Supporting Information

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Fluorimetric Naphthalimide-based Polymer Logic Beads for Acidity and Oxidisability

Matthew Vella Refalo,[a] Nicole V. Farrugia,[a] Alex D. Johnson,[a] Sylwia Klejna,[b] Konrad Szaciłowski[b] and David C. Magri*[a]

[a]Department of Chemistry, Faculty of Science, University of Malta, Msida, MSD 2080, Malta
[b]AGH University of Science and Technology, Academic Centre for Materials and Nanotechnology, Mickiewicza 30, 30-059 Kraków, Poland.

Corresponding author: Prof. Dr David C. Magri
phone: (356) 2340 2276
email: david.magri@um.edu.mt

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1 Experimental

1.1 Chemicals

4-Chloro-1,8-naphthalic anhydride (Alfa Aesar, 94%), 4-bromo-1,8-naphthalic anhydride (Sigma-Aldrich, 95%), 6-aminocaproic acid (Acros Organics, 99+%), 1,4-dioxane (Analar, BDH, 99.5%), piperazine (Alfa Aesar, 99%), 2-methoxyethanol (Carlo Erba, Analytical grade), methanol (Carlo Erba, HPLC grade), hydrochloric acid (Fischer Scientific, 37%), methanesulfonic acid (> 99.5%, Sigma-Aldrich), 1,2-dichloroethane (Analar, BDH, 99.5%), ferrocenecarboxaldehyde (Sigma-Aldrich, 98%), sodium triacetoxyborohydride (Alfa Aesar, 95%), triethylamine (Roth, ≥ 99.5%), *tert*-butyl alcohol (Fischer Scientific, Analytical grade), Tentagel® MB-NH_2 (approx. 0.40 mmol/g loading, Sigma-Aldrich), *N*,*N*-dicyclohexylcarbodiimide (Acros organics, 99%) *N*,*N*-dimethylformamide (Carlo Erba, ACS grade), 2-propanol (Carlo Erba, HPLC grade), ethyl acetate (Carlo Erba, HPLC grade), acetone (Sigma Aldrich, HPLC grade), dichloromethane (Carlo Erba, HPLC grade) and diethyl ether (Sigma-Aldrich, Analytical grade, ≥ 99.5%). The NMR solvents were chloroform-*d* with TMS (Aldrich, 99.8%), deuterium oxide (Carlo Erba, 99.8%), methanol-d_4 (Carlo Erba, 99.8%) and dimethyl sulfoxide-d_6 (Carlo Erba, 99.9%).

1.2 Instrumentation

Syntheses were performed with an IKA C-MAG HS 7 hot plate connected to an IKA ETS-D5 temperature probe. TLC aluminium foils (silica gel matrix with fluorescent indicator 254 nm, Fluka Analytical) were used for column and thin-layer chromatography, respectively. The plates were examined under long wavelength (365 nm) and short wavelength (254 nm) UV light with a UVGL-58 handheld lamp. Melting points were measured with a Stuart SMP11 melting point apparatus.

NMR spectra were acquired with a Bruker Avance III HD NMR spectrometer fitted with an Ascend 500 11.75 Tesla superconducting magnet and a multinuclear 5 mm PABBO probe at a frequency of 500.13 MHz for ^{1}H NMR and 125.76 MHz for ^{13}C NMR. Data were analysed and processed with Topspin version 3.2. Chemical shifts are reported in ppm downfield with respect to TMS at 0.00 ppm at 298 K. Infra-red spectra were recorded using a Shimadzu IR-Affinity-1 spectrophotometer between 4000-400 cm^{-1}. The instrument was calibrated against 1601 cm^{-1} polystyrene absorption peak. IR analyses were performed as KBr

disks or a thin film between NaCl plates. The high resolution mass spectrometry (HRMS) was performed by ESI-ToF outsourced to Medac Ltd (UK). http://medacltd.com/

UV-visible absorption spectra were acquired on a Jasco V-650 spectrophotometer using Hellma Analytics quartz Suprasil cells (100-10-40) with a pathlength of 1.0 cm for solution measurements. The instrument parameters were set at 0.5 nm bandwidth and 400 nm/min scan speed. A blank spectrum was performed on the neat solvent prior to measurement. Fluorescent measurements were acquired with a Jasco FP-8300 spectrophotometer with 1.0 cm Hellma Analytics quartz Suprasil cells (101-10-40). Excitation and emission bandwidths of 2.5 nm, response time 50 msec and a scan rate of 200 nm min^{-1} were used. The optical density was typically 0.10 to prevent inner filter effect.

Images of the beads were taken with an Axiovert 40 CLF fluorescent microscope manufactured by Carl Zeiss MicroImaging with ocular magnifications of ×10 and ×40. The UV light source was a low pressure mercury lamp. A UV filter with an excitation band between 450-490 nm was used. The emission of light started from 515 nm and the beam splitter was adjusted to 510 nm.

2 Synthesis

Synthesis of 6-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)hexanoic acid **5**

1,8-Naphthalic anhydride (0.80 g, 4.0 mmol) and 6-aminohexanoic acid (0.53 g, 4.0 mmol) were dissolved in 20 mL of 2-methoxyethanol and refluxed at 110 °C with stirring for 6 hours. The reaction mixture was monitored by TLC using 9:1 (*v*/*v*) CH_2Cl_2/MeOH. A blue coloured spot was observed with R_f = 0.60 for the product and R_f = 0.93 for the reagent. The solvent was removed by rotatory evaporator. Recrystallisation from ethanol yielded 1.0 g of white crystalline solid in 79% yield. m.p. 135-136 °C; ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ_H 8.60 (d, 2H, *J* = 7.3 Hz, H_a), 8.21 (d, 2H, *J* = 8.4 Hz), 7.76 (t, 2H, *J* = 7.8 Hz), 4.19 (t, 2H, *J* = 7.5 Hz), 2.38 (t, 2H, *J* = 7.5 Hz), 1.80-1.70 (m, 4H), 1.53-1.46 (m, 2H);^{13}C NMR (126 MHz, $CDCl_3$, ppm): 24.4, 26.5, 27.7, 33.9, 40.2, 122.7, 126.9, 128.1, 131.2, 131.7, 133.9, 164.2, 164.3, 179.3; IR (KBr, cm^{-1}): 3412, 3040, 2945, 2864, 1708, 1658, 1625, 1591, 1438, 1385, 1344, 1313, 1261, 1235, 1207, 1167,1138, 1103, 1068, 957, 939, 846, 781, 740.

Synthesis of 6-(6-(4-methylpiperazin-1-yl)-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)hexanoic acid **6**

Compound **6** was synthesised from 0.20 g (0.58 mmol) in 10 mL of 2-methoxyethanol refluxed at 115 °C under constant stirring with 200 μL (1.7 mmol) methylpiperazine for 15 hours. A new green fluorescent spot was observed under long wavelength UV lamp at R_f = 0.26. The product was purified by column chromatography with 9:1 (*v*/*v*) CH_2Cl_2/MeOH and recrystallization from ethyl acetate to give 160 mg of a fine yellow powder in yield 69%. m.p. 137-140 °C; ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ_H 8.58 (d, 1H, *J* = 7.0 Hz), 8.53 (d, 1H, *J* = 7.9 Hz), 8.40 (d, 1H, *J* = 8.5 Hz), 7.69 (t, 1H, *J* = 7.9 Hz), 7.27 (d, 1H, *J* = 8.0 Hz), 4.17 (t, 2H, *J* = 7.5 Hz), 3.30(m, 4H), 2.87 (s, 4H), 2.50 (s, 3H), 2.35 (t, 2H, *J*=7.4 Hz), 1.90-1.70 (m, 4H), 1.60-1.50 (m, 2H); ^{13}C NMR(126 MHz, $CDCl_3$, ppm): 24.9, 26.7, 27.8, 34.7, 40.1, 45.3, 52.3, 54.6, 115.3, 116.9, 123.2, 125.7, 126.2, 129.8, 130.0, 131.1, 132.6, 155.5, 163.9, 164.4, 178.8; MS (ES-TOF, 1.80 mV) m/z (%): 177 (59), 178 (10), 410 (100), 411 (28), 412 (5); HRMS calculated $C_{23}H_{28}N_3O_4$ $[M+H]^{\bullet+}$ 410.2074, found 410.2080.

Synthesis of AND logic gate **7**

Reductive amination of *6-(6-piperazin-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)methyl hexanoate* (110 mg, 0.30 mmol) with ferrocenecarboxaldehyde (71 mg, 0.33 mmol), sodium triacetoxyborohydride (130 mg, 0.60 mmol) and trimethylamine (61 mg, 0.60 mmol) was performed in dried 1,2-dichloroethane under constant stirring in the dark for 3 days. Purification by column chromatography on silica gel with 9:1 (*v*/*v*) CH_2Cl_2/MeOH to give 146 mg of a brown oil in 79% yield. ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ_H 8.54 (d, 1H, *J* = 7.3 Hz), 8.46 (d, 1H, *J* = 8.1 Hz), 8.35 (d, 1H, *J* = 8.4 Hz), 7.64 (t, 1H, *J* = 7.8 Hz), 7.15 (d, 1H, *J* = 8.1 Hz), 4.23 (t, 2H, *J* = 7.6 Hz), 4.17-4.13 (m, 7H), 3.65 (s, 3H), 3.54 (s, 2H), 3.24 (s, 4H), 2.73 (s, 4H), 2.32 (t, *J* = 7.5 Hz), 1.76-1.67 (m, 4H), 1.47-1.41 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$, ppm): 24.7, 26.6, 27.8, 34.0, 40.0, 52.5, 52.9, 58.3, 68.2, 68.6, 70.3, 82.2, 114.8, 116.6, 123.2, 125.5, 126.1, 129.8, 130.3, 131.0, 132.6, 156.0, 164.0, 164.4, 174.1; IR (NaCl, thin film, ν_{max}): 3100, 3066, 2947, 2820, 1732, 1694, 1651, 1589, 1389, 1362, 1234; HRMS (ES-ToF): Calculated $C_{34}H_{38}N_3O_4Fe$ $[M+H]^{\bullet+}$ 608.2212, found 608.2220.

