Nano Fe₃O₄ supported hydrogensulfate ionic liquid catalyzed one pot synthesis of polysubstituted pyridines

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General procedure for the synthesis of catalyst

Preparation of Fe₃O₄@SiO₂: Fe₃O₄ nanoparticles were synthesized by chemical co-precipitation of ferric and ferrous ions in alkali solution. In this procedure a mixture of FeCl₃.6H₂O (2.35 g, 8.7 mmol) and FeCl₂.4H₂O (0.86 g, 4.3 mmol) was dissolved in 40 mL deionized water. The resultant solution under nitrogen atmosphere was left to be stirred for 30 min at 80 °C. Then 5 mL of NH₄OH solution was added with vigorous stirring to produce a black solid and the reaction was continued for another 30 min. The black magnetite nanoparticles were isolated by magnetic decantation, washed several times with deionized water and then dried at 80 °C for 10 h. Fe₃O₄ nanoparticles (1 g) were suspended in a mixture of 100 mL ethanol and NH₃.H₂O (10 mL, 25%) with the help of ultrasonication. Subsequently, 0.4 mL of tetraethoxysilane (TEOS) was added to solution and the mixture was ultrasonicated for 2 h. Afterward silica coated MNPs (MNP@SiO₂) was magnetically separated, washed three times with ethanol and dried at 80 °C for 10 h.

Synthesis of 1-methyl-3-(trimethoxysilylpropyl) imidazolium chloride ([pmim]Cl): A mixture of 0.12 mol (3-chloropropyl)triethoxysilane and 0.12 mol of 1-methylimidazole was refluxed at 78 °C for 24 h under nitrogen atmosphere. The reaction mixture was cooled down and any remaining volatile substances were removed by rotary evaporation. The crude product was additionally washed with Et₂O (5 × 5 ml) and dried under vacuum to afford pure product (slightly yellow viscous oil). ¹H NMR (400 MHz, CDCl₃, TMS): δ = 10.04 (s, 1H), 7.57 (t, J = 2 Hz, 1H), 7.34 (t, J = 1.6 Hz 1H), 4.14 (t, 2H, J = 7.2 Hz), 3.93 (s, 3H), 3.37 (s, 6H) 1.84-1.76 (m, 2H), 0.464-0.423 (m, 2H), ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 137.3, 123.7, 121.9, 51.5, 50.5, 36.3, 23.9, 5.7

Synthesis of 1-methyl-3-(trimethoxysilylpropyl)imidazolium chloride anchored on Fe₃O₄@SiO₂ ()-MNP-[pmim]Cl: [pmim]Cl (0.5 gr, 1.3 mmol) was dissolved in 25 ml of dry toluene and treated with 1 g of previously prepared Fe₃O₄@SiO₂. After heating the slurry at 90 °C for 16 h the resulting solid was then separated by an external magnet and washed with 100 ml of dichloromethane. In the following step, the unreacted ionic liquid was removed by 24 h extraction with boiling dichloromethane (soxhlet extraction). In the next step, the material was dried under high vacuum.

Synthesis of 1-methyl-3-(trimethoxysilylpropyl)imidazolium hydrogensulfate anchored on Fe₃O₄@SiO₂ (MNP-[pmim]HSO₄): In the round bottom flask equipped with stirrer, MNP[pmim]Cl (1gr) was suspended in 20 ml of dry CH₂Cl₂. During vigorous stirring, concentrated H₂SO₄ (1.3 mmol 98%) was introduced drop by drop at 0 °C. Then the mixture was warmed up to the room temperature, and was refluxed for 48 h. Then, the mixture was cooled, filtered and dried.

Scheme S1: Immobilization of ionic liquid on the surface of nanoparticle

Analyses were used to characterize the supported ionic liquid.

Fig S1. FTIR spectra of MNPs(a), MNP@SiO₂ (b), [pim]Cl (c), MNP-[pim]Cl (d), MNP-[pmim]HSO₄ (d)

Fig S2. XRD pattern of MNP (a), MNP [pmim]HSO₄ (b)

Fig S3. The TGA thermogram of (a) MNP@SiO₂ (b) MNP-[pmim]HSO₄

Fig. S4 SEM images of MNP@SiO₂ (left), MNP-[pmim]HSO₄ (right)

Elemental analysis (C:8.36%, H:1.32%, N:2.67% and S:3.19%). The content ratio of C/N (3.13) is very near to the theoretical calculation (3.00).

