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Iron-oxide nanoparticles mediated cyclization of 3-(4-chlorophenyl)-1-hydrazinylisoquinoline to 1-(4,5-dihydropyrazol-1-yl)isoquinolines

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Abstract Iron-oxide nanoparticles were obtained using chitosan templates and their crystalline character and particle size have been confirmed through powder x-ray diffraction and transmission electron microscopy measurements. The particle sizes were found to be 10–25 nm. The diversified chalcones **2** were reacted with 1-hydrazinylisoquinoline **1** in the presence of iron-oxide nanoparticles to the corresponding pyrazolines **3a–j** in high yield and purity. The pyrazolines were characterized by spectroscopic techniques.

Keywords Chalcones · Pyrazolines · Heterocycles · Nanoparticles · Iron oxide

Introduction

Pyrazolines are considered as potential bacteriostatic, fungicidal, anti-cancer, anti-inflammatory, anti-diabetic, anesthetic, and analgesic agents [1–3]. They are extensively used in organic synthesis [4–6]. The synthesis of pyrazolines generally

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involves the condensation of chalcones and hydrazine or its derivatives [7, 8]. In recent years, significant research work has been devoted to pyrazolines synthesis; however, pyrazolines carrying isoquinoline ring substituents has been little attempted. The magnetic nanoparticles are produced through different methodologies [9–12], however, all resulted in aggregated nanoparticles. In order to overcome this, copolymer templates and their application has been reported [13–19]. The current study envisioned the use of chitosan templates for the synthesis Fe_2O_3 nanoparticles by controlled heat treatment. X-ray diffraction (XRD) and transmission electron microscopy (TEM) have been used to characterize the nanoparticles. In our continued interest on isoquinolines and related compounds [20–40], in this paper we report some 3,5-disubstituted pyrazolines with the mediation of iron-oxide nanoparticles obtained through a chitosan template-assisted synthesis.

Results and discussion

The chitosan template provided binding sites for the Fe, which on subsequent controlled heat treatment, generate smaller size and non-agglomerated iron-oxide nanoparticles [41, 42], which are spatially well separated. The morphology and microstructure of the as-prepared samples [41, 42] were detected on a TEM (Tecnai F20 HR TEM) operated at 200 kV and equipped with an energy-dispersive x-ray spectrometer and on a high-resolution TEM (FEI TECNAI F30) with HAADF detector operated at 300 kV.

TEM of the iron-oxide nanoparticles were obtained by dispersing in ethanol and the droplets of the dispersion were placed on copper grids coated with carbon film and dried under natural conditions. The TEM images suggest that the use of chitosan in the material synthesis limits the particle size. The iron-oxide–chitosan mixture generates particles that are significantly smaller.

The x-ray diffraction pattern (Fig. 1a) of iron-oxide nanoparticles are in agreement with the theoretical data and suggest that the crystalline character has been improved in the presence of the template. The crystallite size was found to be between 10 and 25 nm when iron oxide was synthesized using the chitosan template. Figure 1b displays the TEM of the magnetic nanoparticles generated on a chitosan template. The nanoparticles obtained have good uniform distribution of particle morphology, with a size of 10–25 nm. The chemical composition of the catalyst was determined by energy dispersive x-ray (EDX) analysis. The EDX of such particles showed the presence of oxygen and iron atoms (Fig. 2).

In this paper, a series of 3,5-disubstitutedpyrazolines **3a–3j** with different substituents both on the isoquinoline and pyrazoline rings were attempted using iron-oxide nanoparticles. These compounds were obtained by the action of isoquinoline hydrazine, **1** on chalcones **2a–2j**, which in turn generated aldol condensation intermediates of the corresponding aldehydes and ketones in ethanolic NaOH solution (Scheme 1). The chalcones **2a–2j** were confirmed on the basis of their characteristic IR absorption peak at due to the presence of a conjugated

