

Supporting Information

Asymmetric synthesis of hetero-1,2,3,4,5-pentasubstituted ferrocenes

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EXPERIMENTAL SECTION

General Considerations. Unless otherwise stated, all reactions were performed under an argon atmosphere with anhydrous solvents using Schlenk techniques. THF and Et₂O were distilled over sodium/benzophenone. Unless otherwise stated, all reagents were used without prior purification. 2,2,6,6-Tetramethylpiperidine (TMPPH) was distilled under vacuum over CaH₂ and was stored over KOH pellets. All organolithiated reagents were titrated before use.¹ Column chromatography separations were achieved on silica gel (40-63 μm). All Thin Layer Chromatographies (TLC) were performed on aluminum backed plates pre-coated with silica gel (Merck, Silica Gel 60 F254). They were visualized by exposure to UV light. Melting points were measured on a Kofler bench. IR spectra were taken on a Perkin-Elmer Spectrum 100 spectrometer. ¹H, ¹³C and ¹⁹F Nuclear Magnetic Resonance (NMR) spectra were recorded either (i) on a Bruker Avance III spectrometer at 300 MHz and 75.4 MHz, respectively, or (ii) Bruker Avance III HD at 400 MHz and 100 MHz, respectively. ¹H chemical shifts (δ) are given in ppm relative to the solvent residual peak and ¹³C chemical shifts are relative to the central peak of the solvent signal. Cp refers to the unsubstituted cyclopentadienyl ring of ferrocene. Optical rotations were recorded at 20 °C on a Perkin Elmer 341 polarimeter. Enantiomeric ratios (er) were determined by chiral HPLC on a ThermoFischer Ultimate 3000 apparatus. Racemic Ugi's amine ((±)-**7**) was prepared according to Šebesta and Ugi.² 2-Fluoro-1-iodo-3-(trimethylsilyl)ferrocene ((±)-**1**) was prepared according to Erb.³

Safety Considerations. Due to their pyrophoric character, BuLi reagents need to be used only under inert conditions (anhydrous, nitrogen or argon atmosphere) and by people well-trained to the manipulation of reactive organometallics. Due to the inherent dangers of using cryogenic temperatures, experiments should be performed by well-trained people.

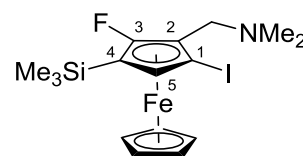
Crystallography. For (±)-**8**, (±)-**10**, (±)-**13**, (*R,S_p*)-**13**, (±)-**14**, (*R,S_p*)-**14**, the X-ray diffraction data were collected using D8 VENTURE Bruker AXS diffractometer at the temperature given in the crystal data. The samples were studied with monochromatized Mo-Kα radiation (λ = 0.71073 Å). The structure was solved by dual-space algorithm using the *SHELXT* program,⁴ and then refined with full-matrix least-square methods based on *F*² (*SHELXL*).⁵ All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions and treated as riding on their parent atom with constrained thermal parameters. The molecular diagrams were generated by MERCURY (version 3.9).

Experimental section.

(±)-2-(Dimethylaminomethyl)-3-fluoro-1-iodo-4-(trimethylsilyl)ferrocene ((±)-2)

*n*BuLi (1.4 M in hexane, 4.70 mL, 6.60 mmol, 1.10 equiv) was added dropwise to a solution of TMPH (1.12 mL, 932 mg, 6.60 mmol, 1.10 equiv) in THF (12.0 mL) at -15 °C. After addition, the reaction was stirred for 5 min at the same temperature before being cooled to -50 °C. After 5 min, compound (±)-**1** was added in one portion and the reaction mixture was stirred at -50 °C for 90 min. Eschenmoser's salt (1.22 g, 6.60 mmol, 1.10 equiv) was added in one portion and the reaction mixture was slowly warmed to rt. Aqueous K₂CO₃ solution (sat., 10 mL) was added and the reaction mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over MgSO₄, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO₂, using PET-EtOAc (70:30) with 1% of NEt₃ to give the title product as an orange oil (2.31 g, 84%).

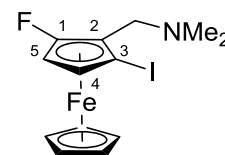
R_f (eluent: PET-EtOAc 70:30 with 5 drops of NEt₃ for 10 mL of eluent) = 0.50. ν_{\max} (film)/cm⁻¹ 2949, 2815, 2767, 1463, 1409, 1385, 1343, 1246, 1179, 1107, 1095, 1082, 1023, 972, 959, 837, 815, 755, 694. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 4.14 (s, 5H, Cp), 4.00 (d, *J* = 1.6 Hz, 1H, H5), 3.65 (d, *J* = 13.2 Hz, 1H, CHH), 3.35 (d, *J* = 13.2 Hz, 1H, CHH), 2.27 (s, 6H, N(CH₃)₂), 0.27 (s, 9H, Si(CH₃)₃). ¹³C NMR (75.4 MHz, CDCl₃): δ (ppm) 136.8 (d, *J* = 273.5 Hz, C3), 75.2 (d, *J* = 14.7 Hz, C2), 73.1 (s, Cp), 71.1 (d, *J* = 6.4 Hz, C5), 61.3 (d, *J* = 21.4 Hz, C4), 55.7 (d, *J* = 3.3 Hz, CH₂), 45.5 (s, N(CH₃)₂), 43.2 (s, C1), -0.3 (s, Si(CH₃)₃). ¹⁹F NMR (282 MHz, CDCl₃): δ (ppm) -181.3. Mass: 459 [M], 415 [M-N(CH₃)₂], 289 [M-I-N(CH₃)₂+H]. Anal. Calcd for C₁₆H₂₃FFeINSi: C, 41.85; H, 5.05; N, 3.05. Found: C, 42.07; H, 5.05; N, 3.35.



(±)-2-(Dimethylaminomethyl)-1-fluoro-3-iodoferrocene ((±)-3)

TBAF (1.0 M in THF, 10.7 mL, 10.7 mmol, 2.50 equiv) was added dropwise to a solution of (±)-**2** (2.00 g, 4.30 mmol, 1.00 equiv) in THF (10.0 mL) at rt. After 5 min, water (10 mL) was added and the reaction mixture was extracted with EtOAc (2 x 20 mL). The combined organic layers were dried over MgSO₄, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO₂, using PET-EtOAc (75:25 to 70:30) with 1% of NEt₃ to give the title product as an orange oil (1.48 g, 89%).

R_f (eluent: PET-EtOAc 70:30 with 5 drops of NEt₃ for 10 mL of eluent) = 0.42. ν_{\max} (film)/cm⁻¹ 2938, 2816, 2768, 1449, 1410, 1371, 1274, 1256, 1179, 1147, 1105, 1015, 1001, 958, 952, 859, 820, 797. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 4.45 (t, *J* = 2.8 Hz, 1H, H5), 4.18 (s, 5H, Cp), 4.15 (dd, *J* = 0.9, 2.2 Hz, 1H, H4), 3.62 (d, *J* = 13.2 Hz, 1H, CHH), 3.38 (d, *J* = 13.2 Hz, 1H, CHH), 2.26 (s, 6H, N(CH₃)₂). ¹³C NMR (75.4 MHz, CDCl₃): δ (ppm) 133.0 (d, *J* = 275.6 Hz, C1), 73.3 (d, *J* = 12.6 Hz, C2), 73.0 (s, Cp), 66.7 (d, *J* = 3.4 Hz, C4), 57.3 (d, *J* = 15.8 Hz, C5), 55.7 (d, *J* = 3.3 Hz, CH₂), 45.3 (s, N(CH₃)₂), 40.7 (d, *J* = 1.5 Hz, C3). ¹⁹F NMR (282 MHz, CDCl₃): δ (ppm) -186.9. Mass: 387 [M], 343 [M-N(CH₃)₂], 217 [M-I-N(CH₃)₂]. Anal. Calcd for C₁₃H₁₅FFeIN: C, 40.35; H, 3.91; N, 3.62. Found: C, 40.47; H, 3.92; N, 3.87.

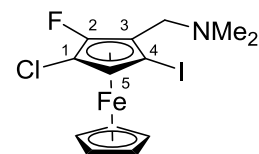


(±)-1-Chloro-3-(dimethylaminomethyl)-2-fluoro-4-iodoferrocene ((±)-4)

*n*BuLi (1.4 M in hexane, 2.70 mL, 3.81 mmol, 1.10 equiv) was added dropwise to a solution of TMPH (642 μ L, 538 mg, 3.81 mmol, 1.10 equiv) in THF (10.0 mL) at -15 °C. After addition, the reaction was stirred for 5 min at the same temperature before being cooled to -78 °C. After 5 min, the LiTMP solution was cannulated onto a solution of (±)-**3** (1.34 g, 3.46 mmol, 1.00 equiv) in THF (10.0 mL) at -78 °C. Quantitative transfer was ensured by washing the LiTMP Schlenk tube with THF (1.0 mL). After 1 h at -78 °C, a solution of hexachloroethane (901 mg, 3.81 mmol, 1.10 equiv) in THF (5.0 mL) was added to the reaction mixture which was slowly warmed to rt. Aqueous K₂CO₃ solution (sat., 10 mL) was added

and the reaction mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over MgSO₄, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO₂, using PET-EtOAc (75:25 to 70:30) with 1% of NEt₃ to give the title product as a red oil (1.26 g, 86%).

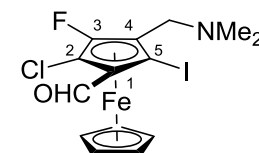
R_f (eluent: PET-EtOAc 70:30 with 5 drops of NEt₃ for 10 mL of eluent) = 0.39. ν_{\max} (film)/cm⁻¹ 2939, 2817, 2770, 1451, 1270, 1256, 1180, 1133, 1107, 1024, 1002, 942, 822, 689. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 4.51 (s, 1H, H5), 4.23 (s, 5H, Cp), 3.58 (d, *J* = 13.3 Hz, 1H, CHH), 3.32 (d, *J* = 13.3 Hz, 1H, CHH), 2.25 (s, 6H, N(CH₃)₂). ¹³C NMR (75.4 MHz, CDCl₃): δ (ppm) 129.4 (d, *J* = 279.6 Hz, C2), 81.6 (d, *J* = 15.9 Hz, C1), 75.2 (s, Cp), 71.9 (d, *J* = 11.7 Hz, C3), 67.4 (s, C5), 55.7 (d, *J* = 3.7 Hz, CH₂), 45.3 (s, N(CH₃)₂), 37.1 (s, C4). ¹⁹F NMR (282 MHz, CDCl₃): δ (ppm) -191.5. Mass: 421 [M], 377 [M-N(CH₃)₂]. Anal. Calcd for C₁₃H₁₄ClFFeIN: C, 37.05; H, 3.35; N, 3.32. Found: C, 37.73; H, 3.41; N, 3.68.



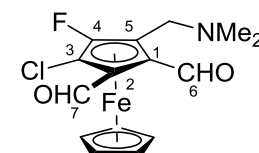
((±)-2-Chloro-4-(dimethylaminomethyl)-3-fluoro-5-iodoferrocenecarboxaldehyde ((±)-5) and ((±)-3-chloro-5-(dimethylaminomethyl)-4-fluoroferrrocene-1,2-dicarboxaldehyde ((±)-6)

*n*BuLi (1.4 M in hexane, 1.76 mL, 2.47 mmol, 1.10 equiv) was added dropwise to a solution of TMPH (418 μ L, 350 mg, 2.47 mmol, 1.10 equiv) in THF (6.6 mL) at -15 °C. After addition, the reaction was stirred for 5 min at the same temperature before being cooled to -78 °C. After 5 min, the LiTMP solution was cannulated onto a solution of ((±)-4 (948 mg, 2.25 mmol, 1.00 equiv) in THF (6.6 mL) at -78 °C. Quantitative transfer was ensured by washing the LiTMP Schlenk tube with THF (1.0 mL). After 1 h at -78 °C, dimethylformamide (192 μ L, 181 mg, 2.47 mmol, 1.10 equiv) was added and the reaction mixture was slowly warmed to 0 °C. Methanol (0.5 mL) was added and the reaction mixture was stirred for 15 min at rt. Volatiles were removed under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO₂, using PET-EtOAc (50:50 to 40:60) with 1% of NEt₃ to give ((±)-5 as a red oil (494 mg, 48%) and ((±)-6 as a red oil (69.0 mg, 8%). **Caution:** both compounds are sensitive and decompose upon exposure to air.

Compound ((±)-5. R_f (eluent: PET-EtOAc 50:50 with 5 drops of NEt₃ for 10 mL of eluent) = 0.46. ν_{\max} (film)/cm⁻¹ 2941, 2821, 2772, 1582, 1459, 1412, 1381, 1256, 1179, 1107, 1096, 1021, 909, 829, 776, 728. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 10.16 (s, 1H, CHO), 4.32 (s, 5H, Cp), 3.55 (d, *J* = 13.4 Hz, 1H, CHH), 3.46 (d, *J* = 13.3 Hz, 1H, CHH), 2.30 (s, 6H, N(CH₃)₂). ¹³C NMR (75.4 MHz, CDCl₃): δ (ppm) 193.3 (s, CHO), 131.5 (d, *J* = 281.6 Hz, C3), 82.3 (d, *J* = 15.4 Hz, C2), 76.7 (s, Cp), 74.4 (s, C4), 65.2 (s, C1), 55.2 (d, *J* = 3.4 Hz, CH₂), 45.4 (s, N(CH₃)₂), 38.9 (s, C5). ¹⁹F NMR (282 MHz, CDCl₃): δ (ppm) -184.2.



Compound ((±)-6. R_f (eluent: PET-EtOAc 50:50 with 5 drops of NEt₃ for 10 mL of eluent) = 0.28. ν_{\max} (film)/cm⁻¹ 2941, 2860, 2822, 2774, 1675, 1455, 1412, 1387, 1355, 1179, 1156, 1087, 1022, 1004, 911, 836, 729. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 10.52 (s, 1H, C₆HO), 10.41 (s, 1H, C₇HO), 4.46 (s, 5H, Cp), 4.05 (d, *J* = 13.0 Hz, 1H, CHH), 3.54 (d, *J* = 13.0 Hz, 1H, CHH), 2.29 (s, 6H, N(CH₃)₂). ¹³C NMR (75.4 MHz, CDCl₃): δ (ppm) 193.5 (s, CHO), 192.2 (s, CHO), 132.0 (d, *J* = 279.2 Hz, C4), 85.2 (d, *J* = 15.3 Hz, C3), 76.5 (s, FcC), 75.3 (s, Cp), 69.6 (s, FcC), 52.4 (d, *J* = 2.5 Hz, CH₂), 44.8 (s, N(CH₃)₂). One signal of FcC missing or overlapping. ¹⁹F NMR (282 MHz, CDCl₃): δ (ppm) -182.1.

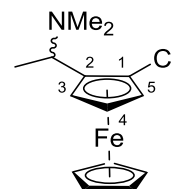


((±)-1-Chloro-2-(α,N,N-trimethylaminomethyl)ferrocene ((±)-8)

*s*BuLi (1.2 M in cyclohexane-hexane (92:8), 14.0 mL, 16.8 mmol, 1.40 equiv) was added dropwise to a solution of compound ((±)-7 (2.52 mL, 3.08 g, 12.0 mmol, 1.00 equiv) in Et₂O (45.0 mL) at 0 °C. After addition, the reaction was stirred for 1 h at the same temperature before being cooled to -78 °C. After 5 min, a solution of hexachloroethane (3.98 g, 16.8 mmol, 1.40 equiv) in THF (15 mL) was added and the reaction mixture was stirred at the same temperature for 15 min before being warmed to 0 °C. Aqueous

K₂CO₃ solution (sat., 30 mL) was added and the reaction mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over MgSO₄, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over neutralized SiO₂, using PET-EtOAc (80:20) with 2% of NEt₃ to give the title product as an orange solid (3.35 g, 96%).

R_f (eluent: PET-EtOAc 90:10 with 10 drops of NEt₃ for 10 mL of eluent, 2 developments on TLC plate first dipped into EtOAc-NEt₃ (50:50) and dried) = 0.55. Mp 50-52 °C. ν_{\max} (film)/cm⁻¹ 2977, 2937, 2824, 2780, 1448, 1393, 1370, 1282, 1255, 1169, 1104, 1072, 1042, 1000, 969, 826, 817, 809, 769, 721. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 4.42 (t, *J* = 1.9 Hz, 1H, H5), 4.16 (s, 5H, Cp), 4.65-4.07 (m, 2H, H3 and H4), 3.80 (q, *J* = 6.9 Hz, 1H, CH), 2.12 (s, 6H, N(CH₃)₂), 1.52 (d, *J* = 6.9 Hz, 3H, CH₃). ¹³C NMR (75.4 MHz, CDCl₃): δ (ppm) 92.7 (C1), 85.9 (C2), 71.0 (Cp), 67.6 (C5), 64.9 (C3 or C4), 64.4 (C3 or C4), 55.5 (CH), 41.2 (N(CH₃)₂), 17.1 (CH₃). Mass: 291 [M], 276 [M-CH₃], 247 [M-N(CH₃)₂], 220 [FcCl]. Anal. Calcd for C₁₄H₁₈ClFeN: C, 57.67; H, 6.22; N, 4.80. Found: C, 57.76; H, 6.26; N, 4.81.



Crystal data for (±)-8. C₁₄H₁₈ClFeN, *M* = 291.59, *T* = 150 K; monoclinic *P* 2₁/*n* (I.T.#14), *a* = 7.4438(13), *b* = 10.970(2), *c* = 16.145(3) Å, β = 94.234(7) °, *V* = 1314.7(4) Å³. *Z* = 4, *d* = 1.473 g.cm⁻³, μ = 1.326 mm⁻¹. A final refinement on *F*² with 3023 unique intensities and 133 parameters converged at ωR_F^2 = 0.0981 (*R_F* = 0.0402) for 2713 observed reflections with *I* > 2σ(*I*). CCDC 1920662.

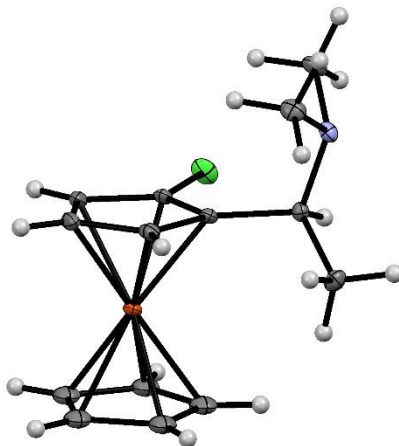


Figure 1. Molecular structure of compound (±)-8 (thermal ellipsoids shown at the 30% probability level).

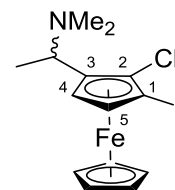
(*R,S_p*)-1-Chloro-2-(*α,N,N*-trimethylaminomethyl)ferrocene (*R,S_p*)-8

By following a similar protocol, starting from (*R*)-7 (2.52 mL, 3.08 g, 12.0 mmol, 1.00 equiv), the title product was obtained as an orange solid (3.23 g, 92%). Analytical data analogous to racemic compound. $[\alpha]_D +0.328$ (*c* 0.01 in CHCl₃).

(±)-2-Chloro-1-iodo-3-(*α,N,N*-trimethylaminomethyl)ferrocene ((±)-9)

*n*BuLi (1.3 M in hexane, 13.8 mL, 18.0 mmol, 3.00 equiv) was added dropwise to a solution of TMPH (3.04 mL, 2.54 g, 18.0 mmol, 3.00 equiv) in THF (40.0 mL) at -15 °C. After addition, the reaction was stirred for 5 min at the same temperature before being cooled to -35 °C. After 5 min, the LiTMP solution was cannulated onto a solution of (±)-8 (1.75 g, 6.00 mmol, 1.00 equiv) in THF (40.0 mL) at -35 °C. Quantitative transfer was ensured by washing the LiTMP Schlenk tube with THF (1.0 mL). After 2 h at -35 °C, iodine (5.33 g, 21.0 mmol, 3.00 equiv) in THF (20 mL) was added and the reaction mixture was stirred for 10 min at -35 °C. At 0 °C, aqueous Na₂S₂O₃ (sat., 30 mL) was added. The reaction mixture was warmed to rt and then extracted with EtOAc (2 x 30 mL). The combined organic layers were dried over MgSO₄, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over neutralized SiO₂, using PET-EtOAc (90:10) with 2% of NEt₃ to give the title product as an orange oil (1.99 g, 80%).

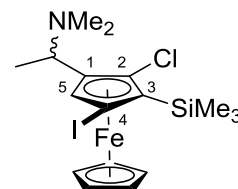
R_f (eluent: PET-EtOAc 90:10 with 10 drops of NEt_3 for 10 mL of eluent, 2 developments on TLC plate first dipped into EtOAc- NEt_3 (50:50) and dried) = 0.43. ν_{max} (film)/ cm^{-1} 2972, 2935, 2819, 2774, 1450, 1369, 1322, 1275, 1259, 1195, 1107, 1068, 1001, 976, 943, 875, 820, 770. ^1H NMR (300 MHz, CDCl_3): δ (ppm) 4.39 (d, $J = 2.8$ Hz, 1H, H5), 4.16 (d, $J = 2.8$ Hz, 1H, H4), 4.14 (s, 5H, Cp), 3.80 (q, $J = 6.9$ Hz, 1H, CH), 2.11 (s, 6H, $\text{N}(\text{CH}_3)_2$), 1.44 (d, $J = 6.9$ Hz, 3H, CH_3). ^{13}C NMR (75.4 MHz, CDCl_3): δ (ppm) 96.7 (C2), 85.4 (C3), 74.1 (Cp), 70.9 (C5), 65.7 (C4), 56.2 (CH), 43.9 (C1), 41.1 ($\text{N}(\text{CH}_3)_2$), 16.0 (CH_3). Mass: 417 [M], 402 [M- CH_3], 373 [M- $\text{N}(\text{CH}_3)_2$], 346 [Fc(D)Cl]. Anal. Calcd for $\text{C}_{14}\text{H}_{17}\text{ClFeIN}$: C, 40.28; H, 4.10; N, 3.35. Found: C, 40.45; H, 4.21; N, 3.53.



(±)-2-Chloro-4-iodo-1-(α , N,N -trimethylaminomethyl)-3-(trimethylsilyl)ferrocene ((±)-10)

$n\text{BuLi}$ (1.3 M in hexane, 930 μL , 1.21 mmol, 1.10 equiv) was added dropwise to a solution of TMPH (204 μL , 171 mg, 1.21 mmol, 1.10 equiv) in THF (1.00 mL) at -15 $^\circ\text{C}$. After addition, the reaction was stirred for 5 min at the same temperature before being cooled to -50 $^\circ\text{C}$. After 5 min, the LiTMP solution was cannulated onto a solution of (\pm)-**9** (460 mg, 1.10 mmol, 1.00 equiv) in THF (1.00 mL) at -50 $^\circ\text{C}$. Quantitative transfer was ensured by washing the LiTMP Schlenk tube with THF (0.5 mL). After 2 h at -50 $^\circ\text{C}$, trimethylsilyl chloride (153 μL , 131 mg, 1.21 mmol, 1.10 equiv) was added dropwise and the reaction mixture was warmed to rt. At 0 $^\circ\text{C}$, aqueous K_2CO_3 solution (sat., 5 mL) was added and the reaction mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over MgSO_4 , filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over neutralized SiO_2 , using PET-EtOAc (90:10) with 2% of NEt_3 to give the title product as an orange solid (319 mg, 59%).

R_f (eluent: PET-EtOAc 90:10 with 10 drops of NEt_3 for 10 mL of eluent, TLC plate first dipped into EtOAc- NEt_3 (50:50) and dried) = 0.35. Mp 97-99 $^\circ\text{C}$. ν_{max} (film)/ cm^{-1} 2942, 2895, 2854, 2816, 2775, 1451, 1369, 1325, 1291, 1253, 1243, 1093, 1085, 946, 913, 835, 819, 757, 738. ^1H NMR (300 MHz, CDCl_3): δ (ppm) 4.53 (s, H5), 4.18 (s, 5H, Cp), 3.81 (q, $J = 6.9$ Hz, 1H, CH), 2.15 (s, 6H, $\text{N}(\text{CH}_3)_2$), 1.46 (d, $J = 6.9$ Hz, 3H, CH_3), 0.49 (s, 9H, $\text{Si}(\text{CH}_3)_3$). ^{13}C NMR (75.4 MHz, CDCl_3): δ (ppm) 97.7 (C2), 90.4 (C1), 76.1 (C5), 74.0 (Cp), 70.8 (C3), 55.4 (CH), 44.6 (C4), 40.9 ($\text{N}(\text{CH}_3)_2$), 15.4 (CH_3), 1.9 ($\text{Si}(\text{CH}_3)_3$). Mass: 489 [M], 474 [M- CH_3], 445 [M- $\text{N}(\text{CH}_3)_2$], 418 [M- $\text{CH}(\text{CH}_3)\text{N}(\text{CH}_3)_2+\text{H}$]. Anal. Calcd for $\text{C}_{17}\text{H}_{25}\text{ClFeINSi}$: C, 41.70; H, 5.15; N, 2.86. Found: C, 41.93; H, 5.22; N, 2.94.



Crystal data for (\pm)-10**.** $\text{C}_{17}\text{H}_{25}\text{ClFeINSi}$, $M = 489.67$, $T = 150$ K; monoclinic $P 2_1/n$ (I.T.#14), $a = 12.213(2)$, $b = 12.0222(19)$, $c = 14.680(2)$ \AA , $\beta = 112.181(6)$ $^\circ$, $V = 1996.0(6)$ \AA^3 . $Z = 4$, $d = 1.629$ $\text{g}\cdot\text{cm}^{-3}$, $\mu = 2.493$ mm^{-1} . A final refinement on F^2 with 4498 unique intensities and 167 parameters converged at $\omega R_F^2 = 0.1336$ ($R_F = 0.0521$) for 3936 observed reflections with $I > 2\sigma(I)$. CCDC 1920661.

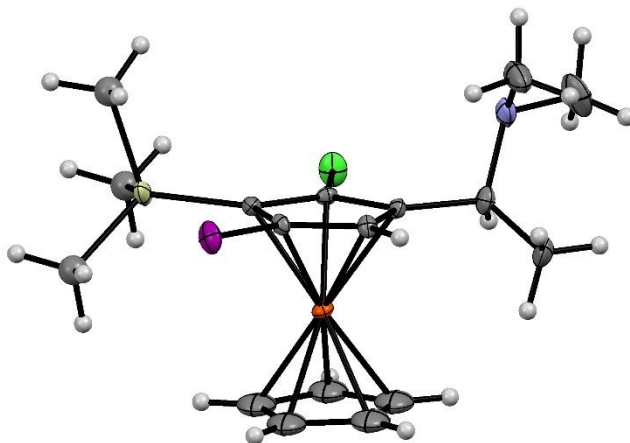
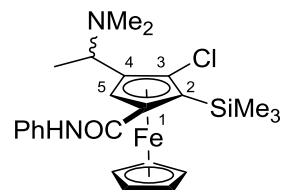


Figure 2. Molecular structure of compound (±)-**10** (thermal ellipsoids shown at the 30% probability level).

(±)-3-Chloro-N-phenyl-4-(α,N,N-trimethylaminomethyl)-2-(trimethylsilyl)ferrocenecarboxamide ((±)-11)

*n*BuLi (1.3 M in hexane, 1.60 mL, 2.00 mmol, 2.00 equiv) was added dropwise to a solution of TMPH (338 μL, 283 mg, 2.00 mmol, 2.00 equiv) in THF (4.00 mL) at -15 °C. After addition, the reaction was stirred for 5 min at the same temperature before being cooled to -35 °C. After 5 min, the LiTMP solution was cannulated onto a solution of (±)-**10** (490 mg, 1.00 mmol, 1.00 equiv) in THF (4.00 mL) at -35 °C. Quantitative transfer was ensured by washing the LiTMP Schlenk tube with THF (0.5 mL). After 2 h at -35 °C, phenyl isocyanate (218 μL, 238 mg, 2.00 mmol, 2.00 equiv) was added dropwise and the reaction mixture was warmed to rt. Aqueous K₂CO₃ solution (sat., 10 mL) was added and the reaction mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over MgSO₄, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over neutralized SiO₂, using PET-EtOAc (90:10) with 2% of NEt₃ to give the title product as an orange solid (46.4 mg, 9.5%, 64.5% brsm).

R_f (eluent: PET-EtOAc 80:20 with 10 drops of NEt₃ for 10 mL of eluent, 3 developments on a TLC plate first dipped into EtOAc-NEt₃ (50:50) and dried) = 0.18. Mp 174-176 °C. ν_{\max} (film)/cm⁻¹ 3368, 2954, 2819, 2777, 1650, 1594, 1515, 1440, 1369, 1338, 1301, 1239, 1201, 1136, 1109, 1095, 1005, 842, 821, 748, 691. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.66 (br s, 1H, NH), 7.53 (d, *J* = 8.6 Hz, 2H, 2 x *o*ArCH), 7.35 (t, *J* = 8.4 Hz, 2H, 2 x *m*ArCH), 7.13 (t, *J* = 7.5 Hz, 1H, *p*ArCH), 4.69 (s, H5), 4.28 (s, 5H, Cp), 3.89 (q, *J* = 6.9 Hz, 1H, CH), 2.18 (s, 6H, N(CH₃)₂), 1.54 (d, *J* = 6.9 Hz, 1H, CH₃), 0.47 (s, 9H, Si(CH₃)₃). ¹³C NMR (75.4 MHz, CDCl₃): δ (ppm) 168.3 (C=O), 18.0 (ArC), 129.3 (2 x *m*ArCH), 124.4 (*p*ArCH), 119.7 (2 x *o*ArCH), 99.7 (C3), 90.3 (C3), 82.4 (C1), 72.7 (Cp), 69.7 (C2), 68.7 (C5), 55.5 (CH), 41.0 (N(CH₃)₂), 15.2 (CH₃), 1.7 (Si(CH₃)₃). Mass: 482 [M], 467 [M-CH₃], 438 [M-N(CH₃)₂], 422, 396. Anal. Calcd for C₂₄H₃₁ClFeN₂OSi: C, 59.69; H, 6.47; N, 5.80. Found: C, 60.26; H, 6.50; N, 5.97.

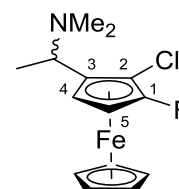


(±)-2-Chloro-1-fluoro-3-(α,N,N-trimethylaminomethyl)ferrocene ((±)-12)

*n*BuLi (1.3 M in hexane, 23.1 mL, 30.0 mmol, 3.00 equiv) was added dropwise to a solution of TMPH (5.10 mL, 4.24 g, 30.0 mmol, 3.00 equiv) in THF (60.0 mL) at -15 °C. After addition, the reaction was stirred for 5 min at the same temperature before being cooled to -35 °C. After 5 min, the LiTMP solution was cannulated onto a solution of (±)-**8** (2.92 g, 10.0 mmol, 1.00 equiv) in THF (60.0 mL) at -35 °C. Quantitative transfer was ensured by washing the LiTMP Schlenk tube with THF (1.0 mL). After 2 h at -35 °C, the reaction mixture was cannulated onto a solution of NFSI (9.46 g, 30.0 mmol, 3.00 equiv) in THF (50 mL) at -35 °C. After addition, the reaction mixture was stirred for 15 min at the same temperature. At 0 °C, an aqueous K₂CO₃ solution (sat., 30 mL) was added and the reaction mixture was

extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over MgSO₄, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over neutralized SiO₂, using PET-EtOAc (90:10) with 2% of NEt₃ to give the title product as an orange solid (807 mg, 26%). Traces of a difluorinated ferrocene derivative were observed by ¹⁹F NMR spectroscopy.

R_f (eluent: PET-EtOAc 90:10 with 10 drops of NEt₃ for 10 mL of eluent, 2 developments on TLC plate first dipped into EtOAc-NEt₃ (50:50) and dried) = 0.36. Mp 69-71 °C. ν_{\max} (film)/cm⁻¹ 3105, 3059, 2970, 2937, 2822, 2781, 1463, 1357, 1288, 1200, 1186, 1105, 1072, 1004, 969, 915, 845, 825, 805, 771, 681. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 4.69 (m, 1H, H5), 4.23 (s, 5H, Cp), 3.75-3.68 (m, 2H, H4 and H7), 2.11 (s, 6H, N(CH₃)₂), 1.44 (d, J = 6.9 Hz, 3H, CH₃). ¹³C NMR (75.4 MHz, CDCl₃): δ (ppm) 131.2 (d, J = 274.1 Hz, C1), 81.4 (d, J = 13.6 Hz, C2), 78.9 (s, C3), 72.4 (Cp), 56.3 (d, J = 2.9 Hz, C4), 55.6 (s, CH), 52.9 (d, J = 14.0 Hz, C5), 41.2 (s, N(CH₃)₂), 16.6 (s, CH₃). Mass: 309 [M], 294 [M-CH₃], 265 [M-N(CH₃)₂], 238 [Fc(Cl)F]. ¹⁹F NMR (282 MHz, CDCl₃): δ (ppm) -192.2. Anal. Calcd for C₁₄H₁₇ClFFeN: C, 54.31; H, 5.53; N, 4.52. Found: C, 54.23; H, 5.53; N, 4.59.



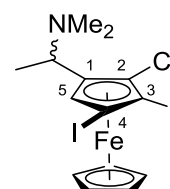
(R,R)-2-Chloro-1-fluoro-3-(α ,N,N-trimethylaminomethyl)ferrocene (R,R)-12

By following a similar protocol, starting from (**R,S**)-**8** (2.92 g, 10.0 mmol, 1.00 equiv), the title product was obtained as an orange solid (807 mg, 26%). Analytical data analogous to racemic compound. [α]_D +0.527 (c 0.01 in CHCl₃).

(\pm)-2-Chloro-3-fluoro-4-iodo-1-(α ,N,N-trimethylaminomethyl)ferrocene (\pm)-13

*n*BuLi (1.4 M in hexane, 1.90 mL, 2.64 mmol, 1.20 equiv) was added dropwise to a solution of TMPH (445 μ L, 373 mg, 2.64 mmol, 1.20 equiv) in THF (6.00 mL) at -15 °C. After addition, the reaction was stirred for 5 min at the same temperature before being cooled to -78 °C. After 5 min, the LiTMP solution was cannulated onto a solution of (\pm)-**12** (681 mg, 2.20 mmol, 1.00 equiv) in THF (6.00 mL) at -78 °C. Quantitative transfer was ensured by washing the LiTMP Schlenk tube with THF (0.5 mL). After 1 h at -78 °C, a solution of iodine (670 mg, 2.64 mmol, 1.20 equiv) was added. The reaction mixture was stirred at the same temperature for 5 min before being warmed to rt and stirred for 10 min. At 0 °C, aqueous Na₂S₂O₃ solution (sat., 20 mL) was added and the reaction mixture was extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over MgSO₄, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over neutralized SiO₂, using PET-EtOAc (90:10) with 2% of NEt₃ to give the title product as an orange solid (871 mg, 91%).

R_f (eluent: PET-EtOAc 90:10 with 10 drops of NEt₃ for 10 mL of eluent, 3 developments on TLC plate first dipped into EtOAc-NEt₃ (50:50) and dried) = 0.53. Mp 89-92 °C. ν_{\max} (film)/cm⁻¹ 2978, 2941, 2860, 1453, 1412, 1372, 1266, 1253, 1196, 1108, 1099, 1069, 1037, 1002, 971, 931, 825, 816, 770, 738, 691. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 4.24 (s, 5H, Cp), 4.10 (s, 1H, H5), 3.68 (q, J = 6.9 Hz, 1H, CH), 2.12 (s, 6H, N(CH₃)₂), 1.43 (d, J = 6.9 Hz, 3H, CH₃). ¹³C NMR (75.4 MHz, CDCl₃): δ (ppm) 131.4 (d, J = 275.0 Hz, C3), 81.0 (s, C1), 80.0 (d, J = 14.2 Hz, C2), 75.4 (s, Cp), 63.0 (s, C5), 55.6 (s, CH), 41.1 (s, N(CH₃)₂), 25.9 (d, J = 14.5 Hz, C4), 16.6 (s, CH₃). ¹⁹F NMR (282 MHz, CDCl₃): δ (ppm) -189.9. Mass: 435 [M], 420 [M-CH₃], 391 [M-N(CH₃)₂], 364 [Fc(I)F(Cl)]. Anal. Calcd for C₁₄H₁₆ClIFFeN: C, 38.61; H, 3.70; N, 3.22. Found: C, 38.70; H, 3.70; N, 3.42.



Crystal data for (\pm)-13. C₁₄H₁₆ClIFFeIN, M = 435.48, T = 150 K; orthorhombic $Fdd2$ (I.T.#43), a = 25.124(4), b = 35.336(6), c = 7.0952(13) Å, V = 6299.0(19) Å³. Z = 16, d = 1.837 g.cm⁻³, μ = 3.084 mm⁻¹. A final refinement on F^2 with 3353 unique intensities and 175 parameters converged at ωR_F^2 = 0.0485 (R_F = 0.0207) for 3310 observed reflections with $I > 2\sigma(I)$. CCDC 1920663.

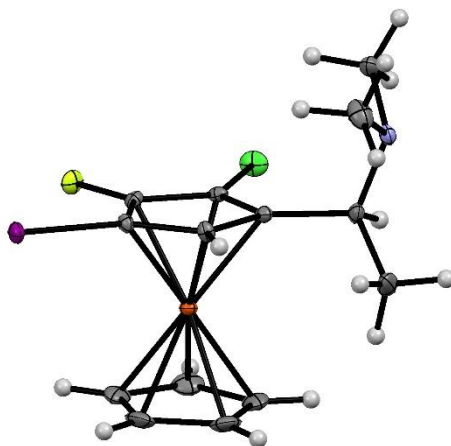


Figure 3. Molecular structure of compound (±)-13 (thermal ellipsoids shown at the 30% probability level).

(R, S_p)-2-Chloro-3-fluoro-4-iodo-1-[α,N,N-trimethylaminomethyl] ferrocene (R, S_p-13)

By following a similar protocol, starting from (R, R_p)-12 (681 mg, 2.20 mmol, 1.00 equiv), the title product was obtained as an orange solid (814 mg, 85%). Analytical data analogous to racemic compound. $[\alpha]_D^{25} +0.667$ (*c* 0.01 in CHCl₃).

Crystal data for (R, S_p)-13. C₁₄H₁₆ClFeIN, *M* = 435.48, *T* = 150 K; orthorhombic *P* 2₁ 2₁ 2₁ (I.T.#19), *a* = 7.6115(19), *b* = 11.500(2), *c* = 17.886(4) Å, *V* = 1565.5(6) Å³. *Z* = 4, *d* = 1.848 g.cm⁻³, μ = 3.102 mm⁻¹. A final refinement on *F*² with 3540 unique intensities and 175 parameters converged at $\omega R_F^2 = 0.0581$ (*R_F* = 0.0241) for 3474 observed reflections with *I* > 2σ(*I*). CCDC 1920665.

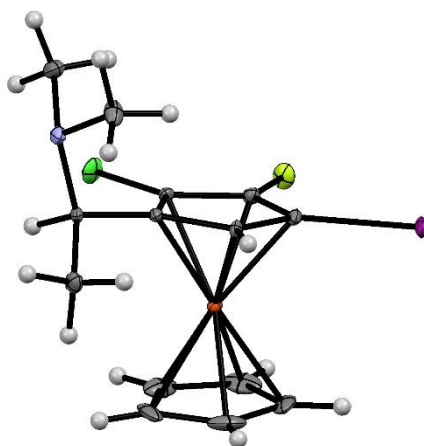


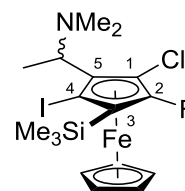
Figure 4. Molecular structure of compound (R, S_p)-13 (thermal ellipsoids shown at the 30% probability level).

(±)-1-Chloro-2-fluoro-4-iodo-5-(α,N,N-trimethylaminomethyl)-3-(trimethylsilyl)ferrocene ((±)-14) and (±)-2-Chloro-3-fluoro-1-(α,N,N-trimethylaminomethyl)-4-(trimethylsilyl)ferrocene ((±)-15)

*n*BuLi (1.4 M in hexane, 942 μL, 1.32 mmol, 1.20 equiv) was added dropwise to a solution of TMPH (223 μL, 187 mg, 1.32 mmol, 1.20 equiv) in THF (3.50 mL) at -15 °C. After addition, the reaction was stirred for 5 min at the same temperature before being cooled to -50 °C. After 5 min, (±)-13 (479 mg, 1.10 mmol, 1.00 equiv) was added in one portion and the reaction mixture was stirred at the same temperature for 4 h. Trimethylsilyl chloride (168 μL, 144 mg, 1.32 mmol, 1.20 equiv) was added dropwise and the reaction mixture was slowly warmed to rt. At 0 °C, aqueous K₂CO₃ solution (sat., 10 mL) was added and the reaction mixture was extracted with EtOAc (2 x 15 mL). The combined organic layers were dried over MgSO₄, filtrated over cotton wool and concentrated under vacuum using a rotary

evaporator to give the crude product. This was purified by column chromatography over neutralized SiO₂, using PET-EtOAc (90:10) with 2% of NEt₃ to give (±)-**14** as an orange solid (387 mg, 69%, 80.5% brsm) and (±)-**15** as an orange oil (57.0 mg, 15%, 16% brsm). Traces of a by-product were observed by ¹⁹F NMR spectroscopy.

Compound (±)-14. R_f (eluent: PET-EtOAc 90:10 with 10 drops of NEt₃ for 10 mL of eluent, TLC plate first dipped into EtOAc-NEt₃ (50:50) and dried) = 0.51. Mp 61-63 °C. ν_{max} (film)/cm⁻¹ 2953, 2818, 2772, 1446, 1384, 1370, 1287, 1248, 1108, 1046, 1003, 840, 818, 758, 731, 714. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 4.27 (s, 5H, Cp), 3.68 (q, *J* = 6.9 Hz, 1H, CH), 2.23 (s, 6H, N(CH₃)₂), 1.81 (d, *J* = 6.9 Hz, 3H, CH₃), 0.46 and 0.45 (2s, 9H, Si(CH₃)₃). ¹³C NMR (75.4 MHz, CDCl₃): δ (ppm) 134.9 (d, *J* = 277.6 Hz, C2), 84.3 (s, C5), 83.4 (d, *J* = 16.7 Hz, C1), 75.1 (s, Cp), 61.0 (d, *J* = 15.2 Hz, C3), 58.0 (s, CH), 43.2 (s, N(CH₃)₂), 38.3 (d, *J* = 3.2 Hz, C4), 16.8 (s, CH₃), 0.9 (s, Si(CH₃)₃). ¹⁹F NMR (282 MHz, CDCl₃): δ (ppm) -181.1. Mass: 507 [M], 492 [M-CH₃], 463 [M-N(CH₃)₂], 436 [FcI(SiMe₃)F(Cl)]. Anal. Calcd for C₁₇H₂₄ClFFeINSi: C, 40.22; H, 4.77; N, 2.76. Found: C, 40.32; H, 4.70; N, 2.87.



Crystal data for (±)-14. C₁₇H₂₄ClFFeINSi, *M* = 507.66, *T* = 150 K; orthorhombic *P* *n* *a* 2₁ (I.T.#33), *a* = 10.3652(11), *b* = 13.2629(14), *c* = 29.267(3) Å, *V* = 4023.3(7) Å³. *Z* = 8, *d* = 1.676 g.cm⁻³, μ = 2.483 mm⁻¹. A final refinement on *F*² with 8585 unique intensities and 427 parameters converged at ω*R*_{*F*}² = 0.0513 (*R*_{*F*} = 0.0241) for 8191 observed reflections with *I* > 2σ(*I*). CCDC 1920664.

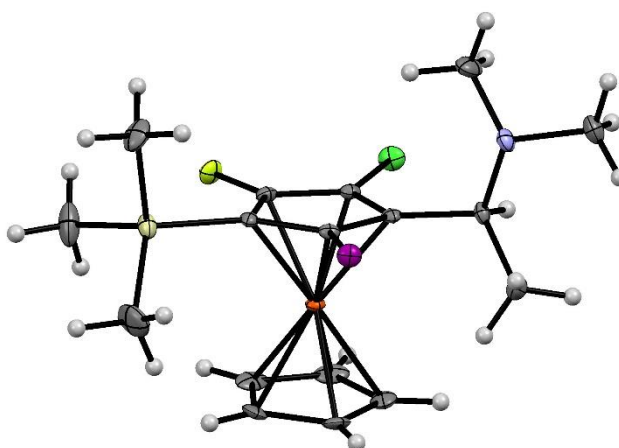
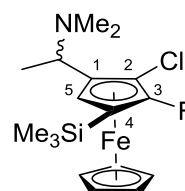


Figure 5. Molecular structure of compound (±)-**14** (thermal ellipsoids shown at the 30% probability level).

Compound (±)-15. R_f (eluent: PET-EtOAc 90:10 with 10 drops of NEt₃ for 10 mL of eluent, TLC plate first dipped into EtOAc-NEt₃ (50:50) and dried) = 0.28. ν_{max} (film)/cm⁻¹ 2955, 2820, 2777, 1434, 1394, 1370, 1289, 1248, 1143, 1107, 1063, 1002, 981, 840, 815, 753, 695. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 4.19 (s, 5H, Cp), 3.70 (q, *J* = 6.9 Hz, 1H, CH), 3.59 (d, *J* = 1.8 Hz, 1H, H5), 2.13 (s, 6H, N(CH₃)₂), 1.45 (d, *J* = 6.9 Hz, 3H, CH₃), 0.29 (s, 9H, Si(CH₃)₃). ¹³C NMR (75.4 MHz, CDCl₃): δ (ppm) 134.9 (d, *J* = 271.5 Hz, C3), 82.7 (d, *J* = 15.9 Hz, C2), 82.5 (s, C1), 72.5 (s, Cp), 60.4 (d, *J* = 5.7 Hz, C5), 56.2 (d, *J* = 19.3 Hz, C4), 55.8 (s, CH), 41.4 (s, N(CH₃)₂), 16.5 (s, CH₃), -0.3 (s, Si(CH₃)₃). ¹⁹F NMR (282 MHz, CDCl₃): δ (ppm) -186.8. Mass: 381 [M], 366 [M-CH₃], 337 [M-N(CH₃)₂], 310 [Fc(SiMe₃)F(Cl)]. Anal. Calcd for C₁₇H₂₅ClFFeNSi: C, 53.48; H, 6.60; N, 3.67. Found: C, 54.16; H, 6.70; N, 3.53.



(*R,S*_p)-1-Chloro-2-fluoro-4-iodo-5-(*α,N,N*-trimethylaminomethyl)-3-(trimethylsilyl)ferrocene (*R,S*_p-14**) and (*R,R*_p)-2-chloro-3-fluoro-1-(*α,N,N*-trimethylaminomethyl)-4-(trimethylsilyl)ferrocene (*R,R*_p-**15**)**

By following a similar protocol, starting from (*R,S*_p)-**13** (479 mg, 1.10 mmol, 1.00 equiv), (*R,S*_p)-**14** was obtained as an orange solid (298 mg, 53%, 61% brsm). Analytical data analogous to racemic

compound. $[\alpha]_D +0.465$ (c 0.01 in CHCl_3). Compound (***R,R***)-**15** was obtained as an orange oil (48 mg, 11%, 13% brsm). Analytical data analogous to racemic compound. $[\alpha]_D +1.02$ (c 0.01 in CHCl_3).

Crystal data for (*R,S_p*)-14. $\text{C}_{17}\text{H}_{24}\text{ClFFeINSi}$, $M = 507.66$, $T = 150$ K; orthorhombic $P 2_1 2_1 2_1$ (I.T.#19), $a = 7.3187(12)$, $b = 12.538(2)$, $c = 21.583(3)$ Å, $V = 1980.5(5)$ Å³. $Z = 4$, $d = 1.703$ g.cm⁻³, $\mu = 2.522$ mm⁻¹. A final refinement on F^2 with 4489 unique intensities and 190 parameters converged at $\omega R_F^2 = 0.0759$ ($R_F = 0.0303$) for 4423 observed reflections with $I > 2\sigma(I)$. CCDC 1920666.

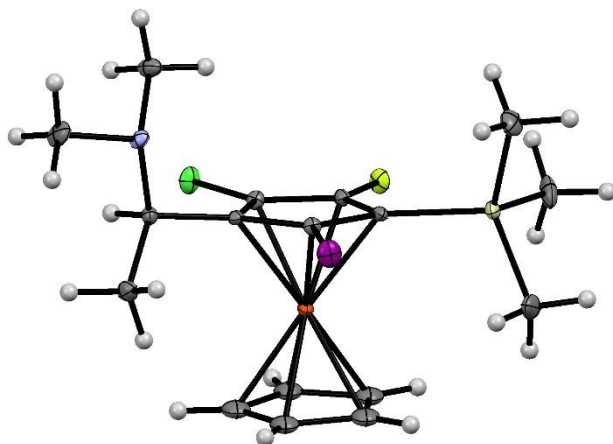
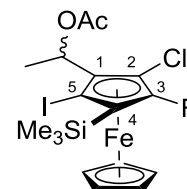


Figure 6. Molecular structure of compound (***R,S_p***)-**14** (thermal ellipsoids shown at the 30% probability level).

(±)-1-(1-Acetoxyethyl)-2-chloro-3-fluoro-5-iodo-4-(trimethylsilyl)ferrocene ((±)-16)

A solution of (**±**)-**14** (76.0 mg, 0.15 mmol, 1.00 equiv) in acetic anhydride (425 μL, 460 mg, 4.50 mmol, 30.0 equiv) was stirred at 110 °C for 1 h. The reaction mixture was cooled to rt and poured onto cold aqueous K_2CO_3 solution (sat., 15 mL). Solid K_2CO_3 was added until pH 8-9 was reached and the reaction mixture was extracted with EtOAc (2 x 15 mL). The combined organic layers were dried over K_2CO_3 , filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over neutralized SiO_2 , using PET-EtOAc (90:10) with 2% of NEt_3 to give the title product as an orange oil (63.0 mg, 80%). A mixture of diastereoisomers in a 1:3 ratio was identified by NMR, minor diastereoisomers identified by *.

R_f (eluent: PET-EtOAc 90:10 with 10 drops of NEt_3 for 10 mL of eluent, TLC plate first dipped into EtOAc- NEt_3 (50:50) and dried) = 0.56. ν_{max} (film)/cm⁻¹ 2957, 1733, 1438, 1413, 1370, 1239, 1115, 1039, 908, 842, 820, 729, 676. ¹H NMR (300 MHz, CDCl_3): δ (ppm) 5.95 (q, $J = 6.7$ Hz, 1H, CH*), 5.89 (q, $J = 6.7$ Hz, 1H, CH), 4.27 (s, 5H, Cp*), 4.25 (s, 5H, Cp), 2.23 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO^*), 1.78 (d, $J = 6.7$ Hz, 3H, CH_3^*), 1.49 (d, $J = 6.7$ Hz, 3H, CH_3), 0.44 (s, 9H, $\text{Si}(\text{CH}_3)_3^*$), 0.43 (s, 9H, $\text{Si}(\text{CH}_3)_3$). ¹³C NMR (75.4 MHz, CDCl_3): δ (ppm) 170.0 (s, C=O*), 169.9 (s, C=O), 135.4 (d, $J = 278.2$ Hz, C3), 135.1 (d, $J = 278.2$ Hz, C3*), 83.4 (s, C1), 81.1 (s, C1*), 80.0 (d, $J = 18.2$ Hz, C2 and C2*), 75.3 (s, Cp*), 75.2 (s, Cp), 69.8 (s, CH and CH*), 60.1 (d, $J = 15.7$ Hz, C4 and C4*), 42.5 (d, $J = 3.3$ Hz, C5), 41.9 (d, $J = 3.3$ Hz, C5*), 21.3 (s, CH_3CO and CH_3CO^*), 20.8 (s, CH_3), 19.9 (s, CH_3^*), 0.6 ((s, $\text{Si}(\text{CH}_3)_3$ and $\text{Si}(\text{CH}_3)_3^*$). ¹⁹F NMR (376 MHz, CDCl_3): δ (ppm) -180.9*, -181.4. Mass: 522 [M], 462 [M-AcOH]. Anal. Calcd for $\text{C}_{17}\text{H}_{21}\text{ClFFeIO}_2\text{Si}$: C, 39.07; H, 4.05. Found: C, 43.66; H, 4.77.



