Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

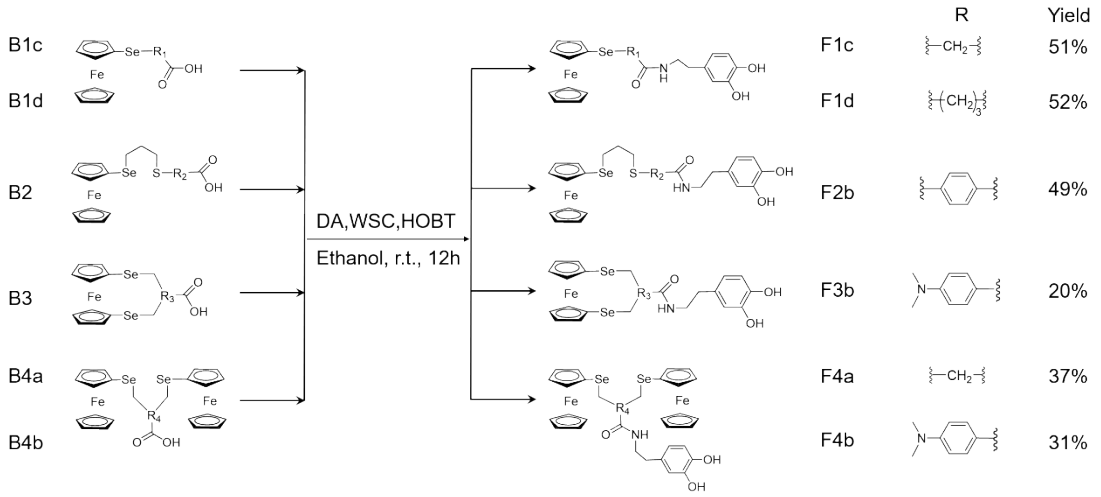
Design of Ferrocenylseleno-dopamine Derivatives to Optimize the Fenton-like Reaction Efficiency and Antitumor Efficacy

Qianya Cheng, [a] Tong Zhou, [a] Qing Xia, [a] Xiulian Lu, [a] Heng Xu, [b] Ming Hu, [a] Su Jing [a,*]

[a] School of Chemistry and Molecular Engineering, Nanjing Tech University, Nanjing 211816, China

[b] Jiangsu Province Institute of Materia Medica, Nanjing Tech University, Nanjing 211816, China

Table of contents



Scheme S1. Synthetic scheme of six new ferrocenylseleno-dopamine derivatives.

The new derivatives were synthesized following the reported methods as shown in **Scheme S1**.[1] The detailed synthetic processes are shown below with related characterization data.

Synthesis of F1c. B1c (0.323 g, 1 mmol), DA (0.189 g, 1 mmol), HOBT (0.135 g, 1mmol), and WSC (0.25 mL, 1 mmol) were placed in a 250 mL three-necked, round-bottomed flask containing dry ethanol (150 mL) under a nitrogen atmosphere; the resulting mixture was stirred at room temperature overnight. Ethanol was removed from the reaction mixture under reduced pressure, the residue was dissolved in dichloromethane (50 mL), and this solution was washed with water three times. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography using dichloromethane/ethyl acetate (3/1 v/v) to obtain a yellow solid. Yield: 0.233 g (51%). M.p. 72.9-74.1 ℃. FT-IR (KBr, $\tilde{\nu}$ cm^{-1}): 3345(w), 2911(m), 2860(m), 2359(m), 1566(m), 1525(m), 1464(m), 1359(m), 1259(m), 1019(m), 796(s), 498(m). ^{1}H NMR (δ, 400MHz, DMSO-d_6): 8.75 (s, 1H), 8.66 (s, 1H), 7.87-7.90 (m, 1H), 6.63-6.42 (m, 3H), 4.32 (m, 2H), 4. 25 (m, 2H), 4.19 (s, 5H), 3.21(s, 2H), 3.12-3.17 (m, 2H), 2.46-2.48 (m, 2H). ^{13}C NMR (δ, 100.6 MHz, DMSO-d_6):169.4, 145.5, 144.0, 130.5, 119.6, 116.4, 115.9, 74.8, 71.4, 69.8, 69.5, 35.0, 31.9. HRMS(ESI-TOF): calcd for $C_{20}H_{21}NO_3SeFe$ $[M+H]^+$ 460.00, found 460.00. Anal. Calcd for $C_{20}H_{21}NO_3SeFe$: C, 52.43; H, 4.62; N, 3.06. Found: C, 52.45; H,4.60; N, 3.05.

Synthesis of F1d. The synthesis was similar as that of **F1c**, except that **B1d** (0.347 g, 1 mmol) was used instead of **B1c**. The target product was obtained as a white solid. Yield: 0.237 g (52%). M.p. 81.7-83.6 ℃. FT-IR (KBr, $\tilde{\nu}$ cm^{-1}): 3351(w), 3312(w), 3095(vs), 2858(m), 2362(m), 1586(m), 1525(m), 1464(m), 1371(m), 1259(m), 988(s), 813(m), 760(m), 495(m). ^{1}H NMR (δ, 400 MHz, DMSO-d_6): 8.75 (s, 1H), 8.65 (s, 1H), 7.91-7.88 (m, 1H), 6.64-6.62 (m, 1H), 6.57 (s, 1H), 6.44-6.42 (m, 1H), 4.37 (t, J = 4.0 Hz, 2H), 4.33 (m, 2H), 4.26 (m, 2H), 4.19 (s, 5H), 3.45 (q, J = 4.0 Hz, 8.0 Hz, 4H), 3.14-3.16 (m, 2H), 2.71 (t, J = 8.0 Hz, 2H), 2.36-2.39 (m, 2H). ^{13}C NMR (δ, 100.6 MHz, DMSO-d_6): 170.9, 145.5, 144.0, 131.2, 119.7, 116.4, 115.9, 74.9, 71.1, 69.8, 69.5, 37.0, 35.1, 24.6. HRMS(ESI-TOF): calcd for $C_{22}H_{25}NO_3SeFe$ $[M]^+$ 487.03, found 486.30. Anal. Calcd for $C_{22}H_{25}NO_3SeFe$: C, 54.34; H, 5.18; N, 2.88. Found: C, 54.32; H,5.20; N, 2.84.

Synthesis of F2b. The synthesis was similar as that of **F1c**, except that **B2** (0.459 g, 1 mmol) was used instead of **B1c**. The target product was obtained as a yellow oil. Yield: 0.292 g (49%). FT-IR (KBr, $\tilde{\nu}$ cm^{-1}): 3512(w), 3124(w), 3005(w), 1608(vs), 1516(m), 1281(m), 819(m), 751(m), 496(m). ^{1}H NMR (δ, 400MHz, DMSO-d_6): 8.77 (s, 1H), 8.65 (s, 1H), 8.47-8.50 (m, 1H), 7.74-7.76 (m, 2H), 7.31-7.34 (m, 2H), 6.61-6.64 (m, 2H), 6.45-6.47 (m,1H), 4.29-4.30 (m, 2H), 4.23-4.24 (m, 2H), 4.17 (s, 5H), 3.07 (t, J = 8.0 Hz, 2H), 2.62-2.65 (m, 4H), 1.83 (t, J = 8.0 Hz, 2H), 1.25 (s, 2H). ^{13}C NMR (δ, 100.6 MHz, DMSO-d_6): 165.9, 146.0, 144.0, 128.2, 127.0, 119.7, 116.5, 116.0, 74.8, 70.9, 69.9, 69.6, 35.1, 31.3, 29.7, 27.7. HRMS (ESI-TOF): calcd for $C_{28}H_{29}NO_3SSeFe$ $[M]^+$ 595.04, found 595.10. Anal. Calcd for $C_{28}H_{29}NO_3SSeFe$: C, 56.58; H, 4.92; N, 2.36. Found: C, 56.60; H,4.90; N, 2.34.

Synthesis of F3b. The synthesis was similar as that of **F1c**, except that **B3** (0.535 g, 1 mmol) was used instead of **B1c**. The target product was obtained as a white solid. Yield: 0.131 g (20%). M.p. 115.9-117.2 ℃**.** FT-IR (KBr, $\tilde{\nu}$ cm^{-1}): 3325(w), 3075(w), 2915(vs), 2359(m), 1644(m), 1602(m), 1520(m), 1410(m), 1359(m), 1193(m), 1112(m), 1026(s), 878(m), 762(m), 487(m). ^{1}H NMR (δ, 400MHz, DMSO-d_6): 8.77 (s, 1H), 8.65 (s, 1H), 8.19 (m, 1H), 7.70, 7.72 (s, 2H), 6.82-6.84 (m, 1H), 6.64 (s, 1H), 6.45-6.47 (m, 1H), 5.76 (s, 1H), 4.34 (m, 4H), 4.25 (m, 4H), 2.51(m, 2H), 1.29-1.31

(m, 2H), 1.31-1.32 (s, 8H). HRMS (ESI-TOF): calcd for $C_{29}H_{30}N_2O_3Se_2Fe$ $[M]^+$ 669.99, found 669.67. Anal. Calcd for $C_{29}H_{30}N_2O_3Se_2Fe$: C, 52.12; H, 4.52; N, 4.19. Found: C, 52.10; H,4.54; N, 4.17.