Attachment of AND logic gate onto Tentagel

Molecular AND logic gate **7** was hydrolysed with sodium hydroxide in 1,4-dioxane and then neutralised with 1 M HCl. Covalent attachment of the acid to the polymer bead was carried out via *N,N'*-dicyclohexylcarbodiimide (DCC) coupling using DMF and HOBt at 40 °C and the reaction left overnight. The orange beads were washed sequentially with DMF, 1:1 (v/v) DMF/ methanol, and methanol.

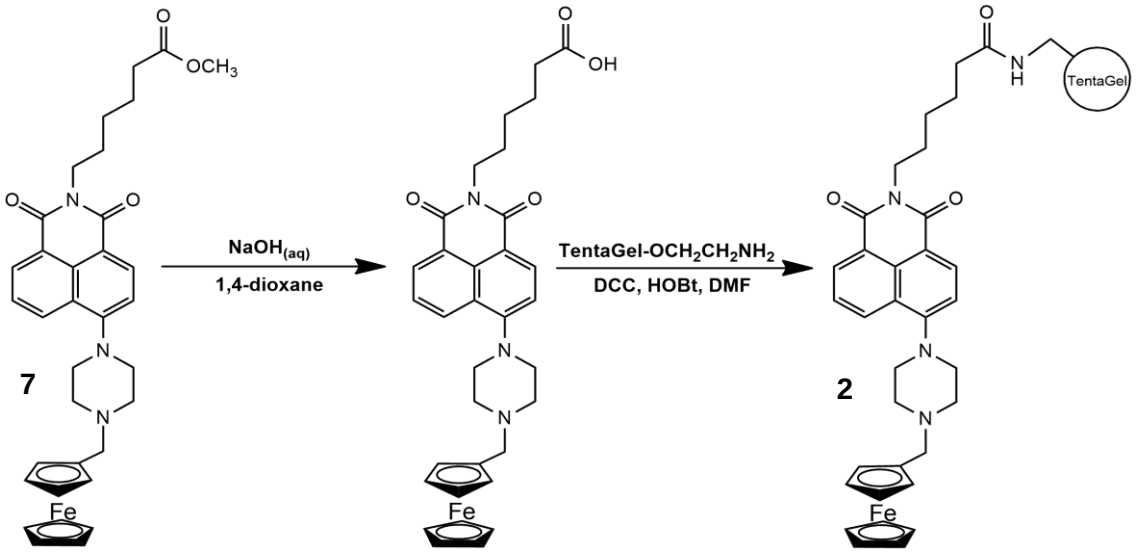

Figure S1. Covalent attachment of **7** onto the polymer bead to yield **2.**

Direct synthesis on beads was performed by attaching the PASS 1 gate to TentaGel via DCC coupling in *tert*-butyl alcohol (HOBt) and *N,N'*-dimethylformamide (DMF) through amide bond formation. The loaded beads were washed with DMF and methanol, respectively. Piperazine and the PASS 1 immobilised logic gate were refluxed in 2-methoxyethanol. The resultant tags were washed with methanol and chloroform prior to reductive amination in dry 1,2-dichloromethane containing ferrocenecarboxaldehyde and sodium triacetoxyborohydride to yield **2**.

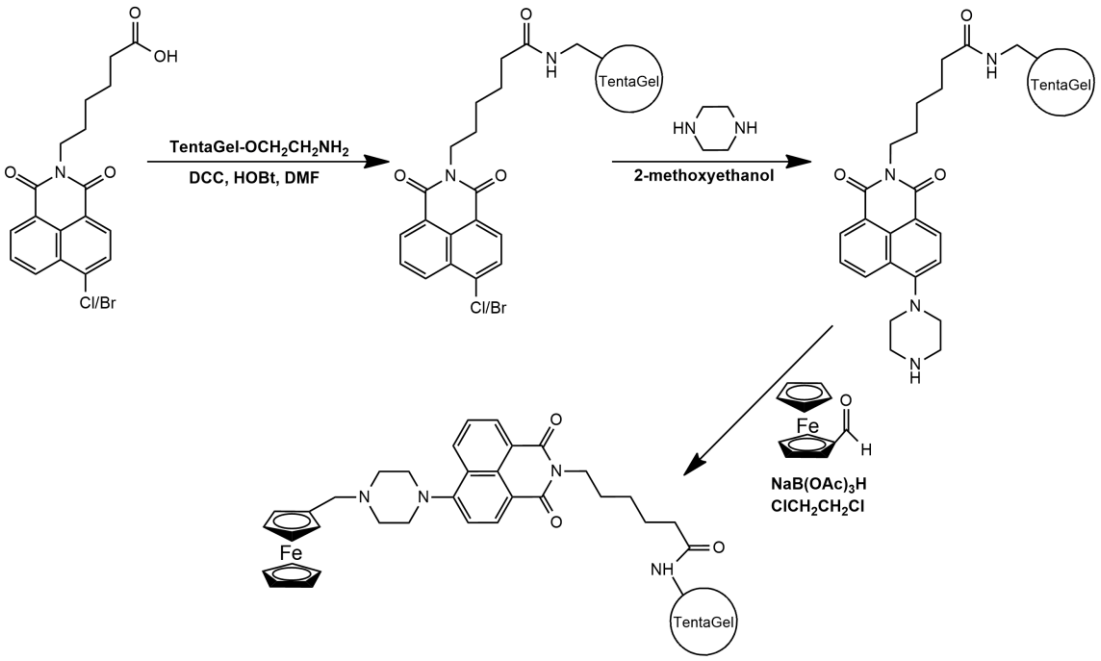

Figure S2. Methodology for the on-bead synthesis of **2.**

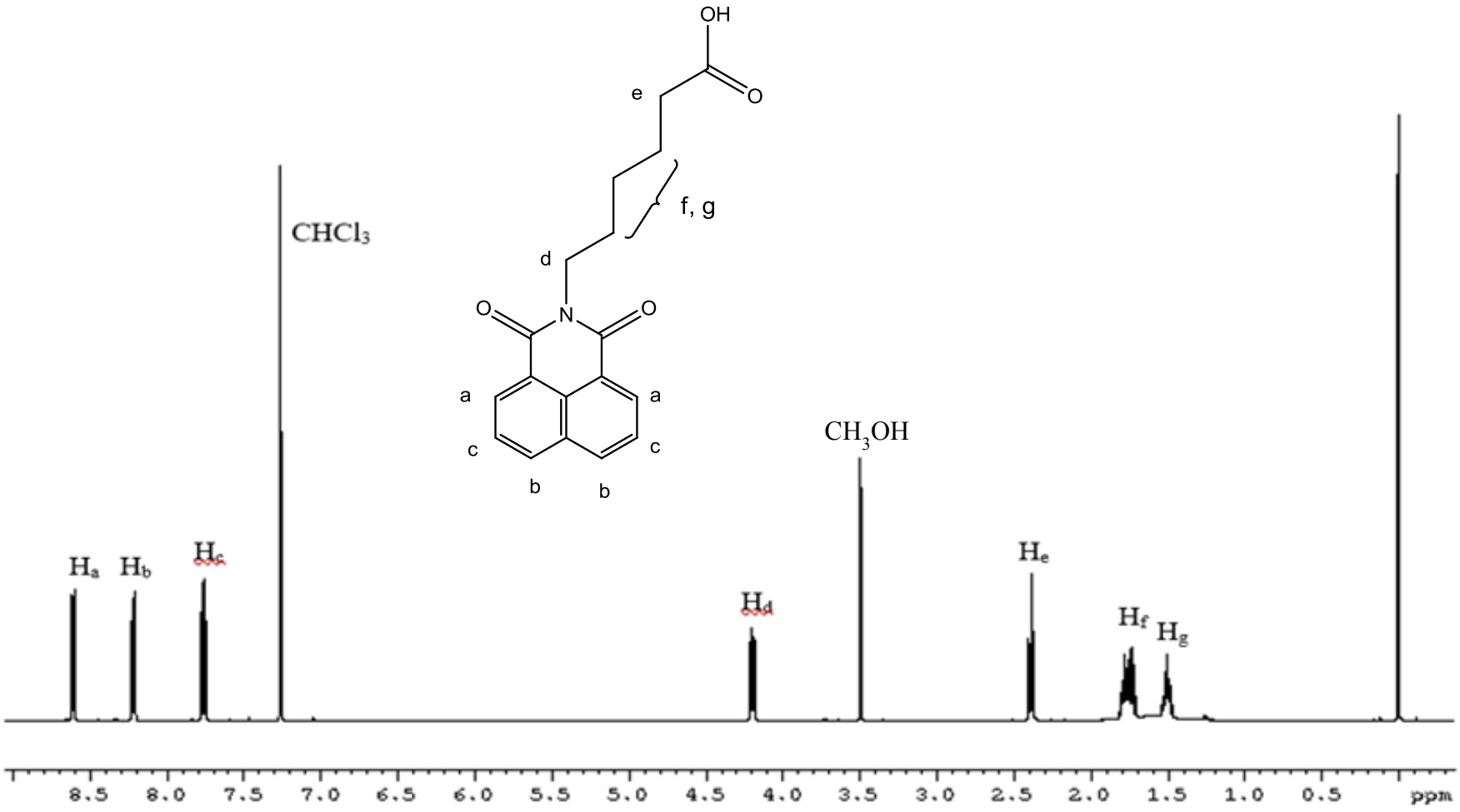

Figure S3. ^{1}H NMR spectrum of **5** in $CDCl_3$ at 500 MHz.

