

Supporting Information

Application of the Curtius rearrangement to the synthesis of 1'-aminoferrocene-1-carboxylic acid derivatives

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Substrates' syntheses

Dimethyl ferrocene-1,1'-dicarboxylate – SI1. Under argon, BuLi (~1.6 M in hexanes, 78.1 mL, 125 mmol, 2.5 equiv) was added to a stirred solution of ferrocene (9.3 g, 50 mmol, 1.0 equiv) and TMEDA (18.7 mL, 14.5 g, 125 mmol, 2.5 equiv) in hexane (250 mL) and the reaction was stirred overnight at room temperature to give a deep red suspension. THF (100 mL) was added and the reaction mixture was cooled to -78 °C. Carbon dioxide was bubbled in the reaction mixture for 15 min and the reaction mixture was slowly warmed to room temperature upon bubbling. EtOAc (150 mL) was added and the organic phase was extracted with NaOH (10%, 3 x 100 mL). The combined aqueous layers were washed with EtOAc (2 x 100 mL) and acidified with HCl (12 M) until pH 1 was reached. The resulting solids were filtrated, washed with H₂O and dried under high vacuum over P₂O₅ to give crude ferrocene-1,1'-dicarboxylic acid. the title product as an orange solid containing 3-5% of ferrocenecarboxylic acid.

The crude product was dissolved in MeOH (150 mL), H₂SO₄ (96%, 1.0 mL) was added dropwise and the reaction mixture was heated at methanol reflux overnight. The reaction mixture was cooled to room temperature and volatiles were removed under vacuum. EtOAc (100 mL) and NaHCO₃ (sat., 100 mL) were added and the layers were separated. The aqueous layer was further extracted with EtOAc (2 x 100 mL). The combined organic layers were dried over MgSO₄, filtrated and concentrated under vacuum to give the crude product. This was purified by column chromatography on silica, eluting with EtOAc/heptane (80:20 to 70:30) to give ferrocene-1,1'-dimethylcarboxylate **SI1** (16.6 g, 70.5%) and methyl ferrocene carboxylate **SI2** (337.0 mg, 3%) as orange solids.

Dimethyl ferrocene-1,1'-dicarboxylate (SI1): mp 112-114 °C (lit.¹ 113.5-114.5 °C); IR (ATR): 3087, 2958, 1698, 1468, 1434, 1373, 1278, 1196, 1143, 1029, 964, 779 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 4.78 (t, *J* = 2.0 Hz, 4H, 4 x FcCH), 4.36 (t, *J* = 2.0 Hz, 4H, 4 x FcCH) 3.78 (s, 6H, 2 x CH₃); ¹³C NMR (75.4 MHz, CDCl₃) δ 170.9 (2 x C=O), 73.1 (2 x FcC), 72.8 (4 x FcCH), 71.7 (4 x FcCH), 51.8 (2 x CH₃). **Methyl ferrocene carboxylate (SI2):** mp 57-58 °C (lit.² 50-56 °C); IR (ATR): 2954, 1709, 1699, 1463, 1373, 1276, 1189, 1136, 1105, 1025, 961, 823 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.78 (t, *J* = 1.7 Hz, 2H, 2 x FcCH), 4.37 (t, *J* = 1.7 Hz, 2H, 2 x FcCH), 4.18 (s, 5H, 5 x FcCH), 3.78 (s, 3H, CH₃); ¹³C NMR (125.7 MHz, CDCl₃) δ 172.4 (C=O), 71.4 (FcC), 71.2 (2 x FcCH), 70.3 (2 x FcCH), 69.9 (5 x FcCH), 51.7 (CH₃).

Sodium ferrocene-1,1'-dicarboxylate (SI3). A solution of NaOH (2.17 g, 54.3 mmol, 8.2 equiv) in water (10 mL) was added to a solution of dimethyl ferrocene-1,1'-dicarboxylate (**SI1**, 2.0 g, 6.6 mmol, 1.0 equiv) in EtOH (10.0 mL) at 70 °C. After 2h at 75 °C, the reaction mixture was cooled to 0 °C and the resulting solids were filtrated, washed with cold EtOH (5 mL), Et₂O (10 mL) and dried under vacuum to give the title product as a yellow solid (2.0 g, 95%). mp > 250 °C; IR (ATR): 3087, 1556, 1477, 1380, 1190, 1067, 1026, 806, 796 cm⁻¹; ¹H NMR (300 MHz, D₂O) δ 4.75 (s, 4H, 4 x FcCH), 4.43 (s, 4H, x FcCH) ; ¹³C NMR (75.4 MHz, D₂O) δ 179.4 (2 x C=O), 77.4 (2 x FcC), 73.1 (4 x FcCH), 71.0 (4 x FcCH).

(9H-Fluoren-9-yl)methanol (SI4). A modified procedure of Chong was followed:³ BuLi (~1.6 M in hexanes, 37.5 mL, 60.0 mmol, 1.0 equiv) was added to a solution of fluorene (10.0 g, 60.0 mmol, 1.0 equiv) in anhydrous THF (250 mL) at 0 °C over 5 min. After 3 min stirring at 0 °C, paraformaldehyde (2.0 g, 66.0 mmol, 1.1 equiv) was added in one portion. The reaction mixture was warmed to room temperature and stirred for 90 min. NaHCO₃ sat. (150 mL) was added and the reaction mixture was extracted with Et₂O (3 x 100 mL). The combined organic layers were dried over MgSO₄, filtrated and concentrated under vacuum to give the crude product. This was purified by recrystallization in hexane/EtOH (600:8) to give the title product as a white solid (3.6 g, 30.5%). mp 100-102 °C (lit.³ 100-101 °C); IR (ATR): 3252 (br), 1444, 1363, 1314, 1048, 1024, 754, 77, 725 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.77 (d, *J* = 7.4 Hz, 2H, ArH), 7.60 (d, *J* = 7.4 Hz, 2H, 2 x ArH), 7.40 (dt, *J* = 7.4, 0.7 Hz, 2H, 2 x ArH), 7.32 (dt, *J* = 7.4, 1.1 Hz, 2H, 2 x ArCH), 4.10 (t, *J* = 6.0 Hz, 1H, CH), 4.01 (t, *J* = 6.0 Hz, 2H, CH₂), 1.64 (t, *J* = 6.0 Hz, 1H, OH); ¹³C NMR (75.4 MHz, CDCl₃) δ 144.5 (2 x ArC), 141.7 (2 x ArC), 127.7 (2 x ArCH), 127.3 (2 x ArCH), 124.9 (2 x ArCH), 120.2 (2 x ArCH), 65.3 (CH₂), 50.6 (CH).

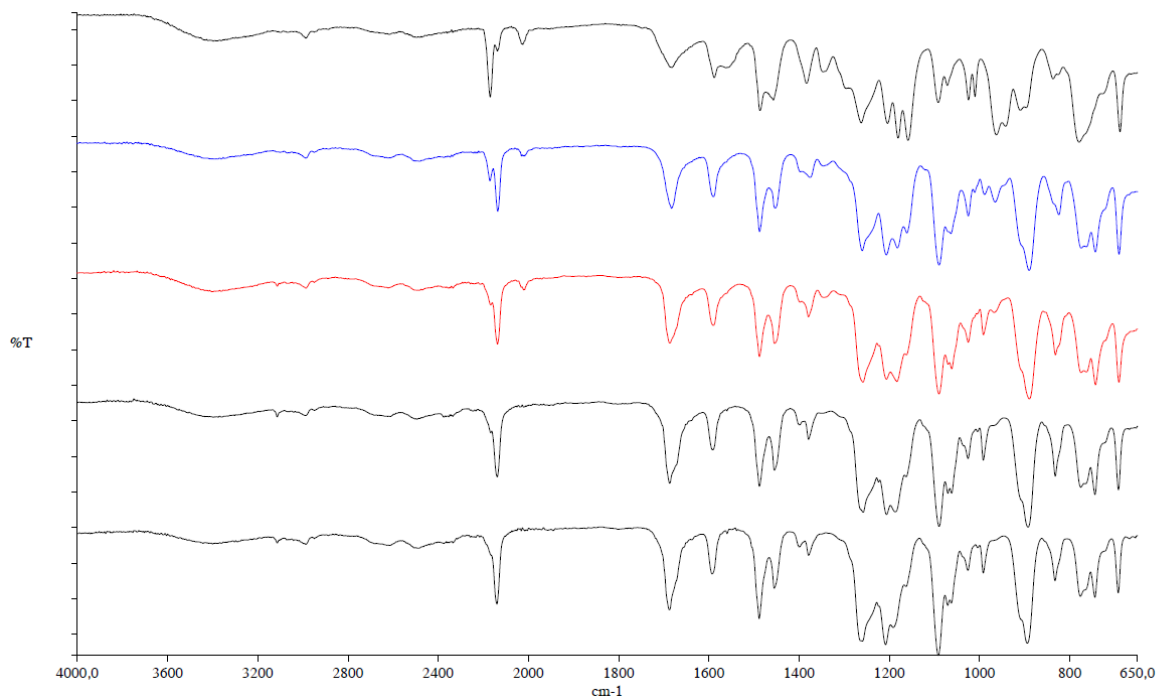
Ferrocene-1,1'-dicarboxylic acid (2). HCl (12 M) was added dropwise to a solution of sodium ferrocene-1,1'-dicarboxylate (**SI3**, 1.0 g, 3.1 mmol, 1.0 equiv) in water (20 mL) at 0 °C until pH 1 was

reached. The resulting solids were filtrated, washed with water and dried under high vacuum over P₂O₅ to give the title product as an orange solid (800 mg, 93%). mp > 250 °C (decomp, lit.⁴ > 250 °C); IR (ATR): 2885 (br), 2557, 1668, 1488, 1404, 1297, 1168, 1032, 917, 840, 751 cm⁻¹; ¹H NMR (300 MHz, DMSO-d⁶) δ 12.32 (br s, 2H, 2 x CO₂H), 4.69 (s, 4H, 4 x FcCH), 4.44 (s, 4H, 4 x FcCH); ¹³C NMR (75.4 MHz, DMSO-d⁶) δ 171.1 (2 x C=O), 73.5 (2 x FcC); 72.6 (4 x FcCH); 71.3 (4 x FcCH).

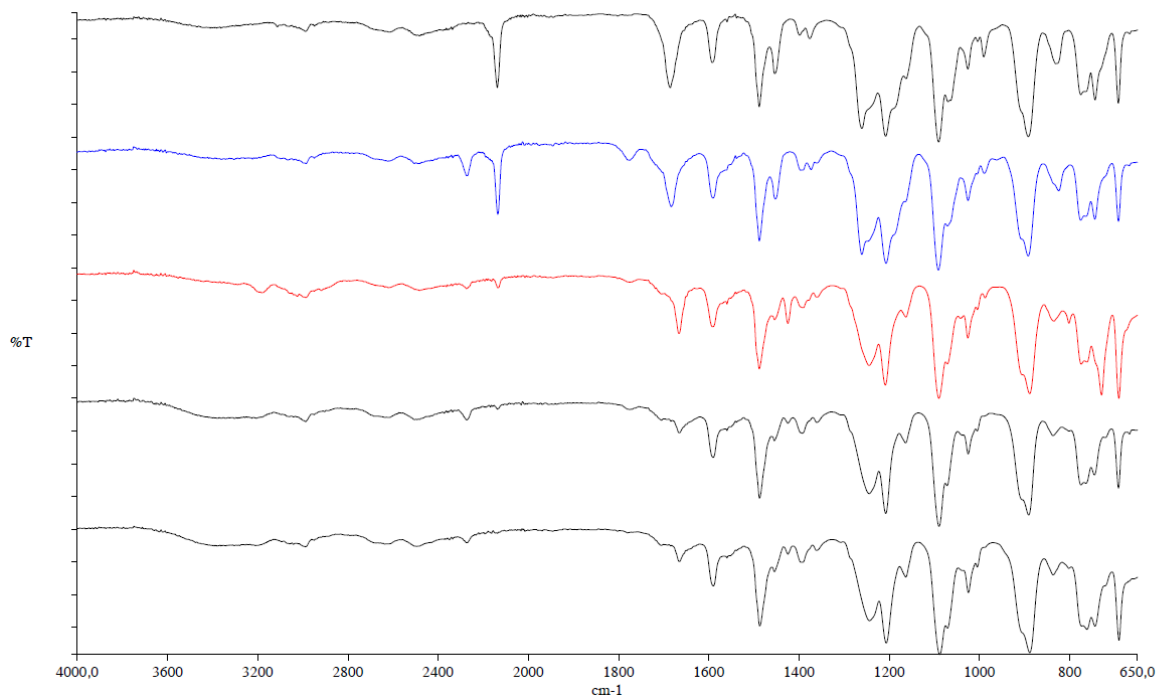
1. Fischer, D. *Acta Crystallogr.* **1964**, *17*, 619.
2. Barišić, L.; Rapić, V.; Pritzkow, H.; Pavlović, G.; Nemet, I. *J. Organomet. Chem.* **2003**, *682*, 131-142.
3. Chong, J. M.; Lajoie, G.; Tjepkema, M. W. *Synthesis* **1992**, *1992*, 819-820.
4. Gao, B.; Yang, B.; Li, T.; Zhang, B. *Synth. Commun.* **2009**, *39*, 2973-2981.

IR spectra of the formation and consumption of 3 and 4

Formation of **3** and **4**: top to bottom (1min, 1h, 2h 3h, 4h).

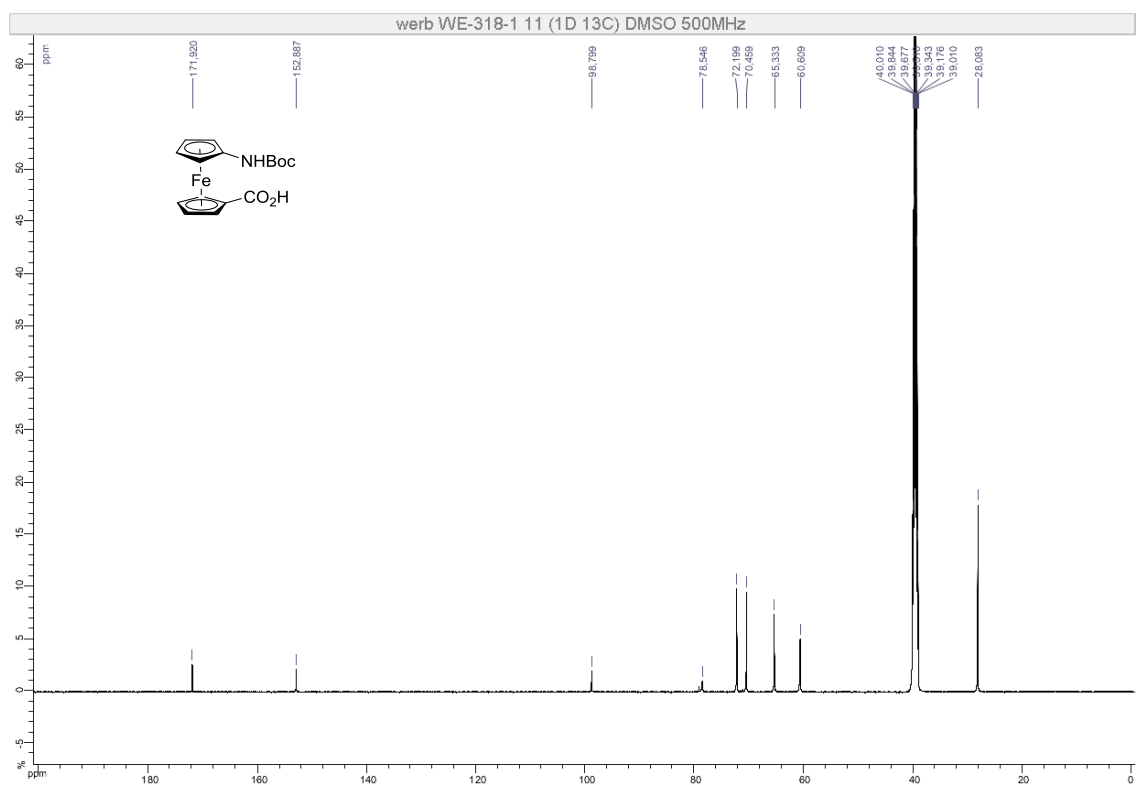
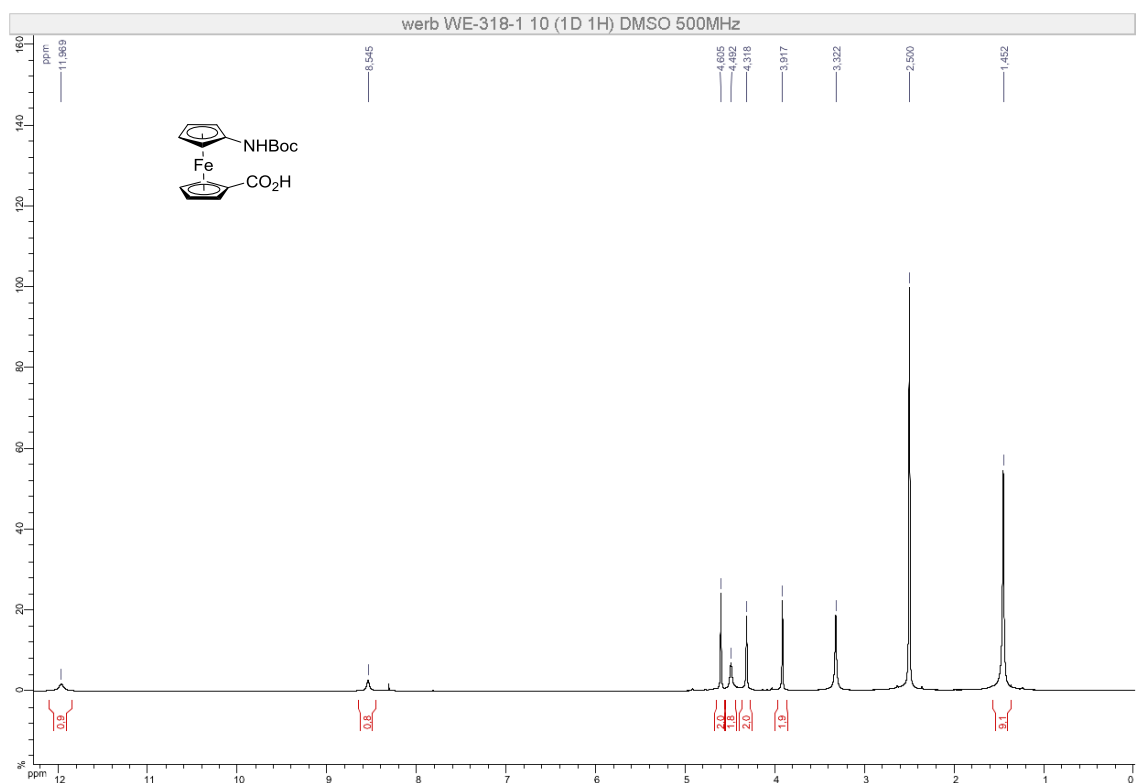


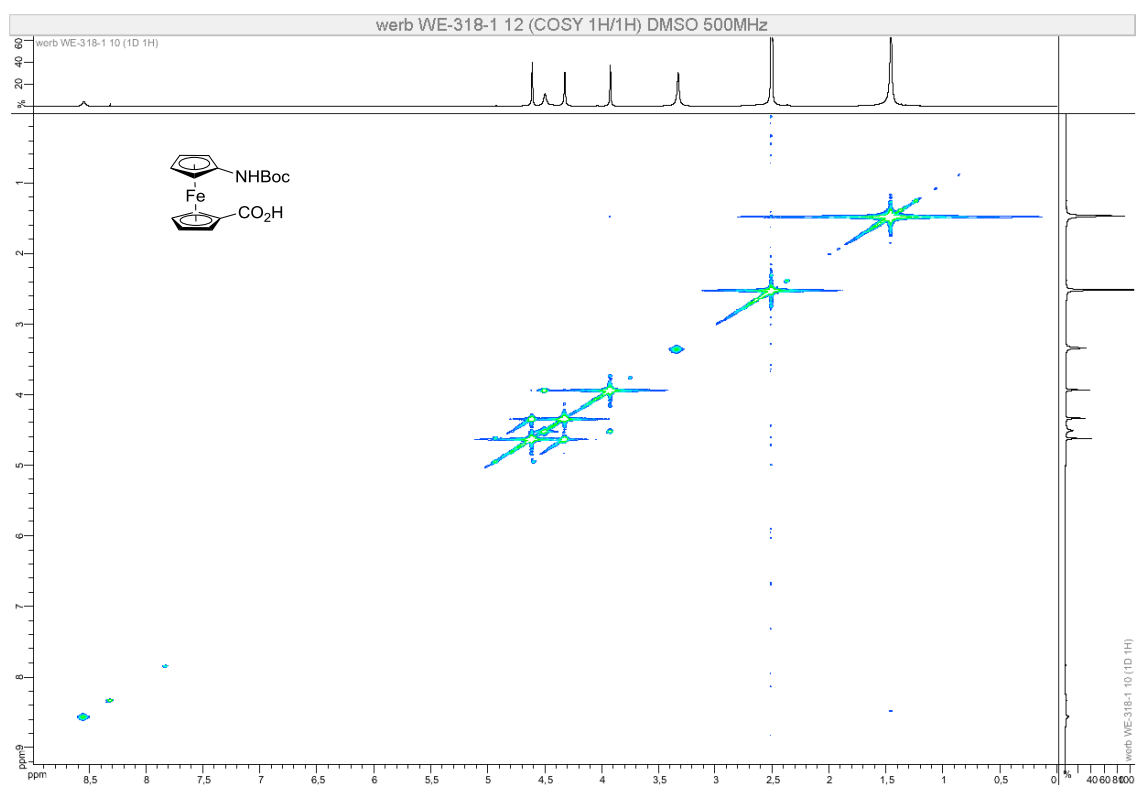
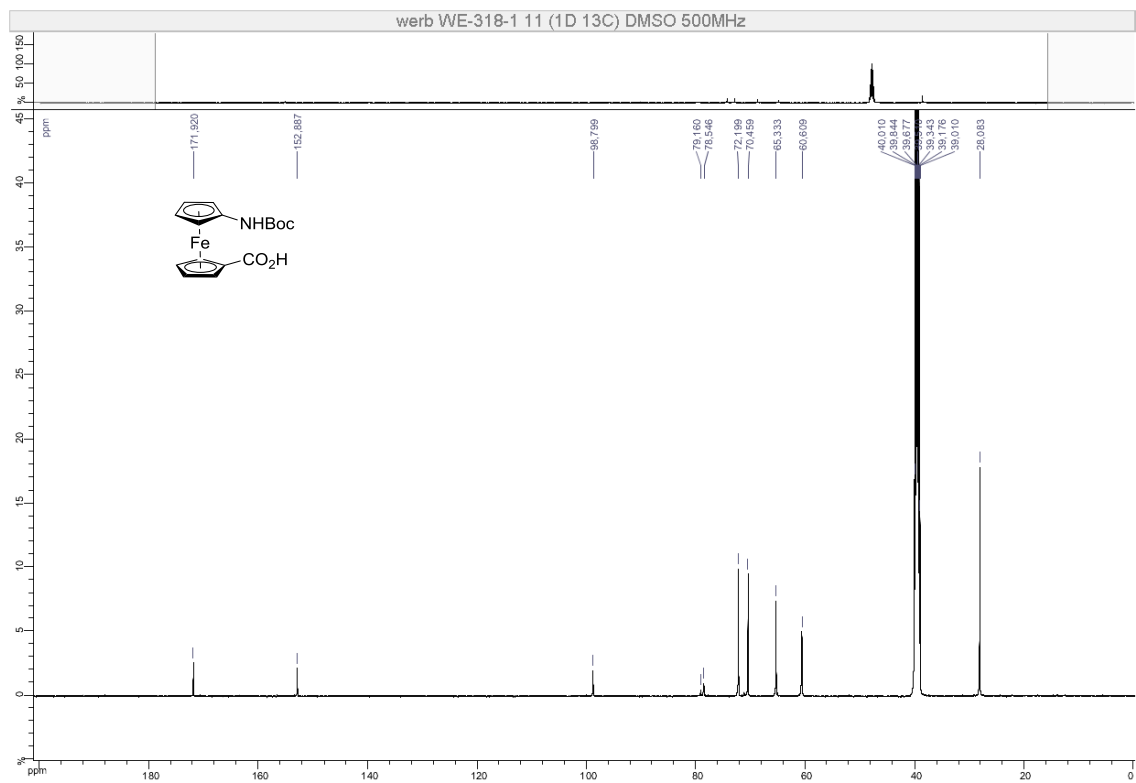
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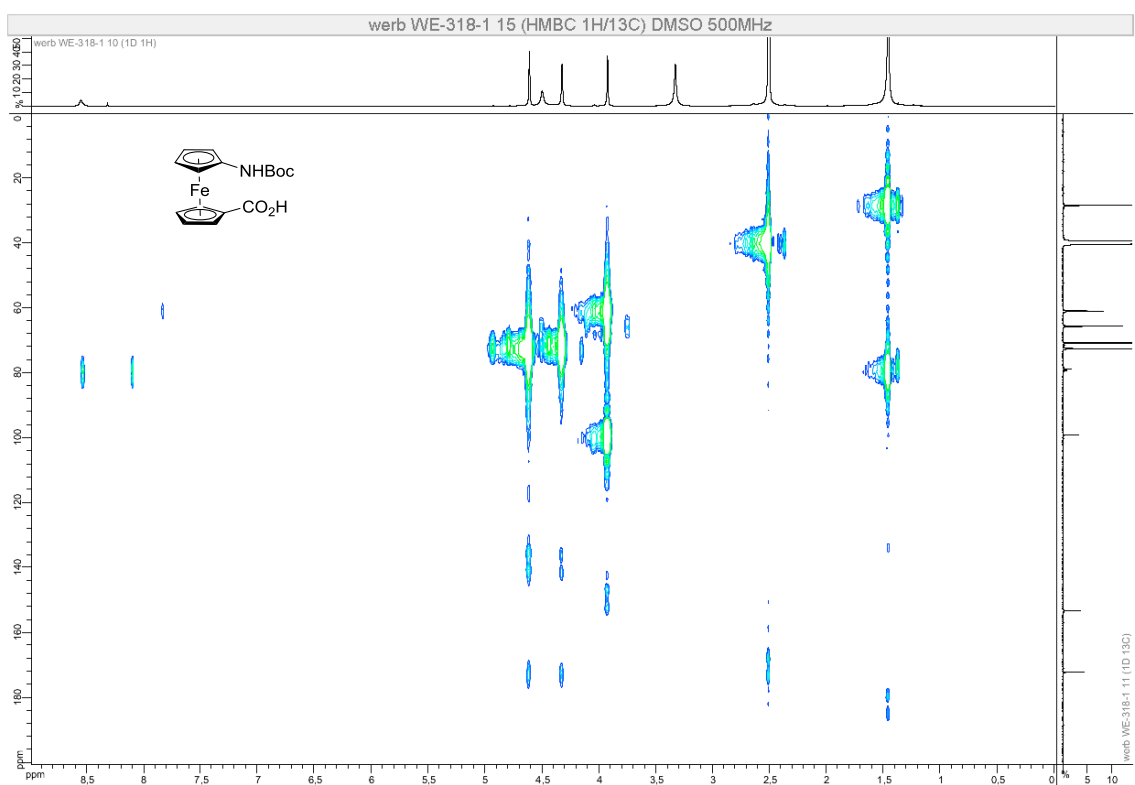
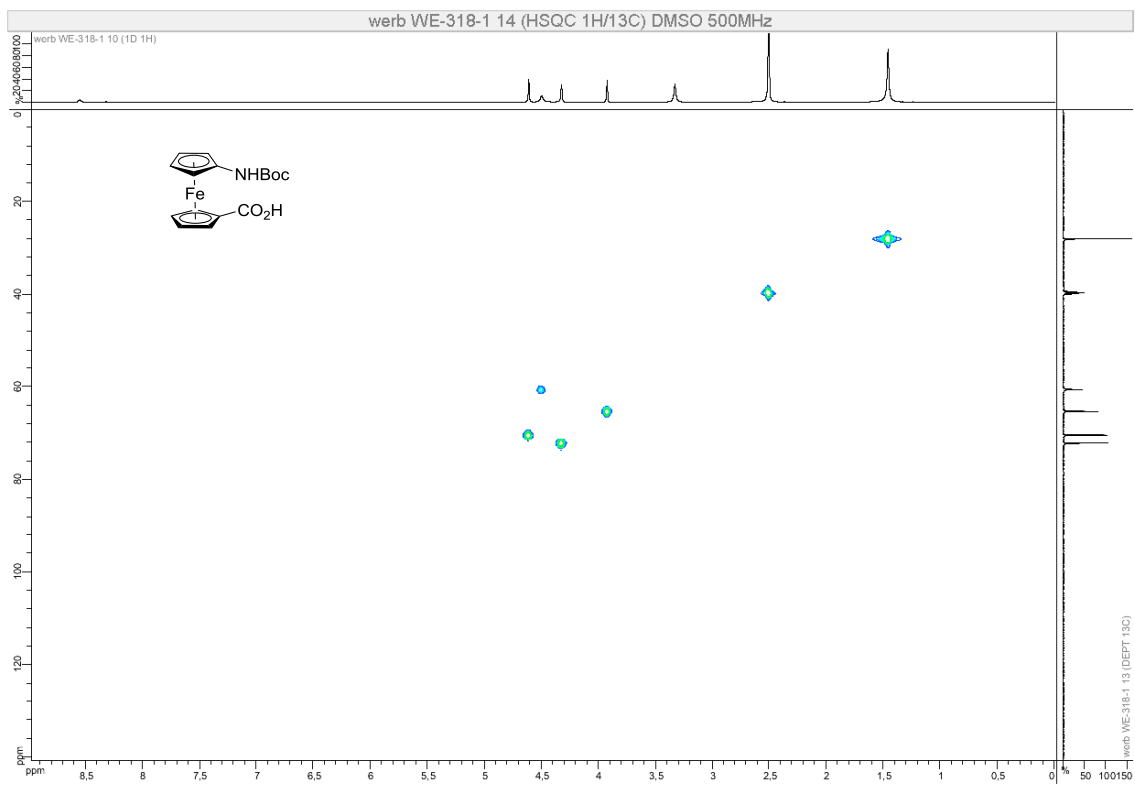


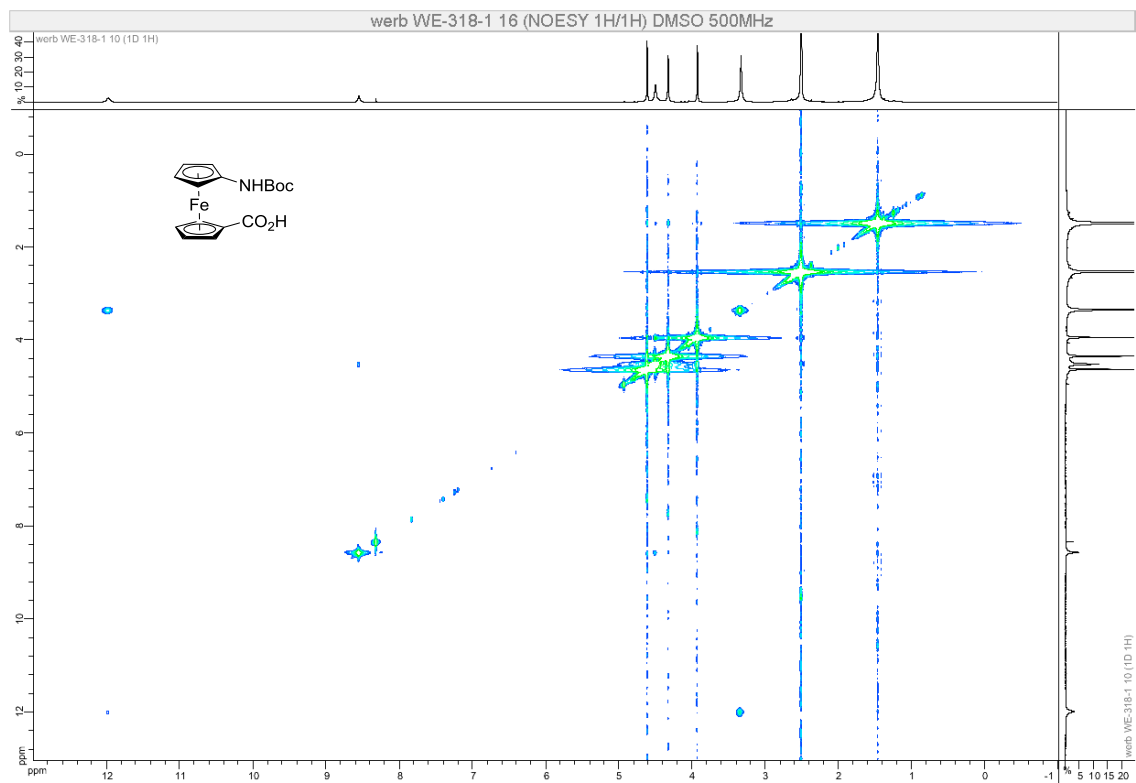
NMR spectra for compounds 1 – 15 and SI1-4

