# *Electronic supplementary information for the manuscript*

## Thiophene-based water-soluble fullerene derivatives as highly efficient antiherpetic pharmaceuticals

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## *Experimental procedures*

Chlorofullerenes $C_{60}Cl_6$ and $C_{70}Cl_8$ were synthesized with quantitative yields as described in P. A. Troshin et al., *Fullerenes, Nanotubes, Carbon Nanostruct.*, **2003**, *11*, 165 and A. B. Kornev et al., *Chem. Commun*., **2011**, 47, 8298. Methyl esters of 2-(thiophen-2-yl)acetic acid, 3-(thiophen-2-yl)propanoic acid, 4-(thiophen-2-yl)butanoic acid were synthesized from commercially available acids using a standard procedure (esterification in methanol in the presence of a catalytic amount of sulfuric acid) (Figure S1). Methyl esters were distilled in vacuo and dried over 4Å molecular sieves, 1,2-dichlorobenzene was distilled.

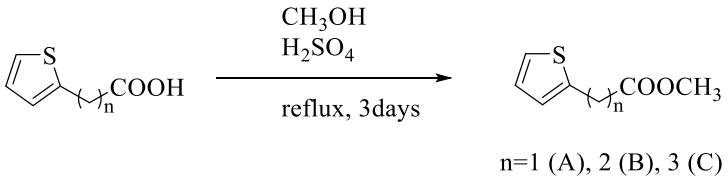


Figure S1. Synthesis of the thiophene-based esters

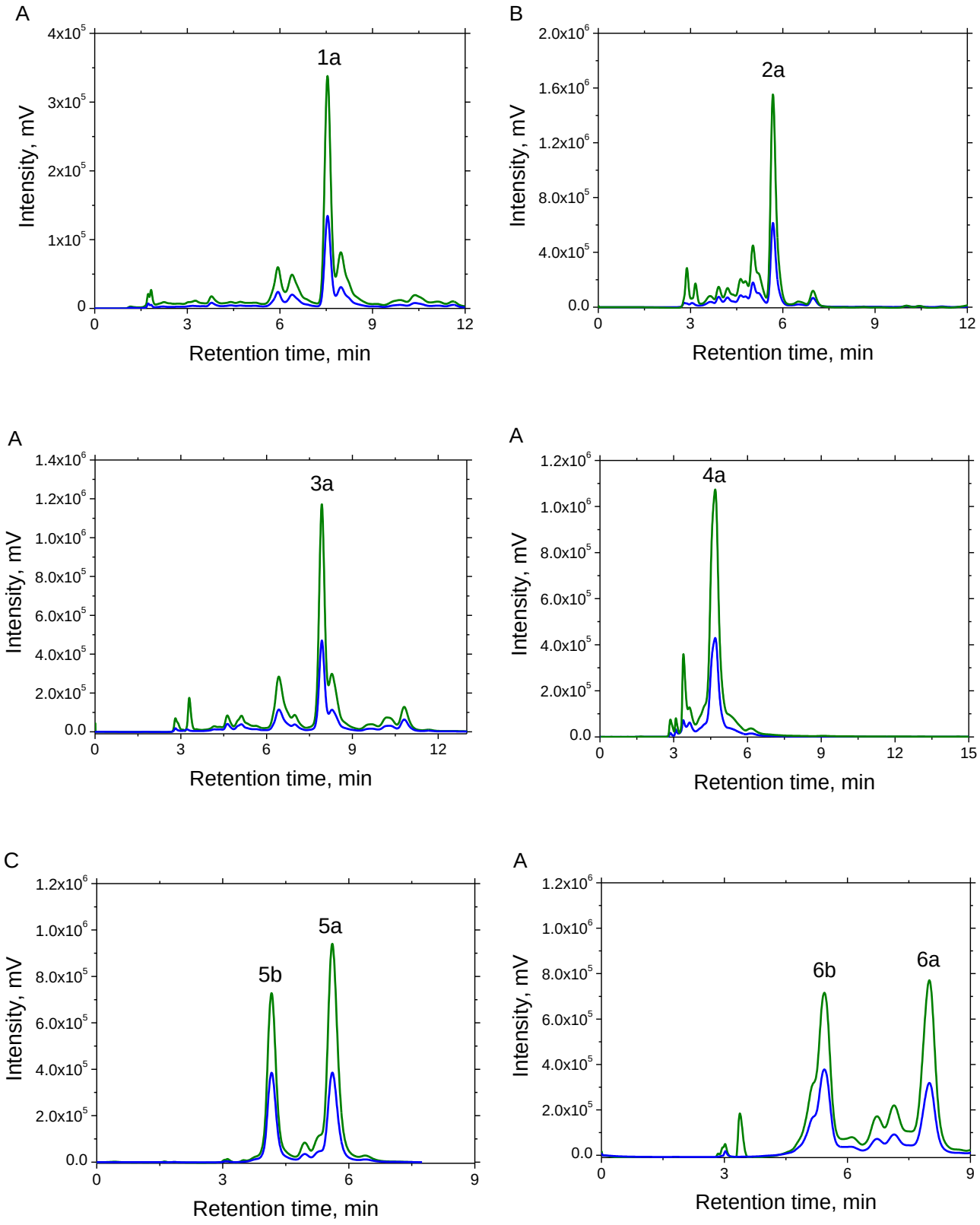


Figure S2. HPLC profiles of the reaction mixtures (Orbit C18 column, elution with toluene/acetonitrile mixtures 30/70 - 20/80 v/v, 30°C, flow rate 1 mL/min. UV/Vis detector: channel 1 – 290 nm (green), channel 2 – 350 nm (blue).

## *Selected spectroscopic data*

***Fullerene-based esters:***

Spectroscopic data for compounds **1a** and **1d** has been reported before (H. J. Huang, O. A. Kraevaya, I.I. Voronov, P.A. Troshin, S.-h. Hsu. *Int. J. Nanomedicine*, **2020**, 15, 2485-2499).

**1b** (yield 94%). $^{1}$H NMR (600 MHz, $CDCl_3$, δ, ppm): 1.89 – 2.05 (m, 10H), 2.29 – 2.47 (m, 10H), 2.75 – 2.92 (m, 10H), 3.63 – 3.76 (m, 15H), 5.40 (s, 1H), 6.63 (d, 1H, *J* = 3.2 Hz), 6.66 (d, 2H, *J* = 3.2 Hz), 6.74 (d, 2H, *J* = 3.2 Hz), 6.89 (d, 1H, *J* = 3.4 Hz), 7.00 (d, 2H, *J* = 3.4 Hz), 7.14 (d, 2H, *J* = 3.4 Hz).

$^{13}$C NMR (151 MHz, $CDCl_3$, δ, ppm): 26.48 ($\underline{C}H_2$), 26.63 ($\underline{C}H_2$), 26.65 ($\underline{C}H_2$), 29.36 ($\underline{C}H_2$), 29.43 ($\underline{C}H_2$), 29.48 ($\underline{C}H_2$), 33.01 ($\underline{C}H_2$), 33.07 ($\underline{C}H_2$), 51.63 ($\underline{C}H_3$), 51.64 ($\underline{C}H_3$), 54.69 ($\underline{C}_{sp3\ fullerene\ cage}$), 55.16 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.54 ($\underline{C}_{sp3\ fullerene\ cage}$), 61.87 ($\underline{C}_{sp3\ fullerene\ cage}$-H), 124.51, 124.53, 124.58, 126.03, 126.33, 126.54, 140.88, 140.89, 143.33, 143.39, 143.45, 144.15, 144.17, 144.28, 144.39, 144.44, 144.47, 144.49, 144.52, 144.75, 144.92, 145.29, 145.79, 146.72, 146.78, 146.97, 146.99, 147.07, 147.68, 148.06, 148.09, 148.17, 148.36, 148.60, 148.67, 148.74, 150.98, 151.53, 152.14, 155.22, 173.64 ($\underline{C}OOCH_3$), 173.67 ($\underline{C}OOCH_3$).

ESI MS: m/z= 1496 ($[M-H]^-$).

**1c** (yield 94%). $^{1}$H NMR (500 MHz, $CDCl_3$, δ, ppm): 1.90 (s, 3H), 3.71 (s, 3H), 3.76 (s, 12H), 3.86 (s, 10H), 6.79 (d, 1H, *J* = 3.6 Hz), 6.83 (d, 1H, *J* = 3.6 Hz), 6.87 – 6.91 (m, 4H), 7.18 (d, 2H, *J* = 3.6 Hz), 7.21 (d, 2H, *J* = 3.5 Hz).

$^{13}$C NMR (126 MHz, $CDCl_3$, δ, ppm): 32.78 ($\underline{C}H_3$), 35.27 ($\underline{C}H_2$), 35.52 ($\underline{C}H_2$), 35.58 ($\underline{C}H_2$), 52.28($\underline{C}H_3$), 52.31 ($\underline{C}H_3$), 52.32 ($\underline{C}H_3$), 53.98 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.49 ($\underline{C}_{sp3\ fullerene\ cage}$), 58.79 ($\underline{C}_{sp3\ fullerene\ cage}$), 61.99 ($\underline{C}_{sp3\ fullerene\ cage}$), 125.31, 126.57, 126.66, 126.69, 126.75, 126.82, 128.25, 129.05, 129.44, 135.52, 135.64, 141.47, 141.60, 142.78, 142.89, 143.01, 143.26, 143.61, 144.18, 144.28, 144.50, 144.77, 144.86, 145.08, 145.85, 146.86, 147.00, 147.18, 147.24, 147.78, 148.15, 148.20, 148.22, 148.55, 148.61, 148.71, 148.79, 150.95, 152.54, 155.90, 159.87, 170.61 ($\underline{C}OOCH_3$), 170.67 ($\underline{C}OOCH_3$), 170.72 ($\underline{C}OOCH_3$).

ESI MS: m/z= 1511 ($[M]^-$).

**2a** (yield 47%). $^{1}$H NMR (500 MHz, $CDCl_3$, δ, ppm): 2.62 – 2.75 (m, 10H), 3.10 (t, 2H, *J* = 7.7 Hz), 3.13 – 3.21 (m, 8H), 3.67 (s, 3H, *J* = 2.3 Hz), 3.71 (s, 6H), 3.72 (s, 6H), 6.68 (d, 1H, *J* = 3.6 Hz), 6.74 (d, 2H, *J* = 3.5 Hz), 6.79 (d, 2H, *J* = 3.5 Hz), 6.81 (d, 1H, *J* = 3.6 Hz), 7.05 (d, 2H, *J* = 3.5 Hz), 7.35 (d, 2H, *J* = 3.6 Hz).

$^{13}$C NMR (126 MHz, CDCl3, δ, ppm): 25.37 ($\underline{C}H_2$), 25.50 ($\underline{C}H_2$), 25.58 ($\underline{C}H_2$), 35.52 ($\underline{C}H_2$), 35.72 ($\underline{C}H_2$), 35.80 ($\underline{C}H_2$), 51.76 ($\underline{C}H_3$), 51.79 ($\underline{C}H_3$), 54.09 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.24 ($\underline{C}_{sp3\ fullerene\ cage}$), 59.63 ($\underline{C}_{sp3\ fullerene\ cage}$), 75.43 ($\underline{C}_{sp3\ fullerene\ cage}$-Cl), 124.24, 124.66, 124.70, 126.97, 127.59,

129.75, 139.00, 140.07, 142.18, 142.57, 142.88, 143.15, 143.49, 143.80, 144.06, 144.09, 144.34, 144.38, 144.59, 144.67, 145.01, 145.28, 145.88, 147.18, 147.35, 147.85, 148.22, 148.30, 148.36, 148.69, 148.75, 148.77, 149.84, 150.43, 153.16, 155.68, 172.66 ($\underline{C}OOCH_3$), 172.70 ($\underline{C}OOCH_3$), 172.74 ($\underline{C}OOCH_3$).

**2b** (yield 89%). $^1$H NMR (500 MHz, $CDCl_3$, δ, ppm): 2.59 – 2.77 (m, 10H), 3.04 – 3.23 (m, 10H), 3.62 – 3.83 (m, 15H), 5.37 (s, 1H), 6.67 (d, 1H, *J* = 2.7 Hz), 6.70 (d, 2H, *J* = 2.7 Hz), 6.77 (d, 2H, *J* = 2.9 Hz), 6.88 (d, 1H, *J* = 3.2 Hz), 6.98 (d, 2H, *J* = 3.3 Hz), 7.13 (d, 2H, *J* = 3.2 Hz).

$^{13}$C NMR (126 MHz, $CDCl_3$, δ, ppm): 25.38 ($\underline{C}H_2$), 25.48 ($\underline{C}H_2$), 25.54 ($\underline{C}H_2$), 35.59 ($\underline{C}H_2$), 35.81 ($\underline{C}H_2$), 51.78 ($\underline{C}H_3$), 51.80 ($\underline{C}H_3$), 54.63 ($\underline{C}_{sp3\ fullerene\ cage}$), 55.12 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.48 ($\underline{C}_{sp3\ fullerene\ cage}$), 61.80 ($\underline{C}_{sp3\ fullerene\ cage}$-H), 124.56, 124.61, 124.64, 126.12, 126.36, 126.59, 128.24, 129.05, 141.12, 141.15, 143.33, 143.39, 143.45, 143.51, 143.55, 144.07, 144.18, 144.29, 144.45, 144.50, 144.70, 144.77, 145.21, 145.70, 146.79, 146.87, 146.95, 147.00, 147.08, 147.69, 148.07, 148.11, 148.18, 148.37, 148.61, 148.69, 148.76, 150.91, 151.40, 152.17, 155.15, 172.69 ($\underline{C}OOCH_3$), 172.71 ($\underline{C}OOCH_3$).

ESI MS: m/z= 1566 ($[M-H]^-$).

**3a** (yield 36%). $^1$H NMR (600 MHz, $CDCl_3$, δ, ppm): 1.91 – 2.07 (m, 10H), 2.33 – 2.45 (m, 10H), 2.77 – 2.92 (m, 10H), 3.64 – 3.74 (m, 15H), 6.65 (d, 1H, *J* = 3.6 Hz), 6.71 (d, 2H, *J* = 3.5 Hz), 6.76 (d, 2H, *J* = 3.5 Hz), 6.82 (d, 1H, *J* = 3.5 Hz), 7.06 (d, 2H, *J* = 3.5 Hz), 7.37 (d, 2H, *J* = 3.5 Hz).

$^{13}$C NMR (126 MHz, $CDCl_3$, δ, ppm): 26.36 ($\underline{C}H_2$), 26.55 ($\underline{C}H_2$), 26.62 ($\underline{C}H_2$), 29.35 ($\underline{C}H_2$), 29.45 ($\underline{C}H_2$), 29.53 ($\underline{C}H_2$), 33.03 ($\underline{C}H_2$), 33.09 ($\underline{C}H_2$), 33.11 ($\underline{C}H_2$), 51.59 ($\underline{C}H_3$), 54.14 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.31 ($\underline{C}_{sp3\ fullerene\ cage}$), 59.66 ($\underline{C}_{sp3\ fullerene\ cage}$), 75.56 ($\underline{C}_{sp3\ fullerene\ cage}$-Cl), 124.13, 124.61, 126.95, 127.59, 129.67, 138.69, 139.79, 142.33, 142.59, 142.93, 143.14, 143.57, 144.17, 144.33, 144.38, 144.58, 144.67, 144.80, 145.01, 145.06, 145.09, 145.42, 145.98, 147.16, 147.18, 147.34, 147.85, 148.20, 148.30, 148.35, 148.66, 148.75, 149.88, 150.56, 153.14, 155.75, 173.59 ($\underline{C}OOCH_3$), 173.62 ($\underline{C}OOCH_3$), 173.63 ($\underline{C}OOCH_3$).

ESI MS: m/z= 1636 ($[M-Cl]^-$).

**3b** (yield 91%). $^1$H NMR (500 MHz, $CDCl_3$, δ, ppm): 3.73 (s, 3H), 3.74 (s, 6H), 3.76 (s, 6H), 3.78 (s, 2H), 3.81 (s, 4H), 3.86 (s, 4H), 5.40 (s, 1H), 6.79 (d, 1H, *J* = 3.6 Hz), 6.82 (d, 2H, *J* = 3.5 Hz), 6.89 (d, 2H, *J* = 3.5 Hz), 6.94 (d, 1H, *J* = 3.6 Hz), 7.05 (d, 2H, *J* = 3.6 Hz), 7.19 (d, 2H, *J* = 3.5 Hz).

$^{13}$C NMR (126 MHz, $CDCl_3$, δ, ppm): 35.40 ($\underline{C}H_2$), 35.48 ($\underline{C}H_2$), 35.57 ($\underline{C}H_2$), 52.28 ($\underline{C}H_3$), 52.33 ($\underline{C}H_3$), 54.59 ($\underline{C}_{sp3\ fullerene\ cage}$), 55.11 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.44 ($\underline{C}_{sp3\ fullerene\ cage}$), 61.80 ($\underline{C}_{sp3\ fullerene\ cage}$-H), 126.10, 126.32, 126.58, 126.82, 126.86, 126.89, 135.29, 135.41, 135.44, 142.59, 142.66, 143.31, 143.35, 143.48, 144.04, 144.20, 144.30, 144.46, 144.51, 144.68, 144.72, 145.19,

145.68, 146.81, 147.00, 147.09, 147.70, 148.09, 148.12, 148.20, 148.39, 148.63, 148.71, 148.77, 150.81, 151.34, 152.23, 155.08, 170.62 ($\underline{C}OOCH_3$), 170.70($\underline{C}OOCH_3$), 170.71 ($\underline{C}OOCH_3$).

ESI MS: m/z= 1636 ($[M-H]^-$).

**4a** (yield 81%). $^1$H NMR (500 MHz, $CDCl_3$, δ, ppm): 3.62 – 3.94 (m, 40H), 6.36 – 7.14 (m, 16H).

$^{13}$C NMR (126 MHz, $CDCl_3$, δ, ppm): 35.40 ($\underline{C}H_2$), 35.54 ($\underline{C}H_2$), 52.32 ($\underline{C}H_3$), 52.41 ($\underline{C}H_3$), 56.59 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.05 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.29 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.48 ($\underline{C}_{sp3\ fullerene\ cage}$), 123.30, 126.21, 126.41, 126.52, 126.63, 126.82, 126.86, 126.88, 131.59, 132.56, 133.83, 134.41, 135.05, 135.10, 135.35, 135.51, 135.63, 141.78, 142.02, 142.39, 142.43, 142.59, 142.62, 143. 151.62, 46, 143.67, 145.31, 145.44, 145.51, 145.79, 146.24, 146.61, 148.02, 148.60, 149.39, 149.50, 150.58, 150.63, 152.04, 152.13, 152.61, 152.66, 152.87, 153.19, 153.93, 154.34, 154.86, 155.16, 160.60, 170.72 ($\underline{C}OOCH_3$), 170.75 ($\underline{C}OOCH_3$), 170.80 ($\underline{C}OOCH_3$).

ESI MS: m/z= 1041 ($[M]^{2-}$).

**5a** (yield 55%). $^1$H NMR (500 MHz, $CDCl_3$, δ, ppm): 2.53 – 2.76 (m, 16H), 2.97– 3.24 (m, 16H), 3.70 (s, 6H), 3.71 – 3.73 (m, 12H), 3.75 (s, 6H), 6.45 (d, 2H, *J* = 3.5 Hz), 6.48 (d, 2H, *J* = 3.5 Hz), 6.55 (d, 2H, *J* = 3.6 Hz), 6.63 (d, 2H, *J* = 3.5 Hz), 6.65 (d, 2H, *J* = 3.5 Hz), 6.68 (d, 2H, *J* = 3.5 Hz), 6.78 (d, 2H, *J* = 3.5 Hz), 6.94 (d, 2H, *J* = 3.5 Hz).

$^{13}$C NMR (126 MHz, $CDCl_3$, δ, ppm): 25.34 ($\underline{C}H_2$), 25.38 ($\underline{C}H_2$), 25.49 ($\underline{C}H_2$), 35.86 ($\underline{C}H_2$), 35.89 ($\underline{C}H_2$), 35.90 ($\underline{C}H_2$), 35.91 ($\underline{C}H_2$), 51.76 ($\underline{C}H_3$), 51.77 ($\underline{C}H_3$), 51.82 ($\underline{C}H_3$), 56.61 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.06 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.29 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.50 ($\underline{C}_{sp3\ fullerene\ cage}$), 124.15, 124.26, 124.58, 126.19, 126.47, 126.60, 126.82, 128.24, 131.60, 132.67, 133.97, 134.50, 135.63, 140.60, 140.97, 141.25, 141.83, 142.20, 142.37, 142.48, 143.09, 143.14, 143.40, 143.53, 143.61, 145.30, 145.44, 145.50, 145.76, 146.24, 146.62, 148.05, 148.61, 149.37, 149.49, 150.53, 150.61, 151.67, 152.04, 152.12, 152.62, 152.84, 153.10, 153.89, 154.25, 154.87, 155.09, 160.74, 172.65 ($\underline{C}OOCH_3$), 172.67 ($\underline{C}OOCH_3$), 172.72 ($\underline{C}OOCH_3$).

ESI MS: m/z= 1097 ($[M]^{2-}$).

**5b** (yield 43%). $^1$H NMR (500 MHz, $CDCl_3$, δ, ppm): 2.49 – 2.83 (m, 18H), 2.93 – 3.29 (m, 18H), 3.65 – 3.76 (m, 27H), 5.43 (s, 1H), 6.41 – 6.59 (m, 8H), 6.61 – 6.95 (m, 8H), 7.10 – 7.22 (m, 2H).

$^{13}$C NMR (126 MHz, $CDCl_3$, δ, ppm): 25.16 ($\underline{C}H_2$), 25.34 ($\underline{C}H_2$), 25.37 ($\underline{C}H_2$), 25.39 ($\underline{C}H_2$), 25.42 ($\underline{C}H_2$), 25.45 ($\underline{C}H_2$), 25.60 ($\underline{C}H_2$), 35.83 ($\underline{C}H_2$), 35.91 ($\underline{C}H_2$), 35.95 ($\underline{C}H_2$), 35.97 ($\underline{C}H_2$), 51.76 ($\underline{C}H_3$), 51.79 ($\underline{C}H_3$), 51.82 ($\underline{C}H_3$), 57.15 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.19 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.39 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.46 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.51 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.60 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.82 ($\underline{C}_{sp3\ fullerene\ cage}$), 58.05 ($\underline{C}_{sp3\ fullerene\ cage}$), 58.26 ($\underline{C}_{sp3\ fullerene\ cage}$), 123.54, 124.07, 124.10, 124.14, 124.23, 124.35, 124.66, 124.76, 125.61, 125.74, 126.18, 126.34, 126.36, 126.40, 126.46, 126.79,

126.83, 126.86, 132.45, 132.89, 133.01, 134.31, 134.52, 135.28, 135.39, 135.85, 136.17, 136.28, 140.95, 141.22, 141.57, 141.60, 141.65, 141.70, 141.88, 142.16, 142.69, 142.73, 142.86, 142.96, 142.98, 143.01, 143.03, 143.06, 143.16, 143.20, 144.12, 144.40, 144.48, 144.77, 146.91, 147.13, 147.16, 147.17, 147.22, 147.51, 147.79, 148.22, 148.33, 148.81, 148.83, 148.85, 148.87, 148.96, 149.15, 149.19, 149.63, 149.65, 151.13, 151.23, 151.29, 151.33, 151.42, 152.11, 152.17, 152.20, 152.35, 152.47, 153.18, 153.39, 153.48, 153.54, 153.63, 153.66, 154.13, 154.24, 154.31, 154.55, 154.64, 154.89, 155.37, 155.44, 155.88, 156.52, 172.70 ($\underline{C}OOCH_3$), 172.76 ($\underline{C}OOCH_3$).

ESI MS: m/z= 1181 ($[M-H]^{2-}$).

**6a** (yield 40%). $^1$H NMR (500 MHz, $CDCl_3$, δ, ppm): 1.84– 2.06 (m, 16H), 2.28 – 2.45 (m, 16H), 2.68 – 2.91 (m, 16H), 3.69 (s, 6H), 3.70 (m, 12H), 3.72 (s, 6H), 6.41 (d, 2H, *J* = 3.5 Hz), 6.45 (d, 2H, *J* = 3.4 Hz), 6.51 (d, 2H, *J* = 3.4 Hz), 6.62 (d, 2H, *J* = 3.4 Hz), 6.65 (d, 2H, *J* = 3.5 Hz), 6.69 (d, 2H, *J* = 3.5 Hz), 6.79 (d, 2H, *J* = 3.4 Hz), 6.96 (d, 2H, *J* = 3.4 Hz).

$^{13}$C NMR (126 MHz, $CDCl_3$, δ, ppm): 26.65 ($\underline{C}H_2$), 26.68 ($\underline{C}H_2$), 26.76 ($\underline{C}H_2$), 29.35 ($\underline{C}H_2$), 29.37 ($\underline{C}H_2$), 29.51 ($\underline{C}H_2$), 32.99 ($\underline{C}H_2$), 33.08 ($\underline{C}H_2$), 51.58 ($\underline{C}H_3$), 51.62 ($\underline{C}H_3$), 56.70 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.16 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.39 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.58 ($\underline{C}_{sp3\ fullerene\ cage}$), 124.08, 124.19, 124.52, 126.09, 126.40, 126.53, 126.74, 131.65, 132.71, 134.03, 134.54, 135.65, 140.35, 140.78, 141.01, 141.83, 141.96, 142.37, 142.46, 143.56, 144.05, 144.11, 144.36, 144.61, 145.35, 145.44, 145.54, 145.77, 146.26, 146.66, 148.07, 148.61, 149.39, 149.48, 150.52, 150.61, 151.80, 152.12, 152.15, 152.63, 152.92, 153.15, 153.88, 154.31, 154.95, 155.13, 160.87, 173.27 ($\underline{C}OOCH_3$), 173.63 ($\underline{C}OOCH_3$), 173.64 ($\underline{C}OOCH_3$), 173.67 ($\underline{C}OOCH_3$).

ESI MS: m/z= 1153 ($[M]^{2-}$).

**6b** (yield 32%). $^1$H NMR (600 MHz, $CDCl_3$, δ, ppm): 1.78–2.12 (m, 18H), 2.16 – 2.51 (m, 18H), 2.61 – 3.01 (m, 18H), 3.58 – 3.80 (m, 27H), 5.45 (s, 1H), 6.29– 7.22 (m, 18H).

$^{13}$C NMR (151 MHz, $CDCl_3$, δ, ppm): 26.60 ($\underline{C}H_2$), 26.68 ($\underline{C}H_2$), 26.75 ($\underline{C}H_2$), 26.78 ($\underline{C}H_2$), 29.36 ($\underline{C}H_2$), 29.38 ($\underline{C}H_2$), 29.47 ($\underline{C}H_2$), 29.56 ($\underline{C}H_2$), 32.99 ($\underline{C}H_2$), 33.00 ($\underline{C}H_2$), 33.04 ($\underline{C}H_2$), 33.08 ($\underline{C}H_2$), 51.60 ($\underline{C}H_3$), 57.25 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.28 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.48 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.59 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.68 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.89 ($\underline{C}_{sp3\ fullerene\ cage}$), 58.12 ($\underline{C}_{sp3\ fullerene\ cage}$), 58.27 ($\underline{C}_{sp3\ fullerene\ cage}$), 124.05, 124.09, 124.17, 124.28, 124.70, 125.46, 125.66, 126.05, 126.25, 126.30, 126.38, 126.69, 126.74, 128.25, 129.05, 132.52, 132.91, 133.07, 134.44, 134.60, 135.31, 135.42, 135.84, 136.21, 136.30, 141.26, 141.35, 141.38, 141.43, 141.48, 141.65, 142.15, 142.53, 142.89, 143.67, 143.93, 143.97, 144.00, 144.02, 144.09, 144.20, 144.42, 144.50, 144.77, 145.07, 146.96, 147.16, 147.20, 147.25, 147.54, 147.78, 148.26, 148.38, 148.84, 148.89, 148.97, 149.16, 149.19, 149.65, 149.67, 150.95, 151.24, 151.29, 151.35, 151.42, 152.13, 152.22, 152.28, 152.36, 152.47, 153.21, 153.50, 153.58, 153.64, 153.68, 153.76, 154.25, 154.29, 154.35, 154.37, 154.58, 154.72, 154.93, 155.41, 155.50, 155.93, 156.62, 173.70 ($\underline{C}OOCH_3$).

ESI MS: m/z= 1244 ($[M-H]^{2-}$).

***Fullerene-based acids:***

Spectroscopic data for compounds **A1a, A4a, A5a, A6a** has been reported before (O. A. Kraevaya et al., *Chem. Commun*., **2020**, *56*, 1179-1182). Yields: 94-98%.

**A1b**. $^{1}$H NMR (500 MHz, $(CD_3)_2SO$, δ, ppm): 3.74 (s, 2H), 3.78 (s, 4H), 3.83 (s, 4H), 5.99 (s, 1H), 6.85 – 6.80 (m, 3H), 6.92 (d, 2H, *J* = 3.4 Hz), 7.03 (d, 1H, *J* = 3.6 Hz), 7.19 (d, 2H, *J* = 3.5 Hz), 7.42 (d, 2H, *J* = 3.5 Hz).