Synthesis of F4a. The synthesis was similar as that of **F1c**, except that **B4a** (0.615 g, 1 mmol) was used instead of **B1c**. The target product was obtained as a white solid. Yield: 0.277 g (37%). M.p. 133.1-136.6 ℃. FT-IR (KBr, $\tilde{\nu}$ cm^{-1}): 3386(w), 3086(w), 2924(w), 2356(vs), 1704(m), 1660(m), 1547(m), 1459(m), 1397(m), 1355(m), 1236(m), 758(m), 504(m). ^1H NMR (δ, 400 MHz, DMSO-d_6): 8.75 (s, 1H), 8.65 (s, 1H), 7.92-7.95 (m, 1H), 6.59-6.64 (m, 1H), 6.58 (s, 1H), 6.45-6.47 (m,1H), 4.23-4.31 (m, 8H), 4.16 (s, 10H), 3.15 (t, J = 8.0 Hz, 2H), 2.74-2.79 (m, 5H), 2.53-2.55(m, 2H). ^{13}C NMR (δ, 100.6 MHz, DMSO-d6): 172.3, 145.6, 144.0, 142.3, 130.7, 119.8, 117.2, 116.0, 74.7, 70.0, 69.8, 69.5, 60.2, 47.4, 35.2, 35.0, 32.0, 21.2. HRMS (ESI-TOF): calcd for $C_{32}H_{33}NO_3Se_2Fe_2$ $[M]^+$ 750.95, found 751.10. Anal. Calcd for $C_{32}H_{33}NO_3Se_2Fe_2$: C, 51.30; H, 4.44; N, 1.87. Found: C, 51.32; H,4.42; N, 1.83.

Synthesis of F4b. The synthesis was similar as that of **F1c**, except that **B4b** (0.721 g, 1 mmol) was used instead of **B1c**. The target product was obtained as a white solid. Yield: 0.271 g (31%). M.p. 133.3-135.1 ℃. FT-IR (KBr, $\tilde{\nu}$ cm^{-1}): 3325(w), 3122(w), 3075(w), 2915(vs), 2359(m), 1644(m), 1602(m), 1520(m), 1410(m), 1359(m), 1187(m), 1008(m), 863(s), 758(m), 494(m). ^1H NMR (δ, 400 MHz, DMSO-d_6): 8.76 (s, 1H), 8.65 (s, 1H), 8.09-8.12 (m, 1H), 7.46-7.48 (m, 2H), 6.57-6.63(m, 2H), 6.42-6.44 (m, 1H), 6.18-6.20 (m, 2H), 4.37 (m, 4H), 4. 33 (m, 4H), 4.20 (s, 10H), 3.45 (t, J = 7.9 Hz, 4H), 3.27-3.32 (m, 2H), 2.62-2.66 (m, 4H), 2.56-2.59 (m, 2H). ^{13}C NMR (δ, 100.6 MHz, DMSO-d_6):145.6, 130.5, 129.2, 121.2, 117.1, 116.0, 111.3, 74.1, 70.5, 70.1, 69.6, 60.2, 55.4, 51.2, 31.7, 31.6, 30.3, 22.6, 21.2, 15.0. HRMS(ESI-TOF): calcd for $C_{39}H_{40}N_2O_3Se_2Fe_2$ $[M]^+$ 686.02, found 686.60. Anal. Calcd for $C_{39}H_{40}N_2O_3Se_2Fe_2$: C, 54.83; H, 4.72; N, 3.28. Found: C,54.81; H,4.70; N, 3.3.

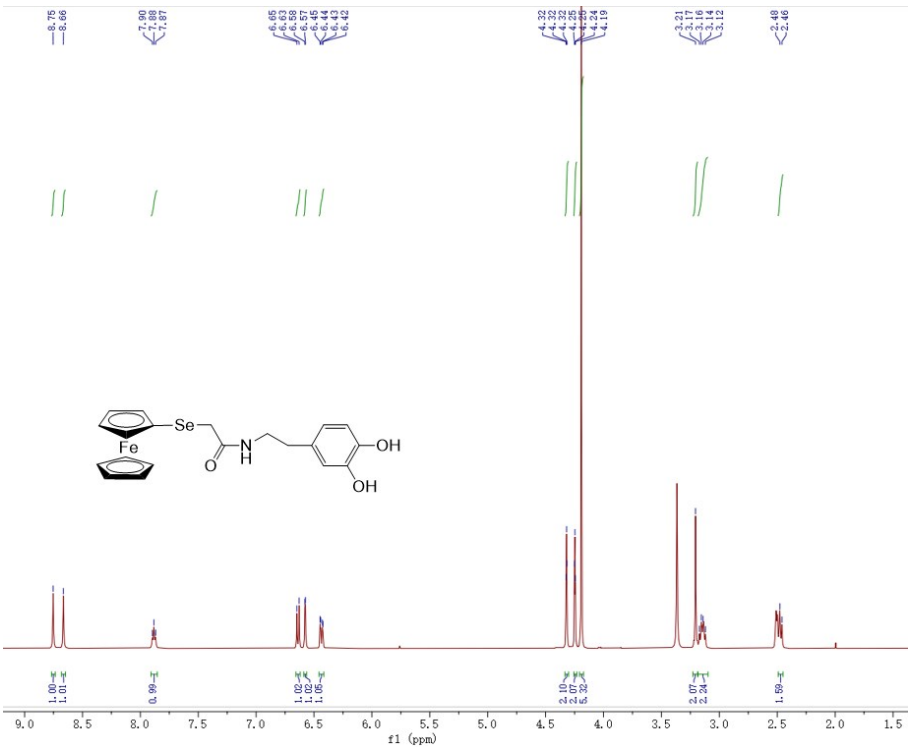


Figure S1. [1] H NMR spectrum of **F1c**.

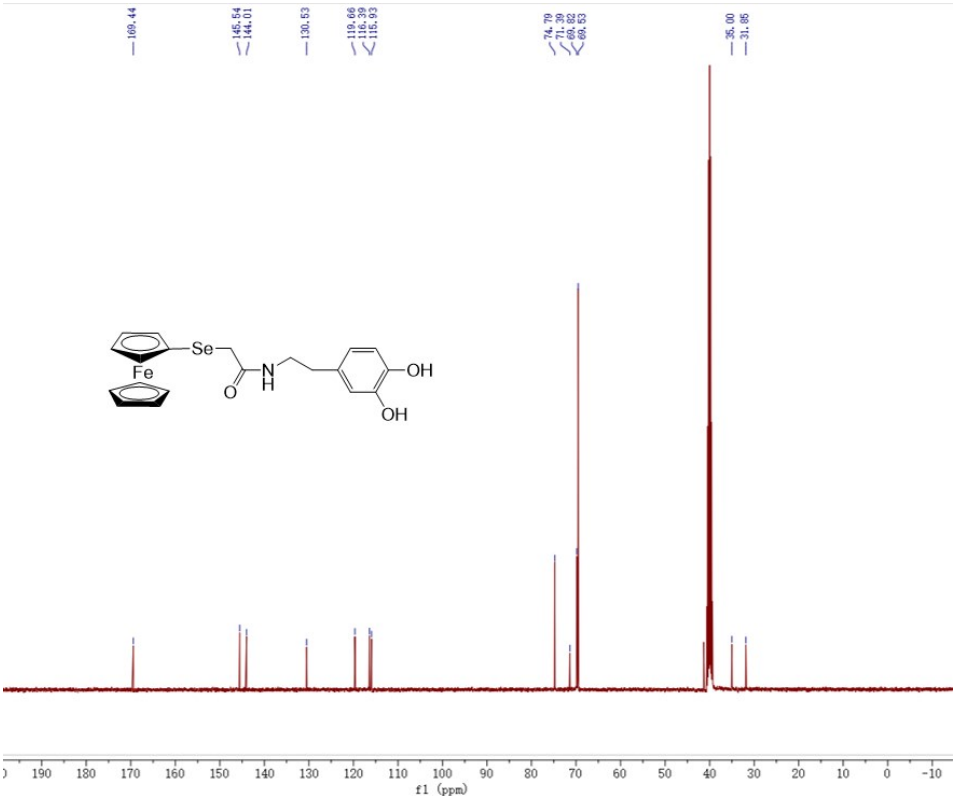


Figure S2. [13] C NMR spectrum of **F1c**.

