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Synthesis of novel ferrocenyl-containing pyrazolo[4,3-c]quinolines

Günseli Turgut Cin*, Seda Demirel, Abban Cakici

Department of Chemistry, Faculty of Art and Sciences, Akdeniz University, Antalya, Turkey

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ABSTRACT

Synthesis of novel ferrocenyl-substituted pyrazolo[4,3-c]quinolines via the Pictet–Spengler reaction is reported. Iminium intermediate formed by the condensation of pyrazole-based arylamine substrates with ferrocenecarboxaldehyde in acidic medium, undergoes 6-endo cyclization with sufficiently reactive aromatic moiety to form a pyrazolo[4,3-c]quinoline ring.

1. Introduction

Pyrazolo[4,3-c]quinolines and their derivatives are known as high-affinity benzodiazepine receptor ligands [1], A_3 adenosine receptor antagonists [1], interleukin 1 [2], acetylcholinesterase [2], NMDA receptor [3] and phosphodiesterase 4 (PDE4) inhibitors [3], anti-cancer [4], anti-inflammatory [2,5] and anti-ulcer [6] agents. Therefore, novel substituted pyrazolo[4,3-c]quinolines represent attractive synthetic targets.

On the other hand, metallocenes are also known to exhibit a wide range of biological activity. Among them, ferrocene has become a useful organometallic compound in the field of pharmaceutical sciences due to its unique structure, different membrane-permeation properties and anomalous metabolism [7,8]. Many ferrocenyl compounds display interesting cytotoxic, anti-tumor, anti-malarial, antifungal and DNA-cleaving activities [9].

Recent studies have suggested that combination of a ferrocenyl moiety with heterocyclic structures may increase their biological activities or create new medicinal properties [7,8,10]. For example, structural variations of established drugs with the ferrocenyl moiety were reported, such as anti-malarial drugs chloroquine (termed ferroquine) [7c,11], quinine, mefloquine, and artemisinin and the anti-cancer drug tamixofen to give ferrocifen [8c,12]. The synthesis of such ferrocene-derived compounds allows the opening up of a potential area of research in designing and synthesizing multifunctional drugs.

Although pyrazolo[4,3-c]quinolines are among intensely studied compounds [1–6,13], surprisingly, ferrocenyl-containing pyrazolo[4,3-c]quinolines have not been encountered in the literature. Therefore, we envisioned the synthesis of novel ferrocenyl-containing pyrazolo[4,3-c]quinoline derivatives that may have significant biological activities. Numerous methods have been developed for the synthesis of substituted pyrazolo[4,3-c]quinolines. In these methods, the pyrazole moiety is typically built up at a later stage of the sequence making the synthetic route lengthy and non-flexible. For instance, condensation of ethyl 4-chloroquinoline-3-carboxylates [1a,13b], 2,3-dihydro-1*H*-quinolin-4-ones [4a] or o-chloro-derivatives of cyano quinolines [5c,d] with various arylhydrazines affords pyrazolo[4,3-c]quinoline ring systems. In contrast to these methods, Kundu et al. [14] described a modified Pictet–Spengler reaction which involves the generation of quinoline ring onto the pyrazole to form pyrazolo[4,3-c]quinolines. In general, a typical Pictet–Spengler reaction is based on the condensation of an aldehyde with an aliphatic amine to form an iminium intermediate which undergoes 6-endo cyclization with sufficiently reactive aromatic moiety to form an *N*-heterocyclic ring in acidic medium [15]. Kundu and his coworkers [14] modified the general procedure of Pictet–Spengler reaction by using designed aromatic amines having an activated heterocyclic ring instead of traditional aliphatic amines. They reported that the iminium ion derived from the arylamine is more electrophilic than the aliphatic

* Corresponding author. Tel.: +90 242 3102306; fax: +90 242 2278911.
E-mail addresses: gturgut@akdeniz.edu.tr (G.T. Cin), sedademirel@akdeniz.edu.tr (S. Demirel), abban@akdeniz.edu.tr (A. Cakici).

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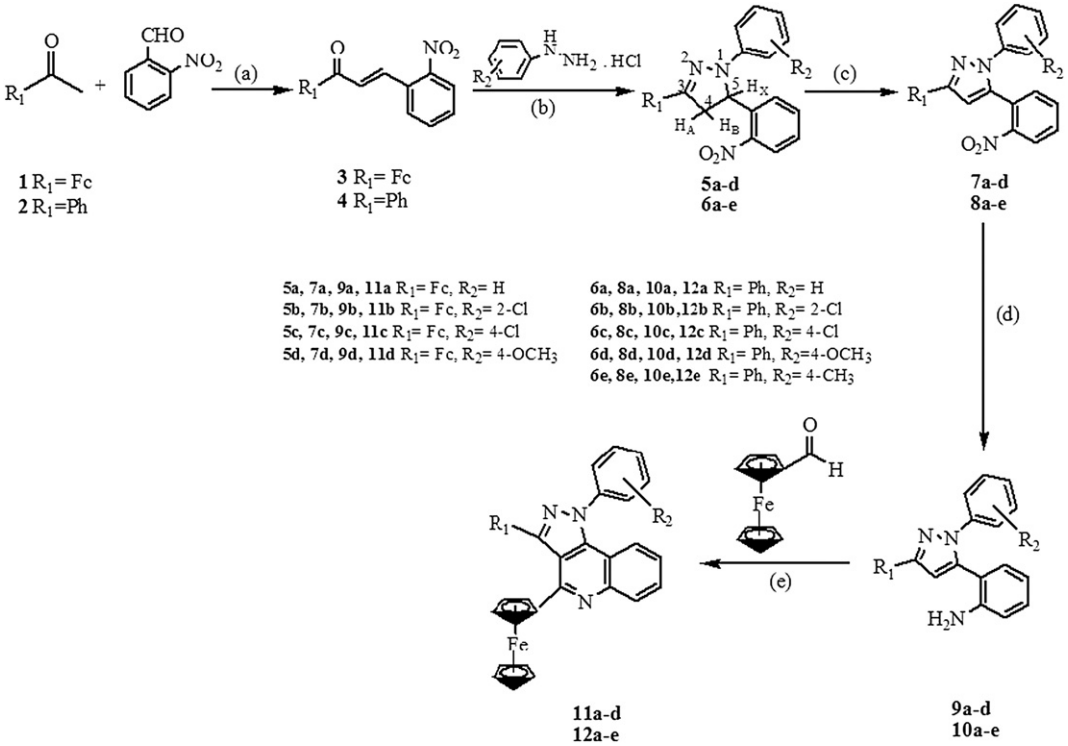
amine [14,16] and it facilitates C–C bond formation. In this respect, the modified Pictet–Spengler reaction has attained considerable importance for the synthesis of various products and novel heterocycles of biological interest [17]. However, to the best of our knowledge, modified Pictet–Spengler reaction has not been used for the synthesis of ferrocenyl-containing pyrazolo[4,3-c] quinolines so far. As part of a project to prepare new ferrocenyl-substituted heterocyclic compounds as potential pharmaceuticals [18], we synthesized novel ferrocenyl-containing pyrazolo[4,3-c] quinolines via modified Pictet–Spengler reaction (Scheme 1). Herein, we report the results of this study.

2. Results and discussion

In this study, we report the synthesis of novel mono and diferrocenyl substituted pyrazolo[4,3-c]quinolines. The synthetic strategy for desired compounds (11–12) in five steps is depicted in Scheme 1. Initially, the chalcones 3 and 4 were synthesized by base-catalyzed Claisen–Schmidt condensation of o-nitrobenzaldehyde with ketones (1–2) in 52 and 88% yields, respectively [19]. The characteristic vibration of carbonyl group in chalcone scaffold was observed at 1648 and 1667 cm^{-1} for compounds 3 and 4, respectively. In the ^{1}H-NMR spectra of these compounds, the olefinic H_α and H_β protons have two doublets at δ 6.88 and 8.07 ppm for 3 and δ 7.40 and 8.15 ppm for 4, respectively. The *E*-configuration of the olefinic group in ferrocenyl chalcone (3) follows from the large ^3J(H,H) coupling constant (15.5 Hz) whereas in phenyl chalcone (4), olefinic group has *Z*-configuration with 9.5 Hz coupling constant. In the ^{13}C-NMR spectra of 3 and 4, the signals at δ 192.4 and 182.3 ppm, respectively, indicate that carbonyl group is present in the chalcone scaffold. The rest of the signals for carbons appeared in the expected regions.

The synthesized chalcones were then treated with arylhydrazinium salts to obtain dihydropyrazoles (5–6) [20]. Among these compounds, 3-ferrocenyldihydropyrazoles (5) (34–53%) were obtained in lower yields than 3-phenyldihydropyrazoles (6) (62–76%). The significantly lower reactivity of 3 than 4 could be attributed to the enhanced electron releasing effect of ferrocenyl substituent which is directly attached to the carbonyl group [20d,21]. The general proposed mechanism for the formation of dihydropyrazole involves first the formation hydrazone followed by the addition of N–H to the olephinic bond of the propenone moiety [22]. Such ring closure was confirmed by the presence of C=N stretching (1583–1607 cm^{-1}) peak in FT-IR spectra of compounds and by the existence of ABX spin system due to three protons attached to the C-4 and C-5 carbon atoms of the dihydropyrazole ring in ^{1}H-NMR spectra of the compounds [14,20]. In ABX spin system, H_A, H_B and H_X protons of dihydropyrazoles (5–6) were depicted by the signals at 2.92–3.30 ppm, 3.90–4.13 ppm and 5.65–6.60 ppm, respectively.

