Supporting Information

for

Copper-catalyzed monoselective C–H amination of ferrocenes with alkylamines

Zhen-Sheng Jia, Qiang Yue, Ya Li, Xue-Tao Xu, Kun Zhang and Bing-Feng Shi

*Beilstein J. Org. Chem.* **2021**, *17*, 2488–2495. doi:10.3762/bjoc.17.165

Full experimental details, compound characterization, and copies of NMR spectra
# Table of contents

1. General information........................................................................................................... S2
2. Structure of substrates....................................................................................................... S3
3. Experimental section ......................................................................................................... S4
4. Screening of reaction conditions....................................................................................... S17
5. General procedures for Cu-catalyzed monoselective C–H amination of ferrocenes with alkylamines......................................................................................................................... S21
6. Gram-scale synthesis ........................................................................................................ S38
7. Removal of directing group. ............................................................................................. S39
8. Mechanistic experiments. .............................................................................................. S40
9. References. ....................................................................................................................... S43
10. NMR spectra. .................................................................................................................. S44
1. General information

All the materials and solvents were purchased from commercial suppliers and used without additional purification. CuI was purchased from Strem. NMR spectra were recorded on a Bruke Avance operating for $^1$H NMR at 400 MHz, $^{13}$C NMR at 100 MHz using TMS as internal standard. The peaks were internally referenced to CDCl$_3$ (7.26 ppm) or residual undeuterated solvent signal of CDCl$_3$ (77.16 ppm for $^{13}$C NMR). The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet, brs = broad singlet. Mass spectroscopy data of the products were collected on an HRMS-TOF instrument using ESI ionization.
2. Structure of substrates

Figure S1: Ferrocene substrates
3. Experimental section

3-1. Preparation of substrates

Substrate 1a is a known compound and was prepared according to the literature.\textsuperscript{[1]} Substrates 1b–m were prepared following the literature procedure. Amines 2a–s are commercially available. All other starting materials, solvents and reagents were purchased and used as received.

**General procedure 1 (for the preparation of 1f–l):**

1) NaOH (2.0 equiv.)
MeOH:H₂O, 60°C, 12 h
2) conv. HCl

**Figure S2:** Secondary amines
\[ N,N'-\text{Dicyclohexylcarbodiimide (DCC, 5.0 mmol, 0.91 g) and 4-dimethylaminopyridine (DMAP, 5.0 mmol, 0.54 g) were added to the solution of ferrocenecarboxylic acid (5.0 mmol, 1.01 g) in dry MeOH (20 mL). The reaction mixture was flushed with argon and stirred at room temperature for 3 h. The reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (ethyl acetate/hexanes = 1/9) to give ferrocenecarboxylic acid methyl ester S1} \]

\[ \text{as orange crystals.} \]

Acetyl chloride (0.43 mL, 6.0 mmol) was added to a suspension of anhydrous aluminum chloride (1.33 g, 10 mmol) in CH\(_2\)Cl\(_2\) (12 mL) at 0 °C and stirred for 15 min. The mixture was then added to a solution of methyl ferrocene-1-carboxylate (1.0 g, 5.0 mmol) in CH\(_2\)Cl\(_2\) (23 mL) at 0 °C over a period of 15 min upon stirring under nitrogen atmosphere. To prevent light-induced degradation, the flask was covered with aluminum foil during the reaction. After 4 h, the reaction mixture was poured into ice water and the resulting precipitate was solubilized by addition of concentrated HCl. The organic layer was separated, and the aqueous layer was extracted with CH\(_2\)Cl\(_2\). The combined organic layers were dried (MgSO\(_4\)) and evaporated to give S2 as orange solid.

A solution of the ester S2 (3.0 mmol) in 15 mL of methanol and 15 mL of 20% NaOH (aq.) was heated under reflux for 12 h. The reaction mixture was cooled and acidified with 5 mL of 20% HCl in an ice bath and then stirred vigorously for a few minutes to make the free acid from the sodium salt. The product was collected by suction filtration, washed with 10 mL of water, and dried. Crude ferrocene carboxylic acid S3 was obtained and used directly for the next step.

Following a reported procedure: In a 50 mL Round-bottomed flask, to a solution of S3 (3.0 mmol), 8-aminoquinoline (3.6 mmol), and DMAP (111 mg, 0.9 mmol) in anhydrous CH\(_2\)Cl\(_2\) (15 mL) was added a solution of N-ethyl-N\(^\prime\)-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC, 1.15 g, 6 mmol) in CH\(_2\)Cl\(_2\) (15 mL) through a dropping funnel at 0 °C under N\(_2\) atmosphere. The reaction mixture was stirred at rt overnight. After completion, the mixture was quenched with NaHCO\(_3\) (10 mL) and diluted with CH\(_2\)Cl\(_2\) (50 mL). The organic layer was washed with aq. 1 N HCl (50 mL), followed by aq. NaHCO\(_3\) (50 mL), aq. NaCl (50 mL), and dried with anhydrous Na\(_2\)SO\(_4\). The solvent was concentrated and the resulting residue was purified by column chromatography using EtOAc/hexane as eluent to afford the desired product 1f-1 as an orange solid.
General procedure 2 (for the preparation of 1c and 1d):

To an oven dried round bottom flask equipped with a stir bar under a N₂(g) atmosphere was added PPh₃MeBr (1.50 equiv). The flask was evacuated and back filled with N₂(g) and dry THF (0.1 M) was added. The resultant mixture was cooled to −78 °C, to which a solution of n-BuLi in hexanes (1.6 M, 1.3 equiv) was added. The solution was allowed to warm to rt and stirred for 30 mins before ketone substrate S₄ was added (1.0 equiv). The reaction was allowed to stir at rt for 4 h before being diluted with hexane and quenched with H₂O. The aqueous layer was separated and washed with hexane (3 × 30 mL). The organic layers were combined, dried (Na₂SO₄), filtered and concentrated in vacuo. The resultant crude alkylferrocenes S₅ were purified via column chromatography.

To a solution of S₅ (4 mmol, 1 equiv) in MeOH (20 mL) was added Pd/C (10 wt %) and the suspension was equipped with H₂ (1 atm) several times. After stirring at rt. for 12 h, the reaction mixture was filtered and the filtrate was concentrated to afford the title compound S₆ as orange oil and used directly in the next step.

A solution of the ester S₆ (3.0 mmol) in 15 mL of methanol and 15 mL of 20% NaOH (aq.) was heated under reflux for 12 h. The reaction mixture was cooled and acidified with 5 mL of 20% HCl in an ice bath and then stirred vigorously for a few minutes to make free acid from the sodium salt. The product was collected by suction filtration at room temperature, washed with 10 mL of water, and dried. Pure 8-ferrocenyl-8-oxooctanoic acid S₇ as red solid.

Following a reported procedure,[4] In a 50 mL Round-bottomed flask, to a solution of S₇ (3.0 mmol), 8-aminoquinoline (3.6 mmol), and DMAP (111 mg, 0.9 mmol) in anhydrous CH₂Cl₂ (15 mL) was added a solution of N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI, 1.15 g, 6 mmol) in CH₂Cl₂ (15 mL) through a dropping funnel at 0 °C under N₂ atmosphere. The reaction mixture was stirred at rt overnight. After completion, the mixture was quenched with
NaHCO₃ (10 mL) and diluted with CH₂Cl₂ (50 mL). The organic layer was washed with aq. 1 N HCl (50 mL), followed by aq. NaHCO₃ (50 mL), aq. NaCl (50 mL), and dried with anhydrous Na₂SO₄. The solvent was concentrated and the resulting residue was purified by column chromatography using EtOAc/hexane as eluent to afford the desired product 1c/1d as an orange solid.

**General procedure 3:**

![Chemical structure of S8, S9, and 1e](image)

A solution of the ester S8 (0.85 g, 3.0 mmol) in 15 mL of methanol and 15 mL of 20% NaOH (aq.) was heated under reflux for 12 h. The reaction mixture was cooled and acidified with 5 mL of 20% HCl in an ice bath and then stirred vigorously for a few minutes to make free acid from the sodium salt. The product S9 was collected by suction filtration at room temperature, washed with 10 mL of water, and dried.

Following a reported procedure:[⁴] In a 50 mL Round-bottomed flask, to a solution of S9 (3.0 mmol), 8-aminoquinoline (3.6 mmol), and DMAP (111 mg, 0.9 mmol) in anhydrous CH₂Cl₂ (15 mL) was added a solution of N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI, 1.15 g, 6 mmol) in CH₂Cl₂ (15 mL) through a dropping funnel at 0 °C under N₂ atmosphere. The reaction mixture was stirred at rt overnight. After completion, the mixture was quenched with NaHCO₃ (10 mL) and diluted with CH₂Cl₂ (50 mL). The organic layer was washed with aq. 1 N HCl (50 mL), followed by aq. NaHCO₃ (50 mL), aq. NaCl (50 mL), and dried with anhydrous Na₂SO₄. The solvent was concentrated and the resulting residue was purified by column chromatography using EtOAc/hexane as eluent to afford the desired product 1e as a yellow solid.
1,1-Dichlorodimethyl ether (15 mmol) was added at 0 °C to a suspension of anhydrous tin tetrachloride (12 mmol) in CH$_2$Cl$_2$ (12 mL) and stirred for 15 min. The mixture was then added at 0 °C to a solution of S1 (2.4 g, 10 mmol) in CH$_2$Cl$_2$ (23 mL) over a period of 15 min upon stirring under nitrogen atmosphere. After 4 h, the reaction mixture was poured into ice water and the resulting precipitate was solubilized by addition of concentrated HCl. The organic layer was separated, and the aqueous layer was extracted with CH$_2$Cl$_2$. The combined organic layers were dried (MgSO$_4$) and evaporated under reduced pressure to give S10 as an orange solid.

To an oven dried round bottom flask equipped with a stir bar under a N$_2$(g) atmosphere was added PPh$_3$BnBr (1.50 equiv). The flask was evacuated and back filled with N$_2$(g) and dry THF (0.1 M) was added. The resultant mixture was cooled to −78 °C to which a solution of n-BuLi in hexanes (1.6M, 1.3 equiv) was added. The solution was allowed to warm to rt and stirred for 30 mins before the crude S10 was added (1.0 equiv). The reaction was allowed to stir at rt for 4 h before diluted with hexane and quenched with H$_2$O. The aqueous layer was separated and washed with hexane (3 × 30 mL). The organic layers were combined, dried (Na$_2$SO$_4$), filtered and concentrated in vacuo. The resultant crude alkenes were purified via column chromatography, afford the desired S11 as an orange solid.

To a solution of S11 (4 mmol, 1 equiv) in MeOH (20 mL) was added Pd/C (10 wt %) and the
suspension was equipped with H₂ (1 atm) several times. After stirring at rt. for 12 h, the reaction mixture was filtered and the filtrate was concentrated to afford the title compound S₁₂ as an orange oil and used directly in the next step.

A solution of the ester S₁₂ (1.04 g, 3.0 mmol) in 15 mL of methanol and 15 mL of 20% NaOH (aq.) was heated under reflux for 12 h. The reaction mixture was cooled and acidified with 5 mL of 20% HCl in an ice bath and then stirred vigorously for a few minutes to make free acid from the sodium salt. The crude product S₁₃ was collected by suction filtration at room temperature, washed with 10 mL of water, and dried.

