



## One pot and efficient pseudo four-component synthesis of 2,4,6-triarylpyridines under solvent-free condition

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### ABSTRACT

This work described an efficient synthesis of 2,4,6-triarylpyridines. This reaction carried out via pseudo four-component reaction between benzylalcohol derivatives, acetophenone and ammonium acetate under conventional heating at 150 °C and solvent free conditions.

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### KEYWORDS

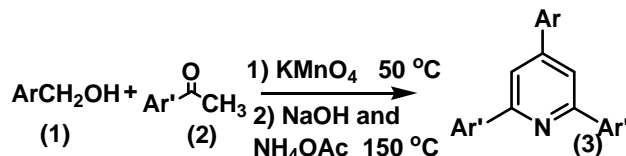
Triarylpyridine;  
Multicomponent;  
Solvent free;  
Benzylalcohol.

### INTRODUCTION

Pseudo multicomponent reactions (PMCRs) are a kind of multicomponent reactions that at least one of the reactant takes part two or more times in reaction steps and the product of the PMCRs contains two or more components of the reactants<sup>[1-4]</sup>.

Pyridines are one of the very interesting heterocyclic compounds. They are useful with their biological activity and exist in some natural products such as NAD nucleotides, pyridoxol (vitamin B<sub>6</sub>), and pyridine alkaloids<sup>[5-9]</sup>. Some examples are used as pharmaceuticals (as antimalarial, vasodilator, anesthetic and anticonvulsant), dyes, additives (as antioxidant), agrochemicals (as fungicidal, pesticidal, and herbicidal), veterinary (as anthelmintic, antibacterial, and antiparasitic), and also in supramolecular chemistry<sup>[9-16]</sup>. 2,4,6-triarylpyridines can also be used as anticoagulants, antimicrobial, antibacterial, anticancer, and anti-HIV activity activities<sup>[17-19]</sup>. 2,4,6-triarylpyridines have been synthesized using various methods and procedures such as reaction between Arylaldehydes, acetophenone and ammonium,

urea, thiourea or their derivatives, in the presence of different catalyst for example Preysslser type heteropolyacid, H<sub>14</sub>[NaP<sub>5</sub>W<sub>30</sub>O<sub>110</sub>], HClO<sub>4</sub>-SiO<sub>2</sub>, Bi(OTf)<sub>3</sub>, pentafluorophenylammonium triflate (PFPAT) and Bi(III)nitrate-Al<sub>2</sub>O<sub>3</sub><sup>[20-28]</sup>. Traditionally, these compounds have been synthesized through the reaction of *N*-phenacylpyridinium salts with  $\alpha,\beta$ -unsaturated ketones in the presence of NH<sub>4</sub>OAc<sup>[29]</sup>.



Scheme 1: One pot and solvent free synthesis of 2,4,6-triarylpyridines (3)

### EXPERIMENTAL

All arylalcohols and acetophenones were obtained from Merck (Germany), and were used without further purification. Melting points were measured with an electro thermal 9100 apparatus. Elemental analyses for

C, H and N were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on an Agilent Technologies (HP) 5973 mass spectrometer operating at an ionization potential of 20 eV.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were measured with Bruker DRX-500 AVANCE (at 500.1 and 125.8 MHz) spectrometer using  $\text{CDCl}_3$  solvent with TMS as an internal standard. Chromatography columns were prepared from Merck silica gel 60 meshes.

### General procedure for the preparation of 2,4,6-triarylpyridine

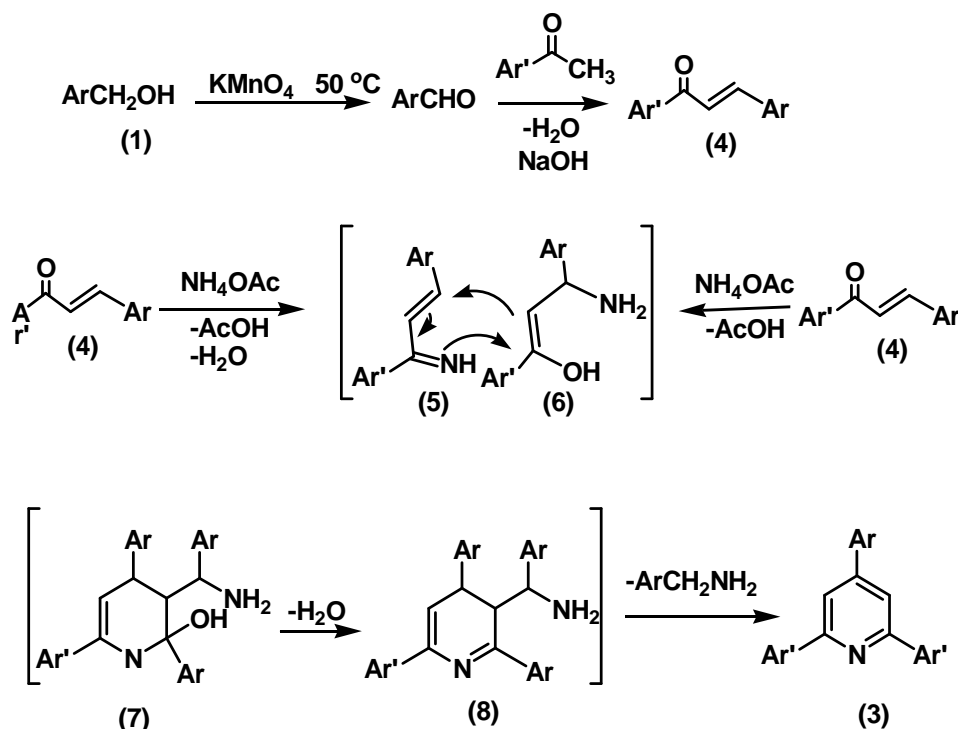
A mixture of benzylalcohol (**1**) (1 mmol) and acetophenone (1 mmol), in the presence of Potassium permanganate  $\text{KMnO}_4$  (0.25 mmol), underwent a solvent free condition at 50-150 °C with  $\text{NH}_4\text{OAc}$  (4 mmol) will produce appropriate 2,4,6-triarylpyridins in good to excellent yields.