$^{13}$C NMR (126 MHz, $(CD_3)_2SO$, δ, ppm): 35.46 ($\underline{C}H_2$), 35.55 ($\underline{C}H_2$), 35.63 ($\underline{C}H_2$), 54.82 ($\underline{C}_{sp3\ fullerene\ cage}$), 55.15 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.77 ($\underline{C}_{sp3\ fullerene\ cage}$), 61.04 ($\underline{C}_{sp3\ fullerene\ cage}$-H), 125.87, 126.72, 126.75, 127.15, 127.25, 127.37, 137.16, 137.59, 137.70, 141.18, 141.24, 142.92, 143.25, 143.34, 144.08, 144.22, 144.32, 144.45, 144.76, 145.28, 145.48, 145.78, 146.65, 146.75, 146.94, 147.03, 147.52, 147.65, 147.97, 148.05, 148.12, 148.28, 148.56, 148.60, 148.68, 151.81, 152.10, 152.95, 155.65, 171.87 ($\underline{C}$OOH), 171.96 ($\underline{C}$OOH), 171.99 ($\underline{C}$OOH).

**A1c**. $^{1}$H NMR (500 MHz, $(CD_3)_2SO$, δ, ppm): 1.88 (s, 3H), 3.73 (s, 2H), 3.84 (s, 8H), 6.73 (d, 1H, *J* = 3.4 Hz), 6.81 (d, 1H, *J* = 3.4 Hz), 6.88 – 6.95 (m, 4H), 7.20 (d, 2H, *J* = 3.4 Hz), 7.24 (d, 2H, *J* = 3.4 Hz).

$^{13}$C NMR (126 MHz, $(CD_3)_2SO$, δ, ppm): 32.93 ($\underline{C}H_3$), 35.30 ($\underline{C}H_2$), 35.58 ($\underline{C}H_2$), 35.62 ($\underline{C}H_2$), 54.10 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.66 ($\underline{C}_{sp3\ fullerene\ cage}$), 58.89 ($\underline{C}_{sp3\ fullerene\ cage}$), 61.97 ($\underline{C}_{sp3\ fullerene\ cage}$), 126.79, 126.86, 127.20, 127.37, 127.44, 129.45, 137.63, 137.86, 137.94, 139.95, 141.33, 141.35, 142.90, 143.19, 143.30, 143.65, 144.11, 144.24, 144.44, 144.47, 144.76, 144.83, 144.85, 145.12, 146.93, 147.12, 147.17, 147.29, 147.75, 148.10, 148.13, 148.14, 148.47, 148.52, 148.65, 148.72, 151.45, 152.90, 156.13, 159.93, 171.79 ($\underline{C}$OOH), 171.93 ($\underline{C}$OOH), 171.99 ($\underline{C}$OOH).

**A1d**. $^{1}$H NMR (500 MHz, $(CD_3)_2SO$, δ, ppm): 1.20 (t, 3H, *J* = 6.9 Hz), 1.97 – 2.06 (m, 2H), 3.76 (s, 2H), 3.84 (s, 8H), 6.82 – 6.86 (m, 2H), 6.90 – 6.96 (m, 4H), 7.07 (d, 2H, *J* = 3.4 Hz), 7.21 (d, 2H, *J* = 3.4 Hz).

$^{13}$C NMR (126 MHz, $(CD_3)_2SO$, δ, ppm): 9.66 ($CH_2\underline{C}H_3$), 32.56 ($\underline{C}H_2CH_3$), 35.34 ($\underline{C}H_2$), 35.57 ($\underline{C}H_2$), 35.61 ($\underline{C}H_2$), 54.31 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.63 ($\underline{C}_{sp3\ fullerene\ cage}$), 59.91 ($\underline{C}_{sp3\ fullerene\ cage}$), 65.20 ($\underline{C}_{sp3\ fullerene\ cage}$), 126.21, 126.79, 127.16, 127.39, 127.52, 130.36, 137.38, 137.63, 138.35, 140.37, 141.90, 142.80, 142.90, 143.16, 143.32, 143.61, 144.11, 144.20, 144.45, 144.51, 144.78, 144.88, 144.91, 145.04, 145.42, 146.93, 147.06, 147.16, 147.23, 147.83, 148.09, 148.12, 148.51, 148.72, 151.08, 153.12, 155.58, 156.04, 171.82 ($\underline{C}$OOH), 171.93 ($\underline{C}$OOH), 171.98 ($\underline{C}$OOH).

**A2a**. $^{1}$H NMR (500 MHz, $(CD_3)_2SO$, δ, ppm): 2.53 – 2.63 (m, 10H), 2.90 – 3.06 (m, 10H), 6.71 (d, 1H, *J* = 3.5 Hz), 6.74 (d, 1H, *J* = 3.6 Hz), 6.85 (d, 2H, *J* = 3.5 Hz), 6.88 (d, 2H, *J* = 3.5 Hz), 7.01 (d, 2H, *J* = 3.5 Hz), 7.30 (d, 2H, *J* = 3.5 Hz).

$^{13}$C NMR (126 MHz, $(CD_3)_2SO$, δ, ppm): 25.15 ($\underline{C}H_2$), 25.40 ($\underline{C}H_2$), 25.49 ($\underline{C}H_2$), 35.23 ($\underline{C}H_2$), 35.67 ($\underline{C}H_2$), 35.75 ($\underline{C}H_2$), 54.03 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.23 ($\underline{C}_{sp3\ fullerene\ cage}$), 59.58 ($\underline{C}_{sp3\ fullerene\ cage}$), 75.52 ($\underline{C}_{sp3\ fullerene\ cage}$-Cl), 125.51, 127.22, 127.87, 129.98, 137.88, 138.93, 142.24, 142.44, 142.79, 143.01, 143.37, 143.88, 144.23, 144.26, 144.38, 144.52, 144.58, 144.89, 145.10, 145.34, 145.66, 145.95, 146.97, 147.01, 147.16, 147.71, 148.07, 148.13, 148.22, 148.50, 148.61, 149.93, 150.54, 153.14, 155.69, 173.67 ($\underline{C}$OOH), 173.75 ($\underline{C}$OOH).

**A2b**. $^1$H NMR (500 MHz, $(CD_3)_2SO$, δ, ppm): 2.50 – 2.62 (m, 10H), 2.87– 3.06 (m, 10H), 5.81 (s, 1H), 6.75 (d, 1H, *J* = 3.4 Hz), 6.77 (d, 2H, *J* = 3.4 Hz), 6.86 (d, 2H, *J* = 3.3 Hz), 6.95 (d, 1H, *J* = 3.5 Hz), 7.08 (d, 2H, *J* = 3.4 Hz), 7.33 (d, 2H, *J* = 3.2 Hz).

$^{13}$C NMR (126 MHz, $(CD_3)_2SO$, δ, ppm): 25.28 ($\underline{C}H_2$), 25.39 ($\underline{C}H_2$), 25.47 ($\underline{C}H_2$), 35.40 ($\underline{C}H_2$), 35.67 ($\underline{C}H_2$), 35.73 ($\underline{C}H_2$), 54.76 ($\underline{C}_{sp3\ fullerene\ cage}$), 55.11 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.69 ($\underline{C}_{sp3\ fullerene\ cage}$), 61.15 ($\underline{C}_{sp3\ fullerene\ cage}$-H), 125.23, 125.34, 126.21, 127.08, 127.12, 139.87, 139.91, 142.93, 143.19, 143.31, 144.03, 144.17, 144.29, 144.41, 144.70, 144.82, 144.92, 145.24, 145.39, 145.42, 145.75, 146.68, 146.87, 146.96, 147.40, 147.59, 147.91, 147.98, 148.06, 148.23, 148.49, 148.54, 148.61, 151.69, 151.99, 152.73, 155.57, 173.71 ($\underline{C}$OOH), 173.76 ($\underline{C}$OOH).

**A3a**. $^1$H NMR (500 MHz, $(CD_3)_2SO$, δ, ppm): 1.65 – 1.88 (m, 10H), 2.14 – 2.31 (m, 10H), 2.65 – 2.85 (m, 10H), 6.71 (d, 1H, *J* = 2.7 Hz), 6.75 (d, 1H, *J* = 3.3 Hz), 6.80 (d, 2H, *J* = 3.0 Hz), 6.84 (d, 2H, *J* = 3.1 Hz), 7.04 (d, 2H, *J* = 3.3 Hz), 7.33 (d, 2H, *J* = 3.2 Hz).

$^{13}$C NMR (126 MHz, DMSO, δ, ppm): 26.59 ($\underline{C}H_2$), 26.81 ($\underline{C}H_2$), 26.94 ($\underline{C}H_2$), 29.05 ($\underline{C}H_2$), 29.17 ($\underline{C}H_2$), 29.22 ($\underline{C}H_2$), 33.12 ($\underline{C}H_2$), 33.20 ($\underline{C}H_2$), 54.07 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.28 ($\underline{C}_{sp3\ fullerene\ cage}$), 59.60 ($\underline{C}_{sp3\ fullerene\ cage}$), 75.66 ($\underline{C}_{sp3\ fullerene\ cage}$-Cl), 125.33, 127.29, 127.91, 137.82, 138.81, 142.31, 142.47, 142.81, 143.04, 143.43, 143.92, 144.25, 144.39, 144.54, 144.59, 144.95, 145.97, 146.15, 146.67, 147.00, 147.03, 147.18, 147.72, 148.14, 148.23, 148.53, 148.54, 148.61, 148.62, 149.92, 150.56, 153.13, 155.67, 174.50 ($\underline{C}$OOH), 174.54 ($\underline{C}$OOH), 174.56 ($\underline{C}$OOH).

**A3b**. $^1$H NMR (500 MHz, $(CD_3)_2SO$, δ, ppm): 1.66 – 1.93 (m, 10H), 2.15 – 2.35 (m, 10H), 2.67 – 2.85 (m, 10H), 5.83 (s, 1H), 6.71 – 6.74 (m, 3H), 6.83 (d, 2H, *J* = 3.6 Hz), 6.95 (d, 1H, *J* = 3.2 Hz) 7.10 (d, 2H, *J* = 3.3 Hz), 7.36 (d, 2H, *J* = 3.4 Hz).

$^{13}$C NMR (126 MHz, $(CD_3)_2SO$, δ, ppm): 26.27 ($\underline{C}H_2$), 26.44 ($\underline{C}H_2$), 28.72($\underline{C}H_2$), 29.03 ($\underline{C}H_2$), 32.66 ($\underline{C}H_2$), 32.68 ($\underline{C}H_2$), 32.74 ($\underline{C}H_2$), 54.74 ($\underline{C}_{sp3\ fullerene\ cage}$), 54.96 ($\underline{C}_{sp3\ fullerene\ cage}$), 56.72 ($\underline{C}_{sp3\ fullerene\ cage}$), 61.88 ($\underline{C}_{sp3\ fullerene\ cage}$-H), 124.72, 126.69, 126.83, 128.75, 128.84, 131.47, 132.07, 139.37, 141.03, 142.51, 142.79, 142.94, 143.60, 143.74, 143.88, 143.99, 144.32, 144.89, 144.93, 145.07, 145.18, 145.26, 145.39, 146.47, 146.57, 146.98, 147.19, 147.51, 147.65, 147.82, 148.08, 148.12, 148.20, 148.54, 148.61, 148.66, 151.24, 174.10 ($\underline{C}$OOH).

**A5b**.$^{1}$H NMR (500 MHz, $(CD_3)_2SO$, δ, ppm): 2.41 – 2.68 (m, 18H), 2.77 – 3.13 (m, 18H), 5.55 (s, 1H), 6.48 (d, 1H, *J* = 3.5 Hz), 6.53 (d, 1H, *J* = 3.2 Hz), 6.55 – 6.73 (m, 12H), 6.76 (d, 1H, *J* = 3.5 Hz), 6.86 (d, 1H, *J* = 3.5 Hz), 6.90 (d, 1H, *J* = 3.3 Hz), 7.21 (d, 1H, *J* = 3.5 Hz).

$^{13}$C NMR (126 MHz, $(CD_3)_2SO$, δ, ppm): 25.26 ($\underline{C}H_2$), 25.30 ($\underline{C}H_2$), 25.46 ($\underline{C}H_2$), 35.83 ($\underline{C}H_2$), 35.85 ($\underline{C}H_2$), 35.90 ($\underline{C}H_2$), 35.95 ($\underline{C}H_2$), 56.49 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.16 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.39 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.44 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.64 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.89 ($\underline{C}_{sp3\ fullerene\ cage}$), 58.04 ($\underline{C}_{sp3\ fullerene\ cage}$), 58.26 ($\underline{C}_{sp3\ fullerene\ cage}$), 124.79, 124.97, 125.14, 125.19, 125.64, 126.22, 126.37, 126.54, 126.58, 126.63, 127.02, 127.12, 128.67, 129.37, 132.56, 132.72, 133.66, 134.58, 135.10, 135.92, 135.99, 136.09, 136.48, 140.27, 140.29, 140.35, 140.41, 140.48, 140.74, 141.18, 141.34, 142.28, 142.79, 143.97, 144.17, 144.27, 144.33, 144.40, 144.53, 144.72, 145.15, 146.76, 146.86, 146.93, 147.01, 147.18, 147.25, 148.11, 148.33, 148.43, 148.78, 148.79, 148.94, 149.00, 149.11, 149.42, 149.51, 150.14, 151.10, 151.21, 151.36, 152.11, 152.23, 152.32, 153.08, 153.57, 153.67, 153.75, 154.04, 154.24, 154.59, 154.96, 155.28, 155.69, 155.77, 156.71, 173.71 ($\underline{C}$OOH), 173.74 ($\underline{C}$OOH), 173.79 ($\underline{C}$OOH), 173.84 ($\underline{C}$OOH).

**A6b**.$^{1}$H NMR (500 MHz, $(CD_3)_2SO$, δ, ppm): 1.61 – 1.91 (m, 18H), 2.12 – 2.34 (m, 18H), 2.59 – 2.91 (m, 18H), 5.58 (s, 1H), 6.48 (d, 1H, *J* = 3.2 Hz), 6.50 – 6.51 (m, 7H), 6.63 (d, 1H, *J* = 3.1 Hz), 6.73 – 6.81 (m, 6H), 6.86 (d, 1H, *J* = 3.4 Hz), 6.93 (d, 1H, *J* = 3.4 Hz), 7.22 (d, 1H, *J* = 3.3 Hz).

$^{13}$C NMR (126 MHz, $(CD_3)_2SO$, δ, ppm): 26.90 ($\underline{C}H_2$), 26.94 ($\underline{C}H_2$), 26.96 ($\underline{C}H_2$), 26.99 ($\underline{C}H_2$), 27.06 ($\underline{C}H_2$), 29.09 ($\underline{C}H_2$), 29.15 ($\underline{C}H_2$), 29.23 ($\underline{C}H_2$), 33.06 ($\underline{C}H_2$), 33.16 ($\underline{C}H_2$), 57.20 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.36 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.42 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.46 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.66 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.67 ($\underline{C}_{sp3\ fullerene\ cage}$), 57.92 ($\underline{C}_{sp3\ fullerene\ cage}$), 58.06 ($\underline{C}_{sp3\ fullerene\ cage}$), 58.17 ($\underline{C}_{sp3\ fullerene\ cage}$), 124.50, 124.77, 124.79, 125.02, 125.52, 126.30, 126.41, 126.69, 127.02, 127.09, 128.68, 129.37, 132.72, 132.90, 133.81, 134.76, 135.29, 136.00, 136.15, 136.41, 140.28, 140.31, 140.38, 140.45, 140.61, 141.25, 141.28, 141.32, 142.25, 142.80, 144.36, 144.60, 144.74, 144.87, 144.95, 145.06, 145.10, 145.15, 145.20, 145.53, 145.81, 146.90, 147.00, 147.10, 147.16, 147.39, 148.15, 148.33, 148.76, 148.80, 148.86, 148.90, 148.95, 149.04, 149.10, 149.45, 149.55, 149.97, 151.06, 151.10, 151.19, 151.21, 151.35, 152.09, 152.18, 152.27, 152.30, 152.33, 153.03, 153.07, 153.11, 153.69, 153.72, 153.77, 153.80, 154.12, 154.24, 154.44, 154.48, 154.82, 155.31, 155.61, 155.82, 156.67, 174.58 ($\underline{C}$OOH), 174.62 ($\underline{C}$OOH).

