Manganese ferrite nanoparticles catalyzed tandem and green synthesis of spirooxindoles

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Experimental Part

The chemicals used in this work were obtained from Fluka and Merck and were used without purification. Melting points were measured on an Electrothermal 9200 apparatus. Mass spectra were recorded on a Shimadzu QP 1100 Ex mass spectrometer operating at an ionization potential of 70 ev. IR spectra were recorded as KBr pellets on a Perkin-Elmer 781 spectrophotometer and an Impact 400 Nicolet FT-IR spectrophotometer. 1H NMR and 13C NMR spectra were recorded in DMSO–d6 solvents on a Bruker DRX-400 spectrometer with tetramethysilane as internal reference. The elemental analyses (C, H, N) were obtained from a Carlo ERBA Model EA 1108 analyzer. X-ray diffraction (XRD) pattern of the as-synthesized material was obtained using a Holland Philips Xpert X-ray powder diffraction (XRD) diffractometer (CuK, radiation, λ = 0.154056 nm), at a scanning speed of 2°/min from 10° to 100° (20). The nanocatalyst was determined using a FEI Quanta 200 scanning electron microscope (SEM) operated at a 20 kV accelerating voltage. The purity determination of the substrates and reaction monitoring were accomplished by TLC on silica-gel polygram SILG/UV 254 plates (from Merck Company).

Typical experimental procedure for the preparation of catalyst

MnFe2O4 nanoparticles has been prepared following the reported standard protocol by co-precipitation of MnCl2 and FeCl3 in water in the presence of sodium hydroxide. Briefly, MnCl2·4H2O and FeCl3·6H2O were taken in molar ratio of Mn2+: Fe3+ = 1:2 to prepare 0.3 mol·L⁻¹ metal ion solution of 100 ml containing 0.1 mol·L⁻¹ Mn2+ and 0.2 mol·L⁻¹ Fe3+, then was slowly dropped into 100 ml NaOH solution of 3 mol·L⁻¹ at the preheated temperature of 95°C. After aging for 2 h with continuous stirring, the mixture was filtered, washed and dried at 60°C for 12 h.

Typical procedure for the preparation of spiro-furo-pyridine-indoline-carbonitriles 5a-l:

A mixture of isatin 1 (1 mmol), malononitrile 2 (1 mmol), anilinolactones 3 (1 mmol), and MnFe2O4 (5 mol%) were taken in PEG-400 (1 mL). The resulting mixture was stirred at 90°C for an appropriate time. After completion of the reaction as indicated by TLC, the reaction mixture was magnetically concentrated with the aid of an external magnet to separate the catalyst. After separation of the catalyst, H2O (10 ml) was added to the reaction mixture and was shaken for a few minutes to
dissolve PEG and precipitate the product. The crude product (insoluble in water) was filtered and re-crystallized by ethanol for more purification. The desired pure product was identified by physical and spectroscopic data.

2-Amino-2',5-dioxo-1-phenyl-5,7-dihydro-1H-spiro[furo[3,4-b]pyridine-4,3' indoline]-3-carbonitrile (5a):

![Chemical structure of 5a]

White powder (Yield: 79%). mp>300°C. IR (KBr) (ν_max/ cm⁻¹): 3385, 2180, 1750, 1683. ¹H NMR (DMSO-d₆, 400 MHz): δ_ppm: 4.34-4.65 (2H, m, OCH₂) 6.03 (2H, s, NH₂), 6.81-7.56 (9H, m, ArH), 10.49 (1H, s, NH). ¹³C NMR (DMSO-d₆, 100 MHz): δ_ppm: 48.2, 60.2, 66.1, 99.2, 109.9, 119.5, 122.5, 125.3, 129.3, 130.7, 134.3, 134.4, 141.8, 152.7, 159.5, 170.0, 178.0. Anal. Calcd for C₂₁H₁₄N₄O₃: C, 68.10; H, 3.81; N, 15.13%; Found C, 68.16; H, 3.87; N, 15.08%; MS: m/z 370.