Following a reported procedure:[⁴] In a 50 mL Round-bottomed flask, to a solution of S₁₃ (3.0 mmol), 8-aminoquinoline (3.6 mmol), and DMAP (111 mg, 0.9 mmol) in anhydrous CH₂Cl₂ (15 mL) was added a solution of N-ethyl-N′-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI, 1.15 g, 6 mmol) in CH₂Cl₂ (15 mL) through a dropping funnel at 0 °C under N₂ atmosphere. The reaction mixture was stirred at rt overnight. After completion, the mixture was quenched with NaHCO₃ (10 mL) and diluted with CH₂Cl₂ (50 mL). The organic layer was washed with aq. 1 N HCl (50 mL), followed by aq. NaHCO₃ (50 mL), aq. NaCl (50 mL), and dried with anhydrous Na₂SO₄. The solvent was concentrated and the resulting residue was purified by column chromatography using EtOAc/hexane as eluent to afford the desired product 1b as an orange solid.

**General Procedure 5:**

A solution of the ester S₁₀ (0.82 g, 3.0 mmol) in 15 mL of methanol and 15 mL of 20% NaOH (aq.) was heated under reflux for 12 h. The reaction mixture was cooled and acidified with 5 mL of 20% HCl in an ice bath and then stirred vigorously for a few minutes to make free acid from the sodium salt. The crude product S₁₄ was collected by suction filtration at room temperature, washed
with 10 mL of water, and dried.

Following a reported procedure:\textsuperscript{[4]} In a 50 mL Round-bottomed flask, to a solution of S\textsubscript{14} (3.0 mmol), 8-aminoquinoline (3.6 mmol), and DMAP (111 mg, 0.9 mmol) in anhydrous CH\textsubscript{2}Cl\textsubscript{2} (15 mL) was added a solution of N-ethyl-N'-[(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI, 1.15 g, 6 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (15 mL) through a dropping funnel at 0 °C under N\textsubscript{2} atmosphere. The reaction mixture was stirred at rt overnight. After completion, the mixture was quenched with NaHCO\textsubscript{3} (10 mL) and diluted with CH\textsubscript{2}Cl\textsubscript{2} (50 mL). The organic layer was washed with aq. 1 N HCl (50 mL), followed by aq. NaHCO\textsubscript{3} (50 mL), aq. NaCl (50 mL), and dried with anhydrous Na\textsubscript{2}SO\textsubscript{4}. The solvent was concentrated and the resulting residue was purified by column chromatography using EtOAc/hexane as eluent to afford the desired product S\textsubscript{15} as a yellow solid.

To a solution of compound S\textsubscript{15} (3 mmol) in methanol (10 mL) was added NaBH\textsubscript{4} (0.2 g, 5 mmol). After stirring for 1 h while cooled with an ice-water bath, methanol was evaporated and the residue was dissolved in EtOAc (50 mL). The organic layer was washed with water (3 × 30 mL) and brine (3 × 30 mL), and dried over MgSO\textsubscript{4}. The volatiles were removed to give pure 1\textsubscript{m} as a yellow solid.

1-((8-Quinolinylamino)carbonyl)-1'-phenethyl-ferrocene (2b)

Substrate 2b was synthesized according to General Procedure 4: orange solid.

\textbf{\textsuperscript{1}H NMR (400 MHz, Chloroform-d)} \(\delta\) 10.26 (s, 1H), 8.85 – 8.79 (m, 1H), 8.77 (dd, \(J = 4.2, 1.6\) Hz, 1H), 8.18 (dd, \(J = 8.2, 1.6\) Hz, 1H), 7.57 (t, \(J = 7.8\) Hz, 1H), 7.51 (d, \(J = 8.1\) Hz, 1H), 7.46 (dd, \(J = 8.3, 4.2\) Hz, 1H), 7.17 (m, \(J = 7.8, 6.9, 3.7\) Hz, 3H), 7.06 – 7.00 (m, 2H), 4.91 (s, 2H), 4.43 (s, 2H), 4.19 (d, \(J = 1.9\) Hz, 2H), 4.14 (d, \(J = 2.0\) Hz, 2H), 2.74 (m, \(J = 9.3, 5.5\) Hz, 2H), 2.65 (m, \(J = 10.2, 6.2\) Hz, 2H).

\textbf{\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3})} \(\delta\) 169.1, 148.4, 141.9, 138.6, 136.5, 134.9, 128.4, 128.3, 128.2, 127.7, 125.9, 121.7, 121.1, 116.3, 90.4, 71.6, 70.1, 69.3, 69.2, 37.6, 30.7.

\textbf{HRMS (ESI)} \textit{m/z}: [M + Na]\textsuperscript{+} Calcd for C\textsubscript{28}H\textsubscript{24}FeN\textsubscript{2}O\textsubscript{4} 483.1130; found:483.1133.
1-((8-Quinolinylamino)carbonyl)-1’-isopropyl-ferrocene (2c)

Substrate 2c was synthesized according to General Procedure 2; orange solid.

\( ^1\)H NMR (400 MHz, Chloroform-d) \( \delta \): 10.28 (d, \( J = 4.7 \) Hz, 1H), 8.95 – 8.84 (m, 1H), 8.82 (dd, \( J = 7.8, 3.4 \) Hz, 1H), 8.19 (d, \( J = 8.0, 2.4, 1.9 \) Hz, 1H), 7.64 – 7.53 (m, 1H), 7.49 (m, \( J = 12.4, 3.8 \) Hz, 2H), 4.92 (p, \( J = 2.4, 1.9 \) Hz, 2H), 4.44 (p, \( J = 2.2 \) Hz, 2H), 4.21 (p, \( J = 2.1, 1.7 \) Hz, 2H), 4.15 (p, \( J = 2.2 \) Hz, 2H), 2.67 (m, \( J = 10.1, 8.9, 7.1, 4.9 \) Hz, 1H), 1.22 – 1.13 (m, 6H).

\( ^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \): 169.3, 148.3, 138.6, 136.5, 134.9, 128.2, 127.7, 121.7, 121.0, 116.2, 98.8, 71.5, 69.3, 69.0, 68.1, 27.3, 23.7.

HRMS (ESI) m/z: [M + H]\(^+\) Calcd for C\(_{23}\)H\(_{23}\)FeN\(_2\)O 399.1082; found: 399.1153.

1-((8-Quinolinylamino)carbonyl)-1’-pentan-3-ferrocene (2d)

Substrate 2d was synthesized according to General Procedure 2; orange solid.

\( ^1\)H NMR (400 MHz, Chloroform-d) \( \delta \): 10.27 (s, 1H), 8.87 (dt, \( J = 4.2, 1.4 \) Hz, 1H), 8.82 (dd, \( J = 7.6, 1.3 \) Hz, 1H), 8.18 (d, \( J = 8.3, 1.3 \) Hz, 1H), 7.57 (t, \( J = 7.9 \) Hz, 1H), 7.53 – 7.49 (m, 1H), 7.49 – 7.43 (m, 1H), 4.89 (q, \( J = 1.6 \) Hz, 2H), 4.41 (q, \( J = 1.5 \) Hz, 2H), 4.20 (q, \( J = 1.5 \) Hz, 2H), 4.11 (q, \( J = 1.5 \) Hz, 2H), 2.27 (q, \( J = 7.2, 6.3 \) Hz, 1H), 1.65 – 1.57 (m, 2H), 1.49 (m, \( J = 14.0, 7.2 \) Hz, 2H), 0.79 (t, \( J = 7.4 \) Hz, 6H).

\( ^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \): 169.3, 148.3, 138.7, 136.5, 135.0, 128.2, 127.7, 121.7, 121.0, 116.2, 97.1, 71.6, 69.1, 69.0, 40.3, 26.7, 11.3.

HRMS (ESI) m/z: [M + Na]\(^+\) Calcd for C\(_{25}\)H\(_{26}\)FeN\(_2\)ONa 449.1287; found: 449.1288.
1-((8-Quinolinylamino)carbonyl)-1’-2-methyl-1-ene-ferrocene (2e)

Substrate 2e was synthesized according to General Procedure 3; yellow solid.

$^1$H NMR (400 MHz, Chloroform-d) δ 10.22 (s, 1H), 8.88 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.83 (dd, $J = 7.6, 1.4$ Hz, 1H), 8.19 (dd, $J = 8.2, 1.6$ Hz, 1H), 7.58 (t, $J = 7.9$ Hz, 1H), 7.53 – 7.46 (m, 2H), 5.10 (s, 1H), 4.88 (t, $J = 1.9$ Hz, 2H), 4.76 (m, $J = 1.6$ Hz, 1H), 4.49 (t, $J = 1.9$ Hz, 2H), 4.40 (t, $J = 1.8$ Hz, 2H), 4.34 (t, $J = 1.9$ Hz, 2H), 2.05 – 1.98 (m, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.9, 148.2, 139.9, 138.6, 136.4, 134.8, 128.1, 127.6, 121.7, 121.0, 116.2, 110.1, 88.2, 72.3, 70.7, 69.7, 67.5, 21.5.

HRMS (ESI) m/z: [M + Na]$^+$ Calcd for C$_{23}$H$_{20}$FeN$_2$ONa 419.0817; found: 419.0817.

1-((8-Quinolinylamino)carbonyl)-1’-acetyl-ferrocene (2f)

Substrate 2f was synthesized according to General Procedure 1; orange solid.

$^1$H NMR (400 MHz, Chloroform-d) δ 10.26 (s, 1H), 8.89 (dd, $J = 4.2, 1.6$ Hz, 1H), 8.81 (dd, $J = 7.4, 1.5$ Hz, 1H), 8.20 (dd, $J = 8.2, 1.6$ Hz, 1H), 7.63 – 7.53 (m, 2H), 7.50 (dd, $J = 8.3, 4.2$ Hz, 1H), 4.99 (t, $J = 1.9$ Hz, 2H), 4.86 (t, $J = 1.9$ Hz, 2H), 4.60 (t, $J = 1.9$ Hz, 2H), 4.49 (t, $J = 1.9$ Hz, 2H), 2.39 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 201.8, 167.6, 148.5, 138.6, 136.6, 134.5, 128.2, 127.7, 121.9, 121.6, 116.5, 80.7, 78.6, 74.2, 72.8, 71.3, 70.1, 27.8.

HRMS (ESI) m/z: [M + H]$^+$ Calcd for C$_{22}$H$_{19}$FeN$_2$O 399.0718; found: 399.0708.
1-((8-Quinolinylamino)carbonyl)-1'-butyryl-ferrocene (2g)

Substrate 2g was synthesized according to **General Procedure 1**: orange solid.

**$^1$H NMR (400 MHz, Chloroform-d)** $\delta$ 10.26 (s, 1H), 8.89 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.82 (dd, $J = 7.4, 1.6$ Hz, 1H), 8.20 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.62 – 7.53 (m, 2H), 7.50 (dd, $J = 8.3, 4.2$ Hz, 1H), 4.98 (t, $J = 1.9$ Hz, 2H), 4.87 (t, $J = 1.9$ Hz, 2H), 4.58 (t, $J = 2.0$ Hz, 2H), 4.48 (t, $J = 1.9$ Hz, 2H), 2.67 (t, $J = 7.4$ Hz, 2H), 1.64 (d, $J = 7.3$ Hz, 2H), 0.86 (t, $J = 7.4$ Hz, 3H).

**$^{13}$C NMR (100 MHz, CDCl$_3$)** $\delta$ 204.1, 167.6, 148.5, 138.6, 136.5, 134.5, 128.2, 127.6, 121.9, 121.5, 116.4, 80.6, 78.5, 74.0, 72.7, 71.0, 70.0, 41.9, 17.8, 14.0.

**HRMS (ESI)** m/z: [M + H]$^+$ Calcd for C$_{24}$H$_{23}$FeN$_2$O$_2$: 427.1031; found: 427.1102.

1-((8-Quinolinylamino)carbonyl)-1'-valeryl-ferrocene (2h)

Substrate 2h was synthesized according to **General Procedure 1**: orange solid.

