Supporting Information

Sequence-selective duplex formation and template effect in recognition-encoded oligoanilines

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1. Experimental Procedures

The reagents, materials and solvents used in the synthesis were bought from international suppliers and used without prior purification. Thin layer chromatography was carried out using Merck 60 F254 silica gel precoated aluminium plates. Column chromatography was carried out manually on Macherey-Nagel silica gel 60 (70-230 mesh). All NMR spectroscopy experiments were carried out on a Bruker AVI250, AVI400, DPX400, AVIII400, 500 MHz AVIII HD Smart Probe, AV600 MHz Cryo spectrometers using the solvent residual signal as the internal standard. All chemical shifts (δ) are reported in ppm and coupling constants given in Hz.

The abbreviations used for the commonly used solvents are: Ac_2O (acetic anhydride), ACN (acetonitrile), DCM (dichloromethane), DMF (dimethylformamide), EtOAc (ethyl acetate), Et_2O (diethyl ether), MeOH (methanol), PE (petroleum ether, distilled fraction boiling from 40 to 60 °C), THF (tetrahydrofuran).

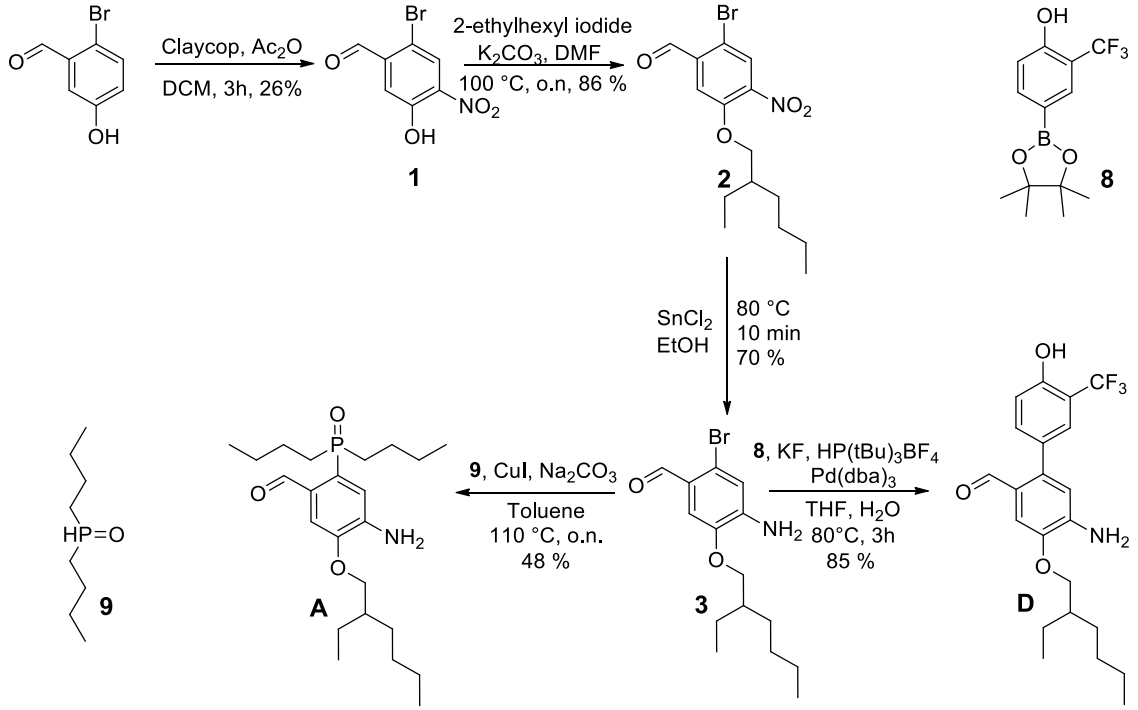
Claycop

The Claycop catalyst used for the nitration of the 2-Bromo-5-hydroxybenzaldehyde has been prepared according to the procedure of Corndis and Laszlo (*Aldrichimica Acta* **1988**, 21, 97). In brief: in a solution of Cu $(NO_3)_2{\cdot}3H_2O$ (20 g) in acetone (1 L flask, the size of the flask is important for an accurate solvent removal) are dispersed 30 g of K 10 montmorillonite clay. The flask is kept at 50 °C in a water bath and the solvent removed under reduced pressure. After 30 minutes the mixture appears as a dry crust adherent to the flask. At this point the light blue solid is crushed and dried again at the rotary evaporator at 50 °C for further 30 minutes. During this work the Claycop has been stored in the dark at room temperature in airtight vials and used up to one month after its preparation.

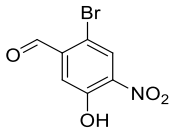
2. Synthesis and characterisation of the monomers

2.1 Synthesis of the bifunctional monomers (-NH_2 and -CO)

The molecules **8, 9** and **10** were prepared according to previously reported procedures. The bifunctional monomers **A** and **D** were synthesized as reported in the following scheme:



2.1.1 Synthesis of 1



1

2-Bromo-5-hydroxybenzaldehyde (500 mg, 2.49 mmol, 1 equiv) was added under stirring to a suspension of claycop (1.5 g) in diethyl ether (15 ml). Then, 3 ml of acetic anhydride were added. The formation of the product was followed via TLC (PE:EtOAc 9:1) over the course of two hours until all the starting material was consumed. The solids were filtered and washed with Et_2O (2x20 ml). The organic fractions were collected, and the solvents removed in vacuum. The crude product was absorbed on silica and purified *via* flash chromatography on silica gel (gradient PE to PE:EtOAc 8:2) giving the desired compound **1** (26% yield) as bright yellow needles.

^{1}H-NMR (500 MHz, chloroform-*d*) δ 10.36 (s, 1H), 10.35 (s, 1H), 8.46 (s, 1H), 7.72(s, 1H).

^{13}C-NMR (126 MHz, chloroform-*d*) δ 189.73, 153.84, 139.06, 136.36, 130.01, 121.70, 113.97.

HRMS(ES+): Calculated for $C_7H_5{}^{79}BrNO_4$ 245.9402 a.m.u.; found 245.9387

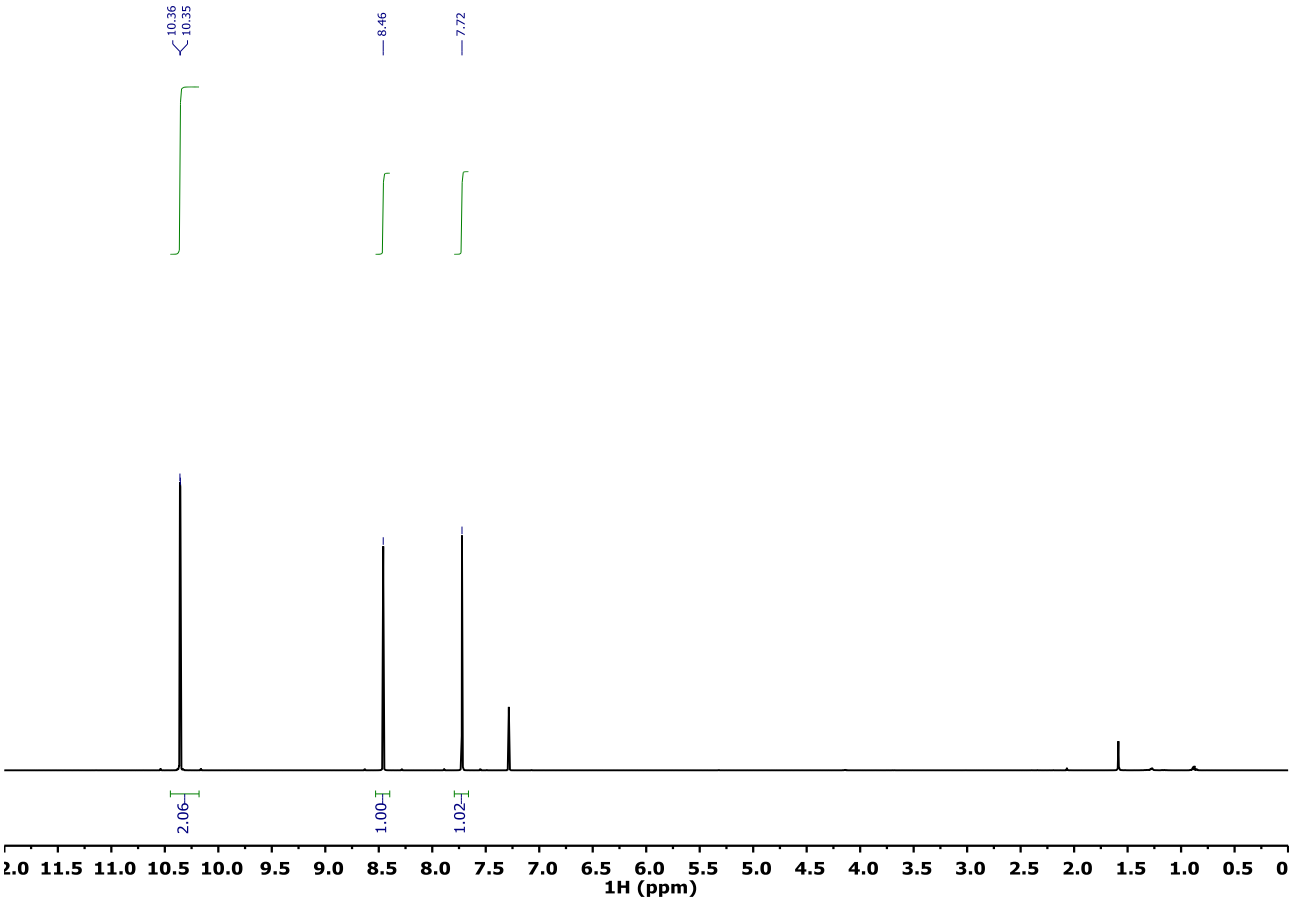


Figure S2.1. ^{1}H-NMR spectrum (500 MHz, chloroform-*d*) of **1**.

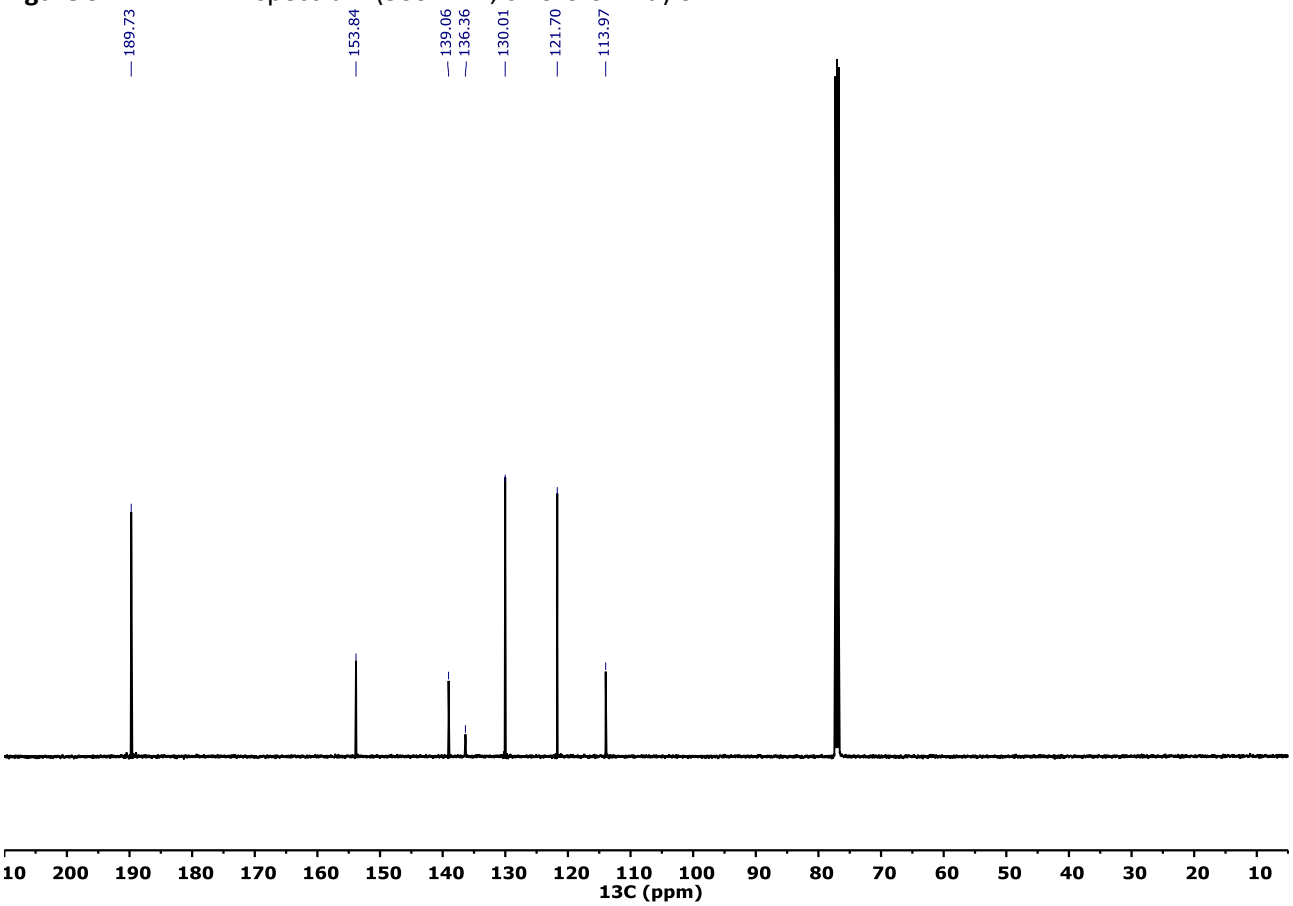
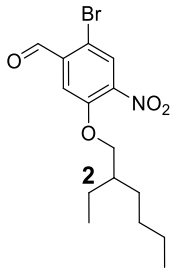


Figure S2.2. ^{13}C-NMR spectrum (126 MHz, chloroform-*d*) of **1**.

2.1.2 Synthesis of 2



Compound **1** (1 g, 4.09 mmol, 1 equiv), 2-Ethylhexyl iodide (2.95 g, 2.20 ml, 12.27 mmol, 3 equiv) and potassium carbonate (2.26 g, 16.36, 4 equiv) were mixed in 6 ml of DMF in a sealed tube. The orange mixture was heated at 100 °C overnight. Once cooled, the resulting yellow solid was partitioned between water and ethyl acetate, the aqueous layer was extracted again with ethyl acetate. The organic fractions were collected, washed with brine, dried over $MgSO_4$ and purified through flash column chromatography (gradient from PE to PE:EtOAC 9:1), giving the desired compound **2** (1.26 g, 86% yield).

^{1}H-NMR (500 MHz, chloroform-*d*) δ 10.35 (s, 1H), 8.06 (s, 1H), 7.62 (s, 1H), 4.06 (m, 2H), 1.80 (m, 1H), 1.60-1.40 (m, 4H), 1.40-1.25 (m, 4H), 0.94 (m, 6H).

^{13}C-NMR (126 MHz, chloroform-*d*) δ 190.23, 151.78, 143.16, 136.17, 130.02, 115.65, 114.74, 72.59, 39.13, 30.19, 28.92, 23.63, 22.92, 14.02, 14.00, 11.04.

HRMS(ES+): Calculated for $C_{15}H_{21}{}^{79}BrNO_4$ 358.0654 a.m.u.; found 358.0672

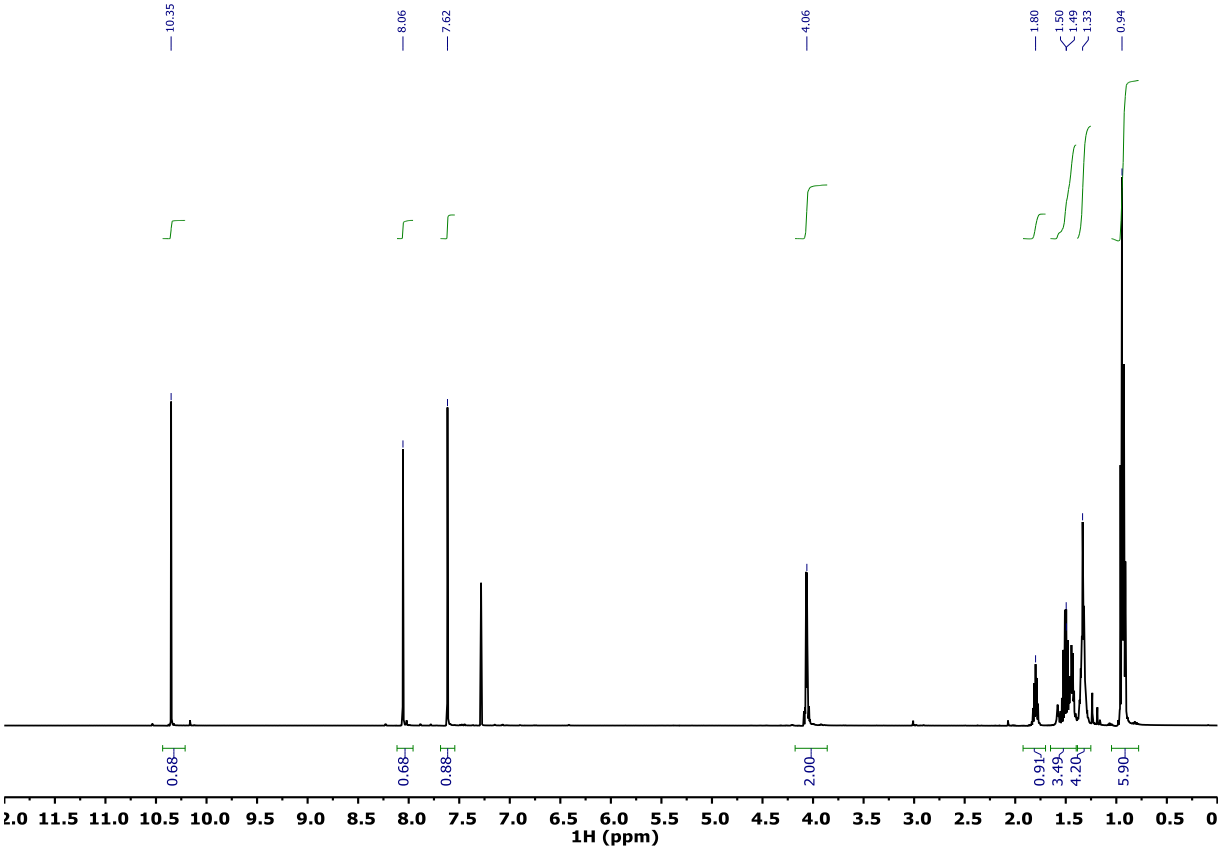


Figure S2.3. ^{1}H-NMR spectrum (500 MHz, chloroform-*d*) of **2**.

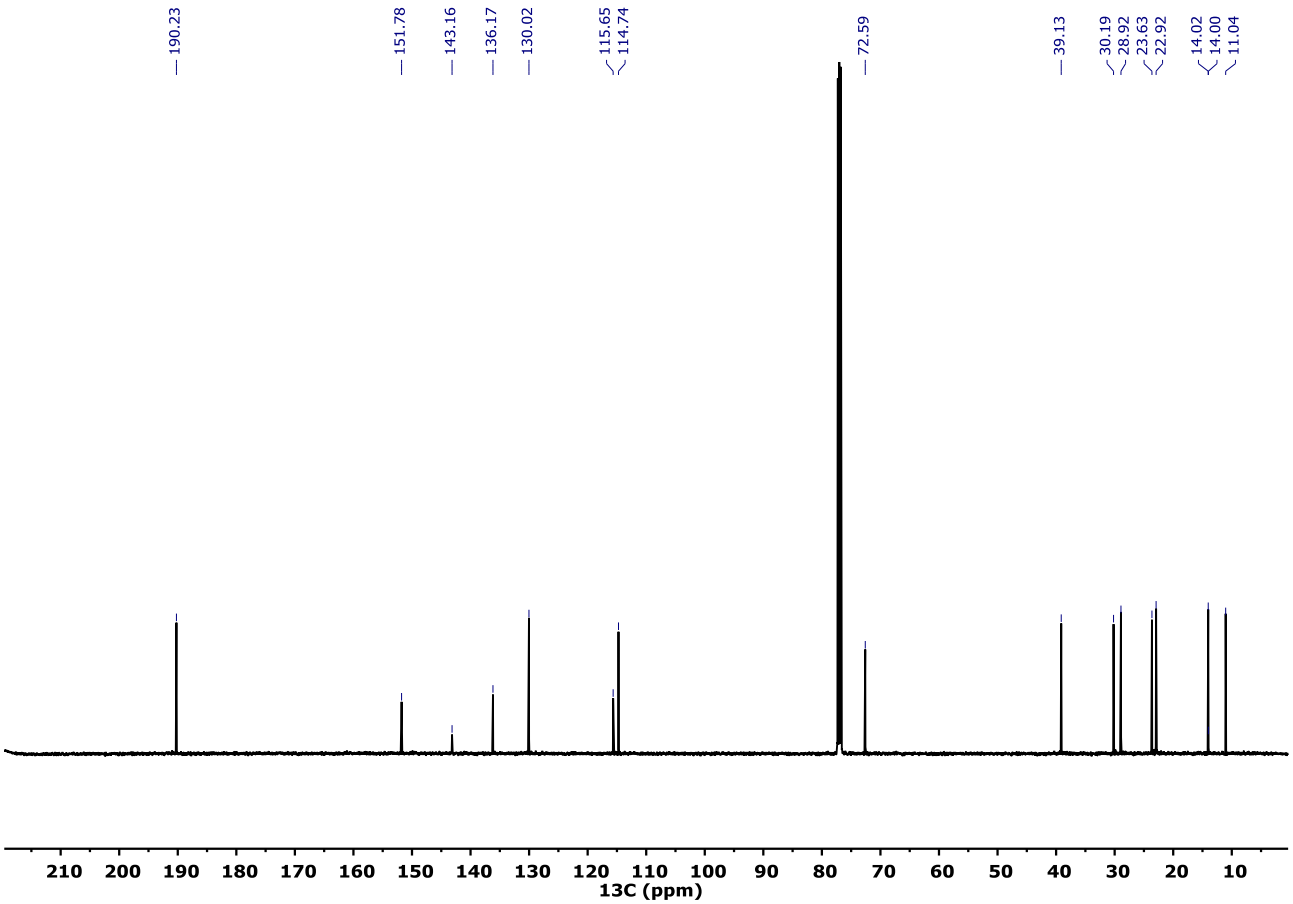
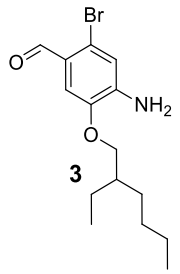


Figure S2.4. ^{13}C-NMR spectrum (126 MHz, chloroform-*d*) of **2**.

2.1.3 Synthesis of 3



Compound **2** (500 mg, 1.40 mmol, 1 equiv) and $SnCl_2$ (1.06 g, 5.60 mmol, 4 equiv) were dissolved in 6 ml of previously degassed EtOH (N_2 bubbling, 15 min) in a sealed tube. The tube was inserted in an oil bath at 80 °C for 10 min. The crude was extracted in $NaHCO_3$ sat/EtOAc, dried over Na_2SO_4 and purified through flash column chromatography (gradient from PE to PE:EtOAC 95:5), giving the desired compound **2** (320 mg, 70% yield).

^{1}H-NMR (500 MHz, chloroform-*d*) δ 10.10 (s, 1H), 7.34 (s, 1H), 6.86 (s, 1H), 4.50 (br s, 2H), 3.96 (m, 2H), 1.79 (m, 1H), 1.53-1.34 (series of m, 8H), 0.96 (m, 6H).

^{13}C-NMR (126 MHz, chloroform-*d*) δ 190.67, 145.53, 143.85, 123.57, 121.46, 116.50, 110.33, 71.11, 39.28, 30.62, 29.04, 24.03, 23.02, 14.06, 11.13.

HRMS(ES+): Calculated for $C_{15}H_{23}{}^{79}BrNO_2$ 328.0912 a.m.u.; found 328.0877

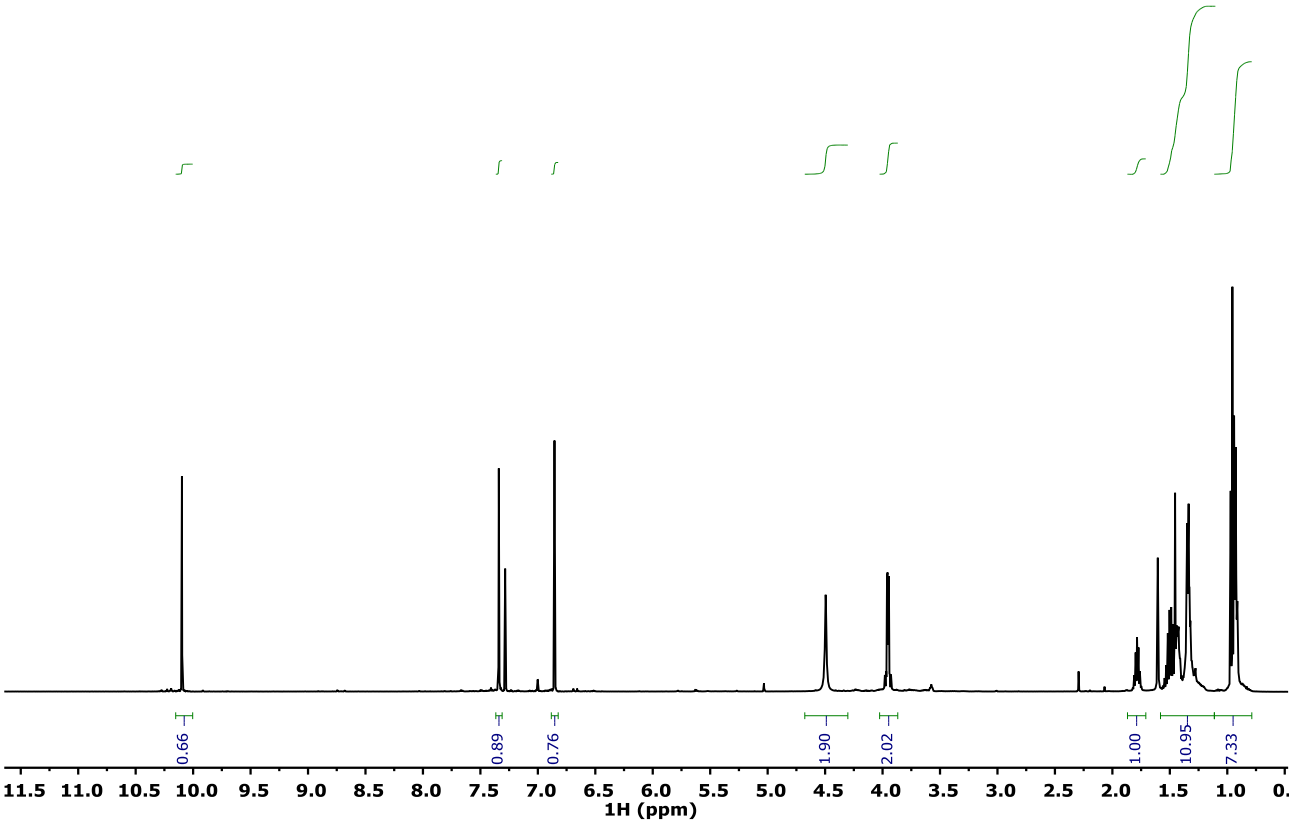


Figure S2.5 ^{1}H-NMR spectrum (500 MHz, chloroform-*d*) of **3**.

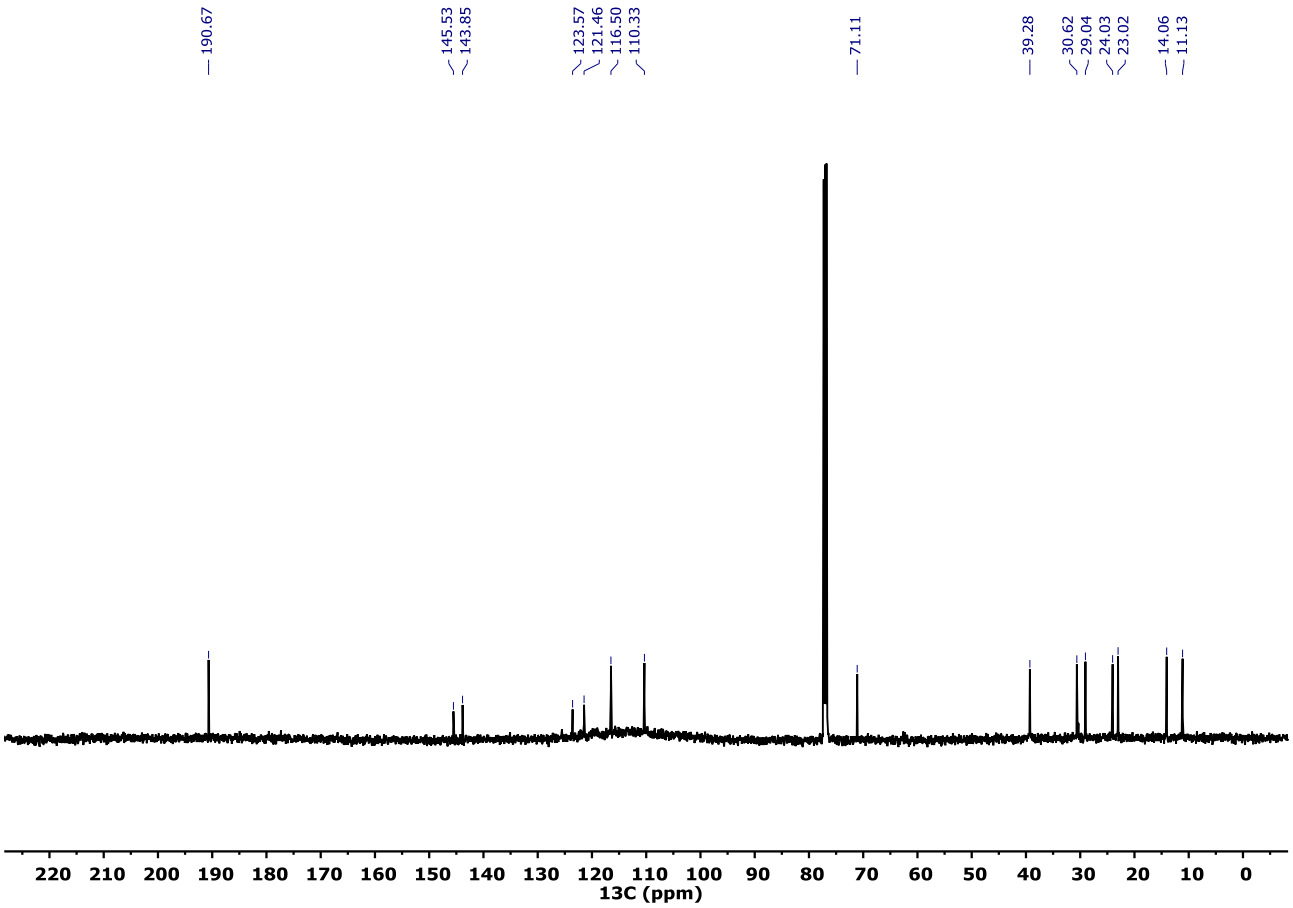
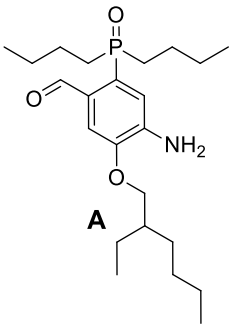


Figure S2.6. ^{13}C-NMR spectrum (126 MHz, chloroform-*d*) of **3**.

2.1.4 Synthesis of A



Compound **3** (100 mg, 0.305 mmol, 1 equiv) was mixed with the phosphine oxide **9** (99 mg, 0.610 mmol, 2 equiv), CuI (58 mg, 0.305 mmol, 1 equiv) and Na_2CO_3 (65 mg, 0.610 mmol, 2 equiv) in 3 ml of degassed toluene (N_2 bubbling, 15 min) and stirred overnight in the dark at 110 °C under inert atmosphere. The rection mixture was extracted with brine/EtOAc (4x) dried over Na_2SO_4 and the solvent evaporated. The crude product was purified through column chromatography (EtOAc), yielding pure **A** (60 mg, 48% yield).

^{1}H-NMR (500 MHz, chloroform-*d*) δ 9.95 (s, 1H), 7.57 (d, J = 12.49 Hz, 1H), 7.33 (d, J = 3.75 Hz, 1H), 4.81 (s, 2H), 4.02 (dd, J = 5.64, 1.77 Hz, 2H), 2.39 – 2.01 (m, 4H), 1.81 (m, J = 6.01 Hz, 1H), 1.72 – 1.17 (m, 17H), 1.09 – 0.58 (m, 1H).

^{13}C-NMR (126 MHz, chloroform-*d*) δ 190.29 (d, J = 2.4 Hz), 146.85 (d, J = 2.62 Hz), 142.24 (d, J = 12.1 Hz), 127.81 (d, J = 53.70 Hz), 127.46 (d, J = 21.1 Hz), 120.29 (d, J = 7.5 Hz), 116.69 (d, J = 10.2 Hz), 71.01, 39.41, 30.64, 29.71, 29.16, 29.10, 24.16, 24.04, 23.89, 23.86, 23.01, 14.07, 13.64, 11.19.

^{31}P-NMR (202 MHz, methanol-d_4) δ 50.19.

HRMS(ES+): Calculated for $C_{23}H_{41}NO_3P$ 410.2824 a.m.u.; found 410.2698

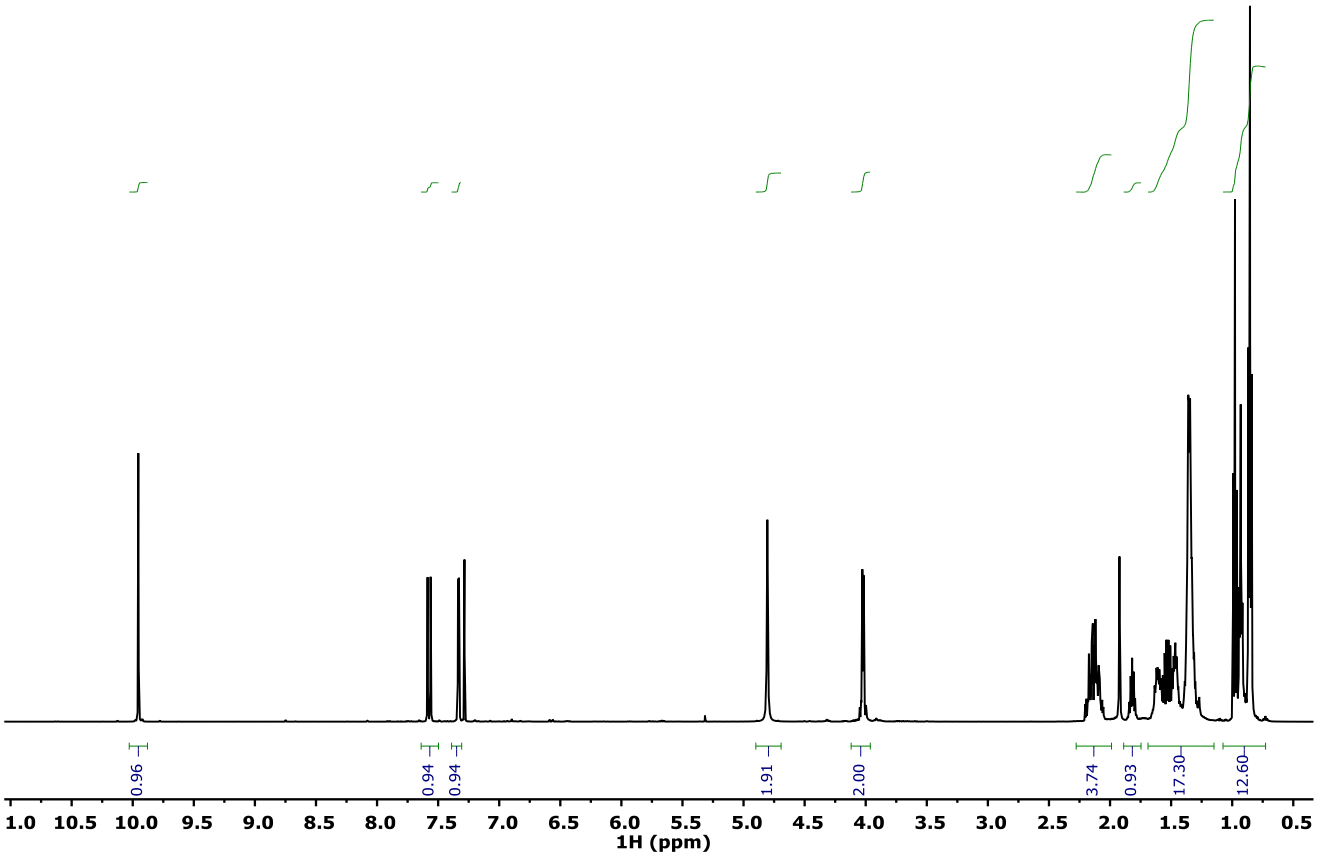


Figure S2.7. ^{1}H-NMR spectrum (500 MHz, chloroform-*d*) of **A**.

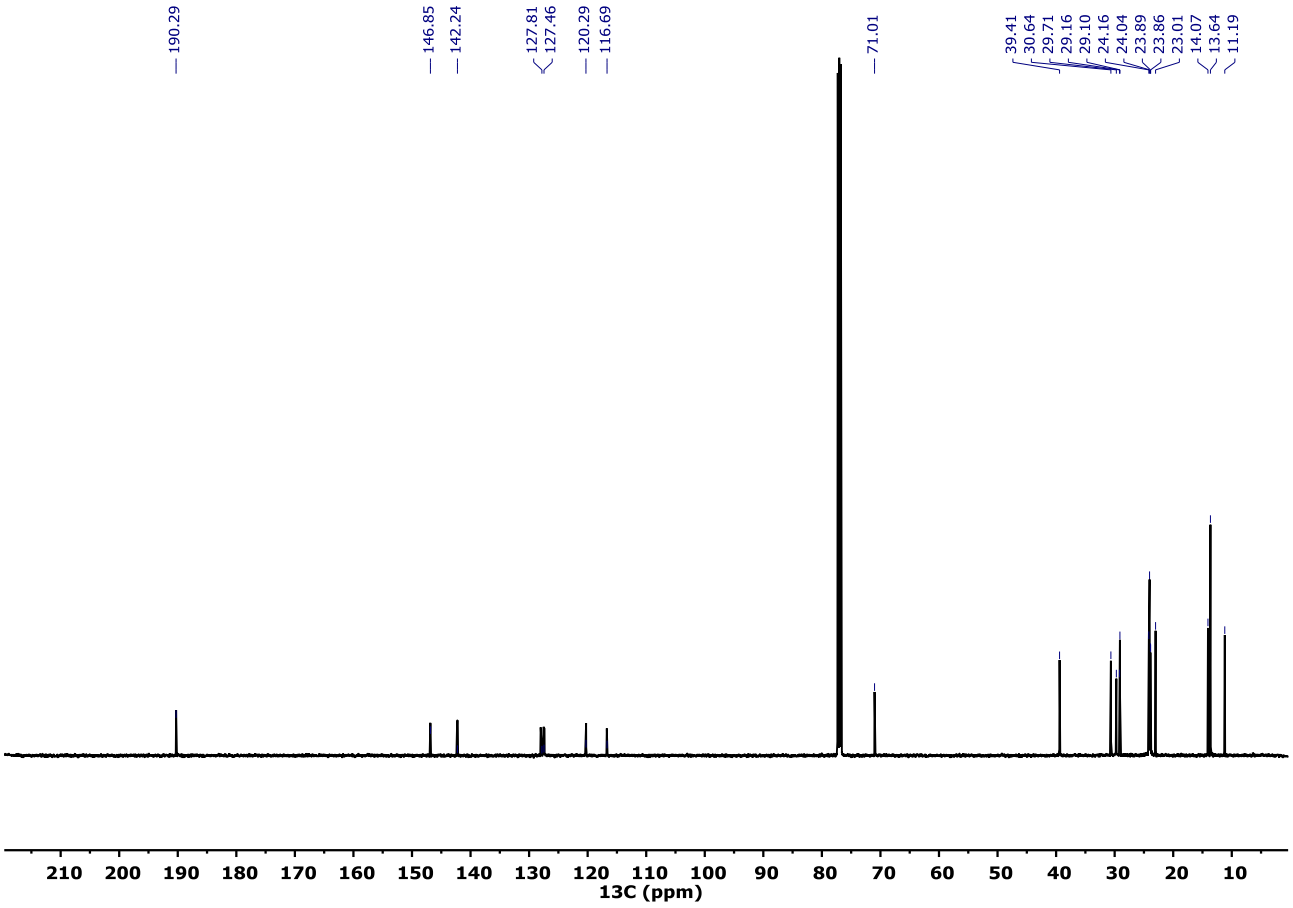


Figure S2.8. ^{13}C-NMR spectrum (126 MHz, chloroform-*d*) of **A**.

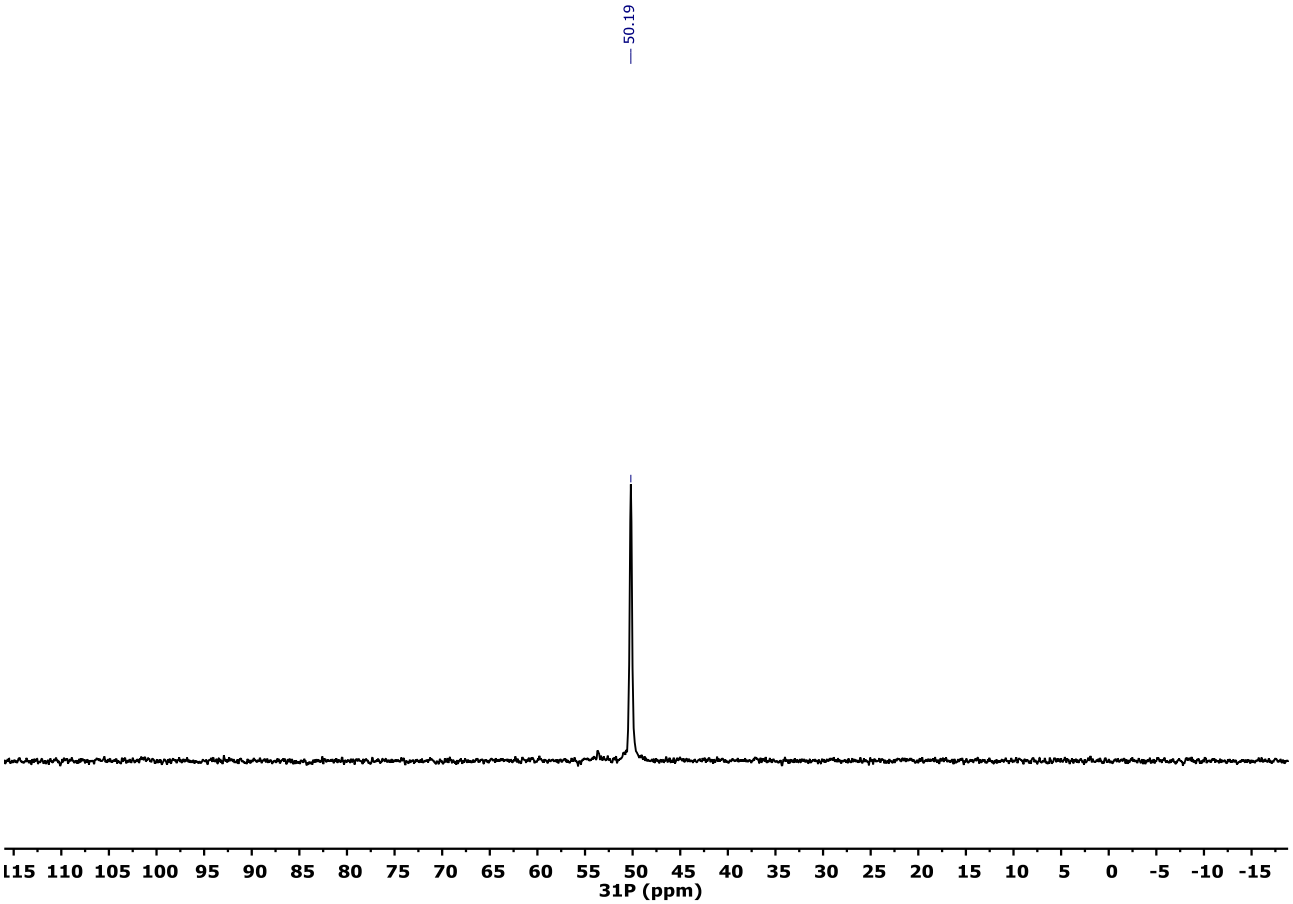


Figure S2.9. ^{31}P-NMR spectrum (202 MHz, methanol-d_4) of **A**.

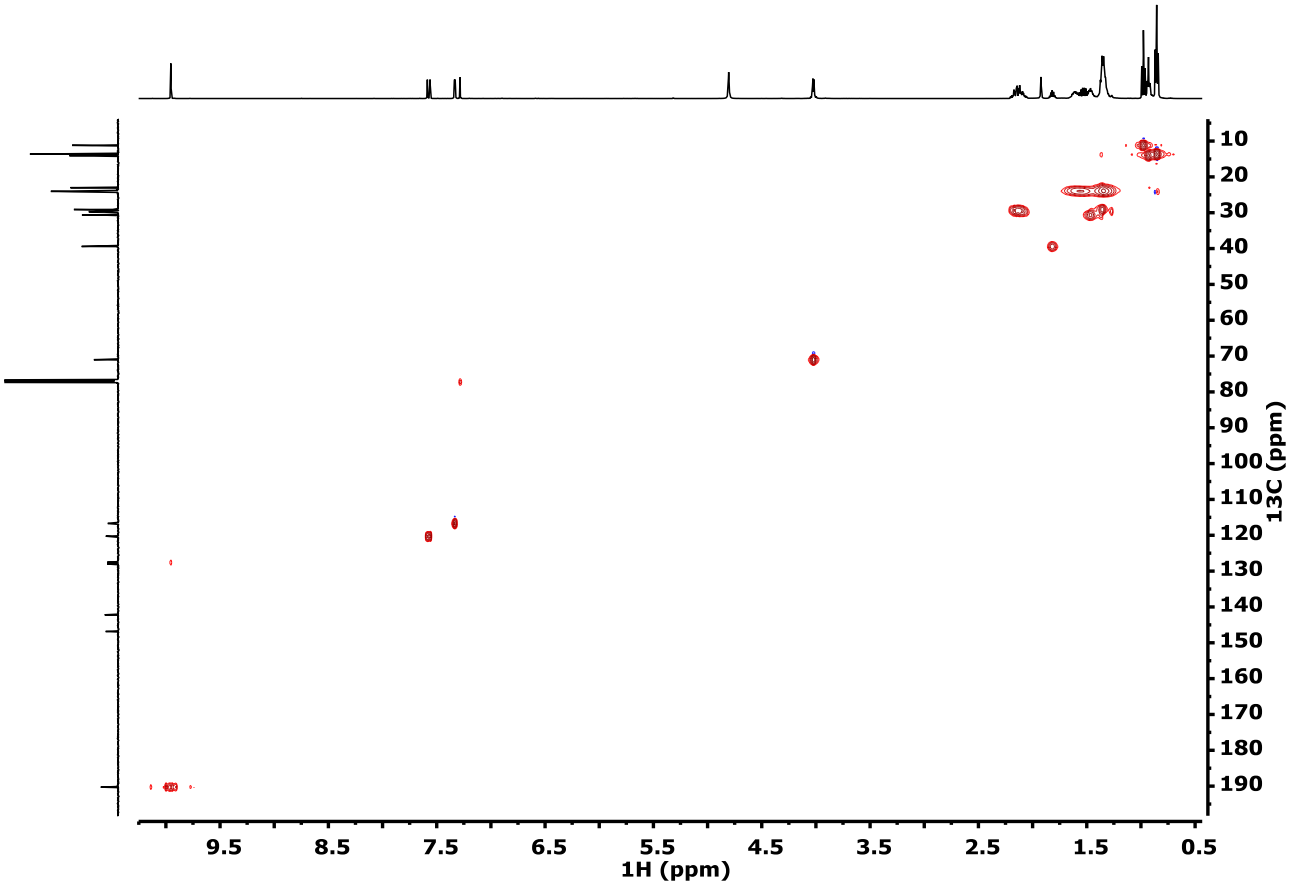
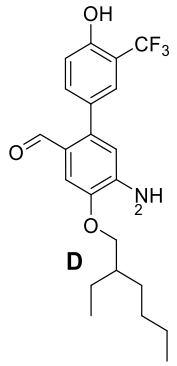


Figure S2.10. ^{1}H -^{13}C-HSQC spectrum (500 MHz, chloroform-*d*) of **A**.

2.1.5 Synthesis of D



D

In a sealed tube compound **3** (400 mg, 1.219 mmol, 1.2 equiv), compound **8** (292 mg, 1.016 mmol, 1 equiv), KF (236 mg, 4.064 mmol, 4 equiv) and $HP(tBu)_3BF_4$ (8.8 mg, 0.031 mmol, 0.03 equiv) were suspended in freshly degassed (N_2 bubbling, 15 min) THF (3 mL) and H_2O (1 mL). Then $Pd_2(dba)_3$ (14.9 mg, 0.0163 mmol, 0.016 equiv) was added and the reaction was stirred under N_2 atmosphere at 80°C for 3 h. Then it was extracted in brine/EtOAc (3x), the organic phases were collected, dried with $MgSO_4$, concentrated under vacuum and purified by flash column chromatography with PE:EtOAc (from 9:1 to 8:2). giving the pure desired monomer **D** (354 mg, 85% yield).

^{1}H-NMR (500 MHz, chloroform-*d*) δ 9.63 (s, 1H), 8.35 (s, 1H), 7.54 (d, J = 2.26 Hz, 1H), 7.49 (s, 1H), 7.33 (dd, J = 8.34, 2.24 Hz, 1H), 7.06 (d, J = 8.34 Hz, 1H), 6.60 (s, 1H), 4.64 (s, 2H), 4.13 – 3.92 (m, 2H), 1.80 (h, J = 6.13 Hz, 1H), 1.61 – 1.39 (m, 4H), 1.40 – 1.24 (m, 4H), 1.02 – 0.85 (m, 6H).

^{13}C-NMR (126 MHz, chloroform-*d*) δ 191.60, 154.62, 145.80, 143.37, 141.75, 134.93, 129.46, 128.04 (q, J = 4.8 Hz), 123.81, 123.77 (q, J = 272.6 Hz), 117.09, 116.86 (q, J = 30.8 Hz), 114.38, 108.70, 70.98, 39.35, 30.66, 29.07, 24.05, 23.03, 14.05, 11.15.

^{19}F-NMR (376 MHz, chloroform-*d*) δ -60.91

HRMS(ES+): Calculated for $C_{22}H_{27}F_3NO_3$ 410.1943 a.m.u.; found 410.1957

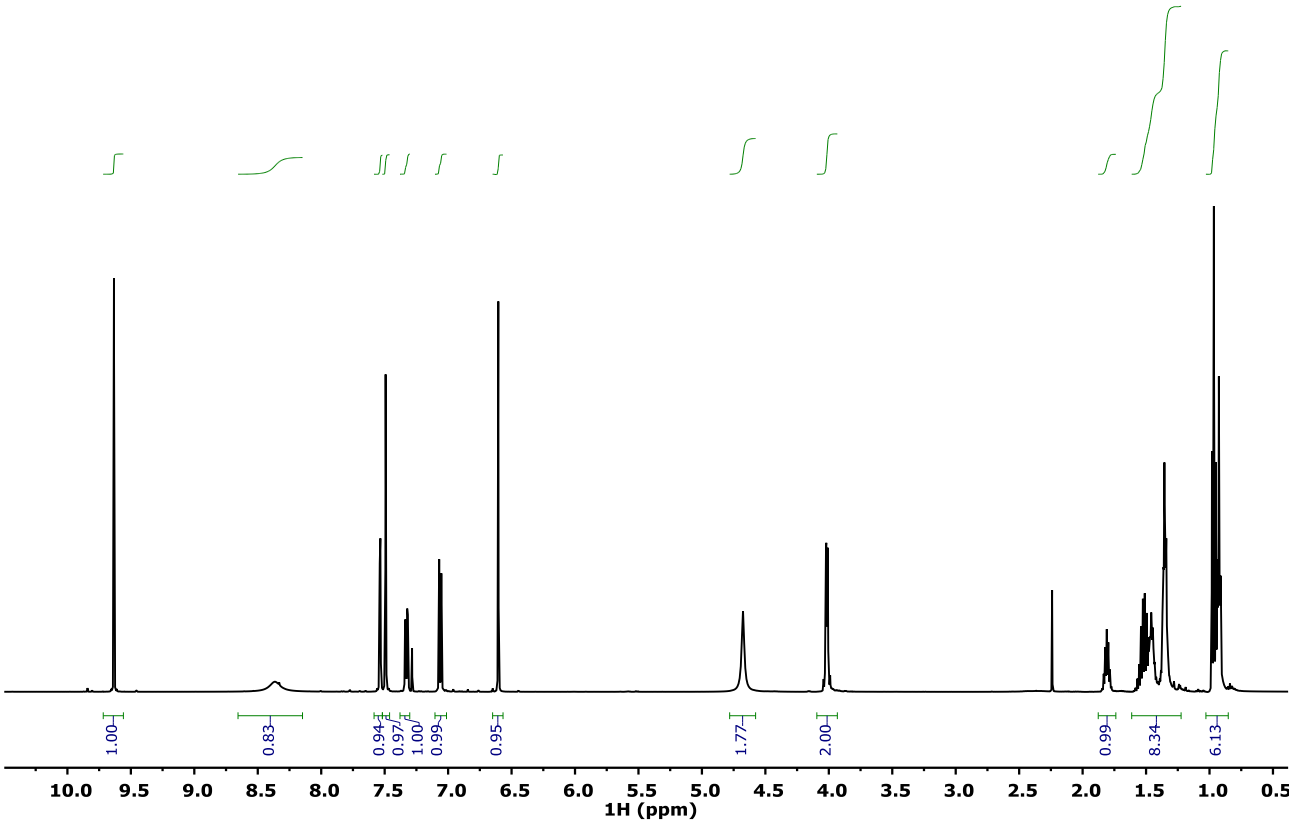


Figure S2.11. ^{1}H-NMR spectrum (500 MHz, chloroform-*d*) of **D**.

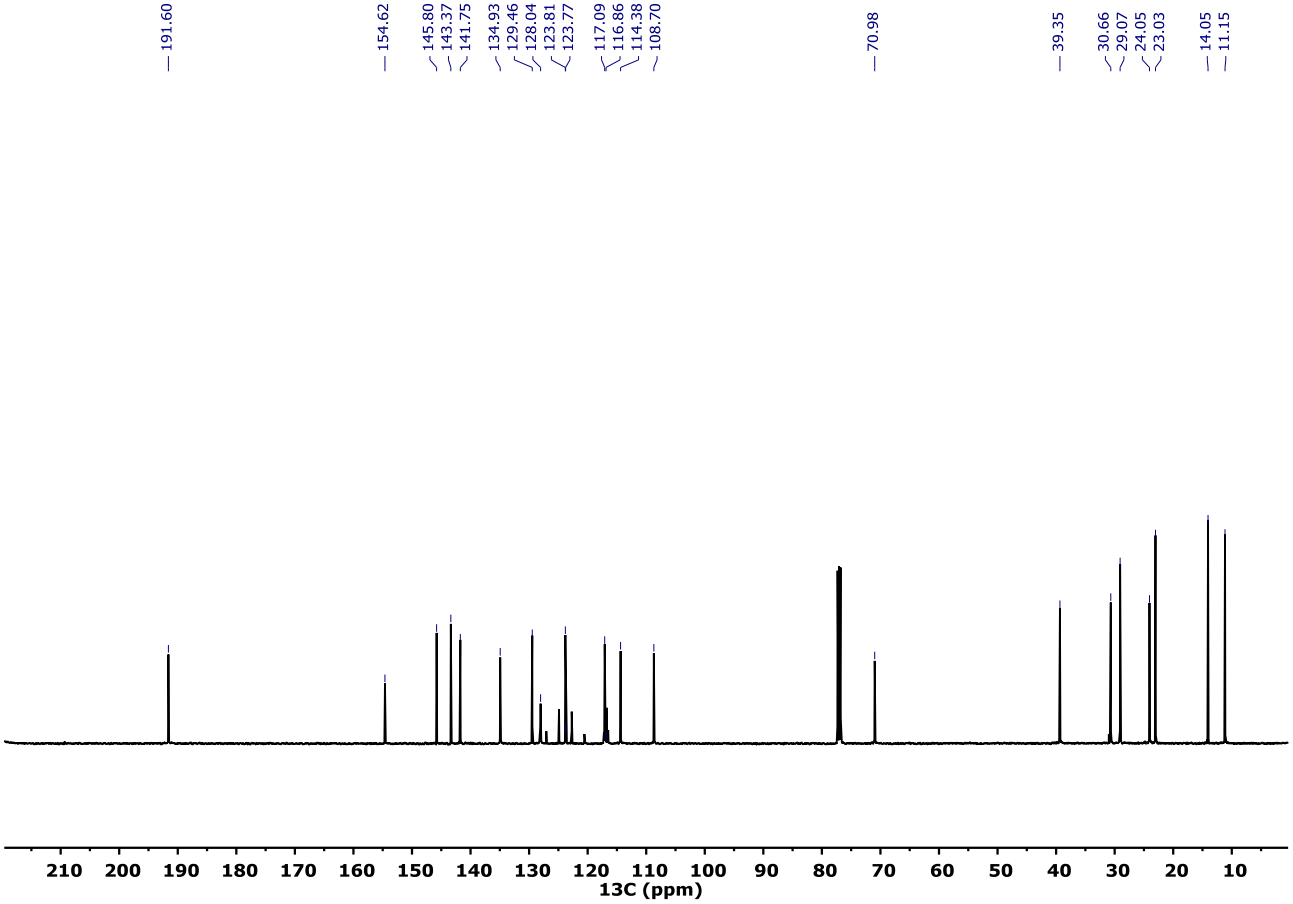


Figure S2.12. ^{13}C-NMR spectrum (126 MHz, chloroform-*d*) of **D**

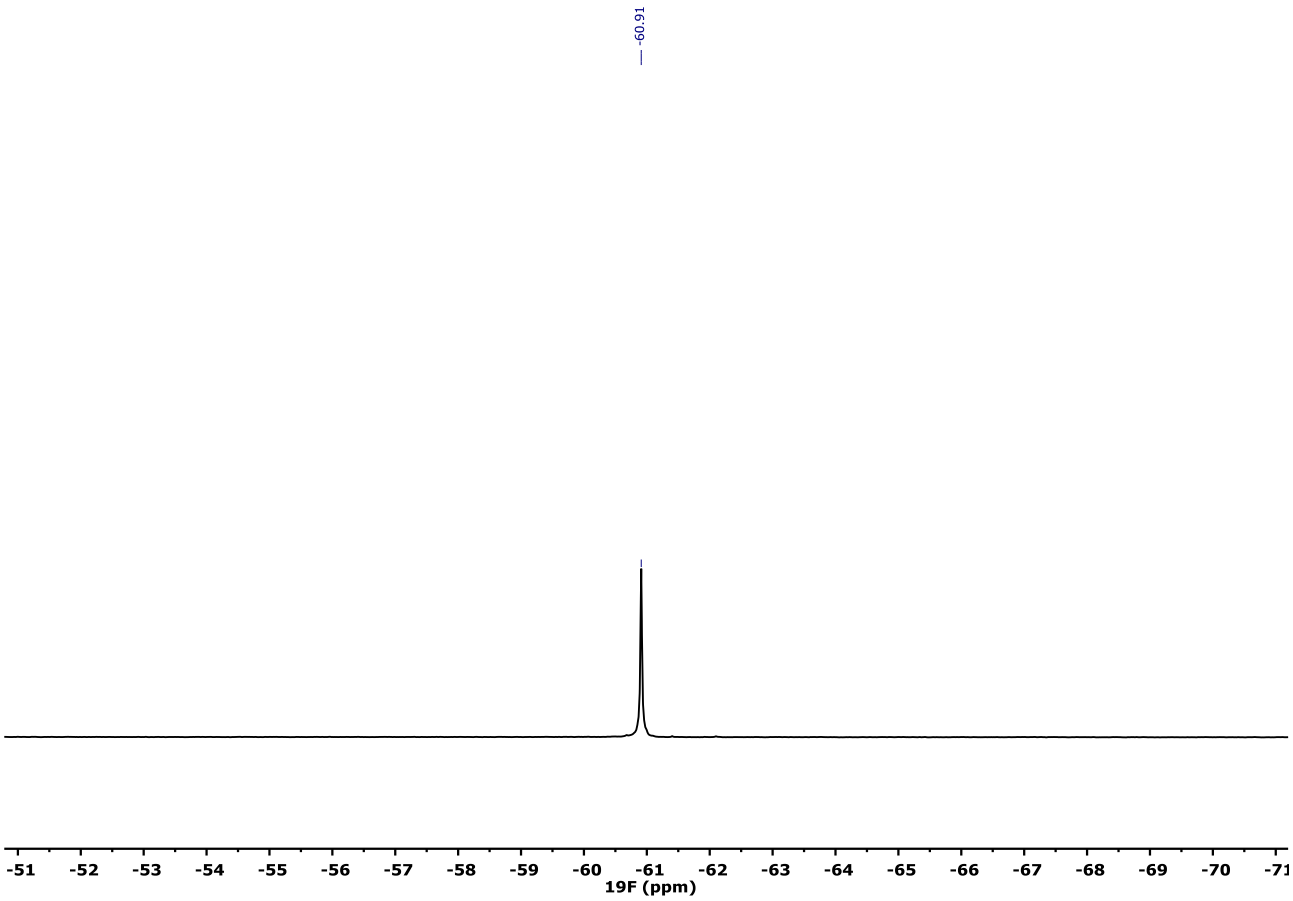


Figure S2.13. ^{19}F-NMR spectrum (376 MHz, chloroform-*d*) of **D**

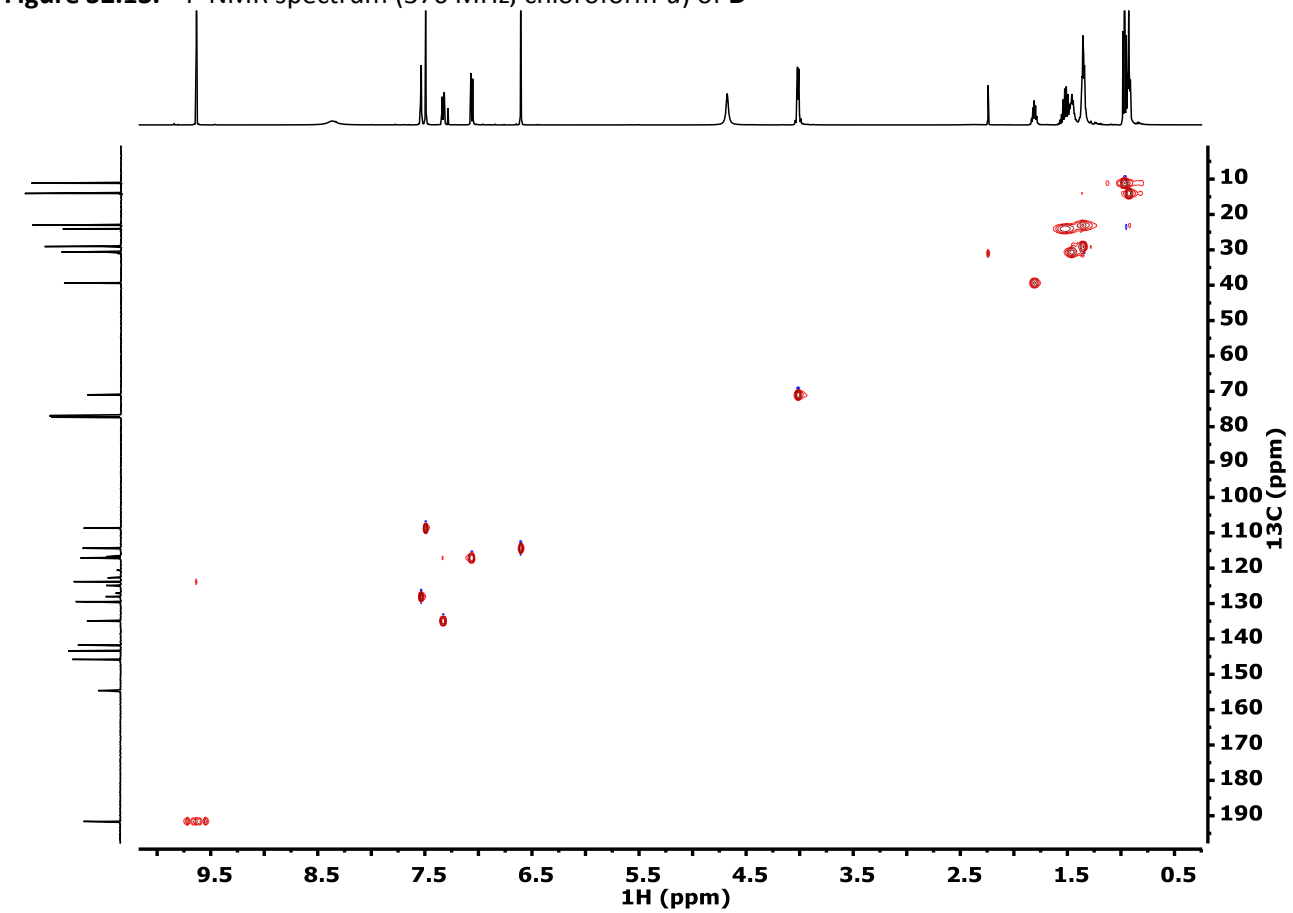
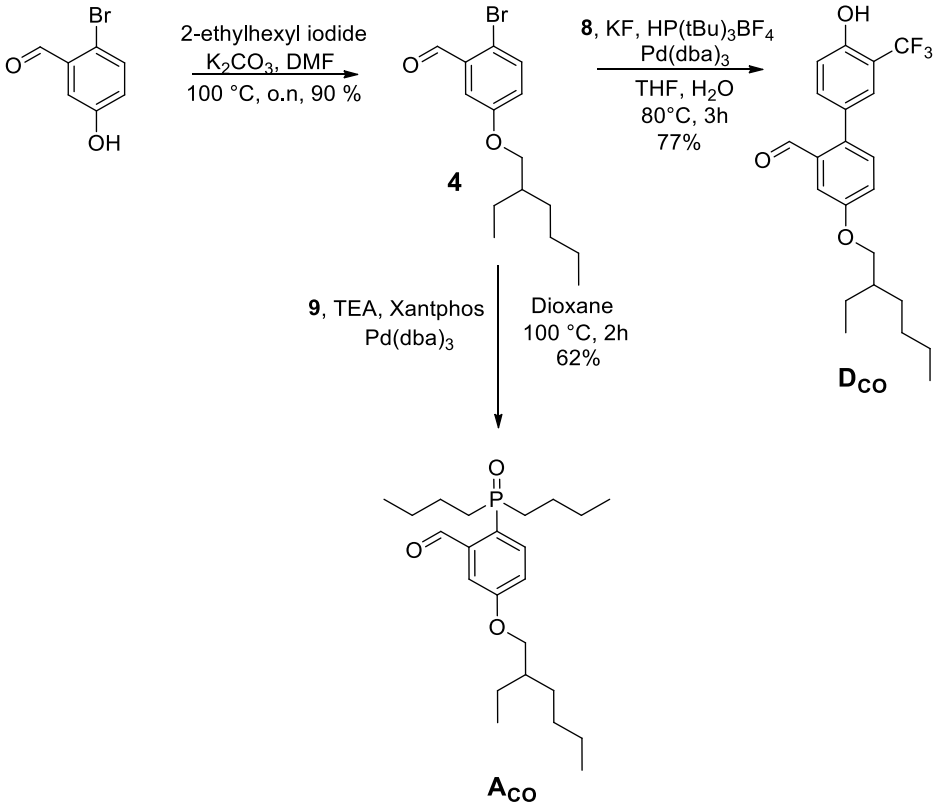


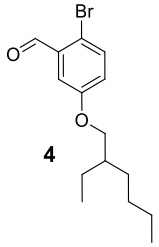
Figure S2.14. ^{1}H -^{13}C-HSQC spectrum (500 MHz, chloroform-*d*) of **D**.

2.2. Synthesis of the mono aldehyde monomers (B_{CO})

The molecules **8** and **9** were prepared according to previously reported procedures. The mono aldehyde monomers $\mathbf{A_{CO}}$ and $\mathbf{D_{CO}}$ were synthesized as reported in the following scheme:



2.1.1 Synthesis of 4



Compound **4** was synthesized starting from 2-Bromo-5-hydroxybenzaldehyde (1 g, 4.97 mmol, 1 equiv) following the procedure described for compound **2** (1.40 g, 90 % yield).

^{1}H-NMR (500 MHz, chloroform-*d*) δ 10.33 (s, 1H), 7.53 (d, J = 8.78 Hz, 1H), 7.43 (d, J = 3.17 Hz, 1H), 7.05 (dd, J = 8.78, 3.20 Hz, 1H), 3.89 (dd, J = 5.73, 2.07 Hz, 2H), 1.88 – 1.67 (m, 1H), 1.59 – 1.27 (m, 8H), 0.93 (dt, J = 8.8154, 7.2758 Hz, 6H).

^{13}C-NMR (126 MHz, chloroform-*d*) δ 191.93, 159.06, 134.47, 133.90, 123.50, 117.62, 113.38, 71.08, 39.26, 30.44, 29.03, 23.80, 23.02, 14.07, 11.08.

HRMS(ES+): Calculated for $C_{14}H_{21}{}^{79}BrNO_3$ 330.0705 a.m.u.;, found 330.0685

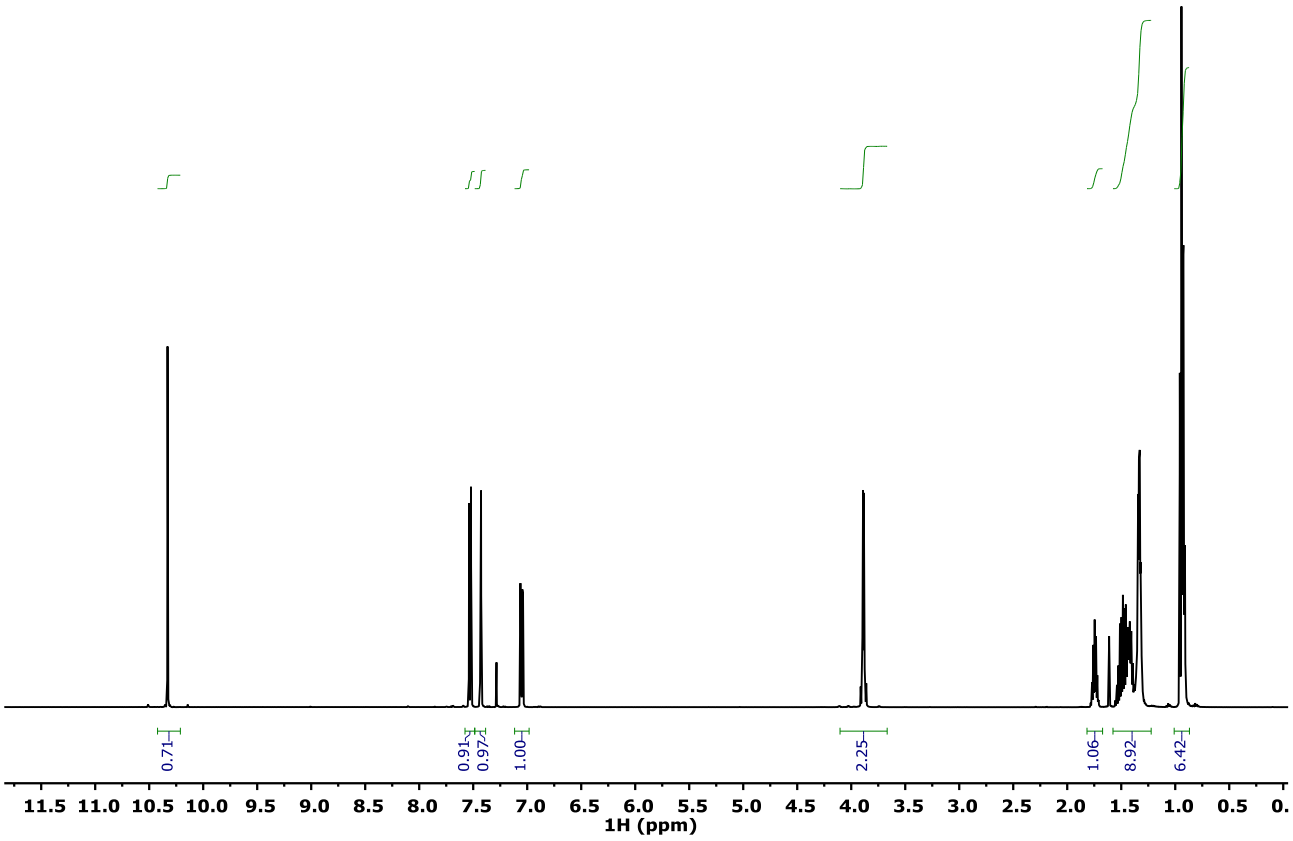


Figure S2.15. ^{1}H-NMR spectrum (500 MHz, chloroform-*d*) of **4**.

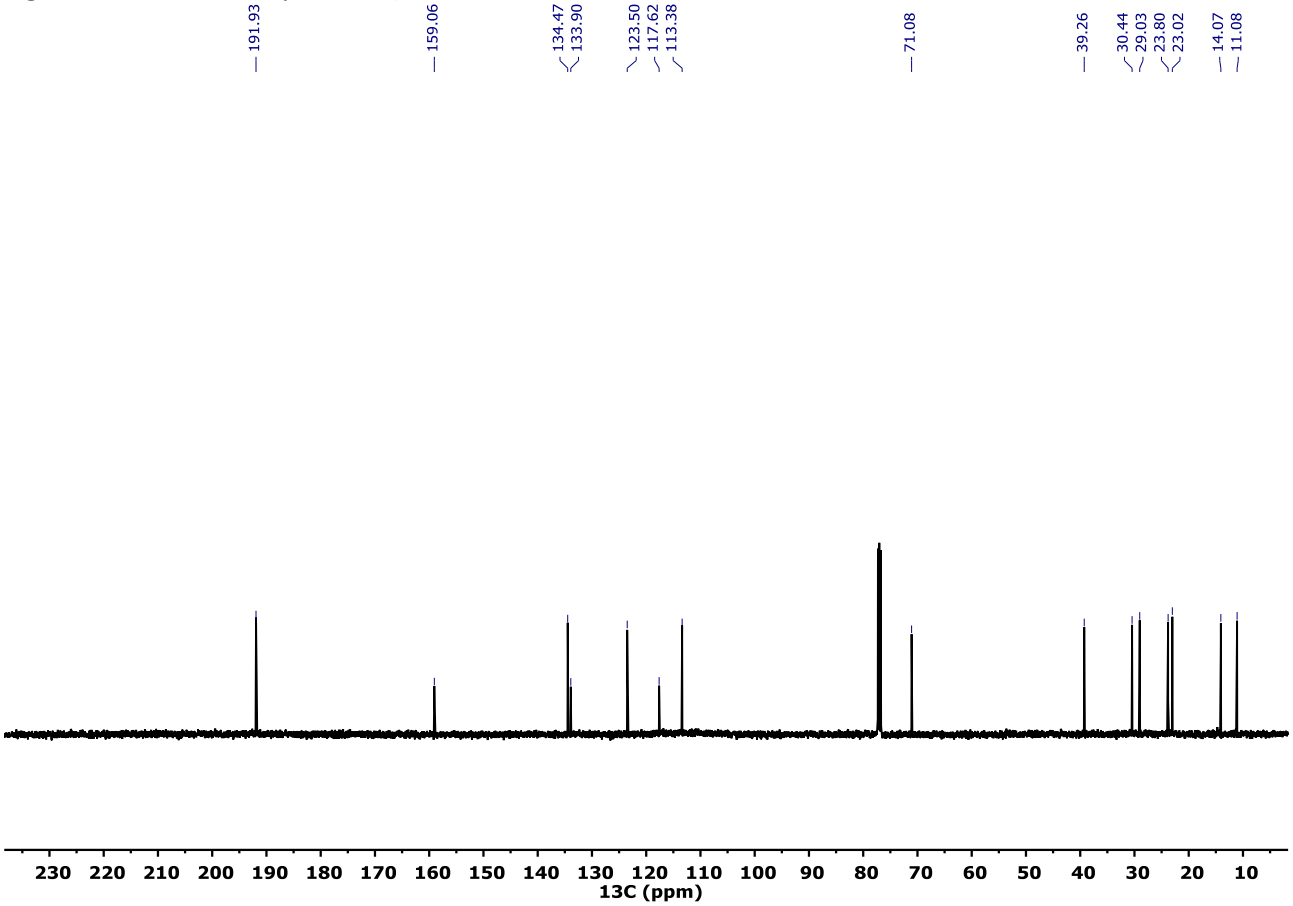
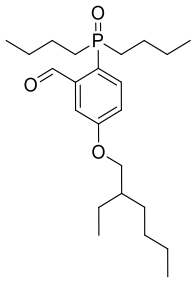


Figure S2.16. ^{13}C-NMR spectrum (126 MHz, chloroform-*d*) of **4**.

2.2.1 Synthesis of A_{CO}



A_{CO}

Compound **4** (0.5 g, 1.596 mmol, 1 equiv) was mixed with the phosphine oxide **9** (388 mg, 2.394 mmol, 1.5 equiv), Xantphos (93 mg, 0.160 mmol, 0.1 equiv) and Pd_2dba_3 (147 mg, 0.160 mmol, 0.1 equiv); finally, previously degassed dioxane (8 mL, N_2 bubbling for 15 min) and triethylamine (484 mg, 667 µl, 4.788 mmol, 3 equiv) were added, and the solution was stirred under nitrogen atmosphere, in dark conditions, for 2 h. The rection mixture was extracted with brine/EtOAc (4x), the organic fractions were collected, dried over Na_2SO_4 and the solvent removed in vacuum. The crude was purified through flash column chromatography EtOAc:MeOH (gradient of MeOH from 0% to 3%) to obtain the pure **A_{CO}** (390 mg, 62% yield).

^{1}H-NMR (400 MHz, chloroform-*d*) δ 10.45 (s, 1H), 8.00 (dd, J = 11.43, 8.50 Hz, 1H), 7.52 (t, J = 2.81 Hz, 1H), 7.22 (ddd, J = 8.44, 2.63, 0.98 Hz, 1H), 3.98 (dd, J = 5.68, 0.91 Hz, 2H), 2.23 – 2.01 (m, 4H), 1.87 – 1.71 (m, 1H), 1.71 – 1.17 (m, 16H), 1.13 – 0.66 (m, 12H).

^{13}C-NMR (101 MHz, chloroform-*d*) δ 193.03 (d, J = 2.42 Hz), 161.99 (d, J = 2.59 Hz), 140.28 (d, J = 7.48 Hz), 136.09 (d, J = 8.35 Hz), 124.44 (d, J = 85.78 Hz), 119.49 (d, J = 9.06 Hz), 118.99 (d, J = 11.03 Hz), 70.97, 39.31, 30.46, 30.14, 29.44, 29.05, 24.15, 24.00, 23.81, 23.76, 23.00, 14.06, 13.61, 11.11.

^{31}P-NMR (202 MHz, methanol-d_4) δ 51.23.

HRMS(ES+): Calculated for $C_{23}H_{40}O_3P$ 395.2715 a.m.u.; found 395.2794

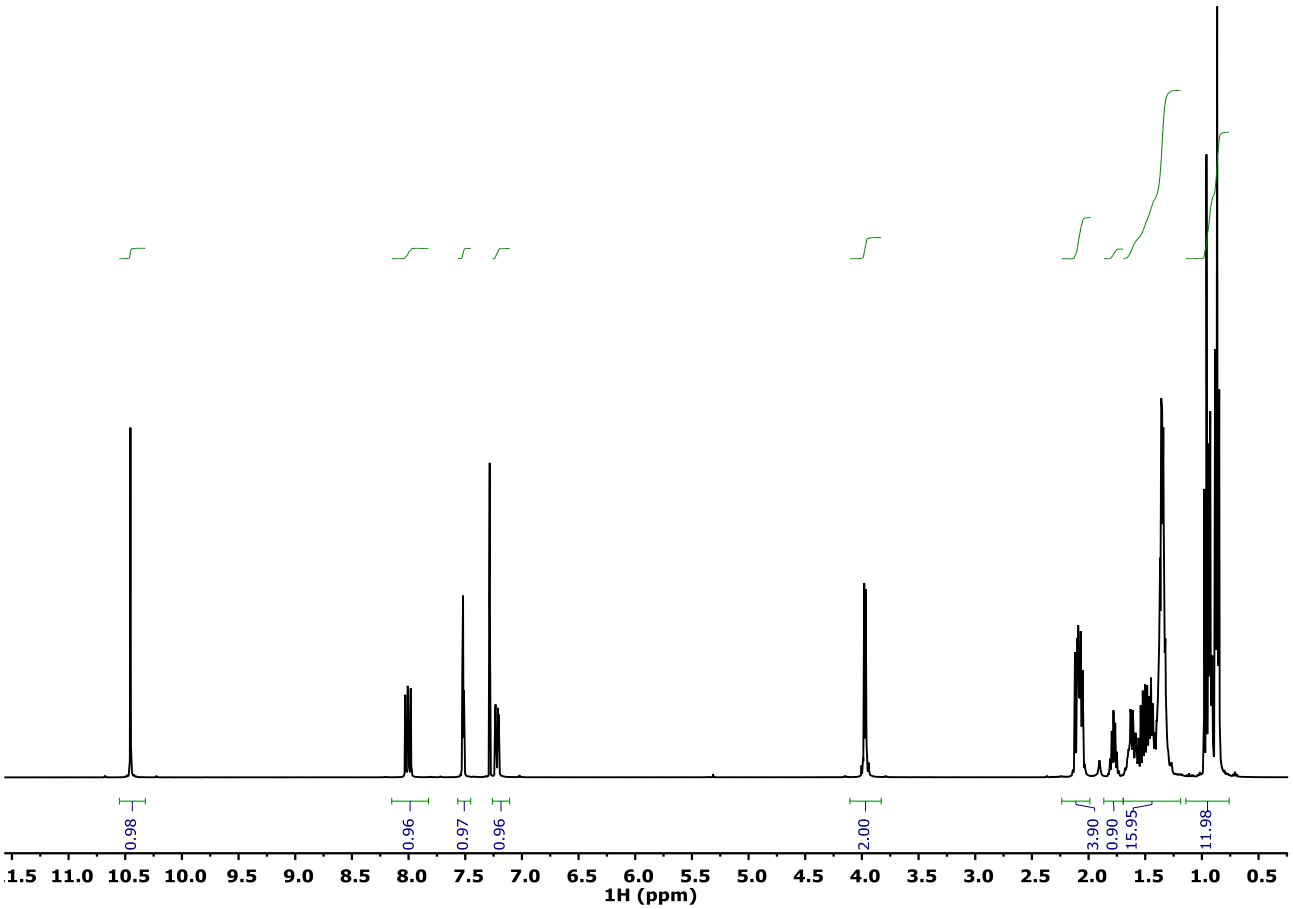


Figure S2.17. ^{1}H-NMR spectrum (400 MHz, chloroform-*d*) of $\mathbf{A_{CO}}$.

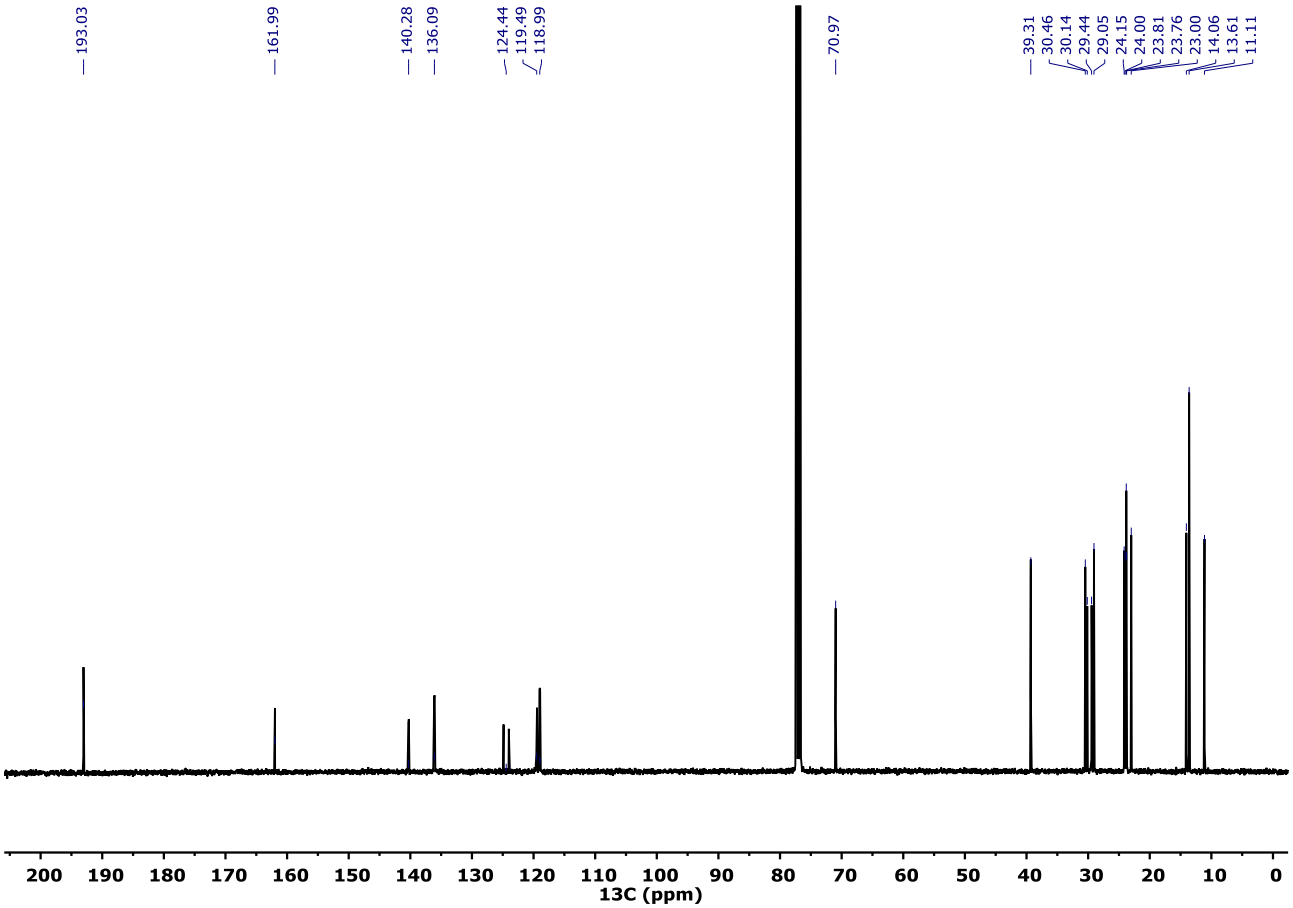


Figure S2.18. ^{13}C-NMR spectrum (101 MHz, chloroform-*d*) of $\mathbf{A_{CO}}$

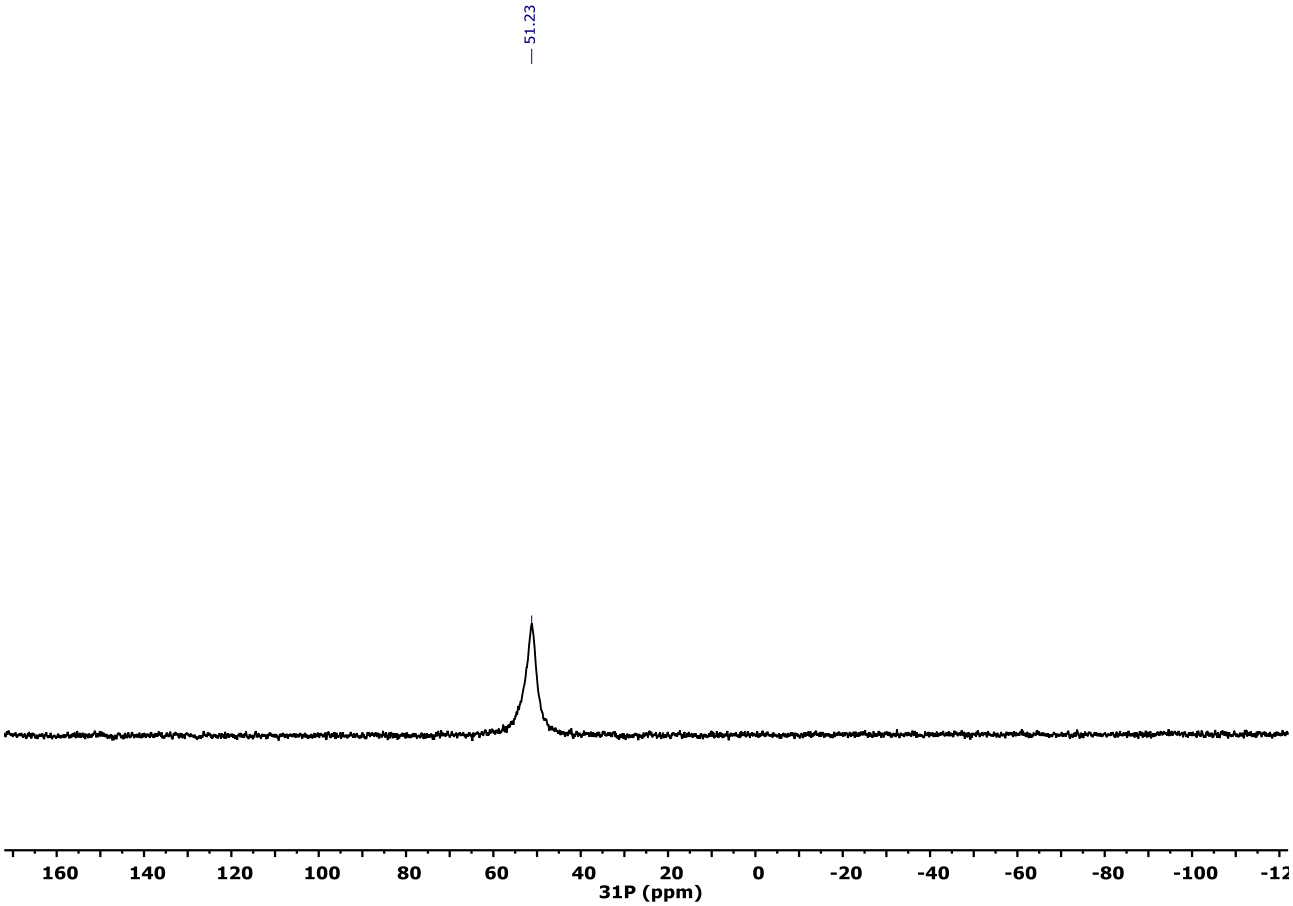


Figure S2.19. ^{31}P-NMR spectrum (202 MHz, methanol-d_4) of $\mathbf{A_{CO}}$.

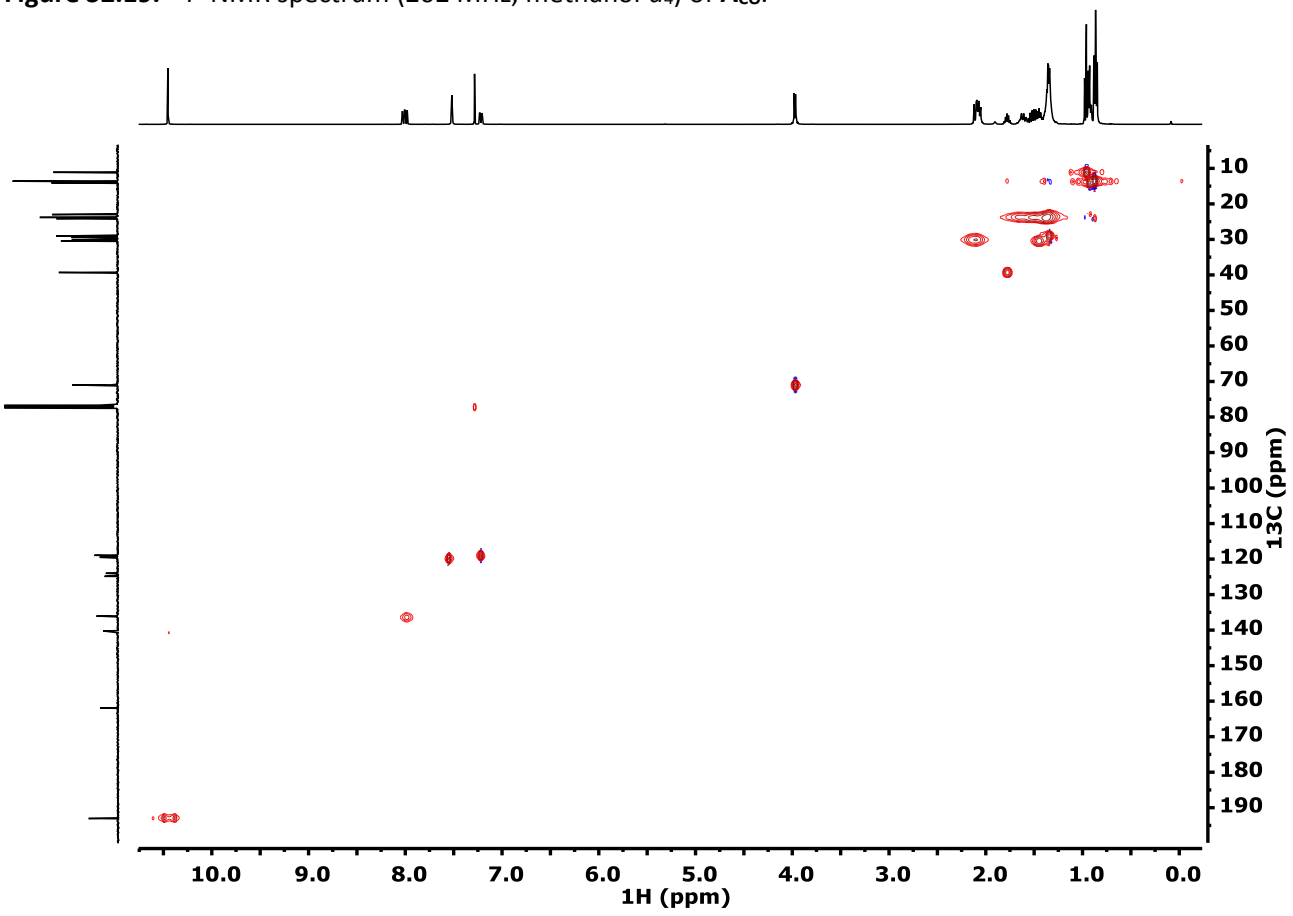


Figure S2.20. ^{1}H -^{13}C-HSQC spectrum (500 MHz, chloroform-d) of $\mathbf{A_{CO}}$.