(*R,S_p*)-1-(1-Acetoxyethyl)-2-chloro-3-fluoro-5-iodo-4-(trimethylsilyl)ferrocene (*R,S_p*-16)

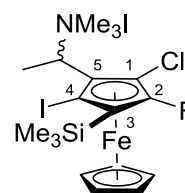
By following a similar protocol, starting from (***R,S_p***)-**14** (76.0 mg, 0.15 mmol, 1.00 equiv), the title product was obtained as an orange oil (64.0 mg, 81%). A mixture of diastereoisomers in a 1:4.5 ratio was identified by NMR, otherwise analytical data analogous to racemic compound. $[\alpha]_D -0.40$ (c 0.01 in CHCl_3). ee = 99.5%, de = 63%. The enantiomeric and diastereoisomeric ratios were determined on

Chiralpak IC-3 column, hexane/iPrOH: 99.5:0.5, 0.25 mL/min, 5 °C, $\lambda = 254$ nm, $t(S, R_p) = 35.71$ min, $t(R, S_p) = 37.91$ min, $t(S, S_p) = 40.72$ min, $t(R, R_p) = 41.83$ min.

(±)-1-Chloro-2-fluoro-4-iodo-5-(α,N,N,N -tetramethylaminomethyl)-3-(trimethylsilyl)ferrocene iodide ((±)-17)

Iodomethane (21.8 μ L, 49.7 mg, 0.35 mmol, 5.00 equiv) was added dropwise to a solution of (±)-**13** (35.5 mg, 0.07 mmol, 1.00 equiv) in CH₃CN (1.00 mL) at rt. After 1 h, volatiles were removed under vacuum using a rotary evaporator to give the crude product. This was triturated with Et₂O (2 mL) and filtrated. The resulting solids were washed with Et₂O (2 x 2 mL) and dried under high vacuum to give the title product as an orange solid (45.4 mg, quant.).

R_f (eluent: PET-EtOAc 50:50 with 10 drops of NEt₃ for 10 mL of eluent, TLC plate first dipped into EtOAc-NEt₃ (50:50) and dried) = 0.00. Mp 149-153 °C (decomp.). ν_{\max} (film)/cm⁻¹ 3445 (br), 2959, 1615, 1486, 1443, 1382, 1277, 1264, 1245, 1045, 849, 826, 758, 724, 701. ¹H NMR (500 MHz, CDCl₃): δ (ppm) 4.91 (q, $J = 7.2$ Hz, 1H, CH), 4.43 (s, 5H, Cp), 3.04 (s, 9H, NMe₃), 2.23 (d, $J = 7.2$ Hz, 1H, CH₃), 0.47 (s, 9H, Si(CH₃)₃). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) 134.9 (d, $J = 276.5$ Hz, C2), 83.3 (d, $J = 17.7$ Hz, C1), 76.1 (s, Cp), 76.0 (s, C5), 68.9 (s, CH), 64.5 (d, $J = 14.9$ Hz, C3), 51.8 (s, NMe₃), 36.9 (s, C4), 16.2 (s, CH₃), 0.8 (d, $J = 1.7$ Hz, Si(CH₃)₃). ¹⁹F NMR (470 MHz, CDCl₃): δ (ppm) -177.9.

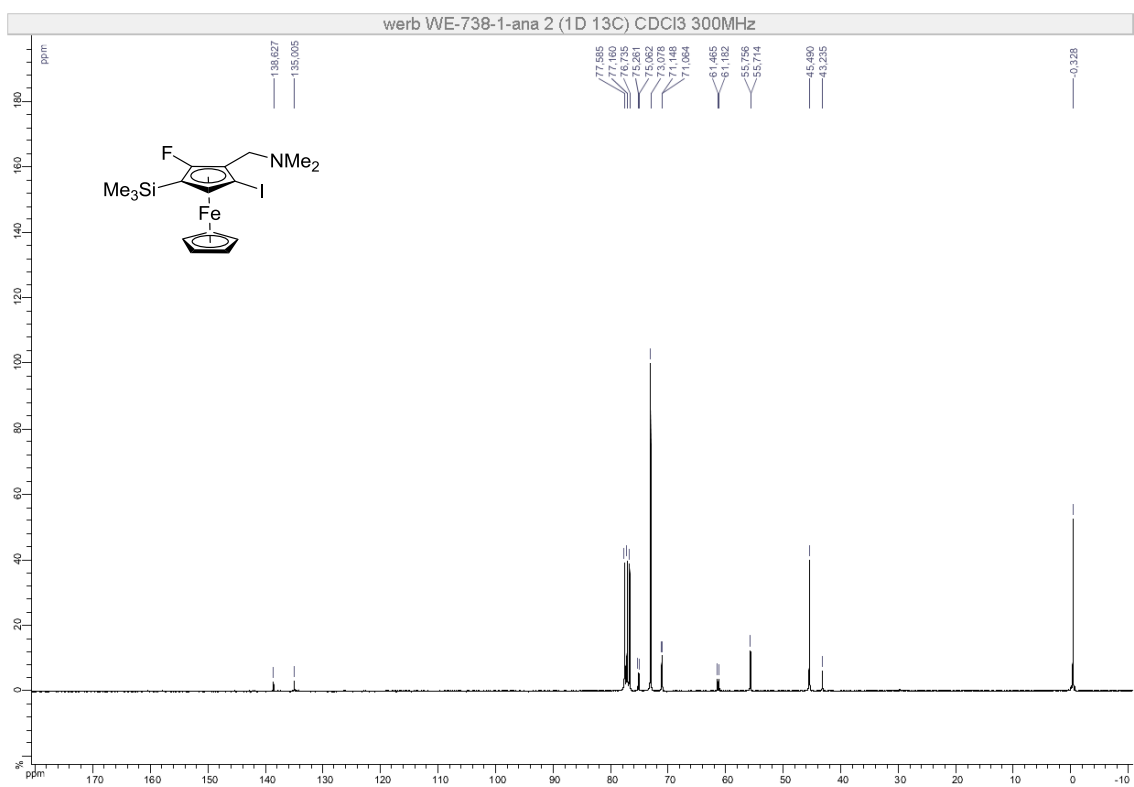
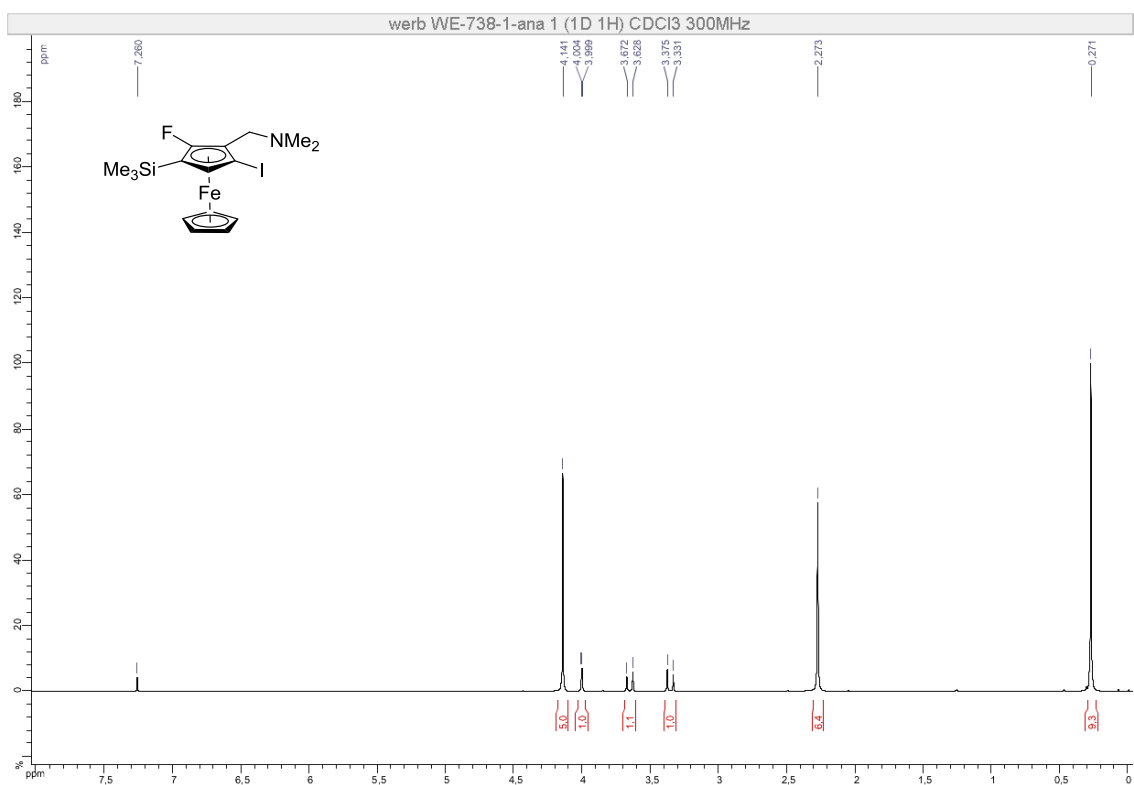


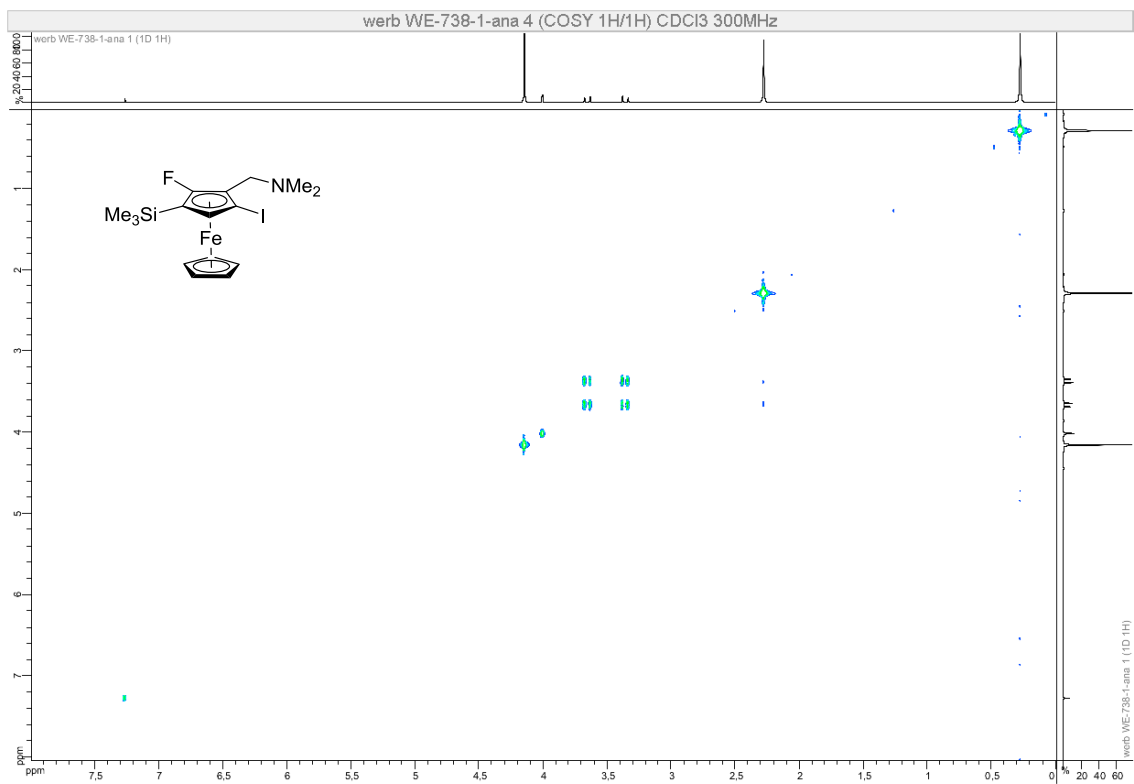
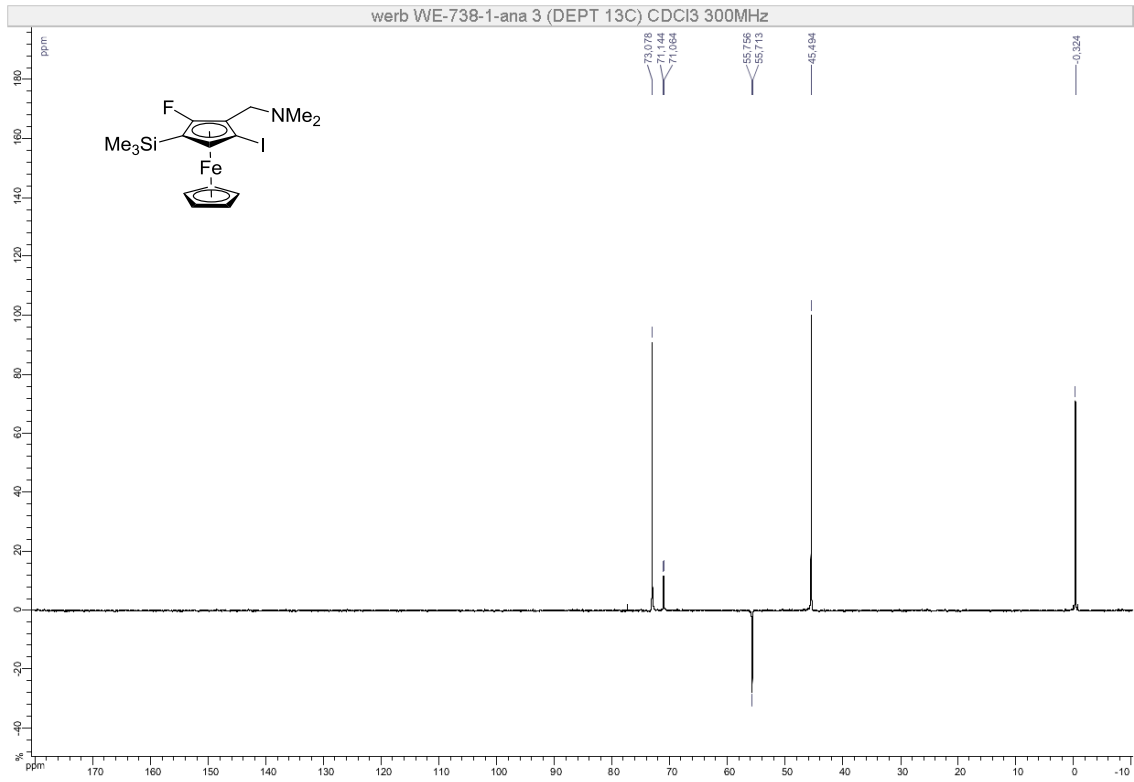
(R,S_p)-1-Chloro-2-fluoro-4-iodo-5-(α,N,N,N -tetramethylaminomethyl)-3-(trimethylsilyl)ferrocene iodide ((R,S_p)-17)

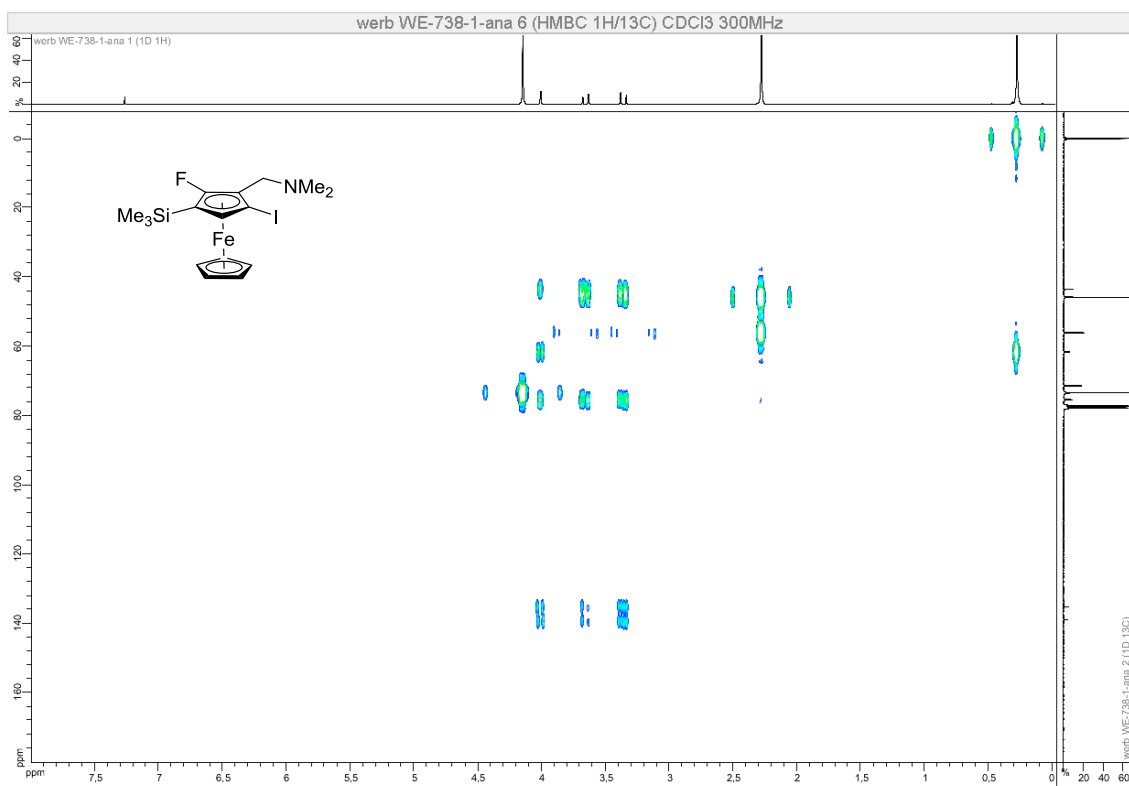
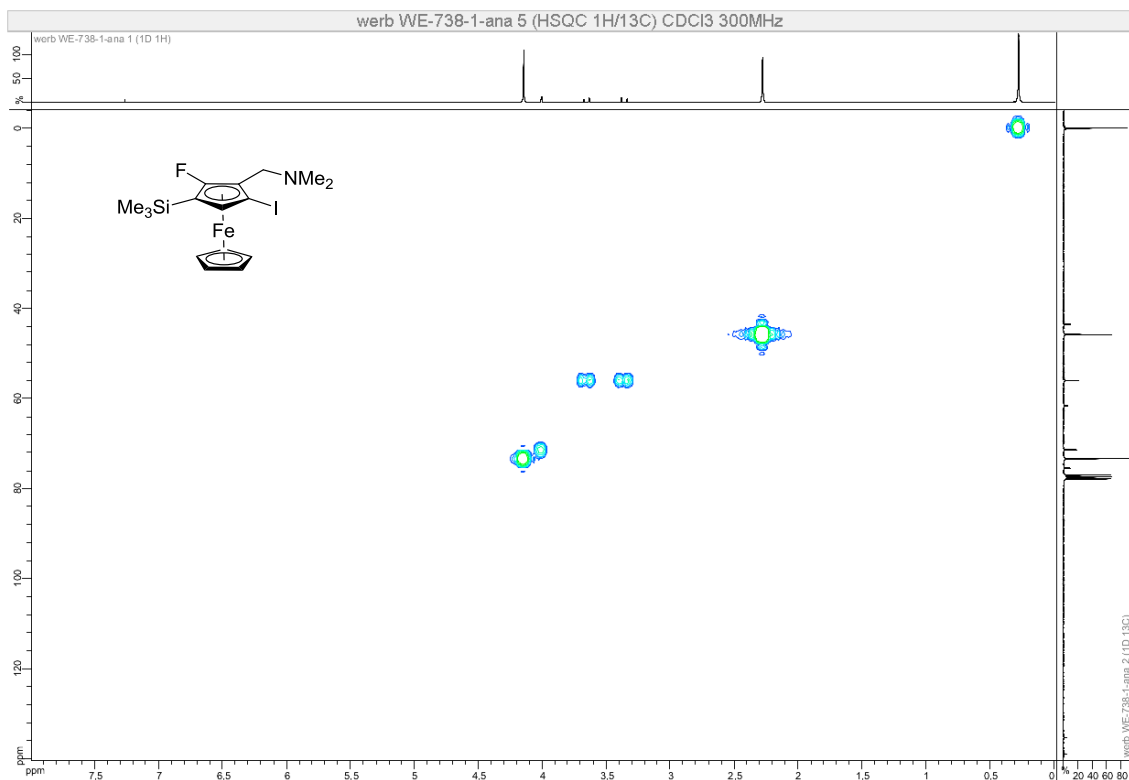
By following a similar protocol, starting from (R,S_p)-**14** (35.5 mg, 0.07 mmol, 1.00 equiv), the title product was obtained as an orange solid (45.3 mg, quant.). Analytical data analogous to racemic compound. $[\alpha]_D +0.643$ (c 0.01 in CH₃CN).

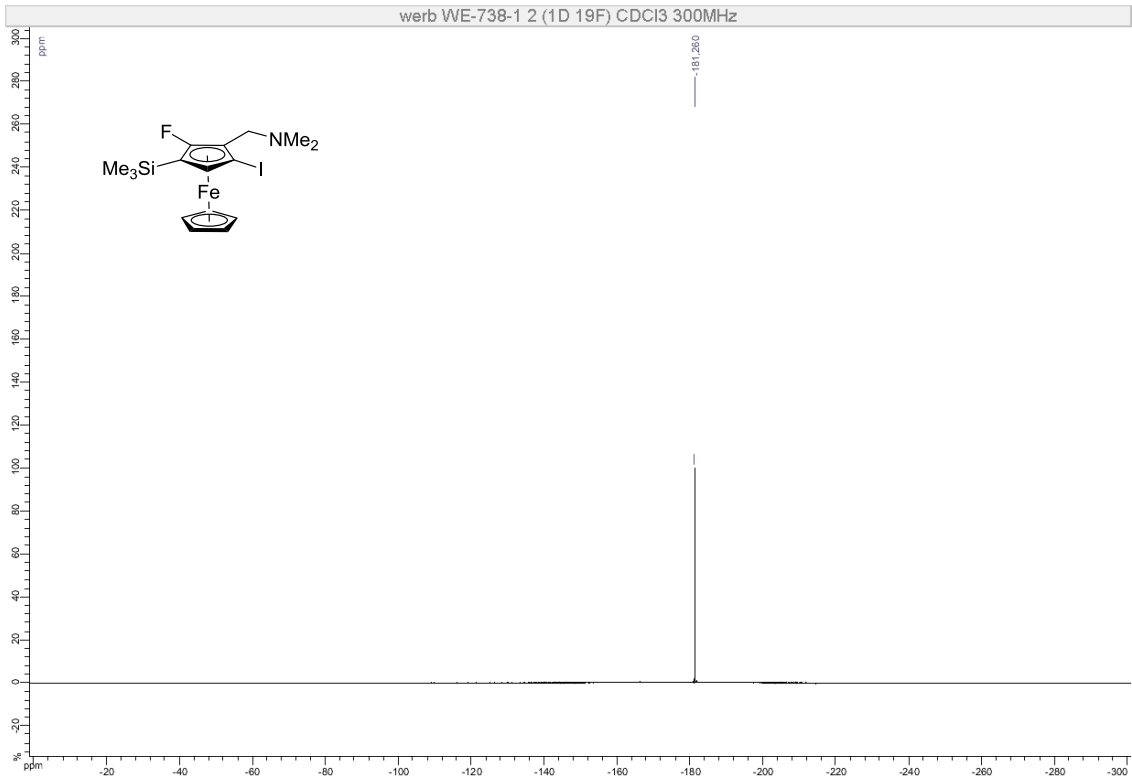
NMR Spectra

Compound (\pm)-2

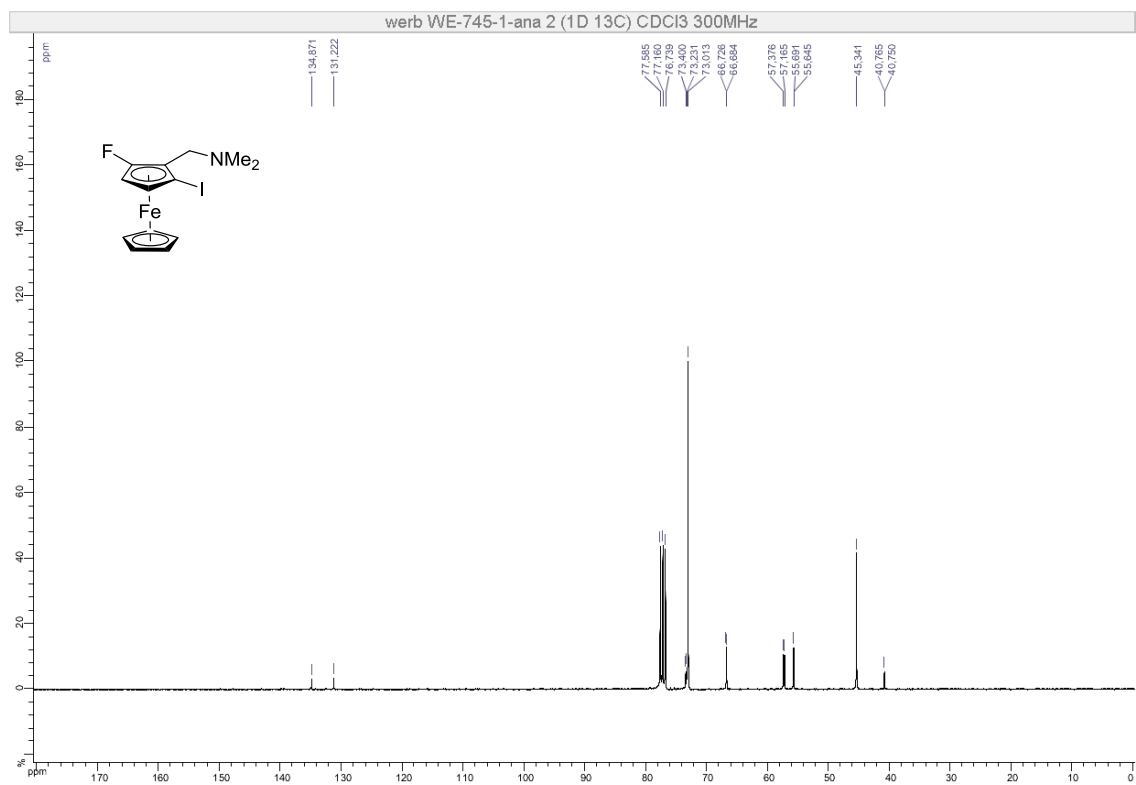
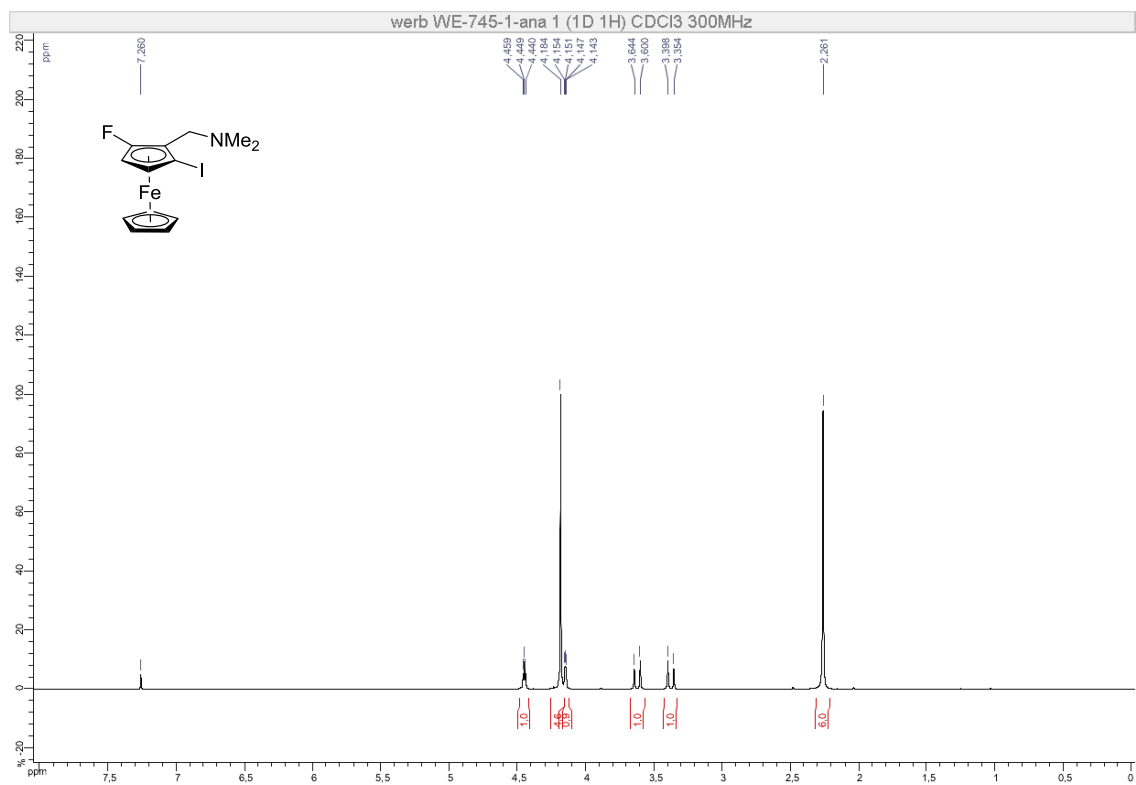


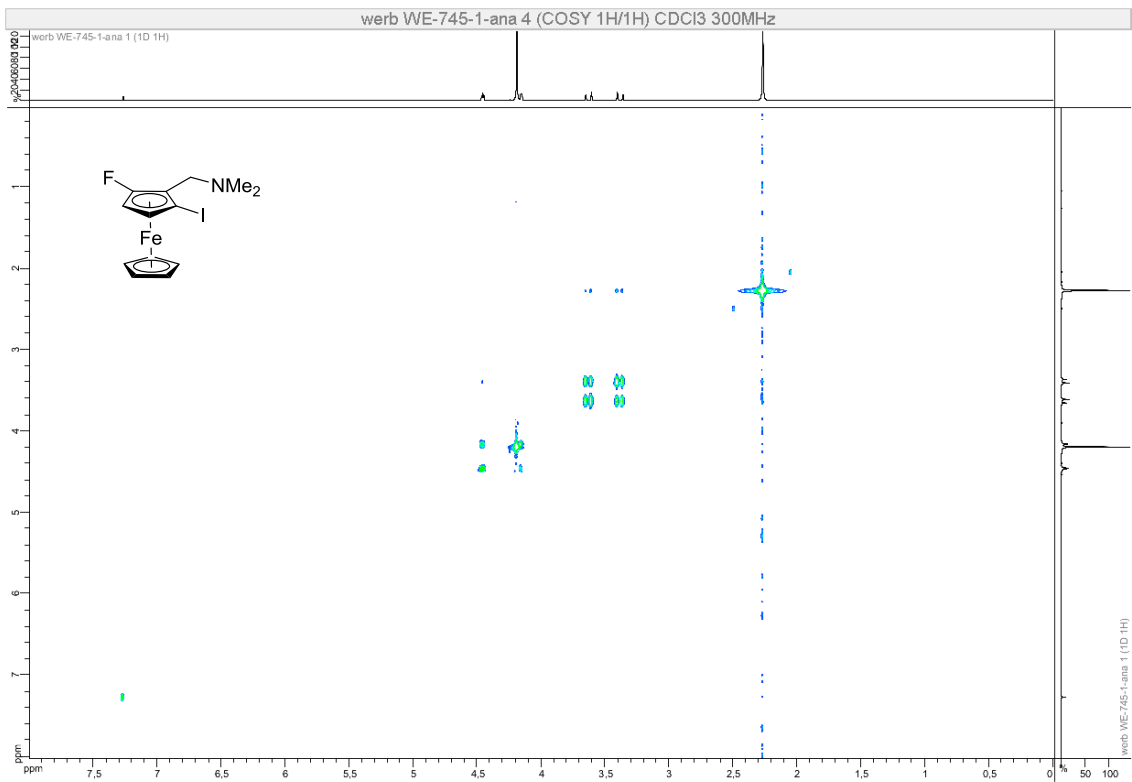
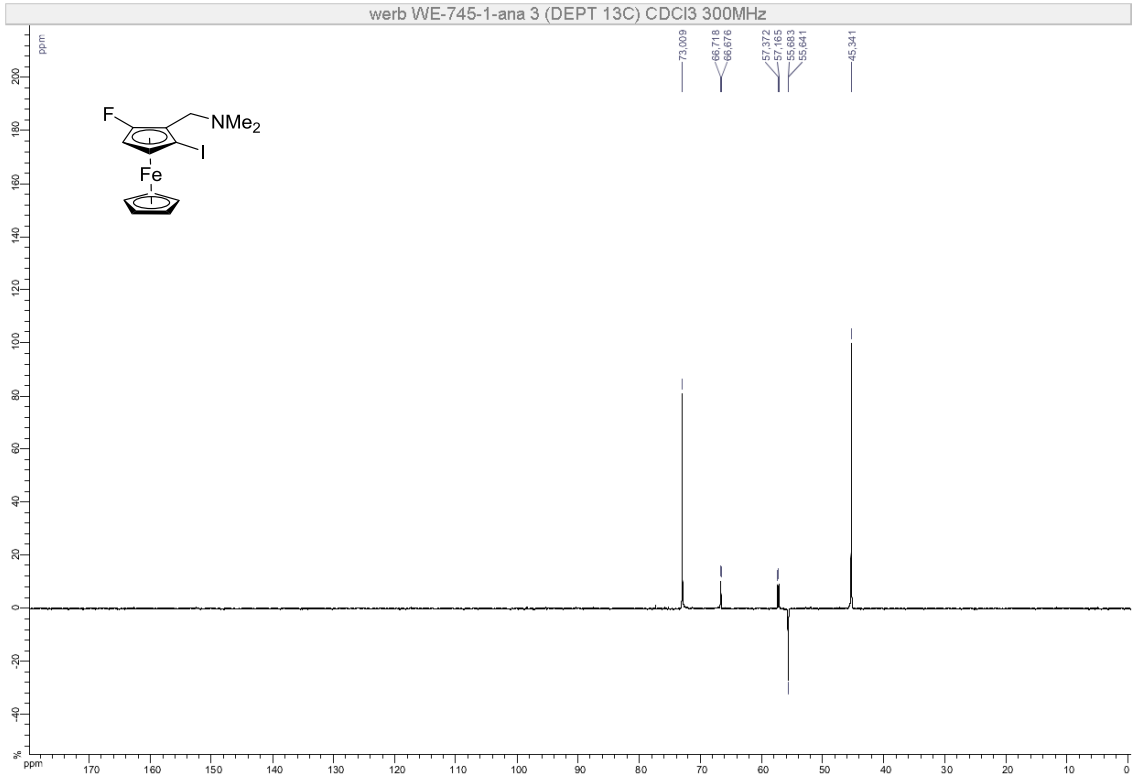


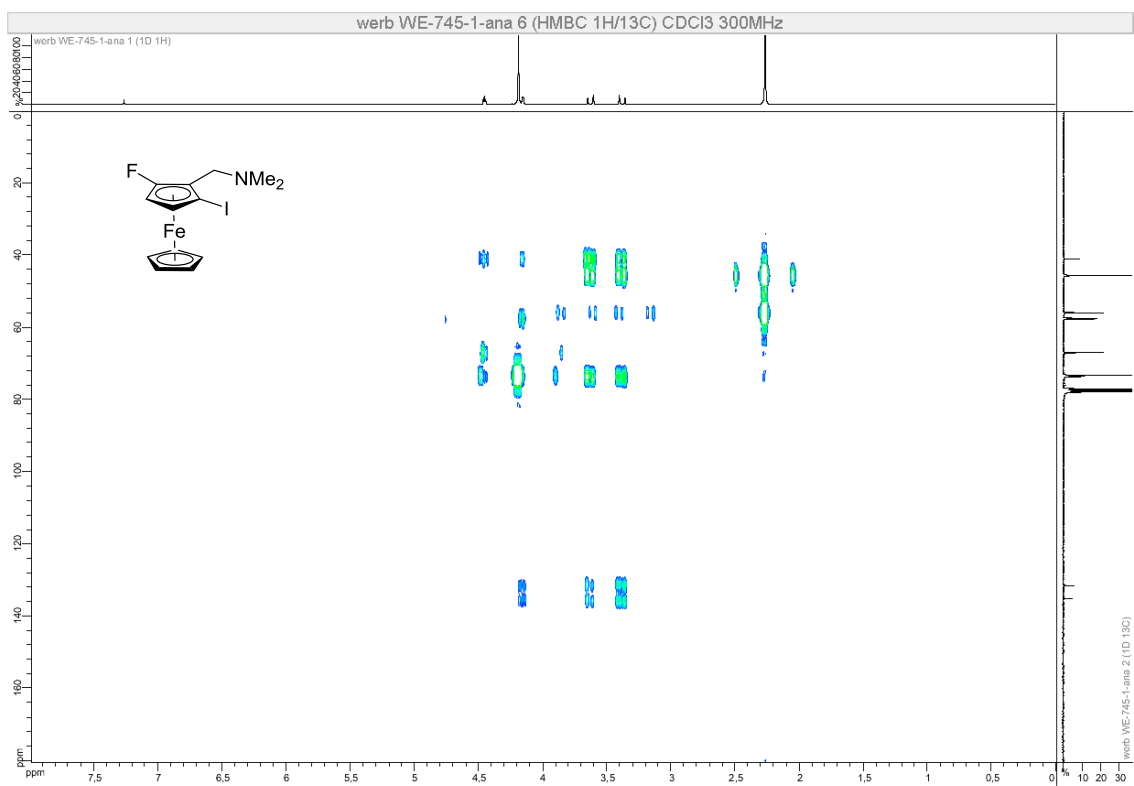
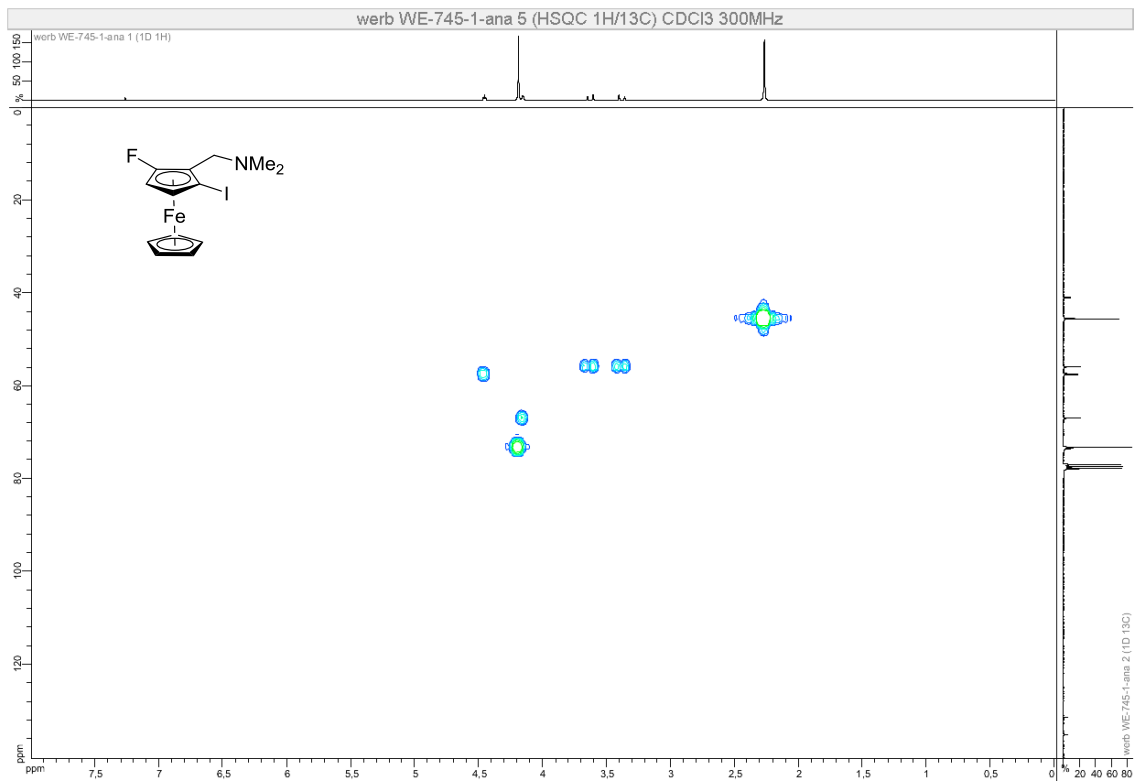


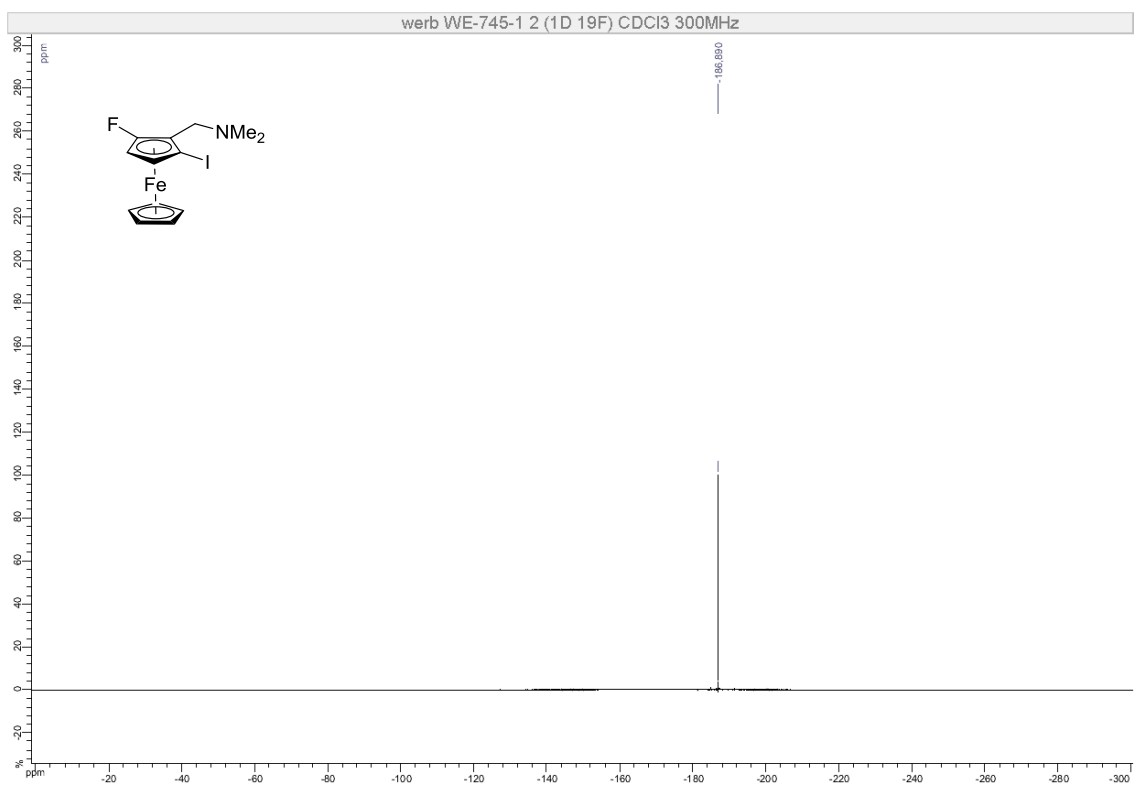
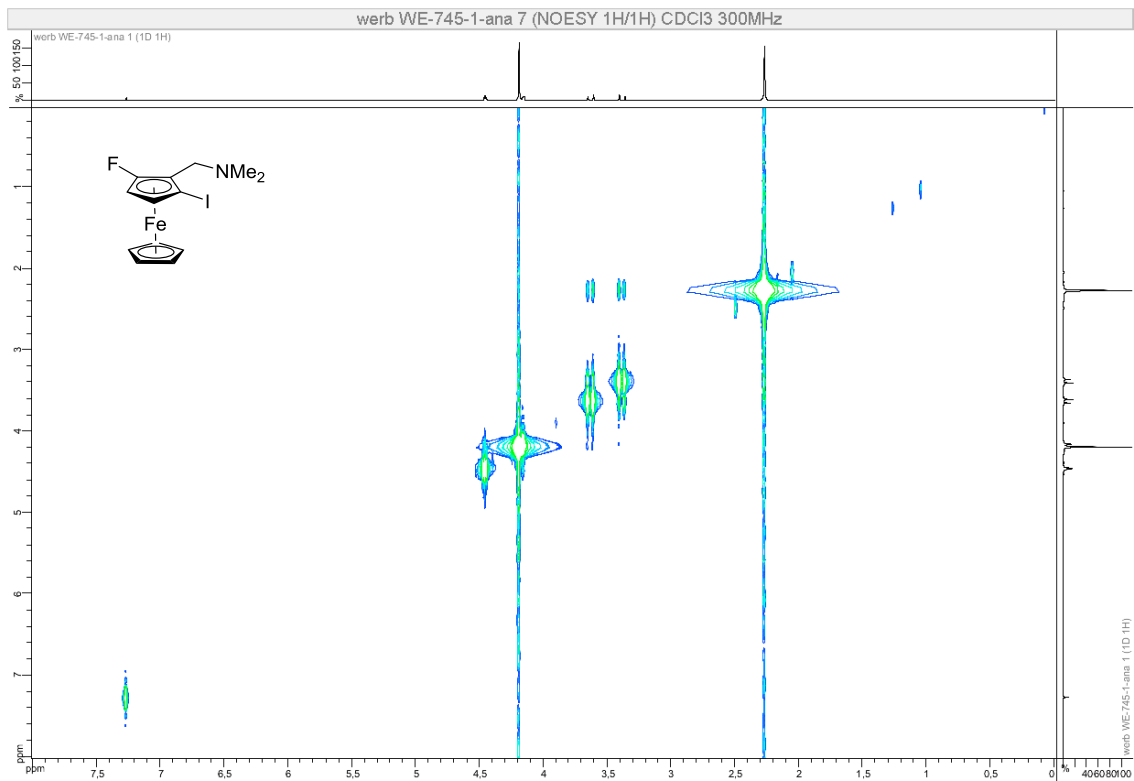


Compound (\pm)-3

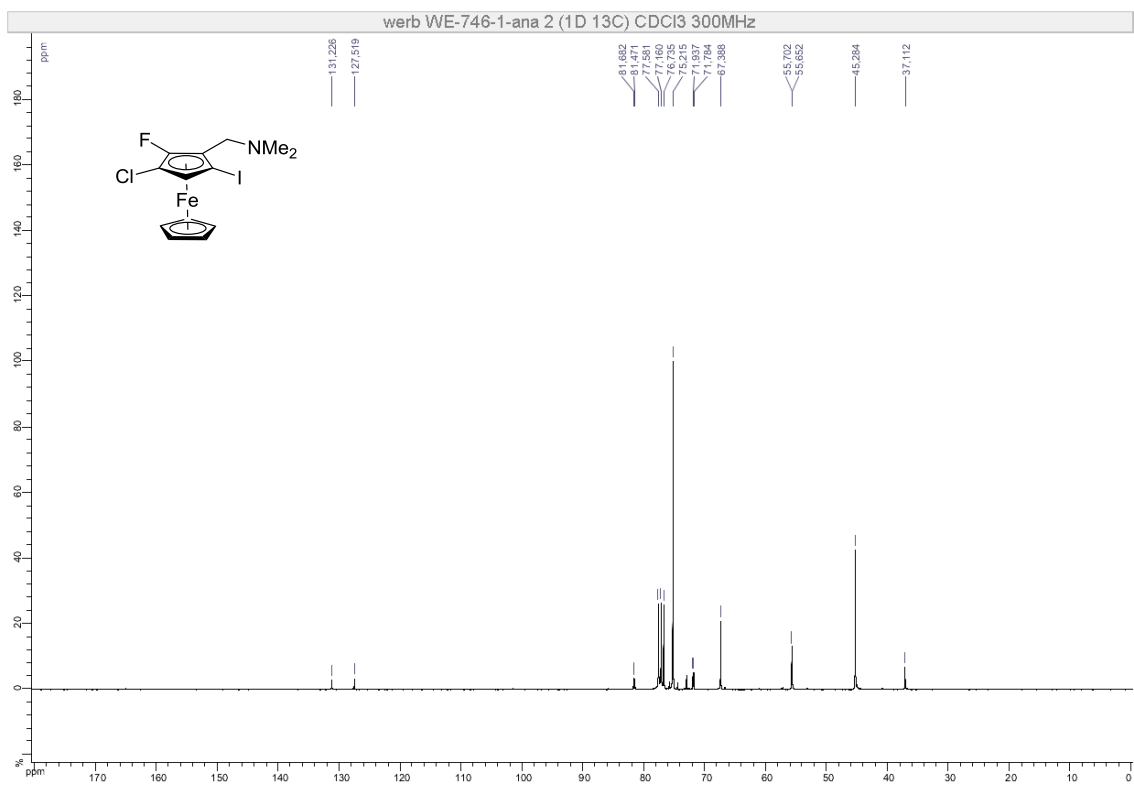
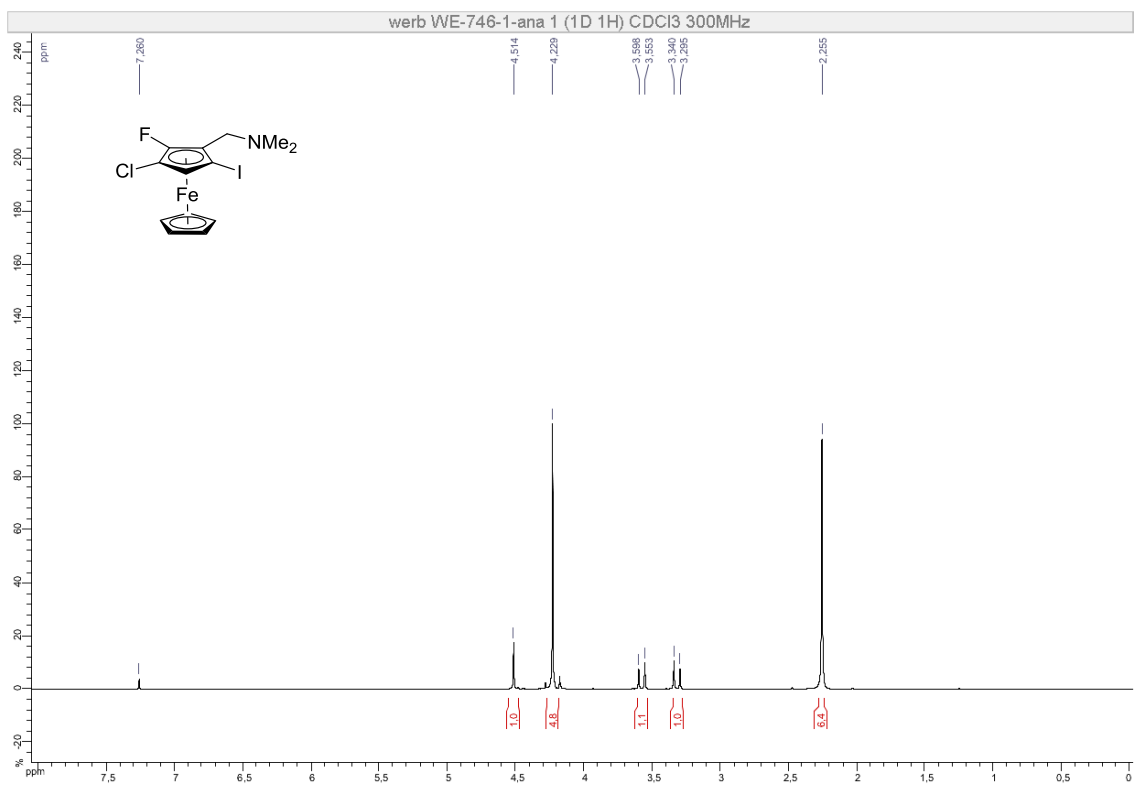