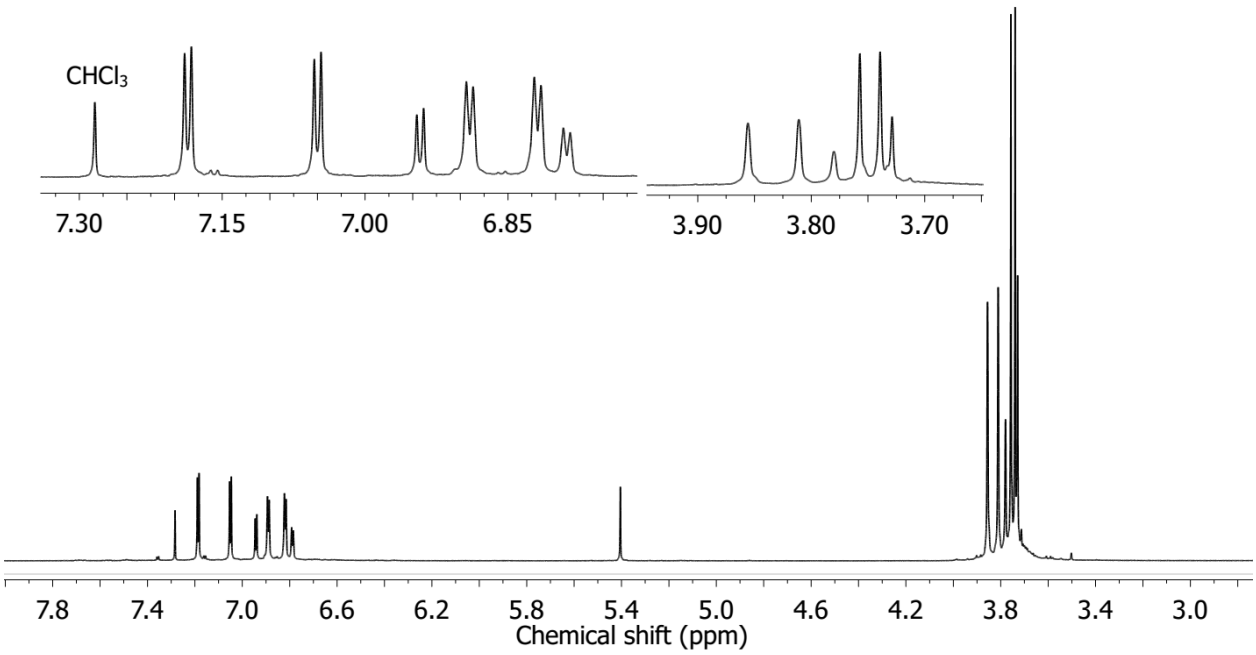


Figure S3. $^{1}$H NMR spectrum of compound **1b**

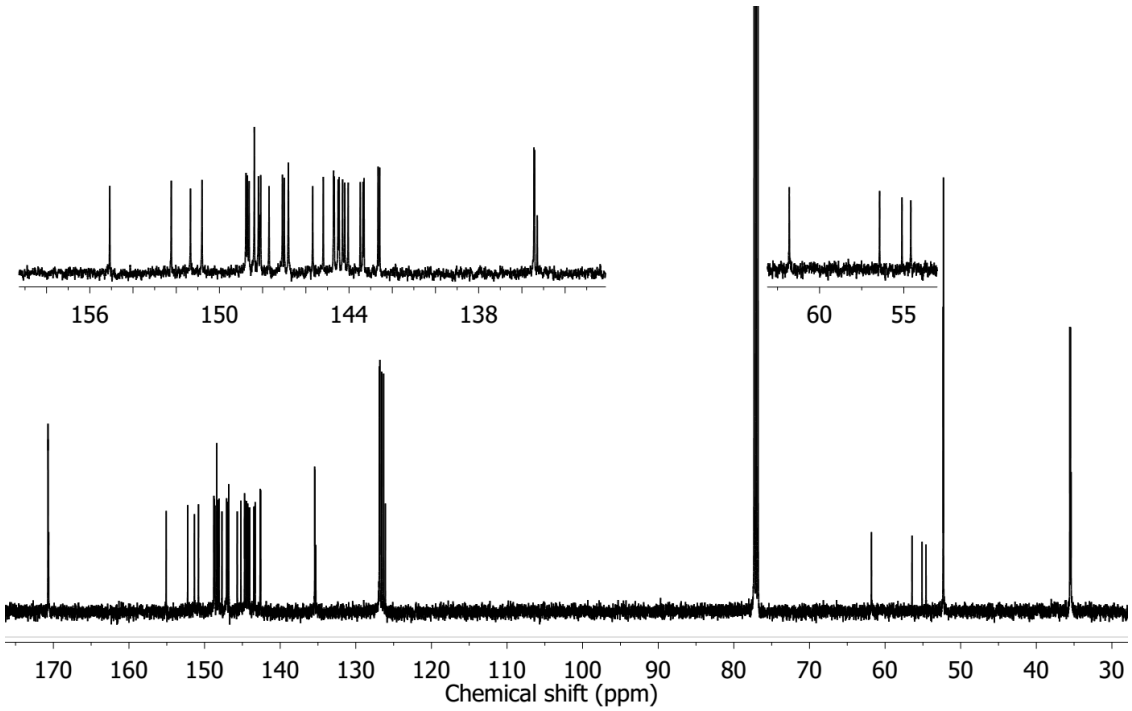


Figure S4. $^{13}$C NMR spectrum of compound **1b**

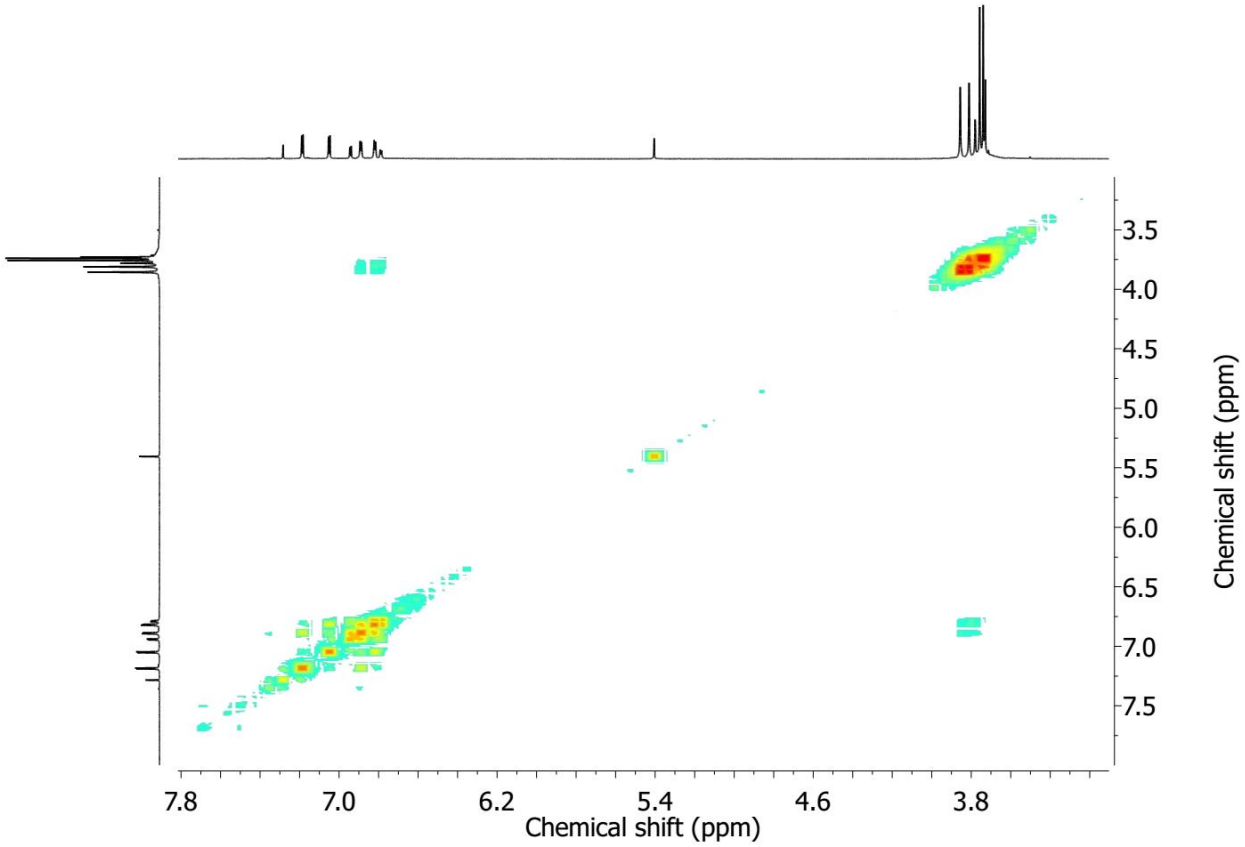


Figure S5. $^{1}$H-$^{1}$H COSY NMR spectrum of compound **1b**

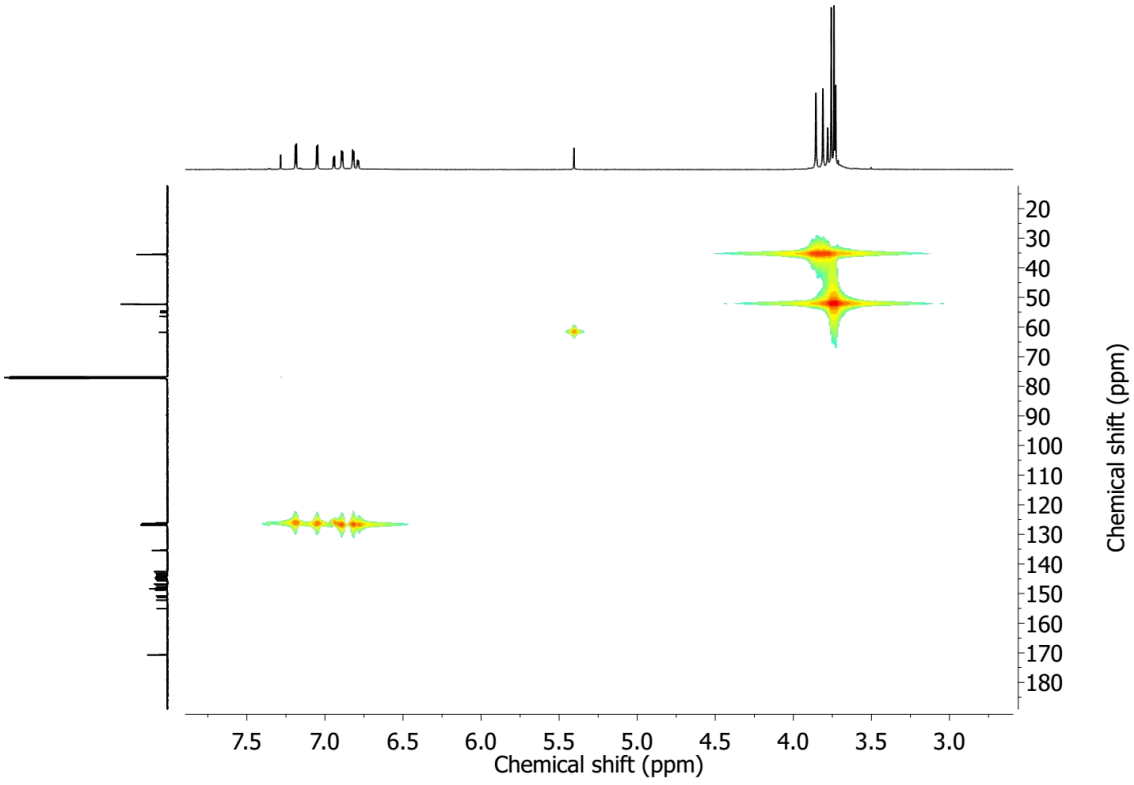


Figure S6. $^{1}$H-$^{13}$C HSQC NMR spectrum of compound **1b**

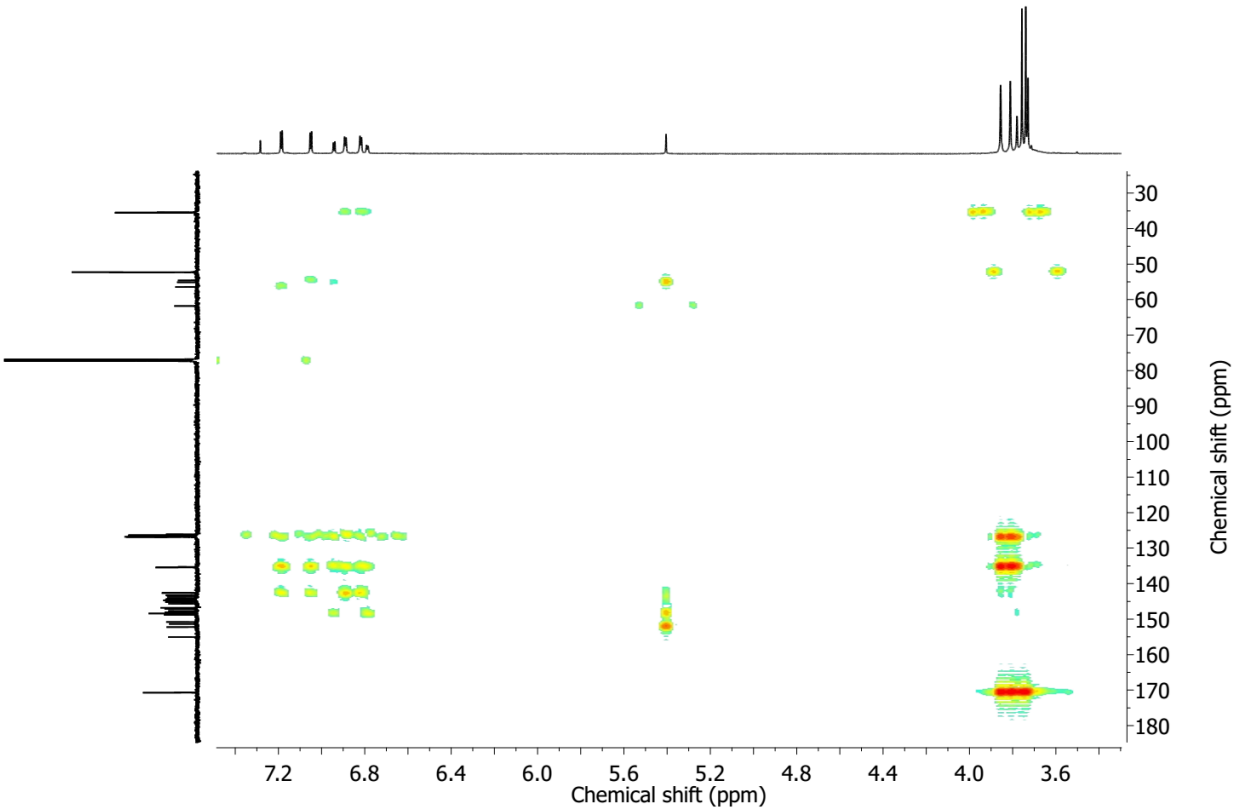


Figure S7. $^{1}H$-$^{13}C$ HMBC NMR spectrum of compound **1b**

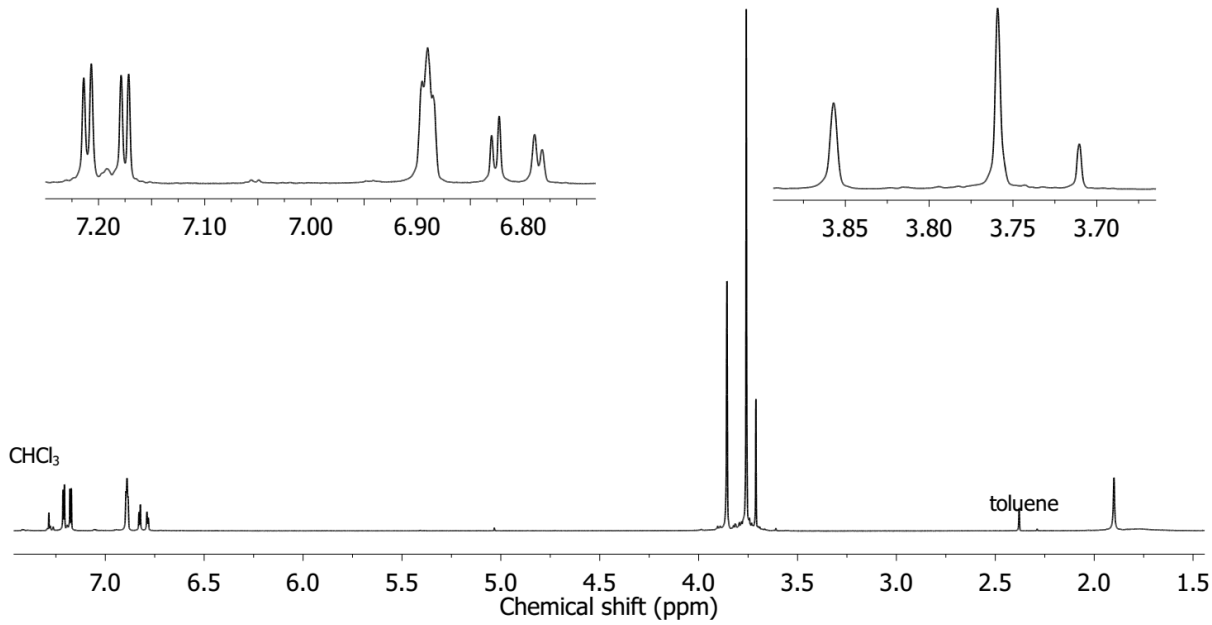


Figure S8. $^{1}H$ NMR spectrum of compound **1c**

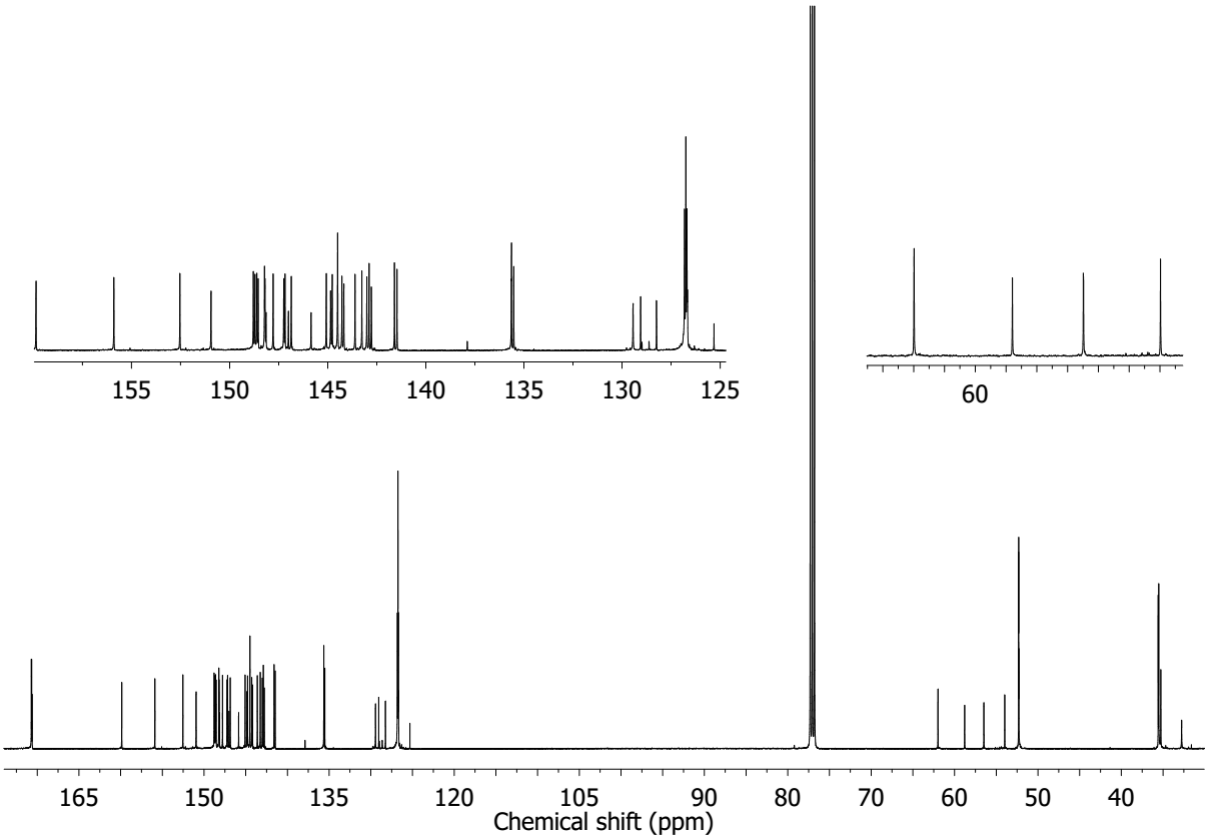


Figure S9. $^{13}$C NMR spectrum of compound **1c**

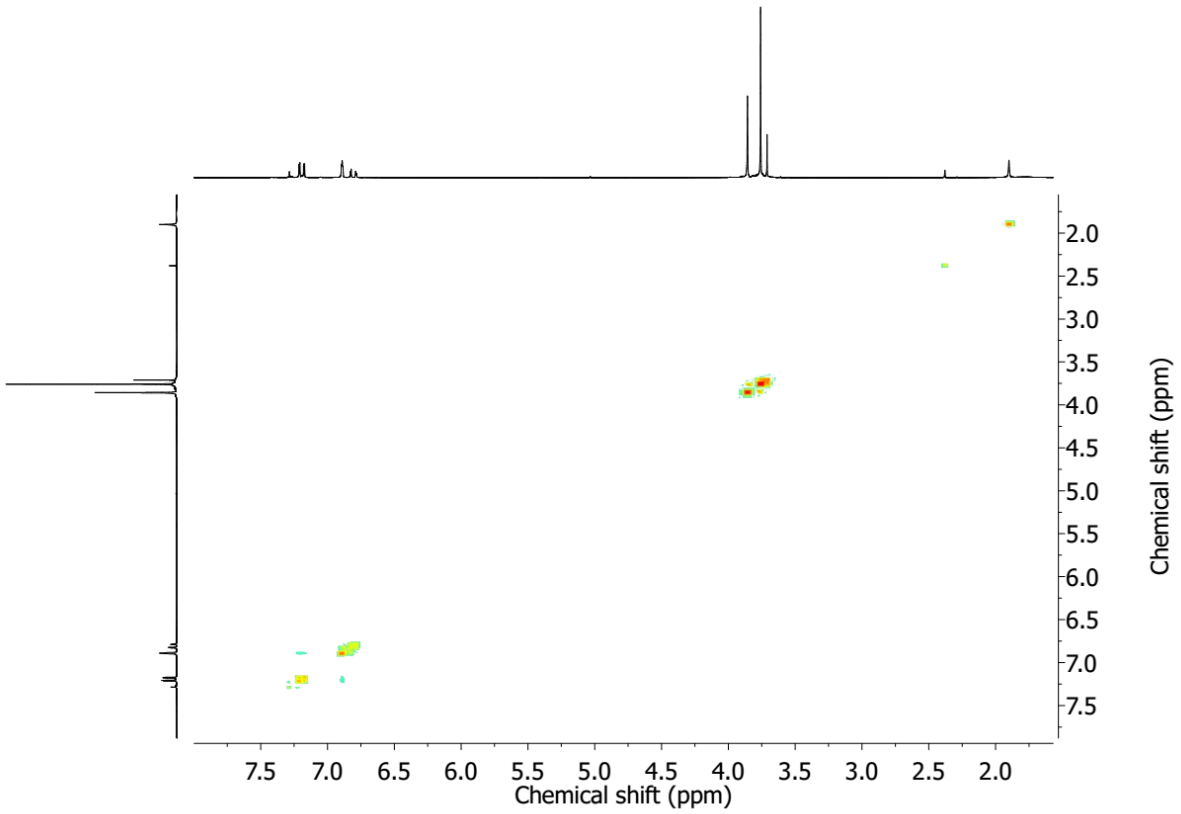


Figure S10. $^{1}$H-$^{1}$H COSY NMR spectrum of compound **1c**

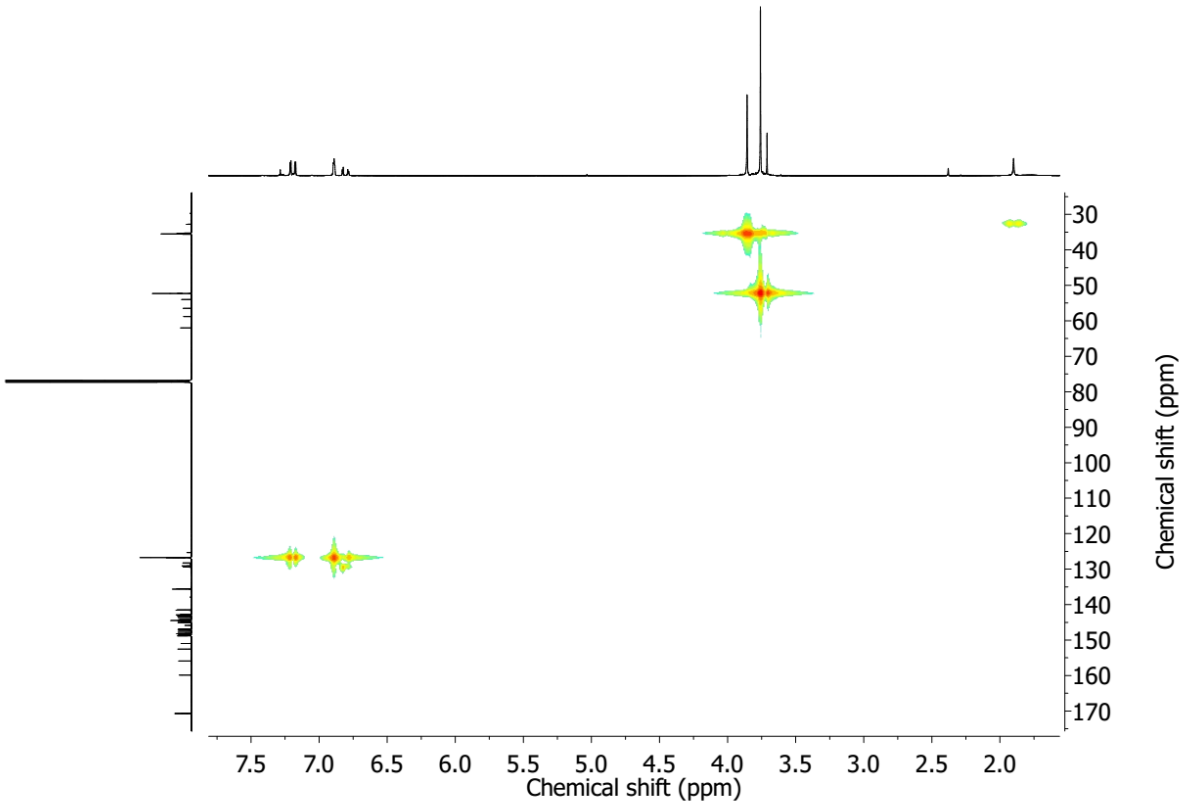


Figure S11. $^{1}$H-$^{13}$C HSQC NMR spectrum of compound **1c**

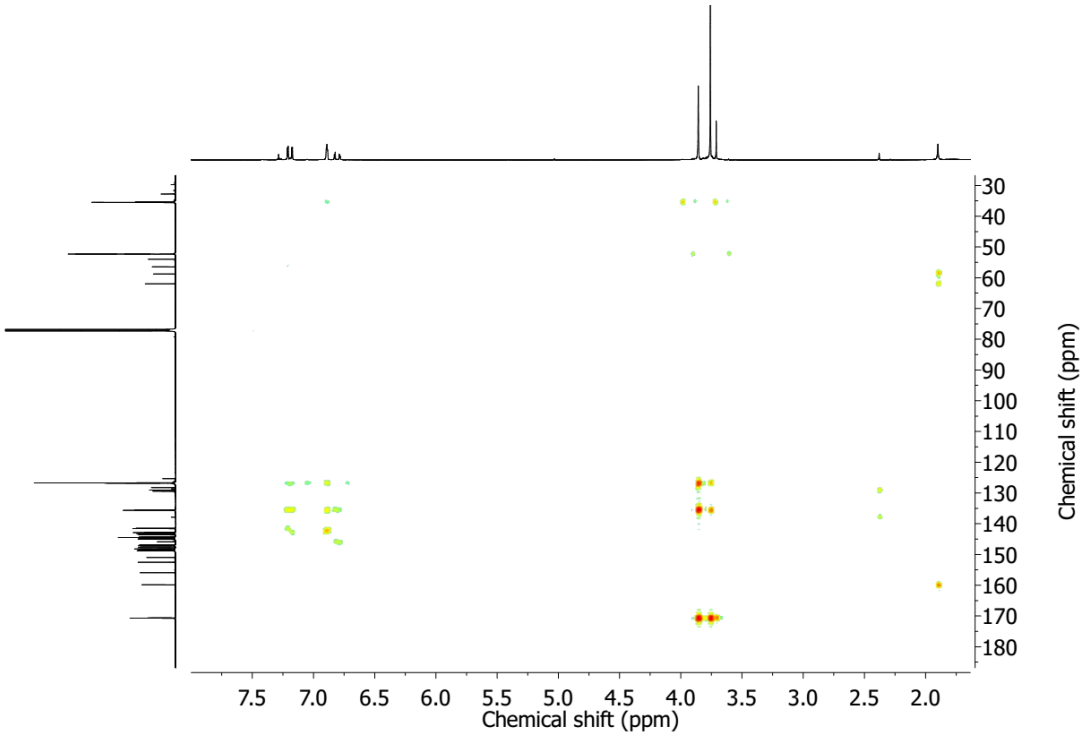


Figure S12. $^{1}$H-$^{13}$C HMBC NMR spectrum of compound **1c**

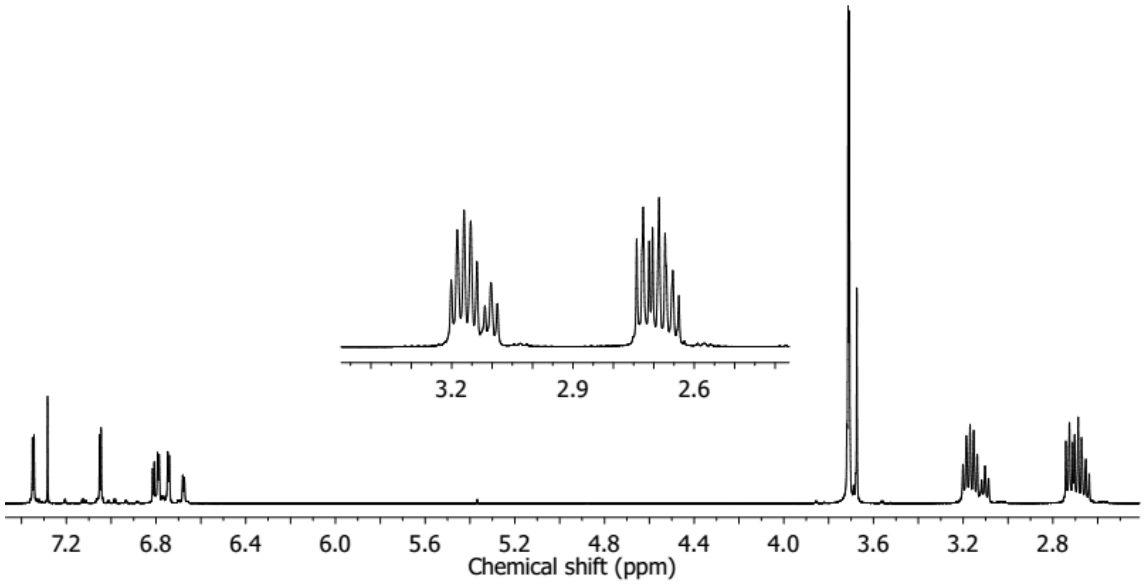


Figure S13. $^{1}$H NMR spectrum of compound **2a**

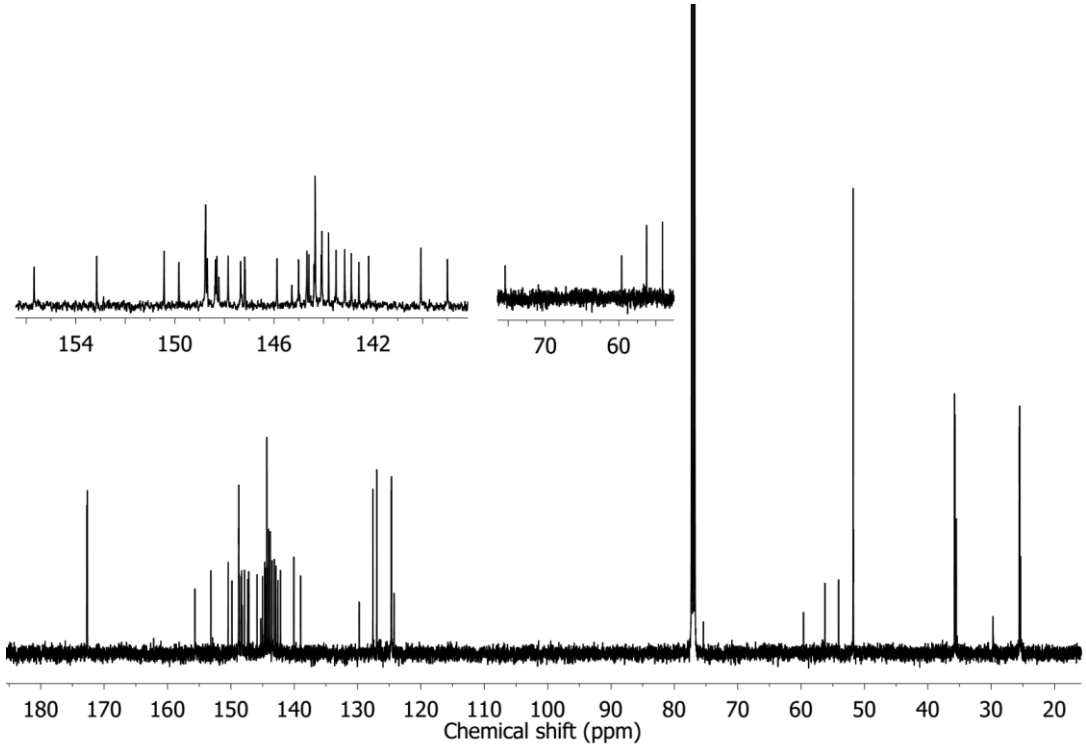


Figure S14. $^{13}$C NMR spectrum of compound **2a**

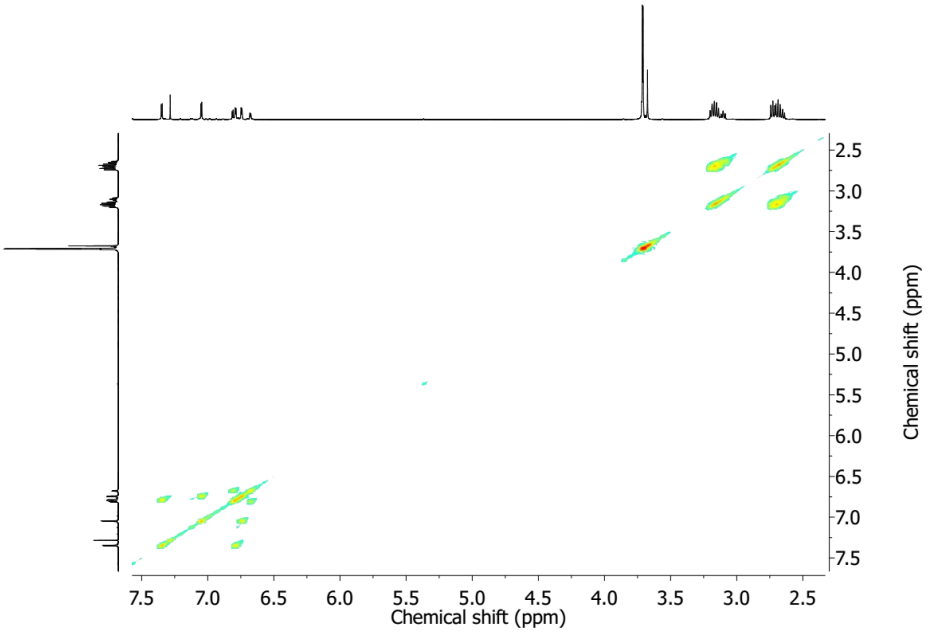


Figure S15. $^{1}$H-$^{1}$H COSY NMR spectrum of compound **2a**

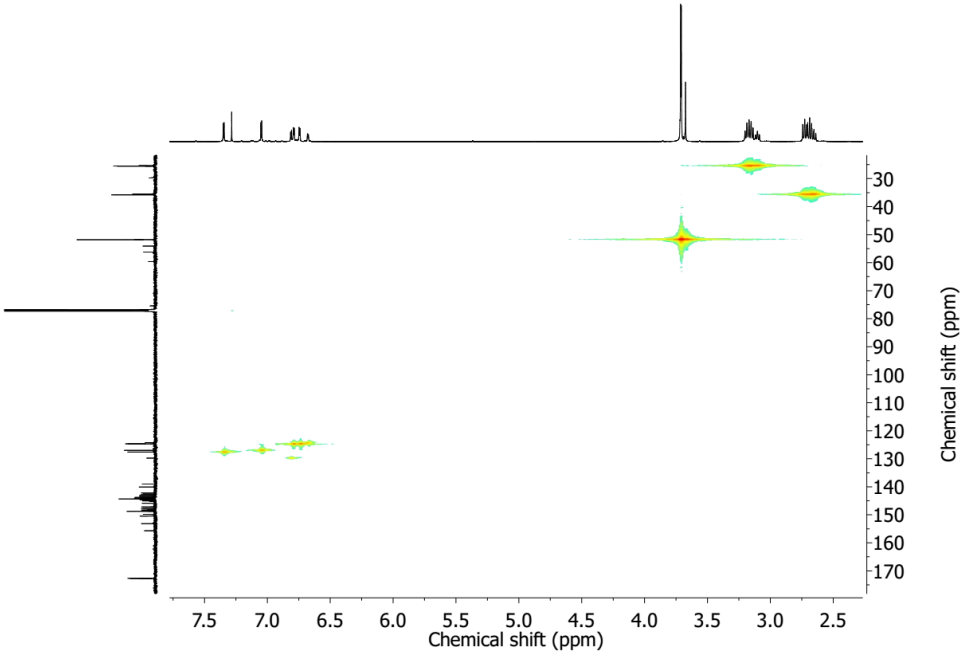


Figure S16. $^{1}$H-$^{13}$C HSQC NMR spectrum of compound **2a**

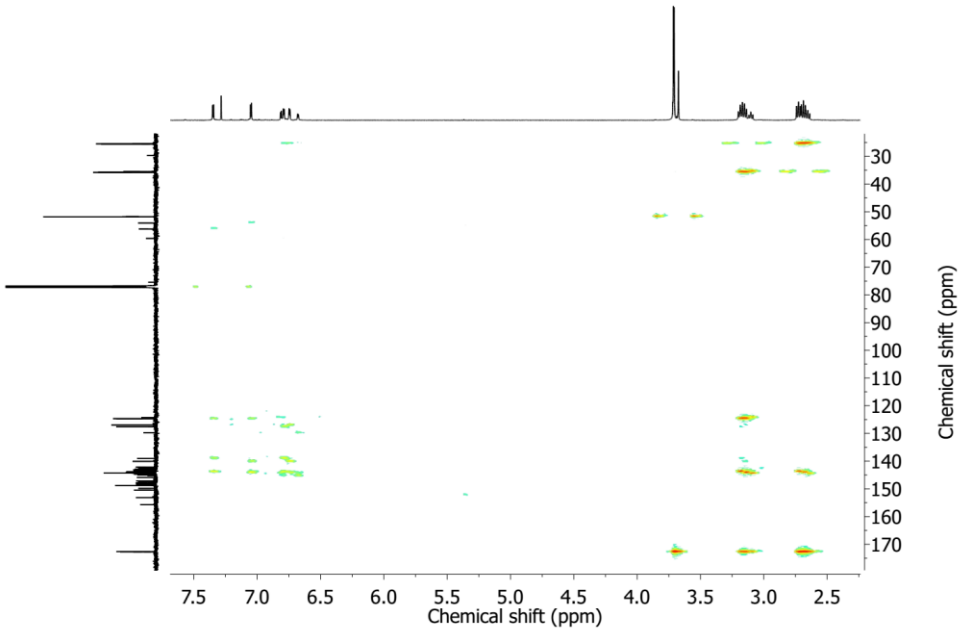


Figure S17. $^{1}H$-$^{13}C$ HMBC NMR spectrum of compound **2a**

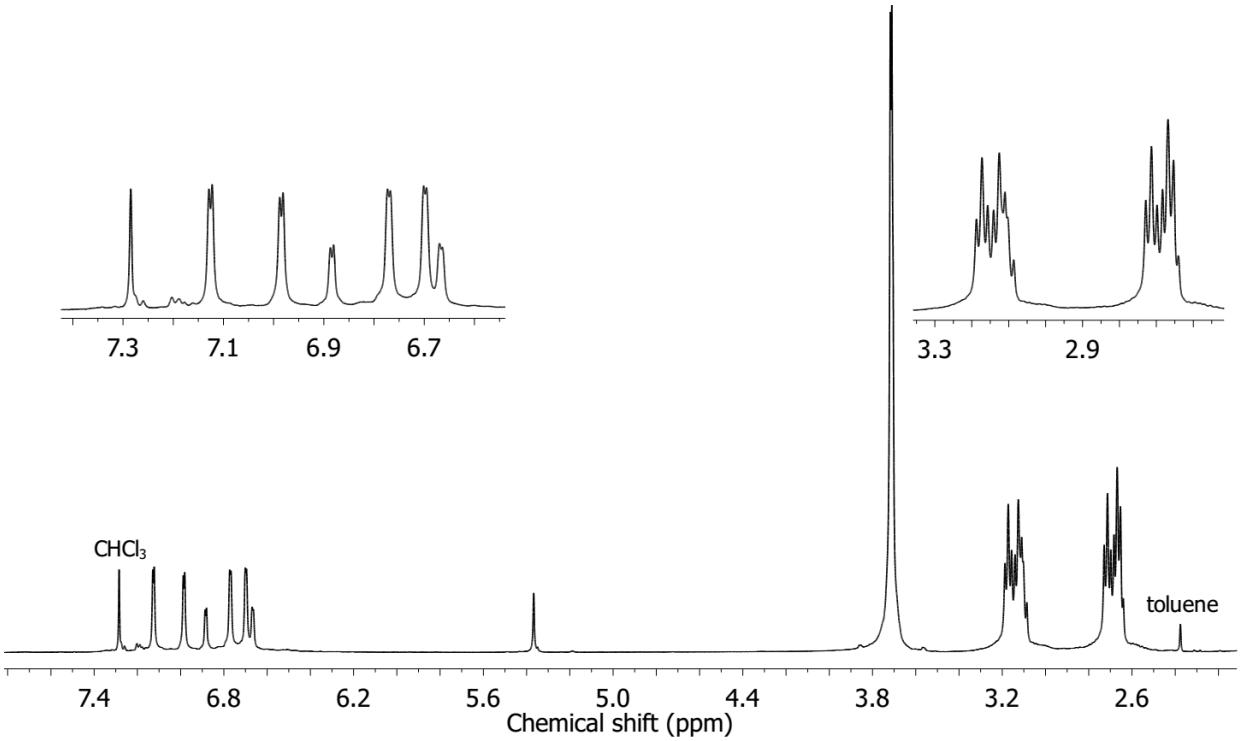


Figure S18. $^{1}H$ NMR spectrum of compound **2b**

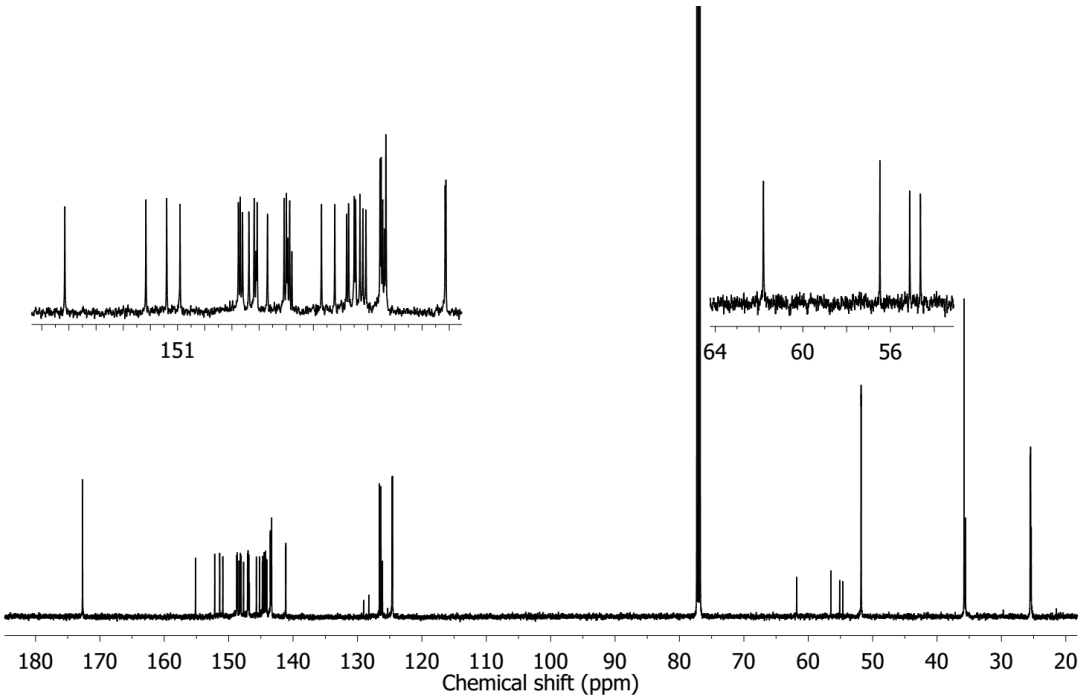


Figure S19. $^{1}$H NMR spectrum of compound **2b**

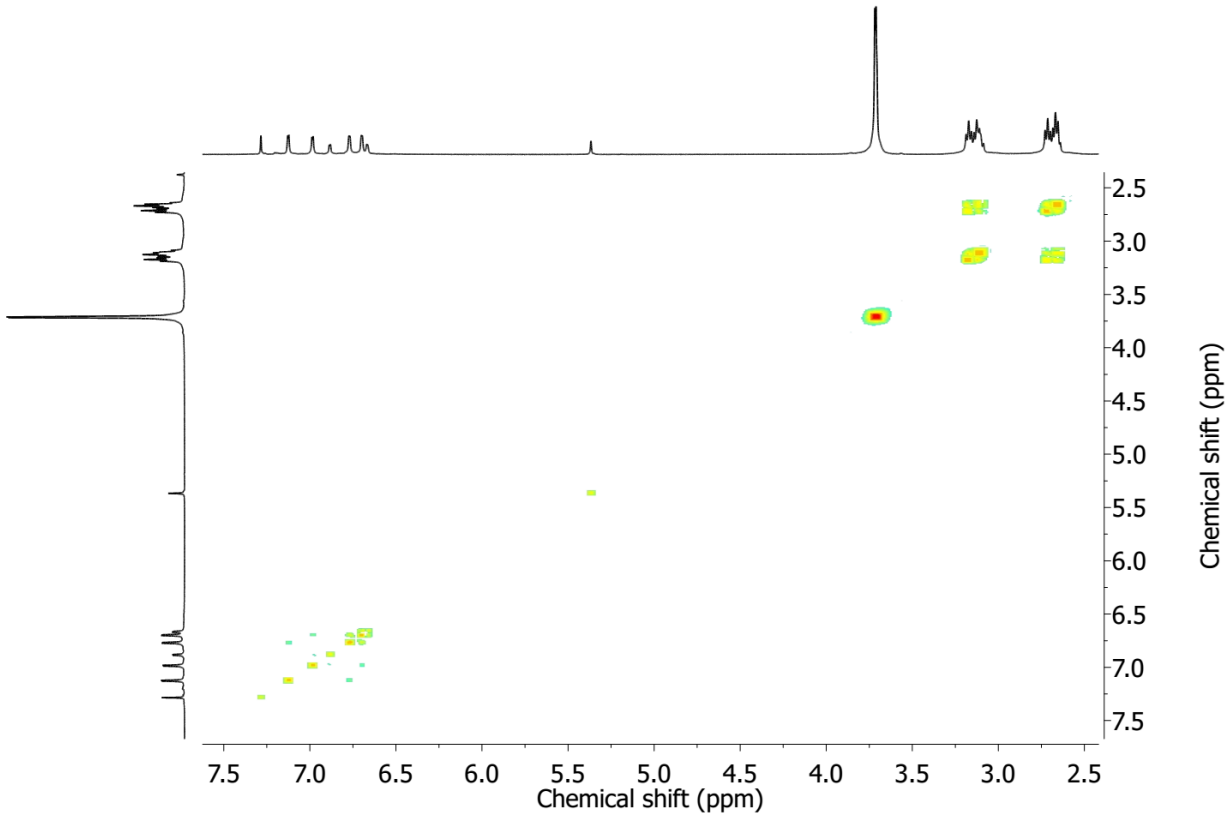


Figure S20. $^{1}$H-$^{1}$H COSY NMR spectrum of compound **2b**

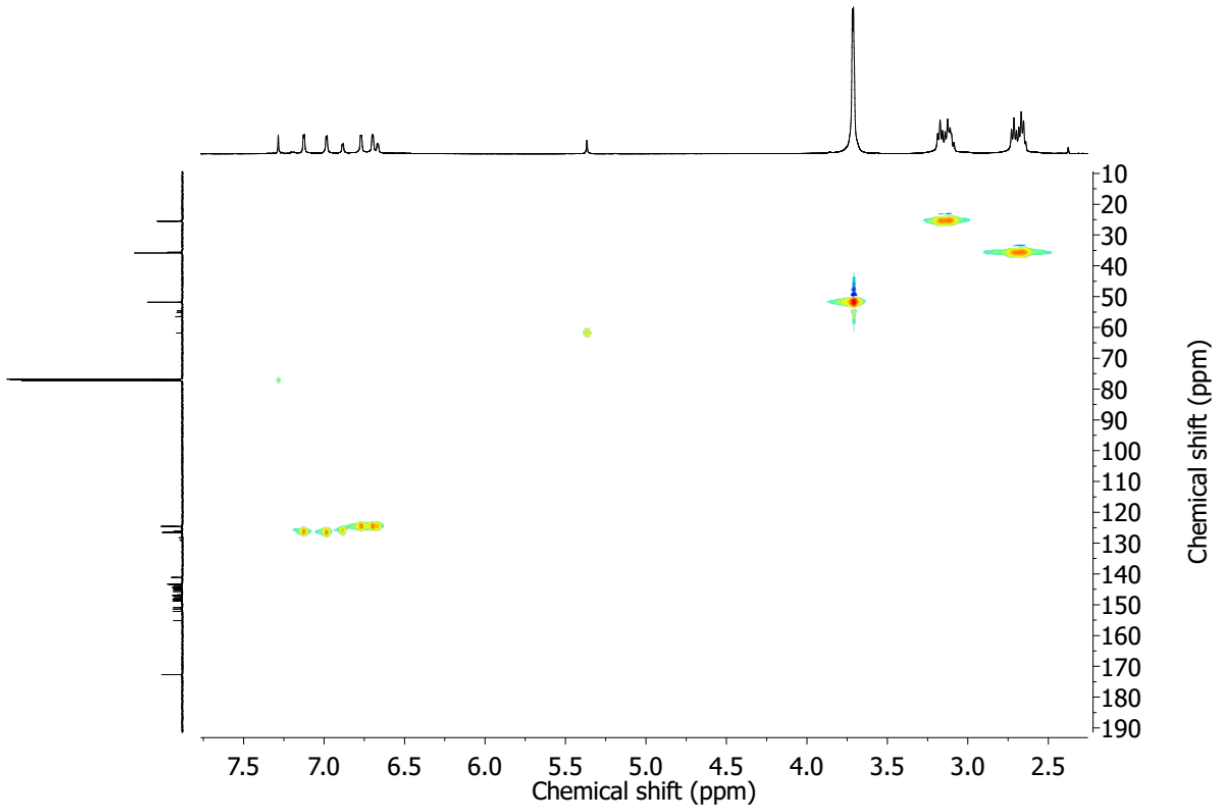


Figure S21. $^{1}$H-$^{13}$C HSQC NMR spectrum of compound **2b**

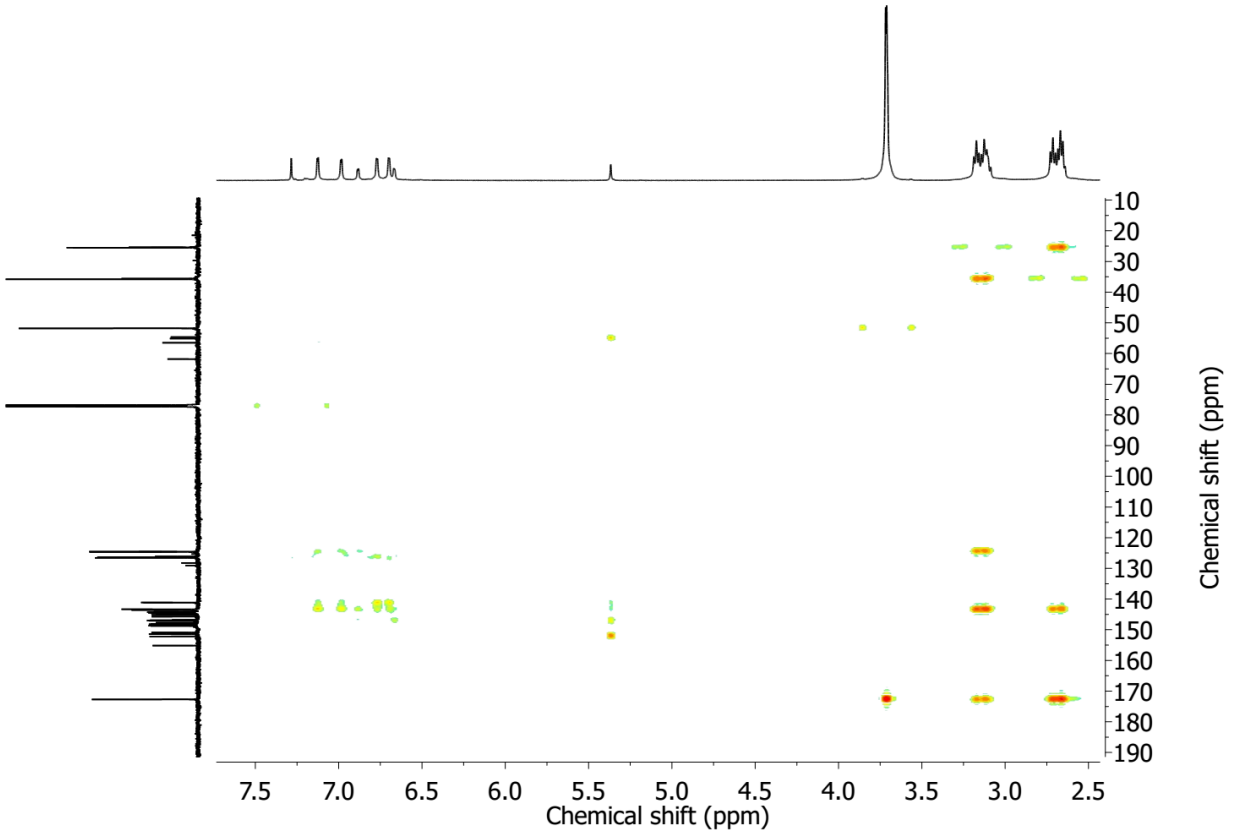


Figure S22. $^{1}$H-$^{13}$C HMBC NMR spectrum of compound **2b**

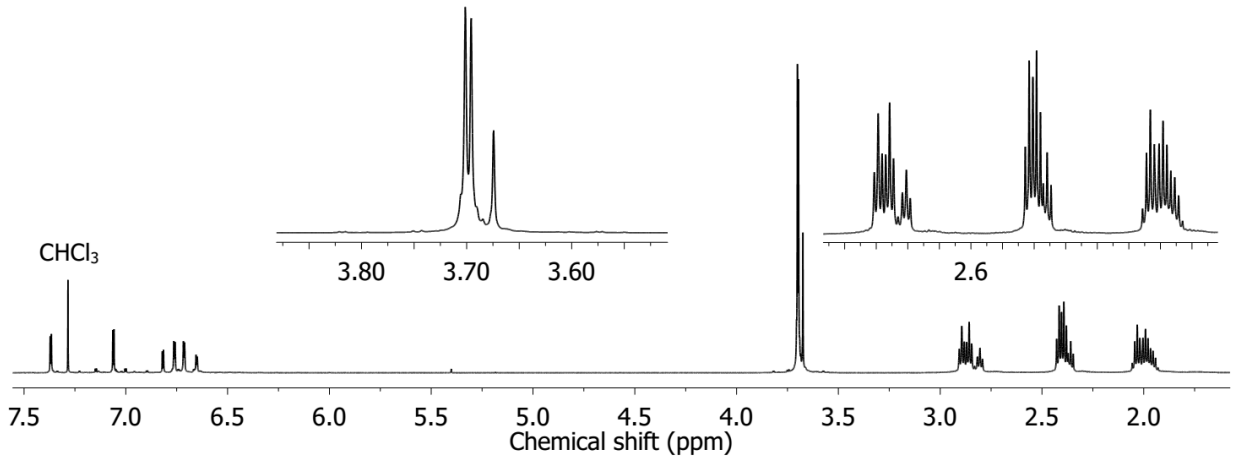


Figure S23. $^{1}$H NMR spectrum of compound **3a**

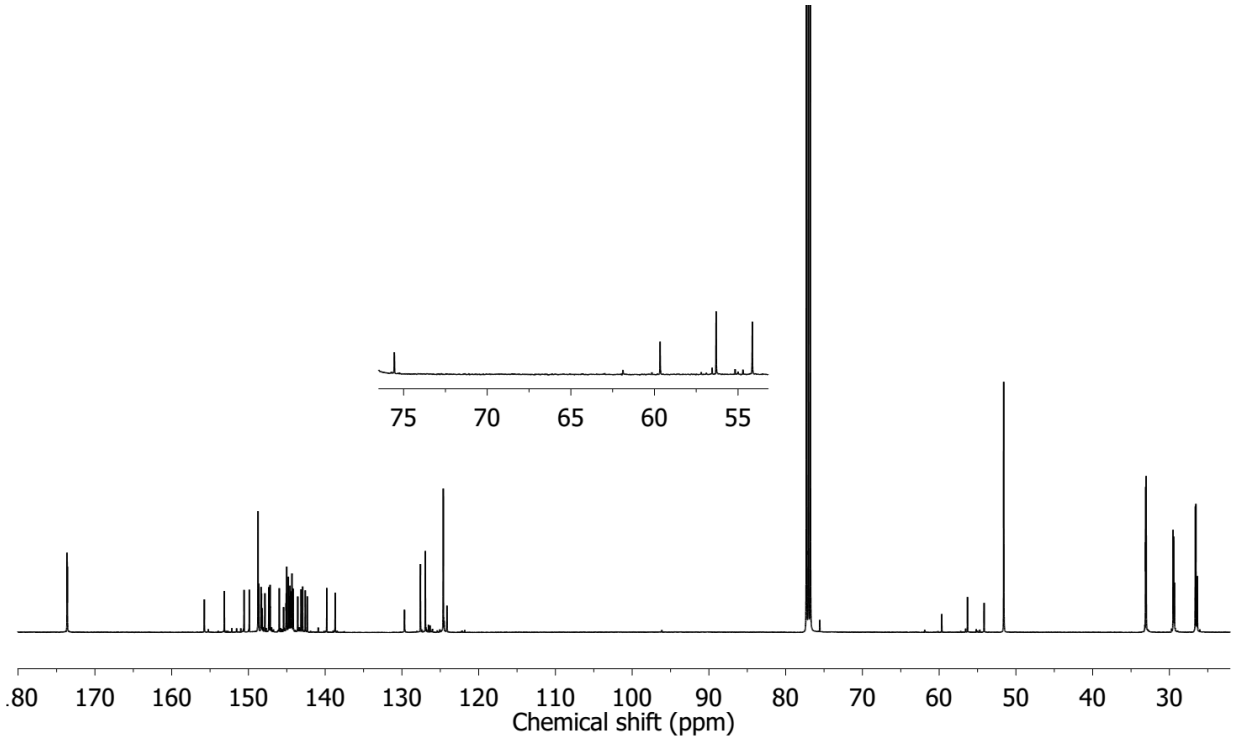


Figure S24. $^{13}$C NMR spectrum of compound **3a**

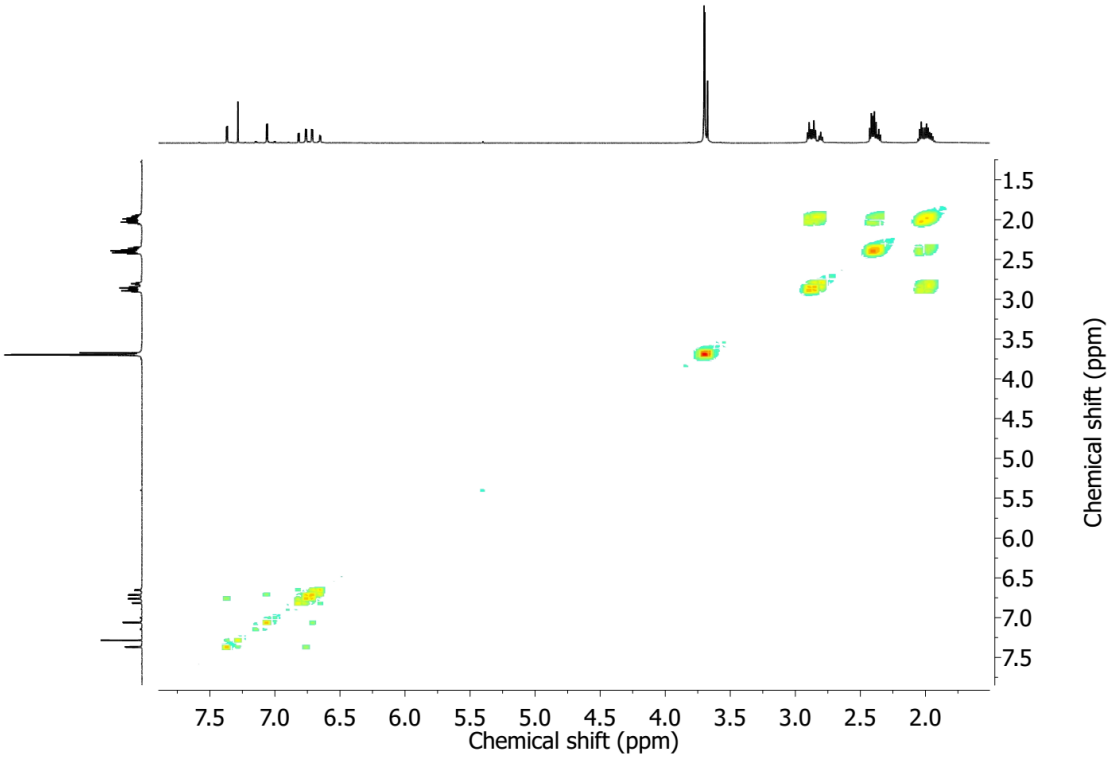


Figure S25. $^{1}$H-$^{1}$H COSY NMR spectrum of compound **3a**

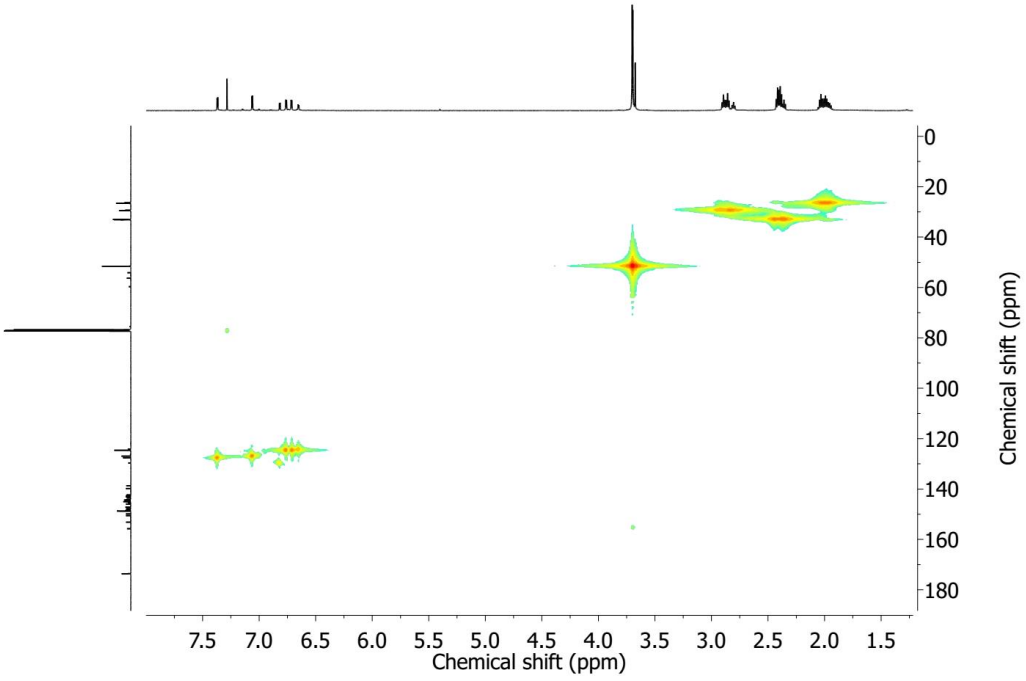


Figure S26. $^{1}$H-$^{13}$C HSQC NMR spectrum of compound **3a**

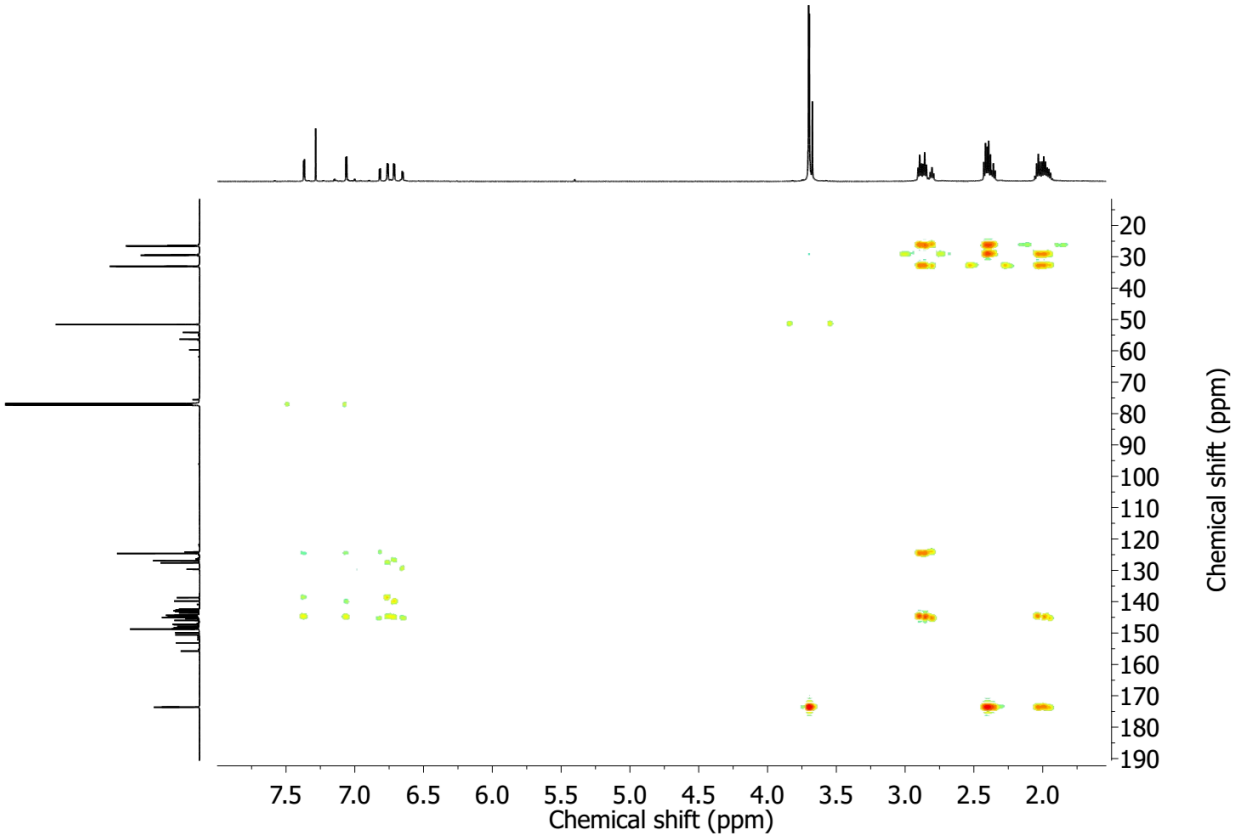


Figure S27. $^{1}H$-$^{13}C$ HMBC NMR spectrum of compound **3a**

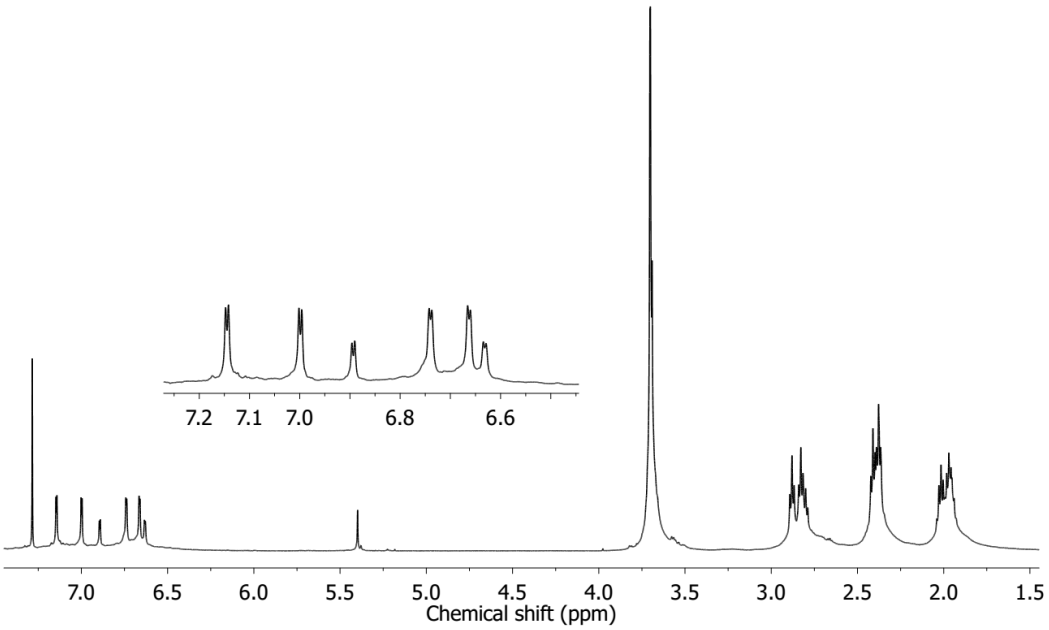


Figure S28. $^{1}H$ NMR spectrum of compound **3b**

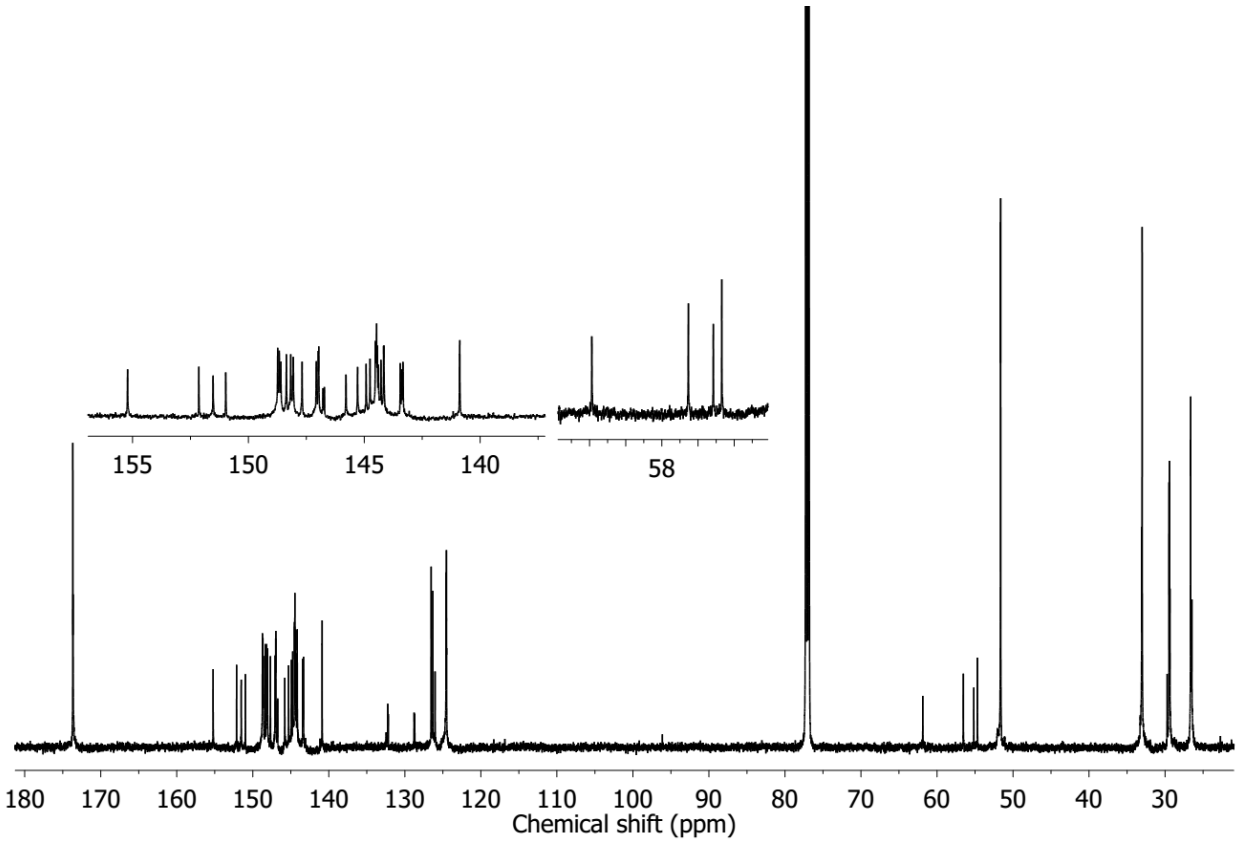


Figure S29. $^{13}$C NMR spectrum of compound **3b**

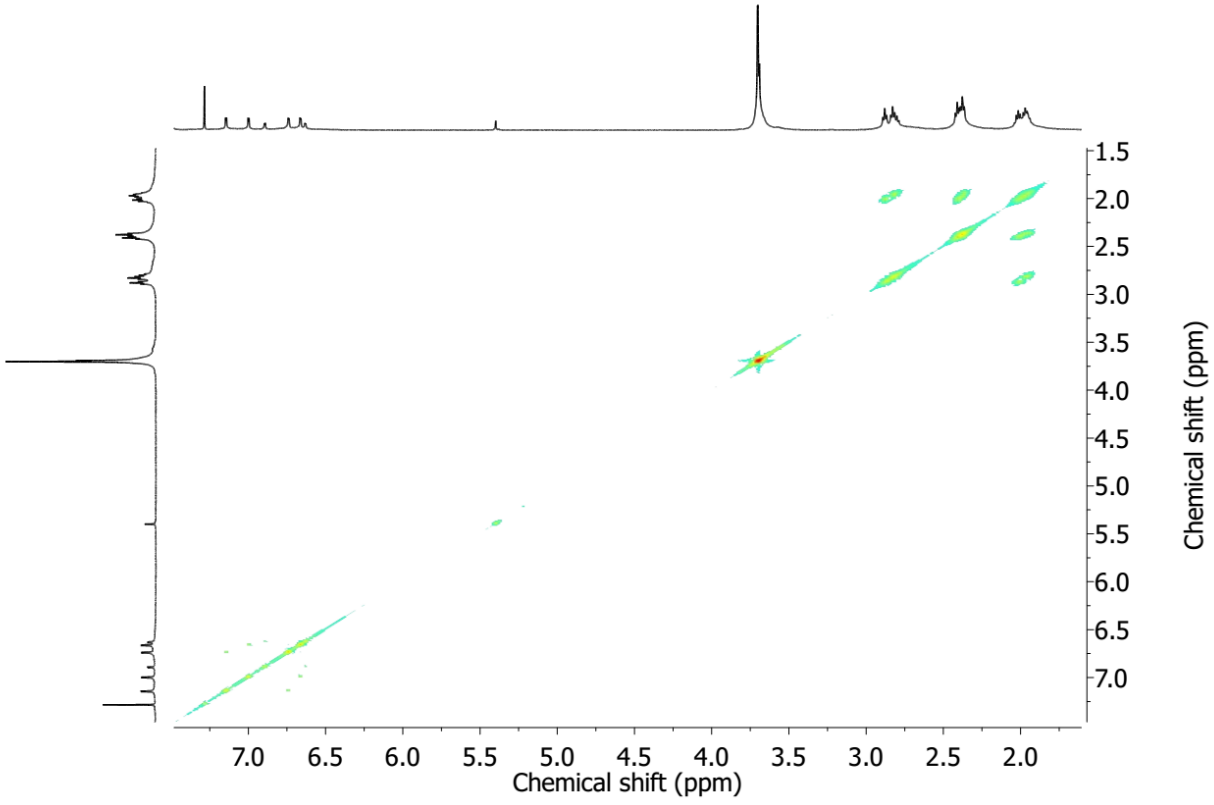


Figure S30. $^{1}$H-$^{1}$H COSY NMR spectrum of compound **3b**

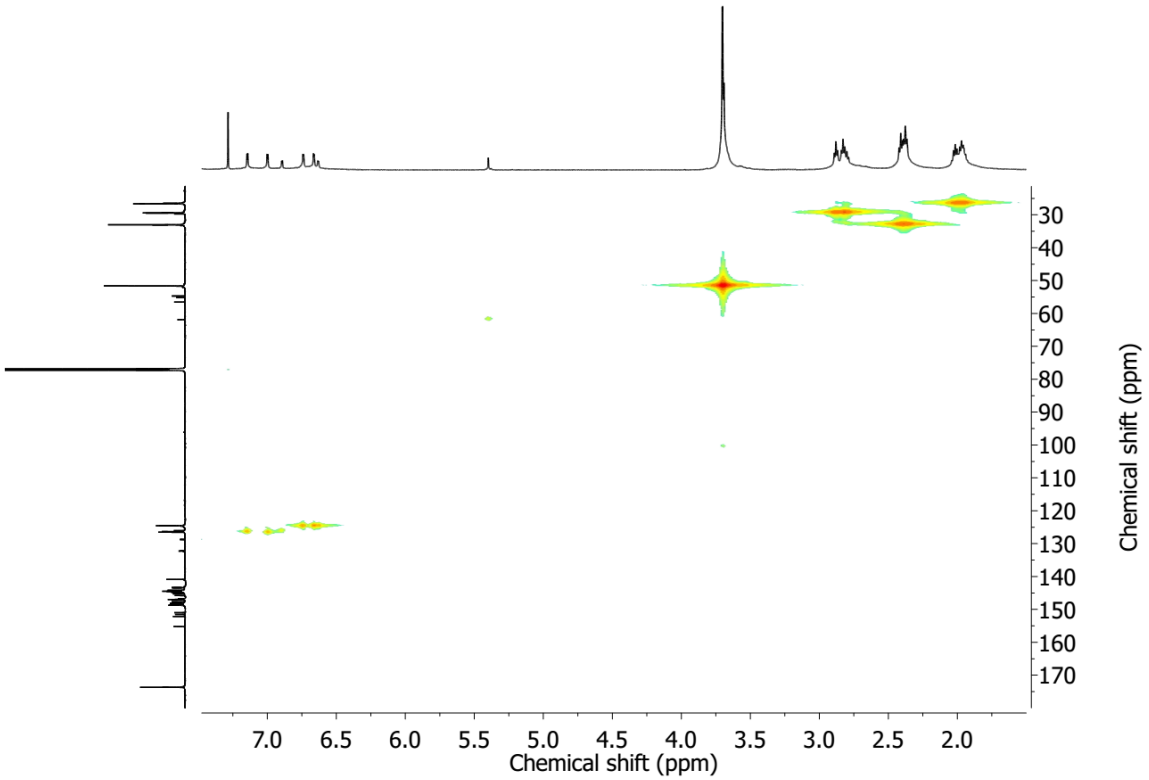


Figure S31. $^{1}$H-$^{13}$C HSQC NMR spectrum of compound **3b**

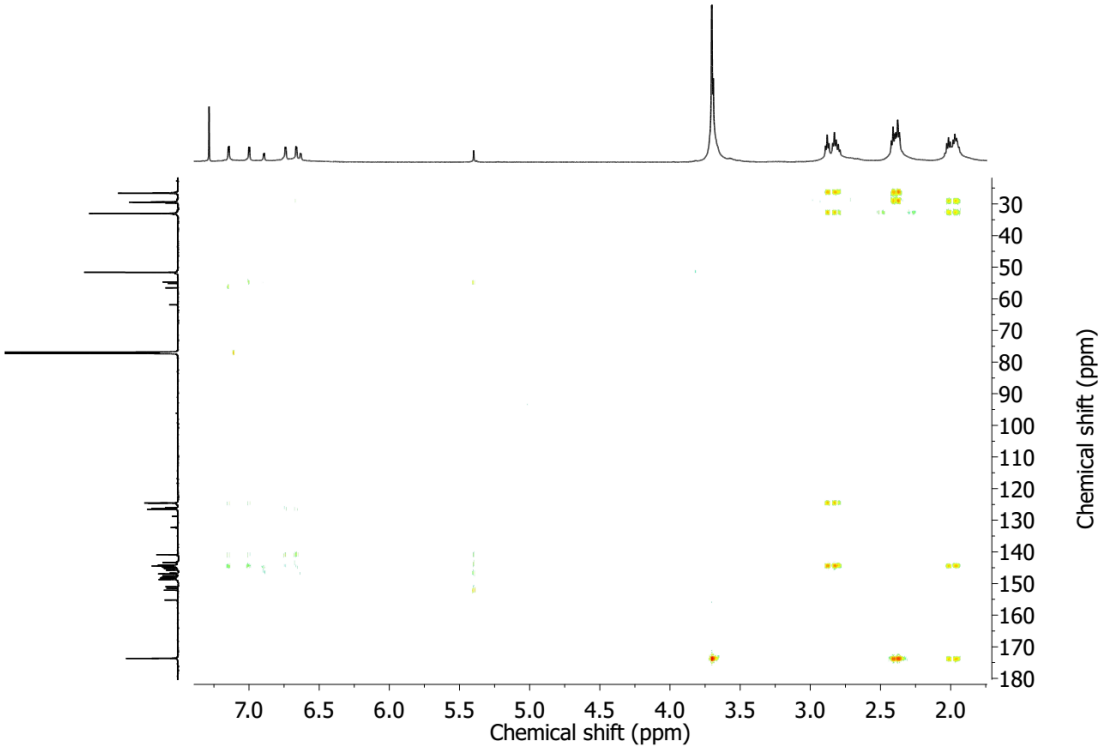


Figure S32. $^{1}$H-$^{13}$C HMBC NMR spectrum of compound **3b**

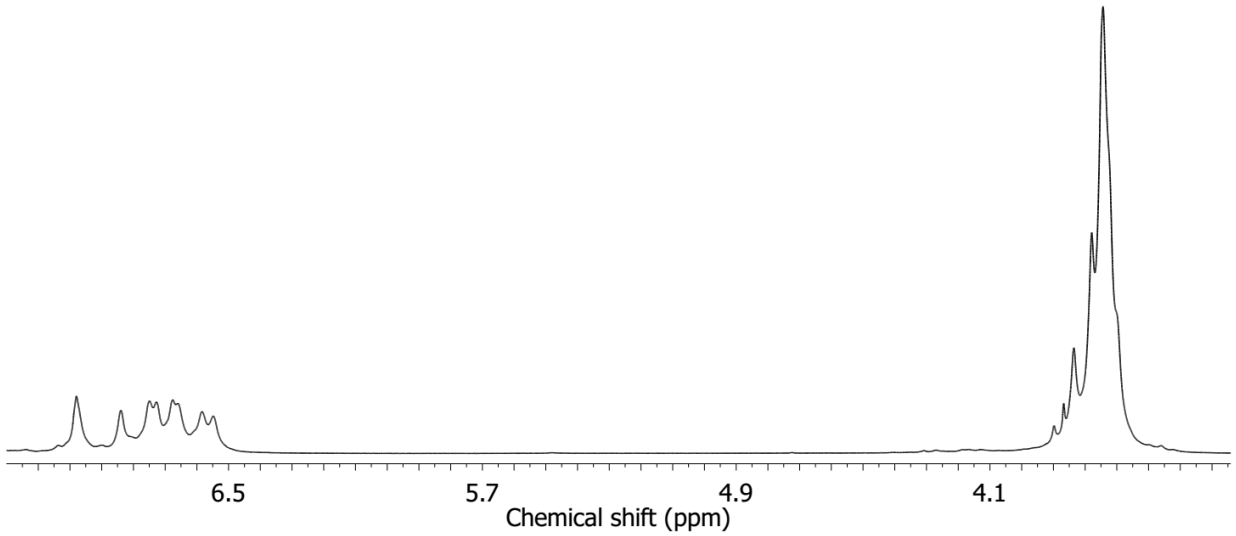


Figure S33. $^{1}$H NMR spectrum of compound **4a**