The synthesis of pyrazoles (7–8) was performed by the reaction of dihydropyrazoles (5–6) with DDQ in DCM/THF (1/1) at room temperature for 5 h and afforded 3-ferrocenylpyrazoles (7) in 48–60% yield [14]. However, synthesis of 3-phenyl substituted pyrazoles (8) could only be achieved by the treatment of 6 with DDQ in dry dioxane at reflux for 7 h with a yield of 45–68% [23]. In the mechanism of oxidation reaction, for both compounds (5–6), the hydride transfer takes place from the 5-position of the dihydropyrazole leading to a stable carbocation. Subsequently, elimination of a proton from the 4-position leads to the formation of pyrazoles, while DDQ is reduced to quinhydrol DDHQ [24]. It is to be noted that the transfer of hydride from 5-position is more difficult for 3-phenyldihydropyrazoles (6) than for 3-ferrocenyldihydropyrazoles (5) due to lower electron releasing effect of phenyl ring compared to the ferrocenyl ring [21]. The most important



Scheme 1. Synthesis of ferrocenyl-substituted pyrazolo[4,3-c]quinolines (**11**–**12**) via modified Pictet–Spengler reaction: (a) KOH, EtOH, rt, 12 h **(3)** and 1 h **(4);** (b) arylhydrazinium hydrochloride, NaOAc, glacial AcOH/H_2O (2/1), reflux 6 h; (c) DDQ, DCM/THF (1/1), rt, 5 h **(7)** and DDQ, dry dioxane, reflux, 7 h **(8)**; (d) $SnCl_2.2H_2O$, glacial AcOH, reflux 10 h; (e) p-TsOH, toluene, reflux 9–11 h.

Table 1
Optimization of reaction involving conversion of **9a** to **11a** and **10a** to **12a** using ferrocenecarboxaldehyde under different Pictet–Spengler protocols.

Entry	Reaction conditions	Time	**11a** (%)	**12a** (%)
1	5% TFA in DCM at r.t.	16 h.	13	24
2	5% TFA in toluene 80 °C	12 h.	31	38
3	*p*-TsOH in toluene at reflux	9 h.	46	54
4	*p*-TsOH in MeOH, r.t.	14 h.	26	38

features of the ^{1}H-NMR and ^{13}C-NMR spectra of the pyrazoles (7–8), that allowed the establishement of their structures, are the resonance of H-4 protons as a singlet between 6.42 and 6.85 ppm and the resonance of C-4 between 105.0 and 106.6 ppm, respectively. The resulting aryl nitropyrazoles (7–8) were then chemoselectively reduced to arylamine substrates (9–10) through catalytic hydrogenation via treatment with $SnCl_2.2H_2O$ in glacial acetic acid with a yield of 67–86% [14]. In the IR spectra of 9–10, N–H asymmetric and symmetric stretching vibrations of amino groups appeared as two weak absorption bands at 3437–3472 cm^{-1} and 3352–3381 cm^{-1}, respectively. In addition, protons of amino group appeared as a broad singlet at 3.57–3.87 ppm in the ^{1}H-NMR spectra.

Finally, arylamine substurates (9–10) were treated with ferrocenecarboxaldehyde under a variety of traditional Pictet–Spengler protocols involving 5% TFA in DCM at room temperature, 5% TFA in neat toluene at 80 °C, p-TsOH in toluene at reflux and p-TsOH in methanol at room temperature (Table 1) [14]. Interestingly, endo cyclization resulting in ferrocenyl-substituted pyrazolo[4,3-c]quinolines (11a-12a) were successfully synthesized under all of the above conditions, but the highest yields were achieved when Pictet–Spengler reactions were carried out in the presence of *p*-TsOH in toluene at reflux (Tables 1 and 2). The reactions were followed by TLC and found to be complete after 9–11 h in 43–68% yields. In the initial stages of the reaction, the TLC exhibited a bright yellow spot due to the formation of Schiff base, which gradually disappeared with the appearance of a new dark yellow spot arising from endo cyclization. Successful synthesis of ferrocenyl pyrazolo[4,3-c]quinolines (11–12) was confirmed by the disappearance of the signals at 6.50–6.86 ppm and 3.57–3.87 ppm in ^{1}H-NMR spectra of the compounds 9–10 which are related to the pyrazole H-4 protons and amine protons, respectively. Moreover, appearance of the new signals at 4.01–4.55 ppm was attributed to the protons of ferrocenyl substituent at position 4 of the pyrazolo[4,3-c]quinolines (11–12). For the case of diferrocenyl substituted pyrazolo[4,3-c]quinolines (11) the signals of protons of ferrocenyl group linked to quinoline ring were shifted to upper field with respect to those of the ferrocenyl group linked to pyrazole ring. These results are in accordance with the ^{13}C-NMR spectra of the compounds (11). As seen in Table 2, 3,4-diferrocenylpyrazolo[4,3-c]quinolines (11) were obtained in lower yields than 4-ferrocenylpyrazolo[4,3-c]quinolines (12). This indicates the lower reactivity of arylamine substrates having ferrocenyl moiety on the pyrazole ring (9) than substrates with phenyl moiety (10) to undergo Pictet–Spengler cyclization. As ferrocenyl group is stronger electron donor than phenyl group [25], presence of such group could enhance the basicity of arylamine substrate leading to a decline in the electrophilicity of imine intermediates [26] (Fig. 1) and thus in its reactivity. On the other hand, there seems to be no effect of *N*-linked phenyl substrates (9–10) on 6-endo cyclization as they give about same yields (Table 2). However, biological activities of these novel *N*-substituted phenyl substrates are expected to be interesting and investigation of this feature is in progress.

3. Conclusion

Nine novel mono and diferrocenyl substituted pyrazolo[4,3-c]quinoline derivatives were synthesized by modified Pictet–Spengler reaction in moderate yields and confirmed by FT-IR, ^{1}H- and ^{13}C-NMR and/or elemental analysis. Studies have shown that mono ferrocenyl-substituted pyrazolo[4,3-c]quinoline derivatives are obtained in higher yields than di-ferrocenyl substituted pyrazolo[4,3-c]quinoline derivatives regardless of the groups on *N*-linked phenyl substrates (**9**–**10**). Our strategy opens up possibilities for the design and synthesis of new pyrazolo[4,3-c]quinolines including different organometallic moieties through modified Pictet–Spengler reaction.

4. Experimental

4.1. General consideration

Nuclear magnetic resonance (^{1}H and ^{13}C) spectra were recorded on a Bruker Spectrospin Avance DPX400 Ultrashield (400 MHz) spectrometer. Chemical shifts are reported in parts per million (δ) downfield from an internal tetramethylsilane reference. Coupling

Table 2
Properties of synthesized ferrocenyl-containing pyrazolo [4,3-c] quinolines (**11**–**12**).

Product	R_1	R_2	Yield (%)	Mp (°C)	Molecule Formula	%C	%H	%N
						Calculated (Found)	Calculated (Found)	Calculated (Found)
11a	Fc	H	46	211–212	$C_{36}H_{27}N_3Fe_2$	70.50 (70.72)	4.44 (4.71)	6.85 (6.78)
11b	Fc	2-Cl	48	192–193	$C_{36}H_{26}ClN_3Fe_2$	66.75 (66.64)	4.05 (3.96)	6.49 (6.39)
11c	Fc	4-Cl	43	194–196	$C_{36}H_{26}ClN_3Fe_2$	66.75 (66.83)	4.05 (4.12)	6.49 (6.30)
11d	Fc	4-OCH_3	47	198–199	$C_{37}H_{29}N_3OFe_2$	69.08 (68.85)	4.54 (4.15)	6.53 (6.28)
12a	Ph	H	54	188–190	$C_{32}H_{23}N_3Fe$	76.05 (76.18)	4.59 (4.66)	8.31 (8.40)
12b	Ph	2-Cl	65	190–192	$C_{32}H_{22}ClN_3Fe$	71.20 (71.08)	4.11 (4.27)	7.78 (7.67)
12c	Ph	4-Cl	57	188–190	$C_{32}H_{22}ClN_3Fe$	71.20 (71.29)	4.11 (4.02)	7.78 (7.69)
12d	Ph	4-OCH_3	53	182–184	$C_{33}H_{25}N_3OFe$	74.03 (73.88)	4.71 (4.53)	7.85 (7.92)
12e	Ph	4-CH_3	68	178–180	$C_{33}H_{25}N_3Fe$	76.31 (75.98)	4.85 (4.77)	8.09 (8.21)

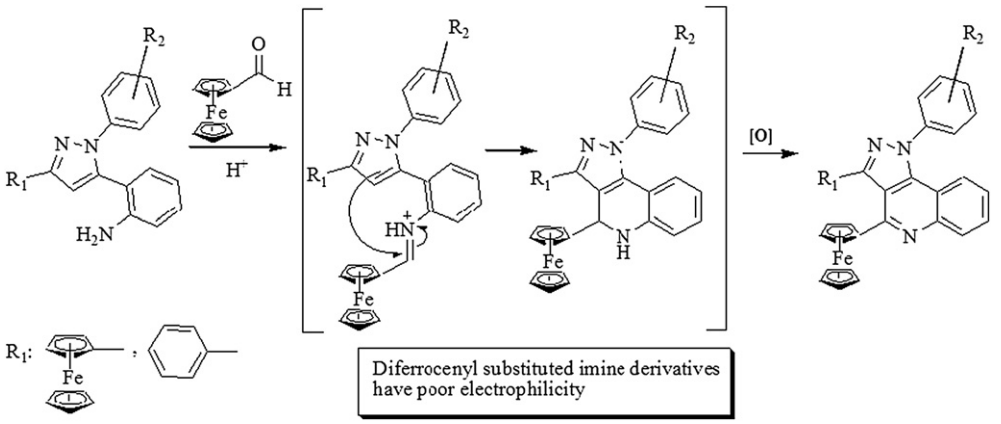


Fig. 1. Mechanism of the formation of ferrocenyl-substituted pyrazolo[4,3-c]quinolines.

constants (*J* values) are reported in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), td (triplet of doublet). All ^{13}C-NMR spectra were determined with complete proton decoupling and reported in ppm. Infrared spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer. Band positions were reported in reciprocal centimeters (cm^{-1}). Elemental analyses were performed on a LECO CHNS-932 instrument. Flash chromatography was performed using thick-walled glass columns and 'flash grade' silica (Merck 230–400 mesh). The relative proportion of solvents in mixed chromatography solvents refers to the volume: volume ratio. All other commercially available reagents and reactants were obtained in reagent grade and used without purification. The experiments were performed in nitrogen atmosphere. Melting points were taken with an electrothermal melting point apparatus.

