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# Synthesis of 2,4,6-triarylpyridines Using $AlPO_4$ Under Solvent-free Conditions

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**Abstract**

A series of 2,4,6-triarylpyridines have been prepared using a variety of aromatic and heteroaromatic aldehydes in the presence of aluminum phosphate ($AlPO_4$) as a heterogeneous catalyst at 120 $^oC$ under solvent-free conditions. The present methodology offers several advantages such as excellent yields, simple procedure, shorter reaction times, milder conditions and the catalyst exhibited remarkable reusable activity.

*Keywords:* Aluminum phosphate; 2,4,6-triarylpyridines; One-pot synthesis; Shorter reaction times; Reusable activity.



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## 1. Introduction

Pyridine ring systems represent an important class of compounds [1] not only for their theoretical interest but also because they constitute the skeleton of some alkaloids [2], of some antitumor antibiotic [3] and because many of these compounds display strong biological activity [4]. These compounds have also attracted considerable attention in recent years because of their wide range of pharmaceutical activities such as antimalarial, vasodilator, anesthetic, anticonvulsant, antiepileptic and agrochemicals such as fungicidal, pesticidal and herbicidal [5-8]. Particularly triarylpyridines are prominent building blockers in supramolecular chemistry with their π-stacking ability, directional H-bonding and coordination. Hence, their synthesis has received much attention. More recently, many improved methods have been developed for the synthesis of 2,4,6-triarylpyridines [9-15].

Heterogeneous catalysts have gained interesting attraction in recent years due to economic and environmental considerations. Especially $AlPO_4$ is a promising acid-base

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catalyst [16-18] in spite of its potential interest, one of the most important aspects with regard to an industrial use. The catalyst is generally inexpensive and can conveniently be handled and removed from the reaction mixture, thus making the experimental procedure simple and eco-friendly.

## 2. Materials and Methods

### 2.1. *General*

All yields refer to isolated products. NMR spectra were recorded on a Varian 200 MHz or Bruker 300 MHz. IR spectra were run on a Perkin-Elmer bio-spectrometer. Mass spectra were recorded on VG micromass 7070H or a Finnigan Met 1020B at 70 eV. The purity of the substances and the progress of the reactions were monitored by TLC on silica gel.

### 2.2. *Typical procedure*

A mixture of an aldehyde (1.0 mmol), an acetophenone (2.0 mmol), $NH_4OAc$ (1.3 mol%) and $AlPO_4$ (10 mmol%) was heated at 120 $^oC$. The progress of reaction was monitored by TLC. After completion of the reaction, hot ethanol was added to the mixture and the insoluble catalyst was filtered off. The filtrate was concentrated and the gummy residue was purified by column chromatography over silica gel using hexane as eluent to obtain pure 2,4,6-triarylpyridines.

