Electronic Supplementary Material (ESI) for Molecular Systems Design & Engineering.

Supporting Information

Synthesis, Structure and stimuli-responsive metallogel of a designer ferrocene appended peptide mimetic

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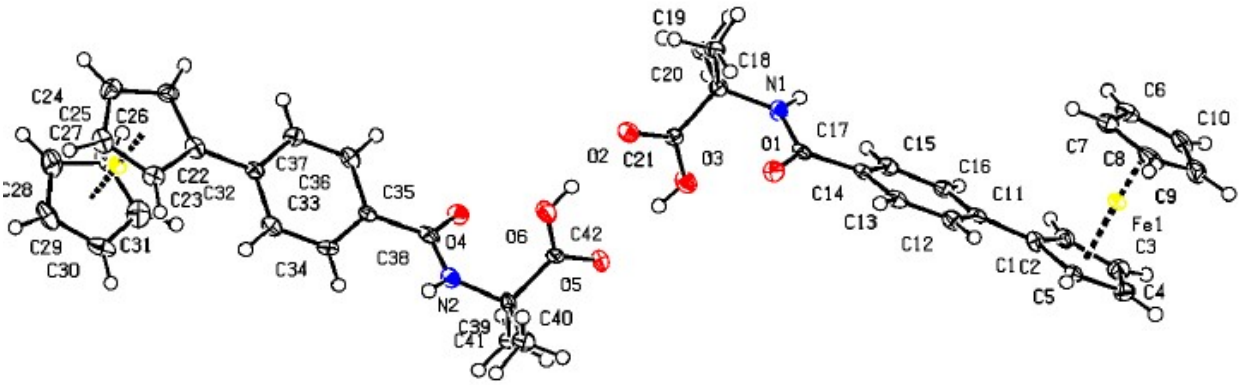

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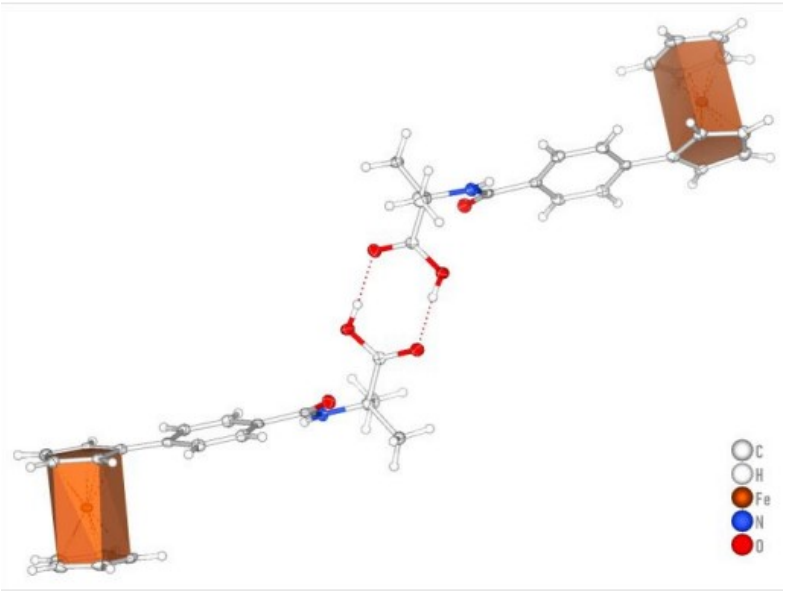

Fig. S1: (a) The ORTEP diagram of peptide mimetic **1** including the atom numbering scheme. Thermal ellipsoids are shown at the level of 50% probability. (b) Peptide mimetic **1** in solid state.

The structure was solved and the space group P21/c (# 14) determined by the ShelXT 2014/5 (Sheldrick, 2014) structure solution program using using iterative methods and refined by full matrix least squares minimisation on F2 using version of olex2.refine 1.5-alpha (Bourhis et al., 2015). All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model. Hydrogen atom positions were calculated geometrically and refined using the riding model.
This structure is based on twinned data -- the embedded de-twinned hklf5 format file has been obtained using PLATON/TWINROTMAT.

A.L.Spek, J. Appl. Cryst. 2003, 36, 7-11. Single-crystal structure validation with the program PLATON

ESI Table S1: Crystal data and structure refinement for peptide mimetic **1**.

Solvent of Crystallization Methanol-water (90:10)

Compound	**FEPBAIBOH**
Formula	$C_{42}H_{42}Fe_2N_2O_6$
$D_{calc.}$/ g cm^{-3}	1.488
μ/mm^{-1}	7.096
Formula Weight	782.502
Colour	clear orangish orange
Shape	needle-shaped
Size/mm^3	0.42×0.37×0.21
T/K	100.01(12)
Crystal System	monoclinic
Space Group	$P2_1/c$
a/Å	15.2027(3)
b/Å	5.7642(1)
c/Å	39.9987(7)
α/°	90
β/°	94.735(2)
γ/°	90
V/Å^3	3493.18(11)
Z	4
Z'	1
Wavelength/Å	1.54184
Radiation type	Cu K_α
Θ_{min}/°	2.22
Θ_{max}/°	68.26
Measured Refl's.	6329
Indep't Refl's	6329
Refl's I≥2 σ(I)	5999
R_{int}	.
Parameters	476
Restraints	0
Largest Peak	0.7889
Deepest Hole	-0.7215
GooF	1.0433
wR_2 (all data)	0.1406
wR_2	0.1397
R_1 (all data)	0.0504
R_1	0.0485

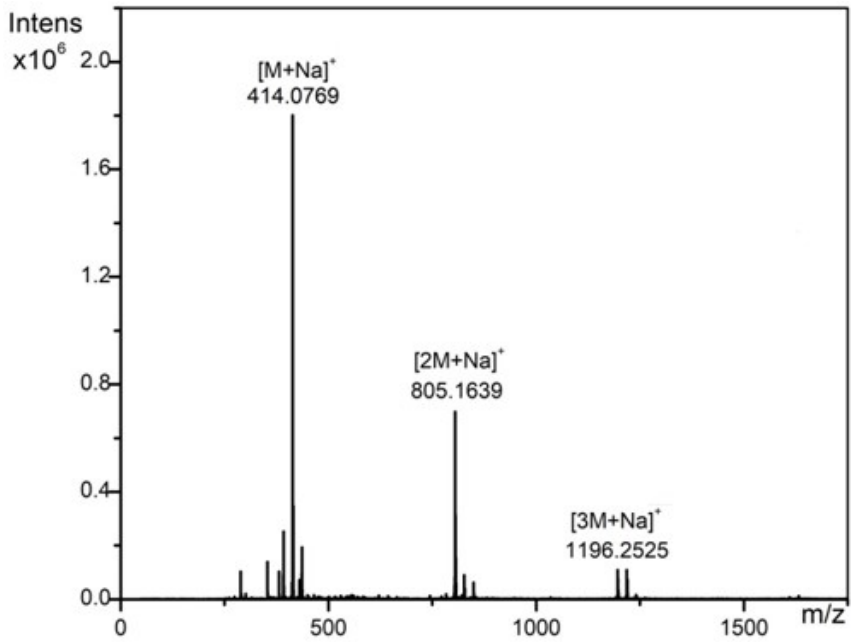

Fig. S2: The HRMS spectra of peptide mimetic **1**.