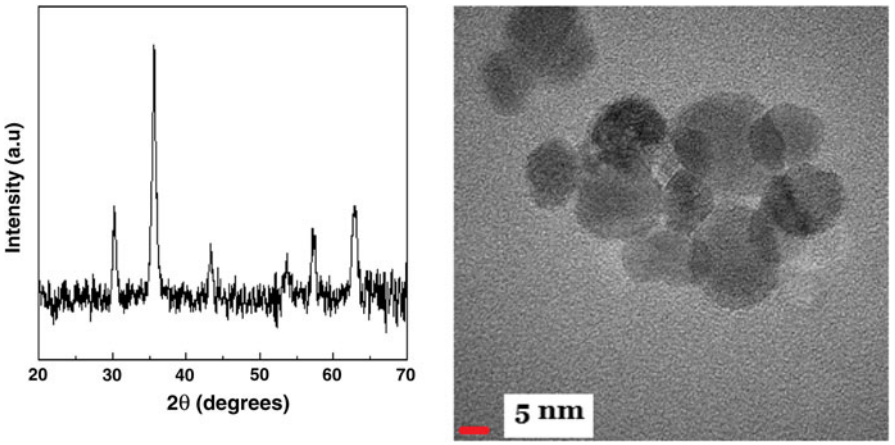


Fig. 1 X-ray diffraction pattern and TEM image of iron-oxide nanoparticles

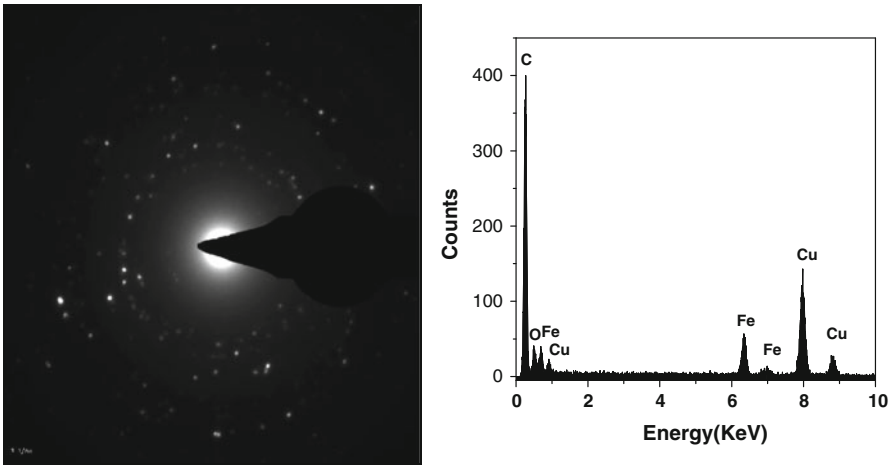
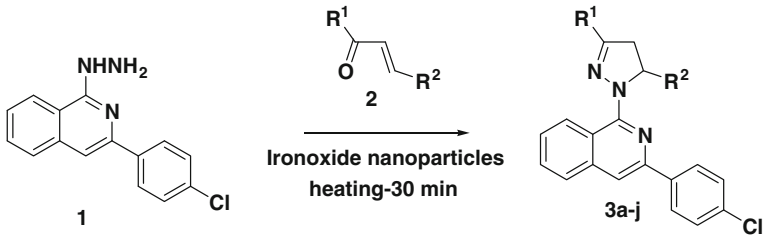


Fig. 2 SAED and EDAX images of iron-oxide nanoparticles



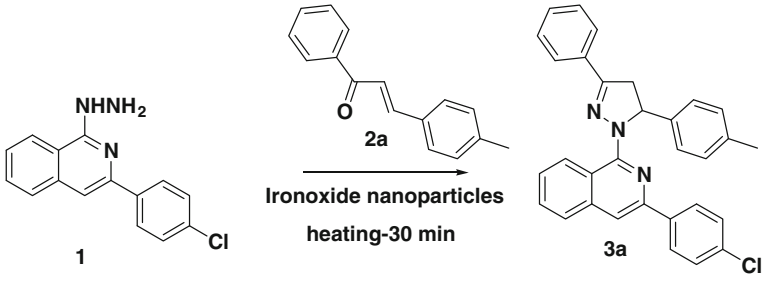
Scheme 1 Cyclization of hydrazine and chalcones in the presence of iron-oxide nanoparticles

carbonyl group and their ^{1}H-NMR spectra suggest the α, β- protons appear in the downfield aromatic region.

The optimization of the reaction condition was carried using condensation of 1-hydrazino-3-(4-chlororpheny)isoquinoline **1** and chalcone **2a** (Scheme 2) as a model reaction. The development of optimized condition, screening of various catalysts, solvents, and catalyst loading was explored as presented in Tables 1, 2, and 3. As shown in Table 1, the reaction proceeds well in the presence of iron-oxide nanoparticles (entry 7). However, other nano-material catalysts (Table 1, entries 2, 3, and 5) and bulk catalysts (Table 1, entries 1, 4, and 6) are less effective and produced lower yields.

The influence of solvents was then explored, which indicated ethanol was as an efficient solvent (Table 2, entry 2) and the methanol, a moderate solvent. Further, to optimize the reaction condition, the amount of iron nanoparticles loading was investigated, which clearly suggested that an optimized amount of 5 mol% catalyst required for the effective conversion (Table 3, entry 5).

