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Melamine Trisulfonic Acid (MTSA) on Neutral Alumina as an efficient catalyst for the synthesis of 2,4,6-Triarylpyridines

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ABSTRACT

Neutral Alumina supported melamine trisulphonic acid (MTSA-Al_2O_3) was found to be highly convenient, green and recyclable heterogeneous catalyst for the synthesis of 2,4,6-triarylpyridines through one-pot two component reaction of substituted chalcones and urea at 120 ℃ under solvent free conditions.

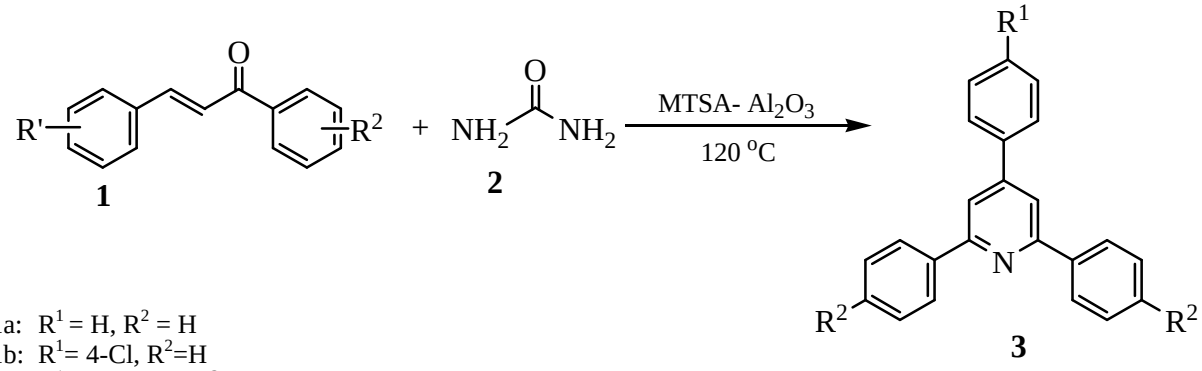
Keywords: 2,4,6-Triarylpyridines,Melamine trisulphonic acid,neutral alumina.

INTRODUCTION

Pyridines are ubiquitous in nature[1]. The pyridyl heterocyclic nucleus is a building block in molecules of natural products, pharmaceuticals such as anticonvulsant, vasodilator, antiepileptic, anaesthetic and agrochemicals such as pesticides and herbicidals[2-5]. Triarylpyridines are widely used in supramolecular chemistry due to their π-stacking ability and directional H-bonding[6].

The general method for synthesis of 2,4,6-triarylpyridines (Krohnke-type pyridines) involves the reaction of N-phenacylpyridinium salts with α,β-unsaturated ketones in the presence of ammonium acetate[7]. A lot of procedures have been developed for the synthesis of 2,4,6-triarylpyridines which include solvent free reaction of chalcones with ammonium acetate[8], reaction of α-ketoketene dithioacetals with methyl ketones in the presence of NH_4OAc[9], solvent free reaction between acetophenones, benzaldehydes and ammonium acetate in the presence of various catalyst for example, $HClO_4$-SiO_2[10], sodium hydroxide[11], I^{12}_2, preyssler type heteropolyacid[13] ionic liquids[14], phase transfer catalysts[15], Lewis acids[16-17] and more recently without a catalyst[18].

However, most of the established methodologies suffer from certain disadvantages such as pollution, high cost, excess reagents, prolonged reaction times, harsh reaction condition, low yields and non-reusability of the catalyst. Melamine trisulfonic acid (MTSA) has received attention now-a-days being a green solid acid and reusable catalyst[19]. MTSA has been used effectively for some organic transformations such as synthesis of coumarins[20], acetylation of amines, phenols and alcohols[21], chemoselective methoxy methylation of alochols[22], regioselective nitration of aromatic compounds[23] and synthesis of polyhydroquinolines[24]. Therefore, here in this methodology, melamine trisulphonic acid on neutral alumina as a solid support is reported. Solid supports have gained considerable interest due to their more surface area, more stability and reusability, low toxicity, greater selectivity and ease of handling[25-26]. To the best of my knowledge, MTSA-Al_2O_3 in one pot-two component synthesis has not been reported so far.