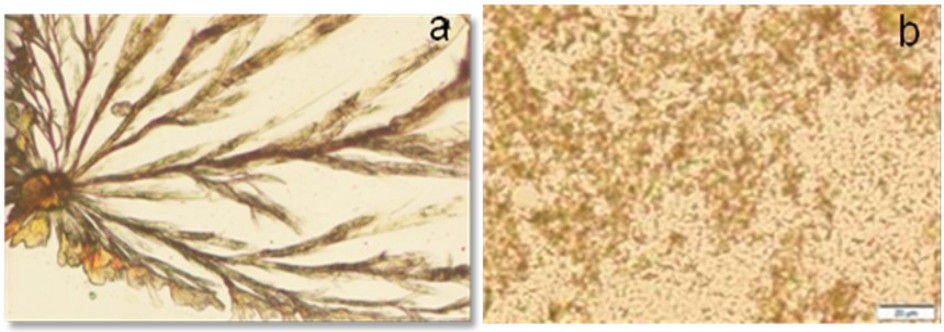

Fig. S3. POM images of peptide mimetic **1** (a) in DMF solution and (b) xerogel from DMF-water.

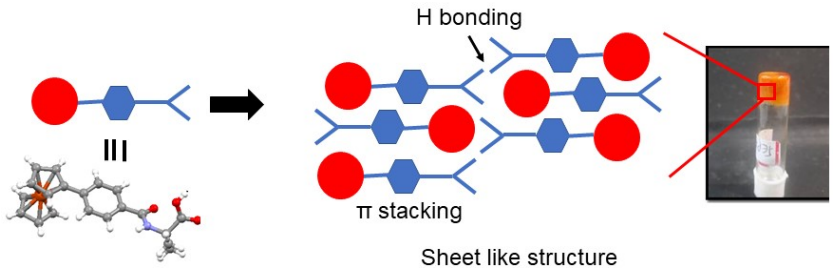

Fig. S4. The proposed model of supramolecular metallogel.

Synthesis and characterization

Synthesis of Compound **2**

Methyl-4-aminobenzoate (1.914 g, 10.2 mmol) from its hydrochloric was dissolved in 10 ml of water and concentrated hydrochloric acid (3 ml) was added intermittent cooling. A solution of sodium nitrite (0.703 g, 10.2 mmol) in 10 ml of water was added slowly to the mixture with stirring under ice-water bath conditions. The resulting palen yellow diazo salt solution was added to a solution of ferrocene (1.860 g, 10.0 mmol) in diethyl ether (50 ml) and allowed to react for 12 h at room temperature. The reactant mixture was then washed with water, the ether layer was dried over anhydrous sodium sulfate and evaporated in vacuo to yield crude product. The crude product was purified by column chromatography (eluent 10:0.5 n-hexane/ethyl acetate). Yield: 65 %.

^{1}H NMR ($CDCl_3$, 400MHz, δppm): 7.94-7.96 (d, 2H, Phenyl ring protons), 7.50-7.52 (d, 2H, phenyl ring protons), 4.71 (d, 2H, [*ortho* on η^5–C_5H_4]), 4.38-4.39 (d, 2H, [*meta* on η^5–C_5H_4]), 4.03 (s, 5H, [η^5–C_5H_4]), 3.92 (s, 3H,-OCH_3). ^{13}C NMR (125MHz, $CDCl_3$, δ in ppm, 298K): 167.27, 145.26, 129.84, 127.44, 125.74, 83.46, 69.93, 66.99, 52.11; ESI-MS (MeOH): m/z (Calc): $C_{19}H_{18}FeO_2$ $[M]^+$ 320.17; found: 320.79.

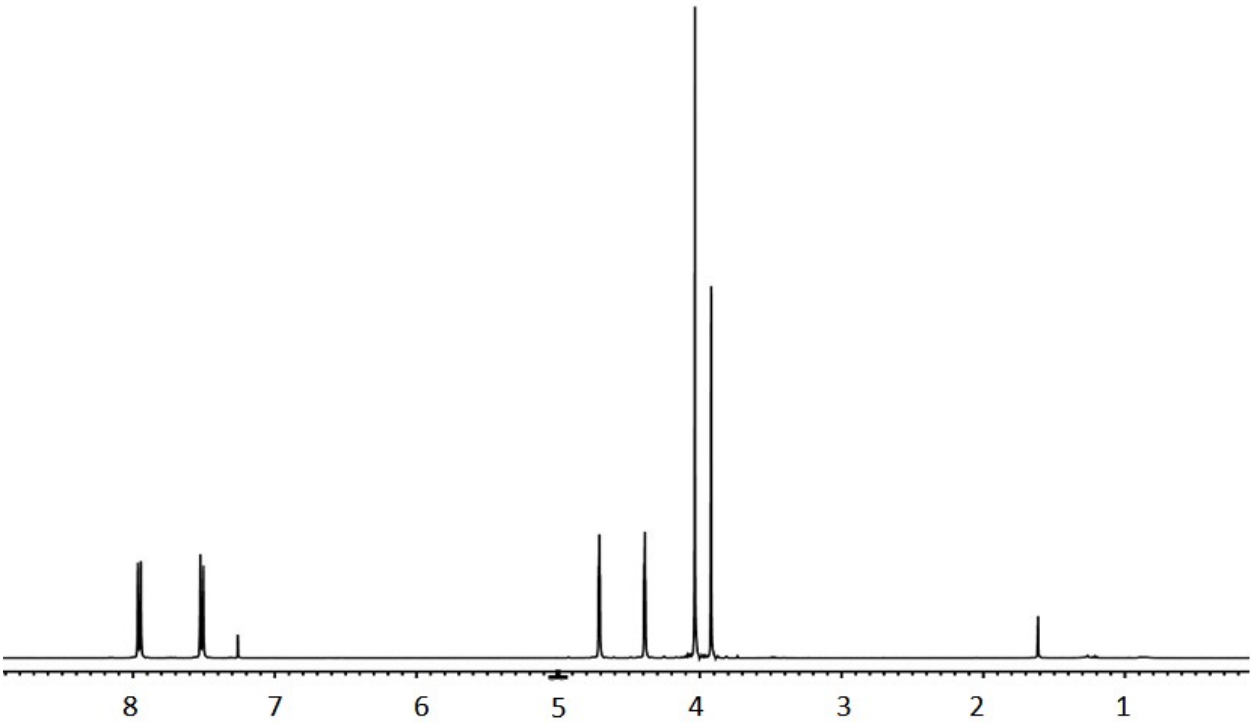

Figure S5. ^{1}H NMR (400 MHz, $CDCl_3$, δ in ppm, 298K) spectrum of Compound **2**

