

Single Point Activation of Pyridines Enables Reductive Hydroxymethylation
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General Experimental Techniques

Chemicals and solvents

Unless stated otherwise, all chemicals were purchased from commercial suppliers (Sigma-Aldrich, Fluorochem, Alfa Aesar) and used without further purification. The magnesium methoxide was purchased from Alfa Aesar as a 6-10% w/w solution in methanol and was titrated using EDTA in the presence of Eriochrome Black T as an indicator. Prilled paraformaldehyde (95% purity) was used in all cases.

Glassware and reaction conditions

Reactions were carried out in oven-dried microwave vials under an atmosphere of air unless otherwise stated.

Analytical techniques

^1H , ^{19}F and ^{13}C NMR spectra were recorded on a Bruker AVIII400 Spectrometer (400 MHz ^1H 376 MHz and 100 MHz respectively) or a Bruker AVII500 (^1H : 500 MHz and ^{13}C : 126 MHz) in CDCl_3 or $\text{DMSO}-d_6$, and referenced to residual solvent peaks. Chemical shifts δ are quoted in parts per million (ppm) to the nearest 0.01 for ^1H and 0.1 for ^{13}C , coupling constants J are quoted in Hz to the nearest 0.1 and splitting are recorded as singlet (s), doublet (d), triplet (t), quartet (q), doublet of a doublet (dd), doublet of a triplet (dt), triplet of a doublet (td), triplet of a triplet (tt), doublet of a doublet of a doublet (ddd), doublet of a doublet of a triplet (ddt) and multiplet (m). Assignments were based upon COSY, HSQC and HMBC experiments. Infrared spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer fitted with an Attenuated Total Reflectance (ATR) sampling accessory. Absorption maxima are quoted in wavenumbers (cm^{-1}). High resolution mass spectra were recorded on a Bruker MicroTof (resolution = 10000 FWHM). Melting points (m.p.) were obtained using a Lecia VMGT heated-stage microscope and are uncorrected.

Chromatography

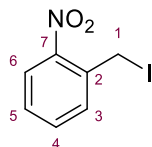
Analytical thin layer chromatography was performed on pre-coated silica gel aluminium sheets from Merck (TLC Silica Gel 60 F_{254s}). Spots were visualized either by the quenching of UV fluorescence or by staining with phosphomolybdic acid, potassium permanganate or vanillin solutions. Preparative flash column chromatography (FCC) was carried out using Geduran Silica Gel 60 (40 μm – 63 μm) from Merck.

The Synthesis of Benzyl Iodides

General Procedure A: Preparation of benzyl iodides

To a solution of the corresponding benzyl chloride or bromide (1.00 equiv.) in acetone (0.5 M) at 0 °C was added NaI (2.00 equiv.) and the reaction mixture was stirred in the dark at room temperature for 16 hours. Reaction was quenched with brine (20 mL) and the aqueous layer extracted with Et₂O (2 x 40 mL). The combined organic layers were dried (MgSO₄), filtered and concentrated *in vacuo*. FCC (0-2% Et₂O in Pentane) afforded the benzyl iodides.

2-Nitrobenzyl iodide (S1)

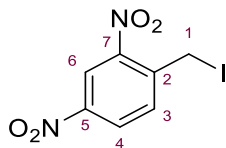


The title compound was prepared by General Procedure A using 2-nitrobenzyl bromide (6.48 g, 30.0 mmol) to give the *iodide* **S1** (7.10 g, 90%) as an orange solid. Spectroscopic data was consistent with that reported in the literature.¹

¹H NMR (400 MHz, CDCl₃) δ 8.04 (dd, *J* = 8.2, 1.4 Hz, 1H, C⁶H), 7.60 – 7.40 (m, 3H, 3 x ArCH), 4.79 (s, 2H, C¹H₂).

¹³C NMR (101 MHz, CDCl₃) δ 147.5 (C⁷), 135.1 (C²), 134.0 (ArCH), 132.4 (ArCH), 129.2 (ArCH), 125.9 (ArCH), 0.0 (C¹H₂).

2,4-Dinitrobenzyl iodide (S2)



Title compound was prepared by General Procedure A using 2,4-dinitrobenzyl bromide (217 mg, 1.00 mmol) to give the *iodide* **S2** (273 mg 89%) as a yellow solid.

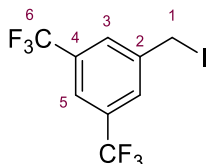
¹H NMR (400 MHz, CDCl₃) δ 8.90 (d, *J* = 2.4 Hz, 1H, C⁶H), 8.40 (dd, *J* = 8.5, 2.4 Hz, 1H, C⁴H), 7.73 (d, *J* = 8.5 Hz, 1H, C³H), 4.84 (s, 2H, 2 x C¹H₂).

¹³C NMR (101 MHz, CDCl₃) δ 141.93 (C²), 133.67 (C⁶H), 128.01 (C⁴H), 121.52 (C³H), -2.78 (C¹H₂), signal for C⁵ and C⁷ not observed.

HRMS (ESI): Exact mass calculated for C₇H₄O₄N₂¹²⁷I [M]⁺: 306.92212, found: 306.92142;

IR (neat) (cm⁻¹): 3124, 2924, 1704, 1603, 1536, 1346, 1198, 1085, 892, 506.

3,5-bis(Trifluoromethyl)benzyl iodide (S3)



Title compound was prepared using General Procedure A using 3,5-bis(trifluoromethyl)benzyl bromide (0.37 mL, 2.00 mmol) to yield the *iodide* **S3** (700 mg, 99%) as a yellow solid. Spectroscopic data was consistent with that reported in the literature.²

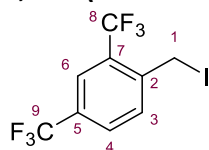
¹H NMR (400 MHz, CDCl₃) δ 7.81 (s, 2H, 2 x C³H), 7.76 (s, 1H, C⁵H), 4.49 (s, 2H, C¹H₂).

¹M. Alajarin, A. Pastor, R.-A. Orenes, J. W. Steed, and R. Arakawa, *Chem. Eur. J.* **2004** 10, 1383–1397.

²D. F. J. Caputo, C. Arroniz, A. B. Dürr, J. J. Mousseau, A. F. Stepan, S. J. Mansfield, and E. A. Anderson, *Chem. Sci.*, 2018,**9**, 5295-5300

¹³C NMR (101 MHz, CDCl₃) δ 142.1, (C²), 132.4 (q, *J* = 33.6 Hz, 2 x C⁴), 128.9 (q, *J* = 3.1 Hz, 2 x C³H), 123.1 (q, *J* = 273 Hz, 2 x C⁶F₃), 122.0 – 121.8 (m, C⁵H), 1.3 (C¹H₂).

2,4-bis(Trifluoromethyl)benzenyl iodide (**S4**)



Title compound was prepared using General Procedure A using 2,4-bis(trifluoromethyl)benzyl bromide (0.38 mL, 2.00 mmol) to yield the *iodide* **S4** (700 mg, 99%) as a yellow oil.

HRMS (ESI): Exact mass calculated for C₉H₅F₆¹²⁷I [M]⁺:

¹H NMR (500 MHz, CDCl₃) δ 7.85 (s, 1H, C⁶H), 7.76 (d, *J* = 8.3 Hz, 1H, C⁴H), 7.70 (d, *J* = 8.2 Hz, 1H, C³H), 4.61 (s, 2H, C¹H₂).

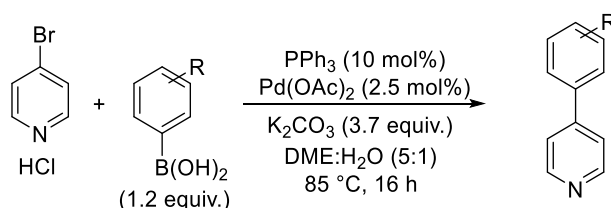
¹³C NMR (126 MHz, CDCl₃) δ 142.3 (C²), 133.6 (C³H), 130.4 (q, *J* = 33.7 Hz, C⁵/C⁷), 129.4 (q, *J* = 3.7 Hz, C⁴H), 128.4 (q, *J* = 31.6 Hz, C⁵/C⁷), 124.05 – 123.52 (m, C⁶H), 123.5 (q, *J* = 274.5 Hz, C⁸F₃/C⁹F₃), 123.30 (q, *J* = 272.3 Hz, C⁸F₃/C⁹F₃), -2.53 (q, *J* = 2.5 Hz, C¹H₂).

¹⁹F NMR (377 MHz, CDCl₃) δ -60.7, -63.0.

IR (neat) (cm⁻¹): 1628, 1345, 1273, 1175, 1119, 1082, 1053, 913, 844, 671

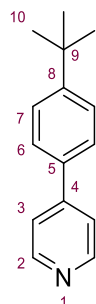
The Synthesis of Pyridine Precursors

General Procedure B: Preparation of 4-Aryl Pyridines



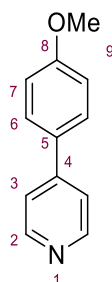
4-Bromopyridine hydrochloride (1.00 equiv.), triphenylphosphine (20 mol%), boronic acid (1.20 equiv.), and potassium carbonate (3.70 equiv.) were added to a 3-necked flask fitted with a reflux condenser. The vessel was evacuated and backfilled with argon three times then dimethoxyethane and water (5:1 0.1 M) were added and solution purged with argon for 10 minutes. Palladium(II) acetate (2.5 mol%) was added and the solution heated at 85°C for 16 hours. The solution was cooled, diluted with 50 mL of water, and extracted with EtOAc (50 mL) three times. The organic layers were combined, dried (MgSO_4), filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography to give the product.

4-(4-(*tert*-Butyl)phenyl)pyridine (**3e**)



The title compound was prepared according to General Procedure B using 4-*tert*-butylphenylboronic acid (2.14 g, 12.0 mmol) and was purified by FCC (10% - 20% EtOAc in pentane) to give *pyridine 3e* (1.78 g, 83%) as a cream solid. The spectroscopic data was consistent with previous reports.³

4-(4-Methoxyphenyl)pyridine (**3f**)

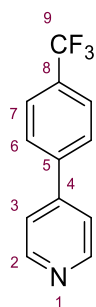


The title compound was prepared according to General Procedure B using 4-methoxyphenylboronic acid (547 mg, 3.60 mmol) and was purified by FCC (10% - 20% EtOAc in pentane) to give *pyridine 3f* (1.60 g, 76%) as a white solid. The spectroscopic data was consistent with previous reports.⁴

³S. Jonsson, F. G. J. Odille, P.-O. Norrby, and K. Wärnmark, *Org. Biomol. Chem.*, 2006, **4**, 1927–1948

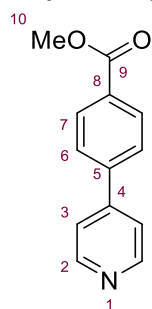
⁴X. Zhang and A. McNally, *Angew. Chem. Int. Ed.*, 2017, **56**, 9833–9836

4-(4-Trifluoromethyl)pyridine (3g)



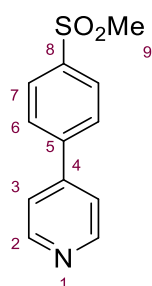
The title compound was prepared according to General Procedure B using 4-trifluoromethylbenzene boronic acid (2.28 g, 12.0 mmol) and was purified by FCC (30% -50% EtOAc in pentane) to give *pyridine* **3g** (1.70 g, 76% yield) as a yellow glass. The spectroscopic data was consistent with previous literature reports.⁵

4-Pyridin-4-yl benzoic acid methyl ester (3h)



The title compound was prepared according to General Procedure B using 4-methoxycarbonylphenylboronic acid (2.16 g, 12.0 mmol) and purified by FCC (30%-50% EtOAc in pentane) to give *pyridine* **3h** (1.60g, 76% yield) as a white solid. The spectroscopic data was consistent with previous literature reports.⁶

4-(4-Methylsulfonylphenyl)pyridine (3i)



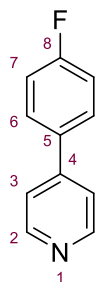
The title compound was prepared according to General Procedure B using 4-methylsulfonylphenylboronic acid (2.40 g, 12.0 mmol) and purified by FCC (10%-20% acetone in CH₂Cl₂) to give *pyridine* **3i** (1.56 g, 67% yield) as a white solid. The spectroscopic data was consistent with previous literature reports.⁷

⁵H. Y. Lee; X. Jiang, D. Lee, *Org. Lett.* **2009**, 11, 2065 - 2068

⁶J. Malineni, R. L. Jezorek, N. Zhang, and V. Percec, *Synthesis*, 2016, **48**, 2795–2807

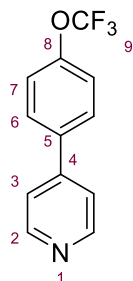
⁷F. Pettersson, P. Svensson, S. Waters, N. Waters, and C. Sonesson, *J. Med. Chem.* 2012, **55**, 3242-3249.

4-(4-Fluorophenyl)pyridine (**3j**)



The title compound was prepared according to General Procedure B using 4-fluorobenzene boronic acid (1.68 g, 12.0 mmol) and was purified by FCC (10% - 20% EtOAc in pentane) to give *pyridine 3j* (1.56 g, 90% yield) as a colourless glass. The spectroscopic data was consistent with previous literature reports.⁸

4-(4-(trifluoromethoxy)phenyl)pyridine (**3k**)



The title compound was prepared according to General Procedure B using 4-trifluoromethoxyphenylboronic acid (2.47 g, 12.0 mmol) and was purified by FCC (10% - 20% EtOAc in pentane) to give *pyridine 3k* (2.19 g, 92%) as a yellow oil.

HRMS (ESI): Exact mass calculated for C₁₃H₈F₃NO [M+H]⁺:240.0631, found: 240.0632

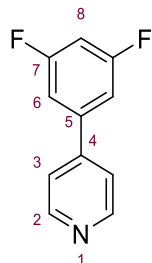
¹H NMR (400 MHz, CDCl₃) δ 8.72 – 8.65 (m, 2H, 2 x C²H), 7.70 – 7.62 (m, 2H, 2 x C⁶H), 7.51 – 7.45 (m, 2H, 2 x C³H), 7.38 – 7.30 (m, 2H, 2 x C⁷H).

¹³C NMR (101 MHz, CDCl₃) δ 150.5 (2 x C²H), 150.1 (C⁸), 147.2 (C⁴), 136.9 (C⁵), 128.7 (2 x C⁶H), 121.7 (2 x C³H), 121.6 (2 x C⁷H), 120.6 (q, *J* = 257.7 Hz, C⁹F₃).

¹⁹F NMR (377 MHz, CDCl₃) δ –57.8.

IR (neat) (cm⁻¹): 2982, 1596, 1516, 1488, 1252, 1207, 1154, 1110, 805, 674.

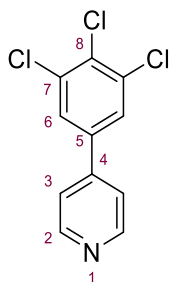
4-(3,5-Difluorophenyl)pyridine (**3l**)



The title compound was prepared according to General Procedure B using 3,5-difluorobenzene boronic acid (1.89 g, 12.0 mmol) and was purified by FCC (10% - 20% EtOAc in pentane) to give *pyridine 3l* (1.67 g, 87% yield) as a cream solid. The spectroscopic data was consistent with previous literature reports.⁴

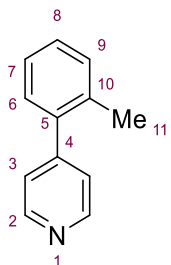
⁸S. Panda, A. Coffin, Q. N. Nguyen, D. J. Tantillo, and J. M. Ready, *Angew. Chem. Int. Ed.* **2016**, 55, 2245-2249

4-(3,4,5-Trichlorophenyl)pyridine (3m)



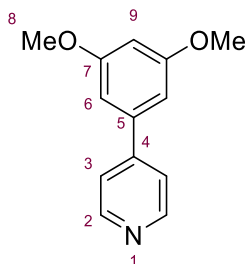
The title compound was prepared using General Procedure B on a 2 mmol scale using 3,4,5-trichlorobenzene boronic acid (540 mg, 2.40 mmol) and purified by FCC (30%-50% EtOAc in pentane) to give *pyridine 3m* (426 mg, 82% yield) as a white solid. The spectroscopic data was consistent with previous literature reports.⁹

4-(2-Methylphenyl)pyridine (3n)



The title compound was prepared according to General Procedure B using 2-methylphenylboronic acid (1.63 g, 12.0 mmol) and purified by FCC (10%-20% EtOAc in pentane) to give *pyridine 3n* (0.94 g, 55% yield) as a colourless oil. The spectroscopic data was consistent with previous literature reports.⁴

4-(3,5-Dimethoxyphenyl)pyridine (3o)



The title compound was prepared according to General Procedure B using 4-trifluoromethoxyphenylboronic acid (2.19 g, 12.0 mmol) and was purified by FCC (20% - 50% EtOAc in pentane) to give *pyridine 3o* (1.74 g, 81%) as a white solid.

m.p. (EtOAc): 56 – 58 °C

HRMS (ESI): Exact mass calculated for C₁₃H₁₄NO₂ [M+H]⁺: 216.1019, found: 216.1020.

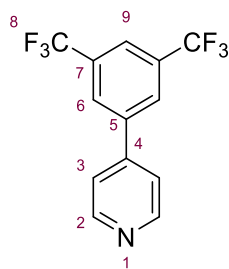
¹H NMR (400 MHz, CDCl₃) δ 8.68 – 8.62 (m, 2H, 2 x C²H), 7.50 – 7.44 (m, 2H, 2 x C³H), 6.75 (d, *J* = 2.2 Hz, 2H, 2 x C⁶H), 6.53 (t, *J* = 2.3 Hz, 1H, C⁹H), 3.85 (s, 6H, 3 x C⁸H₃).

¹³C NMR (101 MHz, CDCl₃) δ 161.5 (2 x C⁷), 150.4 (2 x C²H), 148.5 (C⁴), 140.5 (C⁵), 121.9 (2 x C³H), 105.4 (2 x C⁶H), 100.9 (C⁹H), 55.6 (2 x C⁸H₃).

IR (neat) (cm⁻¹): 2979, 2845, 1586, 1336, 1226, 1198, 1165, 1029, 852, 818.

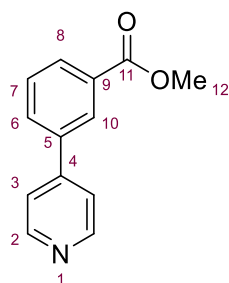
⁹A. Grozavu, H. B. Hepburn, E. P. Bailey, P. J. Lindsay-Scott, T. J. Donohoe, *Chem. Sci.*, 2020, **11**, 8595-8599.

4-(3,5-bis(Trifluoromethyl)phenyl)pyridine (**3p**)



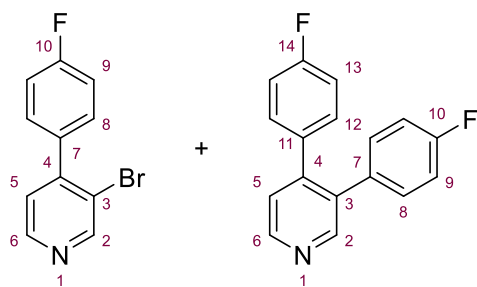
The title compound was prepared according to General Procedure B using 3,5-bis(trifluoromethyl)phenylboronic acid (3.00 g, 12.0 mmol) and purified by FCC (10%-30% EtOAc in pentane) to give *pyridine 3p* (2.12 g, 73% yield) as a white solid. The spectroscopic data was consistent with previous literature reports¹⁰

3-Pyridin-4-yl benzoic acid methyl ester (**3q**)



The title compound was prepared according to General Procedure B using 3-methoxycarbonylphenylboronic acid (2.16 g, 12.0 mmol) and purified by FCC (30%-50% EtOAc in pentane) to give *pyridine 3q* (1.53 g, 72% yield) as a white solid. The spectroscopic data was consistent with previous literature reports.¹¹

3-Bromo-4-(4-fluorophenyl)pyridine (**S5**) and 3,4-bis(4-fluorophenyl)pyridine (**3t**)



The title compound were prepared according to General Procedure B using 3,4-dibromopyridine (2.37 g, 10.0 mmol) and 4-fluorophenylboronic acid (1.52 g, 10.9 mmol) and was purified by FCC (2% EtOAc in pentane) to give *arylp₃pyridine S5* (1.27 g, 51%) as a white solid followed by *bisarylp₃pyridine 3t* (182 mg, 7% yield) as a white solid.

m.p. (EtOAc): 66 - 68 °C

HRMS (ESI): Exact mass calculated for C₁₁H₈BrFN [M+H]⁺: 251.9819, found: 251.9821

¹H NMR (400 MHz, CDCl₃) δ 8.82 (d, *J* = 0.6 Hz, 1H, C²H), 8.55 (d, *J* = 4.9 Hz, 1H, C⁵H), 7.49 – 7.37 (m, 2H, 2 x C⁸H), 7.25 (dd, *J* = 4.9, 0.6 Hz, 1H, C⁶H), 7.22 – 7.11 (m, 2H, 2 x C⁹H).

¹³C NMR (101 MHz, CDCl₃) δ 163.1 (d, *J* = 249.0 Hz, C¹⁰), 152.8, (C²H), 148.9 (C⁴), 148.5 (C⁵H), 134.3 (d, *J* = 3.5 Hz, C⁷), 130.9 (d, *J* = 8.4 Hz, 2 x C⁸H), 125.7 (C⁶H), 121.0 (C³), 115.7 (d, *J* = 21.7 Hz, 2 x C⁹H).

¹⁰ Z.-Y. Liu, Z.-H. Wen, and X.-C. Wang, *Angew. Chem. Int. Ed.*, 2017, **56**, 5817-5820

¹¹ K. Ohkura, M. Terashima, Y. Kanaoka, and K. Seki, *Chem. Pharm. Bull.* 1993, **41**, 1920-1924.

¹⁹F NMR (377 MHz, CDCl₃) δ -112.3 (tt, *J* = 8.6, 5.4 Hz).

IR (neat) (cm⁻¹): 3048, 3011, 2161, 1970, 1605, 1583, 1510, 1470, 1228, 831.

m.p. (EtOAc): 108 - 110 °C

HRMS (ESI): Exact mass calculated for C₁₇H₁₂F₂N [M+H]⁺: 268.0932, found: 268.0932

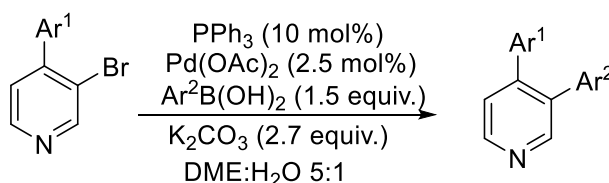
¹H NMR (400 MHz, CDCl₃) δ 8.62 (d, *J* = 5.1 Hz, 1H, C⁵H), 8.61 (d, *J* = 0.7 Hz, 1H, C²H), 7.31 (dd, *J* = 5.0, 0.7 Hz, 1H, C⁶H), 7.16 – 7.05 (m, 4H, 2 x C⁹H + 2 x C¹³H), 7.04 – 6.92 (m, 4H, 2 x C⁸H + 2 x C¹²H).

¹³C NMR (101 MHz, CDCl₃) δ 162.5 (d, *J* = 248.5 Hz, C¹⁰/C¹⁴), 162.3 (d, *J* = 247.6 Hz, C¹⁰/C¹⁴), 151.0 (C²H), 149.0 (C⁵H), 146.7 (C⁴), 134.8 (C³), 134.4 (d, *J* = 3.3 Hz, C⁷/C¹¹), 133.5 (d, *J* = 3.3 Hz, C⁷/C¹¹), 131.4 (d, *J* = 8.0 Hz, C⁸H/C¹²H), 131.0 (d, *J* = 8.3 Hz, C⁸H/C¹²H), 124.5 (C⁶H), 115.5 (d, *J* = 22.0 Hz, C⁹H + C¹³H).

¹⁹F NMR (377 MHz, CDCl₃) δ -113.4 – -113.6 (m), -114.4 – -114.6 (m).

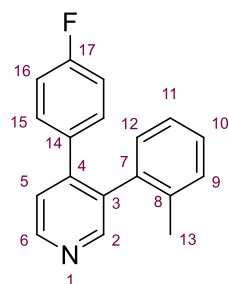
IR (neat) (cm⁻¹): 3050, 3011, 2161, 2034, 1978, 1510, 1228, 1215, 828, 814.

General Procedure C: Preparation of Bisarylpyridines



3-Bromo-4-(4-fluorophenyl)pyridine **S5** (1.5 mmol, 1.00 equiv.), triphenylphosphine (10 mol%), potassium carbonate (2.70 equiv.), and arylboronic acid (1.10 equiv.) were dissolved in a 5:1 mixture of DME:H₂O (0.1 M) which was then purged with Ar for 10 minutes. Pd(OAc)₂ was added and the solution heated for 16 hours at 85 °C. The solution was cooled, diluted with EtOAc and extracted three times with EtOAc. The combined organic layers were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography to give the product.

4-(4-Fluorophenyl)-3-(o-tolyl)pyridine (**3r**)



The title compound was prepared according to General Procedure C using 2-methylphenylboronic acid (150 mg, 1.10 mmol) and purified by FCC (10%-20% EtOAc in pentane) to give *pyridine 3r* (370 mg, 94% yield) as a white solid.

m.p. (EtOAc) 110 - 112 °C;

HRMS (ESI): Exact mass calculated for C₁₈H₁₅FN [M+H]⁺: 268.1183, found: 268.1182.

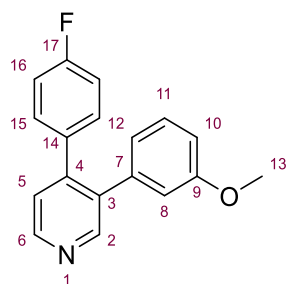
¹H NMR (400 MHz, CDCl₃) δ 8.66 (d, *J* = 5.1 Hz, 1H, C⁵H), 8.54 (d, *J* = 0.6 Hz, 1H, C²H), 7.36 (dd, *J* = 5.1, 0.7 Hz, 1H, C⁶H), 7.23 (dd, *J* = 7.3, 1.7 Hz, 1H, C¹²H), 7.19 (td, *J* = 7.5, 1.6 Hz, 1H, C¹¹H), 7.15 – 7.07 (m, 4H, C⁹H + C¹⁰H + 2 x C¹⁵H), 6.96 – 6.86 (m, 2H, 2 x C¹⁶H), 1.87 (s, 3H, C¹³H₃).

¹³C NMR (101 MHz, CDCl₃) δ 162.6 (d, *J* = 248.4 Hz, C¹⁷), 151.3 (C²H), 148.9 (C⁵H), 147.4 (C⁴), 137.2 (C), 136.2 (C), 135.7 (C), 134.7 (d, *J* = 3.3 Hz, C¹⁴), 130.8 (d, *J* = 8.7 Hz, ArCH + 2 x C¹⁵H), 130.4 (ArCH), 128.2 (C¹²H), 126.0 (C¹¹H), 124.0 (C⁶H), 115.4 (d, *J* = 21.7 Hz, 2 x C¹⁶H), 20.1 (C¹³H₃).

¹⁹F NMR (377 MHz, CDCl₃) δ -113.5 (tt, *J* = 8.8, 5.3 Hz).

IR (neat) (cm⁻¹): 2994, 1602, 1512, 1477, 1218, 831, 779, 756, 746, 729.

4-(4-Fluorophenyl)-3-(3-methoxyphenyl)pyridine (3s)



The title compound was prepared according to General Procedure C using 2-methylphenylboronic acid (167 mg, 1.10 mmol) and purified by FCC (10%-30% EtOAc in pentane) to give *pyridine 3s* (402 mg, 96% yield) as a pale yellow oil.

HRMS (ESI): Exact mass calculated for $C_{18}H_{15}FNO$ $[M+H]^+$: 280.1132, found: 280.1130.

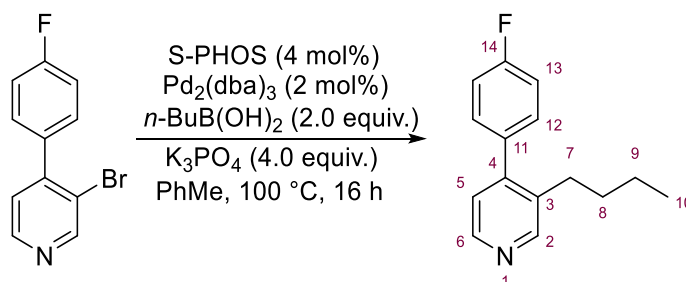
1H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, J = 0.7 Hz, 1H, C^2H), 8.62 (d, J = 5.1 Hz, 1H, C^5H), 7.31 (dd, J = 5.1, 0.7 Hz, 1H, C^6H), 7.20 (dd, J = 8.4, 7.5 Hz, 1H, $C^{11}H$), 7.17 – 7.11 (m, 2H, 2 x $C^{15}H$), 7.02 – 6.92 (m, 2H, 2 x $C^{16}H$), 6.83 (ddd, J = 8.3, 2.6, 1.0 Hz, 1H, $C^{12}H$), 6.72 (ddd, J = 7.6, 1.6, 0.9 Hz, 1H, $C^{10}H$), 6.67 (dd, J = 2.6, 1.6 Hz, 1H, C^8H), 3.68 (s, 3H, $C^{13}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6 (d, J = 248.2 Hz, C^{17}), 159.6 (C^9), 151.1 (C^2H), 148.9 (C^5H), 146.8 (C^4), 139.0 (C), 135.8 (C), 134.7 (d, J = 3.5 Hz, C^{14}), 131.1 (d, J = 8.3 Hz, 2 x $C^{15}H$), 129.6 ($C^{11}H$), 124.6 (C^6H), 122.4 ($C^{10}H$), 115.5 (d, J = 21.5 Hz, 2 x $C^{16}H$), 115.5 (C^8H), 113.4 ($C^{12}H$), 55.3 ($C^{13}H_3$).

^{19}F NMR (377 MHz, $CDCl_3$) δ -113.8 (tt, J = 8.5, 5.2 Hz).

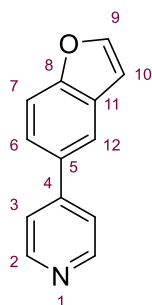
IR (neat) (cm^{-1}): 3039, 2938, 1605, 1512, 1472, 1221, 1160, 1046, 1016, 828.

3-Butyl-4-(4-fluorophenyl)pyridine (3u)



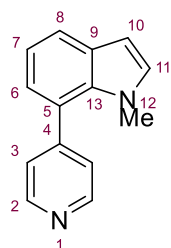
3-Bromo-4-(4-fluorophenyl)pyridine **5S** (1.00 equiv.), S-PHOS (4 mol%), potassium phosphate (4.00 equiv.), and alkylboronic acid (2.00 equiv.) were dissolved in PhMe (8 mL per mmol of aryl bromide) which was then purged with Ar for 10 minutes. $Pd_2(dba)_3$ (2 mol%) was added and the solution heated for 16 hours at 100 °C. The solution was cooled, diluted with EtOAc and extracted three times with EtOAc. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude material was carried through without further purification.

4-(Benzofuran-5-yl)pyridine (3v)



4-Pyridylboronic acid (615 mg, 5.00 mmol), 5-bromobenzofuran (0.75 mL, 6.00 mmol), potassium carbonate (1.80 g, 13.5 mmol), and triphenylphosphine (131 mg, 10 mol%) were dissolved in dioxane:water (25 mL:10 mL). The solution was purged with argon for 10 minutes, then palladium acetate (28 mg, 2.5 mol%) was added. The reaction was heated at 80 °C under argon for 14 hours, then cooled, and diluted with EtOAc (50 mL) and water (50 mL). The solution was separated, and the aqueous layer was extracted with EtOAc (2 x 50 mL, the organic layers were combined, washed with brine, dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by FCC (50% EtOAc in Pentane) to yield *heterocycle 3v* (590 mg, 61% yield) as a white solid. The spectroscopic data was consistent with previous literature reports.¹²

1-Methyl-7-(pyridin-4-yl)-1H-indole (3w)



4-Pyridylboronic acid (830 mg, 6.75 mmol), 7-bromo-1-methyl-1H-indole (945 mg, 4.50 mmol), potassium carbonate (1.55 g, 11.25 mmol), and triphenylphosphine (118 mg, 10 mol%) were dissolved in dioxane:water (40 mL:10 mL). The solution was purged with argon for 10 minutes, then palladium acetate (25 mg, 2.5 mol%) was added. The reaction was heated at 80 °C under argon for 14 hours, then cooled, and diluted with EtOAc (50 mL) and water (50 mL). The solution was separated, and the aqueous layer was extracted with EtOAc (2 x 50 mL, the organic layers were combined, washed with brine, dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by FCC (20%-50% EtOAc in Pentane) to yield *heterocycle 3w* (500 mg, 53% yield) as a white solid.

m.p. (EtOAc) 130 - 132 °C;

HRMS (ESI): Exact mass calculated for C₁₄H₁₃N₂ [M+H]⁺: 209.1073, found: 209.1074.

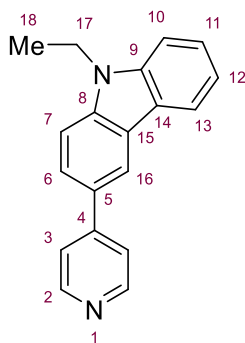
¹H NMR (400 MHz, CDCl₃) δ 8.72 – 8.64 (m, 2H, 2 x C²H), 7.68 (dd, *J* = 7.9, 1.2 Hz, 1H, C⁶H), 7.43 – 7.36 (m, 2H, 2 x C³H), 7.15 (dd, *J* = 7.9, 7.2 Hz, 1H, C⁷H), 7.05 – 6.98 (m, 2H, C⁸H + C¹¹H), 6.58 (d, *J* = 3.1 Hz, 1H, C¹⁰H), 3.36 (s, 3H, C¹²H₃).

¹³C NMR (101 MHz, CDCl₃) δ 149.3 (2 x C²H), 148.9 (C), 133.4 (C), 131.4 (C¹¹H), 130.2 (C), 125.3 (2 x C³H), 124.1 (C⁸H), 123.9 (C), 121.5 (C⁶H), 119.3 (C⁷H), 101.7 (C¹⁰H), 37.2 (C¹²H₃).

IR (neat) (cm⁻¹): 3012, 2160, 2031, 1978, 1511, 1470, 1229, 831, 822, 792.

¹²M. Hagiwara, A. Kobayashi, T. Hosoya, S. Yoshida, and Y. Sumida (Kyoto University), Composition for Activating Neurogenesis, 2019, EP 3508223 A1

9-Ethyl-3-(pyridin-4-yl)-9H-carbazole (3x)



4-Pyridylboronic acid (1.23 g, 10.0 mmol), 3-bromo-9-ethyl-9H-carbazole¹³ (3.28 g, 12.0 mmol), potassium carbonate (3.70 g, 27.0 mmol), and triphenylphosphine (262 mg, 10 mol%) were dissolved in dioxane:water (80 mL:20 mL). The solution was purged with argon for 10 minutes, then palladium acetate (56 mg, 2.5 mol%) was added. The reaction was heated at 80 °C under argon for 14 hours, then cooled, and diluted with EtOAc (100 mL) and water (100 mL). The solution was separated, and the aqueous layer was extracted with EtOAc (2 x 50 mL, the organic layers were combined, washed with brine, dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by FCC (10%-40% EtOAc in Pentane) to yield *heterocycle 3x* (1.00 g, 30% yield) as a white solid.

m.p. (EtOAc) 161 - 163 °C

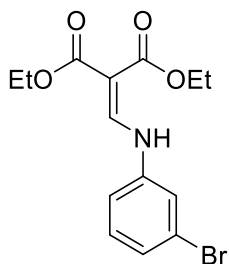
HRMS (ESI): Exact mass calculated for C₁₉H₁₇N₂ [M+H]⁺: 273.1386, found: 273.1386.

¹H NMR (400 MHz, CDCl₃) δ 8.71 – 8.64 (m, 2H, 2 x C²H), 8.40 (d, *J* = 1.8 Hz, 1H, C¹⁶H), 8.17 (dt, *J* = 7.7, 1.0 Hz, 1H, C¹³H), 7.77 (dd, *J* = 8.5, 1.8 Hz, 1H, C⁶H), 7.67 – 7.59 (m, 2H, 2 x C³H), 7.55 – 7.41 (m, 3H, C⁷H + C¹⁰H + C¹¹H), 7.29 (ddd, *J* = 7.9, 7.0, 1.1 Hz, 1H, C¹²H), 4.41 (q, *J* = 7.2 Hz, 2H, C¹⁷H₂), 1.47 (t, *J* = 7.2 Hz, 3H, C¹⁸H₃).

¹³C NMR (101 MHz, CDCl₃) δ 150.3 (C²H), 149.3 (C⁴), 140.6 (C), 140.5 (C), 128.9 (C), 126.4 (C¹¹H), 124.8 (C⁶H), 123.8 (C), 123.0 (C), 121.7 (2 x C³H), 120.7 (C¹³H), 119.5 (C¹²H), 119.2 (C¹⁶H), 109.1 (C⁷H/C¹⁰H), 108.9 (C⁷H/C¹⁰H), 37.9 (C¹⁷H₂), 14.0 (C¹⁸H₃).

IR (neat) (cm⁻¹): 2983, 2161, 1594, 1472, 1459, 1232, 1217, 804, 757, 735.

Ethyl α-carbethoxy-β-*m*-bromoanilinoacrylate (S6)

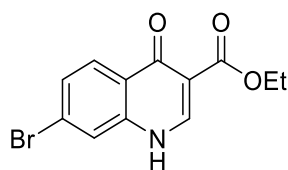


3-Bromoaniline (10 g, 58.1 mmol) and diethyl methoxymethylenemalonate (14 mL, 63.9 mmol) were heated together at 110 °C for 1 hour. The solution was cooled to room temperature which formed a solid, which was broken up and suspended in pentane. The suspension was filtered, washed with pentane, and dried under vacuum to yield *acrylate S6* (19.2 g, 97% yield) as a white solid. Spectroscopic data matched those previously reported.¹⁴

¹³L. Przypis Krzysztof and Z. Walczak, *J. Org. Chem.*, 2019, **84**, 2287–2296

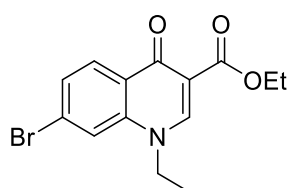
¹⁴D. De, F. M. Krogstad, L. D. Byers, D. J. Krogstad, *J. Med. Chem.*, 1998, **41**, 4918 – 4926.

7-Bromo-4-oxoquinoline-3-carboxylic acid ethyl ester (**S7**)



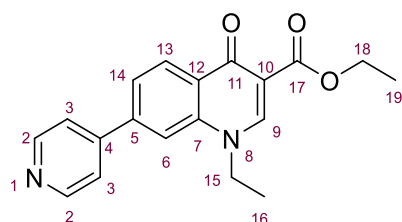
Dowtherm A[®] (50 mL) was heated to 250 °C and Compound **S6** (10.0 g, 29.0 mmol) was added portionwise. The solution was heated at 250 °C for 1 hour before being cooled slowly to room temperature. The resulting suspension was filtered, washed with pentane and dried under vacuum to yield *heterocycle* **S7** (6.99 g, 79% yield) as a colourless solid. Literature NMR spectra in d⁶-DMSO are available. However, in our hands, **S7** was insoluble in DMSO and all other deuterated solvents, no NMR spectra could be obtained and the compound was taken onto to the next step.

N-Ethyl-7-bromo-4-oxoquinoline-3-carboxylic acid ethyl ester (**S8**)



S7 (2.95 g, 10.0 mmol) and potassium carbonate (4.14 g, 30.0 mmol) were suspended in DMF (30 mL) and ethyl iodide (4 mL, 50 mmol) was added. The solution was heated at 80 °C for 5 hours, then poured into water (100 mL). The resulting suspension was filtered and solid was dissolved in CH₂Cl₂ (50 mL), dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by FCC (50-100% EtOAc in pentane) to give *heterocycle* **S8** (2.37 g, 73% yield) as a brown solid. Spectroscopic data matched those previously reported.¹⁵

N-Ethyl-7-(4-pyridine)-4-oxoquinoline-3-carboxylic acid ethyl ester (**3y**)



4-Pyridylboronic acid (553 mg, 4.50 mmol), **S8** (969 mg, 3.00 mmol), potassium carbonate (1.04 g, 7.5 mmol), and triphenylphosphine (79 mg, 10 mol%) were dissolved in dioxane:water (25 mL:10 mL). The solution was purged with argon for 10 minutes, then palladium acetate (17 mg, 2.5 mol%) was added. The reaction was heated at 80 °C under argon for 14 hours, then cooled, and diluted with EtOAc (50 mL) and water (50 mL). The solution was separated, and the aqueous layer was extracted with EtOAc (2 x 50 mL, the organic layers were combined, washed with brine, dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by FCC (0-4% MeOH in CH₂Cl₂) to yield *heterocycle* **3y** (572 mg, 59% yield) as a cream solid. Spectroscopic data matched those previously reported.⁹

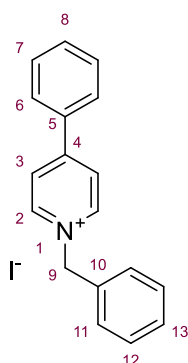
¹⁵ A. L. Choy, A. Eakin, O. Quiroga, B. Sherer (AstraZeneca AB), Heterocyclic Urea Derivatives and Methods of Use Thereof, 2010, US2010317624 A1.

The Synthesis of Pyridinium Salts

General Procedure D: Preparation of benzyl pyridinium iodide salts.

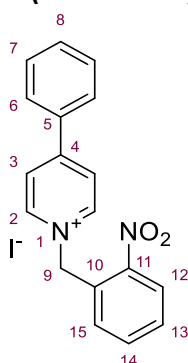
A mixture of the corresponding pyridine (1.00 equiv.) and benzyl iodide (1.50/2.00 equiv.) in acetone (0.5 M) was stirred in the dark at room temperature for 16 hours. Diethyl ether (10 mL) was added and the resulting suspension was sonicated (15 min) and then filtered. The resultant solid was washed with diethyl ether and dried under vacuum to give the benzyl pyridinium iodide salts as crystalline solids.

N-Benzyl-4-phenylpyridinium iodide (**S9**)



The title compound was prepared by General Procedure D using 4-phenyl pyridine (1.41 g, 9.10 mmol) and benzyl iodide (4.78 g 18.2 mmol) to give salt **S9** (3.46 g, 91%) as a yellow solid. Spectroscopic data was consistent with that reported in the literature.¹⁶

N-(2-Nitrobenzyl)-4-phenylpyridinium iodide (**1b**)



The title compound was prepared by General Procedure D using 4-phenyl pyridine (1.41 g, 9.1 mmol) and 2-nitrobenzyl iodide **S1** (4.78 g 18.2 mmol) to give salt **1b** (3.46 g, 91%) as a yellow solid.

m.p. (acetone) 196-198 °C;

HRMS (ESI): Exact mass calculated for C₁₈H₁₅O₂N₂ [M]⁺: 291.11280, found: 291.11275;

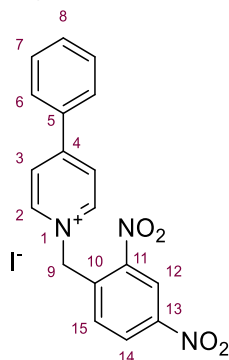
¹H NMR (400 MHz, DMSO) δ 9.18 – 9.08 (d, *J*=7.1 Hz, 2H, 2 x C²H), 8.68 – 8.57 (d, *J*=7.1 Hz, 2H, 2 x C³H), 8.28 (dd, *J* = 8.1, 1.4 Hz, 1H, C¹²H), 8.18 – 8.08 (m, 2H, 2 x ArCH), 7.86 – 7.62 (m, 5H, 5 x ArCH), 7.19 (dd, *J* = 7.7, 1.4 Hz, 1H, C¹⁵H), 6.24 (s, 2H, C⁹H₂).

¹³C NMR (101 MHz, DMSO) δ 155.5 (ArC), 147.5 (ArC), 145.6 (2 x C²H), 135.0 (ArCH), 133.5 (ArC), 132.4 (ArCH), 130.4 (ArCH), 130.0 (C¹⁵H), 129.8 (2 x ArCH), 129.6 (ArC), 128.3 (2 x ArCH), 125.6 (C¹²H), 124.9 (2 x C³H), 59.9 (C⁹H₂).

IR (neat) (cm⁻¹): 1637, 1514, 1440, 1347, 1335, 1200, 861, 790, 772, 747.

¹⁶A. Grozavu, H. B. Hepburn, P. J. Smith, H. K. Potukuchi, P. J. Lindsay-Scott and T. J. Donohoe, *Nat. Chem.*, 2019, **11**, 242-247.

***N*-(2,4-Dinitrobenzyl)-4-phenylpyridinium iodide (**S10**)**

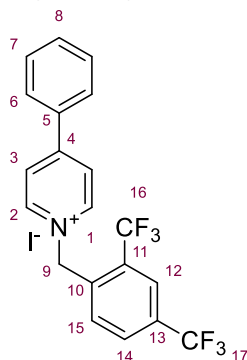


Title compound was prepared by General Procedure D using 4-phenyl pyridine (65.7 mg, 0.42 mmol) and 2,4-bisnitrobenzyl iodide **S2** (261 mg, 0.85 mmol) to give salt **S10** (185 mg, 95%) as a red-brown solid. This compound was found to be highly hygroscopic and water in the atmosphere readily cleaved the bond between N¹ and C⁹. Due to this instability full characterisation data was not obtained.

HRMS (ESI): Exact mass calculated for C₁₈H₁₄O₂N₃[M]⁺ m/z: 336.09788, found 336.09787

¹H NMR (400 MHz, DMSO) δ 9.13 (d, *J* = 6.9 Hz, 2H, 2 x C²H), 8.91 (d, *J* = 2.4 Hz, 1H, C¹²H), 8.68 (d, *J* = 7.1 Hz, 2H, 2 x C³H), 8.51 (dd, *J* = 8.6, 2.4 Hz, 1H, C¹⁴H), 8.18 – 8.10 (m, 2H, 2 x C⁷H), 7.76 – 7.62 (m, 3H, 2 x C⁶H + C⁸H), 7.37 (d, *J* = 8.6 Hz, 1H, C¹⁵H), 6.34 (s, 2H, C⁹H₂).

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-phenylpyridinium iodide (**1c**)**



The title compound was prepared by General Procedure D using 4-phenyl pyridine (517 mg, 3.33 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (2.37 g, 6.66 mmol) to give the pyridinium **1c** (1.51 g, 89%) as a yellow solid.

m.p. (acetone): 221-223 °C

HRMS (ESI): Exact mass calculated for C₂₀H₁₄F₆N [M]⁺ m/z: 382.10250, found: 382.10225

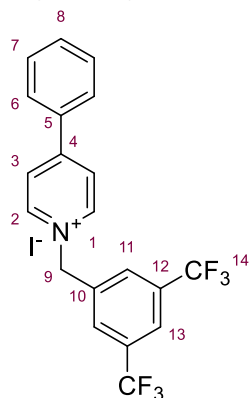
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.13 (d, *J* = 6.9 Hz, 2H, 2 x C²H), 8.63 (d, *J* = 7.1 Hz, 2H, 2 x C³H), 8.22 (s, 1H, C¹²H), 8.13 (m, 3H, 2 x C⁷H + C¹⁴H), 7.72 – 7.64 (m, 3H, 2 x C⁶H + C⁸H), 7.43 (d, *J* = 8.2 Hz, 1H, C¹⁵H), 6.21 (s, 2H, 2 x C⁹H₂).

¹³C NMR (126 MHz, DMSO-*d*₆) δ 155.9 (C), 145.8 (2 x C²H), 136.8 (C), 133.3 (C), 132.6 (C⁸H), 131.0 (C¹⁵H), 130.5 (q, *J* = 3.9 Hz, C¹⁴H), 129.9 (q, *J* = 33.5 Hz, C¹¹/C¹³), 129.8 (2 x C⁶H), 128.4 (2 x C⁷H), 127.8 (q, *J* = 31.7 Hz, C¹¹/C¹³), 124.9 (2 x C³H), 124.0 – 123.5 (m, C¹²H), 123.22 (q, *J* = 274.6 Hz, C¹⁶F₃/C¹⁷F₃), 123.18 (q, *J* = 272.6 Hz, C¹⁶F₃/C¹⁷F₃), 58.9 (q, *J* = 3.1 Hz, C⁹H₂).

¹⁹F NMR (377 MHz, DMSO-*d*₆) δ -59.0, -61.5.

IR (neat) (cm⁻¹): 2984, 2161, 1978, 1639, 1343, 1284, 1270, 1181, 1168, 1137.

***N*-(3,5-bis(trifluoromethyl)benzyl)-4-phenylpyridinium iodide (1d)**



Title compound was prepared by General Procedure D using 4-phenyl pyridine (155 mg, 1.00 mmol) and 3,5-bis(trifluoromethyl)benzyl iodide **S3** (708.1 mg, 2.00 mmol) to give the pyridinium **1d** (435 mg, 88%) as a yellow solid.

m.p. (acetone): >350 °C

HRMS (ESI): Exact mass calculated for C₂₀H₁₄F₆N [M]⁺: 382.1025, found 382.1031

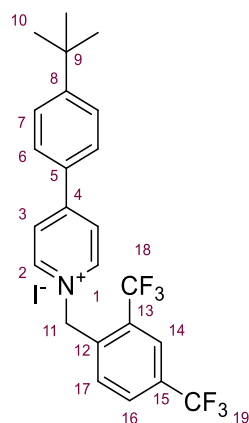
¹H NMR (400 MHz, DMSO) δ 9.30 (d, *J* = 7.1 Hz, 2H, 2 x C²H), 8.57 (d, *J* = 7.1 Hz, 2H, 2 x C³H), 8.4 (d, *J* = 1.7 Hz, 2H, 2 x C¹¹H), 8.23 (s, 1H, C¹³H), 8.12 – 8.06(m, 2H, 2 x ArCH), 7.74 – 7.49 (m, 3H, 3 x ArCH), 5.99 (s, 2H, C⁹H₂).

¹³C NMR (126 MHz, DMSO) δ 155.3 (C⁴), 145.0 (2 x C²H), 137.0 (C), 133.5 (C), 132.3 (ArCH), 130.9 (q, *J* = 33.0 Hz, 2 x C¹²), 130.6 (q, *J* = 3.8 Hz, 2 x C¹¹H), 129.7 (2 x ArCH), 128.3 (2 x ArCH), 125.0 (2 x C³H), 123.7 – 123.2 (m, C¹³H), 123.1 (q, *J* = 273.1 Hz, 2 x C¹⁴F₃), 61.0 (C⁹H₂).

¹⁹F NMR (377 MHz, DMSO) δ –61.2.

IR (neat) (cm⁻¹): 3021, 2960, 1635, 1280, 1167, 1113, 910, 771, 744, 683.

***N*-(2,4-bis(trifluoromethyl)benzyl)-4-(4-(*tert*-butyl)phenyl)pyridinium iodide (1e)**



The title compound was prepared by General Procedure D using 4-(4-(*tert*-butyl)phenyl)pyridine **3e** (423 mg, 2.0 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.06 g, 3.00 mmol) to give the pyridinium **1e** (1.11 g, 98%) as a yellow solid.

m.p. (acetone): 255-257 °C

HRMS (ESI): Exact mass calculated for C₂₄H₂₂NF₆ [M]⁺: 438.16510, found 438.16490

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.10 (d, *J* = 7.0 Hz, 2H, 2 x C²H), 8.61 (d, *J* = 7.0 Hz, 2H, 2 x C³H), 8.23 (s, 1H, C¹⁴H), 8.15 (d, *J* = 8.4 Hz, 1H, C¹⁶H), 8.09 (d, *J* = 8.6 Hz, 2H, 2 x C⁶H), 7.69 (d, *J* = 8.6 Hz, 2H, 2 x C⁷H), 7.44 (d, *J* = 8.2 Hz, 1H, C¹⁷H), 6.20 (s, 2H, 2 x C¹¹H), 1.36 (s, 9H, 3 x C¹⁰H₃).

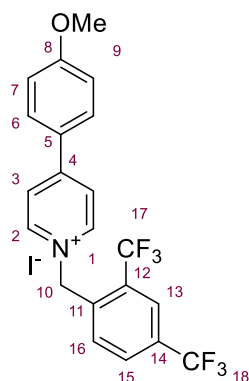
¹³C NMR (126 MHz, DMSO-*d*₆) δ 155.9 (C), 155.7 (C), 145.7 (2 x C³H), 136.8 (C¹²), 131.1 (C¹⁷H), 130.6 – 130.4 (m, C¹⁶H+C), 129.95 (q, *J* = 33.4 Hz, C¹³/C¹⁵), 128.3 (2 x C⁶H), 127.8 (q, *J* = 31.7 Hz, C¹³/C¹⁵), 126.7

(2 x C⁷H), 124.5 (2 x C²H), 124.0 – 123.7 (m, C¹⁴H), 123.18 (q, $J = 274.7$ Hz, C¹⁸F₃/C¹⁹F₃), 123.15 (q, $J = 272.7$ Hz, C¹⁸F₃/C¹⁹F₃), 58.8 (q, $J = 3.4$ Hz, C¹¹H₂), 34.9 (C⁹), 30.8 (3 x C¹⁰H₃).

¹⁹F NMR (377 MHz, DMSO-*d*₆) δ –59.0, –61.5.

IR (neat) (cm⁻¹): 3659, 2981, 1341, 1270, 1182, 1166, 1131, 1084, 1052, 826.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-methoxyphenyl)pyridinium iodide (1f)**



The title compound was prepared by General Procedure D using 4-(4-methoxyphenyl)pyridine **3f** (460 mg, 2.50 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.46 g, 4.20 mmol) to give the pyridinium **1f** (1.23 g, 92%) as a yellow solid.

m.p. (acetone): 215-217 °C

HRMS (ESI): Exact mass calculated for C₂₁H₁₆ONF₆ [M]⁺: 412.1130, found: 412.1131

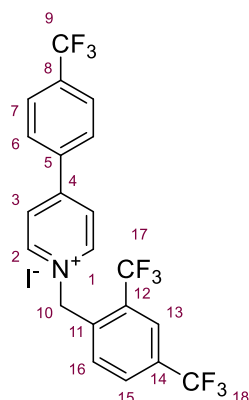
¹H NMR (400 MHz, DMSO) δ 9.02 (d, $J = 7.1$ Hz, 2H, 2 x C²H), 8.57 (d, $J = 7.2$ Hz, 2H, 2 x C³H), 8.22 (s, 1H, C¹³H), 8.18 (d, $J = 9.0$ Hz, 2H, 2 x C⁶H), 8.12 (dd, $J = 8.2, 2.2$ Hz, 1H, C¹⁵H), 7.38 (d, $J = 8.2$ Hz, 1H, C¹⁶H), 7.22 (d, $J = 9.0$ Hz, 2H, 2 x C⁷H), 6.15 (s, 2H, C¹⁰H₂), 3.90 (s, 3H, C⁹H₃).

¹³C NMR (126 MHz, DMSO) δ 163.1 (C⁸), 155.1 (C⁴), 145.4 (2 x C²H), 137.1 (C¹¹), 130.7 (C¹⁶H), 130.5 (q, $J = 3.9$ Hz, C¹⁵H), 130.4 (2 x C⁶H), 129.8 (q, $J = 33.3$ Hz, C¹²/C¹⁴), 127.7 (q, $J = 31.7$ Hz, C¹²/C¹⁴), 125.1 (C⁵), 124.0 – 123.6 (m, C¹³H), 123.5 (2 x C³H), 123.2 (q, $J = 274.6$ Hz, C¹⁷F₃/C¹⁸F₃), 123.1 (q, $J = 272.4$ Hz, C¹⁷F₃/C¹⁸F₃), 115.3 (2 x C⁷H), 58.6 (q, $J = 3.3$ Hz, C¹⁰H₂), 55.8 (C⁹H₃).

¹⁹F NMR (377 MHz, DMSO) δ –59.1, –61.4.

IR (neat) (cm⁻¹): 2981, 1640, 1599, 1344, 1271, 1166, 1122, 1084, 1053, 833.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-(trifluoromethyl) phenyl)pyridinium iodide (1g)**



The title compound was prepared by General Procedure D using 4-(4-(trifluoromethyl) phenyl)pyridine **3g** (446 mg, 2.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.06 g, 3.00 mmol) to give the pyridinium **1g** (987 mg, 85%) as a yellow solid.

m.p. (acetone): 226-228 °C

HRMS (ESI): Exact mass calculated for C₂₁H₁₃NF₉ [M]⁺: 450.08900, found 450.08860

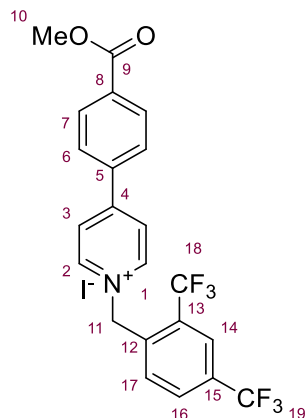
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.22 (d, *J* = 7.0 Hz, 2H, 2 x C²H), 8.69 (d, *J* = 7.1 Hz, 2H, 2 x C³H), 8.32 (d, *J* = 8.2 Hz, 2H, 2 x C⁶H), 8.23 (s, 1H, C¹³H), 8.14 (d, *J* = 8.5 Hz, 1H, C¹⁵H), 8.05 (d, *J* = 8.3 Hz, 2H, 2 x C⁷H), 7.45 (d, *J* = 8.2 Hz, 1H, C¹⁶H), 6.25 (s, 2H, 2 x C¹⁰H₂).

¹³C NMR (126 MHz, DMSO-*d*₆) δ 154.5 (C), 146.2 (2 x C³H), 137.5 (C), 136.7 (C), 131.8 (q, *J* = 32.4 Hz, C⁸/C¹²/C¹⁴), 131.1 (C¹⁶H), 130.5 (d, *J* = 3.8 Hz, C¹⁵H), 130.0 (q, *J* = 33.3 Hz, C⁸/C¹²/C¹⁴), 129.4 (2 x C⁶H), 127.9 (q, *J* = 31.7 Hz, 2 x C⁷H), 126.5 (q, *J* = 3.8 Hz, C⁸/C¹²/C¹⁴), 125.9 (2 x C²H), 124.0 – 123.7 (m, C¹³H), 123.17 (q, *J* = 274.6 Hz, C⁹F₃), 123.15 (q, *J* = 272.4 Hz, 2 x C¹⁷F₃/C¹⁸F₃), 59.2 (q, *J* = 3.4 Hz, C¹⁰H₂).

¹⁹F NMR (376 MHz, DMSO-*d*₆) δ –59.0, –61.5.

IR (neat) (cm⁻¹): 3660, 2981, 1325, 1276, 1167, 1127, 1109, 1084, 1072, 1057.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-(methoxycarbonyl) phenyl)pyridinium iodide (1h)**



The title compound was prepared by General Procedure D using 4-(4-(methoxycarbonyl) phenyl)pyridine **3h** (426 mg, 2.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.06 g, 3.00 mmol) to give the pyridinium **1h** (1.01 g, 89%) as a yellow solid.

m.p. (acetone): 236–238 °C

HRMS (ESI): Exact mass calculated for C₂₂H₁₆O₂NF₆ [M]⁺: 440.10797, found 440.10834

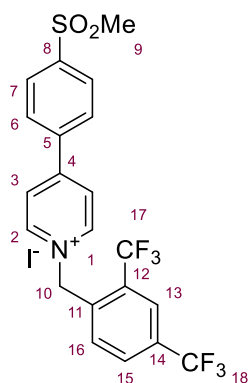
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.19 (d, *J* = 7.0 Hz, 2H, 2 x C²H), 8.68 (d, *J* = 7.0 Hz, 2H, 2 x C³H), 8.26 (d, *J* = 8.8 Hz, 2H, 2 x C⁶H), 8.22 (s, 1H, C¹⁴H), 8.20 (d, *J* = 8.7 Hz, 2H, 2 x C⁷H), 8.13 (d, *J* = 8.4 Hz, 1H, C¹⁶H), 7.44 (d, *J* = 8.2 Hz, 1H, C¹⁷H), 6.24 (s, 2H, 2 x C¹¹H₂), 3.92 (s, 3H, 3 x C¹⁰H₃).

¹³C NMR (126 MHz, DMSO) δ 165.6 (C⁹O), 154.7 (C), 146.2 (2 x C²H), 137.7 (C), 136.7 (C), 132.6 (C), 131.0 (C¹⁷H), 130.5 (d, *J* = 3.8 Hz, C¹⁶H), 130.3 (2 x C⁶H), 130.0 (q, *J* = 33.3 Hz, C¹³/C¹⁵), 128.9 (2 x C⁷H), 127.9 (q, *J* = 31.7 Hz, C¹³/C¹⁵), 125.7 (2 x C³H), 124.1 – 123.6 (m, C¹⁴H), 123.21 (q, *J* = 274.6 Hz, C¹⁸F₃/C¹⁹F₃), 123.17 (q, *J* = 272.7 Hz, C¹⁸F₃/C¹⁹F₃), 59.2 (q, *J* = 3.3 Hz, C¹¹H₂), 52.7 (C¹⁰H₃).

¹⁹F NMR (377 MHz, DMSO) δ –59.00, –61.46.

IR (neat) (cm⁻¹): 3660, 2981, 1719, 1348, 1277, 1179, 1137, 1118, 1084, 1055.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-(methylsulfonyl) phenyl)pyridinium iodide (1i)**



The title compound was prepared by General Procedure D using 4-(4-(methylsulfonyl) phenyl)pyridine **3i** (466 mg, 2.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.06 g, 3.00 mmol) to give the pyridinium **1i** (1.13 g, 96%) as a yellow solid.

m.p. (acetone): 247-249 °C

HRMS (ESI): Exact mass calculated for $C_{21}H_{16}O_2NF_6^{32}S$ [M]⁺: 460.08005, found 460.08010

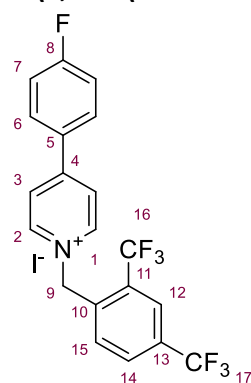
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.23 (d, *J* = 6.7 Hz, 2H, 2 x C²H), 8.70 (d, *J* = 7.1 Hz, 2H, 2 x C³H), 8.36 (d, *J* = 8.6 Hz, 2H, 2 x C⁶H), 8.23 (s, 1H, C¹³H), 8.20 (d, *J* = 8.6 Hz, 2H, 2 x C⁷H), 8.14 (d, *J* = 7.5 Hz, 1H, C¹⁵H), 7.47 (d, *J* = 8.2 Hz, 1H, C¹⁶H), 6.26 (s, 2H, 2 x C¹⁰H₂), 3.35 (s, 3H, C⁹H₃).

¹³C NMR (126 MHz, DMSO-*d*₆) δ 154.3 (C), 146.2 (2 x C²H), 143.6 (C), 138.2 (C), 136.6 (C), 131.1 (C¹⁶H), 130.5 (d, *J* = 3.7 Hz, C¹⁵H), 130.0 (q, *J* = 33.3 Hz, C¹²/C¹⁴), 129.5 (2 x C⁶H), 128.1 (2 x C⁷H), 127.9 (q, *J* = 31.7 Hz, C¹²/C¹⁴), 126.0 (2 x C³H), 124.1 – 123.6 (m, C¹³H), 123.18 (q, *J* = 274.5 Hz, 2 x C¹⁷F₃/C¹⁸F₃), 123.15 (q, *J* = 272.7 Hz, 2 x C¹⁷F₃/C¹⁸F₃), 59.2 (d, *J* = 3.3 Hz, C¹⁰H₂), 43.2 (C⁹H₃).

¹⁹F NMR (376 MHz, DMSO-*d*₆) δ -59.0, -61.5.

IR (neat) (cm⁻¹): 2981, 1703, 1639, 1345, 1274, 1172, 1123, 1085, 1054, 961.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-fluorophenyl)pyridinium iodide (1j)**



The title compound was prepared by General Procedure D using 4-(4-fluorophenyl)pyridine **3j** (345 mg, 2.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.06 g, 3.00 mmol) to give the pyridinium **1j** (1.00 g, 95%) as a yellow solid.

m.p. (acetone): 225-227 °C

HRMS (ESI): Exact mass calculated for $C_{20}H_{13}NF_7$ [M]⁺: 400.09307, found 400.09342

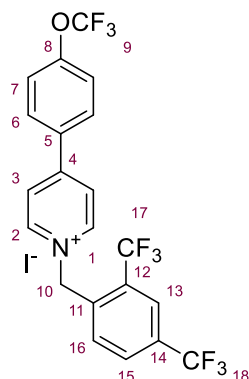
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.12 (d, *J* = 7.1 Hz, 2H, 2 x C²H), 8.61 (d, *J* = 7.1 Hz, 2H, 2 x C³H), 8.28 – 8.19 (m, 3H, 2 x C⁶H and C¹²H), 8.12 (dd, *J* = 8.3, 2.2 Hz, 1H, C¹⁵H), 7.53 (t, *J* = 8.8 Hz, 2H, 2 x C⁷H), 7.41 (d, *J* = 8.2 Hz, 1H, C¹⁴H), 6.20 (s, 2H, 2 x C⁹H₂).

¹³C NMR (126 MHz, DMSO-*d*₆) δ 164.8 (d, *J* = 251.9 Hz, C⁸), 154.8 (C⁴), 145.9 (2 x C²H), 136.8 (C⁵), 131.2 (d, *J* = 9.3 Hz, 2 x C⁶H), 131.0 (C¹⁵H), 130.5 (q, *J* = 4.0 Hz, C¹⁴H), 130.0 (q, *J* = 33.2 Hz, C¹¹/C¹³), 129.9 (q, *J* = 2.9 Hz, C¹⁰), 127.9 (q, *J* = 31.8 Hz, C¹¹/C¹³), 124.9 (2 x C³H), 123.9-123.8 (m, C¹²H), 123.21 (q, *J* = 274.6 Hz, C¹⁶F₃/C¹⁷F₃), 123.17 (q, *J* = 272.7 Hz, C¹⁶F₃/C¹⁷F₃), 117.0 (d, *J* = 22.0 Hz, 2 x C⁷H), 58.9 (q, *J* = 2.8 Hz, C⁹H₂).

¹⁹F NMR (377 MHz, DMSO-*d*₆) δ -59.0, -61.5, -107.2 (tt, *J* = 8.9, 5.2 Hz).

IR (neat) (cm⁻¹): 3009, 2939, 1636, 1497, 1343, 1284, 1265, 1225, 1168, 1136..

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-(trifluoromethoxy) phenyl)pyridinium iodide (1k)**



The title compound was prepared by General Procedure D using 4-(4-(trifluoromethoxy) phenyl)pyridine **3k** (482 mg, 2.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.06 g, 3.00 mmol) to give the pyridinium **1k** (1.07 g, 90%) as a yellow solid.

m.p. (acetone): 210-212 °C

HRMS (ESI): Exact mass calculated for $C_{21}H_{13}ONF_9$ $[M]^+$: 466.08479, found 466.08372

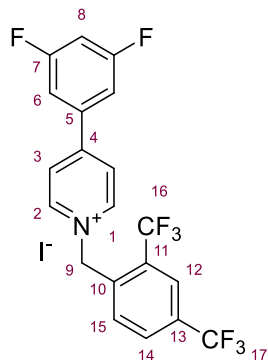
1H NMR (400 MHz, DMSO- d_6) δ 9.17 (d, J = 6.4 Hz, 2H, 2 x C^2H), 8.64 (d, J = 6.9 Hz, 2H, 2 x C^3H), 8.27 (d, J = 8.9 Hz, 2H, 2 x C^6H), 8.22 (s, 1H, $C^{13}H$), 8.13 (d, J = 8.2 Hz, 1H, $C^{15}H$), 7.67 (d, J = 8.3 Hz, 2H, 2 x C^7H), 7.45 (d, J = 8.2 Hz, 1H, $C^{16}H$), 6.22 (s, 2H, 2 x $C^{10}H_2$).

^{13}C NMR (126 MHz, DMSO- d_6) δ 154.5 (C), 151.1 (C), 146.0 (2 x C^2H), 136.7 (C), 132.6 (C), 131.1 ($C^{16}H$), 130.9 (2 x C^6H), 130.5 (d, J = 3.8 Hz, $C^{15}H$), 130.0 (q, J = 33.3 Hz, C^{12}/C^{14}), 127.9 (q, J = 31.6 Hz, C^{12}/C^{14}), 125.3 (2 x C^3H), 124.0 – 123.7 (m, $C^{13}H$), 123.18 (q, J = 274.5 Hz, $C^{17}F_3/C^{18}F_3$), 123.15 (q, J = 272.7 Hz, $C^{17}F_3/C^{18}F_3$), 121.9 (2 x C^7H), 120.0 (q, J = 257.7 Hz, C^9F_3), 59.1 (q, J = 3.3 Hz, $C^{10}H_2$).

^{19}F NMR (376 MHz, DMSO- d_6) δ -56.6, -59.0, -61.5.

IR (neat) (cm^{-1}): 2981, 1638, 1342, 1269, 1212, 1166, 1123, 1084, 1052, 829.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(3,5-difluorophenyl)pyridinium iodide (1l)**



The title compound was prepared by General Procedure D using 4-(3,5-difluorophenyl)pyridine **3l** (382 mg, 2.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.06 g, 3.00 mmol) to give the pyridinium **1l** (714 mg, 65%) as a yellow solid.

m.p. (acetone): 233-235 °C

HRMS (ESI): Exact mass calculated for $C_{20}H_{12}NF_8$ $[M]^+$: 418.08365, found 418.08416

1H NMR (400 MHz, DMSO- d_6) δ 9.22 (d, J = 6.9 Hz, 2H, 2 x C^2H), 8.69 (d, J = 7.1 Hz, 2H, 2 x C^3H), 8.23 (s, 1H, $C^{12}H$), 8.12 (d, J = 7.6 Hz, 1H, $C^{14}H$), 8.04 – 7.91 (m, 2H, 2 x C^6H), 7.64 (tt, J = 9.2, 2.3 Hz, 1H, C^8H), 7.40 (d, J = 8.2 Hz, 1H, $C^{15}H$), 6.22 (s, 2H, 2 x C^9H_2).

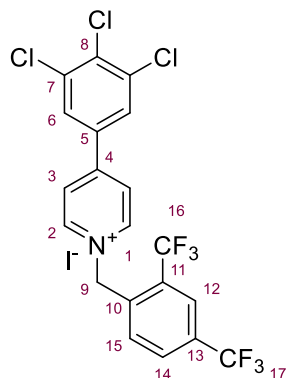
^{13}C NMR (126 MHz, DMSO- d_6) δ 163.1 (dd, J = 247.5, 12.4, Hz, 2 x C^7), 153.3 (C^4), 146.2 (2 x C^2H), 137.2 – 136.0 (m, C^5 + C^{10}), 130.9, ($C^{15}H$), 130.5 ($C^{14}H$), 130.0 (q, J = 33.2 Hz, C^{11}/C^{13}), 127.9 (q, J = 31.8 Hz,

C^{11}/C^{13}), 125.6 (2 x C^3H), 123.9 ($C^{12}H$), 123.17 (q, $J = 275.0$ Hz, $C^{16}F_3/C^{17}F_3$), 123.14 (q, $J = 272.4$ Hz, $C^{16}F_3/C^{17}F_3$), 112.3 – 111.8 (m, 2 x C^6H), 107.7 (t, $J = 26.0$ Hz, C^8H), 59.2 (q, $J = 2.5$ Hz, C^9H_2).

^{19}F NMR (377 MHz, DMSO- d_6) δ -59.0, -61.4, -107.7 (t, $J = 8.5$ Hz).

IR (neat) (cm^{-1}): 2981, 1339, 1275, 1177, 1117, 1084, 1054, 991, 839.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(3,4,5-trichlorophenyl)pyridinium iodide (1m)**



The title compound was prepared by General Procedure D using 4-(3,4,5-trichlorophenyl)pyridine **3m** (186 mg, 0.72 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (530 mg 1.50 mmol) to give the pyridinium **1m** (314 mg, 71%) as a yellow solid.

m.p. (acetone): 277-279 °C

HRMS (ESI): Exact mass calculated for $C_{20}H_{11}N^{35}Cl_3F_6$ $[M]^+$: 483.98558, found 483.98567

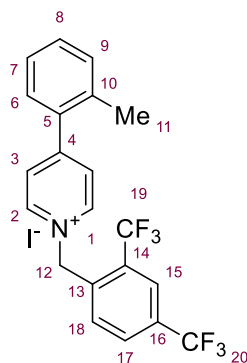
1H NMR (400 MHz, DMSO- d_6) δ 9.22 (d, $J = 7.0$ Hz, 2H, 2 x C^2H), 8.74 (d, $J = 7.1$ Hz, 2H, 2 x C^3H), 8.47 (s, 2H, 2 x C^6H), 8.24 (s, 1H, $C^{12}H$), 8.12 (d, $J = 8.2$ Hz, 1H, $C^{14}H$), 7.36 (d, $J = 8.2$ Hz, 1H, $C^{15}H$), 6.22 (s, 2H, 2 x C^9H_2).

^{13}C NMR (126 MHz, DMSO- d_6) δ 152.4 (C^4), 146.2 (2 x C^2H), 136.7 (C), 134.4 (C), 134.2 (C), 133.8 (C), 130.8 ($C^{15}H$), 130.7 – 130.3 (m, $C^{14}H$), 130.0 (q, $J = 33.2$ Hz, C^{11}/C^{13}), 128.9 (2 x C^6H), 127.8 (q, $J = 31.7$ Hz, C^{11}/C^{13}), 125.7 (2 x C^3H), 124.01 – 123.63 (m, $C^{12}H$), 123.15 (q, $J = 270.0$ Hz, $C^{16}F_3 + C^{17}F_3$), 59.25 (s, C^9H_2).

^{19}F NMR (377 MHz, DMSO- d_6) δ -59.1, -61.4.

IR (neat) (cm^{-1}): 3659, 2981, 1639, 1381, 1347, 1288, 1274, 1186, 1136, 1117.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(o-tolyl)pyridinium iodide (1n)**



The title compound was prepared by General Procedure D using 4-(o-tolyl)pyridine **3n** (285 mg, 2.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.06 g, 3.00 mmol) to give the pyridinium **1n** (815 mg, 93%) as a yellow solid.

m.p. (acetone): 225-257 °C

HRMS (ESI): Exact mass calculated for $C_{21}H_{16}NF_6$ $[M]^+$: 396.11815, found 396.11719

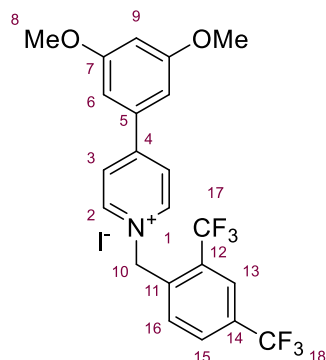
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.12 (d, *J* = 6.9 Hz, 2H, 2 x C²H), 8.31 (d, *J* = 7.0 Hz, 2H, 2 x C³H), 8.24 (s, 1H, C¹⁵H), 8.17 (d, *J* = 8.2 Hz, 1H, C¹⁷H), 7.55 – 7.40 (m, 5H, C⁶H, C⁷H, C⁸H, C⁹H and C¹⁸H), 6.23 (s, 2H, 2 x C¹²H₂), 2.39 (s, 3H, 3 x C¹¹H₃).

¹³C NMR (126 MHz, DMSO-*d*₆) δ 158.5 (C⁴), 145.3 (2 x C²H), 136.5 (C), 135.6 (C), 135.4 (C), 131.5 (ArCH), 131.4 (ArCH), 130.7 (ArCH), 130.6 (C¹⁷H), 130.1 (q, *J* = 33.2 Hz, C¹⁹/C²⁰), 129.8 (ArCH), 128.5 (2 x C³H), 128.0 (q, *J* = 31.7 Hz, C¹⁹/C²⁰), 126.8 (ArCH), 123.9 (C¹⁵H), 123.2 (q, *J* = 271.4 Hz, C¹⁹F₃ + C²⁰F₃), 59.2 (s, C¹²H₂), 19.9 (C¹¹H₃).

¹⁹F NMR (376 MHz, DMSO-*d*₆) δ –58.9, –61.5.

