Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting information

For

Novel Ferrocene-labeled Propargyl amines via CuI Multicomponent Amination/Alkynylation

New Journal of Chemistry

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General remarks:

Chemical and Instrument: All of the reagents purchased were of AR grade and used without further purification. All reactions were monitored by TLC over silica gel plate. The spots on TLC plates were visualized under UV lamp or by iodine vapors. The melting points were determined in capillary tubes on a hot stage apparatus containing silicon oil and are uncorrected. IR spectra were recorded using Perkin-Elmer's Spectrum RX I FTIR spectrophotometer as KBr disc. ^{1}H NMR, ^{13}C NMR spectra were recorded on Bruker Avance DPX-300 MHz or Avance DPX-200 MHz FT Bruker spectrometers, at 27^{o}C using deuteriated solvents and TMS as an internal standard. Data expresses the chemical shift values in δ ppm from downfield to upfield in both ^{1}H NMR and ^{13}C NMR spectra. For all compounds, ^{1}H NMR data is reported in the following order: Chemical shift (multiplicity, number of protons, *J* value, and nature of proton). ESMS mass spectra were recorded on Thermo LCQ advantage ion trap mass spectrometer (USA).

General procedure for the synthesis of 5-6: A mixture of CuI (0.01 mmol) in water (5 mL) was degassed under reduced pressure then nitrogen gas was introduced and after that the mixture was refluxed for 30 min. To this solution piperidine / morpholine (1.5 mmol), Formyl ferrocene (1.0 mmol) and Phenylacetylene (1.2 mmol) was, added and the resulting mixture was refluxed. After completion of the reaction as indicated on TLC, solvent was evaporated and residue was extracted with $CHCl_3$ and water. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated under vacuum to yield an oily residue. The residue was purified by column chromatography over basic Al_2O_3 using hexanes-EtOAc as eluent to obtain the required products in good yield.

General procedure for the synthesis of (2-Formyl-1-chlorovinyl) ferrocene (8)[1]: To 25 mL (0.32 mol) anhyd DMF, 25 mL (0.27 mol) of phosphorus oxychloride was added at 0°C. The resulting viscous, red mixture is transferred to the dropping funnel and added to a magnetically stirred mixture of acetylferrocene 22.8 g (0.1 mol) in anhyd DMF 25 mL (0.32 mol) dropwise over 30 minutes cooled at 0°C. The mixture was stirred at 0°C for 2h during which the colour of the reaction mixture changes from dark brown to olive and ultimately to deep blue. Then 75 mL of diethyl ether is added, and the viscous mixture is stirred vigorously for several minutes. At 0°C, 116 g (0.85 mol) of sodium acetate trihydrate is cautiously added to the reaction mixture in one portion followed by addition of 10 mL of water with vigorous stirring. After 1h, an additional 10 mL of ether is added, and stirring is continued for 3h at rt to ensure complete quenching. After complete quenching, the mixture was diluted with H_2O and extracted with $CHCl_3$. The combined organic phases are carefully washed twice with saturated aqueous sodium

bicarbonate solution and then with water. The combined organic layers was dried over Na_2SO_4, filtered, and concentrated using a rotary evaporator to afford 25.6 g (89%) of (2-formyl-1-chlorovinyl) ferrocene as deep purple crystals after drying under high vacuum.

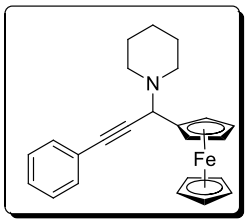
General procedure for the synthesis of ethynyl ferrocene (9)[1]: 2-formyl-1-chlorovinyl ferrocene 26.0 g (95.0 mmol) in 300 mL of anhydrous 1,4-dioxane was refluxed for 5 min. After 5 min of reflux 250 mL of 1N solution of sodium hydroxide (2.5-fold excess) is cautiously added as rapidly as possible in one portion and the reaction was continued at same temperature for 0.5h. After completion of the reaction, the reaction mixture was cooled and poured into ice and neutralized with 1N hydrochloric acid diluted with CH_2Cl_2 and extracted with water. Organic extracts was successively washed twice with saturated aqueous sodium bicarbonate solution and water. The organic phase was dried over Na_2SO_4, filtered. The filtrate was evaporated using a rotary evaporator to afford the orange residue of crude ethynyl ferrocene which was further purified by column chromatography over silica gel using hexane as eluent to yield 75% of pure ethynyl ferrocene which was crystallized to an orange solid.

General procedure for the synthesis of (11-20)

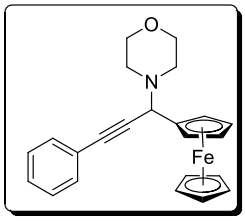
A mixture of CuI (0.01 mmol) in acetonitrile (5 mL) was degassed under reduced pressure then nitrogen gas was introduced and after that the mixture was refluxed for 30 min. To this piperidine / morpholine (1.5 mmol), aldehydes (1.0 mmol) and ethynyl ferrocene (1.0 mmol) was, added and the resulting mixture was refluxed for 2h. After completion of the reaction as indicated on TLC, reaction mixture was extracted with $CHCl_3$ and water. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated under vacuum to yield an oily residue. The residue was purified by column chromatography over basic Al_2O_3 using hexanes-EtOAc as eluent to obtain the required products **11-20** in good yield.

Characterization data of all the compounds:

1-(1-Ferrocenyl-3-phenylprop-2-ynyl)piperidine (5): 92% as yellow solid, mp:153-155°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 7.47 (d, J = 3.2Hz, 2H, ArH), 7.27 (d, J = 3.2Hz, 3H, ArH), 4.56(s, 1H, CH), 4.38(s, 1H, Fc-H), 4.24 (s, 1H, Fc-H) 4.12-4.08 (m, 7H, Fc-H), 2.46 (s, 4H, 2xCH_2), 1.50-1.48 (m, 4H, 2xCH_2), 1.32-1.30 (m, 2H, CH_2); MS (ESI$^+$) *m/z*: = 384.1 $(M+H)^+$ ESI-HR-MS: *m/z*: = 384.1520 calcd. for $C_{24}H_{25}FeN$ $[MH]^+$: 384.1415.

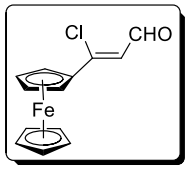


1-(1-Ferrocenyl-3-phenylprop-2-ynyl)morpholine (6):

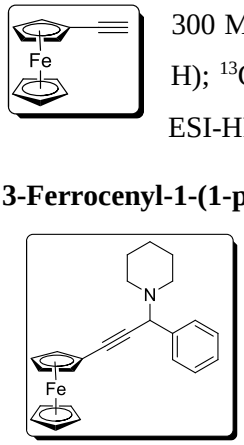


91% as yellow solid; mp 158-165°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 7.57 (d, J = 6.9Hz, 2H, ArH), 7.32-7 23(m, 3H, ArH), 4.64 (s, 1H, CH), 4.40 (s, 2H, Fc-H), 4.15 (s, 7H, Fc-H) 3.68 (s, 4H, 2xCH_2), 2.56 (s, 4H, 2xCH_2); MS (ESI$^+$) *m/z*: = 386.1 (M+H)$^+$ ESI-HR-MS: *m/z*: = 386.1189 calcd. for $C_{23}H_{23}FeNO$ [MH]$^+$: = 386.1207.