4.2. General procedure for the synthesis of **3**–**4**

A solution of o-nitrobenzaldehyde (1 mmol, 151.1 mg) in ethanol (10 ml) was added dropwise to a solution of ketone **(1–2)** (1 mmol) and KOH (1 mmol, 56 mg) in ethanol (20 ml). In case of compound **3**, the mixture was stirred at room temperature for 12 h and then neutralized with 2M HCl. The reaction mixture was extracted with EtOAc (20 ml) for 3 times, then organic phase was dried over magnesium sulfate and evaporated to dryness under reduced pressure to obtain crude solid, which was purified by flash column chromatography on silica gel using hexane/THF (4/1) as eluent to afford **3**. For the compound **4**, the reaction was completed in 1 h and neutralized with 2M HCl. The precipitates were filtered, washed with cold ethanol and dried to afford **4**.

4.2.1. 1-Ferrocenyl-3-(2-nitrophenyl)-2-propen-1-on (**3**)

Yield 52%, red solid, mp 111–112 °C; IR (KBr) ν_{max}: 1648 (C=O), 1606 (C=C), 1525 (NO_2 asym.), 1346 (NO_2 sym.); ^{1}H-NMR ($CDCl_3$) δ: 8.07 (d, 1H, J = 15.5 Hz), 7.99 (d, 1H, J = 8.1 Hz), 7.66–7.59 (m, 2H), 7.49 (t, 1H, J = 7.4 Hz), 6.88 (d, 1H, J = 15.5 Hz), 4.85 (s, 2H), 4.56 (s, 2H), 4.19 (s, 5H); ^{13}C-NMR ($CDCl_3$) δ: 192.4 (C), 148.8 (C), 136.1 (CH), 133.3 (CH), 131.7 (C), 129.9 (CH), 129.3 (CH), 128.4(CH), 124.9 (CH), 79.9 (C), 73.1 (CH), 70.3 (CH), 69.9 (CH).

4.2.2. 3-(2-Nitrophenyl)-1-phenyl-2-propen-1-on (**4**)

Yield 88%, white solid, mp 121–122 °C; IR (KBr) ν_{max}: 1667 (C=O), 1610 (C=C), 1513 (NO_2 asym.), 1341 (NO_2 sym.); ^{1}H-NMR ($CDCl_3$) δ: 8.15 (d, 1H, J = 9.5 Hz), 8.01 (d, 1H, J = 7.6 Hz), 7.95 (d, 2H, J = 7.2 Hz), 7.69 (t, 1H, J = 7.2 Hz), 7.64–7.42 (m, 4H), 7.40 (d, 1H, J = 9.5 Hz), 7.26 (d, 1H, J = 6.8 Hz); ^{13}C-NMR ($CDCl_3$), δ: 182.3 (C), 145.6 (C), 144.2 (CH), 136.8 (C), 134.6 (CH), 130.1 (C), 129.7 (CH), 129.2 (CH), 128.5 (CH), 127.0 (CH), 123.2 (CH), 121.3 (CH), 120.0 (CH).

4.3. General procedure for the synthesis of **5**–**6**

Chalcone (**3**–**4**, 1 mmol), arylhydrazinium hydrochloride derivative (3 mmol) and sodium acetate (12.3 mg, 0.15 mmol,) were dissolved in glacial acetic acid aqueous solution (6 ml, AcOH/H_2O = 2/1). The reaction mixture was refluxed under nitrogen atmosphere for 6 h. Then, it was poured into crushed ice and neutralized with Na_2CO_3. The precipitates were filtered and dried, then purified by flash column chromatography on silica gel using hexane/EtOAc (8/1) as eluent to afford **5**–**6**.

4.3.1. 3-Ferrocenyl-5-(2-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazole (**5a**)

Yield 53%; yellow oil; IR (KBr) ν_{max}: 1596 (C=N), 1525 (NO_2 asym.), 1342 (NO_2 sym.), 1107 cm^{-1} (C–N); ^{1}H-NMR ($CDCl_3$), δ: 8.07 (d, 1H, J = 7.9 Hz), 7.48–7.36 (m, 3H), 7.11–7.08 (m, 2H), 6.81 (d, 2H, J = 7.8 Hz), 6.70 (t, 1H, J = 7.0 Hz), 5.70 (dd, H_x, J_{Ax} = 5.6 Hz, J_{Bx} = 11.7 Hz), 4.55 (s, 2H), 4.28 (s, 2H), 4.00 (s, 5H), 3.92 (dd, H_B, J_{Bx} = 11.7 Hz, J_{AB} = 17.2 Hz), 2.93 (dd, H_A, J_{Ax} = 5.6 Hz, J_{AB} = 17.2 Hz); ^{13}C-NMR ($CDCl_3$), δ: 148.8 (C), 147.4 (C), 144.5 (C), 137.9 (C), 134.5 (CH), 129.1 (CH), 128.5 (CH), 128.3 (CH), 125.5 (CH), 118.9 (CH), 112.7 (CH), 69.8 (C), 69.3 (CH), 66.9 (CH), 66.7 (CH), 60.2 (CH), 44.6 (CH_2); Anal. Calcd for $C_{25}H_{21}N_3O_2Fe$: C, 66.53; H, 4.69; N, 9.31; Found: C, 66.41; H, 4.63; N, 9.38.

4.3.2. 1-(2-Chlorophenyl)-3-ferrocenyl-5-(2-nitrophenyl)-4,5-dihydro-1H-pyrazole (**5b**)

Yield 48%; yellow oil; IR (KBr) ν_{max}: 1583 (C=N), 1524 (NO_2 asym.), 1346 (NO_2 sym.), 1104 (C–N), 753 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 7.92 (d, 1H, J = 7.5 Hz), 7.58 (d, 1H, J = 7.5 Hz), 7.46–7.38 (m, 2H), 7.31–7.27 (m, 1H), 7.13–7.07 (m, 2H), 6.82–6.78 (m, 1H), 6.60 (dd, H_x, J_{Ax} = 4.4 Hz, J_{Bx} = 11.3 Hz), 4.59 (pseudo d, 2H, J = 5.6 Hz), 4.31 (pseudo t, 2H, J = 1.7 Hz), 4.04 (s, 5H), 3.90 (dd, H_B, J_{Bx} = 11.3 Hz, J_{AB} = 17.1 Hz), 2.99 (dd, H_A, J_{Ax} = 4.4 Hz, J_{AB} = 17.1 Hz); ^{13}C-NMR ($CDCl_3$), δ: 150.0 (C), 146.0 (C), 138.0 (C), 137.0 (C), 133.5 (CH), 130.9 (CH), 128.8 (CH), 128.1 (CH), 127.3 (C), 123.4 (CH), 121.4 (CH), 101.0 (CH), 70.1(C), 69.3 (CH), 67.2 (CH), 62.1 (CH), 44.9 (CH), 29.9 (CH_2). Anal. Calcd for $C_{25}H_{20}ClN_3O_2Fe$: C, 61.82; H, 4.15; N, 8.65; Found: C, 61.72; H, 4.10; N, 8.74.

4.3.3. 1-(4-Chlorophenyl)-3-ferrocenyl-5-(2-nitrophenyl)-4,5-dihydro-1H-pyrazole (**5c**)

Yield 47%; yellow oil; IR (KBr) ν_{max}: 1597 (C=N), 1526 (NO_2 asym.), 1345 (NO_2 sym.), 1100 (C–N), 753 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 8.05 (d, 1H, J = 8.0 Hz), 7.47 (t, 1H, J = 7.5 Hz), 7.38–7.32 (m, 2H), 7.00 (d, 2H, J = 8.8), 6.68 (d, 2H, J = 8.8), 5.65 (dd, H_x, J_{Ax} = 5.6 Hz,

J_{Bx} = 12.1 Hz), 4.54 (s, 1H), 4.48 (s, 1H), 4.26 (s, 2H), 3.98 (s, 5H), 3.92 (dd, H_B, J_{Bx} = 12.1 Hz, J_{AB} = 17.4 Hz), 2.92 (dd, H_A, J_{Ax} = 5.6 Hz, J_{AB} = 17.4 Hz); ^{13}C-NMR ($CDCl_3$), δ: 150.0 (C), 146.2 (C), 143.4 (C), 137.0 (C), 134.5 (CH), 129.0 (CH), 128.8 (CH), 128.1 (CH), 125.6 (CH), 124.1 (C), 113.7 (CH), 69.9 (C), 69.3 (CH), 67.0 (CH), 66.8 (CH), 60.1 (CH), 44.7 (CH), 31.9 (CH_2). Anal. Calcd for $C_{25}H_{20}ClN_3O_2Fe$: C, 61.82; H, 4.15; N, 8.65; Found: C, 61.71; H, 4.24; N, 8.58.

