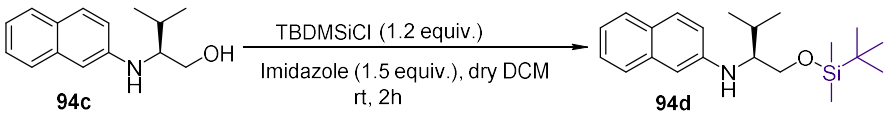
Synthesis of compound **94d** [85]



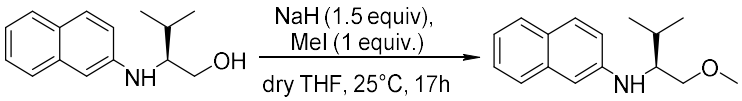
94c **94d**

Yield=93%

To a stirred solution of compound **94c**(1 equiv., 2.2 mmol, 500 mg) in dry DCM (3.73 ml) were added TBDMSiCl (1.2 equiv., 2.64 mmol, 398 mg) and Imidazole (1.5 equiv., 3.3 mmol, 225 mg) at 0°C. The resulting solution was then warmed to room temperature and it was stirred for 2 hours. The reaction mixture was diluted with water and then aqueous layer was extracted three times with dichloromethane. The combined organic layers were dried over $MgSO_4$ and the solvent was removed under vacuum. The desired product was obtained in 93% yield without further purification.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 6.96 – 6.87 (m, 1H), 3.81 (dd, *J* = 10.2, 3.6 Hz, 1H), 3.70 (dd, *J* = 10.2, 4.8 Hz, 1H), 3.34 (dd, *J* = 10.1, 4.7 Hz, 1H), 2.12 (dq, *J* = 13.3, 6.7 Hz, 1H), 1.06 (dd, *J* = 6.8, 3.7 Hz, 5H), 0.91 (s, 7H), 0.04 (d, *J* = 6.6 Hz, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 128.95, 127.57, 126.25, 125.80, 121.91, 118.54, 62.03, 29.24, 25.82, 19.54, 18.81.

Synthesis of compound **94e**[85]

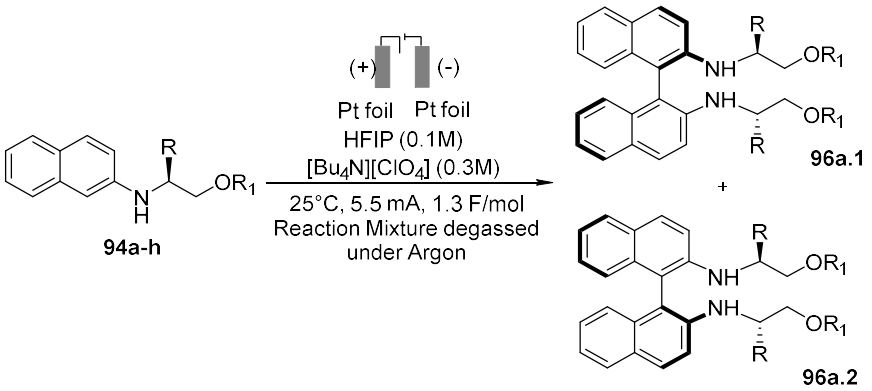


94c **94e**

The amino alcohol **94c** (400mg, 1.74 mmol, 1 equiv.), dissolved in 6 ml of dry THF, was added to a suspension of sodium hydride (63 mg, 2.61 mmol, 1.5 equiv., 60% dispersion in mineral oil) in dry THF (6.3 ml) at 0°C. The mixture was allowed to react at room temperature for 2 h before methyl iodide (371mg, 2.61 mmol, 1.5 equiv.) was added. The mixture was then left to react at room temperature overnight. Distilled water was added, and the ethereal solvent removed under reduced pressure. The residue was extracted three times with dichloromethane and the combined extracts washed with brine, dried over magnesium sulphate and the solvent was removed under reduced pressure. The product was purified by flash column chromatography on silica gel using a hexane/ethyl acetate 8:2 as eluent to afford a yellow solid (after stored in the fridge) in 70% yield.

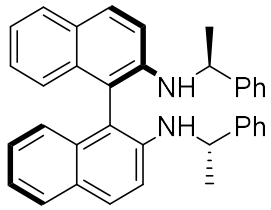
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.01 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.97 (d, *J* = 2.4 Hz, 1H), 3.61 (pd, *J* = 8.9, 4.5 Hz, 1H), 3.47 (s, 3H), 2.20 (h, *J* = 6.8 Hz, 1H), 1.17 (t, *J* = 6.7 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 146.03, 135.48, 129.13, 127.78, 127.47, 126.43, 125.94, 121.89, 118.50, 104.86, 72.35, 59.17, 58.27, 29.87, 19.51, 19.04. **HRMS** calculated 244.1701; found 244.1700. **α_D** [0.7 g/mL] ($CHCl_3$) = -9.34

5.2.5 GENERAL PROTOCOL FOR THE ELECTROCHEMICAL INTERMOLECULAR HOMO-COUPLING OF COMPOUNDS 94a-94h



In a 5 mL IKA ElectraSyn 2.0 vial, equipped with a stir bar, the chiral amine (0.5 mmol, 1equiv.) and Lithium Tetrabutyl ammonium perchlorate (1.5 mmol, 3equiv.) were dissolved in 5 ml of 1,1,1,3,3,3-Hexafluoro-2-propanol. The electrochemical cell was assembled with IKA Platinum foil anode and cathode and the reaction mixture was degassed with Argon for two minutes. Under Argon Atmosphere, the solution was electrolyzed with a constant current of 5.5mA (Cell potential 1.5-2.5V). After 1.3 F/mol were furnished, the reaction mixture was diluted with ethyl acetate and washed two times with brine. The organic phase was than dried over magnesium sulphate and the solvent evaporated under reduced pressure. The crude afforded was purified by column chromatography on flash silica gel to separate the desired diastereoisomers.

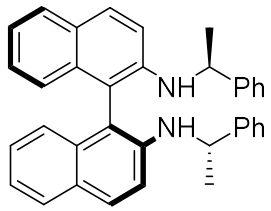
Compound 96a.1



Prepared according to the general procedure starting from **94a**. The product was purified by flash column chromatography on silica gel using a mixture of hexane/ethyl acetate racing from 9.8:0.2 to 9.5:0.5 to afford a white solid (after stored in the fridge) in 18% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 – 7.72 (m, 2H), 7.50 – 7.35 (m, 2H), 7.35 – 7.14 (m, 5H), 7.13 – 7.00 (m, 2H), 4.68 (s, 1H), 4.10 (s, 1H), 1.23 (dd, J = 6.8, 2.7 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 145.69, 144.07, 133.61, 129.50, 128.62, 128.08, 127.68, 126.82, 126.58, 125.81, 123.86, 121.93, 115.05, 53.63, 29.72, 25.14. **HRMS** calculated 493.2644; found 493.2651 α_D [0.1 g/mL] ($CHCl_3$) = -3.27

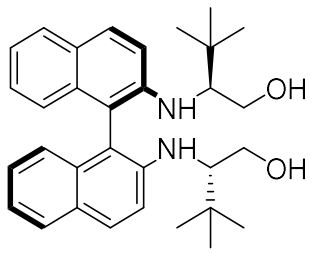
Compound 96a.2



Prepared according to the general procedure starting from **94a**. The product was purified by flash column chromatography on silica gel using a mixture of hexane/ethyl acetate racing from 9.8:0.2 to 9.5:0.5 to afford a yellowish solid (after stored in the fridge) in 29% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J = 9.5 Hz, 2H), 7.22 (qt, J = 6.8, 2.3 Hz, 7H), 7.08 (dd, J = 9.1, 2.7 Hz, 1H), 7.02 – 6.94 (m, 1H), 4.74 (s, 1H), 4.16 (d, J = 5.6 Hz, 1H), 1.36 (dd, J = 7.2, 2.4 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 144.29, 142.55, 132.86, 128.38, 127.41, 126.91, 126.61, 125.72, 125.39, 124.79, 123.27, 120.92, 113.95, 111.03, 52.30, 24.07. **HRMS** calculated 493.2644; found 493.2643 α_D [1.6 g/mL] ($CHCl_3$) = - 67.41

Compound 96b.1

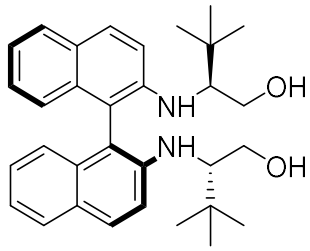


Prepared according to the general procedure starting from **94b**. The product was purified by flash column chromatography on silica gel using hexane/ethyl acetate 8:2 to afford a reddish solid (after stored in the fridge) in 41% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, *J* = 9.0 Hz, 1H), 7.86 – 7.76 (m, 1H), 7.37 (dd, *J* = 9.1, 1.6 Hz, 1H), 7.24 (hept, *J* = 4.7 Hz, 2H), 7.12 – 7.02 (m, 1H), 3.65 (dd, *J* = 11.3, 3.6 Hz, 1H), 3.48 (s, 1H), 3.14 (dd, *J* = 11.3, 7.4 Hz, 1H), 0.82 (s,

9H). **^{13}C-NMR** (75 MHz, $CDCl_3$) δ 145.46, 133.47, 129.98, 128.74, 127.72, 127.30, 122.56, 122.20, 114.71, 111.40, 63.37, 62.39, 34.74, 26.95. **HRMS** calculated 485.3168; found 485.3168. **α_D** [2.16 g/mL] ($CHCl_3$) = -81.23

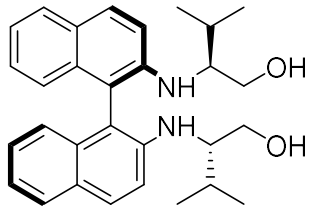
Compound 96b.2



Prepared according to the general procedure starting from **94b**. The product was purified by flash column chromatography on silica gel using hexane/ethyl acetate 8:2 to afford a yellowish solid (after stored in the fridge) in 9% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J = 9.0 Hz, 1H), 7.85 – 7.76 (m, 1H), 7.37 (d, J = 9.1 Hz, 1H), 7.31 – 7.14 (m, 2H), 7.10 (d, J = 7.9 Hz, 1H), 3.79 (dd, J = 11.5, 3.2 Hz, 1H), 3.63 (s, 2H), 3.46 (s, 1H), 3.23 (dd, J = 11.3, 8.5 Hz, 1H), 0.63 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 144.91, 133.86, 129.81, 129.01, 128.09, 126.80, 124.13, 122.20, 114.54, 112.02, 63.85, 62.76, 34.54, 26.67. **HRMS** calculated 485.3168; found 485.3171 **α_D** [0.1 g/mL] ($CHCl_3$) = +23.456

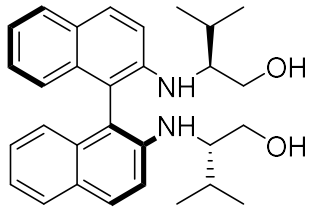
Compound 96c.1



Prepared according to the general procedure starting from **94c**. The product was purified by flash column chromatography on silica gel using hexane/ethyl acetate 7:3 to afford a reddish solid (after stored in the fridge) in 43% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J = 9.0 Hz, 1H), 7.83 (dt, J = 6.2, 3.4 Hz, 1H), 7.33 (d, J = 9.0 Hz, 1H), 7.23 (dt, J = 6.8, 3.4 Hz, 2H), 7.06 (dt, J = 6.1, 3.4 Hz, 1H), 3.57 (dd, J = 17.3, 9.9 Hz, 2H), 3.45 (s, 1H), 3.29 (dd, J = 11.0, 5.9 Hz, 1H), 1.76 – 1.58 (m, 1H), 0.83 (dd, J = 11.6, 6.8 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 144.91, 133.58, 129.94, 128.61, 127.87, 127.16, 122.87, 122.29, 114.99, 112.30, 62.77, 60.79, 30.09, 19.26, 18.86. **HRMS** calculated 457.2855; found 457.2856 . **α_D** [3.5 g/ml] ($CHCl_3$) = -92.27

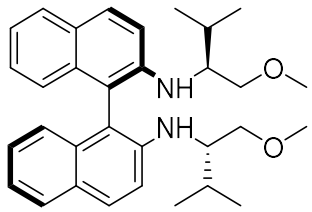
Compound 96c.2



Prepared according to the general procedure starting from **94c**. The product was purified by flash column chromatography on silica gel using hexane/ethyl acetate 7:3 to afford a yellowish solid (after stored in the fridge) in 17% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 9.0 Hz, 1H), 7.81 (d, J = 7.2 Hz, 1H), 7.33 (d, J = 9.1 Hz, 1H), 7.29 – 7.14 (m, 4H), 7.03 (d, J = 8.3 Hz, 1H), 3.70 (dd, J = 11.2, 2.6 Hz, 1H), 3.59 (d, J = 11.2 Hz, 2H), 3.43 (s, 1H), 3.35 (dd, J = 11.2, 6.6 Hz, 1H), 1.57 (q, J = 6.6 Hz, 1H), 0.89 – 0.77 (m, 2H), 0.66 (dd, J = 9.5, 6.7 Hz, 7H). **^{13}C-NMR** (75 MHz, $CDCl_3$) δ 144.19, 134.02, 129.91, 128.60, 128.06, 127.16, 126.84, 124.15, 122.84, 122.49, 122.30, 115.09, 113.29, 62.81, 61.59, 60.81, 30.03, 19.23, 19.06, 18.87, 18.72. **HRMS** calculated 457.2855; found 457.2849. **α_D** [18.75 g/ml] ($CHCl_3$) = -69.99

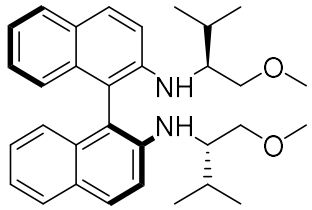
Compound 96e.1



Prepared according to the general procedure starting from **94d**. The product was purified by flash column chromatography on silica gel using a mixture of hexane/ethyl acetate racing from 9.8:0.2 to 9.4:0.6 to afford a yellow solid (after stored in the fridge) in 40% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, *J* = 9.0 Hz, 1H), 7.83 – 7.73 (m, 1H), 7.35 – 7.26 (m, 1H), 7.17 (h, *J* = 5.6 Hz, 2H), 7.00 (d, *J* = 6.5 Hz, 1H), 3.85 (s, 1H), 3.41 (d, *J* = 5.4 Hz, 1H), 3.25 (dd, *J* = 9.5, 4.4 Hz, 1H), 3.05 (dd, *J* = 9.5, 5.5 Hz, 1H), 2.94 (s, 2H), 1.79 (h, *J* = 6.6 Hz, 1H), 0.88 (d, *J* = 6.7 Hz, 3H), 0.74 (d, *J* = 6.7 Hz, 3H). **^{13}C-NMR** (75 MHz, $CDCl_3$) δ 144.89, 133.96, 129.47, 127.94, 127.56, 126.42, 123.94, 121.62, 114.73, 112.28, 73.31, 58.62, 29.73, 19.53, 17.97. **HRMS** calculated 485.3168; found 485.3168 **α_D** [1 g/mL] ($CHCl_3$) = -53.478

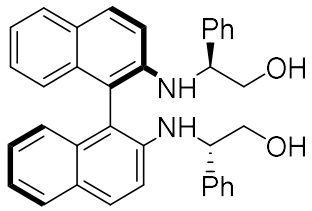
Compound 96e.2



Prepared according to the general procedure starting from **94d**. The product was purified by flash column chromatography on silica gel using a mixture of hexane/ethyl acetate racing from 9.8:0.2 to 9.4:0.6 to afford a beige solid (after stored in the fridge) in 13% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 9.0 Hz, 1H), 7.77 (dd, J = 6.5, 2.6 Hz, 1H), 7.30 – 7.23 (m, 1H), 7.15 (tt, J = 6.7, 4.9 Hz, 2H), 7.04 – 6.96 (m, 1H), 3.70 (d, J = 9.1 Hz, 1H), 3.59 – 3.43 (m, 1H), 3.37 – 3.22 (m, 5H), 3.13 – 2.93 (m, 1H), 1.89 – 1.65 (m, 1H), 0.68 (d, J = 6.8 Hz, 3H), 0.54 (d, J = 6.9 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 144.21, 134.06, 129.47, 127.91, 127.36, 126.50, 124.07, 123.93, 121.60, 114.00, 111.63, 73.65, 58.92, 57.51, 29.49, 19.17, 17.20. **HRMS** calculated 485.3168; found 485.3167. α_D [4 g/ml] ($CHCl_3$) = -21.85

Compound 96f.1

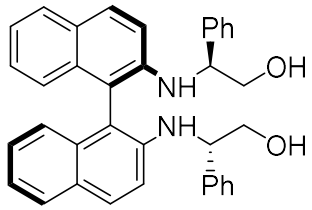


Prepared according to a slightly modified general procedure starting from **94f**. 1.7 F/mol were furnished. The product was purified by flash column chromatography on silica gel using a mixture of hexane/ethyl

acetate racing from 8:2 to 6:4 to afford a brown solid (after stored in the fridge) in 24% yield.

^{1}H NMR). (300 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 7.8, 2.7 Hz, 2H), 7.40 – 7.18 (m, 8H), 7.11 (dd, *J* = 9.4, 4.6 Hz, 2H), 4.69 (s, 1H), 4.36 (s, 1H), 3.61 (dd, *J* = 11.3, 4.4 Hz, 1H), 3.38 (dd, *J* = 11.3, 7.3 Hz, 1H). **^{13}C NMR (**75 MHz, $CDCl_3$) δ 144.04, 140.62, 133.48, 130.01, 128.92, 128.58, 128.20, 127.74, 127.06, 126.73, 123.65, 122.55, 115.21, 112.92, 67.10, 60.25. **HRMS** calculated 525.2542; found 525.2538. α_D [2.45 g/ml] ($CHCl_3$) = +67.48

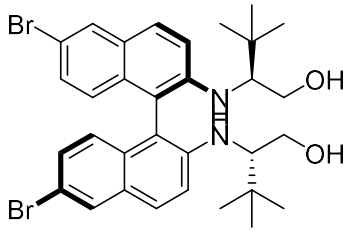
Compound 96f.2



Prepared according to a slight modified general procedure starting from **94f**. 1.7 F/mol were furnished. The product was purified by flash column chromatography on silica gel using a mixture of hexane/ethyl acetate racing from 8:2 to 6:4 to afford a brown solid (after stored in the fridge) in 24% yield

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 8.5 Hz, 2H), 7.41 – 7.07 (m, 8H), 7.02 (d, J = 8.2 Hz, 1H), 4.75 (d, J = 8.3 Hz, 1H), 4.48 (s, 1H), 3.82 (d, J = 13.0 Hz, 1H), 3.37 (t, J = 10.2 Hz, 1H), 3.27 (s, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 143.61, 140.18, 134.02, 129.89, 128.82, 128.65, 128.24, 128.09, 127.50, 126.82, 126.70, 126.50, 126.04, 124.47, 122.52, 115.18, 113.47, 67.30, 60.83, 59.84. **HRMS** calculated 525.2542; found 525.2544. **α_D** [1.25 g/mL] ($CHCl_3$) = -35.96

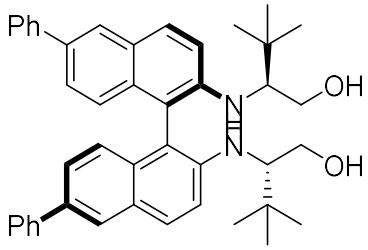
Compound 96g.1



Prepared according to the general procedure starting from **94f**. The product was purified by flash column chromatography on silica gel using hexane/ethyl acetate racing from 95:5 to 7:3 to afford a pinkish solid 58% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, J = 2.0 Hz, 1H), 7.80 (d, J = 9.1 Hz, 1H), 7.37 (d, J = 9.1 Hz, 1H), 7.31 – 7.22 (m, 1H), 6.87 (d, J = 8.9 Hz, 1H), 3.68 (dd, J = 18.0, 10.8 Hz, 2H), 3.47 (dt, J = 11.0, 4.3 Hz, 1H), 3.17 (dd, J = 11.1, 7.2 Hz, 1H), 1.28 (s, 1H), 0.82 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 145.89, 131.94, 130.63, 129.31, 128.73, 124.43, 115.64, 110.74, 63.40, 62.59, 34.67, 26.91. **HRMS** calculated 641.1378; found 641.1367. **α_D** [1.7 g/mL] ($CHCl_3$) = -205.25. **mp**= 298-300°C

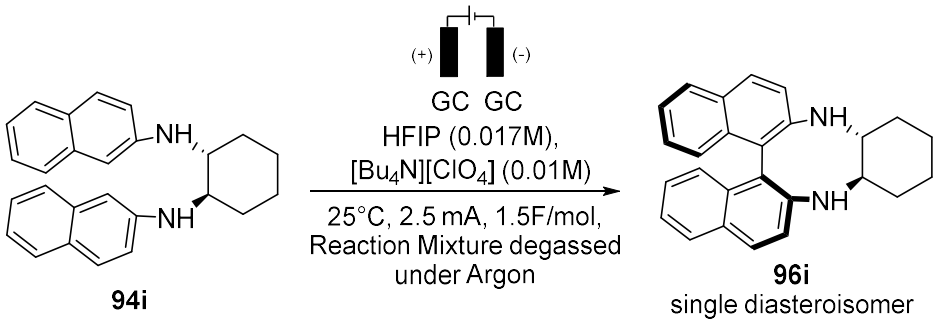
Compound 96h.1



Prepared according to the general procedure starting from **94h**. The product was purified by flash column chromatography on silica gel using hexane/ethyl acetate racing from 95:5 to 7:3 to afford a black oil in 52% yield

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J = 2.1 Hz, 1H), 7.98 (d, J = 9.0 Hz, 1H), 7.69 (d, J = 8.1 Hz, 2H), 7.55 (dd, J = 8.8, 2.0 Hz, 1H), 7.50 – 7.40 (m, 3H), 7.35 (d, J = 7.3 Hz, 1H), 7.18 (d, J = 8.7 Hz, 1H), 3.68 (dd, J = 11.3, 3.7 Hz, 1H), 3.49 (t, J = 3.7 Hz, 1H), 3.27 – 3.13 (m, 1H), 0.84 (s, 9H).**^{13}C-NMR** (75 MHz, $CDCl_3$) δ 145.52, 140.98, 134.92, 132.70, 130.45, 128.79, 128.04, 126.99, 126.64, 123.26, 115.35, 111.43, 63.63, 62.41, 34.76, 26.98. **HRMS** calculated 637.3794; found 637.3805. **α_D** [6.3 g/mL] ($CHCl_3$) = -27.87

5.2.6 GENERAL PROTOCOL FOR THE ELECTROCHEMICAL INTRAMOLECULAR HOMO-COUPLING OF COMPOUND 94i



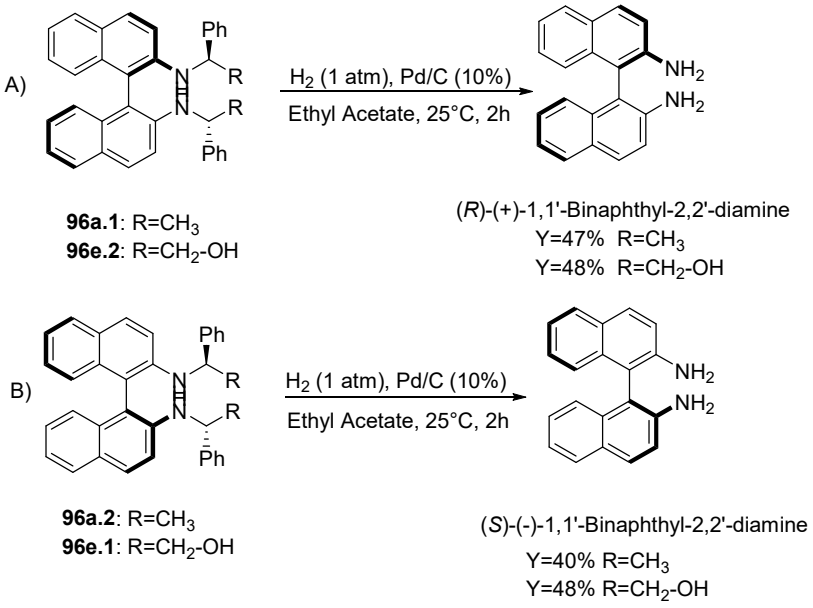
94i **96i** single diasteroisomer

In a 5 mL IKA ElectraSyn vial, equipped with a stir bar, the chiral amine **94i** (0.06 mmol, 1 equiv.) and Lithium Perchlorate (0.037 mmol, 0.6 equiv.) were dissolved in 3.5 ml of 1,1,1,3,3,3-Hexafluoro-2-propanol. The electrochemical cell was assembled with IKA Glassy carbon anode and cathode and the reaction mixture was degassed with Argon for two minutes. Under argon atmosphere, the solution was electrolyzed with a constant current of 2.5 mA (Cell potential 1.5-2.5V). After 1.5 F/mol were furnished, the reaction mixture was diluted with ethyl acetate and washed two times with an equal volume of brine. The organic phase was than dried over magnesium sulphate and the solvent evaporated under reduced pressure. The obtained residue was purified by column chromatography using a

mixture of hexane/ethyl acetate racing from 9.7:0.3 to 9.5:0.5 to afford a brown solid (after stored in the fridge) in 37% yield

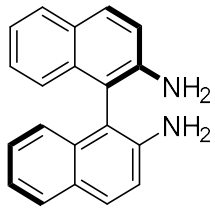
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (dd, J = 17.3, 8.6 Hz, 2H), 7.62 (d, J = 7.5 Hz, 2H), 7.50 (d, J = 8.7 Hz, 1H), 7.45 – 7.33 (m, 3H), 7.09 (p, J = 6.9 Hz, 2H), 6.96 (d, J = 8.7 Hz, 1H), 3.95 (s, 1H), 3.19 (td, J = 10.1, 4.3 Hz, 1H), 3.10 – 2.96 (m, 1H), 2.51 (d, J = 12.8 Hz, 1H), 2.09 (d, J = 12.5 Hz, 1H), 1.86 (d, J = 13.2 Hz, 1H), 1.66 (d, J = 13.3 Hz, 1H), 1.47 – 1.30 (m, 2H), 1.21 – 1.06 (m, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 146.38, 136.05, 133.78, 130.90, 128.53, 128.26, 127.85, 127.76, 127.53, 127.42, 126.16, 125.90, 125.77, 125.24, 124.89, 121.87, 121.60, 117.41, 61.51, 50.91, 33.38, 30.41, 29.73, 25.95, 23.57. **HRMS** calculated 365.2018; found 365.2000. **α_D** [1.34 g/ml] ($CHCl_3$) = -45.52

5.2.7 GENERAL PROCEDURE FOR BYARYL SYSTEMS HYDROGENATION[164]



In a two neck round bottom flask was added 10% Pd/C (0.08 mmol, 2 equiv.), followed by the addition of the chiral byaryl amine **96** (0.05 mmol, 1 equiv.) solubilized in ethyl acetate (6 ml). After three cycle vacuum/hydrogen, the reaction was stirred for 2h at room temperature, monitored by TLC. The suspended Pd/C was then removed by filtration through a celite pad, and the filtrate was evaporated under reduced pressure.

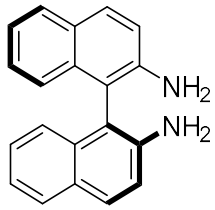
(*R*)-BINAM



Prepared according to the general procedure starting from **96a.1.** and **96e.2** The product was purified by a short flash column chromatography on silica gel using hexane/ethyl acetate 6:4 to afford a white solid in 47% and 48% yield respectively.

Analytical data are in agreement with those obtained for the commercial available *R*-BINAM (CAS N° 18741-85-0). α_D [0.3 g/ml] ($CHCl_3$) = + 57.04

(*S*)-BINAM



Prepared according to the general procedure starting from **96a.1** and **96e.1**. The product was purified by a short flash column chromatography on silica gel using hexane/ethyl acetate 6:4 to afford a white solid in 40 and 48 % yield respectively.

Analytical data are in agreement with those obtained for the commercial available BINAM (CAS N° 18531-95-8). α_D [0.25 g/ml] ($CHCl_3$) = -10.72

5.3 PHOTOCYCLIZATION OF ARYL ENONES UNDER HOMOGENEOUS AND HETEROGENEOUS CONDITIONS

5.3.1 DESCRIPTION OF PHOTOREDOX SET-UP

Construction of Photoreactor#1

A making-off video related to the construction of the photoreactor starting from a sublimator apparatus was already reported in literature[165] The central sublimator glass-piece is first wrapped to the de-sired length with heavy duty aluminium foil to generate a socket for the LED-strip that possesses high heat conductive properties. Around this first layer is then coiled and glued (double sided adhesive tape) the LED-strip which is further secured in place at the top and bottom with electric isolating tape. The cable is guided through the silicon rubber seal by puncturing it. The final reactor is then assembled as presented in **Figure 42**.

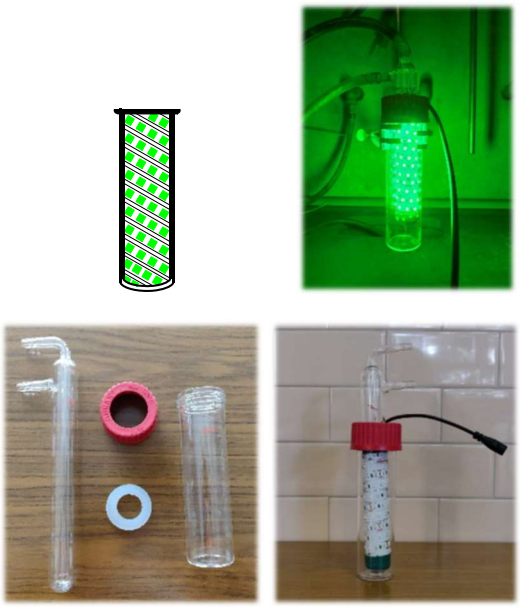


Figure 42: A) Water-cooled photoreactor scheme. B) Assembled photoreactor (on). C) Assembled photoreactor (off). D) Unassembled photoreactor (without LED strip).

Green LEDs characterization

Commercially available SMD LED 2835 60 led/m 24V, with an IP95 “plug and play system” without extra wiring connection were employed in the realization of photoreactor showed in **figure 41**. The LEDs wavelength emission profile together with their specific light intensity (expressed as mW/cm^2) have been determined using a compact CCD spectrometer (model CCS200/M) connected to a multimode optical fiber, purchased by Thorlabs. As clearly depicted in **Figure 43**, green LEDs employed are characterized by an almost monochromatic emission profile showing a maximum of intensity located at ca. 512-514 nm. The light power intensity was thus checked using a Thorlabs PM200 power meter equipped with a S130VC power head with a Si detector. The measured light intensities, though slightly decreasing by moving the maximum of LEDs emission towards longer wavelenghts, resulted to be I = 423.9 ± 0.6 mW/cm^2.

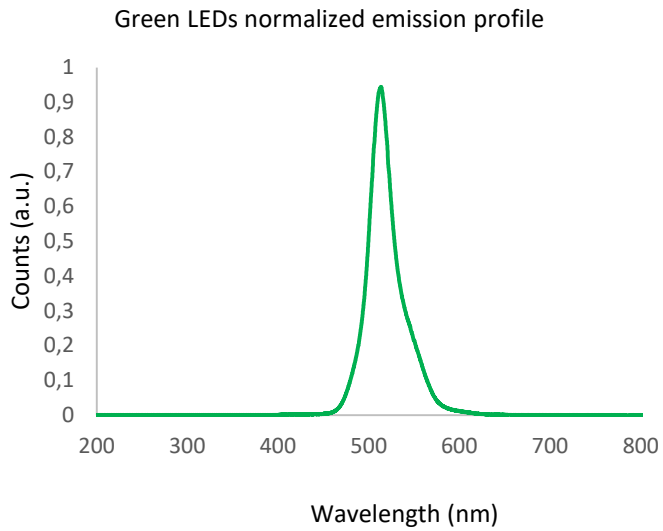


Figure 43: Green LEDs Normalized emission profile.

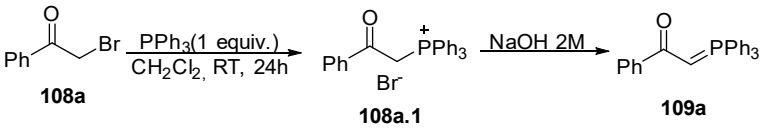
Photochemical Set-up for continuous flow experiments.

A 200 µL coil reactor was used for our purposes This module was constructed using a PFA tubing (1.58 mm outer diameter, 0.508 mm inner diameter, 98.7 cm length, 200 µl effective volume) coiled around the photoreactor. A New Era NE 300 syringe pumps, equipped with two Hamilton gastight syringes, fed the reactant solutions through a T-junction into the above-mentioned PFA tubing (**Figure 44**).

Figure 44: photoreactor #1 with a 200 mL coil reactor.

5.3.2 SYNTHESIS OF STARTING MATERIALS

Synthesis of compound **109a**

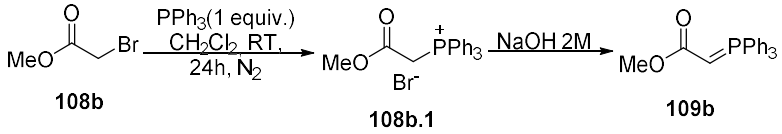


Step 1: A solution of α-bromoacetophenone **108a** (1 eq., 5 mmol, 995 mg) in CH_2Cl_2 (3 mL) was added dropwise over 2 min to a solution of triphenylphosphine (1 eq., 5 mmol, 1,31 g) in CH_2Cl_2 (6 mL). The reaction mixture was stirred at room temperature for 24 h, and the resulting mixture was concentrated under reduced pressure. The resulting precipitate was washed with Et_2O. Compound **109a** was obtained in quantitative yield and used without any purification.[166]

Step 2: In a 1-necked flask, compound **108a.1** (1.5 mmol, 769 mg) was dissolved in a mixture of CH_2Cl_2 (21 mL), then 15 ml of 2M NaOH aqueous solution were added. The reaction was stirred at room temperature for 3 hours and then ethyl acetate (40 mL) was added. The organic layer was recovered and washed with brine, then dried over Na_2SO_4 and evaporated *in vacuum* to yield the target compound in quantitative yield.

Analytical data are in agreement with those reported in literature.[167]

Synthesis of compound **109b**



Step 1

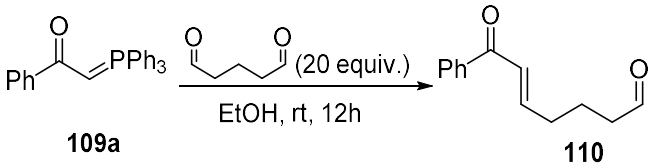
In a 25 mL 2 necked round bottomed flask equipped with an inlet compound **108b** (1 equiv., 2.85 mol, 270 µL) and PPh_3 (1.1 equiv., 3.42 mol, 898 mg) were dissolved in dry-DCM (12 mL). The solution was stirred for 24h under N_2 atmosphere. The reaction mixture was then transferred in a 50 mL round bottomed flask and reduced under vacuum. The obtained white solid (the intermediate salt -1,013 mg).was washed with Et_2O and used in the following step without further purification.

Step 2

The intermediate salt **108b.1** was diluted in DCM (10 mL) in a 50 mL round bottomed flask and 10 mL of NaOH 2M were added to deprotonate the phosphonium salt. The system was reacted for 3 h. The water phase was then separated from CH_2Cl_2 and extracted with Ethyl acetate (3 times). The combined organics were washed with water and brine, dried over Na_2SO_4 and concentrated under vacuo. The product **109b** was obtained as white solid in 79% yield.

Analytical data are in agreement with those reported in literature.[168]

Synthesis compound **110**

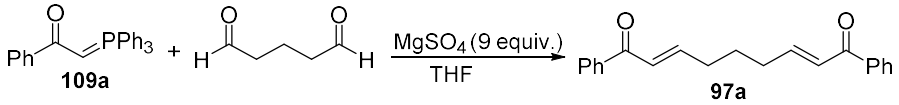


Compound **109a** (1 equiv., 10.5 mmol, 4.0 g) was dissolved in EtOH (80 ml) at room temperature, then glutaric aldehyde (20 equiv. 0.2 mol, 80 ml of 2.6 M) was added. The reaction was stirred for 12h at room temperature. After this time, H_2O was added (200 mL) and the reaction mixture was extracted with Et_2O (3 X 200 ml). Organic layer was washed with HCl 0.2M (3 X 300 ml) and then with brine (3 X 50 ml). Organic phases where then collected, dried with Na_2SO_4 and the solvent was removed by evaporation. The crude

compound was purified by silica gel chromatography (8/2 hexane/Ethyl acetate) affording the pure product **110** as a colourless oil in 62% yield.

Analytical data are in agreement with those reported in literature.[167]

Synthesis of compound **97a**[169]

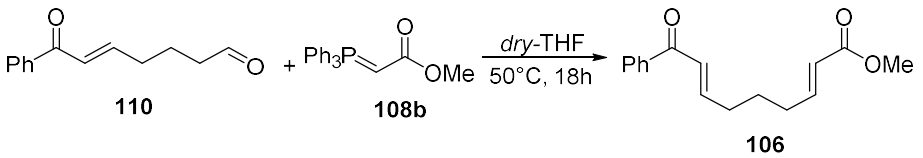


In a 100 ml round-bottom flask, 1-Phenyl-2-(triphenylphosphoranylidene) ethanone **109a** (1.1 equiv; 11 mmol, 4.25 g), glutaraldehyde (1 equiv.; 4.42 mmol, 1.7 ml), $MgSO_4$ (5.30 g), and 50 ml of tetrahydrofuran (THF) were added. The reaction was stirred at room temperature for 48 h, then the resulting mixture was filtered through a Hirsch funnel to remove $MgSO_4$. The filtrate was concentrated under reduced pressure and subsequently purified via column chromatography on silica gel (85/15 hexane/ethyl acetate mixture) as the eluent. The product **97a** was obtained as a yellow oil in 60% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8-7.89 (m, 4H), 7.61-7.52 (m, 2H), 7.51-7.42 (m, 2H), 7.11-7.02 (m, 2H), 6.94 (m, 2H), 2.44-2.37 (q, 4H), 1.84-1.74 (m, 2H).

Analytical data are in agreement with those reported in literature[170]

Synthesis of compound **106**[170]

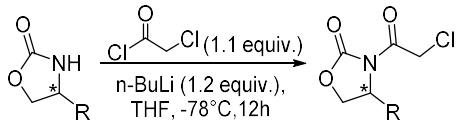


In a 10 mL round-bottomed flask, aldehyde **110** (1,13 equiv., 0,54 mmol, 180.0 mg,) and compound **108b** (1 equiv., 0.47 mmol, 202,25 mg) were dissolved in 9 mL of dry toluene. The reaction mixture was then heated to 50°C and stirred overnight. After this time, the solvent was removed under reduced pressure. The crude product was then purified via flash chromatography (95/05-85/15 hexane/ethyl acetate) to yield the final product as a pale-yellow foaming oil in 47% yield.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.98-7.91 (d, J=7.08, 2 H), 7.61-7.53 (t, J=7.17, J=7.23 2 H), 7.50-7.46 (t, J=7.62, J=7.20 2 H), 7.10-6.89 (m, 3 H), 5.90-5.85 (d, J = 15.86 Hz, 1H), 3.7456 (s, 3H), 2.41-2.26 (m, 4H), 1.77-1.68 (q, 2H).

Analytical data are in agreement with those reported in literature[168]

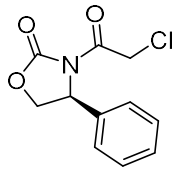
General procedure **A** for the synthesis of chloroacetyl derivatives



111a-c **112a-c**

The desired oxazolidinone (1 equiv., 5.64 mmol) was dissolved in dry THF (30 ml) under nitrogen atmosphere and the resulting mixture was cooled at -78 °C. A 2.5 M solution of n-BuLi (1.2 equiv., 6.77 mmol) was the added. The mixture was stirred for 15 min, then chloroacetyl chloride (1 equiv., 5.64 mmol) was added in one portion. The reaction was monitored by TLC, and when complete, it was quenched with a saturated solution of NH_4Cl. The mixture was allowed to reach RT, then it was diluited with Ethyl acetate and washed with H_2O and brine. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Target product was isolated after chromatographic purification (typically 7/3 hexane/EtOAc).

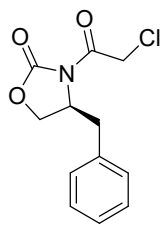
Compound 111a



Synthetized according to the general procedure **A**, starting from (*S*)-4-isopropyloxazolidin-2-one. The product was purified by flash column chromatography on silica gel to afford a white solid in 92% yield

Analytical data are in agreement with those reported in literature.[171]

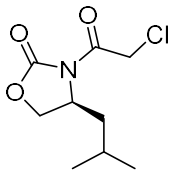
Compound 111b



Synthetized according to the general procedure **A**, starting from (*S*)-4-benzyloxazolidin-2-one The product was purified by flash column chromatography on silica gel to afford a white solid in 71% yield

Analytical data are in agreement with those reported in literature.[172]

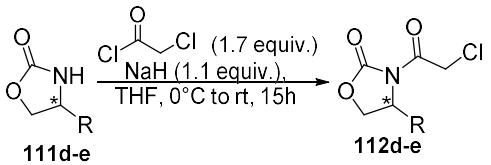
Compound 111c



Synthetized according to the general procedure **A**, starting from. (*S*)-4-benzyloxazolidin-2-one The product was purified by flash column chromatography on silica gel to afford a white solid in 99% yield.

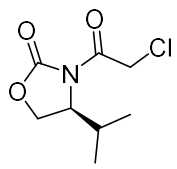
Analytical data are in agreement with those reported in literature.[173]

General procedure **B** for the synthesis of chloroacetyl derivatives **112d-112e**



Freshly washed NaH (1.1 equiv., 2.11 mmol) was loaded in a flame dried Schlenk tube under nitrogen atmosphere, then distilled THF was added (8 ml) and the mixture was cooled at 0 °C. After that, the desired oxazolidinone **111d-e** (1 equiv., 1.92 mmol) was added portion wise, and the reaction was warmed to room temperature. The mixture was stirred for 5 hours. At 0°C. Chloroacetylchloride (1.7 equiv., 3,26 mmol) was the added dropwise, and the reaction mixture was stirred for 15 h at room temperature. After this time, it was filtered on celite pad and the solvent was evaporated under reduced pressure. The crude residue was then dissolved in CH_2Cl_2, washed with $NaHCO_3$, dried over $MgSO_4$, filtered, and the solvent removed under vacuum. Target products **112d-e** were isolated after chromatographic purification (typically 7/3 hexane/EtOAc).

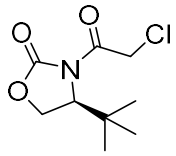
Compound 111d



Prepared according to the general procedure **B**, starting from (*R*)-4-isopropyloxazolidin-2-one. The product was purified by flash column chromatography on silica gel to afford a colorless solid in 45% yield.

Analytical data are in agreement with those reported in literature.[173]

Compound 111e

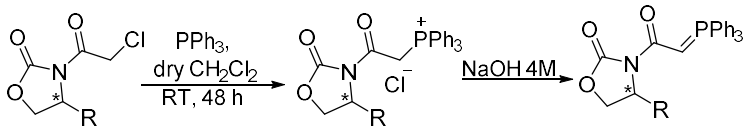


Synthetized according to the general procedure **B**, starting from (S)-4-(tert-butyl) oxazolidin-2-one. The product was purified by flash column chromatography on silica gel to afford a yellow oil in 76% yield.

^{1}H-NMR (300 MHz, $CDCl_3$) = δ 4.73 (dd, J= 25 Hz, 15.46 Hz, 2H), 4.45 (dd, J= 6.96 Hz, 2.2Hz, 1H), 4.37 – 4.29 (m, 2H), 0.96 (s, 9H)

Analytical data are in agreement with those reported in literature.[173]

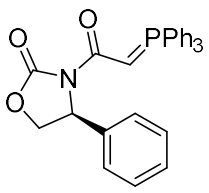
General Procedure **C** for the synthesis of Ylides derivatives



112a-c,e 112.1a-c,e 113a-c,e

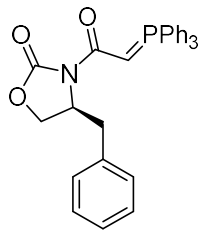
PPh_3 (1.1 equiv., 1.35 mmol) was added to a solution of the desired chloroacetylchloride (1 equiv., 1.23 mmol) in degassed CH_2Cl_2 (10 ml) and the mixture was stirred at rt for 48h under nitrogen. The reaction mixture was concentrated in vacuo and the residue was dissolved in hot water (400 ml), 50°C. After the addition of 4M NaOH aqueous solution, the mixture was shacked for 5 minutes and immediately extracted three times with Ethyl acetate. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. Target product was isolated after chromatographic purification (typically 7/3 hexane/EtOAc).

Compound 113a



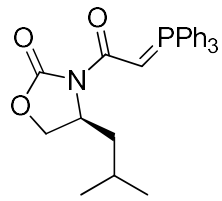
Synthetized according to the general procedure **C** starting from compound **112a.** The product was purified by flash column chromatography on silica gel to afford a white oil in 70% yield. Analytical data are in agreement with those reported in literature.[174]

Compound 113b



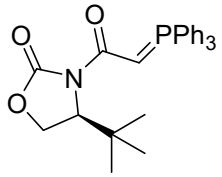
Synthetized according to the general procedure **C** starting from compound **112b**. The product was purified by flash column chromatography on silica gel to afford a white oil in 40% yield. Analytical data are in agreement with those reported in literature[172]

Compound 113c



Synthetized according to the general procedure **C** starting from compound **112c**. The product was purified by flash column chromatography on silica gel to afford a white oil in 40% yield. Analytical data are in agreement with those reported in literature[172]

Compound 113e

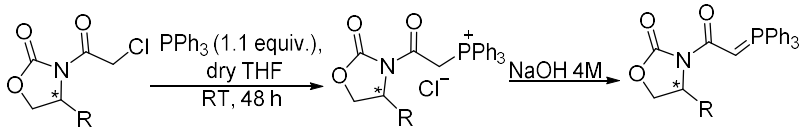


Synthetized according to the general procedure **C** starting from compound **112e**. The product was purified by flash column chromatography on silica gel to afford a white oil in 64% yield.

^{1}H-NMR ($CDCl_3$) = δ 7.70-7.41 (m, 15H), 4.48 (dd, J= 7.33 Hz, 2.30 Hz, 1H), 4.22-4.10 (m, 3H), 0.91 (s, 9H)

Analytical data are in agreement with those reported in literature[174]

General Procedure **D** for the synthesis of Ylides derivatives

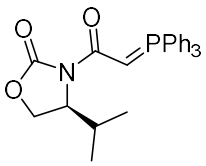


112d **112d.1** **113d**

PPh_3 (1.1 equiv., 2.94 mmol) was added to a solution of the desired chloroacetyl compound **112d** (1 equiv., 2.67 mmol) in dry THF (20 ml) and

the mixture was stirred at RT overnight. Then, it was concentrated under vacuo and the residue was dissolved in hot-water (400 ml). After the addition of 4M NaOH aqueous solution, the mixture was immediately extracted 3 times with Ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. Target product was isolated after chromatographic purification (typically 7/3 hexane/EtOAc).

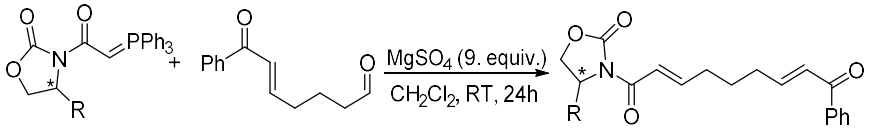
Compound d



Synthetized according to the general procedure **D** starting from compound **112d**. The product was purified by flash column chromatography on silica gel to afford a white oil in 40% yield

Analytical data are in agreement with those reported in literature[172]

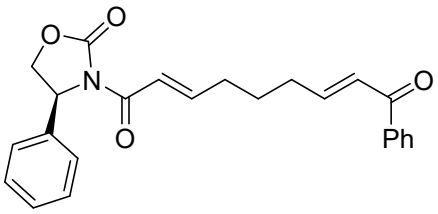
General procedure **E** for the synthesis of enantiopure bisenones



113a-e **110** **103a-e**

Aldehyde **110** (1 equiv., 0.35 mmol) and the desired ylide **113a-e** (1.5 equiv., 0.53 mmol) were dissolved in CH_2Cl_2 (0.5 M), then $MgSO_4$ (9 equiv., 3.15 mmol) was added to the stirred solution. The reaction was allowed to stir for 48h at rt. After this time, the mixture was poured in water and extracted three time with CH_2Cl_2. The organic phases were combined, dried over Na_2SO_4 and the solvent removed in vacuo. The crude was purified by column chromatography of flash silica gel (7/3 hexane/EtOAc).

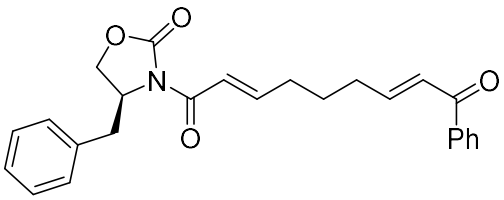
Compound 103a



Prepared according to the general procedure **E** starting from **113a**. The product was purified by flash column chromatography on silica gel to afford a transparent viscous oil in 30% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (t, J = 7.2 Hz, 1H), 7.62 – 7.24 (m, 8H), 7.18 – 6.84 (m, 4H), 5.50 (dt, J = 8.8, 4.4 Hz, 1H), 4.73 (t, J = 8.8 Hz, 1H), 4.30 (dt, J = 12.2, 6.1 Hz, 1H), 2.44 – 2.26 (m, 4H), 1.84 – 1.62 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 199.2, 190.6, 150.6, 148.4, 139.0, 132.6, 129.1, 128.7, 128.5, 126.5, 125.9, 120.9, 69.9, 57.7, 32.1, 32.0, 29.7, 26.5 **HRMS** calculated 389.1612; found 389.1644

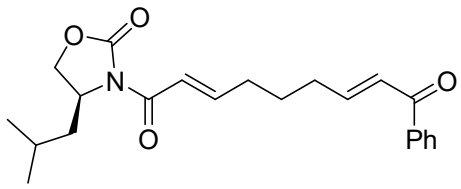
Compound 103b



Prepared according to the general procedure **E** starting from **113b**. The product was purified by flash column chromatography on silica gel to afford a transparent viscous oil in 52% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97-7.95 (d, J=7.5 Hz, 2H), 7.60-7.54 (m, 1H), 7.52-7.46 (m, 2H), 7.38-7.22 (m, 9H), 7.12-7.05 (m, 1H), 6.97-6.91 (d, J=15.53 Hz, 1H), 4.79-4.68 (m,1H), 4.26- 4.16 (m, 2H), 3.39-3.33 (dd, J=13.37, 3.0 Hz, 1H), 2.85-2.74 (m, 2H), 2.44-2.37 (m, 4H), 1.84-1.75 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 190.6, 164.9, 150.7, 150.3, 148.9, 148.4, 135.3, 132.6, 129.4, 128.9, 128.5, 127.3, 126.5, 121.1, 119.9, 66.2, 55.3, 53.4, 37.9, 32.3, 32.0, 29.2, 27.4, 26.6 **HRMS** calculated 403.1784; found 403.17895

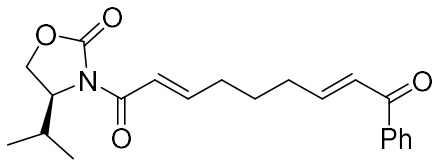
Compound 103c



Prepared according to the general procedure **E** starting from **113c**. The product was purified by flash column chromatography on silica gel to afford a transparent viscous oil in 30% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 – 7.85 (m, 2H), 7.52 (tt, J = 8.5, 4.4 Hz, 3H), 7.35 – 6.84 (m, 4H), 4.55 (dd, J = 18.5, 8.7 Hz, 1H), 4.40 (dd, J = 15.9, 8.1 Hz, 1H), 4.13 (ddd, J = 8.7, 5.8, 2.9 Hz, 1H), 2.37 (dd, J = 13.0, 5.6 Hz, 3H), 1.95 – 1.43 (m, 6H), 0.99 (dt, J = 7.1, 3.6 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 190.6, 164.8, 153.6, 150.1, 149.9, 148.9, 148.5, 137.8, 132.6, 128.5, 126.4, 121.2, 120.1, 67.7, 53.1, 41.5, 32.0, 26.5, 24.8, 23.4, 21.6 .**HRMS** calculated 369.19400; found 369.19433

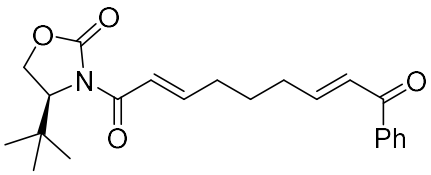
Compound 103d



Prepared according to the general procedure **E** starting from **113d**. The product was purified by flash column chromatography on silica gel to afford a yellow viscous oil in 72% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, J = 6.95 Hz, 1H), 7.57 – 7.43 (m, 2H), 7.09 - 7.00 (m, 2H), 6.89 (d, J = 15.47 Hz, 1H), 6.38 – 6.29 (m, 1H), 4.49 – 4.43 (m, 1H), 4.29 – 4.17 (m, 2H), 2.68 (q, J = 7.48 Hz, 2H), 2.41 – 2.34 (m, 3H), 1.74 – 1.68 (m, 2H) 0.92 – 0.87 (dd, J = 10.71 Hz, 6.94 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 190.9, 164.9, 154, 150.4, 149.1, 138.1, 132.8, 132.7, 128.7, 128.6, 126.5, 120.2, 63.4, 58.5, 32.5, 29.4, 28.6, 27.5, 18.1, 14.8 **HRMS** calculated 378.1681; found 378.1688

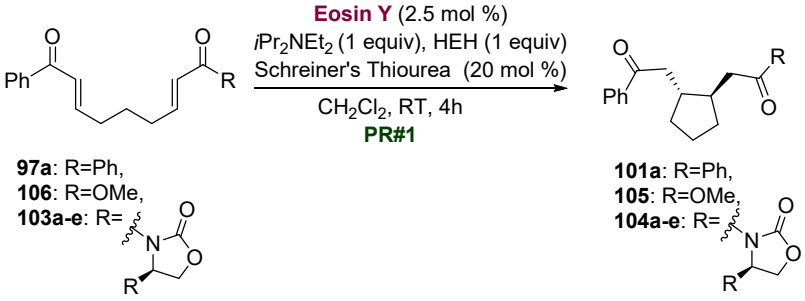
Compound 103e



Prepared according to the general procedure **E** starting from **113e**. The product was purified by flash column chromatography on silica gel to afford a transparent viscous oil in 66% yield.

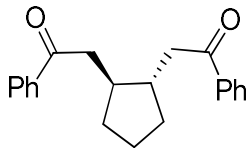
^{1}H-NMR (300 MHz,$CDCl_3$) = δ 7.90 (d, J = 7.4 Hz, 2H), 7.57 – 7.37 (m, 3H), 7.27 (d, J = 15.7 Hz, 1H), 7.16 – 6.95 (m, 2H), 6.88 (d, J = 15.6 Hz, 1H), 4.48 (dd, J = 7.2, 2.1 Hz, 1H), 4.31 – 4.15 (m, 2H), 2.41 – 2.26 (m, 5H), 1.71 (p, J = 7.4 Hz, 2H), 0.91 (s, 9H). **^{13}C-NMR** (75 MHz, $CDCl_3$) = δ 190.8, 165.4, 154.7, 150.3, 148.6, 137.9, 132.9, 128.6, 126.6, 121.3, 65.3, 60.9, 36.0, 32.2, 32.1, 23.6, 25.7. **HRMS** calculated 392.1838; found 392.1847

5.3.3 GENERAL PROCEDURE FOR THE SYNTHESIS OF *TRANS*-CYCLOPENTANE



A 10 ml vial equipped with stirring bar, was filled with the desired bisenone (1 equiv., 1.23 mmol), 1,3-bis(3,5-bis(trifluoromethyl) phenyl)thiourea (0.2 equiv., 0.246 mmol), Eosin Y (0.025 equiv., 0.030 mmol), Hantzsch ester (1 equiv., 1.23 mmol)and iPr_2NEt (1 equiv., 1.23 mmol). All the reagents were dissolved in CH_2Cl_2 (6.15 ml) and the mixture was degassed by three freeze pump thaw cycles under nitrogen. The reaction was irradiated for 4 h using photoreactor#1 and was monitored by TLC. After this time, the irradiation was switched off and the solvent was removed under vacuum. The crude residue was then purified by column chromatography (Hexane/Ethyl acetate 8/2) to afford the pure product as colourless liquid.[96]

Compound *trans*-101a

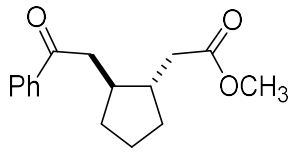


Synthetized according to the general procedure starting from compound **97a**. The product was purified by flash column chromatography on silica gel to afford a transparent viscous oil in 50 % yield

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 – 7.81 (m, 2H), 7.52 (dt, *J* = 30.5, 7.2 Hz, 4H), 3.22 (dd, *J* = 16.5, 4.4 Hz, 2H), 2.96 (dd, *J* = 16.5, 8.2 Hz, 2H), 2.21 (dp, *J* = 16.0, 8.1 Hz, 2H), 2.01 (td, *J* = 13.2, 6.6 Hz, 2H), 1.76 – 1.53 (m, 2H), 1.30 (td, *J* = 15.6, 7.8 Hz, 2H).

Analytical data are in agreement with those reported in literature.[173]

Compound *trans*-105

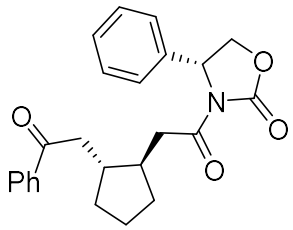


Synthetized according to the general procedure starting from compound **106**. The product was purified by flash column chromatography on silica gel to afford a transparent viscous oil in 37 % yield.