**$^1$H NMR (400 MHz, Chloroform-d)** $\delta$ 10.25 (s, 1H), 8.88 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.82 (dd, $J = 7.4, 1.6$ Hz, 1H), 8.19 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.61 – 7.52 (m, 2H), 7.49 (dd, $J = 8.3, 4.2$ Hz, 1H), 4.97 (t, $J = 1.9$ Hz, 2H), 4.87 (t, $J = 2.0$ Hz, 2H), 4.58 (t, $J = 2.0$ Hz, 2H), 4.47 (t, $J = 1.9$ Hz, 2H), 2.76 – 2.59 (m, 2H), 1.61 – 1.53 (m, 2H), 1.27 – 1.19 (m, 2H), 0.83 (t, $J = 7.3$ Hz, 3H).

**$^{13}$C NMR (100 MHz, CDCl$_3$)** $\delta$ 204.2, 167.6, 148.5, 138.6, 136.5, 134.5, 128.2, 127.6, 121.8, 121.5, 116.4, 80.6, 78.5, 74.0, 72.6, 71.0, 70.0, 39.8, 26.5, 22.6, 14.0.

**HRMS (ESI)** m/z: [M + H]$^+$ Calcd for C$_{25}$H$_{24}$FeN$_2$O$_2$: 441.1187; found: 441.1261.
1-((8-Quinolinylamino)carbonyl)-1’-2-methyl-1-butyryl-ferrocene (2i)

![Structure](image)

Substrate 2i was synthesized according to **General Procedure 1**: orange solid.

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 10.26 (s, 1H), 8.89 (dd, $J = 4.2, 1.6$ Hz, 1H), 8.82 (dd, $J = 7.4, 1.5$ Hz, 1H), 8.20 (dd, $J = 8.3, 1.6$ Hz, 1H), 7.61 – 7.52 (m, 2H), 7.50 (dd, $J = 8.3, 4.2$ Hz, 1H), 4.98 (t, $J = 1.9$ Hz, 2H), 4.86 (t, $J = 1.9$ Hz, 2H), 4.58 (t, $J = 1.9$ Hz, 2H), 4.48 (t, $J = 1.9$ Hz, 2H), 2.56 (d, $J = 6.9$ Hz, 2H), 2.18 (hept, $J = 6.7$ Hz, 1H), 0.89 (d, $J = 6.6$ Hz, 6H).

$^{13}$C NMR (100 MHz, CDCl₃) $\delta$ 203.8, 167.7, 148.5, 138.6, 136.6, 134.6, 128.2, 127.6, 121.9, 121.5, 116.4, 81.0, 78.5, 74.2, 72.7, 71.0, 70.0, 49.0, 25.1, 22.8.

HRMS (ESI) m/z: [M + H]$^+$ Calcd for $\text{C}_{25}\text{H}_{25}\text{FeN}_2\text{O}_2$ 441.1187; found: 441.1259.

1-((8-Quinolinylamino)carbonyl)-1’-2,2-dimethyl-1-propionyl-ferrocene (2j)

![Structure](image)

Substrate 2j was synthesized according to **General Procedure 1**: orange solid.

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 10.27 (s, 1H), 8.89 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.79 (dd, $J = 7.5, 1.6$ Hz, 1H), 8.20 (dd, $J = 8.2, 1.7$ Hz, 1H), 7.61 – 7.52 (m, 2H), 7.50 (dd, $J = 8.3, 4.2$ Hz, 1H), 4.97 (dt, $J = 3.9, 1.9$ Hz, 4H), 4.55 (t, $J = 2.0$ Hz, 2H), 4.46 (t, $J = 2.0$ Hz, 2H), 1.31 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl₃) $\delta$ 209.8, 167.9, 148.5, 138.6, 136.5, 134.7, 128.2, 127.6, 121.8, 121.4, 116.4, 78.3, 78.3, 73.7, 73.3, 72.5, 69.9, 44.6, 28.1.

HRMS (ESI) m/z: [M + H]$^+$ Calcd for $\text{C}_{25}\text{H}_{24}\text{FeN}_2\text{O}_2$ 441.1187; found: 441.1261.
1-((8-Quinolinylamino)carbonyl)-1’-(o-tolyl)acetyl-ferrocene (2k)

Substrate 2k was synthesized according to General Procedure 1: orange solid.

\[^1\text{H NMR (400 MHz, Chloroform-}d\text{)}\delta\text{ 10.24 (s, 1H), 8.85 (dd, } J = 4.2, 1.7 \text{ Hz, 1H), 8.74 (dd, } J = 7.1, 1.9 \text{ Hz, 1H), 8.19 (dd, } J = 8.3, 1.7 \text{ Hz, 1H), 7.60 – 7.51 (m, 3H), 7.49 (dd, } J = 8.3, 4.2 \text{ Hz, 1H), 7.33 – 7.27 (m, 1H), 7.21 – 7.11 (m, 2H), 5.02 (t, } J = 1.9 \text{ Hz, 2H), 4.89 (t, } J = 2.0 \text{ Hz, 2H), 4.65 (t, } J = 1.9 \text{ Hz, 2H), 4.55 (t, } J = 1.9 \text{ Hz, 2H), 2.40 (s, 3H).}\]

\[^{13}\text{C NMR (100 MHz, CDCl}_3\text{)}\delta\text{ 201.6, 167.6, 148.5, 139.6, 138.6, 136.5, 136.1, 134.6, 131.2, 130.1, 128.1, 127.8, 127.6, 125.2, 121.8, 121.5, 116.5, 80.7, 78.6, 74.9, 73.1, 72.8, 70.1, 20.1.}\]

\text{HRMS (ESI) m/z: [M + H]\textsuperscript{+} Calcd for C}_{28}\text{H}_{23}\text{FeN}_2\text{O}_2\text{ 475.1031; found: 475.1104.}\]

1-((8-Quinolinylamino)carbonyl)-1’-p-chlorophenylacetyl -ferrocene (2l)

Substrate 2l was synthesized according to General Procedure 1: orange solid.

\[^1\text{H NMR (400 MHz, Chloroform-}d\text{)}\delta\text{ 10.16 (s, 1H), 8.85 (dd, } J = 4.2, 1.7 \text{ Hz, 1H), 8.70 (dd, } J = 6.7, 2.2 \text{ Hz, 1H), 8.20 (dd, } J = 8.3, 1.7 \text{ Hz, 1H), 7.73 (d, } J = 8.5 \text{ Hz, 2H), 7.59 – 7.52 (m, 2H), 7.50 (dd, } J = 8.3, 4.2 \text{ Hz, 1H), 7.17 (d, } J = 8.5 \text{ Hz, 2H), 5.02 (t, } J = 2.0 \text{ Hz, 2H), 4.99 – 4.94 (m, 2H), 4.73 – 4.63 (m, 2H), 4.53 – 4.43 (m, 2H).}\]

\[^{13}\text{C NMR (100 MHz, CDCl}_3\text{)}\delta\text{ 196.9, 167.3, 148.4, 138.5, 138.1, 137.4, 136.6, 134.4, 129.7, 128.5, 128.1, 127.6, 121.8, 121.6, 116.4, 79.4, 78.9, 74.6, 73.1, 70.6.}\]

\text{HRMS (ESI) m/z: [M + H]\textsuperscript{+} Calcd for C}_{27}\text{H}_{20}\text{ClFeN}_2\text{O}_2\text{ 495.0484; found:495.0560.}\]
1-((8-Quinolinylamino)carbonyl)-1′-methanol-ferrocene (2m)

Substrate 2m was synthesized according to General Procedure 5; yellow solid.

\(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 10.28 (s, 1H), 8.89 – 8.84 (m, 2H), 8.20 (dd, \(J = 8.2, 1.7\) Hz, 1H), 7.61 – 7.52 (m, 2H), 7.49 (dd, \(J = 8.2, 4.2\) Hz, 1H), 4.97 (t, \(J = 1.9\) Hz, 2H), 4.50 (t, \(J = 1.9\) Hz, 2H), 4.38 (s, 2H), 4.32 (t, \(J = 1.9\) Hz, 2H), 4.23 (t, \(J = 1.9\) Hz, 2H).

\(^{13}\)C NMR (100 MHz, CDCl₃) \(\delta\) 170.3, 148.5, 138.6, 136.6, 134.4, 128.2, 127.7, 121.8, 121.7, 116.9, 91.9, 71.4, 69.2, 69.2, 68.7, 60.1.

HRMS (ESI) m/z: [M + Na]^+ Calcd for C₄₁H₁₈FeN₂O₂Na 409.0615; found: 409.0613.
4. Screening of reaction conditions

Table S1. Screening of solvents

| entry | solvents (0.1 M) | yield (%) |
|-------|------------------|-----------|
| 1     | DMF              | 11        |
| 2     | DMSO             | trace     |
| 3     | NMP              | 15        |
| 4     | MeCN             | 32        |
| 5     | iPrOH            | trace     |
| 6     | HFIP             | n.r       |

* Reactions conditions: 1a (0.1 mmol), 2a (0.3 mmol), Cul (20 mol%), K$_2$CO$_3$ (1.0 equiv.), NMO (2.0 equiv.), solvent (0.1 M) under air at 120 °C for 12 h. * Isolated yield.

Table S2. Screening of catalysts

| entry | catalyst (20 mol%) | yield (%) |
|-------|---------------------|-----------|
| 1     | Cu(OAc)$_2$        | 10        |
| 2     | CuCN               | 12        |
| 3     | Cu$_2$O            | n.r       |
| 4     | CuCl               | 18        |
| 5     | Cul                | 32        |
| 6     | TeCu               | trace     |

* Reactions conditions: 1a (0.1 mmol), 2a (0.3 mmol), Catalyst (20 mol%), K$_2$CO$_3$ (1.0 equiv.), NMO (2.0 equiv.), MeCN (0.1 M) under air at 120 °C for 12 h. * Isolated yield.
Table S3. Screening of several bases a

| entry | base (1.0 equiv.) | yield (%)b |
|-------|-------------------|------------|
| 1     | K_2PO_4           | 28         |
| 2     | Cs_2CO_3          | trace      |
| 3     | K_2CO_3           | 32         |
| 4     | DMAP              | 29         |

*a Reactions conditions: 1a (0.1 mmol), 2a (0.3 mmol), Cui (20 mol%), Base (1.0 equiv.), NMO (2.0 equiv.), MeCN (0.1 M) under air at 120 °C for 12 h. b Isolated yield.

Table S4. Screening of several oxidants a

| entry | oxidant (2.0 equiv.) | yield (%)b |
|-------|----------------------|------------|
| 1     | NMO                  | 32         |
| 2     | MnO_2                | trace      |
| 3     | TEMPO                | 23         |
| 4     | O_2                  | 8          |

*a Reactions conditions: 1a (0.1 mmol), 2a (0.3 mmol), Cui (20 mol%), K_2CO_3 (1.0 equiv.), Oxidant (2.0 equiv.), MeCN (0.1 M) under air at 120 °C for 12 h. b Isolated yield.
Table S5. Screening of several additives

| entry | additive (1.0 equiv.) | yield (%) |
|-------|-----------------------|-----------|
| 1     | ![](image)             | 34        |
| 2     | ![](image)             | n.r       |
| 3     | ![](image)             | 33        |
| 4     | ![](image)             | trace     |
| 5     | ![](image)             | n.r       |
| 6     | ![](image)             | 23        |

*a* Reactions conditions: 1a (0.1 mmol), 2a (0.3 mmol), Cul (20 mol%), K₂CO₃ (1.0 equiv.), NMO (2.0 equiv.), additive (1.0 equiv.), MeCN (0.1 M) under air at 120 °C for 12 h. ′ Isolated yield.

