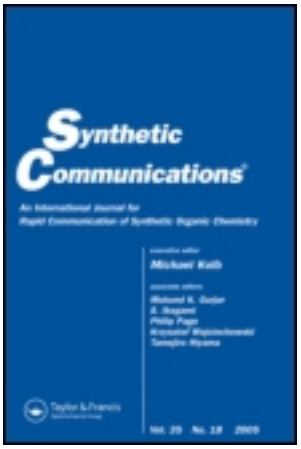

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Efficient Synthesis of Ferrocenylquinolines via the Friedländer Reaction

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EFFICIENT SYNTHESIS OF FERROCENYLQUINOLINES VIA THE FRIEDLÄNDER REACTION

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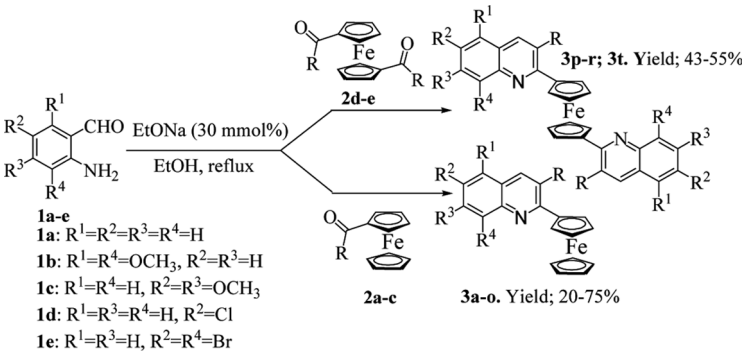
School of Chemistry and Environment, South China Normal University, Guangzhou, China

GRAPHICAL ABSTRACT



Abstract *Acylferrocenes* ***2a–c*** *reacted with* ortho-*aminoarylaldehydes* ***1a–e*** *via the Friedländer condensation reaction to afford the corresponding ferrocenylquinolines* ***3a–o*** *in moderate yields in the presence of sodium ethoxide (30 mmol%) under mild reaction conditions. Under the same reaction conditions, 1,1′-diacetylferrocene* ***2d*** *and 1,1′-dipropionylferrocene* ***2e*** *reacted with* ortho-*aminoaldehydes* ***1a–e*** *to afford the corresponding 1,1′-bis(substituted quinolin-2-yl)ferrocene derivatives* ***3p–t****. The structures of compounds* ***3a–t*** *were determined and characterized by infrared,* ^{1}*H NMR, mass spectrometry, and elemental analysis. The crystal structures of* ***3e*** *and* ***3q*** *were determined by x-ray crystallography.*

Keywords Acylferrocene; ferrocenylquinoline; Friedländer reaction; *o*-aminoarylaldehyde; sodium ethoxide catalysis

INTRODUCTION

The preparation of nitrogen-containing aromatic compounds such as quinolines and pyrroles has been extensively studied for more than a century because of their broad range of biological activities and many potential applications. Many quinolines analogs have been developed as drugs to treat human diseases. Their

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bioactivities include antibacterial,[1] anticancer and antiplatelet,[2] antiasthmatic,[3] anti-inflammatory,[4] and antihypertensive activities[5] and also inhibit tyrosine kinase PDGF-RTK.[6] In addition to medicinal applications, quinoline derivatives have been heavily investigated as ligands for advanced architecture materials through self-assembly.[7,8]

The structural core of quinoline can be synthesized through many conventional reactions such as Skraup, Doebner–Miller, Riehm, Combes, Conrad–Limbach, Knorr, Friedländer, Povarov, Camps, Niementowski, Gould–Jacobs, and Pfitzinger.[9] Many other new synthetic methods for the synthesis of quinoline are currently under exploration. For example, the reactions of aromatic imines with enolizable aliphatic aldehydes in the presence of metal, acidic, and iodine catalysts also led to formation of quinoline derivatives.[10] In addition, the Friedländer reaction, although known for a long time, was recently re-explored and is considered one of the most simple and straightforward methods for the synthesis of quinolines. Friedländer reaction involved the formation of quinoline derivatives by condensation of *ortho*-aminoarylaldehydes or *ortho*-aminoarylketones with an aldehyde or ketone containing a reactive α-methylene group. The Friedländer reaction is generally carried out either by refluxing an aqueous or alcoholic solution of reactants in the presence of acids or bases or heating the reactants at high temperatures without catalysts. Over the past few years, several catalysts such as amines,[11] Brønsted acids,[12] Lewis acids,[13] base,[14] molecular iodine,[15] and proline[16] have all been found to be effective for promoting Friedländer condensation reactions. In addition, microwave irradiation[17] and ionic liquid[18] have also been employed as promoters. On the other hand, many transition-metal complexes,[19] such as ruthenium, palladium, iron, rhodium, and iridium, were found to be effective catalysts for the modified Friedländer reaction.

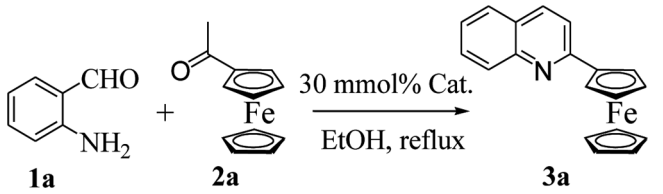
In the light of recent studies,[20] the hybridized molecule between quinoline and ferrocenyl moiety may possess promising biological activities and may find potential medicinal application. For example, ferrocenes have antitumor activity because of metabolic formation of ferricinium ions in situ.[21] In addition, its fascinating sandwich structure motifs have been widely used in organometallic chemistry, materials science, and chiral ligands.[22]

Among extensively studied quinoline derivatives, we are interested in the synthesis of ferrocenyl substituted quinolines because of their promising biological activities and potential applications. In our previous work, we reported that sodium ethoxide is an efficient catalyst in the synthesis of novel six-member ring-fused quinoline derivatives via the Friedländer reaction.[23] In this article, we reported the efficient synthesis of substituted quinolin-2-yl- and 1,1′-bis(substituted quinolin-2-yl)ferrocene derivatives **3a**–**t** via Friedländer reaction in the presence of sodium ethoxide.