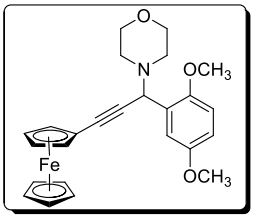
(2-Formyl-1-chlorovinyl) ferrocene (8): 89% as deep purple crystals; mp 76-77°C; IR (KBr) 2851, 1671 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 10.1 (d, J = 7.2Hz, 1H, CHO), 6.42 (d, J = 7.2Hz, 1H, =CH), 4.76 (t, J = 1.7Hz, 2H, Fc-H), 4.58 (d, J = 1.7Hz, 2H, Fc-H), 4.25 (s, 5H, Fc-H); ^{13}C NMR ($CDCl_3$, 50MHz) δ = 190.8, 155.3, 120.3, 80.1, 72.3, 70.8, 68.9, 29.7; MS (ESI$^+$) *m/z*: = 275.0 (M+H)$^+$ ESI-HR-MS: *m/z*: = 274.9906 calcd. for $C_{13}H_{11}FeClO$ [MH]$^+$: = 274.9926.



Ethynylferrocene (9): 75% as orange solid; mp 53-55°C; IR (KBr) 3311, 2112 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 2.71 (s, 1H, CH), 4.19 (m, 2H, Fc-H), 4.21 (s, 5H, Fc-H), 4.46 (m, 2H, Fc-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 63.5, 68.3, 69.6, 71.2; MS (ESI$^+$) *m/z*: = 211.0 (M+H)$^+$ ESI-HR-MS: *m/z*: = 211.0223 calcd. for $C_{12}H_{10}Fe$ [MH]$^+$: = 211.0210.

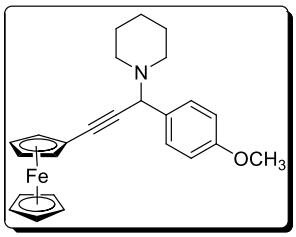


3-Ferrocenyl-1-(1-phenyl,prop-2-ynyl)piperidine (11): 87% as yellow solid; mp 158-160°C; ^{1}H NMR ($CDCl_3$, 300MHz) δ = 7.60 (q, J = 5.6Hz, 2H, ArH), 7.05 (t, J = 8.6Hz, 3H, ArH), 4.64 (s, 1H, CH), 4.46 (s, 2H, Fc-H), 4.22-4.19 (m, 7H, Fc-H), 2.51 (s, 4H, 2xCH_2), 1.61-1.44 (m, 6H, 3xCH_2); MS (ESI$^+$) *m/z*: = 384.1 (M+H)$^+$ ESI-HR-MS: *m/z*: = 384.1425 calcd. for $C_{24}H_{25}FeN$ [MH]$^+$: = 384.1415

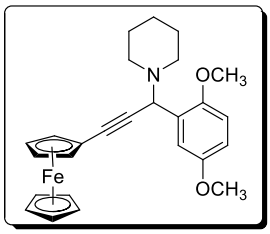


1-(1-2,5-Dimethoxyphenyl,3-ferrocenylprop-2-ynyl)morpholine (12) 76% as yellow solid; mp 160-167°C; ^{1}H NMR ($CDCl_3$, 300MHz) δ = 7.19 (d, J = 6.3Hz, 1H, ArH), 6.80 (t, J = 8.7Hz, 2H, ArH), 4.97 (s, 1H, CH), 4.36 (d, J = 1.5Hz, 2H, Fc-H), 4.12-4.10 (m, 7H, Fc-H), 3.76 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 3.66 (s, 4H, 2xCH_2), 2.69-2.63 (m, 4H, 2xOCH_2); ^{13}C NMR ($CDCl_3$, 50MHz) δ = 148.3, 140.8, 134.6, 129.2, 123.5, 122.8, 88.6, 79.2, 71.7, 71.6, 70.0, 68.9, 67.1, 64.3, 61.5, 49.8; MS (ESI$^+$) *m/z*: = 446.1 (M+H)$^+$ ESI-HR-MS: *m/z*: = 446.1423 calcd. for $C_{25}H_{27}FeNO_3$ [MH]$^+$: = 446.1419

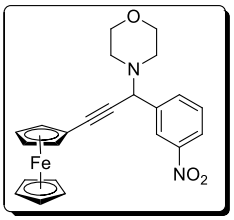
3-Ferrocenyl-1-(1-4-methoxyphenyl, prop-2-ynyl) piperidine (13) : 78% as yellow solid; mp 168-170°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 7.53 (d, J = 8.4Hz, 2H, ArH), 6.90 (d, J = 8.6Hz, 2H, ArH), 4.62 (s, 1H, CH), 4.45 (s, 2H, Fc-H), 4.22-4.18 (m, 7H, Fc-H), 3.81 (s, 3H, OCH_3), 2.52 (s, 4H, 2xCH_2), 1.59-1.43 (m, 6H, 3xCH_2); ^{13}C NMR ($CDCl_3$, 50MHz) δ = 159.0, 131.1, 129.7, 113.4, 85.8, 82.4, 71.6, 71.6, 69.9, 68.5, 65.7, 62.0, 55.3, 50.7, 26.3, 24.7; MS (ESI$^+$) *m/z*: = 414.1 $(M+H)^+$ ESI-HR-MS: *m/z*: = 414.1529 calcd. for $C_{25}H_{27}FeNO$ $[MH]^+$: = 414.1520.



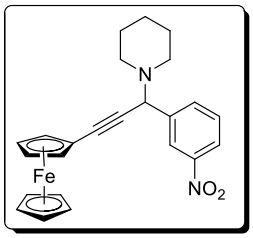
1-(1-2,5-Dimethoxyphenyl,3-ferrocenylprop-2-ynyl)piperidine (14): 75% as yellow solid; mp 155-160°C; ^{1}H NMR ($CDCl_3$, 300MHz) δ = 7.24 (d, J = 5.8Hz, 1H, ArH), 6.85-6.77 (m, 2H, ArH), 5.03 (s, 1H, CH), 4.42 (s, 2H, Fc-H), 4.19-4.15 (m, 7H, Fc-H), 3.81 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 2.62-2.57 (m, 4H, 2xCH_2), 1.58 (s, 4H, 2xCH_2), 1.40 (s, 2H); ^{13}C NMR ($CDCl_3$, 75MHz) δ = 153.4, 151.8, 128.6, 116.6, 113.2, 113.0, 84.4, 83.6, 71.6, 71.6, 69.9, 68.5, 65.8, 57.2, 55.9, 55.7, 51.0, 29.8, 26.2, 24.6; MS (ESI$^+$) *m/z*: = 444.1 $(M+H)^+$ ESI-HR-MS: *m/z*: = 444.1635 calcd. for $C_{26}H_{29}FeNO_2$ $[MH]^+$: = 444.1626.



3-Ferrocenyl-1-(1-3-nitrophenyl,prop-2-ynyl)morpholine (15): 90% as yellow solid; mp 150-155°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 8.49 (s, 1H, ArH), 8.11 (d, J = 7.3Hz, 1H, ArH), 7.94 (d, J = 7.1Hz, 1H, ArH), 7.50 (t, J = 7.9Hz, 1H, ArH), 4.71 (s, 1H, CH), 4.43 (s, 2H, Fc-H), 4.18 (s, 7H, Fc-H) 3.68 (s, 4H, 2xCH_2), 2.56 (t, J = 4.1Hz, 4H, 2xCH_2); MS (ESI$^+$) *m/z*: = 431.1 $(M+H)^+$ ESI-HR-MS: *m/z*: = 431.1038 calcd. for $C_{23}H_{22}FeN_2O_3$ $[MH]^+$: = 431.1058.