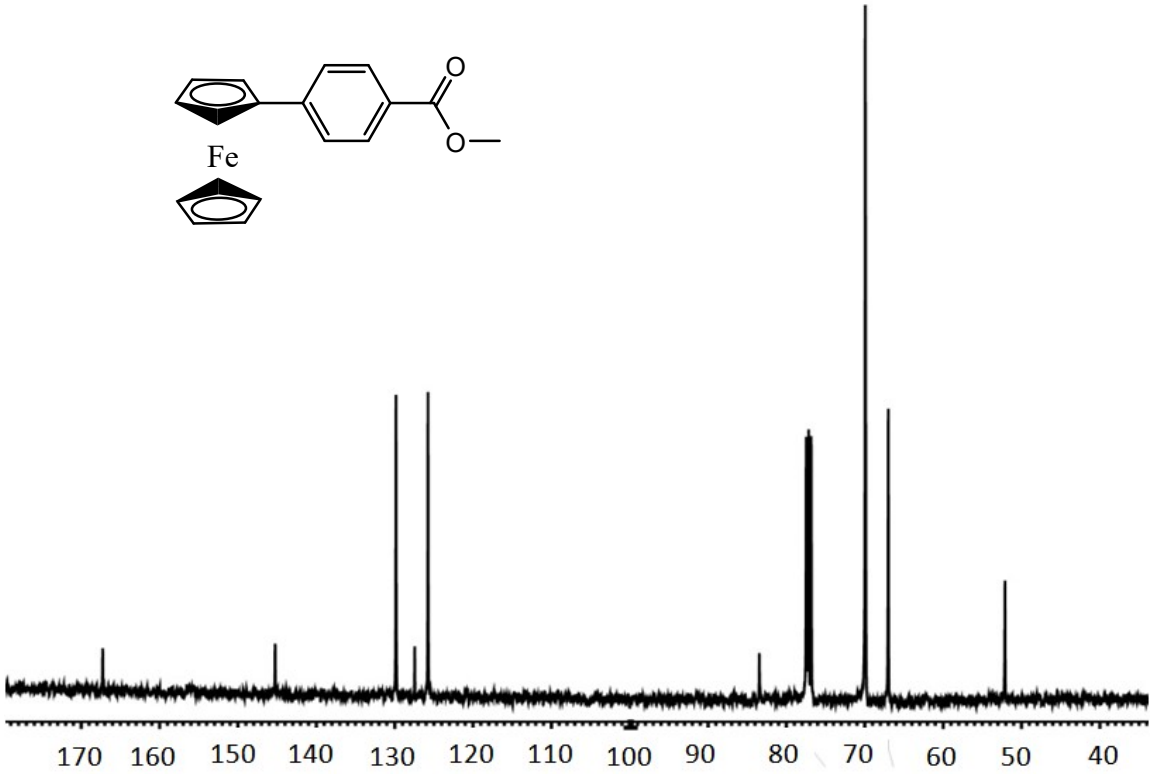

Figure S6. ^{13}C NMR (125 MHz, $CDCl_3$, δ in ppm, 298K) spectrum of Compound **2**

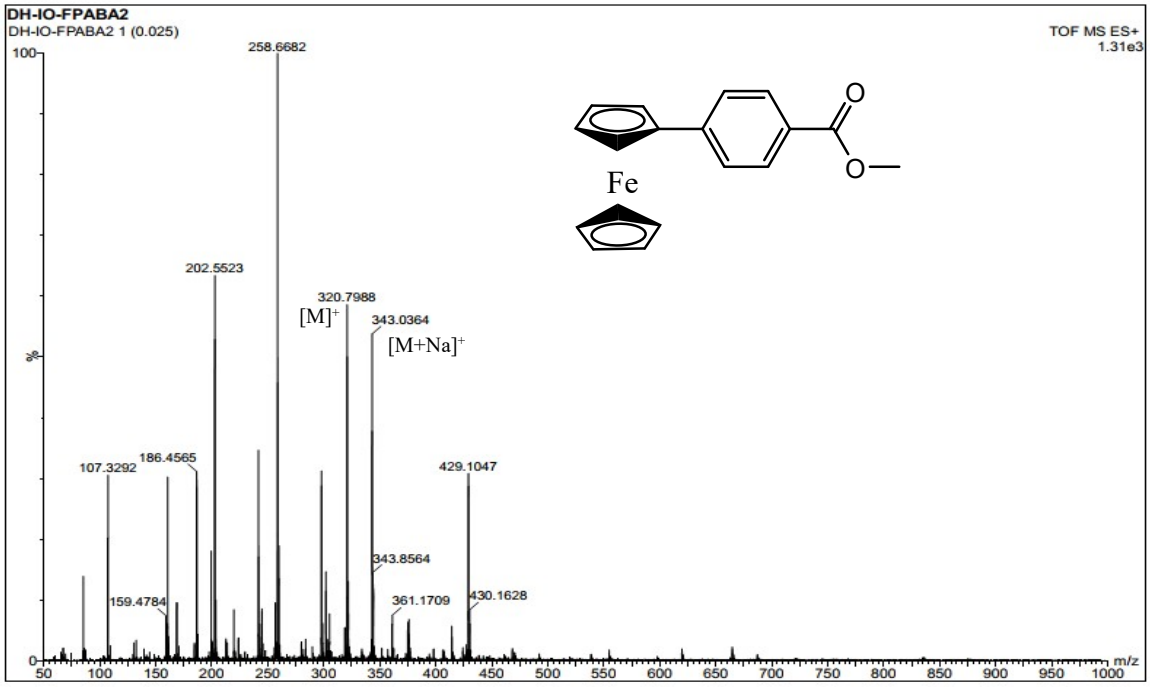

Figure S7. Mass Spectrum of Compound **2**

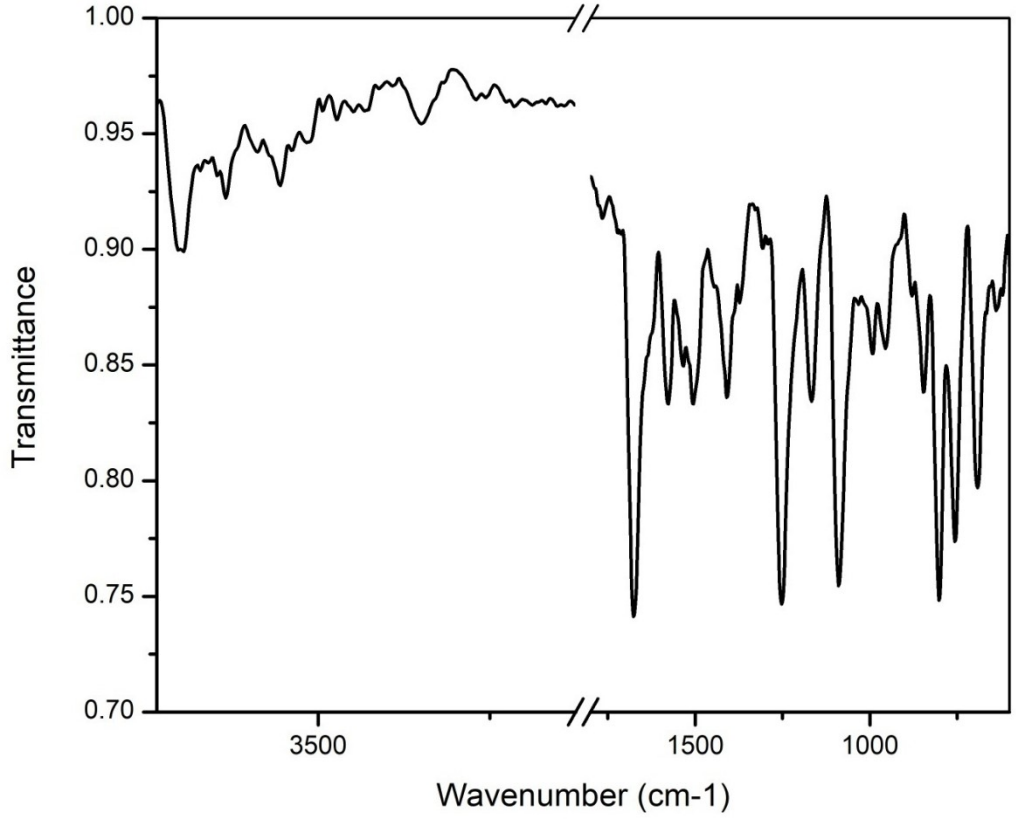

Figure S8. FT-IR Spectrum of Compound **2**

Synthesis of Compound **3**

Para-Ferrocenyl methyl benzoate (**2**) 1.761 g (5.5 mmol) was dissolved in 25 ml methanol and 10 ml of 2 N NaOH in ice water and stirred for 10 hrs. Methanol was evaporated under reduced pressure with rotary evaporator. 25 ml of water was added to the residue, the residue was washed with diethyl ether in separating funnel. The pH of the aqueous layer was adjusted by using 1 M HCl. It was then extracted with ethyl acetate (3 x 50 ml) in separating funnel. The extract in ethyl acetate was dried over anhydrous Na_2SO_4, filtered using separating funnel and cotton wool. The filtrate was evaporated under reduced pressure using rotary evaporator. Yield: 90 %.