RESULTS AND DISCUSSION

The substrates *ortho*-aminoarylaldehyde **1a, 1b, and 1c**, and ferrocenylketone **2a, 2b, 2c, 2d**, and **2e** were prepared according to the reported procedures.[24] At the beginning of our study, we used *ortho*-aminobenzaldehyde **1a** with acetylferrocene **2a** for the condensation in the presence of catalyst (Table 1). For comparison,

Table 1. Catalysts studied in the Friedländer annulation with *ortho*-aminobenzaldehyde (**1a**) and acetylferrocene (**2a**)



1a **2a** **3a**

Entry	Catalyst	Time (h)	Yield[a] (%)
1	Piperidine	48	Trace
2	NEt_3	48	Trace
3	$NH_3 \cdot H_2O$	48	Nr
4	K_2CO_3	16	56
5	KOH	16	67
6	C_2H_5ONa	16	75
7	C_2H_5ONa[b]	16	72
8	C_2H_5ONa[c]	24	50
9	$IrCl_3 \cdot H_2O$	48	Nr
10	$[Ir(cod)Cl]_2$	48	Trace
11	$[Ir(cod)Cl]_2$/dppf	48	Trace

[a]Isolated yield after silica-gel column chromatography.
[b]100 mmol% EtONa was used.
[c]10 mmol% EtONa was used.

a variety of catalysts were screened, and the results are shown in Table 1. It can be seen that all inorganic bases can promote the reaction to a certain degree, and sodium ethoxide was the best. However, in the presence of an organic base such as triethylamine and piperidine as well as the Ir complex, the reaction hardly proceeded, even after a long reaction time. The catalyst loading of sodium ethoxide was then investigated. We found that greater amounts of the catalyst loading (100 mmol%) did not improve the yields (Table 1, entry 7). When the catalyst loading was decreased to 10 mmol%, a much longer reaction time was required with a yield of 50% (Table 1, entry 8).

To optimize the reaction conditions, we conducted this reaction in different solvents [EtOH, tetrahydrofuran (THF), H_2O, CH_3CN, and dioxane]. The results demonstrated that ethanol was the best solvent (Table 2, entry 2). The reaction in

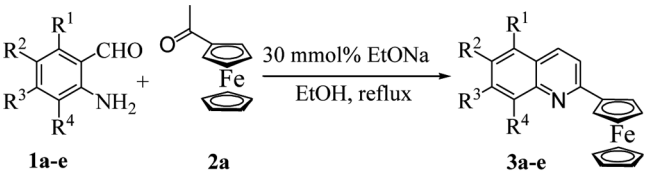
Table 2. (Quinolin-2-yl)ferrocene **3a** was synthesized via the Friedländer reaction in the presence of sodium ethoxide (30 mmol%) in various solvents

Entry	Solvent	Reaction temp. (°C)	Time (h)	Yield (%)
1	H_2O	90	16	Nr
2	EtOH	85	16	75
3	THF	75	16	48
4	Dioxane	90	16	32
5	CH_3CN	85	16	10

THF and dioxane afforded the expected product in 48% and 32% yields, respectively (Table 2, entries 3 and 4). In CH_3CN it gave the desired product in poor yield (10%), and in water the product was not detected. These results promted us to select 30 mmol% of sodium ethoxide as the catalyst and ethanol as the solvent for further study.

We next examine the analogs of reagent **1a** so as to understand the scope and generality of the CH_3CH_2ONa-catalyzed Friedländer reaction. The results of these reactions are summarized in Table 3. As seen from Table 3, the electronic effects of the substituted groups have an impact on the reaction results. The electron donor group such as OCH_3 was observed to give good yields (73% and 69%, respectively) (Table 3, entries 2 and 3). When the substituted group was an electron-withdrawing group such as 5-Cl or 3,5-dibromo, the yields were slightly lower (60% and 63%, respectively) (Table 3, entries 4 and 5). This may be because the electron-withdrawing functional group decreased the reactivity of the amino group

Table 3. Friedländer condensation reaction of *ortho*-aminoarylaldehyde (**1a–e**) with acetylferrocene (**2a**) in the presence of sodium ethoxide catalyst



1a-e **2a** **3a-e**

1a: $R^1=R^2=R^3=R^4=H$
1b: $R^1=R^4=OCH_3$, $R^2=R^3=H$
1c: $R^1=R^4=H$, $R^2=R^3=OCH_3$
1d: $R^1=R^3=R^4=H$, $R^2=Cl$
1e: $R^1=R^3=H$, $R^2=R^4=Br$

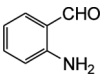
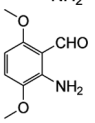
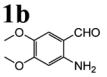
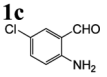
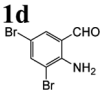
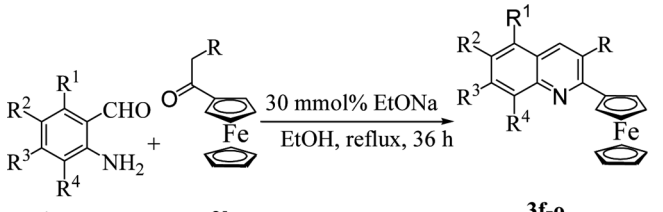
Entry	Substrate **1**	Product **3**	Time (h)	Yield (%)	Mp (°C)
1		**3a**	16	75	143–145
2	 **1b**	**3b**	16	73	141–143
3	 **1c**	**3c**	16	69	171–172
4	 **1d**	**3d**	8	60	154–155
5	 **1e**	**3e**	8	63	161–163

Table 4. Friedländer condensation reaction of *ortho*-aminoarylaldehyde (**1a**–**e**) with acylferrocene (**2b** and **2c**) in the presence of sodium ethoxide catalyst