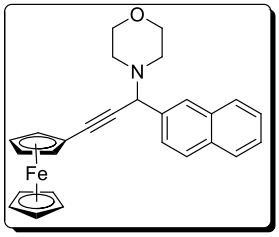


3-Ferrocenyl-1-(1-3-nitrophenyl,prop-2-ynyl)piperidine (16):

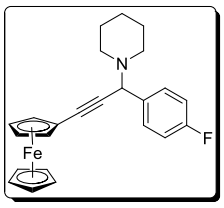


92% as yellow solid; mp 158-165°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 8.50 (s, 1H, ArH), 8.11 (d, J = 7.2Hz, 1H, ArH), 7.97 (s, 1H, ArH), 7.49 (d, J = 7.5Hz, 1H, ArH), 4.73 (s, 1H, CH), 4.43 (s, 2H, Fc-H), 4.18 (s, 7H, Fc-H), 2.48 (m, 4H, 2xCH_2), 1.56-1.41 (m, 6H, 2xCH_2); ^{13}C NMR ($CDCl_3$, 50MHz) δ = 148.3, 141.8, 134.6, 129.0, 123.4, 122.6, 87.8, 80.2, 71.7, 70.0, 68.8, 64.8, 61.9, 50.8, 29.8, 26.2, 24.4; MS (ESI$^+$) *m/z*: = 429.1 $(M+H)^+$ ESI-HR-MS: *m/z*: = 429.1279 calcd. for $C_{24}H_{24}FeN_2O_2$ $[MH]^+$: = 429.1265.

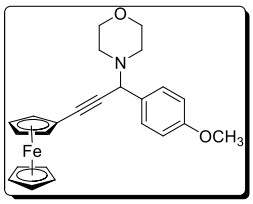
1-(1-(Naphthalen-2-yl)-3-ferrocenylprop-2-ynyl)morpholine (17): 82% as yellow solid; mp 130-135°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 8.40 (d, J = 7.9Hz, 1H, ArH), 7.90-7.80 (m, 3H, ArH), 7.56-7.43 (m, 3H, ArH), 5.29 (s, 1H, CH), 4.48 (d, J = 1.8Hz, 2H, Fc-H), 4.21 (s, 8H, Fc-H), 3.70-3.64 (m, 4H, 2xCH_2), 2.70-2.68 (m, 4H, 2xCH_2); MS (ESI$^+$) *m/z*: = 436.1 (M+H)$^+$ ESI-HR-MS: *m/z*: = 436.1368 calcd. for $C_{27}H_{25}FeNO$ [MH]$^+$: = 436.1364.



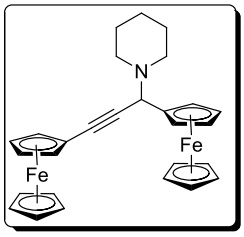
1-(1-4-Fluorophenyl,3-ferrocenylprop-2-ynyl)piperidine (18) : 89% as yellow solid; mp 138-145°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 7.63(d, 2H, ArH), 7.38(t, J=3.6Hz, 2H, ArH), 4.68(s, 1H, CH), 4.46(s, 2H, Fc-H), 4.22-4.19(m, 8H, Fc-H) 2.54(s, 4H, CH_2), 1.65-1.59(m, 4H, CH_2), 1.46(d, 2H, CH_2); MS (ESI$^+$) *m/z*: = 402.1 (M+H)$^+$ ESI-HR-MS: *m/z*: = 402.1329 calcd. for $C_{24}H_{24}FeNF$ [MH]$^+$: = 402.1320



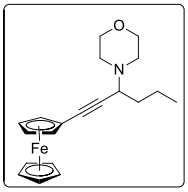
3-Ferrocenyl-1-(1-4-Methoxyphenyl,prop-2-ynyl)morpholine (19): 79% as yellow solid; mp 148-155°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 7.53 (d, J = 8.6Hz, 2H, ArH), 6.91 (d, J = 8.6Hz, 2H, ArH), 4.61 (s, 1H, CH), 4.45 (d, J = 1.3Hz, 2H, Fc-H), 4.21-4.19 (m, 7H, Fc-H), 3.81 (s, 3H, OCH_3), 3.72 (d, J = 3.8Hz, 4H, 2xCH_2), 2.60 (d, J = 3.2Hz, 4H, 2xCH_2); ^{13}C NMR ($CDCl_3$, 50MHz) δ = 159.3, 130.39, 129.86, 113.65, 86.65, 81.54, 72.25, 71.68, 70.30, 69.97, 69.38, 68.70, 67.35, 65.35, 61.72, 55.45, 49.94; MS (ESI$^+$) *m/z*: = 416.1 (M+H)$^+$ ESI-HR-MS: *m/z*: = 416.1333 calcd. for $C_{24}H_{25}FeNO_2$ [MH]$^+$: = 416.1313.



1-(1-Ferrocenyl,3-ferrocenylprop-2-ynyl)piperidine (20): 84% as yellow solid; mp 160-165°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 4.53- 4.09 (m, 19H, CH and FcH), 2.45 (s, 4H, 2xCH_2), 1.50 (s, 4H, 2xCH_2), 1.31(s, 2H, CH_2); ^{13}C NMR ($CDCl_3$, 50MHz) δ = 84.8, 83.4, 83.1, 73.3, 71.5, 71.5, 69.9, 69.7, 69.4, 69.4, 69.3, 68.5, 68.2, 67.6, 66.0, 59.1, 50.3, 29.8, 26.0, 24.5; MS (ESI$^+$) *m/z*: = 492.1 (M+H)$^+$ ESI-HR-MS: *m/z*: = 492.1057 calcd. for $C_{28}H_{29}Fe_2N$ [MH]$^+$: = 492.1077.



3-Ferrocenyl-1-(1-butyl,3-prop-2-ynyl)morpholine (21): 92% as yellow solid; mp 155-158°C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ = 4.38-4.37 (M, 2H, Fc-H), 4.18-4.15 (m, 7H, Fc-H), 3.76-3.75 (m, 4H, 2xCH_2), 3.41-3.38 (m, 1H, CH), 2.71-2.69 (m, 2H, CH_2), 2.56-2.53 (m, 2H, CH_2); 1.67-1.42 (m, 4H, 2xCH_2), 0.97-0.94 (m, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 50MHz) δ = 84.18, 83.15, 71.53, 71.47, 69.91, 68.49, 67.24, 65.54, 57.97, 50.05, 35.25, 19.87, 13.34.