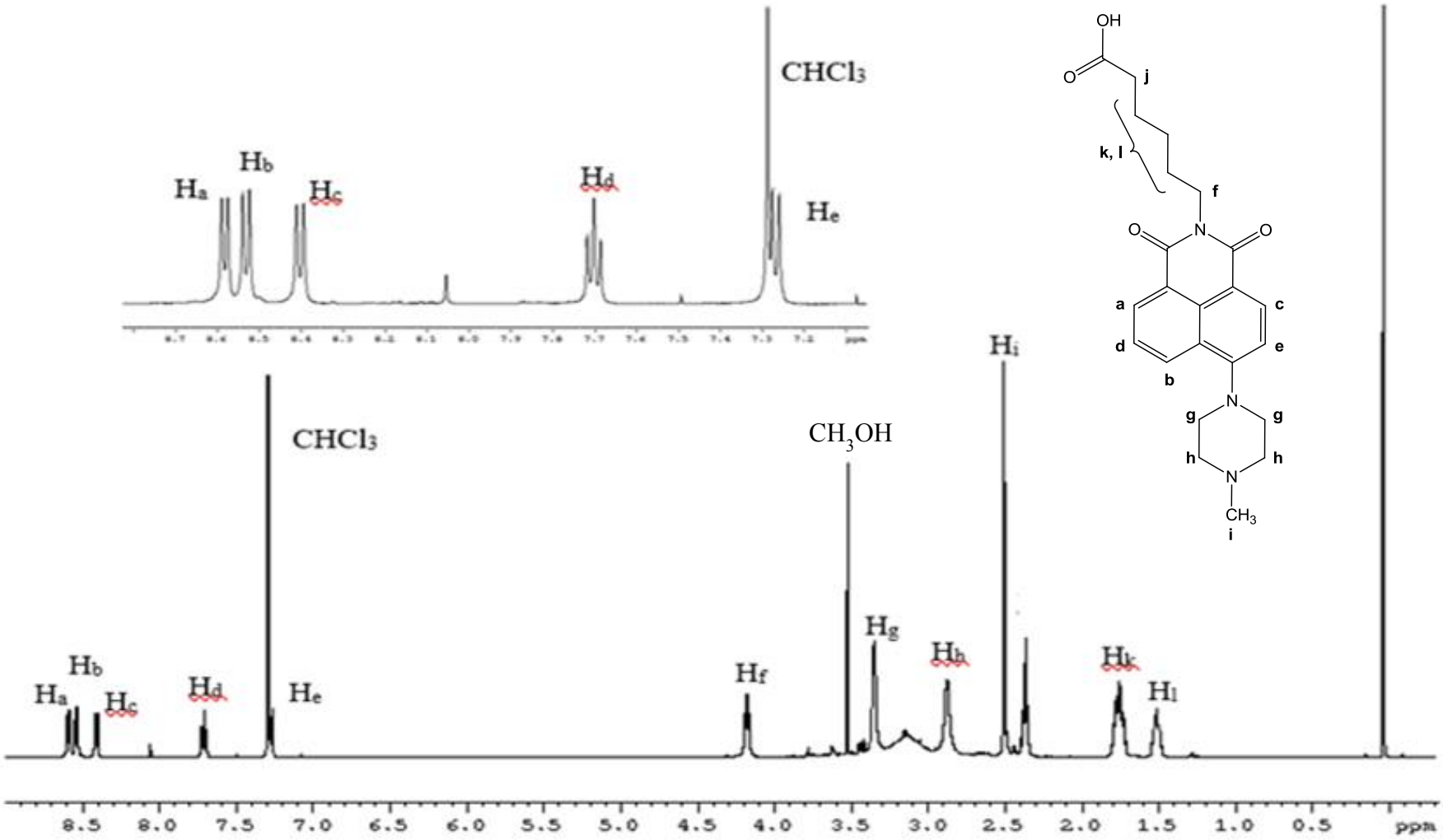

Figure S4. ^{1}H NMR spectrum of **6** in $CDCl_3$ at 500 MHz.

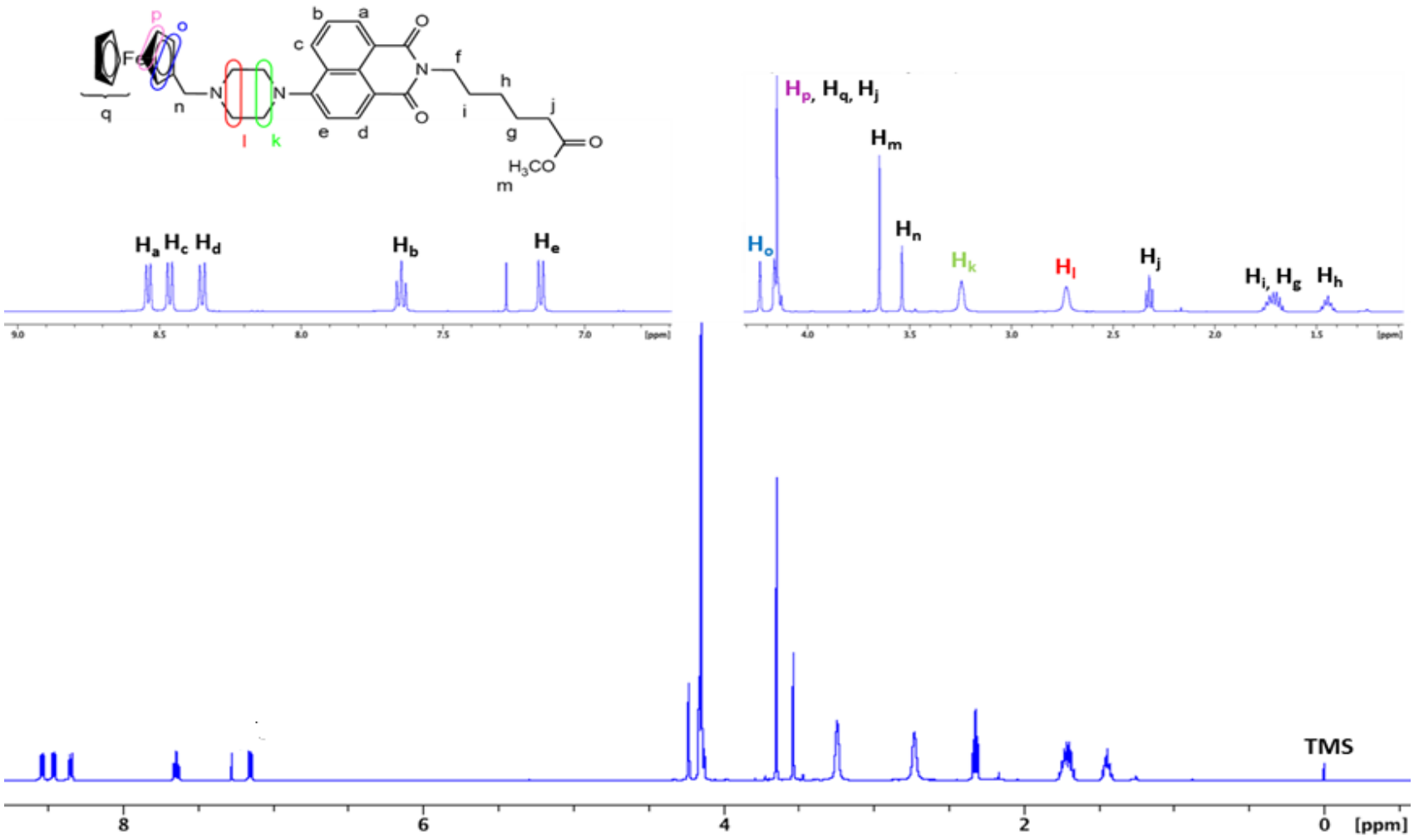

Figure S5. ^{1}H NMR spectrum of **7** in $CDCl_3$ at 500 MHz.