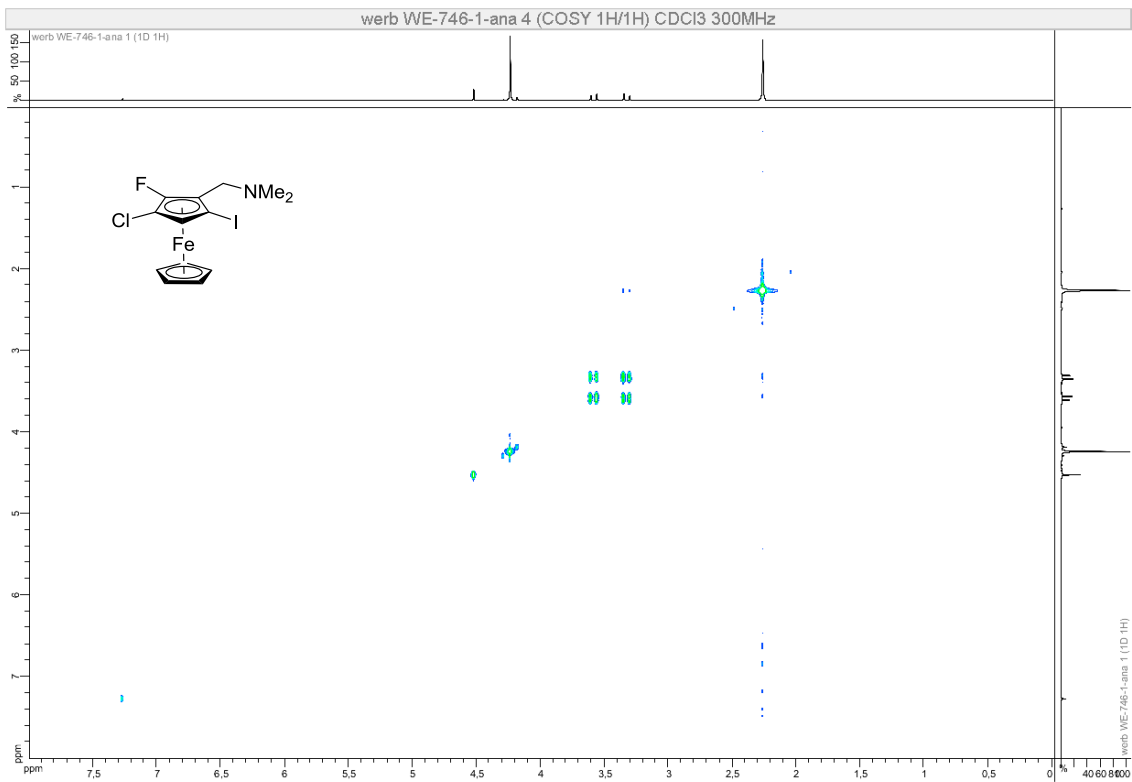
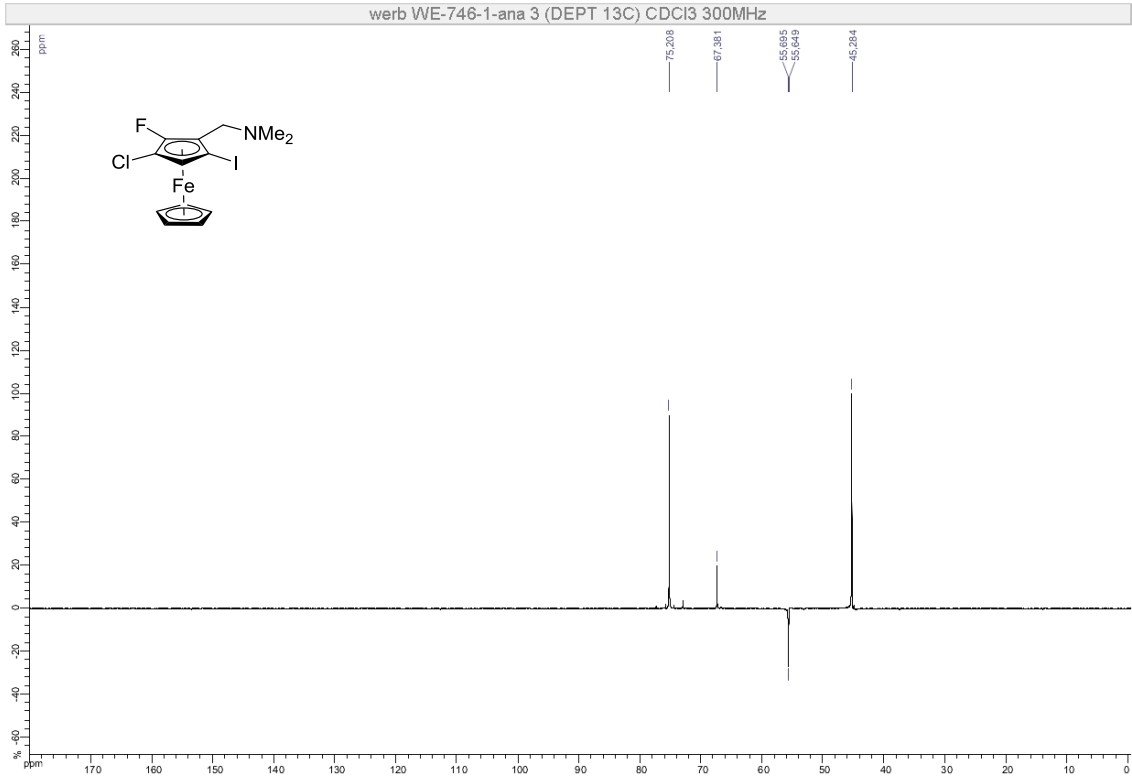


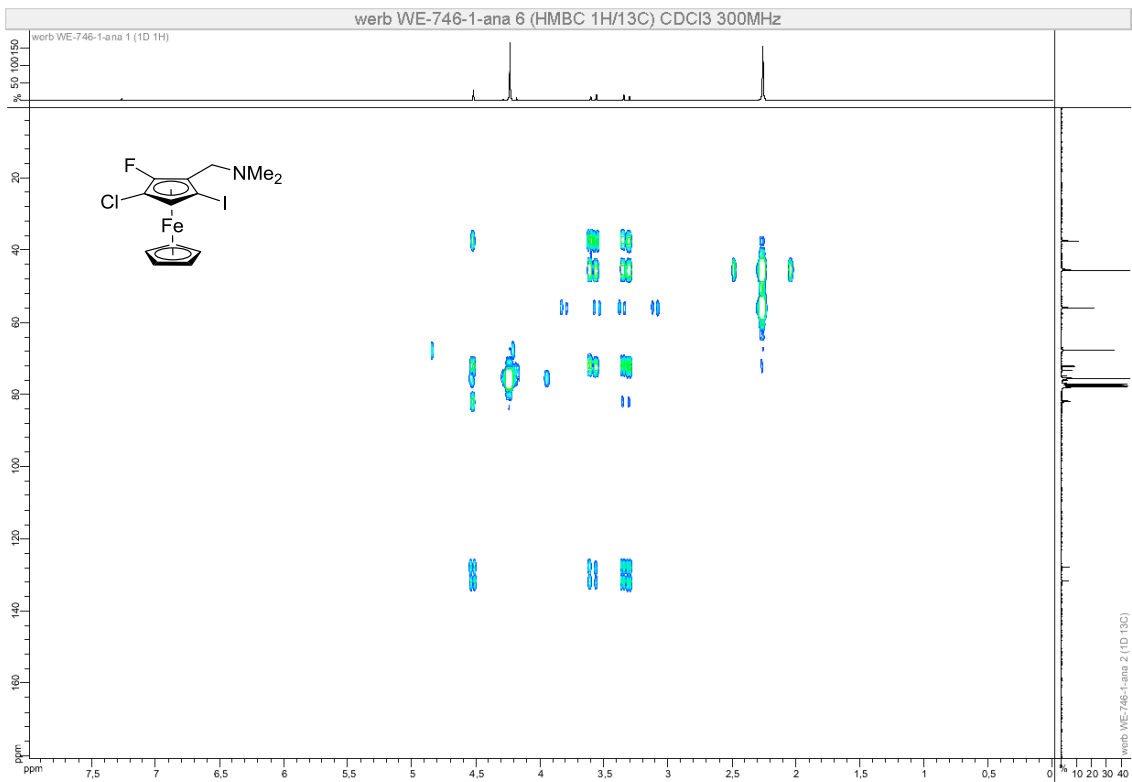
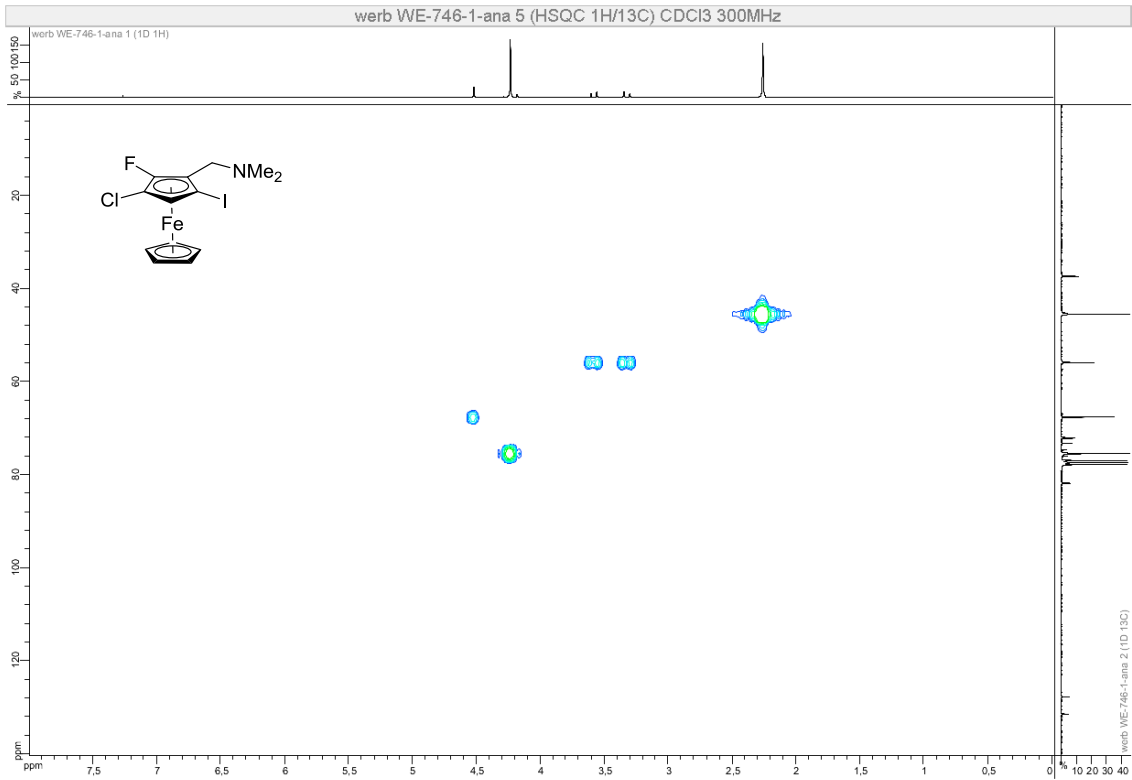


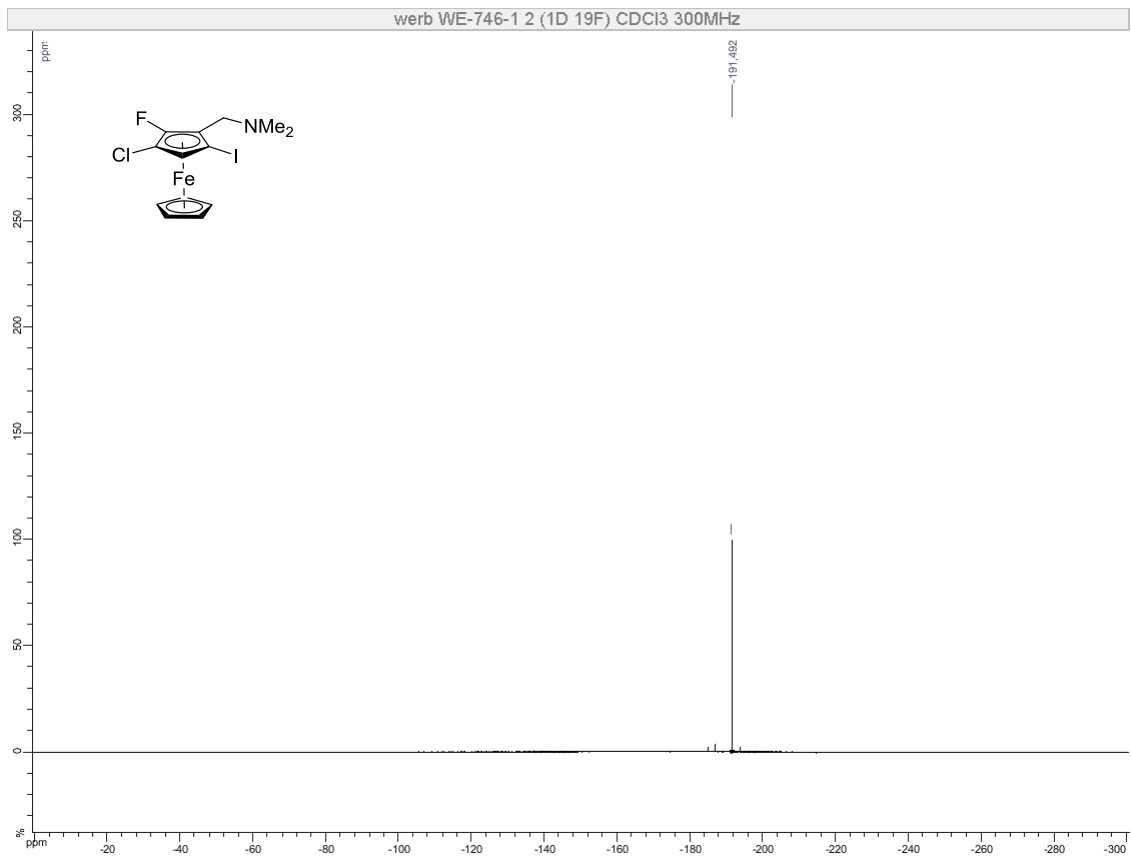


Compound (\pm)-4

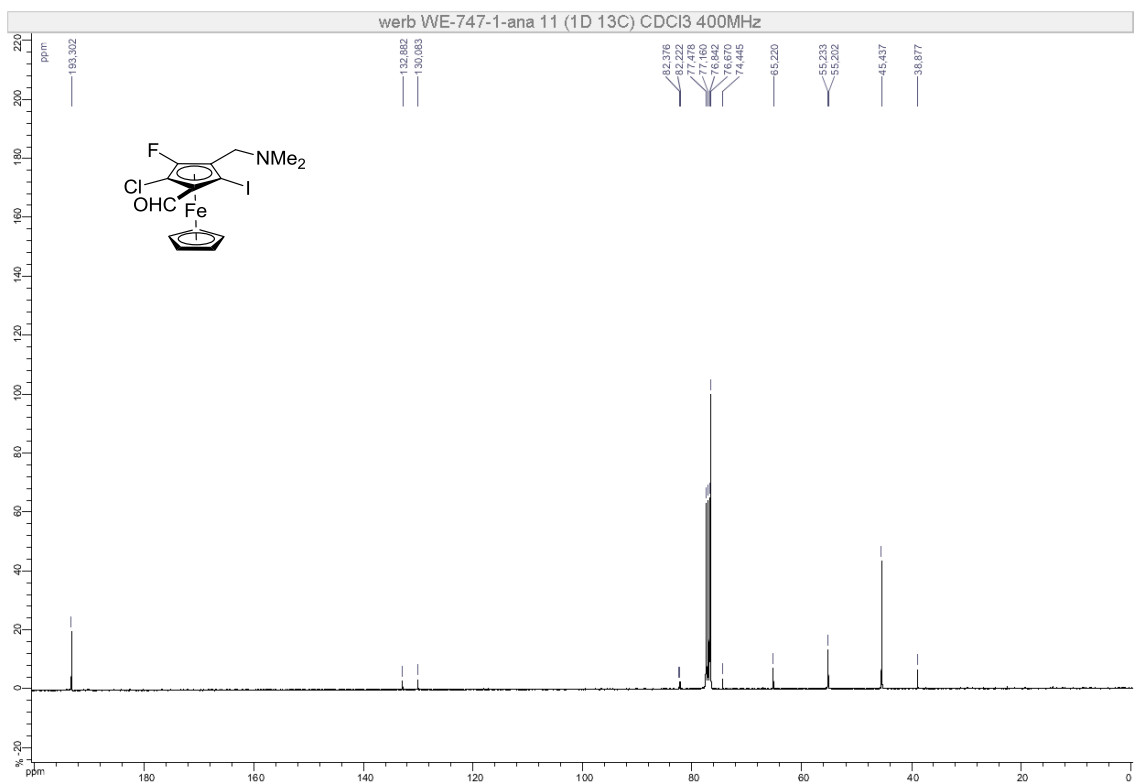
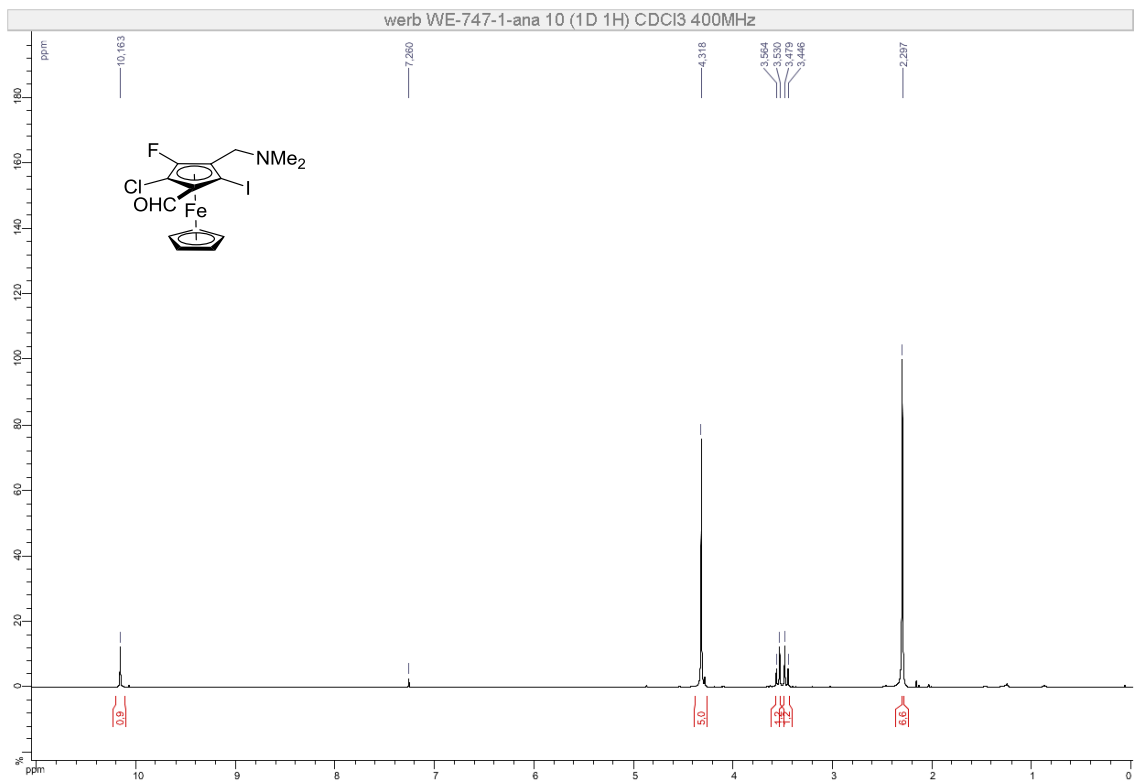


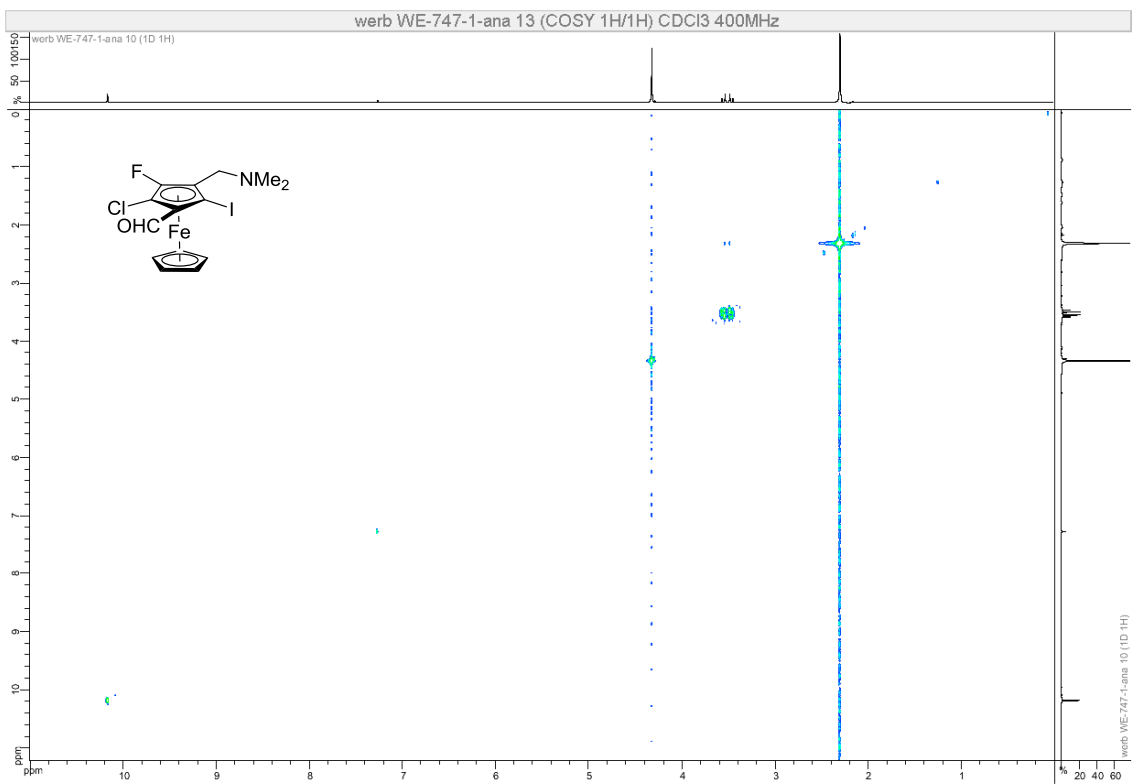
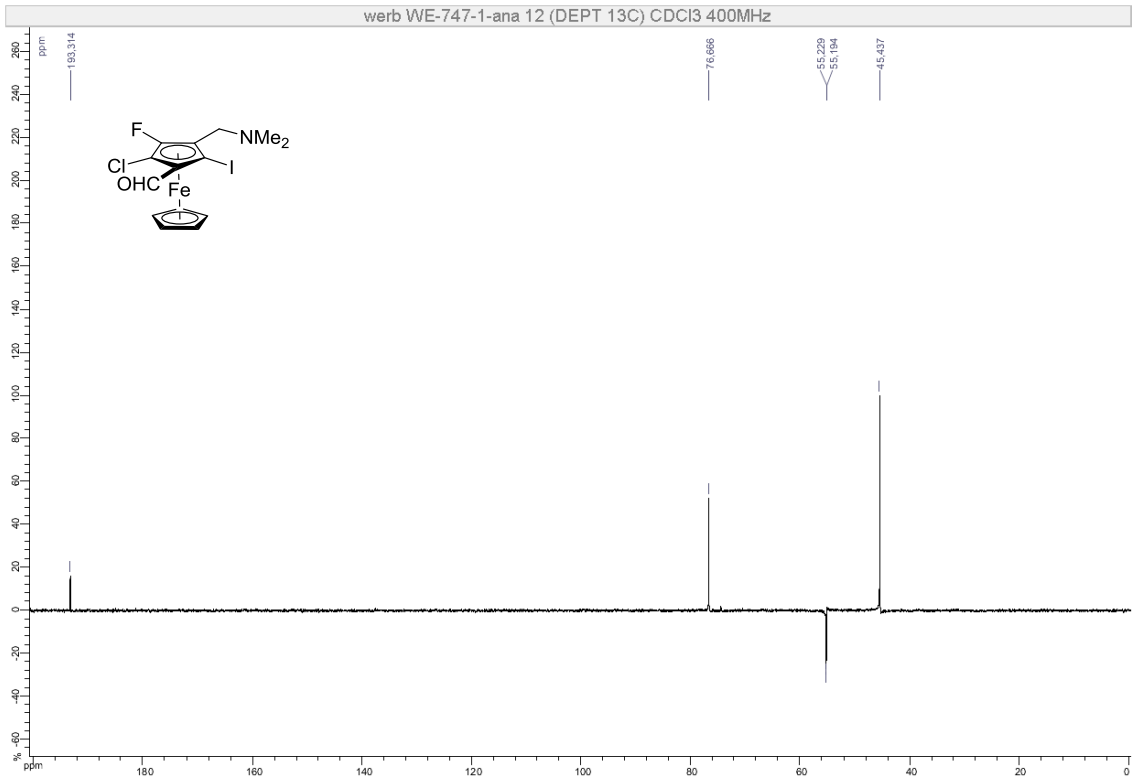


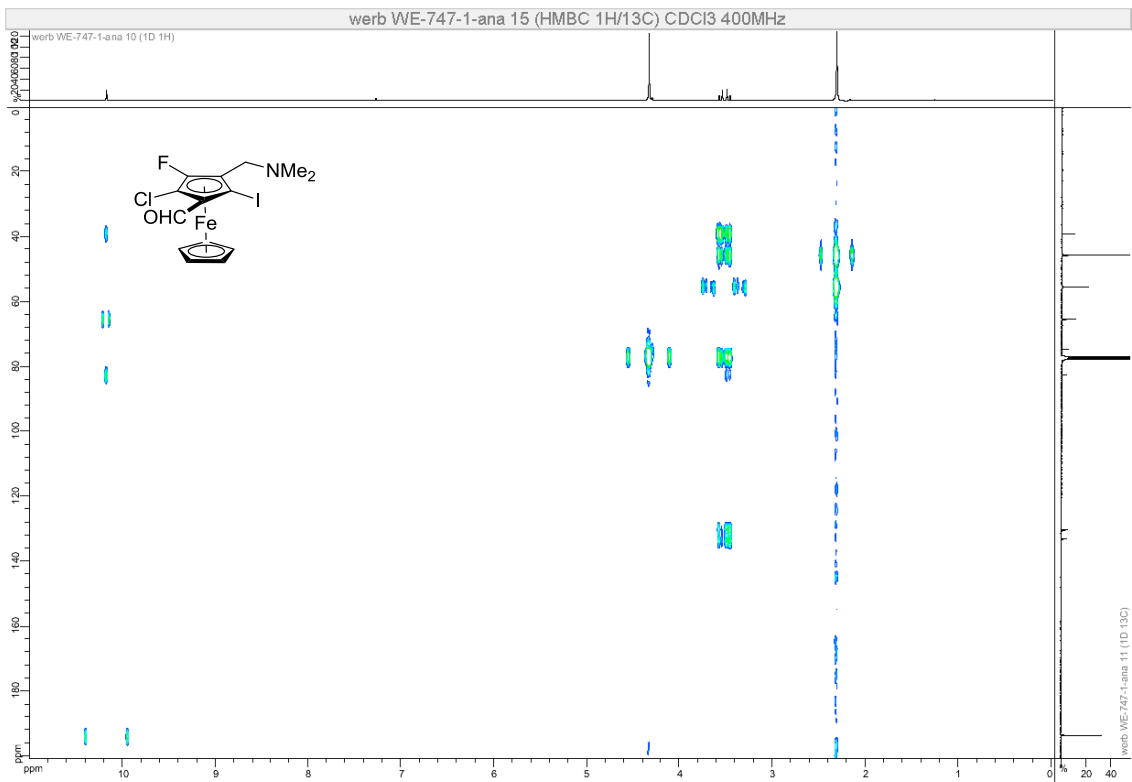
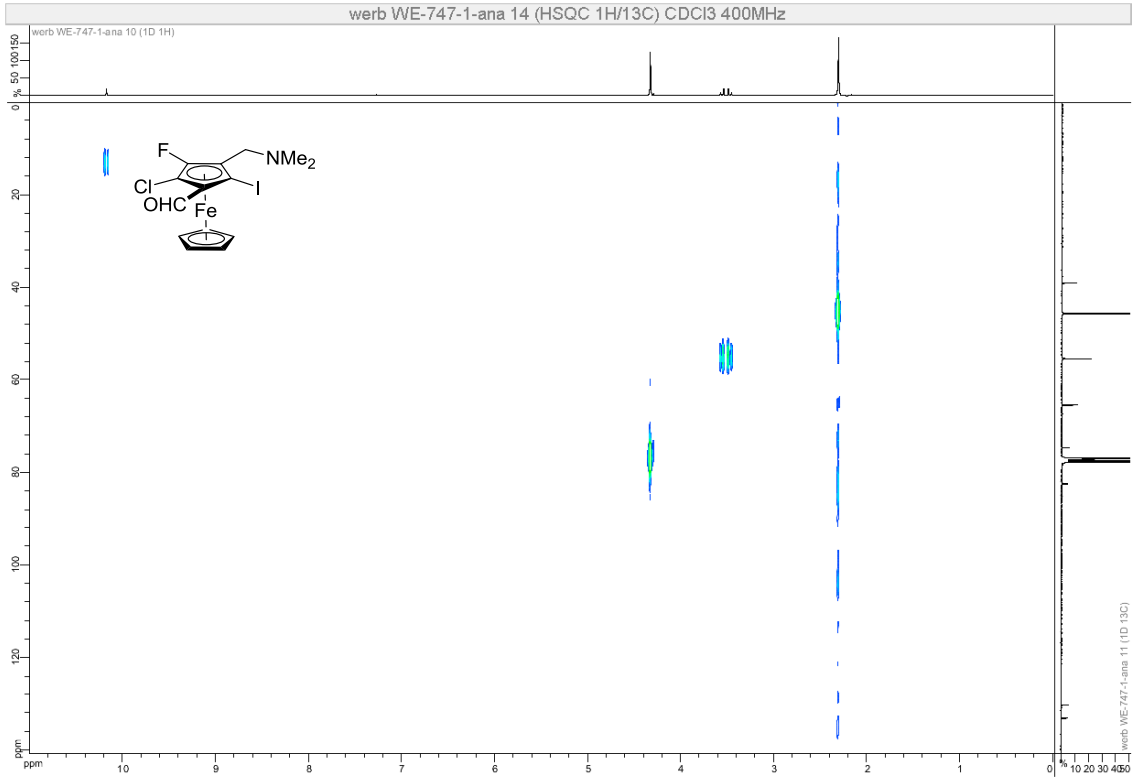


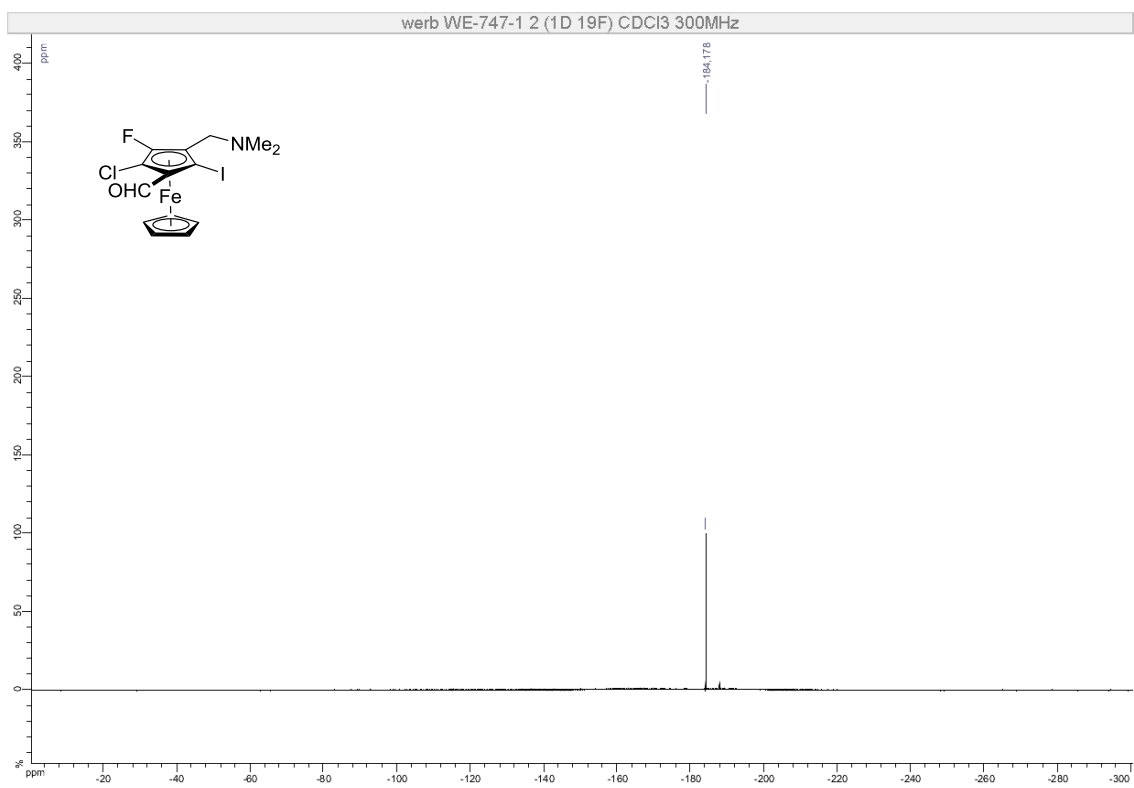
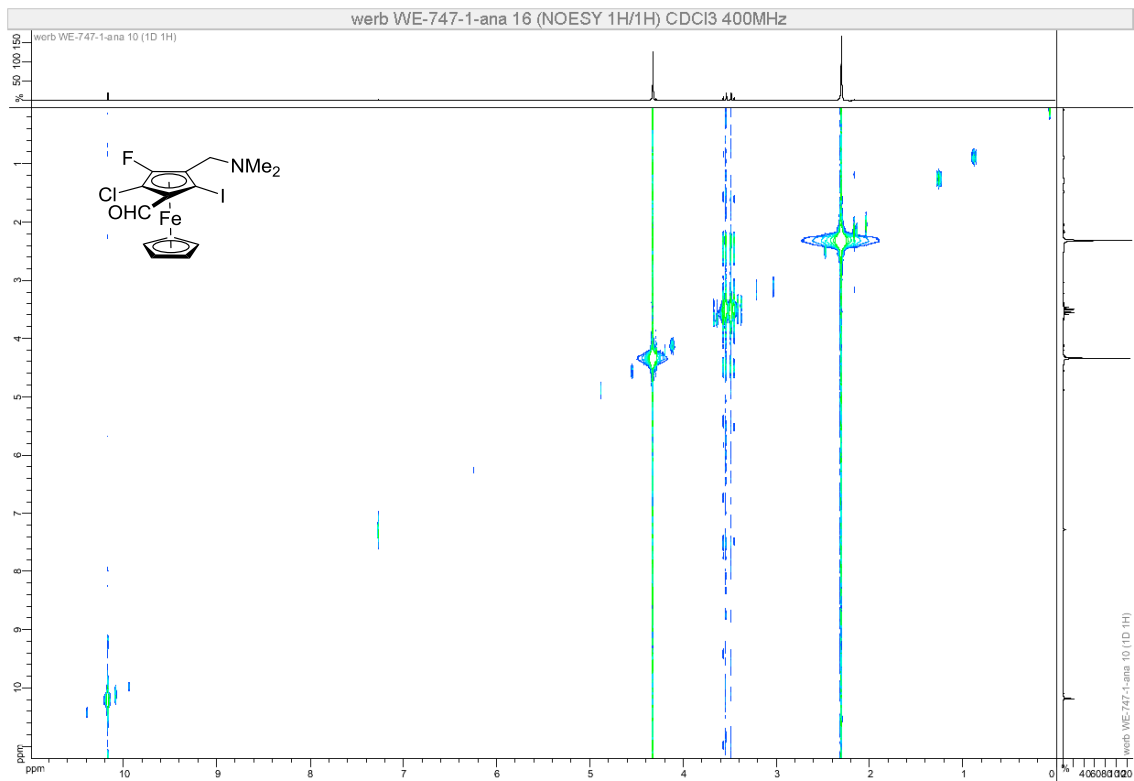


Compound (\pm)-5

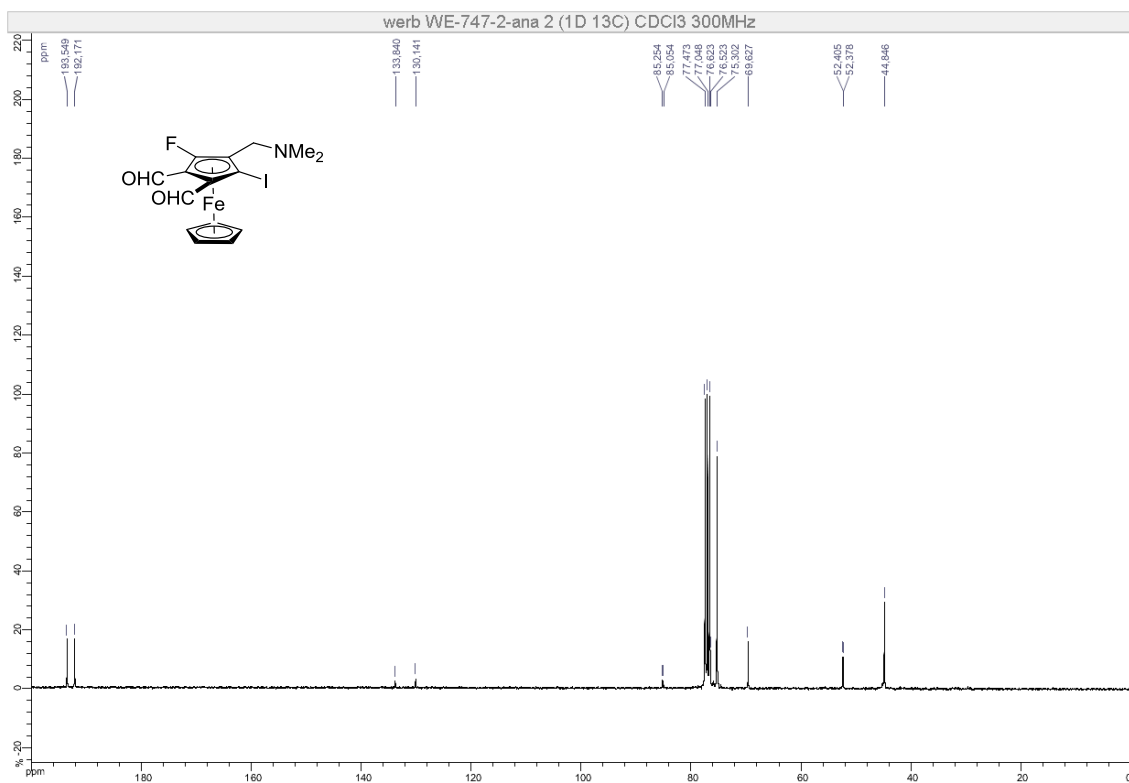
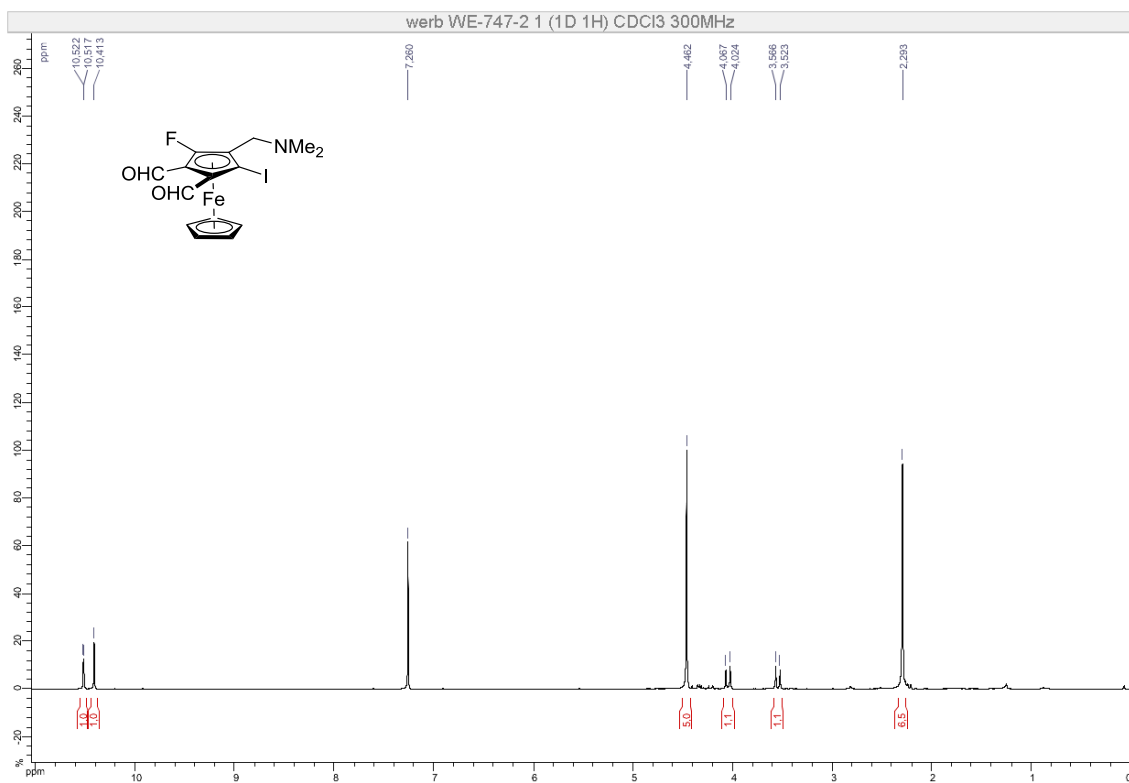


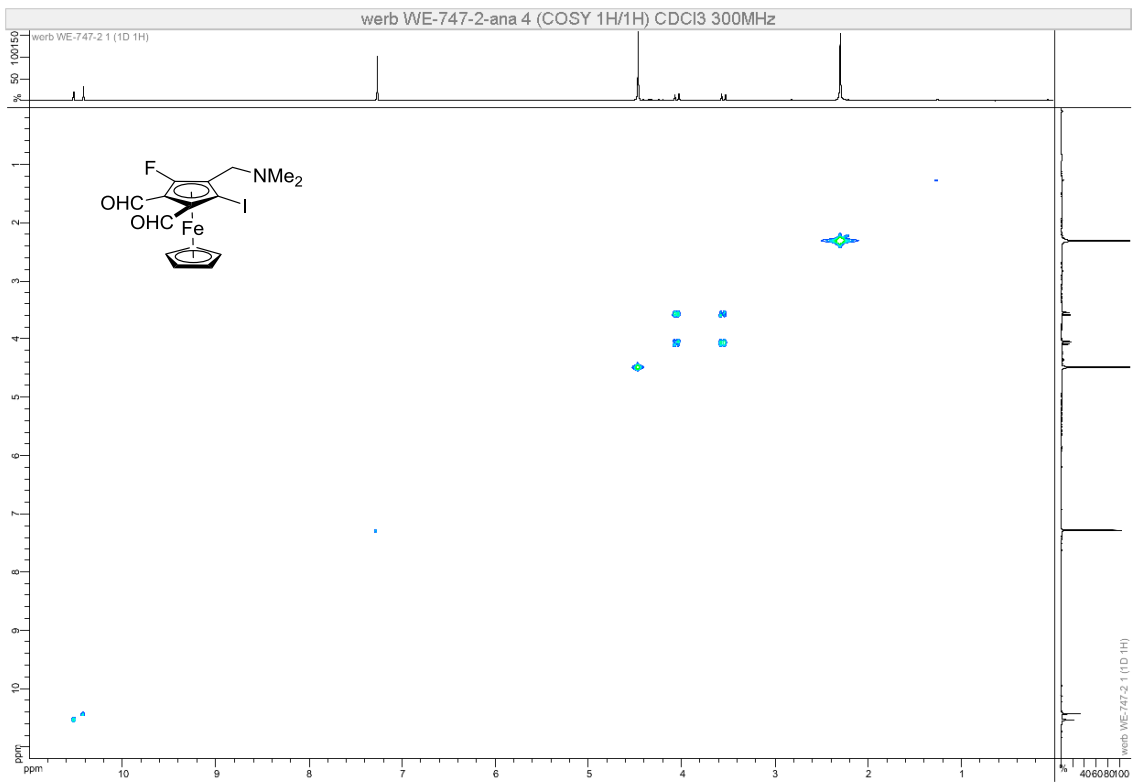
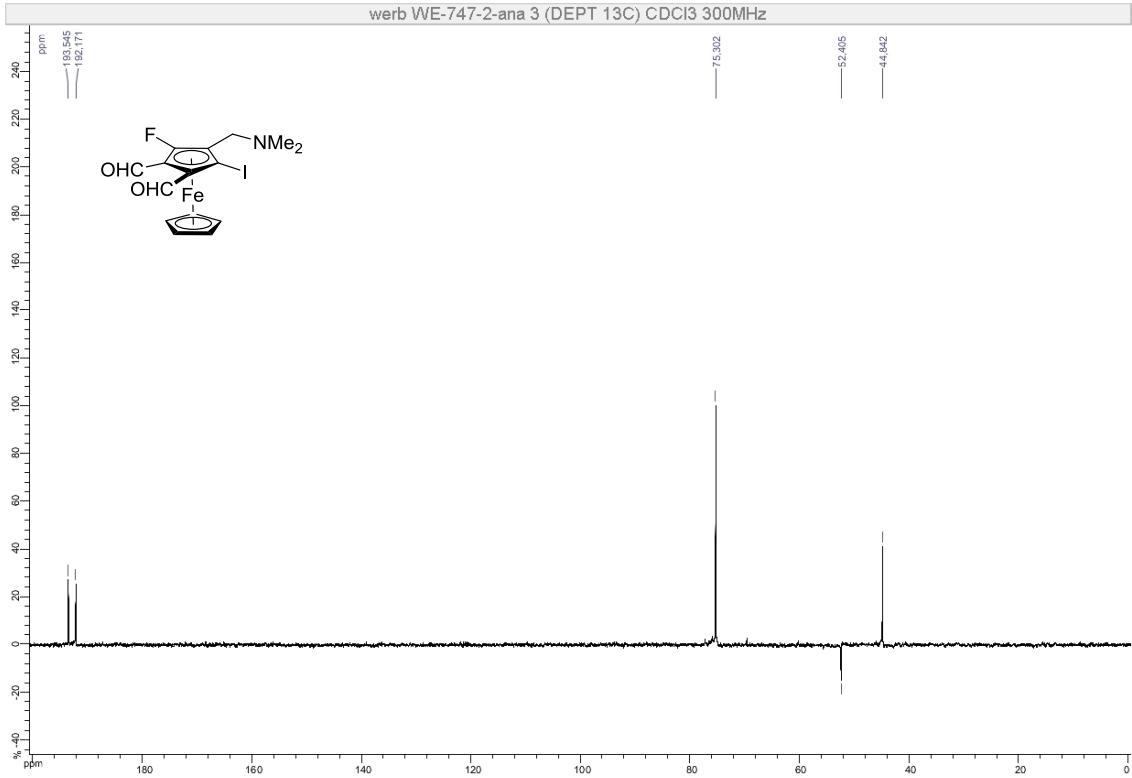


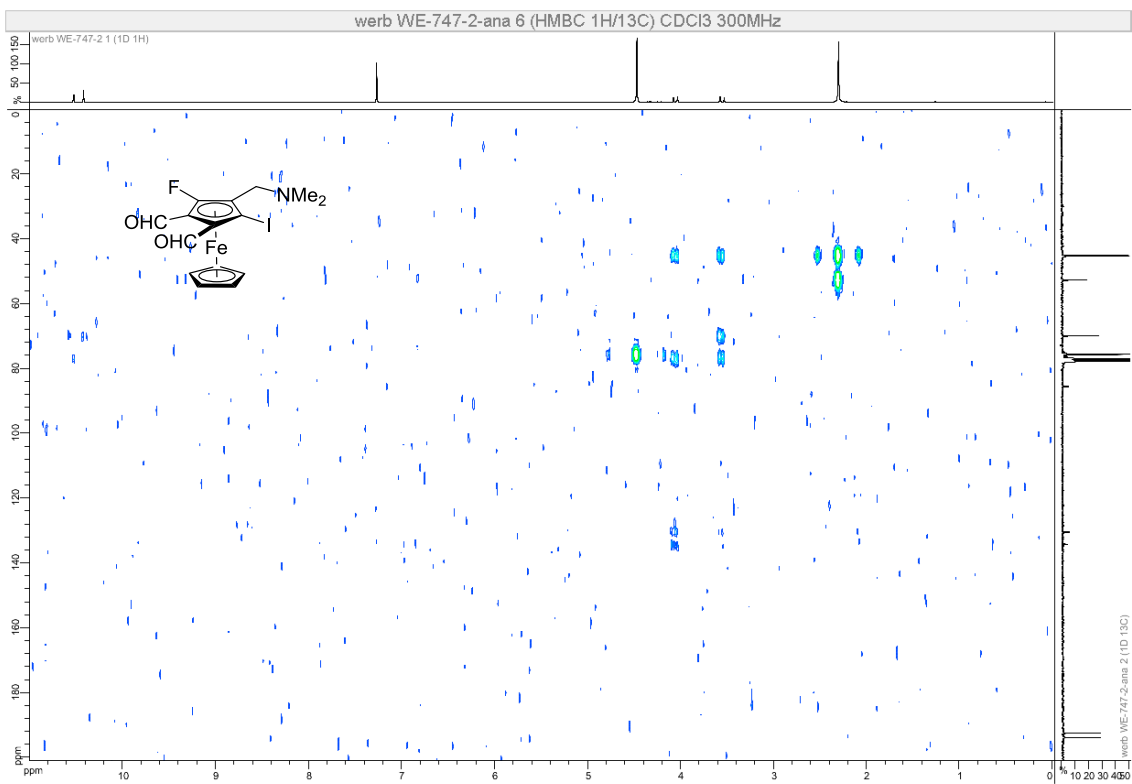
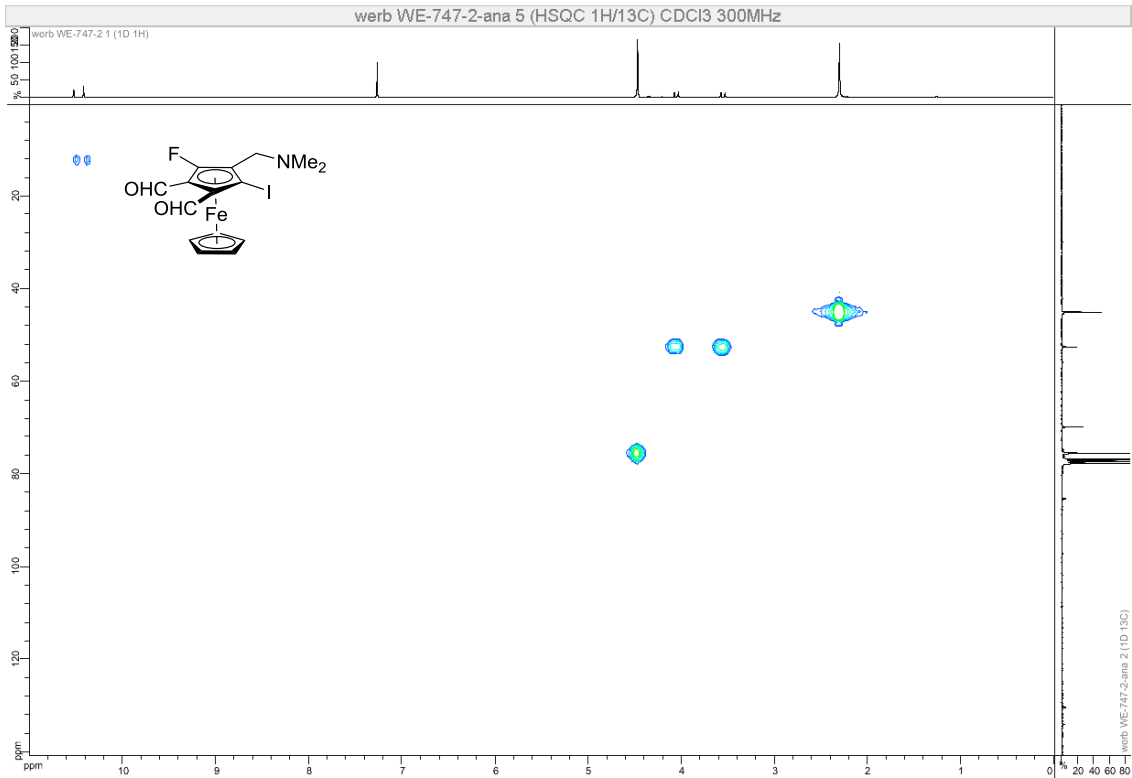