IR (neat) (cm⁻¹): 2981, 1640, 1345, 1269, 1169, 1119, 1084, 1054, 762.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(3,5-dimethoxyphenyl) pyridinium iodide (1o)**



The title compound was prepared by General Procedure D using 4-(3,5-dimethoxyphenyl)pyridine **3o** (430 mg, 2.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.06 g, 3.00 mmol) to give the pyridinium **1o** (1.06 g, 93%) as a yellow solid.

m.p. (acetone): 235-237 °C

HRMS (ESI): Exact mass calculated for C₂₂H₁₈O₂NF₆ [M]⁺: 442.12362, found 442.12302

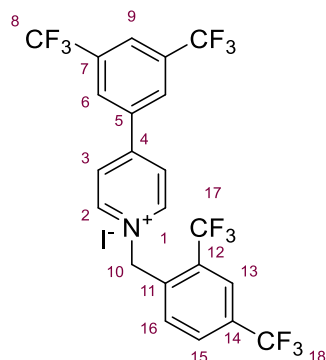
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.12 (d, *J* = 7.1 Hz, 2H, 2 x C²H), 8.65 (d, *J* = 7.0 Hz, 2H, 2 x C³H), 8.22 (s, 1H, C¹³H), 8.12 (d, *J* = 7.6 Hz, 1H, C¹⁵H), 7.39 (d, *J* = 8.2 Hz, 1H, C¹⁶H), 7.25 (d, *J* = 2.2 Hz, 2H, 2 x C⁶H), 6.82 (t, *J* = 2.2 Hz, 1H, C⁹H), 6.21 (s, 2H, 2 x C¹⁰H₂), 3.88 (s, 6H, 6 x C⁸H₃).

¹³C NMR (126 MHz, DMSO-*d*₆) δ 161.4 (2 x C⁷H), 155.8 (C⁴), 145.8 (2 x C²H), 136.9 (C¹¹), 135.3 (C⁵), 130.8, (C¹⁶H), 130.5 (d, *J* = 3.8 Hz, C¹⁵H), 129.9 (q, *J* = 33.3 Hz, C¹²/C¹⁴), 127.8 (q, *J* = 31.8 Hz, C¹²/C¹⁴), 125.3 (2 x C³H), 124.1 – 123.7 (m, C¹³H), 123.22 (q, *J* = 274.4, Hz, C¹⁷F₃/C¹⁸F₃), 123.18 (q, *J* = 272.1, Hz, C¹⁷F₃/C¹⁸F₃), 106.4 (2 x C⁶H), 104.2 (C⁹H), 59.0 (q, *J* = 3.3 Hz, C¹⁰H₂), 55.8 (2 x C⁸H₃).

¹⁹F NMR (377 MHz, DMSO-*d*₆) δ –59.0, –61.4.

IR (neat) (cm⁻¹): 2981, 2889, 1341, 1275, 1182, 1156, 1135, 1115, 1083, 1064.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(3,5-bis(trifluoromethyl) phenyl) pyridinium iodide (1p)**



The title compound was prepared by General Procedure D using 4-(3,5-bis(trifluoromethyl)phenyl)pyridine **3p** (285 mg, 1.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (530 mg, 1.50 mmol) to give the pyridinium **1p** (454 mg, 72%) as a yellow solid.

m.p. (acetone): 259-261 °C

HRMS (ESI): Exact mass calculated for $C_{22}H_{12}NF_{12}$ $[M]^+$: 518.07726, found 518.07581

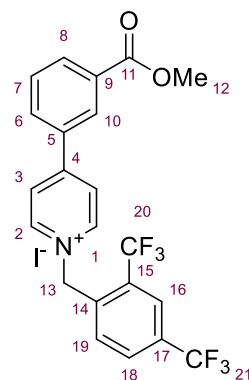
1H NMR (400 MHz, $DMSO-d_6$) δ 9.28 (d, J = 7.1 Hz, 2H, 2 x C^2H), 8.87 (d, J = 7.1 Hz, 2H, 2 x C^3H), 8.78 (s, 2H, 2 x C^6H), 8.45 (s, 1H, C^9H), 8.24 (s, 1H, $C^{13}H$), 8.12 (d, J = 8.1 Hz, 1H, $C^{15}H$), 7.35 (d, J = 8.2 Hz, 1H, $C^{16}H$), 6.28 (s, 2H, 2 x $C^{10}H$).

^{13}C NMR (126 MHz, $DMSO-d_6$) δ 153.1 (C^4), 146.2 (2 x C^2H), 136.9 (C), 136.3 (C), 131.5 (q, J = 33.5 Hz, 2 x C^7), 130.6 ($C^{16}H$), 130.5 (q, J = 3.9 Hz, $C^{15}H$), 130.0 (q, J = 33.3 Hz, C^{12}/C^{14}), 129.5 (q, J = 4.0 Hz, 2 x C^6H), 127.8 (q, J = 31.8 Hz, C^{12}/C^{14}), 126.5 (2 x C^3H), 125.6 – 125.3 (m, C^9H), 123.9 ($C^{13}H$), 123.19 (q, J = 274.6 Hz, $C^{17}F_3/C^{18}F_3$), 123.15 (q, J = 272.7 Hz, $C^{17}F_3/C^{18}F_3$), 123.1 (q, J = 273.2 Hz, 2 x C^8F_3), 59.4 (q, J = 3.5 Hz, $C^{10}H_2$).

^{19}F NMR (377 MHz, $DMSO-d_6$) δ -59.1, -61.1, -61.5.

IR (neat) (cm^{-1}): 2981, 1639, 1345, 1272, 1176, 1122, 1084, 1053, 671.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(3-(methoxycarbonyl) phenyl)pyridinium iodide (**1q**)**



The title compound was prepared by General Procedure D using 4-(3-(methoxycarbonyl)phenyl)pyridine **3q** (427 mg, 2.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.06 g, 3.00 mmol) to give the pyridinium **1q** (1.01 g, 89%) as a yellow solid.

m.p. (acetone): 206-208 °C

HRMS (ESI): Exact mass calculated for $C_{22}H_{16}O_2NF_6$ $[M]^+$: 440.10797, found 440.10828

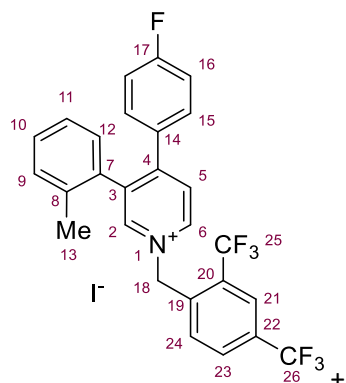
1H NMR (400 MHz, $DMSO-d_6$) δ 9.16 (d, J = 7.0 Hz, 2H, 2 x C^2H), 8.69 (d, J = 7.0 Hz, 2H, 2 x C^3H), 8.57 (t, J = 1.7 Hz, 1H, $C^{10}H$), 8.37 (ddd, J = 7.8, 2.1, 1.1 Hz, 1H, C^8H), 8.27 – 8.21 (m, 2H, C^6H and $C^{16}H$), 8.12 (d, J = 8.1 Hz, 1H, $C^{18}H$), 7.84 (t, J = 7.7 Hz, 1H, C^7H), 7.40 (d, J = 8.2 Hz, 1H, $C^{19}H$), 6.23 (s, 2H, 2 x $C^{13}H_2$), 3.93 (s, 3H, 3 x $C^{12}H_3$).

^{13}C NMR (126 MHz, $DMSO-d_6$) δ 165.6 (C^{11}), 155.1 (C^4), 146.1 (2 x C^2H), 136.9 (C), 134.3 (C), 133.0 (C^8H), 132.6 (C^6H), 131.2 (C), 130.9 ($C^{19}H$), 130.5 (d, J = 4.7 Hz, $C^{18}H$), 130.5 (C^7H), 130.0 (q, J = 33.3 Hz, C^{15}/C^{17}), 128.9 ($C^{10}H$), 127.9 (q, J = 31.7 Hz, C^{15}/C^{17}), 125.7 (2 x C^3H), 124.0 – 123.8 (m, $C^{16}H$), 123.23 (q, J = 274.5 Hz, $C^{20}F_3/C^{21}F_3$), 123.2 (q, J = 272.7 Hz, $C^{20}F_3/C^{21}F_3$), 59.1 (q, J = 3.6 Hz, $C^{13}H_2$), 52.7 ($C^{12}H_3$).

^{19}F NMR (376 MHz, $DMSO-d_6$) δ -59.0, -61.5.

IR (neat) (cm^{-1}): 2981, 1707, 1639, 1345, 1273, 1258, 1181, 1119, 1085, 1054.

***N*-(2,4-bis(trifluoromethyl)benzyl)-4-(4-fluorophenyl)-3-(*o*-tolyl)pyridinium iodide (**1r**)**



The title compound was prepared by General Procedure D using 4-(4-fluorophenyl)-3-(*o*-tolyl)pyridine **3r** (263 mg, 1.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (530 mg, 1.50 mmol) to give the pyridinium **1r** (461 mg, 75%) as a yellow solid.

m.p. (acetone): 252-254 °C

HRMS (ESI): Exact mass calculated for $C_{27}H_{19}NF_7^+ [M]^+$: 490.100, found 490.1398

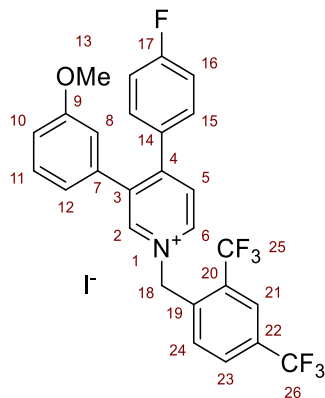
1H NMR (400 MHz, DMSO) δ 9.26 (d, J = 1.6 Hz, 1H, C²H), 9.15 (dd, J = 6.5, 1.6 Hz, 1H, C⁶H), 8.40 (d, J = 6.4 Hz, 1H, C⁵H), 8.23 (s, 1H, C²¹H), 8.15 (d, J = 8.5 Hz, 1H, C²³H), 7.52 (d, J = 8.2 Hz, 1H, C²⁴H), 7.44 – 7.21 (m, 8H, C⁹H, C¹⁰H, C¹¹H, C¹²H, 2 x C¹⁵H + 2 x C¹⁶H), 6.25 (s, 2H, C²H₂), 1.89 (s, 3H, C²H₃).

^{13}C NMR (126 MHz, DMSO) δ 163.20 (d, J = 250.0 Hz, C¹⁷), 155.6 (C⁴), 146.8 (C²), 144.3 (C⁶), 138.9 (C), 136.9 (C¹⁹), 135.7 (C), 133.3 (C), 131.8 (d, J = 8.8 Hz 2 x C¹⁵H), 131.4 (d, J = 3.0 Hz, C¹⁴), 130.8 (C²⁴H), 2 x 130.6 (2 x ArCH), 130.5 (q, J = 3.6 Hz, C²³H), 129.9 (q, J = 33.3 Hz, C²⁰/C²²), 129.6 (ArCH), 128.7 (C⁵), 127.8 (q, J = 31.7 Hz, C²⁰/C²²), 126.4 (ArCH), 123.9 – 123.6 (m, C²¹H), 123.2 (q, J = 274.4 Hz, C²⁵F₃/C²⁶F₃), 123.1 (q, J = 272.5 Hz, C²⁵F₃/C²⁶F₃), 116.0 (d, J = 22.0 Hz, 2 x C¹⁶H), 59.2 (q, J = 3.4 Hz, C¹⁸H₂), 19.3 (C¹³H₃).

^{19}F NMR (377 MHz, DMSO) δ -59.1, -61.4, -109.7 (tt, J = 8.7, 5.2 Hz).

IR (neat) (cm⁻¹): 2979, 2932, 1633, 1600, 1483, 1470, 1340, 1281, 1269, 1163.

***N*-(2,4-bis(trifluoromethyl)benzyl)-4-(4-fluorophenyl)-3-(3-methoxyphenyl)pyridinium iodide (**1s**)**



The title compound was prepared by General Procedure D using 4-(4-fluorophenyl)-3-(3-methoxyphenyl)pyridine **3s** (279 mg, 1.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (530 mg, 1.50 mmol) to give the pyridinium **1s** (495 mg, 78%) as a yellow solid.

m.p. (acetone): 188-190 °C

HRMS (ESI): Exact mass calculated for $C_{27}H_{19}ONF_7^+ [M]^+$: 506.1349, found: 506.1347

1H NMR (400 MHz, DMSO) δ 9.34 (d, J = 1.5 Hz, 1H, C²H), 9.10 (dd, J = 6.5, 1.6 Hz, 1H, C⁶H), 8.33 (d, J = 6.4 Hz, 1H, C⁵H), 8.24 (s, 1H, C²¹H), 8.13 (d, J = 8.0 Hz, 1H, C²³H), 7.49 (d, J = 8.3 Hz, 1H, C²⁴H), 7.43 (ddt, J = 8.3, 5.2, 2.6 Hz, 2H, 2 x C¹⁵H), 7.37 – 7.28 (m, 3H, C¹¹H + 2 x C¹⁶H), 7.02 (ddd, J = 8.4, 2.6, 0.9 Hz, 1H,

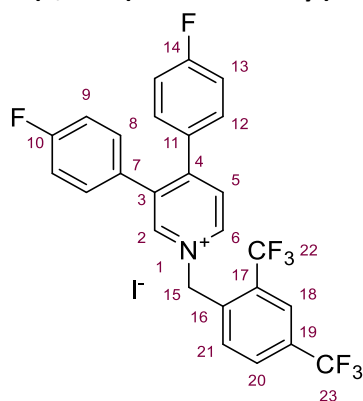
C¹²H), 6.91 (dd, $J = 2.6, 1.6$ Hz, 1H, C⁸H), 6.81 (ddd, $J = 7.7, 1.7, 1.0$ Hz, 1H, C¹⁰H), 6.26 (s, 2H, C¹⁸H₂), 3.69 (s, 3H, C¹³H₃).

¹³C NMR (126 MHz, DMSO) δ 163.1 (d, $J = 249.2$ Hz, C¹⁷), 159.4 (C⁹), 155.3 (C⁴), 146.5 (C²H), 143.9 (C⁶H), 139.1 (C), 137.0 (C¹⁹), 134.9 (C), 132.0 (d, $J = 8.9$ Hz, 2 x C¹⁵H), 131.5 (d, $J = 3.1$ Hz, C¹⁴), 130.5 (C²⁴H), 130.4 (C²³H), 130.1 (C⁵H), 129.8 (q, $J = 33.3$ Hz, C²⁰/C²²), 129.1 (C⁵H), 127.7 (q, $J = 31.9$ Hz, C²⁰/C²²), 123.9 – 123.5 (m, C²¹H), 123.21 (q, $J = 274.5$ Hz, C²⁵F₃/C²⁶F₃), 123.17 (q, $J = 272.7$ Hz, C²⁵F₃/C²⁶F₃), 121.9 (C¹²H), 116.0 (d, $J = 22.1$ Hz, 2 x C¹⁶H), 115.6 (C¹¹H), 114.6 (C¹⁰H), 59.2 (d, $J = 3.5$ Hz, C¹⁸H₂), 55.3 (C¹³H₃).

¹⁹F NMR (377 MHz, DMSO) δ -59.0, -61.4, -110.1 (tt, $J = 8.9, 5.4$ Hz).

IR (neat) (cm⁻¹): 2922, 1632, 1603, 1341, 1274, 1237, 1180, 1163, 1129, 1086.

N-(2,4-bis(Trifluoromethyl)benzyl)pyridinium iodide (1t)



The title compound was prepared by General Procedure D using 3,4-bis(4-fluorophenyl)pyridine **3t** (158 mg, 0.60 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **54** (350 mg, 1.00 mmol) to give the pyridinium **1t** (187 mg, 51%) as a yellow solid.

m.p. (acetone): 205-207°C

HRMS (ESI): Exact mass calculated for C₂₆H₁₆NF₈⁺ [M]⁺: 494.1150, found 494.1140

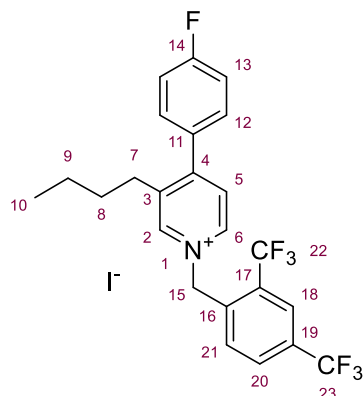
¹H NMR (400 MHz, DMSO) δ 9.34 (d, $J = 1.6$ Hz, 1H, C²H), 9.11 (dd, $J = 6.5, 1.5$ Hz, 1H, C⁶H), 8.34 (d, $J = 6.4$ Hz, 1H, C⁵H), 8.24 (s, 1H, C¹⁸H), 8.13 (d, $J = 8.1$ Hz, 1H, C²⁰H), 7.49 (d, $J = 8.2$ Hz, 1H, C²¹H), 7.44 – 7.38 (m, 2H, 2 x C¹²H), 7.38 – 7.25 (m, 6H, 2 x C⁸H + 2 x C⁹H + 2 x C¹³H), 6.26 (s, 2H, C²H₂).

¹³C NMR (126 MHz, DMSO) δ 163.1 (d, $J = 249.3$ Hz, C¹⁴), 162.5 (d, $J = 247.3$ Hz, C¹⁰), 155.4 (C⁴), 146.5 (C²H), 144.0 (C⁶H), 138.4 (C³), 137.0 (C¹⁶), 132.2 (2 x C⁸H/C¹²H), 132.1 (2 x C⁸H/C¹²H), 131.3 (d, $J = 3.3$ Hz, C⁷/C¹¹), 130.5 (C), 130.4 (q, $J = 3.8$ Hz, C²⁰H), 130.1 (d, $J = 3.2$ Hz, C⁷/C¹¹), 129.8 (q, $J = 33.3$ Hz, C¹⁷/C¹⁹), 129.1 (C⁵H), 127.7 (q, $J = 31.9$ Hz, C¹⁷/C¹⁹), 124.0 – 123.6 (m, C¹⁸H), 123.21 (q, $J = 274.7$ Hz, C²²F₃/C²³F₃), 123.17 (q, $J = 272.7$ Hz, C²²F₃/C²³F₃), 116.1 (d, $J = 22.1$ Hz, 2 x C¹³H), 116.0 (d, $J = 21.9$ Hz, 2 x C⁹H), 59.2 (q, $J = 3.4$ Hz, C¹⁵H₂).

¹⁹F NMR (377 MHz, DMSO) δ -59.0, -61.4, -110.1 (td, $J = 9.0, 4.4$ Hz), -111.9 (tt, $J = 9.0, 5.8$ Hz).

IR (neat) (cm⁻¹): 2980, 1633, 1603, 1493, 1463, 1342, 1270, 1168, 1138, 1122..

***N*-(2,4-bis(trifluoromethyl)benzyl)-3-butyl-4-(4-fluorophenyl)pyridinium iodide (**1u**)**



The title compound was prepared by General Procedure D using 3,4-bis(4-fluorophenyl)pyridine **3u** (158 mg, 0.60 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (350 mg, 1.00 mmol) to give the pyridinium **1u** (187 mg, 51%) as a white wax.

HRMS (ESI): Exact mass calculated for $C_{24}H_{21}NF_8^+$ $[M]^+$: 456.1557, found 456.1552

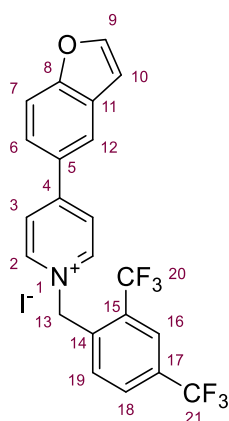
1H NMR (500 MHz, DMSO) δ 9.16 (d, J = 1.6 Hz, 1H, C^2H), 8.98 (dd, J = 6.3, 1.6 Hz, 1H, C^6H), 8.24 (s, 1H, $C^{18}H$), 8.15 (dd, J = 8.2, 1.9 Hz, 1H, $C^{20}H$), 8.12 (d, J = 6.4 Hz, 1H, C^5H), 7.70 – 7.59 (m, 2H, 2 x $C^{12}H$), 7.51 – 7.43 (m, 2H, 2 x $C^{13}H$), 7.39 (d, J = 8.2 Hz, 1H, $C^{21}H$), 6.22 (s, 2H, C^2H_2), 2.84 – 2.76 (m, 2H, C^7H_2), 1.51 – 1.39 (m, 2H, C^8H_2), 1.19 (q, J = 7.4 Hz, 2H, C^9H_2), 0.76 (t, J = 7.3 Hz, 3H, $C^{10}H_3$).

^{13}C NMR (126 MHz, DMSO) δ 163.1 (d, J = 248.4 Hz, C^{14}), 157.0 (C^4), 145.9 (C^2H), 142.8 (C^6H), 140.9 (C^3), 136.8 (C^{16}), 131.8 (d, J = 3.3 Hz, C^{11}), 131.1 (d, J = 8.9 Hz, 2 x $C^{12}H$), 130.8 ($C^{21}H$), 130.4 (q, J = 20.7 Hz, $C^{20}H$), 129.9 (q, J = 33.2 Hz, C^{17}/C^{19}), 128.9 (C^5H), 127.8 (q, J = 31.8 Hz, C^{17}/C^{19}), 124.0 – 123.6 (m, $C^{18}H$), 123.2 (q, J = 274.5 Hz, $C^{22}F_3/C^{23}F_3$), 123.1 (q, J = 272.7 Hz, $C^{22}F_3/C^{23}F_3$), 116.2 (d, J = 21.9 Hz, 2 x $C^{13}H$), 59.3 (q, J = 3.4 Hz, $C^{15}H_2$), 31.2 (C^8H_2), 29.5 (C^7H_2), 21.6 (C^9H_2), 13.4 ($C^{10}H_3$).

^{19}F NMR (377 MHz, DMSO) δ -59.1, -61.4, -110.8 (tt, J = 8.9, 5.3 Hz).

IR (neat) (cm^{-1}): 2981, 1638, 1605, 1500, 1464, 1342, 1276, 1183, 1137, 1123.

4-(Benzofuran-5-yl)-*N*-(2,4-bis(trifluoromethyl)benzyl)pyridinium iodide (1v**)**



The title compound was prepared by General Procedure D using 4-(benzofuran-5-yl)pyridine **3v** (195 mg, 1.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (530 mg, 1.50 mmol) to give the pyridinium **1v** (278 mg, 51%) as a pale yellow solid.

m.p. (acetone): 247-249 °C

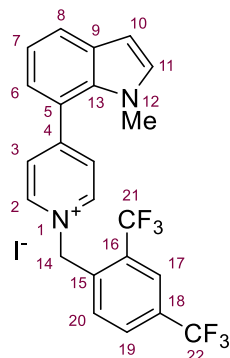
HRMS (ESI): Exact mass calculated for $C_{22}H_{14}ONF_3^+$ $[M]^+$: 422.0974, found 422.0981

1H NMR (500 MHz, DMSO) δ 9.12 (d, J = 6.9 Hz, 2H, 2 x C^2H), 8.67 (d, J = 7.1 Hz, 2H, 2 x C^3H), 8.52 (d, J = 2.0 Hz, 1H, $C^{12}H$), 8.23 (s, 1H, $C^{16}H$), 8.20 (d, J = 2.2 Hz, 1H, C^9H), 8.14 (dd, J = 8.1, 2.1 Hz, 1H, $C^{18}H$), 8.10 (dd, J = 8.7, 2.1 Hz, 1H, C^6H), 7.91 (d, J = 8.7 Hz, 1H, C^7H), 7.43 (d, J = 8.2 Hz, 1H, $C^{19}H$), 7.16 (dd, J = 2.3, 1.0 Hz, 1H, $C^{10}H$), 6.20 (s, 2H, $C^{13}H_2$).

¹³C NMR (126 MHz, DMSO) δ 156.5 (C), 156.3 (C), 148.2 (C⁹H), 145.6 (2 x C²H), 136.9 (C), 131.0 (C¹⁹H), 130.5 (q, J = 3.8 Hz, C¹⁸H), 129.9 (q, J = 33.2 Hz, C¹⁵/C¹⁷), 128.6 (C), 128.4 (C), 127.8 (q, J = 31.6 Hz, C¹⁵/C¹⁷), 124.9 (C⁶H), 124.8 (2 x C³H), 123.9 – 123.6 (m, C¹⁶H), 123.19 (q, J = 274.6 Hz, C²⁰F₃/C²¹F₃), 123.15 (q, J = 272.7 Hz, C²⁰F₃/C²¹F₃), 122.4 (C¹²H), 112.8 (C⁷H), 107.3 (C¹⁰H), 58.8 (q, J = 3.4 Hz, C¹³H₂).
¹⁹F NMR (377 MHz, DMSO) δ -59.0, -61.4.

IR (neat) (cm⁻¹): 3023, 1638, 1343, 1309, 1270, 1193, 1177, 1150, 1134, 1125.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(1-methyl-1H-indol-7-yl)pyridinium iodide (1w)**



The title compound was prepared by General Procedure D using 4-(1-methyl-1H-indol-7-yl)pyridine **3w** (208 mg, 1.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **54** (530 mg, 1.50 mmol) to give the pyridinium **1w** (465 mg, 83%) as a pale yellow solid.

m.p. (acetone): 246-248 °C

HRMS (ESI): Exact mass calculated for C₂₃H₁₇N₂F₆⁺ [M]⁺: 435.1290, found 432.1288

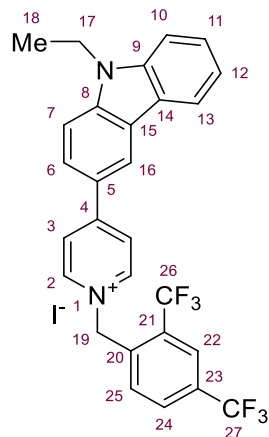
¹H NMR (500 MHz, DMSO) δ 9.12 (d, J = 6.8 Hz, 2H, 2 x C²H), 8.35 (d, J = 6.8 Hz, 2H, 2 x C³H), 8.25 (s, 1H, C¹⁷H), 8.20 (dd, J = 8.3, 2.0 Hz, 1H, C¹⁹H), 7.83 (dd, J = 6.8, 2.1 Hz, 1H, C⁶H), 7.58 (d, J = 8.2 Hz, 1H, C²⁰H), 7.47 (d, J = 3.2 Hz, 1H, C¹¹H), 7.28 – 7.20 (m, 2H, C⁷H + C⁸H), 6.67 (d, J = 3.2 Hz, 1H, C¹⁰H), 6.25 (s, 2H, C¹⁴H₂), 3.48 (s, 3H, C¹²H₃).

¹³C NMR (126 MHz, DMSO) δ 157.1 (C⁴), 144.6 (2 x C²H), 136.5 (C), 133.0 (C¹¹H), 132.6 (C), 131.7 (C²⁰H), 130.6 (q, J = 3.8 Hz, C¹⁹H), 130.4 (ArC), 130.1 (q, J = 33.2 Hz, C¹⁶/C¹⁸), 128.7 (2 x C³H), 128.1 (q, J = 31.6 Hz, C¹⁶/C¹⁸), 125.0 (C⁷H/C⁸H), 124.1 – 123.8 (m, C¹⁷H), 123.7 (C⁶H), 123.2 (q, J = 274.6 Hz, C²¹F₃/C²²F₃), 123.1 (q, J = 272.6 Hz, C²¹F₃/C²²F₃), 120.4 (ArC), 119.3 (C⁷H/C⁸H), 101.7 (C¹⁰H), 59.1 (q, J = 3.1 Hz, C¹⁴H₂), 37.5 (C¹²H₃).

¹⁹F NMR (377 MHz, DMSO) δ -58.93, -61.46.

IR (neat) (cm⁻¹): 1632, 1341, 1308, 1275, 1172, 1129, 1083, 1052, 796, 723.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(9-ethyl-9H-carbazol-3-yl)pyridinium iodide (1x)**



The title compound was prepared by General Procedure D using 4-(9-ethyl-9H-carbazol-3-yl)pyridine **3x** (272 mg, 1.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (530 mg, 1.50 mmol) to give the pyridinium **1x** (606 mg, 97%) as a yellow solid.

m.p. (acetone): 219–221 °C

HRMS (ESI): Exact mass calculated for $C_{28}H_{21}N_2F_6^+$ $[M]^+$: 499.1603, found 499.1601

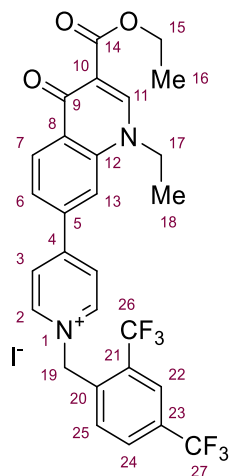
1H NMR (400 MHz, DMSO) δ 9.17 (d, J = 2.0 Hz, 1H, $C^{16}H$), 9.05 (d, J = 7.1 Hz, 2H, 2 x C^2H), 8.74 (d, J = 7.2 Hz, 2H, 2 x C^3H), 8.34 (dt, J = 7.8, 1.0 Hz, 1H, $C^{13}H$), 8.31 (dd, J = 8.8, 2.0 Hz, 1H, C^6H), 8.24 (s, 1H, $C^{22}H$), 8.14 (dd, J = 8.3, 2.0 Hz, 1H, $C^{24}H$), 7.89 (d, J = 8.8 Hz, 1H, C^7H), 7.73 (d, J = 8.3, 0.9 Hz, 1H, $C^{10}H$), 7.57 (ddd, J = 8.3, 7.2, 1.2 Hz, 1H, $C^{11}H$), 7.40 (d, J = 8.3 Hz, 1H, $C^{25}H$), 7.34 (ddd, J = 7.9, 7.2, 0.9 Hz, 1H, $C^{12}H$), 6.17 (s, 2H, $C^{19}H_2$), 4.55 (q, J = 7.1 Hz, 2H, $C^{17}H_2$), 1.37 (t, J = 7.1 Hz, 3H, $C^{18}H_3$).

^{13}C NMR (126 MHz, DMSO) δ 156.5 (C^4), 145.2 (2 x C^2H), 142.2 (2 x C), 140.4 (2 x C), 137.4 (C^{20}), 130.5 ($C^{24}H$ + $C^{25}H$), 129.8 (q, J = 33.3 Hz, C^{21}/C^{23}), 127.7 (q, J = 31.8 Hz, C^{21}/C^{23}), 127.0 ($C^{11}H$), 126.0 (C^6H), 123.9 – 123.7 (m, $C^{22}H$), 123.4 (2 x C^3H), 123.22 (q, J = 274.9 Hz, $C^{26}F_3/C^{27}F_3$), 123.22 (C), 123.17 (q, J = 272.7 Hz, $C^{26}F_3/C^{27}F_3$), 122.4 (C), 121.8 ($C^{16}H$), 121.0 ($C^{13}H$), 120.2 ($C^{12}H$), 110.5 (C^7H), 110.1 ($C^{10}H$), 58.4 (q, J = 3.7 Hz, $C^{19}H_2$), 37.4 ($C^{17}H_2$), 13.8 ($C^{18}H_3$).

^{19}F NMR (377 MHz, DMSO) δ –59.1, –61.4.

IR (neat) (cm^{-1}): 3658, 2980, 2973, 1622, 1590, 1494, 1480, 1343, 1273, 1162.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(3-(ethoxycarbonyl)-1-ethyl-4-oxo-1,4-dihydroquinolin-7-yl)pyridinium iodide (**1y**)**



The title compound was prepared by General Procedure D using 4-(3-(ethoxycarbonyl)-1-ethyl-4-oxo-1,4-dihydroquinolin-7-yl)pyridine **3y** (600 mg, 1.90 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.32 g, 3.70 mmol) to give the pyridinium **1y** (1.13 g, 90%) as an orange solid.

m.p. (acetone): 209–211 °C

HRMS (ESI): Exact mass calculated for $C_{28}H_{23}O_3N_2F_6^+$ $[M]^+$: 549.1607, found 549.1604

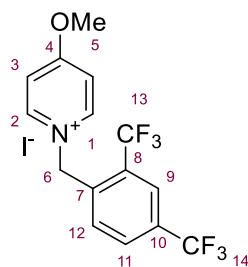
1H NMR (400 MHz, DMSO) δ 9.25 (d, J = 6.4 Hz, 2H, 2 x C^2H + $C^{11}H$), 8.82 (d, J = 7.8 Hz, 3H, 2 x C^2H + $C^{11}H$), 8.46 (d, J = 8.3 Hz, 1H, C^7H), 8.39 (s, 1H, $C^{13}H$), 8.25 (s, 1H, $C^{22}H$), 8.18 – 8.10 (m, 2H, C^6H + $C^{24}H$), 7.42 (d, J = 8.2 Hz, 1H, $C^{25}H$), 6.27 (s, 2H, $C^{19}H_2$), 4.61 (q, J = 7.1 Hz, 2H, $C^{17}H_2$), 4.25 (q, J = 7.0 Hz, 2H, $C^{15}H_2$), 1.43 (t, J = 7.0 Hz, 3H, $C^{18}H_3$), 1.30 (t, J = 7.1 Hz, 3H, $C^{16}H_3$).

^{13}C NMR (126 MHz, DMSO) δ 172.2 (C^9), 164.4 (C^{14}), 154.8 (C^4), 150.0 ($C^{11}H$), 146.0 (2 x C^2H), 139.2 (C), 137.4 (C), 136.8 (C^{20}), 130.8 ($C^{25}H$), 130.5 (q, J = 4.0 Hz, $C^{24}H$), 130.0 (C^8), 129.9 (q, J = 33.4 Hz, C^{21}/C^{23}), 128.0 (C^7H), 127.8 (q, J = 31.7 Hz, C^{21}/C^{23}), 126.3 (2 x C^3H), 124.1 (C^6H), 124.0 – 123.7 (m, $C^{22}H$), 123.2 (q, J = 274.6 Hz, $C^{26}F_3/C^{27}F_3$), 123.1 (q, J = 272.5 Hz, $C^{26}F_3/C^{27}F_3$), 117.6 ($C^{13}H$), 111.0 (C^{10}), 59.9 ($C^{15}H_2$), 59.2 (q, J = 3.3 Hz, $C^{19}H_2$), 48.1 ($C^{17}H_2$), 14.6 ($C^{18}H_3$), 14.3 ($C^{16}H_3$).

^{19}F NMR (377 MHz, DMSO) δ –59.0, –61.4.

IR (neat) (cm^{-1}): 3433, 1720, 1611, 1472, 1348, 1306, 1275, 1219, 1188, 1171.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-methoxypyridinium iodide (**1z**)**



The title compound was prepared by General Procedure D using 4-methoxypyridine (0.2 mL, 2.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.06 g, 3.00 mmol) to give the pyridinium **1z** (853 mg, 92%) as a white solid.

m.p. (acetone): 185-187 °C

HRMS (ESI): Exact mass calculated for $C_{15}H_{12}ONF_6$ $[M]^+$: 336.08176, found 336.08113

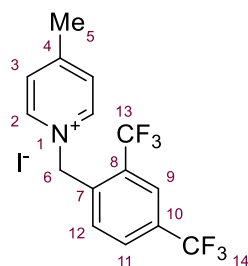
1H NMR (400 MHz, DMSO- d_6) δ 8.89 (d, J = 7.5 Hz, 2H, 2 x C^2H), 8.20 (s, 1H, C^9H), 8.11 (d, J = 8.2 Hz, 1H, $C^{12}H$), 7.73 (d, J = 7.7 Hz, 1H, $C^{11}H$), 7.30 (d, J = 8.2 Hz, 2H, 2 x C^3H), 6.04 (s, 2H, 2 x C^6H), 4.15 (s, 3H, 3 x C^5H).

^{13}C NMR (126 MHz, DMSO- d_6) δ 171.4 (C^4), 147.1 (2 x C^2H), 137.4 (C^7), 130.6 ($C^{12}H$), 130.5 (d, J = 3.8 Hz, $C^{11}H$), 129.8 (q, J = 33.3 Hz, C^8/C^{10}), 127.7 (q, J = 31.8 Hz, C^8/C^{10}), 124.1 – 123.6 (m, C^9H), 123.2 (q, J = 275.3 Hz, $C^{13}F_3 + C^{14}F_3$), 114.0 (2 x C^3H), 58.4 (C^5H_3), 57.9 (q, J = 3.5 Hz, C^6H_2).

^{19}F NMR (377 MHz, DMSO- d_6) δ -59.1, -61.5.

IR (neat) (cm^{-1}): 2981, 1643, 1345, 1269, 1177, 1138, 1085, 1053, 843, 671.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-methylpyridinium iodide (**1aa**)**



The title compound was prepared by General procedure D using 4-methylpyridine (0.2 mL, 2.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.06 g, 3.00 mmol) to give the pyridinium **1aa** (766 mg, 86%) as a pale brown solid.

m.p. (acetone): 192-194 °C

HRMS (ESI): Exact mass calculated for $C_{15}H_{12}NF_6^+$ $[M]^+$: 320.0870, found 320.0868

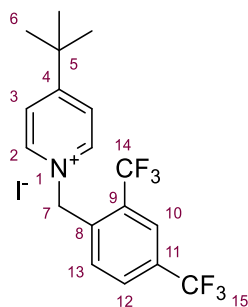
1H NMR (400 MHz, DMSO) δ 8.93 (d, J = 6.8 Hz, 2H, 2 x C^2H), 8.20 (s, 1H, C^9H), 8.13 (dd, J = 8.1, 2.0 Hz, 1H, $C^{11}H$), 8.08 (d, J = 6.1 Hz, 2H, 2 x C^3H), 7.38 (d, J = 8.2 Hz, 1H, $C^{12}H$), 6.14 (s, 2H, C^6H_2), 2.67 (s, 3H, C^5H_3).

^{13}C NMR (126 MHz, DMSO) δ 160.6 (C^4), 144.7 (2 x C^2H), 136.6 (C^7), 131.4 ($C^{12}H$), 130.5 (q, J = 3.9 Hz, $C^{11}H_3$), 130.1 (q, J = 33.2 Hz, C^8/C^{10}), 128.9 (2 x C^3H), 128.0 (q, J = 31.8 Hz, C^8/C^{10}), 124.0 – 123.7 (m, C^9H), 123.1 (q, J = 273.2 Hz, $C^{13}F_3/C^{14}F_3$), 58.9 (q, J = 3.1 Hz, C^6H_2), 21.7 (C^5H_3).

^{19}F NMR (377 MHz, DMSO) δ -59.0, -61.5.

IR (neat) (cm^{-1}): 2981, 1642, 1346, 1282, 1268, 1178, 1139, 1116, 1085, 1053, 670.

***N*-(2,4-bis(trifluoromethyl)benzyl)-4-*tert*-butoxypyridinium iodide (1ab)**



The title compound was prepared by General Procedure D using 4-methylpyridine (0.44 mL, 3.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (1.59 g, 4.50 mmol) to give the pyridinium **1ab** (1.56 g, 99%) as a white solid.

m.p. (acetone): 251-253 °C

HRMS (ESI): Exact mass calculated for $C_{18}H_{18}NF_6^+$ $[M]^+$: 362.1329, found: 362.1338

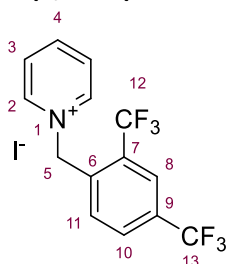
1H NMR (400 MHz, DMSO) δ 8.99 (d, J = 7.0 Hz, 2H, 2 x C^2H), 8.26 (d, J = 7.0 Hz, 2H, 2 x C^3H), 8.22 (s, 1H, $C^{10}H$), 8.15 (d, J = 8.2 Hz, 1H, $C^{12}H$), 7.36 (d, J = 8.2 Hz, 1H, $C^{13}H$), 6.16 (s, 2H, C^7H_2), 1.40 (s, 9H, 3 x C^2H_3).

^{13}C NMR (126 MHz, DMSO) δ 171.4 (C^4), 145.1 (2 x C^2H), 136.6 (C^8), 131.3 ($C^{13}H$), 130.6 (q, J = 3.7 Hz, $C^{12}H$), 130.0 (q, J = 33.2 Hz, C^9/C^{11}), 127.98 (q, J = 31.8 Hz, C^9/C^{11}), 125.6 (2 x C^2H), 124.0 – 123.63 (m, $C^{10}H$), 123.2 (d, J = 274.9 Hz, $C^{14}F_3 + C^{15}F_3$), 58.8 (q, J = 3.3 Hz, C^7H_2), 36.6 (C^5), 29.54 (3 x C^6H_3).

^{19}F NMR (377 MHz, DMSO) δ -59.0, -61.5.

IR (neat) (cm^{-1}): 2972, 1642, 1340, 1271, 1177, 1164, 1129, 1084, 1051, 847.

***N*-(2,4-bis(trifluoromethyl)benzyl)pyridinium (1ac)**



The title compound was prepared by General Procedure D using pyridine (81 μ L, 1.00 mmol) and 2,4-bis(trifluoromethyl)benzyl iodide **S4** (365 mg, 1.20 mmol) to give the pyridinium **1ac** (311 mg, 76%) as a pale yellow solid.

m.p. (acetone): 199-201 °C

HRMS (ESI): Exact mass calculated for $C_{14}H_{10}NF_6^+$ $[M]^+$: 306.0712, found: 306.0710

1H NMR (400 MHz, DMSO) δ 9.09 (dd, J = 6.7, 1.4 Hz, 2H, 2 x C^2H), 8.73 (tt, J = 7.8, 1.3 Hz, 1H, C^4H), 8.28 – 8.22 (m, 2H, 2 x C^3H), 8.20 (d, J = 1.9 Hz, 1H, C^8H), 8.14 (dd, J = 8.2, 2.0 Hz, 1H, $C^{10}H$), 7.44 (d, J = 8.2 Hz, 1H, $C^{11}H$), 6.22 (s, 2H, C^5H_2).

^{13}C NMR (101 MHz, DMSO) δ 147.1 (C^4H), 145.8 (C^2H), 136.2 (C^6), 131.9 ($C^{11}H$), 130.7 ($C^{10}H$), 130.3 (q, J = 33.3 Hz, C^7/C^9), 128.8, 128.2 (q, J = 31.7 Hz, C^7/C^9), 124.3 – 123.6 (m, C^8H), 123.2 (q, J = 273.7 Hz, $C^{12}F_3 + C^{13}F_3$), 59.9 (q, J = 3.2 Hz, C^5H_2).

^{19}F NMR (377 MHz, DMSO) δ -59.0, -61.6.

IR (neat) (cm^{-1}): 3076, 2160, 2033, 1482, 1348, 1274, 1177, 1142, 1122, 1055.

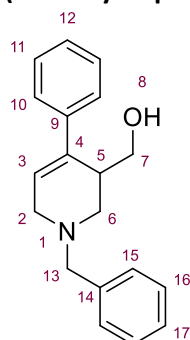
The Synthesis of Tetrahydropyridines

General procedure E:

Substrate (1.00 equiv.), KI (4.00 equiv.), paraformaldehyde (30.0 equiv.), and $[\text{Ru}(p\text{-cymene})\text{Cl}_2]_2$ (2 mol%) was added to a microwave vial. MeOH (0.2 M) and $\text{Mg}(\text{OMe})_2$ (1.00 equiv, 0.89M in MeOH) was added and the solution heated at 65 °C for 16 hours. The solution concentrated under reduce pressure and re-dissolved in CH_2Cl_2 (30 mL), brine (50 mL) and water (50 mL). The solution was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL). The organic layers were combined, dried (MgSO_4), filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (FCC) to furnish amines **2b-2ab**.

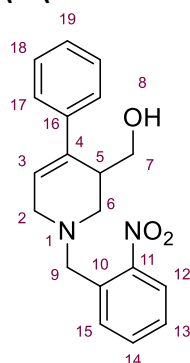
Reaction to form **2k** was also performed in an rbf with a reflux condenser attached and gave exactly the same yield on 0.50 mmol scale.

(*N*-Benzyl-4-phenyl-1,2,3,6-tetrahydropyridin-3-yl)methanol (**2a**)



Salt **1a** (187 mg, 0.50 mmol), KI (332 mg, 2.00 mmol), paraformaldehyde (300 mg, 10.0 mmol), and $[\text{Ru}(p\text{-cymene})\text{Cl}_2]_2$ (6.1 mg, 2 mol%) was added to a microwave vial. MeOH (2.08 mL, 0.2 M) and $\text{Mg}(\text{OMe})_2$ (0.42mL, 0.89M in MeOH) was added and the solution heated at 65 °C for 16 hours. The solution concentrated under reduce pressure and re-dissolved in CH_2Cl_2 (30 mL), brine (50 mL) and water (50 mL). The solution was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL). The organic layers were combined, dried (MgSO_4), filtered, and concentrated *in vacuo*. The product was purified by FCC (10%-20% EtOAc in pentane) to give *amine 2b* (23 mg, 17%) as a yellow oil. Spectroscopic data was consistent with that reported in the literature.¹⁶

(*N*-(2-Nitrobenzyl)-4-phenyl-1,2,3,6-tetrahydropyridin-3-yl)methanol (**2b**)



Salt **1b** (209 mg, 0.50 mmol), KI (332 mg, 2.00 mmol), paraformaldehyde (300 mg, 10.0 mmol), and $[\text{Ru}(p\text{-cymene})\text{Cl}_2]_2$ (6.1 mg, 2 mol%) was added to a microwave vial. MeOH (2.08 mL, 0.2 M) and $\text{Mg}(\text{OMe})_2$ (0.42mL, 0.89M in MeOH) was added and the solution heated at 65 °C for 16 hours. The solution concentrated under reduce pressure and re-dissolved in CH_2Cl_2 (30 mL), brine (50 mL) and water (50 mL). The solution was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL). The organic layers were combined, dried (MgSO_4), filtered, and concentrated *in vacuo*. The product was purified by FCC (20%-50% EtOAc in pentane) to give *amine 2b* (65 mg, 40%) as an orange solid.

m.p.(EtOAc) 124-126 °C;

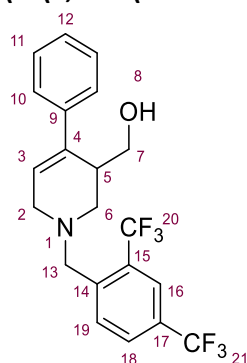
HRMS (ESI): Exact mass calculated for C₁₉H₂₁O₃N₂ [M+H]⁺: 325.15467, found: 325.15454;

¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J* = 7.6 Hz, 1H, C¹²H), 7.64 – 7.54 (m, 2H, 2 x ArCH), 7.45 (ddd, *J* = 8.6, 6.0, 2.9 Hz, 1H, ArCH), 7.41 – 7.19 (m, 5H, 5 x ArCH), 6.02 (dd, *J* = 4.7, 2.2 Hz, 1H, C³H), 4.00 (d, *J* = 14.1 Hz, 1H, C⁹H), 3.88 (d, *J* = 14.0 Hz, 1H, C⁹H₂), 3.67 (dd, *J* = 10.5, 3.1 Hz, 1H, C⁷H₂), 3.60 (ddd, *J* = 10.6, 5.2, 1.3 Hz, 1H, C⁷H₂), 3.38 (dd, *J* = 16.9, 4.7 Hz, 1H, C²H₂), 3.17 (dt, *J* = 11.2, 1.6 Hz, 1H, C⁶H₂), 2.92 (dt, *J* = 16.9, 2.4 Hz, 1H, C²H₂), 2.87 (br s, 1H, C⁵H), 2.69 (dd, *J* = 11.5, 3.3 Hz, 1H, C⁶H₂).

¹³C NMR (101 MHz, CDCl₃) δ 149.9 (ArC), 139.7 (ArC), 136.3 (ArC), 133.0 (ArC), 133.0 (ArCH), 131.4 (ArCH), 128.6 (2 x ArCH), 128.6 (ArCH), 127.5 (ArCH), 126.1 (2 x ArCH), 124.9 (ArCH), 124.1 (C³H), 64.9 (C⁷H), 59.1 (C⁹H), 54.9 (C⁶H), 53.8 (C²H), 39.2 (C⁵H).

IR (neat) (cm⁻¹): 3311, 2928, 2852, 2811, 1726, 1523, 1350, 1127, 1071, 991.

(N-(2,4-bis(Trifluoromethyl)benzyl)-4-phenyl-1,2,3,6-tetrahydropyridin-3-yl)methanol (2c)



The title compound was prepared by general procedure E using salt **1c** (255 mg, 3.00 mmol). Purification by FCC (10%-30% EtOAc in pentane) gave *amine 2c* (916 mg, 73%) as an orange oil.

HRMS (ESI): Exact mass calculated for C₂₁H₂₀F₆NO [M+H]⁺: 416.14436, found: 416.14505

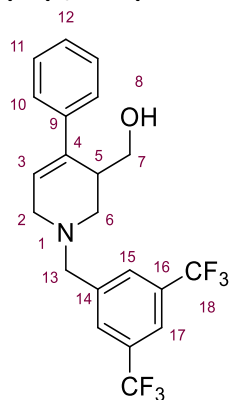
¹H NMR (400 MHz, CDCl₃) δ 7.93 (d, *J* = 1.8 Hz, 1H, C¹⁶H), 7.91 (d, *J* = 8.3 Hz, 1H, C¹⁸H), 7.83 (d, *J* = 8.3, 1.9 Hz, 1H, C¹⁹H), 7.41 – 7.23 (m, 5H, 5 x ArH), 6.08 (dd, *J* = 4.7, 2.2 Hz, 1H, C³H), 4.02 (s, 1H, O⁸H), 3.87 (s, 2H, C¹³H₂), 3.75 (dd, *J* = 10.3, 2.7 Hz, 1H, C⁷H₂), 3.67 (ddd, *J* = 10.3, 4.1, 1.6 Hz, 1H, C⁷H₂), 3.43 (dd, *J* = 16.9, 4.8 Hz, 1H, C²H₂), 3.16 (dt, *J* = 11.2, 1.6 Hz, 1H, C⁶H₂), 2.98 (dt, *J* = 16.9, 2.5 Hz, 1H, C²H₂), 2.89 (brs, 1H, C⁵H), 2.78 (ddd, *J* = 11.1, 3.9, 1.5 Hz, 1H, C⁶H₂).

¹³C NMR (101 MHz, CDCl₃) δ 141.2 (C¹⁴), 139.7 (C), 136.4 (C), 131.5 (C¹⁹H), 129.8 (q, *J* = 31.7 Hz, C¹⁵+C¹⁷), 129.0 (C¹⁸H), 128.7 (2 x ArCH), 127.7 (ArCH), 126.2 (2 x ArCH), 124.1 (C³H), 123.7 (q, *J* = 274.0 Hz, C²⁰F₃/C²¹F₃), 123.5 (q, *J* = 272.4 Hz, C²⁰F₃/C²¹F₃), 123.5 – 123.2 (m, C¹⁶H), 65.4 (C⁷H₂), 58.0 (q, *J* = 2.2 Hz, C¹³H₂), 55.7 (C⁶H₂), 53.8 (C²H₂), 39.1 (C⁵H).

¹⁹F NMR (376 MHz, CDCl₃) δ -59.20, -62.86.

IR (neat) (cm⁻¹): 3376, 2996, 1346, 1283, 1276, 1171, 1126, 1085, 1037, 918.

(N-(3,5-bis(Trifluoromethyl)benzyl)-4-phenyl-1,2,3,6-tetrahydropyridin-3-yl)methanol (2d)



The title compound was prepared by general procedure E using salt **1d** (255 mg, 0.50 mmol). Purification by FCC (20% EtOAc in pentane) gave *amine 2d* (66 mg, 32%) as an orange oil.

HRMS (ESI): Exact mass calculated for $C_{21}H_{20}F_6NO$ $[M+H]^+$: 416.14436, found: 416.14499

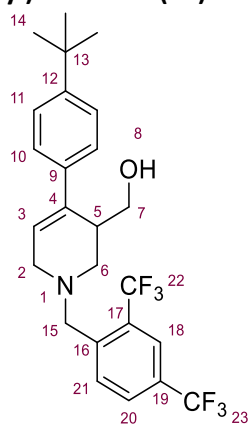
1H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 3H), 7.40 – 7.23 (m, 5H), 6.06 (dd, J = 4.7, 2.2 Hz, 1H), 3.84 (s, 1H), 3.81 (d, J = 13.5 Hz, 1H), 3.75 (dd, J = 10.2, 2.8 Hz, 1H), 3.73 (d, J = 13.5 Hz, 1H), 3.67 (ddd, J = 10.3, 4.3, 1.5 Hz, 1H), 3.42 – 3.32 (m, 1H), 3.17 (dt, J = 11.1, 1.6 Hz, 1H), 2.94 (dt, J = 16.6, 2.4 Hz, 1H), 2.93 – 2.86 (m, 1H), 2.72 (ddd, J = 11.1, 3.8, 1.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.4 (C^{14}), 139.7 (C), 136.6 (C), 132.0 (q, J = 33.3 Hz, 2 x C^{16}), 129.1 (2 x $C^{15}H$), 128.7 (2 x ArCH), 127.7 (ArCH), 126.2 (2 x ArCH), 124.0 (C^3H), 123.5 (q, J = 277.6 Hz, 2 x $C^{18}F_3$), 121.9 – 121.5 (m, $C^{17}H$), 65.3 (C^7H_2), 62.0 ($C^{13}H_2$), 55.4 (C^6H_2), 53.5 (C^2H_2), 39.0 (C^5H).

^{19}F NMR (377 MHz, $CDCl_3$) δ –62.79 (d, J = 2.6 Hz).

IR (neat) (cm^{-1}): 3376, 2921, 1352, 1276, 1168, 1124, 846, 756, 699, 682.

(*N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-(tert-butyl)phenyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2e**)**



The title compound was prepared by General procedure E using salt **1e** (283 mg, 0.50 mmol). Purification by FCC (10%-30% EtOAc in pentane) gave *amine 2e* (157 mg, 66%) as a white solid.

m.p. (acetone): 66-68°C

HRMS (ESI): Exact mass calculated for $C_{25}H_{28}F_6NO$ $[M+H]^+$: 472.20696, found: 472.20642

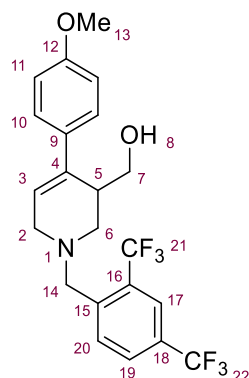
1H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.88 (m, 2H, $C^{18}H$ + $C^{21}H$), 7.83 (dd, J = 8.3, 2.4 Hz, 1H, $C^{20}H$), 7.36 (d, J = 8.7 Hz, 2H, 2 x $C^{10}H$), 7.30 (d, J = 8.7 Hz, 2H, 2 x $C^{11}H$), 6.06 (dd, J = 4.8, 2.2 Hz, 1H, C^3H), 4.02 (s, 1H, OH), 3.86 (s, 2H, $C^{15}H_2$), 3.75 (dd, J = 10.3, 2.7 Hz, 1H, C^7H_2), 3.69 (ddd, J = 10.3, 4.1, 1.5 Hz, 1H, C^7H_2), 3.42 (dd, J = 16.9, 4.7 Hz, 1H, C^2H_2), 3.15 (dt, J = 11.1, 1.6 Hz, 1H, C^6H_2), 2.97 (dt, J = 16.9, 2.5 Hz, 1H, C^2H_2), 2.89 (s, 1H, C^5H), 2.76 (ddd, J = 11.1, 3.9, 1.4 Hz, 1H, C^6H_2), 1.32 (s, 9H, 3 x $C^{14}H_3$).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.7 (C^{12}), 141.2 (C), 136.5 (C), 136.0 (C), 131.5 ($C^{21}H$), 130.0 (q, J = 33.4 Hz, C^{17}/C^{19}), 129.7 (q, J = 31.2 Hz, C^{17}/C^{19}), 129.1 (q, J = 3.8 Hz, $C^{20}H$), 125.8 (2 x $C^{11}H$), 125.6 (2 x $C^{10}H$), 123.7 (q, J = 274.2 Hz, $C^{22}F_3/C^{23}F_3$), 123.5 (q, J = 272.3 Hz, $C^{22}F_3/C^{23}F_3$), 123.4 (C^3H), 123.4 – 123.2 (m, $C^{18}H$), 65.5 (C^7H_2), 58.0 (q, J = 2.2 Hz, $C^{15}H$), 55.8 (C^6H_2), 53.8 (C^2H_2), 38.8 (C^5H), 34.6 (C^{13}), 31.5 (3 x $C^{14}H_3$).

^{19}F NMR (377 MHz, $CDCl_3$) δ –59.2, –62.9.

IR (neat) (cm^{-1}): 3036, 2830, 1344, 1273, 1171, 1121, 1083, 1055, 827, 673.

(N-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-methoxyphenyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2f)



The title compound was prepared by General procedure E using salt **1f** (270 mg, 0.50 mmol). Purification by FCC (5%-30% EtOAc in pentane) gave *amine 2f* (154 mg, 69%) as an orange oil.

HRMS (ESI): Exact mass calculated for C₂₂H₂₂F₆NO₂ [M+H]⁺ 446.1549; found: 446.1549

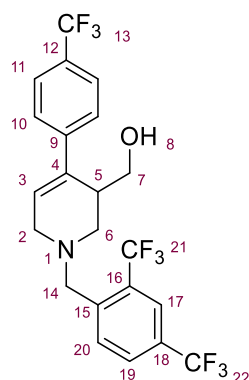
¹H NMR (400 MHz, CDCl₃) δ 7.93 (s, 1H, C¹⁷H), 7.90 (d, *J* = 8.2 Hz, 1H, C²⁰H), 7.83 (dd, *J* = 8.3, 1.9 Hz, 1H, C¹⁹H), 7.30 (d, *J* = 8.9 Hz, 2H, 2 x C¹⁰H), 6.87 (d, *J* = 8.8 Hz, 2H, 2 x C¹¹H), 6.00 (dd, *J* = 4.6, 2.2 Hz, 1H, C³H), 4.06 (s, 1H, OH), 3.86 (s, 2H, C¹⁴H₂), 3.81 (s, 3H, C¹³H₃), 3.75 (dd, *J* = 10.2, 2.7 Hz, 1H, C⁷H₂), 3.67 (ddd, *J* = 10.2, 4.0, 1.6 Hz, 1H, C⁷H₂), 3.41 (dd, *J* = 16.8, 4.7 Hz, 1H, C²H₂), 3.14 (dt, *J* = 11.1, 1.6 Hz, 1H, C⁶H₂), 2.96 (dt, *J* = 16.8, 2.5 Hz, 1H, C²H₂), 2.85 (s, 1H, C⁵H), 2.76 (ddd, *J* = 11.1, 3.8, 1.5 Hz, 1H, C⁶H₂).

¹³C NMR (126 MHz, CDCl₃) δ 159.3 (C¹²), 141.2 (C¹⁵), 135.7 (C), 132.1 (C), 131.5 (C²⁰H), 130.1 (q, *J* = 33.5 Hz, C¹⁶/C¹⁸), 129.7 (q, *J* = 31.2 Hz, C¹⁶/C¹⁸), 129.0 (q, *J* = 4.1 Hz, C¹⁹H), 127.2 (2 x C¹⁰H), 123.7 (q, *J* = 273.2 Hz, C²¹F₃/C²²F₃), 123.5 (q, *J* = 272.3 Hz, C²¹F₃/C²²F₃), 123.3 (m, C¹⁷H), 122.6 (C³H), 114.0 (2 x C¹¹H), 65.5 (C⁷H₂), 58.0 (C¹⁴H₂), 55.8 (C⁶H₂), 55.4 (C¹³H₃), 53.8 (C²H₂), 38.9 (C⁵H).

¹⁹F NMR (377 MHz, CDCl₃) δ -59.2, -62.8.

IR (neat) (cm⁻¹): 2981, 1640, 1599, 1344, 1271, 1166, 1122, 1084, 1053, 833, 671.

(N-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-(trifluoromethyl)phenyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2g)



The title compound was prepared by General procedure E using salt **1g** (289 mg, 0.50 mmol). Purification by FCC (10%-20% EtOAc in pentane) gave *amine 2g* (112 mg, 46%) as a yellow oil.

HRMS (ESI): Exact mass calculated for C₂₂H₁₉F₉NO [M+H]⁺: 484.1317, found: 484.1321

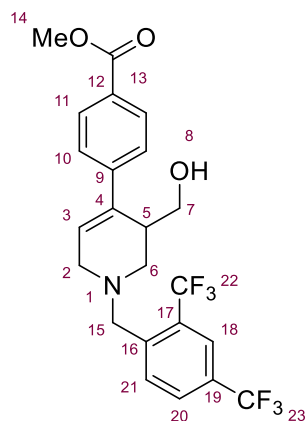
¹H NMR (500 MHz, CDCl₃) δ 7.94 (s, 1H, C¹⁷H), 7.88 (d, *J* = 8.2 Hz, 1H, C²⁰H), 7.84 (dd, *J* = 8.4, 1.9 Hz, 1H, C¹⁹H), 7.59 (d, *J* = 8.2 Hz, 2H, 2 x C¹¹H), 7.47 (d, *J* = 8.1 Hz, 2H, 2 x C¹⁰H), 6.15 (dd, *J* = 4.7, 2.2 Hz, 1H, C³H), 3.96 (s, 1H, OH), 3.87 (s, 2H, C¹⁴H₂), 3.74 (dd, *J* = 10.4, 2.6 Hz, 1H, C⁷H₂), 3.63 (ddd, *J* = 10.4, 4.1, 1.6 Hz, 1H, C⁷H₂), 3.45 (dd, *J* = 17.3, 4.8 Hz, 1H, C²H₂), 3.17 (dt, *J* = 11.2, 1.5 Hz, 1H, C⁶H₂), 3.00 (dt, *J* = 17.2, 2.5 Hz, 1H, C²H₂), 2.89 (brs, 1H, C⁵H), 2.78 (ddd, *J* = 11.1, 3.8, 1.6 Hz, 1H, C⁶H₂).

¹³C NMR (126 MHz, CDCl₃) δ 143.2 (C), 140.9 (C), 135.5 (C), 131.5 (C²⁰H), 130.2 (q, *J* = 33.2 Hz, C¹²/C¹⁶/C¹⁸), 129.8 (q, *J* = 31.3 Hz, C¹²/C¹⁶/C¹⁸), 129.7 (q, *J* = 32.4 Hz, C¹²/C¹⁶/C¹⁸), 129.1 (q, *J* = 3.9 Hz, C¹⁹H), 126.5 (2 x C¹⁰H), 126.2 (C³H), 125.7 (q, *J* = 3.8 Hz, 2 x C¹¹H), 124.3 (q, *J* = 272.0 Hz, C¹³F₃/C²¹F₃/C²²F₃), 123.7 (q, *J* = 274.3 Hz, C¹³F₃/C²¹F₃/C²²F₃), 123.5 (q, *J* = 272.3 Hz, C¹³F₃/C²¹F₃/C²²F₃), 123.5 – 123.4 (m, C¹⁷H), 65.2 (C⁷H₂), 57.9 (C¹⁴H₂), 55.6 (C⁶H₂), 53.7 (C²H₂), 38.9 (C⁵H).

¹⁹F NMR (377 MHz, CDCl₃) δ –59.2, –62.5, –62.9.

IR (neat) (cm⁻¹): 3320, 1346, 1325, 1275, 1166, 1116, 1083, 1069, 1055, 672.

Methyl-4-(1-(2,4-bis(trifluoromethyl)benzyl)-3-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-4-yl)benzoate (2h)



The title compound was prepared by General procedure E using salt **1h** (284 mg, 0.50 mmol). Purification by FCC (10-30% EtOAc in pentane) gave *amine 2h* (148 mg, 62%) as an off-white solid.

m.p. (acetone): 145-147 °C

HRMS (ESI): Exact mass calculated for C₂₃H₂₂F₆NO [M+H]⁺: 474.1498, found:474.1501

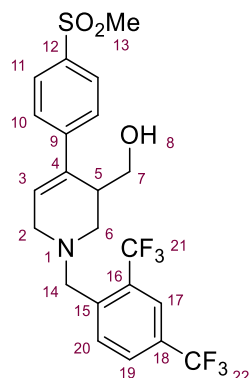
¹H NMR (400 MHz, CDCl₃) δ 8.01 (d, *J* = 8.5 Hz, 2H, 2 x C¹¹H), 7.94 (d, *J* = 1.9 Hz, 1H, C¹⁸H), 7.89 (d, *J* = 8.2 Hz, 1H, C²¹H), 7.83 (dd, *J* = 8.3, 1.8 Hz, 1H, C²⁰H), 7.44 (d, *J* = 8.5 Hz, 2H, 2 x C¹⁰H), 6.19 (dd, *J* = 4.7, 2.3 Hz, 1H, C³H), 3.96 (s, 1H, OH), 3.91 (s, 3H, C¹⁴H₃), 3.87 (s, 2H, C¹⁵H₂), 3.75 (dd, *J* = 10.4, 2.6 Hz, 1H, C⁷H₂), 3.64 (ddd, *J* = 10.4, 4.2, 1.6 Hz, 1H, C⁷H₂), 3.45 (dd, *J* = 17.3, 4.7 Hz, 1H, C²H₂), 3.17 (dt, *J* = 11.2, 1.5 Hz, 1H, C⁶H₂), 2.99 (dt, *J* = 17.3, 2.5 Hz, 1H, C²H₂), 2.92 (s, 1H, C⁵H), 2.78 (ddd, *J* = 11.3, 3.9, 1.5 Hz, 1H, C⁶H₂).

¹³C NMR (126 MHz, CDCl₃) δ 167.0 (C¹³O), 144.1 (C), 141.0 (C), 135.7 (C), 131.5 (C²¹H), 130.2 (q, *J* = 33.5 Hz, C¹⁷/C¹⁹), 130.0 (2 x C¹¹H), 129.8 (q, *J* = 31.0 Hz, C¹⁷/C¹⁹), 129.3 (C), 129.1 (q, *J* = 3.8 Hz, C²⁰H), 126.1 (2 x C¹⁰H + C³H), 123.7 (q, *J* = 274.3 Hz, C²²F₃/C²³F₃), 123.5 (q, *J* = 272.3 Hz, C²²F₃/C²³F₃), 123.5 – 123.2 (m, C¹⁸H), 65.3 (C⁷H₂), 57.9 (q, *J* = 2.0 Hz, C¹⁵H₂), 55.6 (C⁶H₂), 53.8 (C²H₂), 52.3 (C¹⁴H₃), 38.8 (C⁵H).

¹⁹F NMR (376 MHz, CDCl₃) δ –59.2, –62.8.

IR (neat) (cm⁻¹): 3522, 1709, 1630, 1607, 1344, 1283, 1266, 1176, 1170, 1127.

(N-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-(methylsulfonyl)phenyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2i)



The title compound was prepared by General procedure E using salt **1i** (294 mg, 0.50 mmol). Purification by FCC (10%-50% EtOAc in pentane) gave *amine 2i* (136 mg, 55%) as a yellow solid.

m.p. (EtOAc): 95-97 °C

HRMS (ESI): Exact mass calculated for C₂₂H₂₂F₆NOS [M+H]⁺: 494.1195, found: 494.1208

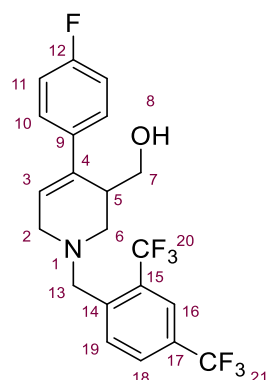
¹H NMR (500 MHz, CDCl₃) δ 7.94 (d, *J* = 1.8 Hz, 1H, C¹⁷H), 7.91 (d, *J* = 8.4 Hz, 2H, 2 x C¹¹H), 7.87 (d, *J* = 8.2 Hz, 1H, C²⁰H), 7.84 (dd, *J* = 8.2, 1.8 Hz, 1H, C¹⁹H), 7.55 (d, *J* = 8.5 Hz, 2H, 2 x C¹⁰H), 6.21 (dd, *J* = 4.8, 2.2 Hz, 1H, C³H), 3.92 (s, 1H, OH), 3.88 (s, 2H, C¹⁴H₂), 3.74 (dd, *J* = 10.4, 2.6 Hz, 1H, C⁷H₂), 3.62 (ddd, *J* = 10.5, 4.3, 1.6 Hz, 1H, C⁷H₂), 3.47 (dd, *J* = 17.4, 4.8 Hz, 1H, C²H₂), 3.18 (dt, *J* = 11.2, 1.5 Hz, 1H, C⁶H₂), 3.06 (s, 3H, C¹³H₃), 3.01 (dt, *J* = 17.5, 2.5 Hz, 1H, C²H₂), 2.90 (s, 1H, C⁵H), 2.78 (ddd, *J* = 11.2, 3.9, 1.5 Hz, 1H, C⁶H₂).

¹³C NMR (126 MHz, CDCl₃) δ 145.2 (C), 140.8 (C), 139.4 (C), 135.2 (C), 131.5 (C²⁰H), 130.3 (q, *J* = 33.6 Hz, C¹⁶/C¹⁸), 129.8 (q, *J* = 31.1 Hz, C¹⁶/C¹⁸), 129.1 (q, *J* = 3.8 Hz, C¹⁹H), 127.9 (2 x C¹¹H), 127.4 (C³H), 127.1 (2 x C¹⁰H), 123.7 (q, *J* = 274.2 Hz, C²¹F₃/C²²F₃), 123.6 – 123.2 (m, C¹⁷H), 123.5 (q, *J* = 272.3 Hz, C²¹F₃/C²²F₃), 65.2 (C⁷H₂), 57.9 (q, *J* = 2.0 Hz, C¹⁴H₂), 55.5 (C⁶H₂), 53.7 (C²H₂), 44.7 (C¹³H₃), 38.9 (C⁵H).

¹⁹F NMR (377 MHz, CDCl₃) δ -59.1, -62.9.

IR (neat) (cm⁻¹): 3326, 2927, 1620, 1346, 1301, 1275, 1171, 1124, 1084, 1055.

(N-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-fluorophenyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2j)



The title compound was prepared by General procedure E using salt **1j** (264 mg, 0.50 mmol). Purification by FCC (5%-20% EtOAc in pentane) gave *amine 2j* (169 mg, 78%) as a yellow oil.

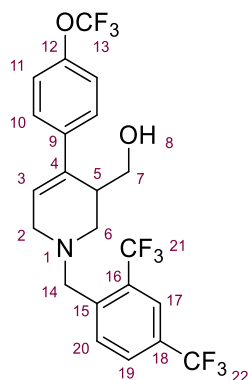
HRMS (ESI): Exact mass calculated for C₂₁H₁₉F₇NO [M+H]⁺: 434.1349, found: 434.1349

¹H NMR (500 MHz, CDCl₃) δ 7.93 (d, *J* = 1.9 Hz, 1H, C¹⁶H), 7.88 (d, *J* = 8.2 Hz, 1H, C¹⁹H), 7.83 (d, *J* = 8.2 Hz, 1H, C¹⁸H), 7.37 – 7.28 (m, 2H, 2 x C¹⁰H), 7.07 – 6.98 (m, 2H, 2 x C¹¹H), 6.02 (dd, *J* = 4.8, 2.2 Hz, 1H, C³H), 4.08 (s, 1H, OH), 3.86 (s, 2H, C¹³H₂), 3.74 (dd, *J* = 10.4, 2.6 Hz, 1H, C⁷H₂), 3.63 (ddd, *J* = 10.4, 4.0, 1.7 Hz, 1H, C⁷H₂), 3.41 (dd, *J* = 17.0, 4.8 Hz, 1H, C²H₂), 3.15 (dt, *J* = 11.2, 1.5 Hz, 1H, C⁶H₂), 2.96 (dt, *J* = 17.0, 2.5 Hz, 1H, C²H₂), 2.83 (s, 1H, C⁵H), 2.77 (ddd, *J* = 11.1, 3.8, 1.6 Hz, 1H, C⁶H₂).

¹³C NMR (126 MHz, CDCl₃) δ 162.5 (d, *J* = 246.5 Hz, C¹²F), 141.0 (C), 135.7 (d, *J* = 3.3 Hz, C⁹), 135.5 (C), 131.5 (C¹⁹H) 130.1 (q, *J* = 33.6 Hz, C¹⁵/C¹⁷), 129.8 (q, *J* = 31.0 Hz, C¹⁵/C¹⁷), 129.1 (q, *J* = 3.7 Hz, C¹⁸H), 127.8 (d, *J* = 8.0 Hz, 2 x C¹⁰H), 124.1 (C³H), 123.7 (q, *J* = 274.2 Hz, C²⁰F₃/C²¹F₃), 123.5 (q, *J* = 272.3 Hz, C²⁰F₃/C²¹F₃), 123.4 (dd, *J* = 6.2, 3.8 Hz, C¹⁶H), 115.5 (d, *J* = 21.3 Hz, 2 x C¹¹H), 65.3 (C⁷H₂), 58.0 (q, *J* = 2.0 Hz, C¹³H₂), 55.7 (C⁶H₂), 53.7 (C²H₂), 39.1 (C⁵H).

IR (neat) (cm⁻¹): 3279, 2922, 1509, 1345, 1275, 1165, 1122, 1083, 1055, 841.

(*N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-(trifluoromethoxy)phenyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2k)



The title compound was prepared by General procedure E using salt **1k** (297 mg, 0.50 mmol). Purification by FCC (5%-20% EtOAc in pentane) gave *amine 2k* (162 mg, 64%) as a yellow oil.

HRMS (ESI): Exact mass calculated for C₂₂H₁₉F₉NO₂ [M+H]⁺: 500.1267, found: 500.1259

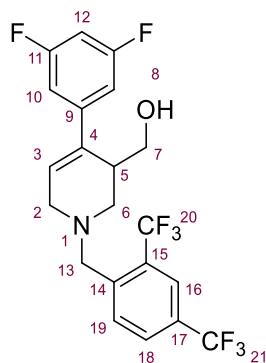
¹H NMR (400 MHz, CDCl₃) δ 7.93 (s, 1H, C¹⁷H), 7.89 (d, *J* = 8.2 Hz, 1H, C²⁰H), 7.83 (dd, *J* = 8.2, 1.8 Hz, 1H, C¹⁹H), 7.38 (d, *J* = 8.8 Hz, 2H, 2 x C¹⁰H), 7.18 (dd, *J* = 8.9, 1.0 Hz, 2H, C¹¹H), 6.10 – 6.04 (m, 1H, C³H), 4.00 (s, 1H, OH), 3.86 (s, 2H, C¹⁴H₂), 3.74 (dd, *J* = 10.4, 2.6 Hz, 1H, C⁷H₂), 3.64 (ddd, *J* = 10.4, 4.1, 1.7 Hz, 1H, C⁷H₂), 3.43 (dd, *J* = 17.1, 4.7 Hz, 1H, C²H₂), 3.16 (dt, *J* = 11.1, 1.5 Hz, 1H, C⁶H₂), 2.97 (dt, *J* = 17.1, 2.4 Hz, 1H, C²H₂), 2.84 (s, 1H, C⁵H), 2.77 (ddd, *J* = 11.1, 3.9, 1.5 Hz, 1H, C⁶H₂).

¹³C NMR (126 MHz, CDCl₃) δ 148.7 (q, *J* = 2.0 Hz, C¹²), 141.0 (C), 138.4 (C), 135.3 (C), 131.5 (C²⁰H), 130.2 (q, *J* = 33.6 Hz, C¹⁶/C¹⁸), 129.8 (q, *J* = 31.1 Hz, C¹⁶/C¹⁸), 129.1 (q, *J* = 3.5 Hz, C¹⁹H), 127.6 (2 x C¹⁰H), 125.0 (C³H), 123.7 (q, *J* = 274.2 Hz, C²¹F₃/C²²F₃), 123.5 (q, *J* = 272.3 Hz, C²¹F₃/C²²F₃), 123.5 – 123.3 (m, C¹⁷H), 121.1 (2 x C¹¹H), 120.6 (q, *J* = 257.1 Hz, C¹³F₃), 65.3 (C⁷H₂), 57.9 (q, *J* = 2.3 Hz, C¹⁴H₂), 55.7, (C⁶H₂), 53.7 (C²H₂), 39.0 (C⁵H).

¹⁹F NMR (377 MHz, CDCl₃) δ -57.9, -59.2, -62.7.

IR (neat) (cm⁻¹): 3245, 2922, 1345, 1275, 1170, 1123, 1083, 1055, 804, 673.

(*N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(3,5-difluorophenyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2l)



The title compound was prepared by General procedure E using salt **1l** (273 mg, 0.50 mmol). Purification by FCC (5%-15% EtOAc in pentane) gave *amine 2l* (132 mg, 59%) as a pale orange oil.

