PEG-400 Catalyzed Reaction for the Synthesis of 2, 4, 6-Triarylpyridines and Crystal Structure of 2,4,6-tris(4'-chlorophenyl)pyridine

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Abstract: An efficient and rapid procedure for synthesizing triarylpyridine compounds under mild reaction conditions has been described. Meanwhile, the crystal structure of 2,4,6-tris(4'-chlorophenyl)pyridine was obtained and determined by X-ray single-crystal diffraction. The procedure is operationally simple, giving good to high product yields.

Keyword: 2, 4, 6-Triarylpyridines, phase transfer catalyst, crystal structure.

2,4,6-Triarylpyridines are prominent synthons in supramolecular chemistry, with their π-stacking ability along with directional π-bonding capacity. In particular, they also are important because of their optical properties [1]. In addition, the excellent thermal stabilities of these pyridines have instigated a growing interest for their use as monomeric building blocks in thin films and organometallic polymers [2].

Recent studies have highlighted the biological activity of triarylpyridines, providing impetus for further studies in utilizing this scaffold in new therapeutic drug classes [3].

Since Kröhnke original report on the synthesis of 2, 4, 6-triarylpyridines [4], there has been a plethora of research targeting their syntheses [5-9]. In general, conventional methods used in the synthesis of substituted pyridines use volatile organic solvents and display only moderate to low yields. Although great success has been obtained, many of these processes suffer from drawbacks such as drastic reaction conditions, long reaction time, low product yields, tedious work-up procedures, the use of toxic metal salts as catalysts, and relatively expensive reagents. Hence, the search for the better method, especially the readily available and green catalysts, is still being actively pursued.

Nevertheless there are no reported simple 'one-pot' procedures for the synthesis of triarylpyridines compounds under phase transfer catalyst. As a non-toxic, inexpensive, thermally stable, recoverable and biologically acceptable reagent, polyethylene glycol (PEG) represents a very attractive medium for organic reactions[10]. To the best of our knowledge, the synthesis of triarylpyridines using PEG-400 as catalyst has not so far been reported.

In this letter, we report a green and one-pot method for the synthesis of triarylpyridines in good to excellent yields by the condensation of various aromatic aldehydes, substituted acetophenones with NH_4OAc catalyzed by PEG-400 under microwave irradiation and solvent-free conditions. The experiment results are summarized in Scheme **1** and Table **1** [11].

Under microwave irradiation, the reaction of an aldehyde with an aromatic ketone in the presence of ammonium acetate and PEG-400 completed within 5-7 min and yielded 3a–3p in 83–95% yields (Scheme **1**). While for the formation of compound **3a**, in microwave irradiation heating mode in the absence of the PEG-400, the reaction time is 8 min and the yield is only 78%, which indicates this reaction can be promoted by the PEG-400.

As seen from Table **1**, the various aromatic aldehydes and acetophenone (Table **1**, entries 1, 5, 9, 13) were converted to the corresponding triarylpyridines in excellent yields under the solvent-free conditions. The results clearly show that a substituent on the phenyl ring, whether electron-donating or electron-withdrawing, did not show any significant effect on the product yields, whereas the substituted acetophenones slightly affect product yields. The use of methyl substituted acetophenone rather increased the yield (Table **1**, entries 2), The use of Cl, Br substituted acetophenones led to a little low yield (Table **1**, entries 3,4) under the similar conditions. Furthermore, the crystal structure of 2,4,6-tris(4'-chlorophenyl)pyridine was obtained and the structure of 2,4,6-tris(4-chlorophenyl)pyridine was confirmed by X-ray diffraction crystallography. In (I) (Fig. **1**), the bond lengths and angles are normal and comparable to those observed reported in the compound [12]. The crystal packing demonstrates no significantly short intermolecular contacts.

In conclusion, we have developed a new and simple procedure for the one-pot synthesis of triarylpyridines mediated by PEG-400 under solvent-free and microwave irradiation conditions. The reaction here has the following advantages: milder conditions, shorter reaction times, environmentally benign and good yields. Our work showed that substantial progress could be made in organic reactions under solvent-free conditions, which have great potential in reducing chemical pollution.