4.3.4. 3-Ferrocenyl-1-(4-methoxyphenyl)-5-(2-nitrophenyl)-4,5-dihydro-1H-pyrazole (**5d**)

Yield 34%; yellow oil; IR (KBr) ν_{max}: 1607 (C=N), 1524 (NO_2 asym.), 1348 (NO_2 sym.), 1104 (C–N); ^{1}H-NMR ($CDCl_3$), δ: 8.16 (d, 1H, J = 7.9), 7.62–7.60 (m, 2H), 7.50–7.46 (m, 1H), 6.85 (d, 2H, J = 6.8 Hz), 6.79 (d, 2H, J = 6.8 Hz), 5.68 (dd, H_x, J_{Ax} = 6.8 Hz, J_{Bx} = 12.1 Hz), 4.66 (q, 1H, J = 1.5 Hz), 4.61 (q, 1H, J = 1.5 Hz), 4.37 (t, 2H, J = 1.8 Hz), 4.25 (s, 5H), 4.03 (dd, H_B, J_{Bx} = 12.1 Hz, J_{AB} = 17.4 Hz), 3.75 (s, 3H), 3.04 (dd, H_A, J_{Ax} = 6.8 Hz, J_{AB} = 17.4 Hz); ^{13}C-NMR ($CDCl_3$), δ: 153.2 (C), 148.1 (C), 147.5 (C), 139.4 (C), 138.2 (C), 134.4 (CH), 128.5 (CH), 125.4 (CH), 114.6 (CH), 114.1 (CH), 69.7 (C), 69.3 (CH), 66.9 (CH), 66.6 (CH), 61.2 (CH), 55.6 (CH_3), 44.7 (CH), 31.6 (CH_2). Anal. Calcd for $C_{26}H_{23}N_3O_3Fe$: C, 64.88; H, 4.82; N, 8.73; Found: C, 64.79; H, 4.77; N, 8.82.

4.3.5. 5-(2-Nitrophenyl)-1,3-diphenyl-4,5-dihydro-1H-pyrazole (**6a**)

Yield 62%; yellow solid; mp 114–116 °C; IR (KBr) ν_{max} (cm^{-1}): 1596 (C=N), 1524 (NO_2 asym.), 1338 (NO_2 sym.), 1127 (C–N); ^{1}H-NMR ($CDCl_3$), δ: 8.06 (d, 1H, J = 8.1 Hz), 7.67 (d, 2H, J = 7.5 Hz), 7.46–7.25 (m, 6H), 7.12 (t, 2H, J = 8.0 Hz), 6.88 (d, 2H, J = 8.0 Hz), 6.74 (t, 1H, J = 7.4 Hz), 5.80 (dd, H_x , J_{Ax} = 6.4 Hz, J_{Bx} = 12.3 Hz), 4.05 (dd, H_B, J_{Bx} = 12.3 Hz, J_{AB} = 17.6 Hz), 3.10 (dd, H_A, J_{Ax} = 6.4 Hz, J_{AB} = 17.6 Hz); ^{13}C-NMR ($CDCl_3$), δ: 152.0 (C), 147.7 (C), 143.1 (C), 137.3 (C), 133.8 (CH), 131.1 (CH), 130.0 (C), 129.3 (CH), 129.1 (CH), 128.7 (CH), 128.2 (CH), 127.4 (CH), 125.2 (CH), 118.4 (CH), 113.2 (CH), 61.4 (CH), 43.2 (CH_2). Anal. Calcd for $C_{21}H_{17}N_3O_2$: C, 73.45; H, 4.99; N, 12.24; Found: C, 73.38; H, 4.92; N, 12.19.

4.3.6. 1-(2-Chlorophenyl)-5-(2-nitrophenyl)-3-phenyl-4,5-dihydro-1H-pyrazole (**6b**)

Yield 65%; yellow oil; IR (KBr) ν_{max}: 1583 (C=N), 1515 (NO_2 asym.), 1334 (NO_2 sym.), 1136 (C–N), 753 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 7.95 (d, 1H, J = 8.2 Hz), 7.78 (d, 2H, J = 7.9 Hz), 7.55–7.38 (m, 6H), 7.35 (t, 1H, J = 7.9 Hz), 7.23–7.15 (m, 2H), 6.89 (t, 1H, J = 7.9 Hz), 6.36 (dd, H_x, J_{Ax} = 5.6 Hz, J_{Bx} = 11.8 Hz), 4.10 (dd, H_B, J_{Bx} = 11.8 Hz, J_{AB} = 17.3 Hz), 3.30 (dd, H_A, J_{Ax} = 5.6 Hz, J_{AB} = 17.3 Hz); ^{13}C-NMR ($CDCl_3$), δ: 150.0 (C), 142.5 (C), 137.4 (C), 133.6 (C), 132.2 (C), 131.1 (CH), 129.3 (CH), 128.6 (CH), 128.5 (CH), 128.2 (CH), 127.3 (CH), 126.1 (C), 124.6 (CH), 123.6 (CH), 121.7 (CH), 62.1 (CH), 43.3 (CH_2). Anal. Calcd for $C_{21}H_{16}ClN_3O_2$: C, 66.76; H, 4.27; N, 11.12; Found: C, 66.62; H, 4.38; N, 11.20.

4.3.7. 1-(4-Chlorophenyl)-5-(2-nitrophenyl)-3-phenyl-4,5-dihydro-1H-pyrazole (**6c**)

Yield 68%; yellow solid; mp 170–173 °C; IR (KBr) ν_{max}: 1597 (C=N), 1526 (NO_2 asym.), 1345 (NO_2 sym.), 1110 (C–N), 753 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 8.04 (d, 1H, J = 8.1 Hz), 7.62 (d, 2H, J = 7.4 Hz), 7.38–7.24 (m, 6H), 7.03 (d, 2H, J = 6.8 Hz), 6.76 (d, 2H, J = 6.8 Hz), 5.75 (dd, H_x, J_{Ax} = 6.4 Hz, J_{Bx} = 12.4 Hz), 4.03 (dd, H_B, J_{Bx} = 12.4 Hz, J_{AB} = 17.7 Hz), 3.08 (dd, H_A, J_{Ax} = 6.4 Hz, J_{AB} = 17.7 Hz); ^{13}C-NMR ($CDCl_3$), δ: 150.8 (C), 143.2 (C), 142.2 (C), 136.8 (C), 134.2 (CH), 133.2 (C), 129.4 (CH), 129.2 (CH), 128.8 (CH), 127.8 (CH), 127.4 (CH), 127.1 (CH), 124.4 (C), 122.8 (CH), 113.2 (CH), 62.4 (CH), 43.3 (CH_2). Anal. Calcd for $C_{21}H_{16}ClN_3O_2$: C, 66.76; H, 4.27; N, 11.12; Found: C, 66.86; H, 4.38; N, 11.04.

4.3.8. 1-(4-Methoxyphenyl)-5-(2-nitrophenyl)-3-phenyl-4,5-dihydro-1H-pyrazole (**6d**)

Yield 71%; yellow oil; IR (KBr) ν_{max}: 1601 (C=N), 1526 (NO_2 asym.), 1347 (NO_2 sym.), 1118 (C–N), ^{1}H-NMR ($CDCl_3$), δ: 8.16 (d, 1H, J = 8.0 Hz), 7.76 (dd, 1H, J = 1.6, 8.0 Hz), 7.56 (d, 2H, J = 8.0 Hz), 7.48–7.34 (m, 5H), 6.96 (d, 2H, J = 8.0 Hz), 6.81 (d, 2H, J = 8.0 Hz), 5.81 (dd, H_x, J_{Ax} = 7.2 Hz, J_{Bx} = 12.4 Hz), 4.13 (dd, H_B, J_{Bx} = 12.4 Hz, J_{AB} = 17.4 Hz), 3.76 (s, 3H), 3.17 (dd, H_A, J_{Ax} = 7.2 Hz, J_{AB} = 17.4 Hz); ^{13}C-NMR ($CDCl_3$), δ: 153.5 (C), 147.5 (C), 146.6 (C), 138.8 (C), 137.8 (C), 134.5 (C), 132.5 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 125.9 (CH), 125.7 (CH), 125.3 (CH), 114.6 (CH), 114.0 (CH), 61.5 (CH), 55.6 (CH_3), 43.2 (CH_2). Anal. Calcd for $C_{22}H_{19}N_3O_3$: C, 70.76; H, 5.13; N, 11.25; Found: C, 70.87; H, 5.21; N, 11.38.

4.3.9. 5-(2-Nitrophenyl)-3-phenyl-1-p-tolyl-4,5-dihydro-1H-pyrazole (**6e**)

Yield 76%; yellow oil; IR (KBr) ν_{max}: 1601 (C=N), 1522 (NO_2 asym.), 1335 (NO_2 sym.), 1133 (C–N); ^{1}H-NMR ($CDCl_3$), δ: 8.16 (d, 1H, J = 8.1 Hz), 7.74 (d, 2H, J = 7.3 Hz), 7.54–7.34 (m, 6H), 7.01 (d, 2H, J = 8.2 Hz), 6.87 (d, 2H, J = 8.2 Hz), 5.85 (dd, H_x, J_{Ax} = 6.8 Hz, J_{Bx} = 12.4 Hz), 4.13 (dd, H_B, J_{Bx} = 12.4 Hz, J_{AB} = 17.6 Hz), 3.16 (dd, H_A, J_{Ax} = 6.8 Hz, J_{AB} = 17.6 Hz), 2.25 (s, 3H); ^{13}C-NMR ($CDCl_3$), δ: 151.2 (C), 144.2 (C), 142.8 (C), 137.4 (C), 134.6 (CH), 133.7 (C), 130.1 (CH), 129.5 (CH), 129.3 (CH), 128.4 (C), 128.1 (CH), 127.8 (CH), 127.5 (CH), 124.2 (CH), 113.4 (CH), 62.6 (CH), 43.1 (CH_2), 22.3 (CH_3). Anal. Calcd for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76; Found: C, 73.76; H, 5.49; N, 11.68.