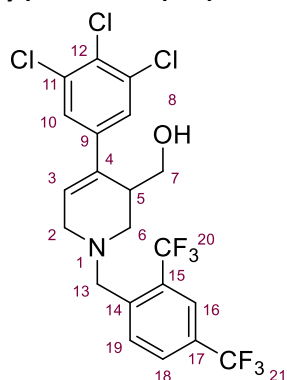
HRMS (ESI): Exact mass calculated for $C_{21}H_{18}F_8NO$ $[M+H]^+$: 452.1255, found: 452.1247

1H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H, $C^{16}H$), 7.91 – 7.79 (m, 2H, $C^{18}H + C^{19}H$), 6.93 – 6.84 (m, 2H, 2 x $C^{10}H$), 6.72 (tt, $J = 8.8, 2.3$ Hz, 1H, $C^{12}H$), 6.13 (dd, $J = 4.8, 2.3$ Hz, 1H, C^3H), 3.86 (s, 2H, $C^{13}H_2$), 3.75 (dd, $J = 10.4, 2.6$ Hz, 1H, C^7H_2), 3.65 (ddd, $J = 10.4, 4.1, 1.7$ Hz, 1H, C^7H_2), 3.43 (dd, $J = 17.3, 4.7$ Hz, 1H, C^2H_2), 3.16 (dt, $J = 10.9, 1.4$ Hz, 1H, C^6H_2), 2.98 (dt, $J = 17.4, 2.4$ Hz, 1H, C^2H_2), 2.83 – 2.70 (m, 2H, $C^6H_2 + C^5H$).
 ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.32 (dd, $J = 247.9, 13.3$ Hz, 2 x $C^{11}F$), 143.1 (t, $J = 9.2$ Hz, C^9), 140.8 (C^{14}), 134.7 (t, $J = 2.5$ Hz, C^4), 131.5 ($C^{19}H$), 130.2 (q, $J = 33.5$ Hz, C^{15}/C^{17}), 129.8 (q, $J = 31.2$ Hz, C^{15}/C^{17}), 129.1 (q, $J = 3.8$ Hz, $C^{18}H$), 126.2 (C^3H), 123.7 (q, $J = 274.2$ Hz, $C^{20}F_3/C^{21}F_3$), 123.5 (q, $J = 272.4$ Hz, $C^{20}F_3/C^{21}F_3$), 123.7 – 123.2 (m, $C^{16}H$), 109.5 – 108.5 (m, 2 x $C^{10}H$), 102.9 (t, $J = 25.4$ Hz, $C^{12}H$), 65.2 (C^7H_2), 57.9 (q, $J = 2.0$ Hz, $C^{13}H_2$), 55.4 (C^6H_2), 53.6 (C^2H_2), 38.8 (C^5H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -59.2, -62.9, -109.9 (t, $J = 8.7$ Hz).

IR (neat) (cm^{-1}): 3264, 2972, 2848, 1345, 1275, 1171, 1118, 1083, 1055, 988.

(N-(2,4-bis(Trifluoromethyl)benzyl)-4-(3,4,5-trichlorophenyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2m)



The title compound was prepared by General procedure E using salt **1m** (287 mg, 0.47 mmol). Purification by FCC (5%-20% EtOAc in pentane) gave the *amine 2m* (124 mg, 51%) as an orange solid.

m.p. (EtOAc): 66-68 °C

HRMS (ESI): Exact mass calculated for $C_{21}H_{17}Cl_3F_6NO$ $[M+H]^+$: 518.0274, found: 518.0274

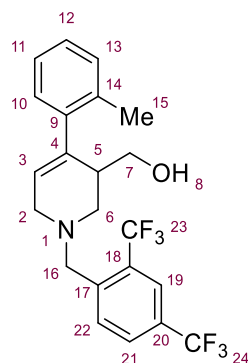
1H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H, $C^{16}H$), 7.89 – 7.79 (m, 2H, $C^{18}H + C^{19}H$), 7.37 (s, 2H, 2 x $C^{10}H$), 6.11 (dd, $J = 4.7, 2.3$ Hz, 1H, C^3H), 3.86 (s, 2H, $C^{16}H_2$), 3.74 (dd, $J = 10.4, 2.4$ Hz, 1H, C^7H_2), 3.62 (ddd, $J = 10.5, 4.0, 1.8$ Hz, 1H, C^7H_2), 3.43 (dd, $J = 17.3, 4.7$ Hz, 1H, C^2H_2), 3.20 – 3.10 (m, 1H, C^6H_2), 2.97 (dt, $J = 17.4, 2.4$ Hz, 1H, C^2H_2), 2.80 – 2.68 (m, 2H, $C^6H_2 + C^5H$).

^{13}C NMR (126 MHz, $CDCl_3$) δ 140.7 (C^{14}), 139.8 (C), 134.5 (2 x C^{11}), 133.9 (C), 131.5 ($C^{19}H$), 130.3 (C), 130.3 (q, $J = 33.6$ Hz, C^{15}/C^{17}), 129.8 (q, $J = 31.2$ Hz, C^{15}/C^{17}), 129.1 (q, $J = 3.8$ Hz, $C^{18}H$), 126.8 (C^3H), 126.5 (2 x $C^{10}H$), 123.7 (d, $J = 274.3$ Hz, $C^{20}F_3/C^{21}F_3$), 123.7 – 123.2 (m, $C^{16}H$), 123.4 (d, $J = 272.3$ Hz, $C^{20}F_3/C^{21}F_3$), 65.1 (C^7H_2), 57.9 (q, $J = 2.4$ Hz, $C^{13}H_2$), 55.4 (C^6H_2), 53.6 (C^2H_2), 38.8 (C^5H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -59.2, -62.9.

IR (neat) (cm^{-1}): 3260, 2981, 1640, 1345, 1269, 1169, 1119, 1084, 1054, 762

(N-(2,4-bis(Trifluoromethyl)benzyl)-4-(o-tolyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2n)



The title compound was prepared by General procedure E using salt **1n** (262 mg, 0.50 mmol). Purification by FCC (5%-20% EtOAc in pentane) gave amine **2n** (144 mg, 67%) as a yellow oil.

HRMS (ESI): Exact mass calculated for $C_{22}H_{22}F_6NO$ $[M+H]^+$: 430.1600, found: 430.1605

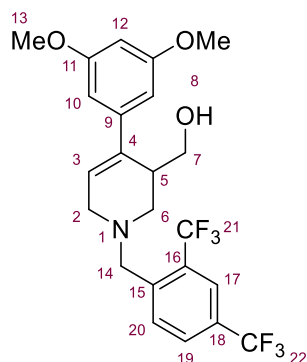
1H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.81 (m, 2H, $C^{19}H$ + $C^{22}H$), 7.77 (dd, J = 8.2, 1.9 Hz, 1H, $C^{21}H$), 7.14 – 7.02 (m, 4H, 4 x ArH), 5.63 – 5.57 (m, 1H, C^3H), 3.80 (s, 2H, $C^{16}H_2$), 3.61 (dd, J = 10.4, 2.7 Hz, 1H, C^7H_2), 3.52 (ddd, J = 10.4, 3.6, 1.8 Hz, 1H, C^7H_2), 3.32 (dd, J = 16.4, 4.5 Hz, 1H, C^2H_2), 3.03 (dt, J = 11.1, 1.6 Hz, 1H, C^6H_2), 2.87 (dt, J = 16.4, 2.4 Hz, 1H, C^2H_2), 2.77 (ddd, J = 11.2, 4.0, 1.6 Hz, 1H, C^6H_2), 2.41 (s, 1H, C^5H), 2.23 (s, 3H, $C^{15}H_3$).

^{13}C NMR (126 MHz, $CDCl_3$) δ 141.1 (C), 141.0 (C), 137.4 (C), 135.8 (C), 131.6 ($C^{22}H$), 130.3 (ArCH), 130.1 (q, J = 33.5 Hz, C^{18}/C^{20}), 129.8 (q, J = 31.1 Hz, C^{18}/C^{20}), 129.1 ($C^{21}H$), 129.1 (ArCH), 127.3 (ArCH), 125.7 (ArCH), 125.3 (C^3H), 123.7 (q, J = 274.2 Hz, $C^{23}F_3/C^{24}F_3$), 123.5 (q, J = 272.3 Hz, $C^{23}F_3/C^{24}F_3$), 123.4 – 123.2 (m, $C^{19}H$), 65.0 (C^7H_2), 58.1 (q, J = 2.4 Hz, $C^{16}H_2$), 55.9 (C^6H_2), 53.3 (C^2H_2), 41.4 (C^5H), 19.8 ($C^{15}H_3$).

^{19}F NMR (377 MHz, $CDCl_3$) δ -59.1, -62.9.

IR (neat) (cm^{-1}): 3658, 2980, 2973, 1345, 1274, 1169, 1123, 1083, 1055, 760.

(N-(2,4-bis(Trifluoromethyl)benzyl)-4-(3,5-dimethoxyphenyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2o)



The title compound was prepared by General procedure E using salt **1o** (285 mg, 0.50 mmol). Purification by FCC (10%-30% EtOAc in pentane) gave the *amine* **2o** (186 mg, 78%) as a viscous red oil.

HRMS (ESI): Exact mass calculated for $C_{23}H_{24}F_6NO_3$ $[M+H]^+$: 476.1655, found: 476.1653

1H NMR (500 MHz, $CDCl_3$) δ 7.93 (s, 1H, $C^{17}H$), 7.89 (d, J = 8.2 Hz, 1H, $C^{19}H$), 7.83 (dd, J = 8.2, 1.9 Hz, 1H, $C^{20}H$), 6.50 (d, J = 2.2 Hz, 2H, 2 x $C^{10}H$), 6.40 (t, J = 2.2 Hz, 1H, $C^{12}H$), 6.07 (dd, J = 4.8, 2.2 Hz, 1H, C^3H), 4.07 (s, 1H, OH), 3.85 (s, 2H, $C^{14}H_2$), 3.79 (s, 6H, 2 x $C^{13}H_3$), 3.74 (dd, J = 10.3, 2.7 Hz, 1H, C^7H_2), 3.67 (ddd, J = 10.3, 4.0, 1.5 Hz, 1H, C^7H_2), 3.41 (dd, J = 17.1, 4.6 Hz, 1H, C^2H_2), 3.14 (dt, J = 11.1, 1.5 Hz, 1H, C^6H_2), 2.96 (dt, J = 17.0, 2.5 Hz, 1H, C^2H_2), 2.82 (brs, 1H, C^5H), 2.76 (ddd, J = 11.1, 3.9, 1.5 Hz, 1H, C^6H_2).

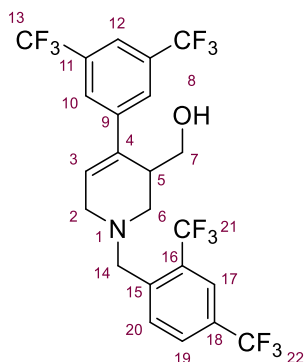
^{13}C NMR (126 MHz, $CDCl_3$) δ 161.0 (2 x C^{11}), 142.0 (C), 141.1 (C), 136.5 (C), 131.5 ($C^{19}H$), 130.1 (q, J = 33.4 Hz, C^{16}/C^{18}), 129.7 (q, J = 31.2 Hz, C^{16}/C^{18}), 129.1 (q, J = 3.9 Hz, $C^{20}H$), 124.4 (C^3H), 123.7 (q, J =

274.1 Hz, C²¹F₃/C²²F₃), 123.5 (q, *J* = 272.4 Hz, C²¹F₃/C²²F₃), 123.5 – 123.2 (m, C¹⁷H), 104.7 (2 x C¹⁰H), 99.5 (C¹²H), 65.5 (C⁷H₂), 58.0 (C¹⁴H₂), 55.7 (C⁶H₂), 55.5 (2 x C¹³H₃), 53.7 (C²H₂), 39.1 (C⁵H).

¹⁹F NMR (377 MHz, CDCl₃) δ –59.2, –62.9.

IR (neat) (cm⁻¹): 3298, 2937, 1592, 1345, 1275, 1155, 1121, 1083, 1055, 842.

(*N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(3,5-bis(trifluoromethyl)phenyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2p)



The title compound was prepared by General procedure E using salt **1p** (323 mg, 0.50 mmol). Purification by FCC (0%-20% EtOAc in pentane) gave *amine 2p* (107 mg, 39%) as an orange oil.

HRMS (ESI): Exact mass calculated for C₂₃H₁₈F₁₂NO [M+H]⁺: 552.1191, found 552.1186

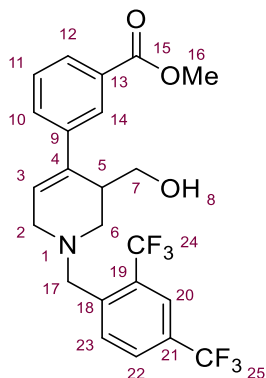
¹H NMR (500 MHz, CDCl₃) δ 7.95 (s, 1H, C¹⁷H), 7.89 – 7.83 (m, 2H, C¹⁹H + C²⁰H), 7.79 (s, 3H, 2 x C¹⁰H + C¹²H), 6.21 (dd, *J* = 4.8, 2.2 Hz, 1H, C³H), 3.89 (s, 2H, C¹⁴H₂), 3.76 (dd, *J* = 10.6, 2.6 Hz, 1H, C⁷H₂), 3.61 (ddd, *J* = 10.6, 4.3, 1.7 Hz, 1H, C⁷H₂), 3.47 (dd, *J* = 17.4, 4.7 Hz, 1H, C²H₂), 3.20 (dt, *J* = 11.2, 1.5 Hz, 1H, C⁶H₂), 3.01 (dt, *J* = 17.4, 2.5 Hz, 1H, C²H₂), 2.90 (s, 1H, C⁵H), 2.80 (ddd, *J* = 11.3, 3.8, 1.6 Hz, 1H, C⁶H₂).

¹³C NMR (126 MHz, CDCl₃) δ 141.9 (C⁹), 140.7 (C¹⁵), 134.5 (C⁴), 132.1 (q, *J* = 33.1 Hz, 2 x C¹¹), 131.5 (C²⁰H), 130.3 (q, *J* = 33.5 Hz, C¹⁶/C¹⁸), 129.9 (q, *J* = 31.3 Hz, C¹⁶/C¹⁸), 129.1 (q, *J* = 3.7 Hz, C¹⁹H), 127.8 (C³H), 126.4 (2 x C¹⁰H), 123.7 (q, *J* = 274.1 Hz, C²¹F₃/C²²F₃), 123.7 – 123.2 (m, C¹⁷H), 123.4 (q, *J* = 272.8 Hz, 2 x C¹³F₃ + C²¹F₃/C²²F₃), 121.6 – 121.2 (m, C¹²H), 65.0 (C⁷H₂), 57.9 (d, *J* = 2.0 Hz, C¹⁴H₂), 55.5 (C⁶H₂), 53.6 (C²H₂), 38.9 (C⁵H).

¹⁹F NMR (377 MHz, CDCl₃) δ –59.2, –62.85, –62.87.

IR (neat) (cm⁻¹): 3659, 2980, 2972, 2889, 1382, 1275, 1164, 1125, 1083, 965, 954.

Methyl-3-(1-(2,4-bis(Trifluoromethyl)benzyl)-3-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-4-yl)benzoate (2q)



The title compound was prepared by General procedure E using salt **1q** (284 mg, 0.50 mmol). Purification by FCC (10-30% EtOAc in pentane) gave *amine 2q* (184 mg, 78%) as a yellow oil.

HRMS (ESI): Exact mass calculated for C₂₃H₂₂F₆NO [M+H]⁺: 474.1498, found:474.1503

¹H NMR (400 MHz, CDCl₃) δ 8.04 (t, *J* = 1.8 Hz, 1H, C¹⁴H), 7.95 (dt, *J* = 9.5, 1.5 Hz, 2H, C¹²H + C²⁰H), 7.89 (d, *J* = 8.2 Hz, 1H, C²³H), 7.83 (dd, *J* = 8.3, 1.9 Hz, 1H, C²²H), 7.56 (ddd, *J* = 7.8, 1.9, 1.2 Hz, 1H, C¹⁰H), 7.41 (t, *J* = 7.8 Hz, 1H, C¹¹H), 6.14 (dd, *J* = 4.7, 2.2 Hz, 1H, C³H), 4.03 (s, 1H, OH), 3.92 (s, 3H, C¹⁶H₃), 3.87

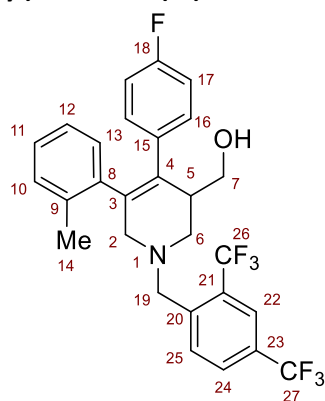
(s, 2H, C¹⁷H₂), 3.75 (dd, *J* = 10.4, 2.6 Hz, 1H, C⁷H₂), 3.63 (ddd, *J* = 10.4, 4.0, 1.6 Hz, 1H, C⁷H₂), 3.44 (dd, *J* = 17.0, 4.7 Hz, 1H, C²H₂), 3.17 (dt, *J* = 11.2, 1.5 Hz, 1H, C⁶H₂), 2.98 (dt, *J* = 16.9, 2.4 Hz, 1H, C²H₂), 2.93 (s, 1H, C⁵H), 2.79 (ddd, *J* = 11.1, 3.8, 1.5 Hz, 1H, C⁶H₂).

¹³C NMR (126 MHz, CDCl₃) δ 167.2 (C¹⁵O), 141.0 (C), 140.0 (C), 135.7 (C), 131.5 (C²³H), 130.8 (C¹⁰H), 130.6 (C), 130.1 (q, *J* = 33.5 Hz, C¹⁹/C²¹), 129.8 (q, *J* = 31.0 Hz, C¹⁹/C²¹), 129.1 (q, *J* = 3.7 Hz, C²²H), 128.82 (C¹¹H/C¹²H), 128.76 (C¹¹H/C¹²H), 127.3 (C¹⁴H), 125.2 (C³H), 123.7 (d, *J* = 274.2 Hz, C²⁴F₃/C²⁵F₃), 123.5 (d, *J* = 272.3 Hz, C²⁴F₃/C²⁵F₃), 123.5 – 123.3 (m, C²⁰H), 65.3 (C⁷H₂), 58.0 (d, *J* = 2.3 Hz, C¹⁷H₂), 55.7 (C⁶H₂), 53.7 (C²H₂), 52.3 (C¹⁶H₃), 38.9 (C⁵H).

¹⁹F NMR (376 MHz, CDCl₃) δ -59.2, -62.8.

IR (neat) (cm⁻¹): 3302, 2954, 1722, 1345, 1275, 1170, 1122, 1083, 1054, 757.

(*N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-fluorophenyl)-5-(*o*-tolyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2r**)**



The title compound was prepared by General procedure E using salt **1r** (309 mg, 0.50 mmol). Purification by FCC (20% EtOAc in pentane) gave *amine 2r* (145 mg, 55%) as a yellow oil.

HRMS (ESI): Exact mass calculated for C₂₈H₂₄F₇NO [M+H]⁺: 524.1819, found: 524.1818

¹H NMR (500 MHz, DMSO) δ 8.19 (t, *J* = 8.5 Hz, 1H, C²⁵H), 8.11 (dd, *J* = 8.1, 2.2 Hz, 1H, C²⁴H), 8.00 (d, *J* = 2.0 Hz, 1H, C²²H), 7.23 – 6.57 (m, 9H, 9 x ArCH), 4.55 – 4.46 (m, 1H, OH), 3.04 – 3.80 (m, 2H, C¹⁹H₂), 3.62 – 3.50 (m, 1H, C⁷H₂), 3.38 (d, *J* = 16.8 Hz, 1H, C²H₂), 3.29 – 3.08 (m, 2H, C⁶H₂ + C⁷H₂), 2.93 – 2.66 (m, 2H, C²H₂ + C⁵H), 2.62 (td, *J* = 11.2, 3.9 Hz, 1H, C⁶H₂), 2.24 (s, 1H, C¹⁴H₃), 1.89 (s, 2H, C¹⁴H₃).

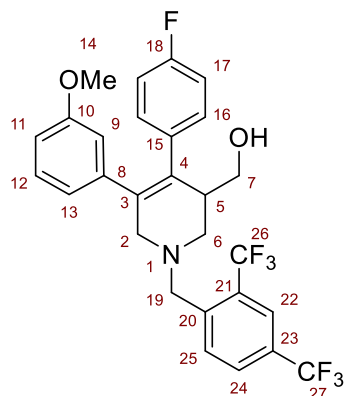
¹³C NMR (126 MHz, DMSO) δ 160.6 (d, *J* = 243.3 Hz, C¹⁸), 160.5 (d, *J* = 243.0 Hz, C¹⁸), 142.9 (C²⁰), 139.5 (C), 139.2 (C), 136.9 (d, *J* = 3.1 Hz, C¹⁵), 136.8 (d, *J* = 3.2 Hz, C¹⁵), 134.4 (C), 134.0 (C), 133.2 (C), 132.7 (C), 131.8 (q, *J* = 2.8 Hz, C²⁵H), 130.4 (d, *J* = 7.9 Hz, 2 x C¹⁶H), 2 x 129.9 (ArCH), 2 x 129.7 (ArCH), 129.6 – 129.3 (m, C²⁴H), 129.2 (C), 128.1 (q, *J* = 32.1 Hz, C²¹/C²³), 128.0 (q, *J* = 33.2 Hz, C²¹/C²³), 2 x 126.9 (ArCH), 125.6 (ArCH), 125.4 (ArCH), 123.6 (q, *J* = 274.3 Hz, C²⁶F₃/C²⁷F₃), 123.5 (q, *J* = 272.3 Hz, C²⁶F₃/C²⁷F₃), 122.8 – 122.6 (m, C²²H), 114.5 (d, *J* = 21.1 Hz, 2 x C¹⁷H), 114.4 (d, *J* = 21.0 Hz, 2 x C¹⁷H), 79.2 (C), 61.4 (C⁷H₂), 61.3 (C⁷H₂), 58.3 (C²H₂), 57.4 (C²H₂), 56.9 (C¹⁹H₂), 56.8 (C¹⁹H₂), 51.7 (C⁶H₂), 51.4 (C⁶H₂), 2 x 43.7 (C⁵H), 19.8 (C¹⁴H₃), 18.9 (C¹⁴H₃).

Due to presence of rotamers that could not be resolved using VT NMR, doubling of majority of the peaks is observed in the ¹³C NMR.

¹⁹F NMR (377 MHz, DMSO) δ -63.9, -67.6.

IR (neat) (cm⁻¹): 3403, 3063, 2849, 1345, 1275, 1171, 1124, 1054, 835, 757.

(*N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-fluorophenyl)-5-(3-methoxyphenyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2s)



The title compound was prepared by General procedure E using salt **1s** (317 mg, 0.50 mmol). Purification by FCC (10–30% EtOAc in pentane) gave *amine 2s* (117 mg, 44%) as a yellow oil.

HRMS (ESI): Exact mass calculated for C₂₈H₂₅F₇NO₂ [M+H]⁺: 540.1768, found: 540.1766

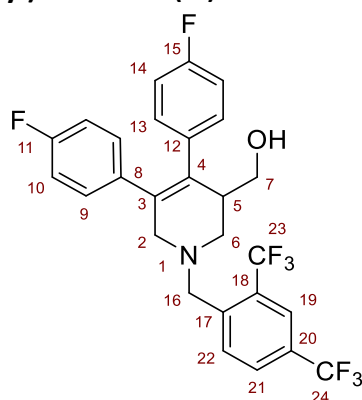
¹H NMR (400 MHz, CDCl₃) δ 7.95 (m, 2H, C²²H + C²⁴H), 7.87 (d, *J* = 8.6 Hz, 1H, C²⁵H), 7.09 – 6.97 (m, 3H, C¹²H + 2 x C¹⁶H), 6.91 – 6.79 (m, 2H, 2 x C¹⁷H), 6.65 (ddd, *J* = 8.3, 2.6, 1.0 Hz, 1H, C¹¹H), 6.58 (ddd, *J* = 7.6, 1.6, 1.0 Hz, 1H, C¹³H), 6.50 (dd, *J* = 2.6, 1.6 Hz, 1H, C⁹H), 4.16 (s, 1H, OH), 3.97 – 3.84 (m, 2H, C¹⁹H₂), 3.72 (d, *J* = 16.6 Hz, 1H, C²H₂), 3.67 (dd, *J* = 10.4, 2.6 Hz, 1H, C⁷H₂), 3.61 (s, 3H, C¹⁴H₃), 3.57 (ddd, *J* = 10.4, 3.9, 1.6 Hz, 1H, C⁷H₂), 3.18 (dt, *J* = 11.2, 1.5 Hz, 1H, C⁶H₂), 3.00 (dd, *J* = 16.6, 2.4 Hz, 1H, C²H₂), 2.91 – 2.83 (m, 1H, C⁶H₂), 2.74 (brs, 1H, C⁵H).

¹³C NMR (126 MHz, CDCl₃) δ 161.7 (d, *J* = 245.7 Hz, C¹⁸), 159.3 (C¹⁰), 141.0 (C⁸), 140.9 (C²⁰), 136.3 (d, *J* = 3.3 Hz, C¹⁵), 136.0 (C⁴), 133.1 (C³), 131.4 (C¹⁴H), 131.0 (d, *J* = 7.8 Hz, 2 x C¹⁶H), 130.2 (q, *J* = 33.5 Hz, C²¹/C²³), 129.8 (q, *J* = 31.0 Hz, C²¹/C²³), 129.1 (C¹¹H + C²⁵H), 123.7 (q, *J* = 274.2 Hz, C²⁶F₃/C²⁷F₃), 123.7 – 123.3 (m, C²²H), 123.5 (q, *J* = 272.3 Hz, C²⁶F₃/C²⁷F₃), 121.9 (C¹¹H), 115.3 (C⁹H), 115.1 (d, *J* = 21.4 Hz, 2 x C¹⁷H), 112.6 (C¹³H), 65.2 (C⁷H₂), 58.3 (C²H₂), 58.0 (q, *J* = 2.2 Hz, C¹⁹H₂), 55.7 (C⁶H₂), 55.2 (C¹⁴H₃), 42.6 (C⁵H).

¹⁹F NMR (377 MHz, CDCl₃) δ –59.2, –62.8, –114.7 – –116.1 (m).

IR (neat) (cm^{–1}): 3372, 2921, 1601, 1508, 1345, 1275, 1169, 1124, 1083, 1053.

(*N*-(2,4-bis(Trifluoromethyl)benzyl)-4,5-bis(4-fluorophenyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2t)



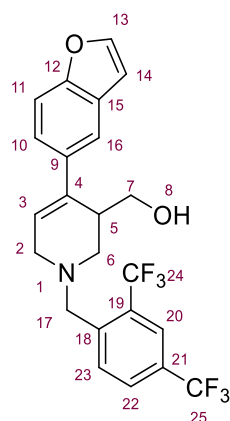
The title compound was prepared by General procedure E using salt **1t** (155 mg, 0.25 mmol). Purification by FCC (10–20% EtOAc in pentane) gave *amine 2t* (49 mg, 37%) as a yellow oil.

HRMS (ESI): Exact mass calculated for C₂₇H₂₂F₈NO [M+H]⁺: 528.1568, found: 528.1564

¹H NMR (400 MHz, CDCl₃) δ 7.98 – 7.91 (m, 2H, C¹⁹H + C²²H), 7.88 (d, *J* = 8.9 Hz, 1H, C²¹H), 7.03 – 6.96 (m, 2H, 2 x C⁹H/C¹³H), 6.97 – 6.91 (m, 2H, 2 x C⁹H/C¹³H), 6.88 – 6.83 (m, 2H, 2 x C¹⁰H/C¹⁴H), 6.83 – 6.76 (m, 2H, 2 x C¹⁰H/C¹⁴H), 4.12 (d, *J* = 5.2 Hz, 1H, OH), 3.97 – 3.84 (m, 2H, C¹⁶H₂), 3.69 (d, *J* = 14.5 Hz, 1H,

IR (neat) (cm⁻¹): 3375, 2923, 1508, 1346, 1275, 1159, 1124, 1054, 833, 674

(4-(Benzofuran-5-yl)-N-(2,4-bis(trifluoromethyl)benzyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2v)



The title compound was prepared by General procedure E using salt **1v** (258 mg, 0.47 mmol). Purification by FCC (20% EtOAc in pentane) gave *amine 2v* (49%) as an orange oil.

HRMS (ESI): Exact mass calculated for C₂₃H₂₀F₆NO₂ [M+H]⁺: 456.1393, found: 456.1387

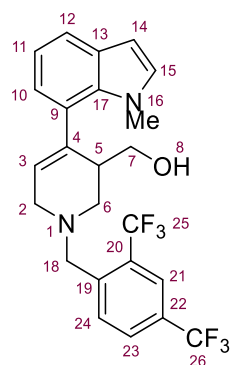
¹H NMR (400 MHz, CDCl₃) δ 7.94 (s, 1H, C²⁰H), 7.91 (d, *J* = 8.1 Hz, 1H, C²³H), 7.84 (dd, *J* = 8.2, 1.9 Hz, 1H, C²²H), 7.62 (d, *J* = 2.2 Hz, 1H, C¹³H), 7.58 (d, *J* = 1.8 Hz, 1H, C¹⁶H), 7.46 (dt, *J* = 8.6, 0.8 Hz, 1H, C¹¹H), 7.31 (dd, *J* = 8.6, 1.9 Hz, 1H, C¹⁰H), 6.74 (dd, *J* = 2.2, 1.0 Hz, 1H, C¹⁴H), 6.05 (dd, *J* = 4.7, 2.2 Hz, 1H, C³H), 4.14 (s, 1H, OH), 3.88 (s, 2H, C¹⁷H₂), 3.75 (dd, *J* = 10.3, 2.7 Hz, 1H, C⁷H₂), 3.66 (ddd, *J* = 10.3, 3.9, 1.6 Hz, 1H, C⁷H₂), 3.44 (dd, *J* = 16.7, 4.7 Hz, 1H, C²H₂), 3.18 (dt, *J* = 11.2, 1.6 Hz, 1H, C⁶H₂), 2.99 (dt, *J* = 16.8, 2.4 Hz, 1H, C²H₂), 2.93 (brs, 1H, C⁵H), 2.82 (ddd, *J* = 11.1, 3.9, 1.6 Hz, 1H, C⁶H₂).

¹³C NMR (101 MHz, CDCl₃) δ 154.7 (C¹²), 145.6 (C¹³H), 141.2 (C¹⁸), 136.7 (C), 135.0 (C), 131.5 (C²³H), 130.0 (d, *J* = 33.0 Hz, C¹⁹/C²¹), 129.4 (d, *J* = 31.2 Hz, C¹⁹/C²¹), 129.1 – 128.9 (m, C²²H), 127.8 (C¹⁵), 123.9 (C³H), 123.7 (d, *J* = 274.1 Hz, C²⁴F₃/C²⁵F₃), 123.5 (q, *J* = 272.4 Hz, C²⁴F₃/C²⁵F₃), 123.5 – 123.2 (m, C²⁰H), 123.0 (C¹⁰H), 118.9 (C¹⁶H), 111.4 (C¹¹H), 106.8 (C¹⁴H), 65.4 (C⁷H₂), 58.0 (d, *J* = 2.1 Hz, C¹⁷H₂), 55.8 (C⁶H₂), 53.8, (C²H₂), 39.7 (C⁵H).

¹⁹F NMR (377 MHz, CDCl₃) δ –59.2, –62.8.

IR (neat) (cm⁻¹): 3325, 2923, 1630, 1345, 1274, 1170, 1122, 1083, 1055, 672.

(N-(2,4-bis(Trifluoromethyl)benzyl)-4-(1-methyl-1H-indol-7-yl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2w)



The title compound was prepared by General procedure E using salt **1w** (141 mg, 0.25 mmol). Purification by FCC (5%-30% EtOAc in pentane) gave the *amine 2w* (78 mg, 67%) as a pale yellow solid.

m.p. (EtOAc): 90-92°C

HRMS (ESI): Exact mass calculated for C₂₄H₂₃F₆N₂O [M+H]⁺: 469.1709, found: 469.1706

¹H NMR (500 MHz, DMSO) δ 8.15 (d, *J* = 8.2 Hz, 1H, C²⁴H), 8.06 (d, *J* = 8.3 Hz, 1H, C²³H), 7.97 (s, 1H, C²¹H), 7.45 (dd, *J* = 7.9, 1.2 Hz, 1H, C¹²H), 7.19 (d, *J* = 3.2 Hz, 1H, C¹⁵H), 6.97 (t, *J* = 7.5 Hz, 1H, C¹¹H), 6.81 (d, *J* = 7.2 Hz, 1H, C¹⁰H), 6.44 (d, *J* = 3.2 Hz, 1H, C¹⁴H), 5.70 (t, *J* = 3.4 Hz, 1H, C³H), 4.12 (t, *J* = 5.1 Hz, 1H,

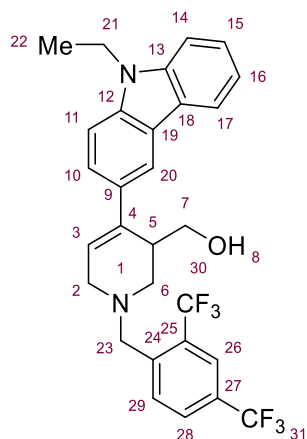
OH), 3.91 (s, 2H, C¹⁸H₂), 3.82 (s, 3H, C¹⁶H₃), 3.54 (td, *J* = 9.6, 5.6 Hz, 1H, C⁷H₂), 3.41 – 3.28 (m, 2H, C⁷H₂ + C²H₂), 3.08 (m, 1H, C²H) 3.03 (dd, *J* = 11.1, 3.7 Hz, 1H, C⁶H₂), 2.74 (dd, *J* = 11.2, 4.1 Hz, 1H, C⁶H₂), 2.65 (s, 1H, C⁵H). C²H at 3.08 hidden underneath the water peak, proven by 2D NMR (COSY)

¹³C NMR (126 MHz, DMSO) δ 142.5 (C¹⁹), 135.2 (C), 133.2 (C), 131.7 (C²⁴H), 130.9 (C¹⁰H), 129.4 (C), 128.8 (q, *J* = 4.6 Hz, C²³H), 128.0 (q, *J* = 30.7 Hz C²⁰ + C²²), 126.1 (C³H), 125.6 (C), 123.1 (q, *J* = 272.9 Hz, C²⁵F₃/C²⁶F₃), 122.2 (m, C¹⁵H + C²¹H), 119.0 (C¹²H), 118.1 (C¹¹H), 100.4 (C¹⁴H), 61.2 (C⁷H₂), 57.0 (C¹⁸H₂), 52.3 (C²H₂), 51.7 (C⁶H₂), 44.1 (C⁵H), 35.4 (C¹⁶H₃). 1 of C²⁵F₃/C²⁶F₃ not observed

¹⁹F NMR (471 MHz, DMSO) δ –58.3, –61.4.

IR (neat) (cm⁻¹): 3056, 2882, 1630, 1345, 1301, 1275, 1171, 1122, 1083, 1053, 796.

(*N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(9-ethyl-9H-carbazol-3-yl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (**2x**)



The title compound was prepared by General procedure E using salt **1x** (313 mg, 0.50 mmol). Purification by FCC (10%-50% EtOAc in pentane) gave *amine 2x* (147 mg, 52%) as an orange solid

m.p. (EtOAc): 107-109°C

HRMS (ESI): Exact mass calculated for C₂₉H₂₇F₆N₂O [M+H]⁺: 533.2022, found:533.2015

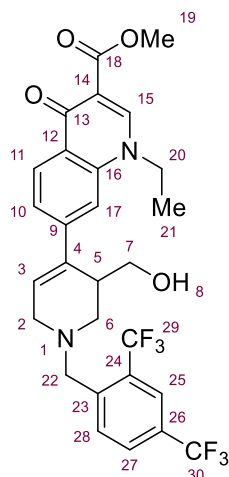
¹H NMR (500 MHz, CDCl₃) δ 8.12 – 8.04 (m, 2H, C¹⁷H + C²⁰H), 7.97 – 7.91 (m, 2H, C²⁶H + C²⁹H), 7.85 (dd, *J* = 8.2, 2.3 Hz, 1H, C²⁸H), 7.53 – 7.44 (m, 2H, C¹¹H + C¹⁴H), 7.43 – 7.35 (m, 2H, C¹⁰H + C¹⁵H), 7.23 (ddd, *J* = 7.9, 7.1, 1.0 Hz, 1H, C¹⁶H), 6.11 (dd, *J* = 4.8, 1.9 Hz, 1H, C³H), 4.37 (q, *J* = 7.2 Hz, 2H, C²¹H₂), 3.90 (s, 2H, C²³H₂), 3.80 (dd, *J* = 10.3, 2.6 Hz, 1H, C⁷H₂), 3.73 (ddd, *J* = 10.3, 3.9, 1.6 Hz, 1H, C⁷H₂), 3.52 – 3.44 (m, 1H, C²H₂), 3.25 – 3.19 (m, 1H, C⁶H₂), 3.12 – 2.98 (m, 2H, C²H₂ + C⁵H), 2.87 (ddd, *J* = 11.1, 3.8, 1.5 Hz, 1H, C⁶H₂), 1.44 (t, *J* = 7.2 Hz, 3H, C²²H₃).

¹³C NMR (126 MHz, CDCl₃) δ 141.3 (C²⁴), 140.5 (C¹²), 139.7 (C), 137.1 (C), 131.5 (C²⁹H), 130.8 (C), 130.0 (q, *J* = 33.5 Hz, C²⁵/C²⁷), 129.7 (q, *J* = 31.1 Hz, C²⁵/C²⁷), 129.1 (q, *J* = 3.8 Hz, C²⁸H), 125.9 (C¹¹H), 124.3 (C¹⁴H), 123.7 (q, *J* = 274.2 Hz, C³⁰F₃/C³¹F₃), 123.5 (q, *J* = 272.3 Hz, C³⁰F₃/C³¹F₃), 123.5 – 123.2 (m, C²⁶H), 123.2 (C), 123.1 (C), 122.8 (C³H), 120.6 (C¹⁷H), 119.0 (C¹⁶H), 118.1 (C²⁰H), 108.7 (C¹⁰H/C¹⁵H), 108.5 (C¹⁰H/C¹⁵H), 65.7 (C⁷H₂), 58.1 (q, *J* = 2.4 Hz, C²³H₂), 56.0 (C⁶H₂), 54.0 (C²H₂), 39.5 (C⁵H), 37.8 (C²¹H₂), 14.0 (C²²H₃).

¹⁹F NMR (377 MHz, CDCl₃) δ –59.2, –62.8.

IR (neat) (cm⁻¹): 3353, 2971, 2885, 1634, 1379, 1160, 1130, 1108, 951, 817.

Methyl 7-(*N*-(2,4-bis(Trifluoromethyl)benzyl)-3-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-4-yl)-1-ethyl-4-oxo-1,4-dihydroquinoline-3-carboxylate (2y)



The title compound was prepared by General procedure E using salt **1y** (169 mg, 0.25 mmol). Purification by FCC (2% MeOH in CH₂Cl₂) gave *amine 2y* (33 mg, 23%) as a pale brown solid.

m.p. (CH₂Cl₂): 129-131 °C

HRMS (ESI): Exact mass calculated for C₂₈H₂₇F₆N₂O₄ [M+H]⁺: 569.1870, found: 569.1870

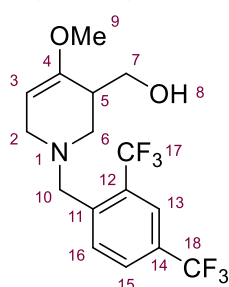
¹H NMR (500 MHz, CDCl₃) δ 8.53 (s, 1H, C¹⁸H), 8.48 (d, *J* = 8.3 Hz, 1H, C¹¹H), 7.94 (d, *J* = 1.8 Hz, 1H, C²⁵H), 7.90 (d, *J* = 8.5 Hz, 1H, C²⁸H), 7.84 (dd, *J* = 8.2, 1.9 Hz, 1H, C²⁷H), 7.42 (d, *J* = 9.3 Hz, 2H, C¹⁰H + C¹⁷H), 6.18 (dd, *J* = 4.9, 2.2 Hz, 1H, C³H), 4.33 – 4.24 (m, 2H, C²⁰H₂), 3.93 (s, 3H, C¹⁹H₃), 3.90 (s, 2H, 22H₂), 3.76 (dd, *J* = 10.5, 2.6 Hz, 1H, C⁷H₂), 3.63 (ddd, *J* = 10.4, 4.4, 1.4 Hz, 1H, C⁷H₂), 3.48 (dd, *J* = 17.4, 4.8 Hz, 1H, C²H₂), 3.21 (d, *J* = 11.2 Hz, 1H, C⁶H₂), 3.03 (d, *J* = 17.3 Hz, 1H, C²H₂), 2.95 (s, 1H, C⁵H), 2.86 – 2.80 (m, 1H, C⁶H₂), 1.55 (t, *J* = 7.2 Hz, 3H, C²¹H₃).

¹³C NMR (126 MHz, CDCl₃) δ 174.2 (C¹³), 166.8 (C¹⁸), 149.2 (C⁹H), 144.7 (C¹⁵), 140.8 (C²³), 139.1 (C¹⁶), 136.1 (C⁴), 131.6 (C²⁸H), 130.2 (q, *J* = 33.6 Hz, C²⁴/C²⁶), 129.8 (q, *J* = 31.1 Hz, C²⁴/C²⁶), 129.1 (q, *J* = 3.7 Hz, C²⁷H), 128.5 (C¹¹H), 127.0 (C³H + C¹²), 123.7 (q, *J* = 274.2 Hz, C²⁹F₃/C³⁰F₃), 123.6 – 123.4 (m, C²⁵H), 123.4 (q, *J* = 272.5 Hz, C²⁹F₃/C³⁰F₃), 123.3 (C¹⁰H), 113.4 (C¹⁷H), 111.0 (C¹⁴), 65.1 (C⁷H₂), 57.9 (C²²H₂), 55.4 (C⁶H₂), 53.7 (C²H₂), 52.3 (C¹⁹H₃), 49.0 (C²⁰H₂), 39.3 (C⁵H), 14.7 (C²¹H₃).

¹⁹F NMR (377 MHz, CDCl₃) δ –59.2, –62.9.

IR (neat) (cm⁻¹): 3373, 2360, 1721, 1614, 1468, 1346, 1276, 1165, 1129, 756.

***N*-(2,4-bis(Trifluoromethyl)benzyl)-4-methoxy-1,2,3,6-tetrahydropyridin-3-yl)methanol (2z)**



N-(2,4-bis(Trifluoromethyl)benzyl)-4-methoxypyridinium iodide **1z** (116 mg, 0.25 mmol, 1.00 equiv.), paraformaldehyde (450 mg, 60.0 equiv.), and [RhCp*Cl₂]₂ (3.1 mg, 2 mol%) was added to a microwave vial. MeOH (0.83 mL, 0.2 M) and Mg(OMe)₂ (0.42 mL, 1.5 equiv, 0.89M in MeOH) was added and the solution heated at 45 °C for 16 hours. The solution concentrated under reduce pressure and re-dissolved in CH₂Cl₂ (30 mL), brine (50 mL) and water (50 mL). The solution was separated, and the aqueous layer was extracted with CH₂Cl₂ (2 x 30 mL). The organic layers were combined, dried

(MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by FCC (5%-30% EtOAc in Pentane) to furnish the *amine 2z* (46 mg, 50%) as a yellow oil.

HRMS (ESI): Exact mass calculated for C₁₆H₁₈F₆NO₂ [M+H]⁺: 370.1236, found: 340.1240.

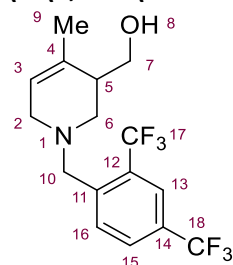
¹H NMR (400 MHz, CDCl₃) δ 7.90 (s, 1H, C¹³H), 7.88 (d, *J* = 8.1 Hz, 1H, C¹⁶H), 7.80 (dd, *J* = 8.2, 2.4 Hz, 1H, C¹⁵H), 4.72 (dd, *J* = 4.6, 2.4 Hz, 1H, C³H), 3.92 (s, 1H, OH), 3.85 (ddd, *J* = 10.2, 3.8, 1.3 Hz, 1H, C⁷H₂), 3.80 (s, 2H, C¹⁰H₂), 3.75 (dd, *J* = 10.2, 3.6 Hz, 1H, C⁷H₂), 3.56 (s, 3H, C⁹H₃), 3.24 (ddt, *J* = 14.5, 4.6, 1.3 Hz, 1H, C²H₂), 2.93 – 2.84 (m, 2H, C²H₂ + C⁶H₂), 2.71 (ddd, *J* = 11.1, 4.4, 1.2 Hz, 1H, C⁶H₂), 2.37 – 2.30 (brs, 1H, C⁵H).

¹³C NMR (101 MHz, CDCl₃) δ 153.6 (C⁴), 141.3 (C¹¹), 131.2 (C¹⁶H), 129.8 (d, *J* = 33.5 Hz, C¹²/C¹⁴), 129.5 (d, *J* = 30.9 Hz, C¹²/C¹⁴), 128.8 (q, *J* = 4.5 Hz, C¹⁵H), 123.6 (q, *J* = 274.2 Hz, C¹⁷F₃/C¹⁸F₃), 123.4 (q, *J* = 272.0 Hz, C¹⁷F₃/C¹⁸F₃), 123.3 – 122.9 (m, C¹³H), 93.0 (C³H), 65.0 (C⁷H₂), 57.5 (d, *J* = 2.1 Hz, C¹⁰H₂), 55.2 (C⁶H₂), 54.5 (C⁹H₃), 51.8 (C²H₂), 40.1 (C⁵H).

¹⁹F NMR (377 MHz, CDCl₃) δ -59.3, -62.9.

IR (neat) (cm⁻¹):

(*N*-(2,4-bis(Trifluoromethyl)benzyl)-4-methyl-1,2,3,6-tetrahydropyridin-3-yl)methanol (2aa)



The title compound was prepared by General procedure E using salt **1aa** (224 mg, 0.50 mmol). Purification by FCC (10%-20% EtOAc in pentane) gave *amine 2aa* (35 mg mg, 20%) as a yellow oil.

HRMS (ESI): Exact mass calculated for C₁₆H₁₈F₆NO [M+H]⁺: 354.1285, found: 354.1287.

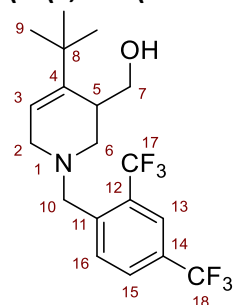
¹H NMR (400 MHz, CDCl₃) δ 7.90 (s, 1H, C¹³H), 7.84 (d, *J* = 8.4 Hz, 1H, C¹⁶H), 7.80 (dd, *J* = 8.5, 1.8 Hz, 1H, C¹⁵H), 5.70 – 5.45 (m, 1H, C³H), 4.36 (s, 1H, OH), 3.86 (ddd, *J* = 10.3, 3.4, 1.8 Hz, 1H, C⁷H₂), 3.80 – 3.74 (m, 3H, C⁷H₂ + C¹⁰H₂), 3.26 – 3.12 (m, 1H, C²H₂), 2.95 (dt, *J* = 11.2, 1.6 Hz, 1H, C⁶H₂), 2.74 (dq, *J* = 15.9, 2.4 Hz, 1H, C²H₂), 2.63 (ddd, *J* = 11.1, 4.0, 1.8 Hz, 1H, C⁶H₂), 2.10 (s, 1H, C⁵H), 1.78 (q, *J* = 1.9 Hz, 3H, C⁹H₃).

¹³C NMR (126 MHz, CDCl₃) δ 141.1 (C¹¹), 132.3 (C⁴), 131.5 (C¹⁶H), 130.0 (q, *J* = 33.5 Hz, C¹²/C¹⁴), 129.7 (q, *J* = 31.0 Hz, C¹²/C¹⁴), 129.0 (q, *J* = 3.7 Hz, C¹⁵H), 123.7 (q, *J* = 274.0 Hz, C¹⁷F₃/C¹⁸F₃), 123.5 (q, *J* = 272.4 Hz, C¹⁷F₃/C¹⁸F₃), 123.4 – 123.1 (m, C¹³H), 121.7 (C³H), 65.1 (C⁷H₂), 58.1 (d, *J* = 2.3 Hz, C¹⁰H₂), 56.1 (C⁶H₂), 53.3 (C²H₂), 41.5 (C⁵H), 21.2 (C⁹H₃).

¹⁹F NMR (377 MHz, CDCl₃) δ -59.2, -62.9.

IR (neat) (cm⁻¹):

(*N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(tert-butyl)-1,2,3,6-tetrahydropyridin-3-yl)methanol (2ab)



The title compound was prepared by General procedure E using salt **1ab** (245 mg, 0.50 mmol). Purification by FCC (10%-20% EtOAc in pentane) gave *amine 2ab* (53 mg mg, 27%) as a yellow oil.

HRMS (ESI): Exact mass calculated for C₁₉H₂₄F₆NO [M+H]⁺: 396.1743, found: 396.1757

¹H NMR (500 MHz, CDCl₃) δ 7.91 (s, 1H, C¹³H), 7.85 (d, *J* = 8.2 Hz, 1H, C¹⁶H), 7.81 (dd, *J* = 8.2, 1.8 Hz, 1H, C¹⁵H), 5.66 (dd, *J* = 4.1, 2.4 Hz, 1H, C³H), 4.78 (s, 1H, OH), 3.92 (ddd, *J* = 10.6, 3.8, 2.2 Hz, 1H, C⁷H₂), 3.82 (dd, *J* = 10.6, 2.2 Hz, 1H, C⁷H₂), 3.78 (s, 2H, C¹⁰H₂), 3.36 (dd, *J* = 16.4, 4.1 Hz, 1H, C²H₂), 2.98 (ddd, *J* = 10.8, 2.1, 1.0 Hz, 1H, C⁶H₂), 2.78 (dt, *J* = 16.4, 2.2 Hz, 1H, C²H₂), 2.53 (dt, *J* = 10.7, 2.7 Hz, 1H, C⁶H₂), 2.41 (s, 1H, C⁵H), 1.12 (s, 9H, 3 x C⁹H₃).

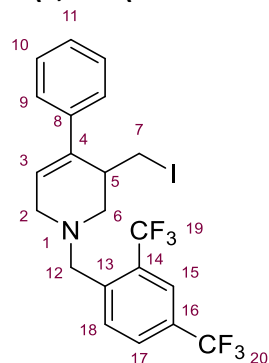
¹³C NMR (126 MHz, CDCl₃) δ 143.4 (C⁴), 141.1 (C¹¹), 131.5 (C¹⁶H), 130.0 (q, *J* = 32.3 Hz, C¹²/C¹⁴), 129.8 (q, *J* = 32.3 Hz, C¹²/C¹⁴), 129.0 (q, *J* = 3.7 Hz, C¹⁵H), 123.7 (q, *J* = 274.2 Hz, C¹⁷F₃/C¹⁸F₃), 123.5 (q, *J* = 272.3 Hz, C¹⁷F₃/C¹⁸F₃), 123.3 (m, C¹³H), 119.5 (C³H), 67.3 (C⁷H₂), 58.0 (q, *J* = 2.0 Hz, C¹⁰H₂), 57.6 (C⁶H₂), 53.9 (C²H₂), 37.4 (C⁵H), 35.5 (C⁸), 30.3 (3 x C⁹H₃).

¹⁹F NMR (377 MHz, CDCl₃) δ -59.1, -62.9.

IR (neat) (cm⁻¹): 3324, 2962, 1345, 1275, 1169, 1122, 1083, 1056, 1029, 672.

Derivatisation of products

N-(2,4-bis(trifluoromethyl)benzyl)-3-(iodomethyl)-4-phenyl-1,2,3,6-tetrahydropyridine (**4**)



Amine **2c** (83 mg, 0.20 mmol), PPh_3 (115 mg, 0.44 mmol) and imidazole (34 mg, 0.50 mmol) were dissolved in CH_2Cl_2 (4 mL). The solution was cooled to 0 °C, I_2 (112 mg, 0.44 mmol) was added and the reaction was allowed to warm to rt. After 2 h the reaction was quenched with an *aq. sat.* solution of $\text{Na}_2\text{S}_2\text{O}_3$ (5 mL). The solution was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The organic layers were combined, dried (MgSO_4), filtered, and concentrated *in vacuo*. The crude material was purified by FCC (0%-2% Et_2O in pentane) to give *iodide 4* (69 mg, 66%) as a yellow oil.

HRMS (ESI): Exact mass calculated for $\text{C}_{21}\text{H}_{19}\text{F}_6\text{NO}^{127}\text{I}$ $[\text{M}+\text{H}]^+$: 526.0461, found: 526.0454.

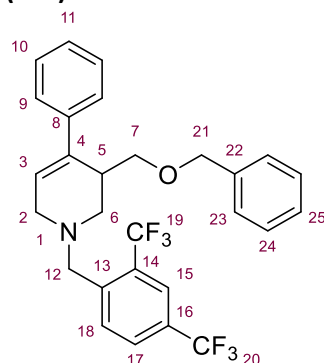
^1H NMR (400 MHz, CDCl_3) δ 8.02 (d, J = 8.2 Hz, 1H, C^{18}H), 7.92 (s, 1H, C^{15}H), 7.84 (d, J = 8.2 Hz, 1H, C^{17}H), 7.40 – 7.27 (m, 5H, 5 x ArCH), 6.02 (dd, J = 4.2, 2.6 Hz, 1H, C^3H), 3.94 – 3.81 (m, 2H, C^{12}H_2), 3.45 (dd, J = 11.0, 9.7 Hz, 1H, C^7H_2), 3.30 (dd, J = 17.4, 4.4 Hz, 1H, C^2H_2), 3.24 – 3.13 (m, 2H, C^6H_2 + C^7H_2), 3.04 (d, J = 11.2 Hz, 1H, C^5H), 2.98 (dt, J = 17.3, 2.5 Hz, 1H, C^2H_2), 2.62 (ddd, J = 11.5, 3.7, 1.6 Hz, 1H, C^6H_2).

^{13}C NMR (126 MHz, CDCl_3) δ 142.2 (C^{13}), 139.1 (C), 137.6 (C), 131.6 (C^{18}H), 129.7 (q, J = 33.9 Hz, $\text{C}^{14}/\text{C}^{16}$), 129.5 (q, J = 31.8 Hz, $\text{C}^{14}/\text{C}^{16}$), 129.0 (C^{17}H), 128.9 (2 x ArCH), 127.8 (ArCH), 125.8 (2 x ArCH), 124.4 (C^3H), 123.8 (q, J = 274.1 Hz, $\text{C}^{19}\text{F}_3/\text{C}^{20}\text{F}_3$), 123.6 (q, J = 272.3 Hz, $\text{C}^{19}\text{F}_3/\text{C}^{20}\text{F}_3$), 123.2 (C^{15}H), 57.5 (C^{12}H_2), 54.5 (C^2H_2), 53.7 (C^6H_2), 41.3 (C^5H), 9.5 (C^7H_2).

^{19}F NMR (377 MHz, CDCl_3) δ -59.5, -62.8.

IR (neat) (cm^{-1}): 2808, 2161, 1348, 1292, 1279, 1167, 1122, 1084, 1057, 757.

3-((Benzyloxy)methyl)-*N*-(2,4-bis(trifluoromethyl)benzyl)-4-phenyl-1,2,3,6-tetrahydropyridine (**S11**)



Amine **2c** (83 mg, 0.20 mmol), 15-crown-5 (80 μL , 0.40 mmol) and benzyl bromide (0.24 mL, 2.00 mmol) were dissolved in THF (1 mL). The solution was cooled to 0 °C and NaH (64 mg, 2.0 mmol) was added portion wise. The reaction mixture was allowed to warm to rt and stir for 2 hours. The reaction was quenched with water (5 mL), the *aq* layer extracted with CH_2Cl_2 (2 x 5 mL), dried (MgSO_4) and concentrated *in vacuo*. The crude material was purified by FCC (0%-4% Et_2O in pentane) to give *amine S11* (72 mg, 73%) as a white solid.

m.p. (EtOAc): 78-80 °C

HRMS (ESI): Exact mass calculated for C₂₈H₂₆F₆NO [M+H]⁺: 506.1911, found: 506.1913.

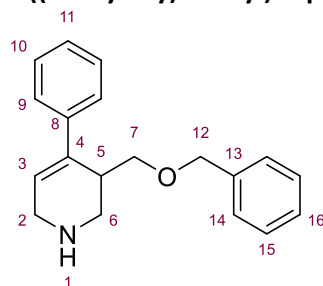
¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, *J* = 8.2 Hz, 1H, C¹⁸H), 7.89 (s, 1H, C¹⁵H), 7.69 (dd, *J* = 7.8, 1.5 Hz, 1H, C¹⁷H), 7.41 – 7.12 (m, 10H, 10 x ArCH), 6.01 (ddd, *J* = 4.5, 2.5, 0.8 Hz, 1H, C³H), 4.45 (d, *J* = 11.8 Hz, 1H, C²¹H₂), 4.32 (d, *J* = 11.8 Hz, 1H, C²¹H₂), 3.90 – 3.75 (m, 2H, C¹²H₂), 3.71 (dd, *J* = 10.0, 9.1 Hz, 1H, C⁷H₂), 3.45 – 3.28 (m, 2H, C²H₂ + C⁷H₂), 3.18 (ddd, *J* = 11.1, 2.4, 1.2 Hz, 1H, C⁶H₂), 3.09 (dt, *J* = 9.8, 3.1 Hz, 1H, C⁵H), 3.01 (dt, *J* = 17.1, 2.5 Hz, 1H, C²H₂), 2.54 (dd, *J* = 11.2, 3.6 Hz, 1H, C⁶H₂).

¹³C NMR (126 MHz, CDCl₃) δ 142.7 (C¹³), 140.0 (C²²), 138.4 (C⁵), 136.2 (C⁴), 131.2 (C¹⁸H), 129.5 (q, *J* = 33.3 Hz, C¹⁴/C¹⁶), 129.3 (q, *J* = 31.3 Hz, C¹⁴/C¹⁶), 128.7 (C¹⁷H + ArCH), 128.5 (2 x ArCH), 127.7 (4 x ArCH), 127.4 (ArCH), 125.8 (2 x ArCH), 124.6 (C³H), 123.8 (q, *J* = 274.2 Hz, C¹⁹F₃/C²⁰F₃), 123.7 (q, *J* = 272.2 Hz, C¹⁹F₃/C²⁰F₃), 123.1 – 122.9 (m, C¹⁵H), 73.1 (C²¹H₂), 70.8 (C⁷H₂), 57.6 (C¹²H₂), 53.8 (C²H₂), 52.0 (C⁶H₂), 38.8 (C⁵H).

¹⁹F NMR (377 MHz, CDCl₃) δ -59.8, -62.7.

IR (neat) (cm⁻¹): 2857, 1348, 1280, 1166, 1118, 1085, 1056, 755, 695, 674.

3-((Benzyloxy)methyl)-4-phenyl-1,2,3,6-tetrahydropyridine (5)



Amine S11 (25 mg, 0.05 mmol) added to a microwave vial, dissolved in DCE (0.13 mL), 1-chloroethyl chloroformate (31 μL, 0.40 mmol) was added and the reaction was sealed and heated to 120 °C for 16 h. The reaction was allowed to cool to rt, the solvent was switched to MeOH (1 mL) and heated to reflux for 4 hours. Purification by FCC (0%-10% MeOH in CH₂Cl₂) gave **amine 5** (11 mg, 77%) as a yellow oil

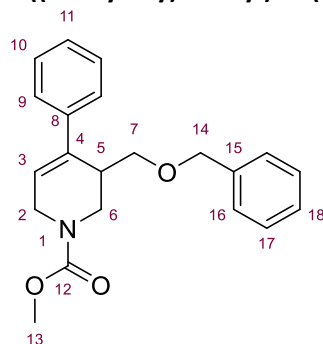
HRMS (ESI): Exact mass calculated for C₁₉H₂₂NO [M+H]⁺: 280.1696, found: 280.1696.

¹H NMR (400 MHz, CDCl₃) δ 7.45 – 7.16 (m, 10H, 10 x ArCH), 5.96 (d, *J* = 3.4 Hz, 1H, C³H), 4.46 (s, 2H, C¹²H₂), 3.85 – 3.71 (m, 2H, C⁶H₂), 3.68 (dd, *J* = 12.5, 2.8 Hz, 1H, C²H₂), 3.60 (dd, *J* = 9.6, 7.0 Hz, 1H, C⁷H₂), 3.49 (dd, *J* = 9.6, 3.4 Hz, 1H, C⁷H₂), 3.27 (dd, *J* = 12.7, 4.8 Hz, 1H, C²H₂), 3.14 (s, 1H, C⁵H).

¹³C NMR (101 MHz, CDCl₃) δ 139.0 (C), 137.9 (C), 137.5 (C), 128.8 (2 x ArCH), 128.5 (2 x ArCH), 128.1 (ArCH), 127.9 (ArCH), 127.8 (2 x ArCH), 126.2 (2 x ArCH), 121.1 (C³H), 73.3 (C¹²H₂), 69.9 (C⁷H₂), 44.4 (C²H₂), 43.1 (C⁶H₂), 35.2 (C⁵H).

IR (neat) (cm⁻¹): 3415, 2922, 2853, 1659, 1639, 1593, 1454, 1092, 1073, 1027.

3-((Benzyloxy)methyl)-N-(2,4-bis(trifluoromethyl)benzyl)-4-phenyl-1,2,3,6-tetrahydropyridine (6)



Amine S11 (25 mg, 0.05 mmol) added to a microwave vial, dissolved in DCE (0.13 mL), methyl chloroformate (31 μL, 0.40 mmol) was added and the reaction was sealed and heated to 120 °C for 16 h. Afterwards the reaction was allowed to cool to rt, diluted with CH₂Cl₂ (5 mL) and quenched with

water (5 mL) The layers were separated, the aqueous layer was extracted with CH₂Cl₂ (2 x 5 mL), dried (MgSO₄) and concentrated *in vacuo*. The crude material was purified by FCC (5%-30% EtOAc in pentane) to give *carbamate 6* (16 mg, 90%) as a pale yellow oil.

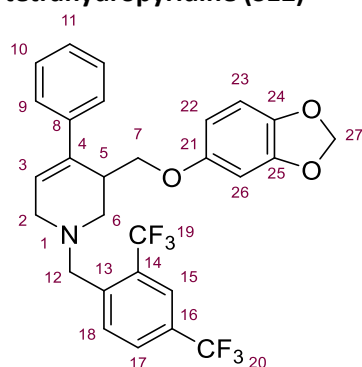
HRMS (ESI): Exact mass calculated for C₂₁H₂₃NO₃⁺Na [M+Na]⁺: 360.1568, found: 360.1570.

¹H NMR (500 MHz, DMSO) δ 7.45 – 7.20 (m, 10H, 10 x ArCH), 6.07 (t, *J* = 3.4 Hz, 1H, C³H), 4.44 (d, *J* = 12.2 Hz, 1H, C¹⁴H₂), 4.38 (d, *J* = 12.1 Hz, 1H, C¹⁴H₂), 4.29 – 4.19 (m, 2H, C²H₂ + C⁷H₂), 3.85 (dt, *J* = 19.1, 2.7 Hz, 1H, C²H₂), 3.66 (s, 3H, C¹³H₃), 3.31 (ddd, *J* = 9.7, 4.0, 1.0 Hz, 1H, C⁶H₂), 3.27 (t, *J* = 9.2 Hz, 1H, C⁶H₂), 3.20 (ddd, *J* = 13.0, 3.7, 0.9 Hz, 1H, C⁷H₂), 3.10 (brs, 1H, C⁵H).

¹³C NMR (126 MHz, DMSO) δ 155.3 (C¹²), 139.0 (C), 138.1 (C), 135.5 (C), 127.9 (2 x ArCH), 127.6 (2 x ArCH), 126.8 (2 x ArCH), 126.7 (2 x ArCH), 125.0 (2 x ArCH), 122.5 (C³H), 71.8 (C¹⁴H₂), 69.1 (C⁷H₂), 51.7 (C¹³H₃), 43.2 (C²H₂), 41.8 (C⁶H₂), 36.9 (C⁵H).

IR (neat) (cm⁻¹): 3414, 2920, 2852, 1754, 1696, 1445, 1265, 1209, 1095, 769.

3-((Benzo[d][1,3]dioxol-5-yloxy)methyl)-*N*-(2,4-bis(trifluoromethyl)benzyl)-4-phenyl-1,2,3,6-tetrahydropyridine (**S12**)



Amine 2c (62 mg, 0.15 mmol), PPh₃ (47 mg, 0.18 mmol) and sesamol (41 mg, 0.30 mmol) were dissolved in THF (1.5 mL). The solution was cooled to 0 °C and DIAD (35 μL, 0.21 mmol) was added dropwise. The reaction was then heated to 50 °C and stirred for 16 h. The reaction was evaporated, the crude redissolved in CH₂Cl₂ (20 mL), washed with NaOH (2 x 20 mL, 1.0 M) and dried (MgSO₄). The crude material was purified by FCC (0%-5% EtOAc in pentane) to give *amine S12* (54 mg, 66%) as a white solid.

m.p. (EtOAc): 110-112 °C

HRMS (ESI): Exact mass calculated for C₂₈H₂₄F₆NO₃ [M+H]⁺: 536.1655, found: 536.1655.

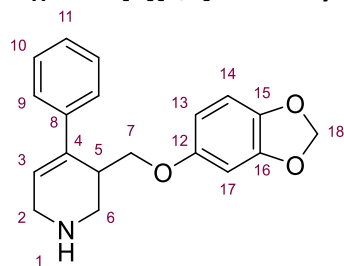
¹H NMR (500 MHz, CDCl₃) δ 7.87 – 7.82 (m, 2H, C¹⁵H + C¹⁸H), 7.44 – 7.39 (m, 2H, C¹¹H + C¹⁷H), 7.38 – 7.32 (m, 2H, 2 x C⁹H/C¹⁰H), 7.32 – 7.27 (m, 2H, 2 x C⁹H/C¹⁰H), 6.65 (d, *J* = 8.5 Hz, 1H, C²³H), 6.27 (d, *J* = 2.5 Hz, 1H, C²⁶H), 6.14 (dd, *J* = 8.5, 2.5 Hz, 1H, C²²H), 6.11 (dd, *J* = 4.6, 2.3 Hz, 1H, C³H), 5.90 (dd, *J* = 9.8, 1.4 Hz, 2H, C²⁷H₂), 4.09 (dd, *J* = 10.3, 8.8 Hz, 1H, C⁷H₂), 3.87 (d, *J* = 14.5 Hz, 1H, C¹²H₂), 3.80 (d, *J* = 15.5 Hz, 1H, C¹²H₂), 3.77 – 3.73 (m, 1H, C⁷H₂), 3.46 (dd, *J* = 17.2, 4.6 Hz, 1H, C²H₂), 3.20 (s, 1H, C⁵H), 3.16 (dd, *J* = 11.1, 1.4 Hz, 1H, C⁶H₂), 3.12 (dt, *J* = 17.1, 2.4 Hz, 1H, C²H₂), 2.53 – 2.40 (m, 1H, C⁶H₂).

¹³C NMR (126 MHz, CDCl₃) δ 154.4 (C²¹), 148.4 (C²⁵), 142.4 (C¹³), 141.7 (C²⁴), 139.7 (C⁸), 135.7 (C⁴), 131.0 (C¹⁸H), 129.3 (q, *J* = 33.3 Hz, C¹⁴/C¹⁶), 129.2 (q, *J* = 31.3 Hz, C¹⁴/C¹⁶), 128.8 (ArCH), 128.7 – 128.5 (m, C¹⁷H), 127.7 (ArCH), 125.7 (ArCH), 125.2 (C³H), 123.8 (q, *J* = 274.1 Hz, C¹⁹F₃/C²⁰F₃), 123.6 (q, *J* = 272.2 Hz, C¹⁹F₃/C²⁰F₃), 123.1 – 122.8 (m, C¹⁵H), 107.9 (C²³H), 105.3 (C²²H), 101.3 (C²⁷H₂), 97.9 (C²⁶H), 68.3 (C⁷H₂), 57.1 (q, *J* = 2.1 Hz, C¹²H₂), 54.2 (C²H₂), 50.8 (C⁶H₂), 38.3 (C⁵H).

¹⁹F NMR (377 MHz, CDCl₃) δ -59.8, -62.8.

IR (neat) (cm⁻¹): 2898, 1629, 1490, 1343, 1271, 1173, 1159, 1119, 1101, 1095.

3-((Benzo[d][1,3]dioxol-5-yloxy)methyl)-4-phenyl-1,2,3,6-tetrahydropyridine (**7**)



Amine **S12** (54 mg, 0.10 mmol) added to a microwave vial, dissolved in DCE (0.25 mL), 1-chloroethyl chloroformate (86 μ L, 0.80 mmol) was added and the reaction was sealed and heated to 120 $^{\circ}$ C for 16 h. The reaction was allowed to cool to rt, the solvent was switched to MeOH (1 mL) and heated to reflux for 4 hours. Purification by FCC (1%-10% MeOH in CH_2Cl_2) gave *amine* **7** (20 mg mg, 65%) as a yellow oil

HRMS (ESI): Exact mass calculated for $\text{C}_{19}\text{H}_{20}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 310.1438, found: 310.1437.

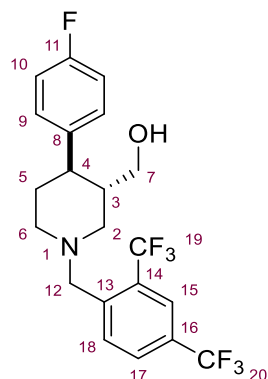
^1H NMR (400 MHz, CDCl_3) δ 7.41 – 7.28 (m, 5H, 5 x ArCH), 6.63 (d, J = 8.5 Hz, 1H, C^{14}H), 6.42 (d, J = 2.4 Hz, 1H, C^{17}H), 6.23 (dd, J = 8.5, 2.5 Hz, 1H, C^{13}H), 6.14 – 6.08 (m, 1H, C^3H), 5.87 (s, 2H, C^{18}H_2), 3.94 (t, J = 9.1 Hz, 1H, C^7H_2), 3.82 – 3.72 (m, 1H, C^7H_2), 3.63 – 3.49 (m, 2H, C^2H_2), 3.47 – 3.39 (m, 1H, C^6H_2), 3.15 – 3.05 (m, 2H, $\text{C}^5\text{H} + \text{C}^6\text{H}_2$), 2.92 (s, 1H, NH).

^{13}C NMR (101 MHz, CDCl_3) δ 154.4 (C^{12}), 148.3 (C^{16}), 141.8 (C^{15}), 140.5 (C^8), 136.2 (C^4), 128.7 (2 x ArCH), 127.5 (ArCH), 127.0 (C^3H), 126.0 (2 x ArCH), 108.0 (C^{14}H), 106.0 (C^{13}H), 101.2 (C^{18}H_2), 98.3 (C^{17}H), 69.0 (C^7H_2), 45.7 (C^2H_2), 45.2 (C^6H_2), 36.4 (C^5H).

IR (neat) (cm^{-1}): 2919, 2160, 2027, 1977, 1630, 1486, 1179, 1035, 757, 698.

Synthesis of Paroxetine

(*trans*-*N*-(2,4-bis(Trifluoromethyl)benzyl)-4-(4-fluorophenyl)piperidin-3-yl)methanol (**8**)



A microwave vial was charged with *amine 2j* (43 mg, 0.10 mmol) and Crabtree's catalyst (16 mg, 20 mol%) evacuated and back filled with argon. Degassed CH_2Cl_2 (2 mL) were added and the reaction mixture was purged with hydrogen for 5 minutes. The reaction was left to stir for 20 h at room temperature under an atmosphere of hydrogen. The d.r. of the crude was 3:1 *trans*:*cis*, however, purification by FCC (0%-10% EtOAc in pentane) gave a single diastereoisomer of *amine 8* (28 mg, 65%) as a yellow oil

HRMS (ESI): Exact mass calculated for $\text{C}_{21}\text{H}_{21}\text{F}_7\text{NO}$ $[\text{M}+\text{H}]^+$: 436.1506, found: 436.1503.

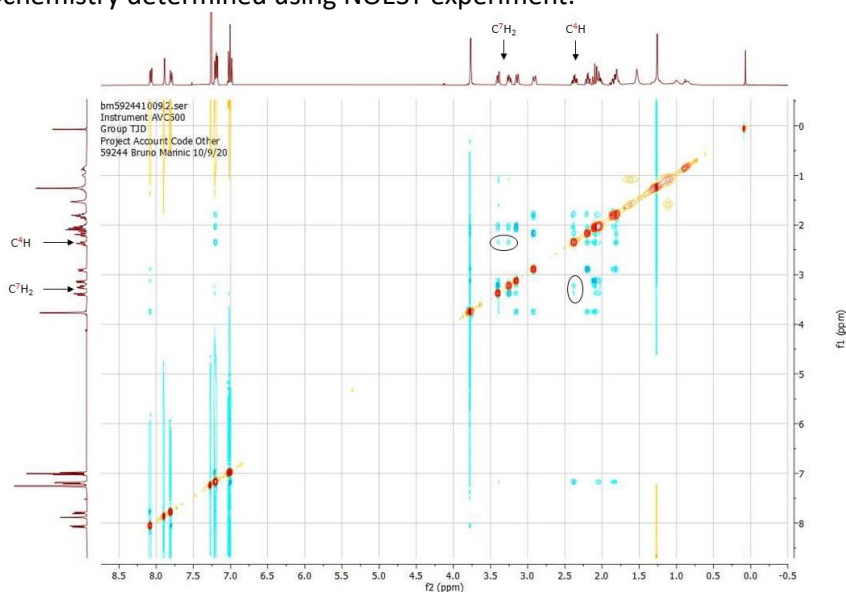
^1H NMR (400 MHz, CDCl_3) δ 8.07 (d, $J = 8.2$ Hz, 1H, C^{18}H), 7.89 (s, 1H, C^{15}H), 7.80 (d, $J = 8.2$ Hz, 1H, C^{17}H), 7.23 – 7.15 (m, 2H, 2 x C^9H), 7.06 – 6.95 (m, 2H, 2 x C^{10}H), 3.77 (s, 2H, C^{12}H_2), 3.40 (dd, $J = 10.8$, 3.1 Hz, 1H, C^7H_2), 3.25 (dd, $J = 10.8$, 6.6 Hz, 1H, C^7H_2), 3.18 – 3.10 (m, 1H, C^2H_2), 2.91 (d, $J = 11.3$ Hz, 1H, C^6H_2), 2.37 (td, $J = 11.0$, 4.9 Hz, 1H, C^4H), 2.19 (td, $J = 11.2$, 3.5 Hz, 1H, C^6H_2), 2.14 – 1.97 (m, 2H, $\text{C}^2\text{H}_2 + \text{C}^3\text{H}$), 1.92 – 1.74 (m, 2H, C^5H_2).

^{13}C NMR (126 MHz, CDCl_3) δ 161.7 (d, $J = 244.3$ Hz, C^{11}), 142.9 (C^{13}), 140.0 (d, $J = 3.3$ Hz, C^8), 130.9 (C^{16}H), 129.4 (q, $J = 33.2$ Hz, $\text{C}^{14}/\text{C}^{16}$), 129.3 (q, $J = 31.3$ Hz, $\text{C}^{14}/\text{C}^{16}$), 128.9 (d, $J = 7.7$ Hz, 2 x C^9H), 128.7 (q, $J = 3.8$ Hz, C^{17}H), 123.8 (d, $J = 274.2$ Hz, $\text{C}^{19}\text{F}_3/\text{C}^{20}\text{F}_3$), 123.7 (d, $J = 272.1$ Hz, $\text{C}^{19}\text{F}_3/\text{C}^{20}\text{F}_3$), 123.3 – 122.9 (m, C^{15}H), 115.6 (d, $J = 21.2$ Hz, 2 x C^{10}H), 64.0 (C^7H_2), 58.4 (q, $J = 2.5$ Hz, C^{12}H_2), 57.7 (C^6H_2), 54.4 (C^2H_2), 44.5 (C^3H), 44.3 (C^4H), 34.7 (C^5H).

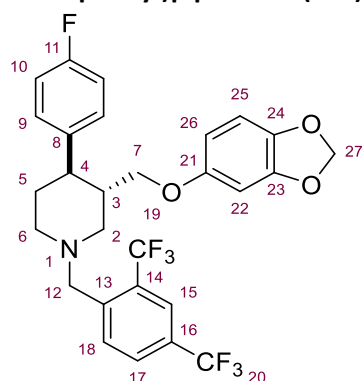
^{19}F NMR (376 MHz, CDCl_3) δ -60.0, -62.7, -115.6 to -118.8 (m).

IR (neat) (cm^{-1}): 3257, 2922, 1510, 1345, 1275, 1168, 1122, 1083, 1053, 831.

Relative stereochemistry determined using NOESY experiment:



***trans*-3-((Benzo[d][1,3]dioxol-5-yloxy)methyl)-*N*-(2,4-bis(trifluoromethyl)benzyl)-4-(4-fluorophenyl)piperidine (**S13**)**



Amine 8 (45 mg, 0.10 mmol), PPh_3 (32 mg, 0.12 mmol) and sesamol (28 mg, 0.20 mmol) were dissolved in THF (1 mL). The solution was cooled to 0 °C and DIAD (47 μL , 0.12 mmol) was added dropwise. The reaction was then heated to 50 °C and stirred for 16 h. The reaction was evaporated, the crude redissolved in CH_2Cl_2 (20 mL), washed with NaOH (2 x 20 mL, 1.0 M) and dried (MgSO_4). The crude material was purified by FCC (0%-20% Et_2O in pentane) to give **amine S13** (46mg, 84%) as a white solid.

m.p. (EtOAc): 100-102 °C

HRMS (ESI): Exact mass calculated for $\text{C}_{28}\text{H}_{25}\text{F}_7\text{NO}_3$ $[\text{M}+\text{H}]^+$: 556.1717, found: 556.1713.

