H); MS(ESI):m/z 307$[M+H]^+$
3i: IR(KBr): 1672 (C=O), 1604 (C=N); 1H NMR(CDCl3): 2.58(s,3H,CH3), 7.94(m, 2H, C3-H, C5-H), 8.10(m, 1H, C4-H), 8.70 (m, 1H, C2-H), 7.13-7.36 (m, 4H, Ar-H); MS(ESI):m/z 357$[M+H]^+$
3j: IR(KBr): 1675 (C=O), 1606 (C=N); 1H NMR(CDCl3): 2.73(s,3H,CH3), 7.92 (m, 2H, C3-H, C5-H), 8.08 (m, 1H, C4-H), 8.66 (m, 1H, C2-H), 7.22-7.54 (m, 4H, Ar-H); MS(ESI):m/z 357$[M+H]^+$

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