Rapid, Metal-Free and Aqueous Synthesis of Imidazo[1,2-*a*]pyridines under Ambient Conditions

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Supporting Information

1. General considerations

Where stated, manipulations were performed under an atmosphere of dry nitrogen by means of standard Schlenk line or glovebox techniques. Anhydrous solvents were prepared by passing the solvent over activated alumina to remove water, copper catalyst to remove oxygen and molecular sieves to remove any remaining water, *via* the Dow-Grubbs solvent system. Deuterated $CDCl_3$, CD_3CN and $(CD_3)_2SO$ were dried over CaH_2, cannula filtered or distilled, and then freeze-pump-thaw degassed prior to use. All other reagents and solvents were used as supplied.

^1H, ^{13}C and ^{19}F NMR spectra were recorded on either a Bruker DPX300 (300/282/75 MHz) spectrometer or a Bruker AV3-400 (400/100 MHz) spectrometer using the residual solvent as an internal standard. The values of chemical shifts are reported in parts per million (ppm) with the multiplicities of the spectra reported as follows: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) and broad (br), values for coupling constants (*J*) are assigned in Hz. Assignment of some ^1H NMR spectra was aided by the use of 2D ^1H-^1H COSY experiments and the assignment of some $^{13}C\{^1H\}$ NMR spectra was aided by $^{13}C\{^1H\}$ DEPT135 experiments. Mass spectra were collected on a Bruker Daltonics (micro TOF) instrument operating in the electrospray mode. Microanalyses were performed using a Carlo Erba Elemental Analyser MOD 1106 spectrometer.

2. Preparation of *N*-propargyl pyridinium bromides 1a-j

General procedure:

2-Aminopyridine derivative (5.0 mmol), propargyl bromide (6.0 mmol, 80 wt. % toluene solution) and 2-propanol (10 mL) were added to a small Schlenk flask and stirred vigorously at 80 ˚C for 2 hours. After this time, the mixture was allowed to cool to room temperature and the excess solvent/propargyl bromide were removed under high vacuum. The resulting crude residue was washed with petroleum ether (2 × 30 mL) and recrystallised from the minimum amount of 2-propanol at -30 ˚C. The resulting precipitate was collected *via* vacuum filtration, rinsed with cold petroleum ether (2 × 20 mL) and dried *in vacuo* to deliver the corresponding *N*-propargyl pyridinium bromides, **1a-i**.

2-Amino-1-(2-propynyl)pyridinium bromide 1a:[1] 2-Aminopyridine was reacted according to the general procedure (*vide supra*), affording the product as a colourless solid. Yield: 0.88 g, 83% yield. ^{1}H NMR (300 MHz, D_2O): δ (ppm) 8.08 (d, *J* = 6.9 Hz, 1H, py*H*), 7.93 (t, *J* = 16.2, 8.4 Hz, 1H, py*H*), 7.17 (d, *J* = 8.4 Hz, 1H, py*H*), 7.01 (t, *J* = 14.1, 6.9 Hz, 1H, py*H*), 5.06 (d, *J* = 2.7 Hz, 2H, CH_2), 3.18 (t, *J* = 5.1, 2.7 Hz, 1H, C≡C*H*). ^{13}C{^{1}H} NMR (100 MHz, D_2O): δ (ppm) 153.8, 143.1, 138.5, 115.2, 113.9, 78.6, 73.2, 43.5. HR-MS (ESI$^+$): *m/z* 133.0756 $[C_8H_9N_2]^+$, calcd. $[M - Br]^+$ 133.0760. Anal. calcd. (%) for $C_8H_9N_2Br$: C 45.10, H 4.26, N 13.15; found C 45.40, H 4.30, N 13.20. Lit. data:[1] ^{1}H NMR (500 MHz, DMSO-d_6) 8.72 (s, 2H, NH_2), 8.23 – 6.85 (m, 4H, py*H*), 5.12 (s, 2H, CH_2), 3.85 (s, 1H, C*H*). ^{13}C NMR (125 MHz, DMSO-d_6) 154.5, 143.6, 139.8, 115.8, 114.0, 80.5, 76.0, 43.9.

4-Methyl-2-amino-1-(2-propynyl)pyridinium bromide 1b: 4-Methyl-2-aminopyridine was reacted according to the general procedure (*vide supra*), affording the product as an off-white solid. Colourless blocks suitable for X-ray crystallographic analysis were obtained *via* slow diffusion of Et_2O vapours into a concentrated MeCN solution of the compound. Yield: 0.87 g, 77% yield. ^{1}H NMR (300 MHz, D_2O): δ (ppm) 7.94 (d, *J* = 7.2 Hz, 1H, py*H*), 6.94 (br s, 1H, py*H*), 6.87 (dd, *J* = 7.2, 1.8 Hz, 1H, py*H*), 5.01 (d, *J* = 2.4 Hz, 2H, CH_2), 3.19 (t, *J* = 5.1, 2.4 Hz, 1H, C≡C*H*), 2.41 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (75 MHz, D_2O): δ (ppm) 156.6, 153.2, 137.6, 116.2, 113.7, 78.7, 73.5, 43.0, 20.9. HR-MS (ESI$^+$): *m/z* 147.0922 $[C_9H_{11}N_2]^+$, calcd. $[M - Br]^+$ 147.0917. Anal. calcd. (%) for $C_9H_{11}N_2Br$: C 47.60, H 4.88, N 12.34; found C 47.20, H 4.80, N 12.20.

5-Methyl-2-amino-1-(2-propynyl)pyridinium bromide 1c: 5-Methyl-2-aminopyridine was reacted according to the general procedure (*vide supra*), affording the product as a pale orange solid. Pale orange blocks suitable for X-ray crystallographic analysis were obtained *via* slow diffusion of Et_2O vapours into a concentrated MeCN solution of the compound. Yield: 0.95 g, 84% yield. ^{1}H NMR (300 MHz, D_2O): δ (ppm) 7.81 (s, 1H, py*H*), 7.77 (d, *J* = 9.0 Hz, 1H, py*H*), 7.04 (d, *J* = 9.0 Hz, 1H, py*H*), 4.96 (s, 2H, CH_2), 3.14 (s, 1H, C≡C*H*), 2.23 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (75 MHz, D_2O): δ (ppm) 152.1, 145.3, 136.1, 124.4, 114.7, 78.6, 73.0, 43.3, 16.2. HR-MS (ESI$^+$): *m/z* 147.0925 $[C_9H_{11}N_2]^+$, calcd. $[M - Br]^+$ 147.0917. Anal. calcd. (%) for $C_9H_{11}N_2Br$: C 47.60, H 4.88, N 12.34; found C 47.40, H 4.80, N 12.30.

6-Methyl-2-amino-1-(2-propynyl)pyridinium bromide 1d: 6-Methyl-2-aminopyridine was reacted according to the general procedure (*vide supra*), affording the product as a colourless solid. Yield: 0.91 g, 80% yield. ^{1}H NMR (400 MHz, D_2O): δ (ppm) 7.77 (dd, *J* = 8.8, 7.2 Hz, 1H, py*H*), 7.02 (d, *J* = 8.8 Hz, 1H, py*H*), 6.88 (d, *J* = 7.2 Hz, 1H, py*H*), 5.02 (s, 2H, CH_2), 2.98 (s, C≡C*H*, weak signal due to H/D exchange), 2.69 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (75 MHz, D_2O): δ (ppm) 157.7, 154.2, 138.7, 117.3, 114.8, 79.8, 74.6, 44.1, 22.0. HR-MS (ESI$^+$): *m/z* 147.0918 [$C_9H_{11}N_2$]$^+$, calcd. [M – Br]$^+$ 147.0917. Anal. calcd. (%) for $C_9H_{11}N_2Br$: C 47.60, H 4.88, N 12.34; found C 47.50, H 4.85, N 12.30.

5-Nitro-2-amino-1-(2-propynyl)pyridinium bromide 1e: 5-Nitro-2-aminopyridine was reacted according to the general procedure (*vide supra*), affording the product as a light brown solid. Yield: 0.85 g, 66% yield. ^{1}H NMR (300 MHz, D_2O): δ (ppm) 9.25 (d, *J* = 2.4 Hz, 1H, py*H*), 8.49 (dd, *J* = 9.9, 2.4 Hz, 1H, py*H*), 7.21 (d, *J* = 9.9 Hz, 1H, py*H*), 5.09 (d, *J* = 2.4 Hz, 2H, CH_2), 3.16 (t, *J* = 5.1, 2.4 Hz, 1H, C≡C*H*). ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ (ppm) 155.1, 139.7, 135.8, 135.4, 115.3, 80.6, 74.2, 44.0. HR-MS (ESI$^+$): *m/z* 178.0618 [$C_8H_8N_3O_2$]$^+$, calcd. [M – Br]$^+$ 178.0611. Anal. calcd. (%) for $C_8H_8N_3BrO_2$: C 37.23, H 3.12, N 16.18; found C 37.30, H 3.05, N 15.80.

2,6-Diamino-1-(2-propynyl)pyridinium bromide 1f: 2,6-Diaminopyridine was reacted according to the general procedure (*vide supra*), affording the product as a hygroscopic, gummy brown solid. Yield: 0.57 g, 50% yield. ^{1}H NMR (300 MHz, D_2O): δ (ppm) 7.77 (t, *J* = 7.8 Hz, 1H, *p*-py*H*), 6.99 (dd, *J* = 7.8 Hz, 2H, *m*-py*H*), 5.02 (s, 2H, CH_2), 2.98 (s, C≡C*H*, weak signal due to H/D exchange). ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ (ppm) 158.1, 157.7 (2C), 104.6, 46.5, 25.0. HR-MS (ESI$^+$): *m/z* 148.0874 [$C_8H_{10}N_3$]$^+$, calcd. [M + H]$^+$ 148.0869. Anal. calcd. (%) for $C_8H_{10}N_3Br$: C 42.13, H 4.42, N 18.42; found C 41.90, H 4.30, N 18.20.

5-Bromo-2-amino-1-(2-propynyl)pyridinium bromide 1g: 5-Bromo-2-aminopyridine was reacted according to the general procedure (*vide supra*), affording the product as a pale orange solid. Yield: 1.20 g, 81% yield. ^{1}H NMR (400 MHz, D_2O): δ (ppm) 8.31 (d, *J* = 1.6 Hz, 1H, py*H*), 8.01 (dd, *J* = 9.6, 1.6 Hz, 1H, py*H*), 7.12 (d, *J* = 9.6 Hz, 1H, py*H*), 5.02 (d, *J* = 2.8 Hz, 2H, CH_2), 3.18 (t, *J* = 5.1, 2.8 Hz, 1H, C≡C*H*). ^{13}C{^{1}H} NMR (100 MHz, D_2O): δ (ppm) 153.0, 145.6, 138.2, 116.4, 106.0, 79.1, 72.7, 43.7. HR-MS (ESI$^+$): *m/z* 210.9865 [$C_8H_8N_2Br^{79}$]$^+$ and 212.9846 [$C_8H_8N_2Br^{81}$]$^+$, calcd. [M – Br]$^+$

210.9865, 212.9845, respectively. Anal. calcd. (%) for $C_8H_8N_2Br_2$: C 32.91, H 2.76, N 9.59; found C 33.10, H 2.60, N 9.60.

5-Iodo-2-amino-1-(2-propynyl)pyridinium bromide 1h: 5-Iodo-2-aminopyridine was reacted according to the general procedure (*vide supra*), affording the product as a pale orange solid. Pale orange blocks suitable for X-ray crystallographic analysis were obtained *via* slow diffusion of Et_2O vapours into a concentrated MeCN solution of the compound. Yield: 1.19 g, 70% yield. ^{1}H NMR (400 MHz, D_2O): δ (ppm) 8.37 (d, *J* = 1.6 Hz, 1H, py*H*), 8.09 (dd, *J* = 9.2, 1.6 Hz, 1H, py*H*), 7.00 (d, *J* = 9.2 Hz, 1H, py*H*), 5.01 (d, *J* = 2.4 Hz, 2H, CH_2), 3.19 (t, *J* = 4.4, 2.4 Hz, 1H, C≡C*H*). ^{13}C{^{1}H} NMR (100 MHz, D_2O): δ (ppm) 153.0, 150.2, 142.9, 116.4, 79.1, 73.6, 72.9, 43.5. HR-MS (ESI$^+$): *m/z* 258.9738 $[C_8H_8N_2I]^+$, calcd. $[M - Br]^+$ 258.9727. Anal. calcd. (%) for $C_8H_8N_2IBr$: C 28.35, H 2.38, N 8.26; found C 28.70, H 2.40, N 8.40.

5-Trifluoromethyl-3-chloro-2-amino-1-(2-propynyl)pyridinium bromide 1i: 5-Trifluoromethyl-3-chloro-2-aminopyridine was reacted according to the general procedure (*vide supra*), affording the product as a colourless solid. Yield: 1.17 g, 74% yield. ^{1}H NMR (300 MHz, D_2O): δ (ppm) 8.56 (bs, 1H, py*H*), 8.36 (bd, *J* = 1.8 Hz, 1H, py*H*), 5.12 (d, *J* = 2.4 Hz, 2H, CH_2), 3.13 (t, *J* = 5.1, 2.4 Hz, 1H, C≡C*H*). ^{13}C{^{1}H} NMR (75 MHz, D_2O): δ (ppm) 152.8, 137.6 (q, $^2J_{C\text{-}F}$ = 10.5 Hz, 1C, C5), 137.3 (q, $^3J_{C\text{-}F}$ = 20.4 Hz, 1C, C4 or C6), 123.5 (q, $^1J_{C\text{-}F}$ = 1077.9 Hz, 1C, *C*F_3), 121.3, 116.4 (q, $^3J_{C\text{-}F}$ = 146.4 Hz, 1C, C4 or C6), 79.9, 72.0, 46.7. ^{19}F{^{1}H} NMR (282 MHz, D_2O): δ (ppm) - 62.65. HR-MS (ESI$^+$): *m/z* 235.0244 $[C_9H_7N_2Cl^{35}F_3]^+$ and 237.0212 $[C_9H_7N_2Cl^{37}F_3]^+$, calcd. $[M - Br]^+$ 235.0244, 237.0215, respectively. Anal. calcd. (%) for $C_9H_7N_2ClF_3Br$: C 34.26, H 2.24, N 8.88; found C 34.30, H 2.10, N 8.80.

2-Amino-1-(2-butynyl)pyridinium bromide 1j: 2-Aminopyridine (0.30 g, 3.20 mmol) and 1-bromo-2-butyne (0.34 mL, 3.88 mmol) were added to a small Schlenk flask and stirred vigorously in ethanol (20 mL) at 80 ˚C for 2 hours. The reaction solvent was concentrated under reduced pressure to *ca*. 4 mL volume and left undisturbed at -30 ˚C for 24 hours. The resulting crystalline product was filtered under vacuum, rinsed with cold diethyl ether (2 × 20 mL) and dried *in vacuo* to provide the product as orange needles. Yield: 0.62 g, 86% yield. ^{1}H NMR (300 MHz, D_2O): δ (ppm) 7.98 (d, *J* = 7.2 Hz, 1H,

py*H*), 7.81 (td, *J* = 15.9, 7.2, 1.5 Hz, 1H, py*H*), 7.01 (d, *J* = 7.2 Hz, 1H, py*H*), 6.89 (td, *J* = 15.9, 7.2, 1.5 Hz, 1H, py*H*), 4.86 (q, *J* = 4.8, 2.4 Hz, 2H, CH_2), 1.82 (t, *J* = 4.8, 2.4 Hz, 3H, CH_3). $^{13}C\{^1H\}$ NMR (75 MHz, D_2O): δ (ppm) 153.7, 142.9, 138.4, 115.1, 113.8, 87.5, 68.4, 44.2, 2.7. HR-MS (ESI$^+$): *m/z* 147.0921 $[C_9H_{11}N_2]^+$, calcd. $[M - Br]^+$ 147.0917. Anal. calcd. (%) for $C_9H_{11}N_2Br$: C 47.60, H 4.88, N 12.34; found 47.59, 4.91, 12.20.

3. Preparation of imidazo[1,2-*a*]pyridines 2a-2j

General procedure

N-Propargyl pyridinium bromide derivative (**1a-i**, 1.0 mmol) was added in a single portion to an aqueous solution of sodium hydroxide (1.0 mmol in 10 mL deionised water) and stirred vigorously at room temperature for 2 minutes. The resulting suspension was extracted with ethyl acetate (2 × 20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure to give analytically pure imidazo[1,2-*a*]pyridines, **2a-i**.

2-Methylimidazo[1,2-a]pyridine 2a:[1] 2-Amino-1-(2-propynyl)pyridinium bromide (**1a**) was reacted according to the general procedure (*vide supra*), affording the product as a colourless oil which solidifies under vacuum at room temperature. Yield: 0.13 g, 100% yield. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.24 (dt, *J* = 6.6, 2.1, 0.9 Hz, 1H, py*H*), 7.58 (d, *J* = 9.0 Hz, 1H, py*H*), 7.49 (s, 1H, im*H*), 7.20 (m, 1H, py*H*), 6.80 (td, *J* = 9.0, 6.6, 0.9 Hz, 1H, py*H*), 2.41 (d, *J* = 0.9 Hz, 3H, CH_3). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ (ppm) 143.2, 140.2, 126.5, 126.1, 115.2, 113.3, 110.2, 13.1. HR-MS (ESI$^+$): *m/z* 133.0759 $[C_8H_9N_2]^+$, calcd. $[M + H]^+$ 133.0760. Anal. calcd. (%) for $C_8H_8N_2$: C 72.70, H 6.10, N 21.10; found C 72.70, H 6.50, N 20.75. Lit. data:[1] ^1H NMR (500 MHz, DMSO-d_6) 8.29 (s, 1H, C*H*), 7.59 – 7.03 (m, 4H, py*H*), 1.21 (s, 3H, CH_3). ^{13}C NMR (125 MHz, DMSO-d_6) 148.0, 140.0, 137.1, 130.8, 130.1, 116.2, 114.5, 34.1.

2,7-Dimethylimidazo[1,2-a]pyridine 2b: 4-Methyl-2-amino-1-(2-propynyl)pyridinium bromide (**1b**) was reacted according to the general procedure (*vide supra*), affording the product as an off-white microcrystalline solid. Yield: 0.14 g, 96% yield. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.87 (d, *J* = 6.6 Hz, 1H, py*H*), 7.20 (s, 1H, im*H*), 7.19 (s, 1H, py*H*), 6.52 (dd, *J* = 6.9, 1.5 Hz, 1H, py*H*), 2.40 (s, 3H,

C*H*$_3$), 2.34 (s, 3H, C*H*$_3$). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 145.6, 143.0, 134.8, 124.4, 115.2, 114.3, 108.8, 21.2, 14.3. HR-MS (ESI$^+$): *m/z* 147.0921 $[C_9H_{11}N_2]^+$, calcd. $[M + H]^+$ 147.0917. Anal. calcd. (%) for $C_9H_{10}N_2$: C 73.94, H 6.79, N 19.16; found C 74.03, H 6.81, N 19.11.

2,6-Dimethylimidazo[1,2-a]pyridine 2c: 5-Methyl-2-amino-1-(2-propynyl)pyridinium bromide (**1c**) was reacted according to the general procedure (*vide supra*), affording the product as a pale yellow microcrystalline solid. Yield: 0.15 g of the product monohydrate, 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.78 (br s, 1H, py*H*), 7.38 (d, *J* = 9.2 Hz, 1H, py*H*), 7.21 (s, 1H, im*H*), 6.93 (dd, *J* = 9.2, 1.6 Hz, 1H, py*H*), 2.40 (s, 3H, C*H*$_3$), 2.25 (s, 3H, C*H*$_3$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 144.2, 143.0, 127.2, 123.1, 121.4, 116.2, 109.3, 18.1, 14.4. HR-MS (ESI$^+$): *m/z* 147.0925 $[C_9H_{11}N_2]^+$, calcd. $[M + H]^+$ 147.0917. Anal. calcd. (%) for $C_9H_{10}N_2(H_2O)$: C 65.83, H 7.37, N 17.06; found C 65.60, H 7.50, N 16.70.

2,5-Dimethylimidazo[1,2-a]pyridine 2d: 6-Methyl-2-amino-1-(2-propynyl)pyridinium bromide (**1d**) was reacted according to the general procedure (*vide supra*), affording the product as a pale yellow microcrystalline solid. Yield: 0.14 g, 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.37 (d, *J* = 9.2 Hz, 1H, py*H*), 7.14 (br s, 1H, im*H*), 7.02 (t, *J* = 9.2, 6.8 Hz, 1H, py*H*), 6.49 (d, *J* = 6.8 Hz, 1H, py*H*), 2.45 (s, 3H, C*H*$_3$), 2.43 (s, 3H, C*H*$_3$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 145.5, 143.3, 133.9, 124.2, 114.1, 110.9, 106.6, 18.7, 14.5. HR-MS (ESI$^+$): *m/z* 147.0920 $[C_9H_{11}N_2]^+$, calcd. $[M + H]^+$ 147.0917. Anal. calcd. (%) for $C_9H_{10}N_2$: C 73.94, H 6.89, N 19.16; found C 73.81, H 7.00, N 19.02.

6-Nitro-2-methylimidazo[1,2-a]pyridine 2e: 5-Nitro-2-amino-1-(2-propynyl)pyridinium bromide (**1e**) was reacted according to the general procedure (*vide supra*), affording the product as a bright yellow solid. Bright yellow needles suitable for X-ray crystallographic analysis were obtained *via* slow evaporation of a weak Et_2O solution of the compound. Yield: 0.17 g, 96% yield. %. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.18 (d, *J* = 2.0 Hz, 1H, im*H*), 7.92 (dd, *J* = 10.0, 2.4 Hz, 1H, py*H*), 7.57 (d, *J* = 10.0 Hz, 1H, py*H*), 7.53 (br s, 1H, py*H*), 2.51 (s, 3H, C*H*$_3$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 147.9, 145.2, 137.1, 125.4, 118.4, 116.4, 112.0, 14.8. HR-MS (ESI$^+$): *m/z* 178.0617 $[C_8H_8N_3O_2]^+$, calcd. $[M + H]^+$ 178.0611. Anal. calcd. (%) for $C_8H_7N_3O_2$: C 54.24, H 3.98, N 23.72; found C 54.15, H 3.89, N 23.62.

5-Amino-2-methylimidazo[1,2-a]pyridine 2f: 2, 6-Amino-1-(2-propynyl)pyridinium bromide (**1f**) was reacted according to the general procedure (*vide supra*), affording the product as a brown solid. Yield: 0.14 g, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.43 (br d, *J* = 5.7 Hz, 1H, im*H*), 7.15 – 7.07 (m, 3H, pyr*H*), 4.92 (br s, 2H, NH_2), 3.53 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 153.9, 142.0, 134.9, 121.6, 119.9, 116.6, 107.6, 28.8. HR-MS (ESI$^+$): *m/z* 148.0871 $[C_8H_{10}N_3]^+$, calcd. $[M + H]^+$ 148.0869. Anal. calcd. (%) for $C_8H_9N_3$: C 65.29, H 6.16, N 28.55; found C 65.41, H 6.08, N 28.44.

6-Bromo-2-methylimidazo[1,2-a]pyridine 2g: 5-Bromo-2-amino-1-(2-propynyl)pyridinium bromide (**1g**) was reacted according to the general procedure (*vide supra*), affording the product as a pale yellow microcrystalline solid. Pale yellow blocks suitable for X-ray crystallographic analysis were obtained *via* slow evaporation of a weak Et_2O solution of the compound. Yield: 0.21 g, 99% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.17 (br s, 1H, im*H*), 7.40 (d, *J* = 9.2 Hz, 1H, py*H*), 7.30 (s, 1H, py*H*), 7.17 (d, *J* = 9.2 Hz, 1H, py*H*), 2.44 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 144.6, 143.6, 127.4, 125.3, 117.6, 109.9, 106.4, 14.5. HR-MS (ESI$^+$): *m/z* 210.9875 $[C_8H_8N_2Br^{79}]^+$ and 212.9854 $[C_8H_8N_2Br^{81}]^+$, calcd. $[M + H]^+$ 210.9865, 212.9845, respectively. Anal. calcd. (%) for $C_8H_7N_2Br$: C 45.53, H 3.34, N 13.27; found C 45.40, H 3.90, N 12.85. (N.B. the compound is highly hydrogrospic and more accurate microanalysis results could not be obtained).

6-Iodo-2-methylimidazo[1,2-a]pyridine 2h: 5-Iodo-2-amino-1-(2-propynyl)pyridinium bromide (**1h**) was reacted according to the general procedure (*vide supra*), affording the product as a yellow solid. Yield: 0.26 g, 100% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.27 (t, *J* = 2.4, 1.2 Hz, 1H, im*H*), 7.30 – 7.23 (m incorporating NMR solvent, 3H, py*H*), 2.43 (d, *J* = 0.8 Hz, 3H, CH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 144.2, 143.7, 131.9, 130.2, 118.0, 109.4, 74.5, 14.4. HR-MS (ESI$^+$): *m/z* 258.9741 $[C_8H_8N_2I]^+$, calcd. $[M + H]^+$ 258.9727. Anal. calcd. (%) for $C_8H_7N_2I$: C 37.23, H 2.73, N 10.86; found C 37.26, H 2.86, N 10.71.

8-Chloro-6-trifluoromethyl-2-methylimidazo[1,2-a]pyridine 2i: 5-Trifluoromethyl-3-chloro-2-amino-1-(2-propynyl)pyridinium bromide (**1i**) was reacted according to the general procedure (*vide supra*), affording the product as a colourless microcrystalline solid. Colourless blocks suitable for X-

ray crystallographic analysis were obtained *via* slow evaporation of a weak Et_2O solution of the compound. Yield: 0.23 g, 98% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.17 (dd, *J* = 1.8, 0.6 Hz, 1H, py*H*), 7.29 (s, 1H, im*H*), 7.17 (dd, *J* = 9.6, 1.8 Hz, 1H, py*H*), 2.43 (s, 3H, C*H*$_3$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 146.3, 142.3, 124.9 (q, $^1J_{C\text{-}F}$ = 1077.9 Hz, 1C, *C*F_3), 123.6, 122.9 (q, $^3J_{C\text{-}F}$ = 21.6 Hz, 1C, C5 or C7), 119.0 (q, $^2J_{C\text{-}F}$ = 11.1 Hz, 1C, C6), 116.5 (q, $^3J_{C\text{-}F}$ = 138.0 Hz, 1C, C5 or C7), 112.7, 14.6, 1.1. ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$): δ (ppm) – 61.92. HR-MS (ESI$^+$): *m/z* 235.0253 $[C_9H_7N_2Cl^{35}F_3]^+$ and 237.0217 $[C_9H_7N_2Cl^{37}F_3]^+$, calcd. $[M + H]^+$ 235.0244, 237.0215, respectively. Anal. calcd. (%) for $C_9H_6N_2ClF_3$: C 46.08, H 2.58, N 11.94; found C 46.10, H 2.60, N 11.80.

2-Ethyl-imidazo[1,2-a]pyridine 2j:[2] 2-Amino-1-(2-butynyl)pyridinium bromide (**1j**) (100 mg, 0.44 mmol) was dissolved in anhydrous *tert*-butanol (10mL) at 30 °C in a small Schleck tube. KO^{t}Bu (54 mg, 0.48 mmol, 1.1 equiv.) was then added in one portion with vigorous stirring. Immediate formation of a white precipitate was observed. The reaction was stirred for 1 hour under nitrogen and the solvent was removed under high vacuum at room temperature to leave a brown oil. ^{1}H NMR spectra of this crude product showed complete conversion of the starting material to product **2j**. Isolated yield after extraction with EtOAc (3 x 20 mL): 31.5 mg, 49% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.04 (dt, *J* = 6.8, 1.1 Hz, 1H), 7.52 (d, *J* = 9.1 Hz, 1H), 7.34 (s, 1H), 7.10 (ddd, J = 9.1, 6.8, 1.3 Hz, 1H), 6.71 (td, *J* = 6.8, 1.1 Hz, 1H), 2.83 (qd, *J* = 7.6, 0.7 Hz, 2H), 1.35 (t, *J* = 7.6 Hz, 3H). ^{1}H NMR (500 MHz, D_2O): δ (ppm) 8.32 (dt, *J* = 6.8, 1.1 Hz, 1H), 7.61 (d, *J* = 0.5 Hz, 1H), 7.49 (dq, *J* = 9.0, 0.7 Hz, 1H) 7.35 (ddd, J = 9.0, 6.8, 1.2 Hz, 1H), 6.93 (td, *J* = 6.8, 1.0 Hz, 1H), 2.79 (qd, *J* = 7.6, 0.7 Hz, 2H), 1.32 (t, *J* = 7.6 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, D_2O): δ (ppm) 148.6, 145.3, 126.7, 126.4, 115.0, 112.7, 109.7, 21.1, 12.9. Lit. data:[2] ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.05 (d, *J* = 7.0 Hz, 1H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.34 (s, 1H), 7.12 (t, *J* = 8.0 Hz, 1H), 6.73 (t, *J* = 6.5 Hz, 1H), 2.84 (q, *J* = 7.5 Hz, 2H), 1.35 (t, J = 7.5 Hz, 3H).