Table S6. Screening of several solvent volumes

| entry | MeCN (v/ml) | yield (%) |
|-------|-------------|-----------|
| 1     | 1.5         | 21        |
| 2     | 1.0         | 34        |
| 3     | 0.8         | 33        |
| 4     | 0.4         | 33        |
| 5     | 0.1         | 34        |
| 6     | neat        | 36\(^{a}\) |

*a* Reactions conditions: 1a (0.1 mmol), 2a (0.3 mmol), Cul (20 mol%), K₂CO₃ (1.0 equiv.), NMO (2.0 equiv.), 2-pyridone (1.0 equiv.) MeCN (v/ml), under air at 120 °C for 12 h. ′ Isolated yield, ″ Morphine (0.5 mmol).
**Table S7.** Screening of several temperatures

| entry | T (°C) | yield (%)<sup>b</sup> |
|-------|--------|------------------------|
| 1     | 140    | 10                     |
| 2     | 120    | 34                     |
| 3     | 100    | 46                     |
| 4     | 80     | 56                     |
| 5     | 60     | 43                     |

<sup>a</sup> Reactions conditions: 1a (0.1 mmol), 2a (0.5 mmol), Cul (20 mol%), \( \text{K}_2\text{CO}_3 \) (1.0 equiv.), NMO (2.0 equiv.), 2-pyridone (1.0 equiv) under air for 12 h. <sup>b</sup> Isolated yield.

**Table S8.** Screening of several times

| entry | t (h) | yield (%)<sup>b</sup> |
|-------|-------|------------------------|
| 1     | 12    | 56                     |
| 2     | 10    | 57                     |
| 3     | 8     | 59                     |
| 4     | 6     | 68                     |
| 5     | 4     | 80                     |
| 6     | 2     | 52                     |

<sup>a</sup> Reactions conditions: 1a (0.1 mmol), 2a (0.5 mmol), Cul (20 mol%), \( \text{K}_2\text{CO}_3 \) (1.0 equiv.), NMO (2.0 equiv.), 2-pyridone (1.0 equiv) under air at 80 °C. <sup>b</sup> Isolated yield.
5. General procedures for Cu-catalyzed monoselective C–H amination of ferrocenes with alkylamines

To a 10 mL Schlenk tube was added 1 (0.1 mmol), 2 (0.5 mmol), K$_2$CO$_3$ (14.0 mg, 1.0 equiv), CuI (3.8 mg, 20 mol%), NMO (23.4 mg, 2.0 equiv) and 2-pyridone (9.5 mg, 1.0 equiv), stirred at 80 °C (aluminum heat transfer block) for 4 h. After cooling to room temperature, the mixture was diluted with DCM, the resulting residue was purified by preparative TLC using Hexane/EtOAc as the eluent to afford the desired product.

1-Morpholino-2-((8-quinolinylamino)carbonyl)-1'-phenethyl-ferrocene (3b)

A purification by flash chromatography in petroleum ether : ethyl acetate = 4 : 1 to give 3b as yellow foam (33.8 mg, 62%).

$^1$H NMR (400 MHz, Chloroform-$d$) δ 12.27 (s, 1H), 9.02 (dd, $J = 7.5, 1.6$ Hz, 1H), 8.87 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.19 (dd, $J = 8.2, 1.7$ Hz, 1H), 7.59 – 7.52 (m, 2H), 7.52 – 7.45 (m, 1H), 7.11 (m $J = 4.6, 1.6$ Hz, 3H), 6.88 (dd, $J = 7.2, 2.4$ Hz, 2H), 4.88 (dd, $J = 2.8, 1.5$ Hz, 1H), 4.30 (dd, $J = 2.7, 1.6$ Hz, 1H), 4.26 (t, $J = 2.8$ Hz, 1H), 4.14 – 3.93 (m, 8H), 3.08 (s, 2H), 2.94 (m, $J = 11.6, 5.9, 3.4$ Hz, 2H), 2.65 – 2.44 (m, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 169.3, 148.1, 141.7, 139.0, 136.3, 136.3, 128.4, 128.3, 128.2, 127.7, 125.8, 121.6, 121.2, 117.6, 112.0, 90.5, 72.7, 71.4, 70.2, 70.1, 69.6, 67.8, 67.2, 66.6, 60.0, 55.5, 37.6, 29.9.

HRMS (ESI) m/z: [M + Na]$^+$ Calcd for C$_{32}$H$_{31}$FeN$_3$O$_2$Na 568.1658; found: 568.1661.
1-Morpholino-2-((8-quinolinylamino)carbonyl)-1'-isopropyl-ferrocene (3c)

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 3c as yellow foam (32.8 mg, 68%).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 12.27 (s, 1H), 9.01 (dd, $J = 7.6, 1.4$ Hz, 1H), 8.95 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.19 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.58 (t, $J = 7.9$ Hz, 1H), 7.55 – 7.46 (m, 2H), 4.87 (dd, $J = 2.8, 1.5$ Hz, 1H), 4.33 (s, 1H), 4.27 (t, $J = 2.8$ Hz, 1H), 4.16 – 4.07 (m, 4H), 4.07 – 3.99 (m, 4H), 3.03 (d, $J = 50.7$ Hz, 4H), 2.60 (m, $J = 6.8$ Hz, 1H), 1.13 (d, $J = 6.8$ Hz, 3H), 1.08 (d, $J = 6.9$ Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 169.6, 148.2, 139.1, 136.4, 136.3, 128.4, 127.7, 121.6, 121.1, 117.5, 111.8, 98.7, 72.2, 71.0, 70.0, 70.0, 68.1, 67.5, 67.4, 66.6, 60.0, 55.5, 27.2, 23.9, 23.5.

HRMS (ESI) m/z: [M + Na]$^+$ Calcd for C$_{27}$H$_{29}$FeN$_3$O$_2$Na 506.1501; found: 506.1497.

1-Morpholino-2-((8-quinolinylamino)carbonyl)-1'-pentan-3-ferrocene (3d)

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 3d as yellow foam (29.6mg, 58%).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 12.28 (s, 1H), 9.02 (dd, $J = 7.7, 1.5$ Hz, 1H), 8.95 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.19 (dd, $J = 8.2, 1.7$ Hz, 1H), 7.58 (t, $J = 7.9$ Hz, 1H), 7.55 – 7.46 (m, 2H), 4.85 (dd, $J = 2.8, 1.5$ Hz, 1H), 4.32 (dd, $J = 2.7, 1.6$ Hz, 1H), 4.23 (t, $J = 2.7$ Hz, 1H), 4.15 – 4.09 (m, 2H), 4.09 (dt, $J = 3.8, 1.3$ Hz, 3H), 4.03 (dd, $J = 6.0, 3.4$ Hz, 5H), 3.09 (s, 2H), 3.00 – 2.89 (m, 2H), 2.18 (tt, $J = 7.4, 5.2$ Hz, 1H), 1.70 – 1.56 (m, 1H), 1.56 – 1.33 (m, 3H), 0.79 (t, $J = 7.4$ Hz, 3H), 0.68 (t, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 169.6, 148.2, 139.1, 136.4, 128.4, 127.7, 121.6, 121.1, 117.5, 111.8, 97.0, 72.3, 70.8, 70.7, 69.8, 68.3, 68.0, 67.6, 66.7, 60.1, 39.9, 26.5, 26.3, 11.3, 11.0.
HRMS (ESI) m/z: [M + Na]^+ Calcd for C_{20}H_{35}FeN_{5}O_{2}Na 534.1814; found: 534.1815.

1-Morpholino-2-((8-quinolinylamino)carbonyl)-1'-2-methyl-1-ene-ferrocene (3e)
A purification by flash chromatography in petroleum ether : ethyl acetate = 4 : 1 to give 3e as yellow foam (26.5 mg, 55%).

^1^H NMR (400 MHz, Chloroform-d) δ 12.21 (s, 1H), 9.02 (dd, J = 7.6, 1.5 Hz, 1H), 8.96 (dd, J = 4.2, 1.7 Hz, 1H), 8.19 (dd, J = 8.3, 1.7 Hz, 1H), 7.58 (t, J = 7.9 Hz, 1H), 7.55 – 7.47 (m, 2H), 5.04 (s, 1H), 4.86 (dd, J = 2.8, 1.5 Hz, 1H), 4.76 – 4.71 (m, 1H), 4.45 (q, J = 1.8 Hz, 1H), 4.41 (q, J = 1.7 Hz, 1H), 4.29 (dd, J = 2.7, 1.6 Hz, 1H), 4.25 (t, J = 1.9 Hz, 2H), 4.21 (t, J = 2.7 Hz, 1H), 4.05 (m, J = 9.8, 6.1, 3.1 Hz, 4H), 3.09 (s, 2H), 2.93 (m, J = 11.7, 5.9, 3.4 Hz, 2H), 1.95 (s, 3H).

^13^C NMR (100 MHz, CDCl_3) δ 168.9, 148.1, 139.7, 139.1, 136.4, 128.4, 127.7, 121.6, 121.1, 117.5, 112.3, 110.4, 88.6, 73.0, 72.0, 71.5, 68.6, 68.5, 68.2, 67.4, 66.6, 60.5, 55.4, 52.8, 21.6.

HRMS (ESI) m/z: [M]^+ Calcd for C_{27}H_{27}FeN_{3}O_{2} 481.1453; found: 481.1449.

1-Morpholino-2-((8-quinolinylamino)carbonyl)-1'-acetyl-ferrocene (3f)
A purification by flash chromatography in petroleum ether : ethyl acetate = 4 : 1 to give 3f as yellow foam (31.9 mg, 66%).

^1^H NMR (400 MHz, Chloroform-d) δ 12.18 (s, 1H), 9.00 – 8.94 (m, 2H), 8.20 (dd, J = 8.3, 1.7 Hz, 1H), 7.61 – 7.55 (m, 2H), 7.54 – 7.49 (m, 1H), 4.97 (dd, J = 2.8, 1.6 Hz, 1H), 4.86 (dt, J = 2.7, 1.3 Hz, 1H), 4.75 (dt, J = 2.6, 1.3 Hz, 1H), 4.50 (m, J = 4.5, 2.6, 1.3 Hz, 2H), 4.35 (dd, J = 2.8, 1.6 Hz, 1H), 4.32 (t, J = 2.8 Hz, 1H), 4.02 (m, J = 14.3, 6.4, 3.1 Hz, 4H), 3.04 (s, 2H), 2.90 (m, J = 11.6, 6.1, 3.1 Hz, 2H), 2.31 (s, 3H).
$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 12.19 (s, 1H), 9.02 – 8.95 (m, 2H), 8.21 (dd, $J = 8.2, 1.7$ Hz, 1H), 7.62 – 7.55 (m, 2H), 7.52 (dd, $J = 8.2, 4.1$ Hz, 1H), 4.98 (dd, $J = 2.8, 1.5$ Hz, 1H), 4.89 (dt, $J = 2.7, 1.3$ Hz, 1H), 4.78 (dt, $J = 2.6, 1.3$ Hz, 1H), 4.48 (m, $J = 2.6, 1.2$ Hz, 1H), 4.35 (dd, $J = 2.8, 1.6$ Hz, 1H), 4.31 (t, $J = 2.8$ Hz, 1H), 4.10 – 3.92 (m, 4H), 3.06 (s, 2H), 2.90 (m, $J = 11.6, 6.2, 3.0$ Hz, 2H), 2.70 – 2.50 (m, 2H), 1.64 – 1.49 (m, 2H), 0.84 (t, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 204.1, 168.2, 148.4, 139.0, 136.5, 135.9, 128.4, 127.7, 121.8, 121.6, 117.7, 113.4, 80.7, 75.5, 74.9, 73.0, 71.5, 71.3, 68.7, 67.9, 66.6, 61.0, 55.2, 42.0, 17.8, 13.9.