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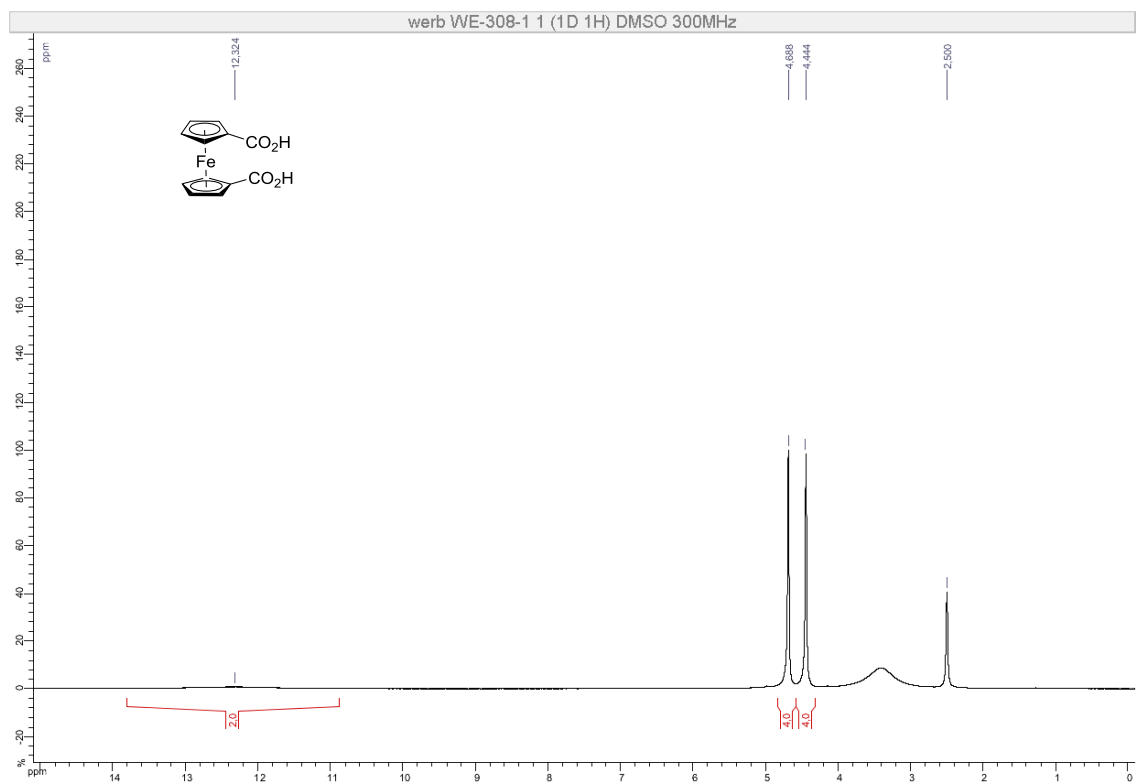


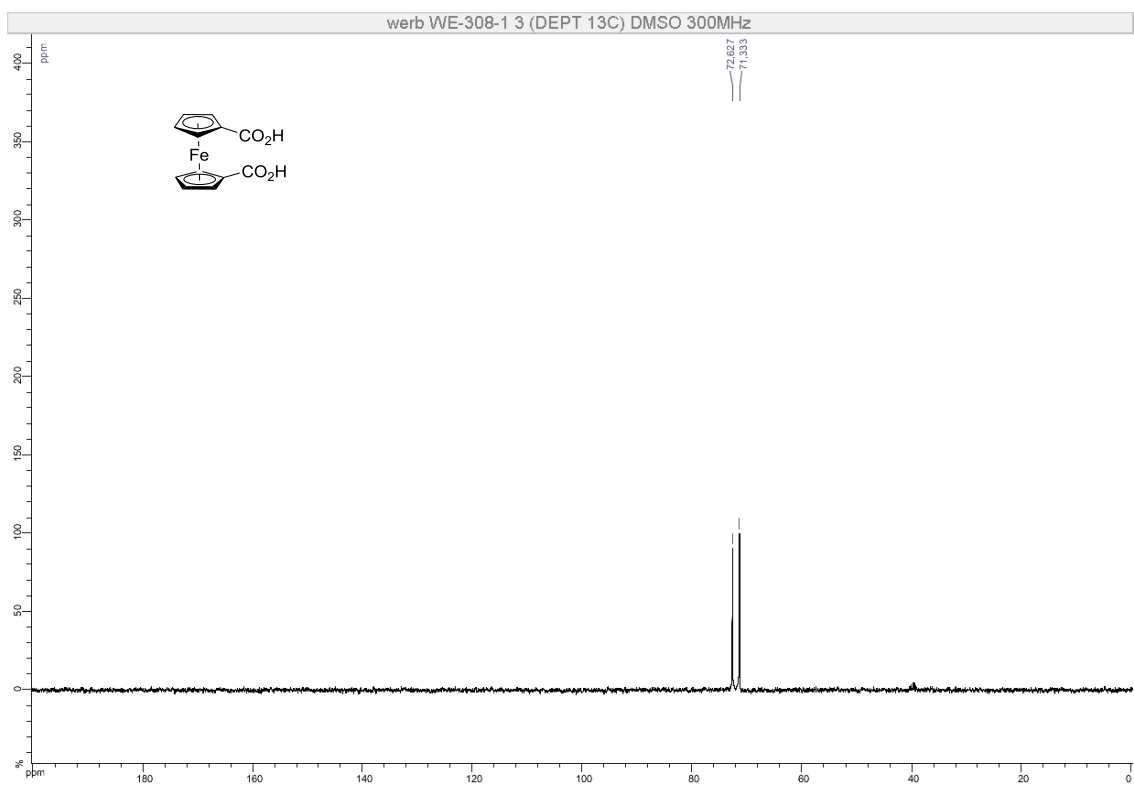
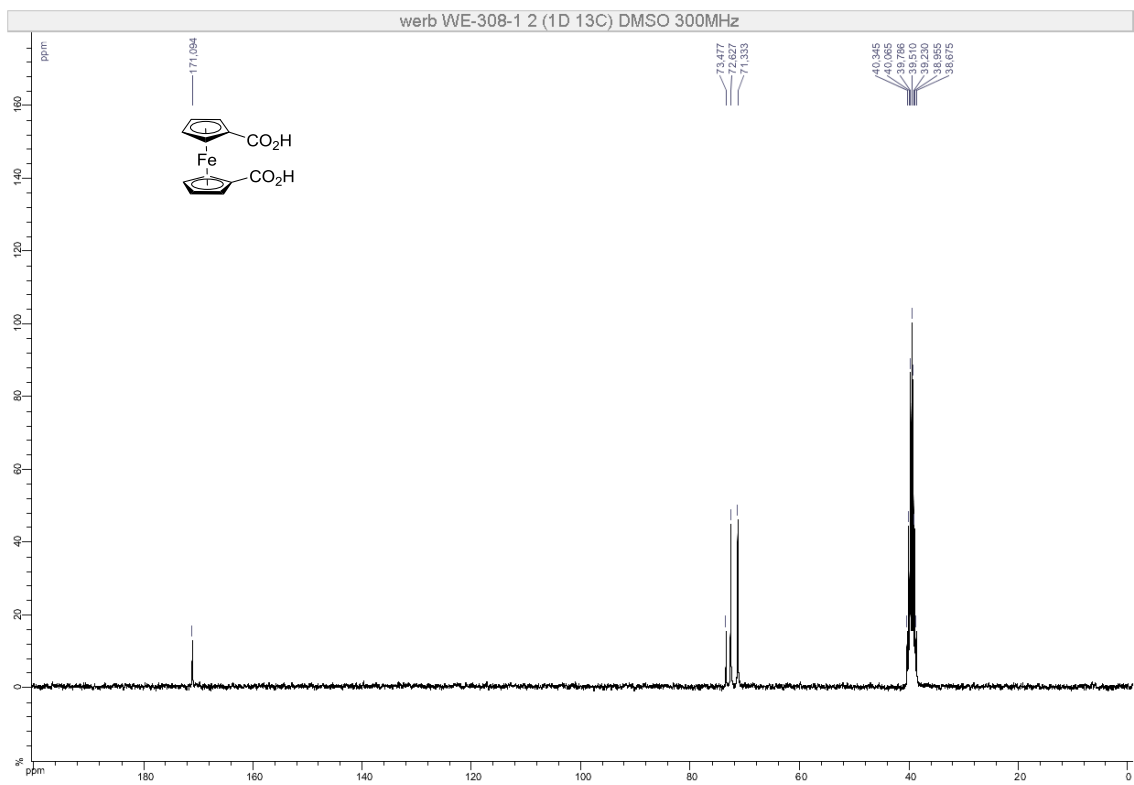




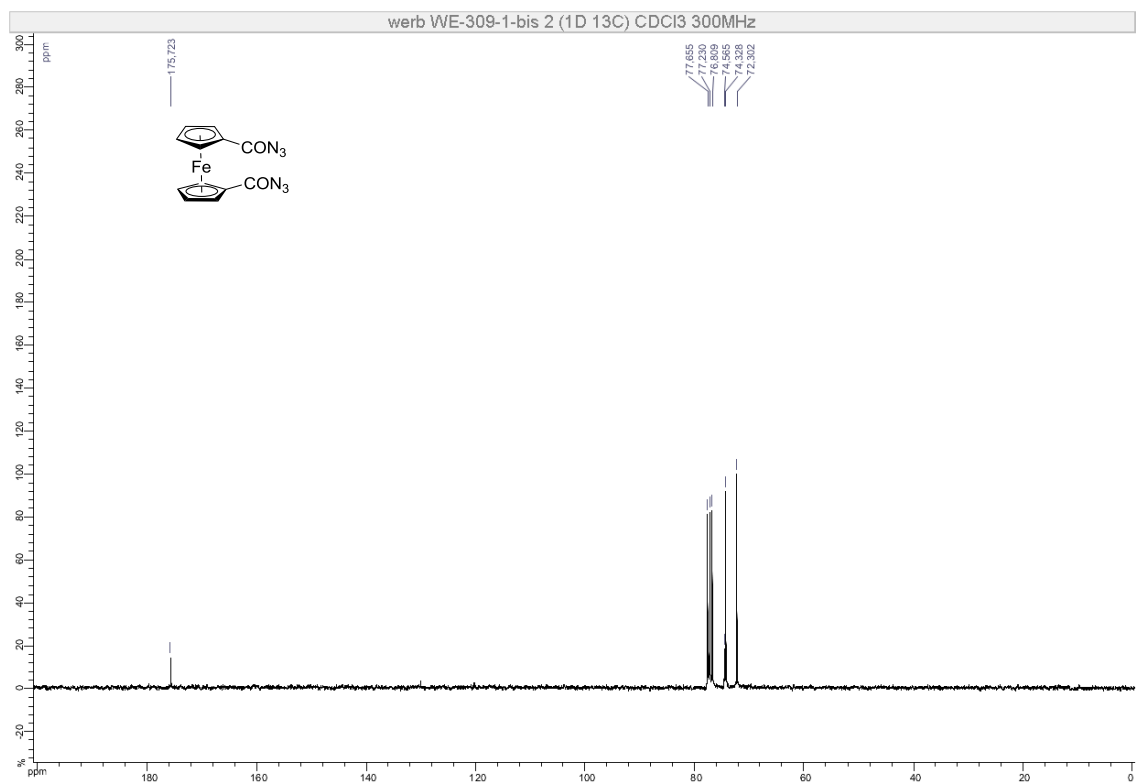
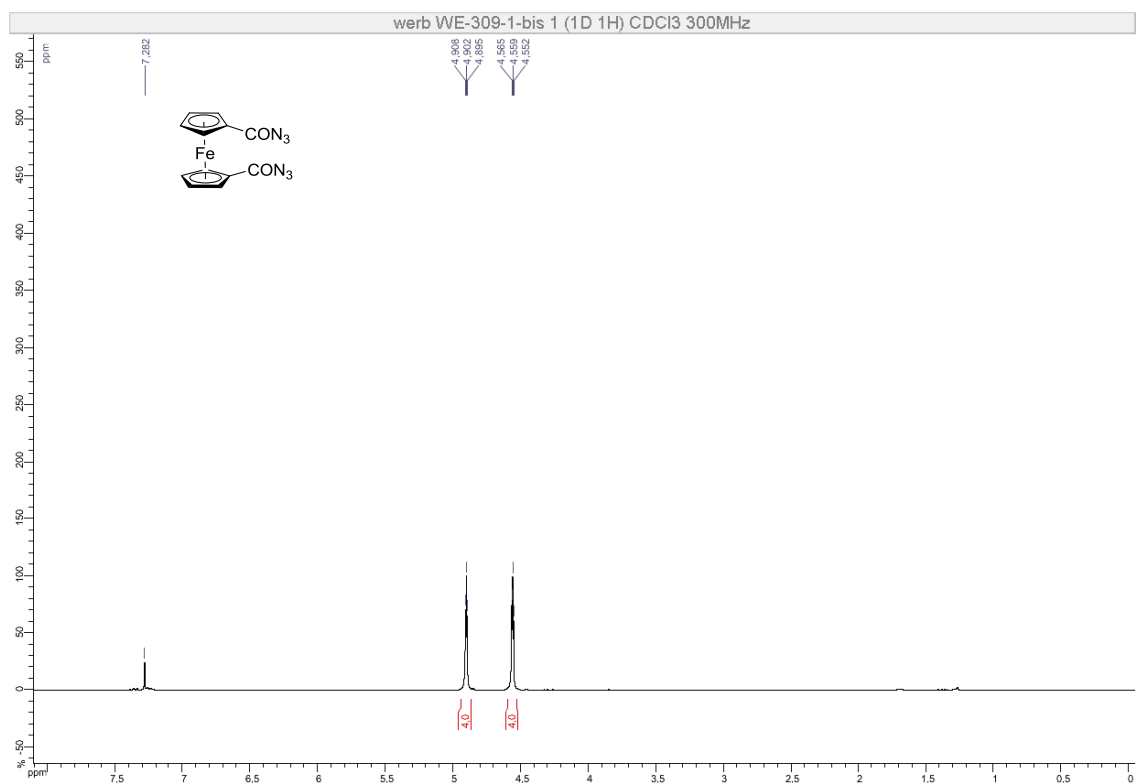


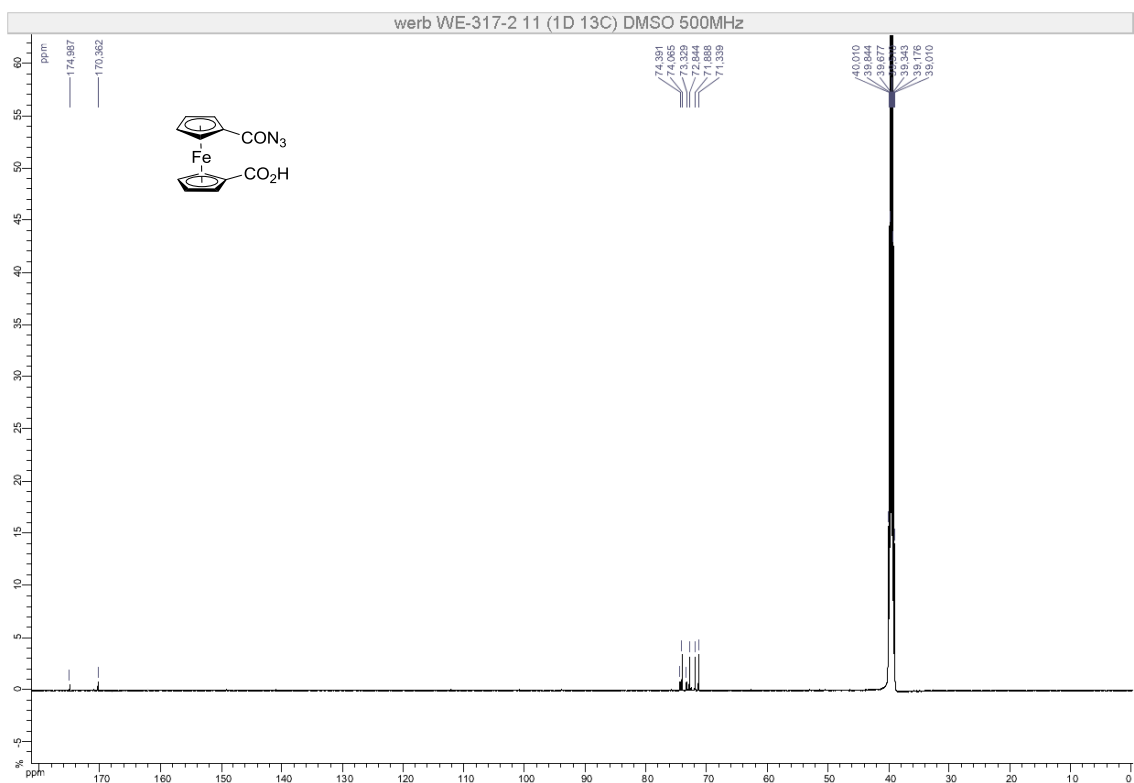
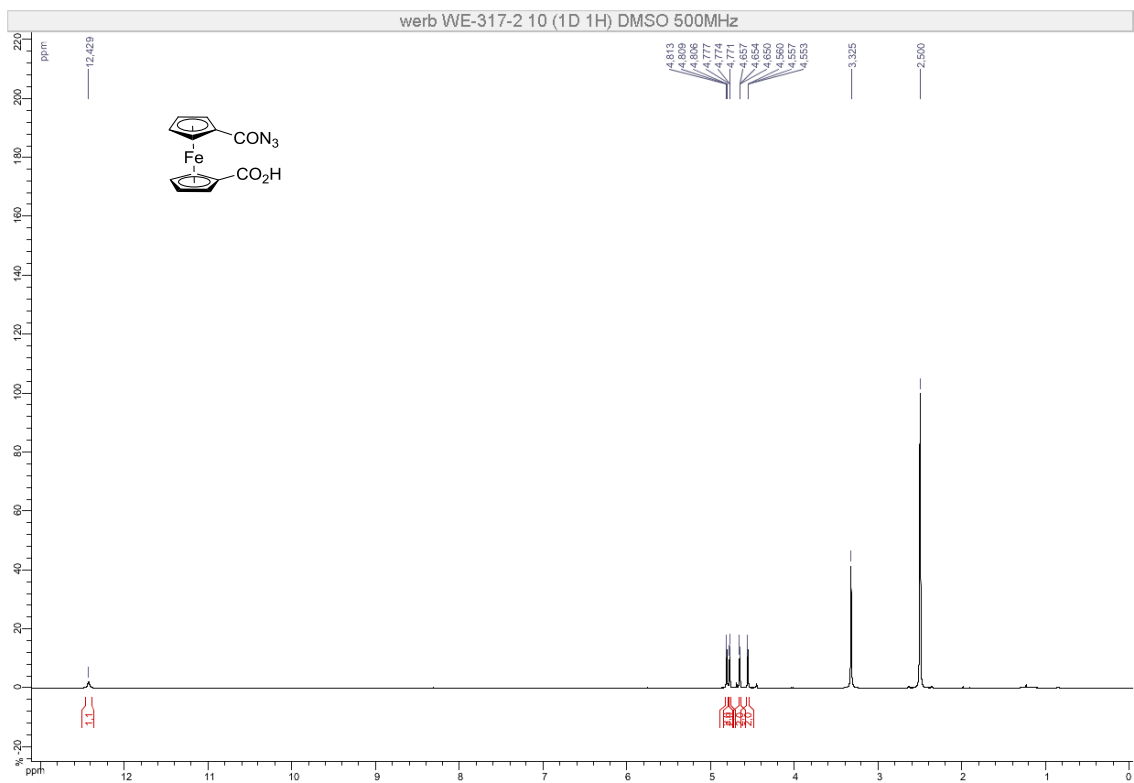
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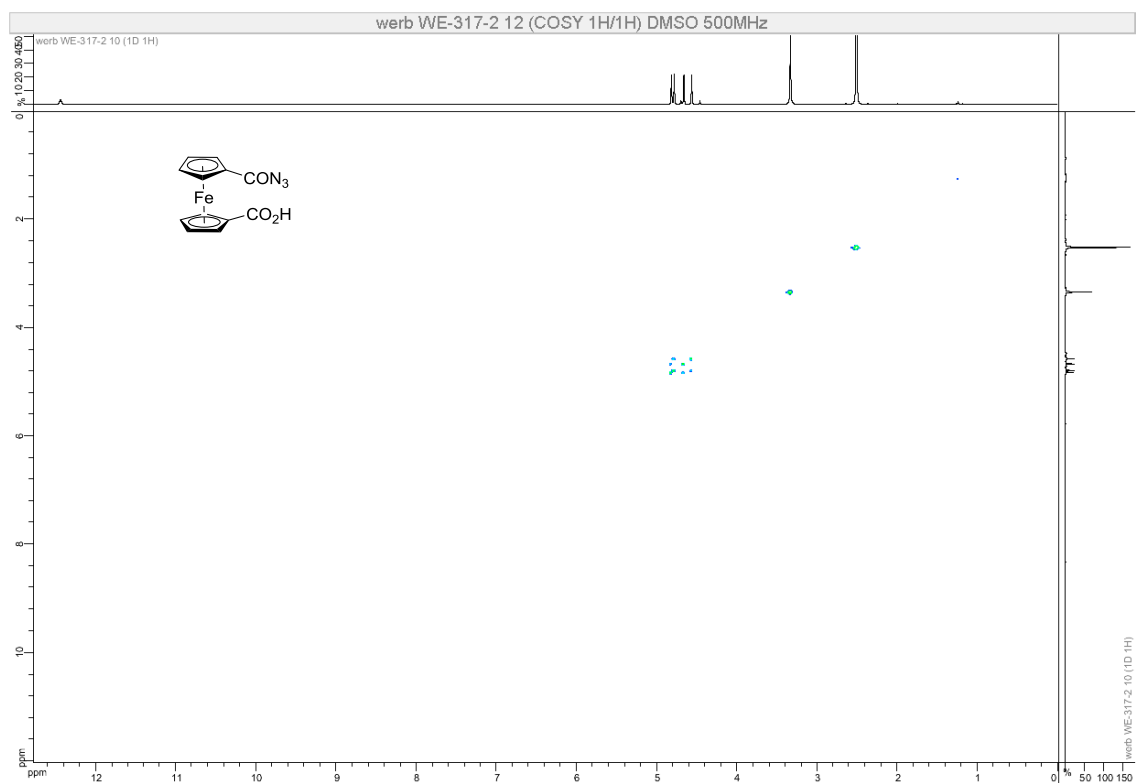
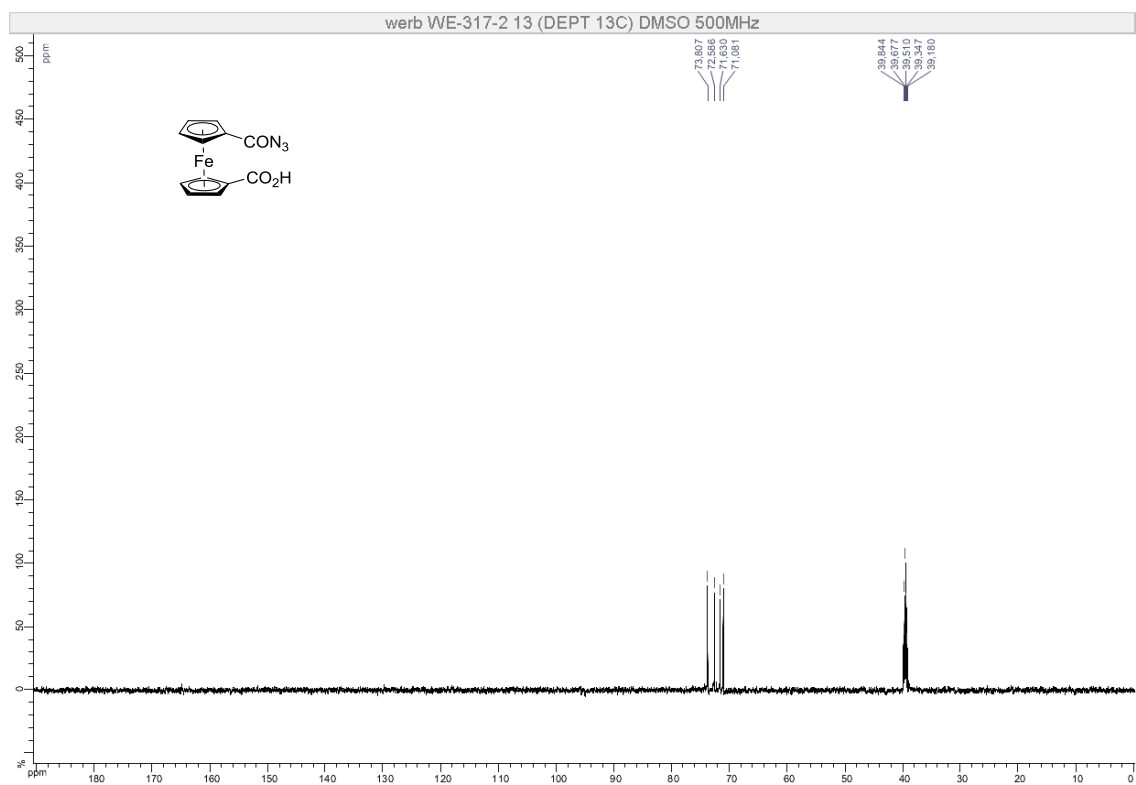


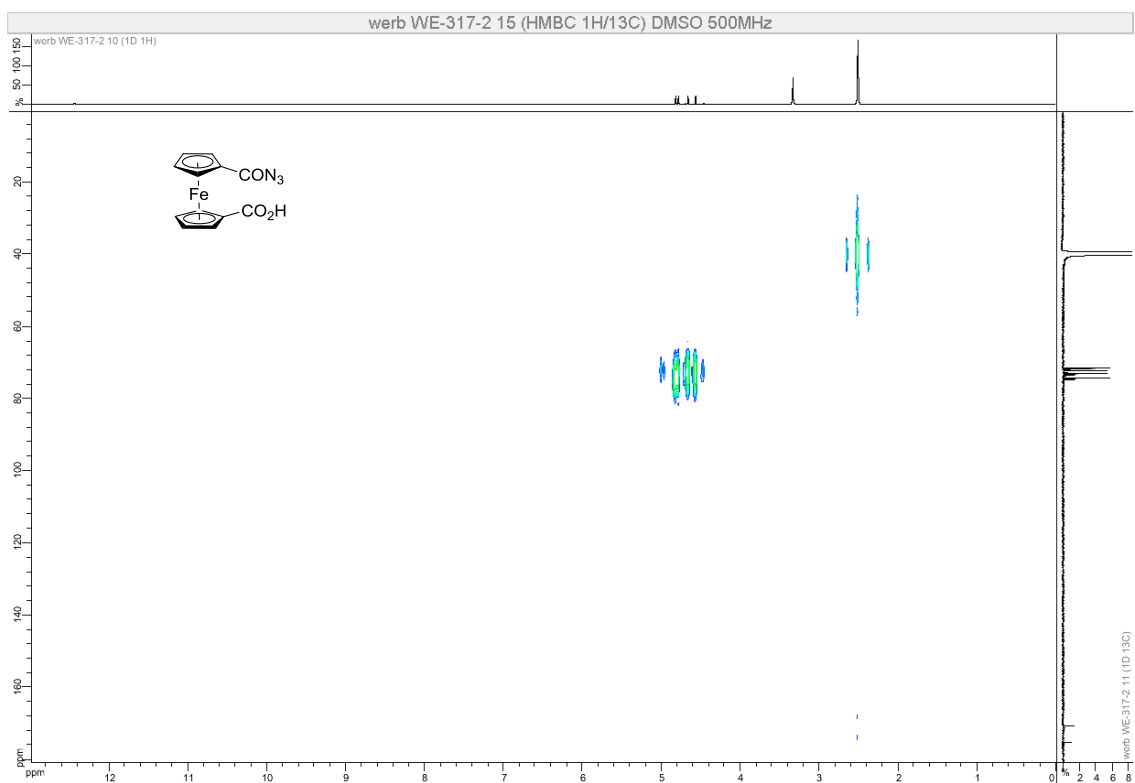
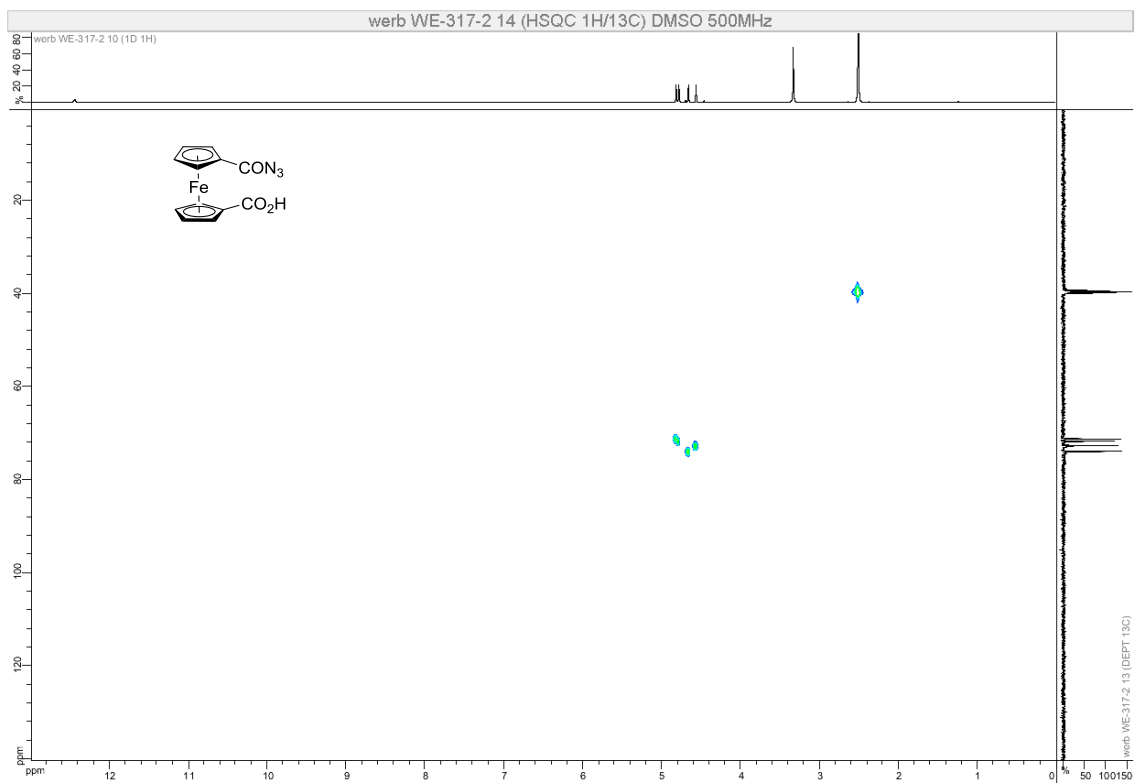