With the optimized result in hand, various pyrazolines were obtained (as shown in Scheme 1; Table 4). The desired products **3a–j,** were obtained in high yield



Scheme 2 3-(4-Chlorophenyl)-1-{5-(4-methylphenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl} isoquinoline

Table 1 Effect of catalyst in the condensation of **1** with chalcone **2a**

Entry	Catalyst	Yield[a] (%)
1	ZnO (bulk)	30
2	ZnO (nanorod)	40
3	ZnO (nanoparticles)	42
4	SnO (bulk)	46
5	SnO (nanoparticles)	48
6	Iron oxide (bulk)	48
7	Iron oxide (nanoparticles)	60

Reaction conditions: **1** (0.1 mmol), **2** (0.11 mmol), catalyst (5 mol%), 1,4-dioxane (10 mL), reflux for 30 min

[a] Isolated yield

Table 2 Effect of solvent in the reaction of **1** with, **2a**

Entry	Base	Yield[a] (%)
1	1,4-dioxane	60
2	Ethanol	94
3	Methanol	79
4	Toluene	54
5	Benzene	52

Reaction conditions: **1** (0.1 mmol), **2a** (0.11 mmol), iron-oxide nanoparticles (5 mol%), solvent (10 mL); reflux for 30 min

[a] Isolated yield

Table 3 Effect of iron-oxide nanoparticles loading in the condensation of **1** and **2a**

Entry	Mol%	Yield[a] (%) **3a**
1	1	20
2	2	56
3	4	68
4	4.5	70
5	5	94
6	5.5	96
7	6	96
8	8	97
9	10	97
10	Nil	Trace

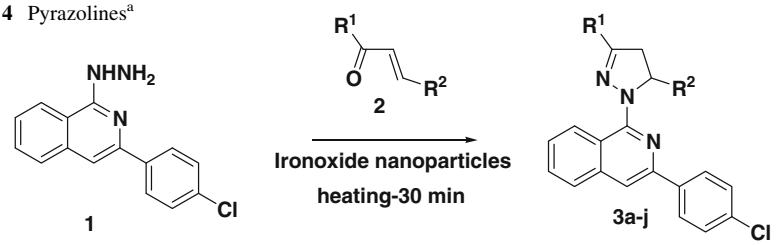
Reaction conditions: **1** (0.1 mmol), **2a** (0.11 mmol), ethanol (10 mL) reflux for 30 min

[a] Isolated yield

(85–97%) and purity. The purified products were characterized by different spectral techniques including ^{1}H, ^{13}C NMR, LC–MS, IR, and CHN analysis.

The proposed mechanism (as depicted in Scheme 3) of the condensation reaction involved the initial nucleophilic addition of the carbonyl carbon of the chalcones. The chalcones adsorbed on the iron-oxide nanoparticles surface were activated for nucleophilic addition due to C=O polarization and increased electrophilicity, towards more nucleophilic nitrogen atoms of the hydrazine with the formation of hydroxyl derivative, which then undergo dehydration and subsequent cyclization to form the pyrazolines product again with the facilitation of the iron-oxide nanoparticles. The advantages of this catalyst include their non-toxicity compared to conventional copper, cobalt, or nickel catalysts, and mild reaction condition requirement; easy removal from the reaction mixture facilitated due to their magnetic properties and further the elimination of auto-oxidation of the desired pyrazolines to the corresponding pyrazoles.

Table 4 Pyrazolines[a]



Entry	R^1	R^2	Yield (%)	Compound
a	C_6H_5	4-$CH_3C_6H_4$	94	3a
b	3-$CH_3C_6H_4$	4-$CH_3C_6H_4$	90	3b
c	4-ClC_6H_4	C_6H_5	84	3c
d	4- Pyridyl-	C_6H_5	91	3d
e	4-FC_6H_4	4-FC_6H_4	89	3e
f	4-FC_6H_4	4-$CH_3C_6H_4$	86	3f
g	3-FC_6H_4	C_6H_5	83	3g
h	3-OHC_6H_4	C_6H_5	90	3h
i	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	94	3i
j	4-OHC_6H_4	C_6H_5	85	3j

Reaction conditions: **1** (0.1 mmol), **2a** (0.11 mmol), iron-oxide nanoparticles (5 mol%), ethanol (10 mL); reflux for 30 min