HRMS (ESI) m/z: [M + Na]$^+$ Caled for C$_{36}$H$_{35}$FeN$_3$O$_3$Na 534.1450; found: 534.1455.

1-Morpholino-2-((8-quinolinylamino)carbonyl)-1’-valeryl-ferrocene (3h)

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 3h as yellow foam (27.8mg, 53%).

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 12.18 (s, 1H), 9.01 – 8.95 (m, 2H), 8.21 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.62 – 7.55 (m, 2H), 7.52 (dd, $J = 8.2, 4.1$ Hz, 1H), 4.98 (dd, $J = 2.8, 1.6$ Hz, 1H), 4.88 (dt, $J = 2.7, 1.4$ Hz, 1H), 4.78 (dt, $J = 2.6, 1.3$ Hz, 1H), 4.48 (pd, $J = 2.5, 1.3$ Hz, 2H), 4.34 (dd, $J = 2.8,$
1.6 Hz, 1H), 4.30 (t, \(J = 2.8\) Hz, 1H), 4.03 (m, \(J = 16.8, 8.1, 5.0\) Hz, 4H), 3.06 (s, 2H), 2.90 (m, \(J = 11.5, 6.2, 3.0\) Hz, 2H), 2.70 – 2.52 (m, 2H), 1.62 – 1.42 (m, 2H), 1.28 – 1.13 (m, 2H), 0.84 (t, \(J = 7.3\) Hz, 3H).

\(\text{\textsuperscript{13}C NMR (100 MHz, CDCl}\textsubscript{3})\) \(\delta\) 204.3, 168.2, 148.4, 139.0, 136.5, 135.9, 128.4, 127.7, 121.8, 121.6, 117.7, 113.4, 80.7, 75.5, 74.9, 73.0, 71.6, 71.3, 68.7, 67.8, 66.6, 61.0, 55.2, 39.9, 26.6, 22.5, 14.0.

HRMS (ESI) \(m/z: [M + Na]^+\) Calcd for C\(_{29}\)H\(_{31}\)FeN\(_3\)O\(_3\)Na 548.1607; found: 548.1608.

1-Morpholino-2-((8-quinolinylamino)carbonyl)-1’-2-methyl-1-butyryl-ferrocene (3i)

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 3i as yellow foam (24.2 mg, 46%).

\(\text{\textsuperscript{1}H NMR (400 MHz, Chloroform-\textsubscript{d})}\) \(\delta\) 12.19 (s, 1H), 9.03 – 8.91 (m, 2H), 8.21 (dd, \(J = 8.3, 1.7\) Hz, 1H), 7.62 – 7.55 (m, 2H), 7.52 (dd, \(J = 8.3, 4.2\) Hz, 1H), 4.98 (dd, \(J = 2.8, 1.6\) Hz, 1H), 4.89 (dt, \(J = 2.6, 1.4\) Hz, 1H), 4.76 (dt, \(J = 2.7, 1.4\) Hz, 1H), 4.47 (dt, \(J = 2.6, 1.3\) Hz, 2H), 4.34 (dd, \(J = 2.8, 1.6\) Hz, 1H), 4.31 (t, \(J = 2.8\) Hz, 1H), 4.10 – 3.92 (m, 4H), 3.06 (s, 2H), 2.90 (m \(J = 11.6, 6.2, 3.0\) Hz, 2H), 2.58 – 2.41 (m, 2H), 2.13 (dt, \(J = 13.5, 6.7\) Hz, 1H), 0.90 (d, \(J = 6.6\) Hz, 3H), 0.84 (d, \(J = 6.7\) Hz, 3H).

\(\text{\textsuperscript{13}C NMR (100 MHz, CDCl}\textsubscript{3})\) \(\delta\) 203.9, 168.2, 148.4, 139.0, 136.5, 135.9, 128.4, 127.7, 121.8, 121.6, 117.6, 113.4, 80.9, 75.8, 75.0, 73.0, 71.5, 71.4, 68.6, 67.9, 66.6, 61.0, 55.1, 49.0, 25.2, 22.8.

HRMS (ESI) \(m/z: [M + Na]^+\) Calcd for C\(_{29}\)H\(_{31}\)FeN\(_3\)O\(_3\)Na 548.1607; found: 548.1609.

1-Morpholino-2-((8-quinolinylamino)carbonyl)-1’-2,2-dimethyl-1-propionyl-ferrocene (3j)

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 3j as yellow
foam (33.6 mg, 64%).

\[^1\text{H NMR (400 MHz, Chloroform-} \text{d}) \delta 12.20 (s, 1H), 8.99 – 8.91 (m, 2H), 8.20 (dd, J = 8.2, 1.7 Hz, 1H), 7.61 – 7.54 (m, 2H), 7.52 (dd, J = 8.3, 4.2 Hz, 1H), 5.02 (dt, J = 2.7, 1.4 Hz, 1H), 4.99 (dd, J = 2.9, 1.5 Hz, 1H), 4.84 (dt, J = 2.6, 1.3 Hz, 1H), 4.42 (m, J = 3.8, 2.6, 1.4 Hz, 2H), 4.32 (dd, J = 2.7, 1.6 Hz, 1H), 4.27 (t, J = 2.8 Hz, 1H), 4.07 – 3.93 (m, 4H), 3.11 (s, 2H), 2.91 (m, J = 11.6, 6.0, 3.2 Hz, 2H), 1.29 (s, 9H).

\[^{13}\text{C NMR (100 MHz, CDCl}_3\text{)} \delta 209.8, 168.4, 148.4, 139.0, 136.5, 135.9, 128.4, 127.7, 121.8, 121.5, 117.6, 113.4, 77.7, 75.3, 75.3, 73.9, 72.6, 71.9, 68.8, 68.5, 66.6, 61.4, 55.1.

HRMS (ESI) m/z: [M + Na]^+ Calcd for C\textsubscript{29}H\textsubscript{31}FeN\textsubscript{3}O\textsubscript{3}Na 548.1607; found: 548.1606.

1-Morpholino-2-((8-quinolinylamino)carbonyl)-1’-(o-tolyl)acetyl-ferrocene (3k)

A purification by flash chromatography in petroleum ether : ethyl acetate = 4 : 1 to give 3k as yellow foam (33.5 mg, 60%).

\[^1\text{H NMR (400 MHz, Chloroform-} \text{d}) \delta 12.18 (s, 1H), 8.95 (dd, J = 4.2, 1.7 Hz, 1H), 8.93 (dd, J = 7.2, 1.9 Hz, 1H), 8.21 (dd, J = 8.3, 1.7 Hz, 1H), 7.61 – 7.55 (m, 2H), 7.54 – 7.48 (m, 2H), 7.36 (td, J = 7.5, 1.5 Hz, 1H), 7.27 (s, 1H), 7.25 – 7.20 (m, 1H), 5.00 (dq, J = 2.5, 1.4 Hz, 2H), 4.73 (dt, J = 2.6, 1.3 Hz, 1H), 4.54 (td, J = 2.6, 1.3 Hz, 1H), 4.47 (dt, J = 2.5, 1.2 Hz, 1H), 4.43 – 4.38 (m, 2H), 3.97 (dt, J = 6.2, 2.9 Hz, 4H), 3.06 (d, J = 8.0 Hz, 2H), 2.89 (dt, J = 11.6, 4.5 Hz, 2H), 2.40 (s, 3H).

\[^{13}\text{C NMR (100 MHz, CDCl}_3\text{)} \delta 201.4, 168.1, 148.4, 139.5, 139.0, 136.5, 136.2, 135.8, 131.3, 130.3, 128.4, 127.8, 127.7, 125.2, 121.8, 121.6, 117.7, 113.7, 80.3, 77.5, 75.8, 73.3, 73.0, 72.8, 68.7, 68.4, 66.5, 61.4, 55.1, 20.1.

HRMS (ESI) m/z: [M + Na]^+ Calcd for C\textsubscript{32}H\textsubscript{29}FeN\textsubscript{3}O\textsubscript{3}Na 582.1450; found: 582.1452.
1-Morpholino-2-((8-quinolinylamino)carbonyl)-1’-p-chlorophenylacetyl-ferrocene (3l)

A purification by flash chromatography in petroleum ether: ethyl acetate = 4:1 to give 3l as yellow foam (26.1 mg, 45%)

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 12.11 (s, 1H), 8.93 (dd, $J = 4.2$, 1.7 Hz, 1H), 8.89 (dd, $J = 7.0$, 2.1 Hz, 1H), 8.21 (dd, $J = 8.2$, 1.7 Hz, 1H), 7.73 (d, $J = 8.5$ Hz, 2H), 7.62 – 7.55 (m, 2H), 7.52 (dd, $J = 8.2$, 4.2 Hz, 1H), 7.28 (d, $J = 8.5$ Hz, 2H), 5.08 (dt, $J = 2.5$, 1.3 Hz, 1H), 4.99 (dd, $J = 2.7$, 1.7 Hz, 1H), 4.89 (dt, $J = 2.7$, 1.3 Hz, 1H), 4.59 (td, $J = 2.5$, 1.3 Hz, 1H), 4.56 (td, $J = 2.6$, 1.2 Hz, 1H), 4.31 (p, $J = 2.7$ Hz, 2H), 4.03 – 3.90 (m, 4H), 3.04 (s, 2H), 2.88 (dd, $J = 11.5$, 5.9, 3.4 Hz, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 196.8, 167.8, 148.3, 139.0, 138.2, 137.5, 136.5, 135.8, 129.8, 128.6, 128.4, 127.7, 121.8, 121.7, 117.7, 113.8, 79.3, 76.3, 75.7, 73.5, 73.4, 73.2, 69.0, 68.7, 66.5, 61.6, 55.0.

HRMS (ESI) m/z: [M + Na]$^+$ Calcd for C$_{31}$H$_{26}$ClFeN$_3$O$_3$Na 602.0904; found: 602.0908.

1-Morpholino-2-((8-quinolinylamino)carbonyl)-1’-methanol-ferrocene (3m)

A purification by flash chromatography in petroleum ether: ethyl acetate = 4:1 to give 3m as yellow foam (34.4 mg, 73%)

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 12.28 (s, 1H), 9.02 (d, $J = 7.3$ Hz, 1H), 8.95 (d, $J = 4.2$ Hz, 1H), 8.21 (d, $J = 8.2$ Hz, 1H), 7.62 – 7.48 (m, 3H), 4.99 (d, $J = 2.6$ Hz, 1H), 4.39 (d, $J = 13.4$ Hz, 3H), 4.30 – 4.24 (m, 2H), 4.21 (d, $J = 5.6$ Hz, 2H), 4.17 (d, $J = 3.2$ Hz, 1H), 4.14 – 3.96 (m, 5H), 3.11 (t, $J = 8.8$ Hz, 2H), 3.01 – 2.92 (m, 2H).
$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 12.30 (s, 1H), 9.00 (dd, $J = 7.7$, 1.5 Hz, 1H), 8.89 (dd, $J = 4.2$, 1.7 Hz, 1H), 8.19 (dd, $J = 8.3$, 1.8 Hz, 1H), 7.59 (t, $J = 7.9$ Hz, 1H), 7.56 – 7.46 (m, 2H), 4.94 (t, $J = 2.2$ Hz, 1H), 4.46 (m, $J = 12.7$, 6.4, 2.2 Hz, 1H), 4.31 (d, $J = 2.8$ Hz, 2H), 4.21 (s, 5H), 4.03 (m, $J = 11.1$, 1.9 Hz, 1H), 2.89 (dt, $J = 11.5$, 2.0 Hz, 1H), 2.59 – 2.49 (m, 1H), 2.19 – 2.09 (m, 1H), 1.41 (d, $J = 6.3$ Hz, 3H), 0.99 (d, $J = 6.3$ Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 169.6, 148.2, 139.2, 136.4, 136.3, 128.4, 127.7, 121.6, 121.2, 117.6, 111.9, 72.1, 71.2, 70.8, 67.1, 66.6, 63.7, 59.8, 58.4, 19.6, 19.0.