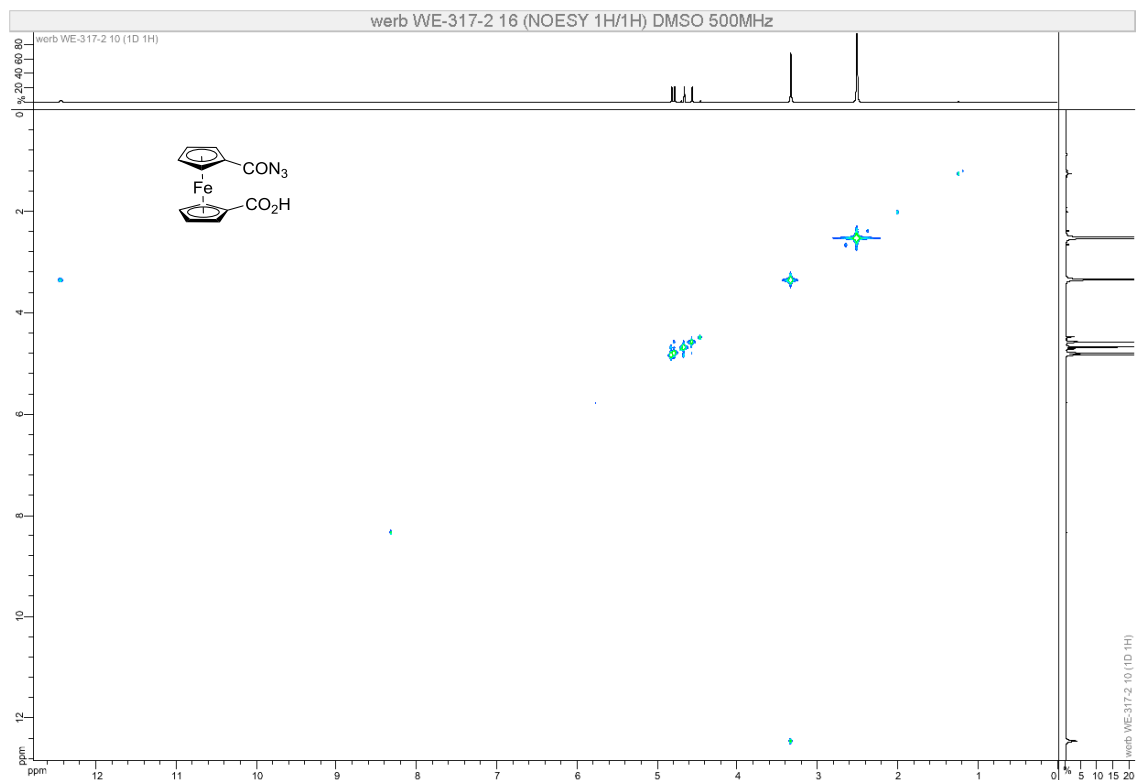
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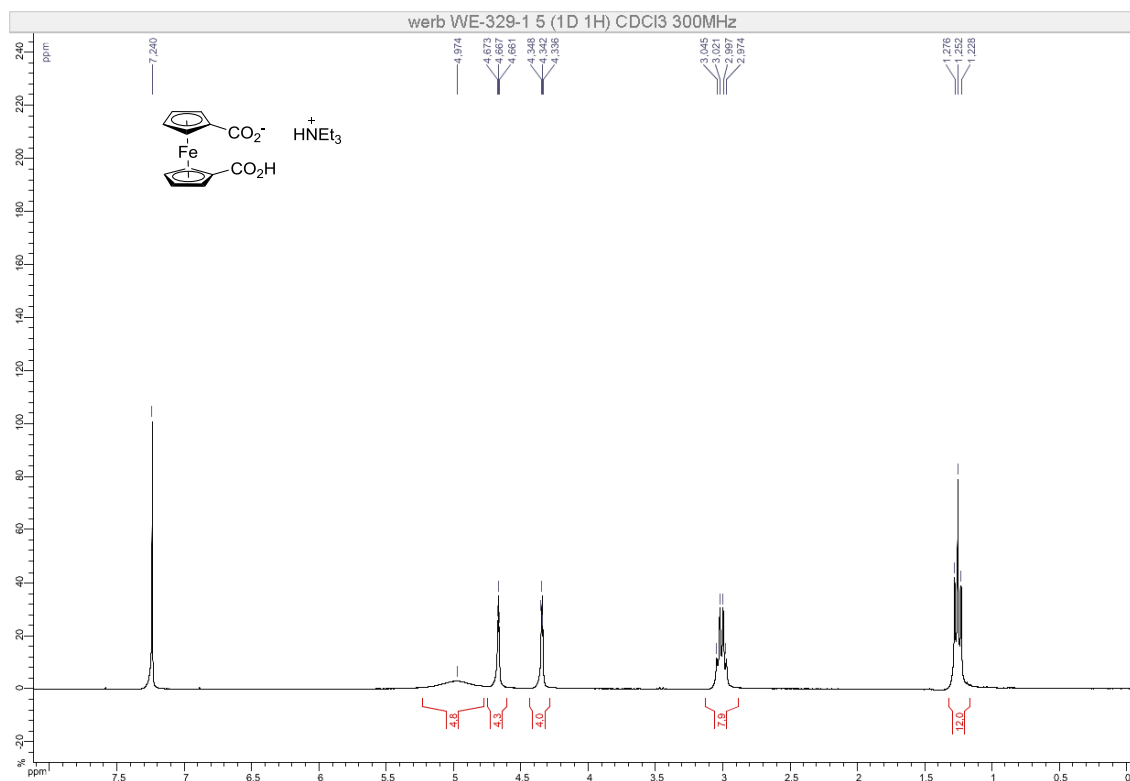


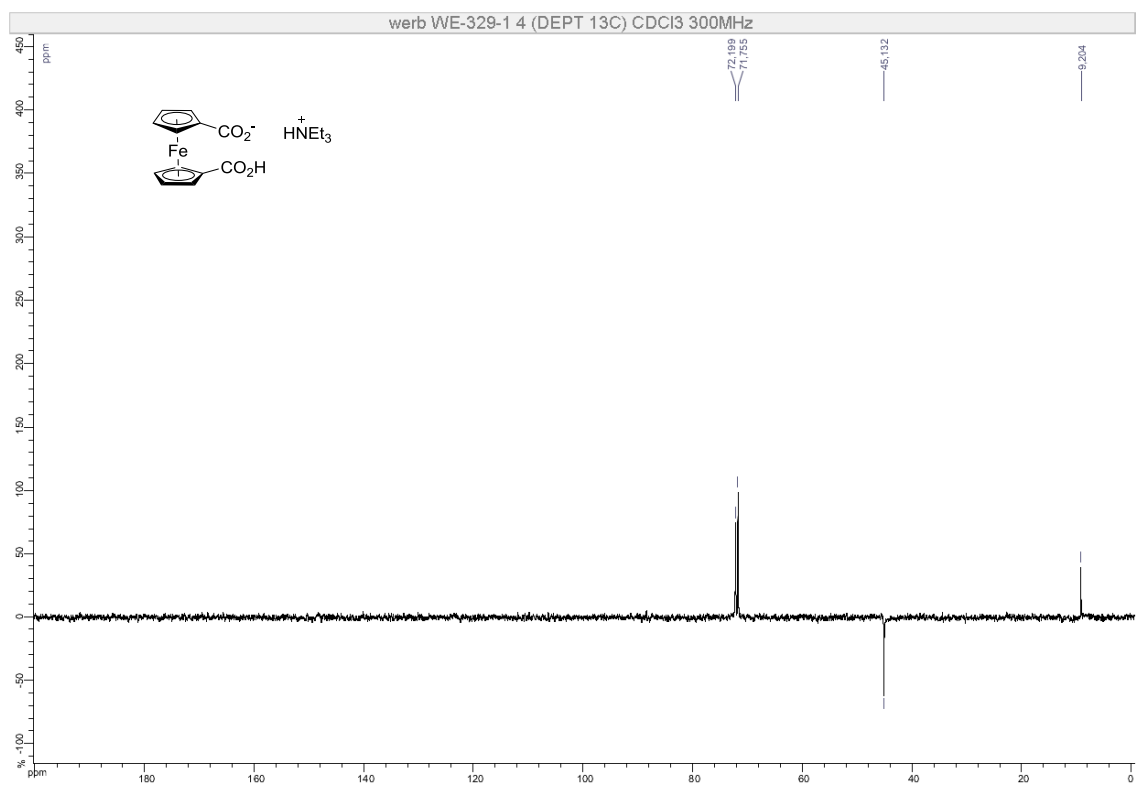
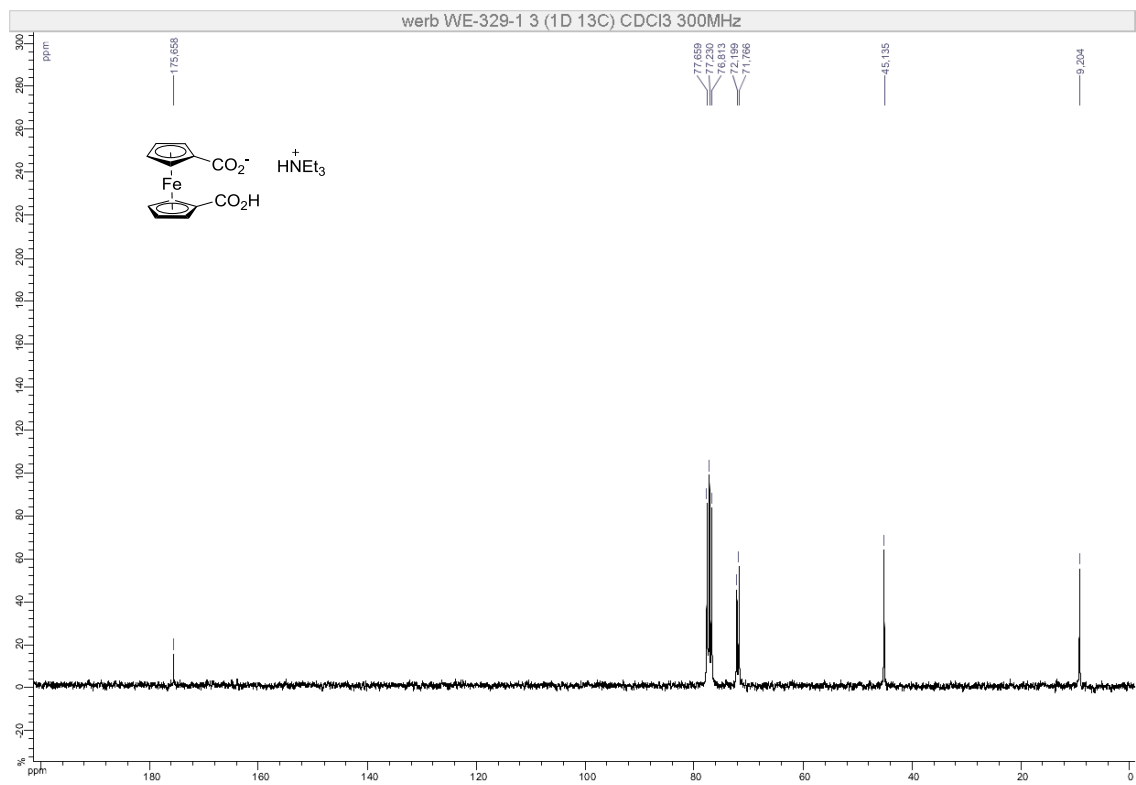


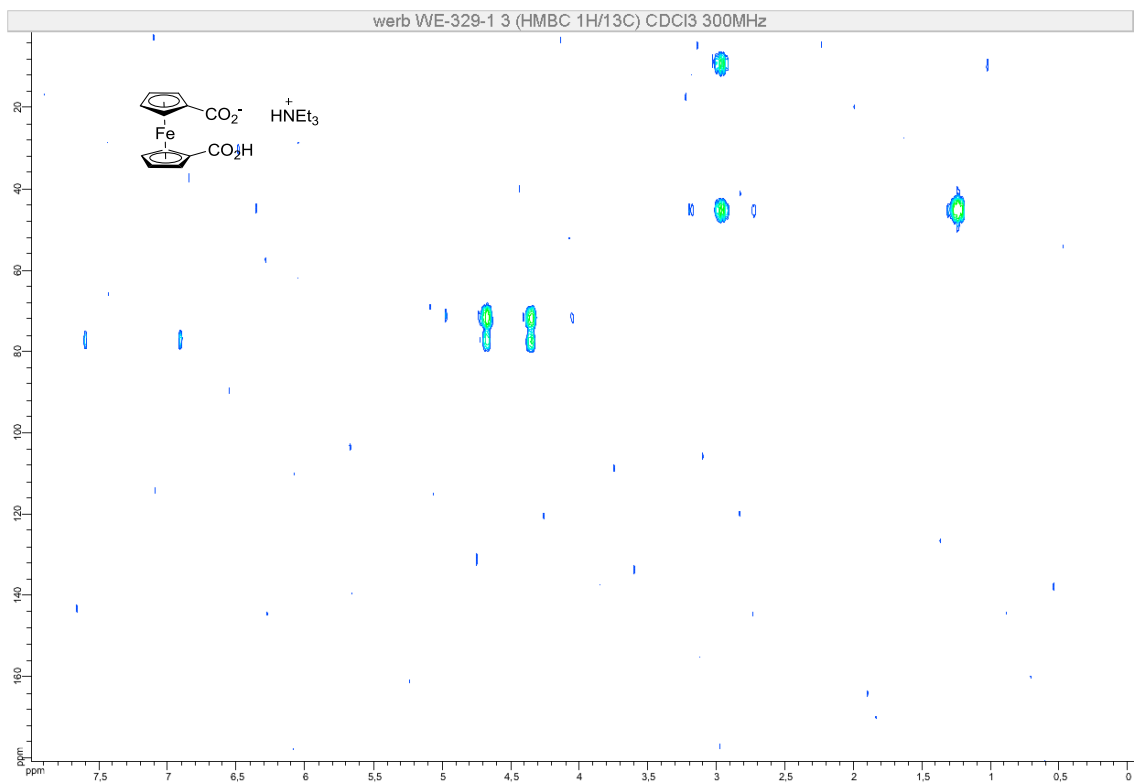




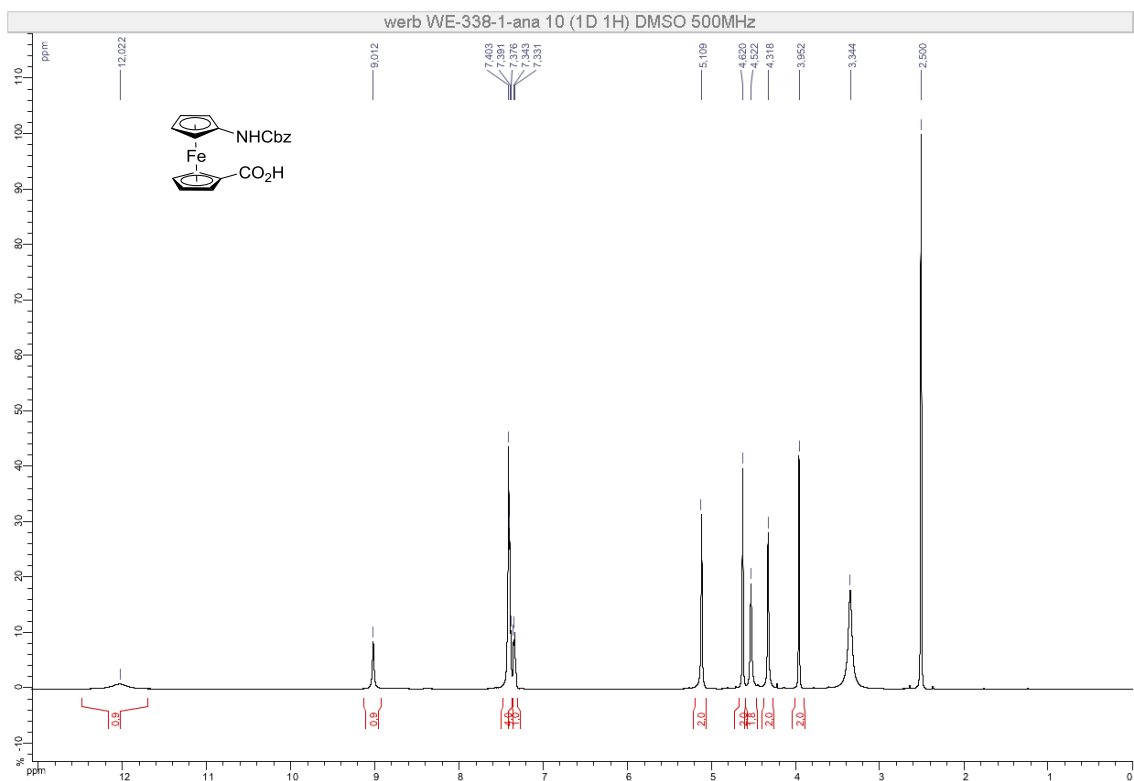
Triethylammonium 1'-carboxyferrocene-1-carboxylate - 5

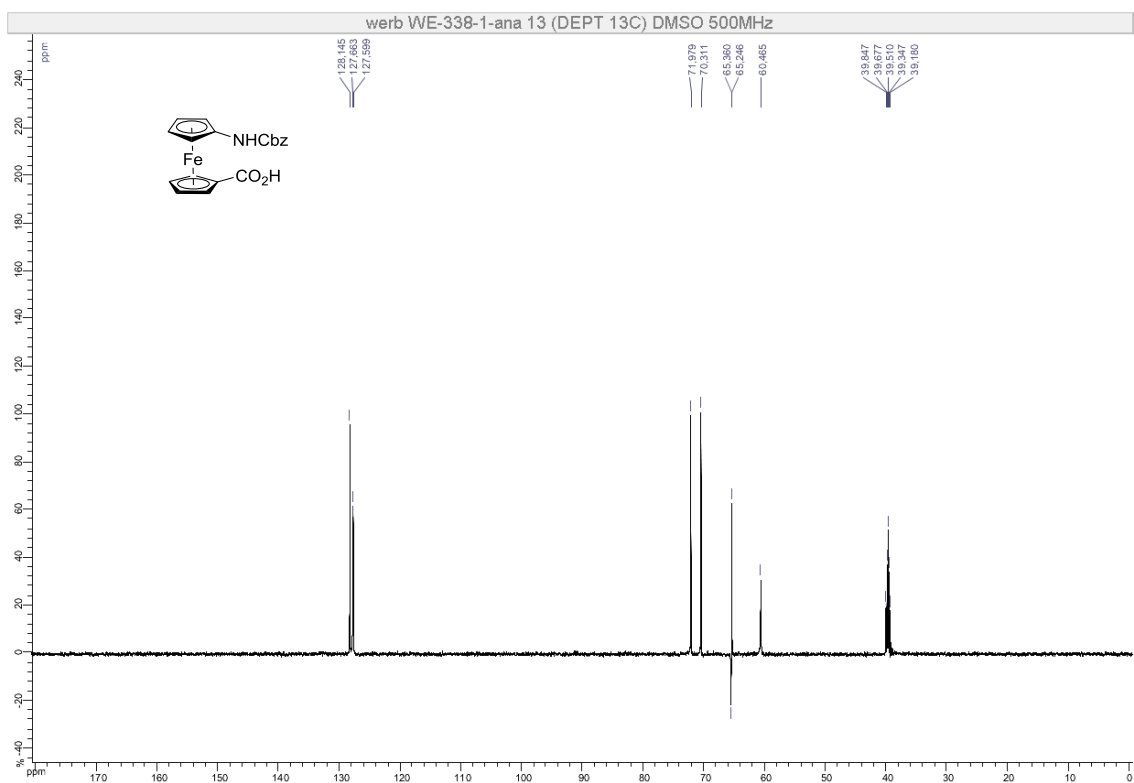
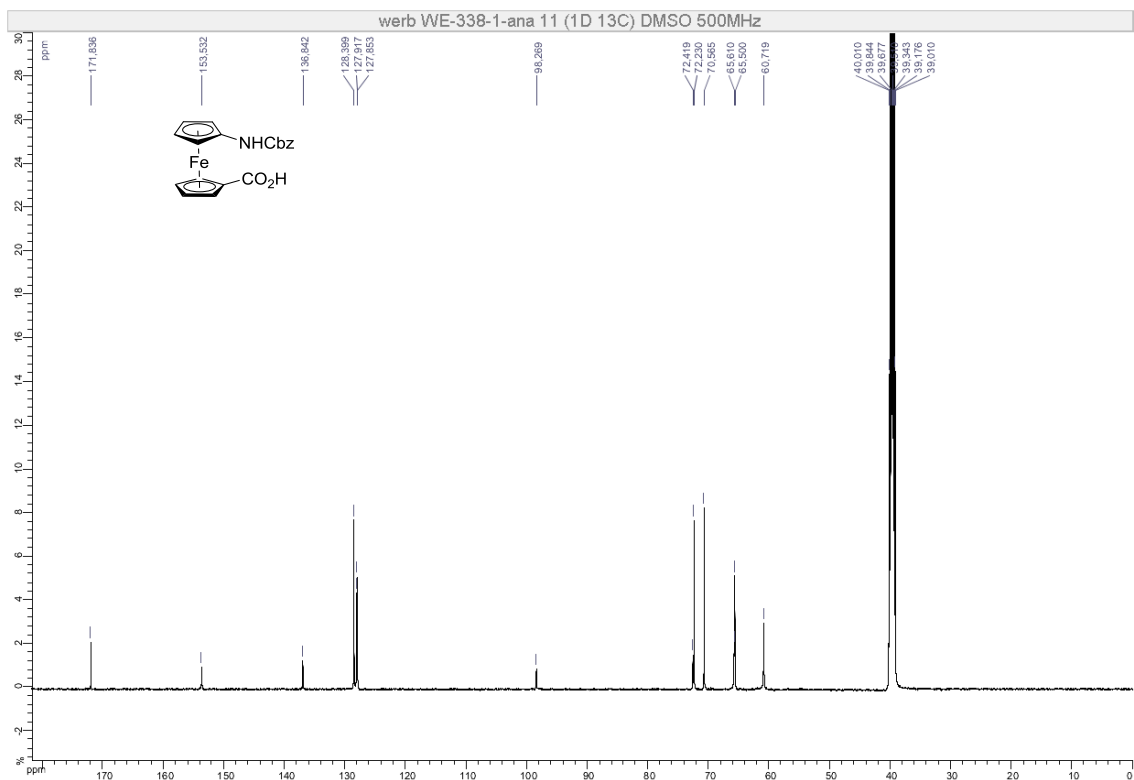


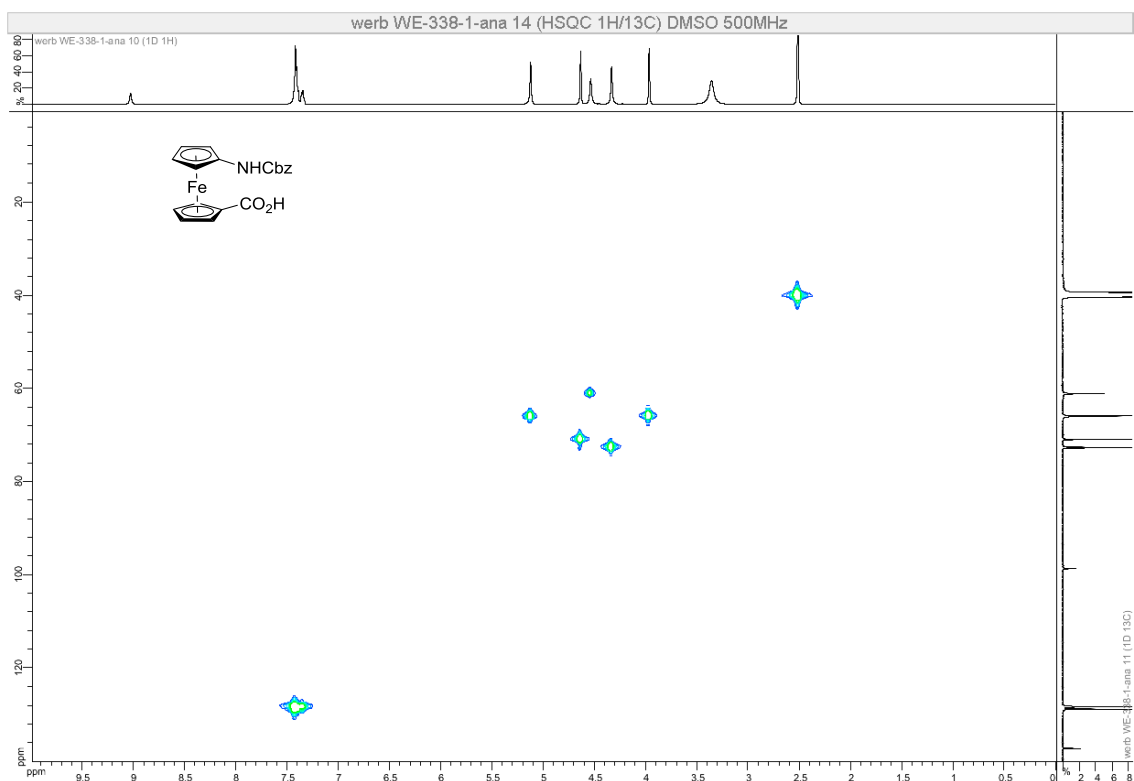
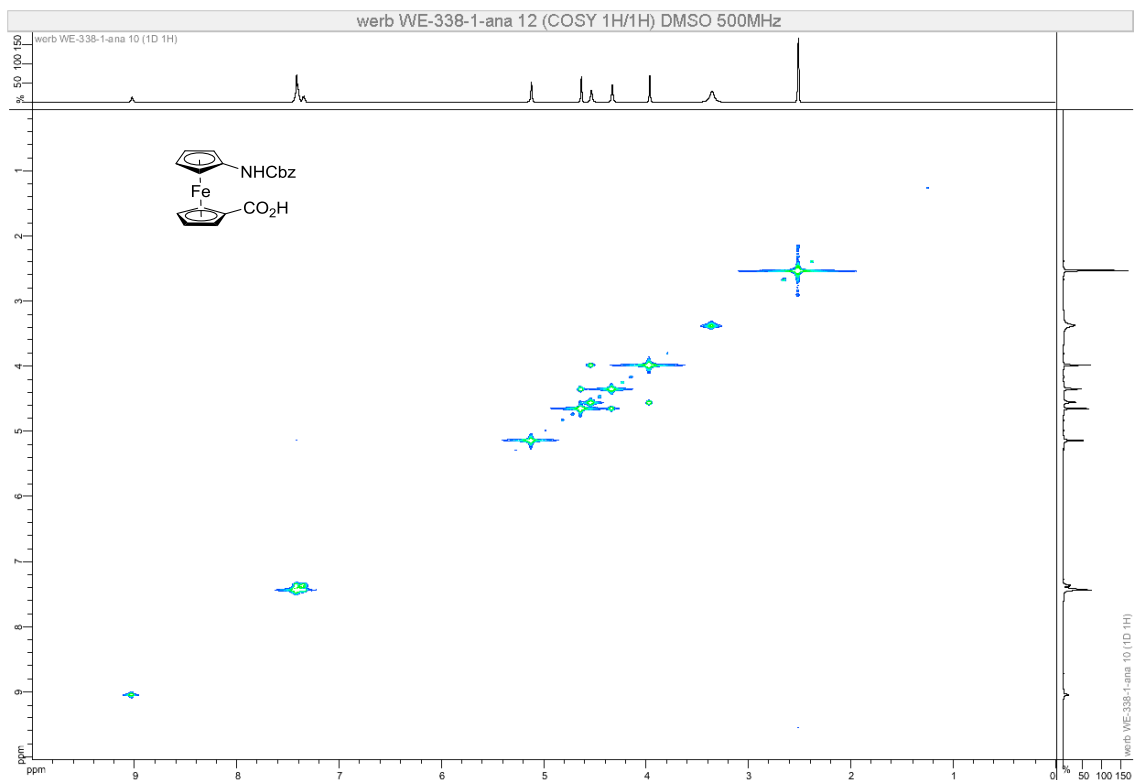


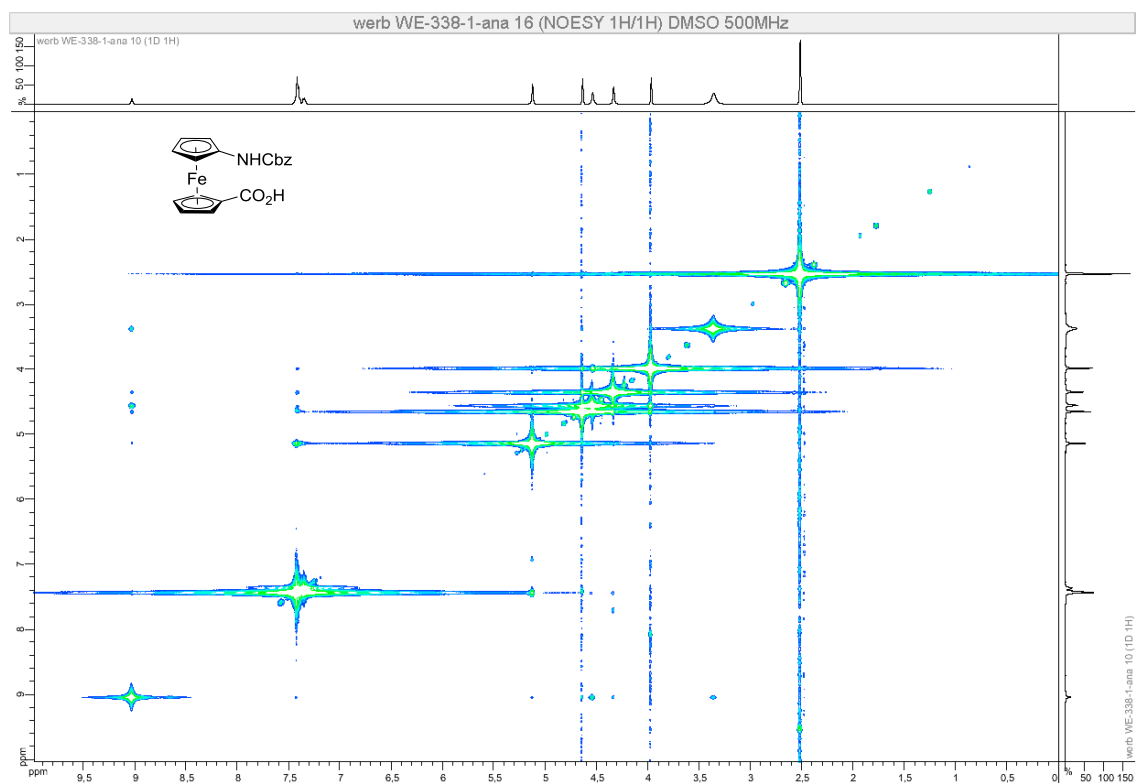
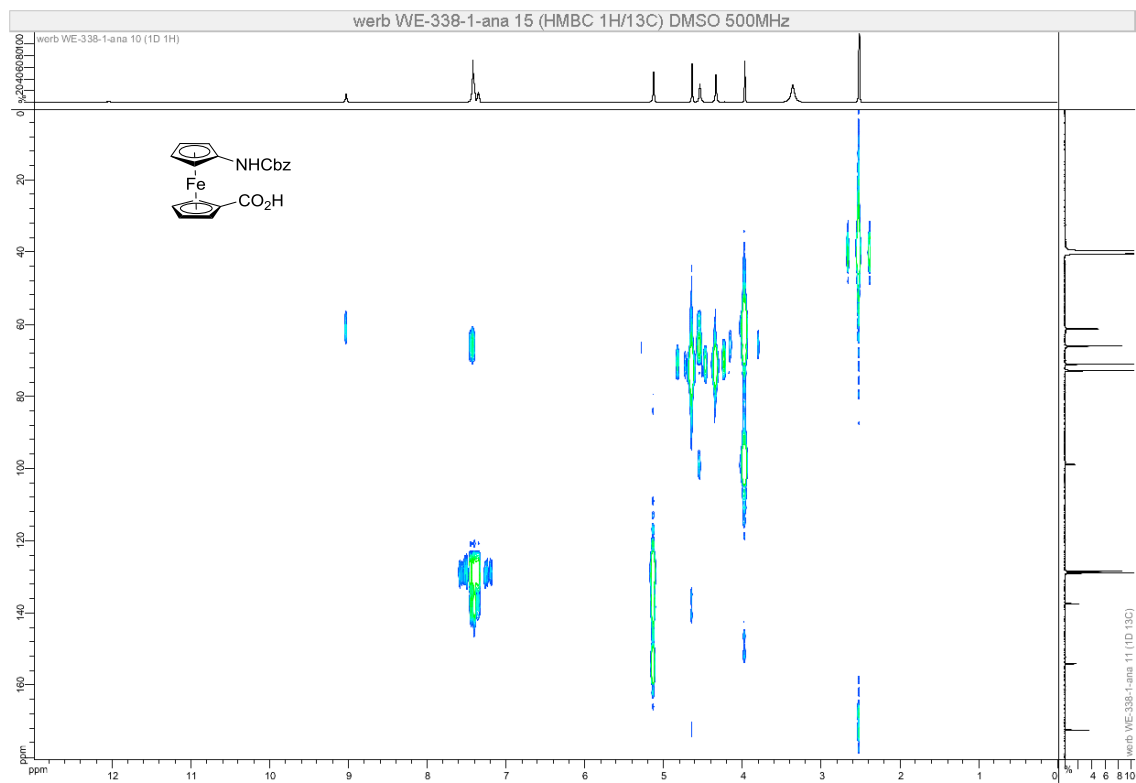