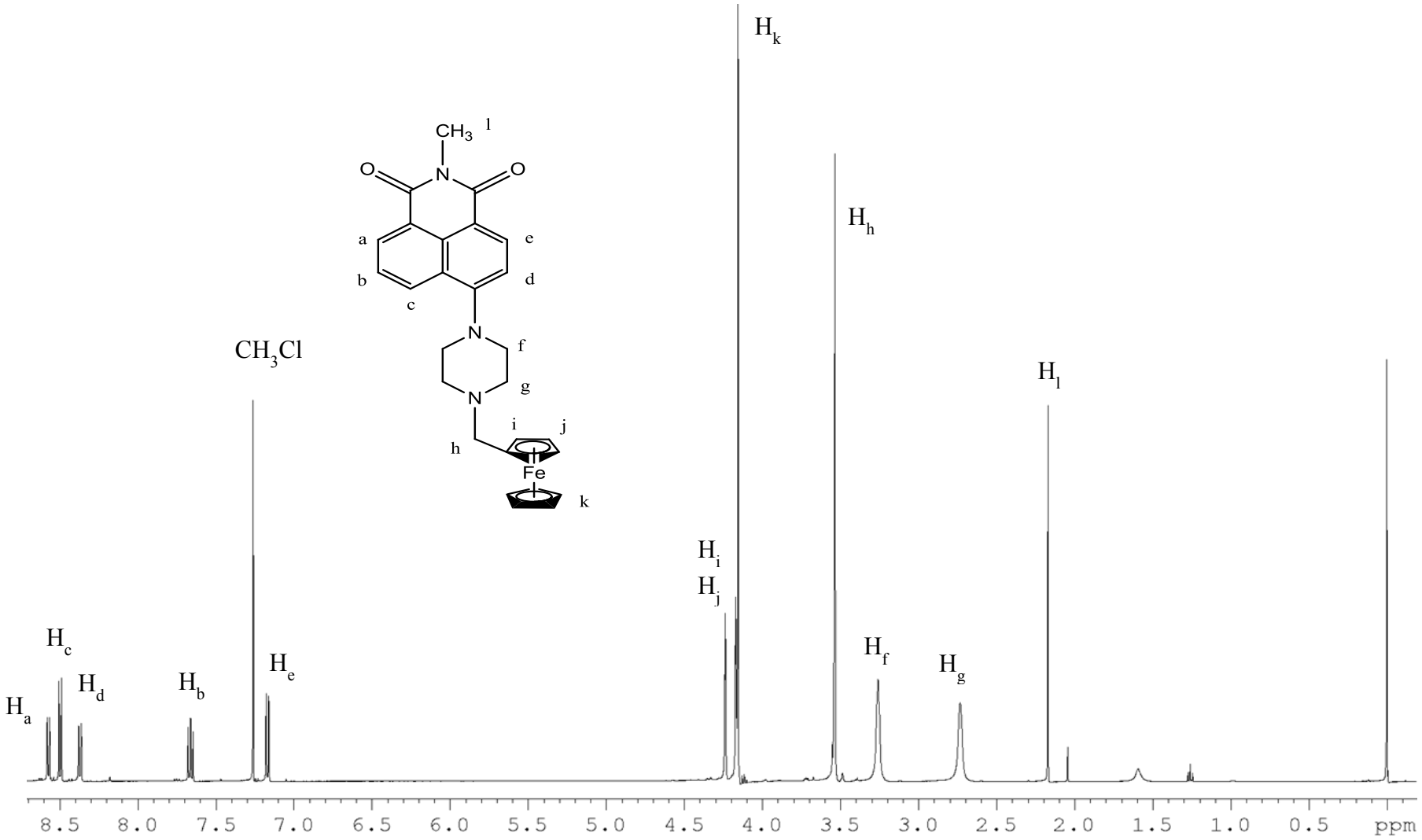

Figure S6. ^{1}H NMR spectrum of **9** in $CDCl_3$ at 500 MHz.

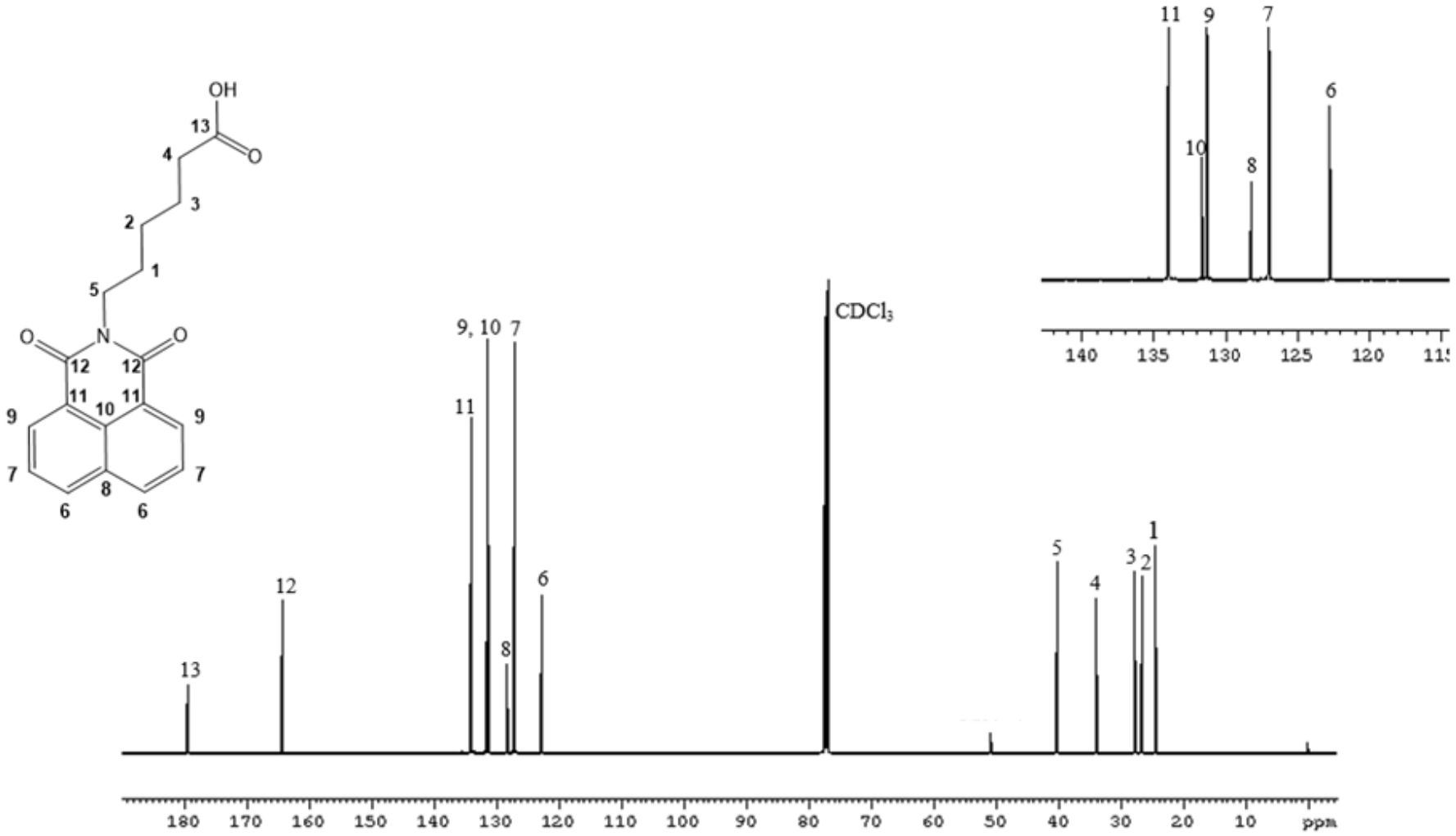

Figure S7. ^{13}C NMR spectrum of **5** in $CDCl_3$ at 126 MHz.