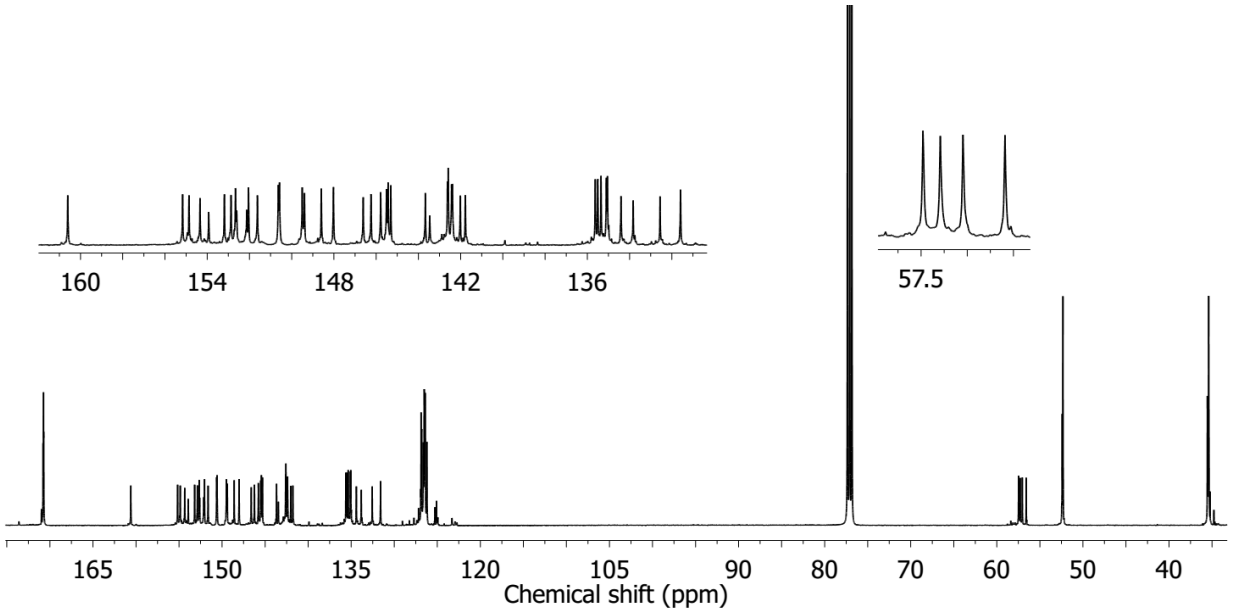


Figure S34. $^{13}$C NMR spectrum of compound **4a**

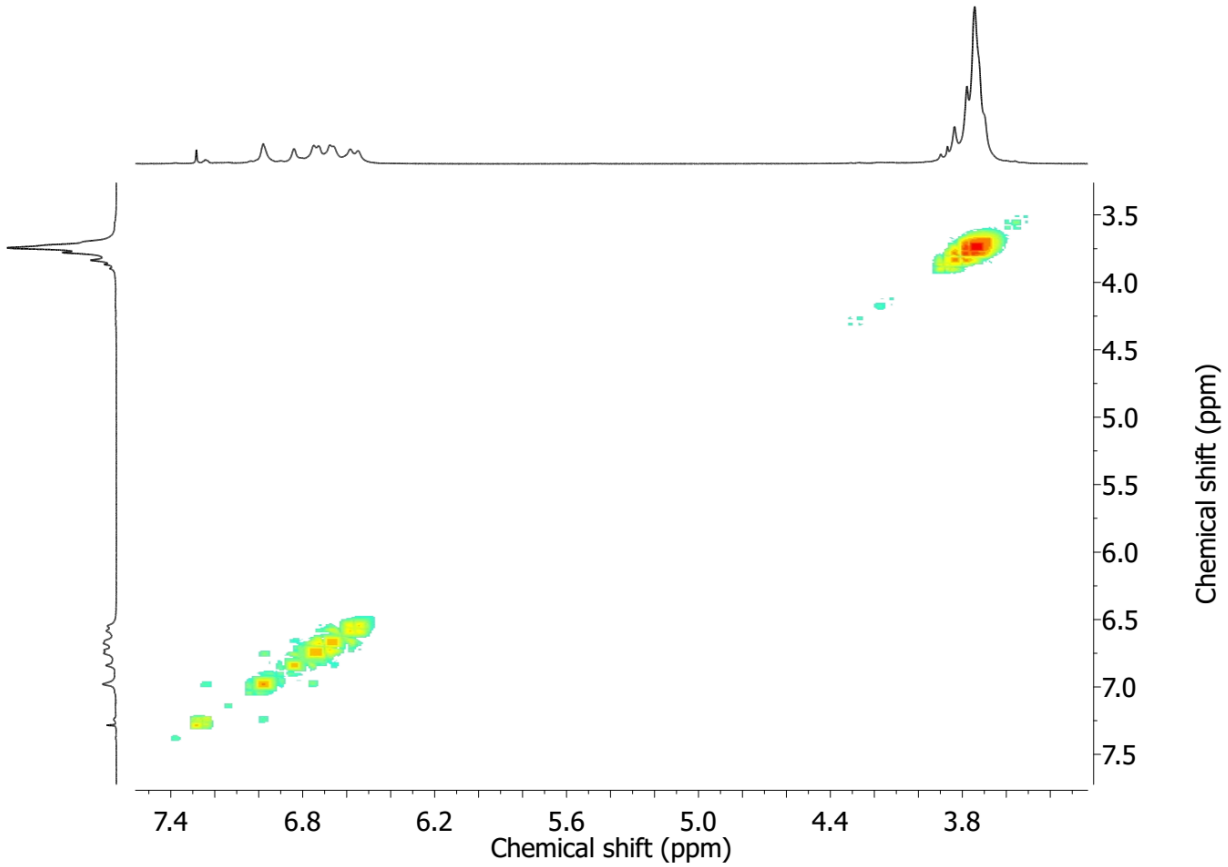


Figure S35. $^{1}$H-$^{1}$H COSY NMR spectrum of compound **4a**

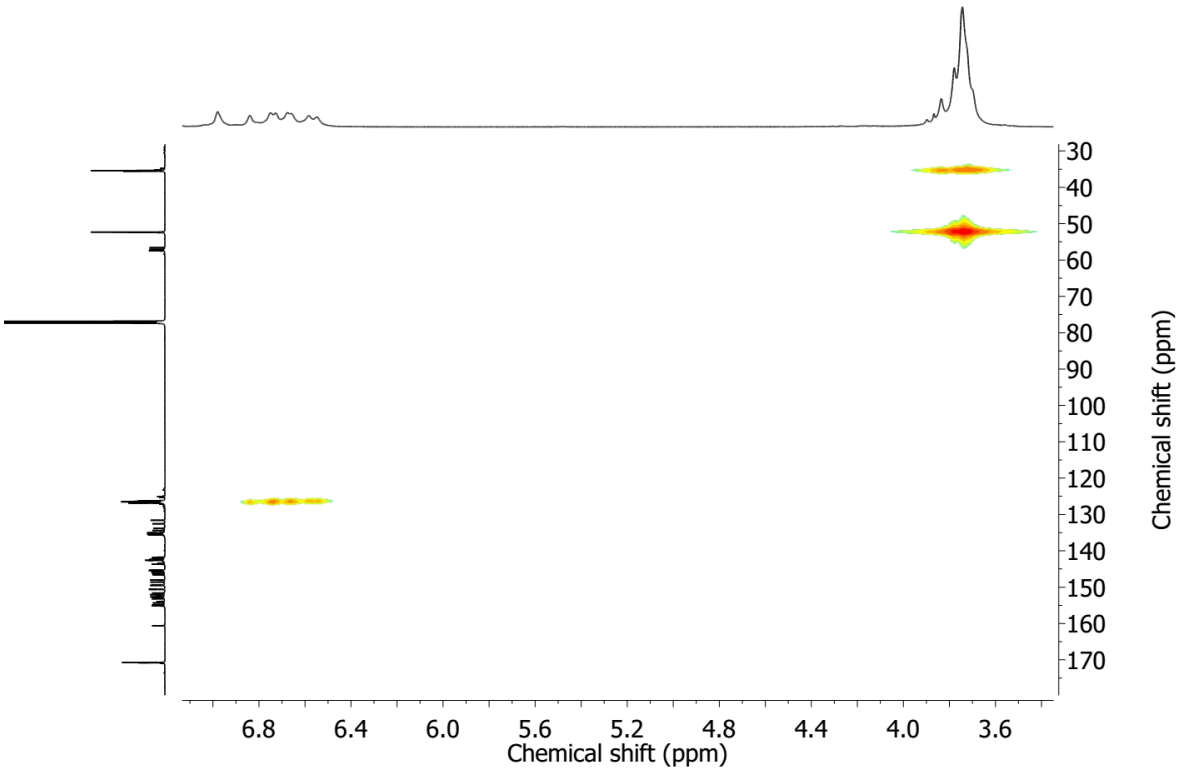


Figure S36. $^{1}$H-$^{13}$C HSQC NMR spectrum of compound **4a**

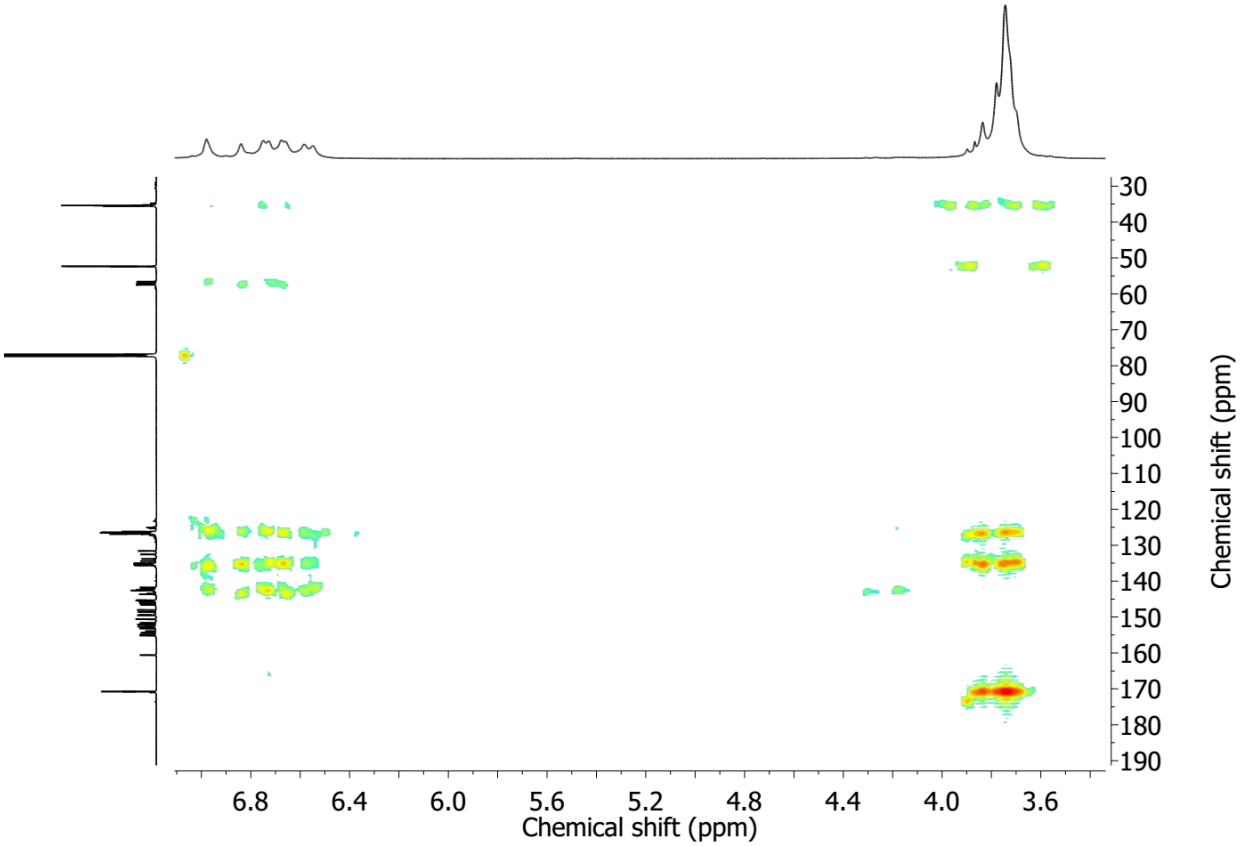


Figure S37. $^{1}H$-$^{13}C$ HMBC NMR spectrum of compound **4a**

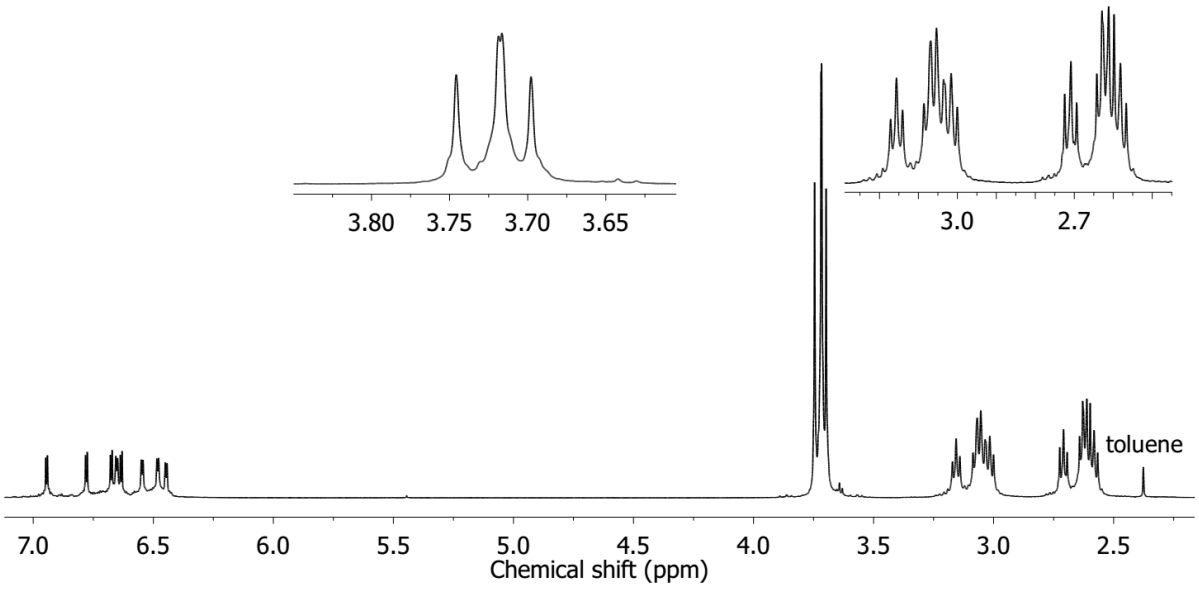


Figure S38. $^{1}H$ NMR spectrum of compound **5a**

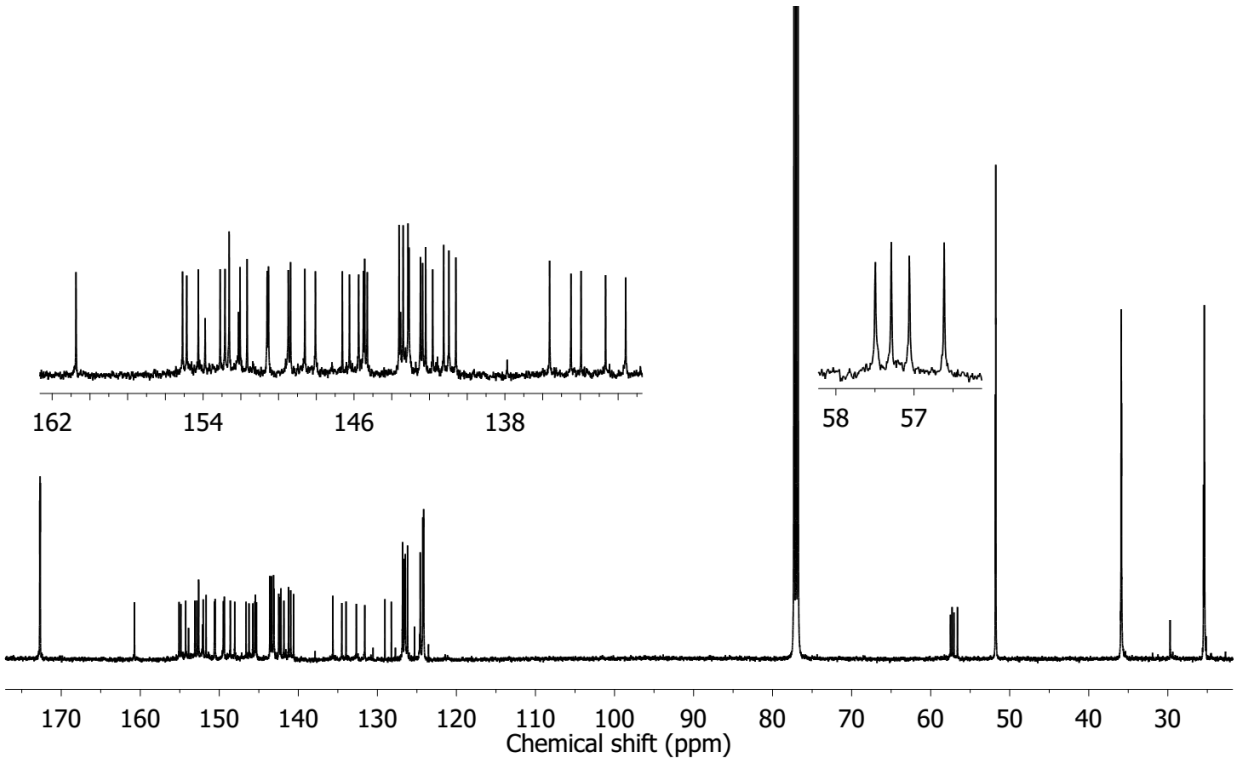


Figure S39. $^{13}$C NMR spectrum of compound **5a**

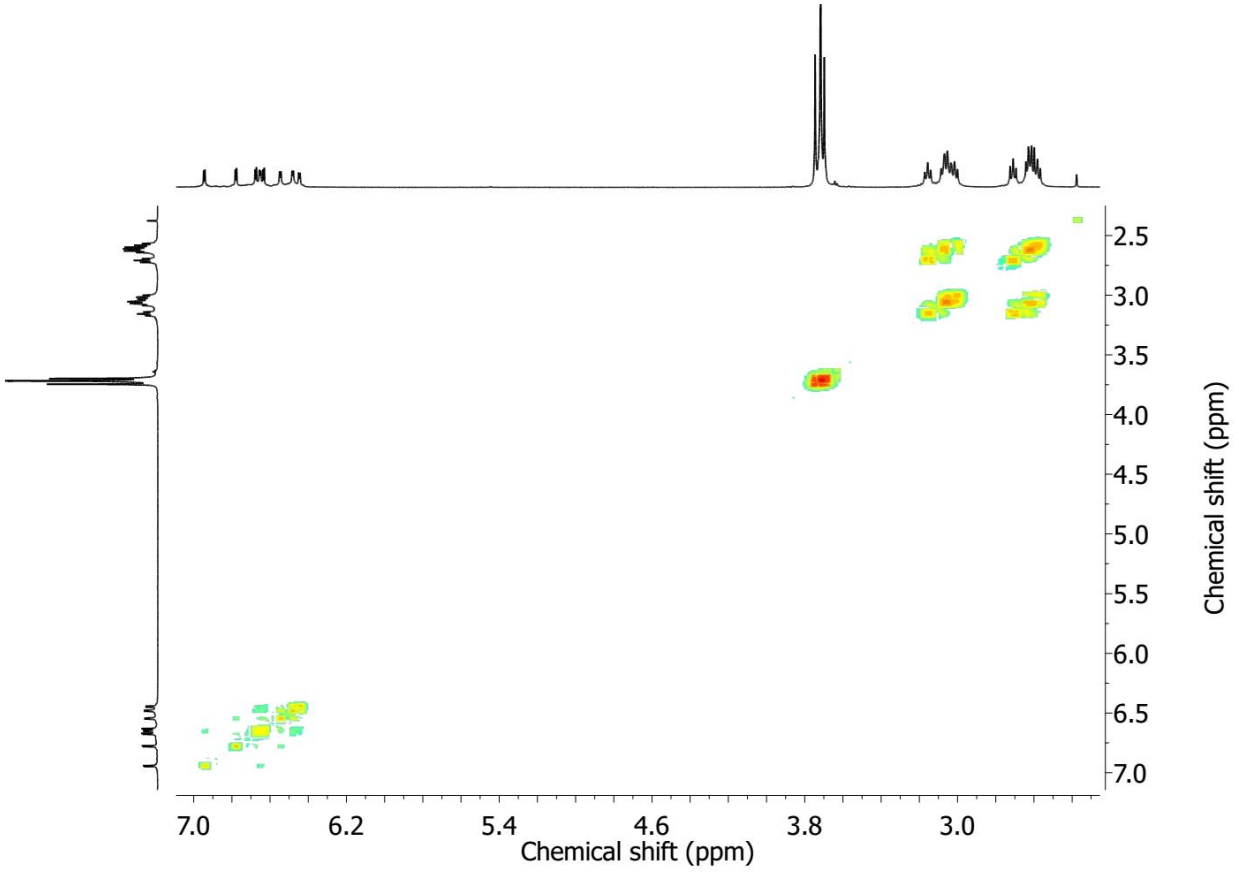


Figure S40. $^{1}$H-$^{1}$H COSY NMR spectrum of compound **5a**

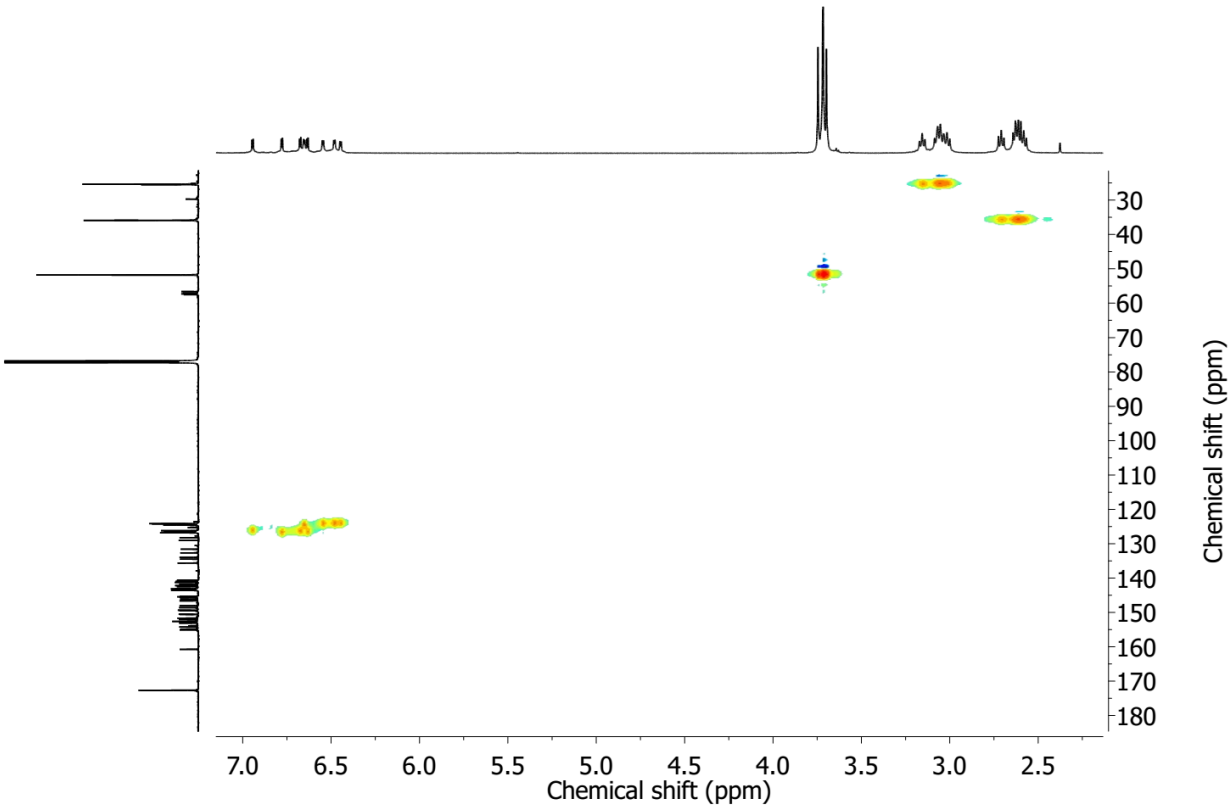


Figure S41. $^{1}H$-$^{13}C$ HSQC NMR spectrum of compound **5a**

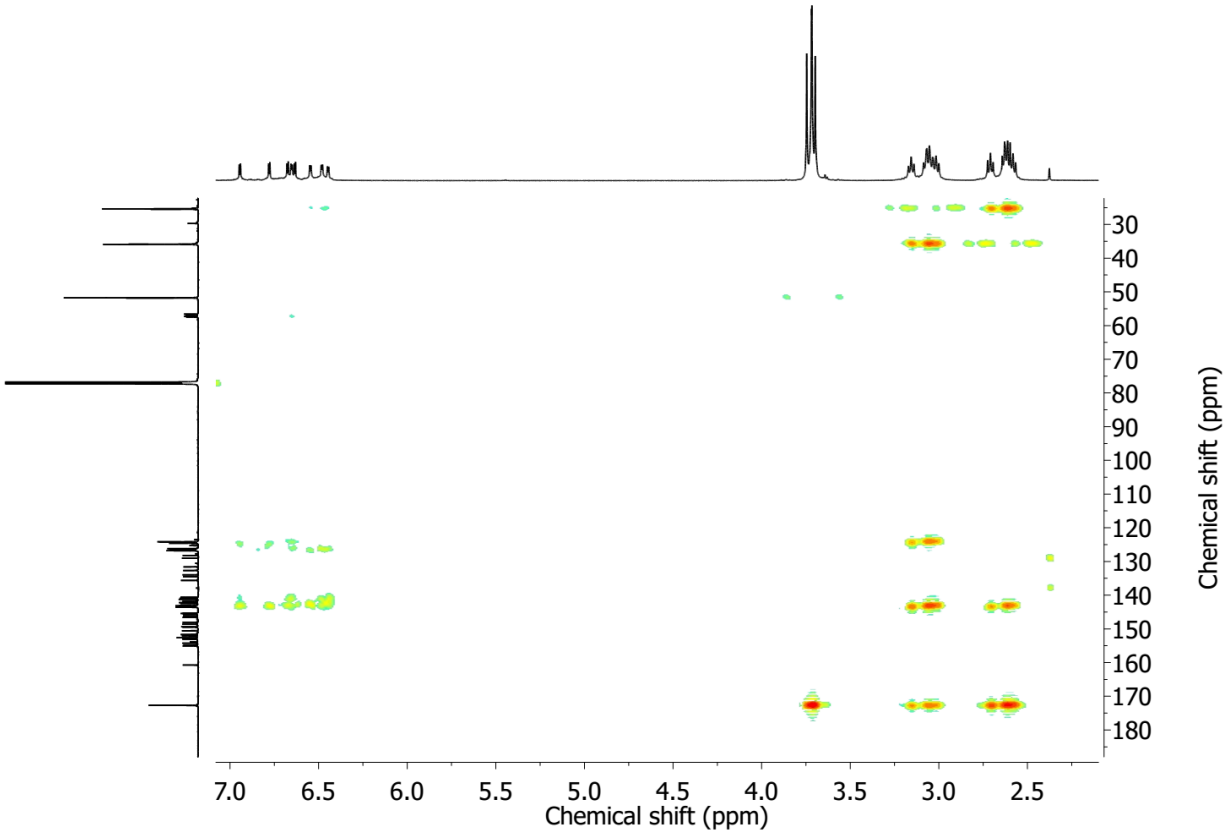


Figure S42. $^{1}H$-$^{13}C$ HMBC NMR spectrum of compound **5a**

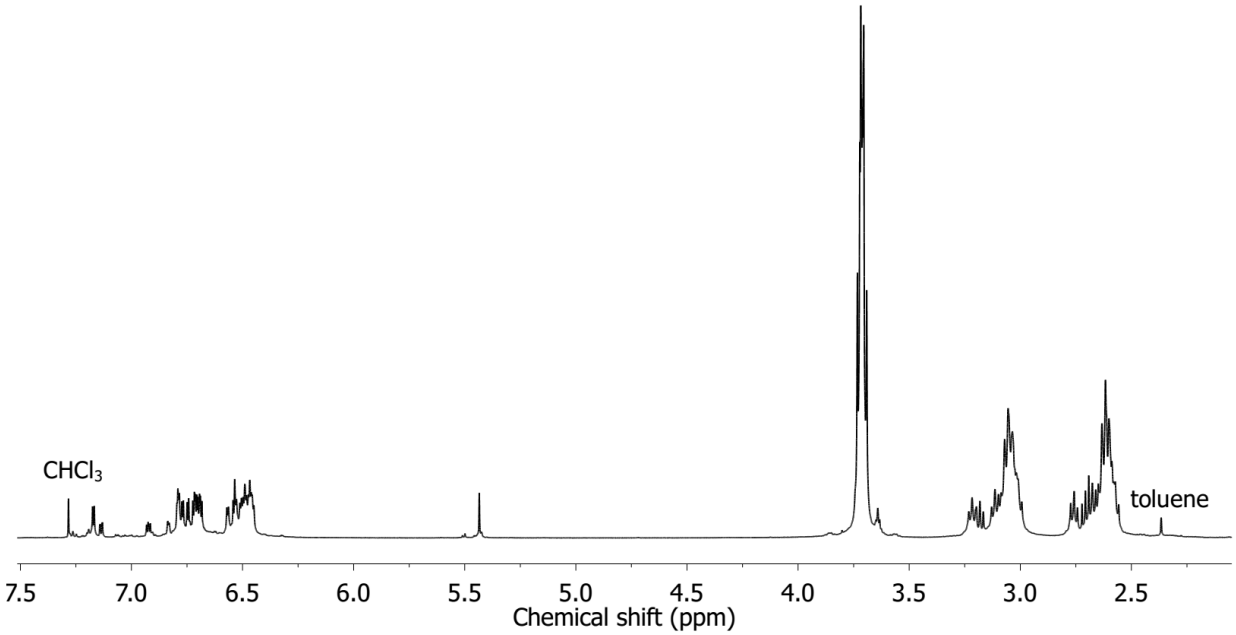


Figure S43. $^{1}$H NMR spectrum of compound **5b**

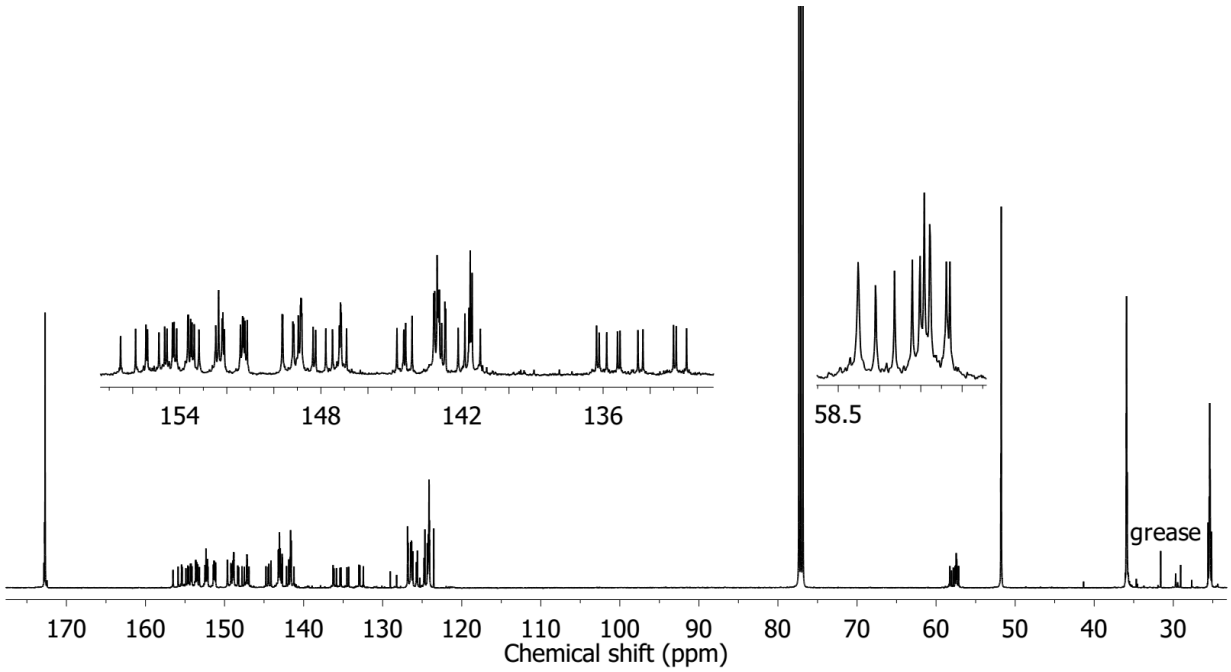


Figure S44. $^{13}$C NMR spectrum of compound **5b**

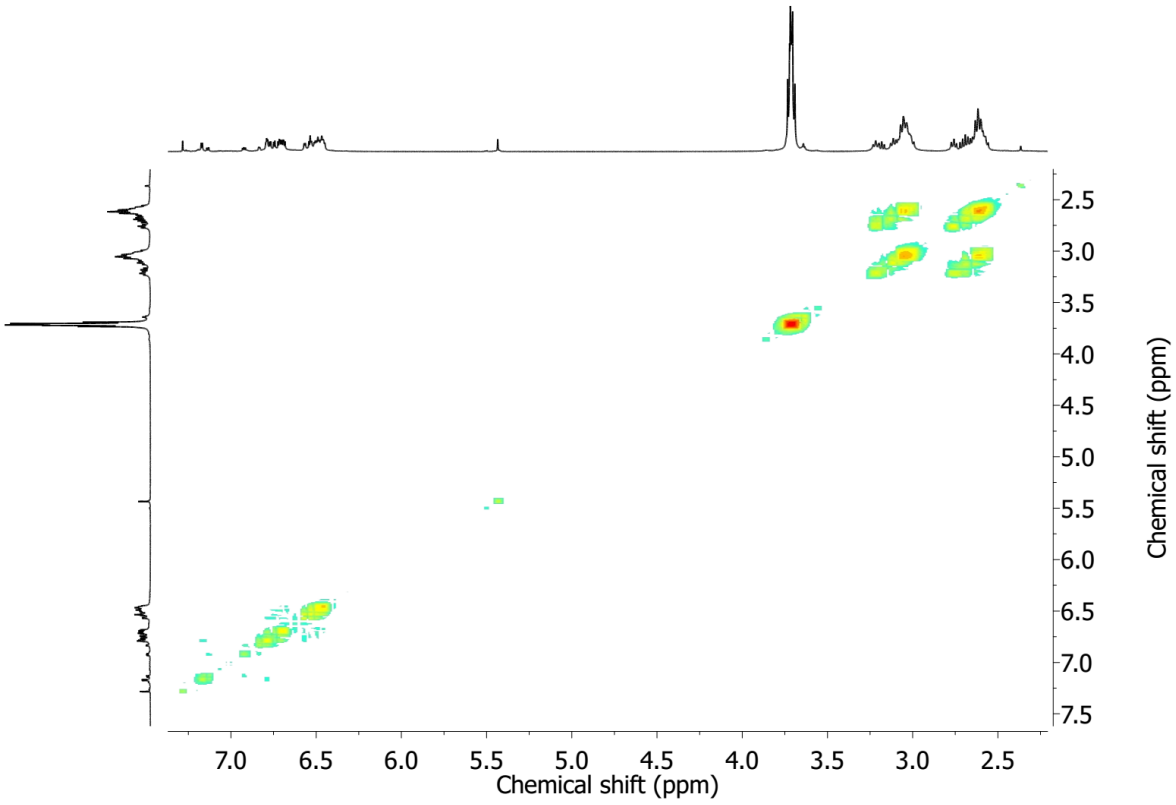


Figure S45. $^{1}$H-$^{1}$H COSY NMR spectrum of compound **5b**

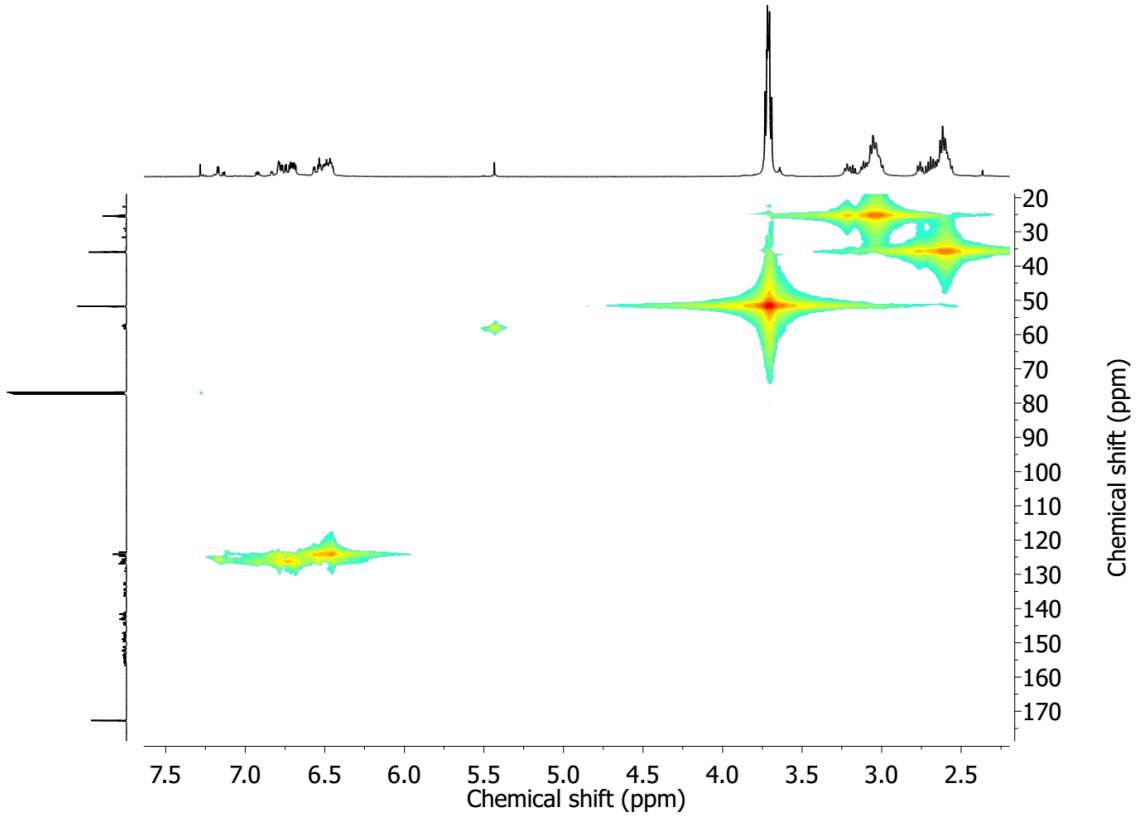


Figure S46. $^{1}$H-$^{13}$C HSQC NMR spectrum of compound **5b**

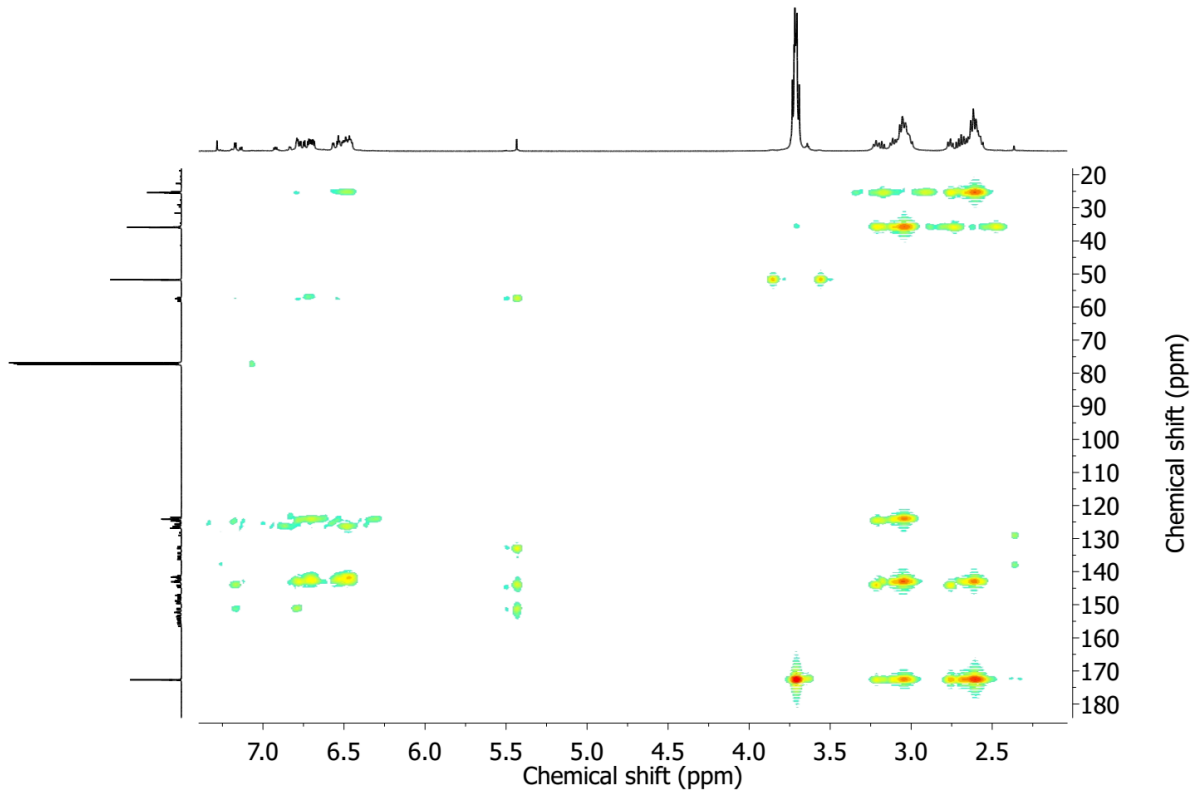


Figure S47. $^{1}H$-$^{13}C$ HMBC NMR spectrum of compound **5b**

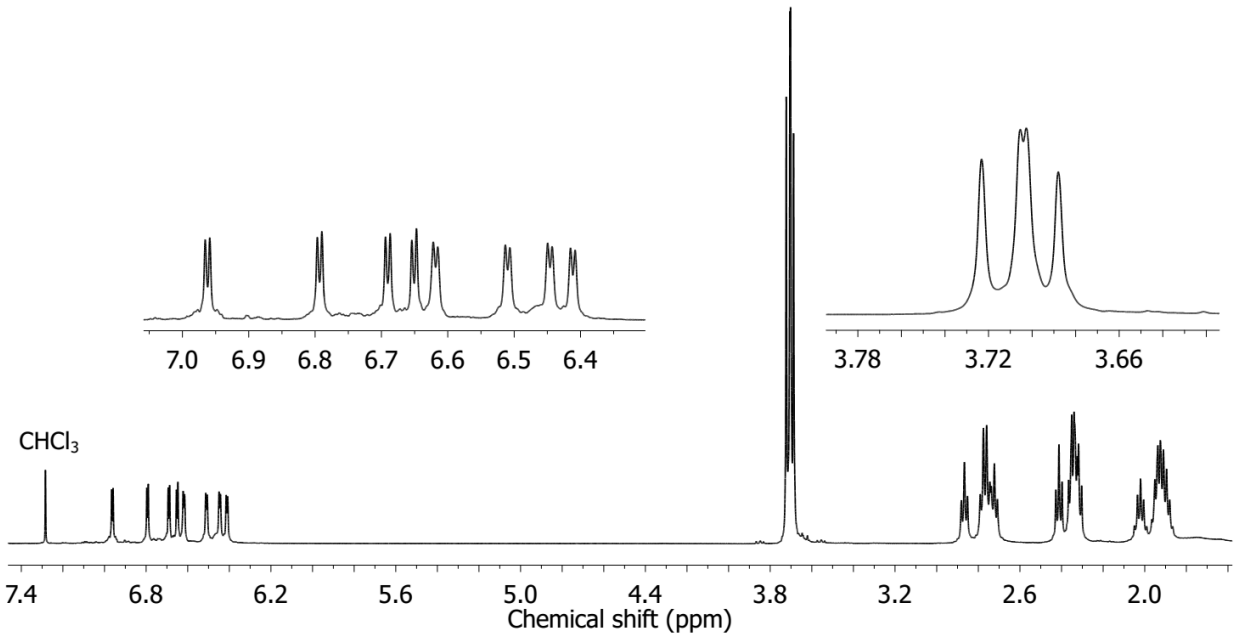


Figure S48. $^{1}H$ NMR spectrum of compound **6a**

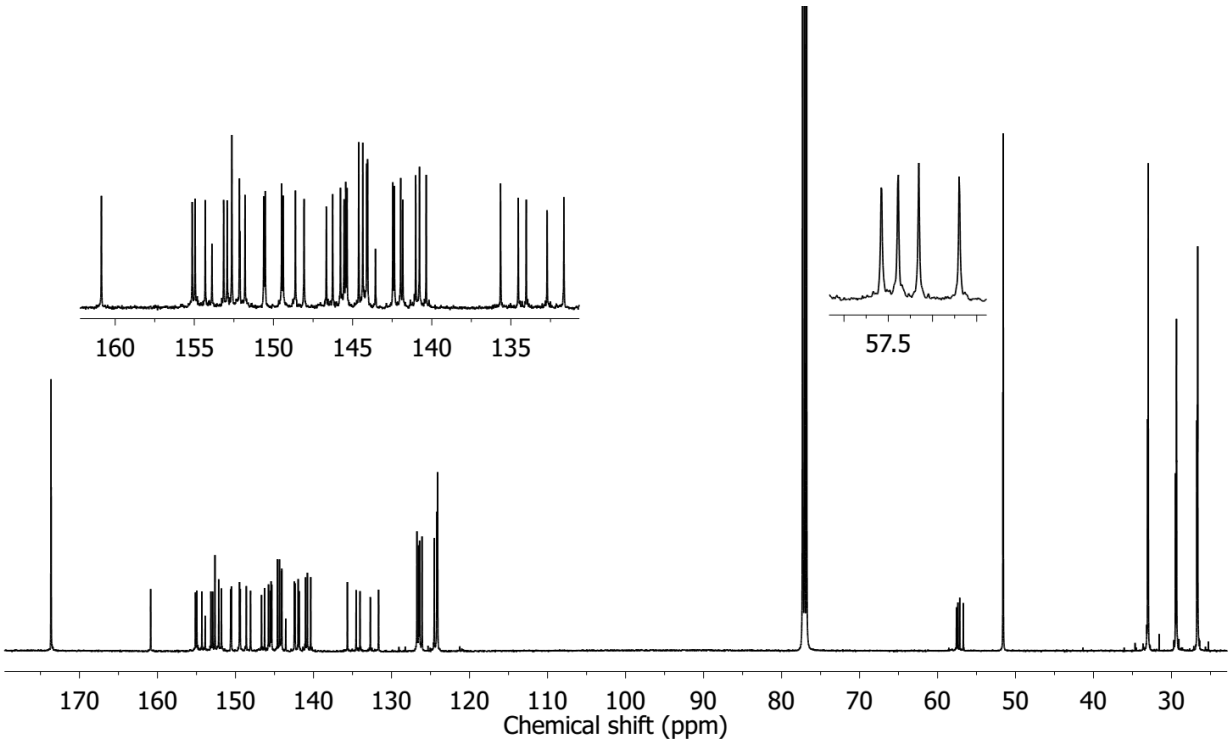


Figure S49. $^{13}$C NMR spectrum of compound **6a**

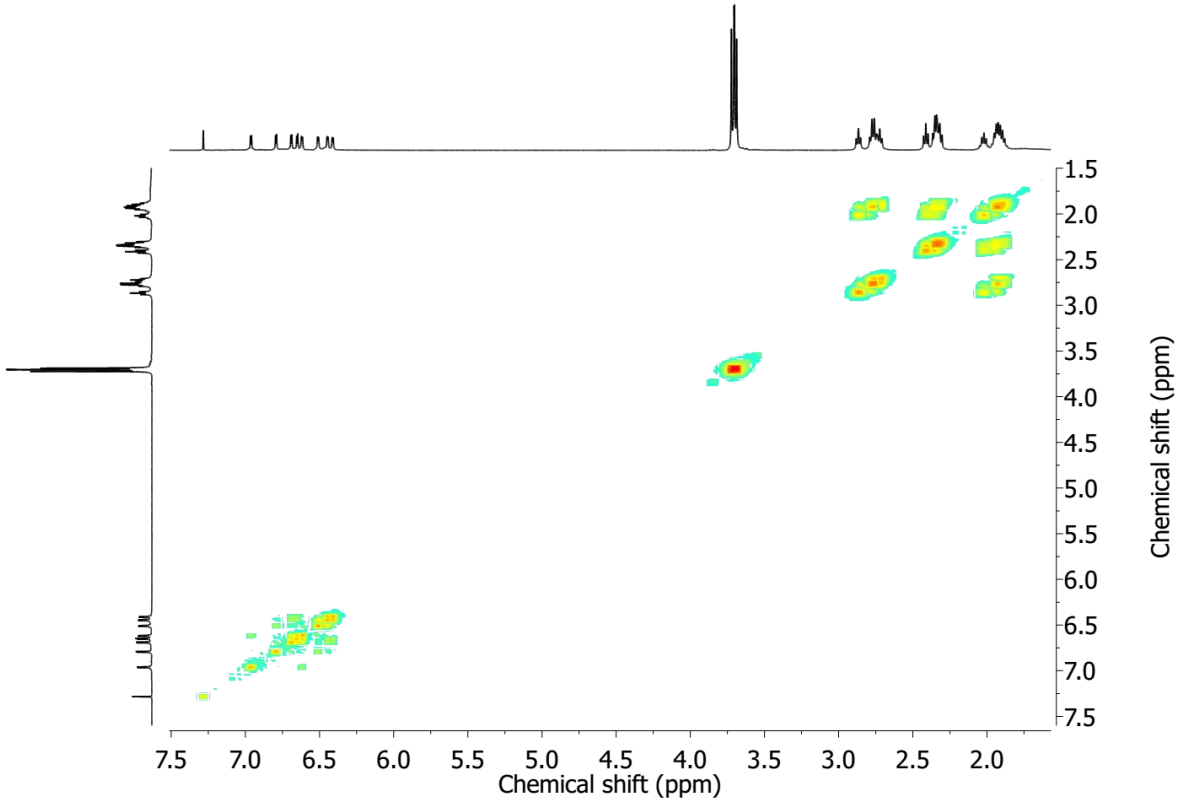


Figure S50. $^{1}$H-$^{1}$H COSY NMR spectrum of compound **6a**

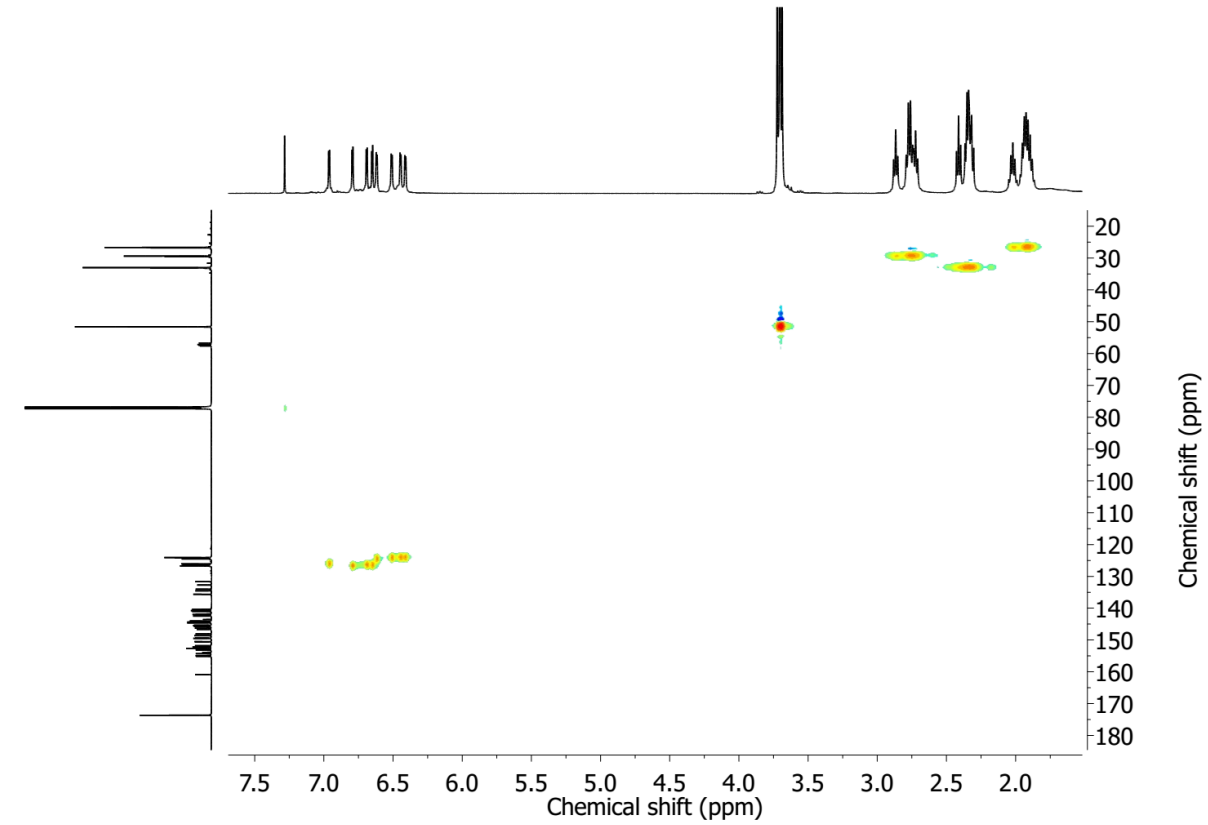


Figure S51. $^{1}$H-$^{13}$C HSQC NMR spectrum of compound **6a**

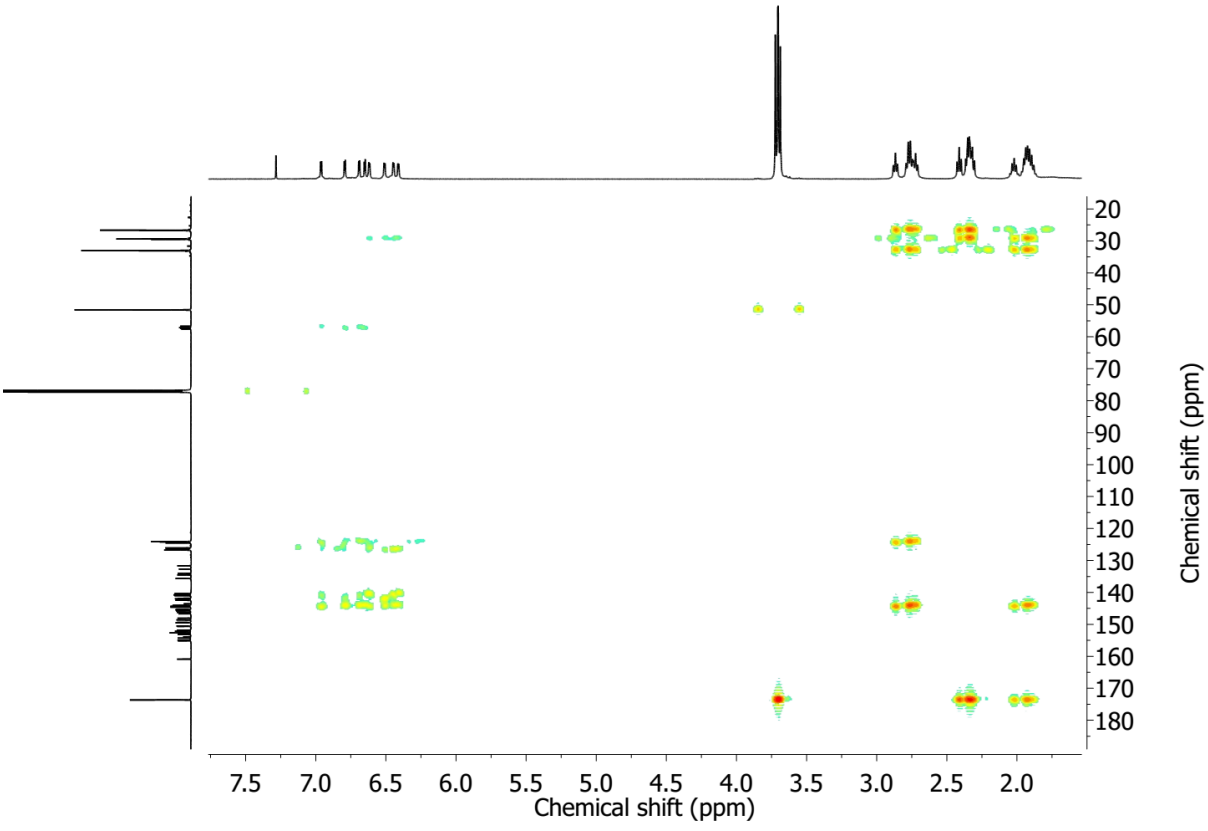


Figure S52. $^{1}$H-$^{13}$C HMBC NMR spectrum of compound **6a**

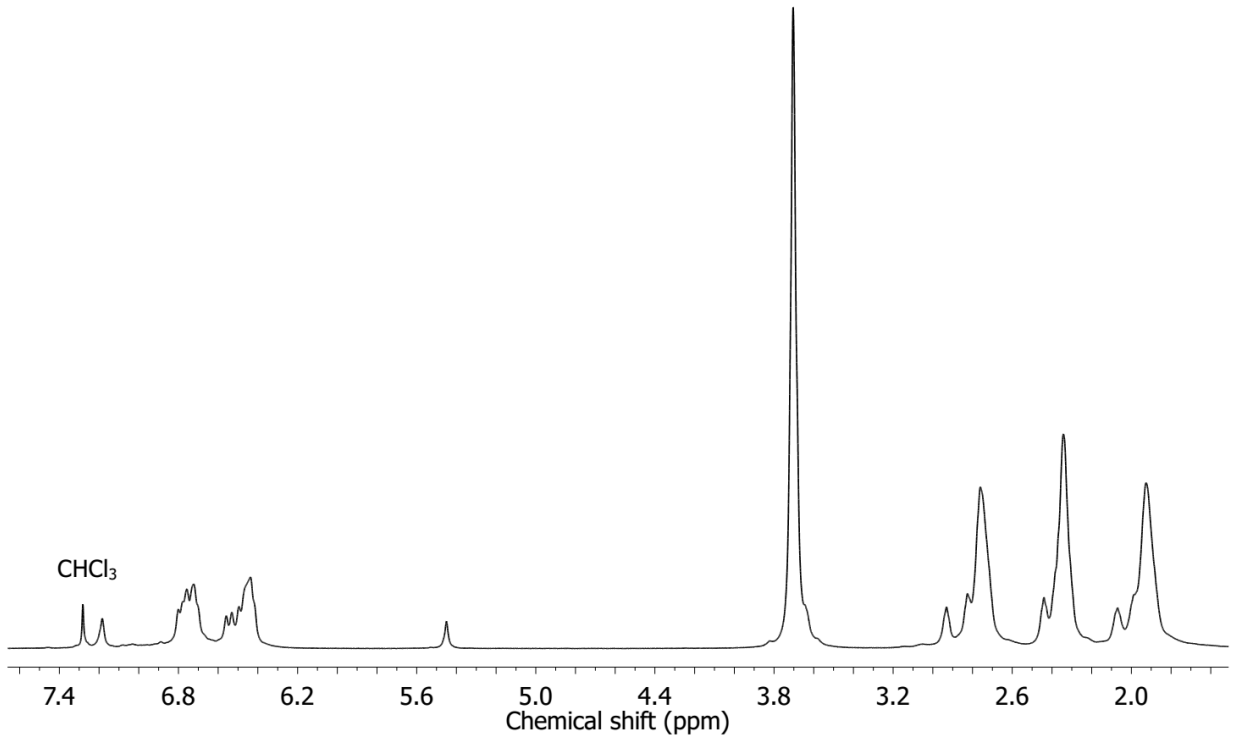


Figure S53. $^{1}$H NMR spectrum of compound **6b**

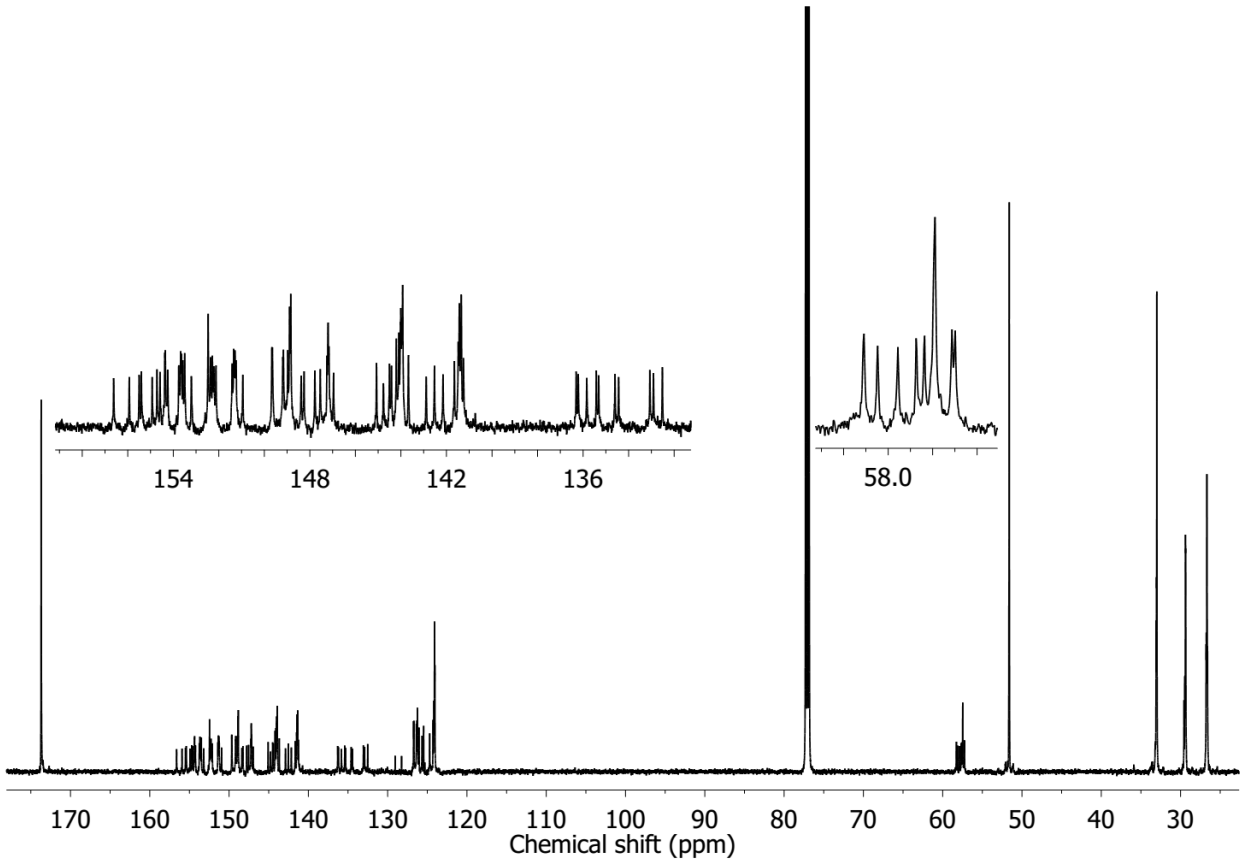


Figure S54. $^{13}$C NMR spectrum of compound **6b**

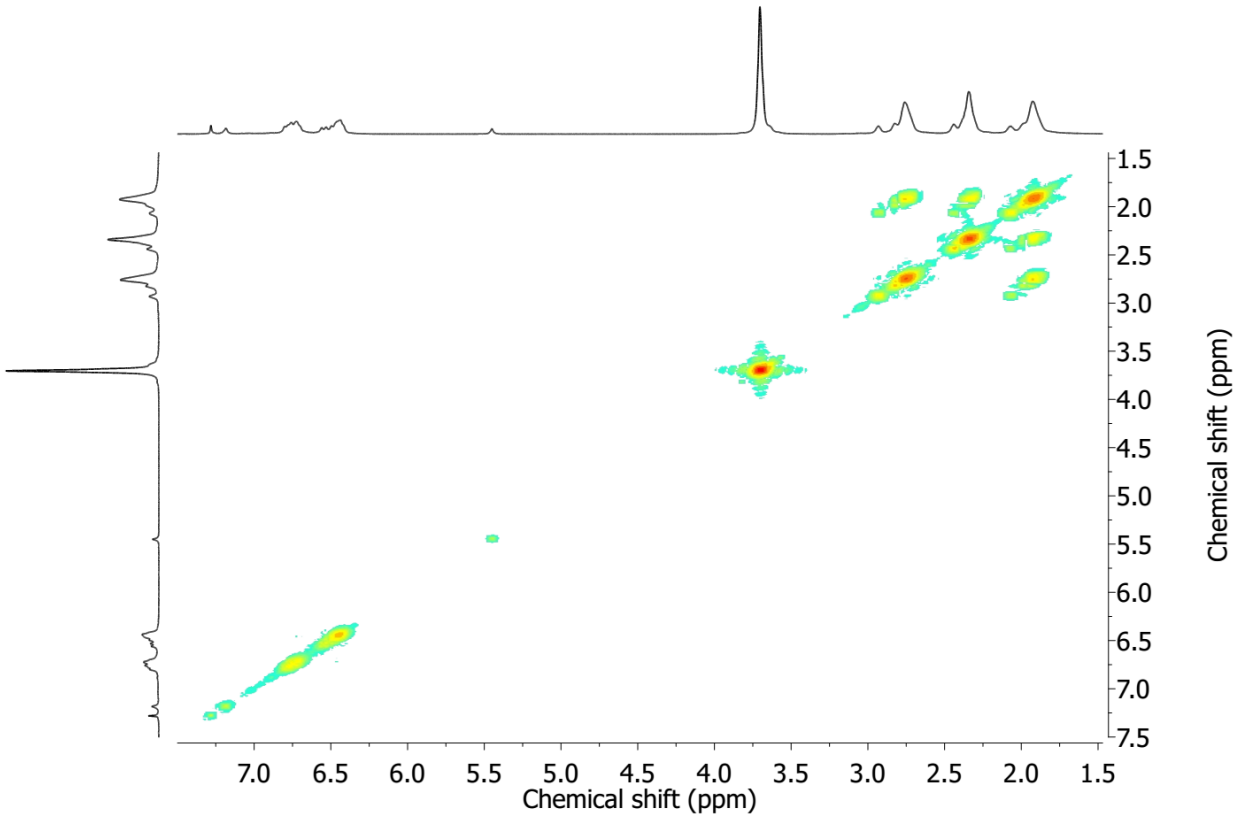


Figure S55. $^{1}$H-$^{1}$H COSY NMR spectrum of compound **6b**

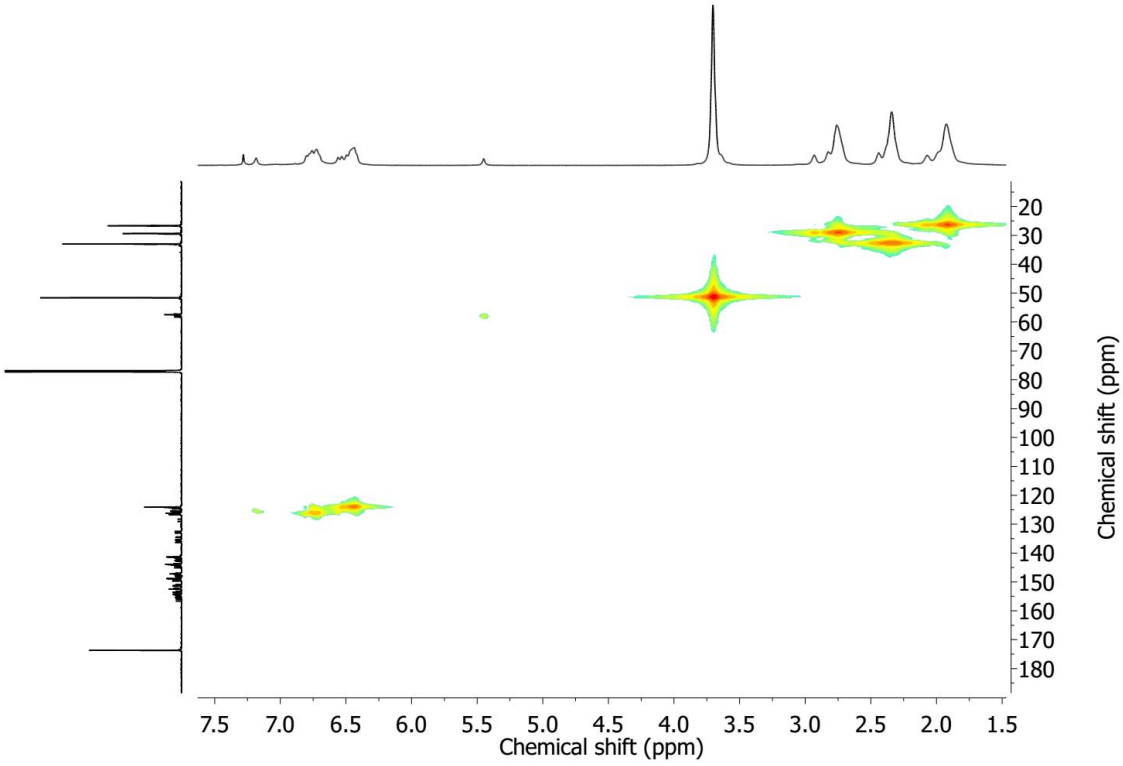


Figure S56. $^{1}$H-$^{13}$C HSQC NMR spectrum of compound **6b**

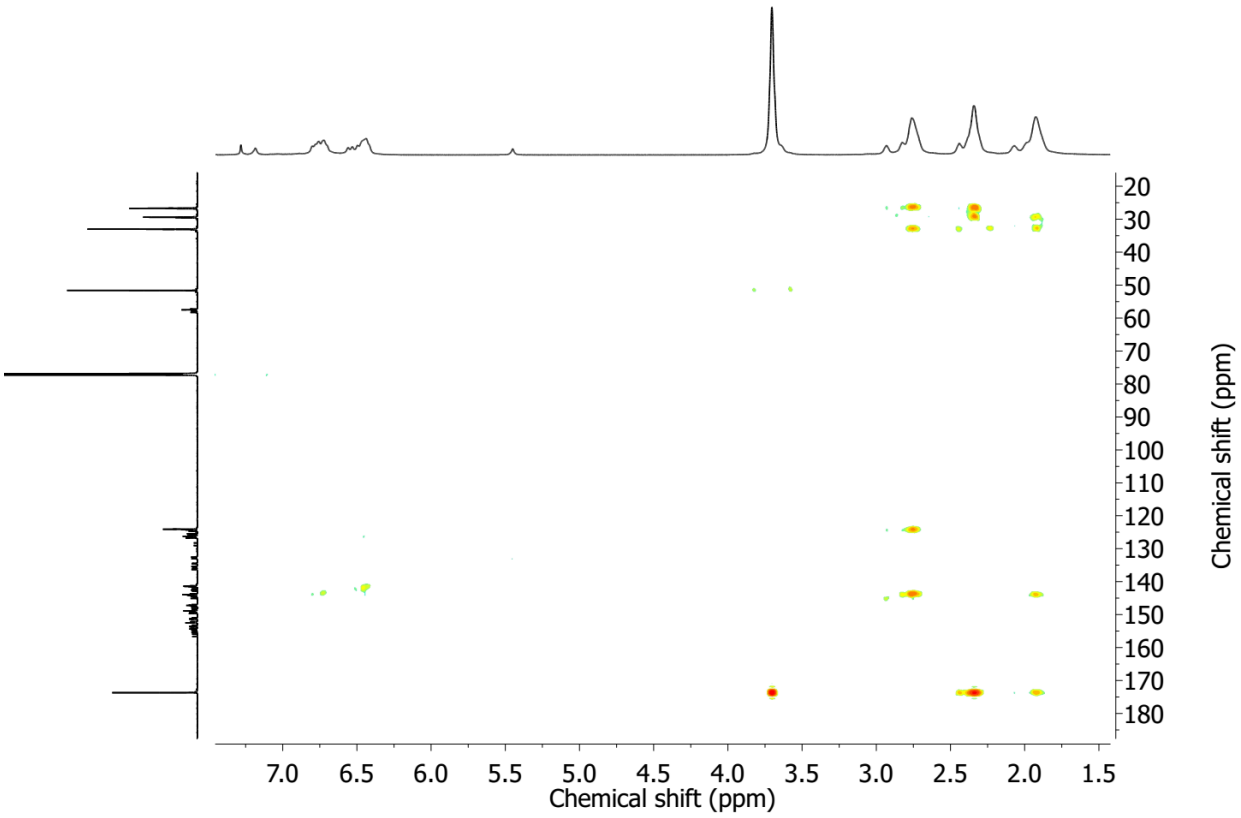


Figure S57. $^{1}H$-$^{13}C$ HMBC NMR spectrum of compound **6b**

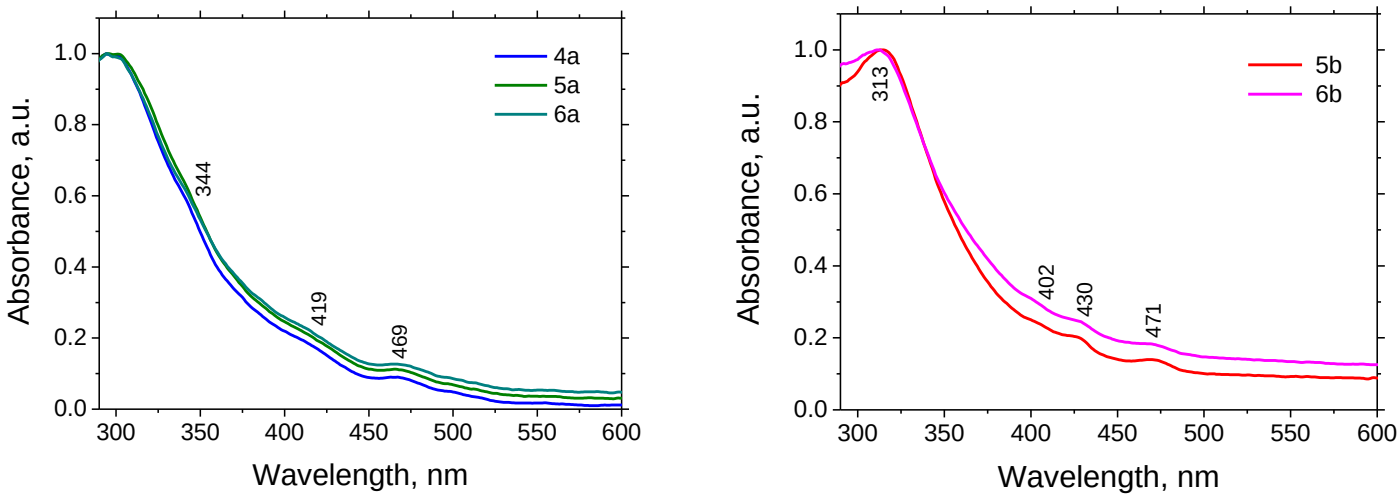


Figure S58. UV-Vis spectra of synthesized $C_{70}$ fullerene derivatives

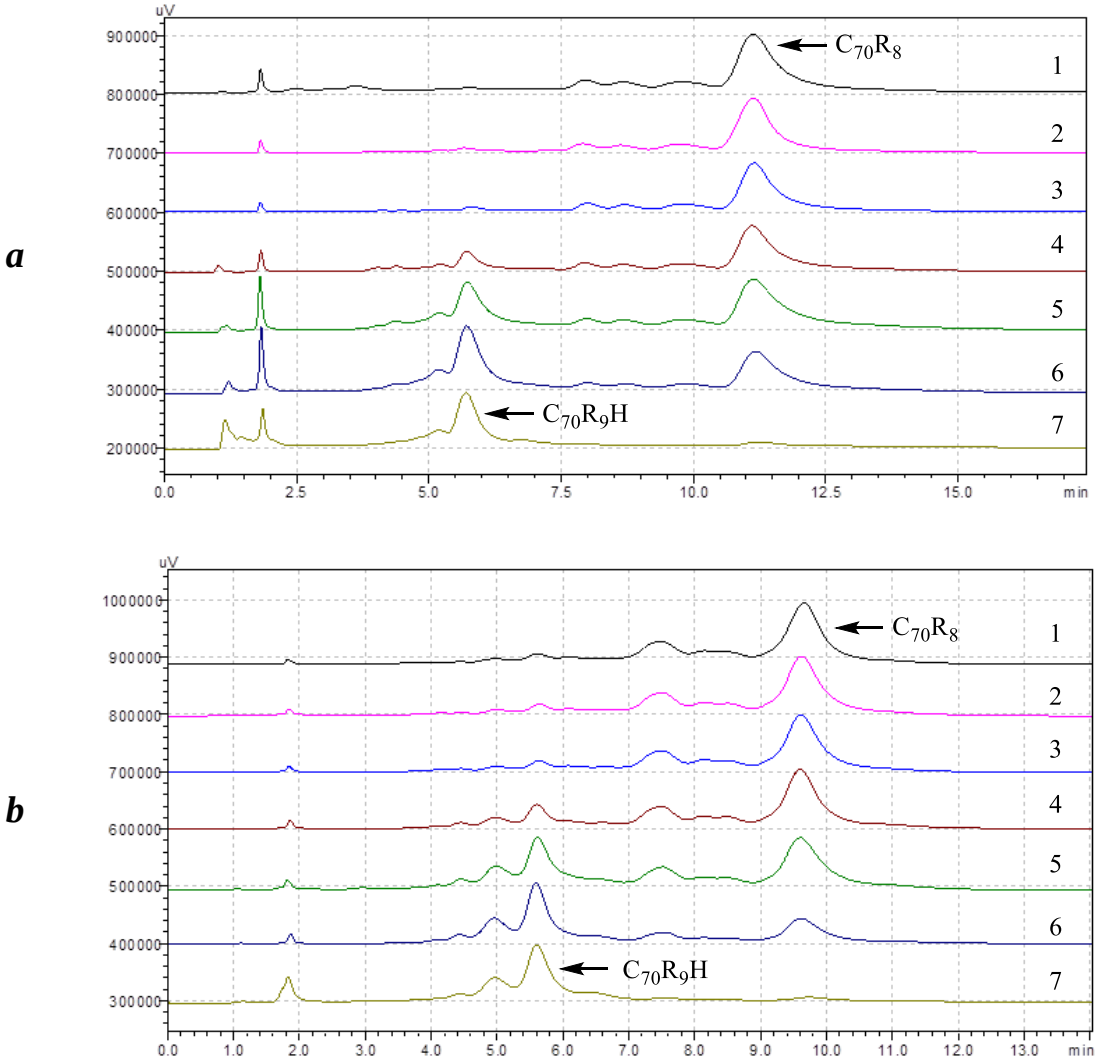


Figure S59. Dynamics of the HPLC profiles for the rections of $C_{70}Cl_8$ with the methyl esters of 3-thienylpropanoic (a) and 4-thienylbutanoic (b) acids at ~ 0.5 h (1), 1 h (2), 1.5 h (3), 2.5 h (4), 3.5 h (5), 4 h (6) and 6 h (7). Conditions: C18 Cosmosil column (nacalai tesque), elution with toluene/acetonitrile mixtures 10/90 (a) or 15/85 (b) v/v, 30°C, flow rate 1 mL/min, UV/Vis detector: 350 nm