2-Amino-2',5-dioxo-1-p-tolyl-5,7-dihydro-1H-spiro[furo[3,4-b]pyridine-4,3'- indoline]-3 carbonitrile (5b):

![Chemical structure of 5b]

White powder (Yield: 83%). mp>300°C. IR (KBr) (ν_max/ cm⁻¹): 3454, 2185, 1721, 1682. ¹H NMR (DMSO-d₆, 400 MHz): δ_ppm: 2.37 (3H, s, CH₃) 4.47-4.64 (2H, m, OCH₂) 5.99 (2H, s, NH₂), 6.82-7.44 (8H, m, ArH), 10.48 (1H, s, NH). ¹³C NMR (DMSO-d₆, 100 MHz): δ_ppm: 21.2, 48.2, 60.0, 66.1, 99.0, 109.8, 119.5, 122.5, 125.3, 128.9, 129.3, 131.2, 131.7, 134.3, 140.3, 141.8, 152.8, 159.6, 170.1, 178.0. Anal. Calcd for C₂₂H₁₆N₄O₃: C, 68.74; H, 4.20; N, 14.58%; Found C,68.69; H, 4.24; N, 14.53%. MS: m/z 384.
2-Amino-1-(4-chlorophenyl)-2',5-dioxo-5,7-dihydro-1H-spiro[furo[3,4-b]pyridine-4,3'-indoline]-3-carbonitrile (5c)

Cream powder (Yield: 80%). mp>300°C. IR (KBr) (νmax/ cm⁻¹): 3334, 2185, 1722, 1683. ¹H NMR (DMSO-d₆, 400 MHz): δppm: 4.52-4.71 (2H, m, OCH₂) 6.21 (2H, s, NH₂), 6.81-7.63 (8H, m, ArH), 10.50 (1H, s, NH). ¹³C NMR (DMSO-d₆, 100 MHz): δppm: 48.2, 60.5, 66.8, 99.3, 109.8, 115.6, 122.5, 125.4, 129.3, 130.7, 131.3, 133.4, 134.3, 135.3, 141.8, 152.7, 159.4, 170.0, 178.0. Anal. Calcd for C₂₁H₁₃ClN₄O₃: C, 62.31; H, 3.24; N%, 13.84%. Found C,62.36; H, 3.30; N, 13.79%. MS: m/z 406, 404.

2-Amino-1-(3-chlorophenyl)-2',5-dioxo-5,7-dihydro-1H-spiro[furo[3,4-b]pyridine-4,3'-indoline]-3-carbonitrile (5d):

Gray powder (Yield: 77%). mp>300°C. IR (KBr) (νmax/ cm⁻¹): 3454, 2186, 1720, 1686. ¹H NMR (DMSO-d₆, 400 MHz): δppm: 4.51-4.73 (2H, m, OCH₂) 6.24 (2H, s, NH₂), 6.81-7.82 (8H, m, ArH), 10.51 (1H, s, NH). ¹³C NMR (DMSO-d₆, 100 MHz): δppm: 48.2, 60.2, 66.1, 99.4, 109.8, 119.4, 122.5, 125.4, 128.2, 129.3, 129.7, 130.8, 132.1, 134.2, 134.6, 135.8, 141.8, 152.6, 159.2, 170.0, 177.9. Anal. Calcd for C₂₁H₁₃ClN₄O₃: C, 62.31; H, 3.24; N, 13.84%. Found C,62.36; H, 3.19; N, 13.78%. MS: m/z 406, 404.
2-Amino-2',5-dioxo-1-p-tolyl-5,7-dihydro-1H-spiro[furo[3,4-b]pyridine-4,3'-indoline]-3-carbonitrile (5e):

White powder (Yield: 80%). mp > 300°C. IR (KBr) (ν_{max}/ cm^{-1}): 3448, 2187, 1713, 1680. \(^1\)H NMR (DMSO-\(d_6\), 400 MHz): δ_{ppm}: 2.30 (3H, s, CH\(_3\)), 4.33-4.70 (2H, m, CH\(_2\)O) 6.06 (2H, s, NH\(_2\)), 6.83-7.46 (8H, m, ArH), 10.52 (1H, s, NH). \(^13\)C NMR (DMSO-\(d_6\), 100 MHz): δ_{ppm}: 17.2, 48.3, 59.7, 66.0, 99.2, 110.0, 119.5, 122.6, 124.8, 128.3, 129.3, 129.8, 131.1, 132.3, 132.9, 134.4, 137.9, 141.7, 152.5, 159.2, 170.0, 177.9. Anal. Calcd for C\(_{22}\)H\(_{16}\)N\(_4\)O\(_3\): C, 68.74; H, 4.20; N, 14.58%;. Found C, 68.69; H, 4.14; N, 14.63%. MS: \(m/z\) 384.

