Highly diastereoselective cyclopropanation of α-methylstyrene catalyzed by a C_2-symmetrical chiral iron porphyrin complex

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Supporting Information

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General methods for synthesis and catalysis

Unless otherwise specified, all reactions were carried out under nitrogen atmosphere employing standard Schlenk techniques and magnetic stirring. THF and benzene were dried by M. Braun SPS-800 solvent purification system. Toluene and α-methylstyrene were distilled over sodium and kept under nitrogen. All the other starting materials were commercial products used as received. (R)-2,2'-dimethoxy-1,1'-binaphthyl-3,3'-diboronic acid[1], and porphyrin **1**[2] were synthesized by methods reported in the literature or by using minor modifications of them. The purity of α-methylstyrene was checked by GC-MS or ^{1}H NMR analysis. NMR spectra were recorded at room temperature on a Bruker AC-300, on a Bruker avance 300-DRX, operating at 300 MHz for ^{1}H, at 75 MHz for ^{13}C or on a Bruker Avance 400-DRX spectrometers, operating at 400 MHz for ^{1}H and at 100 MHz for ^{13}C, or on a Bruker avance 500-DRX spectrometer operating at 500 MHz for ^{1}H and at 125 MHz for ^{13}C. Chemical shift (ppm) are reported relative to TMS. The ^{1}H NMR signals of the compounds described in the following have been attributed by 2D NMR techniques. GC-MS analyses were performed on Shimadzu QP5050A instrument. Infrared spectra were recorded on a Varian Scimitar FTS 1000 spectrophotometer. UV/Vis spectra were recorded on an Agilent 8453E instrument. $[\alpha]_D$ values are given in 10^{-1}deg cm^2 g^{-1}. The ESR spectrum of **2Fe** was recorded from a sample powder at 77 K with a Bruker EMX X-band spectrometer equipped with an Oxford cryostat. Elemental analyses and mass spectra were recorded in the analytical laboratories of Milan University.

Synthesis of compound 2.

In a dried 100 mL Schlenk flask, compound **1**[2] (0.300 g, 2.33×10^{-4}mol), (*R*)-2,2'-dimethoxy-1,1'-binaphthyl-3,3'-diboronic acid (0.226 g, 5.60×10^{-4}mol), tetrakis(triphenyl-phosphine)palladium(0) (0.108 g, 9.34×10^{-5}mol) and potassium carbonate (0.516 g, 3.71×10^{-3}mol) were dissolved in 16.0 mL of toluene, 5.0 mL of ethanol and 8.0 ml of water. The biphasic solution was refluxed under nitrogen atmosphere for 4 hours until the complete consumption of **1** that was monitored by TLC. The resulting mixture was allowed to reach room temperature and the biphasic solution was diluted with 50.0 mL of saturated aqueous NH_4Cl and 50.0 mL of CH_2Cl_2 and then it was separated. The aqueous phase was extracted with an additional 2×50 mL of CH_2Cl_2, and the combined organic phases were washed with 1×50 mL of water and 1×50 mL of saturated aqueous $NaHCO_3$. The organic phase was dried over Na_2SO_4 and filtered. The filtrate was concentrated *in vacuo* and then purified by chromatography (SiO_2 15-40 µm, eluent dichloromethane/methanol = 99.5:0.5). (**2**, 0.143 g, 35%). Elemental Analysis calcd for $C_{120}H_{86}N_8O_8$: C, 81.52; H, 4.90; N, 6.34; found: C, 81.26; H, 4.97; N, 5.94. $\nu_{max}(CH_2Cl_2)/cm^{-1}$: 3685.7 (w), 3412.8 (w), 1711.0 (w), 1676.8 (w), 1519.1 (w), 1445.1 (w), 1418.5 (w), 1359.6 (w), 1305.9 (w), 1240.9 (w), 1101.2 (w), 1009.5 (w). $\nu_{max}(ATR)/cm^{-1}$ 3423.6 (w), 3316.6 (w), 3056.6 (w), 2963.2 (w), 2938.3 (w), 1681.2 (w), 1580.8 (w), 1513.1(w), 1443.3 (w), 1302.5 (w), 1260.6 (w), 1101.6 (w) 1012.3 (w). λ_{max} (CH_2Cl_2)/nm 423, 517, 551, 590, 646 (log ε_M 4.82, 3.57, 3.06, 2.96, 2.71). $[\alpha]_D^{20}$ = -809.524 (c = 7×10^{-4} g/100mL; in CH_2Cl_2). m/z (ESI) 1767.1 [M^+]. ^1H NMR (500 MHz, $CDCl_3$, 298 K) δ 9.07 (d, 2H, *J* = 8 Hz, HAr_{meso}), 9.00 (s, 2H, $H_{\beta pyr}$), 8.95 (s, 2H, $H_{\beta pyr}$), 8.94 (d, 2H, *J* = 4 Hz, $H_{\beta pyr}$), 8.90 (d, 2H, *J* = 8 Hz, HAr_{meso}), 8.88 (d, 2H, *J* = 4 Hz, $H_{\beta pyr}$), 7.98 (dd, 2H, J_1 = 1 Hz, J_2 = 8 Hz, HAr_{meso}), 7.89 (dt, 2H, J_1 = 1 Hz, J_2 = 8 Hz, HAr_{meso}), 7.86 (dt, 2H, J_1 = 1 Hz, J_2 = 8 Hz, HAr_{meso}), 7.85 (s, 2H, NHCO), 7.83 (dd, 2H, J_1 = 1 Hz, J_2 = 8 Hz, HAr_{meso}), 7.70 (d, 4H, *J* = 8 Hz, HAr_{binap}), 7.64 (s, 2H, HAr_{binap}), 7.63 (s, 2H, HAr_{binap}), 7.62 (s, 2H, NHCO), 7.51 (dt, 2H, J_1 = 1 Hz, J_2 = 8 Hz, HAr_{meso}), 7.49 (dt, 2H, J_1 = 1 Hz, J_2 = 8 Hz, HAr_{meso}), 7.32 (s, 2H, HAr_{strap}), 7.27 (m, 2H, HAr_{binap}), 7.19 (s, 2H, HAr_{strap}), 7.07 (m, 2H, HAr_{binap}), 6.90 (d, 2H, *J* = 8 Hz, HAr_{binap}), 6.83 (d, 2H, *J* = 8 Hz, HAr_{binap}), 6.67 (d, 2H, *J* = 8 Hz, HAr_{strap}), 6.39 (d, 2H, *J* = 8 Hz, HAr_{strap}), 6.12 (t, 2H, *J* = 8 Hz, HAr_{strap}), 5.98 (t, 2H, *J* = 8 Hz, HAr_{strap}), 5.91 (d, 2H, *J* = 8 Hz, HAr_{strap}), 5.78 (d, 2H, *J* = 8 Hz, HAr_{strap}), 3.87 (d, 2H, *J* = 8 Hz, CH_2), 3.72 (d, 2H, *J* = 8 Hz, CH_2), 3.66 (d, 2H, *J* = 8 Hz, CH_2), 3.55 (d, 2H, *J* = 8 Hz, CH_2), 2.42 (s, 6H, OMe), 1.89 (s, 6H, OMe), -2.64 (s, 2H, NH_{int}). ^{13}C NMR (125 MHz, $CDCl_3$, 298 K) δ 166.3, 165.6, 154.9(0), 154.8(7), 141.8, 141.5, 138.9, 138.6, 135.4, 135.2, 135.1, 134.2, 133.5, 133.4, 133.0, 132.6, 131.9, 130.9, 130.4(5), 130.4(2), 130.3(9) (2C), 130.3(5) (2C), 130.1, 128.1, 128.0, 127.7, 127.5(3), 127.4(9), 127.4(3), 126.3, 125.7(5), 125.4(4), 125.4(2), 125.1, 124.9, 124.1, 123.1, 122.8, 122.6, 120.6, 115.6, 115.0, 59.9, 59.8, 38.5, 37.9.

Synthesis of complex 2Fe (Fe = $Fe^{III}(OCH_3)$)

In a dried 50 mL Schlenk flask, porphyrin **2** (0.078 g, 4.40×10^{-5}mol) and $FeBr_2$ (0.047 g, 2.20×10^{-4}mol) were dissolved in 25.0 mL of THF. The dark solution was refluxed under nitrogen atmosphere for 24 hours until the complete consumption of **2** that was monitored by TLC. The mixture was evaporated to dryness and the residue purified by chromatography (alumina 0.063-0.200 mm, eluent CH_2Cl_2/CH_3OH = 99.5:0.5). (**2Fe** 0.081 g, 99 %). Elemental analysis: Found: C, 78.83; H, 4.65; N, 6.15. Calc for $C_{121}H_{87}FeN_8O_9$: C, 78.43; H, 4.73; N, 6.05). $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3685.7 (w), 3418.9 (w), 1723.7 (w), 1676.8 (w), 1605.3 (w), 1516.9 (w), 1278.4 (w), 1098.0 (w), 1009.5 (w). $\nu_{max}(ATR)/cm^{-1}$ 3417.6 (w), 2962.0 (w), 2926.0 (w), 2854.1 (w), 1677.1 (w), 1513.6 (w), 1259.2 (w), 1087.3 (w), 1011.4 (w), 795.0 (w). λ_{max} $(CH_2Cl_2)/nm$ 420, 576 (log ε_M 4.58 and 3.35). ESR data (experimental X-band (9.462 GHz) sample powder, 77 K): High spin S =5/2 confirmed by the g tensor values ($g_{\perp}$ = 5.71 and $g_{//}$ = 2.00).$[\alpha]_D^{20}$ = -625.000 (c = $8x10^{-4}$ g/100mL; in CH_2Cl_2). m/z (ESI) 1875.5 $[M+Na^+]$.

Catalytic procedures.

Method a (runs 1-5, Table1): In a typical run, **2Fe** (5.0 mg, 2.70×10^{-6}mol) was dissolved in the desired solvent (5.0 mL) and then α-methylstyrene (0.88 mL,6.75 $x10^{-4}$mol) and ethyl diazoacetate (EDA) (0.028 mL, 2.70×10^{-4}mol) were added. The consumption of EDA was monitored by IR spectroscopy by measuring the decrease of the characteristic N_2 absorbance at 2114 cm^{-1}. The reaction was considered to be finished when the measured EDA absorbance was below 0.03 (by using a 0.5 mm-thickness cell). The solution was then evaporated to dryness and analysed by ^{1}H NMR with 2,4-dinitrotoluene as an internal standard, and by HPLC by using a chiral column (DAI-CEL CHRALCEL, IB, *n*-hexane/*i*-PrOH 99.5:0.5). ***Method b (run 1, Table 2):*** The procedure illustrated for *method a* was repeated by using an equimolar α-methylstyrene/EDA ratio (0.035 mL, 2.70×10^{-4}mol/ 0.028 mL, 2.70×10^{-4}mol). ***Method c (runs 2-4 and 6-9, Table 2):*** 145.0 µL of a **2Fe** toluene solution (3.72×10^{-3}mol/L) was dissolved in 2.0 mL of toluene before adding equimolar amounts of α-methylstyrene and EDA. ***Method d (run 5, Table 2):*** The procedure *e* was repeated by adding EDA dropwise by a syringe pump to the reaction mixture.

