

Electronic Supplementary Information

Molecular hybridization strategy on the design, synthesis, and structural characterization of ferrocene-*N*-acyl hydrazones as immunomodulatory agents

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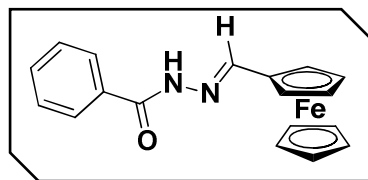
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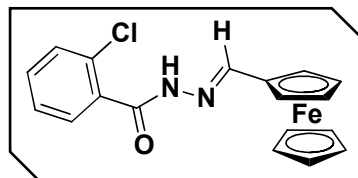
Characterization of the ferrocenyl-*N*-acyl hydrazones **SintMed(141-156)**

(*E*)-*N'*-(Ferrocenylmethylidene)benzohydrazide **SintMed141**



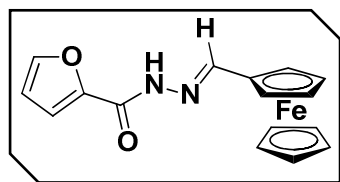
R_f 0.50 (AcOEt/Hexanes 1:1), red powder, yield 93%, mp 178.8-180.5 °C (from dioxane/H₂O 1:1); IR (KBr, ν_{max} cm⁻¹): 3441, 3226 (CONH), 3063 (Ar CH), 1646 (C=O), 1607 (C=C), 1557 (C=N); ¹H NMR (400 MHz; DMSO-*d*₆, δ H ppm): 11.5 (s, 1H, CONH), 8.29 (s, 1H, N=CH), 7.89 (d, 2H, ³*J* = 6.9 Hz, Ar H-2,6), 7.57 (d, 1H, ³*J* = 6.8 Hz, Ar H-4), 7.52 (d, 2H, ³*J* = 6.8 Hz, Ar H-3,5), 4.66 (s, 2H, N=CH-Cp H-2,5), 4.46 (s, 2H, N=CH-Cp H-3,4), 4.24 (s, 5H, Cp-H); ¹³C NMR (100 MHz; DMSO-*d*₆, δ C ppm): 162.3 (1C, C=O), 149.0 (1C, N=CH), 133.6 (1C, Ar C-1), 131.3 (1C, Ar C-4), 128.3 (2C, Ar C-3,5), 127.4 (2C, Ar C-2,6), 78.8 (1C, N=CH-Cp C-1), 70.1 (2C, N=CH-Cp C-3,4), 68.9 (5C, Cp), 67.5 (2C, N=CH-Cp C-2,5); Anal Calcd for C₁₈H₁₆FeN₂O: C, 65.08; H, 4.86; N, 8.43; Found: C, 65.01; H, 4.80; N, 8.51.

(*E*)-*N'*-(Ferrocenylmethylidene)-2-chlorobenzohydrazide **SintMed142**



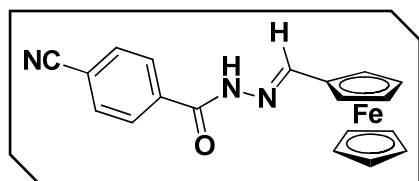
R_f 0.56 (AcOEt/Hexanes 1:1), red powder, yield 91%, mp 156.8-158.1 °C (from dioxane/H₂O 1:1); IR (KBr, ν_{max} cm⁻¹): 3181 (CONH), 2993 (Aliphatic CH), 1641 (C=O), 1598 (C=C), 1547 (C=N); ¹H NMR (400 MHz; DMSO-*d*₆, δ H ppm, \approx 1.8:1 Rotamers mixture): 11.65 (s, CONH minor), 11.57 (s, 1H, CONH), 8.12 (s, 1H, N=CH), 7.88 (s, N=CH), 7.55-7.41 (m, 4H, Ar and minor), 4.66 (s, 2H, N=CH-Cp H-2,5), 4.46 (s, 2H, N=CH-Cp H-3,4), 4.34 (s, N=CH-Cp H-2,5 minor), 4.31 (s, N=CH-Cp H-3,4 minor), 4.23 (s, 5H, Cp-H), 4.15 (s, Cp-H minor); ¹³C NMR (100 MHz; DMSO-*d*₆, δ C ppm, \approx 1.8:1 Rotamers mixture): 167.8 (CONH minor), 161.7 (1C, CONH), 149.1 (1C, N=CH), 144.5 (N=CH minor), 136.1 (Ar C-1 minor), 135.3 (1C, Ar C-1), 131.1, 130.3, 130.2, 129.8, 129.6, 129.2, 128.7, 128.5, 127.1, 126.7 (5C, Ar and minor), 78.8 (N=CH-Cp C-1 minor), 78.5 (1C, N=CH-Cp C-1), 70.2 (2C, N=CH-Cp C-3,4), 69.7 (N=CH-Cp C-3,4 minor), 68.9 (5C, Cp), 68.8 (5C, Cp minor), 67.6 (2C, N=CH-Cp C-2,5), 67.1 (2C, N=CH-Cp C-2,5 minor); Anal Calcd for C₁₈H₁₅FeN₂ClO: C, 58.97; H, 4.12; N, 7.64; Found: C, 58.86; H, 4.18; N, 7.54.

(*E*)-*N'*-(Ferrocenylmethylidene)furan-2-ylcarbohydrazide **SintMed143**



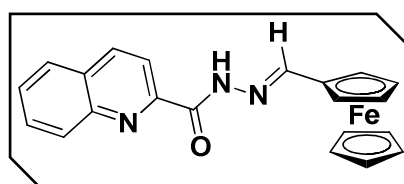
R_f 0.46 (AcOEt/Hexanes 1:1), dark red powder, yield 91%, mp 220.8-222.5 °C (from from dioxane/H₂O 1:1); IR (KBr, ν_{\max} cm⁻¹): 3215 (CONH), 2925 (Aliphatic CH), 1651 (C=O), 1606 (C=C); ¹H NMR (300 MHz; DMSO-*d*₆, δ H ppm): 11.5 (s, 1H, CONH), 8.28 (s, 1H, N=CH); 7.92 (s, 1H, Furyl H-5), 7.25 (s, 1H, Furyl H-3), 6.68 (s, 1H, Furyl H-4), 4.64 (s, 2H, N=CH-Cp H-2,5), 4.44 (s, 2H, N=CH-Cp H-3,4), 4.22 (s, 5H, Cp-H); ¹³C NMR (75 MHz; DMSO-*d*₆, δ C ppm): 153.6 (1C, CONH), 149.1 (1C, N=CH), 146.8 (1C, Furyl C-2), 145.4 (1C, Furyl C-5), 114.3 (1C, Furyl C-3), 111.9 (1C, Furyl C-4), 78.7 (1C, N=CH-Cp C-1), 70.1 (2C, N=CH-Cp C-3,4), 68.9 (5C, Cp), 67.5 (2C, N=CH-Cp C-2,5); Anal Calcd for C₁₆H₁₄FeN₂O₂: C, 59.66; H, 4.38; N, 8.70; Found: C, 59.57; H, 4.45; N, 8.78.

(*E*)-*N'*-(Ferrocenylmethylidene)-4-cyanobenzohydrazide **SintMed144**



R_f 0.50 (AcOEt/Hexanes 1:1), red powder, yield 98%, mp 236.0-237.9 °C (from from dioxane/H₂O 1:1); IR (KBr, ν_{\max} cm⁻¹): 3354, 3229 (CONH), 3090 (Ar CH), 2227 (C≡N), 1650 (C=O), 1611 (C=C), 1565 (C=N); ¹H NMR (300 MHz; DMSO-*d*₆, δ H ppm): 11.8 (s, 1H, CONH), 8.31 (s, 1H, N=CH), 8.05 (br s, 2H, Ar), 8.02 (br s, 2H, Ar), 4.67 (s, 2H, N=CH-Cp H-2,5), 4.45 (s, 2H, N=CH-Cp H-3,4), 4.22 (s, 5H, Cp-H); ¹³C NMR (75 MHz; DMSO-*d*₆, δ C ppm): 160.9 (1C, CONH), 150.2 (1C, N=CH), 137.6 (1C, Ar C-1), 132.4 (2C, Ar), 128.3 (2C, Ar), 118.2 (1C, CN), 113.7 (1C, Ar C-4), 78.4 (1C, N=CH-Cp C-1), 70.3 (2C, N=CH-Cp C-3,4), 68.9 (5C, Cp), 67.6 (2C, N=CH-Cp C-2,5); Anal Calcd for C₁₉H₁₅FeN₃O: C, 63.89; H, 4.23; N, 11.76; Found: C, 63.99; H, 4.18; N, 11.71.

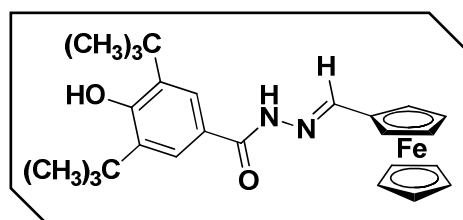
(*E*)-*N'*-(Ferrocenylmethylidene)quinolin-2-ylcarbohydrazide **SintMed145**



R_f 0.66 (AcOEt/Hexanes 1:1), red powder, yield 91%, mp 227.1-228.7 °C (from from dioxane/H₂O 1:1); IR (KBr, ν_{\max} cm⁻¹): 3238 (CONH), 3050 (Ar CH), 1664 (C=O), 1600 (C=C), 1533 (C=N); ¹H NMR (400 MHz; DMSO-*d*₆, δ H ppm): 11.9 (s, 1H, CONH), 8.60 (d, 1H, ³*J* = 8.4 Hz, Quinoline H-4), 8.52 (s, 1H, N=CH),

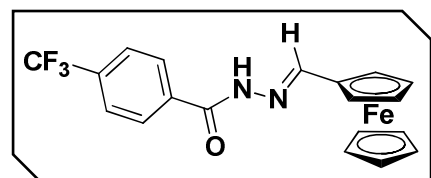
8.21 (d, 1H, $^3J = 8.0$ Hz, Quinoline H-3), 8.20 (d, 1H, $^3J = 8.0$ Hz, Quinoline H-8), 8.11 (d, 1H, $^3J = 8.4$ Hz, Quinoline H-5), 7.92 (t, 1H, $^3J = 7.2$ Hz, Quinoline H-7), 7.75 (t, 1H, $^3J = 7.6$ Hz, Quinoline H-6), 4.69 (s, 2H, N=CH-Cp H-2,5), 4.48 (s, 2H, N=CH-Cp H-3,4), 4.27 (s, 5H, Cp-H); ^{13}C NMR (100 MHz; DMSO- d_6 , δC ppm): 159.7 (1C, C=O), 150.6 (1C, N=CH), 150.0 (1C, Quinoline C-2), 145.8 (1C, Quinoline C-8a), 137.9 (1C, Quinoline C-4), 130.5 (1C, Quinoline C-7), 129.1 (1C, Quinoline C-8), 128.8 (1C, Quinoline C-4a), 128.12 (1C, Quinoline C-5), 128.09 (1C, Quinoline C-6), 118.9 (1C, Quinoline C-3), 78.7 (1C, N=CH-Cp C-1), 70.2 (2C, N=CH-Cp C-3,4), 69.0 (5C, Cp), 67.6 (2C, N=CH-Cp C-2,5); Anal Calcd for $\text{C}_{21}\text{H}_{17}\text{FeN}_3\text{O}$: C, 65.82; H, 4.47; N, 10.96; Found: C, 65.75; H, 4.52; N, 11.03.

(*E*)-*N'*-(Ferrocenylmethylidene)-3,5-*tert*-butyl-4-hydroxybenzohydrazide **SintMed146**



R_f 0.76 (AcOEt/Hexanes 1:1), red powder, yield 97%, mp 256.2-258.4 °C (dec, from from dioxane/ H_2O 1:1); IR (KBr, ν_{max} cm^{-1}): 3627, 3610 (br OH), 3507, 3223 (CONH), 3082 (Ar CH), 2912 (Aliphatic CH), 1640 (C=O), 1607 (C=C), 1556 (C=N); ^1H NMR (400 MHz; DMSO- d_6 , δH ppm): 11.3 (s, 1H, CONH), 8.29 (s, 1H, N=CH), 7.63 (s, 3H, OH and Ar H-2,6), 4.64 (s, 2H, N=CH-Cp H-2,5), 4.43 (s, 2H, N=CH-Cp H-3,4), 4.22 (s, 5H, Cp-H), 1.42 (s, 18H, 2x t Bu); ^{13}C NMR (100 MHz; DMSO- d_6 , δC ppm): 163.3 (1C, C=O), 156.9 (1C, Ar C-4), 148.2 (1C, N=CH), 138.3 (2C, Ar C-3,5), 124.8 (1C, Ar C-1), 124.2 (2C, Ar C-2,6), 79.2 (1C, N=CH-Cp C-1), 69.9 (2C, N=CH-Cp C-3,4), 68.9 (5C, Cp), 67.4 (2C, N=CH-Cp C-2,5), 34.5 (2C, t Bu), 30.1 (6C, t Bu); Anal Calcd for $\text{C}_{26}\text{H}_{32}\text{FeN}_2\text{O}_2$: C, 67.83; H, 7.01; N, 6.08; Found: C, 67.89; H, 6.94; N, 6.13.

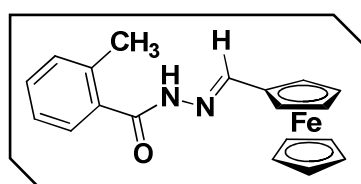
(*E*)-*N'*-(Ferrocenylmethylidene)-4-(trifluoromethyl)benzohydrazide **SintMed147**



R_f 0.74 (AcOEt/Hexanes 1:1), red powder, yield 99%, mp 220.9-222.5 °C (from dioxane/ H_2O 1:1); IR (KBr, ν_{max} cm^{-1}): 3355, 3201 (CONH), 3083, 3053 (Ar CH), 1657 (C=O), 1608 (C=C), 1564 (C=N); ^1H NMR (400 MHz; DMSO- d_6 , δH ppm): 11.7 (s, 1H, CONH), 8.32 (s, 1H, N=CH), 8.10 (d, 2H, $^3J = 5.2$ Hz, Ar H-2,6), 7.90 (d, 2H, $^3J = 6.0$ Hz, Ar H-3,5), 4.68 (s, 2H, N=CH-Cp H-2,5), 4.47 (s, 2H, N=CH-Cp H-3,4), 4.24 (s, 5H, Cp-H); ^{13}C NMR (100 MHz; DMSO- d_6 , δC ppm): 161.1 (1C, C=O), 150.0 (1C,

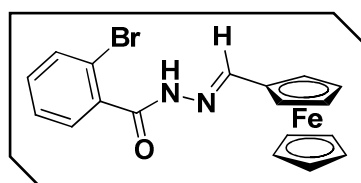
N=CH), 137.4 (1C, Ar C-1), 131.3 (q, 1C, $^2J_{FC} = 31$ Hz, Ar C-4), 128.3 (2C, Ar C-2,6), 125.3 (2C, Ar C-3,5), 126.1 (q, 1C, $^1J_{FC} = 200$ Hz, CF₃), 78.5 (1C, N=CH-Cp C-1), 70.2 (2C, N=CH-Cp C-3,4), 68.9 (5C, Cp), 67.6 (2C, N=CH-Cp C-2,5); ^{19}F NMR (376 MHz; DMSO-*d*₆, δF ppm): -61.2 (s, 1F, CF₃); Anal Calcd for C₁₉H₁₅FeN₂F₃O: C, 57.03; H, 3.78; N, 7.00; Found: C, 56.99; H, 3.83; N, 7.03.

(*E*)-*N'*-(Ferrocenylmethylidene)-2-methylbenzohydrazide **SintMed148**



R_f 0.55 (AcOEt/Hexanes 1:1), red powder, yield 93%, mp 207.9-209.8 °C (from dioxane/H₂O 1:1); IR (KBr, ν_{max} cm⁻¹): 3174 (CONH), 3056 (Ar CH), 2991 (Aliphatic CH), 1643 (C=O), 1600 (C=C), 1559 (C=N); ^1H NMR (400 MHz; DMSO-*d*₆, δH ppm, $\approx 7:3$ Rotamers mixture): 11.4 (s, 1H, CONH and minor), 8.15 (s, 1H, N=CH), 7.89 (s, N=CH minor), 7.43-7.29 (m, 4H, Ar H-3,4,5,6 and minor), 4.64 (s, 2H, N=CH-Cp H-2,5), 4.44 (s, 2H, N=CH-Cp H-3,4), 4.36 (s, N=CH-Cp H-2,5 minor), 4.31 (s, N=CH-Cp H-3,4 minor), 4.23 (s, 5H, Cp-H), 4.17 (s, Cp-H minor), 2.38 (s, 3H, CH₃), 2.30 (s, CH₃ minor); ^{13}C NMR (100 MHz; DMSO-*d*₆, δC ppm, $\approx 7:3$ Rotamers mixture): 170.5 (CONH minor), 164.4 (1C, CONH), 148.4 (1C, N=CH), 144.0 (N=CH minor), 136.1, 135.6, 135.4, 134.4, 130.4, 129.6, 129.4, 128.7, 127.24, 127.17, 125.4, 124.9 (6C, Ar and minor), 78.9 (N=CH-Cp C-1 minor), 78.8 (1C, N=CH-Cp C-1), 70.0 (2C, N=CH-Cp C-3,4), 69.6 (N=CH-Cp C-3,4 minor), 68.8 (5C, Cp), 68.7 (Cp minor), 67.4 (2C, N=CH-Cp C-2,5), 67.0 (N=CH-Cp C-2,5 minor), 19.23 (CH₃ minor), 19.18 (1C, CH₃); Anal Calcd for C₁₉H₁₈FeN₂O: C, 65.92; H, 5.24; N, 8.09; Found: C, 65.99; H, 5.20; N, 8.15.

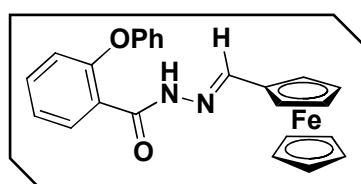
(*E*)-*N'*-(Ferrocenylmethylidene)-2-bromobenzohydrazide **SintMed149**



R_f 0.70 (AcOEt/Hexanes 1:1), red powder, yield 87%, mp 163.4-165.8 °C (dec, from dioxane/H₂O 1:1); IR (KBr, ν_{max} cm⁻¹): 3190 (CONH), 3055 (Ar CH), 1656 (C=O), 1600 (C=C), 1562 (C=N); ^1H NMR (400 MHz; DMSO-*d*₆, δH ppm, $\approx 2:1$ Rotamers mixture): 11.6 (s, CONH minor), 11.5 (s, 1H, CONH), 8.11 (s, 1H, N=CH), 7.87 (s, N=CH minor), 7.71 (d, 1H, $^3J = 8.0$ Hz, Ar H-6), 7.68 (d, $^3J = 8.0$ Hz, Ar H-6 minor), 7.54-7.37 (m, 3H, Ar H-3,4,5 and minor), 4.66 (s, 2H, N=CH-Cp H-2,5), 4.46 (s, 2H, $^3J = 2.8$ Hz, N=CH-Cp H-3,4), 4.34 (s, N=CH-Cp H-2,5 minor), 4.31 (s, N=CH-Cp H-3,4 minor), 4.24 (s,

5H, Cp-H), 4.16 (s, Cp-H minor); ^{13}C NMR (100 MHz; DMSO- d_6 , δC ppm): 162.5 (1C, CONH), 149.0 (1C, N=CH), 144.4 (N=CH minor), 137.5, 132.7, 131.9, 131.2, 130.2, 129.2, 128.5, 127.6, 127.1 (5C, Ar C-1,3,4,5,6 and minor), 119.4 (1C, Ar C-2), 78.9 (N=CH-Cp C-1 minor), 78.6 (1C, N=CH-Cp C-1), 70.2 (2C, N=CH-Cp C-3,4), 69.7 (N=CH-Cp C-3,4 minor), 68.91 (5C, Cp), 68.86 (Cp minor), 67.6 (2C, N=CH-Cp C-2,5), 67.1 (N=CH-Cp C-2,5 minor); Anal Calcd for $\text{C}_{18}\text{H}_{15}\text{FeN}_2\text{BrO}$: C, 52.59; H, 3.68; N, 6.81; Found: C, 52.52; H, 3.71; N, 6.90.

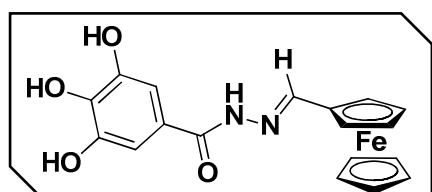
(E)-*N'*-(Ferrocenylmethylidene)-2-phenoxybenzohydrazide **SintMed150**



R_f 0.65 (AcOEt/Hexanes 1:1), red powder, yield 83%, mp 177.9-179.5 °C (dec, from dioxane/ H_2O 1:1); IR (KBr, ν_{max} cm^{-1}): 3308 (CONH), 3060 (Ar CH), 1661 (C=O), 1602 (C=C), 1541 (C=N); ^1H NMR (400 MHz; DMSO- d_6 , δH ppm, $\approx 7:3$

Rotamers mixture): 11.45 (s, CONH minor), 11.38 (s, 1H, CONH), 8.14 (s, 1H, N=CH), 7.84 (s, N=CH minor), 7.67-6.98 (m, 9H, Ar and OPh and minor), 4.62 (s, 2H, N=CH-Cp H-2,5), 4.42 (s, 2H, N=CH-Cp H-3,4), 4.39 (s, N=CH-Cp H-2,5 minor), 4.32 (s, N=CH-Cp H-3,4 minor), 4.20 (s, 5H, Cp-H), 4.12 (s, Cp-H minor); ^{13}C NMR (100 MHz; DMSO- d_6 , δC ppm, $\approx 7:3$ Rotamers mixture): 167.9 (CONH minor), 161.1 (1C, CONH), 156.5, 153.0 (2C, Ar), 148.4 (1C, N=CH), 144.2 (N=CH minor), 131.7, 130.4, 130.2, 129.8, 129.6, 128.8, 128.6, 127.5, 123.6, 123.4, 123.1, 122.9, 120.1, 119.1, 118.4, 118.3, 118.0 (10C, Ar, OPh and minor), 78.9 (N=CH-Cp C-1 minor), 78.7 (1C, N=CH-Cp C-1), 70.1 (2C, N=CH-Cp C-3,4), 69.7 (N=CH-Cp C-3,4 minor), 68.8 (5C, Cp), 68.7 (Cp minor), 67.5 (2C, N=CH-Cp C-2,5), 67.1 (N=CH-Cp C-2,5 minor); Anal Calcd for $\text{C}_{24}\text{H}_{20}\text{FeN}_2\text{O}_2$: C, 67.94; H, 4.75; N, 6.60; Found: C, 67.87; H, 4.82; N, 6.65.

(E)-*N'*-(Ferrocenylmethylidene)-3,4,5-trihydroxybenzohydrazide **SintMed151**

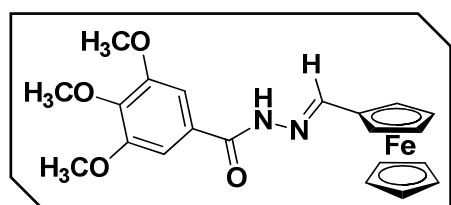


R_f 0.10 (AcOEt), red powder, yield 96%, mp 305.3-306.0 °C (dec, from dioxane/ H_2O 1:1); IR (KBr, ν_{max} cm^{-1}): 3552-3000 (br, OH), 3225 (CONH), 3084 (Ar CH), 1633 (C=O), 1608 (C=C), 1570 (C=N); ^1H NMR (300 MHz;

DMSO- d_6 , δH ppm): 11.2 (s, 1H, CONH), 9.13 (s, 2H, 3,5-OH), 8.77 (s, 1H, 4-OH), 8.23 (s, 1H, N=CH), 6.90 (s, 2H, Ar H-2,6), 4.62 (s, 2H, N=CH-Cp H-2,5), 4.42 (s, 2H, N=CH-Cp H-

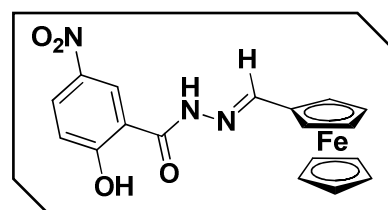
3,4), 4.21 (s, 5H, Cp-H); ^{13}C NMR (75 MHz; DMSO- d_6 , δC ppm): 162.5 (1C, C=O), 147.8 (1C, N=CH), 145.4 (2C, Ar C-3,5), 136.6 (1C, Ar C-4), 123.6 (1C, Ar C-1), 106.9 (2C, Ar C-2,6), 79.2 (1C, N=CH-Cp C-1), 69.9 (2C, N=CH-Cp C-3,4), 68.9 (5C, Cp), 67.4 (2C, N=CH-Cp C-2,5); Anal Calcd for $\text{C}_{18}\text{H}_{16}\text{FeN}_2\text{O}_4$: C, 56.87; H, 4.24; N, 7.37; Found: C, 56.82; H, 4.31; N, 7.32.

(E)-*N'*-(Ferrocenylmethylidene)-3,4,5-trimethoxybenzohydrazide **SintMed152**



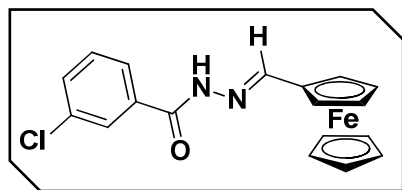
R_f 0.18 (AcOEt/Hexanes 1:1), red powder, yield 90%, mp 237.8-239.5 °C (dec, from dioxane/ H_2O 1:1); IR (KBr, ν_{max} cm^{-1}): 3235 (CONH), 3083 (Ar CH), 2942 (Aliphatic CH), 1646 (C=O), 1608 (C=C), 1582 (C=N); ^1H NMR (400 MHz, DMSO- d_6 , δH ppm): 11.4 (s, 1H, CONH), 8.32 (s, 1H, N=CH), 7.23 (s, 2H, Ar H-2,6), 4.66 (s, 2H, N=CH-Cp H-2,5), 4.45 (s, 2H, N=CH-Cp H-3,4), 4.23 (s, 5H, Cp-H), 3.86 (s, 6H, 3,5-OCH $_3$), 3.73 (s, 3H, 4-OCH $_3$); ^{13}C NMR (100 MHz, DMSO- d_6 , δC ppm): 161.8 (1C, C=O), 152.6 (2C, Ar C-3,5), 149.1 (1C, N=CH), 140.2 (1C, Ar C-4), 128.7 (1C, Ar C-1), 105.0 (2C, Ar C-2,6), 78.8 (1C, N=CH-Cp C-1), 70.1 (2C, N=CH-Cp C-3,4), 68.9 (5C, Cp), 67.5 (2C, N=CH-Cp C-2,5), 60.0 (1C, 4-OCH $_3$), (2C, 3,5-OCH $_3$); Anal Calcd for $\text{C}_{21}\text{H}_{22}\text{FeN}_2\text{O}_4$: C, 59.73; H, 5.25; N, 6.63; Found: C, 59.65; H, 5.22; N, 6.70.