1'-((Benzyloxycarbonyl)amino)ferrocene-1-carboxylic acid - 7

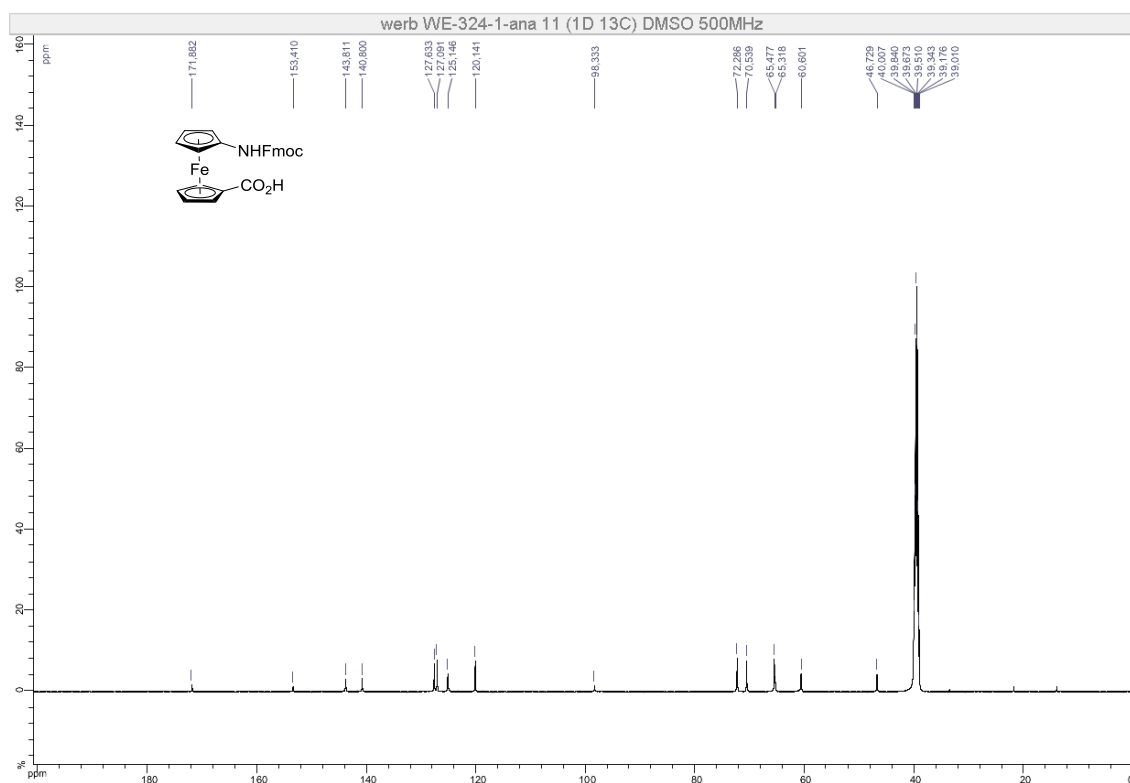
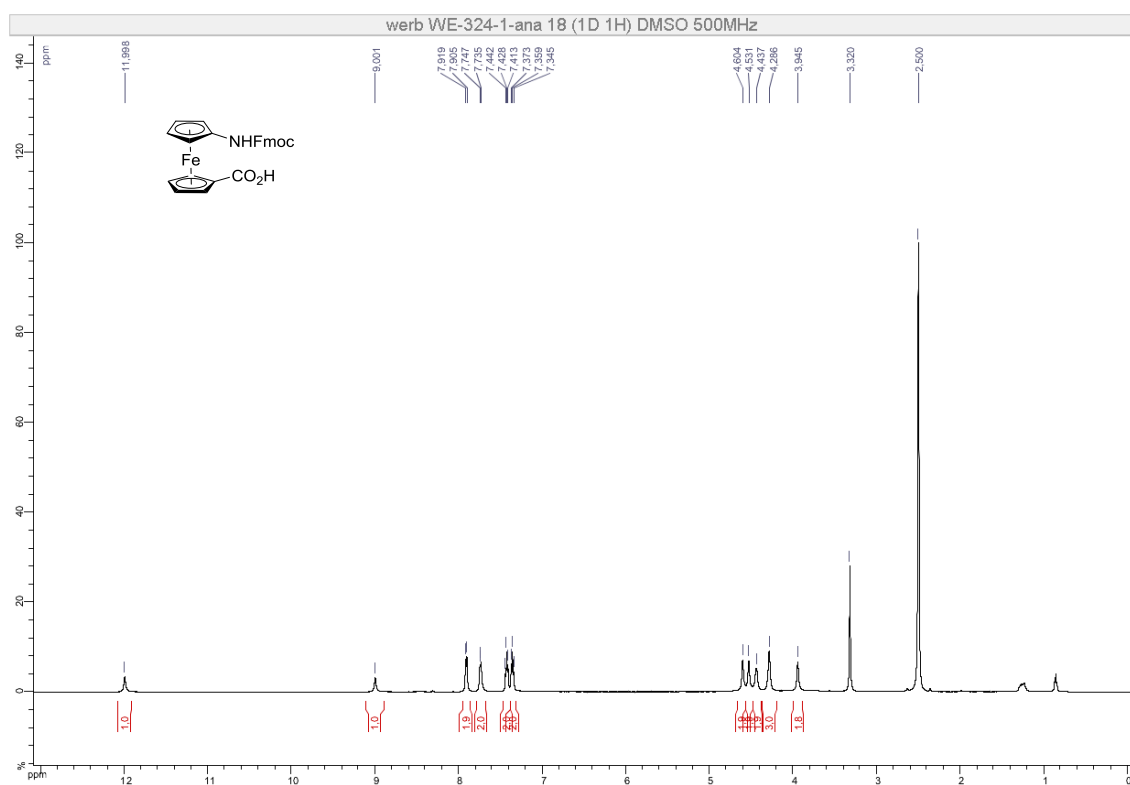


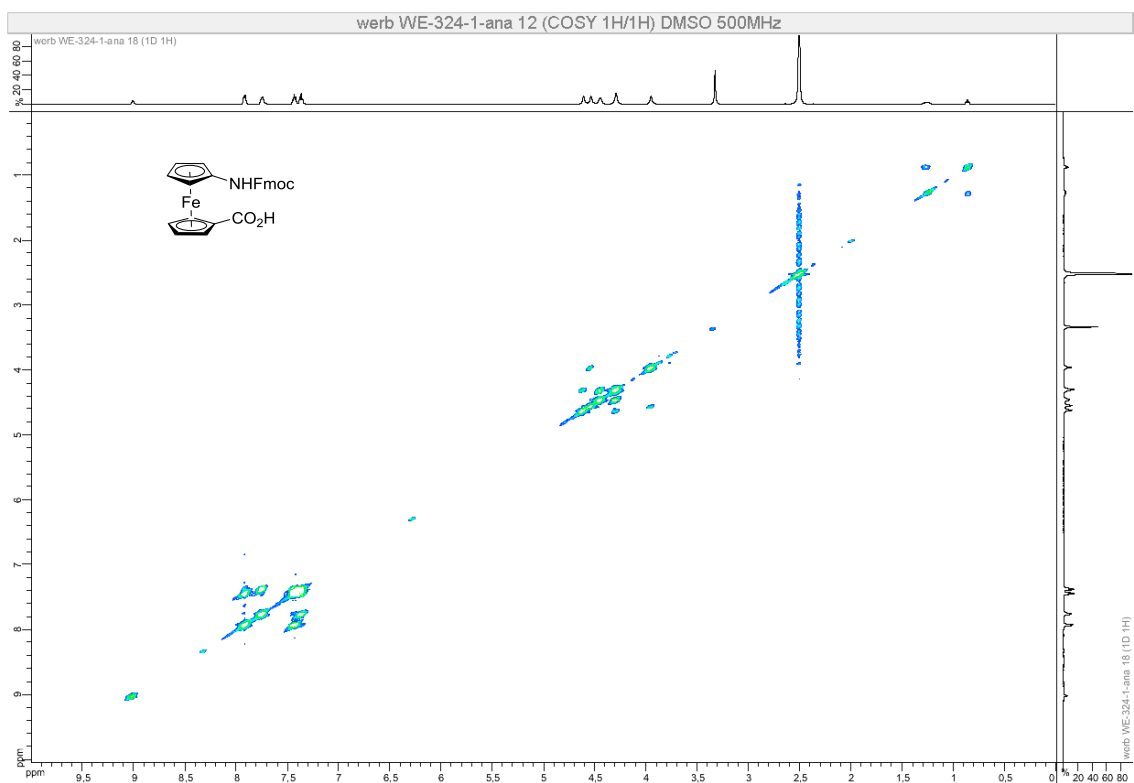
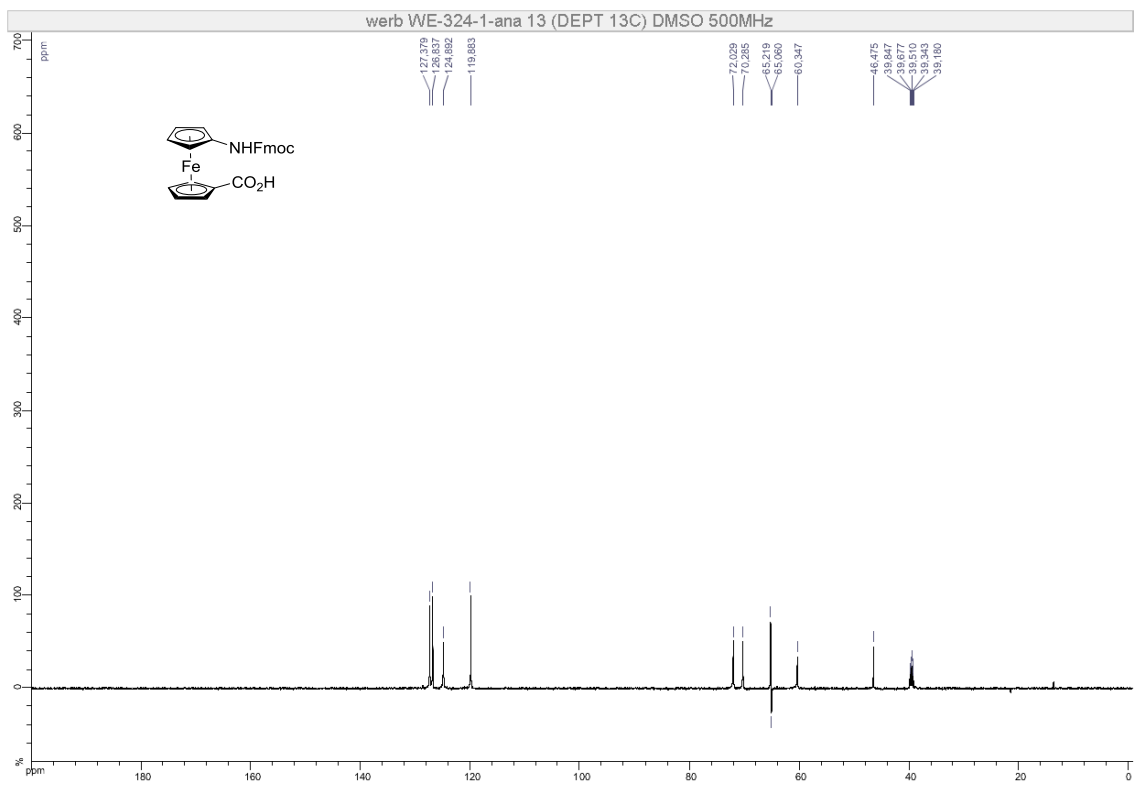


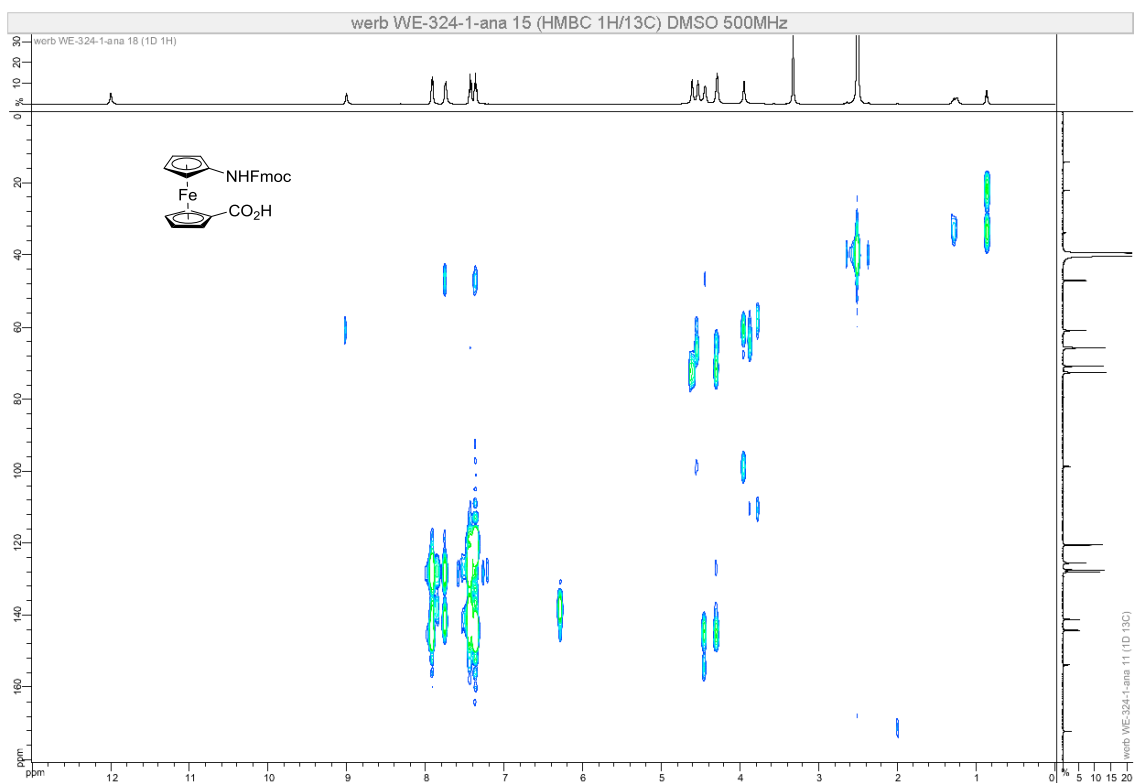
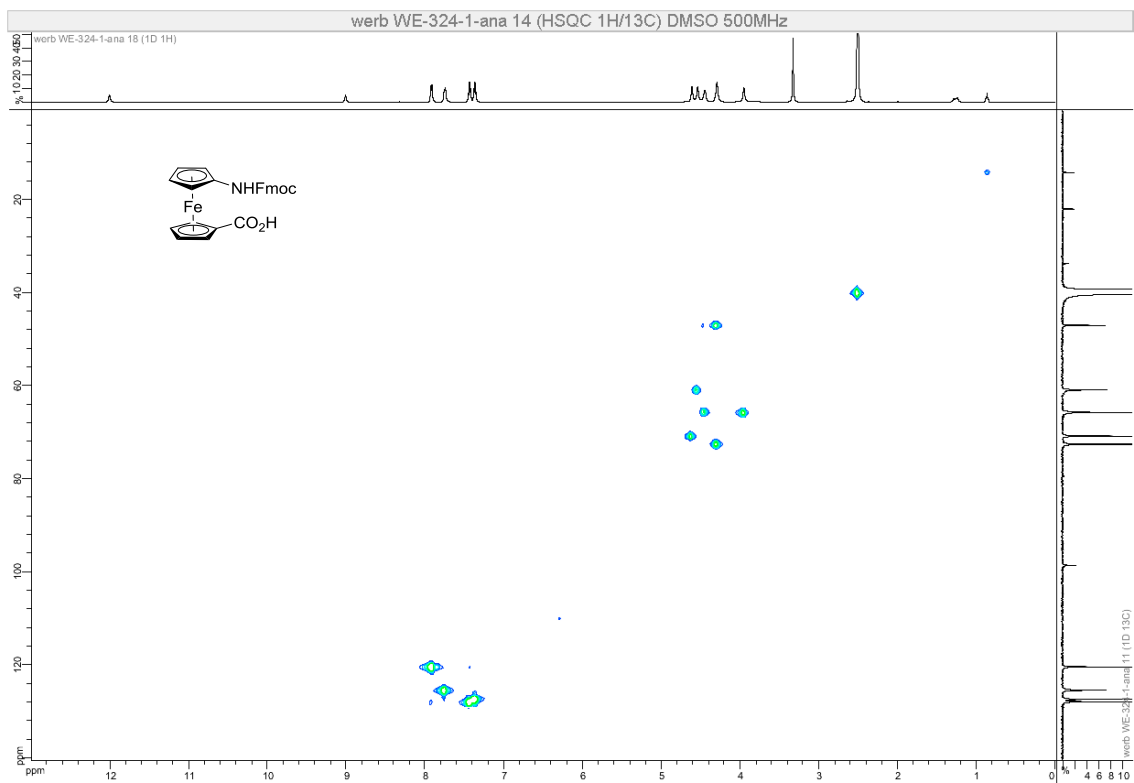


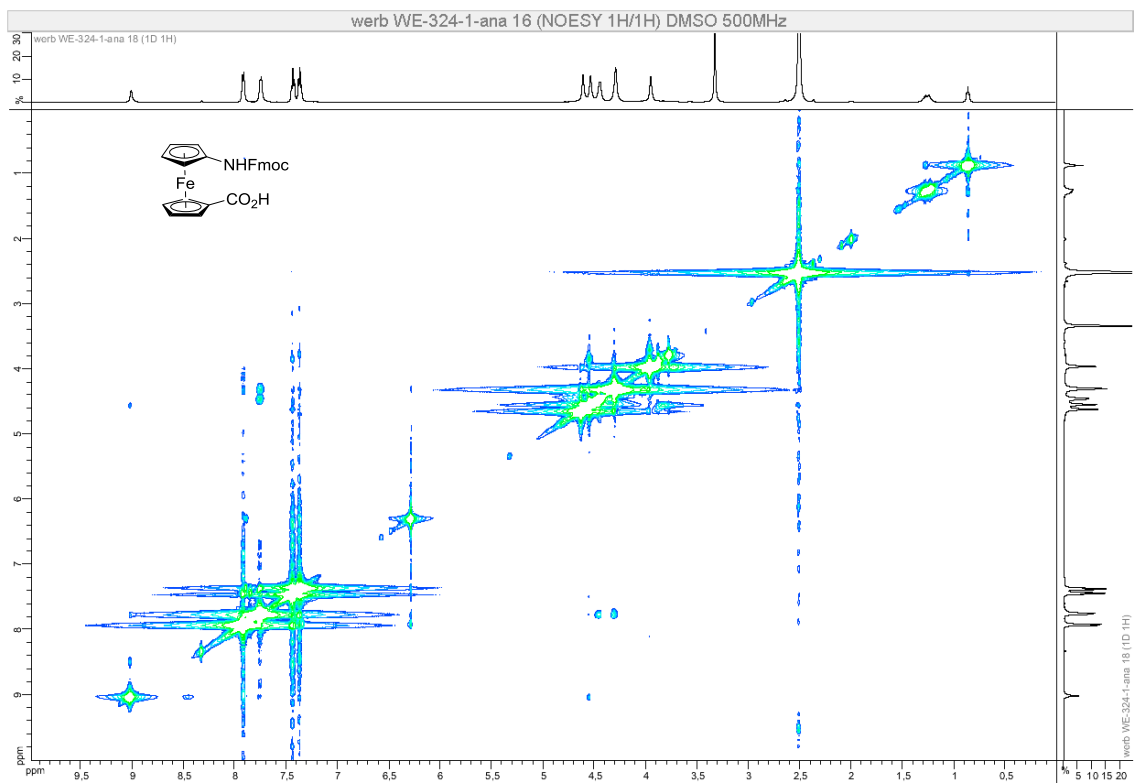


1'-[(Fluoren-9-yl)methoxycarbonyl]amino]ferrocene-1-carboxylic acid - 8

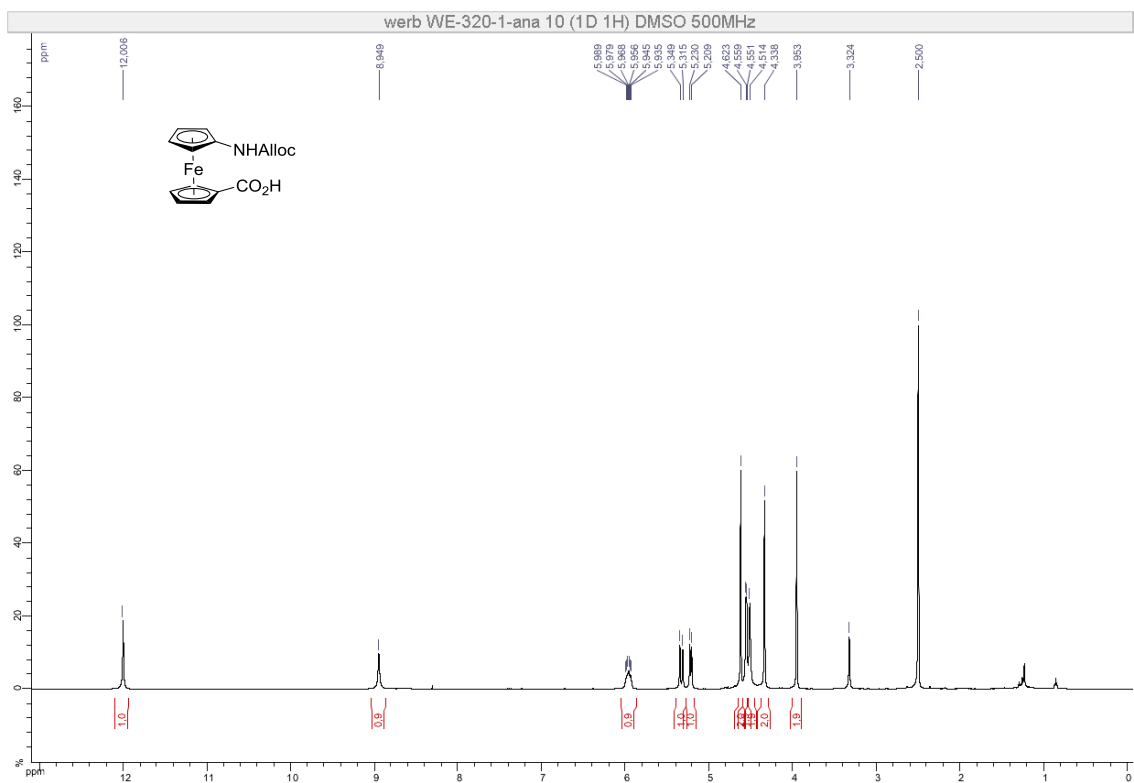


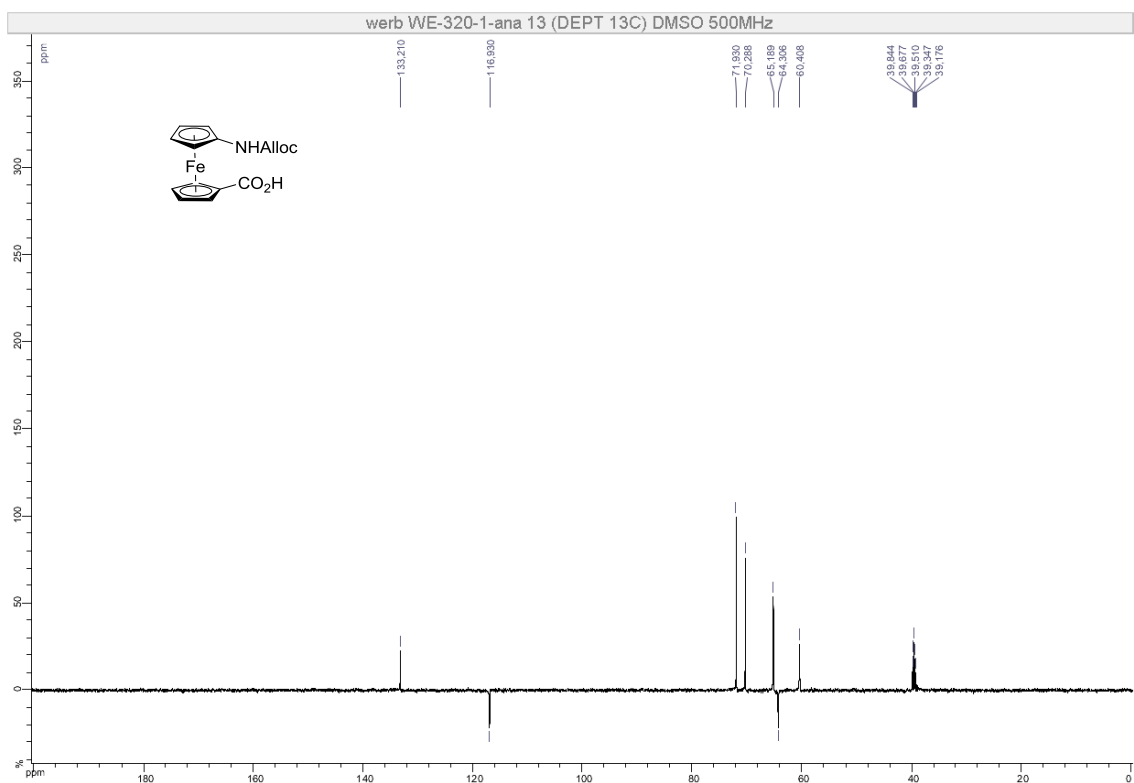
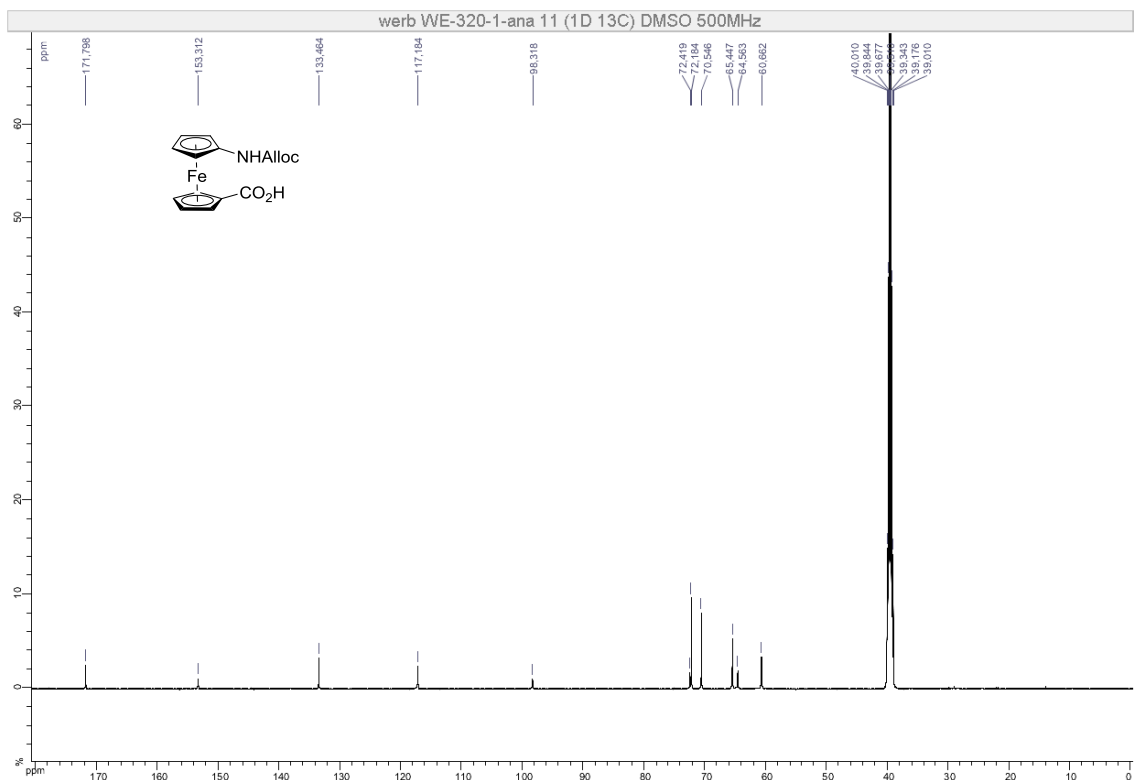


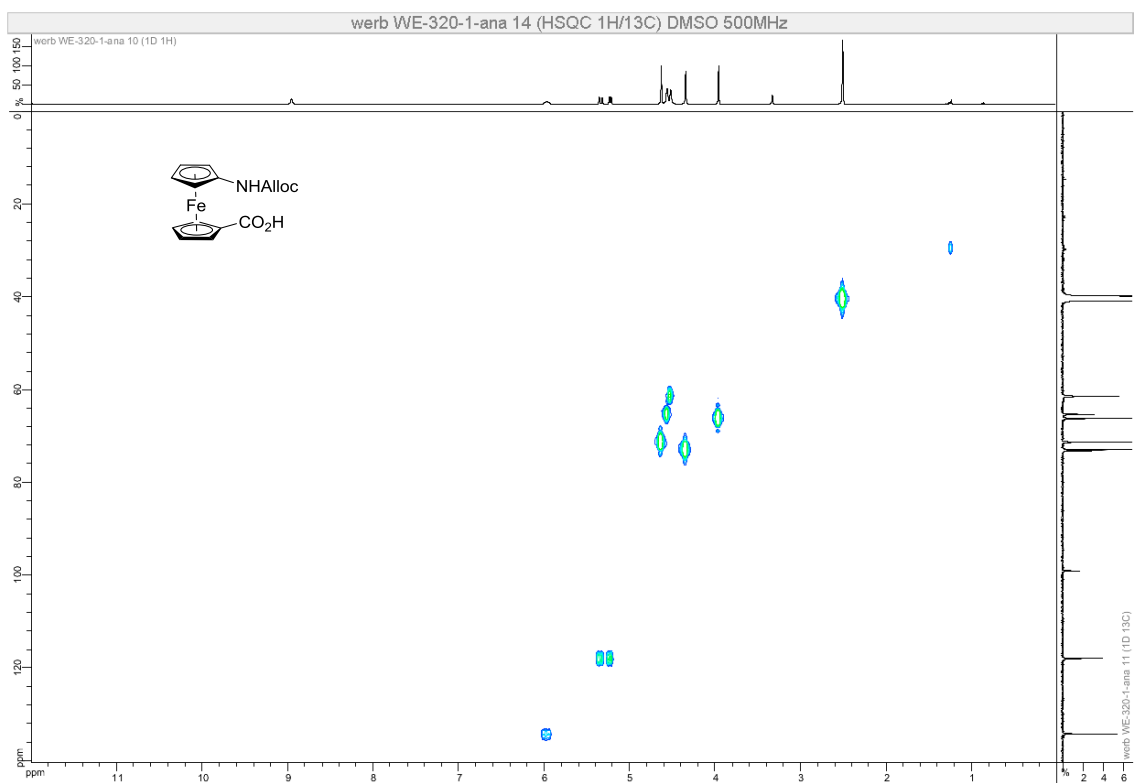
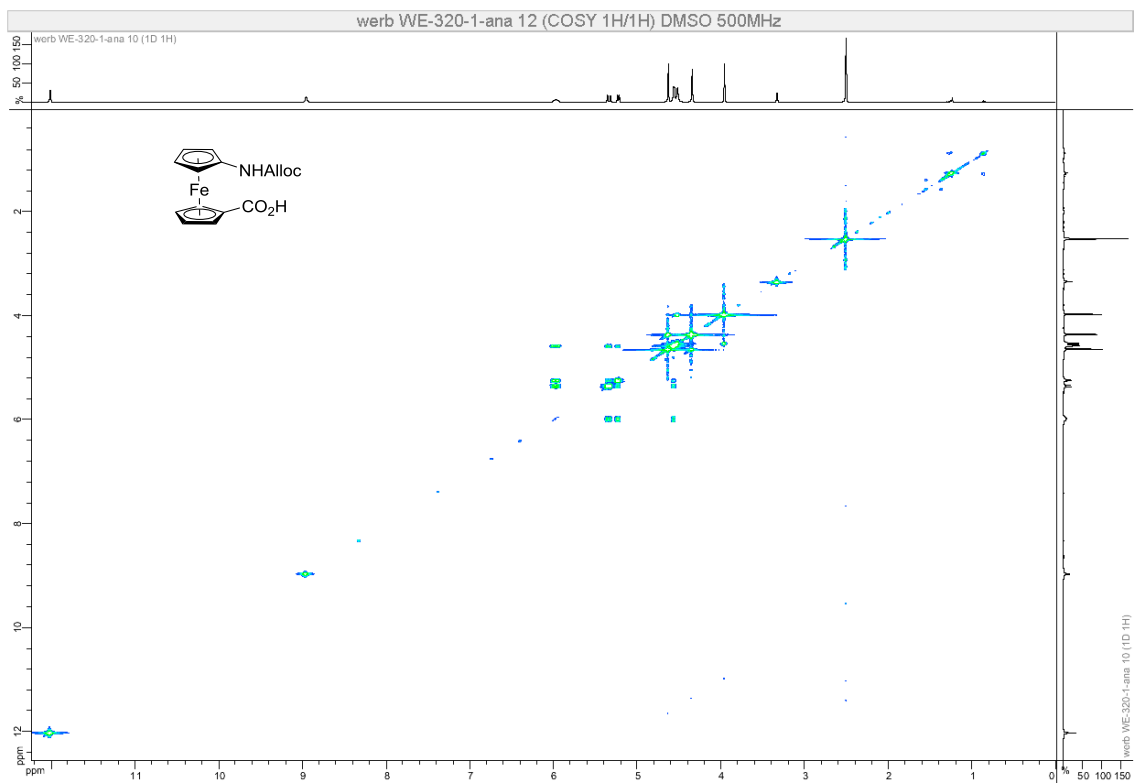