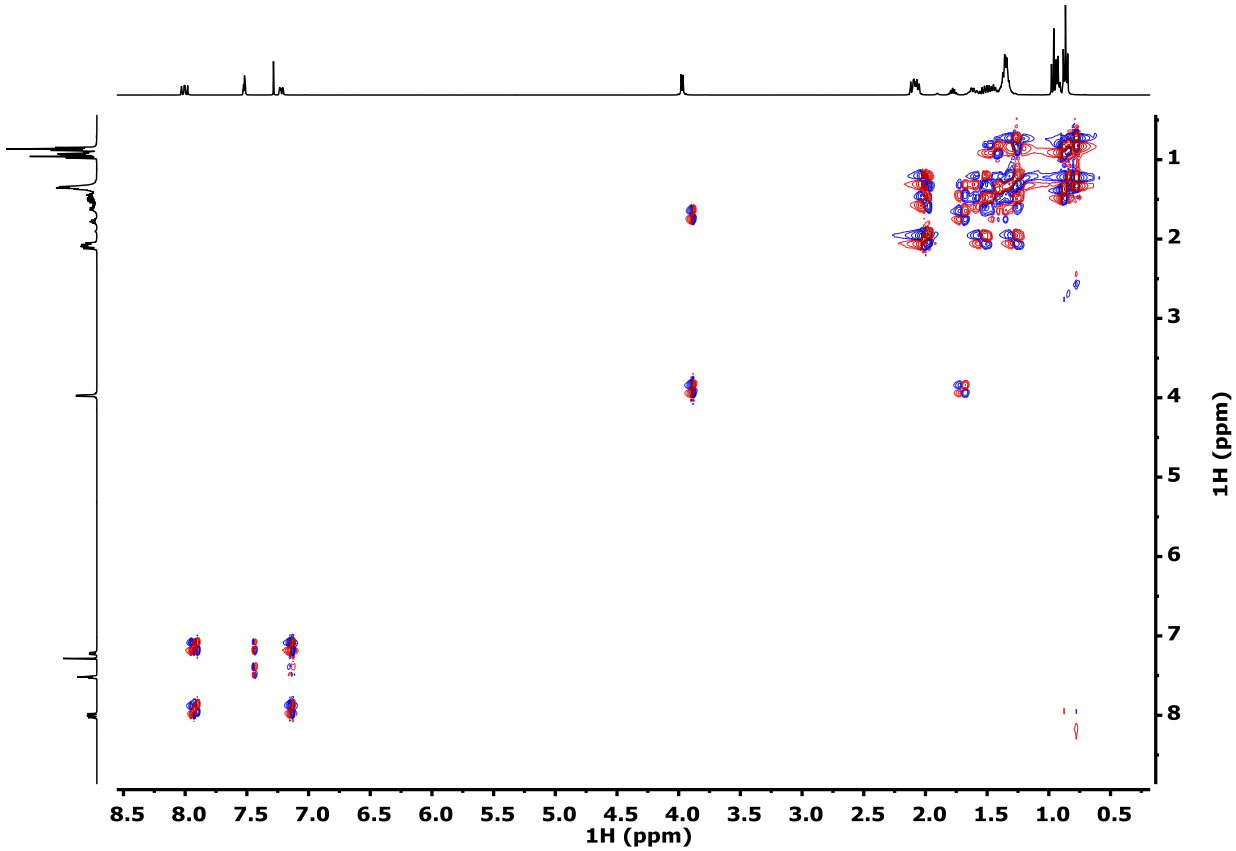
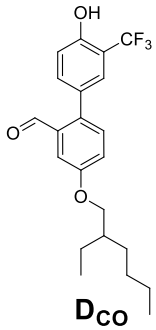


Figure S2.21. ^{1}H -^{1}H-COSY spectrum (126 MHz, chloroform-*d*) of $\mathbf{A_{CO}}$

2.2.2 Synthesis of $\mathbf{D_{CO}}$



$\mathbf{D_{CO}}$

$\mathbf{D_{CO}}$ was synthesized starting from **4** (500 mg, 1.596 mmol, 1 equiv) following the procedure described for compound **D** (485 mg, 77 % yield).

^{1}H-NMR (500 MHz, chloroform-*d*) δ 9.94 (s, 1H), 7.54 (dd, J = 5.08, 2.48 Hz, 2H), 7.41 (dd, J = 8.35, 2.25 Hz, 1H), 7.35 (d, J = 8.46 Hz, 1H), 7.24 (dd, J = 8.46, 2.78 Hz, 1H), 7.08 (d, J = 8.34 Hz, 1H), 6.10 (s, 1H), 4.06 – 3.885(m, 2H), 1.78 (dq, J = 12.77, 6.38 Hz, 1H), 1.63 – 1.29 (m, 9H), 1.07 – 0.86 (m, 6H).

^{13}C-NMR (126 MHz, chloroform-*d*) δ 192.24, 159.25, 153.51, 136.91, 135.17, 134.39, 132.06, 130.18, 128.14 (q, J = 4.9 Hz), 123.84 (q, J = 272.4 Hz), 122.09, 117.78, 116.70 (q, J = 30.8 Hz), 111.18, 70.98, 53.42, 39.34, 30.50, 29.06, 23.86, 23.04, 14.07, 11.10.
^{19}F-NMR (188 MHz, chloroform-*d*) δ -61.31.

HRMS(ES+): Calculated for $C_{22}H_{26}F_3O_3$ 395.1834 a.m.u.; experimental 395.1834 found 395.1894

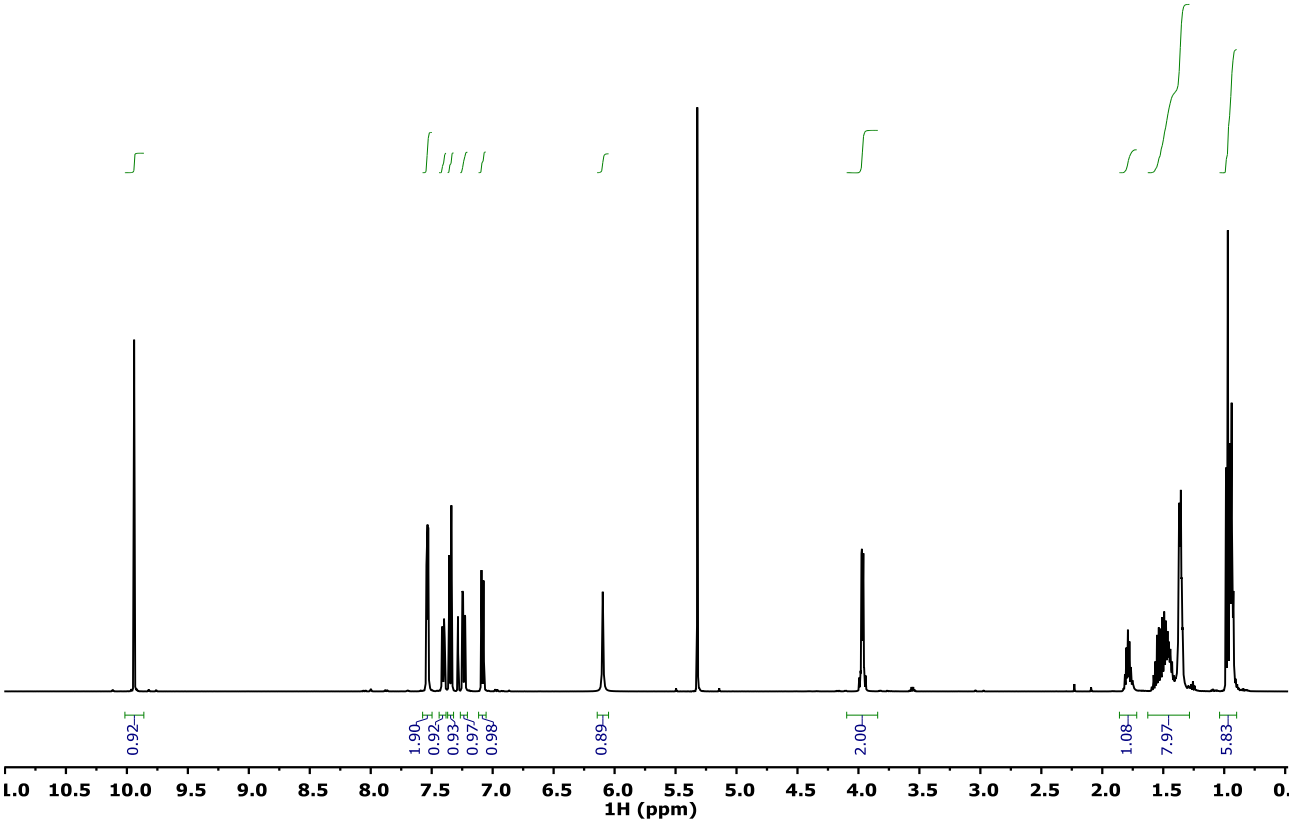


Figure S2.22. ^{1}H-NMR spectrum (500 MHz, chloroform-*d*) of $\mathbf{D_{CO}}$.

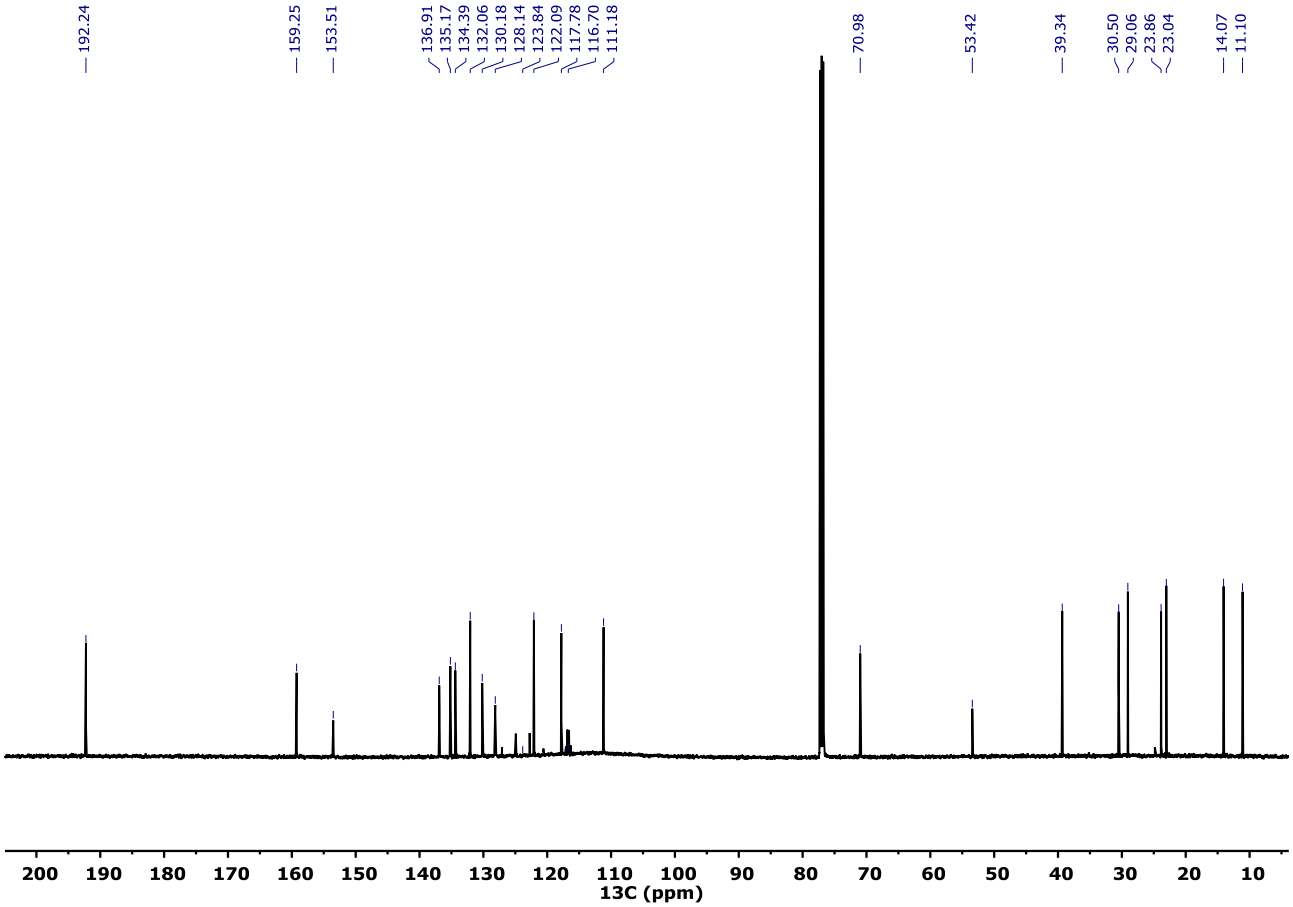


Figure S2.23. ^{13}C-NMR spectrum (126 MHz, chloroform-*d*) of $\mathbf{D_{CO}}$

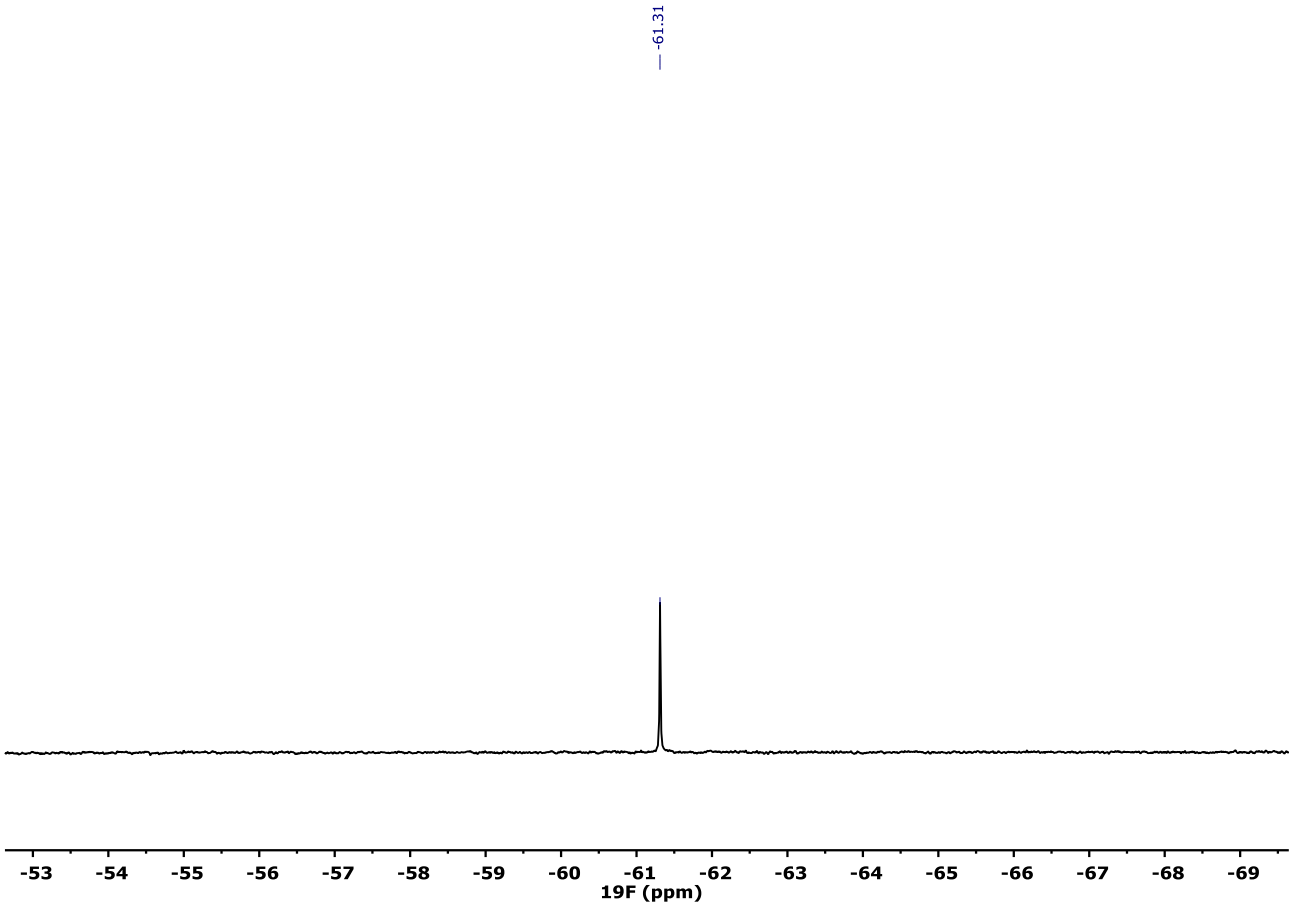


Figure S2.24. ^{19}F-NMR spectrum (188 MHz, chloroform-*d*) of $\mathbf{D_{CO}}$.

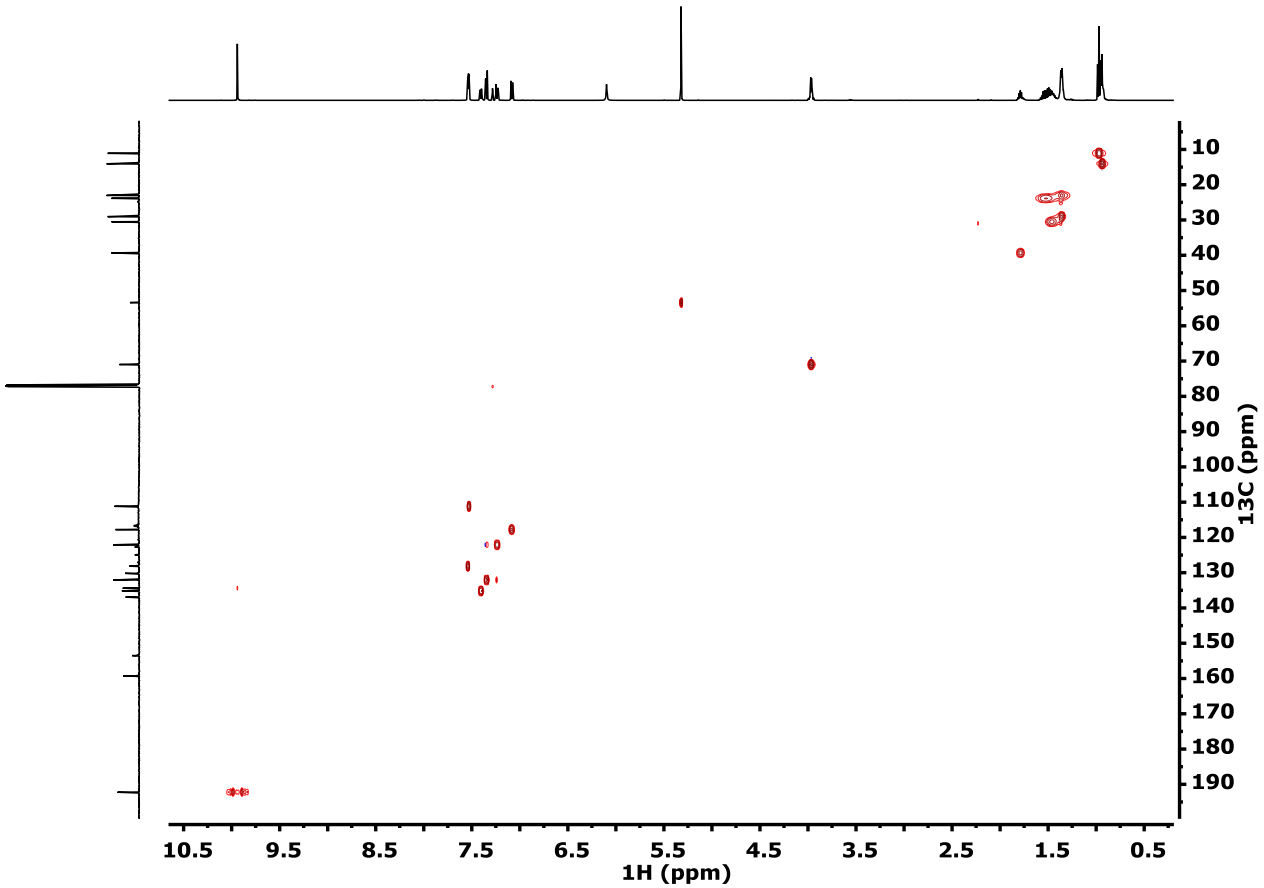


Figure S2.25. ^{1}H -^{13}C-HSQC spectrum (500 MHz, chloroform-*d*) of $\mathbf{D_{CO}}$.

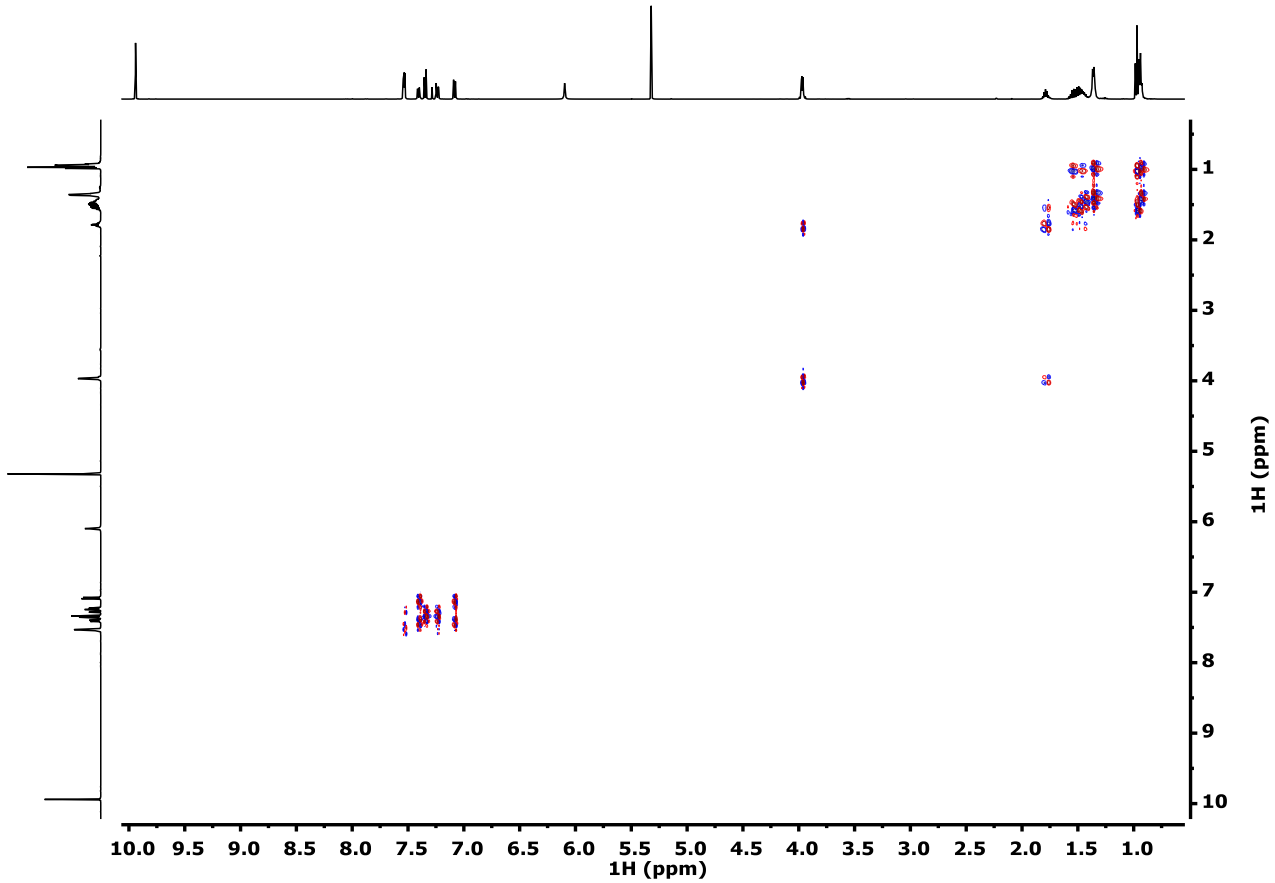
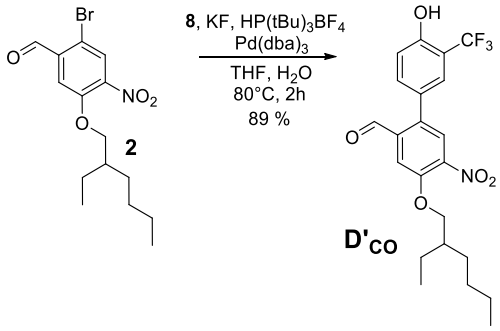


Figure S2.26. ^{1}H -^{1}H-COSY spectrum (500 MHz, chloroform-*d*) of $\mathbf{D_{co}}$

2.3 Synthesis of the mono aldehyde nitro donor D'$_{CO}$

The molecule **8** was prepared according to a previously reported procedure.



The mono aldehyde nitro donor **D'$_{CO}$** was prepared accordingly to the procedure reported for the molecule **D** starting from **2** (500 mg, 1.398 mmol, 1.2 equiv).

^{1}H-NMR δ (600 MHz, chloroform-*d*) δ 9.96 (s, 1H), 7.84 (s, 1H), 7.70 (s, 1H), 7.55 (d, J = 2.25 Hz, 1H), 7.44 (dd, J = 8.38, 2.29 Hz, 1H), 7.13 (d, J = 8.37 Hz, 1H), 5.98 (s, 1H), 4.13 (m, 2H), 1.83 (hep, J = 6.14 Hz, 1H), 1.63 – 1.42 (m, 4H), 1.35 (m, 4H), 0.95 (m, 6H).

^{13}C-NMR (151 MHz, chloroform-*d*) δ 190.20, 154.17, 151.74, 142.64, 136.52, 135.83, 135.00, 128.23, 127.85, 127.37, 123.59 (q, J = 272.79 Hz), 118.39, 117.13 (q, J = 30.88 Hz), 112.96, 72.47, 39.19, 30.25, 28.96, 23.69, 22.95, 14.04, 11.07.

^{19}F-NMR (565 MHz, chloroform-*d*) δ -61.11.

HRMS(ES+): Calculated for $C_{22}H_{25}F_3NO_5$ 440.1685 a.m.u.; found 440.1598

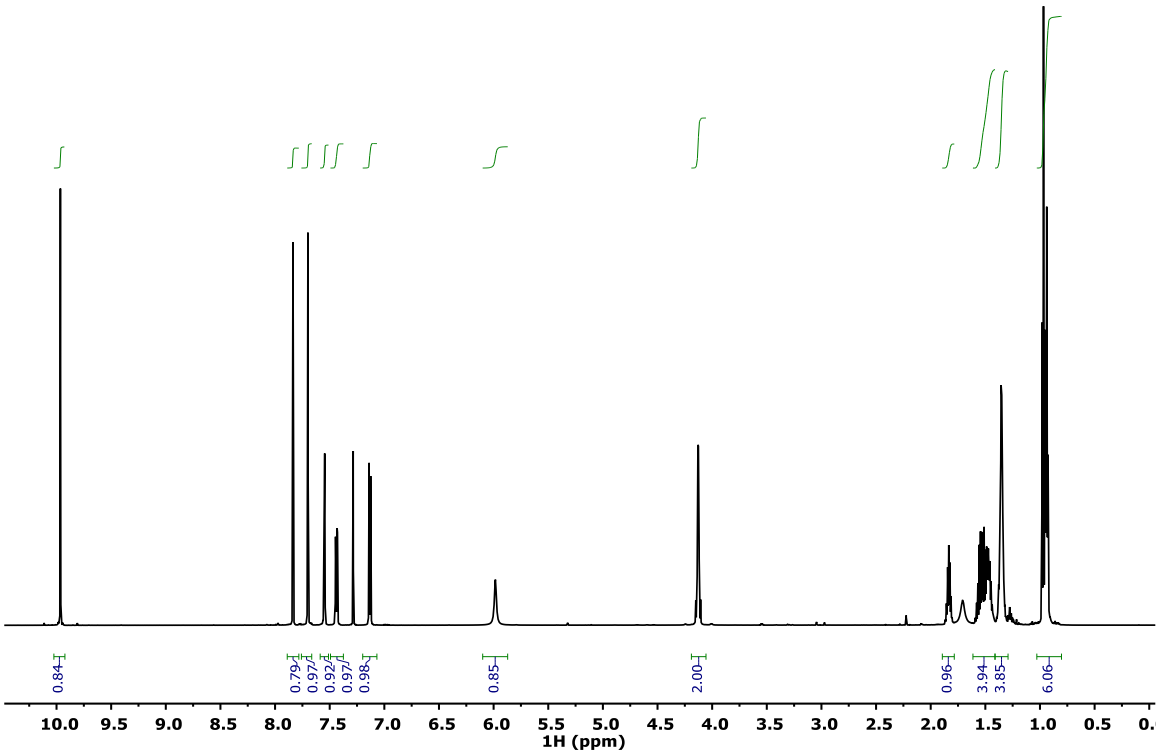


Figure S2.27. ^{1}H-NMR spectrum (600 MHz, chloroform-*d*) of **D'$_{CO}$**.

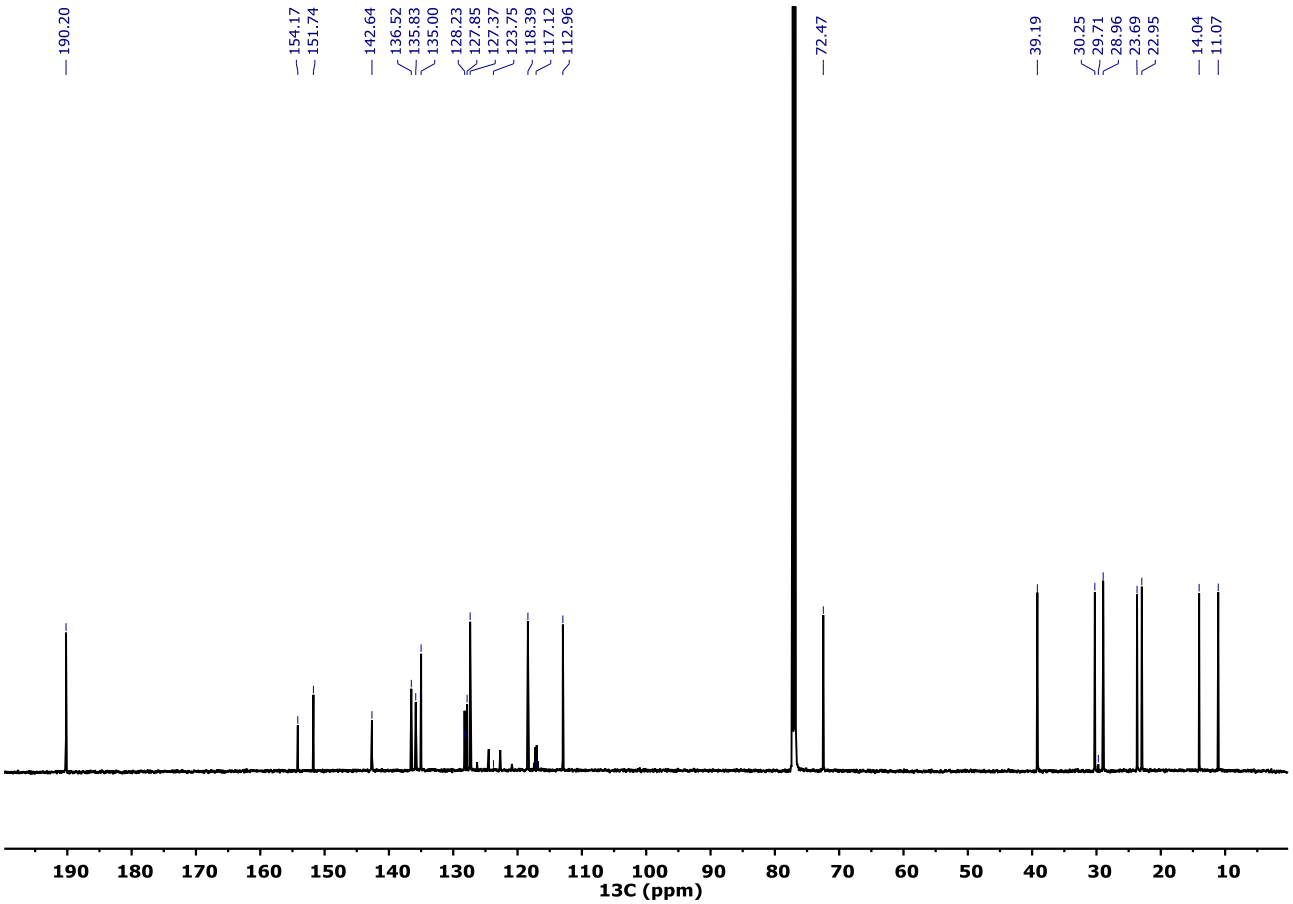


Figure S2.28. ^{13}C-NMR spectrum (151 MHz, chloroform-*d*) of **D'$_{CO}$**.

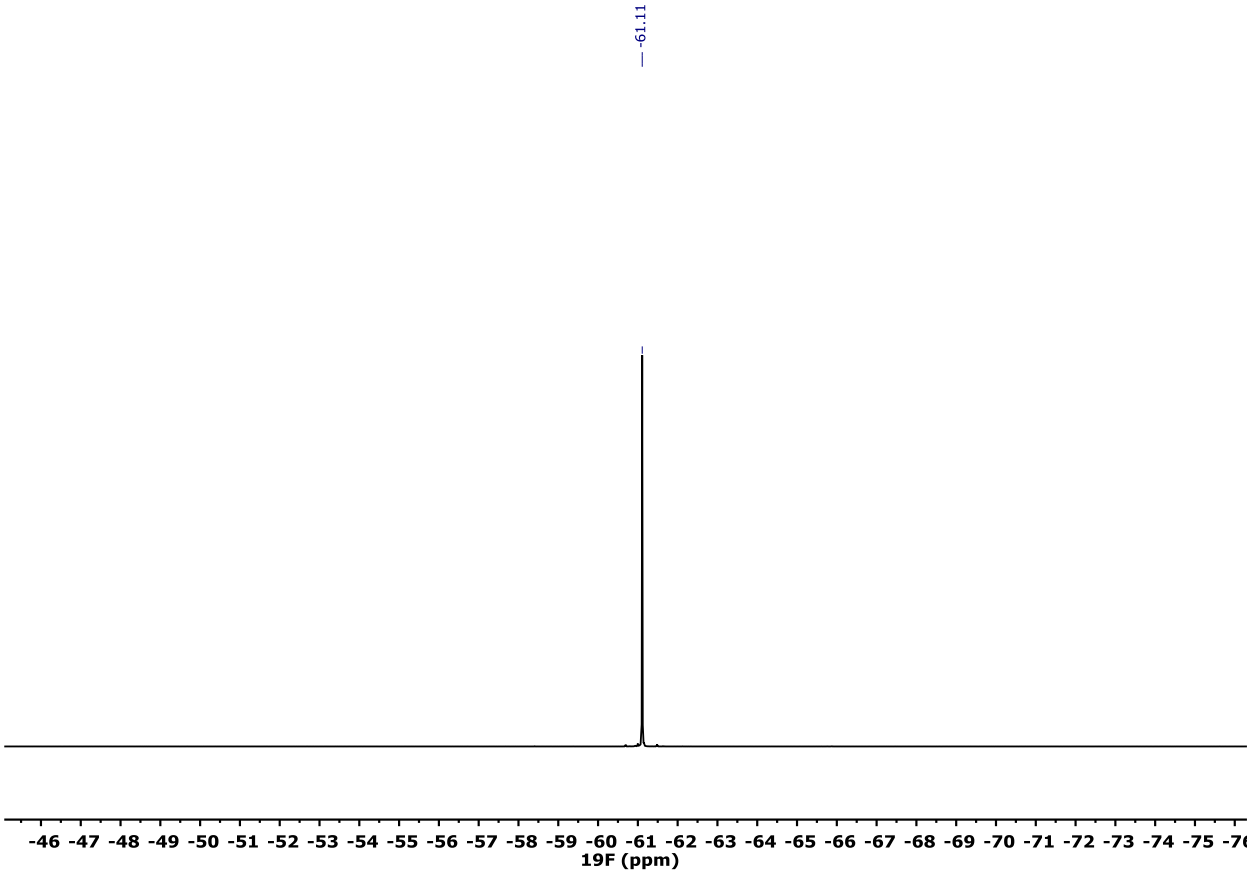


Figure S2.29. ^{19}F-NMR spectrum (565 MHz, chloroform-*d*) of **D'$_{CO}$**.

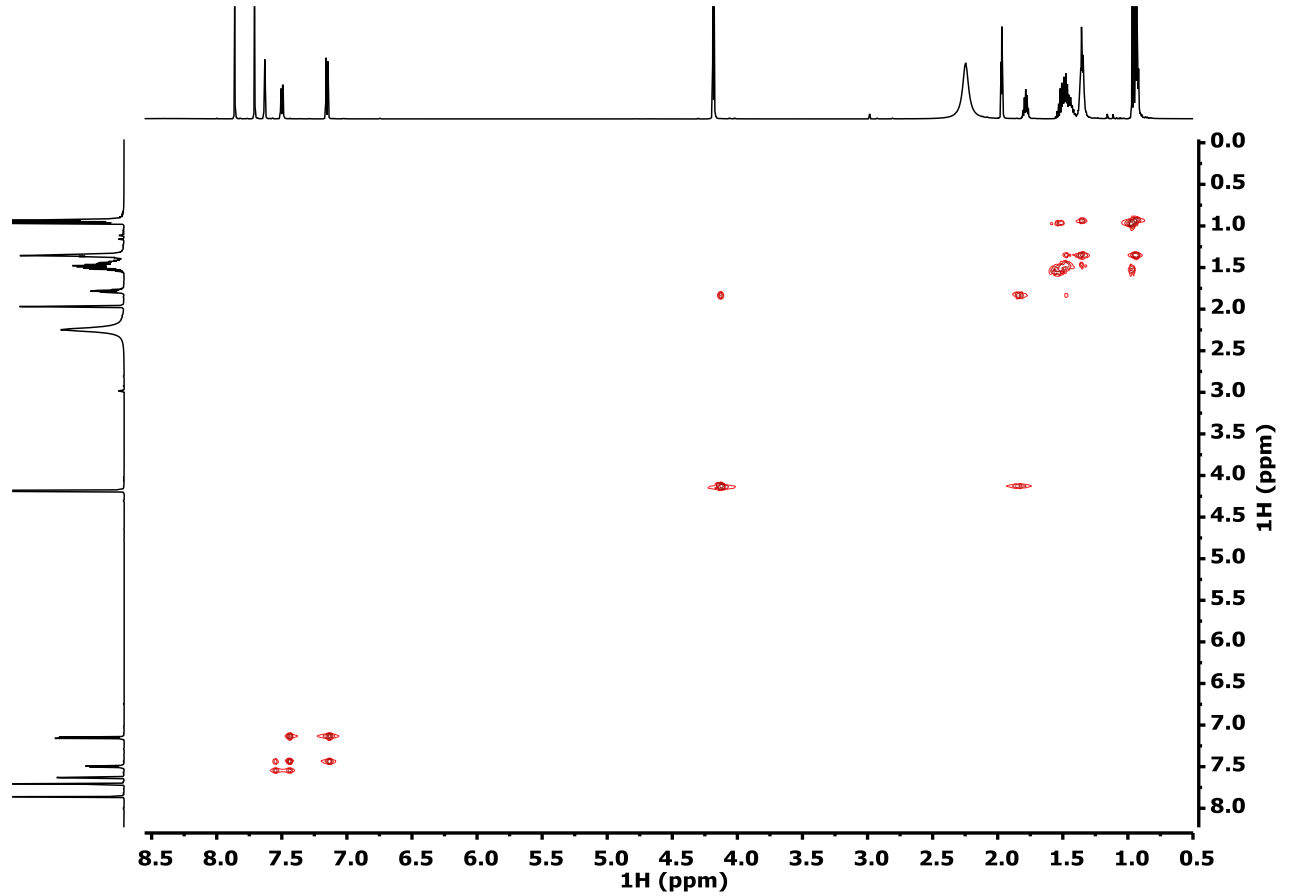


Figure S2.30. ^{1}H-^{1}H COSY spectrum (500 MHz, methanol-d_4) of **D'$_{CO}$**.

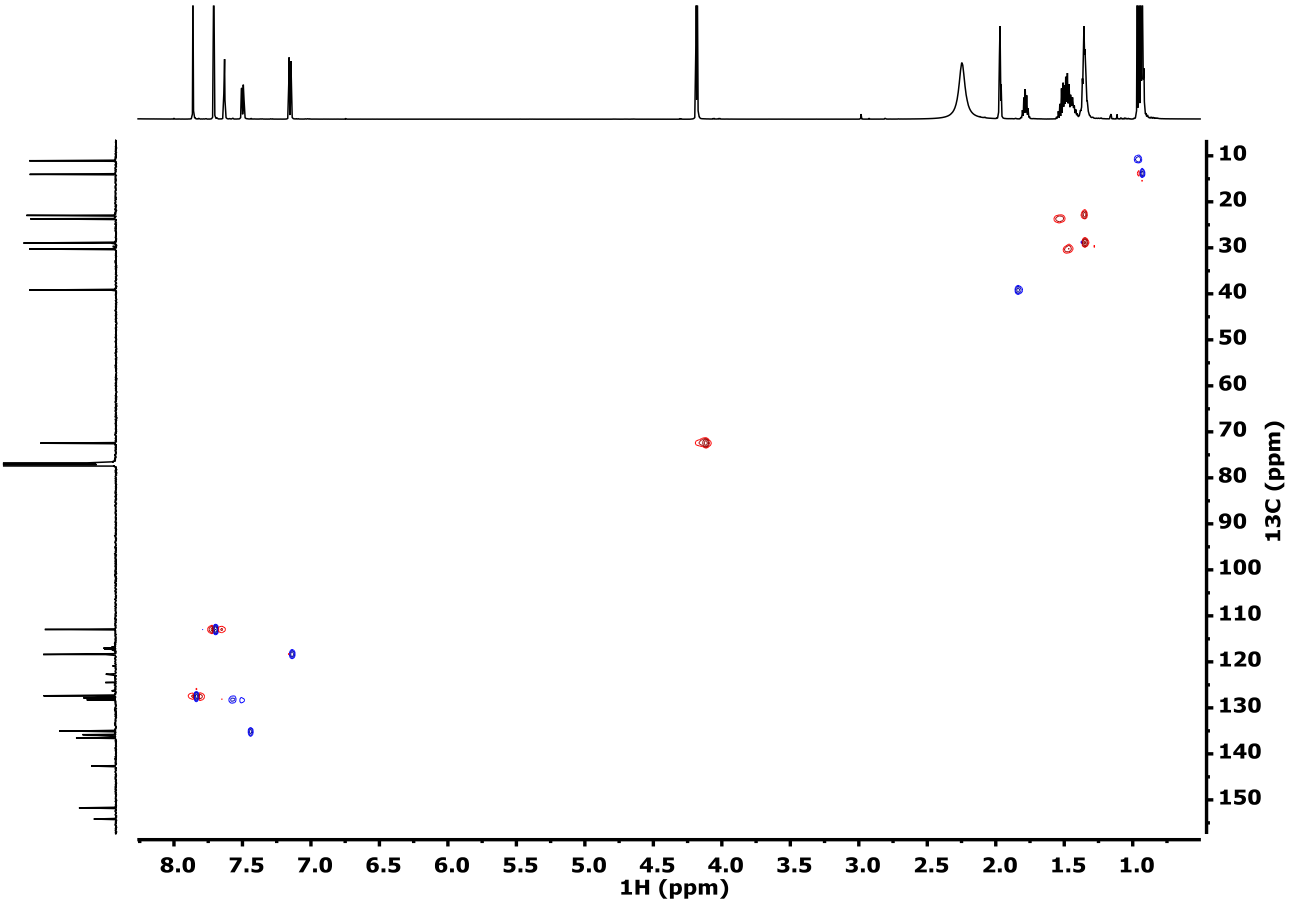
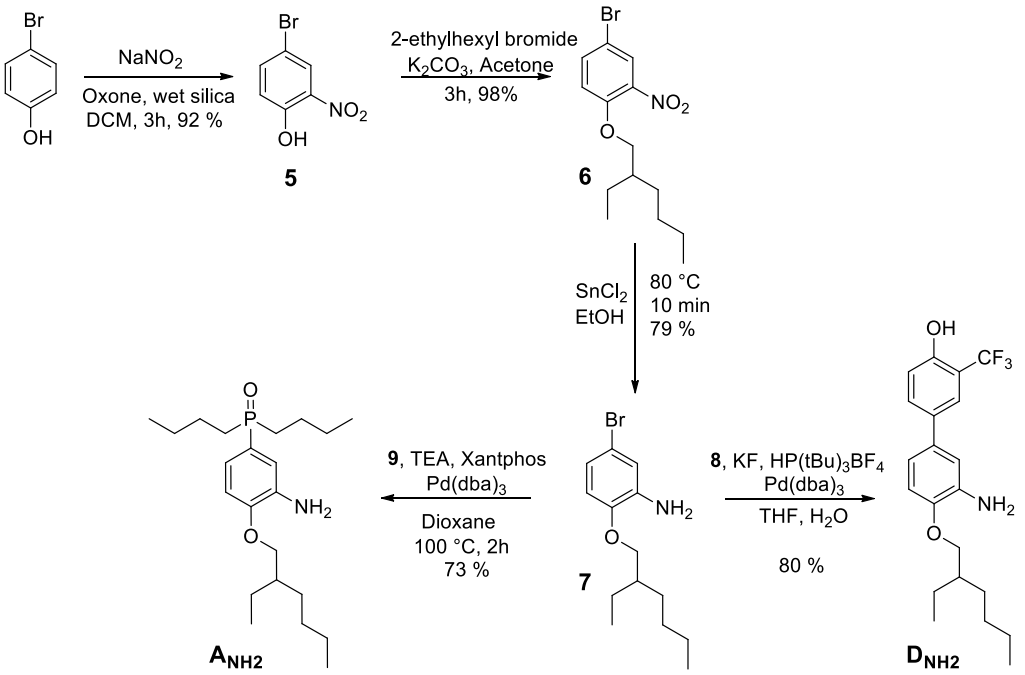


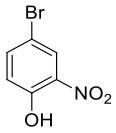
Figure S2.31. Detail of the ^{1}H -^{13}C-HSQC spectrum (126 MHz, chloroform-*d*) of **D'$_{CO}$**. The aldehyde region is omitted for clarity.

2.4 Synthesis of the aniline monomers (B_{NH2})

The molecules **8, 9** and **10** were prepared according to previously reported procedures. The mono aldehyde monomers $\mathbf{A_{NH2}}$ and $\mathbf{D_{NH2}}$ were as reported in the following scheme:



2.4.1 Synthesis of 5



5

With small modifications of a literature procedure (Zolfigol M.A., Bagherzadeh M., Madrakian E., Ghaemi E., Taqian-Nasab A. *One-pot Nitration of Phenols under Mild and Heterogeneous Condition*s. Journal of Chemical Research. **2001**; 140-142) 4-bromophenol (7.5 g, 43.3 mmol, 1 equiv) was added in one portion to a stirred suspension of Oxone® (26 g, 43.3 mmol, 1 equiv), $NaNO_2$ (2.98 g, 43.3 mmol, 1 equiv) and wet silica (4.33 g premixed 50/50 w/w H_2O/silica 400 mesh) in 130 ml of DCM. After 3 h, the solids were filtered, the solvent removed in vacuum and the crude purified *via* flash chromatography on silica gel (gradient PE:EtOAc 9:1 to 8:2) giving the desired compound **5** as bright yellow crystals (8.7 g, 92% yield).

^{1}H-NMR δ (500 MHz, chloroform-*d*) δ 10.51 (s, 1H), 8.28 (t, J = 2.05 Hz, 1H), 7.69 (dd, J = 8.92, 2.41 Hz, 1H), 7.10 (d, J = 8.91 Hz, 1H).

^{13}C-NMR (126 MHz, chloroform-*d*) δ 154.14, 140.36, 134.06, 127.34, 121.75, 111.72.

HRMS(ES+): Calculated for $C_{14}H_{23}{}^{79}BrNO$ 300.0963 a.m.u.; found 300.0947

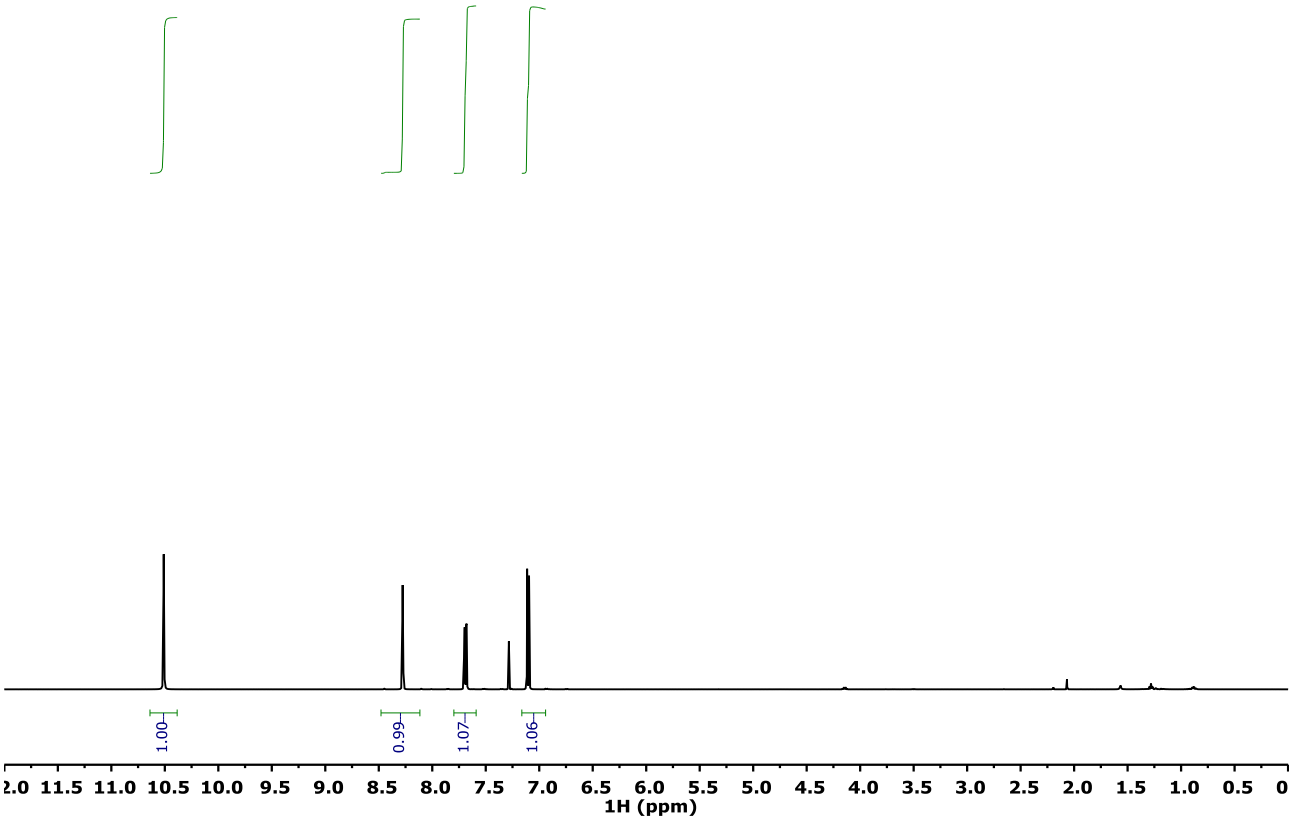


Figure S2.32. ^{1}H-NMR spectrum (500 MHz, chloroform-*d*) of **5**.

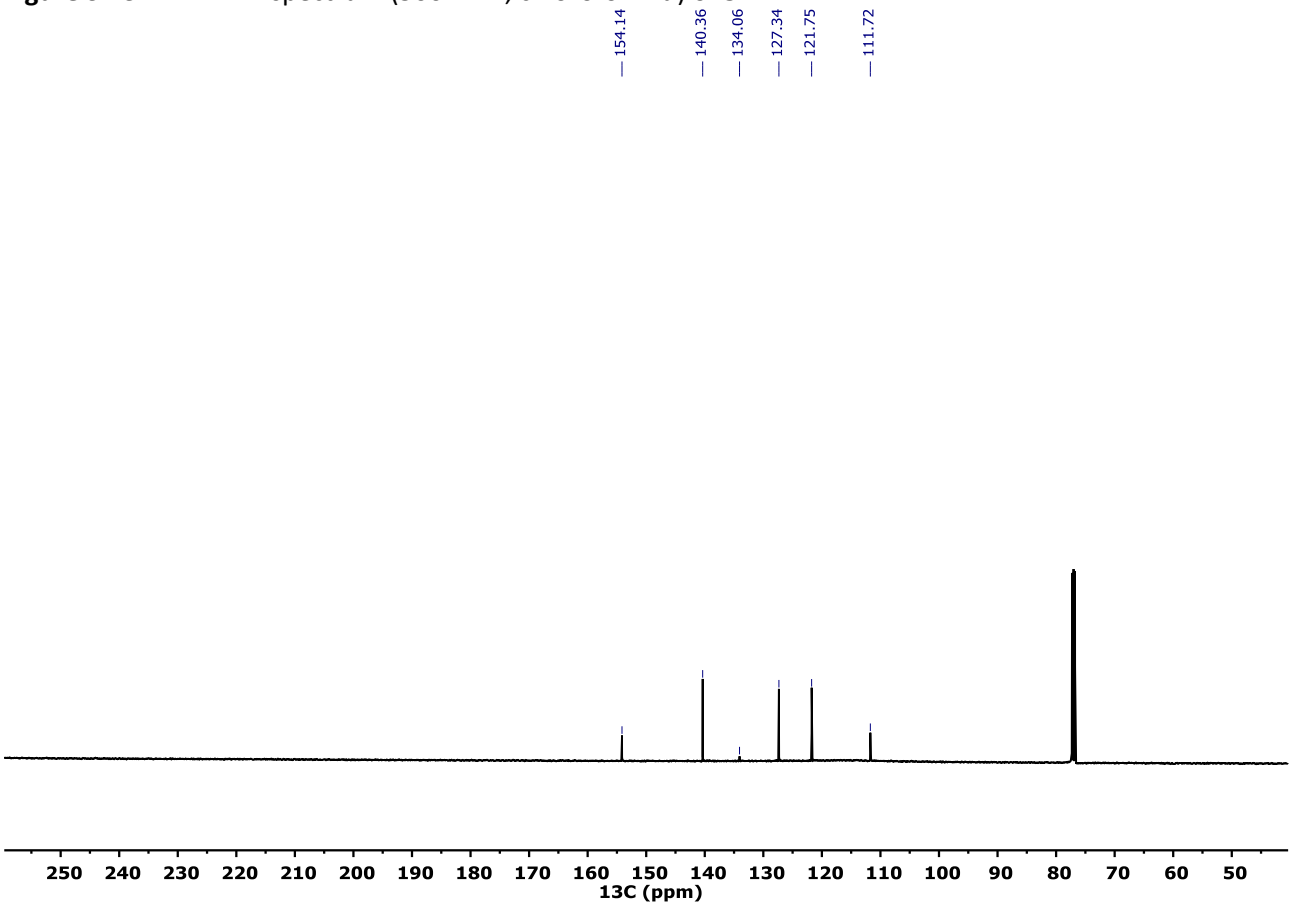
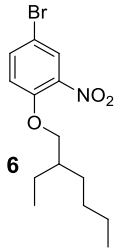


Figure S2.33. ^{13}C-NMR spectrum (126 MHz, chloroform-*d*) of **5**.

2.4.2 Synthesis of 6



Compound **5** (5 g, 22.94 mmol, 1 equiv), K_2CO_3 (6.33 g, 45.87 mmol, 2 equiv) and 2-ethylhexyl bromide (6.64 g, 6.12 ml, 34.41 mmol, 1.5 equiv) were added to 100 ml of acetone. After 3 h, the solids where filtered off, the solvents removed and the crude purified *via* flash chromatography on silica gel (gradient PE to PE:EtOAc 9:1) giving the desired compound **6** as light yellow solid (7.42 g, 98% yield).

^{1}H-NMR (500 MHz, chloroform-*d*) δ 7.9697 (d, J = 2.46 Hz, 1H), 7.62 (dd, J = 8.95, 2.45 Hz, 1H), 6.99 (d, J = 8.92 Hz, 1H), 3.99 (dd, J = 5.58, 1.86 Hz, 2H), 1.78 (hept, J = 6.21 Hz, 1H), 1.67 – 1.40 (m, 4H), 1.40 – 1.17 (m, 4H), 0.93 (m, 6H).

^{13}C-NMR (126 MHz, chloroform-*d*) δ 151.91, 140.22, 136.68, 128.21, 115.93, 111.37, 72.24, 39.24, 30.23, 28.97, 23.65, 22.93, 14.03, 11.05.

HRMS(ES+): Calculated for $C_{14}H_{21}{}^{79}BrNO_3$ 330.0705 a.m.u.; found 330.0621

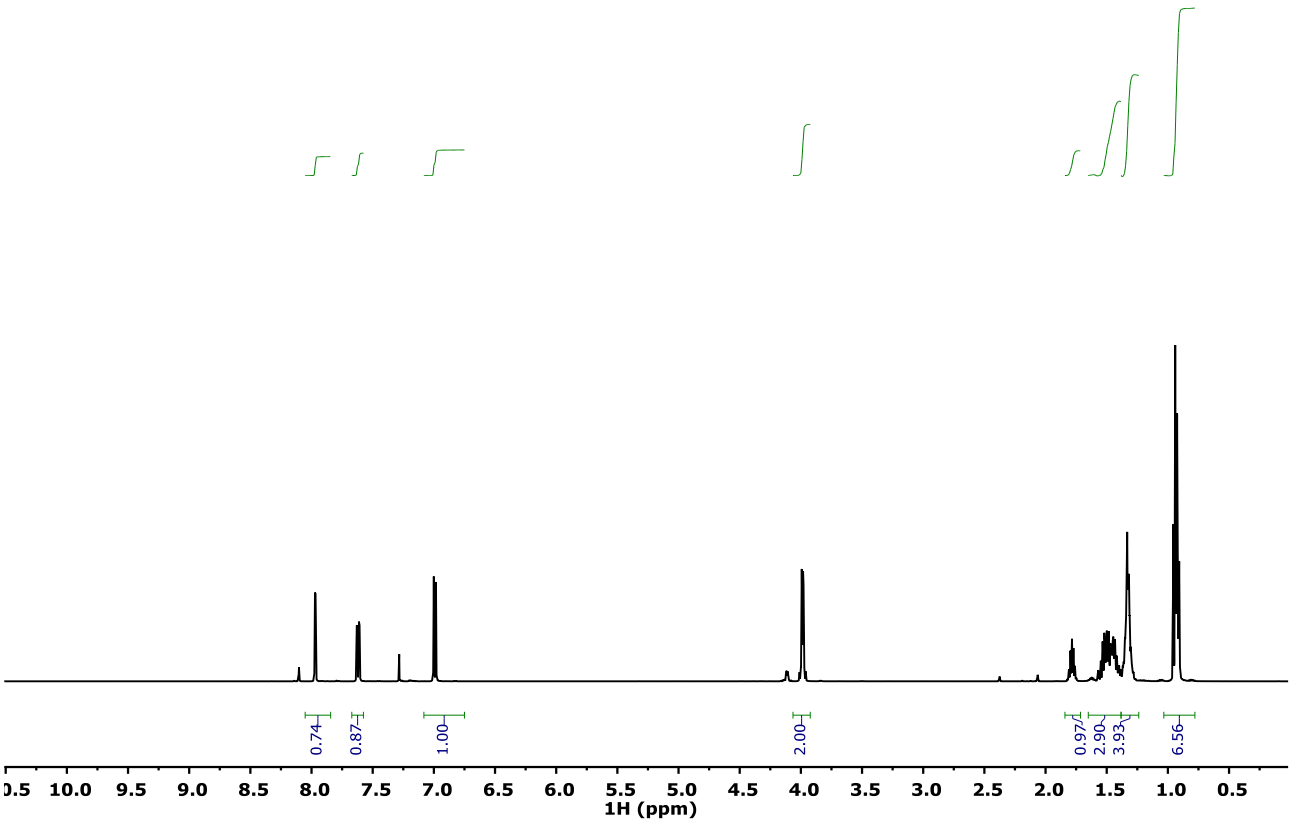


Figure S2.34. ^{1}H-NMR spectrum (500 MHz, chloroform-*d*) of **6**.

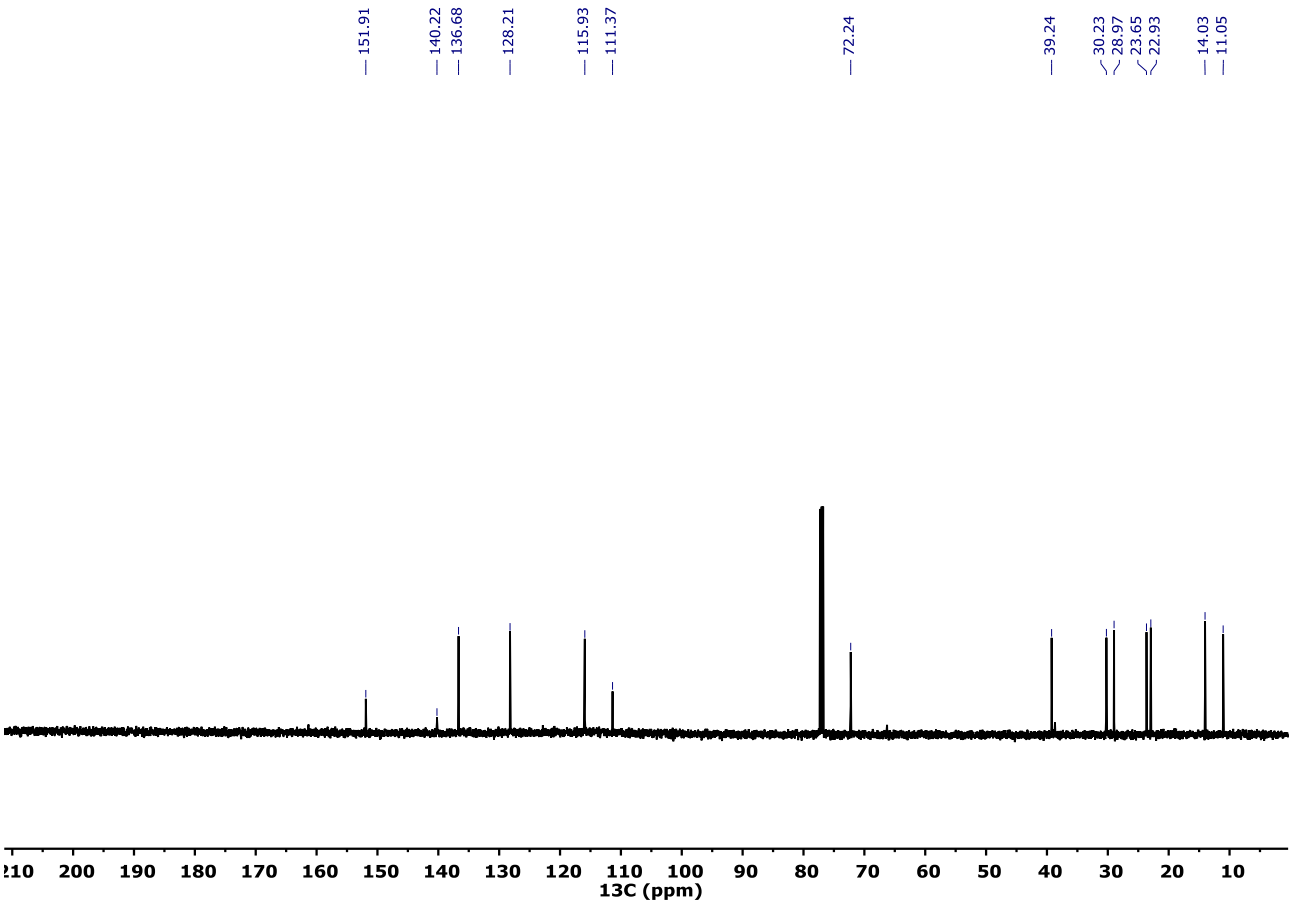
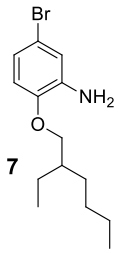


Figure S2.35. ^{13}C-NMR spectrum (126 MHz, chloroform-*d*) of **6**.

2.4.3 Synthesis of 7



7

Compound **7** was synthesized reducing **6** (500 mg, 1.51 mmol, 1 equiv) following the procedure described for compound **3** (358 mg, 79% yield).

^{1}H-NMR (500 MHz, chloroform-*d*) δ 6.84 (d, J = 2.36 Hz, 1H), 6.81 (dd, J = 8.44, 2.37 Hz, 1H), 6.65 (d, J = 8.45 Hz, 1H), 3.87 (m, 4H), 1.77 (hept, J = 6.17 Hz, 1H), 1.62 – 1.31 (m, 9H), 1.01 – 0.84 (m, 6H).

^{13}C-NMR (126 MHz, chloroform-*d*) δ 145.93, 137.89, 120.61, 117.25, 112.98, 112.50, 70.89, 39.43, 30.66, 29.11, 24.03, 23.04, 14.07, 11.17.

HRMS(ES+): Calculated for $C_{14}H_{23}{}^{79}BrNO$ 300.0963 a.m.u.; found 300.0901

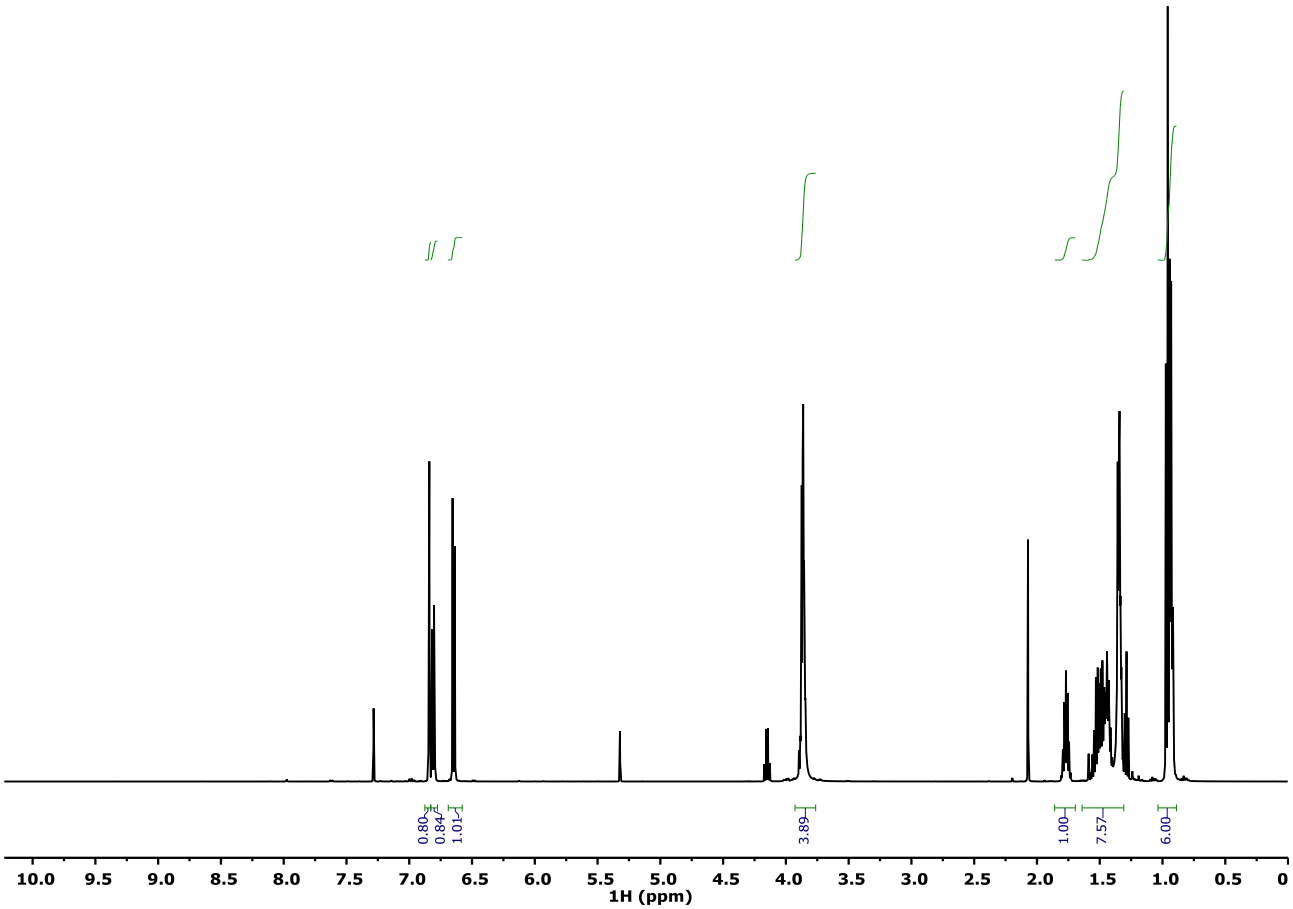


Figure S2.36. ^{1}H-NMR spectrum (500 MHz, chloroform-*d*) of **7**.

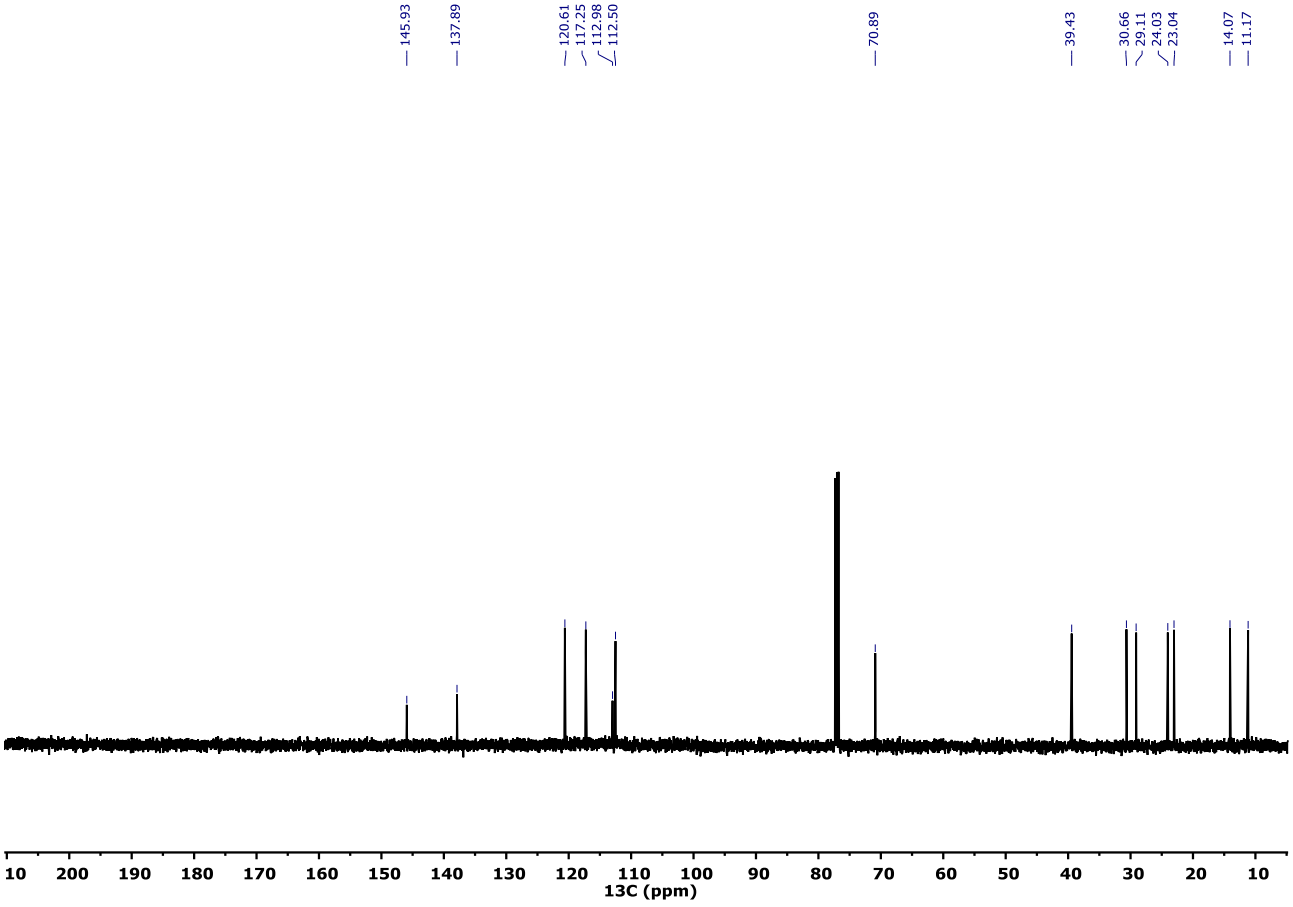
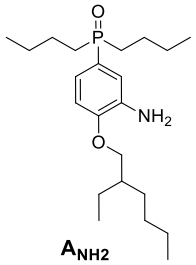


Figure S2.37. ^{13}C-NMR spectrum (126 MHz, chloroform-*d*) of **7**.

2.4.4 Synthesis of A_{NH2}



A_{NH2}

A_{NH2} was synthesized from **7** (200 mg, 0.66 mmol, 1 equiv) following the procedure described for compound **A_{CO}** (184 mg, 73% yield).

^{1}H-NMR (500 MHz, methanol-d_4) δ 7.05 (m, 2H), 6.99 (m, 1H), 3.99 (m, 2H), 2.00 (m, 4H), 1.81 (m, 1H), 1.65 – 1.46 (m, 6H), 1.44 – 1.33 (m, 10H), 0.94 (m, 12 H).

^{13}C-NMR (126 MHz, methanol-d_4) δ 149.73 (d, J = 3.0 Hz), 137.54 (d, J = 14.3 Hz), 121.59 (d, J = 99.8 Hz), 120.61 (d, J = 9.8 Hz), 115.43 (d, J = 11.7 Hz), 110.74 (d, J = 13.9 Hz), 70.38, 53.42, 39.38, 30.35, 28.98, 28.87, 28.43, 23.68, 23.57, 23.22, 22.71, 13.05, 12.56.

^{31}P-NMR (202 MHz, methanol-d_4) δ 47.01.

HRMS(ES+): Calculated for $C_{22}H_{41}NO_2P$ 382.2875 a.m.u.; found 382.3017

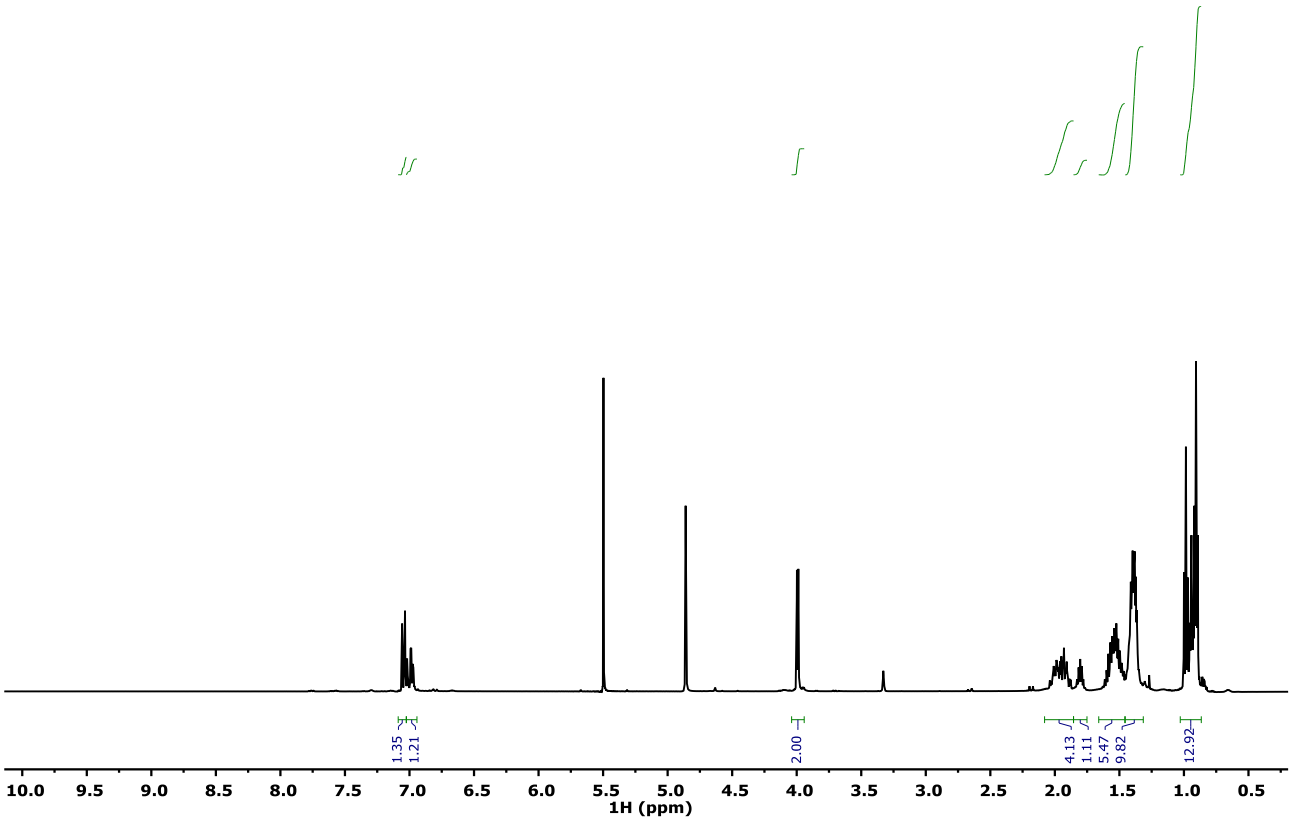


Figure S2.38. ^{1}H-NMR spectrum (500 MHz, methanol-d_4) of **A_{NH2}**.

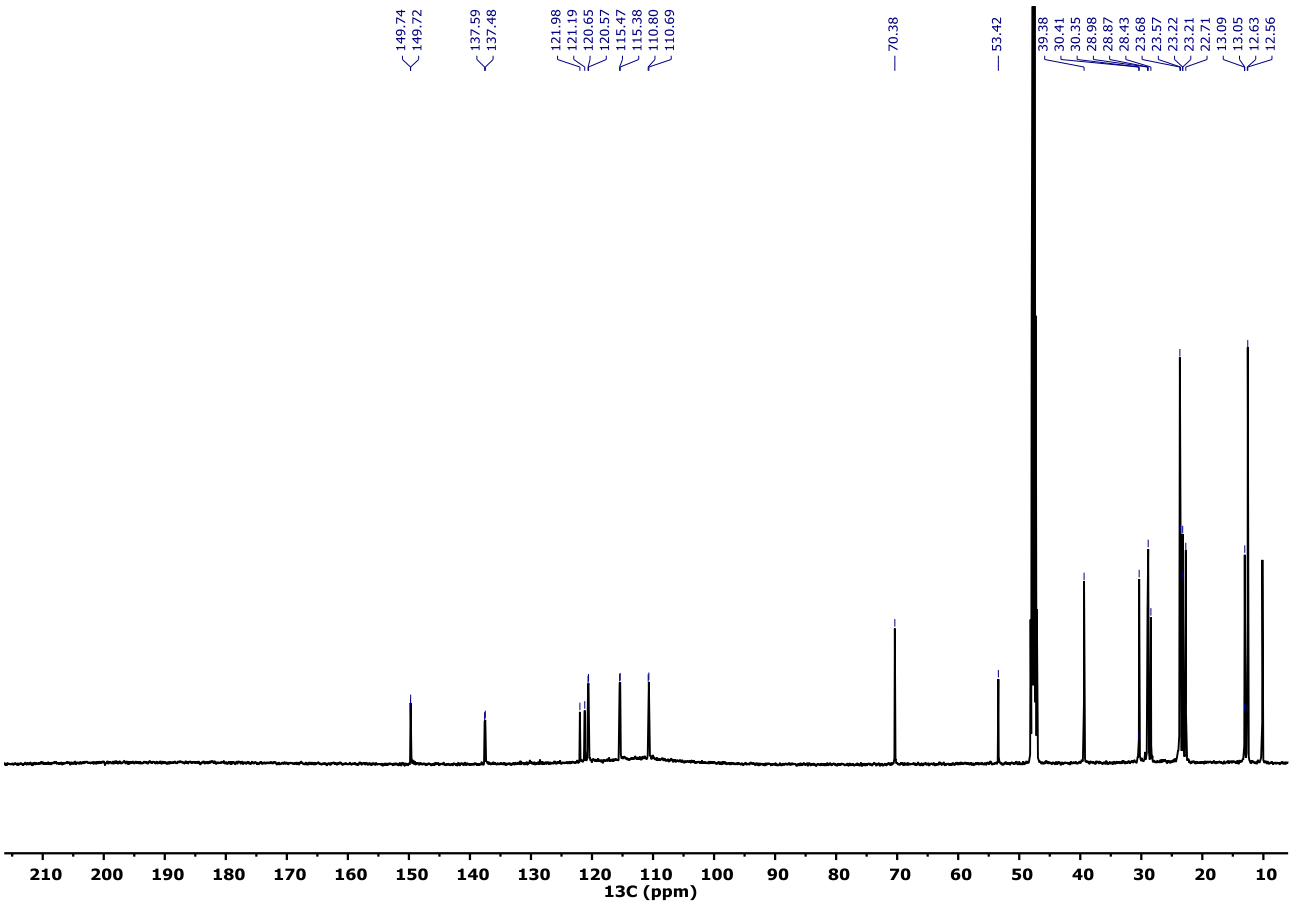


Figure S2.39. ^{13}C-NMR spectrum (126 MHz, methanol-d_4) of $\mathbf{A_{NH2}}$.

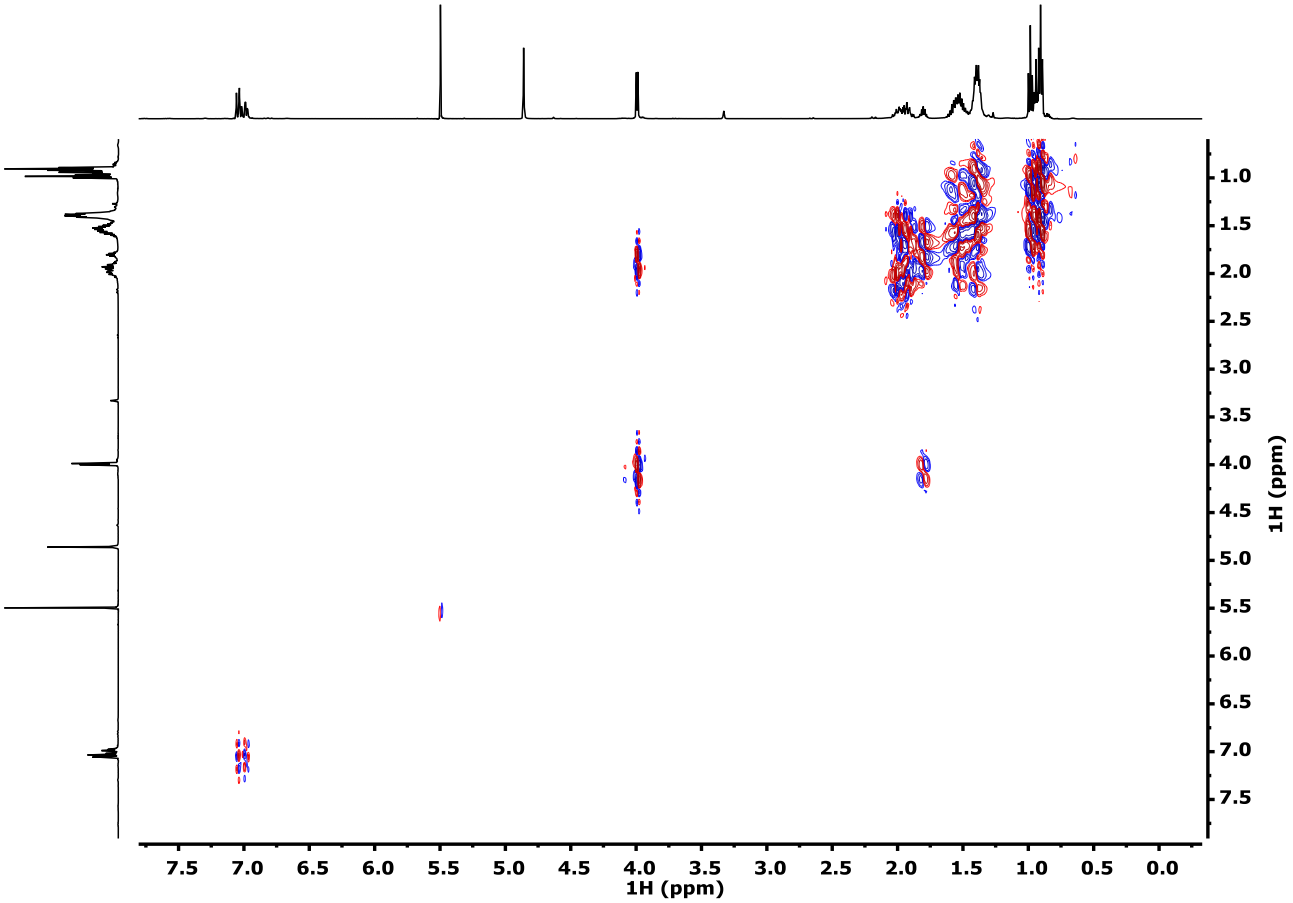


Figure S2.40. ^{1}H-^{1}H COSY spectrum (500 MHz, methanol-d_4) of $\mathbf{A_{NH2}}$.

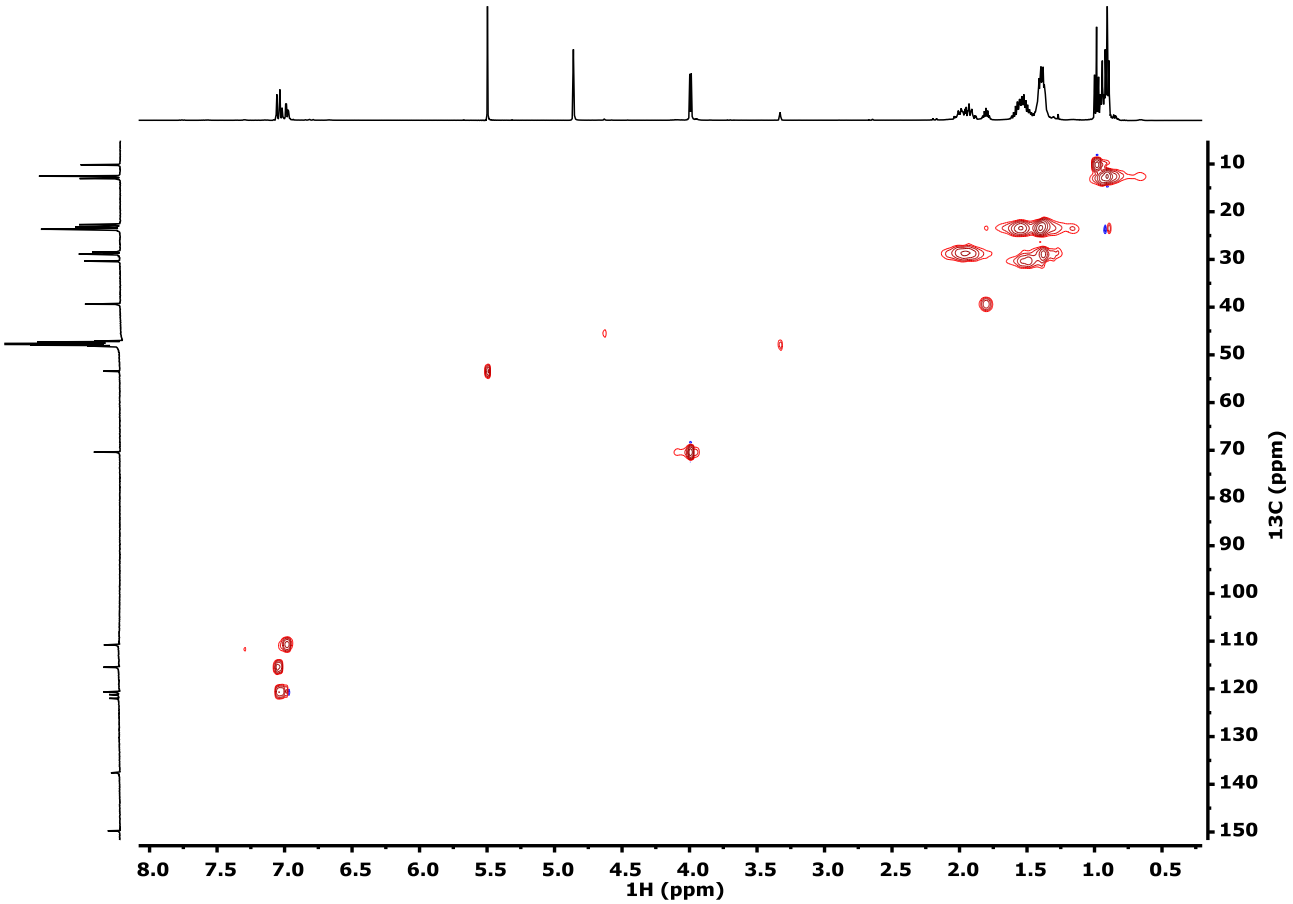


Figure S2.41. ^{1}H-^{13}C HSQC spectrum (500 MHz, methanol-d_4) of $\mathbf{A_{NH2}}$.

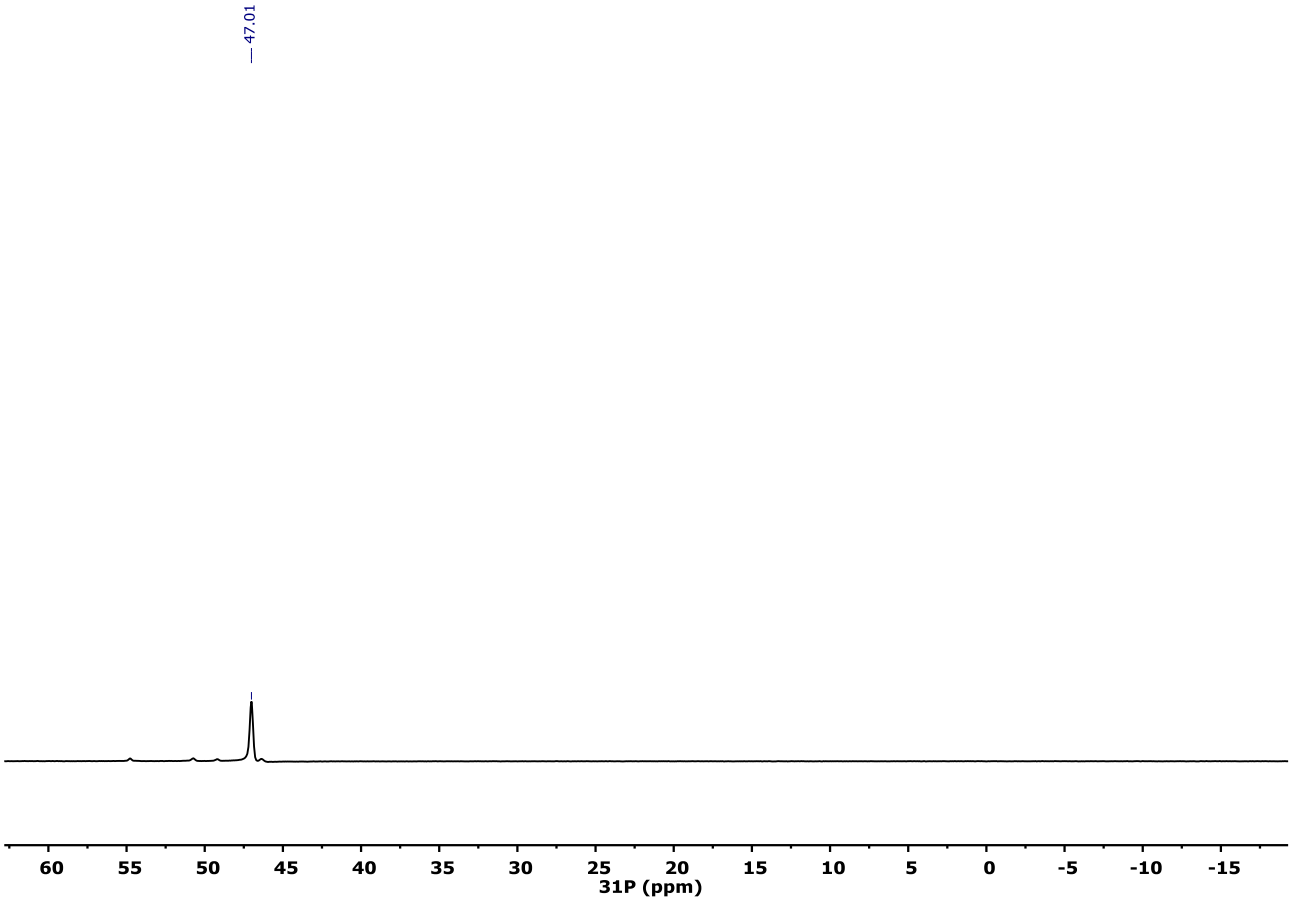
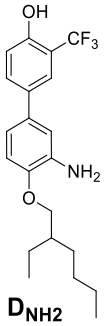


Figure S2.42. ^{31}P-NMR spectrum (202 MHz, methanol-d_4) of $\mathbf{A_{NH2}}$.

2.4.5 Synthesis of D_{NH2}



D_{NH2}

D_{NH2} was synthesized from **7** (200 mg, 0.66 mmol, 1 equiv) following the procedure described for compound **D_{CO}** (201 mg, 80% yield).

^{1}H-NMR (500 MHz, methanol-d_4) δ 7.64 (s, 1H), 7.67 (m, 1H), 7.00 (m, 2H), 6.89 (d, J = 1.31 Hz, 2H), 3.95 (d, J = 5.55 Hz, 2H), 1.79 (m, 1H), 1.69 – 1.45 (m, 4H), 1.38 (m, 4H), 0.97 (m, 6H).