4.4. General procedure for the synthesis of **7**

DDQ (1.1 mmol, 249.7 mg) was dissolved in DCM/THF (1/1) (2 ml) and added to a solution of 4,5-dihydro-1*H*-pyrazole (**5**) compound (1 mmol) in DCM/THF (1/1) in 1 h. The reaction mixture was stirred at room temperature for 5 h under nitrogen atmosphere. Then mixture was evaporated and the crude product was purified by flash column chromatography on silica gel using hexane/EtOAc (8/1) as eluent to afford **7**.

4.4.1. 3-Ferrocenyl-5-(2-nitrophenyl)-1-phenyl-1H-pyrazole (**7a**)

Yield 58%; yellow oil; IR (KBr) ν_{max}: 1593 (C=N), 1524 (NO_2 asym.), 1334 (NO_2 sym.); ^{1}H-NMR ($CDCl_3$), δ: 7.83 (d, 1H, J = 7.8 Hz), 7.53–7.43 (m, 2H) 7.35 (d, 1H, J = 7.8 Hz), 7.19 (s, 5H), 6.42 (s, 1H), 4.72 (s, 2H), 4.25 (s, 2H), 4.07 (s, 5H); ^{13}C-NMR ($CDCl_3$), δ: 150.9 (C), 147.9 (C), 138.3 (C), 137.5 (C), 131.7 (CH), 131.6 (C), 128.8 (CH), 128.0 (CH), 126.3 (CH), 125.1 (CH), 124.3 (CH), 123.5 (CH), 105.0 (CH), 76.9 (C), 68.9 (CH), 67.9 (CH), 65.9 (CH). Anal. Calcd for $C_{25}H_{19}N_3O_2Fe$: C, 66.83; H, 4.26; N, 9.35; Found: C, 66.92; H, 4.19; N, 9.28.

4.4.2. 1-(2-Chlorophenyl)-3-ferrocenyl-5-(2-nitrophenyl)-1H-pyrazole (**7b**)

Yield 48%; yellow oil; IR (KBr) ν_{max}: 1595 (C=N), 1527 (NO_2 asym.), 1346 (NO_2 sym.), 768 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 7.78 (d, 1H, J = 8.0 Hz), 7.48–7.37 (m, 2H), 7.30–7.28 (m, 1H), 7.22–7.19 (m, 4H), 6.46 (s, 1H), 4.75 (s, 2H), 4.25 (s, 2H), 4.10 (s, 5H); ^{13}C-NMR ($CDCl_3$), δ: 150.2 (C), 147.3 (C), 145.6 (C), 143.0 (C), 132.7 (CH), 132.5 (C), 130.3 (C), 130.2 (CH), 129.9 (CH), 129.7 (CH), 127.7 (CH), 120.1 (CH), 105.2 (CH), 75.0 (C), 69.7 (CH), 68.8 (CH), 66.8 (CH). Anal. Calcd for $C_{25}H_{18}ClN_3O_2Fe$: C, 62.07; H, 3.75; N, 8.69; Found: C, 62.20; H, 3.86; N, 8.81.

4.4.3. 1-(4-Chlorophenyl)-3-ferrocenyl-5-(2-nitrophenyl)-1H-pyrazole (**7c**)

Yield 55%; yellow oil; IR (KBr) ν_{max}: 1595 (C=N), 1528 (NO_2 asym.), 1347 (NO_2 sym.), 757 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 7.98 (d, 1H, J = 7.8 Hz), 7.65–7.57 (m, 2H), 7.44 (d, 1H, J = 7.5 Hz), 7.28 (d, 1H, J = 8.9 Hz), 7.23 (d, 1H, J = 8.9 Hz), 6.52 (s, 1H), 4.77 (d, 2H, J = 1.8 Hz), 4.33 (d, 2H, J = 1.8 Hz), 4.14 (s, 5H); ^{13}C-NMR ($CDCl_3$), δ: 152.3 (C), 149.2 (C), 140.1 (C), 138.6 (C), 137.2 (CH), 133.0 (C), 132.6 (C), 130.1 (CH), 129.2 (CH), 125.5 (CH), 124.6 (CH), 106.5 (CH), 77.3 (C), 69.7 (CH), 68.9 (CH), 66.8 (CH). Anal. Calcd for

$C_{25}H_{18}ClN_3O_2Fe$: C, 62.07; H, 3.75; N, 8.69; Found: C, 61.88; H, 3.87; N, 8.84.

4.4.4. 3-Ferrocenyl-1-(4-methoxyphenyl)-5-(2-nitrophenyl)-1H-pyrazole (**7d**)

Yield 60%; yellow oil; IR (KBr) ν_{max}: 1588 (C=N), 1526 (NO_2 asym.), 1346 (NO_2 sym.); ^{1}H-NMR ($CDCl_3$), δ: 7.94 (d, 1H, J = 8.1 Hz), 7.65–7.55 (m, 2H), 7.43 (d, 1H, J = 7.7 Hz), 7.20 (d, 2H, J = 8.9 Hz), 6.82 (d, 2H, J = 8.9 Hz), 6.52 (s, 1H), 4.79 (t, 2H, J = 1.8 Hz), 4.32 (t, 2H, J = 1.8 Hz), 4.15 (s, 5H), 3.80 (s, 3H); ^{13}C-NMR ($CDCl_3$), δ: 158.8 (C), 151.5 (C), 148.9 (C), 147.6 (C), 138.6 (CH), 132.7 (C), 129.7 (CH), 126.2 (CH), 126.1 (CH), 124.4 (CH), 114.2 (CH), 105.6 (CH), 77.2 (C), 69.6 (CH), 68.7 (CH), 66.8 (CH), 55.5 (CH_3). Anal. Calcd for $C_{26}H_{21}N_3O_3Fe$: C, 65.15; H, 4.42; N, 8.77; Found: C, 64.93; H, 4.24; N, 8.59.

4.5. General procedure for the synthesis of **8**

DDQ (1.1 mmol, 249.7 mg) was dissolved in DCM/THF (1/1) (2 ml) and added to a solution of 4,5-dihydro-1*H*-pyrazole (**6**) compound (1 mmol) in DCM/THF (1/1) in 1 h. The reaction mixture was stirred at room temperature for 7 h under nitrogen atmosphere. Then mixture was evaporated and the crude product was purified by flash column chromatography on silica gel using THF/DCM (5/1) as eluent to afford **8**.

4.5.1. 5-(2-Nitrophenyl)-1,3-diphenyl-1H-pyrazole (**8a**)

Yield 45%; yellow oil; IR (KBr) ν_{max}: 1586 (C=N), 1526 (NO_2 asym.), 1346 (NO_2 sym.); ^{1}H-NMR ($CDCl_3$), δ: 7.94 (d, 1H, J = 8.0 Hz), 7.66–7.54 (m, 2H), 7.50–7.44 (m, 3H), 7.39–7.33 (m, 3H), 7.31 (s, 5H), 6.81 (s, 1H); ^{13}C-NMR ($CDCl_3$), δ: 152.2 (C), 149.8 (C), 139.4 (C), 139.3 (C), 135.7 (CH), 132.9 (C), 132.7 (C), 129.9 (C), 129.1 (CH), 128.7 (CH), 128.2 (CH), 127.6 (CH), 125.9 (CH), 125.5 (CH), 124.9 (CH), 124.6 (CH), 105.8 (CH). Anal. Calcd for $C_{21}H_{15}N_3O_2$: C, 73.89; H, 4.43; N, 12.31; Found: C, 74.03; H, 4.61; N, 12.42.

4.5.2. 1-(2-Chlorophenyl)-5-(2-nitrophenyl)-3-phenyl-1H-pyrazole (**8b**)

Yield 60%; yellow oil; IR (KBr) ν_{max}: 1583 (C=N), 1522 (NO_2 asym.), 1353 (NO_2 sym.), 762 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 7.93 (d, 1H, J = 8.1 Hz), 7.85 (dd, 2H, J = 8.0, 0.8 Hz), 7.62–7.49 (m, 3H), 7.46–7.42 (m, 3H), 7.38–7.29 (m, 4H), 6.85 (s, 1H); ^{13}C-NMR ($CDCl_3$), δ: 151.8 (C), 148.2 (C), 141.5 (C), 137.1 (CH), 136.9 (CH), 135.8 (C), 132.9 (C), 132.6 (C), 131.9 (CH), 130.4 (CH), 130.2 (CH), 129.0 (CH), 128.7 (CH), 128.3 (CH), 127.7 (CH), 124.3 (CH), 105.0 (CH). Anal. Calcd for $C_{21}H_{14}ClN_3O_2$: C, 67.21; H, 3.75; N, 11.18; Found: C, 67.36; H, 3.97; N, 11.34.

4.5.3. 1-(4-Chlorophenyl)-5-(2-nitrophenyl)-3-phenyl-1H-pyrazole (**8c**)

Yield 62%; yellow oil; IR (KBr) ν_{max}: 1588 (C=N), 1525 (NO_2 asym.), 1343 (NO_2 sym.), 742 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 7.97 (d, 1H, J = 8.1 Hz), 7.93 (dd, 2H, J = 7.9, 1.2 Hz), 7.67–7.55 (m, 3H), 7.46 (d, 2H, J = 7.3 Hz), 7.43 (d, 2H, J = 7.3 Hz), 7.39–7.35 (m, 3H), 6.80 (s, 1H); ^{13}C-NMR ($CDCl_3$), δ: 152.4 (C), 148.7 (C), 146.9 (C), 139.3 (C), 138.0 (CH), 133.3 (C), 133.1 (CH), 132.7 (CH), 132.5 (C), 132.3 (C), 130.2 (CH), 129.2 (CH), 128.4 (CH), 125.6 (CH), 124.9 (CH), 106.1 (CH). Anal. Calcd for $C_{21}H_{14}ClN_3O_2$: C, 67.21; H, 3.75; N, 11.18; Found: C, 67.36; H, 3.88; N, 11.27.