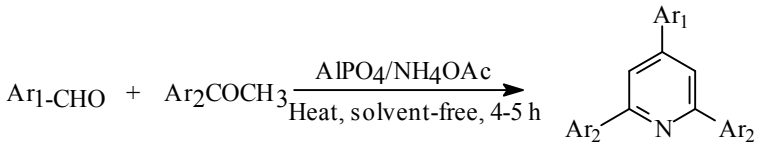
### 2.3. *Spectral data*

Compound **3a:** Colorless crystals, IR (KBr): 3057, 3030, 2923, 1592, 1546, 1492, 1446, 1394, 1276, 1072, 1024, 756, 691 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.35-7.55 (m, 9H, 9CH), 7.73 (d, 2H, *J* = 8.0 Hz, 2CH), 7.89 (s, 2H, 2CH), 8.20 (d, 4H, *J* = 8.0 Hz, 4CH). MS (ESI): 308 (M+1). Compound **3b** : IR (Neat): 3425, 3060, 1680, 1600, 1490, 1095 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): δ 7.40-7.52 (m, 8H, Ar-H), 7.60 (d, *J* = 8.30 Hz, 2H, Ar-H), 7.83 (s, 2H, Ar-H), 8.20 (d, *J* = 6.6 Hz, 4H, Ar-H). Compound **3c:** Pale yellow, IR (KBr): 3059, 2925, 2671, 2555, 1684, 1590, 1423, 1319, 1088, 928, 761, 682 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.10-7.20 (m, 2H, 2CH), 7.38-7.52 (m, 4H, 4CH), 7.70 (d, 2H, *J* = 8.2 Hz, 2CH), 7.80 (s, 2H, 2CH), 8.05 (d, 2H, *J* = 8.2 Hz, 2CH), 8.20 (d, 4H, *J* = 8.0 Hz, 4CH). MS (ESI): 342 (M+1), 344 (M+2). Compound **3d**: IR (KBr): 3050, 2920, 1590, 1545, 1075, 690 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.30-7.50 (m, 8H, 8CH), 7.75 (d, 2H, *J* = 8.2 Hz, 2CH), 7.86 (s, 2H, 2CH), 8.23 (d, 4H, *J* = 8.3 Hz, 4CH). Compound **3e**: IR (KBr): 3060, 3028, 2920, 1590, 1028, 755, 695 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.36-7.57 (m, 4H, 4CH), 7.75-7.90 (m, 4H, 4CH), 7.88 (s, 2H, 2CH), 8.20 (d, 4H, 4CH). Compound **3g** : IR (Neat): 3060, 2925, 1680, 1600, 1470, 1100, 820 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): δ 7.44-7.50 (m, 8H, Ar-H), 7.57 (s, 1H, Ar-H), 7.65 (s, 2H, Ar-H), 8.18 (d, *J* = 6.6 Hz, 4H, Ar-H). Compound **3h** : IR (Neat): 3385, 3195, 1665,

1600, 1400, 828 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): δ 7.43-7.55 (m, 7H, Ar-H), 7.62 (d, *J* = 8.65 Hz, 2H, Ar-H), 7.83 (s, 2H, Ar-H), 8.06 (d, *J* = 8.70 Hz, 4H, Ar-H). Compound **3i:** Colorless crystals, $^1H$ NMR (300 MHz, $CDCl_3$): δ 2.45 (s, 3H, $CH_3$), 7.20 (d, 2H, *J* = 8.0 Hz, 2CH), 7.38-7.50 (m, 3H, 3CH), 7.80 (d, 2H, 2CH), 7.80 (s, 2H, 2CH), 8.09 (d, 2H, *J* = 8.0 Hz, 2CH). MS (ESI): 336 (M+1). Compound **3j** : IR (Neat): 3425, 3060, 1605, 1415, 1242, 1006 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): δ 6.46 (dd, *J* = 3.28 & 1.48 Hz, 1H, Ar-H), 6.96 (d, *J* = 3.44 Hz, 1H, Ar-H), 7.26-7.45 (m, 7H, Ar-H), 7.83 (s, 2H, Ar-H), 8.16 (d, *J* = 7.82 Hz, 4H, Ar-H). Compound **3k** : IR (Neat): 3058, 2920, 1596, 755 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): δ 2.40 (s, 3H, $-CH_3$), 2.56 (s, 3H, $-CH_3$), 7.13-7.26 (m, 9H, Ar-H), 7.73 (s, 2H, Ar-H), 7.82 (d, *J* = 8.15 Hz, 2H, Ar-H), 8.12 (d, *J* = 8.10 Hz, 4H, Ar-H).

## 3. Results and Discussion

We developed for the first time the applicability of a novel recyclable heterogeneous aluminum phosphate for efficient, convenient and facile synthesis of 2,4,6-triarylpyridines by a one-pot reaction of various aldehydes, acetophenones and $NH_4OAc$ at 120 °C (Scheme 1). In addition, to the best of our knowledge, there are no reports on the use of aluminum phosphate as a heterogeneous catalyst for this conversion. This fact has prompted us to investigate $AlPO_4$ for the synthesis of 2,4,6-triarylpyridines in a facile and practical manner (Table 1). Upon screening with *p*-chlorobenzaldehyde, it was found that 10 mol% of $AlPO_4$ is an efficient catalyst to bring about this transformation at 120 °C. In absence of this catalyst no products could be detected even after 10 h and below 10 mol% could not bring about this transformation.