4. Preparation of imidazo[1,2-*a*]pyridinium salts 3

1-(2-Pyridyl)methyl-2-methylimidazo[1,2-a]pyridinium bromide 3ak: 2-Methylimidazo[1,2-*a*]pyridine (**2a**) (0.20 g, 1.5 mmol), 2-bromomethylpyridine hydrobromide (0.40 g, 1.6 mmol) and

acetonitrile (30 mL) were charged to a round-bottomed flask and stirred vigorously at 60 ˚C for 4 hours. Upon cooling to ambient temperature, slow addition of diethyl ether (80 mL) led to precipitation of the product as an off-white microcrystalline solid, which was collected *via* vacuum filtration and rinsed with cold diethyl ether (3 × 30 mL). Recrystallization of the resulting solid from acetonitrile/diethyl ether delivered the pure title compound as a microcrystalline colourless powder. Yield: 0.37 g, 80% yield. ^{1}H NMR (300 MHz, CD_3CN): δ (ppm) 8.68 (d, *J* = 6.9 Hz, 1H, py*H*), 8.42 (d, *J* = 4.5 Hz, 1H, py*H*), 7.99 – 7.86 (m, 3H, im*H* and py*H*), 7.82 (td, *J* = 15.3, 7.8, 1.5 Hz, 1H, *N*-py*H*), 7.50 (d, *J* = 7.8 Hz, 1H, *N*-py*H*), 7.43 (td, *J* = 15.3, 7.8, 1.5 Hz, 1H, *N*-py*H*), 7.31 (dd, *J* = 7.8, 5.1 Hz, 1H, (*N*-py*H*), 5.67 (s, 2H, CH_2), 2.50 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (100 MHz, D_2O): δ (ppm) 151.7, 148.3, 139.2, 137.8, 134.4, 132.8, 128.0, 123.1, 121.3, 116.6, 111.8, 109.5, 47.2, 8.2. HR-MS (ESI$^+$): *m/z* 224.1191 $[C_{14}H_{14}N_3]^+$, calcd. $[M - Br]^+$ 224.1182. Anal. calcd. (%) for $C_{14}H_{14}N_3Br$: C 55.28, H 4.64, N 13.81; found C 55.40 H 5.00, N 13.70.

1-Methyl-2,7-dimethylimidazo[1,2-a]pyridinium iodide 3bl: 2,7-Dimethylimidazo[1,2-*a*]pyridine (**2b**) (0.22 g, 1.5 mmol), methyl iodide (0.19 mL, 3.0 mmol) and acetonitrile (30 mL) were charged to a small round-bottomed flask and stirred vigorously at 60 ˚C for 4 hours. Upon cooling to ambient temperature, slow addition of diethyl ether (40 mL) led to precipitation of the product as an off-white microcrystalline solid, which was collected *via* vacuum filtration and rinsed with cold diethyl ether (3 × 30 mL). Recrystallization of the resulting solid from acetonitrile/diethyl ether delivered the pure title compound as a microcrystalline colourless powder. Yield: 0.40 g, 93% yield. ^{1}H NMR (300 MHz, CD_3CN): δ (ppm) 8.50 (d, *J* = 6.9 Hz, 1H, py*H*), 7.83 (s, 1H, im*H*), 7.72 (s, 1H, py*H*), 7.25 (d, *J* = 6.9 Hz, 1H, py*H*), 3.81 (s, 3H, *N*-CH_3), 2.56 (s, 3H, CH_3), 2.47 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (100 MHz, CD_3CN): δ (ppm) 146.7, 141.0, 135.8, 128.8, 120.1, 112.3, 110.3, 31.6, 21.8, 9.9. HR-MS (ESI$^+$): *m/z* 161.1074 $[C_{10}H_{13}N_2]^+$, calcd. $[M - I]^+$ 161.1073. Anal. calcd. (%) for $C_{10}H_{13}N_2I$: C 41.69, H 4.55, N 9.72; found C 41.60, H 4.50, N 9.55.

1-Methyl-6-bromo-2-methylimidazo[1,2-a]pyridinium iodide 3gl: 6-Bromo-2-methylimidazo[1,2-*a*]pyridine (**2g**) (0.32 g, 1.5 mmol), methyl iodide (0.19 mL, 3.0 mmol) and acetonitrile (30 mL) were charged to a small round-bottomed flask and stirred vigorously at 60 ˚C for 4 hours. Upon cooling to

ambient temperature, slow addition of diethyl ether (40 mL) led to precipitation of the product as an orange microcrystalline solid, which was collected *via* vacuum filtration and rinsed with cold diethyl ether (3 × 30 mL). Recrystallization of the resulting solid from acetonitrile/diethyl ether delivered the pure title compound as a microcrystalline pale orange powder. X-ray quality crystals suitable for crystallographic analysis were obtained *via* slow diffusion of diethyl ether vapours into a concentrated acetonitrile solution of the compound. Yield: 0.48 g, 90 % yield. ^{1}H NMR (300 MHz, CD_3CN): δ (ppm) 8.86 – 8.85 (m, 1H, BrCC*H*N), 8.00 (dd, *J* = 9.9, .8 Hz, 1H, py*H*), 7.89 (br s, 1H, im*H*), 7.83 (d, *J* = 9.9 Hz, 1H, py*H*), 3.86 (s, 3H, *N*-CH_3), 2.50 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (100 MHz, D_2O): δ (ppm) 136.3, 135.6, 128.7, 111.9, 111.1, 110.9, 30.5, 8.9. HR-MS (ESI^+): *m/z* 225.0024 $[C_9H_{10}N_2Br^{79}]^+$ and 227.0004 $[C_9H_{10}N_2Br^{81}]^+$, calcd. $[M - I]^+$ 225.0022, 227.0001, respectively. Anal. calcd. (%) for $C_9H_{10}N_2IBr$: C 30.62, H 2.86, N 7.94; found C 31.01, H 2.83, N 8.20.

1-Allyl-8-chloro-6-trifluoromethyl-2-methylimidazo[1,2-a]pyridinium bromide 3im: 8-Chloro-6-trifluoromethyl-2-methylimidazo[1,2-*a*]pyridine (**2i**) (0.35 g, 1.5 mmol), allyl bromide (0.23 mL, 3.0 mmol) and acetonitrile (30 mL) were charged to a small round-bottomed flask and stirred vigorously at 60 ˚C for 4 hours. Upon cooling to ambient temperature, slow addition of diethyl ether (40 mL) led to precipitation of the product as an off-white microcrystalline solid, which was collected *via* vacuum filtration and rinsed with cold diethyl ether (3 × 30 mL). Recrystallization of the resulting solid from acetonitrile/diethyl ether delivered the pure title compound as a microcrystalline colourless powder. X-ray quality crystals suitable for crystallographic analysis were obtained *via* slow diffusion of diethyl ether vapours into a concentrated acetonitrile solution of the compound. Yield: 0.53 g, 100% yield. ^{1}H NMR (300 MHz, CD_3CN): δ (ppm) 9.95 (s, 1H, py*H*), 8.80 (s, 1H, py*H*), 8.19 (s, 1H, im*H*), 6.19 – 6.06 (m, 1H, C=C*H*CH_2), 5.38 (m, 3H, NCH_2 and C=C*H*), 5.01 (dt, *J* = 17.1, 3.6, 1.8 Hz, 1H, C=C*H*), 2.55 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (100 MHz, D_2O): δ (ppm) 138.4, 136.7, 131.5, 130.2 (q, $^{2}J_{C\text{-}F}$ = 16.4 Hz, 1C, C6), 127.5 (q, $^{3}J_{C\text{-}F}$ = 5.0 Hz, 2C, C5 and C7), 123.2, 120.9 (q, $^{1}J_{C\text{-}F}$ = 107.8 Hz, 1C, CF_3), 120.5, 119.2, 117.7, 115.0, 48.4, 9.4. ^{19}F{^{1}H} NMR (282 MHz, D_2O): δ (ppm) – 61.41. HR-MS (ESI^+): *m/z* 275.0564 $[C_{12}H_{11}N_2Cl^{35}F_3]^+$ and 277.0531 $[C_{12}H_{11}N_2Cl^{37}F_3]^+$ (relative intensities 3:1),

calcd. $[M - Br]^+$ 275.0557, 277.0528, respectively. Anal. calcd. (%) for $C_{12}H_{11}N_2BrClF_3$: C 40.53, H 3.12, N 7.88; found C 40.60, H 3.00, N 7.90.

1-Benzyl-8-chloro-6-trifluoromethyl-2-methylimidazo[1,2-a]pyridinium bromide 3ik: 8-Chloro-6-trifluoromethyl-2-methylimidazo[1,2-*a*]pyridine (**2i**) (0.35 g, 1.5 mmol), benzyl bromide (0.36 mL, 3.0 mmol) and acetonitrile (30 mL) were charged to a small round-bottomed flask and stirred vigorously at 60 ˚C for 4 hours. Upon cooling to ambient temperature, slow addition of diethyl ether (40 mL) led to precipitation of the product as an off-white microcrystalline solid, which was collected *via* vacuum filtration and rinsed with cold diethyl ether (3 × 30 mL). Recrystallization of the resulting solid from acetonitrile/diethyl ether delivered the pure title compound as a microcrystalline colourless powder. X-ray quality crystals suitable for crystallographic analysis were obtained *via* slow diffusion of diethyl ether vapours into a concentrated acetonitrile solution of the compound. Yield: 0.46 g, 75% yield. ^{1}H NMR (300 MHz, CD_3CN): δ (ppm) 9.62 (s, 1H, py*H*), 8.54 (s, 1H, py*H*), 8.21 (s, 1H, im*H*), 7.40 – 7.38 (m, 3H, ph*H*), 7.15 – 7.12 (m, 2H, ph*H*), 6.01 (s, 2H, C*H*$_2$), 2.49 (s, 3H, C*H*$_3$). ^{13}C{^{1}H} NMR (100 MHz, D_2O): δ (ppm) 138.7, 136.9, 134.7, 130.6 (q, $^2J_{C\text{-}F}$ = 16.0 Hz, 1C, C6), 129.2, 128.4, 127.7 (q, $^3J_{C\text{-}F}$ = 10.0 Hz, 2C, C5 and C7), 125.7, 121.1 (q, $^1J_{C\text{-}F}$ = 108.4 Hz, 1C, CF_3), 119.1, 115.3, 49.3, 9.4. ^{19}F{^{1}H} NMR (282 MHz, D_2O): δ (ppm) – 62.56. HR-MS (ESI$^+$): *m/z* 325.0719 $[C_{16}H_{13}N_2ClF_3]^+$ and 327.0689 $[C_{16}H_{13}N_2Cl^{37}F_3]^+$, calcd. $[M + H]^+$ 325.0714, 327.0684. Anal. calcd. (%) for $C_{16}H_{13}N_2BrClF_3$: C 47.38, H 3.23, N 6.91; found C 47.50, H 3.05, N 6.80.

5. Solvent/base screening experiments

Table S1. Summary of solvent/base screening experiments

Entry	Base[a]	Solvent[b]	Time (min)	T (˚C)[c]	Yield (%)[d]
1	Na_2CO_3	H_2O	20	40	94
2		MeOH	20	40	59
3		EtOH	20	40	50
5	K_2CO_3	H_2O	5	40	90
6		MeOH	20	40	77
7		EtOH	20	40	44
9	Cs_2CO_3	H_2O	5	r.t.	93
10		MeOH	5	r.t.	90
11		EtOH	5	r.t.	96
13	KOH	H_2O	2	r.t.	>99

14		MeOH	5	r.t.	95
15		EtOH	20	40	90
17	NaOH	H_2O	2	r.t.	>99
18		MeOH	5	r.t.	95
19		EtOH	5	r.t.	95
21	DABCO	H_2O	2	r.t.	>99
22		MeOH	5	r.t.	97
23		EtOH	5	r.t.	93
25		DMSO (dry)	2	r.t	0
26		DMSO + H_2O (20 mol%)	2	r.t	15
27	NEt_3	H_2O	30	r.t.	48
29		MeOH	30	r.t.	55
30		EtOH	30	r.t.	51
31	$^{i}PrEt_2N$	H_2O	30	r.t.	30
32		MeOH	30	r.t.	39
33		EtOH	30	r.t.	30

[a]Reagent grade bases; [b]MeOH/EtOH are miscible with CH_2Cl_2, therefore deionised H_2O also added during work-up to extract byproducts; [c]temperature required to dissolve base; [d]isolated yield.

6. Sub-stoichometric base reaction

2-amino-1-(2-propynyl)pyridinium bromide, **1a** (0.10 g, 0.47 mmol) was dissolved in a freshly prepared solution of NaOH in deionised water (5 mL of an 18.8 mM stock solution, 0.094 mmoles, 0.2 eq. relative to substrate) and stirred vigorously for 10 minutes. Following reaction, the cyclised product, **2a**, was isolated as above. Yield: 11 mg, 0.086 mmol, 18 %.

7. Labelling experiment

A standard reaction of 4-methyl-2-amino-1-(2-propynyl)pyridinium bromide **1b** (8.0 mg, 0.035 mmol) in a solution of NaOH (2.8 mg, 0.070 mmol) in D_2O (0.40 mL) was performed in an NMR tube with vigorous shaking. ^1H NMR spectrum of the final solution after 10 minutes showed only 1 methyl signal at 2.19 ppm, in contrast to the normally observed 2 methyl signals in product **2b** ($CDCl_3$).

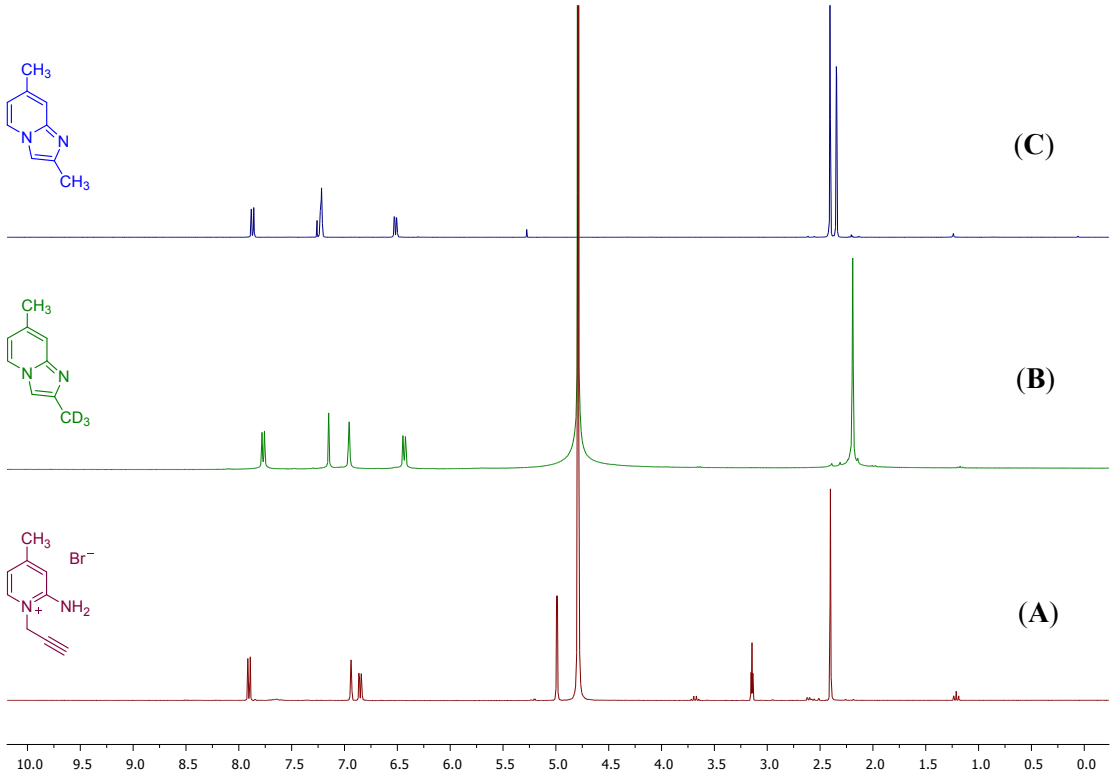
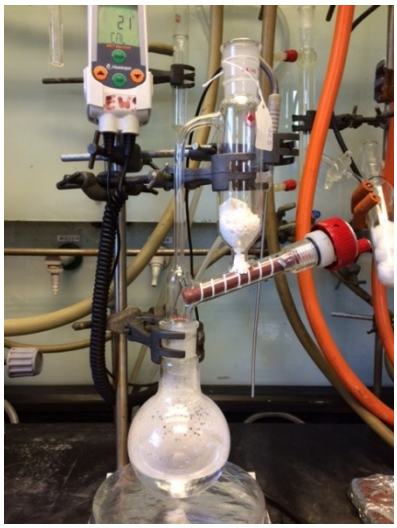
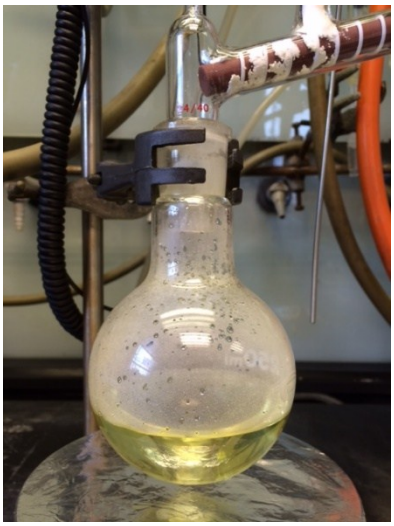


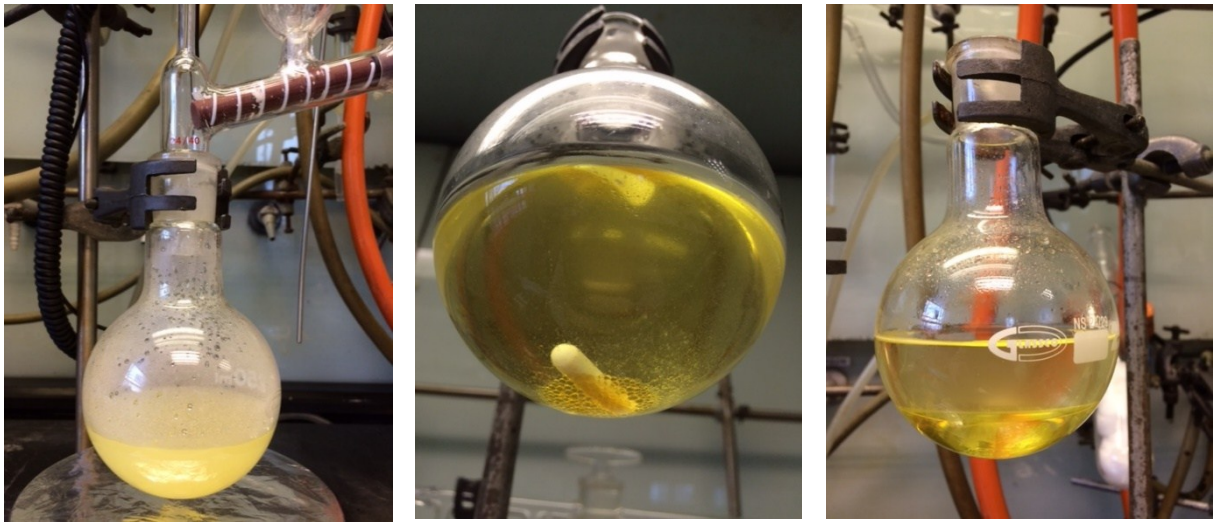
Figure S1. (**A**): ^{1}H NMR (300 MHz, D_2O, 298 K) spectrum of pyridinium bromide **1b**; (**B**): ^{1}H NMR (300 MHz, D_2O, 298 K) spectrum of imidazopyridine **2b** produced in D_2O; (**C**): ^{1}H NMR (300 MHz, $CDCl_3$, 298 K) spectrum of imidazopyridine **2b** produced in H_2O.

8. Scaled up synthesis of imidazo[1,2-*a*]pyridine 2a


Before addition of **1a**


Colour change as soon as addition started


Deeper colour as reaction progressed



Fine suspension at the end of the reaction | Phase separation | Completed phase separation

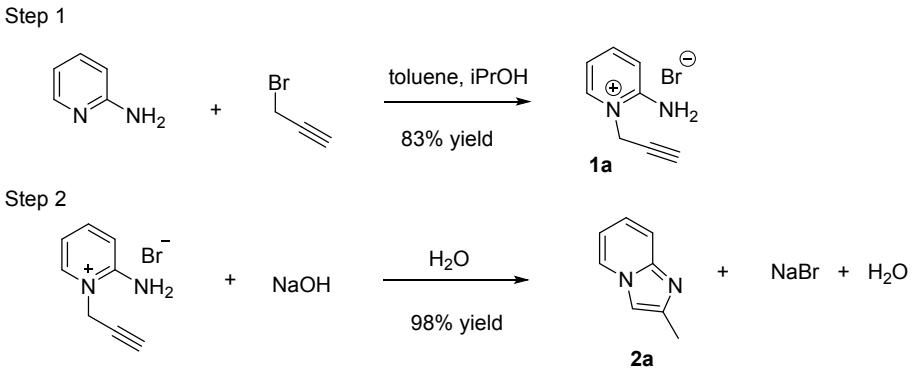
Figure S2. 10 g scale cyclisation reaction of pyridinium bromide, **1a**, to imidazopyridine, **2a**.

2-Aminopyridine (6.12 g, 65.0 mmol), propargyl bromide (11.6 g of an 80 wt.% solution in toluene, 78 mmol, 1.2 equiv) and 2-propanol (200 mL) charged to a round bottomed flask and stirred at 50 °C for 2 hours. After which, a pale yellow solid precipitated from solution. This was filtered and washed with diethyl ether (2 x 30 mL) followed by drying *in vacuo* to give product 1a in 11.1 g (52 mmol, 80% isolated yield).

To a stirring solution of NaOH (1.90 g, 47.5 mmol) in deionised H_2O (70 mL) was added 2-amino-1-(2-propynyl)pyridinium bromide **1a** (10.0 g, 47.0 mmol) *via* powder addition funnel (**a**) over a period of 5 minutes. Immediately upon addition, the solution phase turned yellow (**b** – **d**) and a yellow oil became dispersed as a distinct separate phase (**e**). The oil (product) was subsequently extracted into EtOAc (2 × 30 mL) (**f**), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to afford imidazo[1,2-*a*]pyridine **2a** as a spectroscopically pure pale yellow oil. Yield: 6.12 g, 98% yield.

9. Calculation of green metrics

Our process



Compound In	Product	Waste	MW	Amount (g)
2-Aminopyridine		20% unreacted	94.12	6.12
Propargyl bromide		0.4 eq unreacted	118.96	9.28
Toluene		Toluene	92.14	2.32
Isopropanol		Isopropanol	60.10	157.2
Diethyl ether		Diethyl ether	74.12	42.8
		Excess 2-Aminopyridine	94.12	1.224
		Excess Propargyl bromide	118.96	3.093
	1a		213.08	11.1
1a		2% of **1a**	213.08	10.0
NaOH		1.44 mmol	40.00	1.90
		NaBr	102.89	4.74
H_2O			18.02	70.0
		H_2O	18.02	0.83
	2a		132.17	6.12
EtOAc		EtOAc	88.11	53.4
		Excess **1a**	213.08	0.2
		Excess NaOH	40.00	0.0576

Atom Economy defined as

molecular mass of desired product / molecular mass of all reactants × 100%

$$AE = 132.17 / (118.96 + 94.12 + 40.00) \times 100\% = 52\%$$

E-Factor (excluding water) defined as

Total mass of waste (excluding water as reaction media) for 2 steps (with scaling of the 1st step) / mass of product

EF = {[(2.32 + 157.2 + 42.8 + 1.224 + 3.093) × 10 / 11.1] + (0.2 + 0.0576 + 4.74 + 0.83 + 53.4)}/6.12

186.159459 + 59.2276= 40.1 g waste / g product

E-Factor (including water) defined as

EF = {[(2.32 + 157.2 + 42.8 + 1.224 + 3.093) × 10 / 11.1] + (0.2 + 0.0576 + 4.74 + 0.83 + 53.4 + 70.0)}/6.12

= 51.5 g waste / g product

Effective Mass Yield defined as

Effective mass yield (%) = mass of isolated product × 100% / mass of non-benign reagents (ignoring solvents)

EMY = 6.12 × 100% / [(6.12 + 9.28) × 10 / 11.1 + 1.90] = 39%

Reaction Mass Efficiency as defined by Curzons *et al* .[3]

Mass of isolated product × 100% / total mass of reactants used in reaction

Stage 1: RME = 11.1 × 100% / (6.12 + 9.28) = 72%

Stage 2: RME = 6.12 × 100% / (10.0 + 1.90) = 51%

Process Mass Intensity defined as

Total mass of materials used in 2 reactions (with scaling of the 1st step) / mass of product (not including water)

PMI = ((6.12 + 9.28 + 2.3 + 157.2 + 42.8) × 10.0 / 11.1 + **(**1.90 + 10 + 53.4) / 6.12 = 42.7

Space-time yield defined as

mass of product / total reaction volume × time

Stage 1a

Reaction volume = 218 mL (assuming unknown reactant densities of 1)

STY = 11.1 / (0.218 × 120) = 0.42 $g.L^{-1}.min^{-1}$

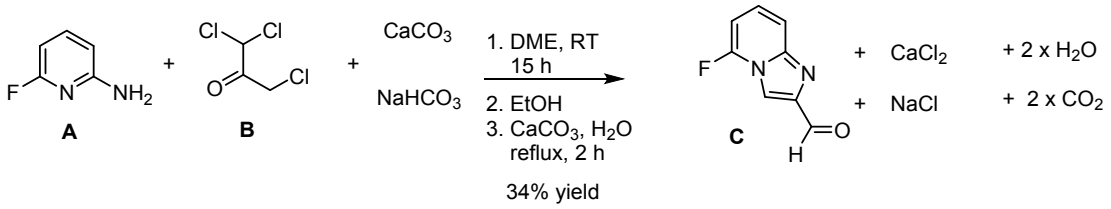
Stage 1b

Reaction volume = 112 mL (maximum process volume)

STY = 6.12 / (0.112 × 5) = 10.9 $g.L^{-1}.min^{-1}$

Literature process 1:

(Sharp *et al.*, *OPRD* **2009**, *13*, 781; Gudmunsson, Boggs, Davids, PCT Int. Appl. WO 2006026703, 2006).



"5-Fluoroimidazo[1,2-a]pyridine-2-carbaldehyde. To a solution of 6-fluoro-2-pyridinamine (Tetrahedron, 2002, 58, 489, incorporated by reference with regard to such) (2.8 g, 25 mmol) in ethylene glycol dimethyl ether (28 mL) was added trichloroacetone (7.9 mL, 75 mmol). The mixture was stirred at room temperature for 15 hours and the resulting precipitate was collected by filtration and refluxed in ethyl alcohol (8 mL) for 4 hours. The reaction mixture was cooled to room temperature, concentrated, dissolved in dichloromethane and washed with saturated aqueous sodium bicarbonate. The organic layer was isolated, dried with magnesium sulfate, and concentrated. The resulting solid was refluxed in aqueous calcium carbonate for 2 hours, cooled to room temperature, and extracted with dichloromethane. The organic layer was dried with magnesium sulfate and concentrated to give 1.4 g (34% yield) 5-fluoroimidazo[1,2-a]pyridine-2-carbaldehyde as a tan solid."

Due to the lack of precise information on the amount of $NaHCO_3$ and $CaCO_3$ employed, calculations were performed using the minimal required amount of these reagents. Solvent required for washing the filtration in step 1 was ignored.

Compound In	Product	Waste	MW	Amount (g)
A		66% unreacted	112.11	2.80
B 3 eq.		2.66 eq. excess	161.41	12.11
H_2O		H_2O		50.0 (est. for both saturated $NaHCO_3$ and $CaCO_3$ (solubility 15 mg/L at 25 °C) based on

				total aqueous volume in literature process 2)
$CaCO_3$			100.09	2.5 (est.)
$NaHCO_3$			84.01	2.1 (est.)
DME		DME	90.12	24.3
Ethanol		Ethanol	46.07	6.31
DCM		DCM	84.93	12 (est.)
$MgSO_4$		$MgSO_4$	120.37	1 (est.)
	C		164.14	1.40
		$CaCl_2$	110.98	0.94
		NaCl	58.44	0.50
		H_2O (product)	18.02	0.31
		CO_2	44.01	0.75
		Excess **B**	161.41	10.74
		Excess **A**	112.11	1.85

Atom Economy defined as

molecular mass of desired product / molecular mass of all reactants × 100%

$$AE = 164.14 / (112.11 + 161.41 + 100.09 + 84.01) \times 100\% = 36\%$$

E-Factor (excluding water) defined as

Total mass of waste / mass of product

$$EF = (24.3 + 6.31 + 12 + 1 + 0.94 + 0.50 + 0.31 + 0.75 + 10.74 + 1.85) / 1.40$$

$$= 41.9 \text{ g waste / g product}$$

E-Factor (including water) defined as

$$EF = (24.3 + 6.31 + 12 + 1 + 0.94 + 0.50 + 0.31 + 0.75 + 10.74 + 1.85 + 50) / 1.40$$

$$= 77.6 \text{ g waste / g product}$$

Effective Mass Yield defined as

Effective mass yield (%) = mass of isolated product × 100% / mass of non-benign reagents (ignoring solvents)

$$EMY = 1.40 \times 100\% / (2.80 + 12.11 + 2.5 + 2.1) = 7.2\ \%$$

Reaction Mass Efficiency as defined by Curzons *et al.*[3]

Mass of isolated product × 100% / total mass of reactants used in reaction

$$EMY = 1.40 \times 100\% / (2.80 + 12.11 + 2.5 + 2.1) = 7.2\ \%$$

Process Mass Intensity defined as

Total mass of materials used in reaction / mass of product (not including water)

$$PMI = (2.8 + 12.11 + 2.5 + 2.1 + 24.3 + 6.31 + 12 + 1) / 1.40 = 45.1$$

Space-time yield defined as

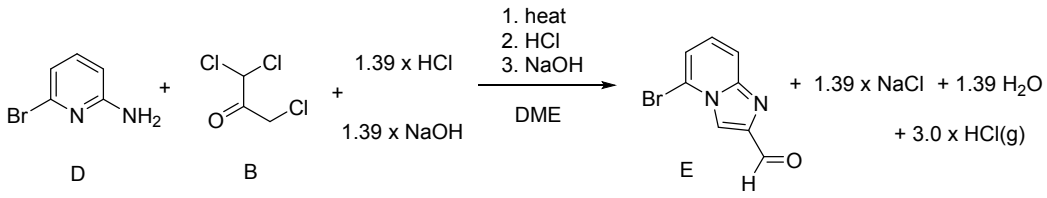
mass of product / total reaction volume × time

$$\text{Reaction volume} = 28 + 7.9 + 2.8 \approx 39\ \text{mL}$$

$$\text{Reaction time} = 15 + 4 + 2 = 21\ \text{hours} = 1260\ \text{mins}$$

$$STY = 1.40 / (0.039 \times 1260) = 0.03\ g.L^{-1}.min^{-1}$$

Literature process 2: Sharp *et al.*, *OPRD* 2009, *13*, 781; Gudmunsson, Boggs, Davids, PCT Int. Appl. WO 2006026703, 2006).