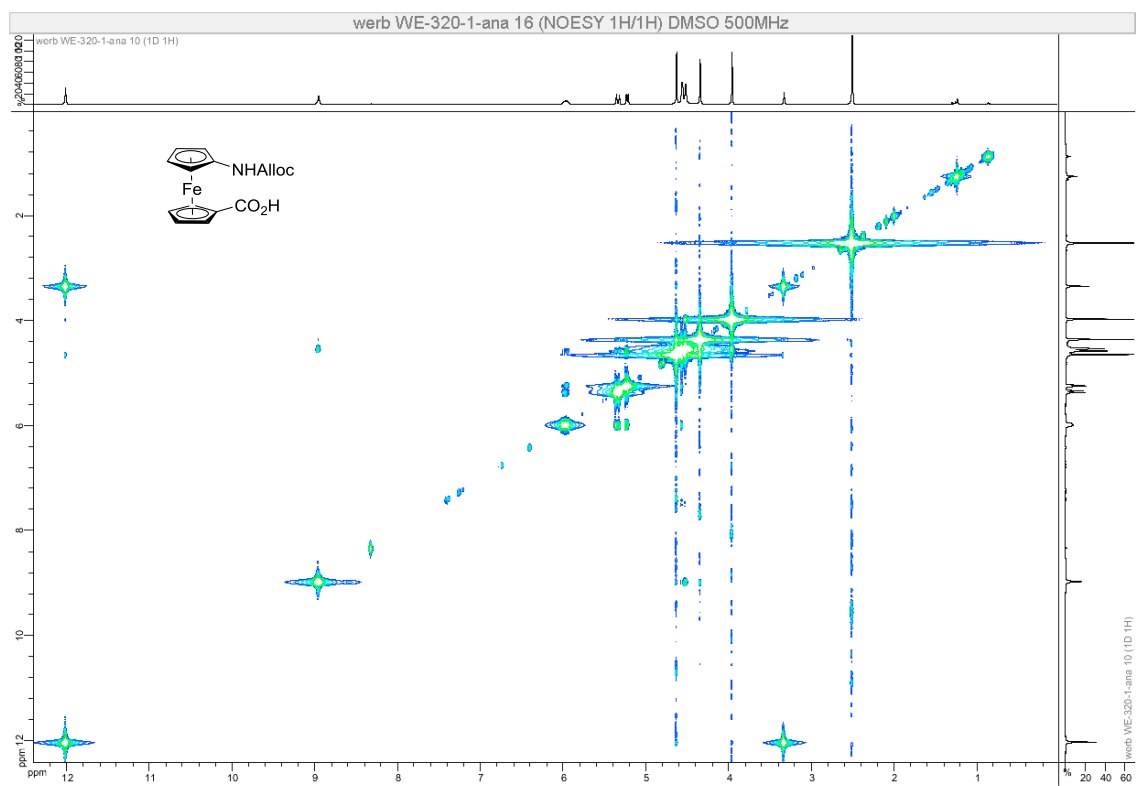
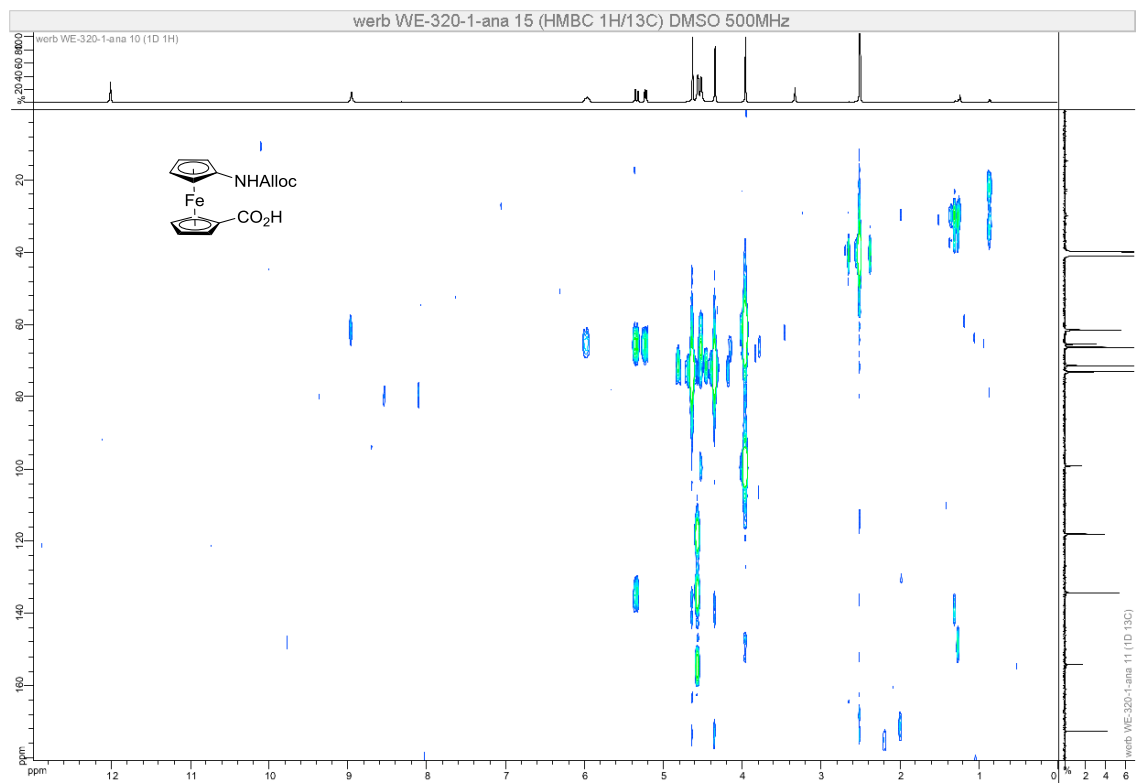


1'-((Allyloxycarbonyl)amino)ferrocene-1-carboxylic acid - 9

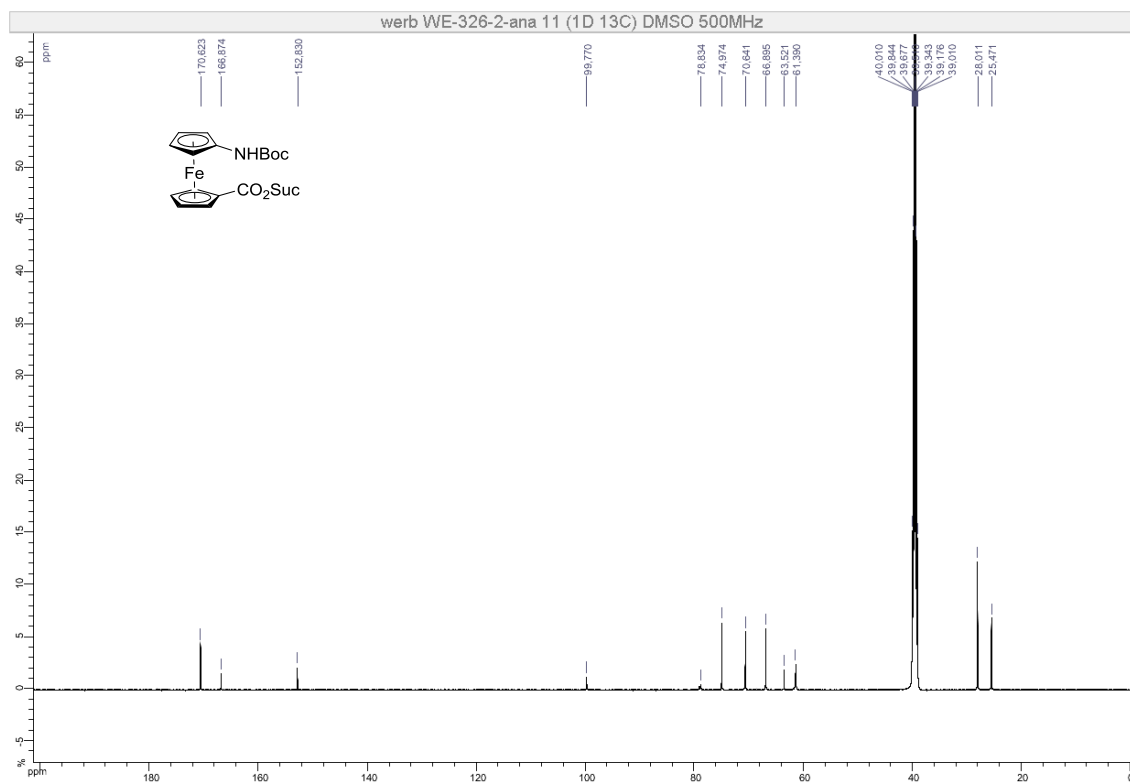
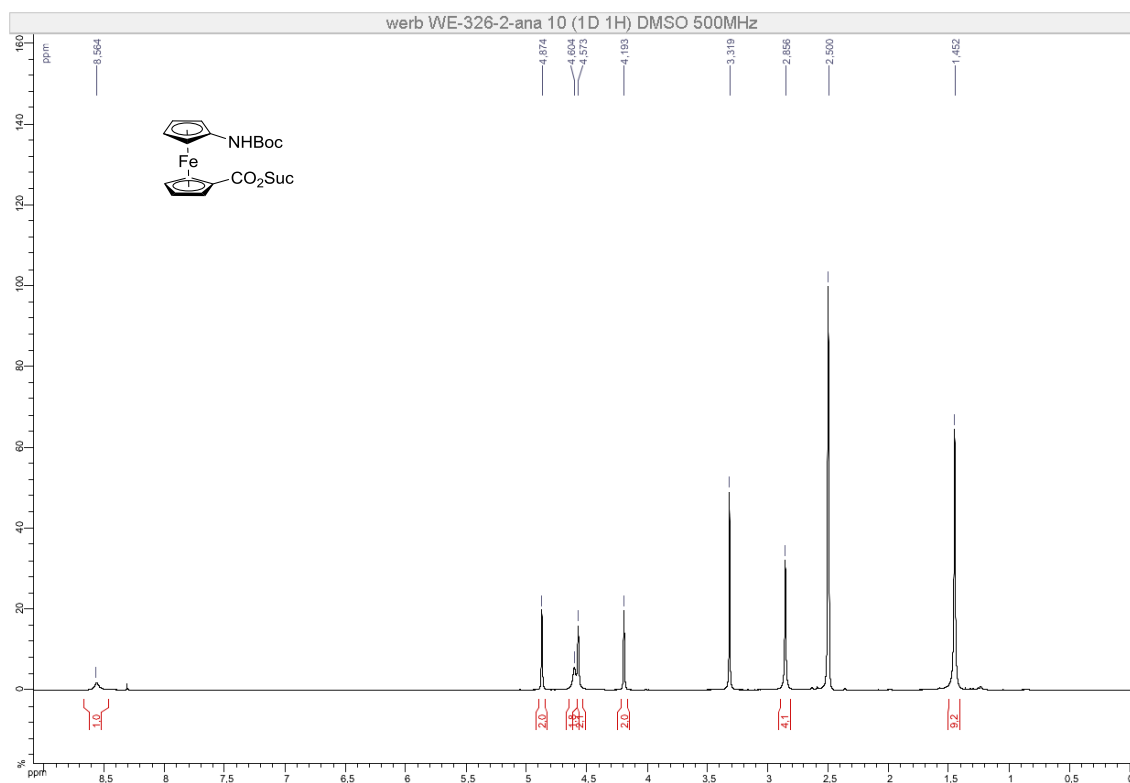


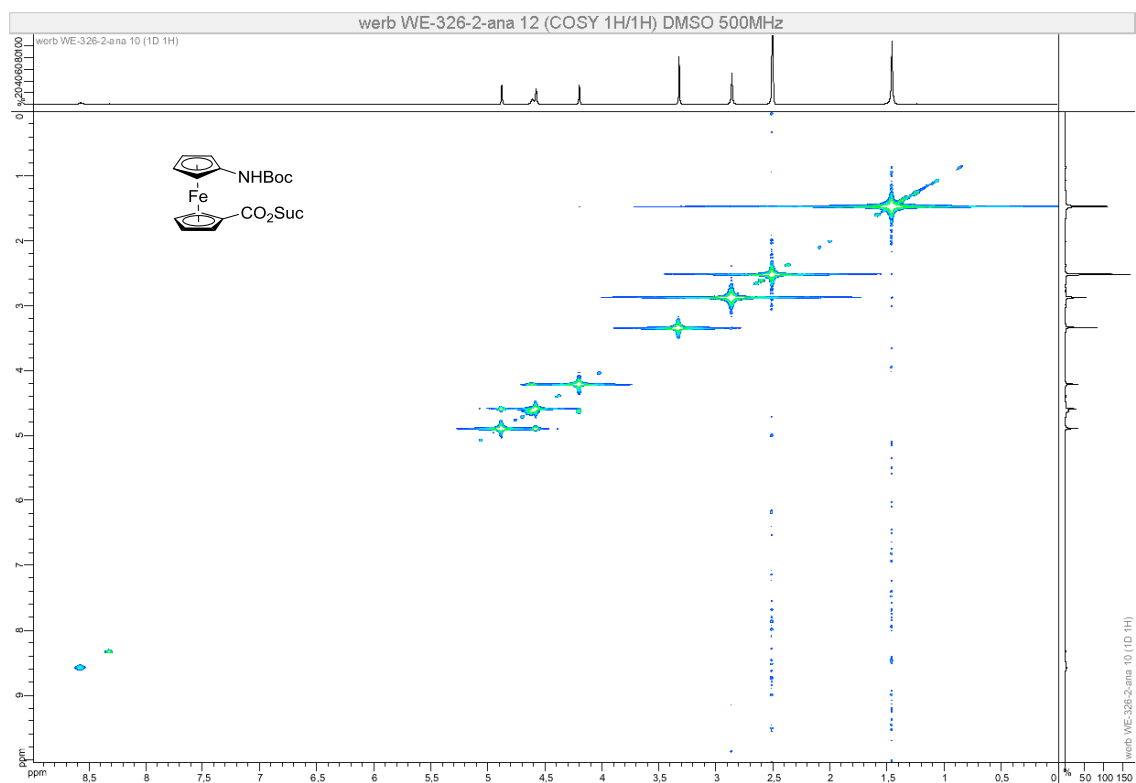
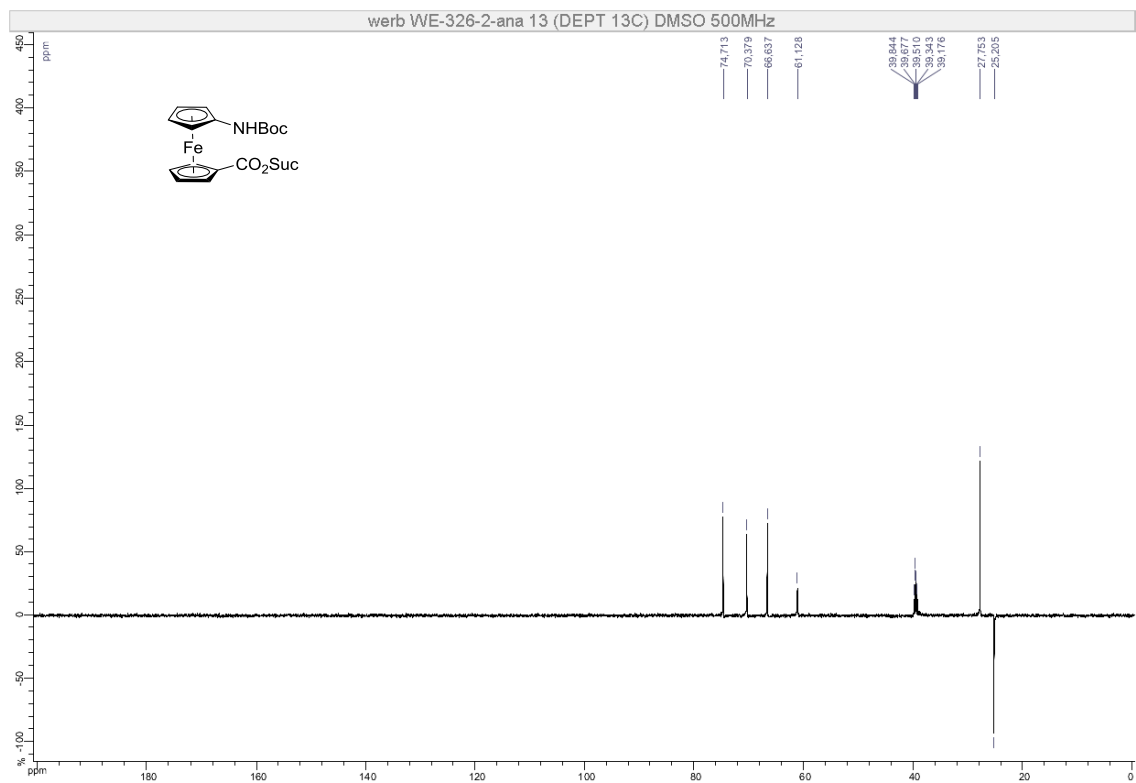


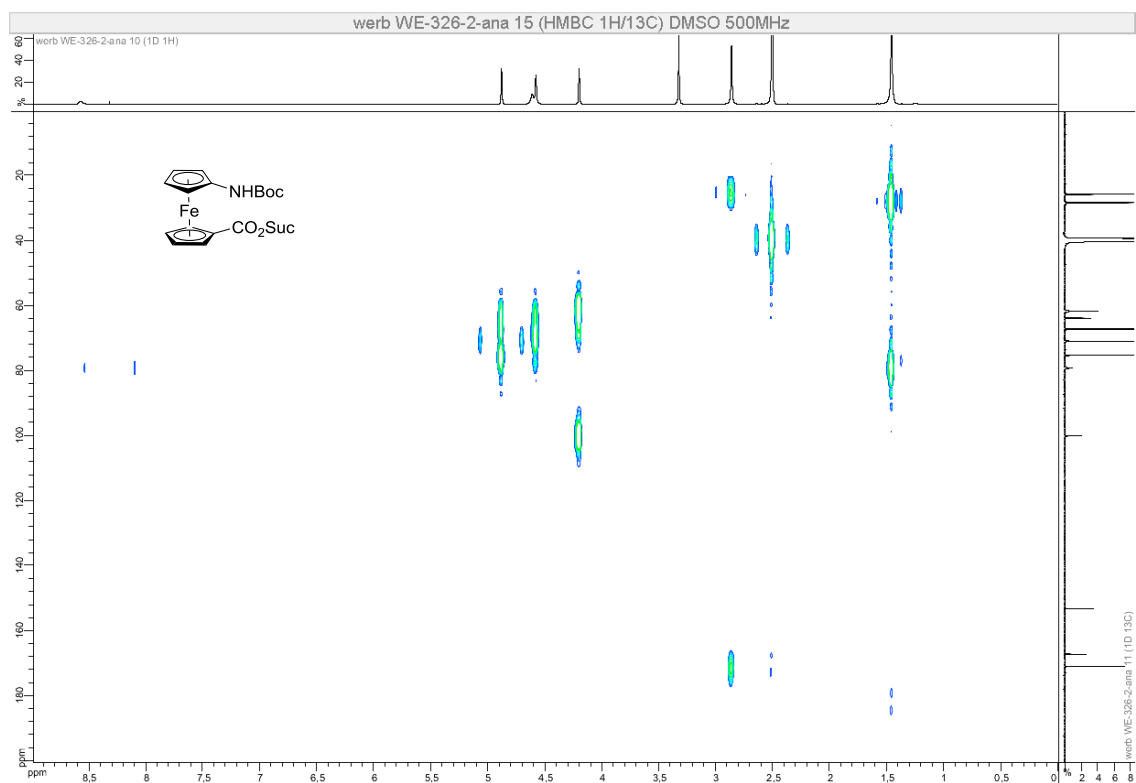
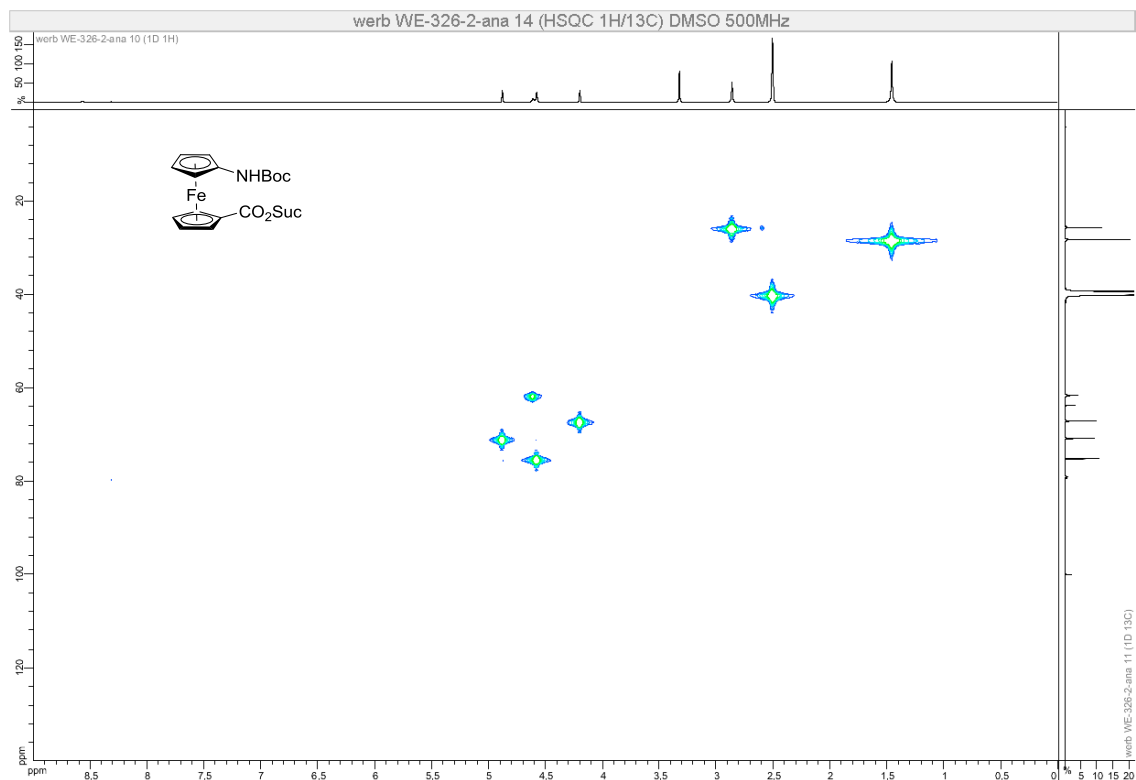


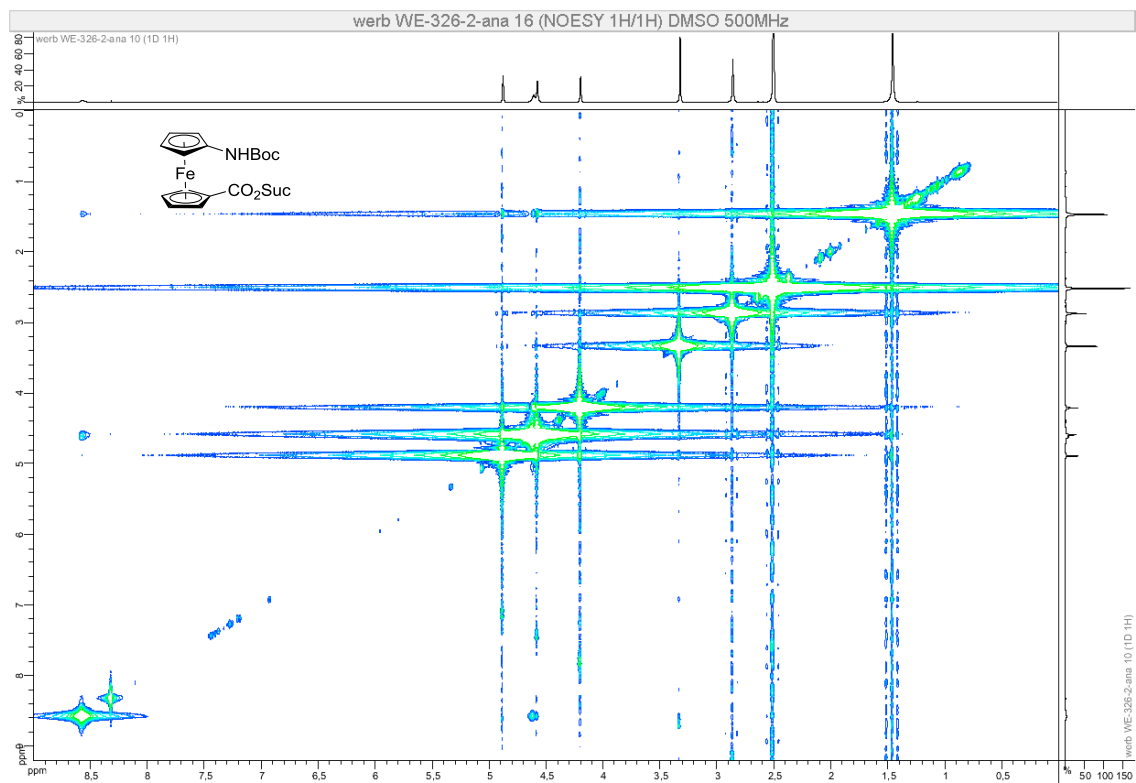


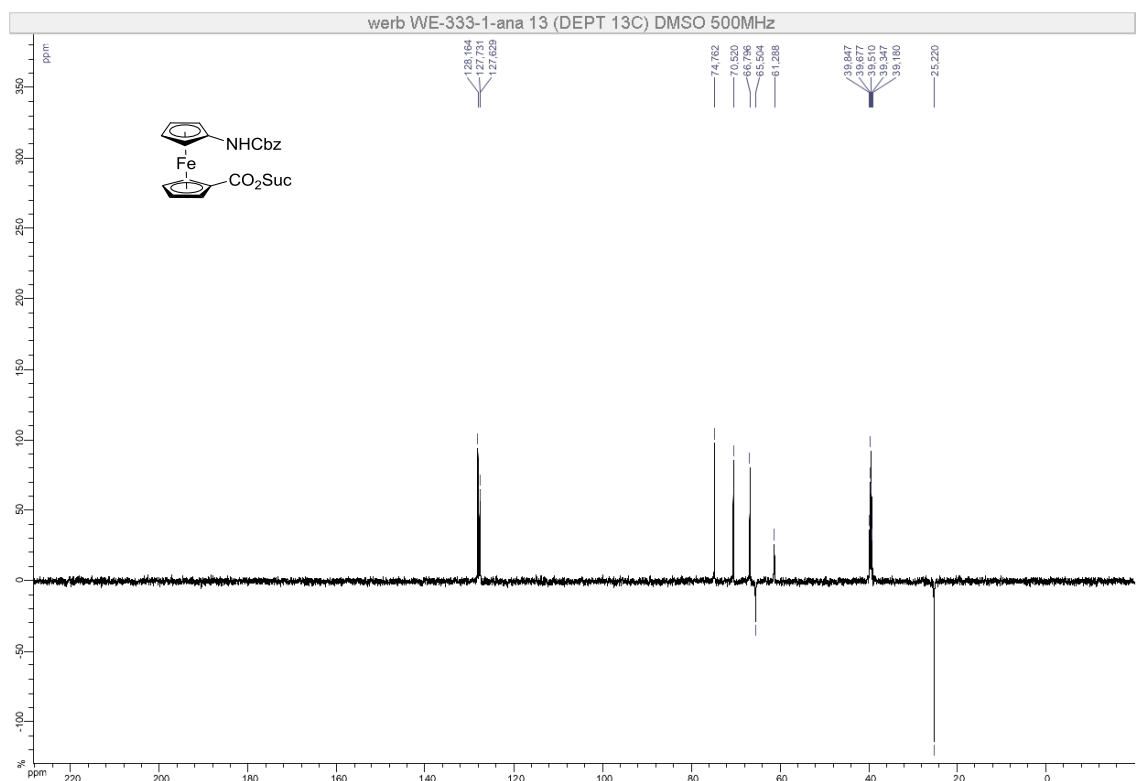
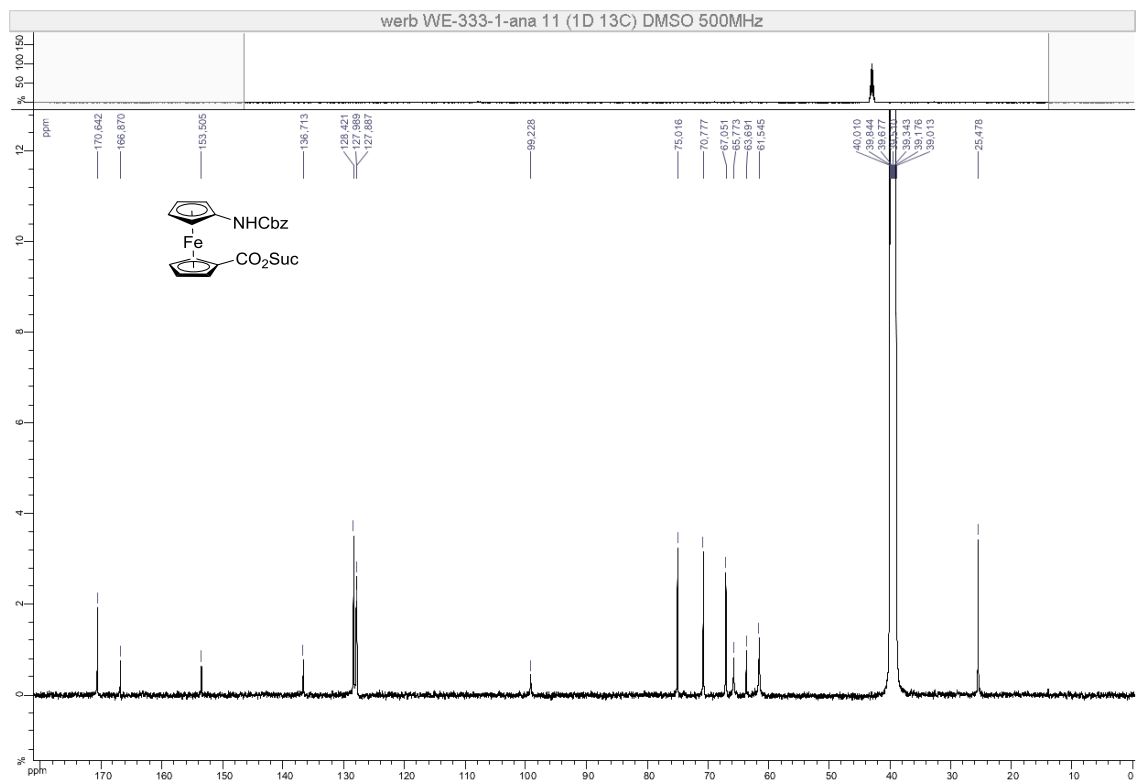
2,5-Dioxopyrrolidin-1-yl 1'-(*tert*-butylcarbonylamino)ferrocene-1-carboxylate - 10