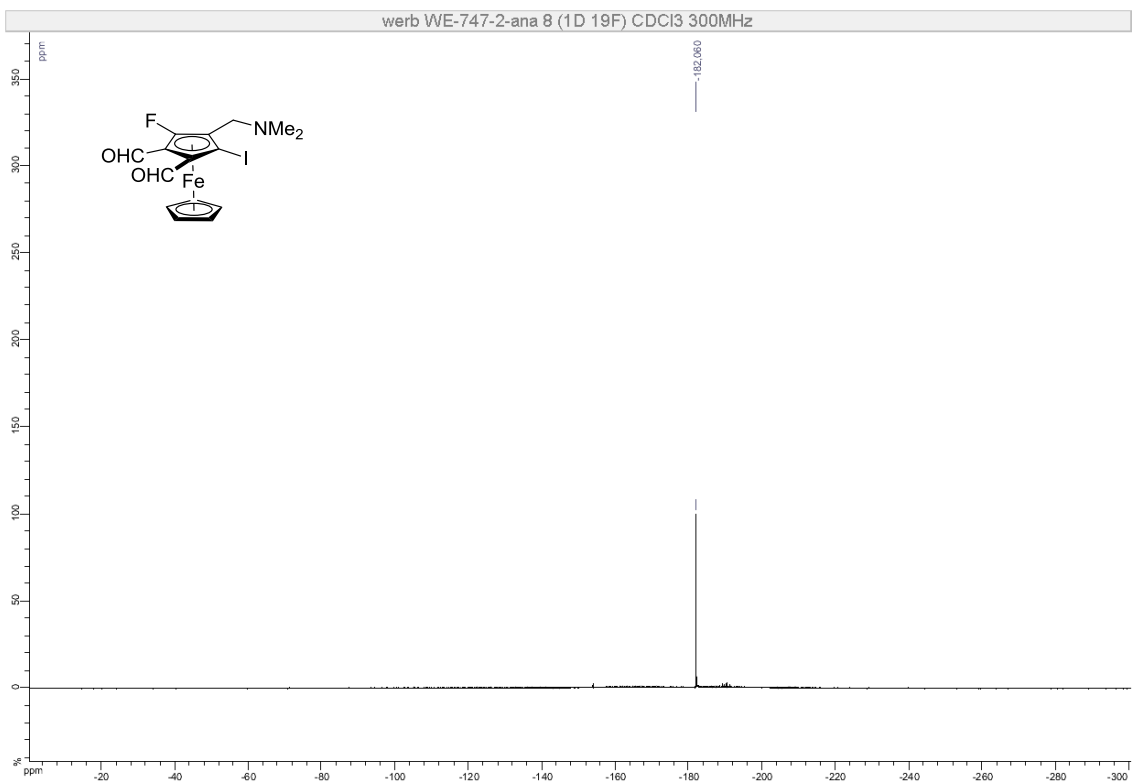
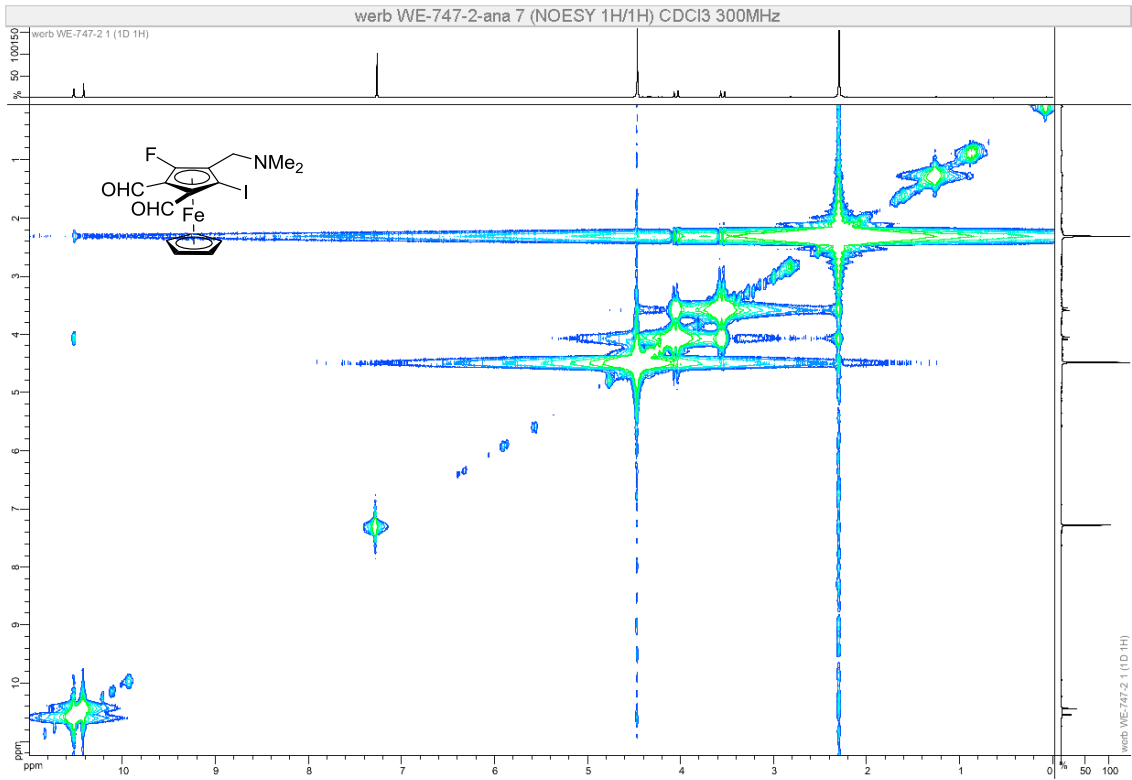


Compound (\pm)-6

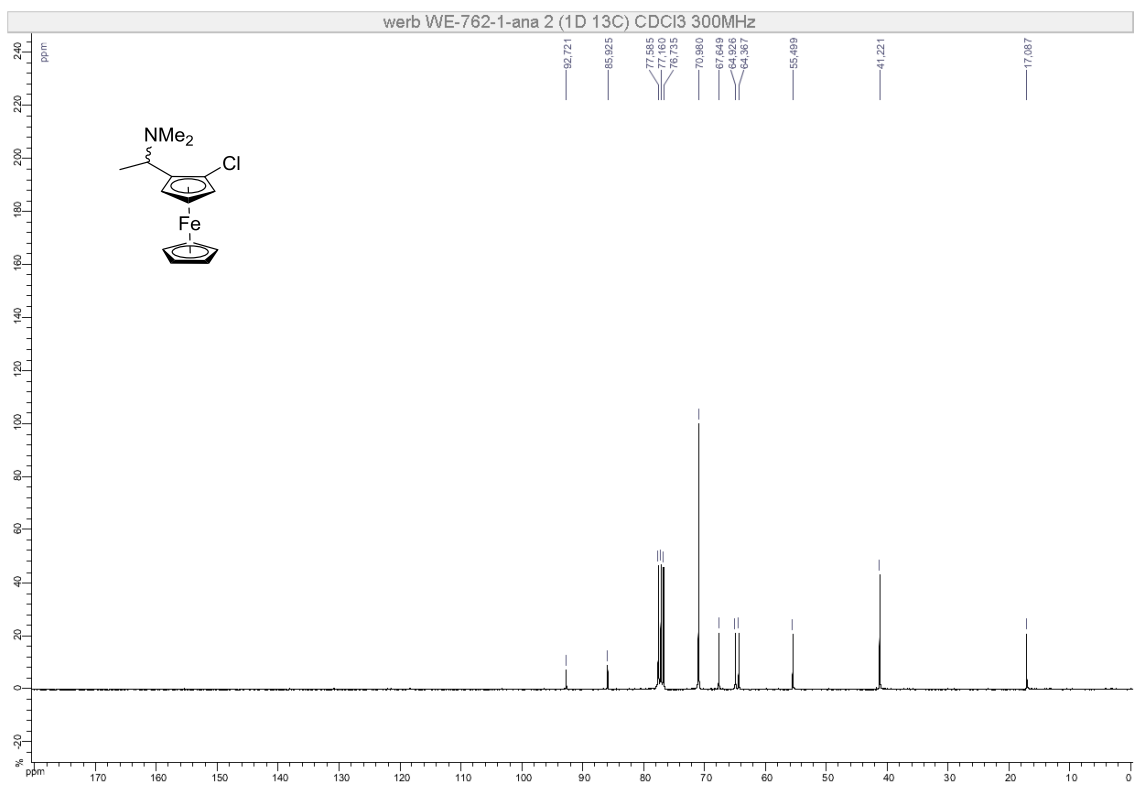
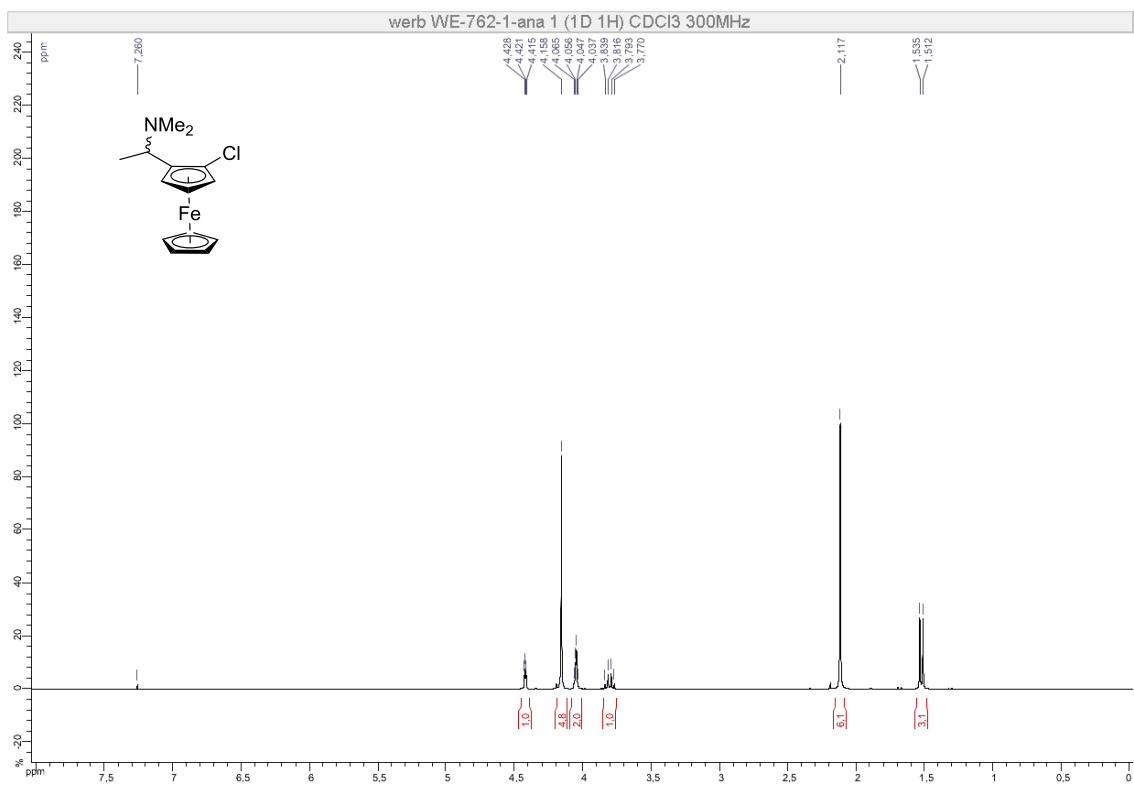


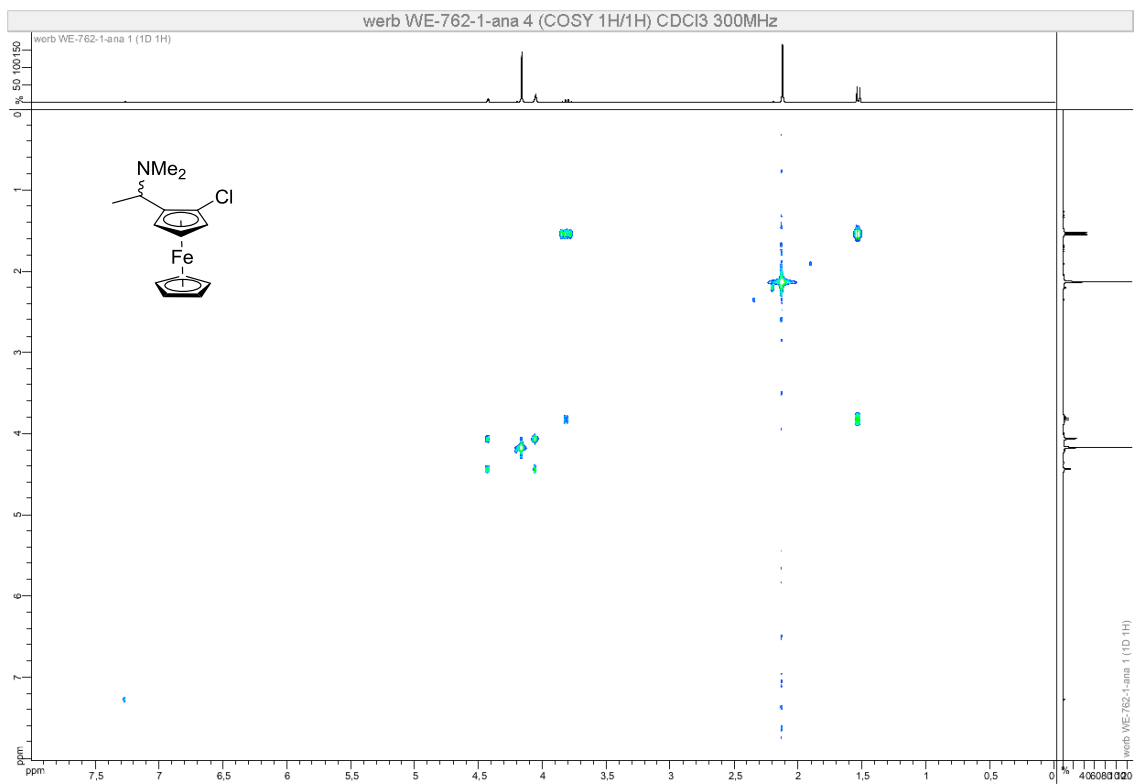
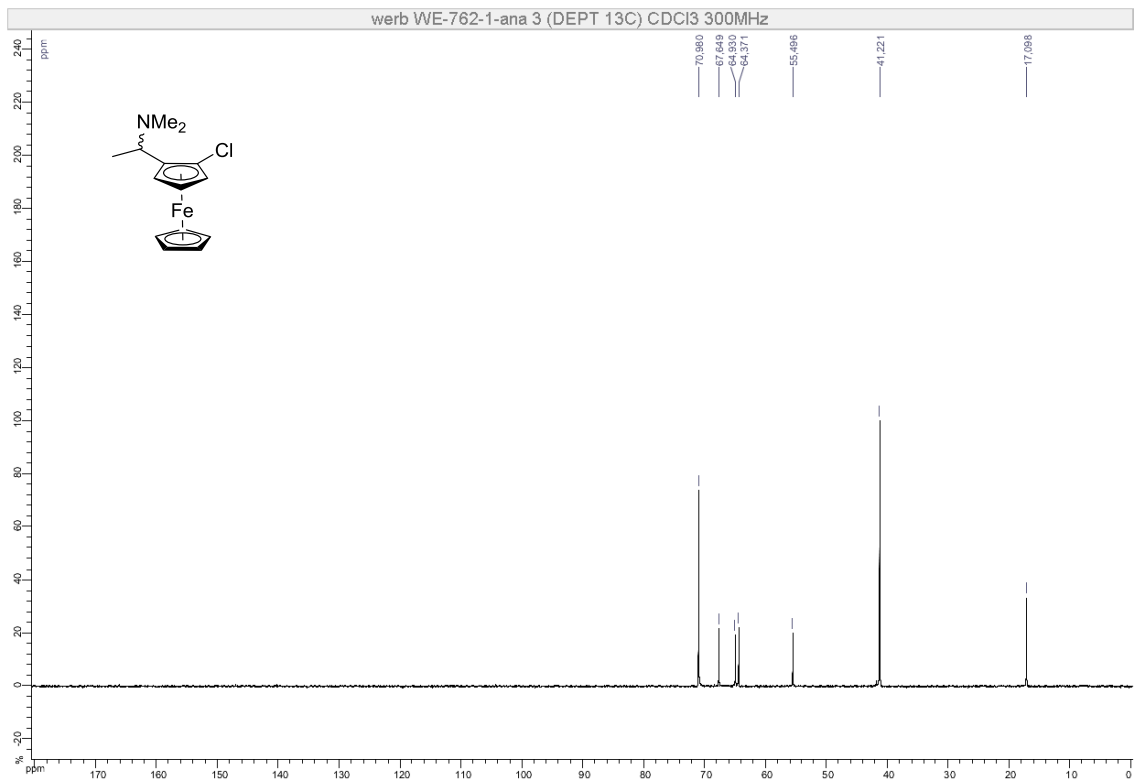


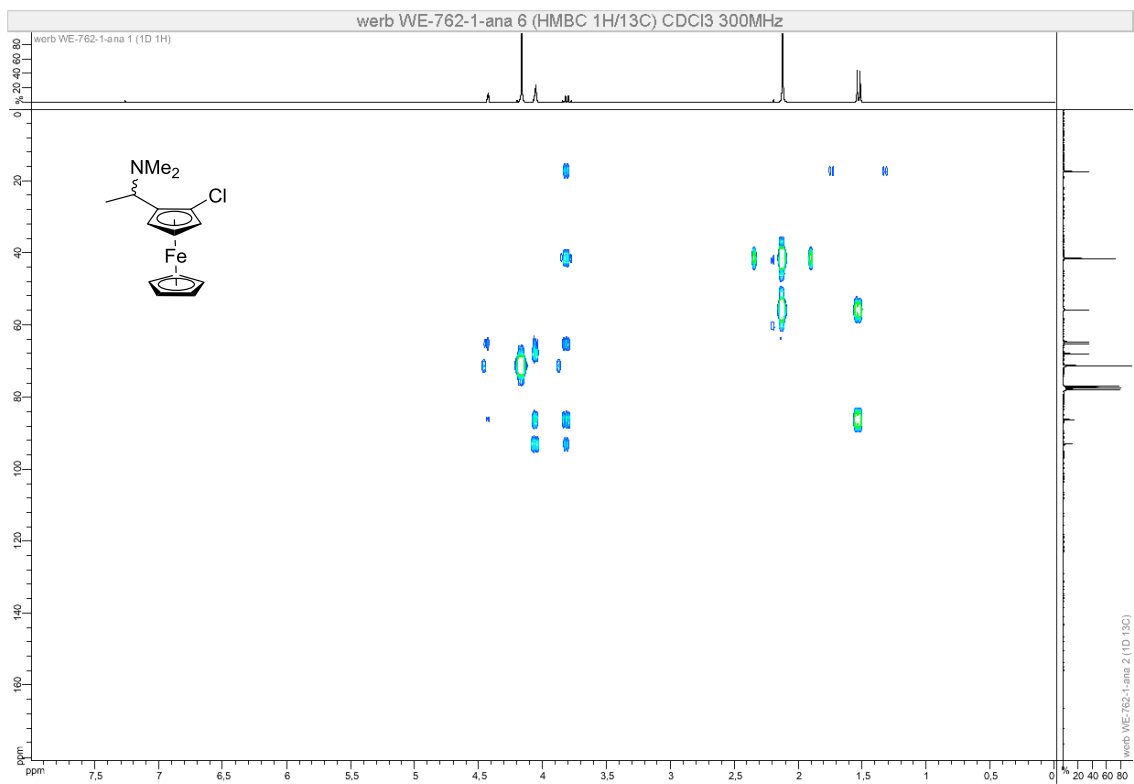
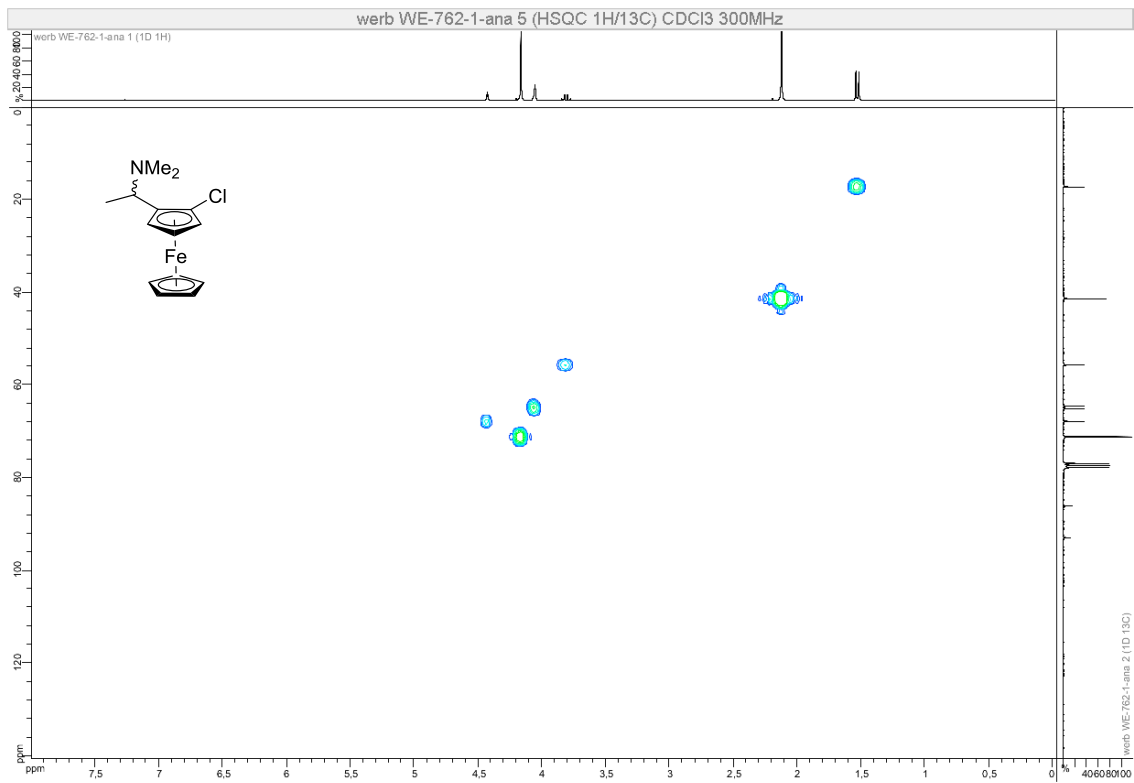


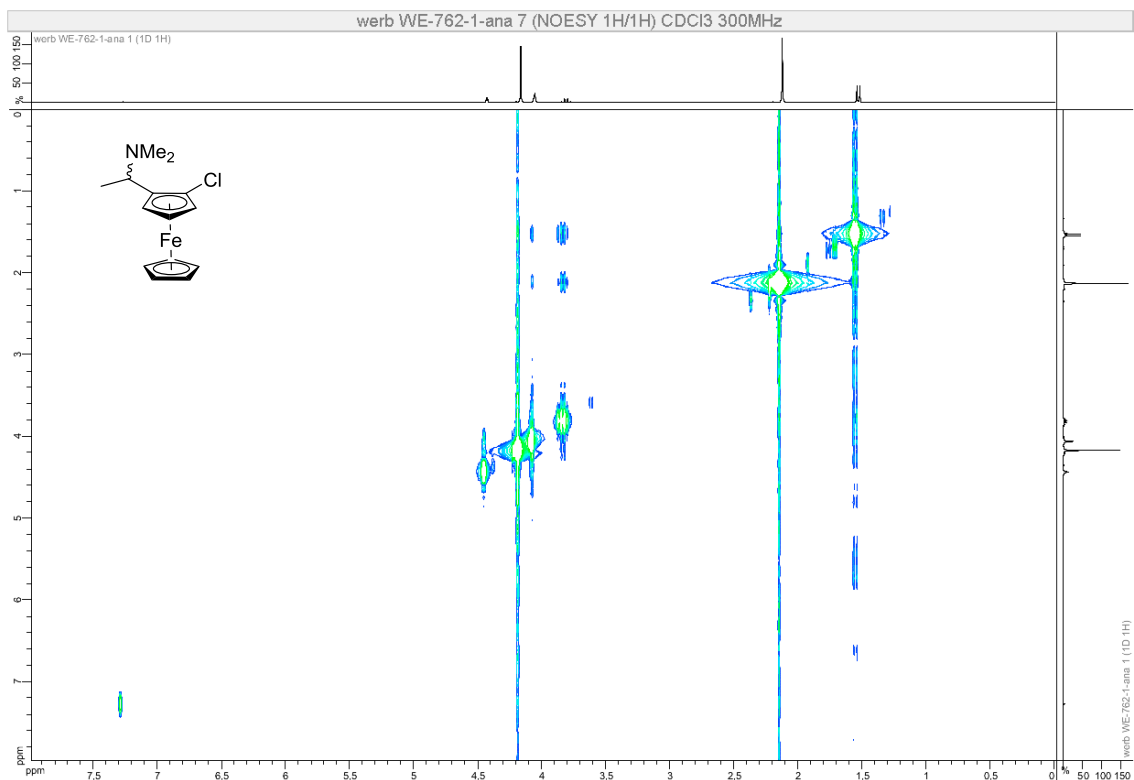


Compound (\pm)-8

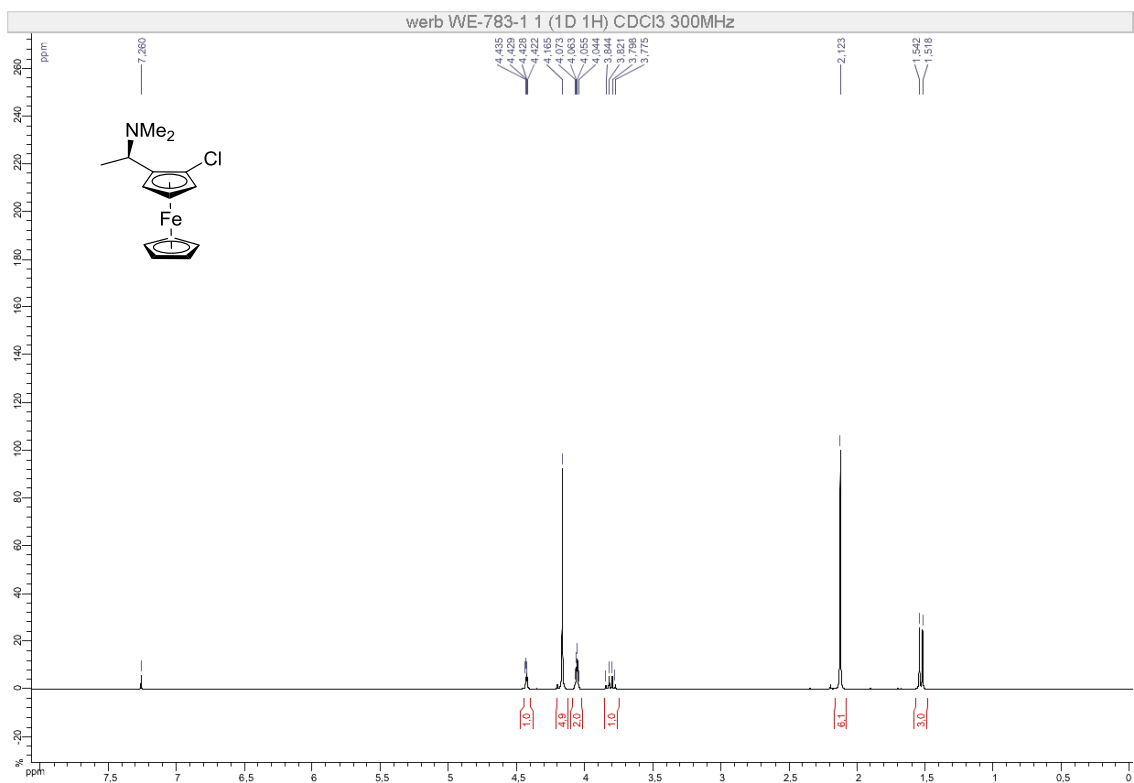




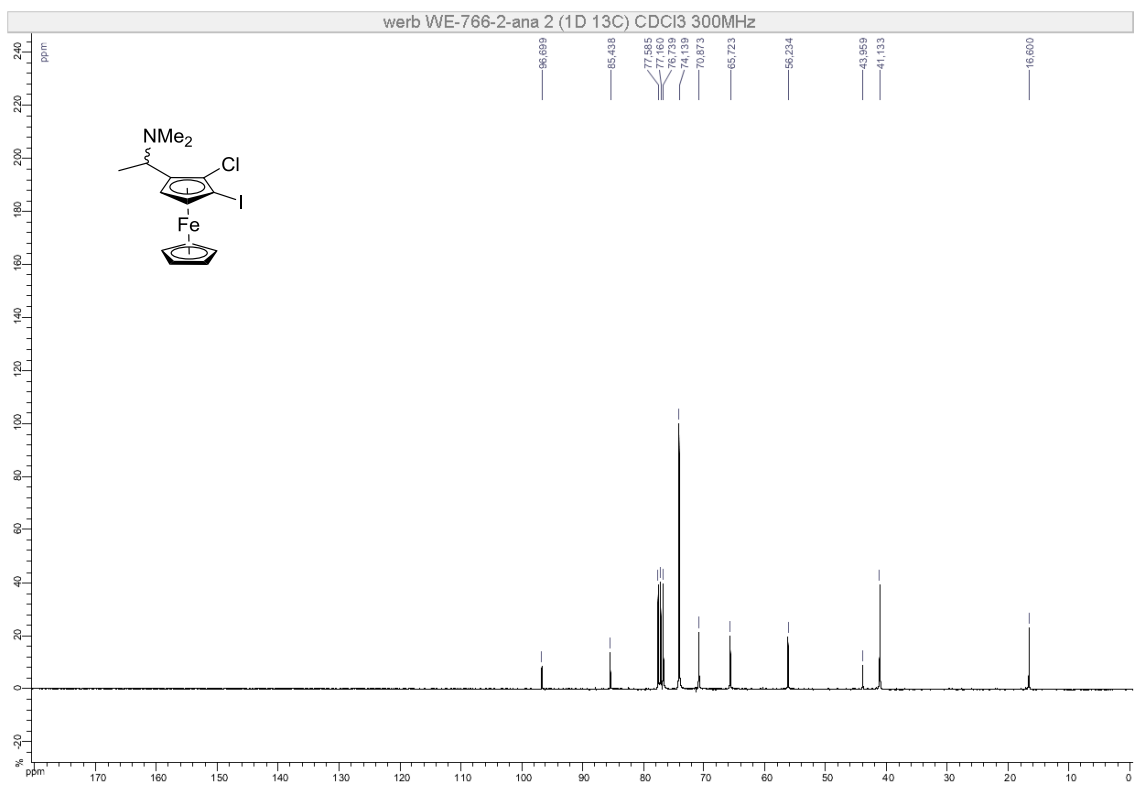
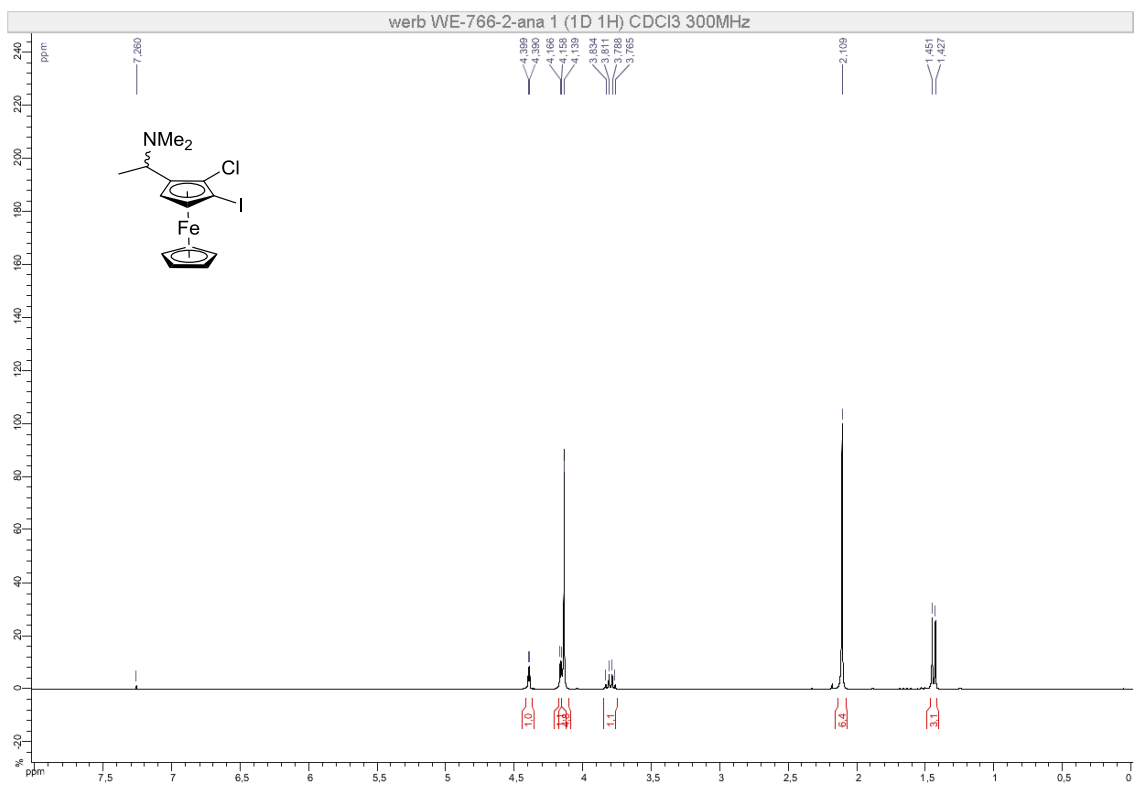


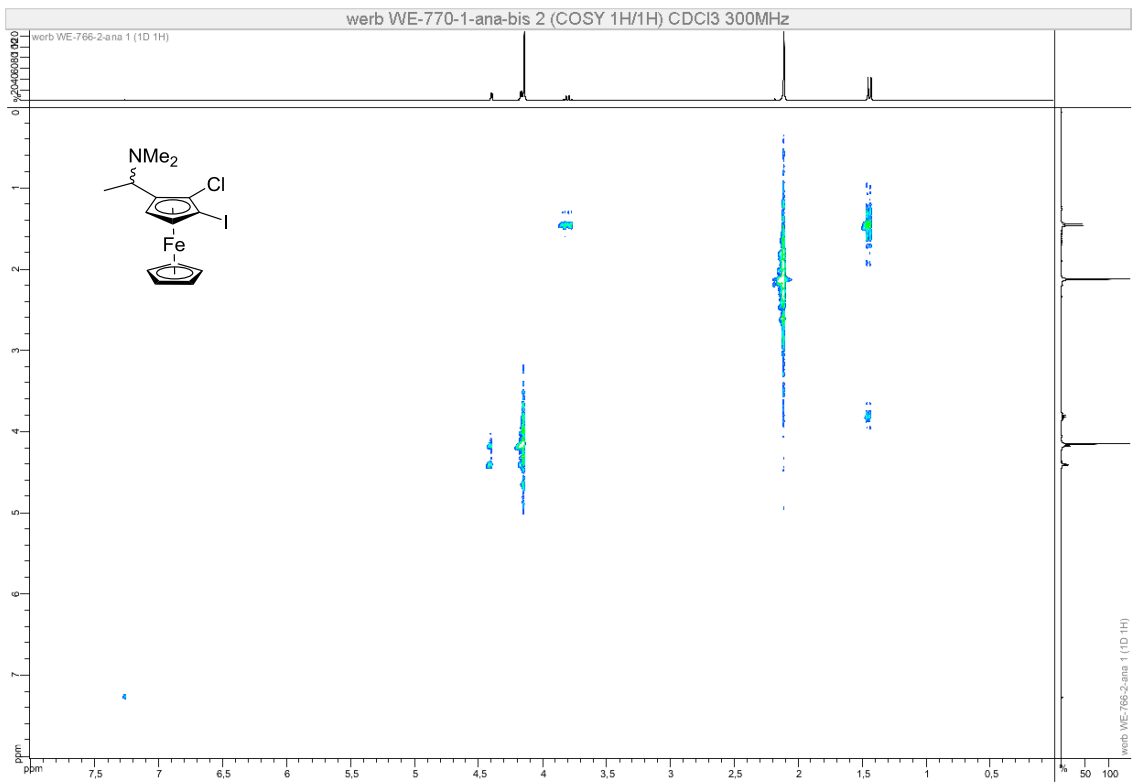
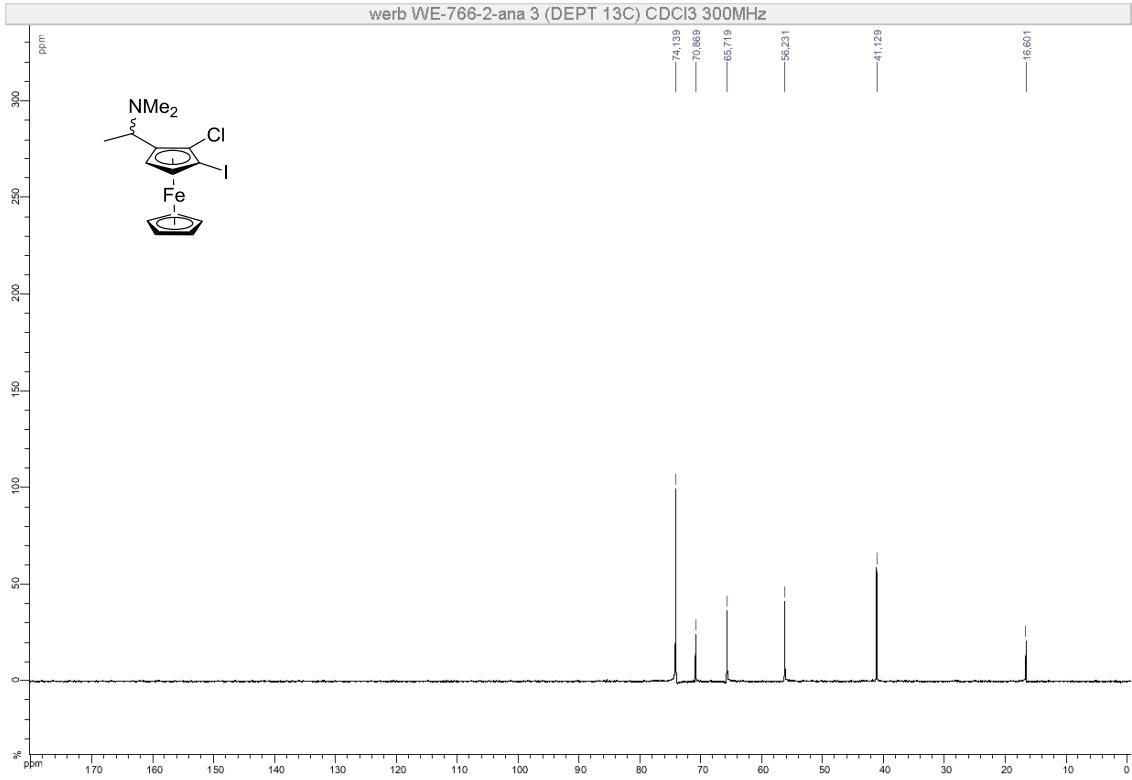


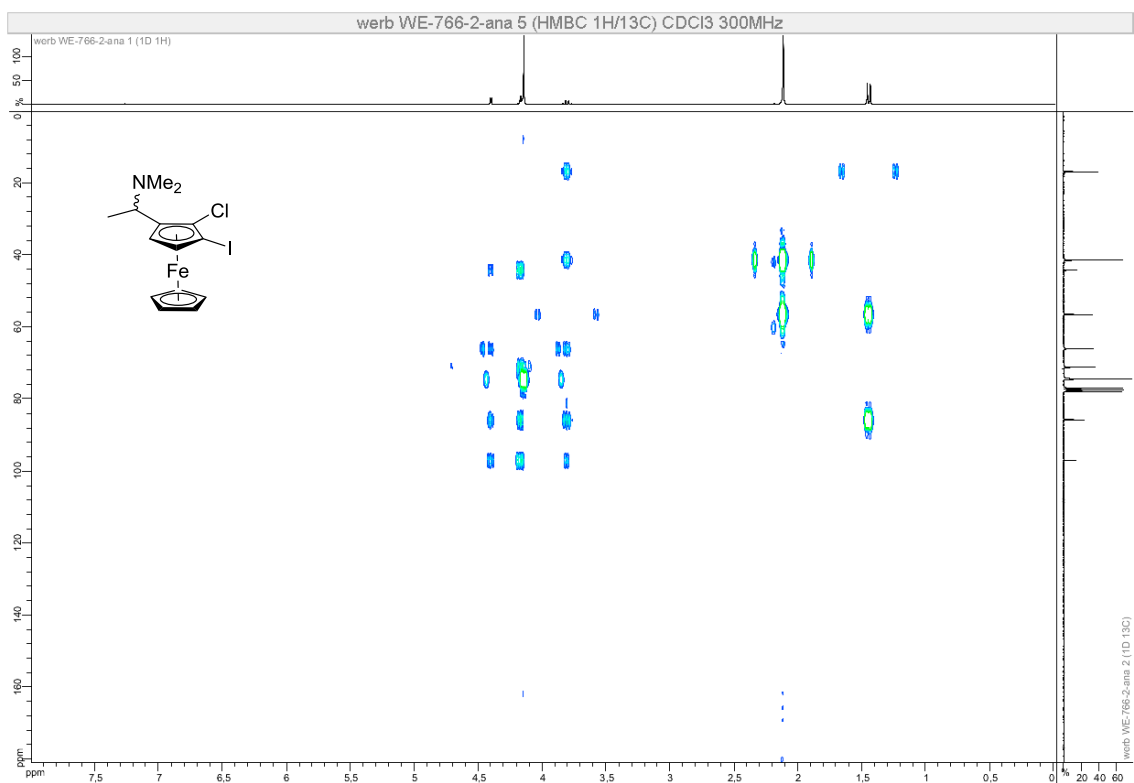
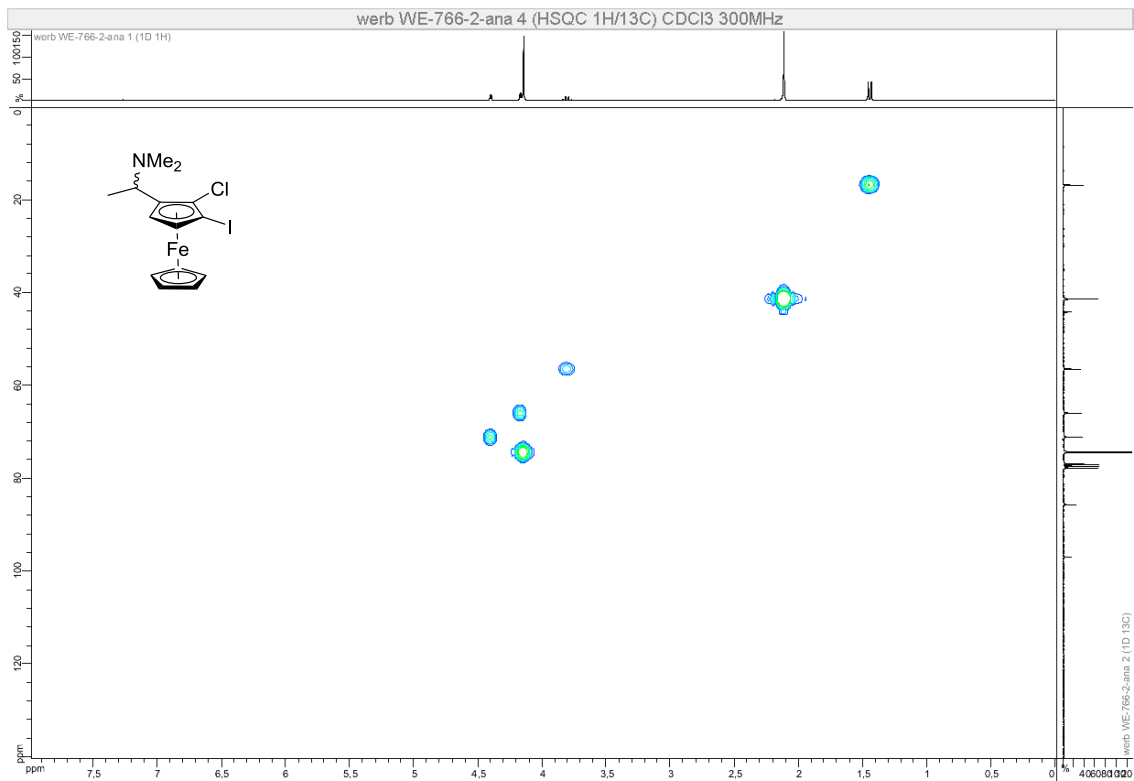
Compound (*R,S*)-8

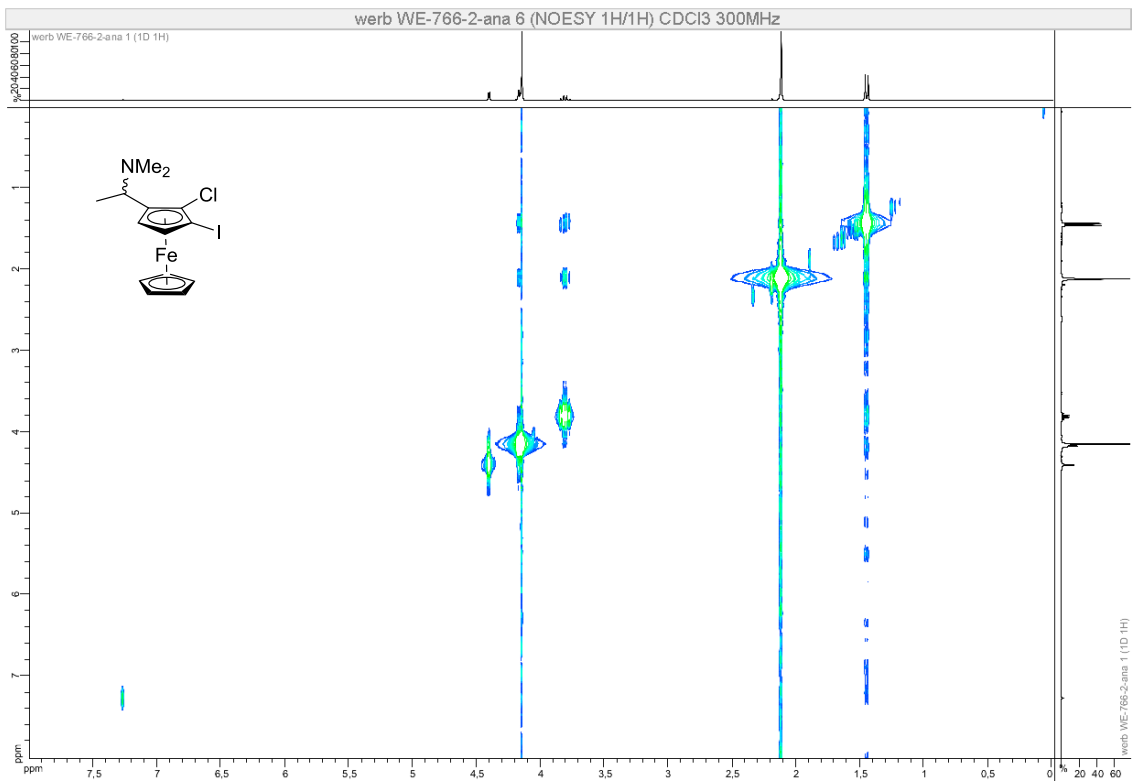


Compound (\pm)-9

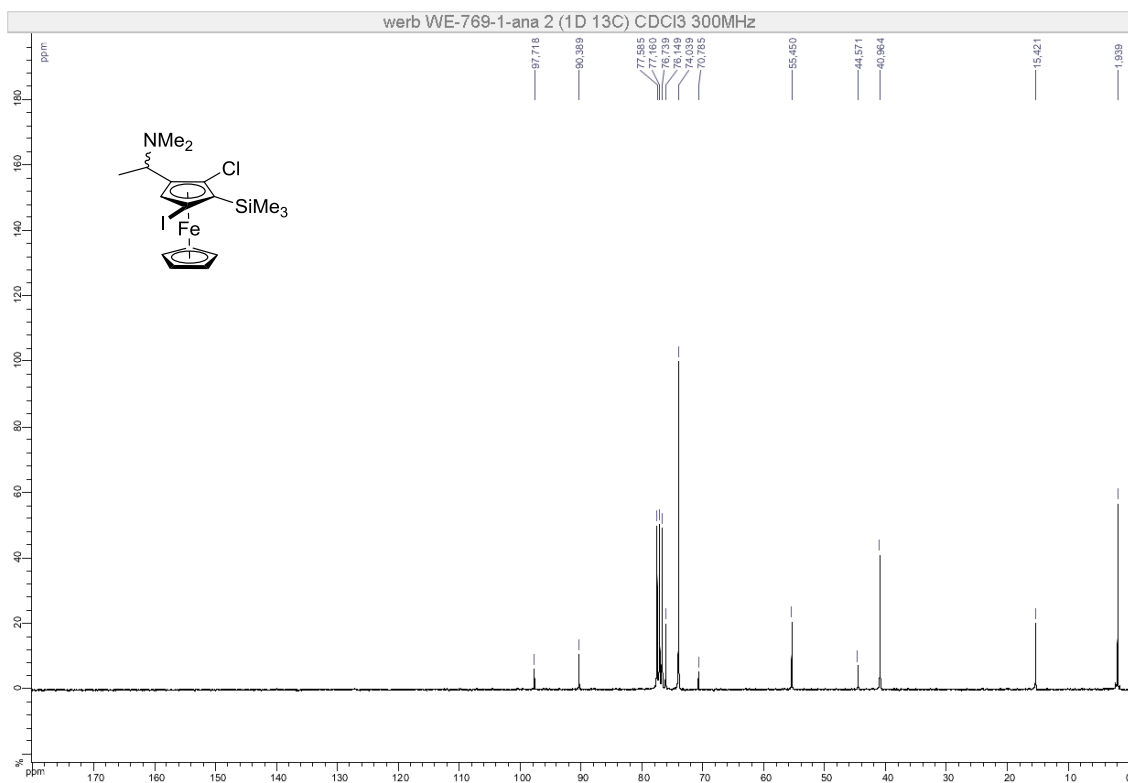
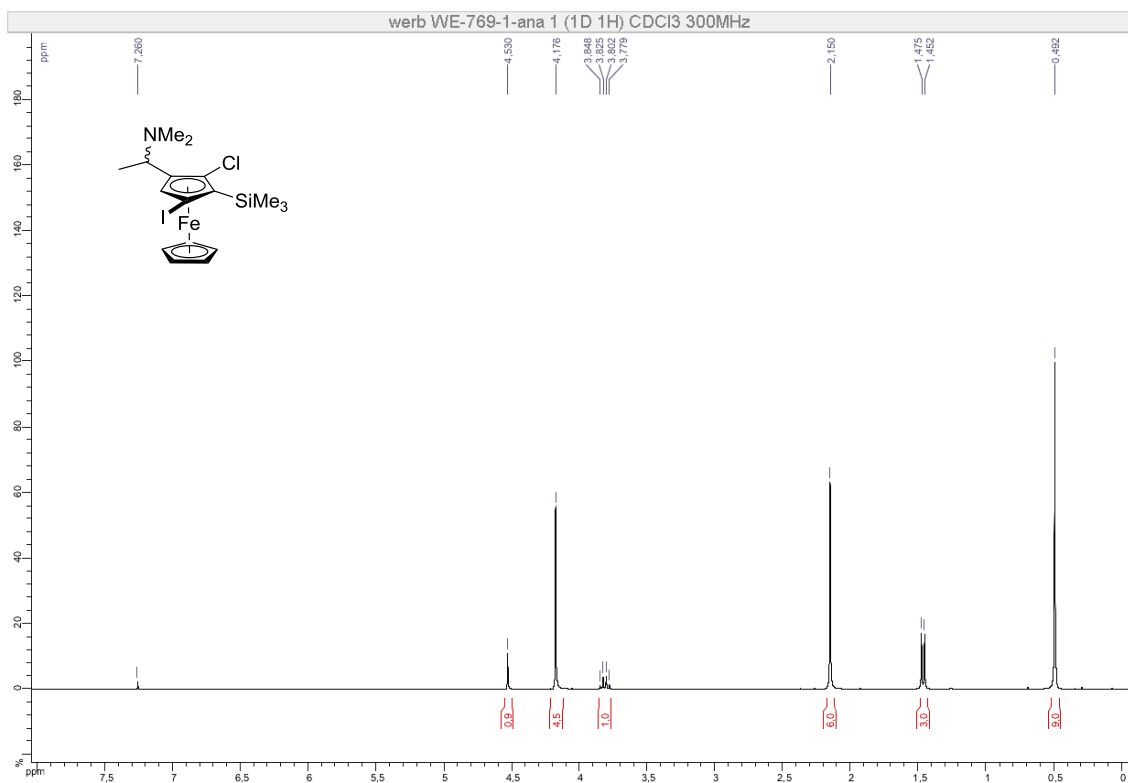