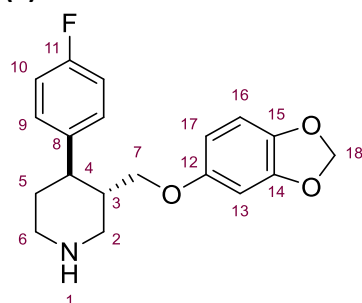
^1H NMR (400 MHz, CDCl_3) δ 8.08 (d, J = 8.2 Hz, 1H, C^{18}H), 7.89 (s, 1H, C^{15}H), 7.81 (dd, J = 8.2, 1.9 Hz, 1H, C^{17}H), 7.24 – 7.14 (m, 2H, 2 x C^9H), 7.04 – 6.94 (m, 2H, 2 x C^{10}H), 6.61 (d, J = 8.4 Hz, 1H, C^{25}H), 6.31 (d, J = 2.5 Hz, 1H, C^{22}H), 6.10 (dd, J = 8.5, 2.5 Hz, 1H, C^{26}H), 5.87 (s, 2H, C^{27}H), 3.85 – 3.72 (m, 2H, C^{12}H), 3.57 (dd, J = 9.5, 2.4 Hz, 1H, C^7H_2), 3.50 – 3.41 (m, 1H, C^7H_2), 3.26 – 3.15 (m, 1H, C^2H_2), 2.92 (ddt, J = 11.3, 4.0, 2.4 Hz, 1H, C^6H_2), 2.51 (td, J = 11.1, 4.9 Hz, 1H, C^4H), 2.32 – 2.16 (m, 3H, C^2H_2 + C^5H + C^6H_2), 1.95 – 1.76 (m, 2H, C^5H_2).

^{13}C NMR (126 MHz, CDCl_3) δ 161.7 (d, J = 244.3 Hz, C^{11}), 154.4 (C^{21}), 148.3 (C^{23}), 142.9 (C^{13}), 141.8 (C^{24}), 139.7 (d, J = 3.2 Hz, C^8), 130.9 (C^{18}H), 129.4 (q, J = 33.3 Hz, $\text{C}^{14}/\text{C}^{16}$), 129.3 (q, J = 31.3 Hz, $\text{C}^{14}/\text{C}^{16}$), 129.0 (d, J = 7.7 Hz, 2 x C^9H), 128.7 (q, J = 3.8 Hz, C^{17}H), 123.8 (q, J = 274.2 Hz, $\text{C}^{19}\text{F}_3/\text{C}^{20}\text{F}_3$), 123.7 (q, J = 272.2 Hz, $\text{C}^{19}\text{F}_3/\text{C}^{20}\text{F}_3$), 123.4 – 123.0 (m, C^{15}H), 115.6 (d, J = 21.2 Hz, 2 x C^{10}H), 108.0 (C^{25}H), 105.7 (C^{26}H), 101.2 (C^{27}H_2), 98.1 (C^{22}H), 69.7 (C^7H_2), 58.3 (q, J = 2.2 Hz, C^{12}H_2), 58.0 (C^2H_2), 54.3 (C^6H_2), 44.1 (C^4H), 42.4 (C^3H), 34.6 (C^5H_2).

^{19}F NMR (377 MHz, CDCl_3) δ -60.0, -62.7, -115.6 to -117.2 (m).

IR (neat) (cm^{-1}): 2918, 2160, 2026, 1503, 1348, 1280, 1198, 1164, 1120, 833.

($\pm$)-Paroxetine



Amine S13 (54 mg, 0.04 mmol) added to a microwave vial, dissolved in DCE (0.13 mL), 1-chloroethyl chloroformate (37 μL , 0.35 mmol) was added and the reaction was sealed and heated to 120 °C for 16 h. The reaction was allowed to cool to rt, the solvent was switched to MeOH (1 mL) and heated to

reflux for 4 hours. Purification by FCC (1%-10% 7N NH₃ MeOH in CH₂Cl₂) gave *Paroxetine* (8 mg, 55%) as a colourless oil. The spectroscopic data was consistent with previous reports.¹⁷

¹H NMR (400 MHz, CDCl₃) δ 7.21 – 7.12 (m, 2H, 2 x C⁹H), 7.03 – 6.92 (m, 2H, 2 x C¹⁰H), 6.62 (d, *J* = 8.4 Hz, 1H, C¹⁶H), 6.33 (d, *J* = 2.5 Hz, 1H, C¹³H), 6.12 (dd, *J* = 8.5, 2.5 Hz, 1H, C¹⁷H), 5.87 (s, 2H, C¹⁸H₂), 3.57 (dd, *J* = 9.4, 3.0 Hz, 1H, C⁷H₂), 3.48 – 3.39 (m, 2H, C²H₂ + C⁷H₂), 3.20 (dt, *J* = 11.6, 3.0 Hz, 1H, C⁶H₂), 2.80 – 2.73 (m, 1H, C⁶H₂), 2.69 (dd, *J* = 12.2, 10.9 Hz, 1H, C²H₂), 2.59 (td, *J* = 11.7, 4.2 Hz, 1H, C⁴H), 2.08 (tdt, *J* = 10.9, 6.9, 3.4 Hz, 1H C³H), 1.87 – 1.77 (m, 1H, C⁵H₂), 1.76 – 1.60 (m, 1H, C⁵H₂).

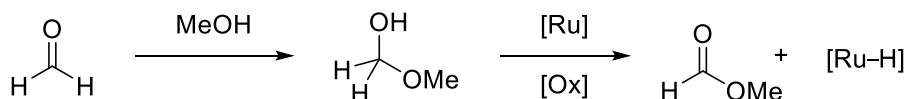
¹³C NMR (101 MHz, CDCl₃) δ 161.67 (d, *J* = 245.0 Hz, C¹¹), 154.6 (C¹²), 148.3 (C¹⁴), 141.7 (C¹⁵), 140.1 (d, *J* = 2.9 Hz, C⁸), 128.9 (d, *J* = 7.7 Hz, 2 x C⁹H), 115.6 (d, *J* = 21.0 Hz, C¹⁰H), 108.0 (C¹⁶H), 105.8 (C¹⁷H), 101.2 (C¹⁸H₂), 98.1 (C¹³H), 69.7 (C⁷H₂), 50.5 (C²H₂), 47.2 (C⁶H₂), 44.7 (C⁴H), 43.1 (C³H), 35.5 (C⁵H₂).

¹⁹F NMR (377 MHz, CDCl₃) δ –116.6.

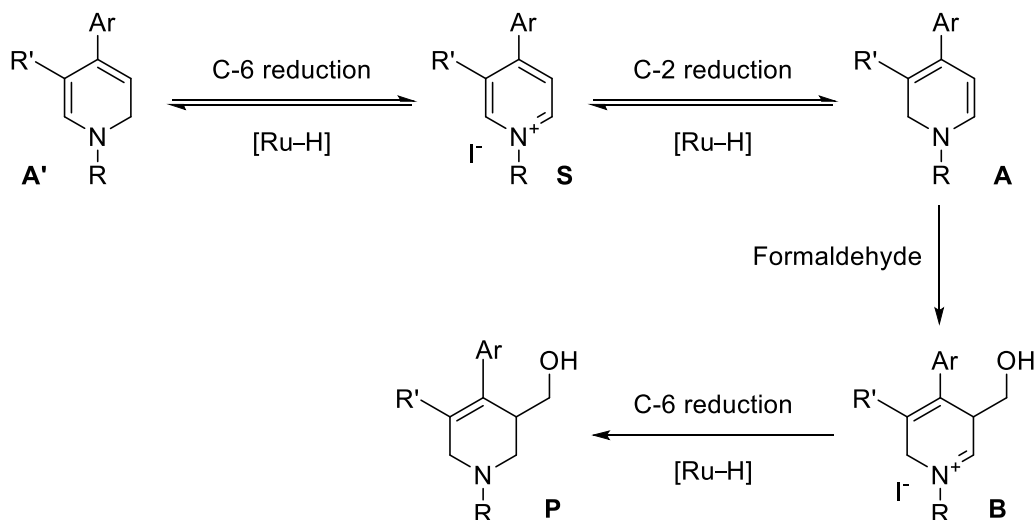
Proposed reaction mechanism

The mechanism of the reaction is thought to proceed via the same pathway we previously reported.¹⁶ Oxidation of paraformaldehyde to methyl formate forms the ruthenium hydride. Reduction can then occur on either C-6 or C-2, with the former forming the inactive enamine **A'** which can be re-oxidised back to the starting material. Reduction at C-2 forms the reactive enamine **A** that then goes on to trap formaldehyde to give iminium **B**. Another reduction at C-6 then generates the final product.

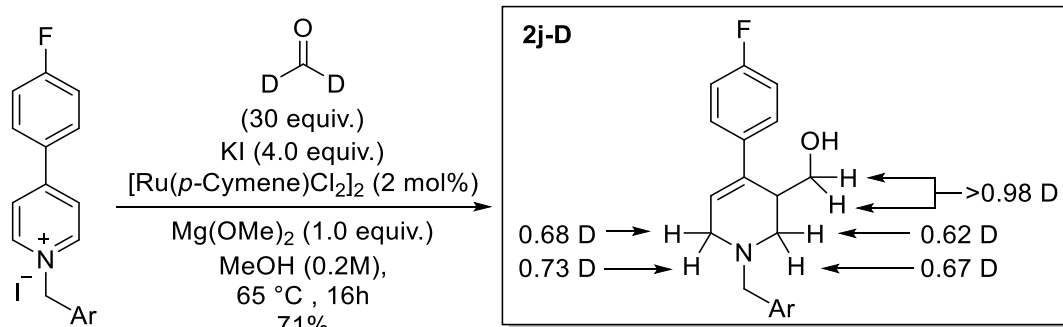
Metal-hydride formation:



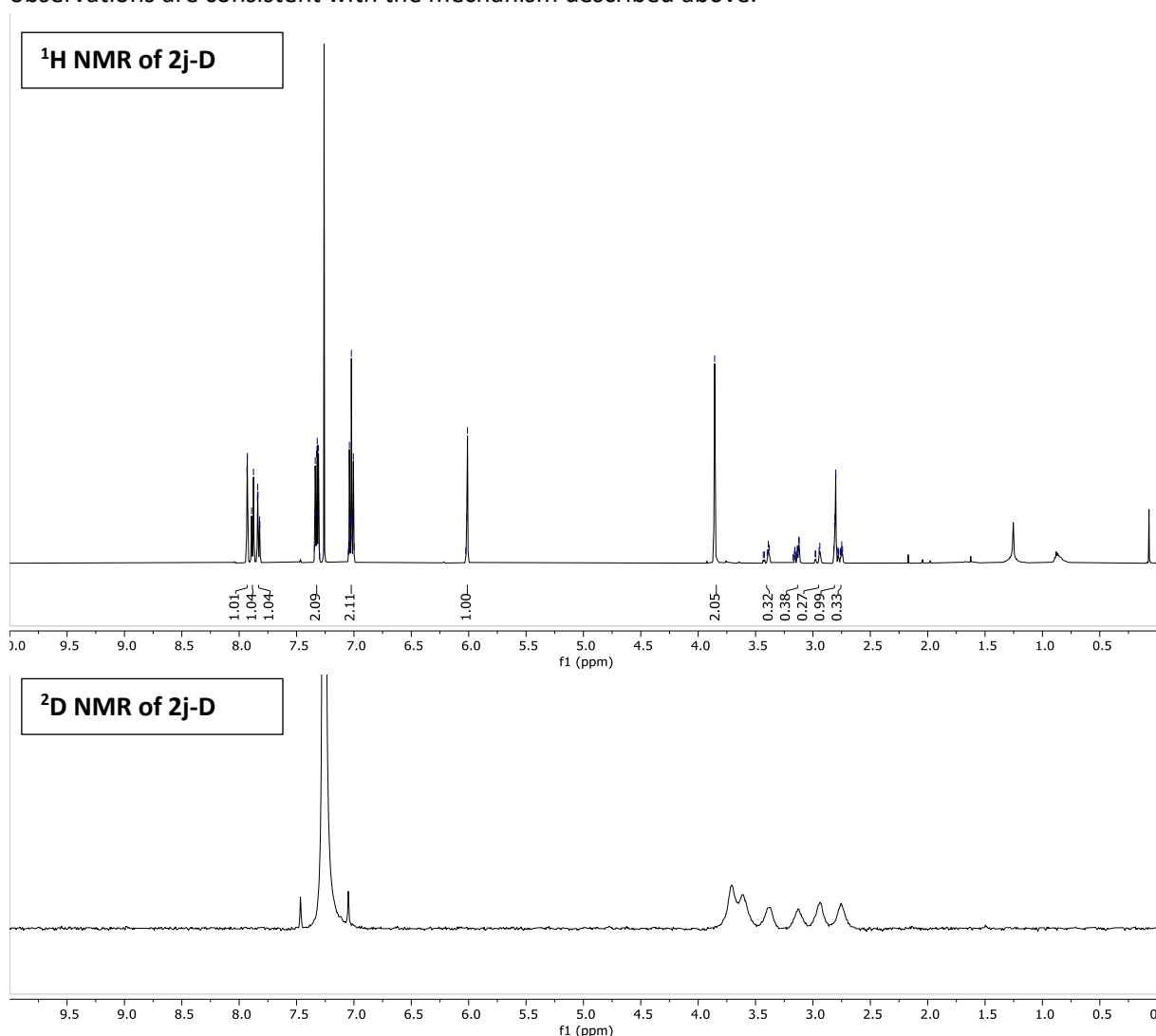
Reaction mechanism:



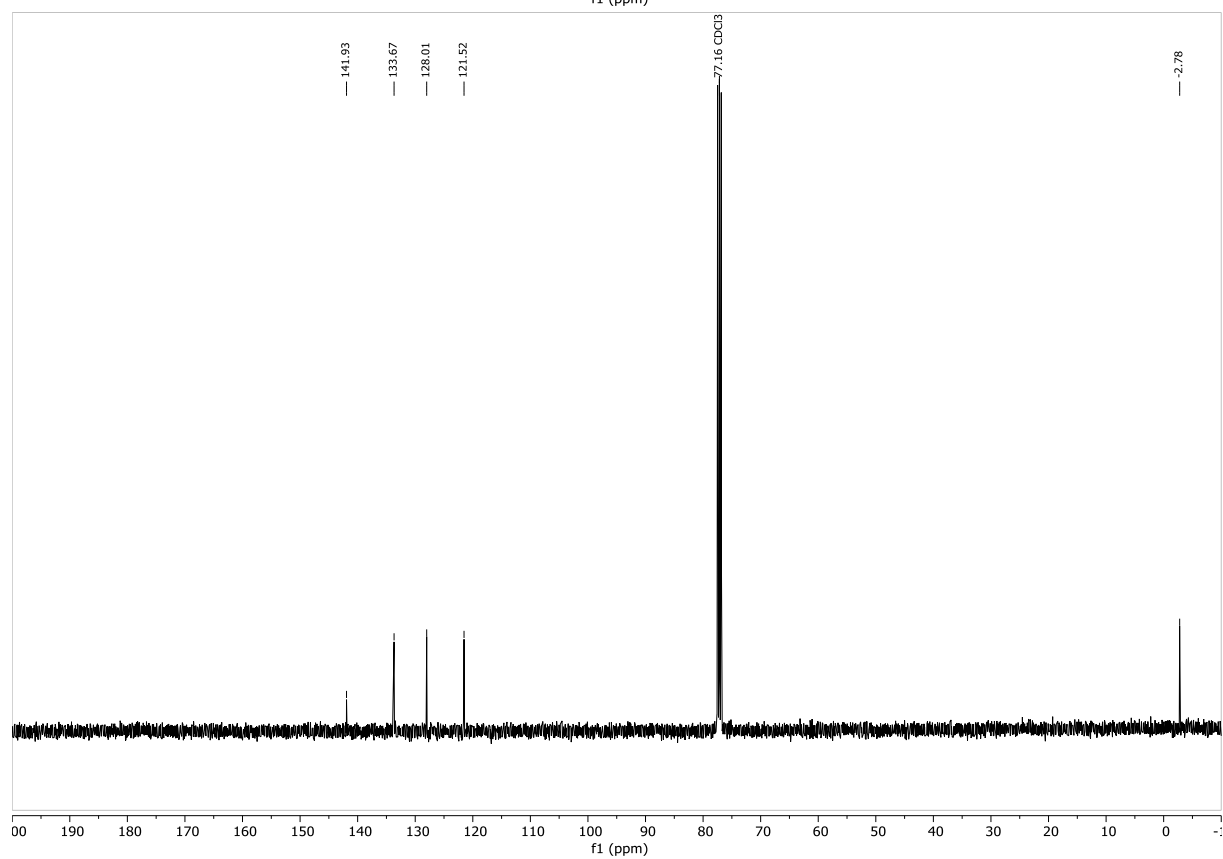
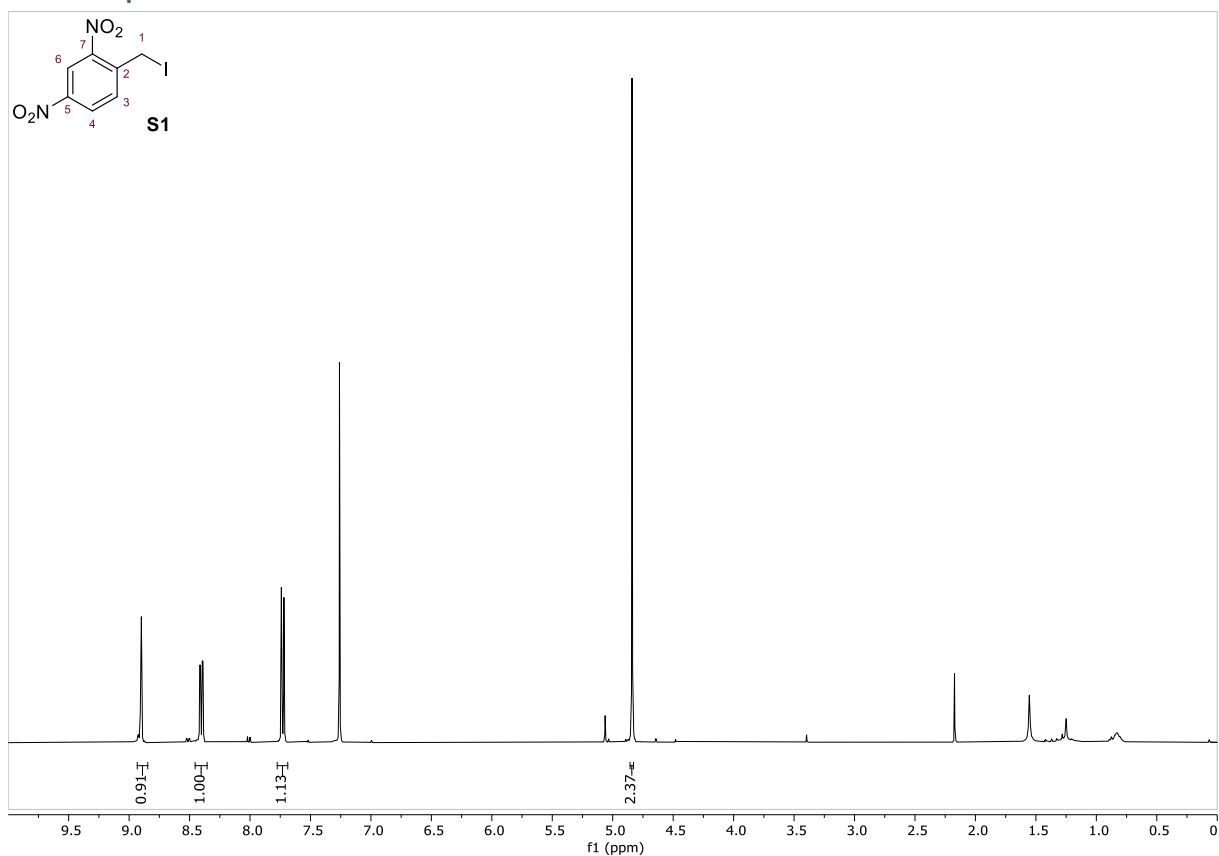
¹⁷ S. Krautwald, M. A. Schafroth, D. Sarlah, and E. M. Carreira, *J. Am. Chem. Soc.*, 2014, **136**, 3020–3023.

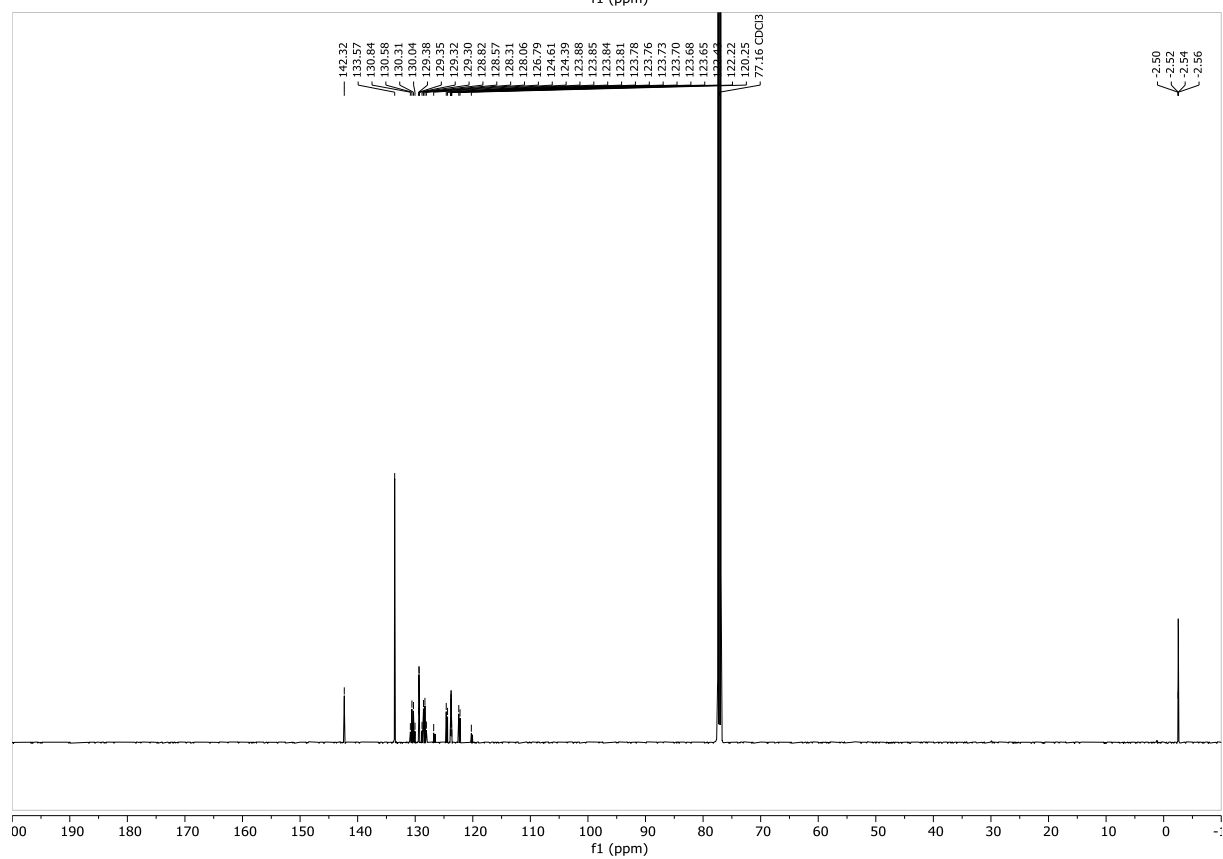
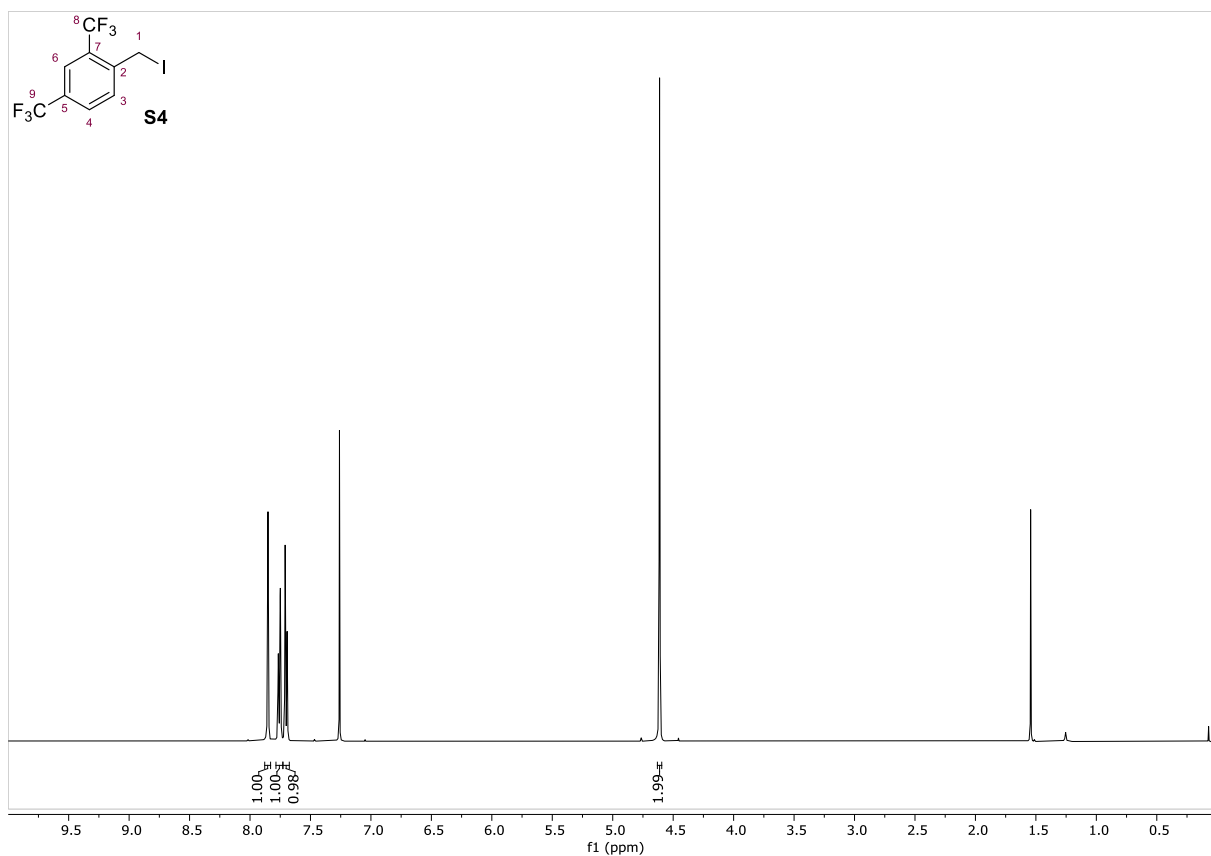


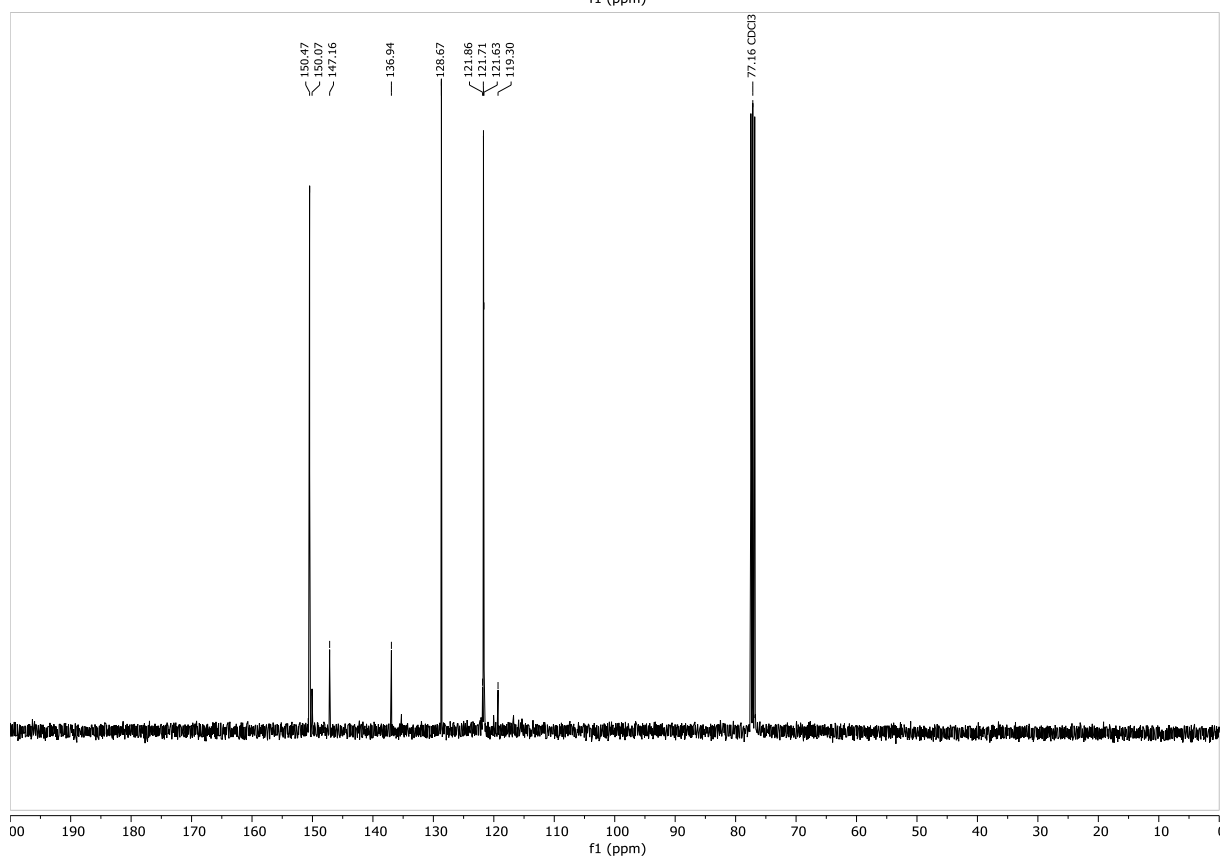
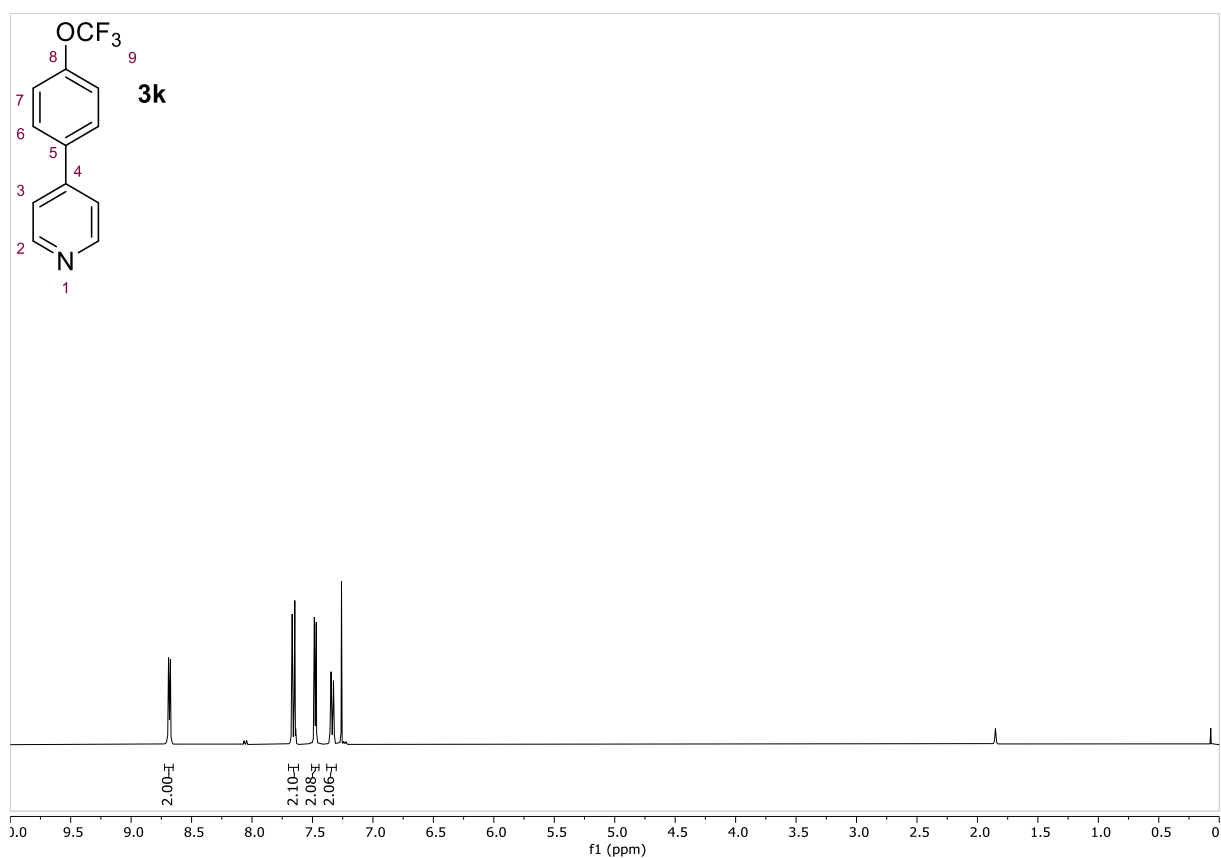
The title compound **2j-D** was prepared by General procedure E using salt **1j** (264 mg, 0.50 mmol) and deuterated paraformaldehyde (480 mg, 15 mmol). Purification by FCC (5%-20% EtOAc in pentane) gave *amine* **2j** (155 mg, 71%) as a yellow oil. Complete deuterium incorporation was observed for the hydroxymethyl group and significant levels of incorporation at the C-2 and C-6 positions. These observations are consistent with the mechanism described above.

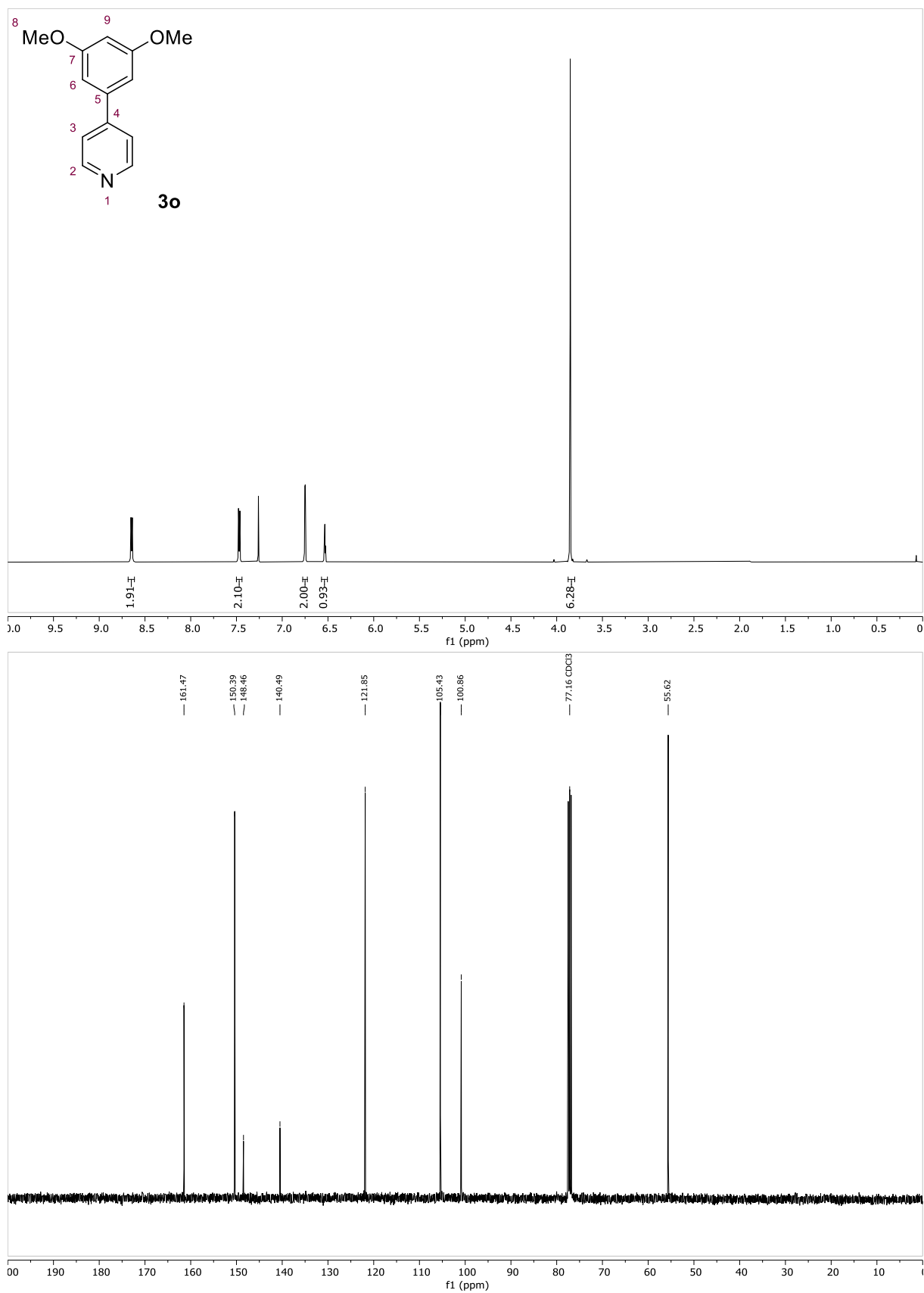


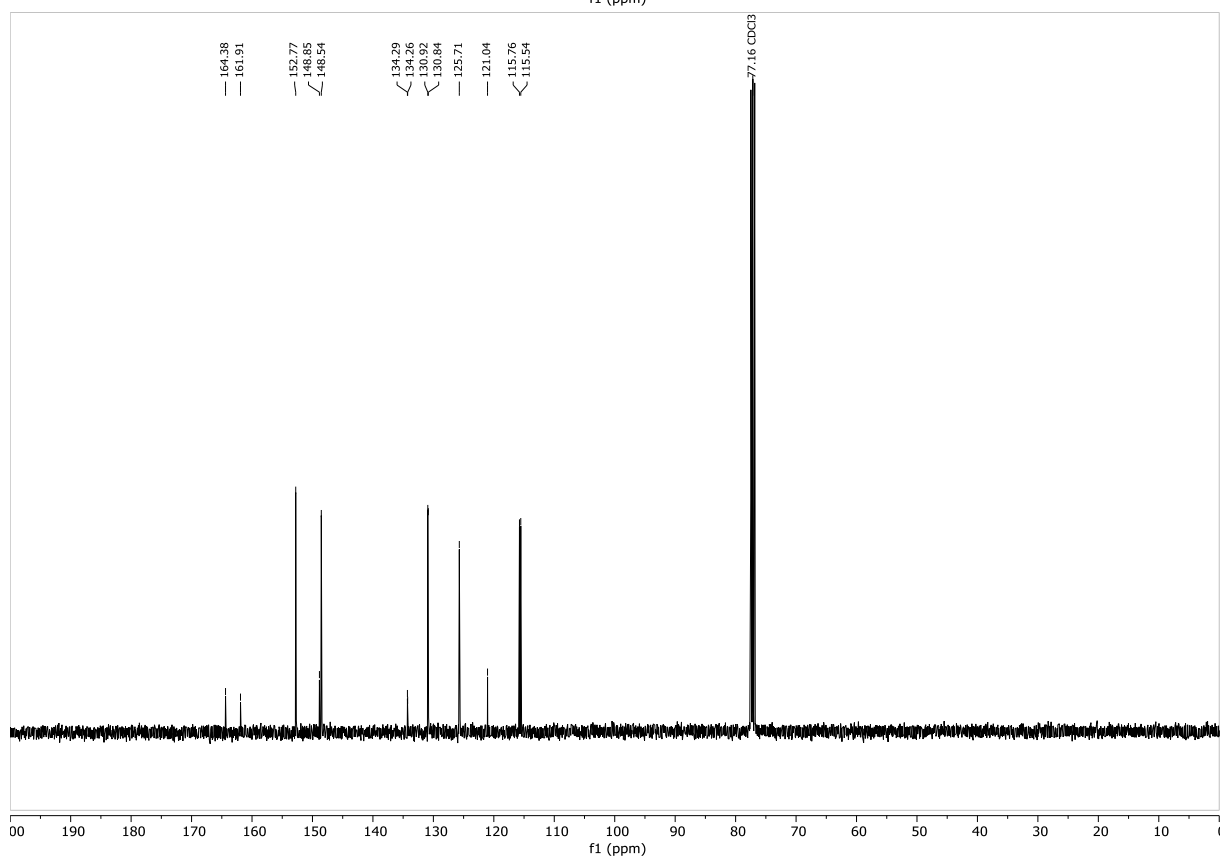
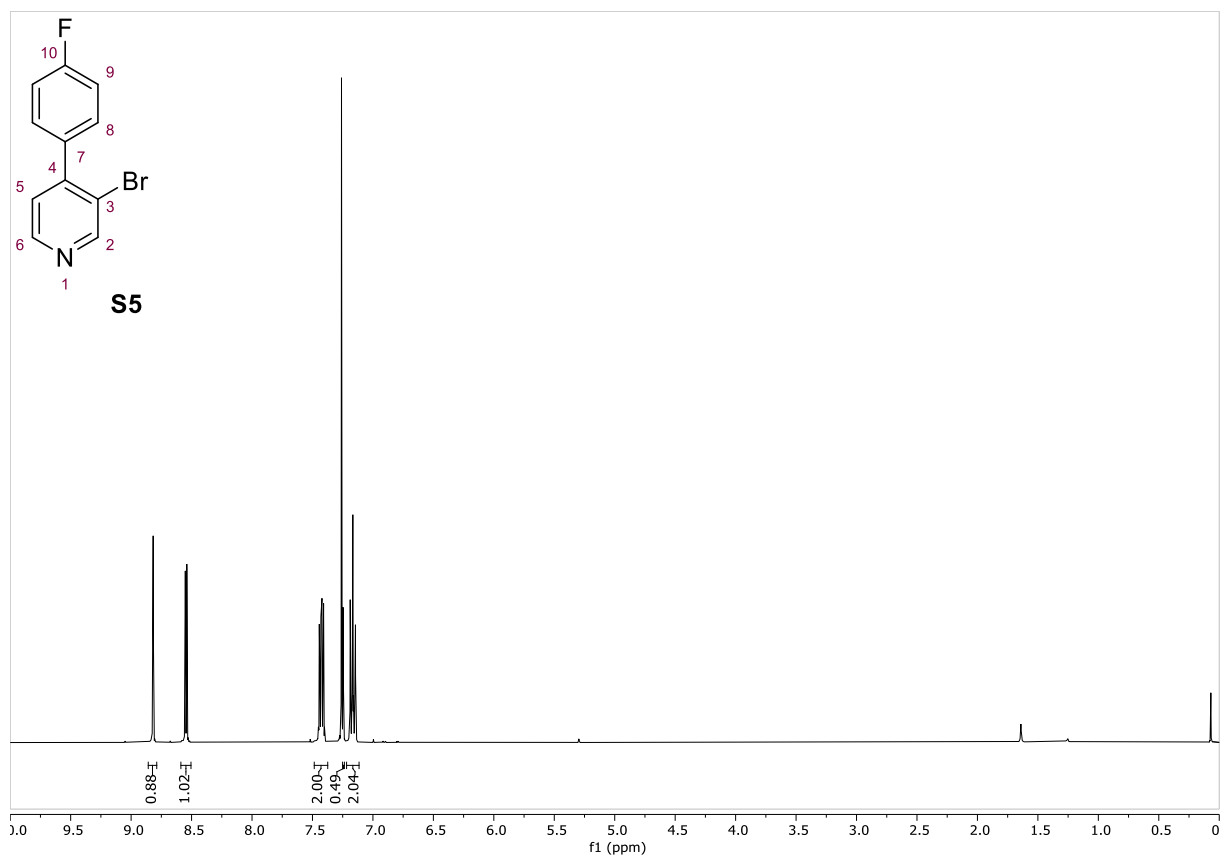
NMR Spectra

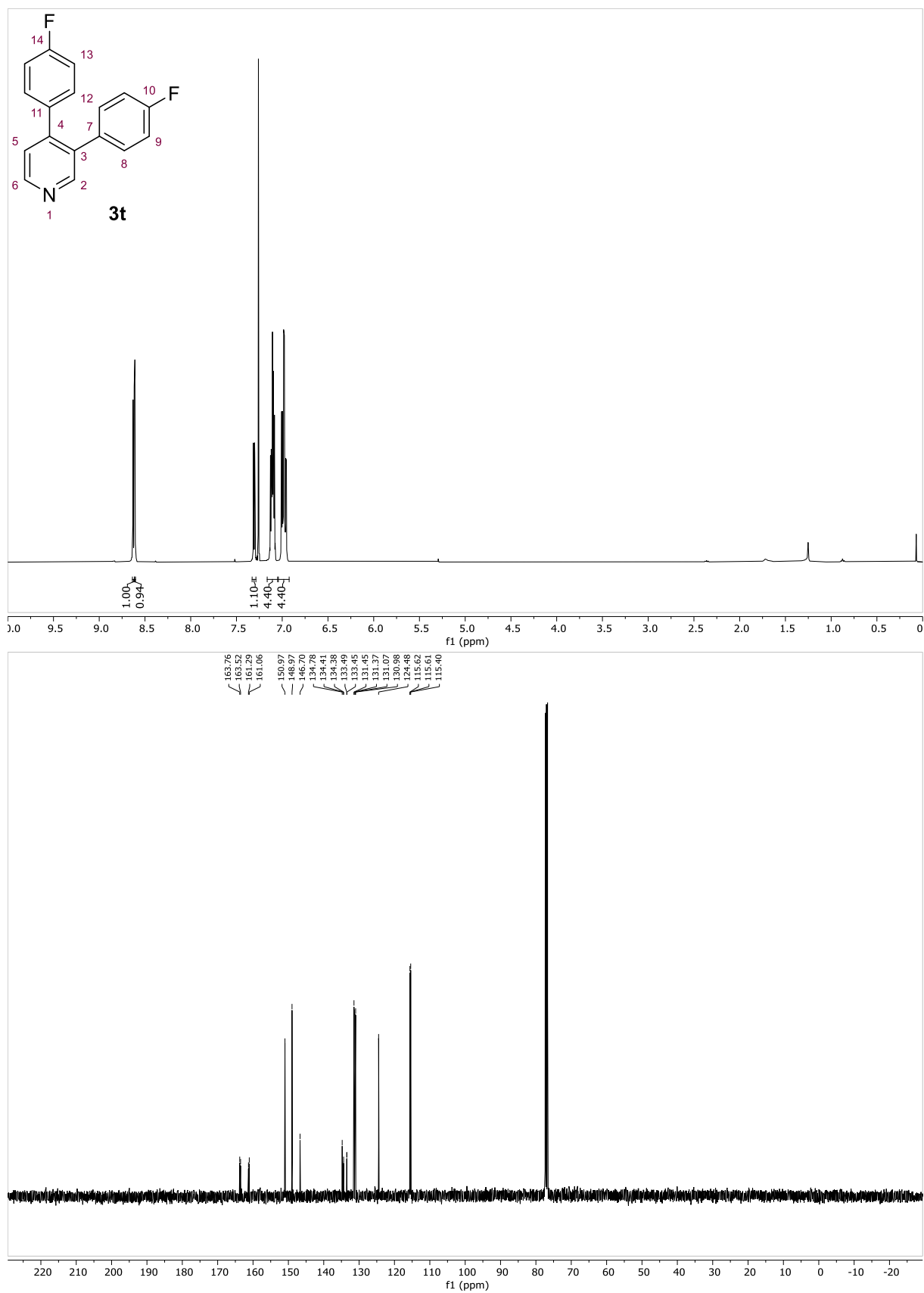


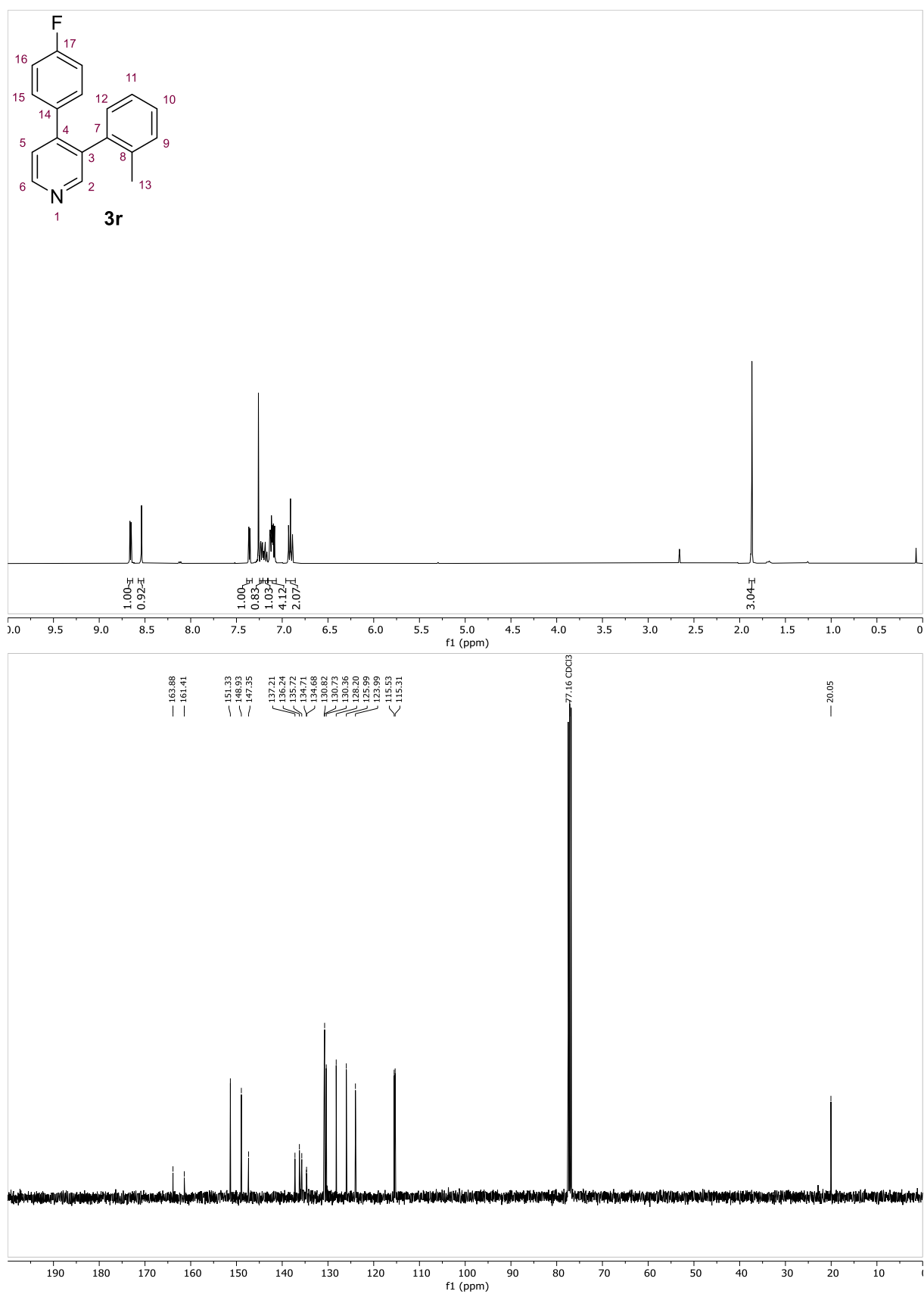


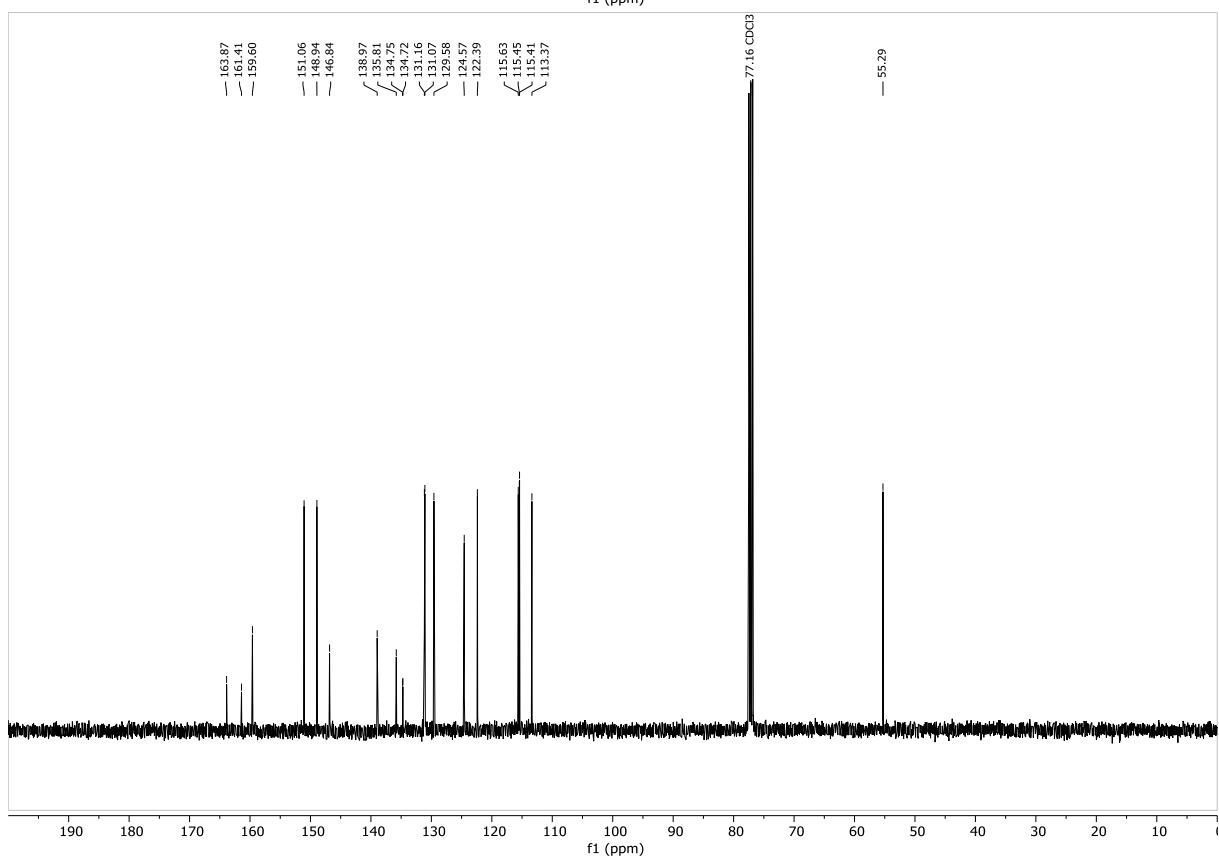
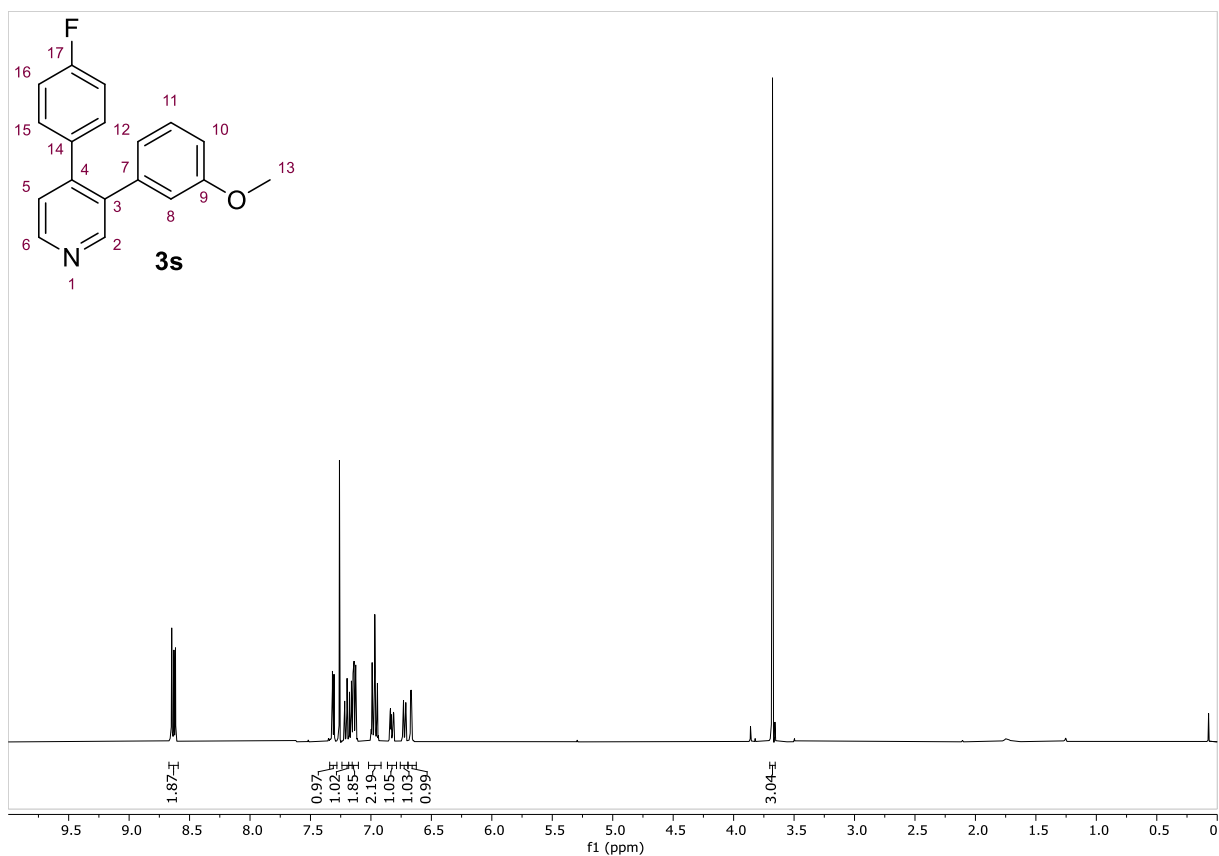


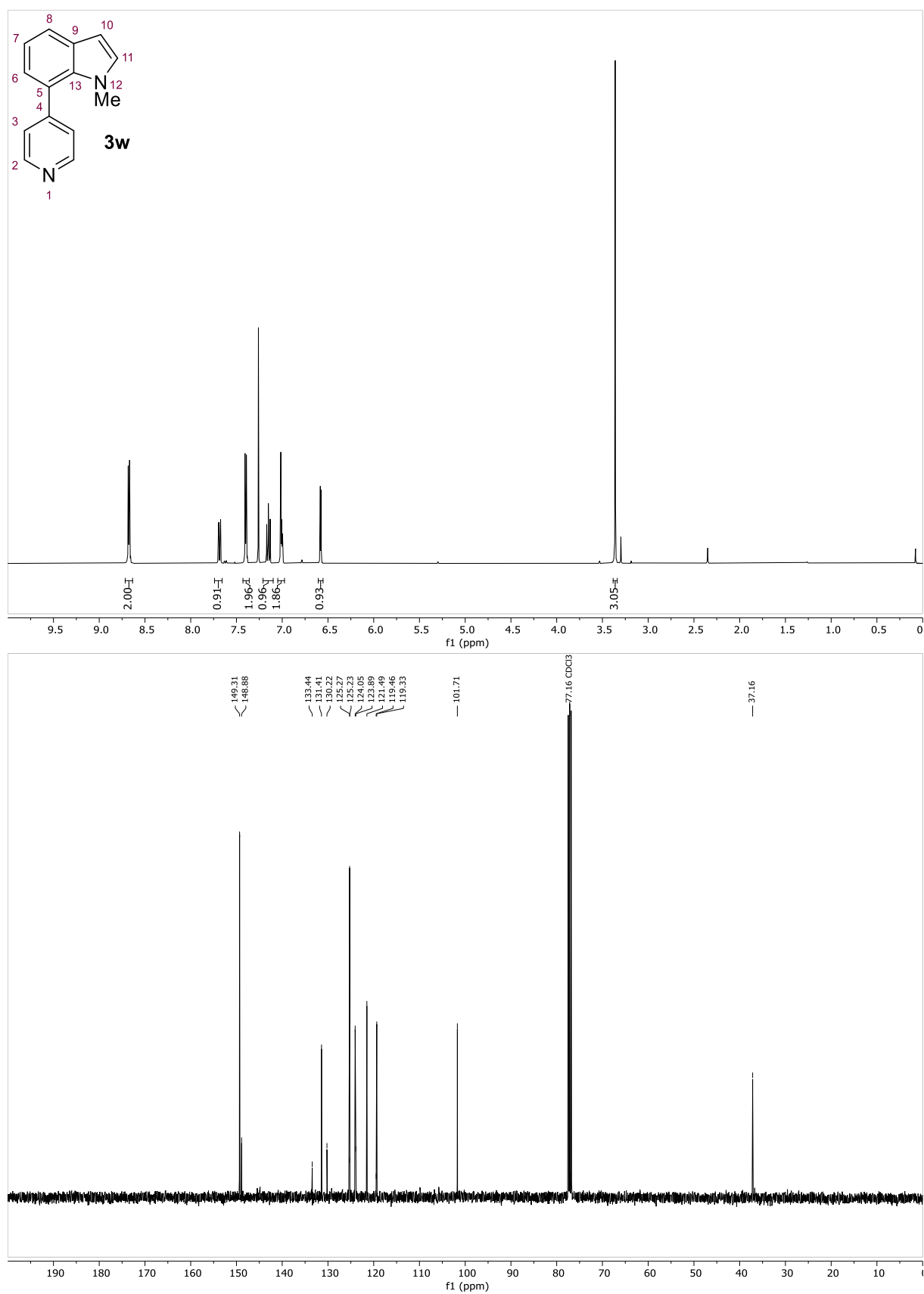


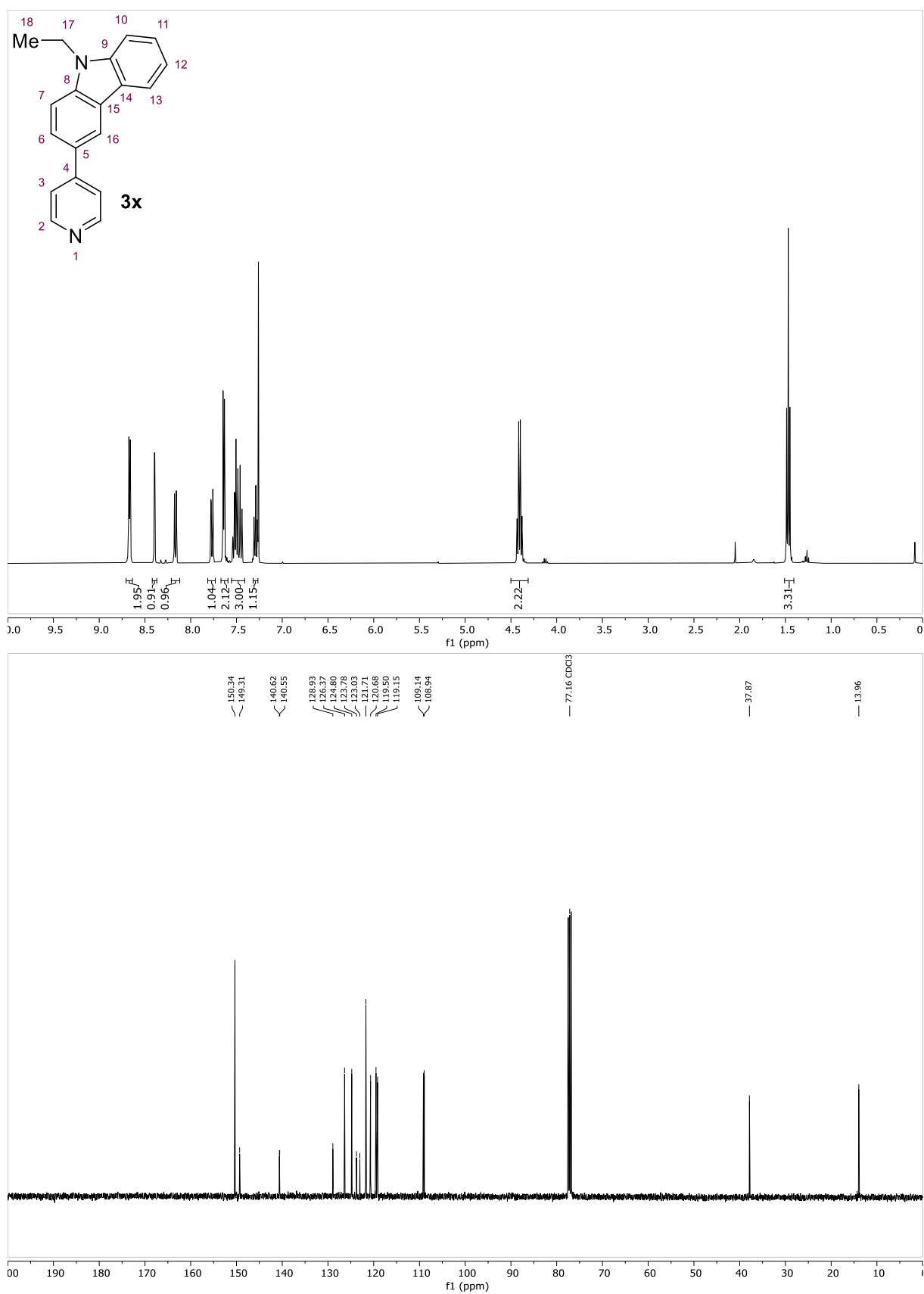


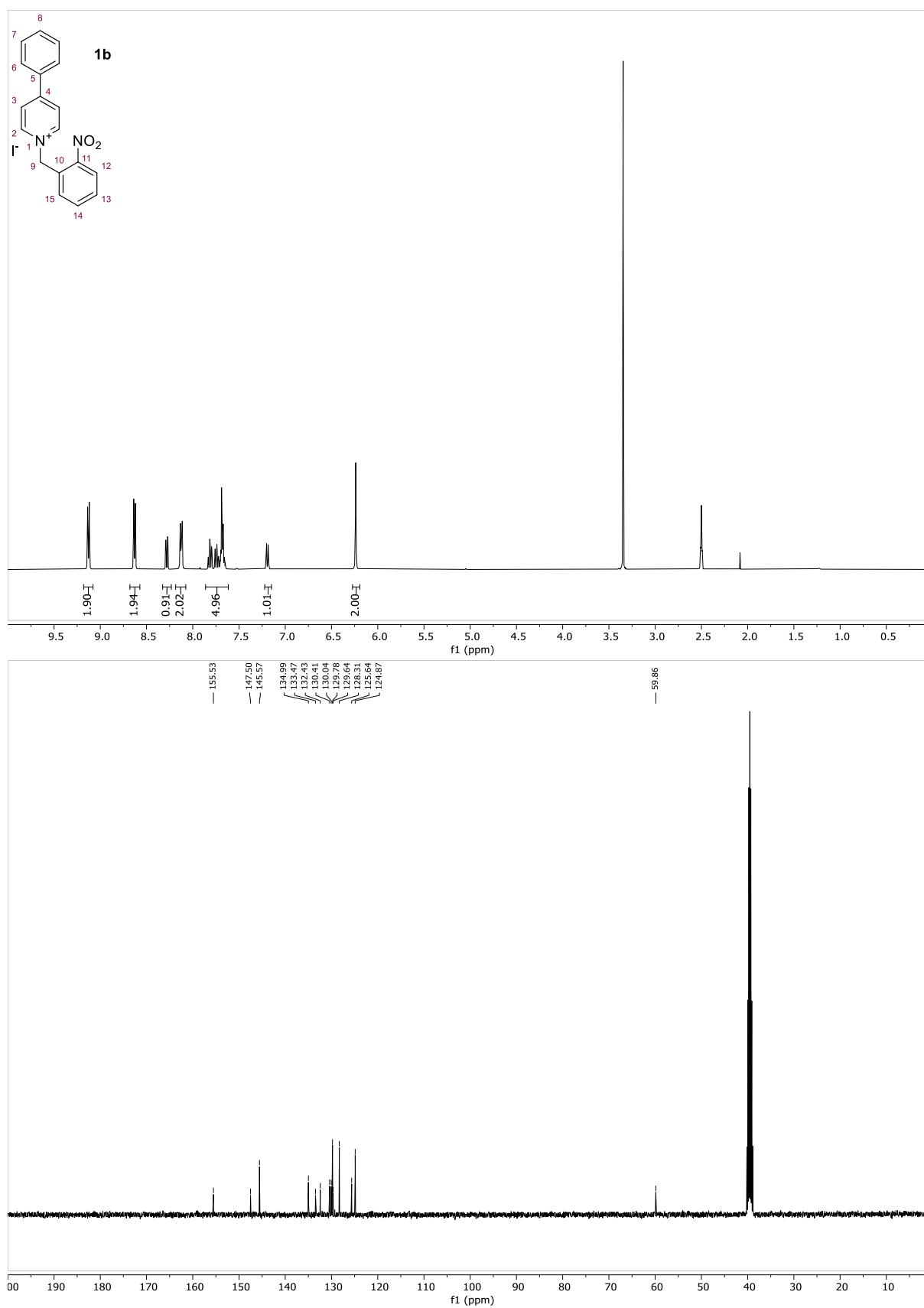


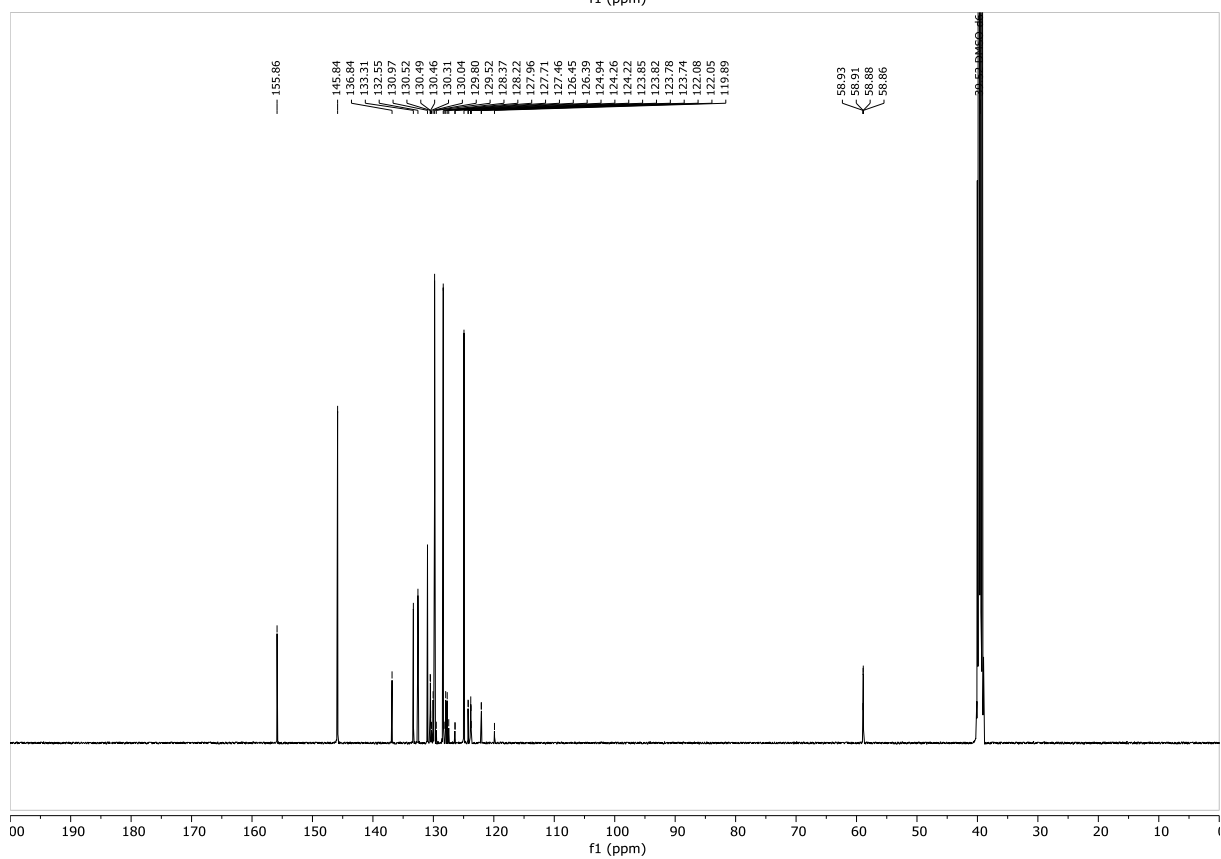
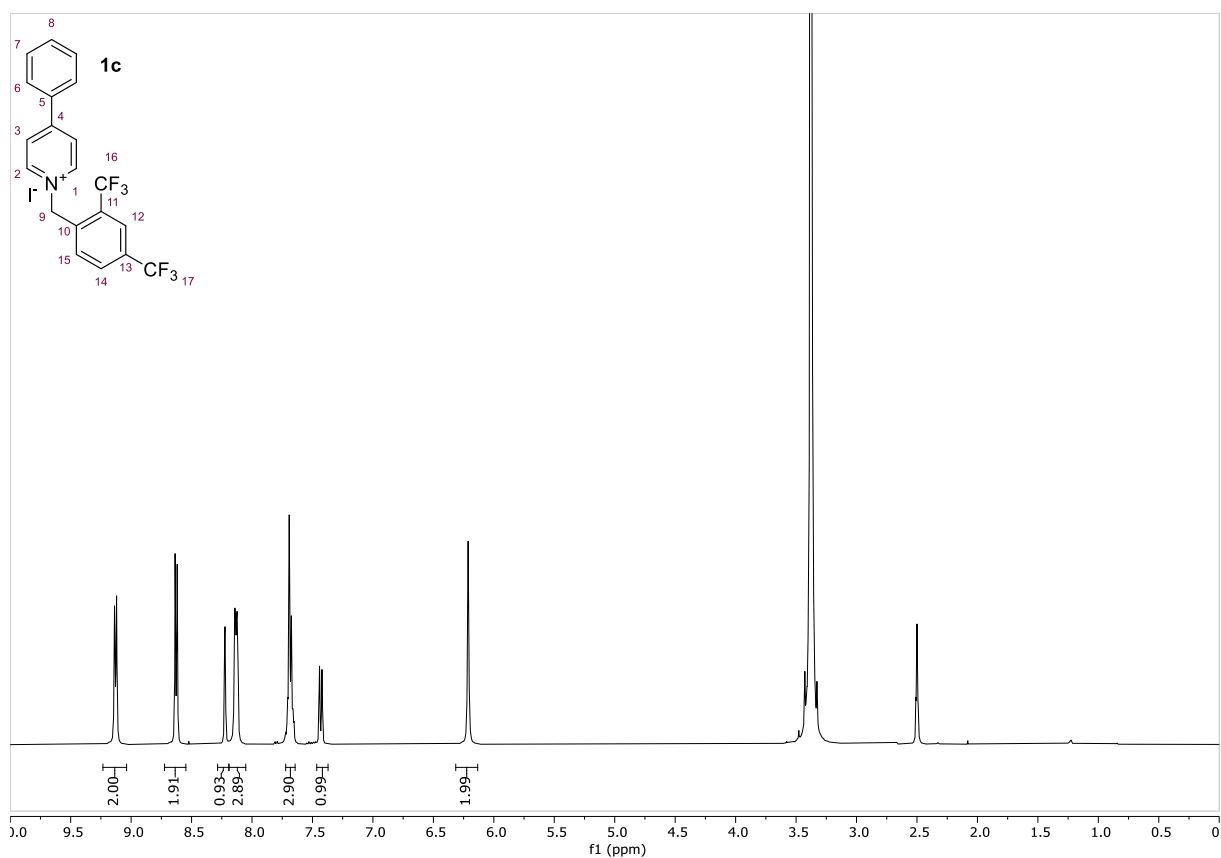