The structures of the isolated products, (**3a-j**), were corroborated by comparison of their mp values, elemental analyses, and their spectral data (mass, IR, high-field  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra) with those of authentic samples (TABLE 1). The mp values, elemental analyses, and spectral data of compounds (**3a-j**), were also in good agreement with those of authentic samples<sup>[28]</sup>.

### RESULT AND DISCUSSION

Mechanistically, it is reasonable to assume that the first step may involve oxidation of benzylalcohols (**1**) to benzaldehyde by  $\text{KMnO}_4$  and then condensation with acetophenone will form chalcone (**4**). The Condensation of ammonia with a molecule of chalcone and Michael addition of ammonia to a second chalcone molecule leading to 2,4-diaryl-1-azadi-ene (**5**) and the 1:1 adduct (**6**) respectively. Azadiene (**5**) and adduct (**6**) probably undergo a formal [4+2] cycloaddition reaction to form tetrahydropyridine intermediate (**7**). Dehydration to dihydropyridine intermediate (**8**) and then oxidative aromatization with removal of the benzyl side chain would yield 2,4,6-triarylpyridine (**3**). This oxidative dealkylation has been previously observed. Isolation of benzylamine from the reaction mixture of ammonium acetate and 1,3-diphenyl-2-propen-1-one, (**3a**), confirms the proposed mechanism (Scheme 2). A similar reaction pathway has been proposed for the reaction between N-(diphenylphosphinyl)-1-ethanimine and aromatic aldehydes in the formation of 2,4,6-triarylpyridines<sup>[28]</sup>.

The product (**3a**) was obtained in 87% yield as colorless crystals, mp 134-135°C, IR (KBr) ( $\nu$  max/



Scheme 2 : The proposed mechanism for the one pot synthesis of 2,4,6-triarylpyridines

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cm<sup>-1</sup>): 1575 (shoulder), 1558, 1516, 1483, 1356, 1256, 1065, 1020, 731, 676. MS, m/z(%): 307 (M<sup>+</sup>, 100), 230 (68), 202 (44), 77 (28). Anal. Calcd for C<sub>23</sub>H<sub>17</sub>N (307.39): C, 89.87; H, 5.57; N, 4.56. Found: C, 89.5; H, 5.5; N, 4.9. <sup>1</sup>H NMR (500.1 MHz, CDCl<sub>3</sub>): δ = 7.40-7.60 (9H, m, 9CH), 7.78 (2H, d, J = 8.0 Hz, 2CH), 7.92 (2H, s, 2CH), 8.23 (4H, d, J = 8.0 Hz, 4CH). <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>): δ = 117.18, 127.21, 127.25, and 128.78 (4CH), 129.04 (C), 129.12 and 129.18 (2CH), 139.09 (C), 139.62 (CH), 150.24 and 157.54 (2C).

TABLE 1 : One pot synthesis of 2,4,6-triarylpyridines

3	Ar'	Ar	mp	Yield %
a	Ph	Ph	135	87%
b	Ph	4-Me-Ph	124	77%
c	Ph	2-Me-Ph	122	84%
d	Ph	4-OMe-Ph	100	79%
e	Ph	4-Cl-Ph	129	80%
f	Ph	4-NO <sub>2</sub> -Ph	202	78%
g	4-Me-Ph	4-Me-Ph	179	82%
h	4-Me-Ph	4-Cl-Ph	201	84%
i	4-Me-Ph	4-OMe-Ph	156	85%
j	4-Me-Ph	Ph	159	89%

## CONCLUSION

In conclusion, we have developed a simple and efficient one pot and pseudo four component synthesis method for the preparation of 2,4,6-triarylpyridines. Solvent-free conditions, use of simple and readily available starting materials, excellent yields, and a simplified purification process are the main advantages of this method. This method appears to have a broad scope with respect to variation in the pyridine 2-or 6- and 4-positions