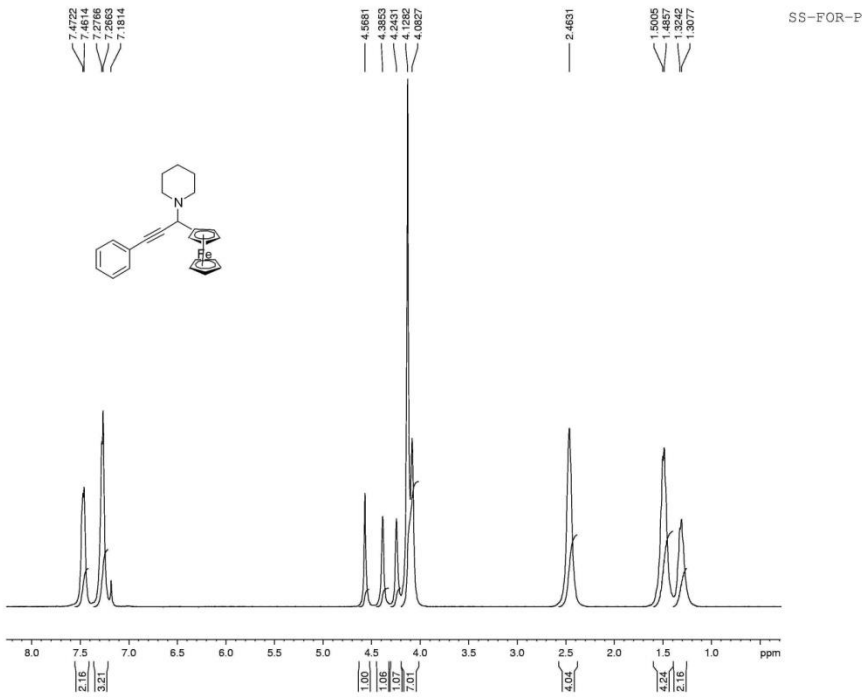


Figure 1. ^{I}H NMR spectra of 5

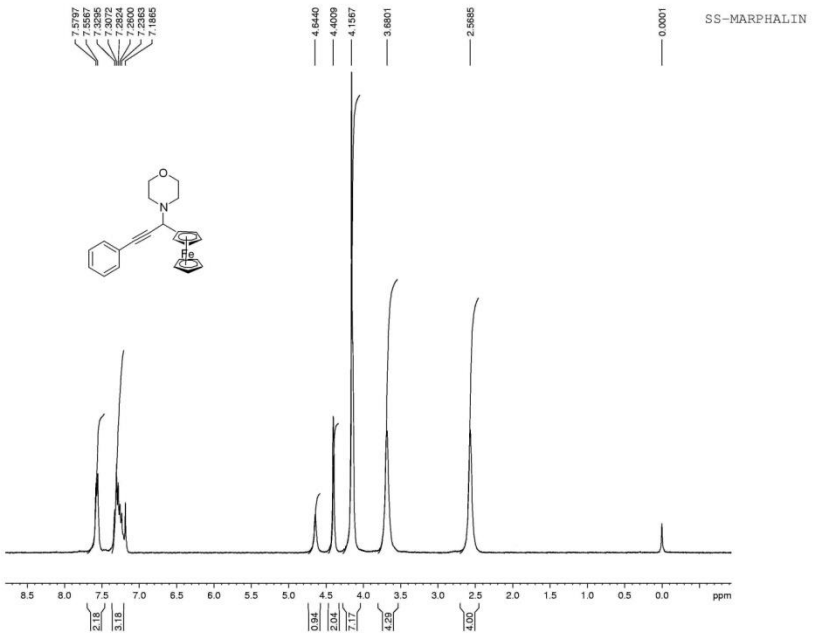


Figure 2. ^{I}H NMR spectra of 6

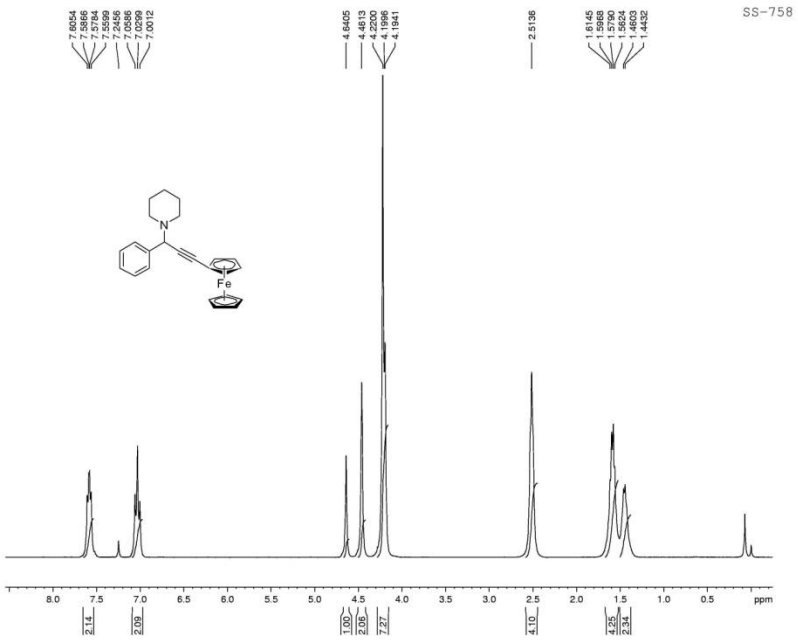


Figure 3. ^{I}H NMR spectra of 11

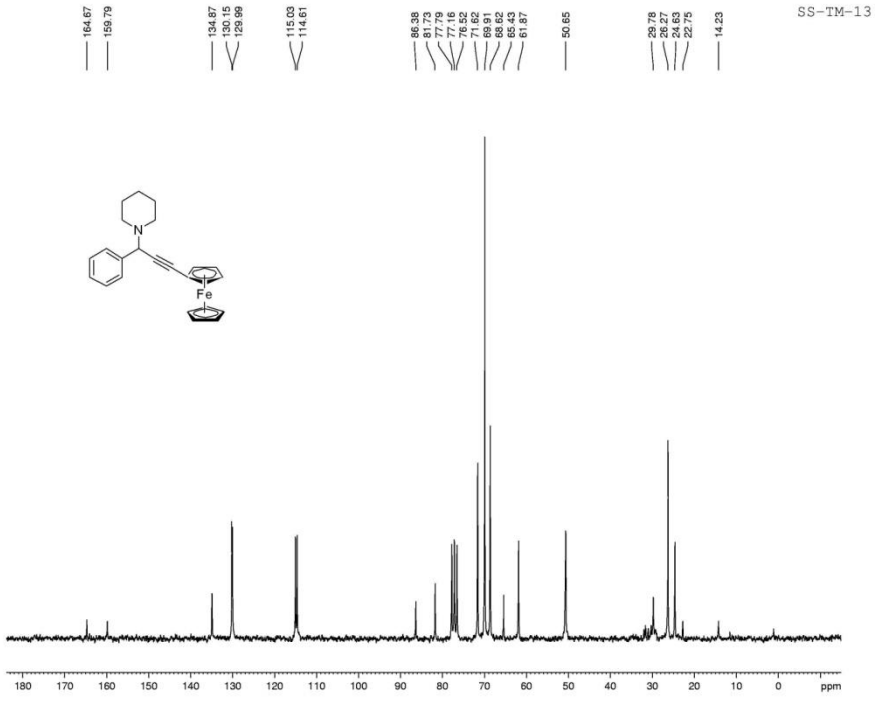


Figure 4. ^{I3}C NMR spectra of 11

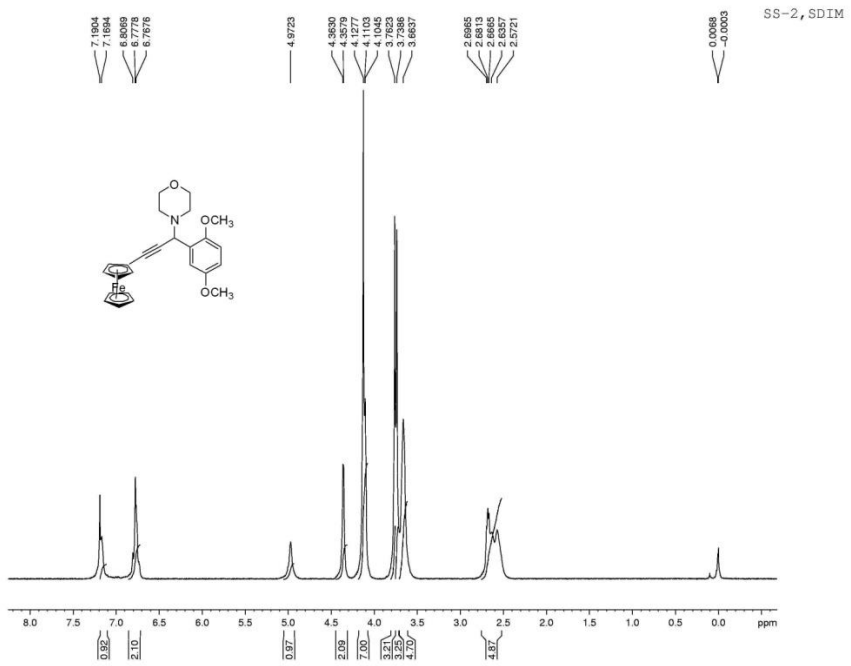


Figure 5. ^{1}H NMR spectra of 12