^{13}C-NMR (126 MHz, methanol-d_4) δ 154.49, 146.73, 136.62, 132.59, 132.44, 130.85, 124.08 (q, J = 5.11 Hz), 124.00 (q, J = 272.13 Hz), 116.65, 116.50 (q, J = 30.59 Hz), 116.42, 113.33, 111.42, 70.44, 39.52, 30.41, 28.90, 23.70, 22.71, 13.02, 10.14.

^{19}F-NMR (376 MHz, chloroform-*d*) δ -60.71

HRMS(ES+): Calculated for $C_{21}H_{27}F_3NO_2$ 382.1994 a.m.u.; found 382.1978

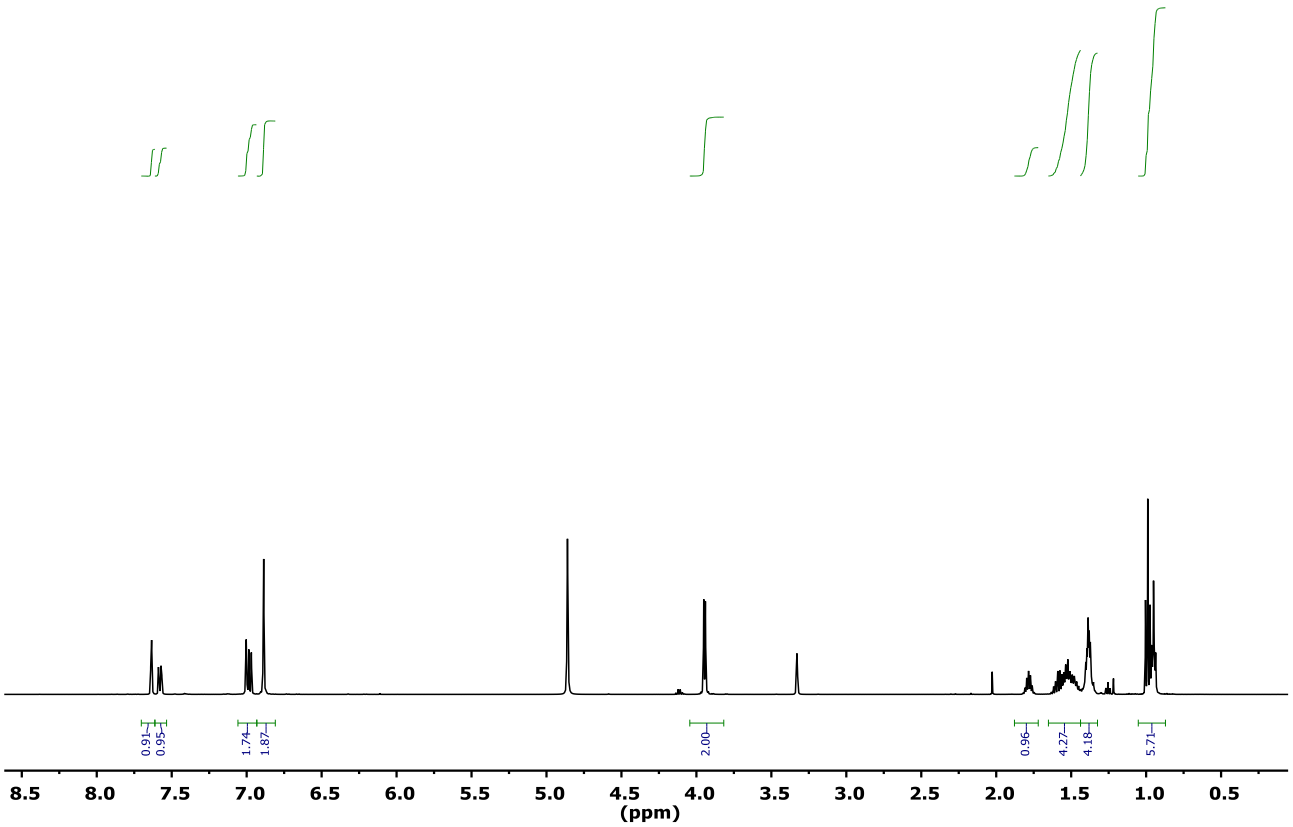


Figure S2.43. ^{1}H-NMR spectrum (500 MHz, methanol-d_4) of **D_{NH2}**.

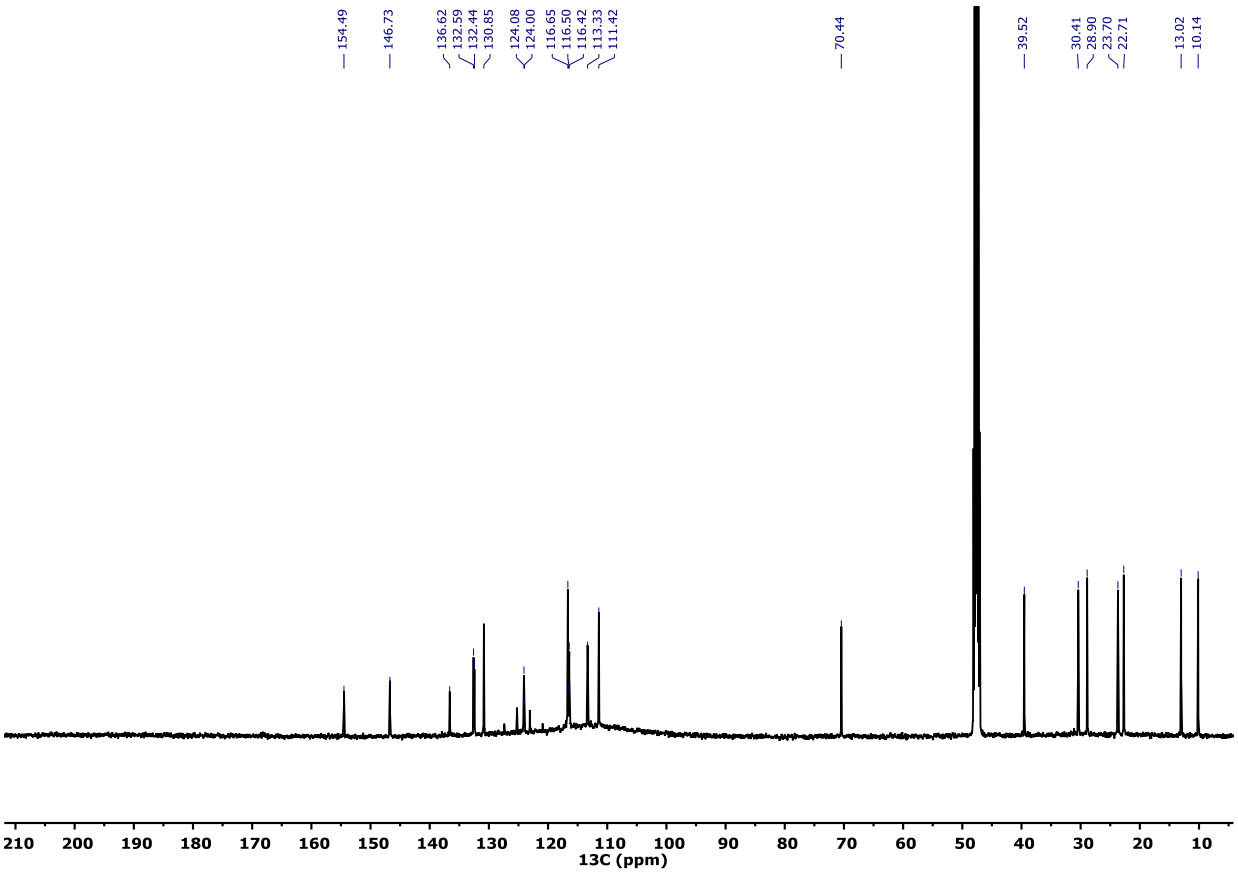


Figure S2.44. ^{13}C-NMR spectrum (126 MHz, methanol-d_4) of $\mathbf{D_{NH2}}$.

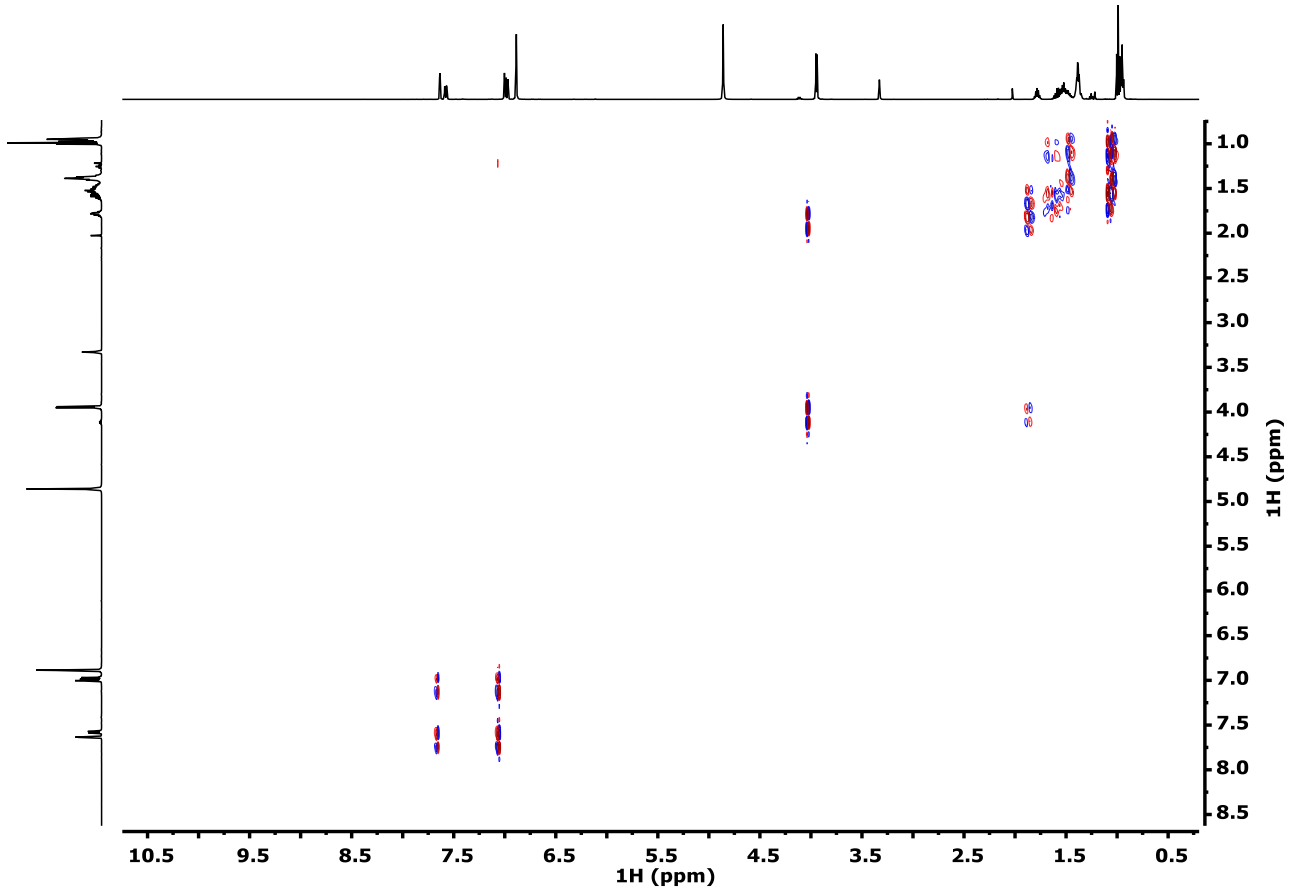


Figure S2.45. ^{1}H-^{1}H COSY spectrum (500 MHz, methanol-d_4) of $\mathbf{D_{NH2}}$.

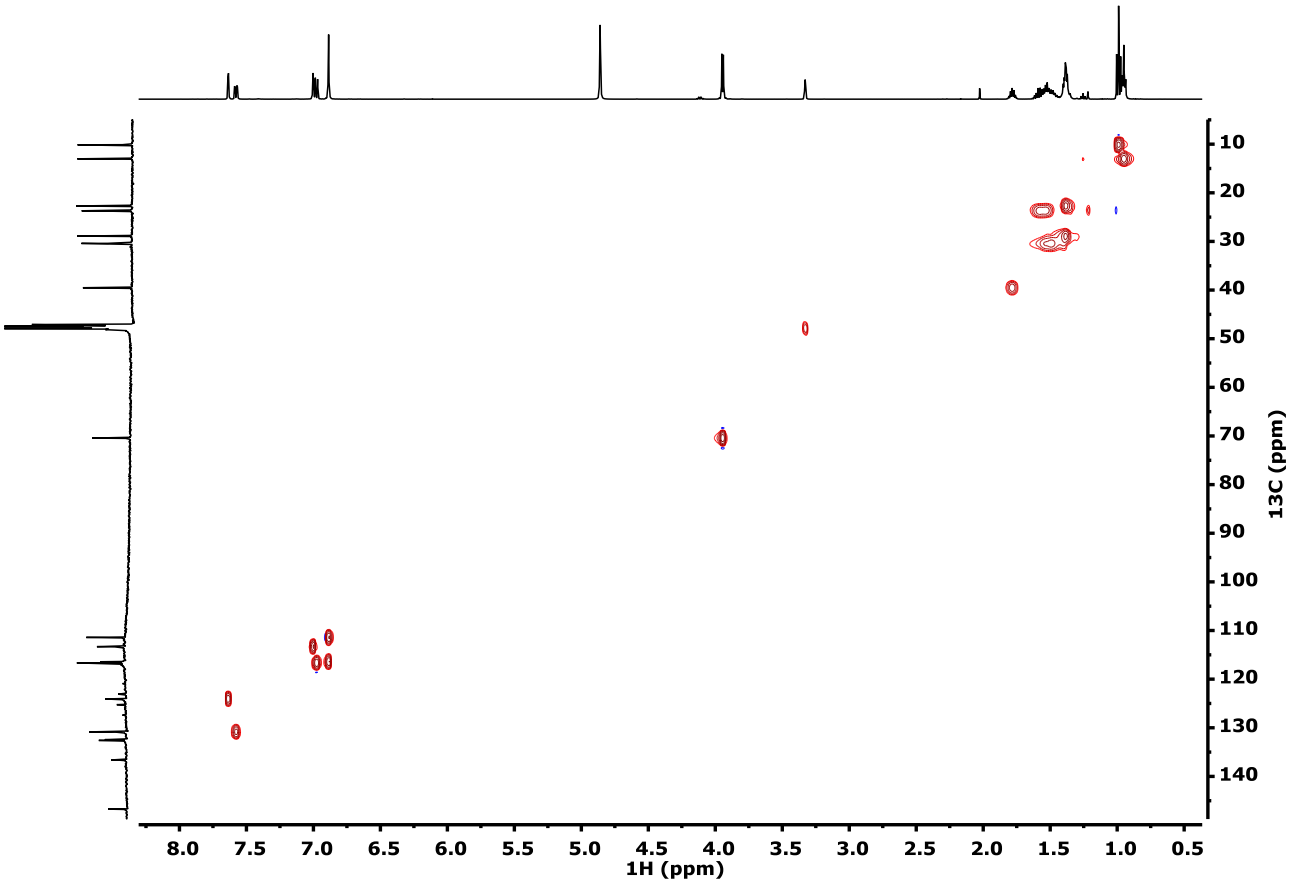


Figure S2.46. ^{1}H-^{13}C HSQC spectrum (500 MHz, methanol-d_4) of $\mathbf{D_{NH2}}$.

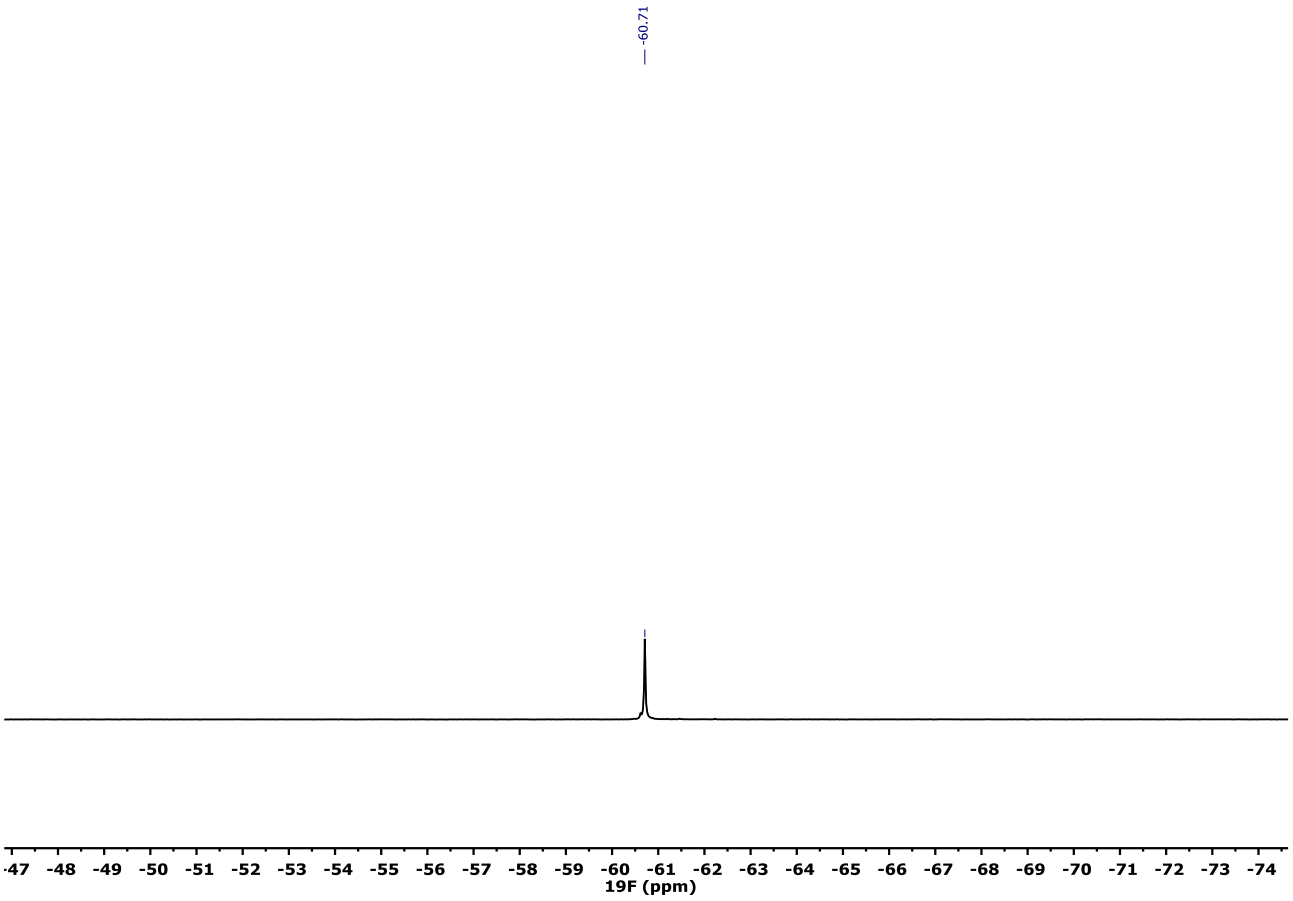
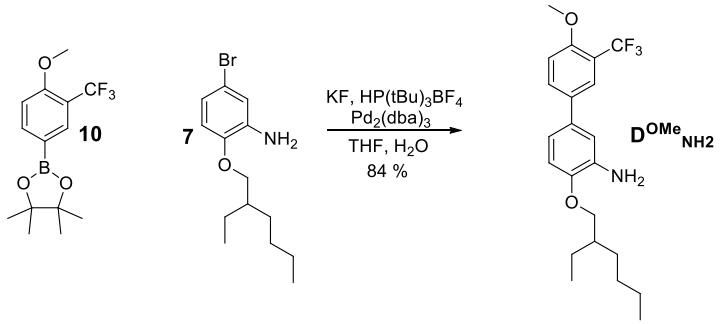


Figure S2.47. ^{19}F spectrum (376 MHz, chloroform-*d*) of $\mathbf{D_{NH2}}$.

2.4.6 Synthesis of D^{OMe}_{NH2}



In a sealed tube compound **7** (200 mg, 0.667 mmol, 1.2 equiv), compound **10** (168 mg, 0.556 mmol, 1 equiv), KF (129 mg, 2.238 mmol, 4 equiv) and $HP(tBu)_3BF_4$ (4.8 mg, 0.017 mmol, 0.03 equiv) were suspended in freshly degassed (N_2 bubbling, 15 min) THF (3 mL) and H_2O (1 mL). Then $Pd_2(dba)_3$ (8.0 mg, 0.0087 mmol, 0.016 equiv) was added and the reaction was stirred under N_2 atmosphere at 80°C for 3 h. Then it was extracted in brine/EtOAc (3x), the organic phases were collected, dried with $MgSO_4$, concentrated under vacuum and purified by flash column chromatography with PE:EtOAc (from 9:1 to 8:2). giving the pure desired monomer $\mathbf{D^{OMe}_{NH2}}$ (185 mg, 84% yield).

^{1}H-NMR (600 MHz, chloroform-*d*) δ 7.75 (d, J = 2.37 Hz, 1H), 7.66 (dd, J = 8.57, 2.40 Hz, 1H), 7.05 (d, J = 8.63 Hz, 1H), 6.96 (d, J = 2.24 Hz, 1H), 6.92 (dd, J = 8.25, 2.22 Hz, 1H), 6.87 (d, J = 8.31 Hz, 1H), 3.95 (s, 5H), 1.81 (m, 1H), 1.71 – 1.17 (m, 7H), 0.98 (t, J = 7.42 Hz, 3H), 0.94 (m, 3H).

^{13}C-NMR (151 MHz, chloroform-*d*) δ 156.31, 146.70, 136.38, 133.58, 132.44, 131.18, 125.37 (q, J = 4.6 Hz), 123.77 (q, J = 273.5 Hz), 118.82 (q, J = 30.7 Hz), 116.99, 113.45, 112.31, 111.55, 70.79, 56.08, 39.50, 30.70, 29.15, 24.07, 23.08, 14.10, 11.20.

^{19}F-NMR (376 MHz, chloroform-*d*) δ -61.31

HRMS(ES+): Calculated for $C_{22}H_{29}F_3NO_2$ 396.2150 a.m.u.; found 396.2198

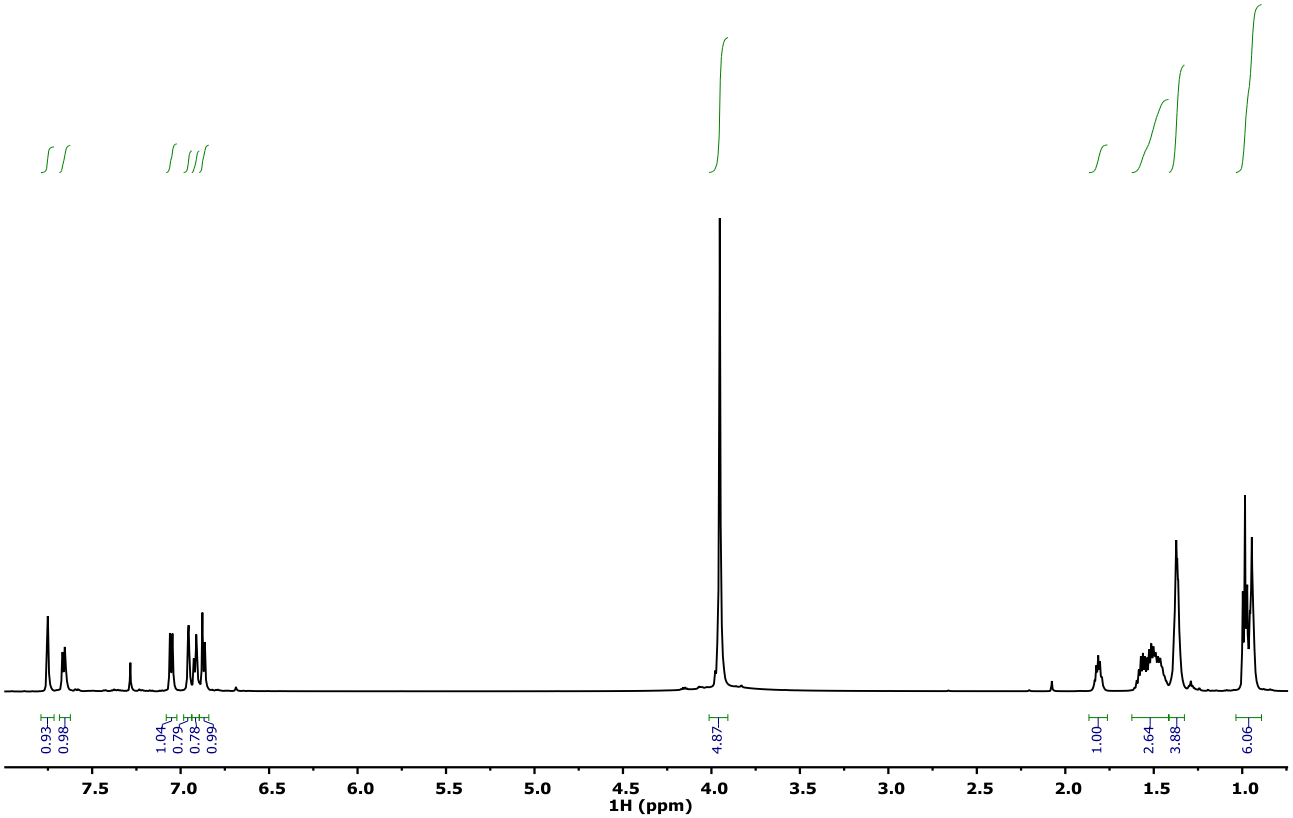


Figure S2.48. ^{1}H-NMR spectrum (600 MHz, chloroform-*d*) of **D$^{OMe}_{NH2}$**

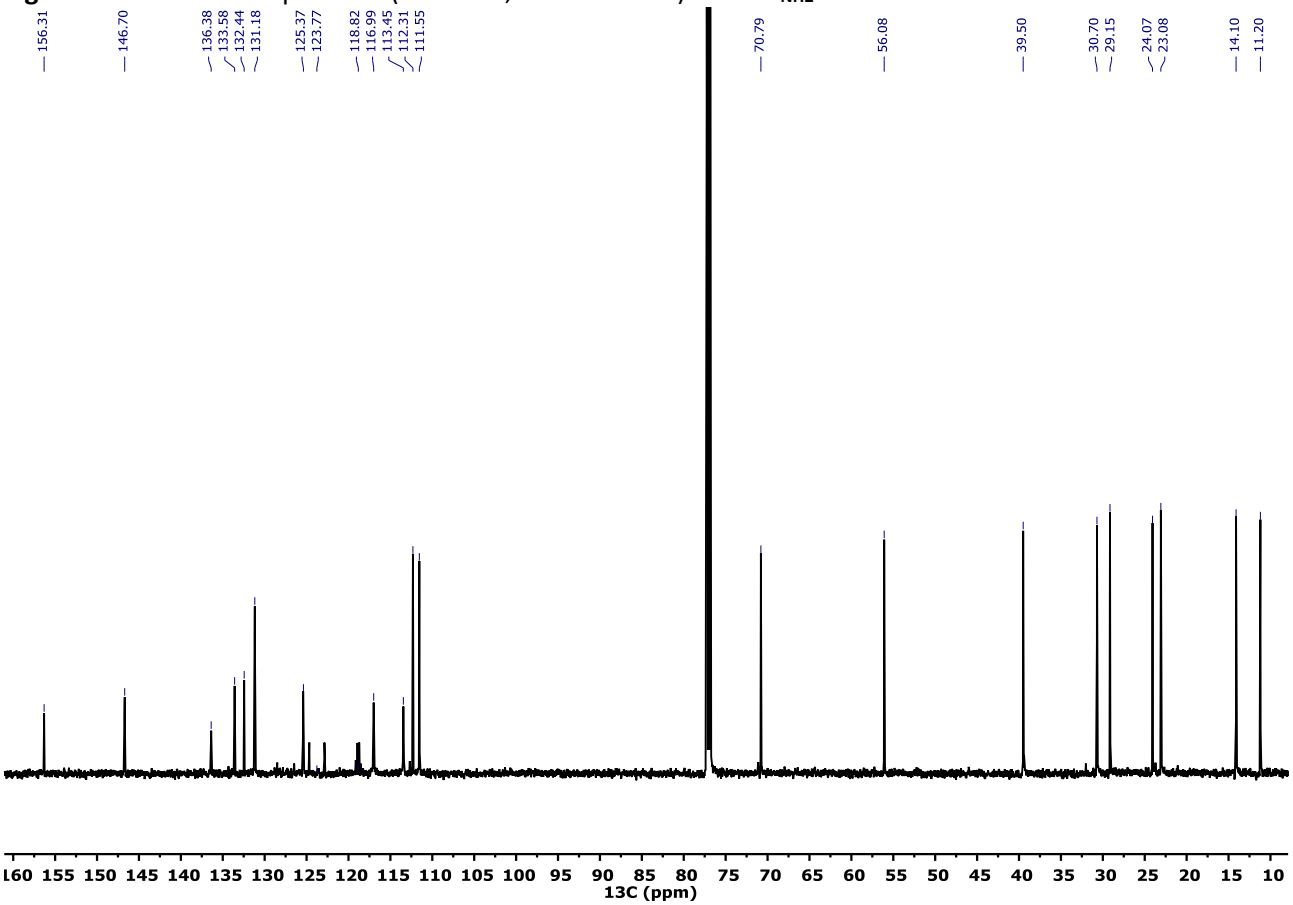


Figure S2.49. ^{13}C-NMR spectrum (151 MHz, chloroform-*d*) of **D$^{OMe}_{NH2}$**

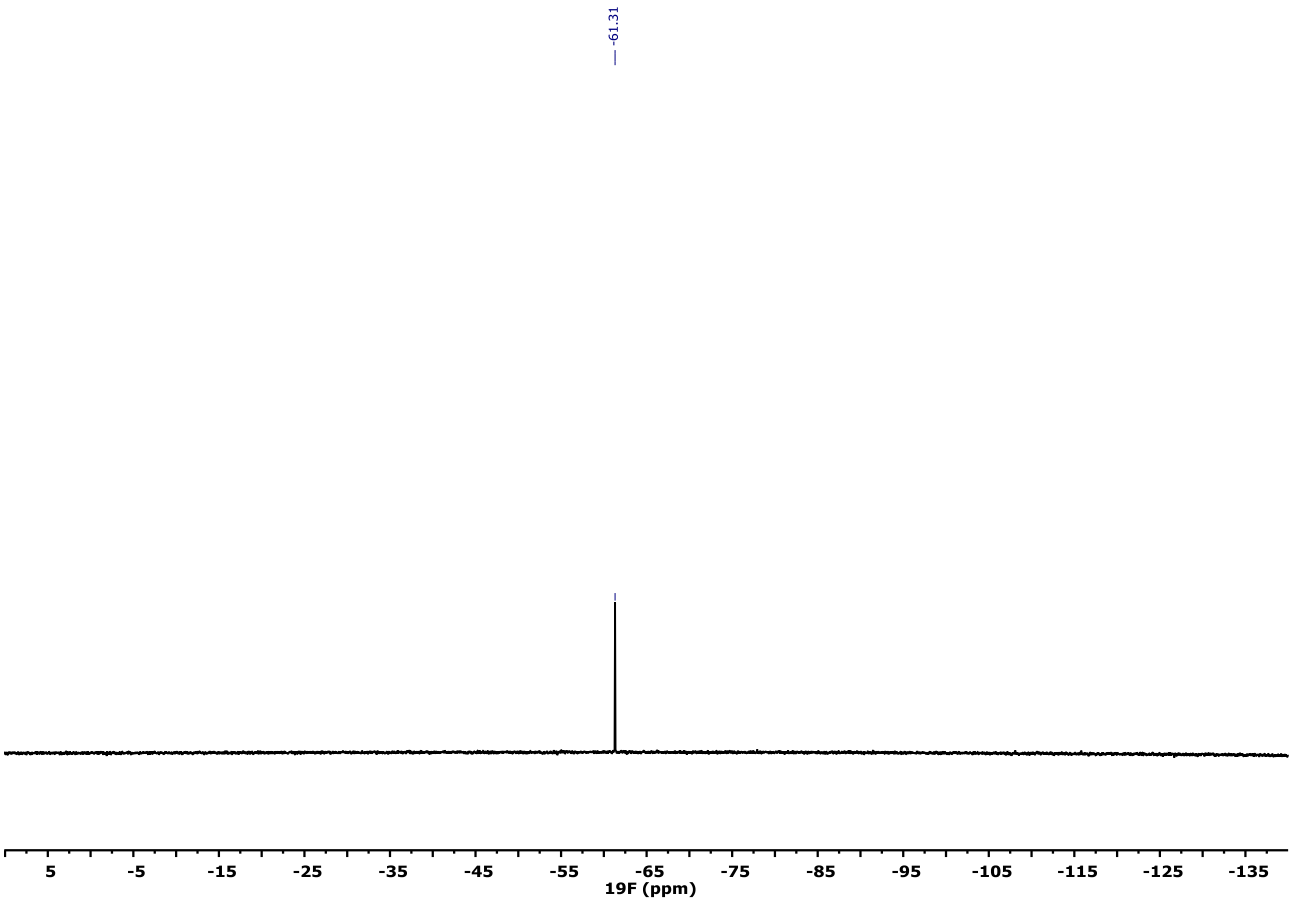
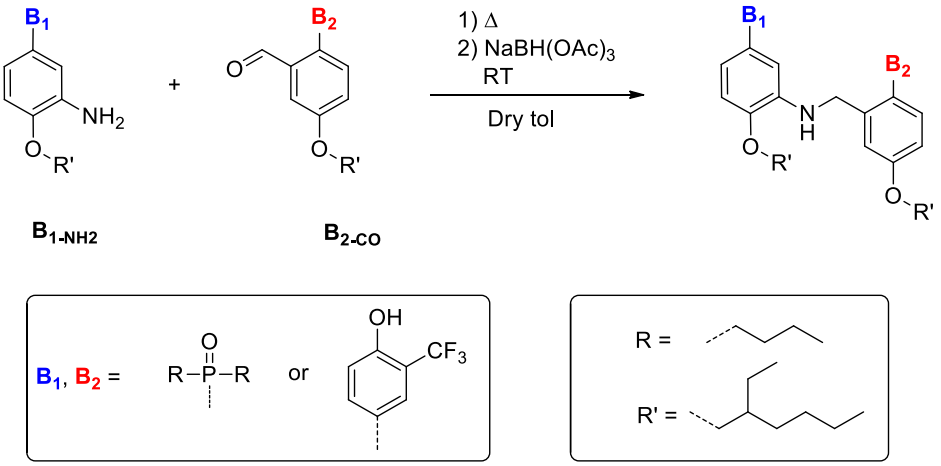


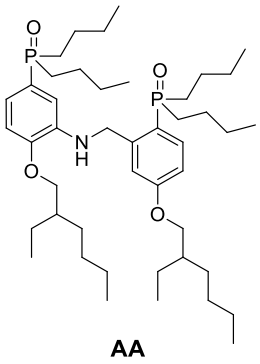
Figure S2.50. ^{19}F-NMR spectrum (376 MHz, chloroform-*d*) of $\mathbf{D^{OMe}_{NH2}}$

3. Synthesis and characterisation of the dimers



Scheme S3.1 general synthesis pathway used for the dimers.

3.1 Synthesis of AA



AA

Dimer **AA** was synthesized via one step reductive amination. Monomers $\mathbf{A_{CO}}$ (36 mg, 0.091 mmol, 1 equiv) and $\mathbf{A_{NH2}}$ (104.5 mg, 0.273 mmol, 3 equiv) were dissolved in dry toluene (2 mL) in a 5 mL flask and the mixture was stirred at 110°C using a dean stark apparatus overnight. Then, $NaBH_4$ (34.5 mg, 0.913 mmol, 10 equiv) was added and the mixture was stirred again for 2 h until complete reduction of the imine (confirmed by ^{1}H-NMR). Then, a saturated solution of NaCl was added and the mixture was stirred until complete solubilisation. Hence, the organic phase was extracted, and the aqueous phase was washed (3x) with EtOAc. The organic layers were collected and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified via flash chromatography (gradient EtOAc to EtOAc: MeOH 9:1), giving the desired dimer (31.9 mg, 46 % yield).

^{1}H NMR (400 MHz, methanol-d_4) δ 7.54 (dd, *J* = 12.10, 8.56 Hz, 1H), 7.20 (t, *J* = 2.69 Hz, 1H), 7.11 – 6.87 (m, 3H), 6.75 (dd, *J* = 11.86, 1.59 Hz, 1H), 4.76 (s, 2H), 4.02 (d, *J* = 5.50 Hz, 2H), 3.91 (d, *J* = 5.62 Hz, 2H), 2.21 – 1.98 (m, 4H), 1.99 – 1.12 (m, 36H), 1.12 – 0.59 (m, 24H).

^{13}C NMR (101 MHz, methanol-d_4) δ 162.07 (d, *J* = 2.66 Hz), 149.35 (d, *J* = 3.40 Hz), 146.65 (d, *J* = 7.92 Hz), 137.80 (d, *J* = 14.71 Hz), 133.77 (d, *J* = 11.95 Hz), 121.73, 120.73, 119.78, 116.02 (d, *J* = 2.66 Hz), 112.66 (d, *J* = 12.45 Hz), 110.08 (d, *J* = 17.01 Hz), 109.94 (d, *J* = 16.99 Hz), 109.78, 70.41, 70.20, 45.73, 39.36, 30.36, 30.25, 29.89, 29.20, 29.06, 28.88, 28.83, 28.38, 23.75, 23.61, 23.60, 23.17, 22.71, 12.59.

^{31}P NMR (202 MHz, methanol-d_4) δ 53.62, 50.94.

HRMS(ES+): Calculated for $C_{45}H_{80}NO_4P_2$ 760.5563 a.m.u.; found 760.5596

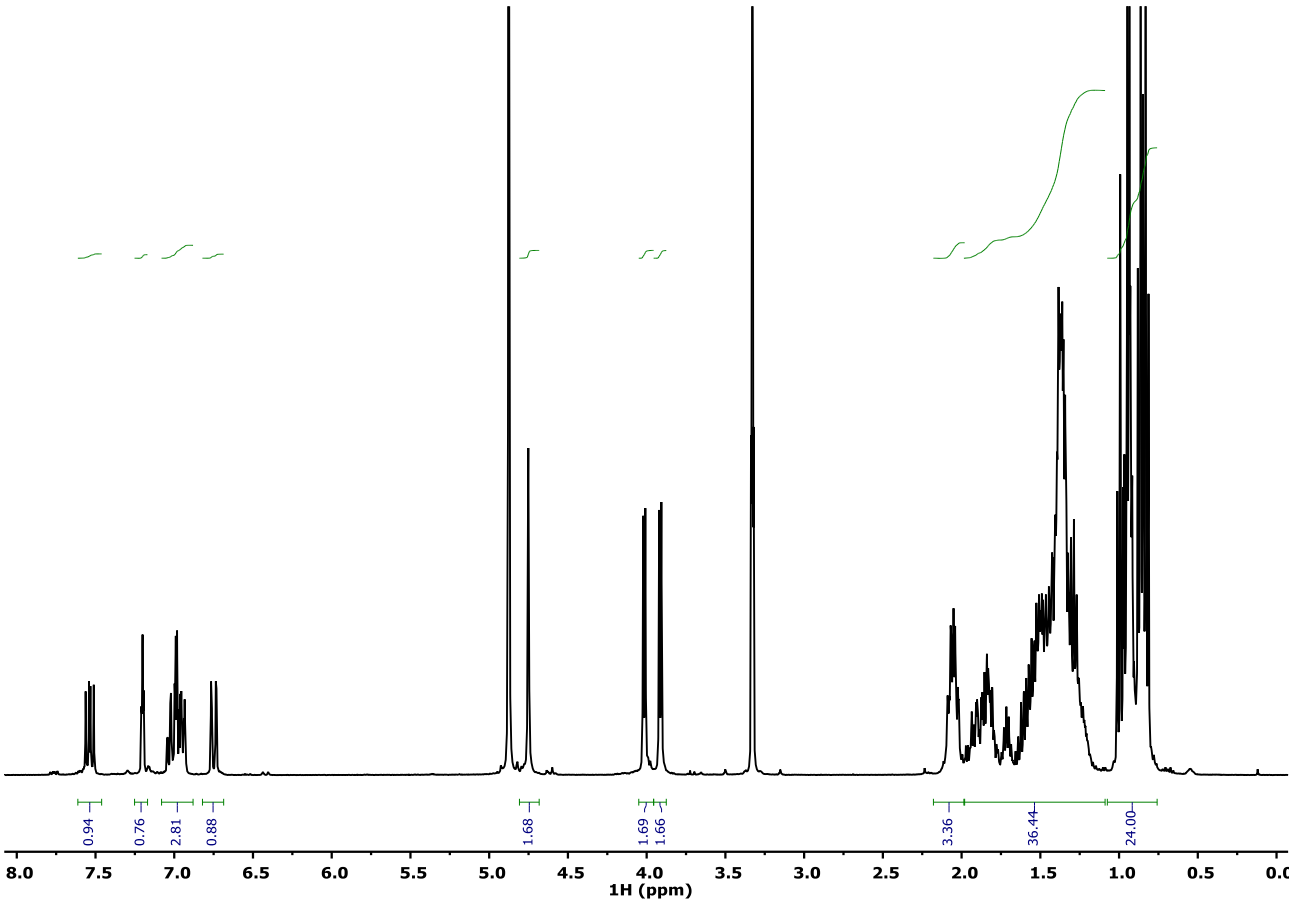


Figure S3.1. ^{1}H-NMR spectrum (500 MHz, methanol-d_4) of **AA**.

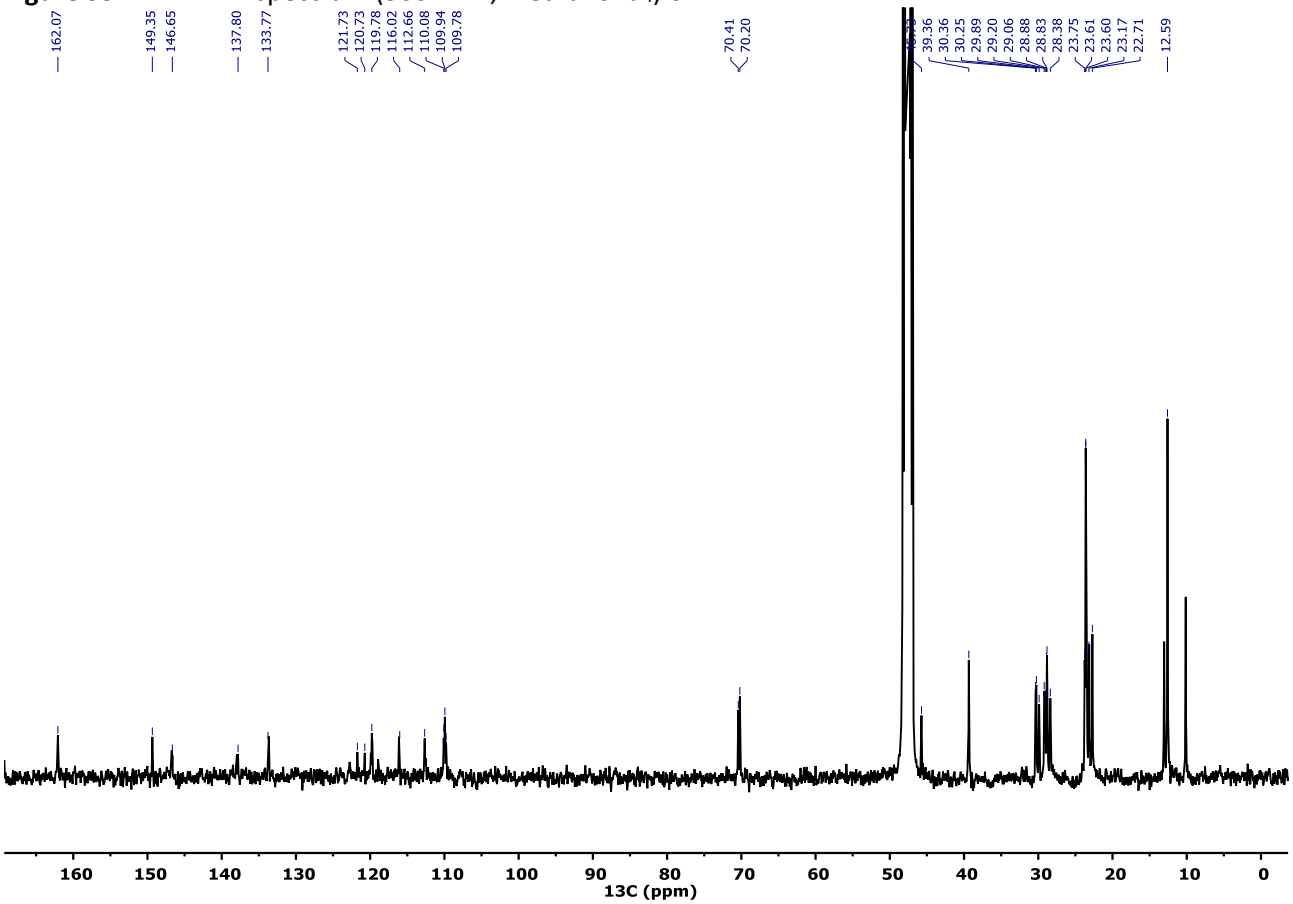


Figure S3.2. ^{13}C-NMR spectrum (126 MHz, methanol-d_4) of **AA**.

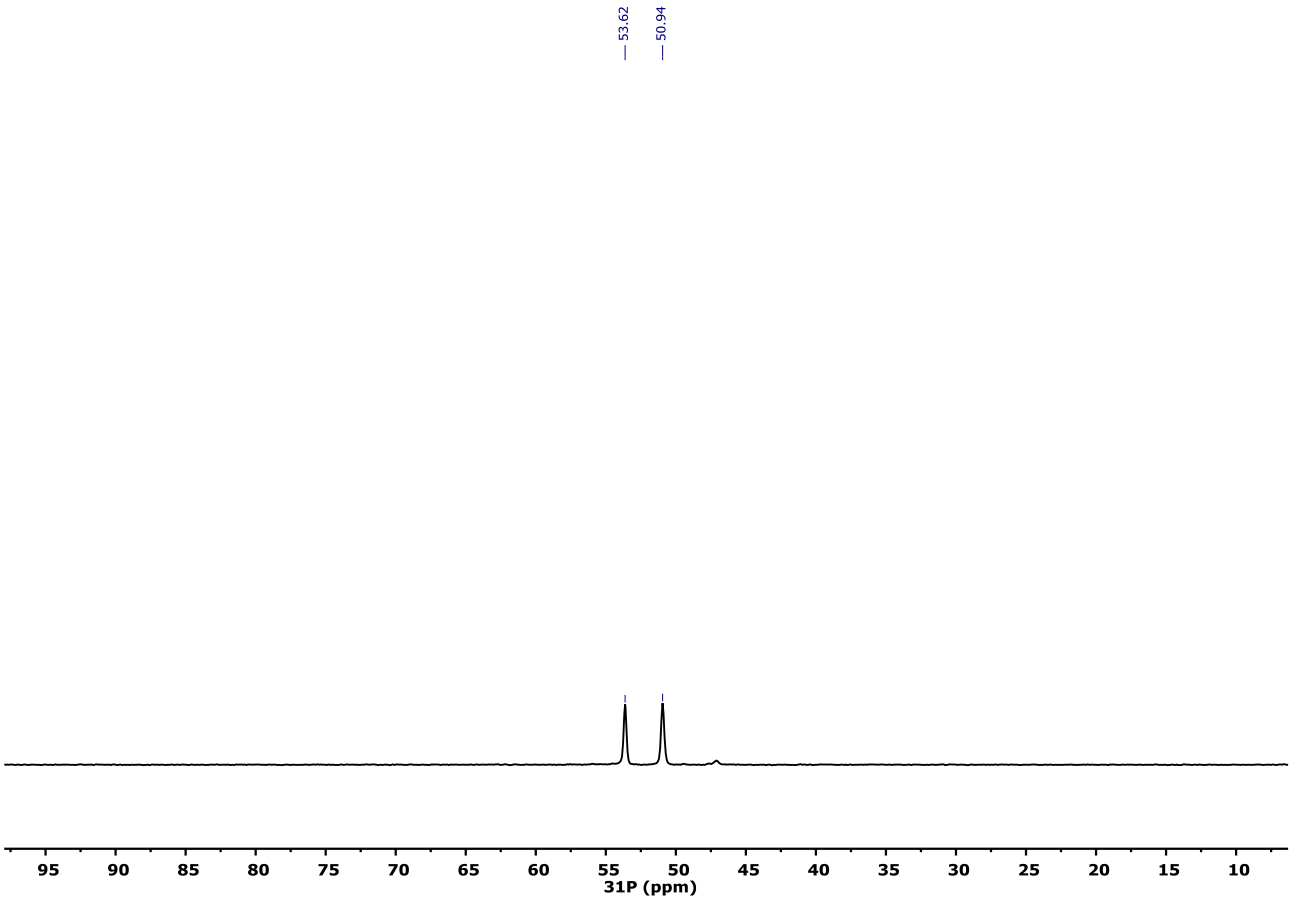


Figure S3.3. ^{31}P-NMR spectrum (202 MHz, methanol-d_4) of **AA**.

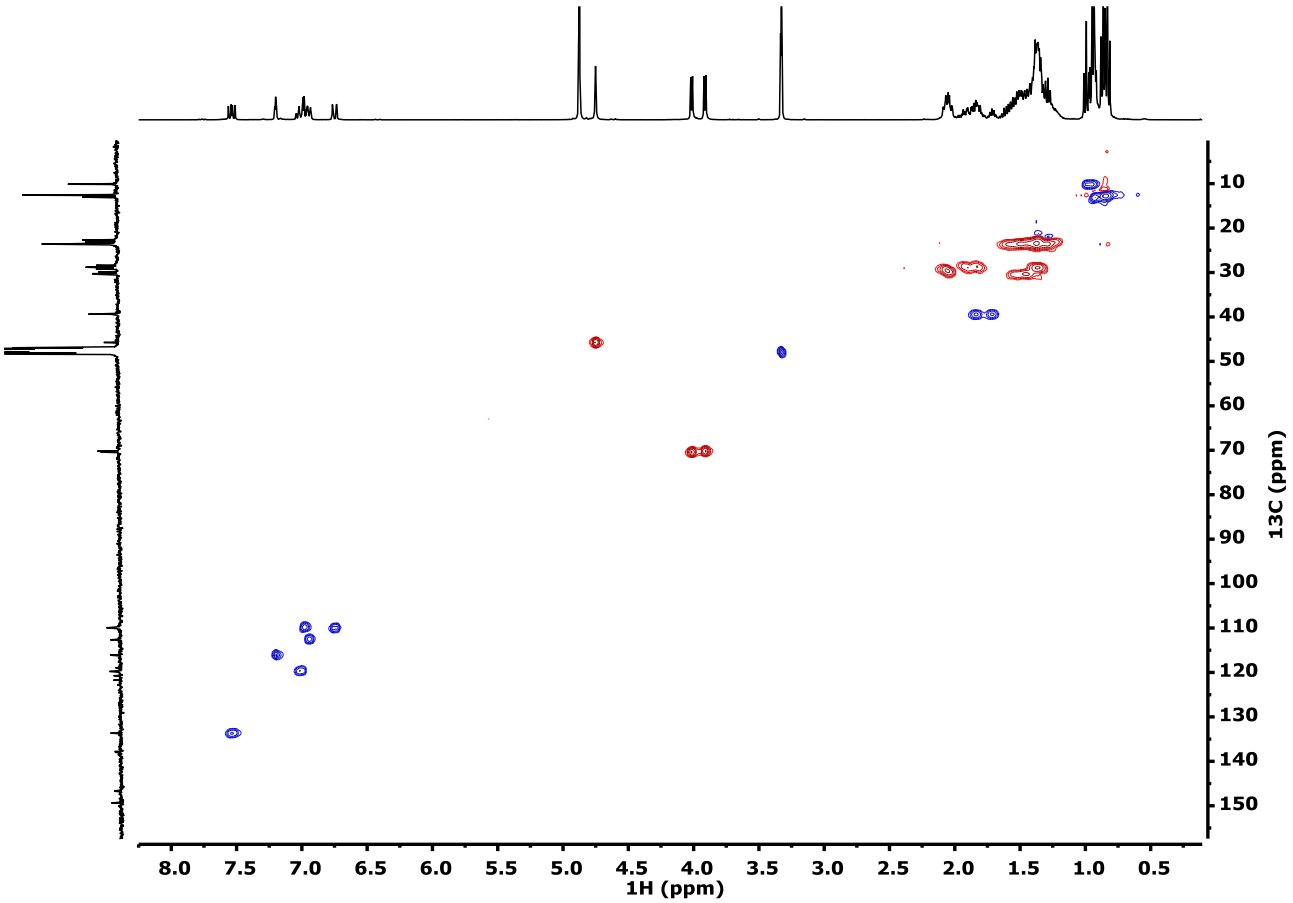


Figure S3.4. ^{1}H-^{13}C HSQC spectrum (500 MHz, methanol-d_4) of **AA**.

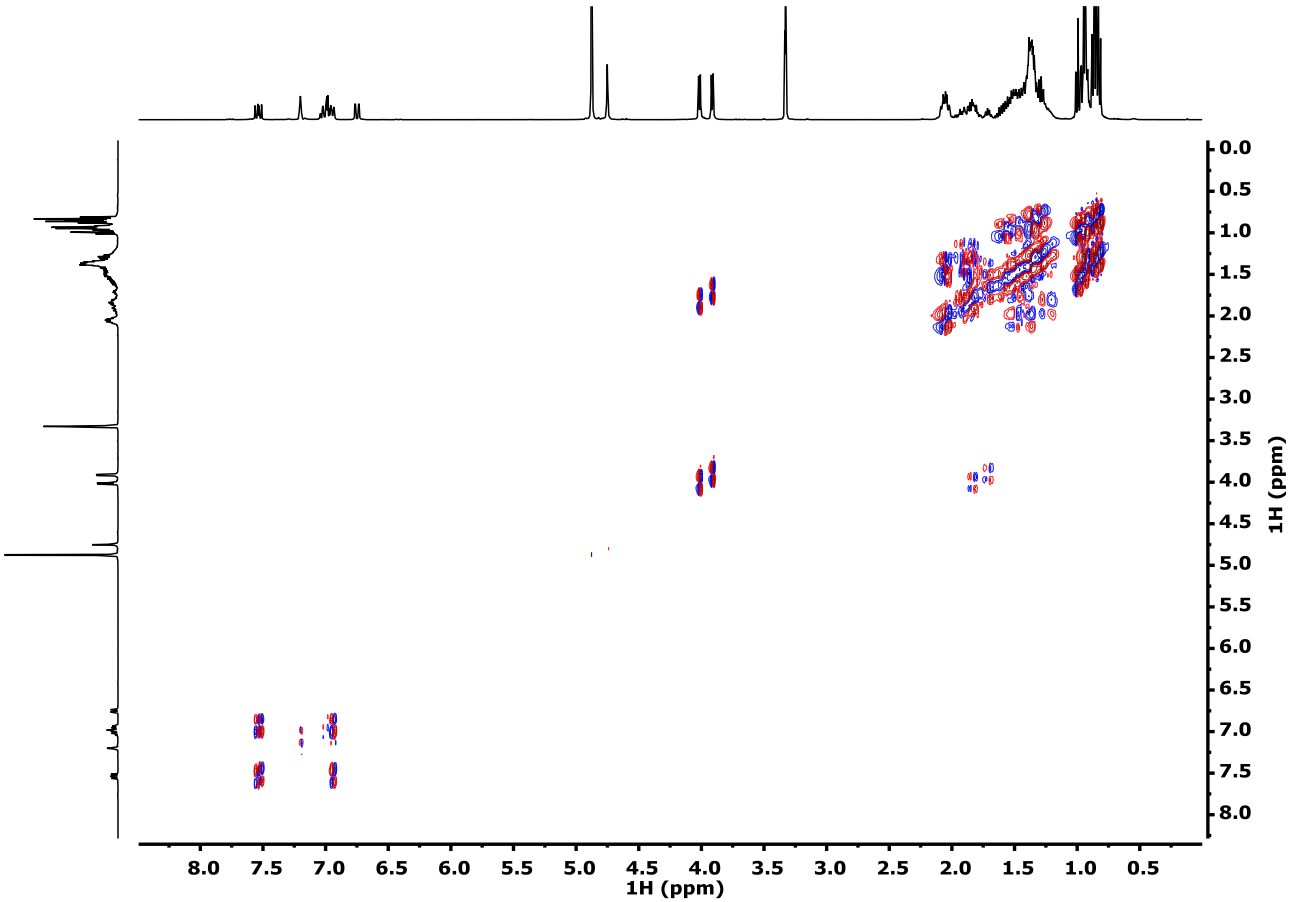
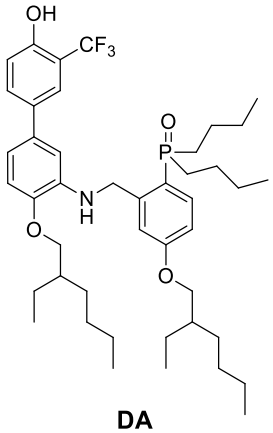


Figure S3.5. ^{1}H-^{1}H COSY spectrum (500 MHz, methanol-d_4) of **AA**.

3.2 Synthesis of DA



DA

Dimer **DA** was synthesized via one step reductive amination. Monomers $\mathbf{A_{CO}}$ (25 mg, 0.063 mmol, 1 equiv) and $\mathbf{D_{NH2}}$ (48.3 mg, 0.127 mmol, 2 equiv) were dissolved in dry toluene (2 mL) in a 5 mL flask and the mixture was stirred at 110°C using a dean stark apparatus overnight. Then, $NaBH(OAc)_3$ (67 mg, 0.067 mmol, 5 equiv) was added and the mixture was stirred again for 2 h until complete reduction of the imine (confirmed by ^{1}H-NMR). Then, a saturated solution of NaCl was added and the mixture was stirred until complete solubilisation. Hence, the organic phase was extracted, and the aqueous phase was washed (3x) with EtOAc. The organic layers were collected and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified via flash chromatography (gradient EP: EtOAc 5:5 to 3:7), giving the desired dimer (33.3 mg, 69 % yield).

^{1}H NMR (600 MHz, methanol-d_4) δ 7.56 (dd, *J* = 12.12, 8.55 Hz, 1H), 7.49 (d, *J* = 2.39 Hz, 1H), 7.48 (d, *J* = 1.98 Hz, 1H), 7.1953 (t, *J* = 2.83 Hz, 1H), 6.94 (ddd, *J* = 9.30, 4.84, 2.55 Hz, 2H), 6.87 (d, *J* = 8.26 Hz, 1H), 6.78 (dd, *J* = 8.19, 2.18 Hz, 1H), 6.71 (d, *J* = 2.18 Hz, 1H), 4.75 (s, 2H), 3.96 (d, *J* = 5.66 Hz, 2H), 3.87 (d, *J* = 5.73 Hz, 2H), 2.13 – 2.00 (m, 4H), 1.80 (h, *J* = 6.08 Hz, 1H), 1.69 – 1.20 (m, 30H), 0.98 (t, *J* = 7.48 Hz, 3H), 0.92 (t, *J* = 7.04 Hz, 3H), 0.89 – 0.79 (m, 12H).

^{13}C NMR (101 MHz, methanol-d_4) δ 162.25 (d, *J* = 2.71 Hz), 154.48, 146.55 (d, *J* = 8.19 Hz), 146.12, 137.89, 133.70 (d, *J* = 12.65 Hz), 132.77 (d, *J* = 18.44 Hz), 130.88, 124.16 (q, *J* = 5.40 Hz), 124.12 (q, J = 271.24 Hz), 119.33, 118.70, 116.61, 116.55 (q, J = 30.62 Hz), 115.40 (d, *J* = 10.71 Hz), 114.65, 112.83 (d, *J* = 12.73 Hz), 110.71, 108.84, 70.64, 70.16, 46.15 (d, *J* = 2.80 Hz), 39.46, 39.03, 30.44, 30.14, 29.69, 29.23, 28.92, 28.66, 23.72, 23.67, 23.63, 23.57, 23.49, 23.46, 22.75, 22.64, 13.10, 12.98, 12.49, 10.20, 10.01.

^{19}F NMR (565 MHz, methanol-d_4) δ -63.52.

^{31}P NMR (202 MHz, methanol-d_4) δ 49.41.

HRMS(ES+): Calculated for $C_{44}H_{66}F_3NO_4P$ 760.4682 a.m.u.; experimental 760.4682 found 760.4807

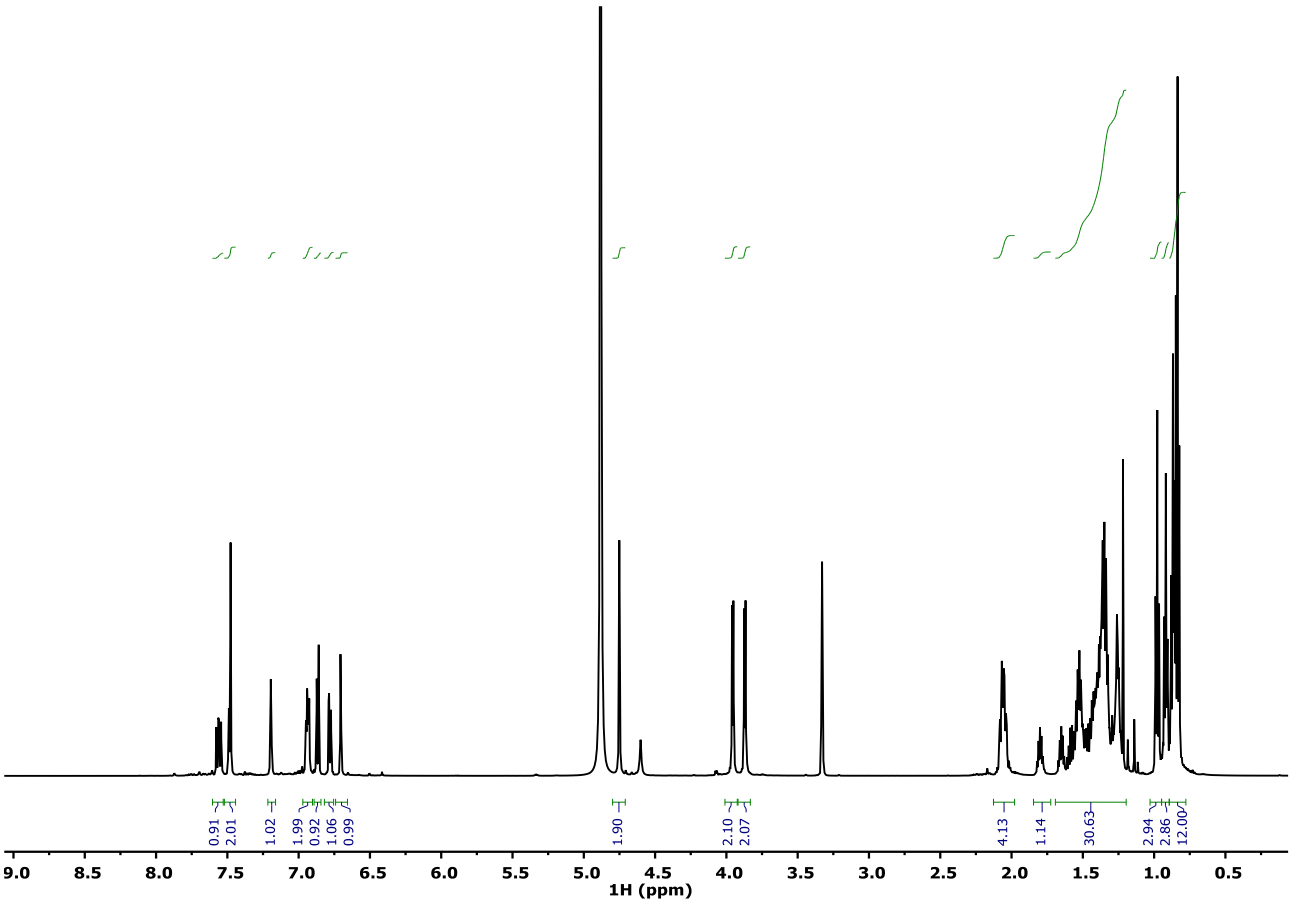


Figure S3.6. ^{1}H-NMR spectrum (600 MHz, methanol-d_4) of **DA**.

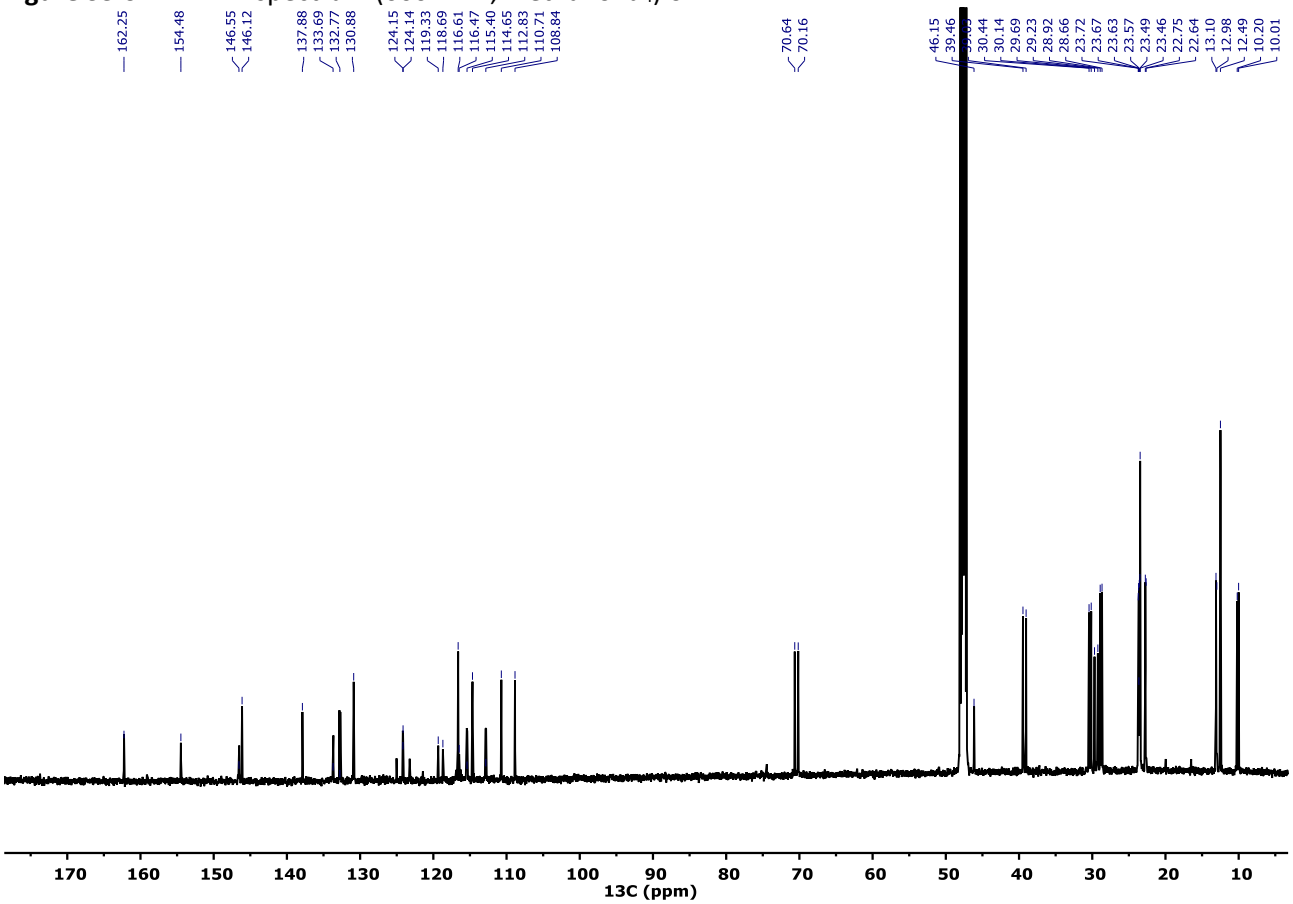


Figure S3.7. ^{13}C-NMR spectrum (151 MHz, methanol-d_4) of **DA**.

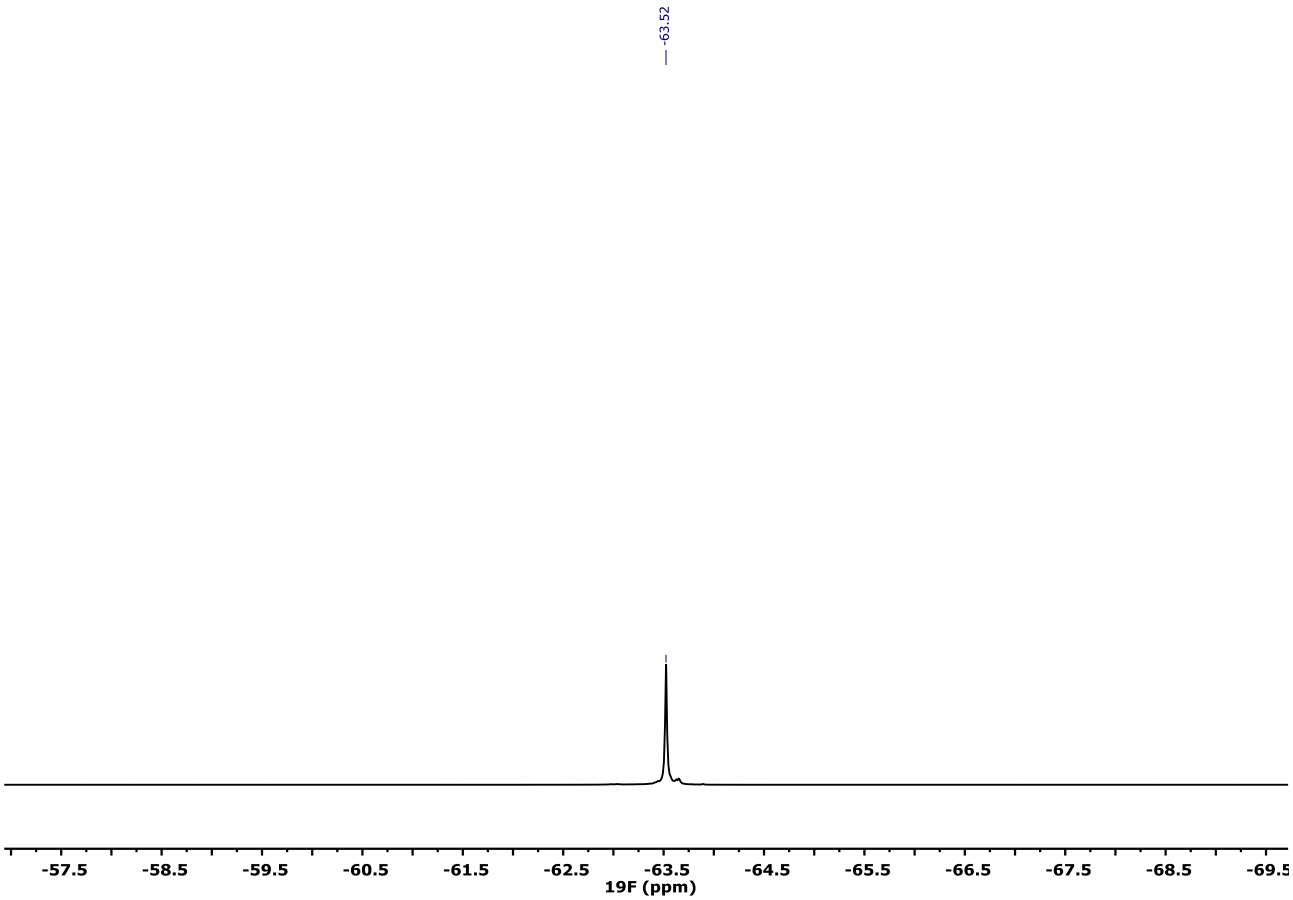


Figure S3.8. ^{19}F-NMR spectrum (565 MHz, methanol-d_4) of **DA**.

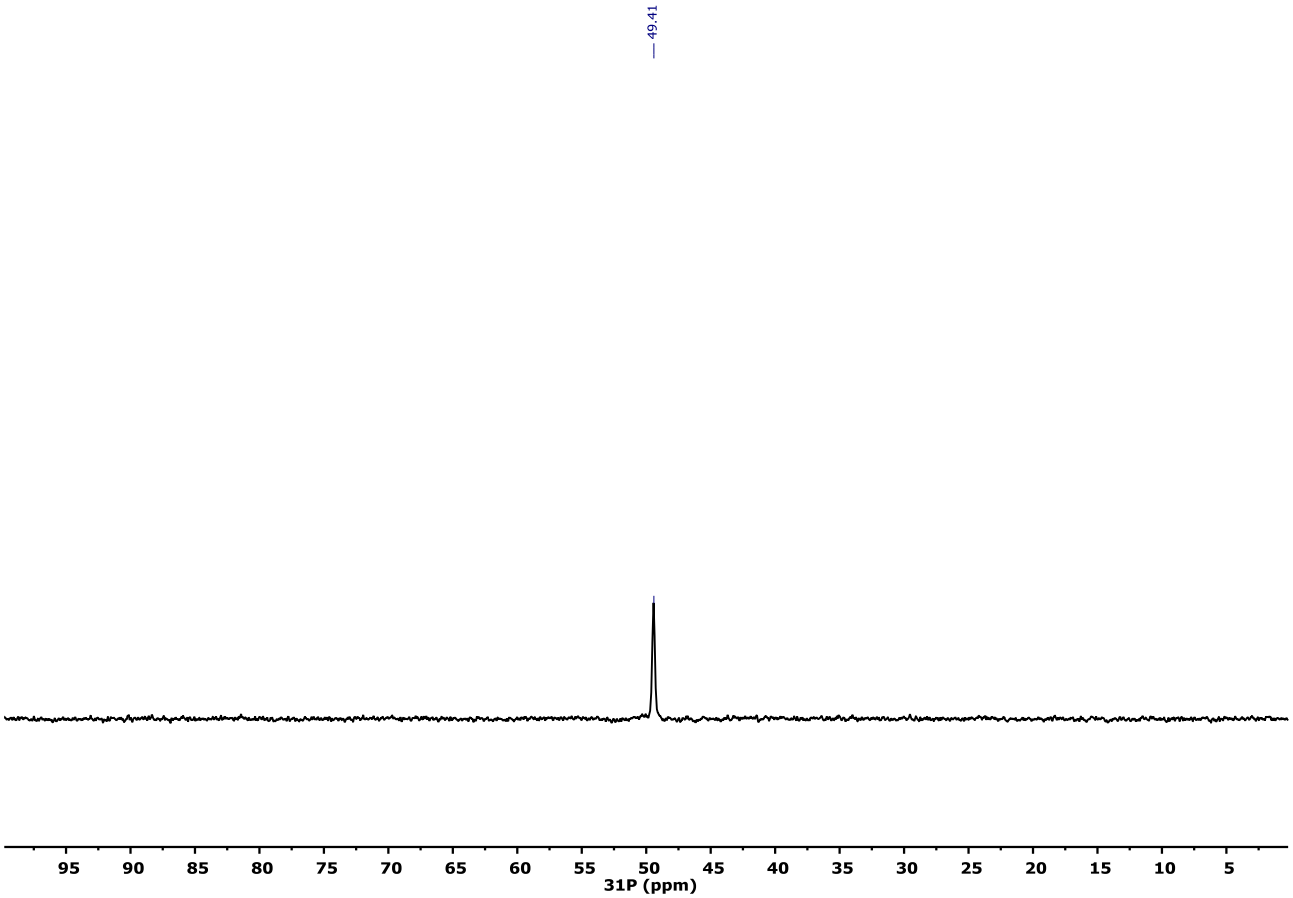


Figure S3.9. ^{31}P-NMR spectrum (202 MHz, methanol-d_4) of **DA**.

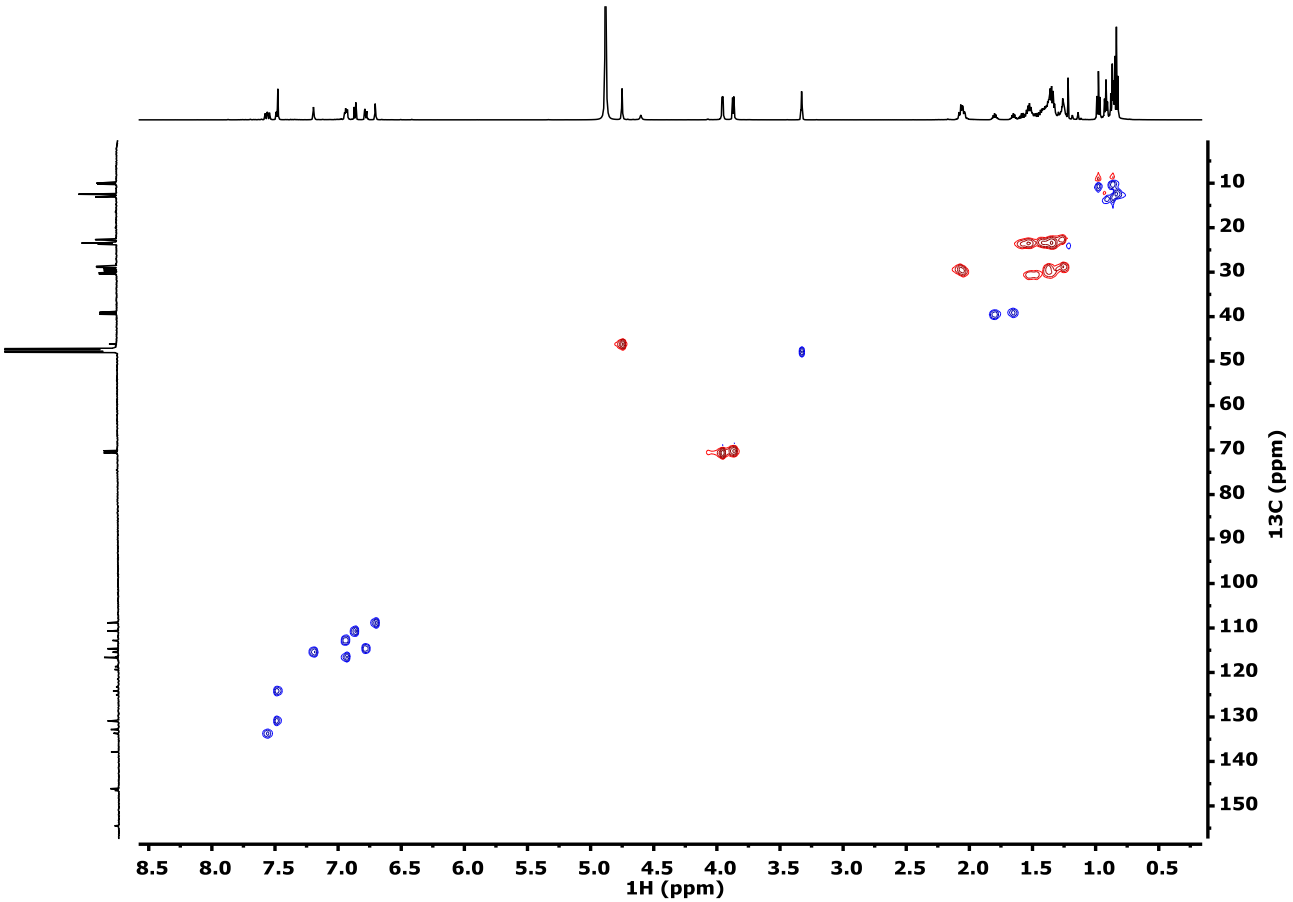


Figure S3.10. ^{1}H-^{13}C HSQC spectrum (600 MHz, methanol-d_4) of **DA**.

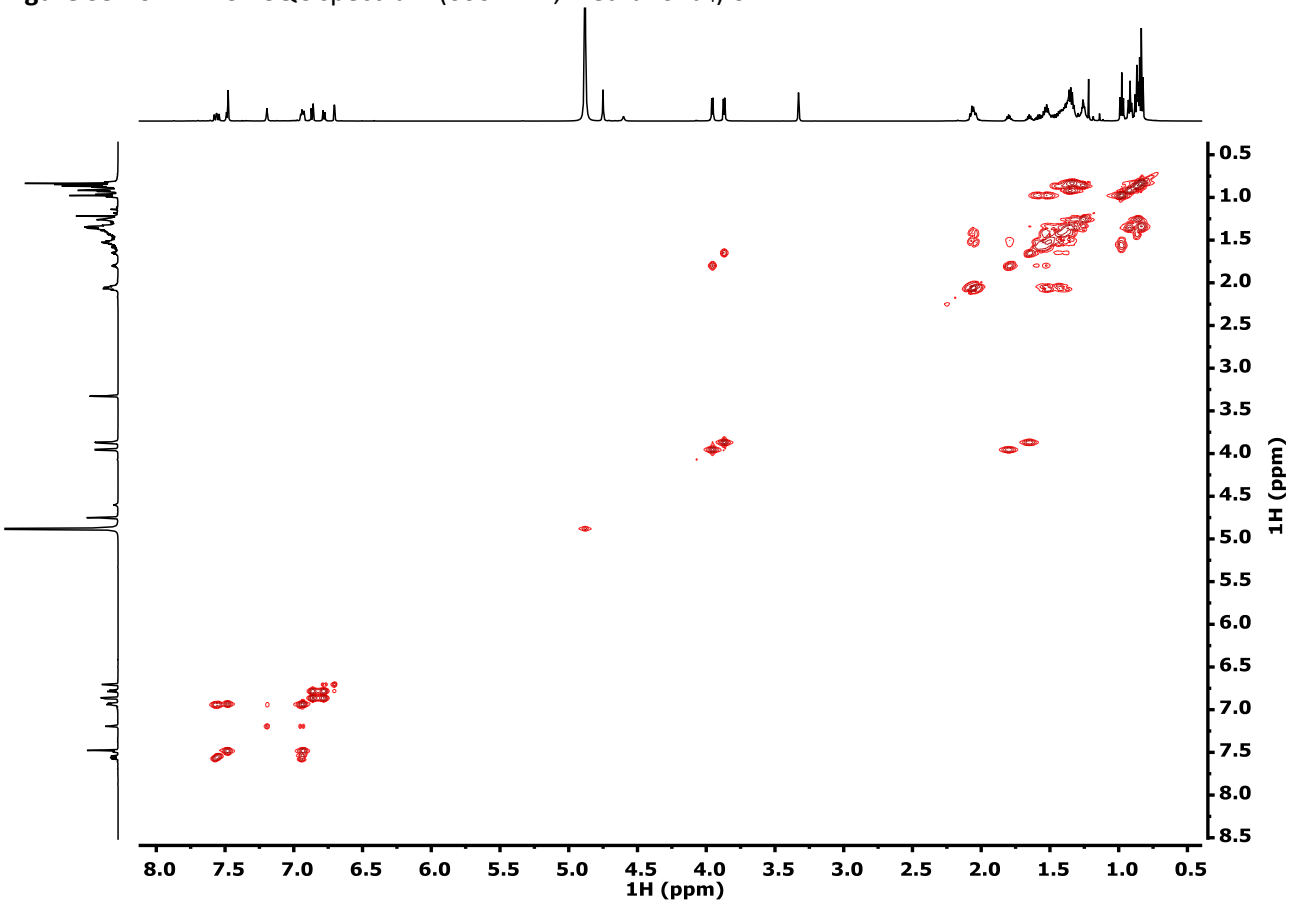
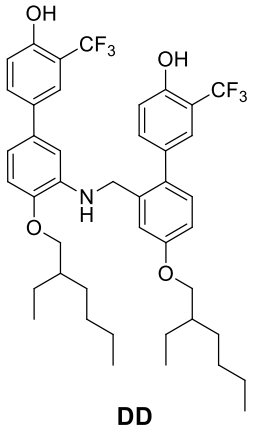


Figure S3.11. ^{1}H-^{1}H COSY spectrum (600 MHz, methanol-d_4) of **DA**.

3.3 Synthesis of DD



DD

Dimer **DD** was synthesized via one step reductive amination. Monomers $\mathbf{D_{CO}}$ (50 mg, 0.127 mmol, 1 equiv) and $\mathbf{D_{NH2}}$ (97 mg, 0.254 mmol, 2 equiv) were dissolved in dry toluene (2 mL) in a 2 mL vial and the mixture was stirred at 40°C overnight. Then, $NaBH(OAc)_3$ (135 mg, 0.043 mmol, 5 equiv) was added and the mixture was stirred again for 2 h until complete reduction of the imine (confirmed by ^{1}H-NMR). Then, a saturated solution of NaCl was added and the mixture was stirred until complete solubilisation. Hence, the organic phase was extracted, and the aqueous phase was washed (3x) with EtOAc. The organic layers were collected and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified via flash chromatography (gradient PE: Et_2O 6:4), giving the desired dimer (79.1 mg, 82 % yield).

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.56 (d, *J* = 2.27 Hz, 1H), 7.51 (d, *J* = 2.01 Hz, 1H), 7.49 (d, *J* = 2.31 Hz, 1H), 7.44 (dd, *J* = 8.39, 2.22 Hz, 1H), 7.20 (d, *J* = 8.43 Hz, 1H), 7.11 (d, *J* = 2.66 Hz, 1H), 6.97 (dd, *J* = 8.42, 6.55 Hz, 2H), 6.92 – 6.89 (m, 1H), 6.81 (t, *J* = 8.72 Hz, 1H), 6.79 (dd, J= 8.27, J= 2.20, 1H), 6.52 (d, *J* = 2.10 Hz, 1H), 5.44 (s, 1H), 5.40 (s, 1H), 4.61 (t, *J* = 5.63 Hz, 1H), 4.27 (d, *J* = 5.12 Hz, 2H), 3.93 (dd, *J* = 5.76, 1.51 Hz, 2H), 3.86 (dd, *J* = 5.76, 2.88 Hz, 2H), 1.79 (p, *J* = 6.11 Hz, 1H), 1.73 (p, *J* = 6.15 Hz, 1H), 1.56 – 1.26 (m, 16H), 0.92 (m, 12H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 159.38, 152.58, 152.27, 146.15, 138.28, 137.94, 134.74, 134.22, 133.31, 132.50, 132.06, 131.67, 131.26, 127.45 (q, J = 4.28 Hz), 124.93 (q, J = 4.40 Hz), 124.17 (q, J = 273.95 Hz), 124.13 (q, J = 272.28 Hz), 118.02, 117.92, 117.63, 117.18, 116.57 (q, J = 30.06 Hz), 116.17 (q, J = 30.42 Hz), 115.14, 114.44, 113.47, 110.54, 108.60, 70.99, 70.57, 60.64, 46.21, 39.39, 39.32, 30.70, 30.51, 29.08, 29.07, 24.11, 23.83, 23.05, 23.03, 14.08, 14.05, 11.13, 11.09.

^{19}F NMR (565 MHz, chloroform-*d*) δ -60.67, -60.72.

ES+: Calculated for $C_{43}H_{52}F_6NO_4$; experimental 760.4 found 760.7

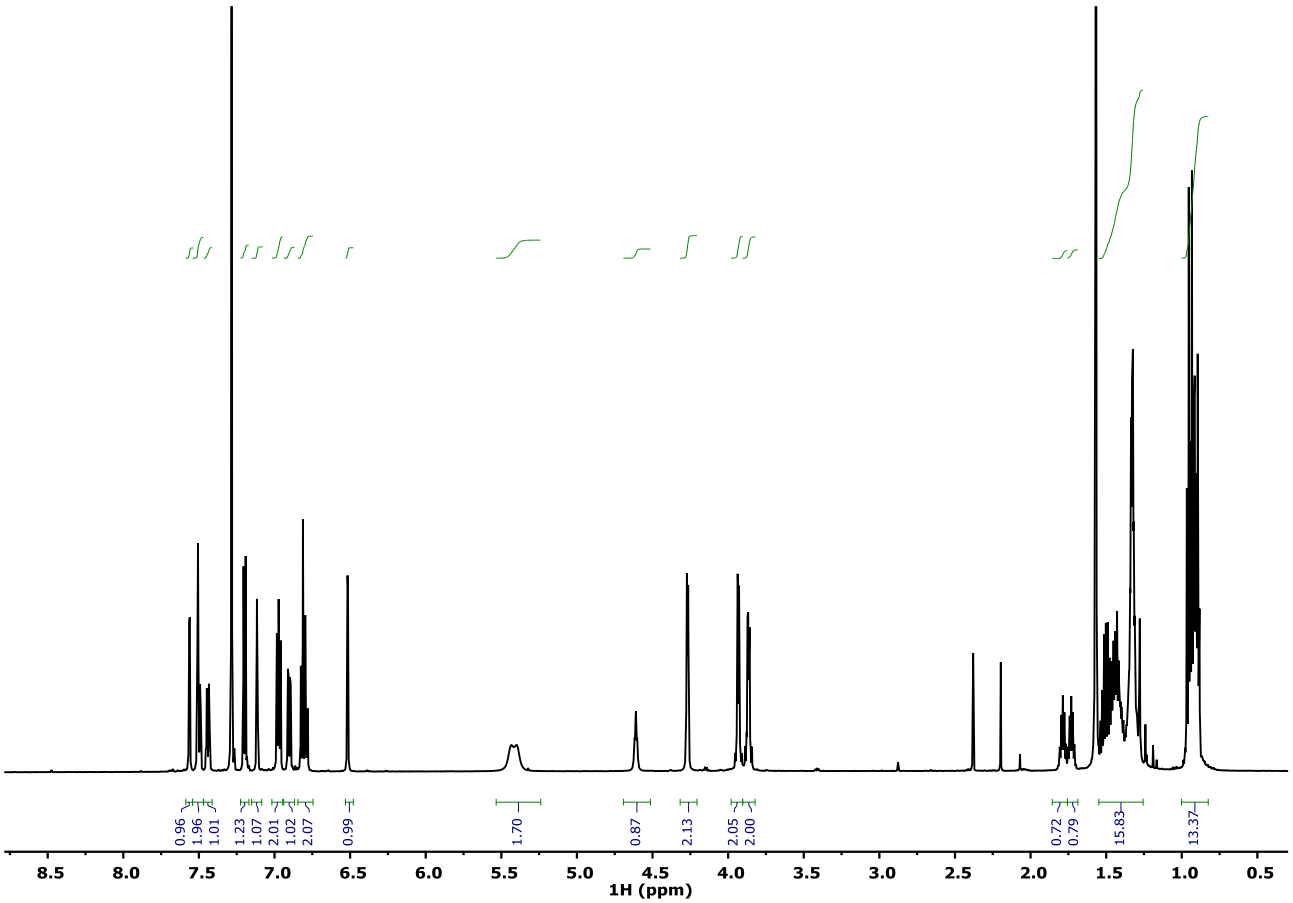


Figure S3.12. ^{1}H-NMR spectrum (600 MHz, chloroform-*d*) of **DD**.

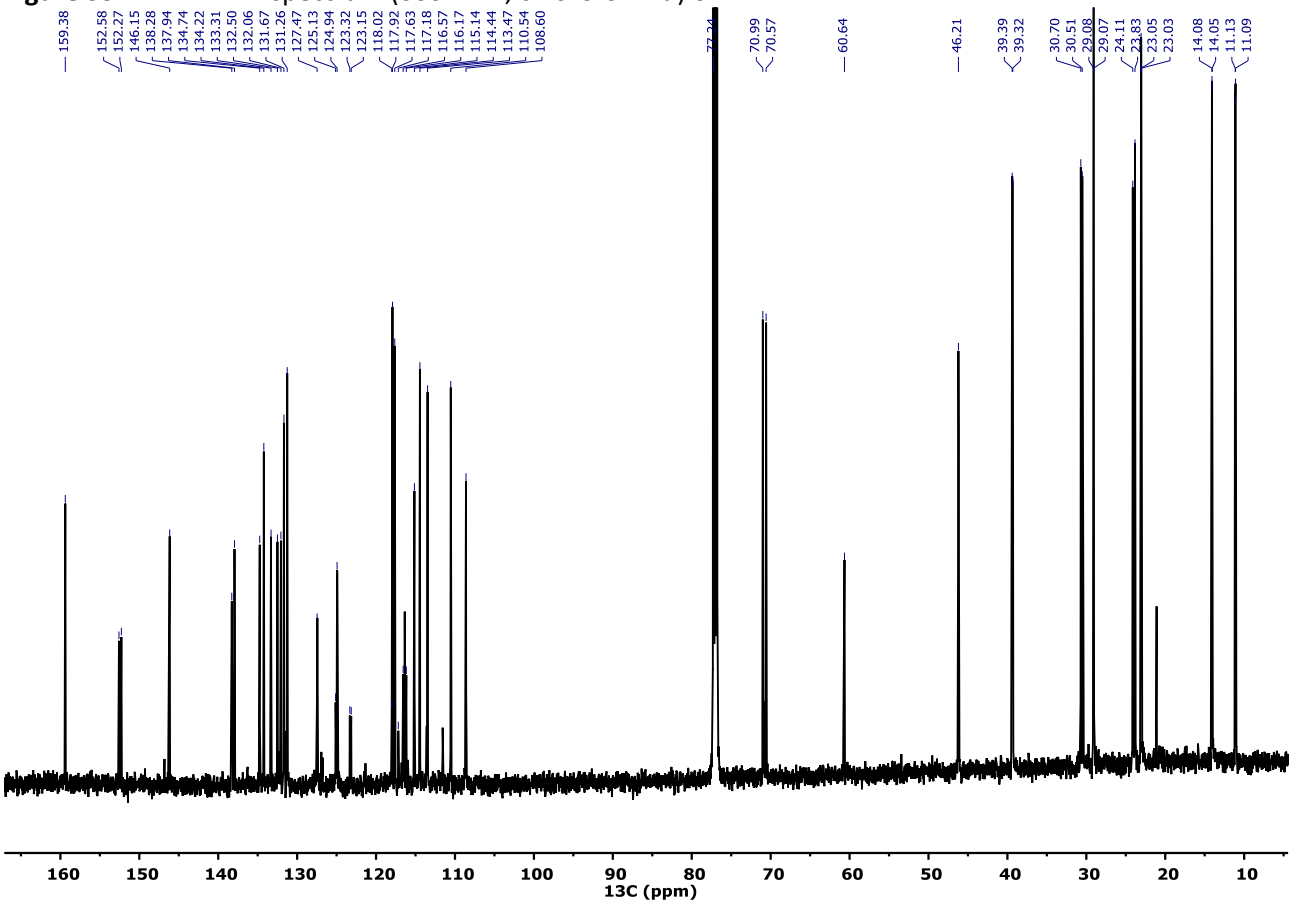


Figure S3.13. ^{13}C-NMR spectrum (151 MHz, chloroform-*d*) of **DD**.

