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Potassium dodeca tangesto cobaltate trihydrate catalysed synthesis of 2-substituted-1,8-naphthyridines under microwave irradiation via Friedlander condensation under solvent free condition

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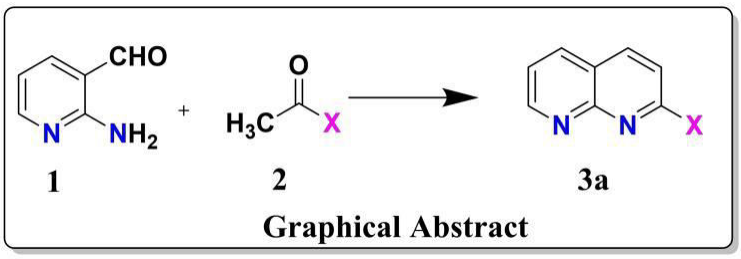
Abstract

2-aminonicotinaldehyde **1** with innumerable methyl ketones **2a-f** in the presence of potassium dodecatangestocobaltate trihydrate ($K_5CoW_{12}O_{40}.3H_2O$) in solvent-free conditions under microwave irradiation furnished the corresponding 1,8-naphthyridines **3a-f** with an excellent yields, eludes contamination difficulties, diminishes reaction time and is accomplished in a 6-8 min via Friedlander condensation (**Scheme I**).

Keywords: 1,8-Naphthyridines, Friedlander condensation, MWI



Graphical Abstract

Introduction

1,8-Naphthyridines have materialized as an imperative class of heterocyclic compounds due to their diverse biological activities[1] and photochemical properties.[2] Gemifloxacin, a compound containing 1,8-naphthyridine staple has touched drug market for the treatment of bacterial infections[3]. In medicinal chemistry and materials science, the development of methods for the synthesis of 1,8-naphthyridines has been of considerable interest to synthetic community including attempts to develop more ecofriendly, safe, and atom economical approaches.[4–5]

1,8-naphthyridines (1) and their derivatives are used as drugs for antimicrobial activities (nalidixic acid, 2),[6–9] antibacterial activities (gemifloxacin, 3),[10-11] shown in below as Fig.I.

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The MW induced organic reactions are becoming popular because of their simplicity and operational convenience[12]. In view of this and in perpetuation of our enduring program to develop environmentally gentle protocols[13]

Use of MW activation in organic synthesis has become a standard tool for organic chemists because of enhancement in rate of reaction, higher yields and improved selectivity in comparison to conventional reactions[14].

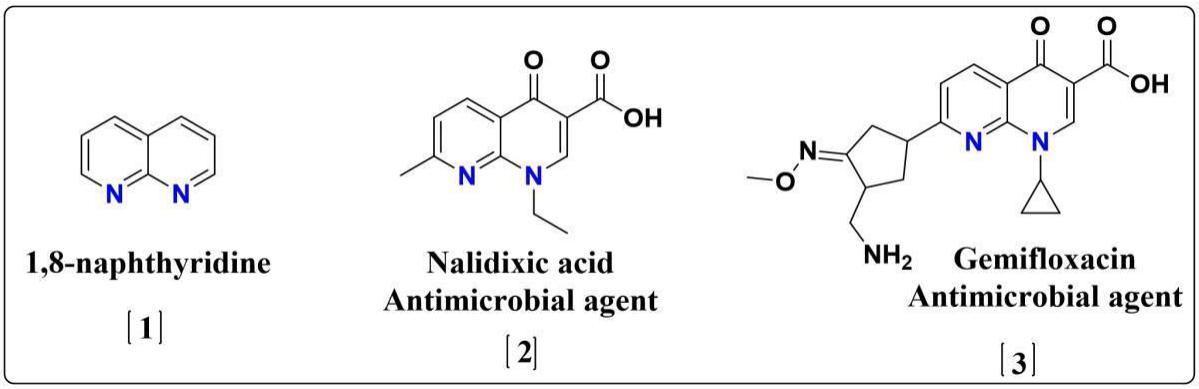
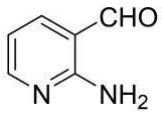
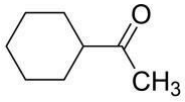
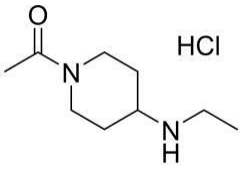
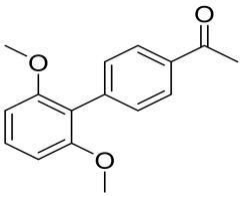
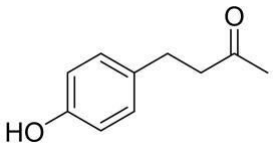
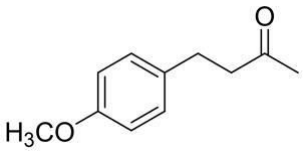
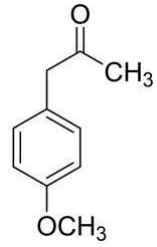