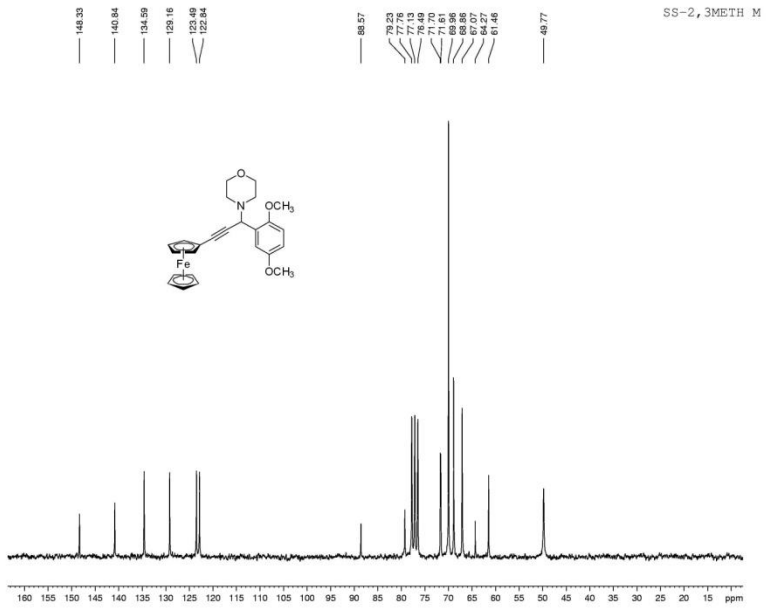


Figure 6. ^{13}C NMR spectra of 12

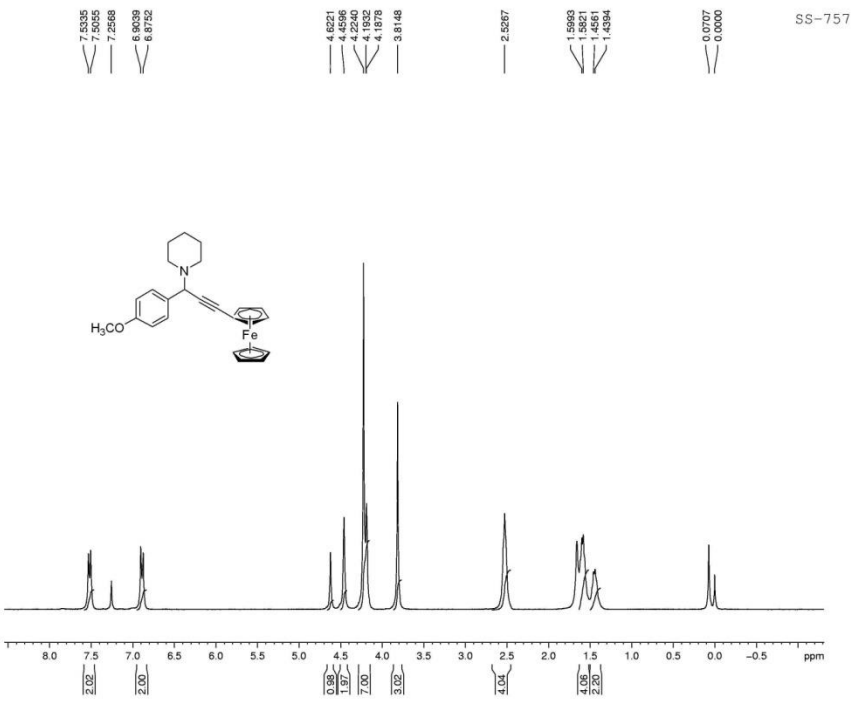


Figure 7. ^{1}H NMR spectra of 13

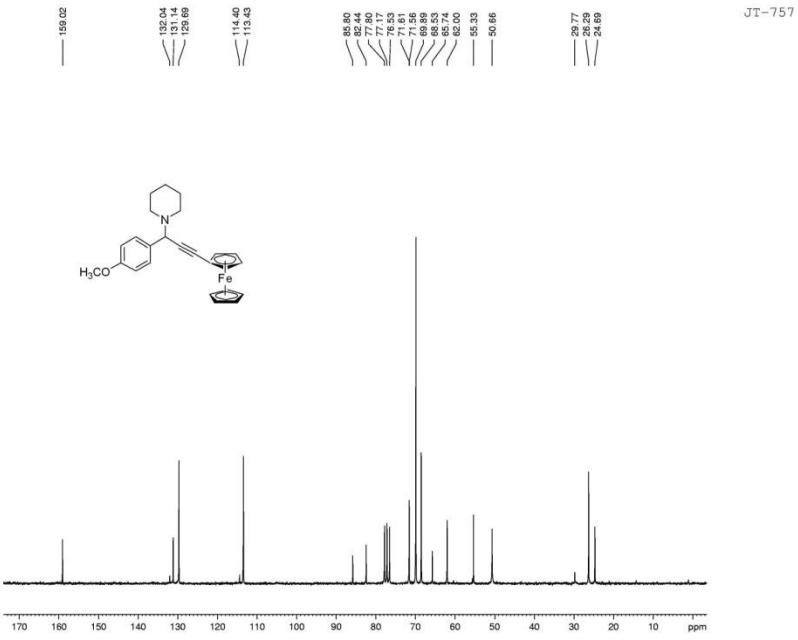


Figure 8. ^{13}C NMR spectra of 13

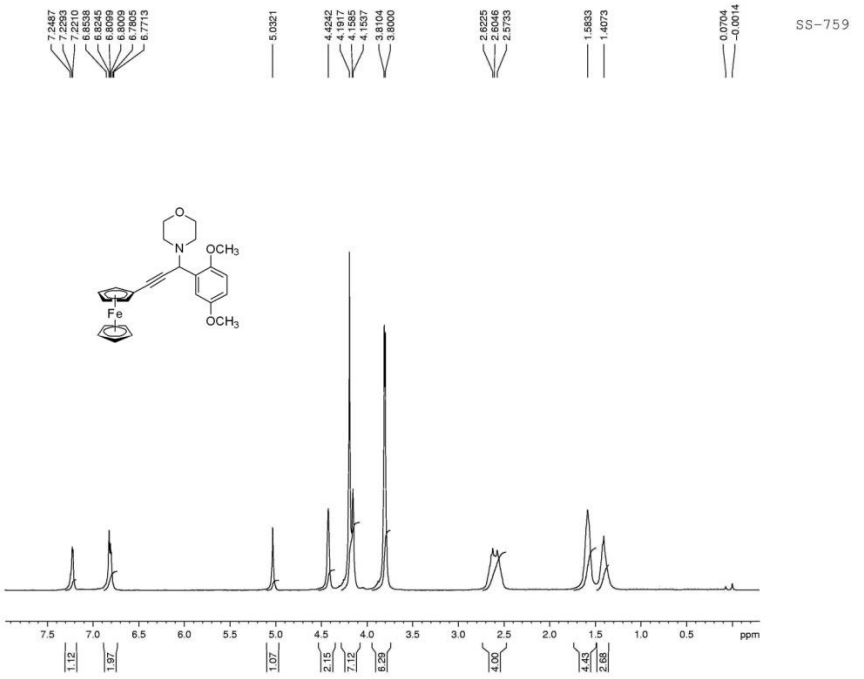


Figure 9. ^{I}H NMR spectra of 14

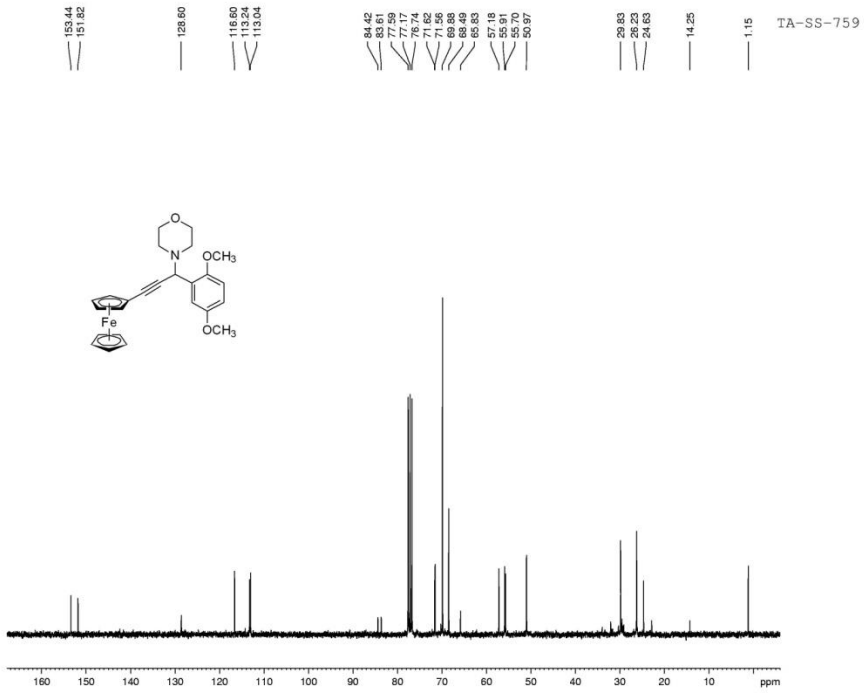