HRMS (ESI) m/z: [M]$^+$ Calcd for C$_{25}$H$_{25}$FeN$_3$O$_3$Na 494.1143; found: 494.1136.

1-(2,6-Dimethylmorpholino)-2-((8-quinolinylamino)carbonyl)ferrocene (4a)

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 4a as yellow foam (25.3mg, 54%).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 11.59 (s, 1H), 8.94 – 8.88 (m, 2H), 8.20 (dd, $J = 8.3$, 1.7 Hz, 1H), 7.62 – 7.52 (m, 2H), 7.48 (dd, $J = 8.3$, 4.2 Hz, 1H), 4.90 (dd, $J = 2.8$, 1.6 Hz, 1H), 4.32 – 4.27 (m, 2H), 4.23 (s, 5H), 4.09 (m, $J = 11.1$, 7.5, 3.0 Hz, 1H), 3.95 – 3.79 (m, 1H), 3.03 – 2.80 (m, 3H), 2.64 (d, $J = 11.2$ Hz, 1H), 1.60 (s, 3H), 1.26 (s, 3H).

HRMS (ESI) m/z: [M]$^+$ Calcd for C$_{26}$H$_{27}$FeN$_3$O$_2$ 469.1453; found: 469.1448.

1-(2,2-Dimethylmorpholino)-2-((8-quinolinylamino)carbonyl)ferrocene (4b)

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 4b as yellow foam (12.2 mg, 26%).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 11.59 (s, 1H), 8.94 – 8.88 (m, 2H), 8.20 (dd, $J = 8.3$, 1.7 Hz, 1H), 7.62 – 7.52 (m, 2H), 7.48 (dd, $J = 8.3$, 4.2 Hz, 1H), 4.90 (dd, $J = 2.8$, 1.6 Hz, 1H), 4.32 – 4.27 (m, 2H), 4.23 (s, 5H), 4.09 (m, $J = 11.1$, 7.5, 3.0 Hz, 1H), 3.95 – 3.79 (m, 1H), 3.03 – 2.80 (m, 3H), 2.64 (d, $J = 11.2$ Hz, 1H), 1.60 (s, 3H), 1.26 (s, 3H).
$^{13}$C NMR (100 MHz, CDCl₃)  δ 169.6, 148.1, 139.3, 136.5, 135.6, 128.4, 127.6, 121.6, 121.5, 118.3, 112.6, 72.2, 71.5, 70.8, 67.3, 66.3, 63.9, 61.6, 59.3, 56.0, 26.2, 24.8.

HRMS (ESI) m/z: [M]$^+$ Calcd for C₂₆H₂₇FeN₃O₂ 469.1453; found: 469.1450.

1-(4-tert-Butoxycarbonyl piperazino)-2-((8-quinolinylamino)carbonyl)ferrocene (4c)

A purification by flash chromatography in petroleum ether : ethyl acetate = 4 : 1 to give 4c as yellow foam (24.3 mg, 45%).

$^1$H NMR (400 MHz, Chloroform-d)  δ 12.31 (s, 1H), 9.00 (dd, J = 7.6, 1.4 Hz, 1H), 8.86 (dd, J = 4.2, 1.6 Hz, 1H), 8.19 (dd, J = 8.3, 1.7 Hz, 1H), 7.58 (t, J = 7.9 Hz, 1H), 7.55 – 7.45 (m, 2H), 4.94 (dd, J = 2.6, 1.6 Hz, 1H), 4.31 (d, J = 2.4 Hz, 2H), 4.22 (s, 5H), 3.75 (s, 4H), 2.88 (dt, J = 10.8, 5.0 Hz, 4H), 1.47 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl₃)  δ 169.6, 155.0, 148.1, 139.1, 136.5, 136.3, 128.5, 127.8, 121.7, 121.2, 117.5, 112.1, 80.0, 72.2, 70.9, 67.0, 66.6, 59.9, 54.8, 28.6.

HRMS (ESI) m/z: [M + Na]$^+$ Calcd for C₂₉H₃₂FeN₄O₃Na 563.1716; found: 563.1719.

1-Piperidino-2-((8-quinolinylamino)carbonyl)ferrocene (4d)

A purification by flash chromatography in petroleum ether: tetrahydrofuran = 12 : 1 to give 4d as yellow foam (37.3 mg, 85%).

$^1$H NMR (400 MHz, Chloroform-d)  δ 12.44 (s, 1H), 9.00 (d, J = 7.6 Hz, 1H), 8.91 (d, J = 3.2 Hz, 1H), 8.18 (d, J = 8.2 Hz, 1H), 7.58 (t, J = 7.9 Hz, 1H), 7.54 – 7.45 (m, 2H), 4.89 (s, 1H), 4.33 – 4.25 (m, 2H), 4.20 (s, 5H), 3.06 (s, 2H), 2.85 (m, J = 11.2, 5.4 Hz, 2H), 1.87 (t, J = 5.9 Hz, 4H), 1.58 (s, 2H).

$^{13}$C NMR (101 MHz, CDCl₃)  δ 170.0, 147.9, 139.4, 136.8, 136.2, 128.4, 127.7, 121.6, 121.0, 117.5, 113.9, 72.3, 70.8, 66.6, 66.2, 59.3, 56.6, 25.8, 24.6.
HRMS (ESI) m/z: [M + H]^+ Calcd for C_{25}H_{26}FeN_{3}O 440.1347; found: 440.1422.

1-(4-Phenylpiperidino)-2-((8-quinolinylamino)carbonyl)ferrocene (4e)

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 4e as yellow foam (30.9 mg, 60%).

$^1$H NMR (400 MHz, Chloroform-d) δ 12.43 (s, 1H), 8.99 (dd, $J = 7.6$, 1.4 Hz, 1H), 8.90 (dd, $J = 4.2$, 1.7 Hz, 1H), 8.21 (dd, $J = 8.3$, 1.7 Hz, 1H), 7.60 (t, $J = 7.9$ Hz, 1H), 7.53 (dd, $J = 8.2$, 1.4 Hz, 1H), 7.47 (dd, $J = 8.2$, 4.2 Hz, 1H), 7.28 (s, 2H), 7.24 (s, 1H), 7.20 (d, $J = 7.2$ Hz, 1H), 7.12 (d, $J = 6.9$ Hz, 2H), 4.91 (dd, $J = 2.8$, 1.6 Hz, 1H), 4.35 (dd, $J = 2.7$, 1.6 Hz, 1H), 4.30 (t, $J = 2.7$ Hz, 1H), 4.23 (s, 5H), 3.94 (d, $J = 11.4$ Hz, 1H), 3.20 (d, $J = 11.8$ Hz, 1H), 2.88 (t, $J = 11.4$ Hz, 1H), 2.70 – 2.59 (m, 1H), 2.52 (m, $J = 11.8$, 7.6, 3.1 Hz, 2H), 2.14 (d, $J = 12.3$ Hz, 1H), 2.07 – 1.94 (m, 1H), 1.65 (d, $J = 12.7$ Hz, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 169.9, 148.4, 146.3, 139.4, 136.4, 128.5, 128.5, 127.7, 127.0, 126.3, 121.4, 121.1, 117.6, 113.3, 72.4, 70.9, 66.6, 66.2, 59.2, 59.1, 53.3, 42.6, 33.6, 32.7.

HRMS (ESI) m/z: [M]^+ Calcd for C_{31}H_{29}FeN_{3}O 515.1660; found: 515.1656.

1-(4-Methoxycarbonylpiperidino)-2-((8-quinolinylamino)carbonyl)ferrocene (4f)

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 4f as yellow foam (28.3 mg, 57%).

$^1$H NMR (400 MHz, Chloroform-d) δ 12.32 (s, 1H), 9.03 (dd, $J = 7.7$, 1.5 Hz, 1H), 9.00 (dd, $J = 4.3$, 1.7 Hz, 1H), 8.17 (dd, $J = 8.2$, 1.8 Hz, 1H), 7.57 (t, $J = 7.9$ Hz, 1H), 7.53 – 7.47 (m, 2H), 4.92 (dd, $J = 2.6$, 1.7 Hz, 1H), 4.31 – 4.27 (m, 2H), 4.20 (s, 5H), 3.76 (d, $J = 11.3$ Hz, 1H), 3.69 (s, 3H), 3.11 (dt, $J = 11.3$, 3.7 Hz, 1H), 2.74 (td, $J = 11.2$, 2.6 Hz, 1H), 2.57 – 2.39 (m, 3H), 2.18 (m, $J = 15.2$, 7.3, 4.0 Hz, 2H), 1.81 (d, $J = 12.9$ Hz, 1H).
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 175.8, 169.8, 148.5, 139.2, 136.5, 136.2, 128.4, 127.6, 121.6, 121.1, 117.4, 112.8, 72.2, 70.9, 66.9, 66.4, 59.5, 57.4, 52.7, 51.8, 41.3, 28.4, 28.0.

HRMS (ESI) m/z: \([M]^+\) Calcd for C\(_{27}\)H\(_{27}\)FeN\(_3\)O\(_3\) 497.1402; found: 497.1398.

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 4g as yellow foam (28.3mg, 61%).

\(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 12.18 (s, 1H), 9.04 (dd, \(J = 7.6, 1.5\) Hz, 1H), 8.94 (dd, \(J = 4.3, 1.7\) Hz, 1H), 8.21 (dd, \(J = 8.2, 1.7\) Hz, 1H), 7.59 (t, \(J = 7.9\) Hz, 1H), 7.57 – 7.48 (m, 2H), 4.94 (dd, \(J = 2.7, 1.6\) Hz, 1H), 4.31 (p, \(J = 2.7\) Hz, 2H), 4.21 (s, 5H), 3.49 (s, 1H), 3.00 – 2.67 (m, 3H), 2.34 (q, \(J = 8.7, 3.6\) Hz, 3H), 2.16 (s, 1H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 169.6, 148.0, 139.0, 136.6, 136.3, 128.5, 127.8, 122.0, 121.8, 121.3, 117.6, 112.1, 72.2, 70.9, 67.1, 66.6, 59.8, 28.8, 28.6, 26.4.

HRMS (ESI) m/z: \([M]^+\) Calcd for C\(_{26}\)H\(_{24}\)FeN\(_4\)O\(_4\) 464.1300; found: 464.1292.

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 4h as yellow foam (26.3mg, 56%).

\(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 12.42 (s, 1H), 9.03 (dd, \(J = 7.6, 1.4\) Hz, 1H), 8.94 (dd, \(J = 4.2, 1.7\) Hz, 1H), 8.17 (dd, \(J = 8.3, 1.7\) Hz, 1H), 7.57 (t, \(J = 7.9\) Hz, 1H), 7.54 – 7.44 (m, 2H), 4.92 (dd, \(J = 2.8, 1.6\) Hz, 1H), 4.31 (dd, \(J = 2.7, 1.5\) Hz, 1H), 4.28 (t, \(J = 2.7\) Hz, 1H), 4.20 (s, 5H), 3.37 (s, 5H), 3.09 (dt, \(J = 10.1, 4.3\) Hz, 1H), 2.76 (m, \(J = 11.7, 8.8, 3.4\) Hz, 2H), 2.21 – 2.00 (m, 4H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 169.9, 148.1, 139.2, 136.5, 136.2, 128.4, 127.6, 121.7, 121.1, 117.5, 112.8, 72.2, 70.8, 66.7, 66.4, 59.6, 55.8, 52.3, 30.7, 30.6.