"2-Amino-6-bromopyridine (D) (3.0 kg, 17.3 mol) and dimethoxyethane (12 L) were combined and stirred at 25 °C under nitrogen. 1,1,3-Trichloroacetone (B) (5.6 kg, 30.3 mol) was added to the solution in a single portion, and the reaction was warmed to 65°C (jacket temperature) and maintained for ~2-4 h until judged complete by HPLC. The reaction was cooled to 10 °C, held for ~1 h and filtered. The solids were rinsed with dimethoxyethane (6 L). The solids were placed back in the reactor and treated with dimethoxyethane (12 L) and 2 N HCl (12 L) and warmed to ~75 °C for 16-20 h or until judged complete by HPLC. The reaction was cooled to ~10 °C, and the pH was adjusted to ~8 with 3N NaOH. The resulting solids were filtered and washed with water (10 L). The solids were dried at 50 °C for 16 h to yield (E) as an off-white solid (2.81 kg, 72% yield)."

Most of the HCl generated by the reaction is assumed to be washed off and evaporated during heating. The NaOH solution is assumed to quench the added amount of 2N HCl in 12 L.

Compound In	Product	Waste	MW	Amount (kg)
D		28% unreacted	173.01	3.0
B (2eq. based on 5.6 kg mass)		128% unreacted	161.41	5.6
DME		DME	90.12	10.41
DME (wash)		DME	90.12	5.21
DME		DME	90.12	10.41
2N HCl			36.46	12.0
3N NaOH			40.00	8.0 (est.)
	E		225.05	2.81
		NaCl	58.44	1.40
H_2O (from HCl and NaOH solution)		H_2O (from HCl and NaOH solution)	18.02	20.0
H_2O (wash)		H_2O (wash)	18.02	10.0
		H_2O (product)	18.02	0.43
		HCl	36.46	1.89
		Excess **D**	173.01	0.84
		Excess **B**	161.41	3.58

Atom Economy defined as

molecular mass of desired product / molecular mass of all reactants × 100%

$$AE = 225.05 / (173.01 + 161.41 + 1.39 \times 36.46 + 1.39 \times 40.00) \times 100\% = 51\%$$

E-Factor (excluding water) defined as

Total mass of waste / mass of product

$$EF = (10.41 + 5.21 + 10.41 + 1.40 + 1.89 + 0.84 + 3.58) / 2.81$$

$$= 12.0 \text{ kg waste / kg product}$$

E-Factor (including water) defined as

$$EF = (10.41 + 5.21 + 10.41 + 1.40 + 1.89 + 0.84 + 3.58 + 20.0 + 10.0 + 0.43) / 2.81$$

$$= 22.8 \text{ kg waste / kg product}$$

Effective Mass Yield defined as

Effective mass yield (%) = mass of product × 100% / mass of non-benign reagents (ignoring solvents)

$$EMY = 2.81 \times 100\% / [3.0 + 5.6 + 0.024 \times (36.46 + 40.00)] = 27\ \%$$

Reaction Mass Efficiency as defined by Curzons *et al*.[3]

Mass of isolated product × 100% / total mass of reactants used in reaction

$$RME = 2.81 \times 100\% / [3.0 + 5.6 + 0.024 \times (36.46 + 40.00)] = 27\ \%$$

Process Mass Intensity defined as

Total mass of materials used in reaction / mass of product (not including water)

$$PMI = (3.0 + 5.6 + 10.41 + 5.21 + 10.41 + 12.0 + 8.0) / 2.81 = 19.4$$

Space-time yield defined as

mass of product / total reaction volume × time

$$\text{Reaction volume} = 12 + 12 + 8 = 32\ L$$

$$\text{Reaction time} = 4 + 1 + 20 = 25\ h\ \text{(not including the 16 h of drying)}$$

$$STY = 2810 / (32 \times 25 \times 60) = 0.059\ g.L^{-1}.min^{-1}$$

10. ^{1}H, ^{13}C and ^{19}F NMR spectral data of *N*-propargyl pyridinium bromides 1a-j

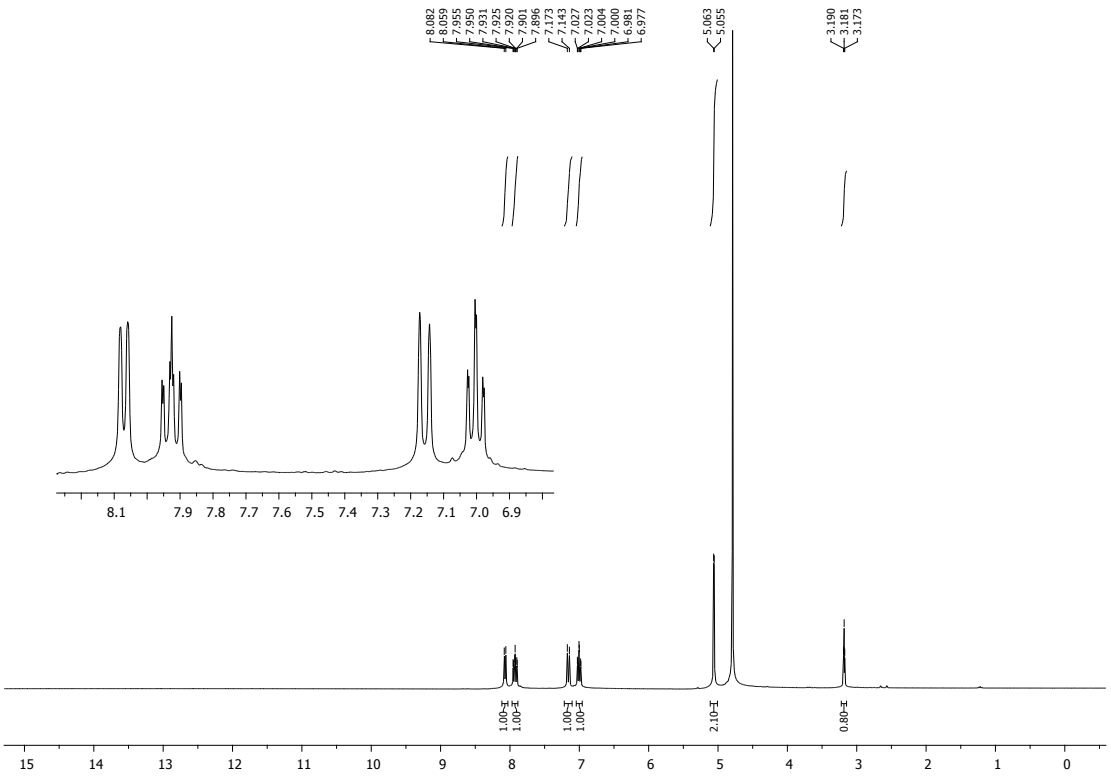


Figure S1. ^{1}H NMR (300 MHz, D_2O) spectrum of compound **1a**.

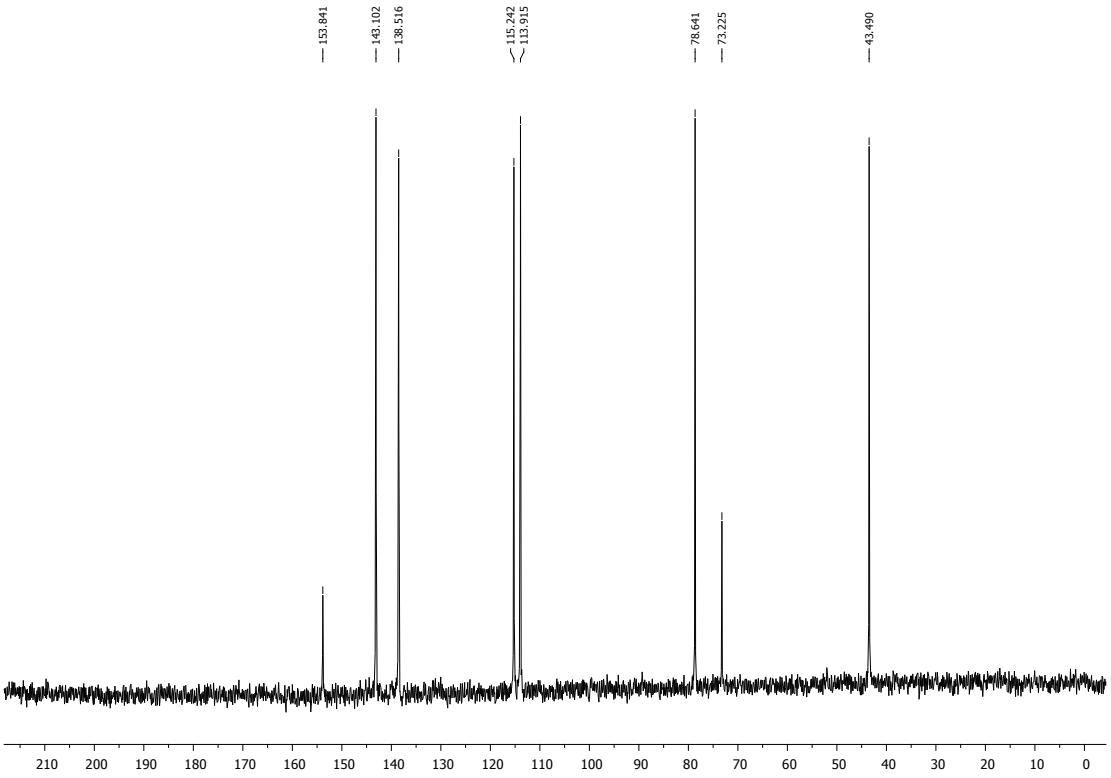


Figure S2. $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O) spectrum of compound **1a**.

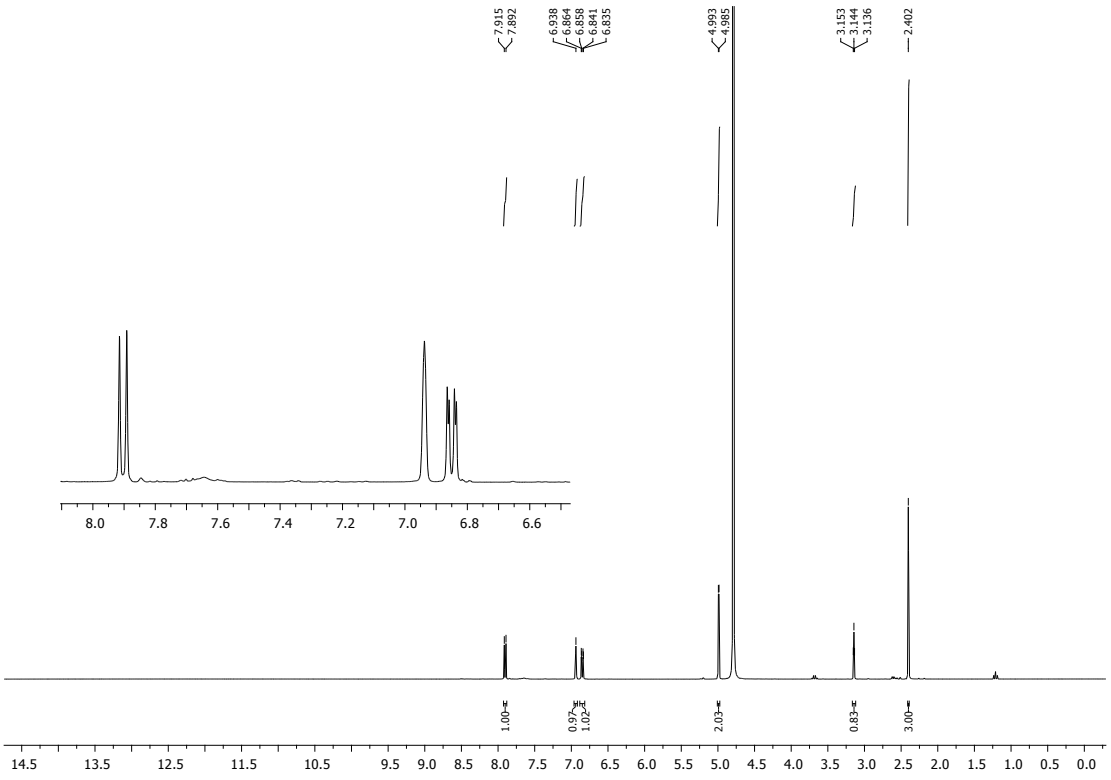


Figure S3. ^{1}H NMR (300 MHz, D_2O) spectrum of compound **1b**.

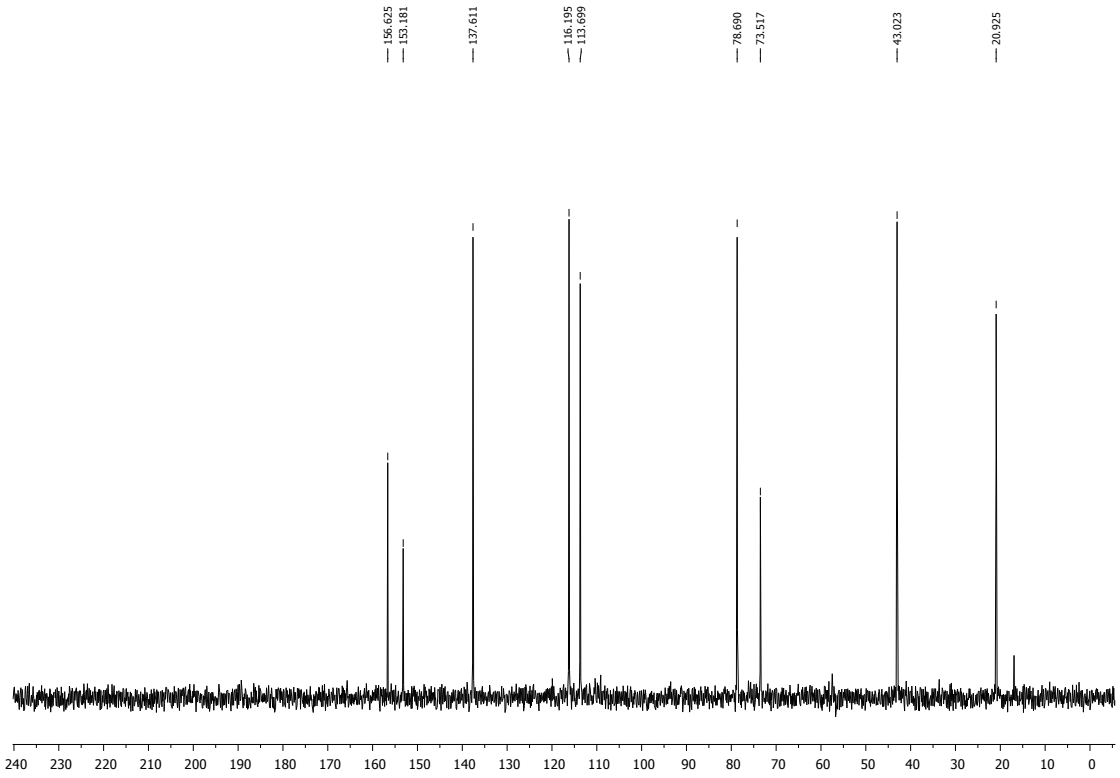


Figure S4. $^{13}C\{^{1}H\}$ NMR (75 MHz, D_2O) spectrum of compound **1b**.

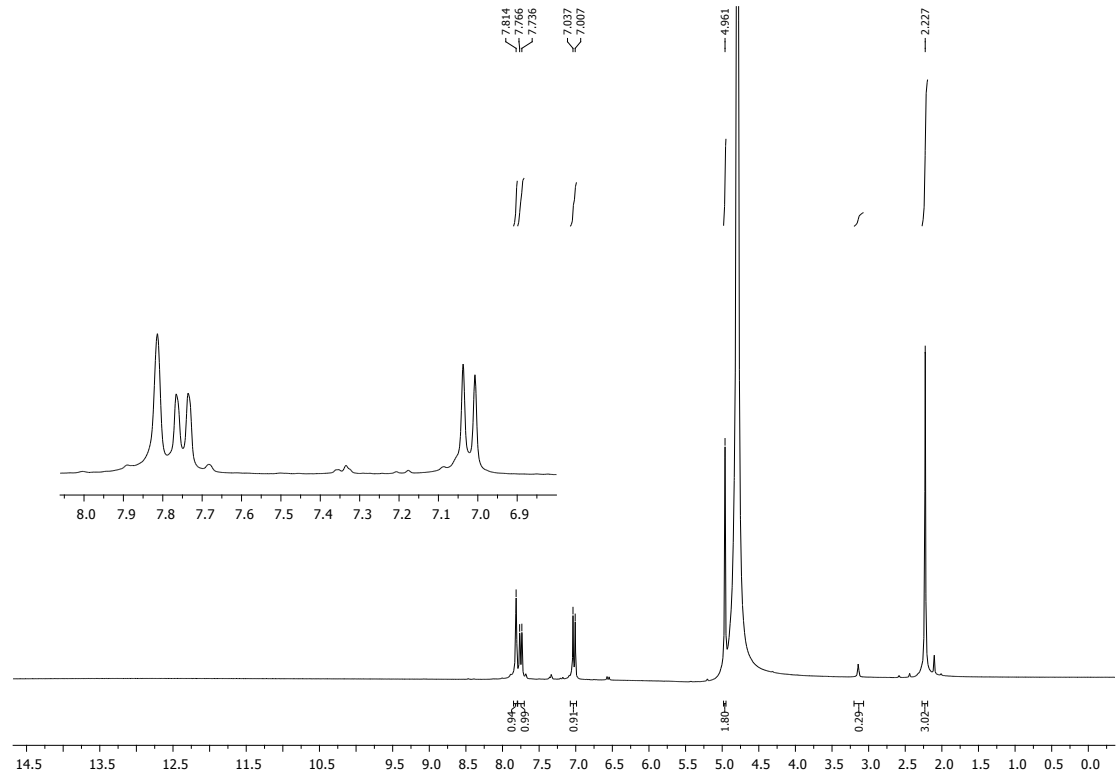


Figure S5. ^{1}H NMR (300 MHz, D_2O) spectrum of compound **1c**.

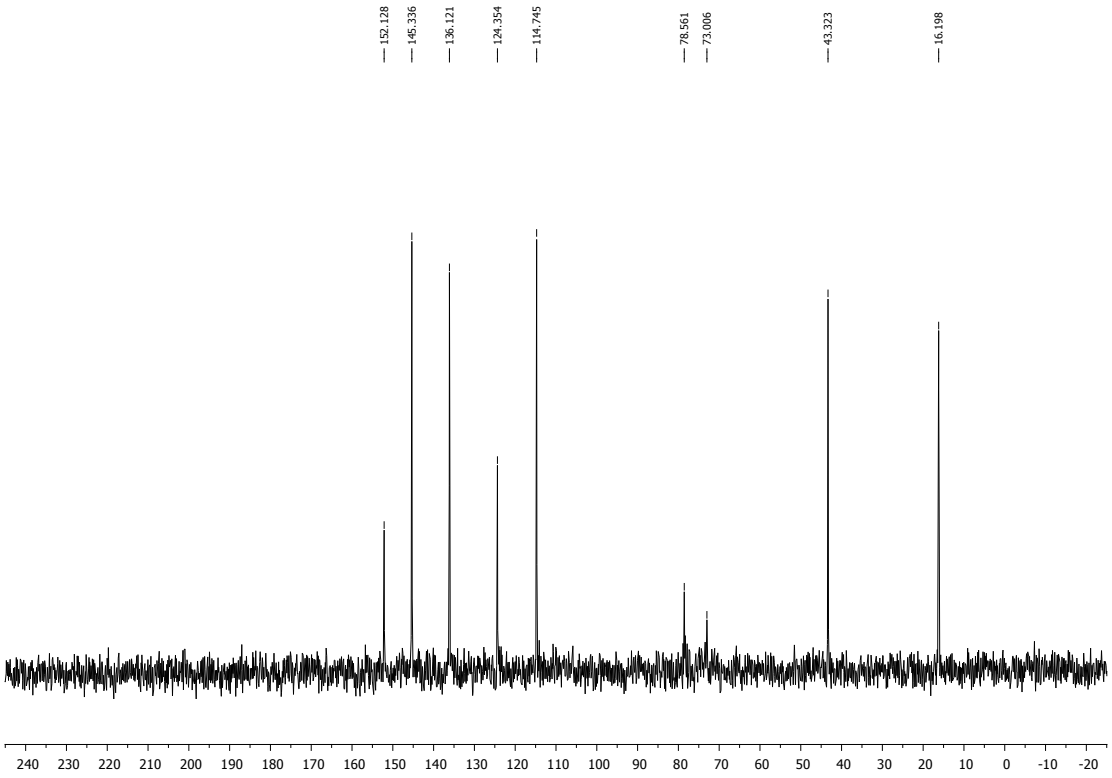


Figure S6. $^{13}C\{^{1}H\}$ NMR (75 MHz, D_2O) spectrum of compound **1c**.

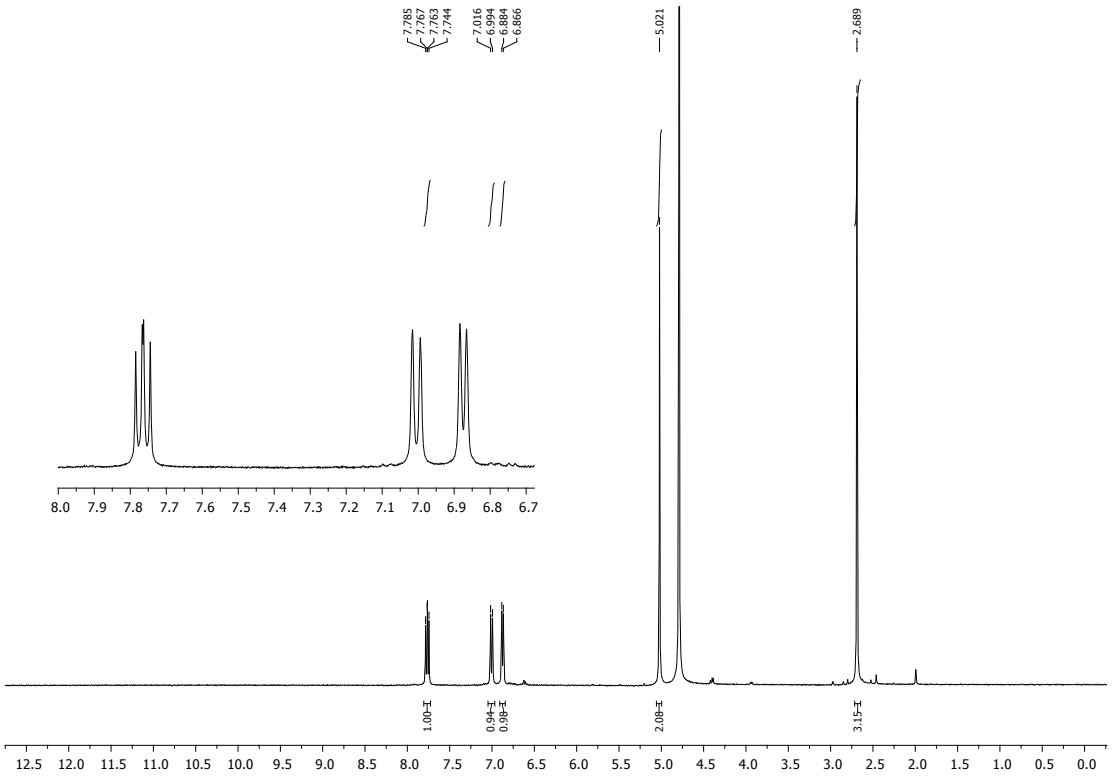


Figure S7. ^{1}H NMR (400 MHz, D_2O) spectrum of compound **1d**.

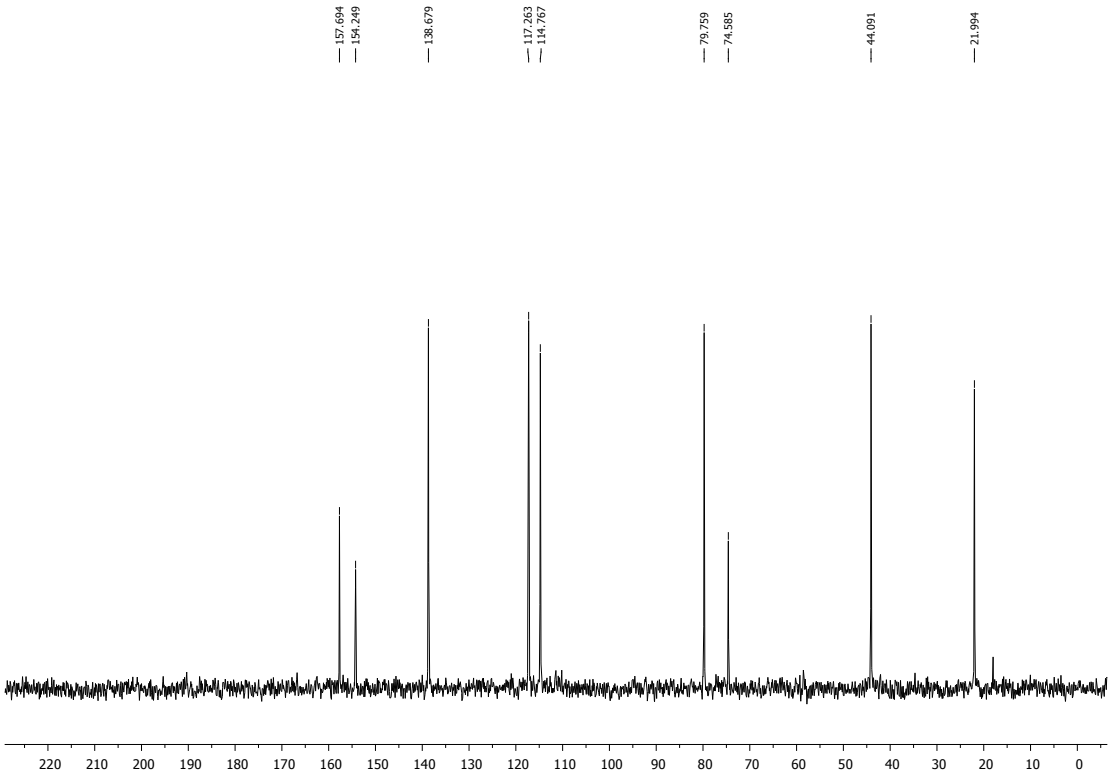


Figure S8. $^{13}C\{^{1}H\}$ NMR (75 MHz, D_2O) spectrum of compound **1d**.

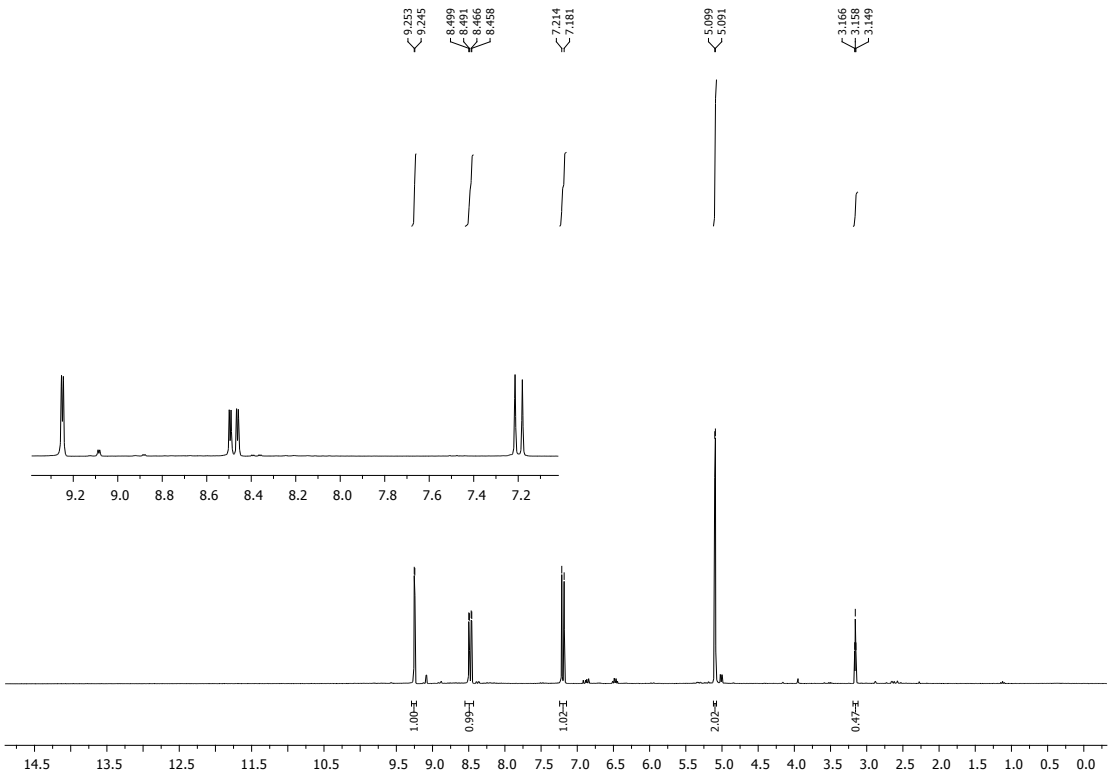


Figure S9. ^{1}H NMR (300 MHz, D_2O) spectrum of compound **1e**.