Analytical data are in agreement with those reported in literature.[175]

^{1}H NMR (300 MHz, CDCl3) δ 7.98 (dd, J = 15.2, 8.1 Hz, 2H), 7.53 (dt, J = 30.0, 7.3 Hz, 3H), 3.67 (s, 3H), 3.17 (dd, J = 16.4, 4.6 Hz, 1H), 3.00 – 2.83 (m, 1H), 2.55 (dd, J = 15.2, 5.0 Hz, 1H), 2.28 (dd, J = 15.1, 8.3 Hz, 1H), 2.16 – 1.89 (m, 2H), 1.72 – 1.56 (m, 2H), 1.38 – 1.19 (m, 4H). **^{13}C-NMR** (75 MHz, CDCl3) δ 199.9, 173.9, 132.9, 128.5, 128.0, 51.4, 43.8, 42.2, 41.2, 39.1, 32.4, 32.1, 29.6, 23.4. **HRMS** calculated 283.1310 found 283.1305

Compound 104a

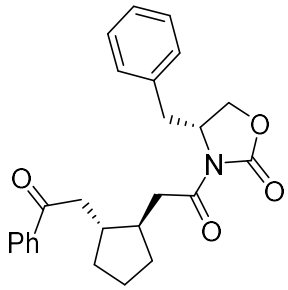


Synthetized according to the general procedure starting from compound **103a**. The product was purified by flash column chromatography on silica gel to afford a light yellow viscous oil in 70 % yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 – 7.84 (m, 2H), 7.65 – 7.20 (m, 8H), 5.43 (ddd, J = 25.3, 8.7, 3.6 Hz, 1H), 4.83 – 4.62 (m, 1H), 4.36 – 4.22 (m, 1H), 3.29 – 3.12 (m, 2H), 3.01 – 2.74 (m, 2H), 2.24 – 1.72 (m, 4H), 1.67 – 1.52 (m, 2H), 1.35 – 1.14 (m, 2H). **^{13}C-NMR** (75 MHz, $CDCl_3$) δ 200.13, 172.45, 153.82, 139.26, 137.69, 132.93, 129.22, 128.59,128.13, 125.98, 70.03, 57.66, 44.32,

43.89, 41.17, 40.80, 40.70, 32.36, 31.95, 23.66. **HRMS** calculated 414.1681; found 414.1677. α_D [0.02 M] ($CHCl_3$) = +17,86

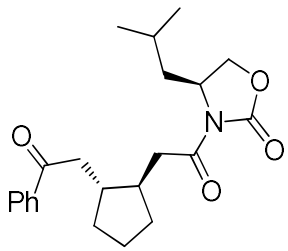
Compound 104b



Synthetized according to the general procedure starting from compound **103b**. The product was purified by flash column chromatography on silica gel to afford a yellow viscous oil in 30 % yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 – 7.91 (m, 2H), 7.67 – 7.14 (m, 8H), 4.82 – 4.51 (m, 1H), 4.35 – 4.05 (m, 2H), 3.43 – 3.14 (m, 2H), 3.00 – 2.64 (m, 3H), 2.33 – 1.91 (m, 4H), 1.75 – 1.55 (m, 3H), 1.50 – 1.18 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 200.1, 172.8, 153.4, 137.2, 135.3, 132.8, 129.4, 128.9, 128.5, 128.1, 127.3, 66.2, 55.2, 43.8, 41.4, 41.1, 40.8, 38.0, 32.4, 32.1, 23.6. **HRMS** calculated 405.1940; found 405.1944 α_D [0.03 M] (CHCl3) = + 41.8

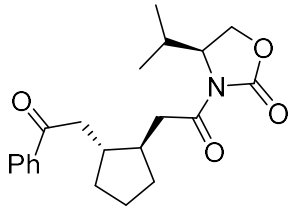
Compound 104c



Synthetized according to the general procedure starting from compound **103c**. The product was purified by flash column chromatography on silica gel to afford a yellow viscous oil in 31 % yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 – 7.78 (m, 2H), 7.69 – 7.34 (m, 3H), 4.61 – 4.28 (m, 2H), 4.21 – 4.02 (m, 1H), 3.41 – 3.03 (m, 2H), 2.96 – 2.73 (m, 2H), 2.26 – 1.87 (m, 4H), 1.82 – 1.19 (m, 8H), 0.99 – 0.93 (m, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 200.0, 172.6, 153.6, 137.2, 132.8, 128.5, 128.0, 67.6, 52.9, 43.7, 41.4, 41.1, 40.7, 32.3, 32.0, 24.8, 23.5, 23.4, 21.5. **HRMS** calculated 371.2097; found 371.3601. α_D [0.06 M] ($CHCl_3$) = + 42.5

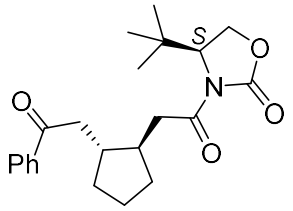
Compound 104d



Synthetized according to the general procedure starting from compound **103d**. The product was purified by flash column chromatography on silica gel to afford a light-yellow viscous oil in 82 % yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 – 7.87 (m, 2H), 7.57 – 7.35 (m, 3H), 4.40 (m, 1H), 4.31 – 4.12 (m, 2H), 3.35 – 3.08 (m, 2H), 2.95 – 2.66 (m, 2H), 2.31 (m, 1H), 2.01 (m, 4H), 1.71 – 1.53 (m, 2H), 1.28 (m, 2H), 0.87 (dd, J = 9.0, 7.0 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 200.1, 172.6, 137.4, 133.0, 128.6, 128.2, 63.5, 58.5, 3.8, 41.8, 41.4, 40.9, 40.6, 32.5, 32.0, 28.5, 23.7, 18.1, 14.8. **HRMS** calculated 380.1838; found 380.1831. **α_D** [0.04 M] ($CHCl_3$) = **-**49.3

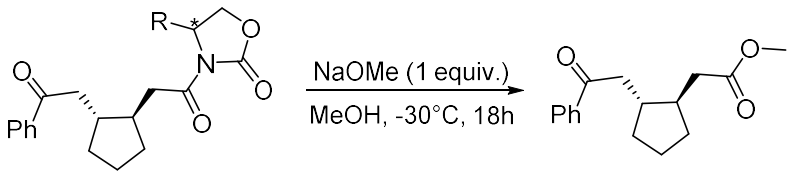
Compound 104e



Synthetized according to the general procedure starting from compound **103e**. The product was purified by flash column chromatography on silica gel to afford a light-yellow viscous oil in 76 % yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (m, 2H), 7.61 – 7.37 (m, 3H), 4.41 (m, 1H), 4.32 – 4.20 (m, 2H), 3.39 – 3.11 (m, 2H), 2.99 – 2.66 (m, 2H), 2.21 – 1.85 (m, 4H), 1.72 – 1.55 (m, 2H), 1.42 – 1.18 (m, 2H), 0.92 (d, J = 4.6 Hz, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 200.3, 173.0, 154.9, 137.3, 132.9, 128.6, 128.2, 65.5, 61.0, 43.8, 41.9, 41.4, 41.0, 35.8, 32.5, 32.0, 29.8, 25.8, 23.8. **HRMS** calculated 394.1994; found 394.2000. **α_D** [0.02 M] ($CHCl_3$) = +47.4

<u>General procedure for the hydrolysis of photocyclized adduct</u>[98]



104a-e ***trans*-105**

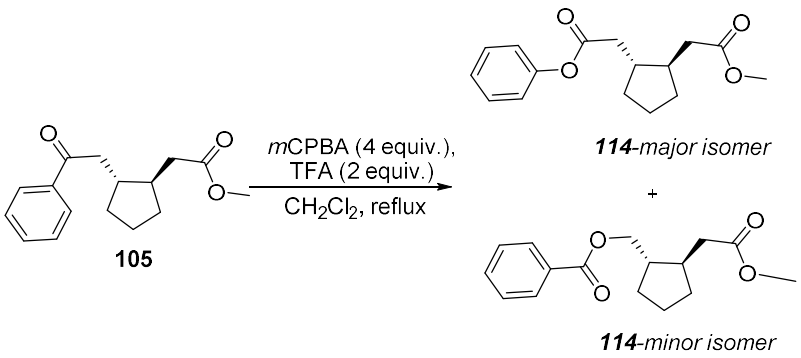
An aqueous solution of NaOMe (0.0612 ml, 0.5 M in MeOH) was added to a -30°C cooled solution of the desired substrate **104a-e** (1 equiv., 0.051 mmol) in MeOH (0.3 ml). The reaction stirred for 18 hours. After this time, it was

quenched with HCl 1M and diluted with 5 of ethyl acetate. The layers were separated, the organic phase was dried over $MgSO_4$ and the solvent removed under reduced pressure. The crude obtained was purified by column chromatography (9/1 hexane/Ethyl acetate) to give the target methyl ester and the recovered oxazolidinone. HPLC analysis: Chiralcel OJH, Hex/IPA 9:1; 0.8 mL/min, 31 bar, λ=210.4 nm, τ minor = 12.39 min, τ major = 11.28 min.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (dd, J = 15.2, 8.1 Hz, 2H), 7.53 (dt, J = 30.0, 7.3 Hz, 3H), 3.67 (s, 3H), 3.17 (dd, J = 16.4, 4.6 Hz, 1H), 3.00 – 2.83 (m, 1H), 2.55 (dd, J = 15.2, 5.0 Hz, 1H), 2.28 (dd, J =15.1, 8.3 Hz, 1H), 2.16 – 1.89 (m, 2H), 1.72 – 1.56 (m, 2H), 1.38 – 1.19 (m, 4H). **^{13}C-NMR** (75 MHz, $CDCl_3$) δ 199.9, 173.9, 132.9, 128.5, 128.0, 51.4, 43.8, 42.2, 41.2, 39.1, 32.4, 32.1, 29.6, 23.4. **HRMS** calculated 283.1310 found 283.1305.

Attribution of absolute configuration.

Synthesis of compound **105** as a mixture of isomers[176]

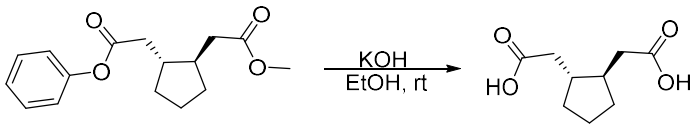


A 10 ml flask was charged with compound **105** (1 equiv., 0.12 mmol), mCPBA (4 equiv., 0.47 mmol), trifluoroacetic acid (2 equiv., 0.24 mmol) and CH_2Cl_2 (1 ml, 0,12 M). The solution was refluxed for 48 h. Then, it was quenched with saturated $NaHCO_3$ aqueous solution and extracted three times with CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered and the solvent was removed under vacuum. The crude was purified by column chromatography (9/1Hexane/chloroform) to give the product as a mixture of isomers (global yield = 65 %).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07-7.96 (m, 1H (minor isomer)), 7.62-7.45 (m, 2H (minor isomer)), 7.42-7.36 (m, 2H (Major isomer)), 7.26-7.21 (dd, J = 18.5, 4.2 Hz, 1H (Major isomer)), 7.12-7.07 (dd, J =8.51, 1.06Hz, 2H (Major isomer)), 4.35-4.23 (m, 1H (minor isomer)), 3.69 (s,3H (Major isomer)), 3.67 (s, 3H (minor isomer)), 2.78 – 2.72 (dd, J=15.23, 4.60, 1H (Major isomer)), 2.60

– 2.25 (m, 7H (major+minor isomer)), 2.08-1.93 (m,7H (major+minor isomer)), 1.57-1.27 (m, 7H (major+minor isomer)).

Synthesis of compound **115**[177]



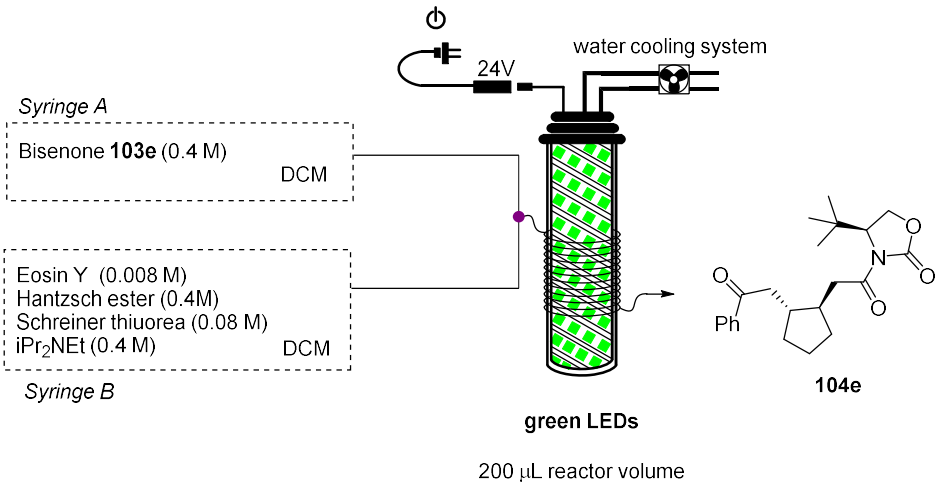
114-*major isomer* **115**

A solution of KOH (10 equiv., 0.54 mmol, 1M) in water was added to a 0°C cooled solution of compound **114** (1 equiv., 0.054 mmol) dissolved in EtOH (0.1 ml). The reaction was allowed to rinse room temperature and stirred for 24 h. After this time, the mixture was cooled to 0°C, and 0.5 ml of HCl 6N were added. The mixture was diluited with ethyl acetate, the two phases were separated and the aqueous phase was extracted 3 times with (3x 0,200 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude product was purified by recrystallization with hot hexanes to obtain the diacid as a white solid in 59% yield. $\boldsymbol{\alpha_D}$ [0.02 M] (MeOH) = +8.5

Analytical data are in agreement with those reported in literature.[177]

Photocatalytic reductive coupling of bisenones under fluidic conditions

Reaction performed using photoreactor #1 and 200 µl coil reactor



The flow reactor was fed by a continuous flow of reagents and reactants: Hamilton gastight syringes were loaded with the needed starting material, whose addition at the defined constant rate was guaranteed by syringe pumps. In a typical experiment, syringe A was filled with a 0.4 M solution of bisenone **103e** in CH_2Cl_2 (total volume 500 µl). Syringe B was filled with a mixture obtained dissolving 2,6 mg (0,004 mmol) of Eosin Y, 50 mg (0.2 mmol) of Hantzsch ester , 20 mg (0.04 mmol) of Schreiner thiourea and 34 µl (0.2 mmol) of *i*PrNEt$_2$ in CH_2Cl_2 (total volume 500 µl). (*note: the concentrations of all reagents in the syringes were doubled with respect to the final concentration, to achieve the desired concentration after mixing*). Syringes A and B were connected to a syringe pump and the reagents were fed into PFA reactor through a T-junction at the desired flow rate (6.66 µL/min for 30 min residence time and 5 µL/min for 40 min residence time) at room temperature. Light irradiation was performed using Green LEDs type-1. A dark shield was used as eye protection system. One reactor volume was discarded before starting sample collection in order to achieve steady-state conditions. Reaction outcome was collected in the dark into a vial and the crude was purified by chromatographic column (eluent hexane:AcOEt 95:05). Conversion was calculated by ^{1}H-NMR of the crude mixture comparing the integration of the multiplet signal at 2.43-2.36 ppm (3H, starting material) with the multiplet signal at 3.38-3.21 ppm (2H, target product). In **Figure 45** is reported the flow setup configuration.

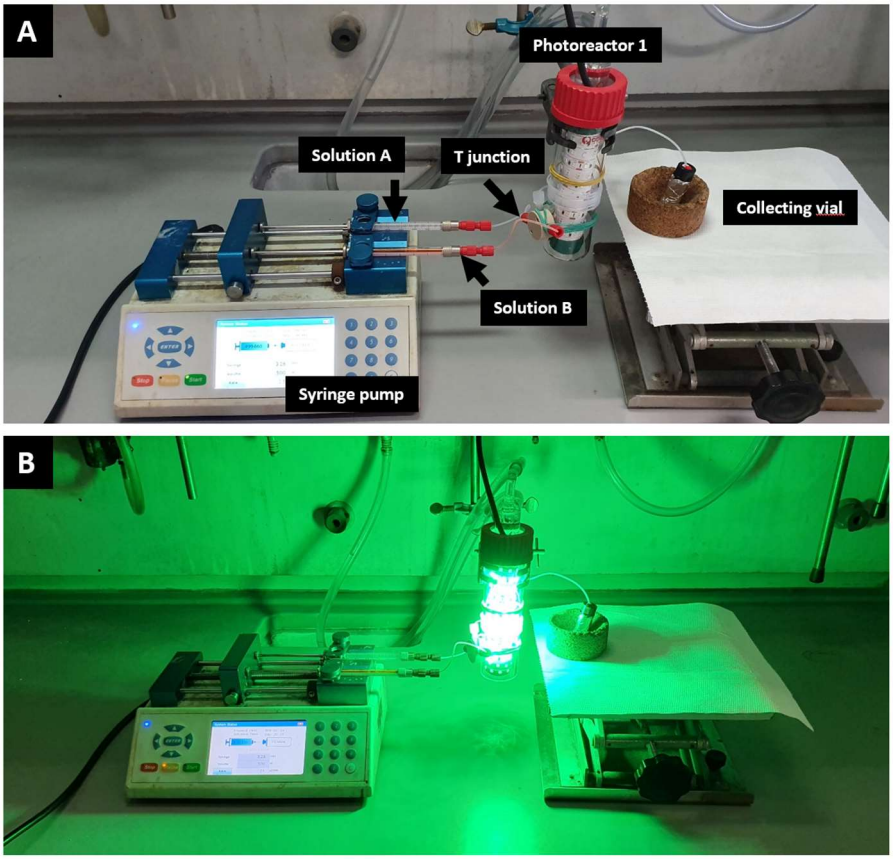
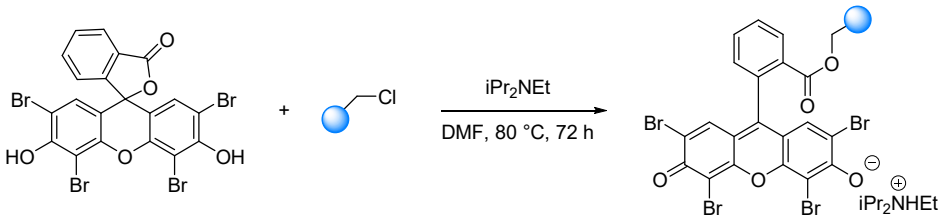


Figure 45– Reaction setup using photoreactor #1. A) Device with green LEDs off, B) Device with green LEDs on.

5.3.4 SYNTHESIS AND CHARACTERIZATION OF IMMOBILIZED EOSIN Y



Eosin Y | Merrifield-Resin f=1.2 mmol/g | Merrifield Eosin Y MR-EY

The synthesis was performed according to literature data.[105]

10.0g (8.33 mmol, 1.00 equiv. , f=1.20 mmol/g) of Merrifield-Resin High-Load 100-200 mesh were introduced in a 250 mL three-necked round bottom flask, then 6.48 g (10.0 mmol, 1.20 equiv.) Eosin Y (hydrogen form) were added. The solid was mechanically stirred and 133 mL of *N,N*-dimethylformamide were added, followed by 3.48 mL (20.0 mmol, 2.40 equiv.) of diisopropylethylamine. After setting the temperature to 80°C the dispersion was stirred for exactly 72 h. After this time, the reaction mixture was poured into an oven-dried glass sintered funnel (pore size 4, pre-weighed) and special care was taken to remove almost all the material out of the flask with generous amounts of methanol. The residue was infused with a mixture of water/THF/methanol and stirred with a glass rod. After infusing for 5 minutes vacuum was attached and the washing liquid was filtered off. Vacuum was detached and the whole process was repeated 15 times. After this generous washing process, the process was repeated for three times using dichloromethane. The washing flasks was changed and the remains in the funnel were dried by running a constant air stream through them for 5 hours by attaching a vacuum. After this time the filter was weighed again and by the difference in weight a preliminary catalyst loading calculated, which amounts to f = 0.168 mmol/g. The catalyst appears as a dark red solid.

Elemental analysis of MR-EY: C 80,73, H 6,54, N 0,28

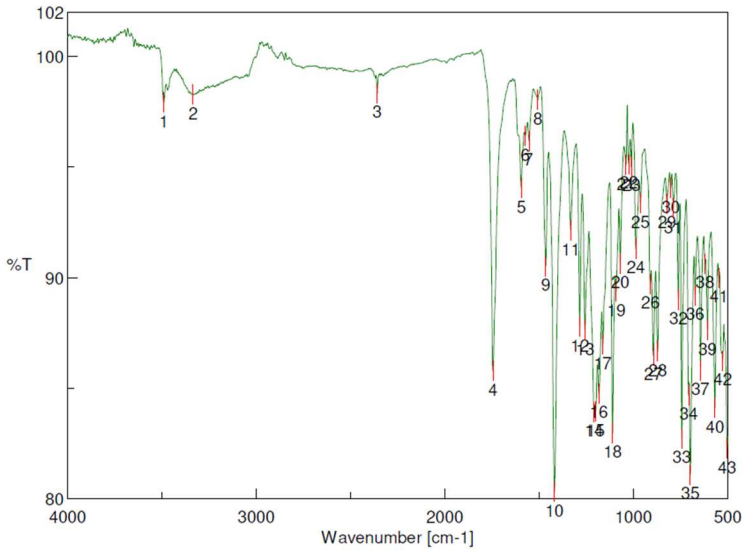
That corresponds to f = 0.2 mmol/g. The gravimetric loading (f = 0.168 mmol/g) was used in the reactions

IR

According to Shajan et all,[178] free Eosin-Y presents characteristic vibrational peaks at 1418 cm^{-1} (peak #4, **Figure 46**) and 1744 cm^{-1} (peak #10, **Figure 46**), which can be assigned to the symmetric vibration of carboxyl group and to the carboxyl (C=O) stretching respectively.

These characteristic vibrational peaks are absent in the functionalized material, meaning that the formation of the ester bond occurs as expected. In addition, two new signals were revealed, at 1717 cm^{-1} (peak #6, **Figure 46**) and 1224 cm^{-1} (peak #18, **Figure 47**) corresponding respectively to the C=O stretching and C-O stretching of an ester group. IR analysis revealed also the presence of aromatic C-H vibrational stretching at 3023 cm^{-1} (peak #1, **Figure 47**) and alkyl C-H stretching at 2919 cm^{-1} (peak #2, **Figure 46**). The strong vibrational peak at 695 cm^{-1} (peak #31 in **Figure 46** and peak #35 in **Figure 48**) present also in unfunctionalized Merrifield resin can be ascribed to C-H bending.

FREE EOSIN Y

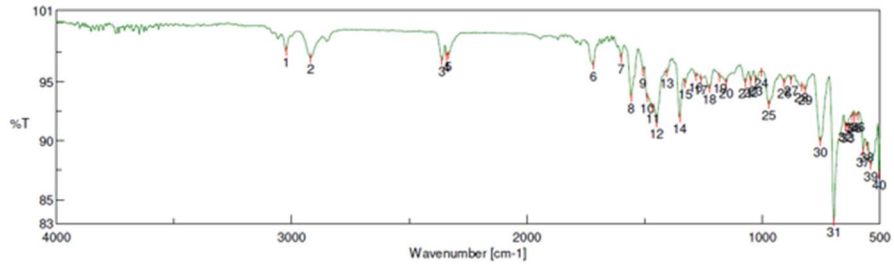


[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity
1	3490.53	97.9091	2	3333.36	98.2743
3	2358.52	98.3286	4	1744.3	85.7776
5	1594.84	94.054	6	1573.63	96.3997
7	1552.42	96.1797	8	1507.1	98.0262
9	1464.67	90.5101	10	1418.39	80.303
11	1332.57	92.1317	12	1284.36	87.7639
13	1256.4	87.6139	14	1209.15	83.9352
15	1200.47	83.9496	16	1183.11	84.7531
17	1161.9	86.9697	18	1110.8	82.9579
19	1091.51	89.376	20	1069.33	90.6198
21	1039.44	95.0855	22	1024.98	95.1521
23	1010.52	95.0133	24	987.375	91.2999
25	962.305	93.3677	26	910.236	89.7067
27	893.844	86.479	28	871.667	86.6542
29	822.491	93.3413	30	802.242	94.0465
31	788.743	93.119	32	761.744	88.9946
33	743.424	82.7185	34	706.783	84.671
35	698.105	81.0845	36	672.071	89.1994
37	644.108	85.7909	38	620.002	90.6393
39	607.467	87.6211	40	567.934	84.1019
41	546.72	90.0026	42	526.471	86.2493
43	503.33	82.2654			

Figure 46: IR of free Eosin Y

MR-EY

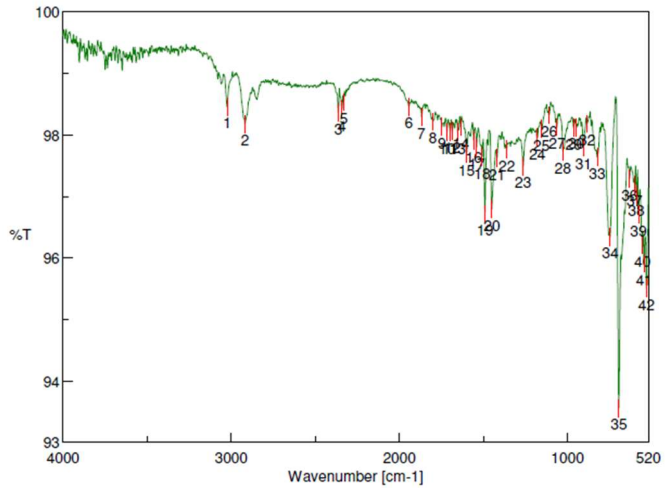


[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3023.84	97.5592	2	2919.7	96.9888	3	2361.41	96.7718
4	2342.12	97.1268	5	2334.41	97.224	6	1717.3	96.3687
7	1600.63	96.9942	8	1557.24	93.6147	9	1507.1	95.7922
10	1489.74	93.622	11	1464.67	92.7665	12	1450.21	91.5185
13	1405.85	95.7442	14	1350.89	91.9488	15	1326.79	94.8462
16	1282.43	95.4103	17	1261.22	95.228	18	1224.58	94.3995
19	1180.22	95.3324	20	1153.22	94.909	21	1071.26	94.9232
22	1049.09	95.027	23	1027.87	95.0948	24	1003.77	95.7739
25	971.947	93.0639	26	905.415	94.898	27	877.452	95.1067
28	834.062	94.5835	29	816.706	94.3724	30	753.066	89.9353
31	695.212	83.1736	32	647.001	91.2193	33	637.358	91.1784
34	618.074	92.0092	35	605.539	92.0167	36	593.968	92.0397
37	570.826	89.0589	38	555.398	89.5108	39	538.042	87.9167
40	503.33	87.1426						

Figure 47: IR of Merrifield resin functionalized with Eosin Y.

MERRIFIELD RESIN



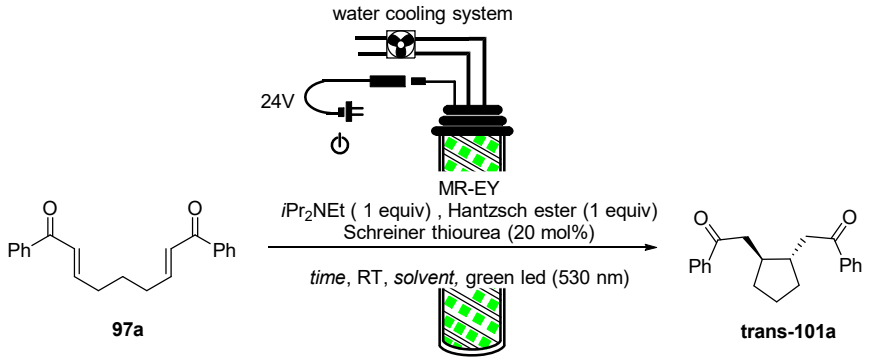
[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity
1	3024.8	98.4576	2	2917.77	98.1782
3	2363.34	98.3592	4	2342.12	98.4145
5	2331.52	98.5331	6	1943.89	98.4564
7	1867.72	98.2918	8	1801.19	98.2166
9	1748.16	98.1347	10	1717.3	98.0474
11	1698.02	98.0488	12	1684.52	98.0611
13	1653.66	98.0505	14	1636.3	98.1273
15	1600.63	97.6927	16	1558.2	97.9059
17	1540.85	97.7991	18	1508.06	97.6418
19	1491.67	96.713	20	1451.17	96.7923
21	1419.35	97.6202	22	1362.46	97.7689
23	1264.11	97.4886	24	1180.22	97.9524
25	1154.19	98.1003	26	1110.8	98.3229
27	1063.55	98.1284	28	1027.87	97.7325
29	964.233	98.1195	30	947.842	98.1235
31	906.379	97.7965	32	884.202	98.1808
33	823.455	97.64	34	747.281	96.3441
35	695.212	93.5571	36	631.573	97.2916
37	600.717	97.1883	38	591.075	97.032
39	578.54	96.7028	40	555.398	96.2056
41	545.756	95.9062	42	531.293	95.5026

Figure 48: IR of unfunctionalized Merrifield resin

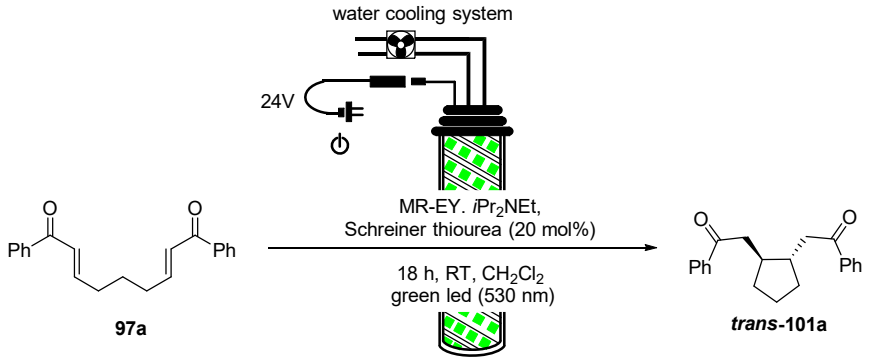
5.3.5 SYNTHESIS OF *TRANS* CYCLOPENTANES USING IMMOBILIZED CATALYST

General procedure for the photocyclization of symmetric bisenones under heterogeneous conditions in the presence of Hantzsch ester and *i*Pr_2NEt (**Table 10**).



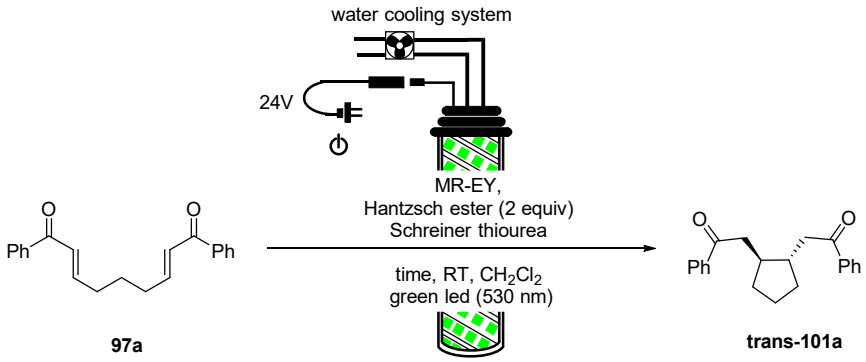
A 10 ml microwave vial with magnetic stirring bar was loaded with MR-Eosin Y, Bisenone **97a** (50 mg, 0.16mmol, 1 equiv), Hantzsch ester (40.5 mg, 0.16 mmol, 1 equiv), *i*Pr_2NEt (27 µl, 0.16 mmol, 1 equiv), 1,3-bis(3,5-bis(trifluoromethyl)phenyl)thiourea (12.5 mg, 0.032 mmol, 20 mol%) and 0.8 ml (0.2 M) of previously degassed CH_2Cl_2 or CH_3CN dry. The tube was then irradiated by using a home-made coil photoreactor LEDs (424 mW/cm^2) and the reaction stirred at room temperature. After the desired time, the reaction mixture was filtered with millipore apparatus (0.1 µm hydrophobic filter) and the MR-EY was copiously washed with dichloromethane. Then, the supported catalyst was recovered as yellowish solid and the crude mixture was concentrated under vacuum.

General procedure for the photocyclization of symmetric bisenones under heterogeneous conditions in the presence of *i*Pr_2NEt (**Table 11**).



A 10 ml microwave vial with magnetic stirring bar was loaded with MR-Eosin Y, Bisenone **97a** (50 mg, 0.16mmol, 1 equiv), *i*Pr_2NEt (1 or 2 equiv), 1,3-bis(3,5- bis(trifluoromethyl)phenyl)thiourea (12.5 mg, 0.032 mmol, 20 mol%) and 0.8 ml (0.2 M) of previously degassed CH_2Cl_2 dry. The tube was then irradiated by using a home-made coil photoreactor LEDs (424 mW/cm^2) and the reaction stirred at room temperature. After the desired time, the reaction mixture was filtered with millipore apparatus (0.1 µm hydrophobic filter) and the MR-EY was copiously washed with dichloromethane. Then, the supported catalyst was recovered as orange solid and the crude mixture was concentrated under vacuum.

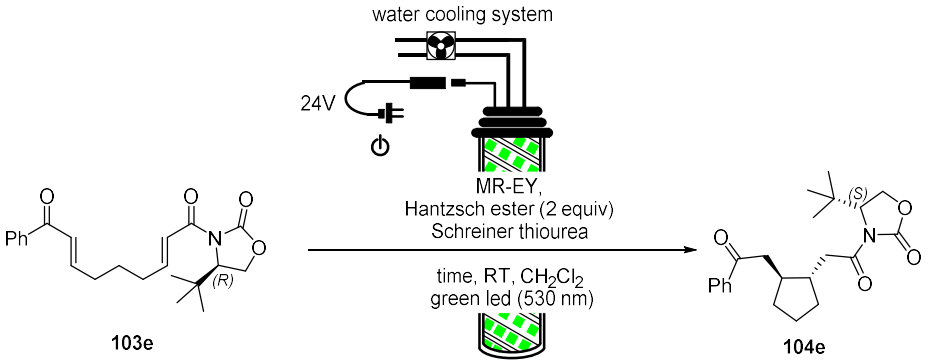
General procedure for the photocyclization of symmetric bisenones under heterogeneous conditions in the presence of Hantzsch ester (**Table 12**).



A 10 ml microwave vial with magnetic stirring bar was loaded with MR-Eosin Y, Bisenone **97a** (0.16 mmol, 1 equiv), Hantzsch ester (0.32 mmol, 2 equiv), 1,3-bis(3,5- bis(trifluoromethyl)phenyl)thiourea and 1.6 ml (0.1 M) of

previously degassed CH_2Cl_2 dry. The tube was then irradiated by using a home-made coil photoreactor LEDs (424 mW/cm^2) and the reaction stirred at room temperature. After the desired time, the reaction mixture was filtered with millipore apparatus (0.1 µm hydrophobic filter) and MR-EY was copiously washed with dichloromethane. Then, the supported catalyst was recovered as yellowish solid and the crude mixture was concentrated under vacuum.

General procedure for the photocyclization of unsymmetric bisenones under heterogeneous conditions (**table 13**)



A 10 ml microwave vial with magnetic stirring bar was loaded with MR-Eosin Y, Bisenones **103e** (50 mg, 0.16mmol, 1 equiv), *i*Pr$_2$NEt (54µl, 0.32 mmol, 2 equiv), 1,3-bis(3,5- bis(trifluoromethyl)phenyl)thiourea (12.5 mg, 0.032 mmol, 20 mol%) and 0.8 ml (0.2 M) of previously degassed DCM dry. The tube was then irradiated by using a home-made coil photoreactor LEDs (424 mW/cm^2) and the reaction stirred at room temperature. After the desired time, the reaction mixture was filtered with millipore apparatus (0.1 µm hydrophobic filter) and MR-EY was copiously washed with dichloromethane. Then, the supported catalyst was recovered as yellowish solid and the crude mixture was concentrated under vacuum.

Catalyst reactivation

Different test have been performed to re-activate the catalyst using a 3 ml vial, equipped with a stirring bar and loaded with 0.006 mmol (35 mg) of inactivated yellowish catalyst. The solid was suspended in organic solvent and compressed air was bubbled inside.

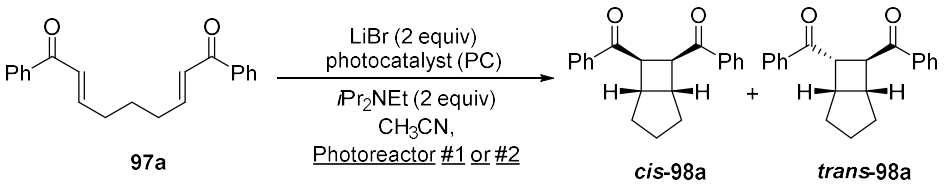
Entry	Solvent	Green Light	Time (H)	Color Change
1	CH_3CN	No	3	No
2	Toluene	No	18	No
3	CH_3CN	Yes	1	Yes

Table 16: Catalyst reactivation tests

In **entry 1**, the catalyst was suspended in 2 ml of CH_3CN and stirred for 3 hours. The catalyst color did not change. In entry 2, a less volatile solvent like Toluene was used to avoid solvent evaporation. Compressed air was bubbled inside for 18h but, also in this case, the color did not change and the catalyst remains inactive. In the last attempt, in entry 3, the same set-up of entry 1 was used and the suspension was irradiated by green light, under compressed air, in air for 30 minutes. After this time, 2 ml of CH_3CN were added and the suspension was stirred and irradiated for other 30 minutes. Then, the suspension was filtered with millipore apparatus (0.1 µm hydrophobic filter) and the MR-EY was recovered as deep pink solid.

5.3.6 SYNTHESIS OF BICYCLO[3.2.0]HEPTANES BY [2+2] PHOTOCYCLOADDITION

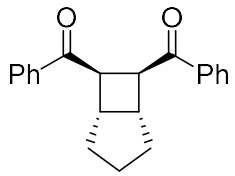
General procedure for the synthesis of compounds **98a** under batch condition



In a typical experiment, aryl-enone **97a** (1 equiv, 0.35 mmol) and i-Pr_2NEt (2 equiv, 122 µL) were introduced into a 10 ml vial containing a magnetic stirring bar under nitrogen atmosphere. Subsequently, a solution of photocatalyst (Eosin Y or Na_2Eosin Y) (0.5 mol% or 0.1 mol%) and LiBr (2 equiv, 0.70 mmol) in dry acetonitrile (3.5 mL), previously sonicated for 10 minutes, was added to the mixture. The resulting solution was degassed

through three freeze-pump-thaw cycles (3 times). After the desired reaction time (h), the solvent was evaporated under vacuum and the crude product was subjected to purification via column chromatography using different hexane/ethyl acetate mixtures (from 95:5 to 85:15). Final yields are reported in **Table 14**.

Compound *cis*-98a

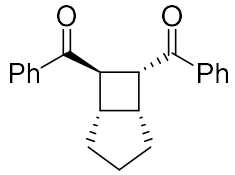


Synthetized according to the general procedure starting from compound **97a**. The product was purified by flash column chromatography on silica gel to afford a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 – 7.65 (m, 1H), 7.47 (t, *J* = 7.3 Hz, 1H), 7.39 (dd, *J* = 18.6, 10.8 Hz, 1H), 3.88 (d, *J* = 4.1 Hz, 1H), 3.23 (td, *J* = 4.2, 2.4 Hz, 1H), 2.11 – 2.00 (m, 1H), 1.92 – 1.87 (m, 1H), 1.85 (dd, *J* = 5.0, 2.5 Hz, 1H), 1.71 (ddd, *J* = 18.3, 13.0, 7.8 Hz, 1H). **MS (APCI+)** m/z (%): calculated for $C_{21}H_{20}O_2$ $(M^+H)^+$: 304.34; found 305.5.

Analytical data are in agreement with those reported in literature.[179,180]

Compound *trans*-98a

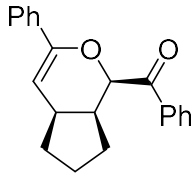


Synthetized according to the general procedure starting from compound **97a**. The product was purified by flash column chromatography on silica gel to afford a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.02-8.00 (d, J=7.14 Hz, 2 H), 7.96-7.93 (d, J=7.14 Hz, 2 H), 7.58-7.53 (d, 2 H), 7.49-7.43 (t, J=7.52, 7.52 Hz, 4 H), 4.60-3.84 (dd, J=7.69, 10.66 Hz, 1 H), 4.30-4.26 (dd, J=7.43 Hz, 1 H), 3.29-3.20 (m, 1 H), 3.09-3.03 (m, 1 H), 2.08-1.99 (q, J = 6.78, 6.78, 6.78 Hz, 1 H), 1.91-1.69 (m, 3 H), 1.56-1.34 (m, 2 H). **MS (APCI+)** m/z (%): calculated for $C_{21}H_{20}O_2$ $(M^+H)^+$: 304.34; found 305.5.

Data are in agreement with those reported in literature. [179,180]

Compound 100a

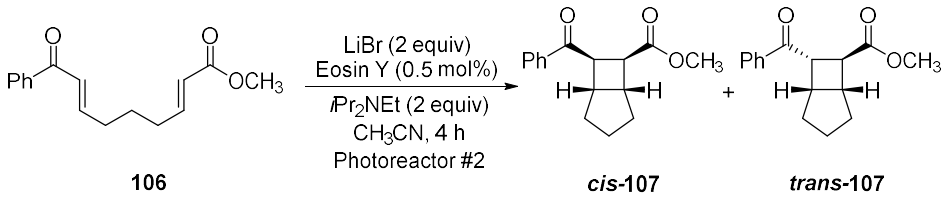


Synthetized according to the general procedure starting from compound **97a**. The product was purified by flash column chromatography on silica gel to afford a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.43 (m, 1H), 1.55 (m, 2H), 1.73 (m, 1H), 1.98 (m, 2H), 2.69 (m, 2H), 4.87 (d, J=7.2 Hz, 1H), 5.51 (d, J=3.9 Hz, 1H), 7.25 (m, 3H), 7.46 (m, 4H), 7.57 (m, 1H), 8.07 (dd, J=7.2, 1.5 Hz, 2H). **MS (APCI+)** m/z (%): calculated for $C_{21}H_{20}O_2$ $(M^+H)^+$: 304.34; found 305.5.

Data are in agreement with those reported in literature. [179,180]

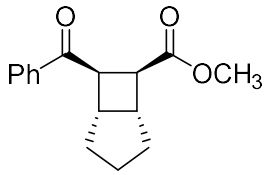
General procedure for the synthesis of compounds **107** under batch condition



106 *cis*-107 *trans*-107

In a 10 ml vial equipped with a magnetic stirring bar, compound **106** (1 equiv, 0.22 mmol) and *i*-Pr_2NEt (2 equiv, 76 µL) were added under N_2 atmosphere. Subsequently, a solution of photocatalyst (Eosin Y) (0.5 mol%) and LiBr (2 equiv, 0.44 mmol) in dry acetonitrile (2.2 mL), previously sonicated for 10 minutes, was added to the mixture. The final mixture was degassed via freeze-pump-thaw cycles (3 cycles). The reaction, carried out using Photoreactor#2, proceeded for 4 h, then the solvent was removed under vacuum, and the crude product was purified by column chromatography using a hexane/ethyl acetate mixture (80:20). Final yields are reported in **Scheme 72**.

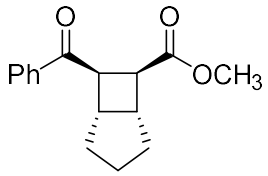
Compound *cis*-107



Synthetized according to the general procedure starting from compound **106**. The product was purified by flash column chromatography on silica gel to afford a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.97-7.77 (d, J = 7.51 Hz, 2H), 7.61-7.52 (t, J = 7.24, 7.24 Hz, 1H), 7.51-7.42 (t, J = 6.94, 8.05 Hz, 2H), 4.39-4.30 (dd, J = 8.36, 9.42 Hz, 1H), 3.67 (s, 3H), 3.47-3.36 (t, J = 7.25, 7.51 Hz, 1H), 3.28-3.17 (m, 1H), 3.07-2.98 (q, J = 6.36, 6.74, 6.74, 1H), 1.81-1.65 (m, 4H), 1.53-1.28 (m, 4H). **^{13}CNMR** (75 MHz, $CDCl_3$): δ 197.39, 175.27, 136.02, 133.14, 128.71, 128.29, 77.42, 77.00, 76.57, 51.81, 44.24, 40.84, 40.75, 39.36, 32.08, 29.69, 27.98, 25.30. **MS (APCI+)** m/z (%): calculated for $C_{16}H_{18}O_3$ $(M^+H)^+$: 258.1; found 260.2.

Compound *trans*-107



Synthetized according to the general procedure B starting from compound **106**. The product was purified by flash column chromatography on silica gel to afford a white solid.

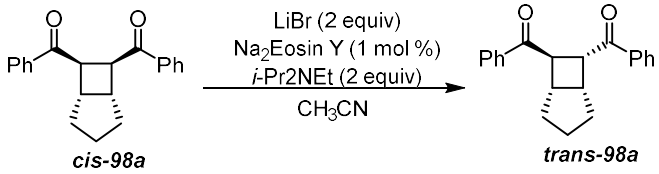
^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.89-7.77 (d, J = 8.20 Hz, 2H), 7.56-7.49 (t, J = 7.09, 7.61 Hz, 1H), 7.48-7.38 (t, J = 7.83, 8.20 Hz, 2H), 3.74-3.67 (dd, J = 4.61, 4.82 Hz, 1H), 3.45 (s, 3H), 3.20-3.05 (m, 2H), 3.03-2.95 (dd, J = 5.10, 4.61 Hz, 1H), 2.00-1.05 (m, 7H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 198.74, 173.65, 136.00, 132.85, 128.51, 128.09, 77.43, 77.01, 76.58, 51.41, 46.69, 43.99, 39.04, 38.86, 32.32, 29.69, 25.17. **MS (APCI+)** m/z (%): calculated for $C_{16}H_{18}O_3$ $(M^+H)^+$: 258.1; found 260.2.

The relative configuration of ***cis*-107** and ***trans*-107** stereoisomers was determined by comparing their NMR signals and coupling constants with those reported in the literature for the ethyl ester analogue derivative.[181]

5.3.7 MECHANISTIC STUDIES

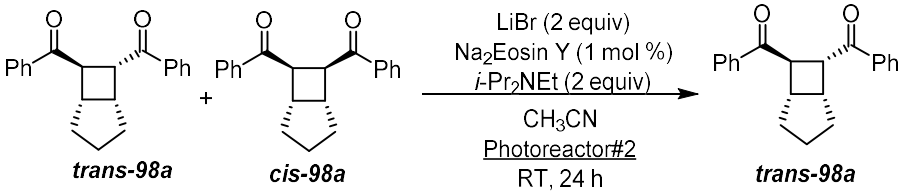
Control experiments

Control experiment #1 (**Scheme 75, A**)



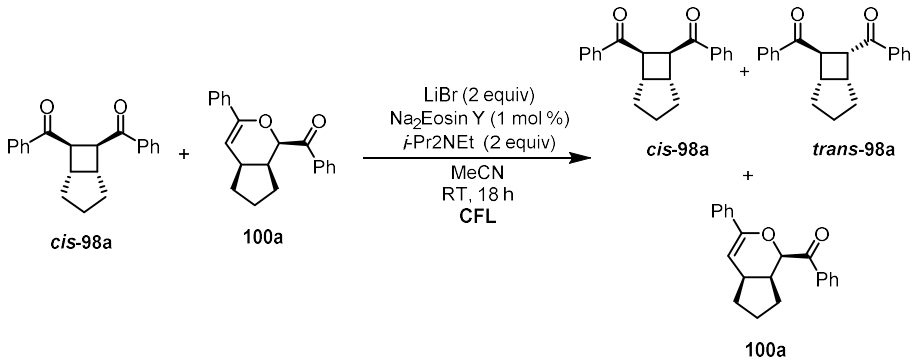
In a 1 ml vial, compound ***cis*-98a** (22 mg, 0.072 mmol), Na_2Eosin Y (1 mol%), LiBr (2 equiv, 12.6 mg), and *i*-Pr_2NEt (2 equiv, 25 µL), were dissolved in 0.7 mL of CH_3CN. The mixture was degassed via freeze-pump-thaw cycles (3 cycles), then stirred for 24 h in the dark. After this time, ^{1}H-NMR revealed the presence of the starting material untouched. The reaction mixture was then subjected to light irradiation for 24 hours using Photoreactor#2 cooled at 26 °C by a fan. After that time, ^{1}H-NMR was acquired, revealing only the presence of compound ***cis*-98a**.

Control experiment #2 (**Scheme 75, B**)



In a 1 ml vial, compound ***cis-98a*** (50 mg, 0.145 mmol), compound ***trans-98a*** (12.5 mg, 0.041), Na_2Eosin Y (1 mol %), LiBr (2 equiv, 33 mg), *i*-Pr_2NEt (2 equiv, 65 µL) were dissolved in 0.7 in 1.4 mL of CH_3CN. The mixture was degassed via freeze-pump-thaw cycles (3 cycles), then stirred for 24 h in the dark. After this time, ^{1}H-NMR revealed the presence of the starting materials untouched. The reaction mixture was then subjected to light irradiation for 24 hours using photoreactor#2 cooled at 26 °C by a fan. After that time, ^{1}H-NMR was acquired, revealing the presence of compound ***cis*-98a** and ***trans*-98a** in the original ratio.

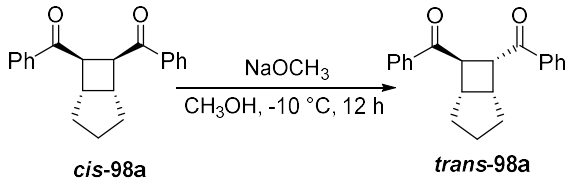
Control experiment #3 (**Scheme 75, C**)



In a 10 ml vial, compound ***cis-98a*** (103 mg, 0.334 mmol), compound **100a** (13.2 mg, 0.043 mmol), Na_2Eosin Y (1 mol %), LiBr (2 equiv, 68.5 mg), and *i*-Pr_2NEt (2 equiv, 135 µL) were dissolved in 3.8 mL of MeCN.The mixture was degassed via freeze-pump-thaw cycles (3 cycles), then stirred for 24 h in the dark. After this time, ^{1}H-NMR revealed the presence of the starting materials untouched. The reaction mixture was then subjected to light irradiation for 24 hours using Photoreactor#2 cooled at 26 °C by a fan. After 24 h, the crude mixture was concentrated under vacuum and analysed by ^{1}H-NMR.

Subsequently, the crude product underwent purification via flash chromatography (eluent: hexane/ethyl acetate starting from 95:05, and gradually shifting to 94:06, and 93:07). Compound ***cis-98a***, **100a** and ***trans-98a*** were recovered in 80 mg, 24 mg, and 9.1 mg respectively.

Control experiment #4 (**Scheme 75, D**)



In a 1 ml vial, compound ***cis*-98a** (13 mg, 0.043 mmol), and NaOMe (162 µL, 0.092 mmol) were dissolved in 343 µL of dry methanol (final concentration 0.15 M). The mixture was sonicated for 10 min in order to dissolve the starting compounds, then the reaction mixture was cooled at -10 °C and stirred for 12 h. The reaction was monitored by TLC. When no starting material was detected, the solvent was removed under vacuum. ^{1}H-NMR of the crude confirms the complete interconversion of ***cis-98a*** in ***trans-98a***.

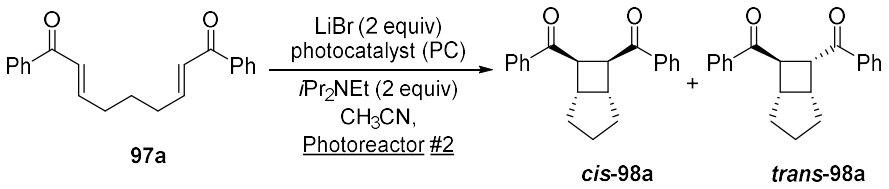
Kinetic study

The reaction has been monitored by HPLC-MS analysis with Trimethoxibenzene (TMB) as external standard. The relative yields at different times have been calculated relating the ratio between the Area of the peaks of the compound (i) to the Area of the peak of TMB ($\frac{A_i}{A_{TMB}}$) with the ratio between the corresponding concentrations ($\frac{C_i}{C_{TMB}}$) and the relative instrument response factor (α) (**1.6** for compound **97a**, **1.7** for compound ***cis-98a***, **0.94** for compound ***trans-98a*** and **0.83** for compound **100a**) following the below equation (**Equation 11**):

$$\frac{A_i}{A_{TMB}} = \alpha \frac{C_i}{C_{TMB}}$$

Equation 11: Relationship between the ratio of the area of the peaks and the ratio of the concentrations.

Kinetic study using Photoreactor#2



This experiment has been performed according to general procedure : aryl-enone **97a** (1 equiv, 0.35 mmol) and *i*-Pr_2NEt (2 equiv, 122 µL) were introduced into a 10 ml vial containing a magnetic stirring bar under nitrogen atmosphere. Subsequently, a solution of photocatalyst (Na_2Eosin Y) (1 mol%) and LiBr (2 equiv, 0.70 mmol) in dry acetonitrile (3.5 mL), previously sonicated for 10 minutes, was added to the mixture. The resulting solution was degassed through three freeze-pump-thaw cycles (3 times). The vial was filled with Argon and has been positioned at a distance from the photoreactor #2 less than 1 cm and it was irradiated for 930 minutes.

The different samples for HPLC analysis were prepared as follow: 100 µL of the solution have been sampled at different reaction time and mixed with 900 µL of a solution CH_3CN/H_2O (60:40) of Trimethoxybenzene (0.01189 M). The obtained samples were analysed with a reverse phase GEMINI 5u-C18 column with a mobile phase CH_3CN/H_2O (60:40).

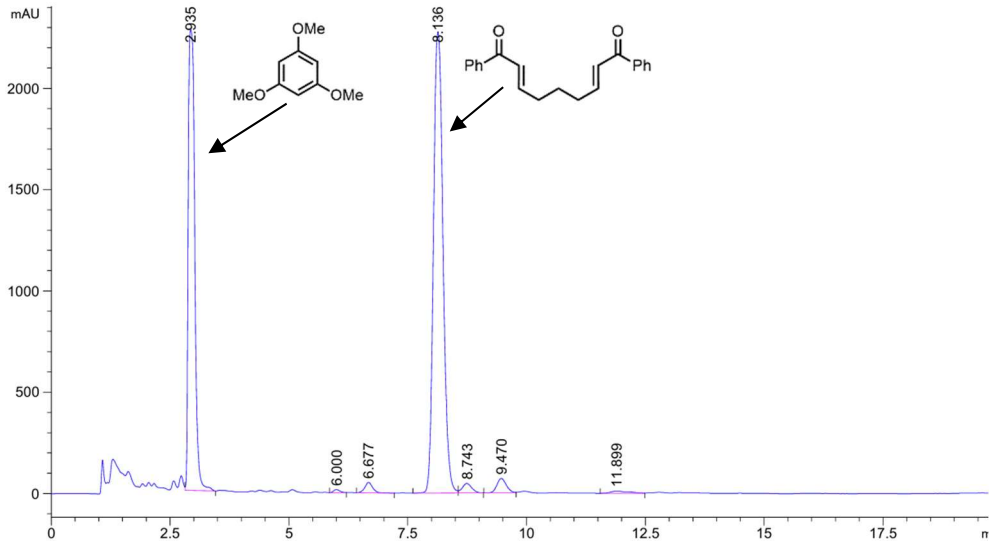
The yields at different time were then calculated from the area of the different peaks (of the corresponding molecules) and were then plot in the **Figure 33**. Here is reported the corresponding values (**Table 17**).

Time (min)	Aryl-enone 97a	*Cis-98a*	*Trans-98a*	100a
0	99,0	0,0	0,0	0,0
5	94,2	4,2	0,0	3,5
15	70,9	8,3	1,4	3,7
20	59,5	12,3	1,5	3,8
30	47,4	30,1	2,8	3,7
60	14,0	64,6	6,8	3,6
90	1,6	87,3	13,0	3,4
150	0,0	90,7	15,1	4,1
210	0,0	90,8	16,5	4,0
240	0,0	91,9	16,9	4,2
300	0,0	91,0	17,2	4,2
330	0,0	91,0	17,9	4,0
360	0,0	90,2	18,1	4,1
420	0,0	91,0	19,1	4,2
510	0,0	87,4	20,0	4,2
600	0,0	68,9	36,8	6,7
720	0,0	23,3	79,9	7,6
780	0,0	23,6	83,4	6,9
840	0,0	21,1	83,8	7,4
900	0,0	18,3	89,3	6,6
930	0,0	16,6	91,3	6,5

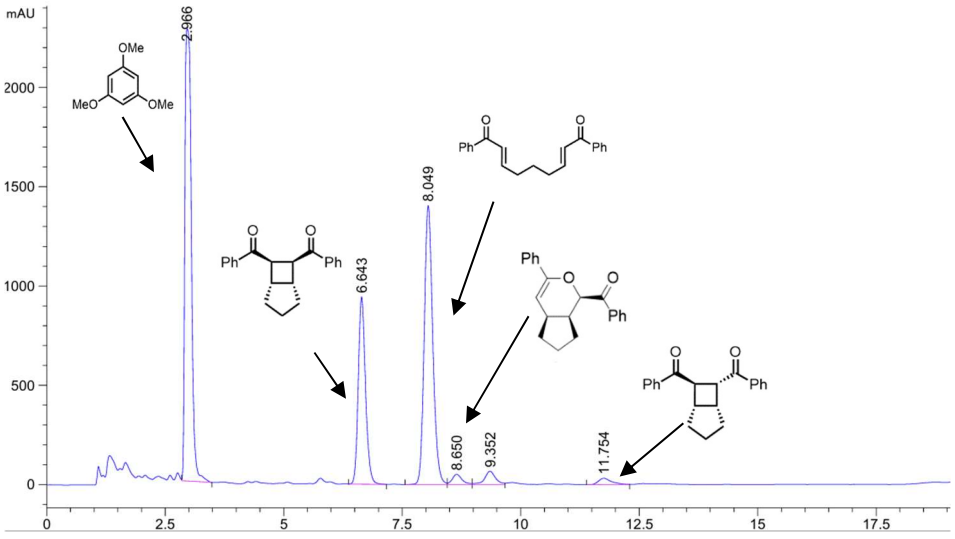
Table 17: Yields of the different compounds (**97a**, ***cis-98a***, ***trans-98a***) at different reaction time.

Some HPLC spectra for this reaction are here reported:

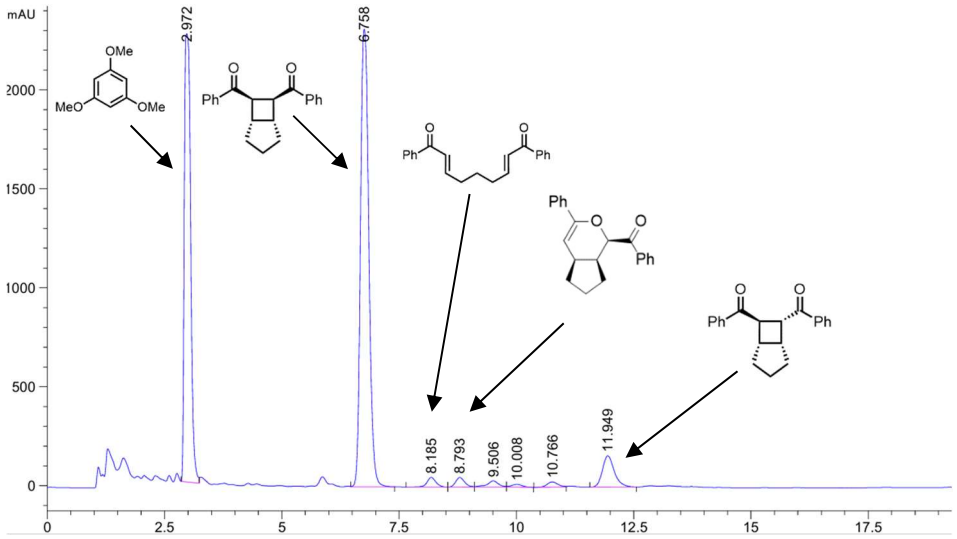
1) HPLC spectra at 0 minutes of irradiation



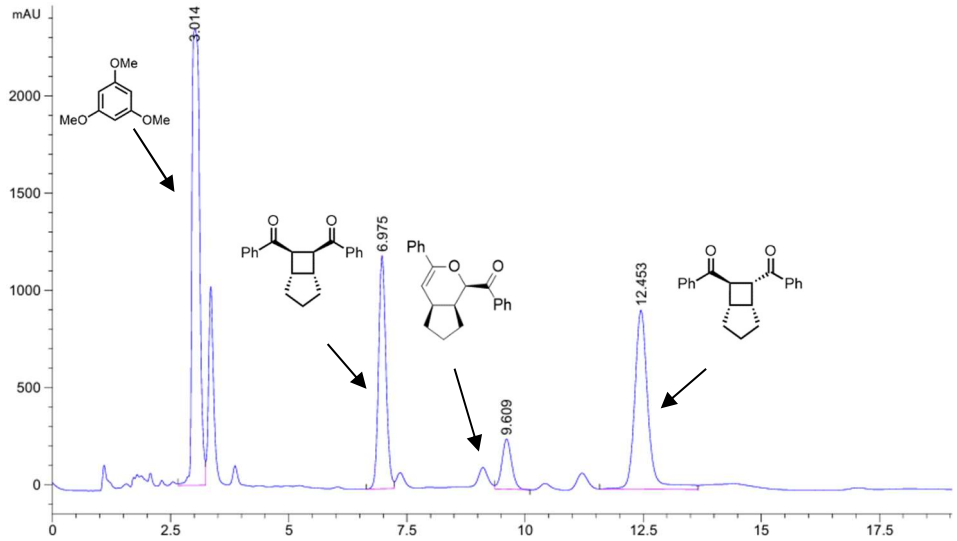
2) HPLC spectra at 30 minutes of irradiation



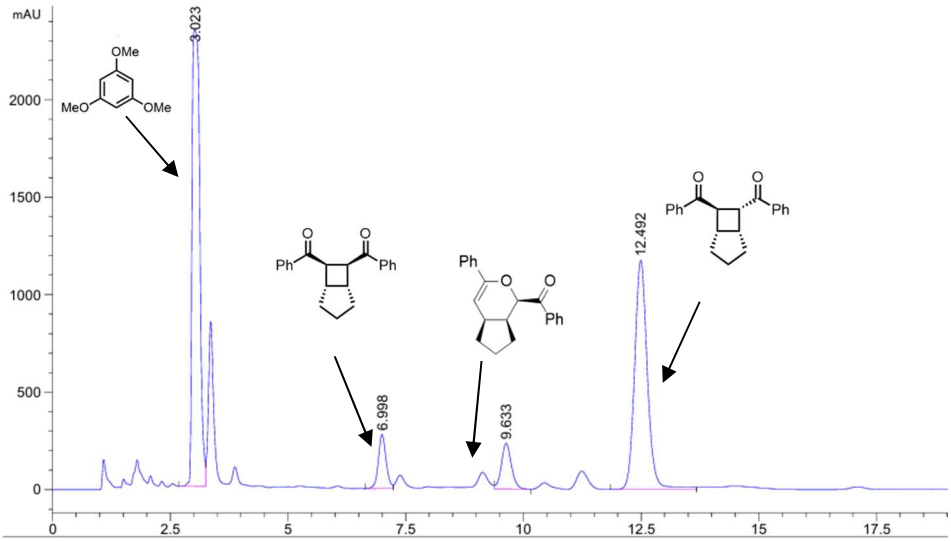
3) HPLC spectra at 120 minutes of irradiation



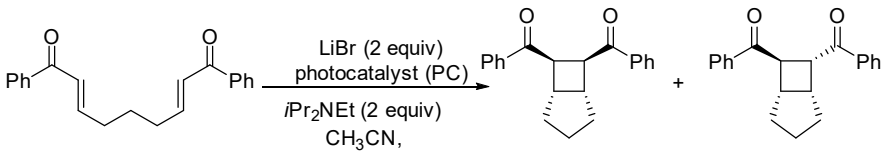
4) HPLC spectra at 800 minutes of irradiation



5) HPLC spectra at 930 minutes of irradiation



Kinetic study using Photoreactor#1



97a ***cis*-98a** ***trans*-98a**

This experiment has been performed according to the following procedure: aryl-enone **97a** (1 equiv, 0.35 mmol) and *i*-Pr_2NEt (2 equiv, 122 µL) were introduced into a 10 ml vial containing a magnetic stirring bar under nitrogen atmosphere. Subsequently, a solution of photocatalyst (Na_2Eosin Y) (1 mol%) and LiBr (2 equiv, 0.70 mmol) in dry acetonitrile (3.5 mL), previously sonicated for 10 minutes, was added to the mixture. The resulting solution was degassed through three freeze-pump-thaw cycles (3 times). The vial was filled with Argon and has been positioned at a distance from the photoreactor #1 less than 1 cm and it was irradiated for 930 minutes.

