



SYNTHESIS OF 2,4,6-TRIARYLPYRIDINES USING TBAHS AS A CATALYST

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ABSTRACT

A simple, efficient and convenient method for the synthesis of 2,4,6-triarylpyridines by a one-pot reaction of aromatic aldehydes, acetophenones and ammonium acetate under solvent free media at 80 °C in the presence of 30 mol% of tetrabutylammonium hydrogen sulphate (TBAHS) is described. The products were formed within 5 – 6 hrs in good to high yields.

Keywords: Tetrabutylammonium hydrogen sulphate, 2,4,6-triarylpyridines, one-pot reaction.

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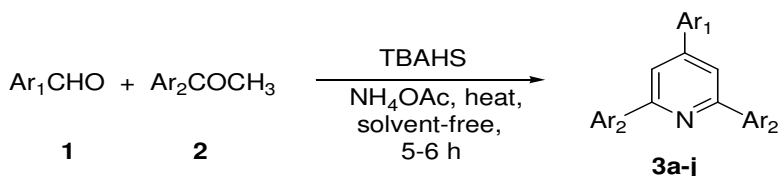
INTRODUCTION

Multicomponent condensation reactions have wide range of applicability in the field of synthetic organic chemistry and it constitute an especially attractive synthetic strategy, since they provide easy and rapid access to large libraries of organic compounds with diverse substitution patterns. Since these are one pot reaction they are easy to carryout than multistep synthesis and these products are formed in a single step and diversity can be achieved by simply varying each component.¹⁻³ In past few years, combinatorial methods using multicomponent reactions have been closely examined as fast and convenient solution for the synthesis of diverse classes of compounds.⁴ In recent, this strategy became important development in the drug discovery in the context of synthesis of biologically active compounds. This method increase the efficiency of the reaction and decrease the number of laboratory operations along with solvents and chemicals used, also reduce the reaction time and facilitate the yield of products than the normal multistep methods.

Pyridine ring systems represent an important class of compounds⁵⁻⁶ not only for their theoretical interest but also because they constitute the skeleton of some alkaloids,⁷⁻¹¹ antitumor, antibiotics.¹² Due to their π -stacking ability, some pyridines are used in supramolecular chemistry.¹³ 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, pesticide and herbicidal.¹⁴⁻¹⁷

Acidic TBAHS act as a phase transfer catalyst and it performs many organic transformations under mild conditions. It has been used for dehydration and cyclization step in Hantzsch reaction and it is easy to handle, inexpensive, thermally stable.¹⁸ To the best of our knowledge there is no report on the synthesis of 2,4,6-triarylpyridines using TBAHS as a reagent. This fact has prompted us to investigate TBAHS for the synthesis of 2,4,6-triarylpyridines in a facile and practical manner. In this communication we report a TBAHS-mediated simple, efficient and convenient three-component reaction with a variety of aromatic aldehydes, acetophenones and ammonium acetate at 120 °C in the preparation of 2,4,6-

triarylpyridines (Scheme 1).



Scheme-1: Synthesis of 2,4,6-triarylpyridines

EXPERIMENTAL

Melting points were recorded on a Buchi 535 melting point apparatus and are uncorrected. All the reactions were monitored by thin layer chromatography performed on precoated silica gel 60F₂₅₄ plates (Merck). IR spectra were recorded on a Perkin-Elmer 683 or a 1310 FT-IR spectrometers with KBr pellets. NMR spectra were recorded on a Varian Unity-400 MHz and BRUKER AMX 300 spectrometers using TMS as an internal standard. Mass spectra were recorded on a VG Micromass 7070H and a Finnigan Mat 1020B mass spectrometers operating at 70eV.

General procedure for the preparation of 2,4,6-triarylpyridines

A mixture of an aldehyde (1.0 mmol), an acetophenone (2.0 mmol), NH₄OAc (1.3 mol%) and TBAHS (30 mol%) were heated at 120 °C. The progress of reaction was monitored by TLC. After completion of the reaction, hot ethanol was added to the mixture and filtered off. The filtrate was concentrated and the gummy residue was purified by column chromatography over silica gel using hexane as eluent to obtain following pure 2,4,6-triarylpyridines.