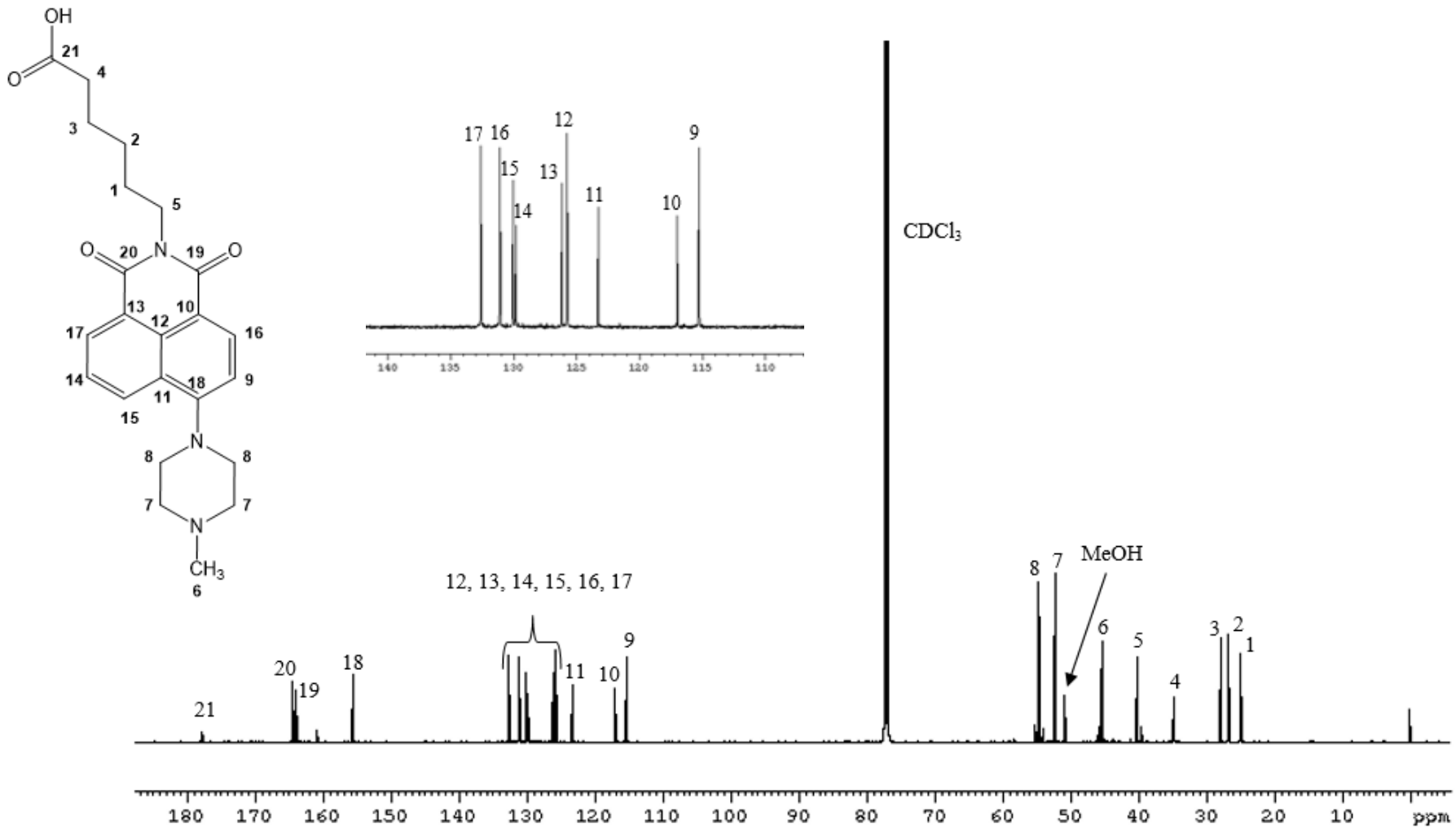

Figure S8. ^{13}C NMR spectrum of **6** in $CDCl_3$ at 126 MHz.

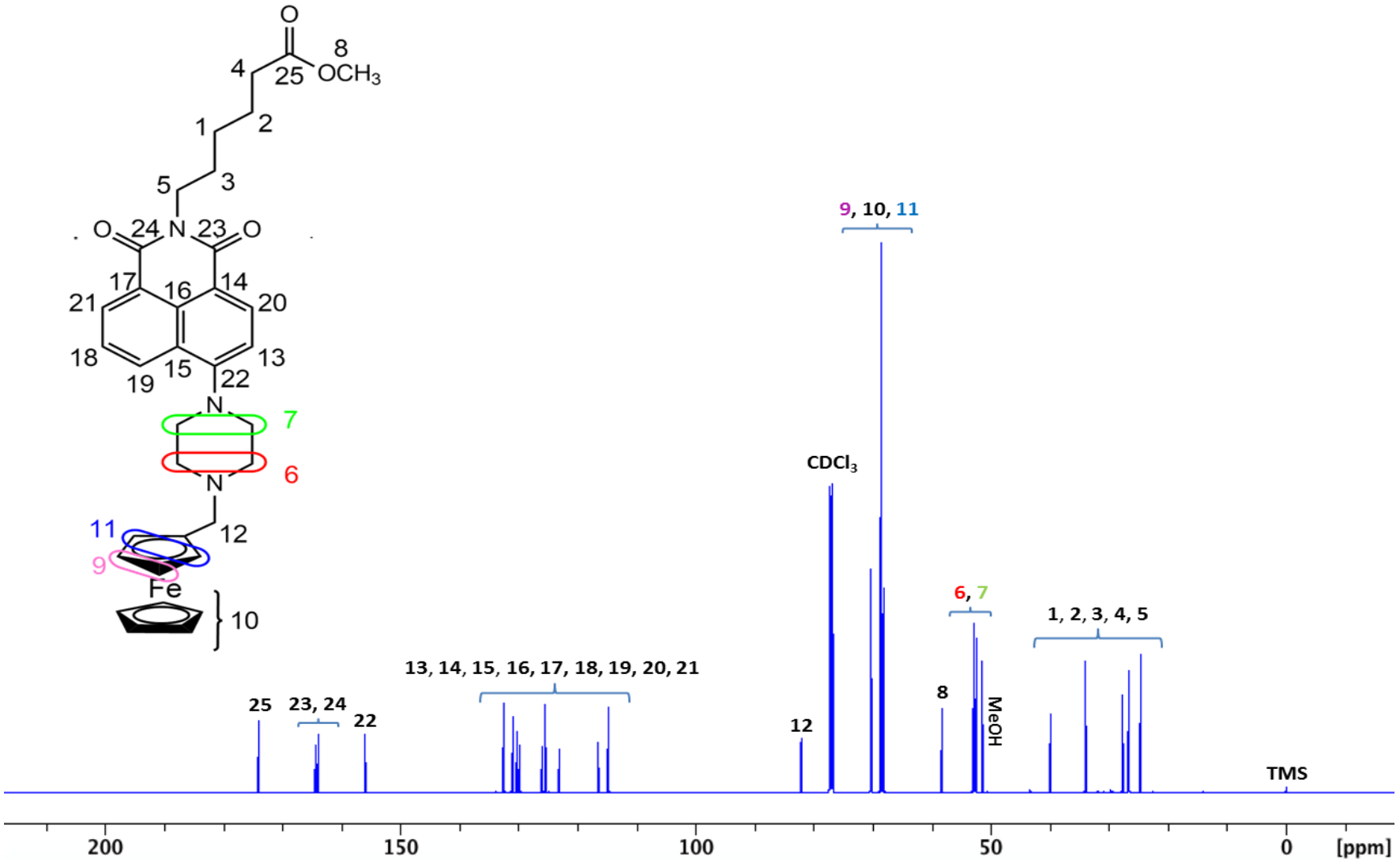

Figure S9. ^{13}C NMR spectrum of **7** in $CDCl_3$ at 126 MHz.

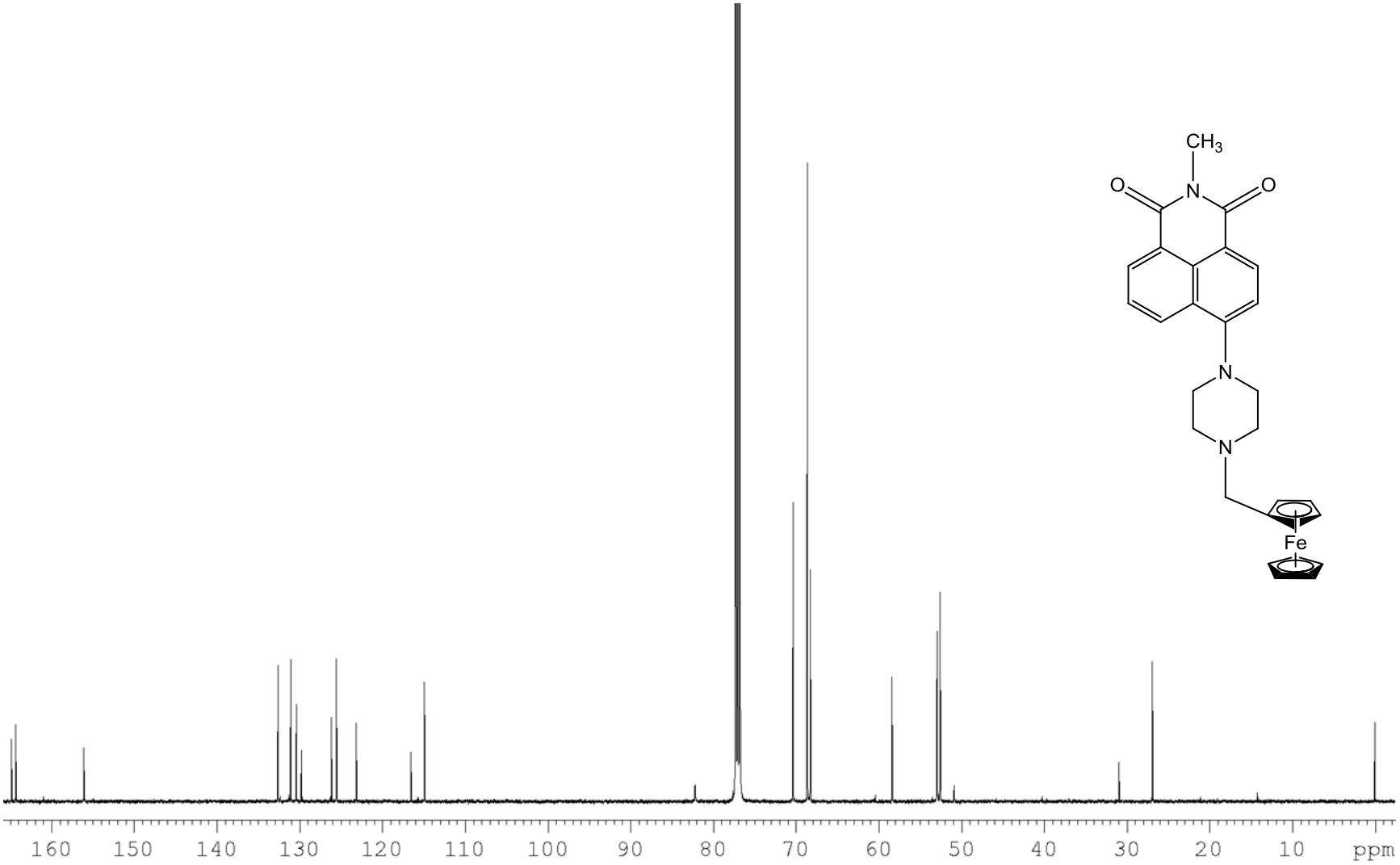

Figure S10. ^{13}C NMR spectrum of **9** in $CDCl_3$ at 126 MHz.