The different samples for HPLC analysis were prepared as follow: 100 µL of the solution have been sampled at different reaction time and mixed with 900 µL of a solution MeCN/H_2O (60:40) of Trimethoxybenzene (0.01189 M). The obtained samples were analysed with a reverse phase GEMINI 5u-C18 column with a mobile phase MeCN/H_2O (60:40).

The product ***cis-98a*** has been obtained after 120 minutes of reaction and no interconversion was observed even after 930 minutes of irradiation.

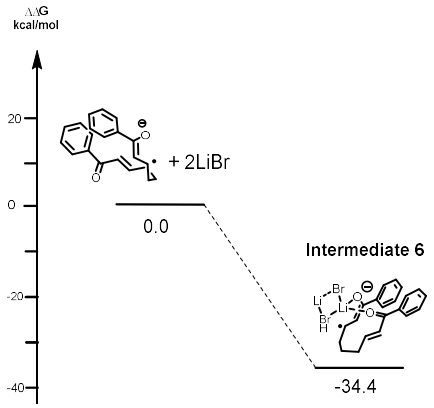
DFT Calculations

Preliminary structures corresponding to intermediates (**97a.3**, **97a.3'**, **101a.1**$_{cis}$, **101a.1**$_{trans}$, **98a.1**$_{cis}$, **98a.1**$_{trans}$ and **100a.1**) and compounds ***cis-98a***, ***trans-98a*** and **100a** were generated through Monte Carlo conformational analysis performed with Molecular Mechanics calculations using the MMFFs force field [109] of the Macromodel package in the Schrodinger suite.[115] All geometries of structures obtained within a 3 kcal/mol range were then fully optimized as minima by DFT approach using the unrestricted M062X functional[182] with the 6-31G(d,p) basis set of the Gaussian package,[111] including solvation effects of acetonitrile using the PCM model.[112] Among these structures, the one exhibiting the lowest energy was selected to construct the reaction profile.

Transition states (**TS1**$_{(97a.3\text{-}101a.1\text{-}cis)}$, **TS1**$_{(97a.3'\text{-}101a.1\text{-}trans)}$, **TS2**$_{(101a.1\text{-}98a.1\text{-}cis)}$, **TS2**$_{(101a.1\text{-}98a.1\text{-}trans)}$ and **TS2**$_{(101a.1\text{-}100a.1)}$) were directly located through a DFT approach, with harmonic vibrational calculations also conducted at the same level of theory, indicating the presence of one imaginary frequency. IRC paths were also calculated to validate the existence of the transition state.

Effects of the coordination with LiBr

The effects of coordination between aryl-enone **97a** and **LiBr** was investigated considering the isodesmic-type reaction showed in **scheme 107**.

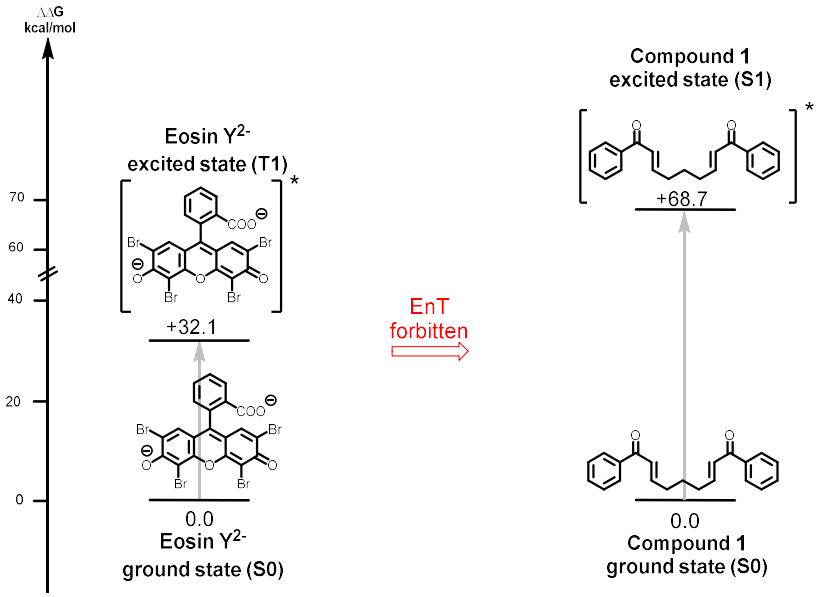


Scheme 107: Effect of coordination with LiBr

Since $\Delta G_{(product\text{-}reactants)}$ = – 34.4 kcal/mol, the coordinative process is favorite.

Energy transfer (EnT) process evaluation

The possibility of the excitation of the starting aryl-enone **97a** by an *EnT* process discussed in the main text has been investigated. The energy required for transition $S_0 \rightarrow T_1$ of Eosin Y^{2-} is 32.1 Kcal/mol, which is less than the energy required for transition $S_0 \rightarrow S_1$ of compound **97a**. According to that, *EnT* process could be excluded (**Scheme 108**).



Scheme 108: Excitation energy of **compound 97a** and **Eosin Y^{2-}**

Free Gibbs energy obtained for all optimized structures

Relative Gibbs Free Energies G (in kcal/mol) and frequencies analysis of transitions states (TS) computed at the (U)M06-2X/6-31G(d,p)/PCM (CH_3CN) Level are reported in **table 18.**

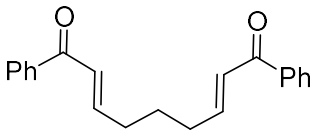
Entry	Compound Name	G (Hartree/particales)	G (kcal/mol)	Imaginary frequency (cm^{-1})	ΔΔG (kca/mol)
1	Intermediate **97a.3**	-6121,08110	-3840978,38774	-	0,0
2	Intermediate **97a.3'**	-6121,06637	-3840969,14969	-	+9,2
3	**TS1**	-6121,06639	-3840969,16161	- 472,94	+9,2
4	**TS1**$_{(97a.3'\text{-}101a.1\text{-}trans)}$,	-6121,01539	-3840937,15848	- 35,35	+41,2
5	Intermediate ***cis-101a.1***	-6121,07729	-3840975,99822	-	+2,4
6	Intermediate ***trans-101a.1***	-6121,07740	-3840976,06536	-	+2,3
7	**TS2**$_{(101a.1\text{-}98a.1\text{-}cis)}$	-6121,07459	-3840974,30711	- 274,71	+4,1
8	**TS2**$_{(101a.1\text{-}98a.1\text{-}trans)}$	-6121,05782	-3840963,77954	- 343,70	+14,6
9	**TS2**$_{(101a.1\text{-}100a.1)}$	-6121,05688	-3840963,18969	- 140,78	+15,2
10	Intermediate ***cis-98a.1***	-6121,08316	-3840979,68039	-	-1,3
11	Intermediate ***trans*-98a.1**	-6121,07591	-3840975,13541	-	+3,3
12	Intermediate **100a.1**	-6121,08303	-3840979,59819	-	-1,2
13	Compound ***cis-98a***	-6120,97308	-3840910,60582	-	-50,6
14	Compound ***trans-98a***	-6120,98379	-3840917,33011	-	-57,3
15	Compound **100a**	-6120,98422	-3840917,59868	-	-57,6
16	Compound **97a**_no LiBr	-962,01341	-603663,41540	-	-
17	LiBr	-2579,46409	-1618613,71648	-	-
18	EosinY	-11430,78194	-7172815,66610	-	-
19	EosinY radical anion	-11428,52147	-7171397,22117	-	-
20	*i*Pr_2NEt	-370,63731	-232574,91203	-	-
21	*i*Pr_2NEt radical cation	-370,44862	-232456,51093	-	-

22	Compound **97a**_LiBr	-6120,97035	-3840908,89274	-	-
23	Intermediate **97a.3**_noLiBr	-962,09810	-603716,55650	-	+34,4

Table 18: Free Gibbs energy obtained for all optimized structures

Geometries (XYZ coordinates)

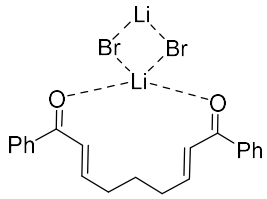
Compound 97a w/o LiBr (charge = 0; spin = 1)



C	3.39327	-1.00706	1.47483
C	4.35379	-1.18151	0.48093
C	3.99541	-1.73630	-0.74909
C	2.67968	-2.12148	-0.97817
C	1.70772	-1.94011	0.01253
C	2.07142	-1.37654	1.23998
C	0.30942	-2.39739	-0.27703
C	-0.80201	-1.82518	0.52559
O	0.10269	-3.20841	-1.16853
C	-2.03725	-2.33418	0.45503
C	-3.21465	-1.80598	1.21264
C	-4.41845	-1.50533	0.30618
C	-4.08471	-0.54376	-0.84706
C	-3.45947	0.72376	-0.35564
C	-2.21861	1.10889	-0.66949
C	-1.62430	2.34097	-0.09383
O	-2.31739	3.19247	0.44513
C	-0.13757	2.51306	-0.16871

C	0.40201	3.76352	0.15446
C	1.77600	3.96344	0.12394
C	2.62710	2.91018	-0.21699
C	2.09995	1.65948	-0.52863
C	0.72157	1.46378	-0.50999
H	3.67203	-0.58115	2.43269
H	5.38178	-0.88538	0.66295
H	4.74302	-1.87050	-1.52378
H	2.38259	-2.56715	-1.92173
H	1.33456	-1.24561	2.02552
H	-0.60209	-0.96550	1.15995
H	-2.20103	-3.19068	-0.20065
H	-2.91979	-0.90525	1.76142
H	-3.51955	-2.55254	1.95650
H	-5.21907	-1.08055	0.92045
H	-4.80271	-2.43877	-0.11816
H	-5.00937	-0.31159	-1.38830
H	-3.40578	-1.03172	-1.55500
H	-4.03560	1.34223	0.33369
H	-1.62141	0.49888	-1.33964
H	-0.27573	4.56579	0.42625
H	2.18801	4.93707	0.36789
H	3.70104	3.06573	-0.23605
H	2.75510	0.83086	-0.78134
H	0.32993	0.47977	-0.74427

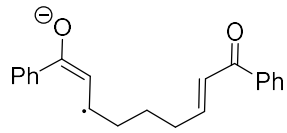
Compound 97a.3 (charge = 0; spin = 1)



C	-5.30558	-0.44406	1.54556
C	-5.24079	-1.80821	1.27102
C	-4.25789	-2.30629	0.41273
C	-3.34406	-1.44020	-0.17274
C	-3.39582	-0.06956	0.11449
C	-4.37973	0.42570	0.97491
C	-2.38091	0.81576	-0.51539
C	-2.11739	2.14782	0.06061
O	-1.75911	0.42142	-1.50970
C	-1.50755	3.08933	-0.67050
C	-1.23161	4.48734	-0.21125
C	0.06202	5.09030	-0.76975
C	1.35082	4.45738	-0.23382
C	1.58322	3.04913	-0.68612
C	2.18737	2.10155	0.04213
C	2.40958	0.75660	-0.52064
O	1.76944	0.36514	-1.50418
C	3.40617	-0.14567	0.11334
C	4.44102	0.34509	0.91472
C	5.35541	-0.53651	1.48526
C	5.22631	-1.90701	1.27197
C	4.18982	-2.40032	0.47625

C	3.28712	-1.52376	-0.11084
Li	-0.00274	-0.32123	-1.11264
Li	-0.24947	-2.82176	0.83507
Br	-0.04793	-2.74480	-1.68401
Br	-0.00511	-0.38954	1.40639
H	-6.07469	-0.05709	2.20512
H	-5.95701	-2.48556	1.72490
H	-4.20723	-3.36947	0.20114
H	-2.56289	-1.81149	-0.83055
H	-4.44172	1.48795	1.18712
H	-2.42793	2.34429	1.08207
H	-1.24431	2.83933	-1.69942
H	-2.06700	5.11277	-0.55405
H	-1.23740	4.52933	0.88370
H	0.05128	5.01598	-1.86434
H	0.07701	6.15705	-0.53008
H	2.19475	5.05868	-0.59830
H	1.38032	4.50744	0.86038
H	1.29189	2.79530	-1.70653
H	2.52459	2.30202	1.05451
H	4.55080	1.41237	1.07758
H	6.16531	-0.15400	2.09690
H	5.93370	-2.59350	1.72598
H	4.08894	-3.46867	0.31498
H	2.46687	-1.89097	-0.72219

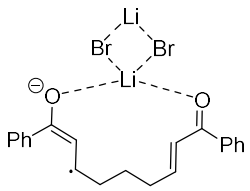
Intermediate 97a.1 w/o LiBr (charge = -1; spin = 2)



C	-0.28760	-2.37428	-0.35506
C	0.82587	-1.94829	0.47382
C	2.10763	-2.36698	0.31484
C	3.26091	-1.86975	1.13783
C	3.45493	0.79710	-0.28435
C	2.18245	1.12044	-0.53805
C	1.56988	2.35444	0.01052
O	2.24416	3.22947	0.53894
C	-2.66903	2.90017	-0.32569
C	-1.82813	3.99235	-0.09791
C	-0.45731	3.79995	0.01389
C	0.08672	2.51672	-0.11743
C	-0.76056	1.42642	-0.33771
C	-2.13726	1.61775	-0.43641
O	-0.09910	-3.09605	-1.39365
C	-1.64769	-1.96022	0.01069
C	-2.69315	-2.17887	-0.92093
C	-4.00429	-1.81988	-0.64415
C	-4.34381	-1.23641	0.58169
C	-3.33078	-1.02871	1.52410
C	-2.01646	-1.37984	1.25102
C	4.11843	-0.43522	-0.81192
C	4.47426	-1.43580	0.29977

H	0.63187	-1.21359	1.25603
H	2.31692	-3.10329	-0.46098
H	2.92237	-1.02461	1.75070
H	3.60795	-2.64094	1.84235
H	4.03712	1.45432	0.36305
H	1.57607	0.46586	-1.15620
H	-3.74071	3.05191	-0.40996
H	-2.24561	4.98996	-0.00755
H	0.21324	4.63324	0.19692
H	-0.36528	0.41653	-0.40526
H	-2.78347	0.75755	-0.58840
H	-2.42748	-2.63927	-1.86662
H	-4.77641	-1.99724	-1.38903
H	-5.37026	-0.96122	0.80097
H	-3.57289	-0.58933	2.48848
H	-1.26677	-1.22173	2.02009
H	3.45234	-0.92012	-1.53235
H	5.03624	-0.15238	-1.34184
H	5.23775	-1.00320	0.95735
H	4.92652	-2.31638	-0.17137

Intermediate 97a.3 (charge = -1; spin = 2)

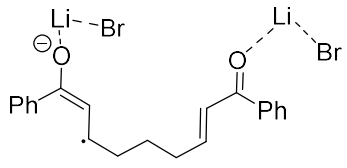


C	-0.27218	0.80692	1.78429

C	0.27266	2.14607	1.65947
C	1.60216	2.32973	1.50937
C	2.28347	3.64669	1.31421
C	1.95506	2.05867	-1.25639
C	0.63438	1.92274	-1.55314
C	-0.04468	0.66811	-1.44498
O	0.48133	-0.18543	1.93010
C	-1.74035	0.58228	1.76100
C	-2.22636	-0.65530	2.20408
C	-3.58847	-0.92935	2.17783
C	-4.48177	0.02489	1.69268
C	-4.00562	1.25203	1.23293
C	-2.64531	1.53185	1.26734
C	2.67527	3.36973	-1.19994
C	3.31463	3.61267	0.17703
Li	1.18916	-1.16721	0.52391
Br	3.58432	-1.33821	-0.04144
Br	0.33970	-3.46347	-0.05571
Li	1.54385	-1.89867	-1.80384
C	-1.49321	0.54767	-1.67461
O	0.61530	-0.40051	-1.14270
C	-2.11571	-0.68111	-1.37793
C	-3.48367	-0.84614	-1.55198
C	-4.26882	0.20132	-2.03402
C	-3.66467	1.42212	-2.33720
C	-2.29783	1.59707	-2.15792
H	-0.40536	2.99211	1.61263

H	2.24261	1.44861	1.56349
H	1.54062	4.43204	1.13002
H	2.80789	3.91289	2.24251
H	2.52463	1.16017	-1.01680
H	0.05291	2.81602	-1.76644
H	-1.51716	-1.38737	2.57642
H	-3.95492	-1.88722	2.53334
H	-5.54534	-0.19046	1.66284
H	-4.69506	1.98521	0.82717
H	-2.28671	2.47417	0.86678
H	3.47344	3.40204	-1.95427
H	1.98280	4.18866	-1.43180
H	3.87549	4.55316	0.16424
H	4.03829	2.81240	0.38009
H	-1.49881	-1.49286	-1.00233
H	-3.94347	-1.79798	-1.30130
H	-5.33792	0.07050	-2.16922
H	-4.26335	2.24464	-2.71737
H	-1.85742	2.55550	-2.41189

Intermediate 97a.3‘(charge = -1; spin = 2)

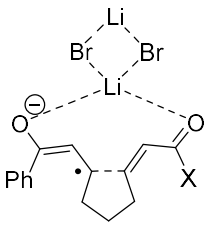


C	-2.85142	0.16833	-1.21696
C	-2.01714	1.37649	-1.30128

C	-0.73238	1.26256	-1.67296
C	0.26451	2.37425	-1.78493
C	0.90288	1.88876	1.16295
C	2.17120	1.64887	0.70604
C	2.93404	0.49954	1.09854
O	-2.47087	-0.90752	-1.69684
C	-4.17748	0.23375	-0.54148
C	-5.07560	-0.82153	-0.74268
C	-6.31459	-0.81657	-0.11556
C	-6.66118	0.23748	0.73069
C	-5.76713	1.28394	0.94697
C	-4.53003	1.28711	0.30974
C	-0.01144	2.99637	0.72014
C	0.16026	3.48536	-0.72699
Li	-1.39653	-2.20923	-0.73170
Br	-1.43102	-1.24654	1.59847
Br	1.06885	-1.96244	-1.30792
Li	0.84071	-0.75030	0.82240
C	4.30821	0.31195	0.62509
O	2.37583	-0.43598	1.81378
C	5.09851	1.34870	0.08427
C	6.39188	1.10520	-0.35934
C	6.94772	-0.17312	-0.26969
C	6.18446	-1.20655	0.27717
C	4.88995	-0.96957	0.72034
H	-2.44990	2.33564	-1.03754
H	-0.36891	0.26300	-1.90730

H	1.25997	1.92459	-1.76165
H	0.16242	2.82325	-2.78253
H	0.52708	1.25527	1.96536
H	2.60469	2.32398	-0.02890
H	-4.78589	-1.63504	-1.39914
H	-7.01065	-1.63171	-0.28239
H	-7.62754	0.24062	1.22439
H	-6.03137	2.09681	1.61465
H	-3.83520	2.09695	0.50394
H	-1.04199	2.64939	0.86219
H	0.08832	3.87028	1.38133
H	1.06337	4.10044	-0.80922
H	-0.67825	4.14988	-0.96461
H	4.70530	2.35915	0.03204
H	6.97827	1.92282	-0.76875
H	7.96005	-0.35772	-0.61403
H	6.60398	-2.20571	0.35505
H	4.28838	-1.76880	1.13982

TS1(97a.3-101a.1-cis) (charge = -1; spin = 2)

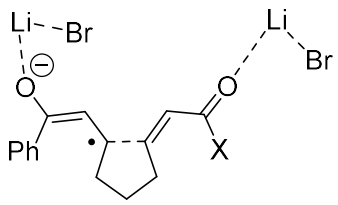


C	-4.70697	-0.83823	-0.85000
C	-3.71528	-1.14990	0.08879
C	-3.54391	-2.48527	0.47799

C	-4.35537	-3.48496	-0.04695
C	-5.34150	-3.16492	-0.97971
C	-5.51121	-1.84130	-1.38295
C	-2.81068	-0.11199	0.67335
O	-1.67731	-0.47717	1.08917
C	-3.25205	1.24572	0.74658
C	-2.40356	2.23845	1.16230
C	-2.79655	3.68751	1.19681
C	-3.11572	4.22491	-0.22175
C	-2.31974	3.46789	-1.30874
C	-1.05568	2.86193	-0.77705
C	-0.58755	1.62469	-1.18066
C	0.60132	0.99155	-0.77213
O	0.74360	-0.29005	-0.90878
C	3.86420	2.99479	1.16101
C	3.20785	3.61676	0.09891
C	2.13606	2.98841	-0.52746
C	1.70822	1.72264	-0.10378
C	2.38111	1.10129	0.95956
C	3.44648	1.73570	1.59016
Li	-0.42990	-1.43767	0.06971
H	-4.83228	0.18515	-1.18919
H	-2.77415	-2.72286	1.20607
H	-4.22130	-4.51348	0.27229
H	-5.97269	-3.94455	-1.39360
H	-6.26841	-1.59004	-2.11842
H	-4.24829	1.49477	0.39349

H	-1.46121	1.93653	1.61051
H	-3.66765	3.83377	1.84654
H	-1.97804	4.26675	1.63138
H	-4.18500	4.13200	-0.43375
H	-2.88776	5.29446	-0.24850
H	-2.10285	4.15212	-2.13993
H	-2.93028	2.65843	-1.72587
H	-0.41364	3.50122	-0.17374
H	-1.27534	0.98156	-1.73317
H	4.70008	3.48716	1.64725
H	3.53864	4.59028	-0.24866
H	1.63954	3.46459	-1.36731
H	2.05193	0.12011	1.29682
H	3.95275	1.24407	2.41488
Br	1.30155	-2.74046	1.25842
Li	2.25377	-1.38124	-0.65021
Br	4.53723	-1.44616	-1.23769

TS1(97a.3'-101a.1-cis) (charge = -1; spin = 2)

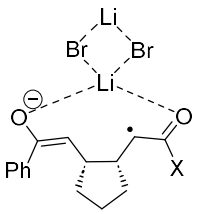


C	2.70713	-1.34316	2.18246
C	1.51042	-1.43103	1.45712
C	1.26602	-2.59963	0.72332
C	2.20111	-3.63275	0.68981

C	3.39532	-3.52378	1.39842
C	3.64021	-2.37469	2.15039
C	0.50072	-0.31950	1.42313
O	-0.73984	-0.66596	1.12739
C	0.90277	0.95654	1.65504
C	-0.03403	1.91983	1.96230
C	0.27803	3.26370	2.59196
C	-0.42509	4.51480	2.02341
C	-0.66173	4.22275	0.51818
C	0.13319	3.14101	-0.14657
C	-0.45195	2.07899	-0.84502
C	0.23481	0.99247	-1.49623
O	-0.42045	-0.01489	-1.84670
C	4.45186	0.99662	-2.22259
C	3.78564	-0.19136	-1.91866
C	2.41413	-0.18090	-1.69410
C	1.70516	1.02358	-1.74196
C	2.37351	2.21059	-2.05515
C	3.74393	2.19457	-2.30092
H	2.90098	-0.46741	2.79363
H	0.33516	-2.68977	0.17006
H	1.99457	-4.52422	0.10483
H	4.12347	-4.32831	1.37539
H	4.55814	-2.28633	2.72358
H	1.96018	1.16058	1.80315
H	-1.07559	1.58710	2.06186
H	-0.05727	3.00704	3.60047

H	1.36216	3.42394	2.63869
H	-1.37823	4.69012	2.52883
H	0.18188	5.41154	2.16961
H	-1.72777	4.05438	0.32719
H	-0.34212	5.04254	-0.12989
H	1.20072	3.34092	-0.29477
H	-1.53602	2.04654	-0.94244
H	5.52208	0.98764	-2.40245
H	4.33610	-1.12472	-1.85729
H	1.87986	-1.09489	-1.45524
H	1.81804	3.14161	-2.12609
H	4.25831	3.11577	-2.55363
Li	-1.76218	-2.11183	1.67160
Li	-1.74556	-0.58417	-0.49102
Br	-3.81774	0.69165	-0.30605
Br	-2.25472	-3.04797	-0.67820

Intermediate cis-101a.1 (charge = -1; spin = 2)

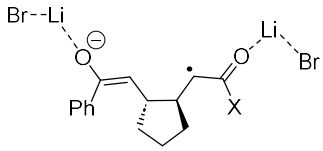


C	4.69745	-0.95379	0.78722
C	3.66422	-1.19785	-0.12460
C	3.46872	-2.49586	-0.61253
C	4.30255	-3.53106	-0.20655
C	5.33216	-3.28095	0.70064

C	5.52466	-1.99422	1.19995
C	2.72707	-0.12594	-0.57642
O	1.58847	-0.44580	-0.98988
C	3.12173	1.24874	-0.51597
C	2.17218	2.34584	-0.77978
C	2.87366	3.68961	-1.01394
C	3.24497	4.19761	0.39958
C	2.28641	3.47511	1.37871
C	1.29715	2.68063	0.50965
C	0.66786	1.48989	1.14609
C	-0.52901	0.94365	0.81606
O	-0.86026	-0.30111	1.12981
C	-3.54989	2.99538	-1.46422
C	-2.98296	3.61365	-0.35086
C	-1.99238	2.96339	0.38148
C	-1.55373	1.68727	0.01255
C	-2.13569	1.07107	-1.10349
C	-3.12340	1.72181	-1.83855
Li	0.31640	-1.41701	0.14751
H	4.84269	0.03900	1.20106
H	2.66345	-2.67536	-1.31817
H	4.15261	-4.53176	-0.59786
H	5.98192	-4.08902	1.02032
H	6.31689	-1.80072	1.91519
H	4.13775	1.48637	-0.21496
H	1.48320	2.04681	-1.57662
H	3.74074	3.60894	-1.67513

H	2.16236	4.37361	-1.48663
H	4.28588	3.95662	0.63459
H	3.15403	5.28457	0.46040
H	1.76117	4.16520	2.04434
H	2.84224	2.77702	2.01585
H	0.53246	3.36342	0.12456
H	1.33216	0.85142	1.73287
H	-4.32441	3.50050	-2.03244
H	-3.32027	4.59938	-0.04595
H	-1.56145	3.43507	1.26042
H	-1.81459	0.07052	-1.38908
H	-3.56274	1.23139	-2.70180
Br	-1.36940	-2.77086	-1.08028
Li	-2.36500	-1.28533	0.70418
Br	-4.67541	-1.25413	1.20841

Intermediate 101a.1 trans (charge = -1; spin = 2)

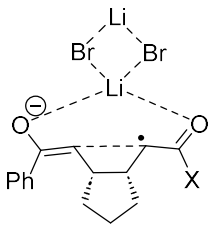


C	2.71679	1.31516	-2.18751
C	1.51940	1.41372	-1.46466
C	1.27945	2.58852	-0.73935
C	2.21937	3.61741	-0.71155
C	3.41412	3.49788	-1.41753
C	3.65470	2.34245	-2.16114
C	0.50440	0.30724	-1.42454

O	-0.73496	0.66162	-1.13312
C	0.90073	-0.97225	-1.64697
C	-0.01209	-2.14743	-1.57329
C	0.26647	-3.28288	-2.56886
C	-0.44344	-4.52666	-1.99274
C	-0.68098	-4.22306	-0.48994
C	0.08998	-2.92630	-0.20719
C	-0.46309	-2.07091	0.85870
C	0.22783	-0.98317	1.50344
O	-0.42318	0.02969	1.84590
C	4.44370	-1.00225	2.23635
C	3.78359	0.18673	1.92315
C	2.41238	0.18120	1.69655
C	1.69763	-1.01954	1.75165
C	2.35987	-2.20750	2.07410
C	3.72998	-2.19627	2.32187
H	2.90741	0.43428	-2.79229
H	0.34818	2.68691	-0.18817
H	2.01618	4.51389	-0.13308
H	4.14605	4.29909	-1.39894
H	4.57307	2.24577	-2.73228
H	1.95738	-1.18233	-1.79203
H	-1.05191	-1.81047	-1.67676
H	-0.06608	-3.03163	-3.57964
H	1.34989	-3.44857	-2.61279
H	-1.39664	-4.70096	-2.49841
H	0.15948	-5.42726	-2.13178

H	-1.74650	-4.04833	-0.30177
H	-0.36625	-5.03984	0.16429
H	1.15633	-3.13023	-0.05595
H	-1.54715	-2.03266	0.95421
H	5.51367	-0.99710	2.41779
H	4.33856	1.11702	1.85618
H	1.88282	1.09604	1.45053
H	1.79988	-3.13536	2.15062
H	4.23959	-3.11811	2.58176
Li	-1.74959	2.10851	-1.68892
Li	-1.74351	0.59582	0.48425
Br	-3.82144	-0.67143	0.30492
Br	-2.24126	3.06325	0.65357

TS2(101a.1-98a.1-cis) (charge = -1; spin = 2)

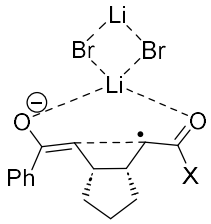


C	1.00974	-1.79207	-0.51212
C	1.65803	-1.32197	0.66481
C	-0.38131	-2.42036	-0.46486
C	-0.03732	-0.29586	-1.30583
C	-1.18068	-1.29139	-1.17109
C	-0.51452	-3.65582	-1.36628
C	-0.73140	-3.06651	-2.76728
C	-1.67365	-1.88333	-2.50112

C	0.01423	0.87737	-0.51264
O	-0.85213	1.11065	0.42546
C	1.16333	1.79835	-0.63426
C	2.31652	1.46364	-1.36356
C	1.13447	3.02417	0.04976
C	3.40188	2.33120	-1.40879
C	2.21880	3.89185	-0.00204
C	3.35876	3.54827	-0.72997
O	0.99612	-0.98832	1.69032
C	3.12556	-1.04624	0.65601
C	3.62306	-0.08216	1.54259
C	4.01609	-1.69360	-0.20988
C	4.97265	0.24856	1.54468
C	5.36828	-1.36476	-0.20461
C	5.84979	-0.38910	0.66697
Li	-0.53159	0.03912	1.99076
Br	-2.85442	-0.78146	2.37329
Li	-2.69128	0.95603	0.61447
Br	-4.43189	1.55883	-0.83473
H	-0.68791	-2.59721	0.56994
H	-2.00118	-0.89640	-0.56986
H	0.35416	-4.31851	-1.30113
H	-1.39978	-4.23043	-1.07112
H	-1.13880	-3.78804	-3.47988
H	0.22101	-2.70556	-3.17602
H	-1.68631	-1.14528	-3.30917
H	-2.69688	-2.25353	-2.37244

H	0.45322	-0.24426	-2.27560
H	2.38597	0.50383	-1.86538
H	0.24682	3.27772	0.61929
H	4.29134	2.04816	-1.96309
H	2.17821	4.83810	0.52839
H	4.20868	4.22224	-0.76356
H	1.65284	-2.11086	-1.32925
H	2.92689	0.41509	2.21004
H	3.66004	-2.46968	-0.87973
H	5.34254	1.00843	2.22583
H	6.04882	-1.87558	-0.87820
H	6.90404	-0.13151	0.66634

TS2(101a.1-98a.1-trans) (charge = -1; spin = 2)

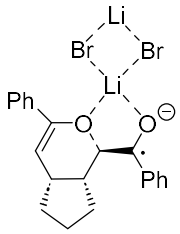


C	-3.93560	2.89791	-1.32866
C	-5.18042	2.27381	-1.25252
C	-5.25749	0.89614	-1.05803
C	-4.09392	0.14397	-0.91768
C	-2.84317	0.76624	-0.98004
C	-2.77257	2.14526	-1.20699
C	-1.56445	-0.00152	-0.88294
C	-1.35595	-1.01690	0.08250
O	-0.63292	0.32534	-1.67330

C	-2.25599	-1.53120	1.16703
C	-0.64321	-0.06033	2.31192
C	-1.43663	-1.33929	2.47425
C	-0.68115	-2.68303	2.68907
C	-1.12195	-3.62187	1.54435
C	-2.46404	-3.05111	1.06185
C	0.65793	0.10509	1.89862
C	1.13737	1.51831	1.69756
O	1.52438	-0.83267	1.67434
C	0.30950	2.51699	1.17238
C	0.79183	3.80877	0.97325
C	2.10911	4.12364	1.30390
C	2.94400	3.13311	1.82060
C	2.46359	1.84019	2.00241
Li	0.99729	-0.49270	-2.13027
Br	1.61697	-2.80621	-1.38018
Li	2.55679	-1.03456	0.19187
Br	3.00023	0.79426	-1.49116
H	-3.87273	3.96912	-1.48986
H	-6.08854	2.85914	-1.35386
H	-6.22431	0.40516	-1.02030
H	-4.15654	-0.93255	-0.78887
H	-1.79587	2.61362	-1.28579
H	-3.19154	-0.96991	1.20647
H	-2.14389	-1.20532	3.30137
H	0.39733	-2.53100	2.68965
H	-0.96964	-3.10743	3.65558

H	-0.39360	-3.58948	0.72642
H	-1.20473	-4.66432	1.86412
H	-3.27051	-3.34484	1.74408
H	-2.73780	-3.37998	0.05381
H	-0.71223	2.26900	0.89777
H	0.13989	4.56877	0.55249
H	2.48510	5.13029	1.15022
H	3.97332	3.36907	2.07405
H	3.11623	1.05440	2.37171
H	-0.37642	-1.48770	0.01792
H	-1.20999	0.84760	2.49985

TS2(101a.1-100a.1) (charge = -1; spin = 2)

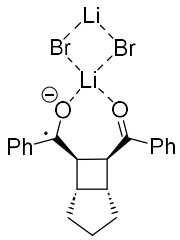


C	-0.49586	3.42115	-0.92427
C	0.58230	2.94681	0.07702
C	-0.18972	2.78616	1.39829
C	-1.33718	3.82772	1.32034
C	-1.22151	4.47895	-0.07455
C	1.44439	1.82577	-0.41109
O	-0.03718	0.48049	-0.83952
C	-1.19963	1.00383	-1.21810
C	-1.44680	2.32681	-1.32807
C	-2.24765	-0.01627	-1.53623

C	-3.61451	0.24246	-1.37930
C	-4.56062	-0.74489	-1.63746
C	-4.15811	-2.01548	-2.05076
C	-2.79881	-2.28574	-2.20716
C	-1.85268	-1.29505	-1.94661
C	2.17604	0.91493	0.40419
C	3.46239	0.35410	-0.09942
C	3.88035	-0.89671	0.37641
C	5.07803	-1.45433	-0.05700
C	5.88537	-0.76610	-0.96286
C	5.48628	0.48494	-1.43077
C	4.28651	1.04307	-0.99990
O	1.68767	0.45244	1.48771
Li	0.10174	-0.46205	0.80258
Li	-1.90420	-2.70096	0.83156
Br	-2.04403	-0.54346	2.06577
Br	0.53743	-2.92097	0.46957
H	-0.02626	3.88426	-1.80459
H	1.27038	3.80190	0.19249
H	-0.60340	1.78030	1.47096
H	0.45924	2.93182	2.26526
H	-2.30216	3.32159	1.42234
H	-1.27977	4.57411	2.11700
H	-0.60626	5.38466	-0.02121
H	-2.19132	4.76190	-0.49438
H	1.83064	1.97766	-1.41649
H	-2.41472	2.63906	-1.71070

H	-3.93437	1.21331	-1.01332
H	-5.61563	-0.52833	-1.50005
H	-4.89648	-2.78637	-2.24754
H	-2.47203	-3.27077	-2.52869
H	-0.79349	-1.50832	-2.04142
H	3.23381	-1.42417	1.06994
H	5.38408	-2.42918	0.31002
H	6.82210	-1.19968	-1.29823
H	6.11621	1.03244	-2.12471
H	4.00213	2.03177	-1.347

Intermediate *cis*-98a.1 (charge = -1; spin = 2)

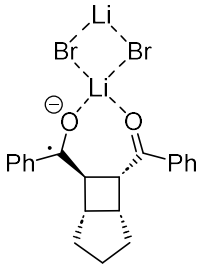


C	-1.98144	3.42450	1.98828
C	-1.74648	4.36485	0.97847
C	-1.03706	3.96384	-0.15812
C	-0.57504	2.66434	-0.28794
C	-0.80108	1.69192	0.72752
C	-1.52419	2.12226	1.87505
C	-0.32540	0.35597	0.53368
C	-0.60196	-0.77722	1.46428
O	0.32831	0.03985	-0.56460
C	0.60871	-1.70443	1.78068
C	-1.34085	-2.04527	0.82930

C	-0.13531	-2.93459	1.17901
C	-0.36075	-3.90308	2.34561
C	-0.31193	-3.00976	3.59504
C	0.80737	-2.00933	3.26739
C	-1.66864	-1.90589	-0.62802
C	-2.75312	-0.96615	-1.02952
O	-1.03254	-2.51511	-1.49228
C	-3.42809	-0.17912	-0.09008
C	-4.39103	0.73442	-0.50877
C	-4.69004	0.85864	-1.86348
C	-4.02700	0.06948	-2.80523
C	-3.05998	-0.83633	-2.38978
Br	3.58181	1.92988	0.57603
Br	2.89490	-1.08848	-2.36758
Li	0.46764	-1.25252	-1.92007
Li	2.12939	0.52350	-0.64152
H	-2.53042	3.71596	2.87941
H	-2.10765	5.38292	1.07622
H	-0.84703	4.67755	-0.95528
H	-0.03561	2.36067	-1.17892
H	-1.72774	1.42877	2.68443
H	-1.11693	-0.45112	2.37063
H	1.52178	-1.39744	1.26445
H	-2.25977	-2.28912	1.37479
H	0.31791	-3.40110	0.30229
H	-1.29430	-4.46685	2.25202
H	0.46317	-4.62456	2.38187

H	-1.26581	-2.48079	3.71666
H	-0.13161	-3.57009	4.51570
H	1.78141	-2.48920	3.41717
H	0.77982	-1.10769	3.88776
H	-3.19608	-0.26041	0.96681
H	-4.90115	1.35245	0.22230
H	-5.44048	1.57214	-2.18836
H	-4.26367	0.16617	-3.85939
H	-2.52777	-1.45254	-3.10690

Intermediate *trans*-98a.1 (charge = -1; spin = 2)

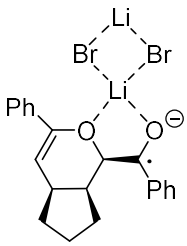


C	5.31368	0.00294	-1.56249
C	5.86394	-0.81761	-0.57709
C	5.03486	-1.48326	0.32391
C	3.65414	-1.33650	0.23654
C	3.09727	-0.51476	-0.74750
C	3.93552	0.15731	-1.64439
C	1.62435	-0.31453	-0.85931
C	0.68568	-1.20700	-0.09756
O	1.19178	0.58606	-1.57867
C	0.77696	-2.74477	-0.33554
C	-0.78213	-1.19158	-0.55590

C	-0.73350	-2.74888	-0.73821
C	-1.45307	-3.57946	0.32784
C	-0.53090	-3.49851	1.55182
C	0.87154	-3.59759	0.93558
C	-1.77498	-0.58011	0.41315
C	-3.16023	-0.57652	0.07822
O	-1.33440	-0.03408	1.50980
C	-3.66889	-1.17796	-1.11279
C	-5.02088	-1.14678	-1.41018
C	-5.93902	-0.52465	-0.55326
C	-5.45885	0.07398	0.62119
C	-4.11241	0.05205	0.93577
Li	1.06728	2.42451	-0.94561
Br	1.74060	2.11371	1.48799
Li	-0.69457	1.65905	1.30478
Br	-1.36150	3.04189	-0.65019
H	5.96044	0.51913	-2.26397
H	6.94053	-0.93725	-0.51147
H	5.46340	-2.11551	1.09400
H	3.01081	-1.84678	0.94425
H	3.49014	0.79161	-2.40369
H	0.78117	-0.93035	0.96259
H	1.49164	-3.03534	-1.10995
H	-0.87515	-0.70215	-1.53393
H	-0.95984	-3.07692	-1.75579
H	-2.46519	-3.21522	0.52463
H	-1.52423	-4.62026	-0.01010

H	-0.65527	-2.52461	2.04065
H	-0.72634	-4.27767	2.29325
H	1.08031	-4.63737	0.65780
H	1.66083	-3.27598	1.62235
H	-2.98523	-1.67347	-1.79687
H	-5.37284	-1.61515	-2.32610
H	-6.99665	-0.50543	-0.79363
H	-6.15526	0.56545	1.29665
H	-3.74721	0.52610	1.84116

Intermediate 100a.1 (charge = -1; spin = 2)

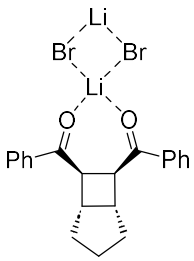


C	0.86816	3.14137	-0.71418
C	1.70142	2.03073	-0.04233
C	1.32566	2.07192	1.46339
C	0.41531	3.30374	1.64625
C	0.69041	4.17306	0.41415
C	1.48031	0.67110	-0.71171
O	0.08406	0.31636	-0.70385
C	-0.79226	1.30017	-1.09625
C	-0.45871	2.59364	-1.16025
C	-2.11242	0.74823	-1.47020
C	-3.28857	1.44301	-1.16337
C	-4.52712	0.92115	-1.51991

C	-4.60573	-0.30319	-2.18723
C	-3.43864	-1.00125	-2.49089
C	-2.19691	-0.48278	-2.12795
C	2.20917	-0.46188	-0.00684
C	3.59254	-0.67861	-0.26381
C	4.29229	-1.70316	0.44430
C	5.63434	-1.94548	0.22236
C	6.36460	-1.19165	-0.70910
C	5.70007	-0.17947	-1.41315
C	4.35653	0.08126	-1.20317
O	1.54145	-1.14478	0.86833
Li	-0.30173	-0.97964	0.77627
Li	-3.31194	-1.39598	0.88979
Br	-1.98321	0.28416	2.14688
Br	-1.53408	-3.08666	0.33843
H	1.39449	3.58026	-1.57071
H	2.76541	2.26314	-0.16046
H	0.81081	1.15806	1.77049
H	2.23306	2.15145	2.06923
H	-0.62924	2.97622	1.64639
H	0.59957	3.83157	2.58558
H	1.62845	4.72645	0.54197
H	-0.10204	4.89816	0.20449
H	1.77659	0.74917	-1.76766
H	-1.20656	3.28839	-1.53222
H	-3.22411	2.37709	-0.61365
H	-5.43333	1.46401	-1.27072
H	-5.57253	-0.71008	-2.46596
H	-3.49316	-1.95544	-3.00556

H	-1.28694	-1.03066	-2.34903
H	3.73656	-2.29557	1.16317
H	6.13063	-2.73577	0.78060
H	7.41813	-1.38598	-0.87853
H	6.24575	0.41889	-2.13848
H	3.88793	0.88061	-1.76973

Compound *cis*-98a (charge = 0; spin = 1)

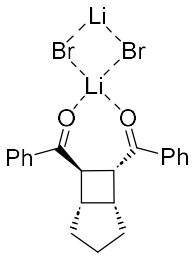


C	4.19415	-0.82120	-2.16042
C	4.47243	0.54283	-2.09225
C	3.47284	1.44949	-1.73659
C	2.19215	0.99481	-1.45258
C	1.91542	-0.37905	-1.50086
C	2.92060	-1.28680	-1.85135
C	0.55830	-0.80690	-1.08492
C	0.31528	-2.15757	-0.46234
O	-0.37546	-0.00728	-1.13879
C	-1.09601	-2.74386	-0.74415
C	-0.08915	-2.03017	1.06847
C	-1.50073	-2.55705	0.74986
C	-1.79106	-3.95920	1.29142
C	-0.96394	-4.88622	0.38729
C	-1.11977	-4.25337	-1.00382

C	0.01483	-0.62440	1.61453
C	1.36455	-0.03297	1.80598
O	-0.99517	0.05323	1.79077
C	2.53306	-0.78978	1.64888
C	3.77573	-0.17088	1.71338
C	3.85688	1.20294	1.93681
C	2.69689	1.96004	2.10243
C	1.45317	1.34558	2.03799
H	4.97086	-1.52228	-2.44573
H	5.47247	0.90092	-2.31467
H	3.69679	2.50920	-1.67461
H	1.40259	1.68055	-1.15354
H	2.71383	-2.35042	-1.90370
H	1.14493	-2.84764	-0.62177
H	-1.65706	-2.15940	-1.47585
H	0.50569	-2.70663	1.69011
H	-2.28531	-1.82559	0.95255
H	-1.54722	-4.05779	2.35359
H	-2.85679	-4.18092	1.16916
H	0.08998	-4.87262	0.69296
H	-1.29708	-5.92593	0.42200
H	-2.09576	-4.52438	-1.42077
H	-0.35272	-4.57147	-1.71601
H	2.48171	-1.85736	1.45849
H	4.67858	-0.75670	1.57990
H	4.82804	1.68592	1.97650
H	2.76420	3.02982	2.26950

H	0.53935	1.92337	2.12376
Li	-1.63604	0.86178	0.05019
Li	-3.30157	3.22330	-0.94106
Br	-3.96926	0.77096	-0.51331
Br	-0.95854	3.22415	-0.00416

Compound *trans*-98a (charge = 0; spin = 1)

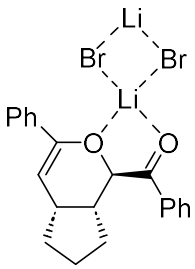


C	-5.37666	-0.18679	-1.57917
C	-5.94624	0.55934	-0.54656
C	-5.13385	1.21125	0.37946
C	-3.75006	1.12484	0.27045
C	-3.17433	0.37916	-0.76248
C	-3.99500	-0.28071	-1.68441
C	-1.70041	0.24133	-0.89697
C	-0.79181	1.12240	-0.07700
O	-1.22882	-0.57760	-1.68459
C	-0.89457	2.66255	-0.31034
C	0.67331	1.13355	-0.52970
C	0.62909	2.69403	-0.66032
C	1.29683	3.50362	0.46042
C	0.31559	3.42118	1.63829
C	-1.05463	3.51233	0.95406

C	1.68808	0.54614	0.41394
C	3.12548	0.57984	0.03569
O	1.33673	0.05408	1.48476
C	3.55751	1.19887	-1.14242
C	4.90952	1.20314	-1.47030
C	5.83166	0.58691	-0.62674
C	5.40520	-0.03331	0.54885
C	4.05724	-0.03433	0.88051
Li	-0.76450	-2.36474	-0.98863
Br	-1.62839	-2.13907	1.39350
Li	0.82611	-1.84327	1.62152
Br	1.64938	-2.69042	-0.57252
H	-6.01151	-0.69365	-2.29790
H	-7.02577	0.63026	-0.46232
H	-5.57757	1.78364	1.18667
H	-3.12099	1.61993	1.00136
H	-3.53341	-0.85849	-2.47807
H	-0.91257	0.83381	0.97527
H	-1.57756	2.94002	-1.11629
H	0.79750	0.64538	-1.50186
H	0.89426	3.05038	-1.65699
H	2.30492	3.15566	0.70515
H	1.38380	4.54486	0.13221
H	0.41641	2.45751	2.15233
H	0.47501	4.20798	2.37890
H	-1.25466	4.54989	0.66470
H	-1.87554	3.18651	1.59889

H	2.84526	1.67943	-1.80551
H	5.24238	1.68449	-2.38331
H	6.88540	0.58793	-0.88596
H	6.12533	-0.51503	1.20143
H	3.70491	-0.51844	1.78541

Compound 100a (charge = 0; spin = 1)



C	0.95588	3.08414	-0.65623
C	1.77868	1.92980	-0.04522
C	1.44906	1.92353	1.47273
C	0.55685	3.15746	1.71823
C	0.82931	4.07058	0.51919
C	1.45368	0.61032	-0.76175
O	0.06828	0.30091	-0.67218
C	-0.78570	1.32139	-1.05945
C	-0.39454	2.59720	-1.10285
C	-2.11665	0.81084	-1.44260
C	-3.27078	1.53815	-1.12990
C	-4.52236	1.05842	-1.49766
C	-4.63455	-0.15575	-2.17906
C	-3.48866	-0.88581	-2.48792
C	-2.23300	-0.40883	-2.11614

C	2.18110	-0.54939	-0.10501
C	3.63688	-0.71883	-0.31634
C	4.31227	-1.65300	0.47986
C	5.67615	-1.85037	0.31602
C	6.37389	-1.11891	-0.64614
C	5.70764	-0.19067	-1.44366
C	4.34160	0.01234	-1.28153
O	1.55315	-1.29600	0.63773
Li	-0.40941	-1.00147	0.78825
Li	-3.41229	-1.36678	0.88335
Br	-2.02657	0.31144	2.12613
Br	-1.60353	-3.07717	0.33066
H	1.47884	3.54126	-1.50386
H	2.84325	2.13249	-0.19370
H	0.93022	1.00949	1.77898
H	2.37608	1.97640	2.04986
H	-0.49121	2.84220	1.71972
H	0.76496	3.64063	2.67553
H	1.78266	4.59564	0.64820
H	0.05004	4.81996	0.35469
H	1.71603	0.68771	-1.82396
H	-1.10793	3.32973	-1.46832
H	-3.17978	2.46298	-0.56845
H	-5.41283	1.62514	-1.24565
H	-5.61219	-0.52984	-2.46553
H	-3.57020	-1.83119	-3.01480
H	-1.33901	-0.97900	-2.34647

H	3.75222	-2.21206	1.22146
H	6.19765	-2.57197	0.93512
H	7.43991	-1.27442	-0.77534
H	6.25045	0.37303	-2.19411
H	3.83770	0.73216	-1.91773

iPr$_2$NEt (charge = 0; spin = 1)

N	-0.00401	0.27285	-0.22387
C	0.29881	1.46160	0.56686
C	1.04005	-0.76390	-0.19467
C	-1.38214	-0.20862	-0.05898
C	-0.30094	2.72998	-0.03418
C	1.67189	-1.03808	1.17965
C	2.12706	-0.42572	-1.21643
C	-1.63457	-1.06787	1.18753
C	-1.85817	-0.93070	-1.32016
H	-0.02063	1.35750	1.61940
H	1.38580	1.58414	0.59104
H	0.56055	-1.69274	-0.52359
H	-1.99760	0.69269	0.04091
H	-0.01426	3.60437	0.55678
H	0.06194	2.86387	-1.05665
H	-1.39322	2.69704	-0.06446
H	2.32593	-1.91279	1.11619
H	2.28588	-0.19473	1.51072
H	0.91924	-1.23181	1.94660
H	2.89713	-1.20278	-1.24170

H	1.69263	-0.32541	-2.21392
H	2.61716	0.52055	-0.96164
H	-2.70327	-1.27951	1.28736
H	-1.11071	-2.02719	1.11841
H	-1.30605	-0.55978	2.09922
H	-2.92165	-1.17456	-1.24183
H	-1.70500	-0.29884	-2.19839
H	-1.31772	-1.87014	-1.47515

iPr$_2$NEt radical cation (charge = -1; spin = 2)

N	-0.00061	0.10869	0.25757
C	0.57315	1.19340	1.03210
C	0.85880	-0.89132	-0.37659
C	-1.45730	0.03379	0.12627
C	0.39141	2.53839	0.31215
C	1.55220	-1.73155	0.70583
C	1.85714	-0.21349	-1.32066
C	-1.96579	-1.28755	0.71451
C	-1.86385	0.21956	-1.34080
H	0.05018	1.20877	1.99471
H	1.62801	0.98452	1.20494
H	0.19967	-1.53876	-0.95704
H	-1.85265	0.86211	0.71885
H	0.83043	3.31415	0.94083
H	0.90167	2.53590	-0.65248
H	-0.66377	2.77360	0.16213
H	2.10951	-2.52350	0.20179

H	2.25605	-1.13471	1.28944
H	0.82450	-2.18959	1.37795
H	2.44396	-0.99843	-1.80139
H	1.34369	0.35833	-2.09619
H	2.54570	0.44148	-0.78124
H	-3.05649	-1.26923	0.67426
H	-1.61869	-2.14746	0.13715
H	-1.65829	-1.39871	1.75595
H	-2.95469	0.23361	-1.38295
H	-1.48871	1.16361	-1.74102
H	-1.51033	-0.60380	-1.96553

5.4 PHOTOELECTROCHEMICAL IRON(III)-CATALYSIS FOR LATE-STAGE C–H FLUOROALKYLATIONS

5.4.1 DESCRIPTION OF ELECTROPHOTOCHEMICAL SET-UP

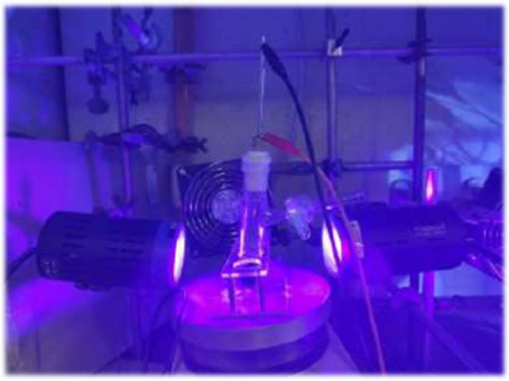
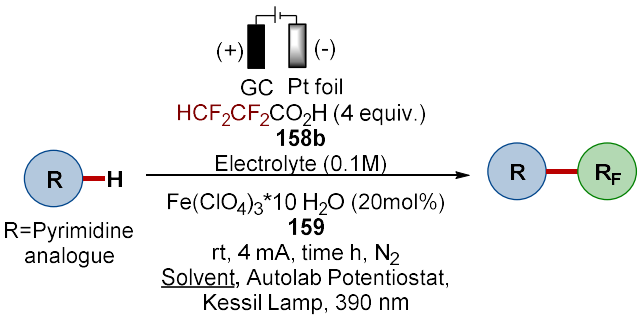


Figure 48: Electrophotochemical set-up

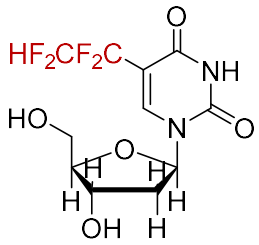
The electrophotochemical setup used to carry out this transformation is shown in **Figure 48**. The reaction mixture (typically 3 ml) and a stirring bar are placed in a 10 ml Schlenk-type undivided electrochemical cell, which is equipped with a cap that holds two stainless steel adapters. These holders can be adjusted within the cell to control the immersion depth of the electrodes in the solution. Additionally, the holders are positioned at a precise, standardized distance to prevent unwanted contact between the glassy carbon (25 mm × 10 mm × 1.5 mm) anode and Platinum (10 mm × 15 mm × 0.25 mm) cathode. The electrochemical cell is connected to a Metrohm MULTI AUTOLAB M204 potentiostat and positioned between two 75 W violet 390 nm LED Kessil lamps, placed on a stirring plate. To prevent overheating, two fans are used as a cooling system.

5.4.2 GENERAL PROCEDURE A FOR LATE-STAGE RADICAL FLUOROALKYLATION IN 2:1 DMSO/H_2O



A 15 mL Schlenk tube (undivided electrochemical cell) was charged with a substrate (1. equiv., 0.3 mmol), $LiClO_4$ (1 equiv. ,0.3 mmol, 32 mg), $Fe(ClO_4)_3{\cdot}10H_2O$ (20 mol% unless stated otherwise, 0.06 mmol, 32 mg) and a stirring bar (0.9 × 0.2 × 0.2 mm) for electrochemical reaction equipped with Platinum (Pt) cathode (25 × 10 × 0.2 mm) and glassy carbon (GC) anode (25 × 10 × 1.5 mm). Then the tube was evacuated and backfilled with nitrogen 3 times. A solution of 3*H*-tetrafluoropropanoic acid (4 equiv., 1.2 mmol, 175 mg,) in 2:1 DMSO/H_2O mixture (3 ml) was added under positive pressure of nitrogen, and the mixture was intensively stirred (1000 rpm) under 390 nm light and a constant current of 4 mA for 12 h. Then the mixture was exposed to air, diluted with 20 mL Ethyl acetate, and 5 mL of saturated aqueous $NaHCO_3$ solution was added. Aqueous layer was extracted with Ethyl acetate (4 × 30 mL), combined organic layers were dried over anhydrous Na_2SO_4, evaporated under reduced pressure and the crude product was purified by column chromatography on silica gel to afford fluoroalkylation products.

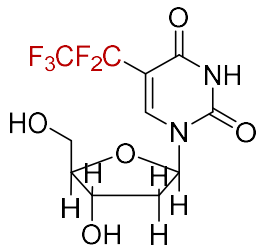
Compound 173



Product **173** was obtained from deoxyuridine (68 mg, 0.3 mmol) and 3*H*-tetrafluoropropionic acid (4 equiv.) according to the general procedure. Column chromatography (DCM/EtOAc, 1:1 to 1:2) afforded the title compound (74 mg, 75%) as a white solid.

^{1}H NMR (300 MHz, MeOH-d_4) δ 8.69 (t, *J* = 1.3 Hz, 1H), 6.52 (tt, *J* = 53.6, 6.1 Hz, 1H, CF_2CF_2H), 6.25 (t, *J* = 6.3 Hz, 1H), 4.42 (dt, *J* = 6.1, 3.9 Hz, 1H), 3.97 (q, *J* = 3.0 Hz, 1H), 3.89 – 3.69 (m, 2H), 2.41 – 2.21 (m, 2H) ppm; **^{13}C NMR** (75 MHz, MeOH-d_4) δ 162.4 (t, *J* = 4.2 Hz), 151.4, 143.8 (t, *J* = 9.4 Hz), 115.3 (tt, *J* = 247.9, 26.4 Hz, CF_2), 110.7 (tt, *J* = 249.2, 34.1 Hz, CF_2H), 105.9 (t, *J* = 24.3 Hz, $\underline{C_q}$-CF_2), 89.3, 87.5, 71.9, 62.3, 42.1 ppm; **^{19}F NMR** (282 MHz, MeOH-d_4) δ -118.7 – -119.1 (m, 2F), -139.3 – -140.8 (m, 2F) ppm; **mp** = 129-130 °C; **IR** (ATR): ṽ = 3400 (br), 1680, 1480, 1299, 1272, 1093, 1015, 785, 594 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{11}H_{12}F_4N_2O_5Na^+$: 351.0575 $[M+Na]^+$, found 351.0578.