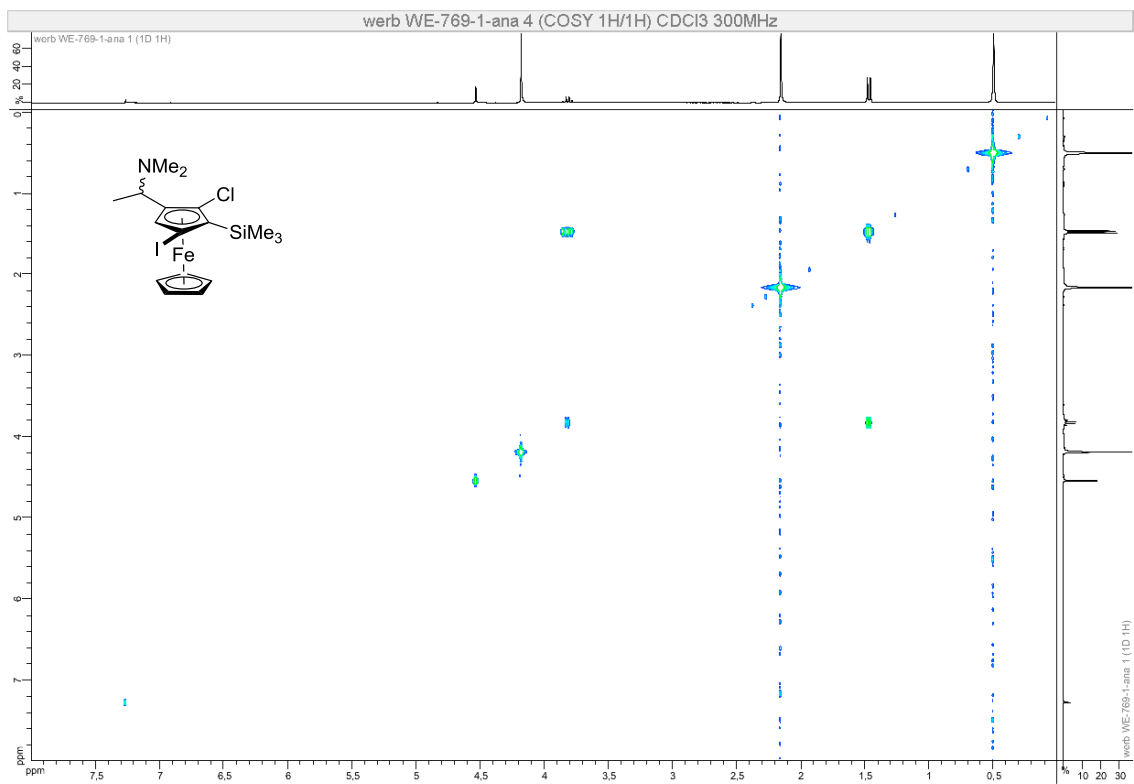
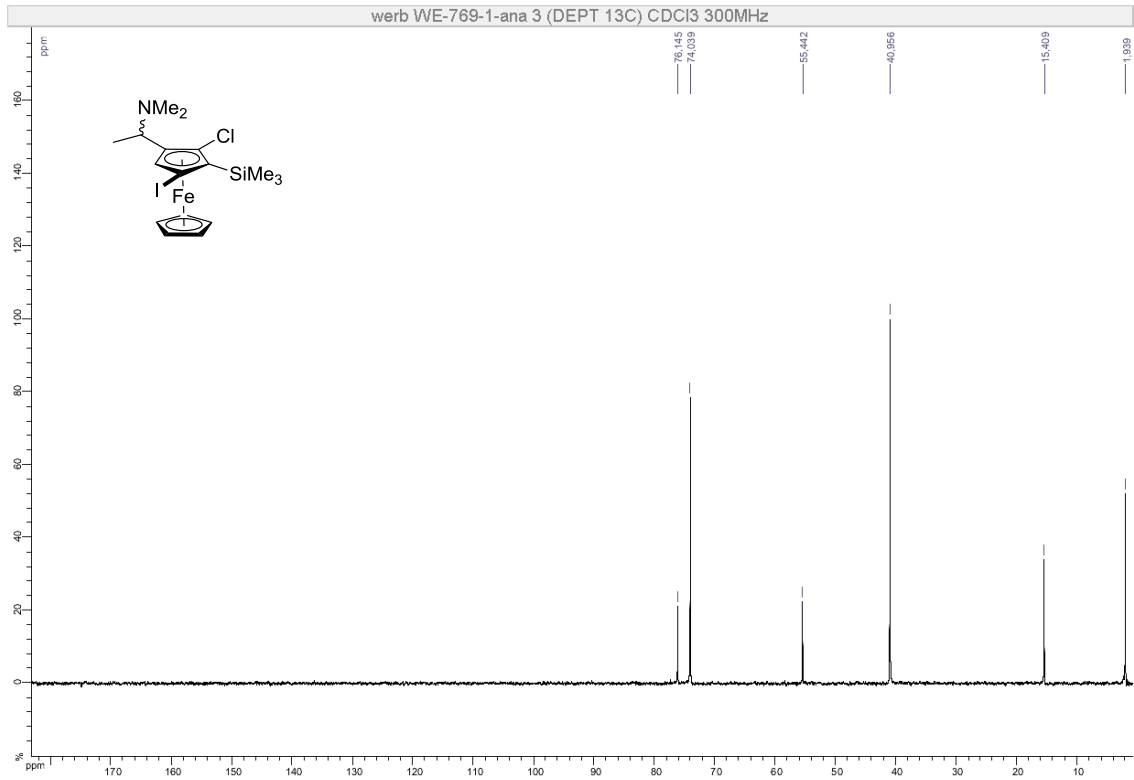


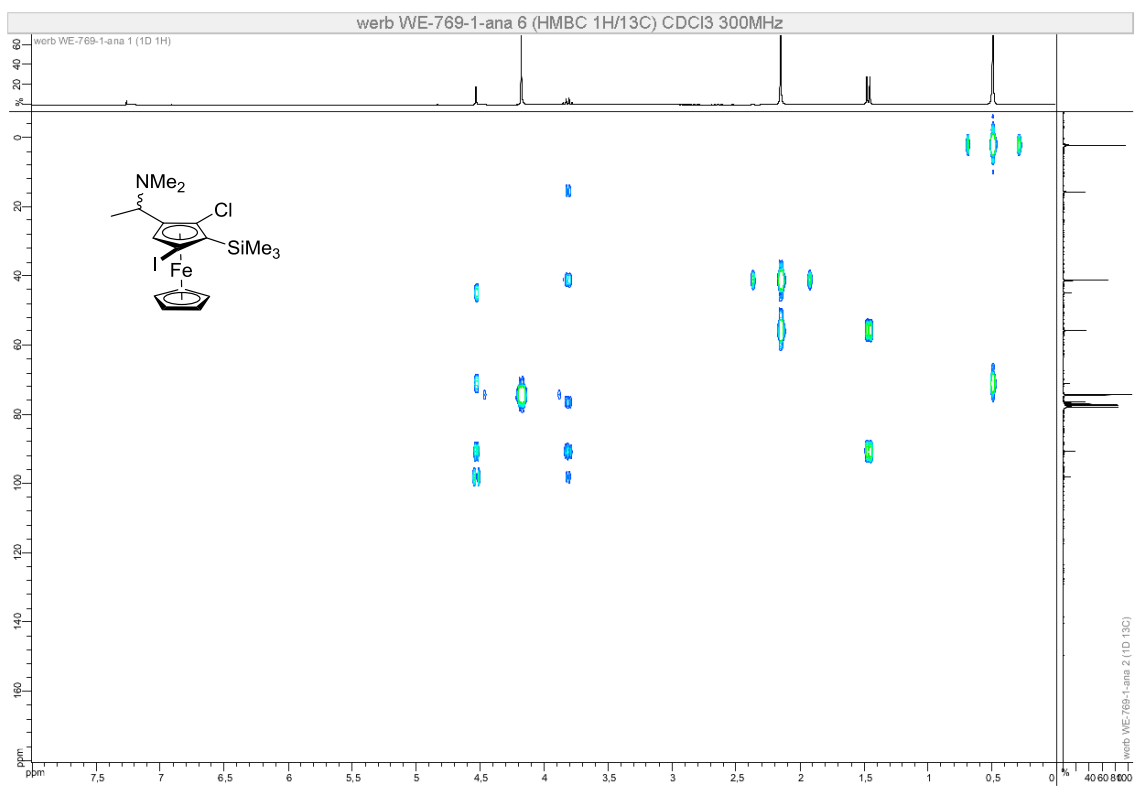
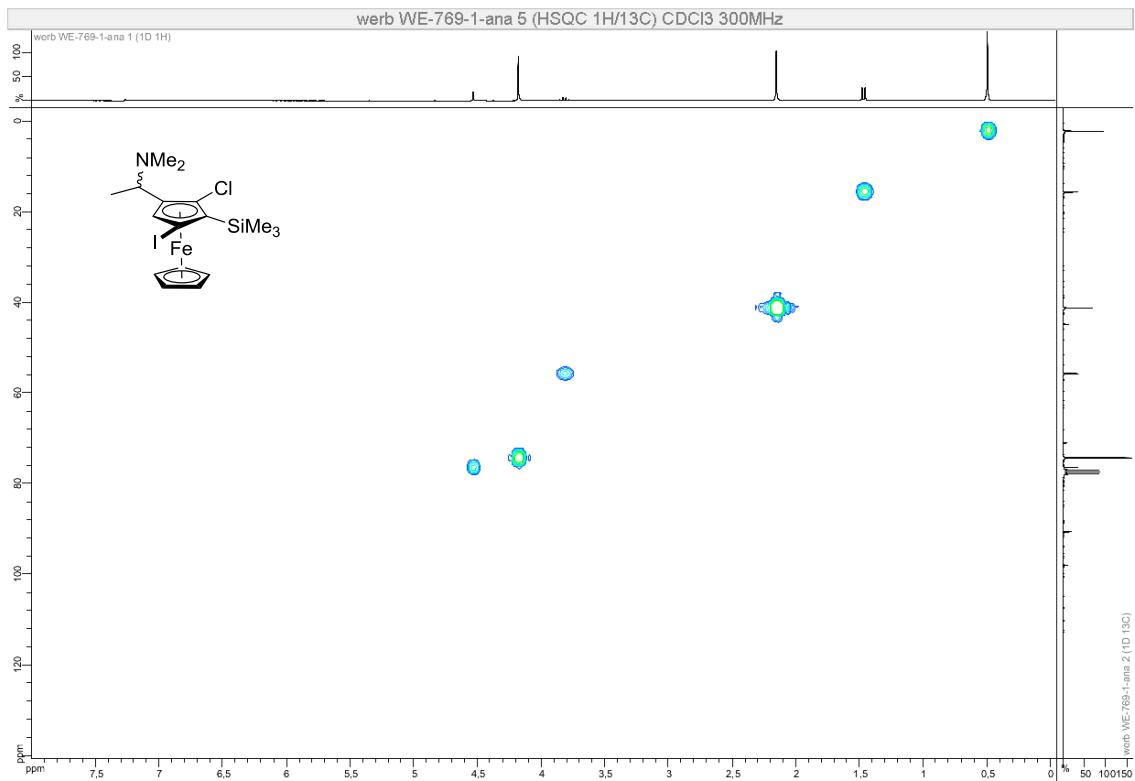


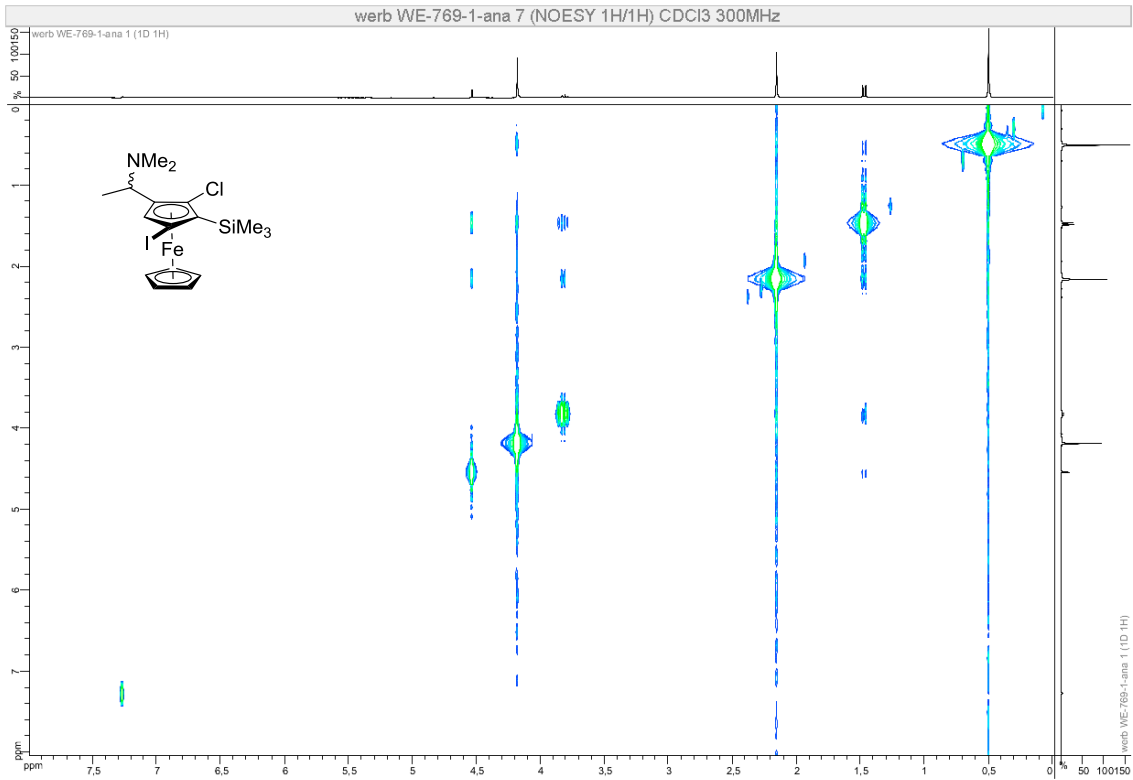


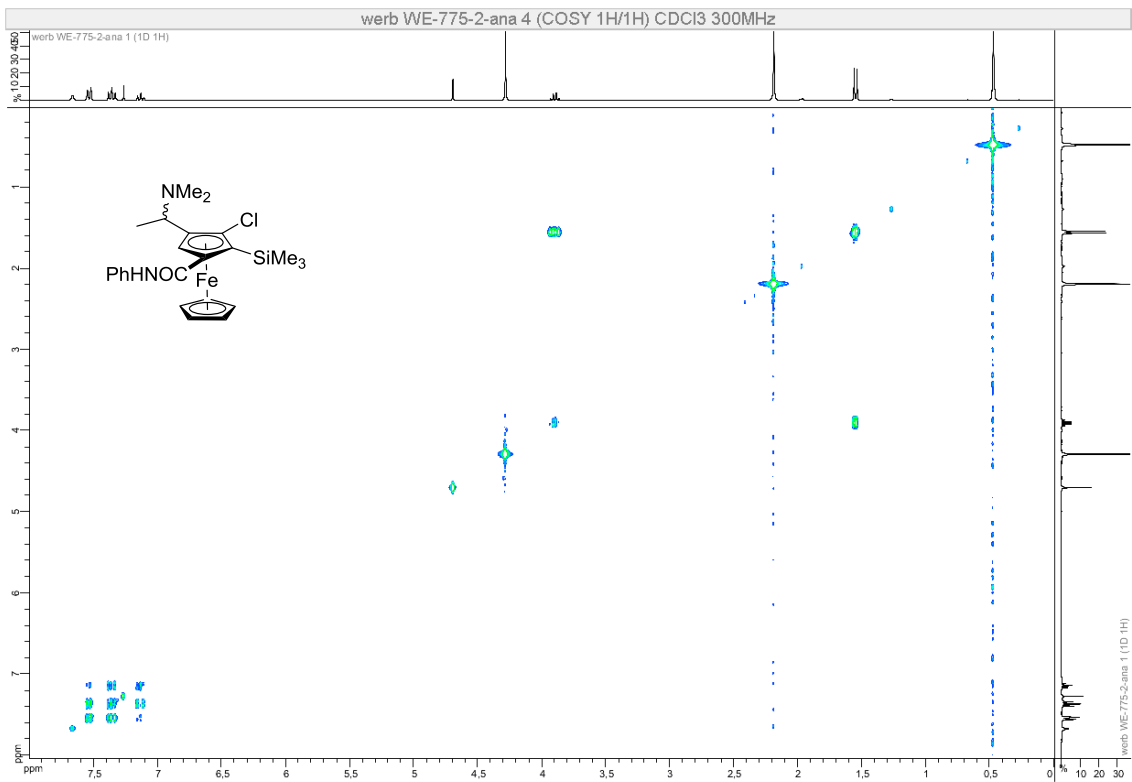
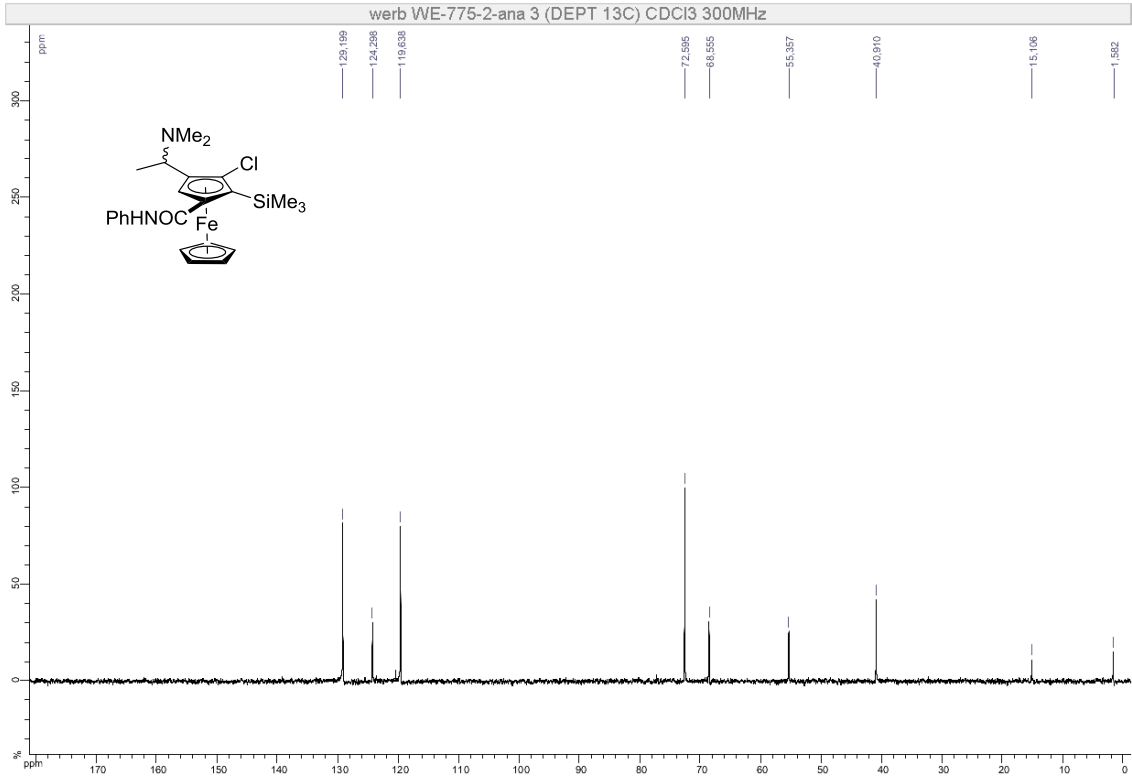
Compound (\pm)-10

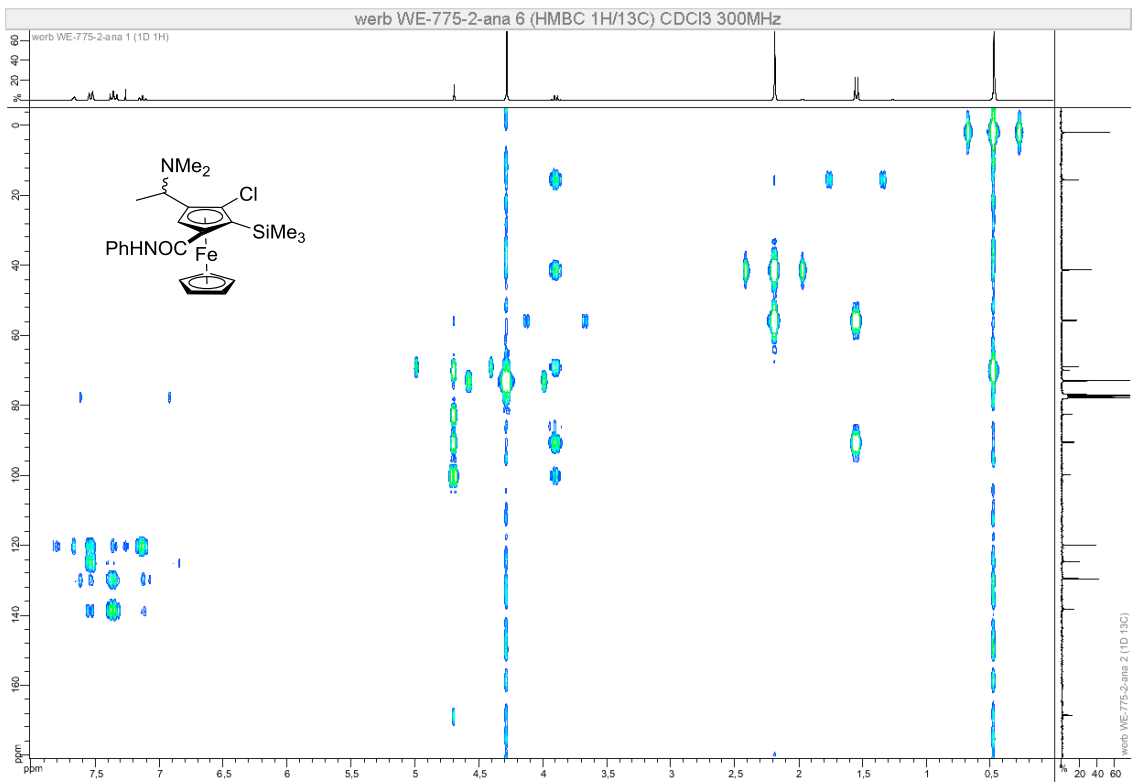
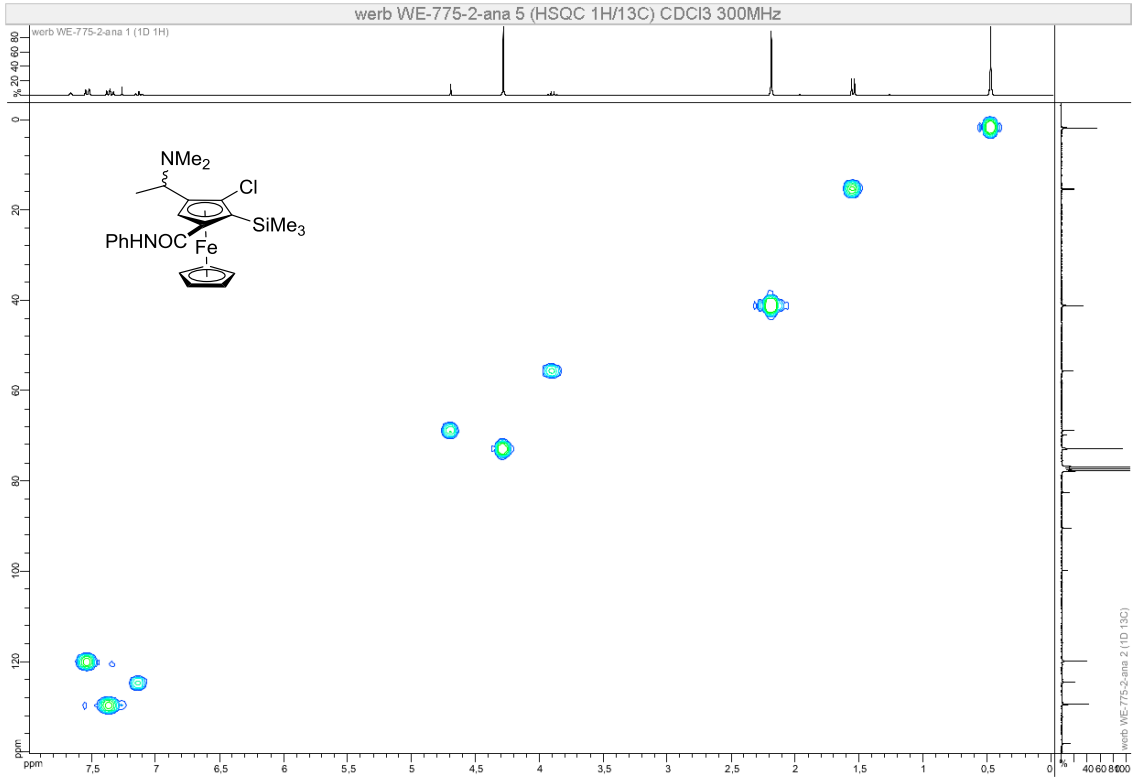


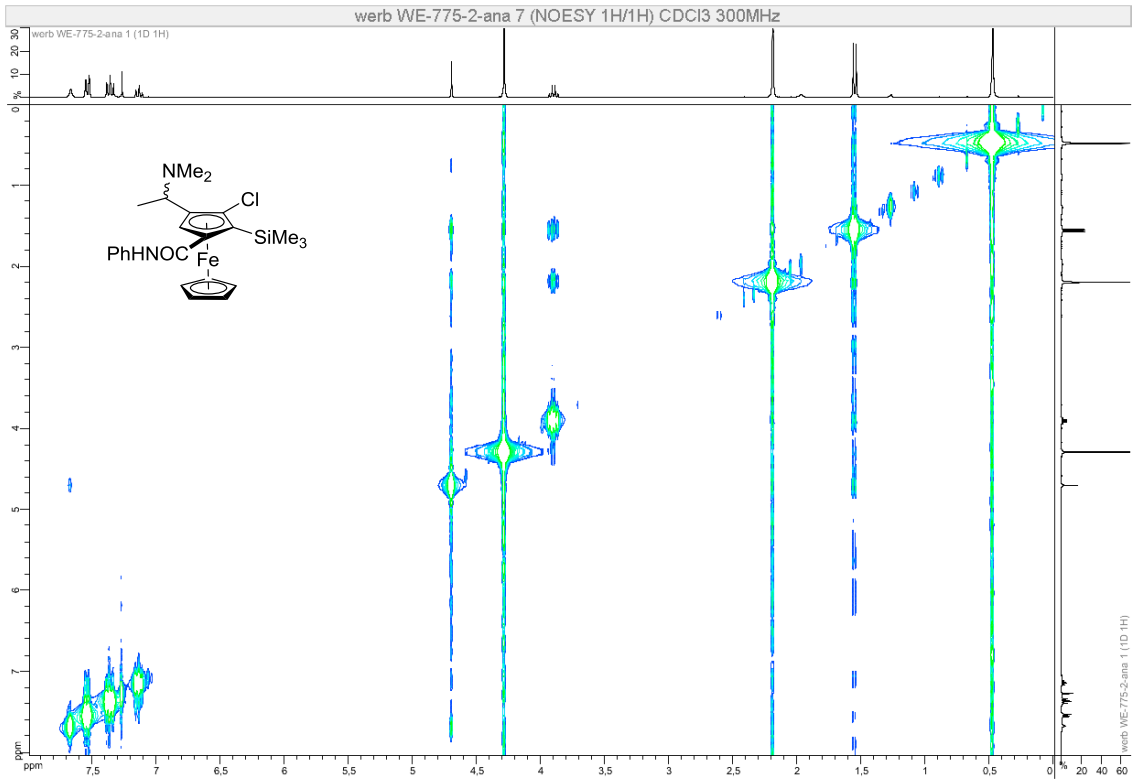




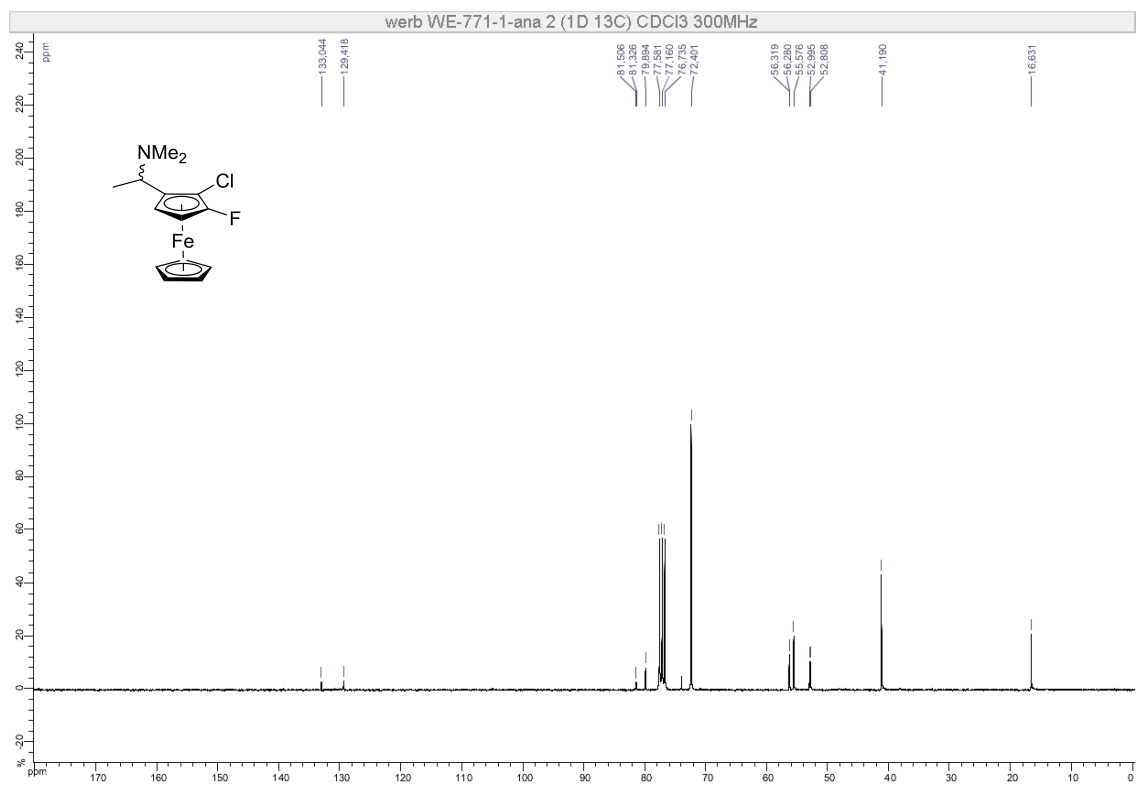
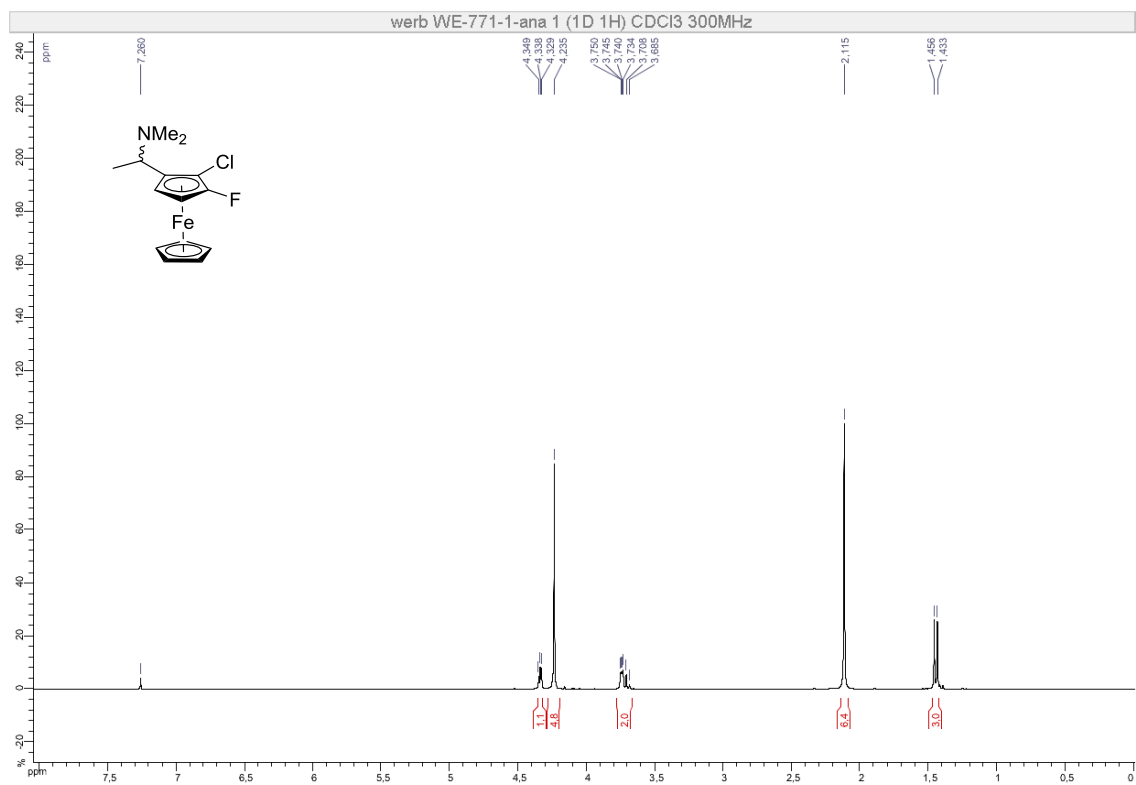


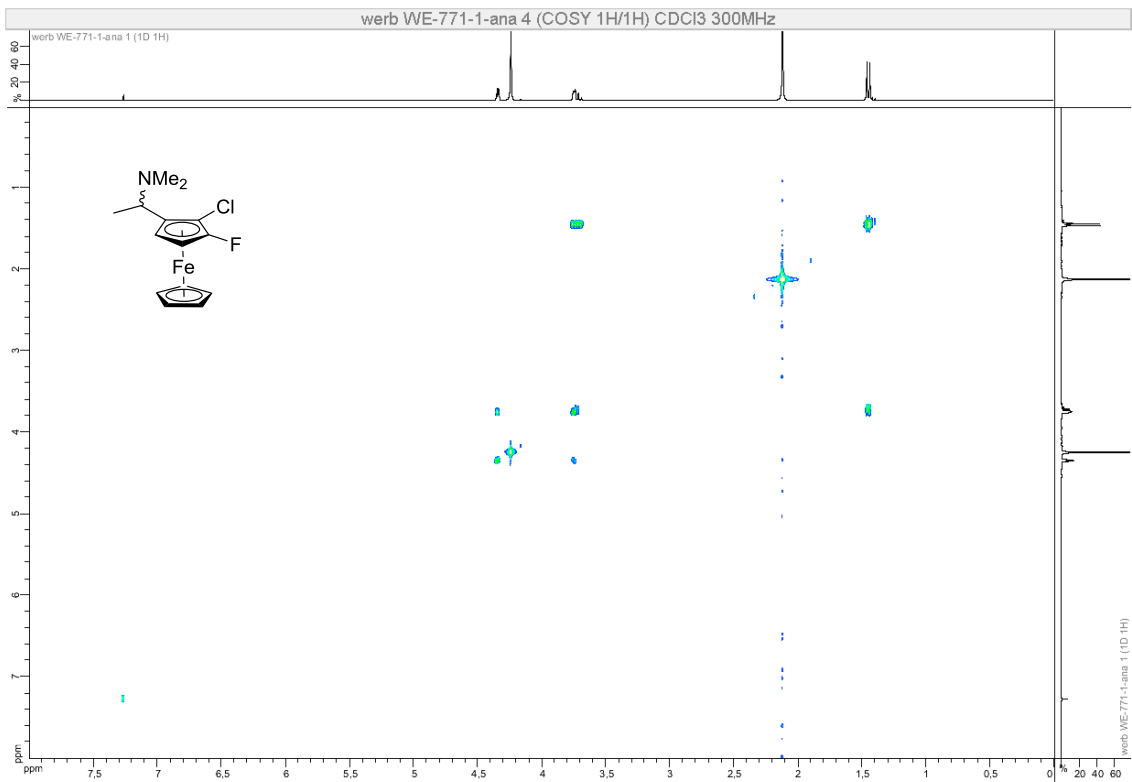
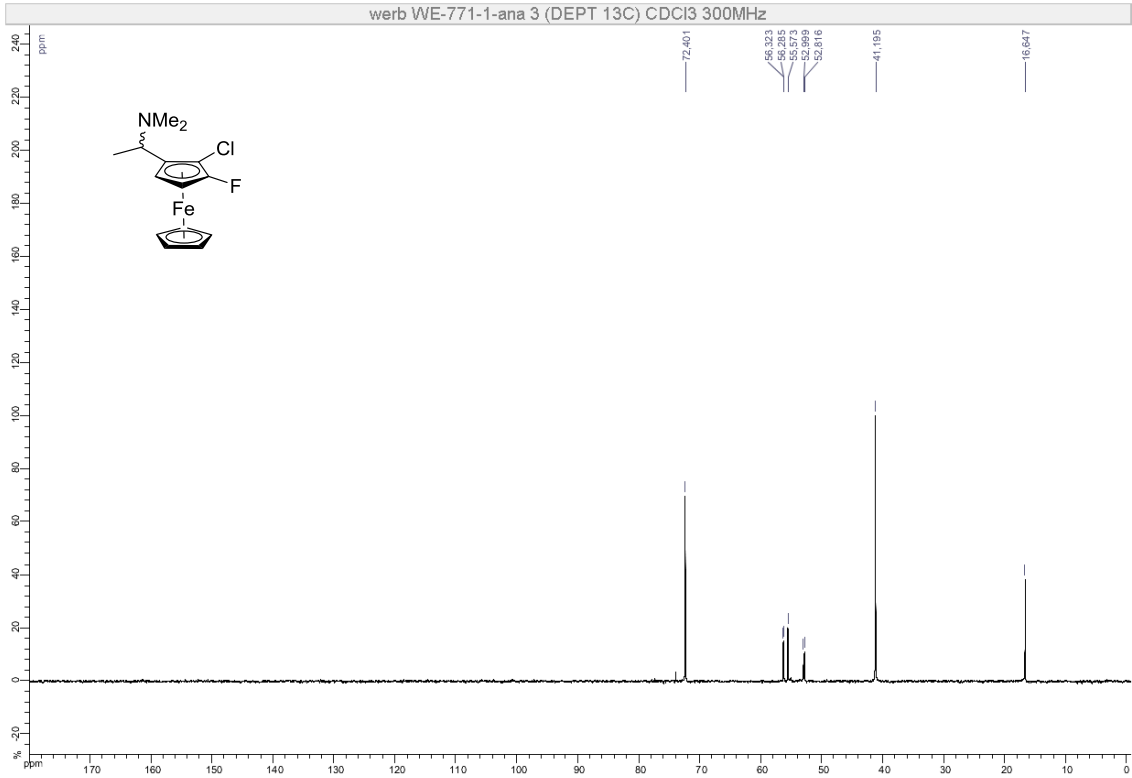


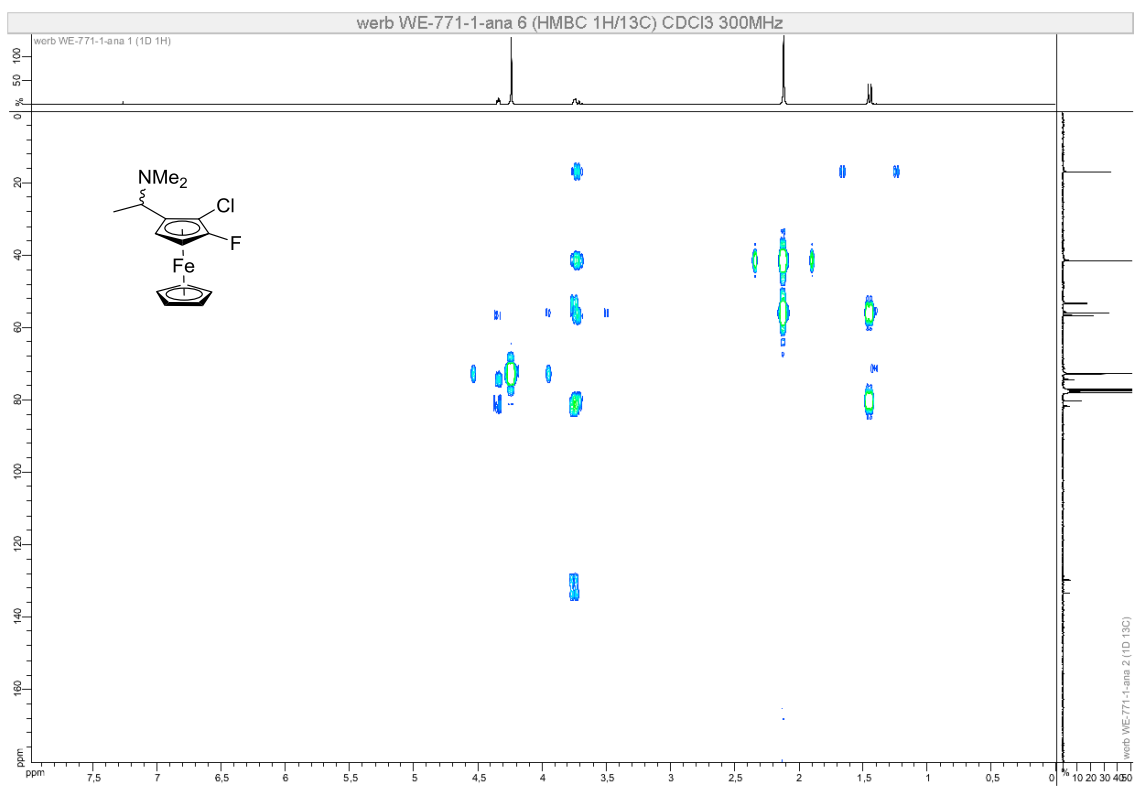
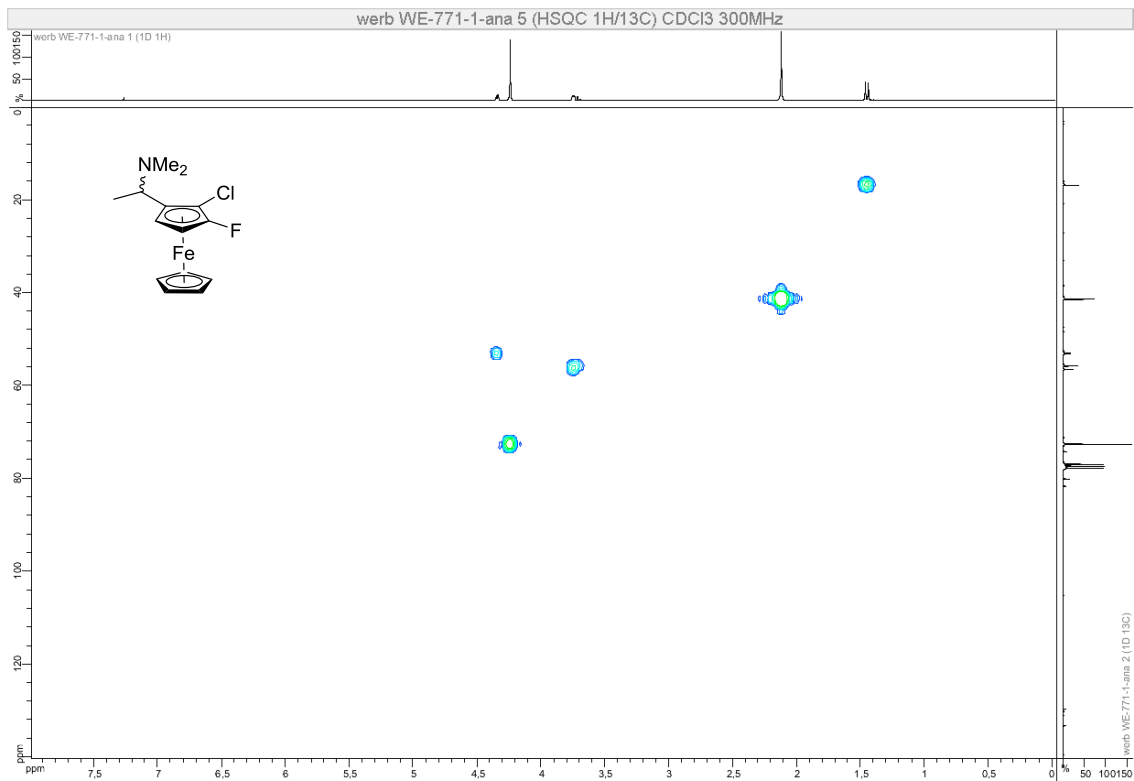