Figure 10. ^{I3}C NMR spectra of 14

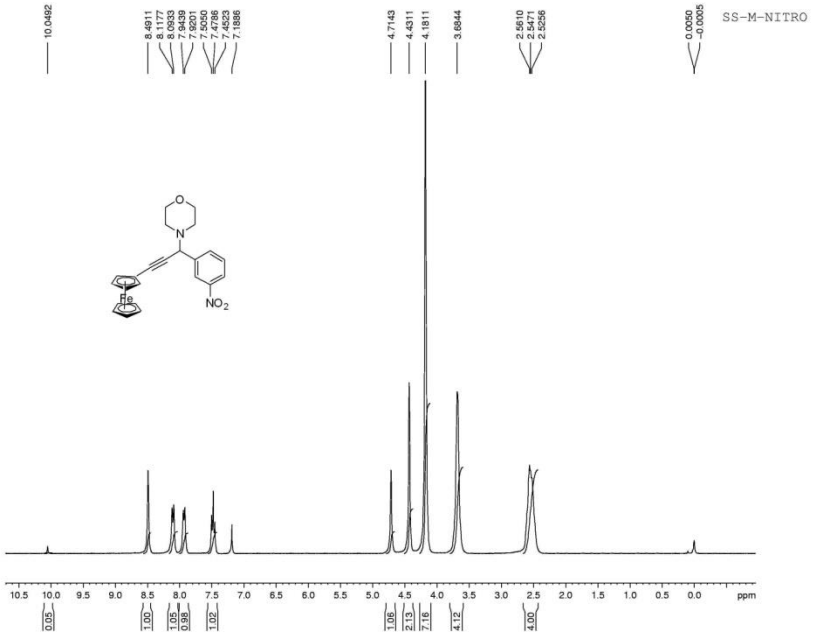


Figure 11. ^{I}H NMR spectra of 15

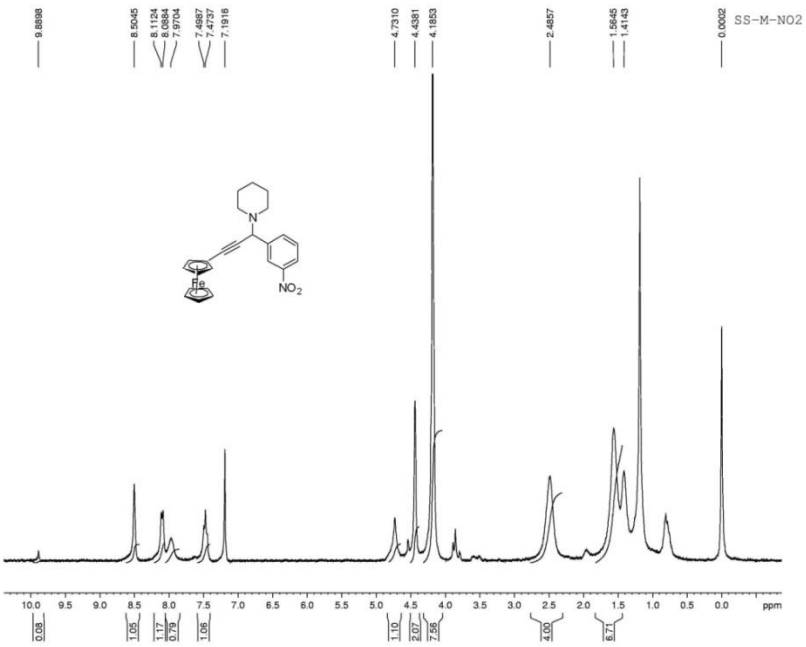


Figure 12. ^{I}H NMR spectra of 16

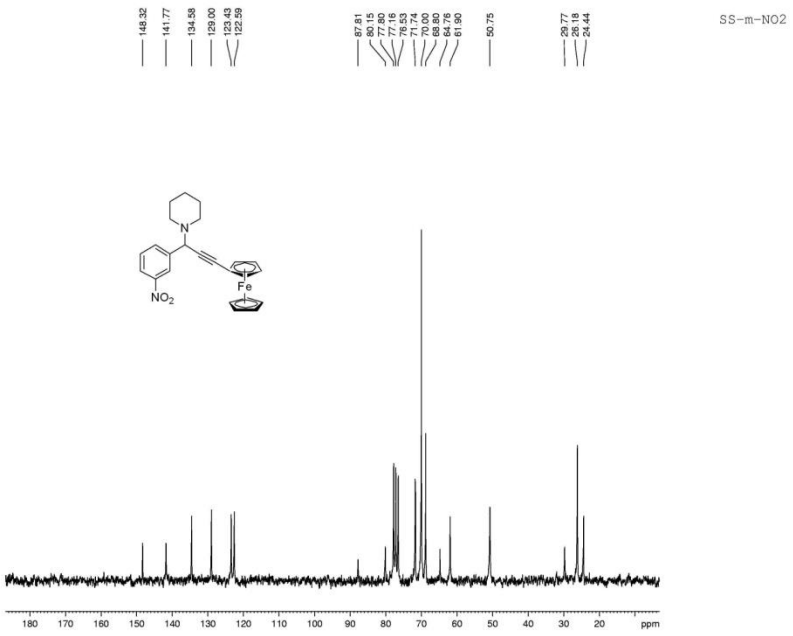


Figure 13. ^{I3}C NMR spectra of 16

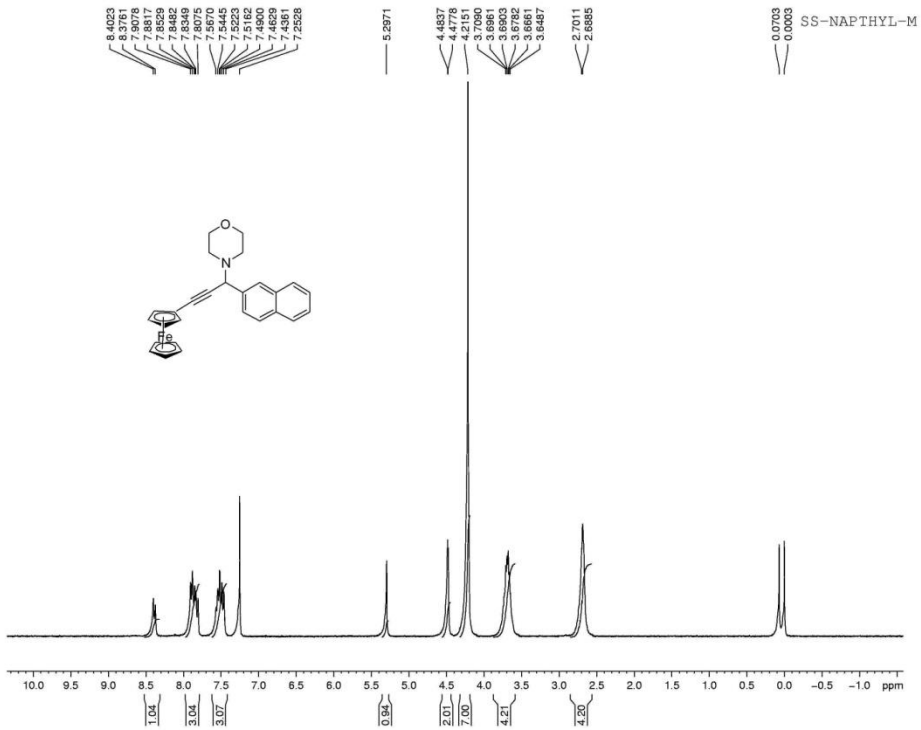


Figure 14. ^{I}H NMR spectra of 17

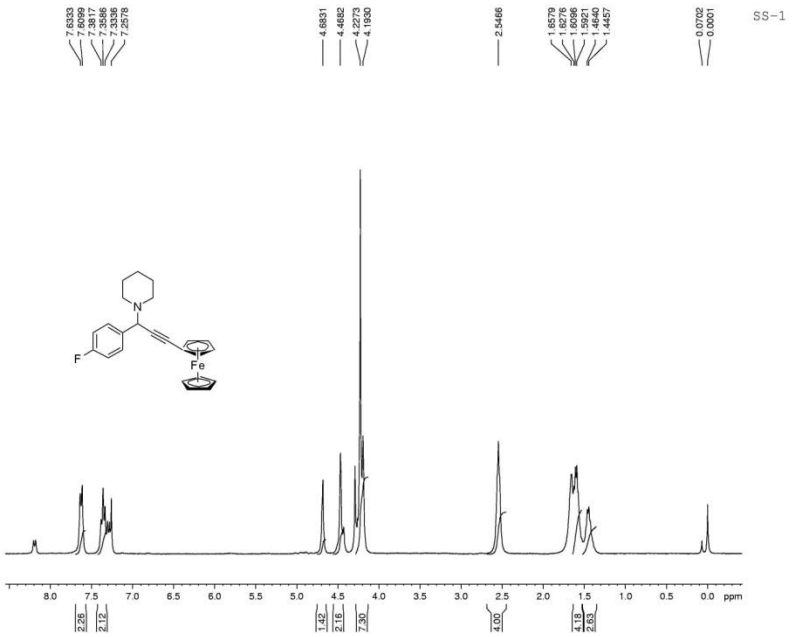