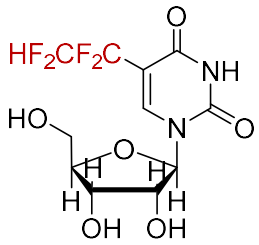
Compound 174



Product **174** was obtained from deoxyuridine (68 mg, 0.3 mmol) and perfluoropropionic acid (4.0 equiv.) according to general procedure, with a <u>reaction time of 36 h</u>. Column chromatography (DCM/EtOAc, 7:3 to 1:2) afforded the title compound (58 mg, 56%) as a colorless oil

^{1}H NMR (300 MHz, MeCN-d_3) δ 9.35 (br s), 8.64 (t, *J* = 1.1 Hz, 1H), 6.11 (t, *J* = 6.0 Hz, 1H), 4.34 (dq, *J* = 6.3, 4.4 Hz, 1H), 3.91 (dt, *J* = 4.4, 2.8 Hz, 1H), 3.73 (qdd, *J* = 12.0, 4.4, 2.8 Hz, 2H), 3.42 (d, *J* = 4.4 Hz, 1H), 3.31 (t, *J* = 4.5 Hz, 1H), 2.37 – 2.16 (m, 2H) ppm; **^{13}C NMR** (75 MHz, MeCN-d_3) δ 159.8 (br), 150.5, 145.3 (t, *J* = 9.7 Hz), 122.5-109.9 (m, CF_2CF_3, signals overlap with solvent), 102.2 (t, *J* = 23.8 Hz), 88.7, 87.3, 70.8, 61.5, 41.9 ppm; **^{19}F NMR** (282 MHz, MeCN-d_3) δ -84.9 (t, *J* = 2.1 Hz, 3F, CF_3), -111.2 – -114.9 (m, 2F, CF_2) ppm; **IR** (ATR): ṽ = 1735, 1680, 1468, 1368, 1210, 1095, 998, 809, 592, 560 cm^{-1}; **HRMS** (ESI) m/z calcd for $C_{17}H_{19}F_4N_2O_9^+$: 471.1021 $[M+H]^+$, found 471.1013.

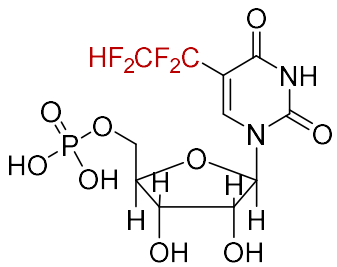
Compound 175



Product **175** was obtained from uridine (73 mg, 0.3 mmol) and 3H-tetrafluoropropionic acid (4 equiv.) according to the general procedure Column chromatography (DCM/EtOAc, 1:1 to 1:2) afforded the title compound (38 mg, 37%) as a colorless oil, which solidifies upon storage.

^{1}H NMR (300 MHz, MeOH-d_4) δ 8.80 (t, *J* = 1.3 Hz, 1H), 6.53 (tt, *J* = 53.6, 6.1 Hz, 1H, CF_2CF_2H), 5.91 (d, *J* = 3.3 Hz, 1H), 4.24 – 4.15 (m, 2H), 4.06 (dt, *J* = 4.8, 2.4 Hz, 1H), 3.91 (dd, *J* = 12.1, 2.5 Hz, 1H), 3.75 (dd, *J* = 12.1, 2.2 Hz, 1H) ppm; **^{13}C NMR** (75 MHz, CD_3CN) δ 162.4 (t, *J* = 4.2 Hz), 151.6, 144.0 (t, *J* = 9.4 Hz), 115.3 (tt, *J* = 247.7, 26.5 Hz, CF_2), 110.7 (tt, *J* = 248.6, 34.4 Hz, CF_2H), 106.0 (t, *J* = 24.3 Hz, C_q-CF_2), 91.4, 86.3, 76.4, 70.8, 61.4 ppm; **^{19}F NMR** (282 MHz, MeOH-d_4) δ -118.6 – -119.0 (m, 2F), -140.1 – -140.6 (m, 2F) ppm; **IR** (ATR): ṽ = 1686, 1474, 1275, 1098, 1058, 1007, 813, 655, 597, 561 cm^{-1}; **HRMS** (ESI) m/z calcd for $C_{11}H_{11}F_4N_2O_6^-$: 343.0559 $[M-H]^-$, found 343.0551.

Compound 176

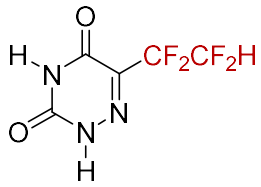


Product **176** was obtained from uridine monophosphoric acid (UMP) disodium salt (111 mg, 0.3 mmol) and 3*H*-tetrafluoropropionic acid (3 equiv.) according to the general procedure 2. Afterwards, the mixture was filtered and concentrated under reduced pressure.

The residue was directly analyzed by NMR and HRMS without further purification due to poor solubility of the product in organic solvents and instability on silica gel. ^{19}F NMR yield 76%.

^{19}F NMR (282 MHz, D_2O) δ -122.8 (td, *J* = 8.4, 5.5 Hz, 2F), -137.8 (dt, *J* = 52.8, 7.8 Hz, 2F) ppm; **^{31}P NMR** (122 MHz, D_2O) δ 4.85 ppm; **HRMS** (ESI) m/z calcd for $C_{11}H_{12}F_4N_2O_9P^-$: 423.0222 $[M-H]^-$, found 423.0217.

Compound 177

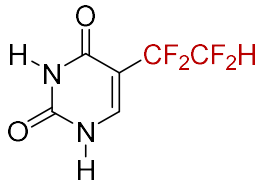


Product **177** was obtained from azauracil (34 mg, 0.3 mmol) and 3*H*-tetrafluoropropionic acid (4.0 equiv.) according to the general procedure.

Column chromatography (DCM/EtOAc, 7:3 to 2:3) afforded the title compound (61 mg, 95%) as a colorless oil

^{1}H NMR (300 MHz, MeOH-d_4) δ 6.53 (tt, *J* = 52.6, 5.7 Hz, 1H, CF_2CF_2H) ppm; **^{13}C NMR** (75 MHz, MeOH-d_4) δ 155.3, 148.9, 134.5 (t, *J* = 25.3 Hz, $\underline{C}_q$-CF_2), 113.0 (tt, *J* = 249.5, 27.0 Hz, CF_2), 110.2 (tt, *J* = 249.9, 31.7 Hz, CF_2H) ppm; **^{19}F NMR** (282 MHz, MeOH-d_4) δ -121.6 (td, *J* = 8.4, 5.5 Hz, 3F), -139.1 – -139.5 (m, 2F) ppm; **IR** (ATR): ṽ = 1690, 1603, 1428, 1270, 1231, 1103, 1013, 820, 755, 545 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_5H_2F_4N_3O_2^-$: 212.0089 $[M-H]^-$, found 212.0098.

Compound 178

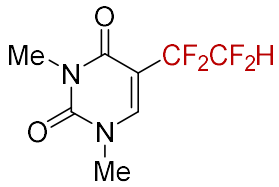


Product **178** was obtained from uracil (34 mg, 0.3 mmol) and 3*H*-tetrafluoropropionic acid (4.0 equiv.) according to the general procedure.

Column chromatography (DCM/EtOAc, 3:1 to 1:1) afforded the title compound (35 mg, 55%) as a white solid

^{1}H NMR (300 MHz, MeCN-d_3) δ 9.26 (br s, 2H, NH), 7.73 (t, *J* = 1.3 Hz, 1H), 6.54 (tt, *J* = 53.4, 6.1 Hz, 1H, CF_2H) ppm; **^{13}C NMR** (75 MHz, MeCN-d_3) δ 162.1 (br), 150.8, 144.25 (t, *J* = 9.4 Hz), 115.2 (tt, *J* = 246.5, 27.4 Hz, CF_2), 110.3 (tt, *J* = 248.7, 33.7 Hz, CF_2H), 104.5 (t, *J* = 24.6 Hz) ppm; **^{19}F NMR** (282 MHz, MeCN-d_3) δ -117.8 – -119.0 (m, 2F), -139.7 (dt, *J* = 53.3, 8.9 Hz, 2F) ppm; **IR** (ATR): ṽ = 1727, 1688, 1224, 1118, 1098, 815, 783, 663, 551, 444 cm^{-1}; **mp** = 221-222 °C (dec.); **HRMS** (ESI) m/z calcd for $C_6H_3F_4N_2O_2^-$: 211.0136 $[M-H]^-$, found 211.0139.

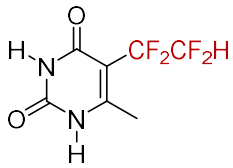
Compound 179



Product **179** was obtained from 1,3-dimethyluracil (42 mg, 0.3 mmol) and 3*H*-tetrafluoropropionic acid (4.0 equiv.) according to general procedure. Column chromatography (Hex/EtOAc, 4:3) afforded the title compound (58 mg, 81%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (t, *J* = 1.3 Hz, 1H, C6-H), 6.50 (tt, *J* = 53.8, 6.1 Hz, 1H, CF_2CF_2H), 3.48 (s, 3H, Me), 3.33 (s, 3H, Me) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.4 (t, *J* = 4.4 Hz), 151.0, 144.2 (t, *J* = 9.5 Hz), 113.8 (tt, *J* = 250.2, 27.7 Hz, CF_2) 109.1 (tt, *J* = 250.4, 33.5 Hz, CF_2H), 104.3 (t, *J* = 24.3 Hz, $\underline{C}_q$-CF_2CF_2H), 37.9, 28.1 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -118.3 (td, *J* = 9.4, 5.7 Hz, 2F), -138.7 (dt, *J* = 53.8, 9.1 Hz, 2F) ppm; **IR** (ATR): $\tilde{\nu}$ = 1713, 1670, 1657, 1640, 1491, 1458, 1097, 1002, 798, 752 cm^{-1}; **HRMS** (ESI) m/z calcd for $C_8H_7F_4N_2O_2^-$: 239.0449 $[M-H]^-$, found 239.0445.

Compound 180

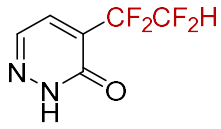


Product **180** was obtained from pseudothymine (38 mg, 0.3 mmol) and 3*H*-tetrafluoropropionic acid (4 equiv.) according to the general procedure.

Column chromatography (hexane/EtOAc, 1:1 to 1:2) afforded the title compound (46 mg, 68%) as a white solid

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.59 (tt, *J* = 53.9, 5.8 Hz, 1H, CF_2CF_2H), 2.34 (t, *J* = 4.0 Hz, 3H, Me) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 164.0 (t, *J* = 4.8 Hz), 158.5, 151.9, 117.3 (tt, *J* = 250.5, 26.9 Hz, CF_2H), 114.5 – 107.7 (m, CF_2), 102.6 (t, *J* = 24.0 Hz), 18.3 – 18.0 (m, 6-Me) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -111.0 – -113.3 (m, 2F), -140.17 (dt, *J* = 53.8, 8.4 Hz) ppm; mp = 140-141 °C; **HRMS** (ESI) m/z calcd for $C_7H_6F_4N_2O_2Na^+$: 249.0258 $[M+Na]^+$, found: 249.0260.

Compound 181

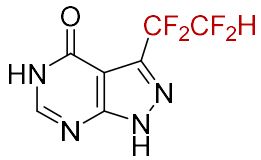


Product **181** was obtained from pyridazine-3(2*H*)-one (29 mg, 0.3 mmol) and 3*H*-tetrafluoropropanoic acid (3.0 equiv.) according to the general procedure.

Column chromatography (DCM/EtOAc, 7:3) afforded the title compound (44 mg, 75%) as a white solid

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, *J* = 4.1 Hz, 1H), 7.76 (dt, *J* = 4.1, 1.3 Hz, 1H), 6.73 (tt, *J* = 53.4, 6.1 Hz, 1H, CF_2CF_2H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.3 (t, *J* = 4.5 Hz), 138.2, 132.9 (t, *J* = 7.8 Hz), 131.9 (t, *J* = 24.0 Hz, $\underline{C}_q$-CF_2), 114.6 (tt, *J* = 249.9, 27.5 Hz), 110.6 (tt, *J* = 249.6, 32.2 Hz) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -123.1 (q, *J* = 7.8 Hz), -140.1 (dt, *J* = 53.3, 8.4 Hz) ppm; **IR** (ATR): $\tilde{\nu}$ = 1670, 1609, 1563, 1273, 1233, 1098, 1011, 871, 806, 669 cm^{-1}; **mp** = 118-119°C; **HRMS** (ESI) m/z calcd for $C_6H_5F_4N_2O^+$: 197.0333 $[M+H]^+$, found 197.0331.

Compound 182



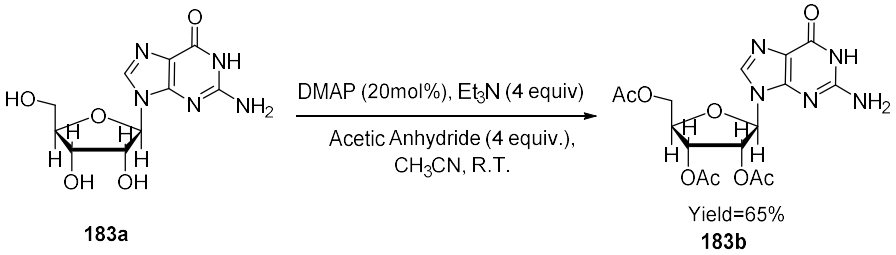
Product **182** was obtained from allopurinol (29 mg, 0.3 mmol) and 3H-tetrafluoropropanoic acid (4.0 equiv.) according to the general procedure.

Column chromatography (DCM/MeOH, 19:1) afforded the title compound (44 mg, 35%) as a white solid

^{1}H NMR (400 MHz, MeOH-d_4): δ 8.06 (s, 1H), 6.81 (tt, *J* = 52.8, 5.6 Hz, 1H, CF_2CF_2H) ppm; **^{13}C NMR** (101 MHz, MeOH-d_4) δ 158.5, 156.6, 149.9, 139.8 (t, *J* = 28.0 Hz, $\underline{C}_q$-CF_2), 113.4 (tt, *J* = 248.0, 25.8 Hz, CF_2), 111.3 (tt, *J* = 249.0, 33.4 Hz, CF_2H), 104.5 ppm; **^{19}F NMR** (377 MHz, MeOH-d_4) δ -117.3 (td, *J* = 9.2, 5.6 Hz), -140.1 (dt, *J* = 52.8, 9.1 Hz) ppm; **mp** = 176–180 °C; **IR** (ATR): $\tilde{\nu}$ = 1680, 1599, 1572, 1482, 1311, 1233, 1103, 983, 907, 815 cm^{-1}; **HRMS** (ESI): m/z calcd. for $C_7H_4F_4N_4ONa^+$: 259.0213 $[M+Na]^+$, found 259.0220.

5.4.3 SYNTHESIS OF PURINE ANALOGUES

Synthesis of compound **183b** [159]

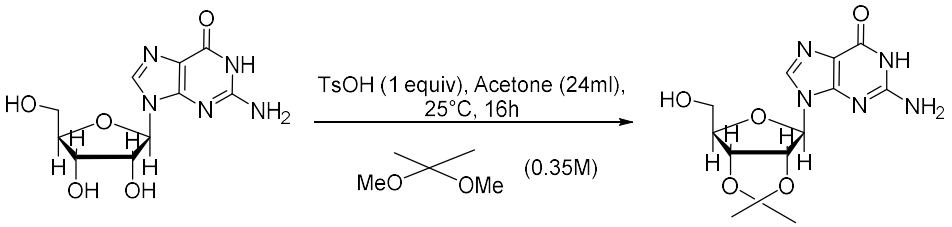


183a **183b**

Guanosine **183a** (500.0 mg, 1.9 mmol, 1.0 equiv.), DMAP (46.0 mg, 0.38 mmol, 0.2 equiv.) and triethylamine (1 mL, 7.6 mmol, 4.0 equiv.) were dissolved in acetonitrile (10 mL). Acetic anhydride (0.78 mL, 7.6 mmol, 4.0 equiv.) was added and the reaction mixture was stirred for 14 h at room temperature. The reaction was stopped by addition of 1 mL methanol and the solution was concentrated to dryness. The crude was then purified by column chromatography on flash silica gel using 200 ml of DCM and 400 ml of DCM:MeOH 95:5. The desired product was achieved as white solid in 65% yield.

Analytical data are in agreement with those reported in literature.[183]

Synthesis of **183c**[160]

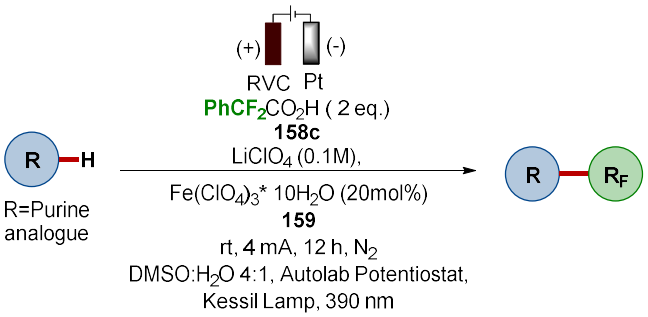


183a **183c**
Yield= 34%

Guanosine **183a** (500 mg, 1.9 mmol) was stirred in acetone (24 mL). p-Toluenesulfonic acid (327 mg, 1.9 mmol) and 2,2- dimethoxypropane (5 mL) were added and the reaction mixture was stirred overnight at 25 °C. The reaction mixture was evaporated to dryness and then dissolved in H_2O (0.5 mL). Solid $NaHCO_3$ (1 equiv., 159 mg) was added cautiously portion wise and the solution was stirred for 2 h. Saturated $NaHCO_3$ (1 mL) was added and the solution was stirred for a further 2 h. The suspension was filtered and the product washed with cold H_2O (2*10 mL) to yield a white solid (200 mg, 34%).

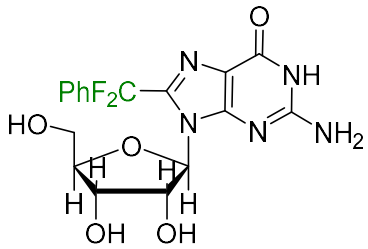
Analytical data are in agreement with those reported in literature.[184]

5.4.4 GENERAL PROCEDURE FOR LATE-STAGE RADICAL FLUOROALKYLATION IN 4:1 DMSO/H_2O



A 15 mL Schlenk tube (undivided electrochemical cell) was charged with a substrate (0.3 mmol), $LiClO_4$ (32 mg, 0.3 mmol), $Fe(ClO_4)_3 \cdot 10H_2O$ (32 mg, 0.06 mmol, 20 mol% unless stated otherwise) and a stirring bar (0.9 × 0.2 × 0.2 mm) for electrochemical reaction equipped with Platinum (Pt) cathode (25 × 10 × 0.2 mm) and Reticulated vitreous carbon (RVC) anode (25 × 10 × 1.5 mm). Then the tube was evacuated and backfilled with nitrogen. α,α-Difluorobenzeneacetic acid (103 mg, 0.6 mmol, 2 equiv.) in 4:1 DMSO/H_2O mixture (3 ml) was added under positive pressure of nitrogen, and the mixture was intensively stirred (1000 rpm) under 390 nm light and a constant current of 4 mA for 12 h. Then the mixture was exposed to air, diluted with 20 mL EtOAc, and 5 mL of saturated aqueous $NaHCO_3$ solution was added. Aqueous layer was extracted with EtOAc (4 × 30 mL), combined organic layers were dried over anhydrous Na_2SO_4, evaporated under reduced pressure and the crude product was purified by column chromatography on silica gel to afford fluoroalkylation products.

Compound 184a

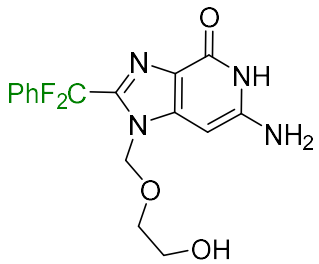


Product **184** was obtained from guanosine (68 mg, 0.3 mmol) and α,α-Difluorobenzeneacetic acid (2 equiv.) according to the general procedure. Column chromatography (DCM/EtOAc 1:1 to EtOAc/MeOH 9:1) afforded **27** (80 mg, 65%) as a yellowish solid.

After chromatography, DMSO residue were removed by trituration with DCM.

^{1}H NMR (300 MHz, DMSO-d_6) δ 10.89 (br s, 1H), 7.56 (s, 5H), 6.60 (br s, 1H), 5.95 (d, *J* = 5.8 Hz, 1H), 5.07 (t, *J* = 5.7 Hz, 1H), 4.23 (dd, *J* = 5.7, 3.6 Hz, 1H), 3.87 (q, *J* = 5.2 Hz, 1H), 3.70 (dd, *J* = 11.8, 4.7 Hz, 1H), 3.55 (dd, *J* = 11.8, 5.7 Hz, 1H) ppm; **^{13}C NMR** (75 MHz, DMSO-d_6) δ 156.5, 154.0, 152.5, 140.5 (m), 133.1 (m), 130.8 (t, *J* = 253.7 Hz, CF_2), 130.5, 128.4, 126.2 (t, *J* = 4.6 Hz), 116.4, 89.7, 86.0, 70.9, 70.7, 62.2 ppm; **^{19}F NMR** (282 MHz, DMSO-d_6) δ -83.4 (d, *J* = 272.8 Hz, 1F), -85.4 (d, *J* = 272.8 Hz, 1F) ppm; **IR** (ATR): ṽ = 3455, 3333, 3217, 3170, 2935, 1694, 1630, 1590, 1078, 1015 cm^{-1}; **mp** = 153-156 °C (dec.); **HRMS** (ESI) m/z calcd for $C_{17}H_{17}F_2N_5O_2Na^+$: 432.1090 $[M+Na]^+$, found 432.1095.

Compound 185

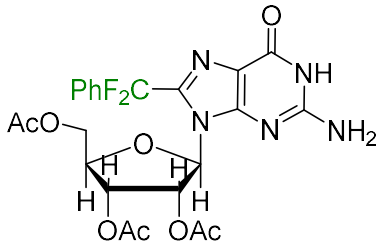


Product **185** was obtained from Aciclovir (67 mg, 0.3 mmol) and α,α-Difluorobenzeneacetic acid (2 equiv.) according to the general procedure. Column chromatography (DCM/EtOAc 1:1 to EtOAc/MeOH 9:1) afforded **185** (68 mg, 64%) as a yellowish solid.

After chromatography, DMSO residue were removed by trituration with DCM.

^{1}H NMR (300 MHz, DMSO-d_6) δ 10.81 (br s, 1H), 7.60 – 7.50 (m, 5H), 6.76 (br s, 2H), 5.49 (br s, 2H), 4.66 (t, *J* = 5.3 Hz, 1H), 3.56 – 3.34 (m, 3H) ppm; **^{13}C NMR** (75 MHz, DMSO-d_6) δ 156.6, 154.7, 153.3, 140.1 (t, *J* = 34.6 Hz), 134.4 (t, *J* = 25.6 Hz), 130.7, 128.4, 126.0 (t, *J* = 5.6 Hz), 117.1 (d, *J* = 238.7 Hz, CF_2), 115.3, 72.2 (CH_2), 70.7 (CH_2), 59.9 (CH_2) ppm; **^{19}F NMR** (282 MHz, DMSO-d_6) δ -87.5 (s, 2F) ppm; **IR** (ATR): ṽ = 3347, 3149, 2921, 1690, 1652, 1605, 1567, 1063, 1022, 691 cm^{-1}; **mp** = 151-153 °C; **HRMS** (ESI) m/z calcd for $C_{15}H_{15}F_2N_5O_3^+$: 352.1216 $[M+H]^+$, found 352.1223.

Compound 184d

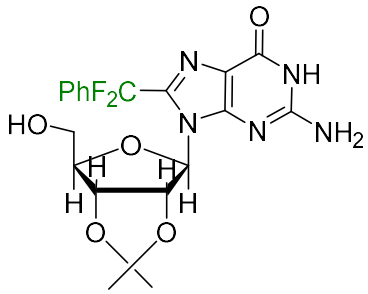


Product **184b** was obtained from guanosine triacetate **183b** (122 mg, 0.3 mmol) and α,α-Difluorobenzeneacetic acid (2 equiv.) according to the general procedure.

Column chromatography (DCM/EtOAc 7:3 to EtOAc afforded **183b** (105 mg, 65%) as a beige sticky oil. After chromatography DMSO residue were removed by fast trituration with H_2O.

^{1}H NMR (300 MHz, DMSO-d_6) δ 11.02 (br s, 1H), 7.54 (s, 5H), 6.75 (br s, 1H), 6.14 (dd, *J* = 6.6, 4.5 Hz, 1H), 6.02 (d, *J* = 4.6 Hz, 1H), 5.65 (t, *J* = 6.1 Hz, 1H), 4.48-4.23 (m, 3H), 2.08 (s, 3H, Me), 2.00 (s, 3H, Me), 1.97 (s, 3H, Me) ppm; **^{13}C NMR** (75 MHz, DMSO-d_6) δ 170.7, 169.9, 169.6, 157.1, 154.8, 153.0, 139.9 (t, *J* = 34.5 Hz), 134.1 (t, *J* = 25.1 Hz), 131.5, 129.0, 126.4 (t, *J* = 5.4 Hz), 117.6 (t, *J* = 235.5 Hz, CF_2), 116.5, 88.0, 80.1, 71.6, 70.6, 63.4, 20.9 (Me), 20.7 (Me), 20.5 (Me) ppm; **^{19}F NMR** (282 MHz, DMSO-d_6) δ -84.1 (d, *J* = 272.3 Hz, 1F), -86.4 (d, *J* = 272.3 Hz, 1F) ppm; **IR** (ATR): ν̃ = 3315, 3154, 2926, 1447, 1687, 1630, 1572, 1370, 1221, 1030, 701 cm^{-1}; **HRMS** (ESI) m/z calcd for $C_{23}H_{24}F_2N_5O_8^+$: 536.1587 $[M+H]^+$, found 536.1600.

Compound 184c



Product **184c** was obtained from guanosine 3,4-acetonide **183b** (106 mg, 0.3 mmol) and α,α-Difluorobenzeneacetic acid (2 equiv.) according to the general procedure 2. Column chromatography (DCM/EtOAc 1:1 to EtOAc/MeOH 8:2) afforded **184c** (105 mg, 80%) as a beige solid.

After chromatography DMSO residue were removed by fast trituration with H_2O..

^{1}H NMR (300 MHz, MeOH-d_4) δ 7.58-7.44 (m, 5H), 6.17 (d, *J* = 3.0 Hz, 1H), 5.43 (dd, *J* = 6.3, 2.9 Hz, 1H), 5.12 (dd, *J* = 6.3, 3.4 Hz, 1H), 4.22 (td, *J* = 5.0, 3.3 Hz, 1H), 3.89 – 3.69 (m, 2H). 1.50 (s, 3H, Me), 1.34 (s, 3H, Me) ppm; **^{13}C NMR** (75 MHz, MeOH-d_4) δ 159.5, 155.6, 153.9, 142.7 (t, *J* = 34.5 Hz), 135.5

(t, *J* = 25.3 Hz), 132.0, 129.6, 127.2 (t, *J* = 5.4 Hz), 118.3 (t, *J* = 238.4 Hz, CF_2), 117.5, 115.2, 92.1, 88.7, 84.6, 83.0, 63.7, 27.7 (Me), 25.7 (Me) ppm; **^{19}F NMR** (282 MHz, MeOH-d_4) δ -87.2 (s, 1F), -87.3 (s, 1F) ppm; **IR** (ATR): ṽ = 3505, 3319, 3209, 2928, 1648, 1568, 1499, 1236, 1027, 762, 693 cm^{-1}; **mp** = 190-191 °C (dec.); **HRMS** (ESI) m/z calcd for $C_{20}H_{21}F_2N_5O_5Na^+$: 472.1403 $[M+Na]^+$, found 472.1412.

Compound 186

Product **186** was obtained from 2-amino-6-chloropurine (51 mg, 0.3 mmol) and α,α-Difluorobenzeneacetic acid

(2 equiv.) according to the general procedure. Column chromatography (DCM/EtOAc 8:2) afforded **186** (37 mg, 40 %) as a yellow solid.

^{1}H NMR (300 MHz, DMSO-d_6) δ 7.65-7.52 (m, 5H, Ph), 6.98 (s, 2H, NH_2) ppm; **^{13}C NMR** (75 MHz, DMSO-d_6) δ 160.5, 155.8, 155.2, 146.7 (t, *J* = 35.1 Hz), 134.0 (t, *J* = 26.3 Hz), 131.1 (br s, CH), 128.9 (CH), 125.6 (t, *J* = 5.6 Hz), 116.2 (t, *J* = 240.3 Hz, CF_2) ppm; **^{19}F NMR** (282 MHz, DMSO-d_6) δ -90.0 (s, 2F) ppm; **IR** (ATR): ṽ = 3503, 3320, 3206, 2927, 1640, 1567, 1524, 1229, 1025, 993, 898, 691 cm^{-1}; mp = 158-162 °C (dec.) **HRMS** (ESI) m/z calcd for $C_{12}H_9F_2N_5Cl^+$: 296.0509 $[M+H]^+$, found 296.0517.

5.4.5 ICP-MS ANALYSIS OF IRON(III) PERCHLORATE DECAHYDRATE

The iron(III) perchlorate hydrate sample material (10-15 mg) was ultra-sonicated in King's water (0.6 mL conc. HCl, 0.2 mL conc. HNO_3; trace metal grad) for 5 h at 50 °C. Then, the sample was diluted to 10 mL with water (LC-MS grade) and sonicated for 10 min at rt. The obtained sample was centrifuged for 20 min at 8000 rpm, decanted in a new vial, and measured on a Thermo Scientific™ iCAP™ RQ. For the analysis of the reaction mixture, a typical batch was evaporated to dryness and was used as the sample material (ca. 10 mg).

Metal	Co	Ni	Cu	Ru	Rh	Pd
Content (ppm)	0.976	11.94	18.72	0.223	1 ppb	48 ppb

5.4.6 SPETTROELECTROCHEMICAL MEASUREMENT

Spectroelectrochemical (SEC) analyses were measured using an AUTOLAB potentiostat with the corresponding SEC cell. Temperature control was ensured with 3 the AUTOLAB Microcell HC. Avantes AvaLight-DH-S-BAL was used as the light source and an Avantes AvaSpec-ULS2048x64-EVO and Avantes AvaSpec-NIR were used for absorption measurement. The evaluation of the SEC data was carried out with the software AvaSoft 8 from Avantes and Nova 2.1. A solution of $Fe(ClO_4)_3 \cdot 10H_2O$ (10 mM) and 2,2-difluoropropionic acid (40 mM) in MeCN (1.5 mL) was prepared. As supporting electrolyte, $LiClO_4$ (0.1 M) was added. The solution was analyzed spectroelectrochemically, and 2 scans (0 V→2.5 V→-1.0 V→0 V) were performed at RT under the rate of 5 mV/s (**Figure 48**).

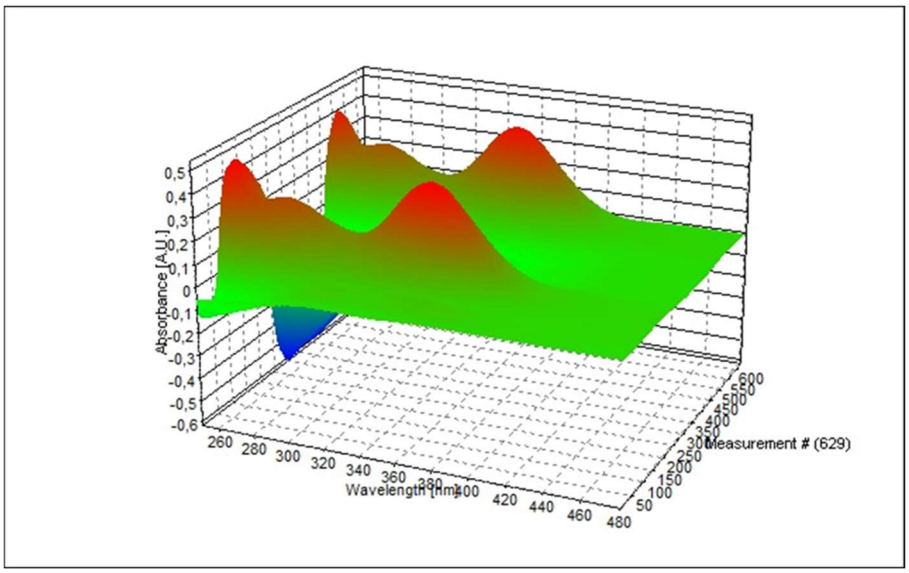


Figure 48: A solution of $Fe(ClO_4)_3 \cdot 10H_2O$ (10 mM), 2,2-difluoropropionic acid (80 mM) and caffeine **157a** (40 mM) in MeCN (1.5 mL) was prepared. As a supporting electrolyte, $LiClO_4$ (0.1 M) was added. The solution was analyzed spectroelectrochemically, and 2 scans (0 V→2.5 V→-1.0 V→0 V) were performed at RT under the rate of 5 mV/s.

5.4.7 EVALUATION OF RADICAL PHILICITY BY DFT CALCULATIONS

All calculation were performed using Gaussian 16, Revision A.03 package[185]. All structures were optimized at the ωB97X-D[185] level of theory with a def2-TZVPP basis set.[186] Analytical frequencies were carried out at the same level of theory in order to identify each stationary point as an intermediate (absence of imaginary frequencies). These also provided thermal and non-thermal corrections to the Gibbs free energy at 298.15 K. The electronic energy was then refined through ωB97X-D[187] single-point calculations on the optimized geometries in combination with a def2-QZVPP basis set.[186] Solvent effects were included implicitly in the single points calculation through the use of the SMD model.[187] In the latter, parameters for acetonitrile, octanol or water were used as implemented in Gaussian 16. Herein, the reported energies are based on gas-phase Gibbs free energies with a def2-TZVPP basis set for which the electronic energies were refined to ωB97X-D with a def2-QZVPP basis set and solvent effects. Nucleophilicity was determined according to[188] taking malononitrile radical as reference, whereas lipophilicity was obtained according to [189].

Structure	E_{HOMO}	E_{LUMO}
$CF_3CF_2CF_2^{\bullet}$	-0.341770	-0.027740
$CHF_2CF_2^{\bullet}$	-0.330560	-0.014880
$CF_3CF_2^{\bullet}$	-0.345840	-0.024140
$ClCF_2^{\bullet}$	-0.334210	-0.021630
$EtCF_2^{\bullet}$	-0.298480	0.016620
$CF_3^{\bullet}$	-0.352600	-0.016710
$CHF_2^{\bullet}$	-0.313560	0.012190
$MeCF_2^{\bullet}$	-0.299850	0.016700
$PhCF_2^{\bullet}$	-0.247610	-0.011850
Malononitrile$^{\bullet}$	-0.359860	-0.097270

Table 19: Calculated HOMO (E_{HOMO}) and LUMO (E_{LUMO}) energies at the ωB97X-D+SMD(Acetonitrile)/def2-QZVPP//ωB97X-D/def2-TZVPP level of theory used in the nucleophilicity determination (all in Hartree).

Structure	$E_{el,O}$	DG_O	$E_{el,W}$	DG_W
$CF_3CF_2CF_2^\bullet$	-813.316433	-813.315094	-813.310952	-813.309613
$CHF_2CF_2^\bullet$	-476.211222	-476.208919	-476.207762	-476.205459
$CF_3CF_2^\bullet$	-575.479616	-575.486370	-575.475315	-575.482069
$ClCF_2^\bullet$	-697.992679	-698.009941	-697.988965	-698.006227
$EtCF_2^\bullet$	-317.020901	-316.974078	-317.016515	-316.969692
$CF_3^\bullet$	-337.634842	-337.649236	-337.632179	-337.646573
$CHF_2^\bullet$	-238.366806	-238.372552	-238.364863	-238.370609
$MeCF_2^\bullet$	-277.701504	-277.681461	-277.698180	-277.678137
$PhCF_2^\bullet$	-469.454051	-469.386622	-469.448248	-469.380819

[a] Subscripts O and W correspond to the octanol and water respectively.

Table 20: Calculated electronic energies (E_{el}) and Gibbs free energies (DG) at the ωB97X-D+SMD(Octanol or Water)/def2-QZVPP//ωB97X-D/def2-TZVPP level of theory used in the lipophilicity determination (all in Hartree).[a]

Cartesian coordinates of the optimized structures

$CF_3CF_2CF_2^\bullet$

Lowest frequency = 36.4373 cm^{-1}

Charge = 0, Multiplicity = 2

10

C	-1.328363	-2.227825	1.766850
C	-0.574884	-0.920855	1.583717
C	-0.318526	-0.486482	0.107329
F	-2.579849	-2.222664	1.371533
F	-0.692848	-3.309287	1.380760
F	-1.278817	0.055277	2.175392
F	0.618917	-1.037682	2.183378
F	0.342922	0.661525	0.078544

F	-1.473269	-0.332605	-0.530623
F	0.397876	-1.410506	-0.522801

$CHF_2CF_2^{\bullet}$

Lowest frequency = 66.5645 cm^{-1}

Charge = 0, Multiplicity = 2

7

C	-1.327824	-2.222999	1.793627
C	-0.577139	-0.924703	1.577437
F	-2.570691	-2.204101	1.353568
F	-0.685845	-3.291873	1.364659
H	-0.439084	-0.695970	0.513702
F	0.633021	-1.017207	2.158339
F	-1.267440	0.079642	2.147602

$CF_3CF_2^{\bullet}$

Lowest frequency = 65.1603 cm^{-1}

Charge = 0, Multiplicity = 2

7

C	-1.203485	-2.167471	1.785856
F	-2.514542	-2.103742	1.750192

F	-0.737139	-3.155362	1.057183
C	-0.501847	-0.836953	1.562992
F	-0.959920	0.061288	2.426181
F	0.805774	-0.984609	1.736121
F	-0.707850	-0.369206	0.326434

$ClCF_2^\bullet$

Lowest frequency = 368.7214 cm^{-1}

Charge = 0, Multiplicity = 2

4

C	-1.297058	-2.173341	1.229050
F	-2.551309	-2.186404	1.622899
F	-0.679740	-3.266558	1.619298
Cl	-0.453927	-0.713826	1.611585

$EtCF_2^\bullet$

Lowest frequency = 92.5366 cm^{-1}

Charge = 0, Multiplicity = 2

10

C	-1.308062	-2.183531	1.753076
C	-0.562836	-0.901860	1.594022
C	-0.331735	-0.515086	0.128375

H	0.388334	-1.008690	2.115462
H	-1.130001	-0.126475	2.108980
H	0.214968	0.425344	0.071852
H	0.248738	-1.277972	-0.388848
H	-1.278565	-0.390499	-0.395500
F	-2.562098	-2.180981	1.299278
F	-0.681613	-3.273237	1.307342

$CF_3^\bullet$

Lowest frequency = 513.6813 cm^{-1}

Charge = 0, Multiplicity = 2

4

C	-1.290034	-2.161494	1.224842
F	-2.543944	-2.163658	1.617585
F	-0.664042	-3.249318	1.613801
F	-0.663796	-1.078478	1.626604

$CHF_2^\bullet$

Lowest frequency = 557.3242 cm^{-1}

Charge = 0, Multiplicity = 2

4

C	-1.281102	-2.146435	1.277813

F	-2.564259	-2.187110	1.590530
F	-0.674452	-3.278923	1.586665
H	-0.764780	-1.254113	1.627825

$MeCF_2^{\bullet}$

Lowest frequency = 194.1401 cm^{-1}

Charge = 0, Multiplicity = 2

7

C	-1.312228	-2.195222	1.789835
C	-0.576798	-0.923569	1.571827
H	0.407036	-0.985657	2.031196
H	-1.128642	-0.099221	2.017695
F	-2.572200	-2.209778	1.358629
F	-0.688181	-3.296339	1.375465
H	-0.455848	-0.729930	0.500304

$PhCF_2^{\bullet}$

Lowest frequency = 117.7002 cm^{-1}

Charge = 0, Multiplicity = 2

14

C	-1.282731	-2.149983	1.525277
F	-2.593460	-2.249382	1.522960

F	-0.709545	-3.332925	1.528170
C	-0.591553	-0.948309	1.522224
C	0.826813	-0.929245	1.523968
C	-1.288244	0.287302	1.518054
C	1.498767	0.271361	1.521656
H	1.372963	-1.861704	1.527069
C	-0.588304	1.471810	1.515821
H	-2.368871	0.290542	1.516607
C	0.805229	1.480076	1.517618
H	2.580784	0.272110	1.522976
H	-1.131706	2.407474	1.512598
H	1.344224	2.417151	1.515843

Malononitrile●

Lowest frequency = 153.4059 cm^{-1}

Charge = 0, Multiplicity = 2

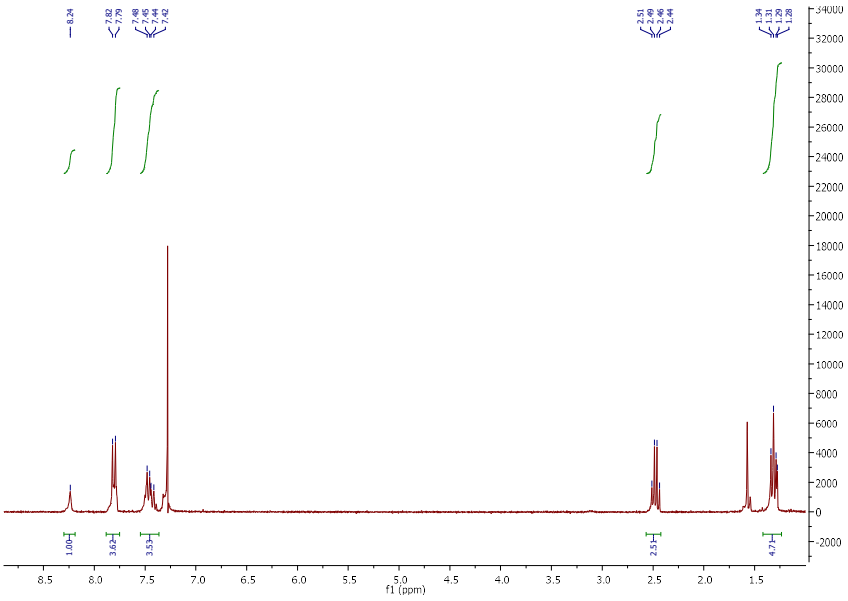
6

C	0.097915	-0.208537	0.302171
H	0.684048	0.618973	0.677924
C	-1.264000	-0.023852	0.066014
N	-2.390684	0.156802	-0.119842
C	0.726045	-1.431384	0.067002
N	1.272460	-2.432960	-0.119625