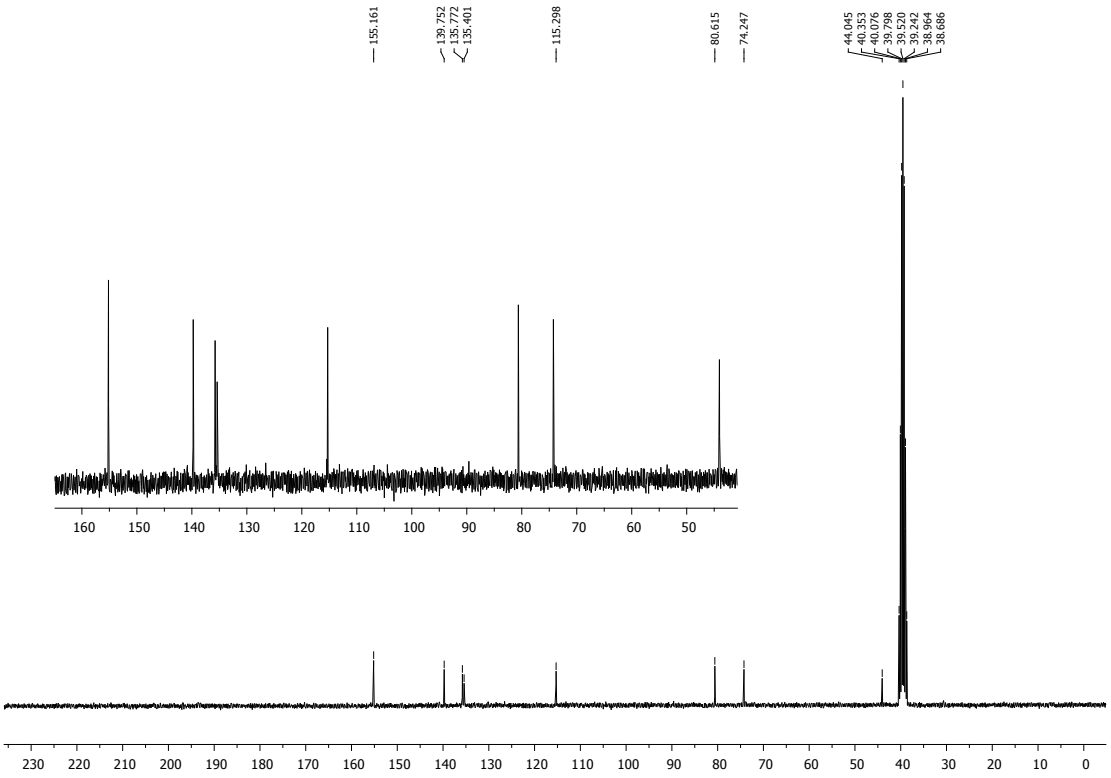


Figure S10. $^{13}C\{^{1}H\}$ NMR (75 MHz, DMSO-d_6) spectrum of compound **1e**.

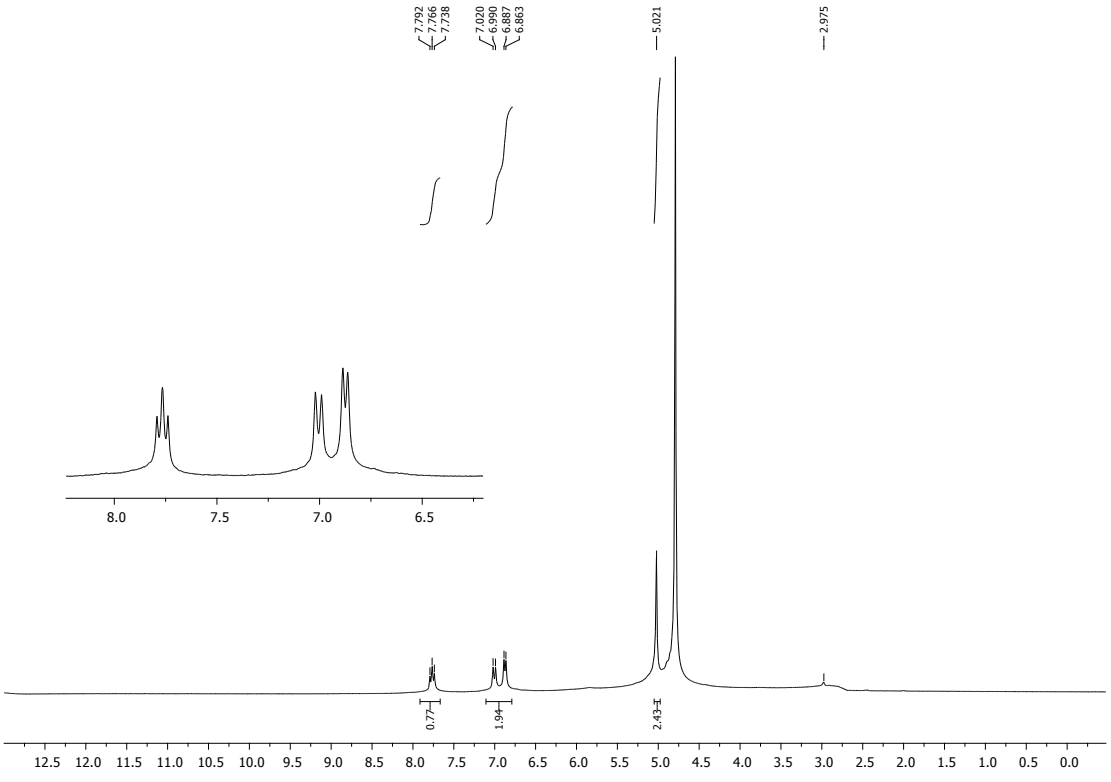


Figure S11. ^{1}H NMR (300 MHz, D_2O) spectrum of compound **1f**.

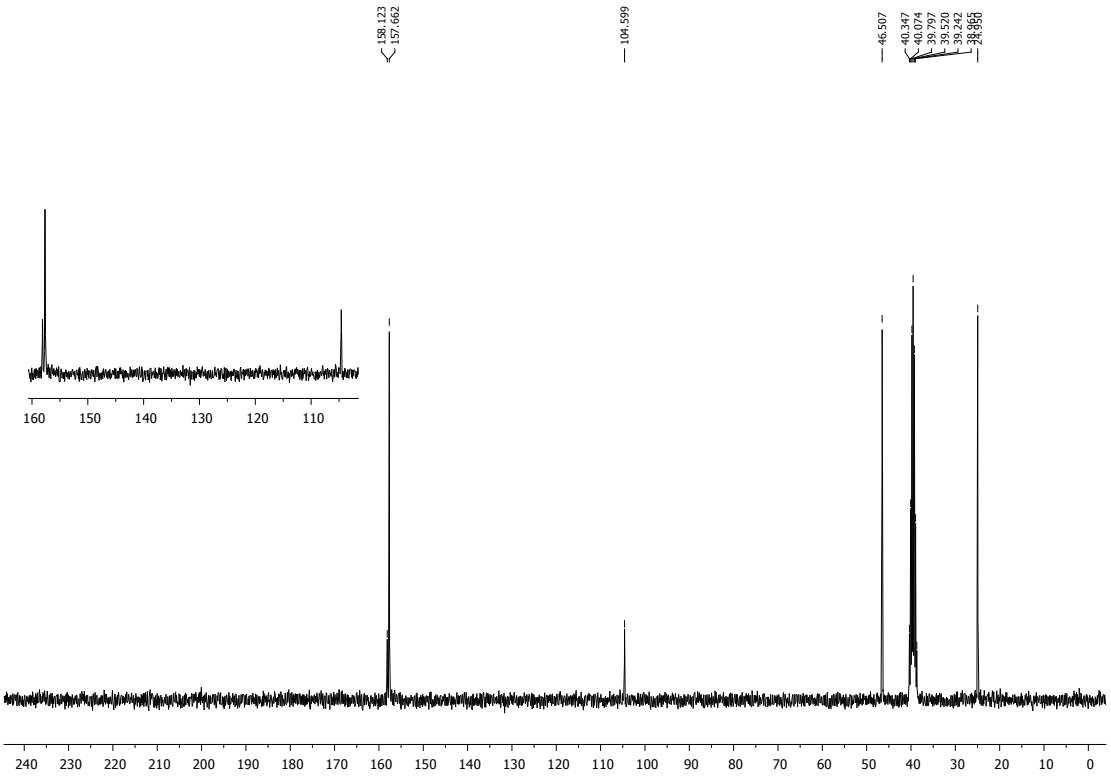


Figure S12. $^{13}C\{^{1}H\}$ NMR (75 MHz, DMSO-d_6) spectrum of compound **1f**.

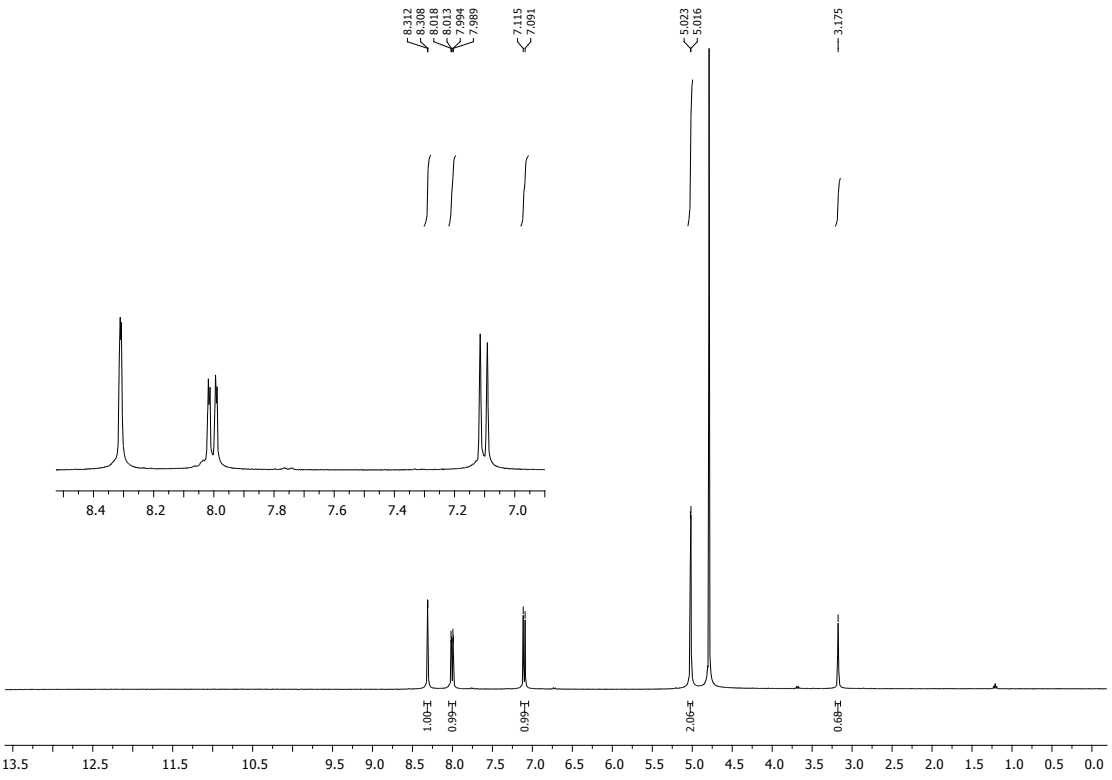


Figure S13. ^{1}H NMR (400 MHz, D_2O) spectrum of compound **1g**.

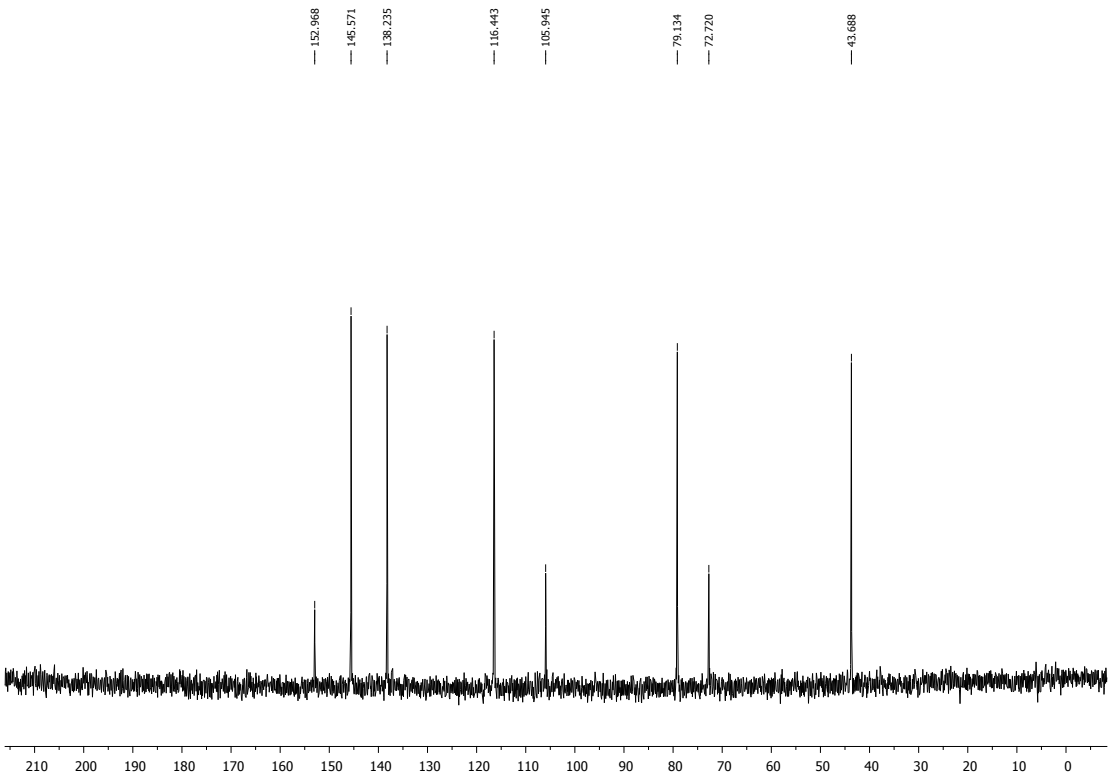


Figure S14. $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O) spectrum of compound **1g**.

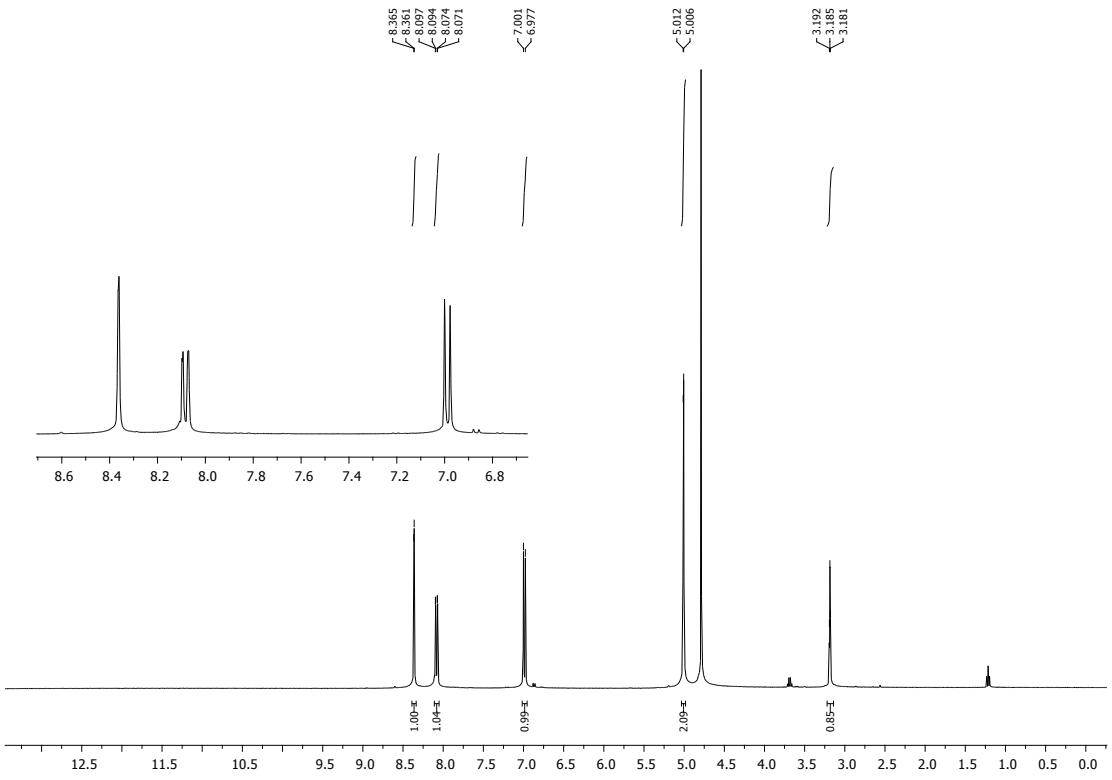


Figure S15. ^{1}H NMR (400 MHz, D_2O) spectrum of compound **1h**.

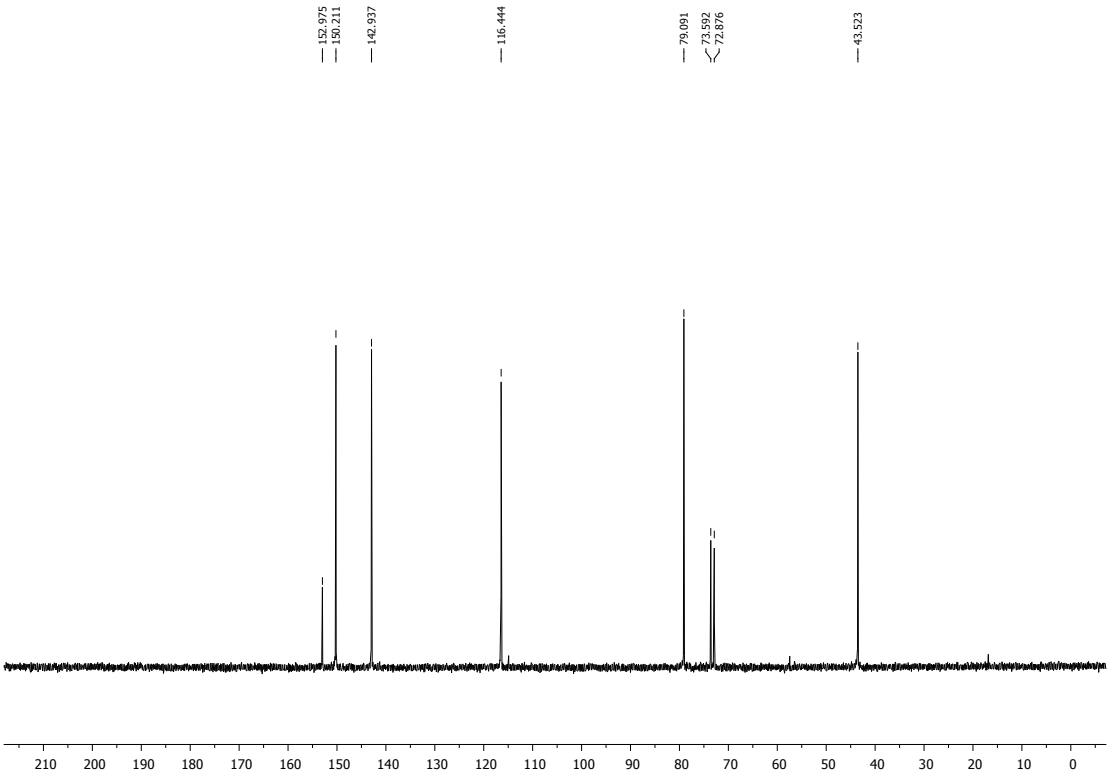


Figure S16. $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O) spectrum of compound **1h**.

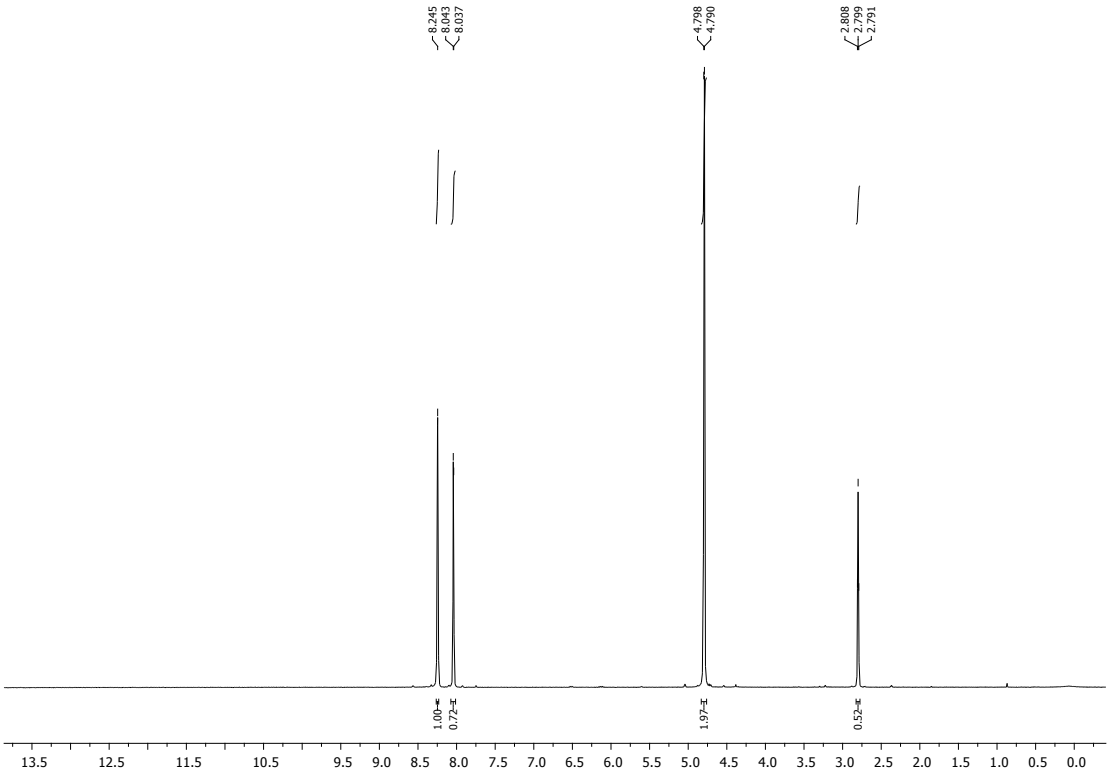


Figure S17. ^{1}H NMR (300 MHz, D_2O) spectrum of compound **1i**.

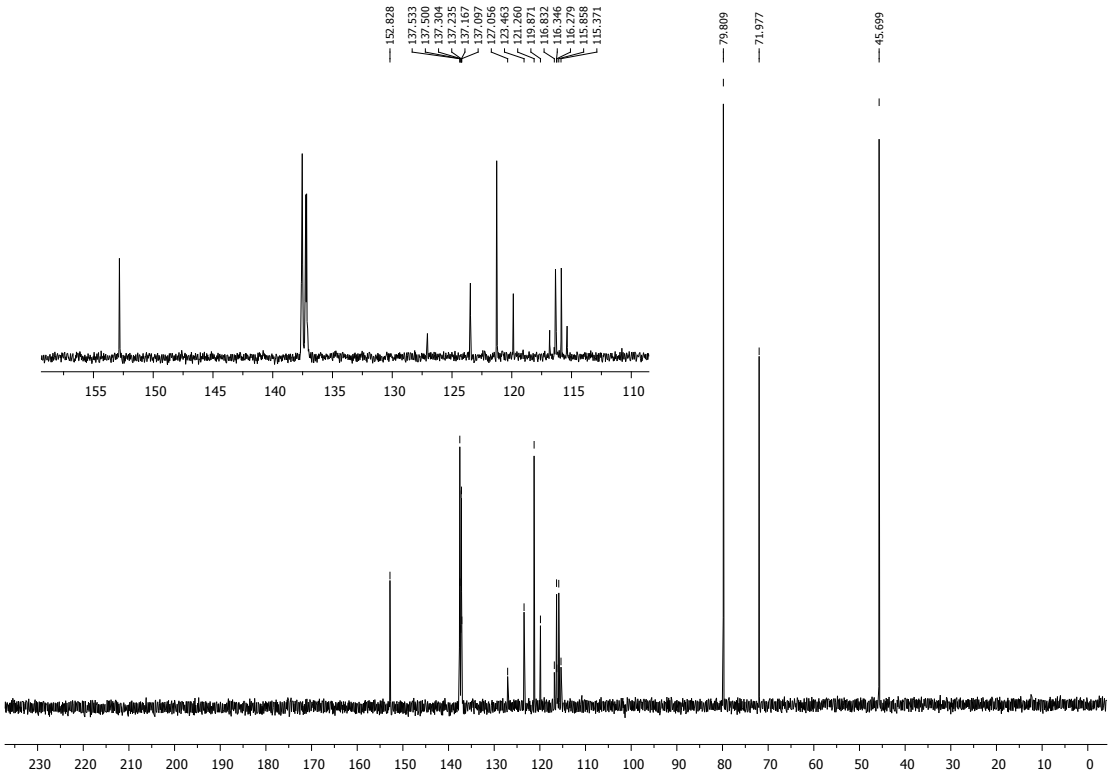


Figure S18. $^{13}C\{^{1}H\}$ NMR (75 MHz, D_2O) spectrum of compound **1i**.

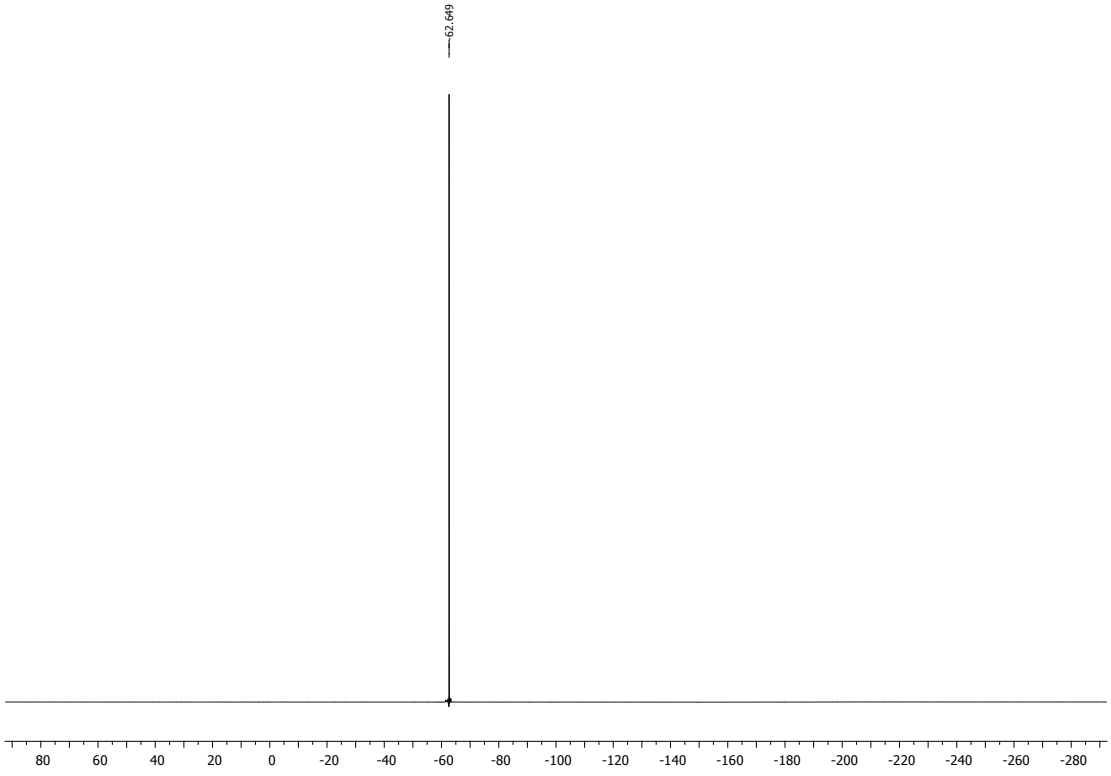


Figure S19. $^{19}F\{^{1}H\}$ NMR (282 MHz, D_2O) spectrum of compound **1i**.

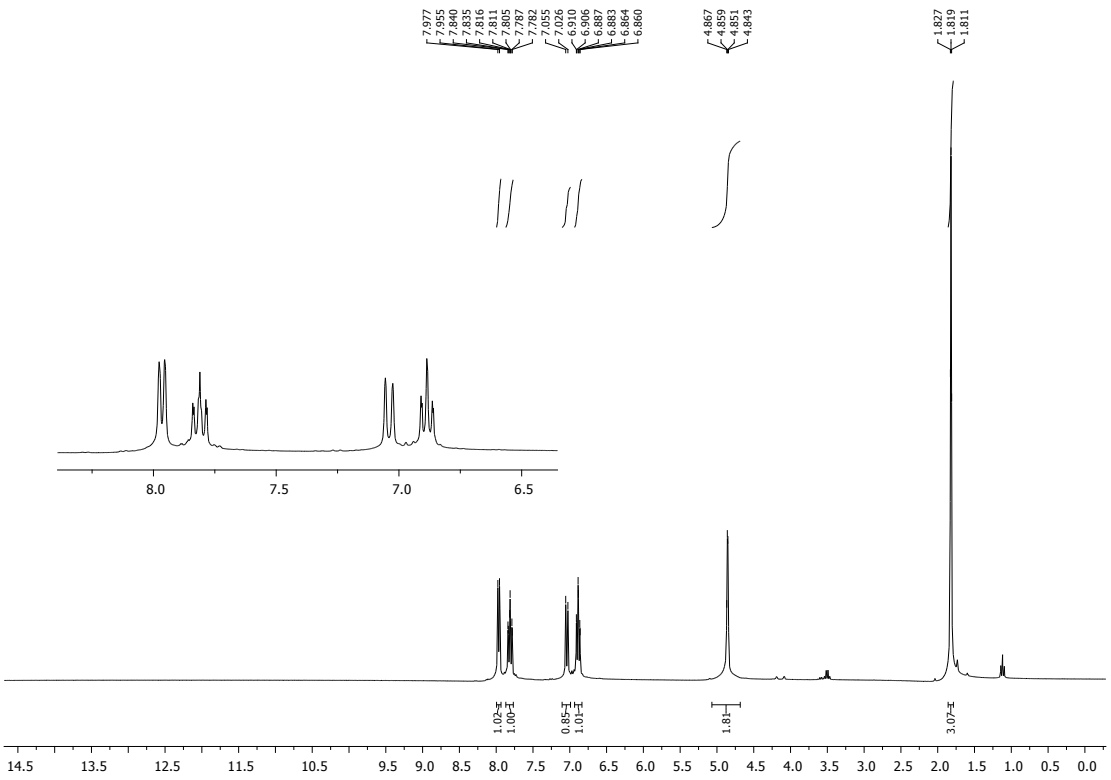


Figure S20. ^{1}H NMR (300 MHz, D_2O) spectrum of compound **1j**.