Recycle of catalyst 2Fe.

α-Methylstyrene (0.421 mL, 3.24×10^{-3}mol) and ethyl diazoacetate (EDA) (0.340 mL, 3.24×10^{-3}mol) were added to a toluene solution (17.0 mL) of **2Fe** (6.0 mg, 3.24×10^{-6}mol) at 0°C under nitrogen atmosphere. The consumption of EDA was monitored by IR spectroscopy by measuring the characteristic N_2 absorbance at 2114 cm^{-1}. After the complete EDA consumption, EDA and α-methystyrene were added again to the catalytic mixture for two more consecutive times. The NMR analyses of the crude revealed 90% of global yield, 98% of *trans*-diastereoselectivity with 75% of ee_{trans}.

UV-Vis spectra.

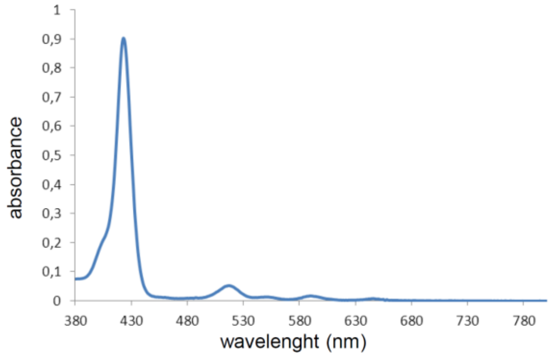


Figure S1. UV-vis spectrum of **2** in CH_2Cl_2

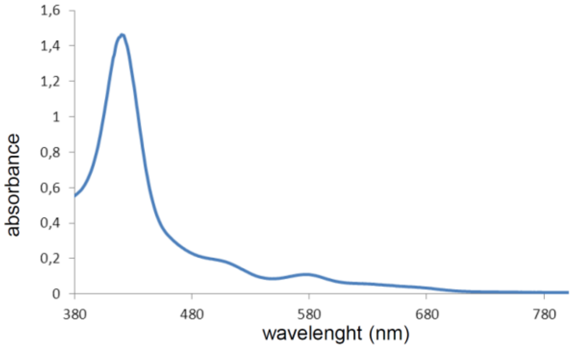


Figure S2. UV-vis spectrum of **2Fe** in CH_2Cl_2

IR spectra.

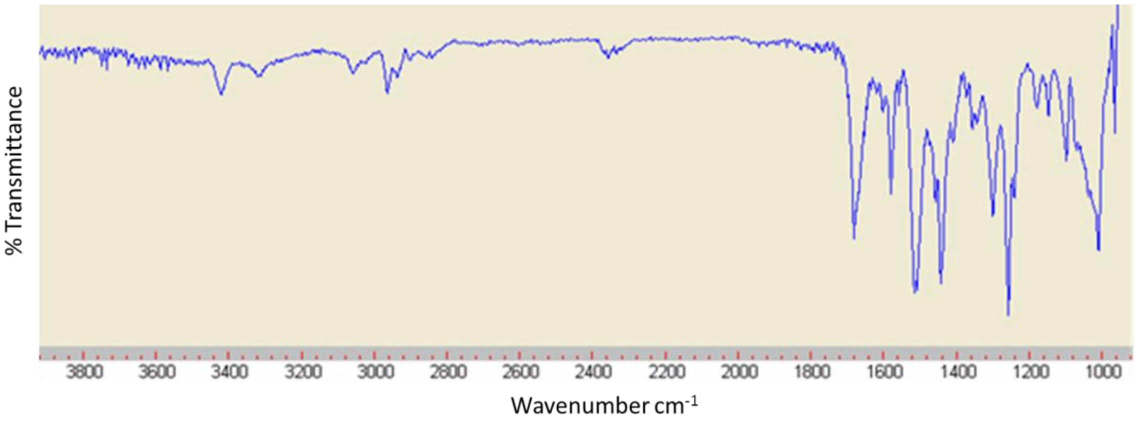


Figure S3. IR spectrum (ATR) of compound **2**

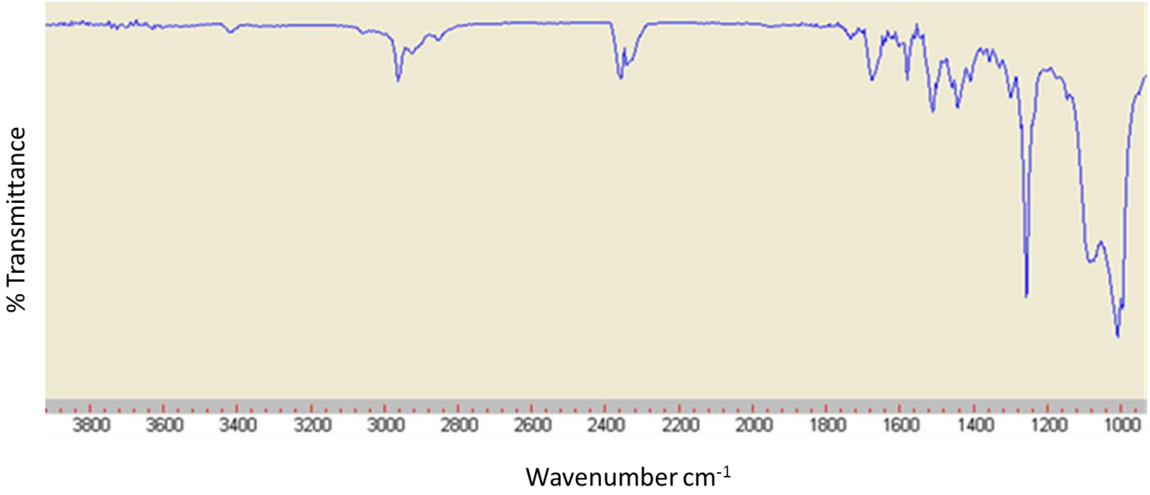


Figure S4. IR spectrum (ATR) of complex **2Fe**

NMR spectra

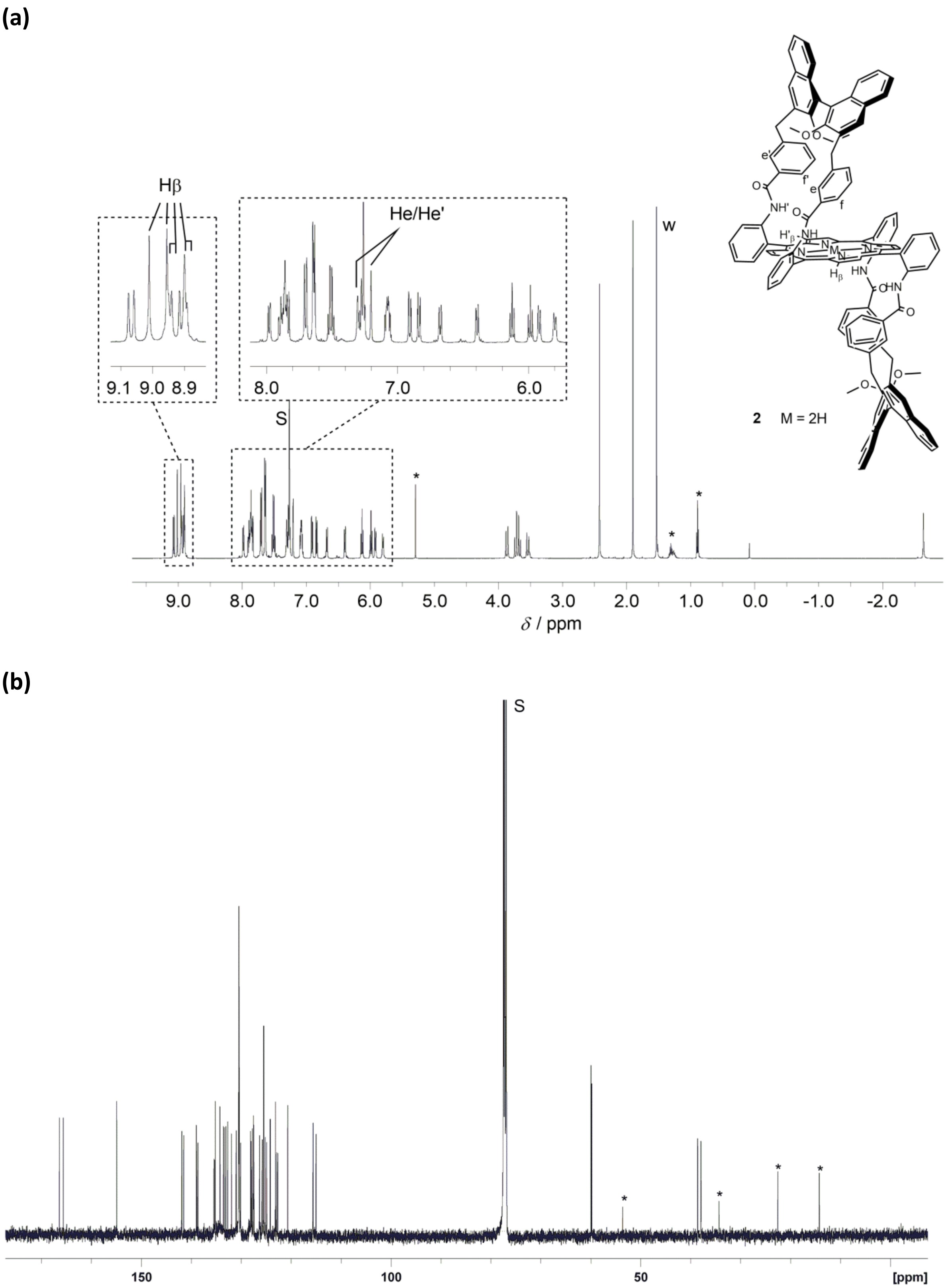


Figure S5. (a) ^{1}H NMR spectrum (500 MHz, 298 K) of compound **2** in $CDCl_3$. **(b)** ^{13}C NMR spectrum (125 MHz, 298 K) of compound **2** in $CDCl_3$. (S = $CHCl_3$, w = water, * = traces of residual solvents or grease).