1a-e **2b-c** **3f-o**

2b: R=CH_3
2c: R=C_6H_5

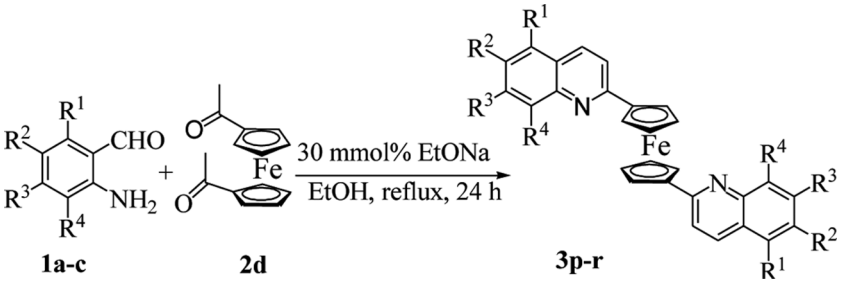
Entry	Substrate **1**	Substrate **2**	Product **3**	Yield (%)	Mp (°C)
1	**1a**	**2b**	**3f**	26	73–74
2	**1b**	**2b**	**3g**	27	164–165
3	**1c**	**2b**	**3h**	20	171–172
4	**1d**	**2b**	**3i**	23	119–121
5	**1e**	**2b**	**3j**	25	154–156
6	**1a**	**2c**	**3k**	24	190–191
7	**1b**	**2c**	**3l**	22	180–181
8	**1c**	**2c**	**3m**	20	177–179
9	**1d**	**2c**	**3n**	23	153–155
10	**1e**	**2c**	**3o**	25	155–156

at the phenyl ring. The reaction involved the formation of an enamine followed by aldol-type cyclization to yield the expected quinolines. In addition, steric effects also influenced the reactivity: *ortho*-aminobenzaldehyde achieved greater yield up to 75% (Table 3, entry 1) than those *ortho*-aminobenzaldehyde with substitutes (Table 3, entries 2–5).

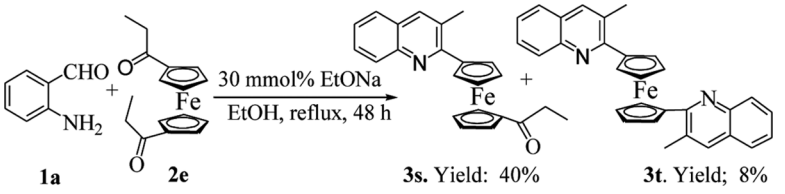
To further investigate the scope of this reaction, ferrocenylketones containing α-methylene such as propionylferrocene **2b** and phenylacetylferrocene **2c** reacted with various substituted *ortho*-aminoarylaldehydes **1a**–**e** to produce a serial of quinoline derivatives, and the results are summarized in Table 4. Surprisingly, we found that the reaction is difficult to proceed and a library synthesis of quinoline **3** was obtained in poor yields even after long reaction times. By comparison of the data in Tables 3 and 4, it can be seen that the steric effects of the substituents on the α-methylene group significantly influenced the reaction results. When the substituent was methyl or phenyl, which have more steric hindrance, the reactivity obviously decreased. Therefore, we afforded lower yields ranging from 20% to 27% (Table 4).

Finally, we also studied the reaction using the substrates of ferrocenyldiketone such as 1,1′-diacetylferrocene **2d** and 1,1′-dipropionylferrocene **2e** with *ortho*-aminoarylaldehyde to synthesize 1,1′-bis(substituted quinolin-2-yl)ferrocenes in the presence of sodium ethoxide catalyst, and the results are summarized in Table 5 and Scheme 1. It can be seen that *ortho*-aminoarylaldehyde **1** underwent double Friedländer condensations with 1,1′-diacylferrocene **2d** or **2e** to afford the corresponding 1,1′-bis(substituted quinolin-2-yl)ferrocenes **3p–r** and **3t**.

Table 5. Friedländer condensation of *ortho*-aminoarylaldehyde (**1a**–**c**) with 1,1′-dipropionylferrocene (**2d**) in the presence of sodium ethoxide catalyst



Entry	Substrate **1**	Product **3**	Yield (%)	Mp (°C)
1	**1a**	**3p**	43	209–211
2	**1b**	**3q**	58	226–228
3	**1c**	**3r**	55	224–226



Scheme 1. Friedländer condensation of *ortho*-aminoarylaldehyde (**1a**) with 1,1′-diacetylferrocene (**2e**) in the presence of sodium ethoxide catalyst.

2-Amino-3,6-dimethoxylbenzaldehyde **1c** and 2-amino-4,5-dimethoxylbenzaldehyde **1d** can react with 1,1′-diacetylferrocene **2d** smoothly to give the corresponding 1,1′-bis[2-(5,8-dimethoxyquinolinyl)]ferrocene **3r** and 1,1′-bis[2-(6,7-dimethoxyquinolinyl)]ferrocene in good yields (58% and 55%, respectively) (Table 5, entries 2 and 3). However, *ortho*-aminobenzaldehyde **1a** reacted with 1,1′-diacetylferrocene **2d** to give 1,1′-bis(quinolin-2-yl)ferrocene in slightly lower yield 43% (Table 5, entry 1). This may be because *ortho*-aminobenzaldehyde **1a** forms a polymer through a self-condensation reaction. Also 1,1′-dipropionylferrocene **2e** reacted with *ortho*-aminobenzaldehyde **1a** to give monoquinolineferrocene **3s** as a major product in 40% yield and bisquinolineferrocene **3t** as a minor product in 8% yield (Scheme 1).

Crystal structures of **3e** and **3q** obtained by solvent evaporation from solution of dichloromethane and ethanol (v/v = 1:1) are shown in Figs. 1 and 2, respectively.