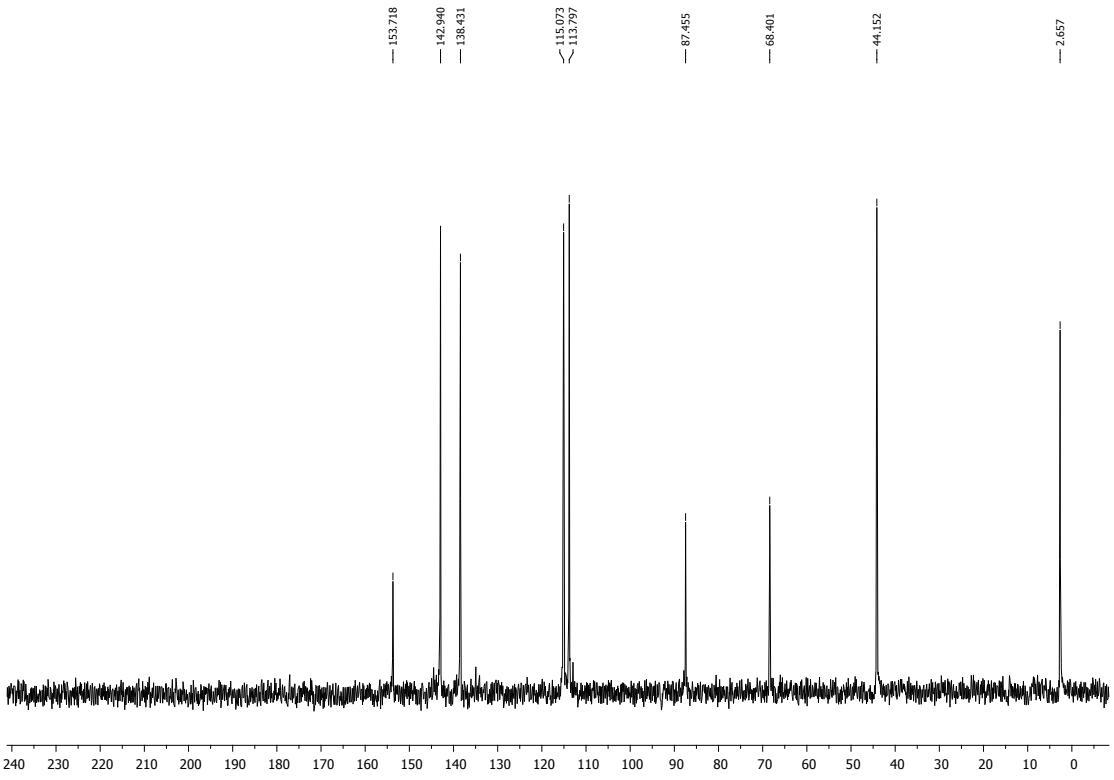


Figure S21. $^{13}C\{^{1}H\}$ NMR (75 MHz, D_2O) spectrum of compound **1j**.

6. ^{1}H, ^{13}C and ^{19}F NMR spectral data of imidazo[1,2-*a*]pyridines, 2a-i

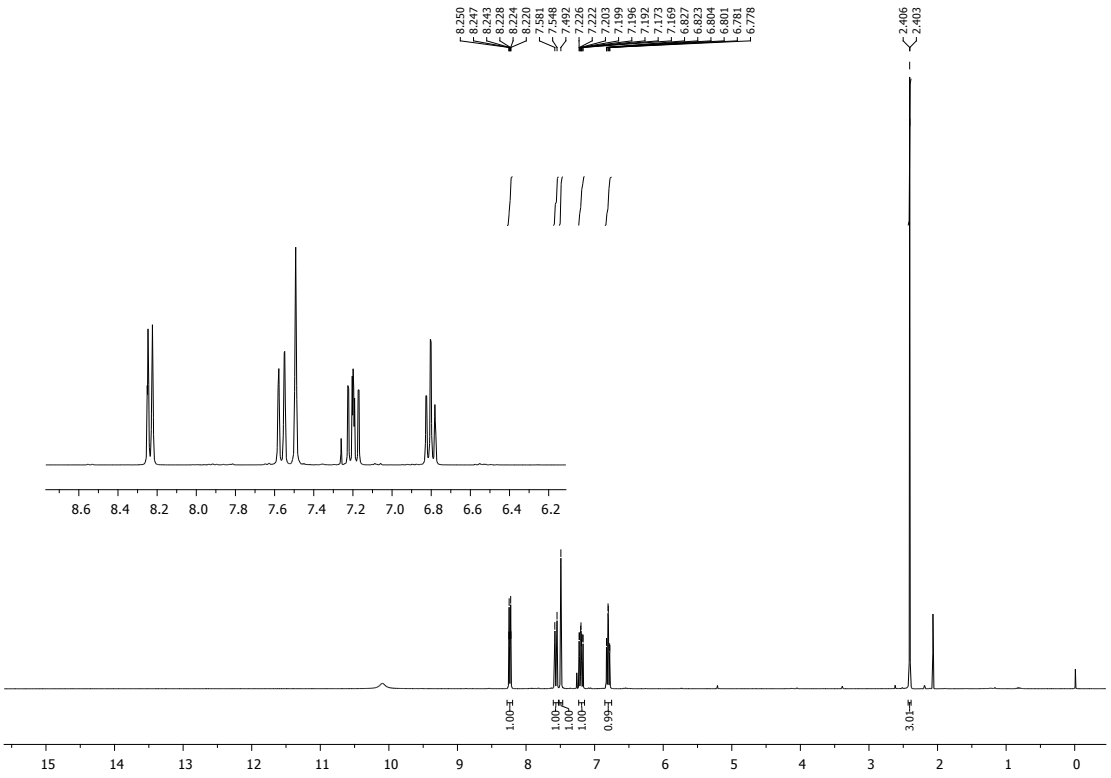


Figure S22. ^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **2a**.

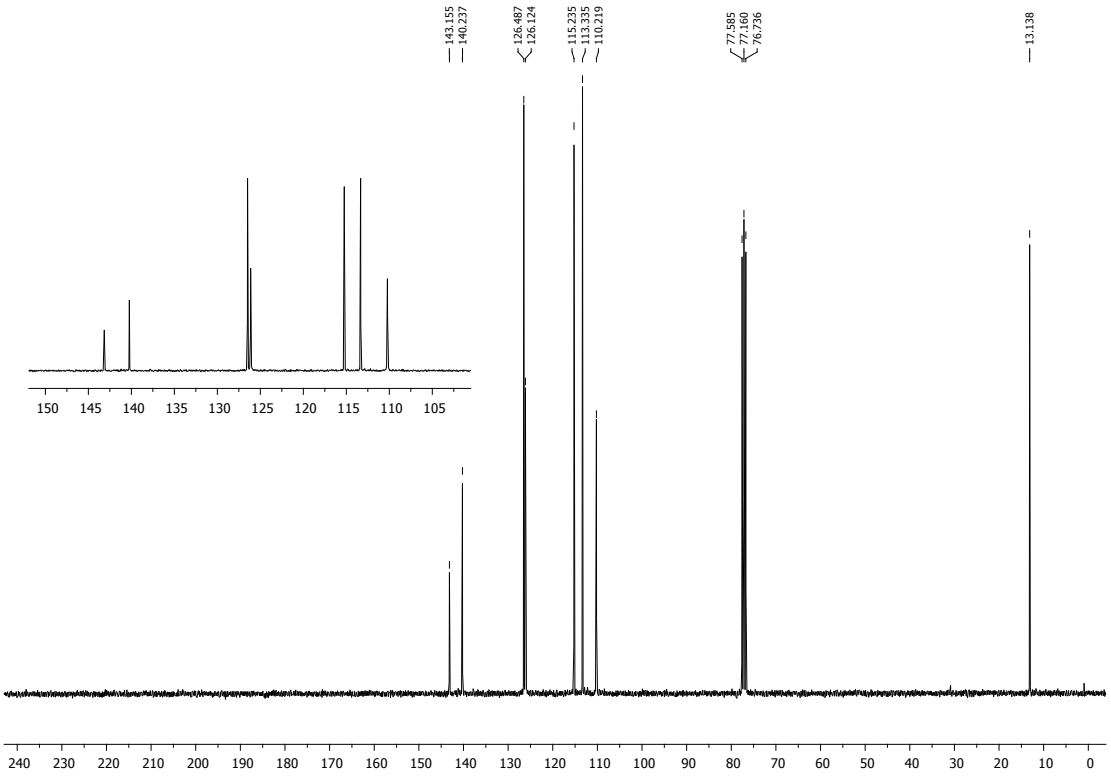


Figure S23. $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) spectrum of compound **2a**.

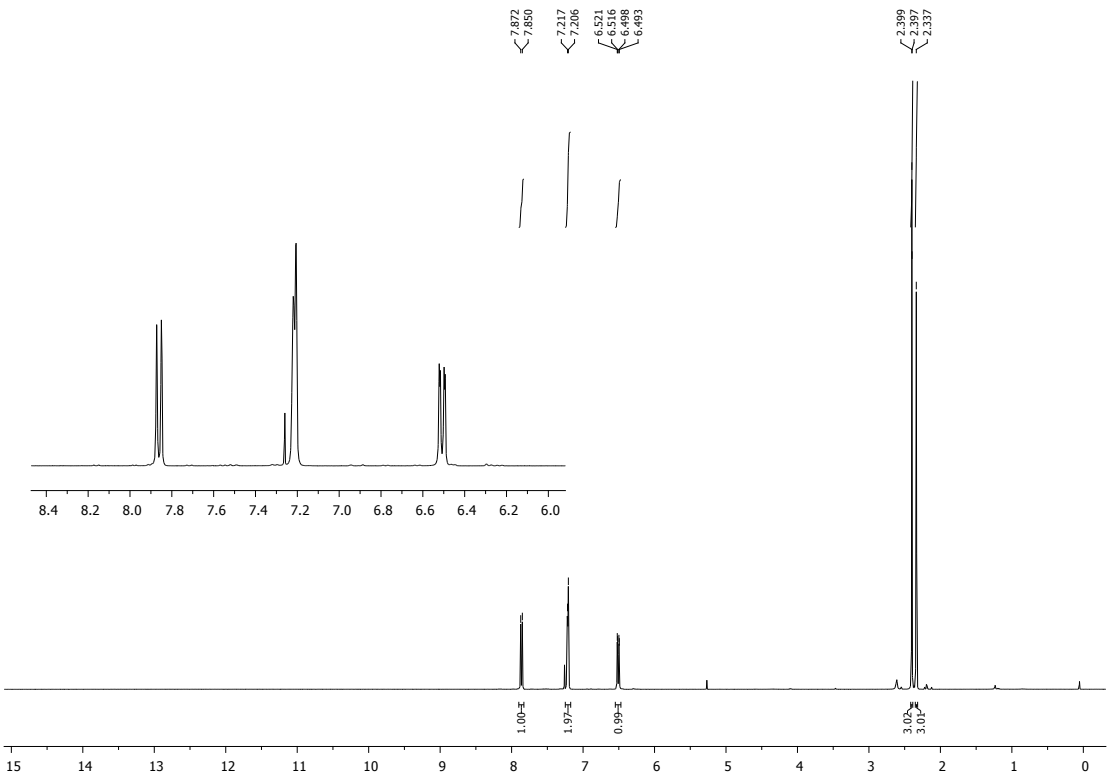


Figure S24. ^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **2b**.

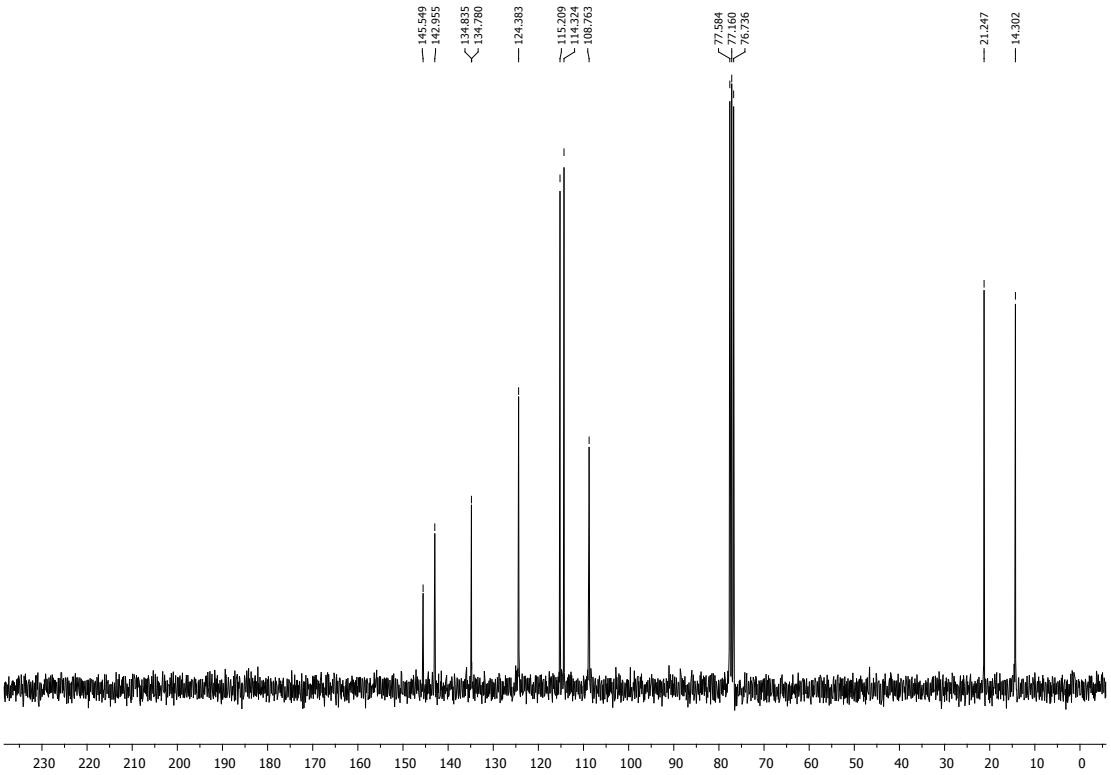


Figure S25. $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) spectrum of compound **2b**.

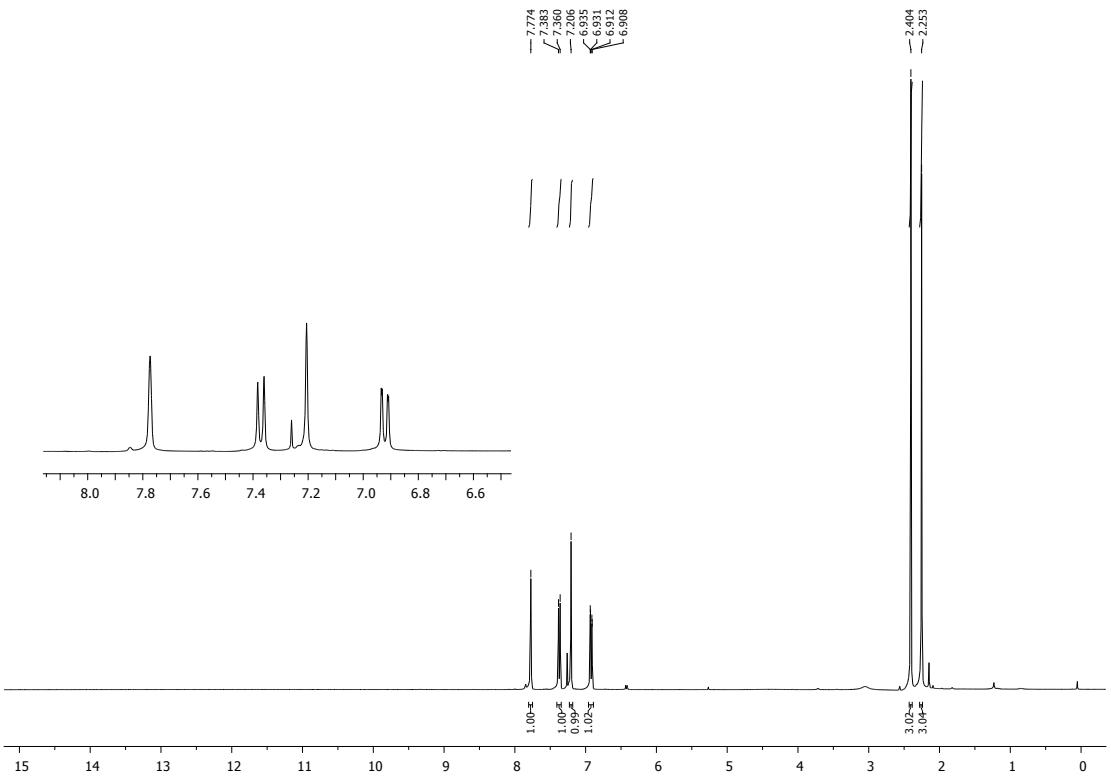


Figure S26. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **2c**.

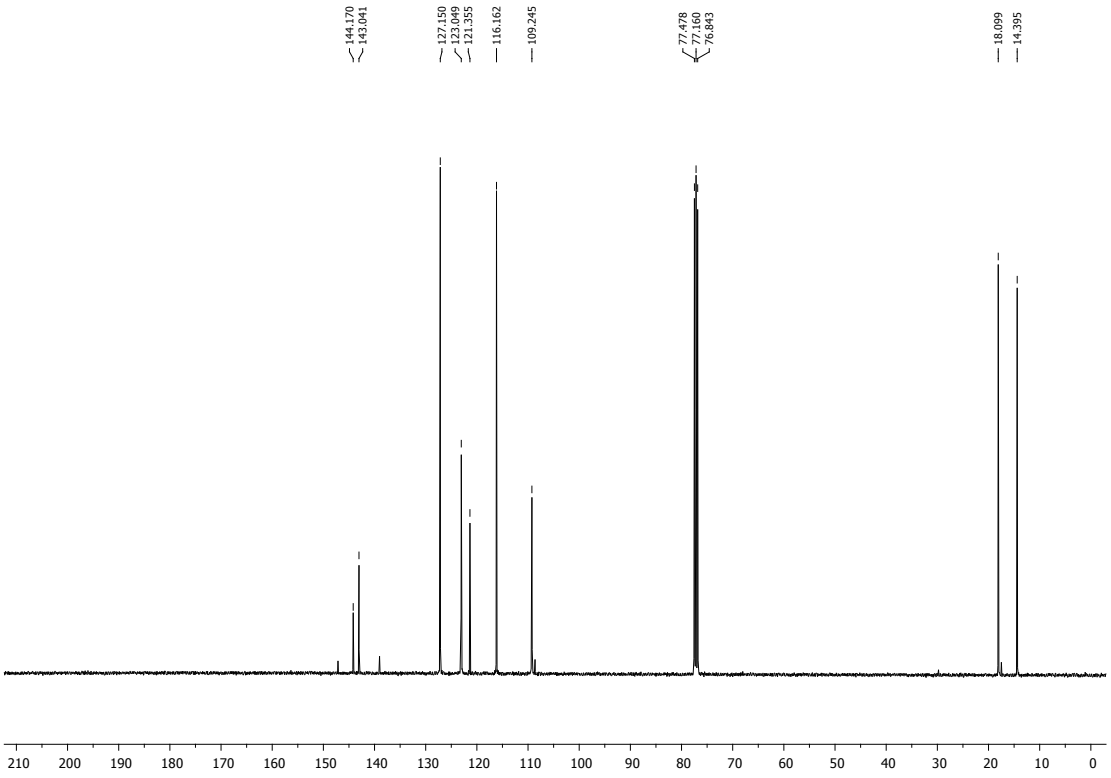


Figure S27. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **2c**.

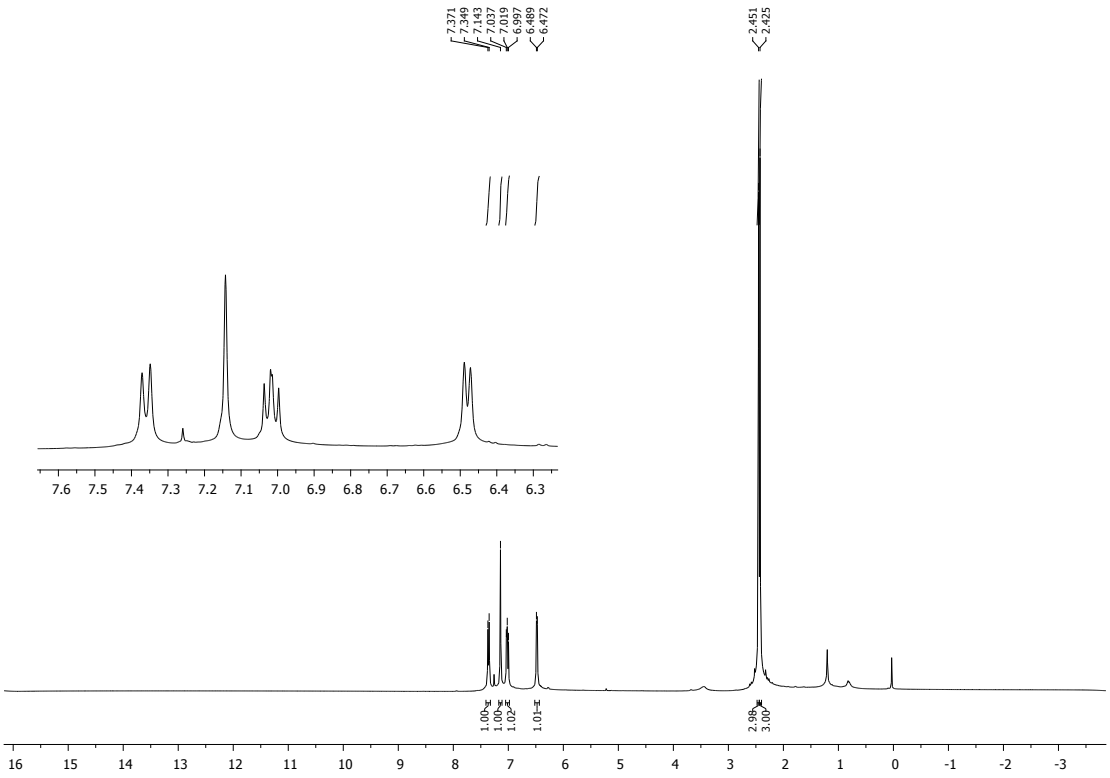


Figure S28. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **2d**.

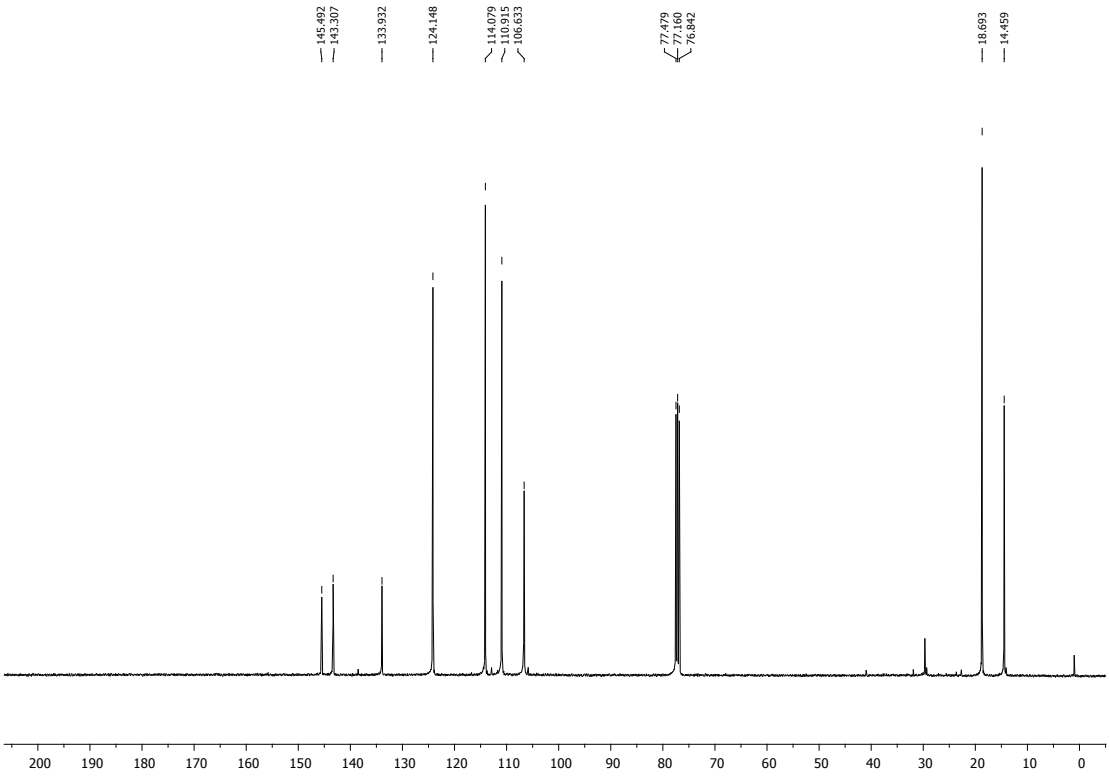


Figure S29. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **2d**.

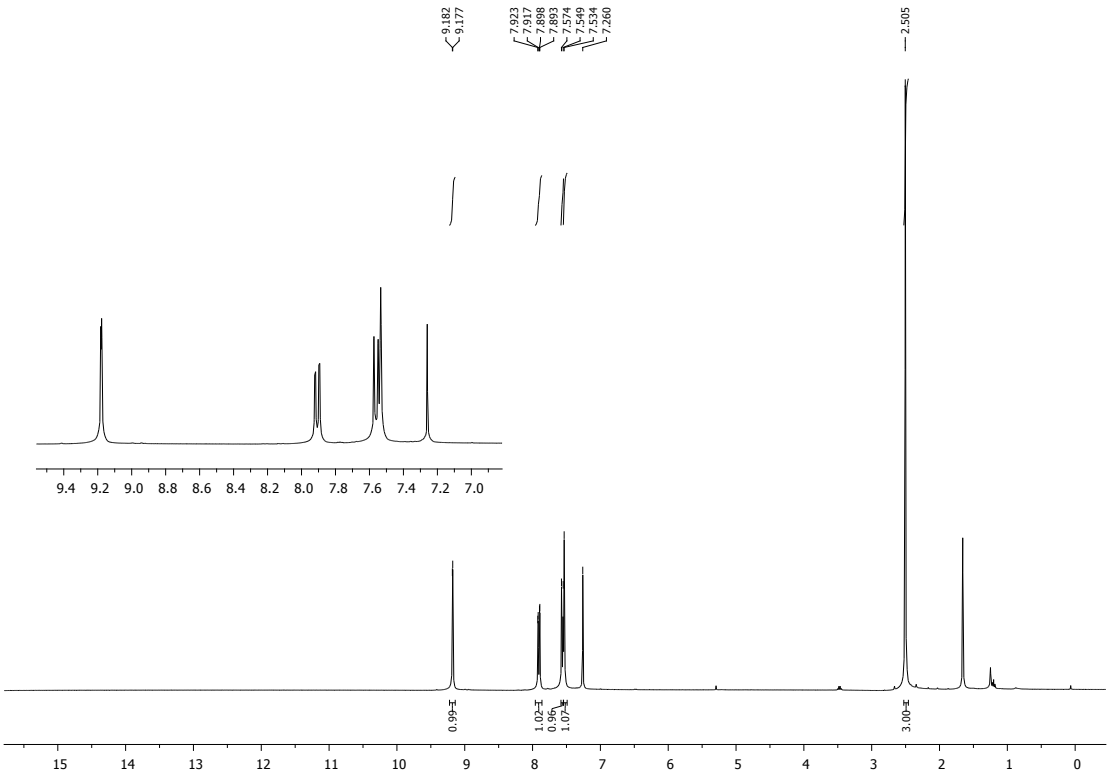


Figure S30. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **2e**.

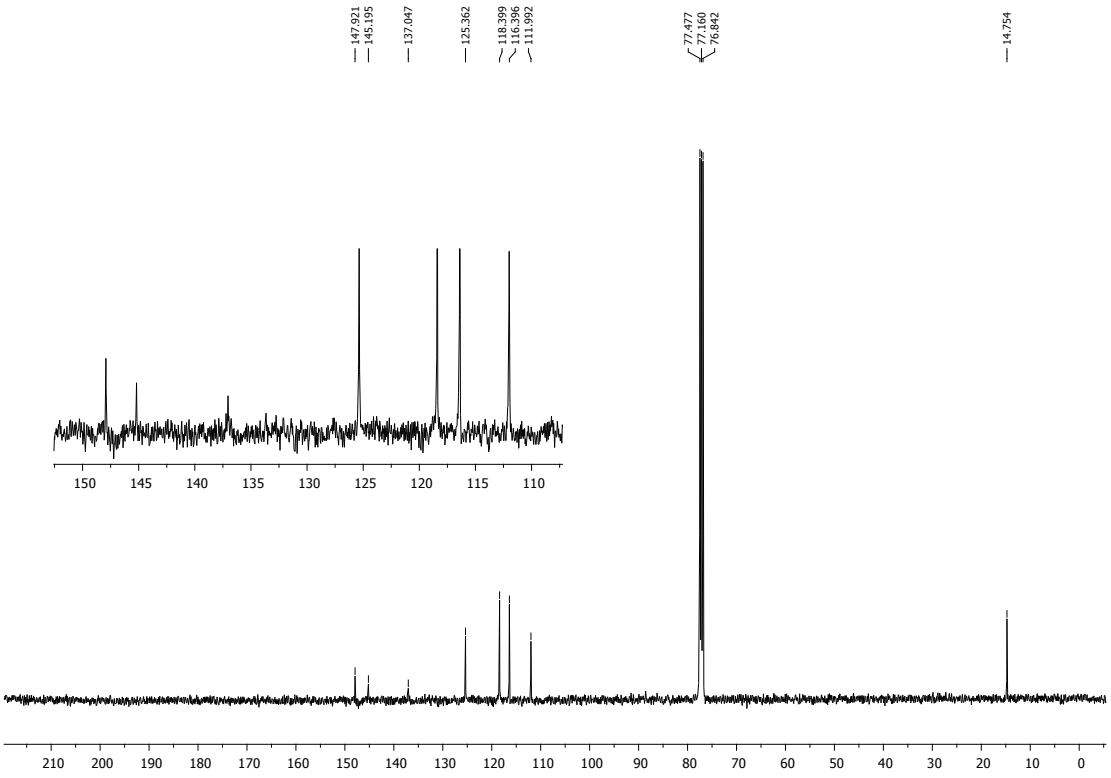


Figure S31. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **2e**.