# *Quantum chemical calculations*

To support the proposed structure of $C_1$-symmetrical fullerene derivatives $C_{70}R_9H$ (**5b** and **6b**), we calculated theoretical $^{13}C$ and $^{1}H$ chemical shifts for isomers B, C and D (fig. S60). The difference between those isomers is in the way the H atom and one of the addends are attached. The optimized structures of B, C, and D isomers are shown in fig. S61.

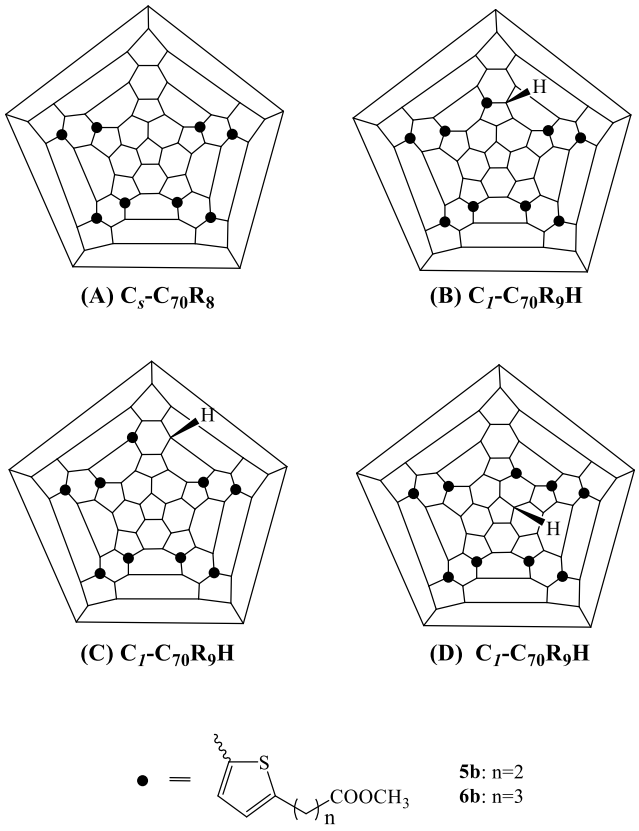


Figure S60. Schlegel diagrams for the fullerene derivatives $C_s$-$C_{70}R_8$ (A) and different isomers of $C_1$-$C_{70}R_9H$ (B-D)

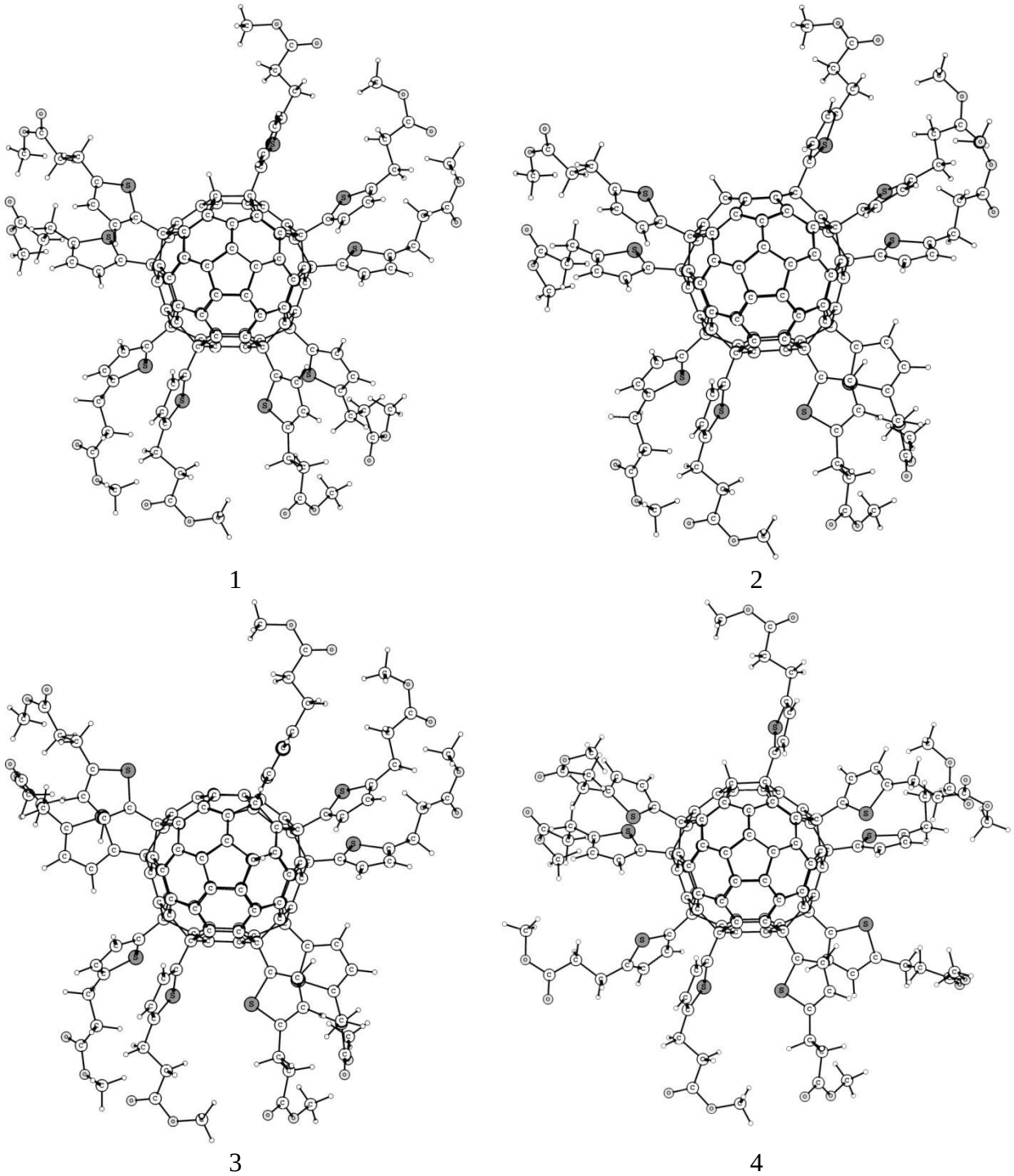


Figure S61. Calculated structures of B (1), C (2) and D (3) isomers of $C_{70}R_9H$ and rotational conformer of B (4)

To reduce the systematic errors in the calculation of chemical shifts, $\delta_{theor}$, in $^{13}C$ NMR spectra the correction correlation formula (1) was used

$$\delta = -4.321 + 0.887\ \delta_{theor}\ (ppm) \qquad (1).$$

Correction formula (1) was obtained from the comparison of the experimental chemical shifts for C ($sp^3$) atoms of the fullerene cage in $^{13}C$ NMR spectra of fullerene derivatives $C_{70}H_{10}$ and $C_{70}Ph_{10}$ with calculated chemical shifts for these compounds. Experimental chemical shifts of C

($sp^3$, cage) atoms for $C_{70}H_{10}$ and $C_{70}Ph_{10}$ are in the range of 45.64 - 48.09 and 60.80 - 67.64 ppm, respectively (A.G. Avent, P.R. Birkett, A.D. Darwish, H.W. Kroto, R.Taylor, D.R.M. Walton, *Tetrahedron*, **1996**, *52*, 14, 5235-5246; H.P. Spielmann, B.R. Weedon, M.S. Meier, *J. Org. Chem.*, **2000**, *65*, 2755-2758).

Formula (1) allows us to describe them with a standard error of 0.3 ppm and a maximum error of 0.5 ppm. The application of this approach for compound $C_{70}Ph_8$ (A.G. Avent, P.R. Birkett, A.D. Darwish, H.W. Kroto, R.Taylor, D.R.M. Walton, *Tetrahedron*, **1996**, *52*, 14, 5235-5246) provides a satisfactory description of the experimental spectra of 60.44 (60.49) 60.60 (61.06) 60.87 (61.15) 61.49 (62.88) ppm (the theoretical chemical shifts for the C ($sp^3$, cage) atoms are given in brackets).

The splitting of the lines in the theoretical spectrum (2.39 ppm) is larger than the experimental one (1.05 ppm). This effect can be attributed to the correlated rotation of phenyl groups, which affect the magnetic shielding constants of $^{13}C$ nuclei and cannot be taken into account in the calculation for a single equilibrium conformation.

For $C_{70}$ derivatives with conformationally non-rigid addends, structures of rotational isomers with close energies are averaged in the experimental spectra due to their mutual transitions in the NMR timescale. Complete theoretical analysis of this case is a non-trivial task.

The structure of compounds $C_s$-$C_{70}R_8$ (**5a**) with a symmetric pattern of attached addends is actually asymmetric due to steric hindrance. Arrangement of the atoms of all -R addends on the fullerene cage differs for the equilibrium structures of $C_s$-$C_{70}R_8$ and $C_1$-$C_{70}R_9H$. The possibility of converting of $C_s$-$C_{70}R_8$ structure to mirror-symmetric one with the same energy leads to averaging of chemical shifts for equivalent positions and to the symmetry of the experimental NMR spectrum (we see only 4 lines instead of 8).