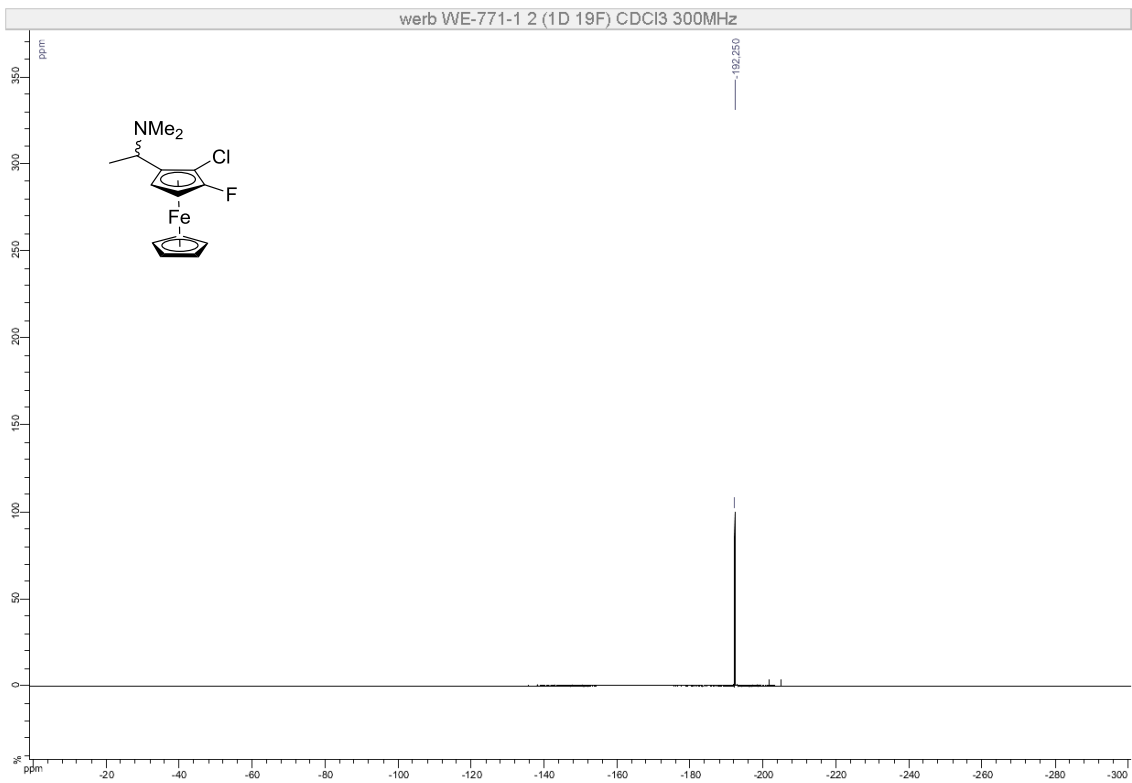


Compound (\pm)-12

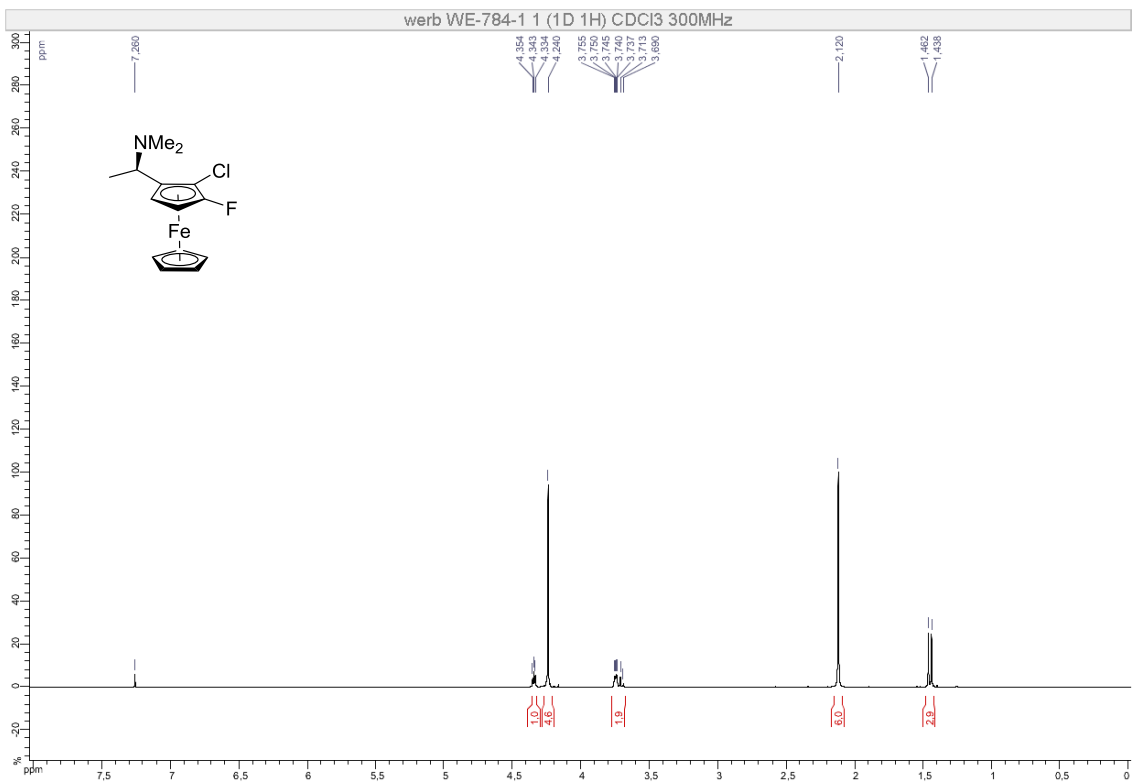


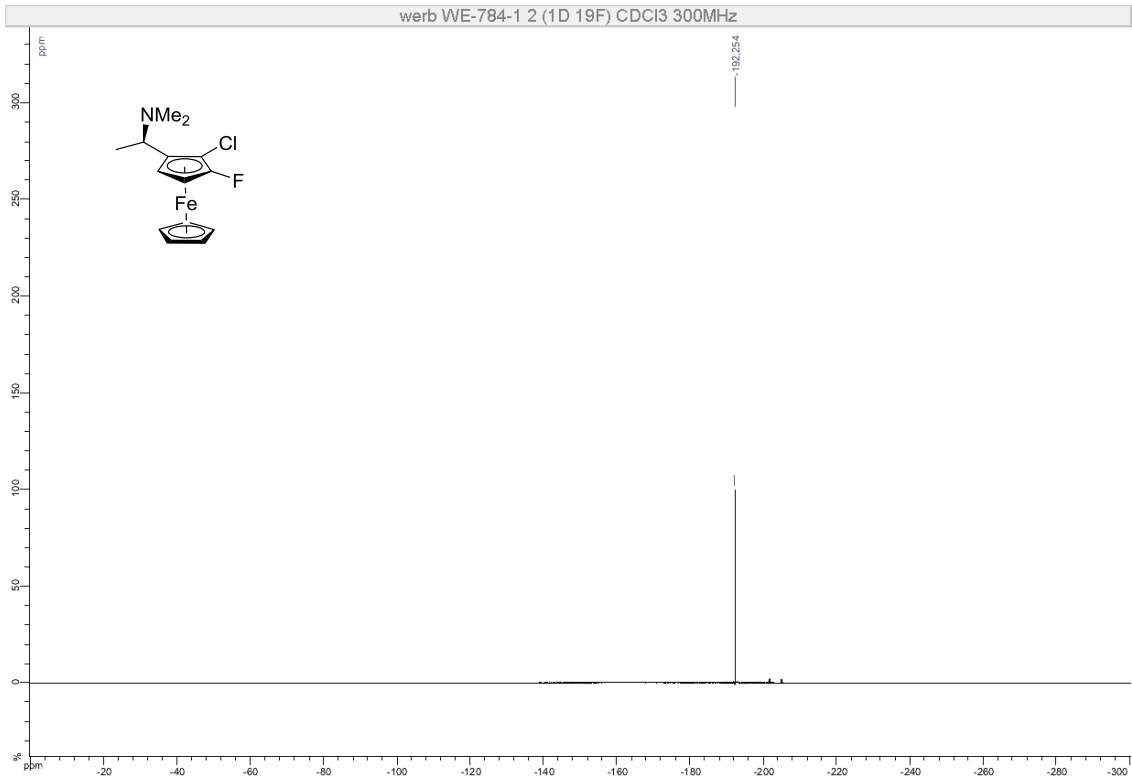




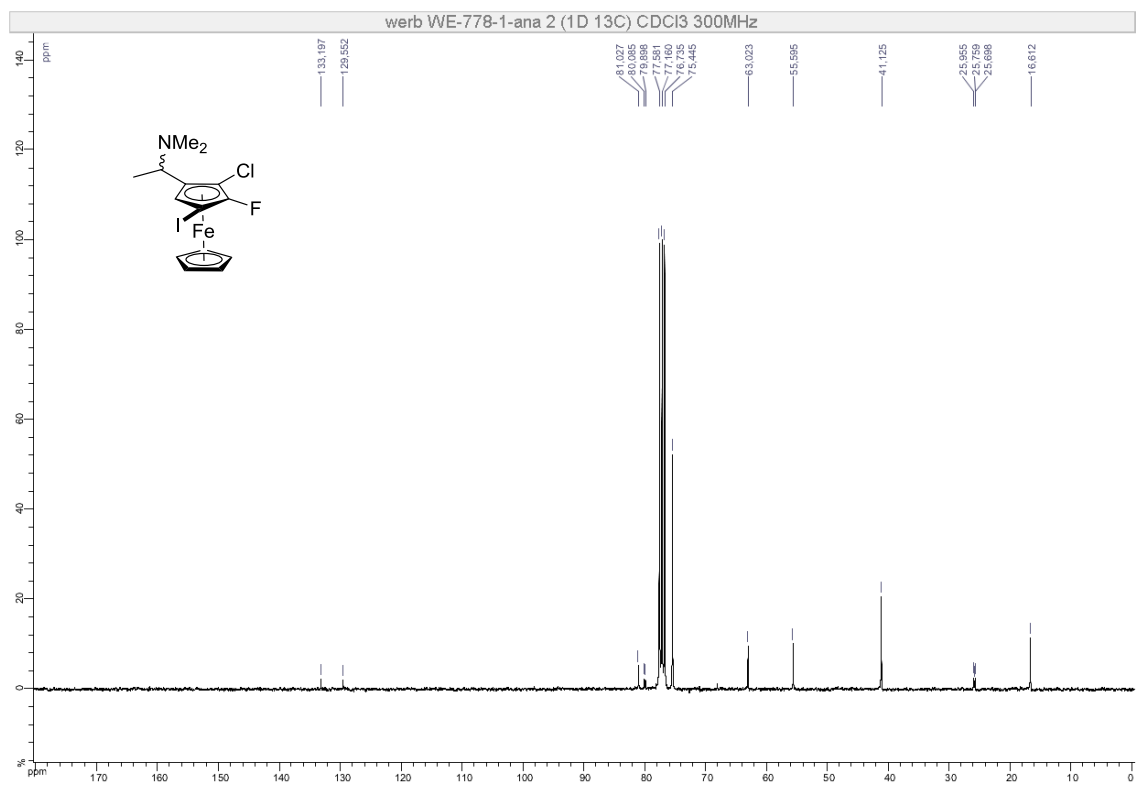
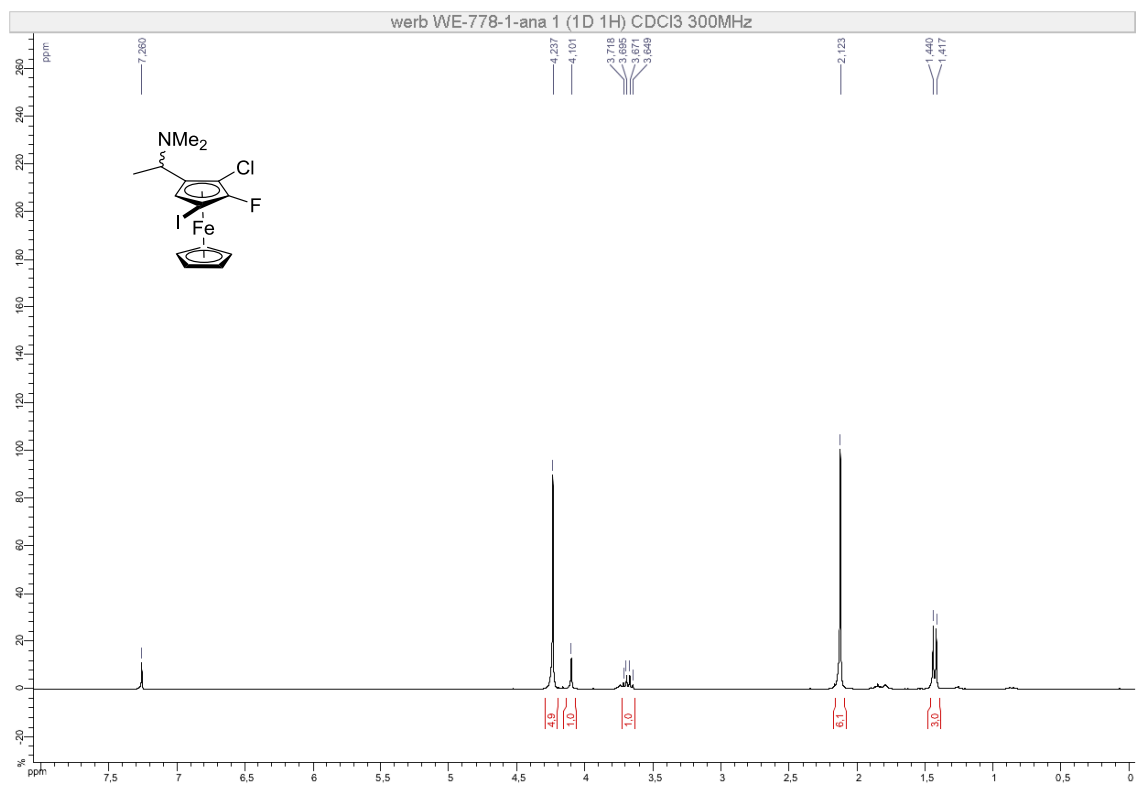


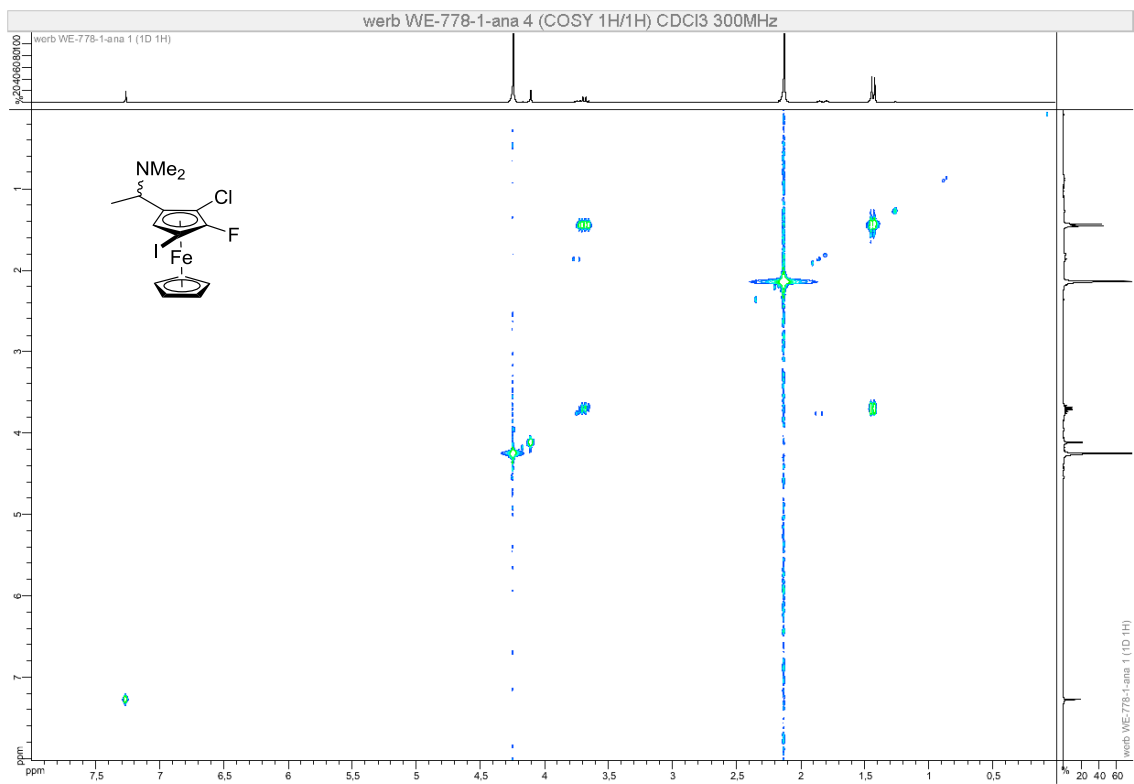
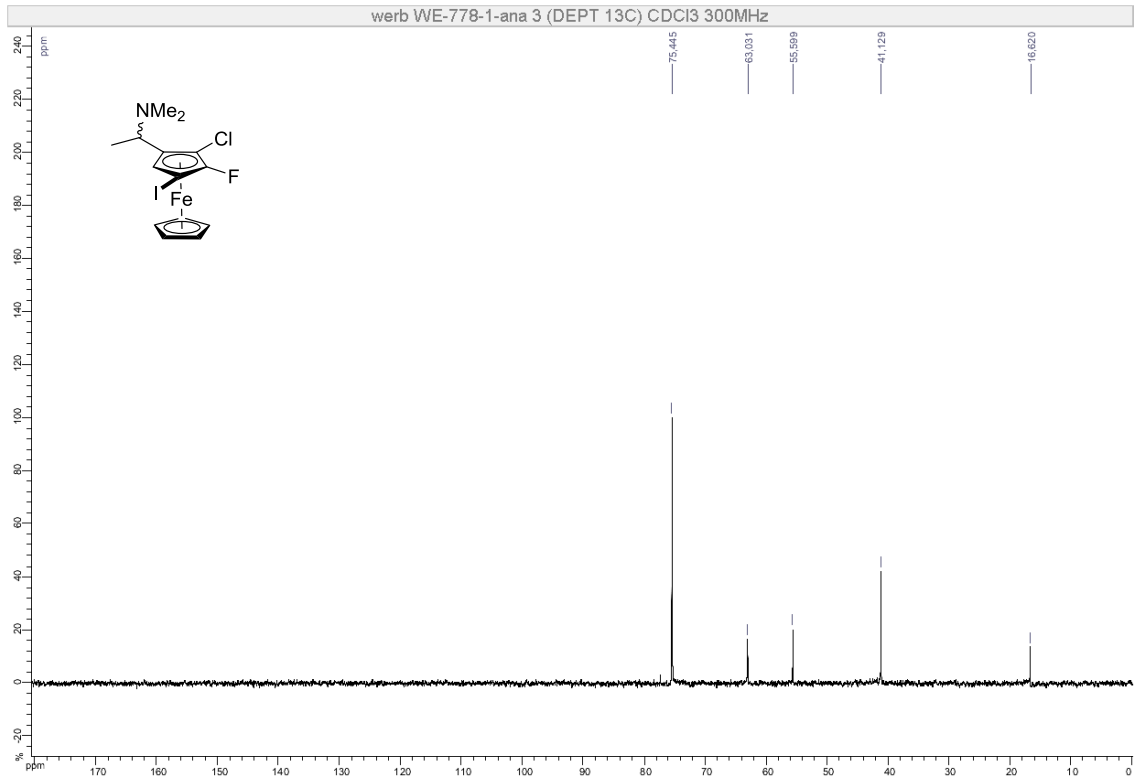
Compound (R,R) -12

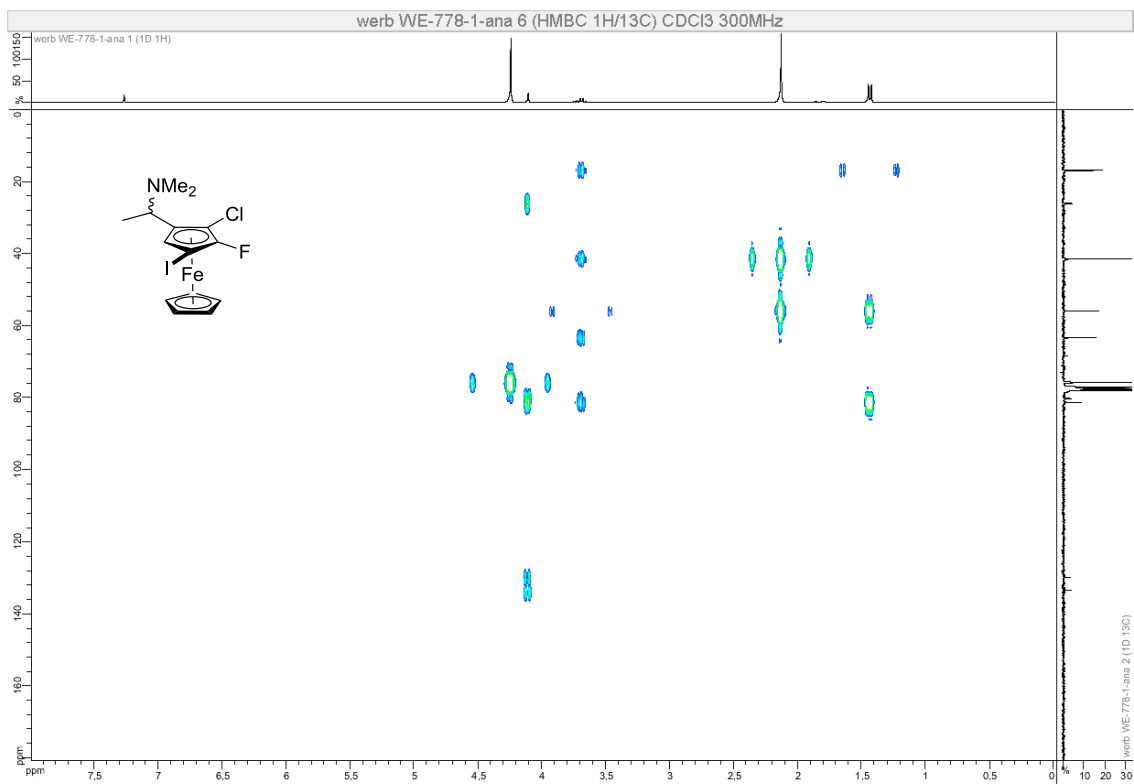
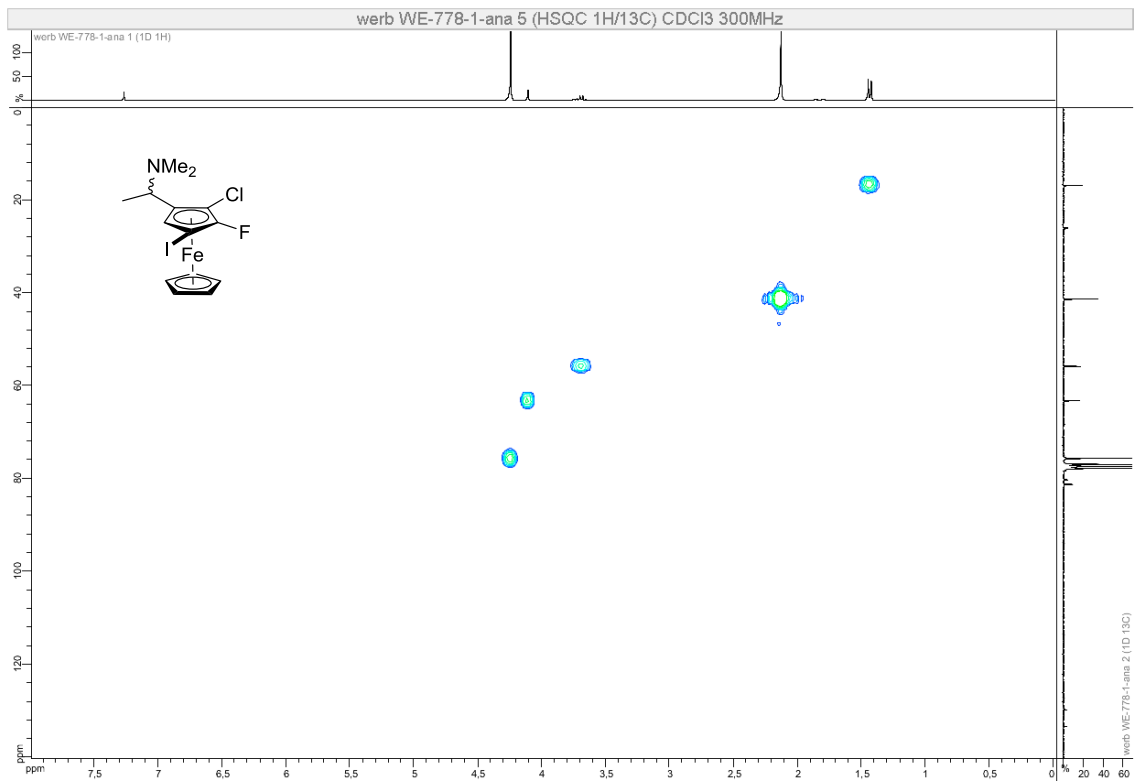


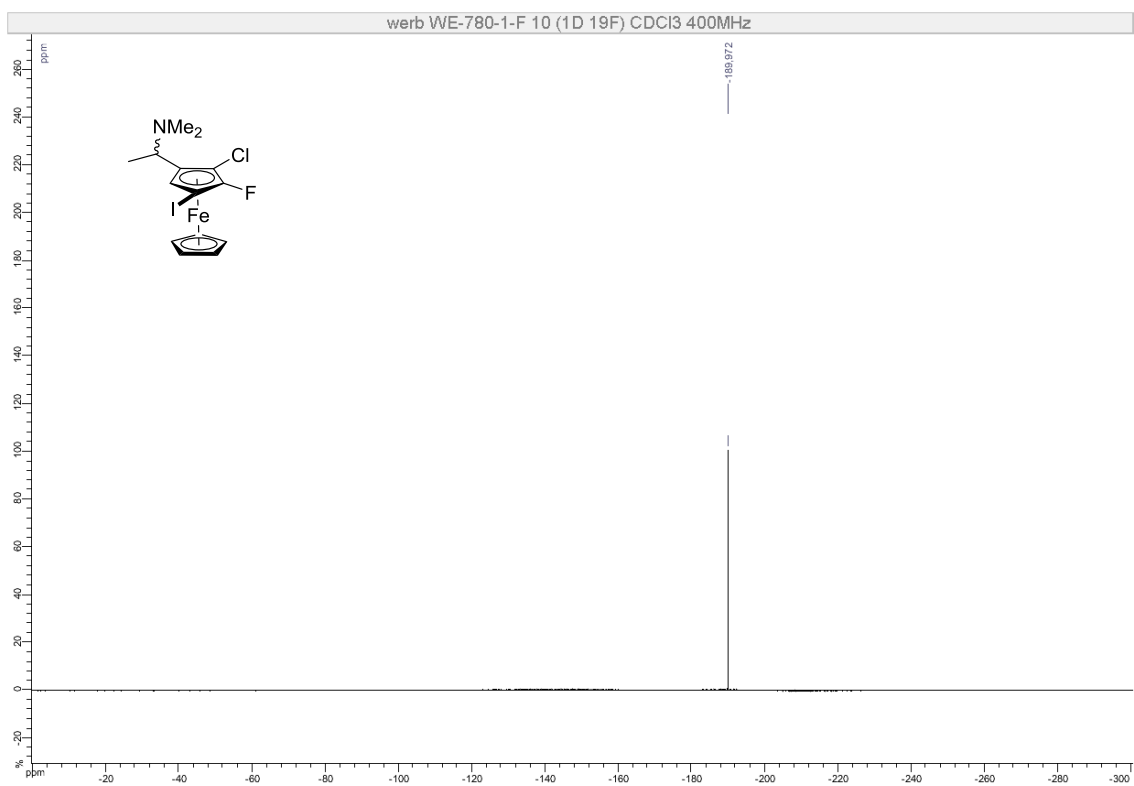
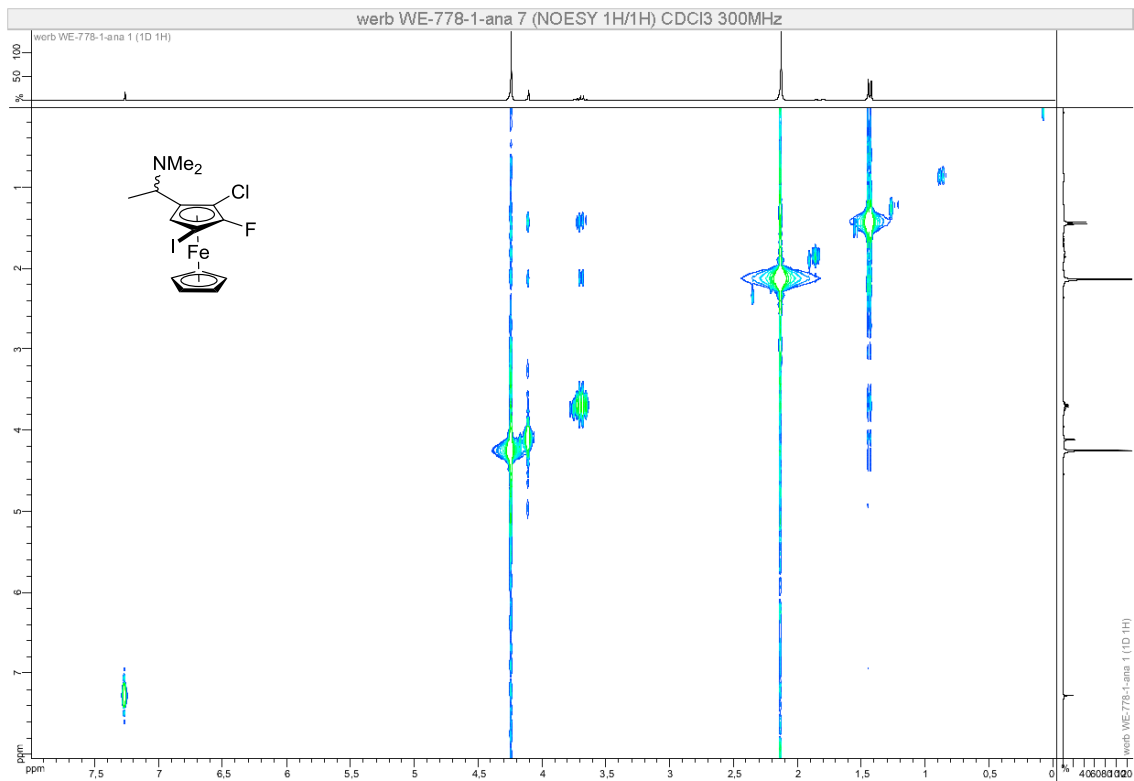


Compound (\pm)-13

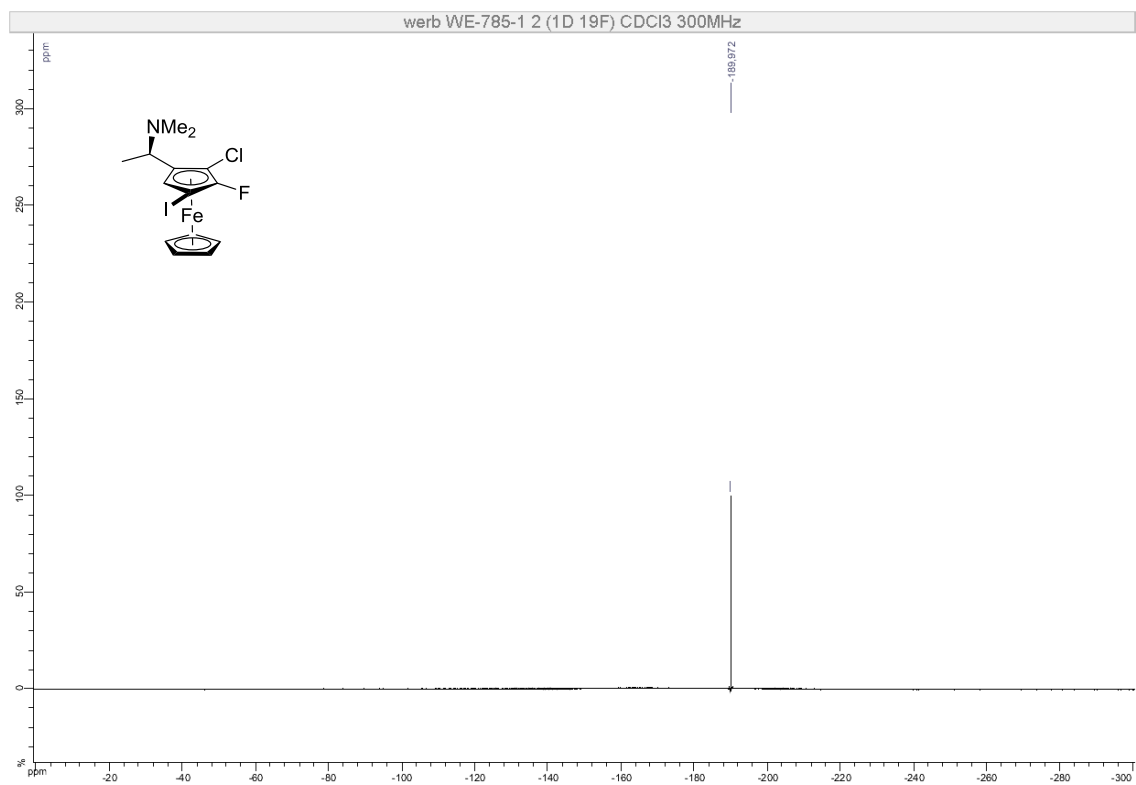
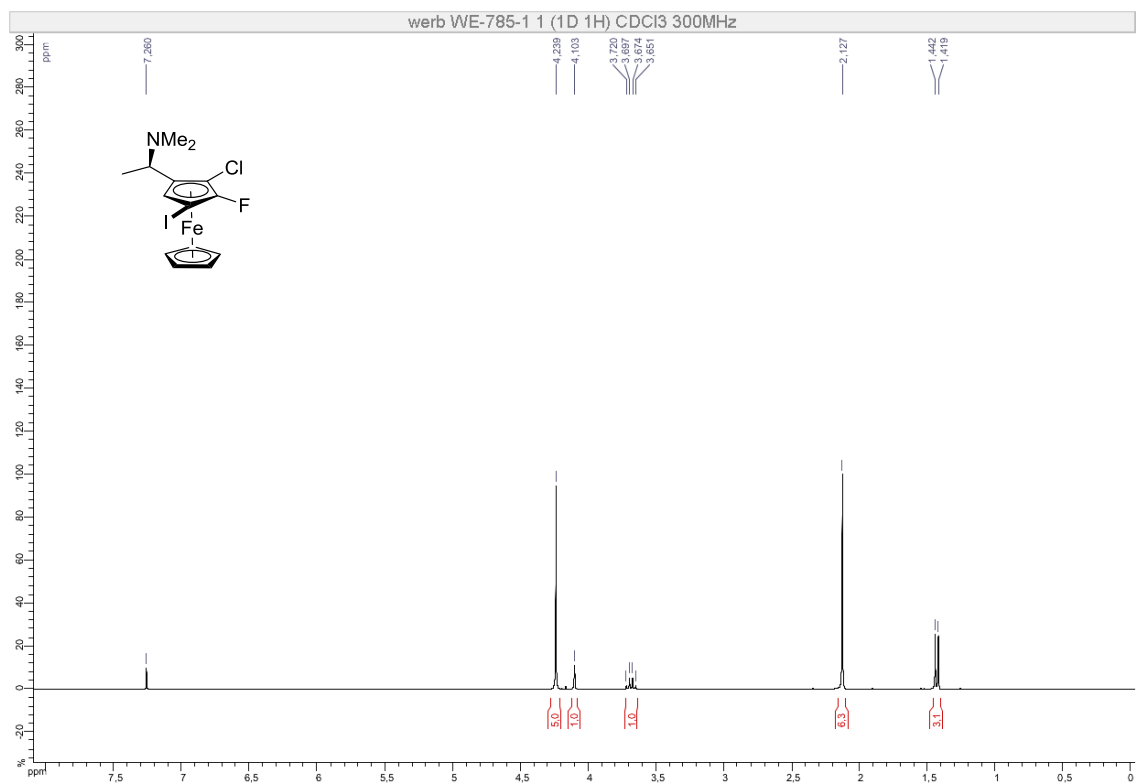




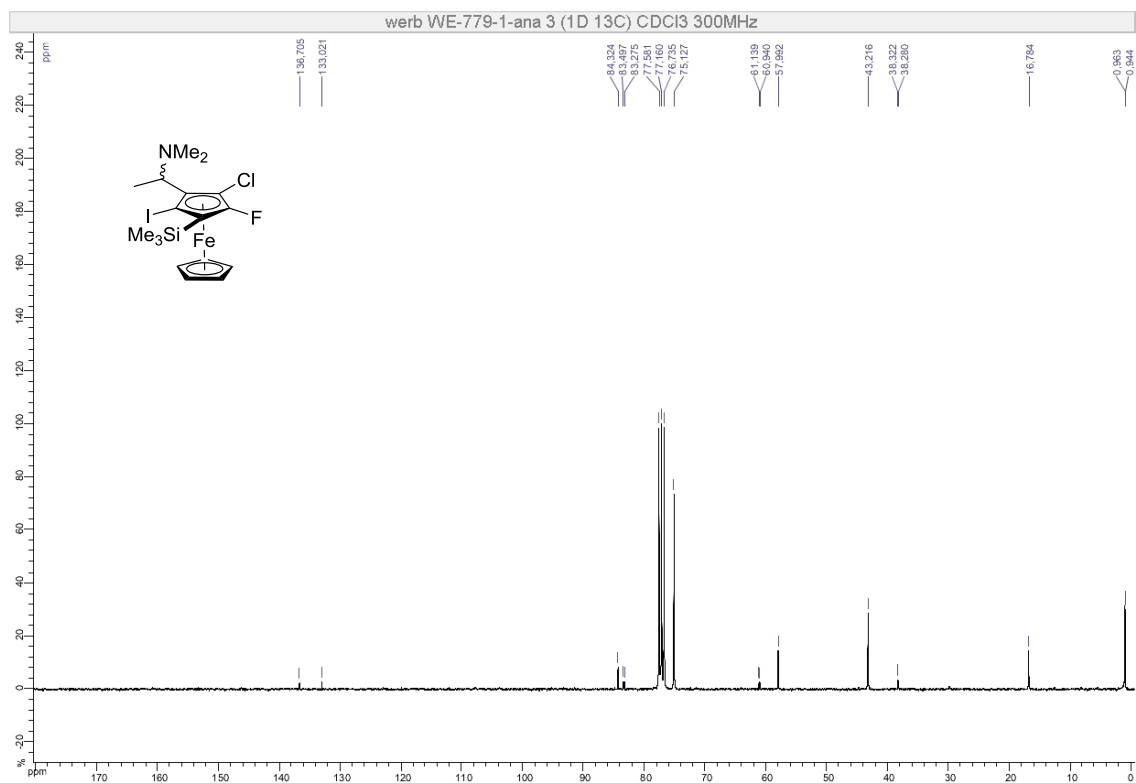
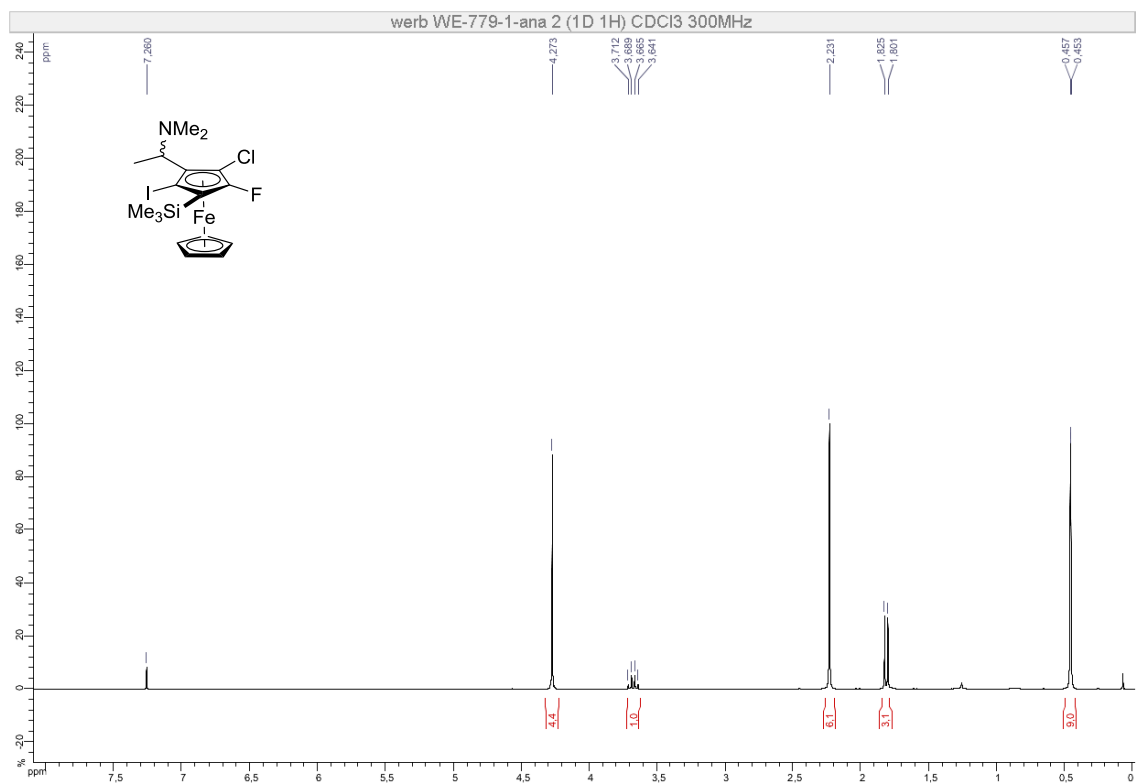


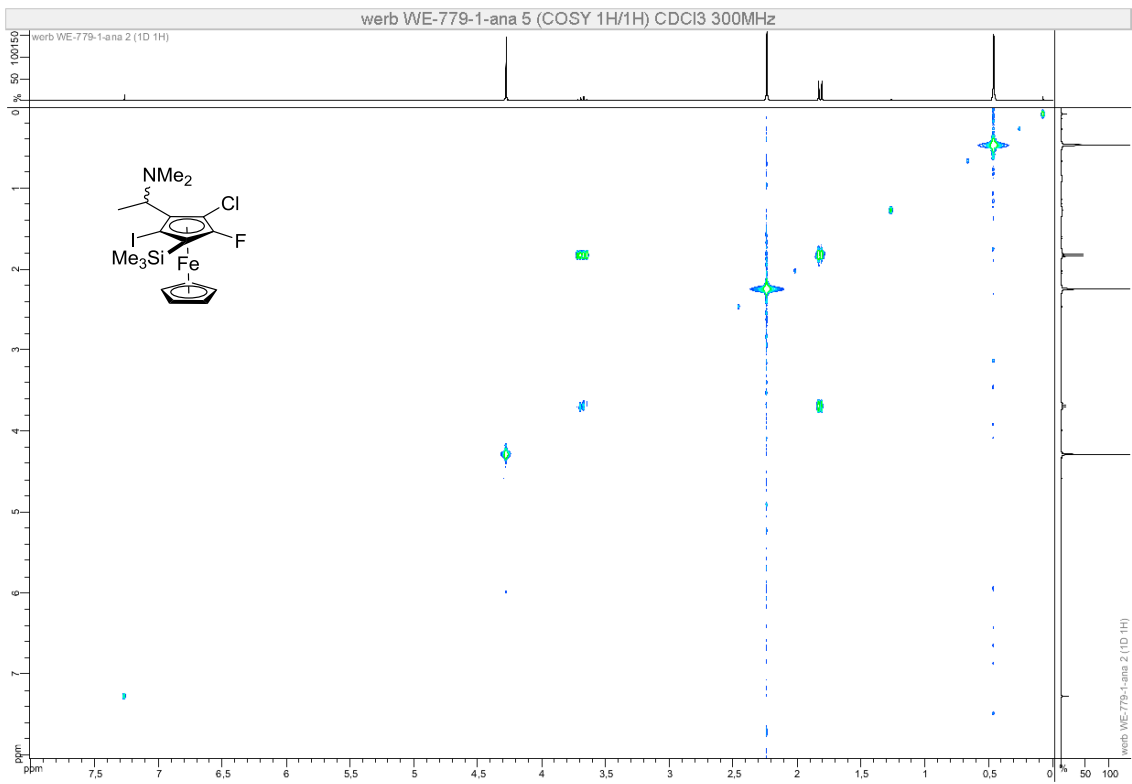
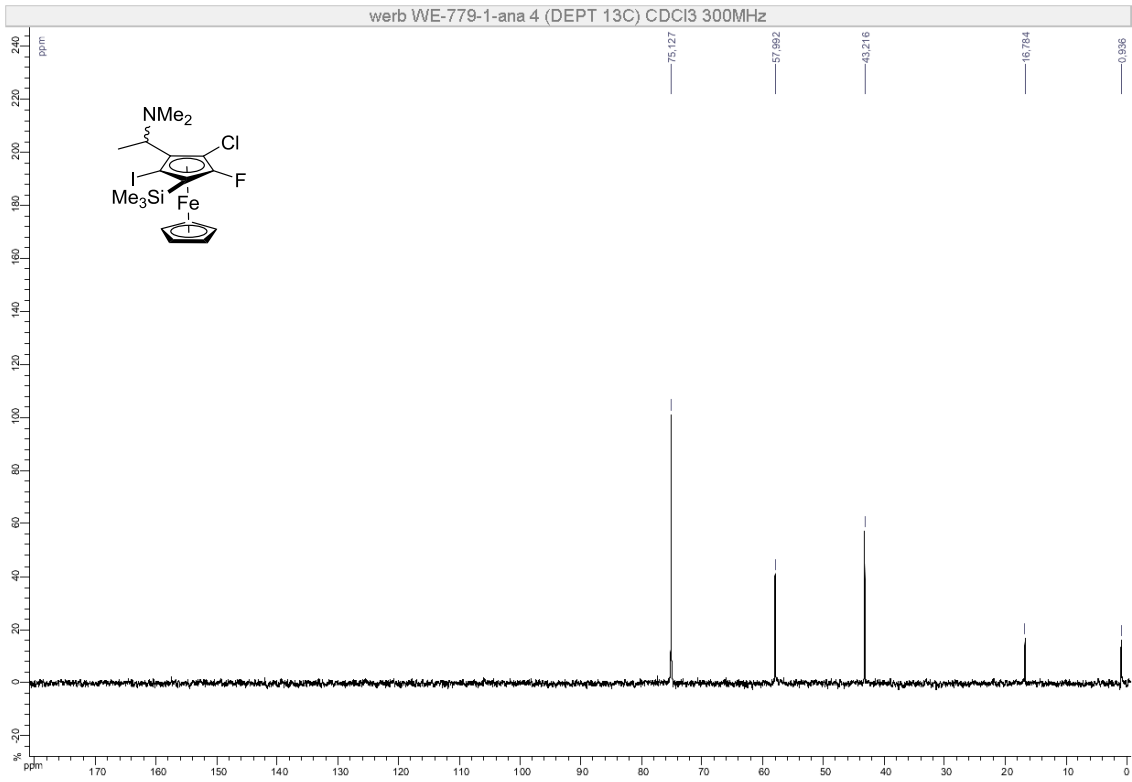


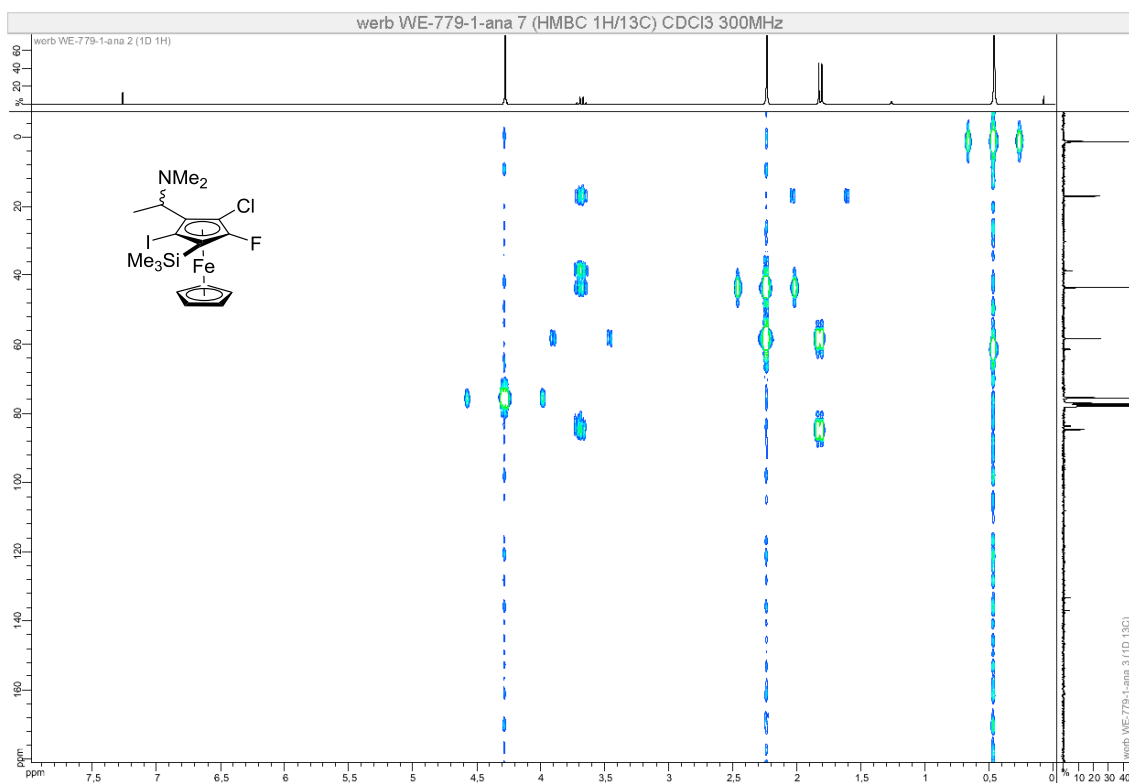
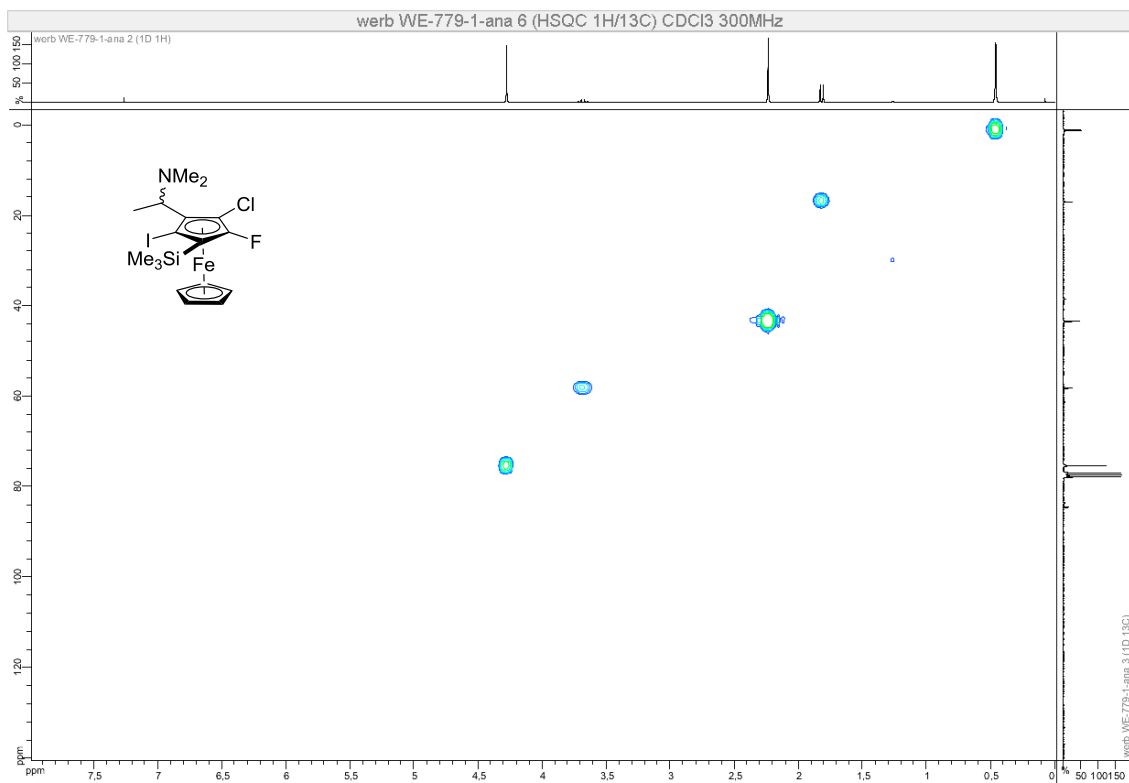
Compound (*R,S*)-13

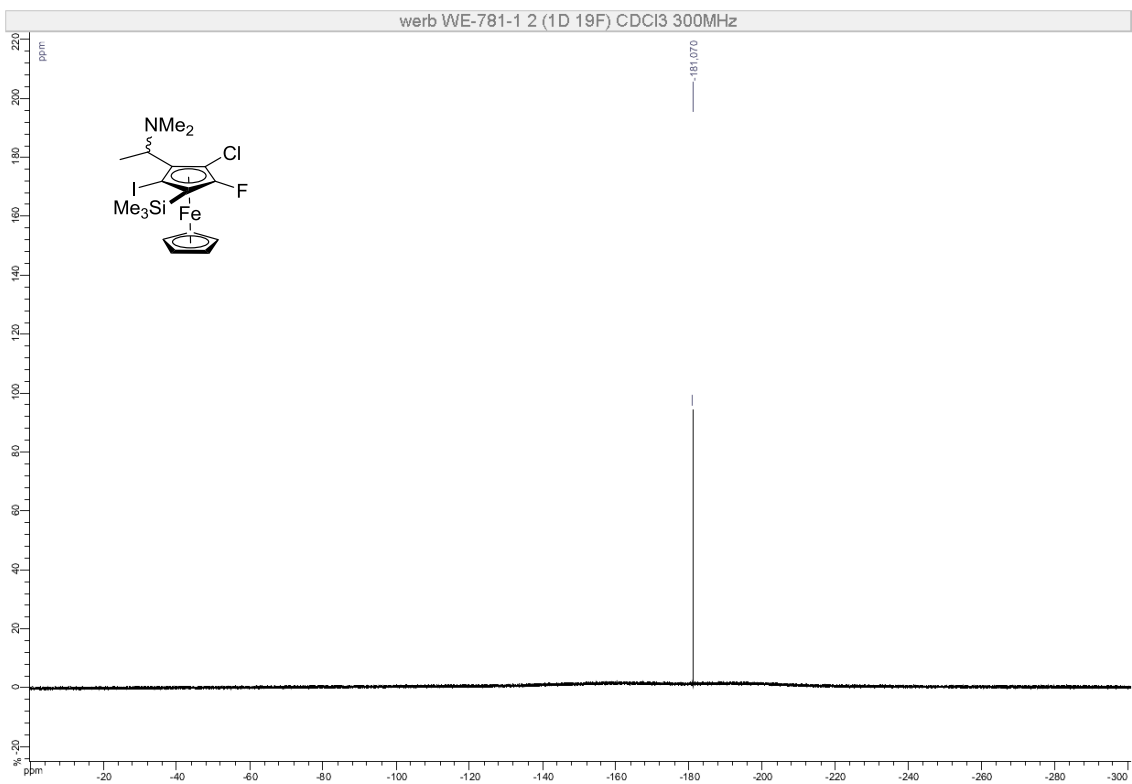
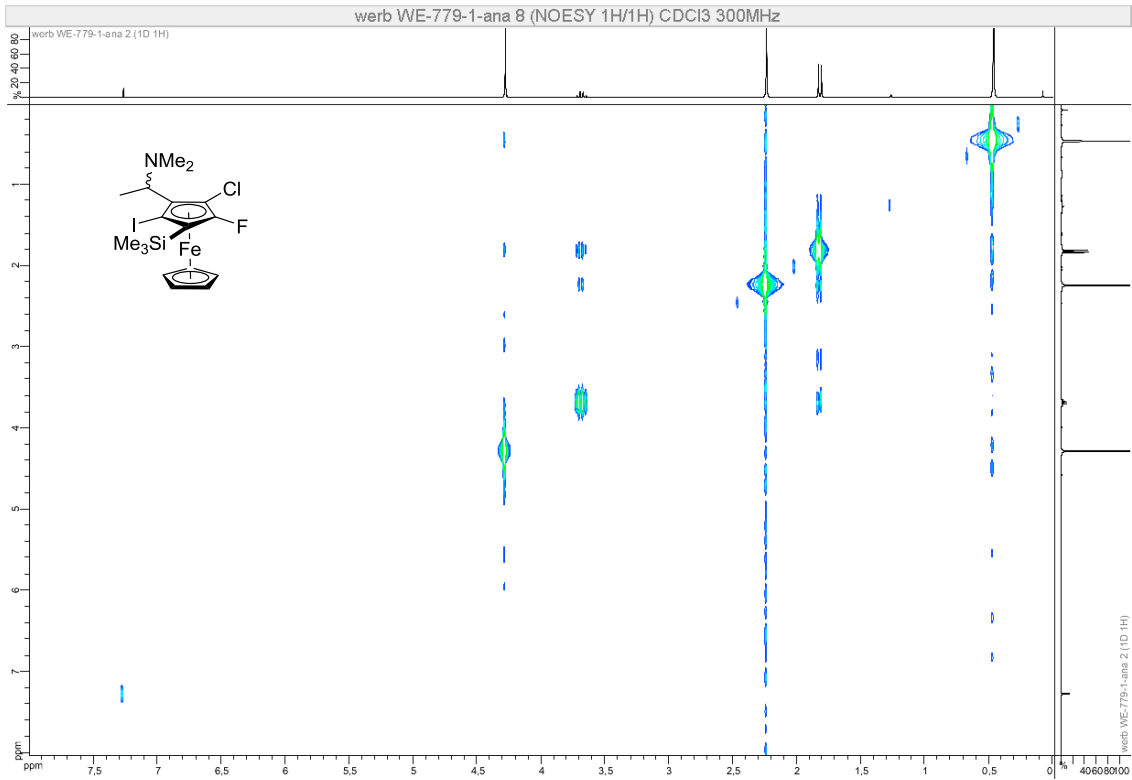