^{1}H NMR (DMSO-d_6, 400MHz, δppm): 12.77-12.85 (b, 1H, Acid OH), 7.86-7.88 (d, 2H, Phenyl ring protons), 7.61-7.63 (d, 2H, phenyl ring protons), 4.84 (d, 2H, [*ortho* on η^5–C_5H_4]), 4.39 (d, 2H, [*meta* on η^5–C_5H_4]), 3.99 (s, 5H, [η^5–C_5H_4]). ^{13}C NMR (125MHz, DMSO-d_6, δ in ppm, 298K): 167.33, 144.59, 129.27, 127.82, 125.57, 82.88, 69.70, 66.77; ESI-MS (MeOH): m/z (Calc): $C_{17}H_{14}FeO_2$ $[M]^+$ 307.04; found: 307.34.

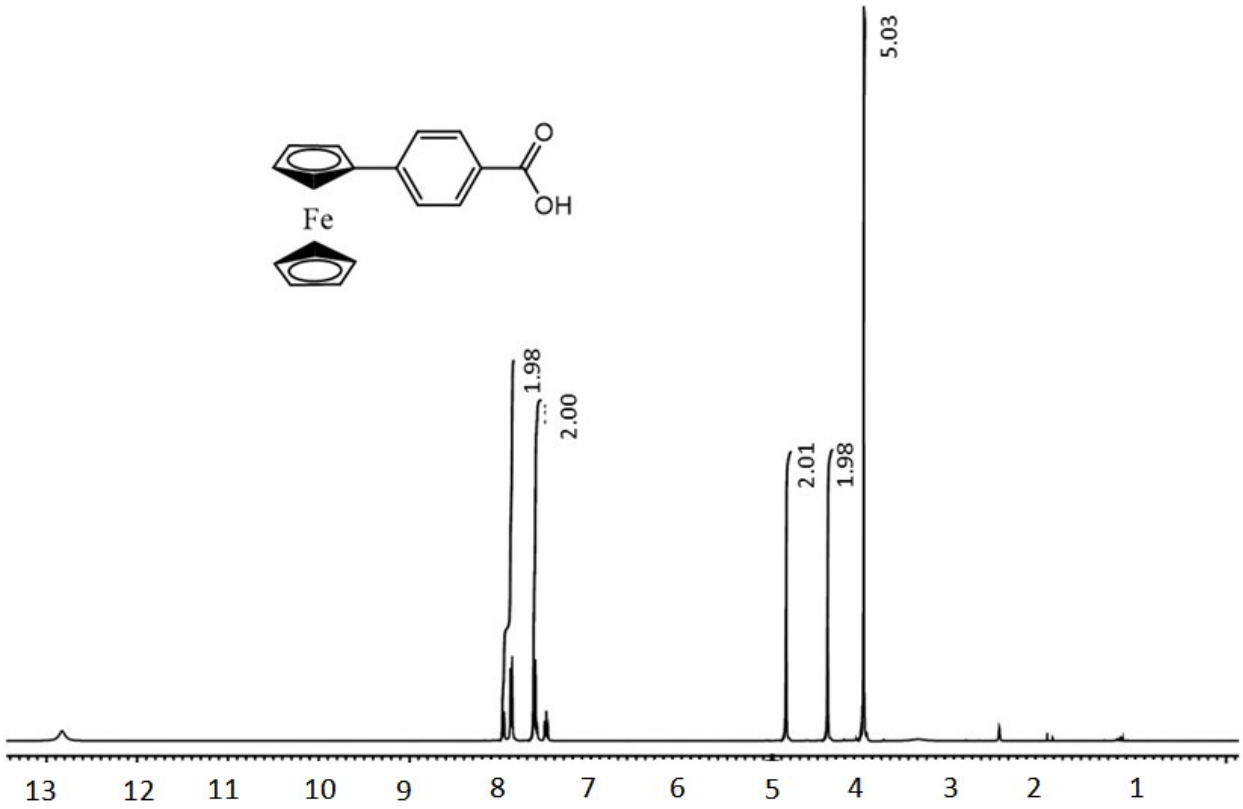

Figure S9. ^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm, 298K) spectrum of Compound **3**

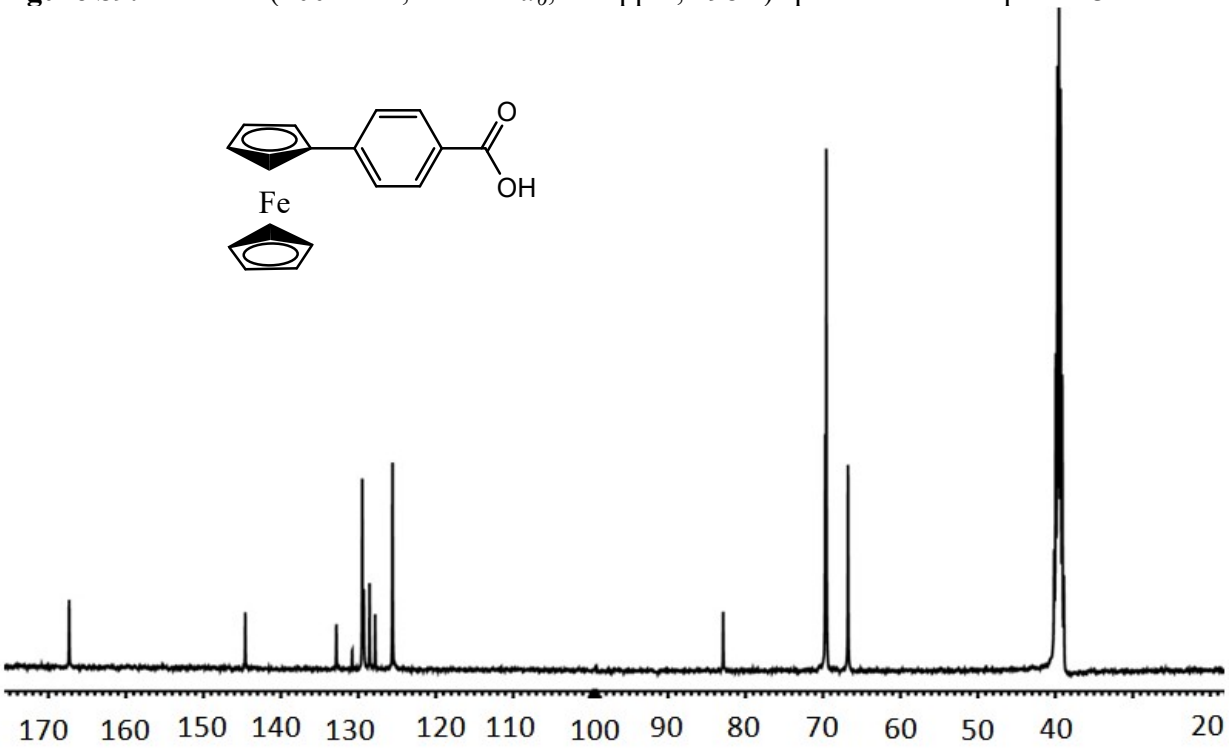

Figure S10. ^{13}C NMR (125 MHz, DMSO-d_6, δ in ppm, 298K) spectrum of Compound **3**