(E)-*N'*-(Ferrocenylmethylidene)-3,4,5-trimethoxybenzohydrazide **SintMed153**



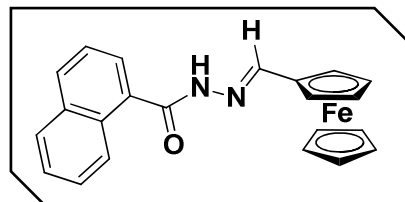
R_f 0.18 (AcOEt/Hexanes 1:1), yellow powder, yield 86%, mp 221.4-222.6 °C (dec, from dioxane/ H_2O 1:1); IR (KBr, ν_{max} cm^{-1}): 3379, 3328, 3255 (CONH, OH), 3095 (Ar CH), 1630 (C=O), 1558 (C=N); ^1H NMR (400 MHz; DMSO- d_6 , δH ppm, \approx 2:1 Rotamers mixture): 13.6 (s, 1H, CONH), 9.23 (s, 1H, Ar H-6), 9.11 (s, Ar H-6 minor), 8.37 and 8.35 (2s, 1H, Ar H-4 major and minor), 8.12 (s, 1H, N=CH), 7.34 (s, 1H, Ar H-3), 4.50 (s, 2H, N=CH-Cp H-2,5), 4.38 (s, 2H, N=CH-Cp H-3,4), 4.16 (s, 5H, Cp-H); ^{13}C NMR (100 MHz; DMSO- d_6 , δC ppm): 167.1 (1C, CONH), 149.0 (1C, N=CH), 136.1 (1C, Ar C-2), 134.4 (1C, Ar C-5), 128.1 (1C, Ar C-4), 127.4 (1C, Ar C-6), 126.3 (1C, Ar C-1), 120.9 (1C, Ar C-3), 78.7 (1C, N=CH-Cp C-1), 69.9 (2C, N=CH-Cp C-3,4), 68.8 (5C, Cp), 67.5 (2C, N=CH-Cp C-2,5); Anal Calcd for $\text{C}_{18}\text{H}_{15}\text{FeN}_3\text{O}_4$: C, 54.99; H, 3.85; N, 10.69; Found: C, 54.92; H, 3.84; N, 10.74.

(*E*)-*N*'-(Ferrocenylmethylidene)-3-chlorobenzohydrazide **SintMed154**



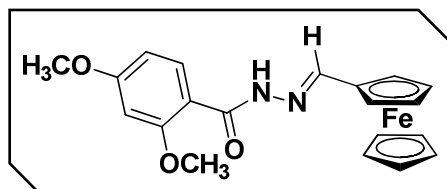
R_f 0.53 (AcOEt/Hexanes 3:7), red powder, yield 98%, mp 225.7-228.2 °C (dec, from dioxane/H₂O 1:1); IR (KBr, ν_{max} cm⁻¹): 3196 (CONH), 3063 (Ar CH), 1643 (C=O), 1608 (C=C), 1568 (C=N); ¹H NMR (400 MHz, DMSO-*d*₆, δ H ppm): 11.6 (s, 1H, CONH), 8.29 (s, 1H, N=CH), 7.95 (s, 1H, Ar H-2), 7.86 (d, 1H, ³*J* = 6.8 Hz, Ar H-6), 7.65 (d, 1H, ³*J* = 7.6 Hz, Ar H-4), 7.55 (t, 1H, ³*J* = 7.6 Hz, Ar H-5), 4.67 (s, 2H, N=CH-Cp H-2,5), 4.46 (s, 2H, N=CH-Cp H-3,4), 4.23 (s, 5H, Cp); ¹³C NMR (100 MHz, DMSO-*d*₆, δ C ppm): 160.8 (C=O), 149.7 (N=CH), 135.6 (1C, Ar C-3), 133.1 (1C, Ar C-1), 131.2 (1C, Ar C-4), 130.3 (1C, Ar C-5), 127.1 (1C, Ar C-2), 126.2 (1C, Ar C-6), 78.6 (1C, N=CH-Cp C-1), 70.2 (2C, N=CH-Cp C-3,4), 68.9 (5C, Cp), 67.5 (2C, N=CH-Cp C-2,5); Anal Calcd for C₁₈H₁₅FeN₂ClO: C, 58.97; H, 4.12; N, 7.64; Found: C, 59.04; H, 4.09; N, 7.58.

(*E*)-*N*'-(Ferrocenylmethylidene)-1-naphthylcarbohydrazide **SintMed155**



R_f 0.68 (AcOEt/Hexanes 1:1), red powder, yield 93%, mp 233.0-234.4 °C (dec, from dioxane/H₂O 1:1); IR (KBr, ν_{max} cm⁻¹): 3185 (CONH), 3035 (Ar CH), 2977, 2845 (Aliphatic CH), 1636 (C=O), 1617 (C=C), 1564 (C=N); ¹H NMR (400 MHz; DMSO-*d*₆, δ H ppm): 11.7 (s, 1H, CONH), 8.24-8.22 (m, 1H, Naphtyl), 8.20 (s, 1H, N=CH), 8.08 (d, 1H, ³*J* = 8.0 Hz, Naphtyl), 8.03-8.00 (m, 1H, Naphtyl), 7.74 (d, 1H, ³*J* = 7.2 Hz, Naphtyl), 7.61-7.58 (m, 3H, Naphtyl), 4.68 (s, 2H, N=CH-Cp H-2,5), 4.47 (s, 2H, N=CH-Cp H-3,4), 4.26 (s, 5H, Cp-H); ¹³C NMR (100 MHz; DMSO-*d*₆, δ C ppm): 163.9 (C=O), 148.9 (N=CH), 133.1, 133.0, 130.2, 130.0, 128.2, 126.8, 126.3, 125.6, 125.1, 124.9 (10C, Naphtyl), 78.8 (1C, N=CH-Cp C-1), 70.1 (2C, N=CH-Cp C-3,4), 68.9 (5C, Cp), 67.5 (2C, N=CH-Cp C-2,5); Anal Calcd for C₂₂H₁₈FeN₂O: C, 69.13; H, 4.75; N, 7.33; Found: C, 69.21; H, 4.73; N, 7.36.

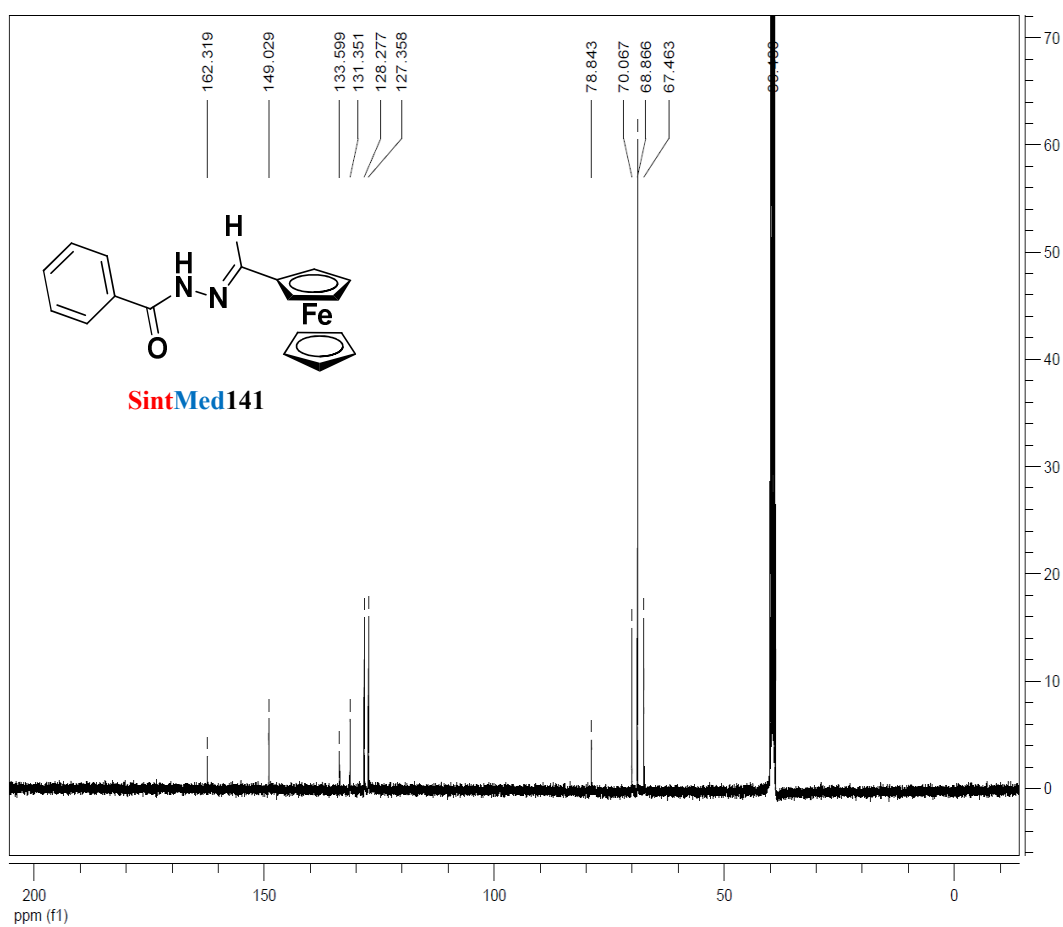
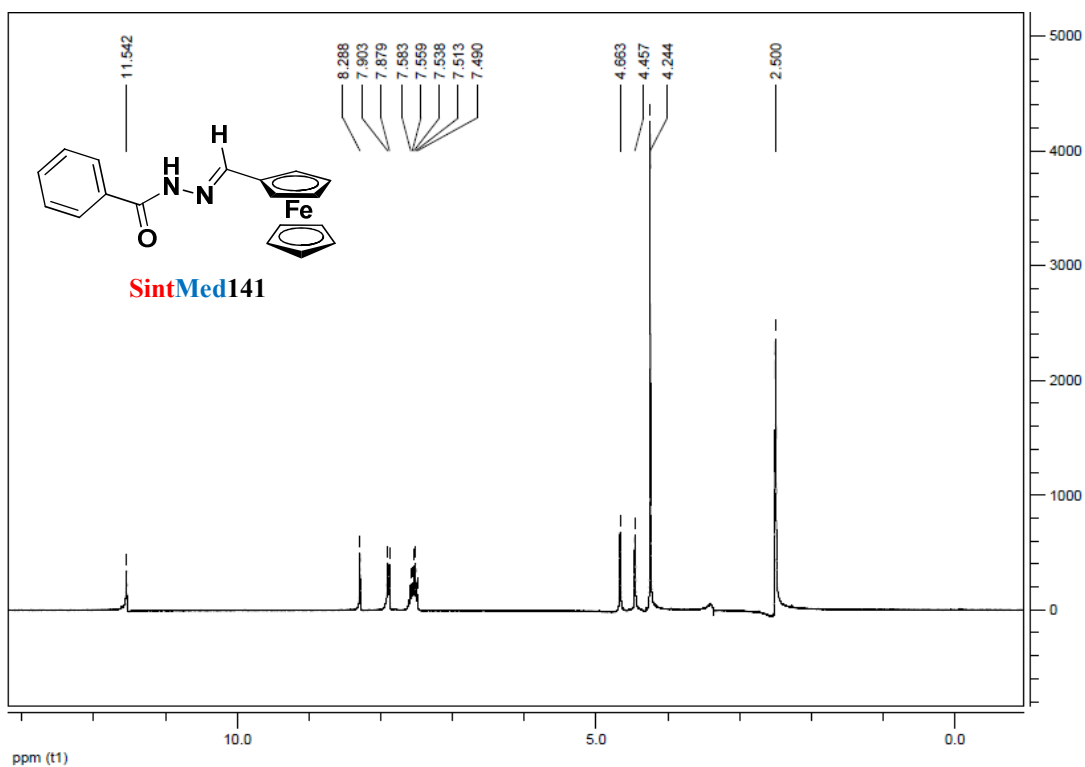
(*E*)-*N*'-(Ferrocenylmethylidene)-2,4-dimethoxybenzohydrazide **SintMed156**

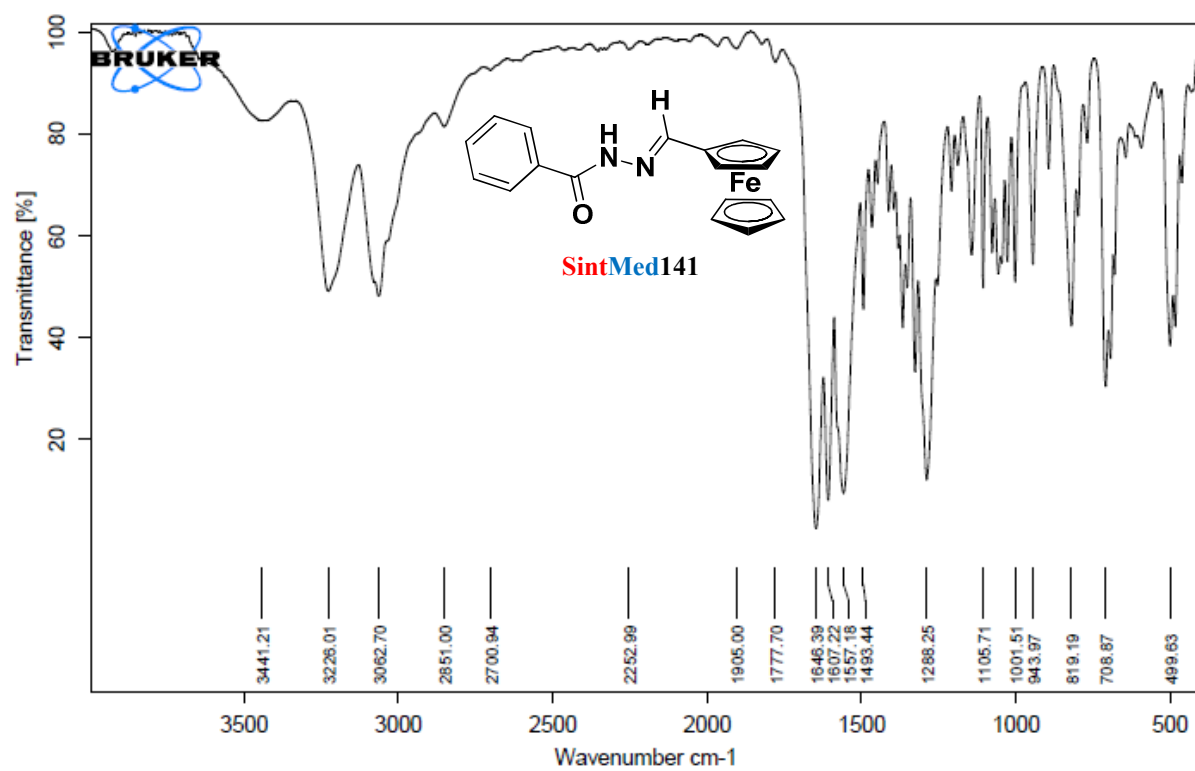


R_f 0.32 (AcOEt/Hexanes 1:1), red powder, yield 87%, mp 123.9-126.6 °C (dec, from dioxane/H₂O 1:1); IR

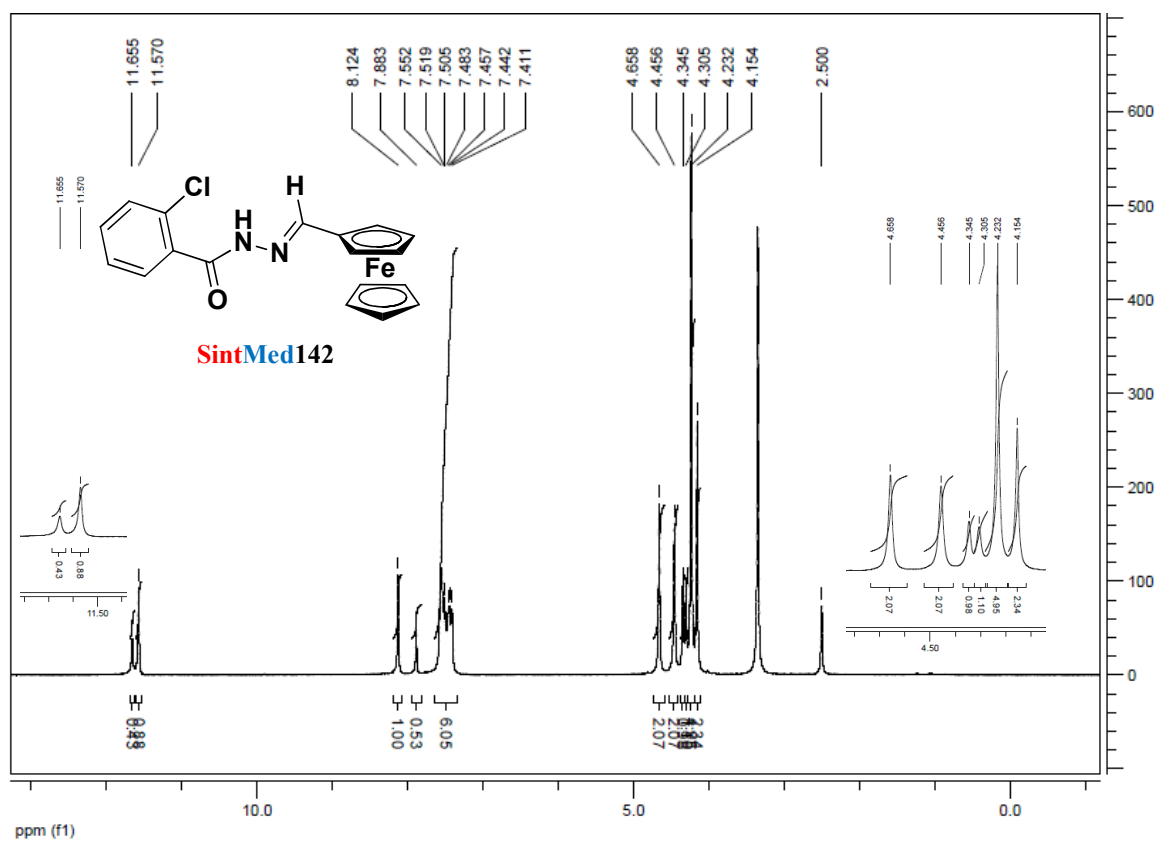
(KBr, ν_{\max} cm^{-1}): 3223 (CONH), 3083 (Ar CH), 2836 (Aliphatic CH), 1641 (C=O), 1603 (C=C), 1561 (C=N); ^1H NMR (400 MHz; $\text{DMSO-}d_6$, δH ppm): 11.4 (s, 1H, CONH), 8.30 (s, 1H, N=CH), 7.55 (d, 1H, $^3J = 8.0$ Hz, Ar H-5), 7.48 (s, 1H, Ar H-3), 7.07 (d, 1H, $^3J = 8.8$ Hz, Ar H-6), 4.65 (s, 2H, N=CH-Cp H-2,5), 4.44 (s, 2H, N=CH-Cp H-3,4), 4.23 (s, 5H, Cp-H), 3.84 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3); ^{13}C NMR (100 MHz; $\text{DMSO-}d_6$, δC ppm): 161.8 (C=O), 151.4 (1C, Ar C-4), 148.5 (1C, Ar C-2), 148.2 (N=CH), 125.6 (Ar C-1), 120.7 (1C, Ar C-5), 110.9 (1C, Ar C-6), 110.7 (1C, Ar C-3), 79.0 (1C, N=CH-Cp C-1), 70.0 (2C, N=CH-Cp C-3,4), 68.9 (5C, Cp), 67.4 (2C, N=CH-Cp C-2,5), 55.5 (2C, $2\times\text{OCH}_3$); Anal Calcd for $\text{C}_{20}\text{H}_{20}\text{FeN}_2\text{O}_3$: C, 61.24; H, 5.14; N, 7.14; Found: C, 61.16; H, 5.15; N, 7.09.

NMR and IR spectra of Fc-NAH **SintMed**(141-156)

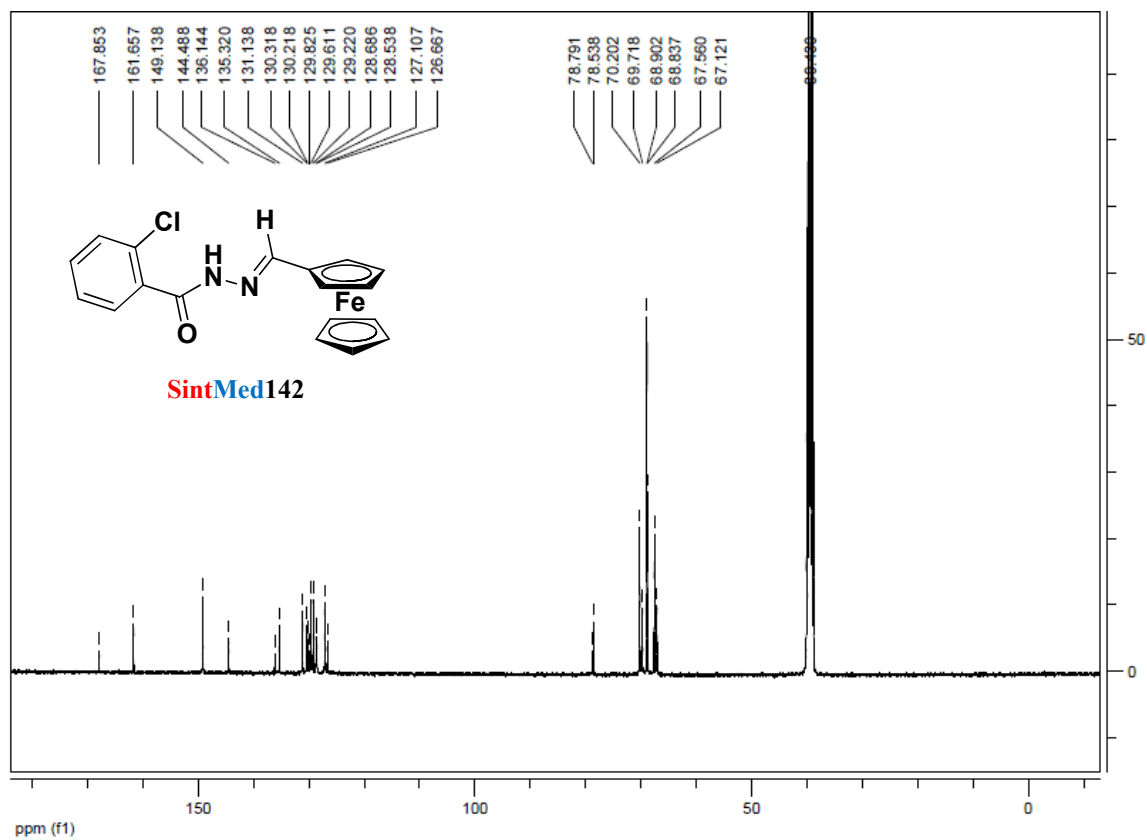




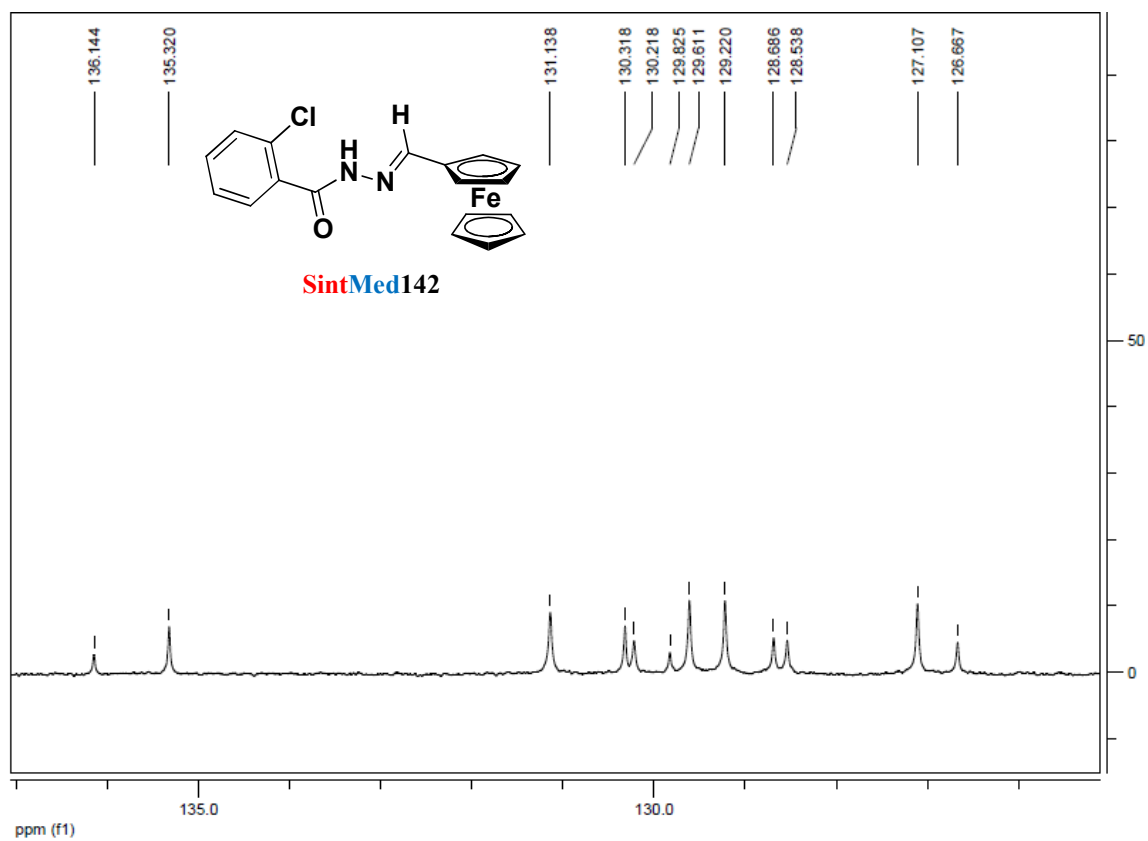
IR spectrum of SintMed141



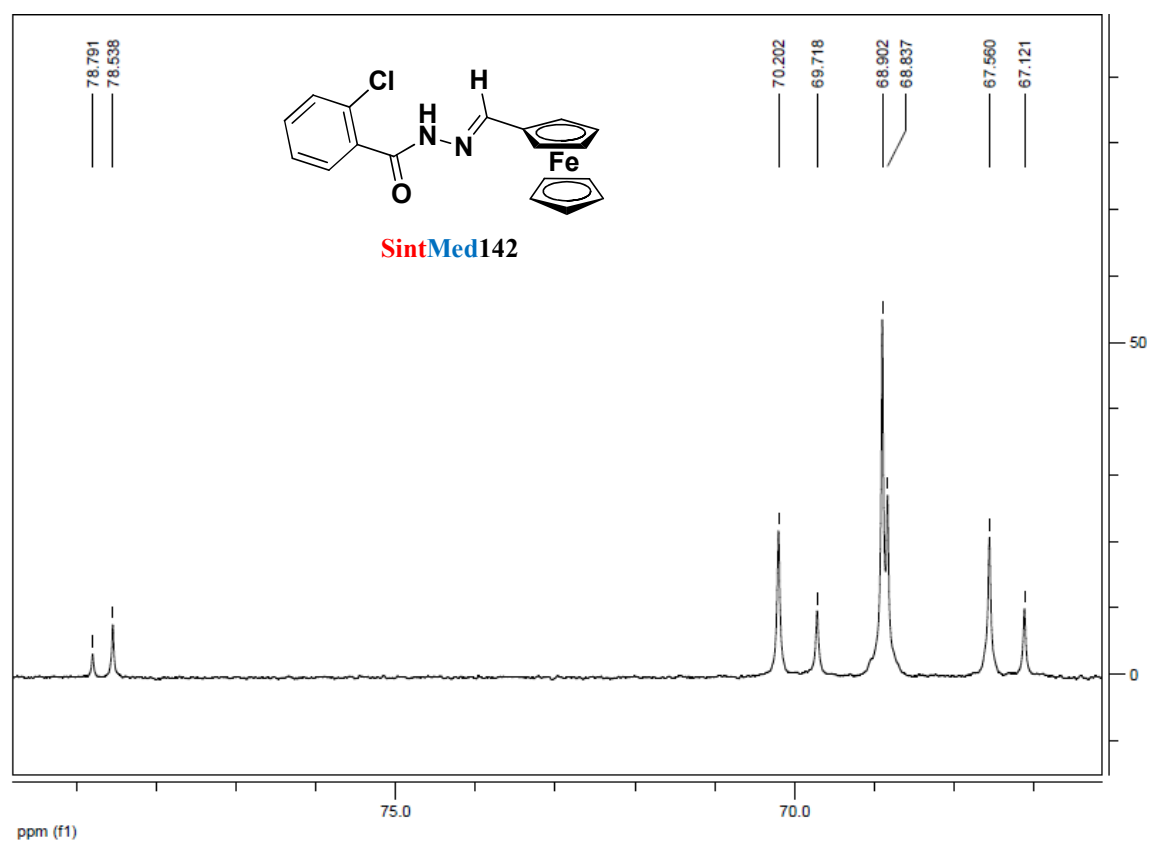
¹H NMR spectrum of **SintMed142** (400 MHz, DMSO-*d*₆)