5.5 NMR SPECTRA

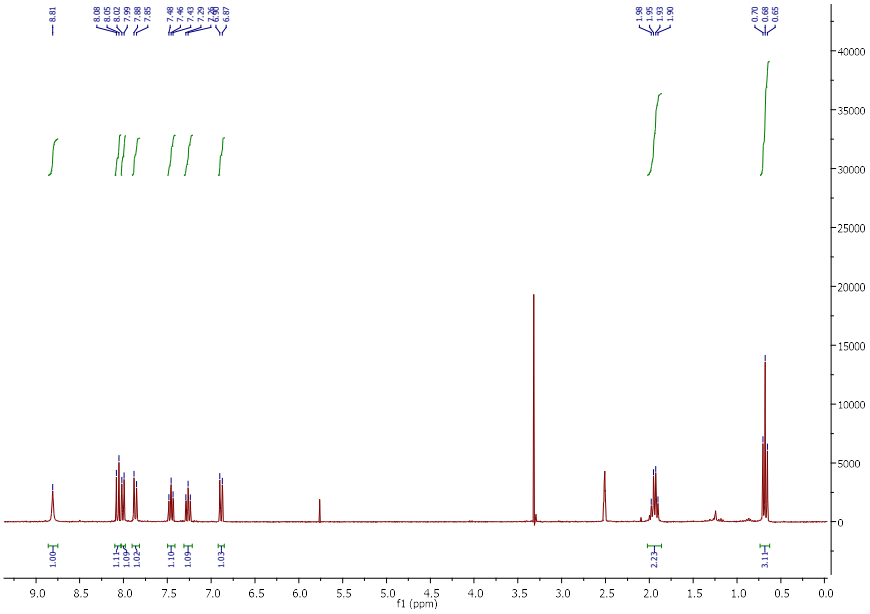
COMPOUND **67**

^{1}H-NMR of **67**, CDCl3, 300MHz



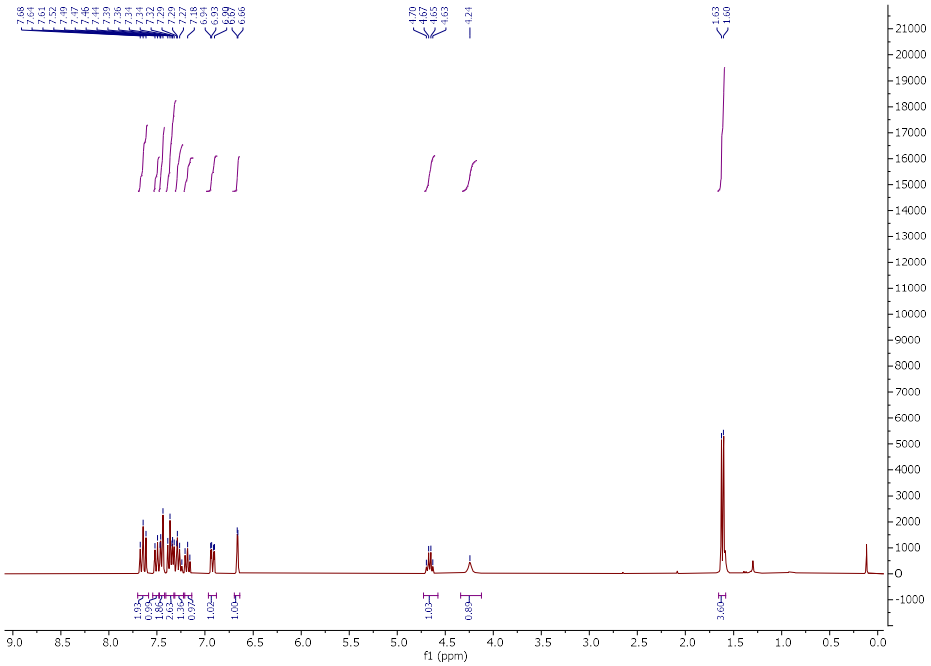
COMPOUND **83**

^{1}HNMR of **83**, $CDCl_3$, 300MHz

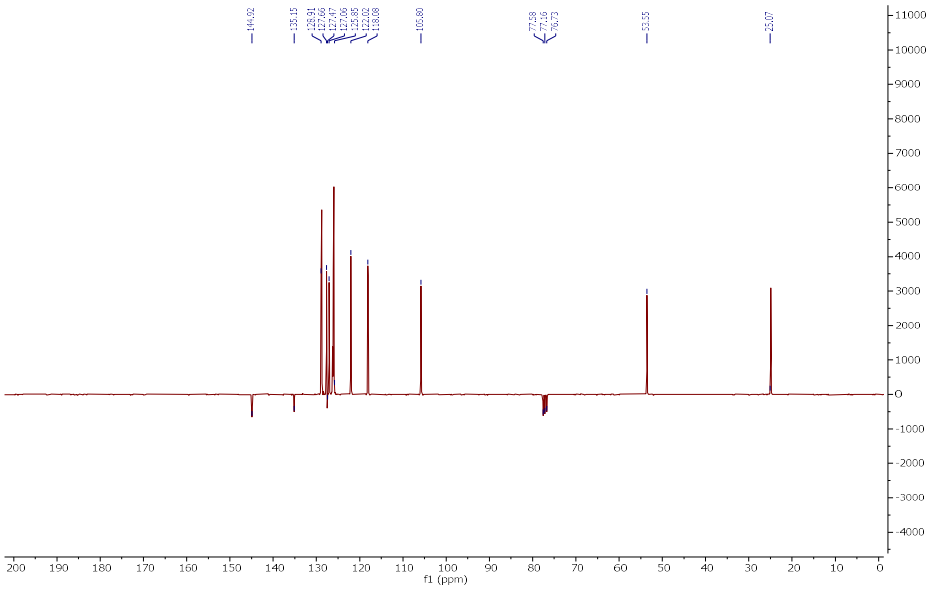


COMPOUND **94a**

^{1}HNMR of **94a**, $CDCl_3$, 300MHz

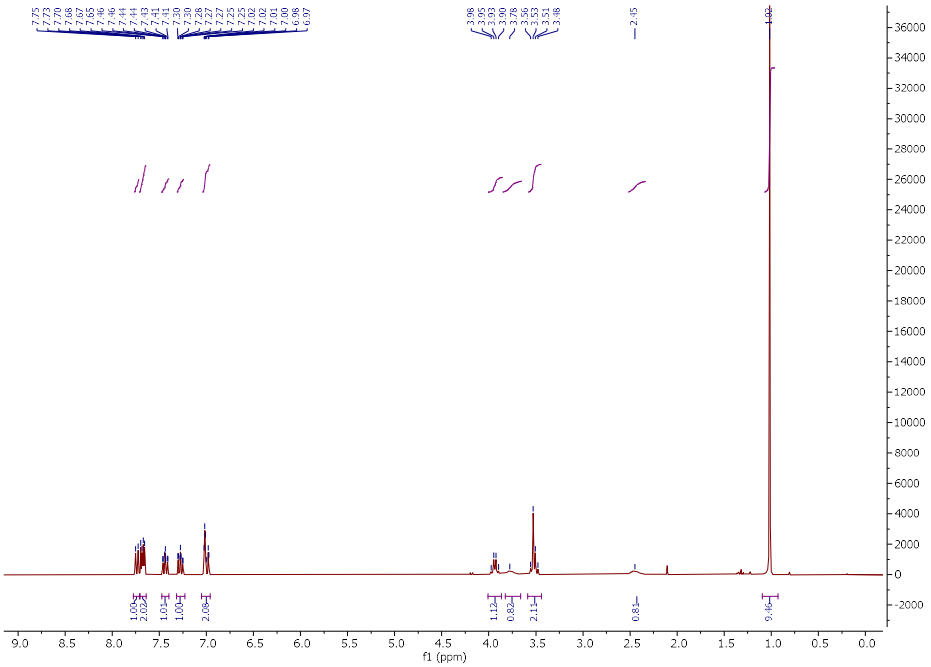


^{13}CNMR of **94a**, $CDCl_3$, 75MHz

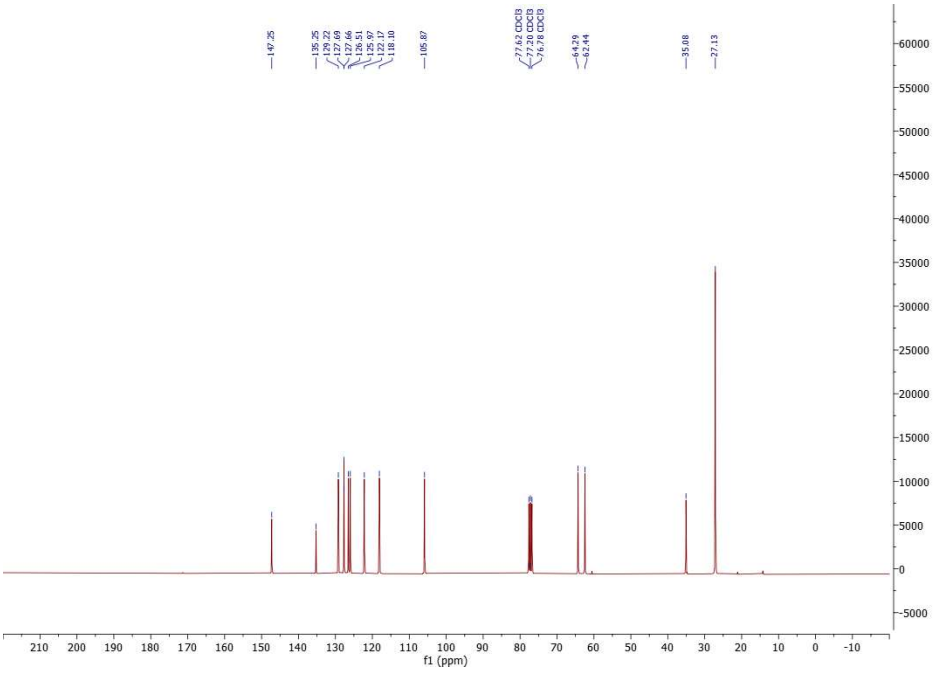


COMPOUND **94b**

^{1}HNMR of **94b**, $CDCl_3$, 300MHz

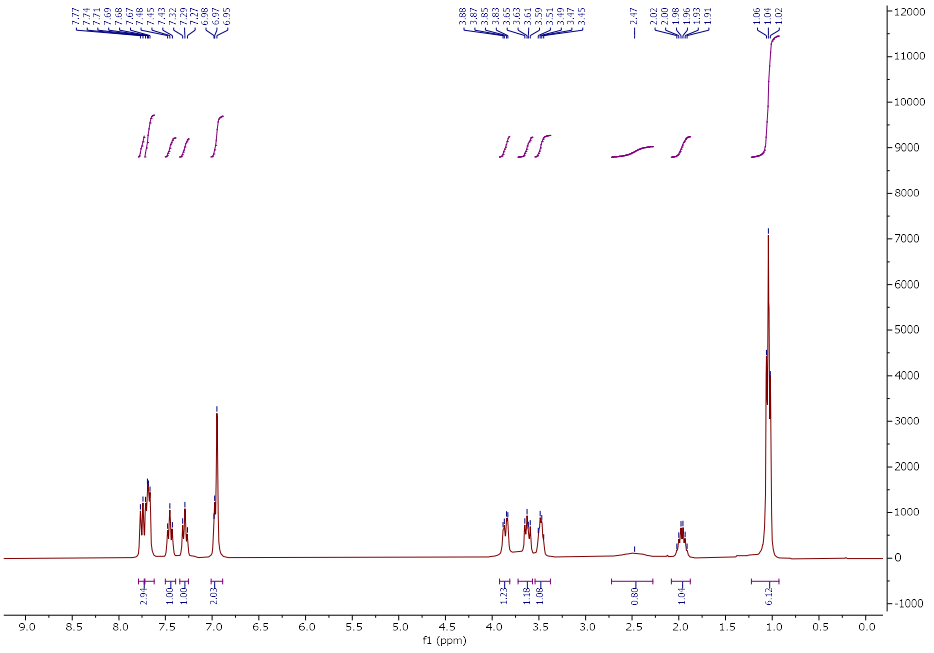


^{13}CNMR of **94b**, $CDCl_3$, 75 MHz

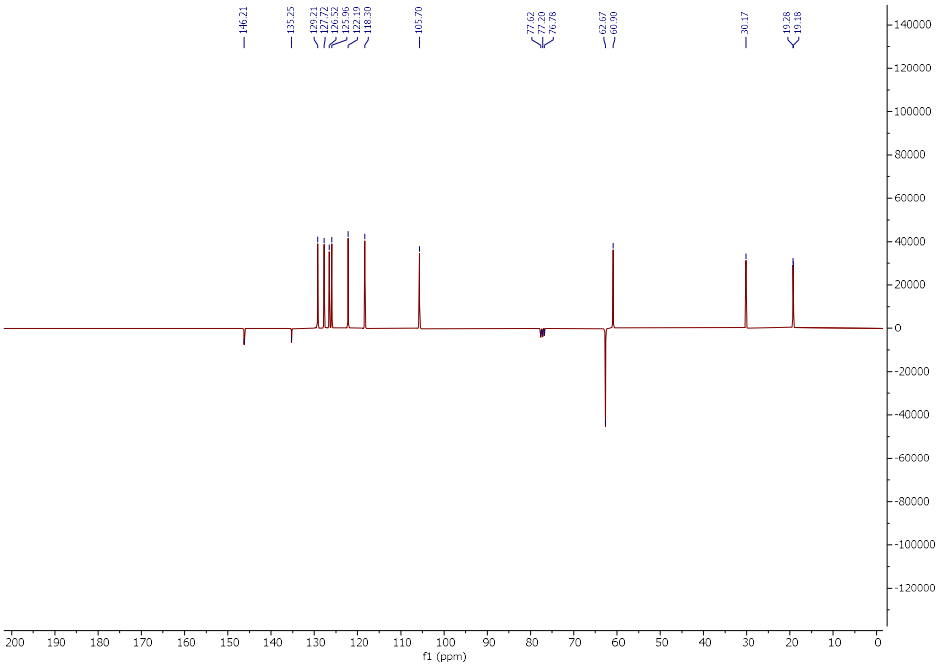


COMPOUND **93c**

^{1}HNMR of **93c**, $CDCl_3$, 300MHz

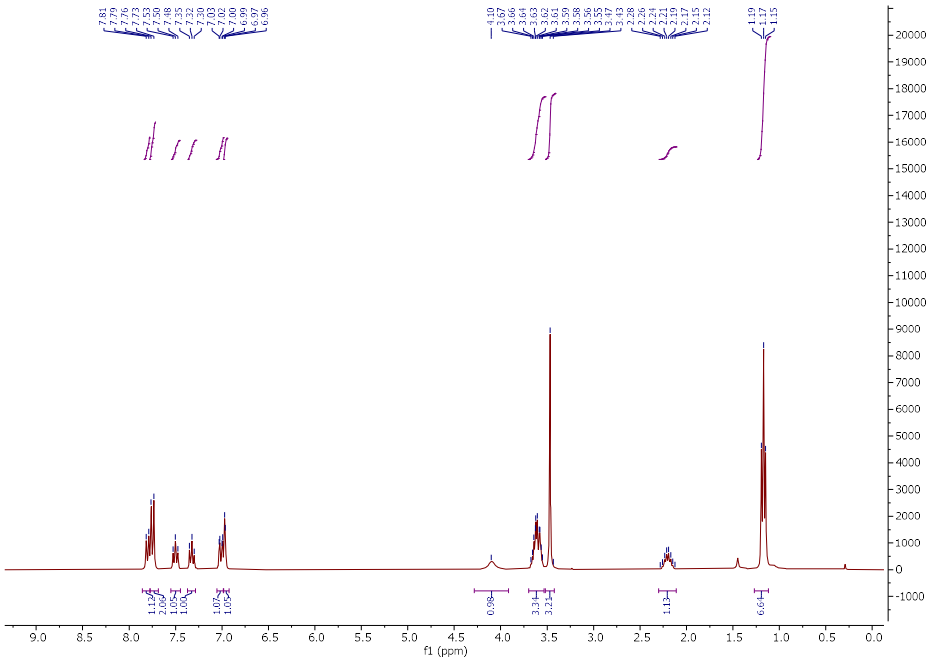


^{13}CNMR of **93c**, $CDCl_3$, 75 MHz

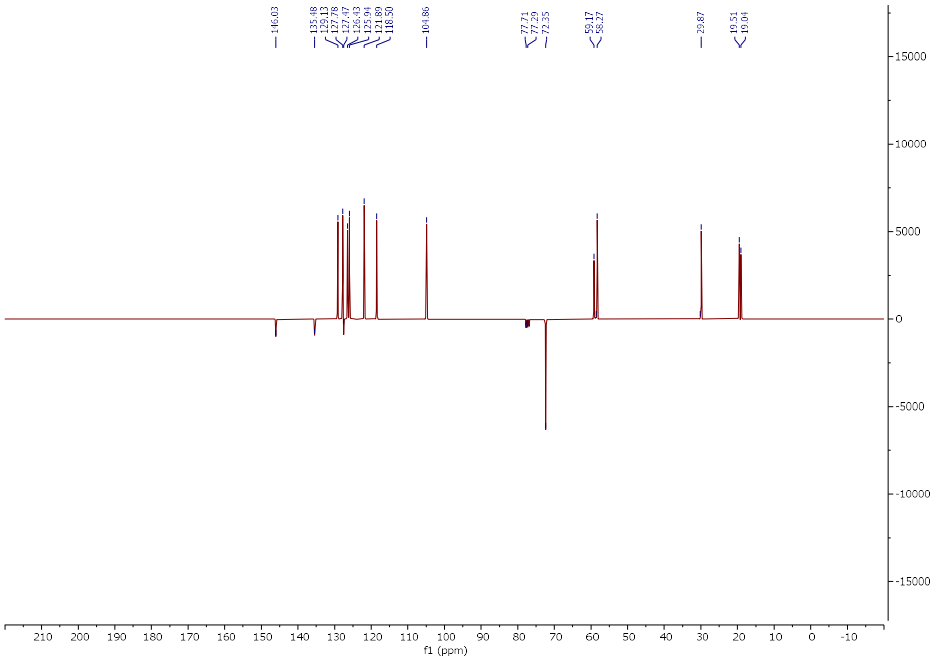


COMPOUND **93e**

^{1}HNMR of **93e**, $CDCl_3$, 300MHz

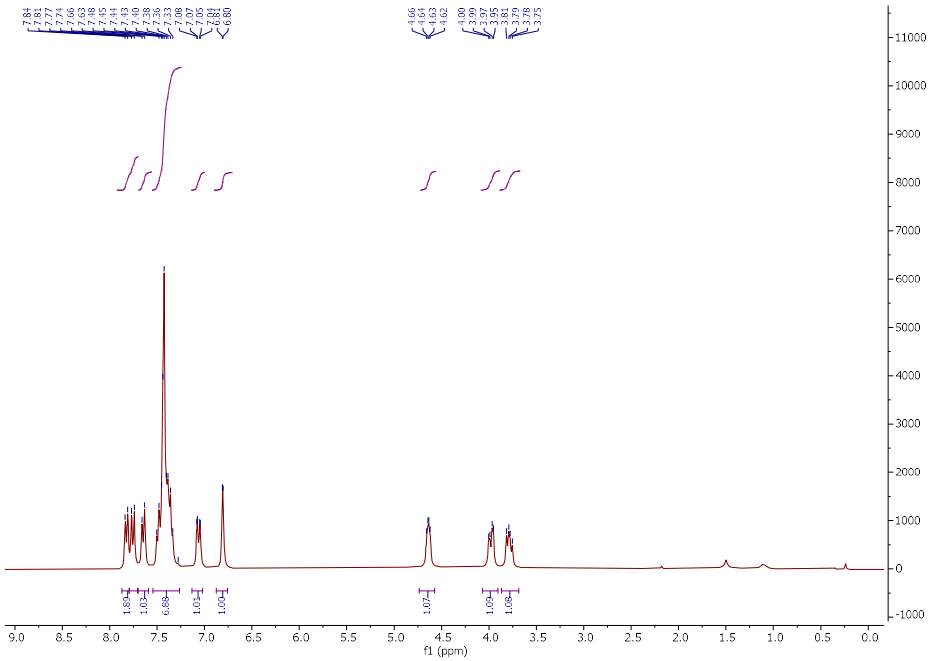


^{13}CNMR of **93e**, $CDCl_3$, 75 MHz

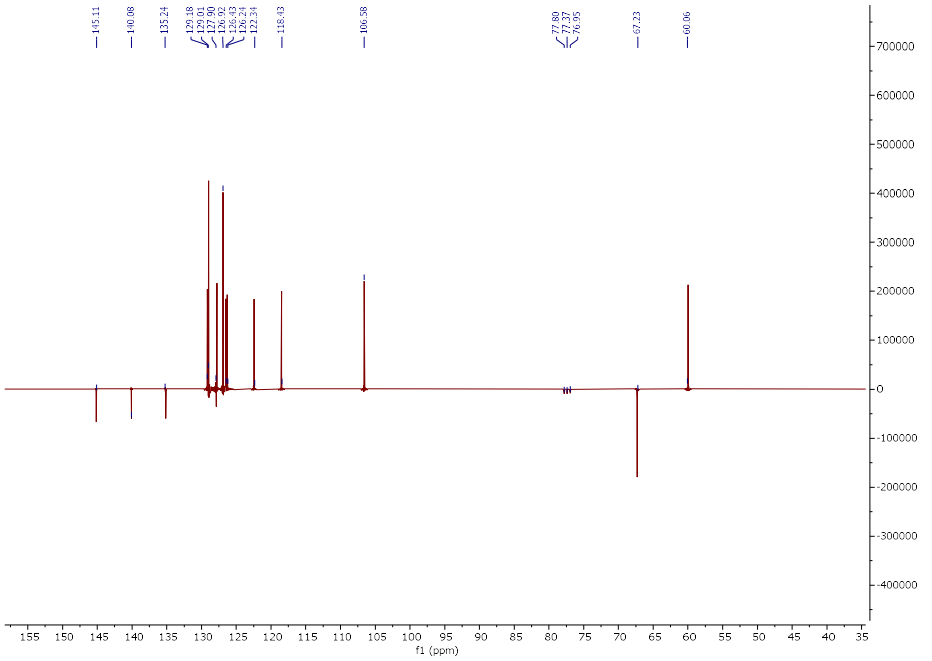


COMPOUND **93f**

^{1}HNMR of **93f**, $CDCl_3$, 300MHz

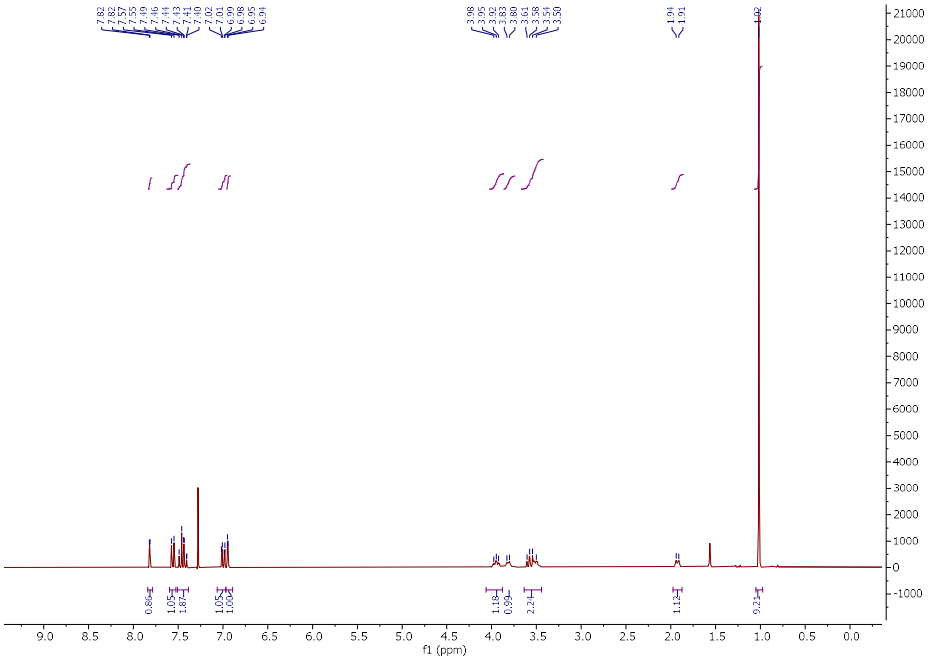


^{13}CNMR of **93f**, $CDCl_3$, 75 MHz

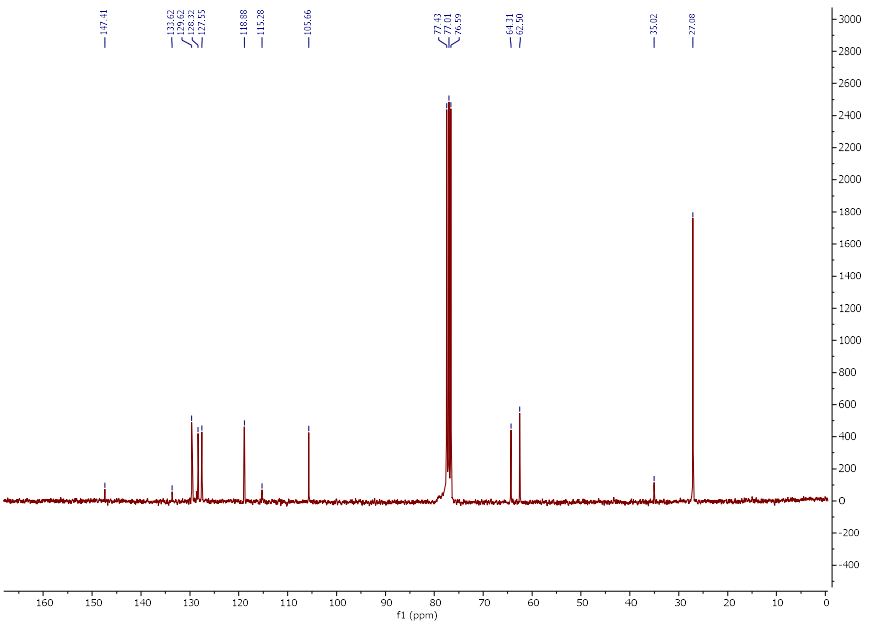


COMPOUND **93g**

^{1}HNMR of **93g,** $CDCl_3$, 300MHz

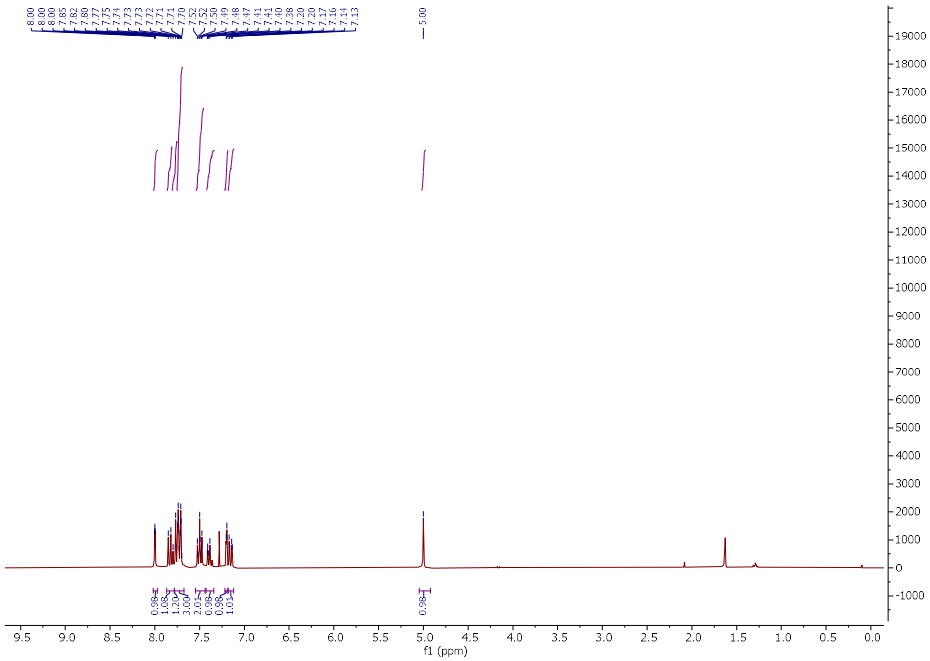


^{13}CNMR of **93g,** $CDCl_3$, 75 MHz

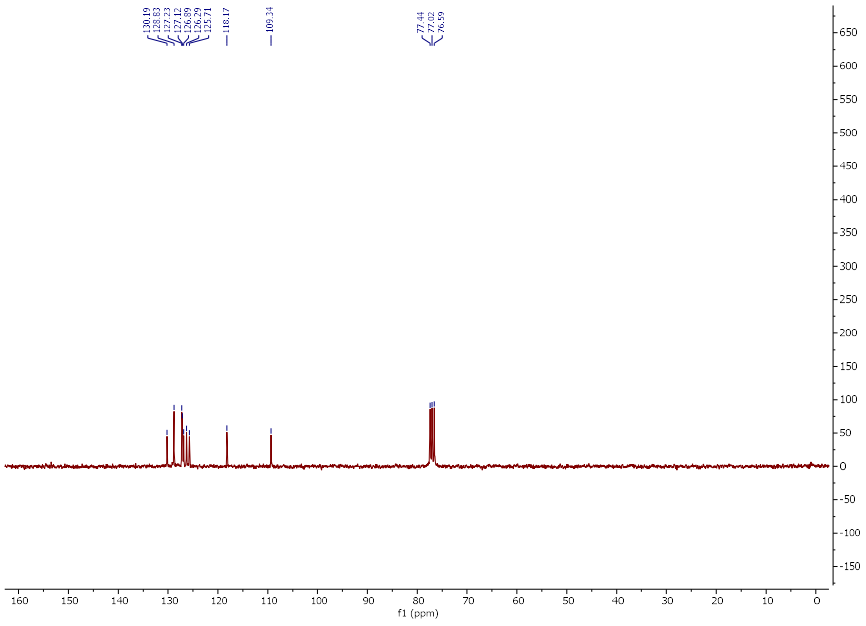


COMPOUND **h**

^{1}HNMR of **h**, $CDCl_3$, 300 MHz

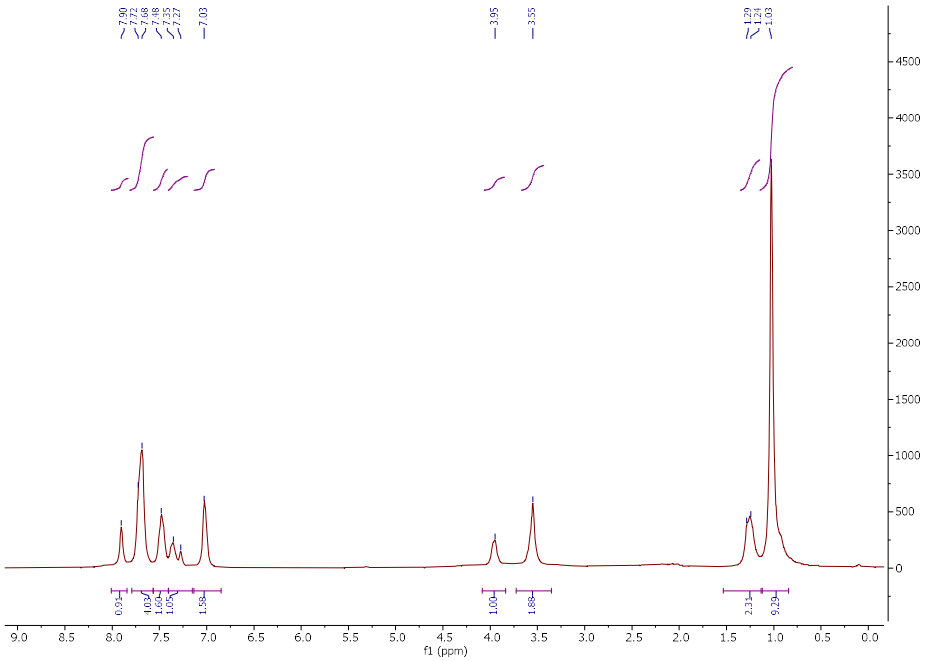


^{13}CNMR of **h,** $CDCl_3$, 75 MHz

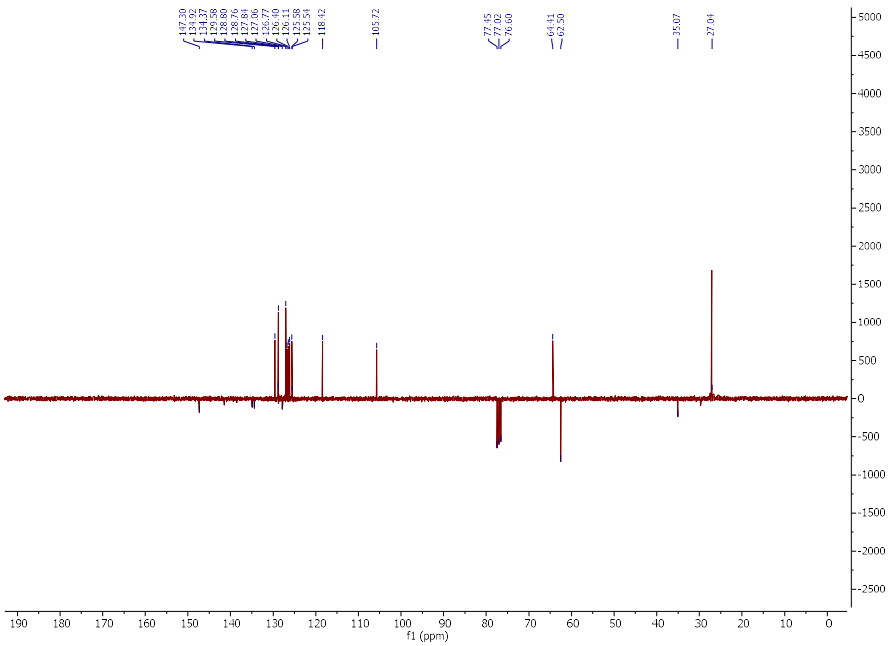


COMPOUND **93h**

^{1}HNMR of **93h**, $CDCl_3$, 300MHz

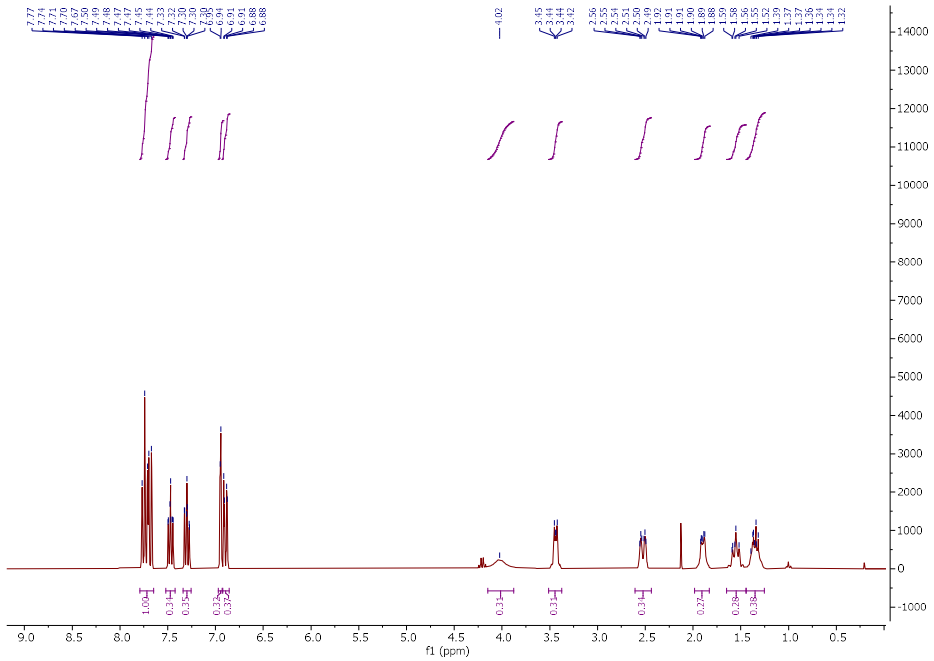


^{13}CNMR of **93h**, $CDCl_3$, 75 MHz

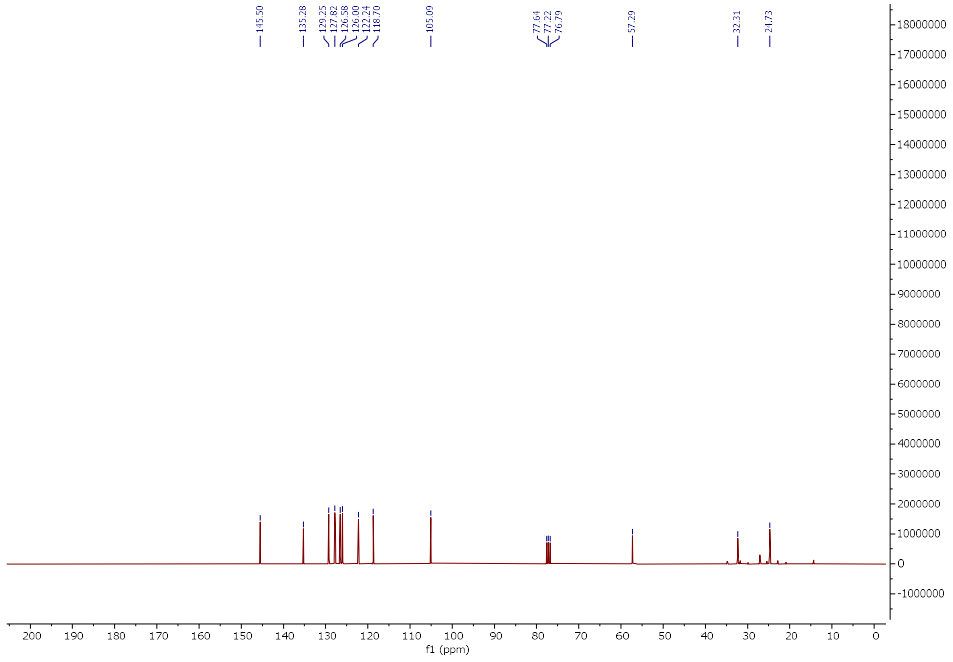


COMPOUND **93i**

^{1}HNMR of **93i**, $CDCl_3$, 300 MHz

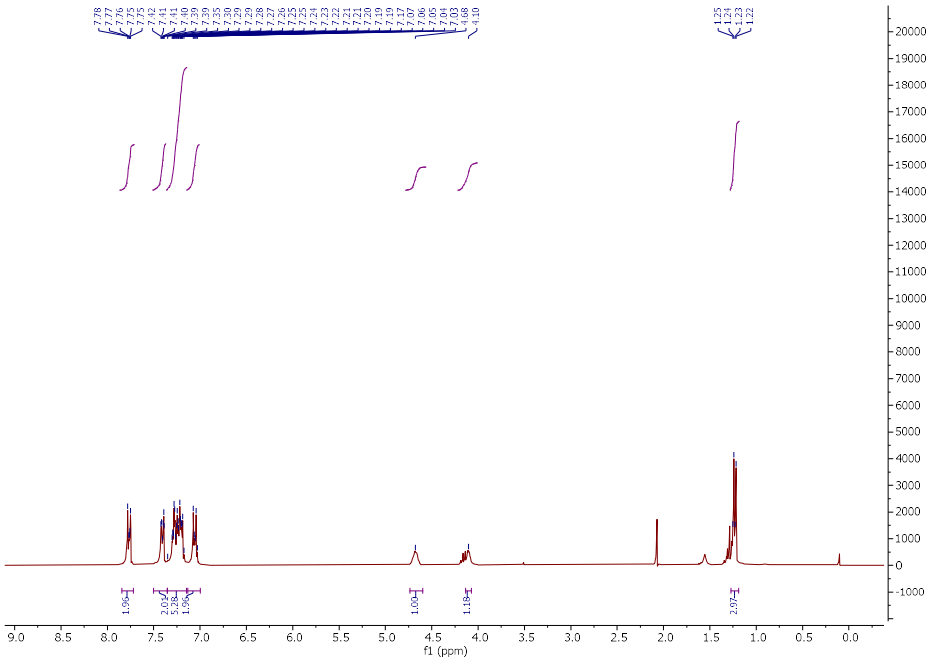


^{13}CNMR of **93i**, $CDCl_3$, 75 MHz

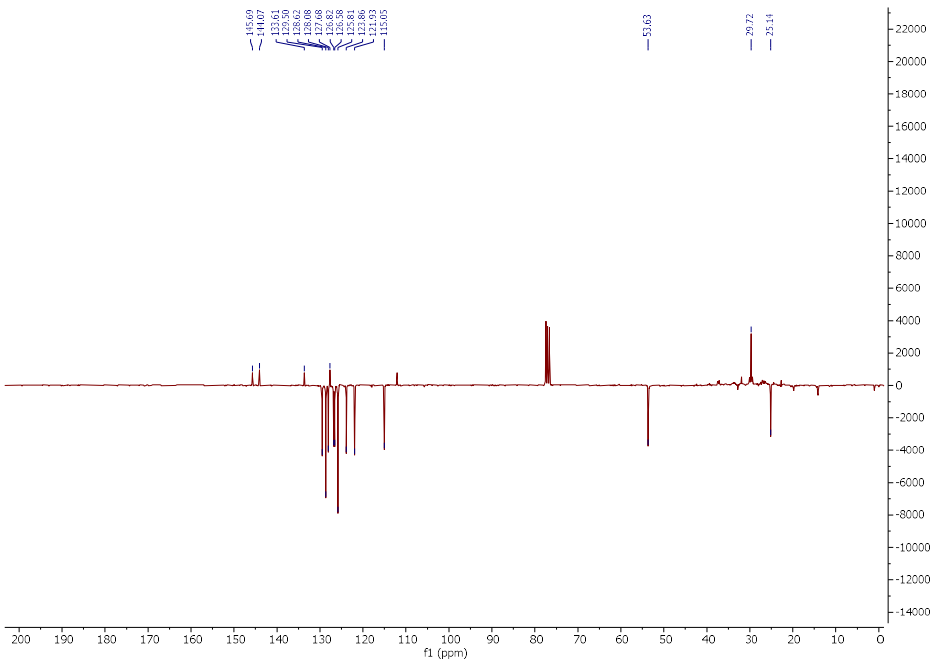


COMPOUND **96a.1**

^{1}HNMR of **96a.1**, $CDCl_3$, 300 MHz

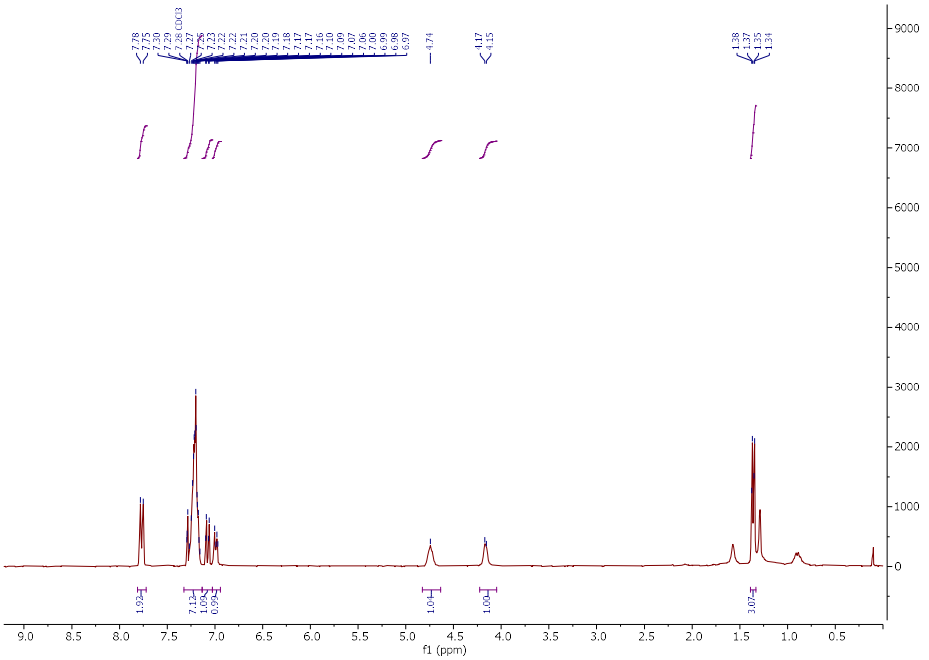


^{13}CNMR of **96a.1**, $CDCl_3$, 75 MHz

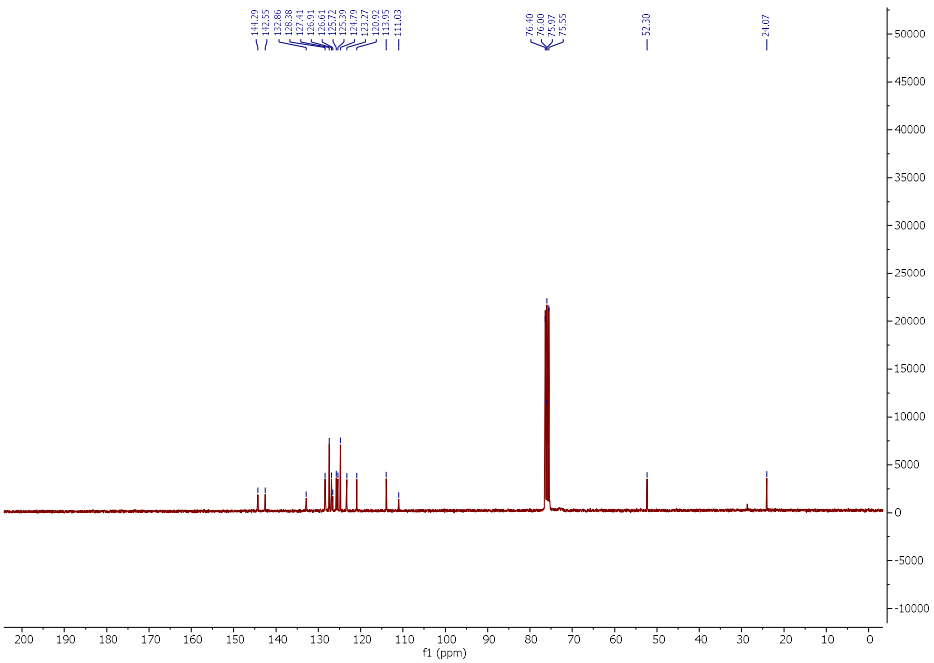


COMPOUND **96a.2**

^{1}HNMR of **96a.2,** $CDCl_3$, 300 MHz

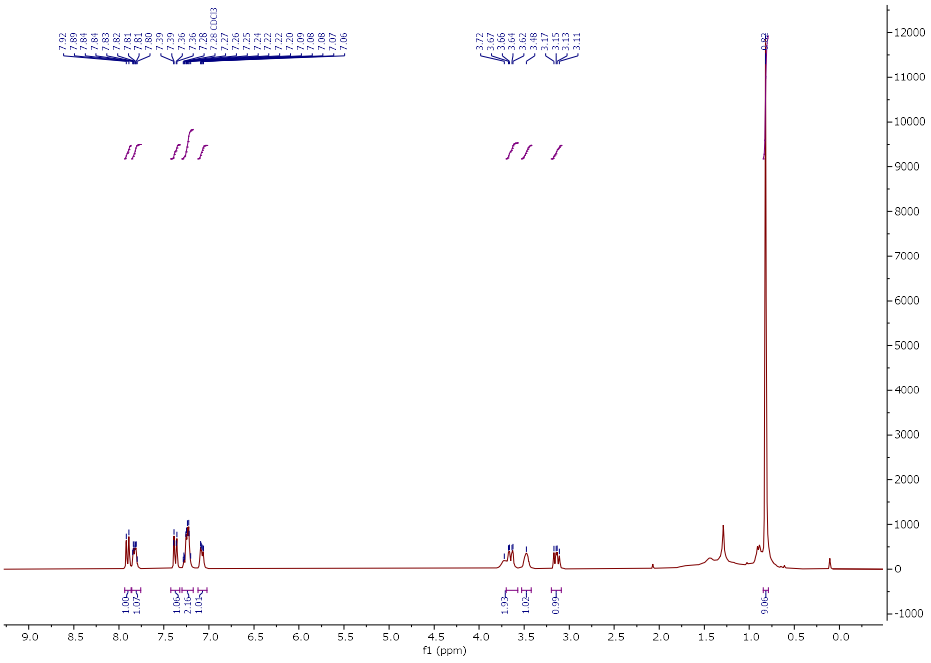


^{13}CNMR of **96a.2**, $CDCl_3$, 75 MHz

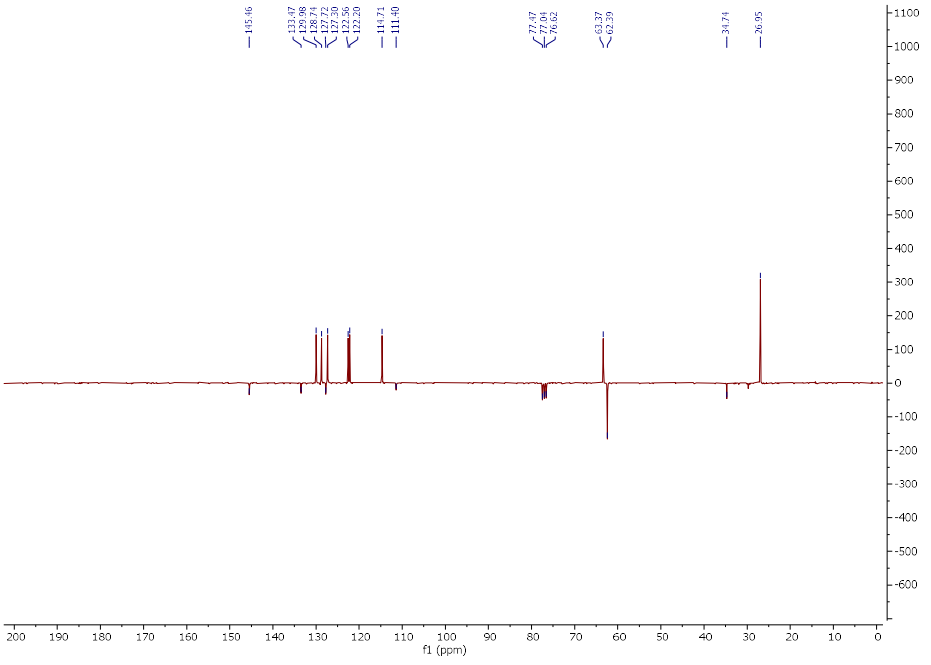


COMPOUND **96b.1**

^{1}HNMR of **96b.1**, $CDCl_3$, 300 MHz

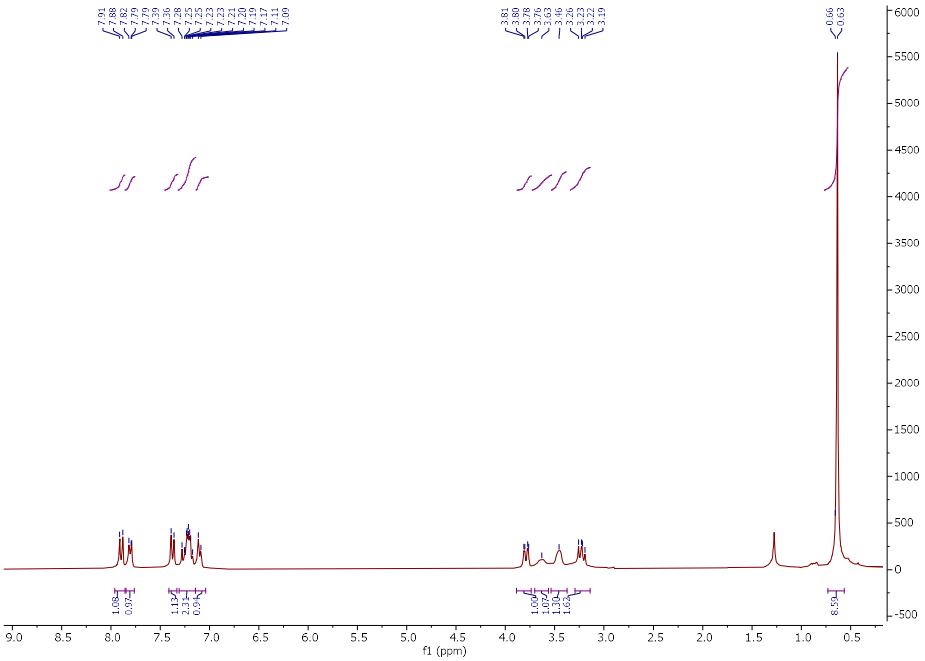


^{13}CNMR of **96b.1**, CDCl3, 75 MHz

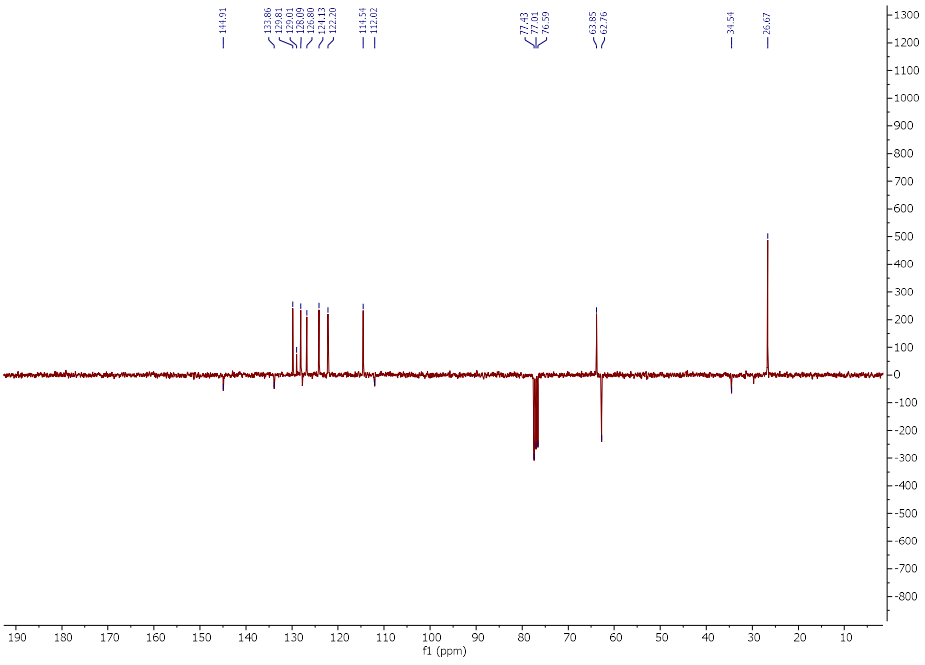


COMPOUND **96b.2**

^{1}HNMR of **96b.2**, $CDCl_3$, 300 MHz

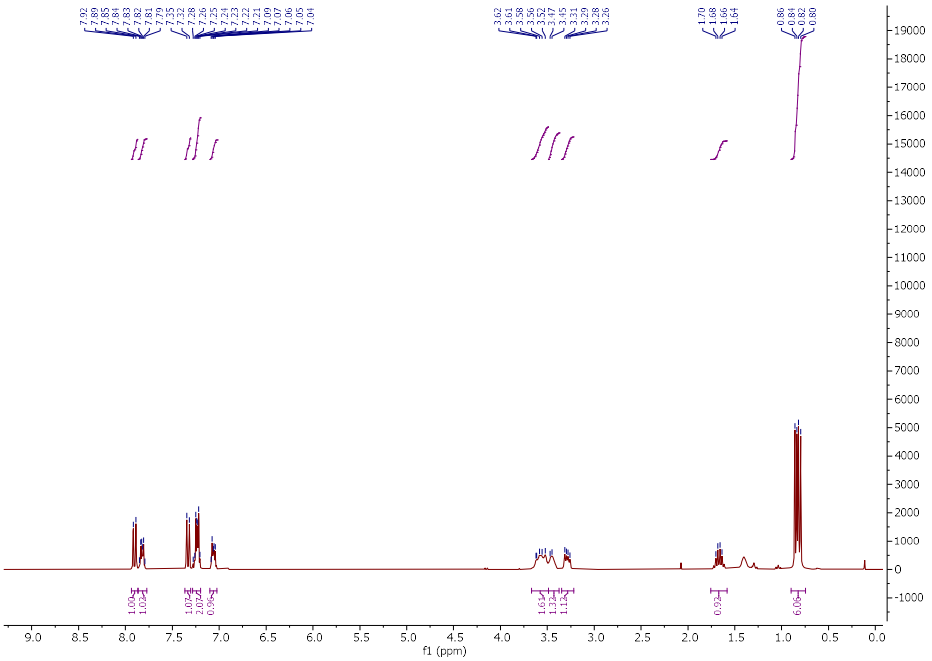


^{13}CNMR of **96b.2**, CDCl3, 75 MHz

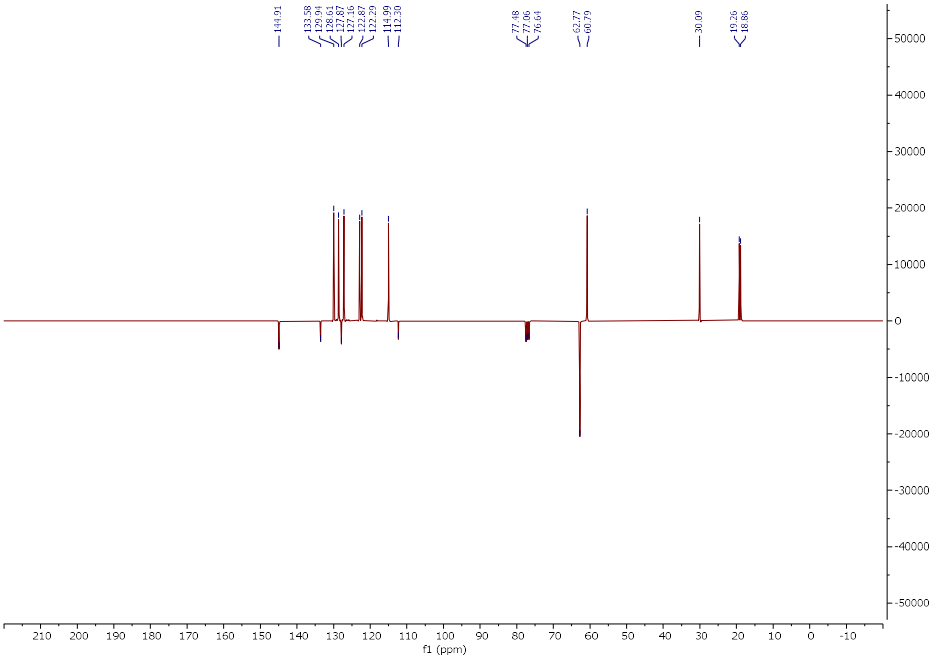


COMPOUND **96c.1**

^{1}HNMR of **96c.1**, $CDCl_3$, 300 MHz

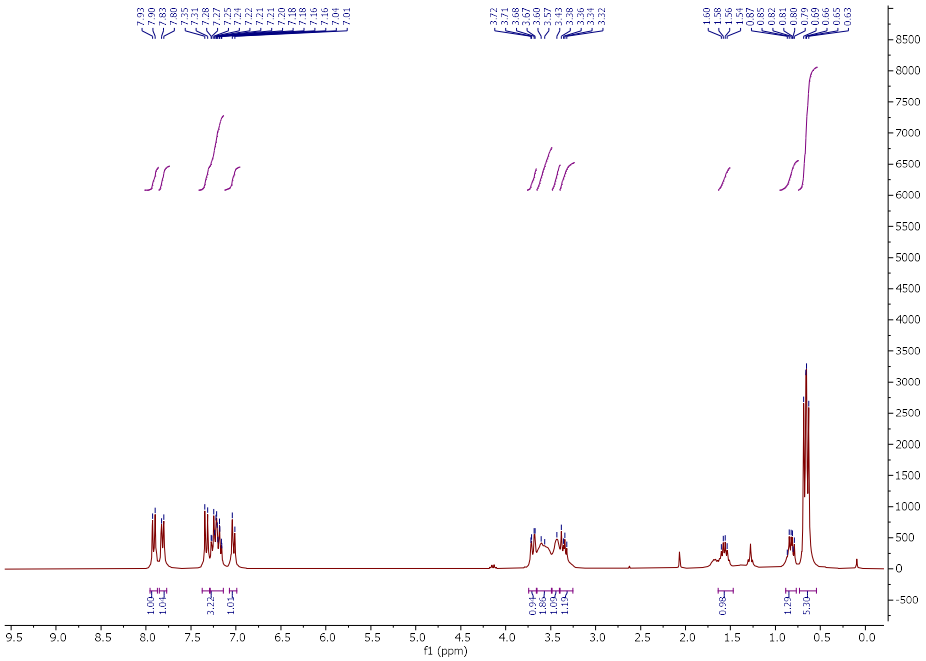


^{13}CNMR of **96c.1**, $CDCl_3$, 75 MHz

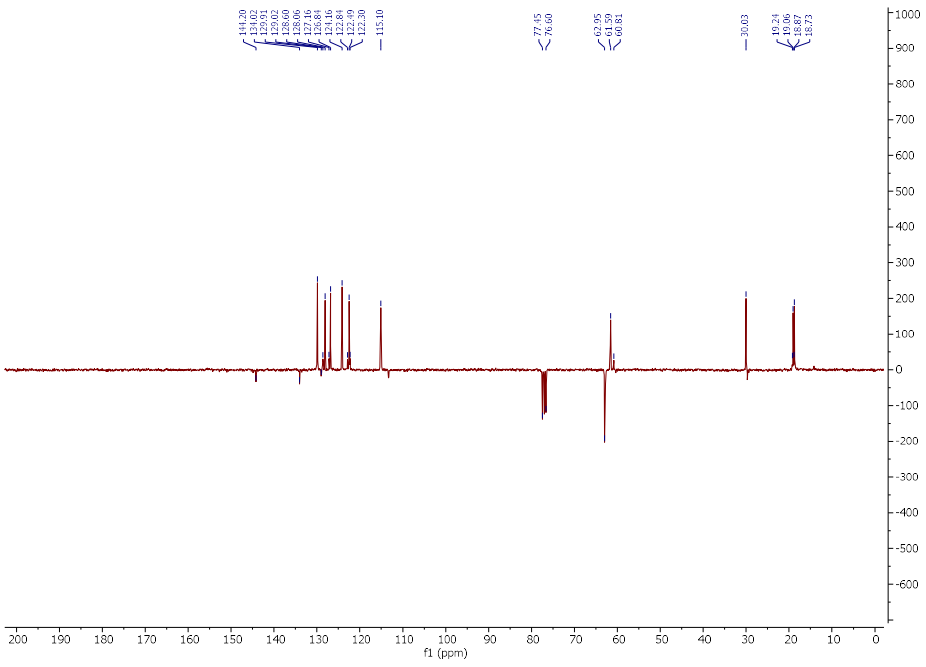


COMPOUND **96c.2**

^{1}HNMR of **96c.2**, $CDCl_3$, 300 MHz

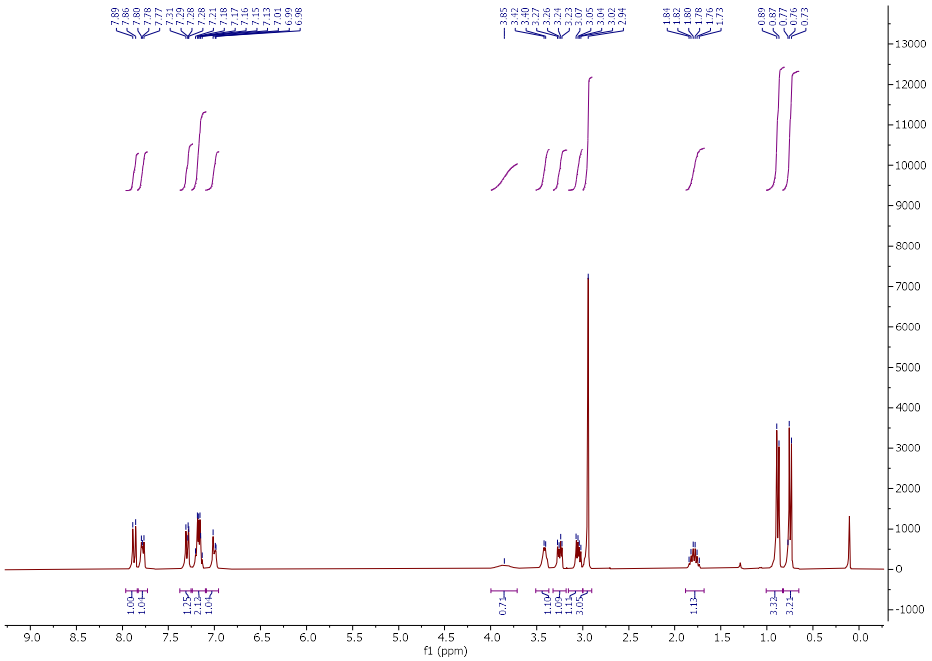


^{13}CNMR of **96c.2**, $CDCl_3$, 75 MHz

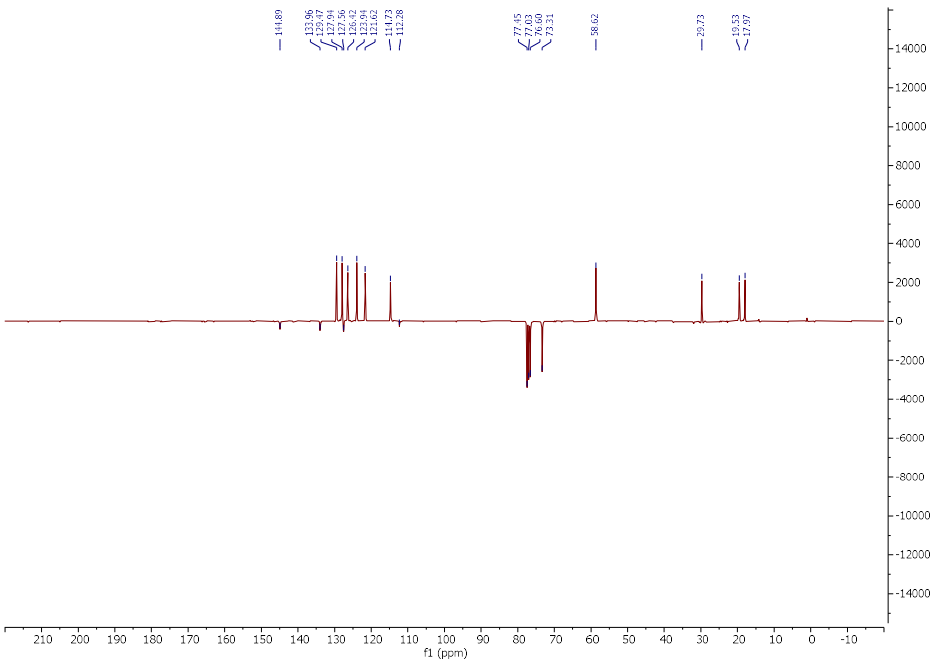


COMPOUND **96e.1**

^{1}HNMR of **96e.1**, $CDCl_3$, 300 MHz

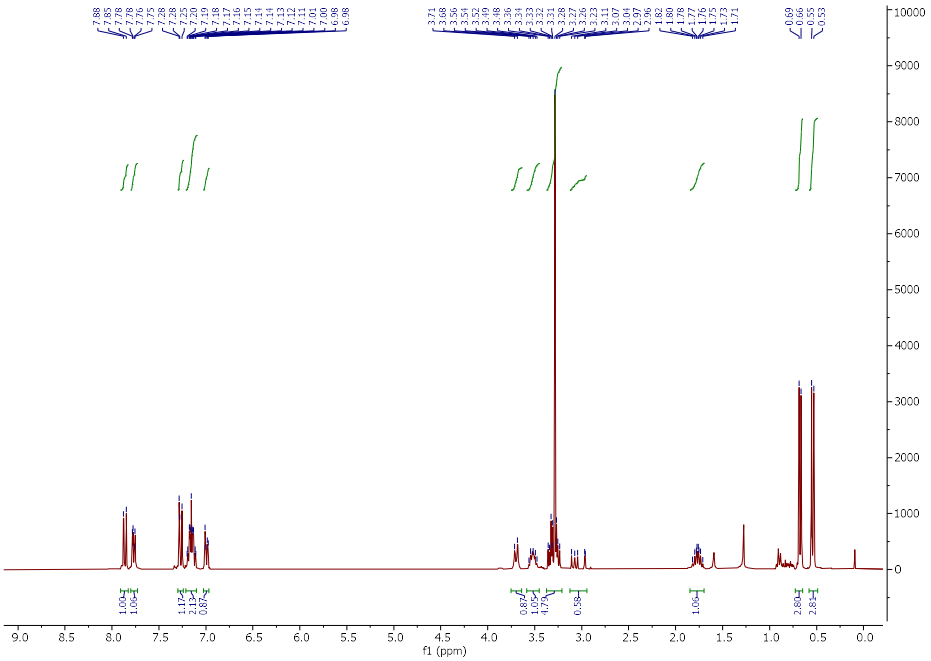


^{13}CNMR of **96e.1**, $CDCl_3$, 75 MHz

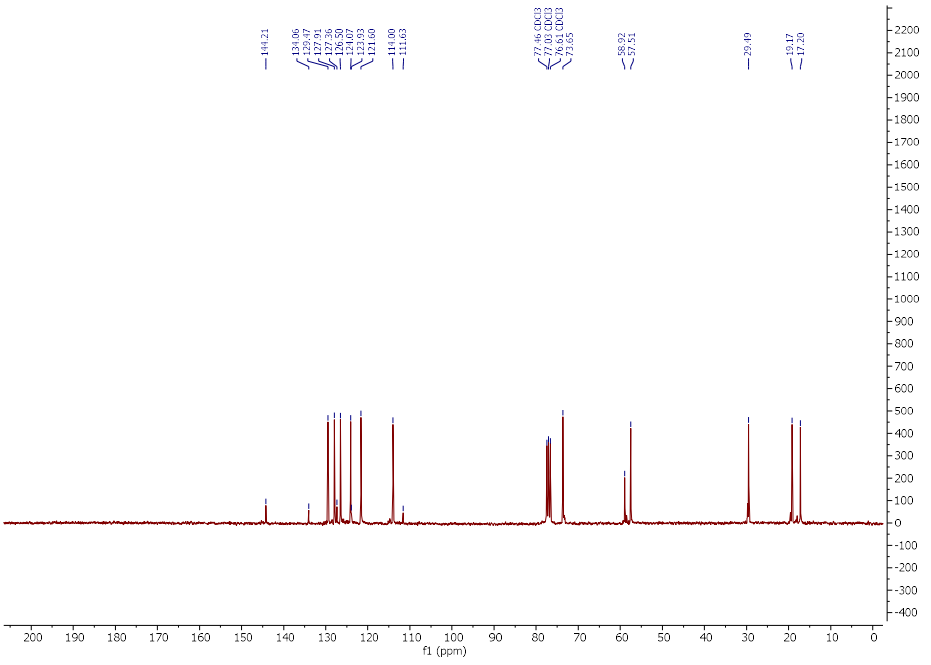


COMPOUND **96e.2**

^{1}HNMR of **96e.2**, $CDCl_3$, 300 MHz

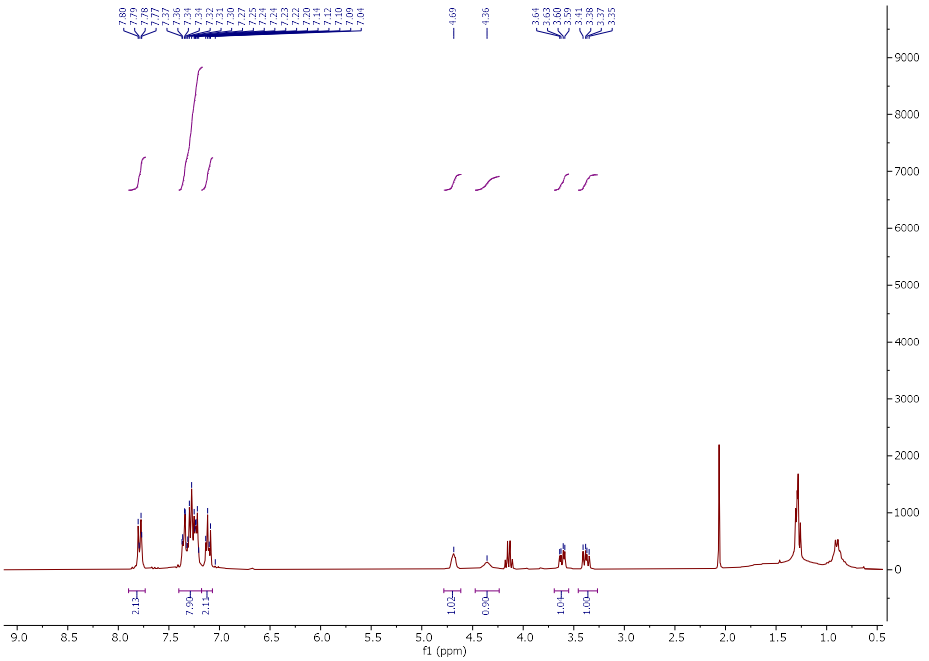


^{13}CNMR of **96e.2**, $CDCl_3$, 75 MHz

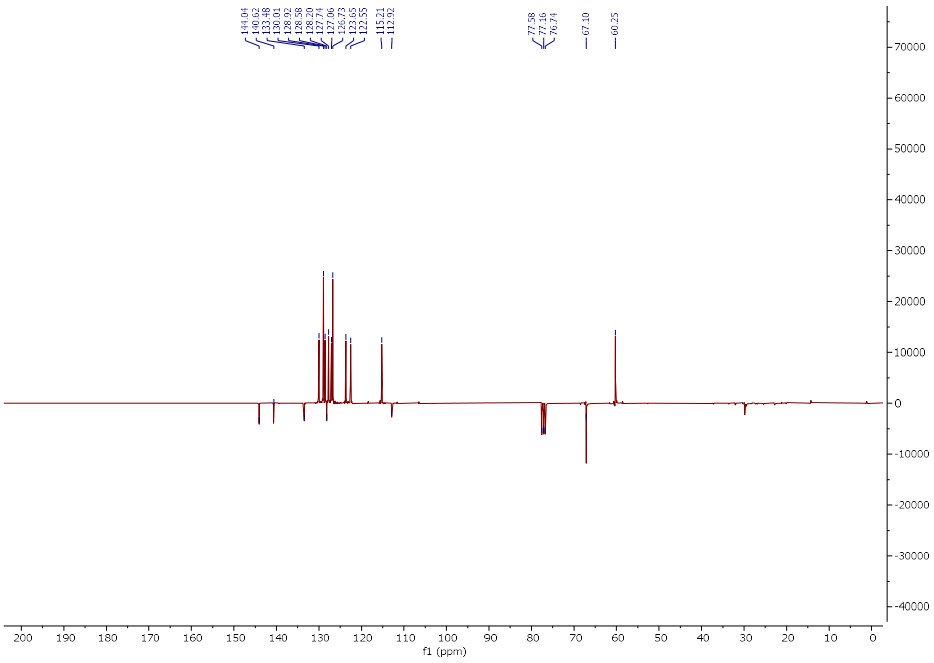


COMPOUND **96f.1**

^{1}HNMR of **96f.1**, $CDCl_3$, 300 MHz

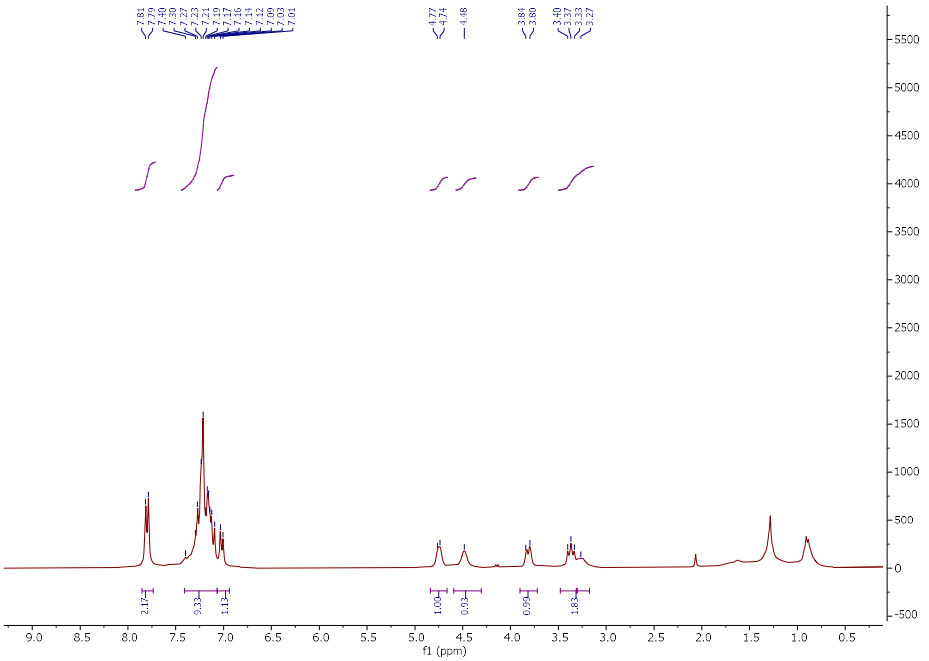


^{13}CNMR of **96f.1**, $CDCl_3$, 75 MHz

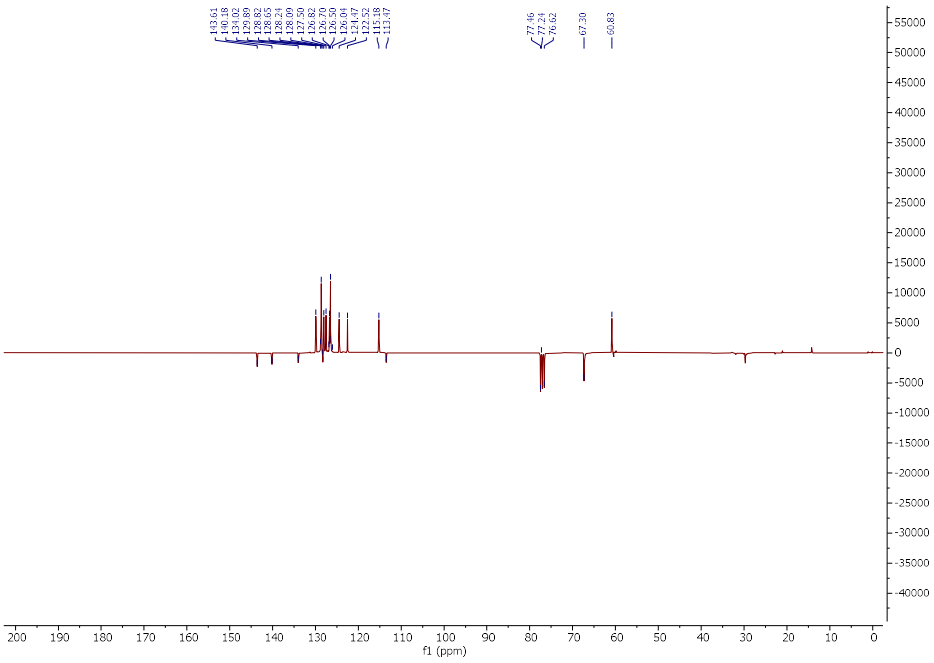


COMPOUND **96f.2**

^{1}HNMR of **96f.2**, $CDCl_3$, 300 MHz

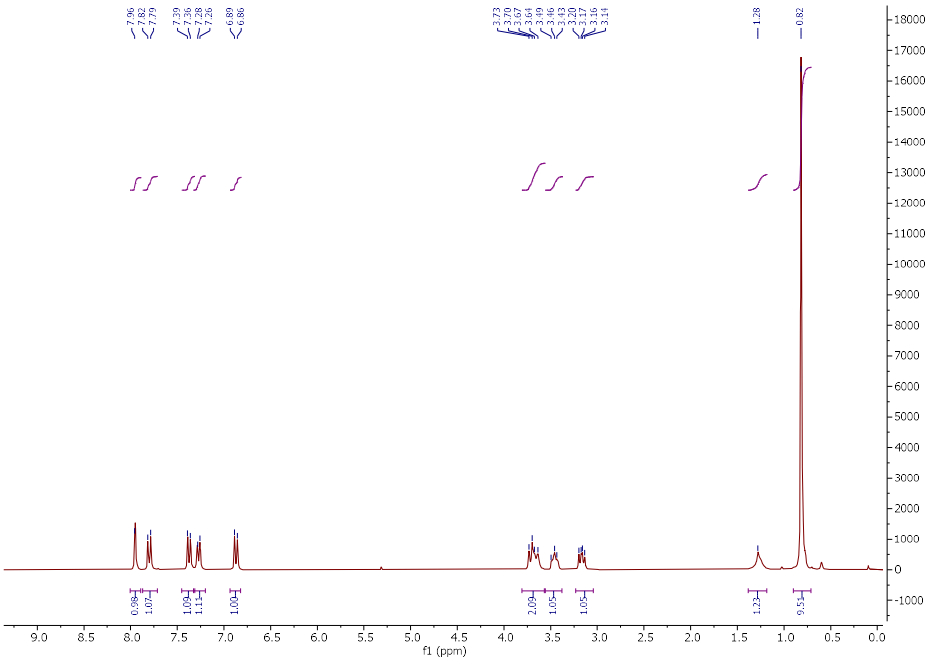


^{13}CNMR of **96f.2**, CDCl3, 75 MHz

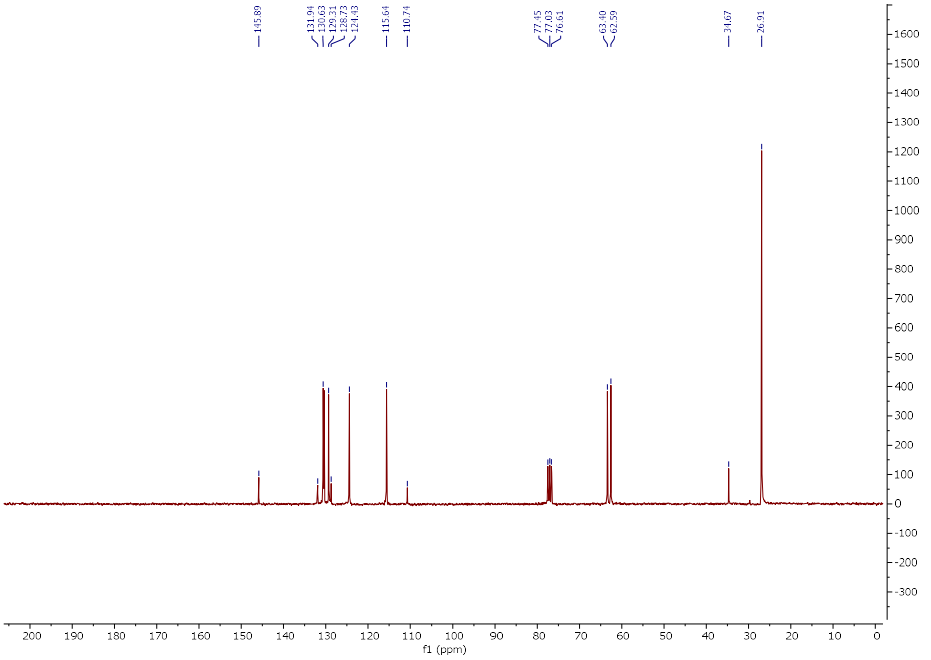


COMPOUND **96g.1**

^{1}HNMR of **96g.1**, $CDCl_3$, 300 MHz

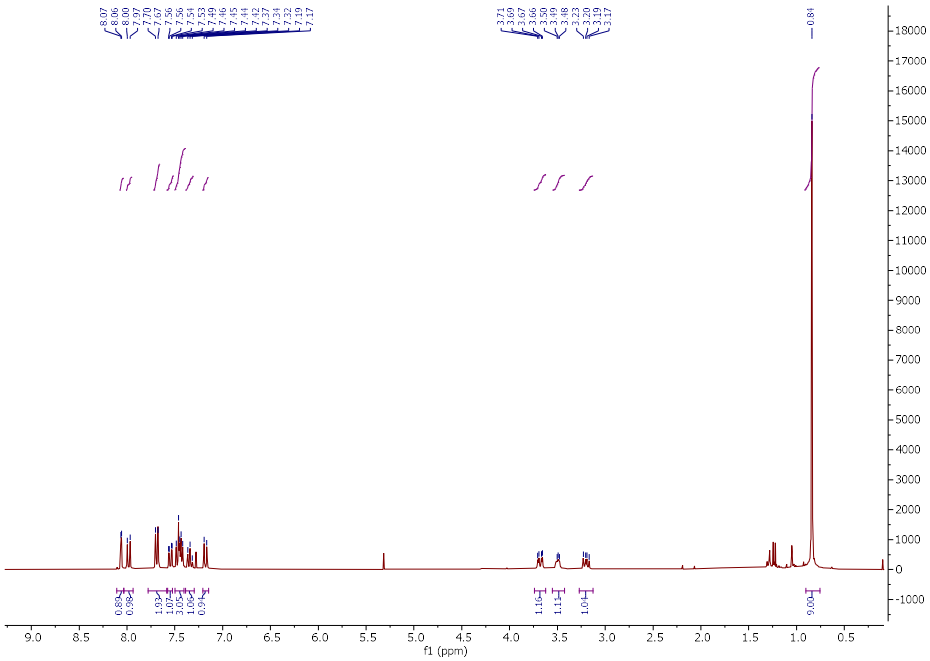


^{13}CNMR of **96g.1**, $CDCl_3$, 75 MHz

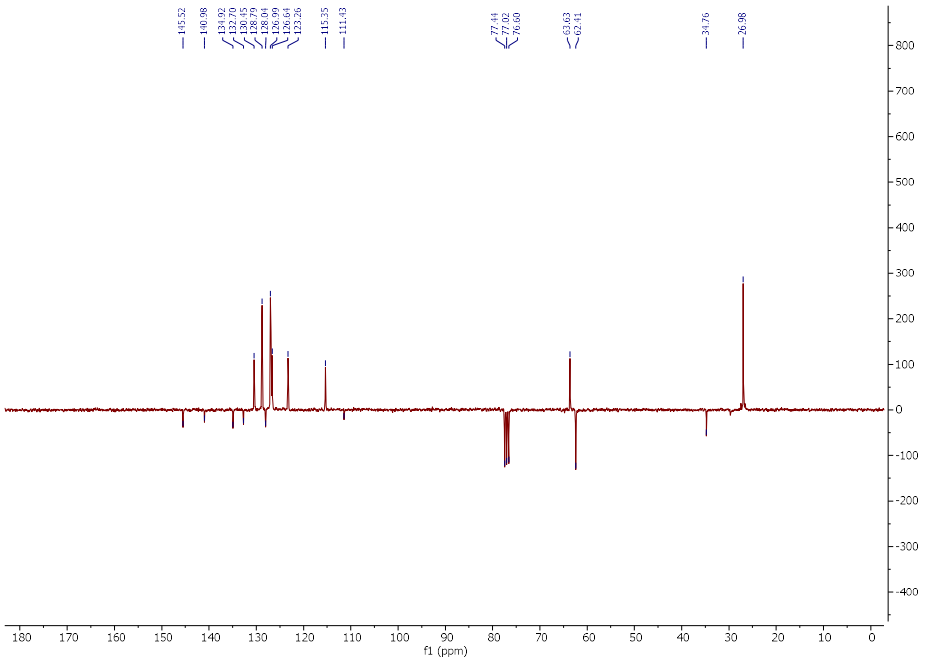


COMPOUND **96h.1**

^{1}HNMR of **96h.1**, $CDCl_3$, 300 MHz

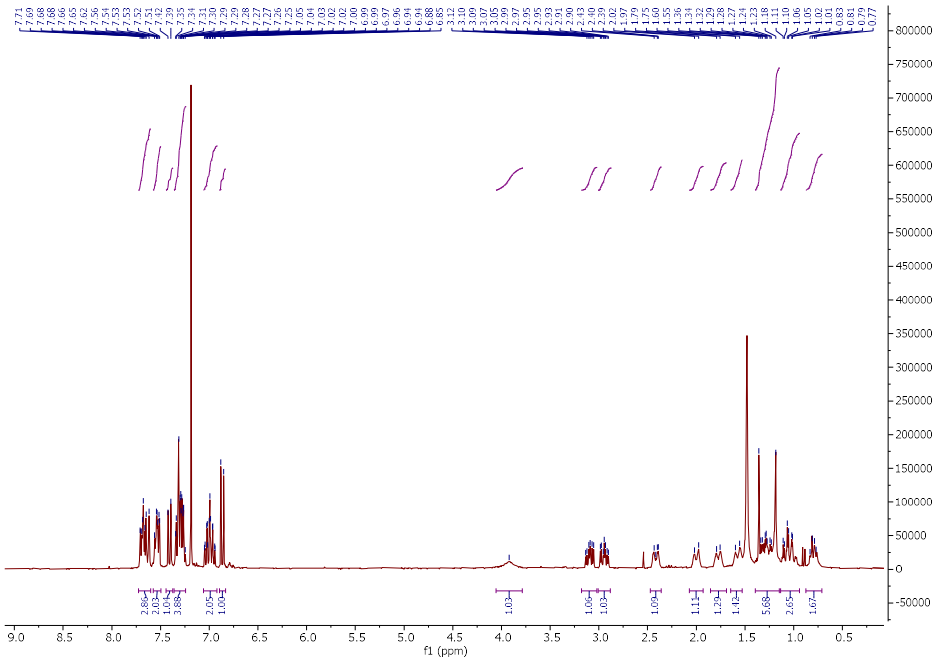


^{13}CNMR of **96h.1**, $CDCl_3$, 75 MHz

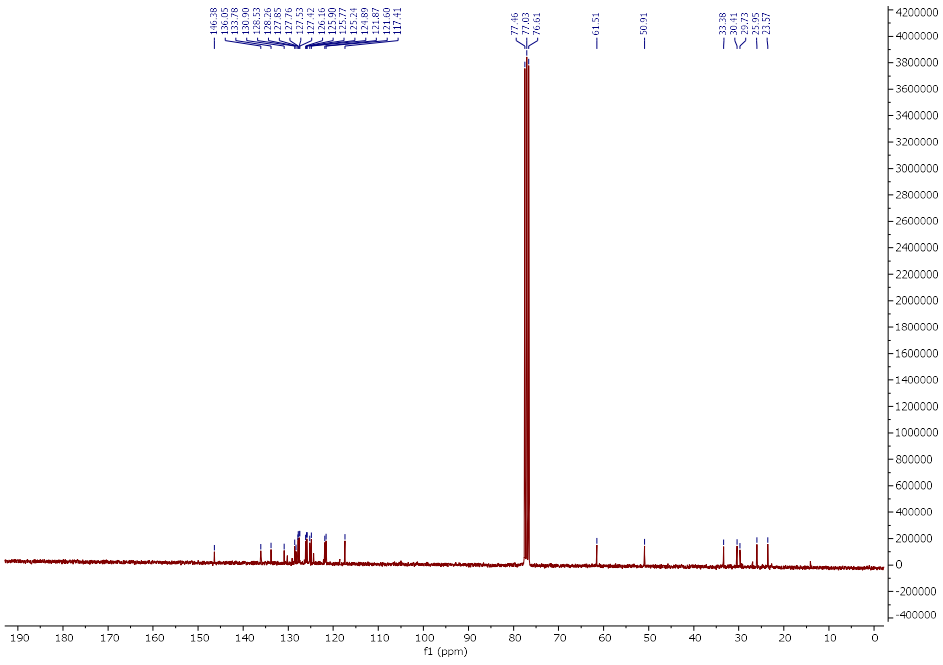


COMPOUND **96i.1**

^{1}HNMR of **96i.1**, $CDCl_3$, 300 MHz

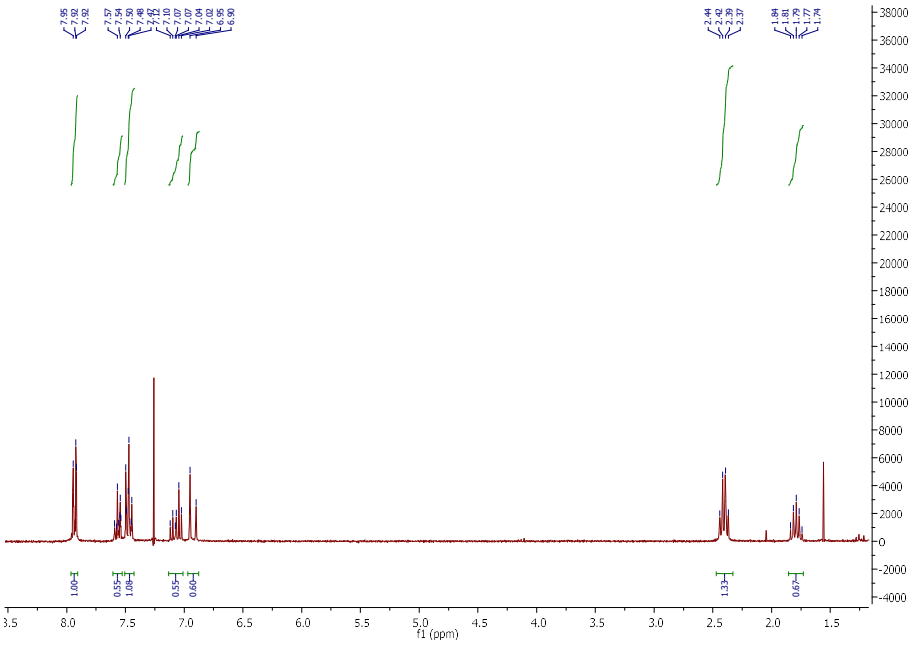


^{13}CNMR of **96i.1**, $CDCl_3$, 75 MHz



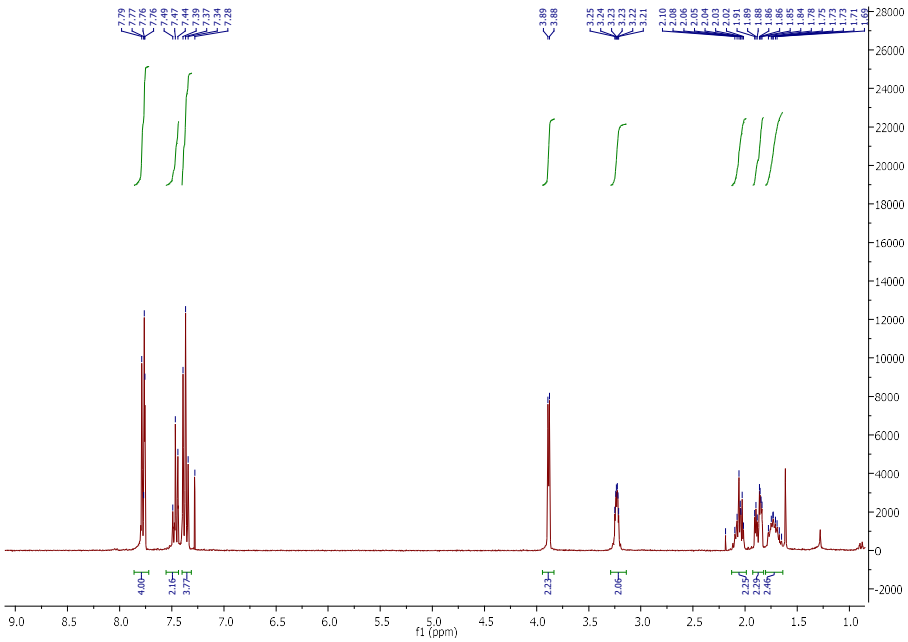
COMPOUND **97a**

^{1}HNMR of **97a**, $CDCl_3$, 300 MHz

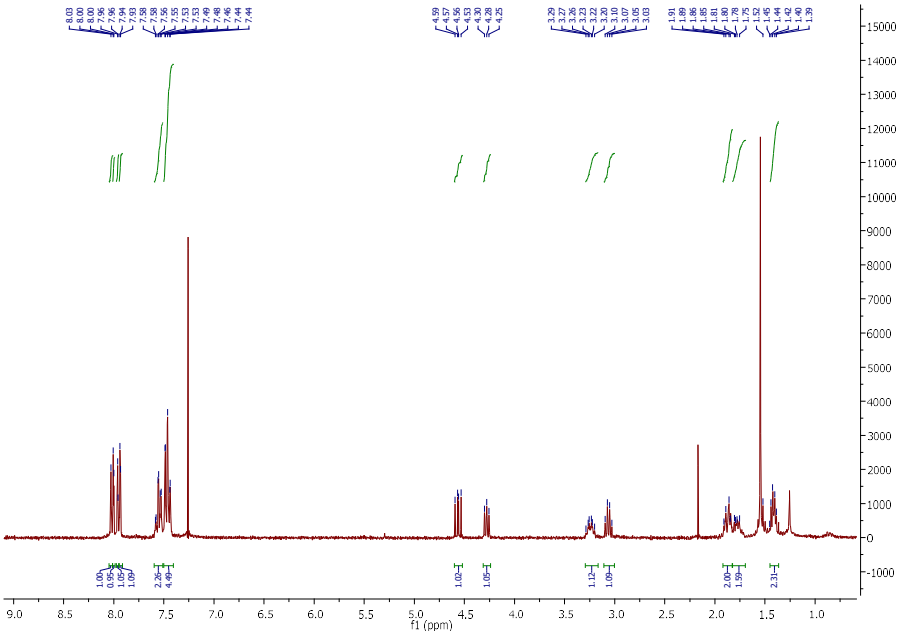


COMPOUND **98a**

^{1}HNMR of ***cis*-98a**, $CDCl_3$, 300 MHz

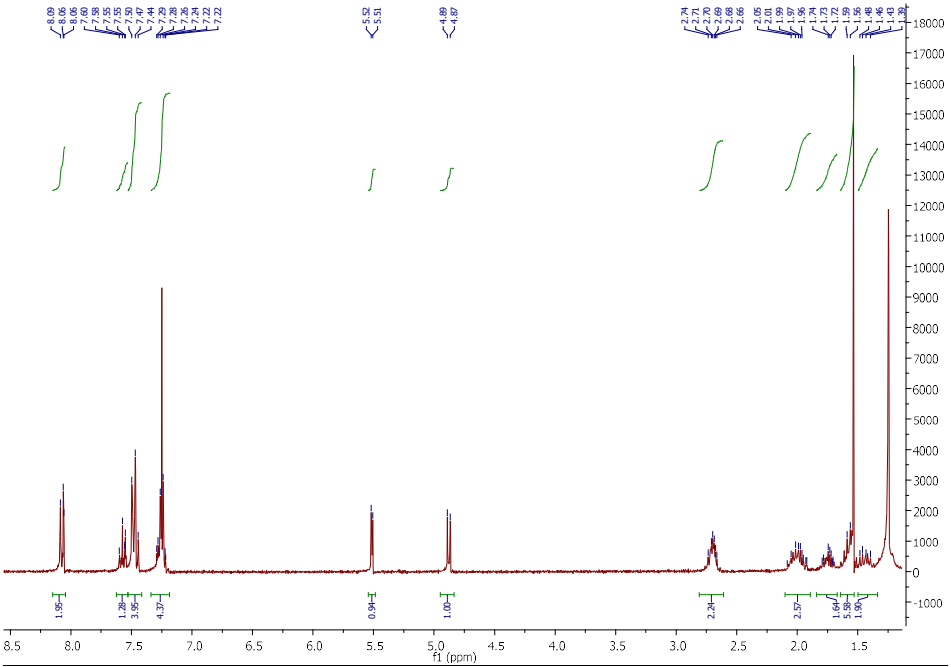


^{1}HNMR of ***trans*-98a**, $CDCl_3$, 300 MHz