[a] Isolated yield

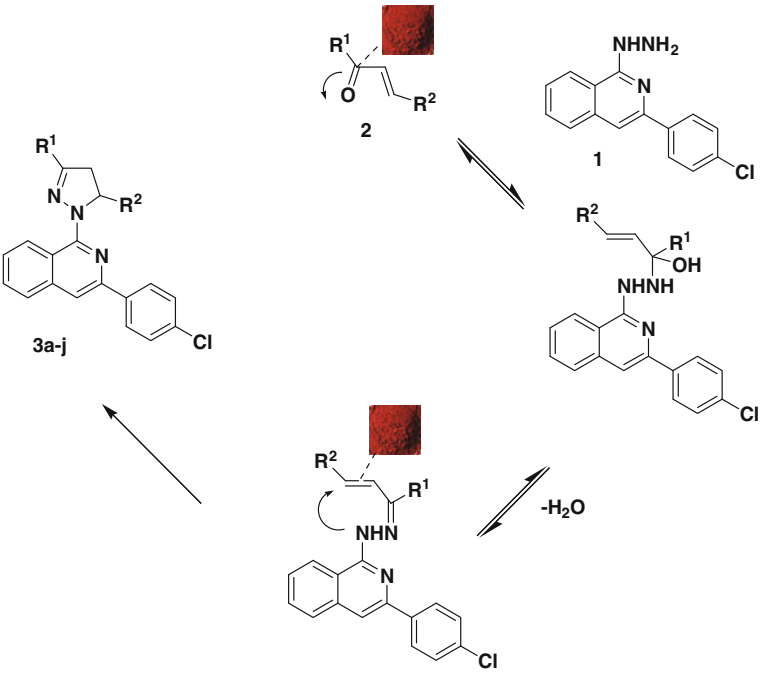
Experimental methods

The chemicals and reagents were purchased from Aldrich Chemicals (India) and solvents were purchased from S.D. Fine Chemicals (India). Melting points were taken on an Elchem microprocessor-based DT apparatus in open capillary tubes. IR spectra were obtained on a Nucon infrared spectrophotometer, India (KBr disc). NMR spectra were recorded on a Bruker 500 spectrometer, India, and chemical shifts are reported in parts per million (δ) relative to tetramethylsilane (TMS) as an internal standard.

General procedure for the preparation of 3,5-disubstituted-pyrazolines (**3a**–**3j**)

The chalcones **2a**–**2j** were prepared by stirring a mixture of the appropriate aldehyde and ketones (0.1 mol of each) in ethanolic NaOH solution (80 mL) for several hours at room temperature until a yellow to orange color had developed. Then, the reaction mixture was filtered and the resulting precipitate was washed with 3% aqueous HCl. The crude material was recrystallized from ethanol (96%) to obtain a bright-yellow crystalline product. The structures of these chalcones were established on the basis of their chemical properties and spectral data.

Method A: Chalcones **2a**–**2j** (0.05 mol) were dissolved in dry acetic acid (100 mL) was then reacted with an appropriate isoquinoline hydrazine **1** for several



Scheme 3 Mechanism of the reaction

hours at 90–100 °C until the cyclization was complete and a deep-orange color developed. The reaction mixture was then evaporated in vacuo to separate the acetic acid, and the residue was recrystallized from ethanol or acetonitrile to obtain the pure crystalline pyrazolines **3a–j**.

Method B: A solution of chalcones **2a–2j** (0.05 mol), in ethanol (10 mL) was refluxed with an appropriate isoquinoline hydrazine, **1** in the presence of 5 mol% iron-oxide nanoparticles until the cyclization was complete and a deep-orange color developed. The reaction mixture was then filtered to remove iron-oxide nanoparticles and evaporated in vacuo, and the residue was re-crystallized from ethanol or acetonitrile to obtain the pure crystalline pyrazolines **3a–j**. The structures of these compounds were established on the basis of their chemical properties and spectral analysis.

The chalcones when reacted with isoquinolinylhydrazines 1, cyclizes through α,β-unsaturated hydrazone to give a 2-pyrazoline ring **3a–3j** in the presence of a suitable cyclizing agent like dry acetic acid under prolonged refluxing condition or with iron-oxide nanoparticles in 30 min. All the structures of products were appropriately established by spectroscopic data and analytical methods. In general, the pyrazolines exhibited C=N stretching vibrations in the $\nu \sim$ 1,650–1,450 cm^{-1} range. In addition, ^{1}H-NMR spectra of these compounds generally exhibit an AMX pattern for the presence of two diastereotopic protons (CH_2 protons of the pyrazoline ring) at C-4 resonated as a pair of doublets of doublets at $\sim\delta$ 3.30 ppm (H_A), $\sim\delta$ 3.90 ppm (H_B) and one single proton at the C-5 position appear as

doublets of doublets, due to vicinal coupling with the two magnetically non-equivalent protons of the methylene group at position 4 of the pyrazoline ring. The ^{13}C NMR data of pyrazolines exhibited the chemical shift values of the carbon atoms at $\sim\delta$ 25–43 ppm (C-4), $\sim\delta$ 64 ppm (C-5), and $\delta \sim$ 150 ppm (C-3) of the 2-pyrazoline ring.