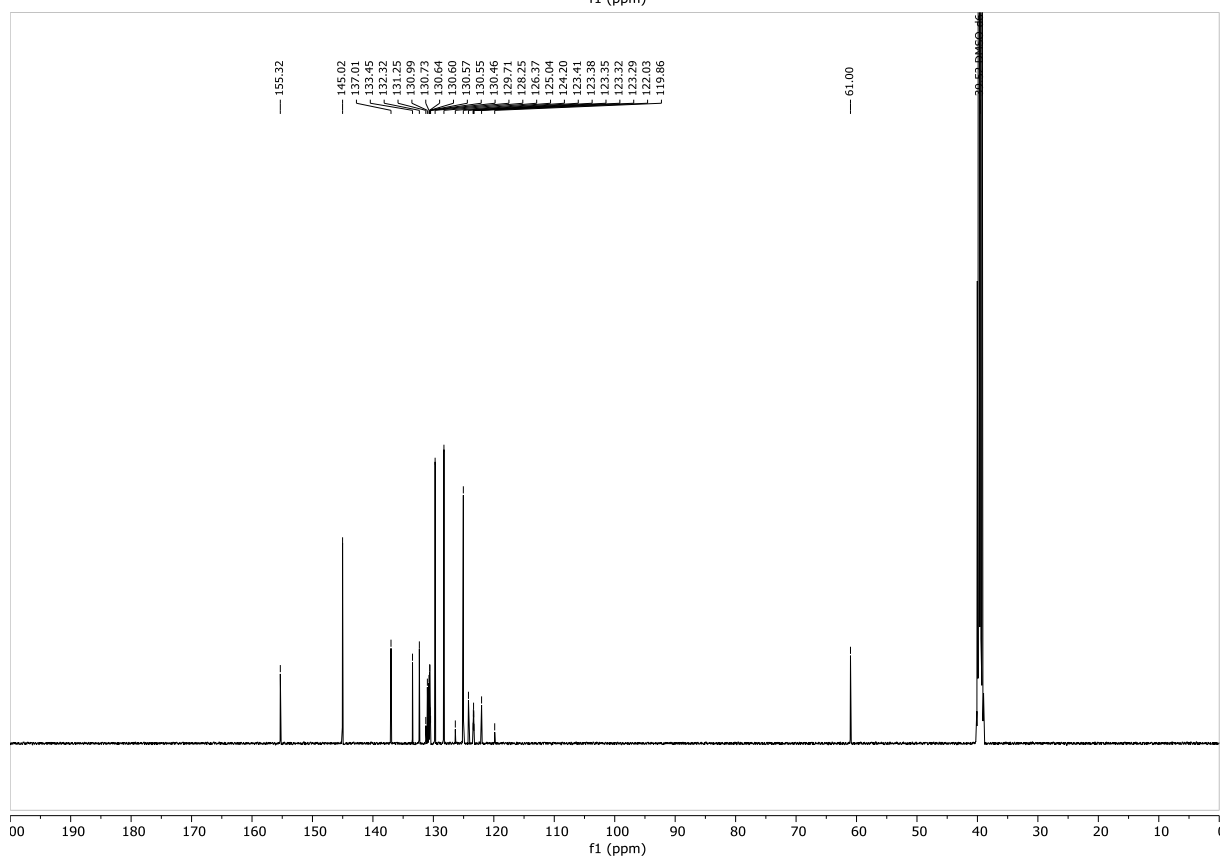
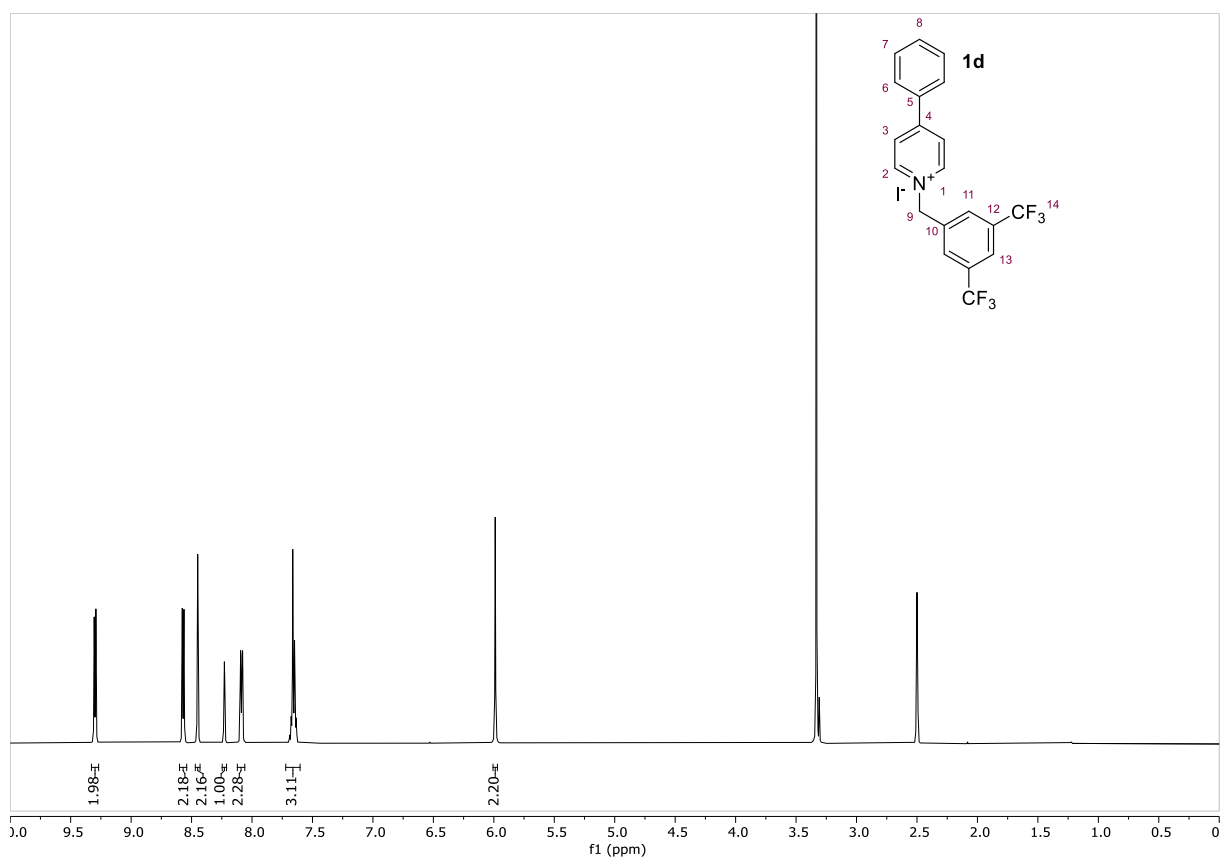


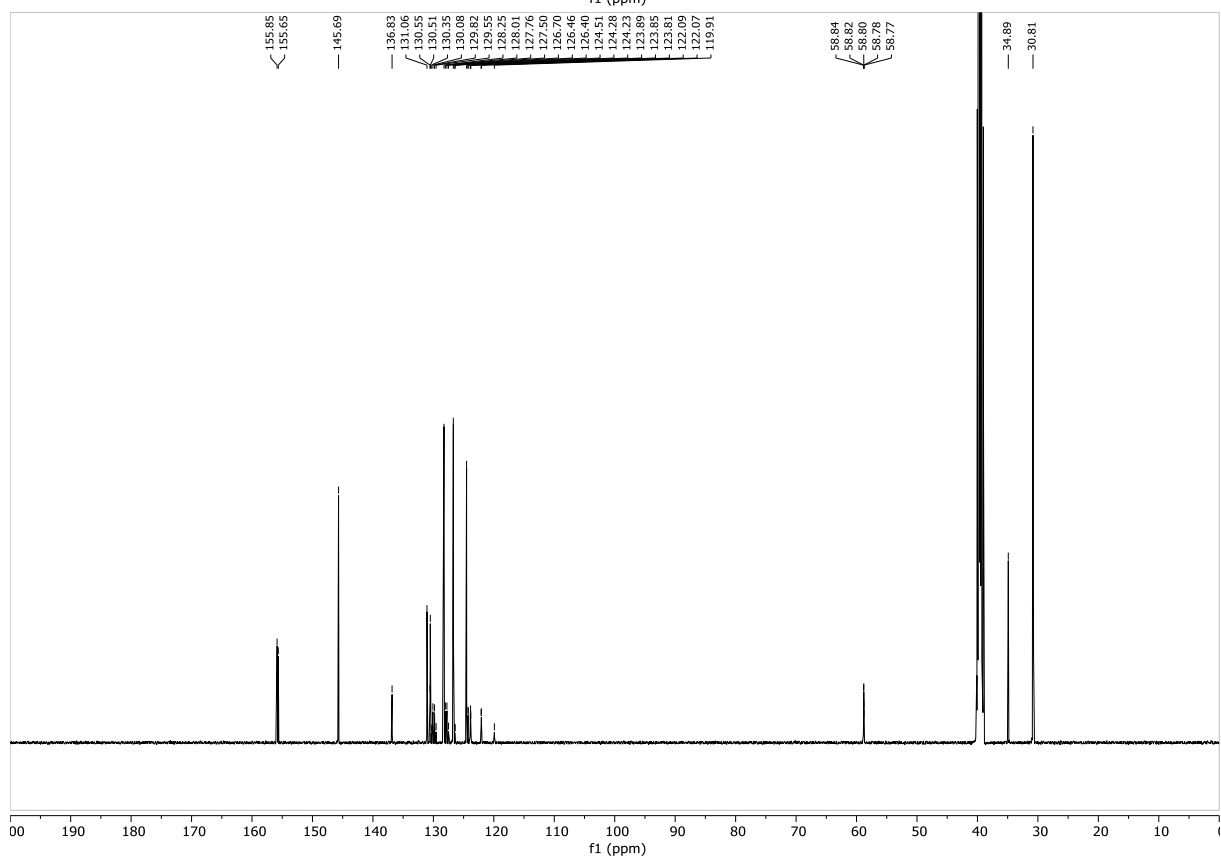
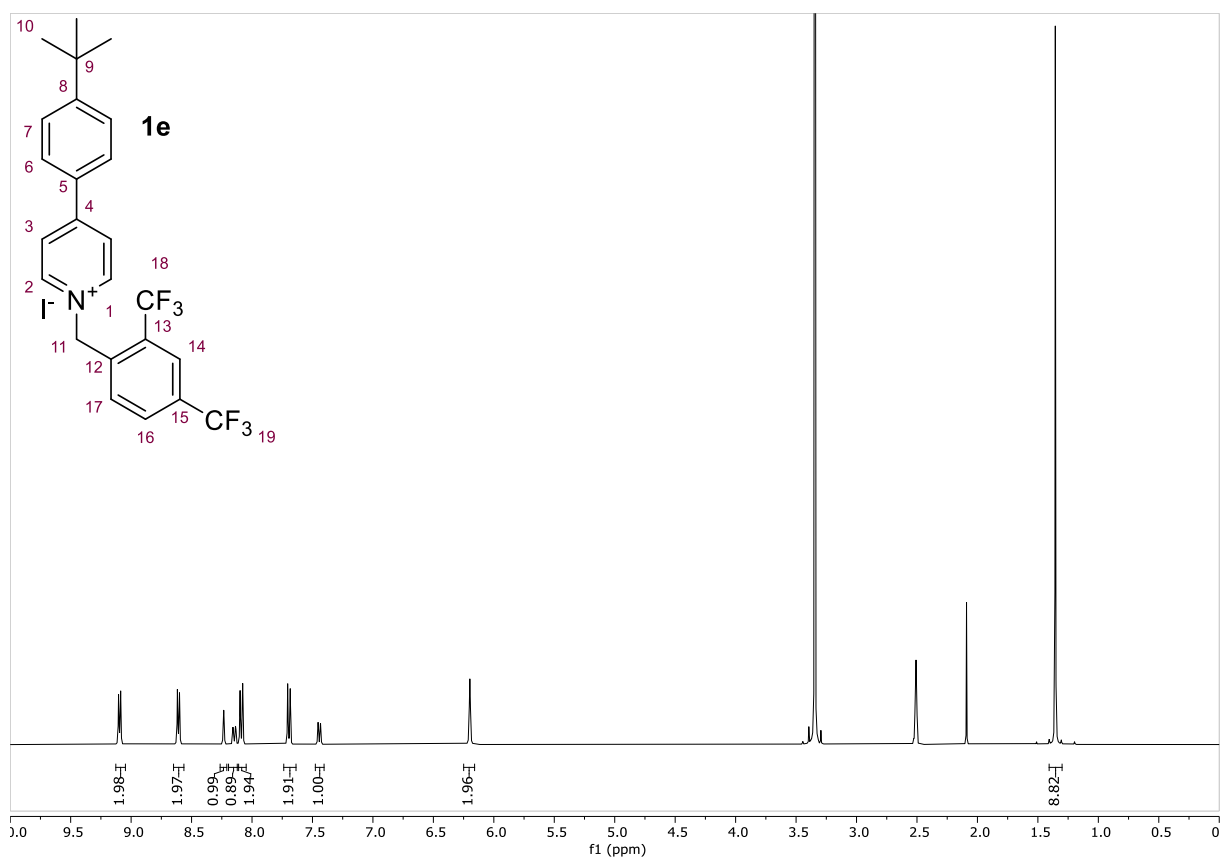


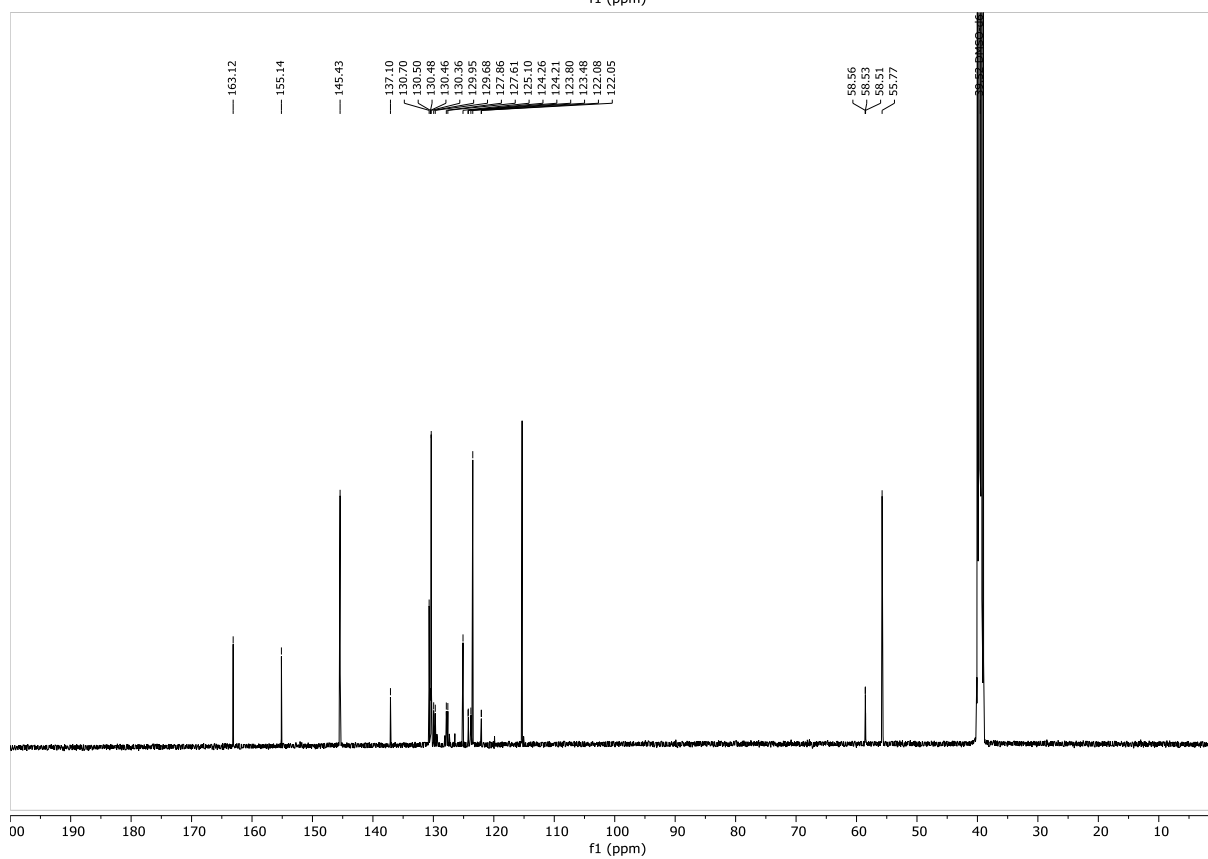
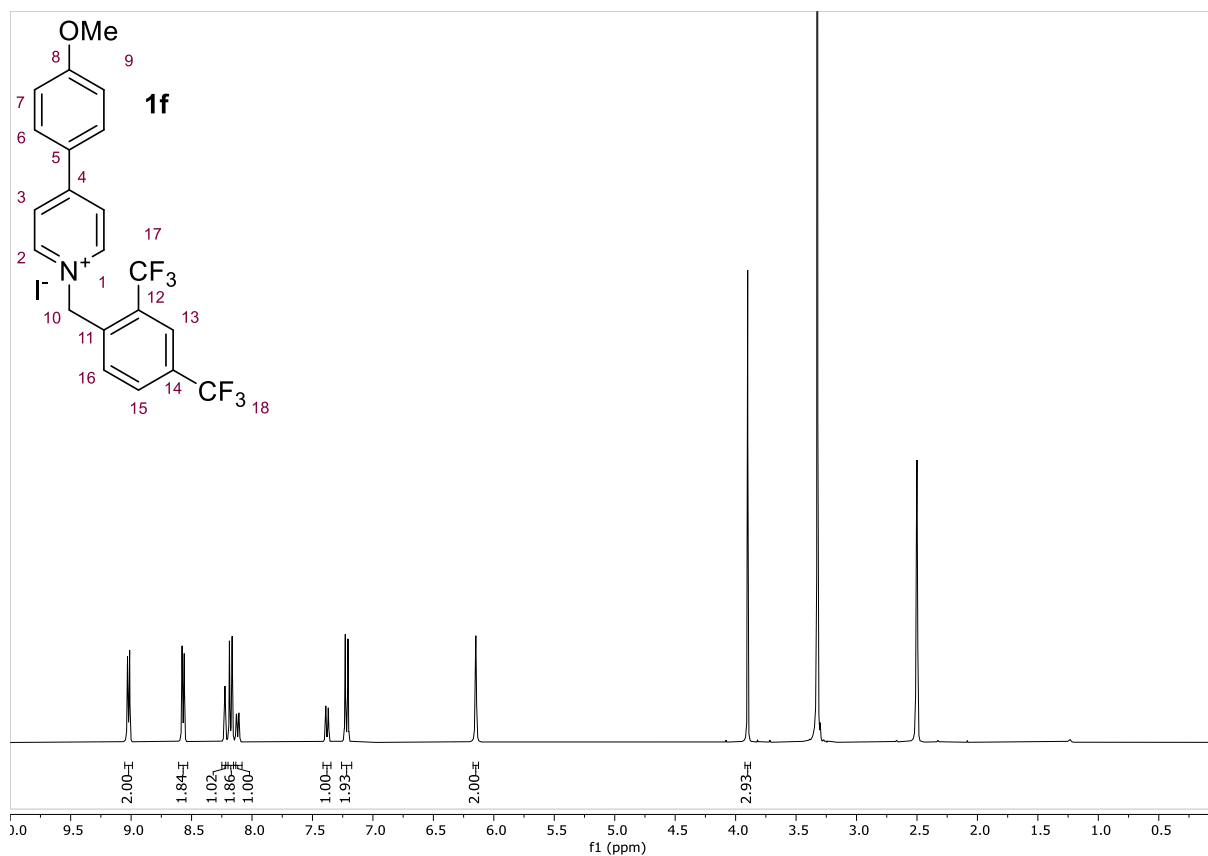


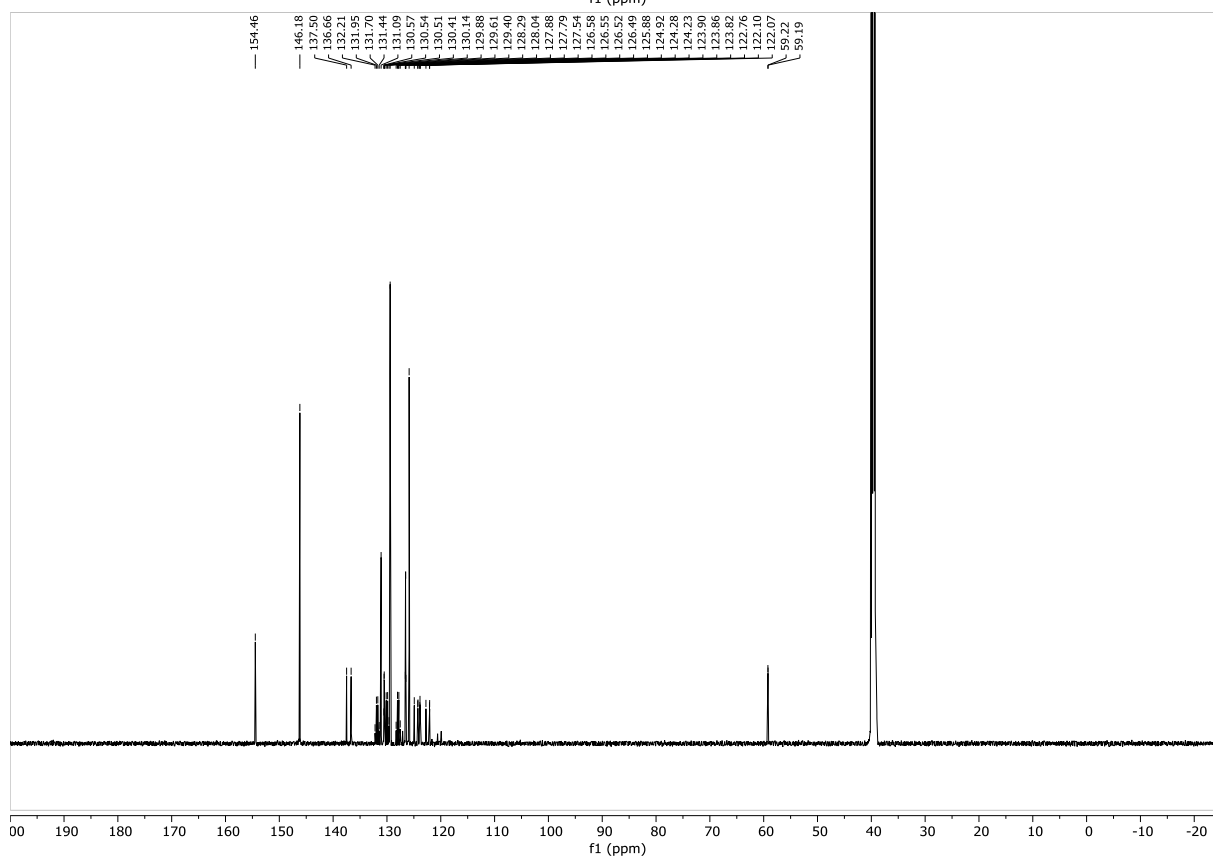
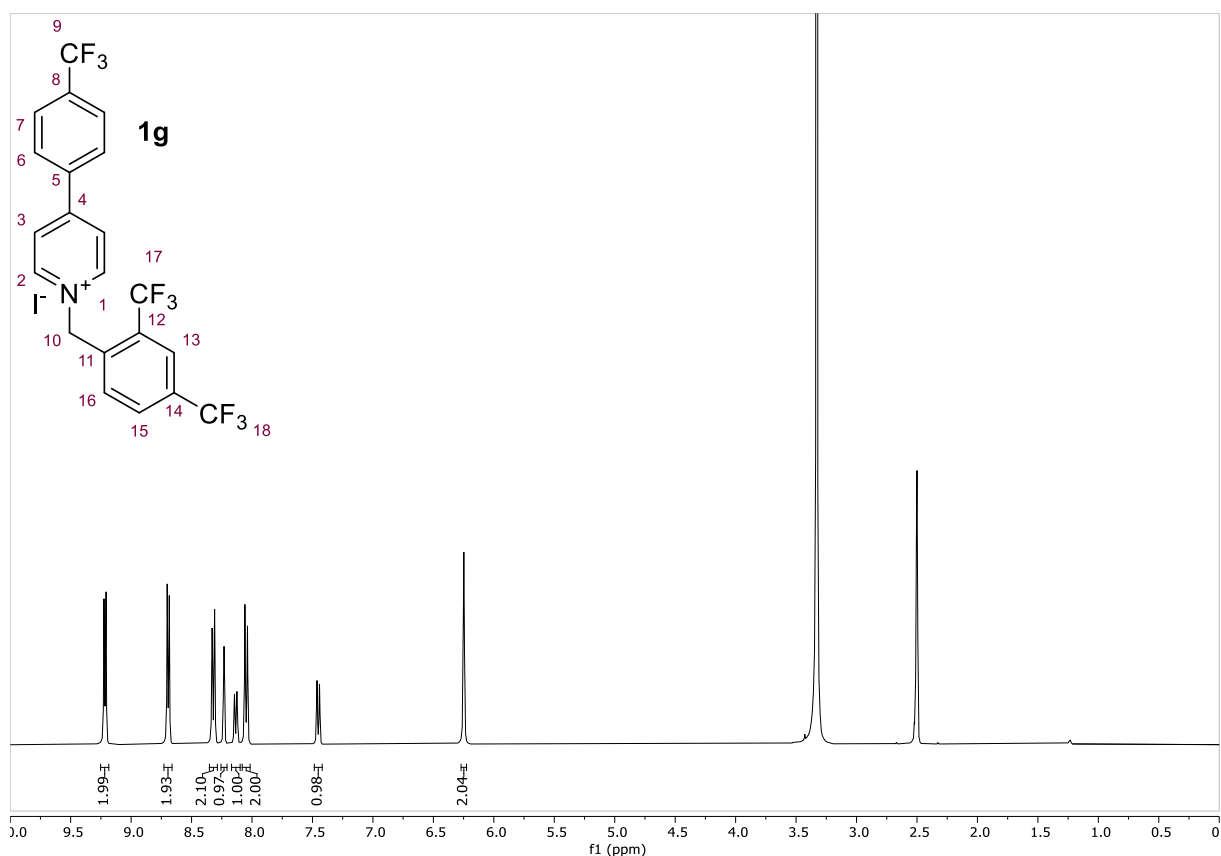


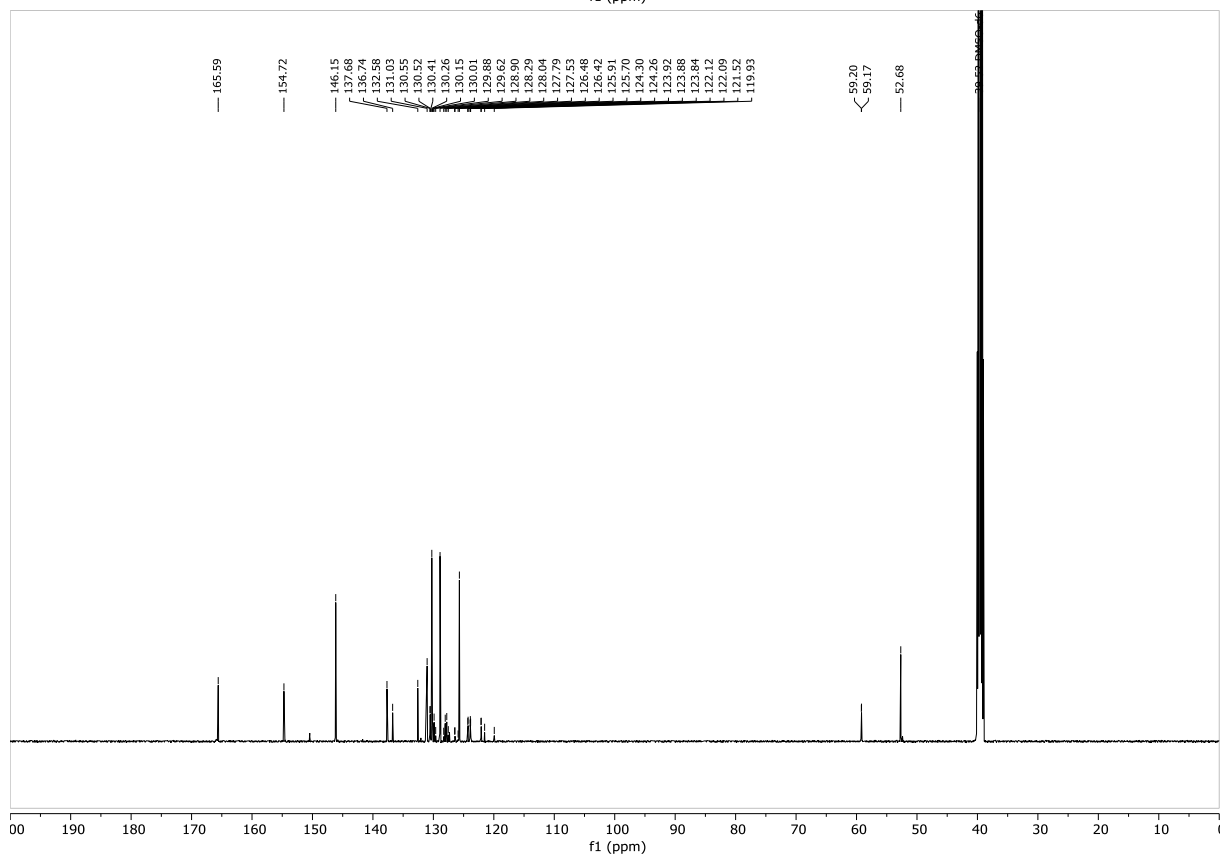
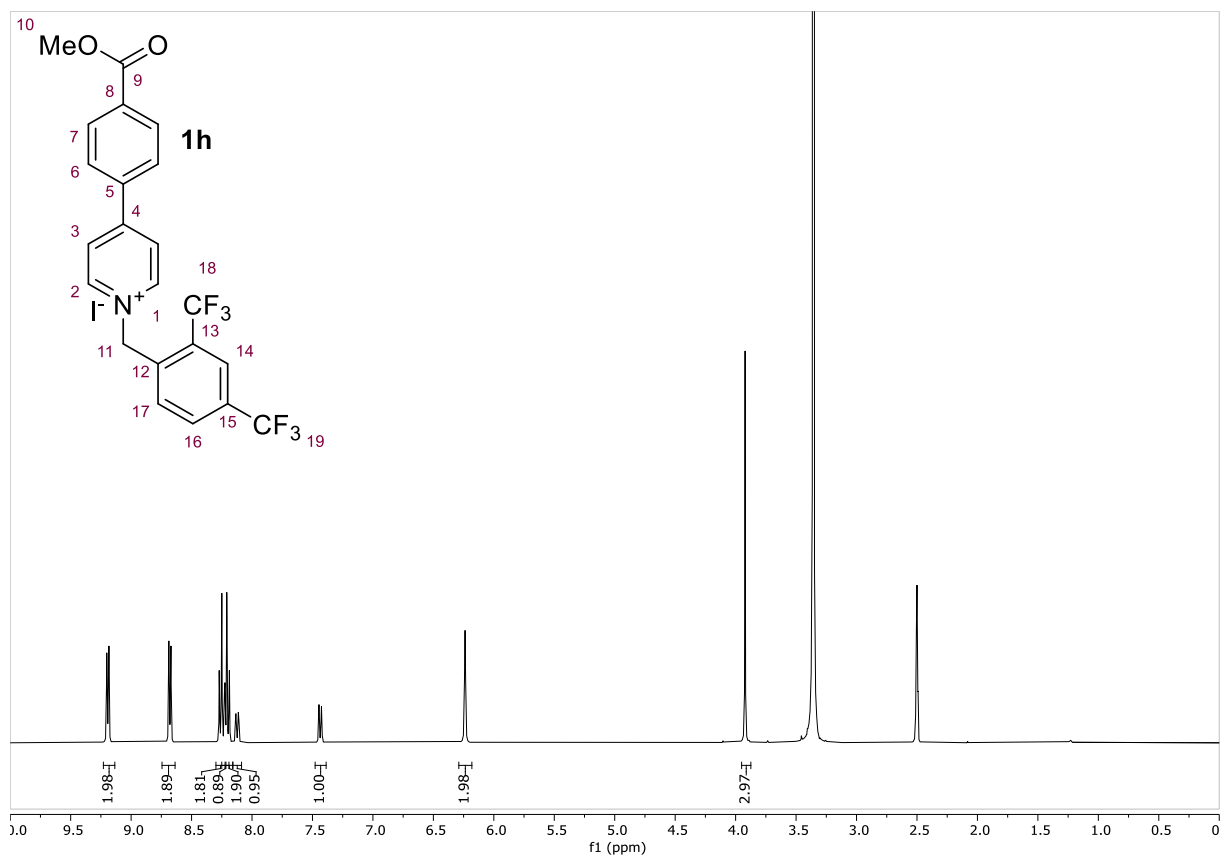


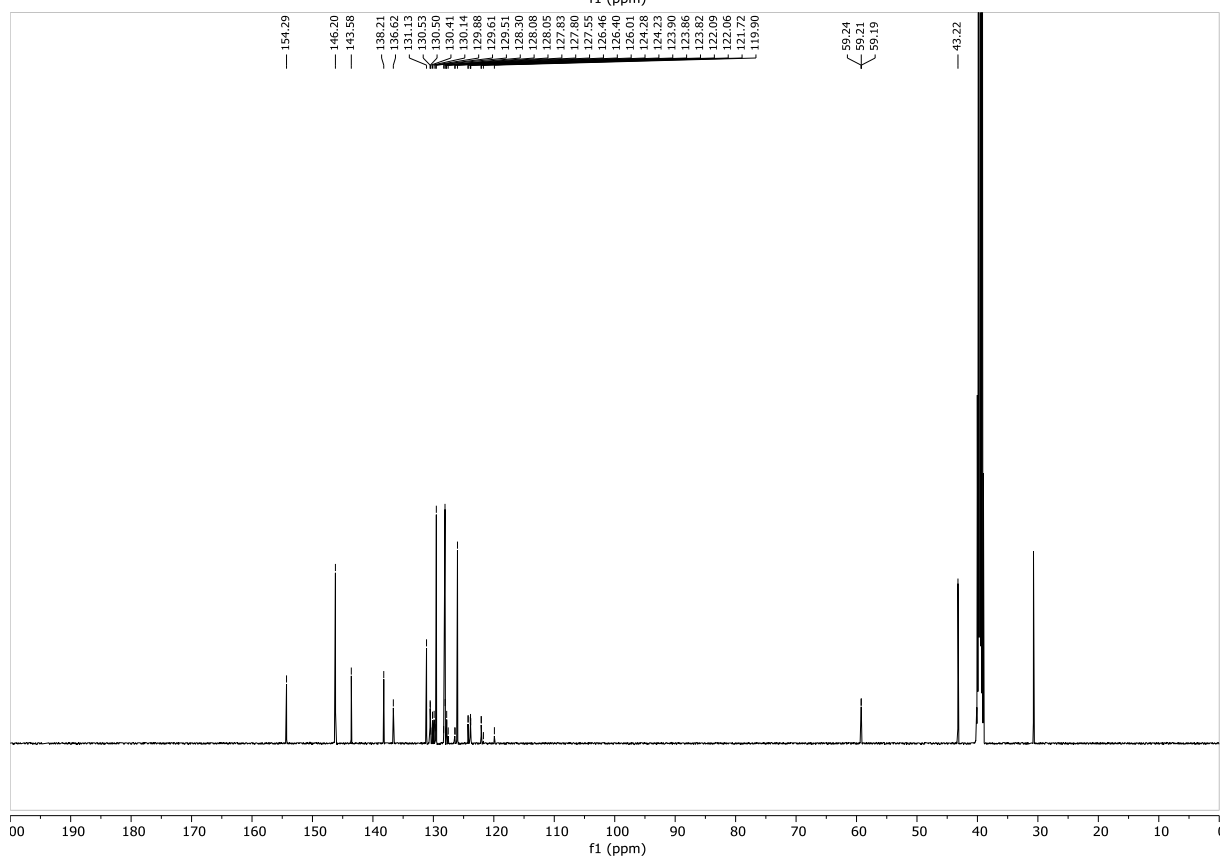
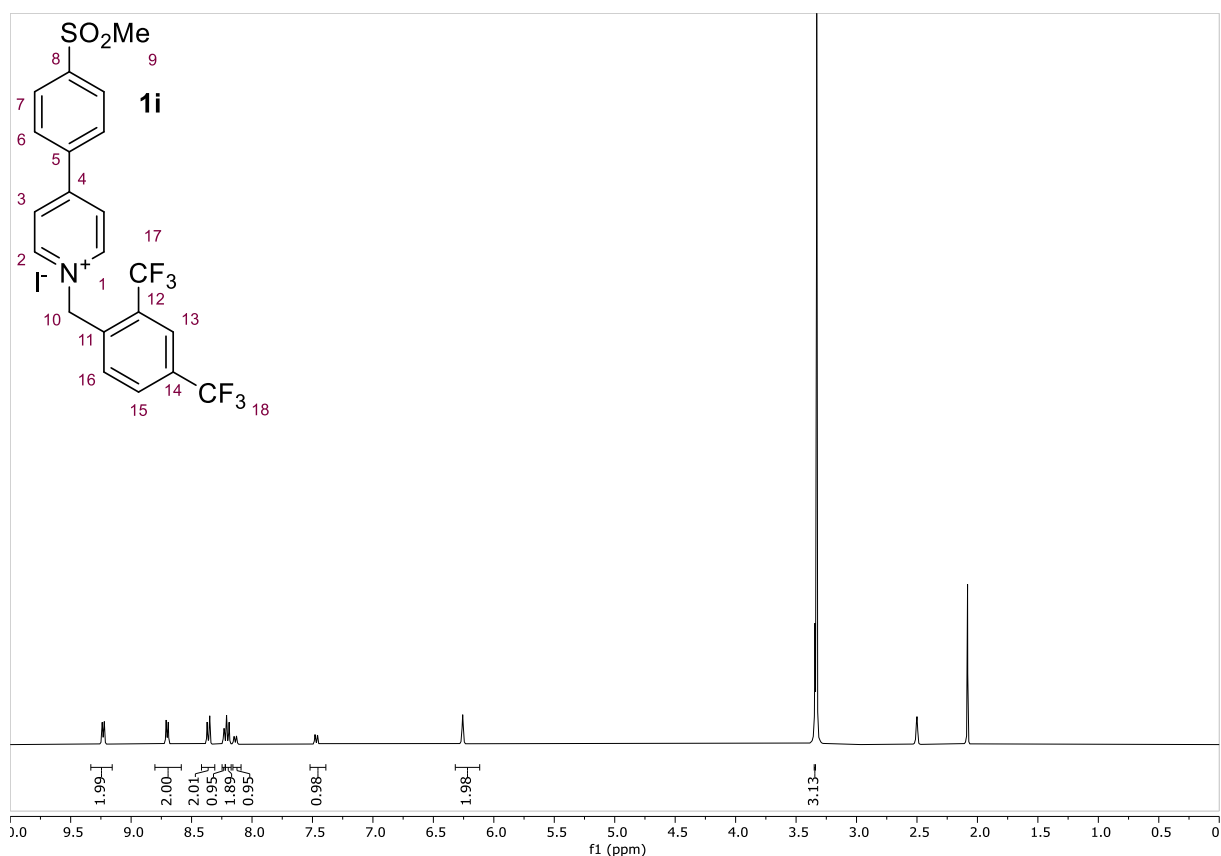


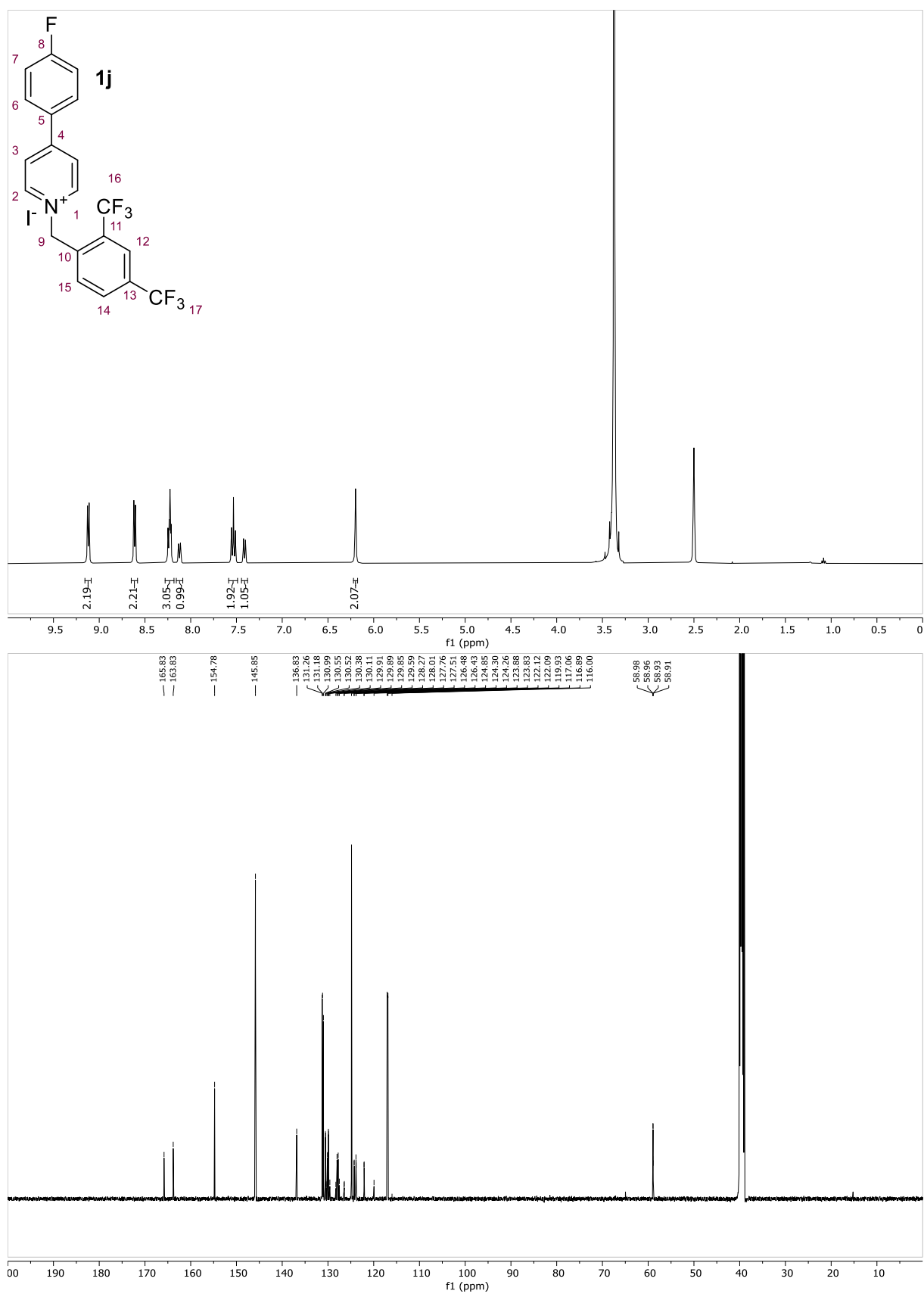


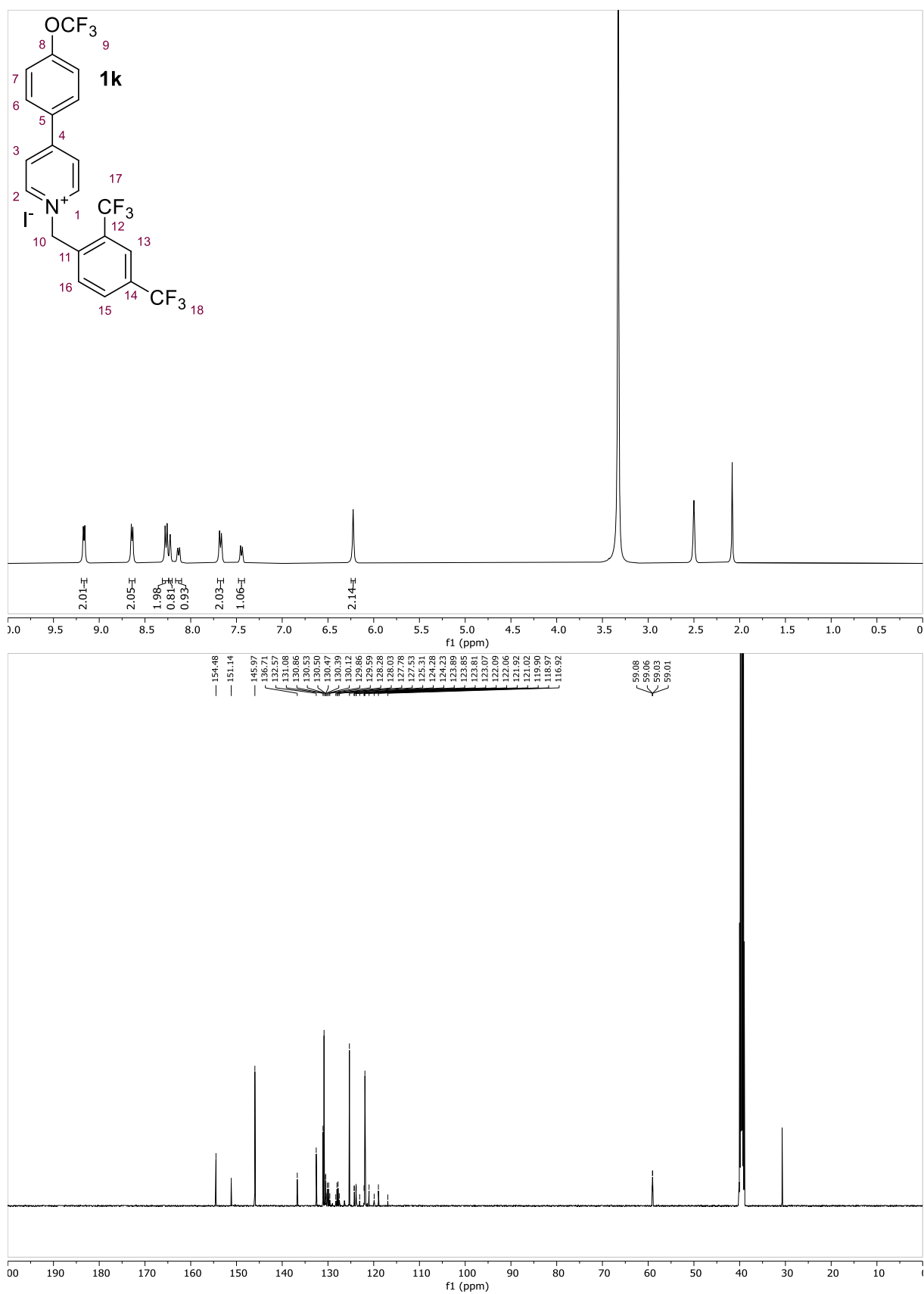


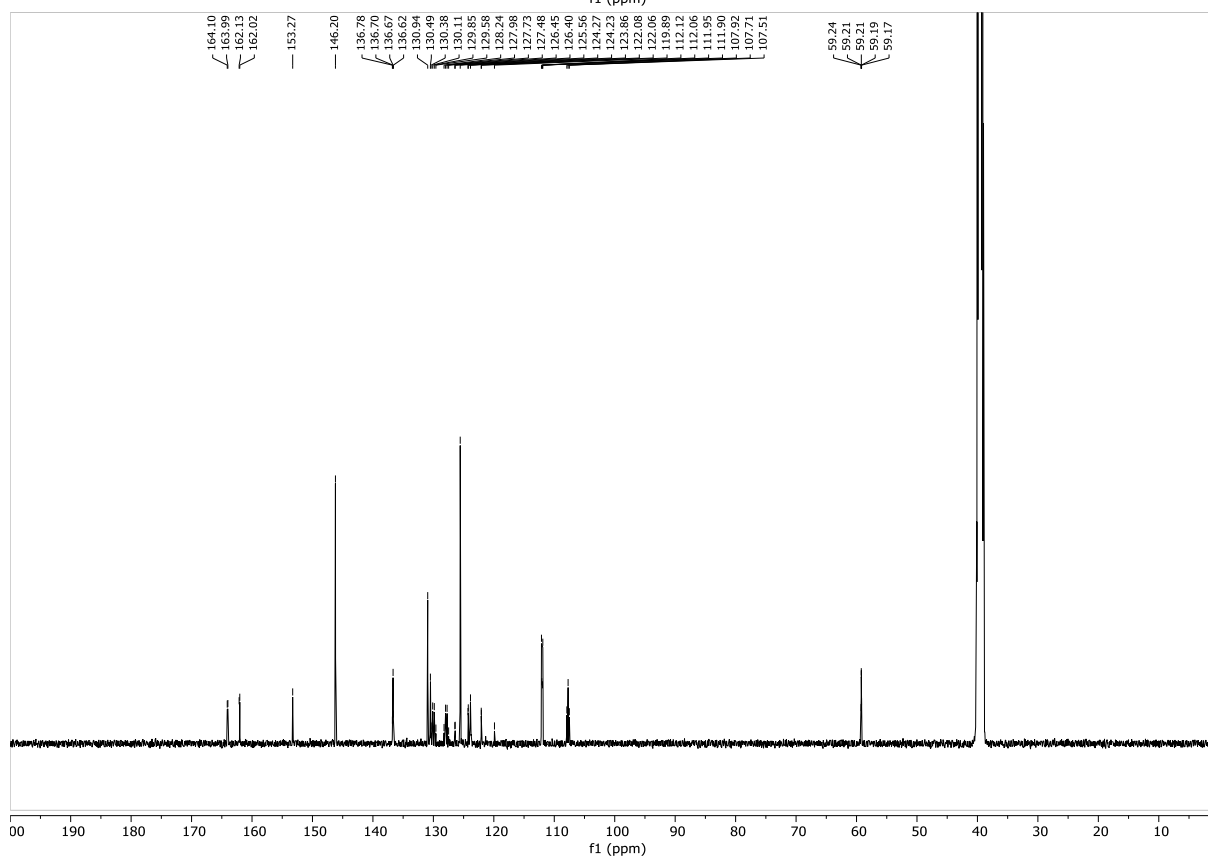
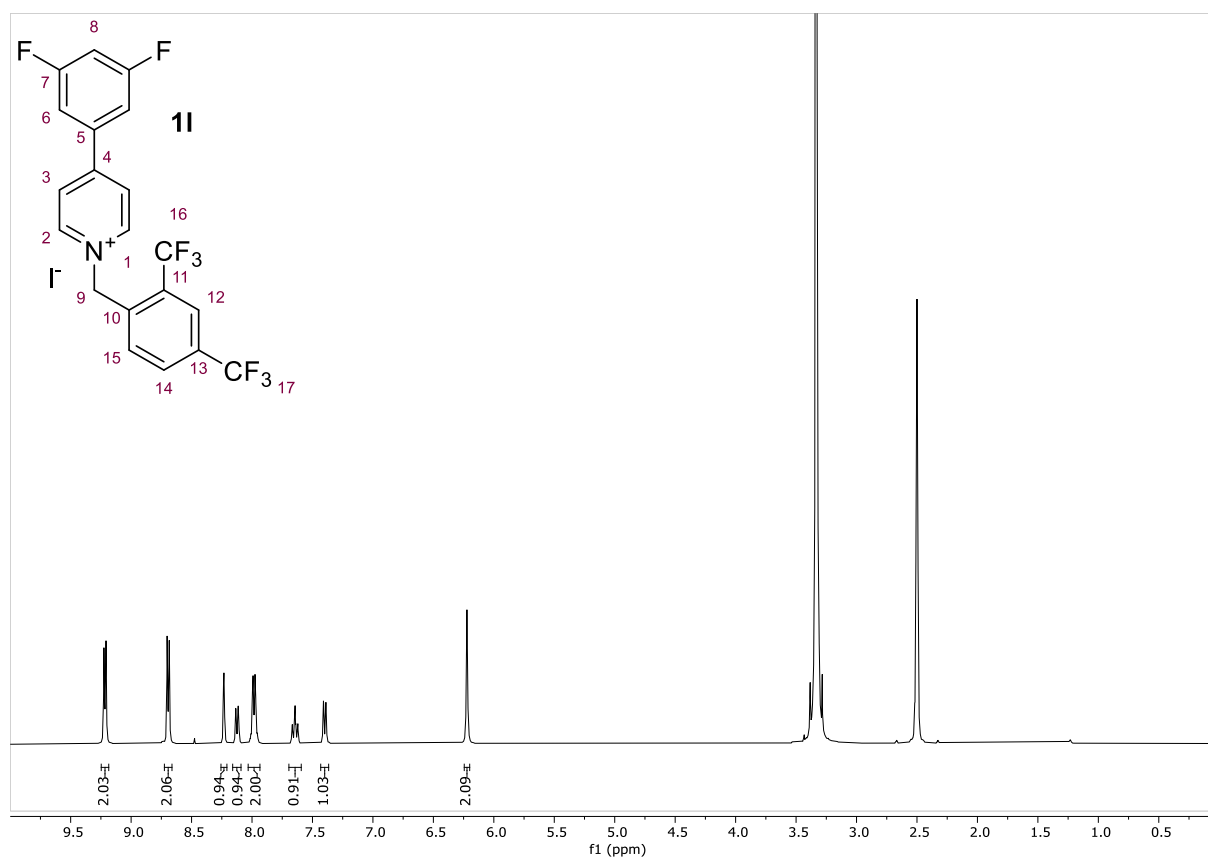


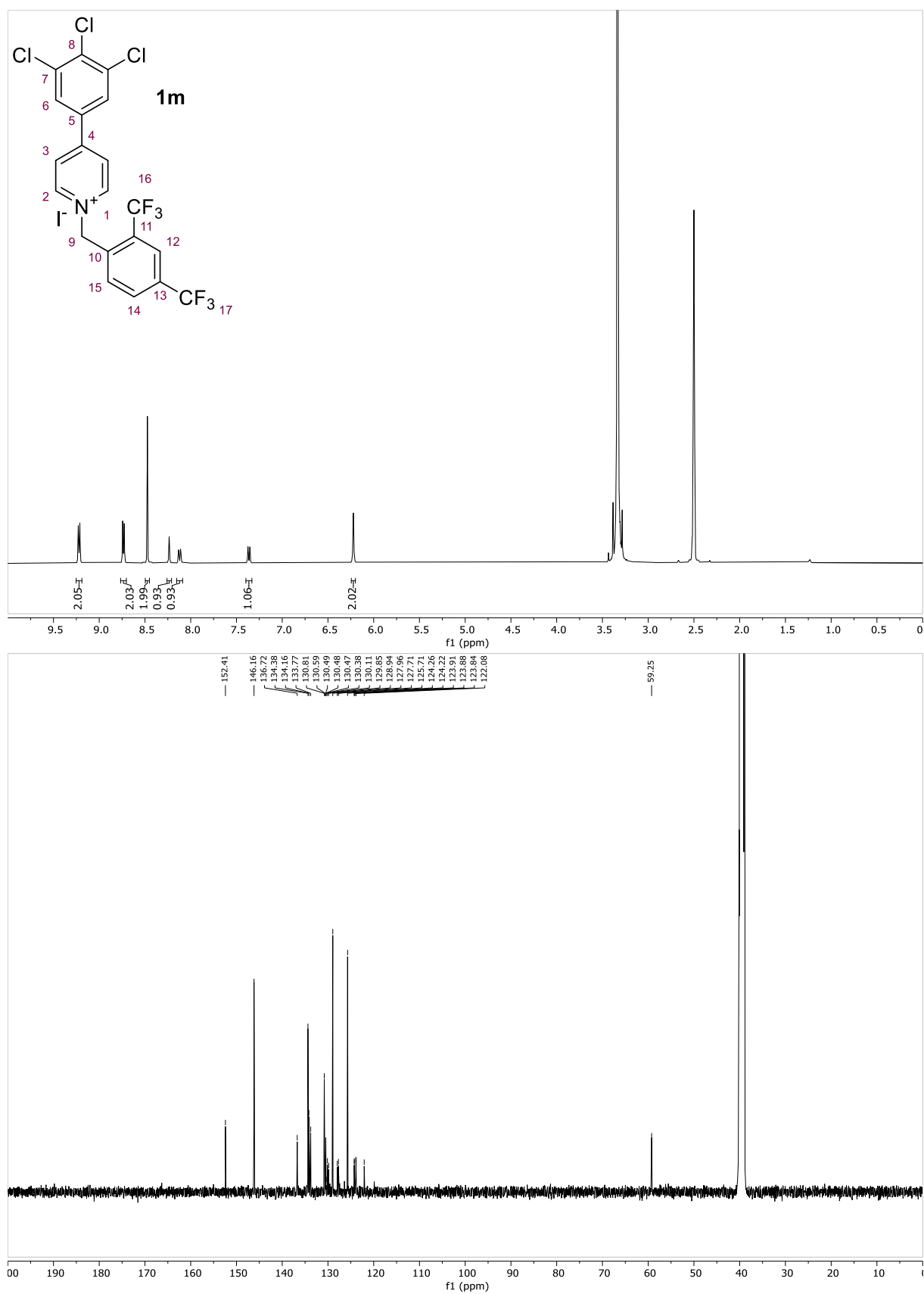


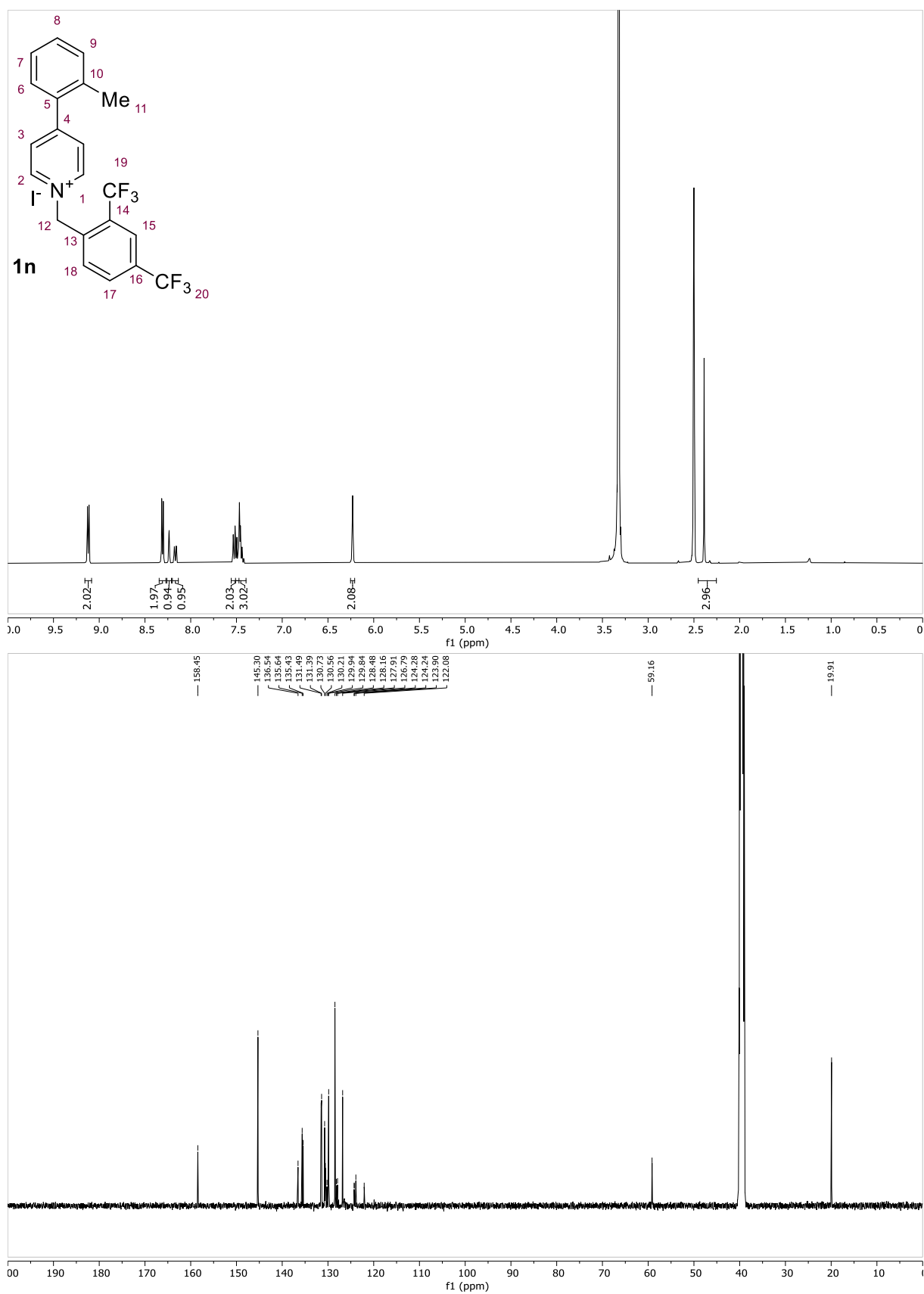


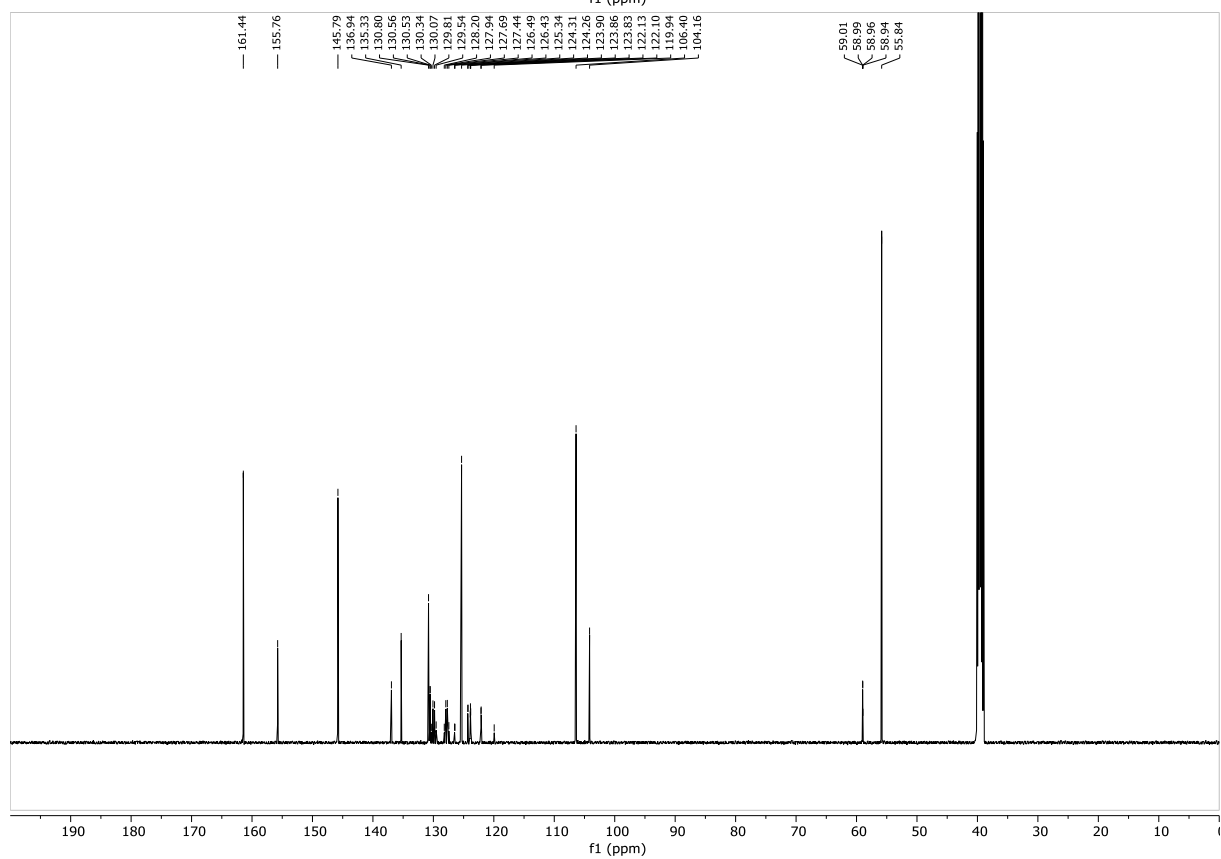
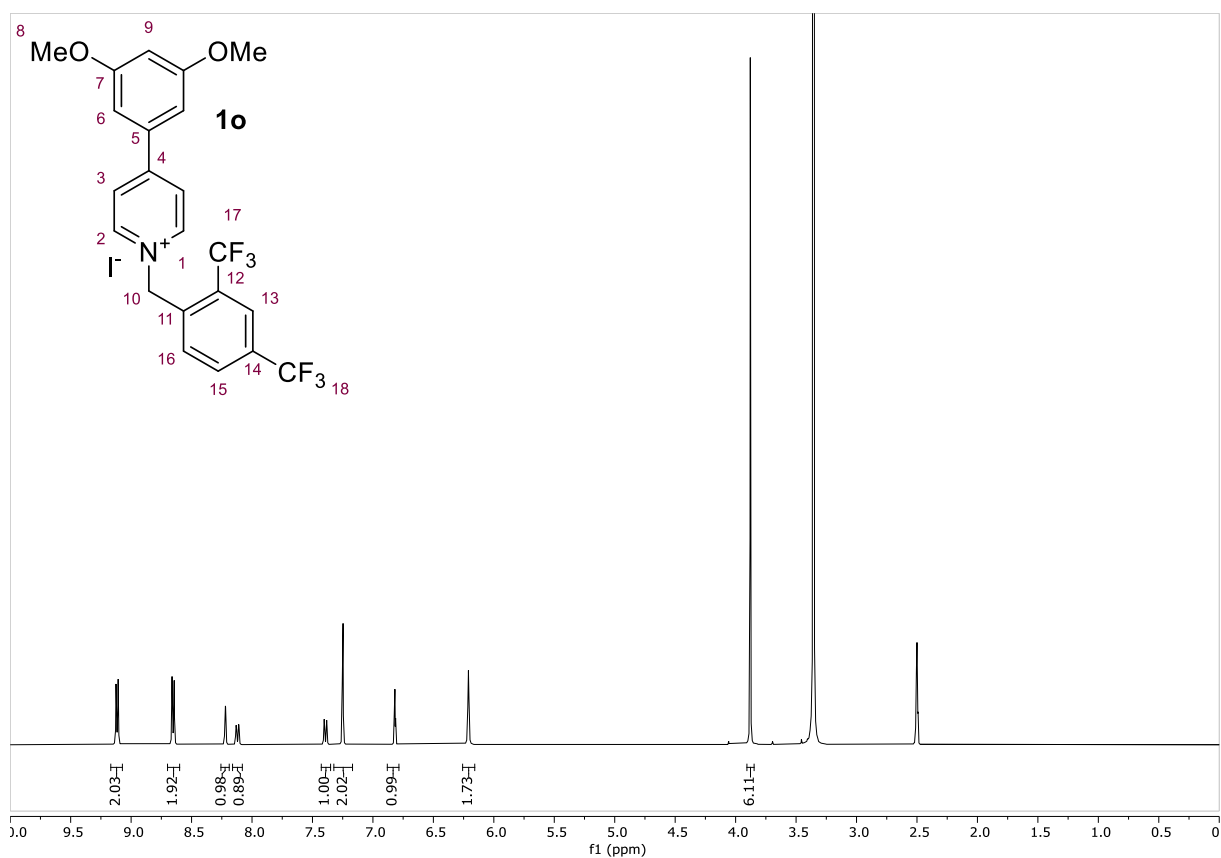


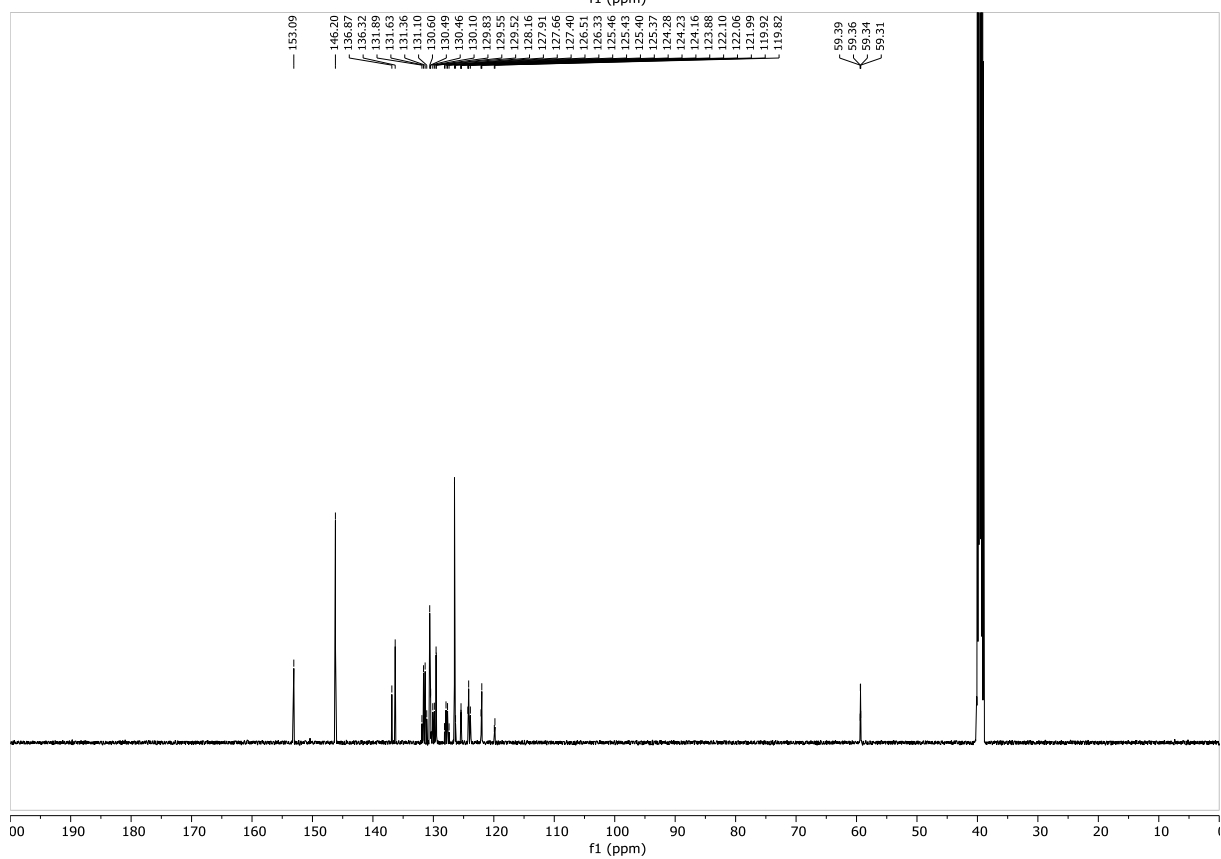


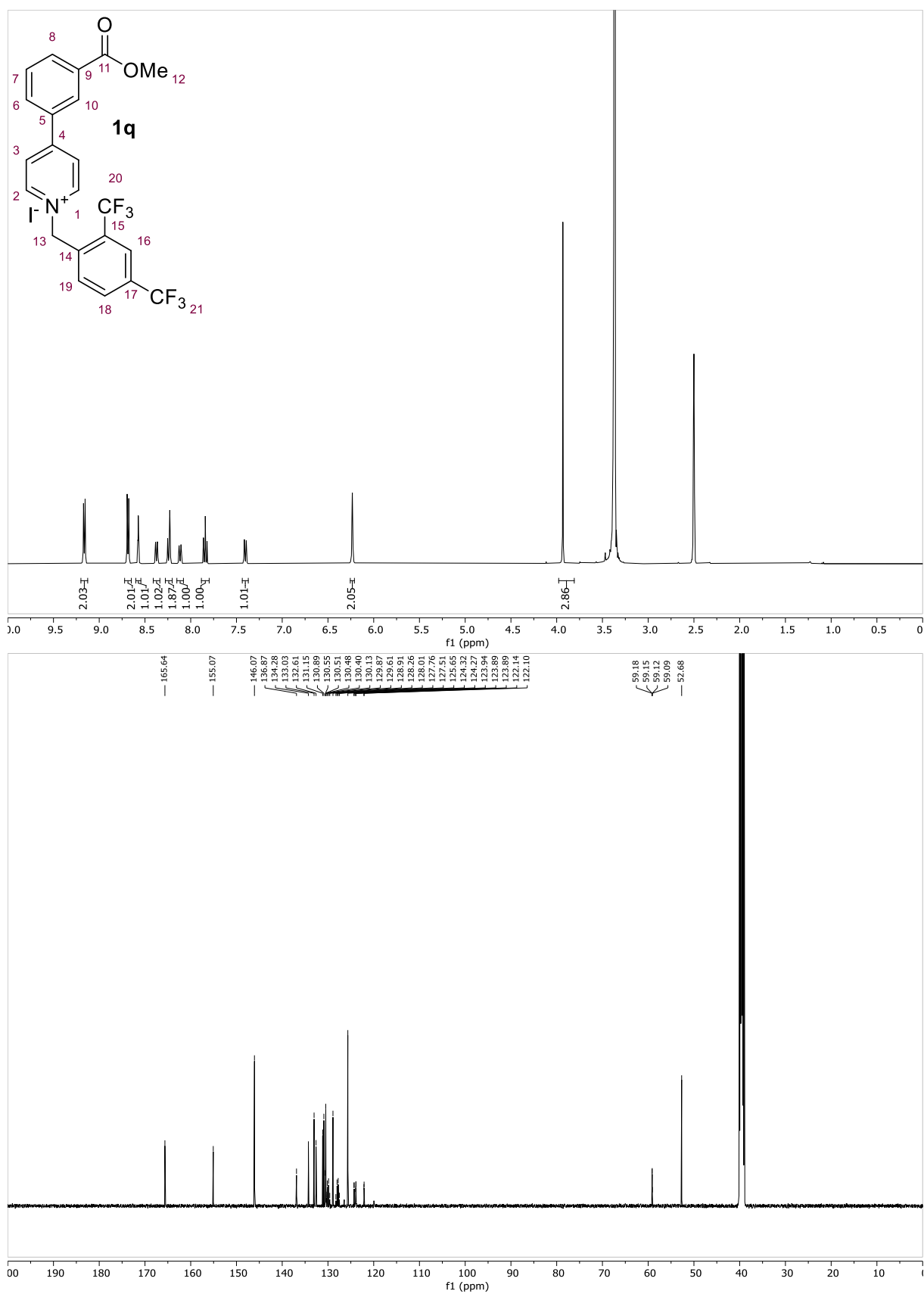


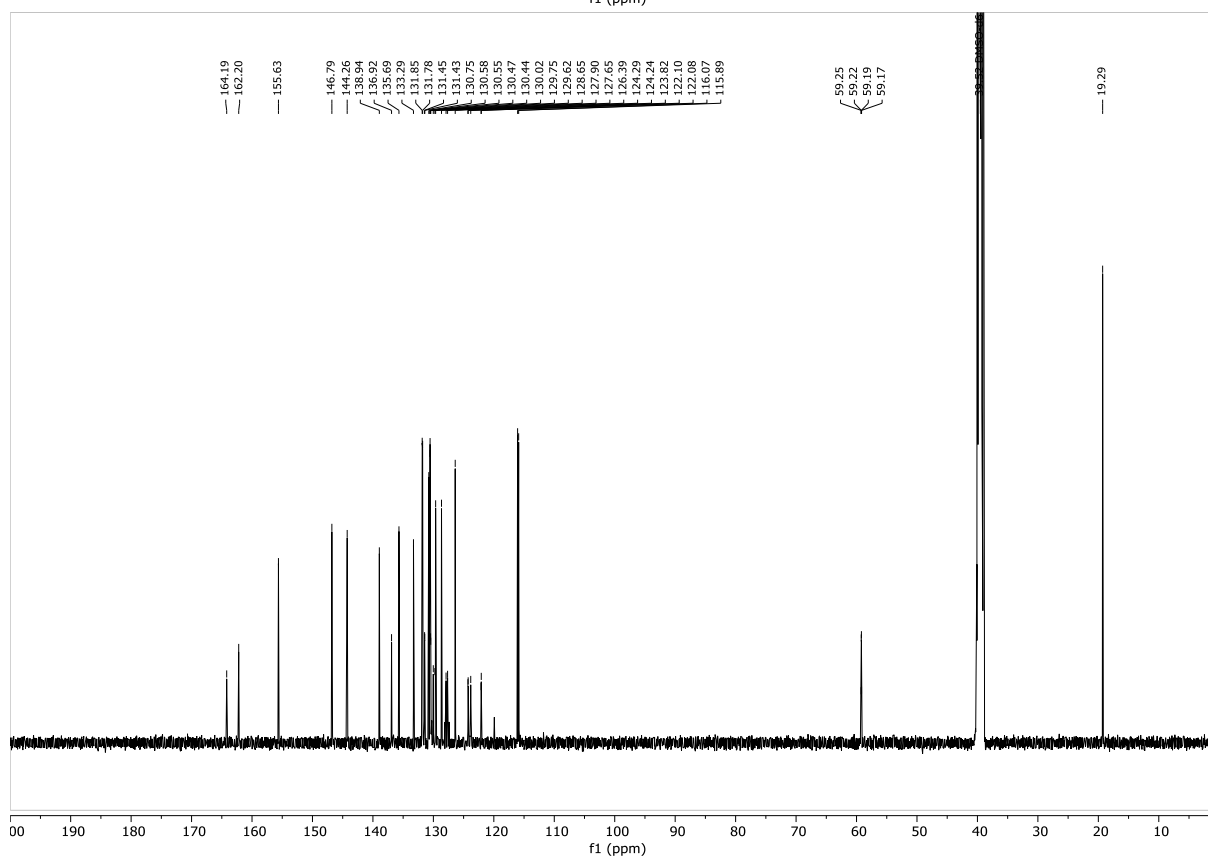
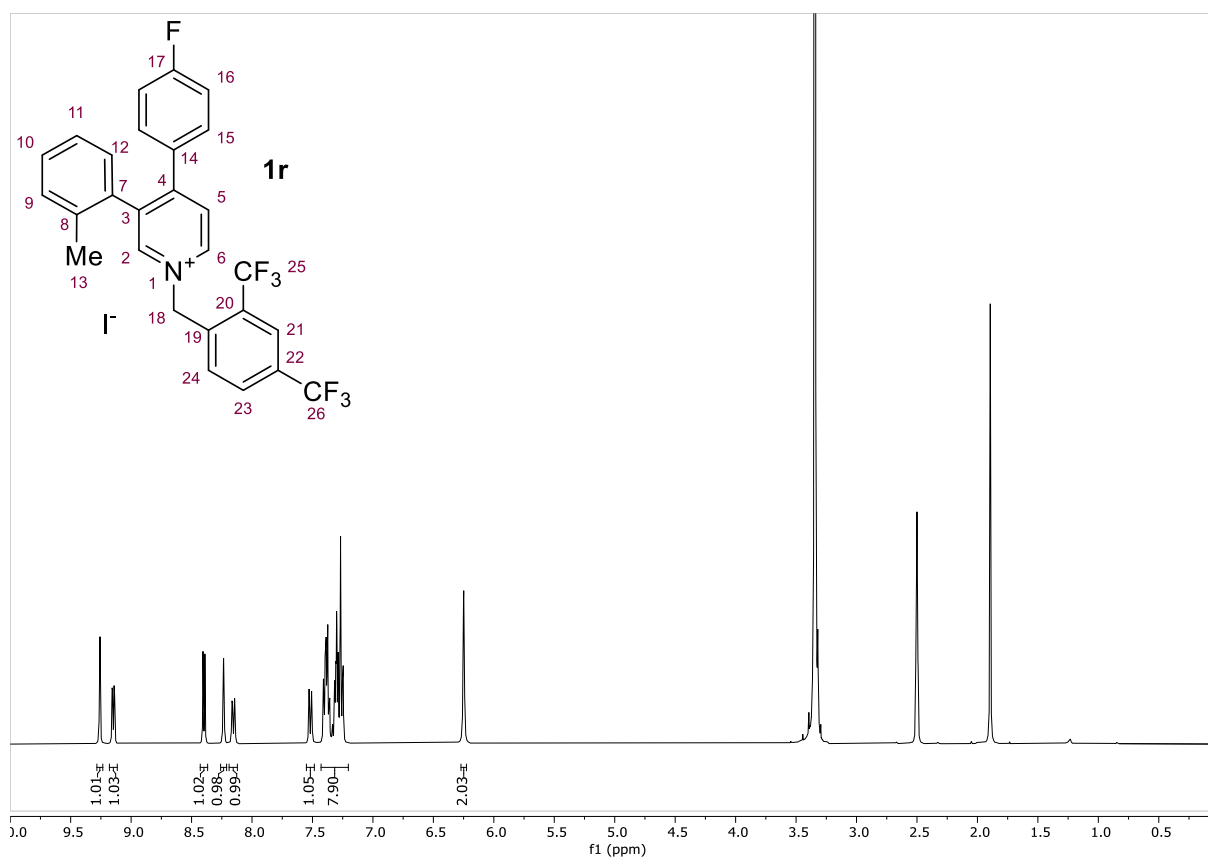