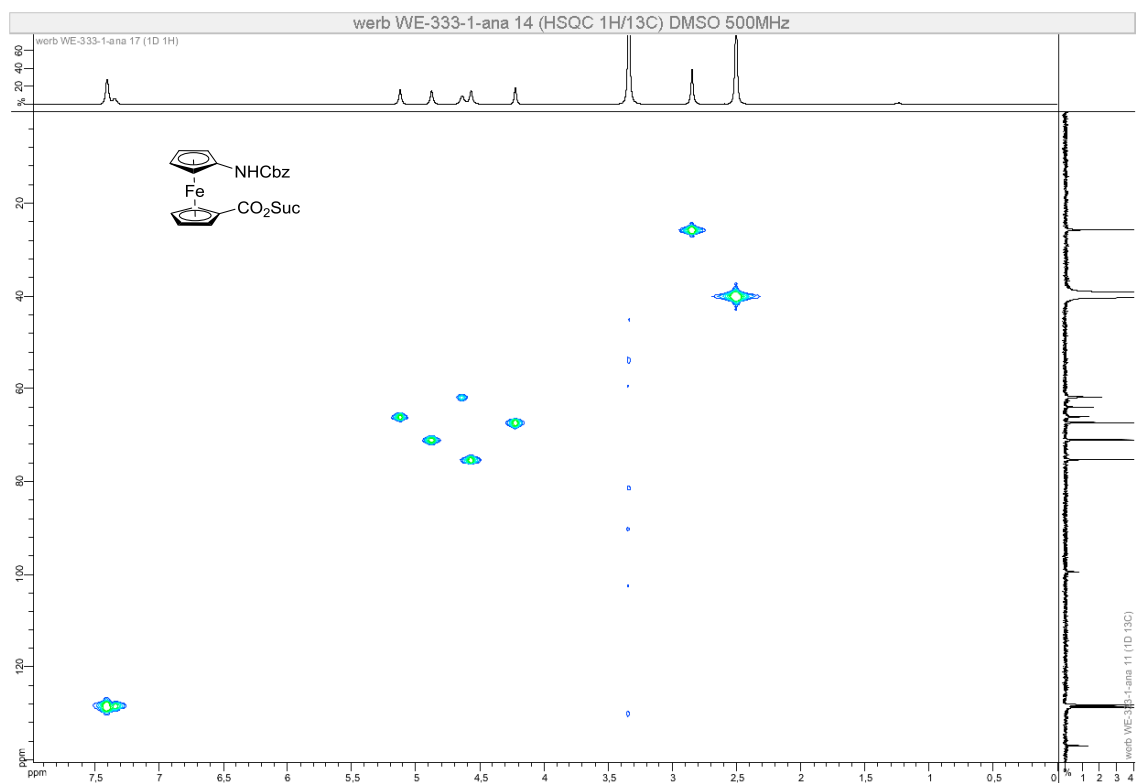
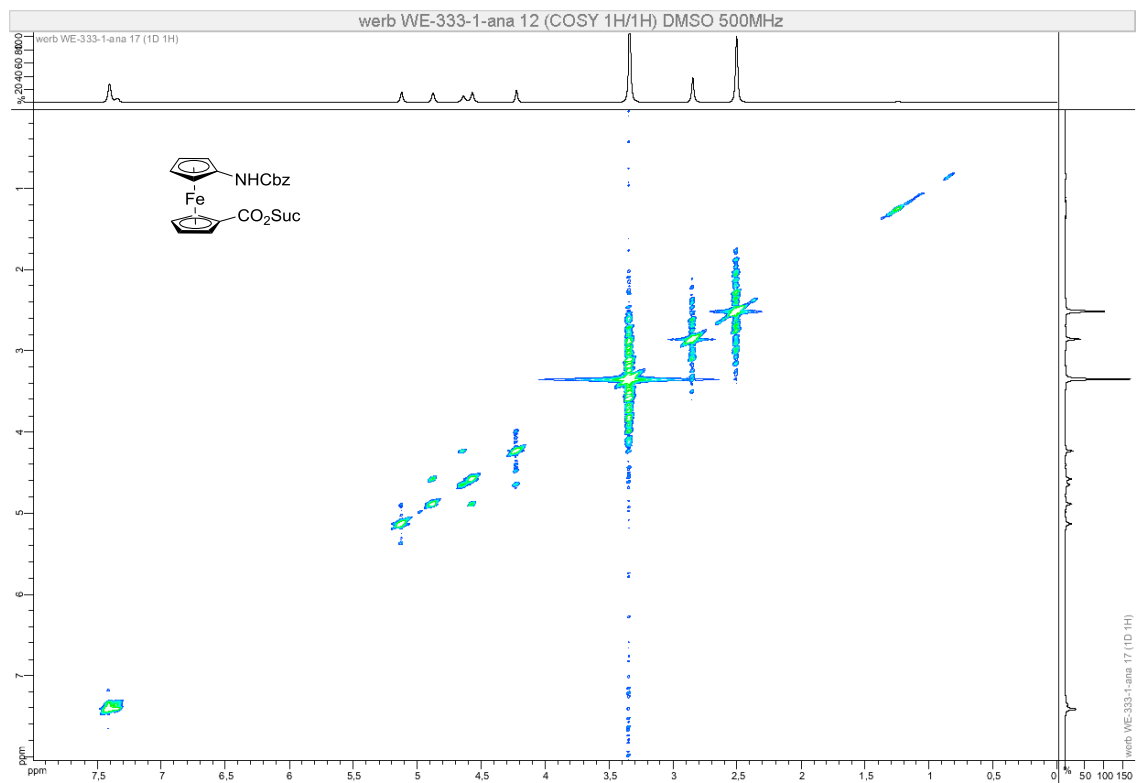


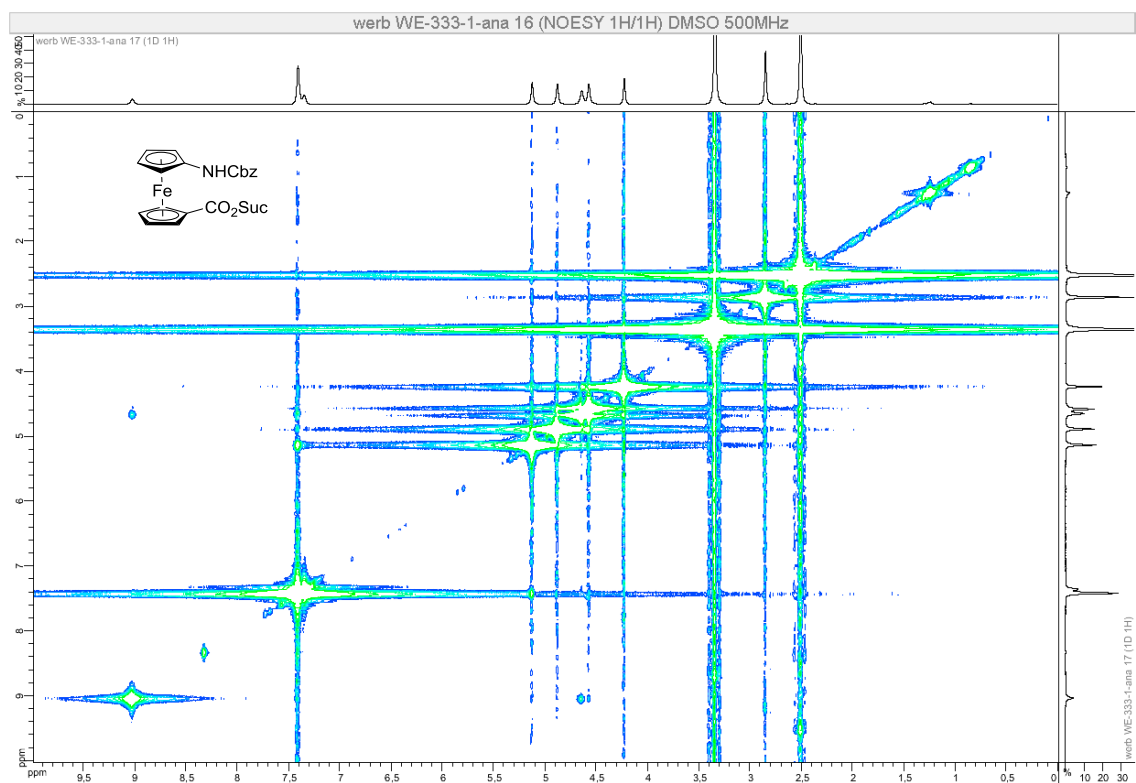
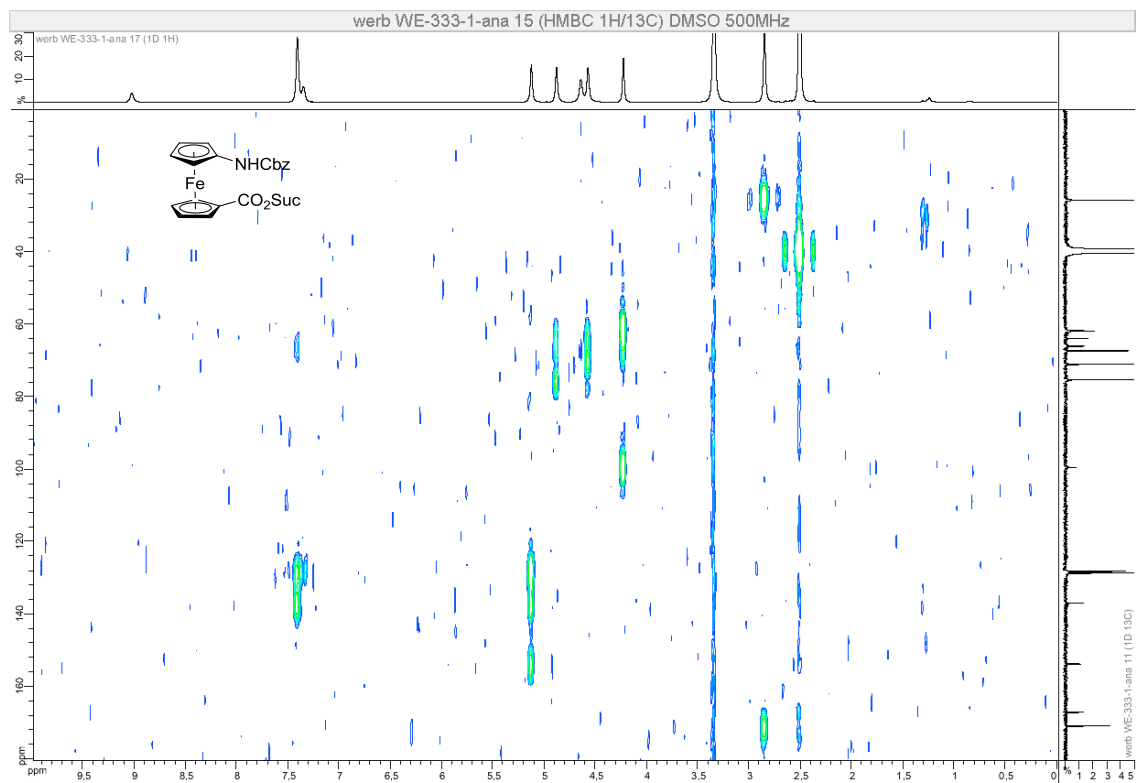




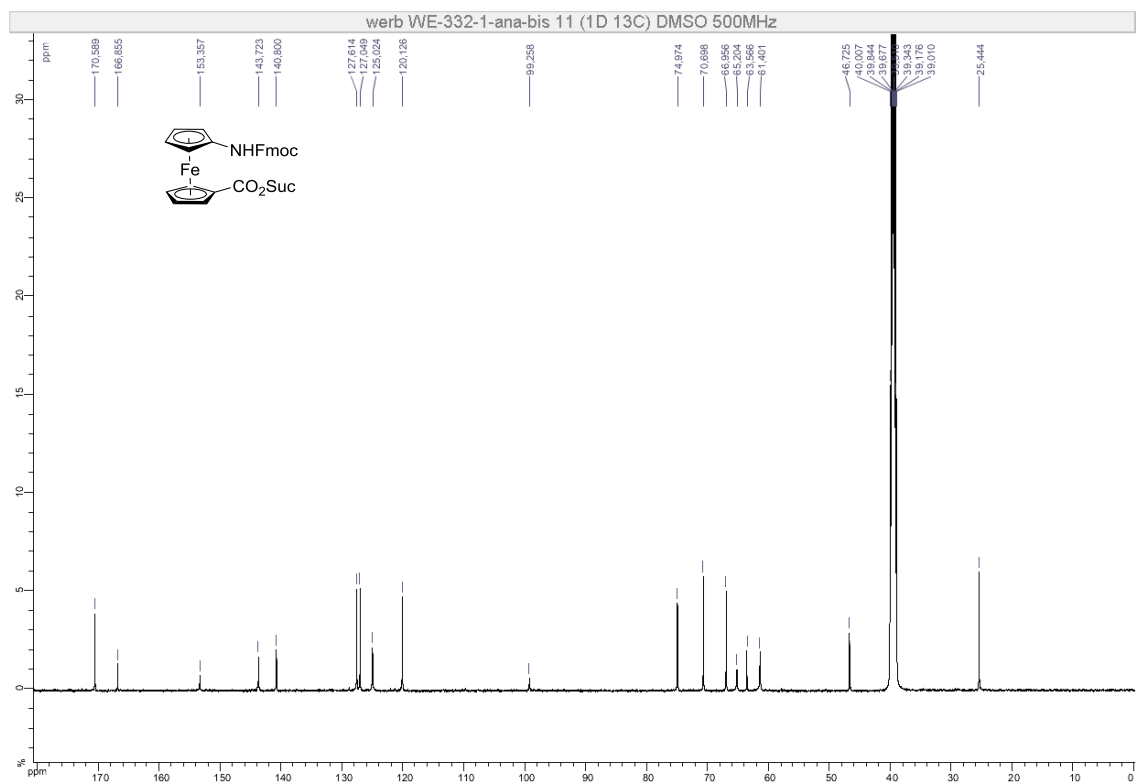
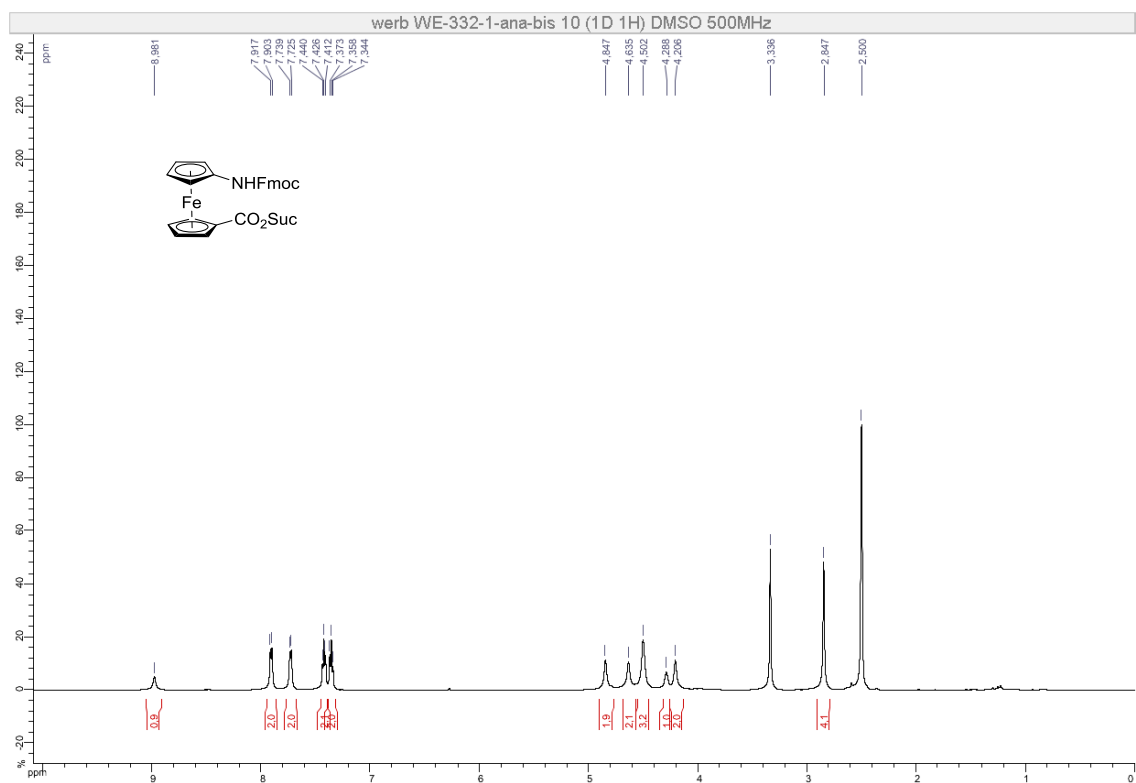


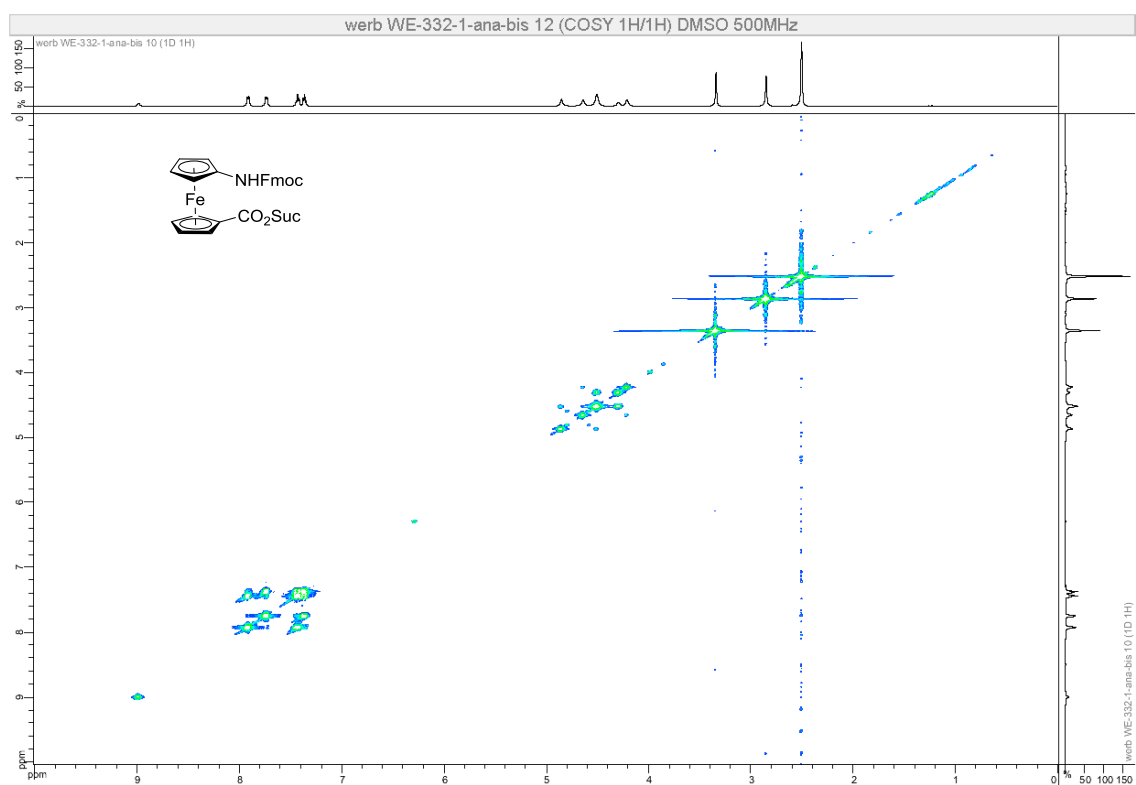
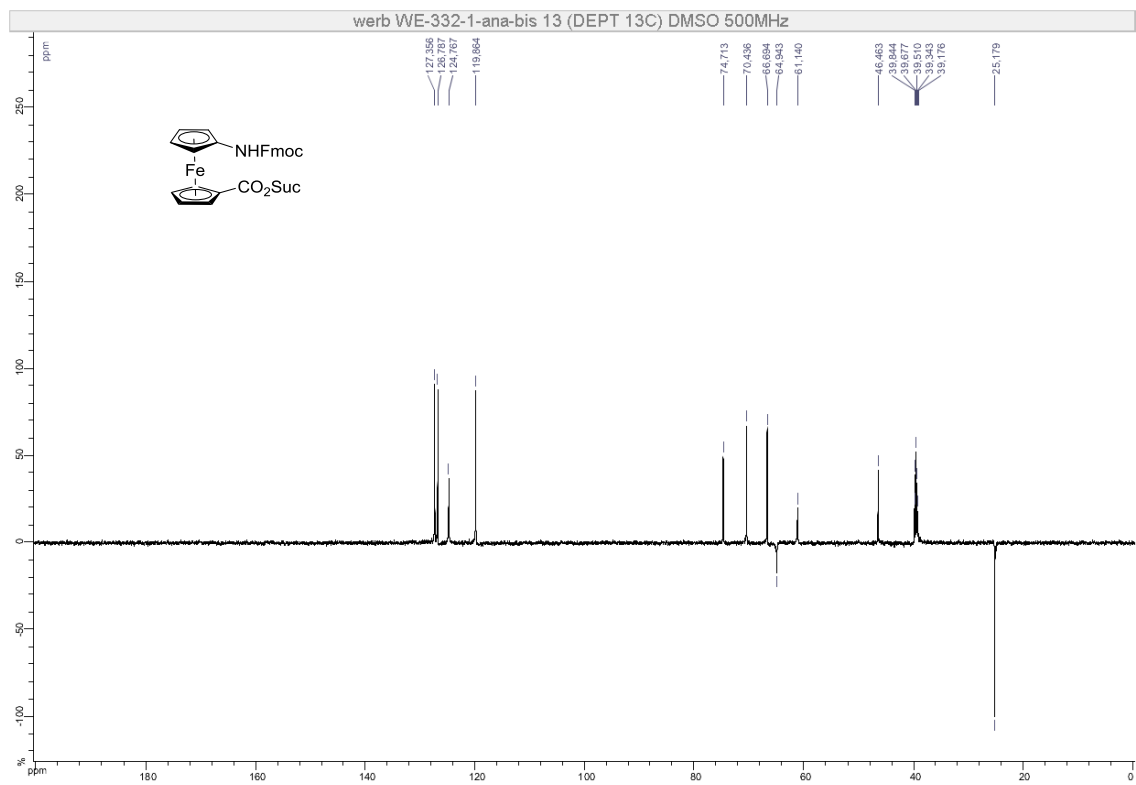


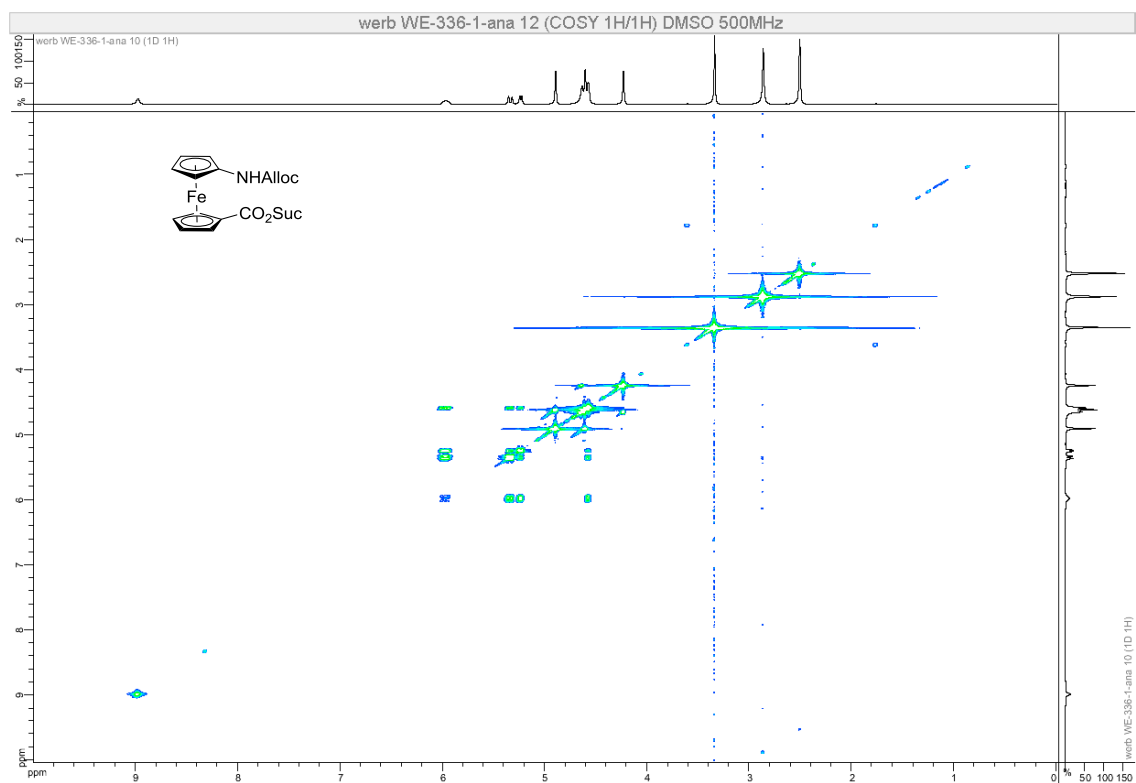
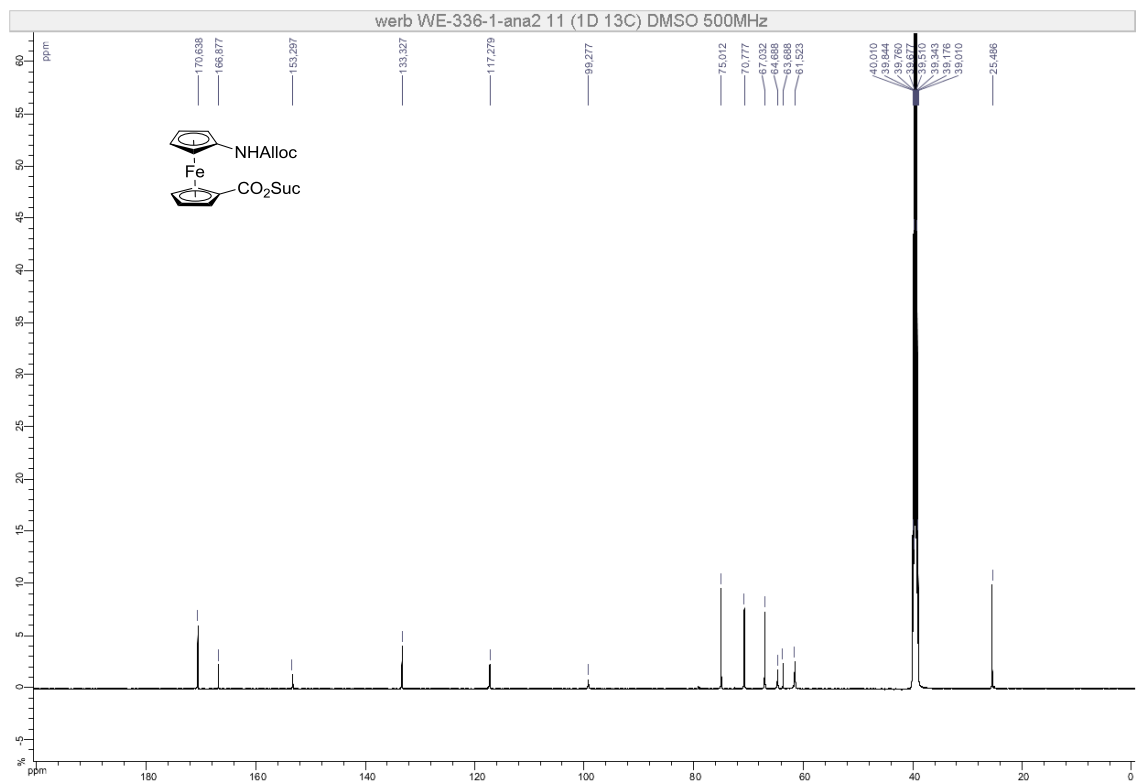


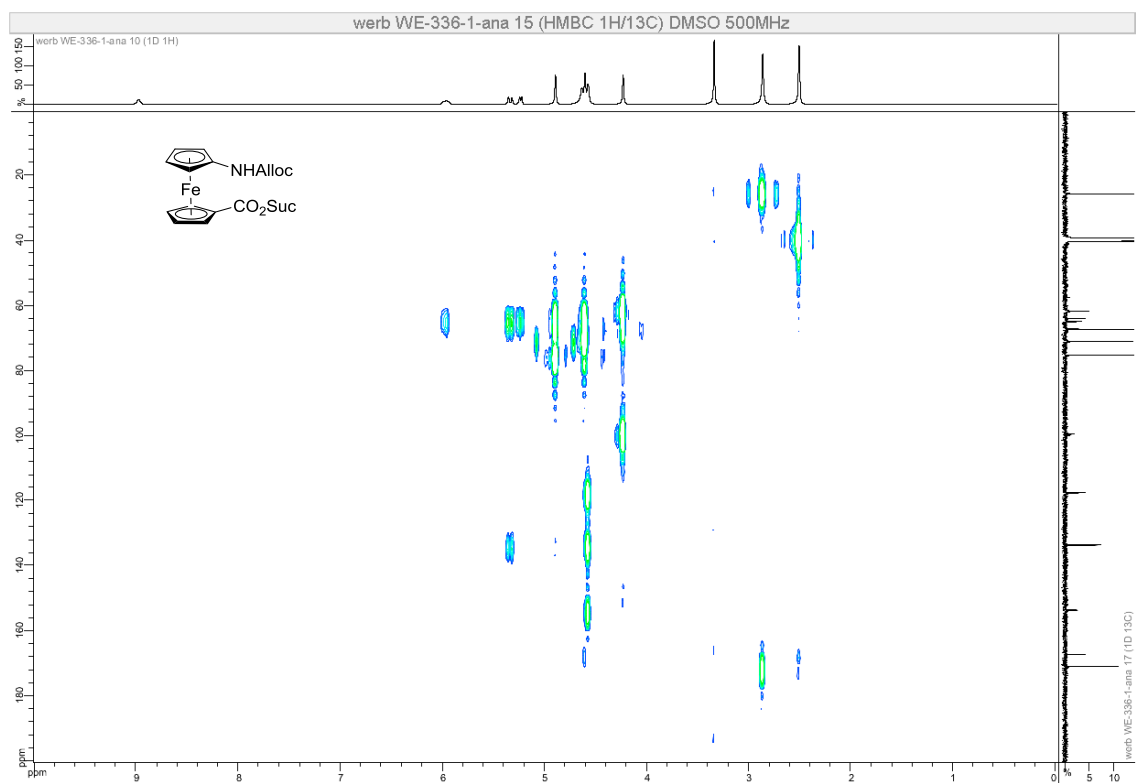
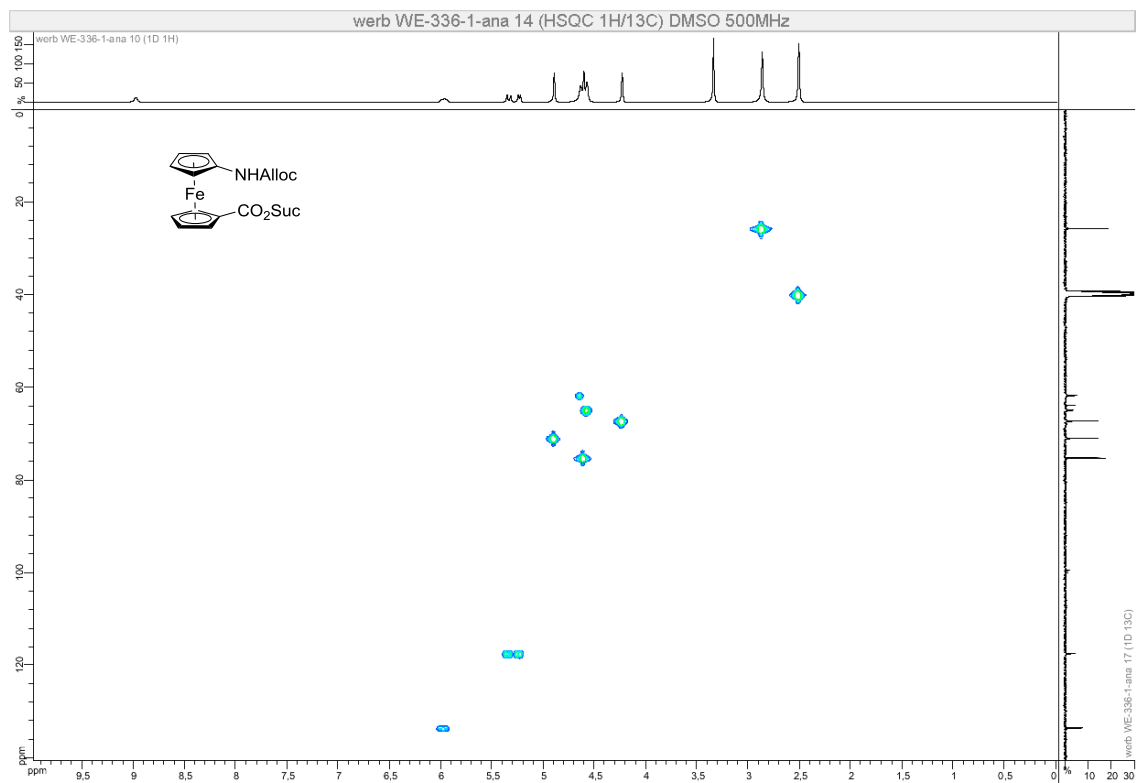


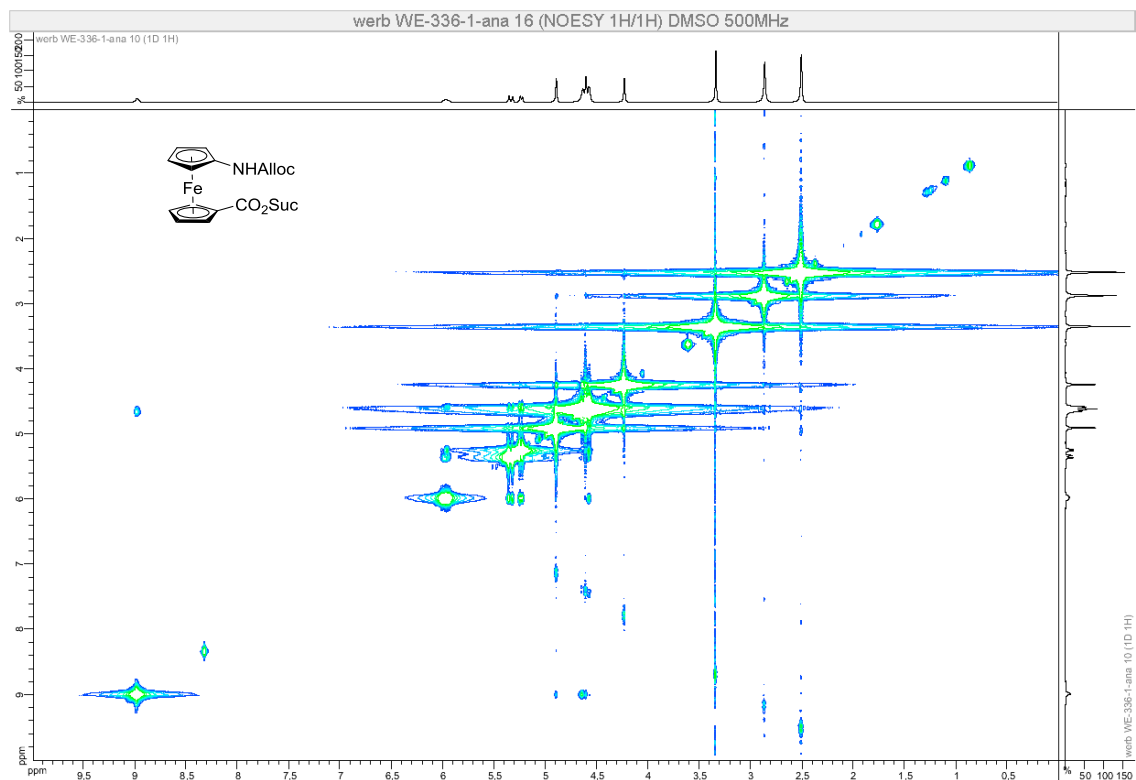
2,5-Dioxopyrrolidin-1-yl 1'-[((fluoren-9-yl)methoxycarbonyl)amino]ferrocene-1-carboxylate - 12