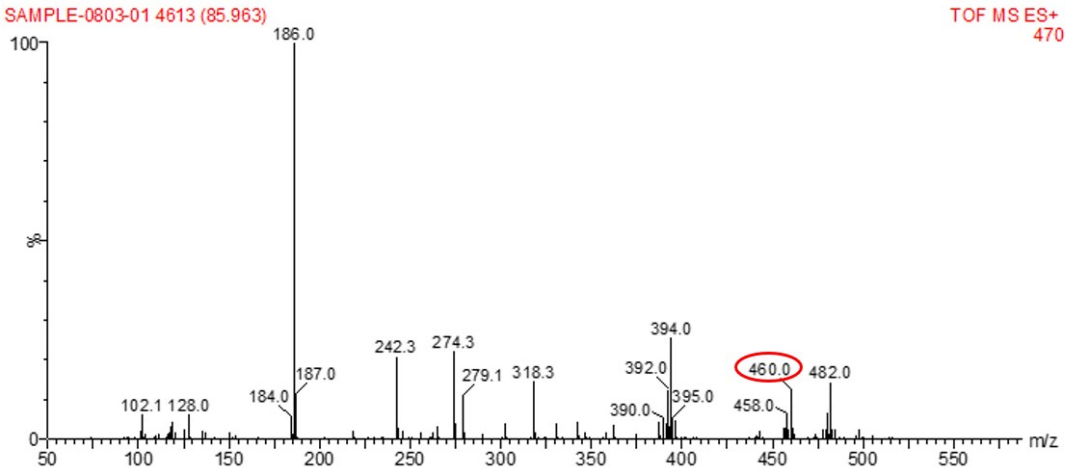


Figure S3. MS spectrum of **F1c**.

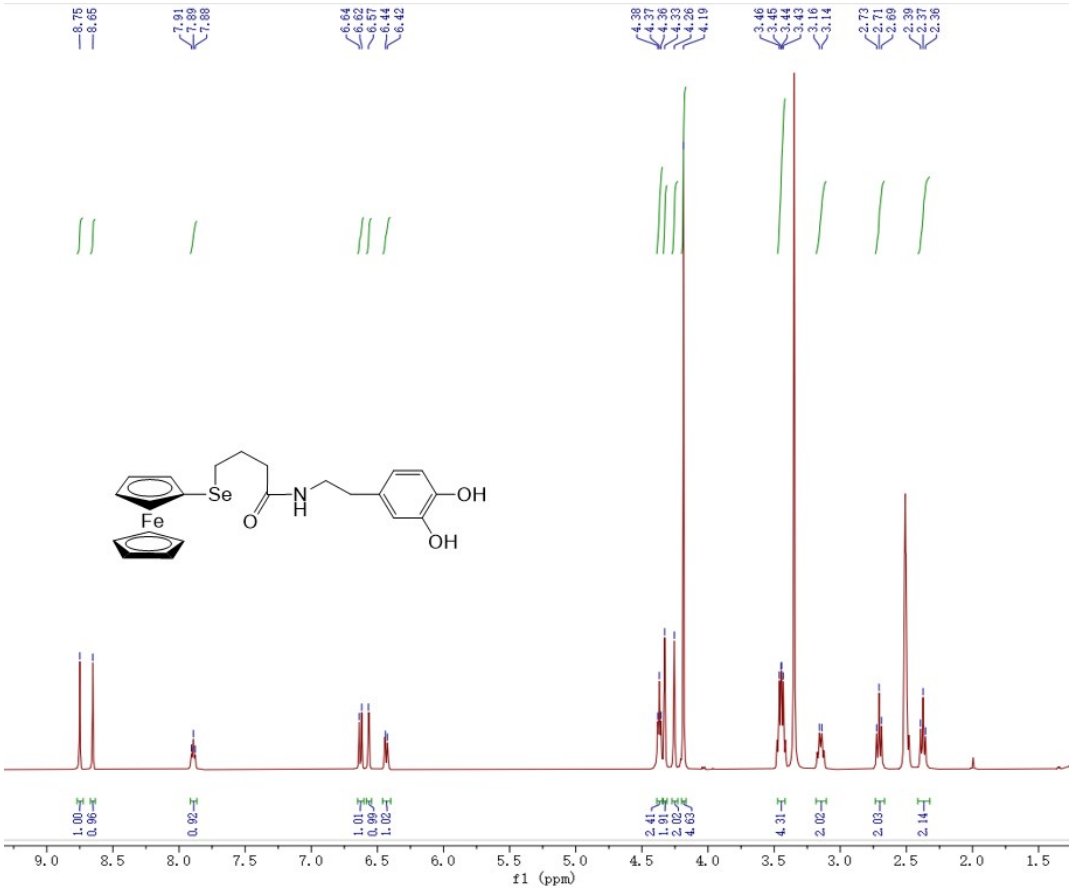


Figure S4. ^{1}H NMR spectrum of **F1d**.

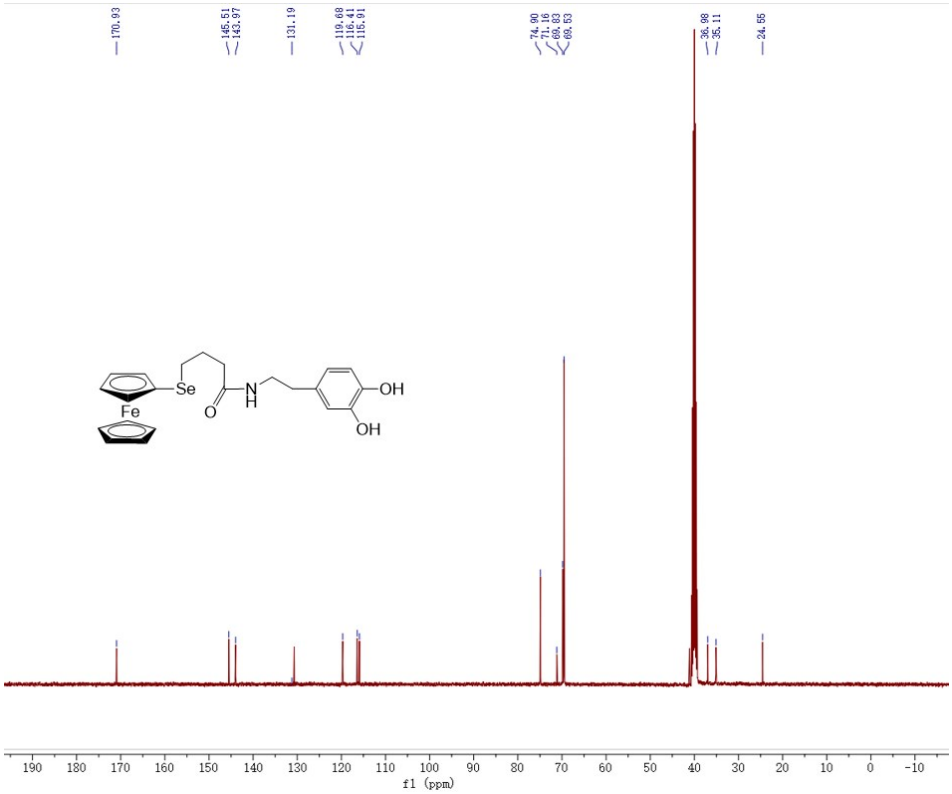


Figure S5. ^{13}C NMR spectrum of **F1d**.

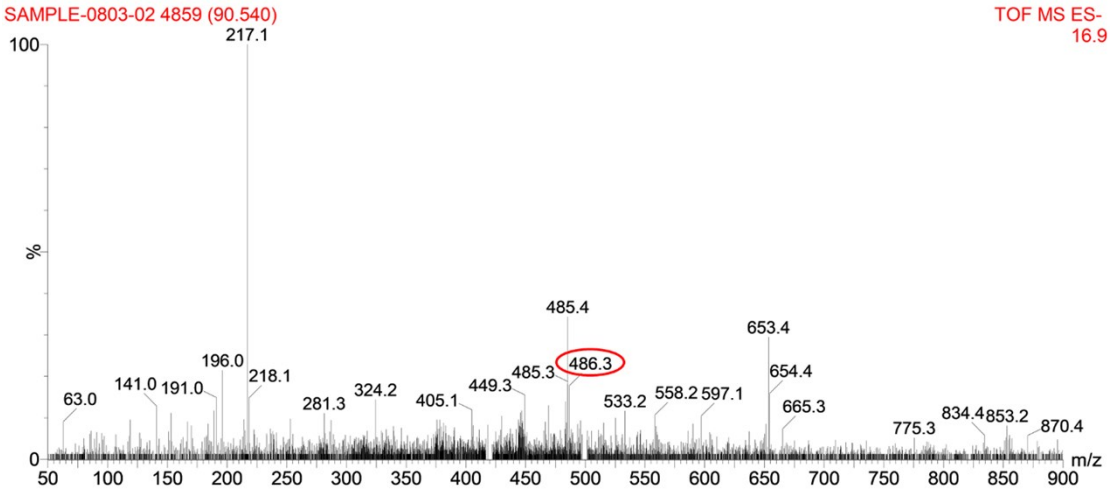


Figure S6. MS spectrum of **F1d**.