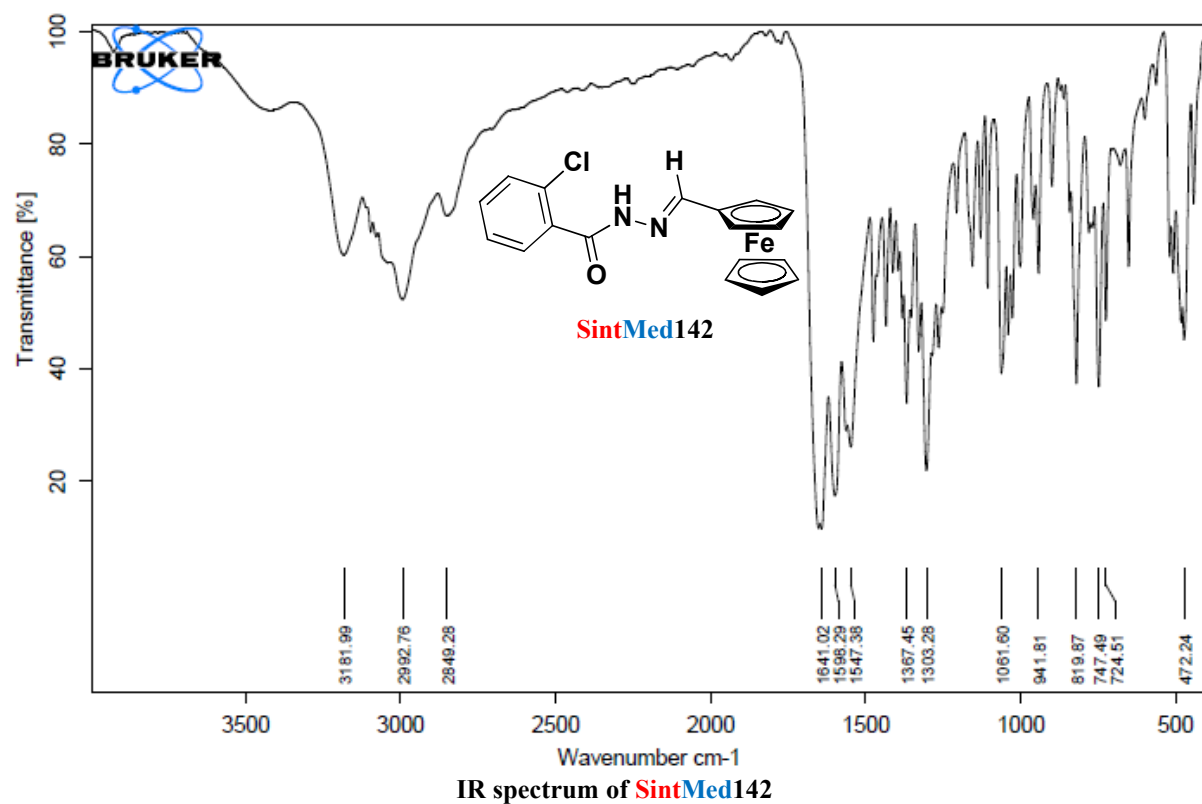
^{13}C NMR spectrum of SintMed142 (100 MHz, DMSO-*d*₆)

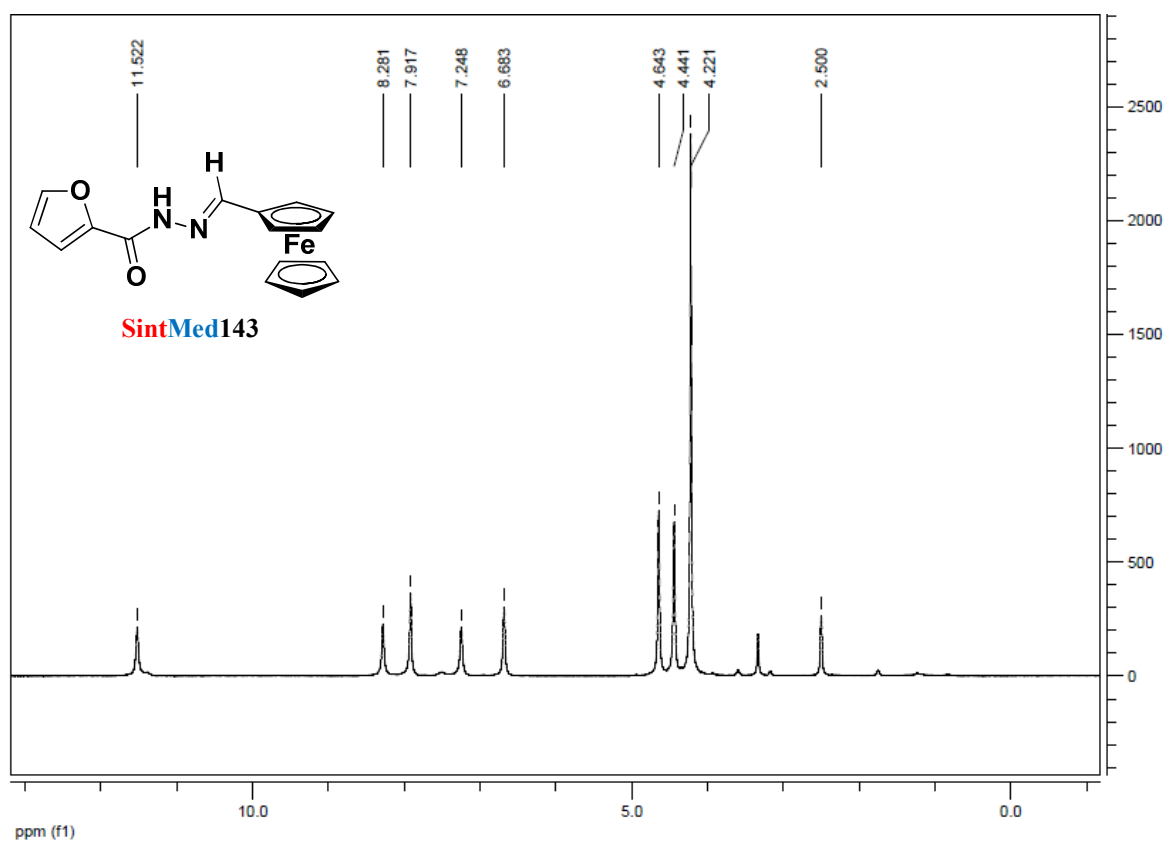


¹³C NMR spectrum expansion of SintMed142 (100 MHz, DMSO-*d*₆)

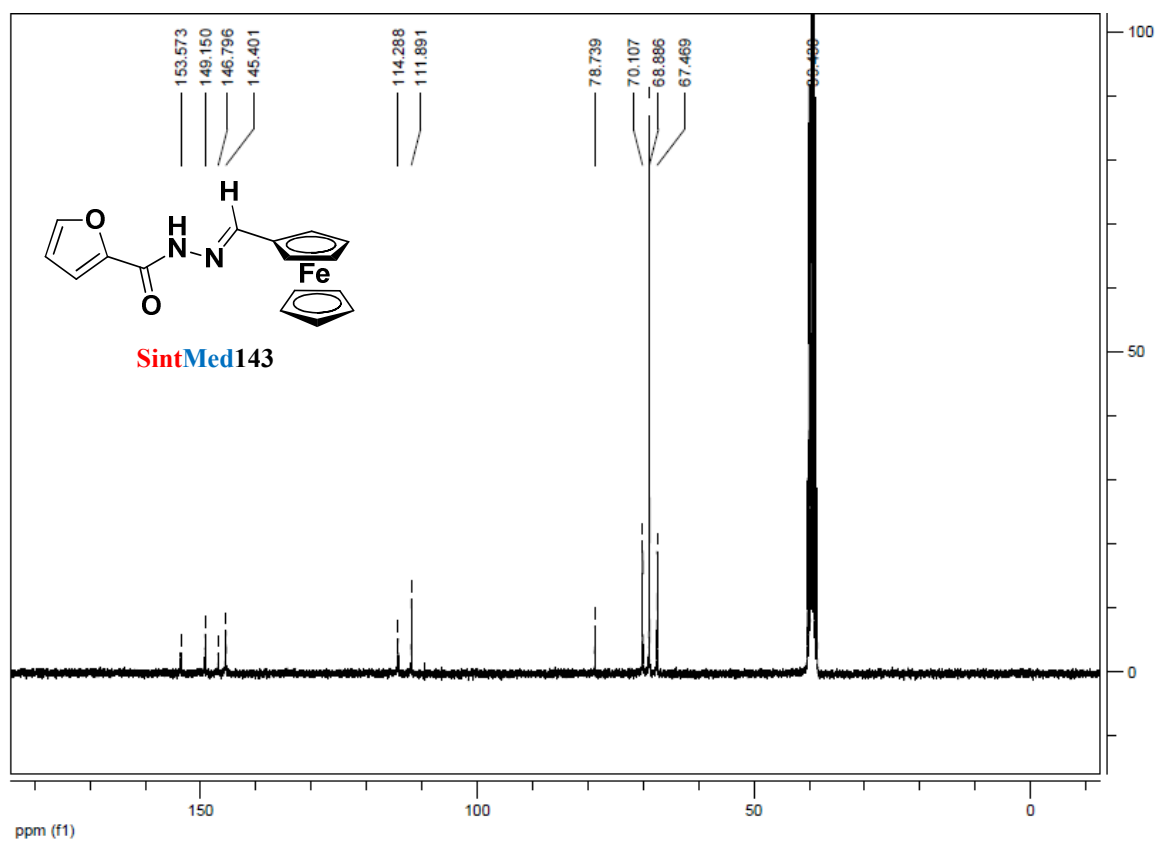


¹³C NMR spectrum expansion of SintMed142 (100 MHz, DMSO-*d*₆)

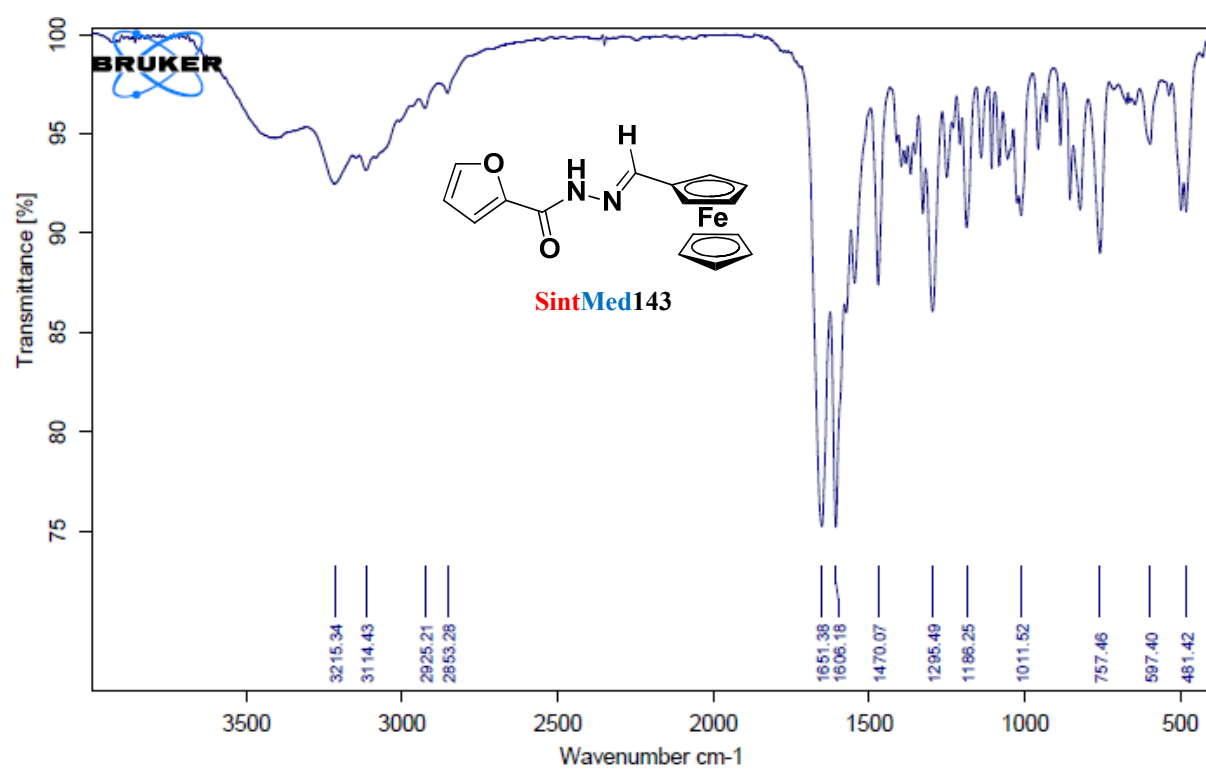




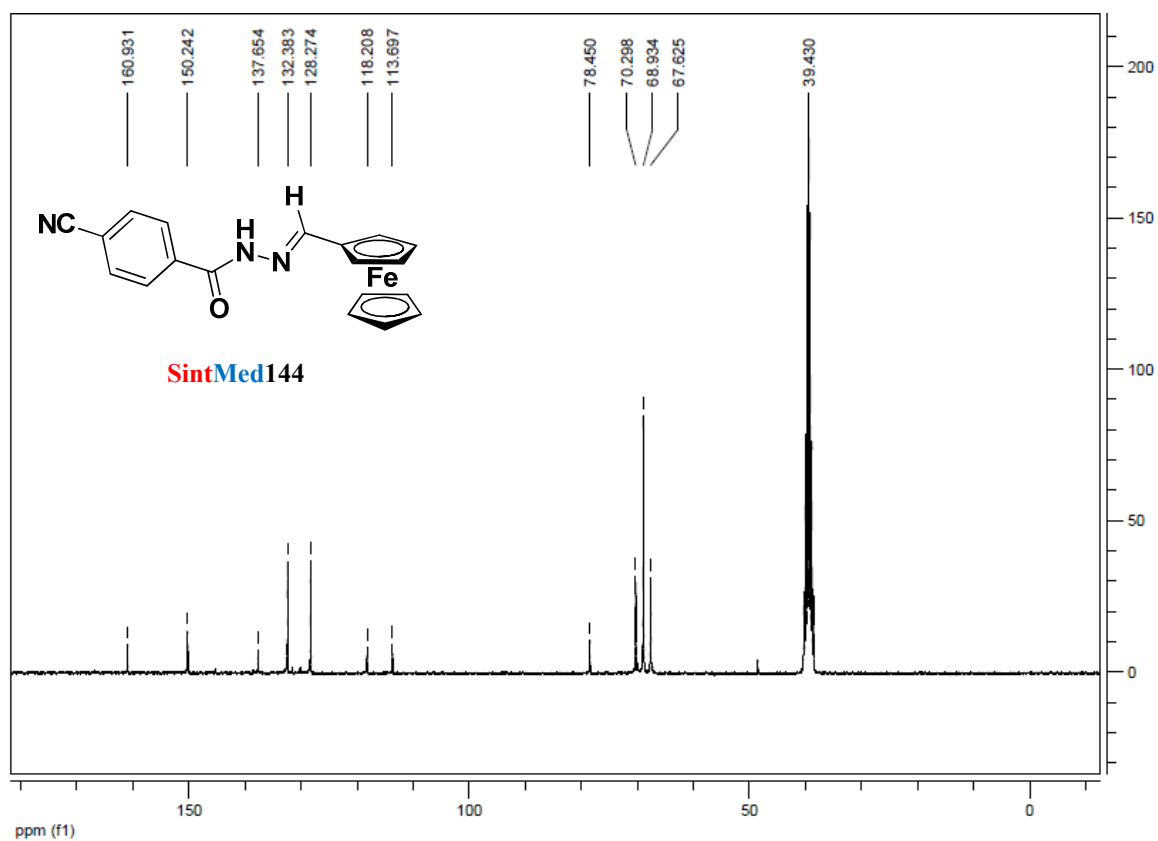
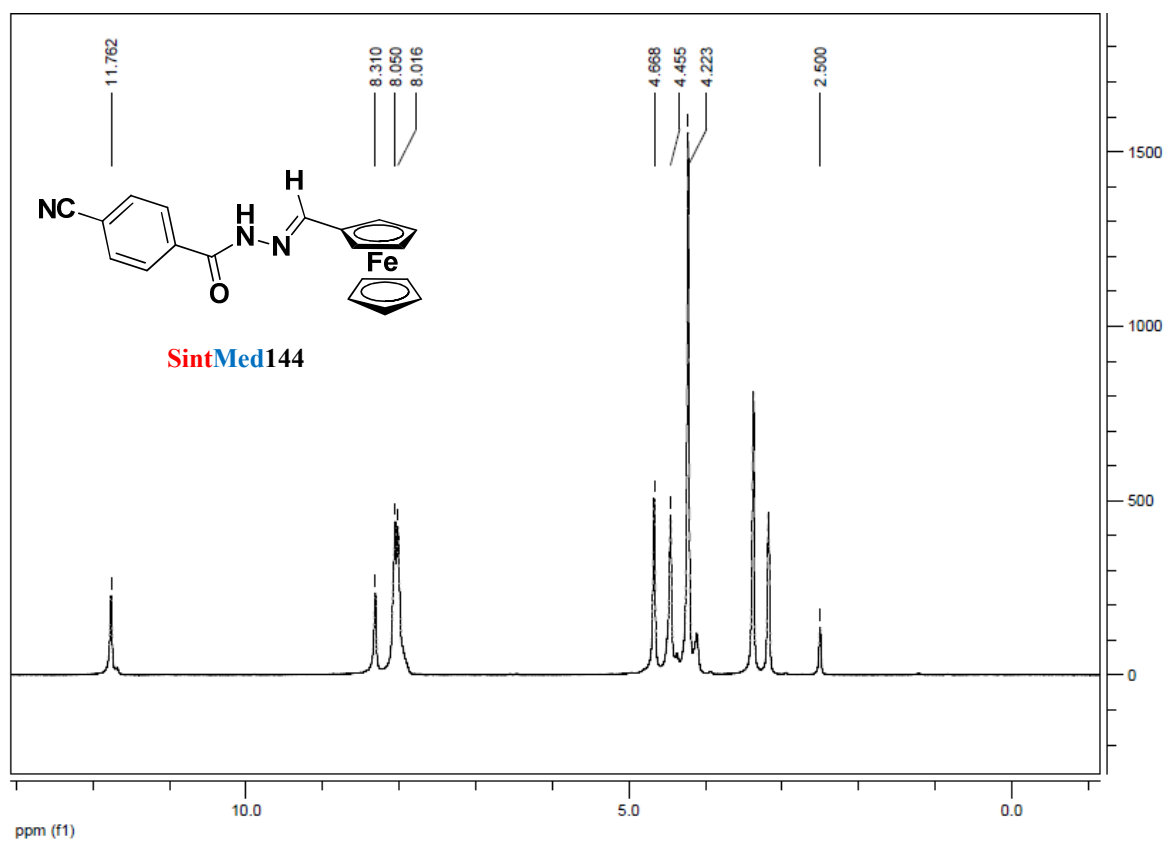
¹H NMR spectrum of **SintMed143** (300 MHz, DMSO-*d*₆)



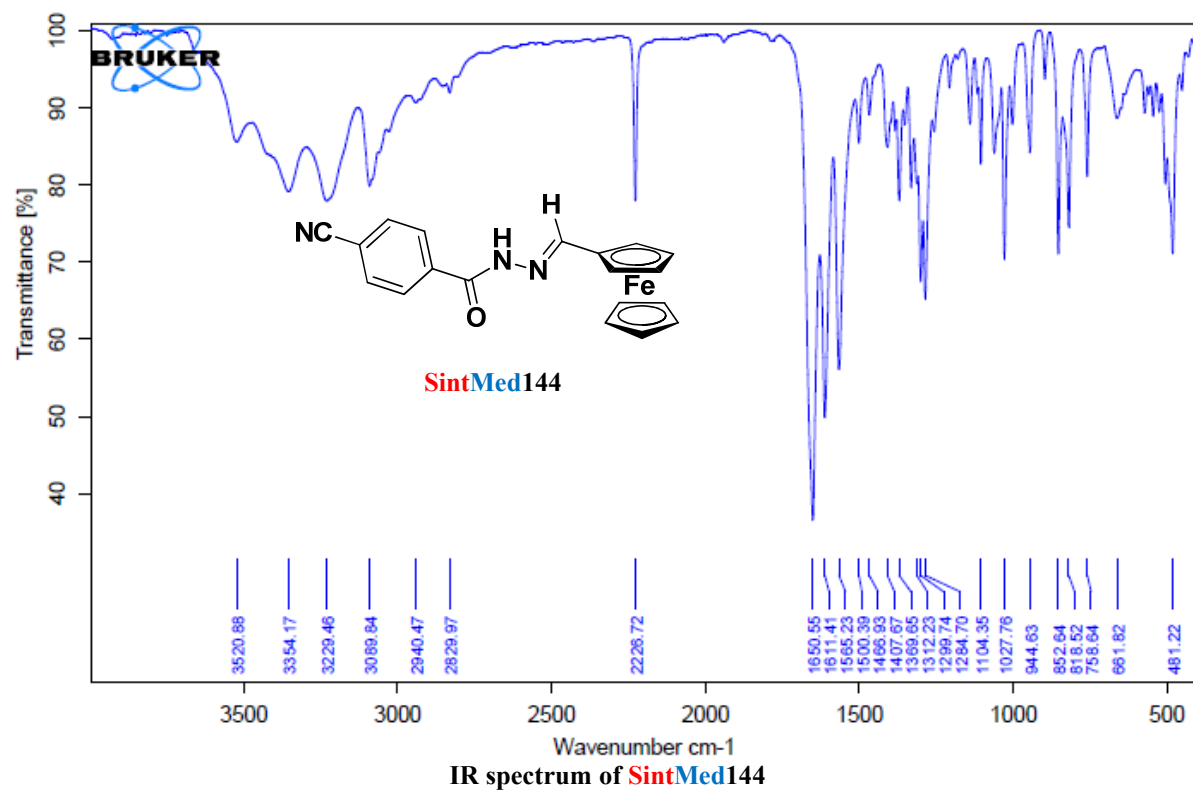
¹³C NMR spectrum of **SintMed143** (75 MHz, DMSO-*d*₆)

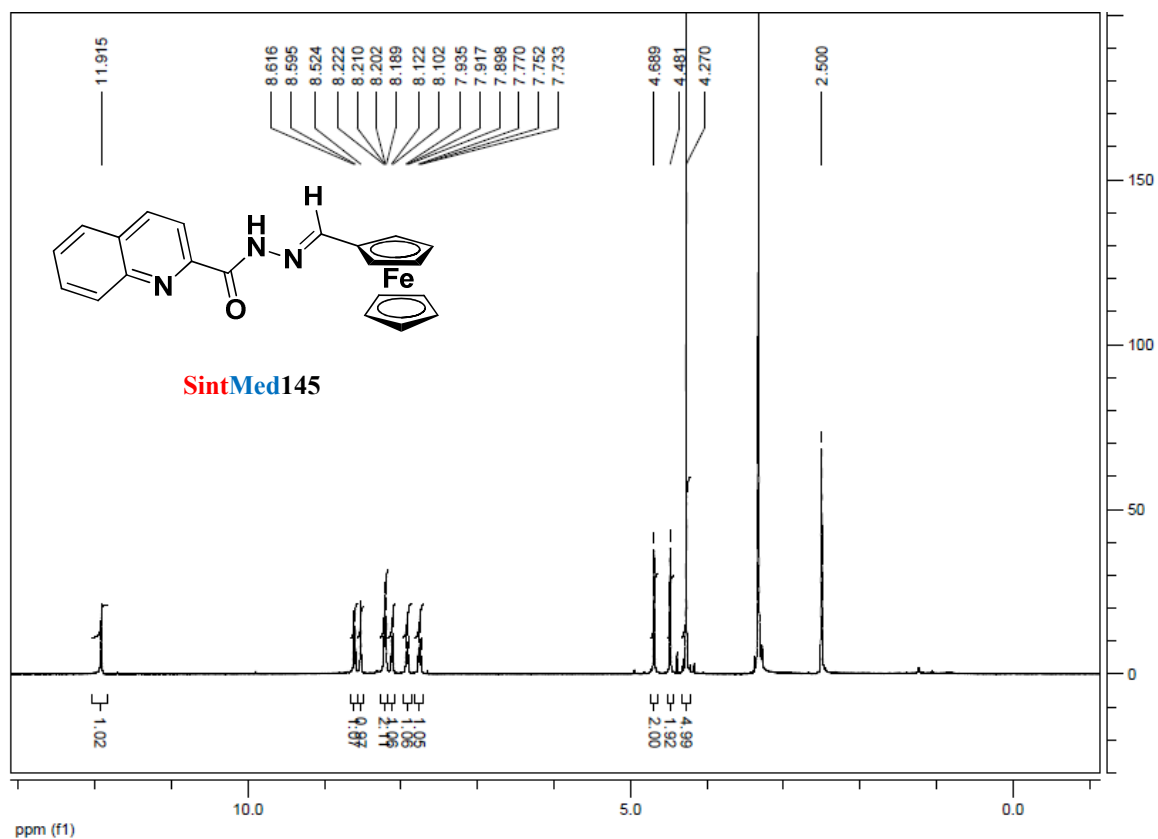


IR spectrum of SintMed143

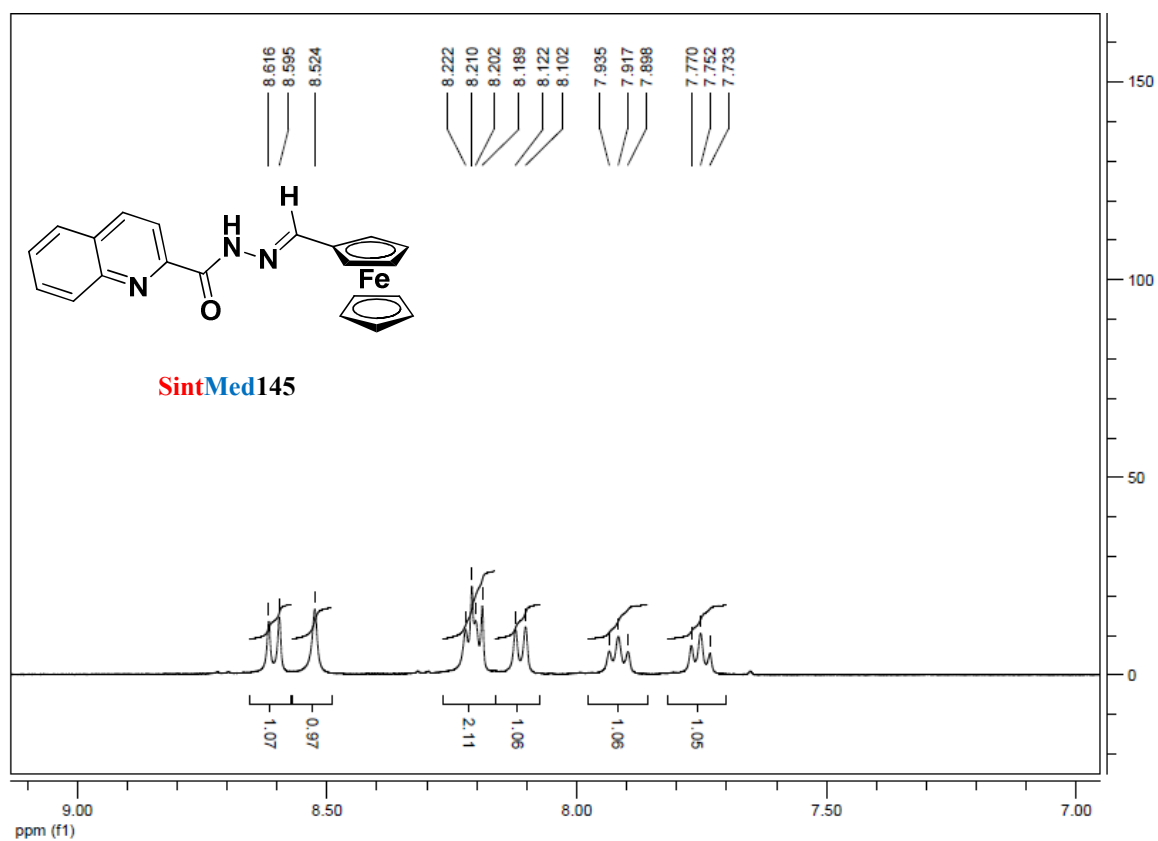


¹³C NMR spectrum of **SintMed144** (75 MHz, DMSO-*d*₆)