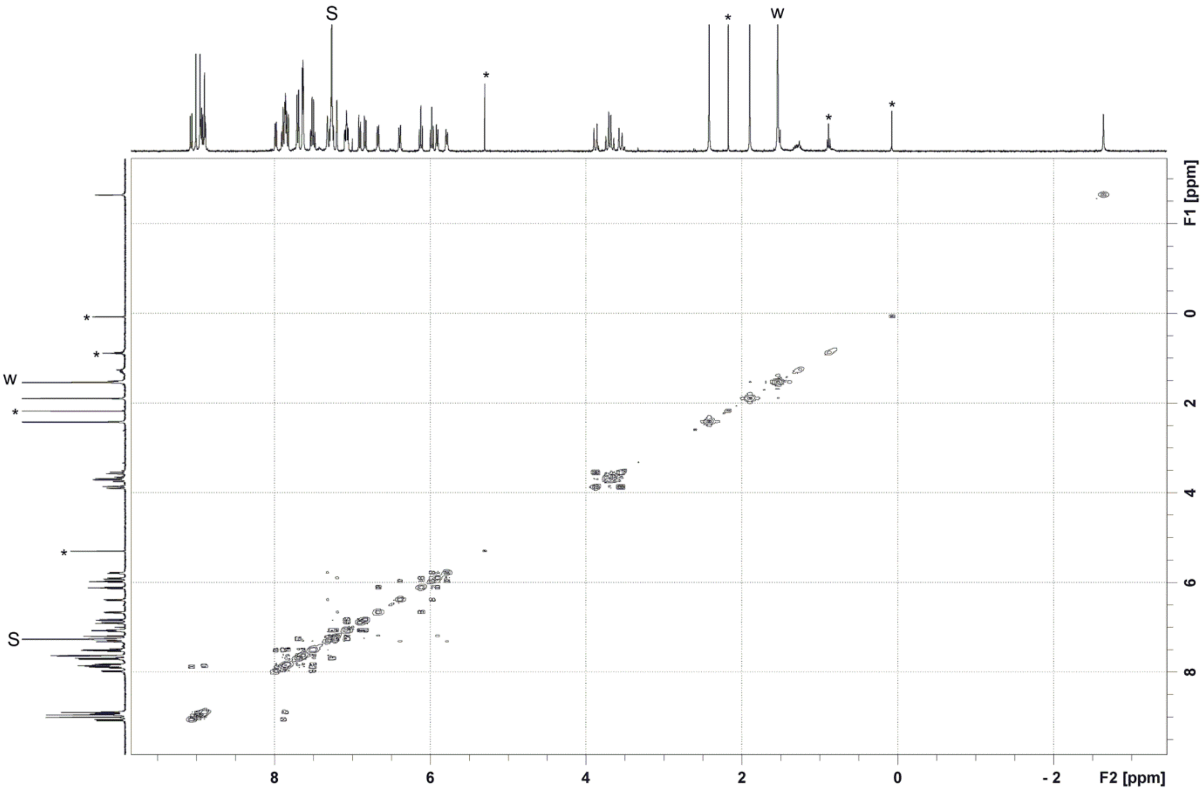


Figure S6. COSY 2D NMR spectrum (500 MHz, 298 K) of compound **2** in $CDCl_3$ (S = $CHCl_3$, w = water, * = traces of residual solvents or grease).

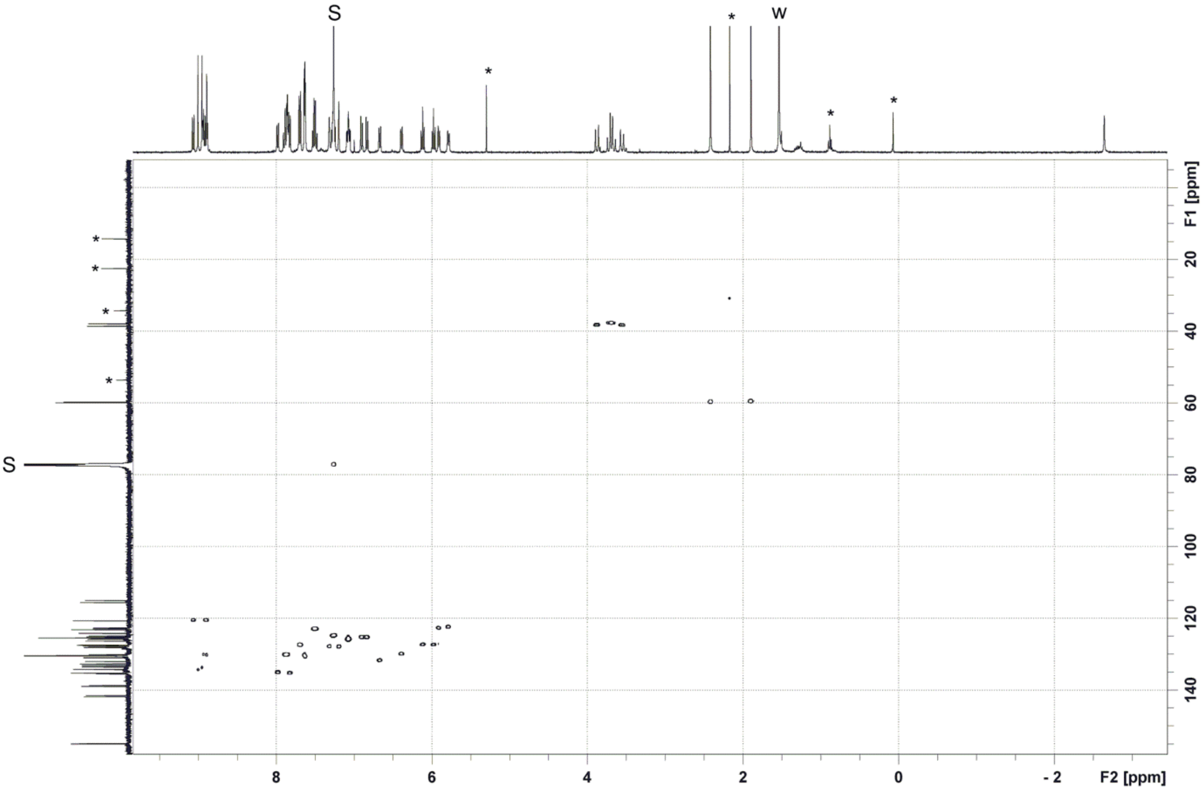
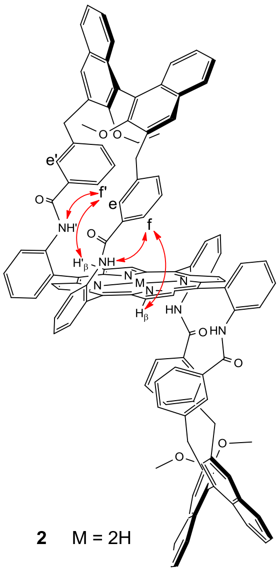


Figure S7. HMQC 2D NMR spectrum (500 MHz, 298 K) of compound **2** in $CDCl_3$ (S = $CHCl_3$, w = water, * = traces of residual solvents or grease).



2 M = 2H

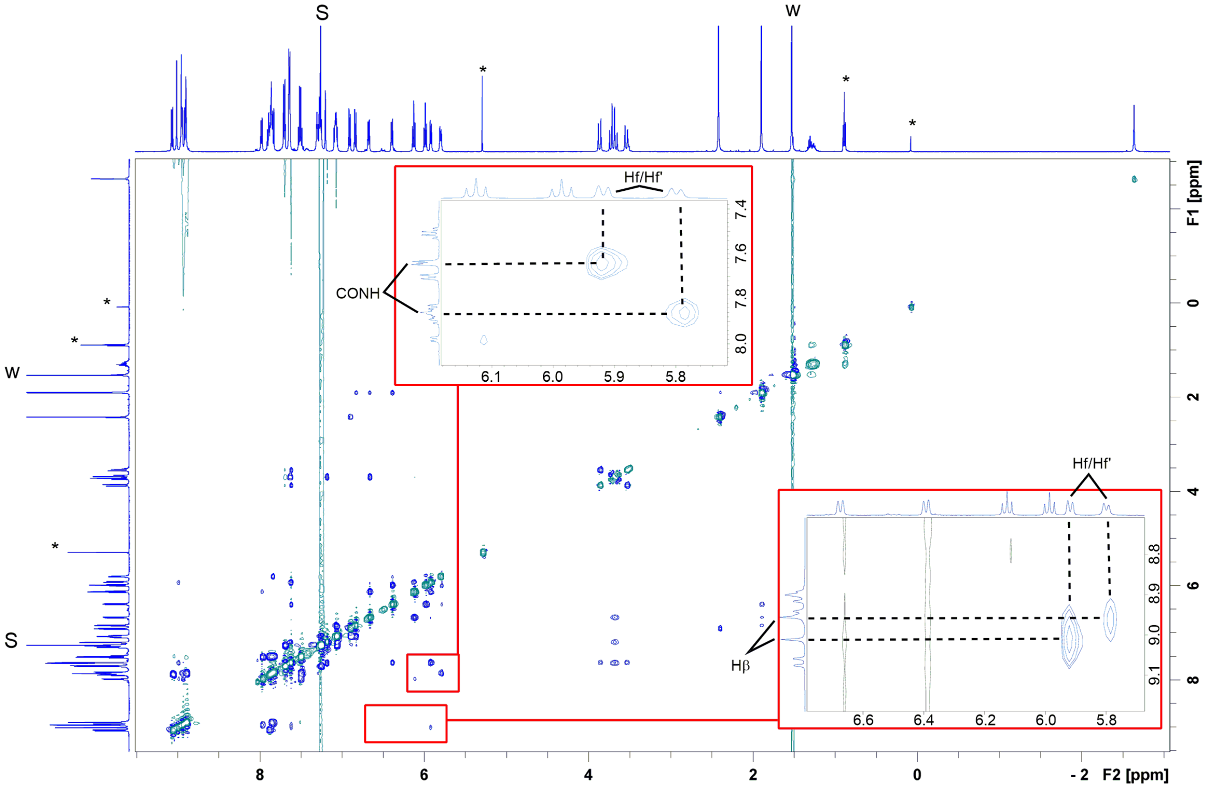


Figure S8. ROESY 2D NMR spectrum (500 MHz, 298 K) of compound **2** in $CDCl_3$ (S = $CHCl_3$, w = water, * = traces of residual solvents or grease). Expanded regions showing NOE cross-peaks between Hf and both the amide and Hβ protons.