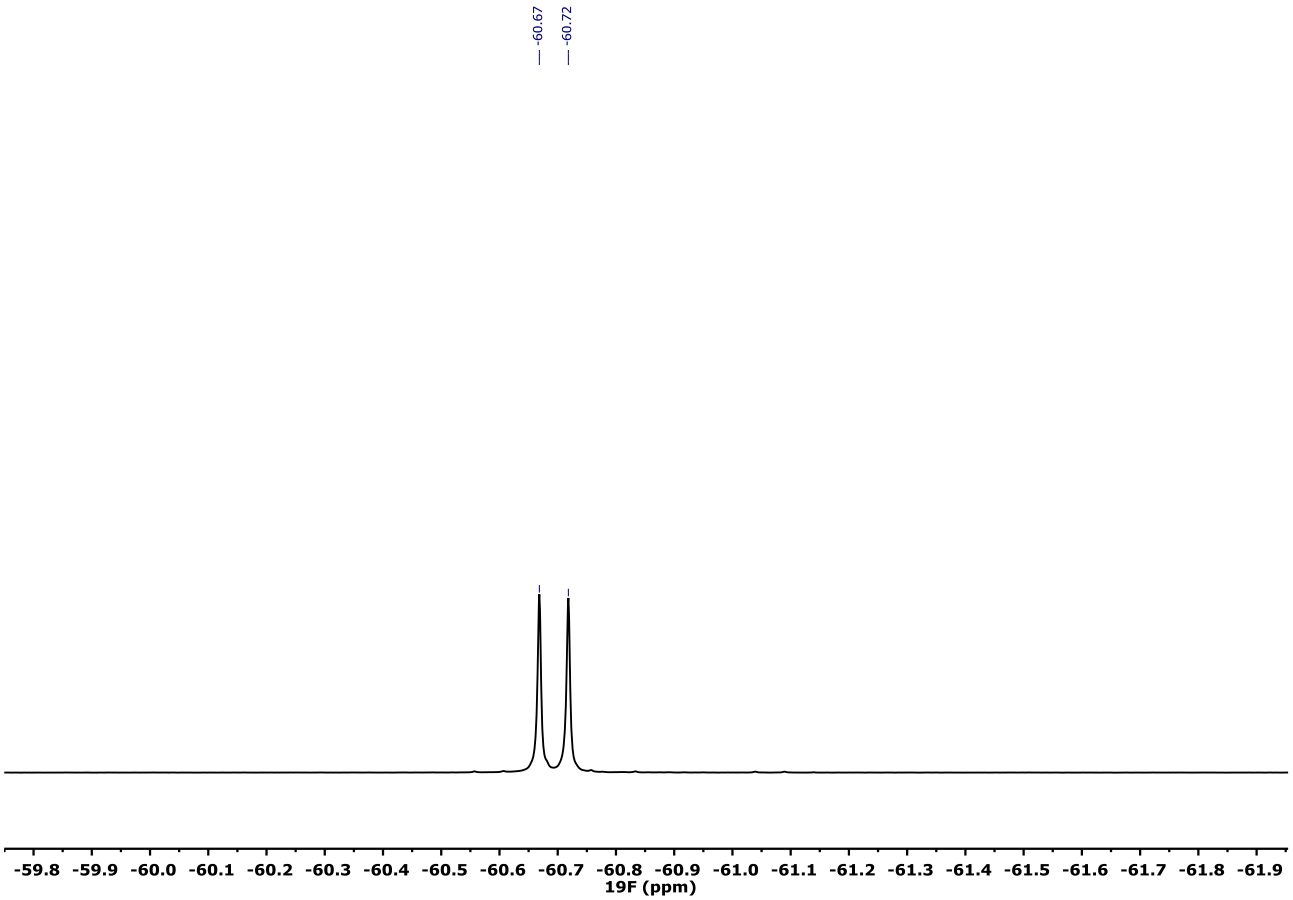


Figure S3.14. ^{19}F-NMR spectrum (565 MHz, chloroform-*d*) of **DD**.

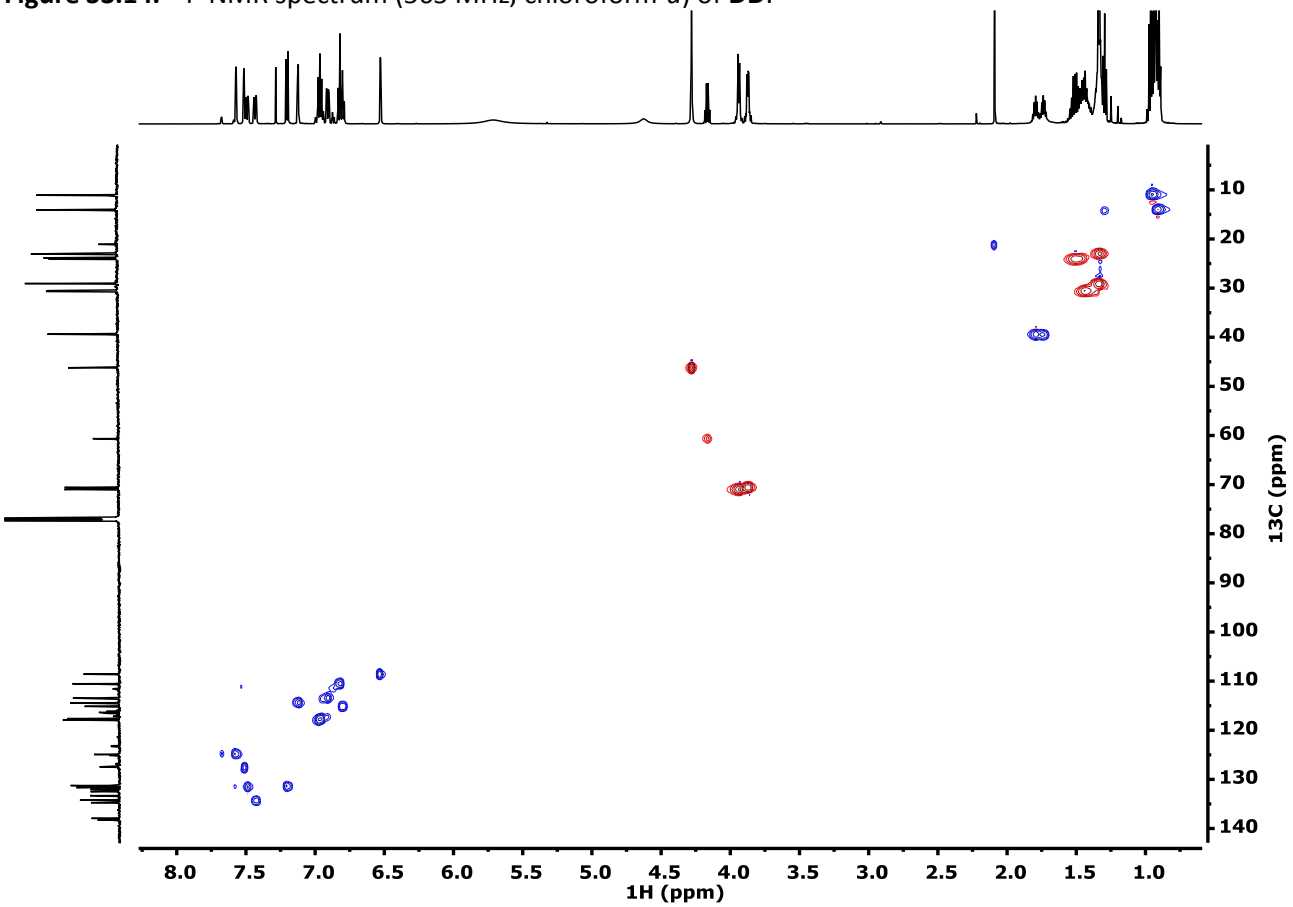


Figure S3.15. ^{1}H-^{13}C HSQC spectrum (600 MHz, chloroform-*d*) of **DD**.

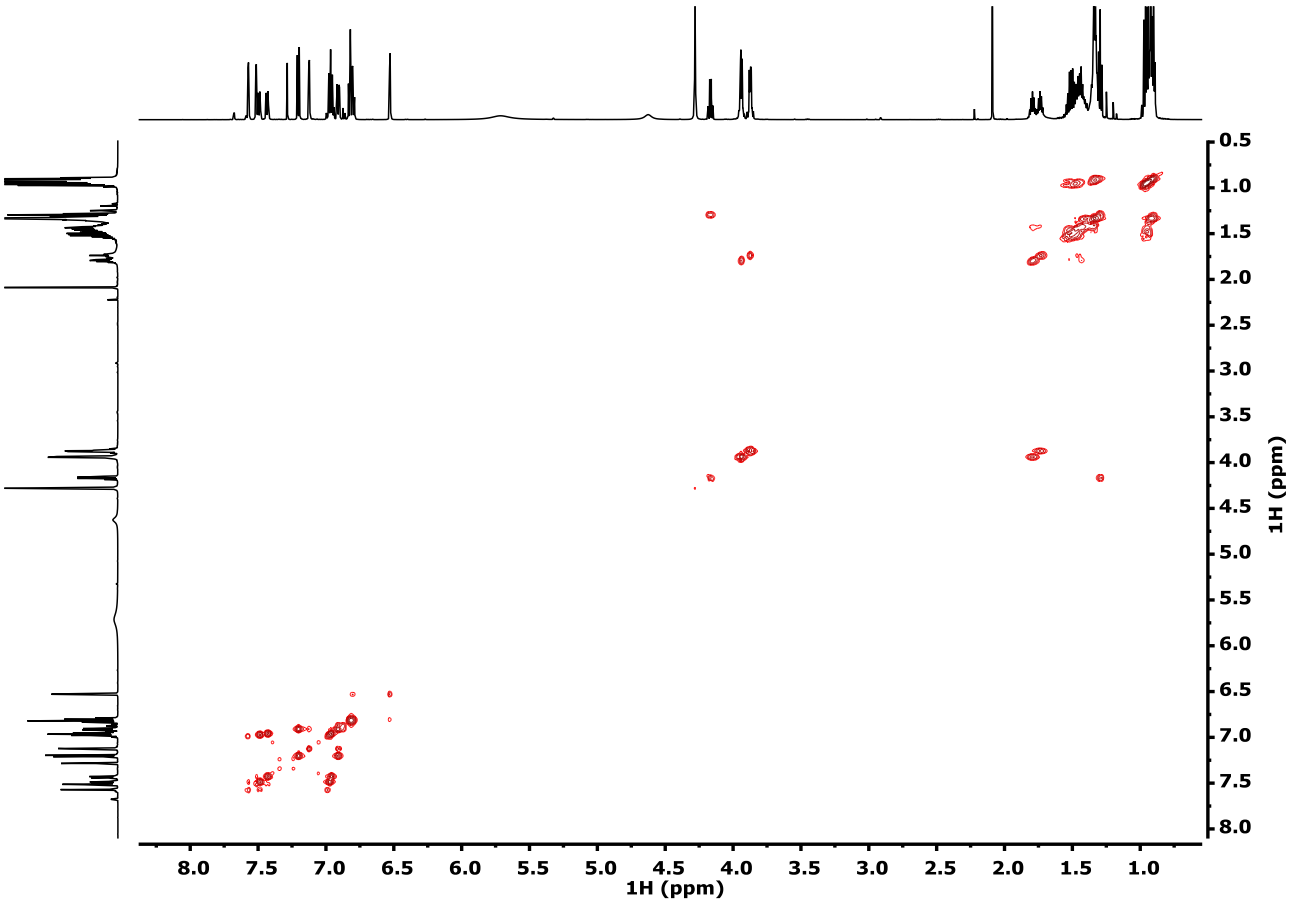


Figure S3.16. ^{1}H-^{1}H COSY spectrum (600 MHz, chloroform-*d*) of **DD**.

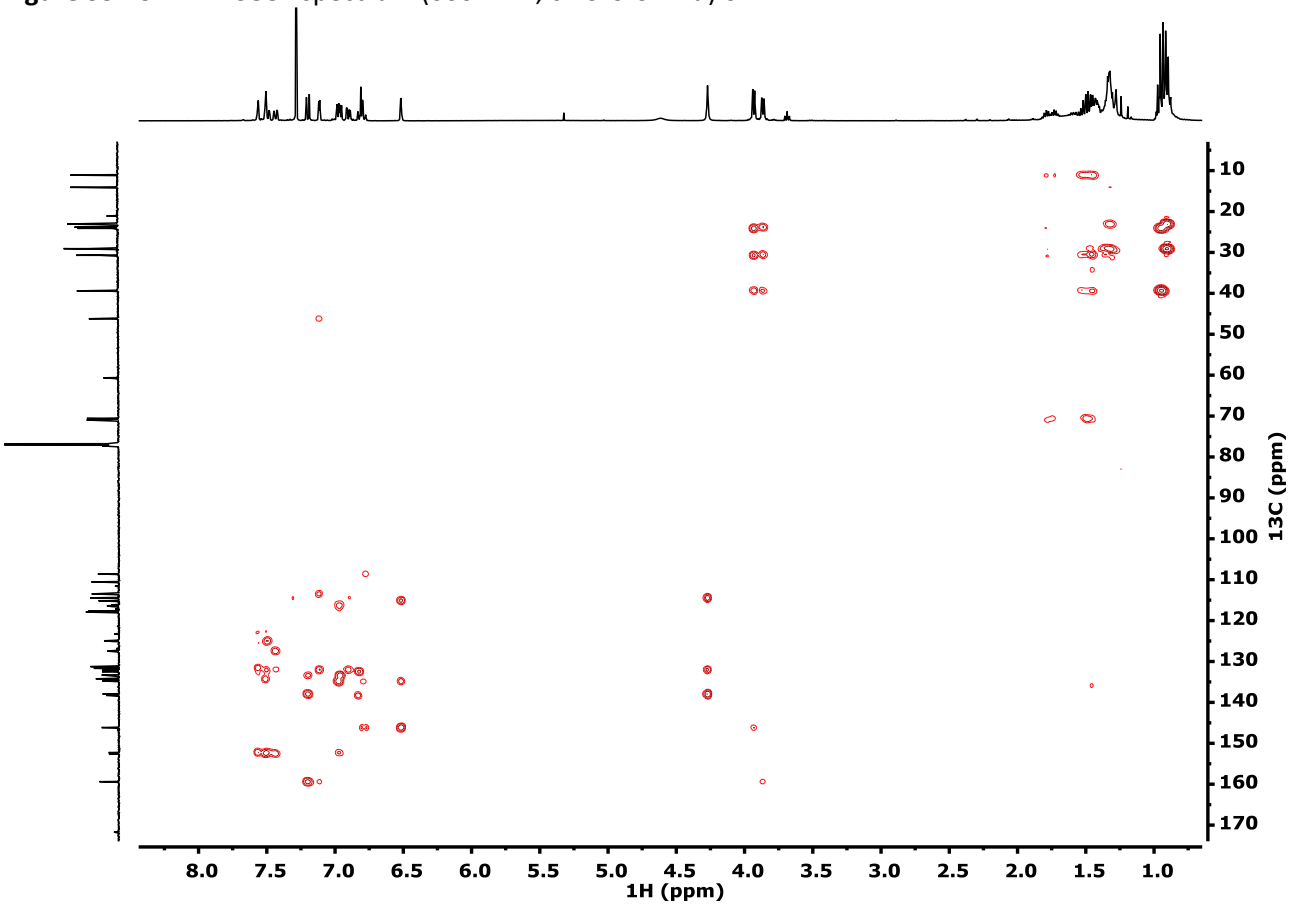


Figure S3.17. ^{1}H-^{13}C HMBC spectrum (400 MHz, chloroform-*d*) of **DD.**

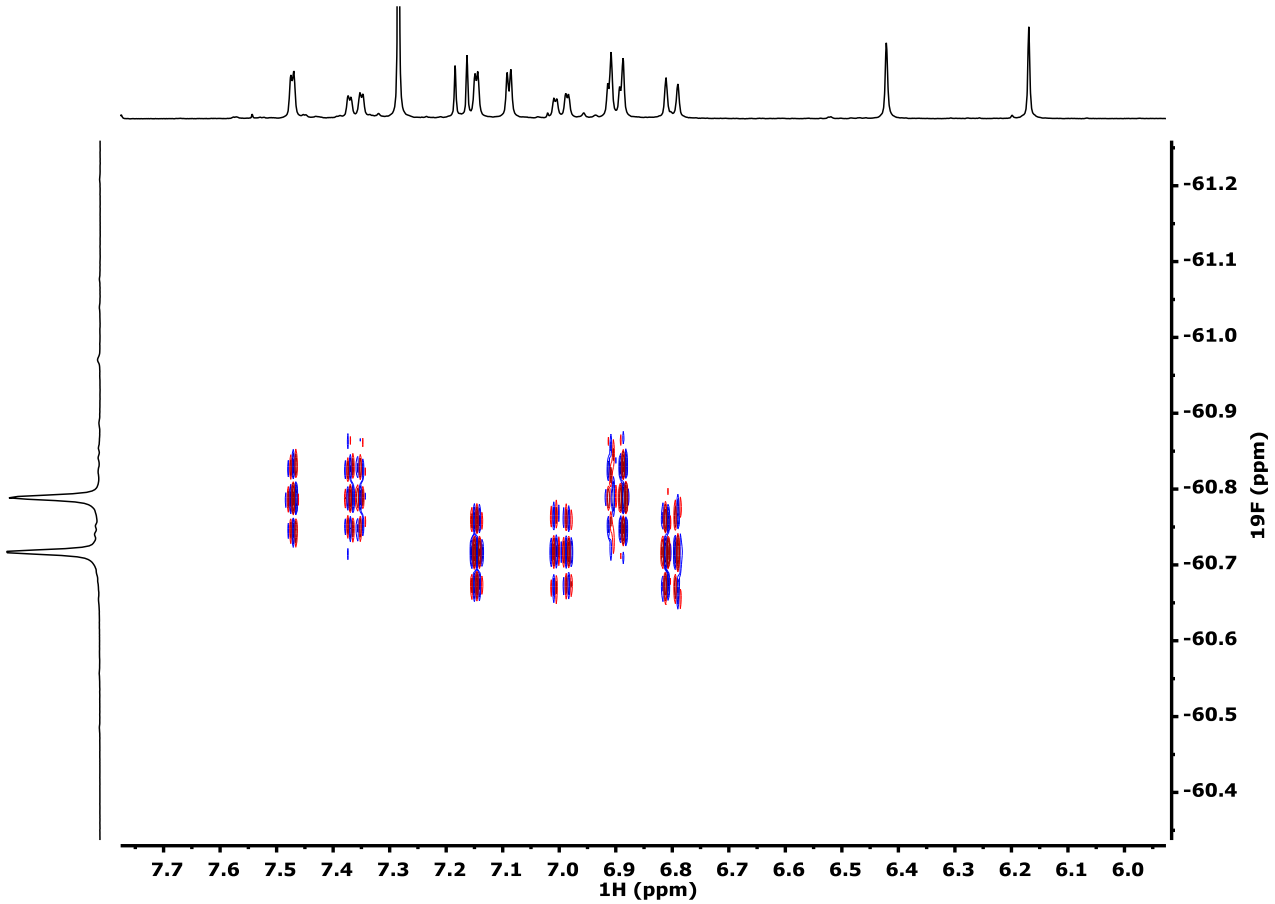
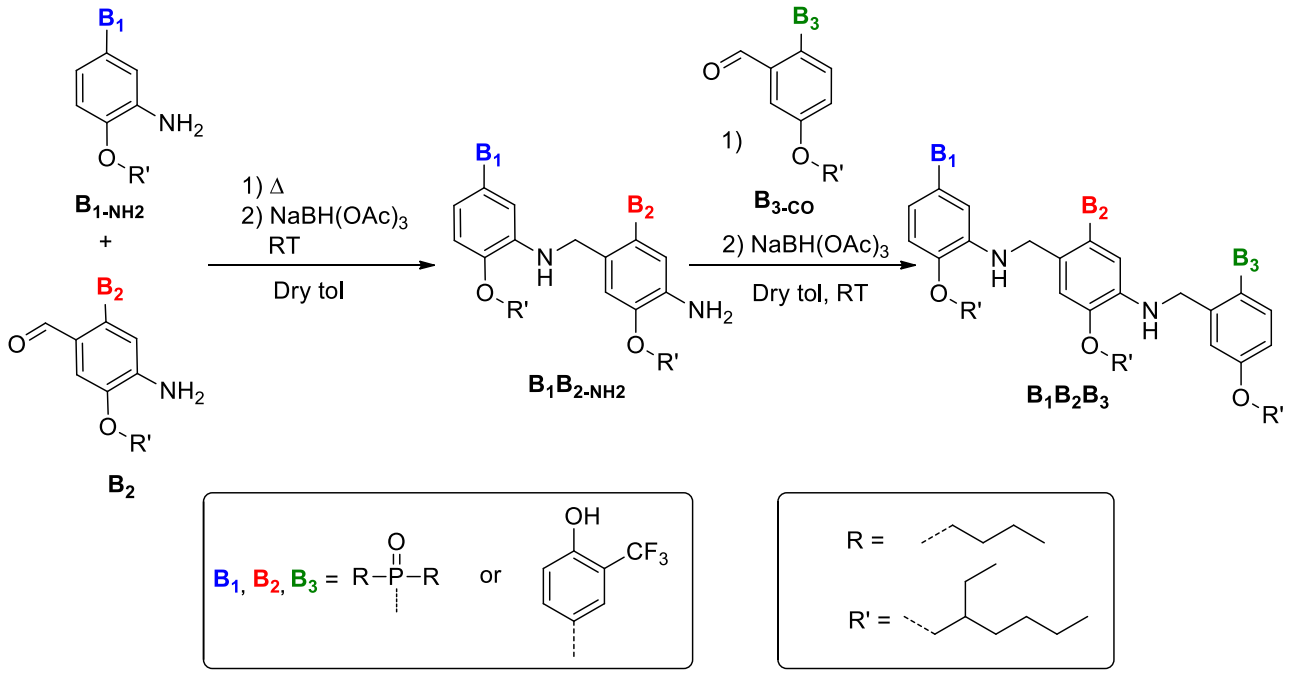


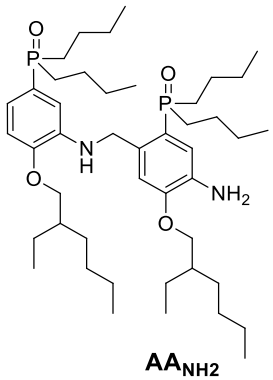
Figure S3.18. ^{1}H-^{19}F HMBC spectrum (400 MHz, chloroform-*d*) of **DD.**

4. Synthesis and characterisation of the trimers



Scheme S4.1 general synthesis pathway used for all the trimers.

4.1 Synthesis of AA_{NH2}



AA_{NH2}

Intermediate $\mathbf{AA_{NH2}}$ was synthesized via one step reductive amination. Monomers **A** (29.5 mg, 0.072 mmol, 1 equiv) and $\mathbf{A_{NH2}}$ (165 mg, 0.432 mmol, 6 equiv) were dissolved in dry toluene (0.5 mL) in a 2 mL vial and the mixture was stirred at 40°C overnight. Then, 9.15 mg (0.043 mmol, 0.6 equiv) of $NaBH(OAc)_3$ were added. The mixture was let to react another day, then a second addition of $NaBH(OAc)_3$ (76 mg, 0.360 mmol, 5 equiv) was made to complete the reduction of the imine (confirmed by ^{1}H-NMR). Then, a saturated solution of NaCl was added and the mixture was stirred until complete solubilisation. Hence, the organic phase was extracted, and the aqueous phase was washed (3x) with EtOAc. The organic layers were collected and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified via flash chromatography (gradient ACN: MeOH 95:5 to 9:1), giving the desired dimer (51.7 mg, 93 % yield).

^{1}H NMR (400 MHz, acetonitrile-d_3) δ 7.02 (d, *J* = 3.25 Hz, 1H), 6.95 – 6.82 (m, 3H), 6.78 (d, *J* = 12.55 Hz, 1H), 5.97 (br t, 1H), 4.58 (d, *J* = 5.67 Hz, 2H), 4.20 (s, 2H), 3.96 (d, *J* = 5.47 Hz, 2H), 3.92 (d, *J* = 5.38 Hz, 2H), 2.03 – 1.65 (m, 12H), 1.63 – 1.10 (m, 36H), 0.94 (m, 12H), 0.81 (m, 12H).

^{13}C NMR (101 MHz, acetonitrile-d_3) δ 148.71 (d, J = 3.07 Hz), 148.04 (d, J = 2.79 Hz), 138.03 (d, *J* = 13.41 Hz), 136.14 (d, *J* = 14.27 Hz), 134.21 (d, *J* = 6.69 Hz), 124.10 (d, *J* = 96.34 Hz), 121.57 (d, *J* = 92.03 Hz), 118.70 (d, *J* = 8.70 Hz), 116.47 (d, *J* = 13.90 Hz), 113.57 (d, *J* = 11.94 Hz), 110.84 (d, *J* = 12.42 Hz), 109.66 (d, *J* = 13.64 Hz), 70.32 (d, *J* = 36.36 Hz), 45.47, 39.38, 30.64, 30.34 (d, *J* = 6.52 Hz), 29.94 (d, *J* = 2.96 Hz), 29.24, 28.88 (d, *J* = 5.42 Hz), 23.91, 23.79, 23.77, 23.75, 23.71, 23.65, 23.62, 23.58, 22.83, 13.47 (d, *J* = 3.02 Hz), 13.05, 10.57 (d, *J* = 7.04 Hz).

^{31}P NMR (162 MHz, acetonitrile-d_3) δ 44.36, 39.74

HRMS(ES+): Calculated for $C_{45}H_{81}N_2O_4P_2$ 775.5672 a.m.u.; found 775.5717

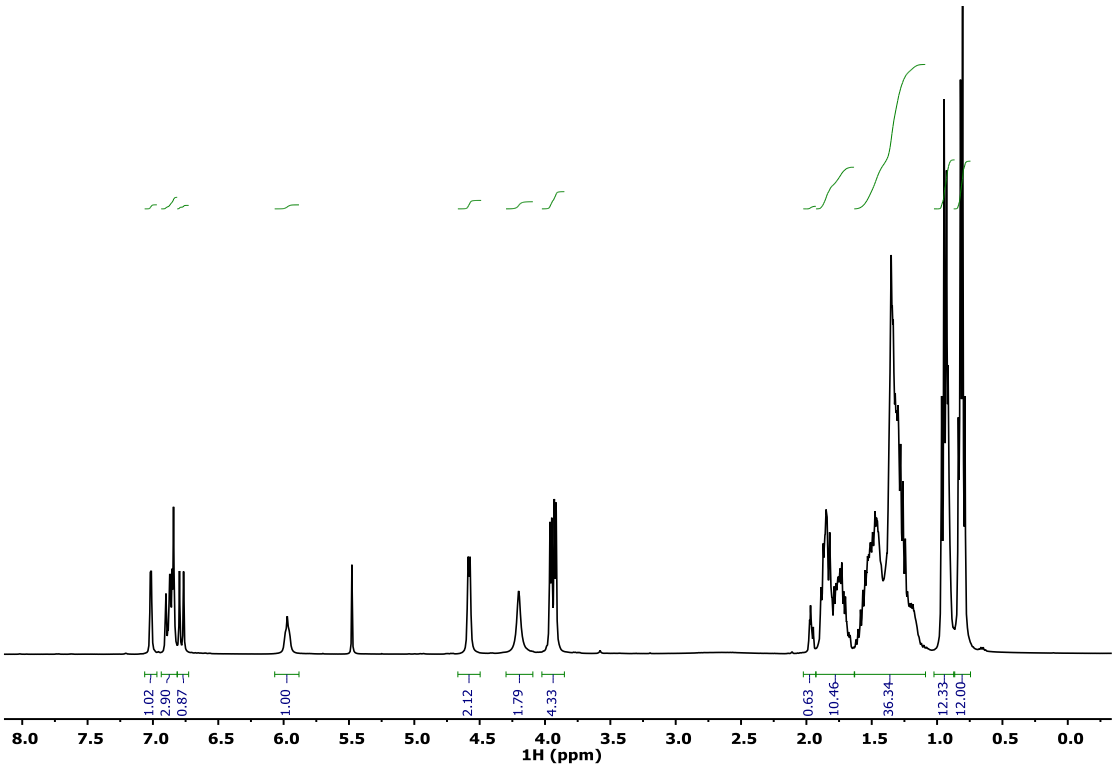


Figure S4.1. ^{1}H-NMR spectrum (400 MHz, acetonitrile-d_3) of $\mathbf{AA_{NH2}}$.

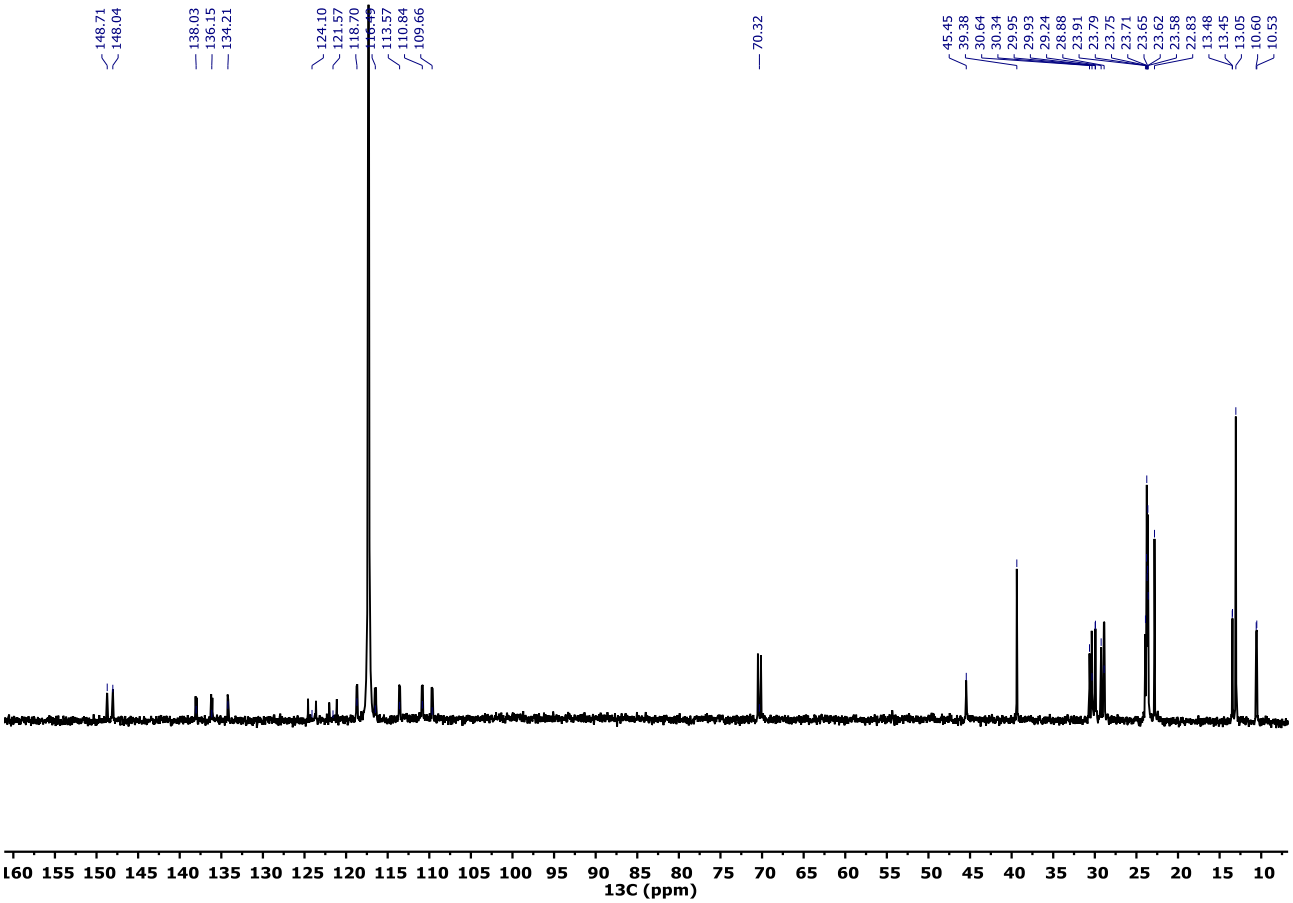


Figure S4.2. ^{13}C-NMR spectrum (101 MHz, acetonitrile-d_3) of $\mathbf{AA_{NH2}}$.

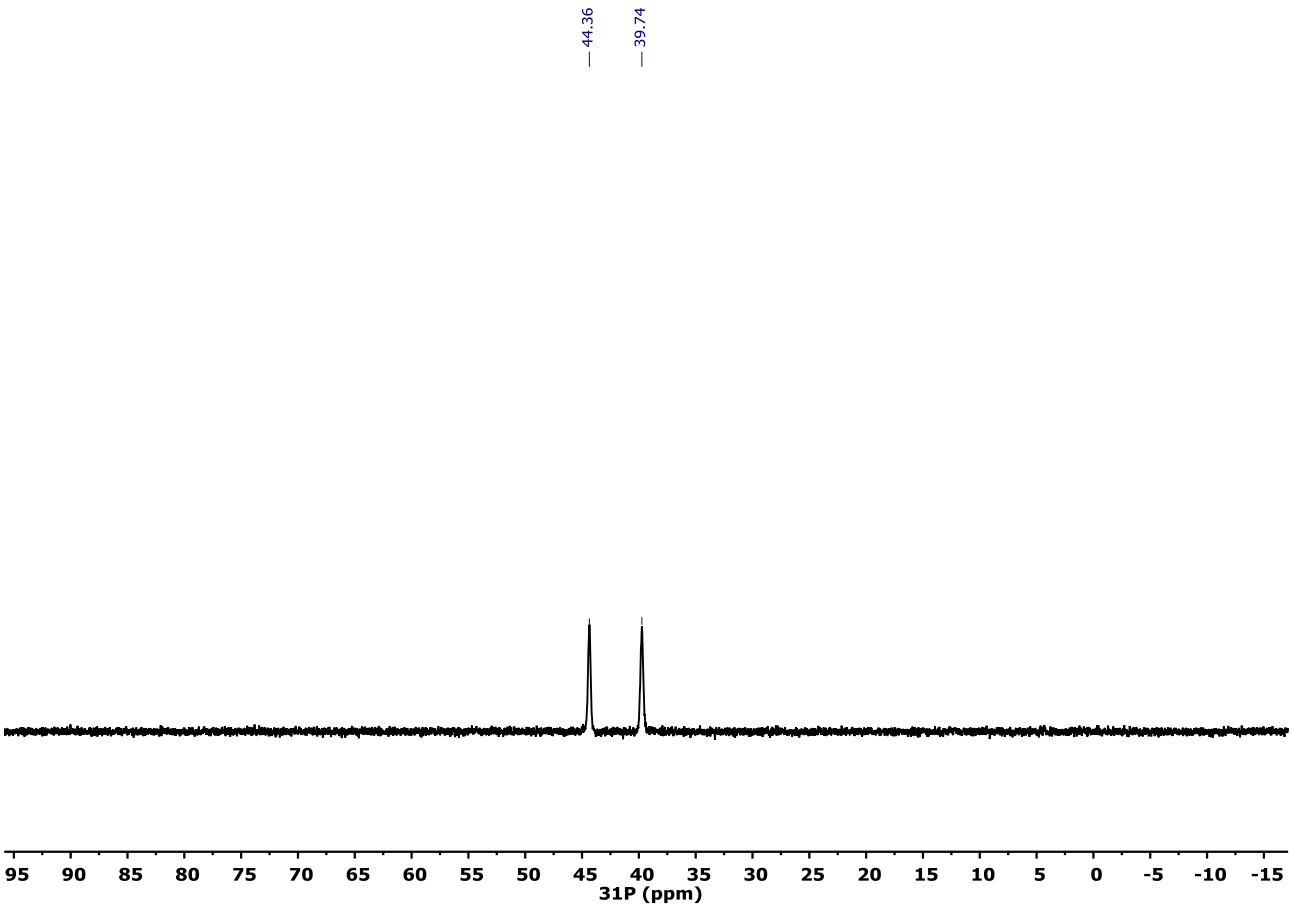


Figure S4.3. ^{31}P-NMR spectrum (162 MHz, acetonitrile-d_3) of **AA_{NH2}**.

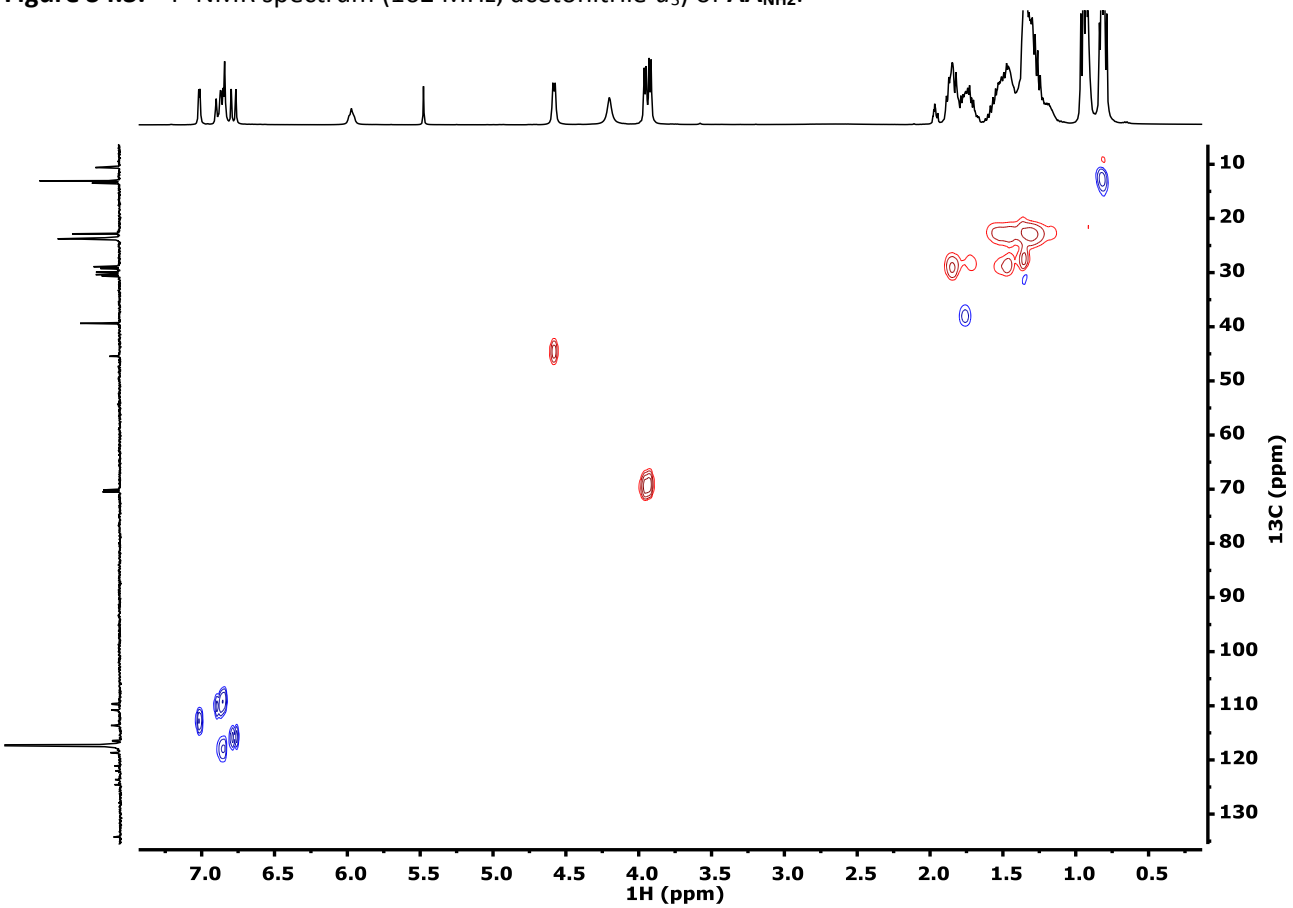


Figure S4.4. ^{1}H-^{13}C HSQC spectrum (400 MHz, acetonitrile-d_3) of **AA_{NH2}**.

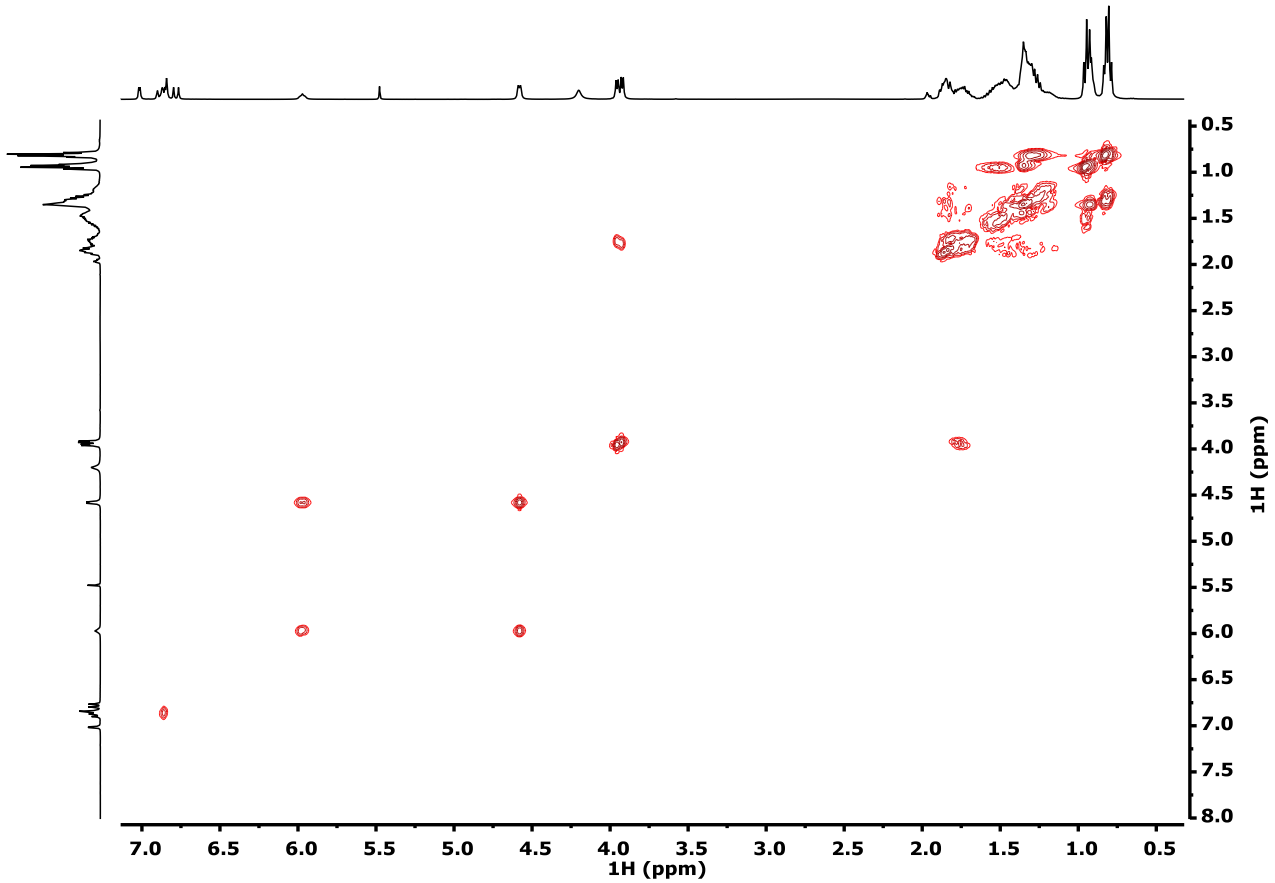
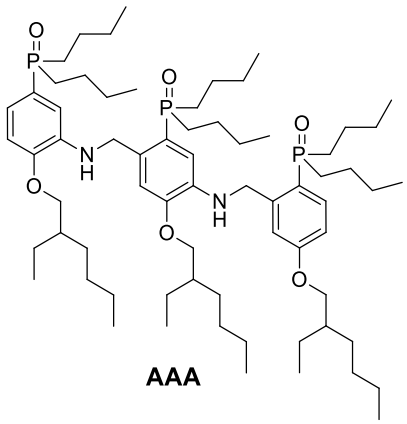


Figure S4.5. ^{1}H-^{1}H COSY spectrum (400 MHz, acetonitrile-d_3) of $\mathbf{AA_{NH2}}$.

4.2 Synthesis of AAA



AAA

AA_{NH2} (21 mg, 0.028 mmol, 1 equiv) and **A_{CO}** (12.2 mg, 0.031 mmol, 1.1 equiv) were dissolved in a 2 mL vial with dry toluene (0.3 mL) and stirred over weekend at room temperature. Then, 1.8 mg (0.008 mmol, 0.3 equiv) of $NaBH(OAc)_3$ were added. The mixture was let to react other 24 h, before a second addition of $NaBH(OAc)_3$ (29.7 mg, 0.14 mmol, 5 equiv) to complete the reduction of the imine (confirmed by ^{1}H-NMR). Then, a saturated solution of NaCl was added and the mixture was stirred until complete solubilisation. Hence, the organic phase was extracted, and the aqueous phase was washed (3x) with EtOAc. The organic layers were collected and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified via flash chromatography (EtOAc: MeOH 97:3), giving the desired trimer (20.7 mg, 64 % yield).

^{1}H-NMR (400 MHz, acetonitrile-d_3) δ 7.40 (dd, J = 11.76, 8.54 Hz, 1H), 7.06 (t, J = 2.70 Hz, 1H), 6.97 (d, J = 3.42 Hz, 1H), 6.94 – 6.76 (m, 4H), 6.52 (d, J = 13.07 Hz, 1H), 6.05 (t, J = 6.98 Hz, 1H), 5.88 (t, J = 6.85 Hz, 1H), 4.70 (d, J = 6.68 Hz, 2H), 4.53 (d, J = 6.65 Hz, 2H), 3.98 (d, J = 5.49 Hz, 2H), 3.90 (d, J = 5.51 Hz), 3.87 (d = 5.55 Hz, 2H), 2.02 – 1.04 (m, 73H), 1.02 – 0.87 (m, 18H), 0.82 (m, 12H), 0.73 (t, J = 7.18 Hz, 6H).

^{13}C-NMR (101 MHz, acetonitrile-d_3) δ 161.38 (d, J = 2.69 Hz), 148.72 (d, J = 2.80 Hz), 147.86 (d, J = 2.50 Hz), 147.37 (d, J = 7.3447 Hz), 138.20, 138.07, 136.22 (d, J = 14.37 Hz), 133.53, 133.40, 133.35, 133.29, 124.63, 123.67, 122.19, 121.46, 121.27, 120.54, 118.46 (d, J = 8.87 Hz), 116.16 (d, J = 10.30 Hz), 112.94 (d, J = 11.99 Hz), 111.88 (d, J = 12.51 Hz), 111.70 (d, J = 15.91 Hz), 110.70 (d, J = 12.46 Hz), 109.63 (d, J = 13.58 Hz), 70.39, 70.33, 70.08, 45.32, 39.48, 39.36, 39.19, 31.65, 30.87, 30.42, 30.33, 30.25, 30.20, 29.91, 29.73, 29.37, 29.23, 28.92, 28.88, 28.76, 23.87, 23.85, 23.81, 23.77, 23.73, 23.71, 23.64, 23.56, 22.87, 22.80, 22.78, 13.49, 13.45, 13.40, 13.12, 13.03, 12.98, 10.60, 10.46, 10.43.

^{31}P-NMR (202 MHz, methanol-d_4) δ 49.98, 49.51, 47.19.

HRMS(ES+): Calculated for $C_{68}H_{120}N_2O_6P_3$ 1153.8359 a.m.u.; found 1153.8296

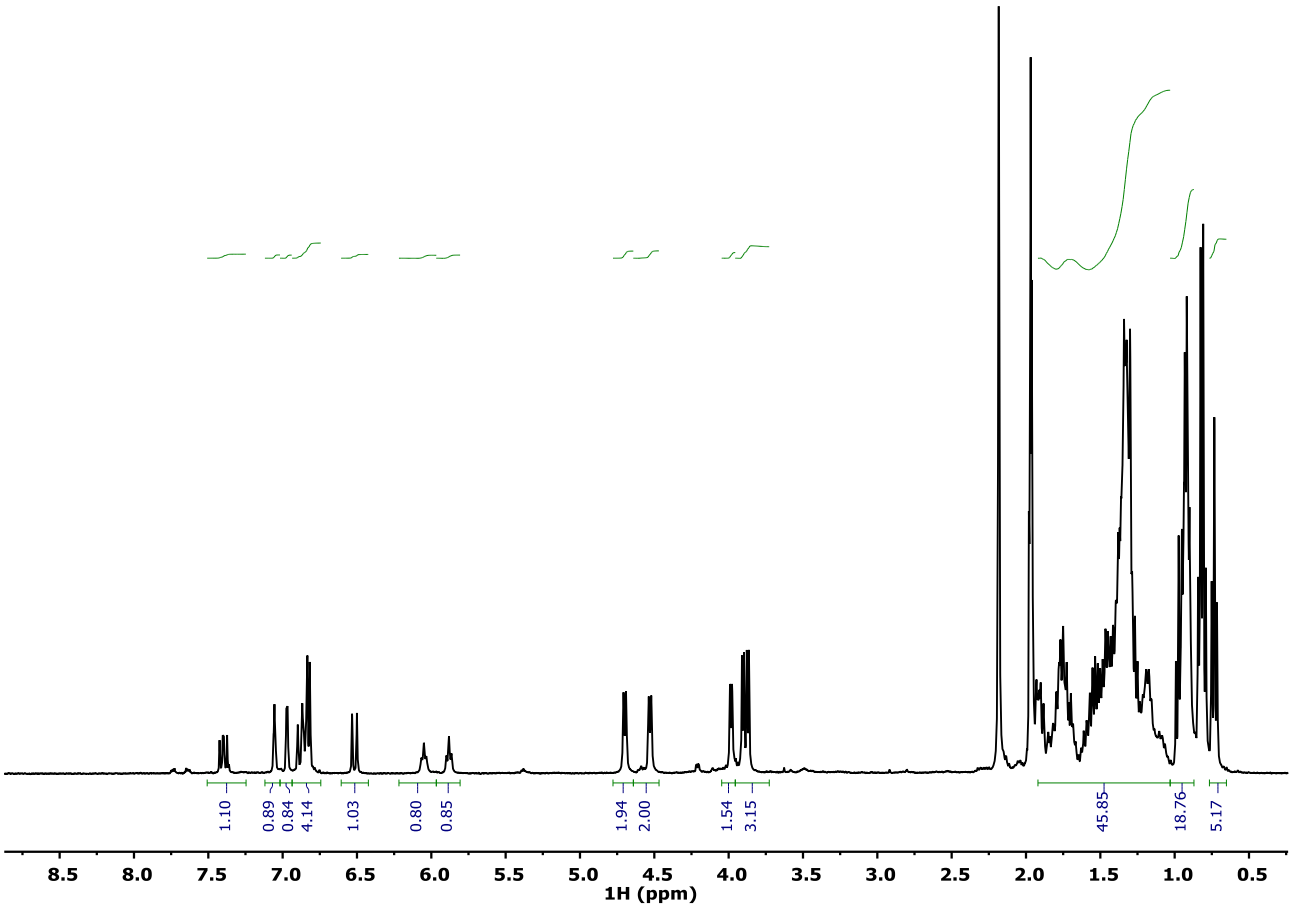


Figure S4.6. ^{1}H-NMR spectrum (400 MHz, acetonitrile-d_3) of **AAA**.

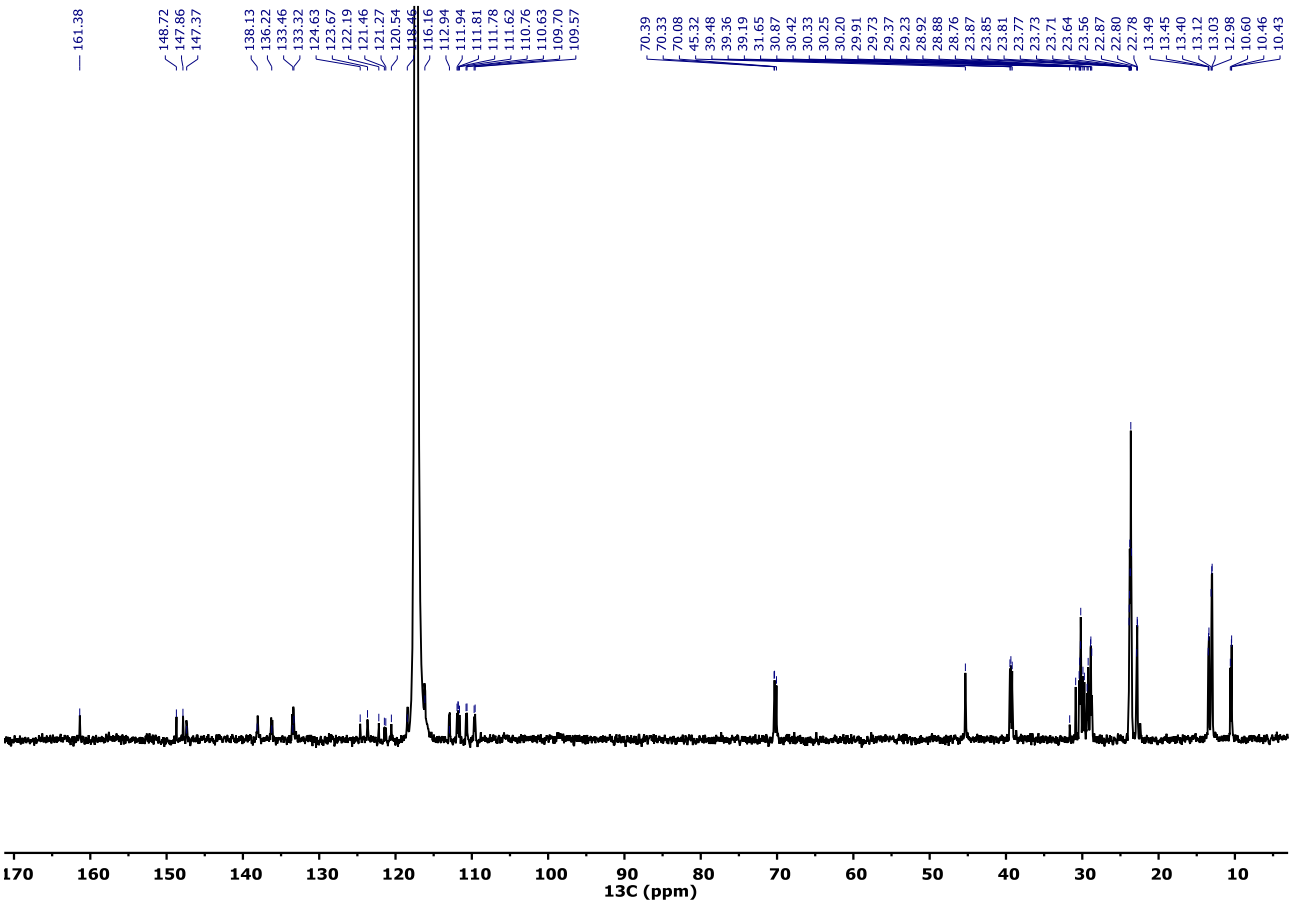


Figure S4.7. ^{13}C-NMR spectrum (101 MHz, acetonitrile-d_3) of **AAA**.

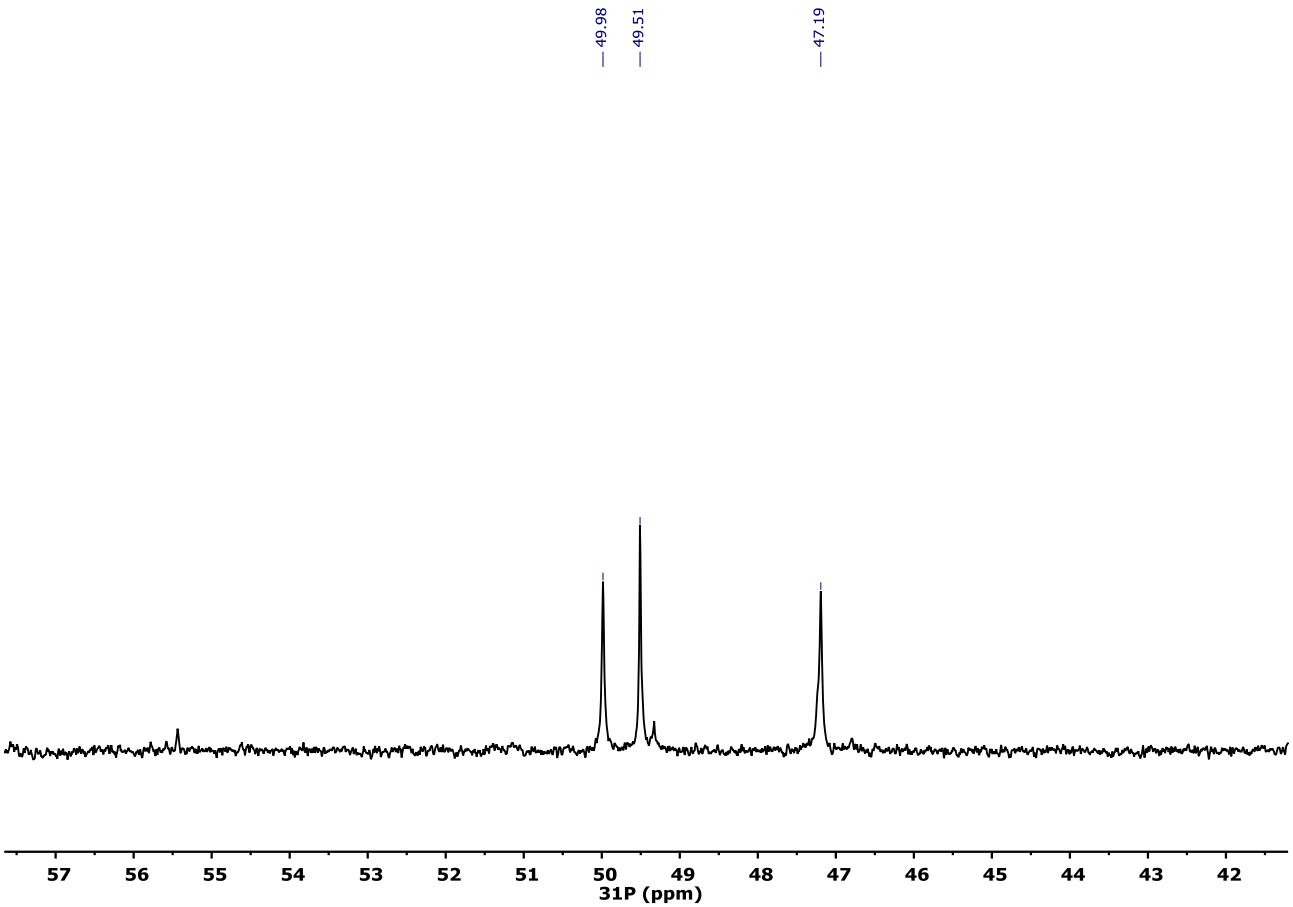


Figure S4.8. ^{31}P-NMR spectrum (202 MHz, methanol-d_4) of **AAA**.

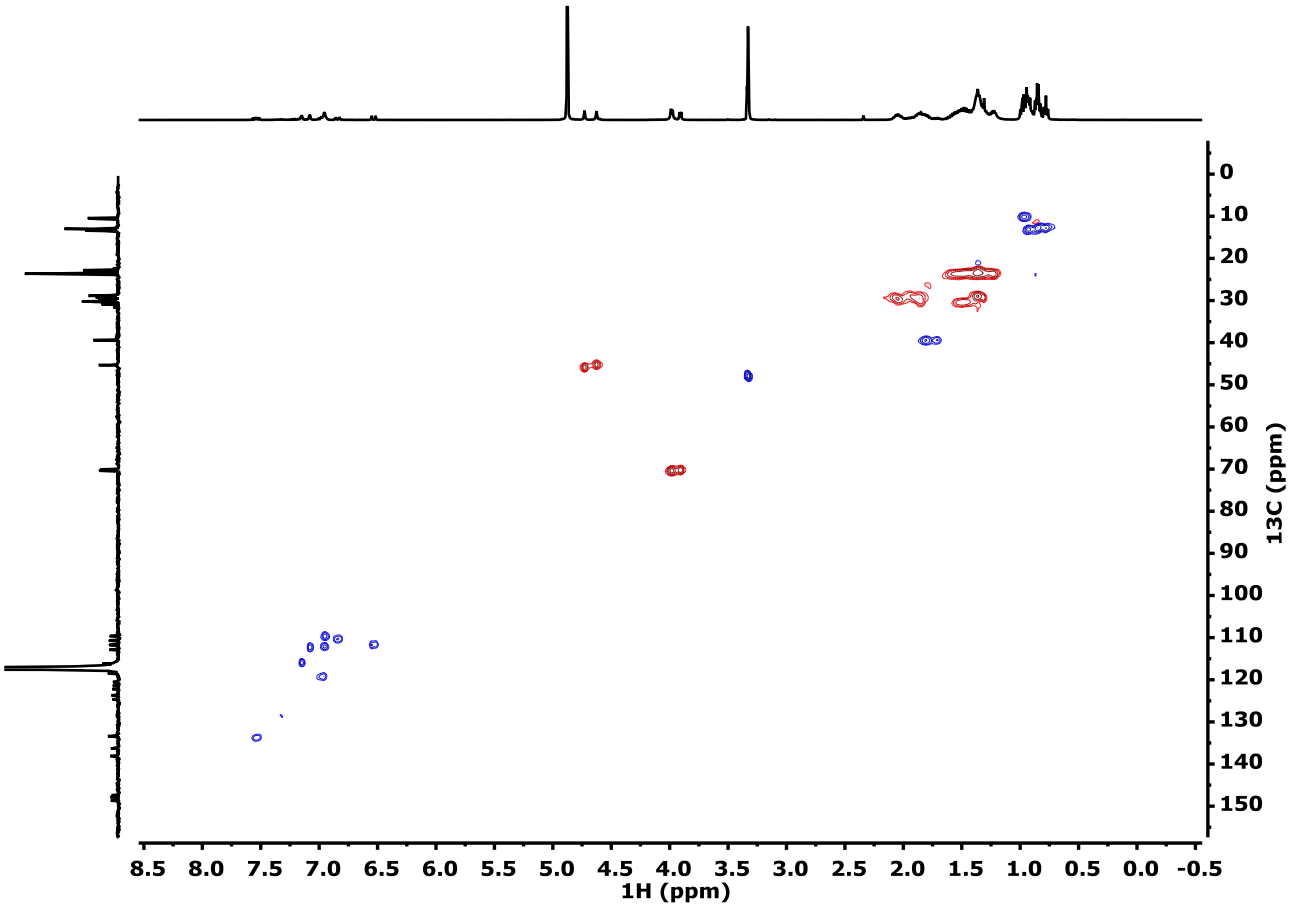


Figure S4.9. ^{1}H-^{13}C HSQC spectrum (500 MHz, methanol-d_4) of **AAA**.

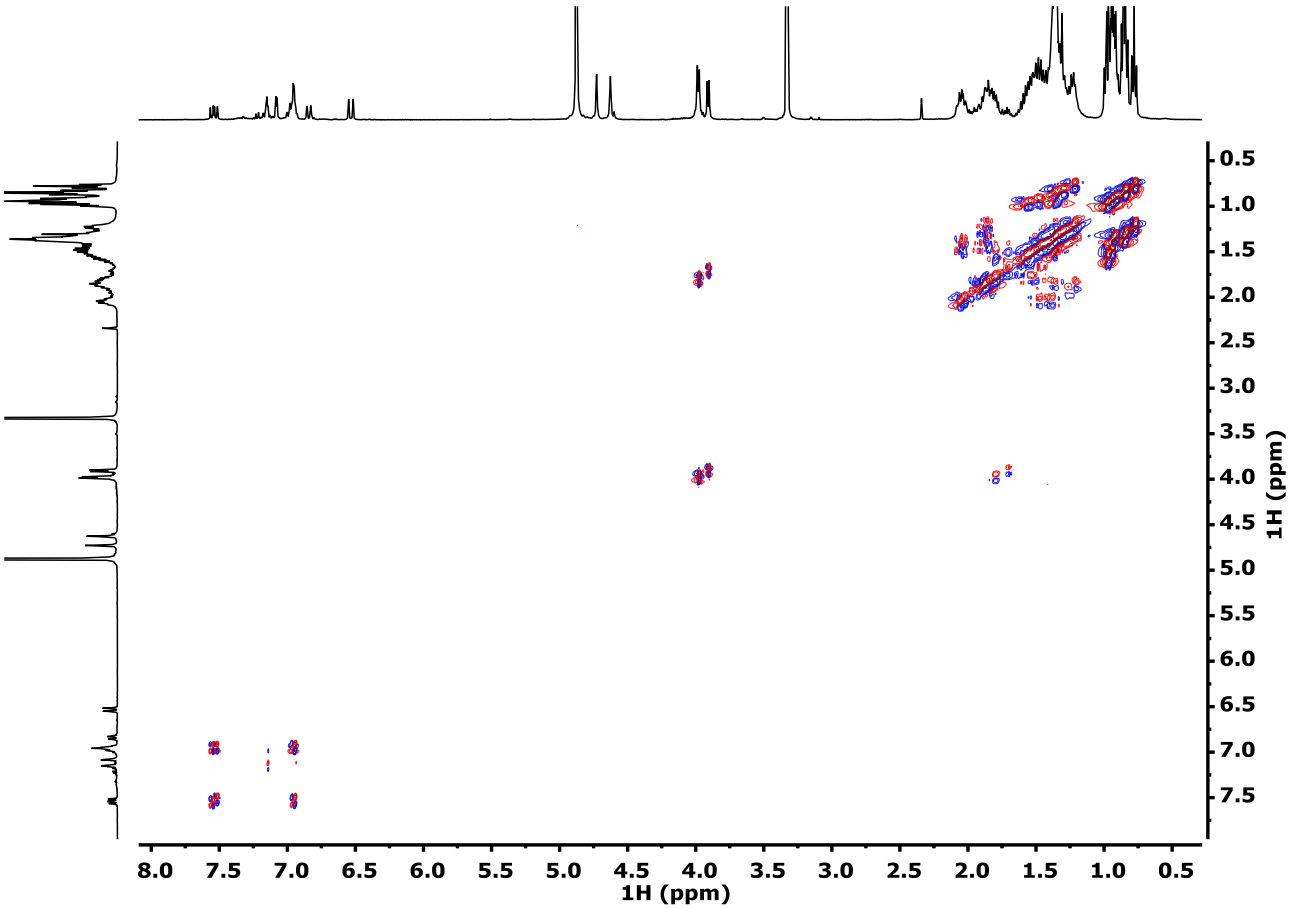
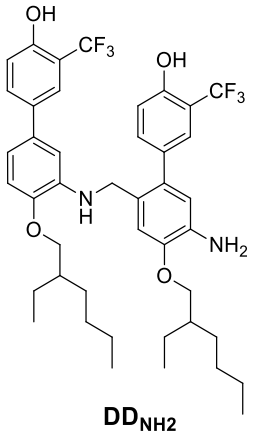


Figure S4.10. ^{1}H-^{1}H COSY spectrum (500 MHz, methanol-d_4) of **AAA**.

4.3 Synthesis of DD_{NH2}



DD_{NH2}

Intermediate DD_{NH2} was synthesized via one step reductive amination. Monomers **D** (35 mg, 0.085 mmol, 1 equiv) and D_{NH2} (98 mg, 0.256 mmol, 3 equiv) were dissolved in dry toluene (1 mL). The round bottom flask was equipped with a dean-stark filled with 3 Å molecular sieves and the mixture was stirred at 40°C overnight. Then, the mixture was cooled to room temperature and 91 mg (0.429 mmol, 5 equiv) of $NaBH(OAc)_3$ were added. The mixture was let to react 2 h until complete reduction of imine was reached (confirmed by ^{1}H-NMR). Then, a saturated solution of NaCl was added and the mixture was stirred until complete solubilisation. Hence, the organic phase was extracted, and the aqueous phase was washed (3x) with EtOAc. The organic layers were collected and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified via flash chromatography (gradient PE: Et_2O 8:2 to 6:4), giving the desired dimer (52.3 mg, 79 % yield).

^{1}H-NMR (500 MHz, acetonitrile-d_3) δ 7.76 (s, 2H), 7.60 (d, *J* = 2.17 Hz, 1H), 7.53 (d, *J* = 2.06 Hz, 1H), 7.51 (d, *J* = 2.29 Hz, 1H), 7.42 (dd, *J* = 8.35, 2.06 Hz, 1H), 7.01 (dd, *J* = 15.28, 8.41 Hz, 2H), 6.95 (s, 1H), 6.84 (d, *J* = 8.24 Hz, 1H), 6.78 (dd, *J* = 8.18, 2.12 Hz, 1H), 6.60 (s, 1H), 6.53 (d, *J* = 2.17 Hz, 1H), 4.65 (s, 1H), 4.20 (s, 2H), 4.10 (s, 1H), 3.92 (d, *J* = 5.61 Hz, 2H), 3.86 (d, *J* = 5.61 Hz, 2H), 1.73 (m, 2H), 1.60 – 1.23 (m, 18H), 1.02 – 0.80 (m, 12H).

^{13}C-NMR (126 MHz, acetonitrile-d_3) δ 153.73, 153.64, 146.14, 146.09, 138.44, 136.40, 134.15, 133.44, 132.89, 132.69, 132.20, 131.43, 127.16 (q, J = 4.93 Hz), 125.56, 124.52 (q, J = 5.15 Hz), 123.72, (q, J = 271.11 Hz) 123.64 (q, J = 272.23 Hz), 117.29, 116.62, 116.35 (q, J = 30.25 Hz), 116.08 (q, J = 29.13 Hz), 115.77, 114.36, 111.94, 110.85, 108.29, 70.79, 70.58, 45.11, 39.27, 39.23, 30.42, 30.31, 28.83, 28.77, 23.81, 23.70, 22.77, 13.36, 13.36, 10.51, 10.45.

^{19}F-NMR (565 MHz, methanol-d_4) δ -63.51, -63.60.

HRMS(ES+): Calculated for $C_{43}H_{53}F_6N_2O_4$ 775.3910 a.m.u.; found 775.3895

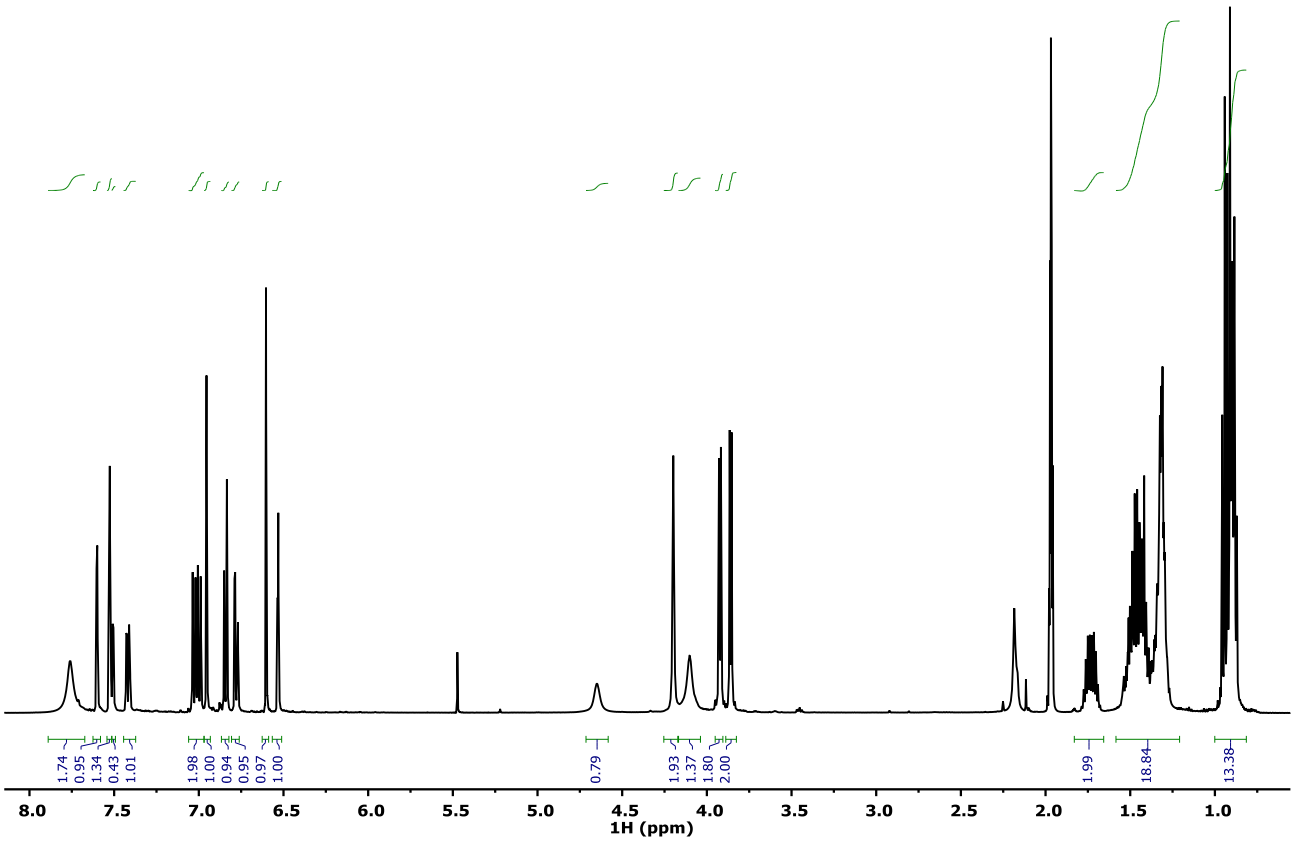


Figure S4.11. ^{1}H-NMR spectrum (500 MHz, acetonitrile-d_3) of **DD$_{NH2}$**.

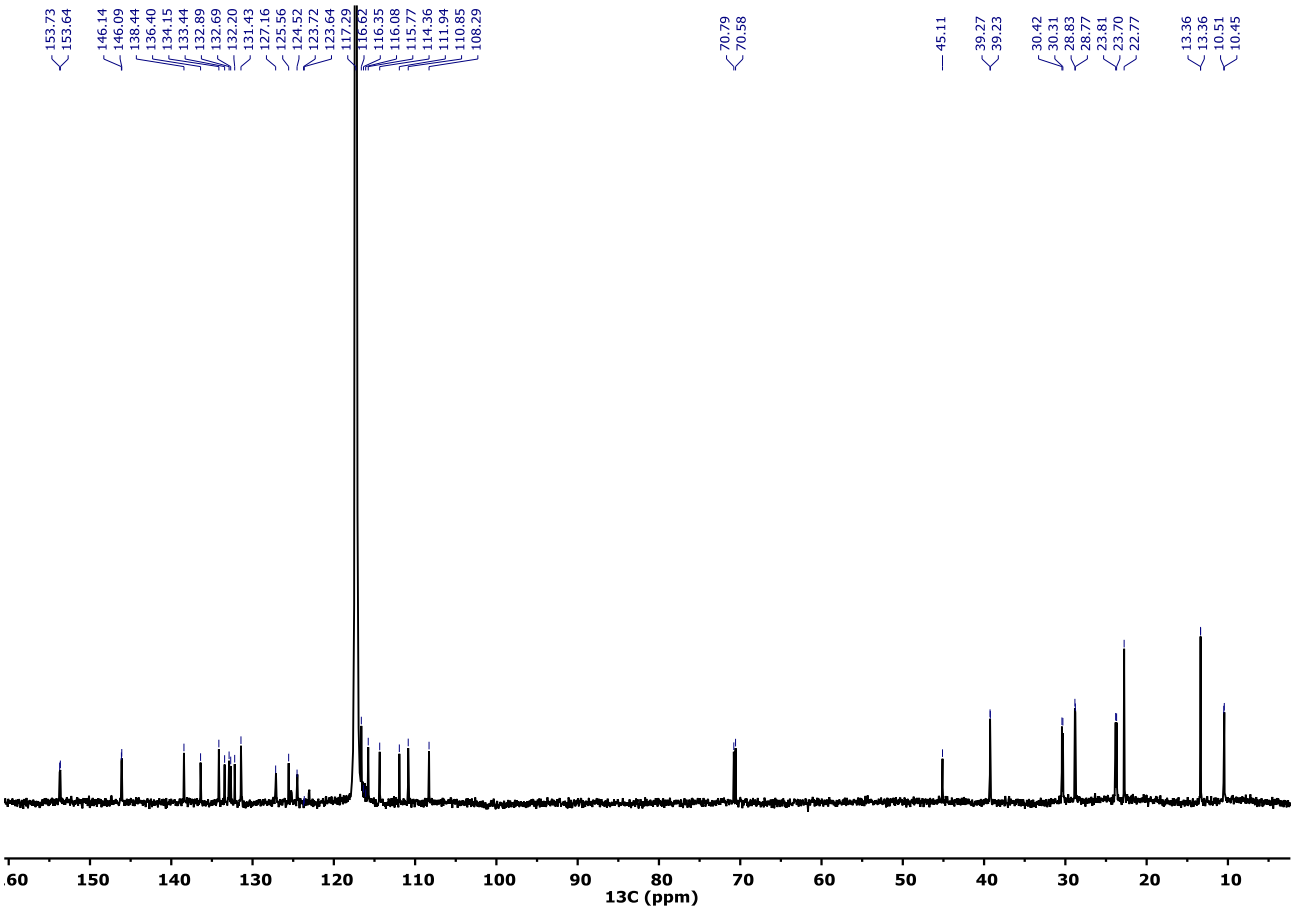


Figure S4.12. ^{13}C-NMR spectrum (126 MHz, acetonitrile-d_3) of **DD$_{NH2}$**.

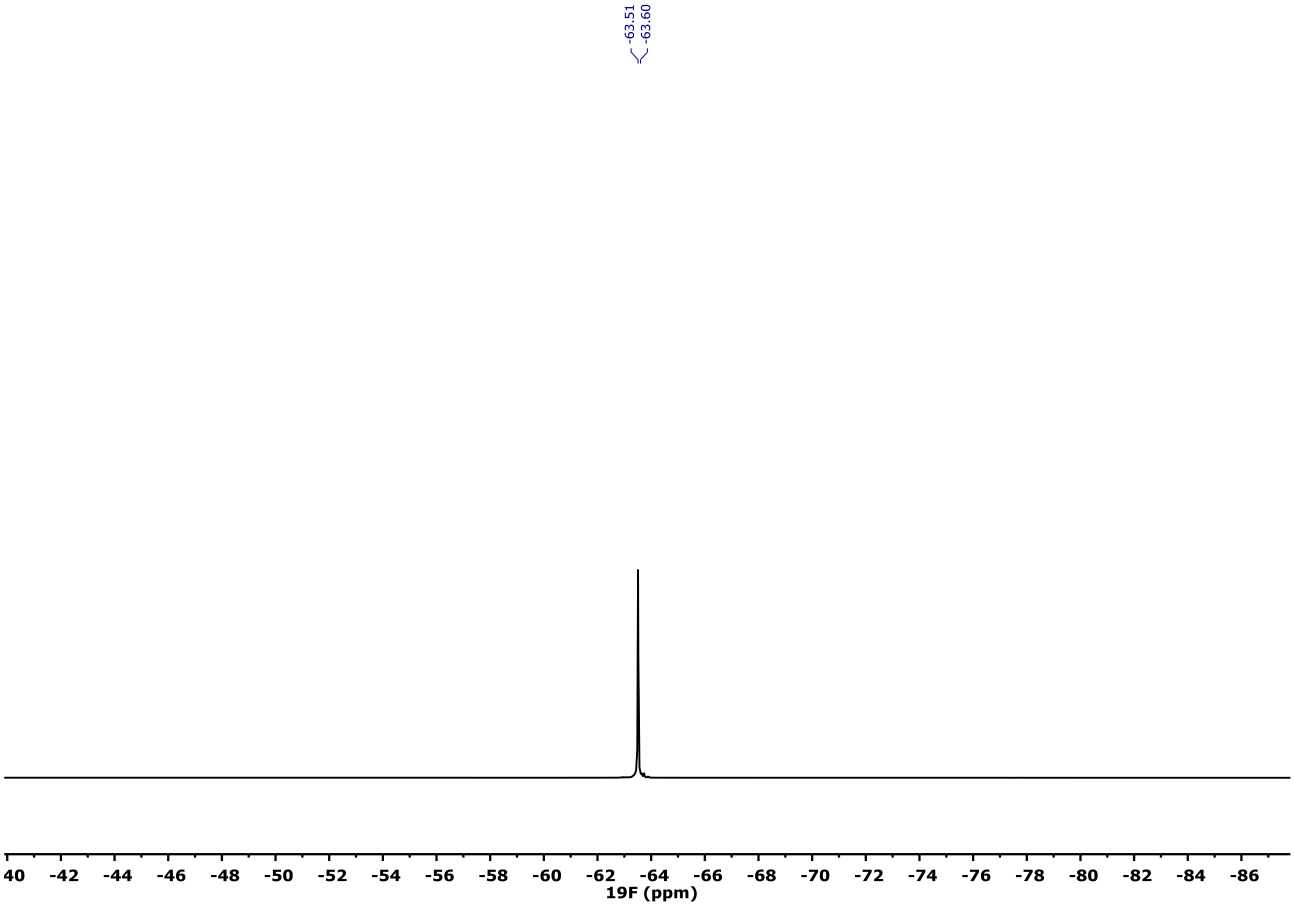


Figure S4.13. ^{19}F-NMR spectrum (565 MHz, methanol-d_4) of **DD$_{NH2}$**.

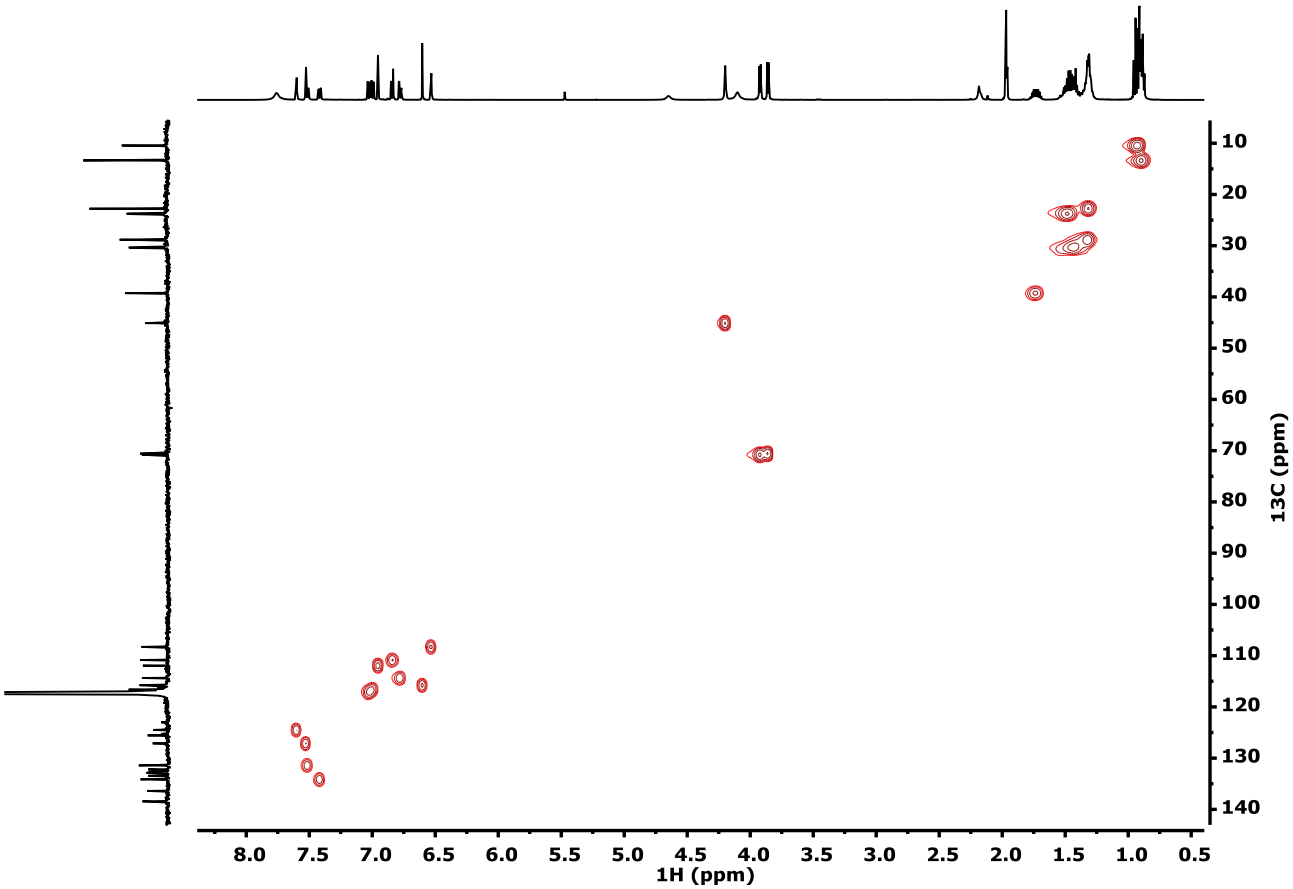


Figure S4.14. ^{1}H-^{13}C HSQC spectrum (500 MHz, acetonitrile-d_3) of **DD$_{NH2}$**.

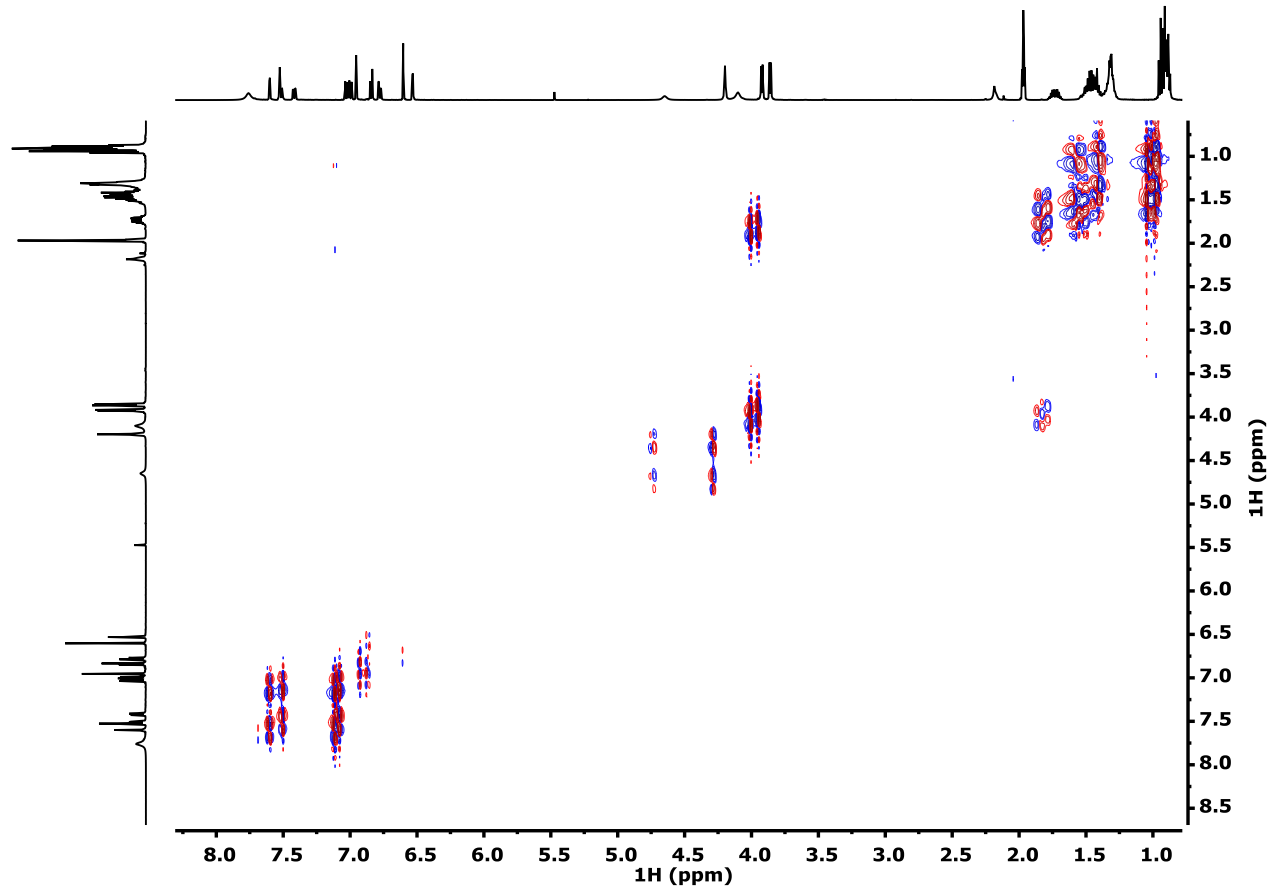
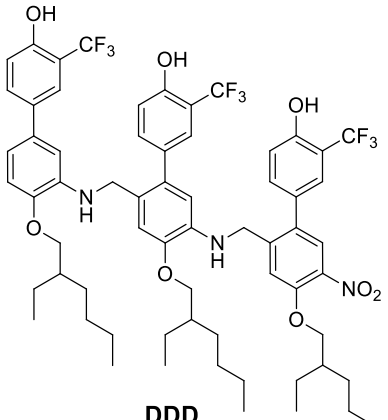


Figure S4.15. ^{1}H-^{1}H COSY spectrum (500 MHz, acetonitrile-d_3) of $\mathbf{DD_{NH2}}$.

4.4 Synthesis of DDD



DDD

Trimer **DDD** was synthesized via one step reductive amination. Dimer $\mathbf{DD_{NH2}}$(24 mg, 0.031 mmol, 1 equiv) and $\mathbf{D'_{CO2}}$ (40.8 mg, 0.093 mmol, 3 equiv) were dissolved in a 2 mL vial with dry toluene (0.5 mL). The mixture was stirred over weekend, then $NaBH(OAc)_3$ (32.8 mg, 0.156 mmol, 5 equiv) was added and the mixture stirred for 2 h until complete reduction of the imine (confirmed by ^{1}H-NMR). Then, a saturated solution of NaCl was added and the mixture was stirred until complete solubilisation. Hence, the organic phase was extracted, and the aqueous phase was washed (3x) with EtOAc. The organic layers were collected and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified via flash chromatography (gradient PE:Et_2O 6:4 to Et_2O), giving the desired trimer (24.9 mg, 67 % yield).

^{1}H-NMR (600 MHz, acetonitrile-d_3) δ) δ 7.70 (s, 1H), 7.57 (d, *J* = 2.18 Hz, 1H), 7.50 (d, *J* = 1.96 Hz, 1H), 7.48 (dd, *J* = 8.50, 2.18 Hz, 2H), 7.38 (dd, *J* = 8.12, 2.04 Hz, 2H), 7.34(s, 1H), 7.27 (dd, *J* = 8.34, 2.02 Hz, 1H), 7.09 – 6.95 (m, 3H), 6.95 (s, 1H), 6.83 (d, *J* = 8.28 Hz, 1H), 6.77 (dd, *J* = 8.17, 2.18 Hz, 1H), 6.50 (d, *J* = 2.07 Hz, 1H), 6.10 (s, 1H), 5.00 (t, *J* = 6.27 Hz, 1H), 4.62 (s, 1H), 4.33 (d, *J* = 6.10 Hz, 2H), 4.17 (d, *J* = 5.01Hz, 2H), 3.93 (d, *J* = 5.56 Hz, 2H), 3.92 – 3.890(m, 2H), 3.87 (d, *J* = 5.67 Hz, 2H), 1.79 – 1.69 (m, 2H), 1.69 – 1.61 (m, 1H), 1.59 – 1.19 (m, 30H), 0.97 – 0.76 (m, 18H).

^{13}C-NMR ^{13}C NMR (101 MHz, chloroform-*d*) δ 153.32, 152.53, 152.22, 152.20, 146.36, 146.07, 144.05, 138.40, 138.27, 136.63, 134.74, 134.07, 133.77, 132.51, 132.44, 131.64, 131.51, 130.72, 127.46 (q, J = 5.34 Hz), 127.22 (q, J = 4.90 Hz), 127.18, 125.42, 124.85 (q, J = 4.94 Hz), 122.84, 122.67, 122.40, 121.38, 118.08, 117.88, 117.59, 116.83(q, J = 30.06 Hz), 116.58 (q, J = 30.42 Hz), 116.27 (q, J = 30.63 Hz), 114.95, 113.87, 111.66, 110.84, 110.44, 108.67, 71.99, 70.95, 70.91, 62.86, 46.31, 45.88, 39.32, 39.25, 34.83, 30.66, 30.64, 30.27, 29.05, 29.03, 28.95, 24.08, 23.63, 23.02, 22.94, 18.88, 14.02, 14.02, 14.01, 11.11, 11.08, 11.04.

^{19}F-NMR (565 MHz, chloroform-*d*) δ -60.72, -60.73, -60.95.