EXPERIMENTAL

Melting points were obtained on a XT-4 microscopic melting-point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian XL

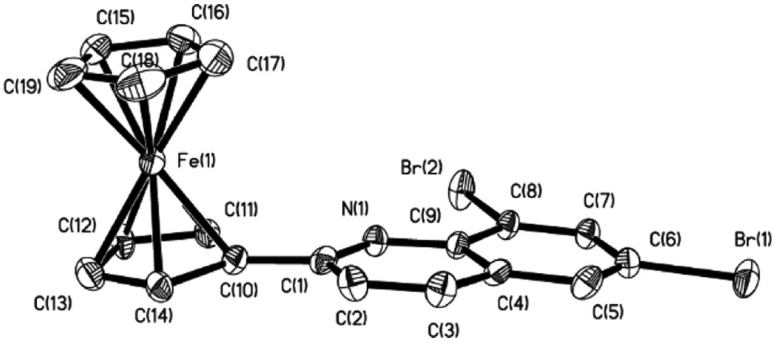


Figure 1. Crystal structure of compound **3e** showing the atom labeling scheme. Hydrogen atoms have been omitted for clarity. The data are as follows: Crystal system is triclinic, space group *P-1* with unit cell dimensions of $a = 10.8239(15)$ Å^3, $b = 11.3478(16)$ Å, $c = 13.5025(19)$ Å, $\alpha = 89.332(2)°$, $\beta = 81.543(2)°$, $\gamma = 89.446(2)°$, $V = 1640.3(4)$ Å, $Z = 17$. Absorption coefficient is 14.014 cm^{-1}.

400-MHz spectrometer (at 400 and 100 MHz, respectively) with $SiMe_4$ as the internal standard in $CDCl_3$. Infrared (IR) spectra were recorded on a Perkin-Elmer 1730 Fourier transform (FT)–IR spectrometer as KBr pellets. Mass Spectrometry (MS) data were obtained using a VGZAB-HS mass spectrometer. Elemental analysis was performed on a Elemental Varioel spectrometer. Bruker Smart CCD Apex II was used for single-crystal x-ray diffraction.

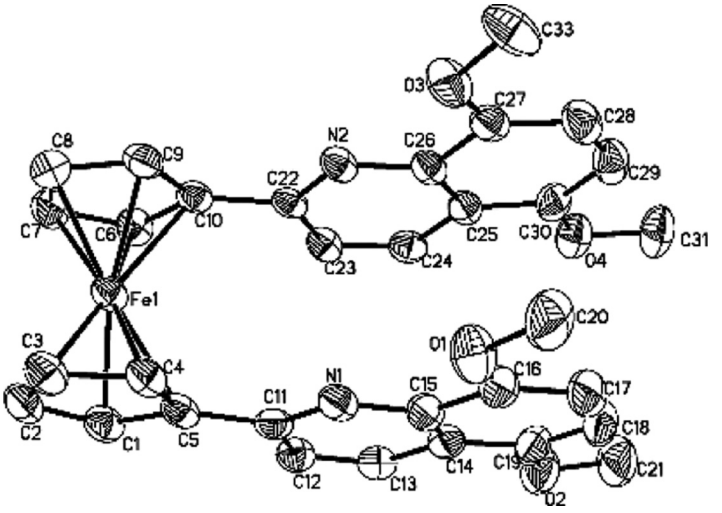


Figure 2. Crystal structure of compound **3q** showing the atom labeling scheme. Hydrogen atoms have been omitted for clarity, the data are as follows: Crystal system is orthorhombic, space group P with unit cell dimensions of $a = 15.387(9)$ Å^3, $b = 21.783(12)$ Å, $c = 15.387$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, $V = 5157(4)$ Å, $Z = 8$. Absorption coefficient is 0.627 cm^{-1}.

General Procedure for the Synthesis of (Substituted quinolin-2-yl)ferrocene 3a–O, and 1,1′-Bis(substituted quinolin-2-yl)ferrocene 3p–3t

Sodium ethoxide (0.3 mmol) was added to a solution of *o*-aminoarylaldehyde **1** (1 mmol) and acylferrocene **2** (1 mmol) in absolute anhydrous ethanol (15 ml). The solution was stirred at reflux for the designated time. The mixture was cooled to room temperature. The solvent was removed under vacuum, and the residue was purified by flash column chromatography on silica gel with petroleum ether / ethyl acetate to afford the expected product.

(Quinolin-2-yl)ferrocene (3a)

Red brown solid; mp 143–145 °C; IR (KBr, cm^{-1}): 3086, 3058, 2924, 2851, 1615, 1598, 1556, 1510, 1424, 1282, 1127, 1105, 1091, 907, 824, 757; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, $J = 3.6$ Hz, 1H, Ar-H), 8.03 (d, $J = 3.6$ Hz, 1H, Ar-H), 7.74 (d, $J = 8.8$ Hz, 1H, Ar-H), 7.66 (t, $J = 8.4$ Hz, 1H, Ar-H), 7.57 (d, $J = 8.4$ Hz, 1H, Ar-H), 7.46 (t, $J = 8.0$ Hz, 1H, Ar-H), 5.07 (t, $J = 2.0$ Hz, 2H, Fc-H_α),), 4.47 (t, $J = 2.0$ Hz, 2H, Fc-H_β), 4.06 (s, 5H, Fc-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 148.1, 135.3, 129.2, 128.9, 127.3, 126.5, 125.2, 119.3, 83.8, 70.3, 69.6, 67.8; MS (ESI): $m/z = 314$ $[M+H]^+$. Anal. calcd. for $C_{19}H_{15}FeN$: C, 72.87; H, 4.83; N, 4.47. Found: C, 72.64; H, 4.59; N, 4.40.