4.5.4. 1-(4-Methoxyphenyl)-5-(2-nitrophenyl)-3-phenyl-1H-pyrazole (**8d**)

Yield 64%; yellow oil; IR (KBr) ν_{max}: 1594 (C=N), 1525 (NO_2 asym.), 1343 (NO_2 sym.); ^{1}H-NMR ($CDCl_3$), δ: 8.14 (d, 1H, J = 8.0 Hz), 7.97 (d, 2H, J = 7.6 Hz), 7.73 (dd, 1H, J = 7.6, 1.8 Hz), 7.47–7.35 (m, 5H), 6.93 (d, 2H, J = 8.8 Hz), 6.80 (d, 2H, J = 8.8 Hz), 6.65 (s, 1H), 3.75 (s, 3H); ^{13}C-NMR ($CDCl_3$), δ: 158.7 (C), 153.5 (C), 151.8 (C), 146.6 (C), 135.5 (CH), 134.5 (C), 132.9 (C), 132.4 (C), 129.5 (CH), 128.9 (CH), 128.7 (CH), 128.6 (CH), 127.7 (CH), 125.7 (CH), 125.4 (CH), 114.6 (CH), 106.6 (CH), 55.6 (CH_3). Anal. Calcd for $C_{22}H_{17}N_3O_3$: C, 71.15; H, 4.61; N, 11.31; Found: C, 71.02; H, 4.74; N, 11.12.

4.5.5. 5-(2-Nitrophenyl)-3-phenyl-1-p-tolyl-1H-pyrazole (**8e**)

Yield 68%; yellow oil; IR (KBr) ν_{max}: 1601 (C=N), 1528 (NO_2 asym.), 1349 (NO_2 sym.); ^{1}H-NMR ($CDCl_3$), δ: 7.93 (d, 1H, J = 8.1 Hz), 7.74 (d, 2H, J = 7.7 Hz), 7.65–7.53 (m, 3H), 7.48–7.42 (m, 3H), 7.19 (d, 2H, J = 7.9 Hz), 7.10 (d, 2H, J = 7.9 Hz), 6.79 (s, 1H), 2.37 (s, 3H); ^{13}C-NMR ($CDCl_3$), δ: 152.8 (C), 148.5 (C), 146.7 (C), 138.4 (C), 136.2 (CH), 134.2 (C), 133.6 (C), 133.3 (CH), 133.0 (CH), 132.5 (C), 132.2 (CH), 130.1 (CH), 129.2 (CH), 128.2 (CH), 125.8 (CH), 123.2 (CH), 106.2 (CH), 23.2 (CH_3). Anal. Calcd for $C_{21}H_{17}N_3O_2$: C, 74.35; H, 4.82; N, 11.82; Found: C, 74.50; H, 4.75; N, 11.92.

4.6. General procedure for the synthesis of **9**–**10**

$SnCl_2.2H_2O$ (5 mmol, 1125 mg) was added to compound (**7**–**8**) (1 mmol) in glacial acetic acid (5 ml) at room temperature under nitrogen atmosphere. The reaction mixture was refluxed for 10 h and purified by flash column chromatography on silica gel using hexane/EtOAc (8/1) as eluent to afford **9**–**10**.

4.6.1. 2-(3-Ferrocenyl-1-phenyl-1H-pyrazol-5-yl)-phenylamine (**9a**)

Yield 72%; yellow oil; IR (KBr) ν_{max}: 3456 (N–H asym.), 3377 (N–H sym.), 1597 (C=N); ^{1}H-NMR ($CDCl_3$), δ: 7.28 (d, 2H, J = 7.8 Hz), 7.19 (t, 3H, J = 7.8 Hz), 7.12–7.07 (m, 2H), 6.91 (d, 1H, J = 7.6 Hz), 6.63–6.59 (m, 1H), 6.50 (s, 1H), 4.67 (t, 2H, J = 1.7 Hz), 4.21 (t, 2H, J = 1.7 Hz), 4.04 (s, 5H), 3.70 (br s, 2H); ^{13}C-NMR ($CDCl_3$), δ: 152.0 (C), 144.7 (C), 140.3 (C), 131.1 (C), 130.0 (CH), 128.8 (CH), 126.8 (CH), 123.7 (CH), 118.2 (CH), 116.0 (C), 115.5 (CH), 115.0 (CH), 106.6 (CH), 78.0 (C), 69.6 (CH), 68.7 (CH), 66.9 (CH). Anal. Calcd for $C_{25}H_{21}N_3Fe$: C, 71.61; H, 5.05; N, 10.02; Found: C, 71.73; H, 5.12; N, 10.14.

4.6.2. 2-[1-(2-Chlorophenyl)-3-ferrocenyl-1H-pyrazol-5-yl]-phenylamine (**9b**)

Yield 67%; yellow oil; IR (KBr) ν_{max}: 3437 (N–H asym.), 3352 (N–H sym.), 1577 (C=N), 753 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 7.28–7.21 (m, 2H), 7.18–7.15 (m, 4H), 6.98–7.03 (m, 1H), 6.82 (d, 1H, J = 7.6 Hz), 6.52 (s,1H), 4.76 (s, 2H), 4.25 (s, 2H), 4.10 (s, 5H), 3.80 (br s, 2H); ^{13}C-NMR ($CDCl_3$), δ: 151.2 (C), 144.8 (C), 143.8 (C), 142.0 (C), 134.0 (C), 131.2 (CH), 130.9 (CH), 128.8 (CH), 128.6 (CH), 124.7 (CH), 123.5 (CH), 118. 7 (CH), 115.8 (CH), 114.2 (C), 106.3 (CH), 77.2 (C), 69.6 (CH), 68.6 (CH), 66.8 (CH). Anal. Calcd for $C_{25}H_{20}ClN_3Fe$: C, 66.18; H, 4.44; N, 9.26; Found: C, 66.09; H, 4.58; N, 9.19.

4.6.3. 2-[1-(4-Chlorophenyl)-3-ferrocenyl-1H-pyrazol-5-yl]-phenylamine (**9c**)

Yield 76%; yellow oil; IR (KBr) ν_{max}: 3439 (N–H asym.), 3358 (N–H sym.), 1619 (C=N), 753 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 7.33 (d, 2H, J = 8.5 Hz), 7.28 (d, 2H, J = 8.5 Hz), 7.22 (t, 2H, J = 7.6 Hz), 7.05 (d, 1H, J = 7.6 Hz), 6.76 (d, 1H, J = 7.6 Hz), 6.59 (s, 1H), 4.77 (d, 2H, J = 1.6 Hz), 4.34 (d, 2H, J = 1.6 Hz), 4.15 (s, 5H), 3.82 (br s, 2H); ^{13}C-NMR ($CDCl_3$), δ: 152.1 (C), 145.0 (C), 141.7 (C), 135.2 (C), 131.1 (C), 130.3 (CH), 128.9 (CH), 125.0 (CH), 124.7 (CH), 118.4 (CH), 115.6 (CH), 114.0 (C), 106.9 (CH), 77.9 (C), 69.6 (CH), 68.8 (CH), 66.9 (CH). Anal. Calcd for $C_{25}H_{20}ClN_3Fe$: C, 66.18; H, 4.44; N, 9.26; Found: C, 66.38; H, 4.30; N, 9.44.

4.6.4. 2-[3-ferrocenyl-1-(4-methoxyphenyl)-1H-pyrazol-5-yl]-phenylamine (**9d**)

Yield 86%; yellow oil; IR (KBr) ν_{max}: 3451 (N–H asym.), 3377 (N–H sym.), 1617 (C=N); ^{1}H-NMR ($CDCl_3$), δ: 7.28 (t, 2H, J = 7.8 Hz),

7.23 (d, 2H, $J = 8.7$ Hz), 7.12 (d, 1H, $J = 7.8$ Hz), 6.83 (d, 2H, $J = 8.7$ Hz), 6.82 (d, 1H, $J = 7.8$ Hz), 6.60 (s, 1H), 4.79 (t, 2H, $J = 1.6$ Hz), 4.32 (t, 2H, $J = 1.6$ Hz), 4.14 (s, 5H), 3.81 (br s, 2H), 3.78 (s, 3H); ^{13}C-NMR ($CDCl_3$), δ:152.7 (C), 151.5 (C), 148.1 (C), 146.3 (C), 132.0 (C), 130.1 (CH), 125.7 (CH), 122.6 (CH), 118.3 (CH), 116.2 (CH), 113.5 (CH), 112.8 (C), 106.8 (CH), 77.6 (C), 69.6 (CH), 68.6 (CH), 66.9 (CH), 55.3 (CH_3). Anal. Calcd for $C_{26}H_{23}N_3OFe$: C, 66.50; H, 5.16; N, 9.35; Found: C, 66.63; H, 5.26; N, 9.23.