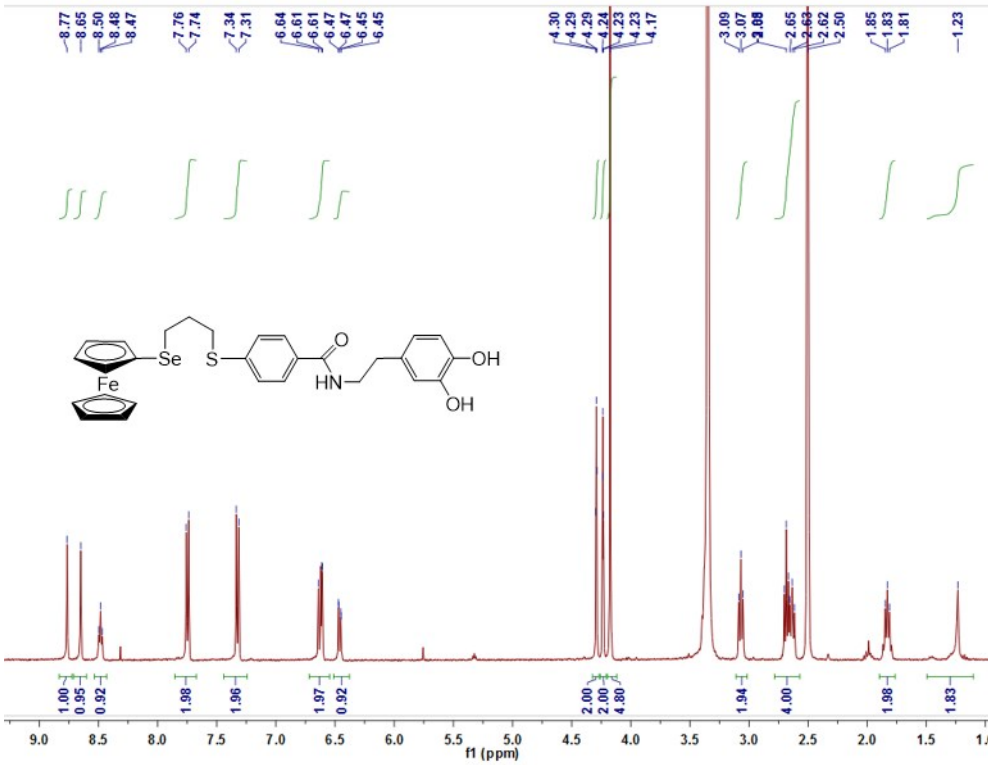


Figure S7. [1] H NMR spectrum of **F2b**.

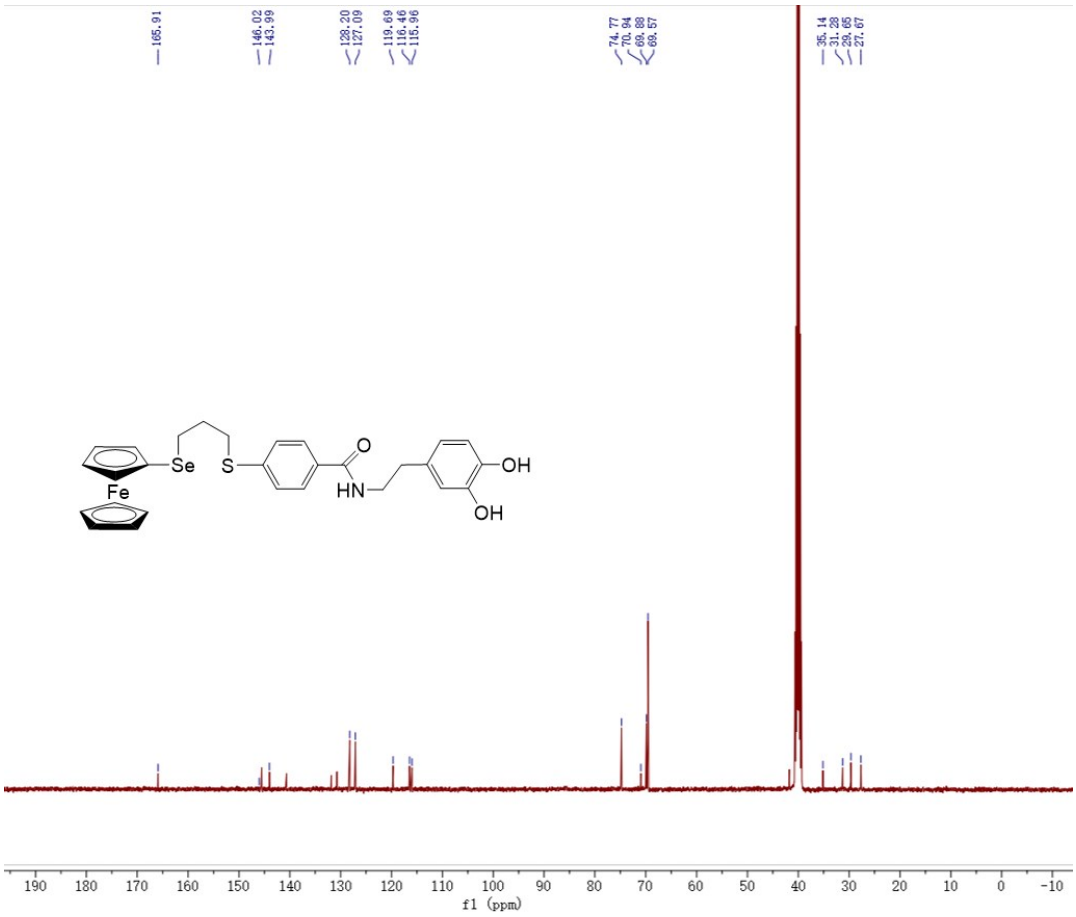


Figure S8. [13] C NMR spectrum of **F2b**.

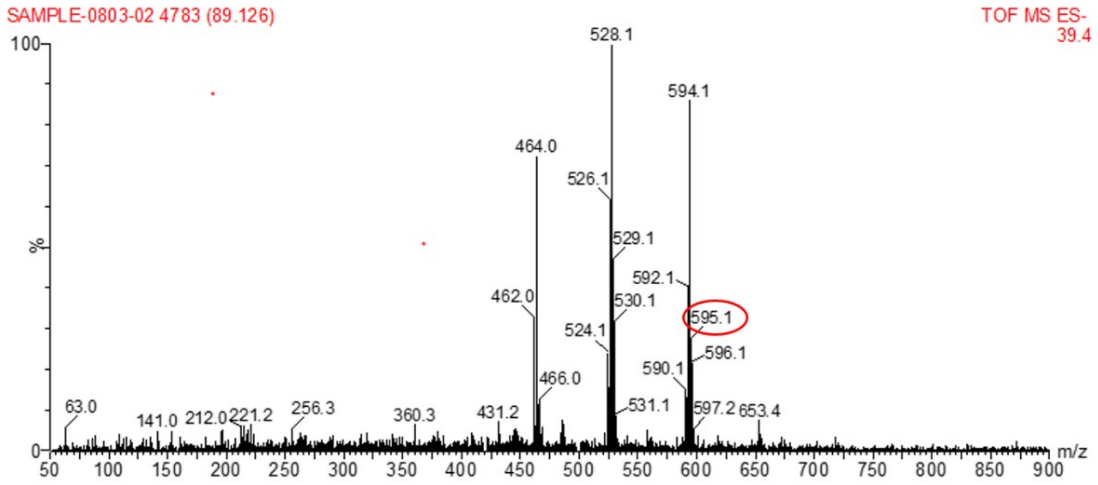


Figure S9. MS spectrum of **F2b**.

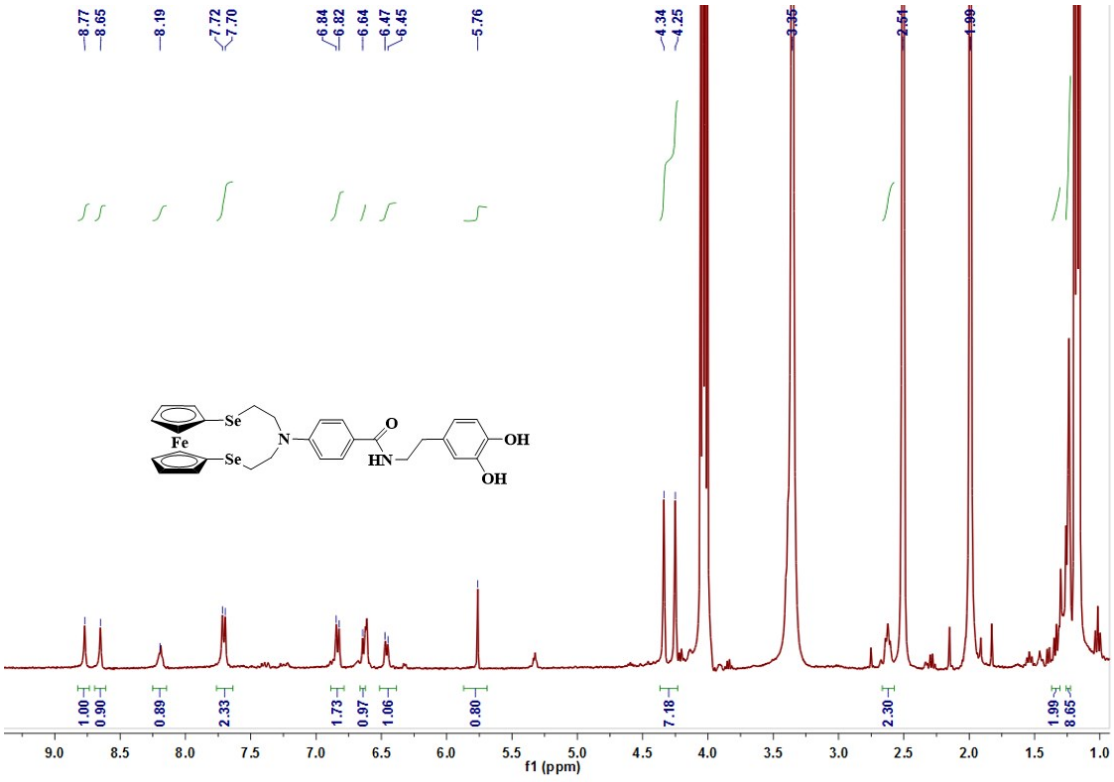


Figure S10. [1] H NMR spectrum of **F3b**.