General procedure for the synthesis of triarylpyridines

To a mixture of aldehyde (1.0 mmol), ketone (2.0 mmol), ammonium acetate (1.3 mmol) was added MNP-([pmim]HSO₄) (0.012 gr, 1.2 mol%) and the resulting mixture was stirred at 100°C for the specific period of time. The progress of the reaction was monitored by TLC. After completion of the reaction, EtOAc (10 ml) was added and cooled reaction mixture. The catalyst was separated by an external magnet, washed with EtOAc, dried and reused for a consecutive run under the same reaction conditions. Evaporation of the organic solvent under reduced pressure gave the crude products. Pure products were obtained by recrystallization by aqueous EtOH. The products were characterized with IR, ¹HNMR and ¹³CNMR spectra.

Scheme S2: Synthesis of triarylpyridines catalyzed by MNP-([pmim]HSO₄)

Table S2: Synthesis of 2,4,6-triphenylpyridine^a

Entry	Ar ¹	Ar ²	Time (min)	Yield ^b	M. p (°C) ^{Ref}
1	C ₆ H ₅ -	C ₆ H ₅ -	50	90	133-134 ^[41]
2	4-FC ₆ H ₄ -	C ₆ H ₅ -	55	87	204-206 ^[41]
3	4-ClC ₆ H ₄ -	C ₆ H ₅ -	45	95	124-125 ^[41]
4	4-BrC ₆ H ₄ -	C ₆ H ₅ -	40	90	102-104 ^[41]
5	4-NO ₂ C ₆ H ₄ -	C ₆ H ₅ -	40	85	196-198 ^[41]
6	4-MeC ₆ H ₄ -	C ₆ H ₅ -	60	90	122-124 ^[41]
7	4-MeOC ₆ H ₄ -	C ₆ H ₅ -	70	87	99-100 ^[43]
8	4-OHC ₆ H ₄ -	C ₆ H ₅ -	75	87	195-197 ^[43]
9	4-N(Me) ₂ C ₆ H ₄ -	C ₆ H ₅ -	80	90	138-140 ^[31]
10	Pyridine-4yl	C ₆ H ₅ -	65	83	187-190 ^[31]
11	Thiophen-2-yl	C ₆ H ₅ -	85	78	161-163 ^[41]
12	Furan-2-yl	C ₆ H ₅ -	80	75	179-181 ^[41]
13	C ₆ H ₅ -	4-ClC ₆ H ₄ -	45	85	126-128 ^[40]
14	4-ClC ₆ H ₄ -	4-ClC ₆ H ₄ -	35	90	269-270 ^[41]
15	4-MeC ₆ H ₄ -	4-ClC ₆ H ₄ -	50	89	118-119 ^[40]
16	4-MeOC ₆ H ₄	4-ClC ₆ H ₄ -	45	88	190-191 ^[40]

^a Conditions: aldehyde/acetophenone/NH₄OAc/MNP-[pmim]HSO₄: 1/2/1.3/0.012, 120 °C, solvent-free.^b Yields refer to pure isolated products

4-(4-Fluorophenyl)-2,6-di phenyl pyridine (Table S2, entry 2): ¹HNMR (400 MHz, DMSO-d₆, δ/ppm): 7.49-7.51 (m, 2H), 7.55-7.57 (m, 4H), 7.86 (b, 3H), 7.88 (b, 2H), 8.21-8.23 (m, 5H). ¹³C NMR (100 MHz, DMSO-d₆, δ/ppm): 112.7, 116.8, 118.5, 127.6, 127.9, 128.8, 129.2, 129.4, 132.9, 139.0, 143.6, 143.2, 157.9. IR (KBr disc): (cm⁻¹): 1600, 1542, 1514, 1246, 1179, 1026, 826, 753. m/z (ESI) 325.1 (M⁺, 100%), 320.1 (50%), 172.1 (16.4%), 171.2 (14.6%), 154.1 (6.7%), 153.2 (4.2%).

4-(4-Choloro)-2,6-di phenyl pyridine (Table S2, entry 3): ¹HNMR (400 MHz, DMSO-d₆, δ/ppm): 7.13-7.19 (m, 2H), 7.28-7.35 (m, 3H), 7.58-7.62 (m, 2H), 7.63-7.72 (m, 3H), 7.74-7.76 (m, 2H), 7.95 (s, 2H), 8.10 (d, 2H, *J*= 7.2 Hz). ¹³C NMR (100 MHz, DMSO-d₆, δ/ppm): 114.3, 115.0, 115.1, 115.6, 117.8, 120.0, 127.0, 128.3, 128.4, 128.8, 128.9, 133.9, 134.1, 141.2, 147.1, 157.7.