4.6.5. 2-(1,3-Diphenyl-1H-pyrazol-5-yl)-phenylamine (**10a**)

Yield 68%; yellow oil; IR (KBr) ν_{max}: 3470 (N–H asym.), 3381 (N–H sym.), 1598 (C=N); ^{1}H-NMR ($CDCl_3$), δ: 7.96 (d, 2H, $J = 7.8$ Hz), 7.49–7.43 (m, 3H), 7.39–7.28 (m, 5H), 7.19 (td, 1H, $J = 7.3$, 1.6 Hz), 7.01 (dd, 1H, $J = 7.6$, 1.2 Hz), 6.86 (s, 1H), 6.73 (td, 2H, $J = 7.0$, 1.0 Hz), 3.85 (br s, 2H); ^{13}C-NMR ($CDCl_3$), δ: 152.1 (C), 144.7 (C), 141.1 (C), 140.1 (C), 133.0 (C), 131.1 (CH), 130.1 (CH), 128.7 (CH), 128.1 (CH), 127.1 (CH), 125.8 (CH), 123.8 (CH), 118.3 (CH), 116.0 (CH), 115.6 (CH), 114.8 (C), 106.0 (CH). Anal. Calcd for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49; Found: C, 81.23; H, 5.66; N, 13.32.

4.6.6. 2-[1-(2-Chlorophenyl)-3-phenyl-1H-pyrazol-5-yl]-phenylamine (**10b**)

Yield 74%; yellow oil; IR (KBr) ν_{max}: 3465 (N–H asym.), 3378 (N–H sym.), 1615 (C=N), 762 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 7.94 (d, 2H, $J = 7.5$ Hz), 7.48 (d, 2H, $J = 7.5$ Hz), 7.33–7.28 (m, 4H), 7.23 (td, 2H, $J = 7.3$, 1.5 Hz), 6.95 (dd, 1H, $J = 7.3$, 1.5 Hz), 6.87 (dd, 2H, $J = 7.3$, 1.5 Hz), 6.84 (s, 1H), 3.84 (br s, 2H); ^{13}C-NMR ($CDCl_3$), δ:152.7 (C), 144.8 (C), 144.2 (C), 140.1 (C), 133.2 (C), 132.3 (C), 130.0 (CH), 129.7 (CH), 129.4 (CH), 128.7 (CH), 128.2 (CH), 127.6 (CH), 127.4 (CH), 121.5 (CH), 119.4 (CH), 116.1 (CH), 115.3 (C), 106.1 (CH). Anal. Calcd for $C_{21}H_{16}ClN_3$: C, 72.93; H, 4.66; N, 12.15; Found: C, 73.10; H, 4.52; N, 12.01.

4.6.7. 2-[1-(4-Chlorophenyl)-3-phenyl-1H-pyrazol-5-yl]-phenylamine (**10c**)

Yield 79%; yellow oil; IR (KBr) ν_{max}: 3468 (N–H asym.), 3375 (N–H sym.), 1617 (C=N), 765 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 7.93 (d, 2H, $J = 7.2$ Hz), 7.45 (t, 2H, $J = 7.2$ Hz), 7.37 (d, 2H, $J = 7.3$ Hz), 7.27 (d, 2H, $J = 7.3$ Hz), 7.20 (td, 2H, $J = 7.2$, 1.5 Hz), 6.98 (dd, 1H, $J = 7.4$, 1.3 Hz), 6.84 (s, 1H), 6.73 (td, 2H, $J = 7.4$, 1.3 Hz), 3.83 (br s, 2H); ^{13}C-NMR ($CDCl_3$), δ: 152.4 (C), 144.7 (C), 141.1 (C), 138.6 (C), 132.8 (C), 131.0 (CH), 130.4 (CH), 129.7 (CH), 129.2 (C), 128.6 (CH), 128.1 (CH), 127.7 (CH), 125.8 (CH), 118.4 (CH), 115.6 (CH), 115.2 (C), 106.2 (CH). Anal. Calcd for $C_{21}H_{16}ClN_3$: C, 72.93; H, 4.66; N, 12.15; Found: C, 73.15; H, 4.52; N, 12.34.

4.6.8. 2-[1-(4-Methoxyphenyl)-3-phenyl-1H-pyrazol-5-yl]-phenylamine (**10d**)

Yield 77%; yellow oil; IR (KBr) ν_{max}: 3472 (N–H asym.), 3380 (N–H sym.), 1608 (C=N); ^{1}H-NMR ($CDCl_3$), δ: 7.96 (d, 2H, $J = 7.6$ Hz), 7.47 (t, 2H, $J = 7.6$ Hz), 7.37 (d, 2H, $J = 8.8$ Hz), 7.34 (d, 2H, $J = 8.8$ Hz), 7.20 (td, 1H, $J = 7.6$, 1.6 Hz), 7.01 (dd, 1H, $J = 7.4$, 1.2 Hz), 6.73 (td, 2H, $J = 7.4$, 1.2 Hz), 6.86 (s, 1H), 3.87 (br s, 2H), 3.80 (s, 3H); ^{13}C-NMR ($CDCl_3$), δ: 158.6 (C), 151.8 (C), 144.8 (C), 141.1 (C), 133.3 (C), 133.1 (C), 131.2 (CH), 129.6 (CH), 128.7 (CH), 128.0 (CH), 125.6 (CH), 118.2 (CH), 116.0 (CH), 115.1 (CH), 114.0 (C), 105.5 (CH), 55.4 (CH_3). Anal. Calcd for $C_{22}H_{19}N_3O$: C, 77.40; H, 5.61; N, 12.31; Found: C, 77.53; H, 5.39; N, 12.48.

4.6.9. 2-(3-Phenyl-1-p-tolyl-1H-pyrazol-5-yl)-phenylamine (**10e**)

Yield 81%; yellow oil; IR (KBr) ν_{max}: 3460 (N–H asym.), 3371 (N–H sym.), 1611 (C=N); ^{1}H-NMR ($CDCl_3$), δ: 7.94 (d, 2H, $J = 7.4$ Hz), 7.42 (t, 2H, $J = 7.2$ Hz), 7.36 (d, 1H, $J = 7.3$ Hz), 7.30 (d, 2H, $J = 8.2$ Hz), 7.19 (t, 1H, $J = 7.4$ Hz), 7.11 (d, 2H, $J = 8.2$ Hz), 7.00 (dd, 1H, $J = 7.5$, 1.1 Hz), 6.72 (t, 2H, $J = 7.5$ Hz), 6.86 (s, 1H), 3.57 (br s, 2H), 2.35 (s, 3H); ^{13}C-NMR ($CDCl_3$), δ: 151.9 (C), 144.5 (C), 141.0 (C), 137.6 (C), 136.9 (C), 133.1 (C), 130.3 (CH), 130.2 (CH), 130.0 (CH), 129.9 (CH), 129.5 (CH), 127.7 (CH), 123.7 (CH), 119.1 (CH), 116.4 (CH), 115.1 (C), 105.8 (CH), 22.6 (CH_3) Anal. Calcd for $C_{22}H_{19}N_3$: C, 81.20; H, 5.89; N, 12.91; Found: C, 81.41; H, 5.76; N, 13.05.

4.7. General procedure for the synthesis of ferrocenyl-containing pyrazolo [4,3-c] quinolines (**11**–**12**)

Compound (**9**–**10**) (1 mmol), ferrocenylcarboxaldehyde (1 mmol, 214.1 mg) and p-tolylsulphonic acid (p-TsOH) (0.1 mmol, 19.0 mg) were dissolved in toluene (8 ml) and refluxed for 9–11 h under nitrogen atmosphere. The mixture was purified by flash column chromatography on silica gel using hexane/EtOAc (8/1) as eluent to afford **11**–**12**. For all the compounds (**11**–**12**) data related to percent yields, melting points (m.p) and elemental analyses are reported in Table 2.

4.7.1. 3,4-Diferrocenyl-1- phenyl-1H-pyrazolo[4,3-c]quinoline (**11a**)

Yellow solid; IR (KBr) ν_{max}: 1595 (C=N), 1562, 1506, 1447 (C=C); ^{1}H-NMR ($CDCl_3$), δ: 8.14 (d, 1H, $J = 7.9$ Hz), 7.66–7.63 (m, 2H), 7.62–7.47 (m, 5H), 7.21–7.17 (m, 1H), 4.54 (t, 2H, $J = 1.8$ Hz) 4.27 (t, 2H, $J = 1.8$ Hz), 4.07 (t, 2H, $J = 1.8$ Hz), 4.03 (t, 2H, $J = 1.8$ Hz), 4.02 (s, 5H), 4.01 (s, 5H); ^{13}C-NMR ($CDCl_3$), δ: 156.0 (C), 146.2 (C), 145.9 (C), 141.3 (C), 140.1 (C), 129.7 (CH), 129.6 (CH), 129.4 (CH), 128.6 (CH), 127.2 (CH), 124.9 (C), 121.4 (CH), 115.0 (C), 85.9 (C), 79.0 (CH), 72.0 (CH), 71.4 (CH), 69.8 (CH), 69.7 (CH), 68.0 (CH), 67.6 (CH).

4.7.2. 1- (2-Chlorophenyl)-3,4-diferrocenyl-1H-pyrazolo[4,3-c] quinoline (**11b**)

Yellow solid; IR (KBr) ν_{max}: 1596 (C=N), 1560, 1506, 1446 (C=C); ^{1}H-NMR ($CDCl_3$), δ: 8.24 (d, 1H, $J = 7.7$ Hz), 7.78–7.72 (m, 2H), 7.66–7.60 (m, 1H), 7.37–7.19 (m, 4H), 4.83 (t, 2H, $J = 1.6$ Hz), 4.51 (t, 2H, $J = 1.6$ Hz), 4.26 (t, 2H, $J = 1.6$ Hz), 4.17 (t, 2H, $J = 1.6$ Hz), 4.11 (s, 5H), 4.09 (s, 5H); ^{13}C-NMR ($CDCl_3$), δ: 159.3 (C), 146.8 (C), 144.3 (C), 143.4 (C), 138.7 (C), 135.5 (C), 131.1 (CH), 130.9 (CH), 130.3 (CH), 129.9 (CH), 129.8 (CH), 128.0 (CH), 125.0 (CH), 124.3 (C), 121.6 (CH), 115.7 (C), 86.3 (C), 81.9 (C), 72.3 (CH), 71.8 (CH), 70.1 (CH), 69.9 (CH), 68.2 (CH), 67.7 (CH).