1-(4-Cyanopiperidin-1-yl)-2-((8-quinolinylamino)carbonyl)ferrocene (4g)

1-(4-Methoxypiperidino)-2-((8-quinolinylamino)carbonyl)ferrocene (4h)
HRMS (ESI) m/z: [M]⁺ Calcd for C_{26}H_{27}FeN_{3}O_{4} 469.1453; found: 469.1449.

1-(1,4-Dioxaa-8-azaspiro[4.5]decane)-2-((8-quinolinylamino)carbonyl)ferrocene (4i)

A purification by flash chromatography in petroleum ether : ethyl acetate = 4 : 1 to give 4i as yellow foam (31.3 mg, 63%).

$^1$H NMR (400 MHz, Chloroform-d) δ 12.45 (s, 1H), 9.06 (dd, $J = 7.7$, 1.5 Hz, 1H), 8.98 (dd, $J = 4.2$, 1.7 Hz, 1H), 8.17 (dd, $J = 8.3$, 1.7 Hz, 1H), 7.57 (t, $J = 7.9$ Hz, 1H), 7.53 – 7.47 (m, 2H), 4.93 (dd, $J = 2.9$, 1.5 Hz, 1H), 4.34 (t, $J = 2.1$ Hz, 1H), 4.29 (t, $J = 2.7$ Hz, 1H), 4.20 (s, 5H), 4.00 (s, 4H), 3.21 (s, 2H), 3.02 (dt, $J = 11.3$, 5.5 Hz, 2H), 2.23 – 1.98 (m, 4H).

$^{13}$C NMR (100 MHz, CDCl₃) δ 169.9, 148.1, 139.2, 136.6, 136.3, 128.4, 127.7, 121.8, 121.1, 117.4, 112.4, 107.5, 72.1, 70.9, 66.8, 66.5, 64.5, 60.0, 53.7, 34.9.

HRMS (ESI) m/z: [M]⁺ Calcd for C_{27}H_{27}FeN_{3}O_{4} 497.1402; found: 497.1394.

1-(4,4-Difluoropiperidino)-2-((8-quinolinylamino)carbonyl)ferrocene (4j)

A purification by flash chromatography in petroleum ether : ethyl acetate = 4 : 1 to give 4j as yellow foam (10.9 mg, 23%).

$^1$H NMR (400 MHz, Chloroform-d) δ 12.27 (s, 1H), 9.08 (dd, $J = 7.7$, 1.5 Hz, 1H), 8.87 (dd, $J = 4.3$, 1.7 Hz, 1H), 8.20 (dd, $J = 8.2$, 1.7 Hz, 1H), 7.59 (t, $J = 7.9$ Hz, 1H), 7.56 – 7.47 (m, 2H), 4.96 (t, $J = 2.2$ Hz, 1H), 4.33 (d, $J = 2.2$ Hz, 2H), 4.21 (s, 5H), 3.26 (s, 2H), 3.04 (m, $J = 11.7$, 7.0, 4.4 Hz, 2H), 2.58 – 2.24 (m, 4H).

$^{13}$C NMR (100 MHz, CDCl₃) δ 169.6, 147.8, 139.0, 136.0, 136.3, 128.5, 127.8, 121.8, 121.3, 117.6, 111.4, 72.2, 70.9, 67.1, 66.7, 60.1, 34.4, 34.2, 33.9.

HRMS (ESI) m/z: [M + Na]⁺ Calcd for C_{25}H_{25}F₂FeN_{3}O_{4}Na 498.1051; found: 498.1054.
1-(1,2,3,4-Tetrahydroquinolino)-2-((8-quinolylamino)carbonyl)ferrocene (4k)

A purification by flash chromatography in petroleum ether : tetrahydrofuran = 12 : 1 to give 4k as yellow foam (2.4 mg, trace).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 11.35 (s, 1H), 8.84 (dd, $J = 7.7, 1.4$ Hz, 1H), 8.68 (dd, $J = 8.3, 1.4$ Hz, 1H), 7.70 (t, $J = 7.9$ Hz, 1H), 7.43 (dd, $J = 8.3, 1.4$ Hz, 1H), 7.39 (dd, $J = 8.3, 4.2$ Hz, 1H), 6.98 – 6.91 (m, 1H), 6.79 (t, $J = 7.8$ Hz, 1H), 6.58 (t, $J = 7.3$ Hz, 1H), 6.36 (d, $J = 8.3$ Hz, 1H), 5.11 (dd, $J = 2.9, 1.6$ Hz, 1H), 4.53 – 4.44 (m, 2H), 4.34 (s, 5H), 4.31 (dd, $J = 2.7, 1.6$ Hz, 1H), 3.76 (td, $J = 10.6, 3.1$ Hz, 1H), 2.98 (m, $J = 11.4, 5.6$ Hz, 2H), 2.85 (m, $J = 11.0, 10.0, 5.3$ Hz, 1H), 2.21 (d, $J = 5.4$ Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.1, 147.7, 139.3, 138.5, 136.2, 135.0, 131.9, 128.6, 128.2, 127.6, 126.7, 124.6, 121.5, 121.4, 121.2, 119.1, 117.3, 115.0, 74.8, 71.2, 67.6, 67.0, 65.2, 53.6, 27.8, 22.8.

HRMS (ESI) m/z: [M + H]$^+$ Calcd for C$_{29}$H$_{26}$FeN$_3$O 488.1347; found: 488.1415.

1-Thiomorpholinolino-2-((8-quinolylamino)carbonyl)ferrocene (4l)

A purification by flash chromatography in petroleum ether : ethyl acetate = 4 : 1 to give 4l as yellow foam (13.3 mg, 29%).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 12.29 (s, 1H), 9.10 – 8.99 (m, 2H), 8.21 (dd, $J = 8.2, 1.7$ Hz, 1H), 7.59 (t, $J = 7.9$ Hz, 1H), 7.55 – 7.49 (m, 2H), 4.94 (dd, $J = 2.8, 1.6$ Hz, 1H), 4.32 (t, $J = 2.8$ Hz, 1H), 4.29 (dd, $J = 2.8, 1.6$ Hz, 1H), 4.20 (s, 5H), 3.46 (s, 2H), 3.12 (m, $J = 21.0, 10$ Hz, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 169.6, 148.1, 139.0, 136.5, 136.4, 128.5, 127.8, 121.8, 121.2, 117.5, 113.6, 72.1, 70.9, 66.9, 66.7, 60.3, 57.5, 27.6.

HRMS (ESI) m/z: [M + Na]$^+$ Calcd for C$_{24}$H$_{23}$FeN$_3$OSNa 480.0803; found: 480.0804.
1-(4,4-Dioxothiomorpholino)-2-((8-quinolinylamino)carbonyl)ferrocene (4m)

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 4m as yellow foam (32.8 mg, 67%).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 12.02 (s, 1H), 9.12 (dd, $J = 7.5$, 1.6 Hz, 1H), 9.06 (dd, $J = 4.3$, 1.7 Hz, 1H), 8.24 (dd, $J = 8.3$, 1.7 Hz, 1H), 7.61 (t, $J = 7.8$ Hz, 2H), 7.59 – 7.51 (m, 2H), 5.02 (dd, $J = 2.9$, 1.5 Hz, 1H), 4.39 (t, $J = 2.8$ Hz, 1H), 4.35 (dd, $J = 2.7$, 1.5 Hz, 1H), 4.23 (s, 5H), 3.73 (s, 4H), 3.46 (d, $J = 9.4$ Hz, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 169.0, 148.4, 138.8, 137.1, 136.0, 128.6, 127.9, 122.1, 121.7, 117.8, 110.8, 72.0, 71.1, 67.6, 67.2, 61.0, 53.8, 51.9.

HRMS (ESI) m/z: [M + Na]$^+$ Calcd for C$_{24}$H$_{23}$FeN$_3$O$_3$SNa 512.0702; found: 512.0700.

1-(N-Methylphenyl)-2-((8-quinolinylamino)carbonyl)ferrocene (4n)

A purification by flash chromatography in petroleum ether : tetrahydrofuran= 12 : 1 to give 4n as yellow foam (8.3 mg, 18%).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 11.69 (s, 1H), 8.82 – 8.76 (m, 2H), 8.10 (dd, $J = 8.2$, 1.7 Hz, 1H), 7.49 (t, $J = 7.9$ Hz, 1H), 7.45 – 7.39 (m, 2H), 7.06 (dd, $J = 8.8$, 7.2 Hz, 2H), 6.78 (d, $J = 7.8$ Hz, 2H), 6.69 (t, $J = 7.3$ Hz, 1H), 5.09 (dd, $J = 2.9$, 1.5 Hz, 1H), 4.51 (t, $J = 2.8$ Hz, 1H), 4.35 (s, 6H), 3.88 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.6, 150.9, 148.1, 139.1, 136.1, 135.7, 128.6, 128.1, 127.6, 121.5, 120.9, 119.5, 116.6, 116.3, 107.3, 74.1, 71.2, 67.3, 67.1, 65.4, 44.1.

HRMS (ESI) m/z: [M + Na]$^+$ Calcd for C$_{27}$H$_{23}$FeN$_3$ONa 484.1083; found: 484.1086.
1-(N-Benzylmethyl)-2-((8-quinolinylamino)carbonyl)ferrocene (4o)

A purification by flash chromatography in petroleum ether : tetrahydrofuran = 12 : 1 to give 4o as yellow foam (7.1 mg, 15%).

$^1$H NMR (400 MHz, Chloroform-d) δ 12.27 (s, 1H), 8.93 (d, J = 7.6 Hz, 1H), 8.59 (dd, J = 4.2, 1.7 Hz, 1H), 8.16 (dd, J = 8.2, 1.7 Hz, 1H), 7.58 (t, J = 7.9 Hz, 1H), 7.52 (d, J = 8.2 Hz, 1H), 7.45 – 7.38 (m, 3H), 7.26 – 7.19 (m, 3H), 4.95 (s, 1H), 4.49 (d, J = 13.1 Hz, 1H), 4.32 (s, 1H), 4.26 (s, 6H), 3.85 (d, J = 13.1 Hz, 1H), 2.71 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl₃) δ 169.7, 148.9, 148.3, 139.5, 137.2, 136.1, 129.9, 128.3, 128.2, 127.6, 127.4, 121.4, 121.2, 117.7, 113.3, 72.5, 70.9, 66.9, 66.3, 62.9, 60.5, 43.9.

HRMS (ESI) m/z: [M]$^+$ Calcd for C₂₅H₂₅FeN₃O 475.1347; found: 475.1340.

1-(4-(4-Chlorophenyl)-4-hydroxypiperidin-1-yl)-2-((8-quinolinylamino)carbonyl)ferrocene (4p)

A purification by flash chromatography in petroleum ether : ethyl acetate = 4 : 1 to give 4p as yellow foam (35.6 mg, 63%).

$^1$H NMR (400 MHz, Chloroform-d) δ 12.41 (s, 1H), 8.96 (d, J = 7.5 Hz, 1H), 8.71 (d, J = 2.6 Hz, 1H), 8.21 (d, J = 8.3 Hz, 1H), 7.59 (t, J = 7.9 Hz, 1H), 7.53 (d, J = 8.2 Hz, 1H), 7.43 (dd, J = 8.2, 4.2 Hz, 1H), 7.28 (d, J = 8.7 Hz, 3H), 7.23 (d, J = 8.6 Hz, 3H), 4.89 (s, 1H), 4.38 (s, 1H), 4.30 (t, J = 2.7 Hz, 1H), 4.21 (s, 5H), 3.68 (d, J = 10.7 Hz, 1H), 3.31 – 3.20 (t, 1H), 2.99 – 2.86 (m, 2H), 2.71 (m, J = 12.7, 4.4 Hz, 1H), 2.41 – 2.29 (m, 1H), 2.13 – 2.02 (m, 1H), 1.88 (s, 1H), 1.60 (d, J = 13.5 Hz, 1H).