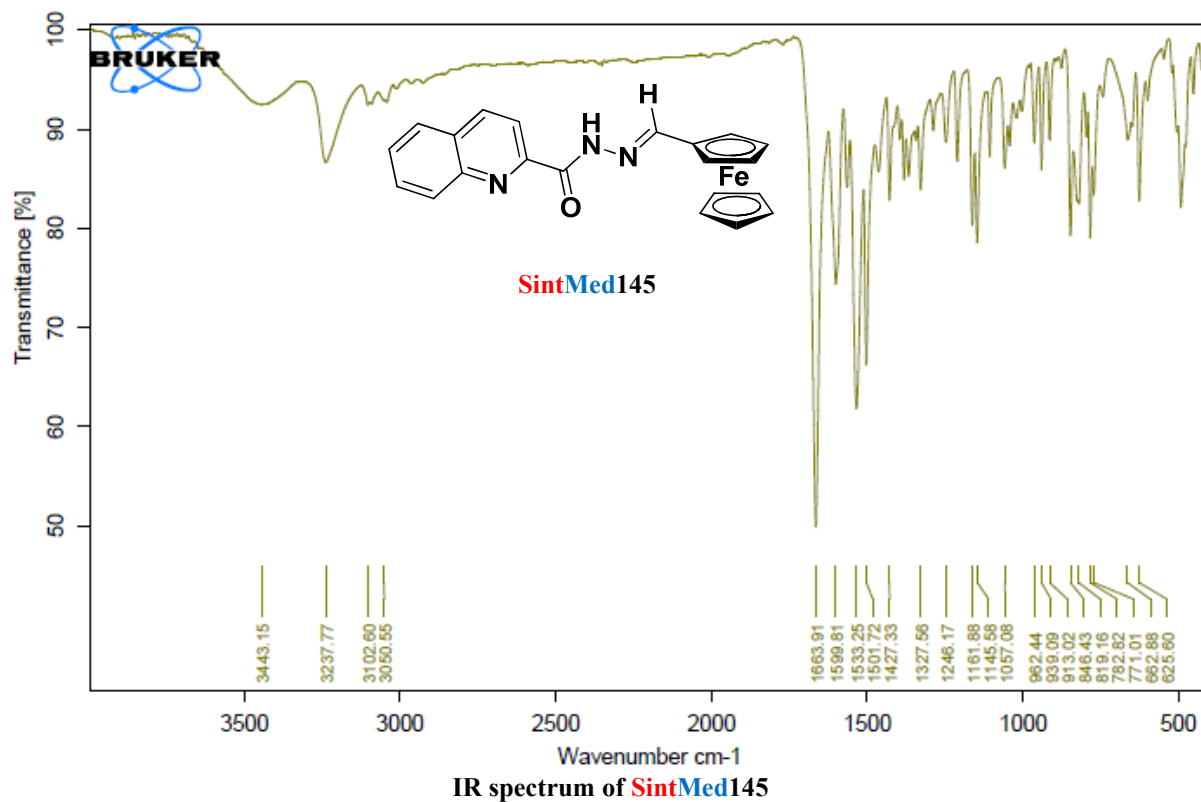
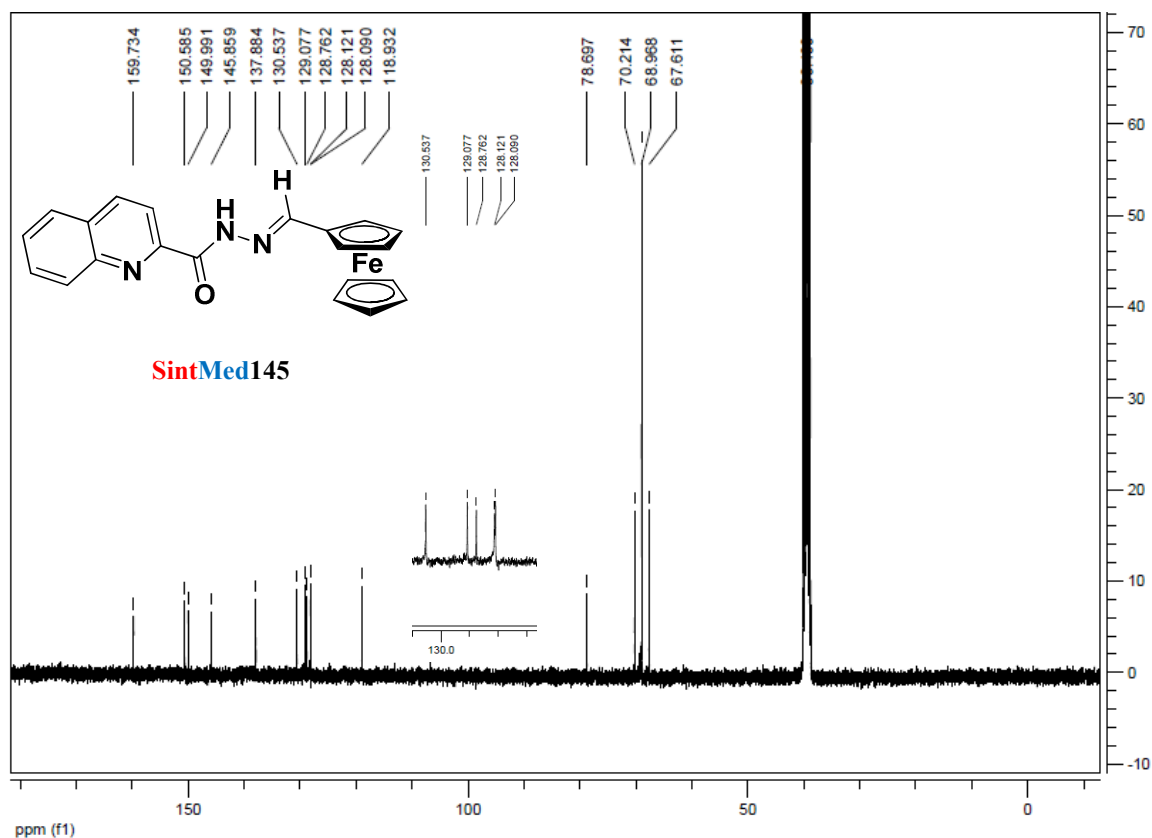


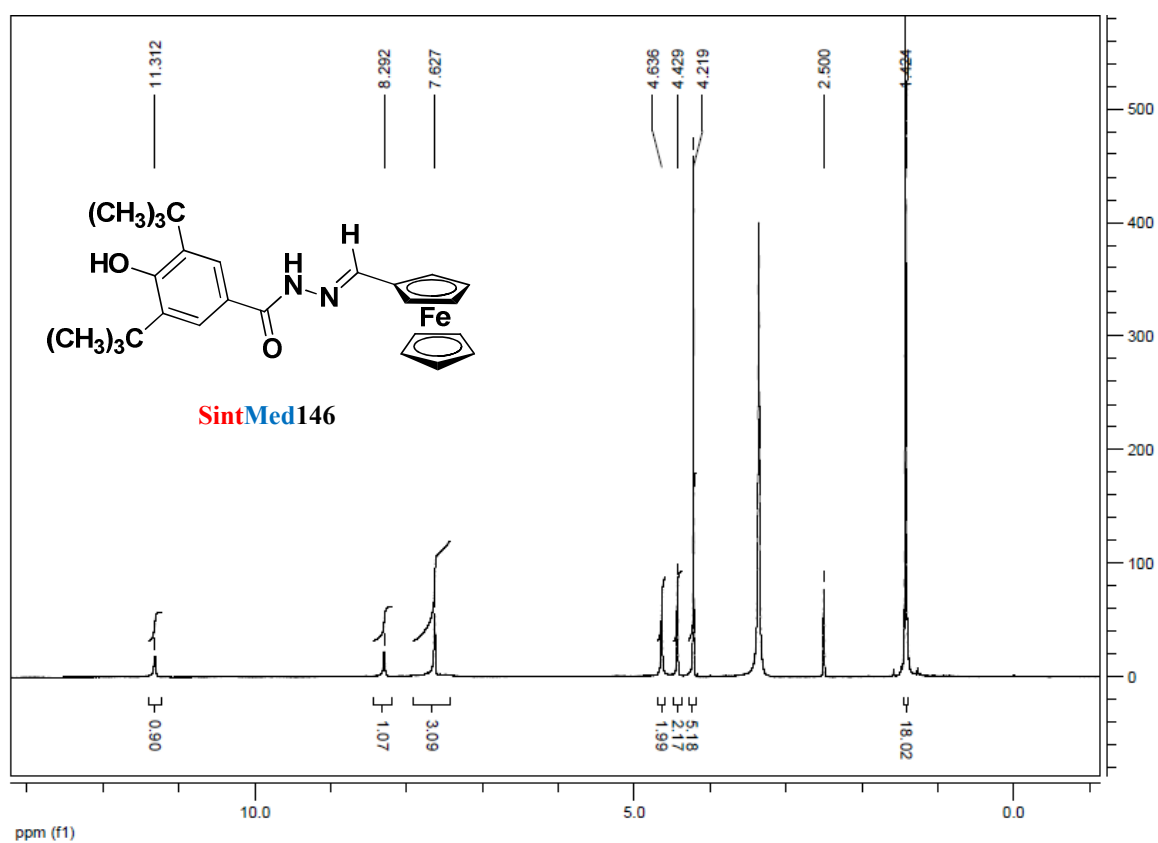


¹H NMR spectrum of **SintMed145** (400 MHz, DMSO-*d*₆)

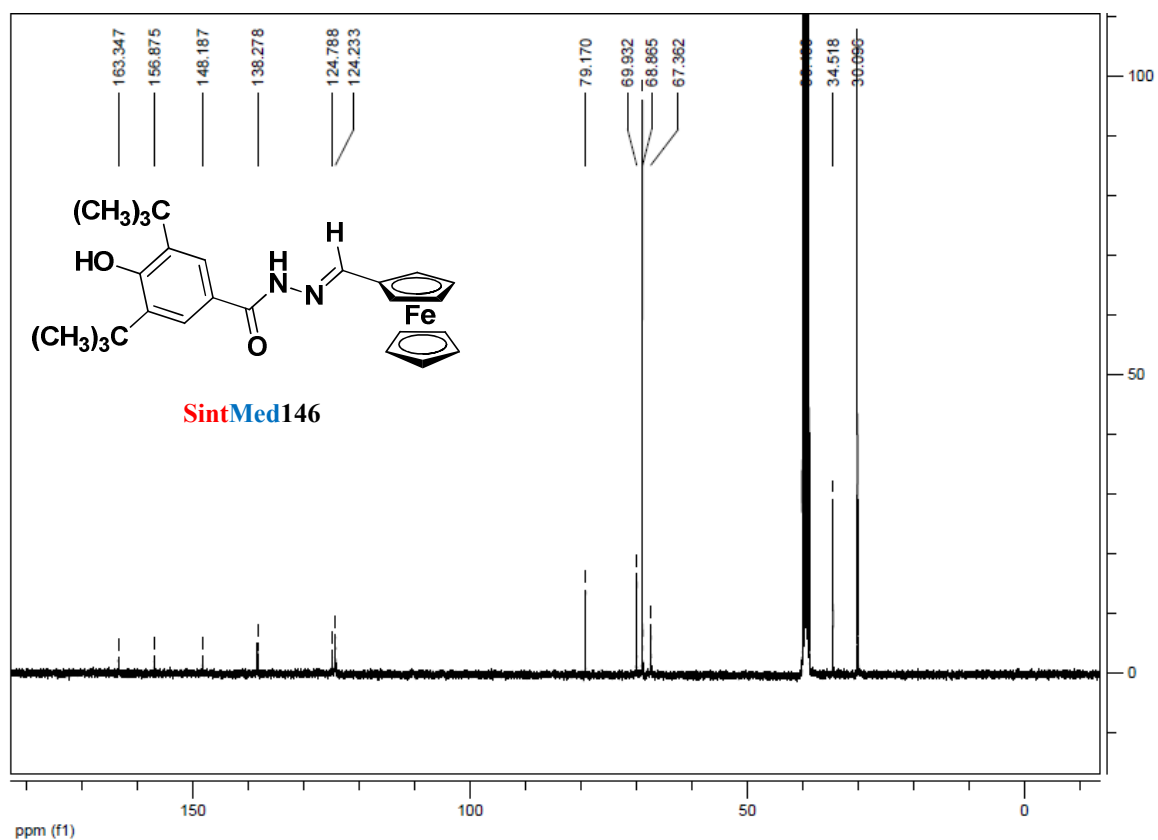


¹H NMR spectrum expansion of **SintMed145** (400 MHz, DMSO-*d*₆)

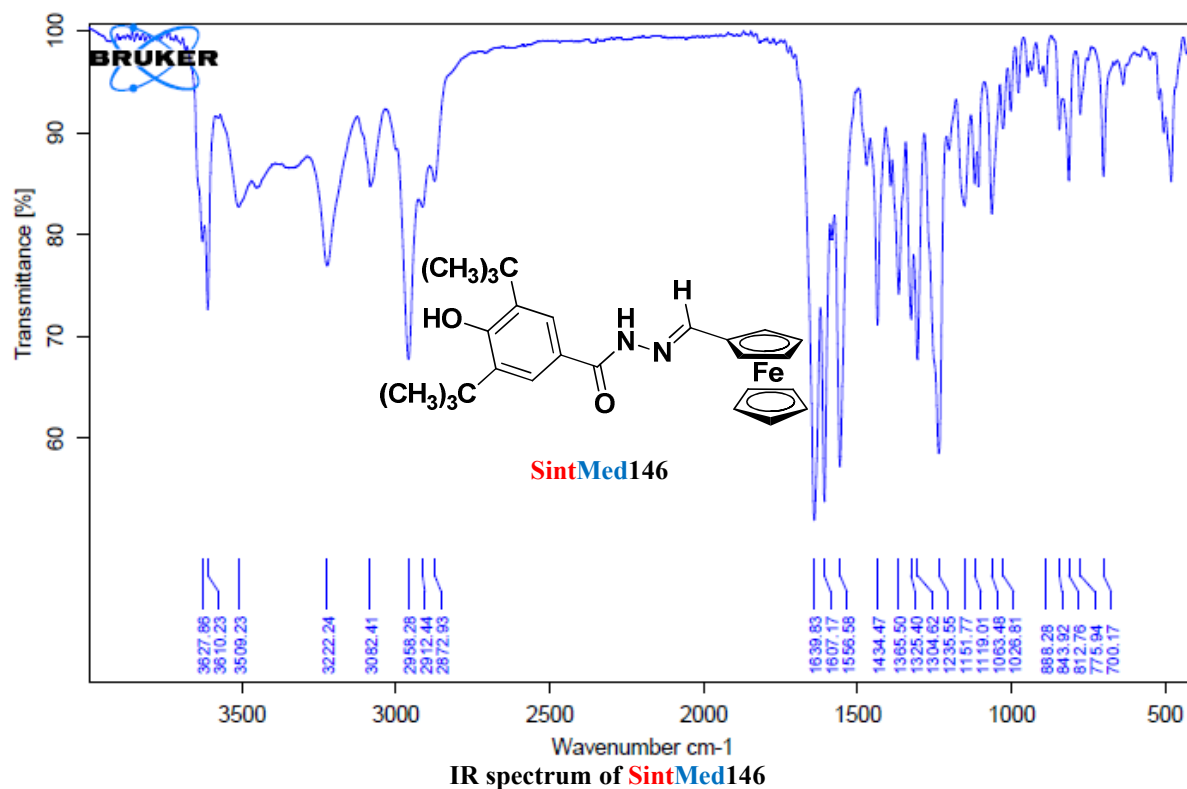


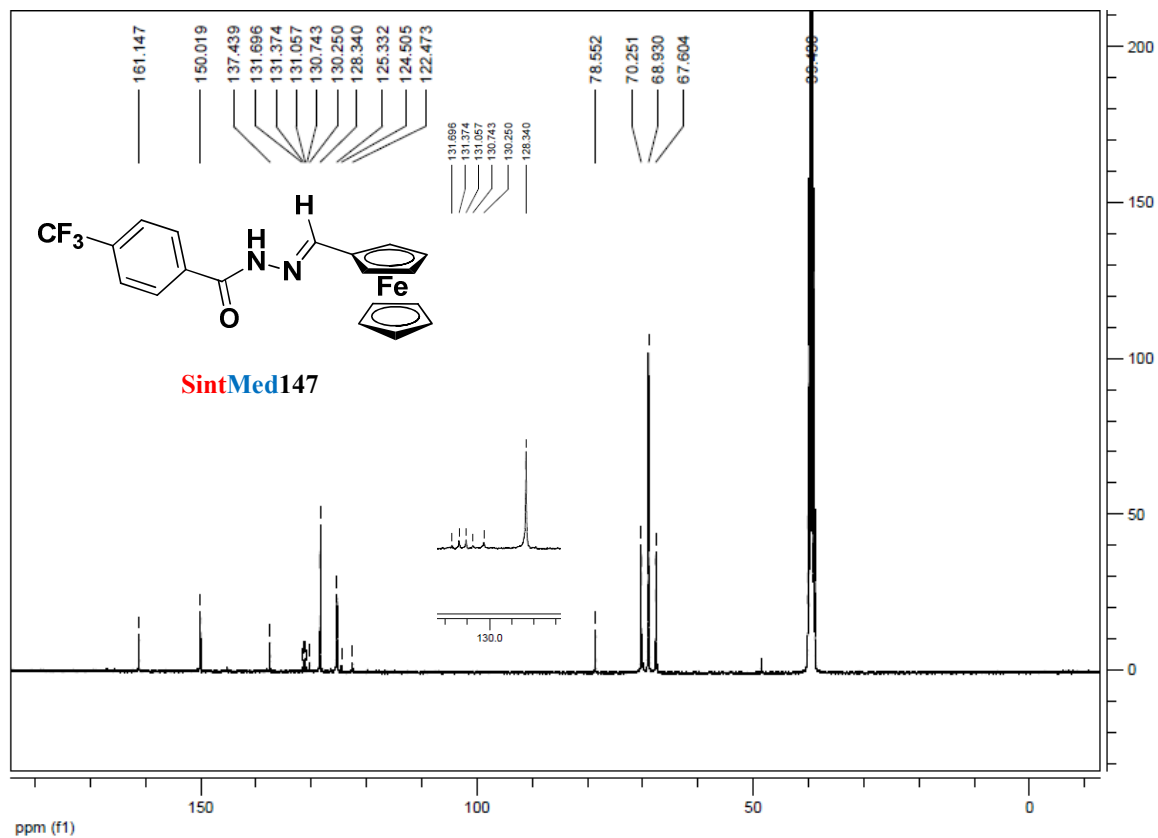
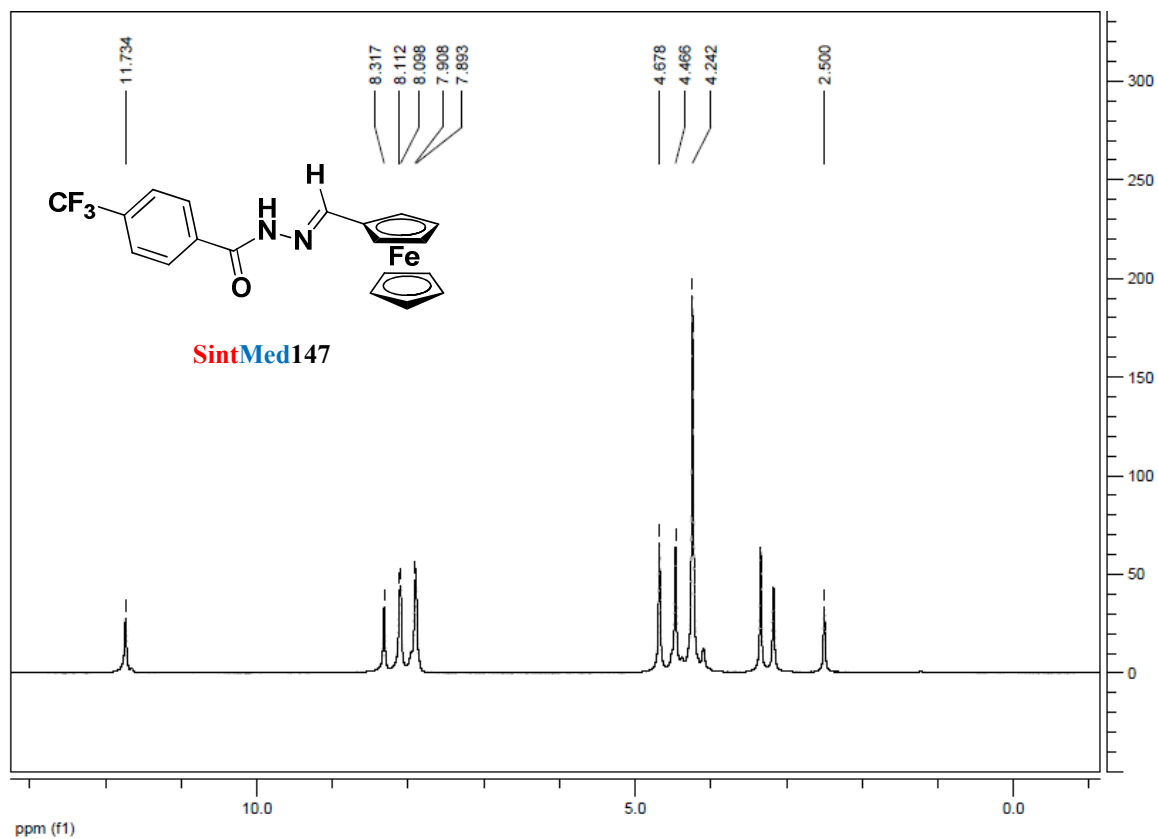


¹H NMR spectrum of SintMed146 (400 MHz, DMSO-*d*₆)