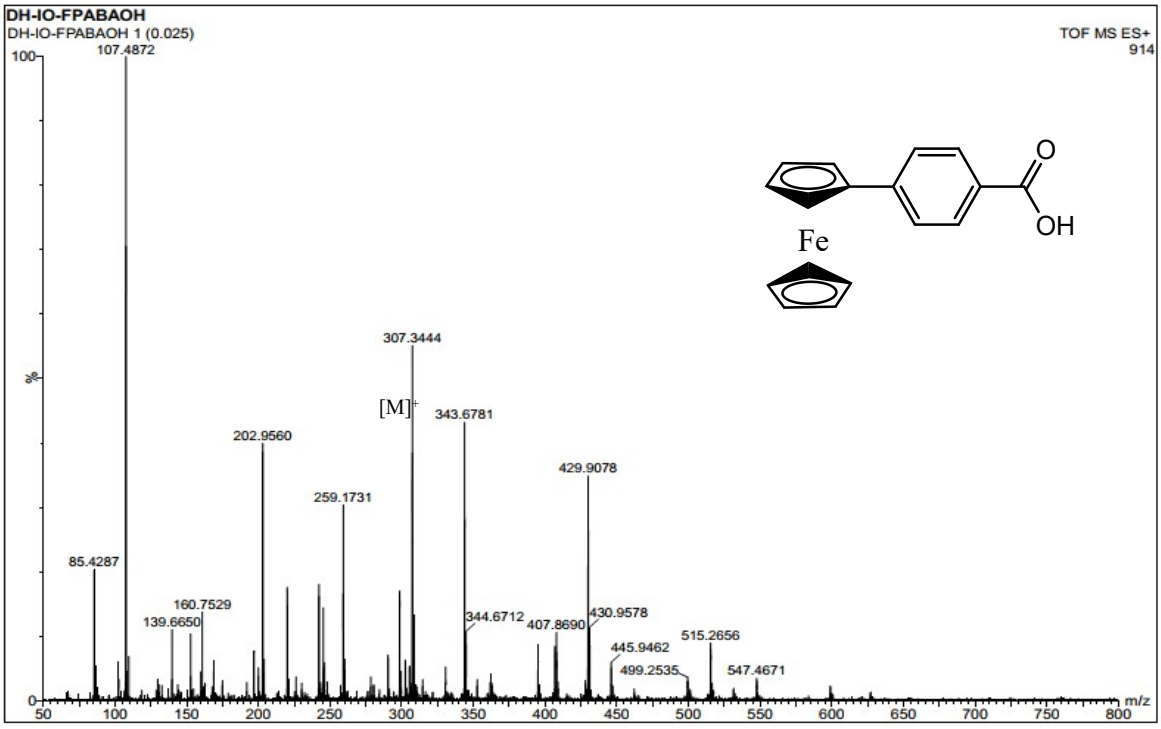

Figure S11. Mass Spectrum of Compound **3**

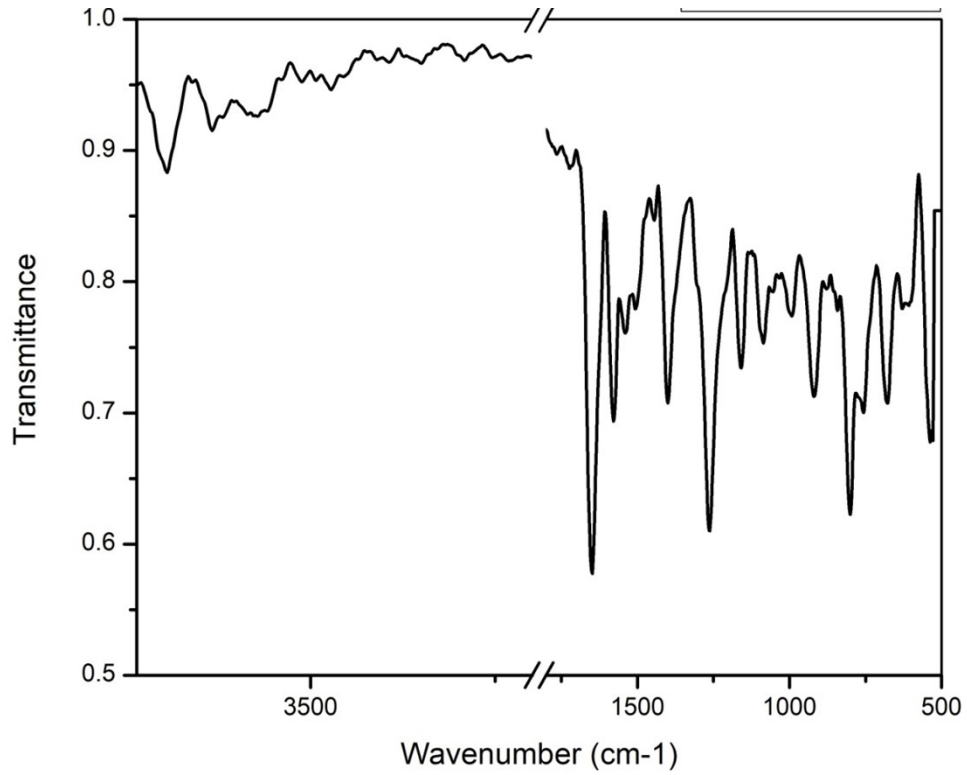

Figure S12. FT-IR Spectrum of Compound **3**

Synthesis of Compound **4**

Para-Ferrocenyl methyl benzoic acid (**3**) 1.530 g (5 mmol) was dissolved in 20 mL of dry DCM and 5 ml of dry DMF under ice−water bath conditions, followed by the addition of 1.547 g (7.5 mmol) of DCC and 1.148 g (7.5 mmol) of HOBt. 1.152 g (7.5 mmol) AIB-Ome (**iii**) from its hydrochloric was then added to the solution. The reaction mixture was stirred for 48 h at room temperature. After the completion of the reaction, DCM was evaporated, and the residue was dissolved in ethyl acetate (40 mL) and was put in fridge for 3 h for dicyclohexylurea (DCU) to precipitate, dicyclohexylurea (DCU) was filtered off and water (50 ml) was added and stirred at room temperature for 30 min and subsequently, the ethyl acetate layer was washed with 2 M HCl (3 × 50 mL), brine (2 × 50 mL), 1 M sodium carbonate (3 × 50 mL), and brine (2 × 50 mL), respectively. The organic layer was dried over anhydrous sodium sulfate and evaporated under vacuum to yield compound **4** as solid. The product was purified by silica gel using hexane/ethyl acetate (4/1) as eluent. Yield: 58 %.

^{1}H NMR ($CDCl_3$, 500MHz, δppm): 7.69-7.70 (d, 2H, Phenyl ring protons), 7.48-7.50 (d, 2H, phenyl ring protons), 6.79 (s, 1H, AiB-NH), 4.68 (s, 2H, [*ortho* on η^5–C_5H_4]), 4.36 (s, 2H, [*meta* on η^5–C_5H_4]), 3.87 (s, 5H, [η^5–C_5H_4]), 3.78 (s, 3H, OCH_3) 1.42 (s, 6H, Aib-CH_3). ^{13}C NMR (125MHz, $CDCl_3$, δ in ppm, 298K): 175.44, 166.55, 143.67, 131.70, 127.22, 125.68, 83.61, 69.70, 66.84, 60.46, 56.95, 52.84, 24.92, 21.12, 14.29; ESI-MS (MeOH): m/z (Calc): $C_{22}H_{23}FeO_2$ $[M]^+$ 406.11; found: 406.02.