$^{13}$C NMR (100 MHz, CDCl₃) δ 170.0, 148.2, 147.0, 139.4, 136.4, 136.6, 136.3, 133.0, 128.6, 128.4, 127.8,
HRMS (ESI) m/z: [M]⁺ Caled for C₃₁H₂₈ClFeN₃O₂ 565.1219; found: 565.1215.

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 4q as yellow foam (31.1 mg, 60%).

1H NMR (400 MHz, Chloroform-d) δ 12.43 (s, 1H), 9.02 (d, J = 7.7 Hz, 1H), 8.82 (d, J = 2.5 Hz, 1H), 8.32 (d, J = 4.7 Hz, 2H), 8.16 (d, J = 6.6 Hz, 1H), 7.59 (t, J = 7.9 Hz, 1H), 7.51 (d, J = 6.8 Hz, 1H), 7.42 (dd, J = 8.3, 4.2 Hz, 1H), 6.50 (t, J = 4.8 Hz, 1H), 4.95 (s, 1H), 4.31 (s, 2H), 4.24 (s, 5H), 4.19 m, J = 6.3, 3.3 Hz, 4H), 3.17 (m, J = 10.7, 5.0 Hz, 2H), 2.99 (m, J = 10.8, 4.9 Hz, 2H).

13C NMR (100 MHz, CDCl₃) δ 169.7, 161.8, 157.9, 148.1, 139.2, 136.4, 128.5, 127.8, 121.7, 121.2, 117.6, 112.2, 110.0, 100.9, 72.3, 70.9, 67.1, 66.6, 59.9, 55.0, 43.6.

HRMS (ESI) m/z: [M + Na]⁺ Caled for C₂₈H₂₆FeN₆ONa 541.1410; found: 541.1412.

A purification by flash chromatography in petroleum ether : ethyl acetate= 4 : 1 to give 4r as yellow foam (40.1 mg, 70%).

1H NMR (400 MHz, Chloroform-d) δ 12.40 (s, 1H), 9.02 (d, J = 6.3 Hz, 1H), 8.96 (d, J = 2.6 Hz, 1H), 8.15 (d, J = 8.2 Hz, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.57 (t, J = 7.9 Hz,
1H), 7.54 – 7.41 (m, 3H), 7.35 (t, J = 7.5 Hz, 1H), 4.98 (s, 1H), 4.41 (s, 1H), 4.35 (t, J = 2.8 Hz, 1H), 4.25 (s, 5H), 3.93 (t, J = 5.0 Hz, 4H), 3.41 – 3.32 (m, 2H), 3.24 – 3.14 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl₃) δ 169.7, 164.2, 152.9, 148.6, 139.1, 136.4, 136.3, 127.7, 127.7, 124.1, 124.0, 121.8, 121.2, 120.7, 117.5, 112.1, 72.3, 70.9, 67.1, 66.6, 60.0, 55.0, 49.9.

HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{31}H_{27}$FeN₅OSNa 596.1178; found: 596.1181.
6. Gram-scale synthesis

![Chemical reaction diagram]

**Procedure for 6 mmol scale reaction of 1a:**

To a 50 mL Schlenk tube was added 1a (6 mmol), 2a (30.0 mmol), K₂CO₃ (840.0 mg, 1.0 equiv), CuI (228 mg, 20 mol%), NMO (1.4 g, 2.0 equiv) and 2-pyridone (570 mg, 1.0 equiv). The reaction mixture was stirred at 80 °C (aluminum heat transfer block) for 24 h. After cooling to room temperature, the mixture was diluted with DCM, The crude mixture was purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 10:1 to 4:1) affording the desired product 3a as yellow solid, 1.32 g, 50% yield.
7. Removal of directing group.

The product 3a (44.1 mg, 0.1 mmol, 1.0 equiv.) was dissolved in MeOH (1 mL) and KOH (1.12 g, 20 mmol, 20.0 equiv.) was added. The reaction mixture was refluxed with stirring for 12 h (The reaction was detected by TLC). The reaction mixture was cooled to room temperature and extracted with ethyl acetate (30 mL) and water (2 × 30 mL). The combined aqueous phase was acidified with 2 M HCl to pH = 2 and extracted with ether (3 × 30 mL). The combined ether phase was washed with brine (45 mL) and dried with Na2SO4 and was concentrated under reduced pressure to give the crude product that used directly in the next step.

K2CO3 (0.6 mmol), DMF (2.0 ml) and (bromomethyl)benzene (1.6 mmol) were charged in reaction vessel equipped with magnetic stirring bar under nitrogen atmosphere. The mixture was stirred at rt for 12 h. Ethyl acetate (10 mL) and 10% aqueous Na2S2O3 (20 mL) were added to the mixture and the organic phase extracted by three potions of EtOAc. Combined organic layer was dried over MgSO4 and the solvent evaporated in vacuo. Further purification was carried out by silica gel column chromatography using EtOAc/hexane to afford the desired 5 (30.4 mg, 75% yield)

Benzyl 2-morpholinoferrocenezoate (5).

1H NMR (400 MHz, Chloroform-d) δ 7.45 (d, J = 6.7 Hz, 2H), 7.40 (t, J = 7.2 Hz, 2H), 7.34 (t, J = 7.1 Hz, 1H), 5.32 (d, J = 12.4 Hz, 1H), 5.20 (d, J = 12.4 Hz, 1H), 4.73 (dd, J = 2.8, 1.6 Hz, 1H), 4.25 (dd, J = 2.8, 1.7 Hz, 1H), 4.18 (s, 6H), 3.79 (t, J = 4.7 Hz, 4H), 3.08 (m, J = 10.1, 4.9 Hz, 2H), 2.91 – 2.81 (m, 2H).

13C NMR (100 MHz, CDCl3) δ 171.4, 136.7, 128.7, 128.3, 128.3, 114.5, 69.7, 68.9, 67.1, 65.9, 65.8, 62.2, 61.7, 53.7.

HRMS (ESI) m/z: [M + H]+ Calcd for C22H24FeNO3 406.1107; found: 406.1098.
8. Mechanistic Experiments.

8.1 Synthesis of deuterated substrate.

1a (1.0 mmol), CD$_3$CO$_2$D (10 ml) and Pd(OAc)$_2$ (10 mol %) were charged in reaction vessel equipped with magnetic stirring bar under O$_2$ atmosphere. The mixture was at rt. for 12 h. Ethyl acetate (10 mL) and 10% aqueous NaHCO$_3$ (10 mL) were added to the mixture and the organic phase extracted by three potions of EtOAc. Combined organic layer was dried over magnesium sulfate and the solvent evaporated in vacuo. Further purification was carried out by silica gel column chromatography using EtOAc/hexane to afford the desired 2a (27.3 mg, 81% yield).
8.2 H/D exchange experiment

To a 10 mL Schlenk tube was added 1a (0.1 mmol), CD₃CO₂D (0.2 mmol), K₂CO₃ (14.0 mg, 1.0 equiv), CuI (3.8 mg, 20 mol %), NMO (23.4 mg, 2.0 equiv) and 2-pyridone (9.5 mg, 1.0 equiv), stirred at 80 °C (aluminum heat transfer block) for 4 h. After cooling to room temperature, the mixture was diluted with DCM, the resulting residue was purified by preparative TLC using Hexane/EtOAc as the eluent to afford the desired product. No H/D exchange was observed at the ortho-position of 1a.
8.3 KIE experiment

To a 50 mL Schlenk tube was added 1a (0.1 mmol), or 1a-d (0.1 mmol), 2a (0.5 mmol), K₂CO₃ (14.0 mg, 1.0 equiv), CuI (3.8 mg, 20 mol %), NMO (23.4 mg, 2.0 equiv) and 2-pyridone (9.5 mg, 1.0 equiv), the tube was sealed up a cap and evacuated then refilled with air and kept stirring at 80 °C (aluminum heat transfer block). Then immediately quenched with DCM. The corresponding yield of each product was determined by ¹H NMR. A whole set of experiments was performed two times and their average values were used for the KIE calculation. KIE = \( k_{H}/k_{D} = 2.4 \).

| Time (min) | 1  | 5  | 10 | 15 | 25 | 35 |
|------------|----|----|----|----|----|----|
| 3a         | 0  | 6  | 13 | 25 | 40 | ---|
| 3a-d       | 0  | 2  | ---| 7  | 15 | 25 |
9. References.

1) Sattar, M.; Praveen, C.; Prasad, D.; Verma, A.; Kumar, S.; Kumar, S. Adv. Synth. Catal. **2016**, 358, 240.

2) Ivan, S.; Jakub, V.; Dusan, B.; Andrej. K. *Tetrahedron*. **2015** 71, 8876-8884.

3) Daniela, H.; Harald, H.; and Peter, G. *J. Med. Chem.* **2009**, 52, 6860–6870.

4) Zubeda, B.; Bhavania, D.; Sridharb, B.; Basireddy, V.; Subba, R. *Synthesis*. **2018**, 50, 4089–4096.

5) Siu, Juno C.; Parry, Joseph B.; and Lin, S. *J. Am. Chem. Soc.* **2019**, 141, 2825–2831.
10. NMR Spectra.

2b-^1^H NMR

[Diagram of 2b-^1^H NMR spectrum]

2b-^1^3C NMR

[Diagram of 2b-^1^3C NMR spectrum]
2c-\textsuperscript{1}H NMR

2c-\textsuperscript{13}C NMR
2e-¹H NMR

2e-¹³C NMR
2f-^1^H NMR

2f-^13^C NMR
2g-$^1$H NMR

2g-$^{13}$C NMR
$2h^3\text{H NMR}$

$2h^{13}\text{C NMR}$
2k-$^1$H NMR

2k-$^{13}$C NMR
3b-$^1$H NMR

3b-$^{13}$C NMR
3d-$^1$H NMR

3d-$^{13}$C NMR
3e-\textsuperscript{1}H NMR

3e-\textsuperscript{13}C NMR
3g-$^1$H NMR

3g-$^{13}$C NMR
3h-\(^1\)H NMR

3h-\(^{13}\)C NMR
3i-$^1$H NMR

3i-$^{13}$C NMR
$3k^{1}H$ NMR

$3k^{13}C$ NMR
3l-^1^H NMR

3l-^1^C NMR
3m$^1$H NMR

3m$^{13}$C NMR
4b-$^1$H NMR

4b-$^{13}$C NMR
4d-^3^H NMR

4d-^1^3^C NMR
4e-^1^H NMR

![4e-^1^H NMR spectrum]

4e-^13^C NMR

![4e-^13^C NMR spectrum]
4g-$^1$H NMR

4g-$^{13}$C NMR
4i-^1H NMR

![4i-^1H NMR spectrum](image)

4i-^13C NMR

![4i-^13C NMR spectrum](image)
4j-^1H NMR

4j-^13C NMR
4k-^1^H NMR

4k-^13^C NMR
$4m^-\text{H NMR}$

$4m^-\text{C NMR}$
4n-^1^H NMR

4n-^1^3^C NMR
$^{40}$H NMR

$^{40}$C NMR
4p-^1^H NMR

4p-^{13}C NMR
4r-^1^H NMR

4r-^1^3^C NMR
5-¹H NMR

5-¹³C NMR