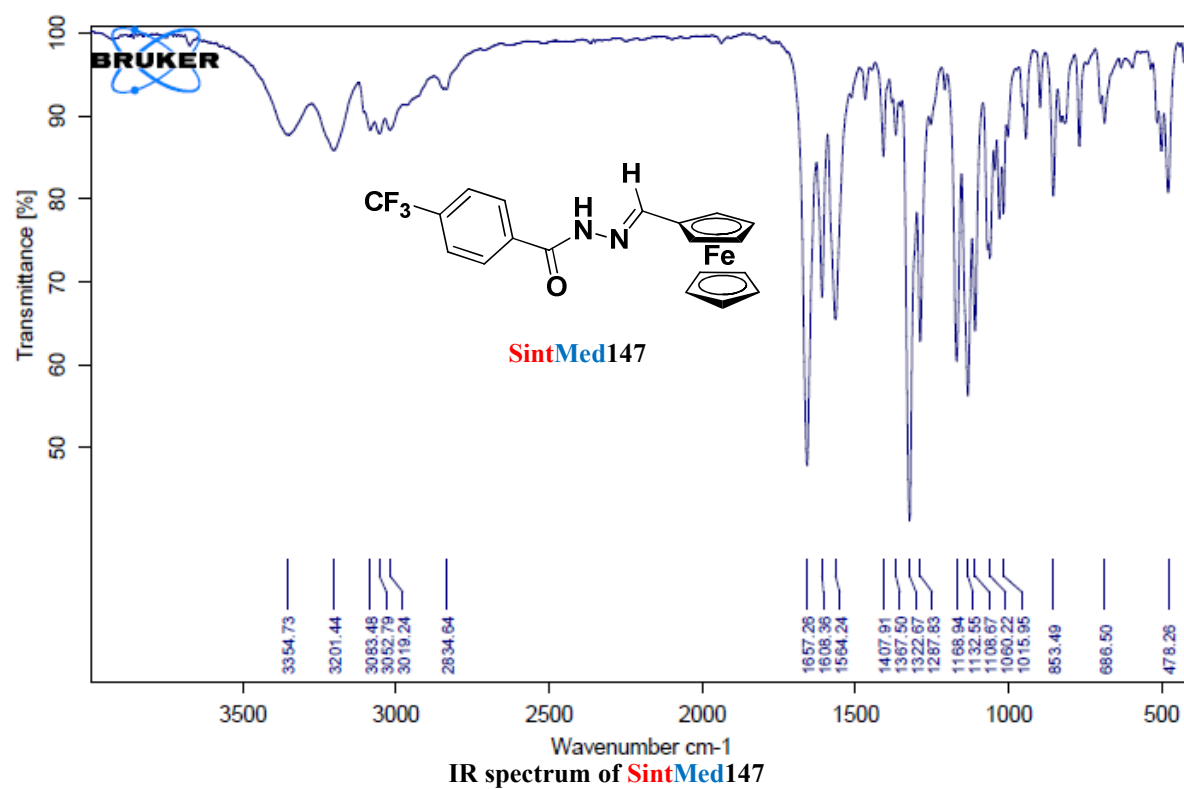


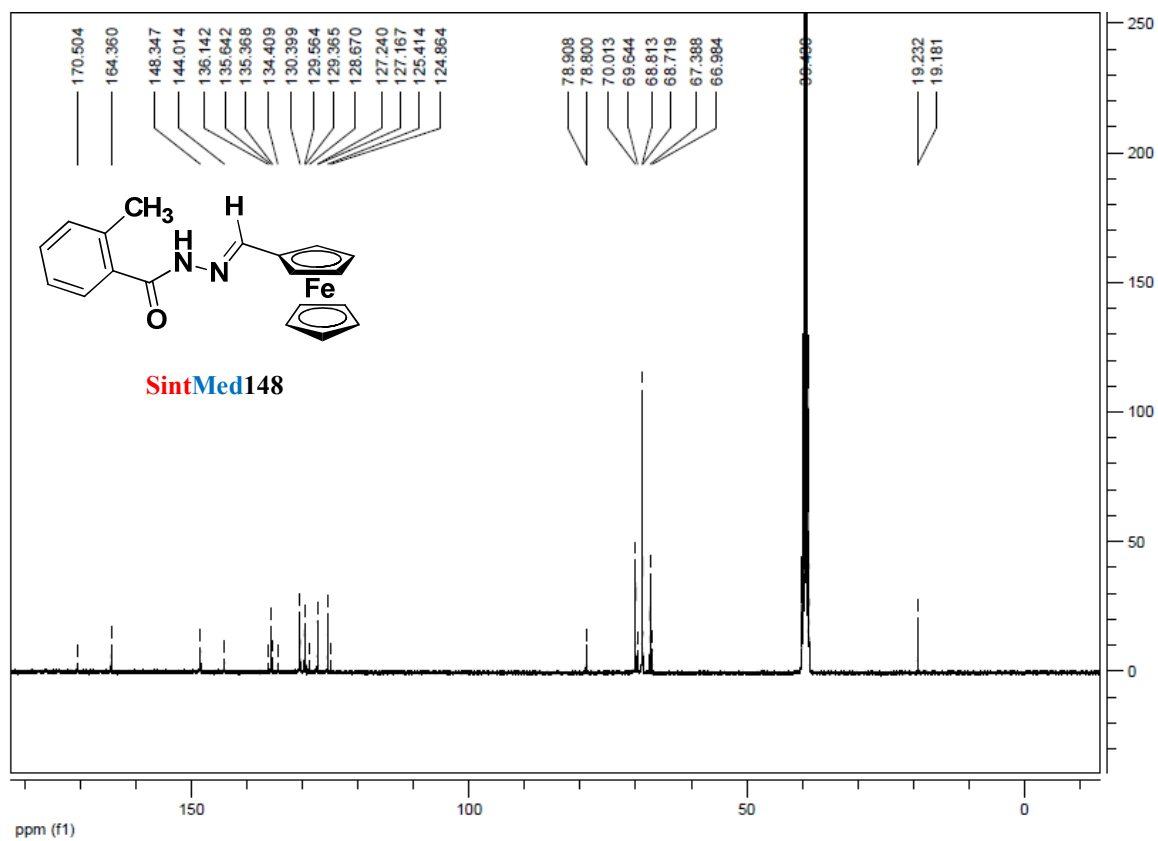
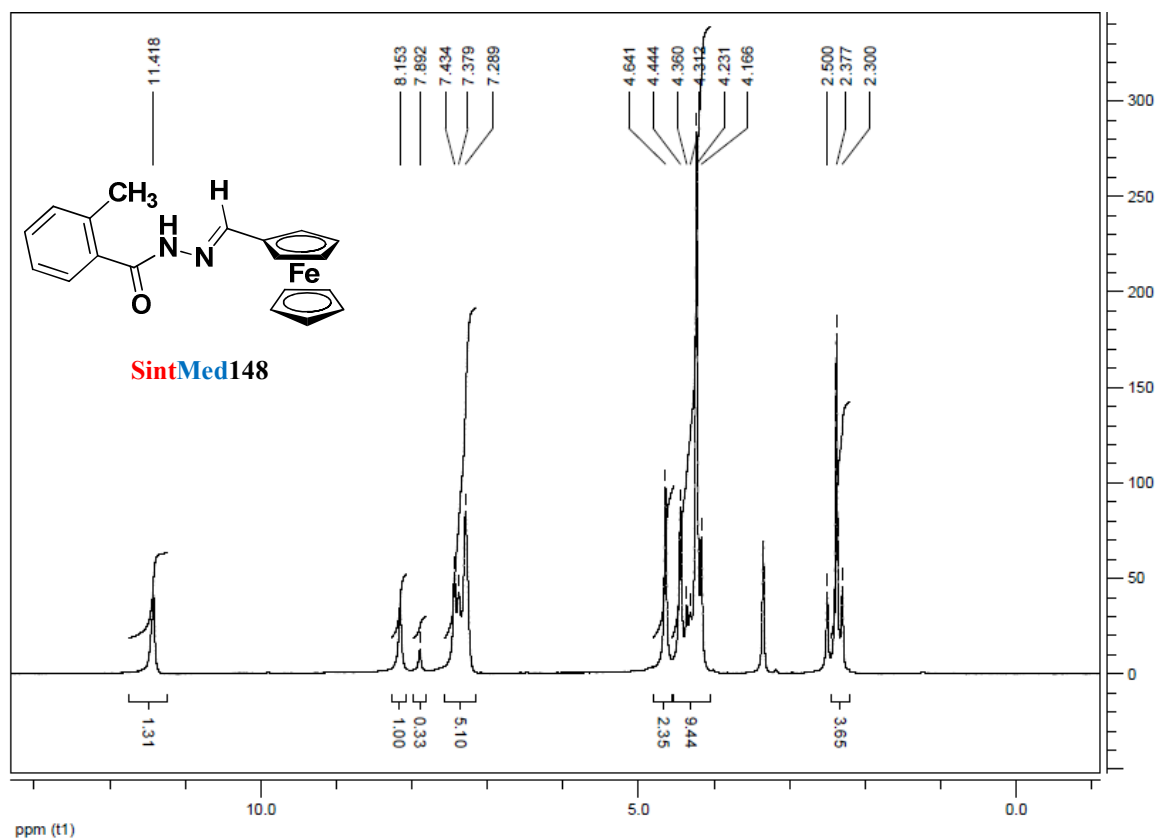
¹³C NMR spectrum of SintMed146 (100 MHz, DMSO-*d*₆)

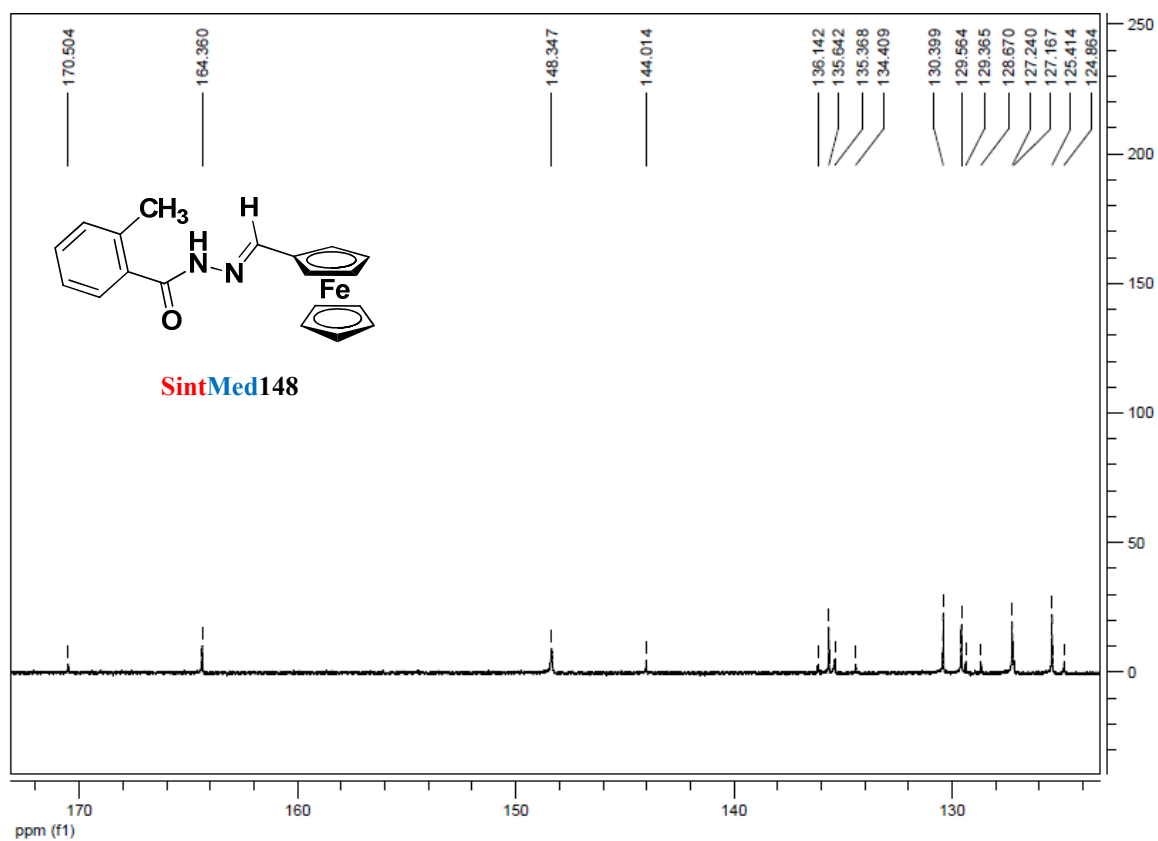




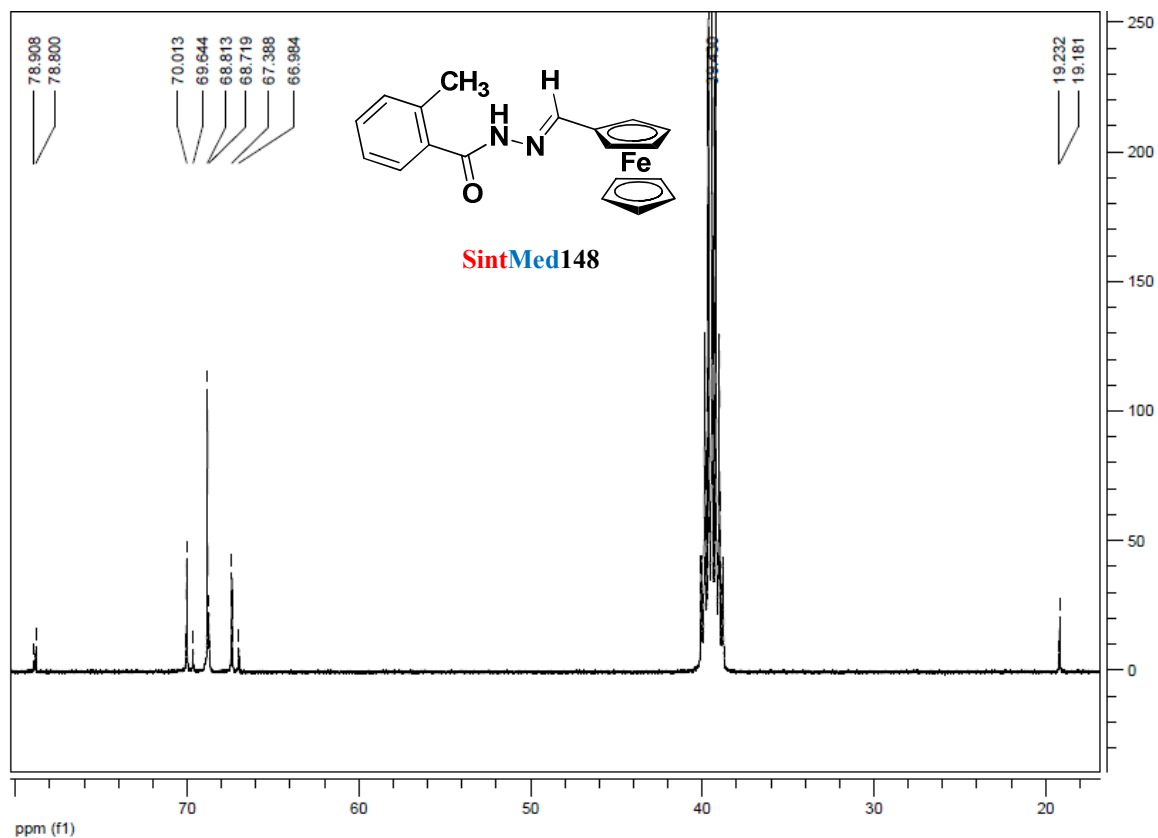
¹³C NMR spectrum of **SintMed147** (100 MHz, DMSO-*d*₆)



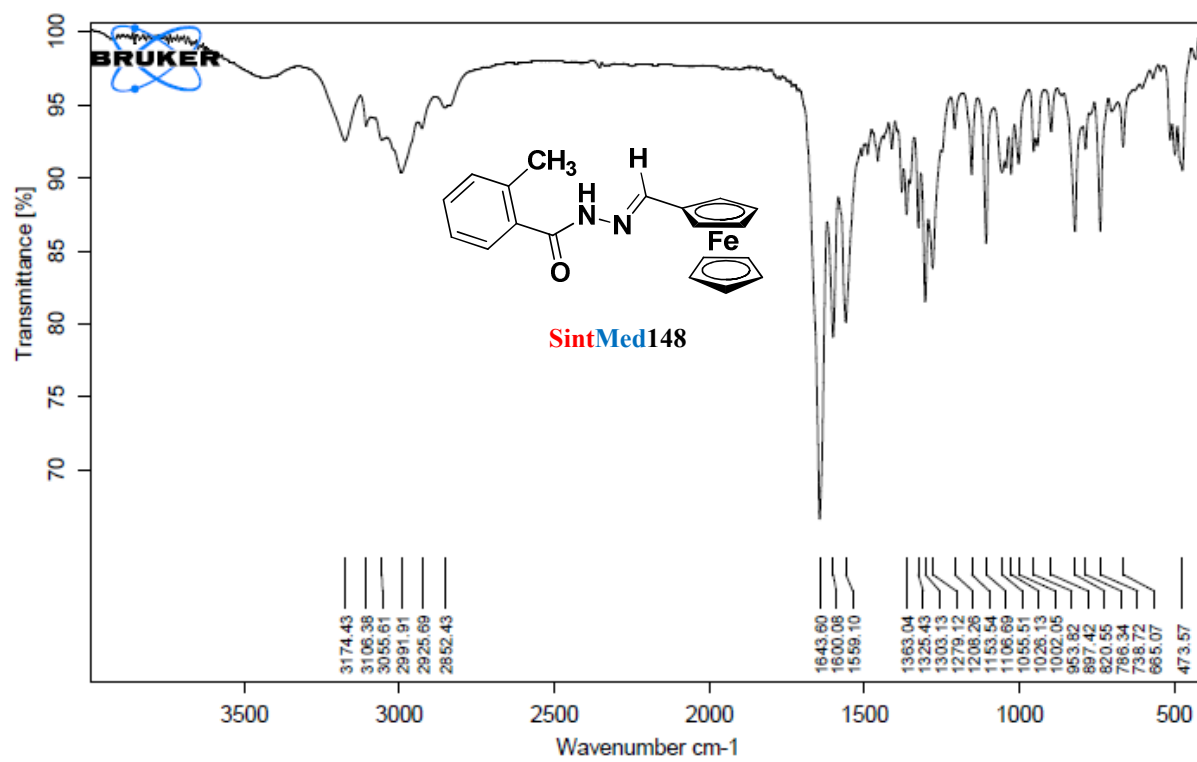




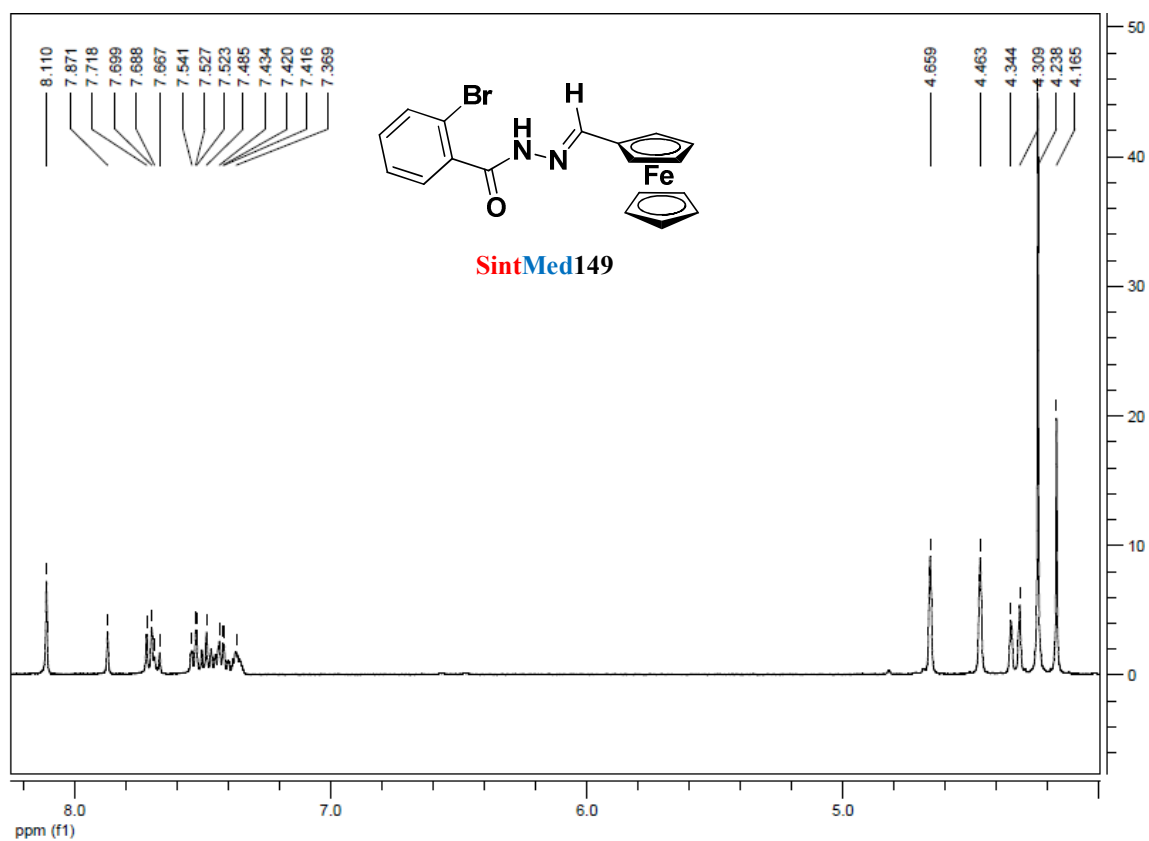
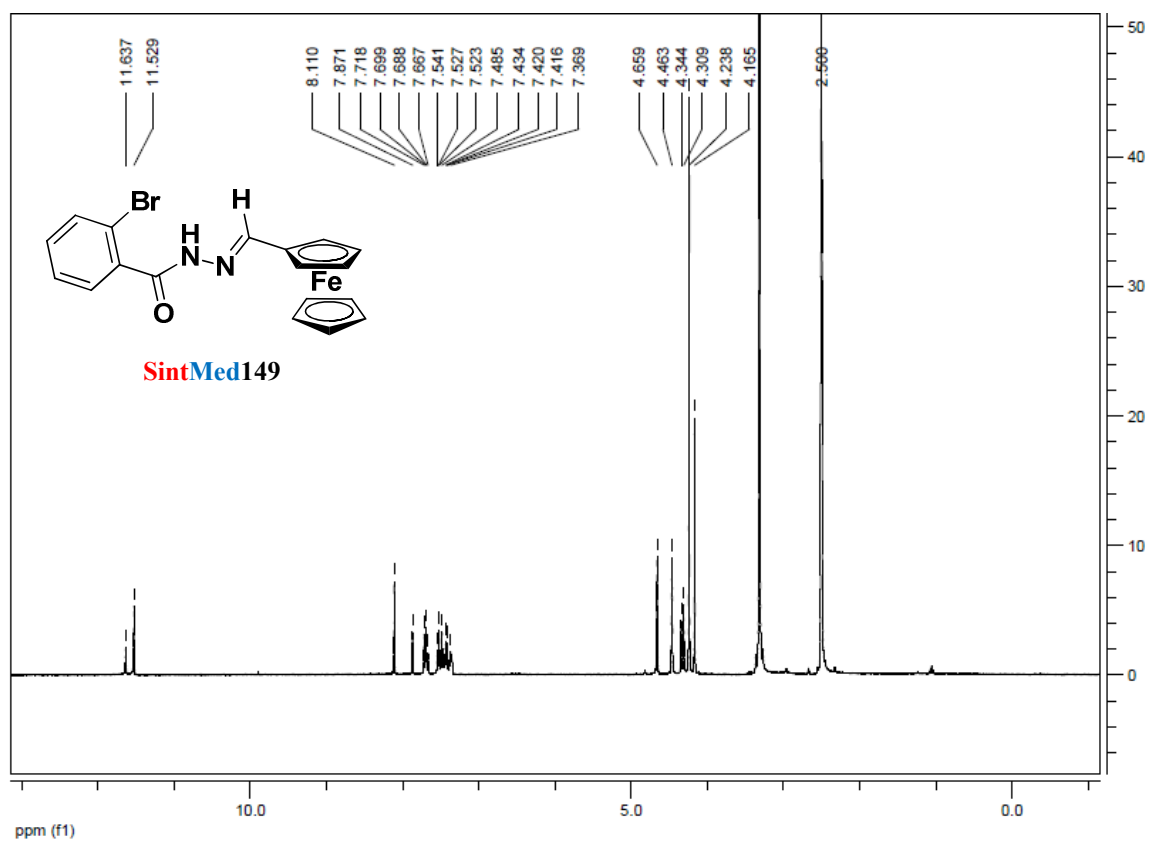
¹³C NMR spectrum expansion of **SintMed148** (100 MHz, DMSO-*d*₆)

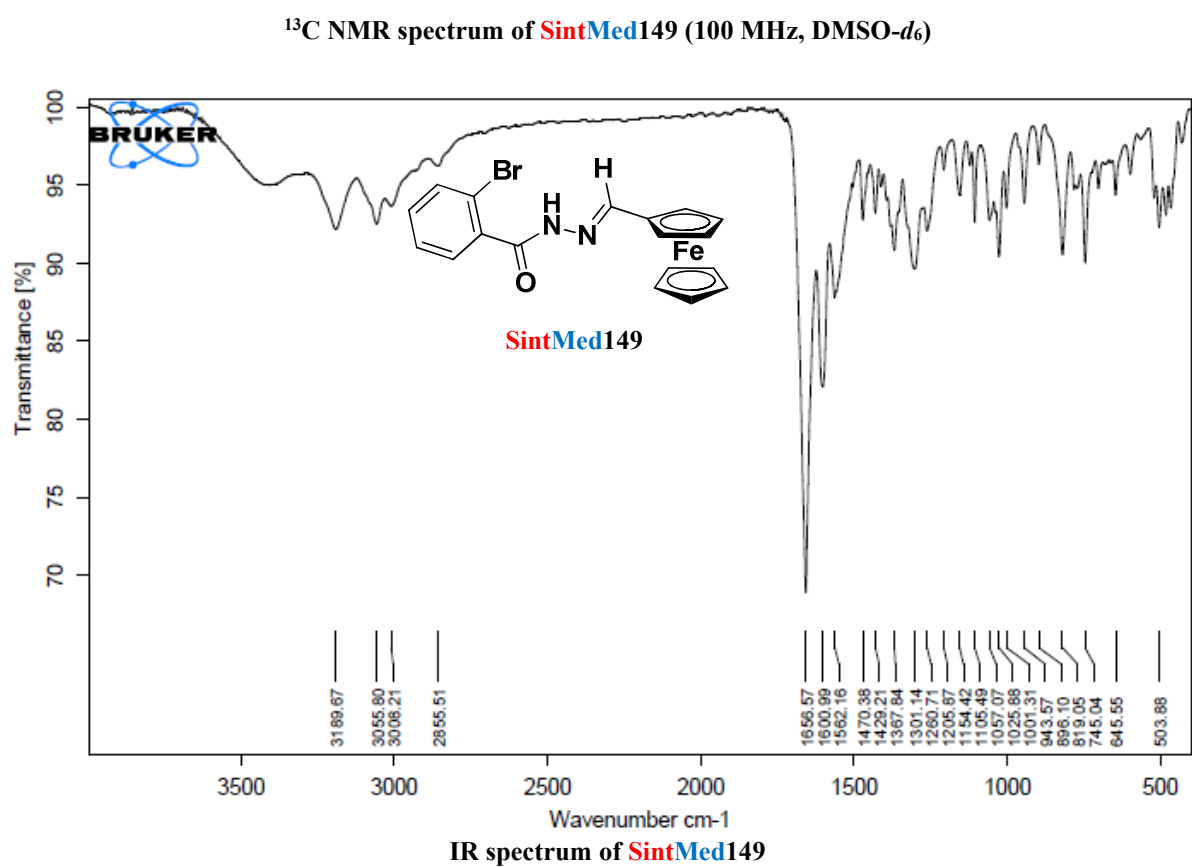
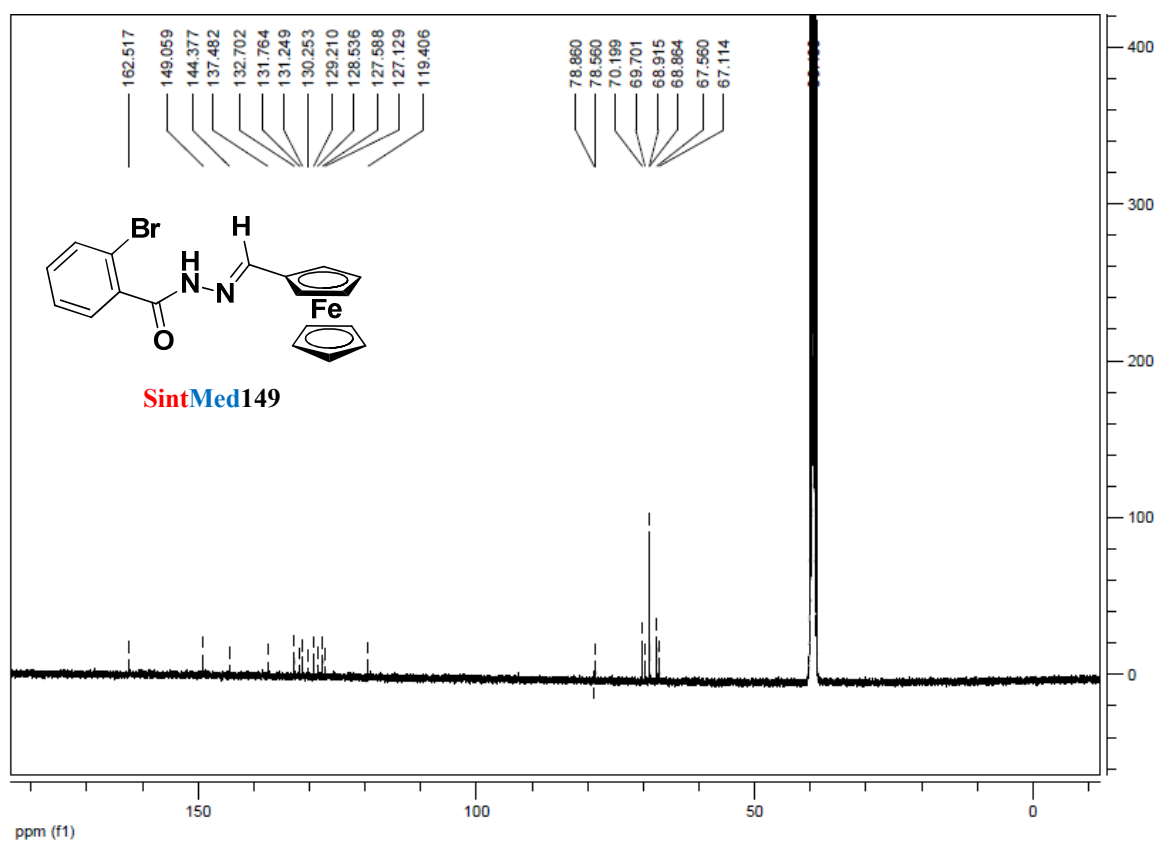