3-(4-Chlorophenyl)-1-{5-(4-methylphenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl} isoquinoline (**3a**)

Yellow solid, mp 151–152 °C, IR (cm^{-1}) 3,051, 3,019, 2,910, 1,614, 1,592, 1,567, 1,513, 1,496, 1,410, 1,351, 1,204, 1,143, 1,053, 902, 828, 786, 756. ^{1}H NMR (DMSO-D_6): δ 9.33–9.30 (d, 1H, $J = 7.71$ Hz), 7.97–7.94 (d, 2H, $J = 8.52$ Hz), 7.88–7.82 (m, 4H), 7.73–7.61 (m, 4H), 7.51–7.44 (m, 4H), 7.35–7.32 (d, 2H, $J = 7.89$ Hz),7.11–7.08 (d, 2H, $J = 7.86$ Hz), 6.16–6.098 (t, 1H, $J = 8.46$ Hz), 3.96–3.86 (t, 1H, $J = 12.03$ Hz), 3.25–3.08 (m, 1H), 2.15 (s, 3H). ^{13}C NMR (DMSO-D_6): 152.0, 151.9, 145.8, 140.9, 139.5, 138.0, 136.4, 133.4, 132.4, 130.5, 129.9, 129.5, 129.2, 128.8, 128.4, 128.3, 127.8, 126.7, 126.5, 126.3, 119.5, 110.0, 64.1, 21.0. LC–MS: m/e 474.16, $C_{31}H_{24}ClN_3$ requires Mol. wt.: 473.17. Elemental analysis, calculated: C, 78.55; H, 5.10; Cl, 7.48; N, 8.87%. Found: C, 78.61; H, 5.06; N, 8.81%.

3-(4-Chlorophenyl)-1-{5-(4-methylphenyl)-3-(3-methyl phenyl)-4,5-dihydro-1*H*-pyrazol-1-yl} isoquinoline (**3b**)

Yellow solid, mp 135–136.5 °C, IR (cm^{-1}) 2,921, 2,865, 1,552, 1,493, 1,455, 1,409, 1,331, 1,089.4, 1,054, 1,033, 1,012, 879, 816, 780, 750, 717, 682, 545. ^{1}H NMR (DMSO-D_6): δ 9.32–9.29 (d, 1H, $J = 8.31$ Hz),7.96–7.93 (d, 2H, $J = 8.61$ Hz), 7.87–7.81 (m, 2H), 7.72–7.61 (m, 4H), 7.46–7.43 (d, 2H, $J = 8.58$ Hz), 7.39–7.23 (m, 4H), 7.10–7.07 (d, 2H, $J = 7.86$ Hz), 6.14–6.07 (t, 1H, $J = 8.28$ Hz), 3.92–3.82 (t, 1H, $J = 11.88$ Hz), 3.14–3.06 (dd, 1H, $J = 8.22$,17.52 Hz), 2.20 (s, 3H), 2.4 (s, 3H). ^{13}C NMR (DMSO-D_6): 152.1, 151.9, 145.8, 140.9, 139.5, 138.4, 138.0, 136.4, 133.4, 132.3, 130.6, 130.5, 129.5, 129.1, 128.8, 128.4, 127.8, 127.1, 126.7, 126.3, 123.7, 119.5, 110.0, 64.0, 21.5, 21.0. LC–MS: m/e 489.18., $C_{32}H_{26}ClN_3$ requires Mol. wt.: 487.18. Elemental analysis, calculated: C, 78.76; H, 5.37; N, 8.61%. Found: C, 78.69; H, 5.29; N, 8.54%.

3-(4-Chlorophenyl)-1-{5-phenyl-3-(4-chloro phenyl)-4,5-dihydro-1*H*-pyrazol-1-yl} isoquinoline (**3c**)

Yellow solid, mp 221–222 °C, IR (cm^{-1}) 3,058, 2,954, 2,921, 1,611, 1,588, 1,546, 1,494, 1,435, 1,400, 1,367, 1,331, 1,236, 1,141, 1,089, 1,057, 1,008, 961, 899, 873, 818, 749, 671, 646, 592. ^{1}H NMR (DMSO-D_6), 9.31–9.29 (d, 1H, $J = 8.40$ Hz), 7.92–7.85 (m, 6H), 7.74–7.71 (t, 1H, $J = 6.8$ Hz), 7.67–7.64 (t, 1H, $J = 6.8$ Hz), 7.58–7.55 (d, 2H, $J = 8.4$ Hz), 7.47–7.44 (m, 4H), 7.34–7.30 (t, 2H, $J = 7.60$ Hz), 7.21–7.18 (t, 1H, $J = 7.6$ Hz), 6.2–6.15 (t, 1H, $J = 8.8$ Hz), 3.98–3.91 (dd, 1H, $J = 12.00$, 5.60 Hz), 3.21–3.14 (q, 1H). ^{13}C NMR (DMSO-D_6): 151.9 8, 149.5,