(5,8-Dimethoxyquinolin-2-yl)ferrocene (3b)

Brown solid; mp 141–143 °C; IR (KBr, cm^{-1}): 3086, 2933, 2833, 1617, 1600, 1570, 1518, 1478, 1459, 1399, 1304, 1257, 1164, 1105, 1079, 800, 724; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, $J = 8.8$ Hz, 1H, Ar-H), 7.62 (d, $J = 8.8$ Hz, 1H, Ar-H), 6.92 (d, $J = 8.4$ Hz, 1H, Ar-H), 6.70 (d, $J = 8.4$ Hz, 1H, Ar-H), 5.09 (s, 2H, Fc-H_α), 4.45 (s, 2H, Fc-H_β), 4.05 (s, 8H, Fc-H, OCH_3), 3.96 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 149.2, 148.9, 140.5, 130.2, 119.7, 119.3, 108.0, 102.9, 84.3, 70.2, 69.6, 68.2, 56.6, 55.7; MS (ESI): $m/z = 374$ $[M+H]^+$. Anal. calcd. for $C_{21}H_{19}FeNO_2$: C, 67.58; H, 5.13; N, 3.75. Found: C, 67.32; H, 5.39; N, 4.05.

(6,7-Dimethoxyquinolin-2-yl)ferrocene (3c)

Brown solid; mp 171–172 °C; IR (KBr, cm^{-1}): 3079, 2985, 2927, 1617, 1596, 1499, 1465, 1432, 1337, 1244, 1215, 1160, 1002, 886, 853; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, $J = 8.4$ Hz, 1H, Ar-H), 7.44 (d, $J = 8.8$ Hz, 1H, Ar-H), 7.39 (s, 1H, Ar-H), 6.99 (s, 1H, Ar-H), 5.00 (t, $J = 2.0$ Hz, 2H, Fc-H_α), 4.42 (t, $J = 1.6$ Hz, 2H, Fc-H_β), 4.05 (s, 5H, Fc-H), 4.04 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 152.4, 149.1, 145.2, 134.0, 122.0, 117.8, 108.2, 105.4, 84.6, 70.1, 69.7, 67.7, 56.2, 56.1; MS (ESI): $m/z = 374$ $[M+H]^+$. Anal. calcd. for $C_{21}H_{19}FeNO_2$: C, 67.58; H, 5.13; N, 3.75. Found: C, 67.38; H, 5.32; N, 3.97.

(6-Chloroquinolin-2-yl)ferrocene (3d)

Brown solid; mp 154–155 °C; IR (KBr, cm^{-1}): 3086, 3050, 2956, 2851, 1615, 1598, 1504, 1444, 1331, 1187, 1071, 854, 826; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93

(d, $J = 8.8$ Hz, 1H, Ar-H), 7.87 (d, $J = 8.4$ Hz, 1H, Ar-H), 7.66 (d, $J = 2.0$ Hz, 1H, Ar-H), 7.54 (dd, $J = 2.5$ Hz, $J = 6.8$ Hz, 1H, Ar-H), 7.50 (d, $J = 8.4$ Hz, 1H, Ar-H), 5.01 (t, $J = 2.0$ Hz, 2H, Fc-H_α), 4.43 (t, $J = 2.0$ Hz, 2H, Fc-H_β), 4.01 (s, 5H, Fc-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 146.6, 134.4, 130.8, 130.5, 130.1, 127.2, 126.1, 120.2, 83.4, 70.6, 69.6, 67.9; MS (ESI): m/z = 348 $[M+H]^+$. Anal. calcd. For $C_{19}H_{14}ClFeN$: C, 65.65; H, 4.06; N, 4.03. Found: C, 65.39; H, 4.26; N, 4.22.

(6,8-Dibromoquinolin-2-yl)ferrocene (3e)

Brown solid; mp 145–146 °C; IR (KBr, cm^{-1}): 3086, 3050, 2920, 2847, 1617, 1590, 1502, 1458, 1313, 1281, 1187, 1107, 1005, 970, 861, 820; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H, Ar-H), 7.86 (d, $J = 8.4$ Hz, 1H, Ar-H), 7.81 (s, 1H, Ar-H), 7.51 (d, $J = 8.8$ Hz, 1H, Ar-H), 5.10 (d, $J = 1.6$ Hz, 2H, Fc-H_α), 4.49 (d, $J = 1.6$ Hz, 2H, Fc-H_β), 4.03 (d, $J = 0.8$ Hz, 5H, Fc-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 144.5, 136.1, 135.3, 129.8, 128.8, 126.1, 121.1, 118.5, 83.5, 71.4, 70.3, 68.8; MS (ESI): m/z = 472 $[M+H]^+$. Anal. calcd. for $C_{19}H_{13}Br_2FeN$: C, 48.45; H, 2.78; N, 2.97. Found: C, 48.22; H, 3.02; N, 3.19.

(3-Methylquinolin-2-yl)ferrocene (3f)

Brown solid; mp 73–74 °C; IR (KBr, cm^{-1}): 3092, 3050, 2956, 2851, 1615, 1598, 1494, 1444, 1408, 1328, 1274, 1130, 1106, 1070, 1033, 876, 819, 755; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, $J = 6.0$ Hz, 1H, Ar-H), 7.83 (s, 1H, Ar-H), 7.68 (d, $J = 8.0$ Hz, 1H, Ar-H), 7.60 (t, $J = 7.6$ Hz, 1H, Ar-H), 7.43 (t, $J = 7.2$ Hz, 1H, Ar-H), 5.09 (s, 2H, Fc-H_α), 4.44 (s, 2H, Fc-H_β), 4.09 (s, 5H, Fc-H), 2.76 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 146.7, 136.6, 129.2, 128.9, 128.4, 126.8, 126.5, 125.5, 85.3, 70.0, 69.8, 69.5, 21.4; MS (ESI): $m/z = 328$ $[M+H]^+$. Anal. calcd. for $C_{20}H_{17}FeN$: C, 73.41; H, 5.24; N, 4.28. Found: C, 73.21; H, 5.51; N, 4.47.