Fig. I Biologically active 1,8-naphthyridines

Table I---- List of purchased reactants are depicted below

Entry	Name	Structure	Sigma- Aldrich CAS number
1	2-aminonicotinaldehyde		7521-41-7
2a	1-cyclohexylethan-1-one		823-76-7
2b	1-(4-(Ethylamino) piperidin-1-yl) ethan-1-one hydrochloride		PH019162

2c	1-(2′,6′-Dimethoxy-[1,1′-biphenyl]-4-yl)ethan-1-one		PH014655
2d	4-(4-Hydroxyphenyl)2-butanone		5471-51-2
2e	4-(4-Methoxyphenyl)2-butanone		104-20-1
2f	4-Methoxyphenylacetone		122-84-9

Experimental section

Melting points were determined using a Cintex melting point apparatus and are uncorrected. TLC was performed by using Merck silica gel 60F254 precoated plates (0.25 mm) and column chromatography was performed by using Silica gel (particle size 100-200 mesh). Proton nuclear Magnetic Resonance (400 MHz) and Carbon Nuclear Magnetic Resonance (100 MHz) spectrums were logged on Bruker AC-300 spectrophotometer in $CHCl_3$with *TMS* as reference. Mass spectrum was documented on JEOL SX-102 spectrophotometer. All the chemicals and reagents used in present investigation were purchased from Sigma- Aldrich Chemical Company.

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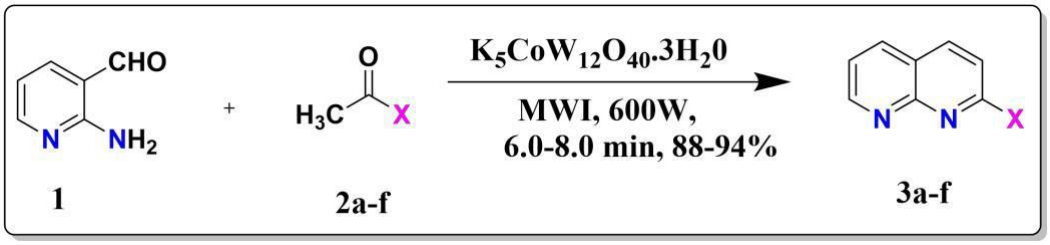
Results and discussions

The Friedlander condensation of 2-aminonicotinaldehyde **1** with various methyl ketones **2a-f** in the presence of potassium dodecatangestocobaltate trihydrate ($K_5CoW_{12}O_{40}.3H_2O$) in solvent-free conditions was subjected to MW irradiation at 600 W 6.0-8.0 mins furnished the corresponding 2-aryl-1,8-naphthyridines **3a-f** (**Scheme I**).This method provides an easy access to 1,8-naphthyridines in fairly good yields, avoids pollution problems, reduces reaction time and is completed in a few minutes.



Scheme I

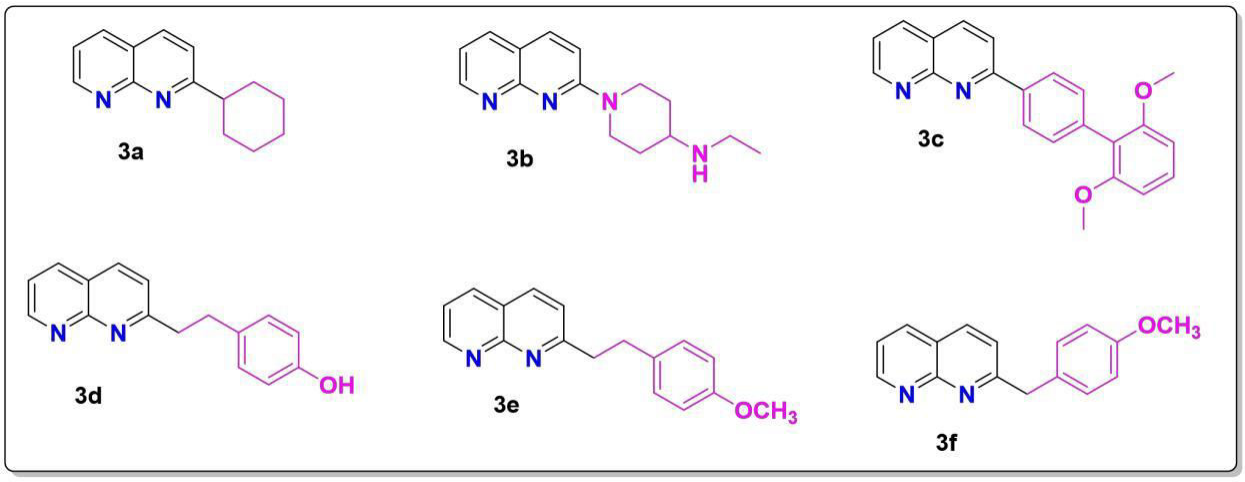


Fig. II Structures of compounds 3a-f

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Table IIPhysical and analytical data of 2-substituted-1,8-naphthyridines