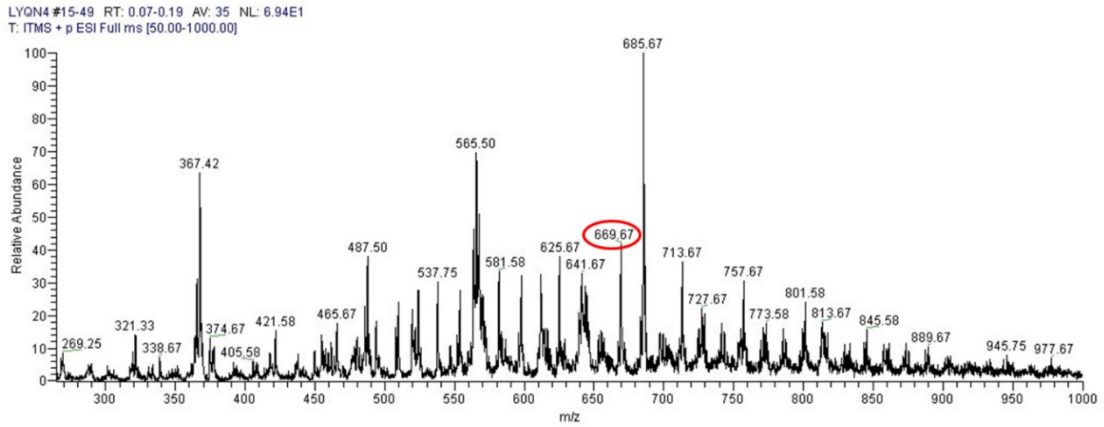


Figure S11. MS spectrum of **F3b**.

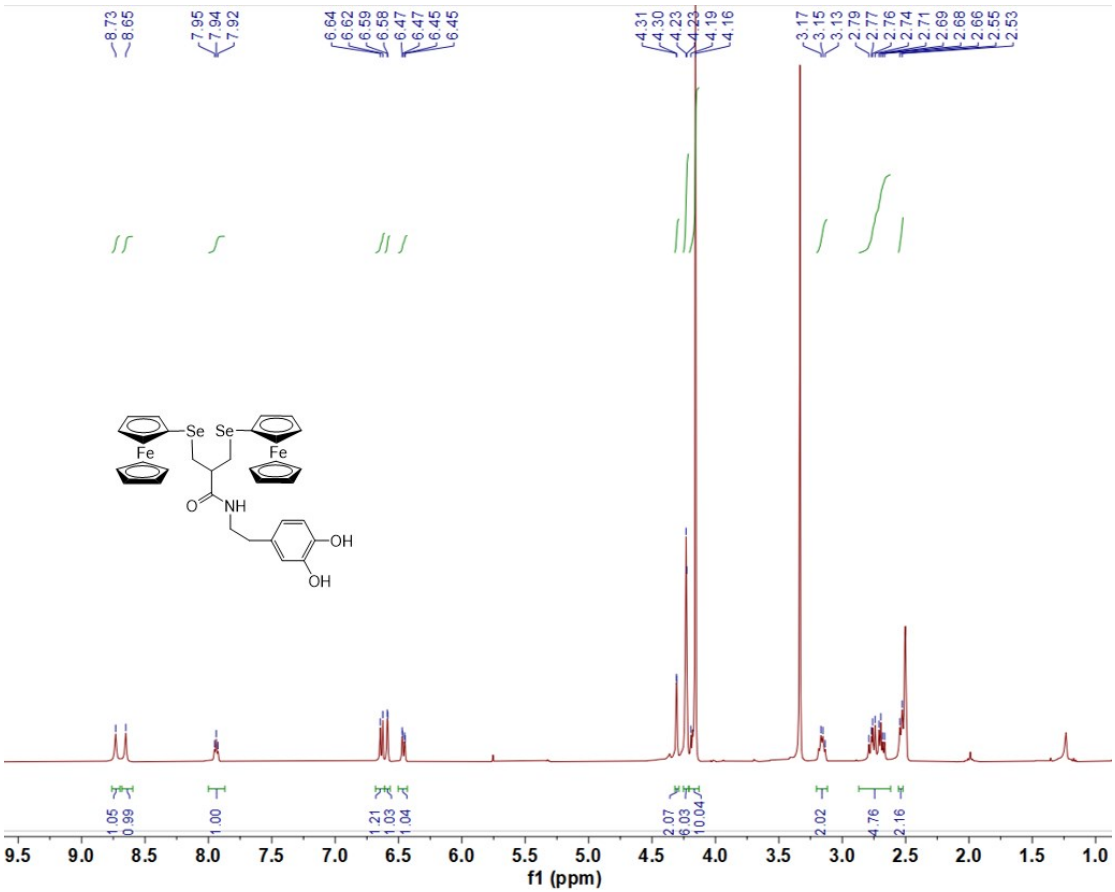


Figure S12. [1] H NMR spectrum of **F4a**.

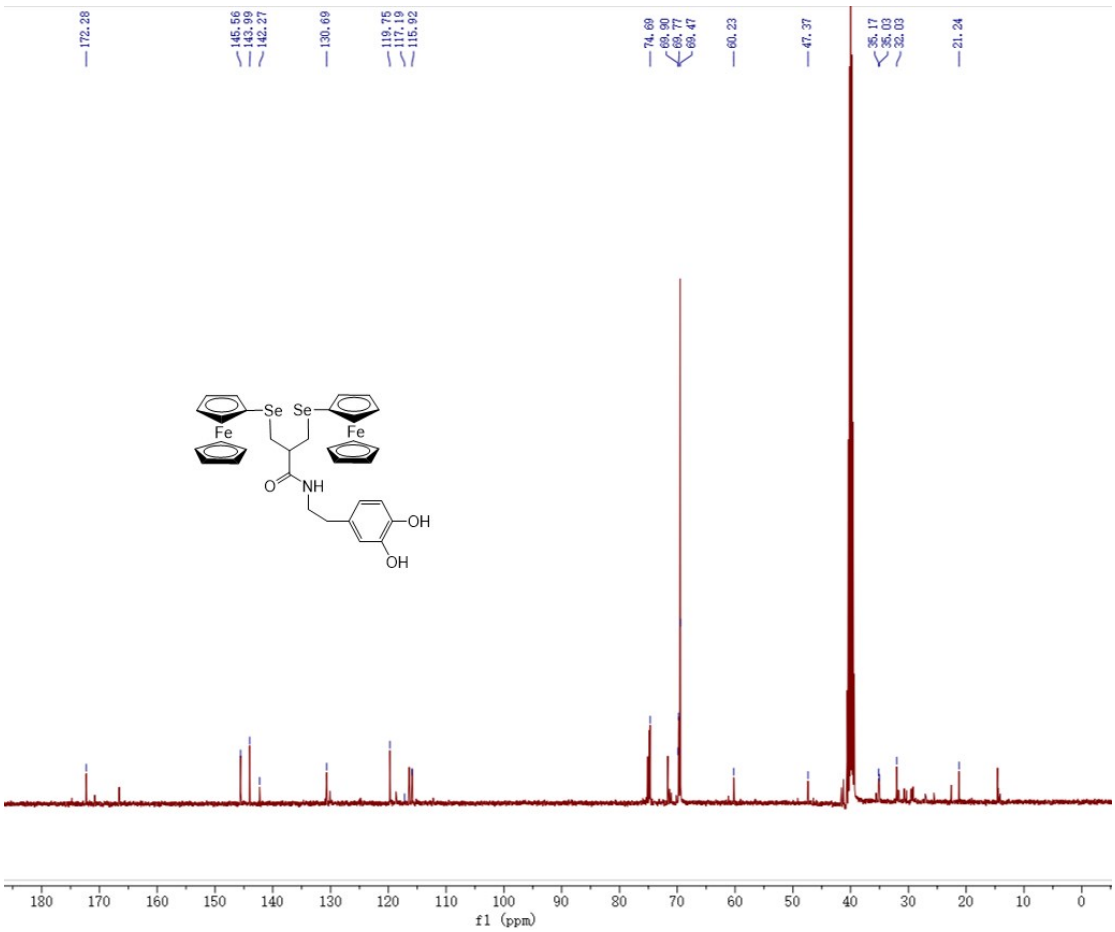


Figure S13. ^{13}C NMR spectrum of **F4a**.