(3-Methyl-5,8-dimethoxyquinolin-2-yl)ferrocene (3g)

Brown solid; mp 164–165 °C; IR (KBr, cm^{-1}): 3091, 2935, 2833, 1617, 1597, 1463, 1433, 1389, 1341, 1262, 1180, 1112, 1009, 876, 797; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H, Ar-H), 6.83 (d, $J = 8.4$ Hz, 1H, Ar-H), 6.66 (d, $J = 8.4$ Hz, 1H, Ar-H), 5.09 (t, $J = 2.0$ Hz, 2H, Fc-H_α), 4.42 (t, $J = 1.6$ Hz, 2H, Fc-H_β), 4.09 (s, 5H, Fc-H), 4.02 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 2.78 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 149.3, 148.3, 138.9, 131.5, 128.9, 119.9, 106.8, 102.8, 85.7, 70.1, 69.8, 69.4, 56.5, 55.7, 21.4; MS (ESI): $m/z = 388$ $[M+H]^+$. Anal. calcd. for $C_{22}H_{21}FeNO_2$: C, 68.23; H, 5.47; N, 3.62. Found: C, 68.42; H, 5.55; N, 3.90.

(3-Methyl-6,7-dimethoxyquinolin-2-yl)ferrocene (3h)

Brown solid; mp 171–172 °C; IR (KBr, cm^{-1}): 3087, 2949, 2826, 1617, 1597, 1497, 1462, 1336, 1341, 1237, 1146, 1019, 1009, 898, 818; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H, Ar-H), 7.35 (s, 1H, Ar-H), 6.92 (s, 1H, Ar-H), 5.01 (s, 2H, Fc-H_α), 4.40 (s, 2H, Fc-H_β), 4.08 (d, $J = 0.8$ Hz, 5H, Fc-H), 4.01 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 2.72 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7,

151.6, 149.2, 143.4, 135.4, 127.2, 122.2, 107.7, 104.2, 85.8, 69.6, 69.5, 69.3, 56.1, 55.9, 21.2; MS (ESI): $m/z = 388$ $[M+H]^+$. Anal. calcd. for $C_{22}H_{21}FeNO_2$: C, 68.23; H, 5.47; N, 3.62. Found: C, 67.96; H, 5.73; N, 3.48.

(6-Chloro-3-methylquinolin-2-yl)ferrocene (3i)

Brown solid; mp 119–121 °C; IR (KBr, cm^{-1}): 3086, 2963, 2833, 1618, 1593, 1485, 1403, 1383, 1235, 1270, 1070, 886, 824; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, $J = 8.8$ Hz, 1H, Ar-H), 7.72 (s, 1H, Ar-H), 7.65 (s, 1H, Ar-H), 7.52 (d, $J = 8.8$ Hz, 1H, Ar-H), 5.08 (s, 2H, Fc-H_α), 4.46 (s, 2H, Fc-H_β), 4.10 (s, 5H, Fc-H), 2.72 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 145.1, 135.6, 130.9, 130.4, 130.2, 129.3, 127.3, 125.2, 84.8, 70.0, 69.5, 21.4; MS (ESI): $m/z = 362$ $[M+H]^+$. Anal. calcd. for $C_{20}H_{16}ClFeN$: C, 66.42; H, 4.46; N, 3.87. Found: C, 66.12; H, 4.66; N, 3.72.

(6,8-Dibromo-3-methylquinolin-2-yl)ferrocene (3j)

Brown solid; mp 154–156 °C; IR (KBr, cm^{-1}): 3456, 3369, 3086, 3050, 2923, 2851, 1608, 1584, 1481, 1442, 1396, 1318, 1267, 1106, 1033, 1070, 947, 890, 824; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H, Ar-H), 7.77 (s, 1H, Ar-H), 7.69 (s, 1H, Ar-H), 5.13 (s, 2H, Fc-H_α), 4.47 (s, 2H, Fc-H_β), 4.10 (s, 5H, Fc-H), 2.69 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 142.3, 135.6, 134.6, 131.0, 128.3, 128.3, 125.6, 118.2, 84.4, 70.6, 70.2, 69.7, 21.1; MS (ESI): $m/z = 486$ $[M+H]^+$. Anal. calcd. for $C_{20}H_{15}Br_2FeN$: C, 49.53; H, 3.12; N, 2.89. Found: C, 49.30; H, 3.32; N, 3.12.

(3-Phenylquinolin-2-yl)ferrocene (3k)

Brown solid; mp 193–194 °C; IR (KBr, cm^{-1}): 3101, 3057, 2925, 2854, 1729, 1620, 1589, 1485, 1441, 1272, 1106, 1088, 1019, 816, 755; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, $J = 8.4$ Hz, 1H, Qu-H), 7.87 (s, 1H, Qu-H), 7.74 (d, $J = 8.4$ Hz, 1H, Qu-H), 7.68 (t, $J = 8.0$ Hz, 1H, Qu-H), 7.50–7.44 (m, 4H, Ar-H), 7.40–7.37 (m, 2H, Ar-H, Qu-H), 4.50 (t, $J = 2.0$ Hz, 2H, Fc-H_α), 4.23 (t, $J = 1.8$ Hz, 2H, Fc-H_β), 3.98 (s, 5H, Fc-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 147.9, 141.3, 137.1, 134.7, 130.2, 129.7, 129.4, 128.7, 128.1, 127.8, 126.4, 126.2, 84.8, 71.0, 70.1, 69.9; MS (ESI): $m/z = 390$ $[M+H]^+$. Anal. calcd. for $C_{25}H_{19}FeN$: C, 77.14; H, 4.92; N, 3.60. Found: C, 76.98; H, 5.16; N, 3.88.