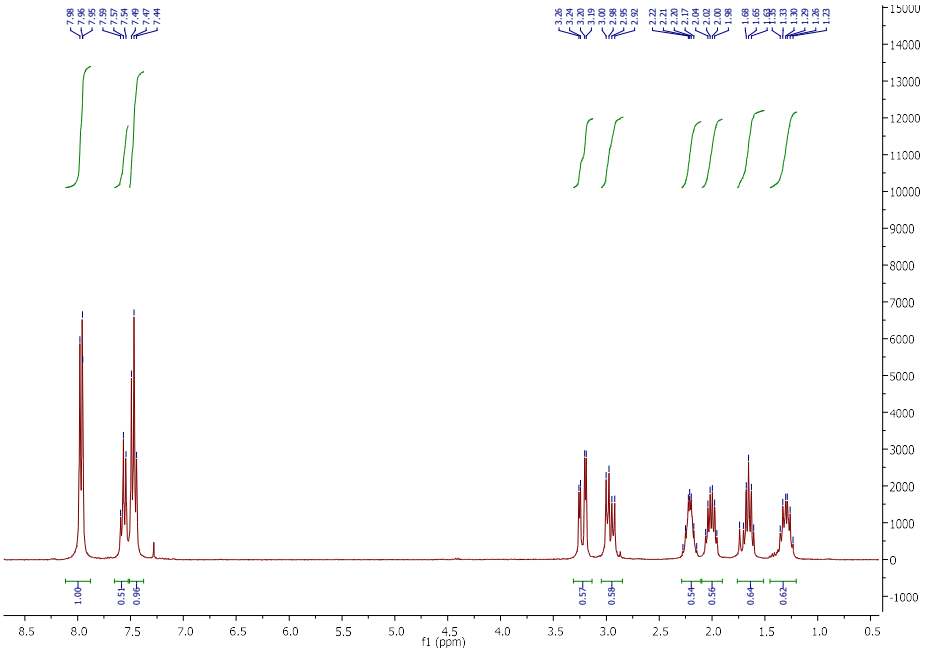
COMPOUND **100a**

^{1}HNMR of **100a**, $CDCl_3$, 300 MHz



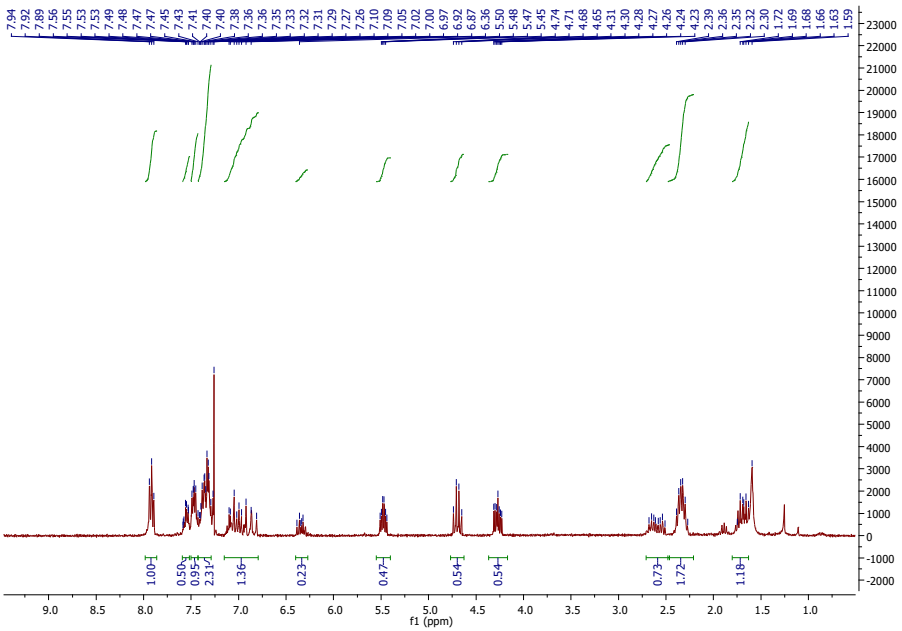
COMPOUND **101a**

^{1}HNMR of **101a**, $CDCl_3$, 300 MHz

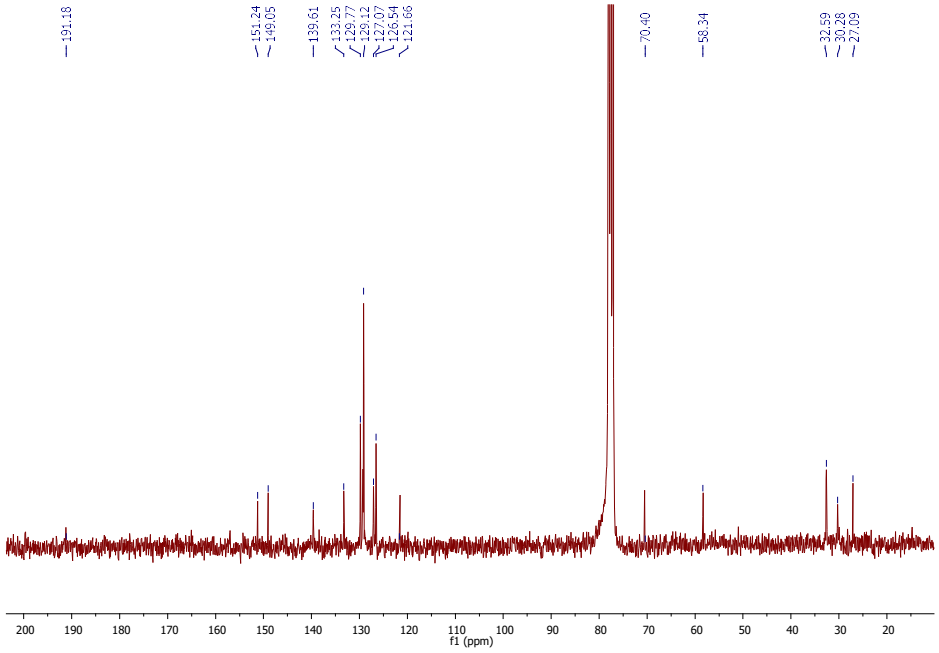


COMPOUND **103a**

^{1}HNMR of **103a**, $CDCl_3$, 300 MHz

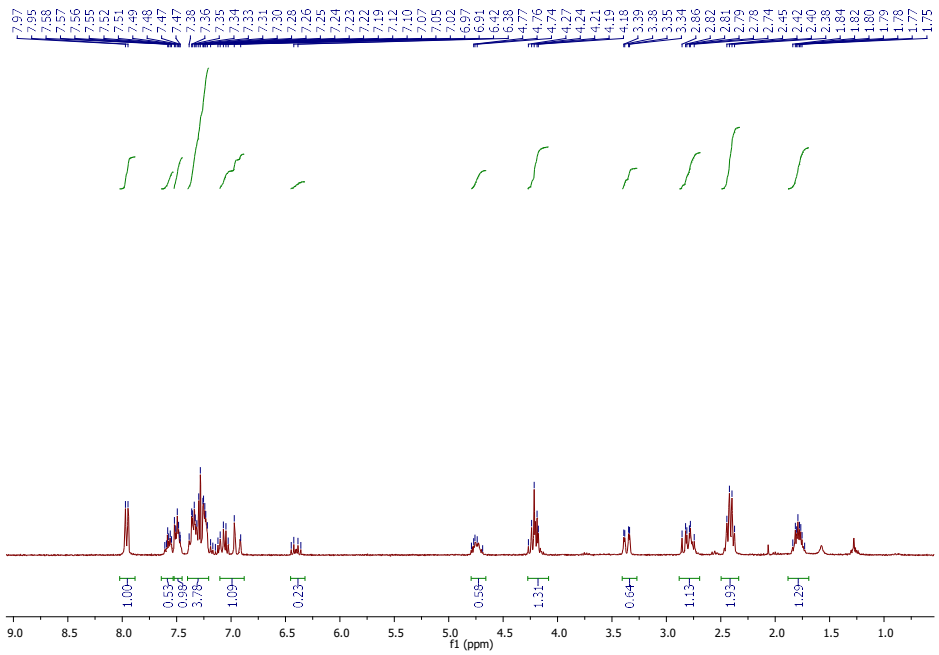


C^{13}NMR of **103a**, $CDCl_3$, 75 MHz

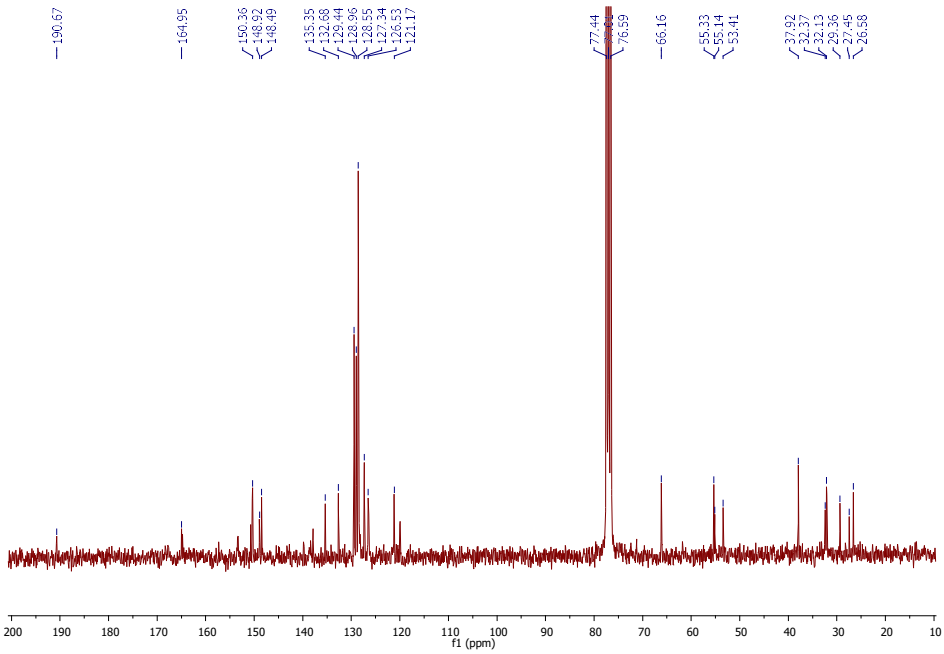


COMPOUND **103b**

^{1}HNMR of **103b**, $CDCl_3$, 300 MHz

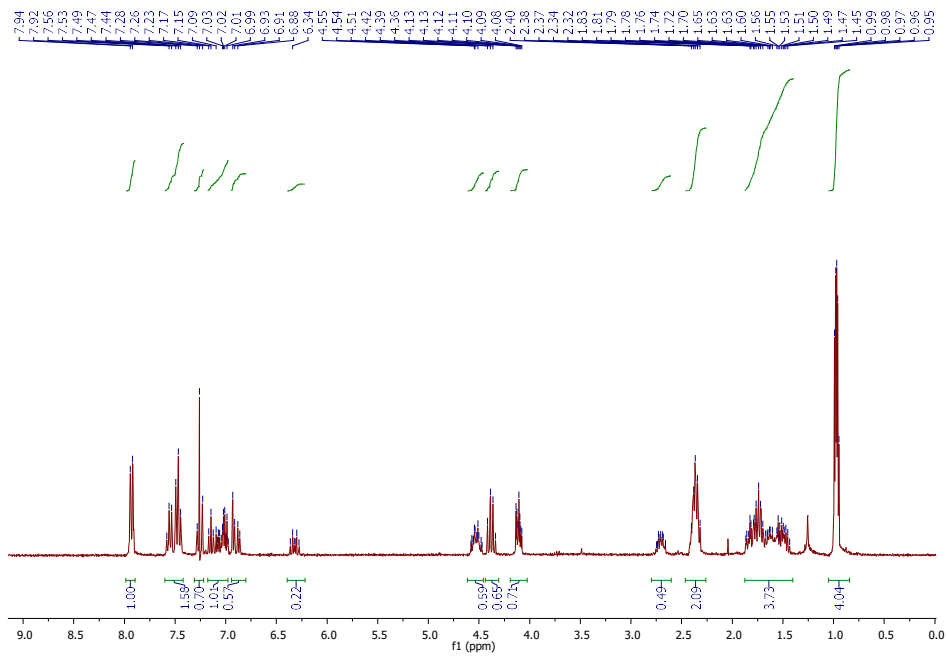


C^{13}NMR of **103b**, $CDCl_3$, 75 MHz

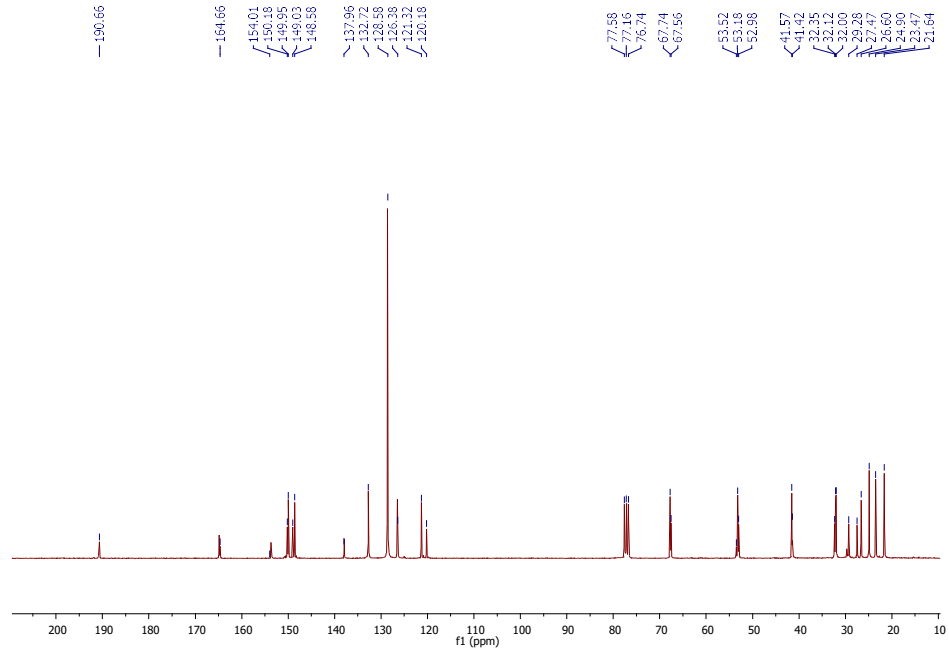


COMPOUND **103c**

^{1}HNMR of **103c**, $CDCl_3$, 300 MHz

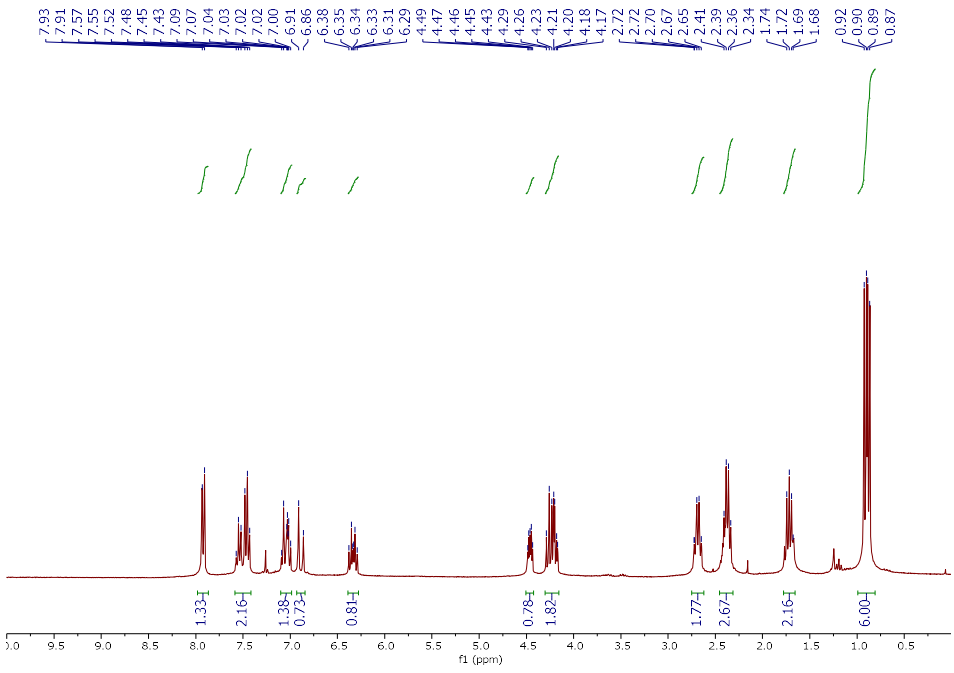


C^{13}NMR of **103c**, $CDCl_3$, 75 MHz

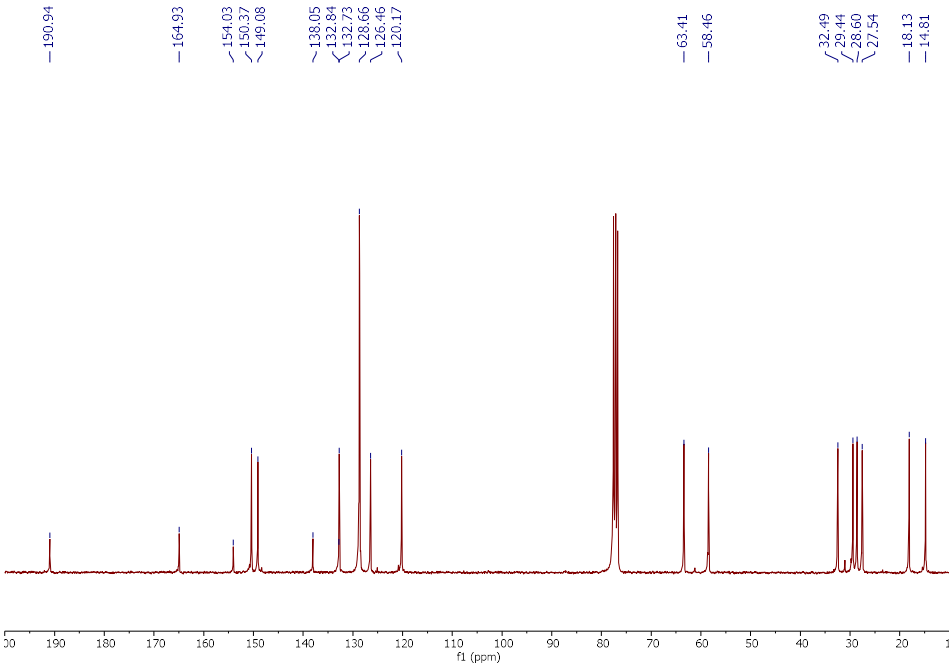


COMPOUND **103d**

^{1}HNMR of **103d**, $CDCl_3$, 300 MHz

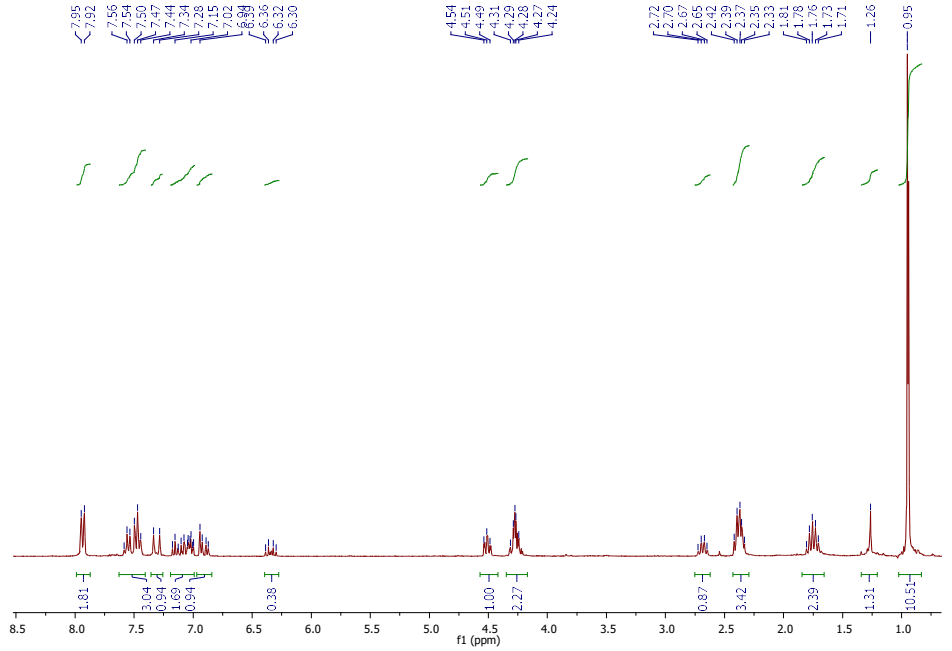


C^{13}NMR of **103d**, $CDCl_3$, 75 MHz

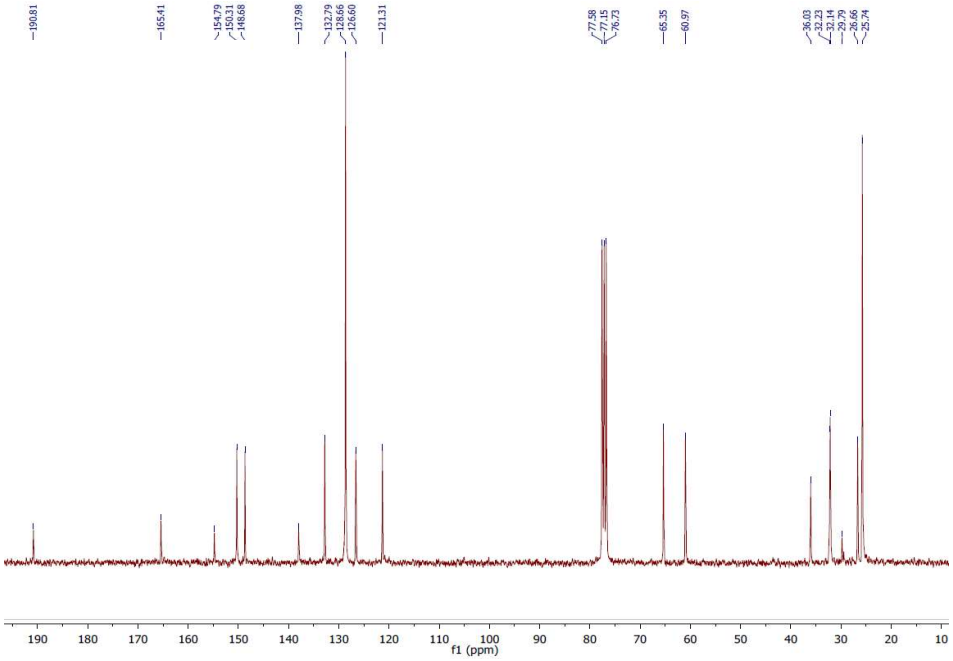


COMPOUND **103e**

^{1}HNMR of **103e**, $CDCl_3$, 300 MHz

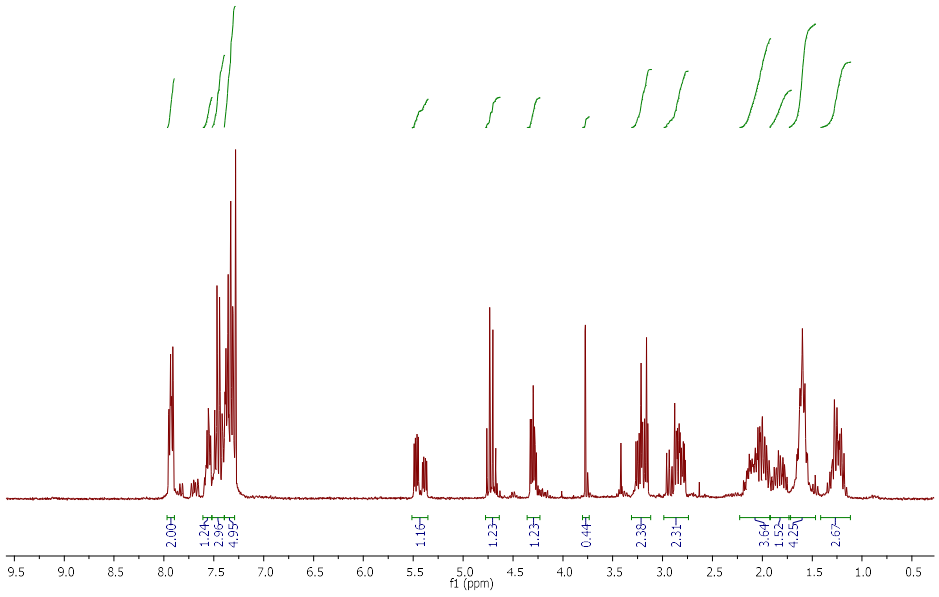


C^{13}NMR of **103e**, $CDCl_3$, 75 MHz

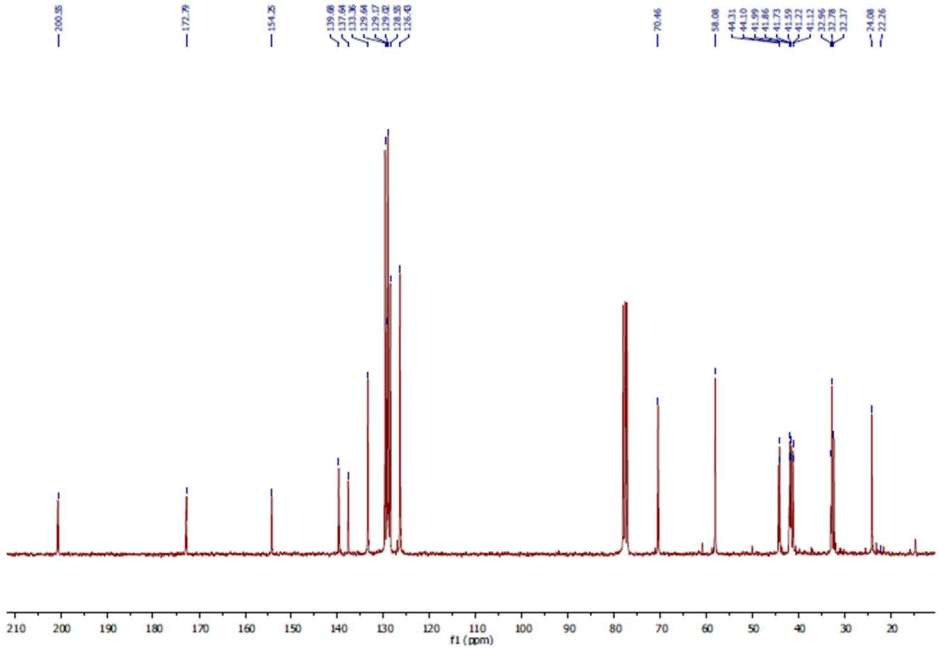


COMPOUND **104a**

^{1}HNMR of **104a**, $CDCl_3$, 300 MHz

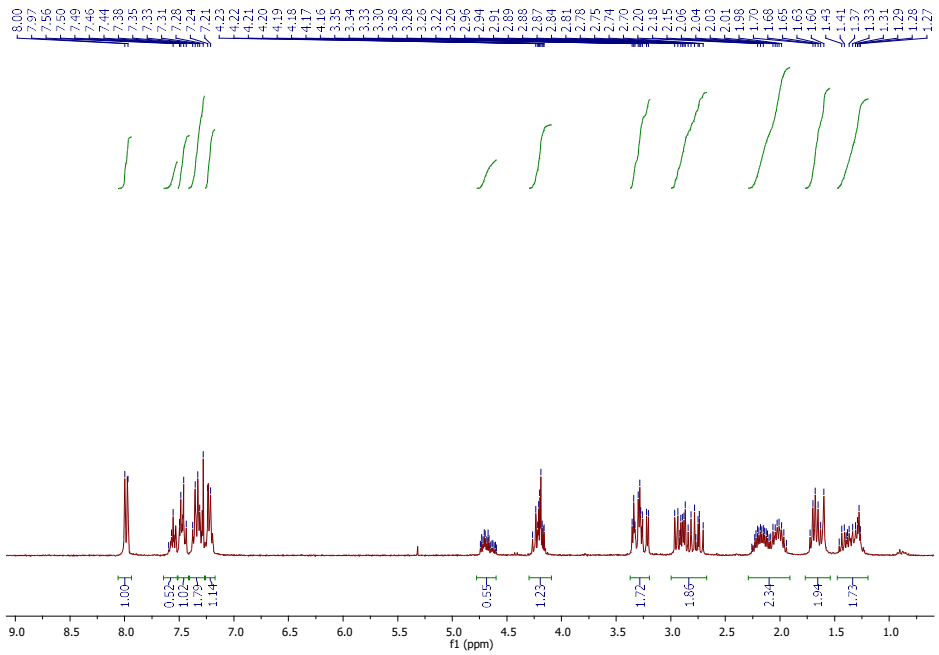


C^{13}NMR of **104a**, $CDCl_3$, 75 MHz

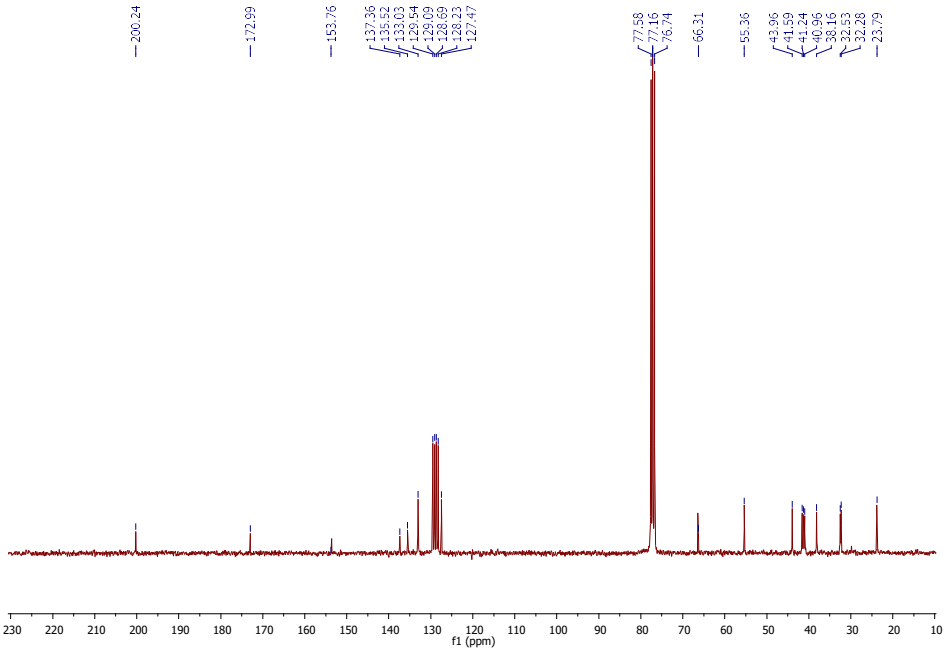


COMPOUND **104b**

^{1}HNMR of **104b**, $CDCl_3$, 300 MHz

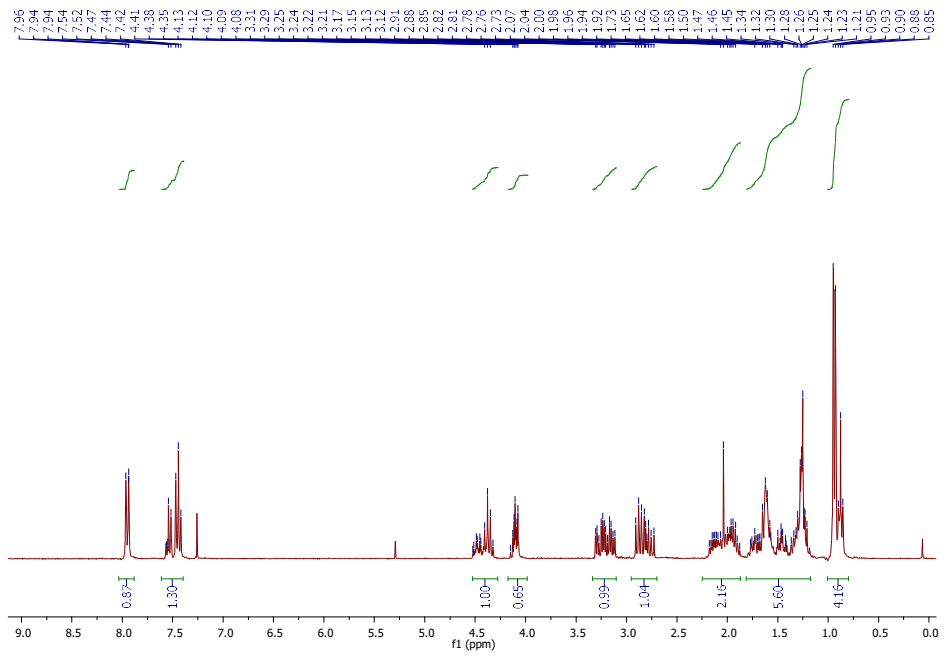


C^{13}NMR of **104b**, $CDCl_3$, 75 MHz

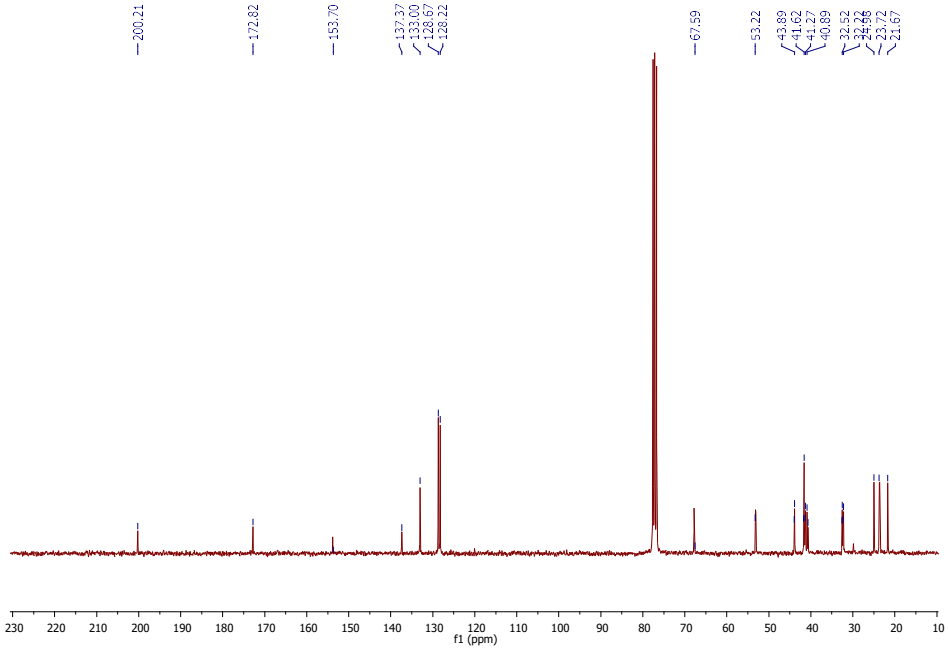


COMPOUND **104c**

^{1}HNMR of **104c**, $CDCl_3$, 300 MHz

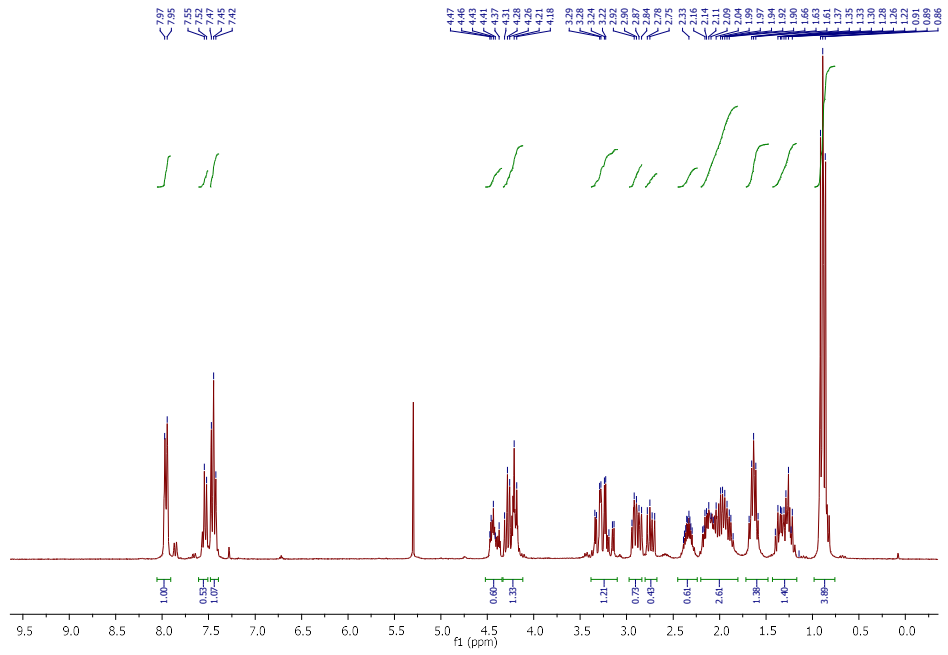


C^{13}NMR of **104c**, $CDCl_3$, 75 MHz

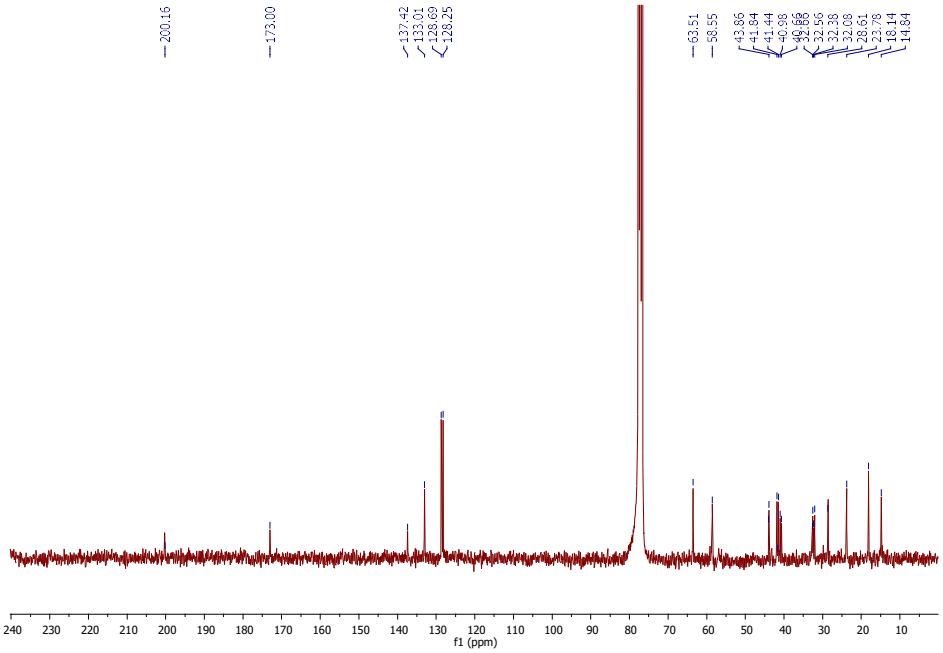


COMPOUND **104d**

^{1}HNMR of **104d**, $CDCl_3$, 300 MHz

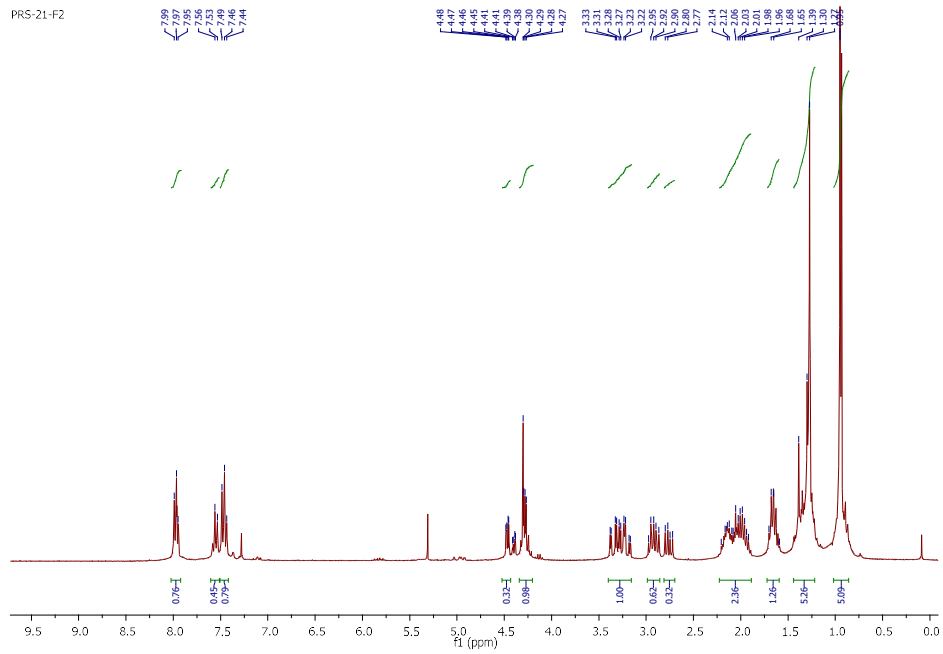


C^{13}NMR of **104d**, $CDCl_3$, 75 MHz

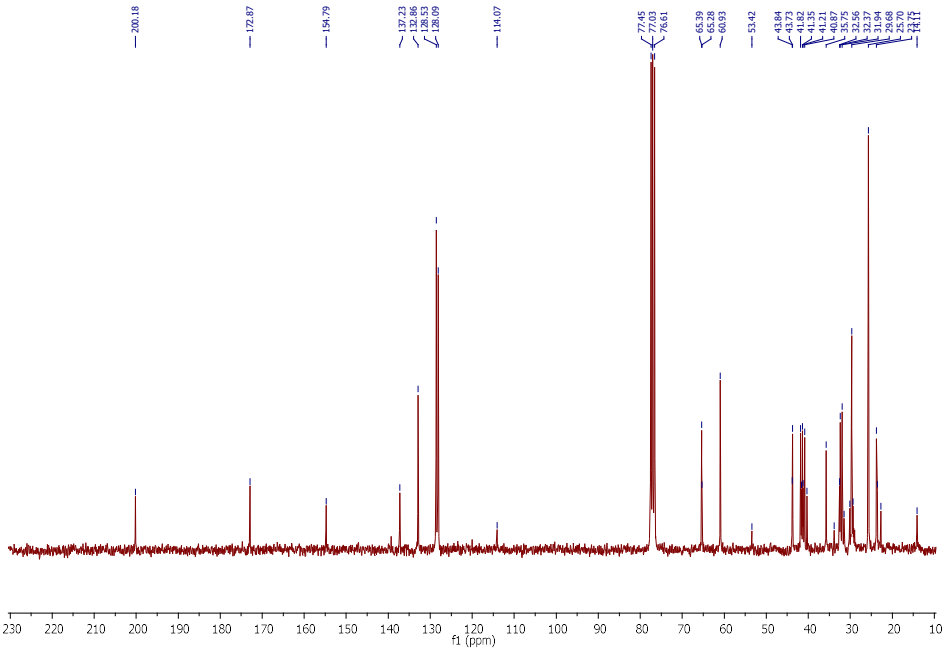


COMPOUND **104e**

^{1}HNMR of **104e**, $CDCl_3$, 300 MHz

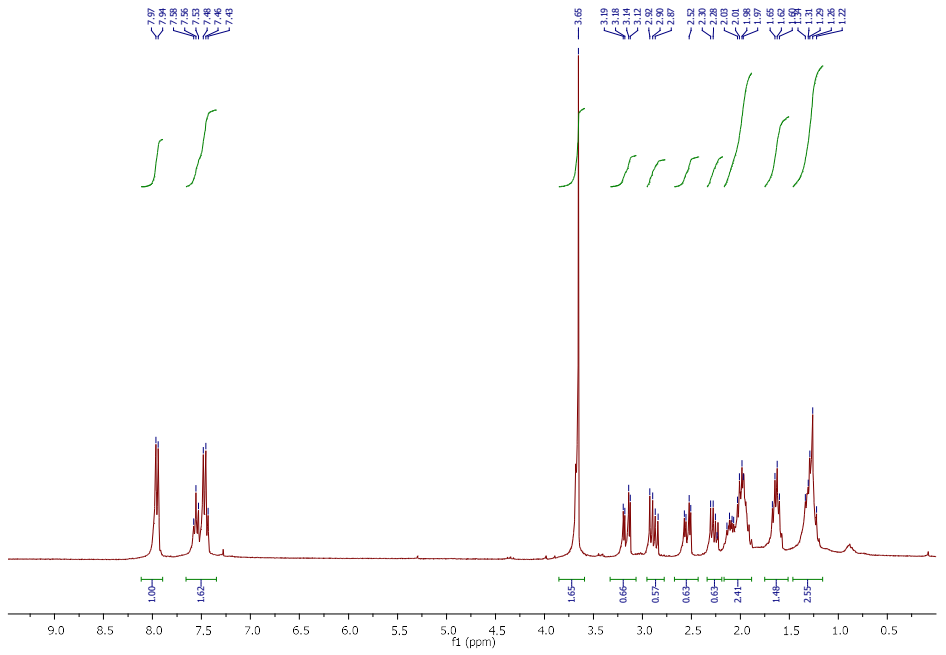


C^{13}NMR of **104e**, $CDCl_3$, 75 MHz

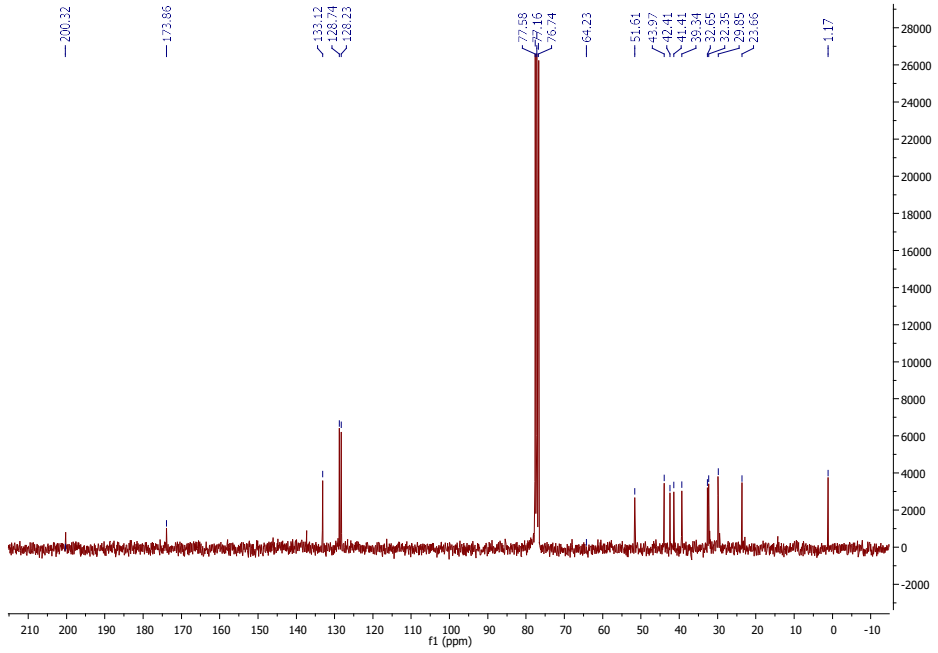


COMPOUND **105**

^{1}HNMR of **105**, $CDCl_3$, 300 MHz

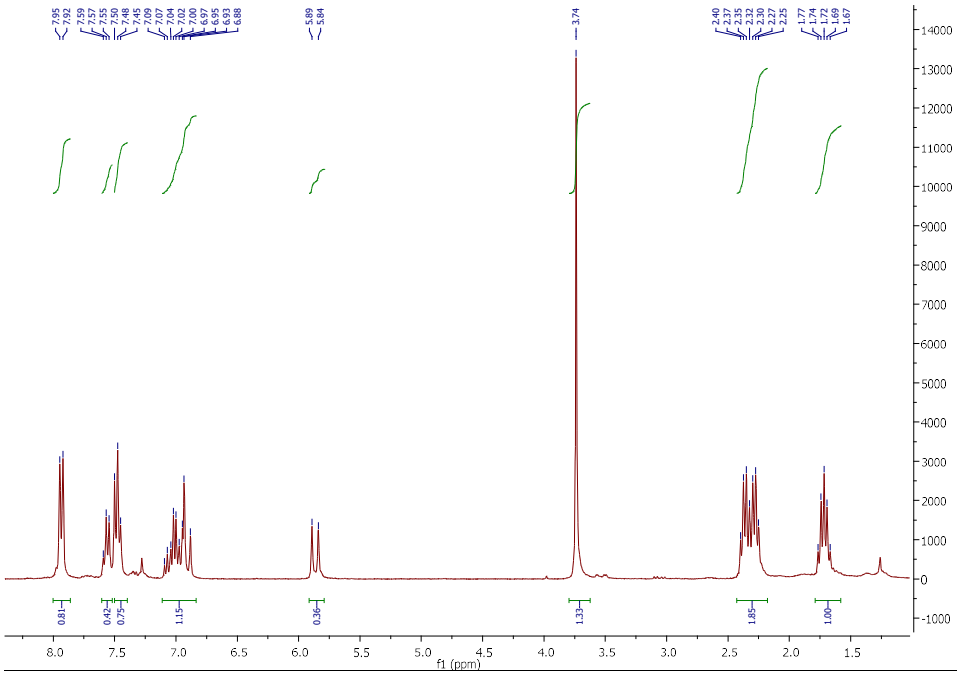


C^{13}NMR of **105**, $CDCl_3$, 75 MHz



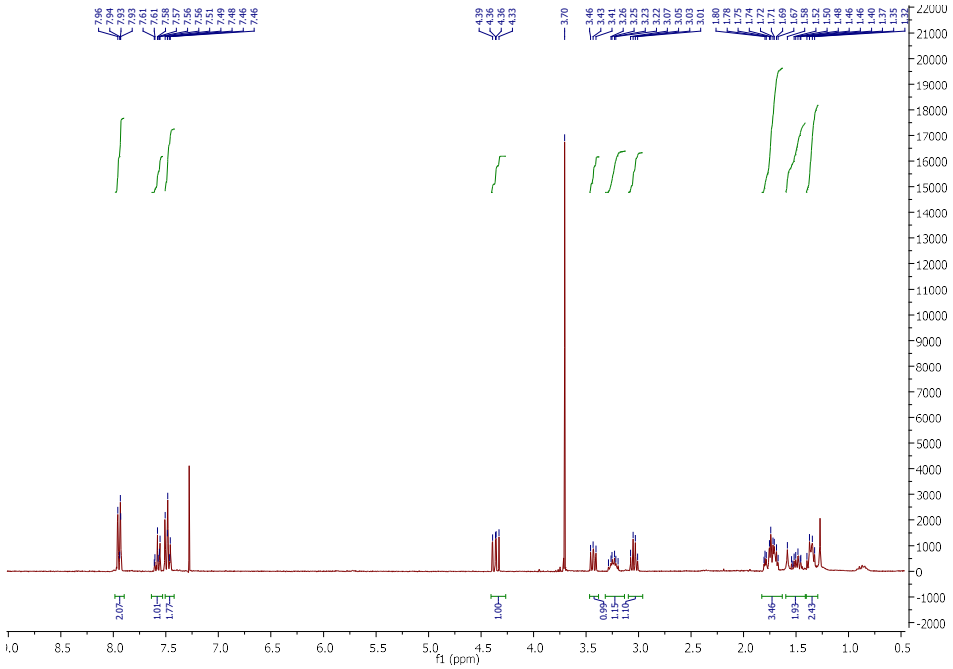
COMPOUND 106

^{1}HNMR of **106**, $CDCl_3$, 300 MHz

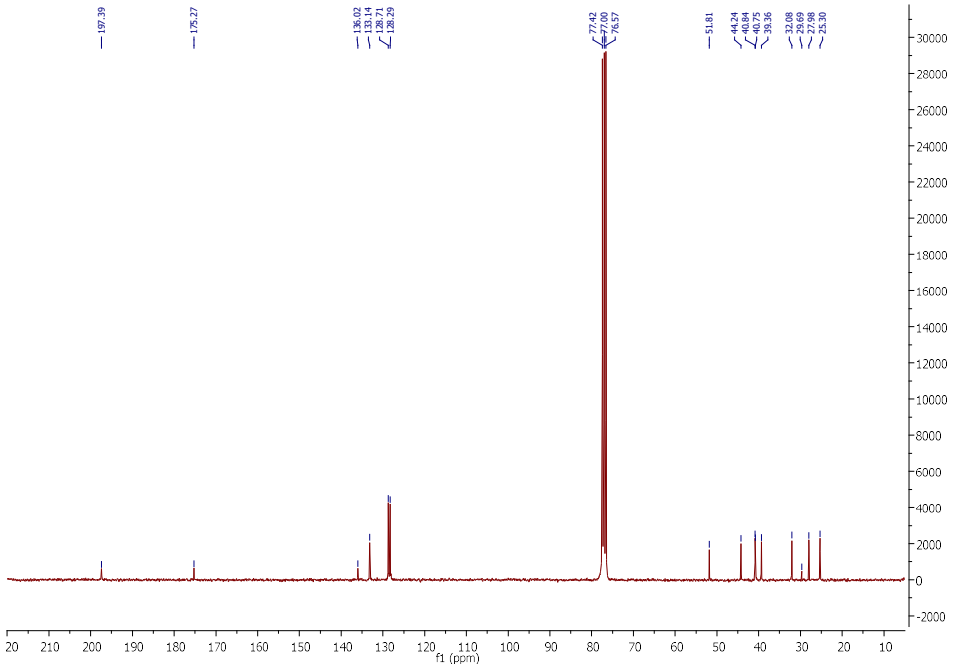


COMPOUND *cis*-107

^{1}HNMR of ***cis*-107**, $CDCl_3$, 300 MHz

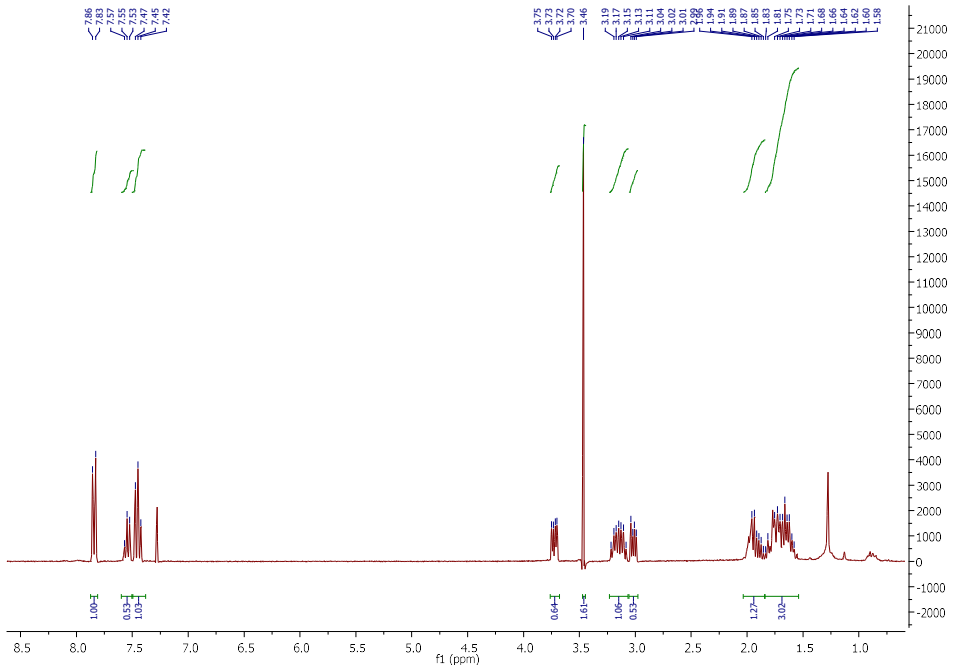


C^{13}NMR of ***cis*-107**, $CDCl_3$, 75 MHz

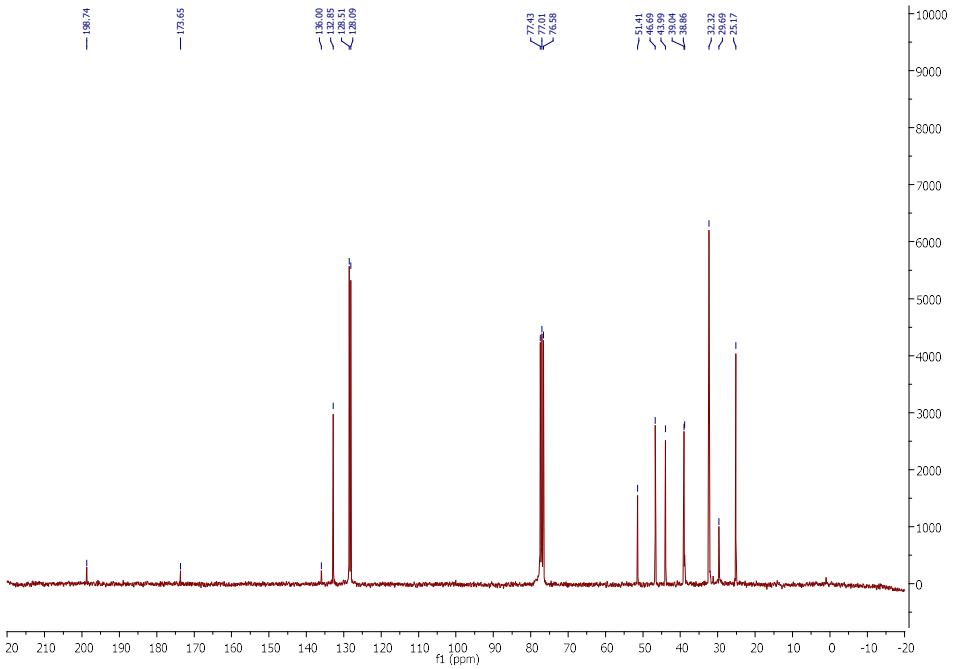


COMPOUND *trans*-107

^{1}HNMR of ***trans*-107**, $CDCl_3$, 300 MHz

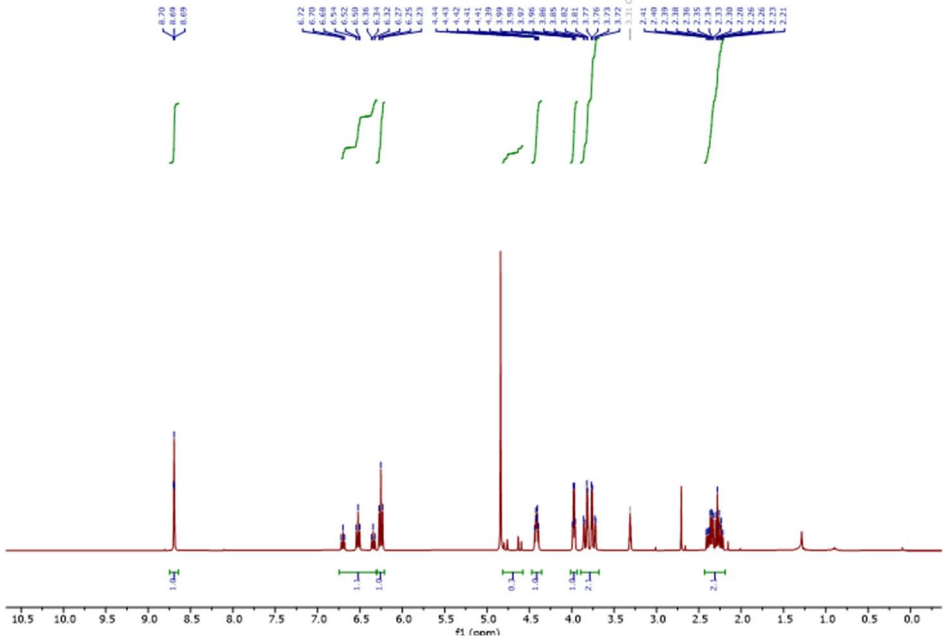


C^{13}NMR of ***trans*-107**, $CDCl_3$, 75 MHz

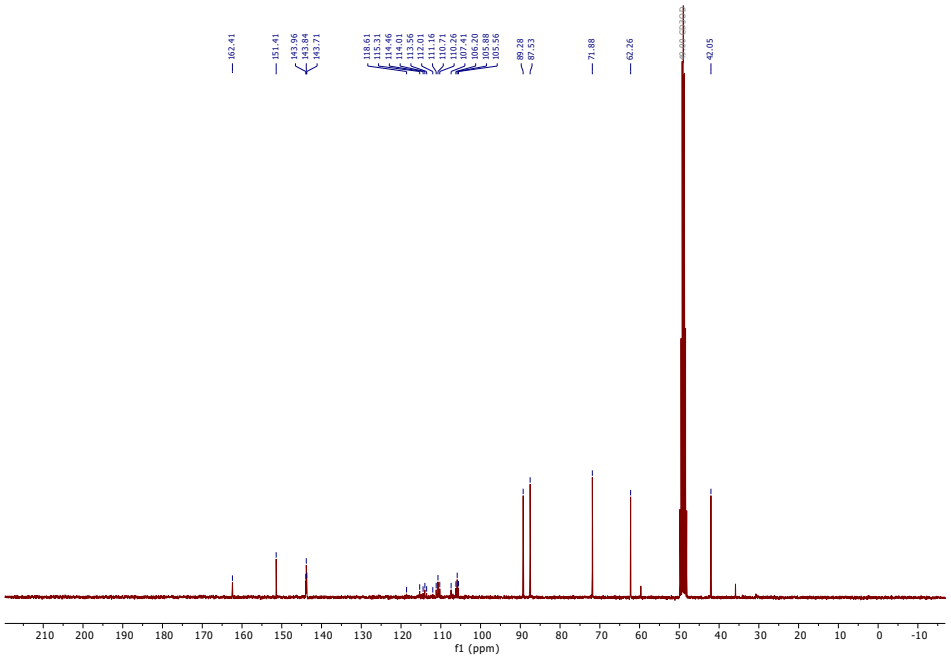


COMPOUND 173

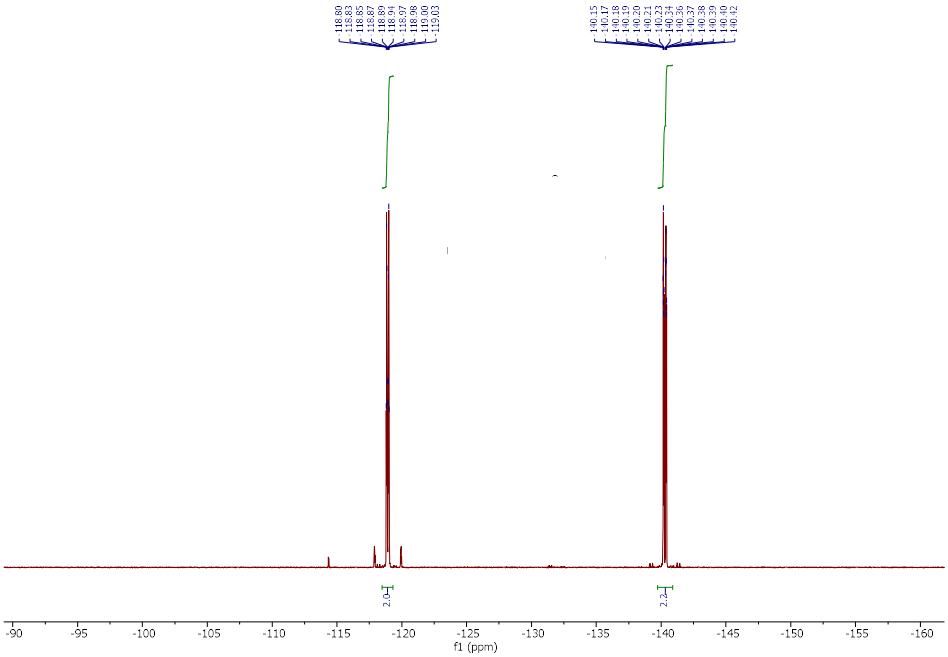
^{1}HNMR of **173**, MeOH-d_4, 300 MHz



C^{13}NMR of **173**, MeOH-d_4, 75 MHz

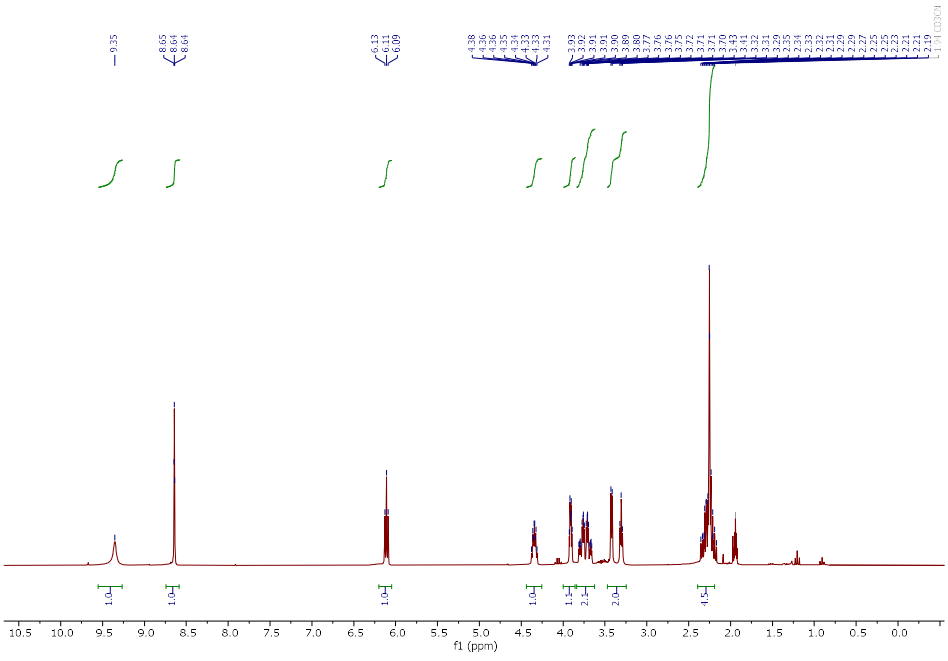


^{19}F NMR of **173**, MeOH-d_4, 282 MHz

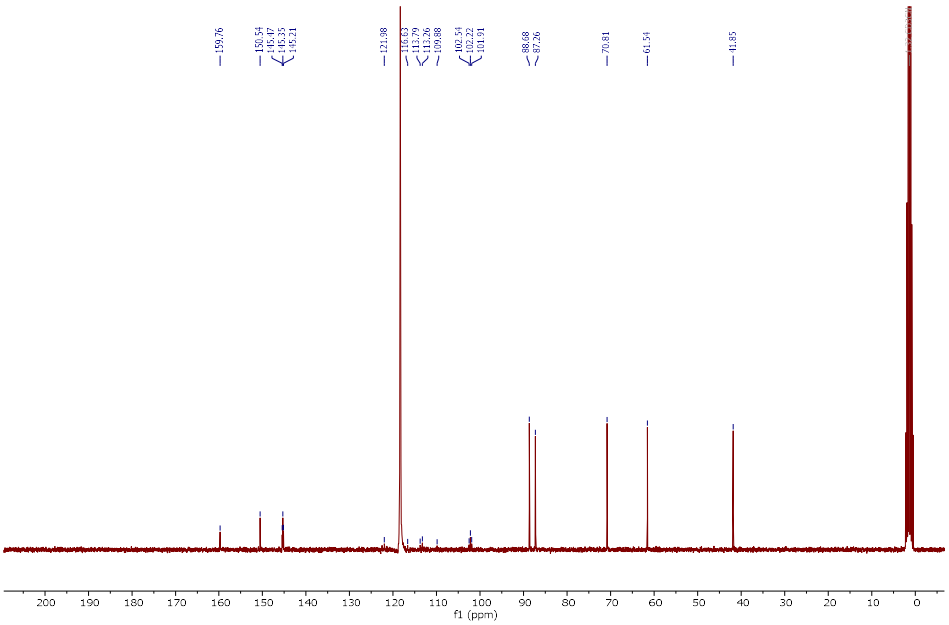


COMPOUND 174

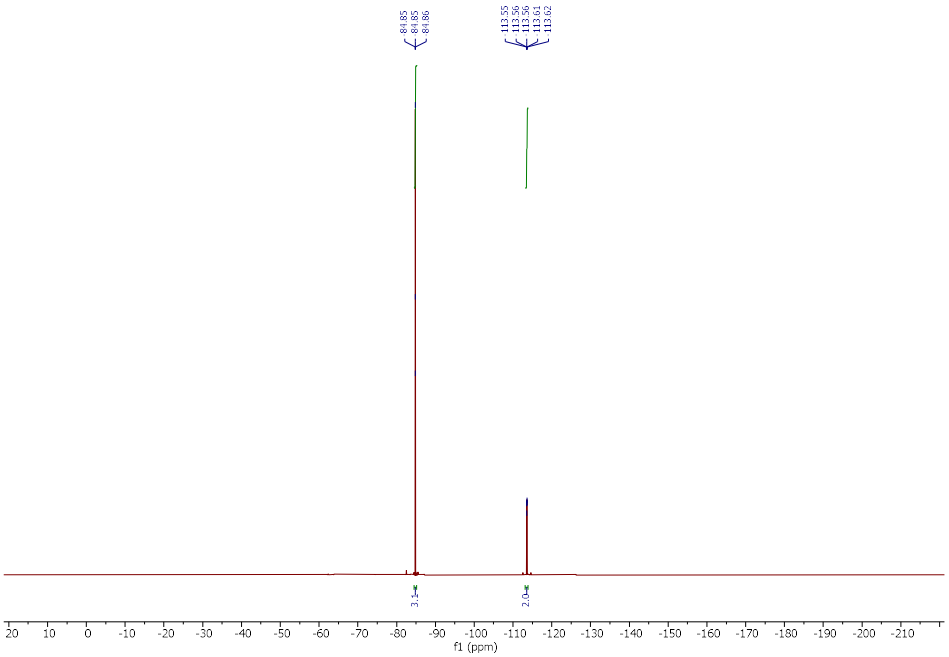
^{1}HNMR of **174**, CD_3CN, 300 MHz



^{13}CNMR of **174**, CD_3CN, 75 MHz

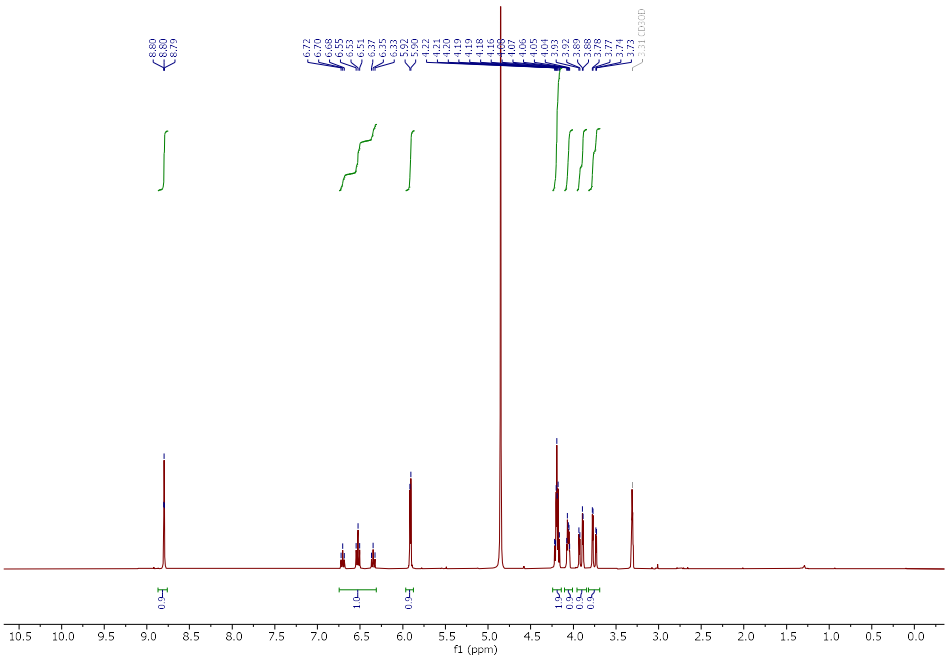


^{19}FNMR of **174**, CD_3CN, 282 MHz

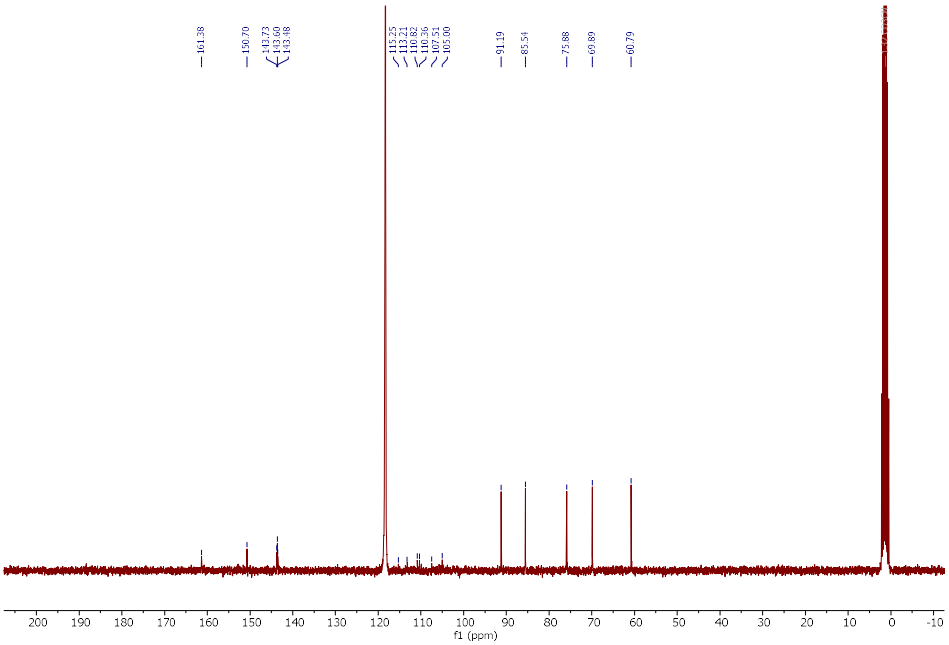


COMPOUND 175

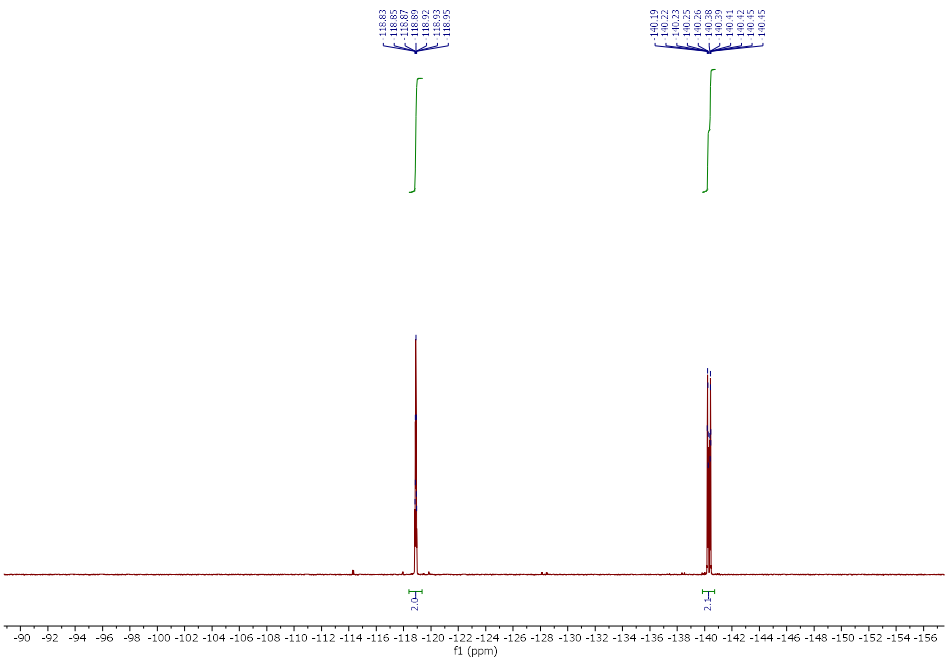
^{1}HNMR of **175**, CD_3OD, 300 MHz



^{13}CNMR of **175**, CD_3OD, 75 MHz

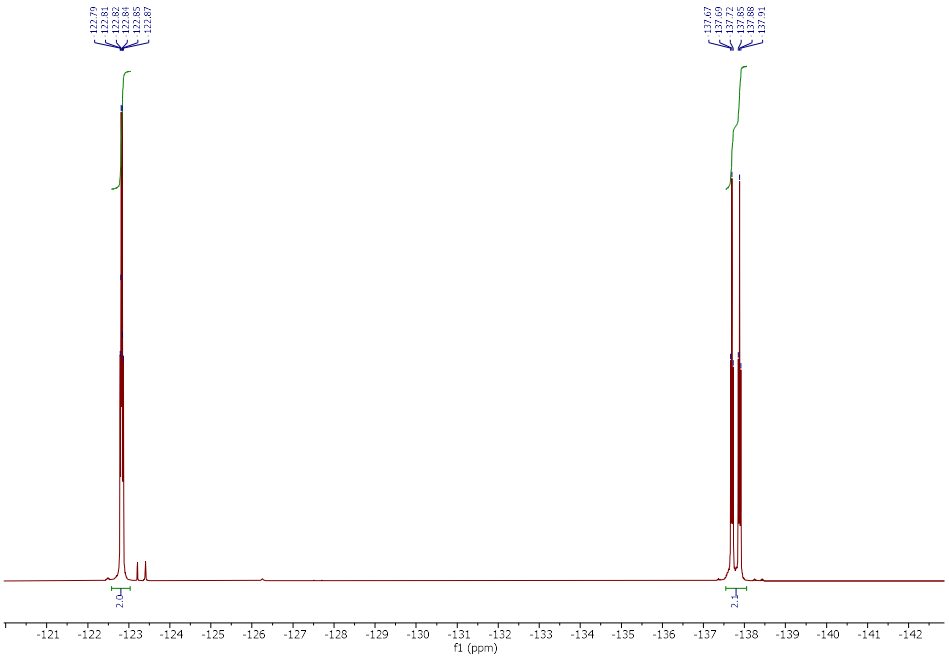


^{19}FNMR of **175**, CD_3OD, 282 MHz

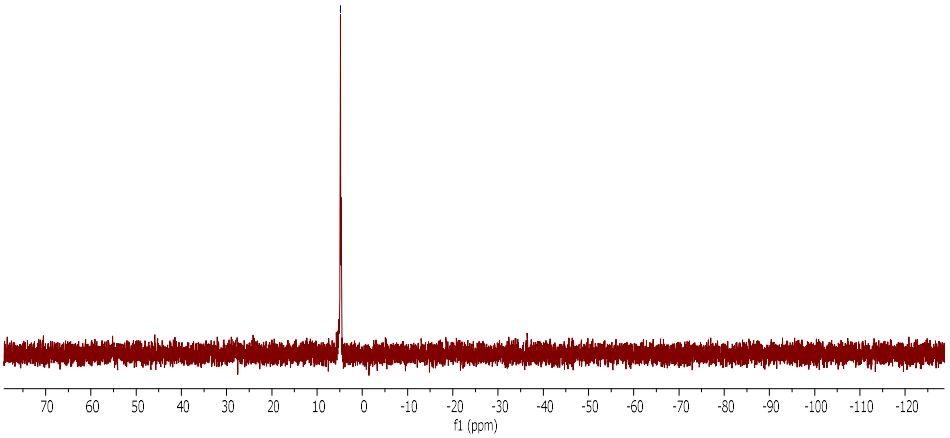


COMPOUND 176

^{19}FNMR of **176**, D_2O, 282 MHz

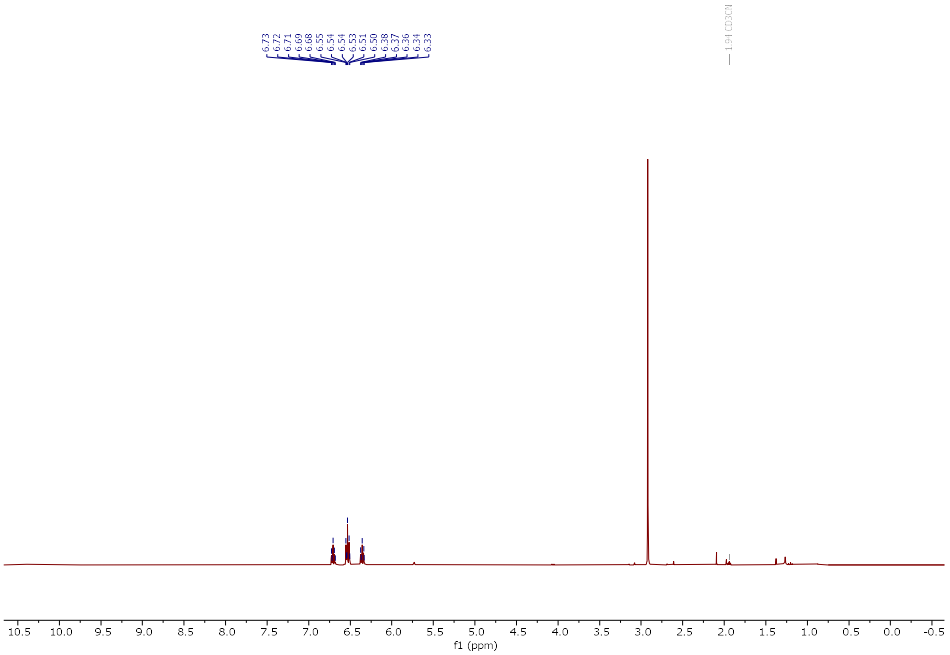


^{31}PNMR of **176**, D_2O, 122 MHz

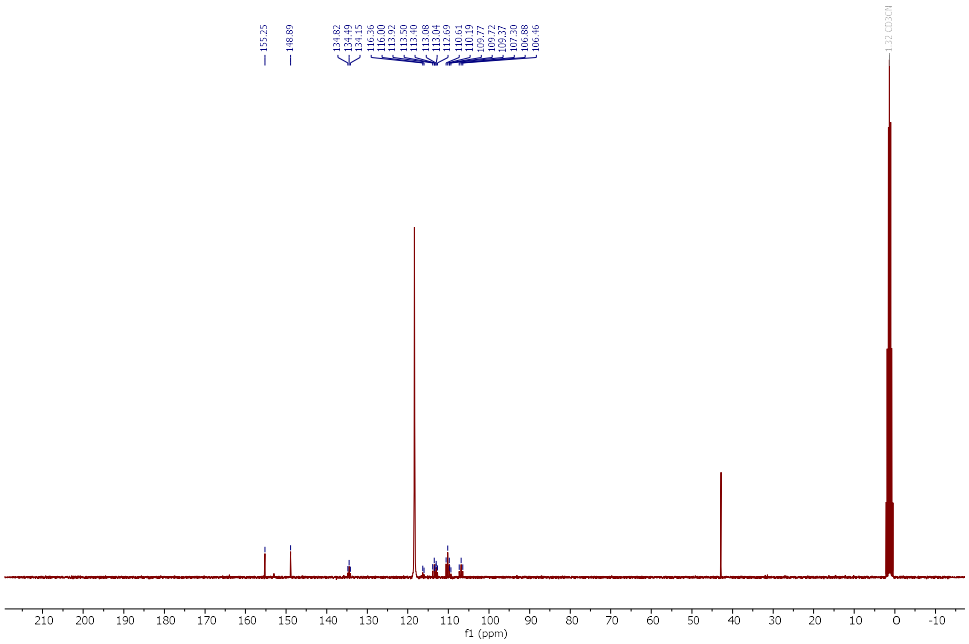


COMPOUND 177

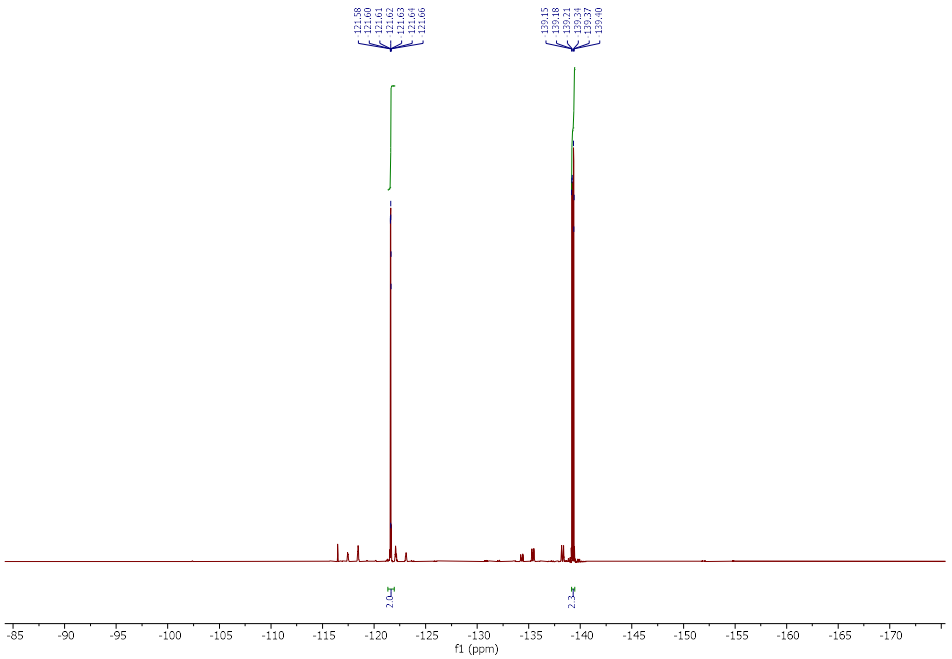
^{1}HNMR of **177**, CD_3CN, 300 MHz



^{13}CNMR of **177**, CD_3CN, 75 MHz

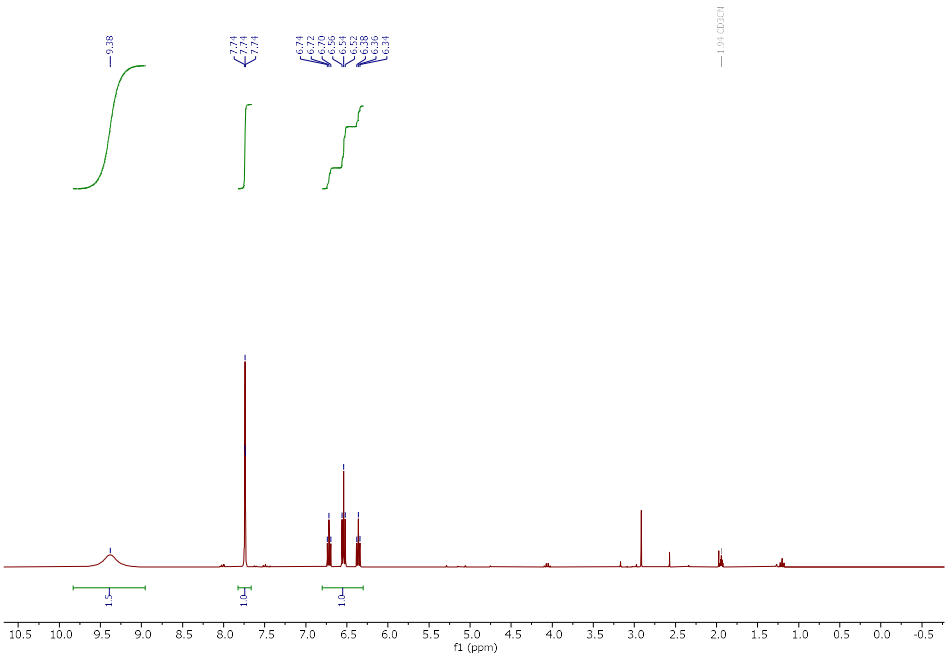


^{19}FNMR of **177**, CD_3CN, 282 MHz

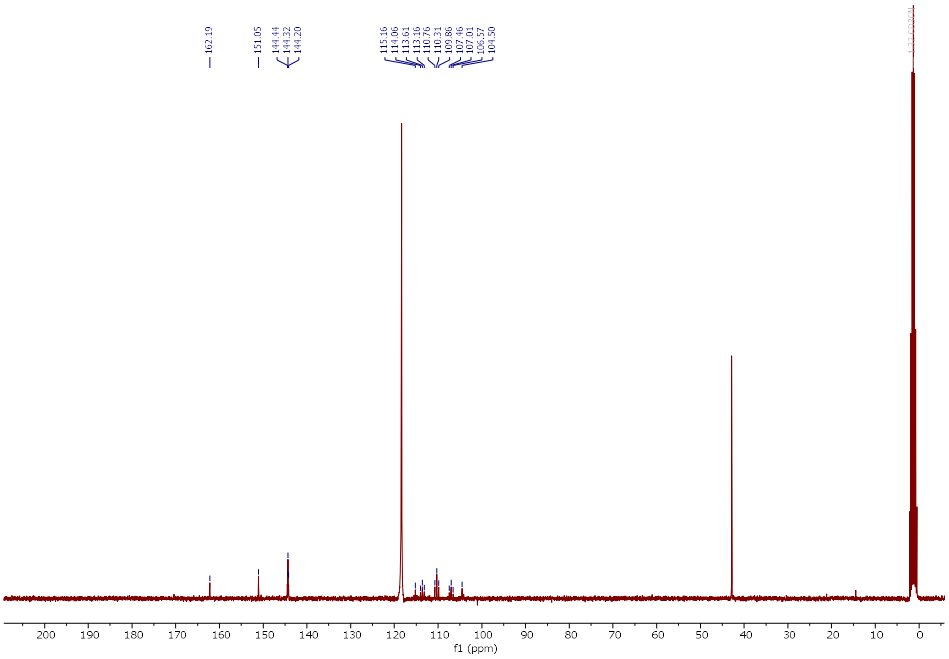


COMPOUND 178

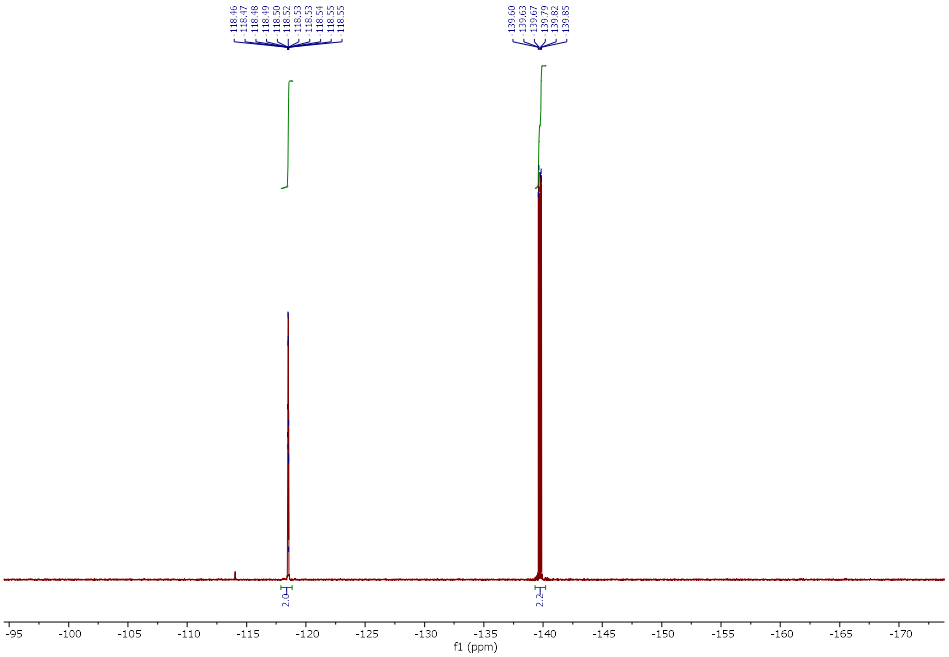
^{1}HNMR of **178**, CD_3CN, 300 MHz



^{13}CNMR of **178**, CD_3CN, 75 MHz

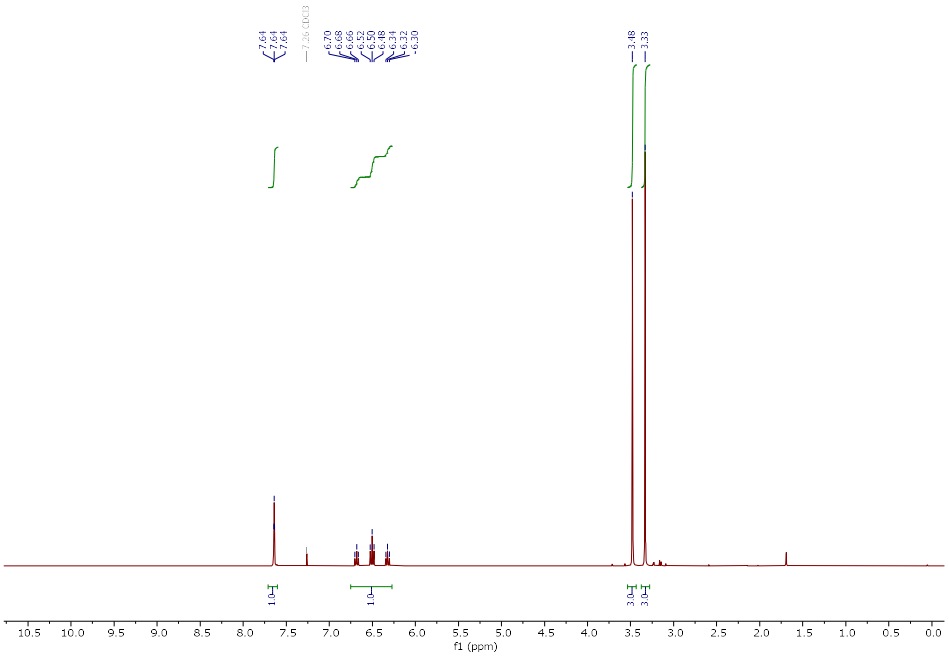


^{19}FNMR of **178**, CD_3CN, 282 MHz

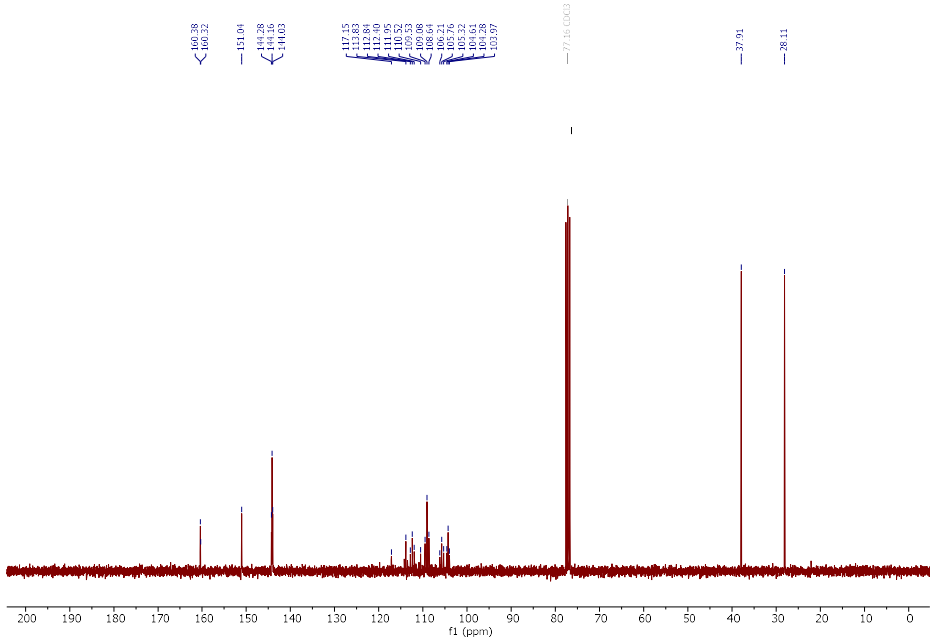


COMPOUND 179

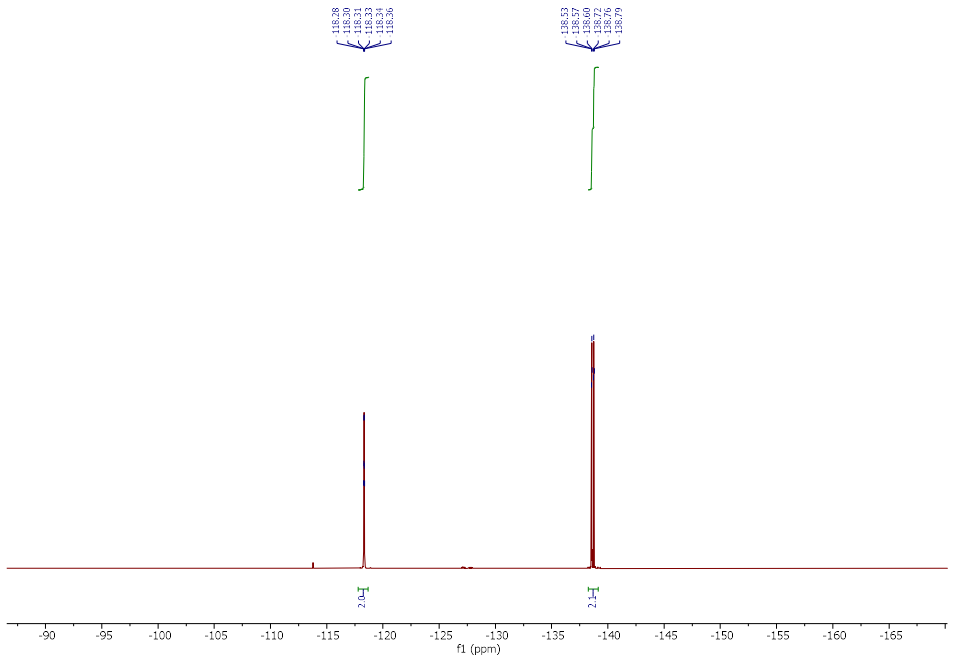
^{1}HNMR of **179**, CD_3Cl_3, 300 MHz



^{13}CNMR of **179**, CD_3Cl_3, 75 MHz

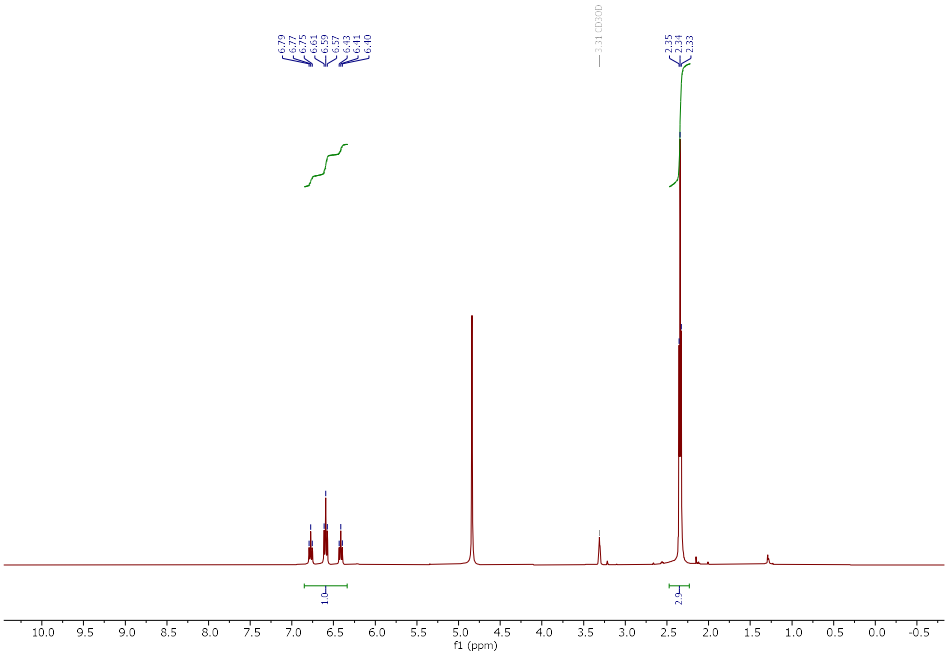


^{19}FNMR of **179**, CD_3Cl_3, 282 MHz

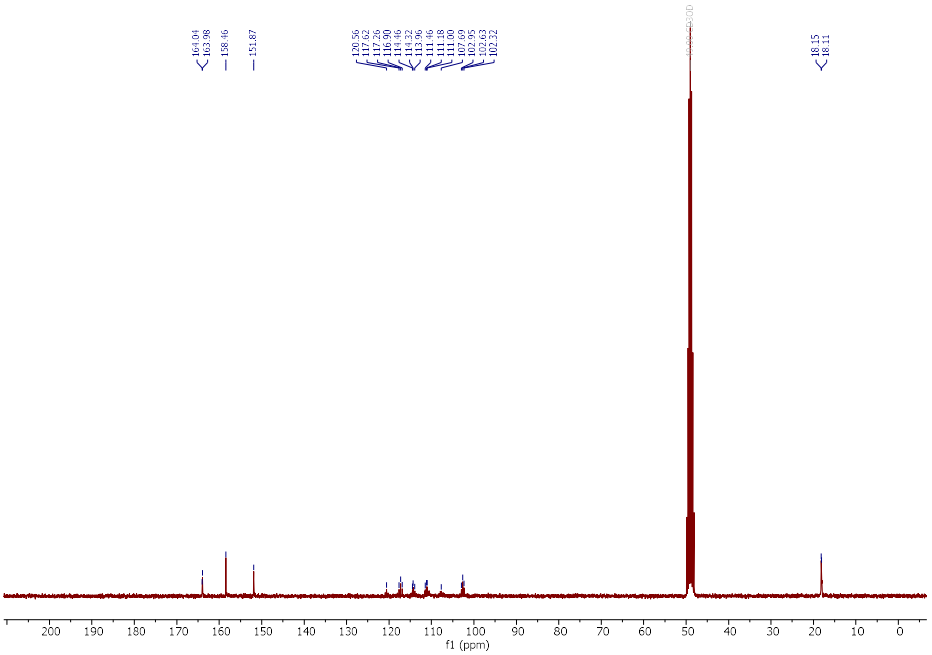


COMPOUND 180

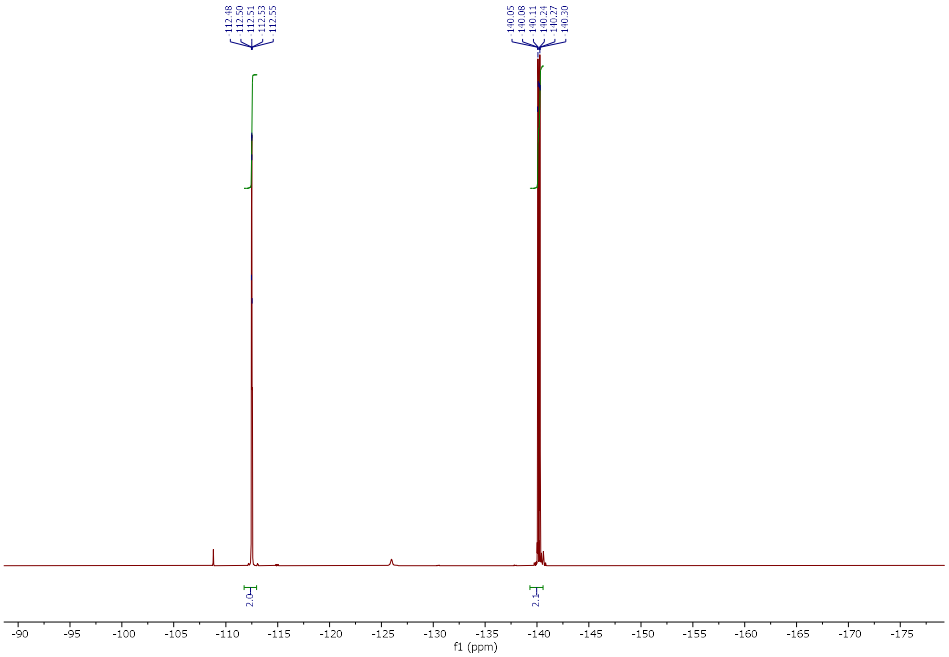
^{1}HNMR of **180**, CD_3OD, 300 MHz