1a: R^1 = H, R^2 = H
1b: R^1= 4-Cl, R^2=H
1c: R^1 = 4-OCH_3, R^2 = H
1d: R^1 = 4-Br, R^2 = H
1e: R^1 = H, R^2 = OCH_3
1f: R^1 = 4-$N(CH_3)_2$, R^2 = H
1e: R^1 = 3-NO_2, R^2 = H
1f: R^1 = 4-OH, R^2 = H
1g: R^1 =4-CH_3, R^2 = H

The substrate chalcones 1a-1i were prepared by well known Claisen-Schmidt condensation[27]. The catalyst was prepared by adsorbing MTSA[28] (5% w/w) on neutral alumina and activation of the air-dried mixture in a hot air-oven at 110 °C for 6 h. The catalyst was reactivated, each time, before use.

Subsequent reactions of 1a-1i with urea 2(2:1M) and a stoichiometric amount of MTSA-Al_2O_3 were carried out in a thermostatically controlled hot air oven at 120 °C for 2=2.5 hrs. The resulting products 3a-i (75-90% yield) were isolated with chloroform, purified by column chromatography and analysed by spectral methods such as, HREIMS, IR, ^{1}H-NMR and ^{13}C-NMR (Table-1).

Experiments were carried to determine the effect of temperature and the catalyst amount on the rate of the reaction. It was observed that at 120 °C and in the presence of 5% (w/w) of the catalyst, the reaction proceeded towards the formation of triphenylpyridine in short reaction time and high yield. Increase in the amount of catalyst did not have any effect on yield and the reaction time. The reusability of the catalyst is one of the most important benefits. The catalyst can be recovered and reused for five additional times without a considerable change in the reaction times and yield.

Table-1: Two component reaction of substituted chalcones and urea at 120 °C.

Entry	R^1	R^2	Time(h)	Yield (%)	m.p(°C)	
					Found	Reported
3a	H	H	2.5	76	133-134	130-131
3b	4-Cl	H	1.8	86	124-126	122-124
3c	4-OCH_3	H	2.0	90	99-100	100-101
3d	4-Br	H	2.0	85	164-166	166-167
3e	H	OCH_3	2.5	86	132-133	---
3f	4-$N(CH_3)$	H	2.5	85	133-134	138-139
3g	3-NO_2	H	4	70	124-126	---
3h	4-OH	H	3.0	62	263-264	---
3i	4-CH_3	H	1.5	78	116-117	118-119

The mechanism of the reaction may be rationalised as involving β-oxygenation of the MTSA activated chalcones enolate which may then undergo Michael addition with second α,β-unsaturated ketone to form a 1,5-diketone enolate adduct. Subsequent heteroannulation with urea via condensation, retro aldol disproportionation and dehydration may lead to the formation of 2,4,6-triaryl pyridine after hydrolysis.

MATERIALS AND METHODS

Melting points were determined with an electrothermal melting point apparatus and are uncorrected. FTIR spectra were obtained on a Nicolet Magna 550 Fourier transform Infrared spectrophotometer as KBr disc. ^{1}H and ^{13}C NMR spectra (400 MHz, 100 MHz) were recorded on a Brucker Advance DRX-400 spectrometer. Elemental analysis were carried out on a EA2400II elemental analyser.

General method for the synthesis of 2,4,6-triarylpyridine (3): Chalcones (1a-1i) and urea in the molar ratio 2:1 with stoichiometric amount of MTSA-Al_2O_3 were grinded in pestle-mortar. Then this mixture was transferred in a stoppered round bottom flask and kept in a hot air oven at 120 °C for 1.5 to 3 hrs. The resulting products 3a-i (62-90% yield) were isolated with chloroform, purified by column chromatography over silica gel.

Spectral data

2,4,6-triarylpyridine, **3a** White solid. **IR:** υmax 3025, 1605 (C=C), 1548 (C=N), 1494, 1420, 1359, 1157, 1028, 872, 731, 720 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.23(s, 2H), 7.49(dd, J = 8.4, 5.2 Hz, 5H), 7.53(dd, J = 8.4, 5.1 Hz, 4H), 7.7(m,4H), 8.2(d, J = 8.2Hz, 2H). **^{13}C-NMR($CDCl_3$):** δ_C 116.3, 125.9, 126.1, 127.3, 128.4, 128.7, 129.2, 125.8, 135.1, 139.4, 141.3, 153.7. **HREIMS:** m/z (rel. Int.) 307.0155(M^+). **Anal. Calcd. For $C_{23}H_{17}N$:** C 89.87, H 5.57, N 4.56; **Found:** C 89.54, H 5.43, N 4.67%

3b. Colourless crystals. 4-(4-chlorophenyl)-2,6-diphenylpyridine.