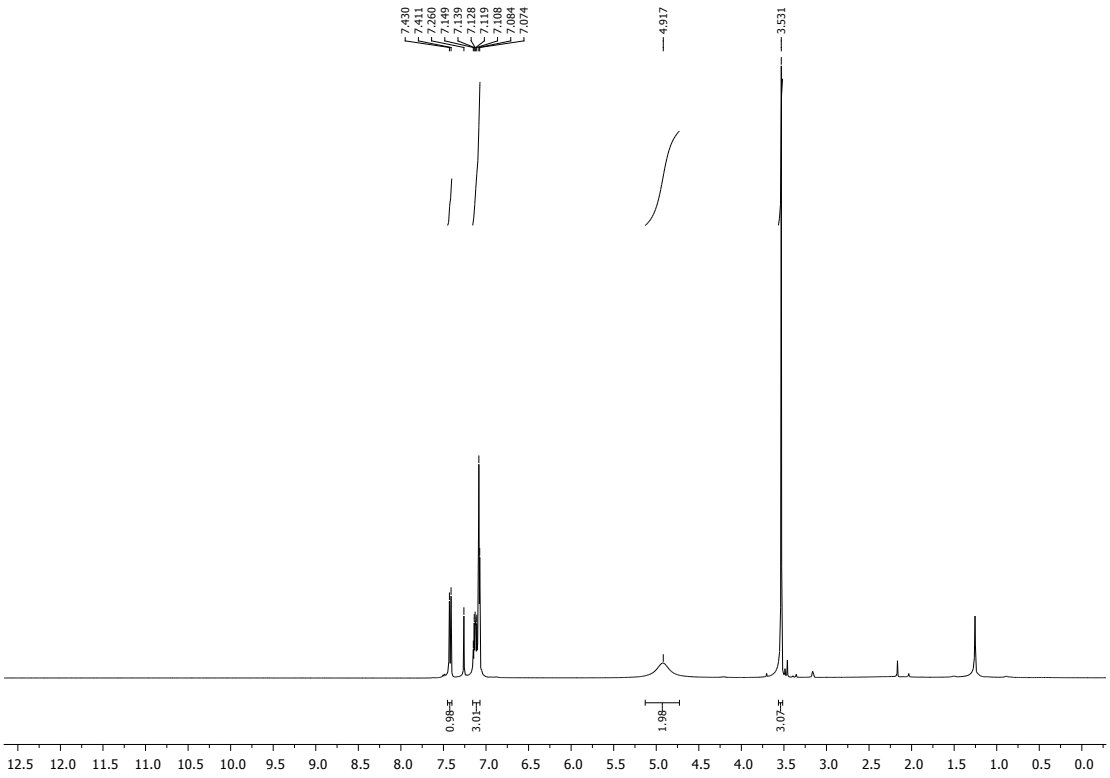


Figure S32. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **2f**.

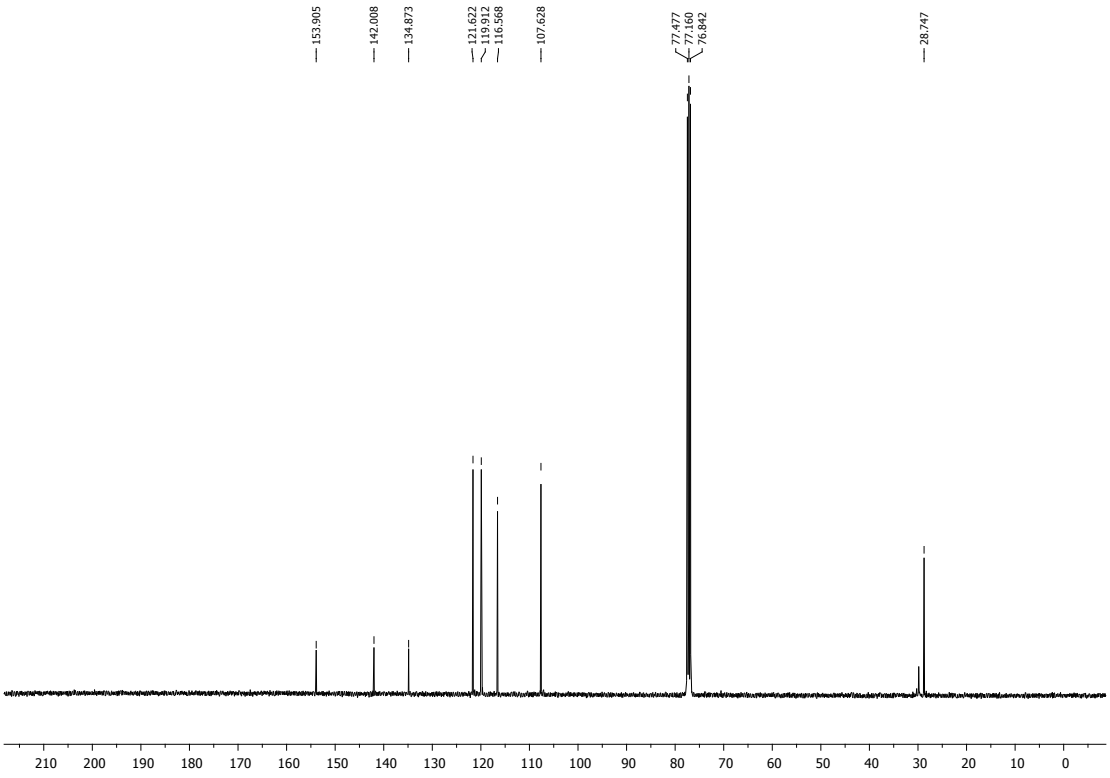


Figure S33. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **2f**.

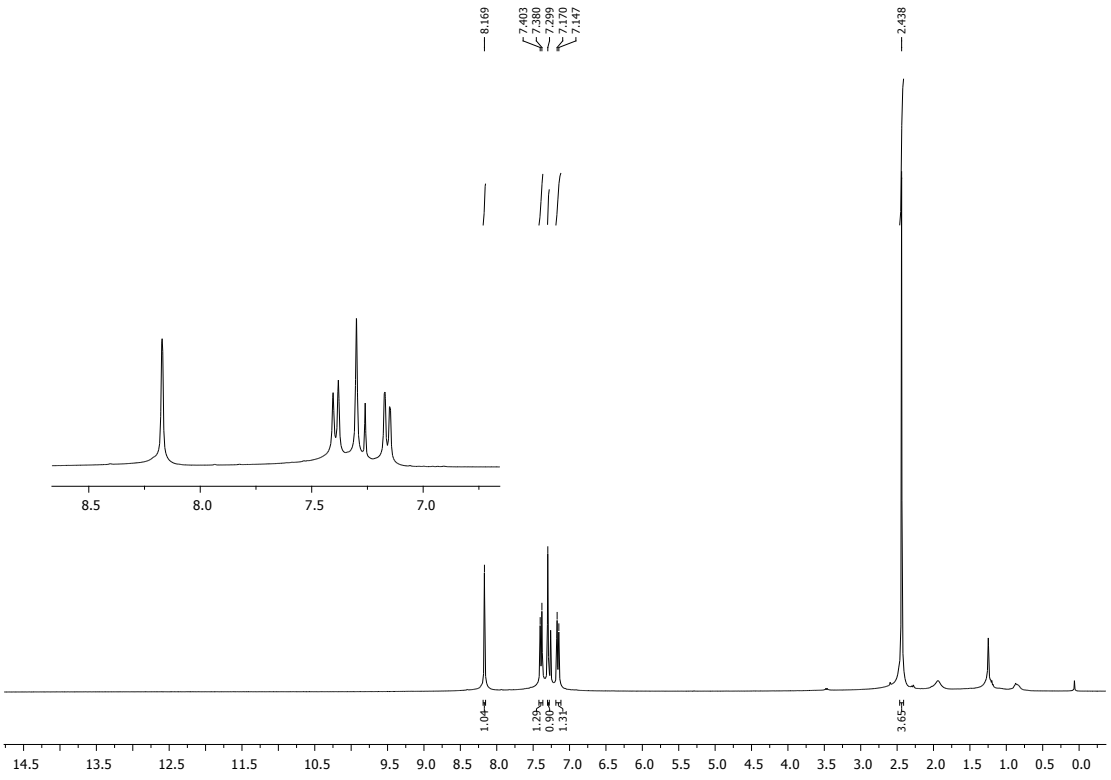


Figure S34. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **2g**.

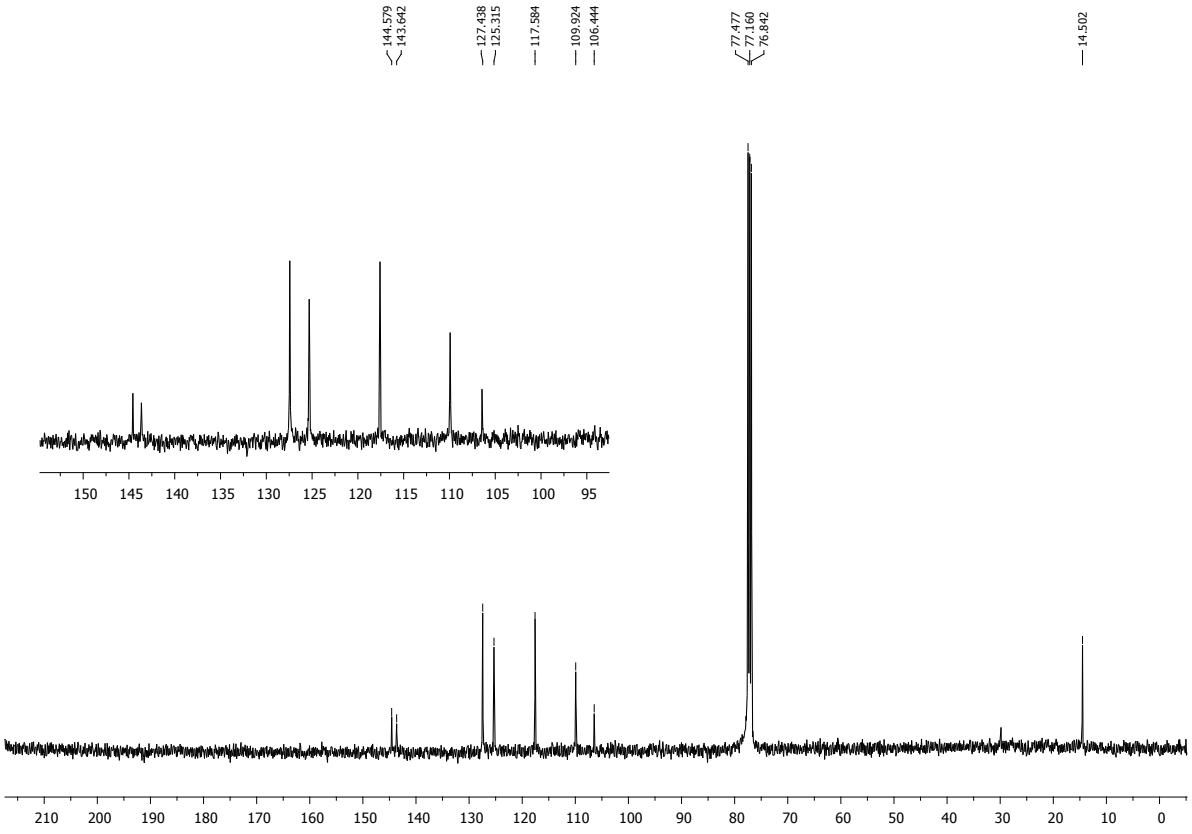


Figure S35. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **2g**.

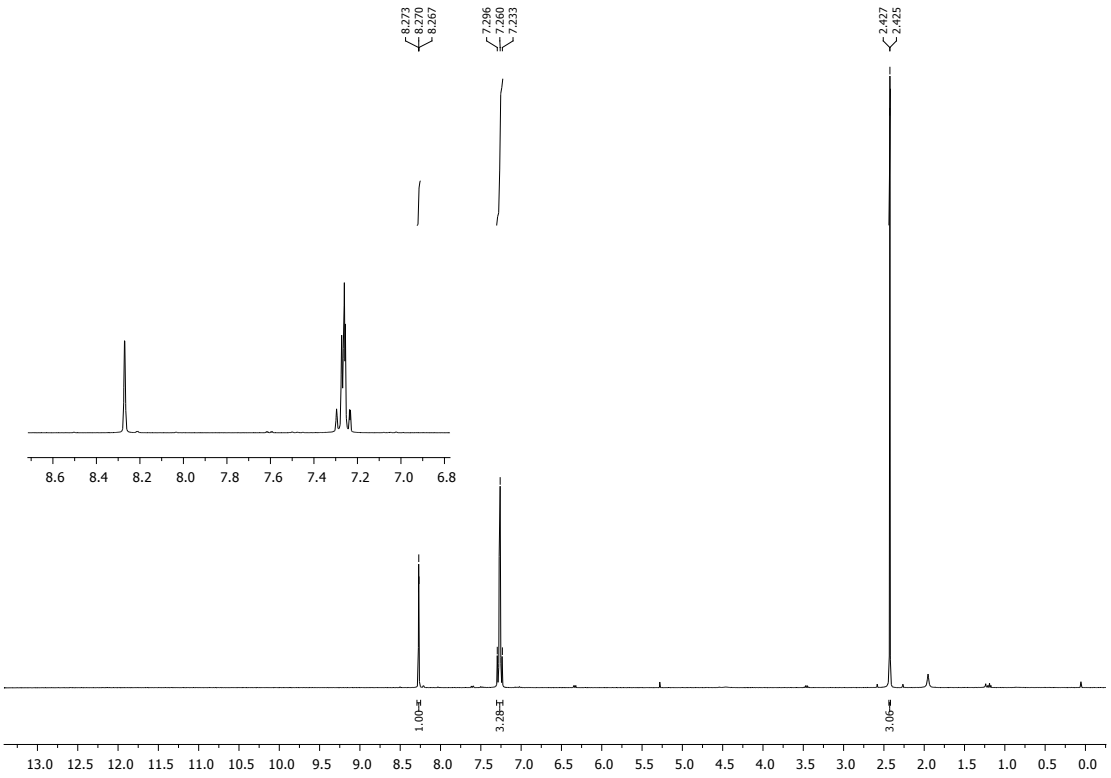


Figure S36. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **2h**.

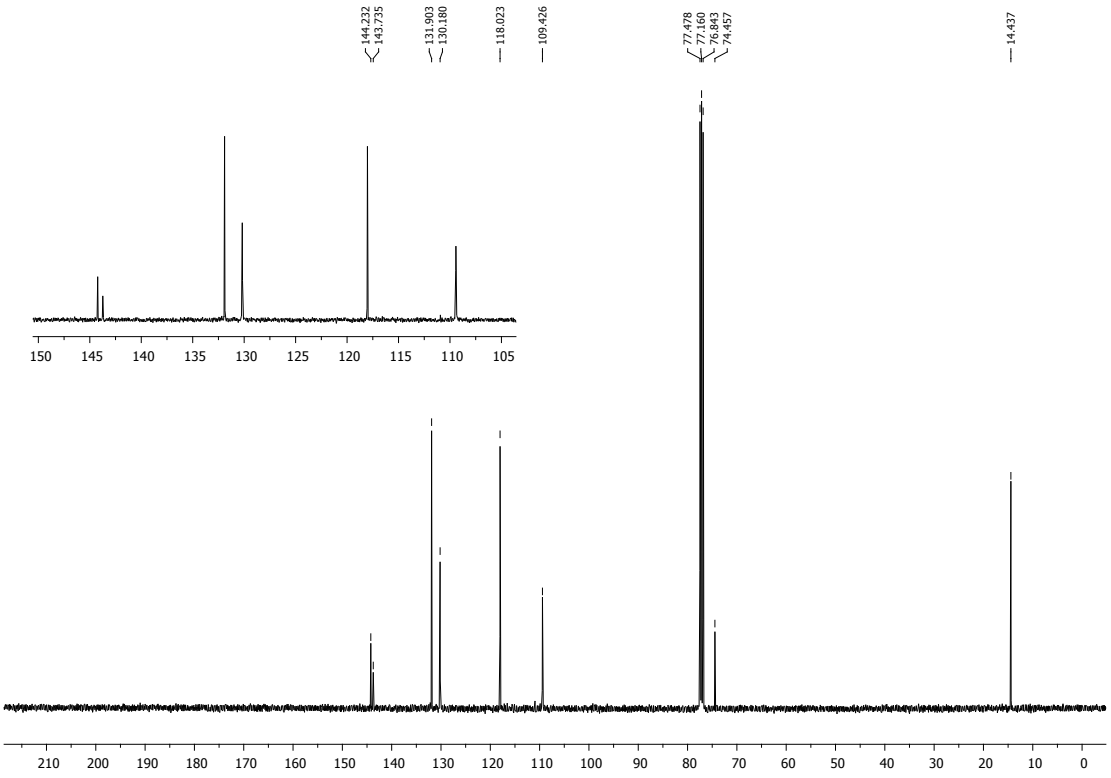


Figure S37. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **2h**.

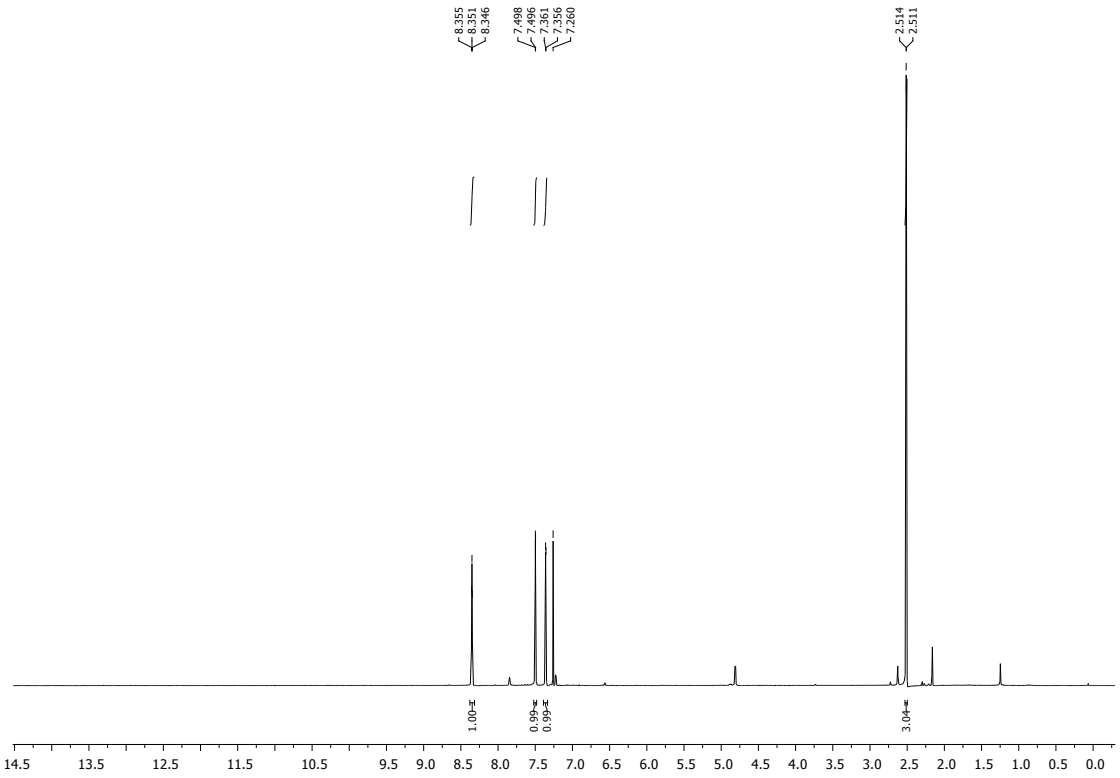


Figure S38. ^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **2i**.

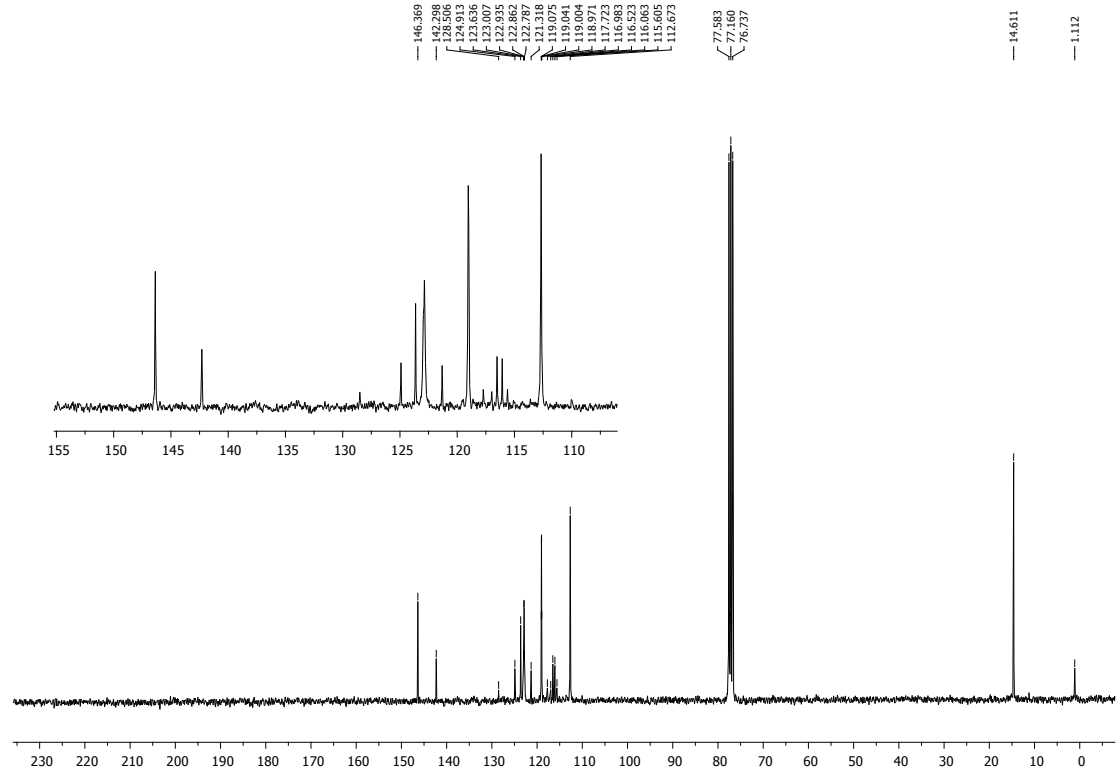


Figure S39. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **2i**.

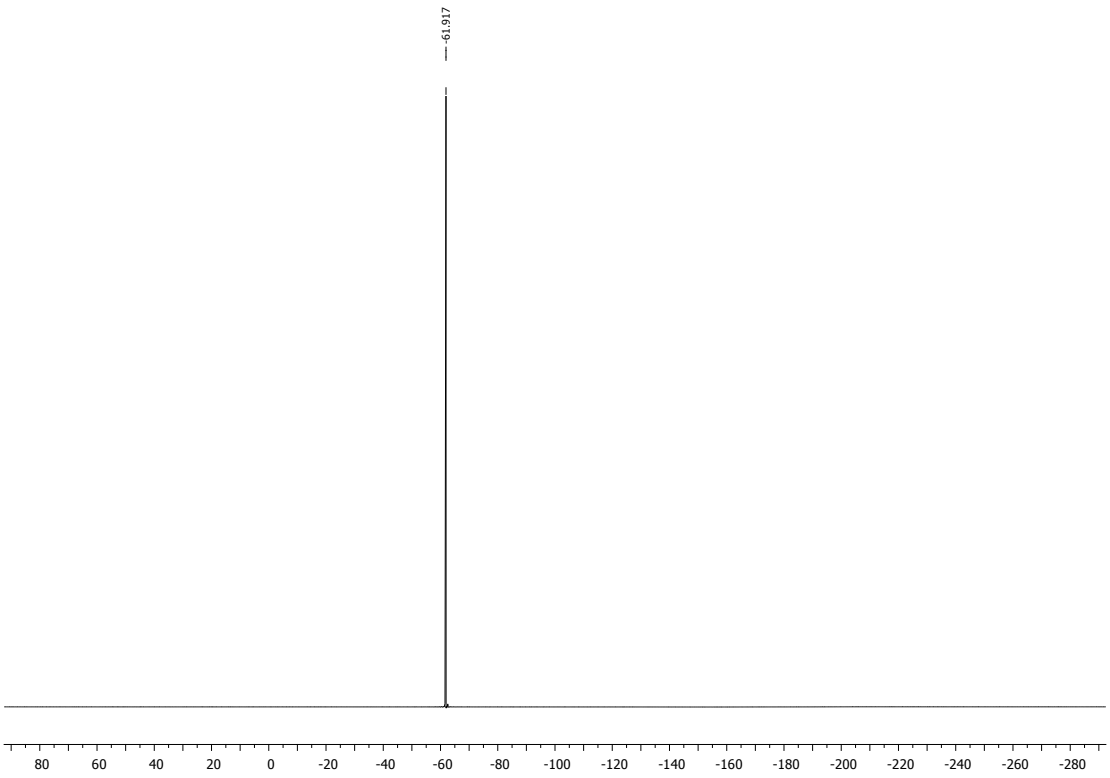


Figure S40. $^{19}F\{^{1}H\}$ NMR (282 MHz, $CDCl_3$) spectrum of compound **2i**.

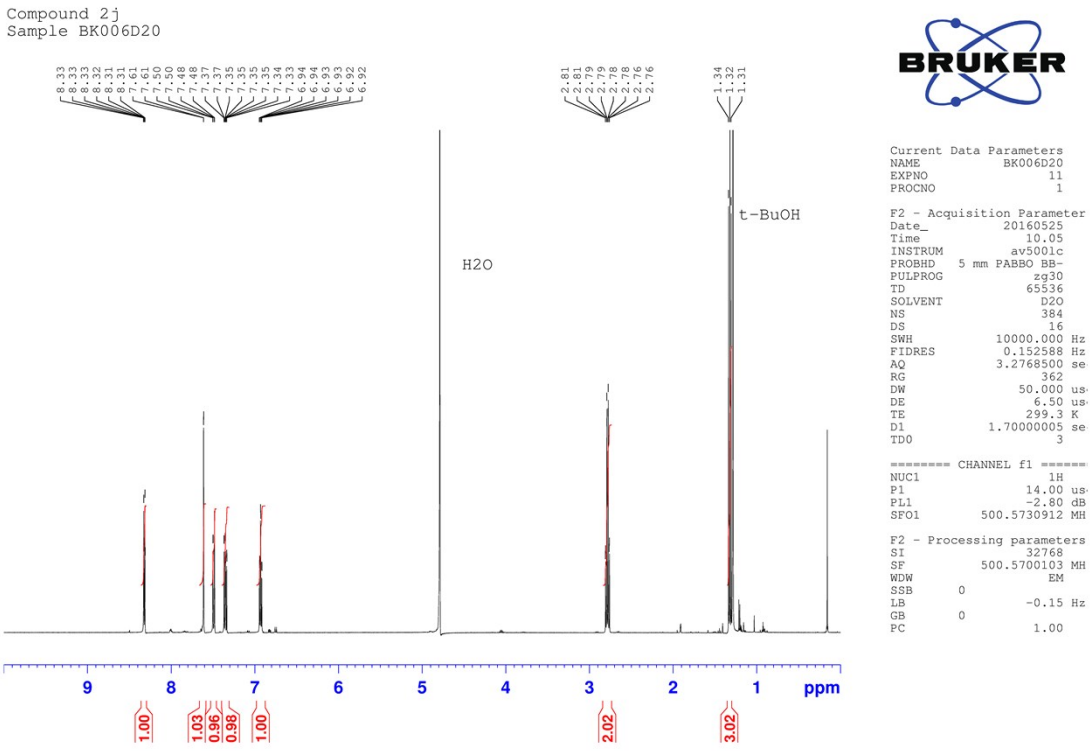


Figure S41. ^{1}H NMR (500 MHz, D_2O) spectrum of compound **2j**.

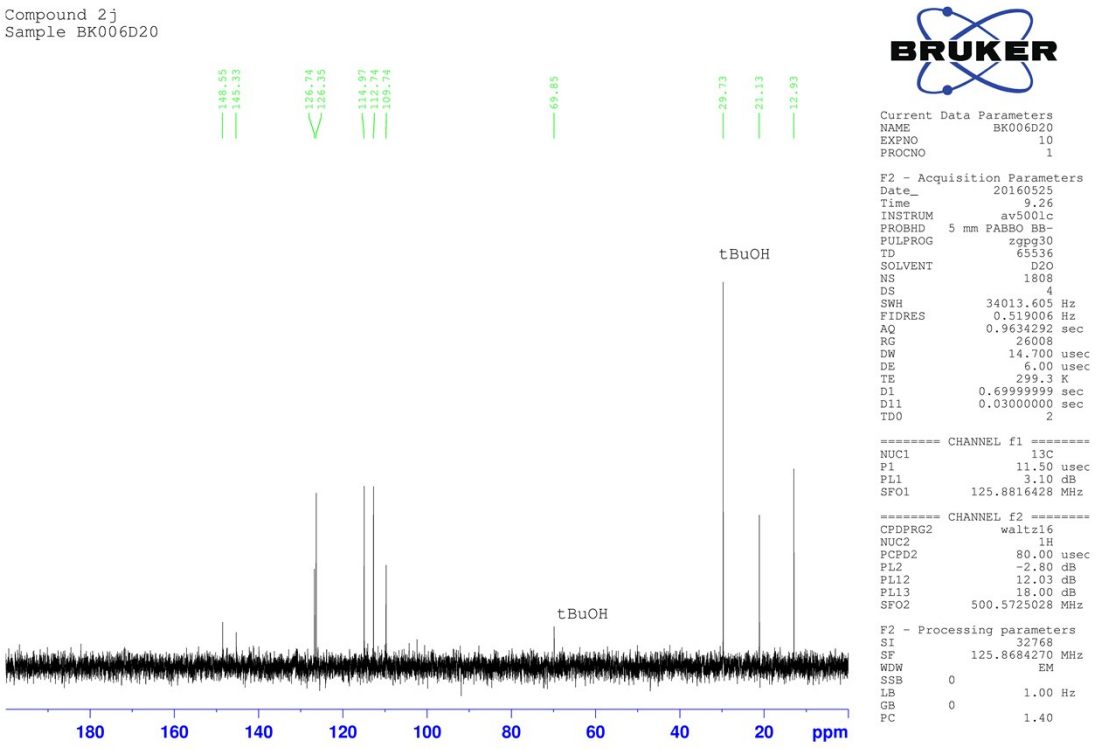


Figure S42. $^{13}C\{^{1}H\}$ NMR (125 MHz, D_2O) spectrum of compound **2j**.