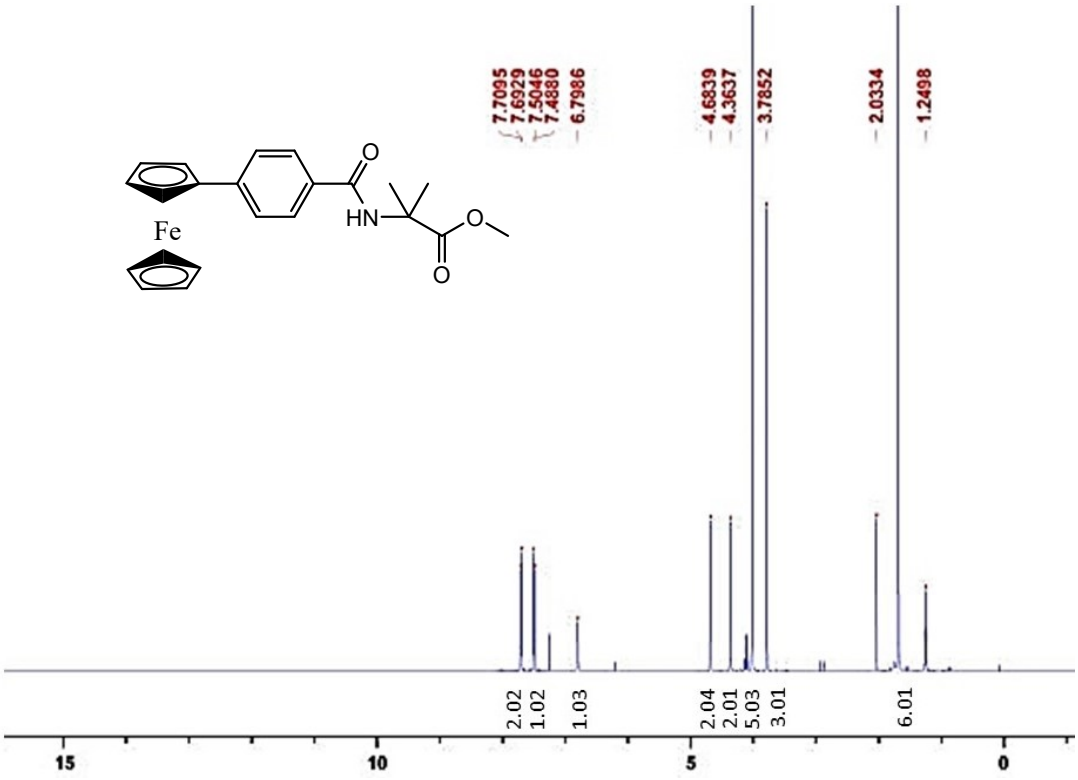

Figure S13. ^{1}H NMR (500 MHz, $CDCl_3$, δ in ppm, 298K) spectrum of Compound **4**

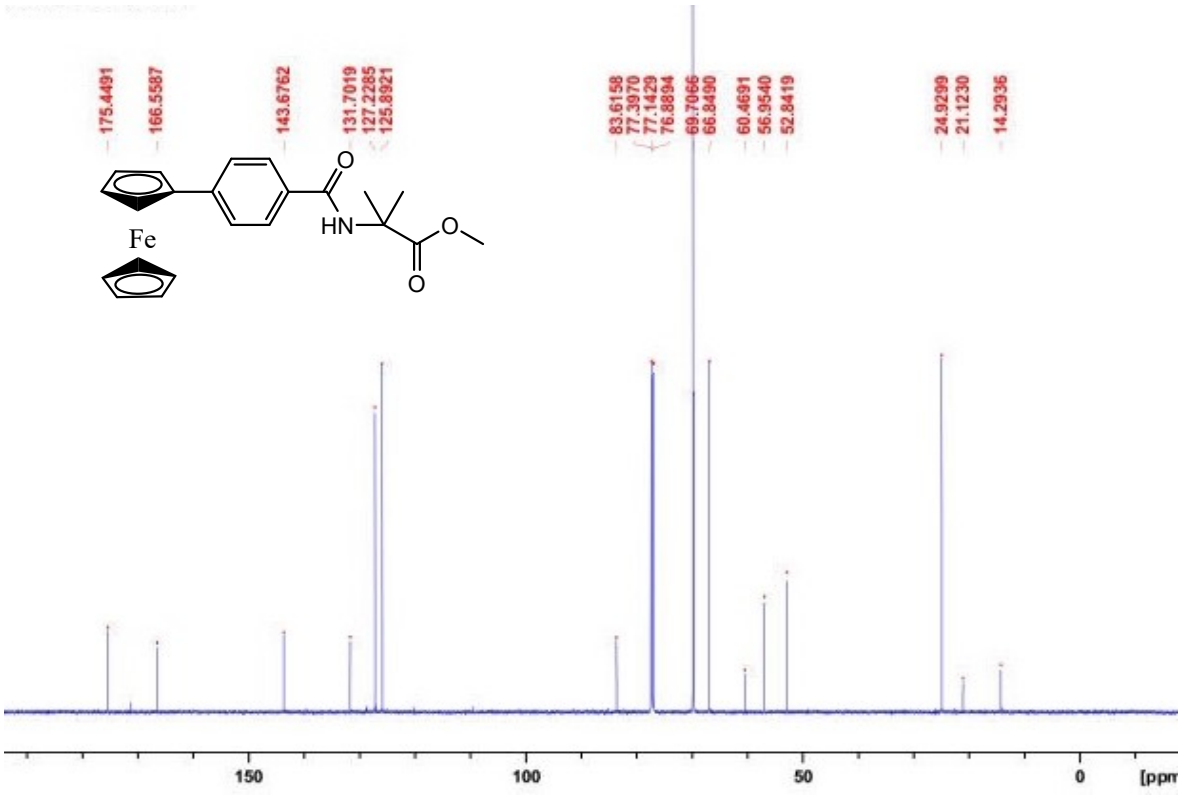

Figure S14. ^{13}C NMR (125 MHz, $CDCl_3$, δ in ppm, 298K) spectrum of Compound **4**

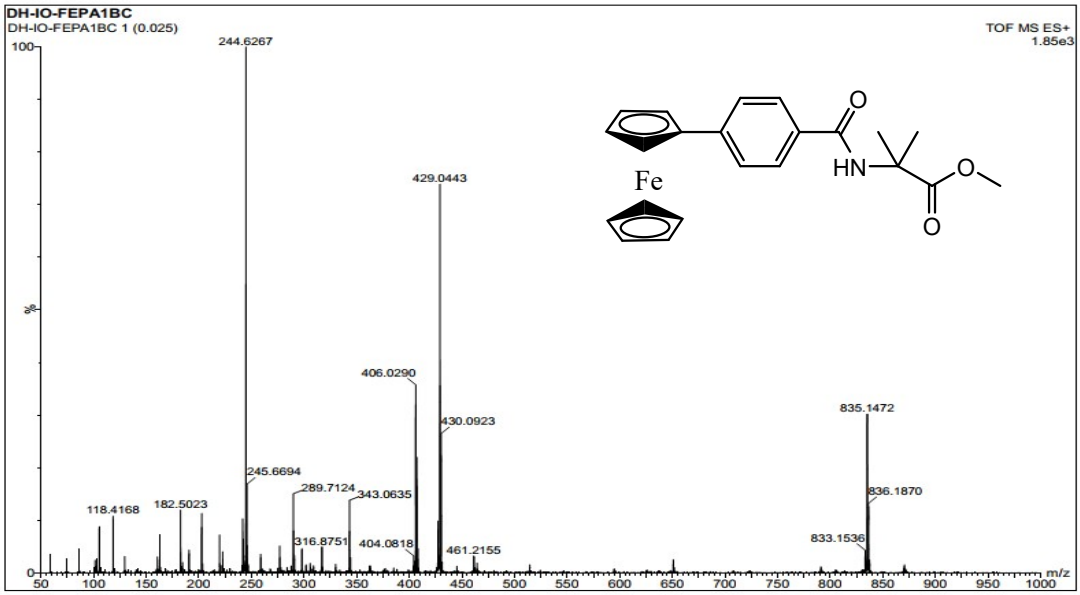

Figure S15. Mass Spectrum of Compound **3**.