^{13}CNMR of **180**, CD_3OD, 75 MHz

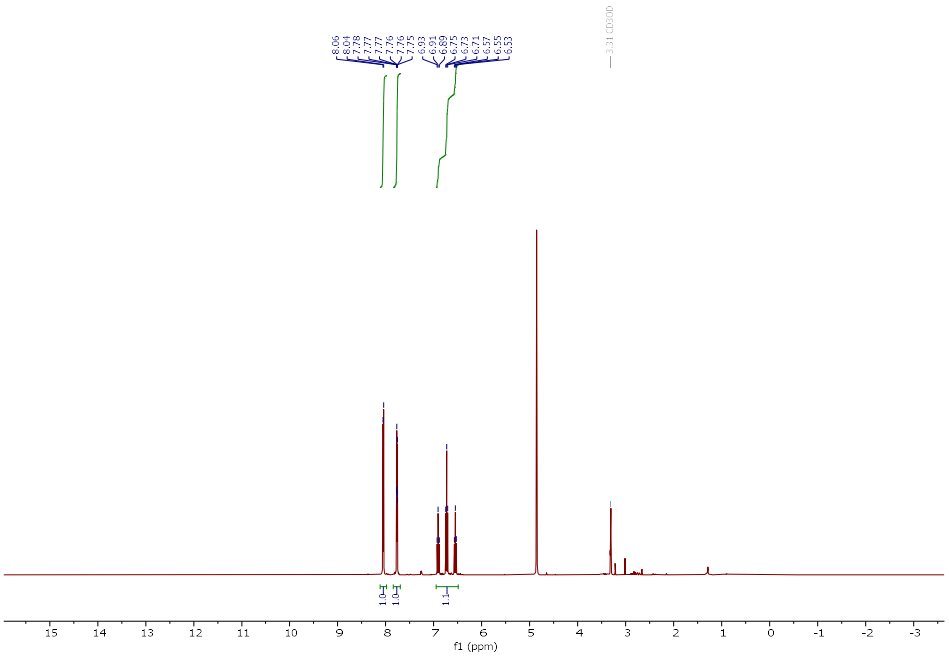


^{19}FNMR of **180**, CD_3OD, 282 MHz

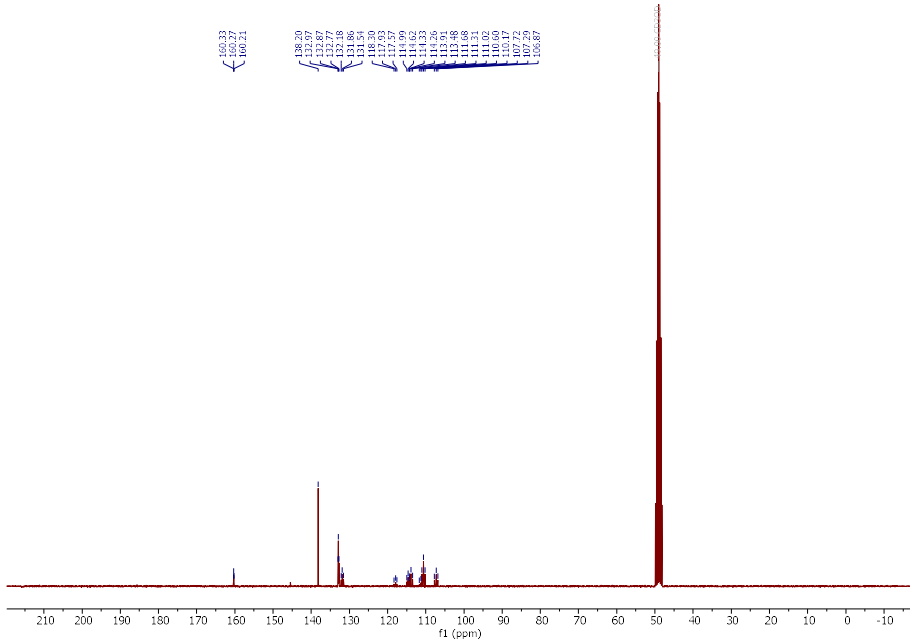


COMPOUND 181

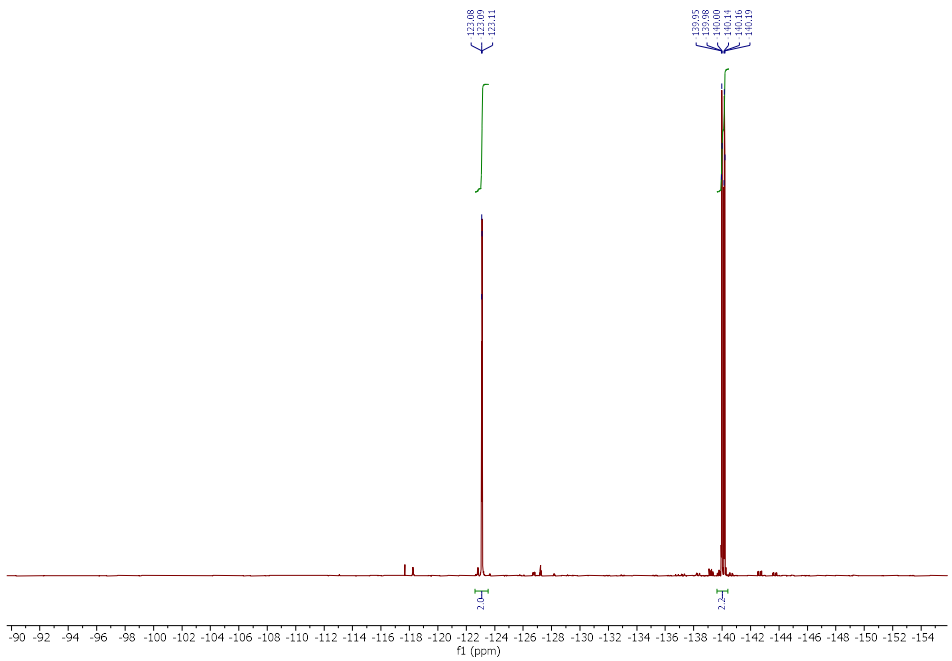
^{1}HNMR of **181**, CD_3OD, 300 MHz



^{13}CNMR of **181**, CD_3OD, 75 MHz

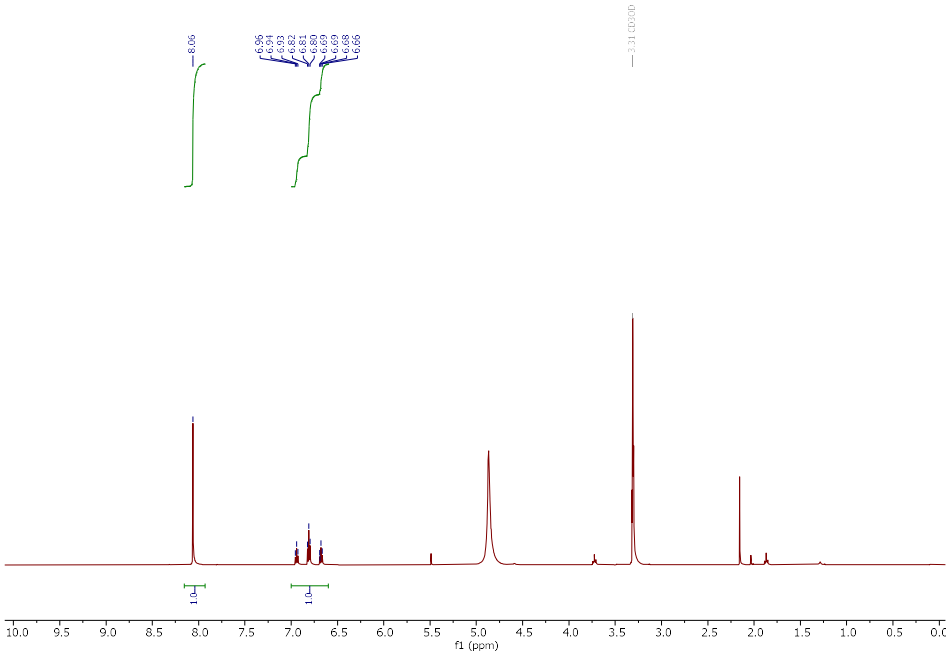


^{19}FNMR of **181**, CD_3OD, 282 MHz

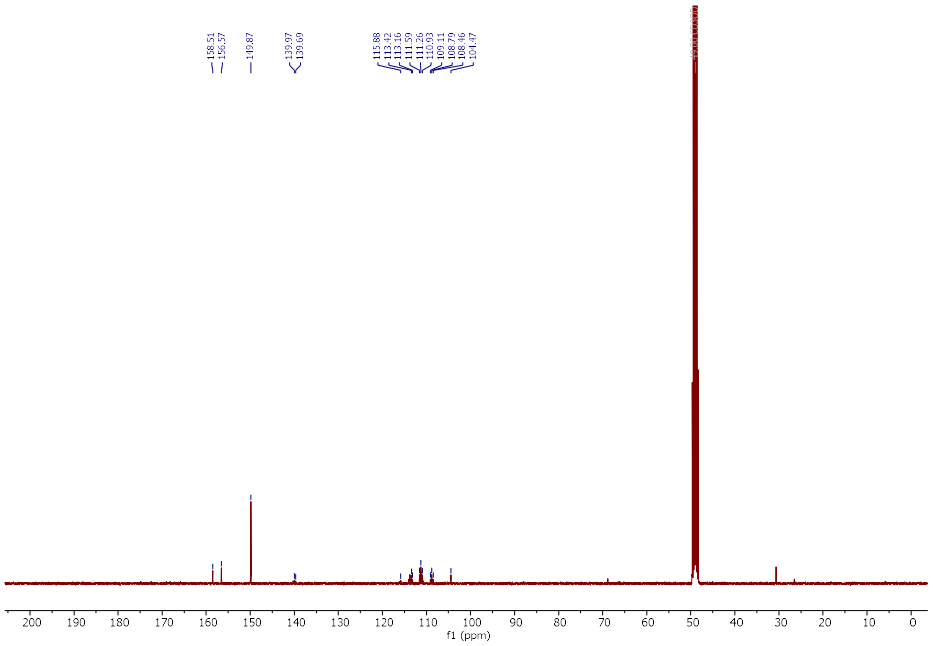


COMPOUND 182

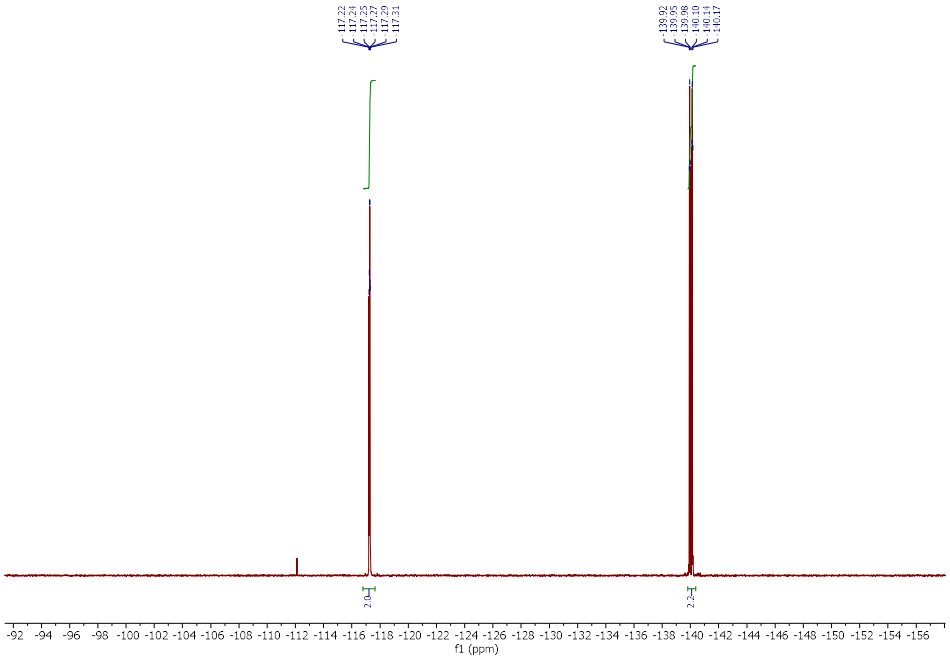
^{1}HNMR of **182**, CD_3OD, 400 MHz



^{13}CNMR of **182**, CD_3OD, 101 MHz

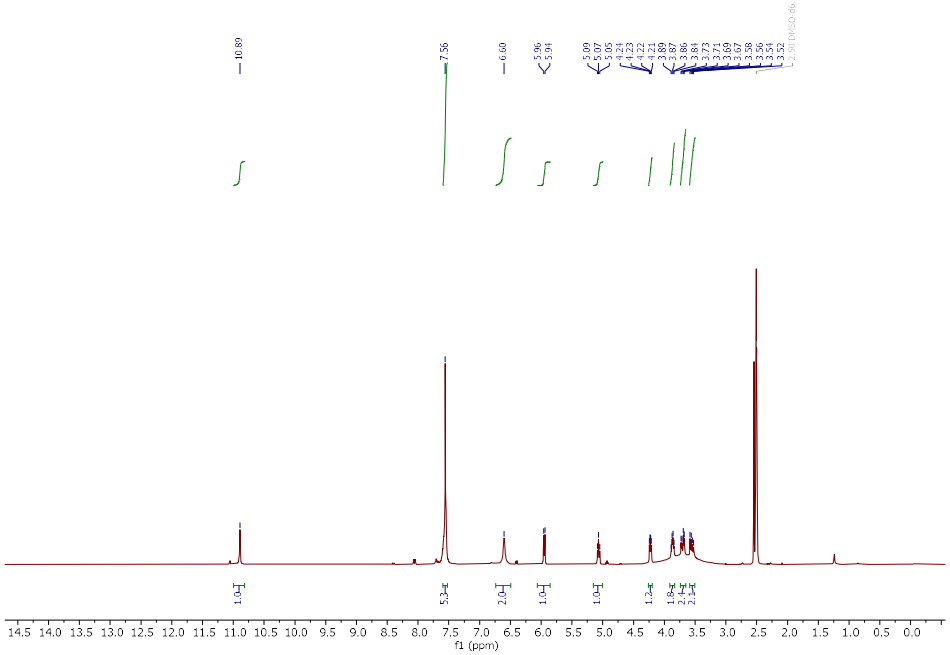


^{19}F NMR of **182**, CD_3OD, 377 MHz

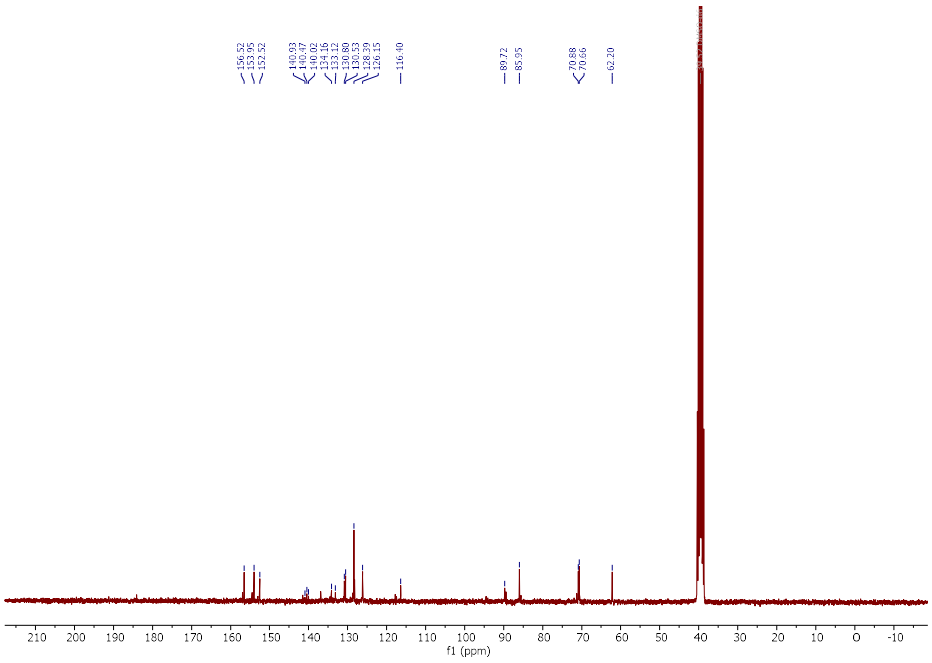


COMPOUND 184 a

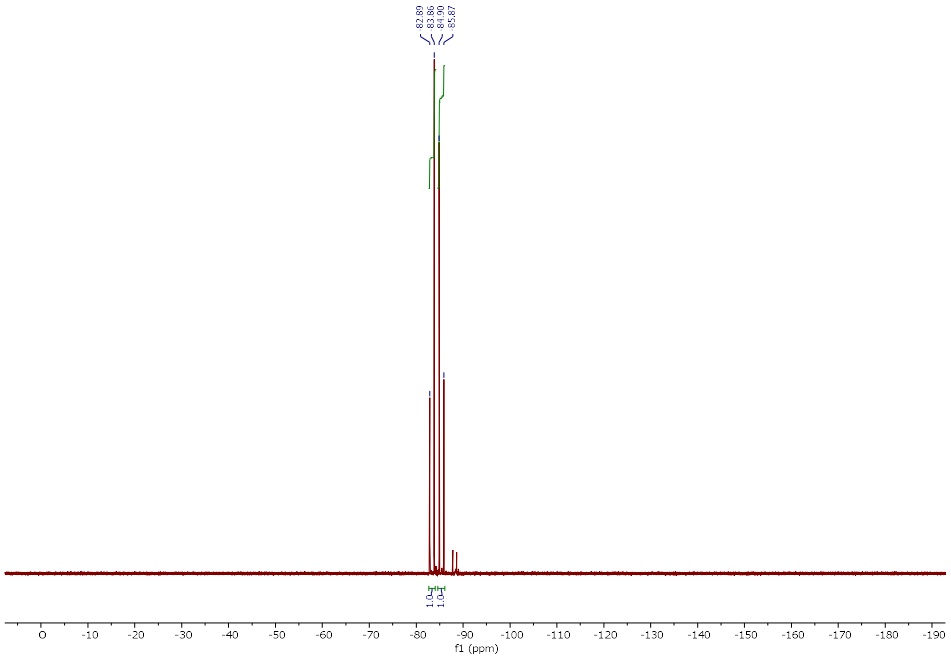
^{1}HNMR of **184a**, DMSO-d_6, 300 MHz



^{13}CNMR of **184a**, DMSO-d_6, 75 MHz

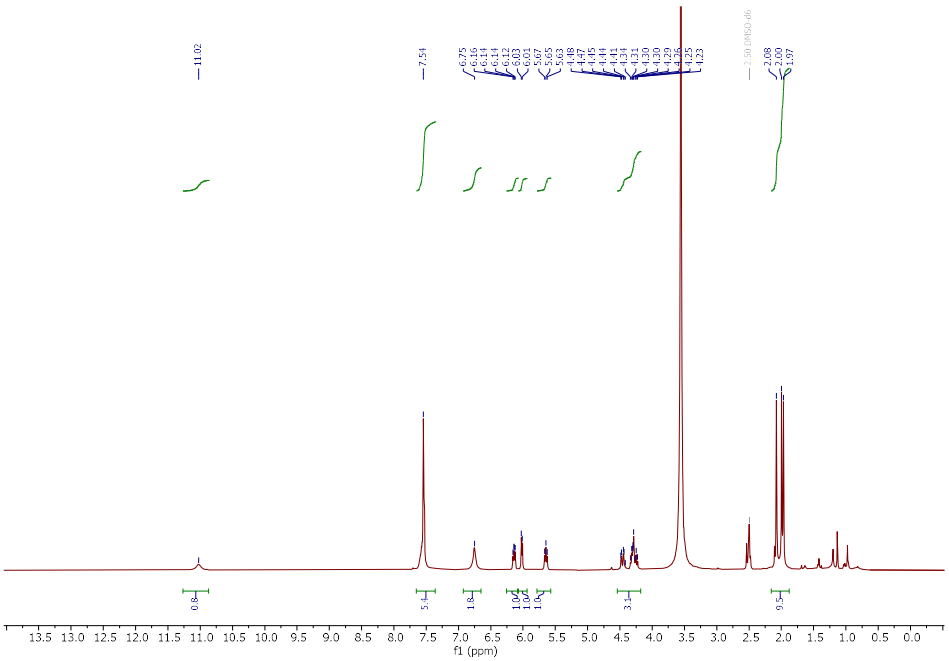


^{19}FNMR of **184a**, DMSO-d_6, 282 MHz

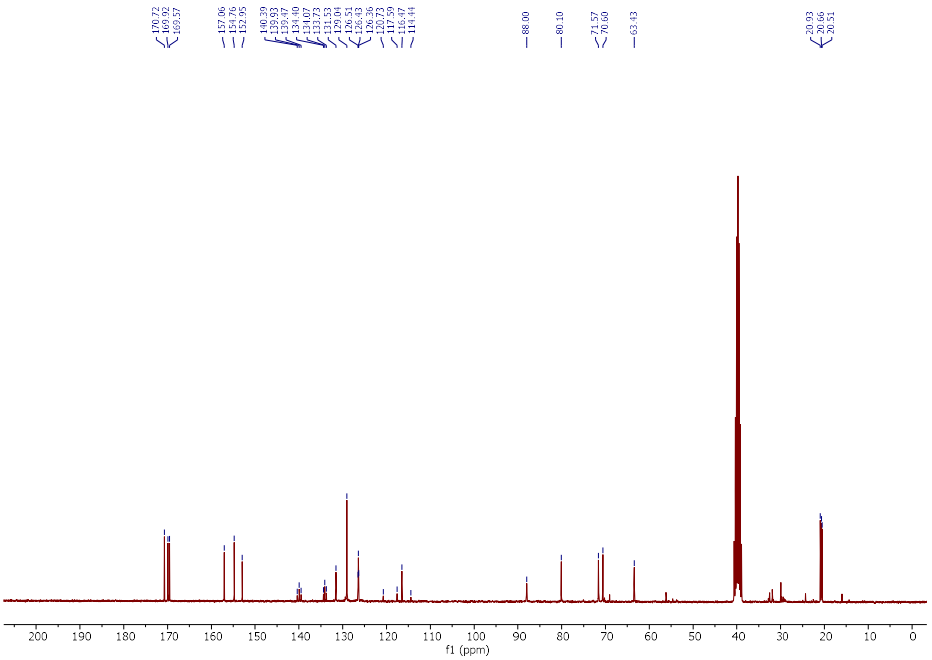


COMPOUND 184 b

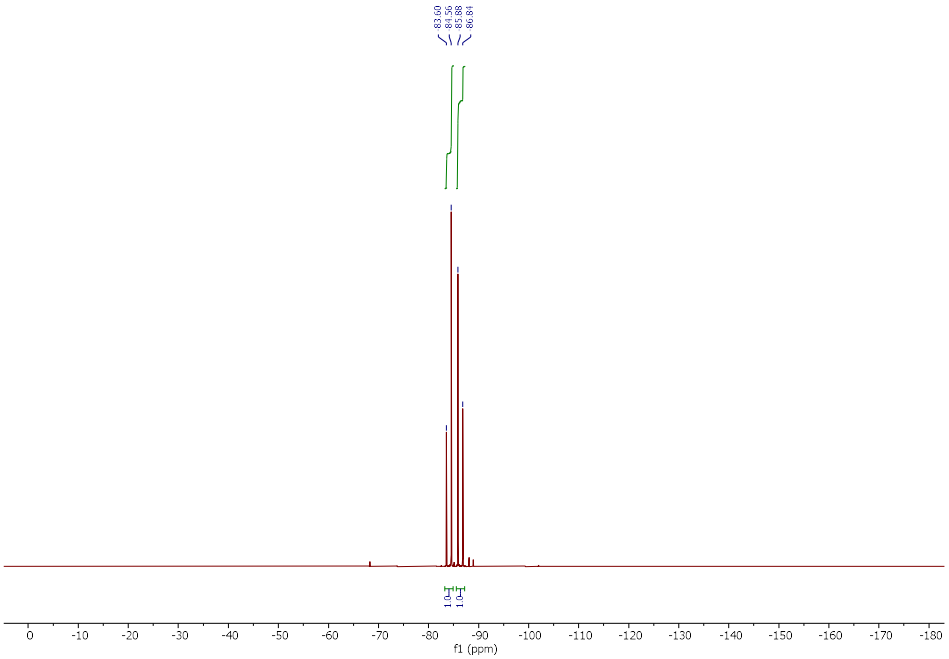
^{1}HNMR of **184b**, DMSO-d_6, 300 MHz



^{13}CNMR of **184b**, DMSO-d_6, 75 MHz

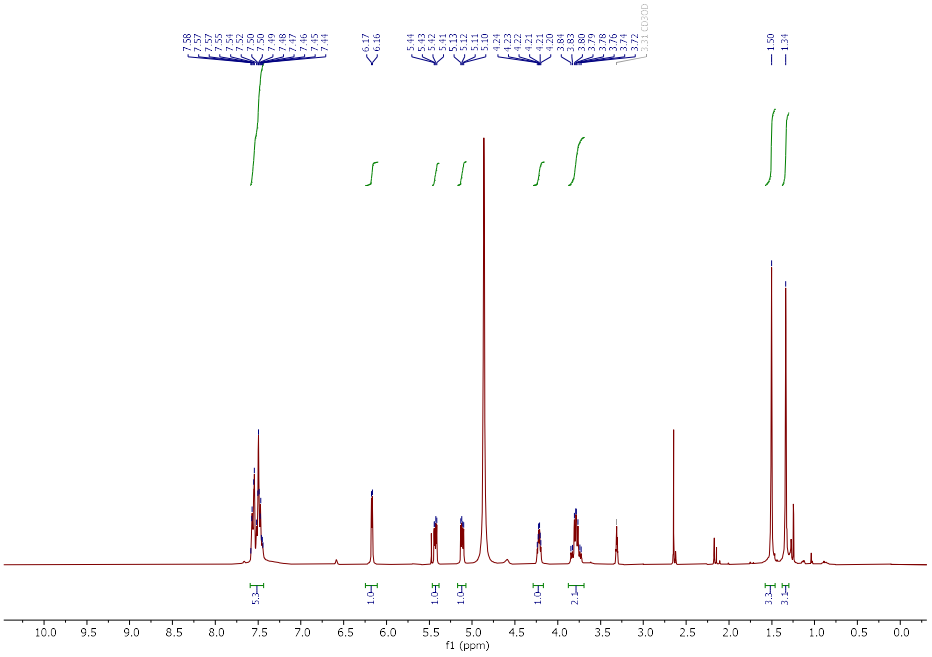


^{19}FNMR of **184b**, DMSO-d_6, 282 MHz

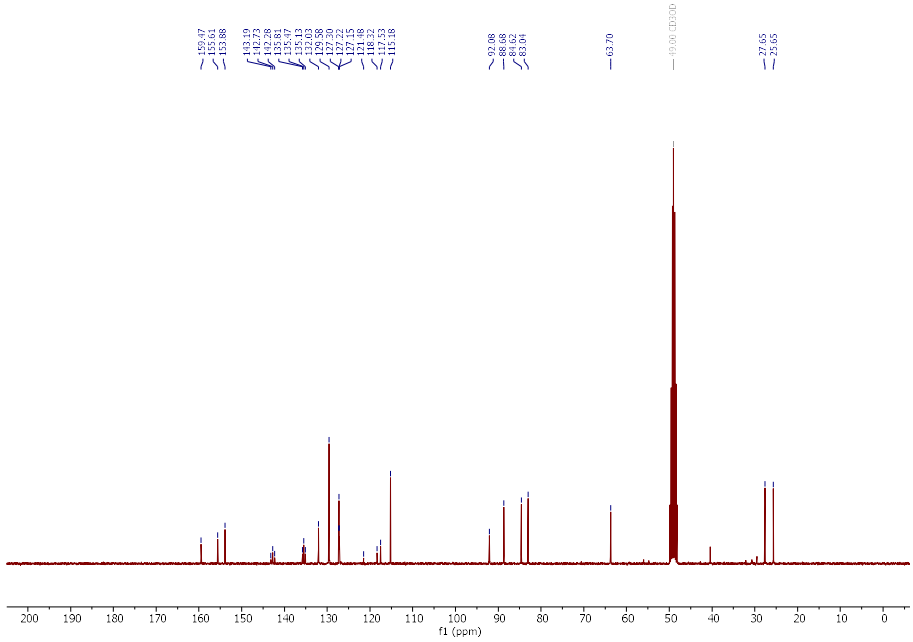


COMPOUND 184 c

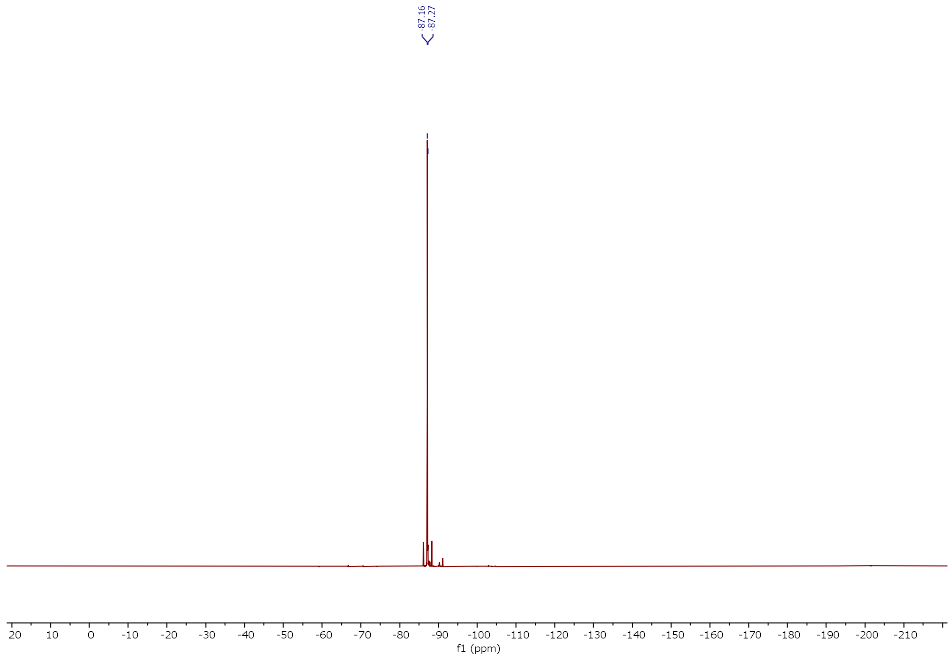
^{1}HNMR of **184c**, CD_3OD, 300 MHz



^{13}CNMR of **184c**, CD_3OD, 75 MHz

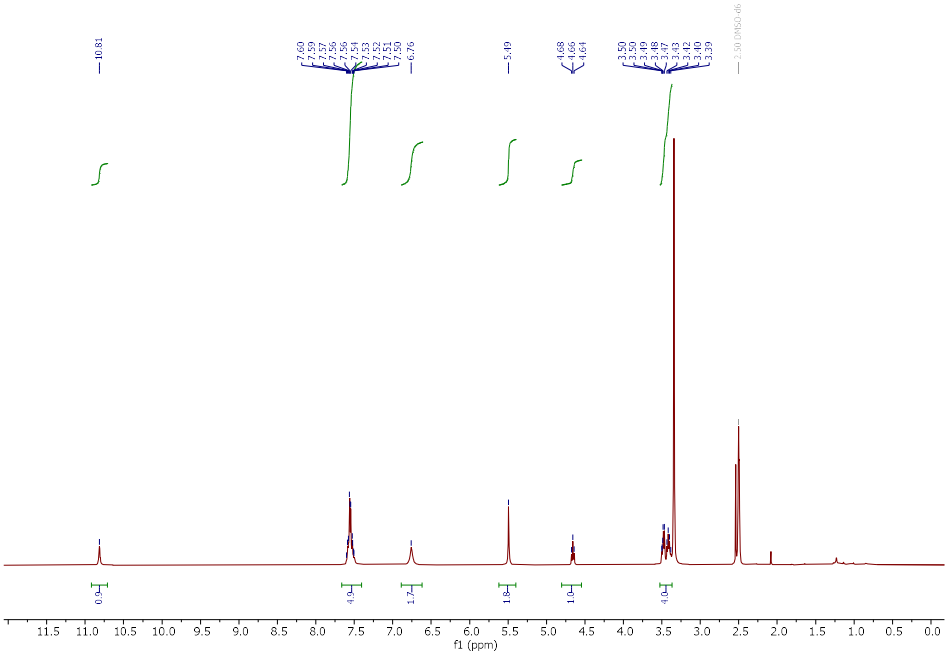


^{19}FNMR of **184c**, CD_3OD, 282 MHz

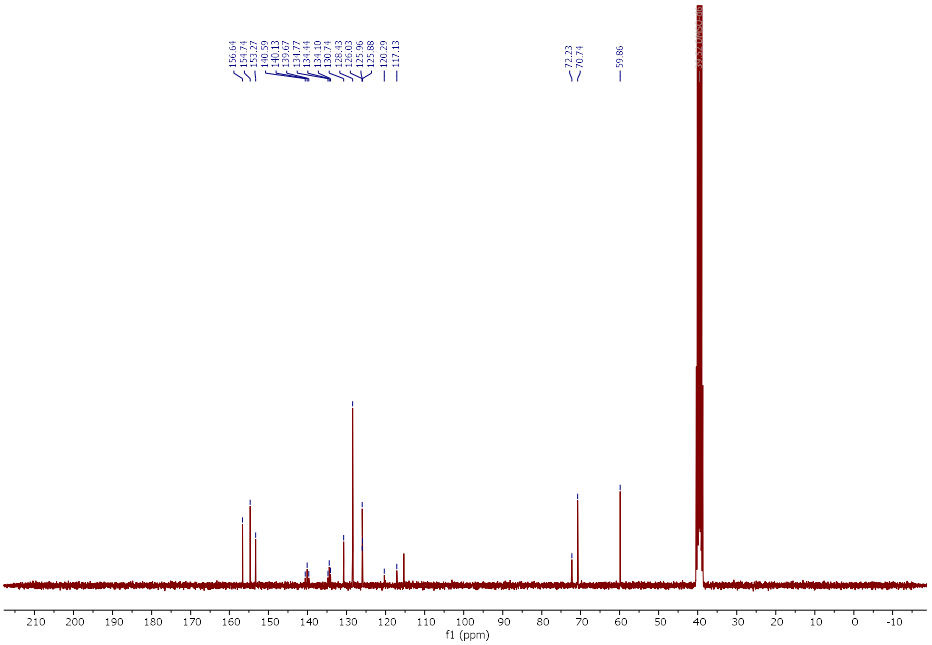


COMPOUND 185

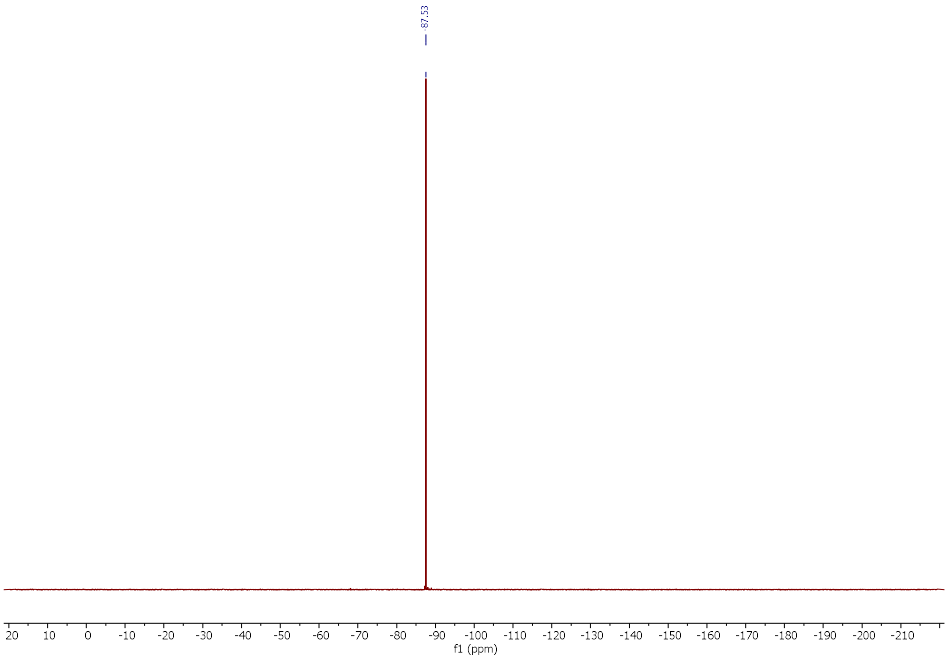
^{1}HNMR of **185**, DMSO-d_6, 300 MHz



^{13}CNMR of **185**, DMSO-d_6, 75 MHz

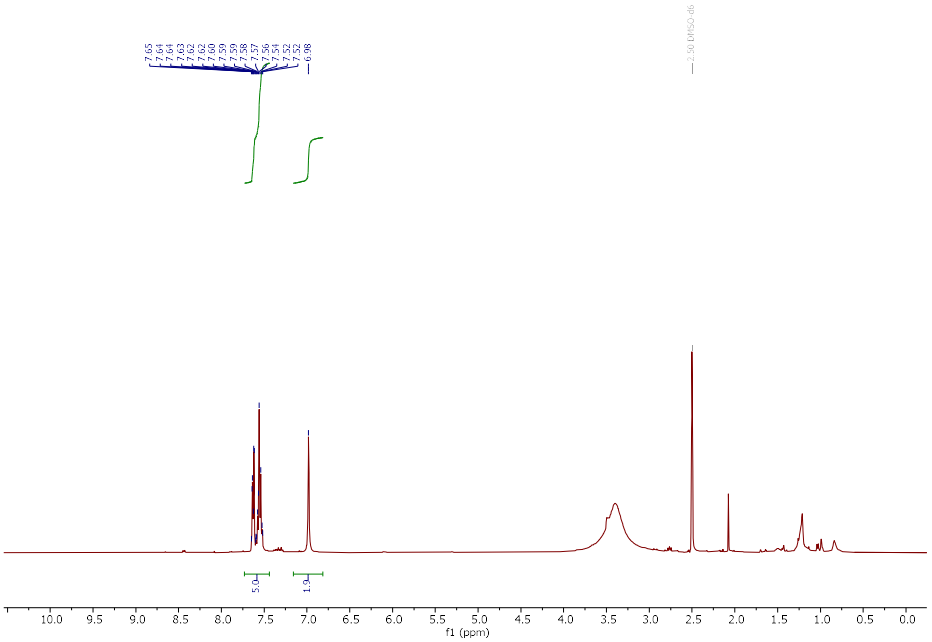


^{19}FNMR of **185**, DMSO-d_6, 282 MHz

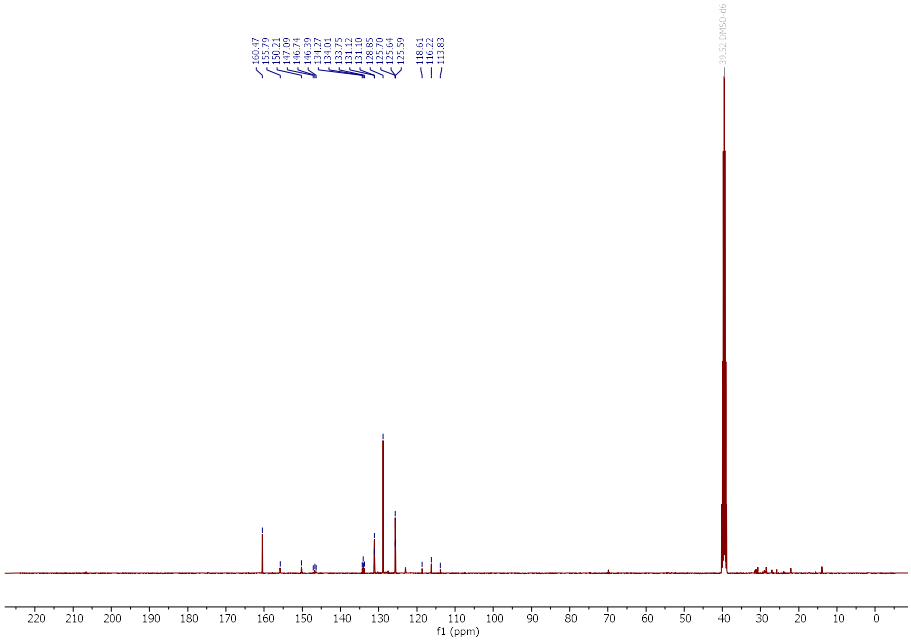


COMPOUND 186

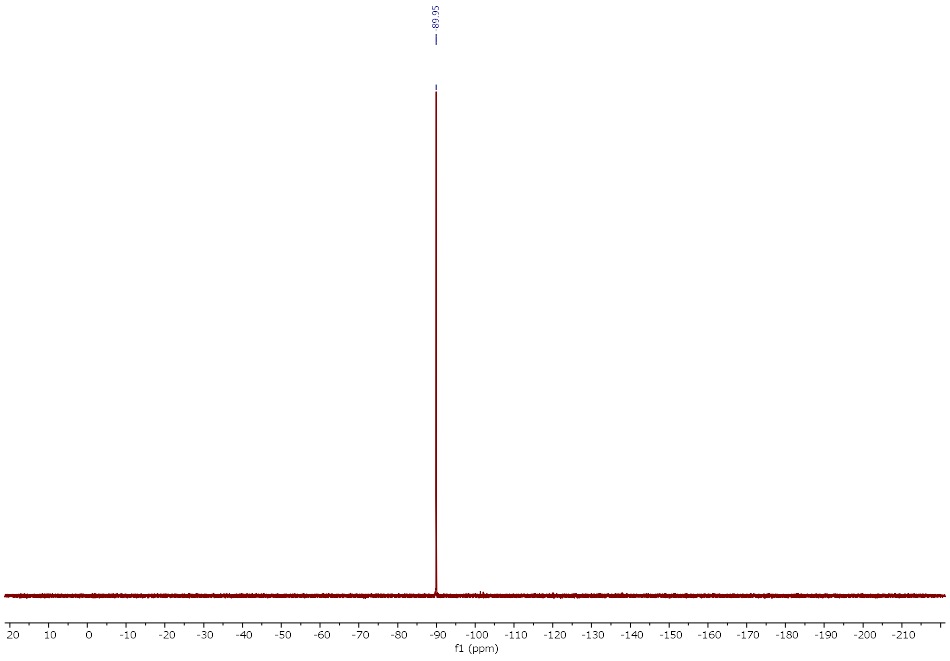
^{1}HNMR of **186**, DMSO-d_6, 300 MHz



^{13}CNMR of **186**, DMSO-d_6, 75 MHz



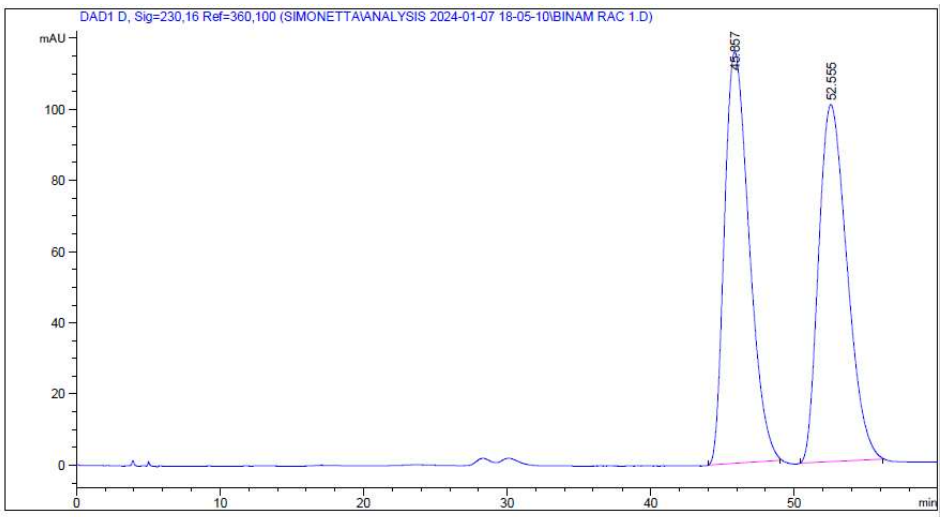
^{19}FNMR of **186**, DMSO-d_6, 282 MHz



5.6 HPLC ANALYSIS

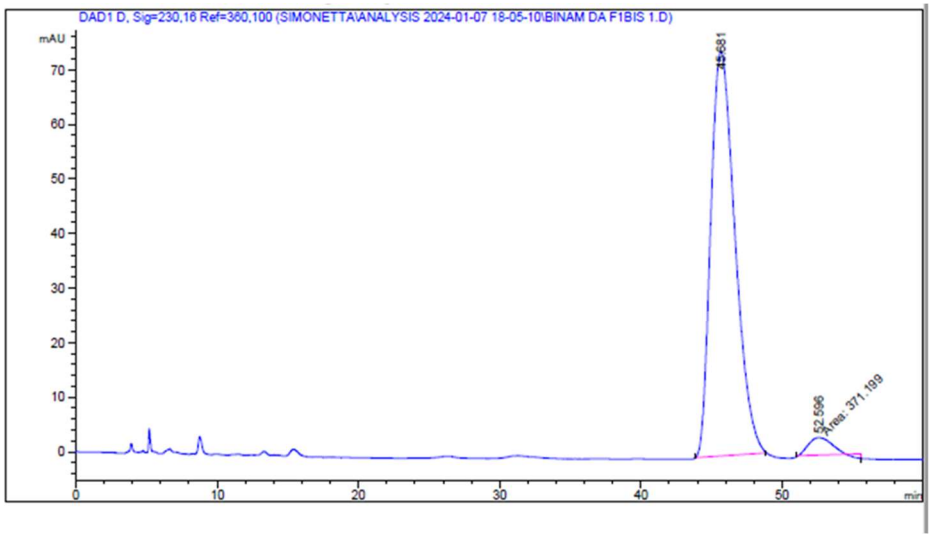
HPLC condition for BINAM Racemic mixture separation

Chiralcel OD; hex:ipa 95:5; 0.8 ml/min; 40 bar. Tr_1= 45.65 min, *R*-BINAM; Tr_2= 52.55 min *S*-BINAM

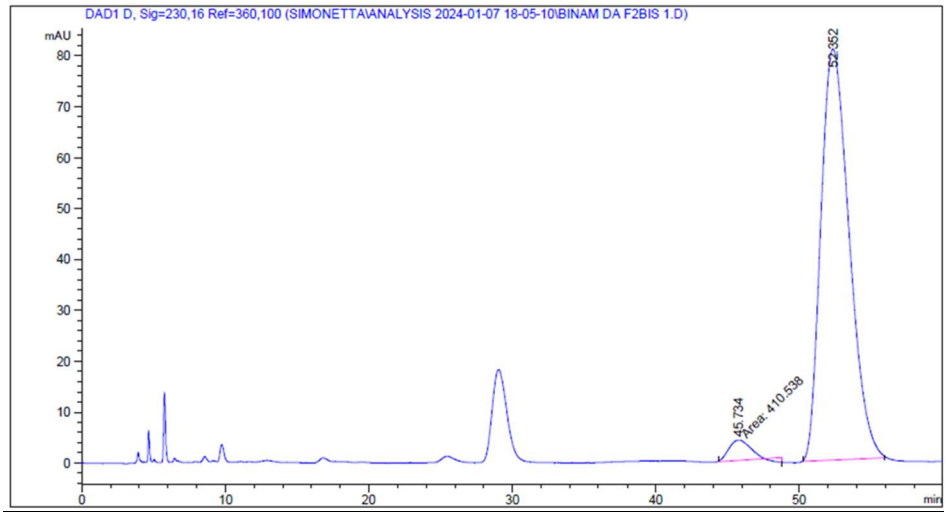


HPLC analysis of (*R*)-(+)-1,1'-Binaphthyl-2,2'-diamine (*R*-BINAM) obtained from the hydrogenation of 96a.1 and 96f.2 and subsequent chromatographic purification

Chiralcel OD; hex:ipa 95:5; 0.8 ml/min; 40 bar. Tr_1= 45.65 min, *R*-BINAM

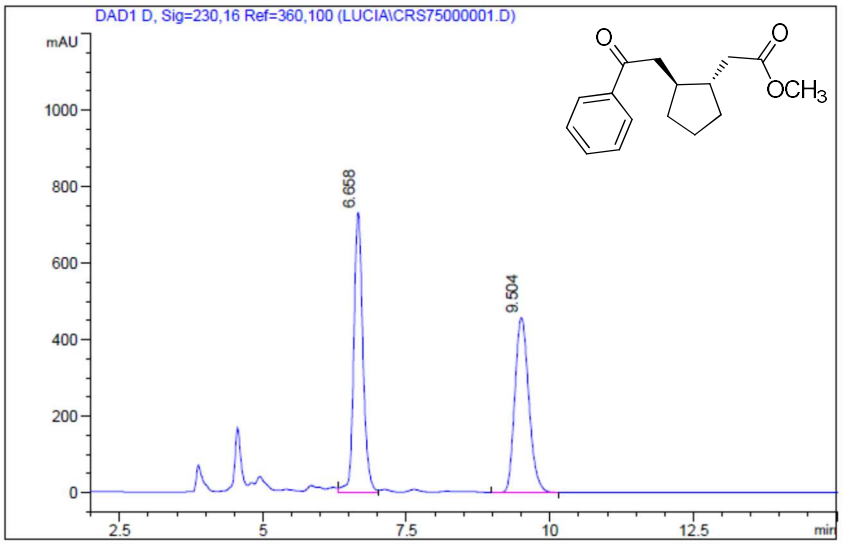


HPLC analysis of (*S*)-(+)-1,1'-Binaphthyl-2,2'-diamine (*S*-BINAM) obtained from the hydrogenation of **96a.2** and **96f.1** as crude product.
Chiralcell OD; hex:ipa 95:5; 0.8 ml/min; 40 bar. Tr_2= 52.55 min *S*-BINAM



Hplc condition of racemic **105**

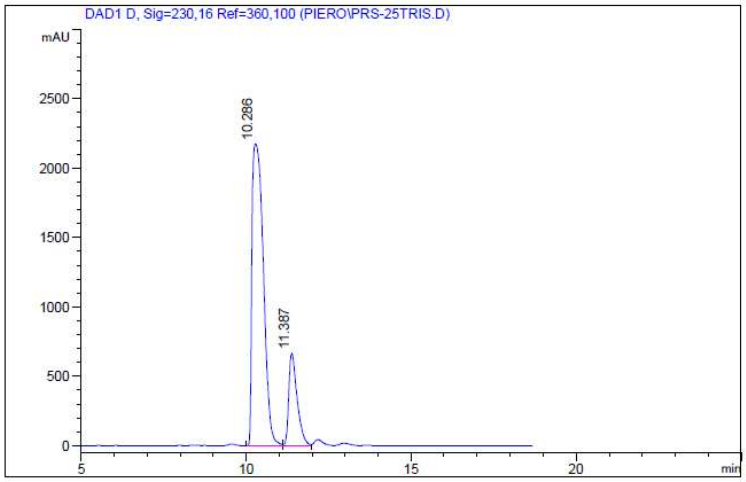
chiralpak OD-H, Hex/IPA 9:1; 0.8 mL/min, pressione 41 bar



Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	6.658	VV	0.169	8061.383	51.005	
2	9.504	VB	0.264	7743.552	48.995	

Hplc analysis of enantioenriched **105** (deriving from **104e**)
Chiralcel OJH, Hex/IPA 9:1; 0.8 mL/min, pressione 31 bar



Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	10.286	VV	0.388	51984.641	81.448	
2	11.387	VV	0.265	11841.128	18.552	

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RINGRAZIAMENTI

Al termine di questo faticoso ma avvincente percorso ad ostacoli, chiamato dottorato, vorrei ringraziare tutti coloro che, in un modo o nell'altro, hanno contribuito al raggiungimento di questo traguardo. La "luna" della citazione di Caparezza, rappresenta per me questa "piccola vittoria" con l'auspicio che possa essere un passo significativo verso l'esplorazione di altri pianeti. Il "raggiungimento della luna" è stata un'enorme occasione di crescita professionale e umana, una possibilità unica di mettersi costantemente alla prova.

Per questo motivo non posso che ringraziare il Professor Maurizio Benaglia per avermi concesso l'opportunità di entrare a far parte del suo gruppo, per essere stato un ottimo mentore, di una eccezionale umanità. Un enorme ringraziamento lo devo al Professor Sergio Rossi per essere stato una fonte di suggerimenti preziosi e un punto di riferimento in qualsiasi circostanza, nonostante tutte le mie lamentale sui "non" risultati della ricerca. Ringrazio, inoltre, le professoresse Alessandra Puglisi e Laura Raimondi per il costante contributo scientifico e umano fornito al gruppo.

Ci tengo particolarmente a esprimere la mia gratitudine nei confronti del "Benaglia group" che, nel corso di questi anni in cui la mia famiglia era lontana per motivi logistici, ha rappresentato la mia casa.