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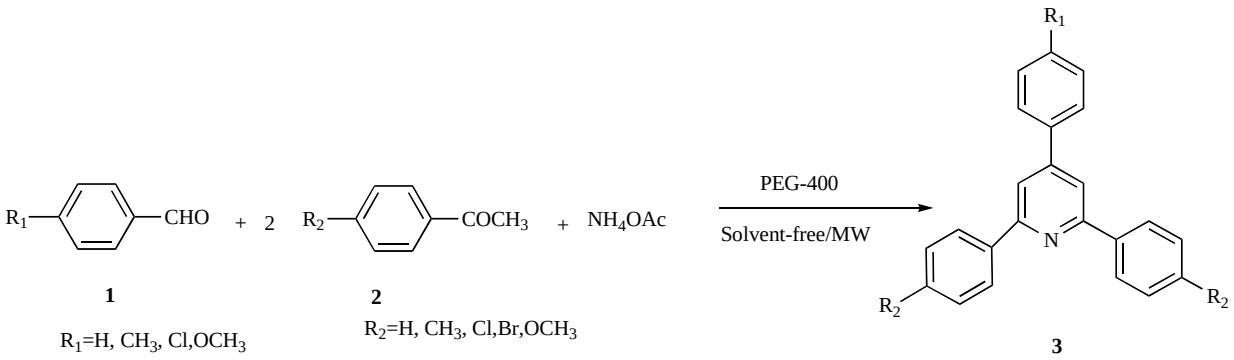


Scheme 1.

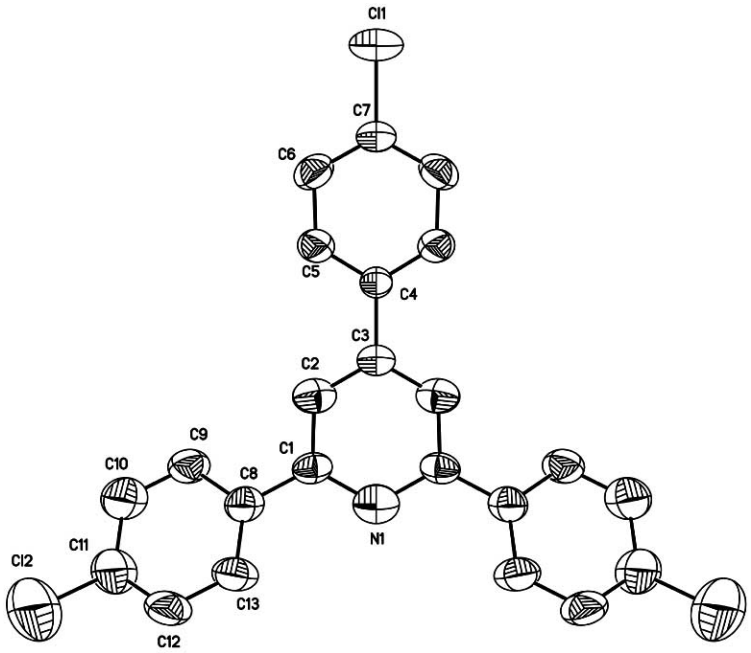
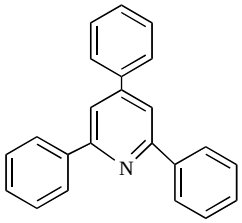
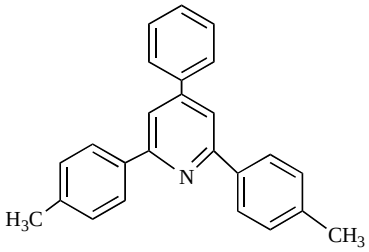
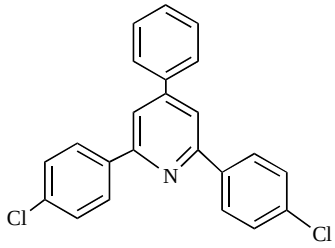
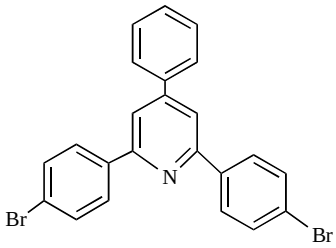
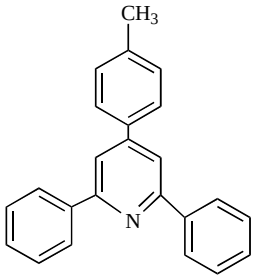
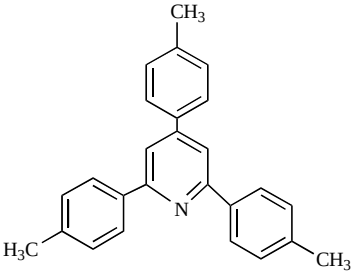
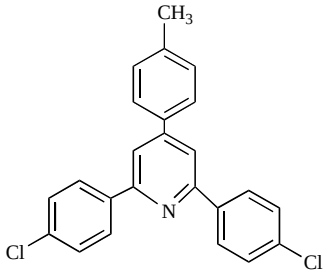
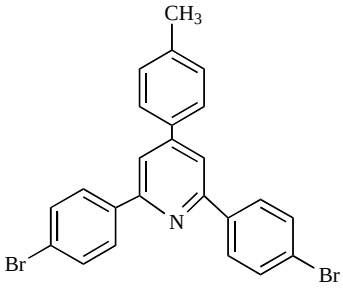


Fig. (1).