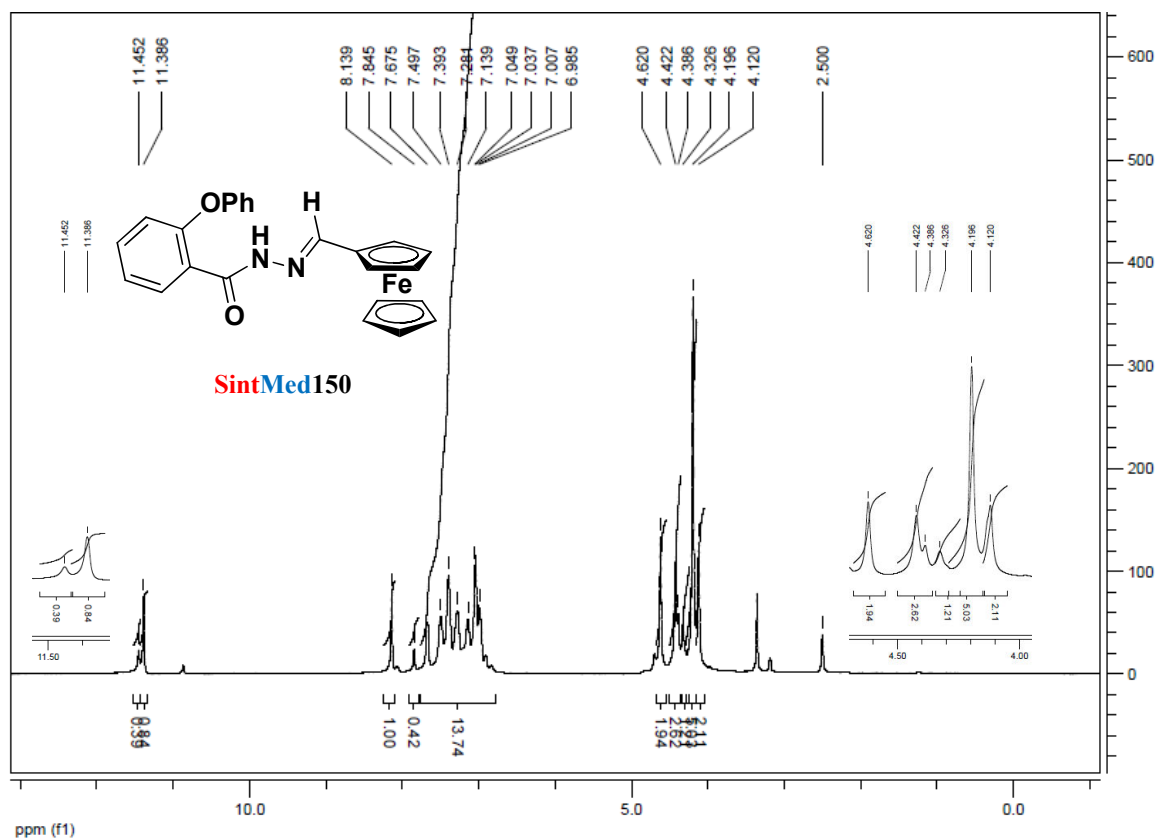
¹³C NMR spectrum expansion of **SintMed148** (100 MHz, DMSO-*d*₆)



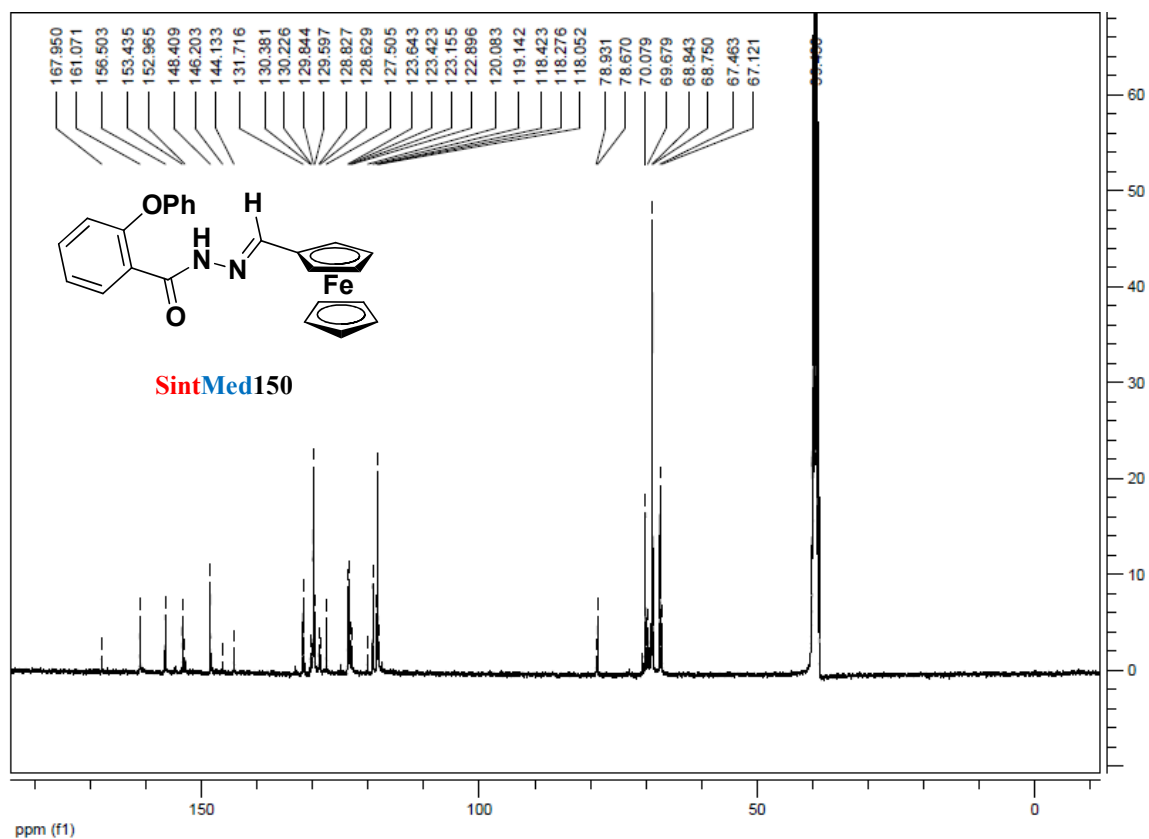
IR spectrum of SintMed148



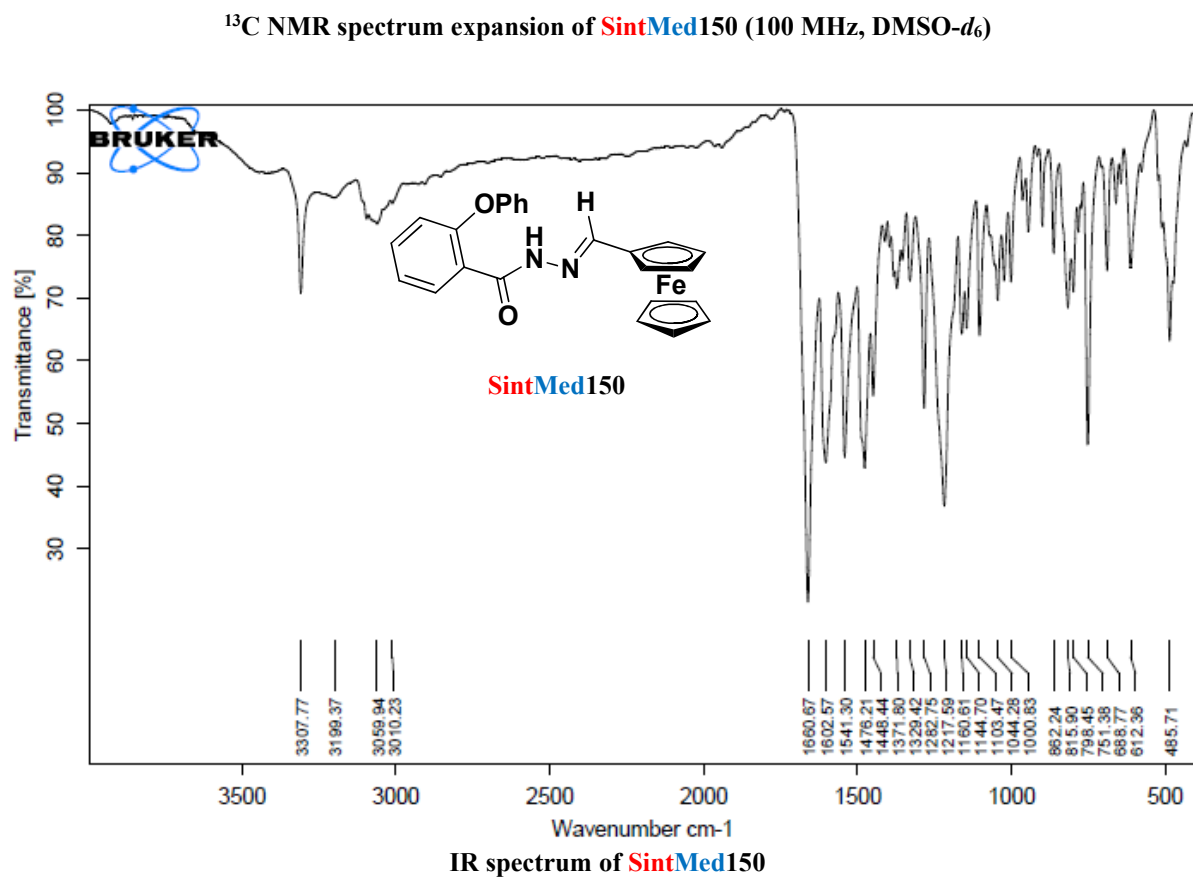
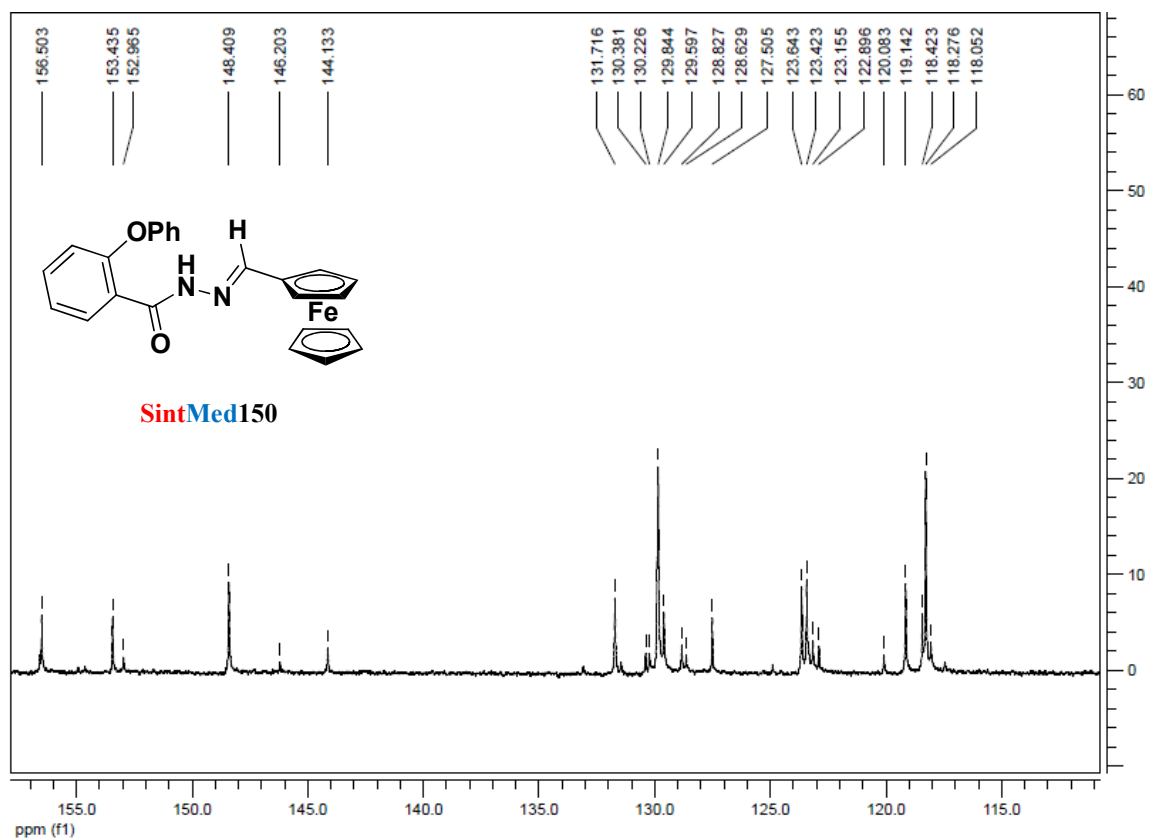


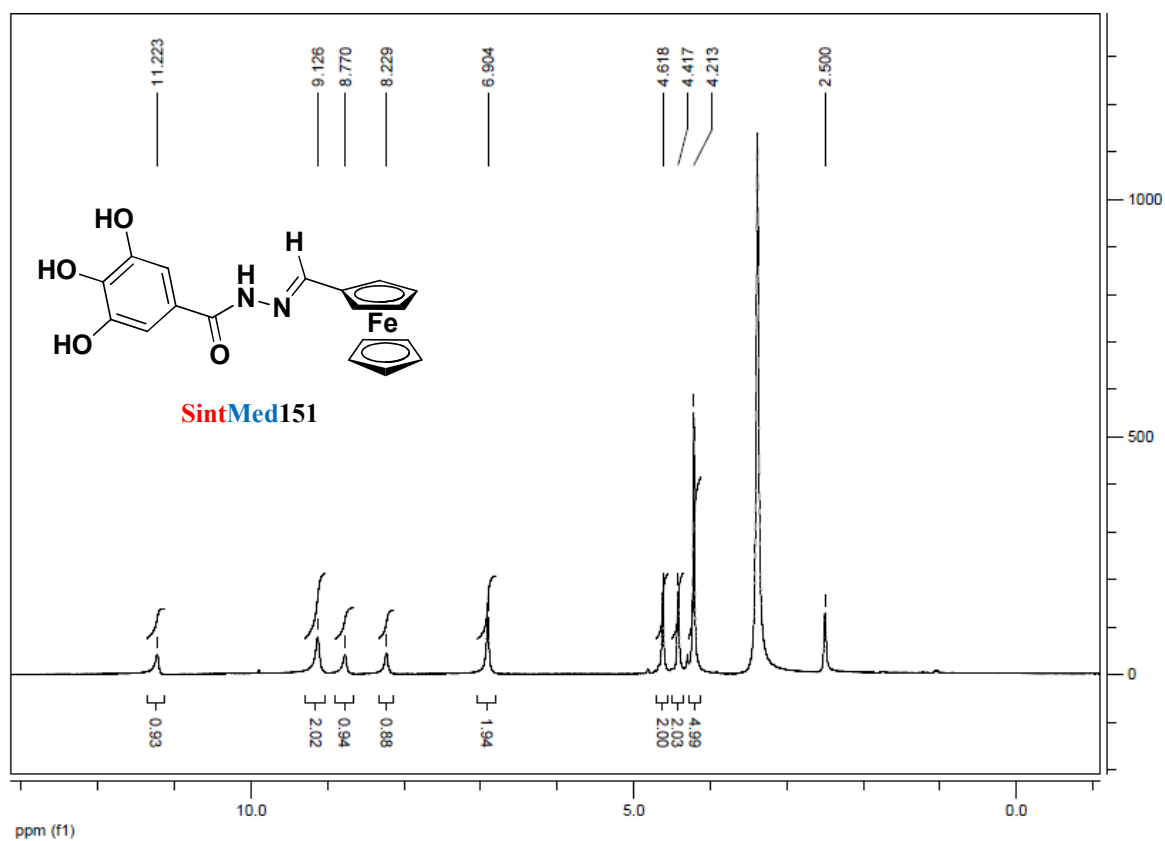


¹H NMR spectrum of SintMed150 (400 MHz, DMSO-*d*₆)

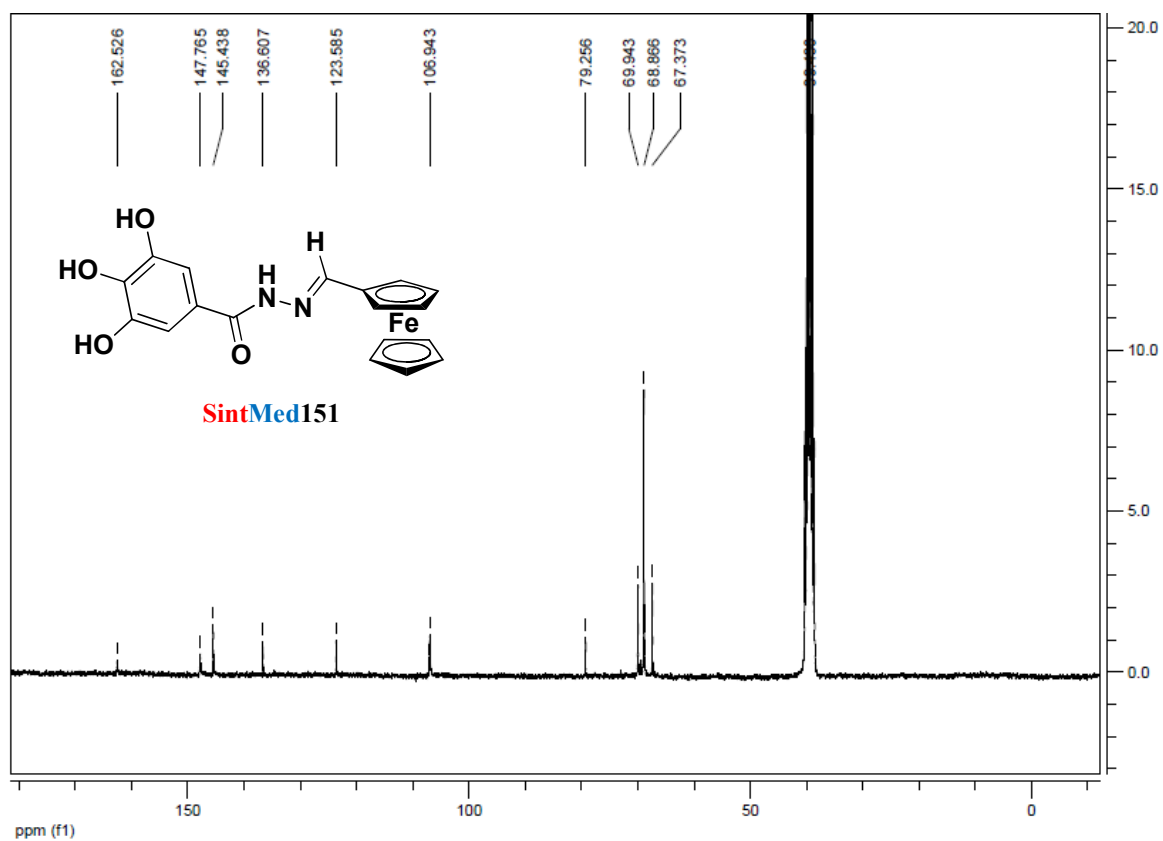


¹³C NMR spectrum of SintMed150 (100 MHz, DMSO-*d*₆)

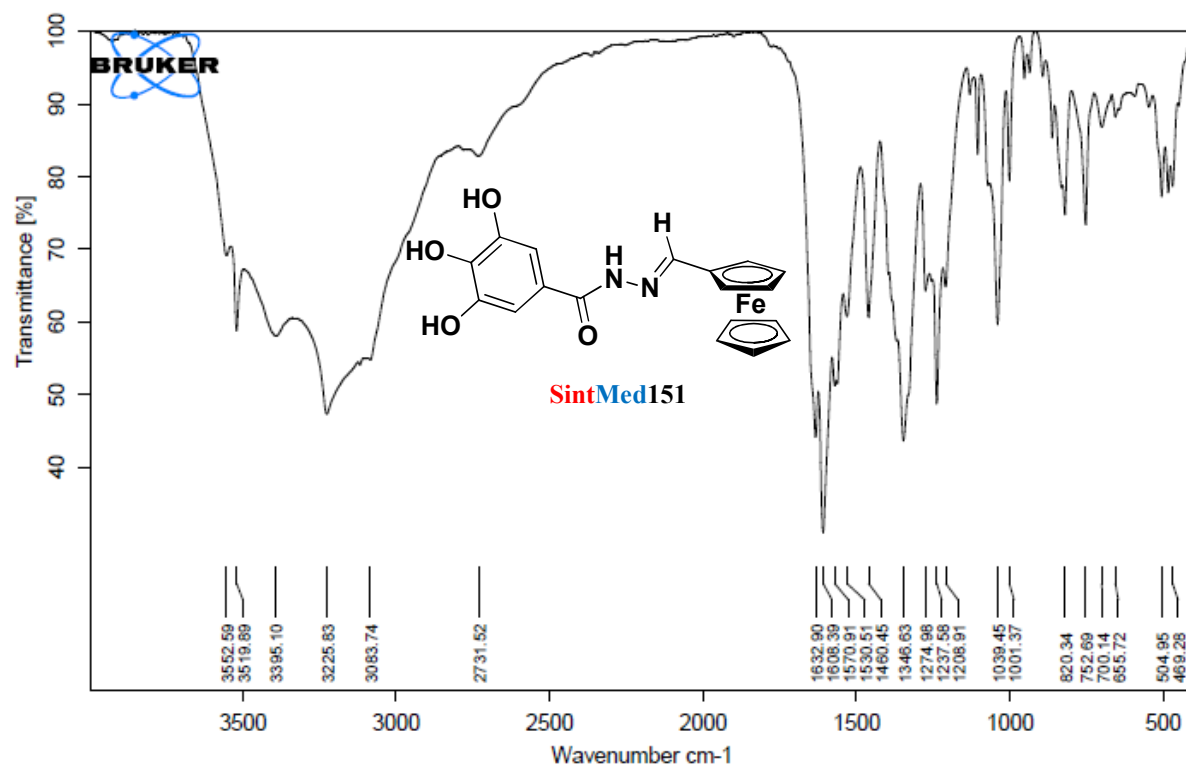




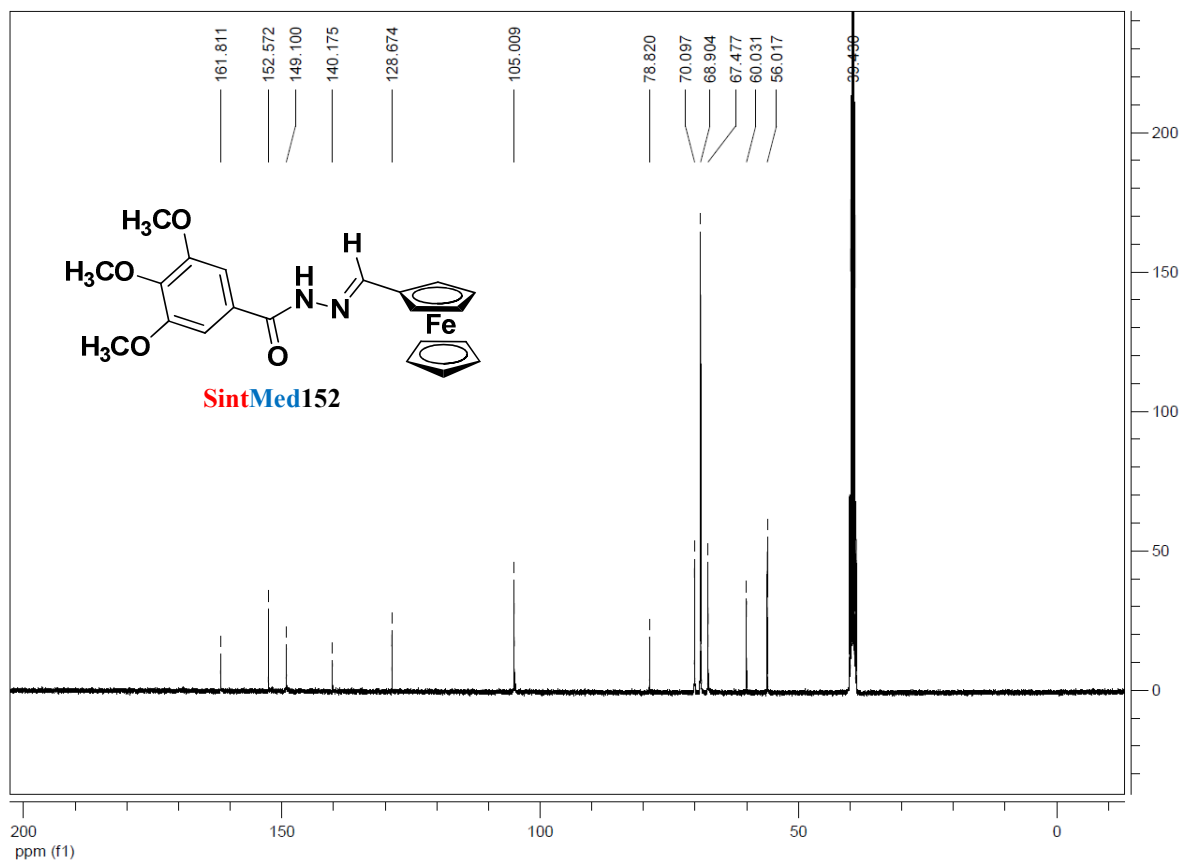
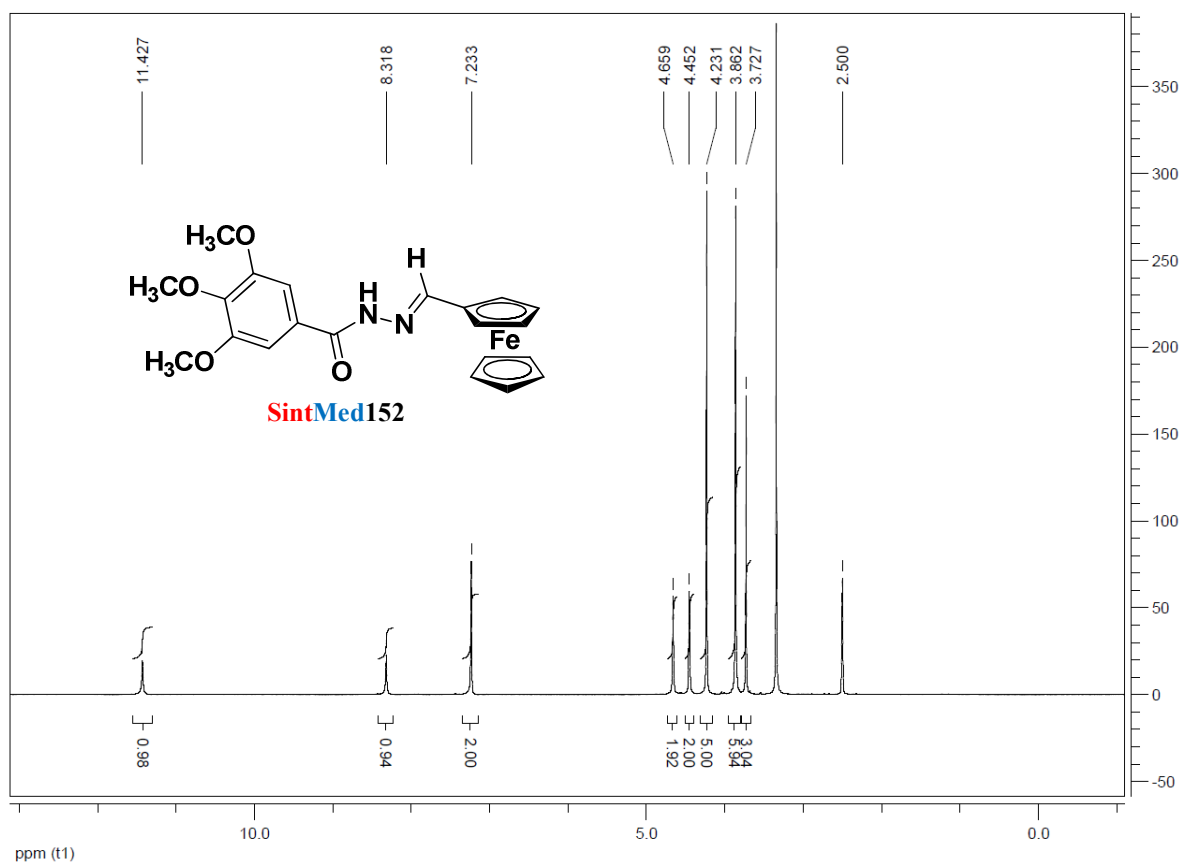
¹H NMR spectrum of **SintMed151** (300 MHz, DMSO-*d*₆)