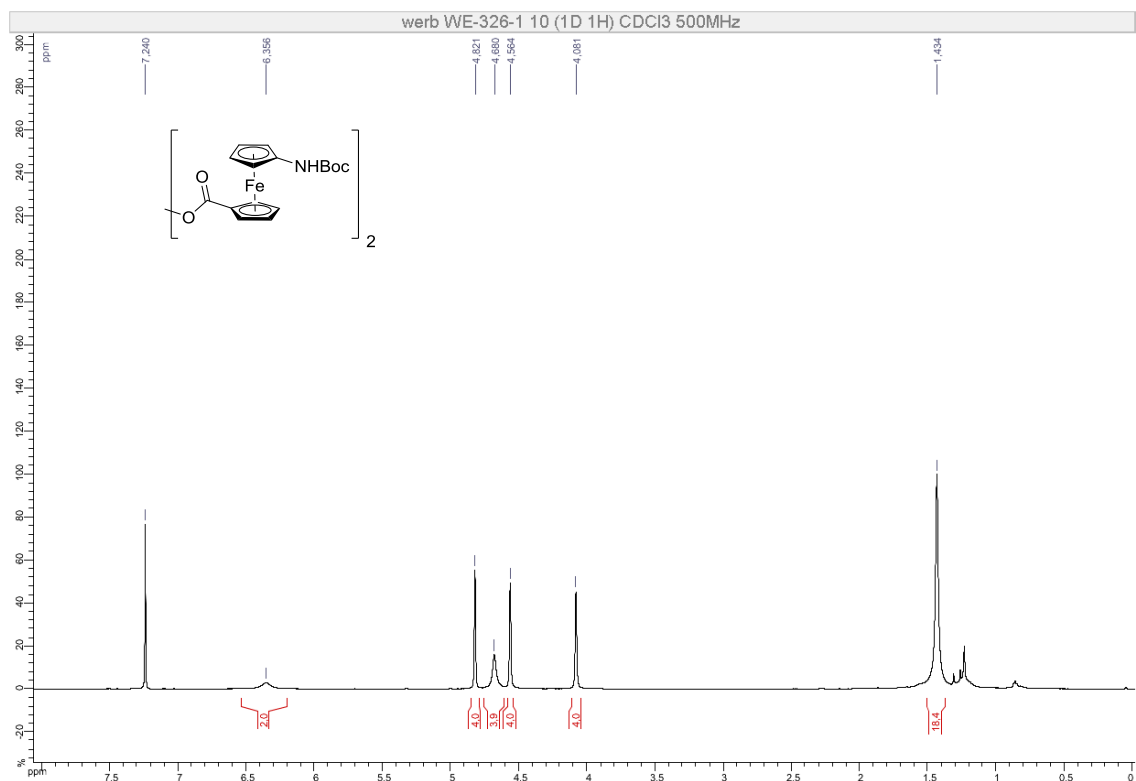


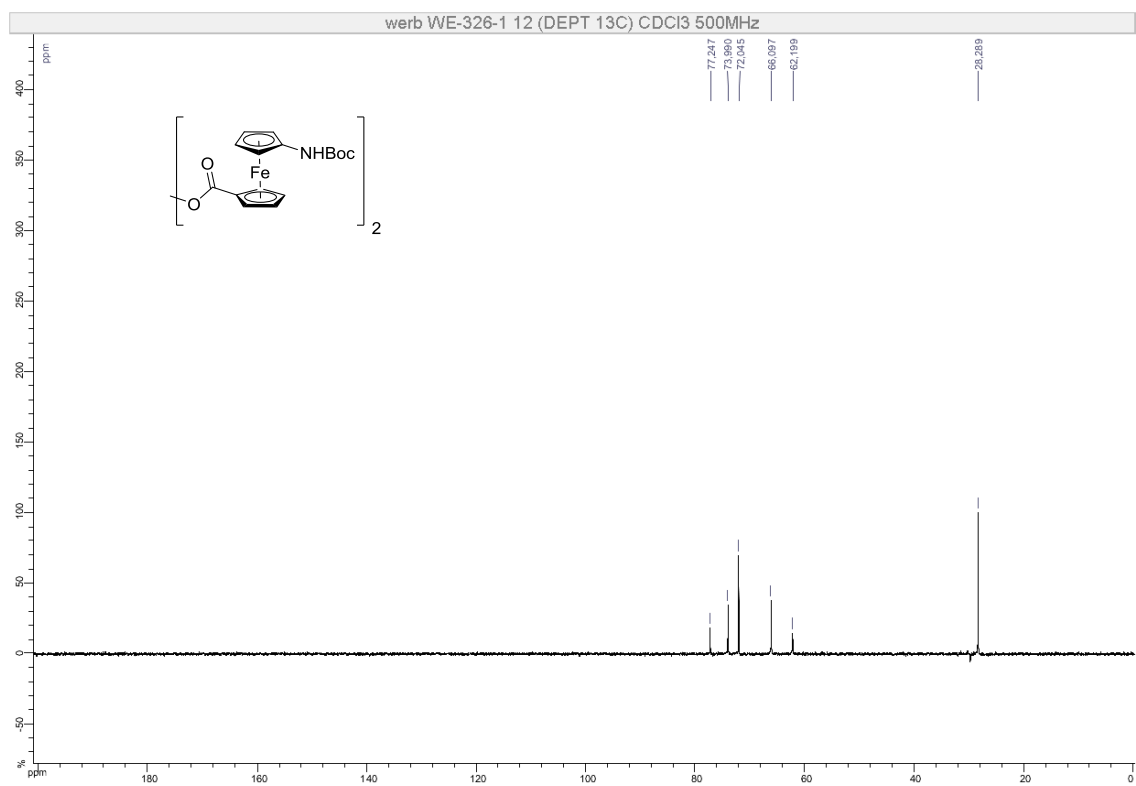
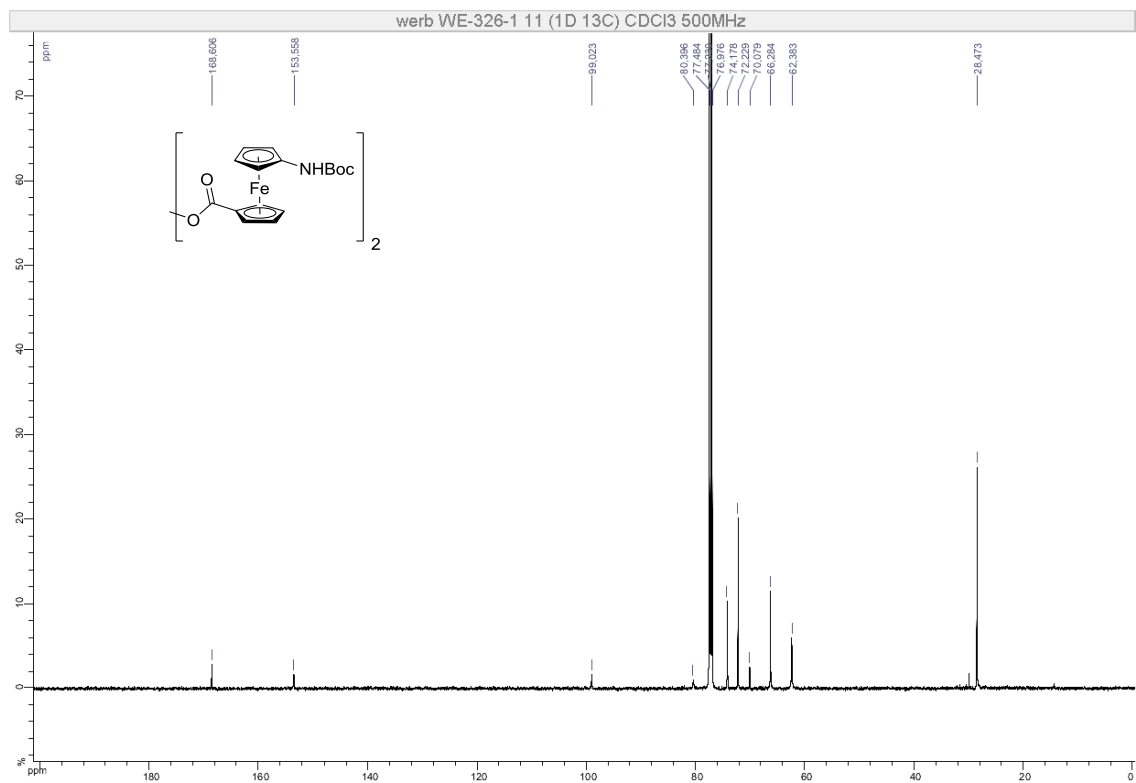


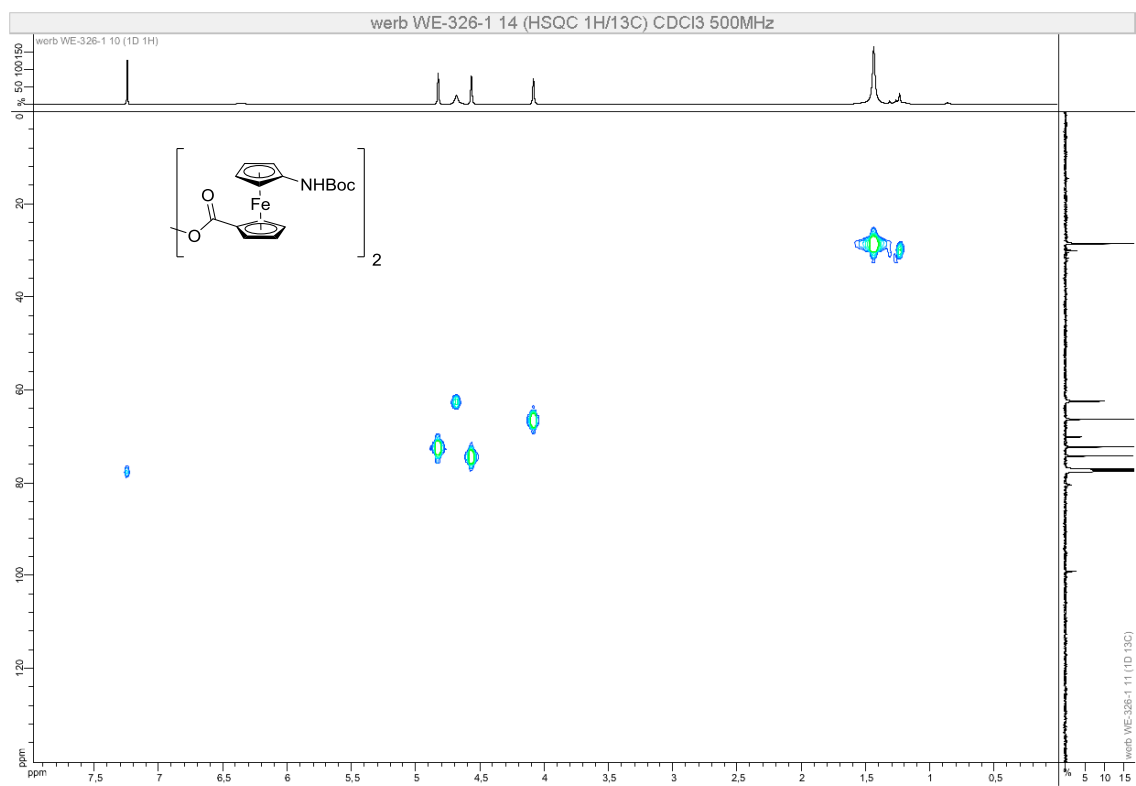
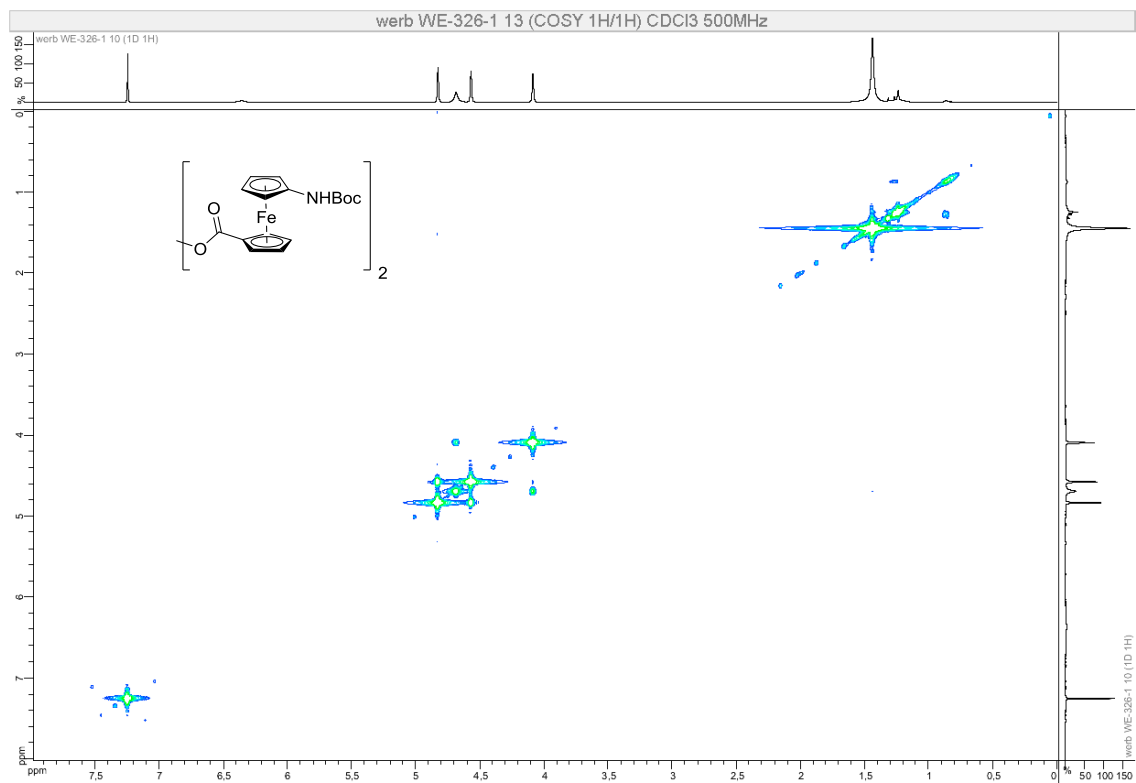




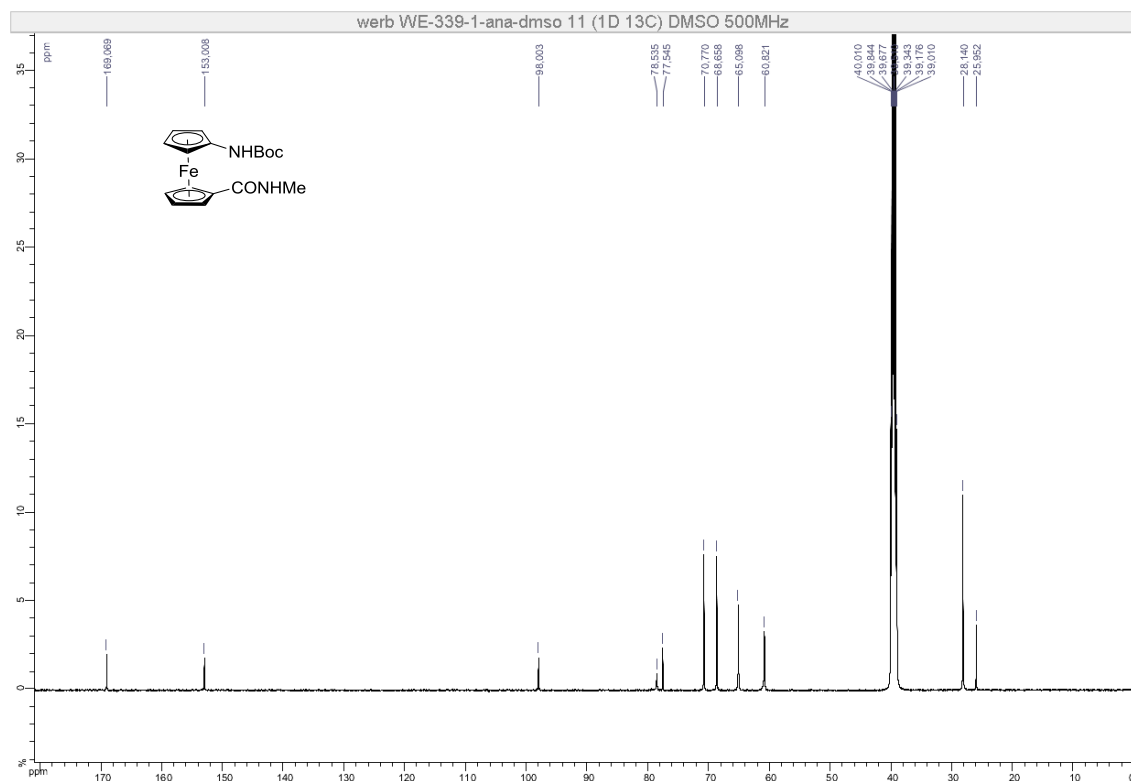
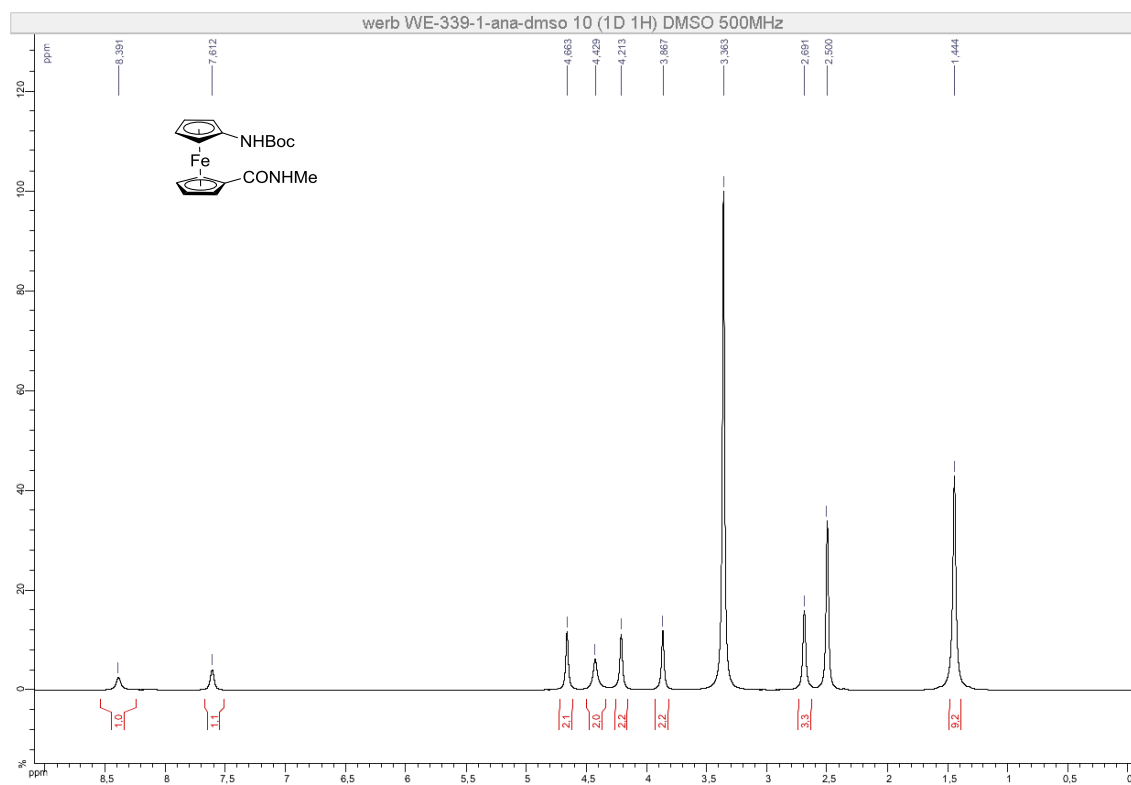
1'-((*tert*-Butoxycarbonyl)amino)ferrocene-1-carboxylic anhydride - 14

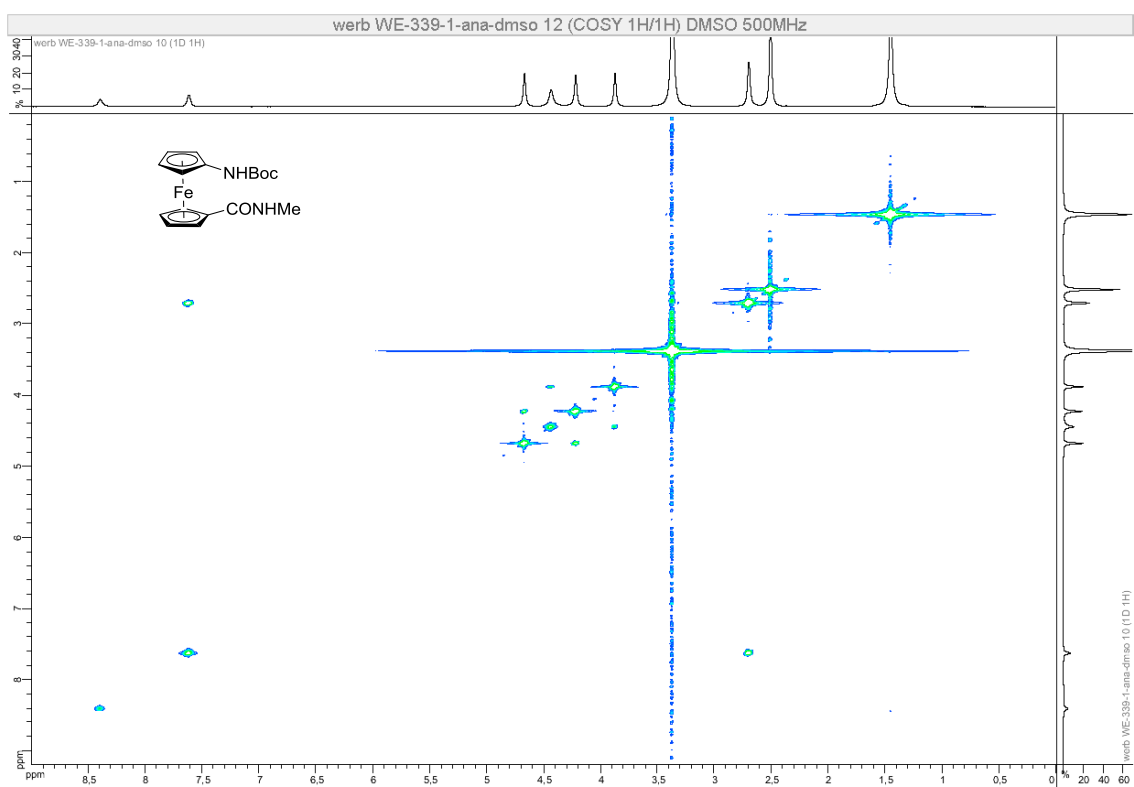
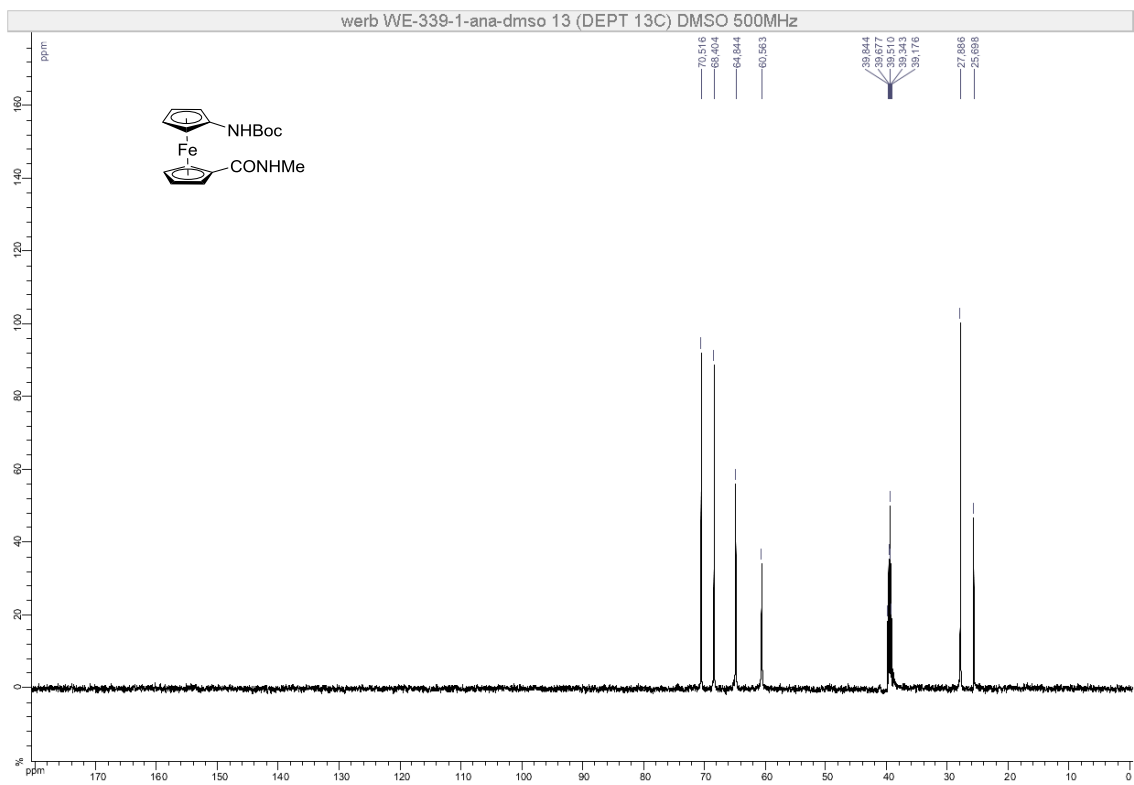


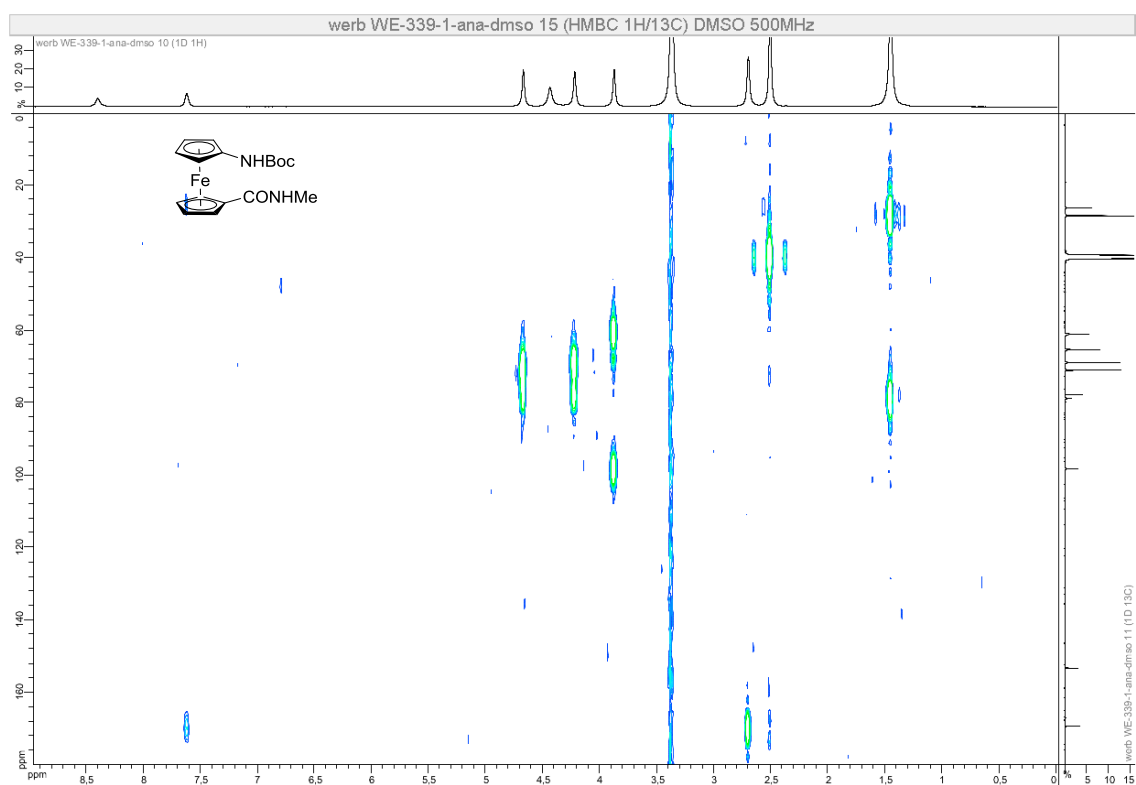
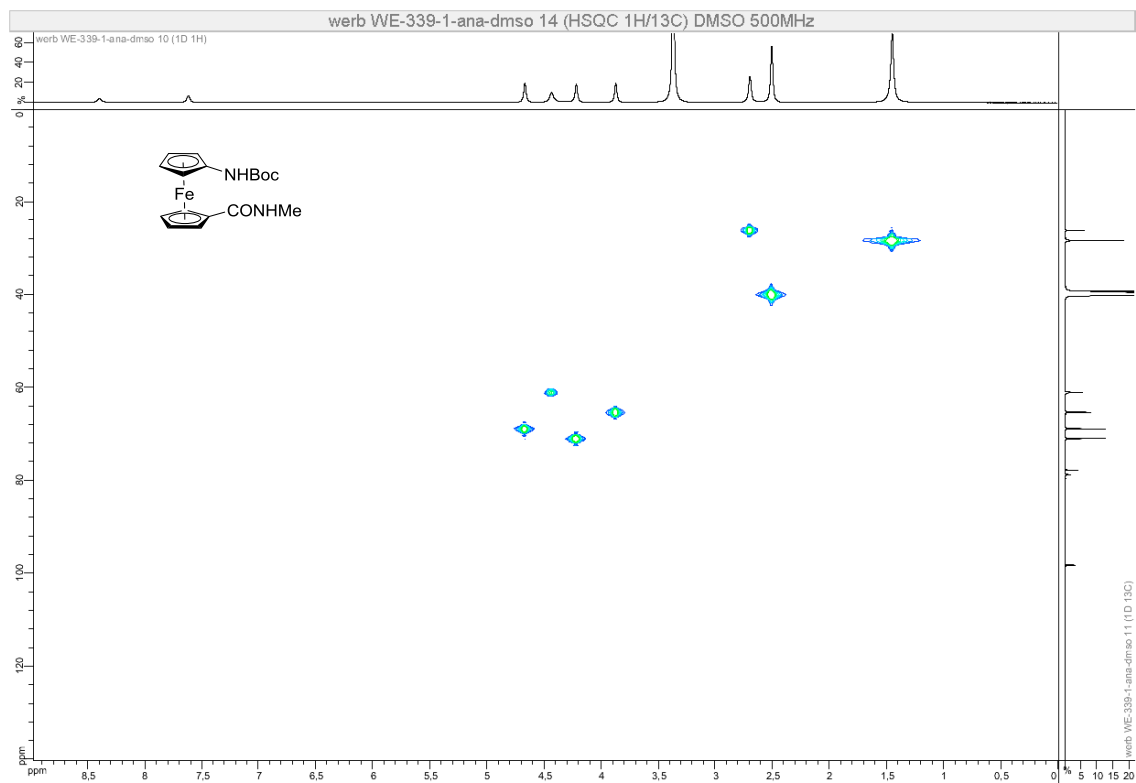