2-Amino-1-(2,4-dichlorophenyl)-2',5-dioxo-5,7-dihydro-1H-spiro[furo[3,4-b]pyridine-4,3'-indoline]-3-carbonitrile (5f):

Cream powder (Yield: 79%). mp > 300°C. IR (KBr) (ν_{max}/ cm^{-1}): 3453, 2186, 1753, 1687. \(^1\)H NMR (DMSO-\(d_6\), 400 MHz): δ_{ppm}: 4.41-4.80 (2H, m, OCH\(_2\)) 6.43 (2H, s, NH\(_2\)), 6.83-7.98 (7H, m, ArH), 10.56 (1H, s, NH). \(^13\)C NMR (DMSO-\(d_6\), 100 MHz): δ_{ppm}: 48.2, 59.7, 66.0, 100.1, 110.0, 119.3, 122.8, 124.9, 129.4, 129.8, 130.6, 131.1, 133.4, 134.2, 135.4, 136.7, 141.7, 152.3, 158.7, 169.8, 177.7. Anal. Calcd for C\(_{21}\)H\(_{12}\)Cl\(_2\)N\(_4\)O\(_3\): C, 57.42; H, 2.75; N, 12.76%;. Found C, 57.48; H, 2.69; N, 12.81%. MS: \(m/z\) 440, 438.
Due to very low solubility of the products 5g, we cannot report the $^{13}$C NMR data for this product.

2-Amino-1-(4-bromophenyl)-2',5-dioxo-5,7-dihydro-1H-spiro[furo[3,4-b]pyridine-4,3'-indoline]-3-carbonitrile (5g):

![Chemical Structure]

Cream powder (Yield: 75%). mp>300°C. IR (KBr) ($\nu_{max}$/ cm$^{-1}$): 3448, 2192, 1742, 1694. $^1$H NMR (DMSO-$d_6$, 400 MHz): $\delta_{ppm}$: 4.51-4.72 (2H, m, OCH$_2$) 6.21 (2H, s, NH$_2$), 6.81-7.78 (7H, m, ArH), 10.47 (1H, s, NH). Anal. Calcd for C$_{21}$H$_{13}$BrN$_4$O$_3$: C, 56.14; H, 2.92; N, 12.47%. Found C, 56.19; H, 2.87; N, 12.53. Ms: $m/z$ 450, 448

2-Amino-5'-bromo-2',5-dioxo-1-phenyl-5,7-dihydro-1H-spiro[furo[3,4-b]pyridine-4,3'-indoline]-3-carbonitrile (5h):

![Chemical Structure]

White powder (Yield: 73%). mp>300°C. IR (KBr) ($\nu_{max}$/ cm$^{-1}$): 3340, 2182, 1726, 1675. $^1$H NMR (DMSO-$d_6$, 400 MHz): $\delta_{ppm}$: 4.45-4.66 (2H, m, OCH$_2$) 6.12 (2H, s, NH$_2$), 6.80-7.65 (8H, m, ArH), 10.64 (1H, s, NH). $^{13}$C NMR (DMSO-$d_6$, 100 MHz): $\delta_{ppm}$: 48.5, 59.4, 66.3, 98.3, 111.9, 114.3, 119.3, 128.2, 129.2, 129.5, 130.7, 132.1, 134.3, 136.5, 141.2, 152.9, 159.9, 170.1, 177.7. Anal. Calcd for C$_{21}$H$_{13}$BrN$_4$O$_3$: C, 56.14; H, 2.92; N, 12.47%. Found C, 56.20; H, 2.87; N, 12.52%. Ms: $m/z$ 450, 448.
2-Amino-5'-bromo-2',5-dioxo-1-o-tolyl-5,7-dihydro-1H-spiro[furo[3,4-b]pyridine-4,3'-indoline]-3-carbonitrile (5i):