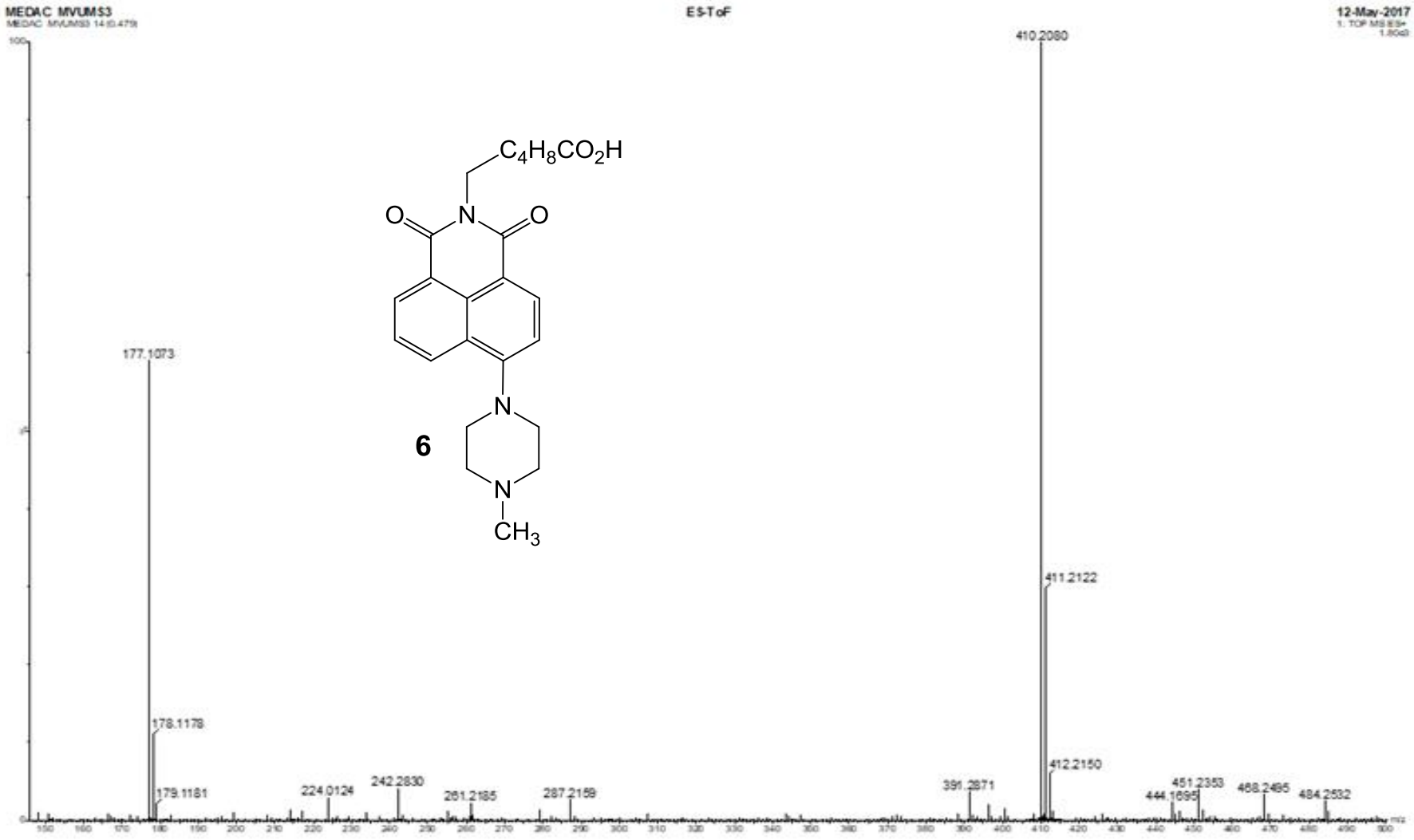

Figure S11. HRMS of compound **6**.

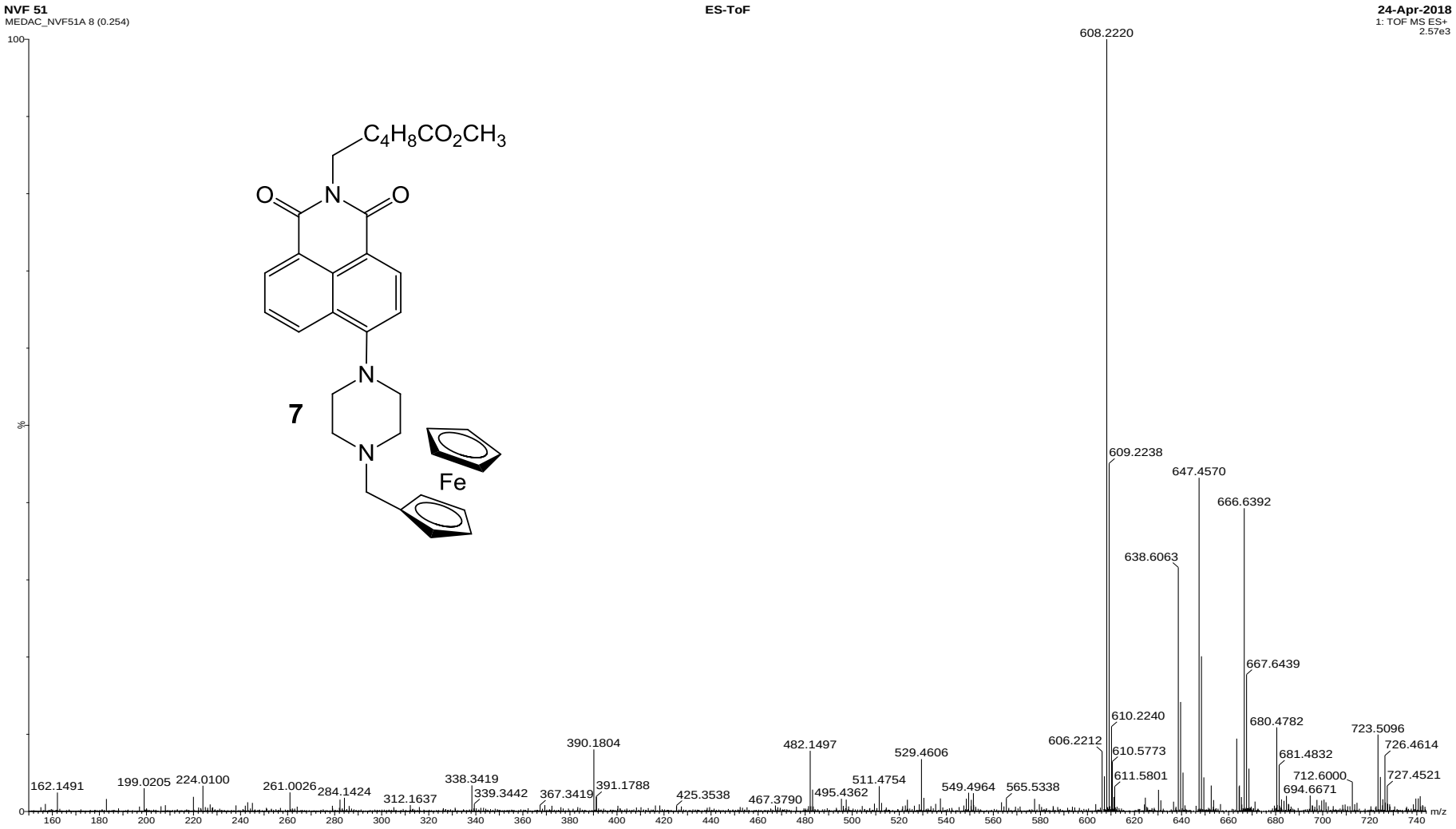

Figure S12. HRMS of compound **7**.