HRMS(ES+): Calculated for $C_{65}H_{77}F_9N_3O_8$ 1198.5567 a.m.u.; found 1198.5594

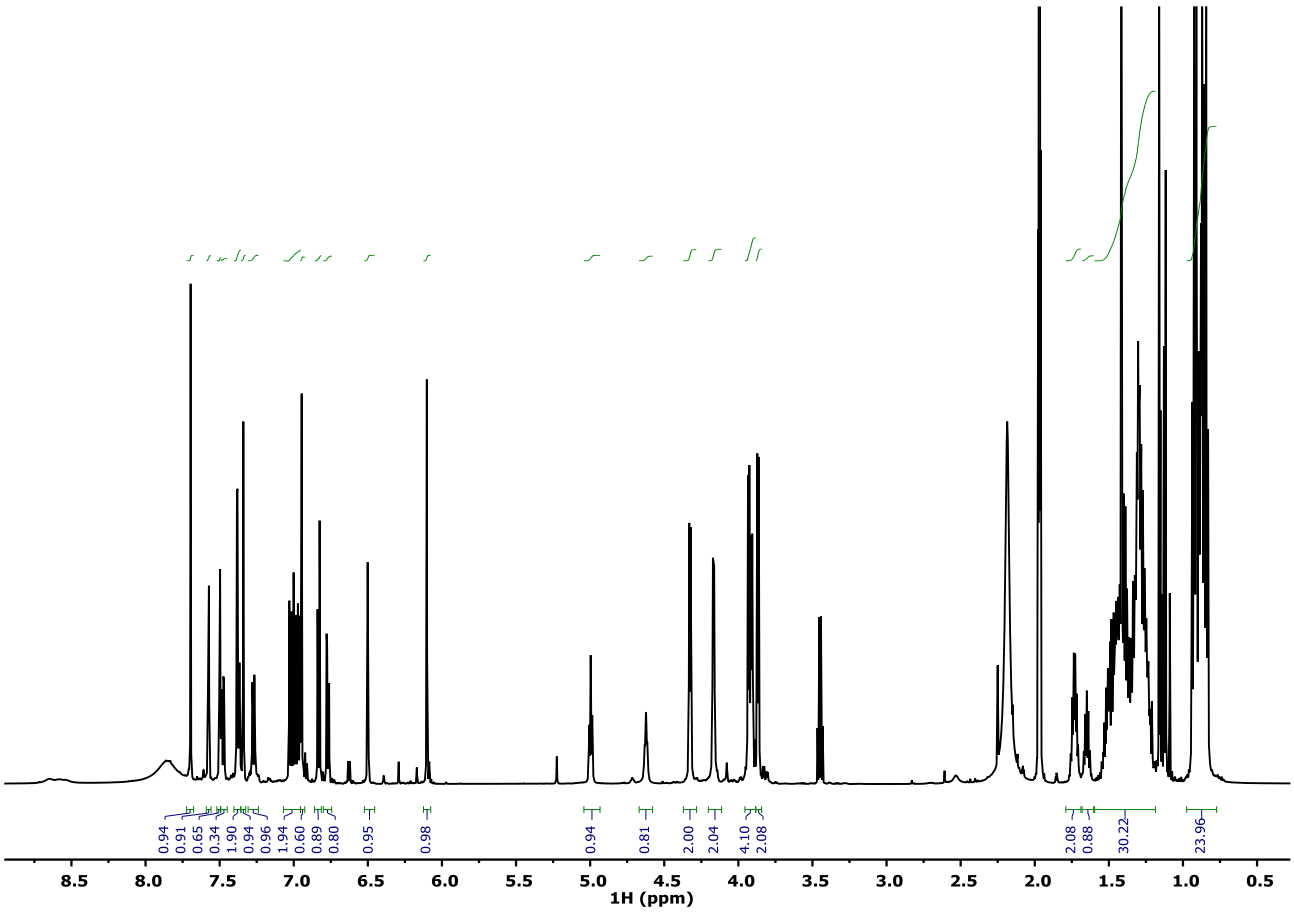


Figure S4.16. ^{1}H-NMR spectrum (600 MHz, acetonitrile-d_3) of **DDD**.

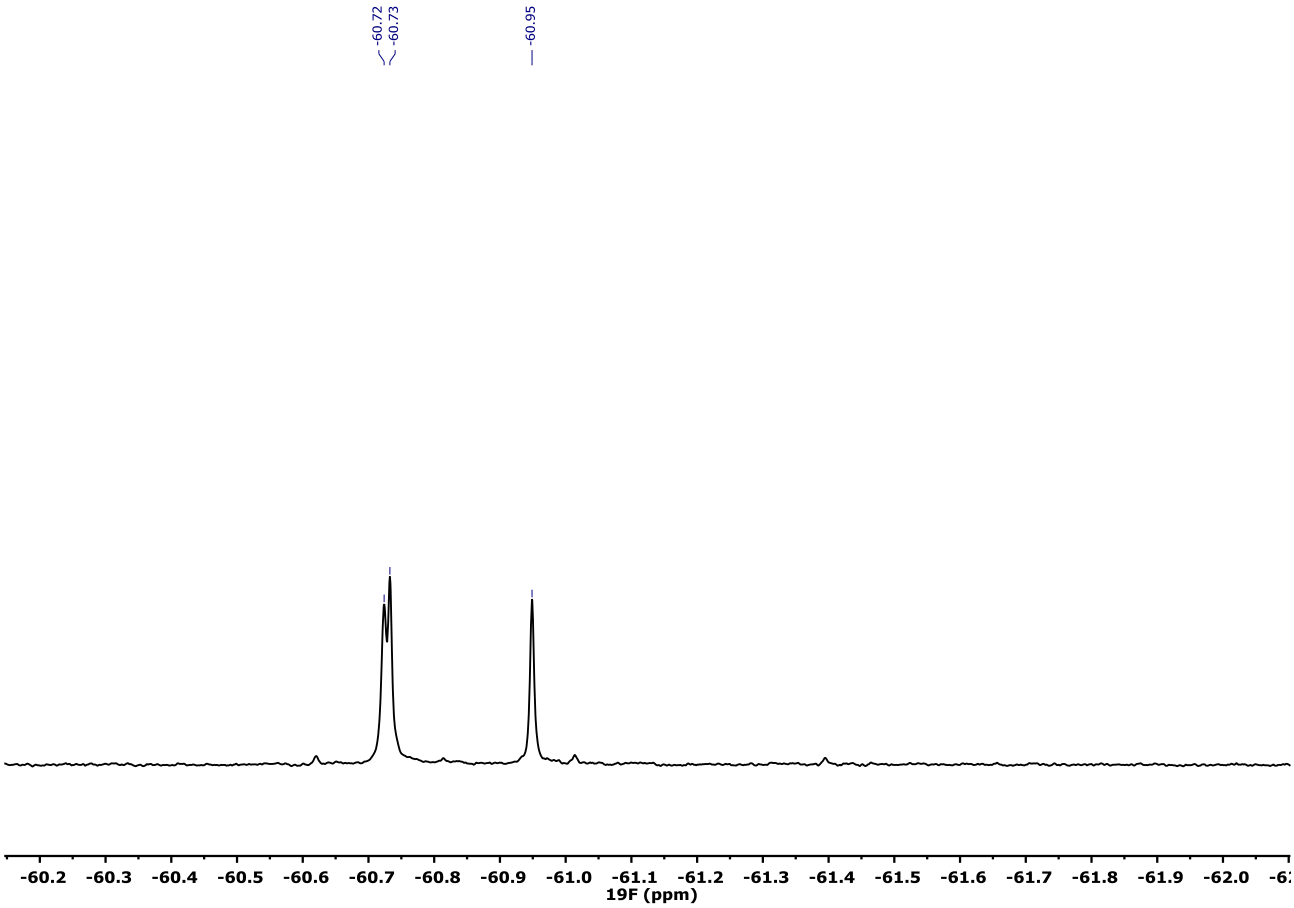
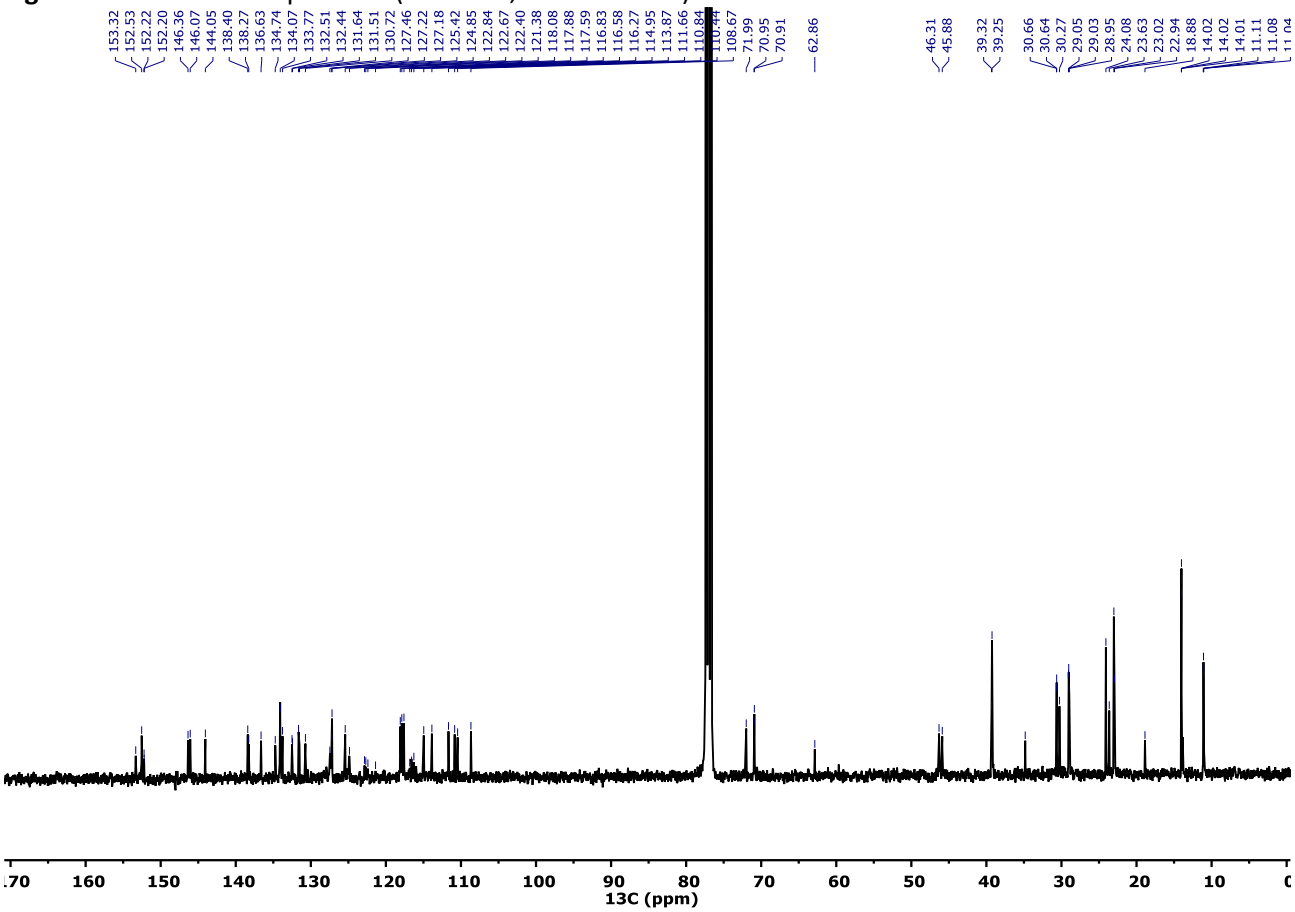


Figure S4.17. ^{19}F-NMR spectrum (565 MHz, chloroform-*d*) of **DDD**.



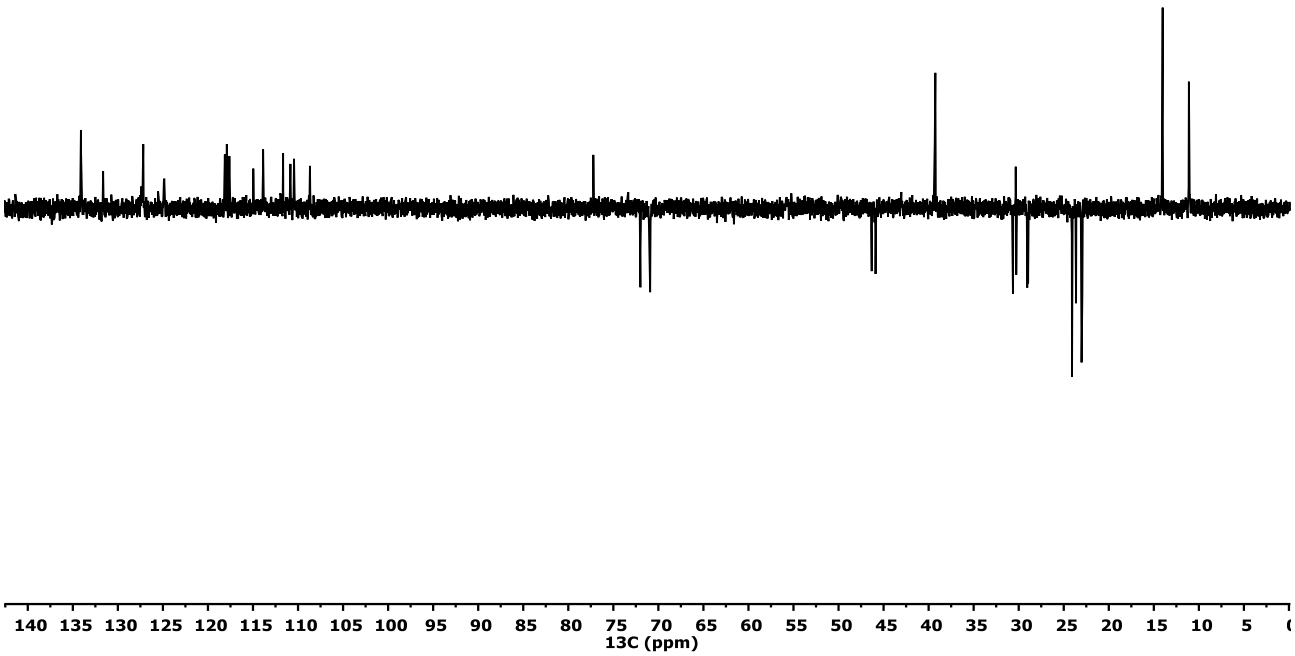


Figure S4.18. ^{13}C-NMR and DEPT spectra (101 MHz, chloroform-*d*) of **DDD**.

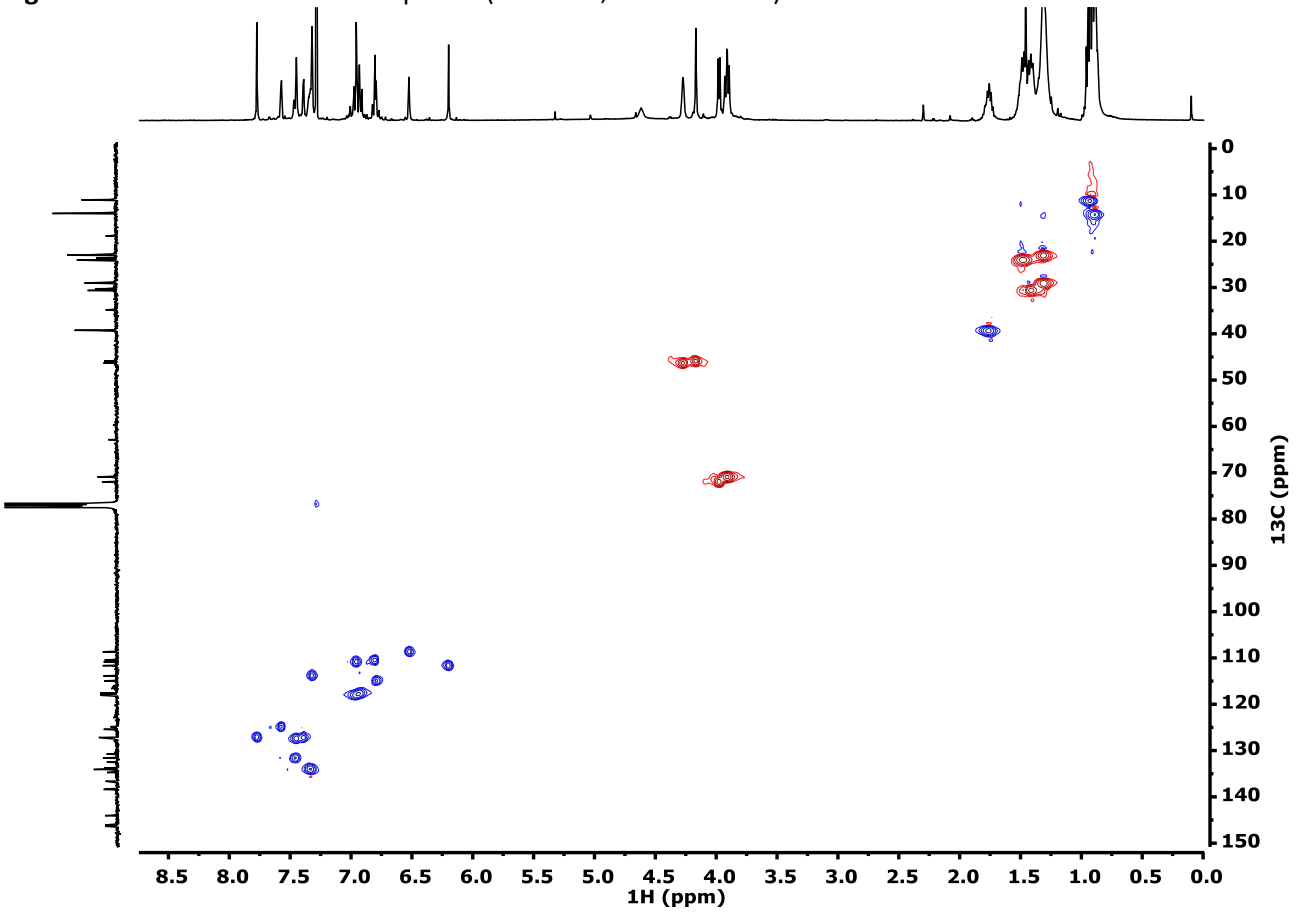


Figure S4.19. ^{1}H-^{13}C HSQC spectrum (400 MHz, chloroform-*d*) of **DDD**.

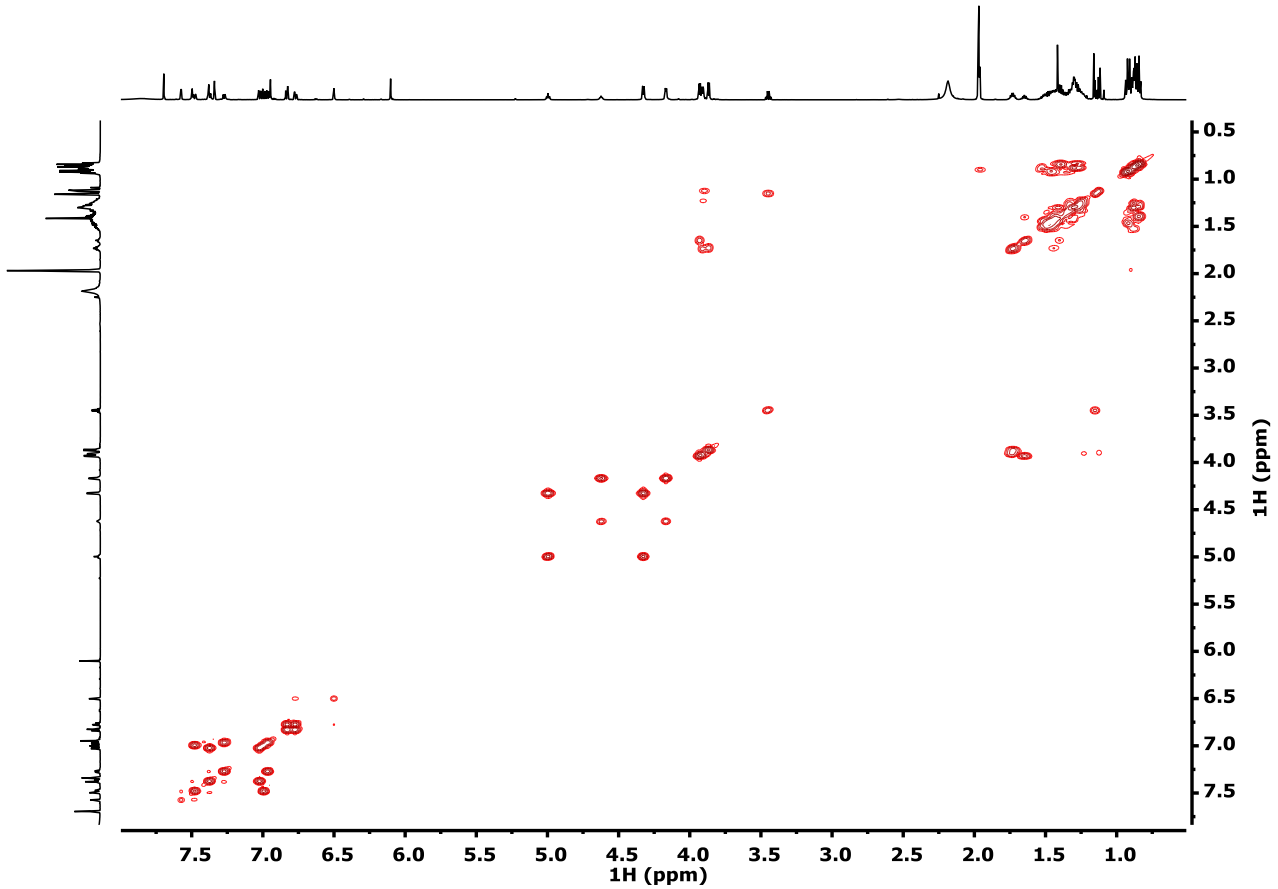


Figure S4.20. ^{1}H-^{1}H COSY spectrum (400 MHz, chloroform-*d*) of **DDD**.

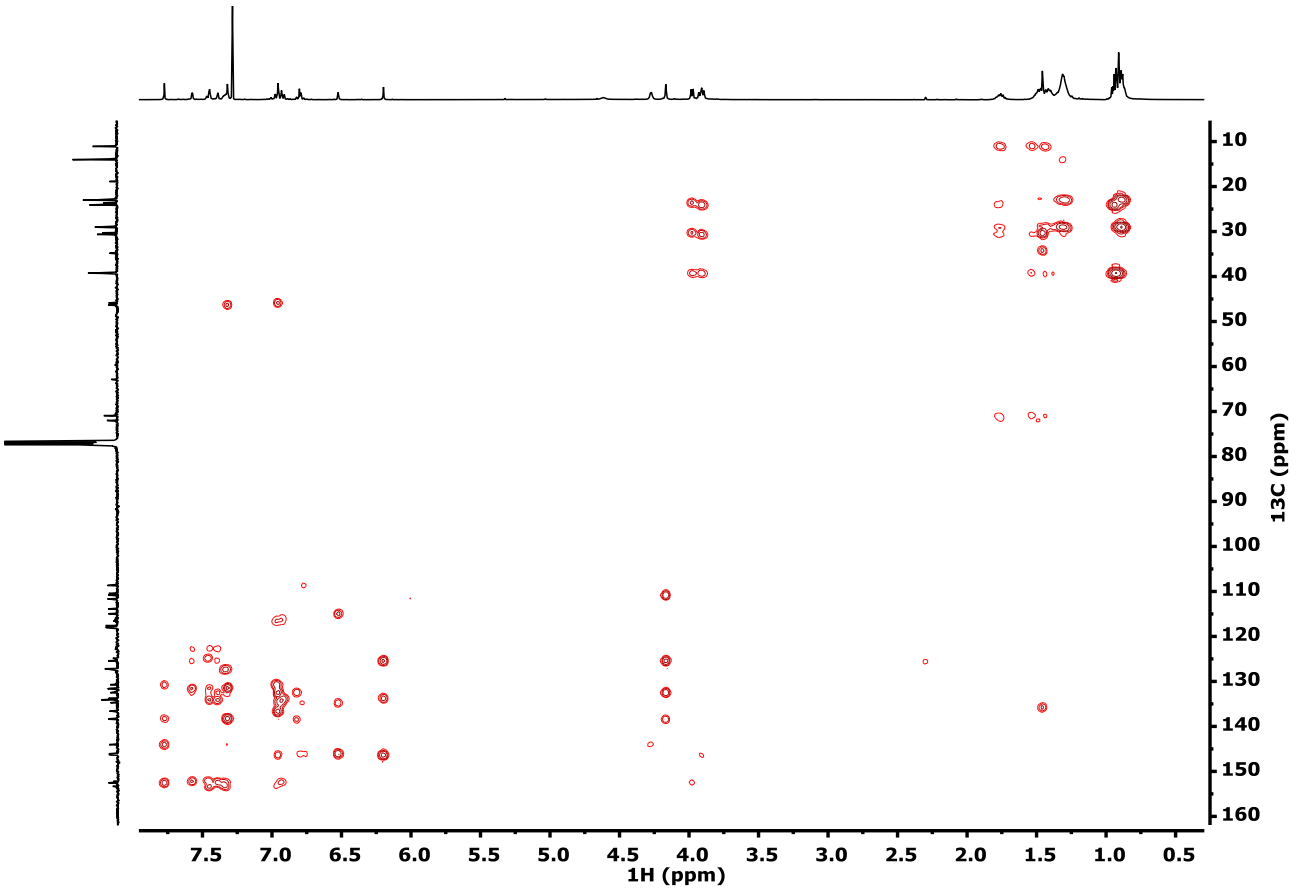


Figure S4.21. ^{1}H-^{13}C HMBC spectrum (400 MHz, chloroform-*d*) of **DDD**.

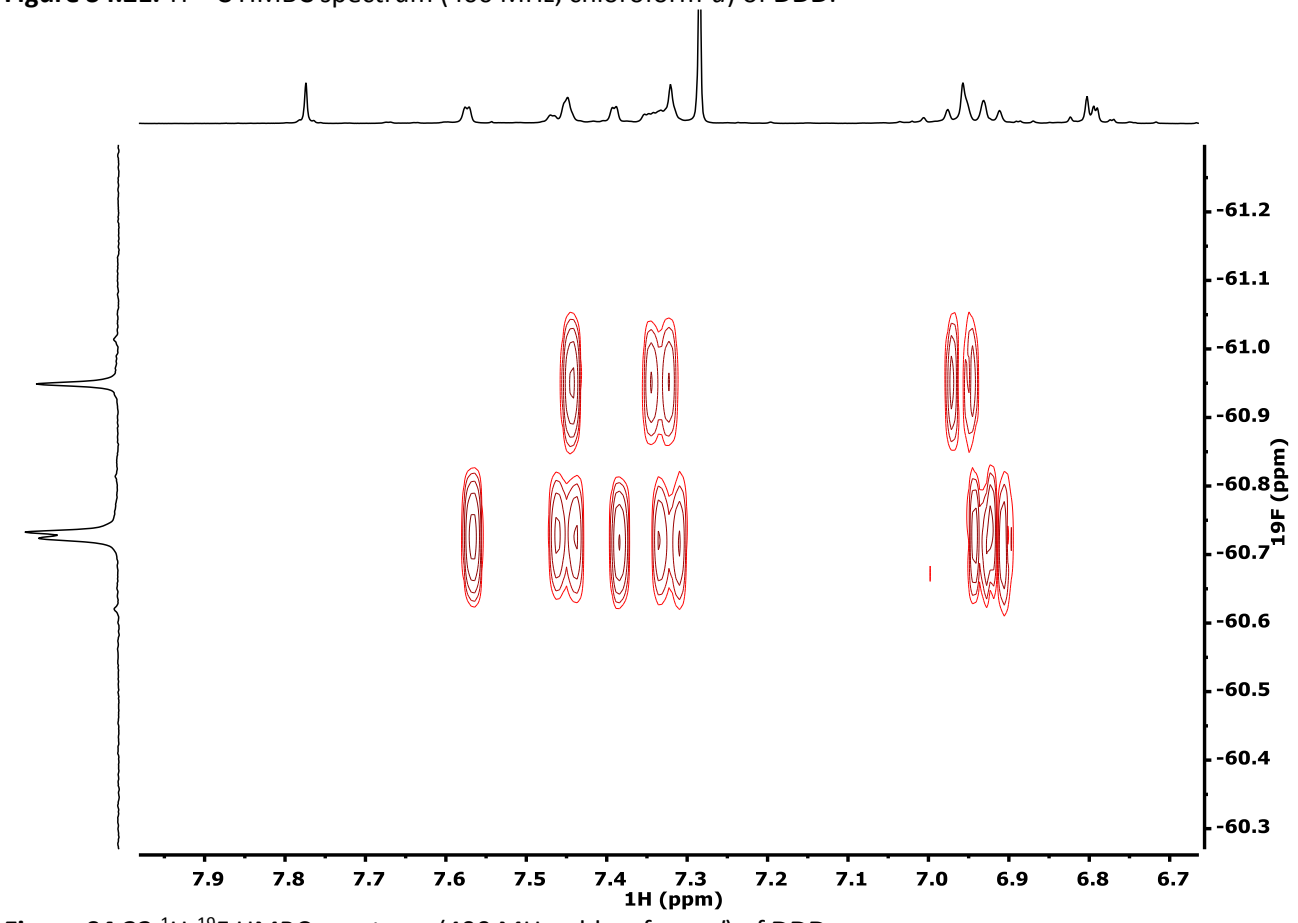
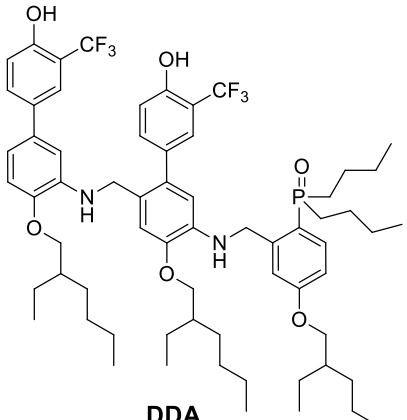


Figure S4.22. ^{1}H-^{19}F HMBC spectrum (400 MHz, chloroform-*d*) of **DDD**.

4.5 Synthesis of DDA



DDA

Trimer **DDA** was synthesized via one step reductive amination. Dimer $\mathbf{DD_{NH2}}$ (28.0 mg, 0.036 mmol, 1 equiv) and $\mathbf{A_{co}}$ (28.5 mg, 0.124 mmol, 2 equiv) were dissolved in a 2 mL vial with dry toluene (0.5 mL). The mixture was stirred over weekend, then 38.3 mg (0.180 mmol, 5 equiv) of sodium $NaBH(OAc)_3$ were added and the reaction mixture stirred for 2 h until complete the reduction of the imine (confirmed by ^{1}H-NMR). Then, a saturated solution of NaCl was added and the mixture was stirred until complete solubilisation. Hence, the organic phase was extracted, and the aqueous phase was washed (3x) with EtOAc. The organic layers were collected and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified via flash chromatography gradient (PE: EtOAc 4:6 to EtOAc) giving the desired trimer (23.3 mg, 56 % yield).

^{1}H-NMR (600 MHz, methanol-d_4) δ 7.54 (dd, *J* = 12.11, 8.57 Hz, 1H), 7.51 (d, *J* = 2.29 Hz, 1H), 7.41 (dd, *J* = 8.49, 2.33 Hz, 1H), 7.33 (d, *J* = 2.20 Hz, 1H), 7.29 (dd, *J* = 8.34, 2.22 Hz, 1H), 7.14 (t, *J* = 2.85 Hz, 1H), 6.97 – 6.91 (m, 3H), 6.88 (d, *J* = 8.392 Hz, 1H), 6.82 (d, *J* = 8.24 Hz, 1H), 6.78 – 6.73 (m, 1H), 6.52 (d, *J* = 2.17 Hz, 1H), 6.41 (s, 1H), 4.68 (s, 2H), 4.18 (s, 2H), 3.91 (dd, *J* = 5.65, 3.39 Hz, 2H), 3.88 (d, *J* = 5.71 Hz, 2H), 3.82 (d, *J* = 5.80 Hz, 2H), 2.01 (m, 4H), 1.74 (m, 2H), 1.62 (q, *J* = 6.16 Hz, 1H), 1.57 – 1.18 (m, 40H), 0.99 – 0.83 (m, 18H), 0.80 (t, *J* = 7.25 Hz, 6H).

^{13}C-NMR (151 MHz, methanol-d_4) δ 162.28, 154.59, 154.41, 146.38 (d, J = 8.41 Hz), 146.14 (d, J = 9.96 Hz), 138.15, 136.59, 133.67 (d, J = 13.35 Hz), 133.55, 132.85, 132.72, 132.29, 128.53, 127.81, 126.91 (q, J = 5.34 Hz), 124.67 (q, J = 271.18 Hz), 124.32 (q, J = 272.01 Hz) 124.07 (q, J = 4.86 Hz), 123.88, 119.24, 118.61, 116.61, 116.38 (d, J = 29.36 Hz), 116.33 (d, J = 30.12 Hz), 116.07, 115.14 (d, J = 11.13 Hz), 114.53, 112.88 (d, J = 12.79 Hz), 112.07, 110.76, 110.64, 108.83, 70.71, 70.64, 70.19, 46.12, 45.40, 39.38, 39.28, 39.01, 30.52, 30.38, 30.16, 29.60, 29.15, 28.88, 28.84, 28.70, 23.83, 23.68, 23.60, 23.50, 23.45, 23.43, 23.40, 22.72, 22.66, 13.07, 12.47, 10.22.

^{19}F-NMR (565 MHz, methanol-d_4) δ -63.43, -63.47.

^{31}P-NMR (202 MHz, methanol-d_4) δ 49.48

HRMS(ES+): Calculated for $C_{66}H_{92}F_6N_2O_6P$ 1153.6597 a.m.u.; found 1153.6548

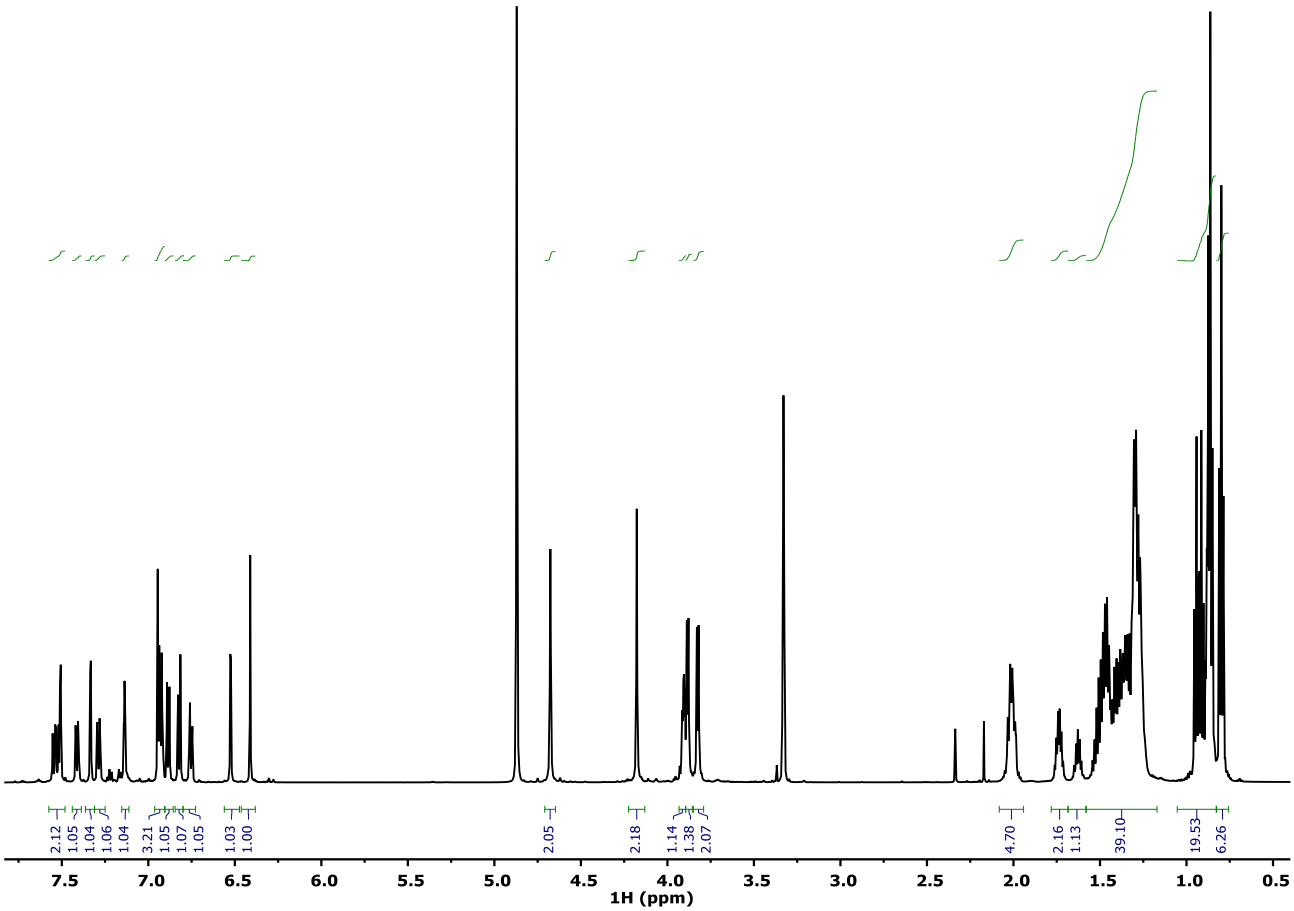


Figure S4.23. ^{1}H-NMR spectrum (600 MHz, methanol-d_4) of **DDA**.

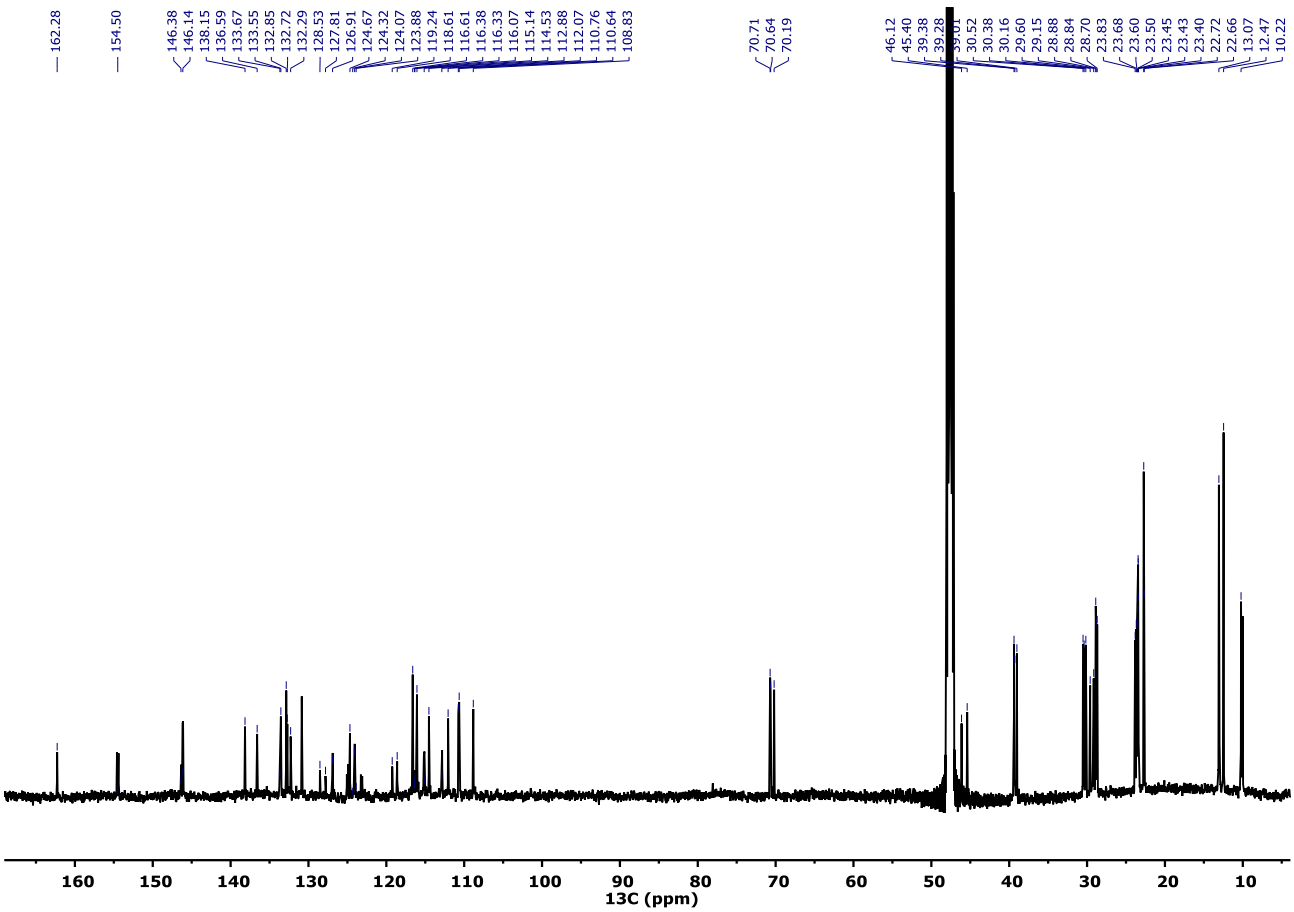


Figure S4.24. ^{13}C-NMR spectrum (151 MHz, methanol-d_4) of **DDA**.

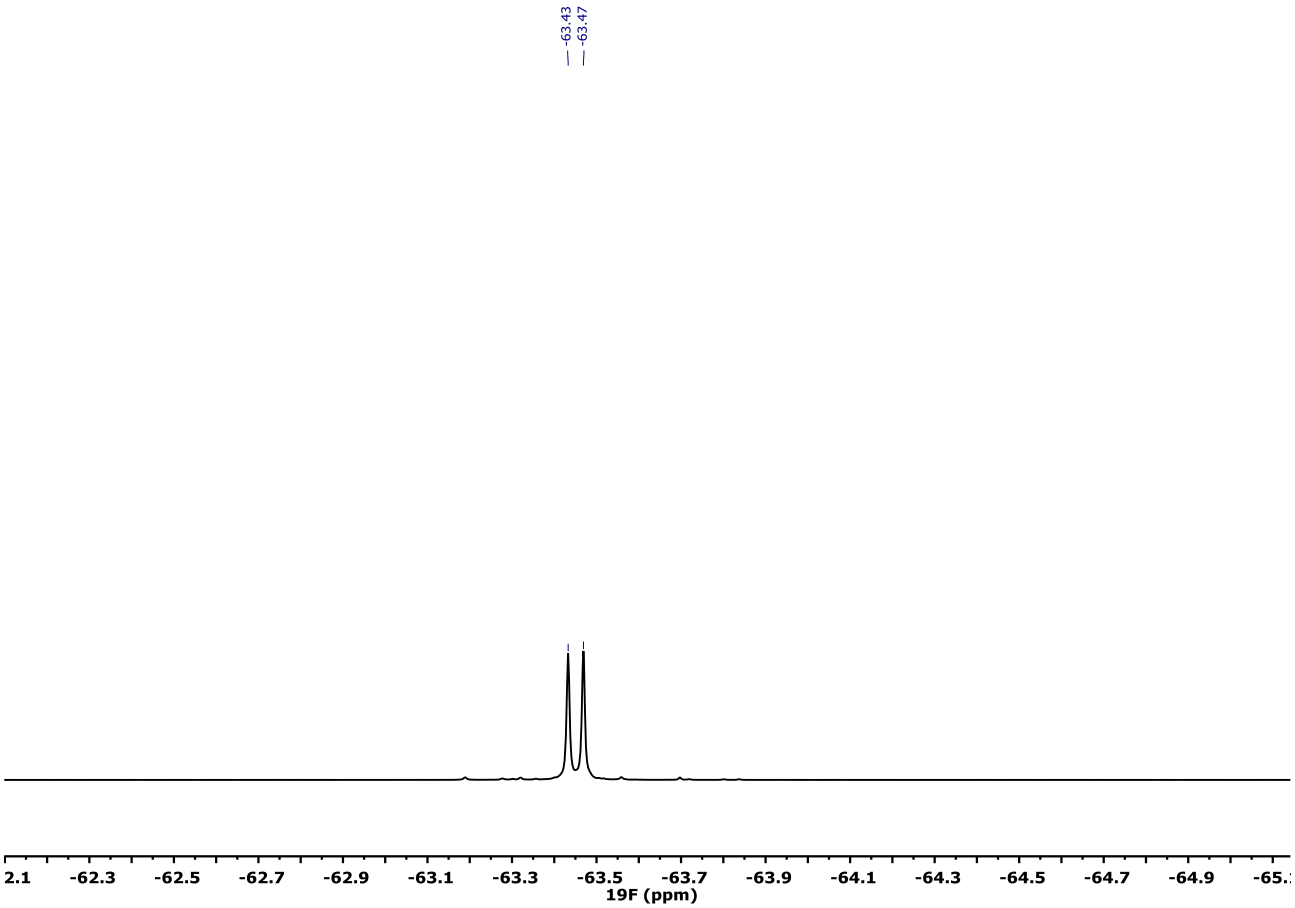


Figure S4.25 ^{19}F-NMR spectrum (565 MHz, methanol-d_4) of **DDA**.

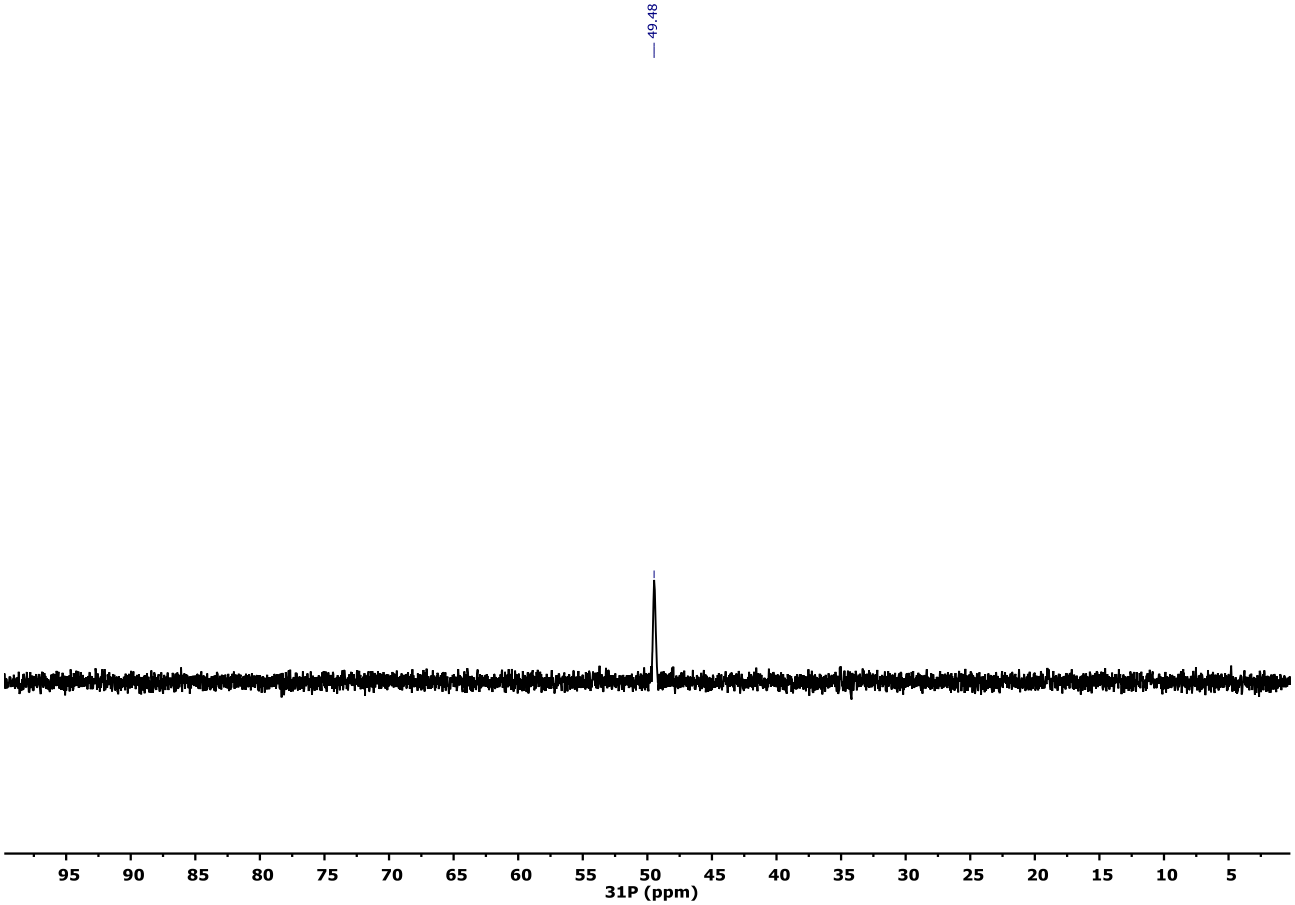


Figure S4.26. ^{31}P-NMR spectrum (202 MHz, methanol-d_4) of **DDA**.

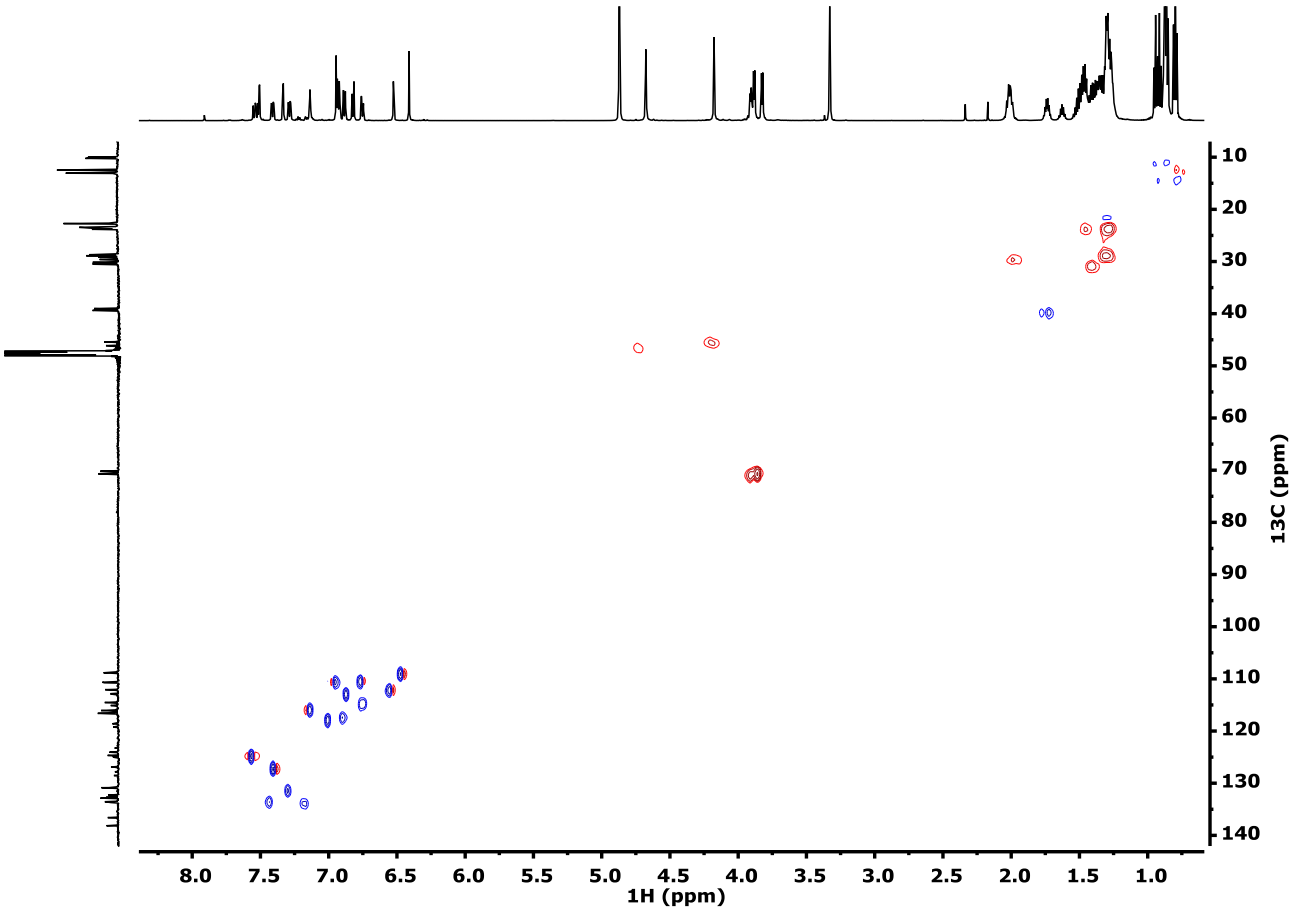


Figure S4.27. ^{1}H-^{13}C HSQC spectrum (600 MHz, methanol-d_4) of **DDA**.

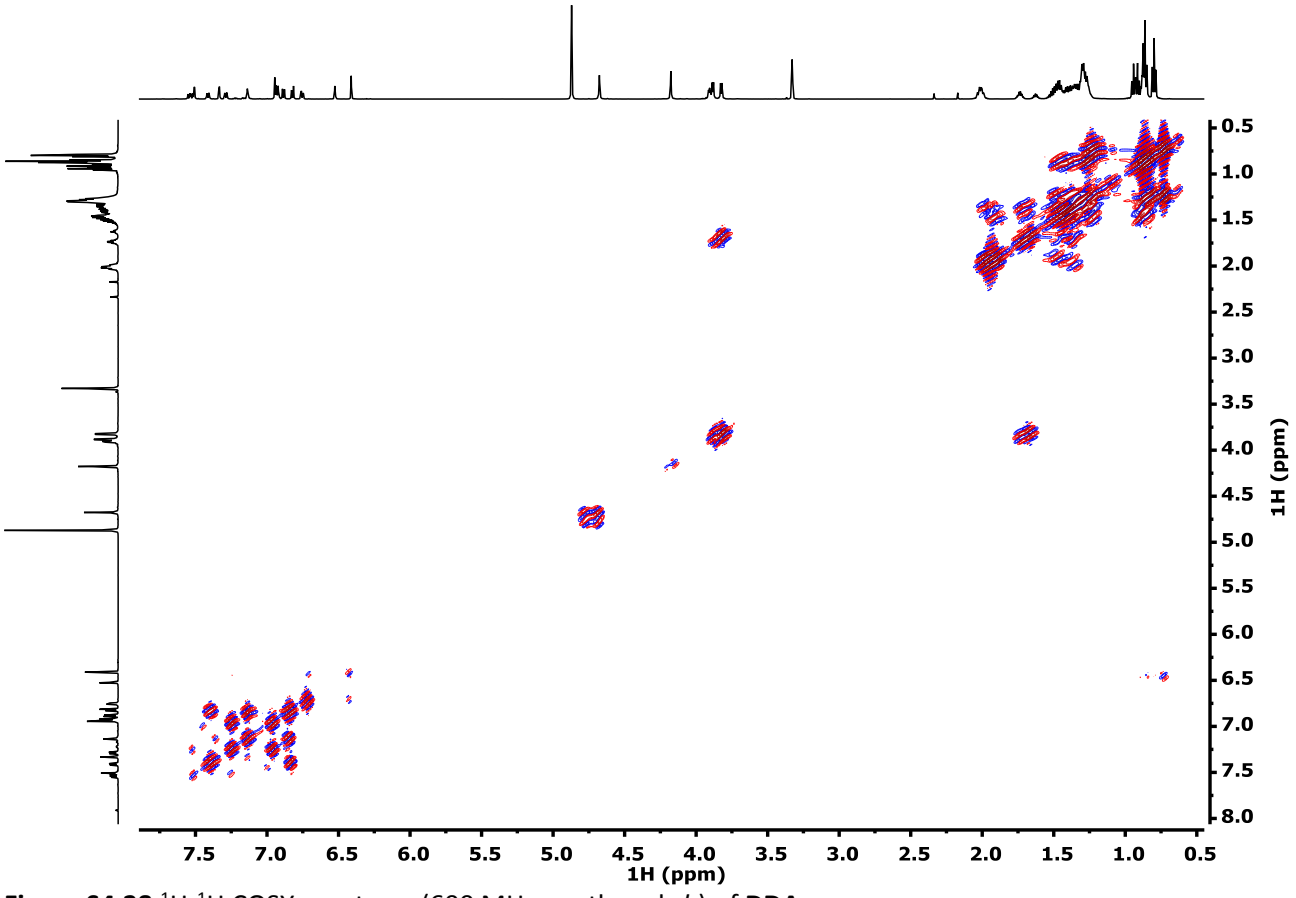


Figure S4.28. ^{1}H-^{1}H COSY spectrum (600 MHz, methanol-d_4) of **DDA**.

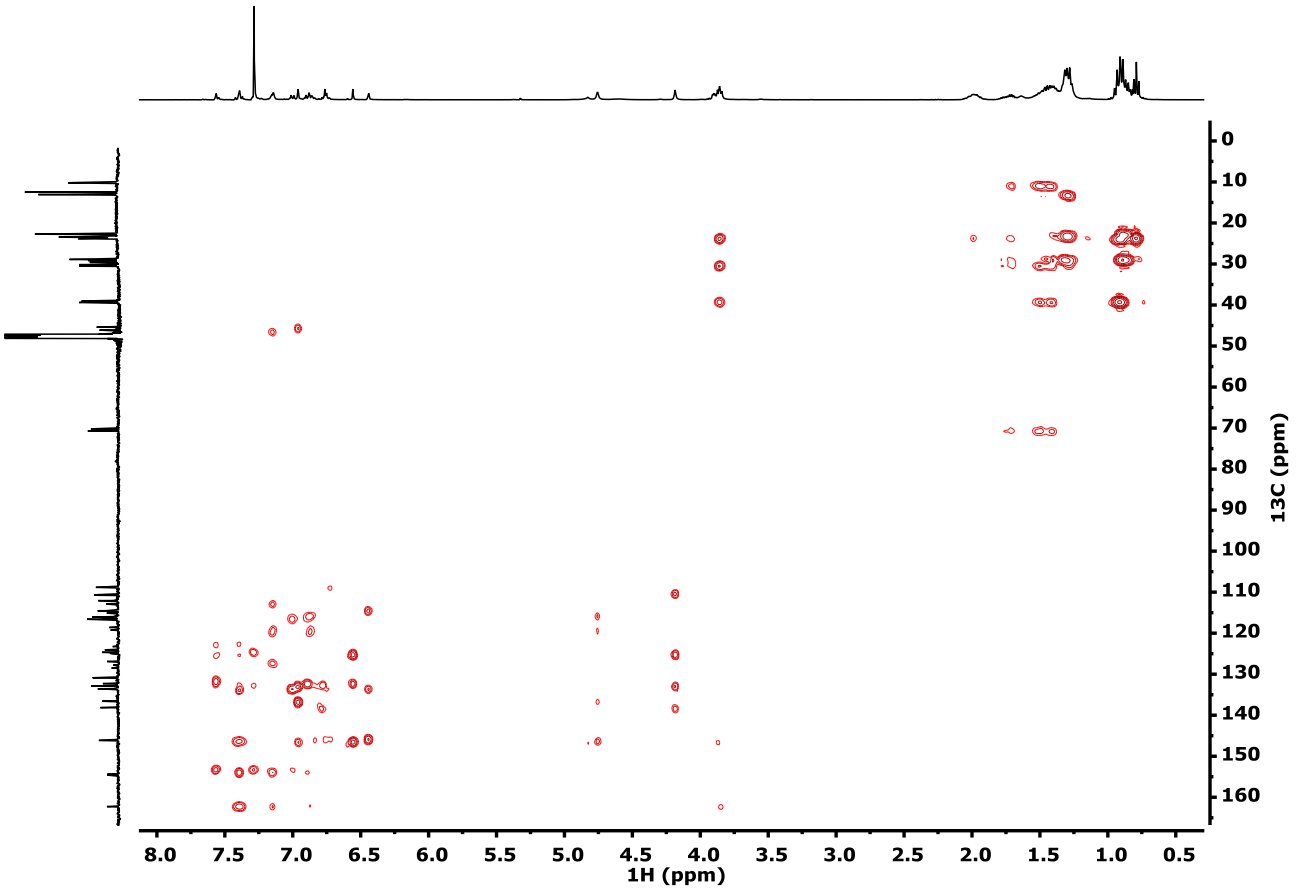


Figure S4.29. ^{1}H-^{13}C HMBC spectrum (400 MHz, chloroform-*d*) of **DDA**.

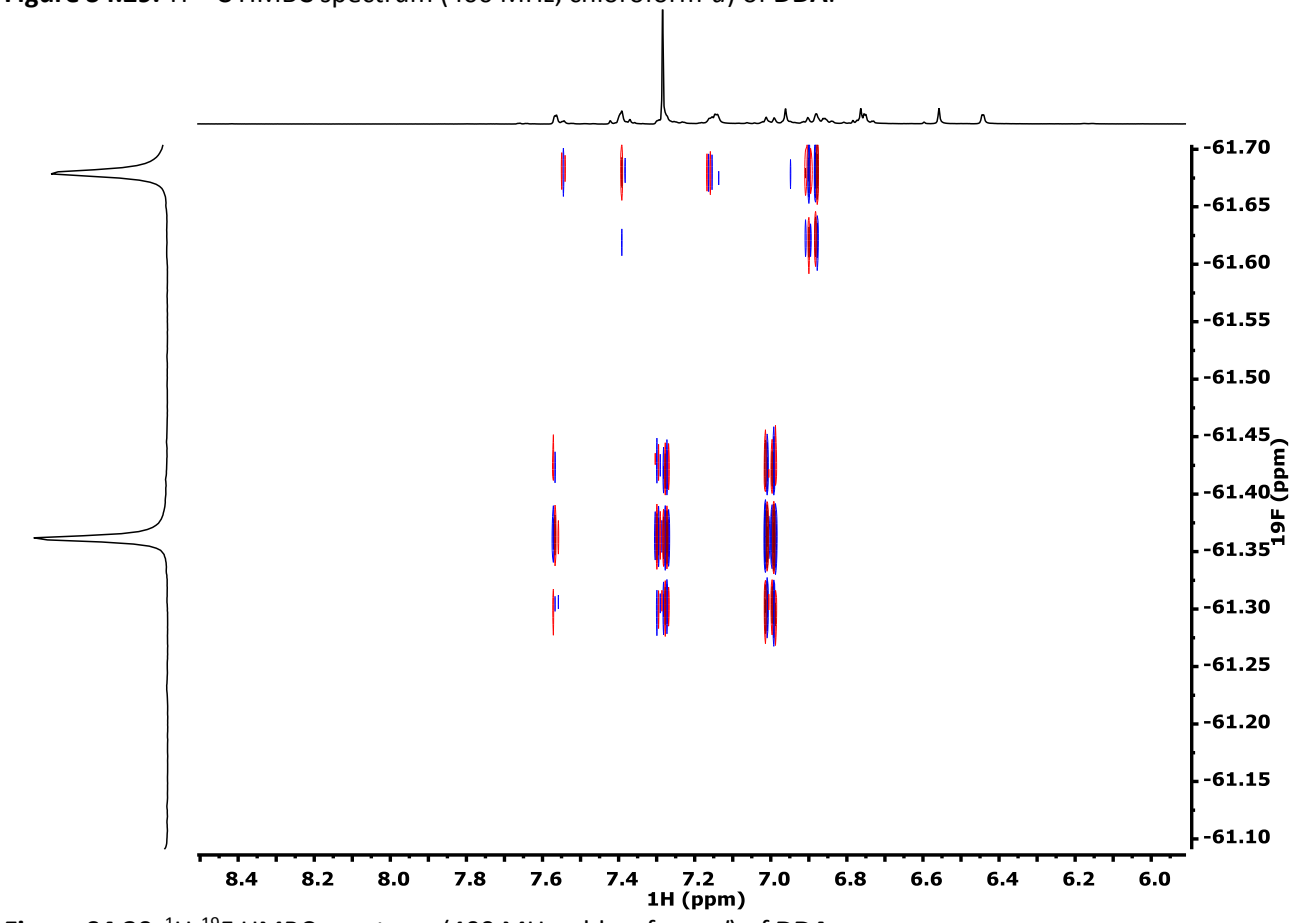
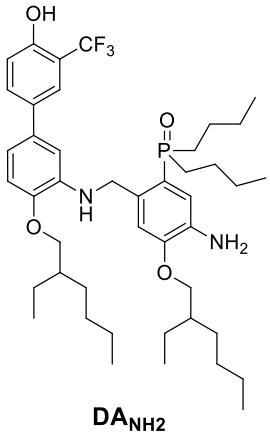


Figure S4.30. ^{1}H-^{19}F HMBC spectrum (400 MHz, chloroform-*d*) of **DDA**.

4.6 Synthesis of DA_{NH2}



DA_{NH2}

Intermediate DA_{NH2} was synthesized via one step reductive amination. Monomers **A** (68 mg, 0.166 mmol, 1 equiv) and D_{NH2} (190 mg, 0.498 mmol, 3 equiv) were dissolved in dry toluene (1 mL). The round bottom flask was equipped with a dean-stark filled with 3 Å molecular sieves and the mixture was refluxed at 120°C overnight. Then, the mixture was cooled to room temperature and 24.6 mg (0.116 mmol, 0.7 equiv) of $NaBH(OAc)_3$ were added. The mixture was let to react another day, then a second addition of $NaBH(OAc)_3$ (175.9 mg, 0.829 mmol, 5 equiv) was made to complete the reduction of the imine (confirmed by ^{1}H-NMR). Then, a saturated solution of NaCl was added and the mixture was stirred until complete solubilisation. Hence, the organic phase was extracted, and the aqueous phase was washed (3x) with EtOAc. The organic layers were collected and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified via flash chromatography (gradient PE: EtOAc 2:8 to EtOAc), giving the desired dimer (112.9 mg, 88 % yield).

^{1}H-NMR (500 MHz, methanol-d_4) δ 7.55 (d, J = 2.29 Hz, 1H), 7.52 (dd, J = 8.44, 2.37 Hz, 1H), 7.07 (d, J = 3.71 Hz, 1H), 7.00 (d, J = 12.83 Hz, 1H), 6.95 (d, J = 8.43 Hz, 1H), 6.87 (d, J = 8.12 Hz, 1H), 6.83 – 6.76 (m, 2H), 4.65 (s, 2H), 3.98 – 3.93 (m, 2H), 3.88 (d, J = 5.63 Hz, 2H), 2.03 (m, 4H), 1.79 (p, J = 6.06 Hz, 1H), 1.69 (p, J = 6.10 Hz, 1H), 1.63 – 1.17 (m, 17H), 0.97 (t, J = 7.48 Hz, 3H), 0.95 – 0.76 (m, 15H).

^{13}C-NMR (126 MHz, methanol-d_4) δ 154,45, 149.34, 146.18, 138.09, 135.74 (d, J = 14.38 Hz), 134.42 (d, J = 7.90 Hz), 134.36, 132.82 (d, J = 21.53 Hz), 130.92, 124.13 (q, J = 5.74 Hz), 123.99 (q, J = 273.35 Hz) 119.54, 118.78, 117.54 (d, J = 13.76 Hz), 116.60, 116.54 (q, J = 31.07 Hz), 114.59, 112.82 (d, J = 12.30 Hz), 110.69, 109.07, 70.50 (d, J = 31.68 Hz), 45.85, 39.49, 39.08, 30.46, 30.22, 29.77, 29.23, 28.93, 28.70, 23.72, 23.60, 23.55, 23.49, 22.74, 22.65.

^{19}F-NMR (376 MHz, methanol-d_4) δ -63.54.

^{31}P-NMR (202 MHz, methanol-d_4) δ 49.43.

HRMS(ES+): Calculated for $C_{44}H_{67}F_3N_2O_4P$ 775.4791 a.m.u.; found 775.4806

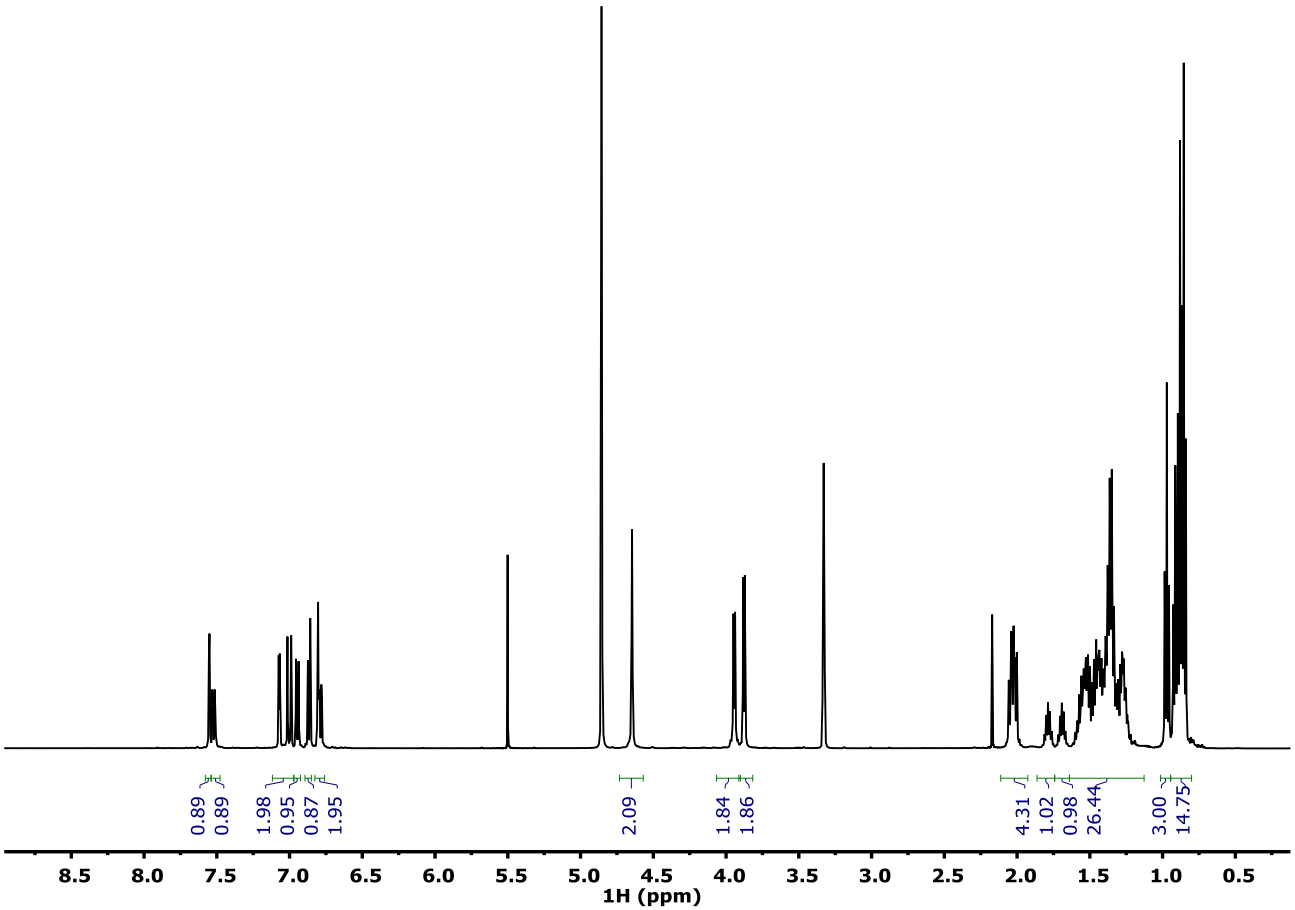


Figure S4.31. ^{1}H-NMR spectrum (500 MHz, methanol-d_4) of **DA_{NH2}**.

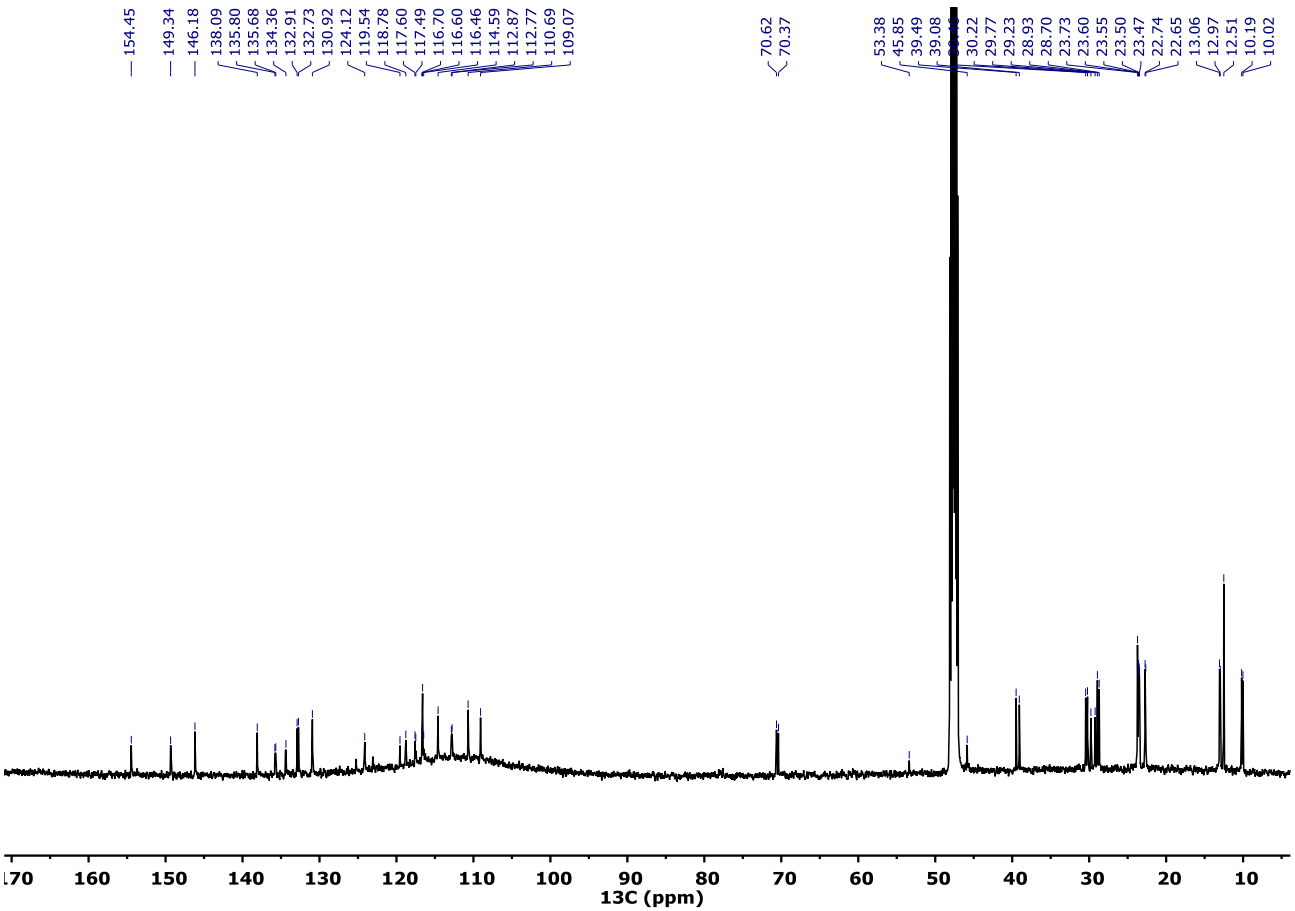


Figure S4.32. ^{13}C-NMR spectrum (126 MHz, methanol-d_4) of **DA_{NH2}**.

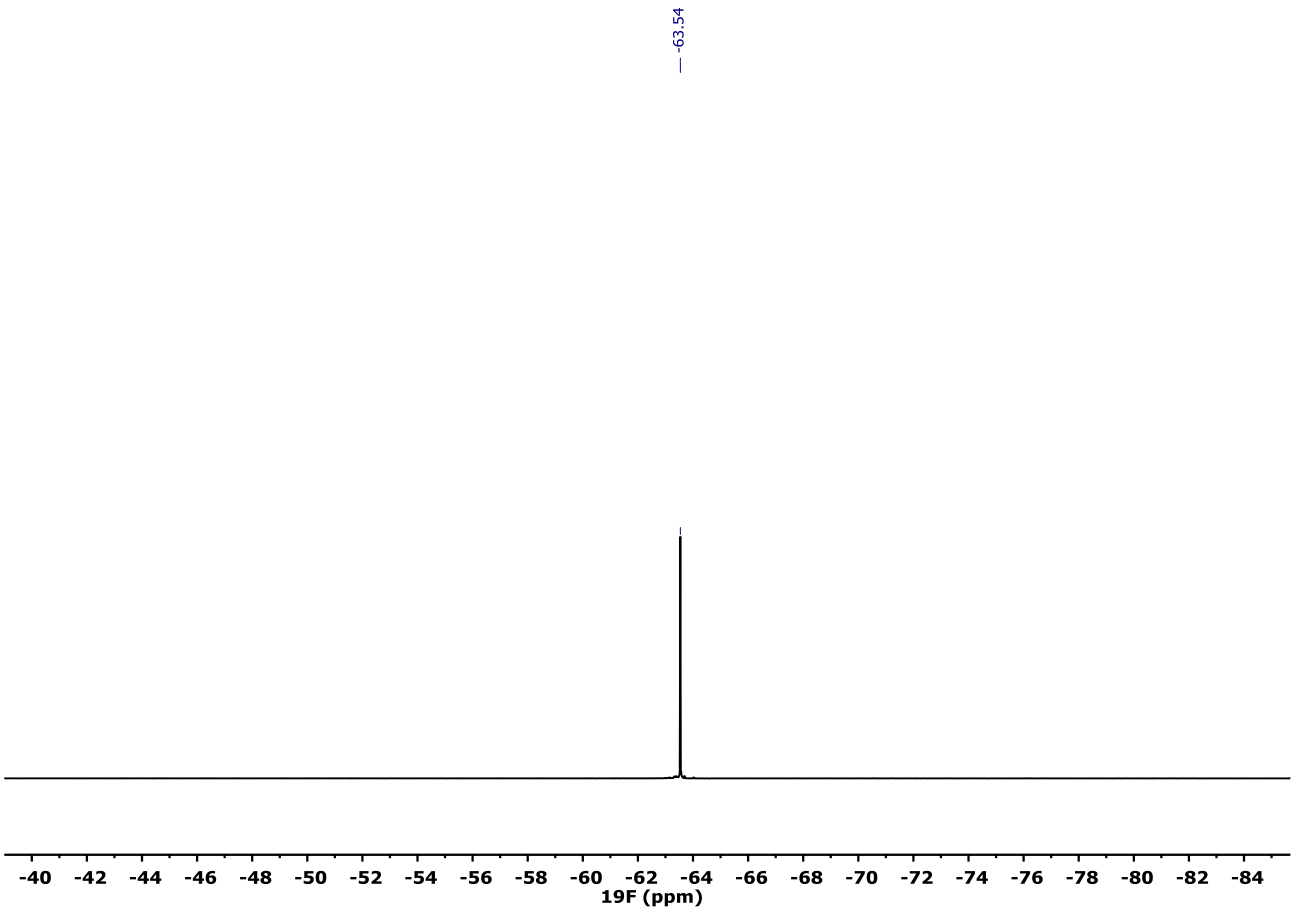


Figure S4.33. ^{19}F-NMR spectrum (376 MHz, methanol-d_4) of $\mathbf{DA_{NH2}}$.

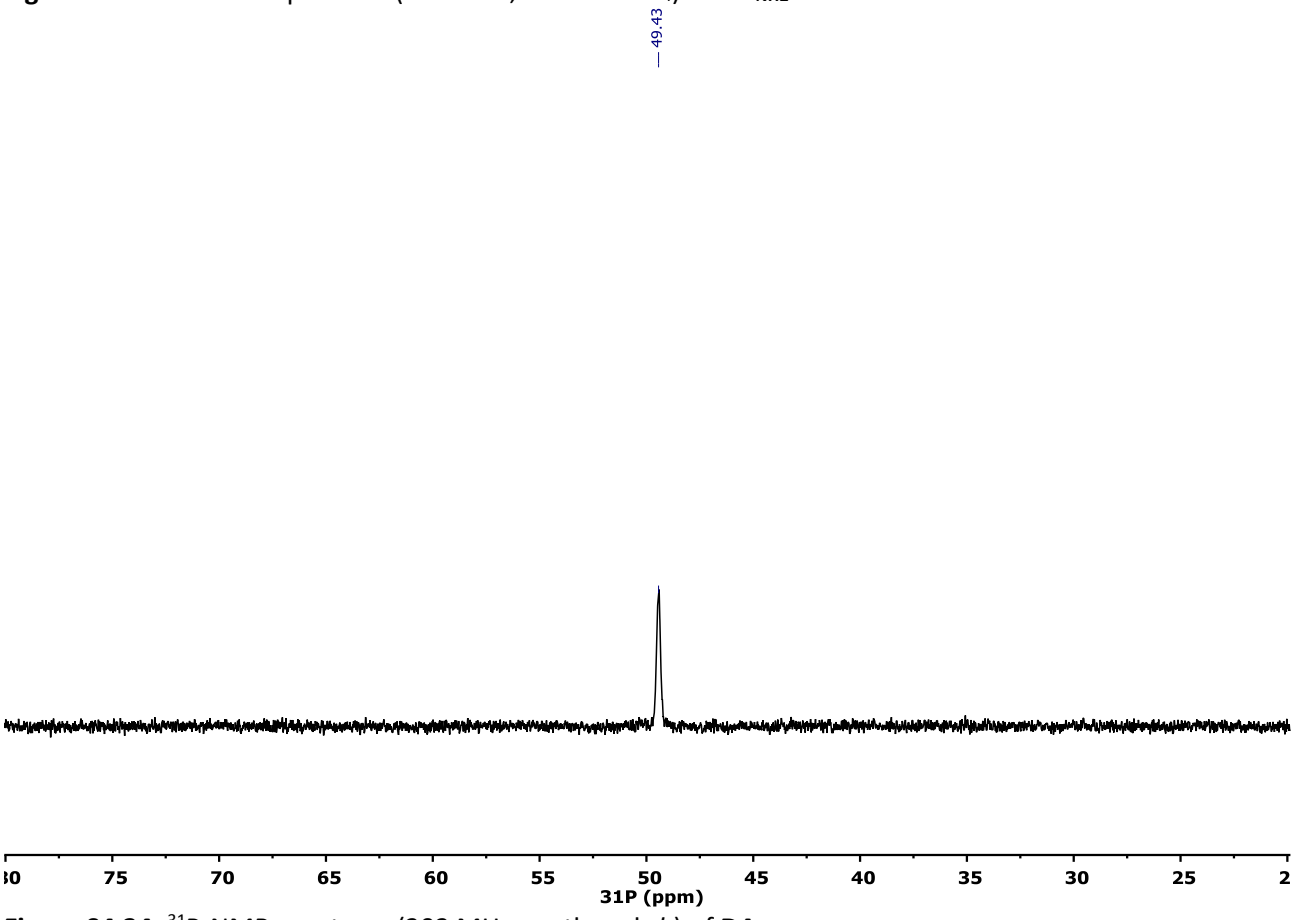


Figure S4.34. ^{31}P-NMR spectrum (202 MHz, methanol-d_4) of $\mathbf{DA_{NH2}}$.

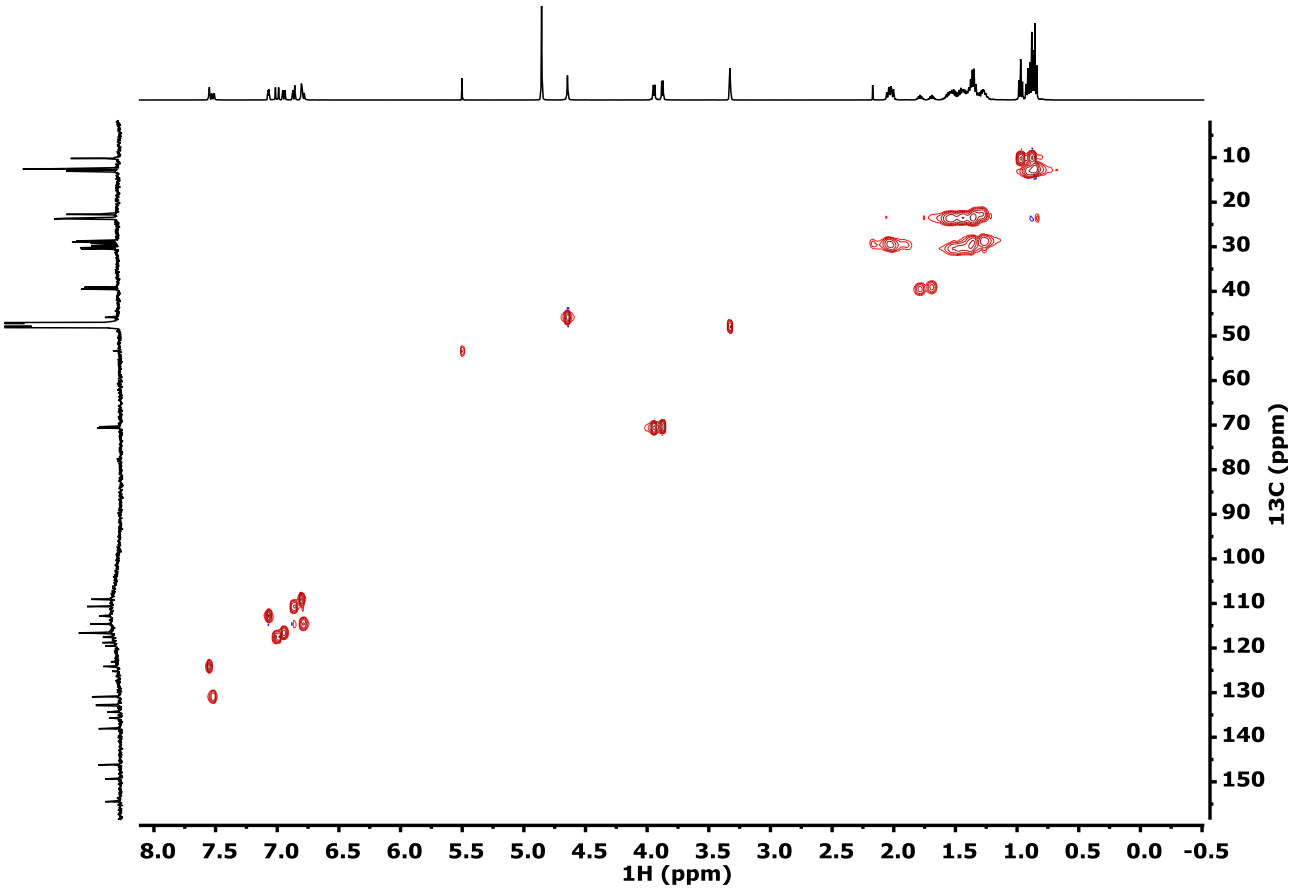


Figure S4.35. ^{1}H-^{13}C HSQC spectrum (500 MHz, methanol-d_4) of **DA$_{NH2}$**.

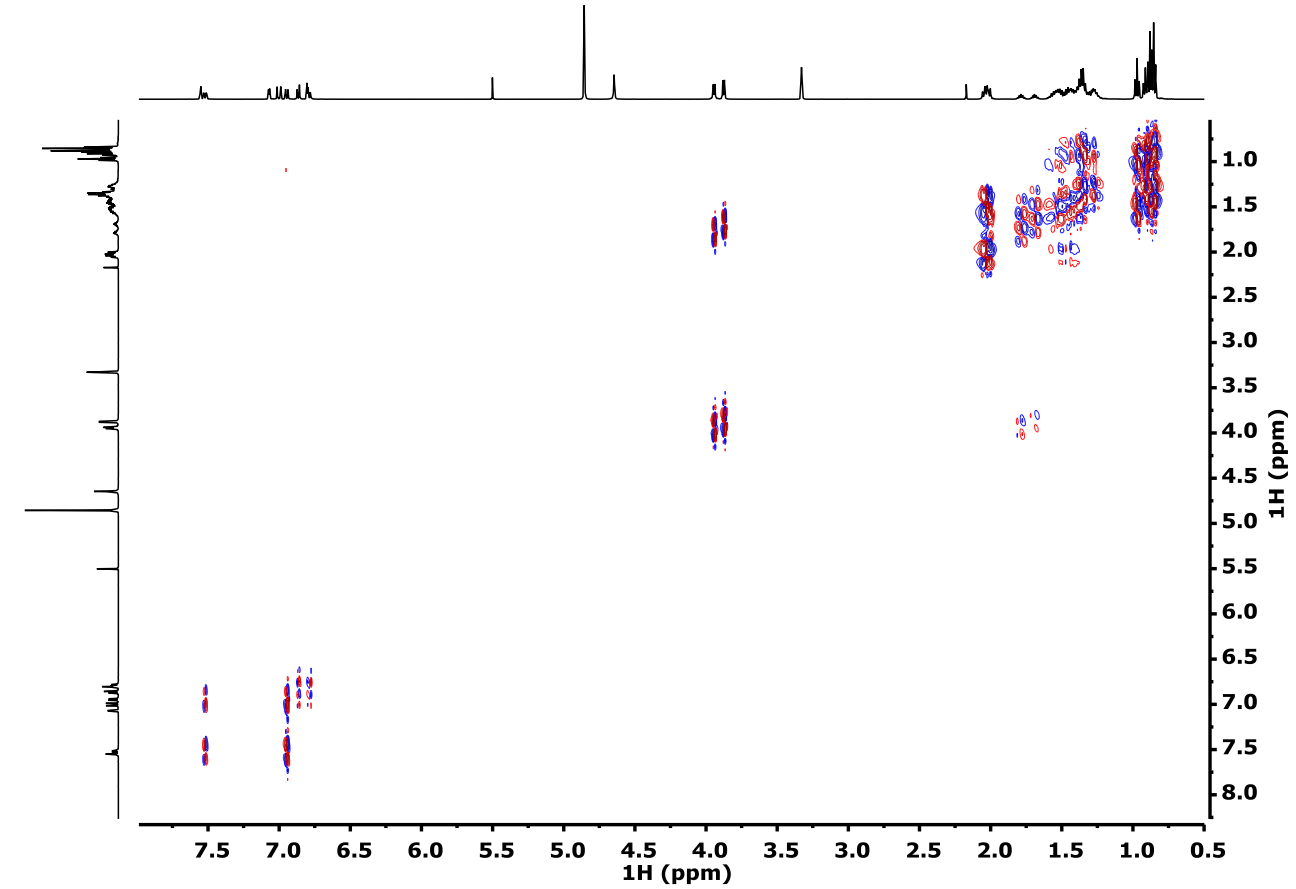
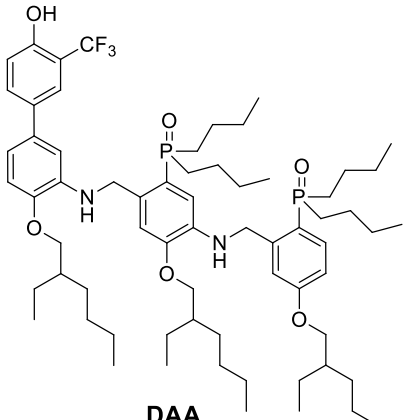


Figure S3.36. ^{1}H-^{1}H COSY spectrum (500 MHz, methanol-d_4) of **DA$_{NH2}$**.

4.7 Synthesis of DAA



DAA

Trimer **DAA** was synthesized via one step reductive amination. Dimer $\mathbf{DA_{NH2}}$(32 mg, 0.041 mmol, 1 equiv) and $\mathbf{A_{CO}}$ (48.9 mg, 0.124 mmol, 3 equiv) were dissolved in a 2 mL vial with dry toluene (0.5 mL). The mixture was stirred over weekend, then 2.9 mg (0.014 mmol, 0.3 equiv) of sodium $NaBH(OAc)_3$ were added. The mixture was let to react another day, then a second addition of $NaBH(OAc)_3$ (43.45 mg, 0.205 mmol, 5 equiv) was made to complete the reduction of the imine (confirmed by ^{1}H-NMR). Then, a saturated solution of NaCl was added and the mixture was stirred until complete solubilisation. Hence, the organic phase was extracted, and the aqueous phase was washed (3x) with EtOAc. The organic layers were collected and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified via flash chromatography (gradient EtOAc to EtOAc: MeOH 9:1), giving the desired trimer (28.3 mg, 60 % yield).

^{1}H NMR (400 MHz, methanol-d_4) δ 7.64 – 7.41 (m, 3H), 7.16 (t, *J* = 2.81 Hz, 1H), 7.05 (d, *J* = 3.64 Hz, 1H), 6.94 (dd, *J* = 8.59, 3.15 Hz, 2H), 6.90 – 6.81 (m, 2H), 6.76 (dd, *J* = 8.19, 2.11 Hz, 1H), 6.55 (d, *J* = 13.43 Hz, 1H), 4.71 (s, 2H), 4.67 (s, 2H), 3.93 (d, *J* = 5.61 Hz, 2H), 3.89 (d, *J* = 5.63, 4H), 1.96 (m, 8H), 1.83 – 1.12 (m, 46H), 1.02 – 0.84 (m, 18H), 0.78 (m, 12H).

^{13}C NMR (202 MHz, methanol-d_4) δ 162.02 (d, J = 2.80 Hz), 154.44 (d, J = 1.68 Hz), 148.59 (d, J = 3.20 Hz), 147.01, 146.94, 146.15, 138.06, 136.35, 136.20, 133.95, 133.83, 133.76, 132.92, 132.60, 130.90, 124.17 (q, J = 271.33 Hz), 124.07 (q, J = 5.16 Hz), 119.87, 119.13, 118.91, 118.17, 116.59, 116.55 (q, J = 30.42 Hz), 116.15, 116.05, 114.27, 112.44, 112.30, 112.28, 112.16, 111.87, 111.71, 110.62, 108.93, 70.54, 70.32, 70.18, 46.11 (d, J = 3.18 Hz), 45.36 (d, J = 3.07 Hz), 39.49, 39.30, 39.16, 30.41, 30.26, 30.13, 29.79, 29.45, 29.11, 28.93, 28.82, 28.75, 23.75, 23.68, 23.60, 23.54, 23.45, 23.42, 22.76, 22.71, 13.09, 13.05, 12.65, 12.54, 10.16, 10.14, 10.08.

^{19}F NMR (376 MHz, methanol-d_4) δ -63.46.

^{31}P NMR (202 MHz, methanol-d_4) δ 50.27, 49.55.