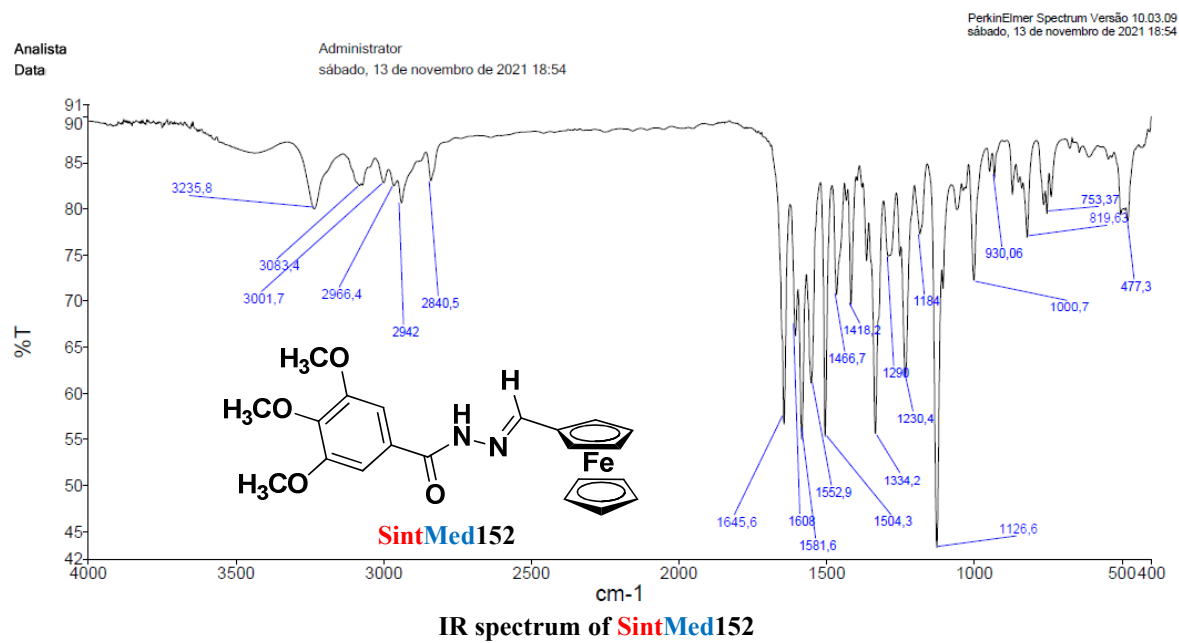
¹³C NMR spectrum of **SintMed151** (75 MHz, DMSO-*d*₆)

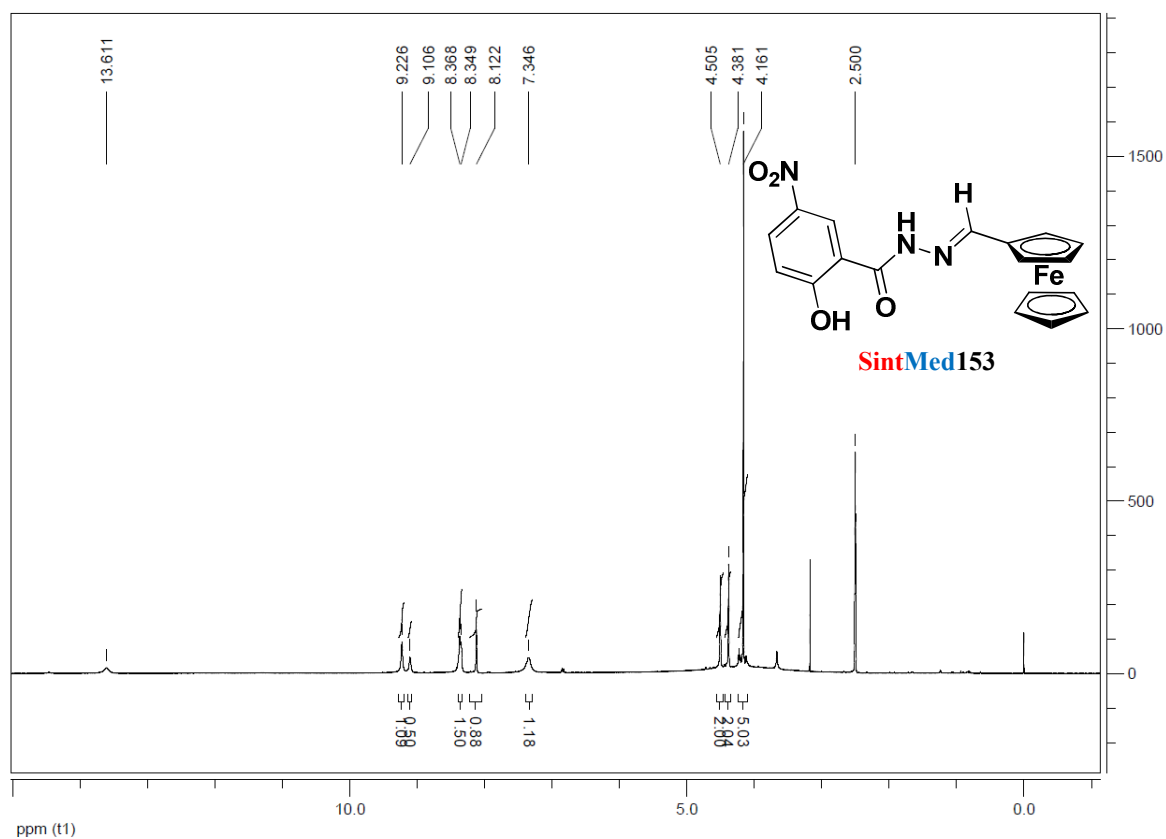


IR spectrum of SintMed151

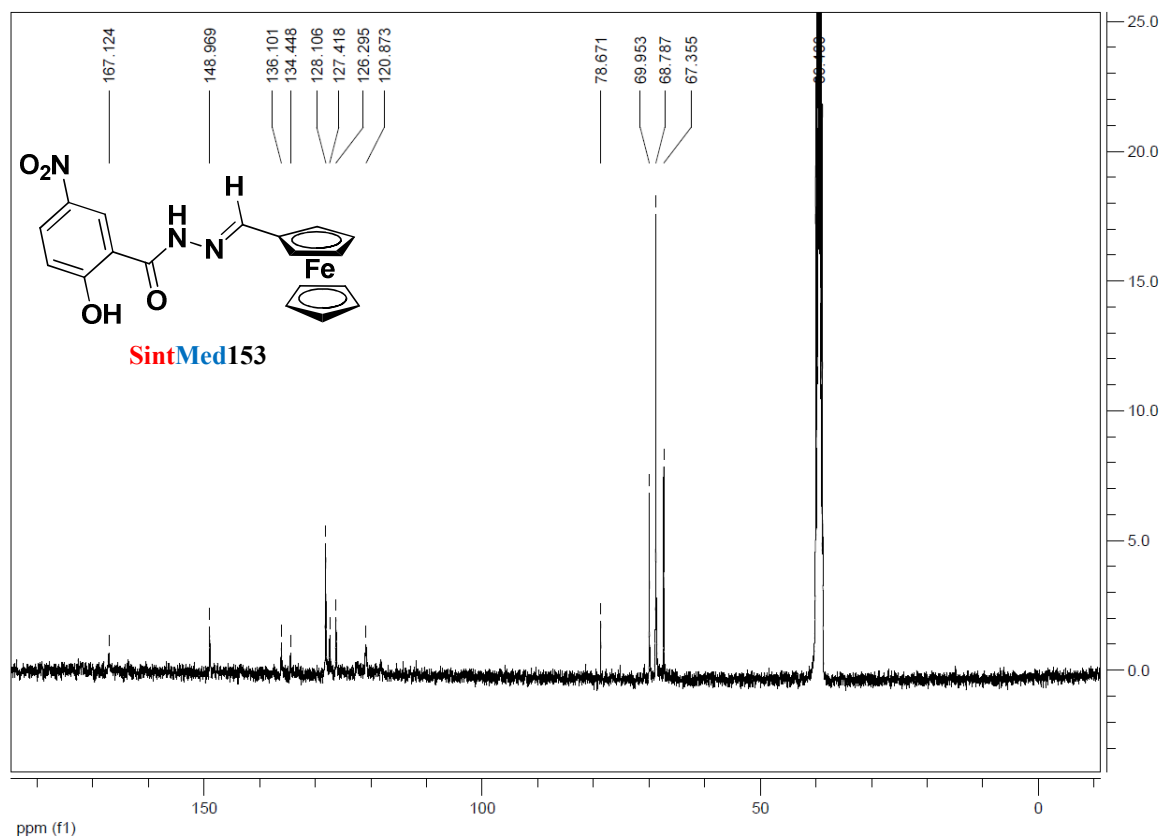


¹³C NMR spectrum of **SintMed152** (100 MHz, DMSO-*d*₆)

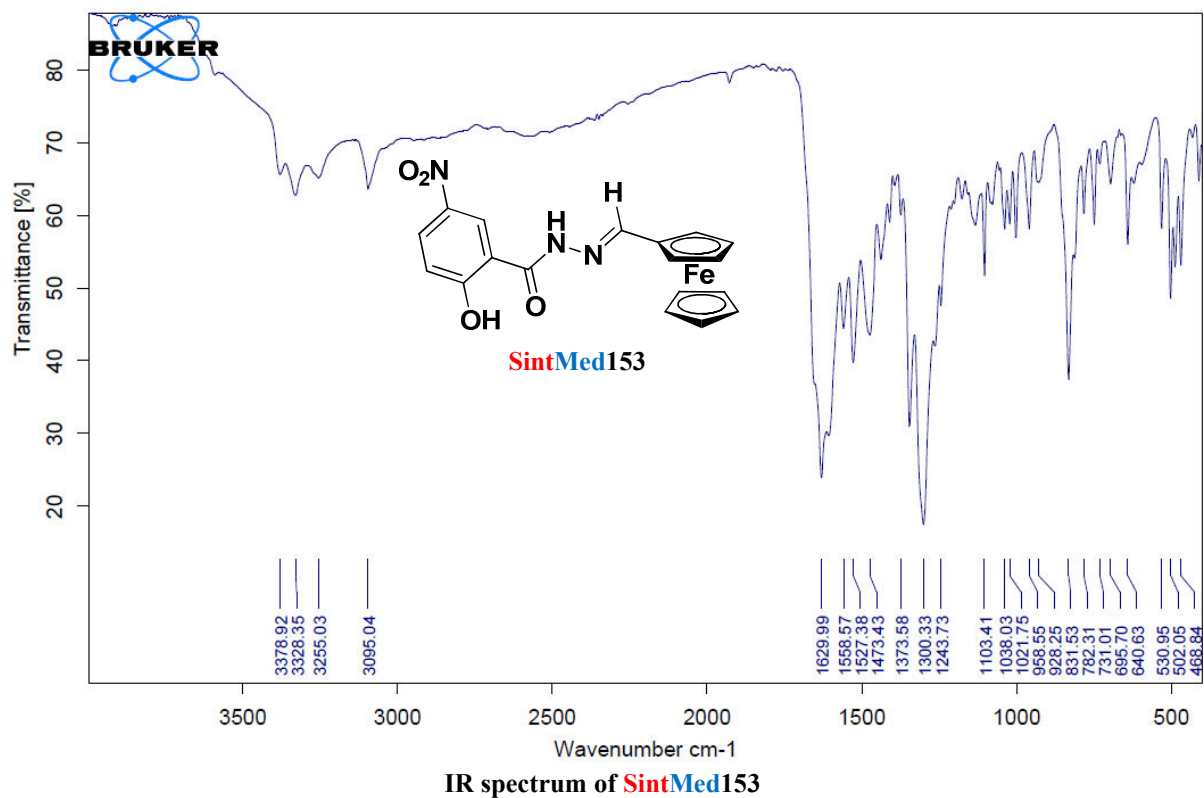


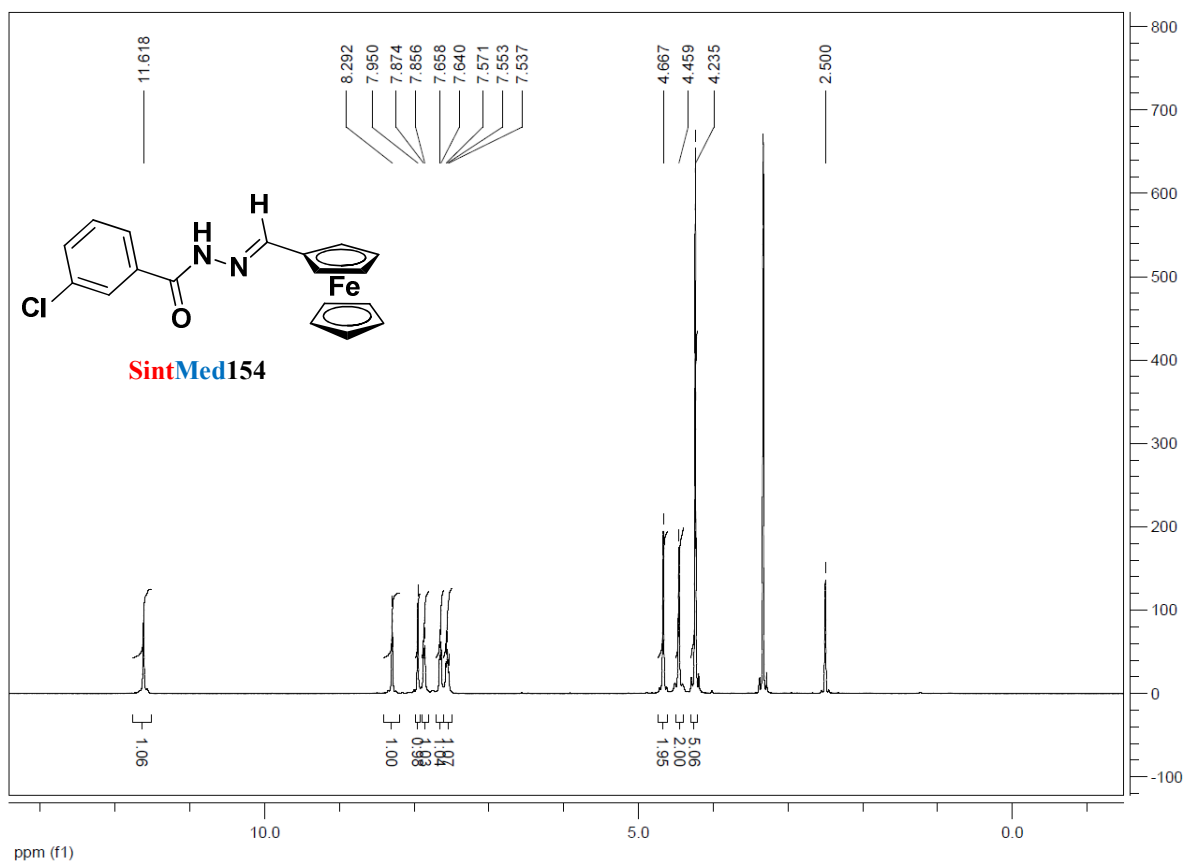


¹H NMR spectrum of SintMed153 (400 MHz, DMSO-*d*₆)

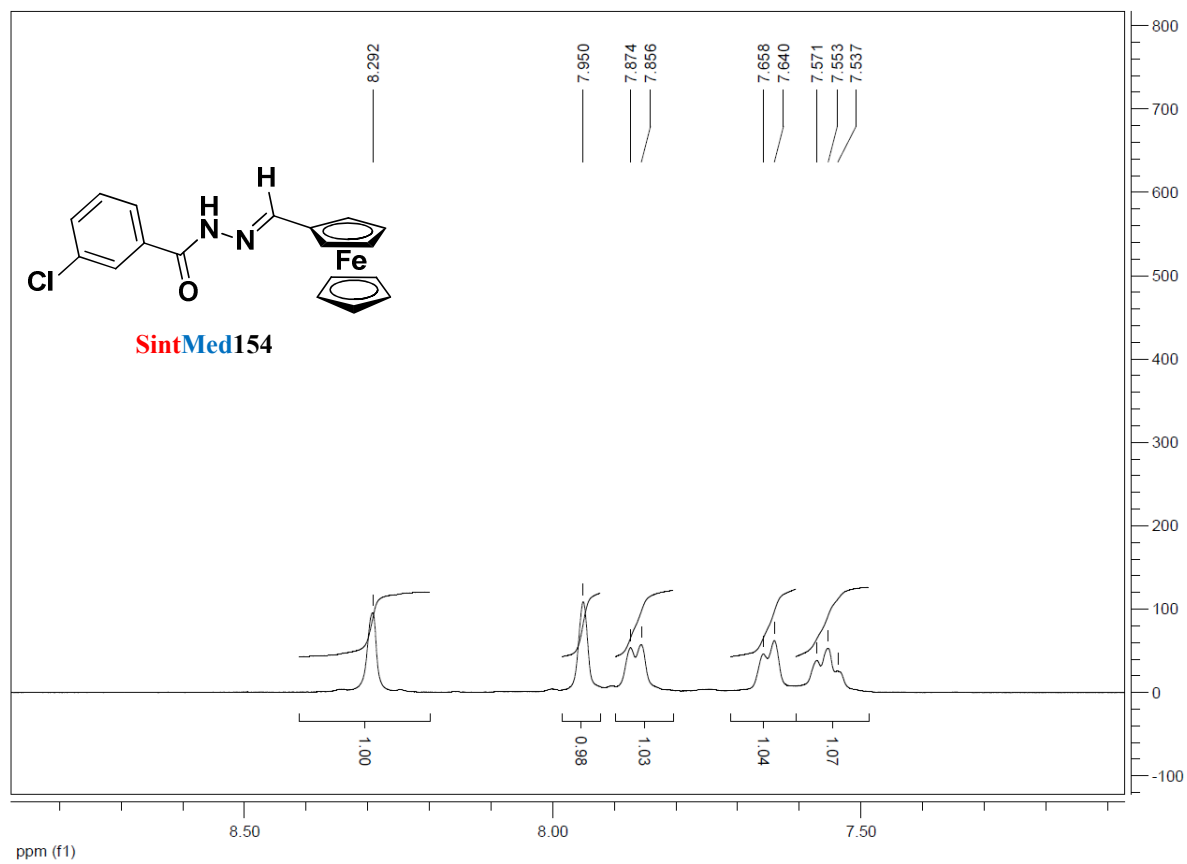


¹³C NMR spectrum of SintMed153 (100 MHz, DMSO-*d*₆)

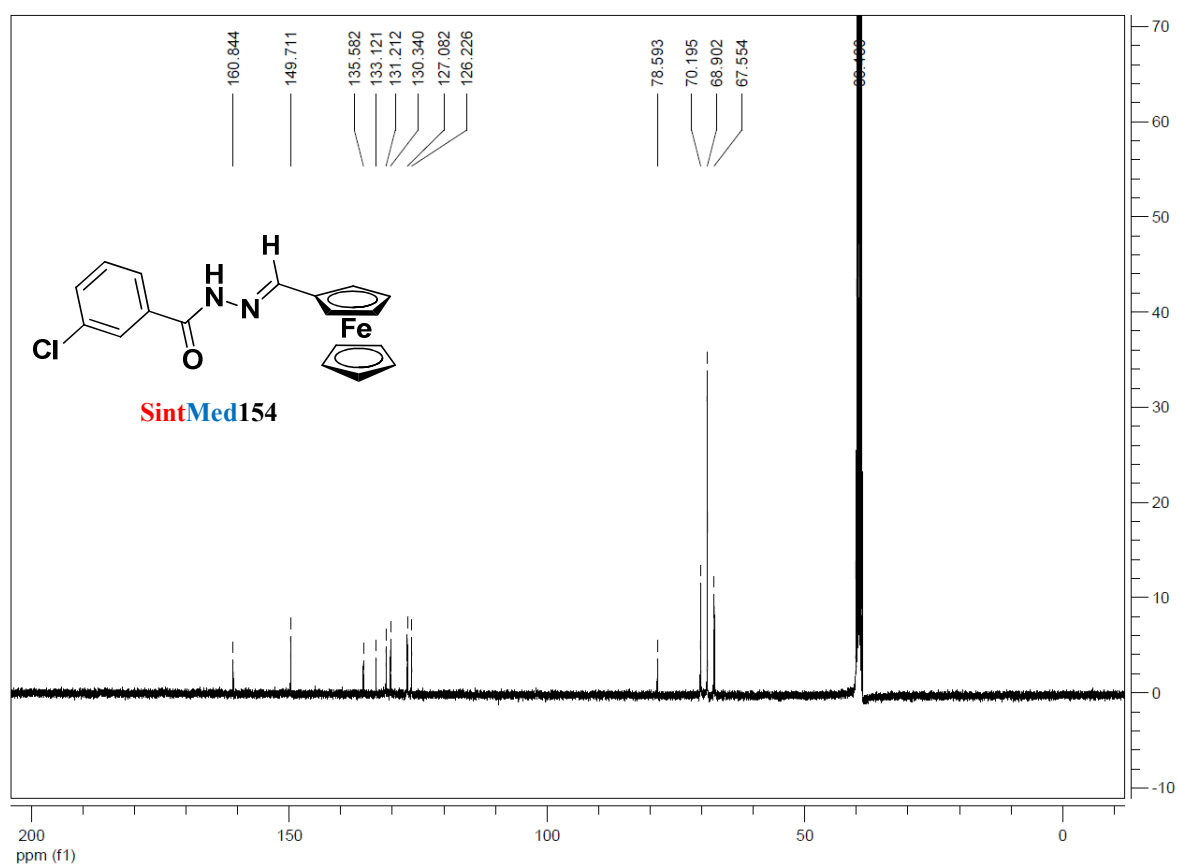




¹H NMR spectrum of **SintMed154** (400 MHz, DMSO-*d*₆)

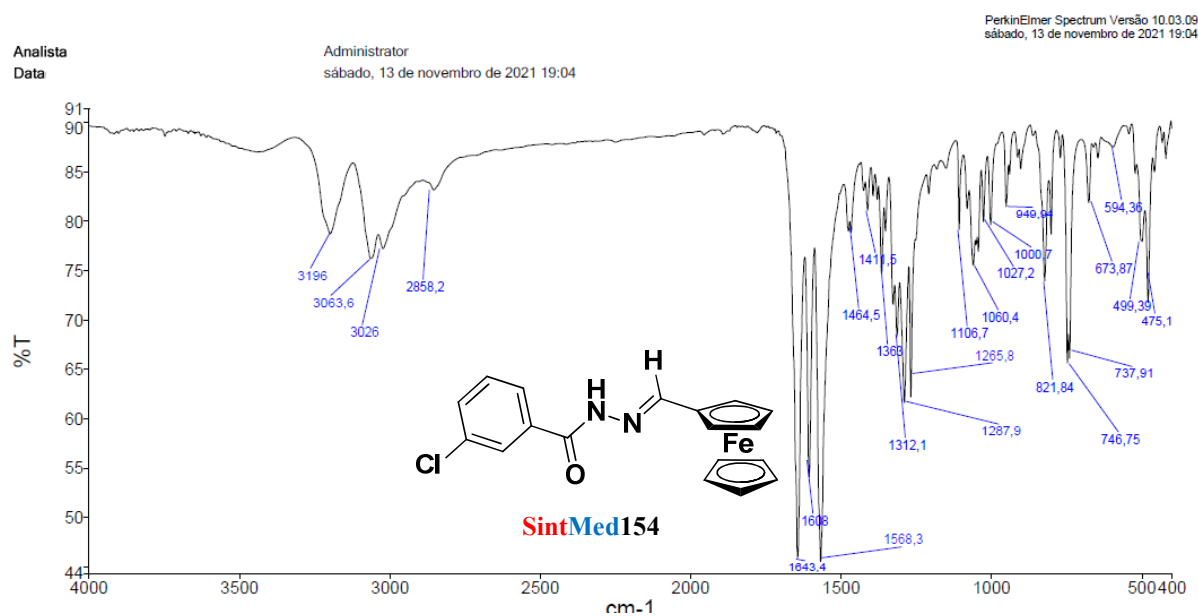


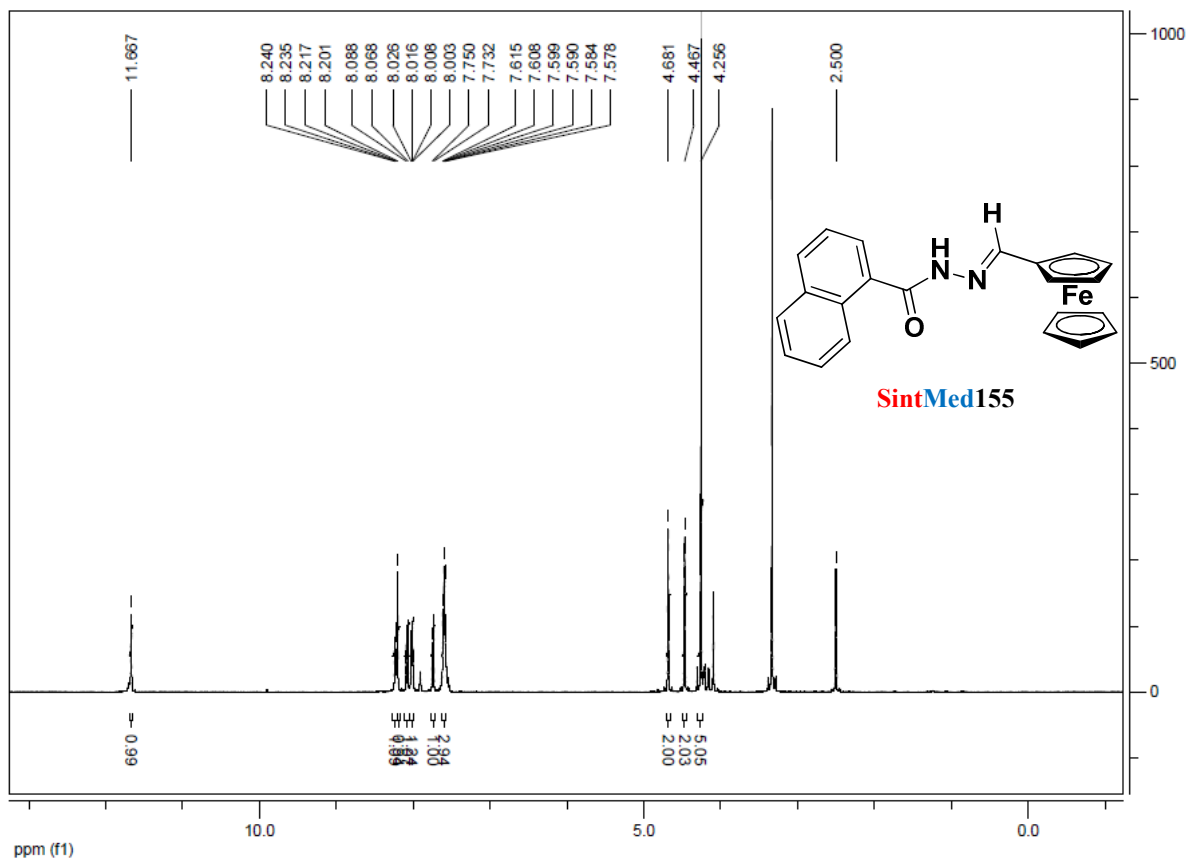
¹H NMR spectrum expansion of SintMed154 (400 MHz, DMSO-*d*₆)