Figure 15. ^{I}H NMR spectra of 18

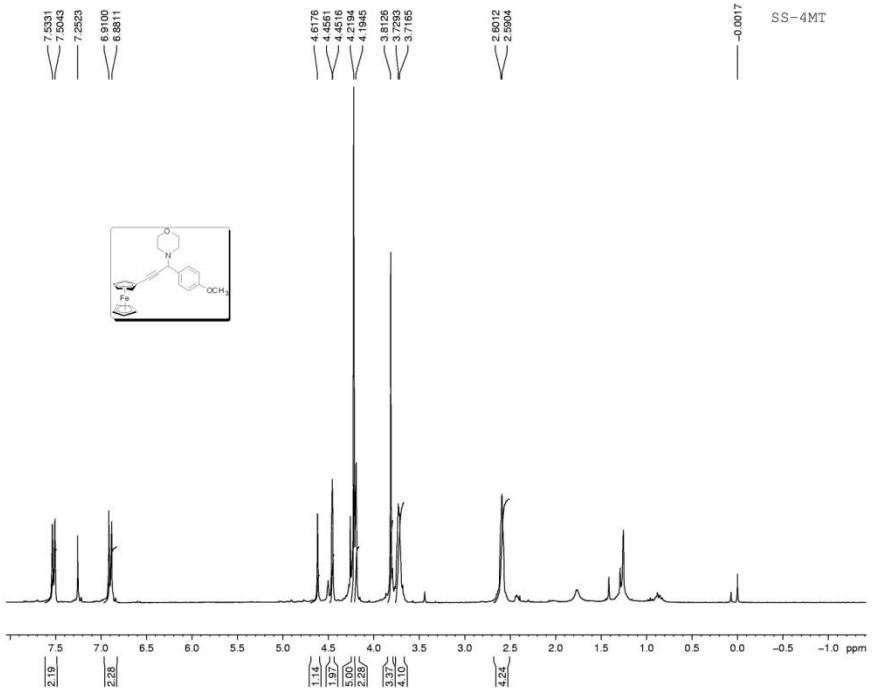


Figure 16. ^{I}H NMR spectra of 19

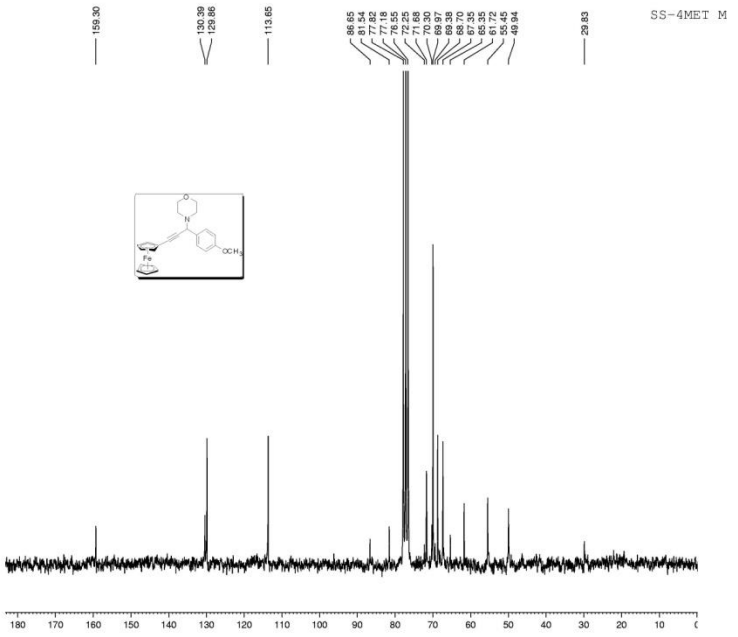


Figure 17. ^{13}C NMR spectra of 19

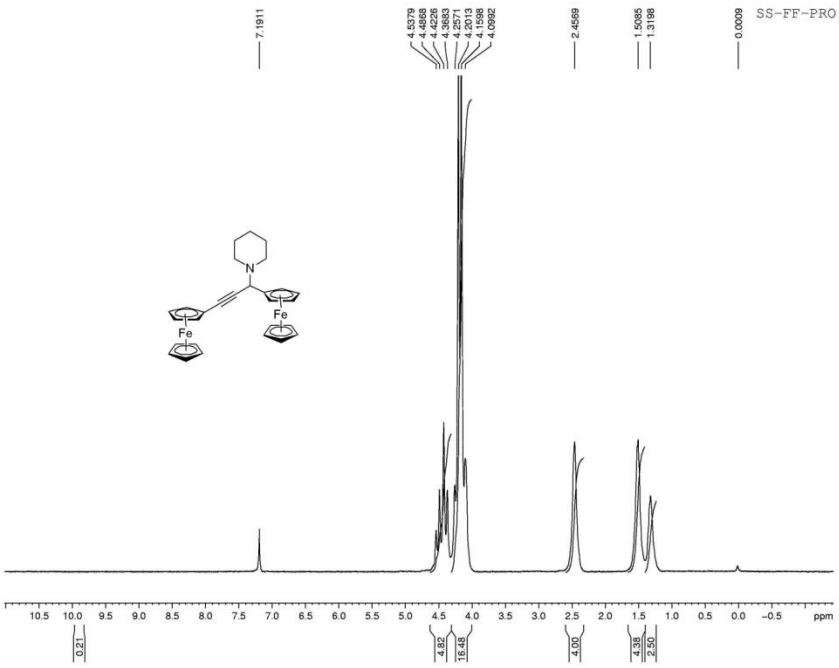


Figure 18. ^{1}H NMR spectra of 21

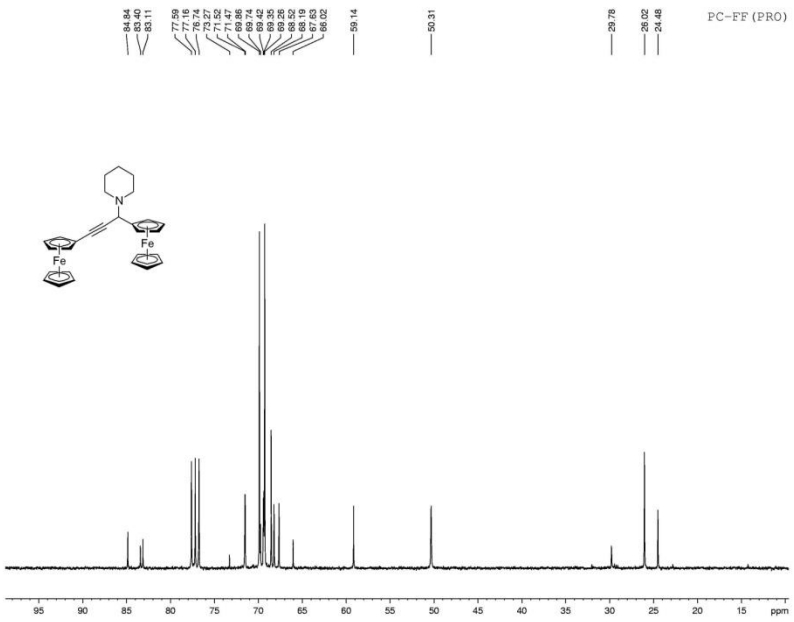


Figure 19. ^{13}C NMR spectra of 21