Compound (\pm)-14

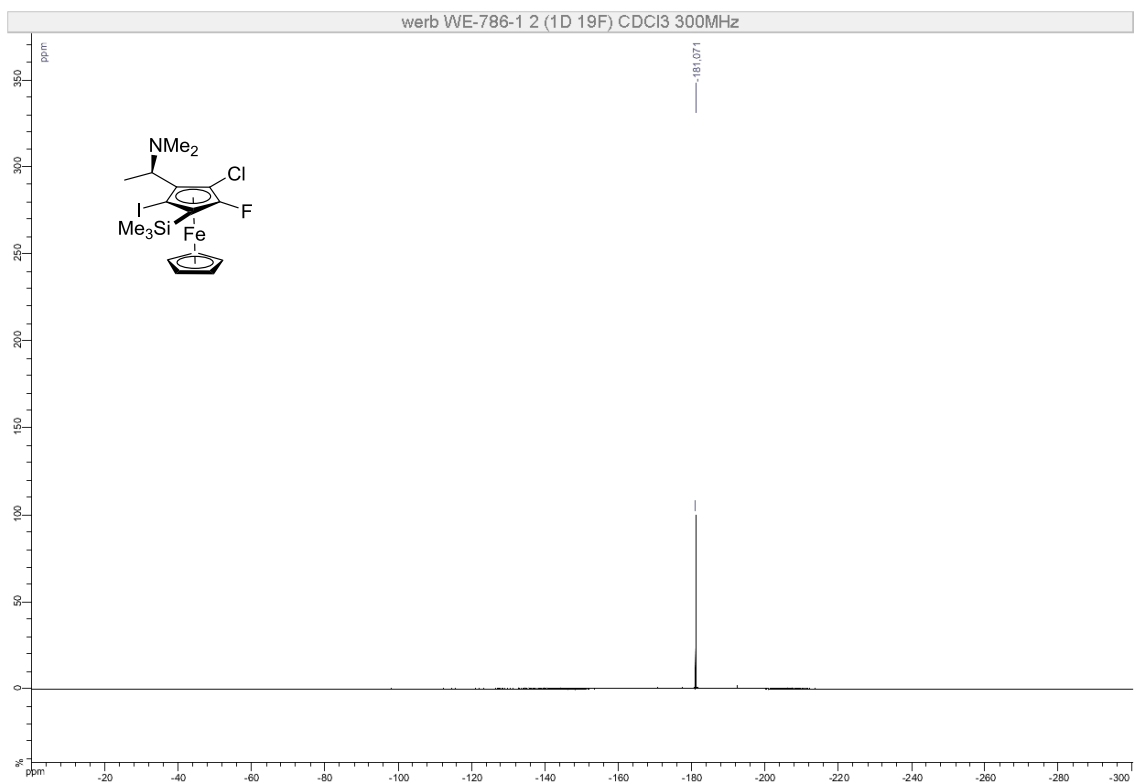
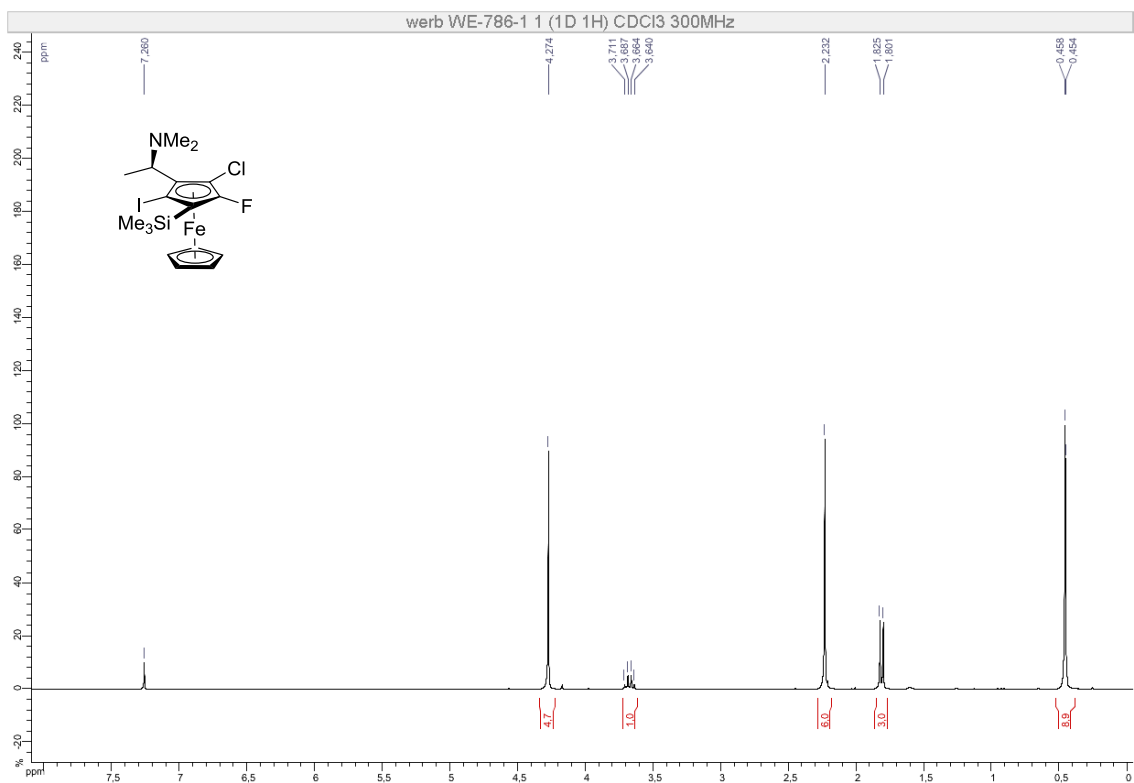




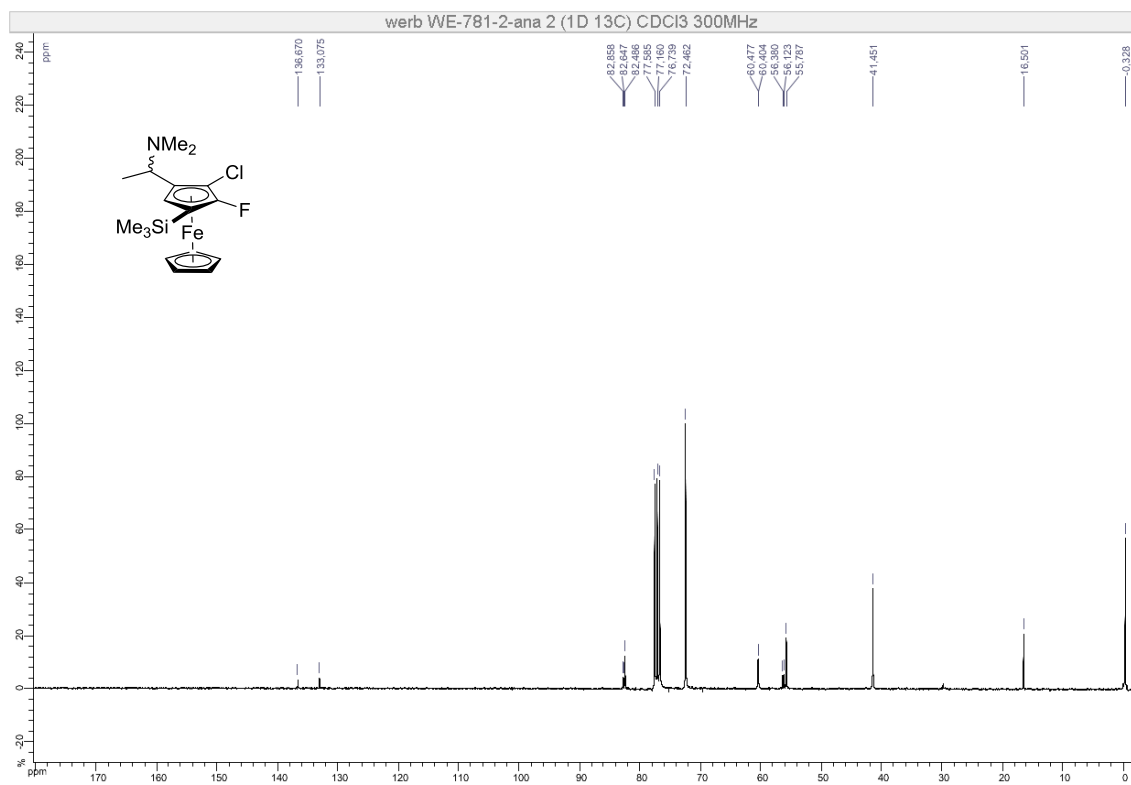
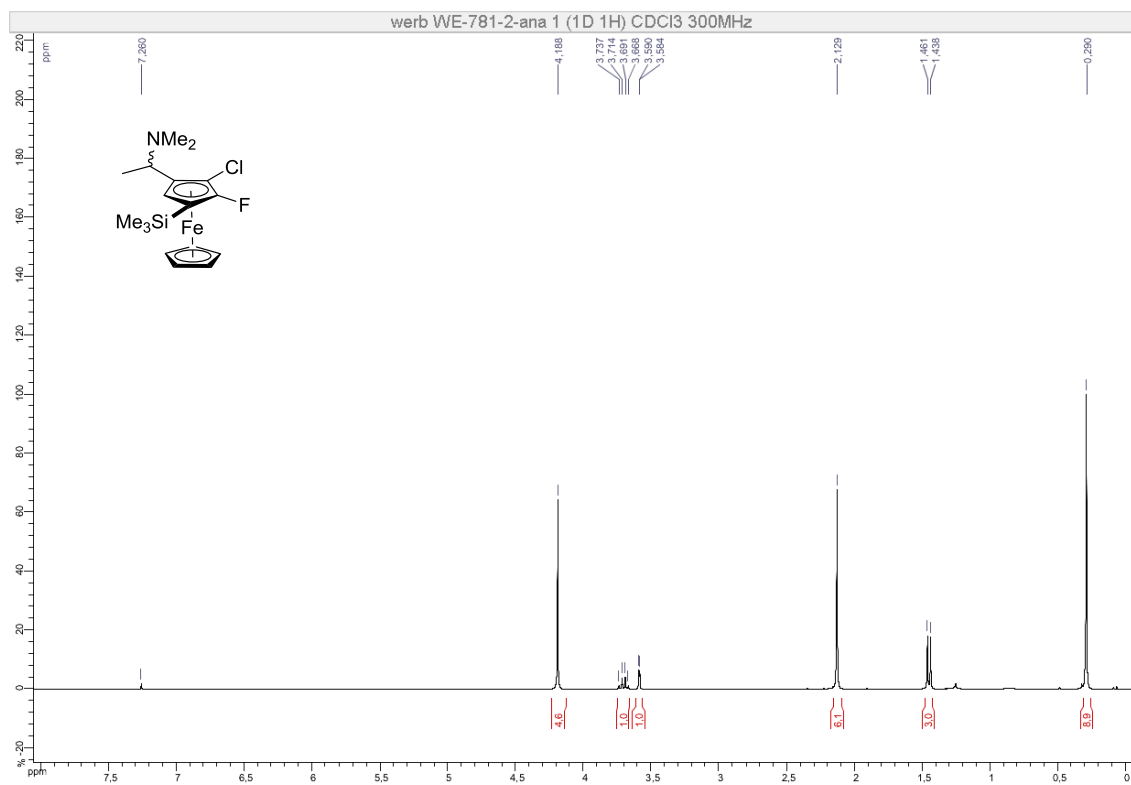


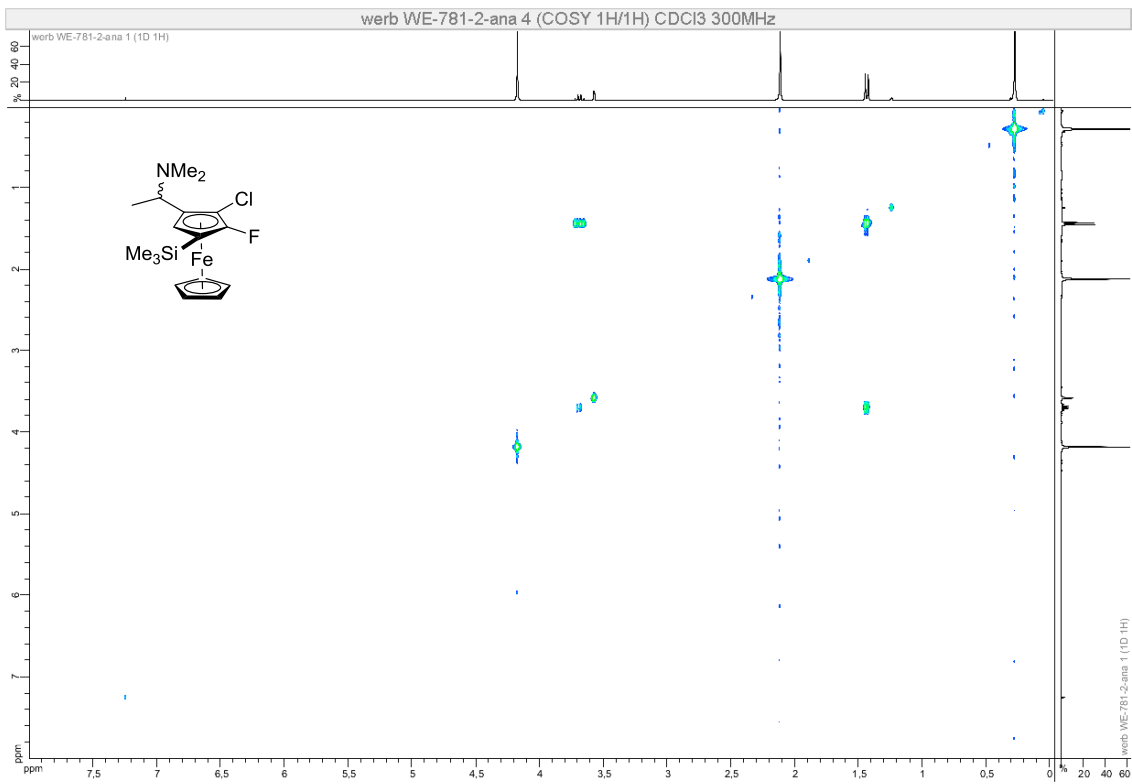
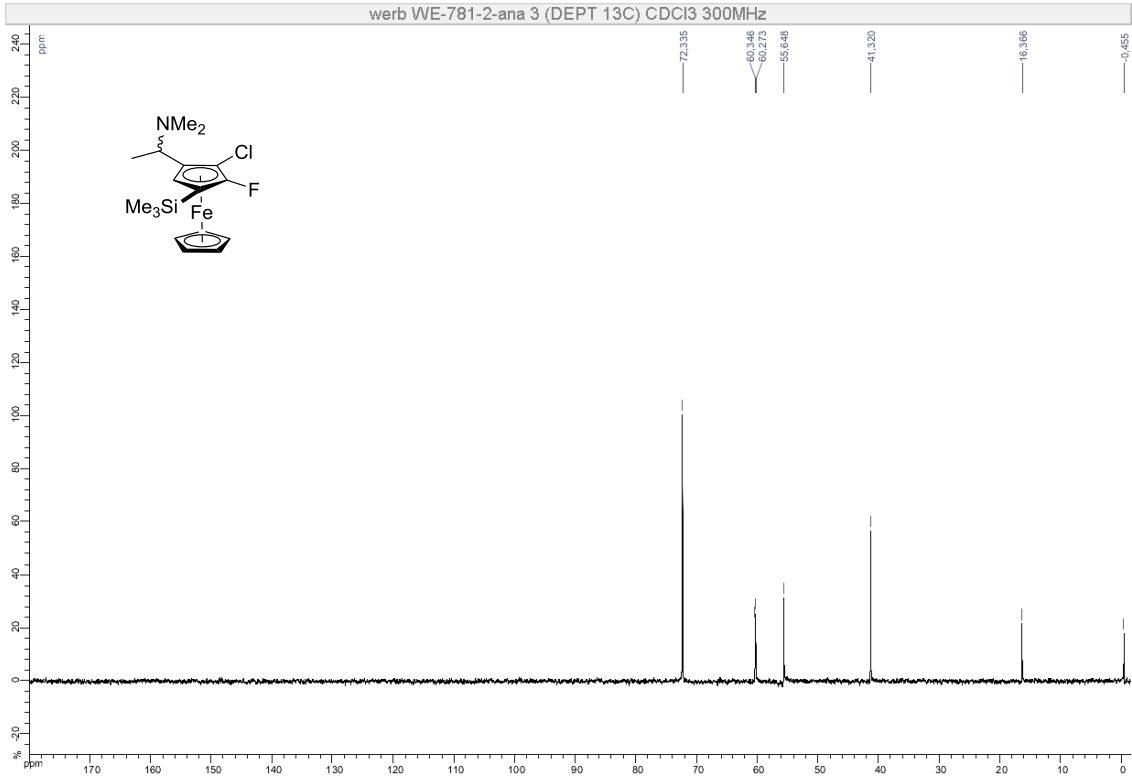


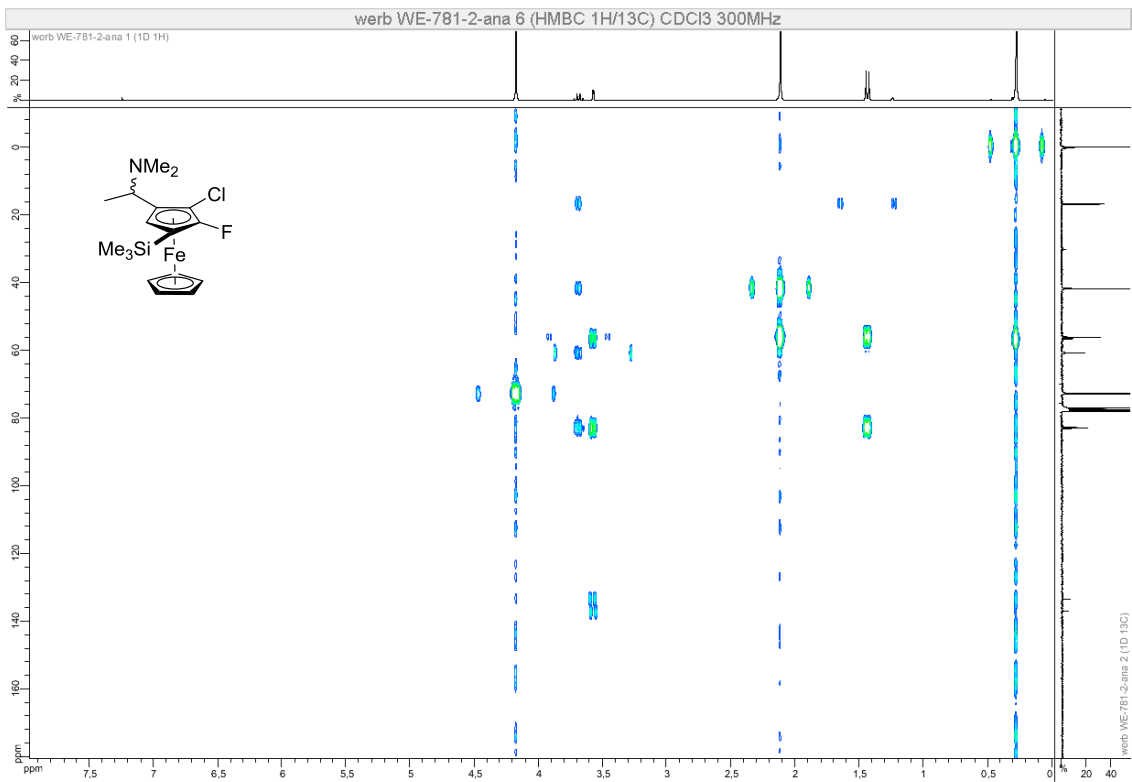
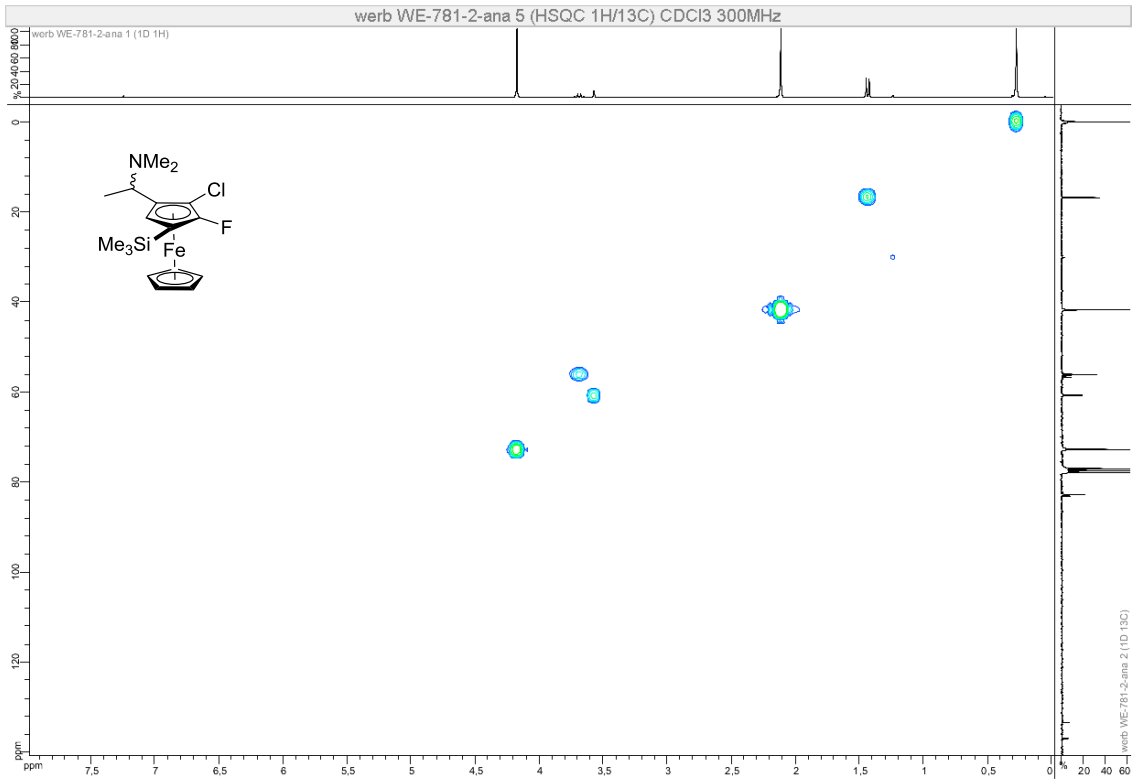
Compound (*R,S*)-14

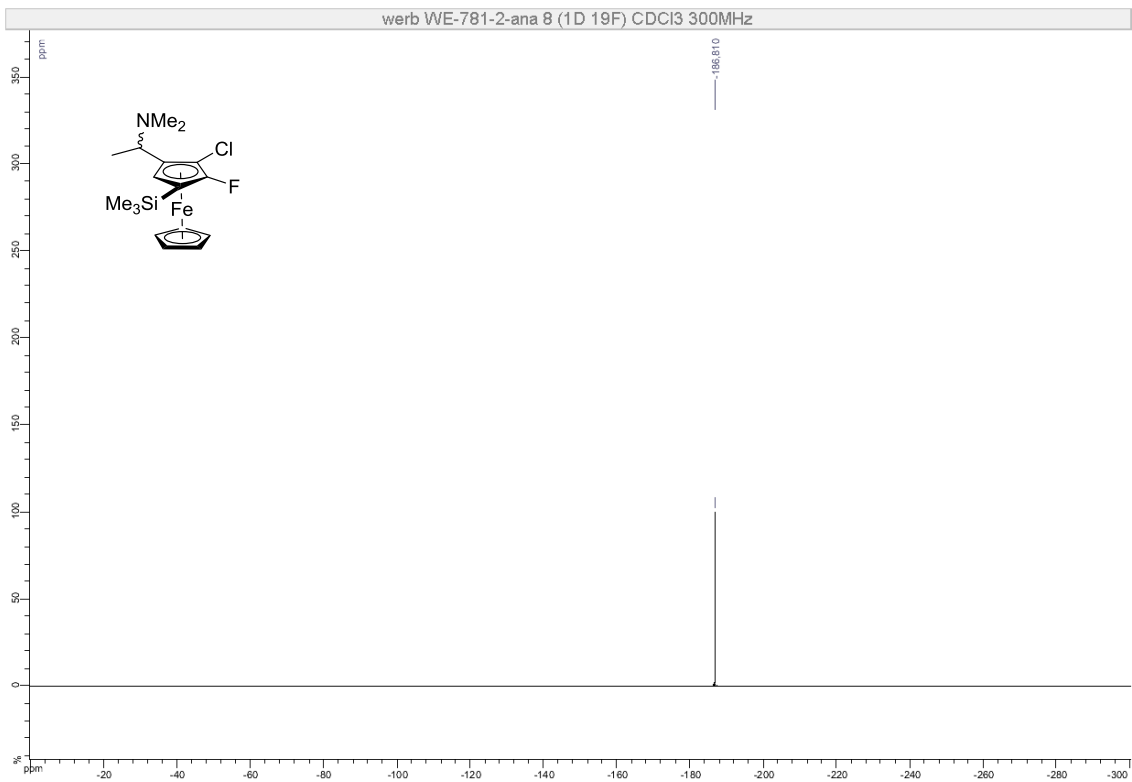
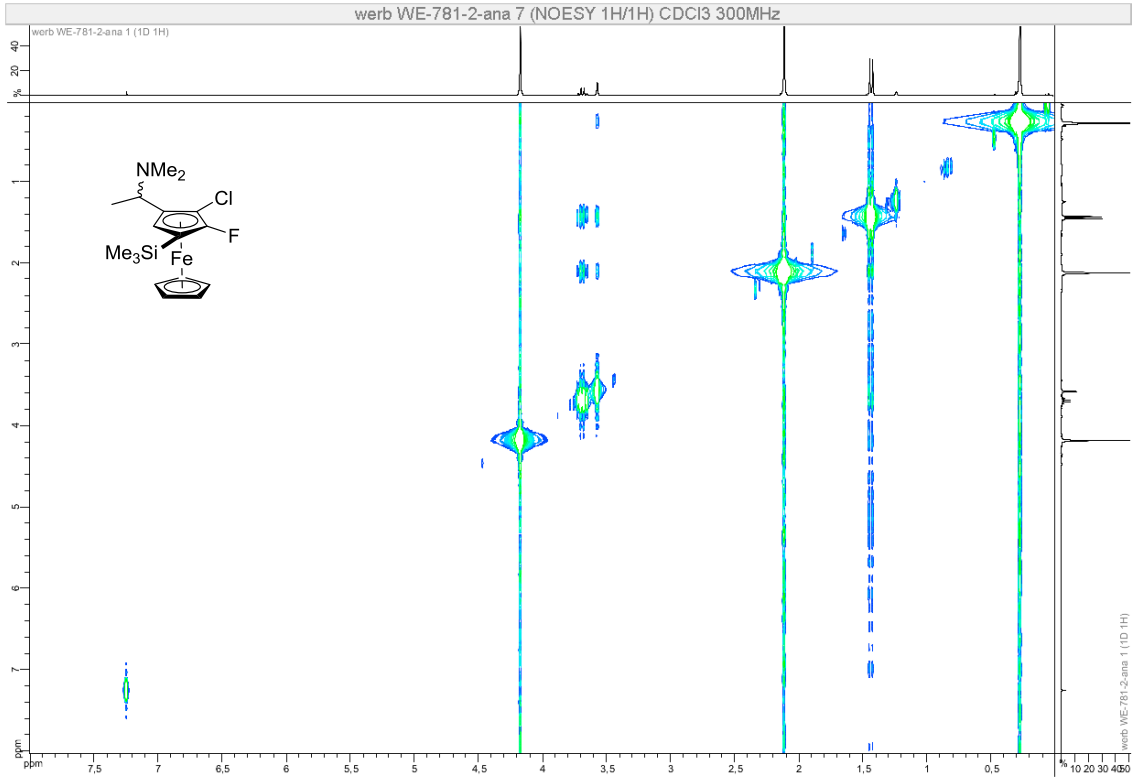


Compound (\pm)-15

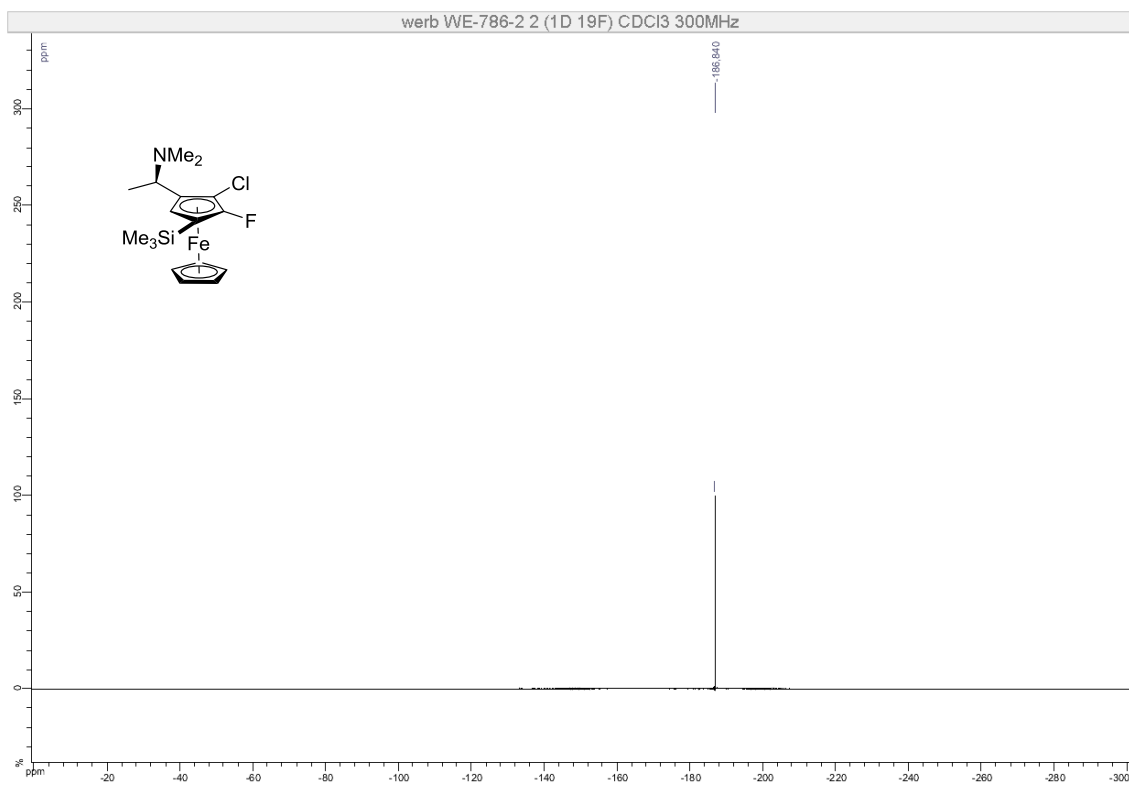
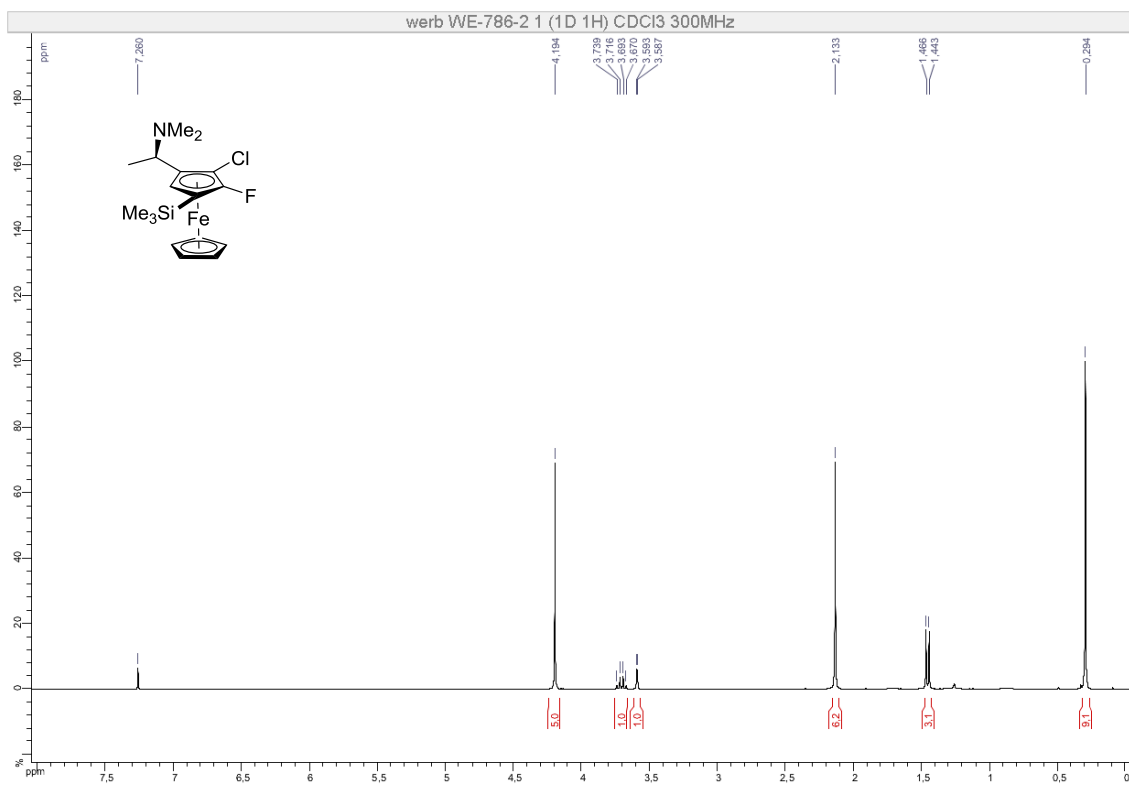




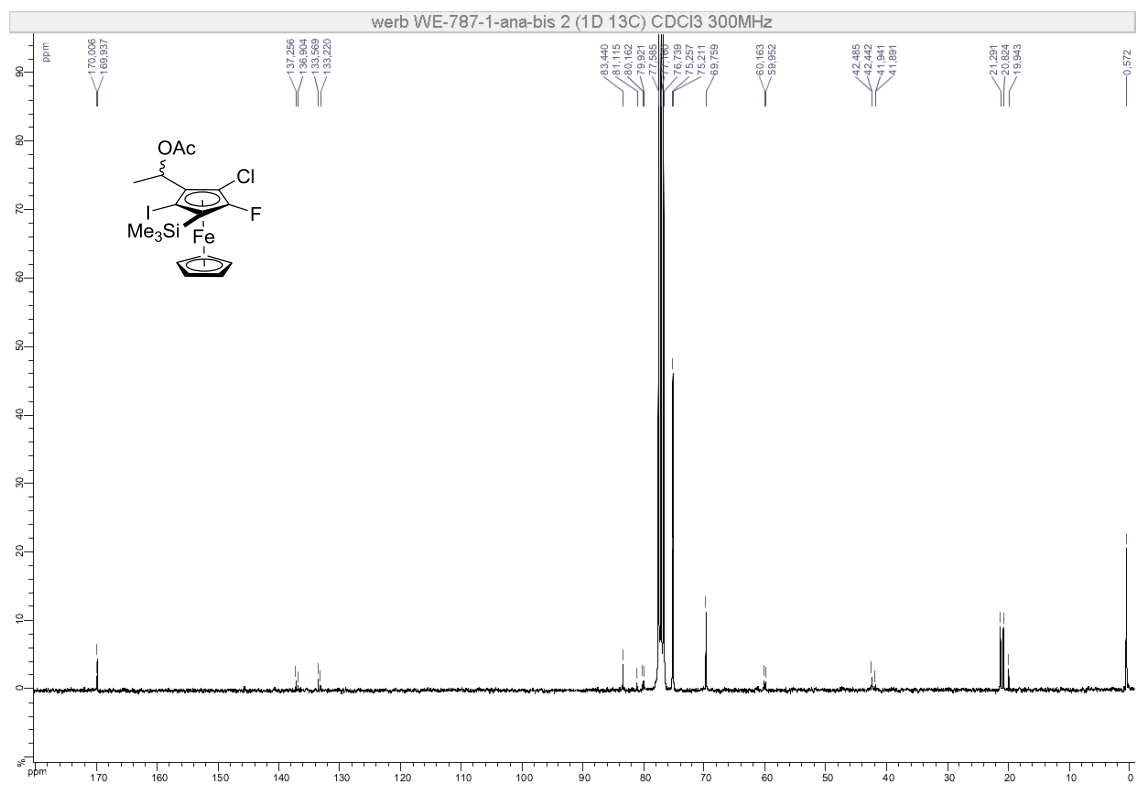
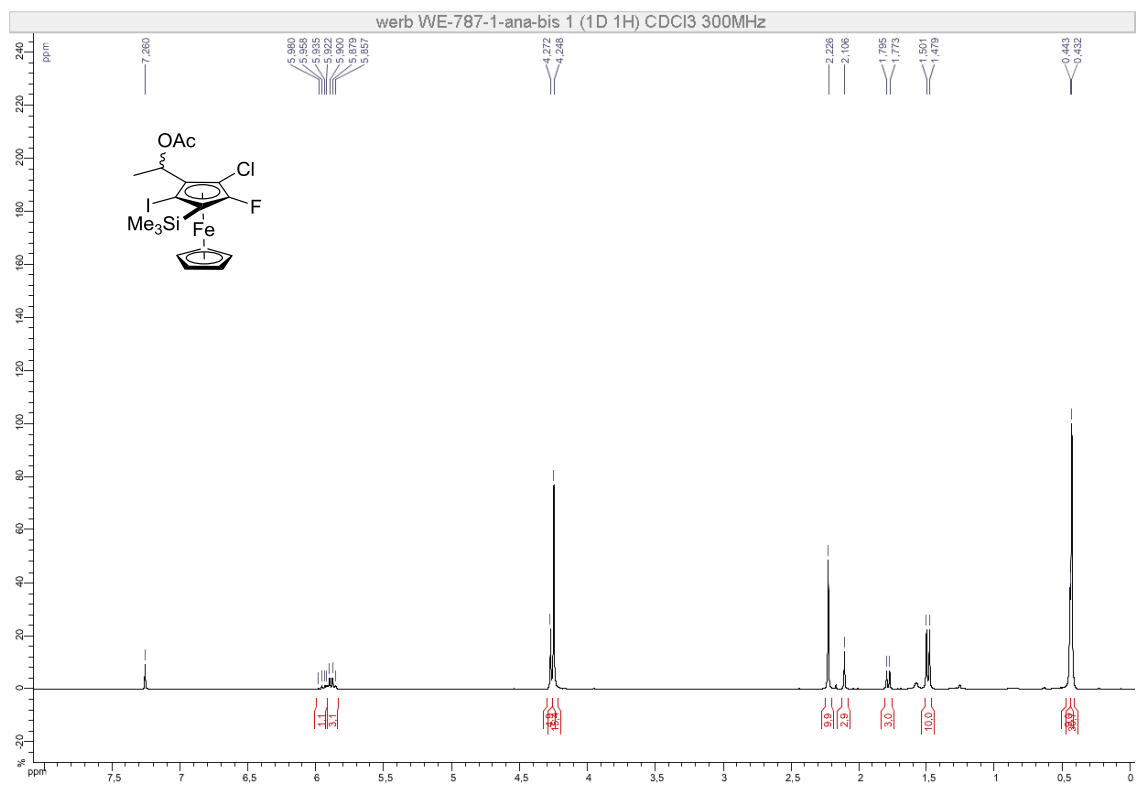


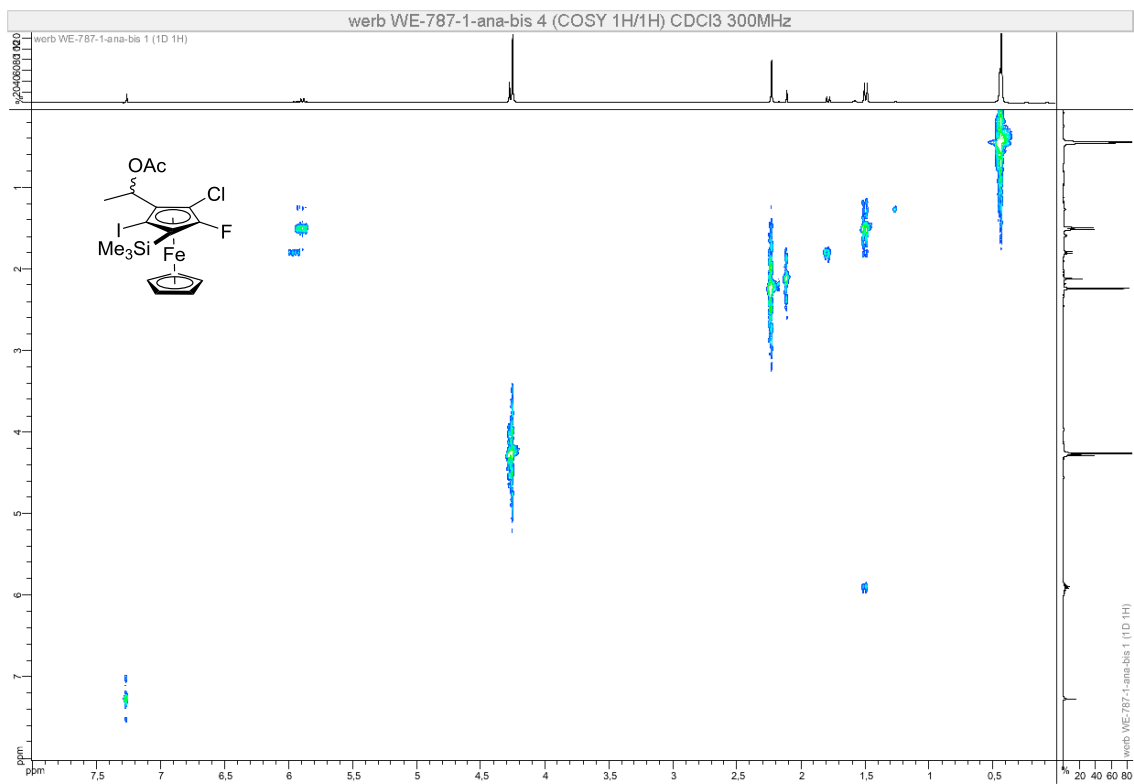
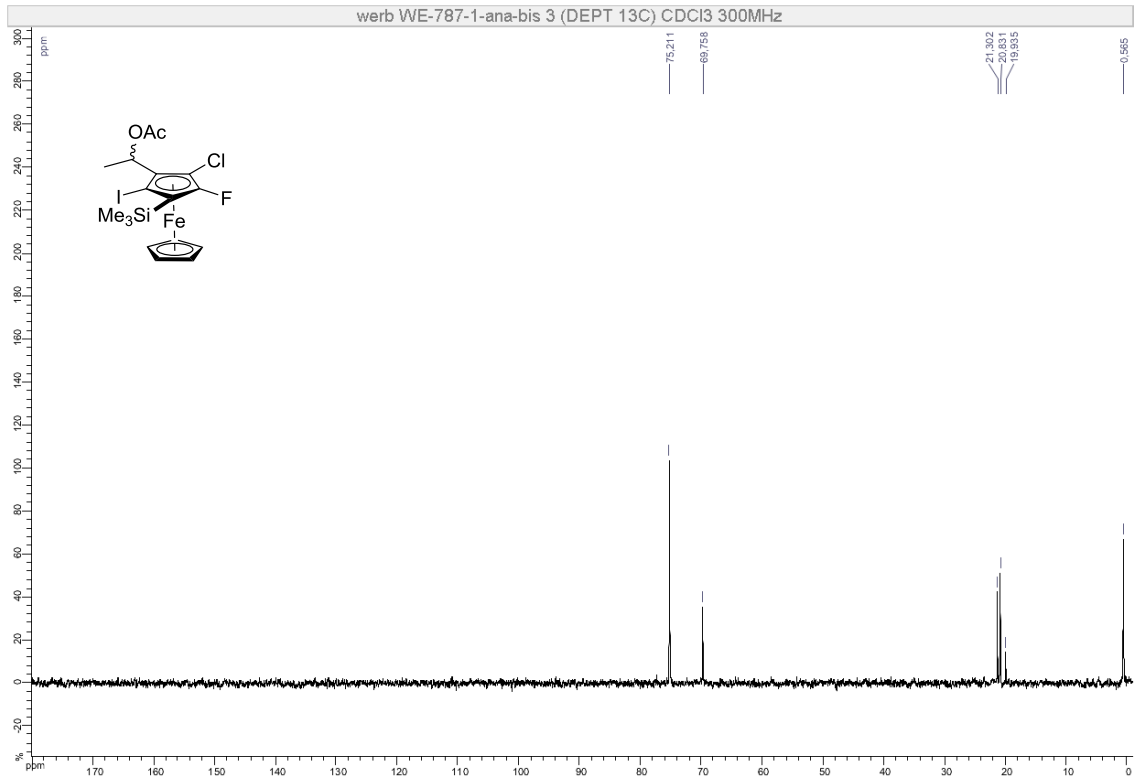


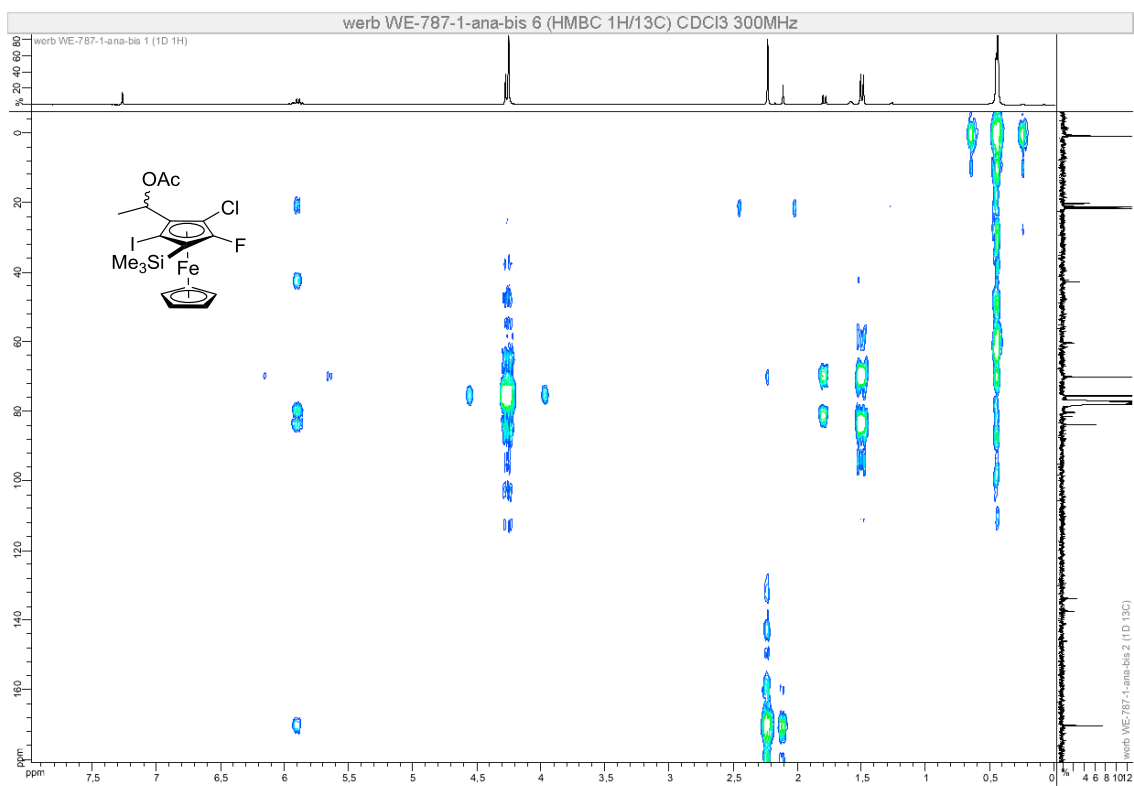
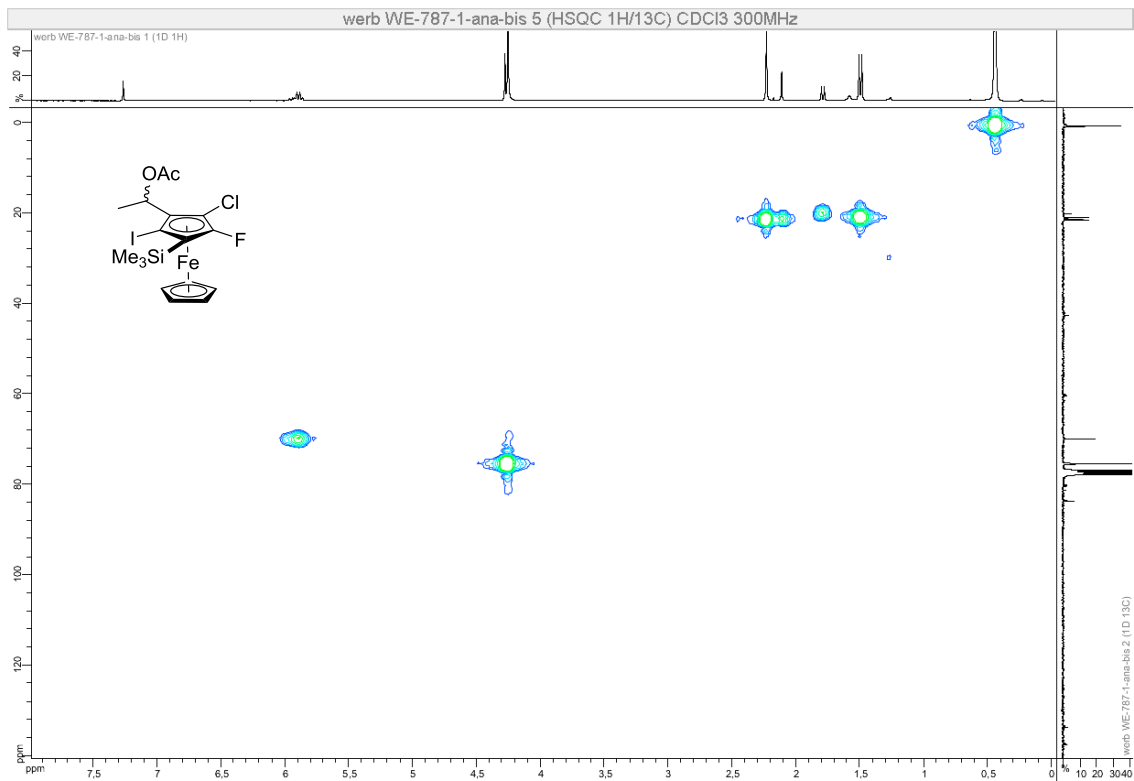
Compound (*R,R*)-15