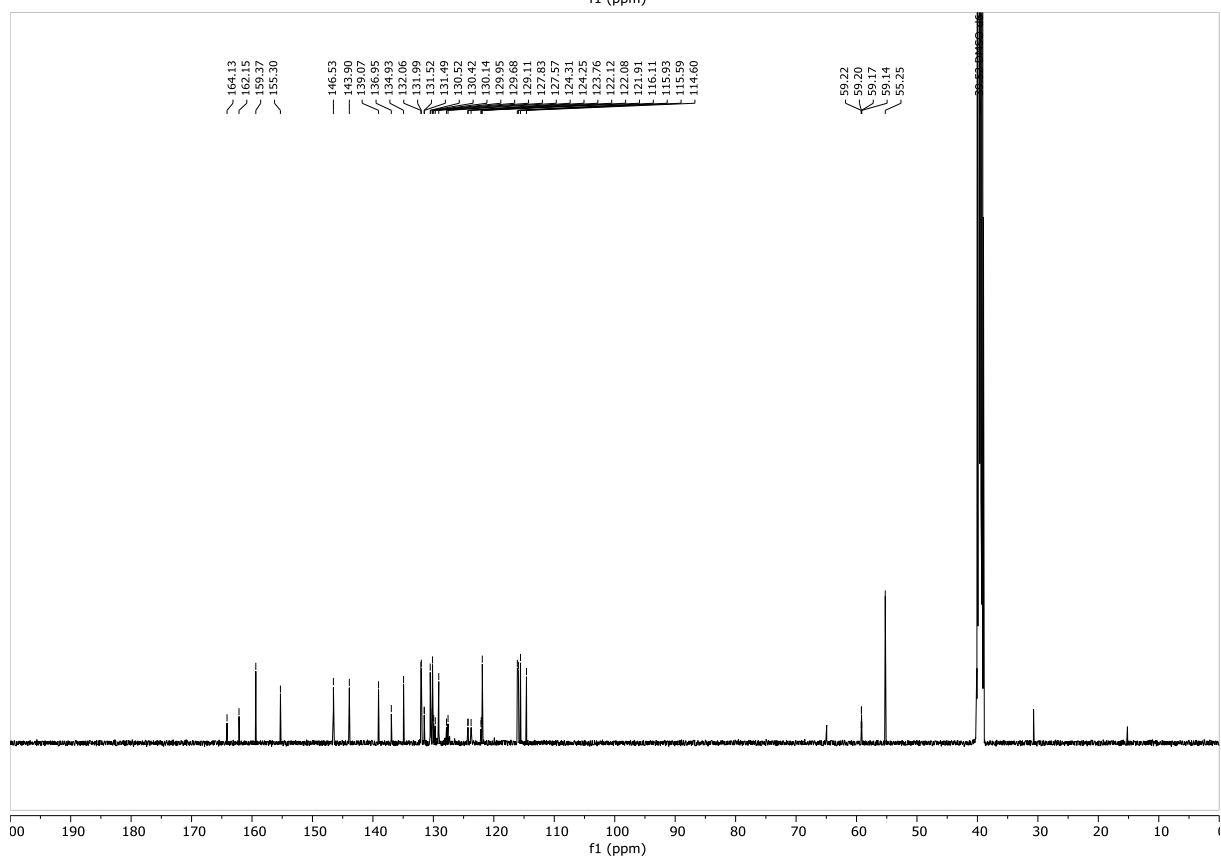
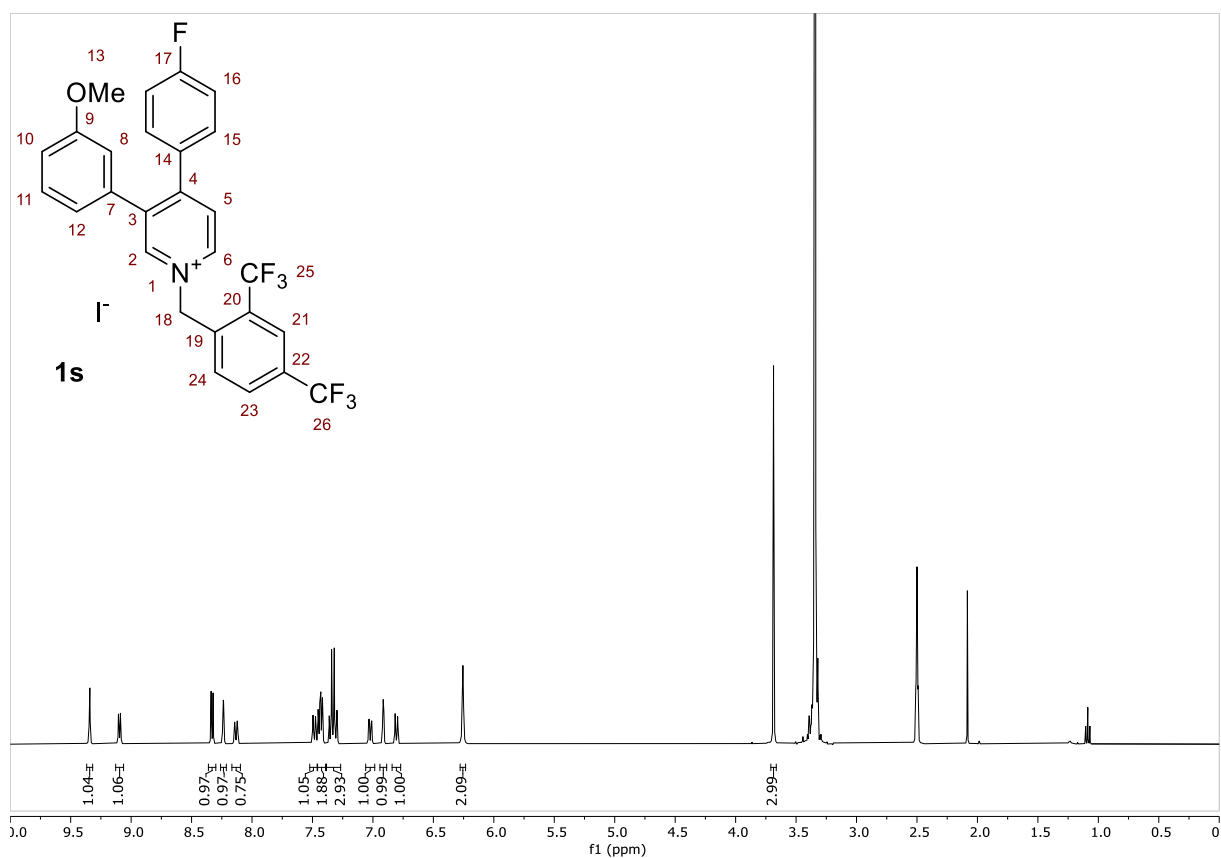


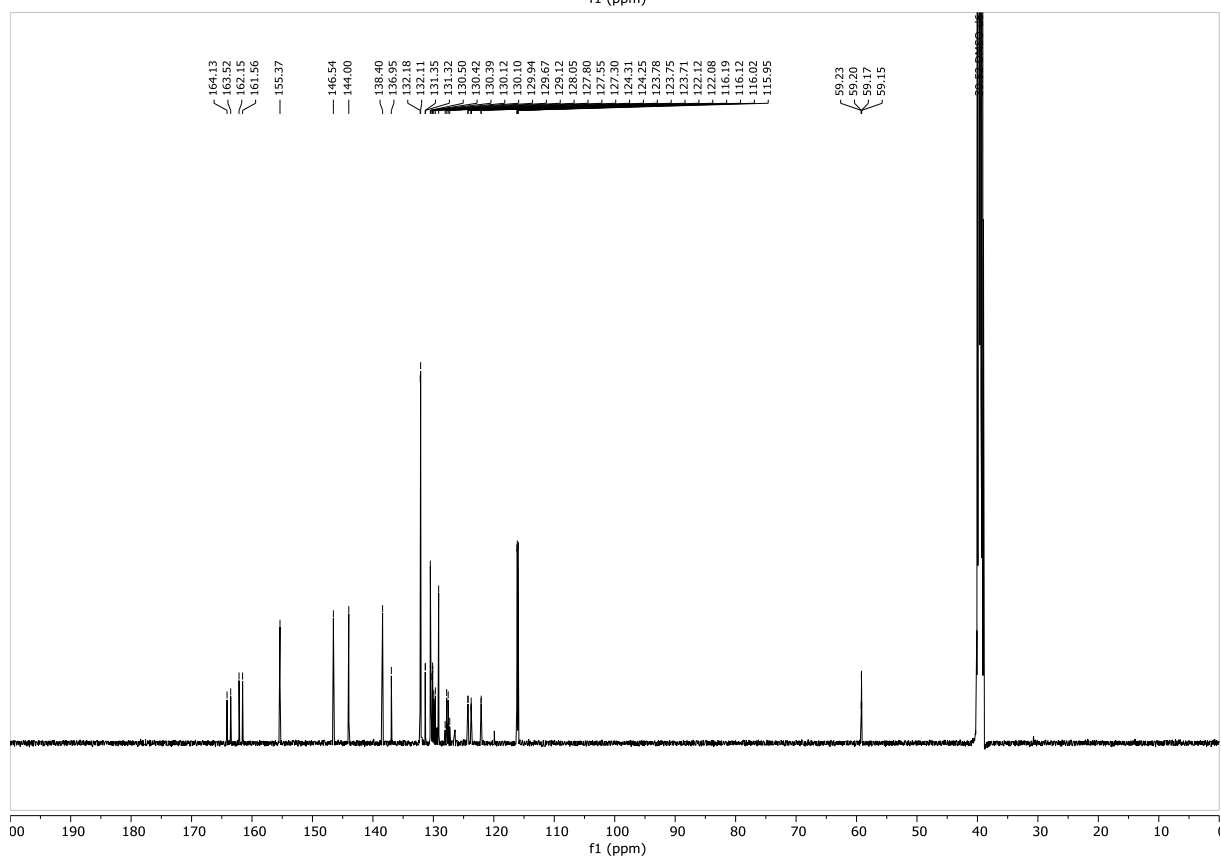
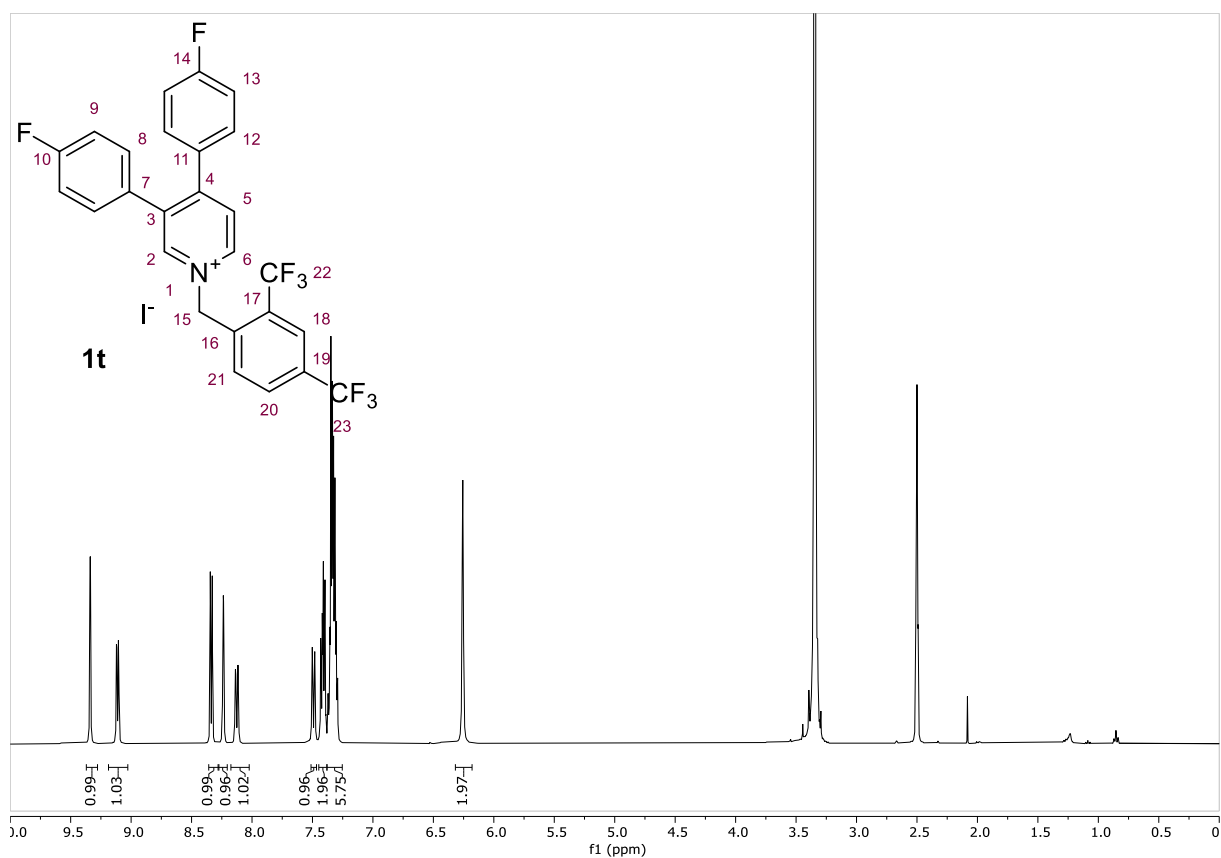


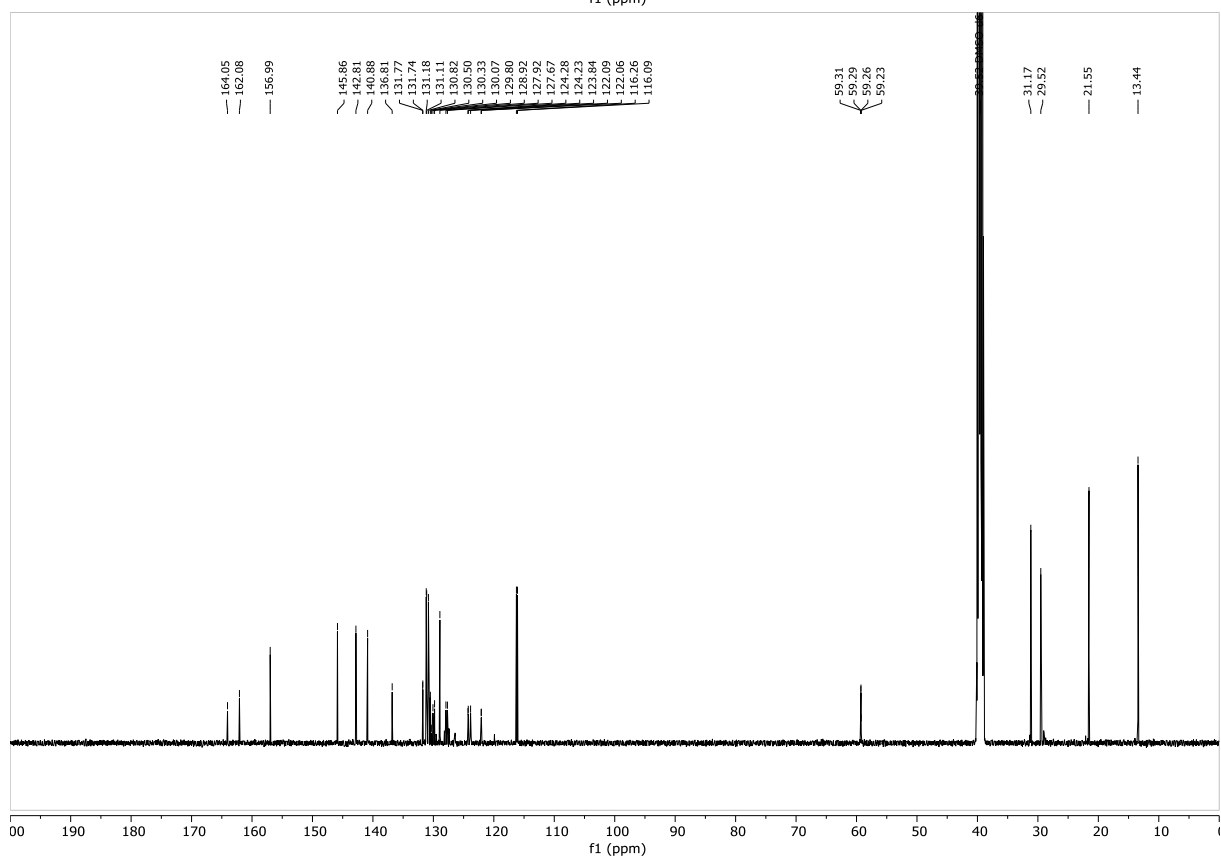
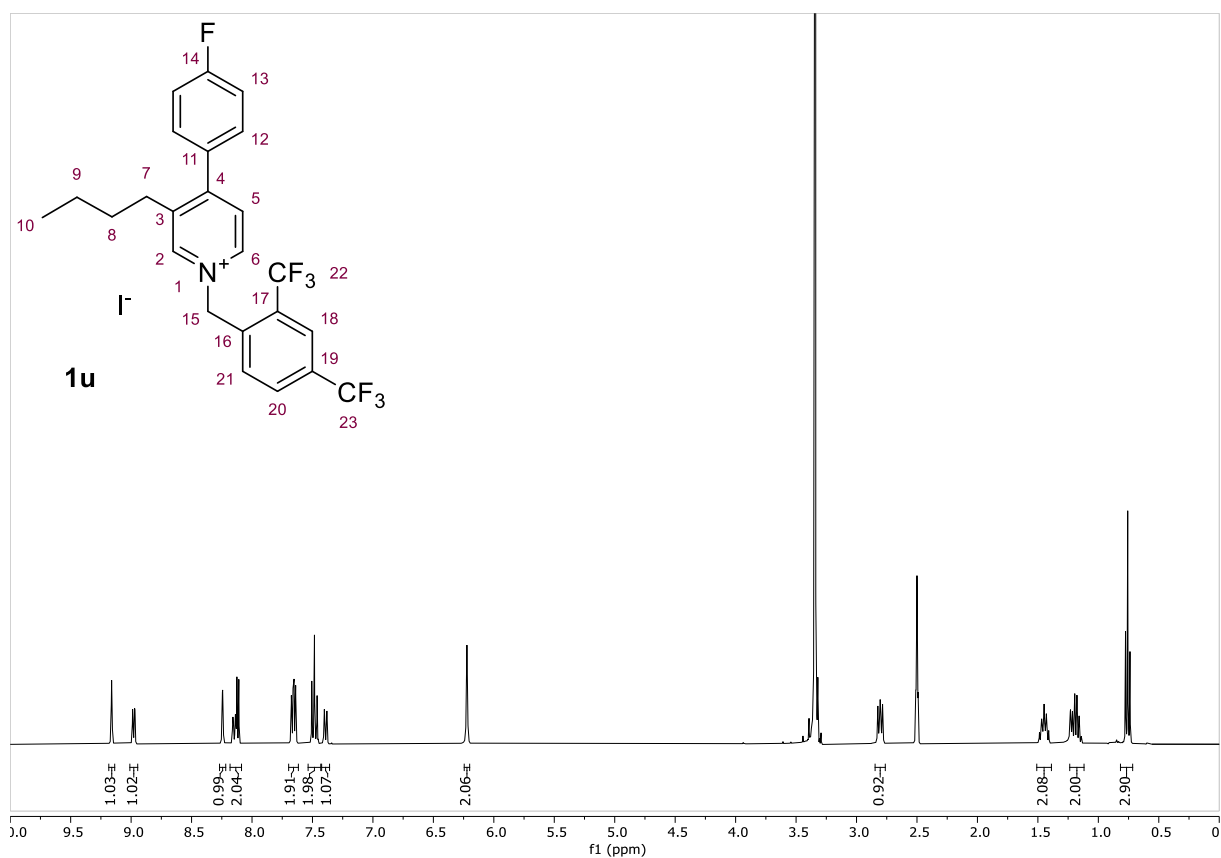


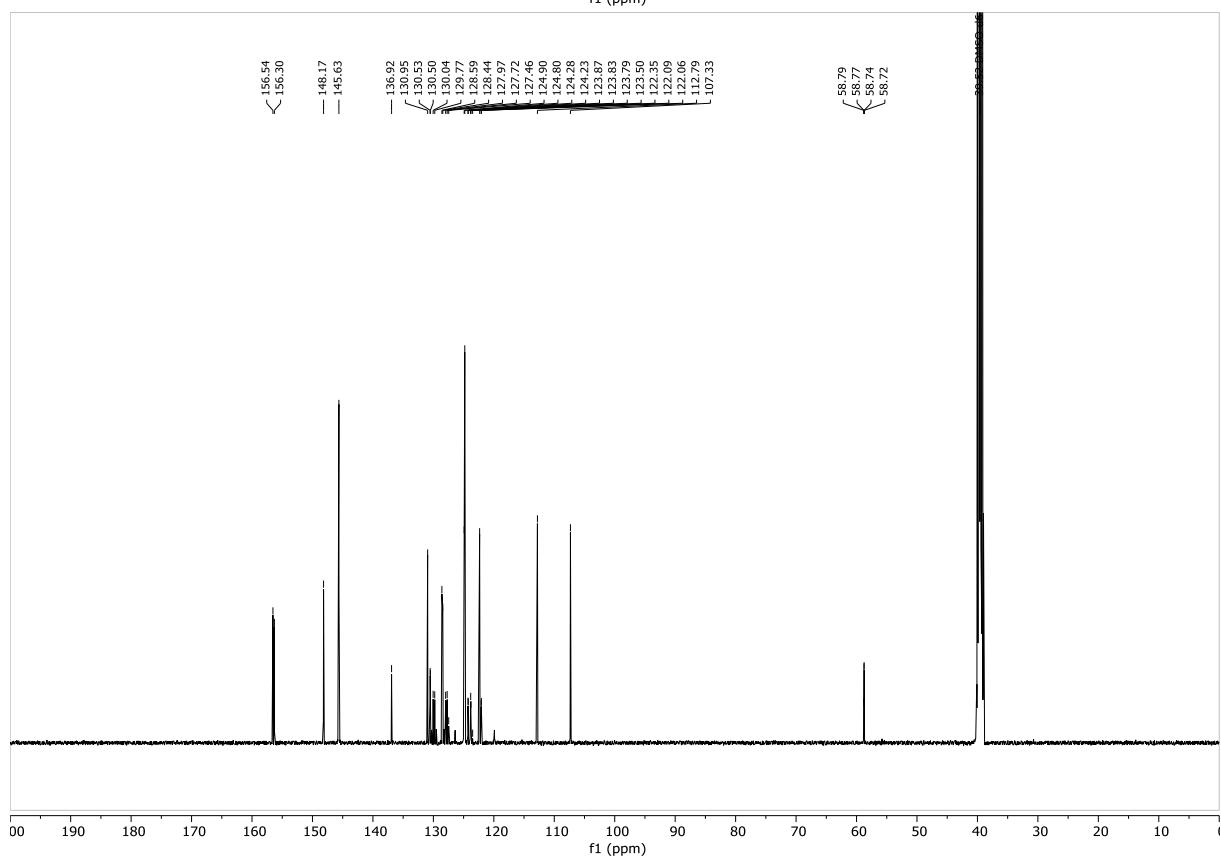
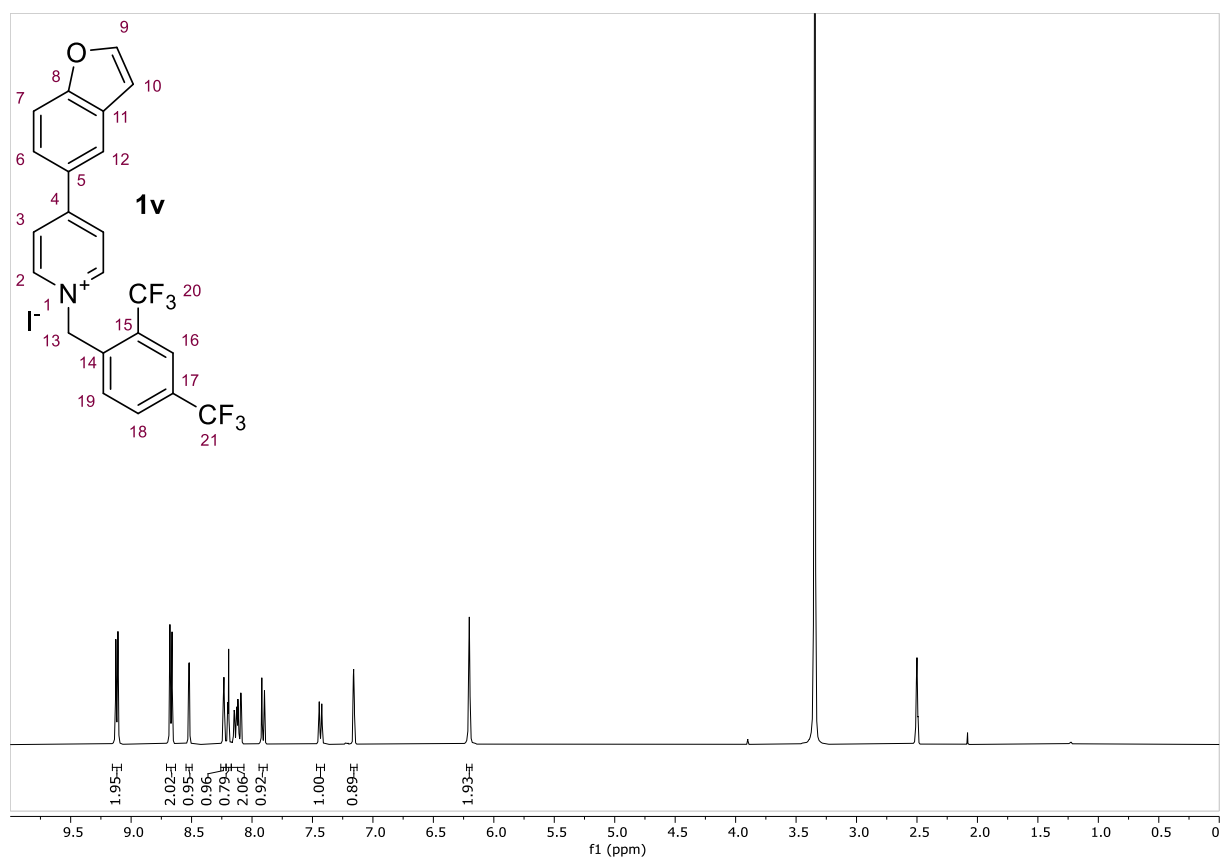


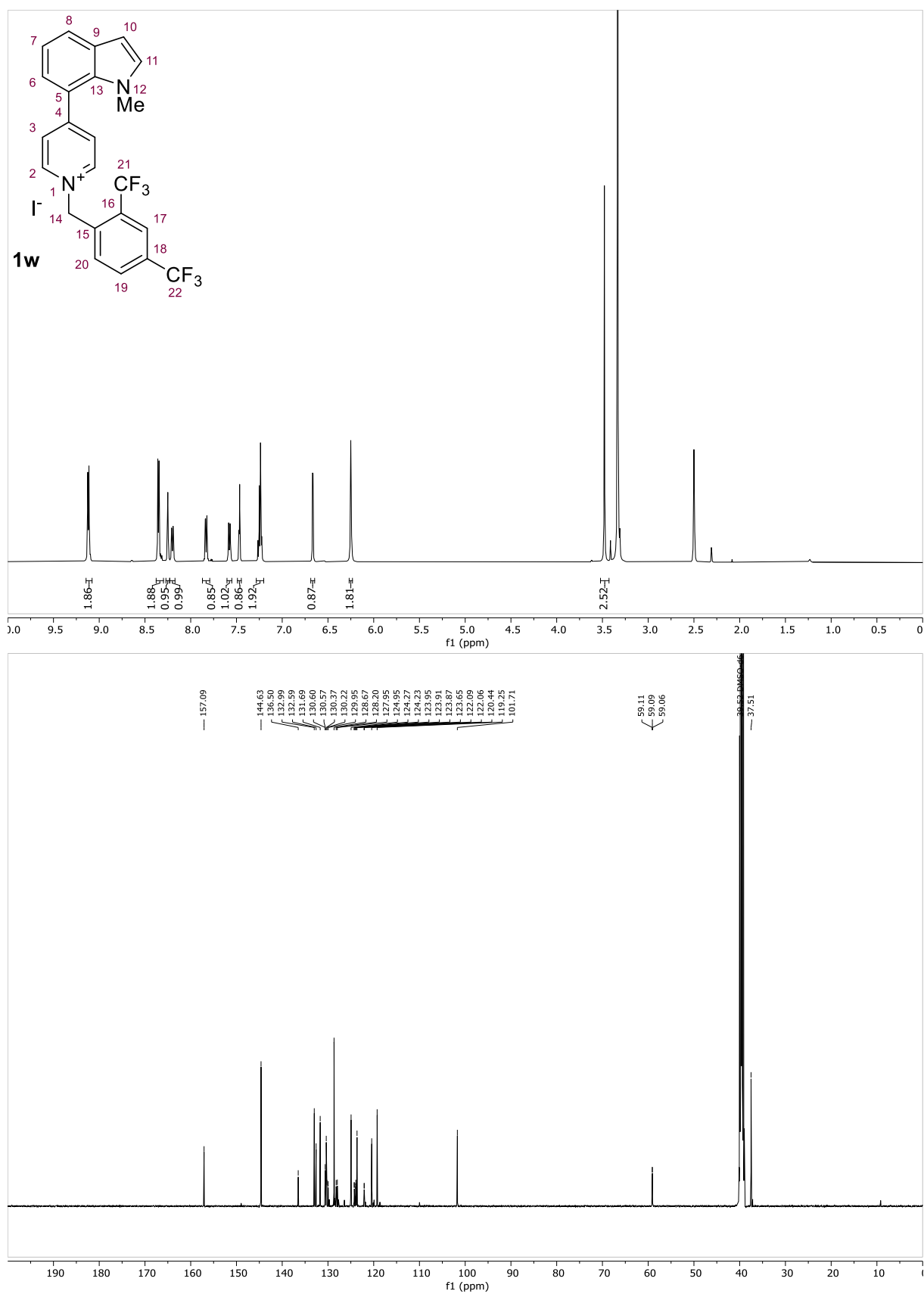


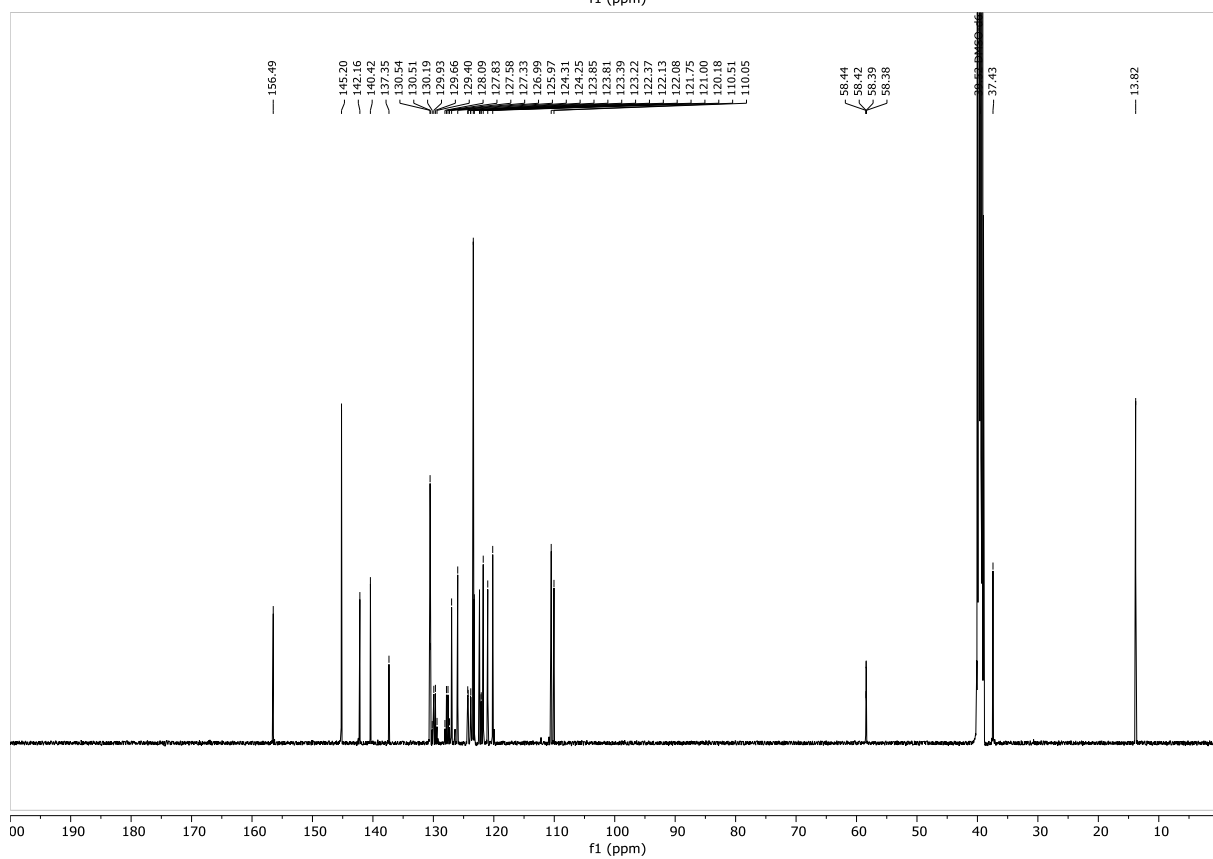
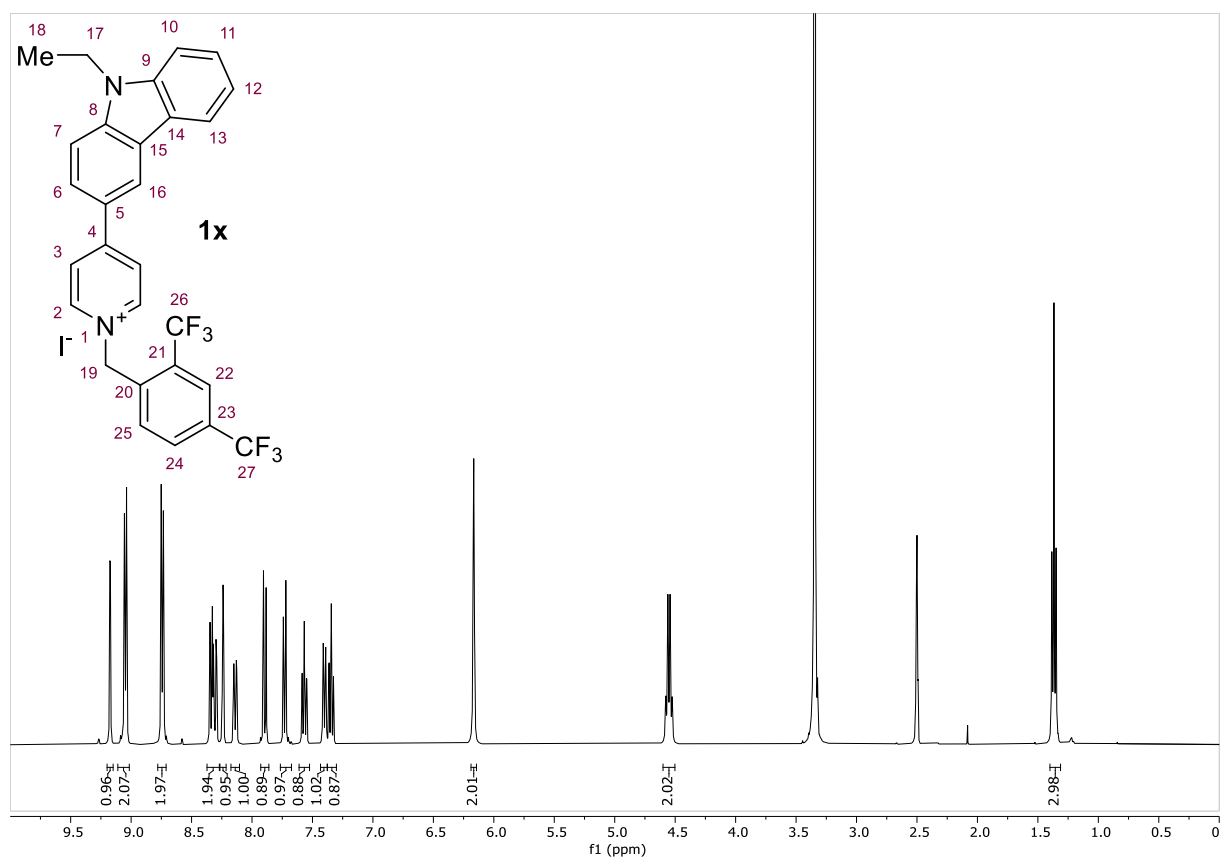


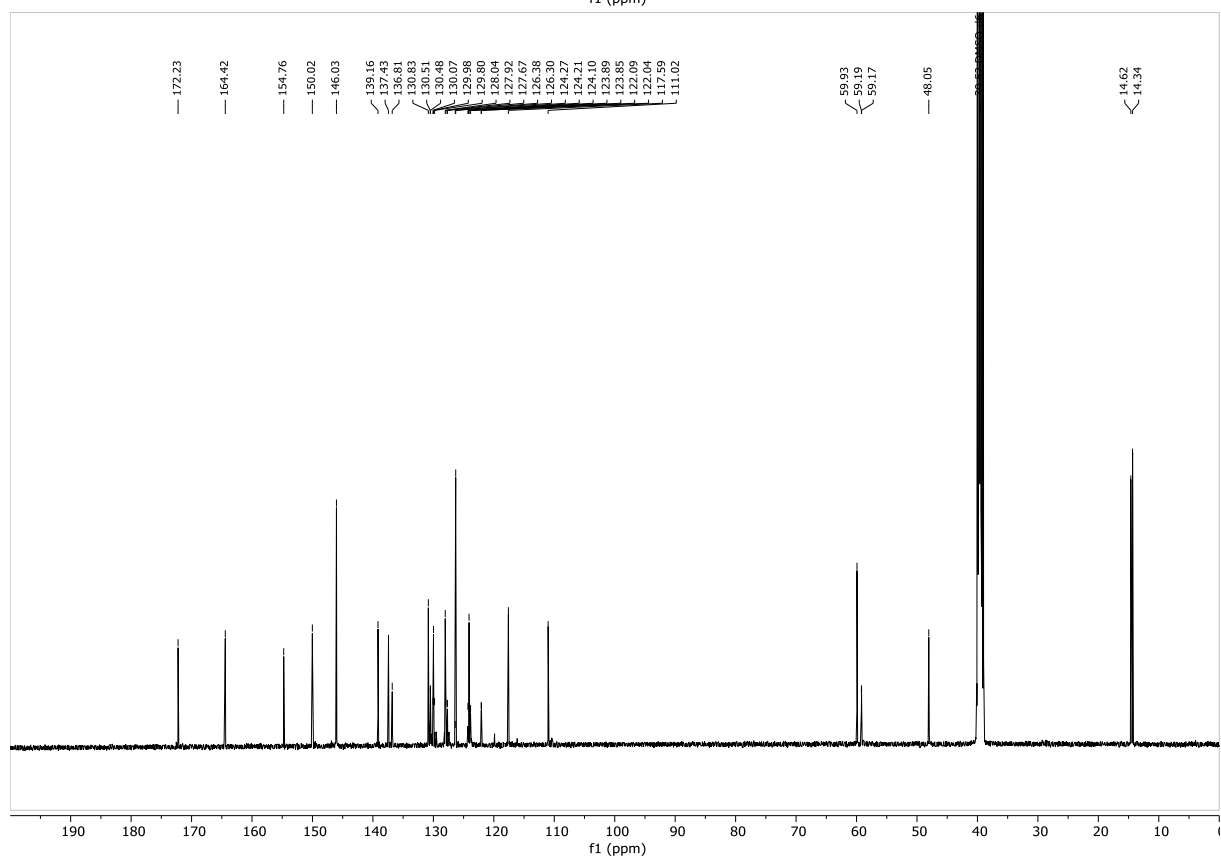
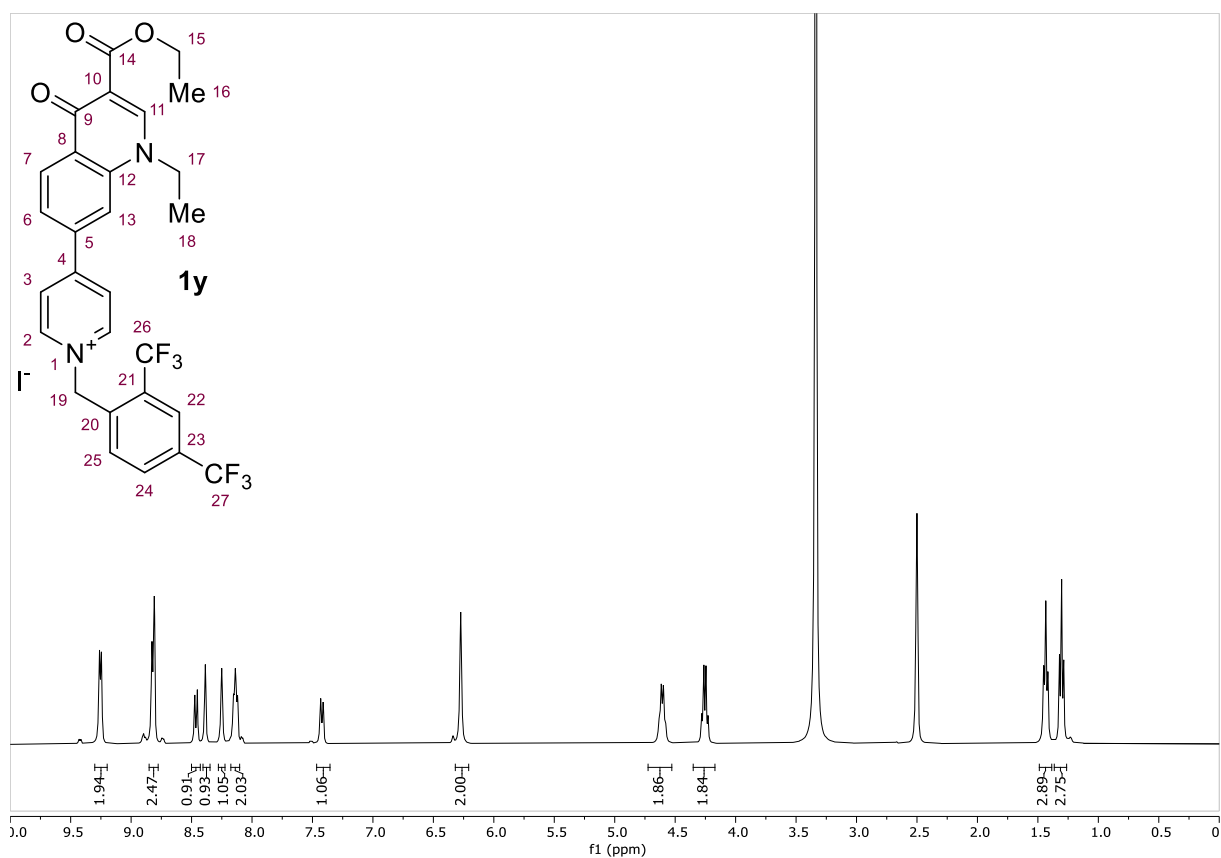


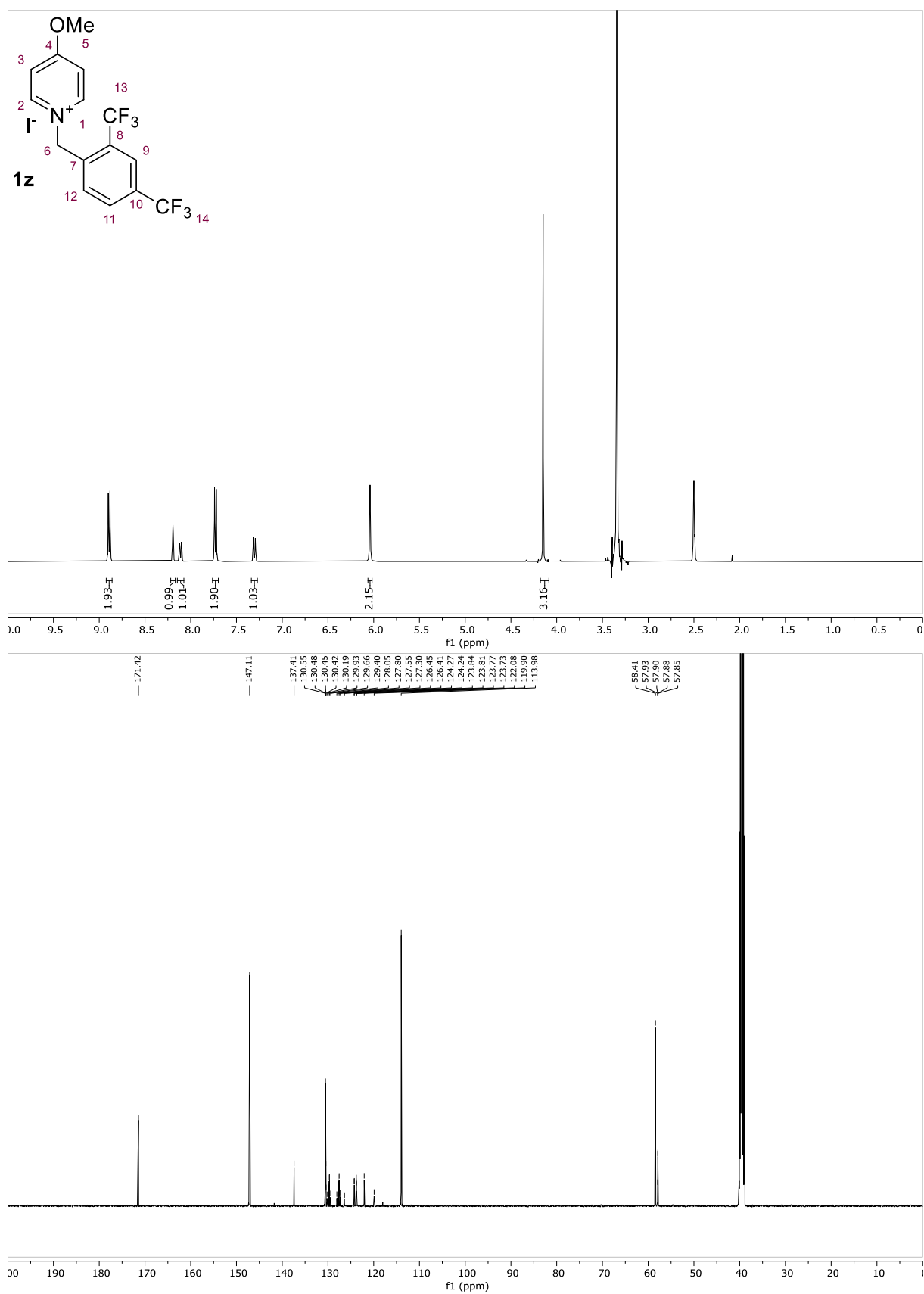


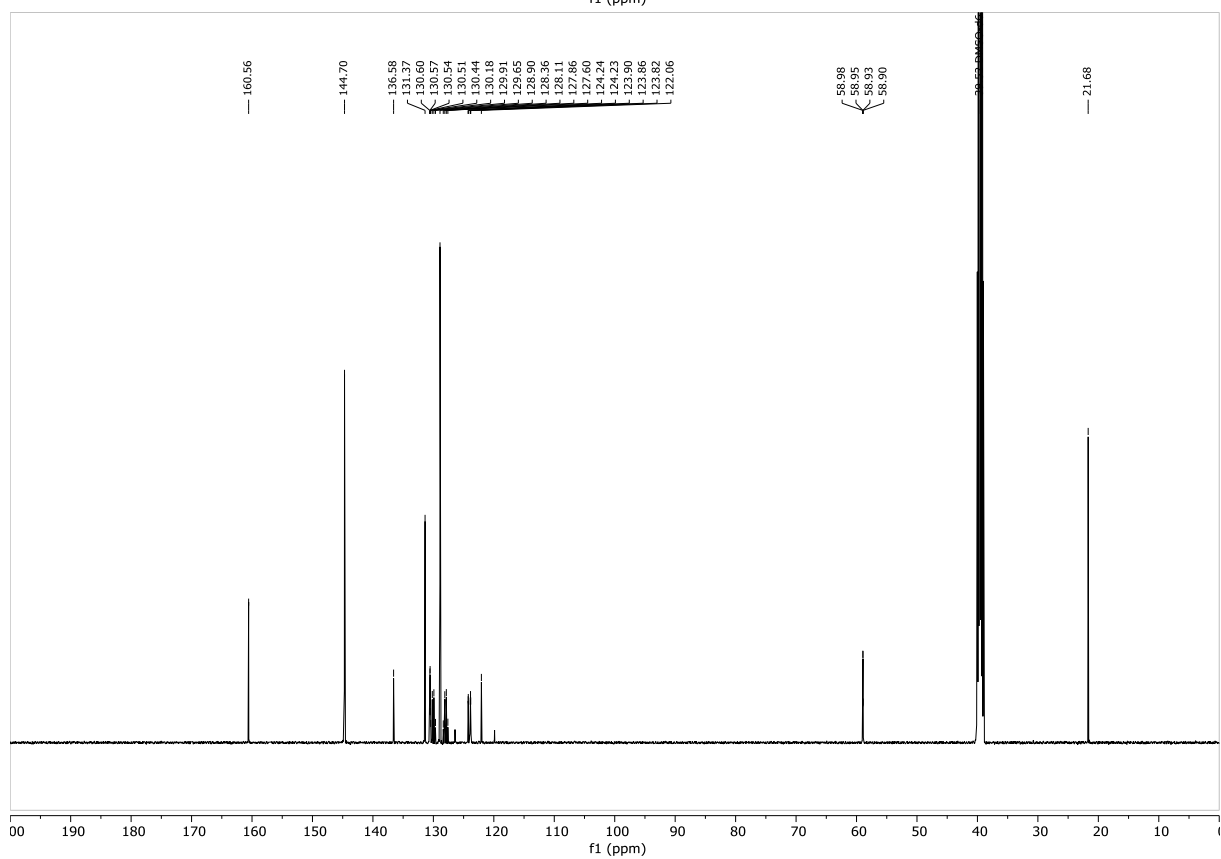
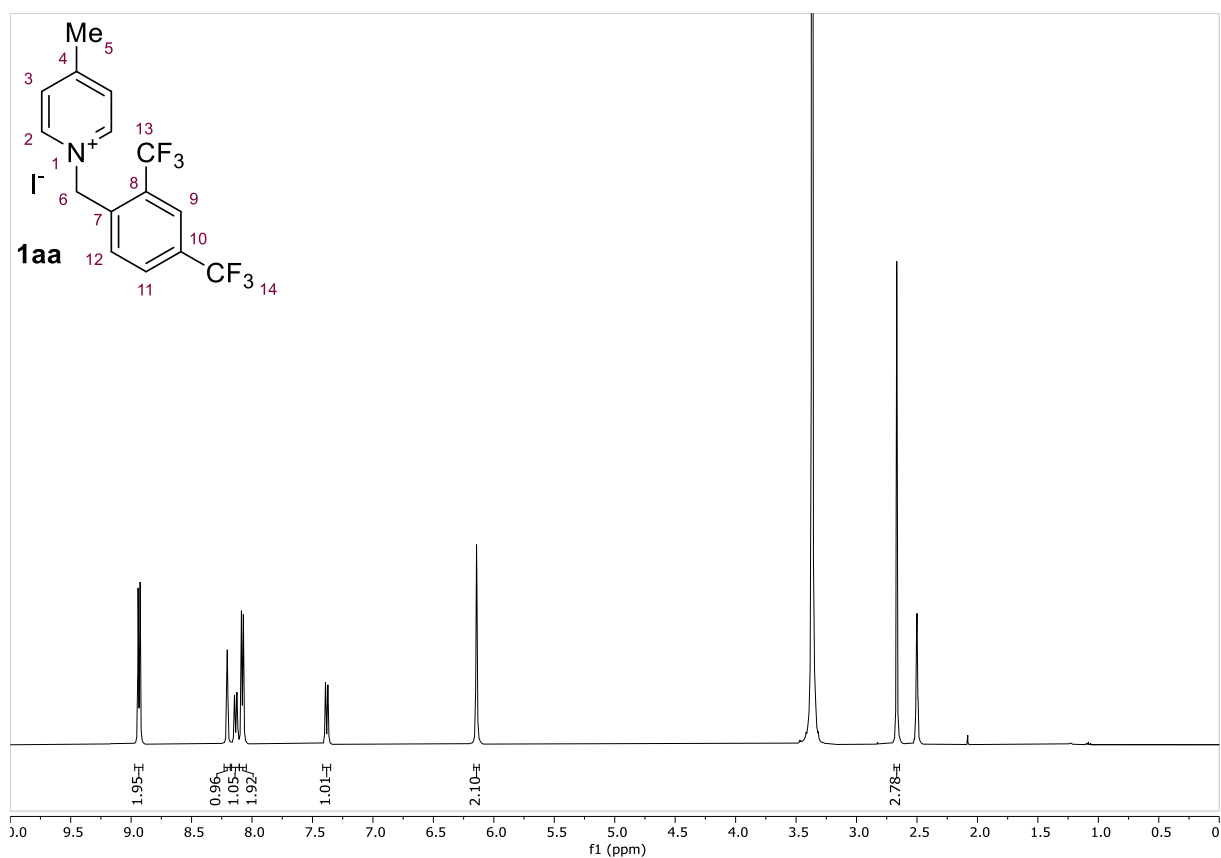


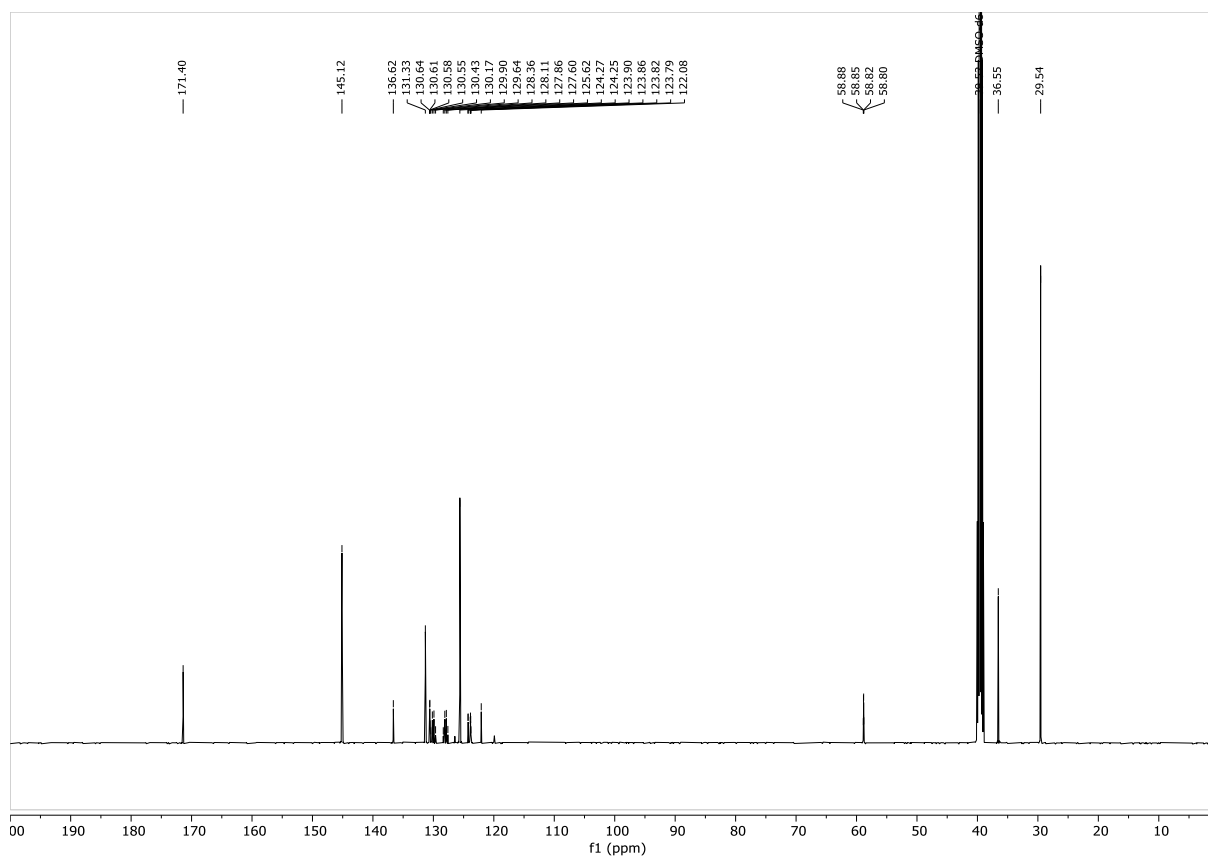
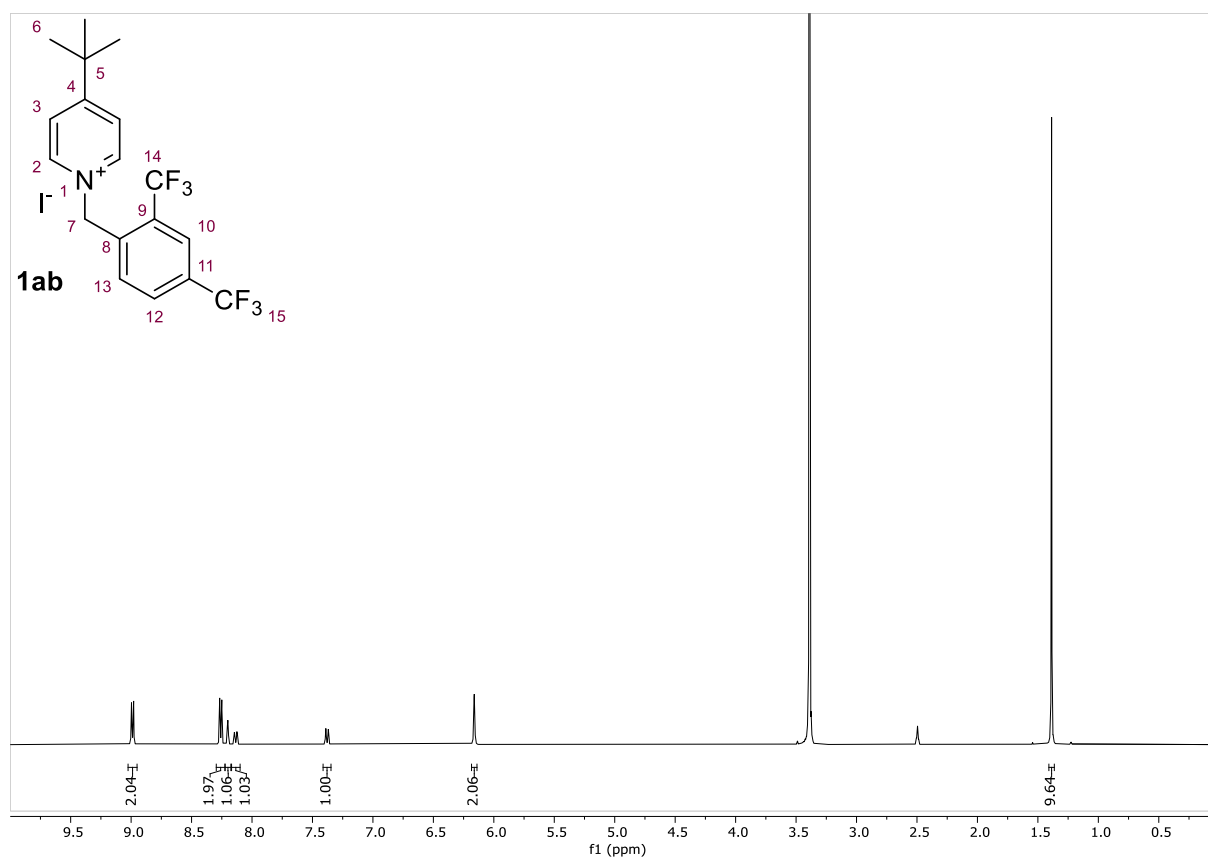


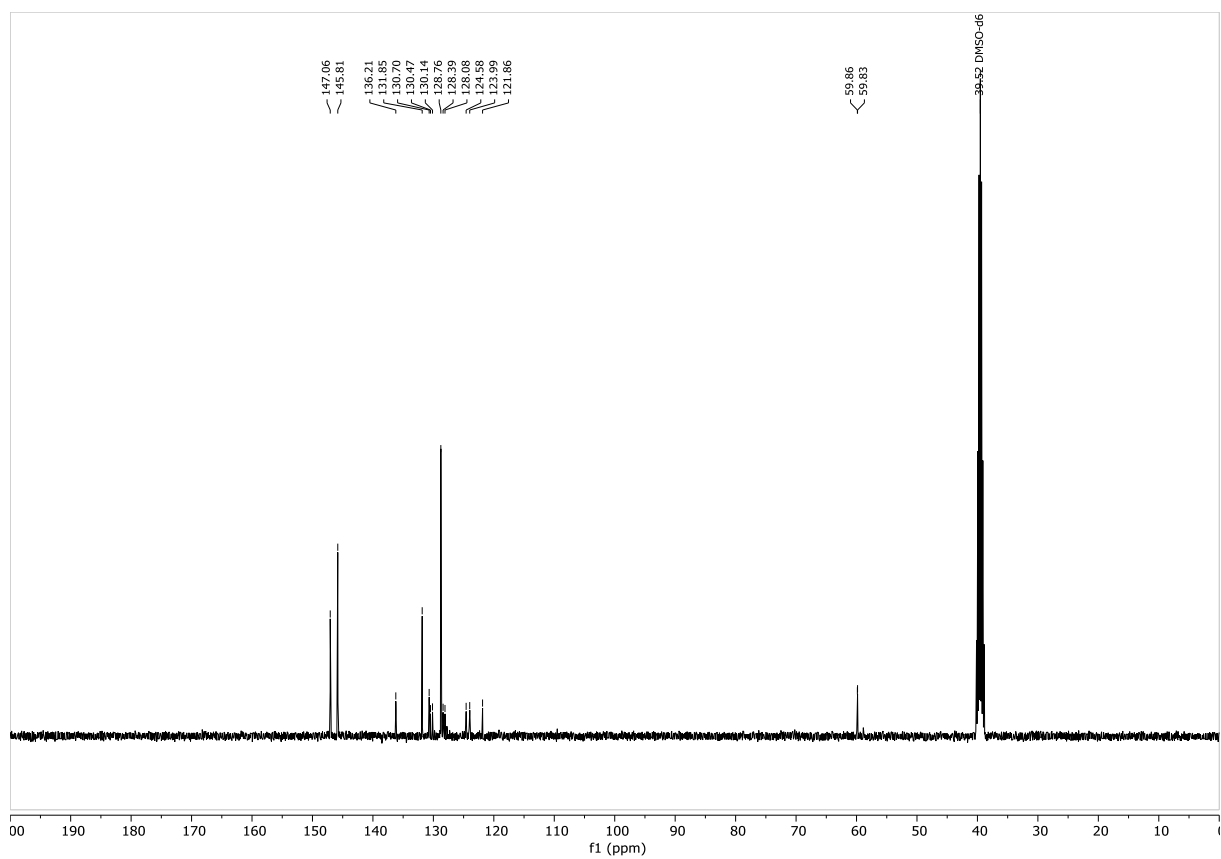
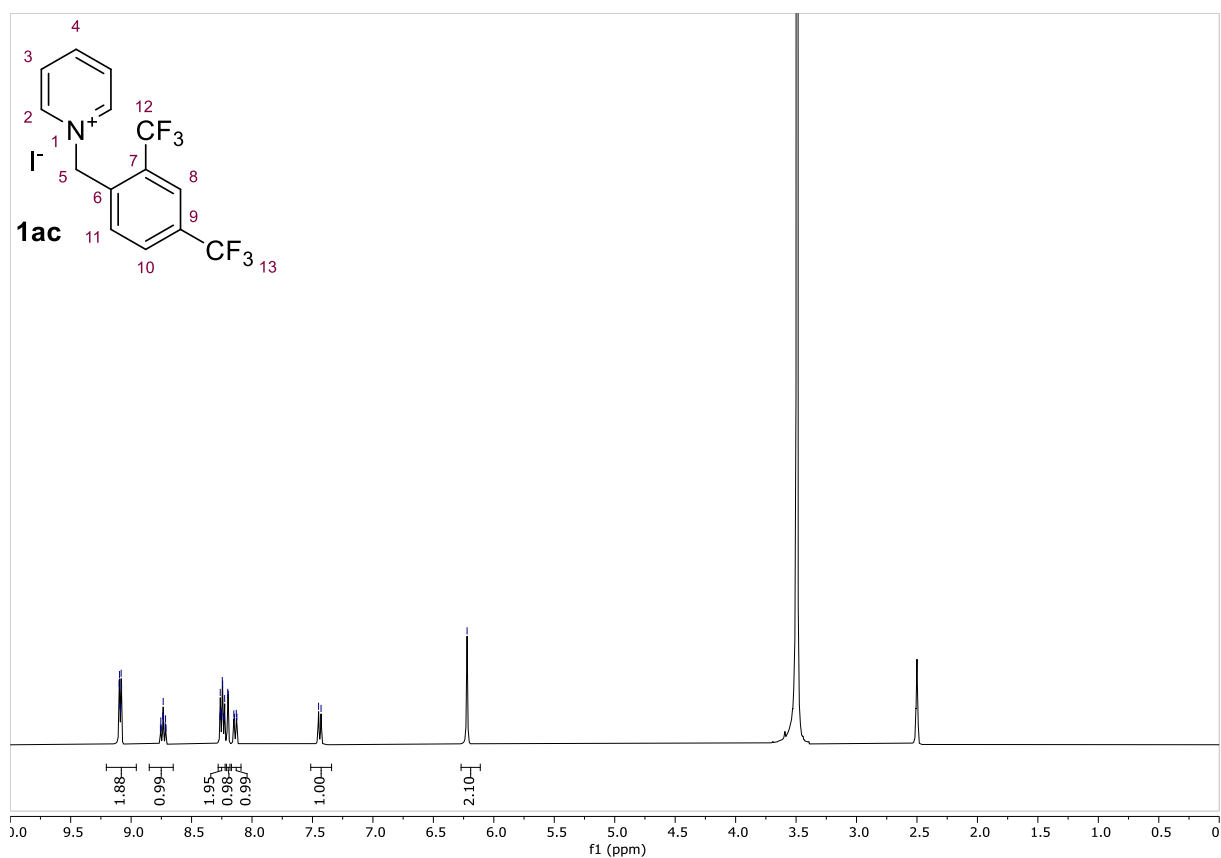


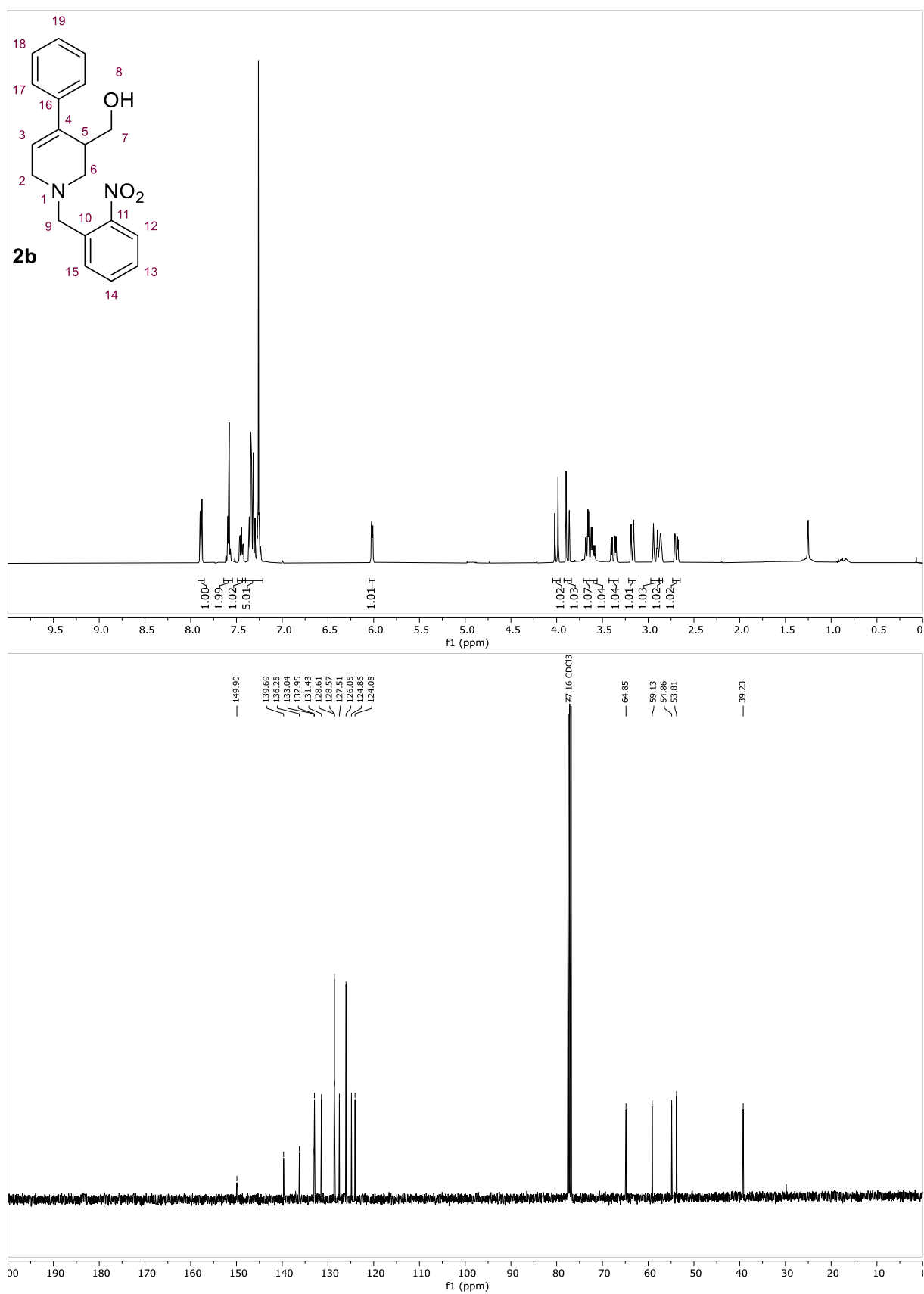


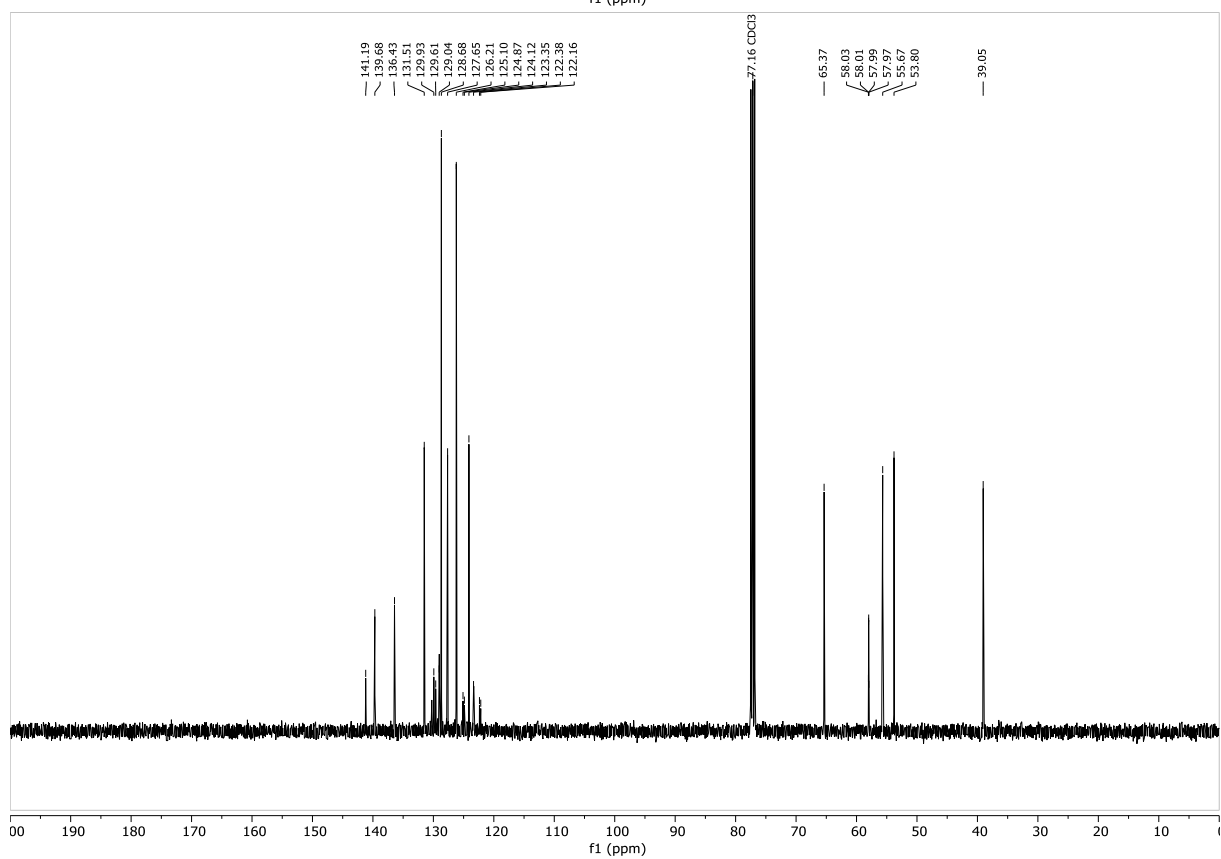
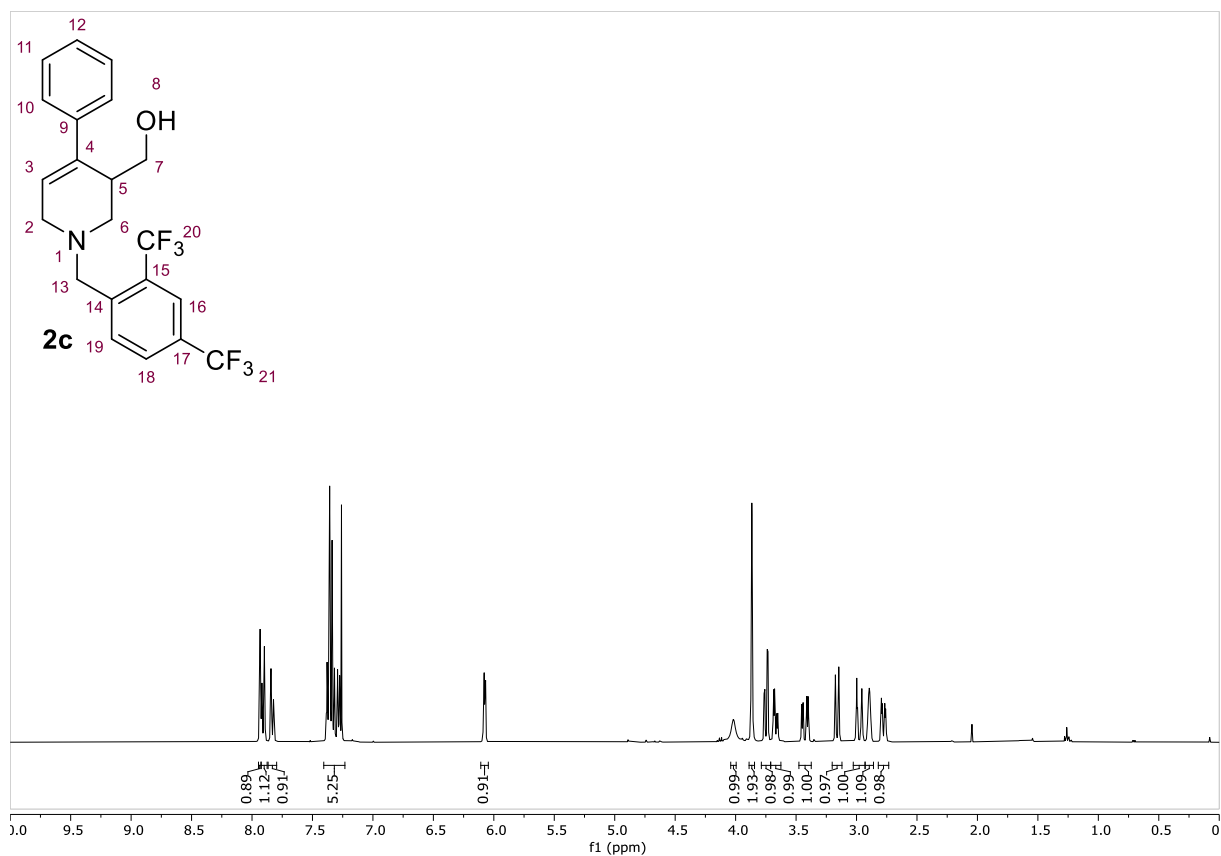