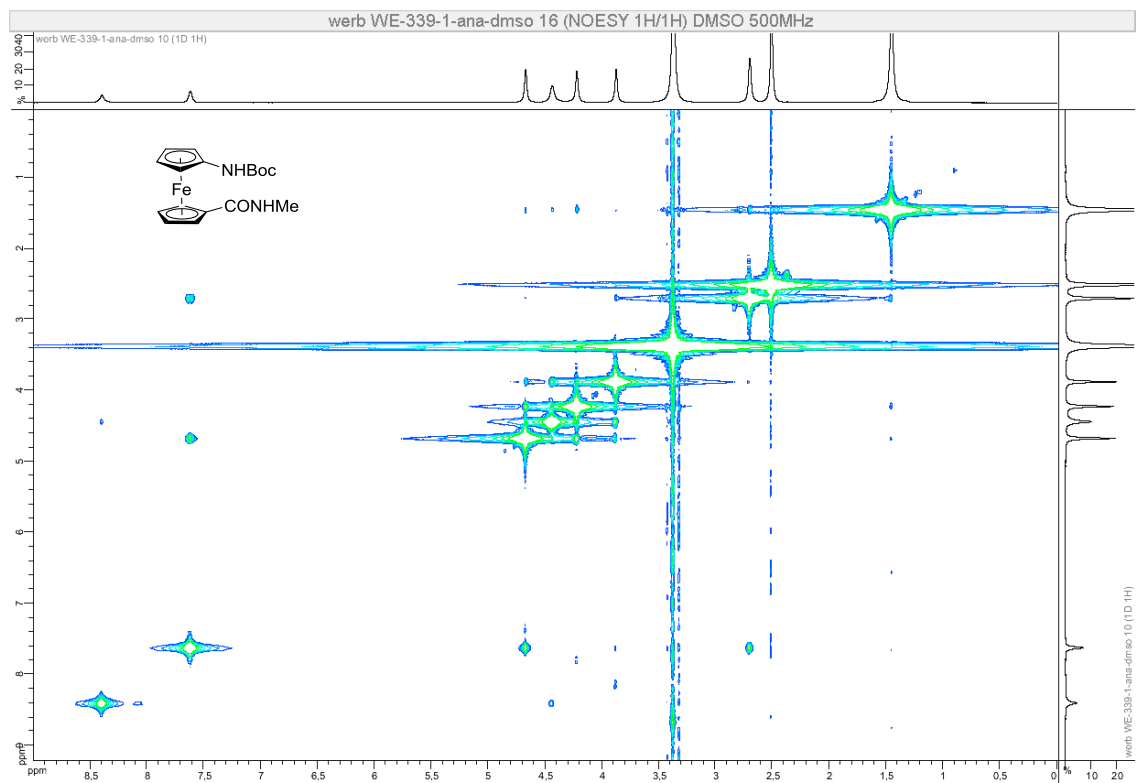


***N*-methyl 1'-((*tert*-butoxycarbonyl)amino)ferrocene-1-carboxamide - 15**

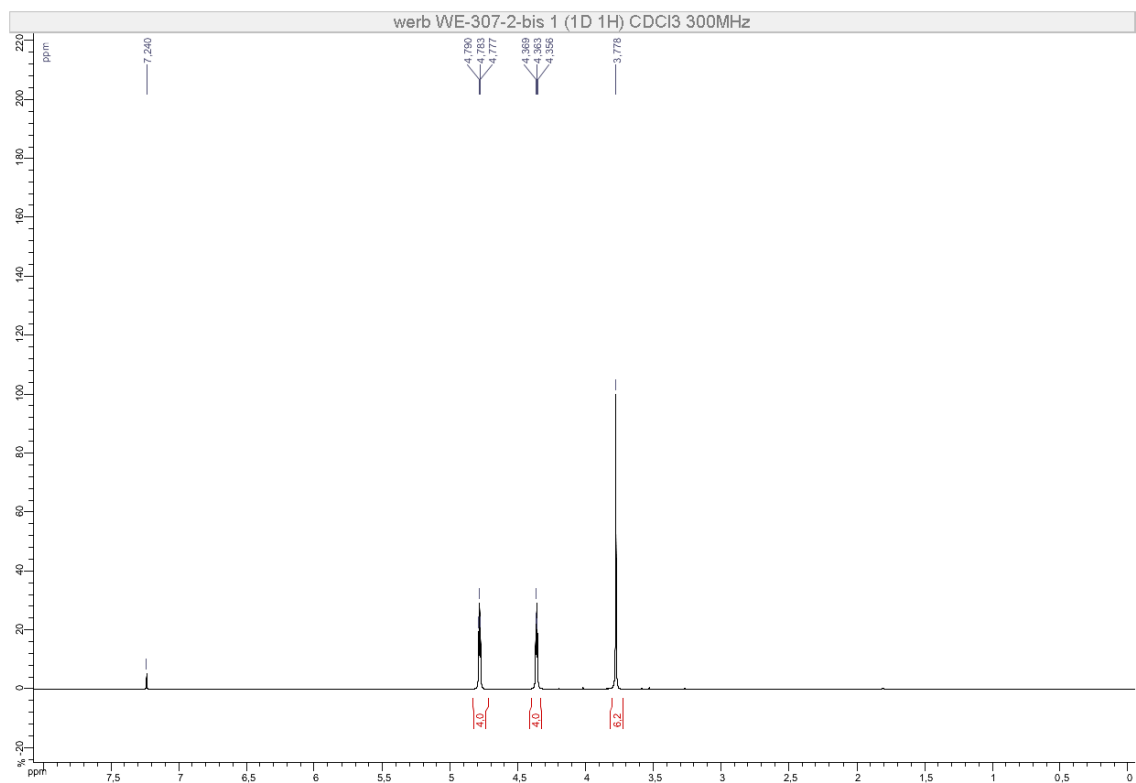


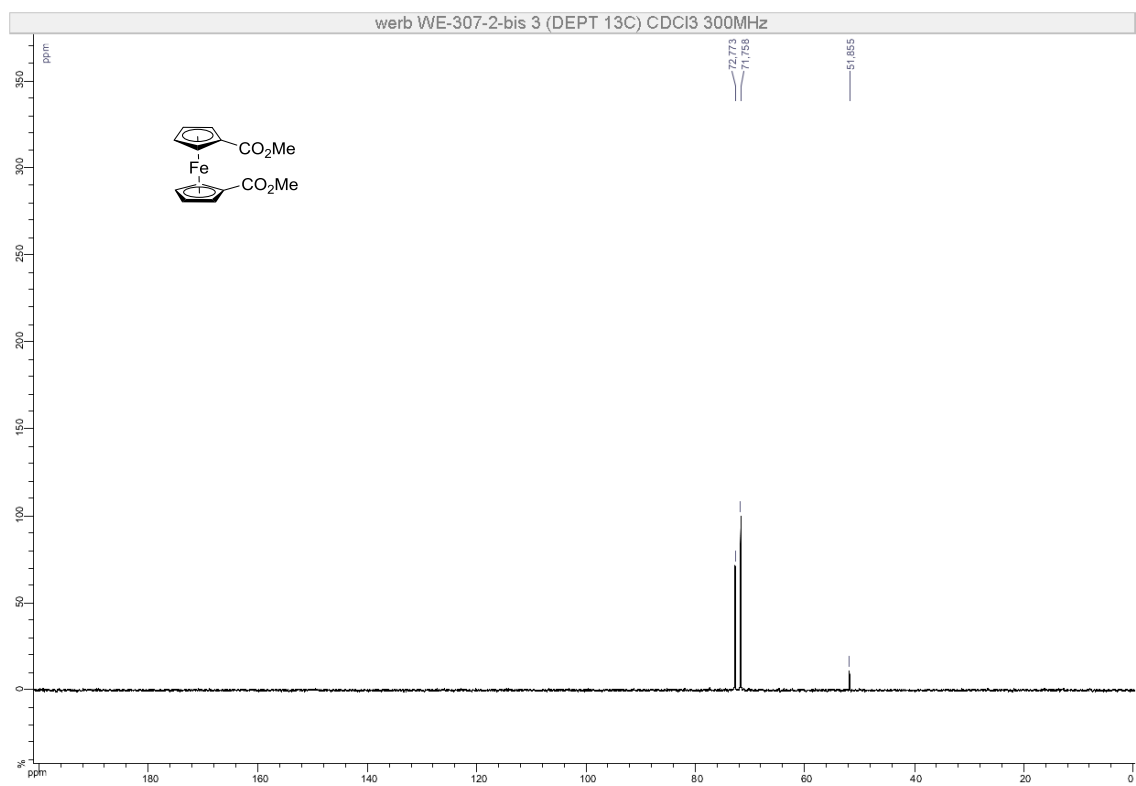
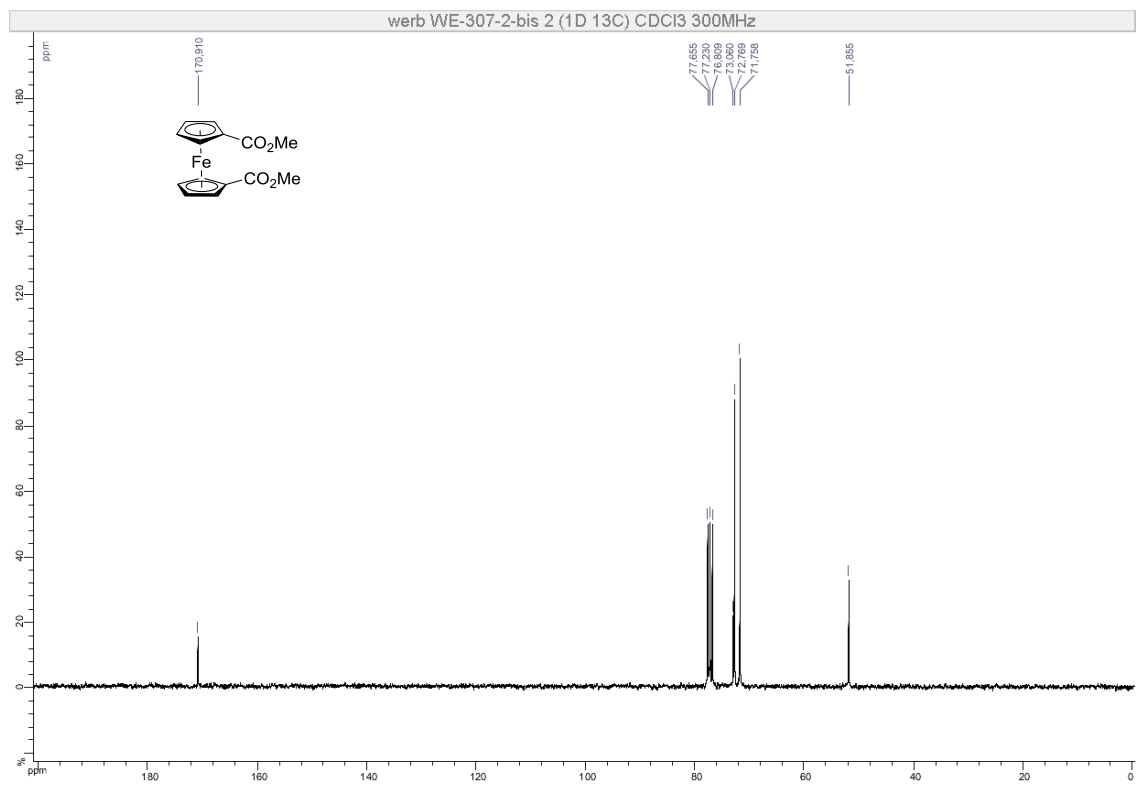




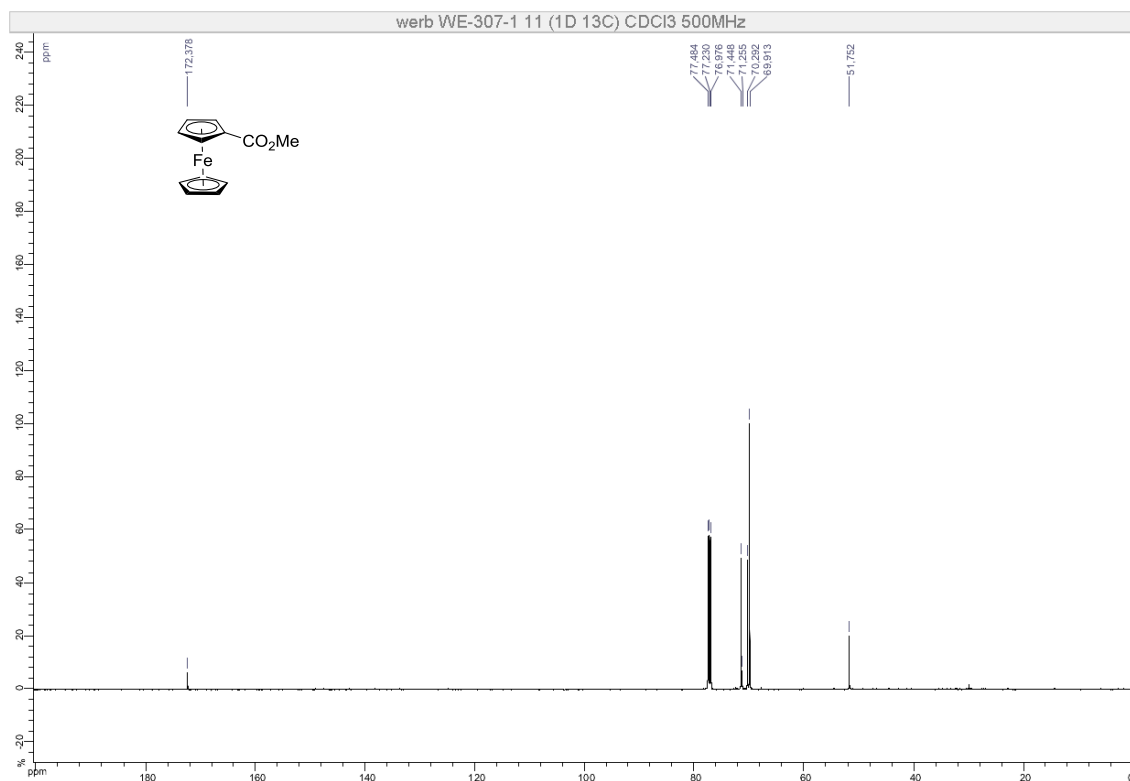
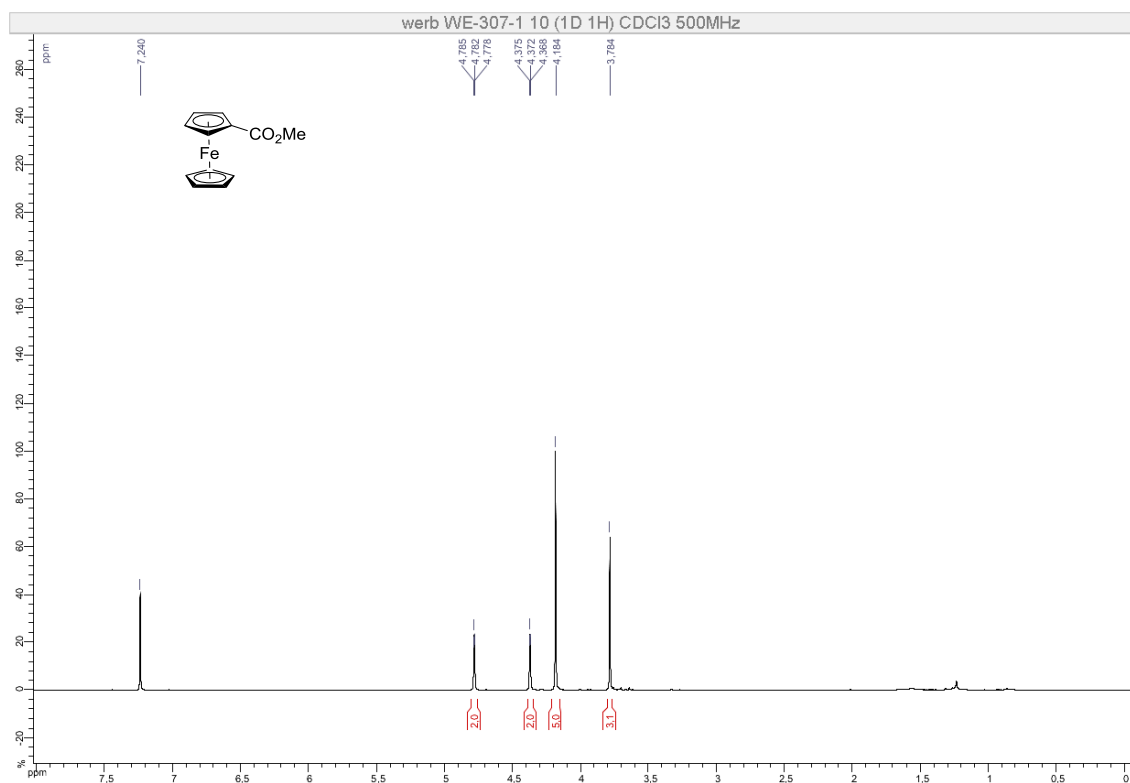


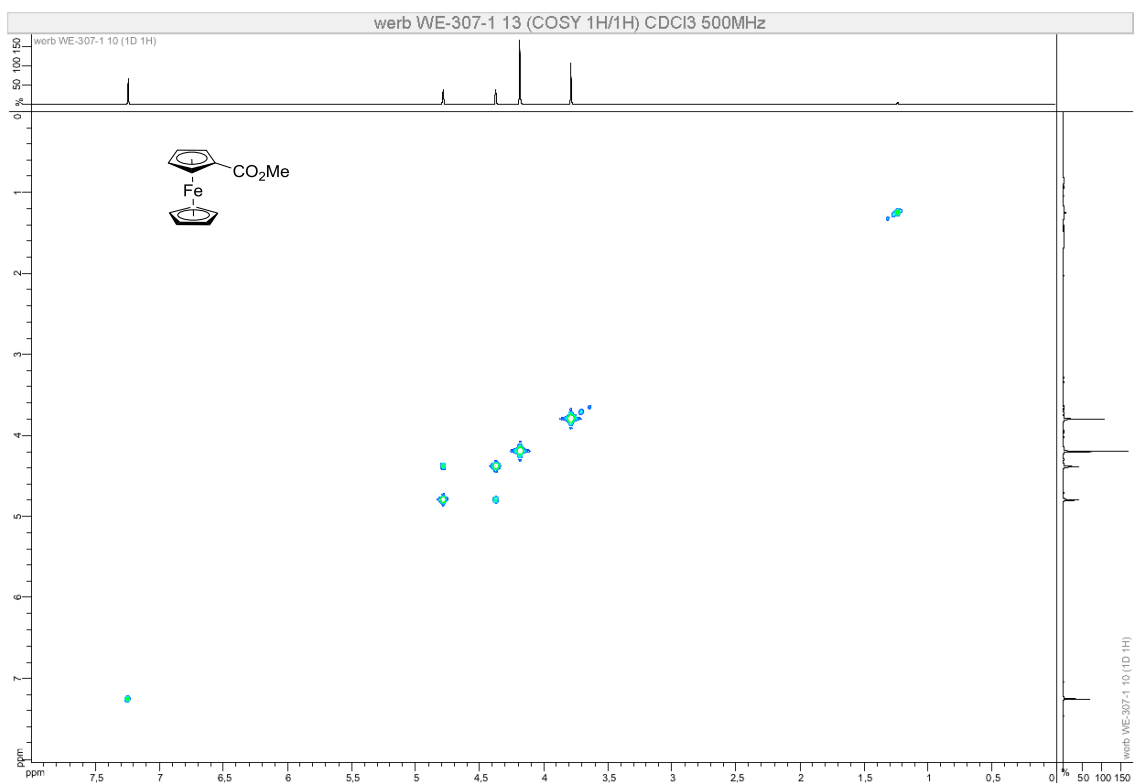
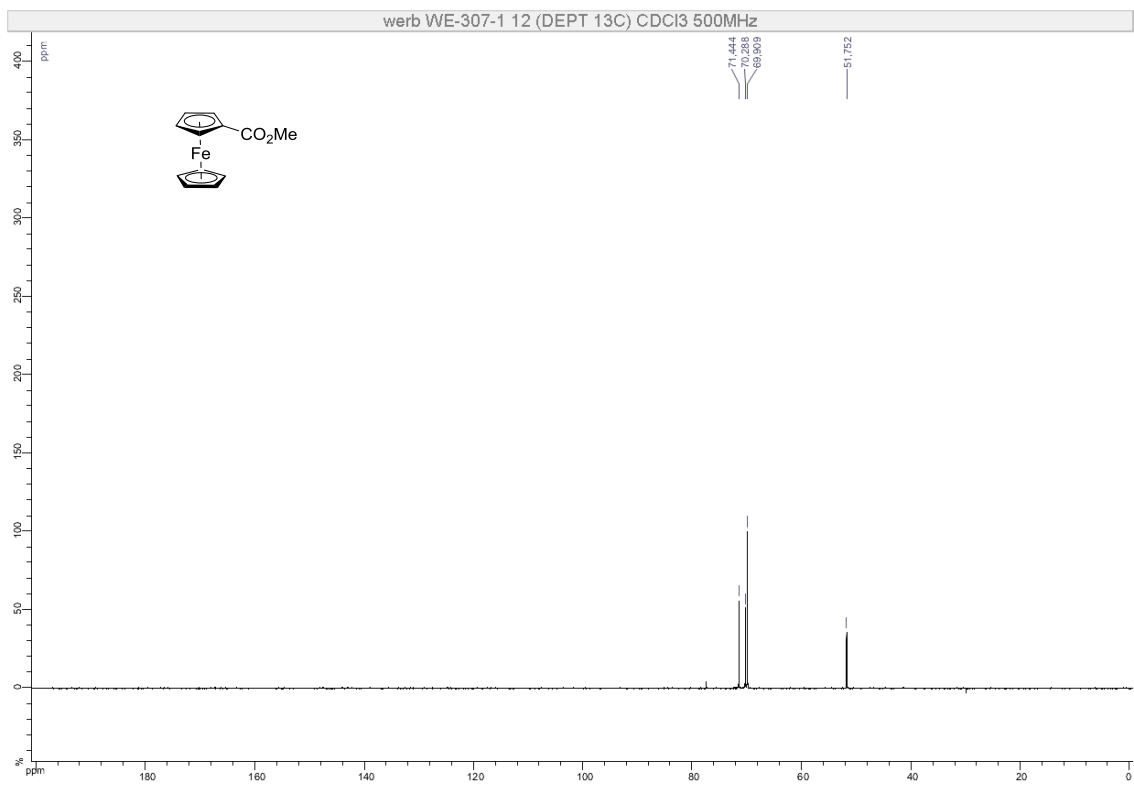
Dimethyl ferrocene-1,1'-dicarboxylate – SII

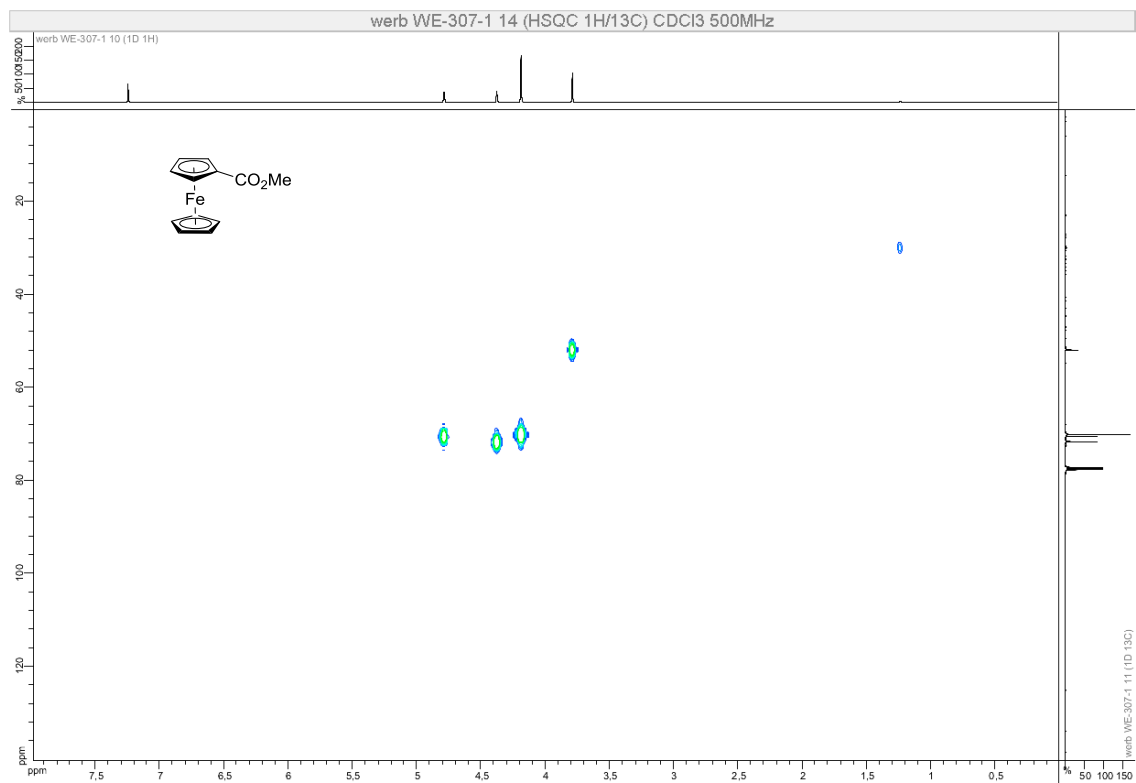




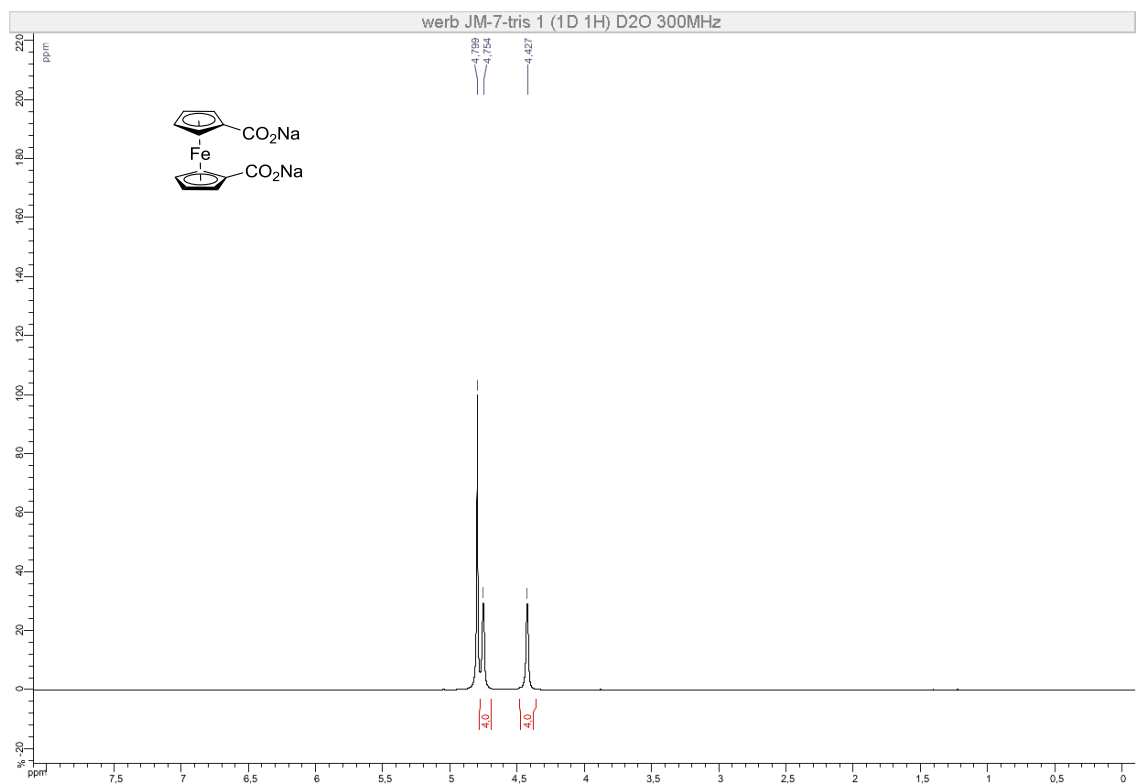
Methyl ferrocene carboxylate – SI2

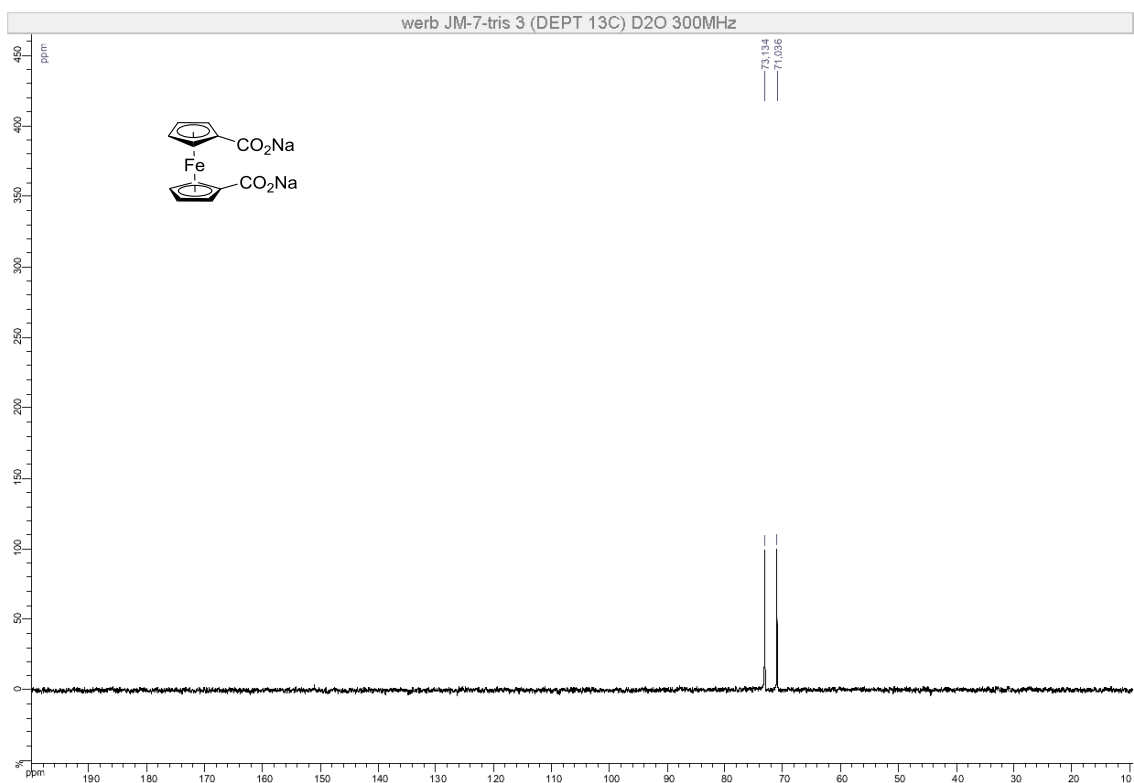
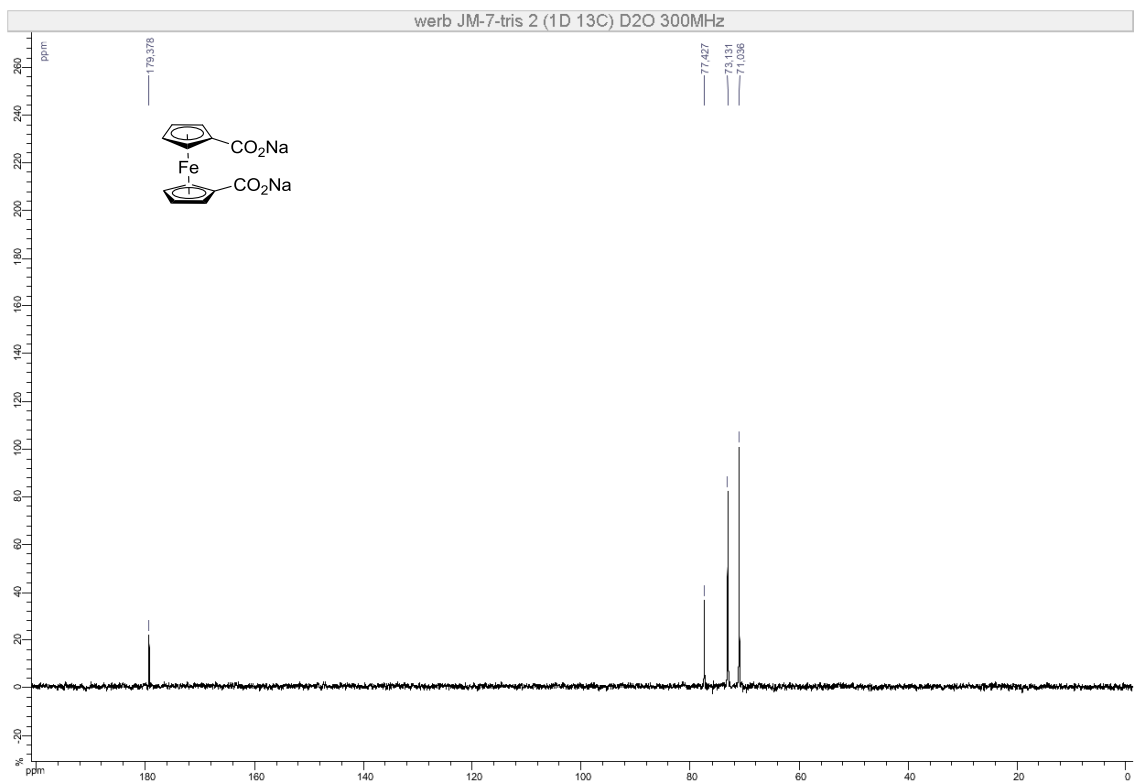






Sodium ferrocene-1,1'-dicarboxylate – SI3





(9H-Fluoren-9-yl)methanol – SI4