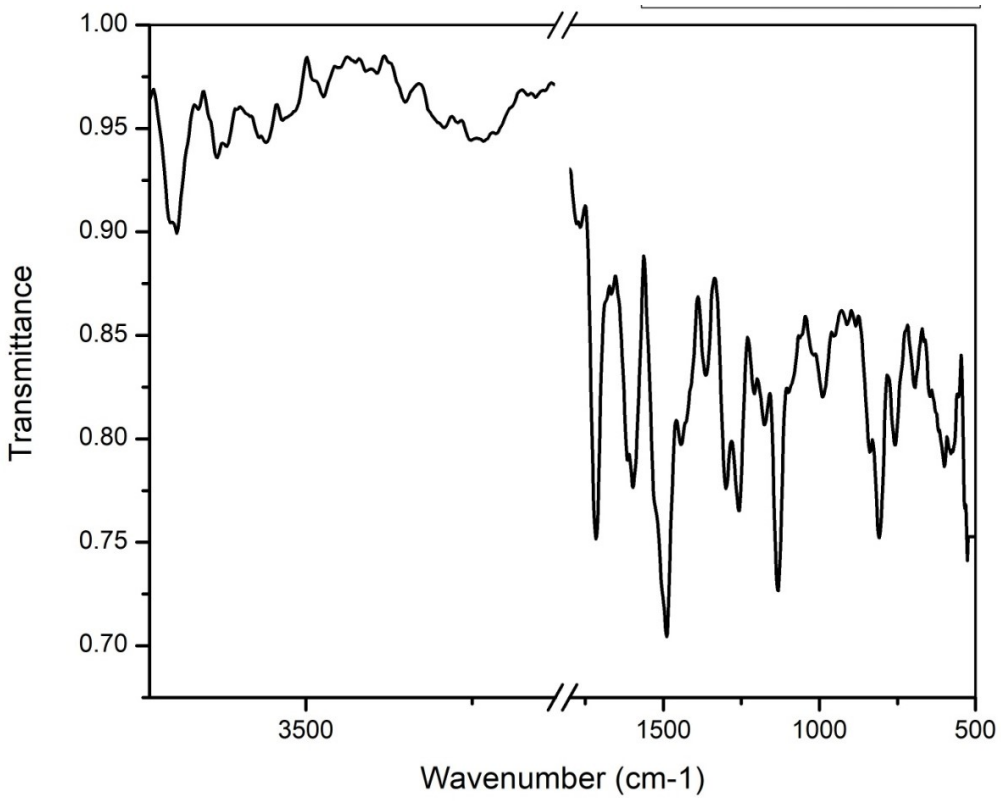

Figure S16. FT-IR Spectrum of Compound **4**

Synthesis of Compound **1**

Compound (4) 2.026 g (5 mmol) was dissolved in 25 ml methanol and 10 ml of 2 N NaOH in ice water and stirred for 10 hrs. Methanol was evaporated under reduced pressure with rotary evaporator. 25 ml of water was added to the residue, the residue was washed with diethyl ether in separating funnel. The pH of the aqueous layer was adjusted by using 1 M HCl. It was then extracted with ethyl acetate (3 x 50 ml) in separating funnel. The extract in ethyl acetate was dried over anhydrous Na_2SO_4, filtered using separating funnel and cotton wool. The filtrate was evaporated under reduced pressure using rotary evaporator. Yield: 80 %.

^{1}H NMR (DMSO-d_6, 400MHz, δppm): 12.27-12.32 (b, 1H, Acid OH), 8.52 (s, 1H, AiB-NH), 7.92-7.94 (d, 2H, Phenyl ring protons), 7.72-7.75 (d, 2H, phenyl ring protons), 5.00-5.01 (s, 2H, [*ortho* on η^5–C_5H_4]), 4.52-4.53 (s, 2H, [*meta* on η^5–C_5H_4]), 4.14-4.15 (s, 5H, [η^5–C_5H_4]), 1.64 (s, 6H, Aib-CH_3). ^{13}C NMR (125MHz, DMSO-d_6, δ in ppm, 298K): 175.64, 172.15, 176.04, 162.15, 143.41, 131.86, 127.70, 125.19, 83.23, 69.52, 66.60, 55.38, 25.07; ESI-MS (MeOH): m/z (Calc): $C_{21}H_{21}FeO_3$ $[M]^+$ 392.09; found: 392.16.