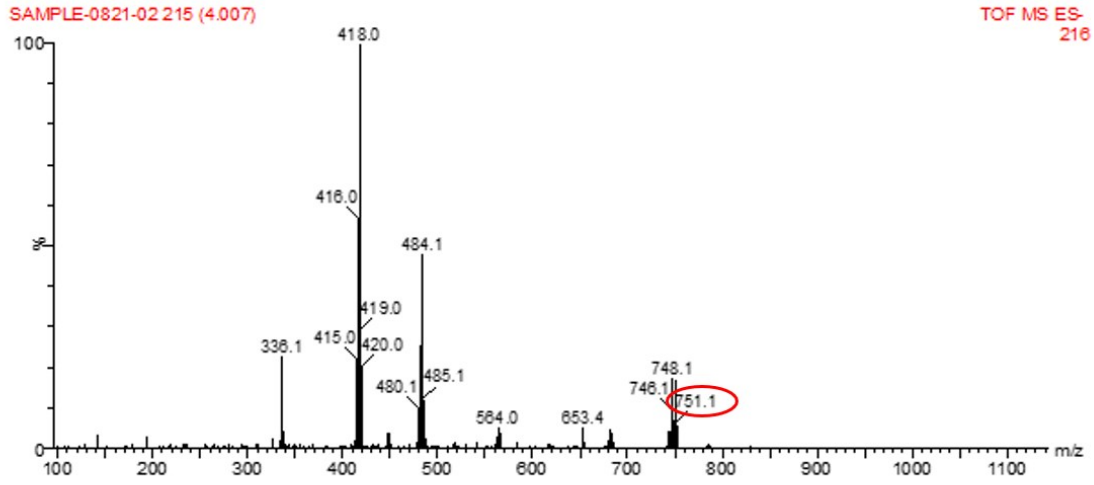


Figure S14. MS spectrum of **F4a**.

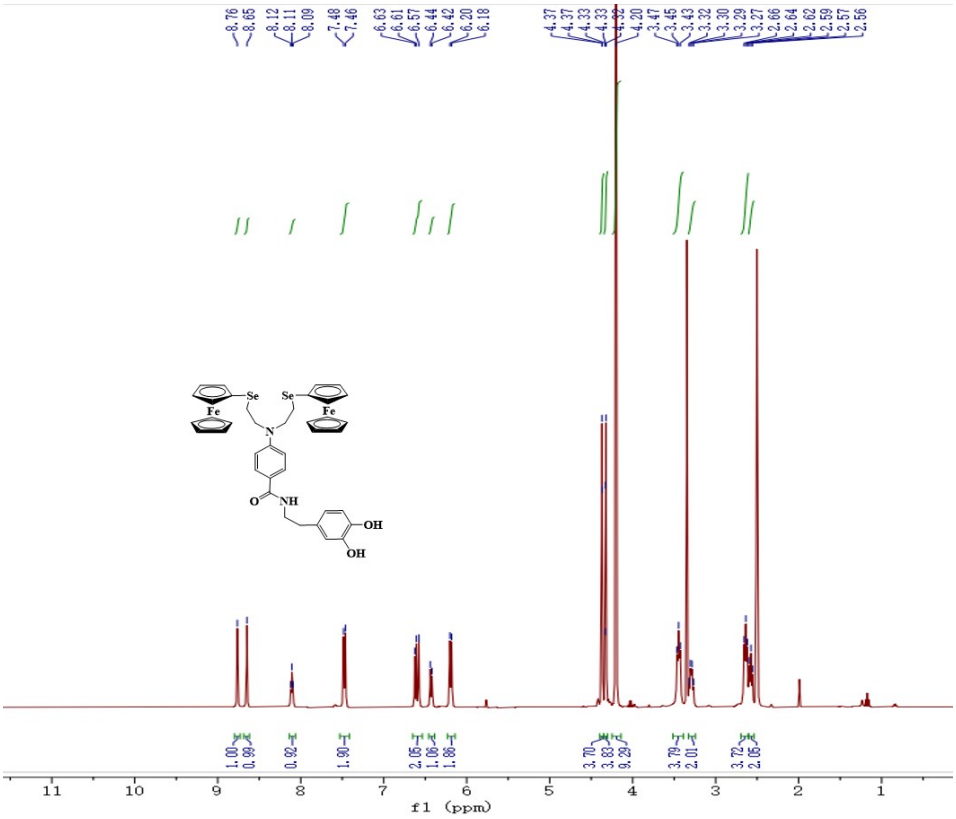


Figure S15. [1] H NMR spectrum of **F4b**.

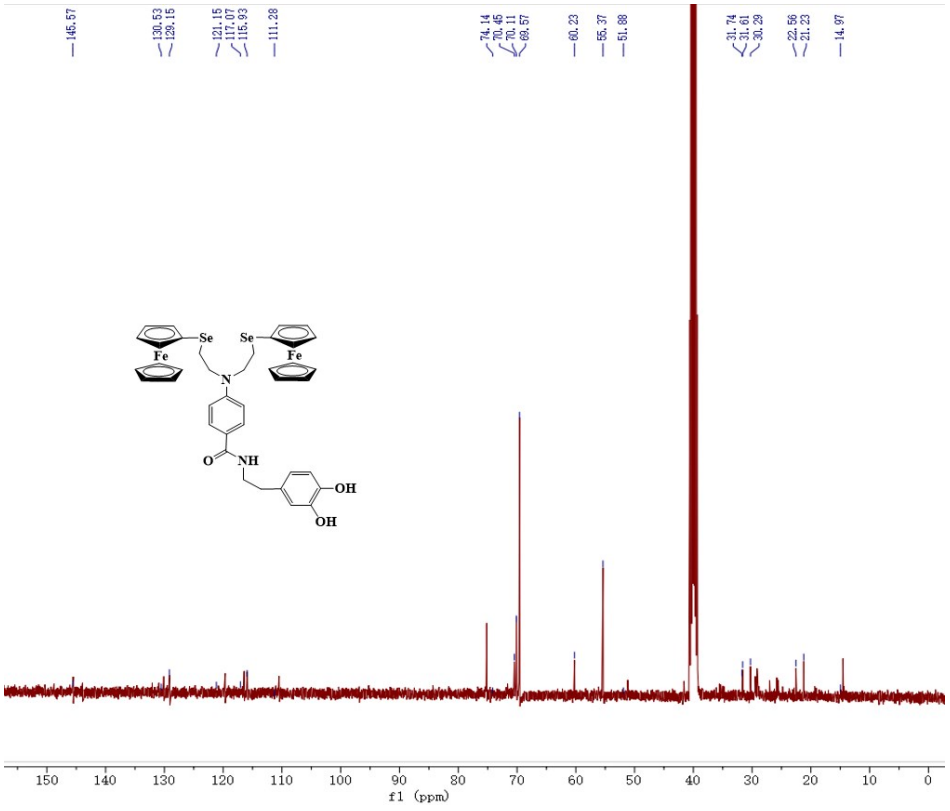


Figure S16. [13] C NMR spectrum of **F4b**.

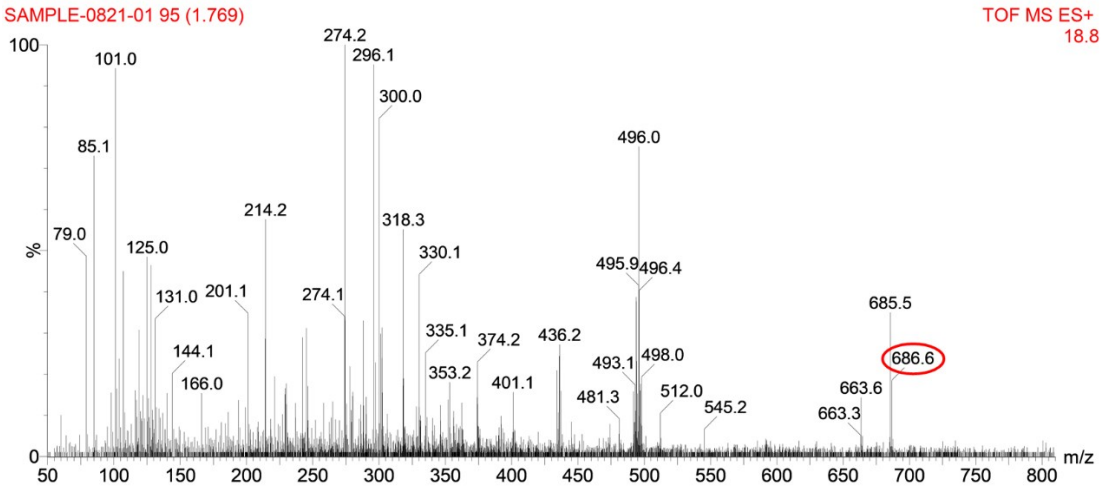


Figure S17. MS spectrum of **F4b**.