Entry	Reaction Time (min)	m.p. ° C	Yield (%)	Mol. Formula	Found (%) (Calcd)		
					C	H	N
3a	6.5	202	88	$C_{14}H_{16}N_2$	79.33 (79.21	7.63 7.60	13.34 13.20)
3b	7.5	187	90	$C_{15}H_{20}N_4$	70.32 (70.28	7.88 7.86	22.00 21.86)
3c	8.0	255	94	$C_{22}H_{18}N_2O_2$	77.21 (77.17	5.32 5.30	8.28 8.18)
3d	6.0	186	92	$C_{16}H_{14}N_2O$	76.90 (76.78	5.67 5.64	11.26 11.19)
3e	7.0	218	90	$C_{17}H_{16}N_2O$	77.34 (77.25	6.12 6.10	10.74 10.60)
3f	8.0	224	88	$C_{16}H_{14}N_2O$	76.90 (76.78	5.66 5.64	11.33 11.19)

Table III ----- Mass spectral data of compounds 3a-f

Entry	**MS(LC-MSD) $[M+H]^+$ *m/z***
3a	213.12
3b	257.13
3c	343.14
3d	250.11
3e	265.13
3f	250.11

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Table IV --- ^{1}H NMR & ^{13}C NMR data of compounds 4a-f

Entry	^{1}H NMR data (400 MHz, $CHCl_3$) (, ppm)	^{13}C NMR data (100 MHz, $CHCl_3$) (, ppm)
3a	8.87 (d, *J* = 8.9 Hz, 1H), 8.22 (d, *J* = 6.1 Hz, 2H), 7.70 – 7.25 (m, 2H), 2.87 – 2.58 (m, 1H), 2.39 (dd, *J* = 13.4, 5.6 Hz, 2H), 2.00 – 1.56 (m, 8H).	170.08, 156.80, 152.03, 135.88, 135.24, 121.74, 116.78, 114.81, 40.71, 31.45, 25.91, 24.84.
3b	8.83 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.33 – 7.88 (m, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 7.5 Hz,1H), 3.70 – 3.34 (m, 2H), 3.34 – 2.88 (m, 3H), 2.72 – 2.38 (m, 2H), 2.09 – 1.42 (m, 4H), 1.09 (dd, *J* = 11.8, 5.5 Hz, 4H).	161.38, 155.15, 154.02, 137.18, 134.45, 119.61, 115.48, 107.48, 59.04, 48.63, 42.38, 31.02, 14.34.
3c	8.90 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.28 – 8.21 (m, 1H), 8.18 – 8.05 (m, 3H), 7.75 (dd, *J* = 27.1, 7.5 Hz, 3H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 6.68 (d, *J* = 7.5 Hz, 2H), 3.81 (s, 6H).	157.14, 156.49, 152.11, 137.83, 135.90, 134.64, 134.35, 131.67, 125.23, 121.99, 117.78, 116.02, 104.90.
3d	8.88 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.37 – 8.10 (m, 2H), 7.69 – 7.31 (m, 2H), 7.01 (d, *J* = 7.5 Hz, 2H), 6.73 (d, *J* = 7.5 Hz, 2H), 3.53 (s, 1H), 3.26 – 2.72 (m, 4H).	136.45, 136.16, 132.00, 129.30, 120.51, 120.10, 116.73, 114.84, 36.31, 30.64.
3e	8.88 (d, *J* = 7.5 Hz, 1H), 8.21 (dd, *J* = 22.9, 7.4 Hz, 2H), 7.70 – 7.33 (m, 2H), 7.15 (d, *J* = 7.5 Hz, 2H), 6.85 (d, *J* = 7.5 Hz, 2H), 3.81 (s, 3H), 3.00 (qd, *J* = 9.7, 7.4 Hz, 4H).	162.08, 158.62, 156.60, 152.86, 136.45, 136.16, 132.59, 128.66, 120.51, 120.10, 114.84, 114.59, 56.03, 36.31, 30.64.
3f	8.90 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.20 (dd, *J* = 24.9, 8.2 Hz, 2H), 7.73 – 7.36 (m, 2H), 7.02 (dd, *J* = 173.6, 7.5 Hz, 4H), 4.33 (s, 2H), 3.80 (s, 3H).	159.01, 158.15, 156.60, 152.86, 138.96, 136.16, 131.16, 130.31, 121.26, 120.51, 114.84, 56.03, 43.04.

Conclusion

Herein, we have reported an efficient solvent-free synthesis of 1,8-naphthyridines using potassium dodecatangestocobaltate trihydrate as catalyst under MWI.

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