146.6, 143.2, 139.4, 138.1, 135.0, 133.8, 131.0, 129.8, 128.9, 128.6, 128.3, 128.2, 127.9, 127.2, 127.1, 127.1, 126.0, 125.9, 119.7, 110.2, 64.7, 40.9. LC–MS: m/e 494.11, $C_{30}H_{21}Cl_2N_3$ requires Mol. Wt.: 493.11. Elemental analysis, calculated: C, 72.88; H, 4.28; N, 8.50%. Found: C, 72.81; H, 4.21; N, 8.45%.

3-(4-Chlorophenyl)-1-{5-phenyl-3-(4-Pyridyl)-4,5-dihydro-1*H*-pyrazol-1-yl} isoquinoline (**3d**)

Yellow solid, mp 137–138.5 °C, IR (cm^{-1}) 3,026, 2,955, 2,920, 2,851, 2,361, 2,336, 1,701, 1,588, 1,494, 1,429, 1,334, 1,260, 1,135, 1,089, 1,057, 1,009, 900, 872, 808, 749, 717, 672. ^{1}H NMR (DMSO-D_6), 9.29-9.26 (d, 1H, $J = 8.22$ Hz), 8.68–8.66 (d, 2H, $J = 5.52$ Hz), 7.78–7.65 (m, 3H), 7.62–7.60 (d, 4H, $J = 6.18$ Hz), 7.54–7.48 (m, 2H), 7.35–7.32 (d, 4H, $J = 8.31$ Hz), 7.13–7.11 (d, 2H, $J = 7.83$ Hz), 6.18–6.29 (t, 1H, $J = 8.56$ Hz), 3.89–3.65 (q, 1H), 3.21–3.14 (q, 1H). ^{13}C NMR (DMSO-D_6): 151.5, 150.0, 147.8, 146.6, 139.8, 139.4, 137.9, 137.00, 134.0, 129.9, 129.5, 129.3, 129.1, 128.7, 128.4, 128.0, 127.9, 127.2, 126.2, 125.9, 119.9, 119.7, 110.9, 64.7, 40.3. LC–MS: 461.2, $C_{29}H_{21}ClN_4$ requires Mol. wt.: 460.15. Elemental analysis, calculated: C, 75.56; H, 4.59; N, 12.15%. Found: C, 75.61; H, 4.52; N, 12.18%.

3-(4-Chlorophenyl)-1-{5-(4-fluoro phenyl)-3-(4-fluoro phenyl)-4,5-dihydro-1*H*-pyrazol-1-yl} isoquinoline (**3e**)

Yellow solid, mp 201–202 °C, IR (cm^{-1}) 3,053, 2,922, 1,603, 1,554, 1,508, 1,491, 1,405, 1,330, 1,294, 1,216, 1,172, 1,153, 1,129, 1,092, 1,053, 1,010, 962, 899, 874, 816, 749, 716, 671, 645, 592. ^{1}H NMR (DMSO-D_6), 9.30–9.28 (d, 1H, $J = 8.64$ Hz), 7.93–7.85 (m, 6H), 7.74–7.70 (t, 1H, $J = 8.00$ Hz), 7.66–7.62 (t, 1H, $J = 8.36$ Hz), 7.52–7.45 (m, 4H), 7.36–7.32 (t, 2H, $J = 8.88$ Hz), 7.16–7.12 (t, 2H, $J = 8.88$ Hz), 6.19–6.14 (t, 1H, $J = 8.56$ Hz), 3.96–3.89 (q, 1H), 3.21–3.14 (q, 1H). ^{13}C NMR (DMSO-D_6): 164.6, 163.0, 162.1, 160.6, 152.0, 149.6, 146.5, 139.4, 139.0, 139.0, 138.1, 133.9, 129.8, 128.6, 128.6, 128.4, 128.2, 127.9, 127.9, 127.8, 127.6, 127.5 127.2, 125.9, 119.7, 115.2, 115.0, 115.7, 115.5, 110.5, 63.2, 41.1. LC–MS: m/e 496.2, $C_{30}H_{20}ClF_2N_3$ requires Mol. wt.: 495.13. Elemental analysis, calculated: C, 72.65; H, 4.06; N, 8.47%. Found: C, 72.71; H, 4.01; N, 8.39%.