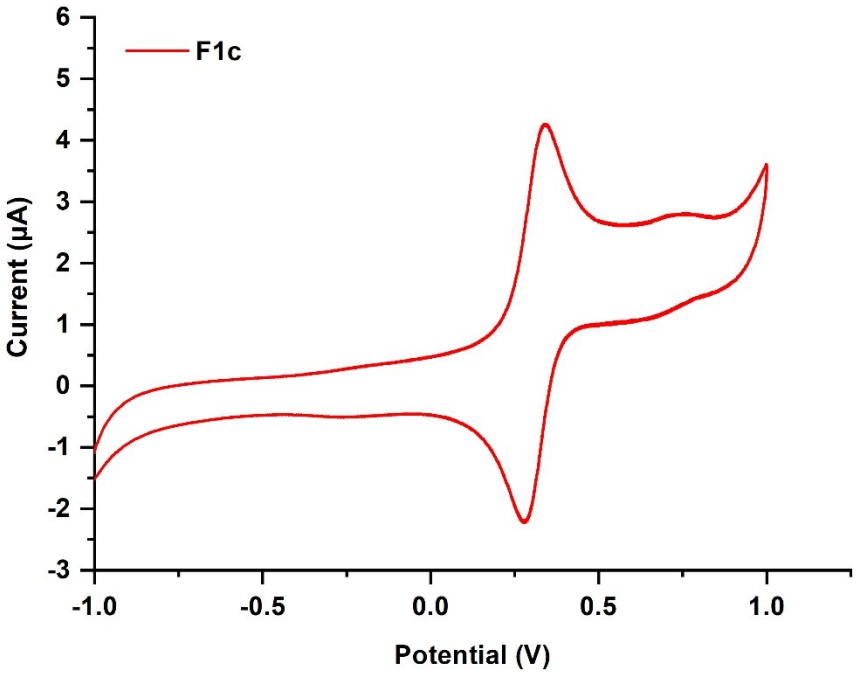


Figure S18. Cyclic voltammograms of **F1c** in CH_3CN/MeOH (v: v = 1:1).

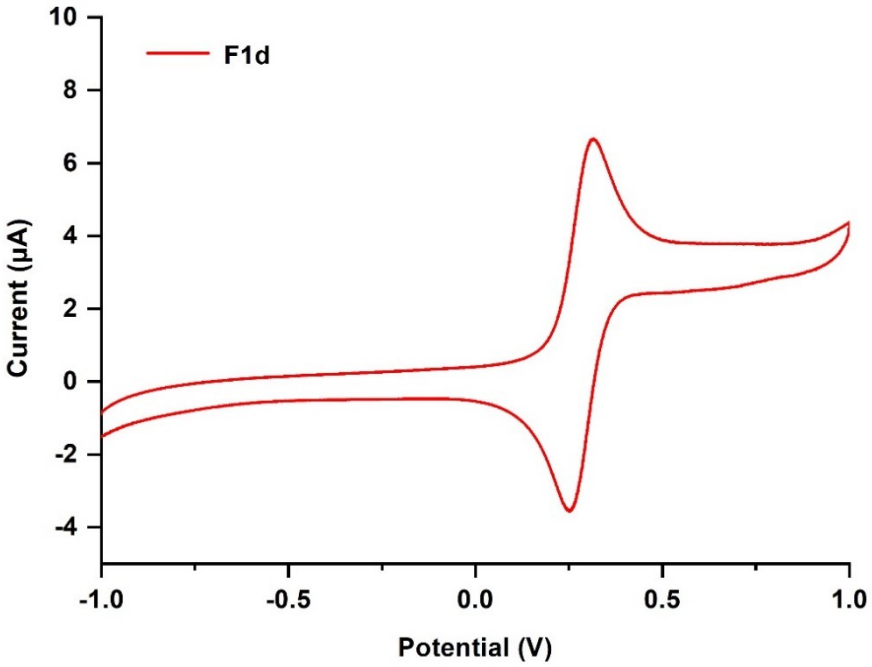


Figure S19. Cyclic voltammograms of **F1d** in CH_3CN/MeOH (v:v = 1:1).

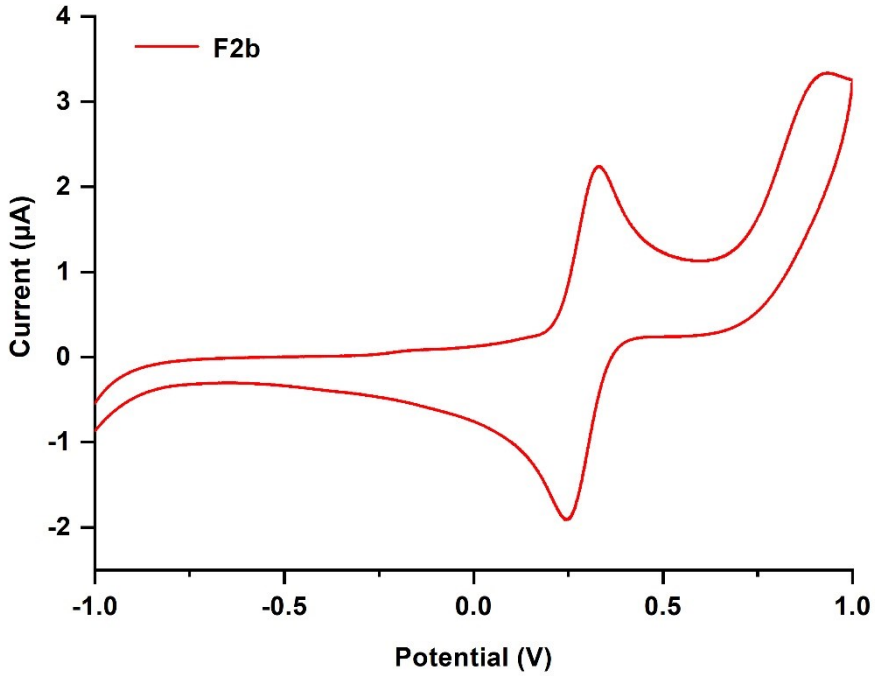


Figure S20. Cyclic voltammograms of **F2b** in CH_3CN/MeOH (v:v = 1:1).

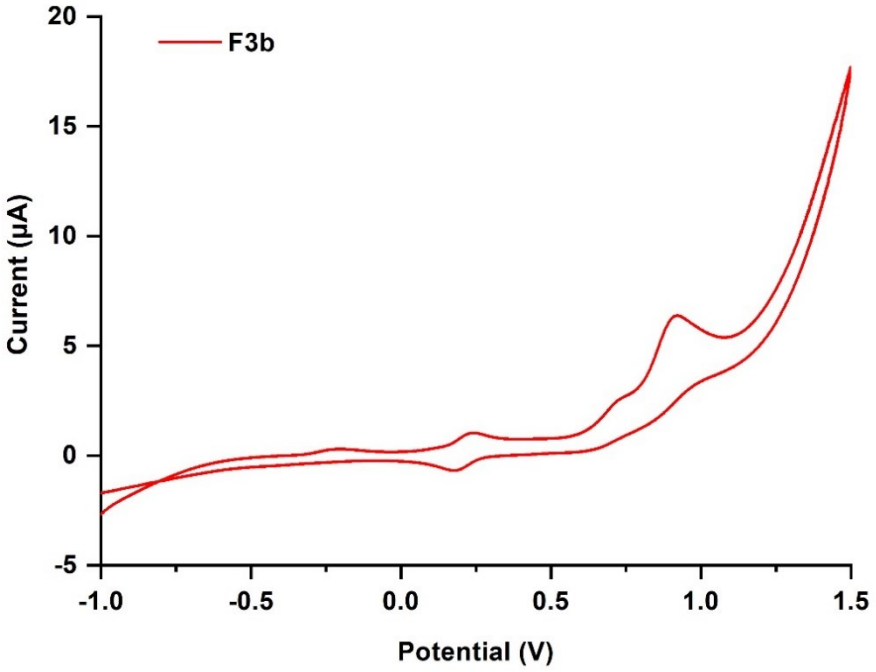


Figure S21. Cyclic voltammograms of **F3b** in CH_3CN/MeOH (v:v = 1:1).

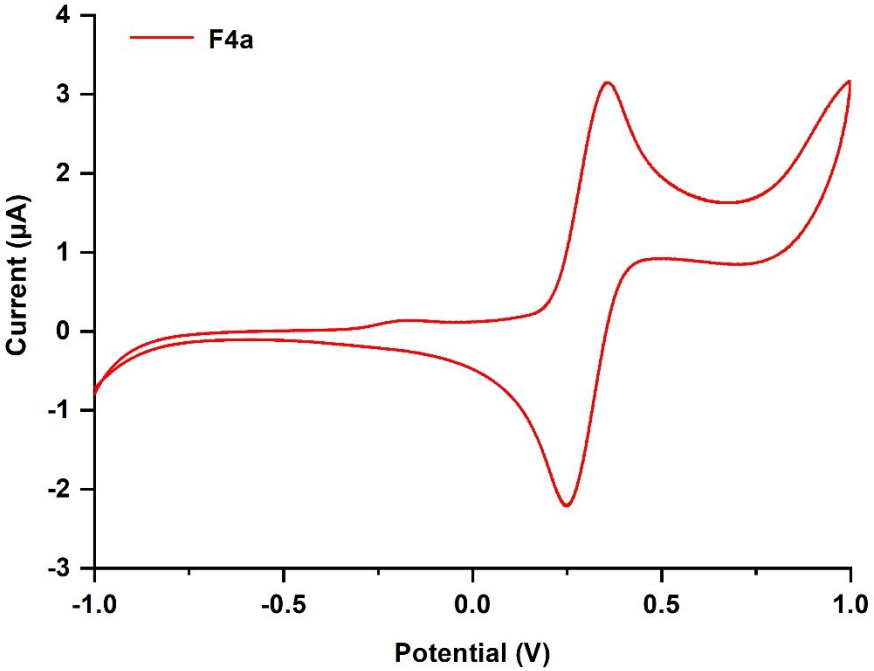


Figure S22. Cyclic voltammograms of **F4a** in CH_3CN/MeOH (v:v = 1:1).