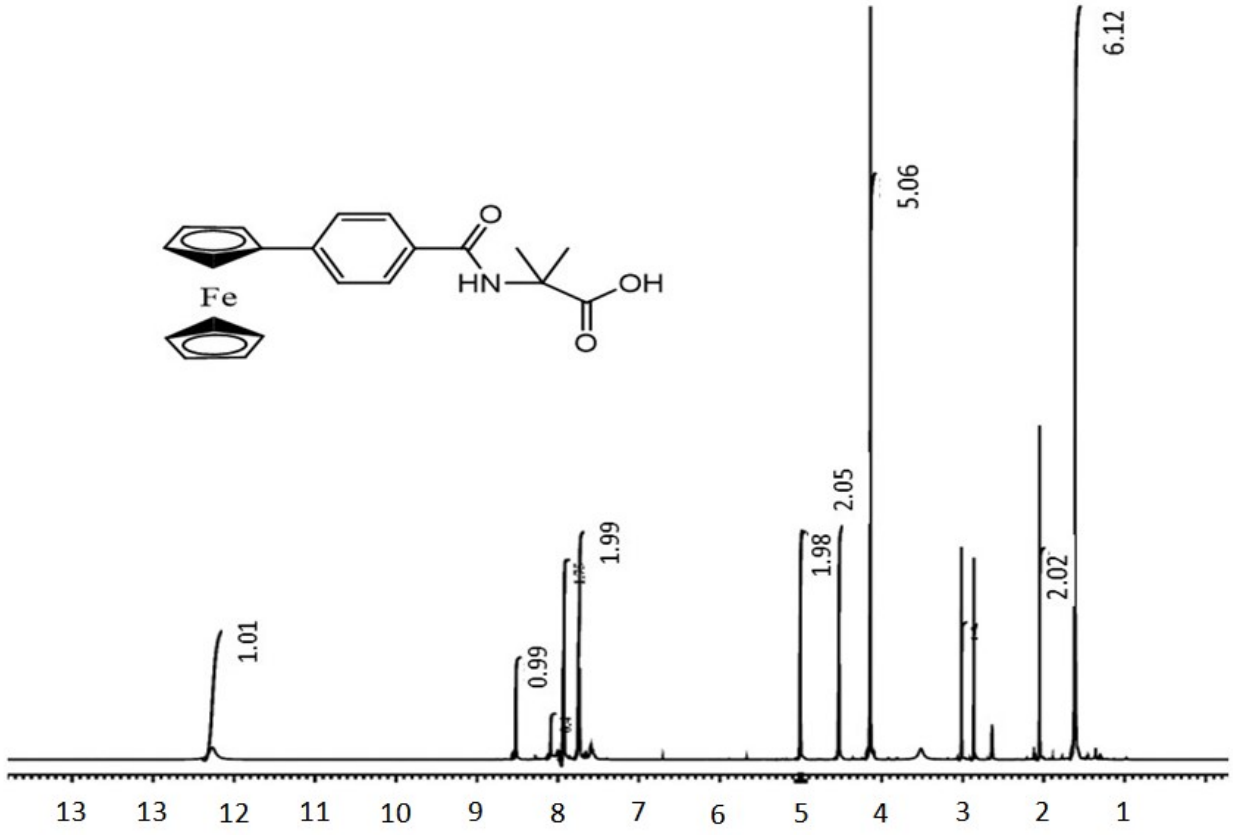

Figure S17. ^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm, 298K) spectrum of Compound **1**

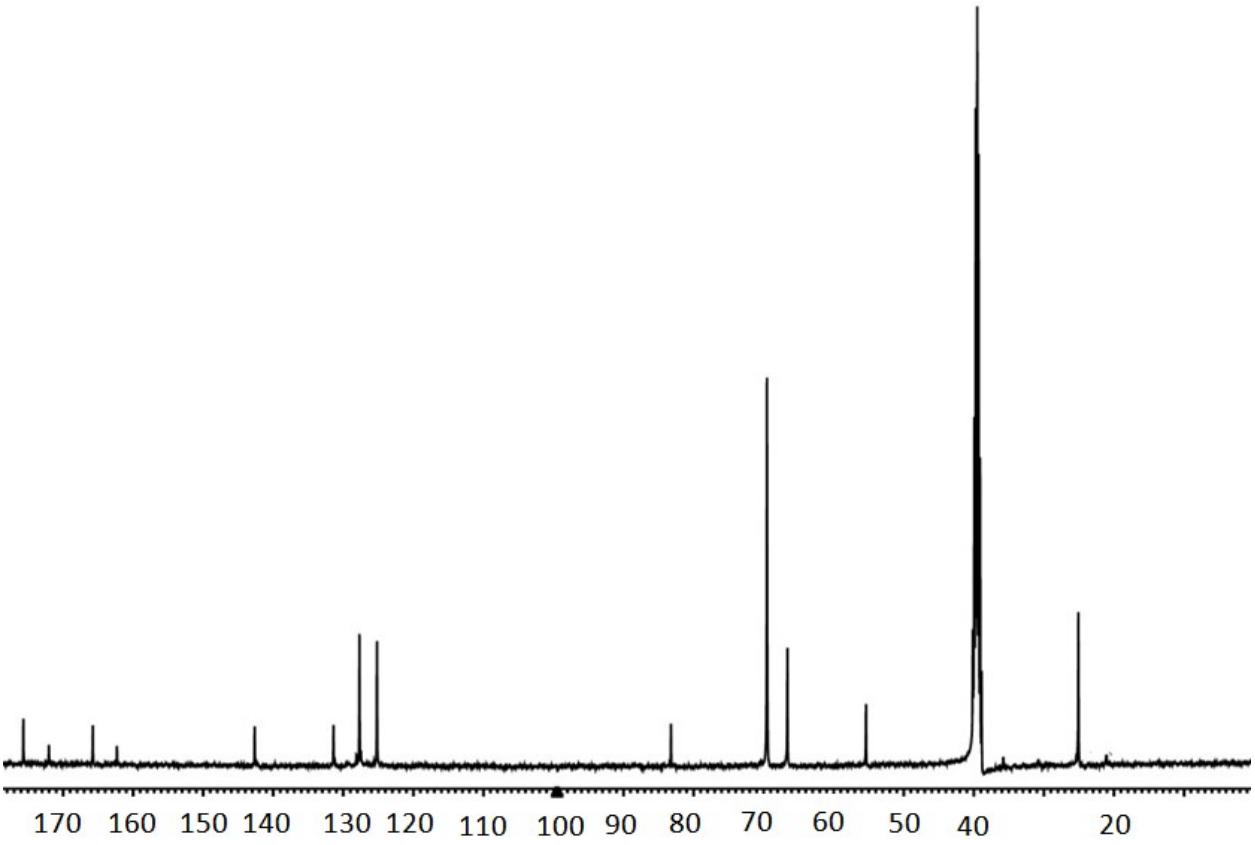

Figure S18. ^{13}C NMR (125 MHz, DMSO-d_6, δ in ppm, 298K) spectrum of Compound **1**

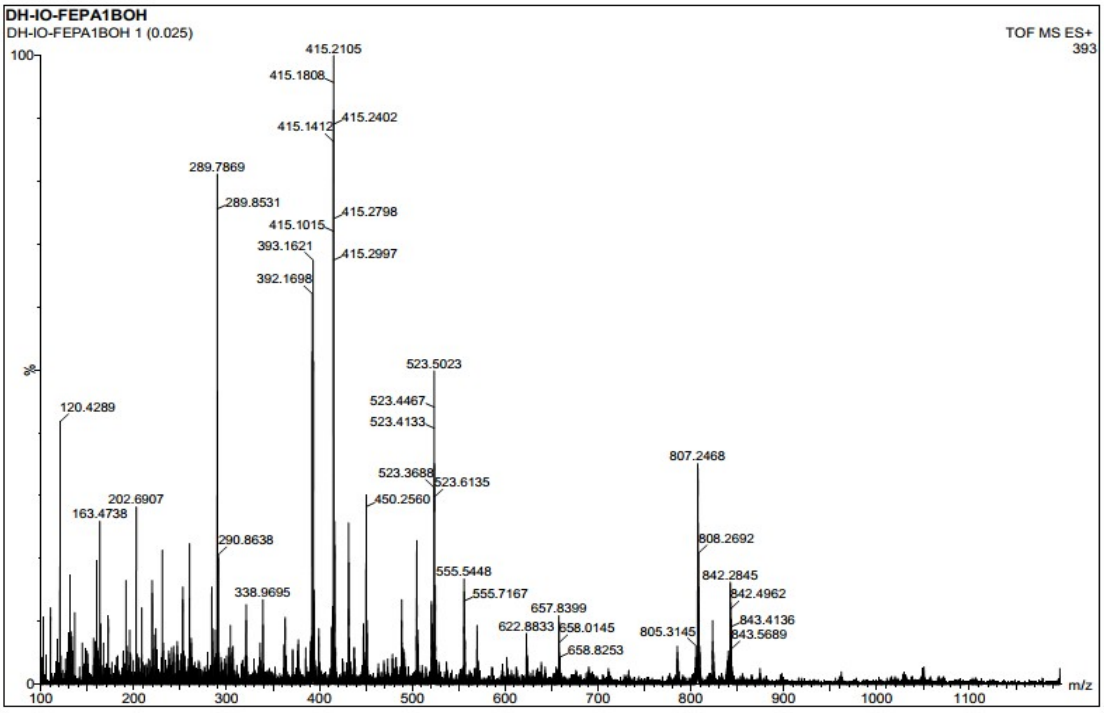

Figure S19. Mass Spectrum of Compound **1**