**1** **2** **3a-k**

**Scheme 1**

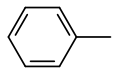
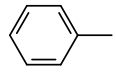
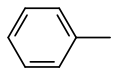
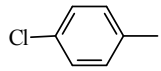
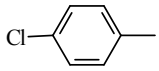
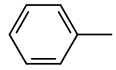
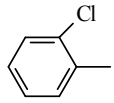
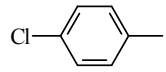
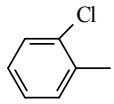
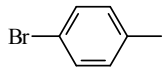
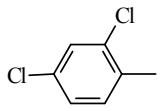
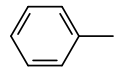
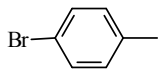
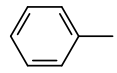
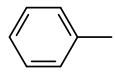
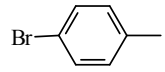
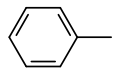
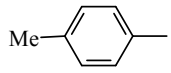
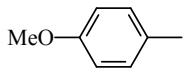
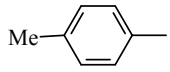
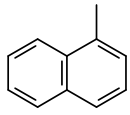
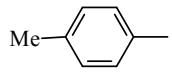
Table 1. Synthesis of 2,4,6-triarylpyridines using different catalysts.

| Sl. | Catalyst | Time (h) | Yield (%) | Ref. |
|---|---|---|---|---|
| 1. | $H_{14}[NaP_5W_{30}O_{110}]$ | 3.5-7.0 | 58-98 | 14 |
| 2. | $HClO_4$-$SiO_2$ | 4.0-6.0 | 69-88 | 15 |
| 3. | $AlPO_4$ | 4.0-5.0 | 76-90 | - |

Encouraged by the results obtained for *p*-chlorobenzaldehyde with acetophenone and $NH_4OAc$, we investigated a number of other aldehydes to probe their behavior under the current catalytic conditions. Thus, a range of symmetrical 2,4,6-triarylpyridines **3a-k** were

synthesized by heating a mixture of aldehydes, acetophenones and $NH_4OAc$ in the presence of $AlPO_4$ at 120 $^oC$ for 4-6 h under solvent-free conditions in 68-88% yields. The effect of the nature of substituents on the aromatic ring showed no obvious effect on this conversion as they were obtained in high yields with short reaction time. The results are summarized in Table 2.

Table 2. Solvent-free synthesis of 2,4,6-triarylpyridine derivatives catalyzed by $AlPO_4$.

| Entry | $Ar_1$ | $Ar_2$ | Time (h) | Yield (%)[a] |
|---|---|---|---|---|
| **a** |  |  | 4 | 87 |
| **b** |  |  | 4 | 88 |
| **c** |  |  | 4 | 90 |
| **d** |  |  | 4 | 89 |
| **e** |  |  | 5 | 76 |
| **f** |  |  | 4 | 87 |
| **g** |  |  | 5 | 78 |
| **h** |  |  | 5 | 80 |
| **i** |  |  | 5 | 88 |
| **j** |  |  | 4 | 90 |
| **k** |  |  | 5 | 75 |

[a]Yield refer to isolated products

*Reusability of the catalyst:* Next, we investigated the reusability and recycling of $AlPO_4$. At first, we put *p*-chloro benzaldehyde (20 mmol), acetophenone (40 mmol), $NH_4OAc$ (26 mmol) and $AlPO_4$ (1 g,) together, and then the mixture was heated at 120 $^oC$. When the reaction was completed, the catalyst was separated by simple filtration by diluting with excess hot ethanol and recovered $AlPO_4$ was reused in subsequent reactions without significant decrease in activity even after four runs.

## 5. Conclusions

In conclusion, we have developed a novel and facile method for the synthesis of 2,4,6-triarylpyridines in the presence of solid supported $AlPO_4$ as a heterogeneous catalyst at 120 $^oC$. Present methodology offers very attractive features such as shorter reaction times, higher yields and will have wide scope in organic synthesis. This simple procedure combined with ease of recovery and reuse of the catalyst makes this method economic, benign, and a waste-free chemical process for the synthesis of 2,4,6-triarylpyridines.

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