Cream powder (Yield: 76%). mp>300°C. IR (KBr) (νmax/ cm⁻¹): 3348, 2178, 1718, 1680. ¹H NMR (DMSO-d₆, 400 MHz): δppm: 2.36 (3H, s, CH₃), 4.43-4.84 (2H, m, OCH₂) 6.07 (2H, s, NH₂), 6.78-7.54 (7H, m, ArH) 10.70 (1H, s, NH). ¹³C NMR (DMSO-d₆, 100 MHz): δppm: 21.3, 48.5, 59.3, 66.2, 98.2, 111.9, 114.3, 119.4, 128.2, 128.9, 129.2, 130.0, 131.2, 131.6, 132.1, 136.6, 140.4, 141.1, 153.0, 160.0, 170.1, 177.7. Anal. Calcd for C₂₂H₁₅BrN₄O₃: C, 57.04; H, 3.26; N, 12.09%. Found C, 57.10; H, 3.32; N, 12.14%. Ms: m/z 464, 462.

2-Amino-5'-nitro-2',5-dioxo-1-phenyl-5,7-dihydro-1H-spiro[furo[3,4-b]pyridine-4,3'-indoline]-3-carbonitrile (5j):

Cream powder (Yield: 81%). mp>300°C. IR (KBr) (νmax/ cm⁻¹): 3352, 2188, 1735, 1674. ¹H NMR (DMSO-d₆, 400 MHz): δppm: 4.50-4.68 (2H, m, OCH₂) 6.23 (2H, s, NH₂), 7.05-8.31 (8H, m, ArH), 11.25 (1H, s, NH). ¹³C NMR (DMSO-d₆, 100 MHz): δppm: 48.5, 58.6, 66.5, 97.7, 110.2, 119.2, 121.2, 126.8, 129.2, 129.5, 130.7, 134.2, 135.0, 143.3, 148.4, 153.2, 160.4, 170.1, 178.7. Anal. Calcd for C₂₁H₁₃N₅O₅: C, 60.72; H, 3.15; N, 16.86%. Found C, 60.68; H, 3.20; N, 16.91%. Ms: m/z 415.
2-Amino-1-(4-bromophenyl)-5'-nitro-2',5-dioxo-5,7-dihydro-1H-spiro[furo[3,4-b]pyridine-4,3'-indoline]-3-carbonitrile (5k):

Cream powder (Yield: 84%). mp>300°C. IR (KBr) (νmax/ cm⁻¹): 3362, 2187, 1735, 1692. ¹H NMR (DMSO-d₆, 400 MHz): δppm: 4.57-4.69 (2H, m, OCH₂) 6.40 (2H, s, NH₂), 7.07-8.33 (7H, m, ArH), 11.24 (1H, s, NH). ¹³C NMR (DMSO-d₆, 100 MHz): δppm: 48.5, 58.5, 66.5, 97.9, 110.2, 119.1, 121.3, 124.2, 126.8, 131.5, 133.6, 133.7, 135.0, 143.3, 148.4, 153.1, 160.1, 170.0, 178.6. Anal. Calcd for C₂₁H₁₂BrN₅O₅: C, 51.03; H, 2.45; N, 14.17%. Found C,51.09; H, 2.51; N, 14.12%. Ms: m/z 495, 493.

2-Amino-1-(3-chlorophenyl)-5'-nitro-2',5-dioxo-5,7-dihydro-1H-spiro[furo[3,4-b]pyridine-4,3'-indoline]-3-carbonitrile (5l):

Cream powder (Yield: 85%). mp>300°C. IR (KBr) (νmax/ cm⁻¹): 3362, 2180, 1741, 1689. ¹H NMR (DMSO-d₆, 400 MHz): δppm: 4.56-4.74 (2H, m, OCH₂) 6.42 (2H, s, NH₂), 7.07-8.37 (7H, m, ArH), 11.24 (1H, s, NH). ¹³C NMR (DMSO-d₆, 100 MHz): δppm: 48.5, 58.5, 66.6, 97.9, 110.3, 119.3, 121.5, 126.9, 128.2, 129.6, 131.0, 132.1, 134.6, 135.0, 135.5, 143.3, 148.4, 153.1, 160.1, 170.1, 178.7. Anal. Calcd for C₂₁H₁₂ClN₅O₅: C, 56.07; H, 2.69; N, 15.57%. Found C,56.12; H, 2.64; N, 15.61%. Ms: m/z 451, 449.