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## REFERENCES

- [1] A. Shaabani, F. Hajishaabaha, M. Mahyari, H. Mofakham, S. W. Ng; *Tetrahedron*, **67**, 8360-8366 (2011).
- [2] R. Ghahremanzadeh, T. Amanpour, A. Bazgir; *Tetrahedron Lett.*, **51**, 4202-4204 (2010).
- [3] V. Nair, V. Varghese, B. P. Babu, C. Sinu, E. Suresh; *Org. Biomol. Chem.*, **8**, 761-764 (2010).
- [4] B. Mohammadi, M. Shafieey, H. Kazemi, A. Ramazani; *Chinese Chemical Letters*, **24**, 497-499 (2013).
- [5] D. Chang-Yih, W. Yang-Chang, W. Shang-Kwei; *Phytochemistry*, **29**, 2689-2691 (1990).
- [6] E. A. Couladouros, A. T. Strongilos, E. Neokosmidis; *Tetrahedron Letters*, **48**, 8227-8229 (2007).
- [7] M. Frater-Schröder, M. Mahrer-Busato; *Bioorganic Chemistry*, **4**, 332-341 (1975).
- [8] D. A. Bender; *Vitamin B6: Physiology*, in: B. Caballero, (Ed); *Encyclopedia of Human Nutrition (Third Edition)*, Academic Press, Waltham, 340-350 (2013).
- [9] M. Srivastava, P. Rani, N. P. Singh, R. A. Yadav; *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, **120**, 274-286 (2014).
- [10] G. W. Cave, M. J. Hardie, B. A. Roberts, C. L. Raston; *European Journal of Organic Chemistry*, 3227-3231 (2001).
- [11] I. J. Enyedy, S. Sakamuri, W. A. Zaman, K. M. Johnson, S. Wang; *Bioorganic & Medicinal Chemistry Letters*, **13**, 513-517 (2003).
- [12] A. D. Pillai, P. D. Rathod, F. P. X. M. Patel, M. Nivsarkar, K. K. Vasu, H. Padh, V. Sudarsanam; *Biochemical and Biophysical Research Communications*, **301**, 183-186 (2003).
- [13] V. Klimešová, M. Svoboda, K. Waisser, M. Pour, J. Kaustová; *Il Farmaco*, **54**, 666-672 (1999).
- [14] B. Y. Kim, J. B. Ahn, H. W. Lee, S. K. Kang, J. H. Lee, J. S. Shin, S. K. Ahn, C. I. Hong, S. S. Yoon; *European Journal of Medicinal Chemistry*, **39**, 433-447 (2004).
- [15] H. Behbehani, H. M. Ibrahim, S. Makhseed, M. H. Elnagdi, H. Mahmoud; *European Journal of Medicinal Chemistry*, **52**, 51-65 (2012).
- [16] N. S. A. M. Khalil; *Carbohydrate Research*, **341**, 2187-2199 (2006).
- [17] A. K. Patel, N. H. Patel, M. A. Patel, D. I. Brahmabhatt; *Arkivoc*, **11**, 28-38 (2010).
- [18] M. Ghazzali, K. Al-Farhan, A. El-Faham, J. Reedijk; *Polyhedron*, **29**, 2829-2832 (2010).
- [19] M. F. Abdel-Megeed, B. E. Badr, M. M. Azaam, G. A. El-Hiti; *Bioorganic & Medicinal Chemistry*, **20**, 2252-2258 (2012).

- [20] P.V.Shinde, V.B.Labade, J.B.Gujar, B.B.Shingate, M.S.Shingare; Tetrahedron Letters, **53**, 1523-1527 (2012).
- [21] N.Montazeri, S.Mahjoob; Chinese Chemical Letters, **23**, 419-422 (2012).
- [22] A.R.Khosropour, I.Mohammadpoor-Baltork, F.Kiani; Comptes Rendus Chimie, **14**, 441-445 (2011).
- [23] A.K.Verma, S.Koul, A.P.S.Pannu, T.K.Razdan; Tetrahedron, **63**, 8715-8722 (2007).
- [24] L.Nagarapu, Aneesa, R.Peddiraju, S.Apuri; Catalysis Communications, **8**, 1973-1976. (2007)
- [25] M.M.Heravi, K.Bakhtiari, Z.Darogheha, F.F.Bamoharram; Catalysis Communications, **8**, 1991-1994 (2007).
- [26] A.Kumar, S.Koul, T.K.Razdan, K.K.Kapoor; Tetrahedron Letters, **47**, 837-842 (2006).
- [27] M.D.Bowman, M.M.Jacobson, B.G.Pujanauski, H.E.Blackwell; Tetrahedron, **62**, 4715-4727 (2006).
- [28] M.Adib, H.Tahermansouri, S.A.Koloogani, B.Mohammadi, H.R.Bijanzadeh; Tetrahedron Letters, **47**, 5957-5960 (2006).
- [29] F.Kröhnke, W.Zecher, D.Drechsler, K.Pfleghar, K.E.Schnalke, W.Weis; Angewandte Chemie, **74**, 811-817 (1962).