4-(4-Bromophenyl)-2,6-di phenyl pyridine (Table S2, entry 4): ¹H NMR (400 MHz, DMSO-d₆, δ/ppm): 6.84-6.89 (m, 2H), 6.99 (d, 2H, *J* = 8.8 Hz), 7.26 (d, 2H, *J* = 8.8 Hz), 7.41 (t, 2H, *J* = 7.6 Hz), 7.51 (s, 4H), 7.95 (d, 2H, *J* = 2.4 Hz), 8.02 (d, 2H, *J* = 7.2 Hz). ¹³C NMR (100 MHz, DMSO-d₆, δ/ppm): 114.7, 115.1, 115.6, 118.1, 128.3, 128.8, 129.0, 133.4, 133.6, 134.2, 140.1, 140.2, 146.8, 146.9, 157.0.

4-(4-Nitrophenyl)-2,6-di phenyl pyridine (Table S2, entry 5): ¹HNMR (400 MHz, DMSO-d₆, δ/ppm): 8.11 (d, 2H, *J*= 7.6 Hz), 7.83 (s, 2H), 7.59 (d, 2H, *J*= 7.2 Hz), 7.54-7.48 (m, 4H), 7.43 (t, 2H, *J*= 7.2 Hz), 7.26 (d, 2H, *J*= 8 Hz), 7.15 (t, 2H, *J*= 7.2 Hz). ¹³C NMR (100 MHz, DMSO-d₆, δ/ppm): 112.2, 120.7, 121.2, 125.1, 125.9, 127.6, 127.8, 130.4, 130.6, 135.0, 140.9, 141.2, 144.4, 156.4, 159.2.

4-(Thiophen-2-yl)-2,6-di phenyl pyridine (Table S2, entry 11): ¹HNMR (400 MHz, DMSO-d₆, δ/ppm): 7.06 (d, 2H, *J*= 8 Hz), 7.12 (s, 1H), 7.13 (d, 1H, *J*= 3.2 Hz), 7.17(d, 2H, *J*= 8.8 Hz), 7.26 (s, 2H), 7.35-7.40 (m, 2H), 7.42-7.46 (m, 1H), 7.51 (d, 1H, *J*= 6.8 Hz), 7.84 (d, 2H, *J*= 8 Hz), 7.91 (d, 2H, *J*= 2 Hz). ¹³C NMR (100 MHz, DMSO-d₆, δ/ppm): 122.8, 125.7, 126.2, 126.3, 127.5, 128.4, 129.0, 129.3, 130.2, 131.9, 132.6, 136.0, 139.4, 156.3.

2,4,6-Tri-4-choloro phenyl pyridine (Table S2, entry 14): ¹HNMR (400 MHz, DMSO-d₆, δ/ppm): 6.92 (d, 2H, *J*= 8.4 Hz), 7.25-7.29 (m, 3H), 7.47-7.48 (m, 4H), 7.77-7.79 (m, 3H), 7.92 (s, 2H), 8.20 (d, 2H, *J*= 4.8 Hz). ¹³C NMR (100 MHz, DMSO-d₆, δ/ppm): 112.0, 121.6, 126.5, 126.7, 129.3, 130.5, 131.5, 132.0, 132.1, 136.2, 138.9, 142.1, 143.8, 151.3, 157.4.

4-(4-Methoxy phenyl)-2,6-di-4-choloro phenyl pyridine (Table S2, entry 16): ¹HNMR (400 MHz, DMSO-*d*₆, δ/ppm): 3.88 (s, 3H), 6.97 (d, 2H, *J*= 8.4 Hz), 7.41 (t, 2H, *J*= 6.4 Hz), 7.46-7.49 (m, 3H), 7.57-7.58 (m, 3H), 7.62 (d, 2H, *J*= 8.8 Hz), 8.08 (d, 2H, *J*= 7.2 Hz), 8.28 (s, 2H). ¹³C NMR (100 MHz, DMSO-*d*₆, δ/ppm): 55.3, 115.9, 120.7, 125.8, 127.3, 127.5, 128.6, 130.4, 133.7, 141.2, 143.5, 144.7, 158.2.