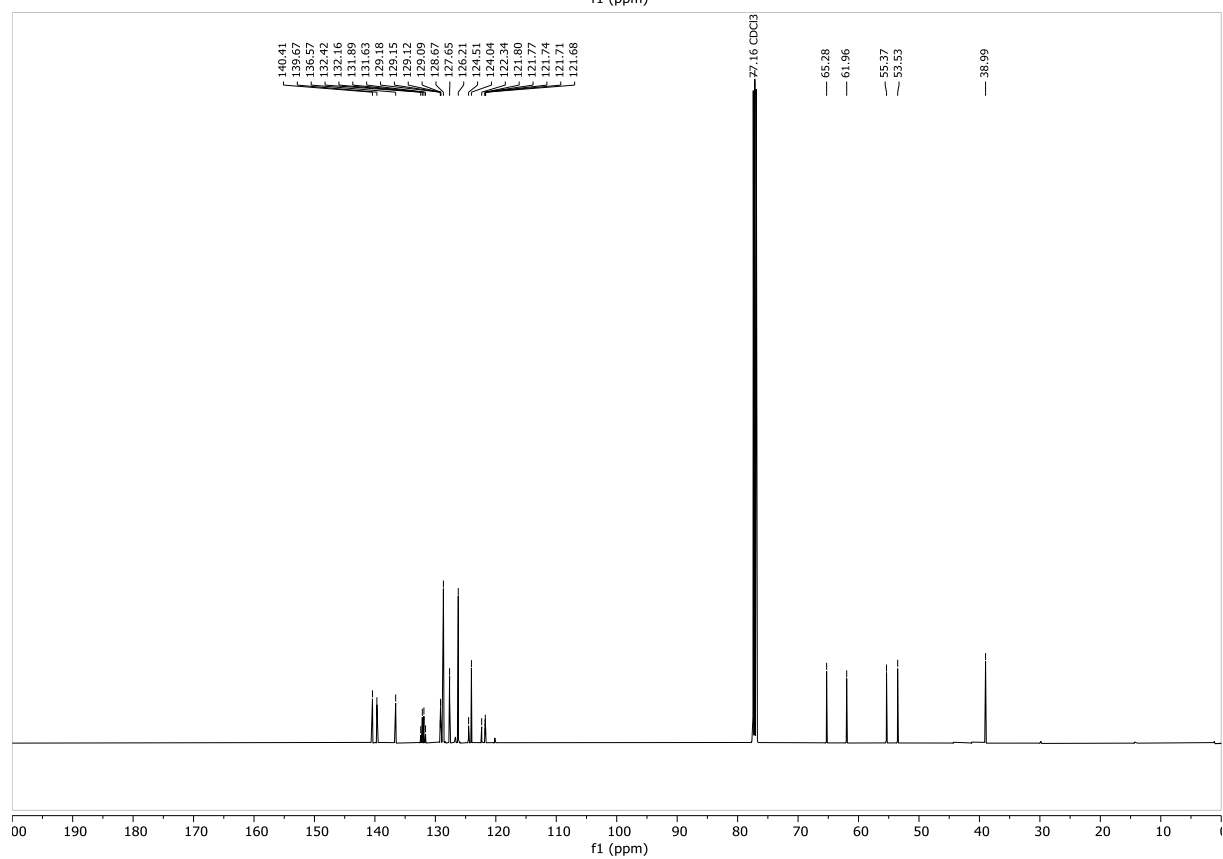


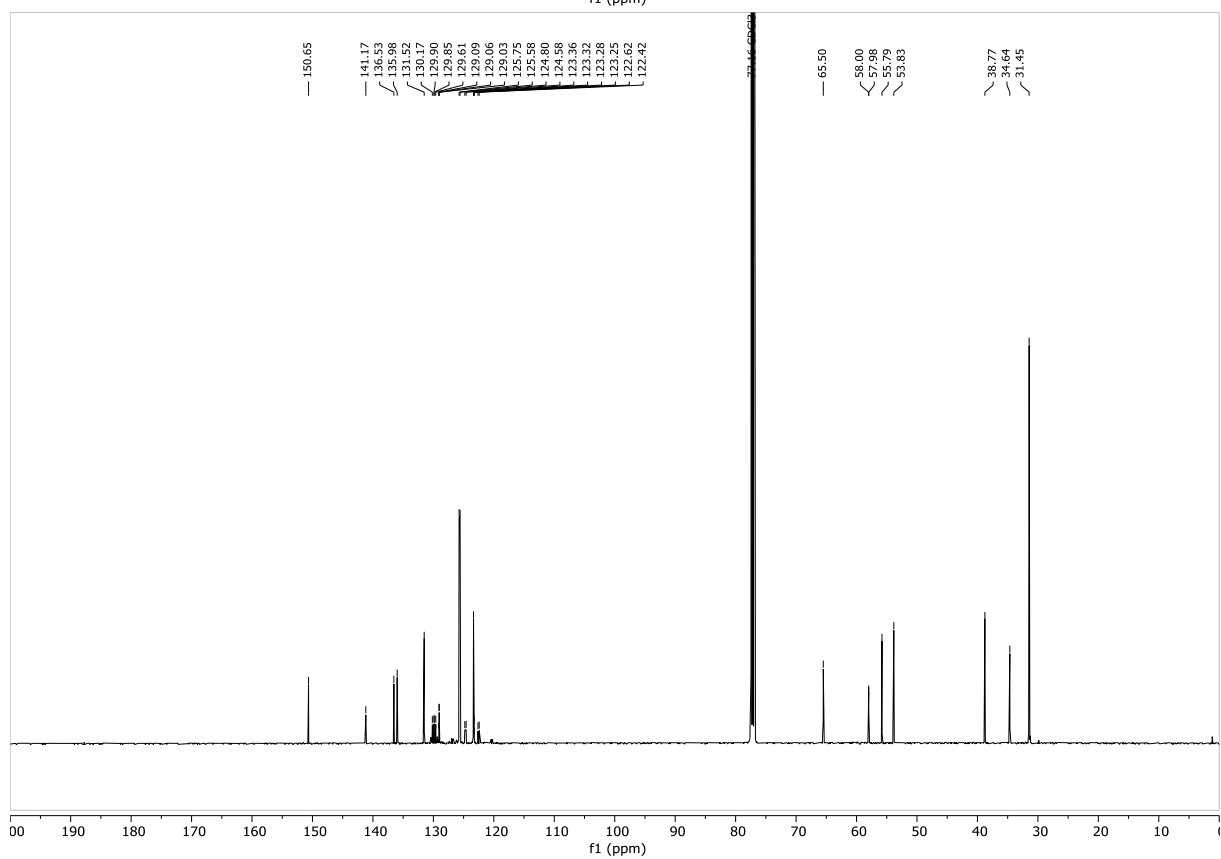
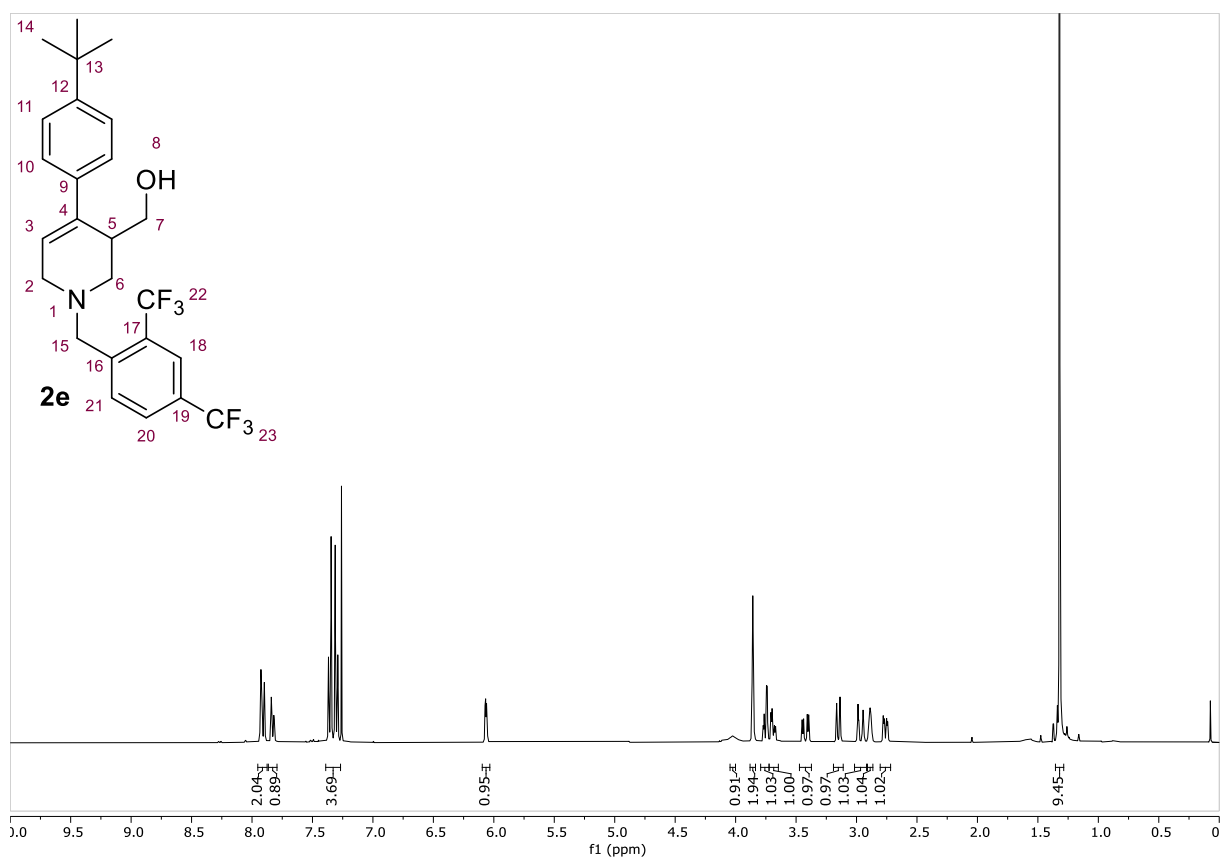


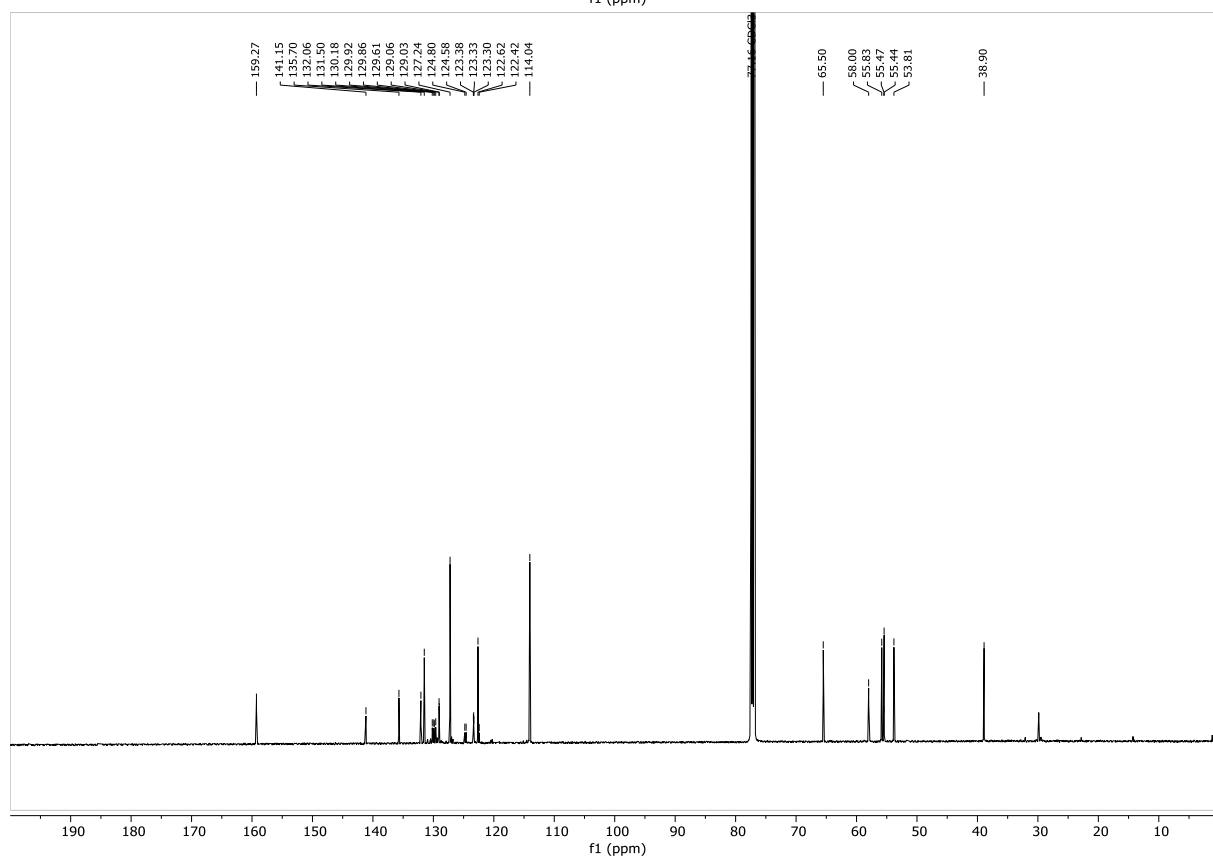
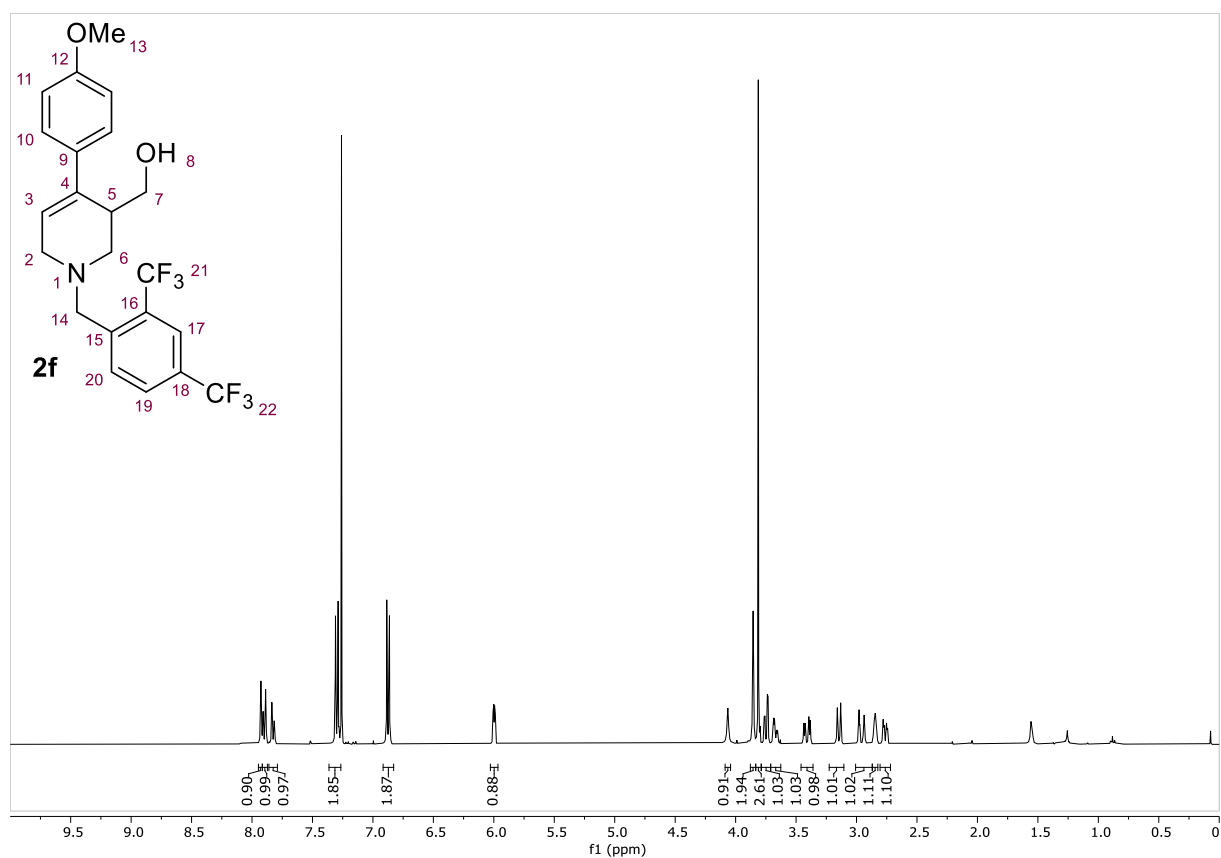


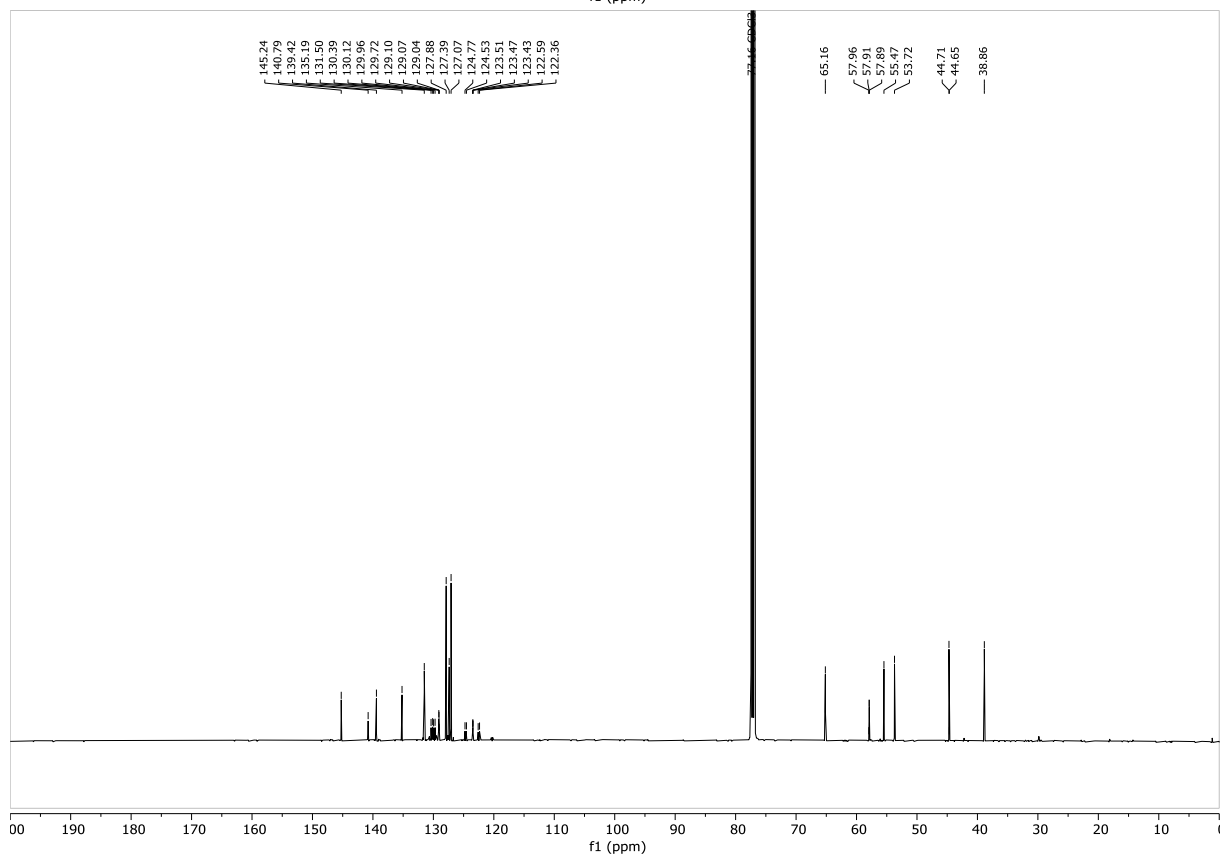
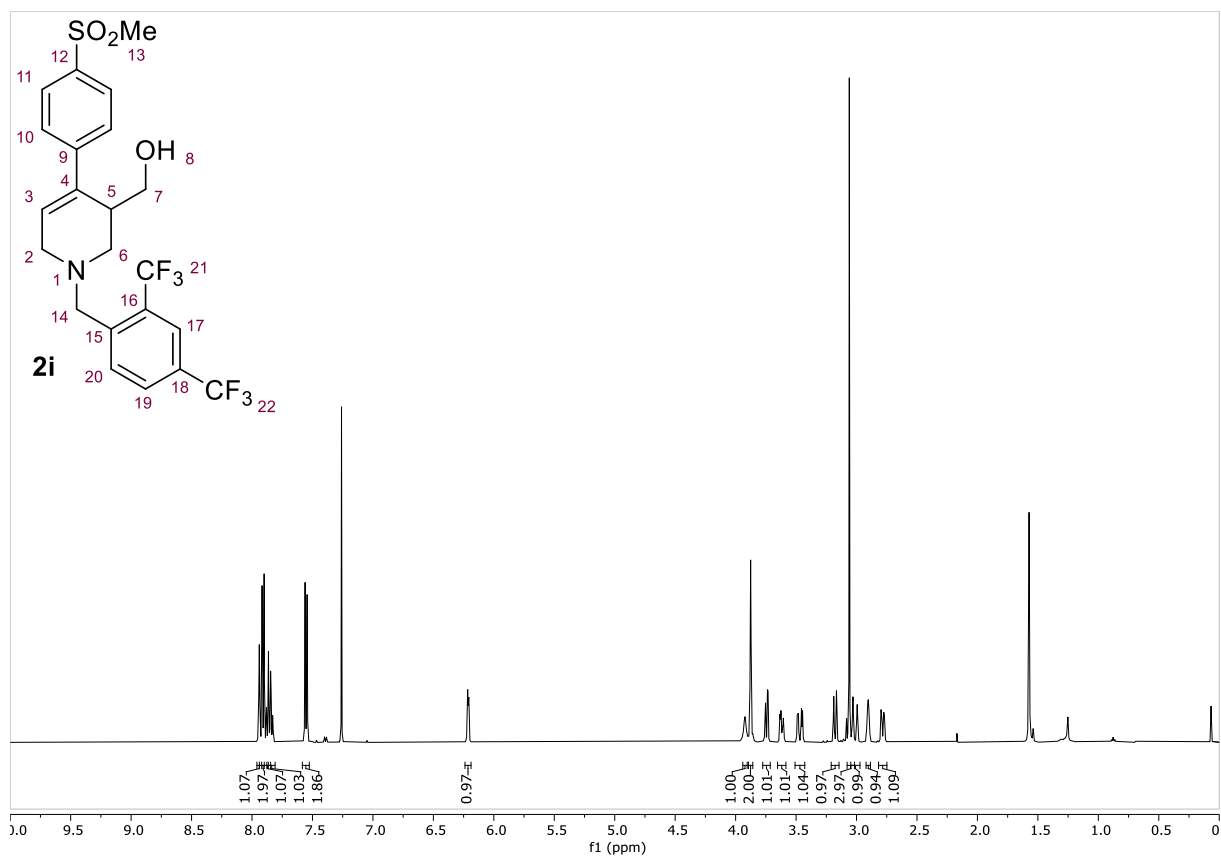


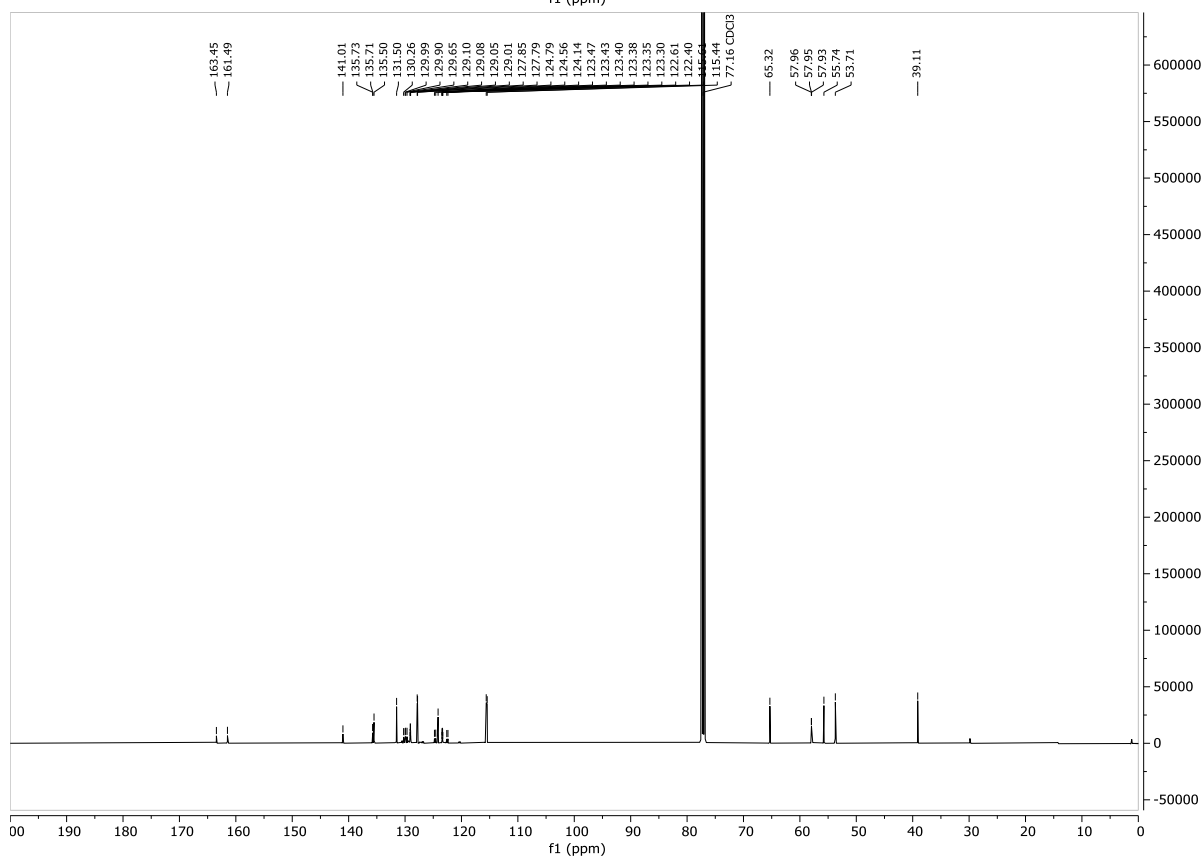
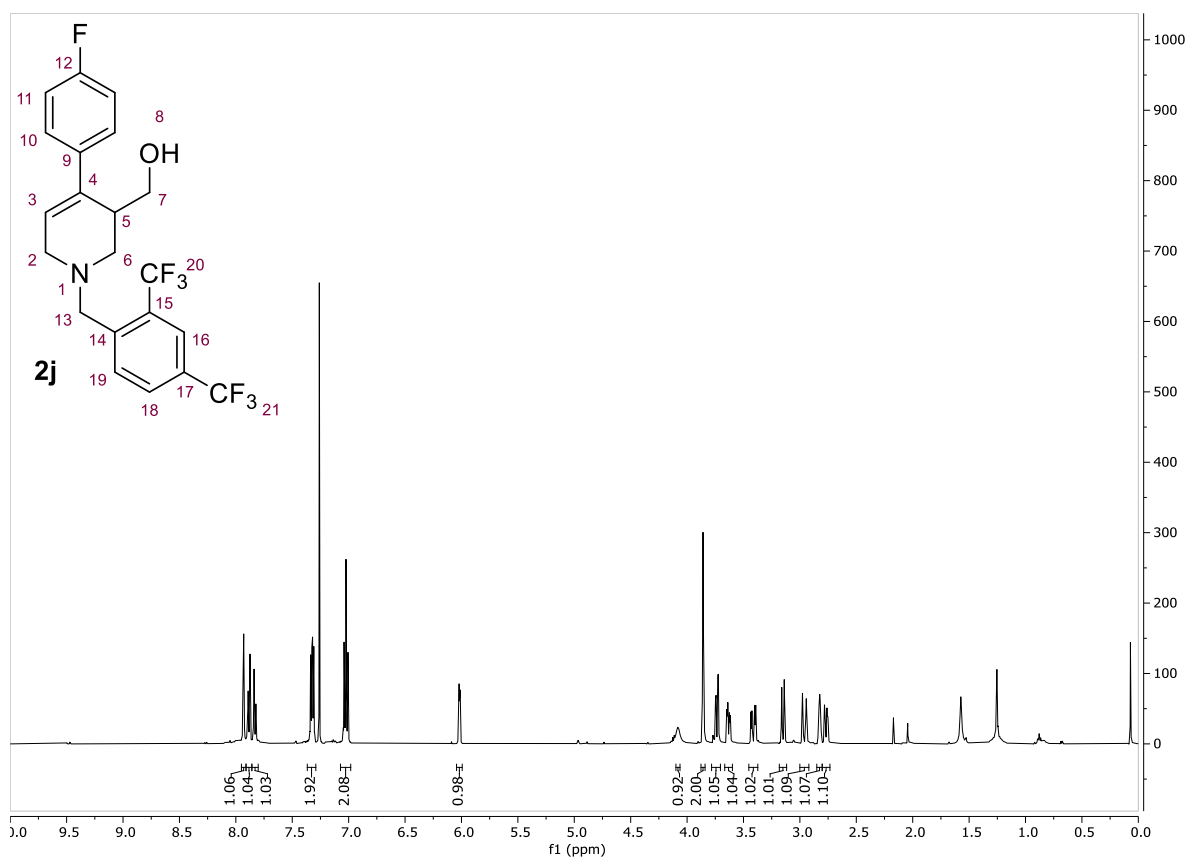


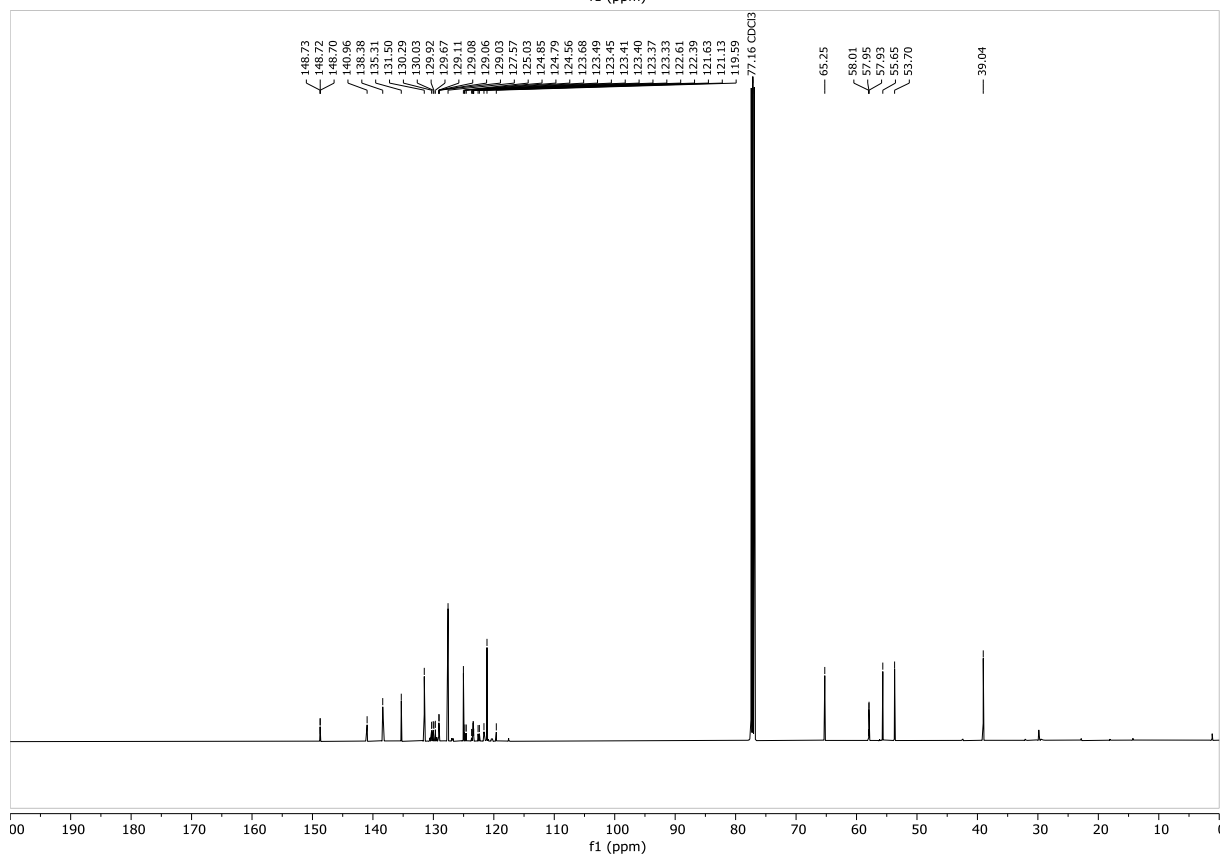
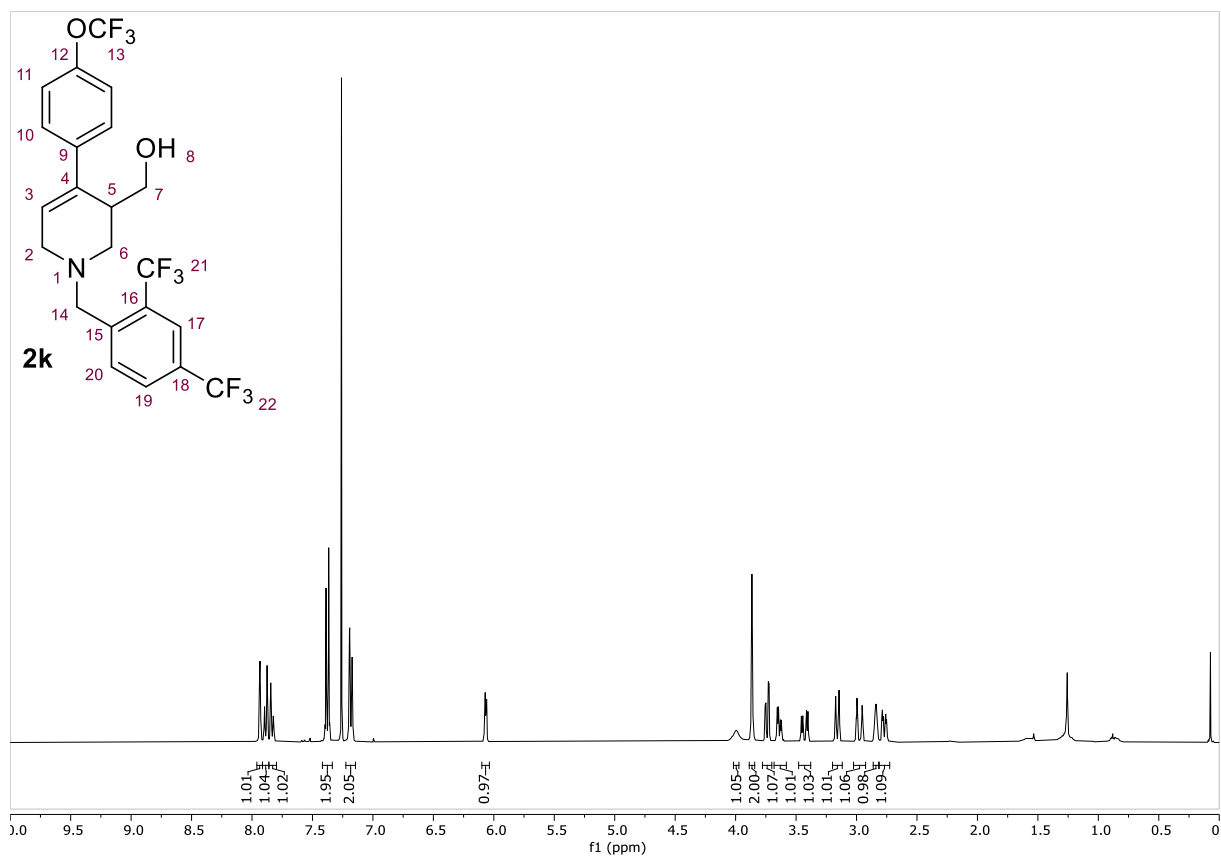


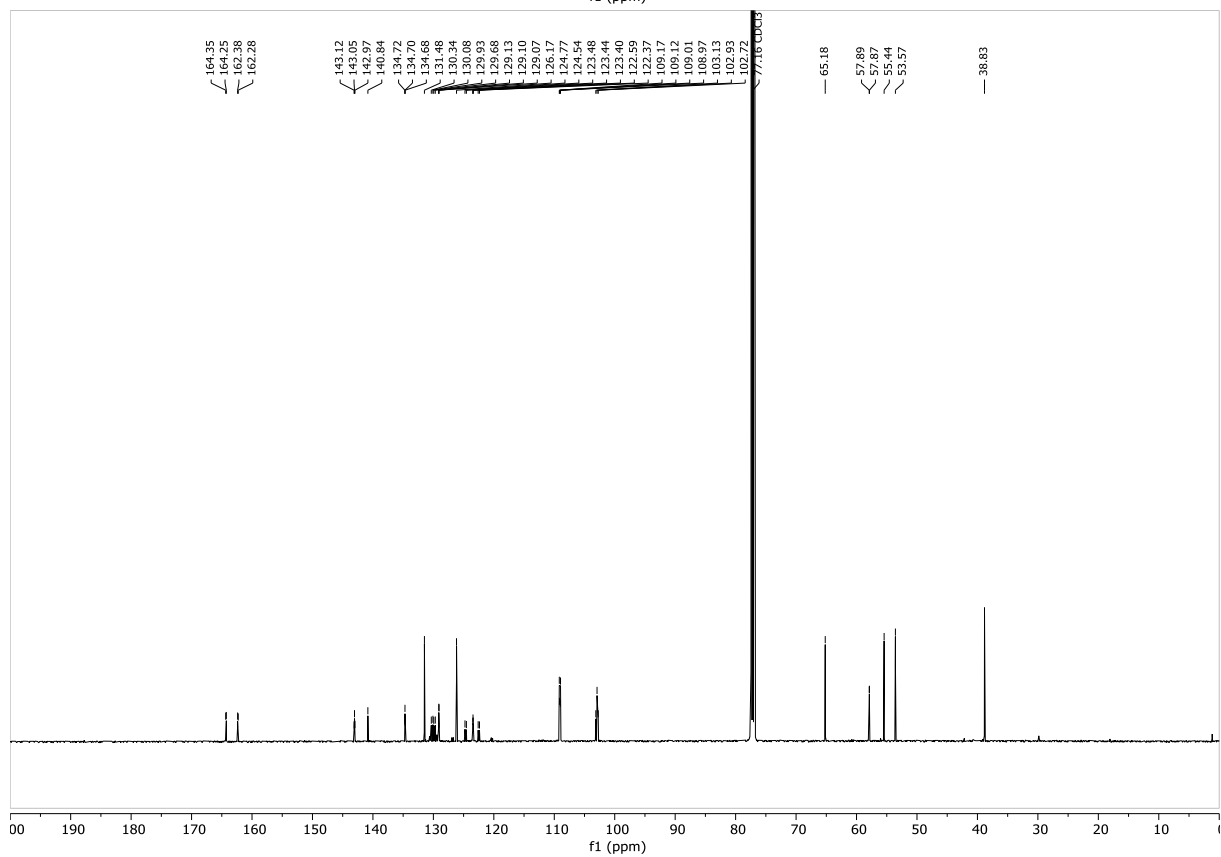
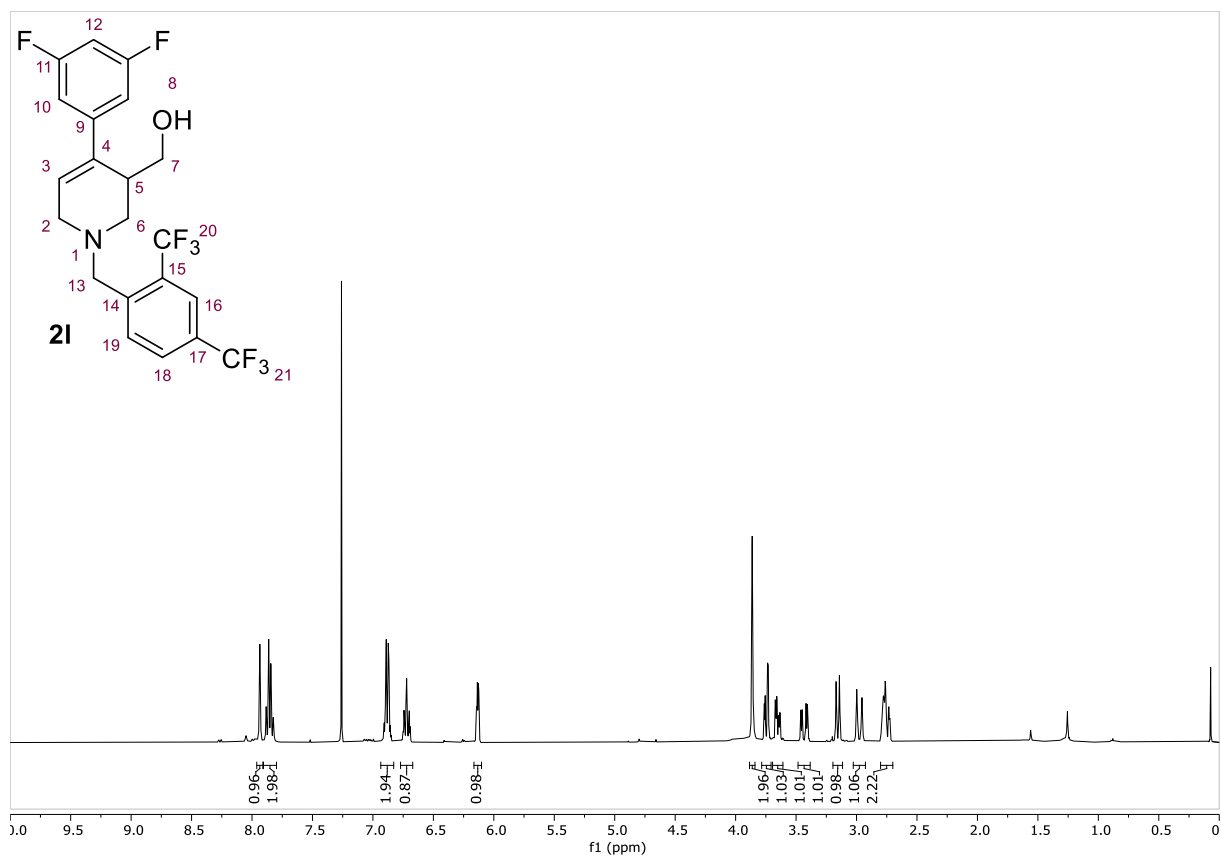


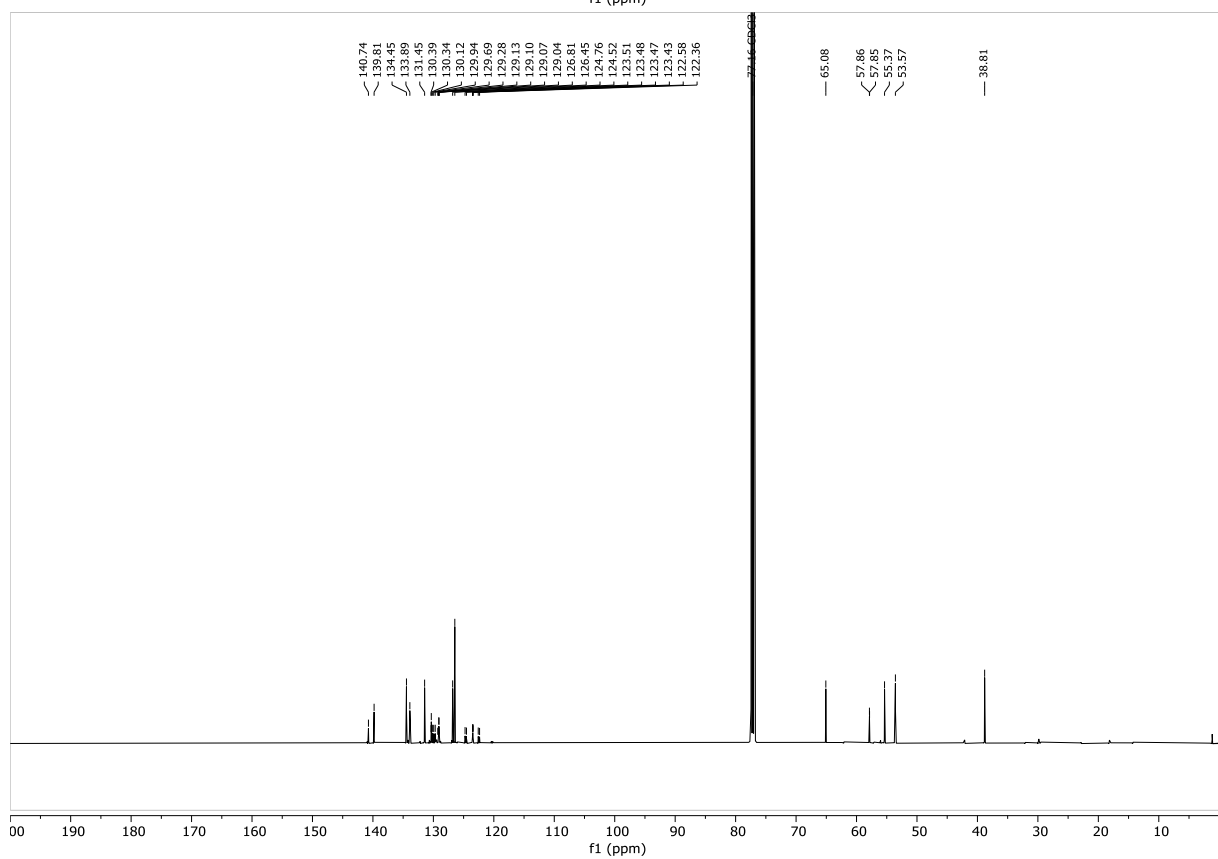
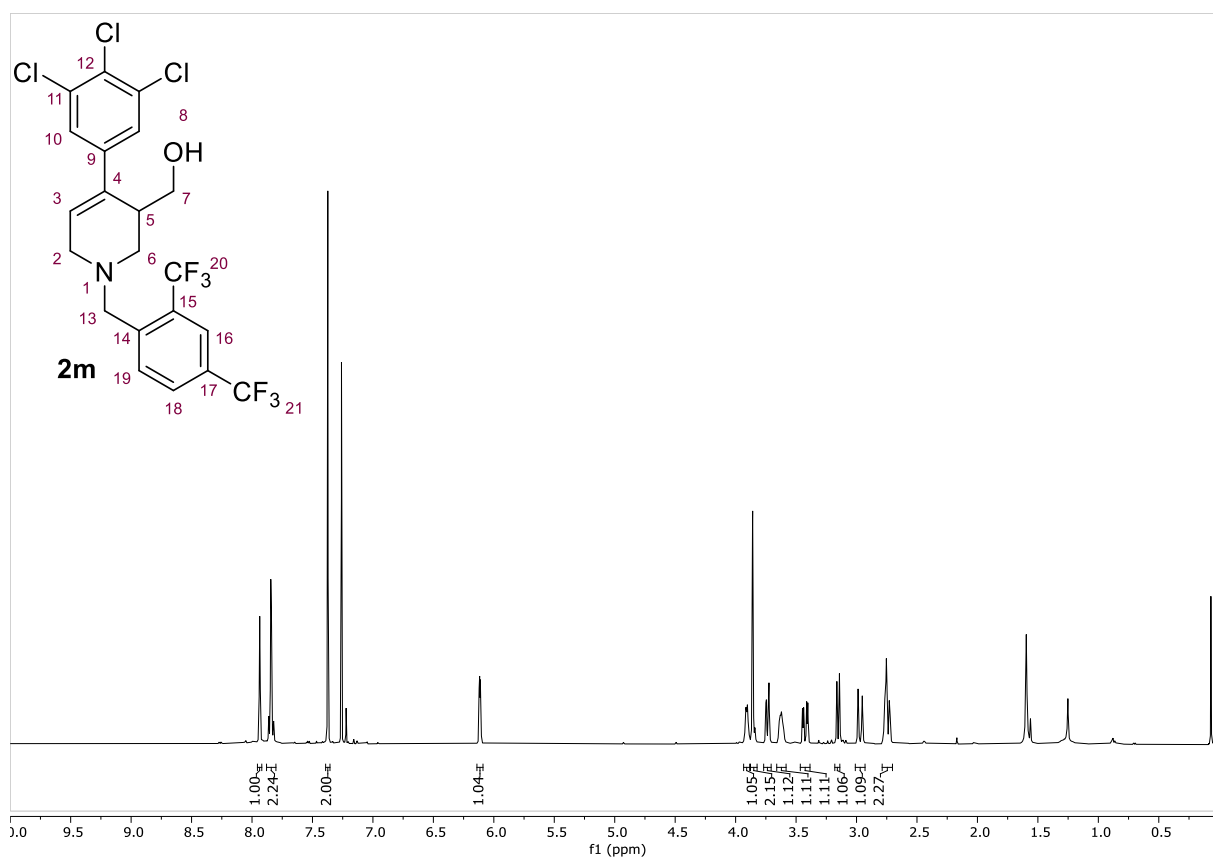


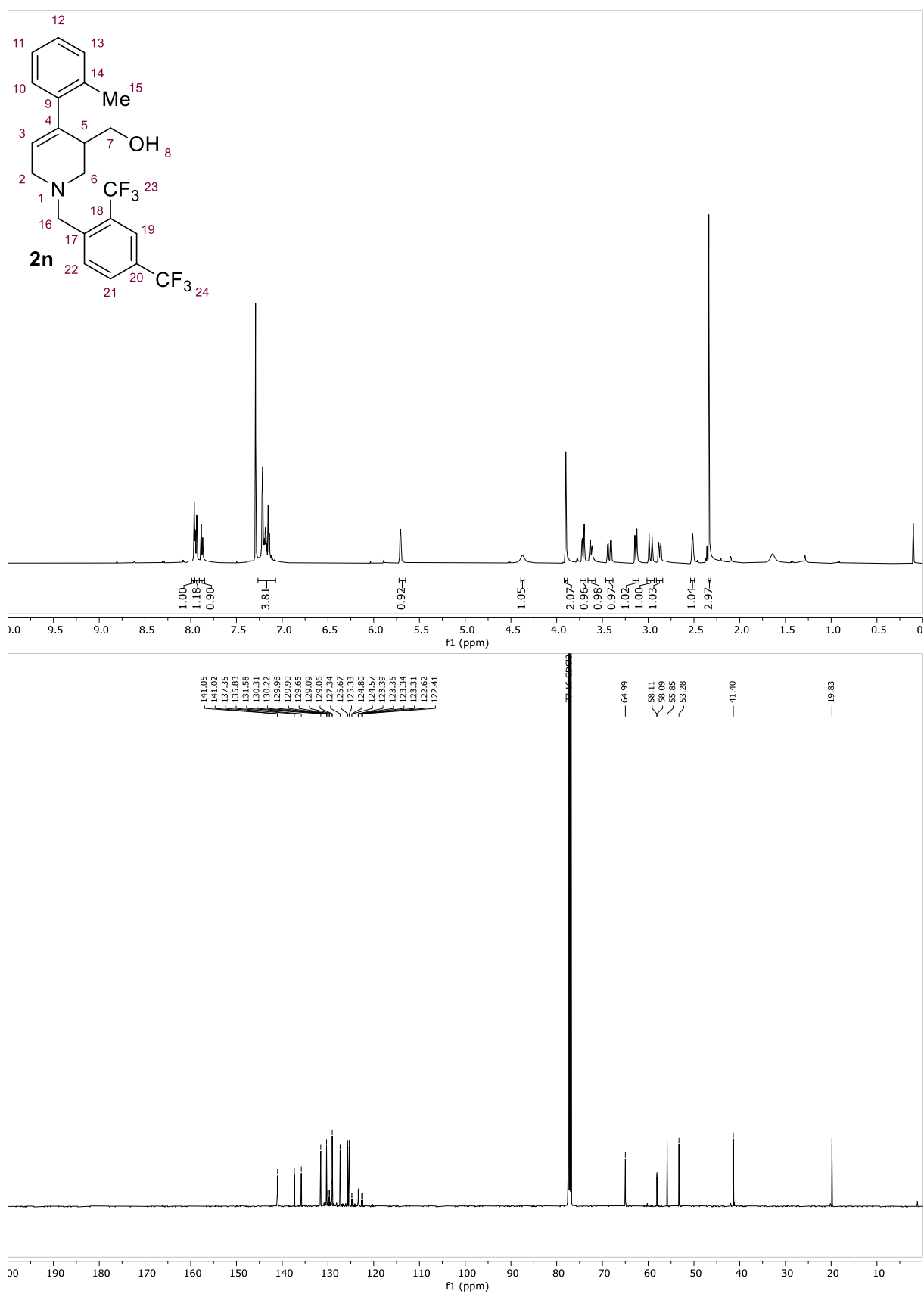


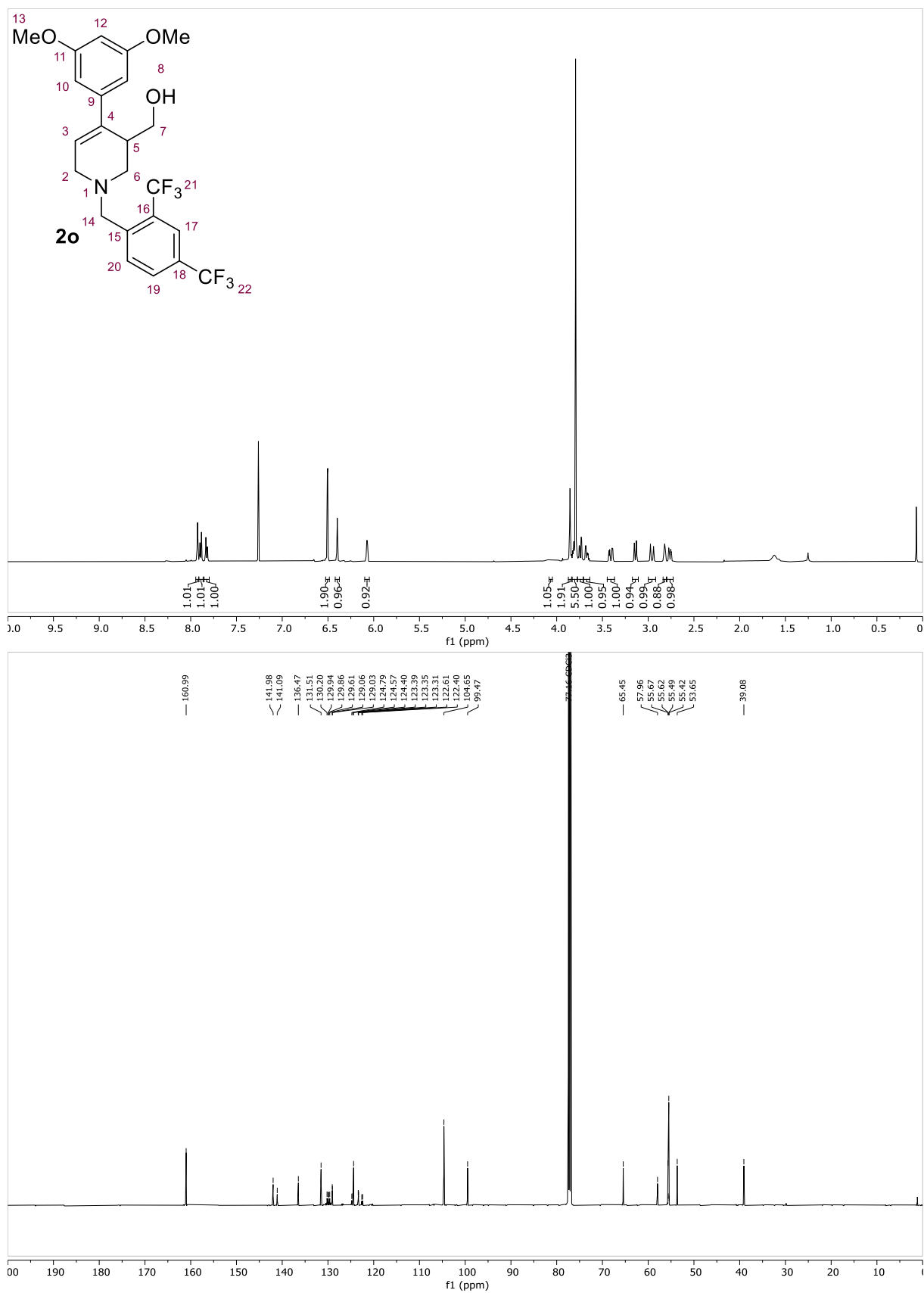


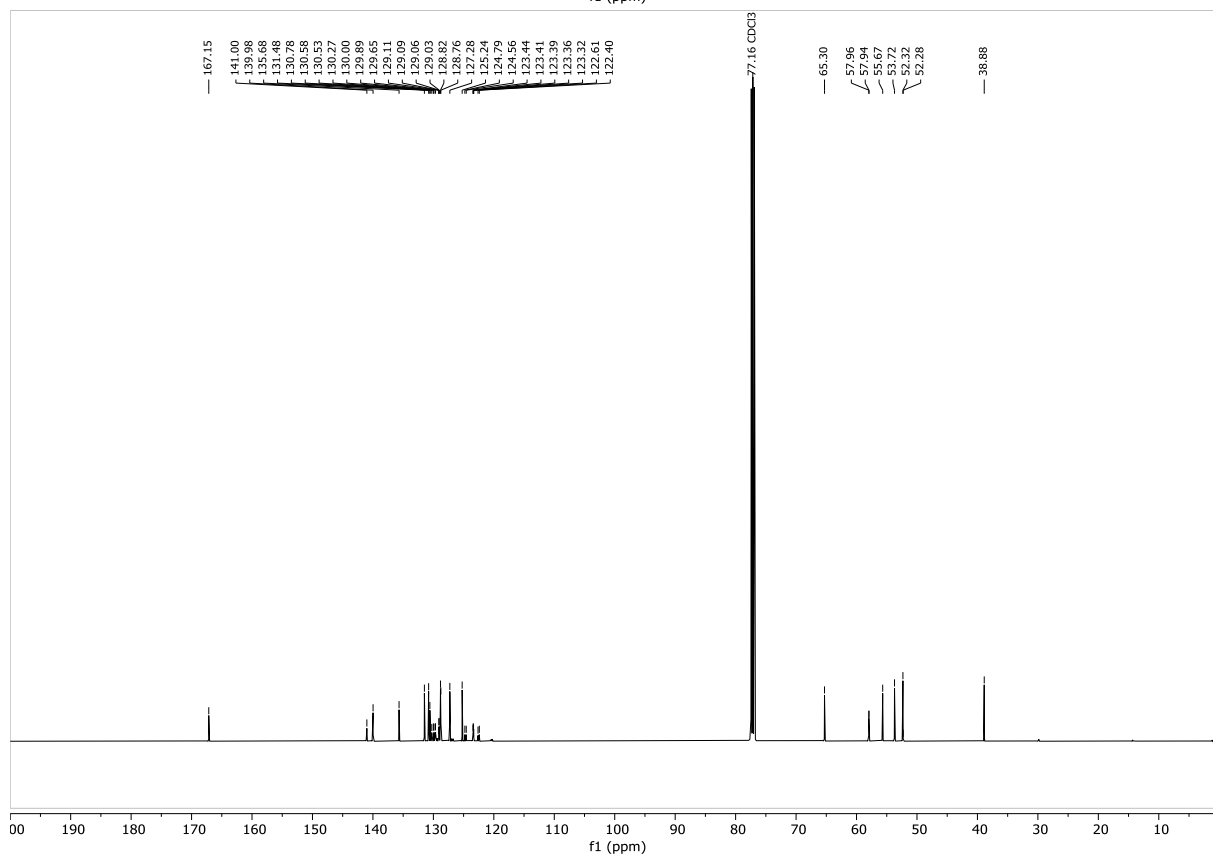
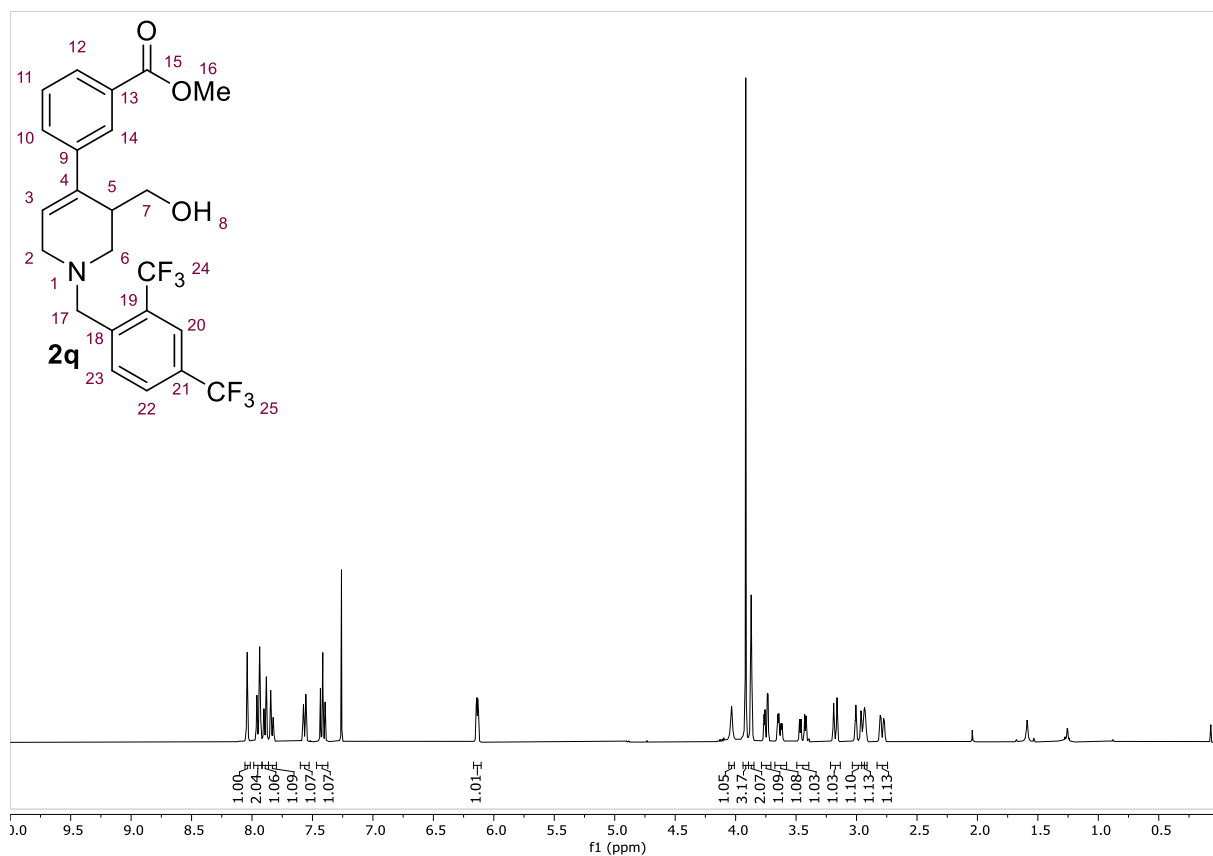


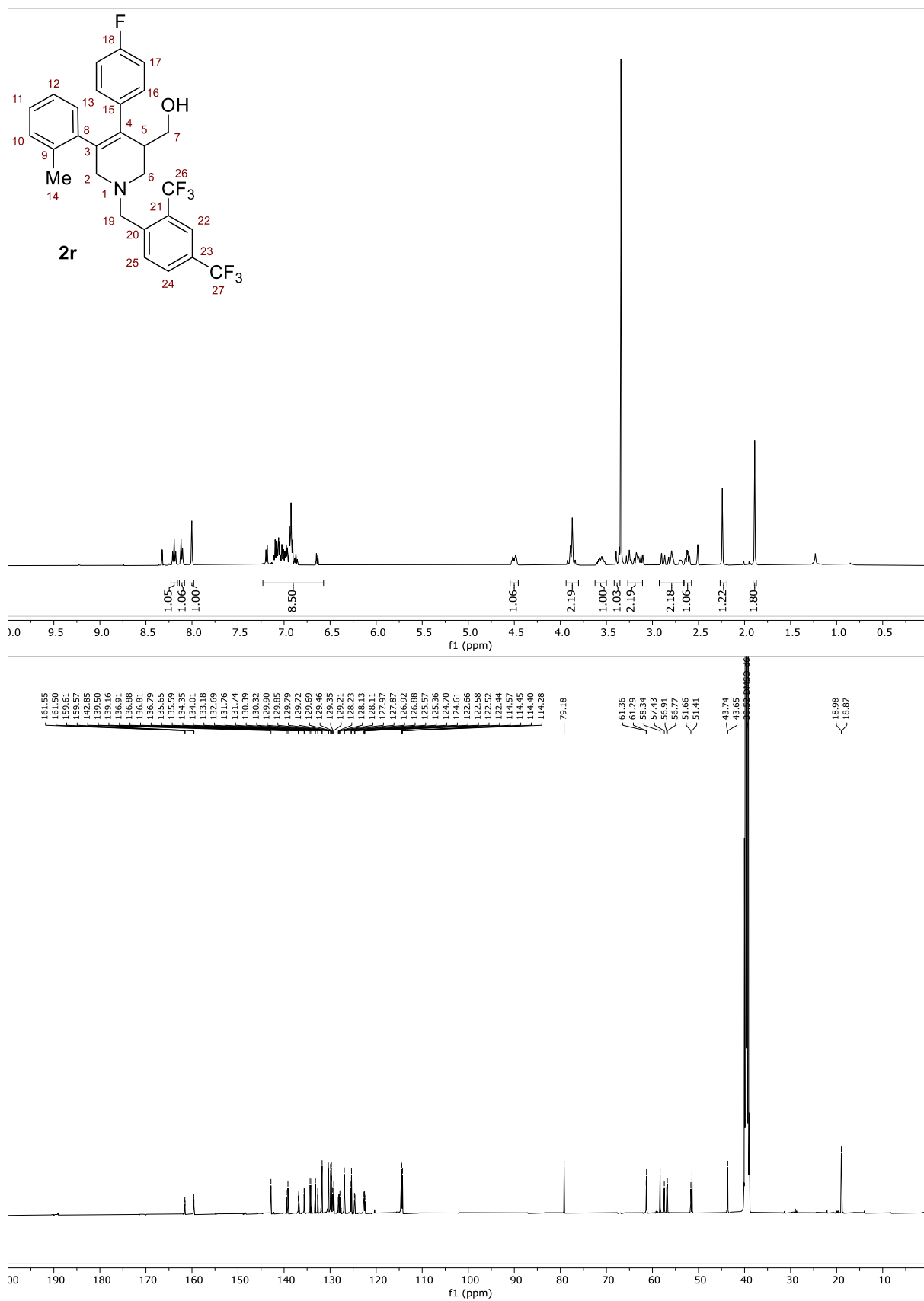




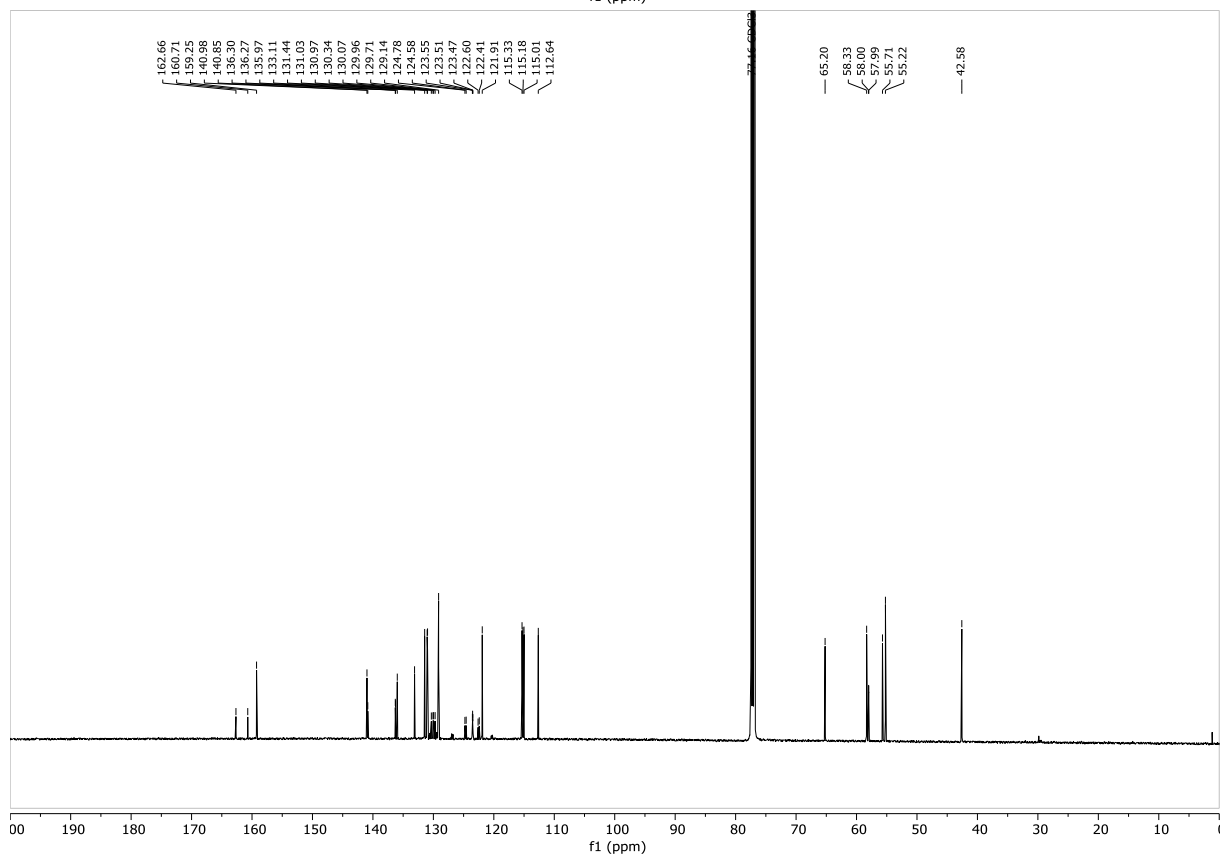
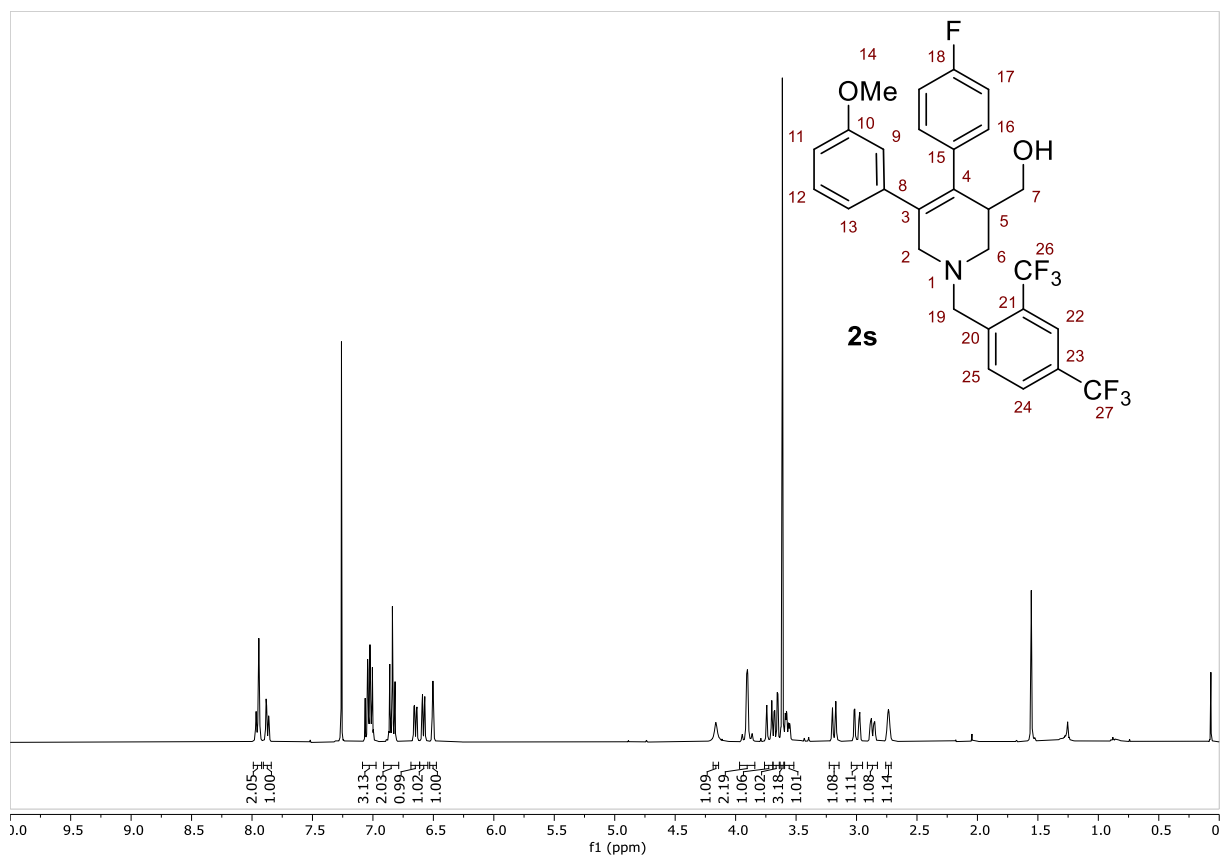