Taking this into account, chemical shifts were averaged for equivalent substituents in the equilibrium structure of $C_{70}R_8$. As a result of calculations, the following chemical shifts were obtained: 46.30 (56.61) 57.59 (57.06) 58.03 (57.29) 58.75 (57.50) ppm (experimental values are given in brackets for comparison). The difference in chemical shifts for the extreme lines is 2.45 ppm, which is 2.5 times higher than the experimental difference of 0.89 ppm. However, the ratio of differences in the chemical shifts of adjacent signals (2.3 : 0.9 : 1) is approximately the same as in the experimental spectra (2.1 : 1.1: 1).

The theoretical chemical shifts found for C ($sp^3$, cage) atoms of compound $C_s$-$C_{70}R_9$ (**5b**), including isomers B,C, D are following:

B: 57.03, 57.16, 57.58, 57.60, 57.85, 57.86, 58.47, 58.51, 58.86, 58.87 ppm;

C: 37.83, 47.61, 55.55, 56.00, 56.32, 56.71, 56.96, 57.64, 58.22, 58.66 ppm;

D: 44.86, 56.49, 57.19, 57.42, 57.68, 57.69, 57.70, 57.76, 57.81, 57.83 ppm.

Spectra of isomers B, C, D are qualitatively different. Only a spectrum of isomer B is close enough to the experimental one:

experimental: 57.15, 57.19, 57.39, 57.46, 57.51, 57.60, 57.82, 58.05, 58.26 ppm.

The difference between chemical shifts of the extreme lines is 1.84 ppm, which is also quite close to the experimental 1.11 ppm. For C and D isomers, some lines (37.83, 47.61, 44.86) are strongly displaced from the main region.

An additional calculation was performed for the rotational isomer B in which 4 addends are rotated approximately by 180 degrees around the C($C_{70}$)-C axes (higher in energy). The calculation showed that the chemical shifts lied in a narrow range from 57.43 to 59.01 ppm, and the displacements of individual lines did not exceed 1.4 ppm.

Additionally, isomer B has the lowest energy, while C and D isomers are higher than B by 41.6 and 11.6 kcal/mol, respectively. For all these structures, the locations of seven addends don't vary significantly, and the main contribution to the difference in energies comes from the positional isomery.

Note that the calculation of relative energies of similar isomers (B, C, D) for $C_{70}(CF_3)_{10}$ with bulky addends shows that the D isomer has lower energy, which is in agreement with the experimental data (I.E. Kareev, I.V. Kuvychko, A.A. Popov, S.F. Lebedkin, S.M. Miller, O.P. Anderson, S.H. Strauss, O.V. Boltalina, *Angew. Chem., Int. Ed*., **2005**, *44*, 7984).

The chemical shifts in the experimental $^1$H NMR spectra of $C_{70}H_{10}$ are in the range of 5.26 - 5.42 ppm, which means that the calculated values (5.61 to 5.81 ppm) are shifted on average by 0.37 ppm. Accepting an empirical correction of -0.37 ppm for $^1$H NMR spectra of $C_1$-$C_{70}R_9H$, we obtain a $^1$H chemical shift estimate of 5.27, 4.67, and 5.04 ppm for B, C, and D isomers, respectively. The best agreement with the experimental value of 5.43 ppm (H atom bound fullerene cage) is also observed for B isomer.

To verify the theoretical conclusions, additional calculations were performed using the less wide basis Λ1 H [6s 2p / 2s 1p] C, O, [10s 7p 3d / 3s 2p 1d], S [14s 11p 3d / 4s 3p 1d] for chemical shifts of $C_{70}R_9H$ isomers B, C, D.