3-(4-chlorophenyl)-1-{5-(4-methylphenyl)-3-(4-fluoro phenyl)-4,5-dihydro-1*H*-pyrazol-1-yl} isoquinoline (**3f**)

Yellow solid, mp 186–187 °C, IR (cm^{-1}) 3,053, 2,956, 2,919, 1,596, 1,551, 1,512, 1,490, 1,436, 1,353, 1,330, 1,296, 1,229, 1,144, 1,087, 1,054, 1,010, 897, 873, 814, 748, 716, 677, 593. ^{1}H NMR (DMSO-D_6), 9.29–9.26 (d, 1H, $J = 8.31$ Hz), 7.95–7.92 (d, 2H, $J = 8.55$ Hz), 7.87–7.81 (m, 4H), 7.69–7.62 (m, 2H), 7.45–7.43 (d, 2H, $J = 8.49$ Hz), 7.34–7.28 (m, 4H), 7.09–7.07 (d, 2H, $J = 7.8$ Hz), 6.09–6.16 (t, 1H, $J = 8.46$ Hz), 3.96–3.86 (q, 1H), 3.25–3.08 (q, 1H), 2.18 (s, 3H). ^{13}C NMR (DMSO-D_6): 164.8, 161.6 151.9, 151.2, 145.8, 140.8, 139.5, 138.0, 136.4, 133.4, 130.5, 129.5, 129.1, 129.0, 128.8, 128.7, 128.4, 128.3, 127.8, 126.7, 126.3, 119.5,

116.4, 116.1, 110.1, 64.2, 21.0. LC–MS: m/e 492.2, $C_{31}H_{23}ClFN_3$ requires Mol. wt.: 491.16. Elemental analysis, calculated: C, 75.68; H, 4.71; N, 8.54%. Found: C, 75.62; H, 4.65; N, 8.47%.

3-(4-Chlorophenyl)-1-{5-phenyl-3-(3-fluoro phenyl)-4,5-dihydro-1*H*-pyrazol-1-yl} isoquinoline (**3g**)

Yellow solid, mp 175–176 °C, IR (cm^{-1}) 3,029, 2,927, 2,361, 2,336, 1,595, 1,611, 1,572, 1,552, 1,491, 1,455, 1,418, 1,353, 1,371, 1,331, 1,278, 1,177, 1,155, 1,132, 1,083, 1,053, 1,028, 926, 885, 860, 814, 749, 697, 673. ^{1}H NMR (DMSO-D_6), 9.29–9.27 (d, 1H, $J = 8.52$ Hz), 7.91–7.88 (m, 4H), 7.74–7.52 (m, 6H), 7.50–7.42 (m, 4H), 7.33–7.18 (m, 4H), 6.18–6.17 (t, 1H, $J = 8.46$ Hz), 3.94–3.92 (q, 1H), 3.24–3.13 (q, 1H). ^{13}C NMR (DMSO-D_6): 164.8, 161.6, 151.1, 145.8, 140.8, 143.7, 139.5, 138.0, 136.4, 133.4, 130.6, 129.0, 129.0, 128.8, 128.7, 128.3, 128.2, 127.8, 127.4, 126.9, 126.4, 119.4, 113.2, 110.4, 64.7, 21.0. LC–MS: 478.2, $C_{30}H_{21}ClFN_3$ requires Mol. wt.: 477.14. Elemental analysis, calculated: C, 75.39; H, 4.43; N, 8.79%. Found: C, 75.36; H, 4.37; N, 8.71%.

3-(4-Chlorophenyl)-1-{5-phenyl-3-(3-hydroxy phenyl)-4,5-dihydro-1*H*-pyrazol-1-yl} isoquinoline (**3h**)

Yellow solid, mp 212.5–213.5 °C, IR (cm^{-1}) 3,468, 3,411, 3,028, 2,927, 2,361, 2,336, 1,595, 1,551, 1,493, 1,455, 1,420, 1,371, 1,352, 1,337, 1,278, 1,187, 1,137, 1,087, 1,057, 1,027, 1,010, 960, 910, 878, 857, 821, 748, 701.2, 677.3, 648.5, 621.4, 588.3, 546.6. ^{1}H NMR (DMSO-D_6), 9.61–9.92 (bs, 1H), 9.32–9.30 (d, 1H, $J = 8.48$ Hz), 7.88–7.84 (d, 3H, $J = 8.60$ Hz), 7.78 (s, 1H), 7.70–7.62 (m, 2H), 7.43–7.40 (d, 4H, $J = 7.08$ Hz), 7.31–7.25 (m, 4H), 7.22–7.16 (m, 2H), 6.87–6.84 (d, 1H, $J = 7.88$ Hz), 6.11–6.06 (t, 1H, $J = 8.44$ Hz), 3.91–3.81 (t, 1H, $J = 8.40$ Hz), 3.11–3.04 (q, 1H). ^{13}C NMR (DMSO-D_6): 157.5, 151.6, 151.4, 145.3, 143.3, 139.0, 137.5, 133.0, 132.9, 130.0, 129.8, 128.5, 128.2, 127.8, 127.3, 126.8, 126.1, 125.8, 118.9, 117.2, 116.7, 112.3, 109.5, 64.0, 40.7. LC–MS: m/e 476.2, $C_{30}H_{22}ClN_3O$ requires Mol. wt.: 475.15. Elemental analysis, calculated: C, 75.70; H, 4.66;; N, 8.83%. Found: C, 75.64; H, 4.58; N, 8.76%.