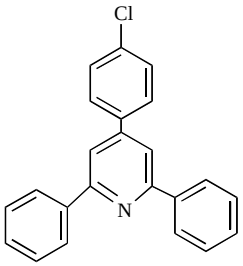
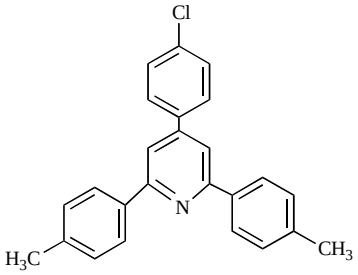
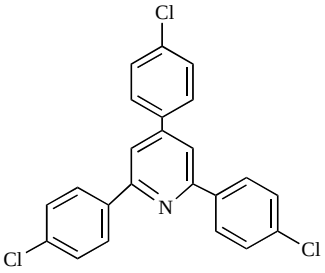
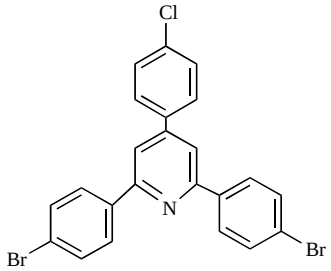
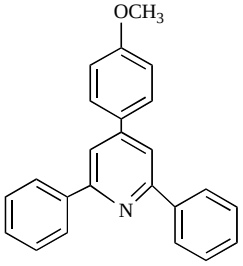
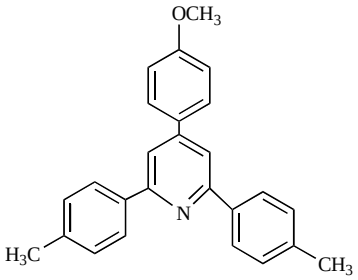
Table 1. Synthesis of 2, 4, 6- Triarylpyridines with Various Aromatic Aldehydes, Substituted Acetophenones with NH_4OAc Catalyzed by PEG-400 Under Microwave Irradiation and Solvent-Free Conditions[a]

Entry	R_1	R_2	Product[b]		Time (Min)	Yield (%)[c]
1	H-	H		**3a**	5	90 [13]
2	H-	CH_3		**3b**	5	94 [13]

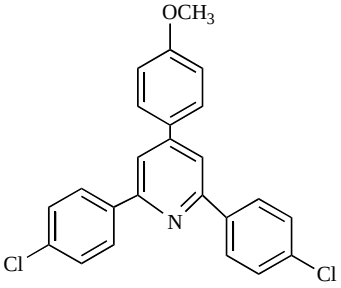
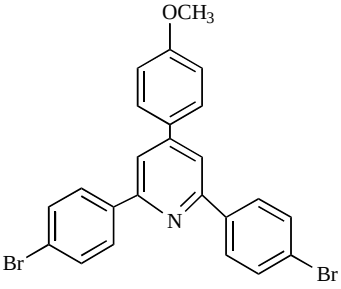
(Table 1). Contd…..

Entry	R_1	R_2	Product[b]		Time (Min)	Yield (%)[c]
3	H-	Cl		**3c**	6	87 [13]
4	H-	Br		**3d**	7	83 [13]
5	CH_3-	H		**3e**	5	91 [13]
6	CH_3-	CH_3		**3f**	5	95 [13]
7	CH_3-	Cl		**3g**	6	89 [14]
8	CH_3-	Br		**3h**	6	85

(Table 1). Contd…..

Entry	R_1	R_2	Product[b]		Time (Min)	Yield (%)[c]
9	Cl-	H		**3i**	6	91 [6]
10	Cl-	CH_3		**3j**	6	93
11	Cl-	Cl		**3k**	7	86
12	Cl-	Br		**3l**	7	85
13	CH_3O-	H		**3m**	5	92 [15]
14	CH_3O	CH_3		**3n**	5	95 [15]

(Table 1). Contd…..

Entry	R_1	R_2	Product[b]		Time (Min)	Yield (%)[c]
15	CH_3O	Cl		**3o**	5	87 [8]
16	CH_3O	Br		**3p**	6	86

[a]Reaction conditions: aromatic aldehydes (5 mmol), substituted acetophenones (10 mmol) and NH_4OAc(5 mmol), PEG-400 (2 mmol) under microwave irradiation (375W) and solvent-free conditions.
[b]All the compounds was characterized by ^{1}H-NMR, ^{13}C-NMR, MS.
[c]Isolated yield.