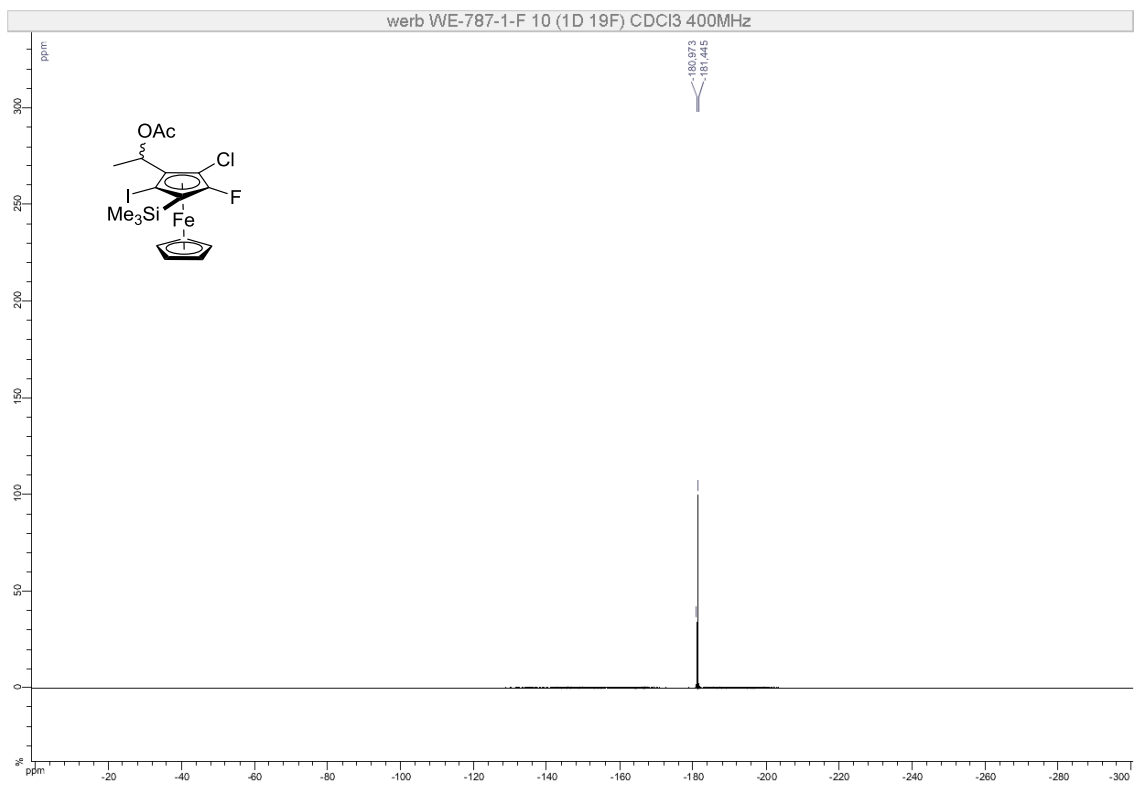
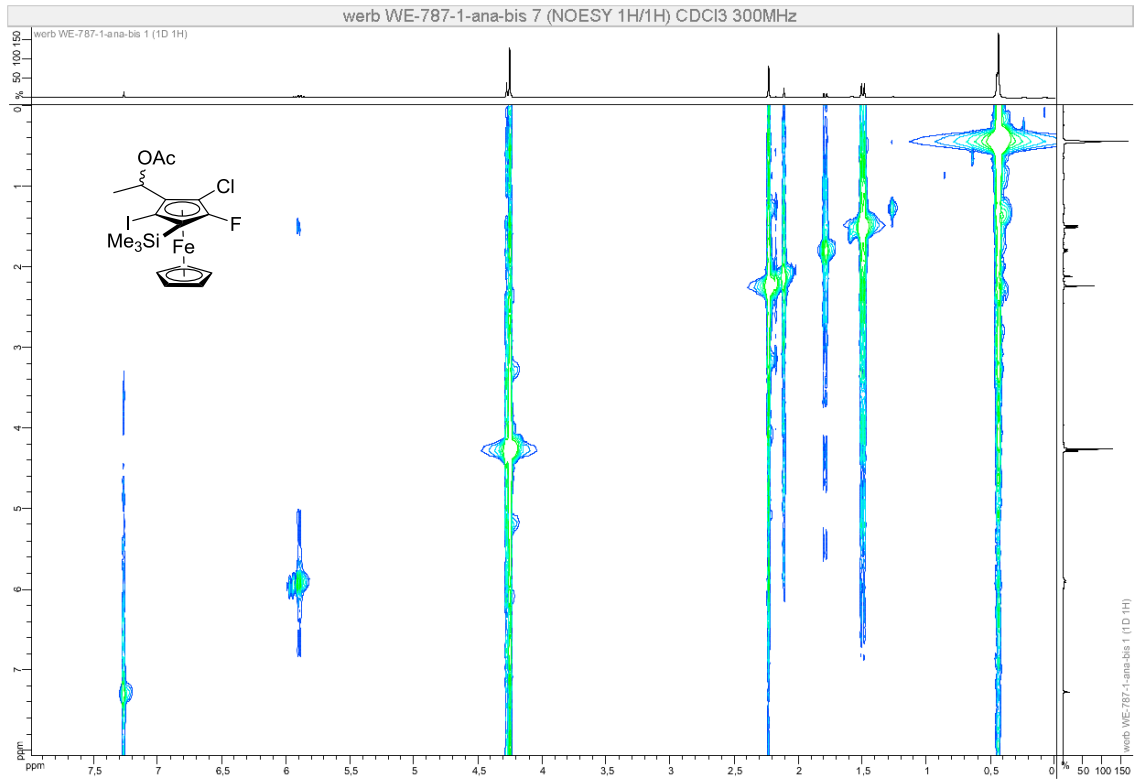


Compound (\pm)-16

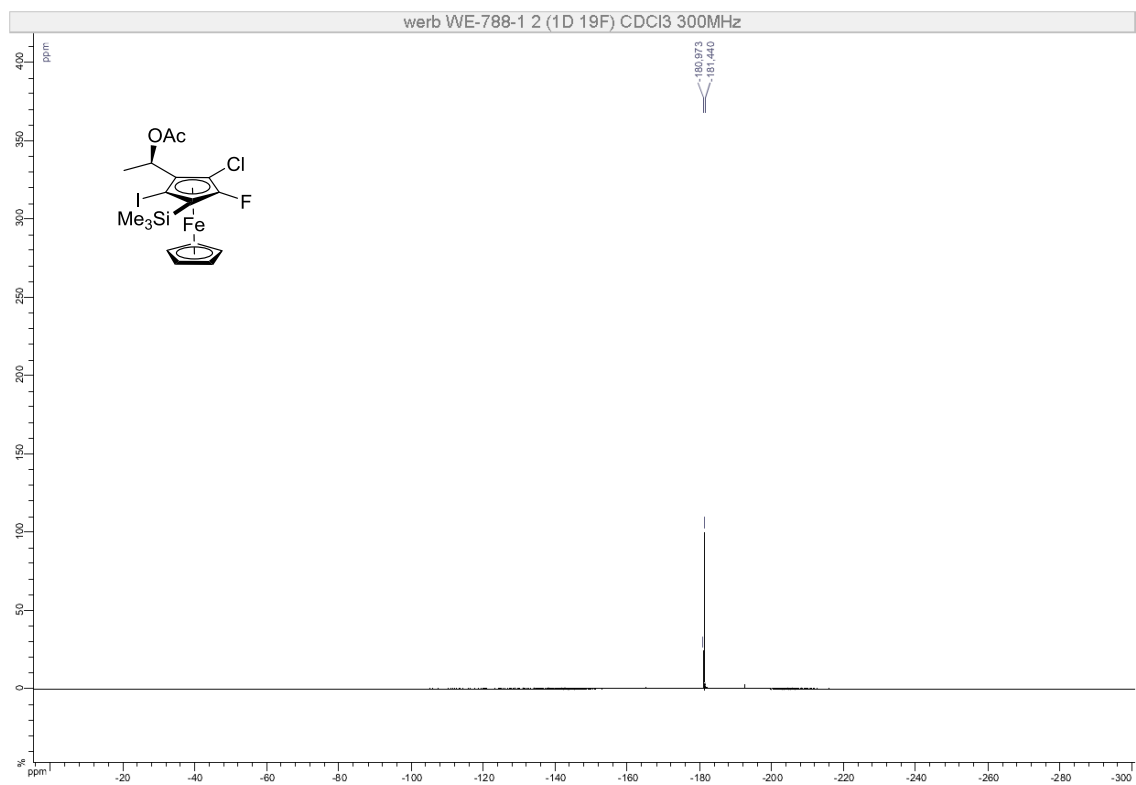
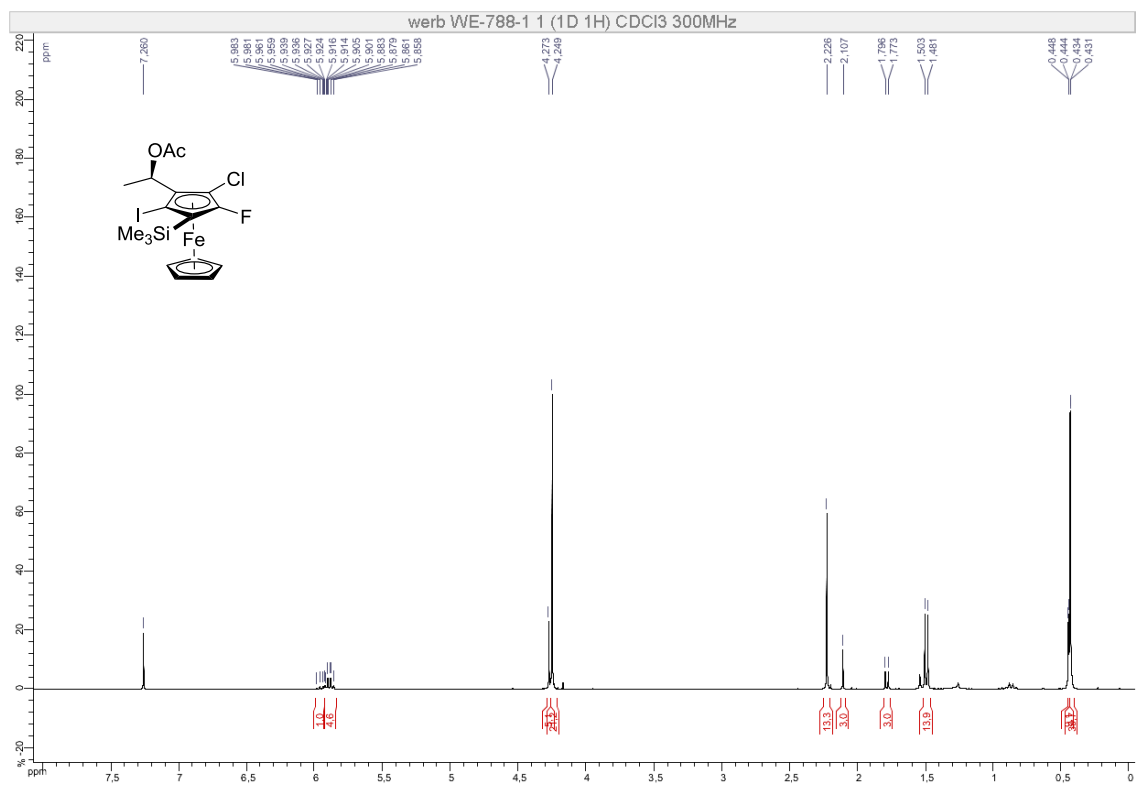




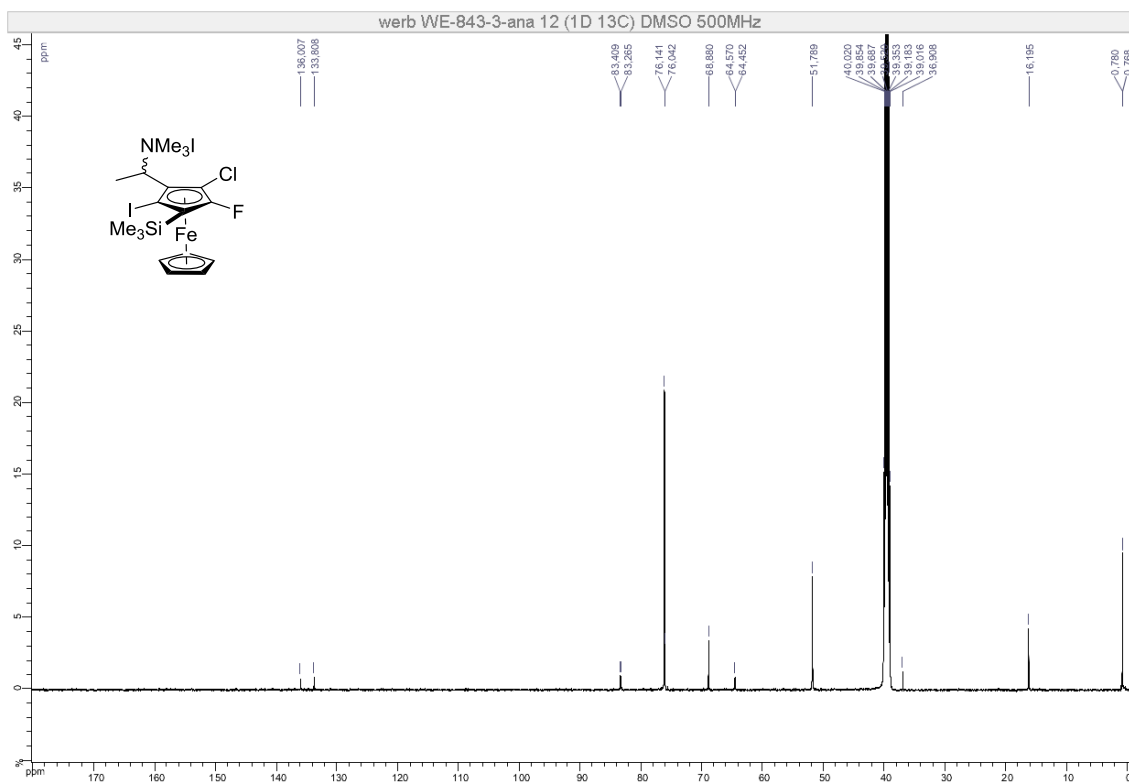
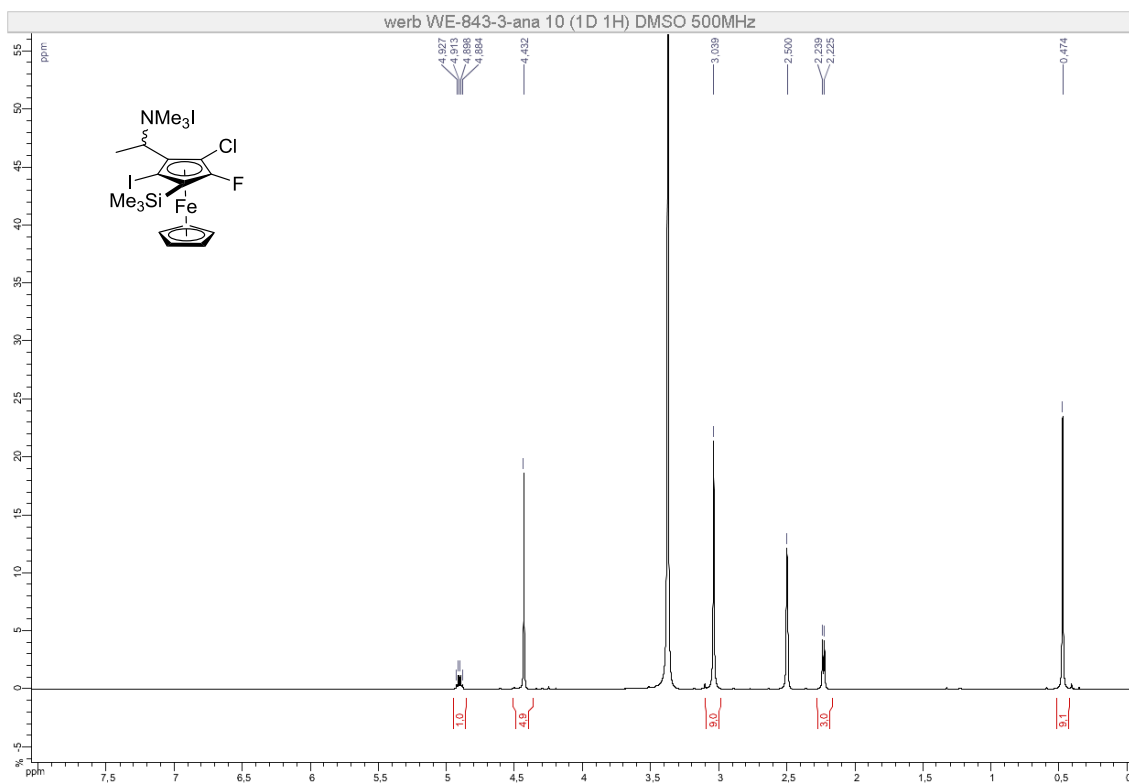


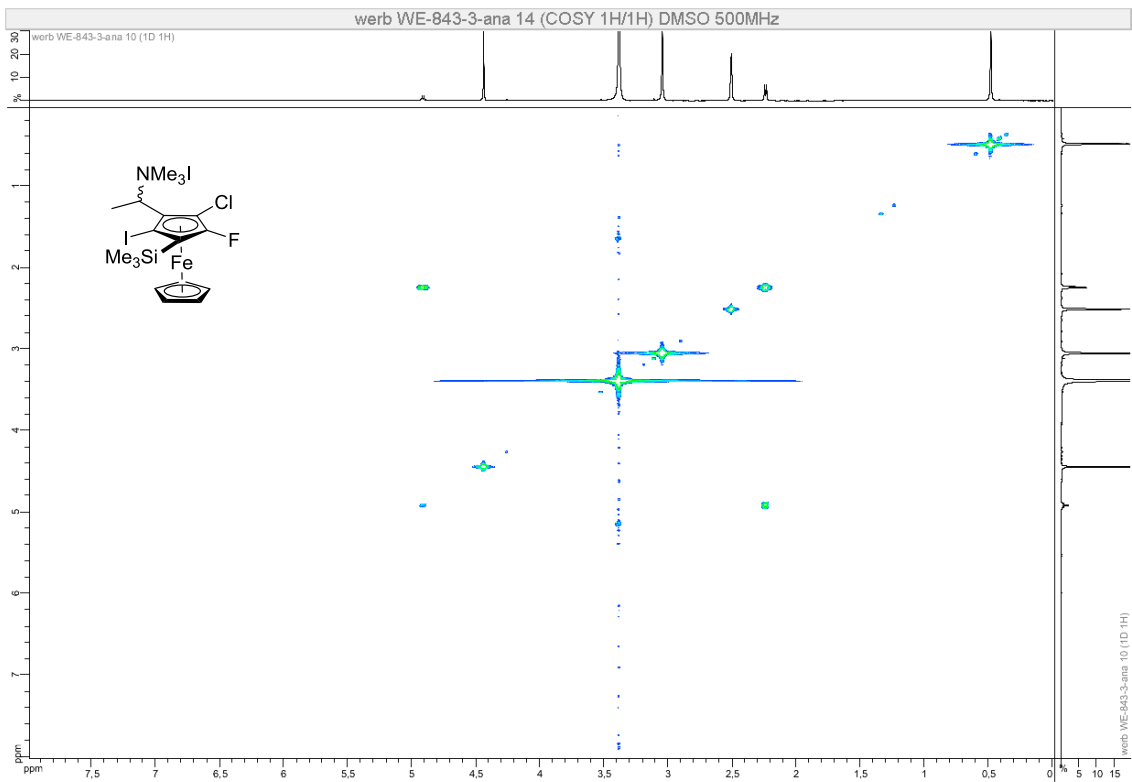
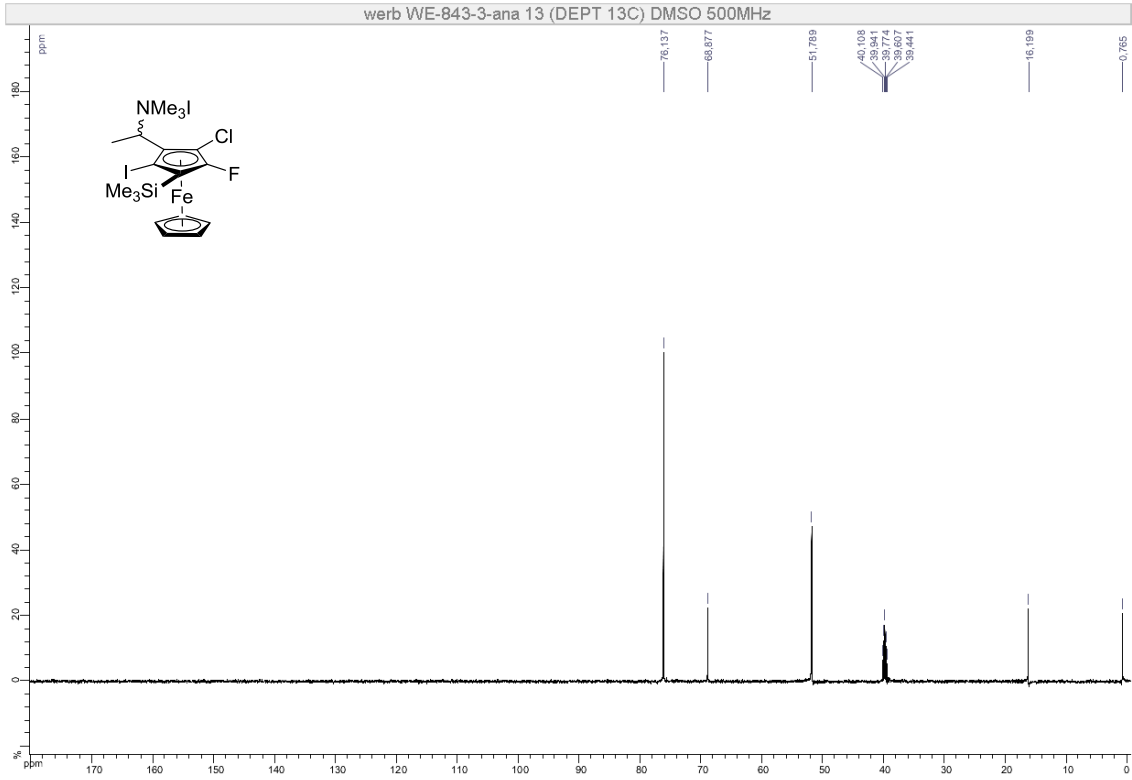


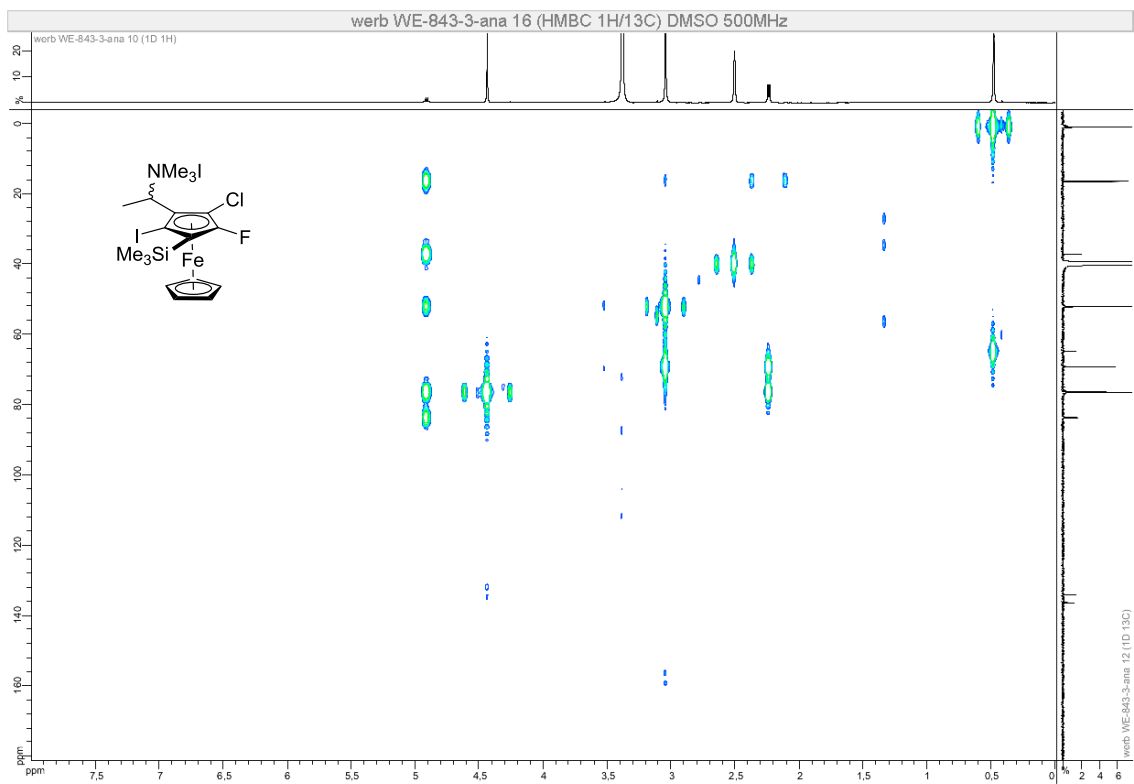
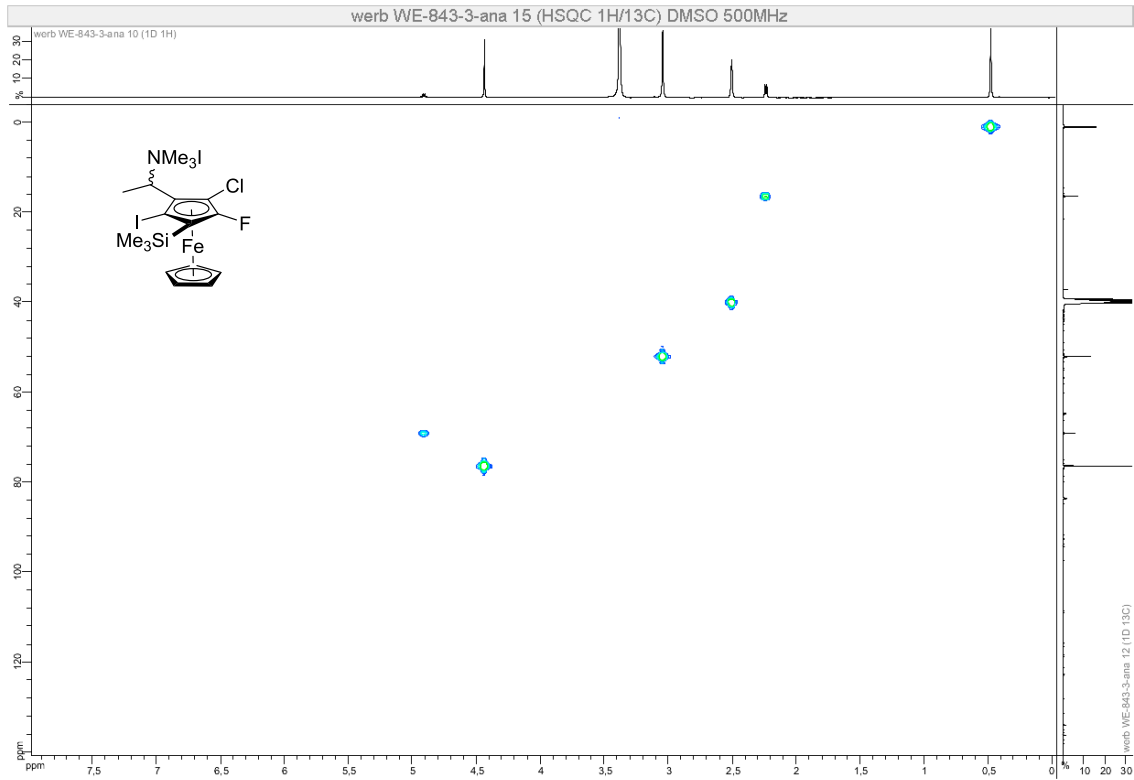
Compound (*R,S*)-16

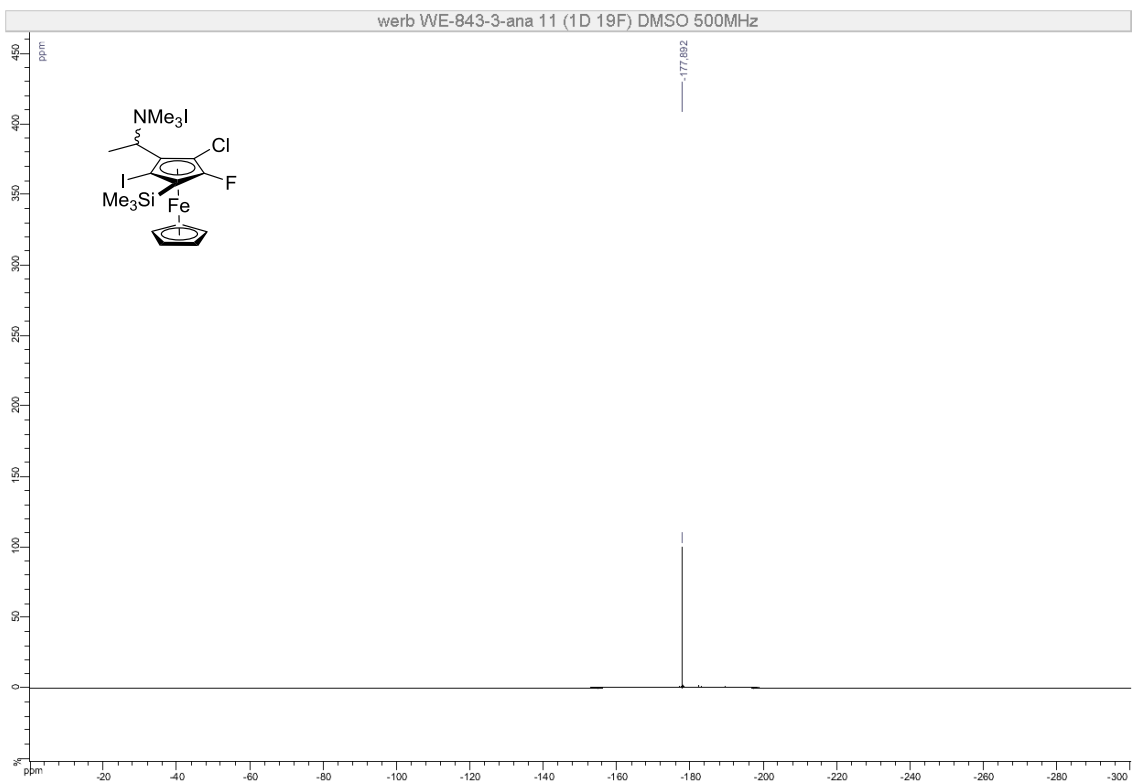
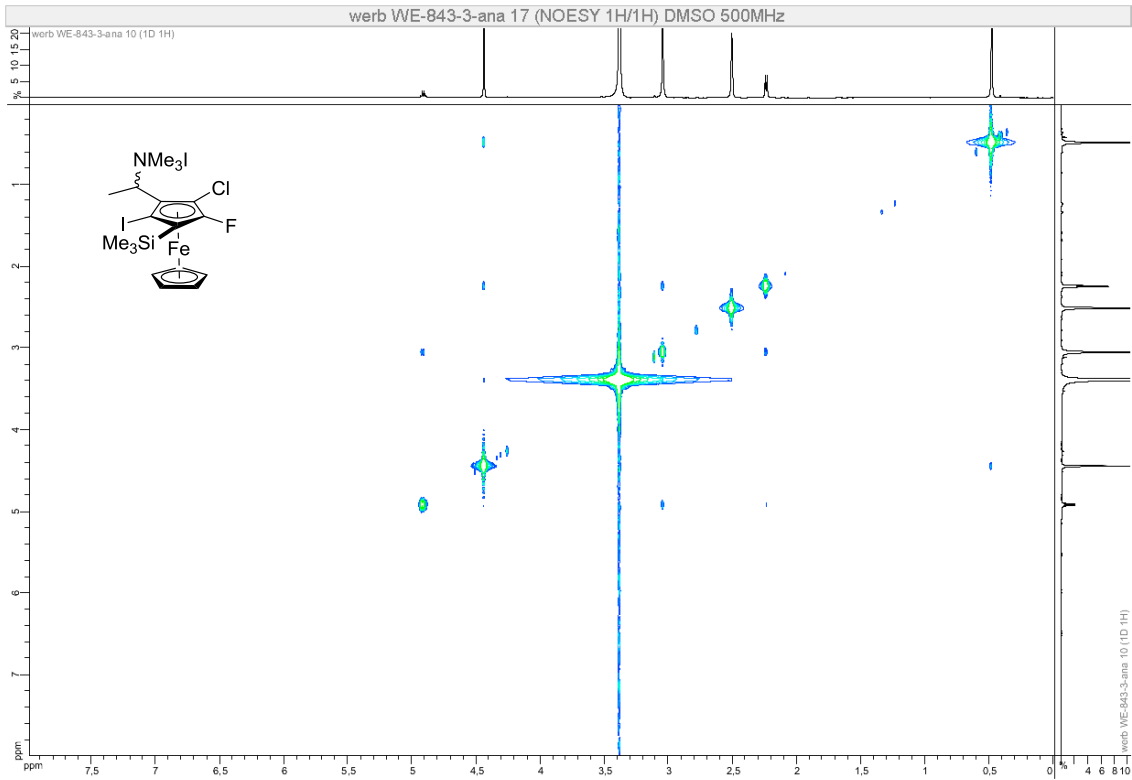


Compound (\pm)-17

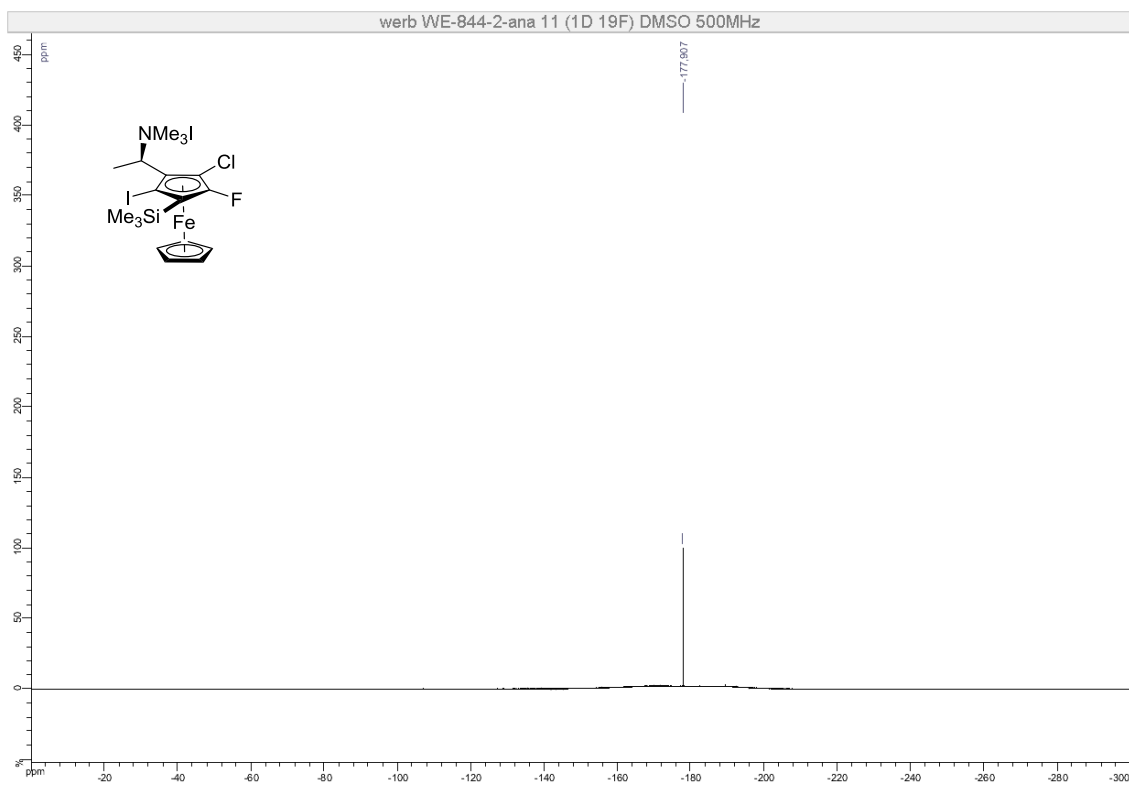
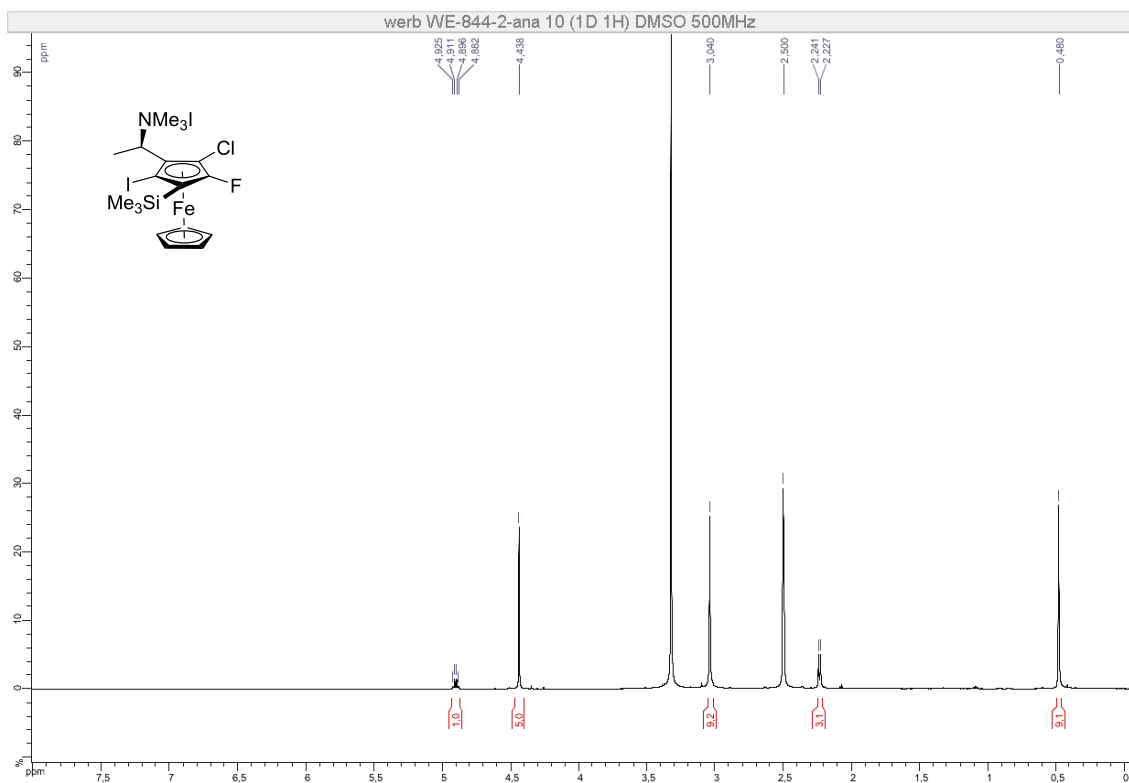






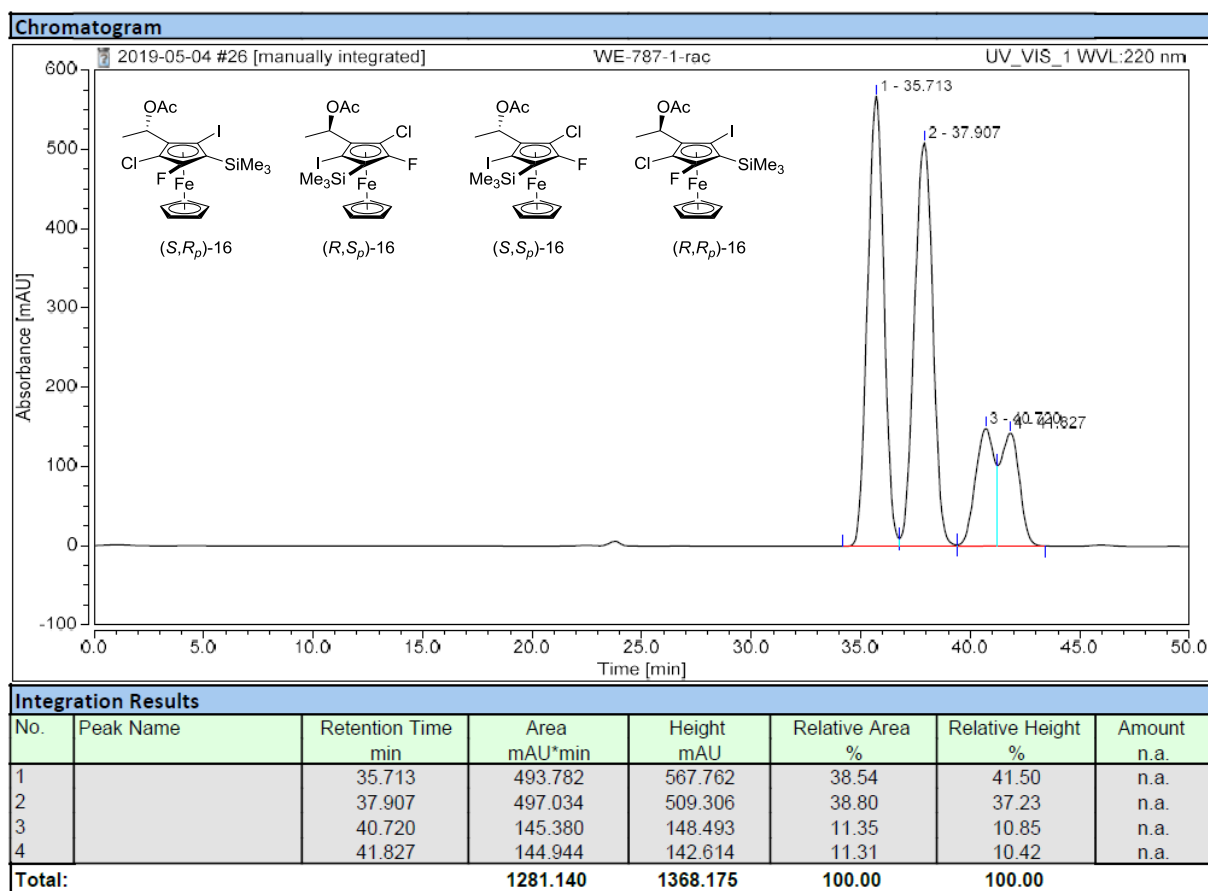


Compound ((*R,S*)-17)

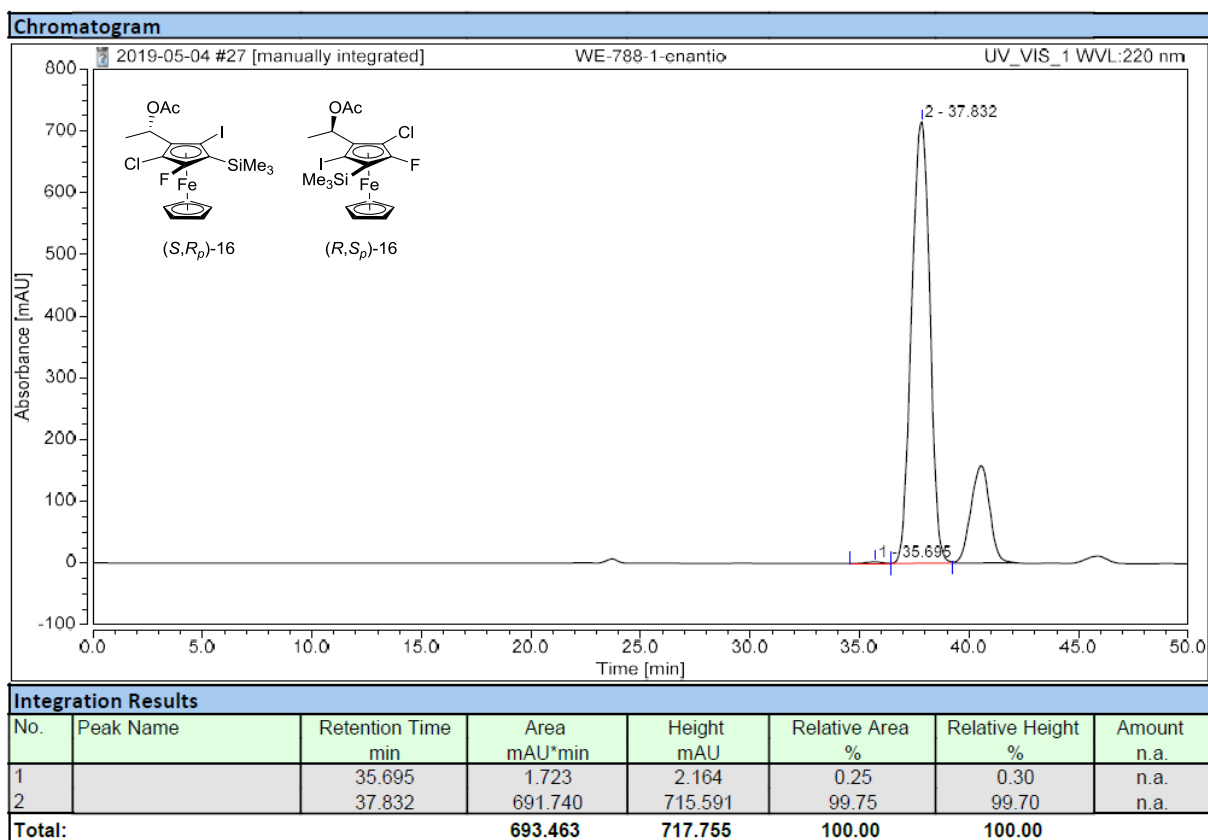
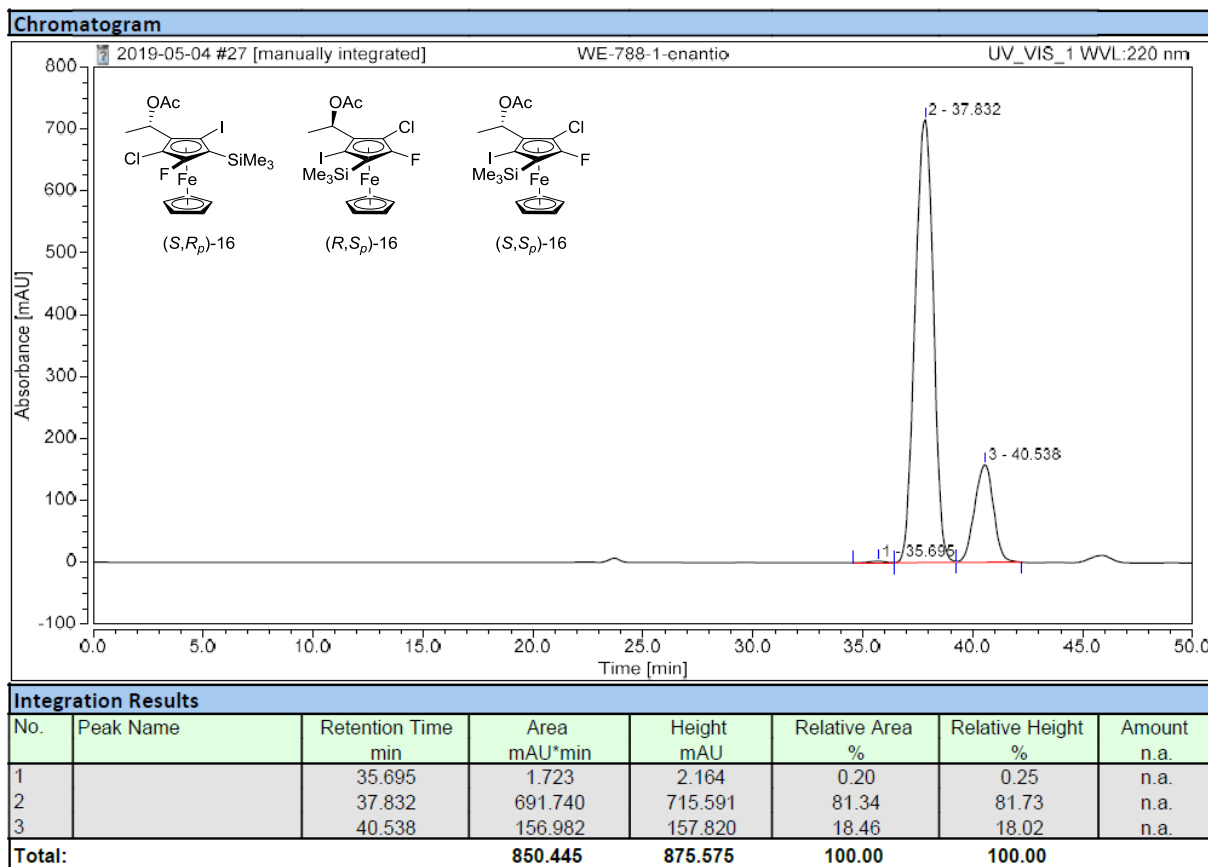


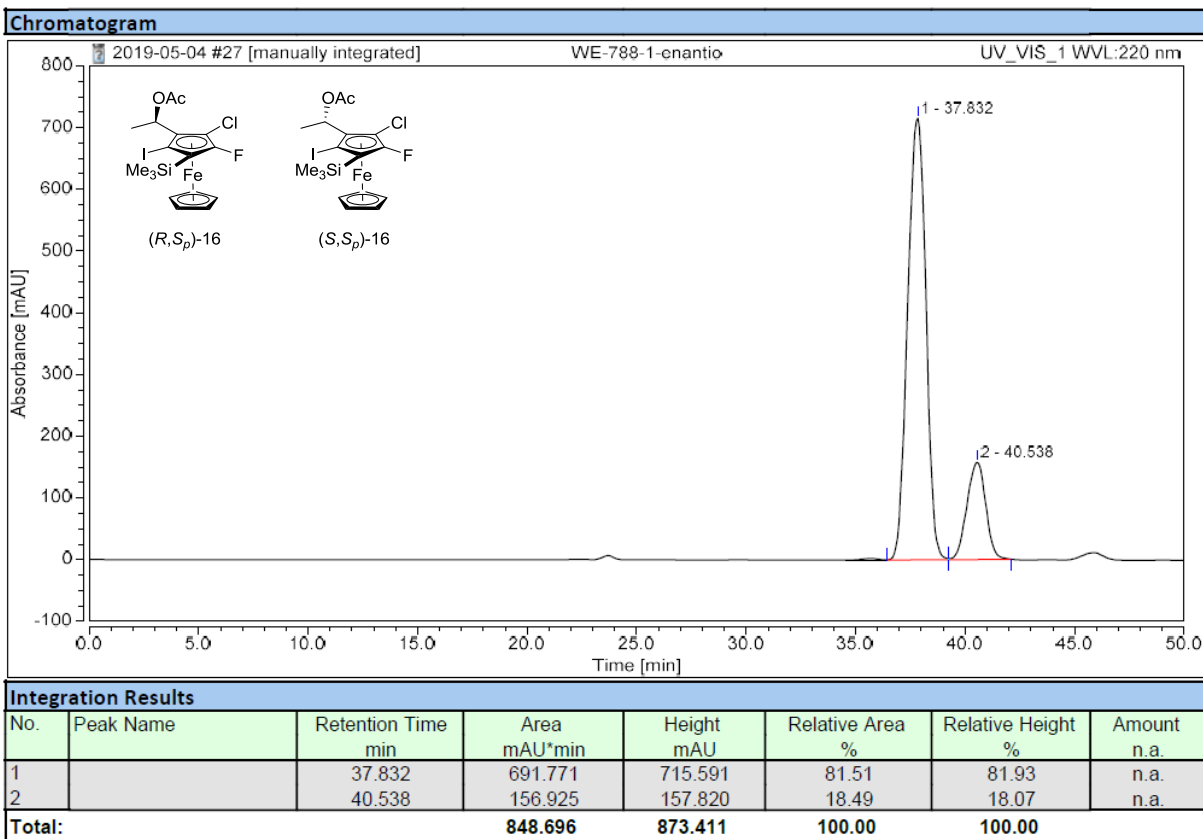
HPLC Chromatograms of compounds (*R,S*)-, (*S,R*)-, (*S,S*)- and (*R,R*)-16.

Chiralpak IC-3 column, hexane/iPrOH: 99.5:0.5, 0.25 mL/min, 5 °C, $\lambda = 254$ nm, t (*S,R*) = 35.71 min, t (*R,S*) = 37.91 min, t (*S,S*) = 40.72 min, t (*R,R*) = 41.83 min.



Chiralpak IC-3 column, hexane/iPrOH: 99.5:0.5, 0.25 mL/min, 5 °C, $\lambda = 254$ nm, $t(S,R_p) = 35.71$ min, $t(R,S_p) = 37.91$ min, $t(S,S_p) = 40.72$ min, (R,R_p) too low to be identified. ee = 99.5%, de = 63%.





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