3-(4-Chlorophenyl)-1-{5-(4-methylphenyl)-3-(4-methyl phenyl)-4,5-dihydro-1*H*-pyrazol-1-yl} isoquinoline (**3i**)

Yellow solid, mp 206.5–207.5 °C, IR (cm^{-1}) 3,727, 3,625, 3,021, 2,920, 2,854, 2,361, 2,336, 1,893, 1,734, 1,651, 1,608, 1,590, 1,551, 1,514, 1,491, 1,437, 1,371, 1,331, 1,298, 1,237, 1,183, 1,142, 1,087, 1,054, 1,027, 961, 898, 872, 808, 742, 711, 669, 640, 595, 542. ^{1}H NMR (DMSO-D_6), 9.43–9.41 (d, 1H, $J = 8.36$ Hz), 7.74–7.68 (m, 5H), 7.64–7.55 (m, 2H), 7.47 (s, 1H), 7.38–7.31 (m, 4H), 7.29–7.24 (m, 2H), 7.13–7.11 (d, 2H, $J = 7.96$ Hz), 6.15–6.10 (q, 1H), 3.78–3.70 (q, 1H), 3.19–3.13 (q, 1H), 2.41(s, 3H), 2.30 (s, 3H). ^{13}C NMR (DMSO-D_6): 152.1, 150.7, 146.5, 140.5, 139.4, 139.3, 138.2, 133.7, 129.6, 129.6, 129.3, 129.1, 128.5, 128.2, 127.89 126.9, 125.9, 125.6, 119.8, 109.7, 64.0, 41.1, 21.4, 21.0. LC–MS: m/e 488.2,

$C_{32}H_{26}ClN_3$ requires Mol. wt.: 487.18. Elemental analysis, calculated: C, 78.76; H, 5.37; N, 8.61%. Found: C, 78.68; H, 5.29; N, 8.55%.

3-(4-Chlorophenyl)-1-{5-phenyl-3-(4-hydroxy phenyl)-4,5-dihydro-1*H*-pyrazol-1-yl} isoquinoline (**3j**)

Yellow solid, mp 75–76.5 °C, IR (cm^{-1}) 3,561, 3,027, 2,921, 2,851, 2,361, 2,336, 1,701, 1,603, 1,552, 1,518, 1,494, 1,432, 1,353, 1,333, 1,245, 1,167, 1,140, 1,088, 1,053, 1,010, 820, 750, 695, 597. ^{1}H NMR (DMSO-D_6), 9.42–9.39 (d, 1H, $J = 8.22$ Hz), 7.74–7.54 (m, 6H), 7.48–7.46 (d, 4H, $J = 6.75$ Hz), 7.37–7.19 (m, 6H), 6.93–6.90 (d, 2H, $J = 8.55$ Hz), 6.15–6.10 (q, 1H), 3.78–3.70 (q, 1H), 3.18–3.10 (q,1H). ^{13}C NMR (DMSO-D_6): 156.8, 150.5, 146.5, 143.5, 139.4, 138.2, 133.7, 129.6, 128.5, 128.2, 127.8, 127.7, 126.9, 126.9, 125.9, 125.5, 125.2, 119.7, 115.6, 109.7, 64.3, 41.1. LC–MS: m/e 477.0, $C_{30}H_{22}ClN_3O$ requires Mol. wt.: 475.15. Elemental analysis, calculated: C, 75.70; H, 4.66; N, 8.83%, Found: C, 75.68; H, 4.59; N, 8.77%.

Conclusions

An efficient, simple, and high-yielding method for the iron-oxide nanoparticles mediated cyclization of 3-(4-chlorophenyl)-1-hydrazinylisoquinoline to 1-(4,5-dihydropyrazol-1-yl)isoquinolines was established. The advantages of this catalyst include their non-toxicity, mild reaction condition requirement, easy removal from reaction mixture, and elimination of auto-oxidation of the desired pyrazolines to the corresponding pyrazoles.

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