ACKNOWLEDGEMENTS

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DATA FOR SELECTED COMPOUNDS

3a; Mp 133-135˚C (lit[13]136-137˚C) ^{1}H NMR (400M Hz, CD_3Cl) δ = 8.13 (d, J=8.6, 4H), 7.82 (s, 2H), 7.76-7.43 (m, 11H); ^{13}C NMR (100M Hz, CD_3Cl) δ =157.45, 150.15, 139.52, 139.01, 129.08, 129.01, 128.94, 128.67, 127.14, 127.10, 117.08; MS (m/e, %): 307 (M^+, 100), 230 (M^+-C_6H_5, 21.3), 77 (C_6H_5, 18.21).

3h: Mp 258-260˚C ^{1}H NMR (200M Hz, CD_3Cl) δ = 8.05 (d, J=8.4, 4H), 7.84 (s, 2H), 7.80-7.31 (m, 8H), 2.44 (s, 3H); ^{13}C NMR (100M Hz, CD_3Cl) δ = 156.28, 150.40, 139.36, 138.20, 132.33, 131.87, 129.87, 128.61, 126.94, 123.56, 116.84, 21.26; MS (m/e, %): 481(M^++4, 43.22), 479 (M^++2,100), 477 (M^+, 48.80), 464 (M^+- CH_3, 20.90)

3j: Mp 193-195˚C ^{1}H NMR (200M Hz, CD_3Cl) δ = 8.08 (d, J=8.2, 4H), 7.82 (s, 2H), 7.69-7.29 (m, 8H), 2.47 (s, 6H); ^{13}C NMR (100M Hz, CD_3Cl) δ = 157.47, 148.79, 139.13, 137.57,136.52, 135.04, 129.40, 129.24, 128.42, 126.98, 116.20, 21.31; MS (m/e, %): 371 (M^++2, 34.39), 369 (M^+, 100), 334 (M^+-Cl, 21.39);

3k; Mp 271-273˚C ^{1}H NMR (400M Hz, CD_3Cl) δ = 8.12 (d, J=7.2, 4H), 7.81 (s, 2H), 7.68-7.46 (m, 8H); ^{13}C NMR (100M Hz, CD_3Cl) δ = 156.48, 149.35, 137.46, 137.03, 135.45, 129.40, 128.94, 128.41, 128.35, 116.81; MS (m/e, %): 411 (M^++2, 58.49), 409 (M^+, 100), 374 (M^+-Cl, 30.51).

3l: Mp 286-288˚C ^{1}H NMR (200M Hz, CD_3Cl) δ = 8.04 (d, J=7.2, 4H), 7.80 (s, 2H), 7.65-7.52 (m, 8H); ^{13}C NMR (100M Hz, CD_3Cl) δ = 156.53, 149.29, 137.96, 137.00, 135.45, 131.88, 129.38, 128.60, 128.32, 126.94,116.83; MS (m/e, %): 481 (M^++4, 47.32), 499 (M^++2, 58.49), 497 (M^+, 53.12), 462 (M^+-Cl, 14.73);

3p: Mp 293-295˚C ^{1}H NMR (200M Hz, CD_3Cl) δ = 8.28 (d, J=8.4, 4H), 7.96 (s, 2H), 7.80-7.16 (m, 8H), 3.98 (s, 3H); ^{13}C NMR (100M Hz, CD_3Cl) δ = 162.3, 156.2, 148.6, 139.2, 130.8, 129.0, 128.5, 128.4, 127.4, 117.1, 114.4, 55.6; MS (m/e, %): 499 (M^++4, 51.23), 497 (M^++2,100), 495 (M^+, 48.74), 416 (M^+-Br, 20.41)

The crystal data of the compound **3k**: orthorhombic system , space group *Pnma*, a = 1.8811(2) nm, b = 2.1663(3) nm, c = 4.7237(8) nm, α = 90.00°, β = 90.00°, γ = 90.00°, Dc = 1.410 g.cm^{-3}, V = 1.9249(5) nm^{-3}, Z = 4.

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[11] General Procedure for Synthesis of 2, 4, 6-triarylpyridines: Substituted acetophenones (10 mmol) was added dropwise to aromatic aldehydes (5 mmol) in 50 mL flask, then NH_4OAc (5 mmol) and PEG-400 (2 mmol) was added to the above mixture at room temperature. Then the mixture was irradiated in microwave (375W) in an open flask for 5-7min. The reaction mixture left to cool to room temperature and added 10ml water, the mixture was filtered and given crude product, the title compound was recrystallized from appropriate solvent to analytical purity.

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