Un ringraziamento speciale va ai miei amici e colleghi Emanuela e Jacopo (J) che ormai rappresentano dei punti di riferimento importanti qui a Milano, con i quali ho condiviso ogni momento di questo percorso, all'interno e all'esterno dell'università. A loro non posso che aggiungere Monica e Niccolò, compagni di viaggi e congressi, nella disperazione della ricerca e "nelle gioie dei Gin Tonic". Inoltre, vorrei ringraziare Chiara e Milena per essere state degli ottimi esempi di coerenza, costanza e precisione, nonostante la distanza che purtroppo ci separa.

A questo importante elenco, non posso che aggiungere i miei preziosi amici e collaboratori Stefano e Tommaso per avermi sopportato e ascoltato, nonostante spesso avrebbero voluto teletrasportarsi altrove. Ringrazio inoltre tutti i tesisti che ho avuto modo di seguire nel corso di questi anni per aver insegnato a me più di quanto io abbia insegnato a loro: Luca Orsi, Luca Rota, Silvia Granelli, Giulia Bonfanti e, il sopracitato, Tommaso Benettin.

Il conseguimento di questo significativo traguardo, lo devo anche e soprattutto alla mia famiglia. Ringrazio particolarmente mia madre e mio

padre, a cui ho deciso di dedicare questo lavoro, per essere stati degli ottimi esempi di vita e di coesione. Li ringrazio per la loro lungimiranza nel fornirmi gli strumenti necessari per affrontare tutte le circostanze, per avermi mostrato determinazione e passione nel raggiungimento dei propri obiettivi. Li ringrazio per aver supportato la scelta di allontanarmi dalla mia amata Puglia, anche se a malincuore, per costruire il futuro che desidero. Li ringrazio inoltre per aver sempre creduto nelle mie potenzialità, festeggiando per i successi e normalizzando i fallimenti.

Ringrazio mio fratello Domenico per essere una garanzia da 29 anni, una fonte inesauribile di consigli (soprattutto culinari e sui ristoranti di Milano) e un confidente fidato. Inoltre, non posso che ringraziare gli altri elementi imprescindibili della mia famiglia: Ilaria, gli zii, i cugini ed infine i miei nonni, quelli che ci sono e quelli che purtroppo fisicamente non ci sono più, ma che per me ci sono sempre.

Un ringraziamento speciale va a Fabio, il miglior compagno di vita che potessi desiderare, indubbiamente una delle persone più intelligenti che conosca. Sicuramente questo percorso non sarebbe lo stesso senza la sua vicinanza e il suo supporto. Ringrazio la sua instancabile volontà di scegliermi ogni giorno per costruire un bellissimo futuro insieme. Inoltre, non posso che esprimere la mia gratitudine nei confronti della sua preziosa famiglia che, da diversi anni, mi ha accolta come una di loro.

Ci tengo a ringraziare particolarmente la famiglia che mi sono scelta, quella costituita dai “miei amici di giù”: Alessia, Giuseppe, Grazia, Martina, Ilaria, Gianmarco, Francesco e Michele. Ringrazio infinitamente la loro capacità di essere sempre presenti, anche se fisicamente distanti e di trovare sempre il modo per alleggerire le giornate, attraverso meme, messaggi e citazioni. Nonostante sia difficile o quasi impossibile organizzare viaggi insieme (ho l’ansia solo a pensarci), rimangono i momenti più belli e divertenti che continuerò sempre a costruire con voi. Ringrazio Robertina (anche definita come mia sorella adottiva dalla pelle bianca) per essere mia amica da prima che io possa ricordare, dispensatrice di leggerezza e pessime decisioni.

Infine, ma non per importanza, vorrei ringraziare la mia ex-coinquilina Pierangela per i bellissimi momenti trascorsi insieme nella palazzina di Via Battistotti Sassi e per quelli futuri che vivremo. Ti ringrazio per aver reso il mio arrivo a Milano meno complicato, nonostante le zone rosse, le mascherine e il Covid.

Questo lungo percorso, durato 4 anni mi ha permesso di crescere come ricercatrice, come donna e come amica; mi ha insegnato a fare un passo indietro quando è necessario e uno in avanti quando è possibile dare un piccolo contributo. Mi ha insegnato a presentare di fronte ad un pubblico di persone a cui interessa la mia ricerca e a quelle che semplicemente preferiscono altro. Ho reimparato ad apprezzare la diversità delle cose, delle culture, delle persone e ho visto come la scienza possa unire tutto ciò, valorizzandone i singoli aspetti. Ho avuto la conferma di come la ricerca sia una grande risorsa per la società, un motore costante che favorisce innovazione e sviluppo, abbattendo complottismi, pregiudizi e mancanza d'informazione. Spero che la ricerca possa diventare un'aspirazione per molti, così come lo è per me.