IR: υ_{max} 3050, 1605, 1548, 1494, 1385, 1350, 1148, 1090, 1018, 920, 865, 720 cm^{-1}. **^{1}H-NMR(400 MHz,$CDCl_3$):** δ 7.29(d, J = 2.9Hz, 2H), 7.40(d, J = 7.2 Hz, 4H), 7.52(dd, J = 7.2, 2.2 Hz, 2H), 7.58(ddd, J = 8.0, 7.1, 2.2 Hz, 4H), 8.20(dd, J = 8.0, 2.2 Hz, 4H). **^{13}C-NMR($CDCl_3$):** δ_C 116.8, 127.2, 128.4, 129.2, 133.9, 135.1, 135.2, 139.4, 155.9, 160.3. **HREIMS:** m/z (rel. Int.) 343 (M^+) **Anal. Calcd. For $C_{23}H_{16}ClN$:** C 80.81, H 4.72, N 4.10, Cl 10.37. **Found:** C 80. 73, H 4.61, N 4.07, Cl 10.30.

3c. 4-(4-methoxyphenyl)-2,6-diphenylpyridine

Colourless needles, **IR:** υ_{max} 3020, 1610, 1555, 1494, 1420, 1359, 1157, 1028, 870, 720 cm^{-1}. **^{1}H-NMR(400 MHz, $CDCl_3$):** δ 3.86(s, 3H), 7.03(d, J = 8.7 Hz, 2H), 7.30(s, 1H), 7.48(ddd, J = 6.9, 8.4, 6.9 Hz, 5H), 7.69(d, J = 8.3 Hz, 2H), 7.84(s, 2H), 8.19(d, J = 8.36 Hz, 4H). **^{13}C-NMR($CDCl_3$):** δ_C 55.3, 114.4, 116.5, 127.0,128.2, 128.6, 128.9,131.2, 139.6, 149.5, 157.4, 160.4. **HREIMS:** m/z(rel. Int.) 308 (M^+). **Anal. Calcd. For $C_{24}H_{19}NO$:** C 85.43, H 5.68, N 4.15, O 4.74. **Found:** C 85.48, H 5.64, N 4.10, O 4.78.

3d: 4-(4-Bromophenyl)-2,6-diphenylpyridine

Colourless crystals, **IR:** υ_{max} 3050, 1605, 1545, 1490, 1385, 1350, 1140, 1096, 920, 760, 720 cm^{-1}. **^{1}H-NMR(400 MHz, $CDCl_3$):** δ 7.28(s, 2H), 7.39(dd, J = 8.7, 2.3 Hz, 4H), 7.52(dd, J = 8.7, 2.3 Hz, 2H), 7.58(ddd, J=8.3, 2.4, 8.3 Hz, 4H), 7.72(d, J=8.7Hz, 2H), 8.28(ddd, J=8.3, 2.4, 8.3Hz, 2H). **^{13}C-NMR(CDCl3):** δ_C 116.5,116.7, 127.2, 128.5,131.1, 132.3, 132.5, 135.3, 139.1, 150.2, 160.3. **HREIMS: m/z(rel. Int.):** 387(M^+) **Anal. Calcd. For $C_{23}H_{16}BrN$:** C 80.81, H 4.72, N 4.10, Br 10.37. **Found:** C 80.73, H 4.6, N 4.61, Br 10.30.

3e: 2,6-bis(4-methoxyphenyl)-4-phenylpyridine

White solid. **IR(KBr):** 3065, 2833, 1608, 1545, 1512, 833, 773, 583 cm^{-1}. **^{1}H-NMR(400 MHz, $CDCl_3$):** δ 8.30(s,4H), 8.06-8.2(m, 4H), 7.57-7.53(m, 3H), 7.11(s, 4H), 3.84(s, 6H). **^{13}C-NMR(100 MHz):** δ 55.1, 113.9, 114.8, 127.2, 128.1, 1290.0,131.3, 139.9, 149.2, 155.9, 160.1. **HREIMS:** m/z (rel. Int.) 368 (M^+ + H, 100). **Anal. Calcd. For $C_{25}H_{21}NO_2$:** C 81.72, H 5.76, N 3.81. **Found:** C 81. 85, H 5.66, N 3.76.