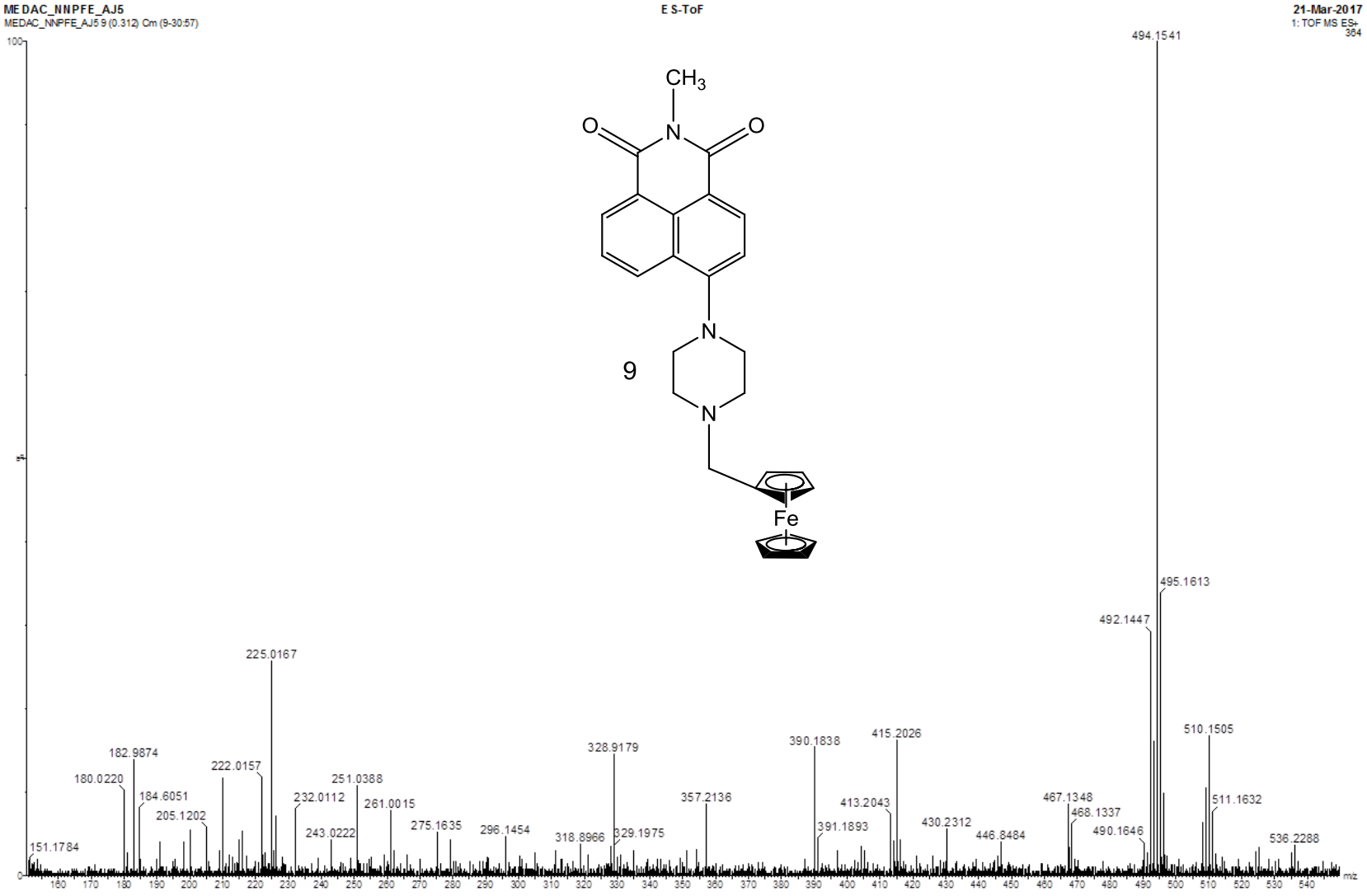

Figure S13. HRMS of compound **9**.

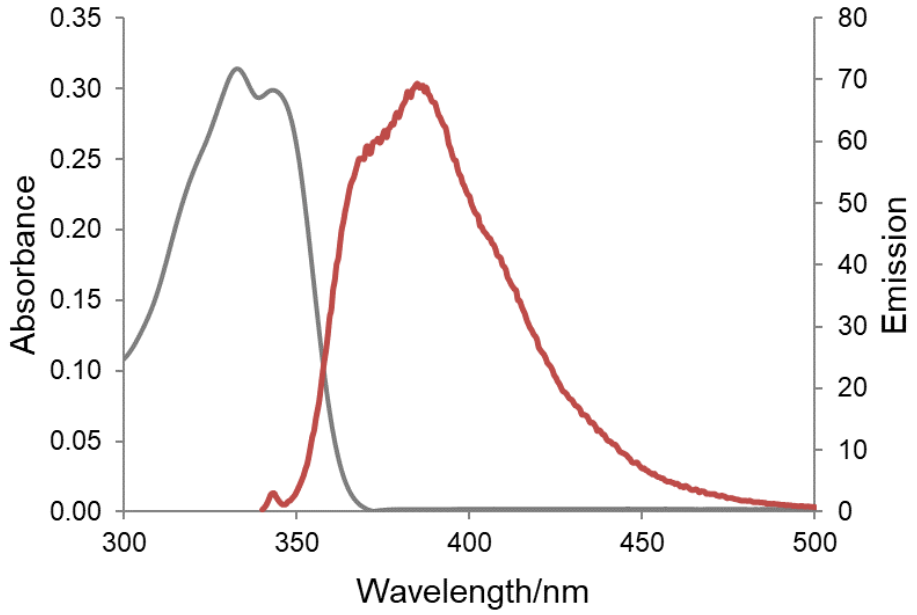

Figure S14. UV-visible absorbance and emission spectra of 22 μM **5** in 1:1 (*v*/*v*) methanol/water at pH 6.5. λ_{ex} = 343 nm.

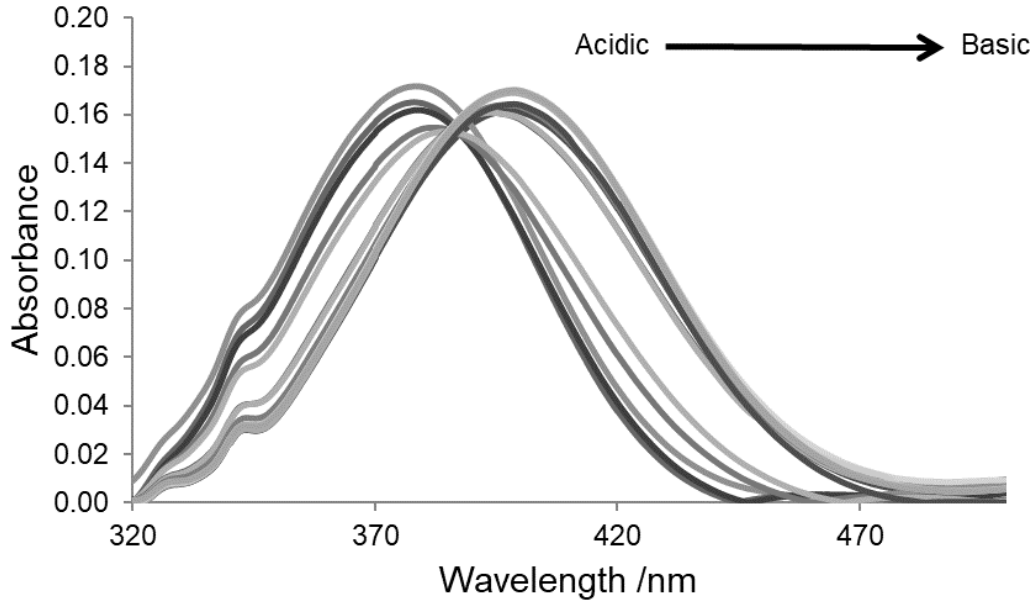

Figure S15. UV-visible absorbance spectra of 16 μM **6** in 1:1 (*v*/*v*) methanol/water between pH 3-10.

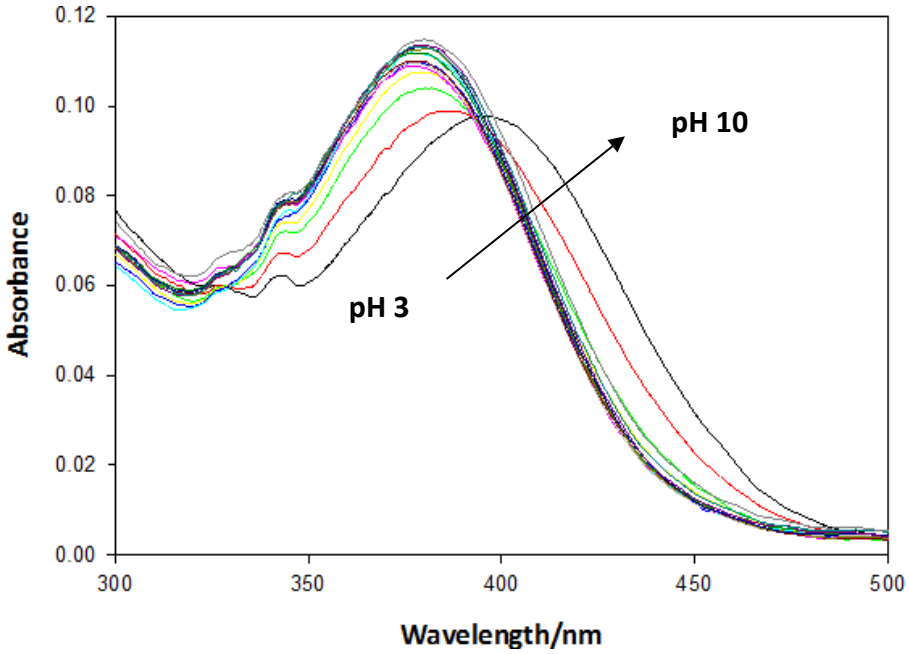

Figure S16. UV-visible absorbance spectra of 6 μM **7** in 9:1 (*v*/*v*) methanol/water with 7.6-480 μM methanesulfonic acid.