7. ^{1}H, ^{13}C and ^{19}F NMR spectral data of imidazo[1,2-*a*]pyridinium salts, 3a-e, 5a

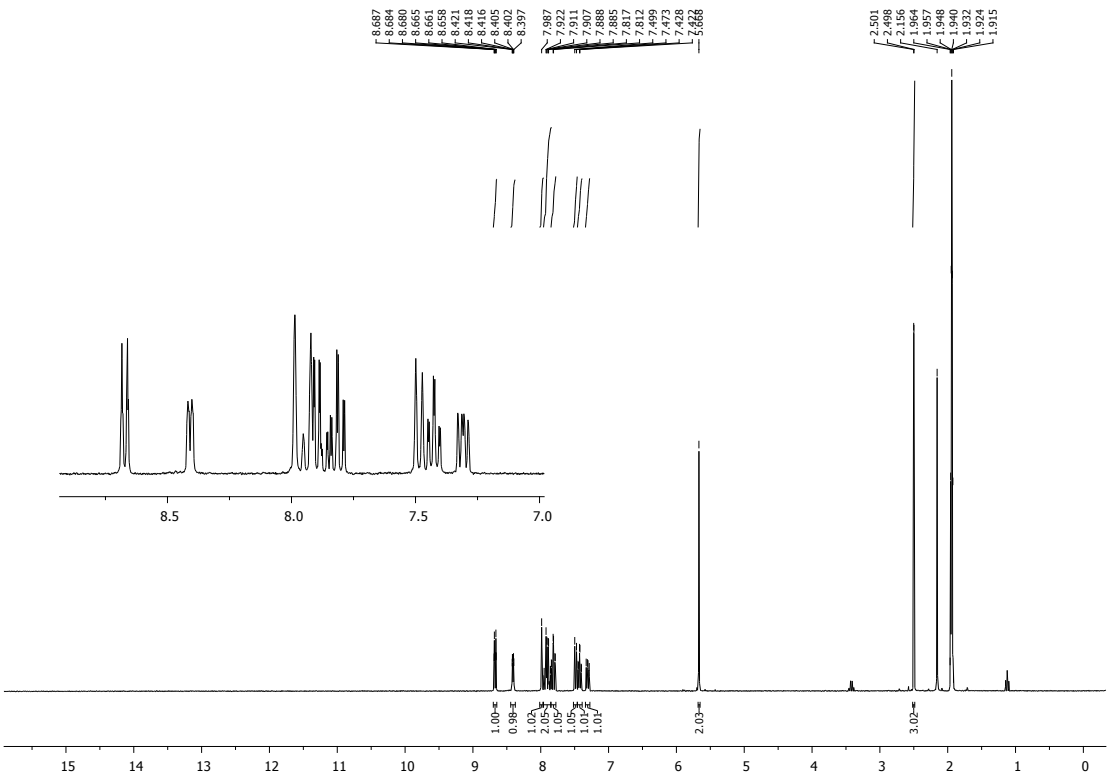


Figure S43. ^{1}H NMR (300 MHz, CD_3CN) spectrum of compound **3a**.

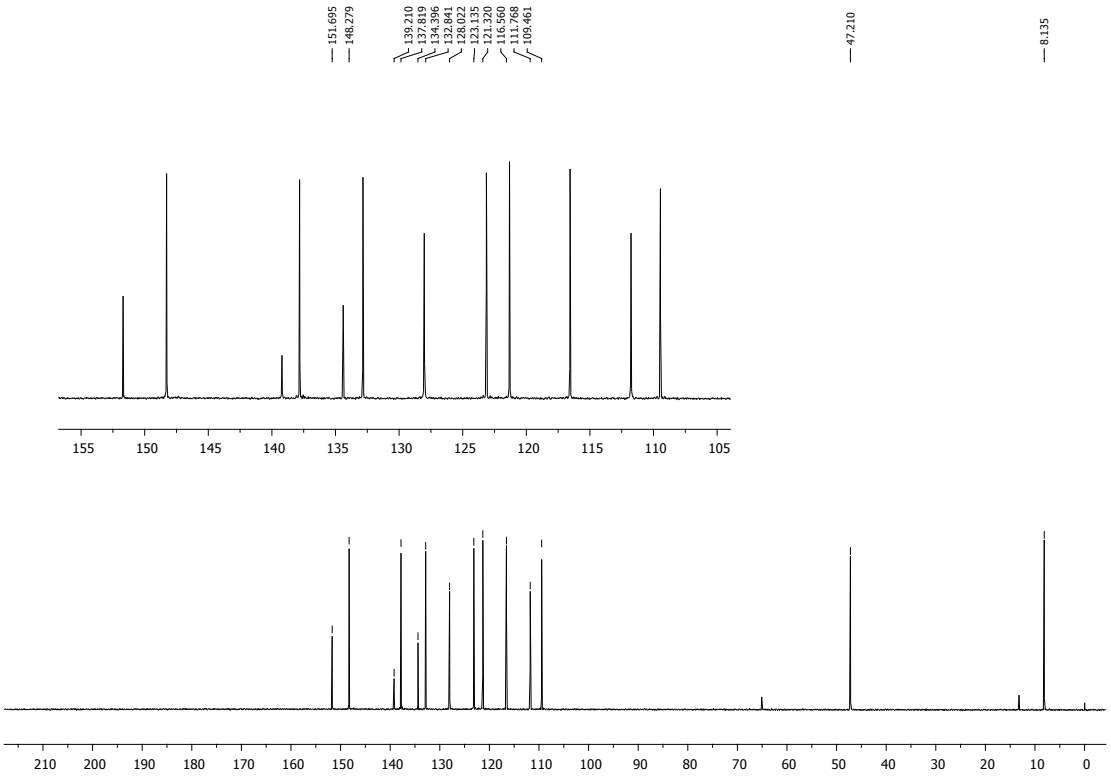


Figure S44. $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O) spectrum of compound **3a**.

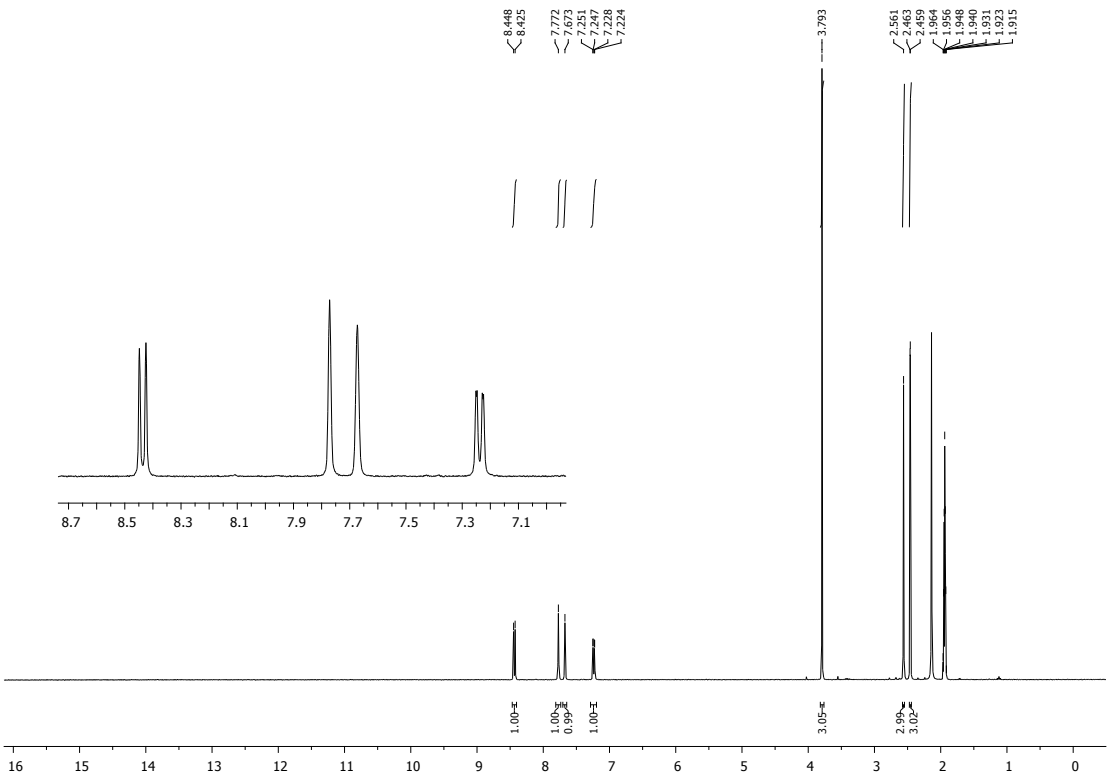


Figure S45. ^{1}H NMR (300 MHz, CD_3CN) spectrum of compound **3b**.

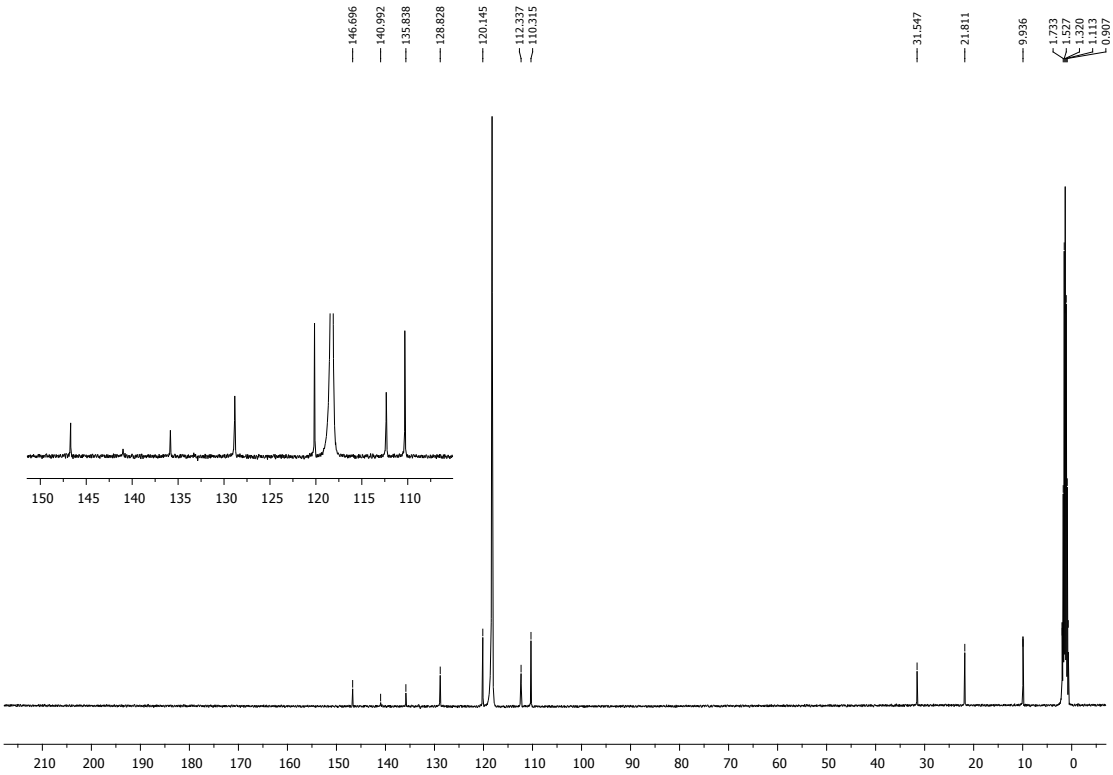


Figure S46. $^{13}C\{^{1}H\}$ NMR (100 MHz, CD_3CN) spectrum of compound **3b**.

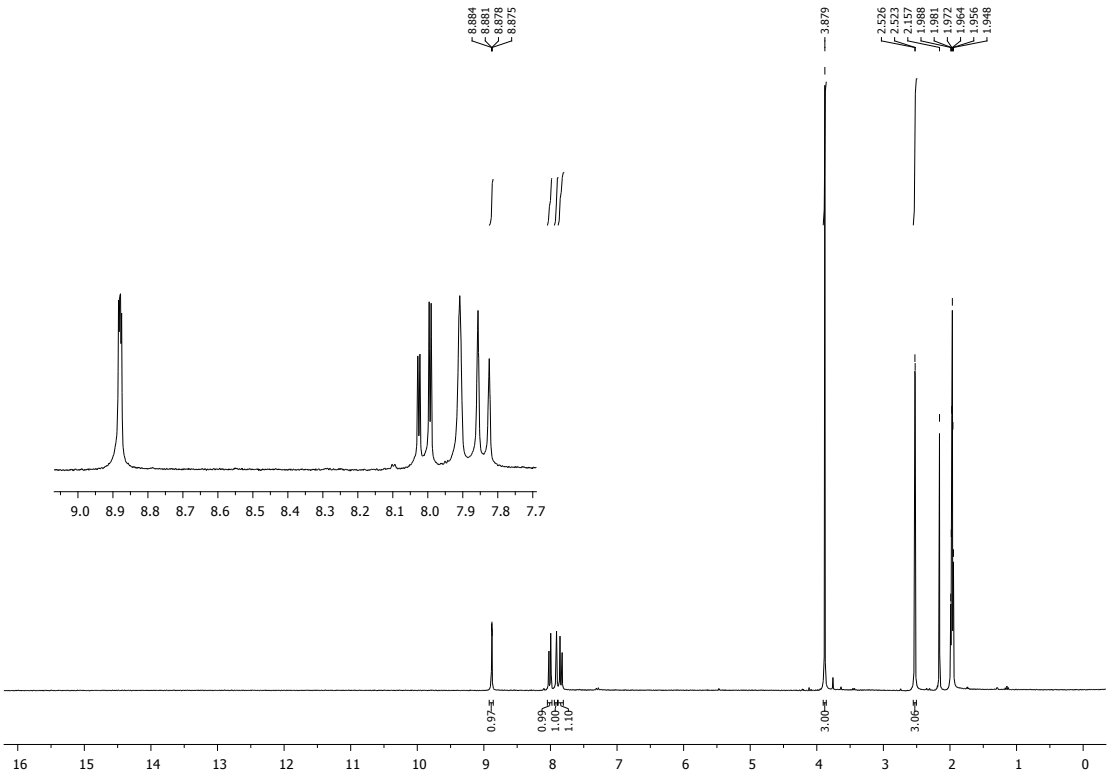


Figure S47. ^{1}H NMR (300 MHz, CD_3CN) spectrum of compound **3c**.

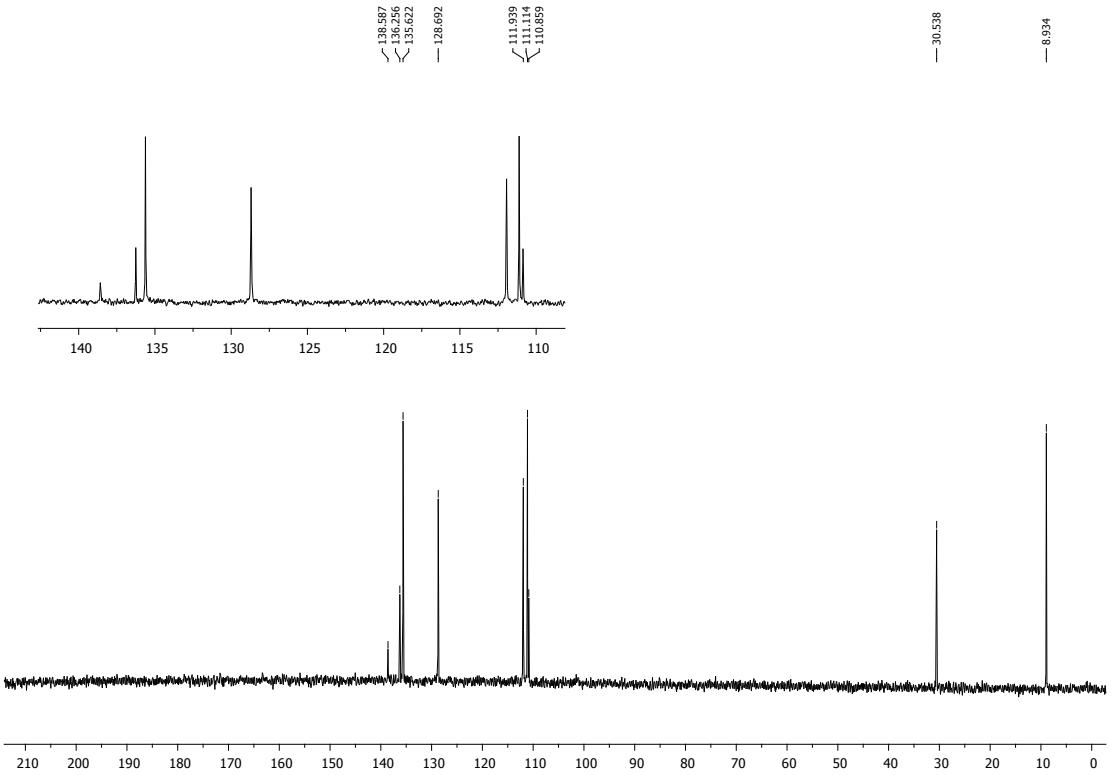


Figure S48. $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O) spectrum of compound **3c**.

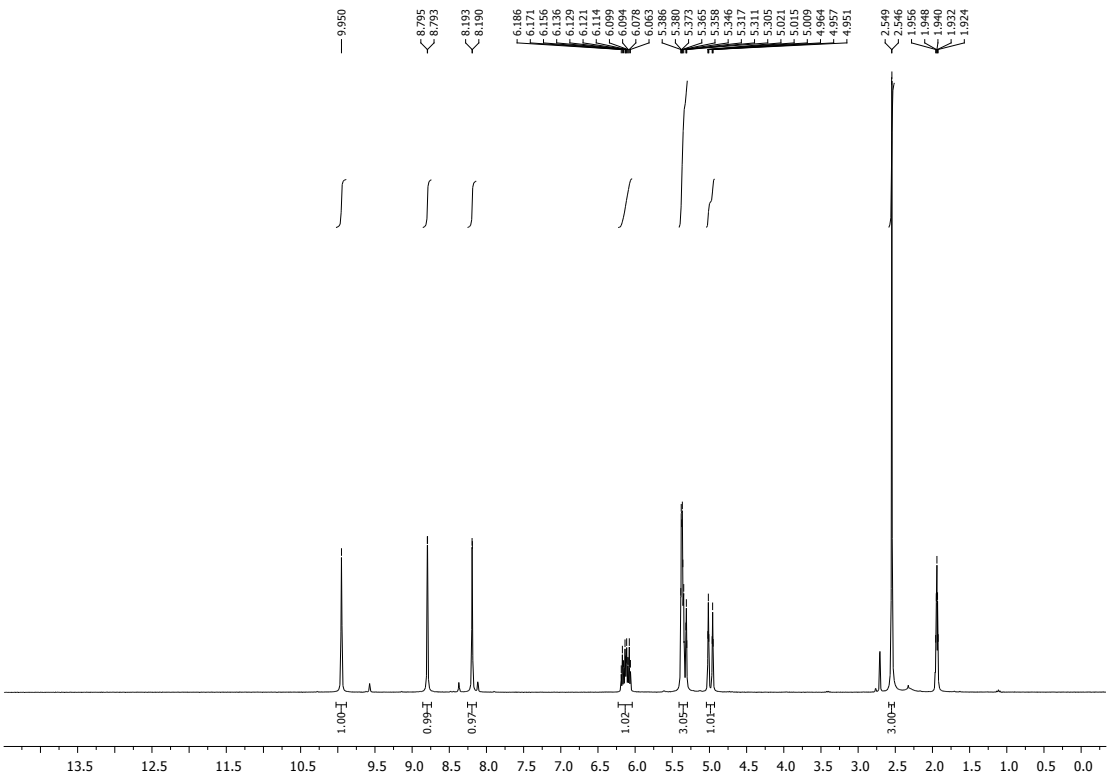


Figure S49. ^{1}H NMR (300 MHz, CD_3CN) spectrum of compound **3d**.

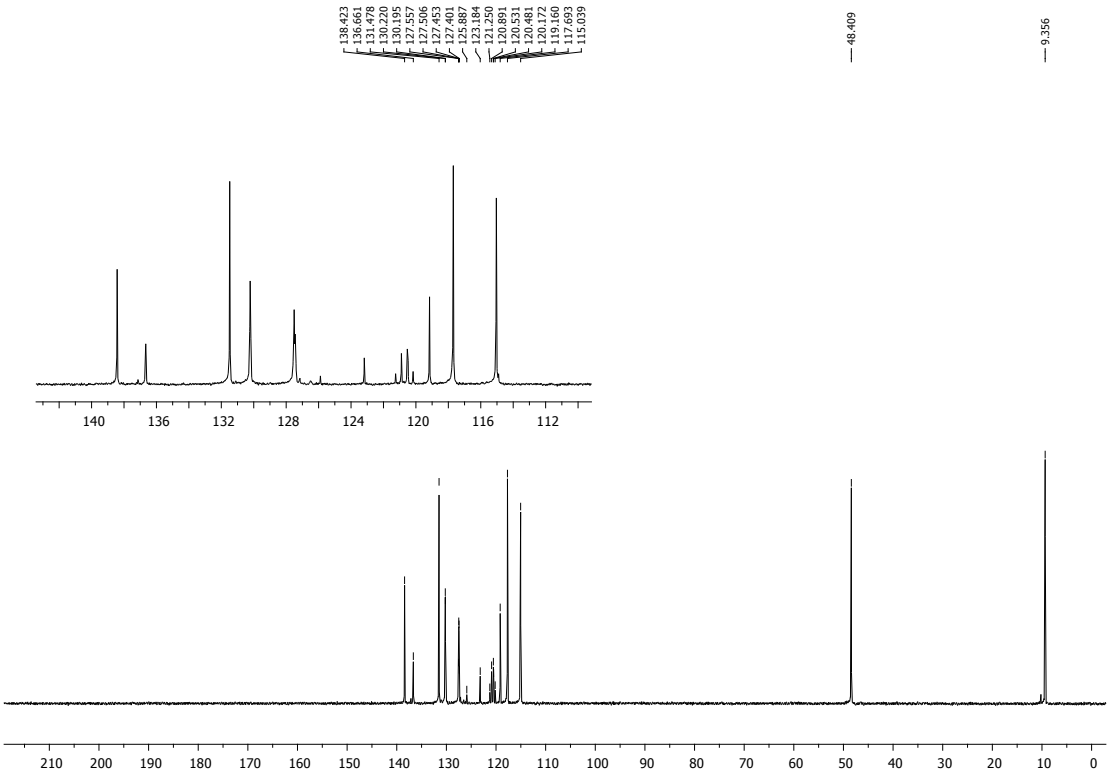


Figure S50. $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O) spectrum of compound **3d**.

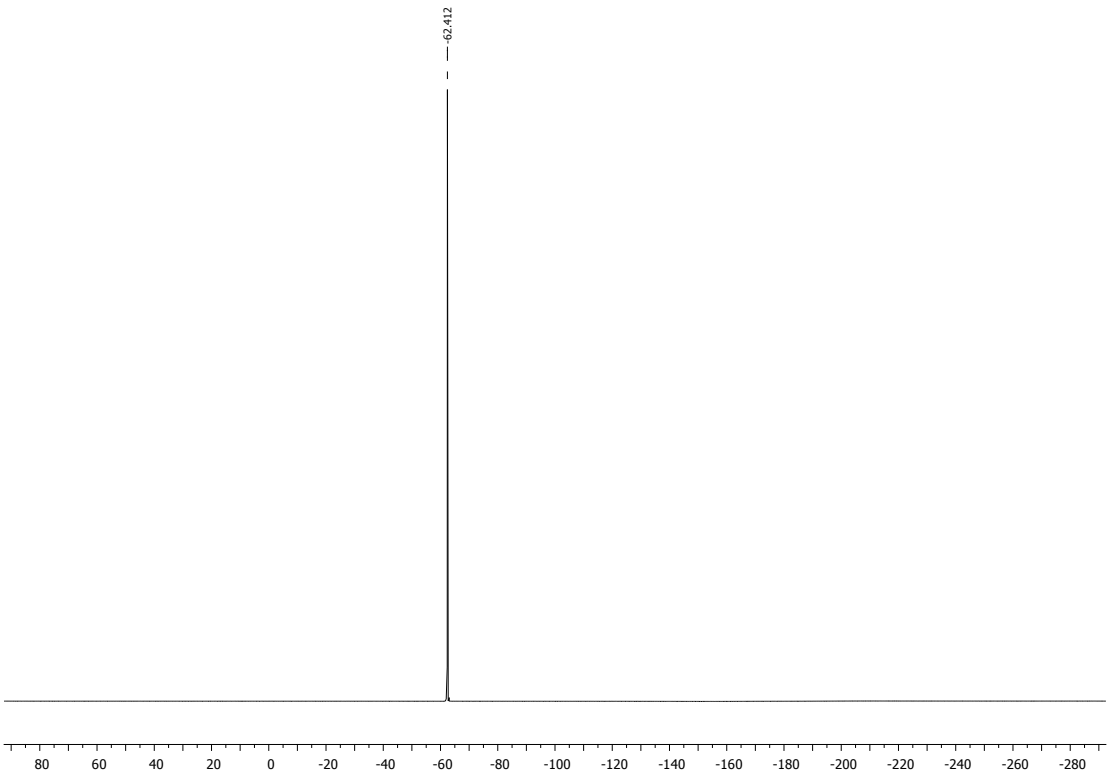


Figure S51. $^{19}F\{^{1}H\}$ NMR (282 MHz, D_2O) spectrum of compound **3d**.

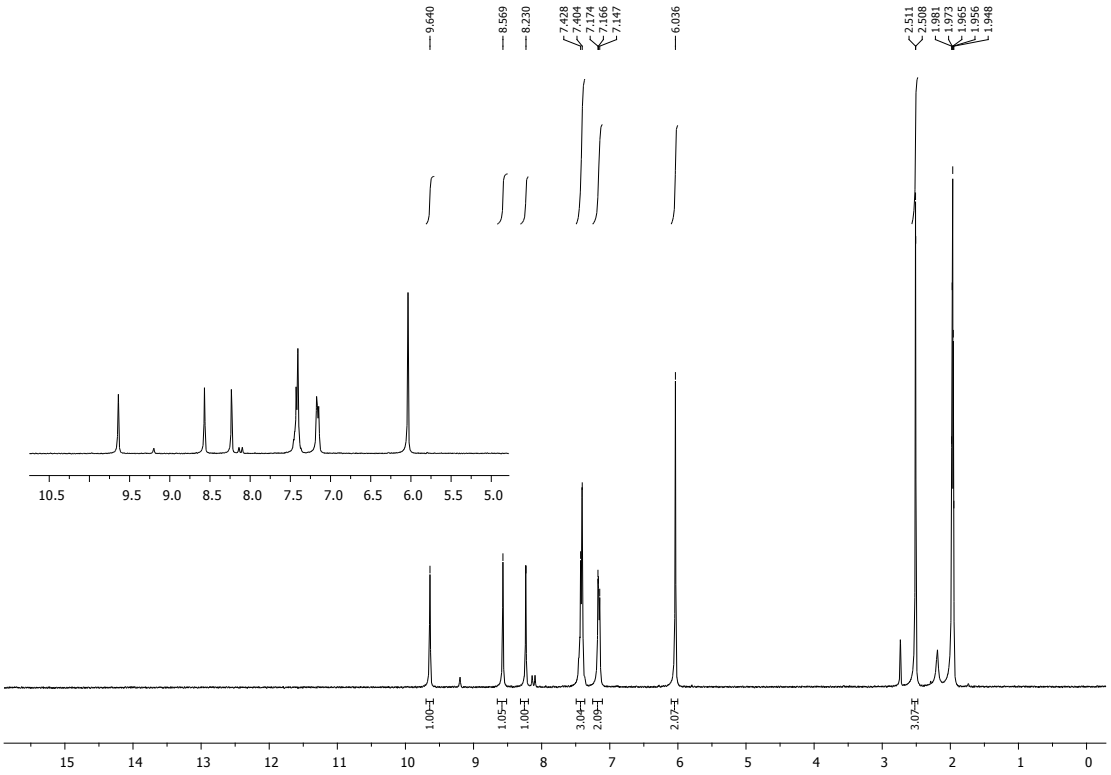


Figure S52. ^{1}H NMR (300 MHz, CD_3CN) spectrum of compound **3e**.