In a similar approach for constructing a correction correlation relation that looks like

$$\delta = 0.688 + 0.865\ \delta_{theor}\ (ppm) \qquad (2)$$

the following results were obtained for isomers:

B: 56.87, 57.00, 57.62, 57/87, 57.89, 58.15, 58.39, 58.48, 58.59, 58.70 ppm;

C: 37.52, 47.64, 55.47, 56.10, 56.16, 56.73, 56.88, 57.65, 58.10, 58.52 ppm;

D: 44.73, 55.21, 57.19, 57.27, 57.44, 57.54, 57.58, 57.73, 57.74, 58.72 ppm;

which qualitatively do not differ from the data in the Λ2 basis.

Thus, obtained results allowed us to univocally identify the structure of the compound as **5b** as B isomer. Similar results can be obtained for compound **6b**, which has very close experimental chemical shifts.

# *Biological assays*

***Table S1. Antiviral activity of the water-soluble fullerene derivatives against human immunodeficiency virus (HIV-1, HIV-2)***

| **Compound** | **Cytotoxicity** $CC_{50}$[a] **, μM** | **Antiviral activity** $EC_{50}$[b]**, μM** | | |
|---|---|---|---|---|
| | | **HIV-1 NL4.3** | **HIV-1 BaL** | **HIV-2 ROD** |
| ***K1a***[c] | 53.7 | 0.85 | 2.26 | nd |
| ***K1b*** | 61 | 1.81 | nd | 4.03 |
| ***K1c*** | 23 | 2.58 | nd | 4.65 |
| ***K1d*** | 25 | 2.19 | nd | 5.72 |
| ***K2a*** | 50 | 5.19 | nd | 3.06 |
| ***K2b*** | 59.3 | 1.90 | 2.99 | nd |
| ***K3a*** | > 100 | 2.05 | 2.31 | 1.79 |
| ***K3b*** | > 100 | 1.57 | 2.87 | 1.31 |
| ***K4a***[c] | > 100 | 1.09 | 2.31 | 1.75 |
| ***K5a***[c] | > 100 | 1.58 | 5.13 | 4.13 |
| ***K5b*** | > 100 | **0.70** | 5.4 | 1.81 |
| ***K6a***[c] | > 100 | 0.93 | 2.49 | 5.52 |
| ***K6b*** | > 100 | 2.05 | 3.37 | 1.72 |

[a]$CC_{50}$ -50% cytotoxic concentration in TZM-bl cell cultures. [b]$EC_{50}$ - 50% effective concentration or compound concentration required to inhibit HIV- induced cytopathogenic effect in TZM-bl cell cultures. [c]This data has been reported before (O. A. Kraevaya et al., *Chem. Commun*., **2020**, *56*, 1179-1182) and given here for the comparison. nd=not determined

***Table S2. Antiviral activity of the water-soluble fullerene derivatives against influenza viruses***

| Compound | Cytotoxicity, μM | | Antiviral activity $EC_{50}$[c], μM | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Influenza A/H1N1 A/Ned/378/05 | | Influenza A/H3N2 A/HK/7/87 | | Influenza B B/Ned/537/05 | |
| | $CC_{50}$[a] | MCC[b] | visual CPE score | MTS | visual CPE score | MTS | visual CPE score | MTS |
| ***K1a*** | 1.9 | 4 | >100 | >100 | >100 | >100 | >100 | >100 |
| ***K2b*** | 50.6 | 20 | >100 | >100 | **0.5** | **0.7** | >100 | >100 |
| ***Zanamivir*** | >100 | >100 | 0.08 | 0.01 | 9 | 3 | 0.2 | 0.01 |
| ***Amantadine*** | >100 | >100 | >100 | 0.5 | 20 | 1.3 | >100 | >100 |

[a]$CC_{50}$ - 50% cytotoxic concentration, as determined by measuring the cell viability with the colorimetric formazan-based MTS assay. [b]MCC - minimum compound concentration that causes a microscopically detectable alteration of normal cell morphology. [c]$EC_{50}$ - 50% effective concentration, or concentration producing 50% inhibition of virus-induced cytopathic effect, as determined by visual scoring of the CPE, or by measuring the cell viability with the colorimetric formazan-based MTS assay.