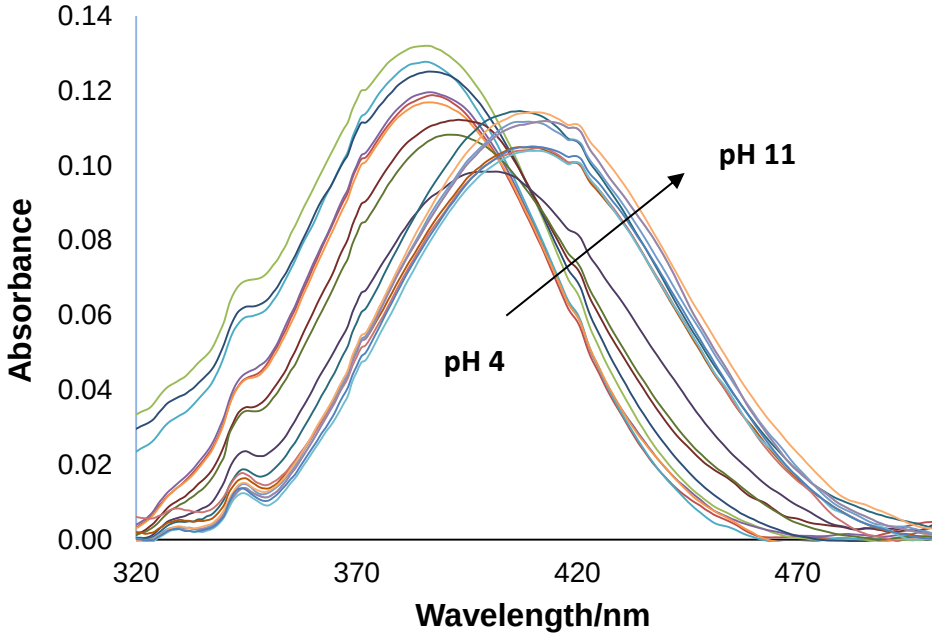

Figure S17. UV-visible absorbance spectra of 5 μM **9** in 1:1 (*v*/*v*) methanol/water with 7.6-480 μM methanesulfonic acid.

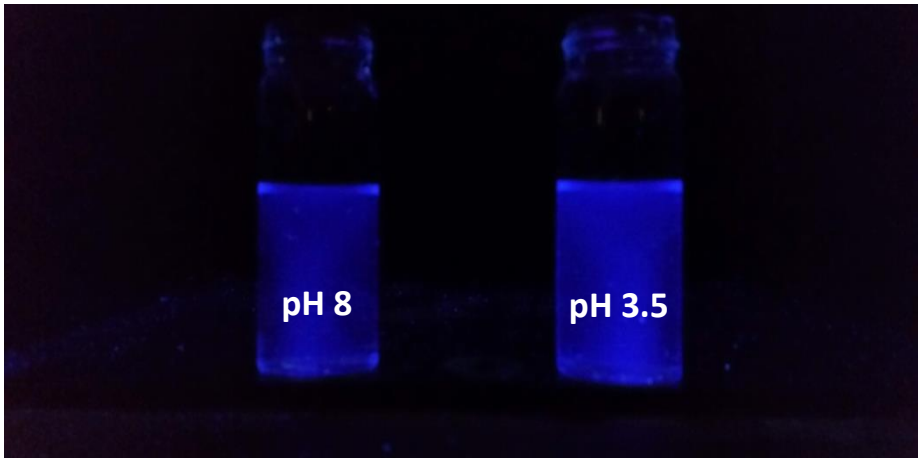

Figure S18. Solutions of 22 μM PASS 1 logic gate **5** in 1:1 (*v*/*v*) MeOH/H_2O irradiated with a 365 nm UV handheld lamp.

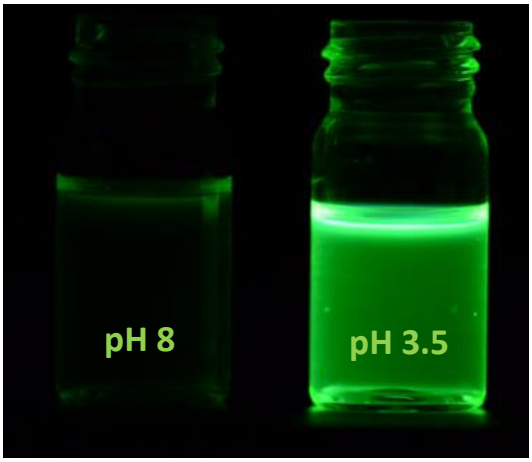

Figure S19. Solutions of 16 μM YES logic gate **6** in 1:1 (*v*/*v*) MeOH/H_2O irradiated with a 365 nm UV handheld lamp adjusted with 0.1 M KOH and 0.1 M methanesulfonic acid.

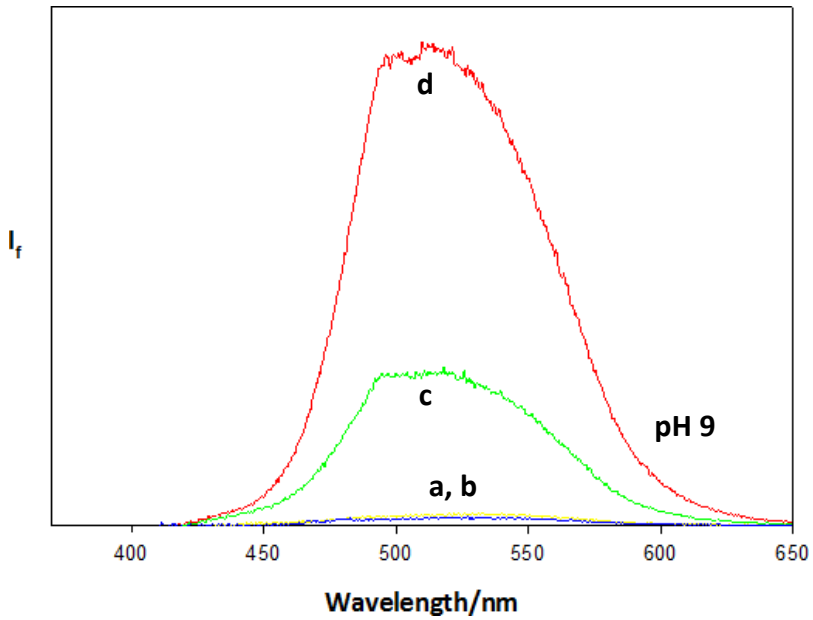

Figure S20. Fluorescence spectra of 6 μM **7** in 9:1 (*v*/*v*) MeOH/H_2O λ_{max} = 400 nm. The input conditions are (a) low H^+, low Fe^{3+}, (b) low H^+ and high Fe^{3+}, (c) high H^+ and low Fe^{3+}, (d) high H^+ and Fe^{3+} at 100 μM, 126 μM, and 70 μM, OH, H^+ and Fe^{3+}.

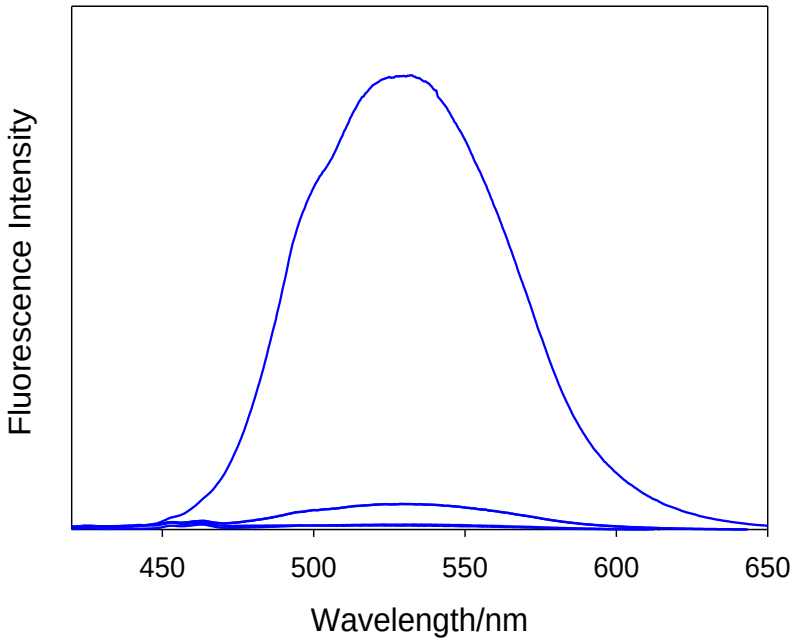

Figure S21. Fluorescence spectra of 6 μM **8** in 1:1 (*v*/*v*) MeOH/H_2O, λ_{max} = 399 nm. Inputs methanesulfonic acid and iron(III) sulfate pentahydrate at 0.2 mM and 10 μM, respectively. Reproduced with permission of the RSC. *New. J. Chem*. 2015, **39**, 3349.