3f. 4-(2,6-Diphenylpyridine-4-yl)-N,N-dimethylbenzamine $C_{25}H_{22}N_2$): Yellow solid

IR(KBr): 3037, 2936, 1598, 1525, 1489, 1442, 1398, 1352, 1233, 1199, 1168, 1068, 1023, 818, 773, 695 cm^{-1}. **^{1}H NMR(400 MHz, DMSO-d_6):** δ 8.27-8.30(d, 4H, J = 7.2 Hz, ArH), 8.10(s, 2H, ArH), 7.90-7.93(d, 2H, J = 8.4 Hz, ArH). 7.44-7.55(m, 6H, ArH), 6.82-6.84(d, 2H, J = 8.4 Hz, ArH), 3.19(s, 3H, CH_3). **^{13}C-NMR(100 MHz, DMSO, d_6):** δ 40.20, 114.8, 118.0,127.4, 127.6, 128.3, 129.3, 136.2, 150.1, 152.0, 155.2. **Anal. Calcd. For $C_{25}H_{22}N_2$:** C 85.68, H 6.33, N 7.99. **Found:** C 85.62, H 6.29, N 7.94. **HREIMS:** m/z(rel. Int.), 350(M^+ + H, 100)

3g. 4-(3-nitrophenyl)-2,6-diphenylpyridine: Yellow solid.

IR(KBr): 1603, 1526, 1438, 1397, 1350, 775, 740, 690 cm^{-1}. **^{1}H-NMR(400 MHz, DMSO-d_6):** δ 8.84(s, 1H), 8.51(d, 1H, J = 7.5 Hz), 8.38-8.28(m, 7H), 7.86(t, 1H, J = 7.9 Hz), 7.64-7.49(m, 6H). **^{13}C-NMR(100 MHz, DMSO-d_6):** δ 117.3, 122.6, 124.3, 127.5, 129.1, 129.8, 131.0, 134.6, 138.9, 139.9, 147.8, 149.0, 157.1. **HREIMS (m/z rel. Int.):** 353(M^+ + H, 100) **Anal. Calcd. For $C_{23}H_{16}N_2O_2$:** C 78.39, H 4.58, N 7.95. **Found:** C 78.48, H 4.52, N 8.01.

3h. 4-(4-hydroxyphenyl)-2,6-diphenylpyridine: White solid.

IR(KBr): 3197, 1603, 1546, 1519, 1398, 839, 776, 696 cm^{-1}. **^{1}H-NMR(400 MHz, DMSO-d_6):** δ 9.90(s, 1H), 8.32(d, 4H, J = 7.5 Hz), 8.13(s, 2H), 7.93(d, 2H, J = 8.1 Hz), 7.57-7.47(m, 6H), 6.95(d, 2H, J = 8.1 Hz). **^{13}C-NMR(100 MHz, DMSO-d_6):** δ 116.1, 116.3, 127.3, 128.5, 129.1, 129.5, 139.4, 149.8, 156.7, 159.2. **HREIMS (m/z rel. Int.):** 324(M^+ + H, 100). **Anal. Calcd. For $C_{23}H_{17}NO$:** C 85.42, H 5.30, N 4.33. **Found:** C 85. 51, H 5.34, N 4.26. **Found:** C 85 51, H 5. 34, N 4.26.

3i: 2,6-Diphenyl-4-p-tolylpyridine $C_{24}H_{19}N$: White solid
IR(KBr): υ_{max} 3034, 2936, 1598, 1543, 1442, 1398, 1286, 1254, 1203, 1170, 1036, 871, 775, 691 cm^{-1}. **^{1}H NMR(400 MHz):** δ 8.29-8.3(d, 4H, J = 7.2 Hz, ArH), 8.14(s, 2H, ArH), 7.92-7.94(d, 2H, J = 7.6Hz, Ar-H), 7.51-7.55(t, 4H, J = 7.2 Hz, ArH), 7.46-7.48(t, 2H, J=7.2 Hz, ArH), 7.34-7.36(d, 2H, J = 7.6 Hz, ArH), 2.48(s, 3H, CH_3). **^{13}C NMR(100 MHz):** δ 21.25, 116.6, 127.3, 127.5, 129.1, 129.6, 130.1, 135.1, 139.4, 149, 156.9. **HREIMS m/z(rel int.):** 320(M^+ +4, 100%). **Anal. Calcd. For $C_{24}H_{19}N$:** C 89.68, H 5.96, N 4.36. **Found:** C 89.62, H 5.90, N 4.32.

CONCLUSION

In conclusion, an efficient method for the synthesis of 2,4,6-triarylpyridines catalysed by melamine trisulphonic acid on neutral alumina is reported. Moreover high yields of the products, relatively short reaction times, ease of preparation, easy work-up procedure, low toxicity and reusability of the catalyst are the other advantages of this method.

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