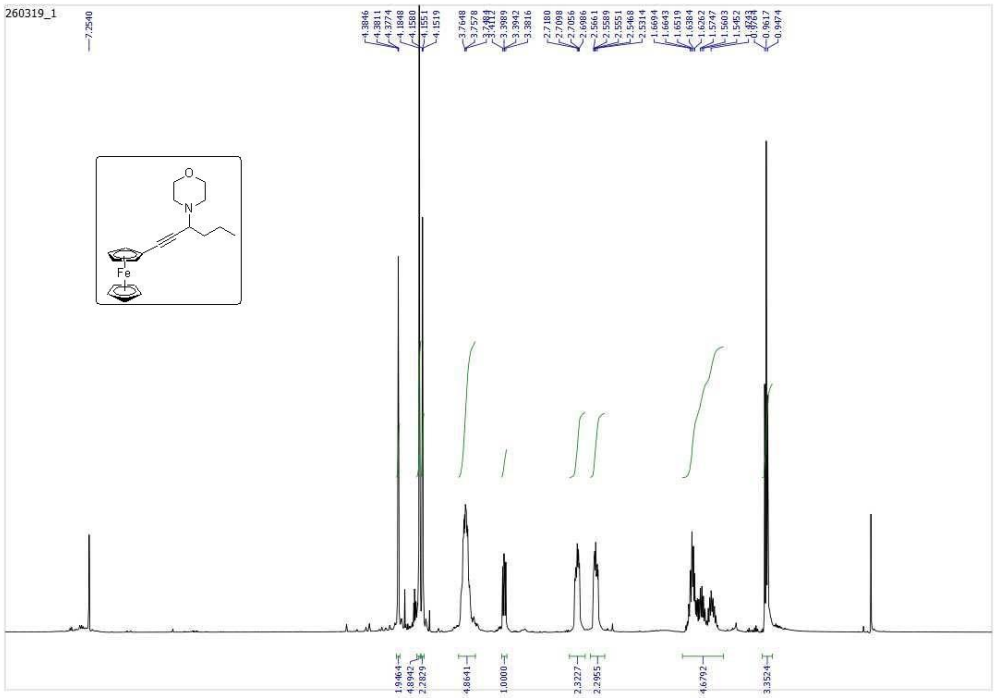


Figure 20. ^{1}H NMR spectra of 20

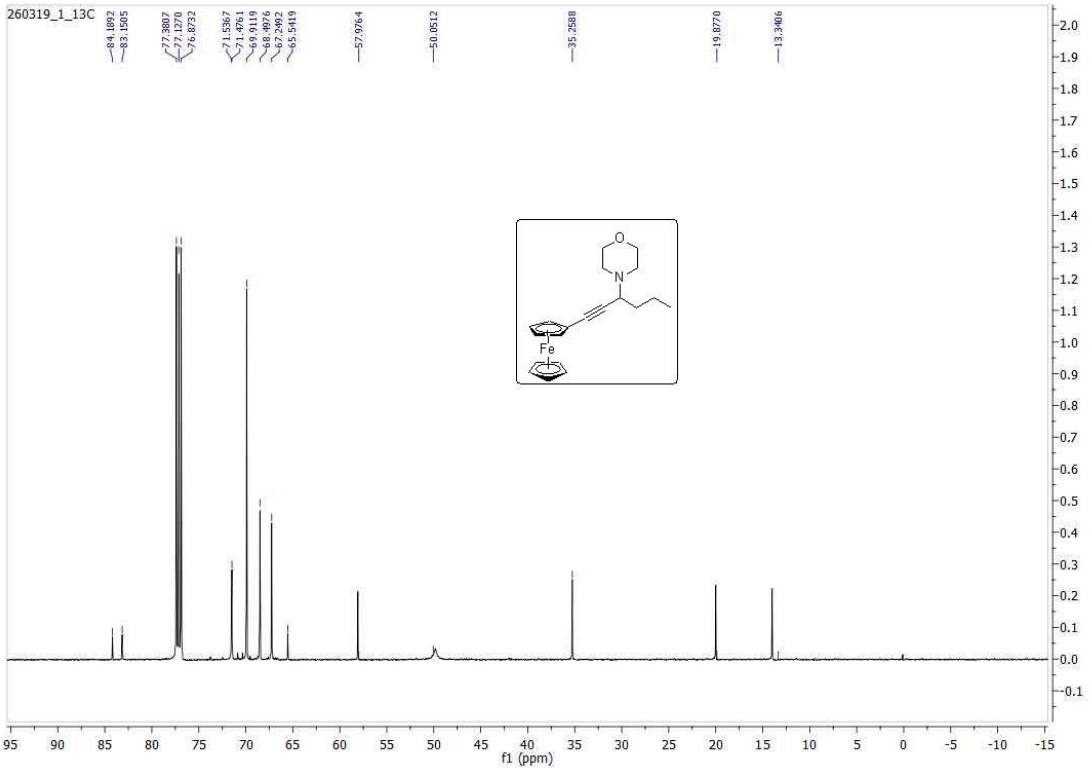


Figure 21. ^{13}C NMR spectra of 20

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1. Submitted by Johann Polin and Herwig Schottenberger. Checked by Bruce Anderson and Stephen F. Martin,. Organic Syntheses, Coll. Vol. 9, p.411 (1998); Vol. 73, p.262 (1996).