MS-ESI spectra

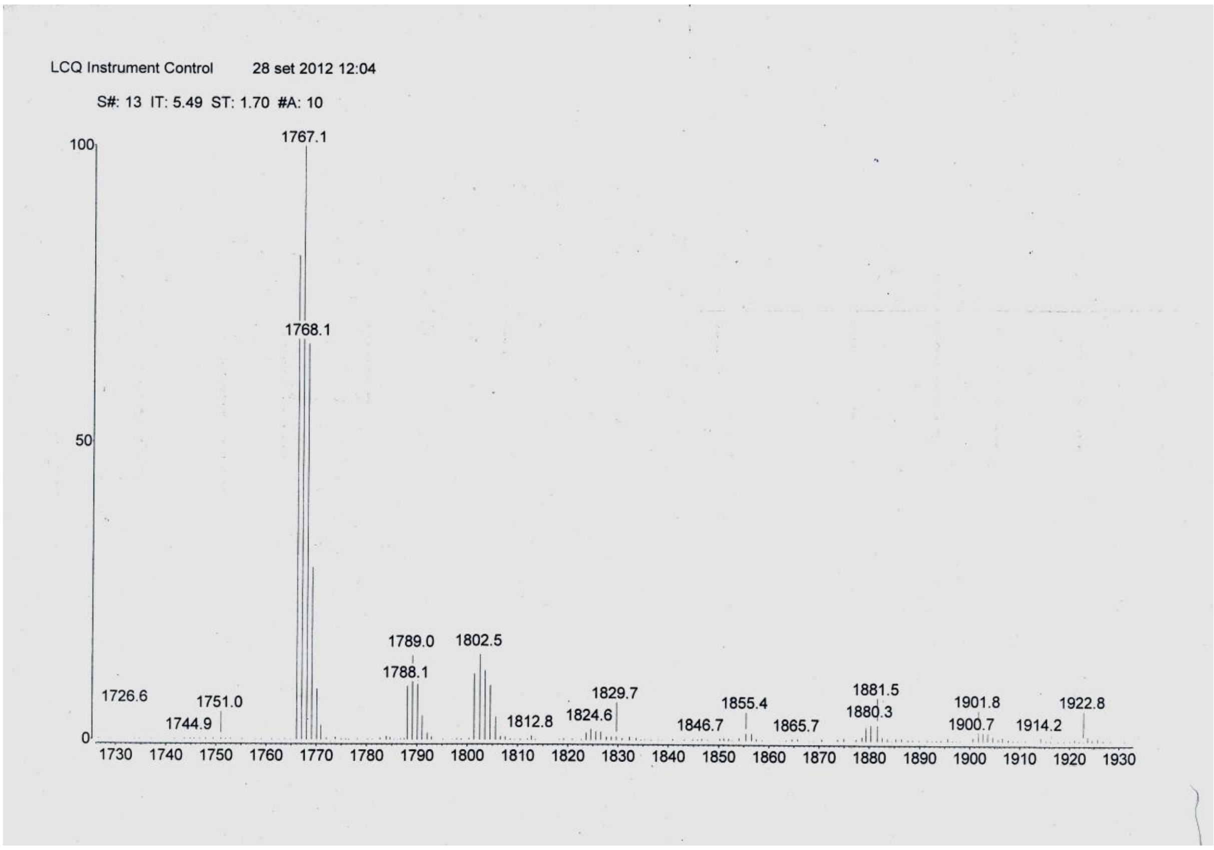
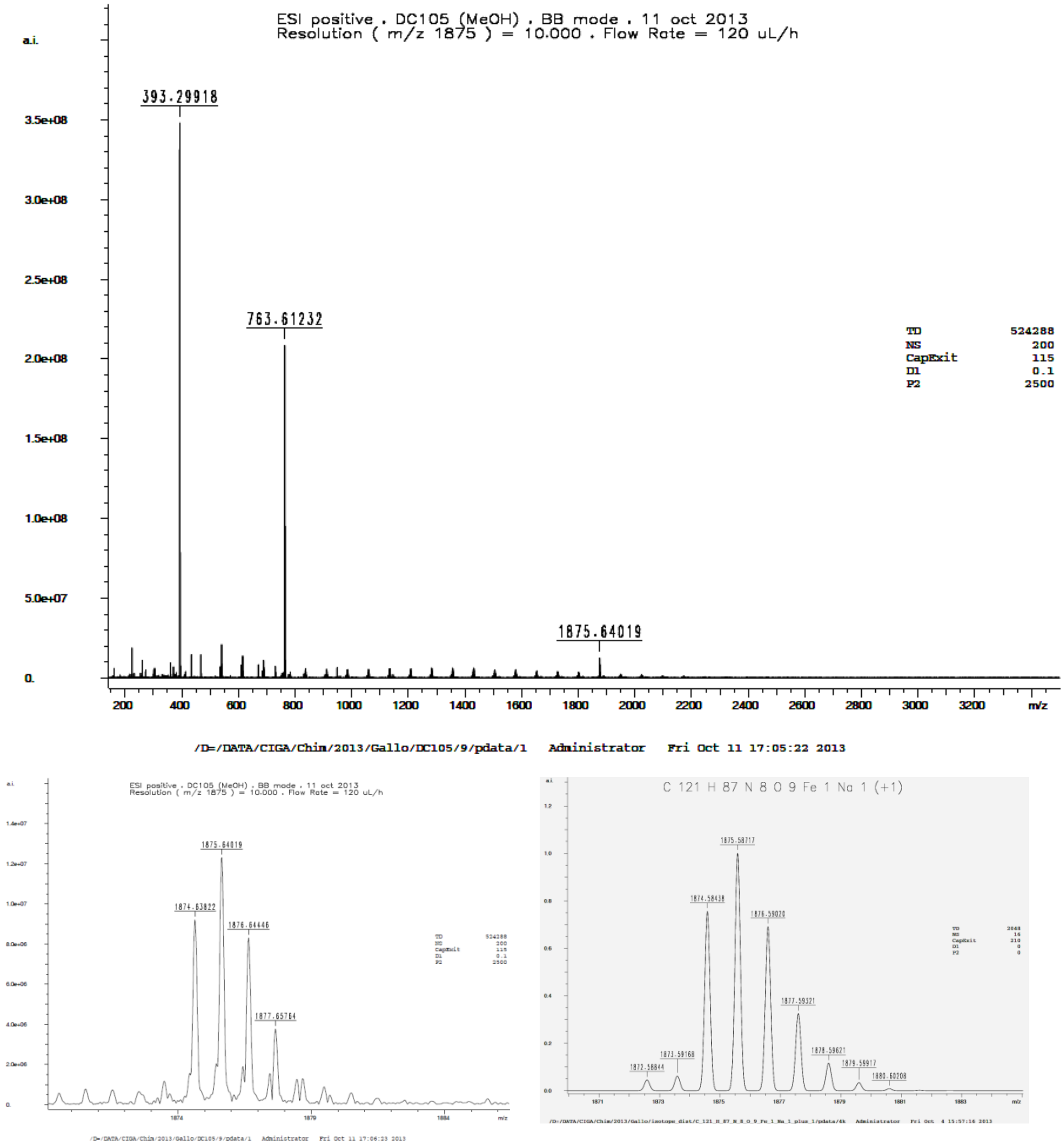


Figure S9. MS-ESI spectrum of compound **2** [M$^+$]



a) Experimental MS-ESI spectrum **b) Simulation of MS-ESI spectrum**

Figure S10. MS-ESI spectrum of complex **2Fe** [M+Na$^+$]

NMR and HPLC spectra of catalytic reactions

Legend	**S**	Internal standard 2,4-dinitrotoluene
	⬭	Maleate
	⬯	Fumarate
	△	α-methylstyrene
	☆	Cyclopropane *trans*
	□	Cyclopropane *cis*

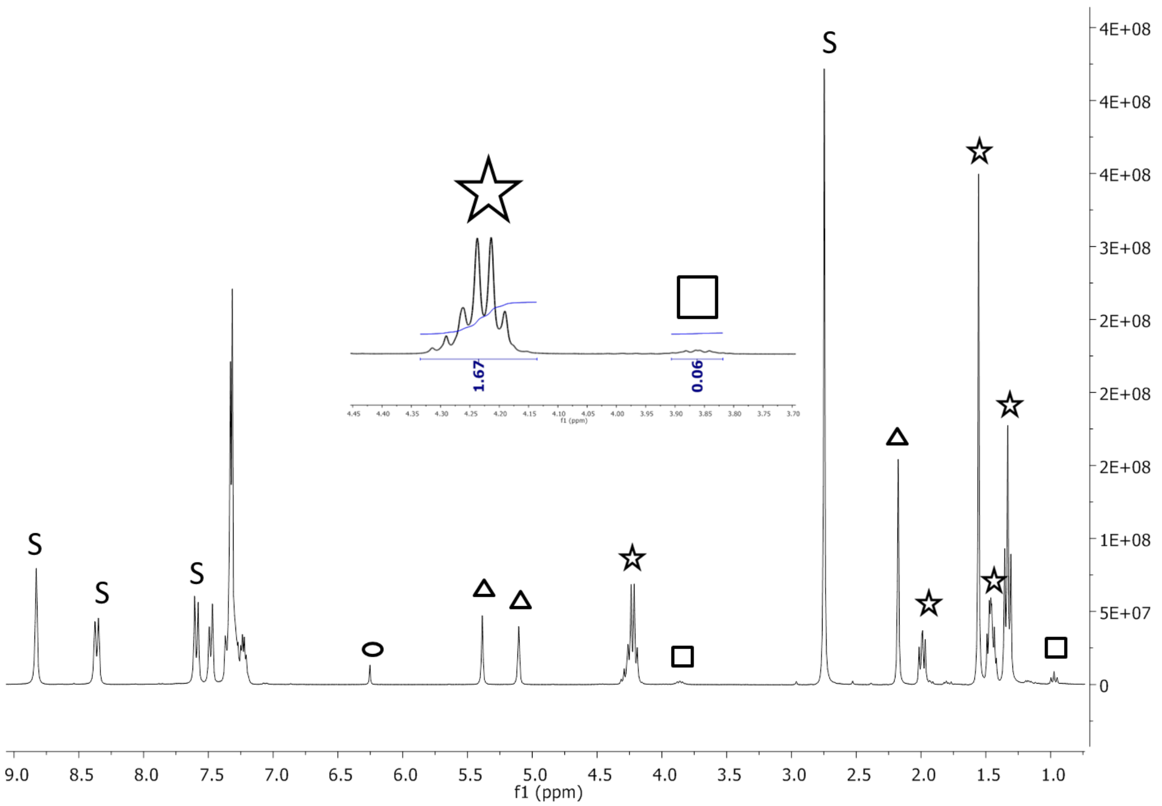


Figure S11. ^{1}H NMR (CDCl$_3$) spectrum of entry 1, Table 1.

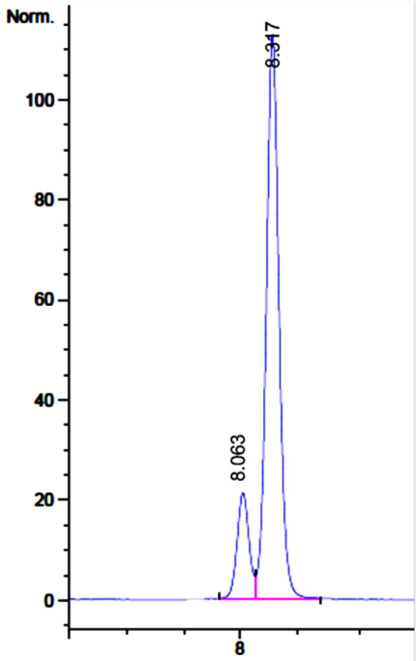


Figure S12. HPLC spectrum of entry 1, Table 1.

DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5

peak	time (min)	area percent
1	8.063	14,066
2	8.317	85,936
		100,000

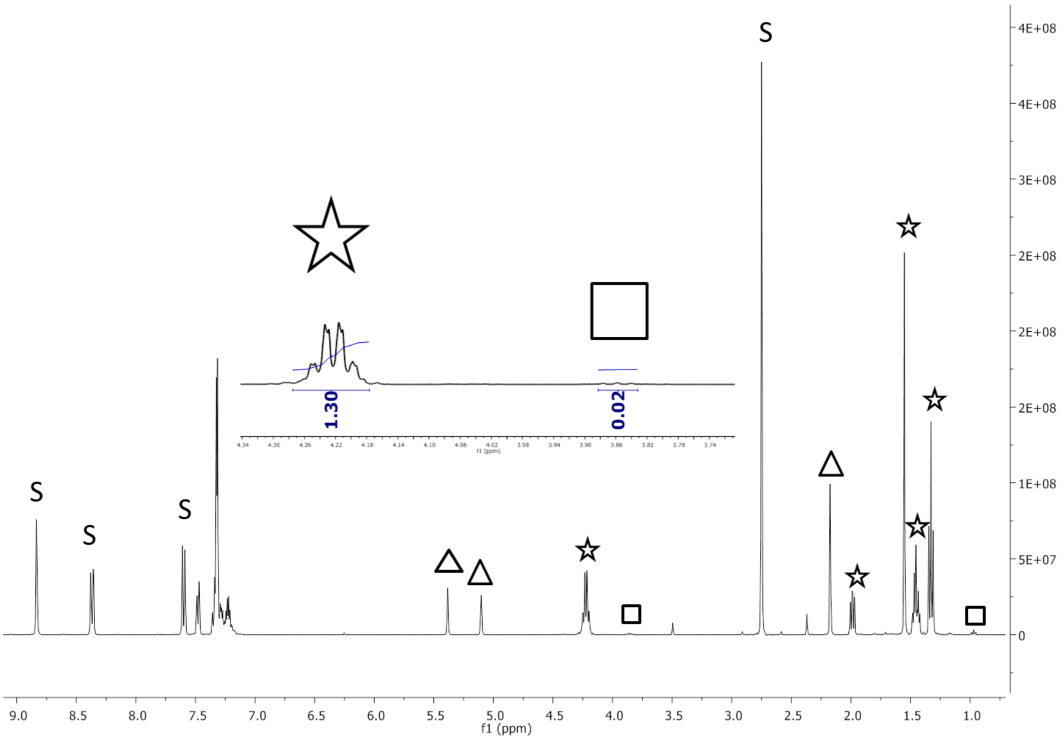


Figure S13. ^{1}H NMR ($CDCl_3$) spectrum of entry 2, Table 1.

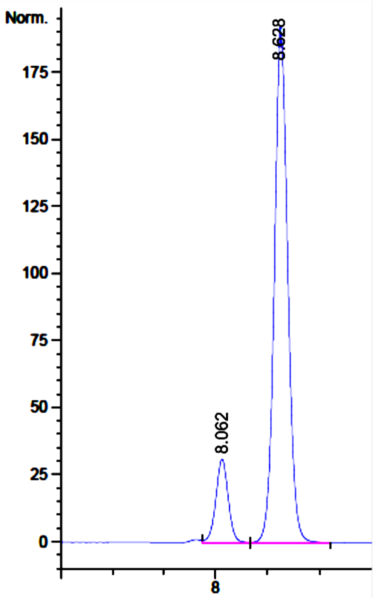


Figure S14. HPLC spectrum of entry 2, Table 1.

DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5

peak	time (min)	area percent
1	8.062	12,656
2	8.628	87,344
		100,000

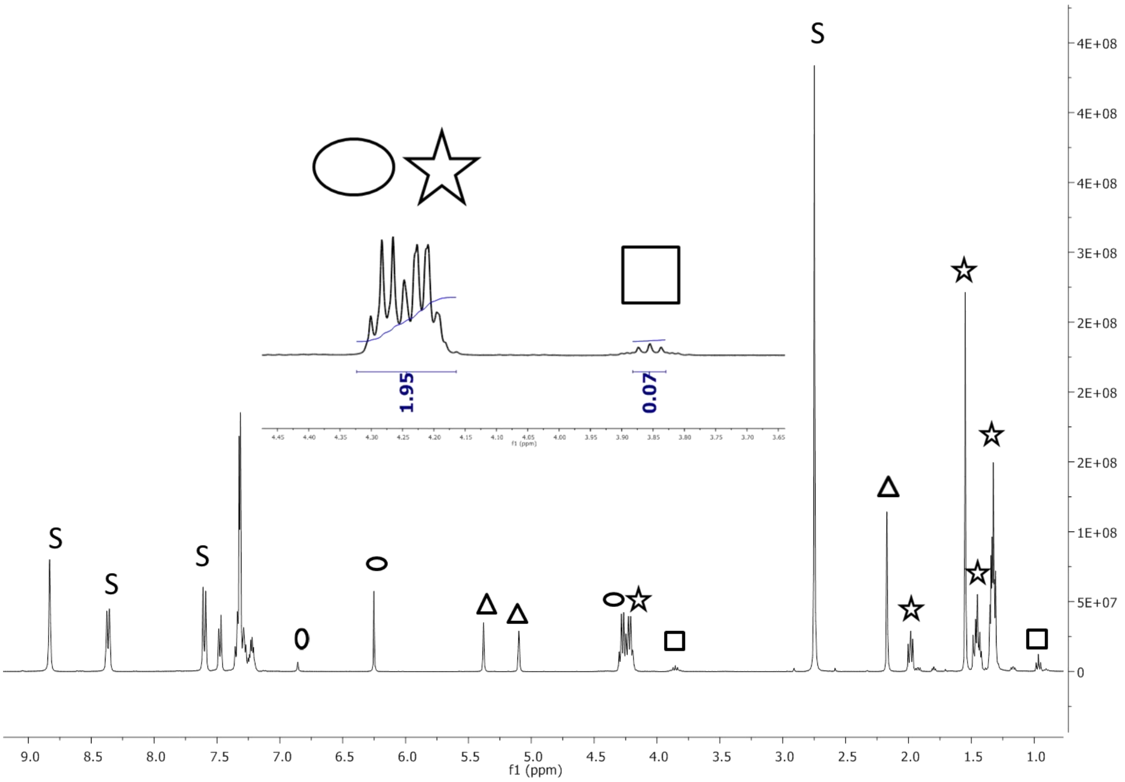


Figure S15. ^{1}H NMR (CDCl$_3$) spectrum of entry 4, Table 1.

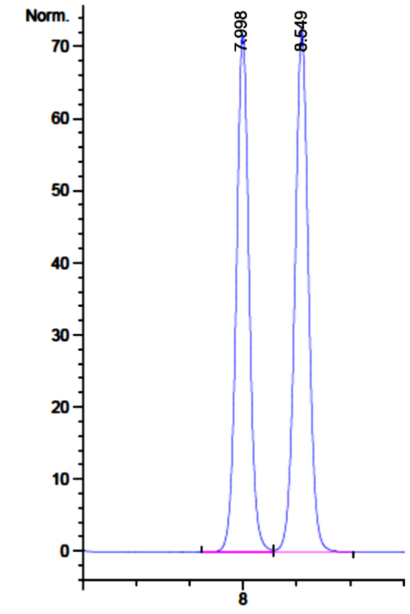


Figure S16. HPLC spectrum of entry 4, Table 1.

DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5

peak	time(min)	area percent
1	7.998	30.381
2	8.549	69.919
		100,000

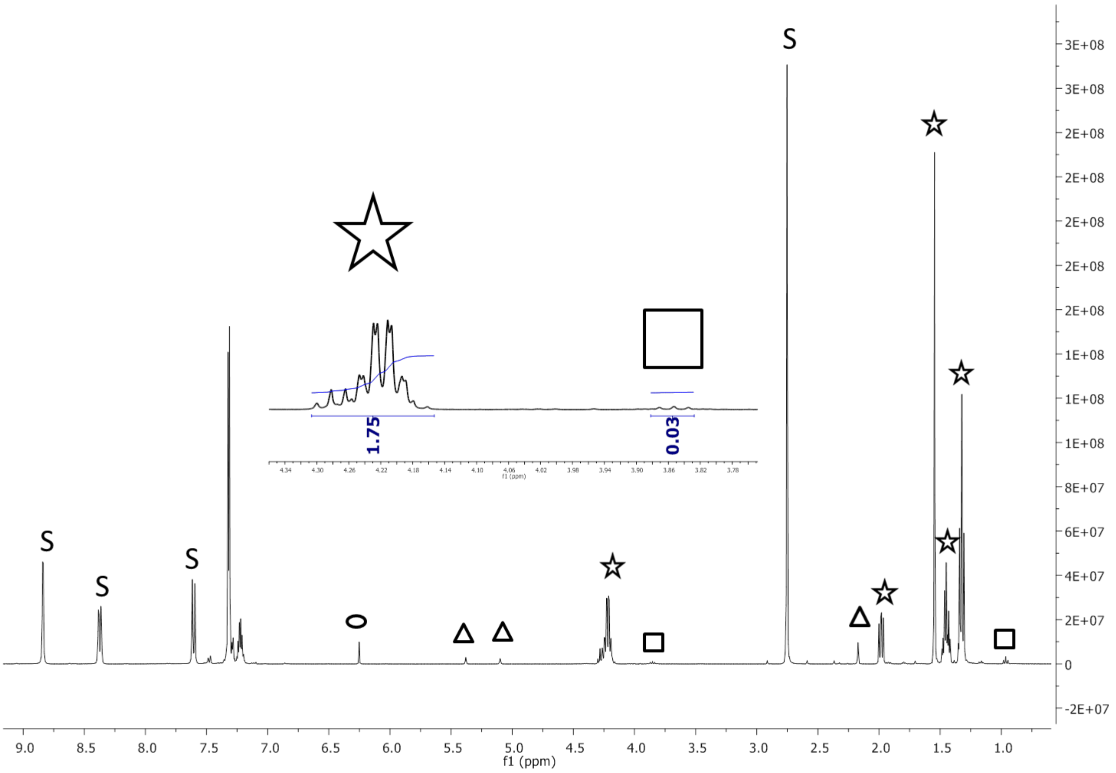


Figure S17. ^{1}H NMR ($CDCl_3$) spectrum of entry 5, Table 1.

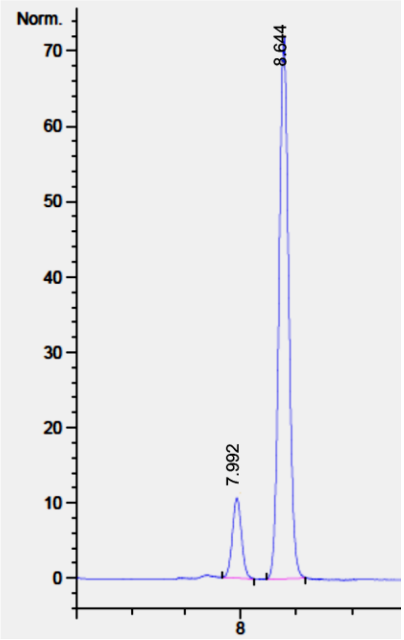


Figure S18. HPLC spectrum of entry 5, Table 1.

DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5

peak	time (min)	area percent
1	7.992	12,322
2	8.644	87,678
		100,000

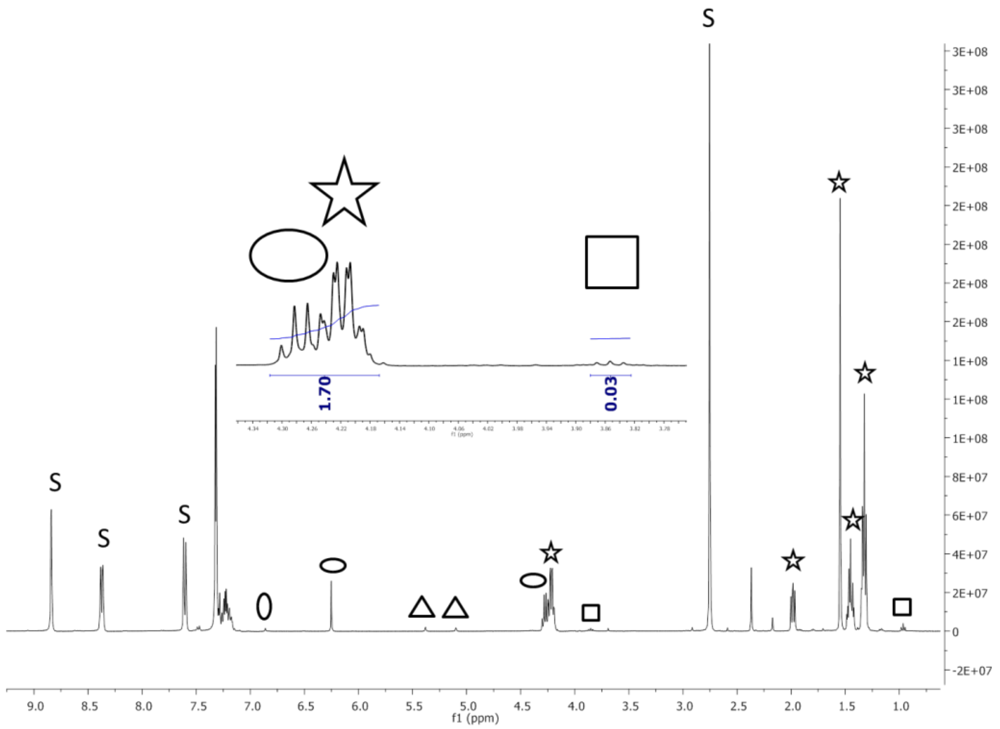


Figure S19. ^{1}H NMR ($CDCl_3$) spectrum of entry 1, Table 2.

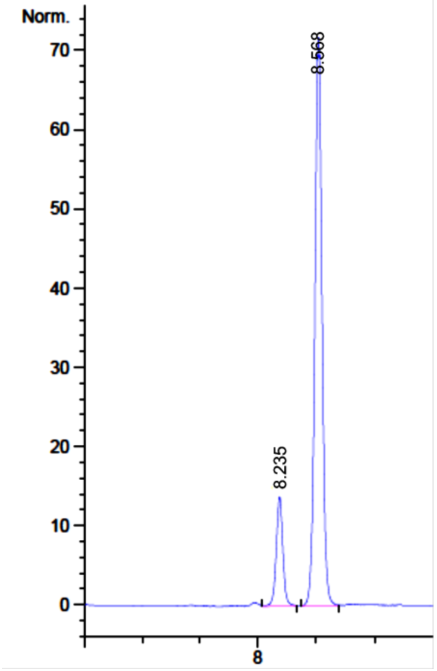


Figure S20. HPLC spectrum of entry 1, Table 2.

DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5

peak	time (min)	area percent
1	8.325	13,663
2	8.568	86,337

100,000

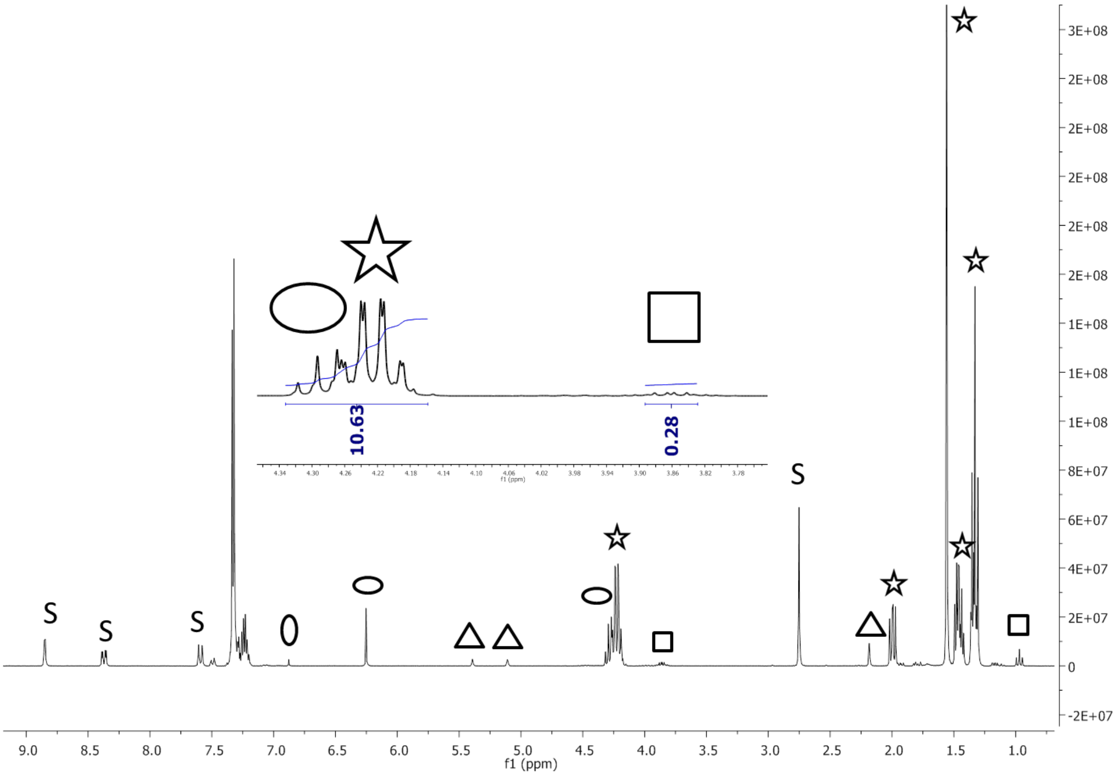


Figure S21. ^{1}H NMR ($CDCl_3$) spectrum of entry 2, Table 2.

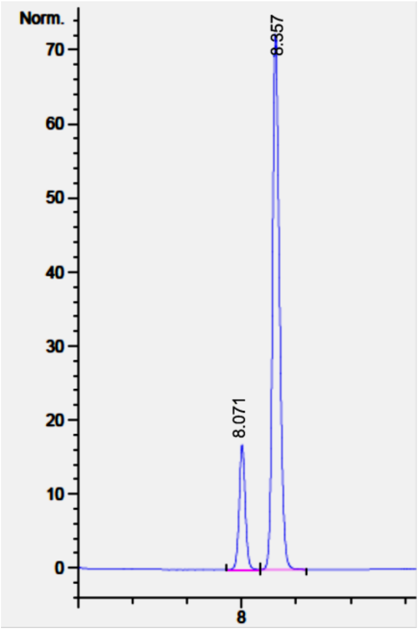


Figure S22. HPLC spectrum of entry 2, Table 2.

DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5

peak	time (min)	area percent
1	8.071	16,205
2	8.357	83,795
		100,000

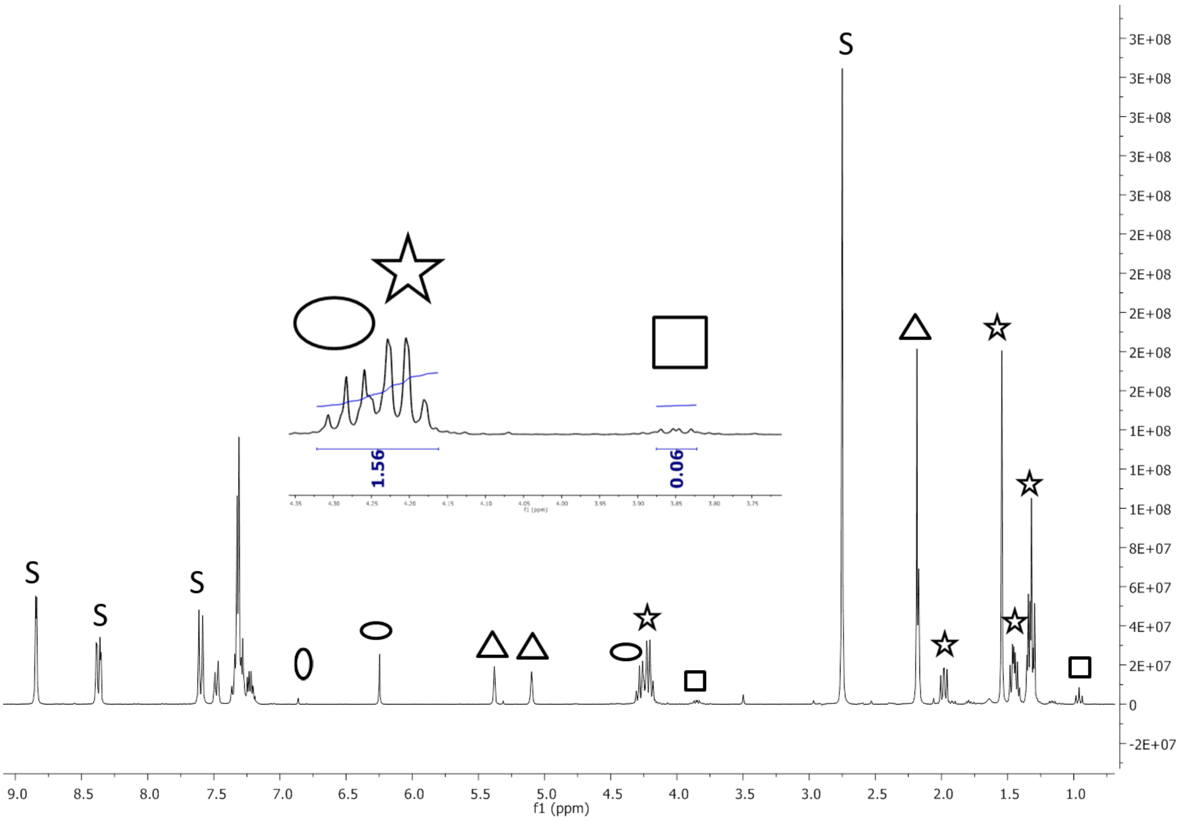


Figure S23. ^1H NMR ($CDCl_3$) spectrum of entry 3, Table 2.

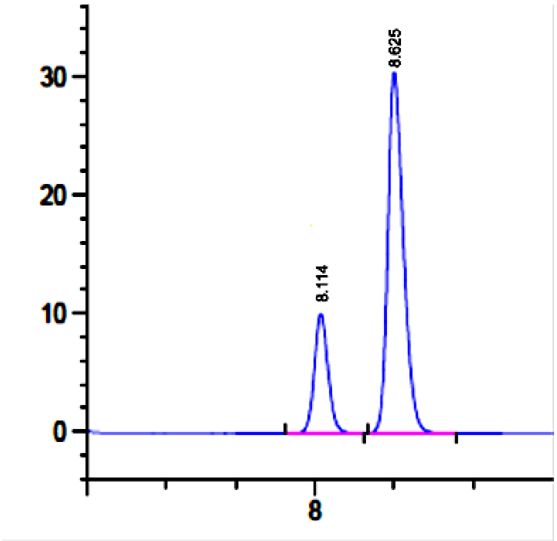


Figure S24. HPLC spectrum of entry 3, Table 2.