HRMS(ES+): Calculated for $C_{67}H_{106}F_3N_2O_6P_2$ 1153.7478 a.m.u.; found 1153.7503

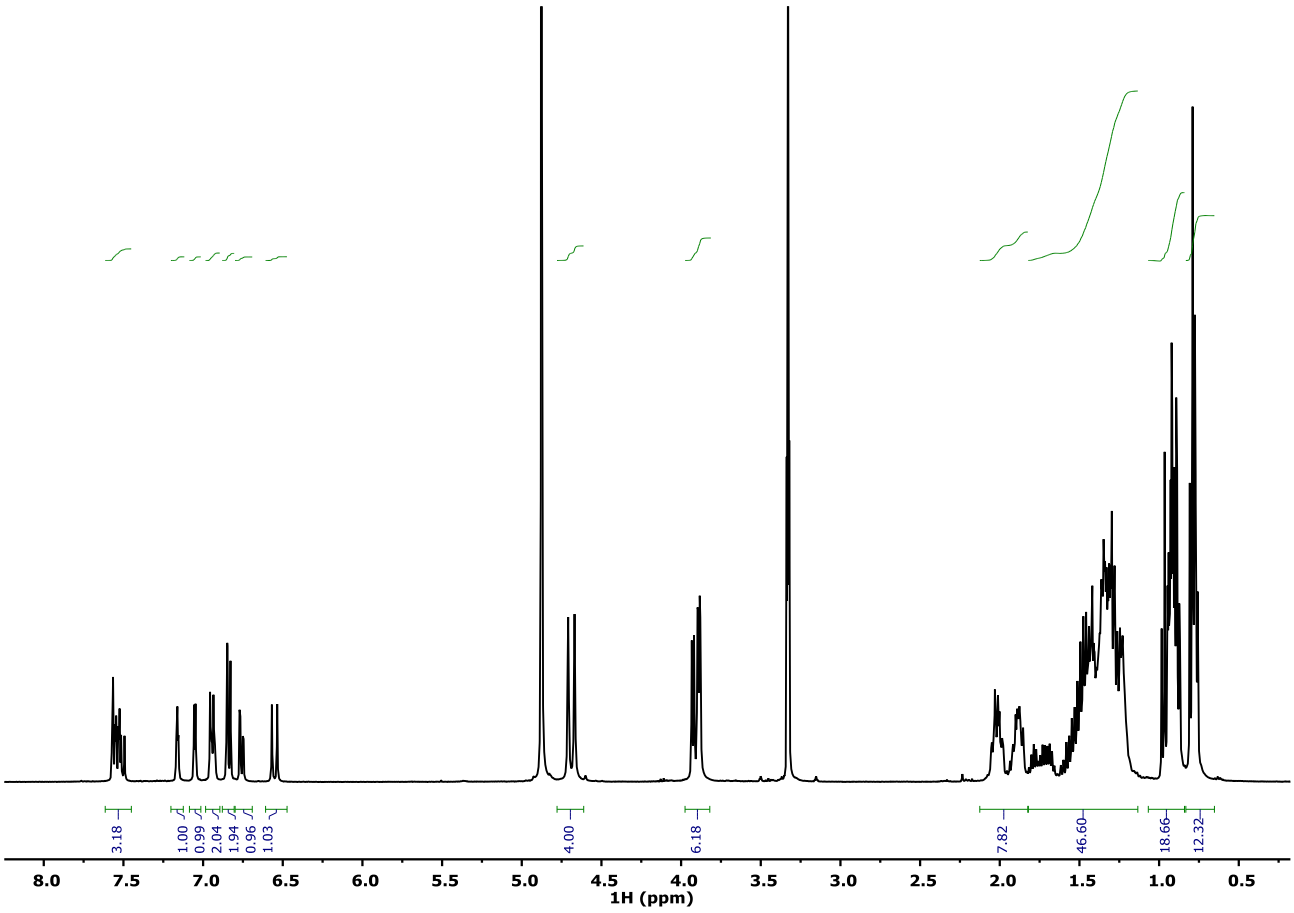


Figure S4.37. ^{1}H-NMR spectrum (500 MHz, methanol-d_4) of **DAA**.

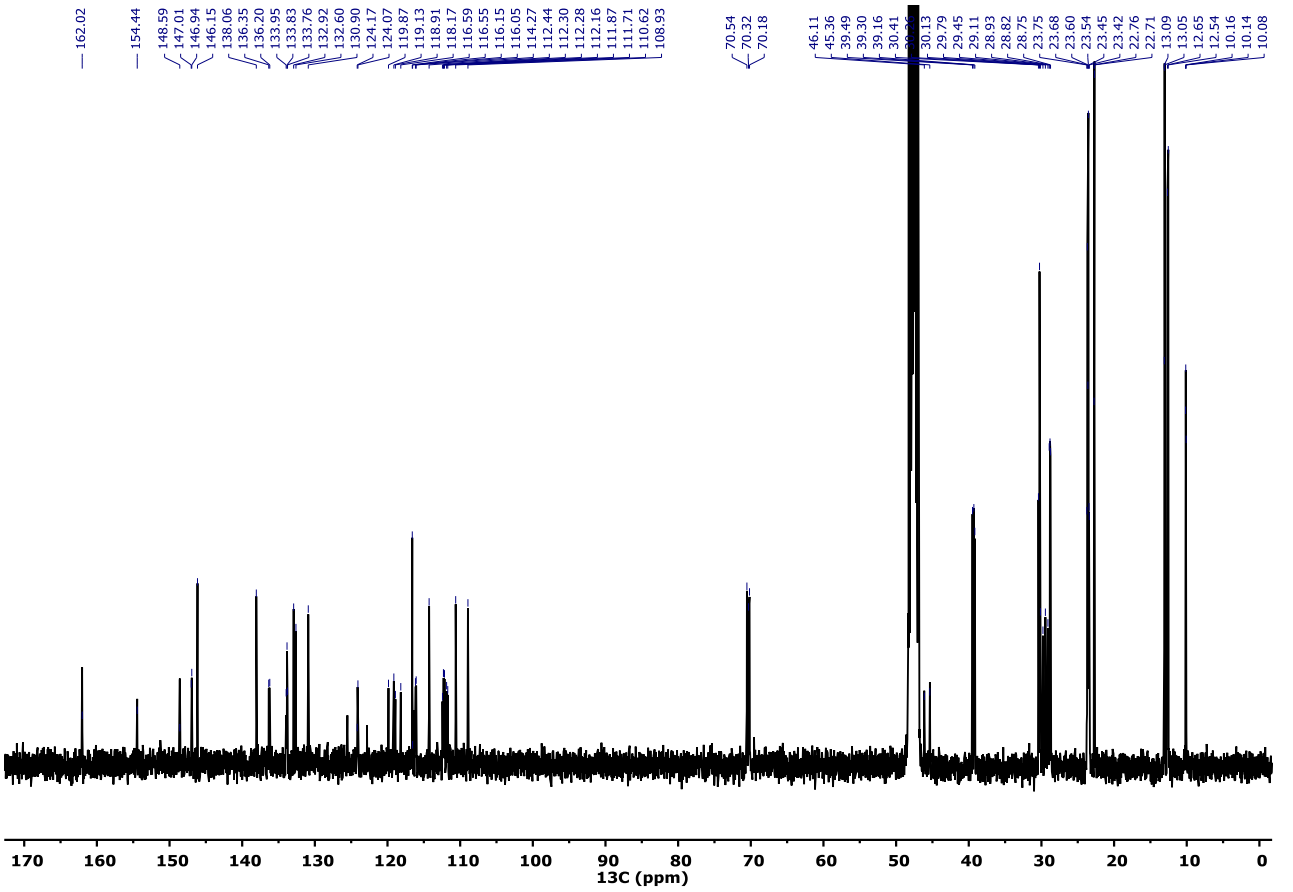


Figure S4.38. ^{13}C-NMR spectrum (126 MHz, methanol-d_4) of **DAA**.

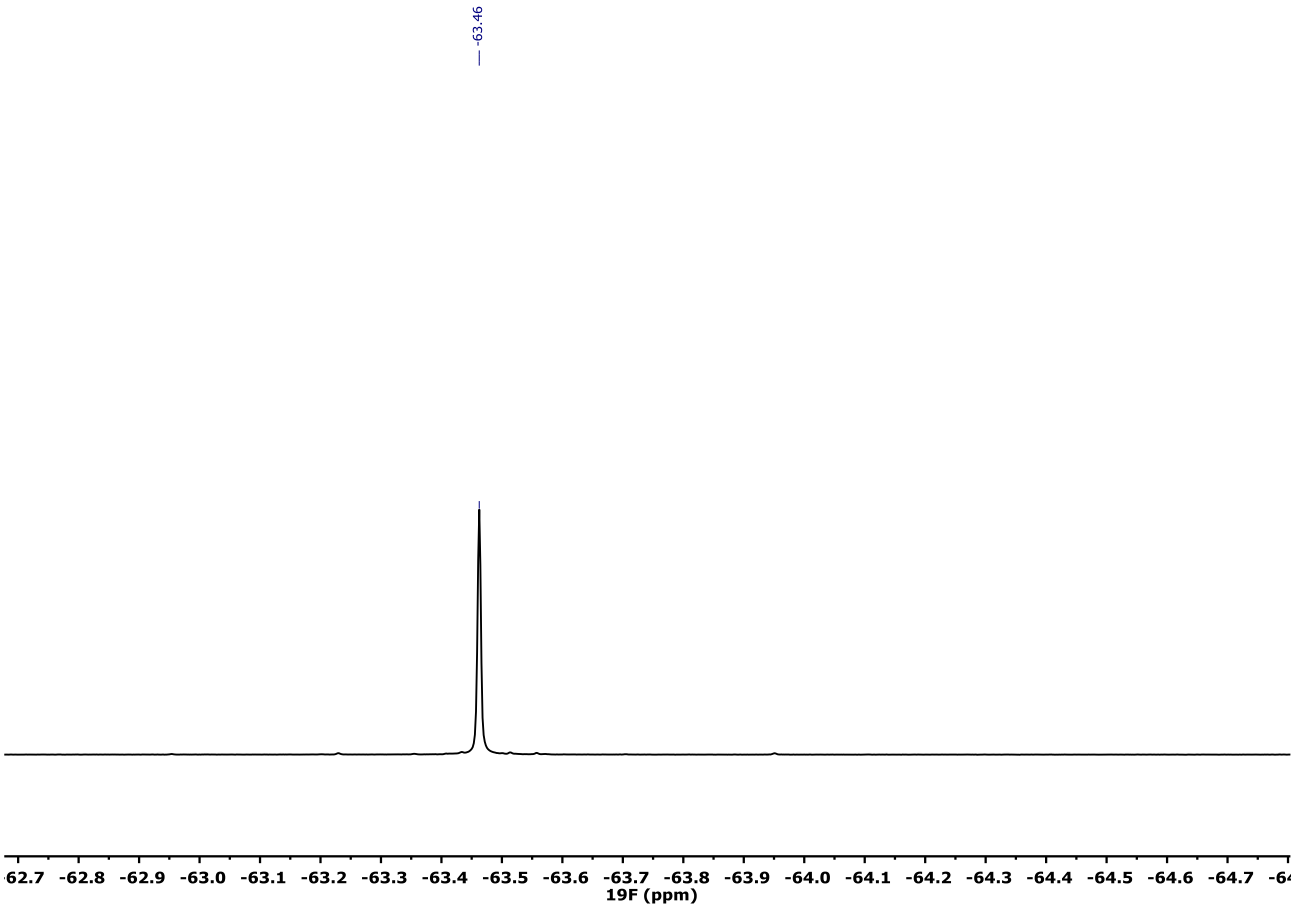


Figure S4.39. ^{19}F-NMR spectrum (376 MHz, methanol-d_4) of **DAA**.

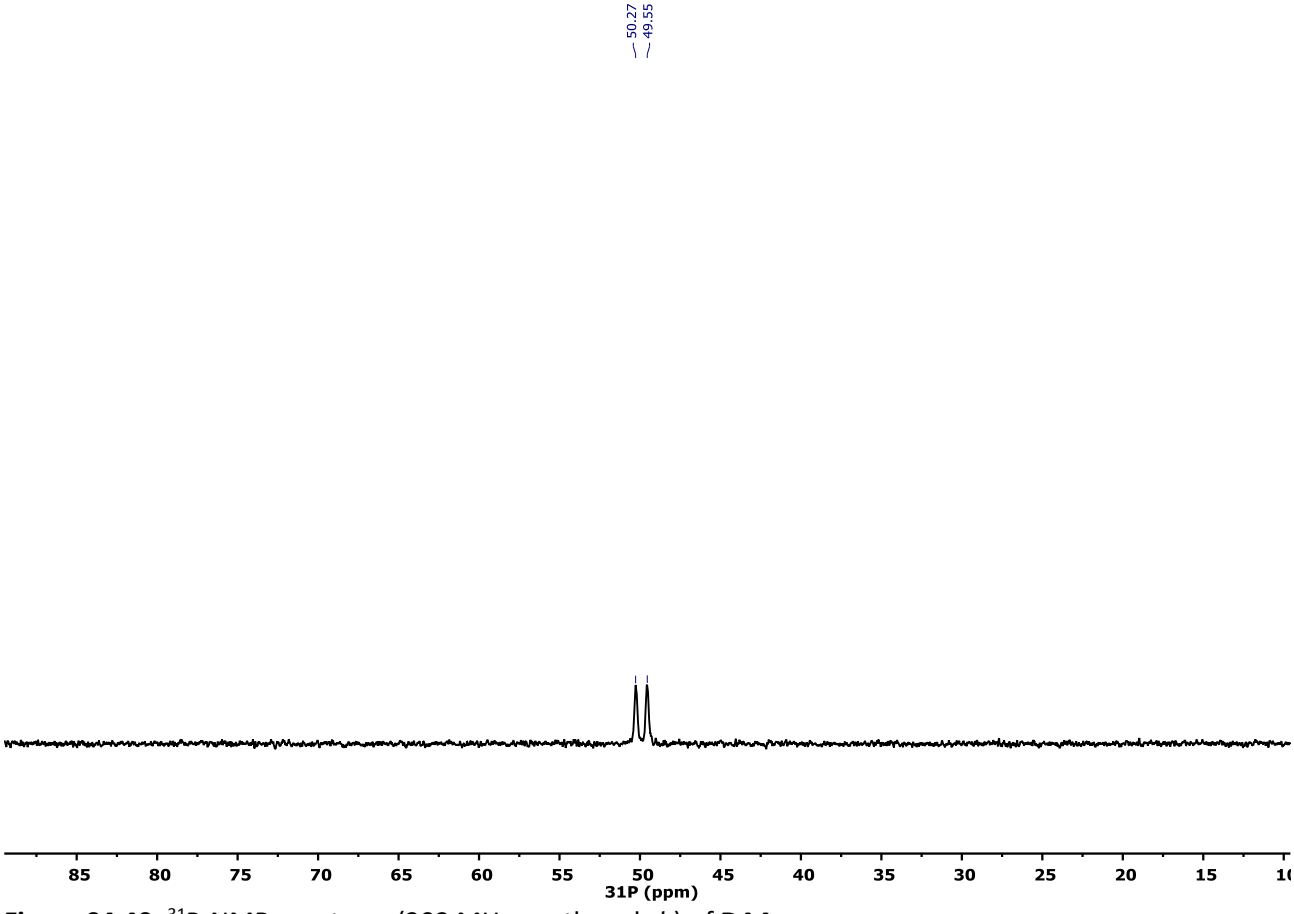


Figure S4.40. ^{31}P-NMR spectrum (202 MHz, methanol-d_4) of **DAA**.

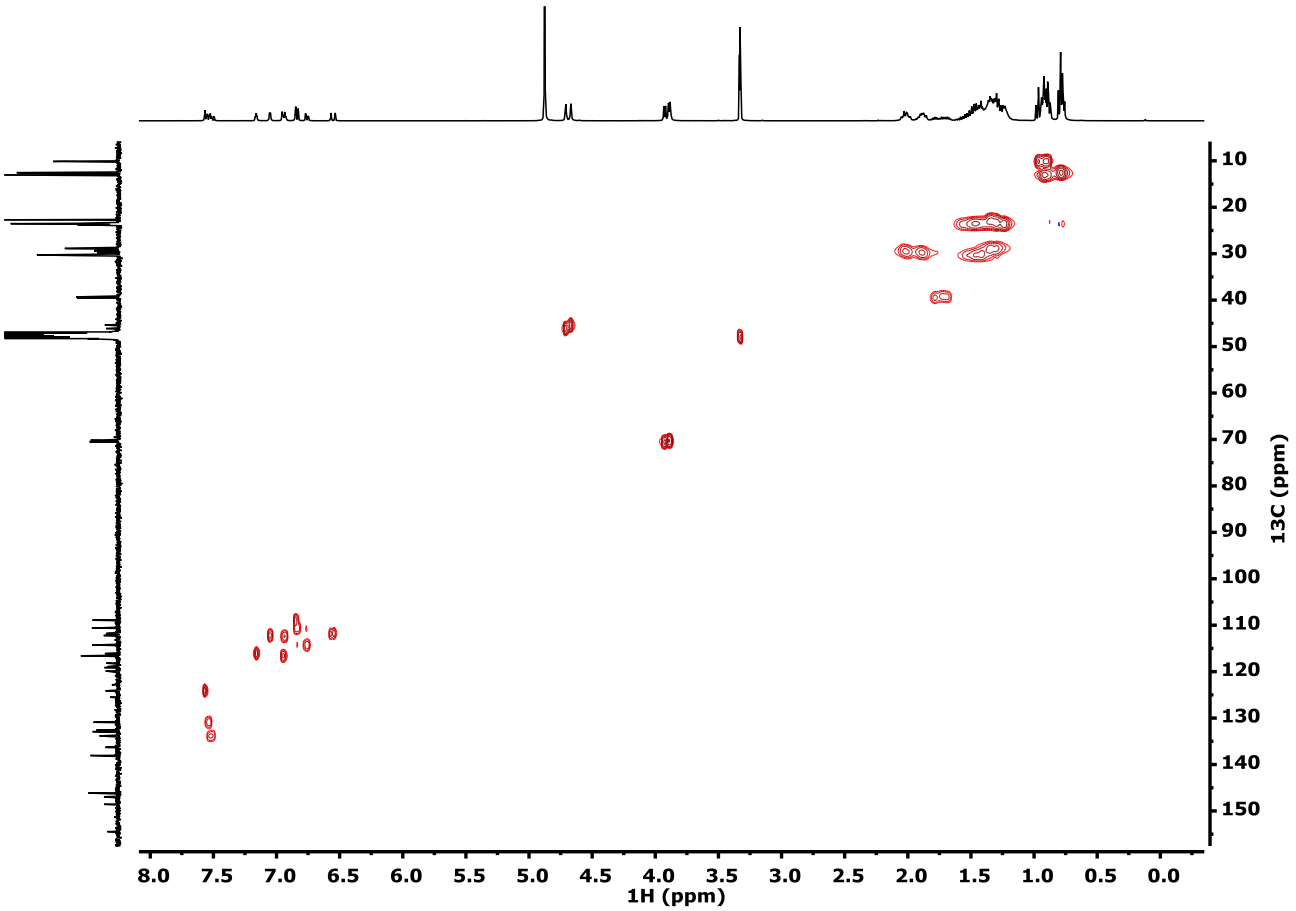


Figure S4.41. ^{1}H-^{13}C HSQC spectrum (400 MHz, methanol-d_4) of **DAA**.

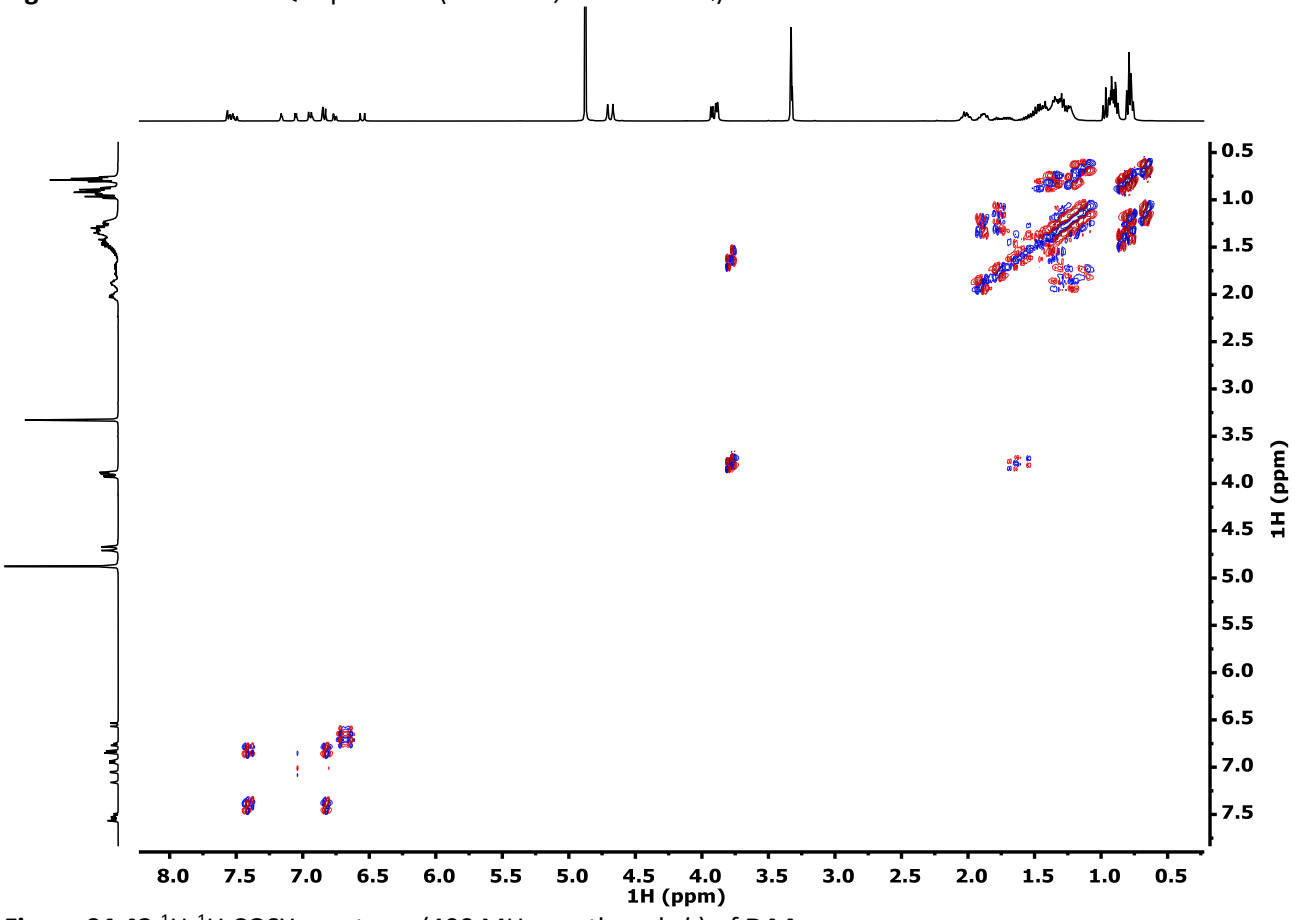
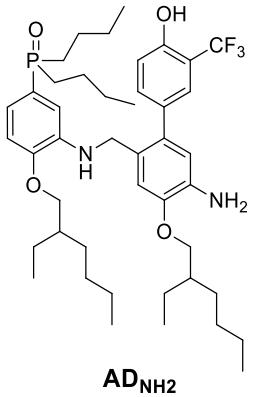


Figure S4.42. ^{1}H-^{1}H COSY spectrum (400 MHz, methanol-d_4) of **DAA**.

4.8 Synthesis of AD_{NH2}



AD_{NH2}

Intermediate **AD_{NH2}** was synthesized via reductive amination. Monomers **D** (83 mg, 0.201 mmol, 1 equiv) and **A_{NH2}** (230 mg, 0.603 mmol, 3 equiv) were dissolved in dry toluene (1 mL). The round bottom flask was equipped with a dean-stark filled with 3 Å molecular sieves and the mixture was refluxed overnight. Then, the mixture was cooled to room temperature and 21.4 mg (0.101 mmol, 0.5 equiv) of $NaBH(OAc)_3$ were added. The mixture was let to react another day, then a second addition of $NaBH(OAc)_3$ (214 mg, 1.01 mmol, 5 equiv) was made to complete the reduction of the imine (confirmed by ^{1}H-NMR). Then, a saturated solution of NaCl was added and the mixture was stirred until complete solubilisation. Hence, the organic phase was extracted, and the aqueous phase was washed (3x) with EtOAc. The organic layers were collected and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified via flash chromatography (gradient EtOAc 100% to 2% MeOH: EtOAc), giving the desired dimer (127.6 mg, 82 % yield).

^{1}H-NMR (500 MHz, methanol-d_4) δ 7.44 (d, J = 2.19 Hz, 1H), 7.39 (dd, J = 8.41, 2.24 Hz, 1H), 7.23 (t, J = 7.55 Hz, 1H), 7.19 – 7.15 (m, 1H), 7.02 – 6.91 (m, 4H), 6.69 (s, 1H), 6.45 (dd, J = 11.76, 1.74 Hz, 1H), 4.20 (s, 2H), 3.99 (dq, J = 6.76, 3.92 Hz, 2H), 3.88 (d, J = 5.58 Hz, 2H), 1.94 – 1.65 (m, 6H), 1.63 – 1.14 (m, 32H), 1.05 – 0.75 (m, 22H).

^{13}C-NMR (126 MHz, methanol-d_4) δ 154.68, 149.28 (d, J = 2.81 Hz), 146.73, 138.12 (d, J = 14.35 Hz), 135.71, 133.62, 132.82, 131.89, 128.52, 127.81, 126.70 (q, J = 4.70 Hz) 125.63, 124.90, 123.99 (q, J = 272.72 Hz), 121.59, 120.79, 119.52 (d, J = 9.05 Hz), 116.57, 116.16 (q, J = 30.30 Hz), 116.13, 110.99, 110.18 (d, J = 13.15 Hz), 109.70 (d, J = 14.21 Hz), 70.62, 70.38, 45.1015, 39.42, 39.22, 30.42, 30.38, 28.91, 28.87, 28.83, 28.37, 23.76, 23.69, 23.55, 23.44, 23.11, 23.08, 22.71, 22.70, 13.04, 12.99, 12.47, 10.15.

^{19}F-NMR (188 MHz, acetonitrile-d_3) δ -62.92.

^{31}P-NMR (162 MHz, acetonitrile-d_3) δ 44.75.

HRMS(ES+): Calculated for $C_{44}H_{67}F_3N_2O_4P$ 775.4791 a.m.u.; found 775.3895

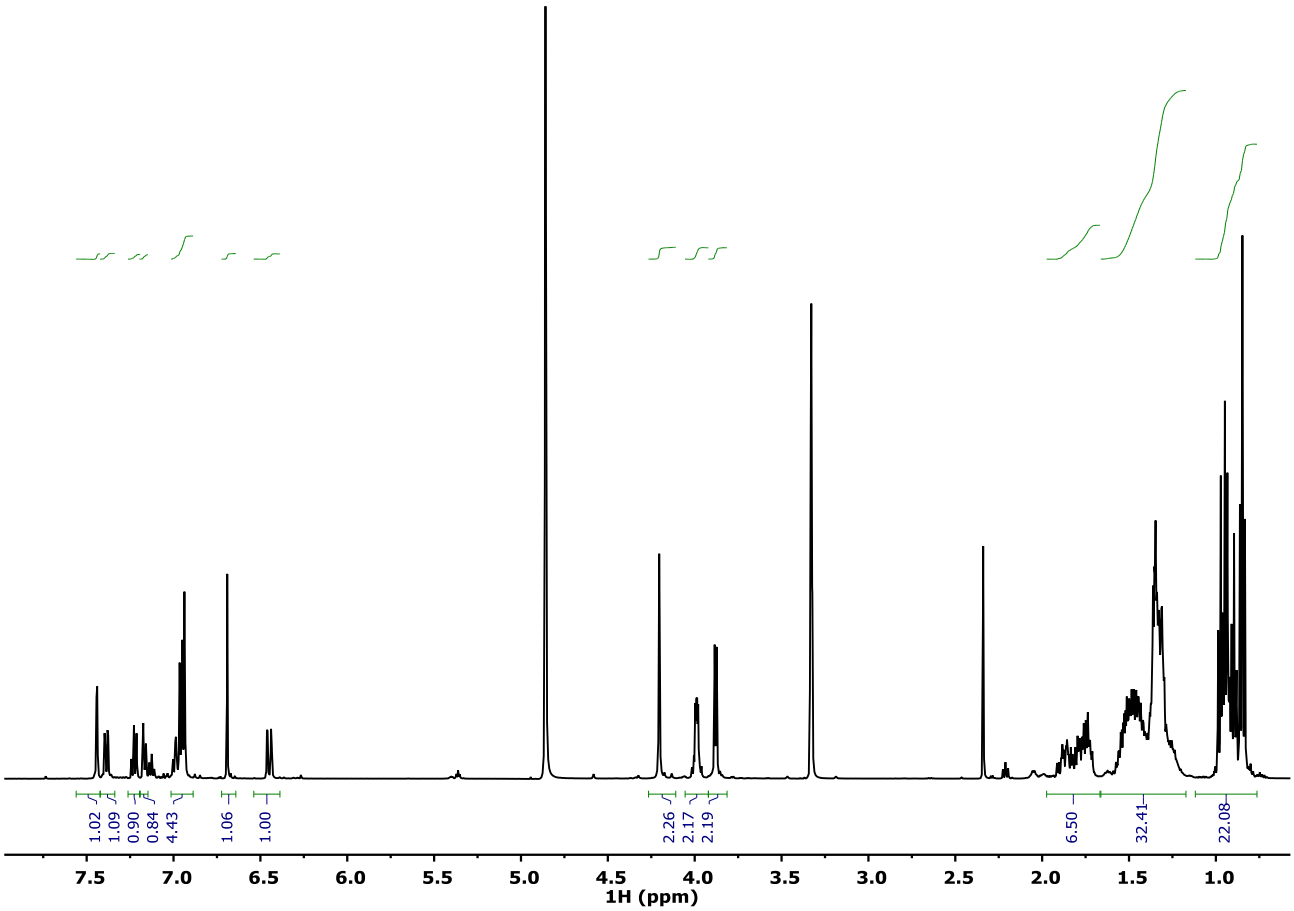


Figure S4.43. ^{1}H-NMR spectrum (500 MHz, methanol-d_4) of **AD$_{NH2}$**.

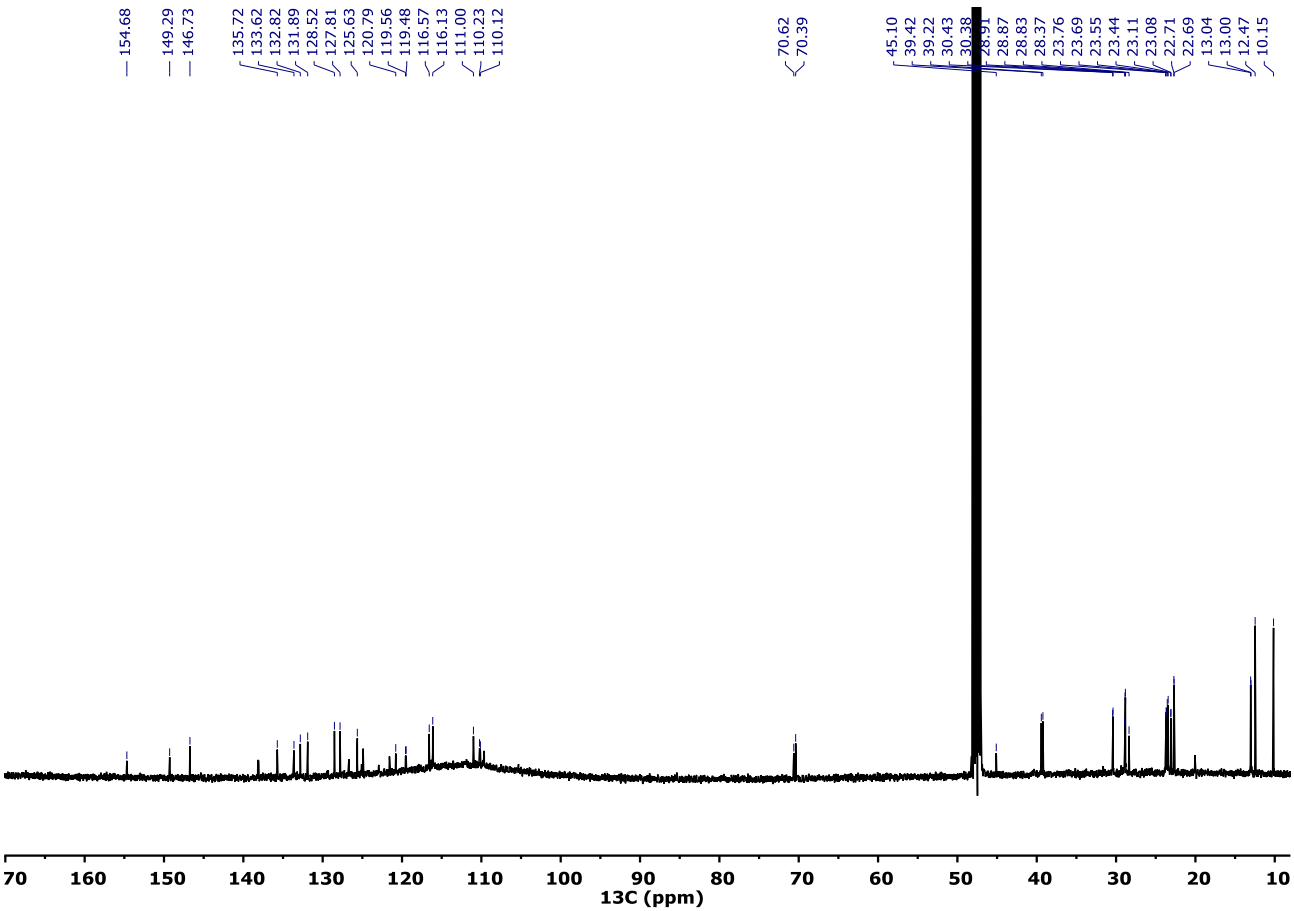


Figure S4.44. ^{13}C-NMR spectrum (126 MHz, methanol-d_4) of **AD$_{NH2}$**.

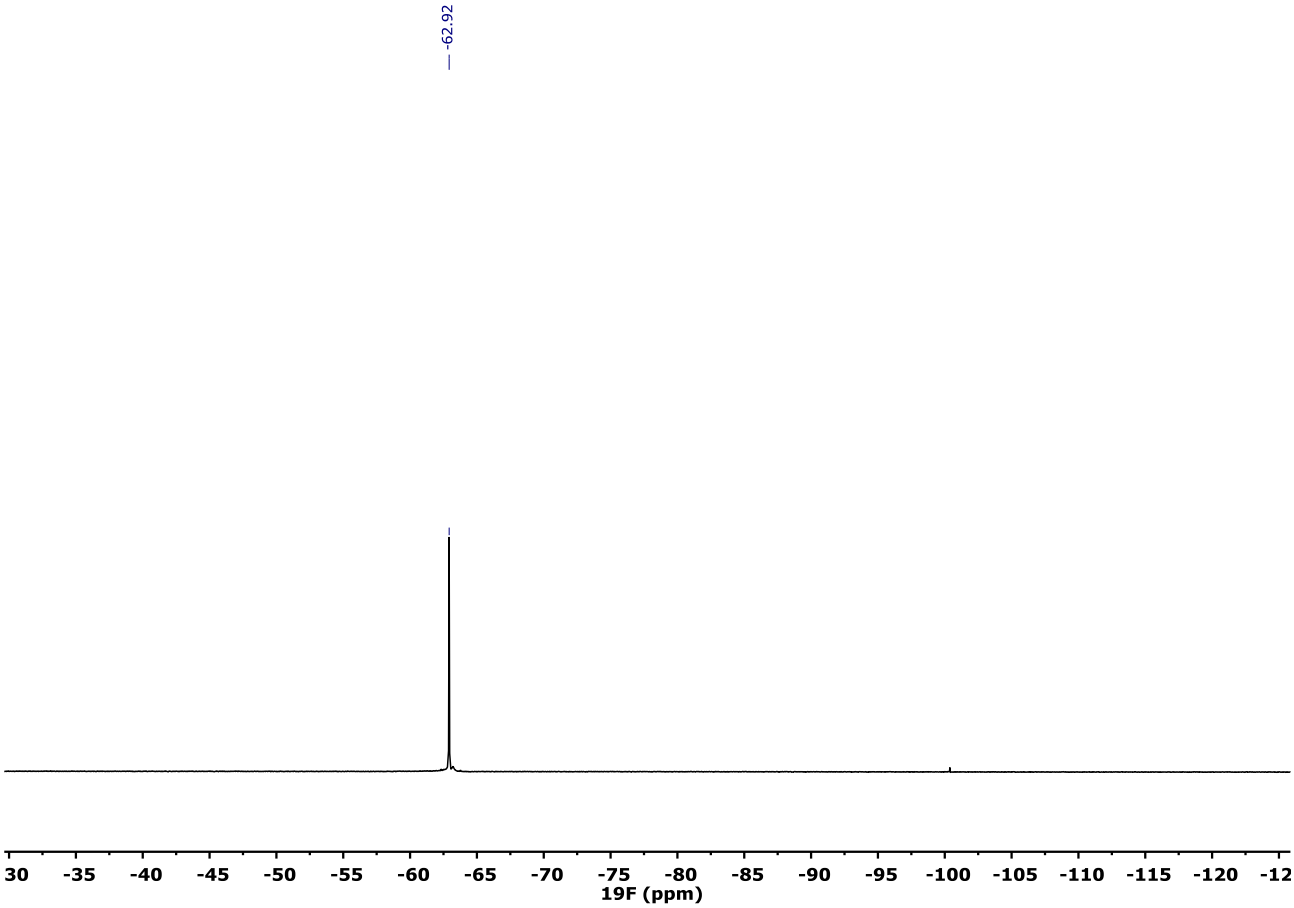


Figure S4.45. ^{19}F-NMR spectrum (188 MHz, acetonitrile-d_3) of $\mathbf{AD_{NH2}}$.

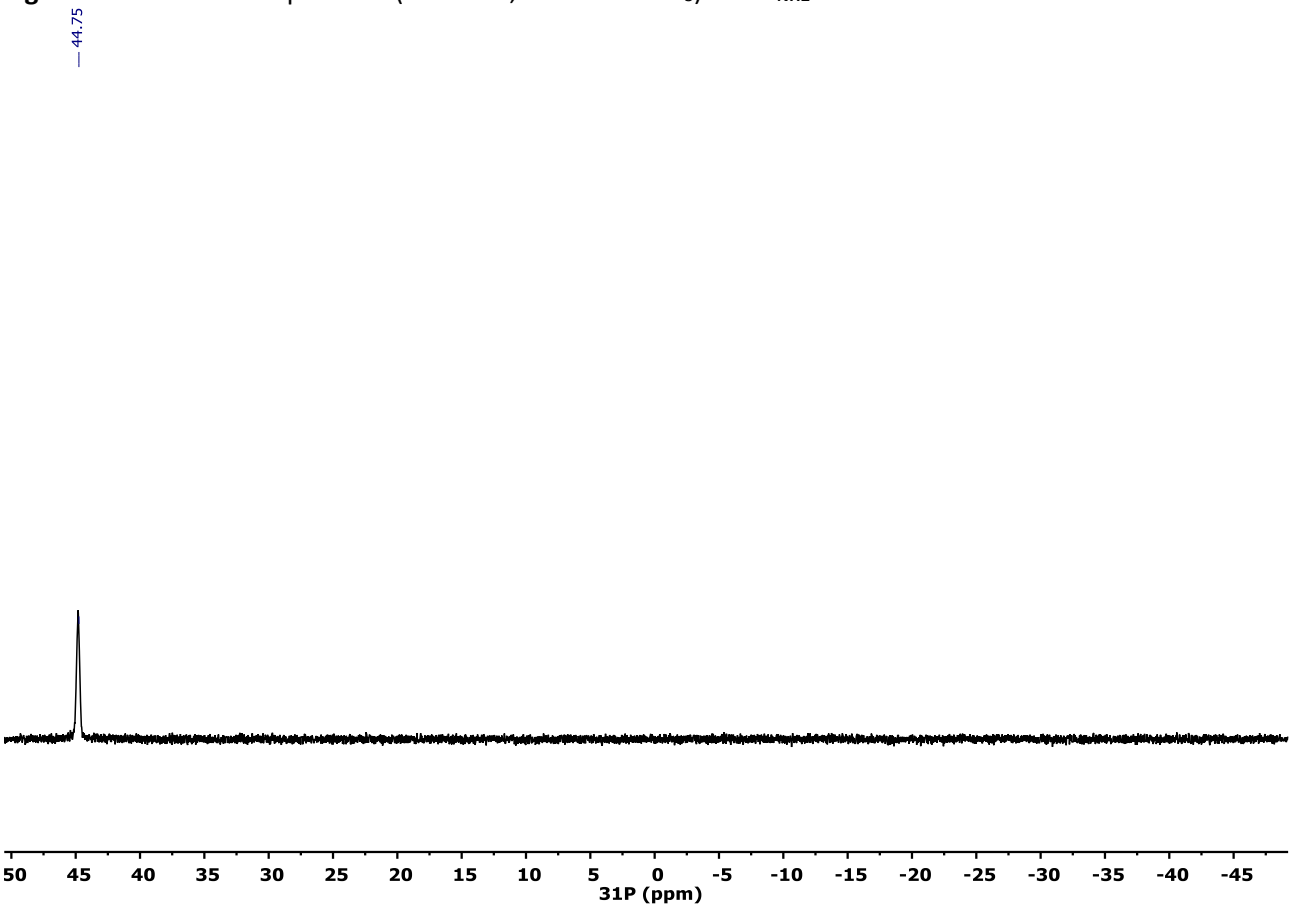


Figure S4.46. ^{31}P-NMR spectrum (162 MHz, acetonitrile-d_3) of $\mathbf{AD_{NH2}}$.

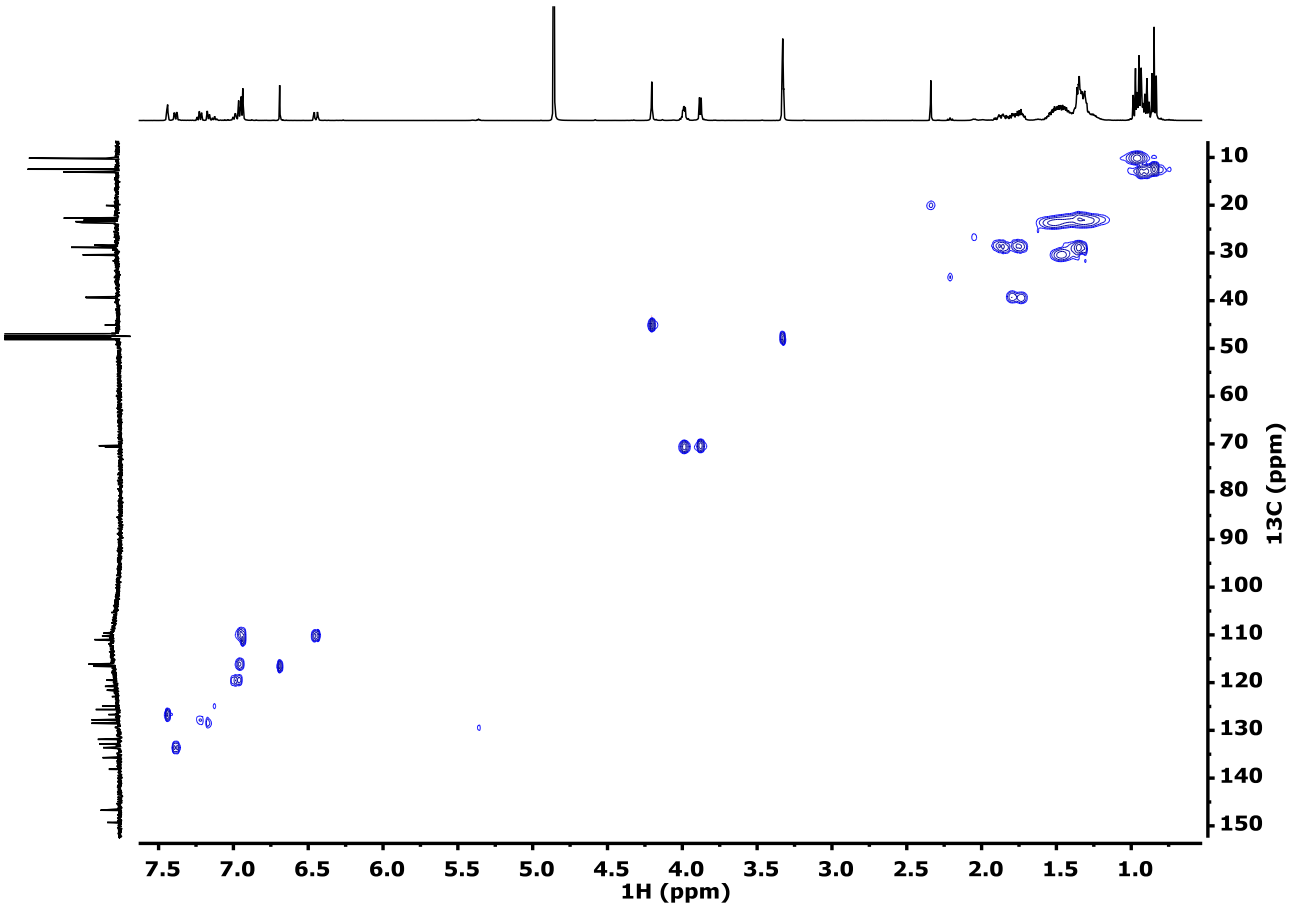


Figure S4.47. ^{1}H-^{13}C HSQC spectrum (500 MHz, methanol-d_4) of **AD$_{NH2}$**.

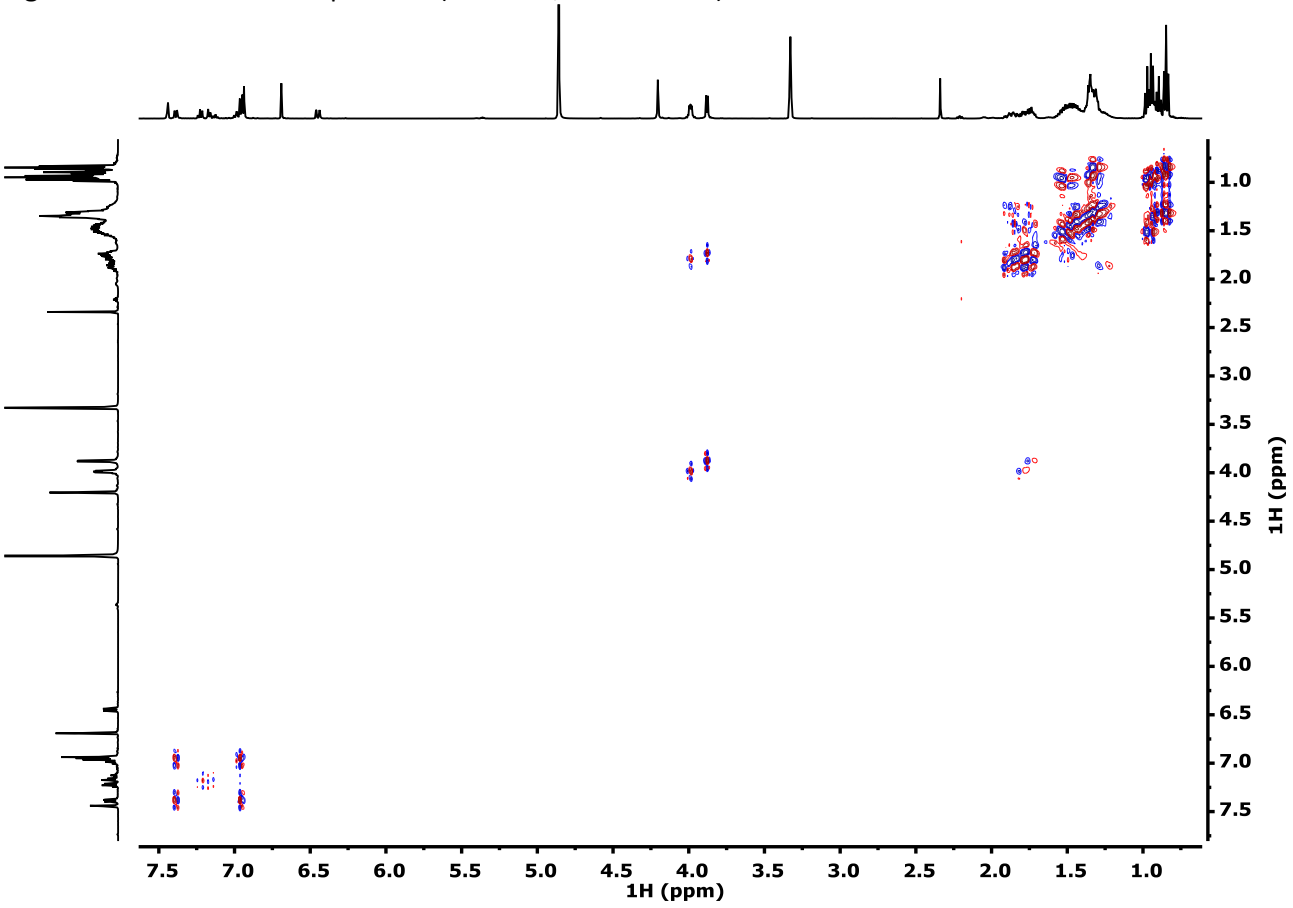
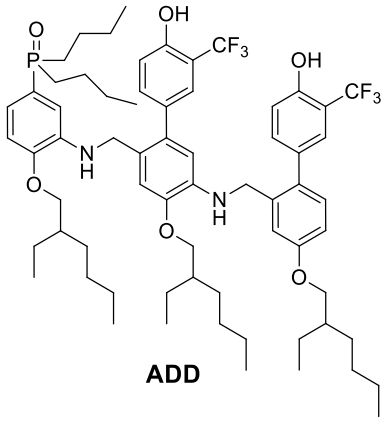


Figure S4.48. ^{1}H-^{1}H COSY spectrum (500 MHz, methanol-d_4) of **AD$_{NH2}$**.

4.9 Synthesis of ADD



ADD

Trimer **ADD** was synthesized via reductive amination. Dimer $\mathbf{AD_{NH2}}$ (52 mg, 0.067 mmol, 1 equiv) and $\mathbf{D_{CO}}$ (79.4 mg, 0.201 mmol, 3 equiv) were dissolved in dry toluene (0.5 ml) in a 2 mL vial. The mixture was stirred over weekend, then 8.5 mg (0.040 mmol, 0.6 equiv) of $NaBH(OAc)_3$ were added. The mixture was let to react another day, then a second addition of $NaBH(OAc)_3$ (70 mg, 0.336 mmol, 5 equiv) was made to complete the reduction of the imine (confirmed by ^{1}H-NMR). Then, a saturated solution of NaCl was added and the mixture was stirred until complete solubilisation. Hence, the organic phase was extracted, and the aqueous phase was washed (3x) with EtOAc. The organic layers were collected and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified via flash chromatography (gradient PE: EtOAc 4:6 to EtOAc), giving the desired trimer (43.4 mg, 56 % yield).

^{1}H-NMR (400 MHz, methanol-d_4) δ 7.39 (d, *J* = 1.96 Hz, 1H), 7.31 (d, *J* = 2.08 Hz, 1H), 7.30 – 7.22 (m, 2H), 7.12 (d, *J* = 8.44 Hz, 1H), 7.07 (d, *J* = 2.57 Hz, 1H), 7.01 – 6.89 (m, 4H), 6.89 – 6.83 (m, 2H), 6.36 (dd, *J* = 11.74, 1.66 Hz, 1H), 6.18 (s, 1H), 4.22 (s, 2H), 4.16 (s, 2H), 3.96 (dd, *J* = 5.56, 2.99 Hz, 2H), 3.85 (d, *J* = 5.62 Hz, 4H), 1.7563 (m, 8H), 1.58 – 1.14 (m, 40H), 1.03 – 0.83 (m, 18H), 0.79 (t, *J* = 7.15 Hz, 6H).

^{13}C-NMR (101 MHz, methanol-d_4) δ 159.03, 154.89 (d, J = 1.98 Hz), 154.75 (d, J = 2.16 Hz), 149.29 (d, J = 3.01 Hz), 146.16, 138.18, 138.03, 136.98, 133.68, 133.56, 132.70, 132.54, 132.00, 131.39, 130.82, 126.97 (q, J = 4.94 Hz), 126.70 (q, J = 5.13 Hz), 125.37 (d, J = 2.97 Hz), 123.76, 122.67 (d, J = 2.27 Hz), 121.58, 120.59, 119.56, 119.47, 116.46, 116.30, 116.14, 115.99, 113.65, 113.02, 111.80, 110.16, 110.05, 109.74, 109.59, 70.64, 70.60, 70.10, 60.13, 45.55, 45.06, 39.28, 39.27, 39.19, 30.45, 30.43, 30.29, 28.97, 28.82, 28.82, 28.28, 23.75, 23.57, 23.53, 23.39, 23.07, 23.03, 22.71, 22.71, 22.69, 13.07, 13.05, 13.02, 12.48, 12.48, 10.21, 10.16, 10.12.

^{19}F-NMR (188 MHz, methanol-d_4) δ -63.75, -63.93.

^{31}P-NMR (202 MHz, methanol-d_4) δ 47.42.

HRMS(ES+): Calculated for $C_{66}H_{92}F_6N_2O_6P$ 1153.6597 a.m.u.; found 1153.6584

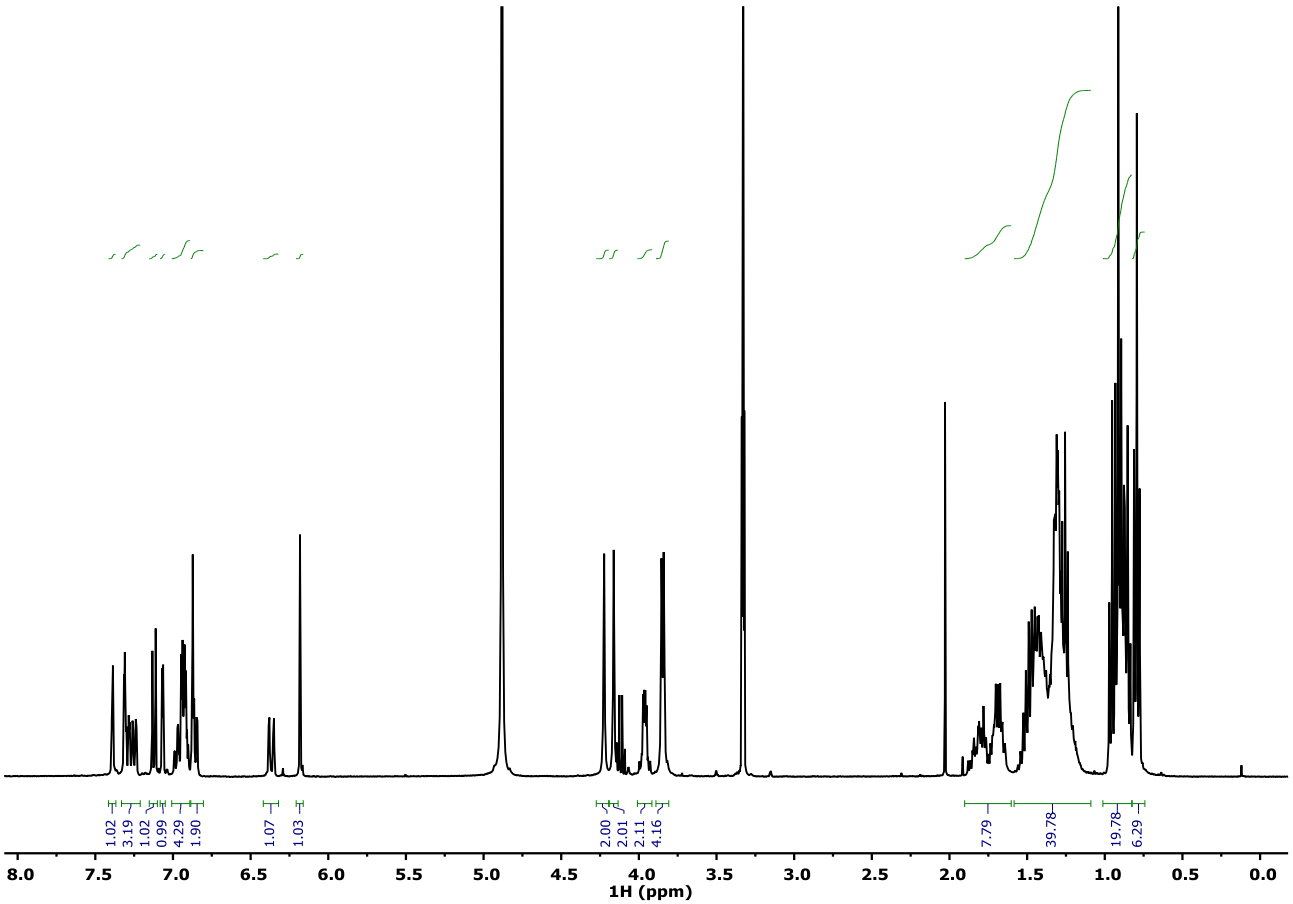


Figure S4.49. ^{1}H-NMR spectrum (400 MHz, methanol-d_4) of **ADD**.

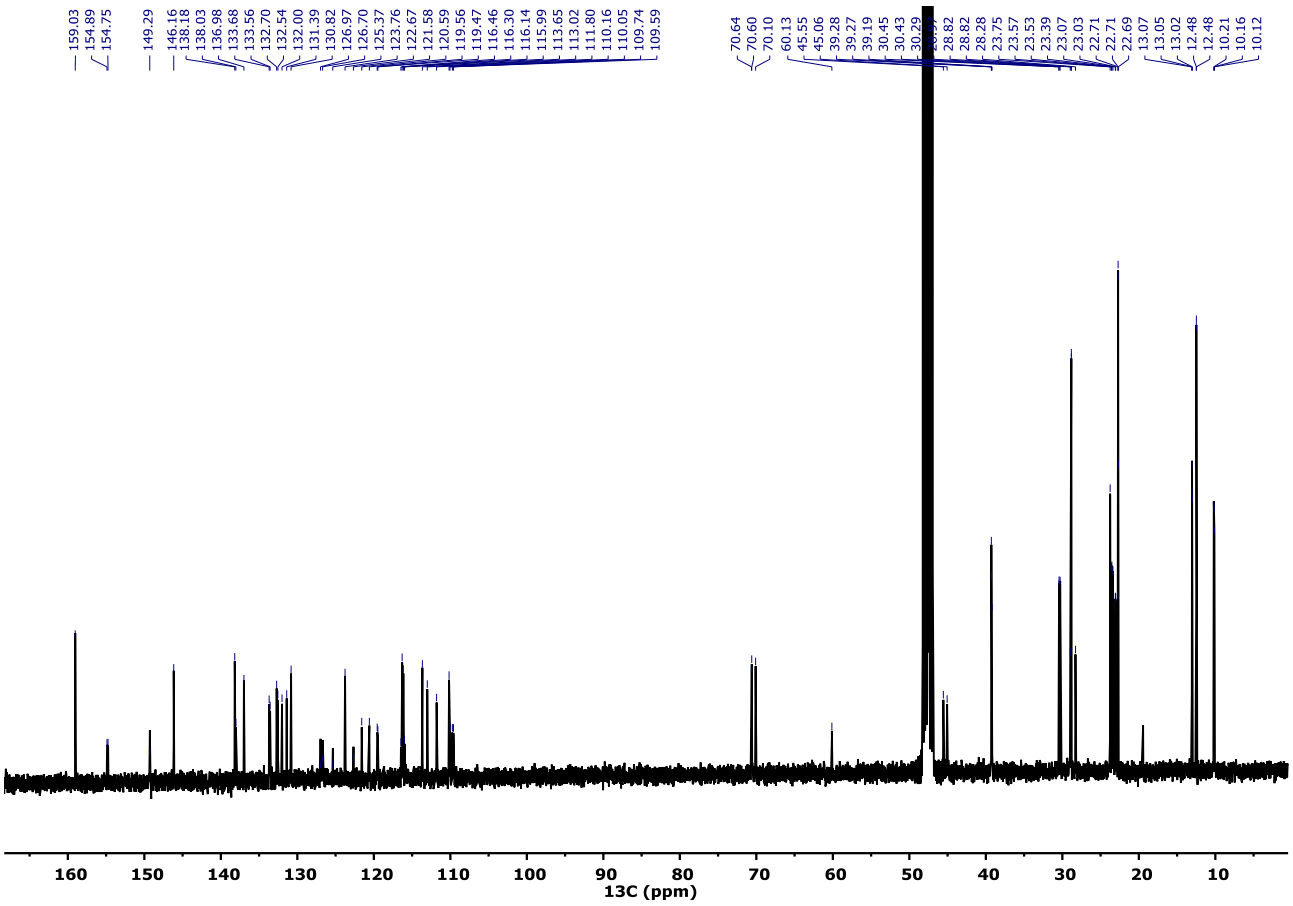


Figure S4.50. ^{13}C-NMR spectrum (101 MHz, methanol-d_4) of **ADD**.

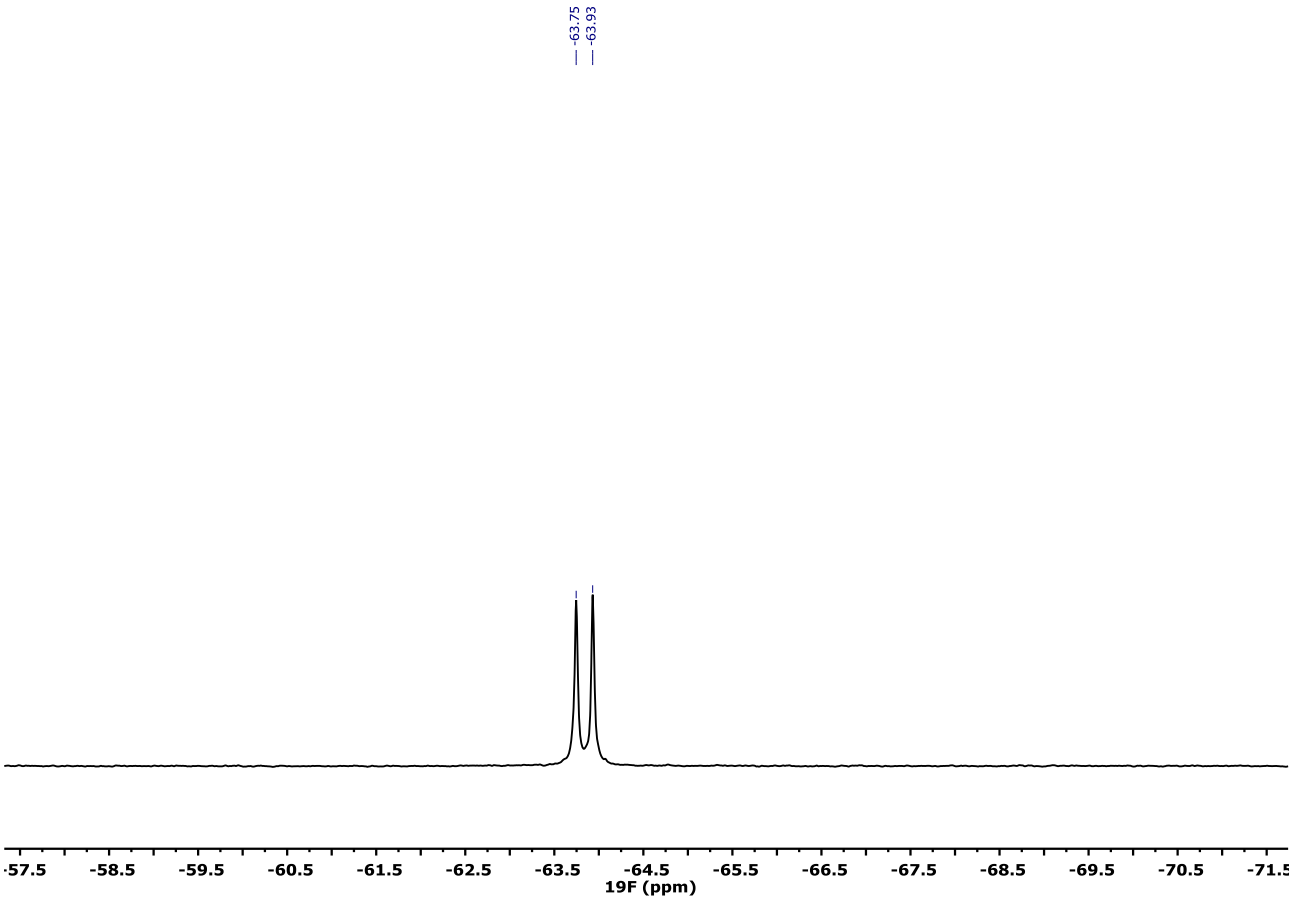


Figure S4.51. ^{19}F-NMR spectrum (188 MHz, methanol-d_4) of **ADD**.

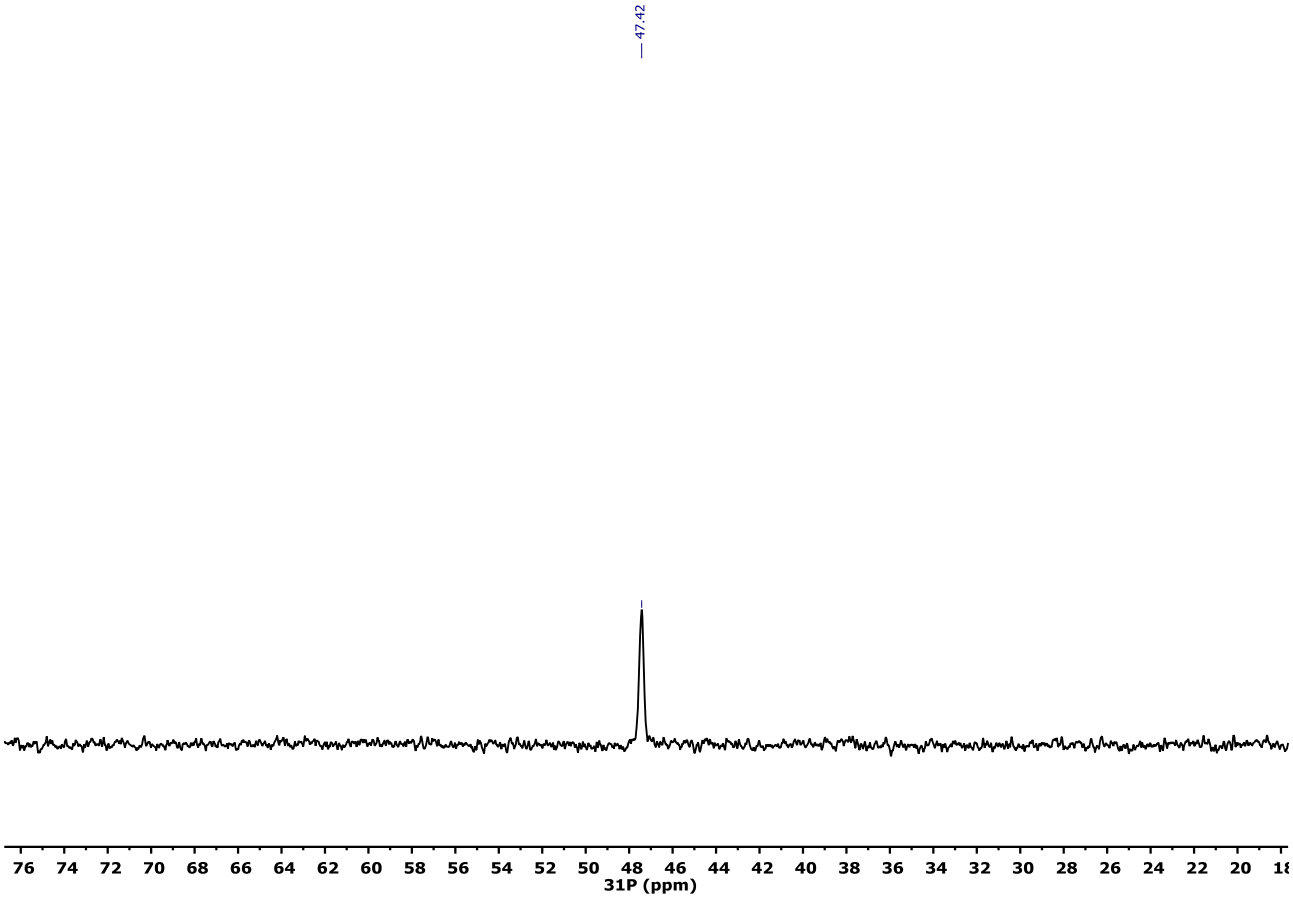


Figure S4.52. ^{31}P-NMR spectrum (202 MHz, 400 MHz, methanol-d_4) of **ADD**.

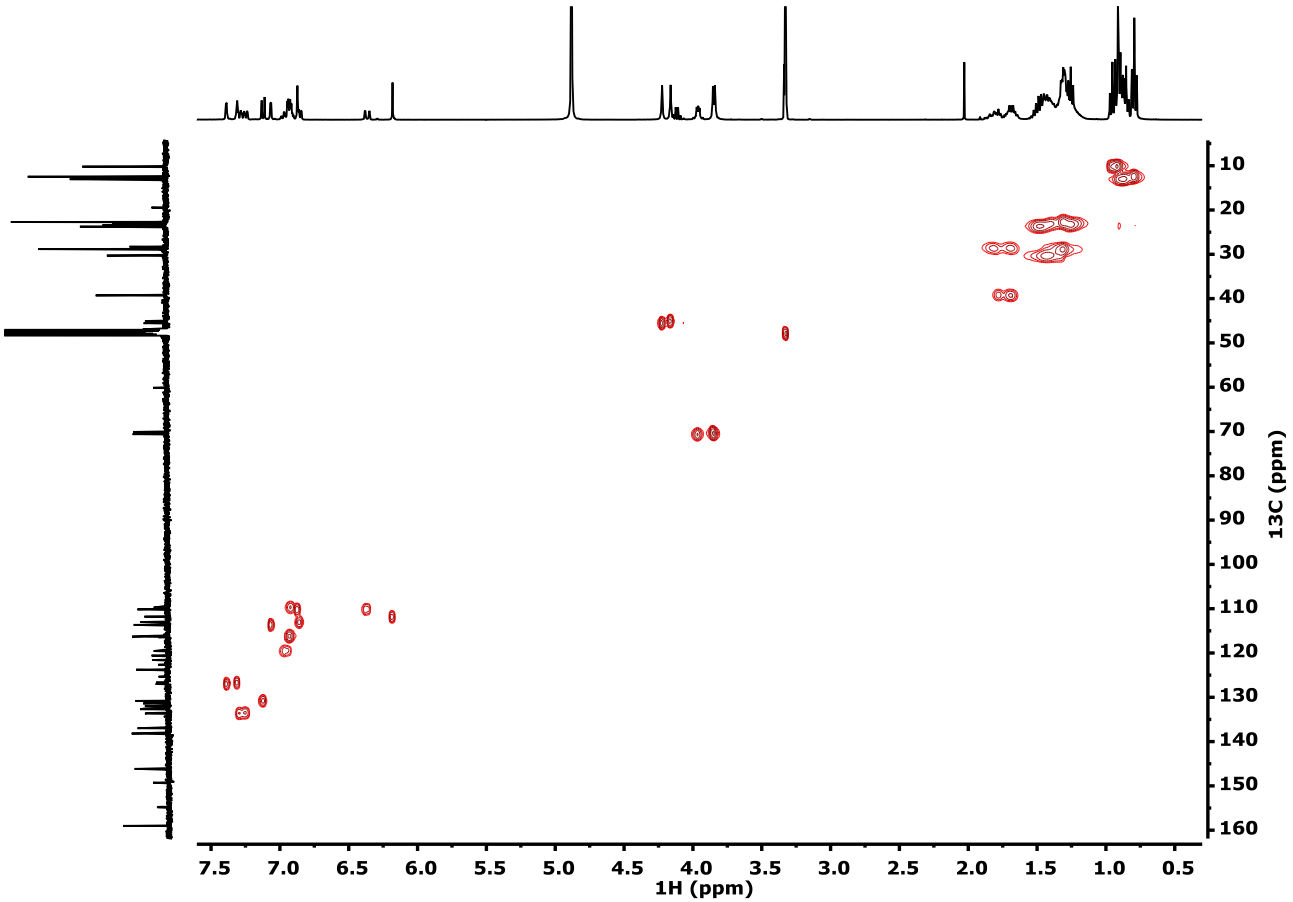


Figure S4.53. ^{1}H-^{13}C HSQC spectrum (400 MHz, methanol-d_4) of **ADD**.

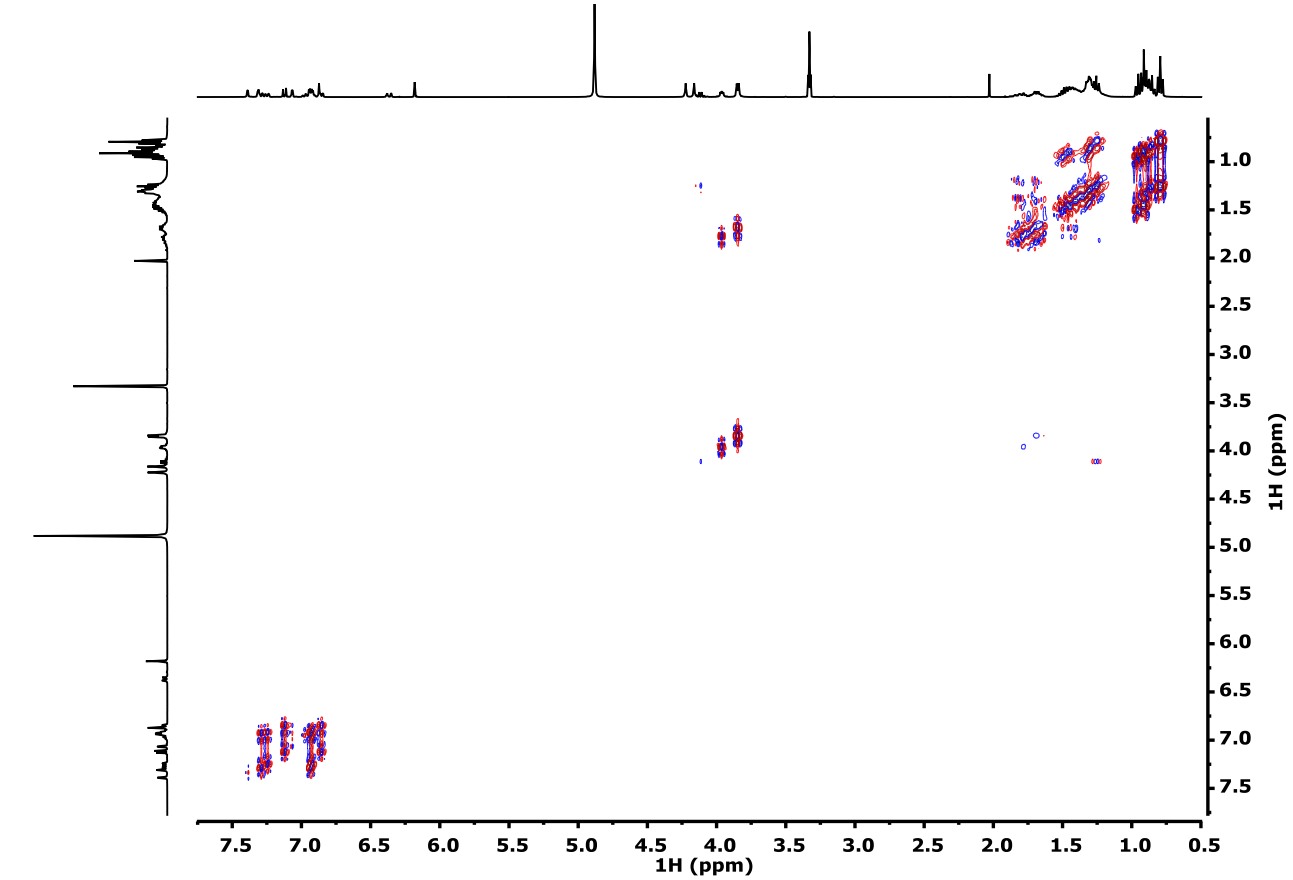


Figure S4.54. ^{1}H-^{1}H COSY spectrum (400 MHz, methanol-d_4) of **ADD**.

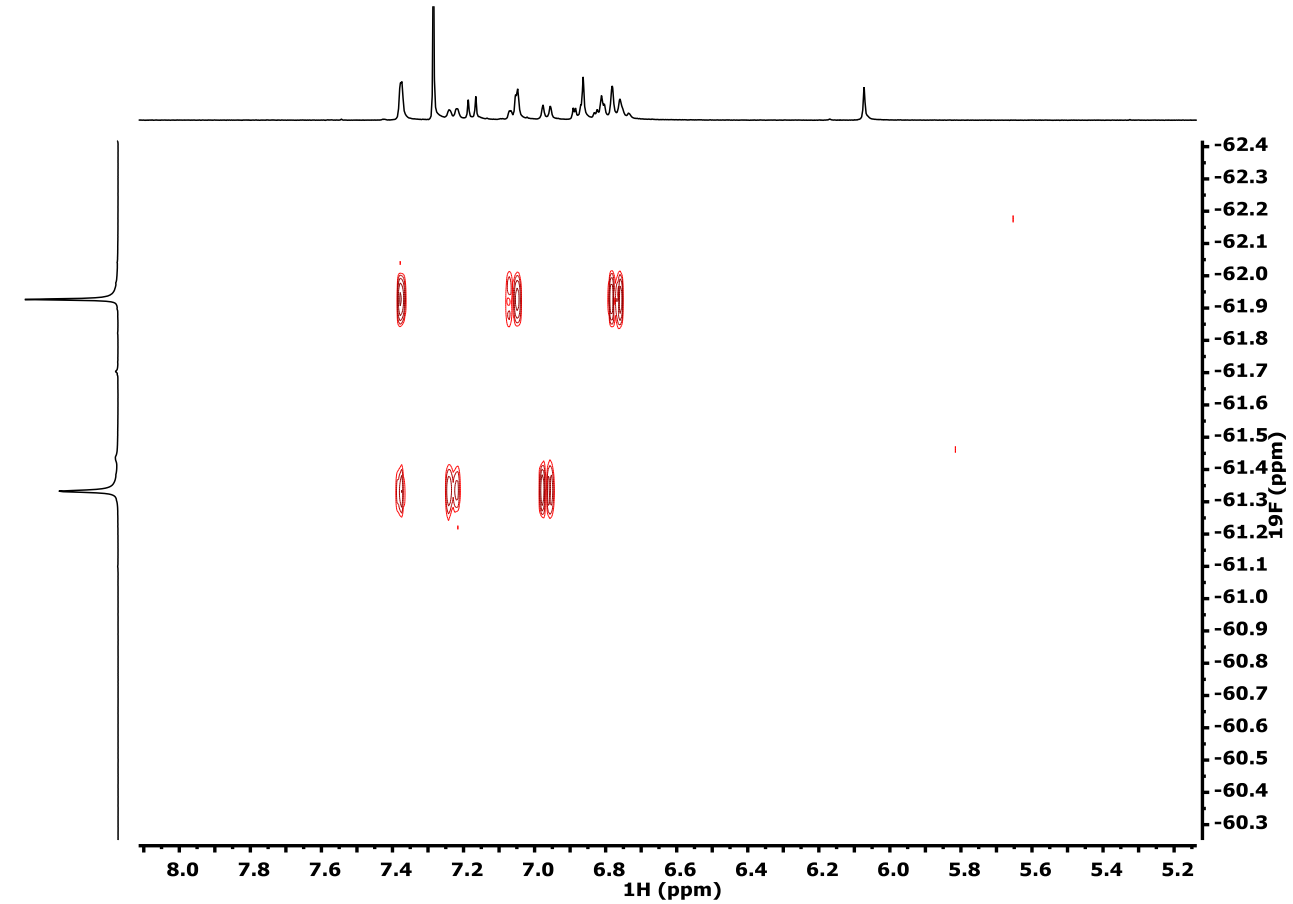


Figure S4.55. ^{1}H-^{13}C HMBC spectrum (400 MHz, chloroform-*d*) of **ADD**.

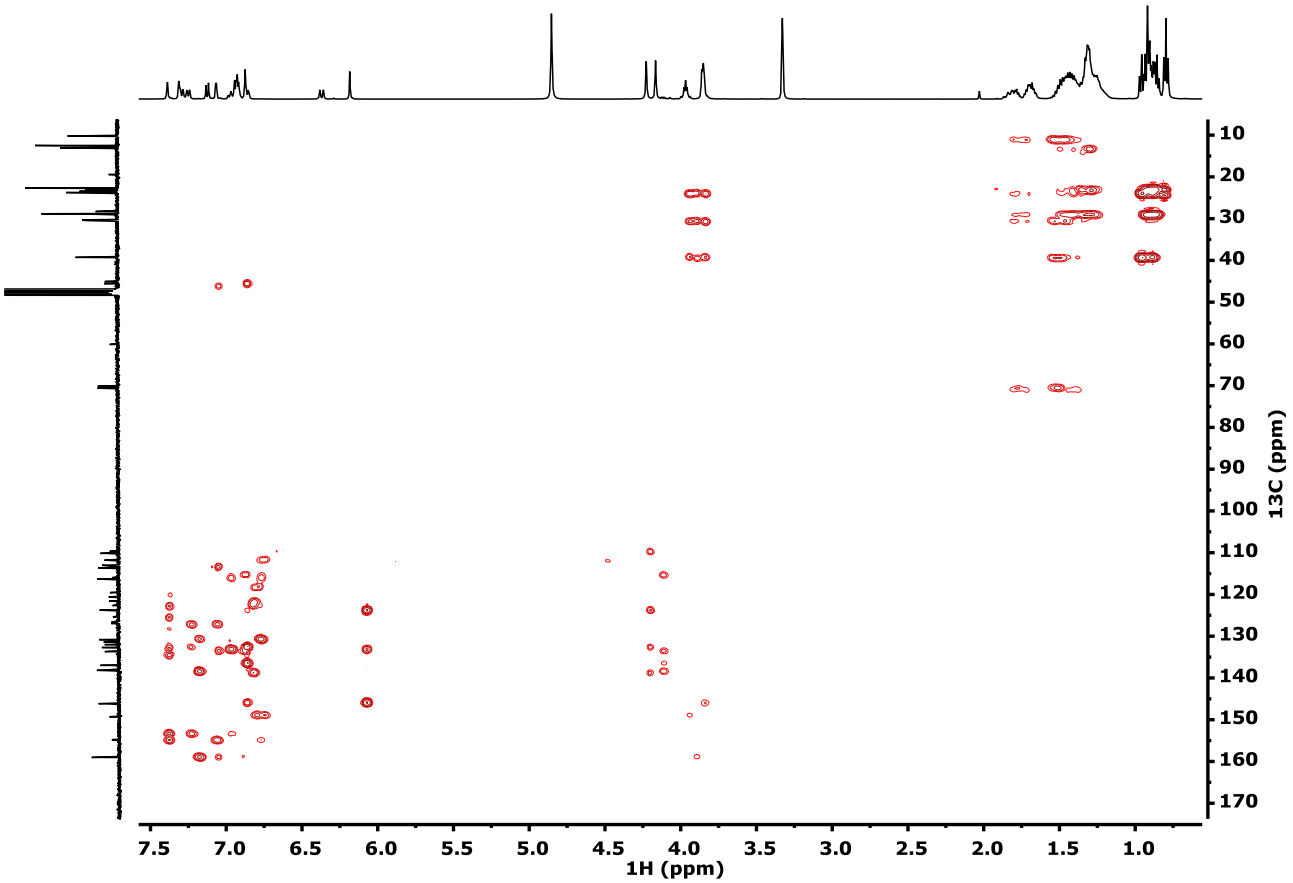


Figure S4.56. ^{1}H-^{19}F HMBC spectrum (400 MHz, chloroform-*d*) of **ADD**.

5. Characterization of the duplex formation

The binding constants were measured through ^{19}F and ^{1}H-NMR shift titrations performed, according to the availability, on Bruker Avance III instruments operating at 600 MHz (Cryo), 500 MHz, 400 MHz or 200 MHz.

During a typical experiment, the host was dissolved in chloroform-*d* (freshly filtered on alumina) or toluene-d_8 at a known concentration; the guest was dissolved at a known concentration in the host solution.

The **D** rich oligomer was normally chosen as host, so to have more than one ^{19}F signal to follow. To minimize the interference of the 1,3 folding in the case of the heterotrimers, the election host was the oligomer that experiences a more pronounced folding (e.g., **DAA** vs **DDD**).

Known volumes of the so prepared guest solution were added to the 5 mm NMR tube containing 500 µl of host solution and a spectrum was recorded after each addition at 298 K. The chemical shifts of the host -CF_3 or -OH resonances were plotted as a function of the guest concentration and analysed using a tailored Microsoft Excel-based software. The binding constants and limiting complexation-induced changes in chemical shifts the host reported in the tables were obtained by fitting the titration data to a 1:1 binding isotherm.

Errors were calculated as two times the standard deviation from the average value (95% confidence limit).

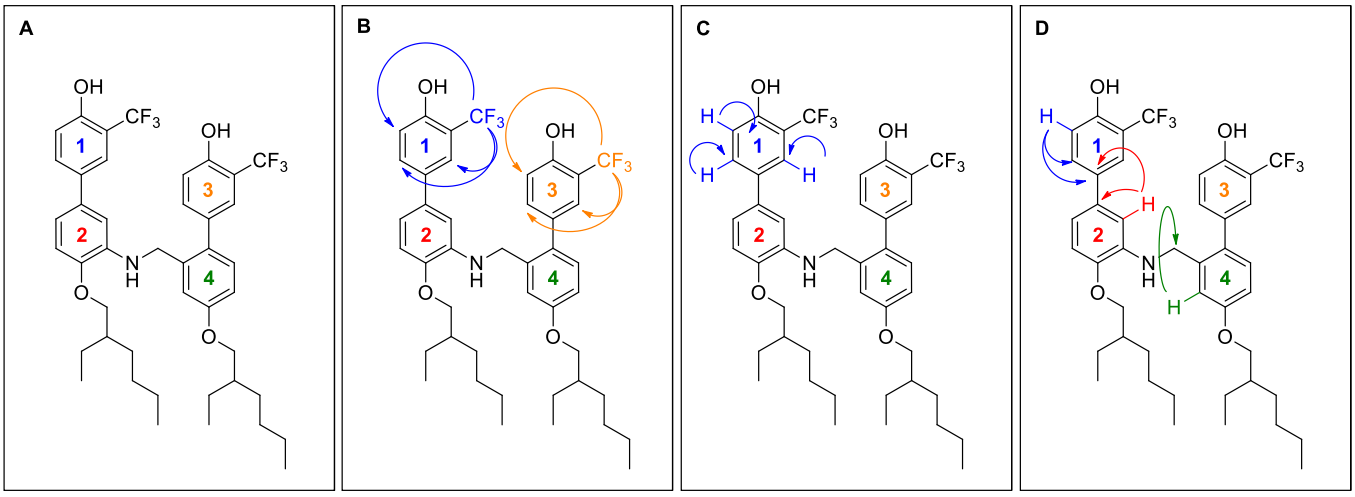
Self-association constants of mixed dimers were measured the same way using a 3 mm tube, starting at a known concentration (60 mM), and registering a spectrum after every dilution.

5.1 Assignation of ^{19}F signals

As discussed in the main text, the backbone of the system under analysis is not symmetrical and this generates a different separate signal for each -OH and -CF_3 residuals of the **D** bases (that are the ones normally followed in the titration experiments). To have a deeper insight on the properties of the duplex assignation of the CF_3 signals was necessary.

The signals were assigned by 2D-NMR experiments (reported in the sections 3 and 4 of this SI in the characterizations of each molecule), we proceeded as follows (*Scheme 5.1*):

- **A.** ^{1}H-^{1}H COSY was used to identify the protons belonging to the different aromatic rings.
- **B.** ^{1}H-^{19}F HMBC showed the correlations between the -CF_3 and all the three protons of the upper ring.
- **C.** ^{1}H-^{13}C HSQC was used to identify the proton-carbon correlations for each ring.
- **D.** long range ^{1}H-^{13}C HMBC allowed to determine the connections between the lower and upper ring of each **D** residual. The cross peaks involving the benzylic carbons where particularly useful to order the residuals from the -CO terminus to the -NH_2 terminus (each benzyl carbon gives a cross peak with the H on the same ring).



Scheme S5.1: Schematic representation of the ^{19}F assignation workflow. Example on the dimer **DD**. For clarity, not all the useful connections are shown.

#	CO-terminus → NH₂-terminus								
	1			2			3		
	δ_{free}	δ_{bound}	$\delta\Delta$	δ_{free}	δ_{bound}	$\delta\Delta$	δ_{free}	δ_{bound}	$\delta\Delta$
D_{CO}	-61,32	-63,01	-1,69	--	--	--	--	--	--
DD	-60,68	-62,05	-1,37	-60,73	-62,20	-1,47	--	--	--
DDD	-60,74	-62,00	-1,26	-60,74	-62,20	-1,47	-60,97	-62,38	-1,41
DDA	-60,89	-61,49	-0,60	-60,72	-61,89	-1,17	--	--	--
ADD	--	--	--	-60,70	-61,89	-1,19	-61,98	-61,88	0,10
DAA	-60,70	-62,09	-1,38	--	--	--	--	--	--

Table S5.1: Chemical shifts of the different CF_3 signals and their variations upon binding (from titration fitting).

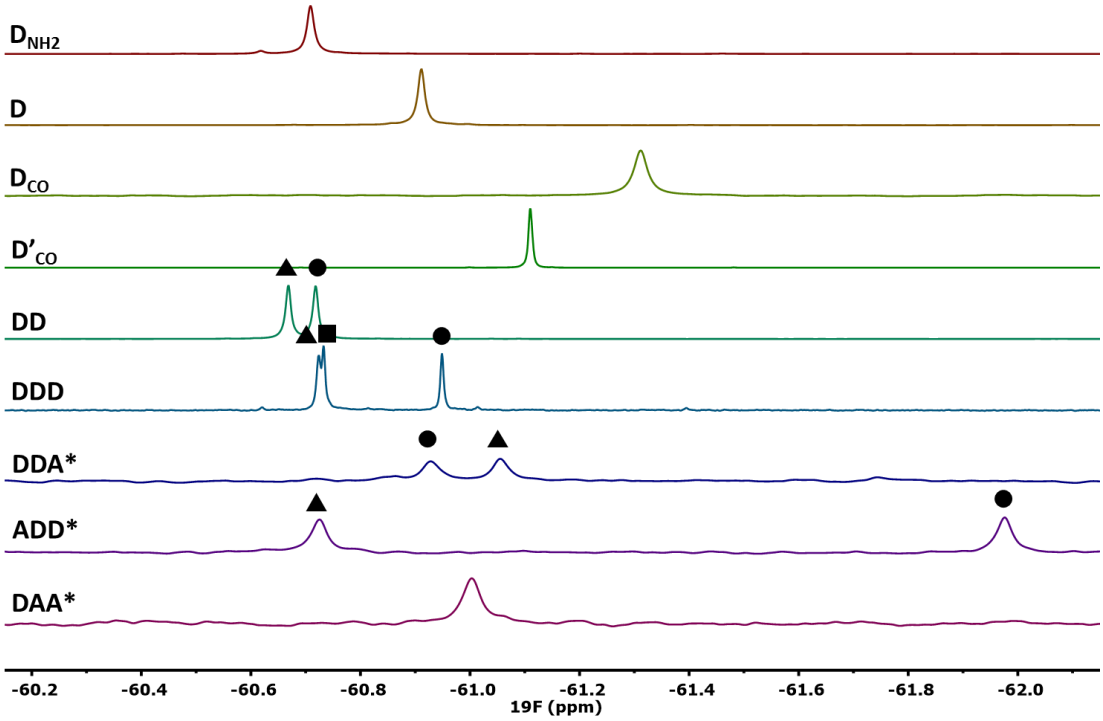


Figure S5.1: ^{19}F NMR spectra in chloroform-*d* of D-containing monomers and oligomers used in the work. ▲ indicates the CO- terminus; ■ indicates the central base; ● indicates the -NH_2 terminus. * The signals of the heterotrimers shift according to the concentration, the spectra shown in the figure are recorded at a concentration of 0.1 mM. Different S/N ratio and linewidth are due to the different instruments used.

5.2 NMR titrations in chloroform-*d*

5.2.1 D_{CO} vs A_{CO}

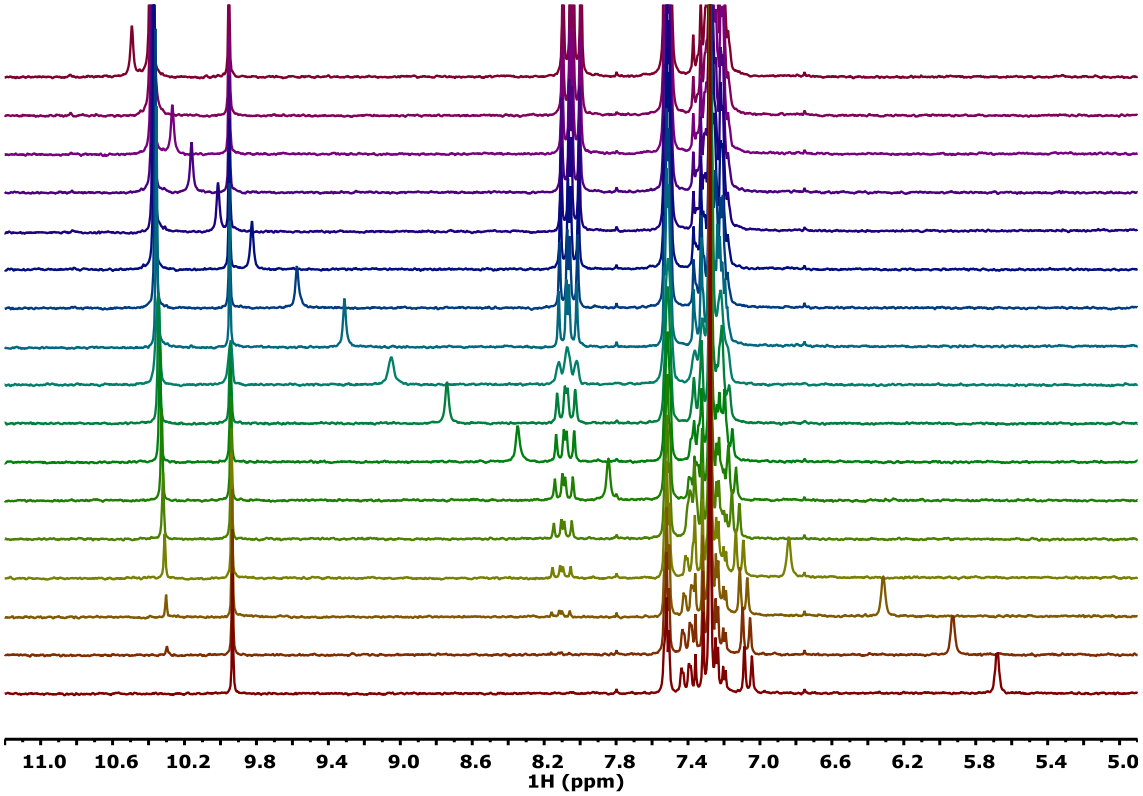


Figure S5.2: ^{1}H NMR titration of **A_{CO}** (40.6 mM) into **D_{CO}** (2.3 mM) in chloroform-*d*. Spectra recorded (bottom to top) for 0, 3, 8, 16, 26, 36, 51, 66, 81, 96, 116, 141, 166, 226, 256, 296 µl of **A_{CO}** added into 500 µl of **D_{CO}**.