***Table S3. Antiviral activity of the water-soluble fullerene derivatives against human cytomegalovirus (HCMV)***

| Compound | $CC_{50}$, µg/mL | Exposure scheme | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Microbicidal[a] | | Prophylactic[b] | | Virulicide[c] | | Therapeutic[d] | |
| | | $EC_{50}$, µg/mL | SI | $EC_{50}$, µg/mL | SI | $EC_{50}$, µg/mL | SI | $EC_{50}$, µg/mL | SI |
| ***K1a*** | 70 | - | - | - | - | - | - | 9,6 | 7,3 |
| ***K1b*** | 608 | 16.9 | 36 | 324 | 2 | 27.6 | 22 | 23.4 | 26 |
| ***K2b*** | 15 | - | - | - | - | - | - | - | - |
| ***K3a*** | 201 | - | - | 2.5 | 80 | - | - | 5.3 | 38 |
| ***K3b*** | 1181 | - | - | 5.2 | **227** | - | - | 16.2 | 73 |
| ***K1c*** | 515 | 12 | 43 | 16.1 | 32 | 20.7 | 25 | 19.8 | 26 |
| ***K1d*** | 608 | 55.3 | 11 | 19.6 | 31 | 38.1 | 16 | - | - |
| ***K4a*** | 1222 | 10.4 | **118** | - | - | 8 | >**122** | 10 | **122** |
| ***K5a*** | 1321 | 220.2 | 6 | 30.7 | 43 | 16.7 | 79 | 133.8 | 10 |
| ***K5b*** | 1100 | - | - | - | - | 7.8 | **141** | 10.3 | **107** |
| ***K6a*** | 1386 | 28.9 | 48 | 37.5 | 37 | 16.9 | 82 | 46.2 | 30 |
| ***K6b*** | 1267 | - | - | - | - | 12,5 | **101** | 14,9 | 85 |

[a] cells were incubated for 1 h with the compounds and then were infected with the virus

[b] cells were incubated for 24 h with the compounds and then were infected with the virus

[c] the mixture of virus and compounds was incubated for 1 hour and introduced into the cell culture for 1 hour, then washed and fresh culture medium was added

[d] cells were infected with the virus and after 1 hour the compounds were introduced

***Table S4. Antiviral activity of the water-soluble fullerene derivatives against herpes simplex virus type 1 (HSV1)***

| **Compound** | **$CC_{50}$, μg/mL** | **Exposure scheme** | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | **Microbicidal[a]** | | **Prophylactic[b]** | | **Virulicide[c]** | | **Therapeutic[d]** | |
| | | **$EC_{50}$, μg/mL** | **SI** | **$EC_{50}$, μg/mL** | **SI** | **$EC_{50}$, μg/mL** | **SI** | **$EC_{50}$, μg/mL** | **SI** |
| ***K1a*** | 734 | 1,3 | **565** | 5,5 | **133** | 5,1 | **144** | 15,7 | 46,7 |
| ***K1b*** | 136 | 0,6 | **227** | 9,2 | 15 | 0,93 | **146** | 7,5 | 18 |
| ***K2b*** | 291 | 2,5 | **144** | - | - | 5,5 | 52 | 15,2 | 18,8 |
| ***K3a*** | 905 | 15 | 60 | 84 | 11 | 3,3 | **3013** | - | - |
| ***K3b*** | 1124 | 17 | 66 | 201 | 6 | 4 | **281** | 32 | 35 |
| ***K1c*** | 25 | 0,06 | **417** | 1,8 | 14 | 1,5 | 17 | 16,3 | 1,5 |
| ***K1d*** | 85 | 0,6 | **142** | 8,4 | 10 | 0,19 | **447** | 15 | 6 |
| ***K4a*** | 173 | 6,5 | 27 | - | - | 5,7 | 30 | 27,2 | 6 |
| ***K5a*** | 4038 | 0,1 | **40380** | <0,1 | **>40380** | 2,3 | **1756** | - | - |
| ***K5b*** | 1006 | 31 | 32 | - | - | 13,7 | 73 | - | - |
| ***K6a*** | 4000 | 0,1 | **40000** | 0,5 | **8000** | <0,1 | **>40000** | 29 | **138** |
| ***K6b*** | 844 | 31 | 27 | 0,1 | **8128** | 11,8 | 71 | - | - |

a, b, c, d - as in *the Table S3*

***Determination of the acute toxicity of compound K5a in mice***

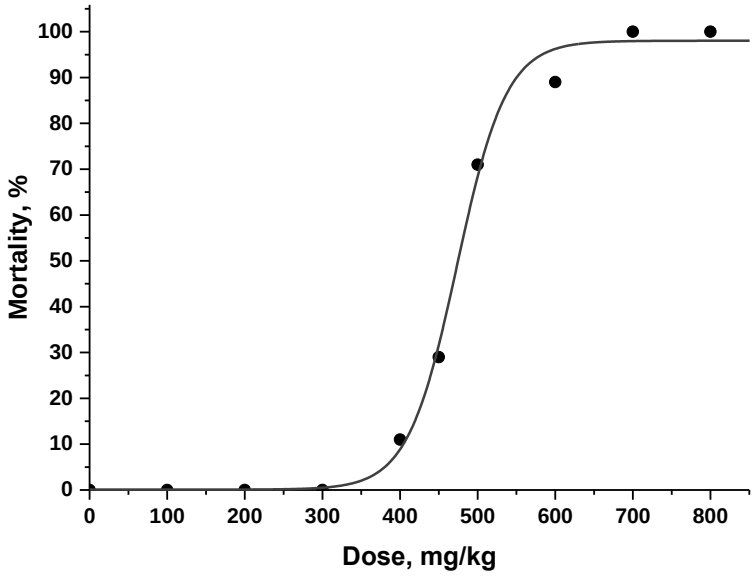


Figure 62. The dose-effect curve of the dependence of the percentage of mortality of laboratory animals on the dose of **K5a** with intraperitoneal administration