(5,8-Dimethoxy-3-phenylquinolin-2-yl)ferrocene (3l)

Brown solid; mp 180–181 °C; IR (KBr, cm^{-1}): 3086, 2934, 2832, 1616, 1589, 1496, 1461, 1384, 1368, 1269, 1230, 1110, 1002, 799; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H, Qu-H), 7.48-7.38 (m, 5H, C_6H_5-H), 6.95 (d, $J = 8.4$ Hz, 1H, Qu-H), 6.69 (d, $J = 8.4$ Hz, 1H, Qu-H), 4.55 (s, 2H, Fc-H_α), 4.22 (s, 2H, Fc-H_β), 4.11 (s, 3H, OCH_3), 3.97 (s, 5H, Fc-H), 3.93 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 150.0, 149.7, 141.6, 140.5, 134.4, 132.3, 130.3, 128.7, 128.1, 119.8, 109.4, 103.5, 85.3, 71.2, 70.3, 70.2, 57.9, 56.3; MS (ESI): $m/z = 450$ $[M+H]^+$. Anal. calcd. for $C_{27}H_{23}FeNO_2$: C, 72.17; H, 5.16; N, 3.12. Found: C, 71.94; H, 4.96; N, 3.36.

(6,7-Dimethoxy-3-phenylquinolin-2-yl)ferrocene (3m)

Brown solid; mp 177–179 °C; IR (KBr, cm^{-1}): 3086, 3057, 2932, 2826, 1662, 1591, 1496, 1448, 1386, 1338, 1278, 1151, 1010, 821, 702; ^1H NMR (400 MHz, $CDCl_3$) δ 7.01 (s, 1H, Qu-H), 7.42 (s, 4H, C_6H_5-H), 7.36 (s, 1H, C_6H_5-H), 7.35 (s, 1H, Qu-H), 6.97 (s, 1H, Qu-H), 4.44 (s, 2H, Fc-H_α), 4.18 (s, 2H, Fc-H_β), 4.08 (s, 3H, OCH_3), 3.98 (s, 8H, Fc-H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 152.4, 149.4, 144.4, 141.2, 135.2, 132.5, 129.8, 128.1, 127.4, 121.3, 107.7, 104.7, 84.8, 70.2, 69.5, 69.1, 56.2, 56.0; MS (ESI): $m/z = 450$ $[M+H]^+$. Anal. calcd. for $C_{27}H_{23}FeNO_2$: C, 72.17; H, 5.16; N, 3.12. Found: C, 71.94; H, 4.96; N, 3.36.

(6-Chloro-3-phenylquinolin-2-yl)ferrocene (3n)

Brown solid; mp 153–155 °C; IR (KBr, cm^{-1}): 3094, 3057, 2925, 1603, 1585, 1494, 1472, 1405, 1365, 1269, 1184, 1106, 1001, 880, 827; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, $J = 8.8$ Hz, 1H, Qu-H), 7.78 (s, 1H, Qu-H), 7.71 (d, $J = 2.4$ Hz, 1H, Qu-H), 7.60 (dd, $J = 2.0$ Hz, $J = 2.8$ Hz, 1H, Qu-H), 7.48–7.46 (m, 3H, C_6H_5-H), 7.38–7.36 (m, 2H, C_6H_5-H), 4.49 (s, 2H, Fc-H_α), 4.25 (s, 2H, Fc-H_β), 3.99 (s, 5H, Fc-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 145.7, 140.2, 135.5, 134.9, 131.0, 130.4, 130.0, 129.4, 128.1, 127.7, 126.3, 125.8, 83.7, 70.5, 69.6; MS (ESI): $m/z = 424$ $[M+H]^+$. Anal. calcd. for $C_{25}H_{18}ClFeN$: C, 70.87; H, 4.28; N, 3.31. Found: C, 70.62; H, 4.57; N, 3.59.

(6,8-Dibromo-3-phenylquinolin-2-yl)ferrocene (3o)

Brown solid; mp 155–156 °C; IR (KBr, cm^{-1}): 3082, 2924, 2847, 1581, 1530, 1468, 1439, 1355, 1282, 1184, 1079, 1019, 1002, 881, 795, 701; ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H, Qu-H), 7.85 (s, 1H, Qu-H), 7.76 (s, 1H, Qu-H), 7.45 (s, 3H, C_6H_5-H), 7.34 (s, 2H, C_6H_5-H), 4.53 (s, 2H, Fc-H_α), 4.27 (s, 2H, Fc-H_β), 3.99 (s, 5H, Fc-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 143.0, 139.5, 135.7, 135.7, 135.4, 129.4, 129.1, 128.4, 128.0, 127.5, 125.7, 118.4, 83.4, 71.1, 70.0; MS (ESI): $m/z = 548$ $[M+H]^+$. Anal. calcd. for $C_{25}H_{17}Br_2FeN$: C, 54.89; H, 3.13; N, 2.56. Found: C, 55.01; H, 3.36; N, 2.80.

1,1′-Bis(quinolin-2-yl)ferrocene (3p)

Following the general procedure, using *o*-aminobenzaldehyde **1a** (2 mmol), 1,1′-diacetylferrocene **2d** (1 mmol), and sodium ethoxide (0.6 mmol), **3p** was obtained as a brown solid; mp 209–211 °C. IR (KBr, cm^{-1}): 3050, 2924, 2847, 1732, 1619, 1599, 1556, 1512, 1424, 1091, 1028, 908, 819, 749; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, $J = 8.4$ Hz, 2H, Ar-H), 7.58 (d, $J = 3.6$ Hz, 2H, Ar-H), 7.39 (s, 4H, Ar-H), 7.19 (d, $J = 8.4$ Hz, 2H, Ar-H), 6.98 (d, $J = 8.4$ Hz, 2H, Ar-H), 5.04 (s, 4H, Fc-H_α),), 4.42 (s, 4H, Fc-H_β); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 148.0, 134.9, 129.0, 128.7, 127.4, 126.3, 125.0, 119.1, 85.6, 71.2, 68.9; MS (ESI): $m/z = 441$ $[M+H]^+$. Anal. calcd. for $C_{28}H_{20}FeN_2$: C, 76.38; H, 4.58; N, 6.36. Found: C, 76.10; H, 4.83; N, 6.40.