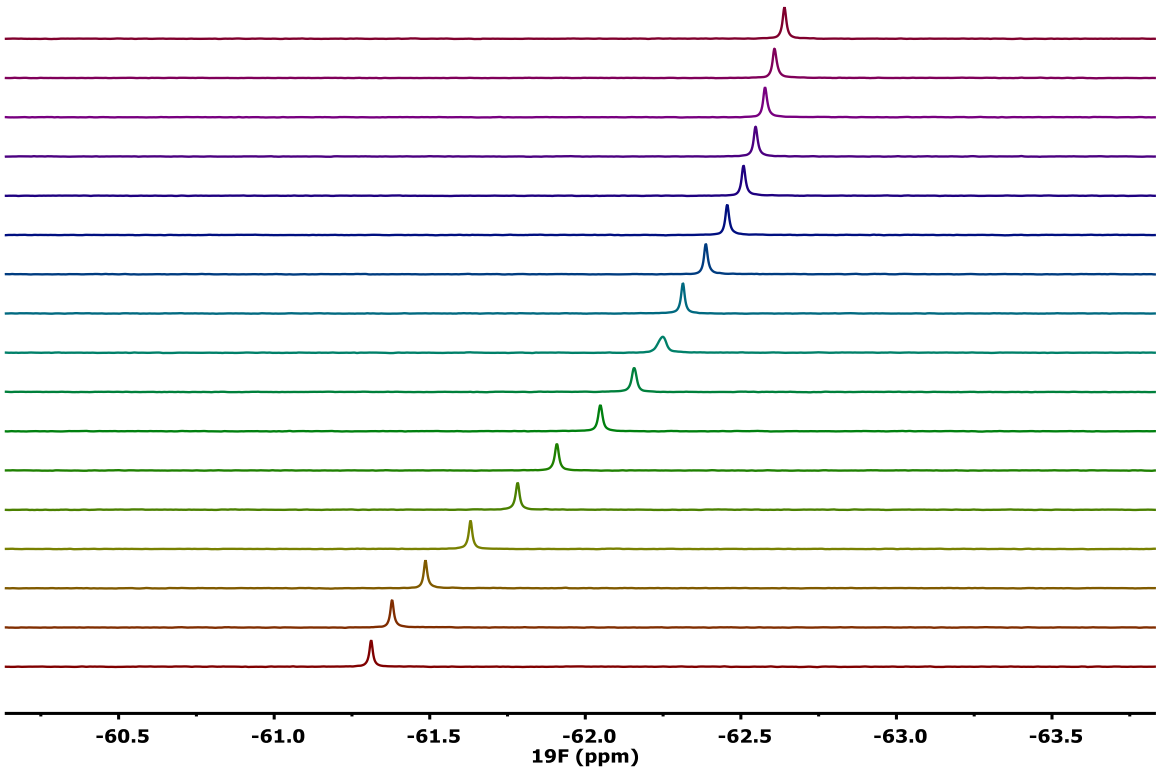


Figure S5.3: ^{19}F NMR titration of **A_{CO}** (40.6 mM) into **D_{CO}** (2.3 mM) in chloroform-*d*. Conditions as in *Figure 5.1*.

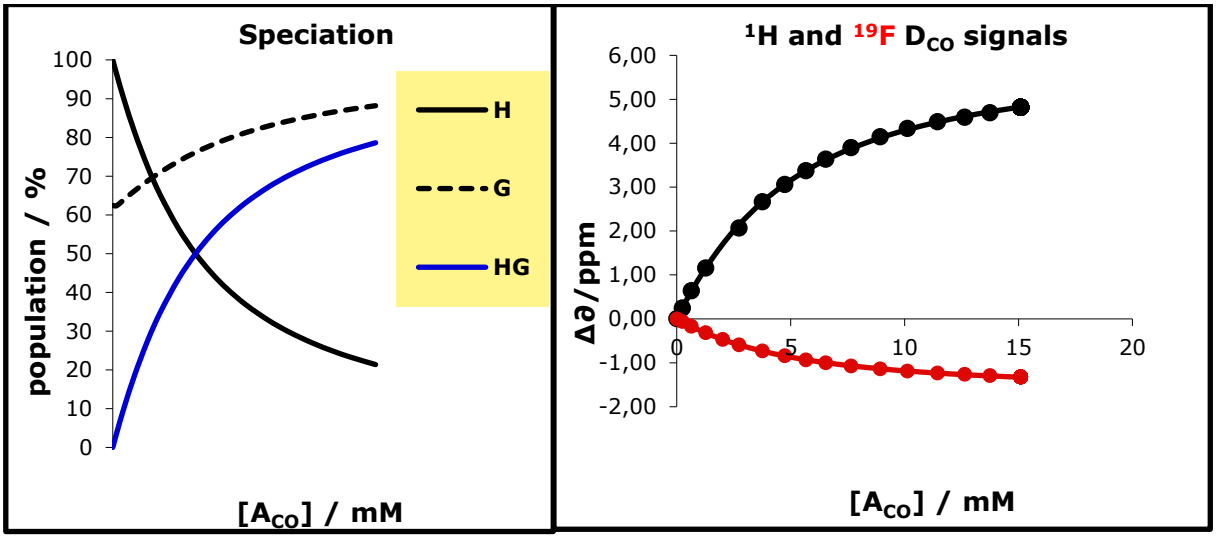


Figure S5.4: Plot of the change in chemical shift of the $\mathbf{D_{CO}}$ ^{19}F (**red**) and ^{1}H (**black**) signal in chloroform-*d* as a function of [$\mathbf{A_{CO}}$] (the line represents the best fit to a 1:1 binding isotherm) and speciation as a function of [$\mathbf{A_{CO}}$] obtained from the average of the two constants.

5.1.2 DD vs AA

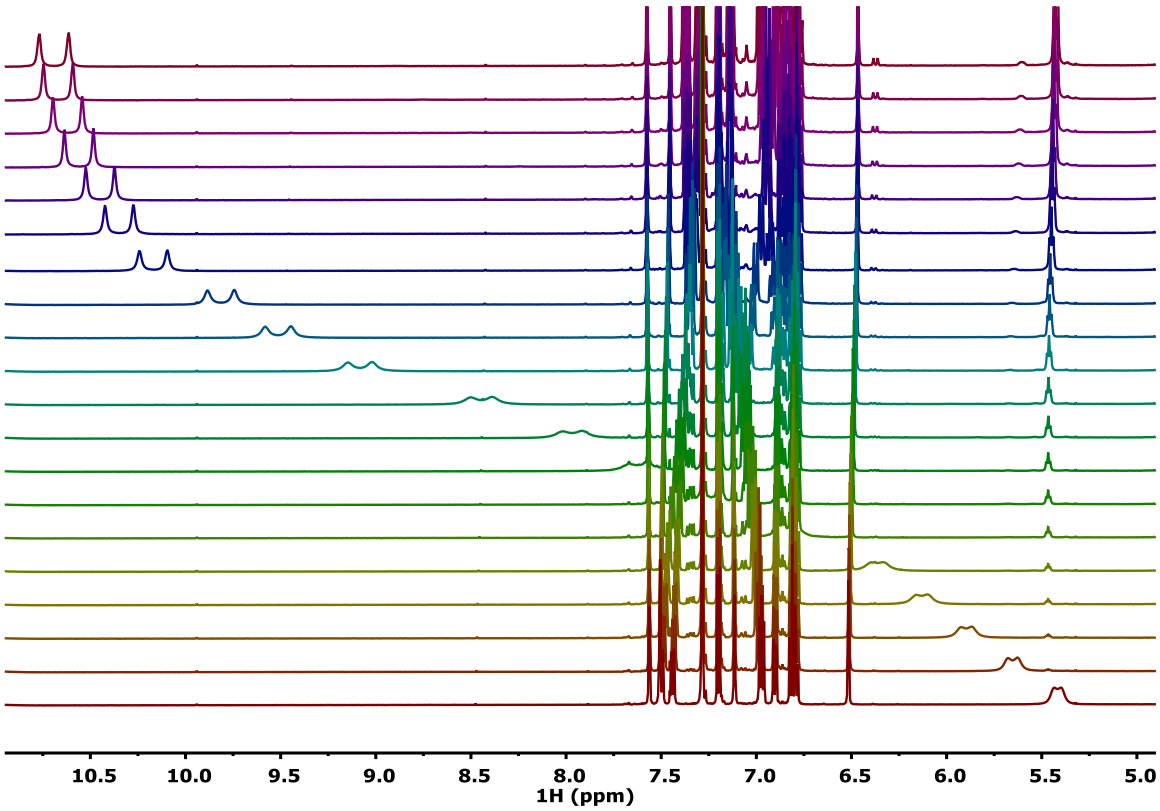


Figure S5.5: ^{1}H NMR titration of **AA** (10.0 mM) into **DD** (2.3 mM) in chloroform-*d*. Spectra recorded (bottom to top) of 0, 5, 10, 15, 20, 30, 40, 50, 60, 75, 100, 125, 150, 200, 300, 400, 500, 700, 900 µl of **AA** into 500 µl of **DD**.

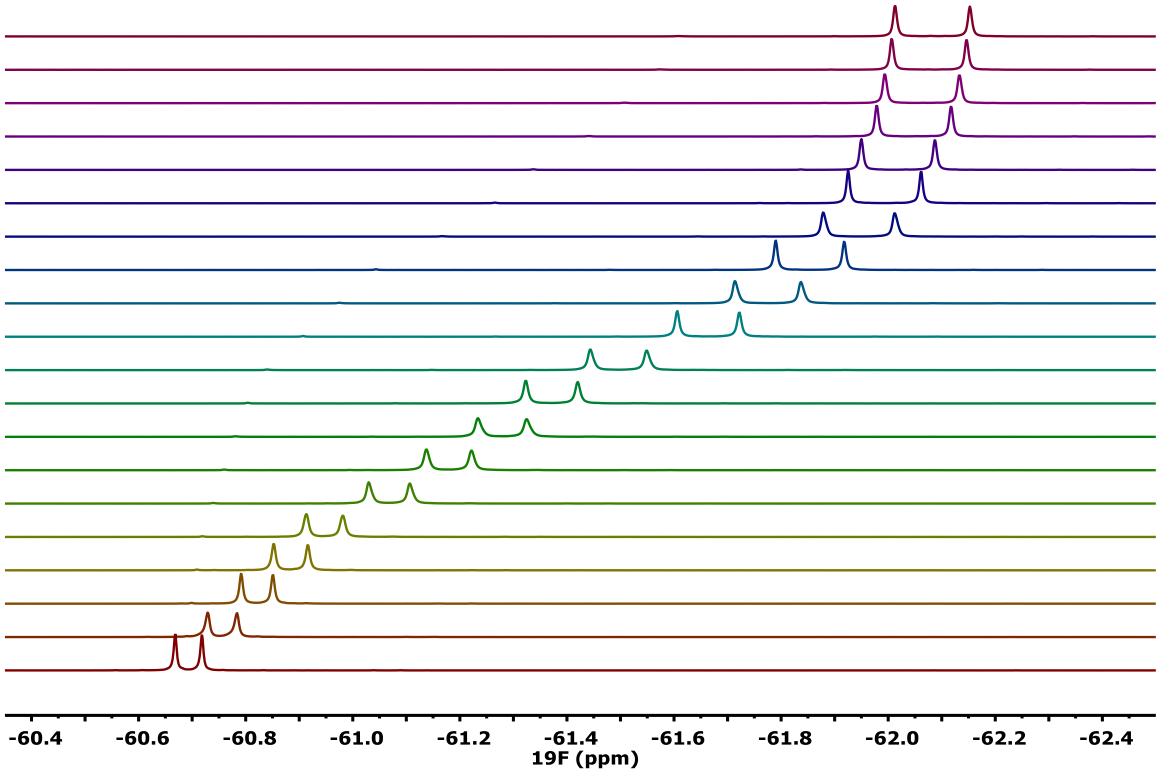


Figure S5.6: ^{19}F NMR titration of **AA** (10.0 mM) into **DD** (2.3 mM) in chloroform-*d*. Conditions as in *Figure 5.4*.

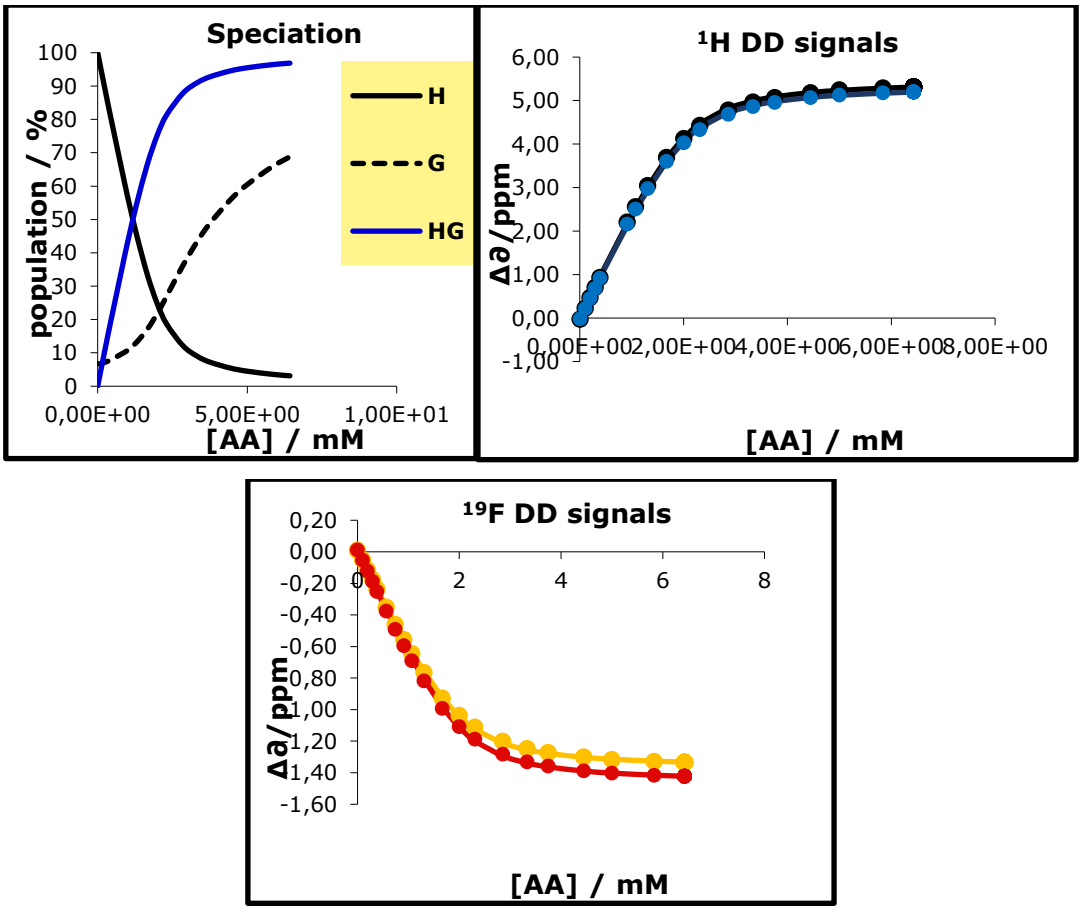


Figure S5.7: Plot of the change in chemical shift of the **DD** ^{19}F (**red** and **orange**) and ^{1}H (**black** and **blue**) signals in chloroform-*d* as a function of [**AA**] (the line represents the best fit to a 1:1 binding isotherm) and speciation as a function of [**AA**] obtained from the average of the four constants.

5.2.3 DDD vs AAA

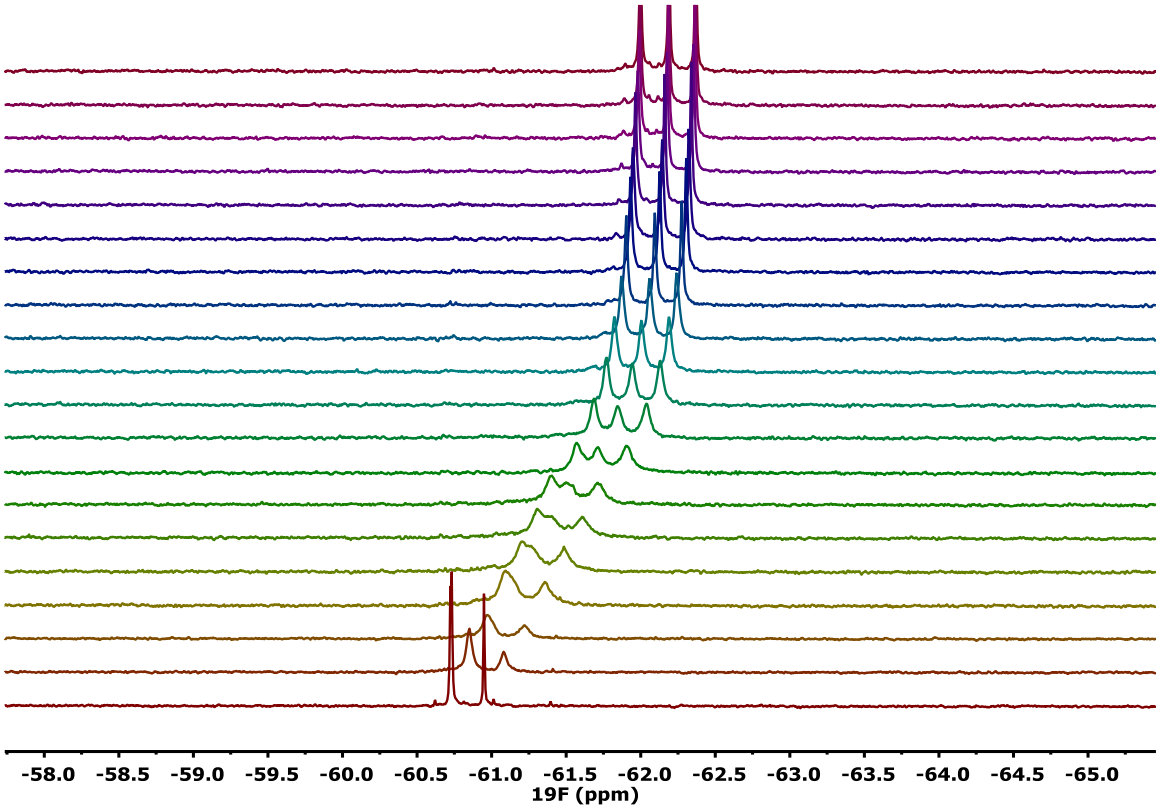


Figure S5.8: ^{19}F NMR titration of **AAA** (1.0 mM) into **DDD** (0.1mM) in chloroform-*d*. Spectra recorded (bottom to top) for 0, 5, 10, 15, 20, 25, 30, 40, 50, 60, 70, 85, 100, 125, 150, 200, 300, 500, 700, 900 µl of **AAA** into 500 µl of **DDD**.

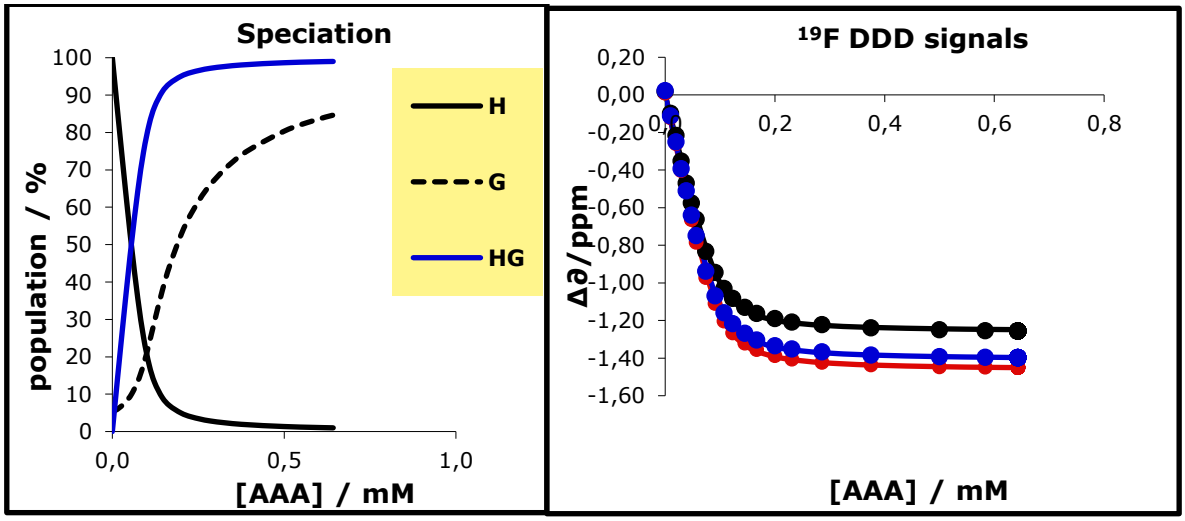


Figure S5.9: Plot of the change in chemical shift of the **DDD** ^{19}F (**black**, **blue**, and **red**) signals in chloroform-*d* as a function of [**AAA**] (the line represents the best fit to a 1:1 binding isotherm) and speciation as a function of [**AAA**] obtained from the average of the three constants. At the concentrations required for a successful titration of the trimers the ^{1}H NMR signals of the -OH moieties could not be used for the estimation of the binding constants under reasonable spectra acquisition times.

5.2.4 DDA vs AAA

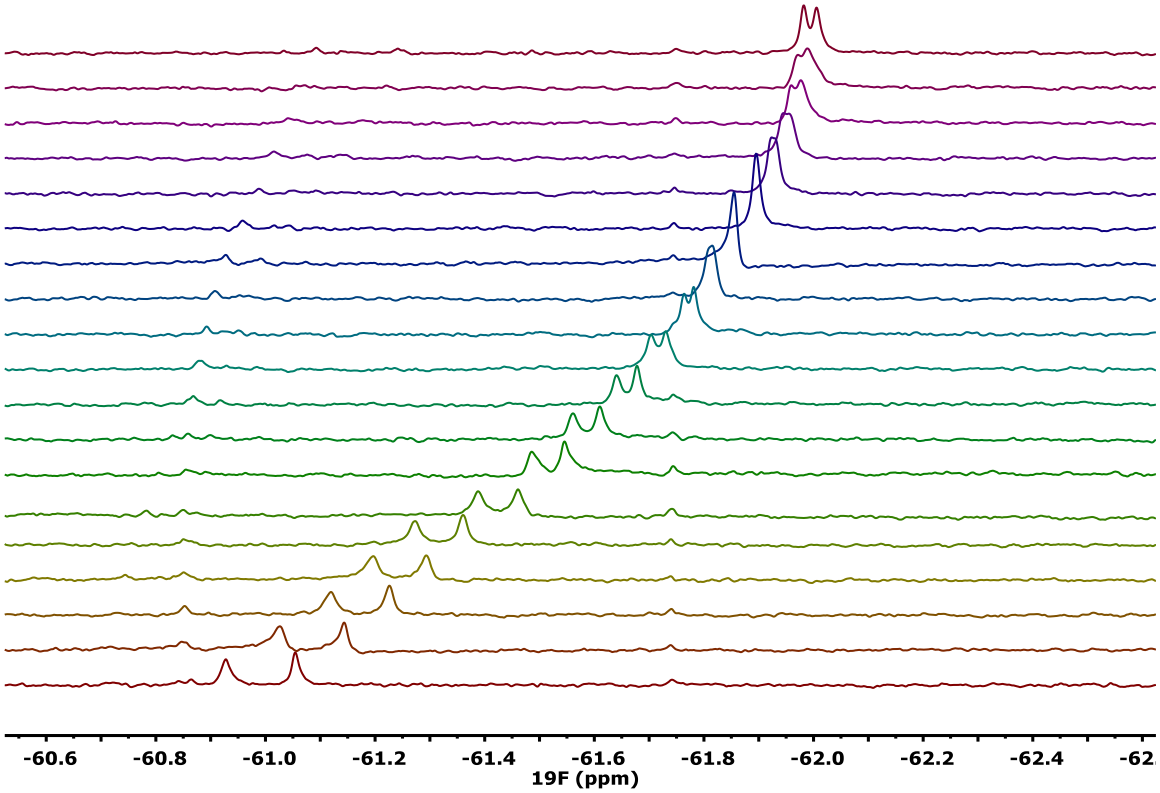


Figure S5.10: ^{19}F NMR titration of **AAA** (2 mM) into **DDA** (0.1 mM) in chloroform-*d*. Spectra recorded (bottom to top) for 0, 5, 10, 15, 20, 30, 40, 50, 65, 80, 100, 120, 150, 190, 240, 300, 360, 460, 660 µl of **AAA** into 500 µl of **DDA**.

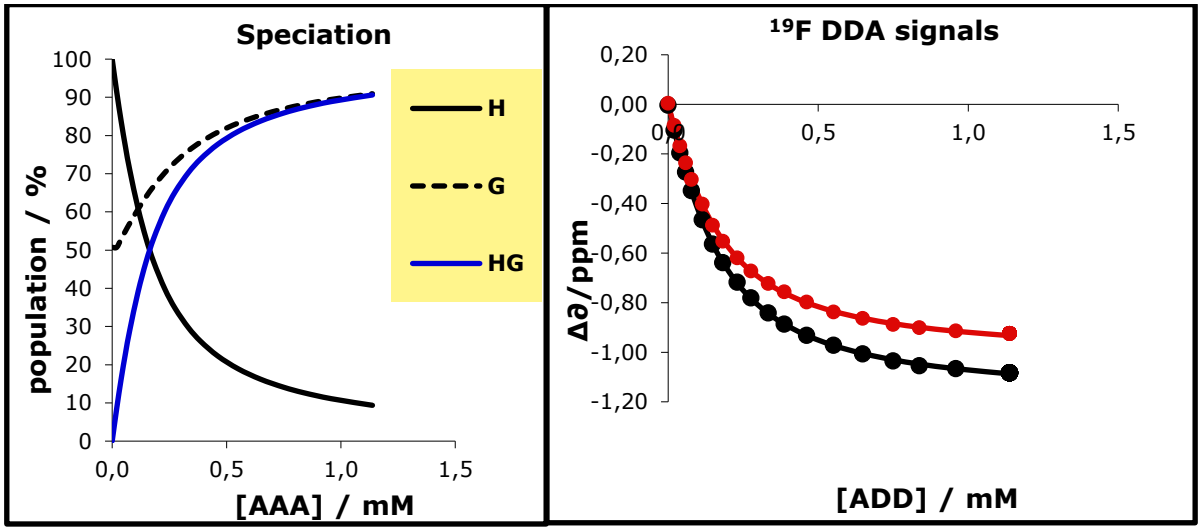


Figure S5.11: Plot of the change in chemical shift of the **DDA** ^{19}F (**black** and **red**) signals in chloroform-*d* as a function of [**AAA**] (the line represents the best fit to a 1:1 binding isotherm) and speciation as a function of [**AAA**] obtained from the average of the two constants.

5.2.5 ADD vs AAA

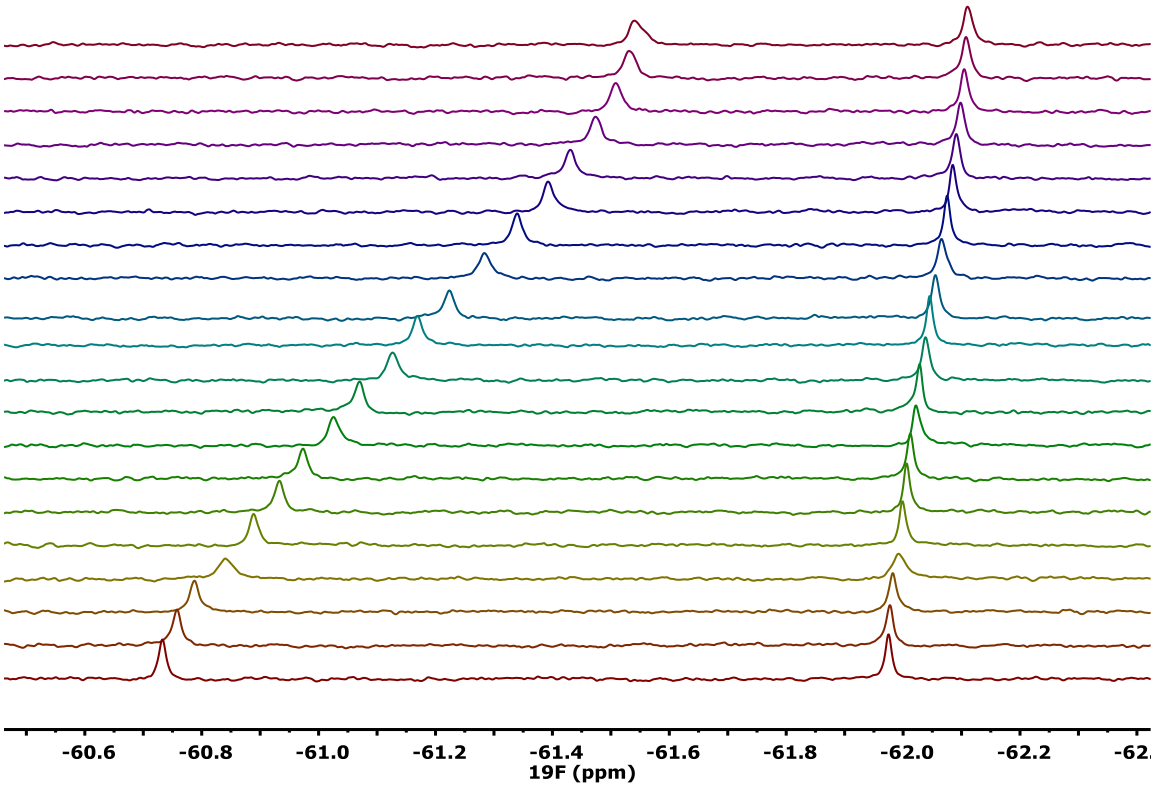


Figure S5.12: ^{19}F NMR titration of **AAA** (2 mM) into **ADD** (0.1 mM) in chloroform-*d*. Spectra recorded (bottom to top) for 0, 5, 10, 20, 30, 40, 50, 65, 80, 100, 120, 150, 190, 240, 300, 360, 460, 560, 660, 800 µl of **AAA** into 500 µl of **ADD**.

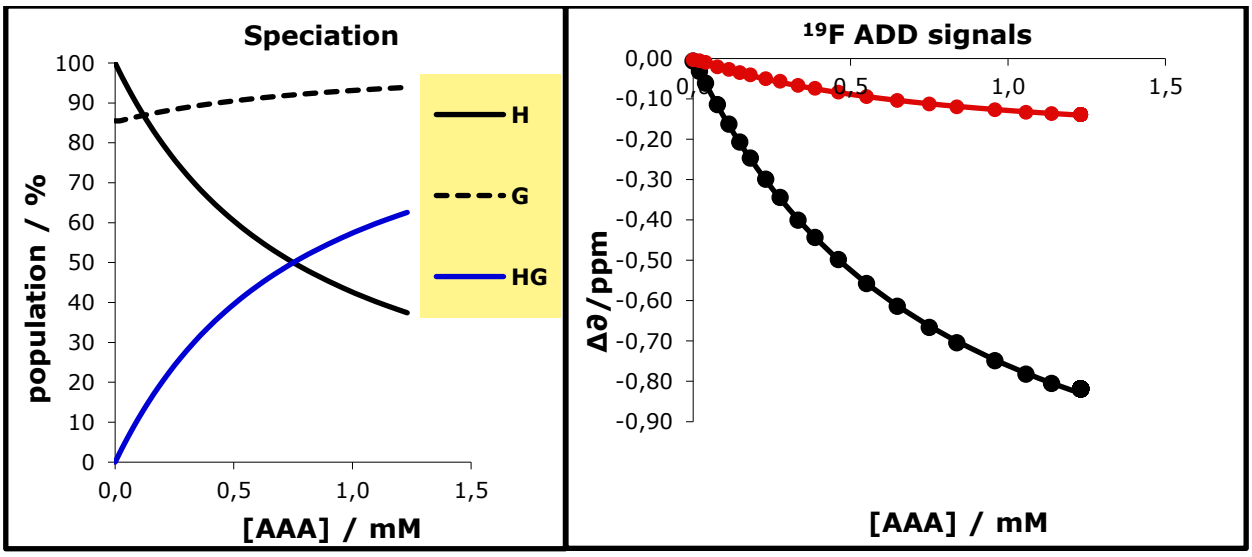


Figure S5.13: Plot of the change in chemical shift of the **ADD** ^{19}F (**black** and **red**) signals in chloroform-*d* as a function of [**AAA**] (the line represents the best fit to a 1:1 binding isotherm) and speciation as a function of [**AAA**] obtained from the average of the two constants.

5.2.6 DAA vs DDD

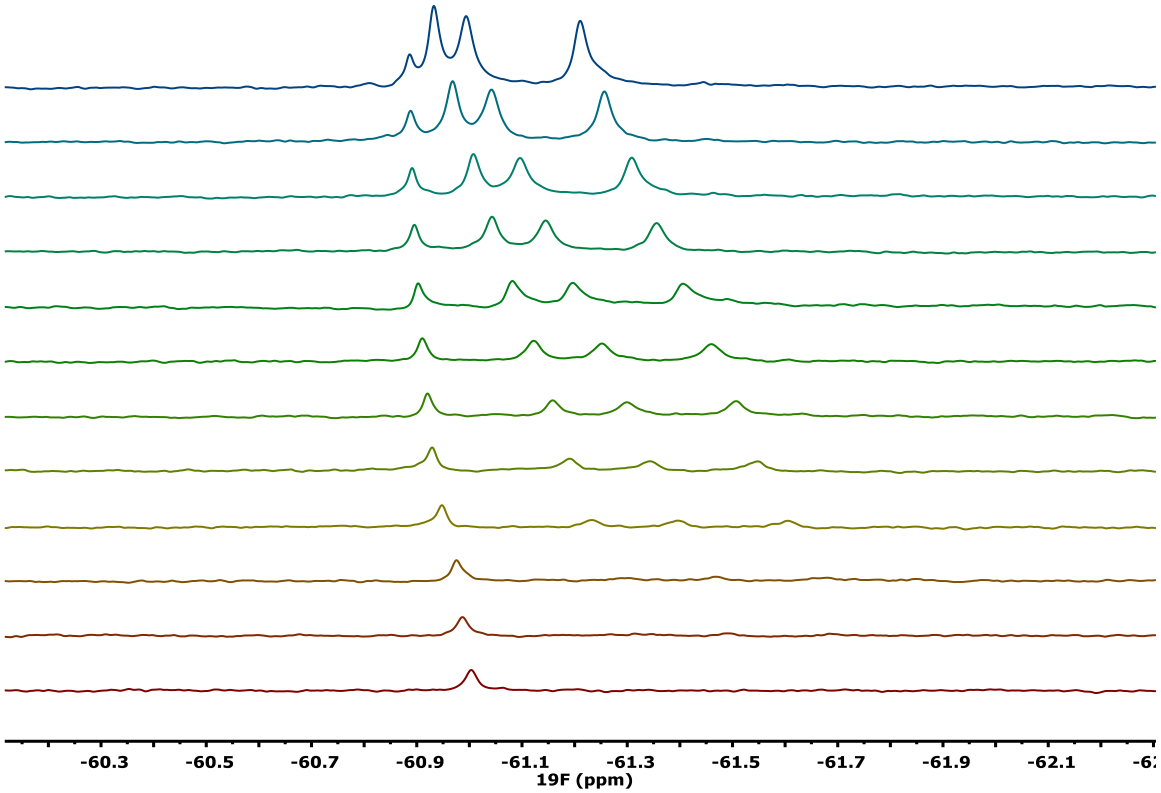


Figure S5.14: ^{19}F NMR titration of **DDD** (2 mM) into **DAA** (0.1 mM) in chloroform-*d*. Spectra recorded (bottom to top) for 0, 5, 10, 20, 30, 40, 50, 65, 80, 100, 130, 170 µl of **DDD** into 500 µl of **DAA**.

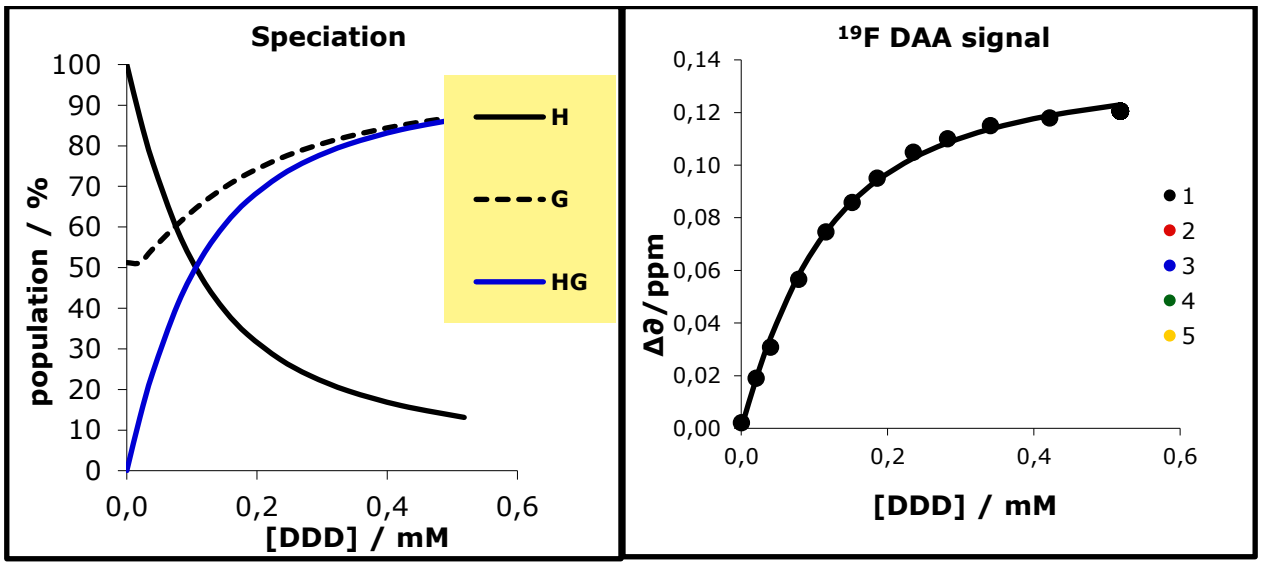


Figure S5.15: Plot of the change in chemical shift of the **DAA** ^{19}F (**black**) signal in chloroform-*d* as a function of [**DDD**] (the line represents the best fit to a 1:1 binding isotherm) and speciation as a function of [**DDD**].

5.2.7 DDA vs DAA

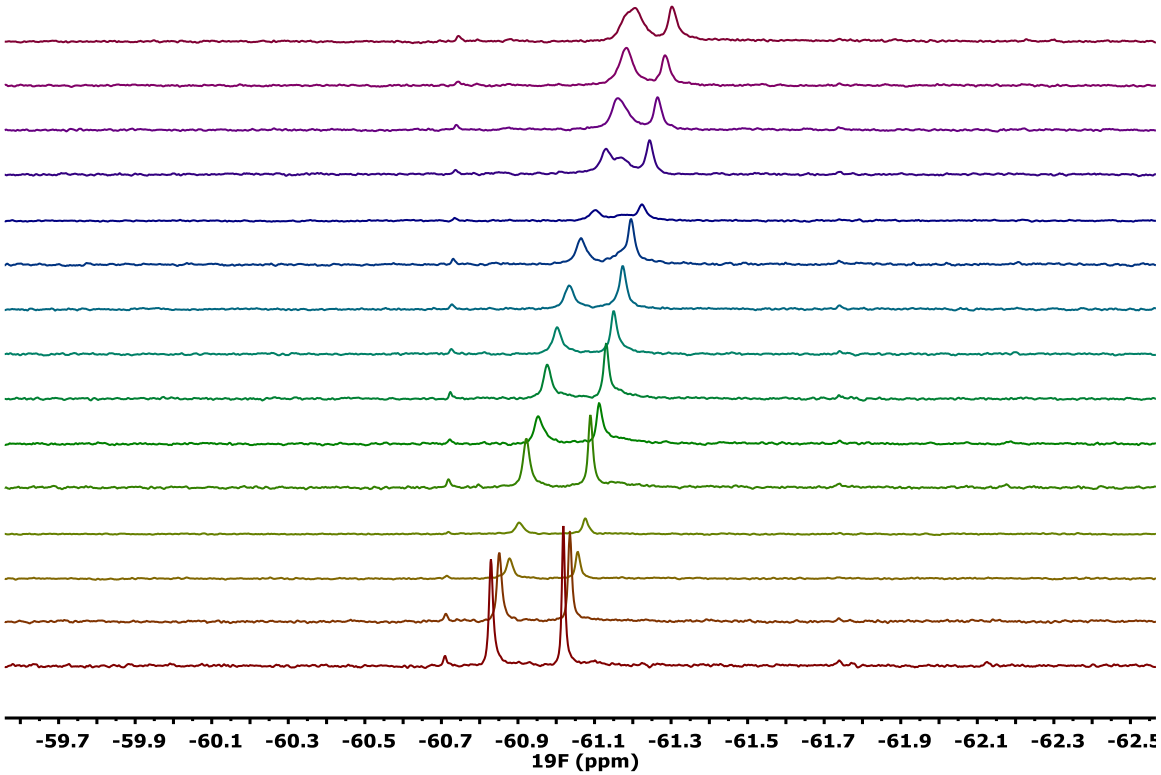


Figure S5.16: ^{19}F NMR titration of **DAA** (0.5 mM) into **DDA** (0.05 mM) in chloroform-*d*, partial. Spectra recorded (bottom to top) for 0, 3, 6, 9, 12, 16, 20, 24, 29, 34, 40, 46, 52, 58 µl of **DAA** into 500 µl of **DDA**.

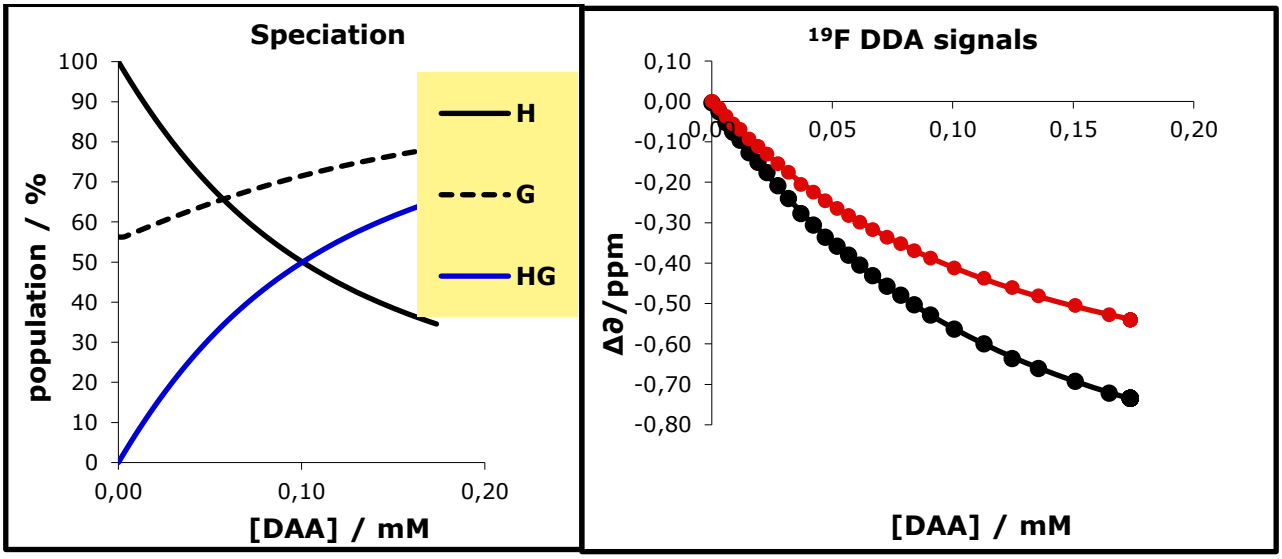


Figure S5.17: Plot of the change in chemical shift of the **DDA** ^{19}F (**black** and **red**) signals in chloroform-*d* as a function of [**DAA**] (the line represents the best fit to a 1:1 binding isotherm) and speciation as a function of [**DAA**] obtained from the average of the two constants.

5.2.8 ADD vs DAA

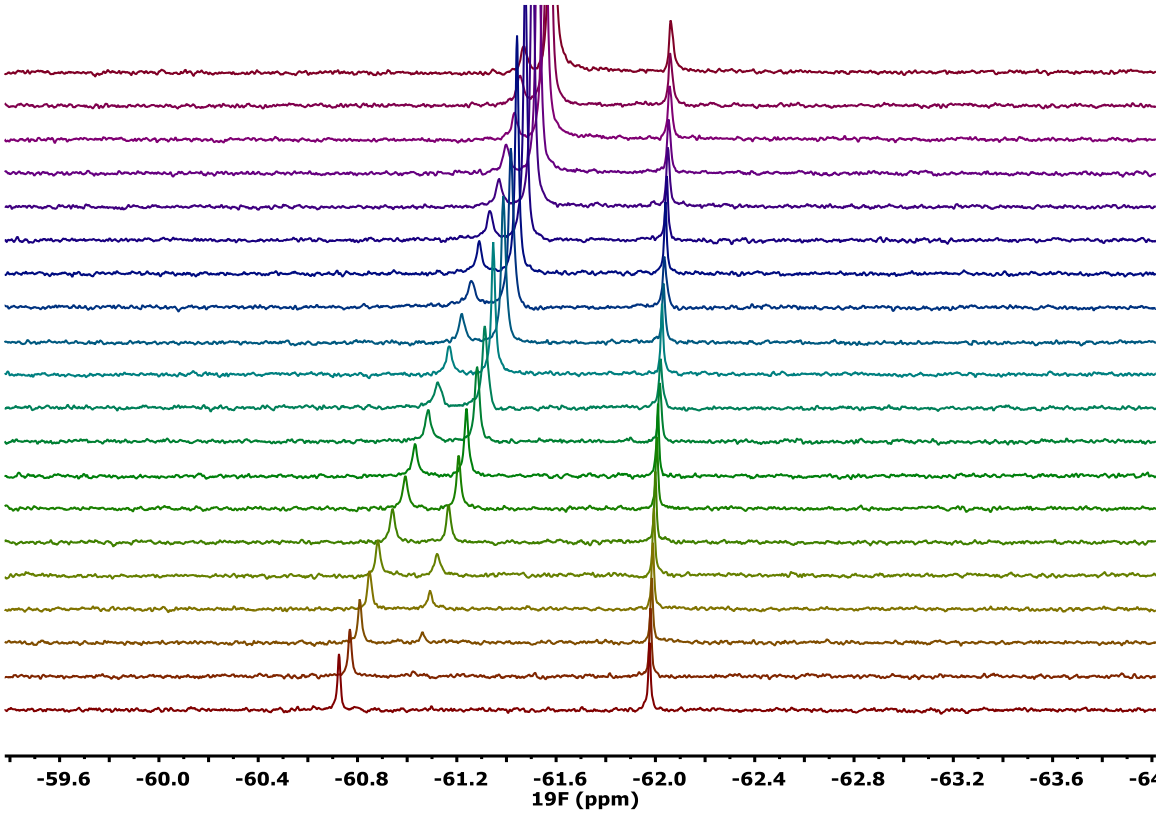


Figure S5.18: ^{19}F NMR titration of **DAA** (2 mM) into **ADD** (0.1 mM) in chloroform-*d*. Spectra recorded (bottom to top) of 0, 5, 10, 15, 20, 30, 40, 50, 65, 80, 100, 130, 160, 190, 240, 300, 360, 460, 560, 660 µl of **DAA** into 500 µl of **ADD**.

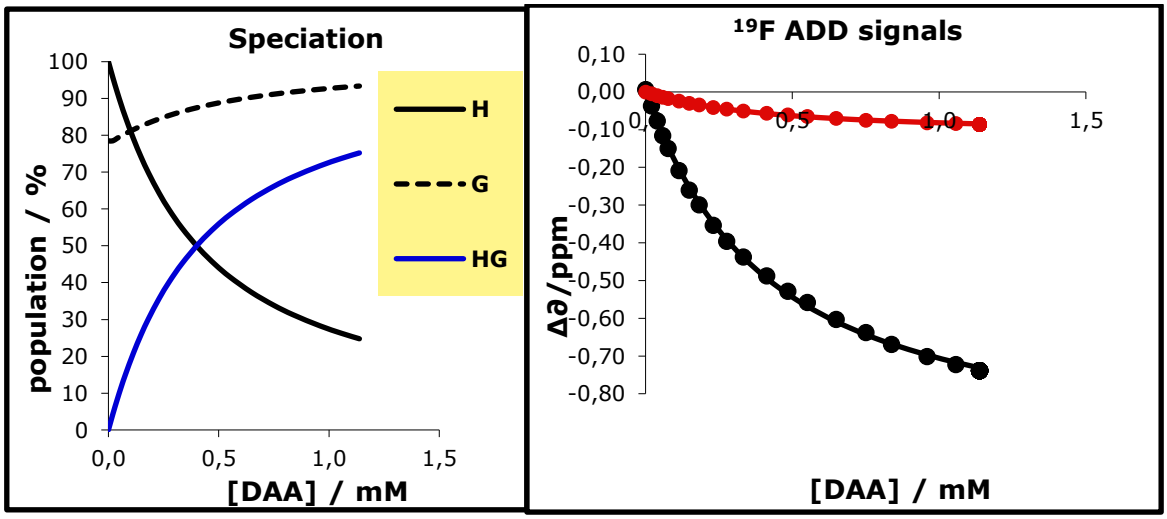


Figure S5.19: Plot of the change in chemical shift of the **ADD** ^{19}F (**black** and **red**) signals in chloroform-*d* as a function of [**DAA**] (the line represents the best fit to a 1:1 binding isotherm) and speciation as a function of [**DAA**] obtained from the average of the two constants.

5.2.9 DA dilution

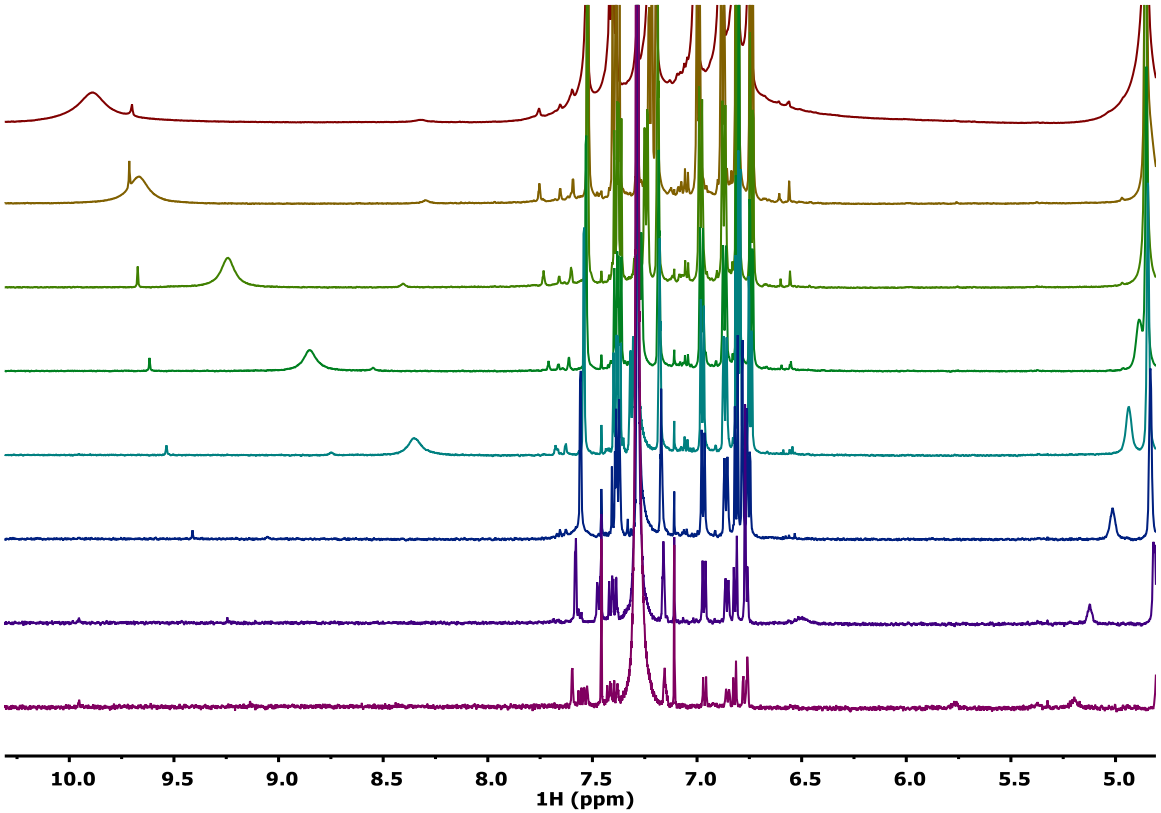


Figure S5.20: ^{1}H spectra of the dilution titration of **DA** (top to bottom 60, 30, 10, 5, 2.5, 1, 0.25, 0.05 mM) in chloroform-*d*.

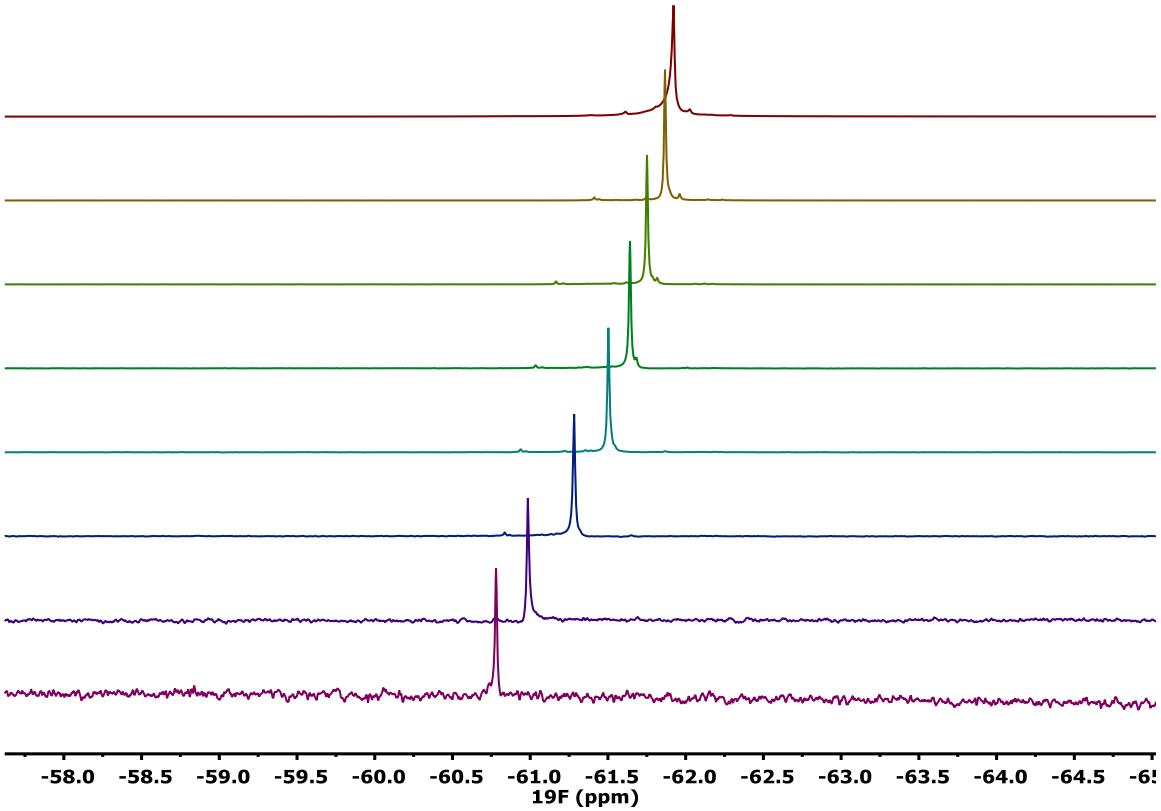


Figure S5.21: ^{19}F spectra of the dilution titration of **DA** (top to bottom 60, 30, 10, 5, 2.5, 1, 0.25, 0.05 mM) in chloroform-*d*.

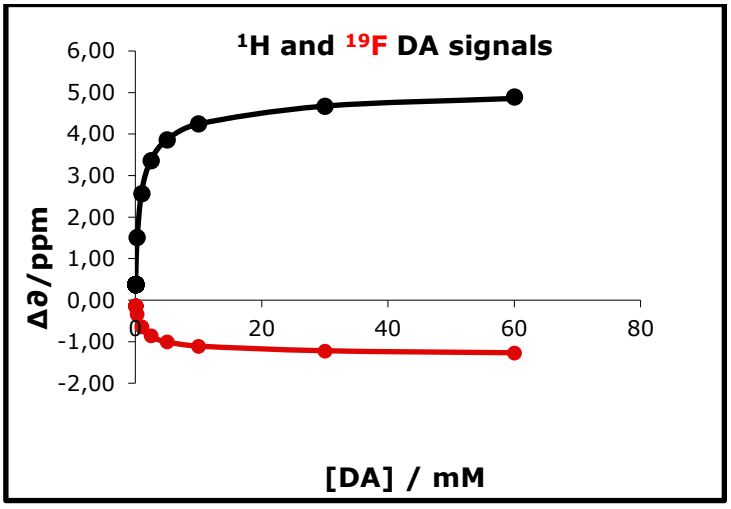


Figure S5.22: Plot of the change in chemical shift upon dilution of a solution of the **DA** ^{19}F (**red**) and ^{1}H (**black**) signals in chloroform-*d* as a function of [**DA**] (the line represents the best fit to a 1:1 binding isotherm).

5.2.10 DDA dilution

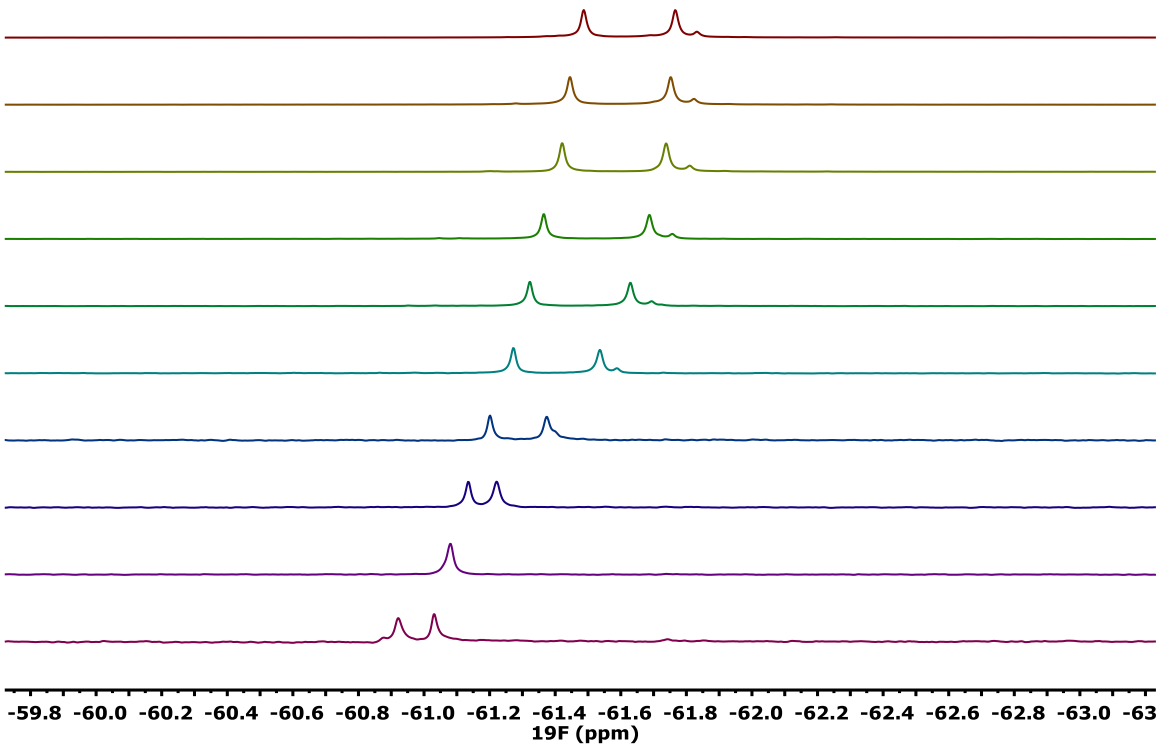


Figure S5.23: ^{19}F spectra of the dilution titration of **DDA** (top to bottom 50, 30, 20, 10, 5, 2.5, 1, 0.5, 0.25, 0.1 mM) in chloroform-*d*.

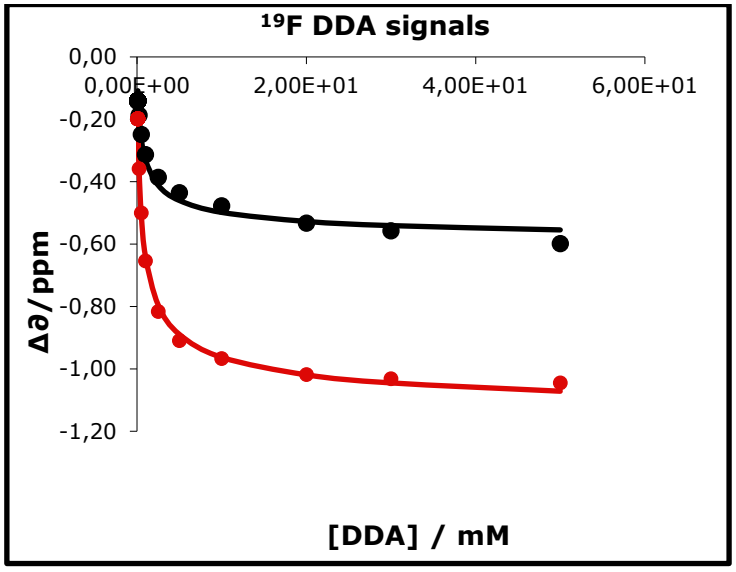


Figure S5.24: Plot of the change in chemical shift upon dilution of a solution of the **DDA** ^{19}F signals in chloroform-*d* as a function of [**DDA**] (the line represents the best fit to a 1:1 binding isotherm).

5.2.11 DAA dilution

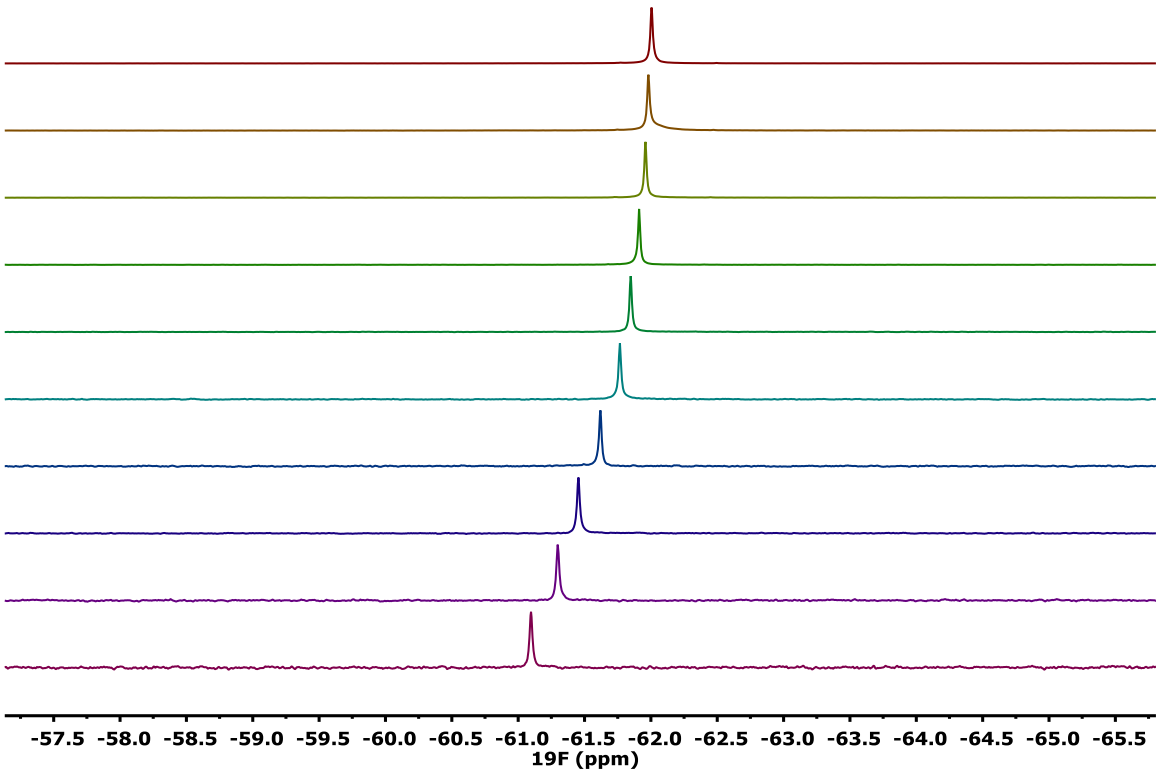


Figure S5.25: ^{19}F spectra of the dilution titration of **DAA** (top to bottom 50, 30, 20, 10, 5, 2.5, 1, 0.5, 0.25, 0.1 mM) in chloroform-*d*.

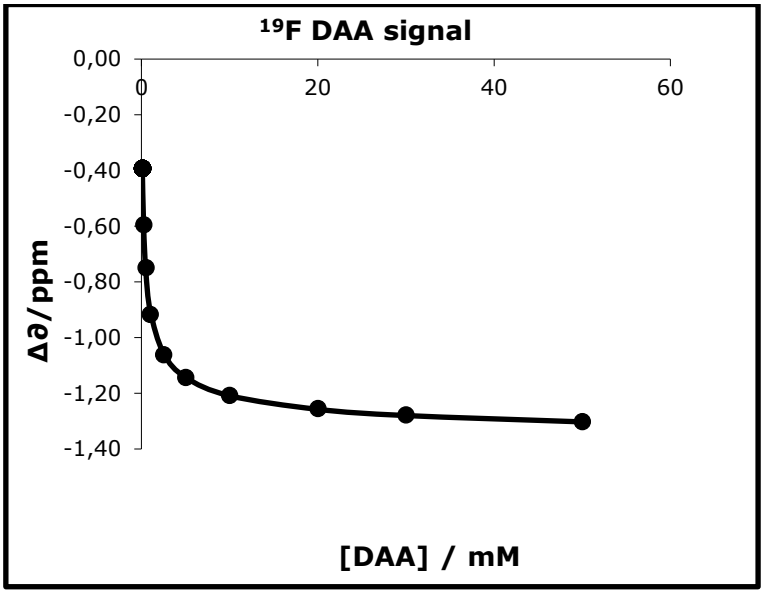


Figure S5.26: Plot of the change in chemical shift upon dilution of a solution of the **DAA** ^{19}F signal in chloroform-*d* as a function of [**DAA**] (the line represents the best fit to a 1:1 binding isotherm).

5.1.12 ADD dilution

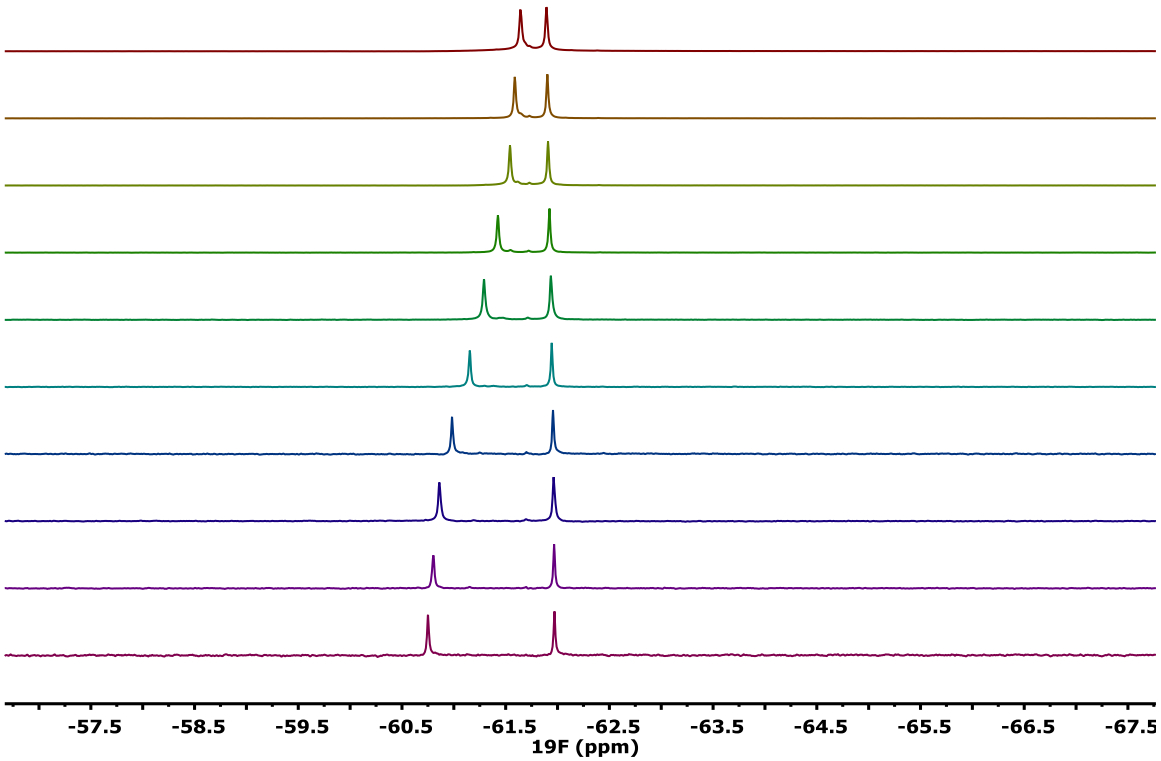


Figure S5.27: ^{19}F spectra of the dilution titration of **ADD** (top to bottom 50, 30, 20, 10, 5, 2.5, 1, 0.5, 0.25, 0.1 mM) in chloroform-*d*

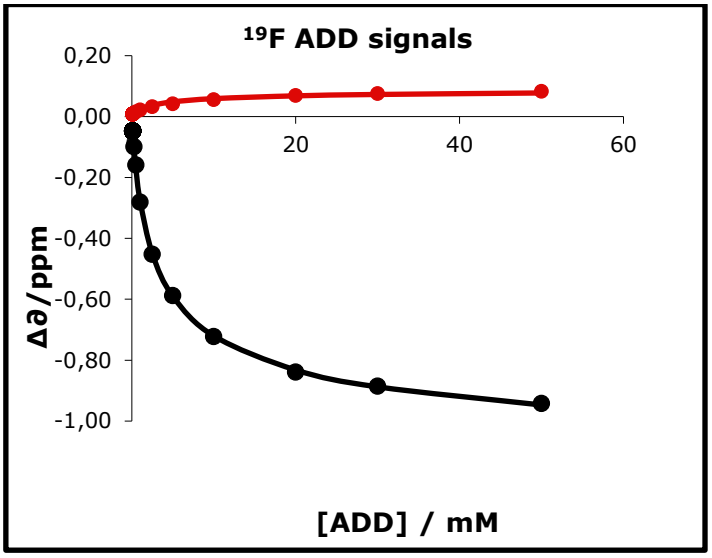


Figure S5.28: Plot of the change in chemical shift upon dilution of a solution of the **ADD** ^{19}F signal in chloroform-*d* as a function of [**ADD**] (the line represents the best fit to a 1:1 binding isotherm).

5.3 Titrations in toluene-d_8

5.3.1 D_{CO} vs A_{CO}

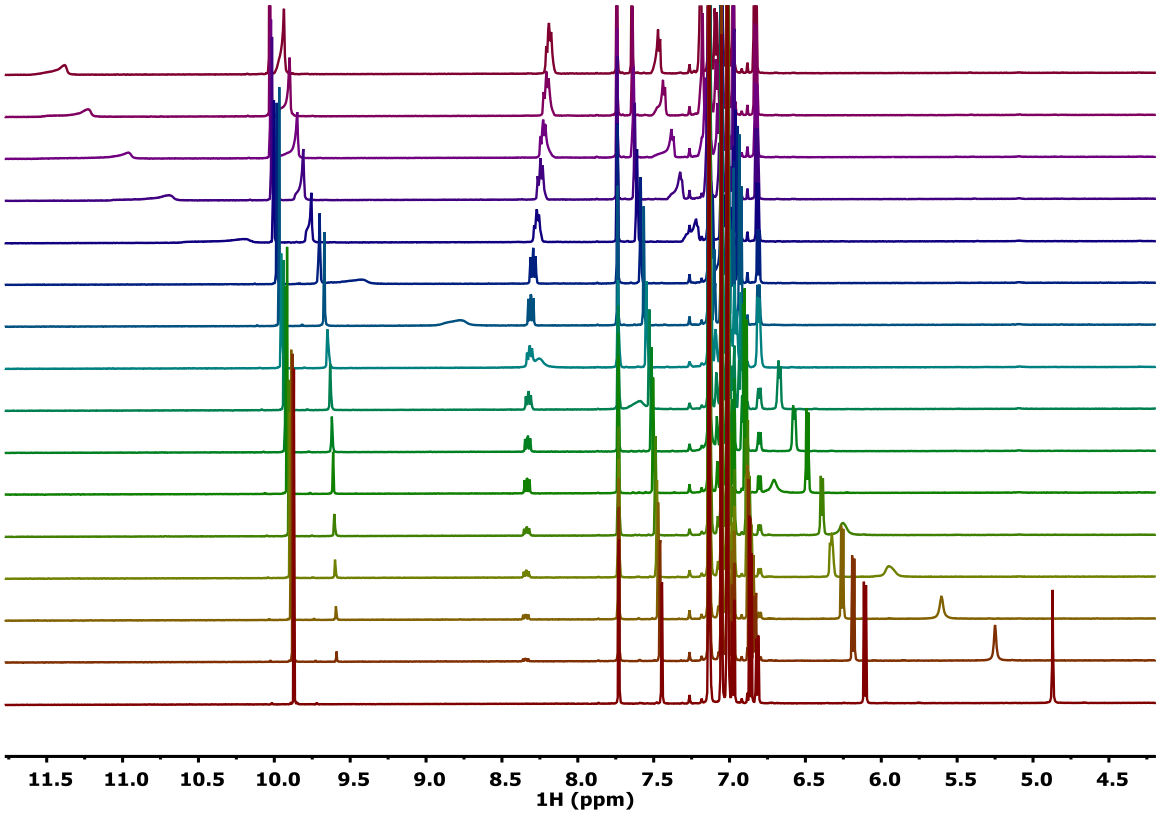


Figure S2.29: ^{1}H NMR titration of $\mathbf{A_{CO}}$ (6.7 mM) into $\mathbf{D_{CO}}$ (2.3 mM) in toluene-d_8. Spectra recorded (bottom to top) for 0, 10, 20, 30, 40, 55, 70, 90, 120, 150, 200, 300, 400, 600, 800, 950 of $\mathbf{A_{CO}}$ added into 500 µl of $\mathbf{D_{CO}}$.

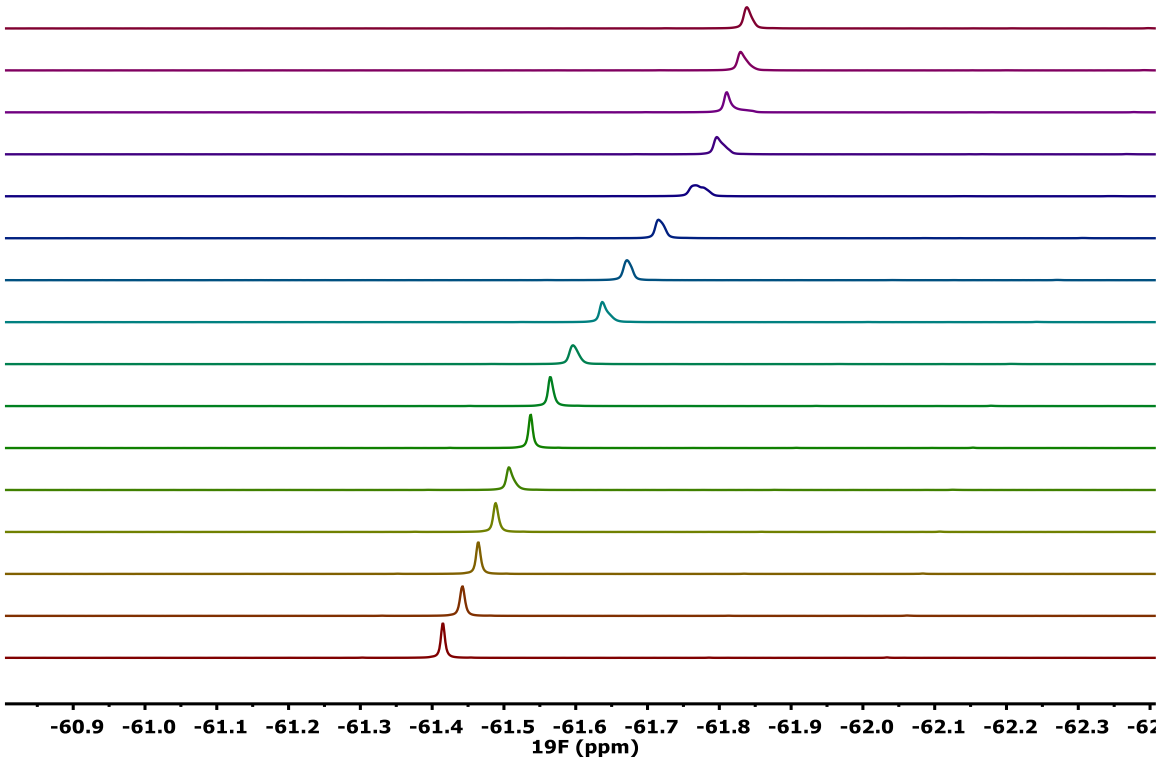


Figure S2.30: ^{19}F NMR titration of $\mathbf{A_{CO}}$ (6.7 mM) into $\mathbf{D_{CO}}$ (2.3 mM) in toluene-d_8. Conditions as in *Figure 2.28*.

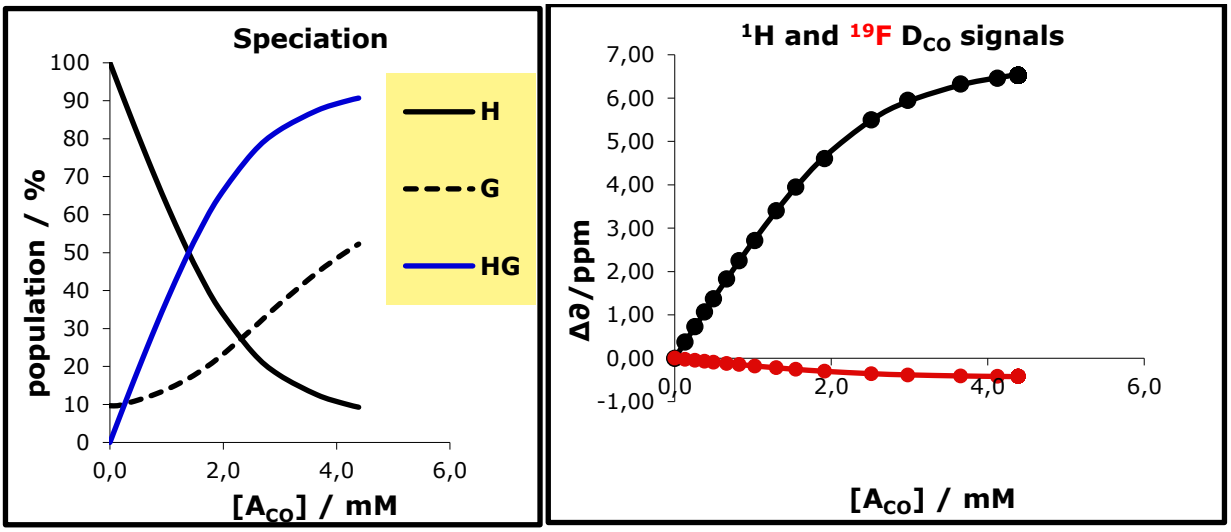


Figure S2.31: Plot of the change in chemical shift of the $\mathbf{D_{CO}}$ ^{19}F (**red**) and ^{1}H (**black**) signal in toluene-d_8 as a function of [$\mathbf{A_{CO}}$] (the line represents the best fit to a 1:1 binding isotherm) and speciation as a function of [$\mathbf{A_{CO}}$] obtained from the average of the two constants.

5.3.2 DD vs AA

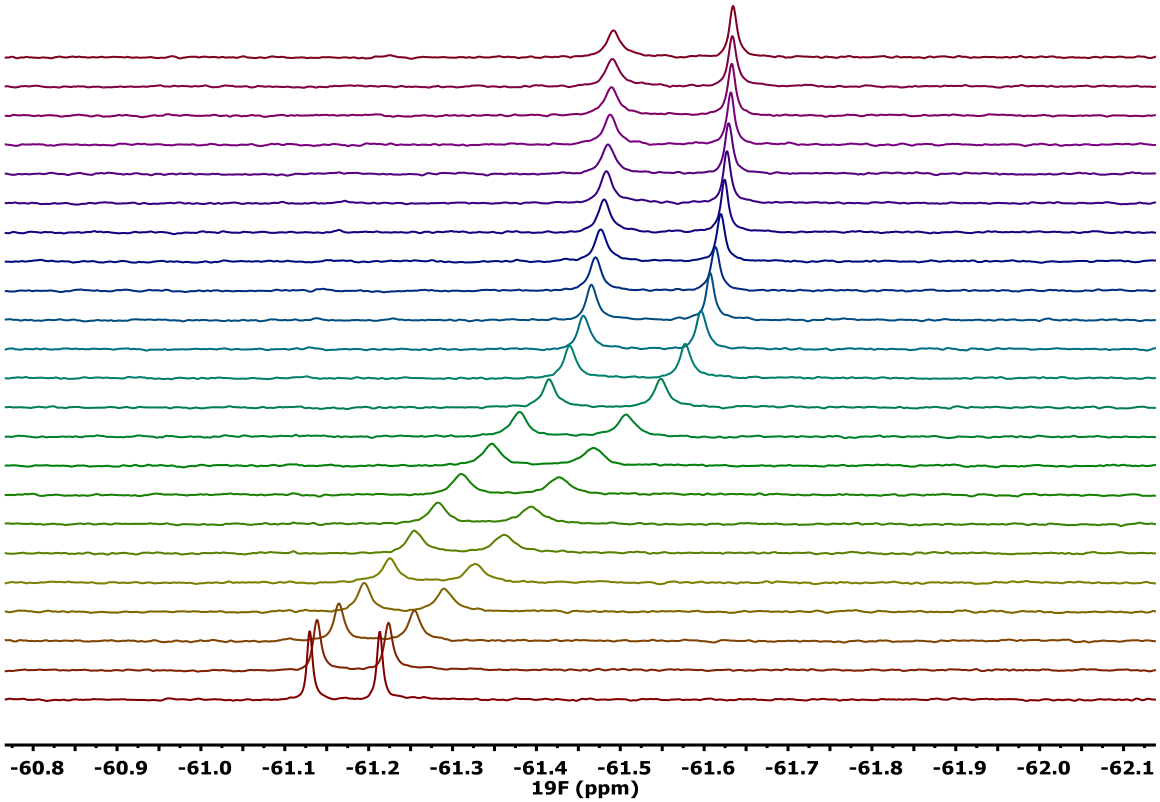


Figure S2.32: ^{19}F NMR titration of **AA** (0.2 mM) into **DD** (0.05 mM) in toluene-d_8. Spectra recorded (bottom to top) for 0, 5, 10, 15, 25, 35, 45, 55, 65, 80, 95, 115, 135, 155, 175, 195, 225, 260, 300, 450, 600, 750, 900 µl of **AA** added into 500 µl of **DD**.

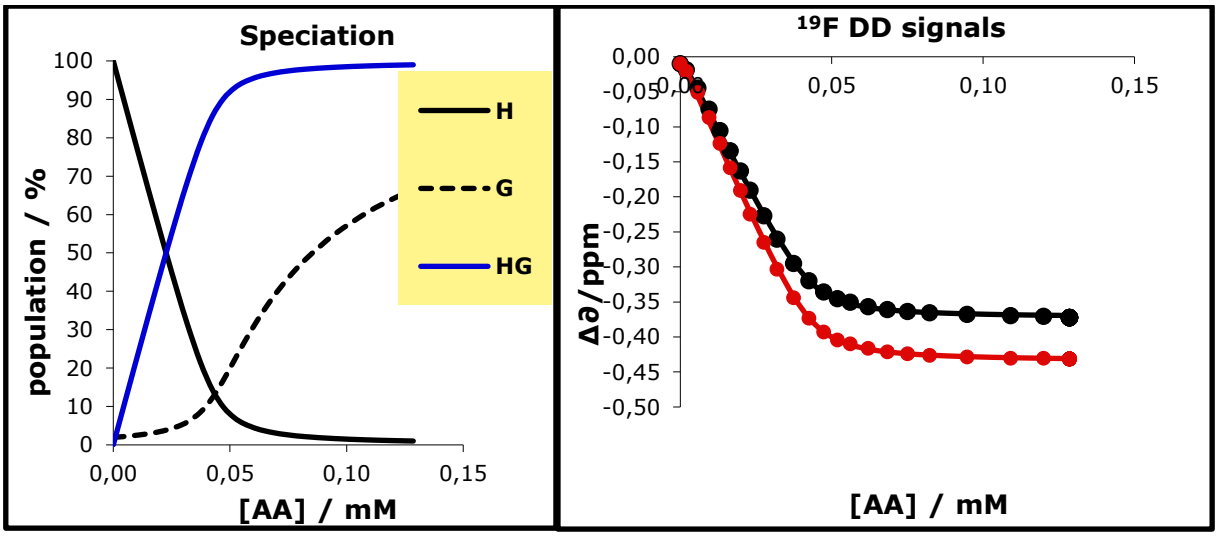


Figure S2.33: Plot of the change in chemical shift of the **DD** ^{19}F signals in toluene-d_8 as a function of [**AA**] (the line represents the best fit to a 1:1 binding isotherm) and speciation as a function of [**AA**] obtained from the average of the two constants.

5.3.3 DA dilution

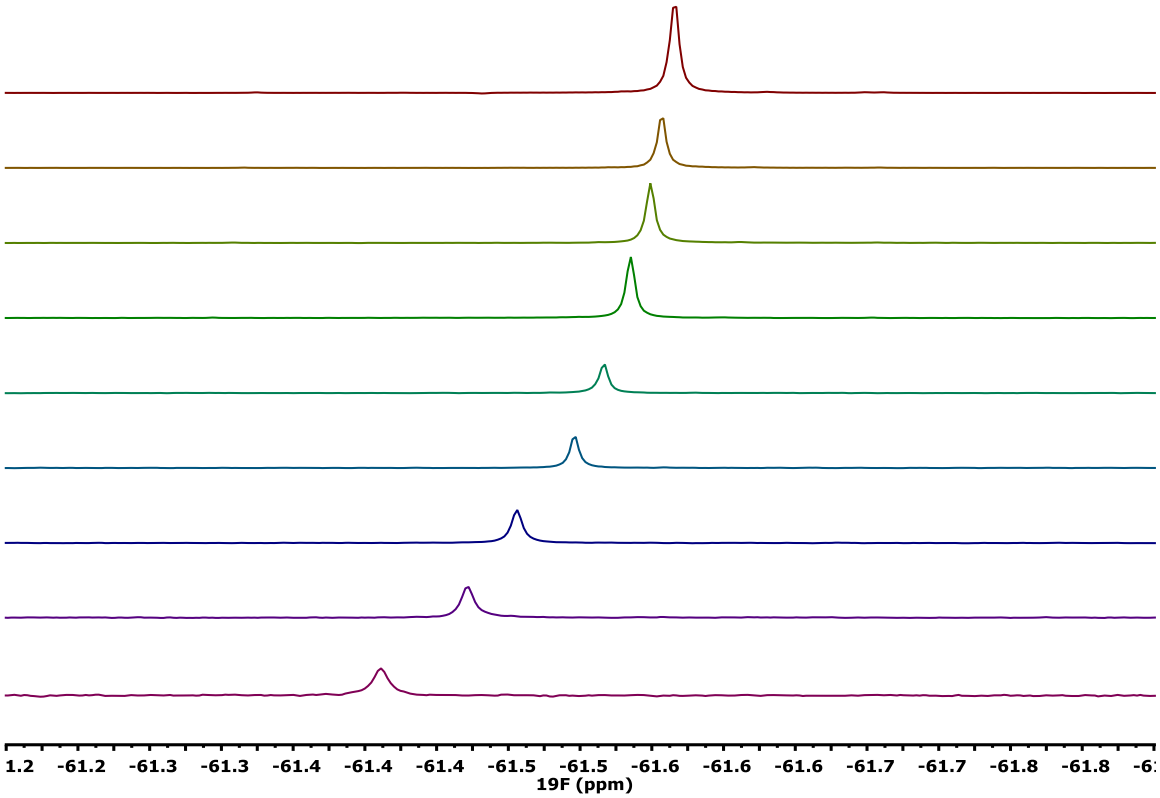


Figure S2.34: ^{19}F spectra of the dilution titration of **DA** (top to bottom 30, 10, 5, 2, 1.2, 0.7, 0.4, 0.2, 0.1) in toluene-d_8.

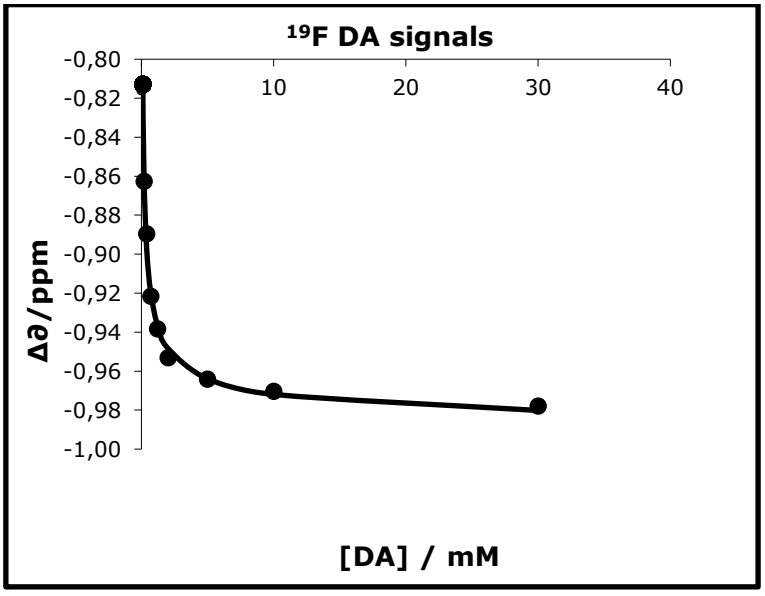


Figure S2.35: Plot of the change in chemical shift upon dilution of a solution of the **DA** ^{19}F signal in toluene-d_8 as a function of [**DA**] (the line represents the best fit to a 1:1 binding isotherm).

6. Variable temperature denaturation experiments

The variable temperature (VT) experiments to assess the thermal denaturation properties of the presented system were performed following the -CF_3 resonances of a 2 mM solution of length-complementary oligomers in 1,1,2,2-tetrachloroethane (TCE-d_2) upon heating from 233 to 373 K in a screw cap NMR tube on a Bruker Avance III 400 MHz instrument. Data were fitted using *Equation S6.1* to extract the transition melting temperature T_m (assumptions: 1. Only the duplex and single strand oligomers are present; 2. ΔH_N° and ΔS_N° are temperature independent; 3. the heat capacity change between free and bound states is zero).

$$\delta = \delta_f + (\delta_b - \delta_f)\left(\frac{1+4e^{-\left\{\frac{\Delta H_N^\circ}{R}\left(\frac{1}{T}-\frac{1}{T_{m,N}}\right)\right\}}-\sqrt{1+8e^{-\left\{\frac{\Delta H_N^\circ}{R}\left(\frac{1}{T}-\frac{1}{T_{m,N}}\right)\right\}}}}{4e^{-\left\{\frac{\Delta H_N^\circ}{R}\left(\frac{1}{T}-\frac{1}{T_{m,N}}\right)\right\}}}\right) \qquad \text{(S6.1)}$$

Table S6.1: Summary of the parameters obtained from the fitting of the VT experimental data with equation (1)

	T_m (K)	$\Delta H°_N$ (kJ mol^{-1})	δ_f (ppm)	Δ_b(ppm)
D●A	289	-23	-58.4	-61.0
DD●AA	351; 357	-31; -34	-57.7; -57.9	-60.6; 60.6
DDD●AAA	399; 429; 438	-31; -34; -37	-56.0; -56.0; -57.0	-60.7; -60.7; -61.0

6.1 D●A

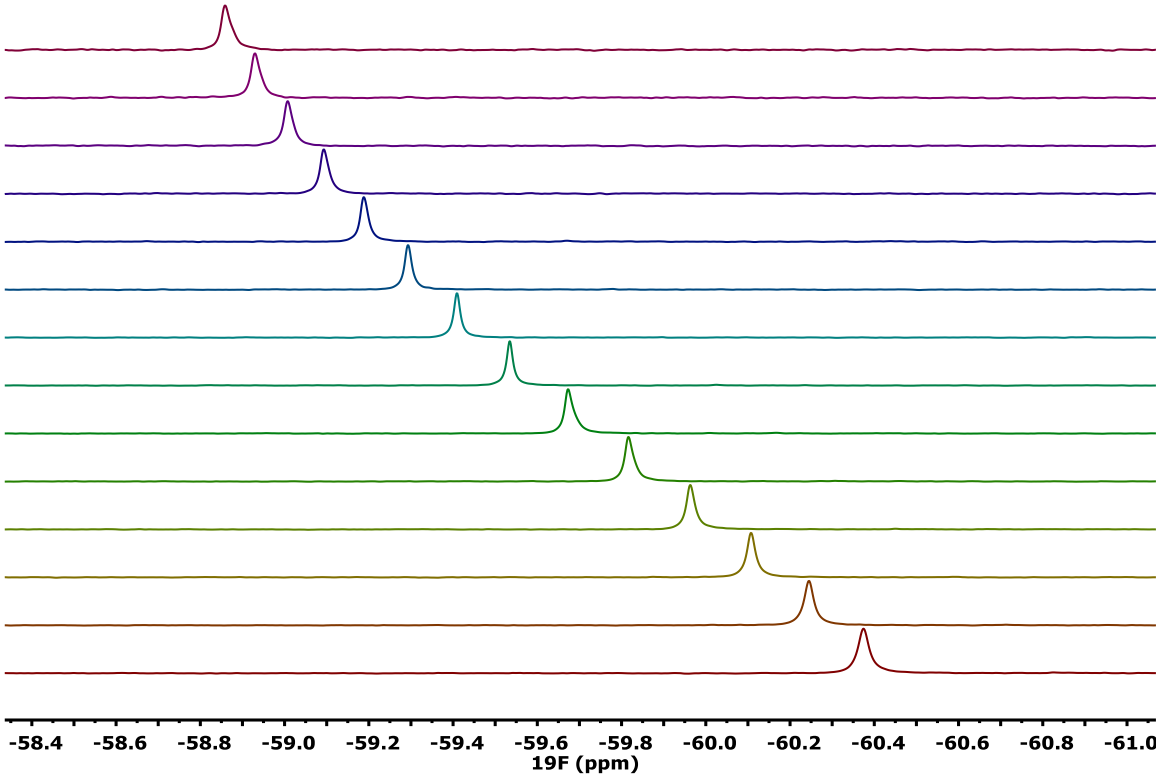


Figure S6.1: ^{19}F spectra of the $\mathbf{D_{co}}$ signal for the VT experiments done on a mixture of $\mathbf{D_{co}}$ (2 mM) and $\mathbf{A_{co}}$ (2 mM) in TCE-d_2. From bottom to top 243, 253, 263, 273, 283, 293, 303, 313, 323, 333, 343, 353, 363, 373 K.