4.7.3. 1- (4-Chlorophenyl)-3,4-diferrocenyl-1H-pyrazolo[4,3-c] quinoline (**11c**)

Yellow solid; IR (KBr) ν_{max}: 1598 (C=N), 1565, 1510, 1448 (C=C); ^{1}H-NMR ($CDCl_3$), δ: 8.23 (d, 1H, $J = 7.6$ Hz), 7.70 (d, 2H, $J = 8.4$ Hz), 7.64 (d, 2H, $J = 8.4$ Hz), 7.61 (d, 1H, $J = 8.4$ Hz), 7.35–7.31 (m, 2H), 4.63 (d, 2H, $J = 1.6$ Hz), 4.35 (d, 2H, $J = 1.6$ Hz), 4.17 (d, 2H, $J = 1.6$ Hz), 4.14 (d, 2H, $J = 1.6$ Hz), 4.11 (s, 5H), 4.10 (s, 5H); ^{13}C-NMR ($CDCl_3$), δ: 156.2 (C), 146.8 (C), 146.0 (C), 140.1 (C), 139.8 (C), 135.2 (C), 130.0 (CH), 129.9 (CH), 129.8 (CH), 128.8 (CH), 128.4 (CH), 125.1 (C), 121.2 (CH), 114.8 (C), 85.7 (C), 78.8 (C), 72.0 (CH), 71.5 (CH), 69.9 (CH), 69.7 (CH), 68.1 (CH), 67.7 (CH).

4.7.4. 3,4-Diferrocenyl-1-(4-methoxyphenyl)-1H-pyrazolo[4,3-c] quinoline (**11d**)

Yellow solid; IR (KBr) ν_{max}: 1596 (C=N), 1566, 1510, 1444 (C=C); ^{1}H-NMR ($CDCl_3$), δ: 8.22 (d, 1H, $J = 8.4$ Hz), 7.68–7.62 (m, 2H), 7.57 (d, 1H, $J = 8.2$ Hz), 7.31 (d, 2H, $J = 8.8$ Hz), 7.19 (d, 2H, $J = 8.8$ Hz), 4.64 (t, 2H, $J = 1.6$ Hz), 4.37 (t, 2H, $J = 1.6$ Hz), 4.16 (t, 2H, $J = 1.6$ Hz), 4.13 (t, 2H, $J = 1.6$ Hz), 4.10 (s, 10H), 4.0 (s, 3H); ^{13}C-NMR ($CDCl_3$), δ: 160.3 (C), 156.1 (C), 145.9 (C), 140.3 (C), 134.1 (C), 129.6 (C), 128.5 (CH), 128.2 (CH), 124.9 (C), 121.3 (CH), 115.1 (C), 114.9 (CH), 85.9 (C), 79.1(C), 72.0 (CH), 71.4 (CH), 69.8 (CH), 69.7 (CH), 68.0 (CH), 67.6 (CH), 55.7 (CH_3).

4.7.5. 4-Ferrocenyl-1,3-diphenyl-1H-pyrazolo[4,3-c]quinoline (**12a**)

Yellow solid; IR (KBr) ν_{max}: 1598 (C=N), 1564, 1512, 1448 (C=C); ^{1}H-NMR ($CDCl_3$), δ: 8.25 (d, 1H, J = 8.4 Hz), 7.72–7.63 (m, 5H), 7.55 (d, 1H, J = 8.3 HZ), 7.36 (d, 2H, J = 8.4 Hz), 7.32–7.22 (m, 5H), 4.54 (t, 2H, J = 1.5 Hz), 4.1 (s, 5H), 4.07 (t, 2H, J = 1.5 Hz); ^{13}C-NMR ($CDCl_3$), δ: 157.9 (C), 147.2 (C), 145.9 (C), 139.7 (C), 136.9 (C), 133.1 (C), 130.1 (CH), 129.8 (CH), 129.7 (CH), 129.6 (CH), 128.8 (CH), 127.9 (CH), 127.4 (CH), 126.5 (CH), 125.1 (CH), 121.5 (C), 120.1 (CH), 119.3 (C), 85.4 (C), 71.6 (CH), 69.8 (CH), 68.1 (CH).

4.7.6. 1-(2-Chlorophenyl)-4-ferrocenyl-3-phenyl-1H-pyrazolo[4,3-c]quinoline (**12b**)

Yellow solid; IR (KBr) ν_{max}: 1614 (C=N), 1562, 1510, 1451 (C=C), 768 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 8.27 (d, 1H, J = 8.0 Hz), 7.73–7.63 (m, 4 H), 7.60 (d, 1H, J = 8.0 Hz), 7.35 (d, 2H, J = 8.0 Hz), 7.31–7.22 (m, 5H), 4.54 (t, 2H, J = 1.8 Hz), 4.10 (s, 5H), 4.08 (t, 2H, J = 1.8 Hz); ^{13}C-NMR ($CDCl_3$), δ: 157.6 (C), 147.2 (C), 145.8 (C), 142.8 (C), 136.7 (C), 133.2 (C), 133.1 (C), 130.2 (CH), 129.8 (CH), 129.5 (CH), 129.3 (CH), 128.2 (CH), 127.9 (CH), 127.6 (CH), 127.4 (CH), 127.3 (CH), 125.1 (CH), 122.2 (C), 121.4 (CH), 119.3 (C), 85.3 (C), 71.5 (CH), 69.8 (CH), 68.2 (CH).

4.7.7. 1-(4-Chlorophenyl)-4-ferrocenyl-3-phenyl-1H-pyrazolo[4,3-c]quinoline (**12c**)

Yellow solid; IR (KBr) ν_{max}: 1616 (C=N), 1564, 1512, 1449 (C=C), 767 (C–Cl); ^{1}H-NMR ($CDCl_3$), δ: 8.26 (d, 1H, J = 8.3 Hz), 7.66 (d, 2H, J = 8.8 Hz), 7.62 (d, 2H, J = 8.8 Hz), 7.59 (d, 1H, J = 8.3 Hz), 7.35 (d, 2H, J = 8.3 Hz), 7.30–7.22 (m, 5H), 4.53 (t, 2H, J = 1.8 Hz), 4.10 (s, 5H), 4.07 (t, 2H, J = 1.8 Hz); ^{13}C-NMR ($CDCl_3$), δ: 156.2 (C), 148.7 (C), 146.2 (C), 139.5 (C), 135.4 (C), 133.0 (C), 131.1 (C), 129.9 (CH), 129.8 (CH), 129.0 (CH), 128.6 (CH), 128.1 (CH), 127.8 (CH), 127.2 (CH), 125.8 (CH), 123.0 (C), 121.3 (CH), 115.0 (C), 85.6 (C), 71.6 (CH), 70.0 (CH), 68.1 (CH).

4.7.8. 4-Ferrocenyl-1-(4-methoxyphenyl)-3-phenyl-1H-pyrazolo[4,3-c]quinoline (**12d**)

Yellow solid; IR (KBr) ν_{max}: 1608 (C=N), 1561, 1516, 1446 (C=C); ^{1}H-NMR ($CDCl_3$), δ: 8.27 (d, 1H, J = 8.4 Hz), 7.74–7.59 (m, 5H), 7.35 (dd, 3H, J = 6.8, 1.2 Hz), 7.31 (d, 2H, J = 8.0 Hz), 7.24 (d, 2H, J = 8.0 Hz), 4.55 (d, 2H, J = 1.6 Hz), 4.11 (s, 5H), 4.09 (d, 2H, J = 1.6 Hz), 3.43 (s, 3H); ^{13}C-NMR ($CDCl_3$), δ: 156.1 (C), 149.1 (C), 147.8 (C), 141.2 (C), 139.5 (C), 135.4 (C), 130.1 (C), 129.9 (CH), 129.0 (CH), 128.6 (CH), 128.1 (CH), 127.8 (CH), 125.3 (CH), 121.5 (CH), 121.3 (C), 120.0 (C), 114.9 (CH), 85.6 (C), 71.6 (CH), 69.7 (CH), 68.1 (CH), 55.5 (CH_3).

4.7.9. 4-Ferrocenyl-3-phenyl-1-p-tolyl-1H-pyrazolo[4,3-c]quinoline (**12e**)

Yellow solid; IR (KBr) ν_{max}: 1601(C=N), 1561, 1511, 1437 (C=C); ^{1}H-NMR ($CDCl_3$), δ: 8.25 (d, 1H, J = 8.4 Hz), 7.58 (d, 2H, J = 8.2 Hz), 7.44 (d, 2H, J = 8.2 Hz), 7.68 (t, 1H, J = 8.4 Hz), 7.38 (d, 2H, J = 8.4 Hz), 7.34–7.22 (m, 5H), 4.55 (t, 2H, J = 1.8 Hz), 4.10 (s, 5H), 4.07 (t, 2H, J = 1.8 Hz), 2.56 (s, 3H); ^{13}C-NMR ($CDCl_3$), δ: 156.1 (C), 148.1 (C), 146.1 (C), 140.1 (C), 139.7 (C), 138.4 (C), 133.3 (C), 130.9 (CH), 130.3 (CH), 129.8 (CH), 128.8 (CH), 128.7 (CH), 127.9 (CH), 127.7 (CH), 127.2 (CH), 125.1 (CH), 121.6 (C), 114.9 (C), 85.8 (C), 71.6 (CH), 69.8 (CH), 68.1 (CH), 29.4 (CH_3).

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Appendix. Supplementary material

Supplementary data related to this article can be found online, at doi:10.1016/j.jorganchem.2010.10.006.

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