1,1′-Bis(5,8-dimethoxyquinolin-2-yl)ferrocene (3q)

Following the general procedure, using 2-amino-3,6-dimethoxybenzaldehyde **1b** (2 mmol), 1,1′-diacetylferrocene **2d** (1 mmol), and sodium ethoxide (0.6 mmol), **3q** was obtained as a orange solid; mp 226–228 °C. IR (KBr, cm^{-1}): 3072, 3000, 2934, 2826, 1621, 1600, 1459, 1434, 1399, 1257, 1203, 1164, 1107, 1080, 799; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, $J = 8.8$ Hz, 2H, Ar-H), 7.28 (d, $J = 8.8$ Hz, 2H, Ar-H), 6.83 (d, $J = 8.4$ Hz, 2H, Ar-H), 6.59 (d, $J = 8.4$ Hz, 2H, Ar-H), 4.99 (s, 4H, Fc-H_α), 4.35 (s, 4H, Fc-H_β), 4.01 (s, 6H, OCH_3), 3.89 (s, 6H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 149.1, 148.8, 140.4, 129.9, 119.5, 118.9, 107.8, 102.5, 85.7, 71.4, 69.5, 56.5, 55.6; MS (ESI): $m/z = 561$ $[M+H]^+$. Anal. calcd. for $C_{32}H_{28}FeN_2O_4$: C, 68.58; H, 5.04; N, 5.00. Found: C, 68.40; H, 5.20; N, 5.30.

1,1′-Bis(6,7-dimethoxyquinolin-2-yl)ferrocene (3r)

Following the general procedure, using 2-amino-4,5-dimethoxybenzaldehyde **1c** (2 mmol), 1,1′-diacetylferrocene **2d** (1 mmol), and sodium ethoxide (0.6 mmol), **3r** was obtained as a brown solid, mp 224–226 °C. IR (KBr, cm^{-1}): 3086, 3000, 2936, 2833, 1621, 1598, 1500, 1466, 1432, 1337, 1245, 1203, 1129, 1029, 857; ^1H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, $J = 8.4$ Hz, 2H, Ar-H), 7.09 (s, 2H, Ar-H), 6.89 (d, $J = 8.4$ Hz, 2H, Ar-H), 6.58 (s, 2H, Ar-H), 4.98 (t, $J = 1.6$ Hz, 4H, Fc-H_α), 4.38 (t, $J = 2.0$ Hz, 4H, Fc-H_β), 3.97 (s, 6H, OCH_3), 3.95 (s, 6H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 151.7, 148.5, 144.7, 133.1, 121.5, 117.2, 107.6, 104.9, 85.9, 70.7, 68.4, 56.0, 55.8; MS (ESI): $m/z = 561$ $[M+H]^+$. Anal. calcd. for $C_{32}H_{28}FeN_2O_4$: C, 68.58; H, 5.04; N, 5.00. Found: C, 68.83; H, 5.32; N, 4.76.

1-(3-Methylquinolin-2-yl)-1′-propionylferrocene (3s)

Following the general procedure, using *o*-aminobenzaldehyde **1a** (2 mmol), 1,1′-dipropionylferrocene **2e** (1 mmol), and sodium ethoxide (0.6 mmol), **3s** was obtained as a brown solid, mp 109–111 °C. IR (KBr, cm^{-1}): 3050, 2975, 1672, 1596, 1494, 1450, 1409, 1376, 1246, 1050, 879, 756; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, $J = 8.4$ Hz, 1H, Qu-H), 7.86 (s, 1H, Qu-H), 7.69 (d, $J = 8.0$ Hz, 1H, Qu-H), 7.61 (t, $J = 7.6$ Hz, 1H, Qu-H), 7.45 (t, $J = 7.6$ Hz, 1H, Qu-H), 5.13 (s, 2H, Fc-H_α), 4.69 (s, 2H, Fc-H_β), 4.42 (d, $J = 16.0$ Hz, 4H, Fc-H), 2.66 (s, 3H, CH_3), 2.44 (q, $J = 7.2$ Hz, 2H, CH_2), 0.88 (t, $J = 7.2$ Hz, 3H, CH_2-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.7, 156.9, 146.8, 137.1, 129.4, 128.9, 128.8, 127.1, 126.8, 126.1, 87.0, 80.2, 73.5, 71.6, 71.4, 70.7, 32.9, 21.8, 8.1; MS (ESI): $m/z = 384$ $[M+H]^+$. Anal. calcd. for $C_{23}H_{21}FeNO$: C, 72.08; H, 5.52; N, 3.65. Found: C, 71.97; H, 5.79; N, 3.39.

1,1′-Bis[(3-methylquinolin-2-yl)]ferrocene (3t)

Following the general procedure, using *o*-aminobenzaldehyde **1a** (2 mmol), 1,1′-dipropionylferrocene **2e** (1 mmol), and sodium ethoxide (0.6 mmol), **3t** was obtained as a brown solid, mp 229–230 °C. IR (KBr, cm^{-1}): 3036, 2956, 2923, 1618, 1597, 1494, 1443, 1410, 1280, 1037, 887, 746; ^1H NMR (400 MHz, $CDCl_3$) δ

7.89 (d, $J = 8.4$ Hz, 2H, Ar-H), 7.56 (t, $J = 7.2$ Hz, 2H, Ar-H), 7.39 (t, $J = 7.2$ Hz, 2H, Ar-H), 7.28 (d, $J = 8.0$ Hz, 2H, Ar-H), 6.51 (s, 2H, Ar-H), 5.28 (s, 4H, Fc-H_α), 4.44 (s, 4H, Fc-H_β), 2.29 (s, 6H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 146.1, 136.1, 128.5, 128.3, 128.1, 126.4, 126.4, 125.0, 86.3, 71.0, 70.5, 21.4; MS (ESI): $m/z = 469$ $[M+H]^+$. Anal. calcd. for $C_{30}H_{24}FeN_2$: C, 76.93; H, 5.16; N, 5.98. Found: C, 77.12; H, 5.45; N, 6.22.

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