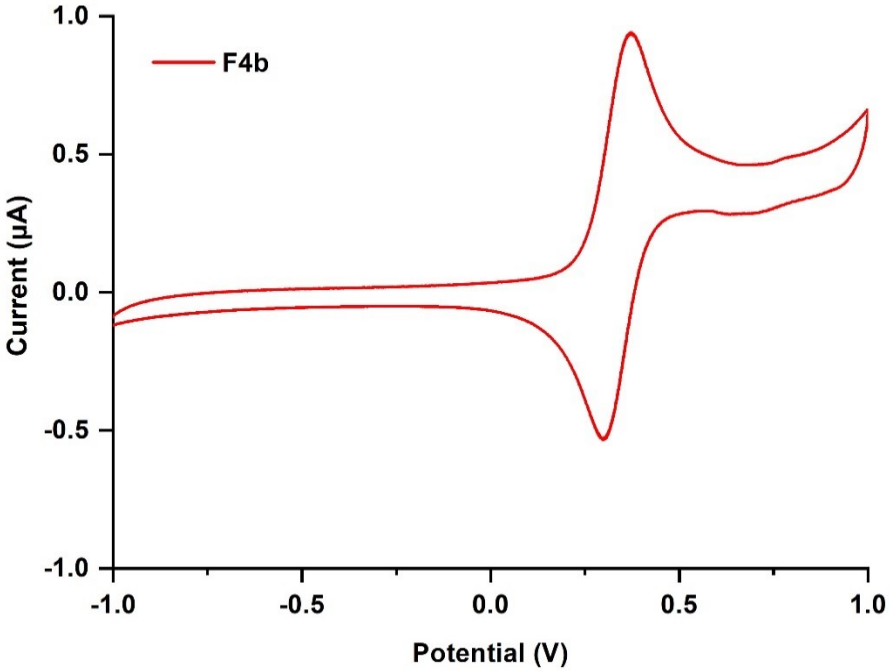


Figure S23. Cyclic voltammograms of **F4b** in CH_3CN/MeOH (v:v = 1:1).

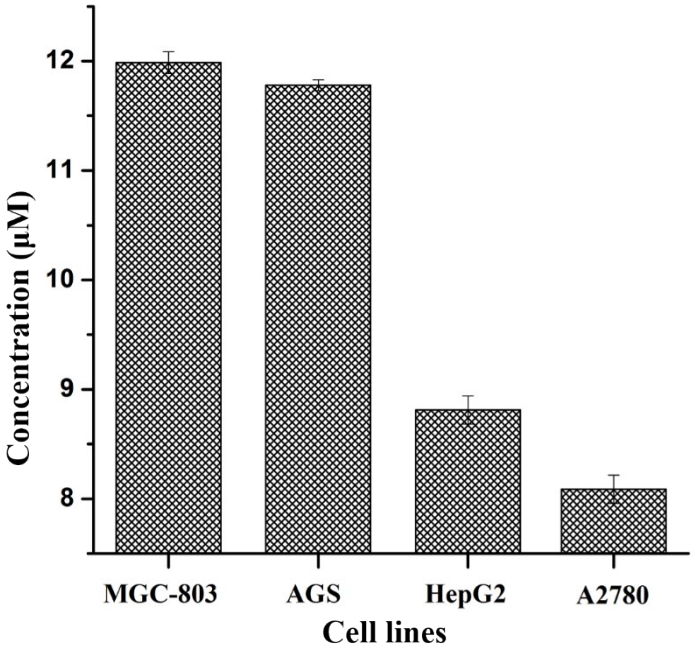


Figure S24. H_2O_2 concentration in different cell line.

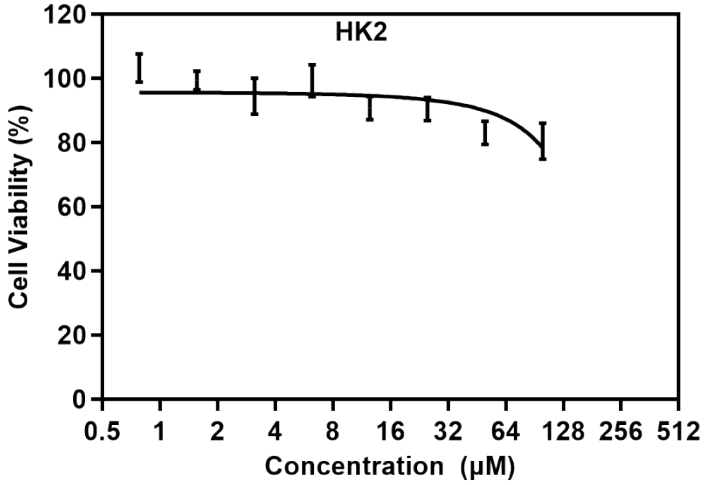


Figure S25. Anticancer activity of **F4b** in HK2 cells.

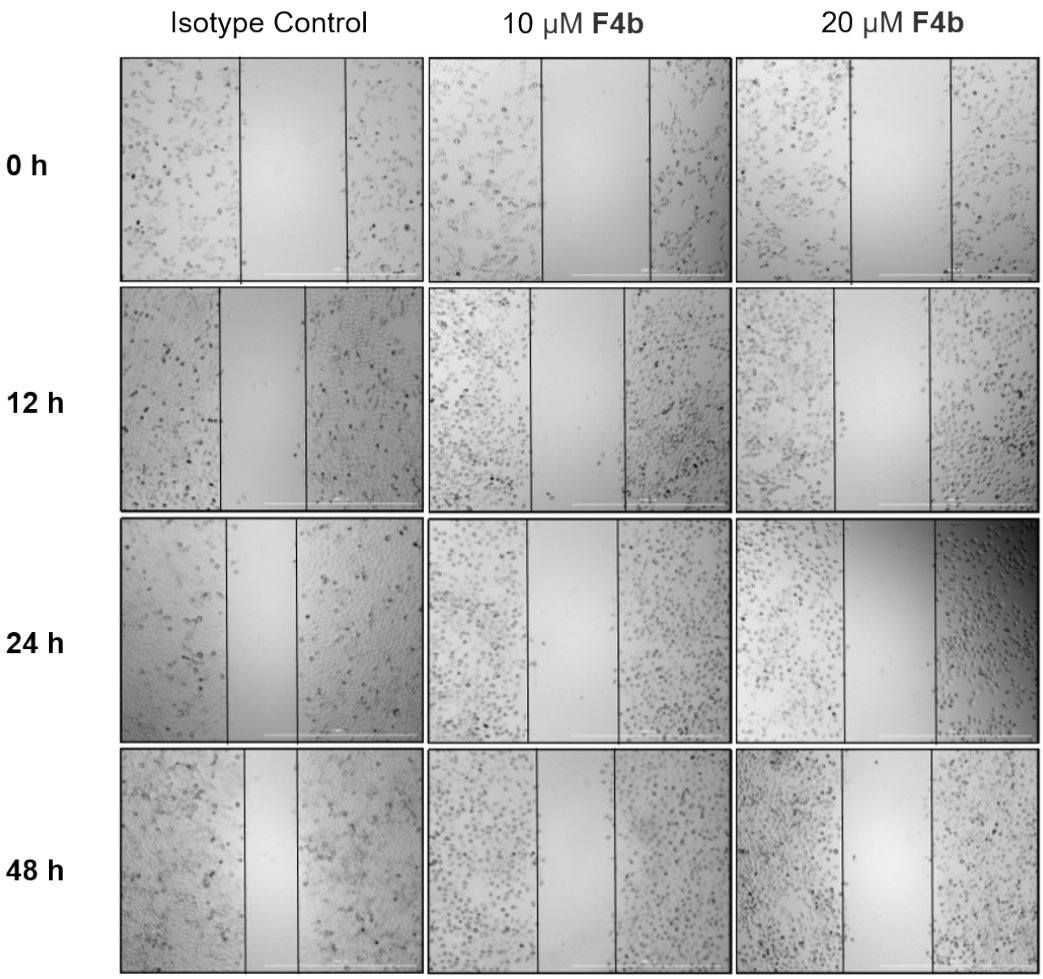


Figure S26. Migration of the cell front observed at different time intervals in scratch assays performed on MGC-803 cells after treatment with **F4b**.

Reference

1. H. Y. Zhou, M. Li, J. Qu, S. Jing, H. Xu, J. Z. Zhao, J. Zhang and M. F. He, *Organometallics* 2016, **35**, 1866-1875.