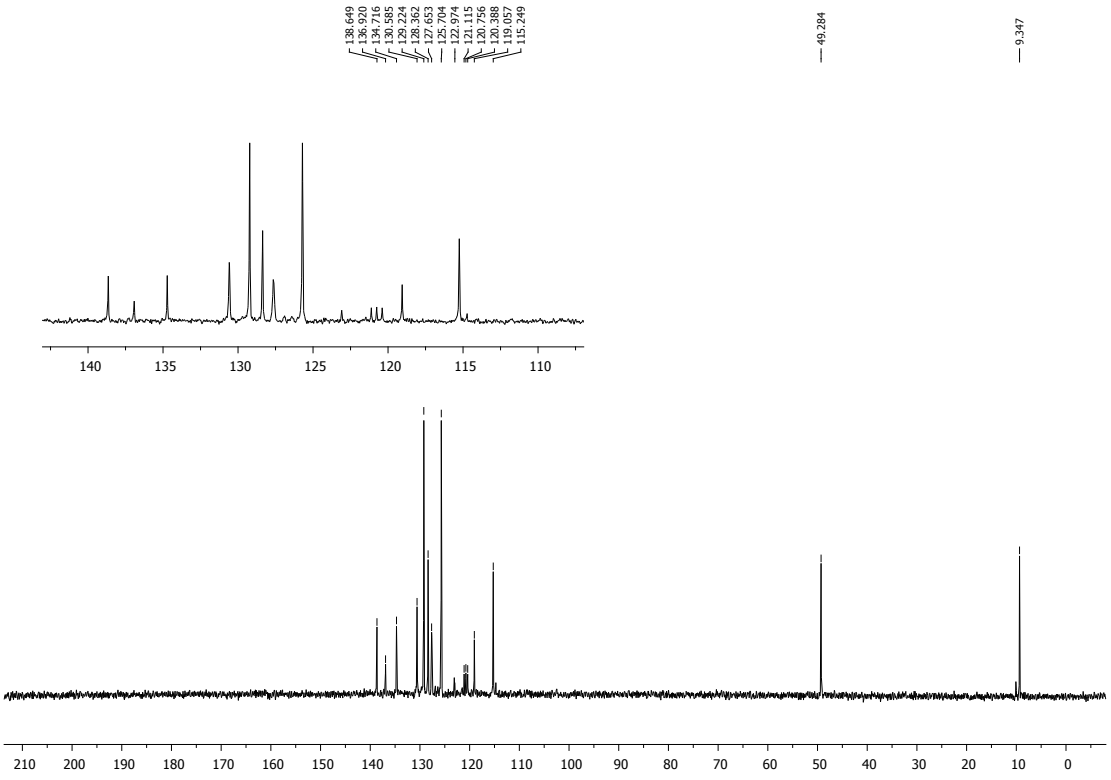


Figure S53. $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O) spectrum of compound **3e**.

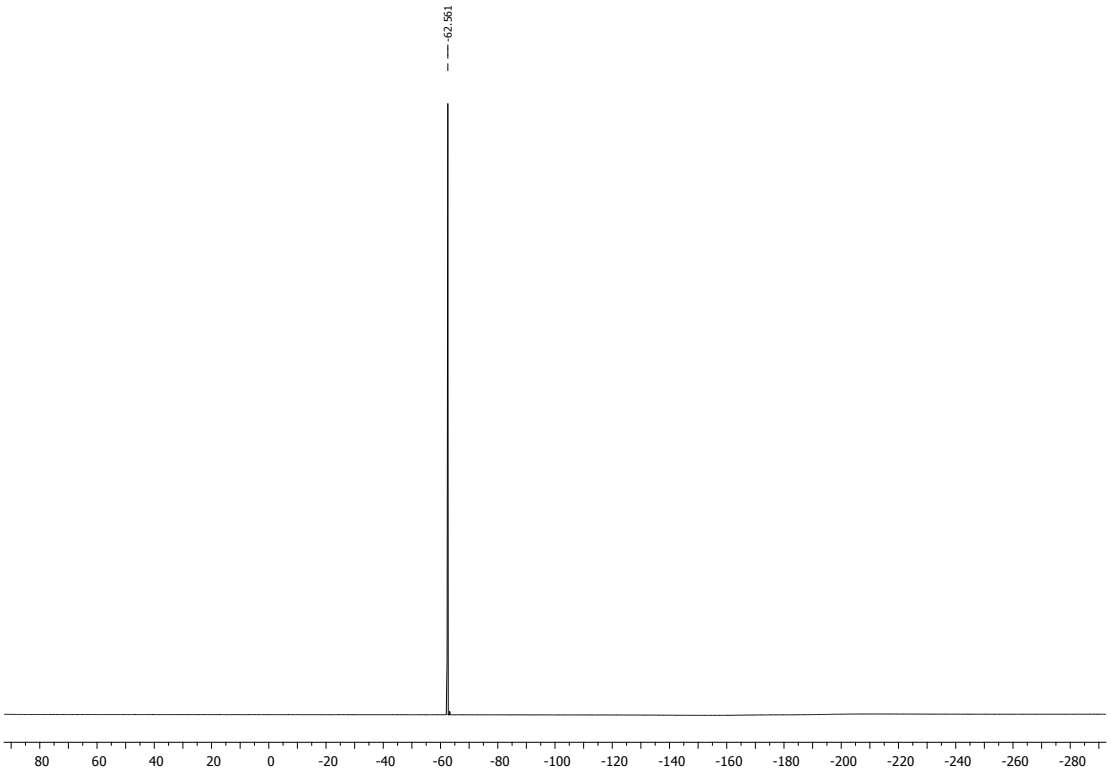


Figure S54. $^{19}F\{^{1}H\}$ NMR (282 MHz, D_2O) spectrum of compound **3e**.

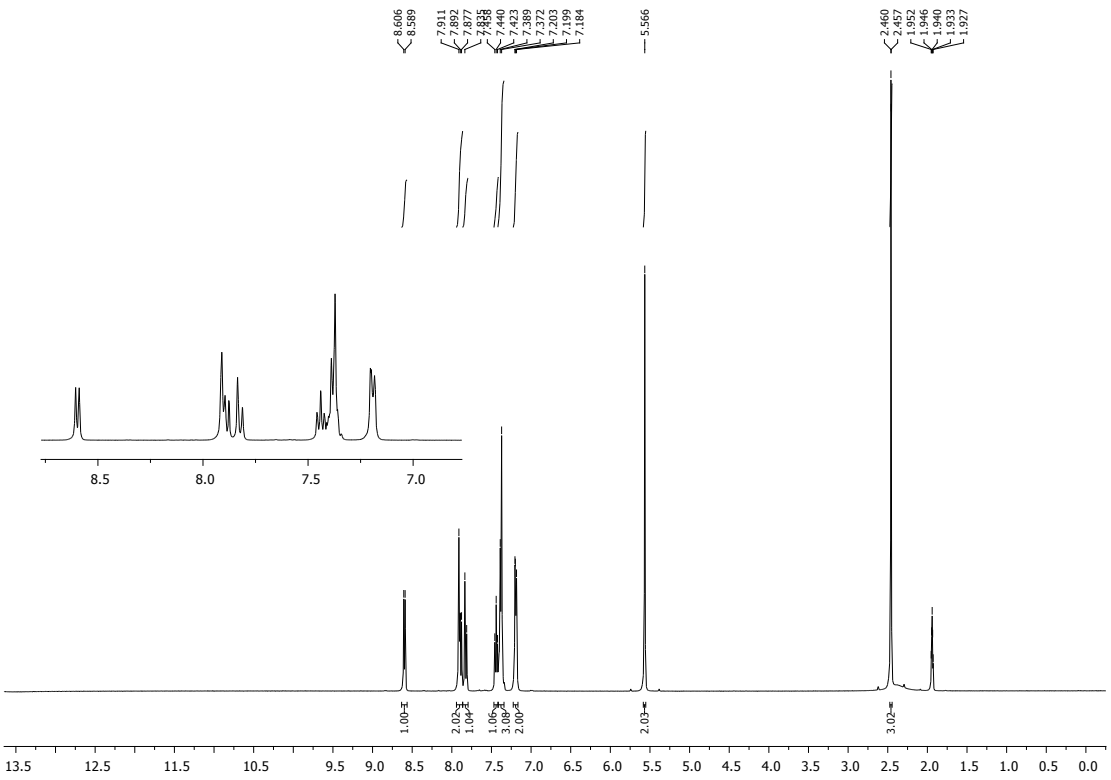


Figure S55. ^{1}H NMR (400 MHz, CD_3CN) spectrum of compound **5a**.

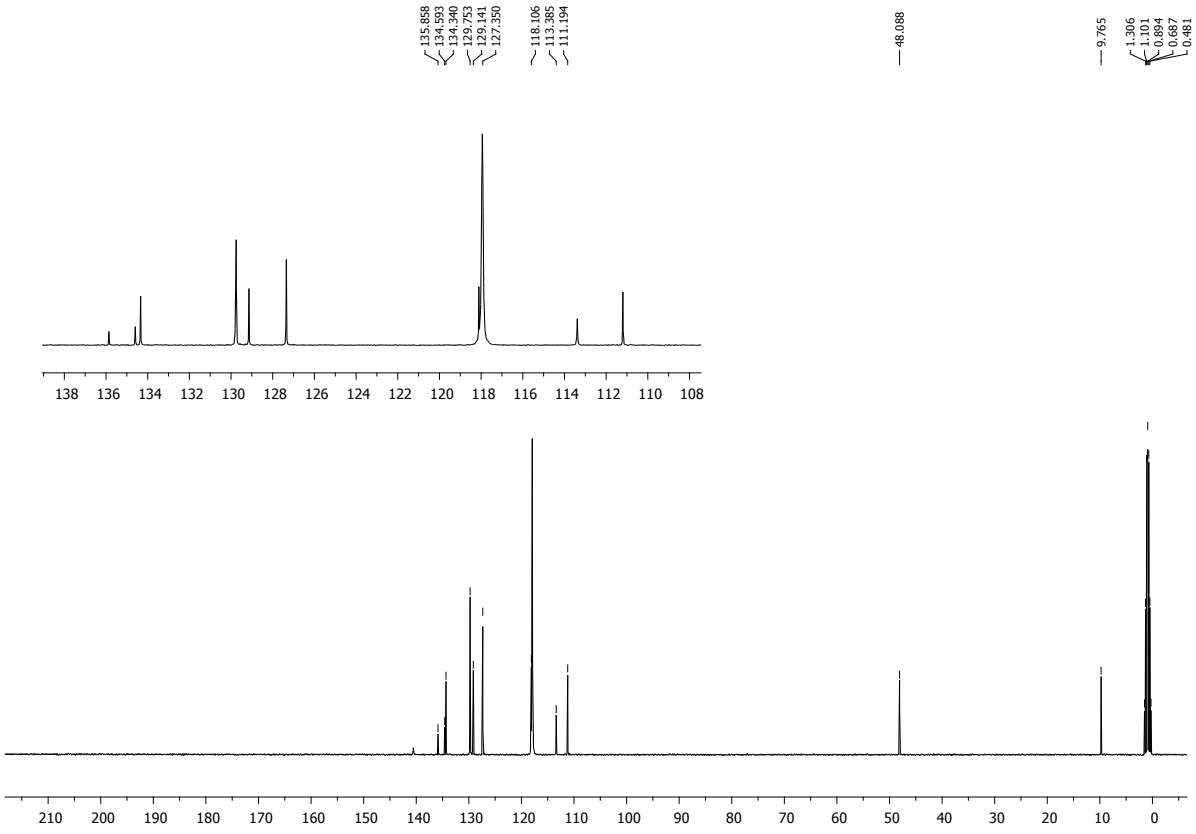
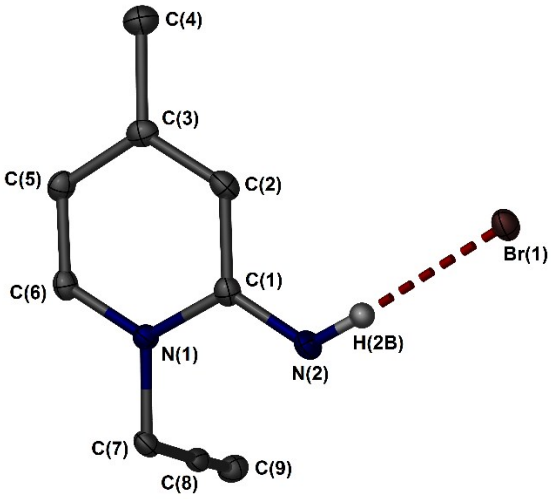


Figure S56. $^{13}C\{^{1}H\}$ NMR (100 MHz, CD_3CN) spectrum of compound **5a**.

11. Crystallographic details

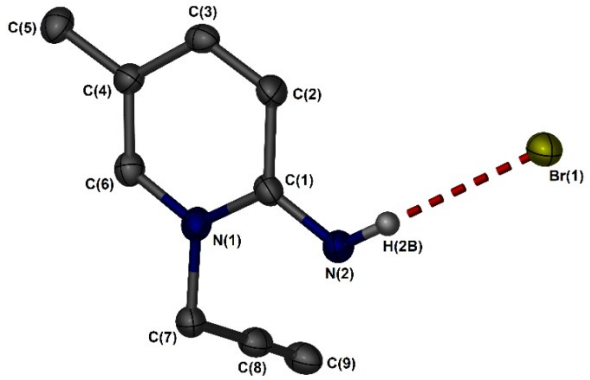
X-Ray diffraction data were collected on an Agilent SuperNova diffractometer fitted with an Atlas CCD detector with Mo Kα radiation (λ = 0.7107 Å) or Cu Kα radiation (λ = 1.5418 Å). Crystals were mounted under oil on nylon fibres. Data sets were corrected for absorption using a multiscan method, and the structures were solved by direct methods using SHELXS-97 or SHELXT and refined by full-matrix least squares on F2 using ShelXL-97, interfaced through the program Olex2.[4] Molecular graphics for all structures were generated using POV-RAY in the X-Seed program.



Crystallographic details for compound 1b.

Identification code	MRC210
Empirical formula	$C_9H_{11}BrN_2$
Formula weight	227.11
Temperature/K	120.01(10)
Crystal system	monoclinic
Space group	C2/c
a/Å	16.7925(7)
b/Å	8.3062(4)
c/Å	15.0809(7)
α/°	90.00
β/°	108.294(5)
γ/°	90.00
Volume/Å^3	1997.21(15)
Z	8
ρ_{calc}g/cm^3	1.511
μ/mm^{-1}	4.066
F(000)	912.0
Crystal size/mm^3	0.3168 × 0.3047 × 0.2242

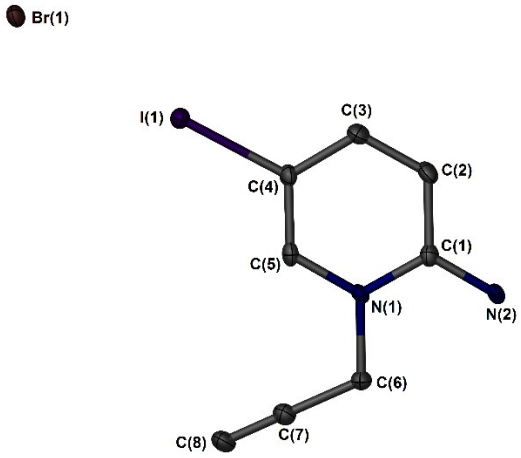
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.34 to 62.36
Index ranges	-23 ≤ h ≤ 23, -10 ≤ k ≤ 12, -13 ≤ l ≤ 21
Reflections collected	6872
Independent reflections	2841 [R_{int} = 0.0520, R_{sigma} = 0.0688]
Data/restraints/parameters	2841/0/110
Goodness-of-fit on F^2	1.071
Final R indexes [I>=2σ (I)]	R_1 = 0.0442, wR_2 = 0.0869
Final R indexes [all data]	R_1 = 0.0623, wR_2 = 0.0961
Largest diff. peak/hole / e $Å^{-3}$	0.67/-0.63



Crystallographic details for compound 1c.

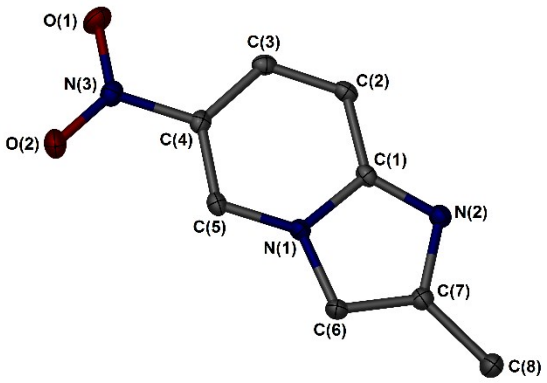
Identification code	MRC278
Empirical formula	$C_9H_{11}BrN_2$
Formula weight	227.11
Temperature/K	120.01(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	7.4282(7)
b/Å	14.9520(14)
c/Å	8.9188(7)
α/°	90.00
β/°	94.547(9)
γ/°	90.00
Volume/$Å^3$	987.45(15)
Z	4
$\rho_{calc}g/cm^3$	1.528
μ/mm^{-1}	5.251
F(000)	456.0
Crystal size/mm^3	0.2292 × 0.0982 × 0.0286
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	11.58 to 148.48
Index ranges	-6 ≤ h ≤ 9, -18 ≤ k ≤ 15, -10 ≤ l ≤ 11
Reflections collected	3789
Independent reflections	1930 [R_{int} = 0.0626, R_{sigma} = 0.0784]
Data/restraints/parameters	1930/0/110
Goodness-of-fit on F^2	1.086

Final R indexes [I>=2σ (I)]	R_1 = 0.0686, wR_2 = 0.1740
Final R indexes [all data]	R_1 = 0.0849, wR_2 = 0.1896
Largest diff. peak/hole / e Å^{-3}	1.32/-0.87



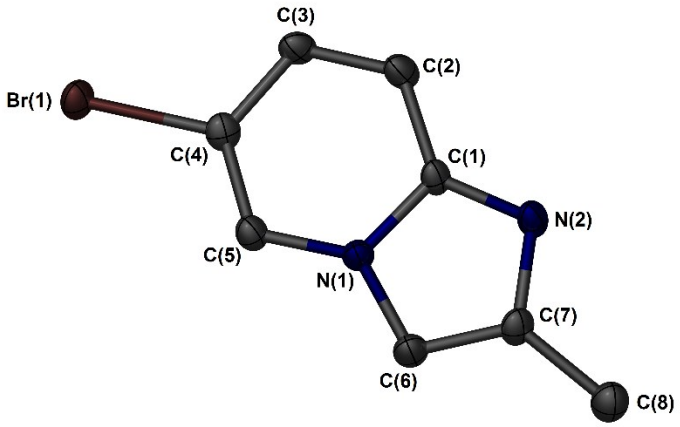
Crystallographic details for compound 1h.

Identification code	MRC214
Empirical formula	$C_8H_8BrIN_2$
Formula weight	338.97
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	6.0553(4)
b/Å	14.8323(10)
c/Å	12.4390(10)
α/°	90.00
β/°	103.295(8)
γ/°	90.00
Volume/Å^3	1087.24(14)
Z	4
ρ_{calc}g/cm^3	2.071
μ/mm^{-1}	6.573
F(000)	632.0
Crystal size/mm^3	0.2118 × 0.1382 × 0.0712
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.44 to 62.5
Index ranges	$-8 \le h \le 8$, $-13 \le k \le 21$, $-17 \le l \le 17$
Reflections collected	6777
Independent reflections	3055 [R_{int} = 0.0453, R_{sigma} = 0.0691]
Data/restraints/parameters	3055/0/109
Goodness-of-fit on F^2	1.030
Final R indexes [I>=2σ (I)]	R_1 = 0.0401, wR_2 = 0.0692
Final R indexes [all data]	R_1 = 0.0602, wR_2 = 0.0781
Largest diff. peak/hole / e Å^{-3}	1.26/-0.74



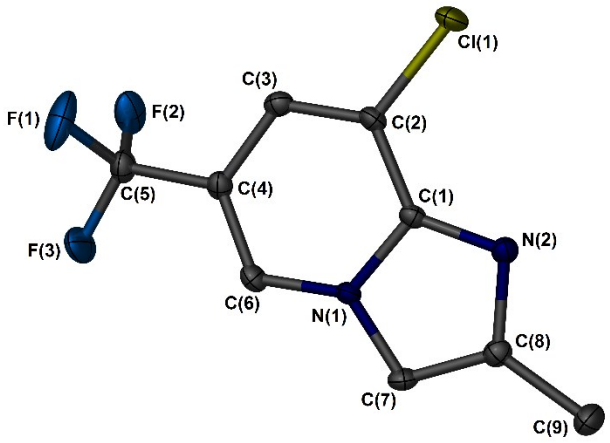
Crystallographic details for compound 2e.

Identification code	MRC218
Empirical formula	$C_8H_7N_3O_2$
Formula weight	177.17
Temperature/K	119.99(14)
Crystal system	trigonal
Space group	R-3
a/Å	24.304(2)
b/Å	24.304(2)
c/Å	6.8579(5)
α/°	90.00
β/°	90.00
γ/°	120.00
Volume/Å^3	3508.1(5)
Z	18
ρ_{calc}g/cm^3	1.509
μ/mm^{-1}	0.113
F(000)	1656.0
Crystal size/mm^3	0.23 × 0.0982 × 0.0286
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.24 to 62.48
Index ranges	$-17 \leq h \leq 33$, $-25 \leq k \leq 31$, $-9 \leq l \leq 7$
Reflections collected	4157
Independent reflections	2171 [R_{int} = 0.0311, R_{sigma} = 0.0540]
Data/restraints/parameters	2171/0/119
Goodness-of-fit on F^2	1.102
Final R indexes [I>=2σ (I)]	R_1 = 0.0526, wR_2 = 0.1269
Final R indexes [all data]	R_1 = 0.0719, wR_2 = 0.1374
Largest diff. peak/hole / e Å^{-3}	0.27/-0.32



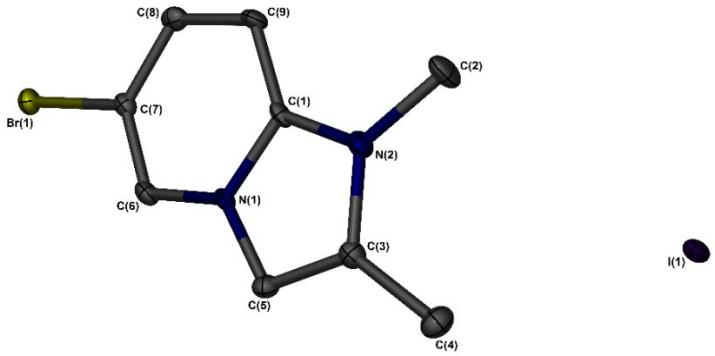
Crystallographic details for compound 2g.

Identification code	MRC000(2g)
Empirical formula	$C_8H_7BrN_2$
Formula weight	211.07
Temperature/K	120.01(16)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	3.9883(6)
b/Å	17.853(2)
c/Å	11.2011(12)
α/°	90.00
β/°	91.622(11)
γ/°	90.00
Volume/Å^3	797.27(17)
Z	4
ρ_{calc}g/cm^3	1.758
μ/mm^{-1}	6.457
F(000)	416.0
Crystal size/mm^3	0.223 × 0.0777 × 0.0292
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.32 to 148.54
Index ranges	$-4 \leq h \leq 4$, $-17 \leq k \leq 21$, $-11 \leq l \leq 13$
Reflections collected	4773
Independent reflections	1576 [R_{int} = 0.0828, R_{sigma} = 0.0702]
Data/restraints/parameters	1576/0/101
Goodness-of-fit on F^2	1.060
Final R indexes [I>=2σ (I)]	R_1 = 0.0667, wR_2 = 0.1730
Final R indexes [all data]	R_1 = 0.0797, wR_2 = 0.1847
Largest diff. peak/hole / e Å^{-3}	1.88/-1.09



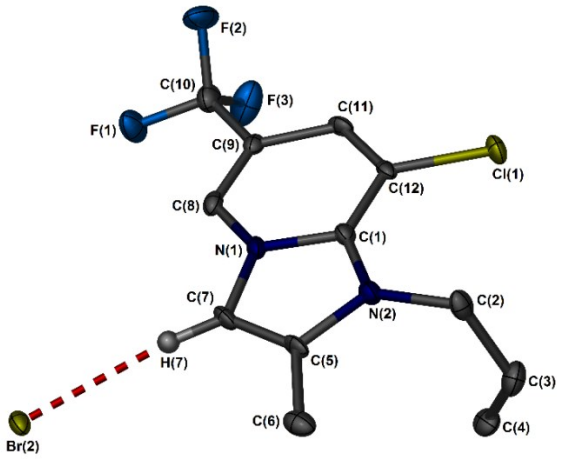
Crystallographic details for compound 2i.

Identification code	MRC196
Empirical formula	$C_9H_6ClF_3N_2$
Formula weight	234.61
Temperature/K	120.01(15)
Crystal system	monoclinic
Space group	I2/a
a/Å	12.0869(14)
b/Å	8.1608(10)
c/Å	19.776(3)
α/°	90.00
β/°	102.192(12)
γ/°	90.00
Volume/Å^3	1906.7(4)
Z	8
ρ_{calc}g/cm^3	1.635
μ/mm^{-1}	0.411
F(000)	944.0
Crystal size/mm^3	0.26 × 0.1011 × 0.03
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.06 to 62.4
Index ranges	$-17 \leq h \leq 12$, $-11 \leq k \leq 11$, $-24 \leq l \leq 27$
Reflections collected	6222
Independent reflections	2707 [R_{int} = 0.0512, R_{sigma} = 0.0780]
Data/restraints/parameters	2707/0/137
Goodness-of-fit on F^2	1.091
Final R indexes [I>=2σ (I)]	R_1 = 0.0707, wR_2 = 0.1274
Final R indexes [all data]	R_1 = 0.1075, wR_2 = 0.1426
Largest diff. peak/hole / e Å^{-3}	0.32/-0.33



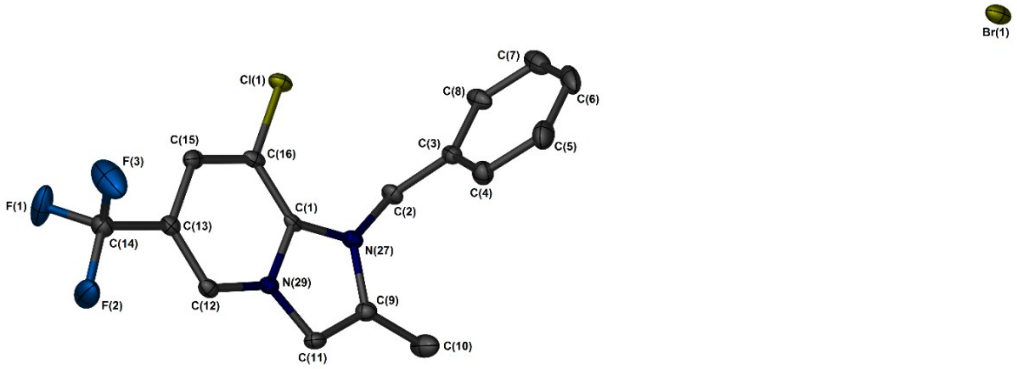
Crystallographic details for compound 3bi.

Identification code	MRC207
Empirical formula	$C_9H_{10}BrIN_2$
Formula weight	353.00
Temperature/K	120.00(13)
Crystal system	monoclinic
Space group	C2/c
a/Å	16.4865(9)
b/Å	10.7791(5)
c/Å	13.0845(8)
α/°	90.00
β/°	110.686(6)
γ/°	90.00
Volume/Å^3	2175.3(2)
Z	8
ρ_{calc}g/cm^3	2.156
μ/mm^{-1}	6.575
F(000)	1328.0
Crystal size/mm^3	0.16 × 0.09 × 0.07
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.2 to 62.42
Index ranges	$-12 \leq h \leq 22$, $-15 \leq k \leq 15$, $-18 \leq l \leq 18$
Reflections collected	7183
Independent reflections	3102 [R_{int} = 0.0497, R_{sigma} = 0.0687]
Data/restraints/parameters	3102/0/120
Goodness-of-fit on F^2	1.072
Final R indexes [I>=2σ (I)]	R_1 = 0.0432, wR_2 = 0.0761
Final R indexes [all data]	R_1 = 0.0588, wR_2 = 0.0819
Largest diff. peak/hole / e Å^{-3}	1.07/-0.70



Crystallographic details for compound 3im.

Identification code	MRC213
Empirical formula	$C_{12}H_{11}BrClF_3N_2$
Formula weight	355.59
Temperature/K	120.00(11)
Crystal system	triclinic
Space group	P-1
a/Å	11.0577(11)
b/Å	11.1824(12)
c/Å	12.0726(12)
α/°	98.874(9)
β/°	103.354(9)
γ/°	103.785(9)
Volume/Å^3	1375.6(2)
Z	4
ρ_{calc}g/cm^3	1.717
μ/mm^{-1}	3.204
F(000)	704.0
Crystal size/mm^3	0.2673 × 0.1112 × 0.0797
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.78 to 62.4
Index ranges	$-16 \leq h \leq 15$, $-14 \leq k \leq 14$, $-16 \leq l \leq 13$
Reflections collected	15562
Independent reflections	7699 [R_{int} = 0.0935, R_{sigma} = 0.1715]
Data/restraints/parameters	7699/0/348
Goodness-of-fit on F^2	1.024
Final R indexes [I>=2σ (I)]	R_1 = 0.0760, wR_2 = 0.1161
Final R indexes [all data]	R_1 = 0.1488, wR_2 = 0.1499
Largest diff. peak/hole / e Å^{-3}	2.07/-0.68



Crystallographic details for compound 3ik.

Identification code	MRC227
Empirical formula	$C_{16}H_{13}BrClF_3N_2$
Formula weight	405.64
Temperature/K	120.02(16)
Crystal system	monoclinic
Space group	I2/a
a/Å	22.7475(15)
b/Å	11.3014(7)
c/Å	27.0251(16)
α/°	90.00
β/°	104.181(6)
γ/°	90.00
Volume/Å^3	6735.8(7)
Z	16
ρ_{calc}g/cm^3	1.600
μ/mm^{-1}	2.628
F(000)	3232.0
Crystal size/mm^3	0.1218 × 0.076 × 0.0505
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.38 to 62.3
Index ranges	-25 ≤ h ≤ 33, -15 ≤ k ≤ 16, -32 ≤ l ≤ 37
Reflections collected	26483
Independent reflections	9663 [R_{int} = 0.0634, R_{sigma} = 0.0993]
Data/restraints/parameters	9663/36/414
Goodness-of-fit on F^2	1.040
Final R indexes [I>=2σ (I)]	R_1 = 0.0660, wR_2 = 0.1191
Final R indexes [all data]	R_1 = 0.1118, wR_2 = 0.1368
Largest diff. peak/hole / e Å^{-3}	1.64/-1.08

12. References

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