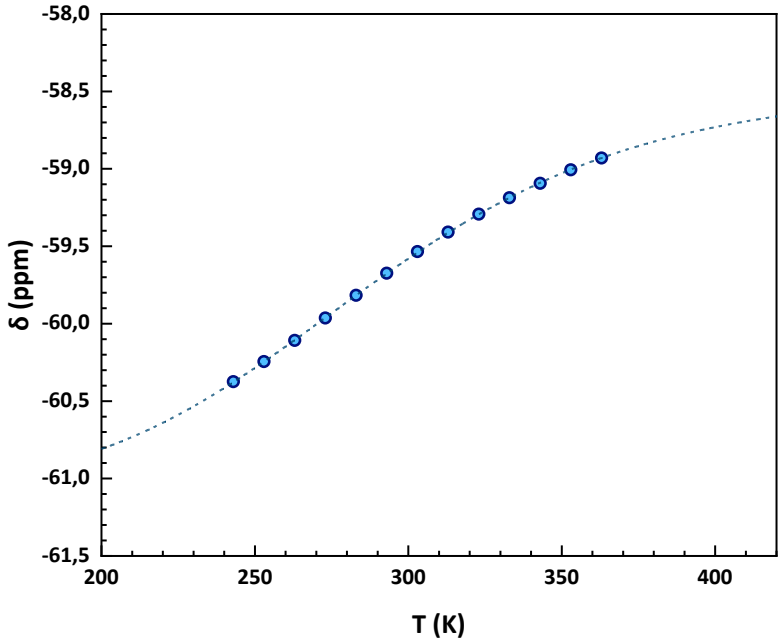


Figure S6.2: Plot of the ^{19}F chemical shift of the $\mathbf{D_{co}}$ signal vs temperature for the VT experiment and best fit of the data according to the model previously exposed.

6.2 DD●AA

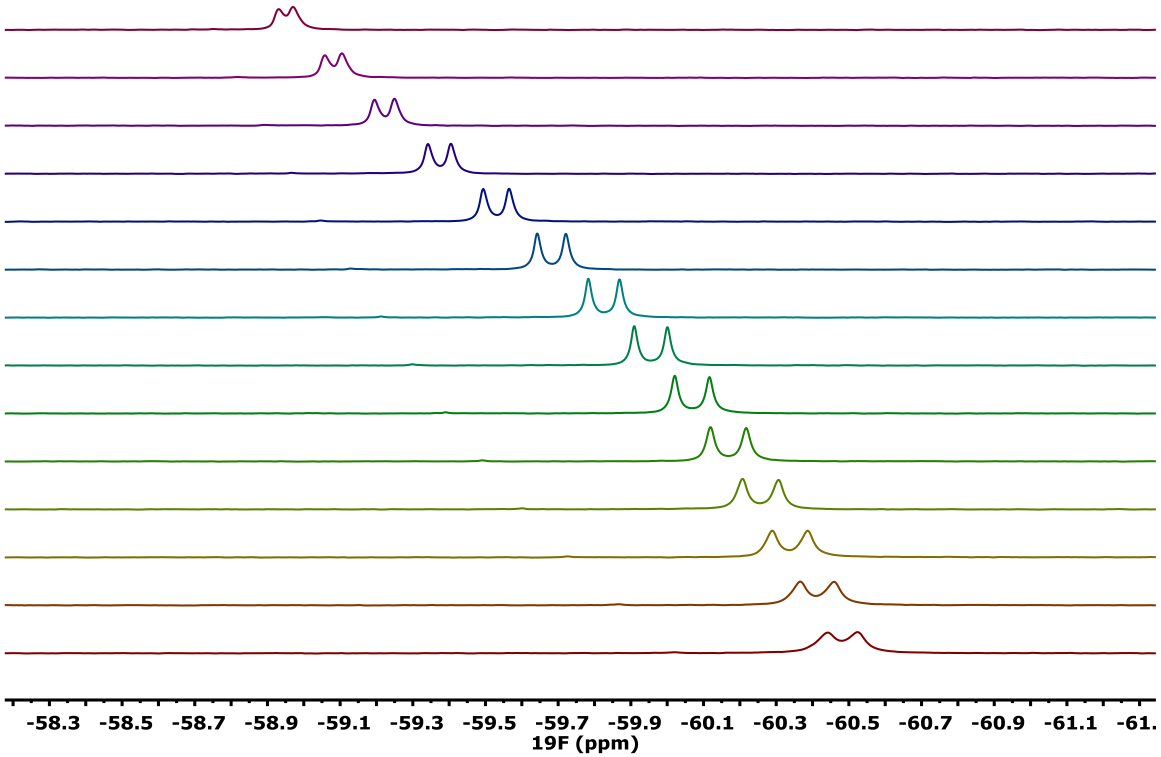


Figure S6.3: ^{19}F spectra of the **DD** signals for the VT experiments done on a mixture of **DD** (2 mM) and **AA** (2 mM) in TCE-d_2. From bottom to top 243, 253, 263, 273, 283, 293, 303, 313, 323, 333, 343, 353, 363, 373 K.

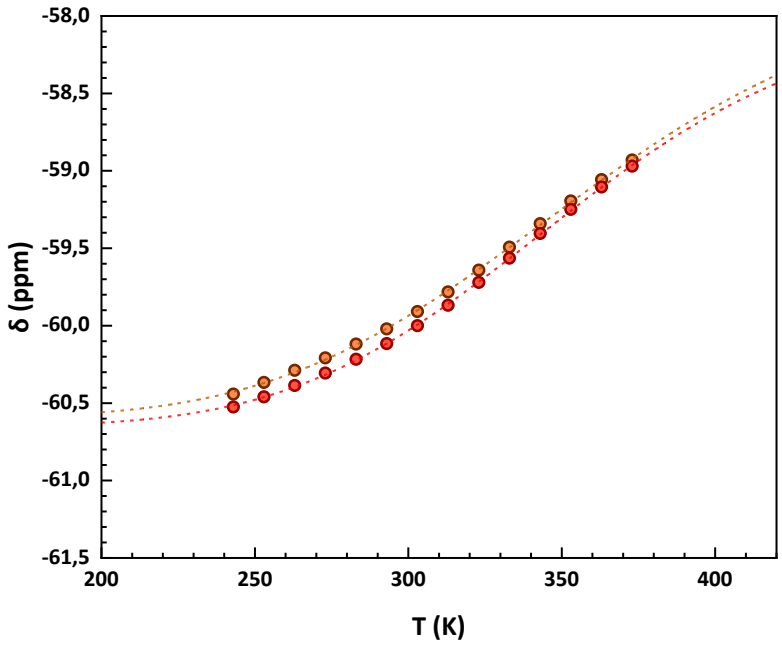


Figure S6.4: Plot of the ^{19}F chemical shift of the **DD** signal vs temperature for the VT experiment and best fit of the data according to the model previously exposed.

6.3 DDD●AAA

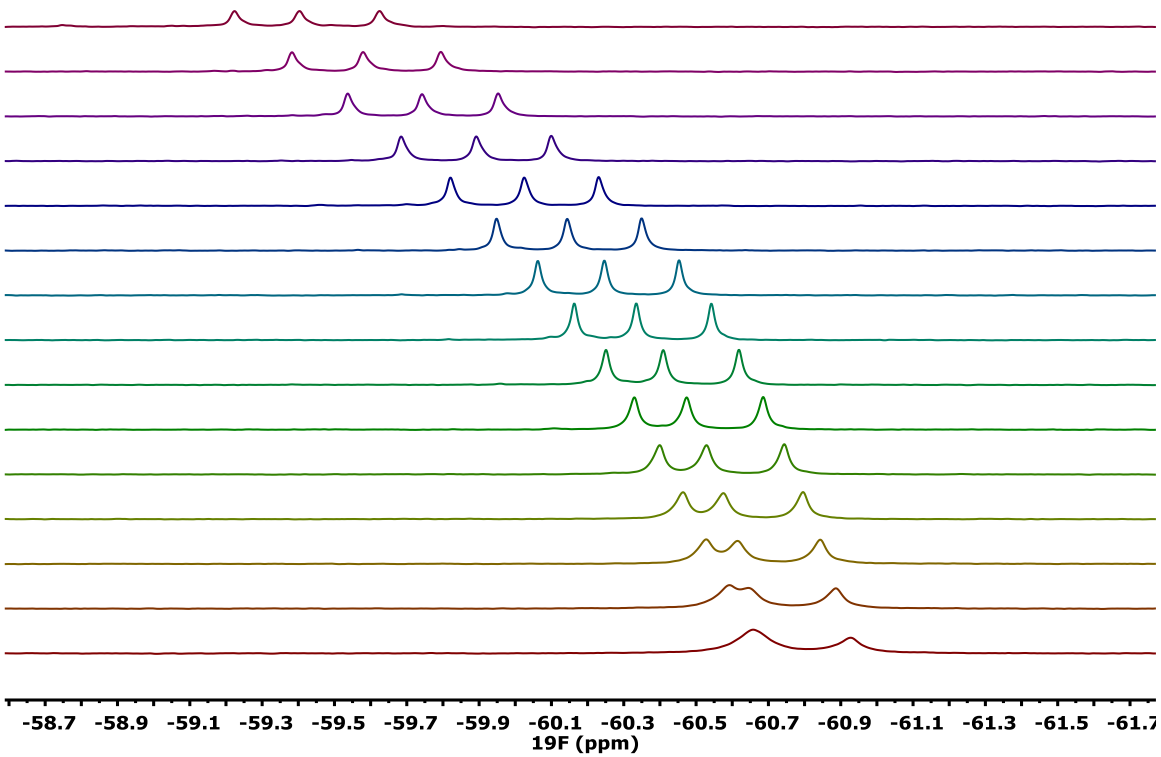


Figure S6.5: ^{19}F spectra of the **DDD** signals for the VT experiments done on a mixture of **DDD** (2 mM) and **AAA** (2 mM) in TCE-d_2. From bottom to top 233, 243, 253, 263, 273, 283, 293, 303, 313, 323, 333, 343, 353, 363, 373 K.

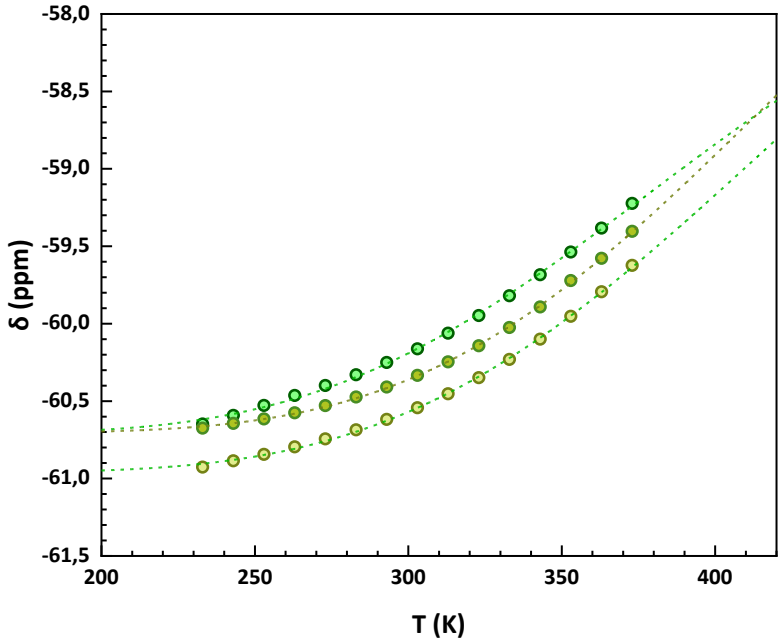


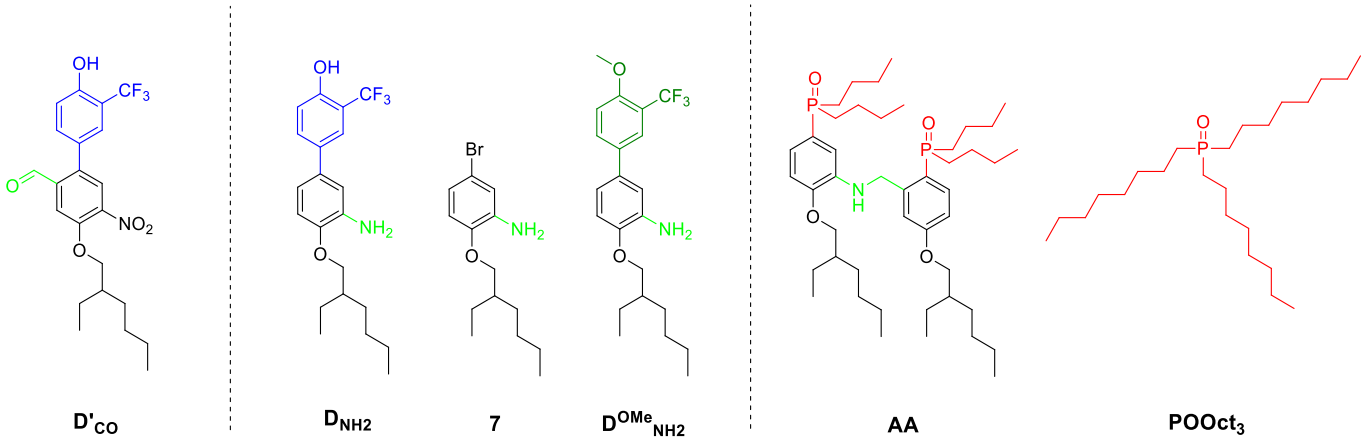
Figure S6.6: Plot of the ^{19}F chemical shift of the **DDD** signal vs temperature for the VT experiment and best fit of the data according to the model previously exposed.

7. Templated experiments

The kinetics of imine formation were followed, under different experimental conditions, through ^{1}H-NMR spectra recorded on a 400 MHz Bruker Avance III instrument at 298 K.

During a typical experiment, stock solutions of the selected monomers (structures reported in *Scheme S7.1*) were freshly prepared in toluene-d_8 at a known concentration. A known volume of the aldehyde monomer (**D'$_{CO}$**) and either the complementary templating dimer (**AA**) or a non-templating control (POOct$_3$) were added to an NMR tube. Finally, a known volume of the aniline solution (**D$_{NH2}$**, **7**, or **D$^{OMe}_{NH2}$**) was added and the final volume adjusted to 600 µl. The tube was quickly flame-sealed and vigorously shaken. The reactions were heated at 70 °C immersing the tube in a thermostated oil bath. Spectra were recorded at regular intervals removing the tube from the thermostated bath for maximum 15 minutes.

Aldehyde and imine signals were integrated, and the relative integral values were plotted versus the reaction time.



Scheme S7.1: chemical structures of the molecules used in for the templated experiments.

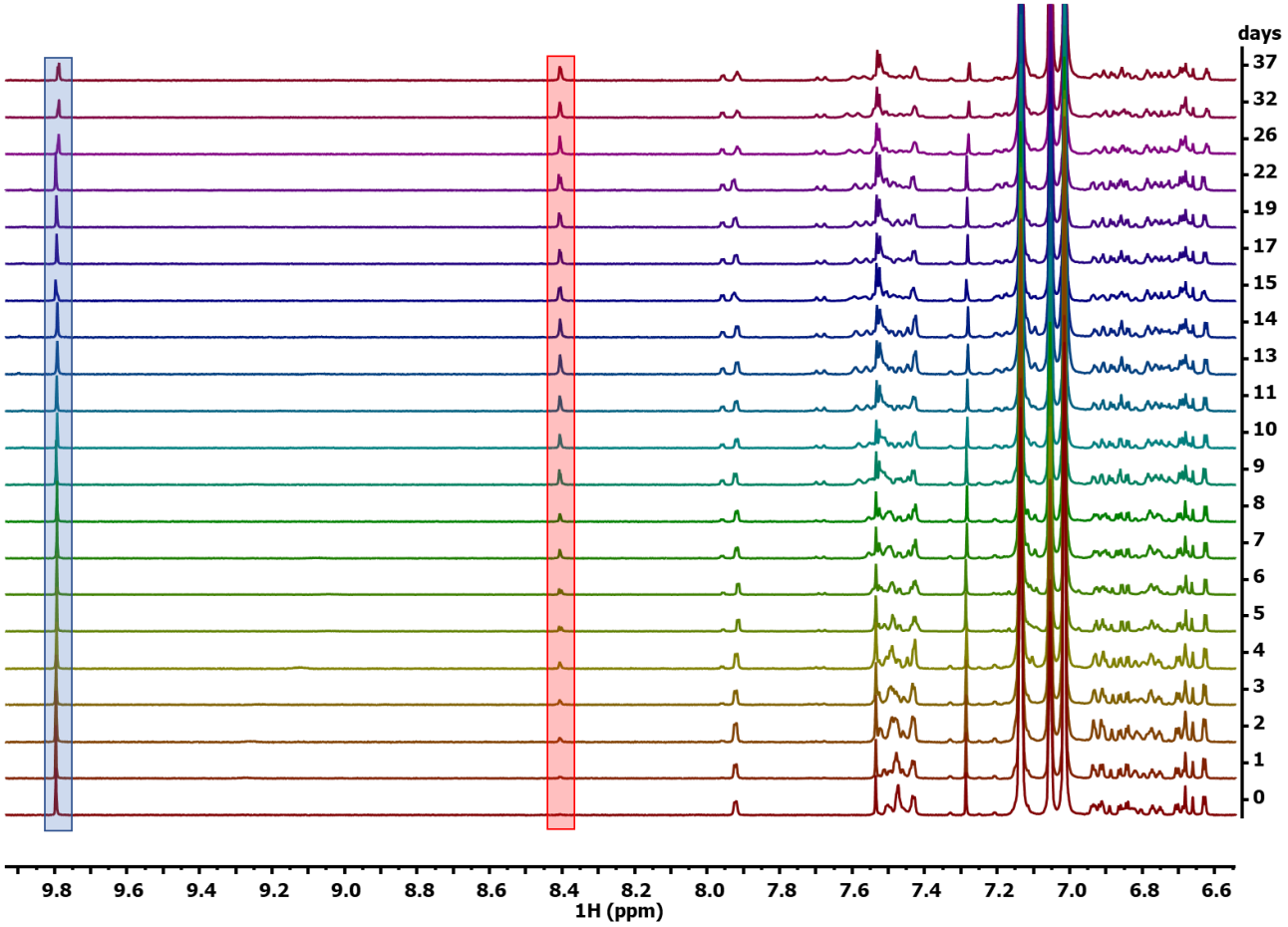
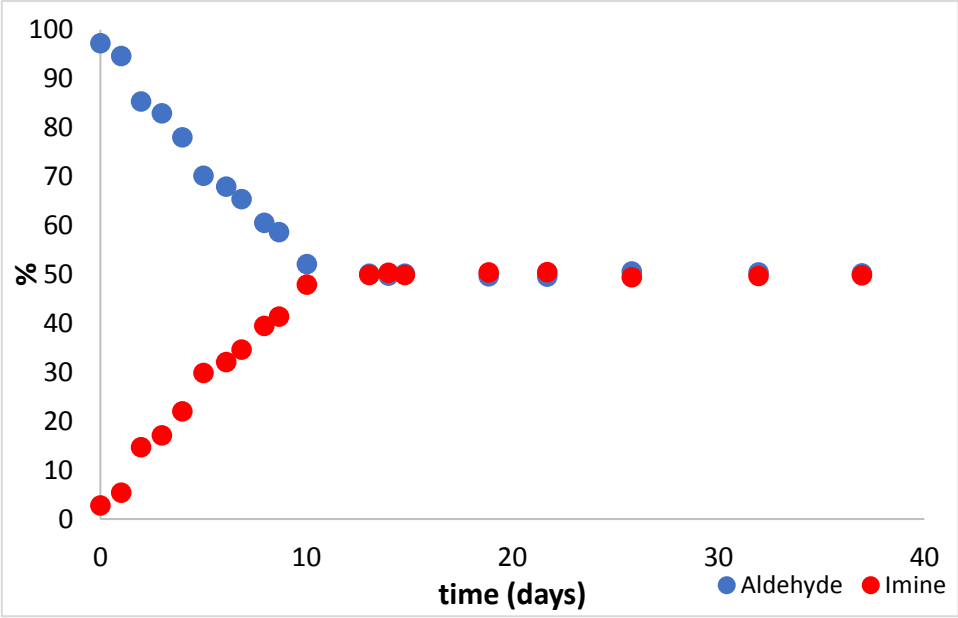


Figure S7.1: Partial ^{1}H spectrum (400 MHz, toluene-d_8) of the kinetic of formation of imine between $\mathbf{D_{NH2}}$ and $\mathbf{D'_{CO}}$ with template **AA** all at 1 mM concentration. The blue rectangle highlights the aldehyde peak, the red rectangle highlights the imine peak. Relative integrated intensities of the two peaks are reported in *Graph 7.1*.



Graph S7.1: formation of imine between the amine $\mathbf{D_{NH2}}$ and the aldehyde $\mathbf{D'_{CO}}$ with **AA** as template, all at 1 mM concentration (reaction in toluene-d_8 at 70°C). Relative integrated intensities as a function of reaction time obtained from integration of the imine C**H**=N and C**H**=O signals of the ^{1}H NMR spectra reported in *Figure S7.1*

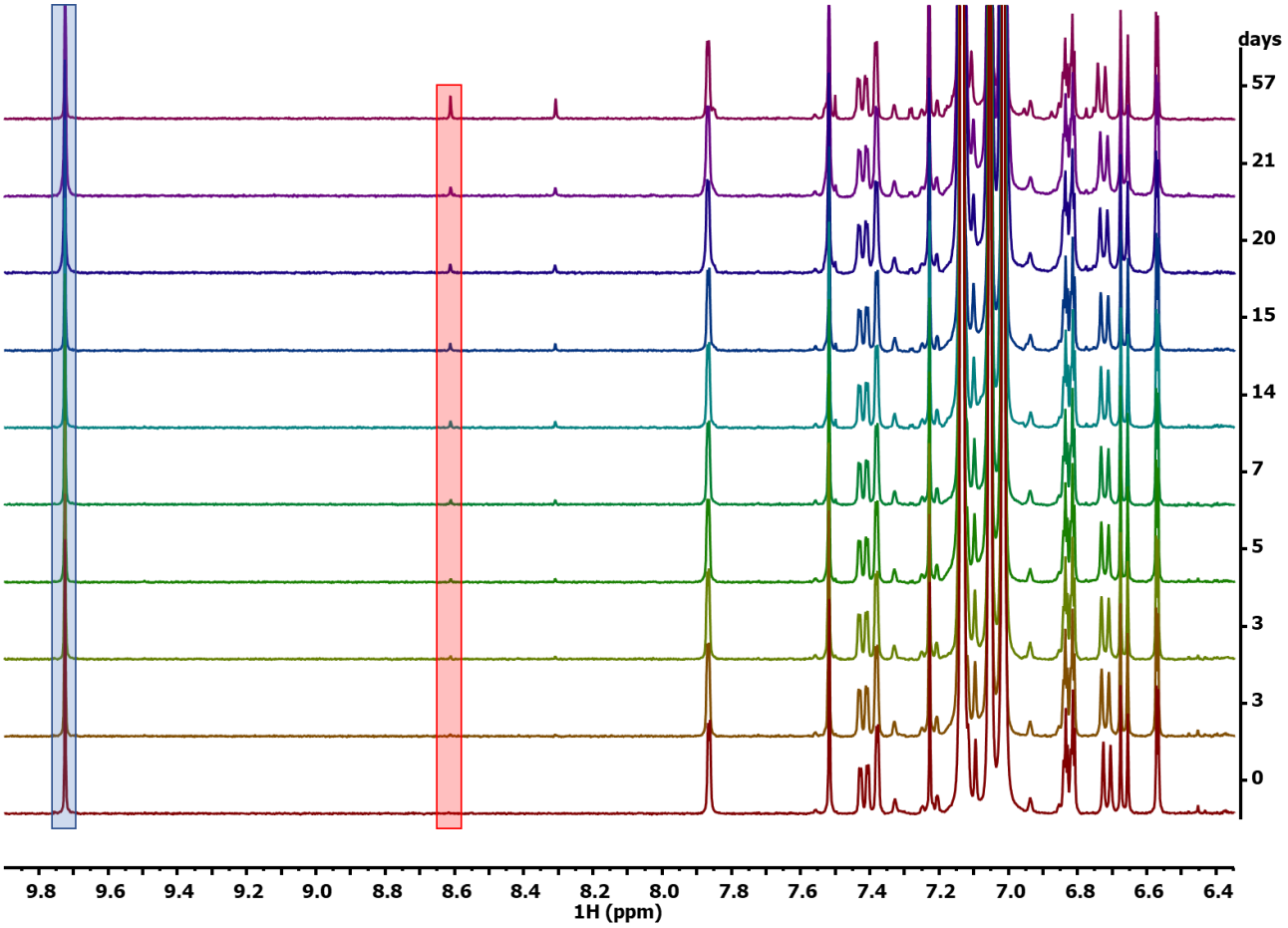
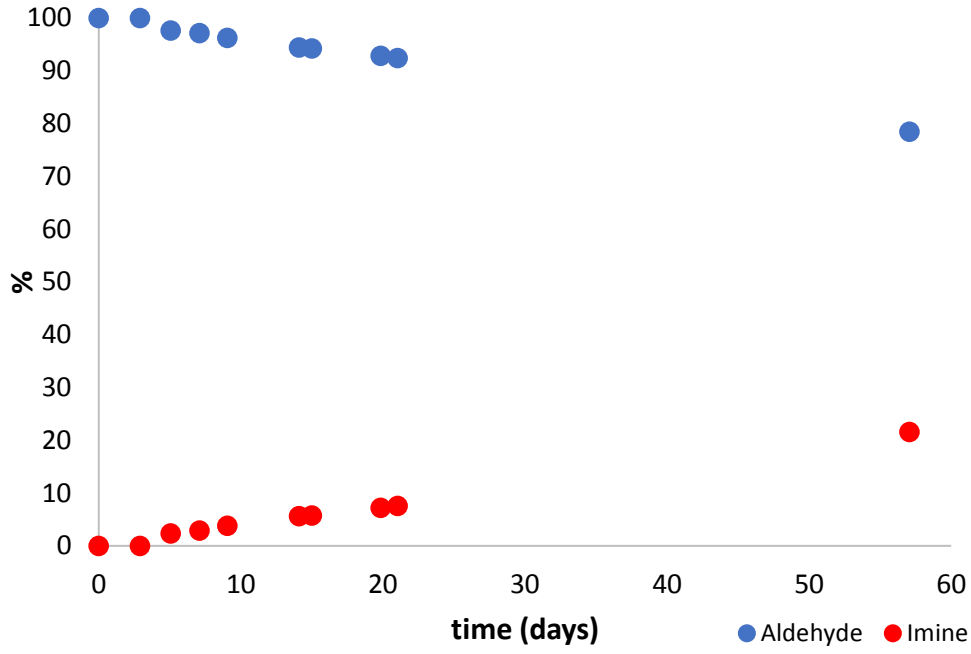


Figure S7.2: Partial ^{1}H spectrum (400 MHz, toluene-d_8) of the kinetic of formation of imine between $\mathbf{D_{NH2}}$ and $\mathbf{D'_{CO}}$ with $POOct_3$ as control, all at 1 mM concentration. The blue rectangle highlights the aldehyde peak, the red rectangle highlights the imine peak. Relative integrated intensities of the two peaks are reported in *Graph 7.2*.



Graph S7.2: formation of imine between the amine $\mathbf{D_{NH2}}$ and the aldehyde $\mathbf{D'_{CO}}$ with $POOct_3$ as control, all at 1 mM concentration (reaction in toluene-d_8 at 70°C). Relative integrated intensities as a function of reaction time obtained from integration of the imine C**H**=N and C**H**=O signals of the ^{1}H NMR spectra reported in *Figure S7.2*

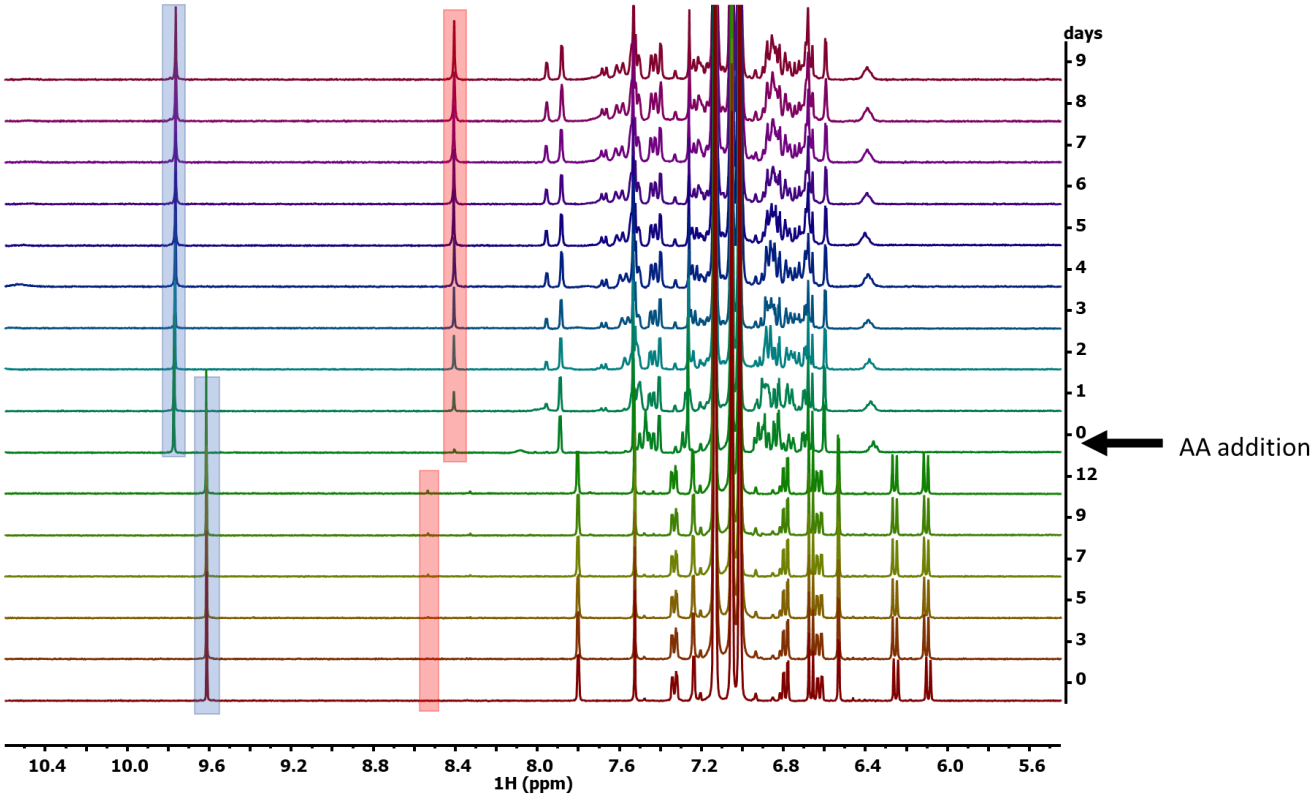
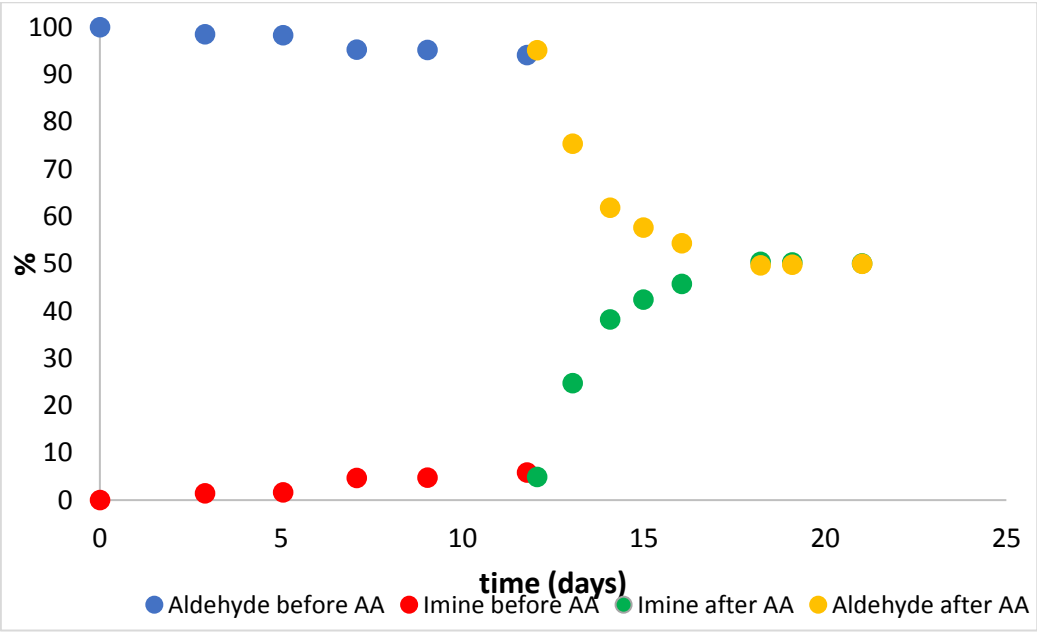


Figure S7.3: Partial ^{1}H spectrum (400 MHz, toluene-d_8) of the kinetic of formation of imine between $\mathbf{D_{NH2}}$ and $\mathbf{D'_{CO}}$, followed prior and after the addition of **AA** as a template (all at 1 mM concentration). The blue rectangle highlights the aldehyde peak, the red rectangle highlights the imine peak. Relative integrated intensities of the two peaks are reported in *Graph 7.3*.



Graph S7.3: formation of imine between the amine $\mathbf{D_{NH2}}$ and the aldehyde $\mathbf{D'_{CO}}$ at 1 mM concentration (reaction in toluene-d_8 at 70°C). Relative integrated intensities as a function of reaction time obtained from integration of the imine C**H**=N and C**H**=O signals of the ^{1}H NMR spectra reported in *Figure S7.3*. Imine peak before addition of template **AA** is in **red**, after addition is in **green**. Aldehyde peak before addition of **AA** is in **blue**, after addition of template AA in **yellow**.

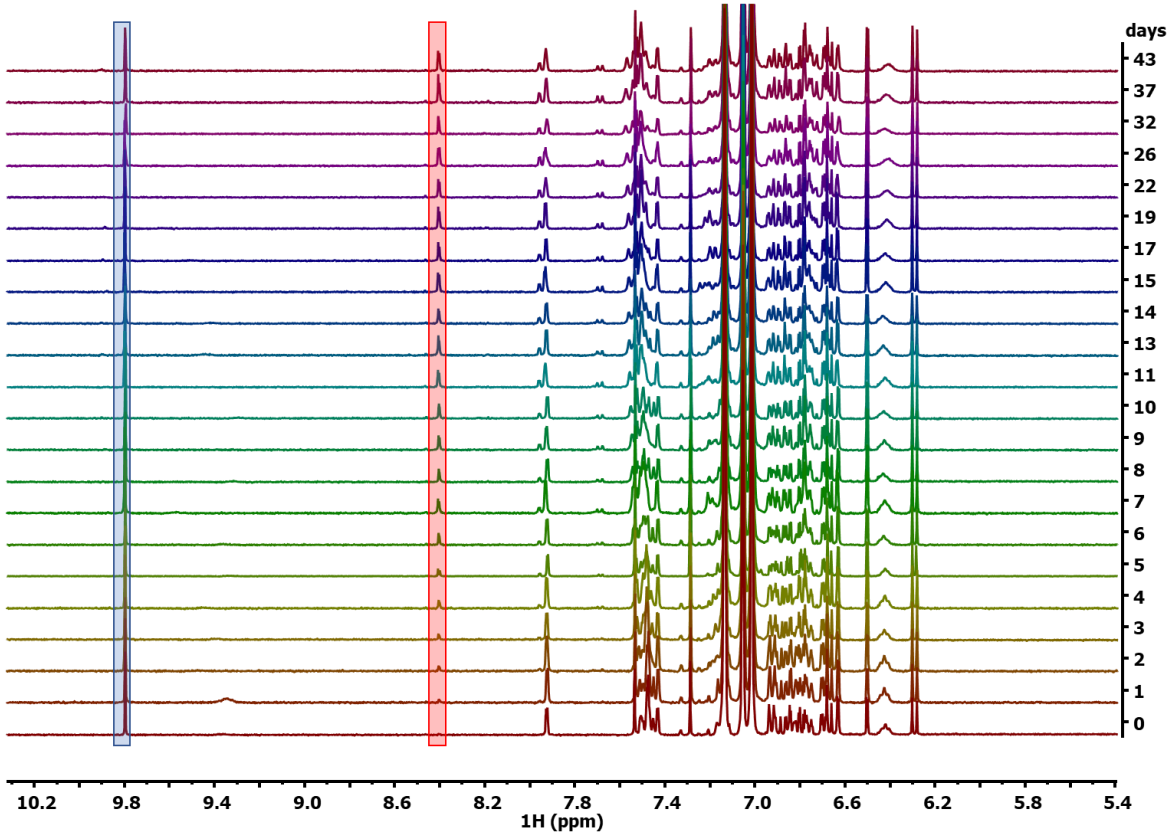
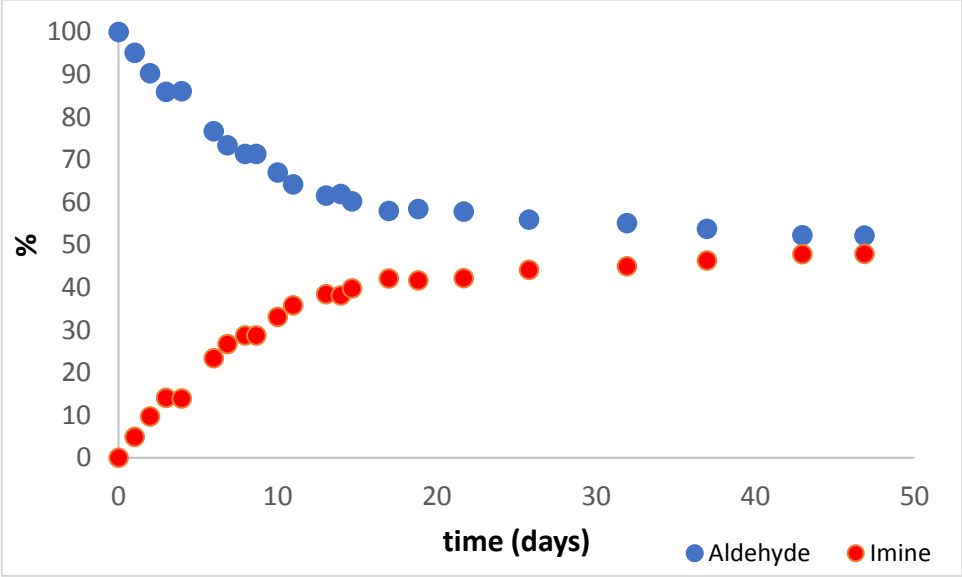


Figure S7.4: Partial ^{1}H spectrum (400 MHz, toluene-d_8) of the kinetic of formation of imine between $\mathbf{D_{NH2}}$, **7** (as competing base lacking the recognition unit) and $\mathbf{D'_{CO}}$ with **AA** as template, all at 1 mM concentration. The blue rectangle highlights the aldehyde peak, the red rectangle highlights the imine peak. Relative integrated intensities of the two peaks are reported in *Graph 7.4*.



Graph S7.4: formation of imine between the amines $\mathbf{D_{NH2}}$, **7** and $\mathbf{D'_{CO}}$ with **AA** as template, all at 1 mM concentration (reaction in toluene-d_8 at 70°C). Relative integrated intensities as a function of reaction time obtained from integration of the imine C**H**=N and C**H**=O signals of the ^{1}H NMR spectra reported in *Figure S7.4*

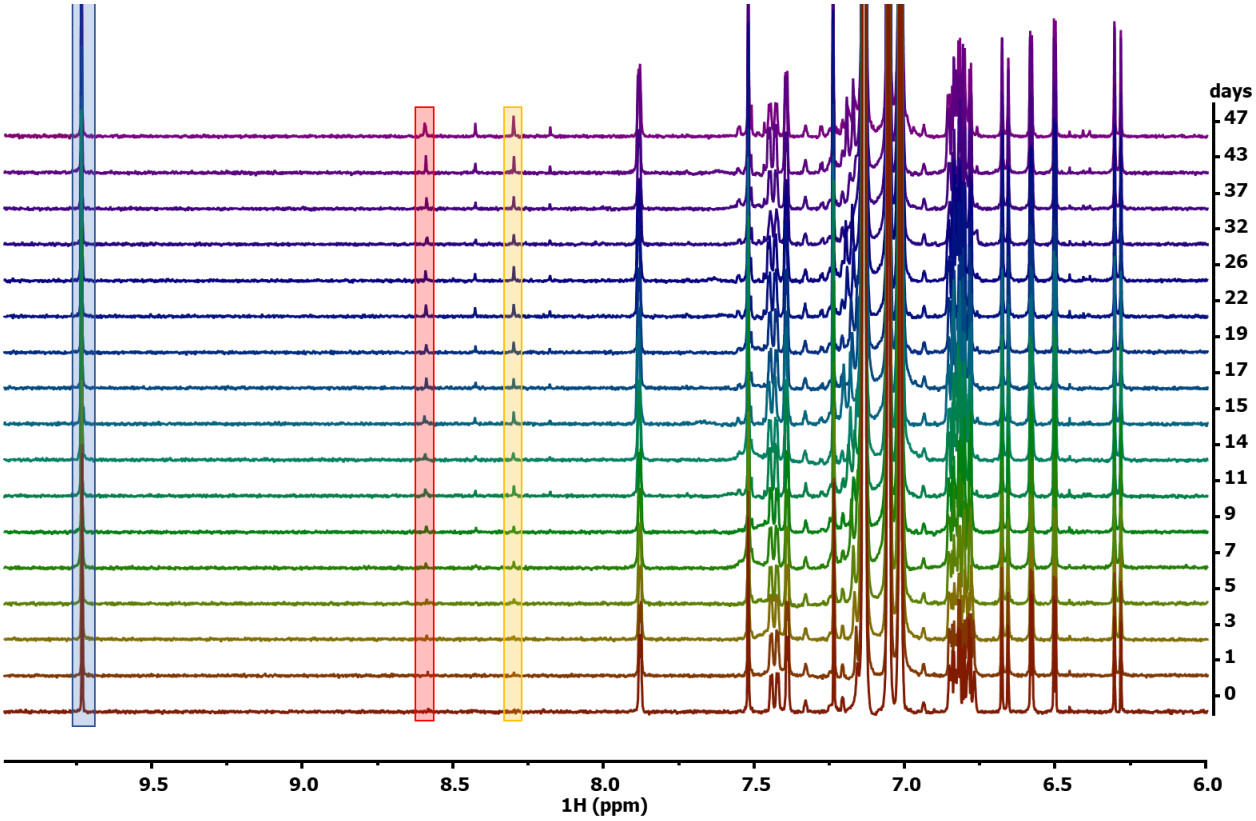
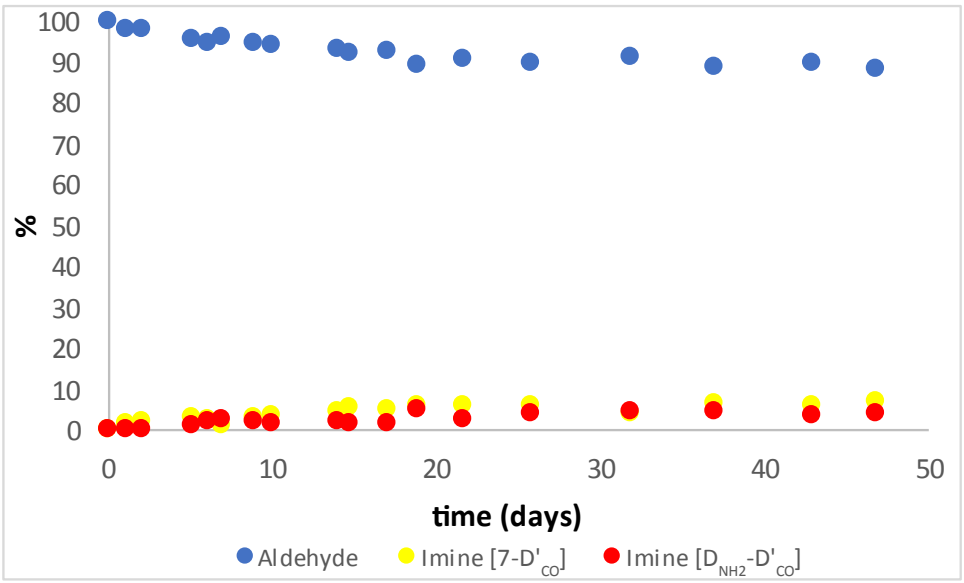


Figure S7.5: Partial ^{1}H spectrum (400 MHz, toluene-d_8) of the kinetic of formation of imine between $\mathbf{D_{NH2}}$, **7** (as competing base lacking the recognition unit) and $\mathbf{D'_{CO}}$ with $POOct_3$ as control, all at 1 mM concentration. The blue rectangle highlights the aldehyde peak, the red and yellow rectangles highlight the imine peak. Relative integrated intensities of the peaks are reported in *Graph 7.5*.



Graph S7.5: formation of imine between the amines $\mathbf{D_{NH2}}$, **7** and $\mathbf{D'_{CO}}$ with $POOct_3$ as a control, all at 1 mM concentration (reaction in toluene-d_8 at 70°C). Relative integrated intensities as a function of reaction time obtained from integration of the imine C**H**=N and C**H**=O signals of the ^{1}H NMR spectra reported in *Figure S7.5*. Imine peak from the reaction of **7** and $\mathbf{D'_{CO}}$ is in **yellow** ($7\text{-}D'_{CO}$); imine peak from the reaction $\mathbf{D_{NH2}}$ and $\mathbf{D'_{CO}}$ is in **red** ($D_{NH2}\text{-}D'_{CO}$). Aldehyde peak is reported in **blue**.

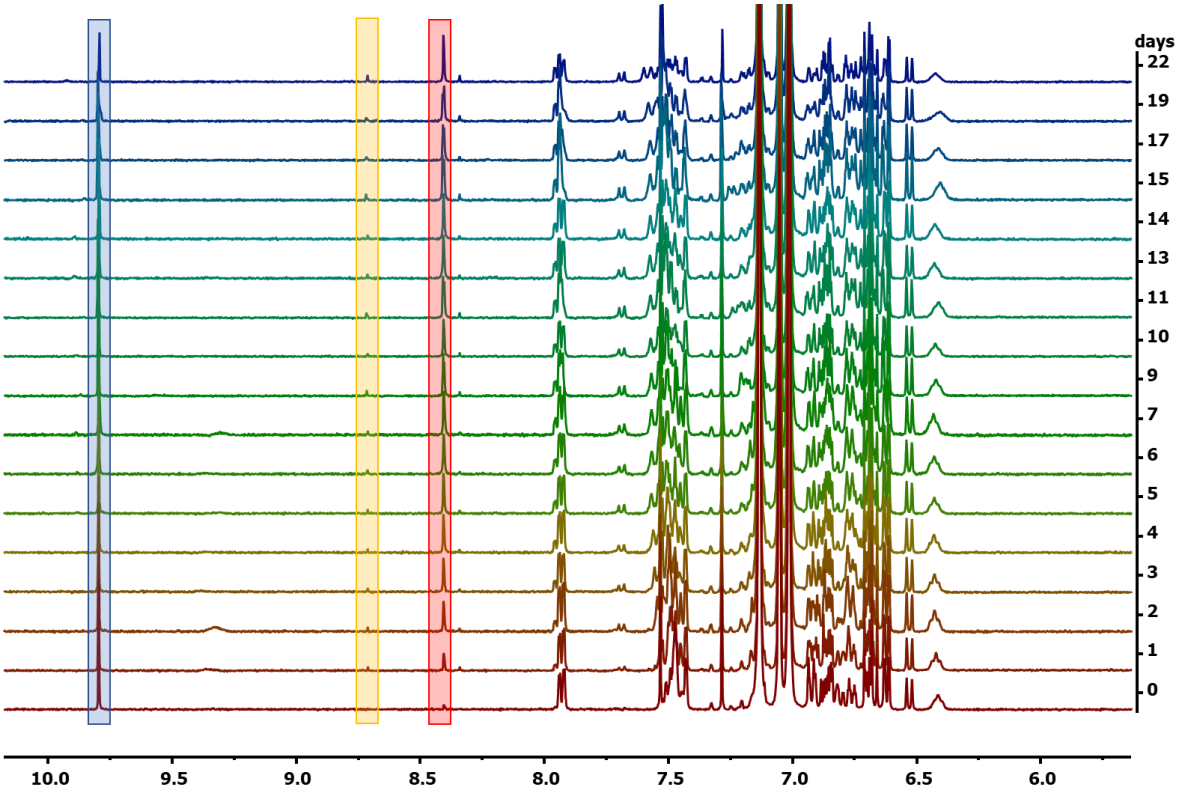
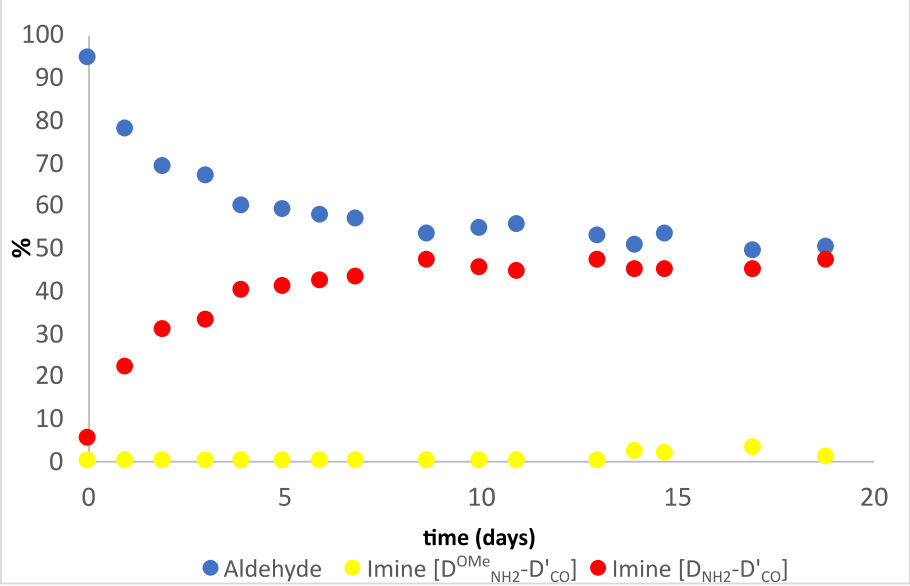


Figure S7.6: Partial ^{1}H spectrum (400 MHz, toluene-d_8) of the kinetic of formation of imine between $\mathbf{D_{NH2}}$, $\mathbf{D^{OMe}_{NH2}}$ (as competing base with mutated recognition unit) and $\mathbf{D'_{CO}}$ with **AA** as template, all at 1 mM concentration. The blue rectangle highlights the aldehyde peak, the red and yellow rectangles highlight the imine peak. Relative integrated intensities of the peaks are reported in *Graph 7.6*.



Graph S7.6: formation of imine between the amines $\mathbf{D_{NH2}}$, $\mathbf{D^{OMe}_{NH2}}$and $\mathbf{D'_{CO}}$ with **AA** as a template, all at 1 mM concentration (reaction in toluene-d_8 at 70°C). Relative integrated intensities as a function of reaction time obtained from integration of the imine C**H**=N and C**H**=O signals of the ^{1}H NMR spectra reported in *Figure S7.6*. Imine peak from the reaction of $\mathbf{D^{OMe}_{NH2}}$ and $\mathbf{D'_{CO}}$ is in **yellow** (D^{OMe}_{NH2}-D'_{CO}); imine peak from the reaction $\mathbf{D_{NH2}}$ and $\mathbf{D'_{CO}}$ is in **red** (D_{NH2}-D'_{CO}). Aldehyde peak is reported in **blue**.

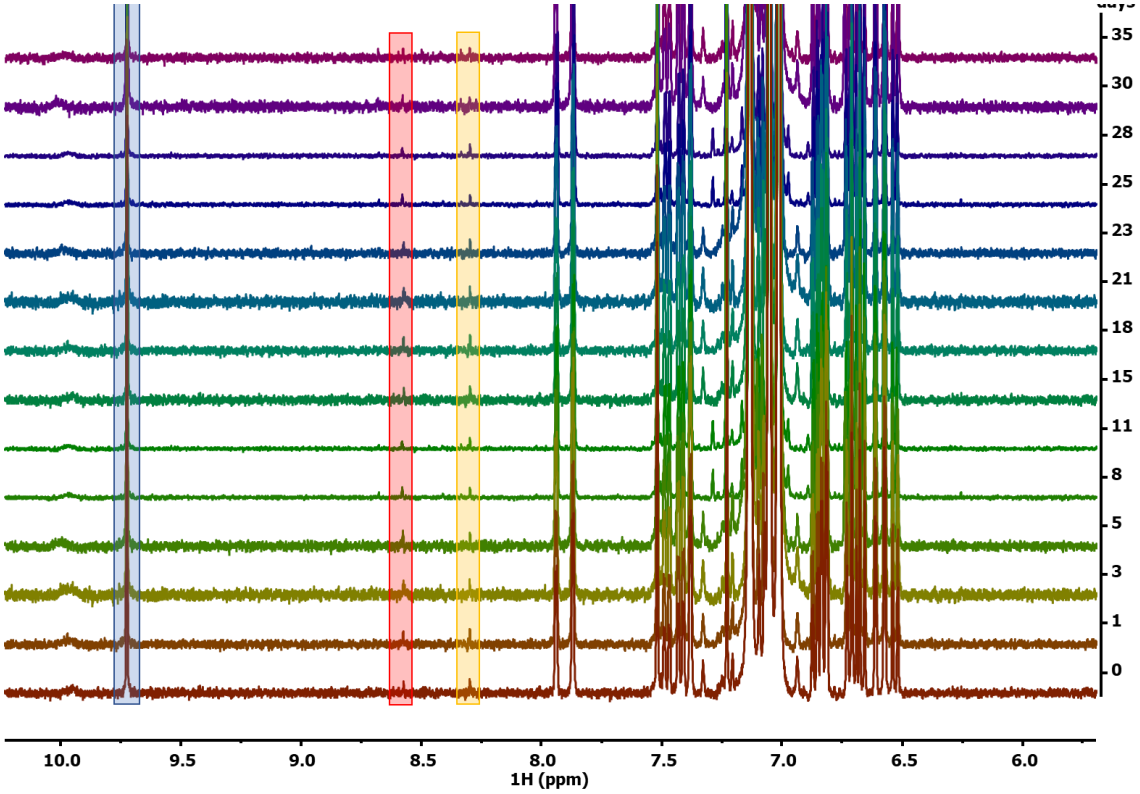
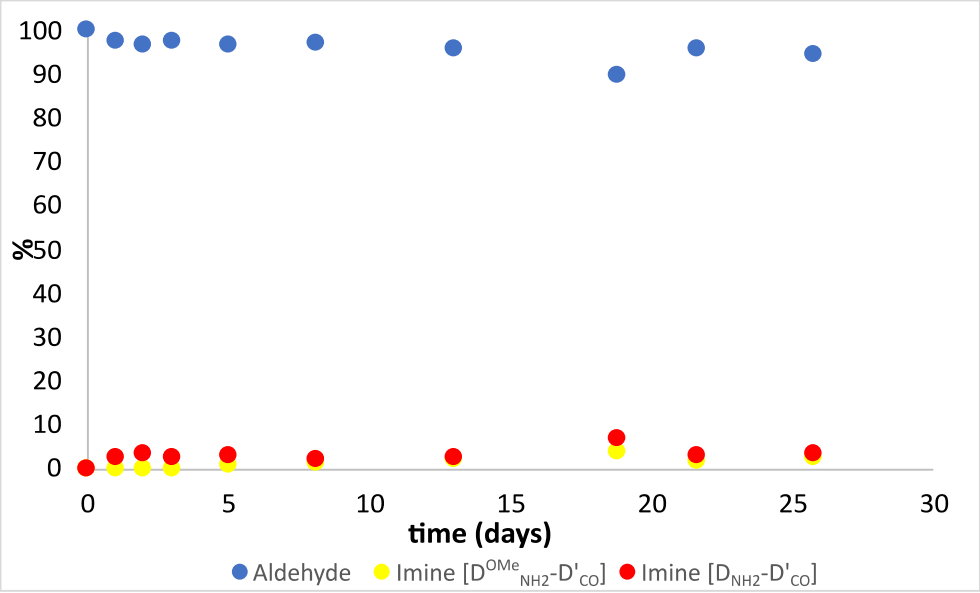


Figure S7.7: Partial ^{1}H spectrum (400 MHz, toluene-d_8) of the kinetic of formation of imine between $\mathbf{D_{NH2}}$, $\mathbf{D^{OMe}_{NH2}}$ (as competing base with mutated recognition unit) and $\mathbf{D'_{CO}}$ with $POOct_3$ as non-templating control, all at 1 mM concentration. The blue rectangle highlights the aldehyde peak, the red and yellow rectangles highlight the imine peak. Relative integrated intensities of the peaks are reported in *Graph 7.7.*



Graph S7.7: formation of imine between the amines $\mathbf{D_{NH2}}$, $\mathbf{D^{OMe}_{NH2}}$and $\mathbf{D'_{CO}}$ with **AA** as a template, all at 1 mM concentration (reaction in toluene-d_8 at 70°C). Relative integrated intensities as a function of reaction time obtained from integration of the imine C**H**=N and C**H**=O signals of the ^{1}H NMR spectra reported in *Figure S7.7*. Imine peak from the reaction of $\mathbf{D^{OMe}_{NH2}}$and $\mathbf{D'_{CO}}$ is in **yellow** (D^{OMe}_{NH2}-D'_{CO}); imine peak from the reaction of $\mathbf{D_{NH2}}$ and $\mathbf{D'_{CO}}$ is in **red** (D_{NH2}-D'_{CO}). Aldehyde peak is reported in **blue**.

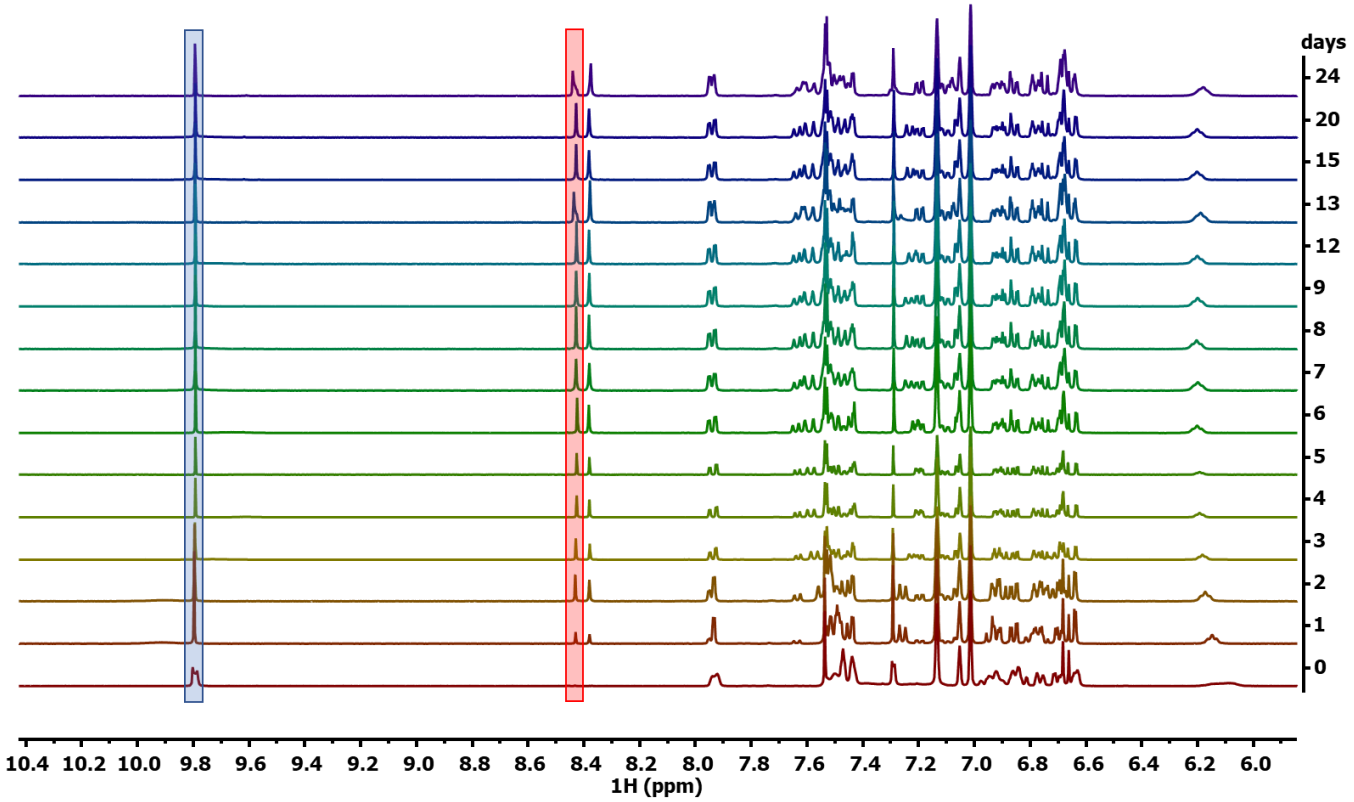
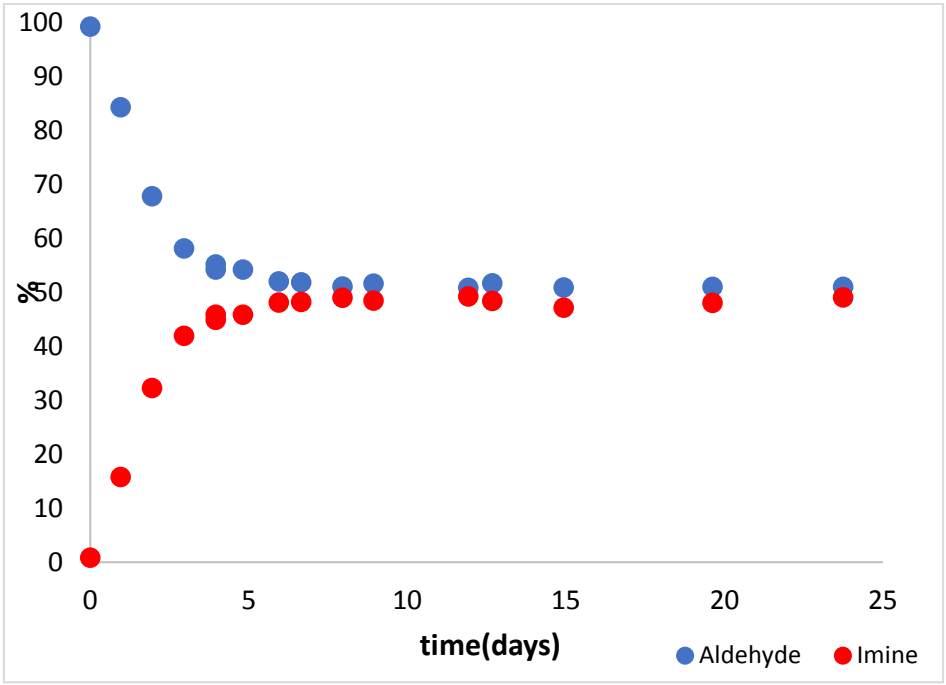


Figure S7.8: Partial ^{1}H spectrum (400 MHz, toluene-d_8) of the kinetic of formation of imine between $\mathbf{D_{NH2}}$ and $\mathbf{D'_{CO}}$ with **AA** as template, all at 10 mM concentration. The blue rectangle highlights the aldehyde peak, the red rectangle highlights the imine peak. Relative integrated intensities of the two peaks are reported in *Graph 7.8*.



Graph S7.8: formation of imine between the amines $\mathbf{D_{NH2}}$, and $\mathbf{D'_{CO}}$ with **AA** as template, all at 10 mM concentration (reaction in toluene-d_8 at 70°C). Relative integrated intensities as a function of reaction time obtained from integration of the imine C**H**=N and C**H**=O signals of the ^{1}H NMR spectra reported in *Figure S7.8*

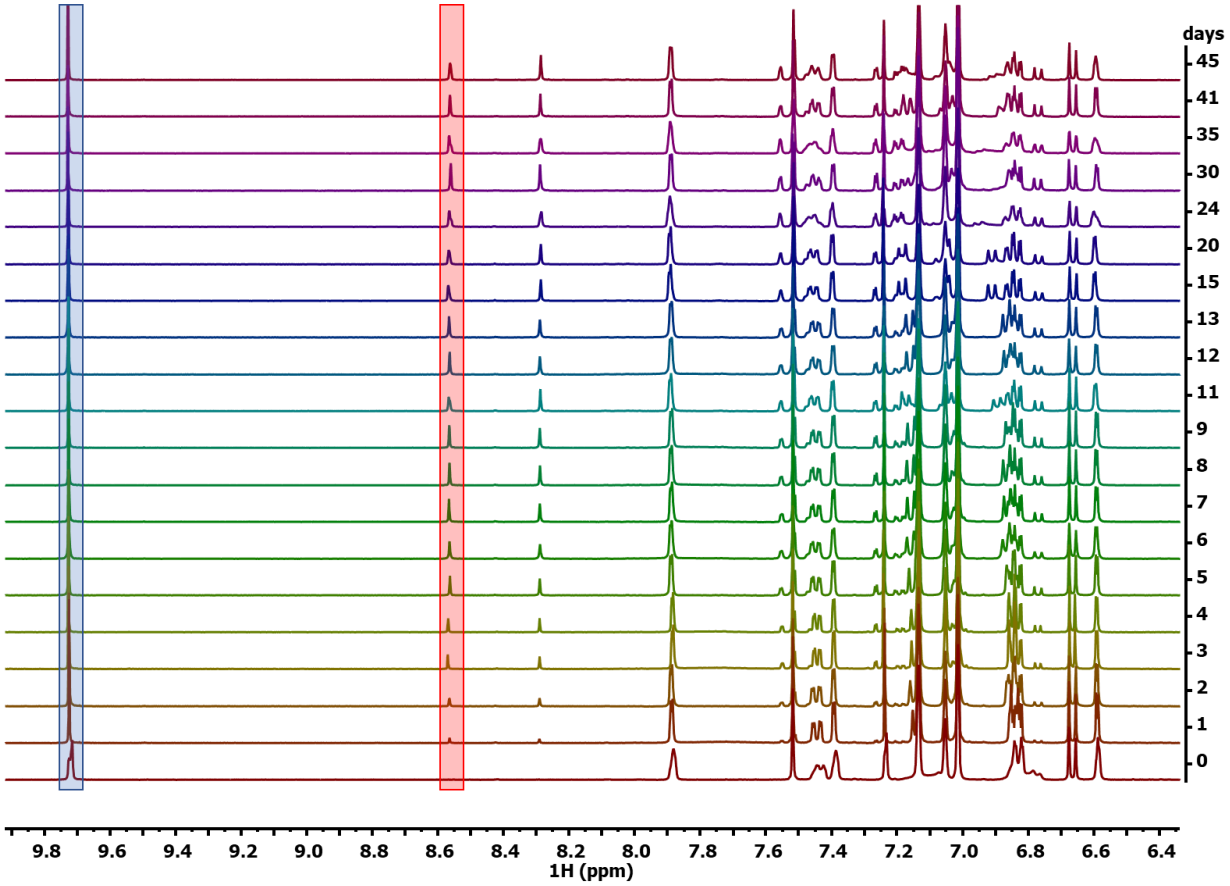
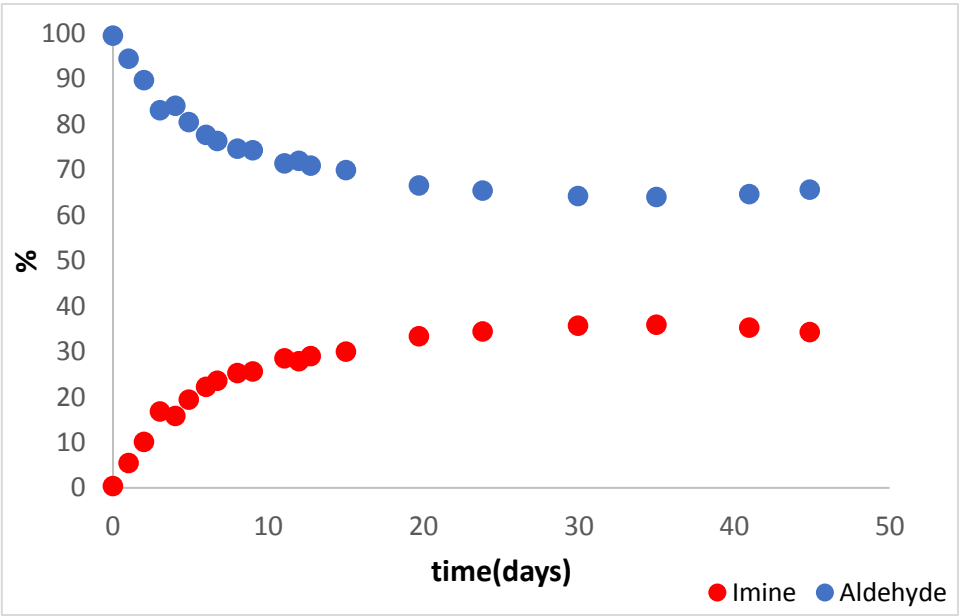


Figure S7.9: Partial ^{1}H spectrum (400 MHz, toluene-d_8) of the kinetic of formation of imine between $\mathbf{D_{NH2}}$ and $\mathbf{D'_{CO}}$ with $POOct_3$ as control, all at 10 mM concentration. The blue rectangle highlights the aldehyde peak, the red rectangle highlights the imine peak. Relative integrated intensities of the two peaks are reported in *Graph 7.9*.



Graph S7.9: formation of imine between the amines $\mathbf{D_{NH2}}$, and $\mathbf{D'_{CO}}$ with $POOct_3$ as template, all at 10 mM concentration (reaction in toluene-d_8 at 70°C). Relative integrated intensities as a function of reaction time obtained from integration of the imine C**H**=N and C**H**=O signals of the ^{1}H NMR spectra reported in *Figure S7.9*

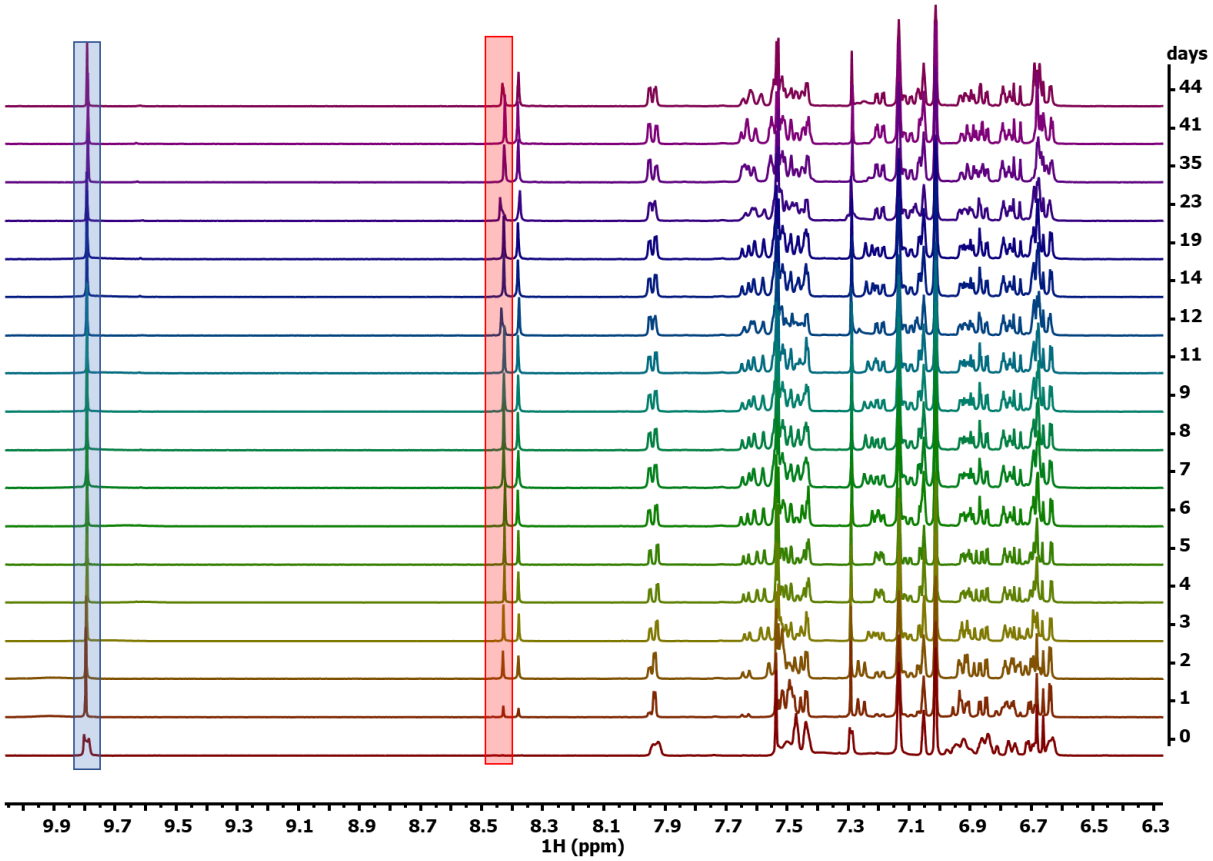
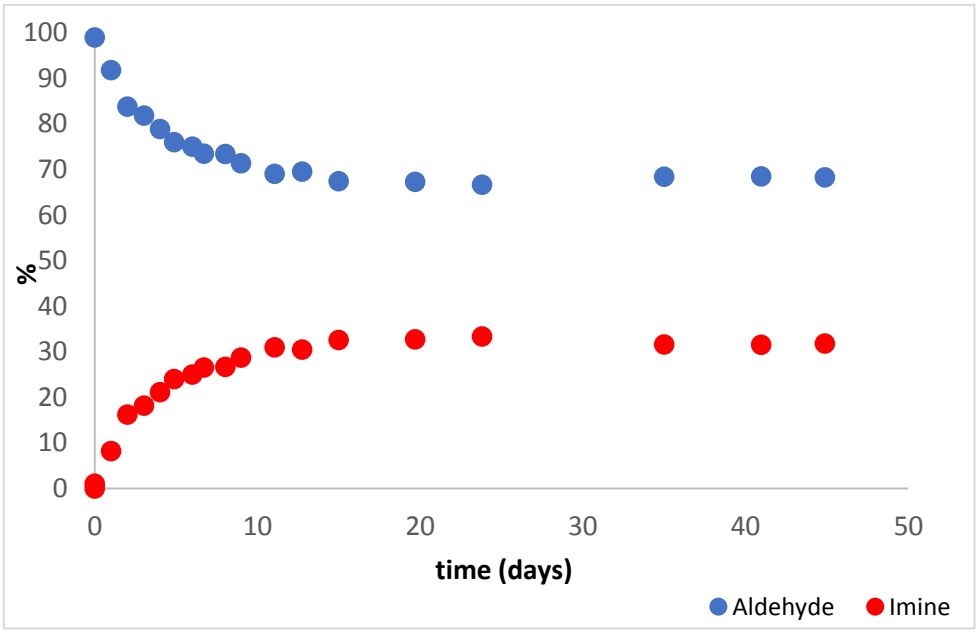
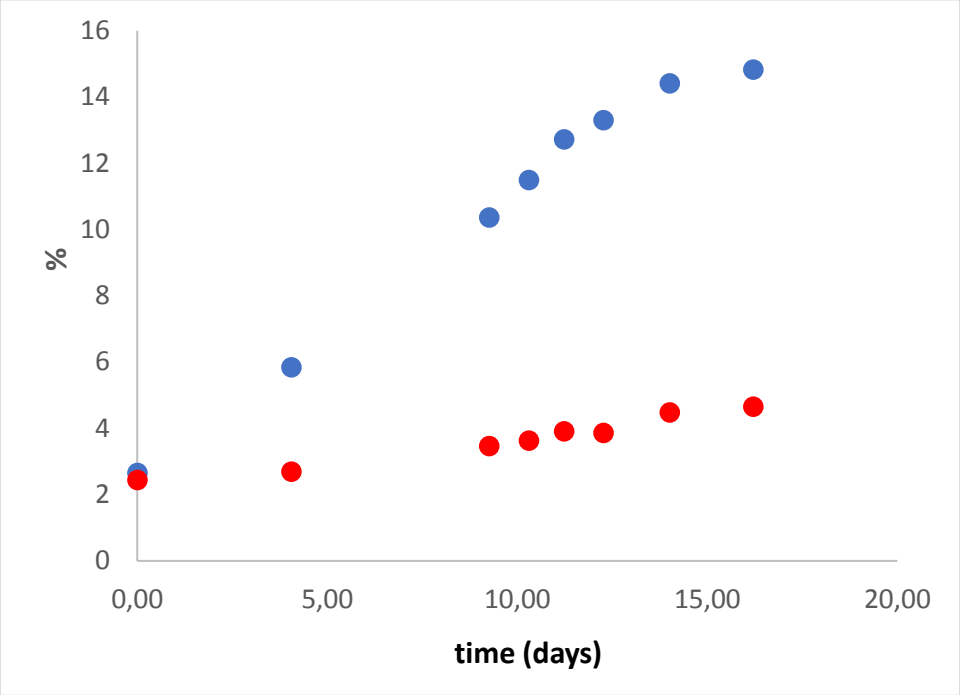


Figure S7.10: Partial ^{1}H spectrum (400 MHz, toluene-d_8) of the kinetic of formation of imine between $\mathbf{D_{NH2}}$ and $\mathbf{D'_{CO}}$ with $POOct_3$ as control, all at 10 mM concentration. The blue rectangle highlights the aldehyde peak, the red rectangle highlights the imine peak. Relative integrated intensities of the two peaks are reported in *Graph 7.10*.



Graph S7.10: formation of imine between the amine $\mathbf{D_{NH2}}$ and the aldehyde **D'CO** with $POOct_3$ as control, all at 1 mM concentration (reaction in toluene-d_8 at 70°C). Relative integrated intensities as a function of time obtained from integration of the imine C**H**=N and C**H**=O signals of the ^{1}H NMR spectra reported in *Figure S7.10*

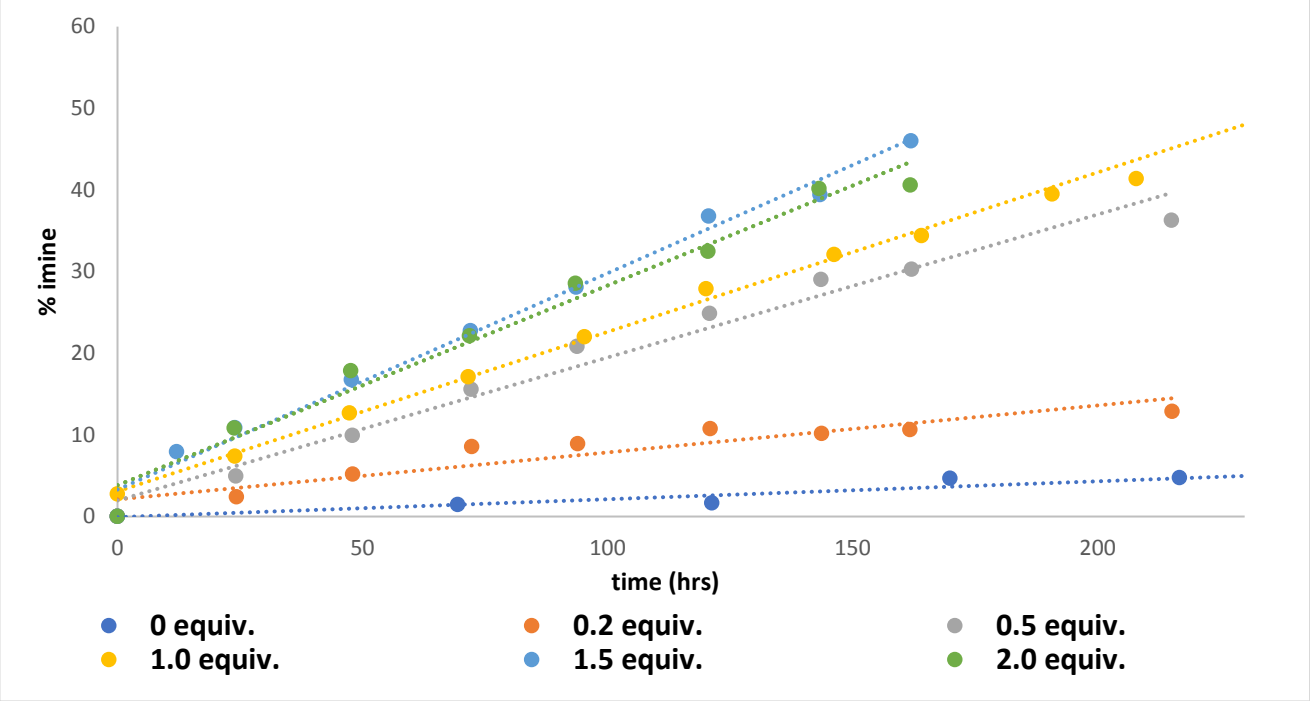


Graph S7.11: Preliminary experiment: (blue) formation of imine between the amine $\mathbf{D_{NH2}}$ and the aldehyde $\mathbf{D_{CO}}$ with **AA** as template, all at 10 mM concentration (reaction in toluene-d_8 at 60°C); (red) formation of imine between the amine $\mathbf{D_{NH2}}$ 10 mM and the aldehyde $\mathbf{D_{CO}}$ 10 mM with $\mathbf{POOct_3}$ 20 mM as control, (reaction in toluene-d_8 at 60°C); Relative integrated intensities as a function of time obtained from integration of the imine C**H**=N and C**H**=O signals of the ^{1}H NMR spectra.

8. Initial rate experiments

AA equivalents	Curve equation	R^2	Initial Rate [mmol*hrs^{-1}]
0.0	y= 0.0219x – 0.0769	0.9266	0.0219
0.2	y= 0.0575x + 2.0969	0.9072	0.0575
0.5	y= 0.1519x + 1.9643	0.8907	0.1519
1.0	y= 0.1851x + 3.0770	0.9262	0.1851
1.5	y= 0.2223x + 4.1447	0.9202	0.2223
2.0	y= 0.2476x + 4.5149	0.9260	0.2476

Table S8.1: Summary of the initial rate formation of Imine between the amine $\mathbf{D_{NH2}}$ and the aldehyde $\mathbf{D'_{CO}}$ at 1 mM concentration (reaction in toluene-d_8 at 70°C) at different concentrations of template **AA**.



Graph S8.1: Plot of the initial rate formation of Imine between the amine $\mathbf{D_{NH2}}$ and the aldehyde $\mathbf{D'_{CO}}$ at 1 mM concentration (reaction in toluene-d_8 at 70°C) at different concentrations of template AA. The relative curve equation and initial rate are reported in *Table S8.1*

9. ITC titration experiments

ITC titration experiments have been used to estimate the association constants of duplex formation for the trimers **AAA** and **DDD** in chloroform-*d* as comparison and confirmation of the constants obtained through the NMR titrations. In a typical experiment one of the components of the complex (the host, H) was dissolved in chloroform-*d* (freshly filtered on basic alumina) with a concentration in the range 50-100 µM and the solution was loaded into the sample cell of the PEAQ-ITC microcalorimeter (Malvern). A solution of the second component (the guest, G), in chloroform-*d* (freshly filtered on basic alumina) in a concentration 8-10 times higher than the host, was loaded into the injection syringe. The titration consisted in 19 injections (at 298 K), the first one with a volume of 0.4 µL (always discarded from the analysis), the others of 2 µL. The thermogram peaks were integrated using the instrument analysis, subtracting the contribution of the control titrations (solvent vs solvent and G vs solvent) and the resulting data were fit to a 1:1 binding isotherm.

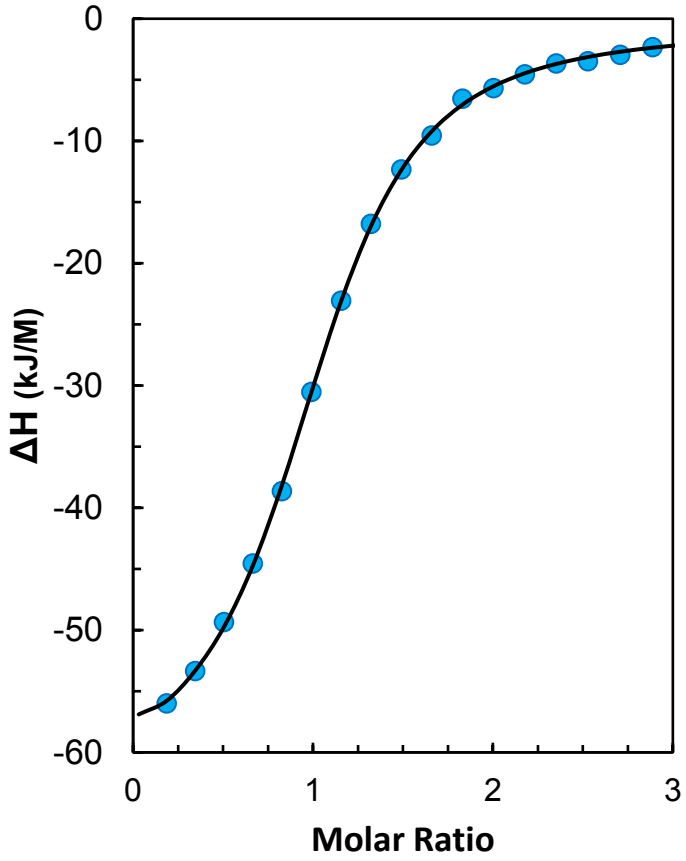


Figure S9.1: ITC titration of **DDD** (1 mM in the syringe) into **AAA** (70 µM in the cell) in chloroform-*d* at 298 K. The black line represents the best fit to a 1:1 binding isotherm. log*K* = 5.2 ± 0.1 (M^{-1}).

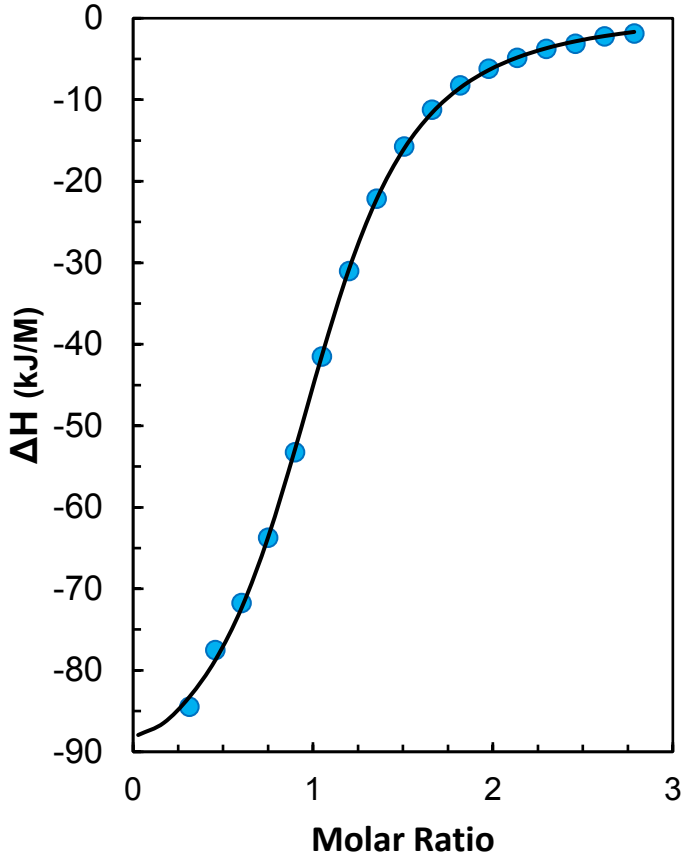


Figure S9.2: ITC titration of **AAA** (1 mM in the syringe) into **DDD** (70 µM in the cell) in chloroform-*d* at 298 K. The black line represents the best fit to a 1:1 binding isotherm. log*K* = 5.2 ± 0.1 (M^{-1})

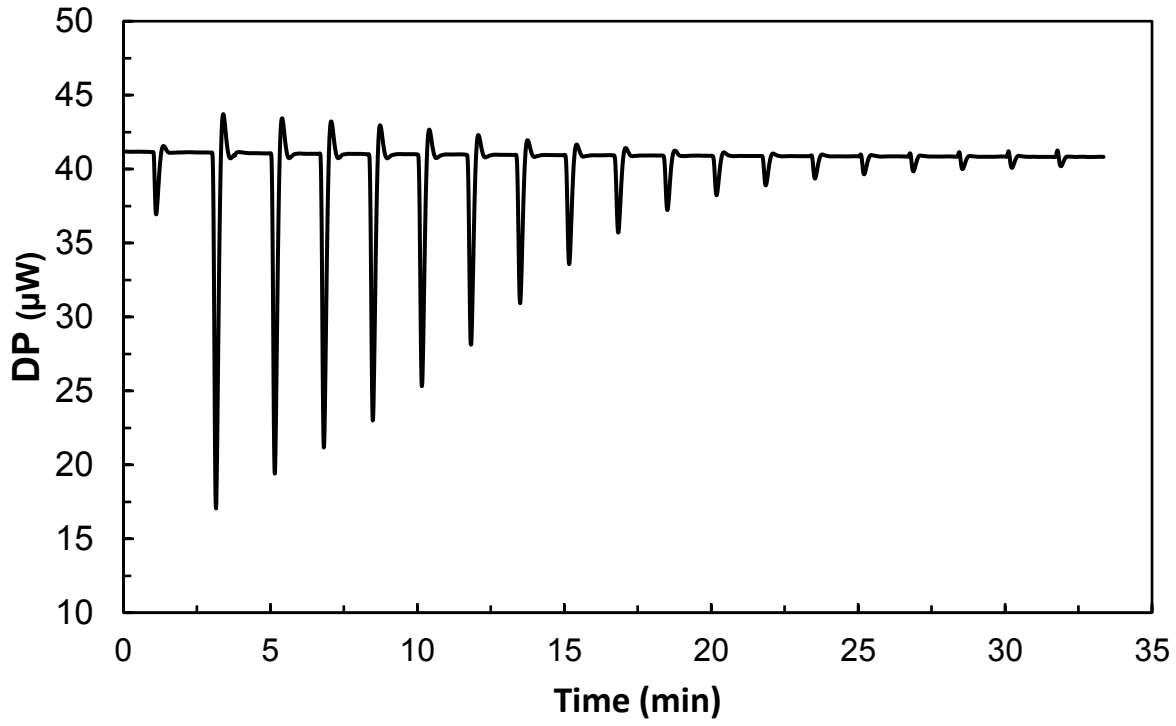


Figure S9.3: Example of raw thermogram from an ITC titration of **AAA** (1 mM in the syringe) into **DDD** (70 µM in the cell) in chloroform-*d* at 298 K.

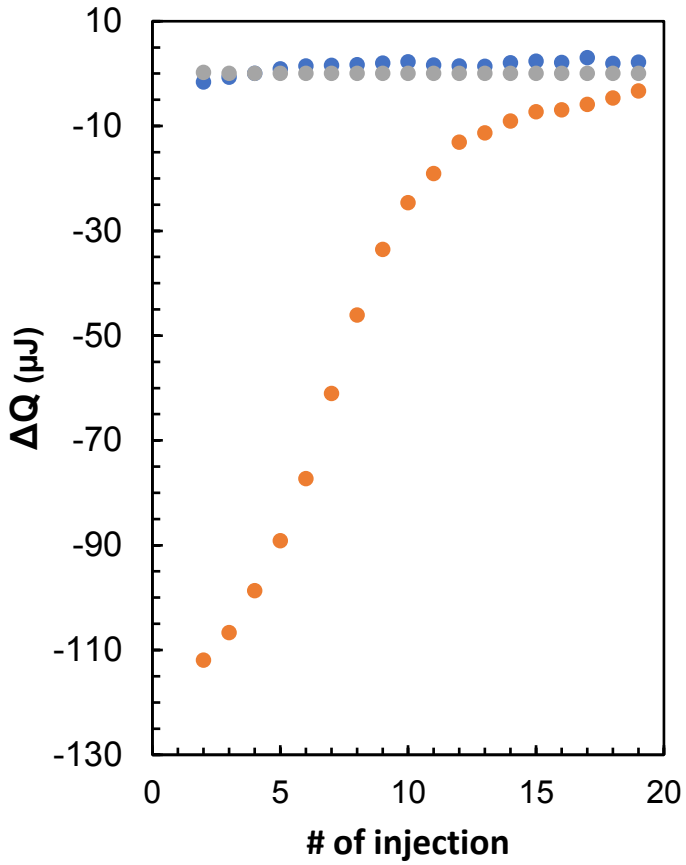


Figure S9.4: Comparison of integrated heat plot vs injection number for the **DDD** vs **AAA** titration and the control titrations: chloroform-*d* vs chloroform-*d* (grey), **DDD** vs chloroform-*d* (blue), **DDD** vs **AAA** (orange).