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DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5
          peak              time(min)           area percent
            1                   8.114                 20,998
            2                   8.625                 79,002

                                                     100,000
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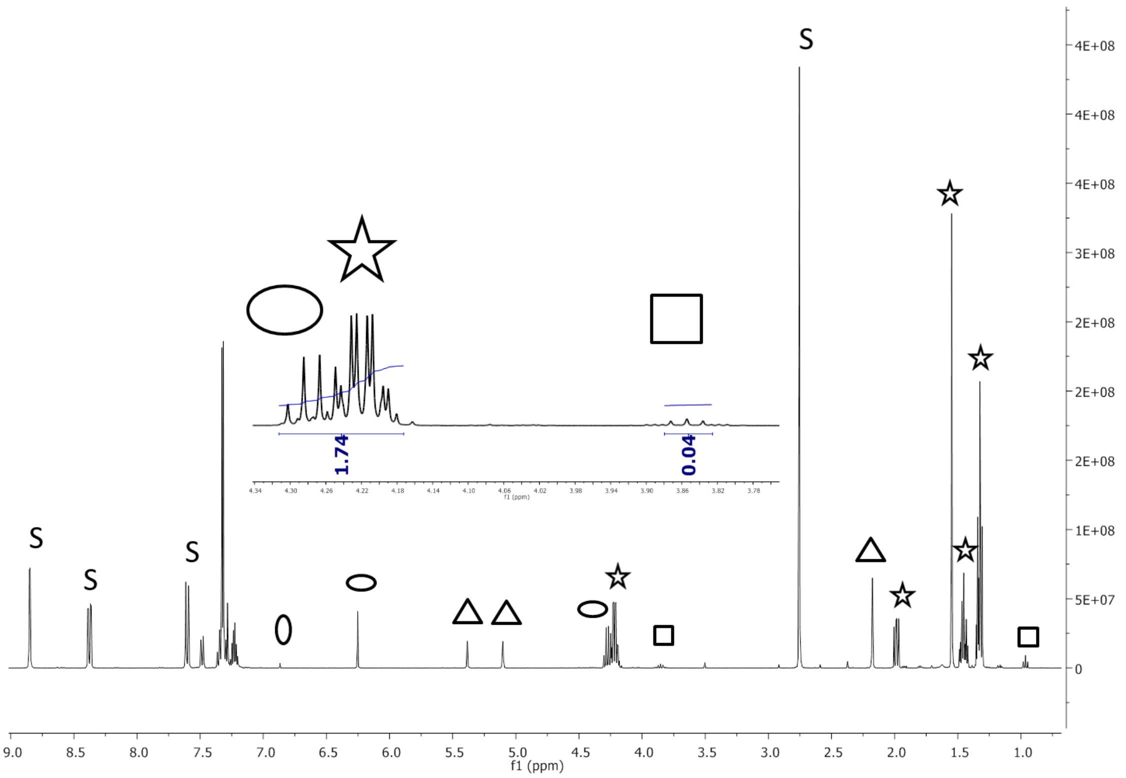

Figure S25. ^{1}H NMR (CDCl$_3$) spectrum of entry 4, Table 2.

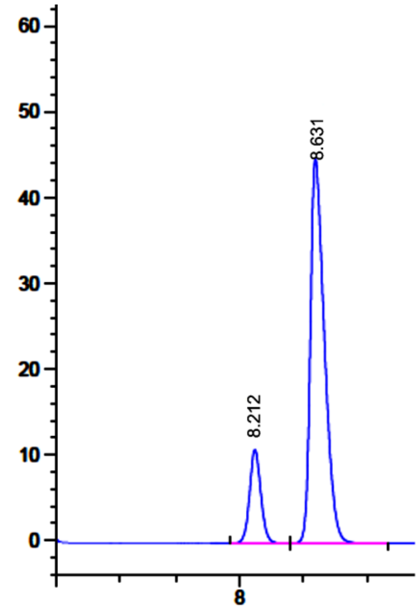

Figure S26. HPLC spectrum of entry 4, Table 2.

DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5

peak	time(min)	area percent
1	8.212	11,255
2	8.631	88,745
		100,000

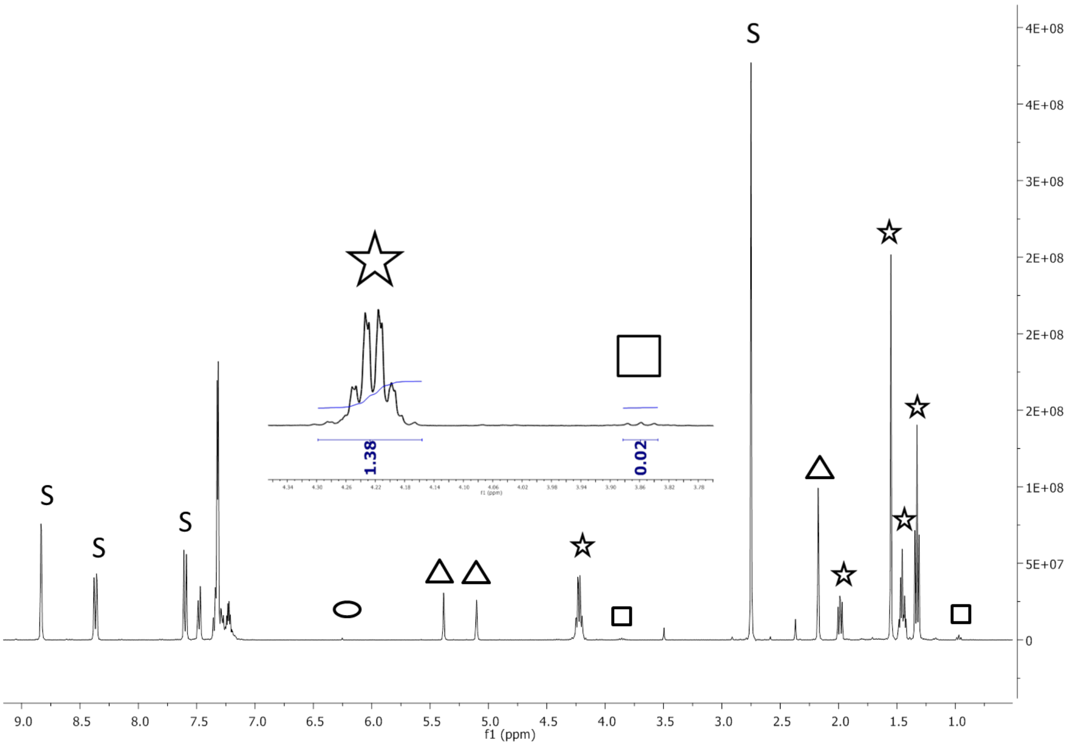

Figure S27. ^{1}H NMR (CDCl$_3$) spectrum of entry 5, Table 2.

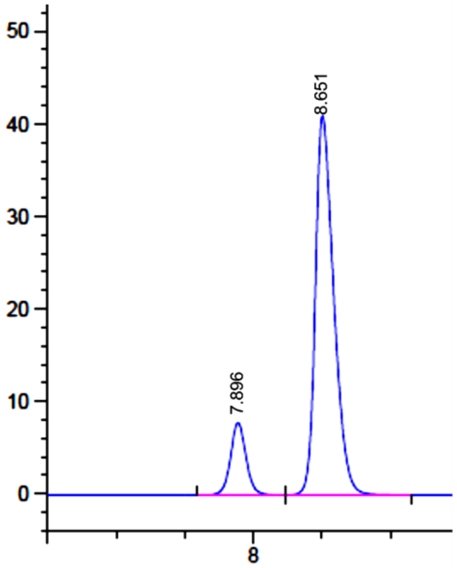

Figure S28. HPLC spectrum of entry 5, Table 2.

DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5

peak	time(min)	area percent
1	7.896	13,029
2	8.651	86,971
		100,000

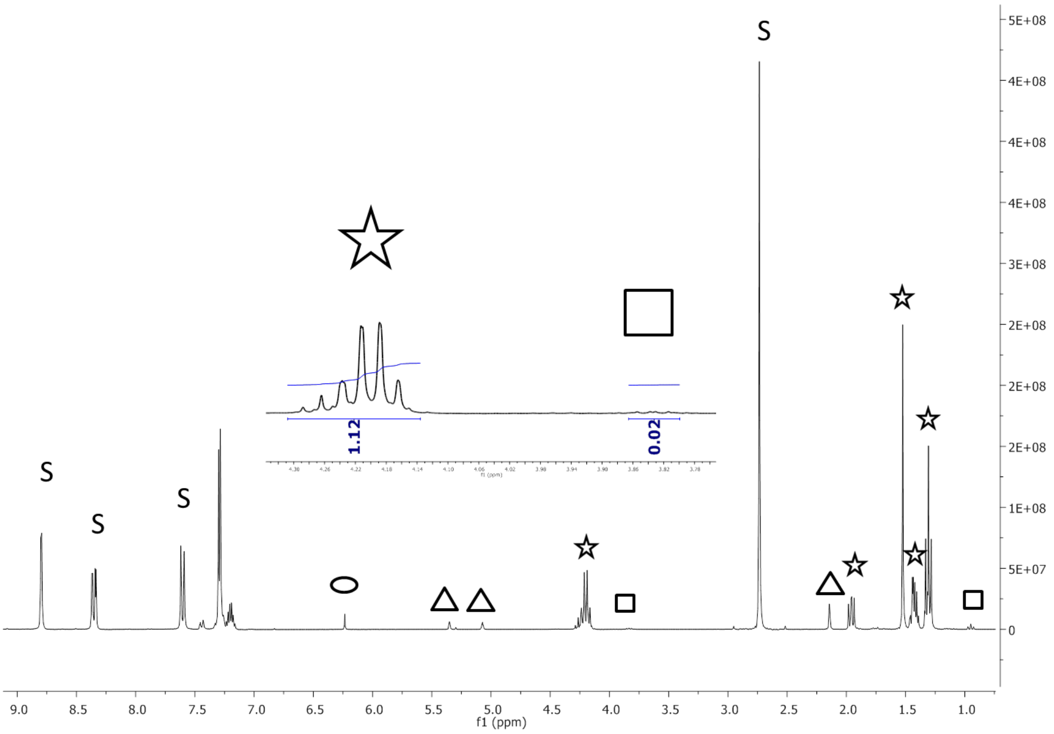

Figure S29. ^{1}H NMR (CDCl$_3$) spectrum of entry 6, Table 2.

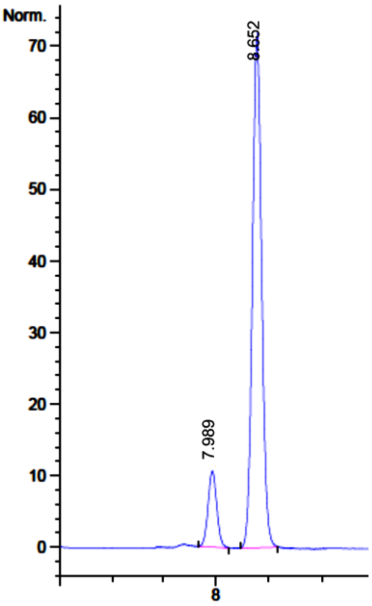

Figure S30. HPLC spectrum of entry 6, Table 2.

DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5

peak	time(min)	area percent
1	7.989	10,551
2	8.652	89,449
		100,000

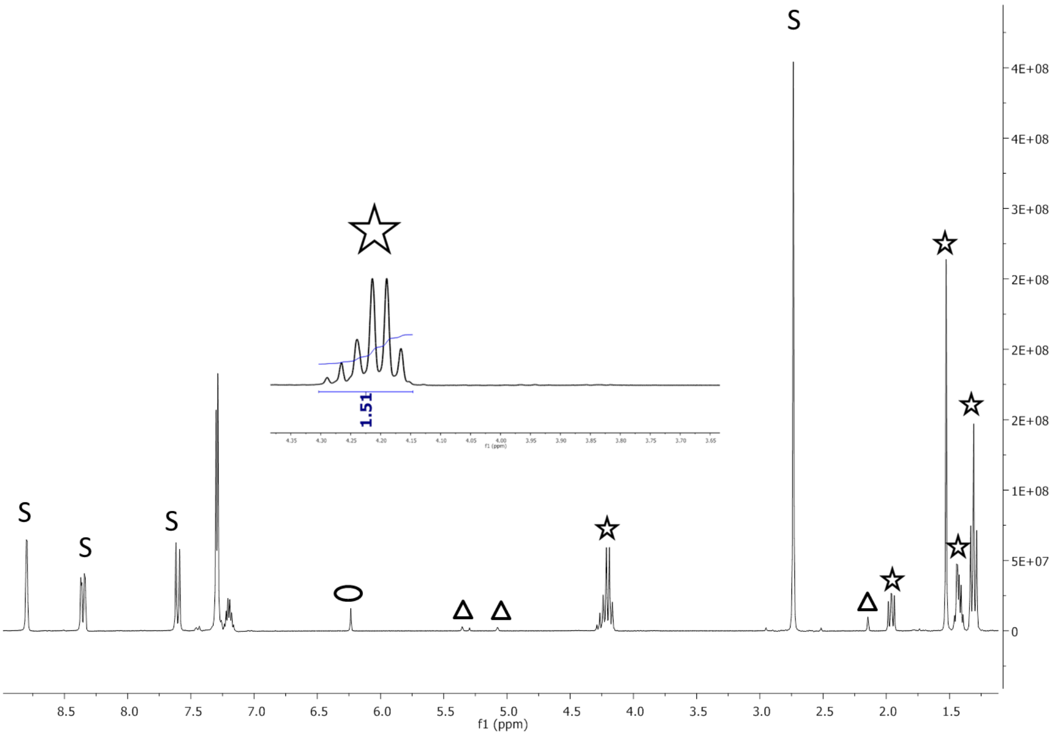

Figure S31. ^{1}H NMR ($CDCl_3$) spectrum of entry 7, Table 2.

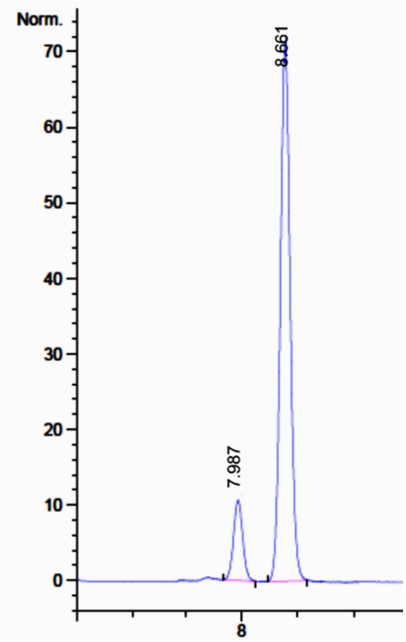

Figure S32. HPLC spectrum of entry 7, Table 2.

DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5

peak	time (min)	area percent
1	7.987	10,638
2	8.661	89,362
		100,000

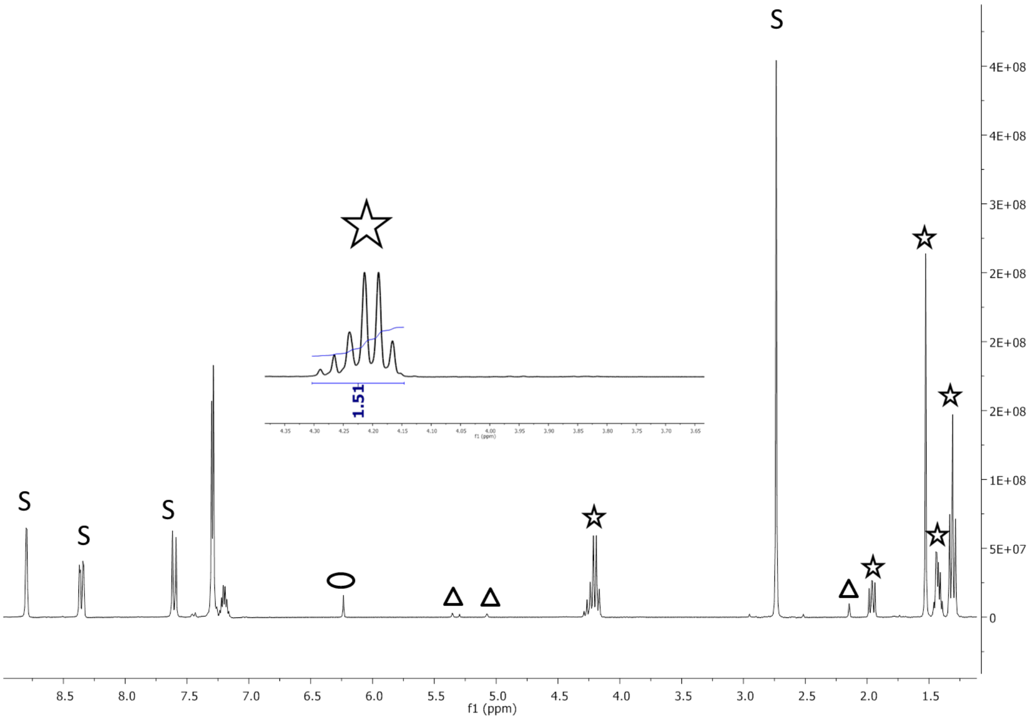

Figure S33. ^{1}H NMR (CDCl$_3$) spectrum of entry 8, Table 2.

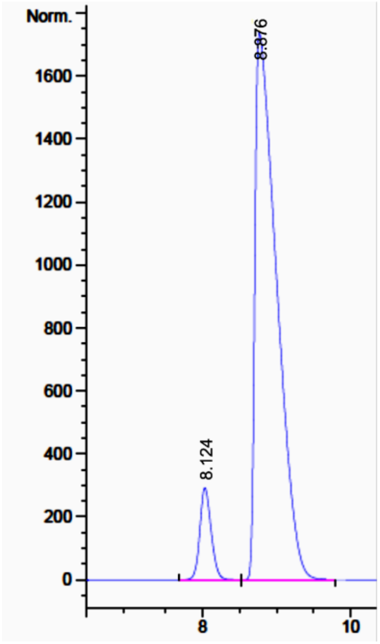

Figure S34. HPLC spectrum of entry 8, Table 2.

DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5

peak	time (min)	area percent
1	8.124	6,666
2	8.876	93,334
		100,000

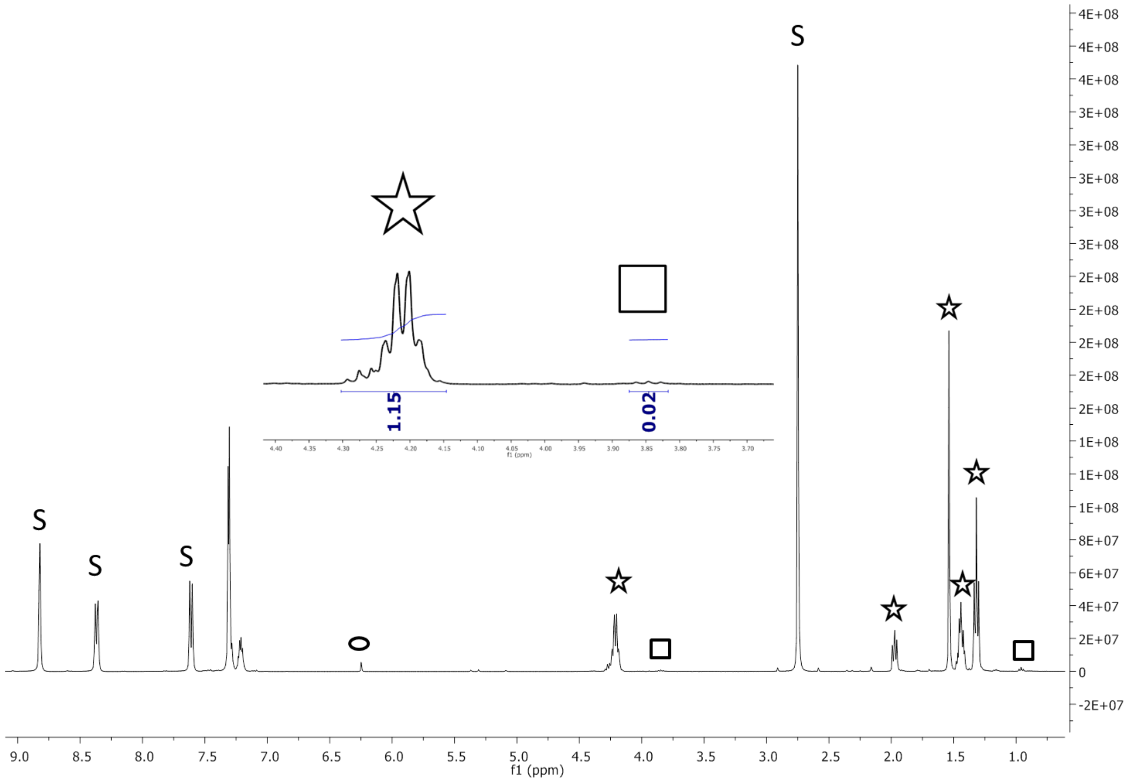

Figure S35. ^{1}H NMR ($CDCl_3$) spectrum of entry 9, Table 2.

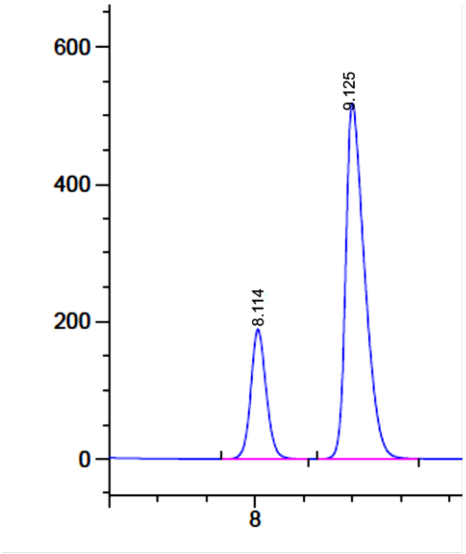

Figure S36. HPLC spectrum of entry 9, Table 2.

DAI-CEL CHRALCEL, IB, n-hexane/i-PrOH 99.5:0.5

peak	time(min)	area percent
1	8.114	21,743
2	9.125	78,257
		100,000

References.

1) X.-W. Zou, L.-F. Zheng, L.-L. Wu, L.-L. Zong and Y.-X. Cheng, *Chin. J. Chem.*, 2008, **26**, 373-378.

2) Z. Halime, S. Balieu, B. Najjari, M. Lachkar, T. Roisnel and B. Boitrel, *J. Porphyrins Phthalocyanines*, 2010, **14**, 412-420.