Representative spectral data

Compound 3a: Colorless crystals, m.p. 132-133 °C (Lit.,¹⁹ m.p. 134-135 °C). IR (KBr): ν_{\max} 3060, 3030, 2923, 1585, 1550, 1275, 1100, 755, 695 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 7.35-7.55 (m, 9H, Ar-H), 7.78 (d, 4H, *J* = 8.2 Hz, Ar-H), 8.22 (d, 4H, *J* = 8.0 Hz, Ar-H). ESI-MS: 308 [M+Na].

Compound 3b: Colorless crystals, m.p. 178-180 °C (Lit.,²⁰ m.p. 180-181 °C). IR (KBr): ν_{\max} 3059, 2924, 1683, 1491, 692 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 7.40-7.52 (m, 8H, Ar-H), 7.67 (d, 4H, *J* = 8.3 Hz, Ar-H), 7.80 (s, 2H, Ar-H), 8.15 (d, 4H, *J* = 7.0 Hz, Ar-H). ESI-MS: 342 [M+Na].

Compound 3j: Colorless crystals, m.p. 170-172 °C (Lit.,¹⁹ m.p. 168-170 °C). IR (KBr): ν_{\max} 3059, 2923, 1605, 1412 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 6.94 (d, 1H, *J* = 3.65 Hz, Ar-H), 7.39-7.51 (m, 8H, Ar-H), 7.90 (s, 2H, Ar-H), 8.17 (d, 4H, *J* = 6.58 Hz, Ar-H).

RESULTS DISCUSSION

Upon screening with 4-chlorobenzaldehyde, it was found that TBAHS with low loading (30 mol%) 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.

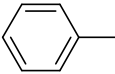
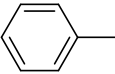
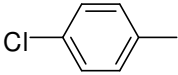
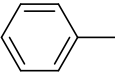
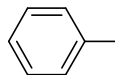
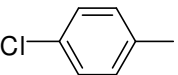
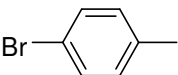
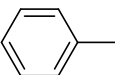
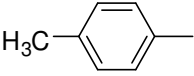
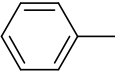
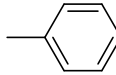
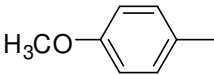
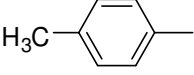
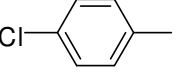
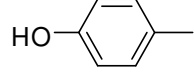
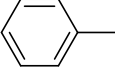
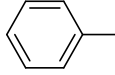
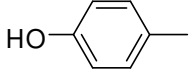
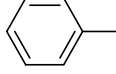

Encouraged by the results obtained from 4-chlorobenzaldehyde with acetophenone and NH₄OAc, we investigated a number of other aldehydes to probe their behavior under the current catalytic conditions. Thus, a range of symmetrical 2,4,6-triarylpyridines **3a-j** were synthesized by heating a mixture of aldehydes, acetophenones and NH₄OAc in the presence of 30 mol% of TBAHS for 5-6 h under solvent-free conditions in 70-75% yields. The effect of the nature of substituent 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 1.

CONCLUSION

In summary, we have developed a convenient approach for the synthesis of 2,4,6-triarylpyridine derivatives with excellent yields and short reaction times which involves the use of inexpensive catalyst TBAHS. Furthermore, the present procedure is readily amenable to parallel synthesis and generation of

combinatorial arylpyridine libraries.

Table 1: TBAHS - Catalyzed synthesis of 2,4,6-triarylpyridine derivatives^a

Entry	Ar ₁	Ar ₂	Time (h)	Yield ^b (%)
a			5	70
b			5	75
c			5	72
d			6	68
e			5	70
f			6	72
g			5	75
h			6	65
i			6	68
j			6	75

^aAll the products were characterized by ¹H NMR, IR and mass spectroscopy.

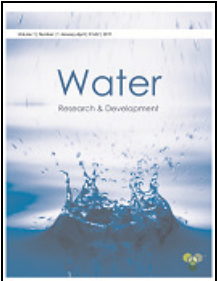
^bIsolated yields.

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[RJC-767/2011]

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