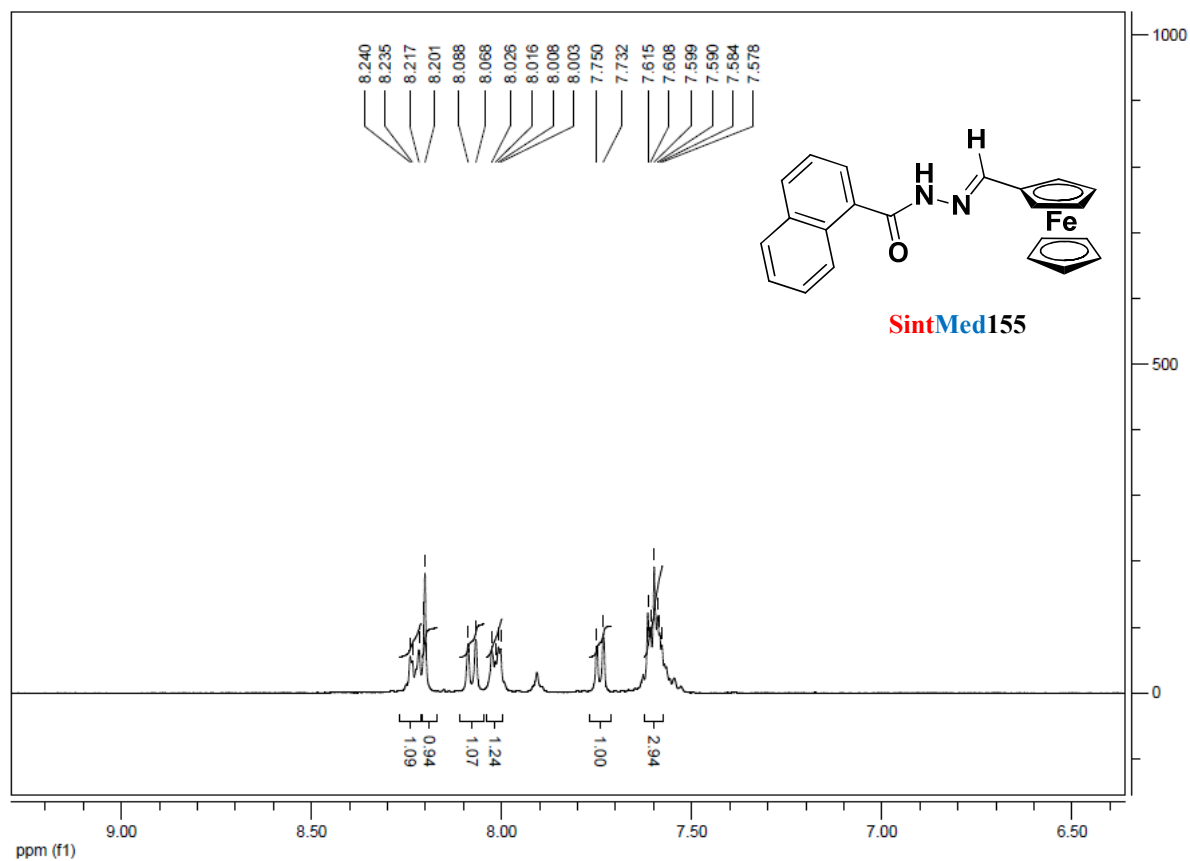
¹³C NMR spectrum of SintMed154 (100 MHz, DMSO-*d*₆)

IR spectrum of SintMed154

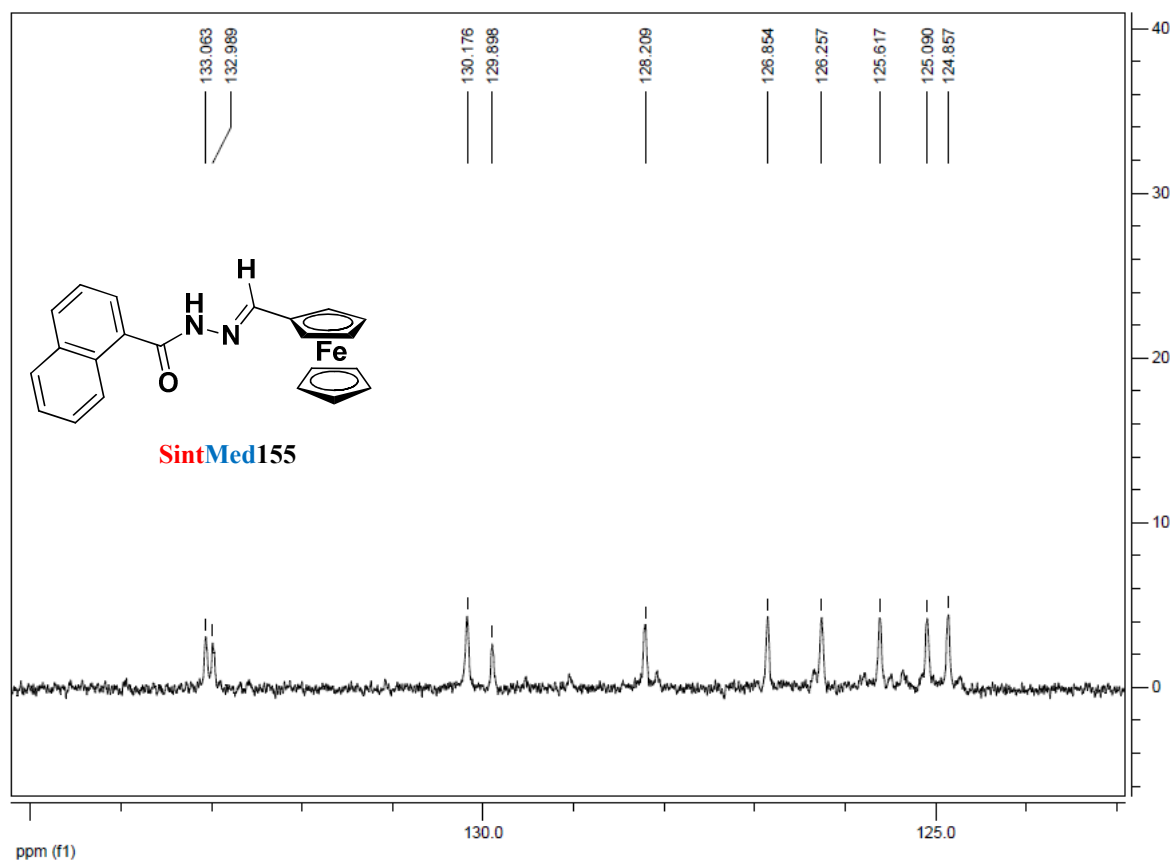
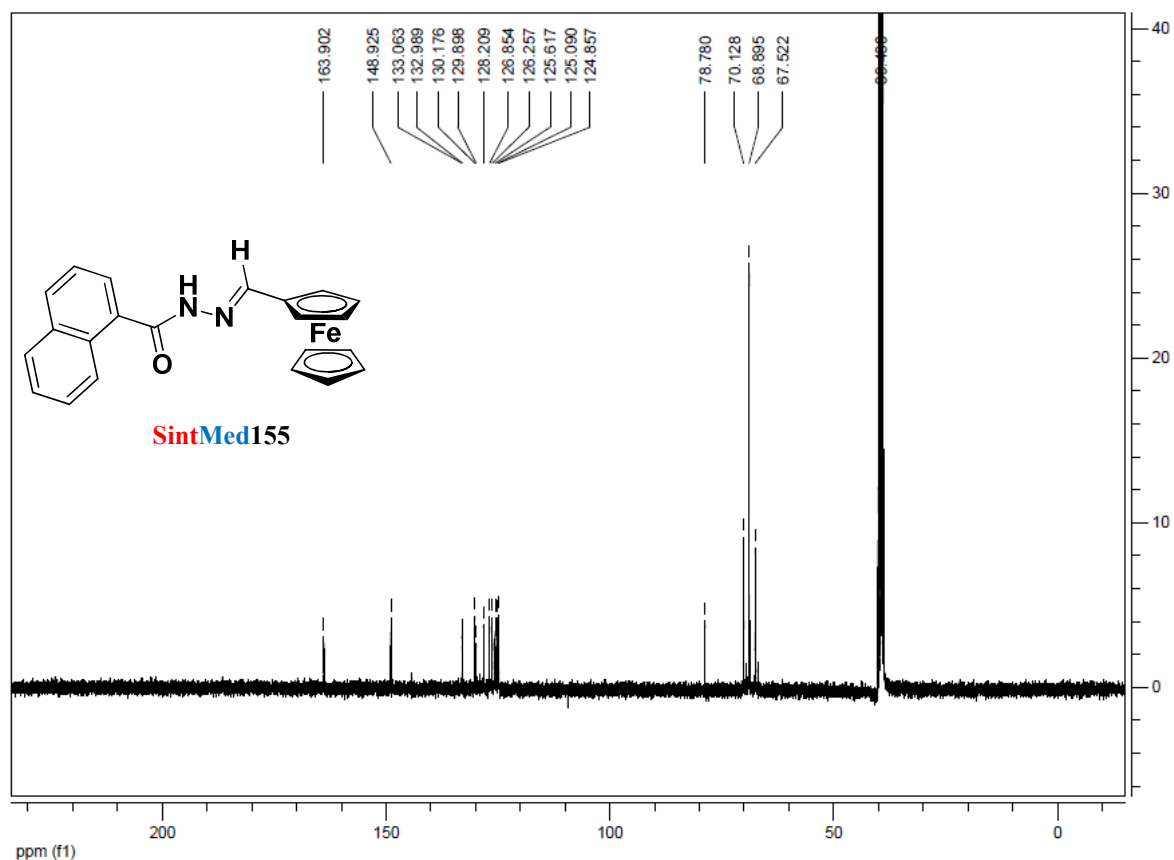




¹H NMR spectrum of SintMed155 (400 MHz, DMSO-*d*₆)

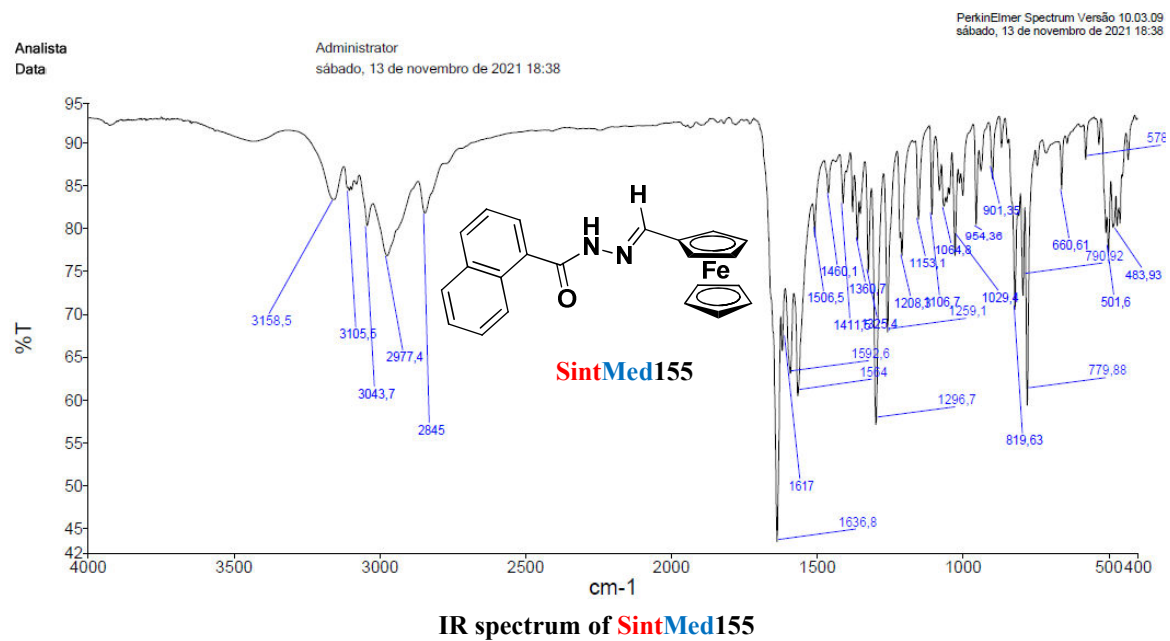


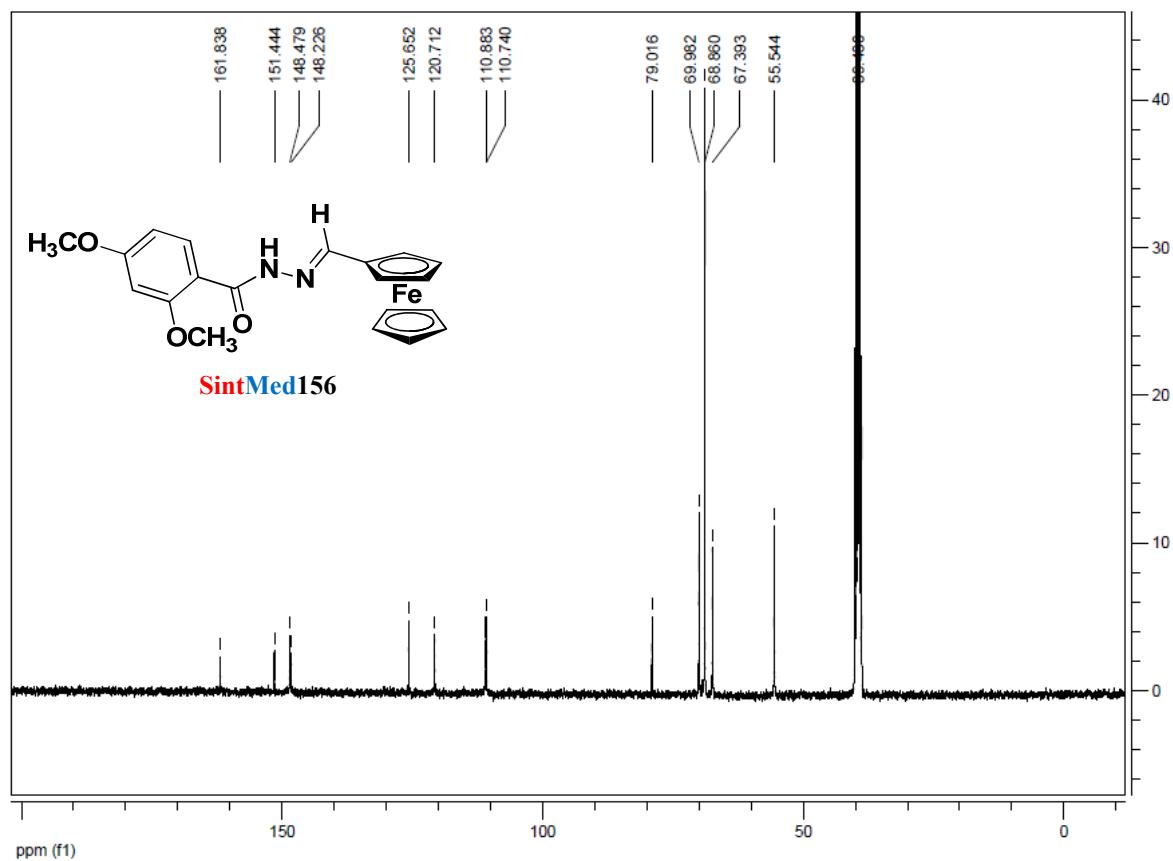
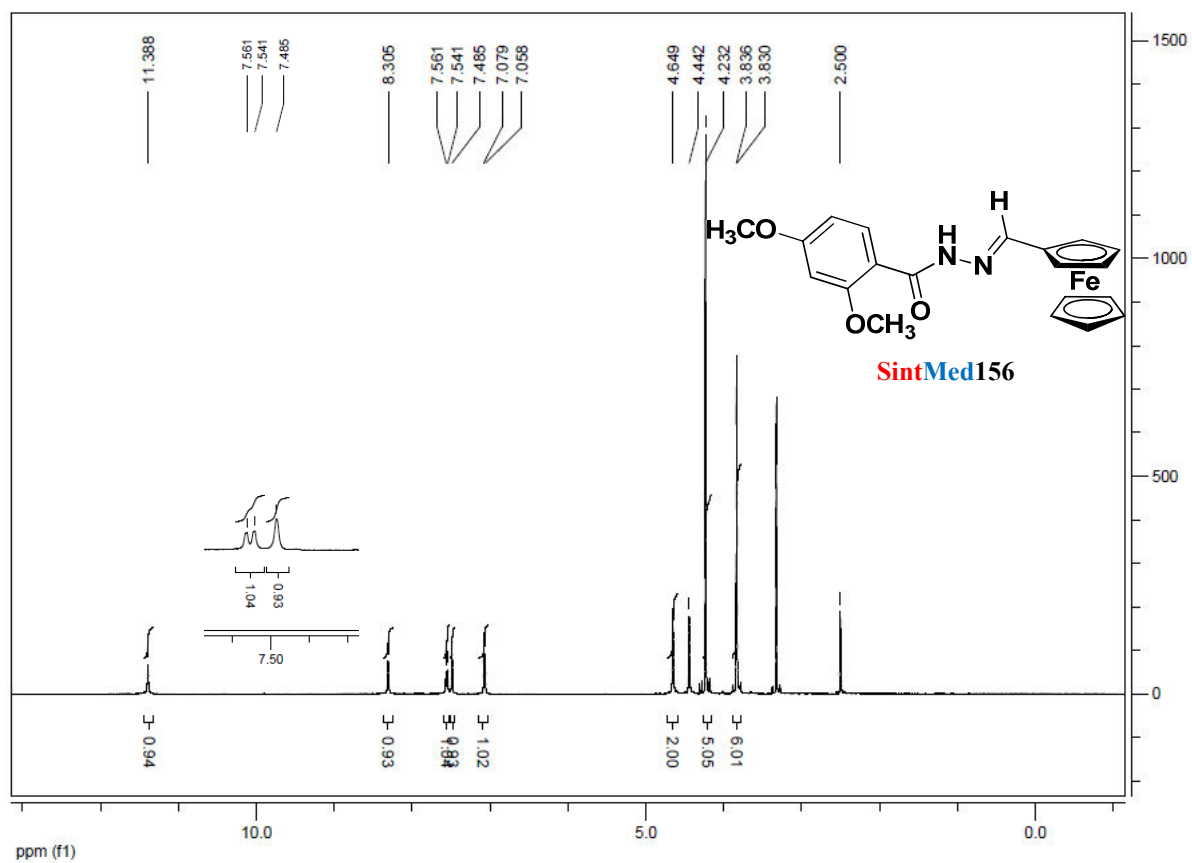
¹H NMR spectrum expansion of SintMed155 (400 MHz, DMSO-*d*₆)



¹³C NMR spectrum of **SintMed155** (100 MHz, DMSO-*d*₆)

¹³C NMR spectrum expansion of **SintMed155** (100 MHz, DMSO-*d*₆)

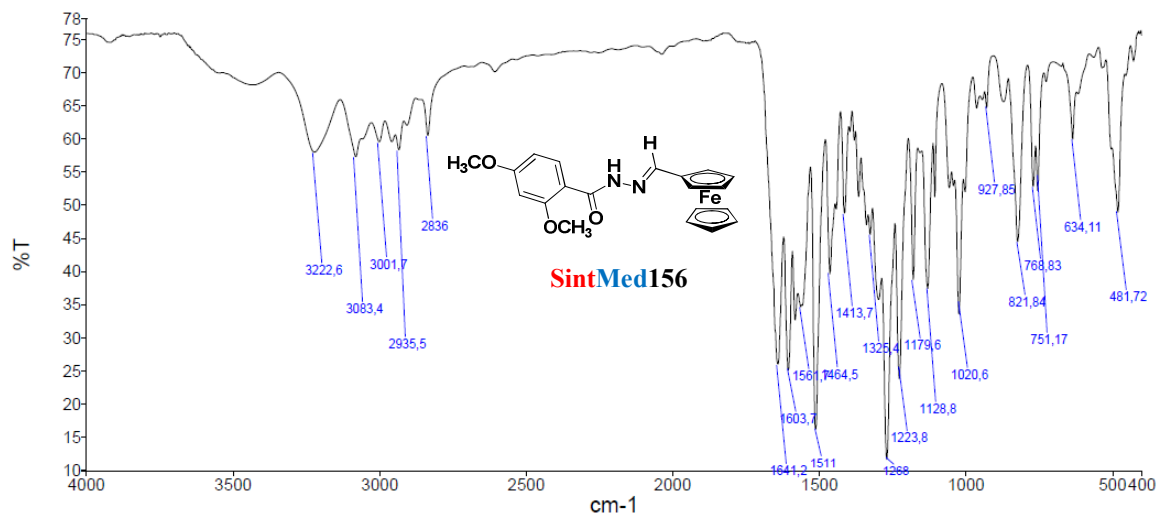




Analista
Data

Administrator
sexta-feira, 12 de novembro de 2021 18:32

PerkinElmer Spectrum Versão 10.03.09
sexta-feira, 12 de novembro de 2021 18:32



IR spectrum of SintMed156

X-ray crystallographic data of SintMed149

The X-ray crystallographic studies reveal that the complex crystallizes in the triclinic system with the P-1 space group and exhibits two molecules in the asymmetric unit. As shown in **Fig. S1**, the obtained crystal structure corroborates with the results from the other characterization techniques. These two molecules of the asymmetric unit are similar, being the main difference in the overlapping of the ferrocene rings, which in one approaches the eclipsed conformation, while the other is more similar to the staggered conformation.

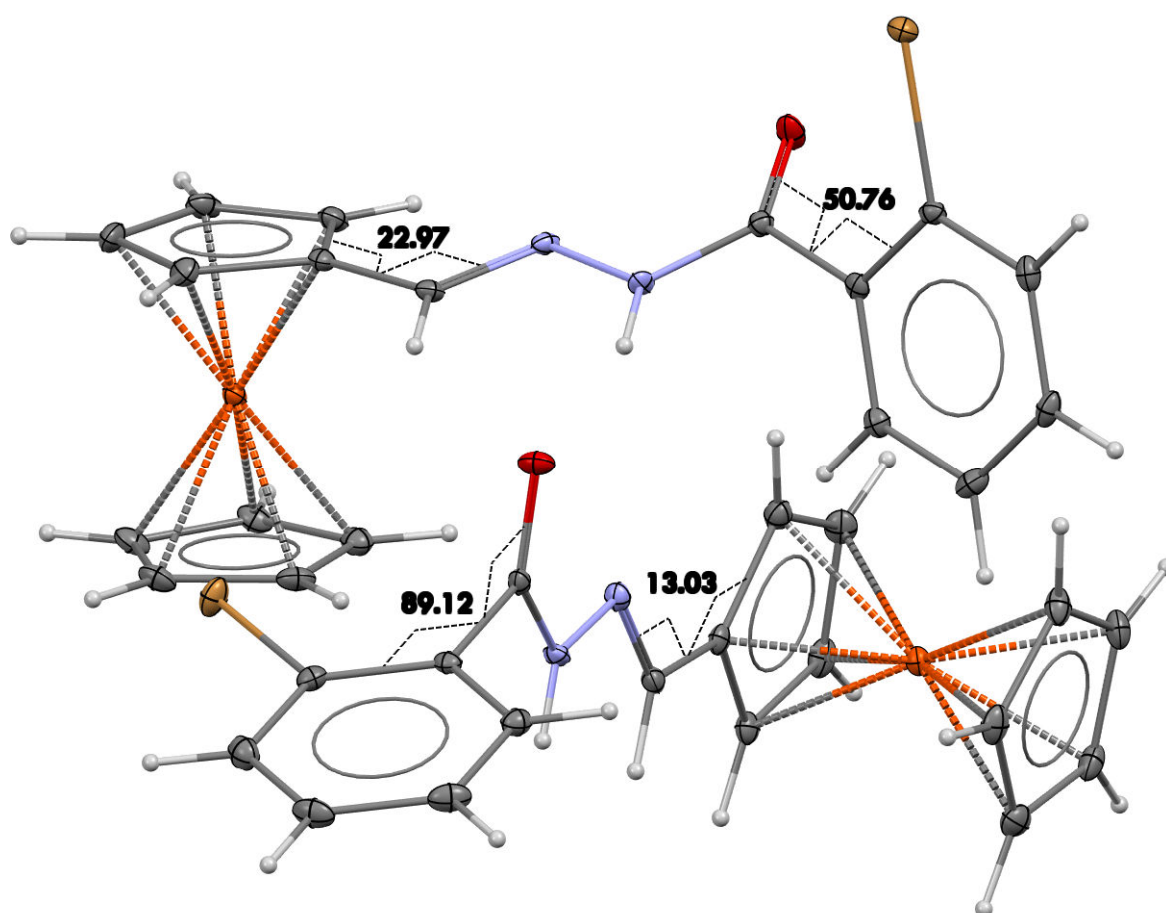


Figure S1. Representation of the asymmetric unit and torsion angles presented by the complex SintMed149.

Another important difference between these two molecules is the torsion angles presented between the plane of the ferrocene ring and the C=N bond and the six-member aromatic ring and the C=O bond, as shown in **Figure S1**. These different angles presented by equivalent molecules confirm the high fluxionality of these molecules.

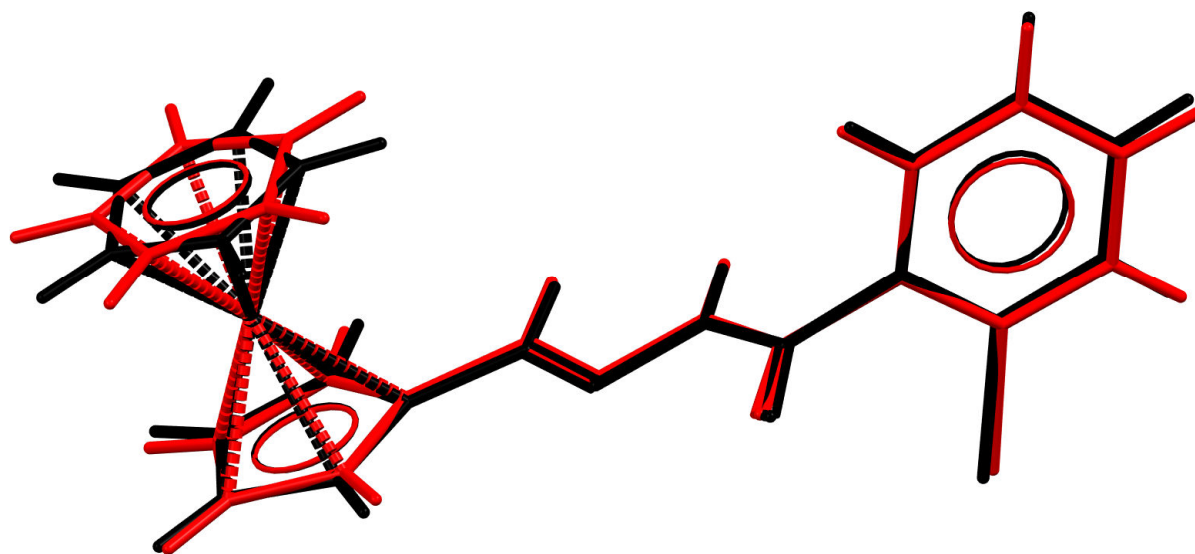


Figure S2. Superposition of the two structures present in the asymmetric unit obtained in the crystallographic studies of compound **SintMed149**.

Table S1. Crystal data and structure refinement for complex **SintMed149**.

CCDC code	2214776
Empirical formula	C ₁₈ H ₁₅ BrFeN ₂ O
Formula weight	411.08
Temperature/K	100.01(10)
Crystal system	triclinic
Space group	P-1
a/Å	7.3780(2)
b/Å	10.3437(3)
c/Å	21.0830(6)
α/°	88.551(3)
β/°	89.580(2)
γ/°	81.369(2)
Volume/Å ³	1590.22(8)
Z	4
ρ _{calc} /cm ³	1.717
μ/mm ⁻¹	3.466
F(000)	824.0
Crystal size/mm ³	0.215 × 0.072 × 0.026
Radiation	Mo Kα (λ = 0.71073)
2θ range for data collection/°	5.484 to 54.2
Index ranges	-9 ≤ h ≤ 9, -13 ≤ k ≤ 13, -26 ≤ l ≤ 27
Reflections collected	28737
Independent reflections	7025 [R _{int} = 0.0389, R _{sigma} = 0.0357]
Data/restraints/parameters	7025/0/415
Goodness-of-fit on F ²	1.028
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0274, wR ₂ = 0.0569
Final R indexes [all data]	R ₁ = 0.0363, wR ₂ = 0.0591
Largest diff. peak/hole / e Å ⁻³	0.42/-0.31