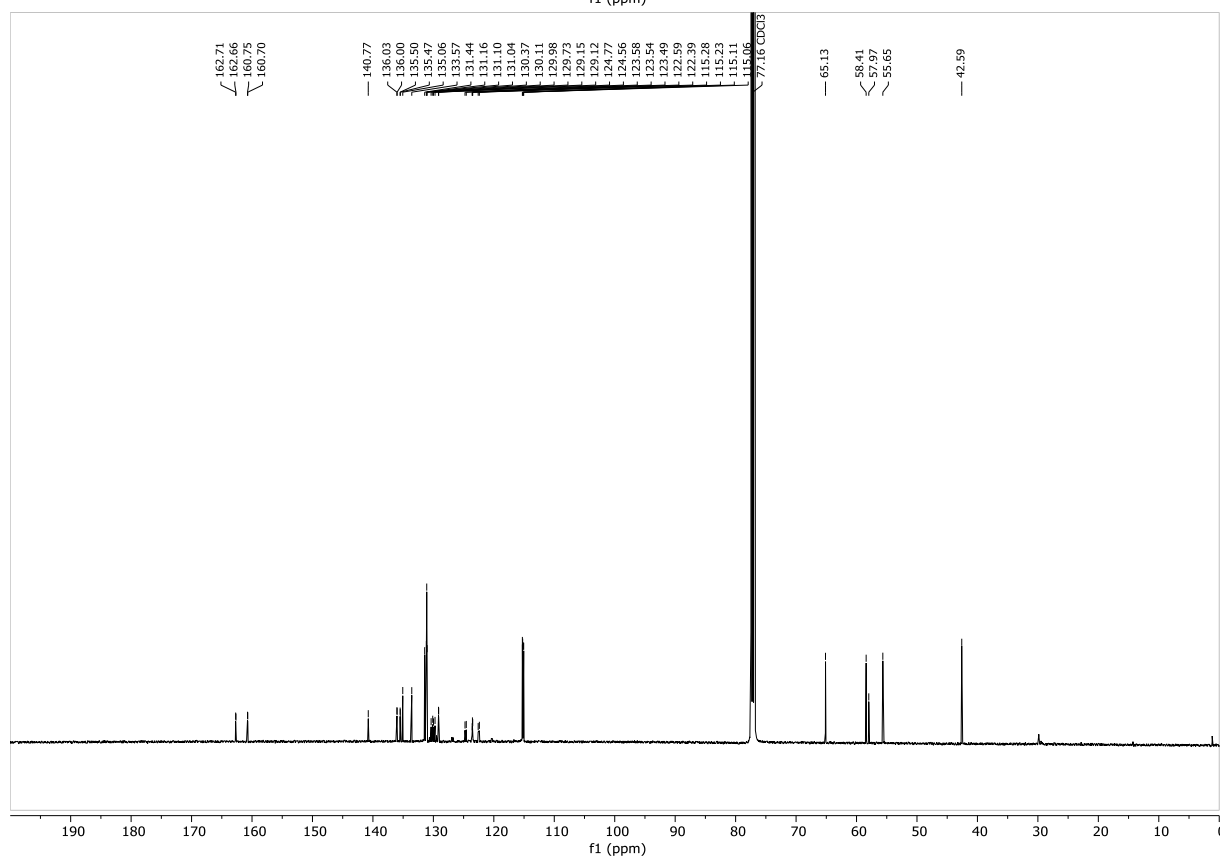
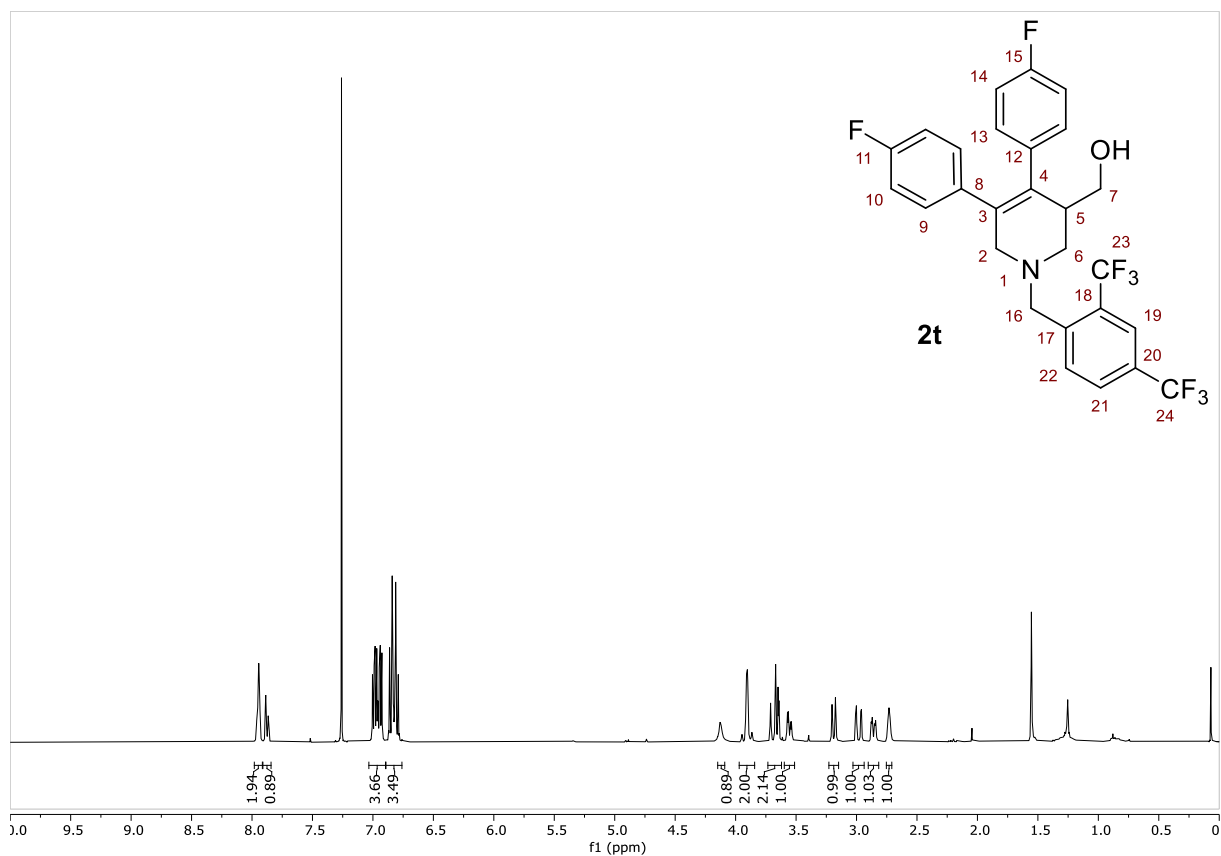


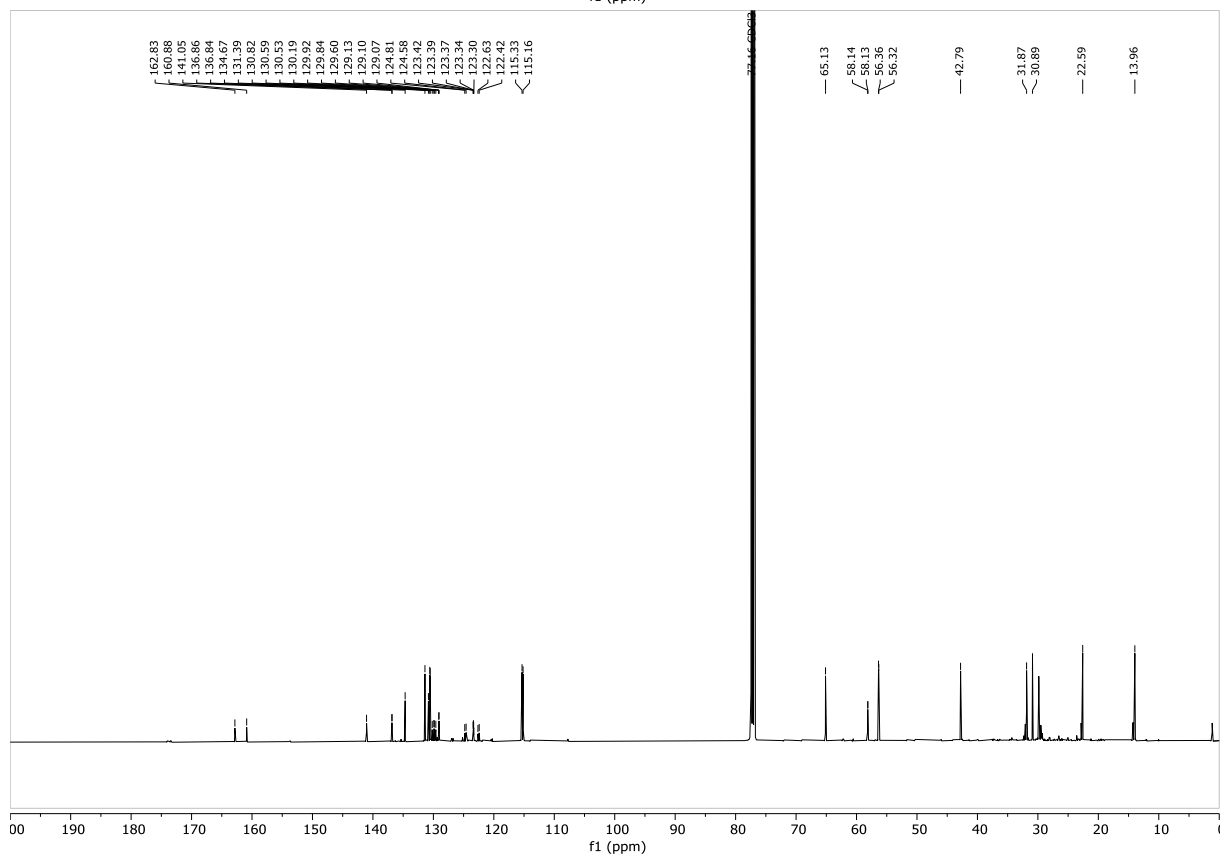
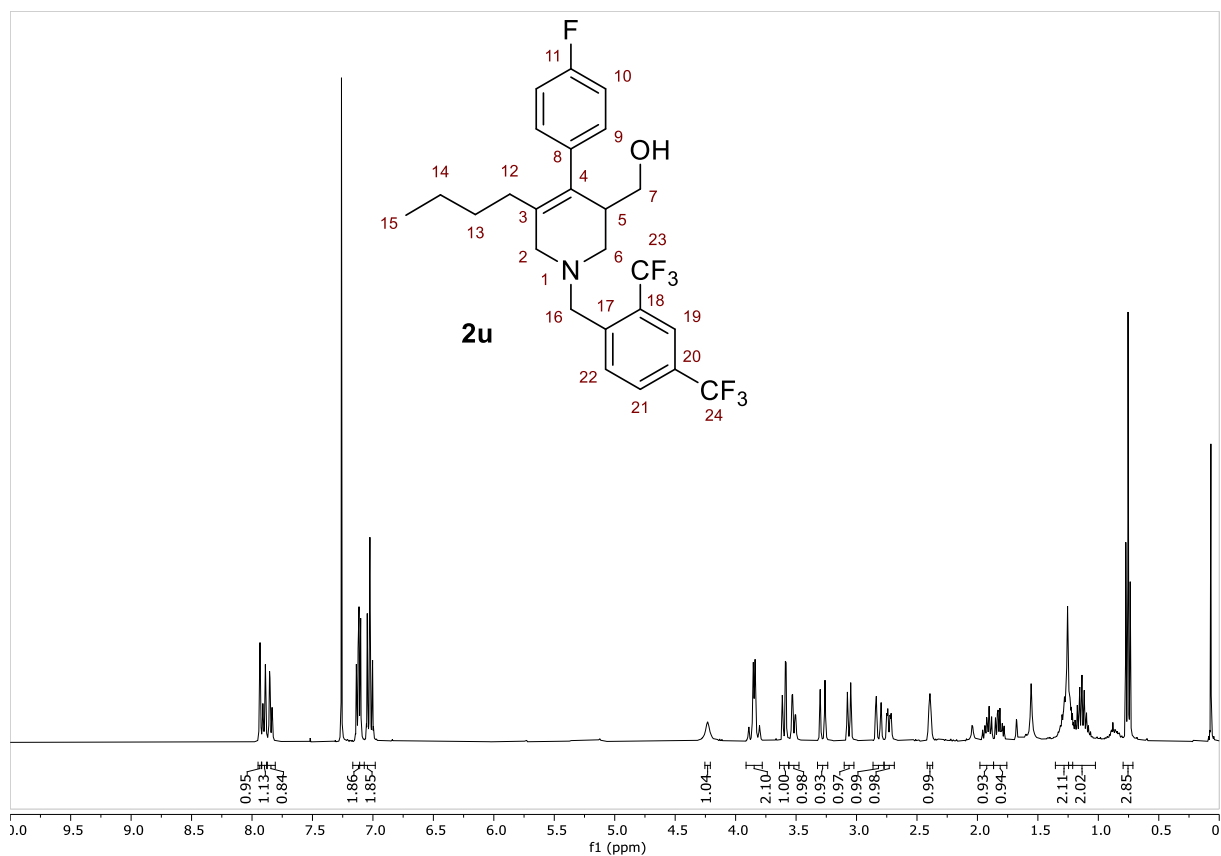


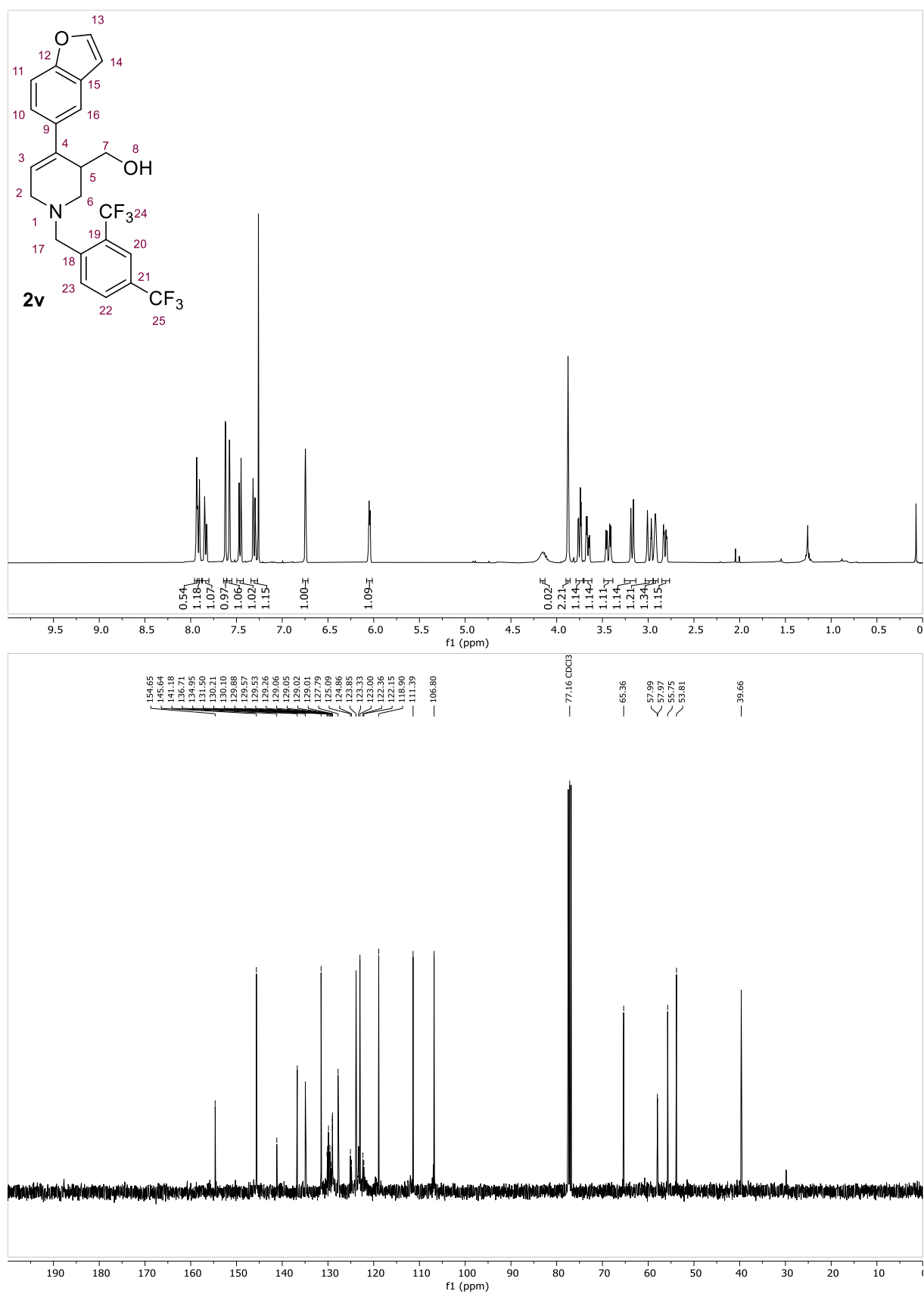


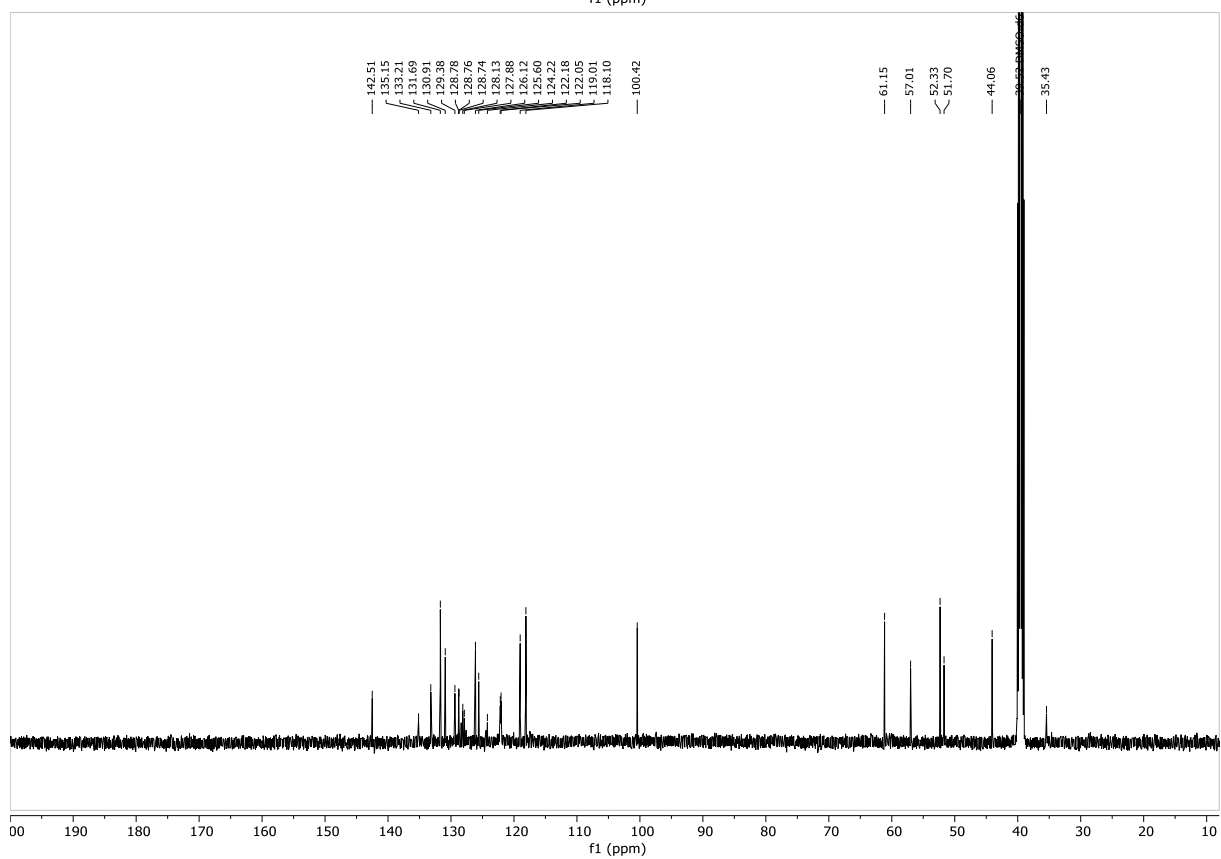
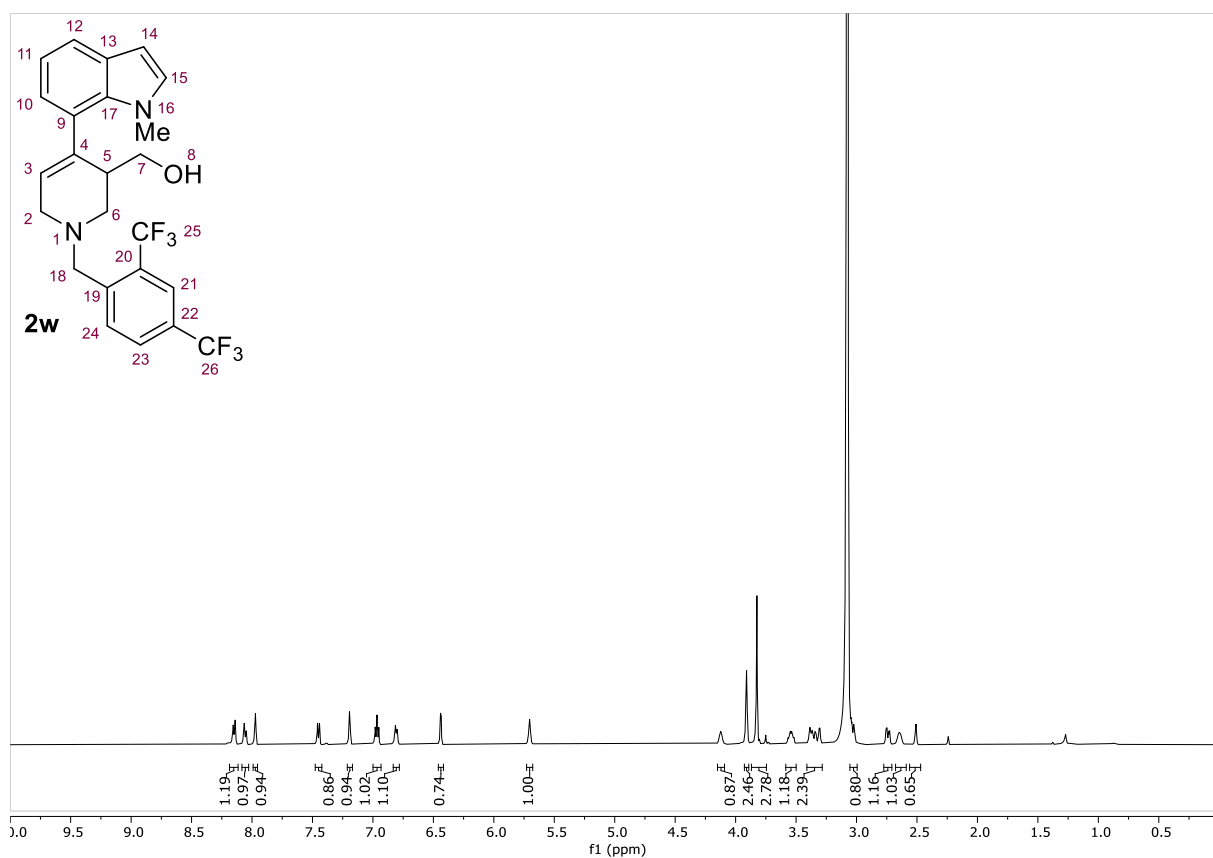
This compound showed rotameric behaviour at RT that could not be resolved using VT NMR.

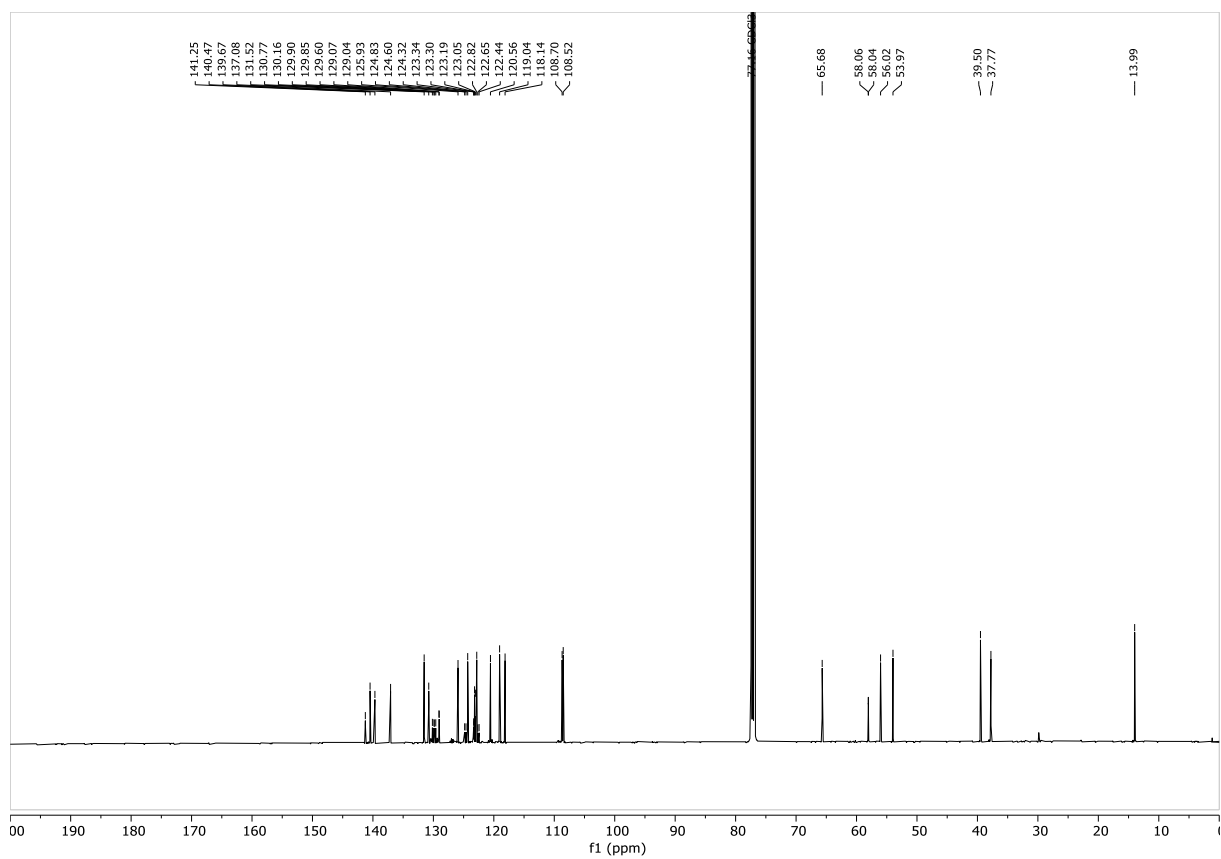
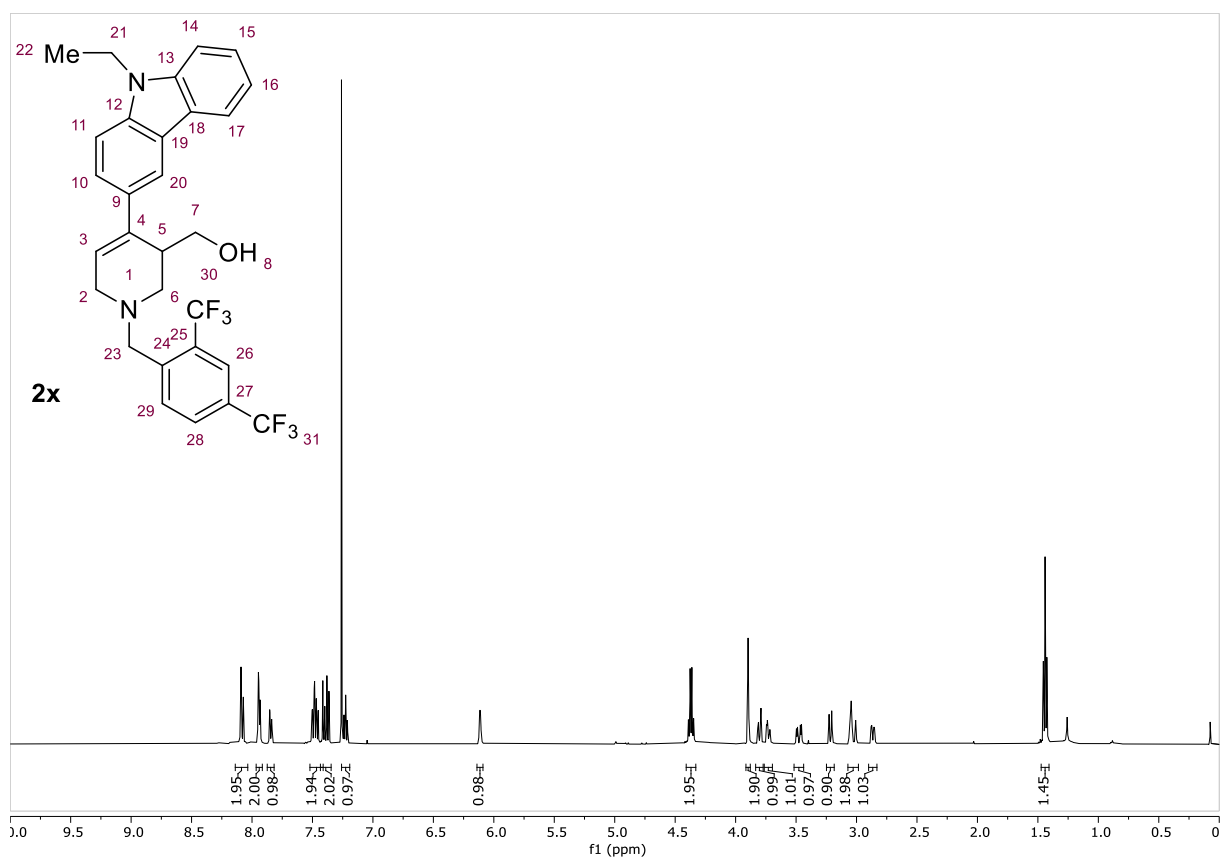


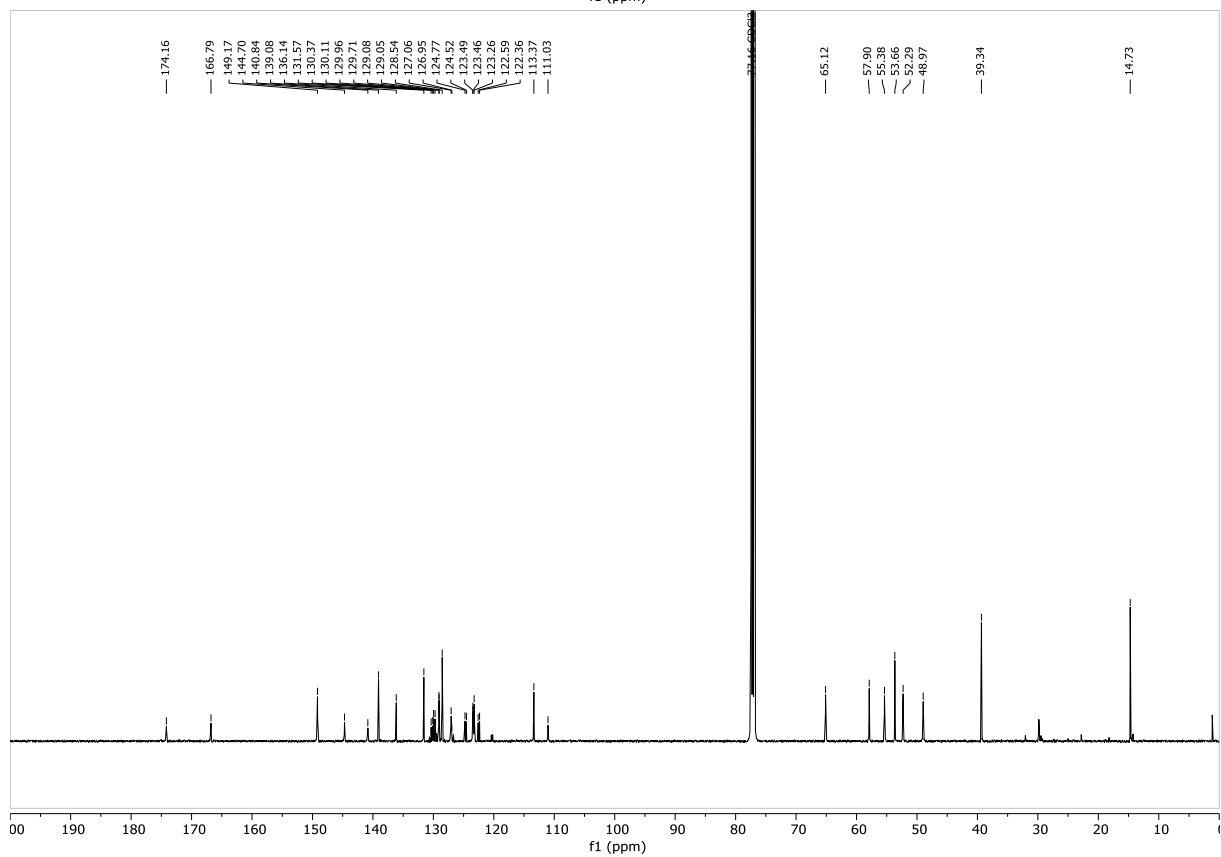
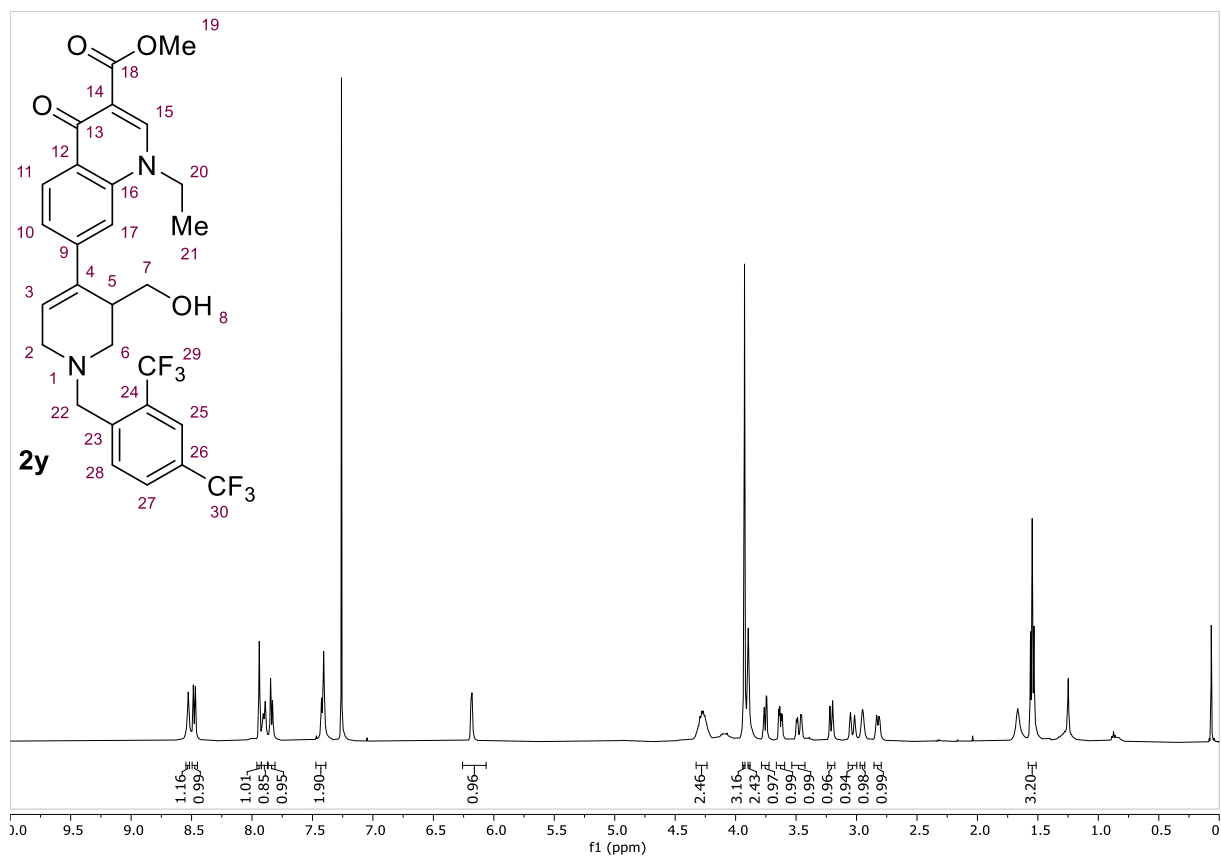


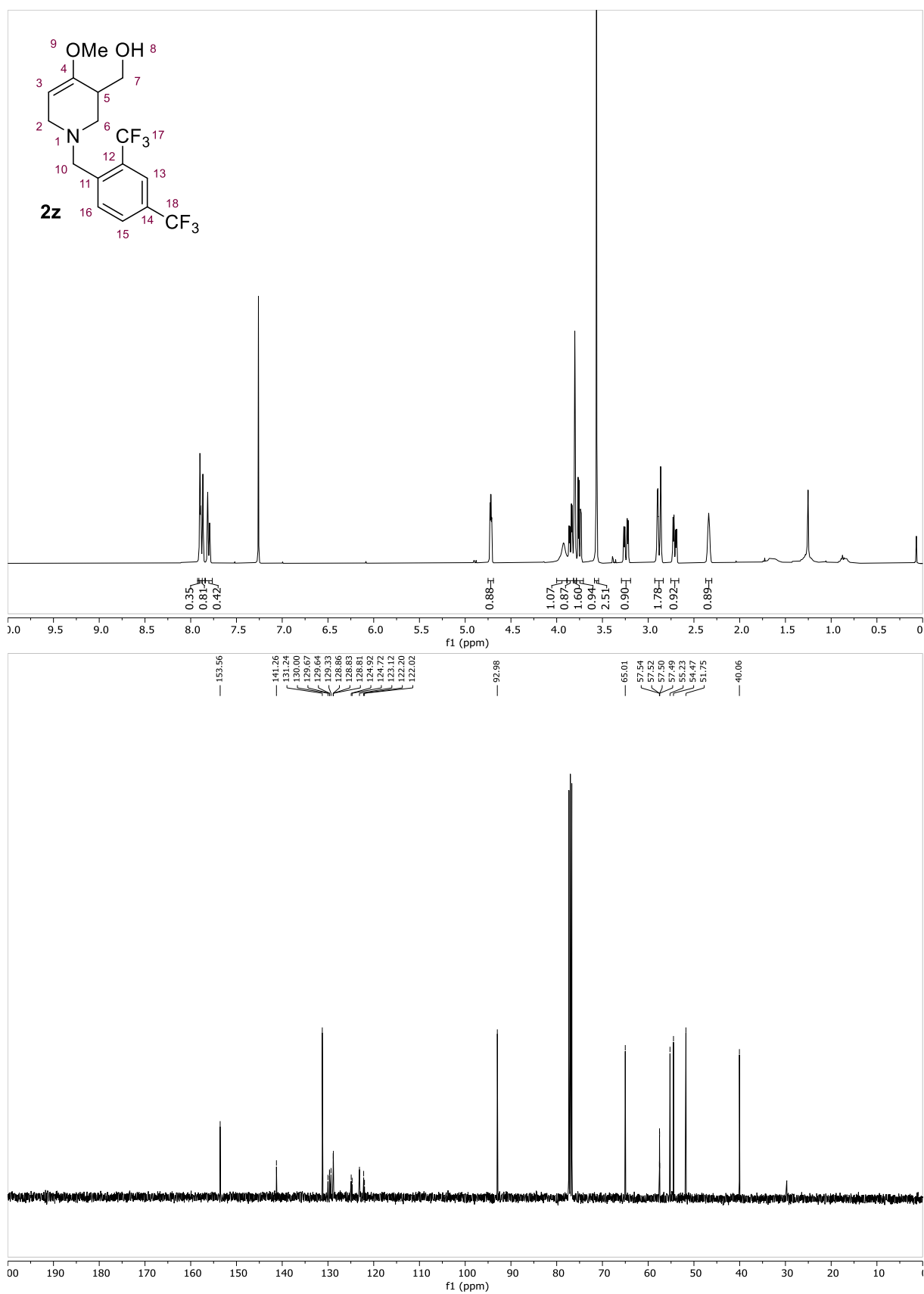


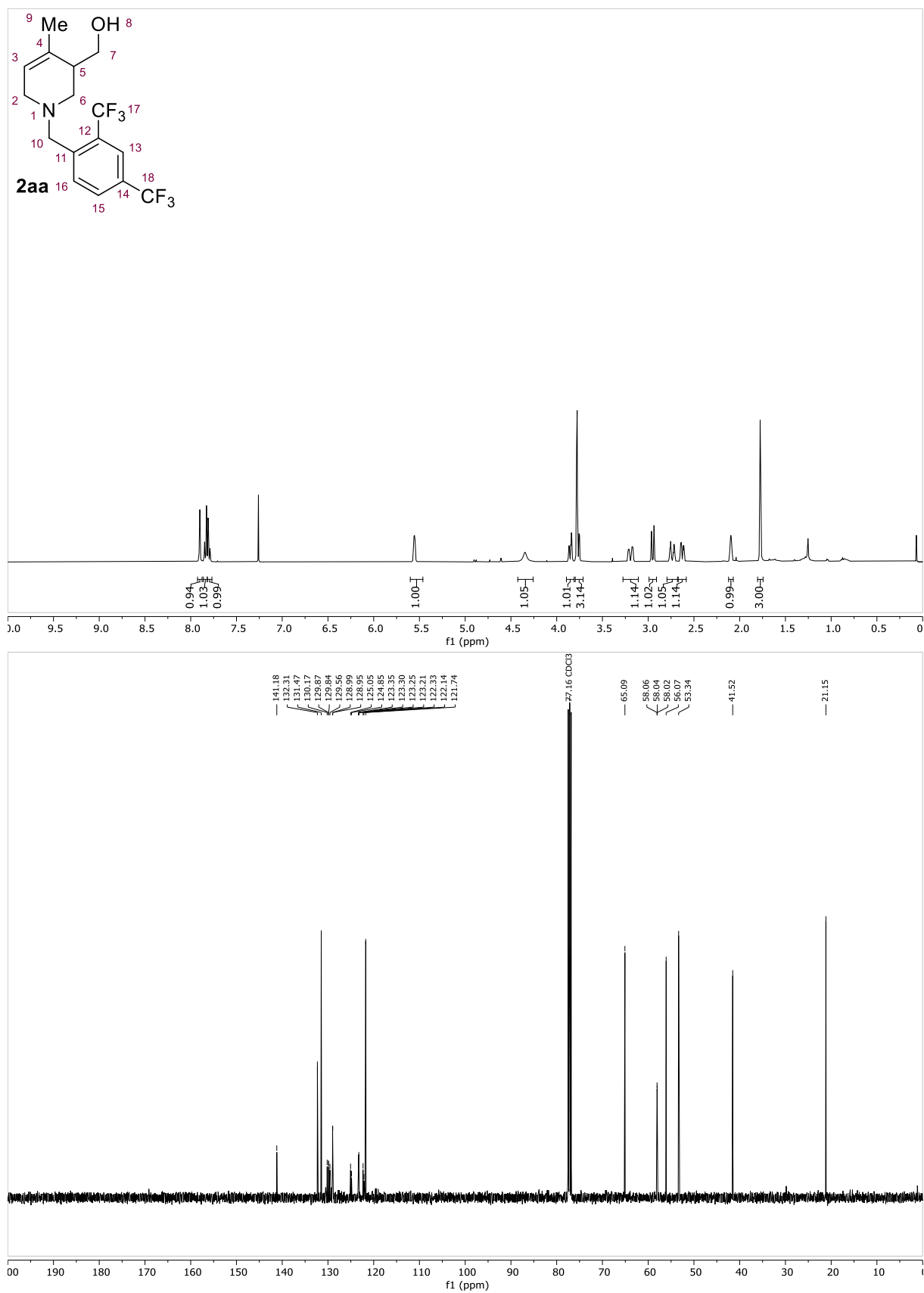


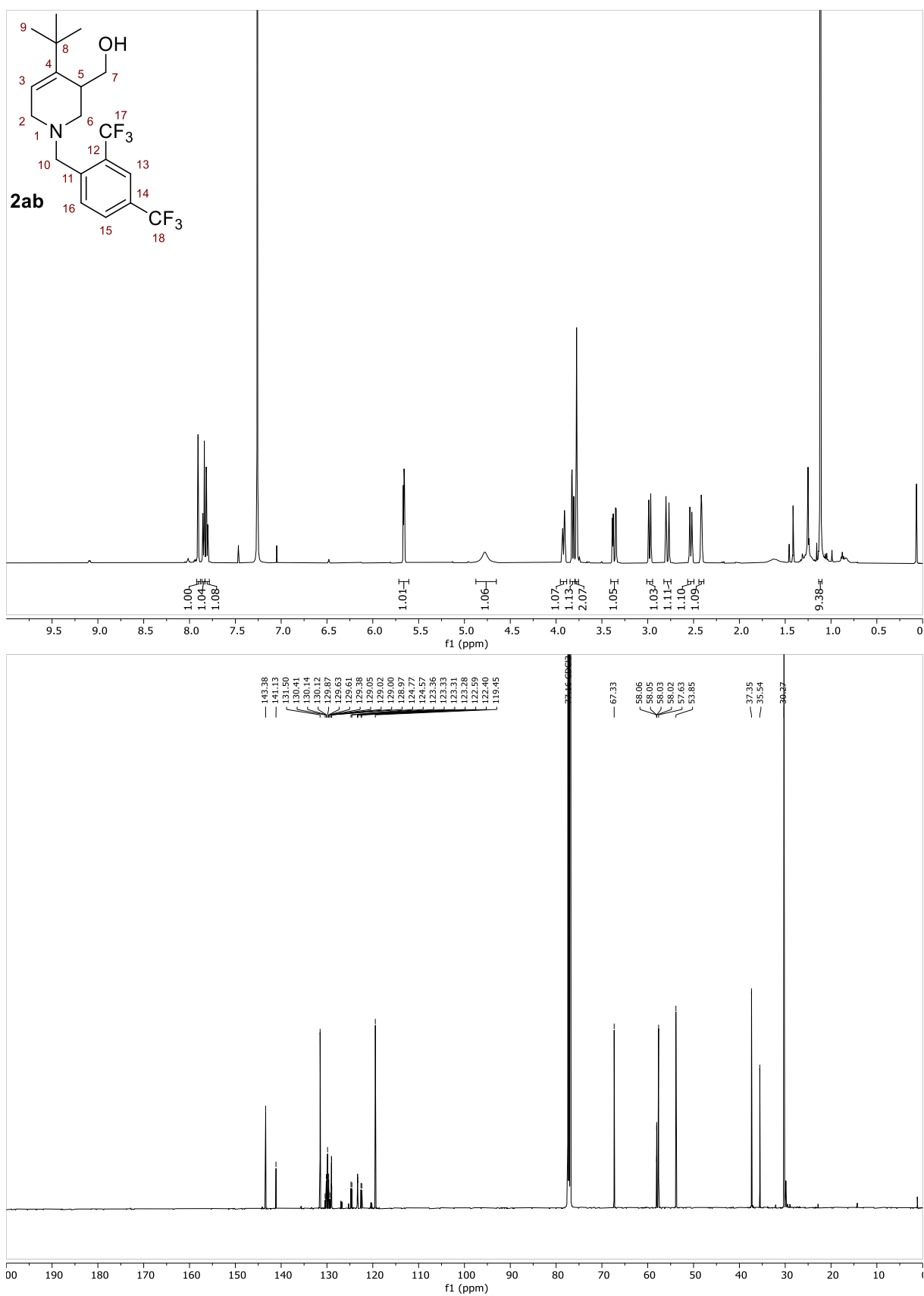


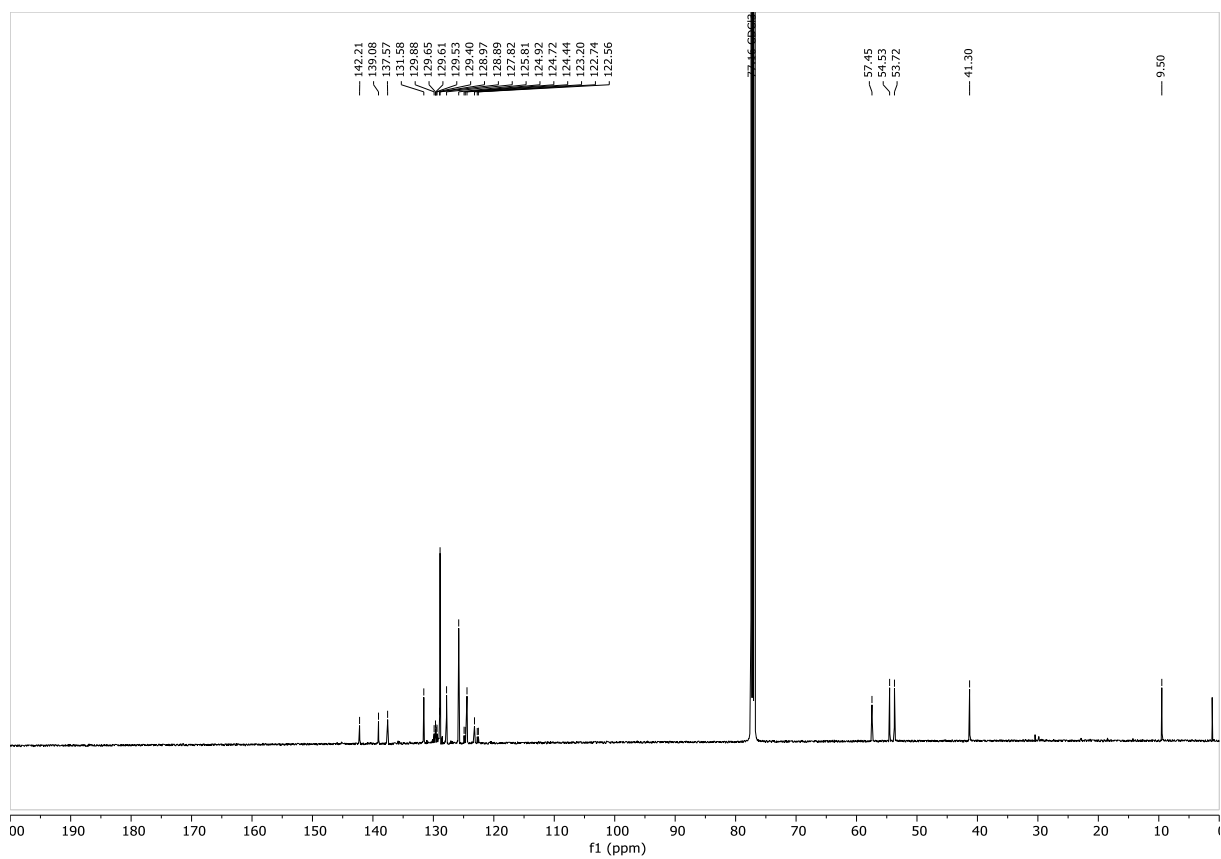
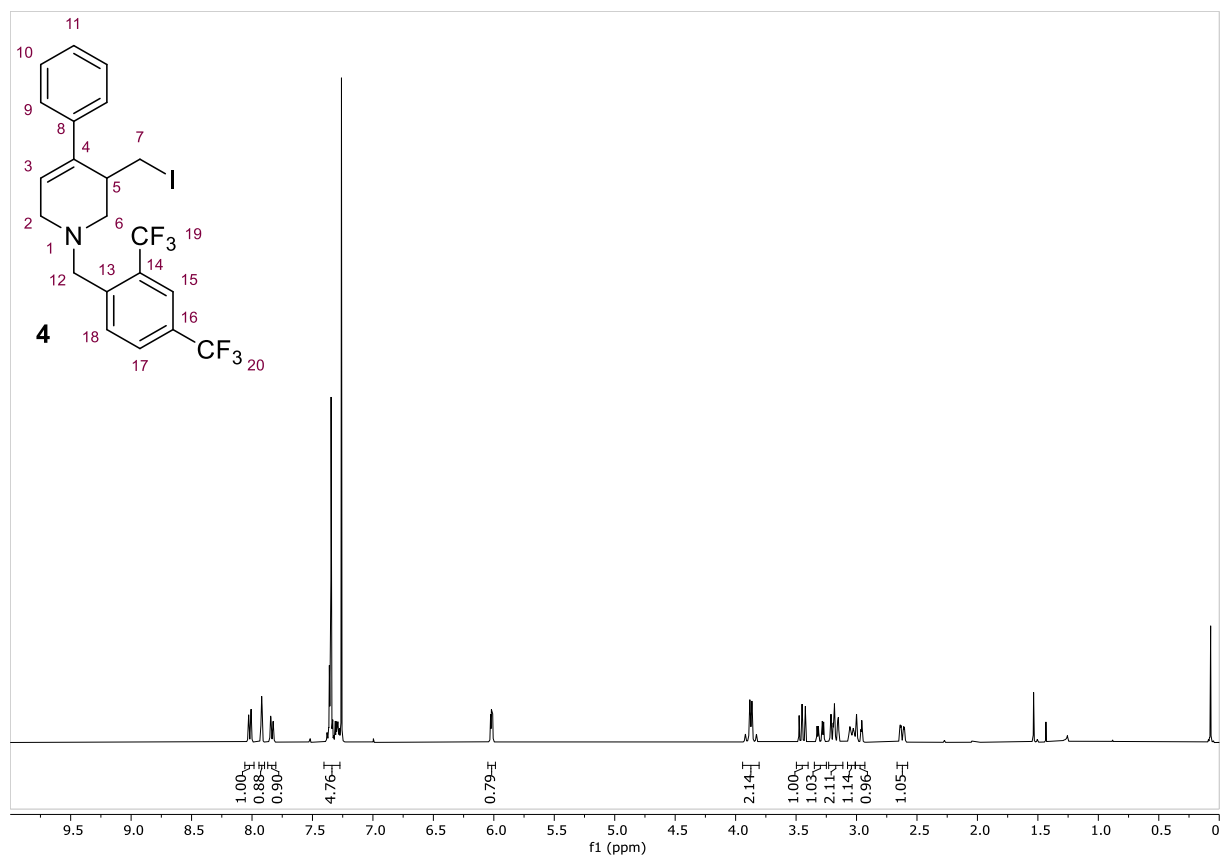


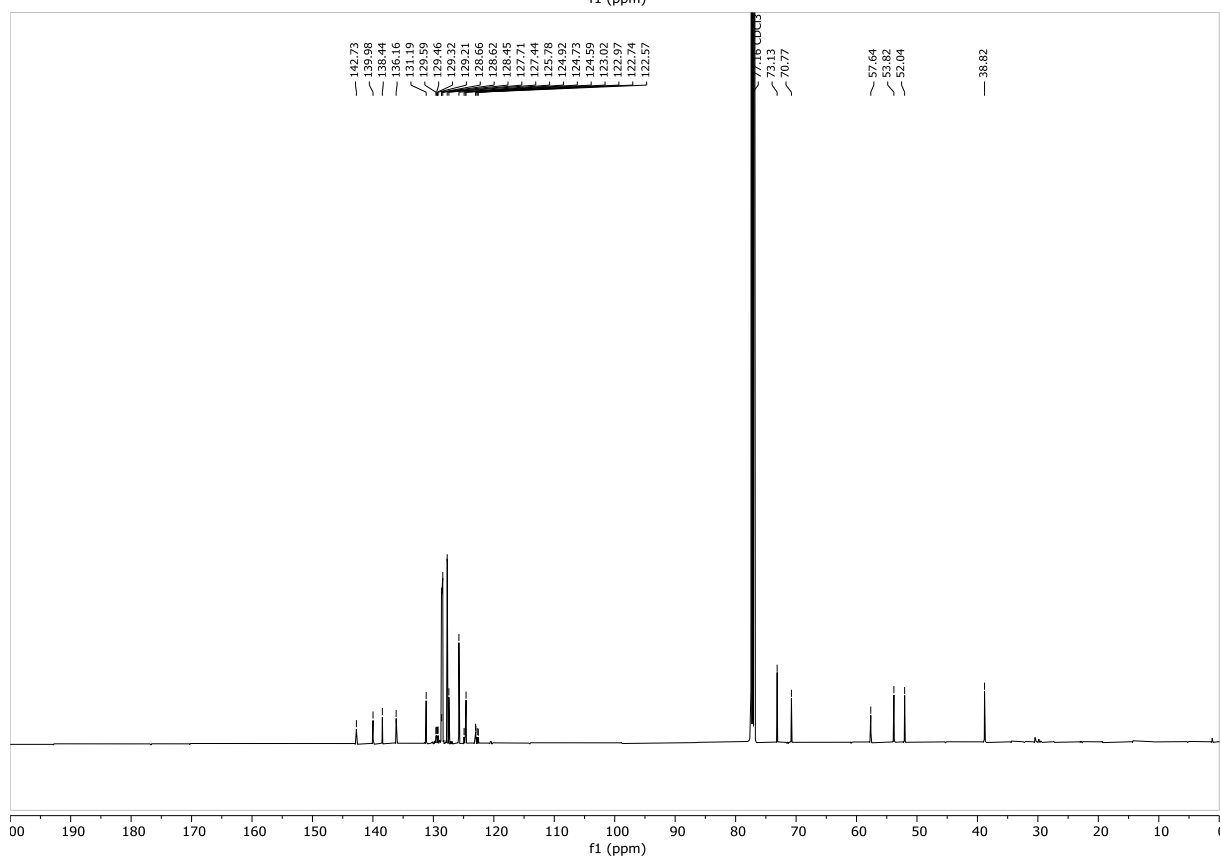
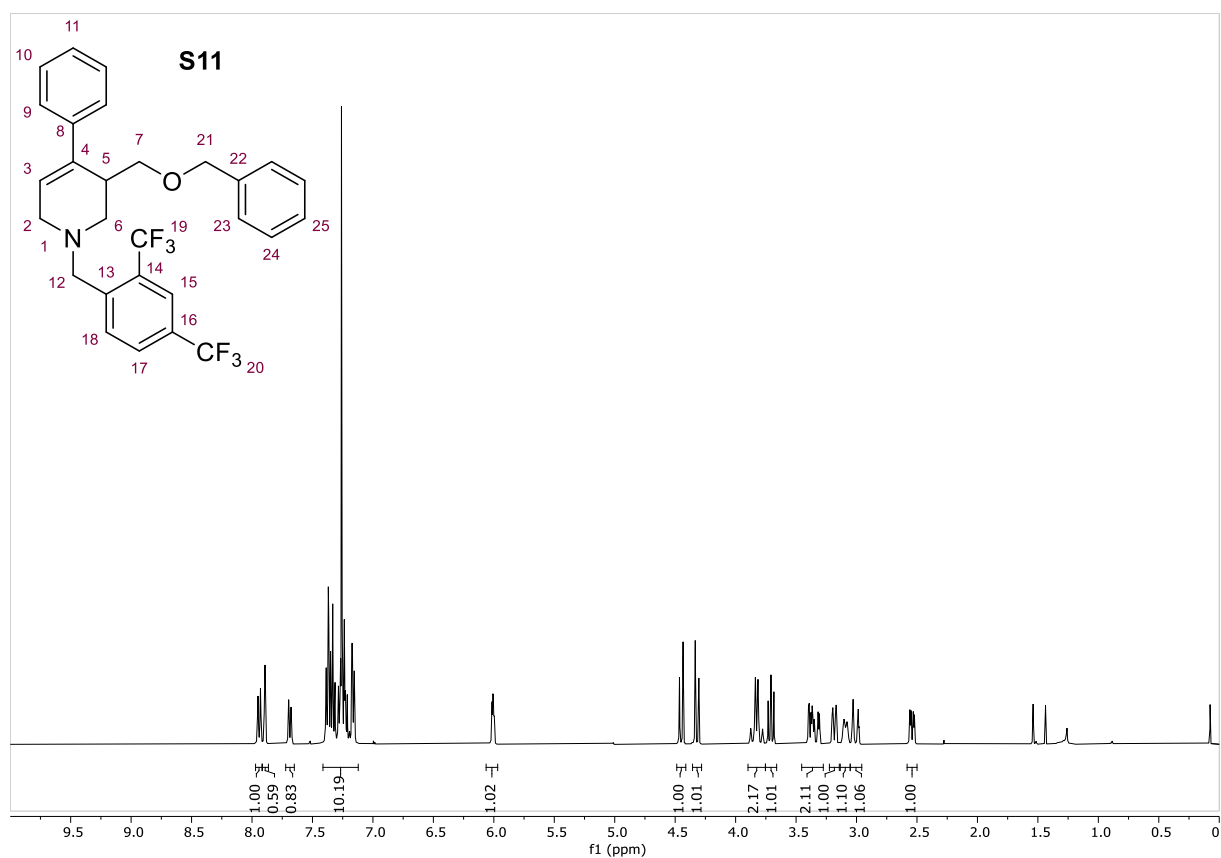


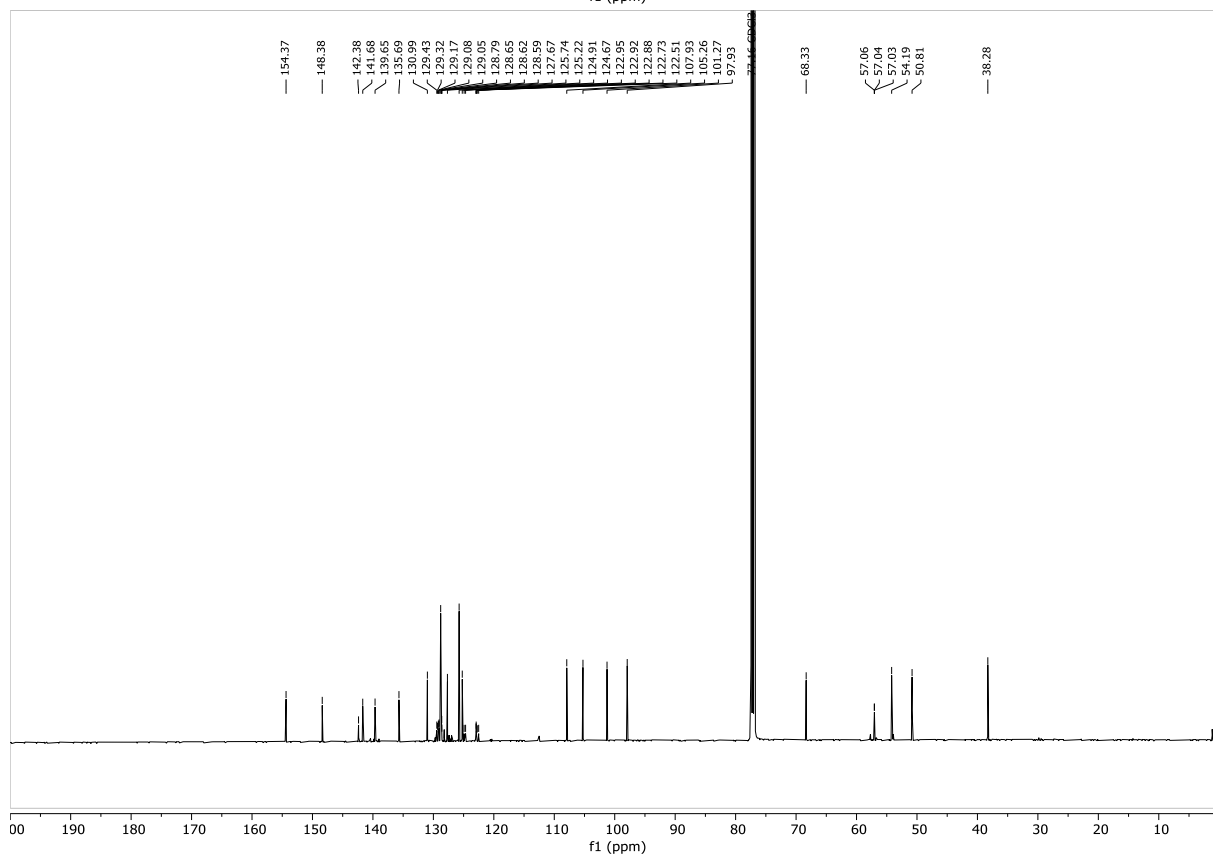
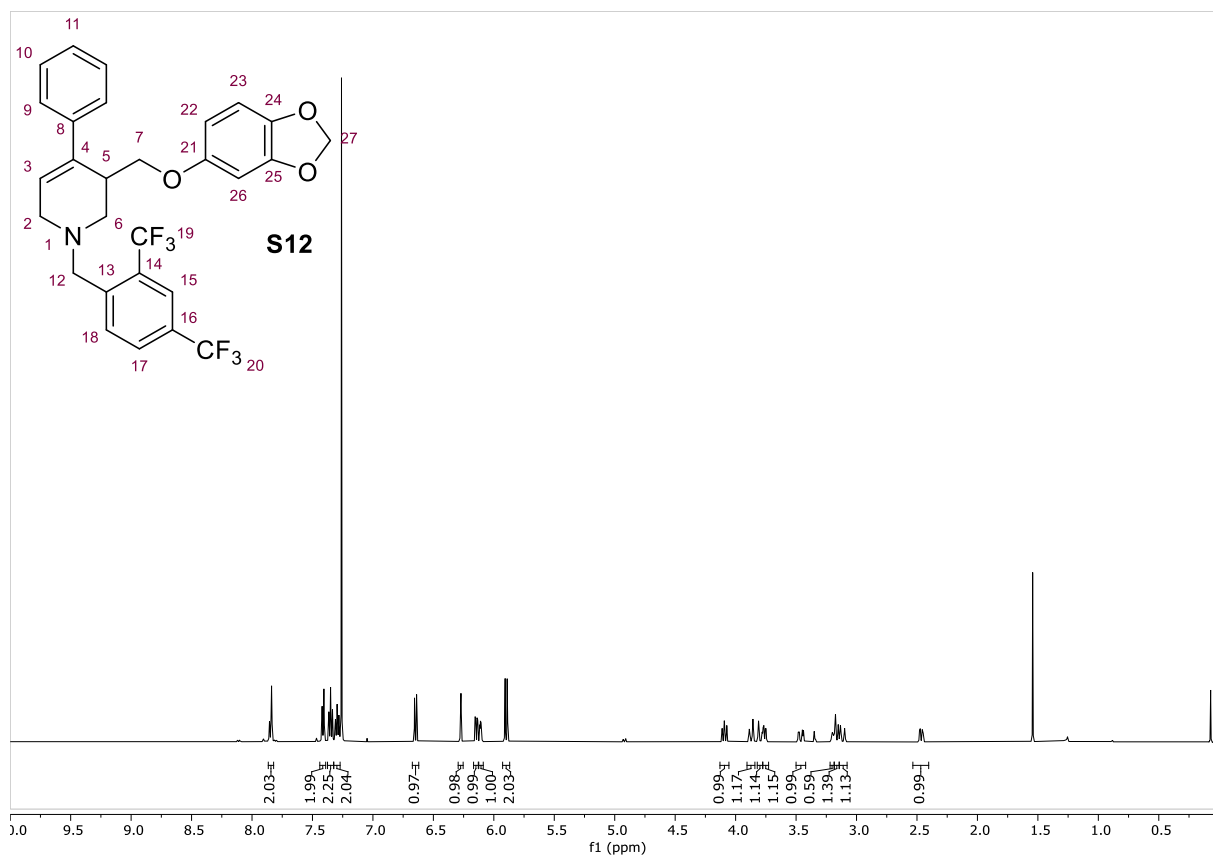


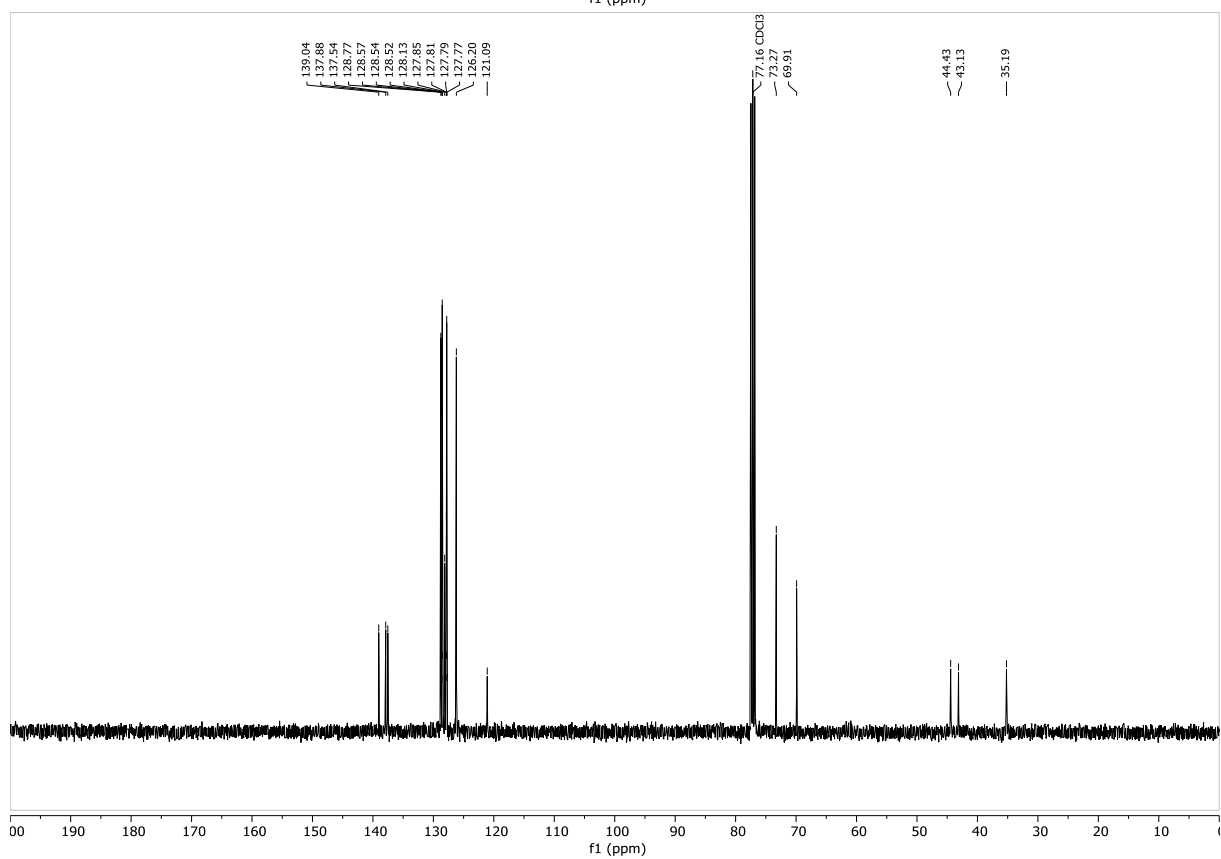
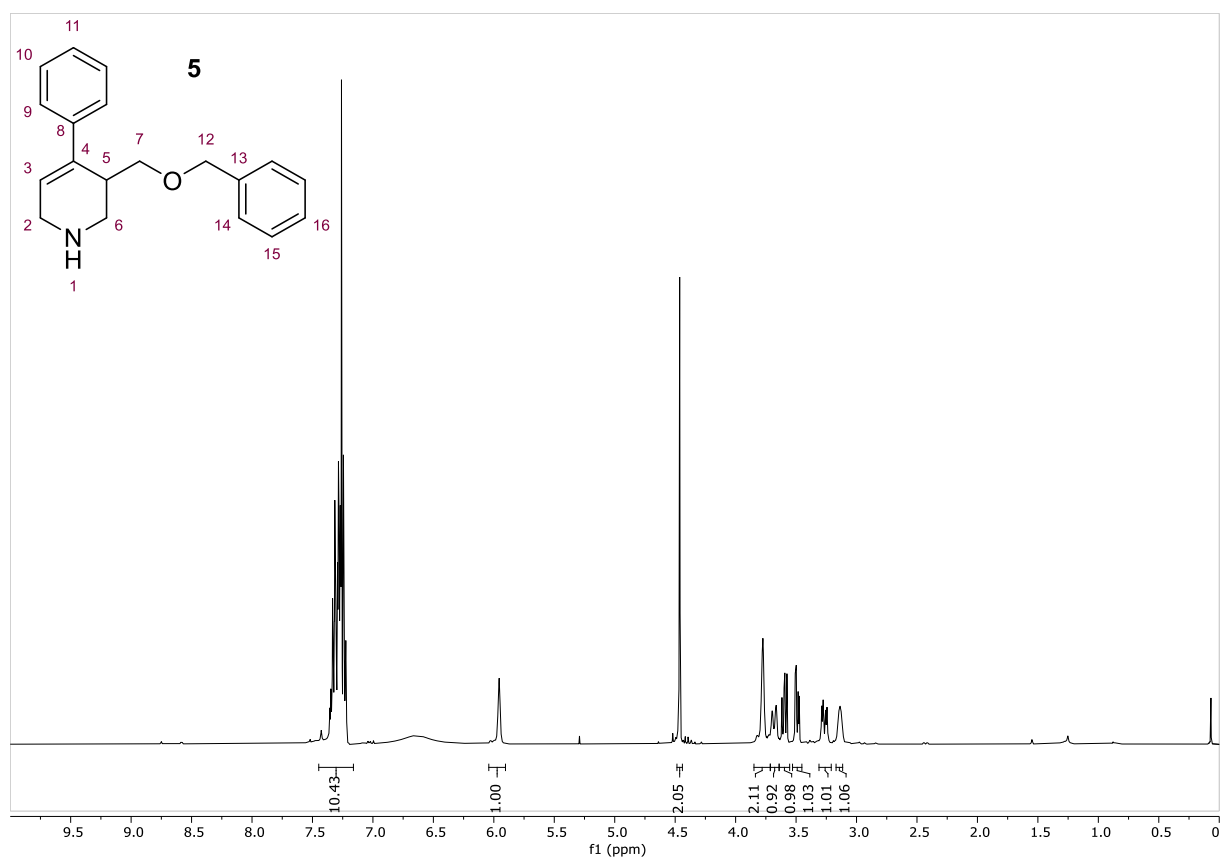


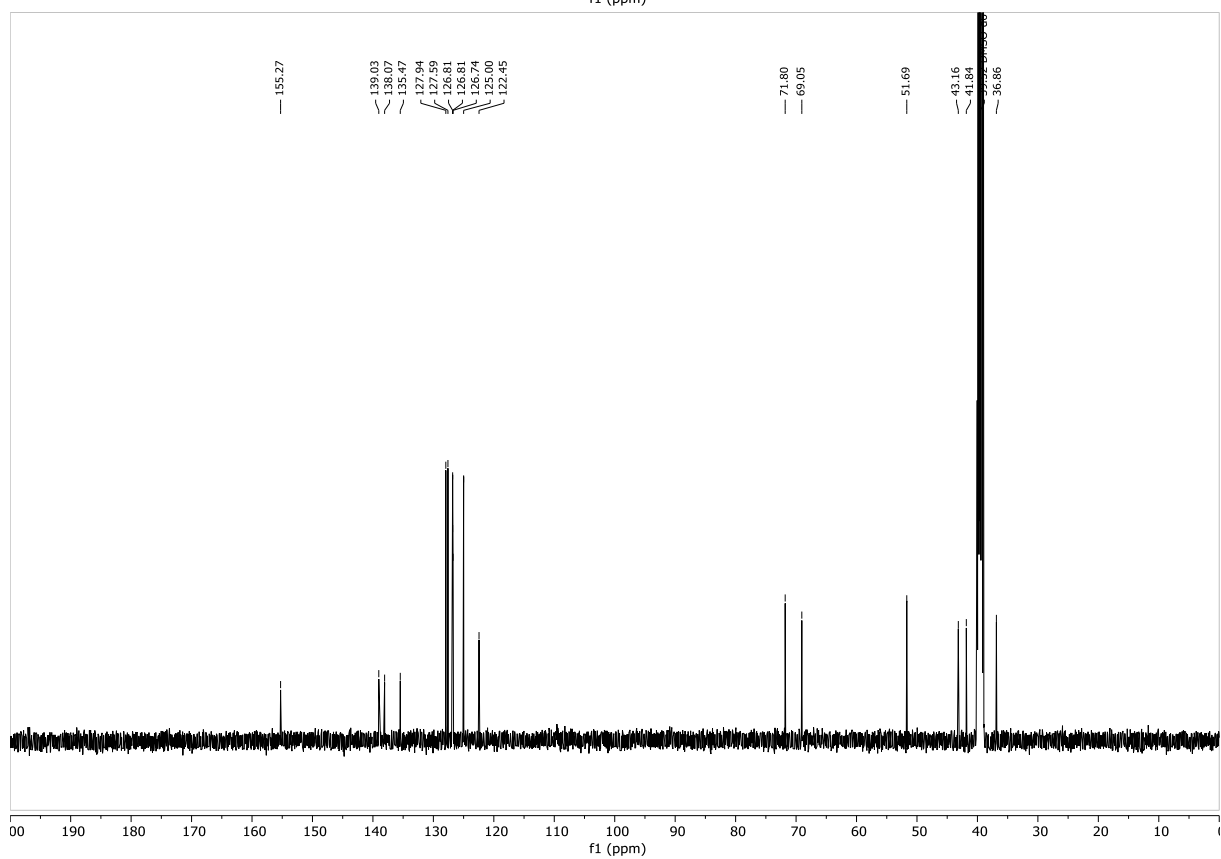
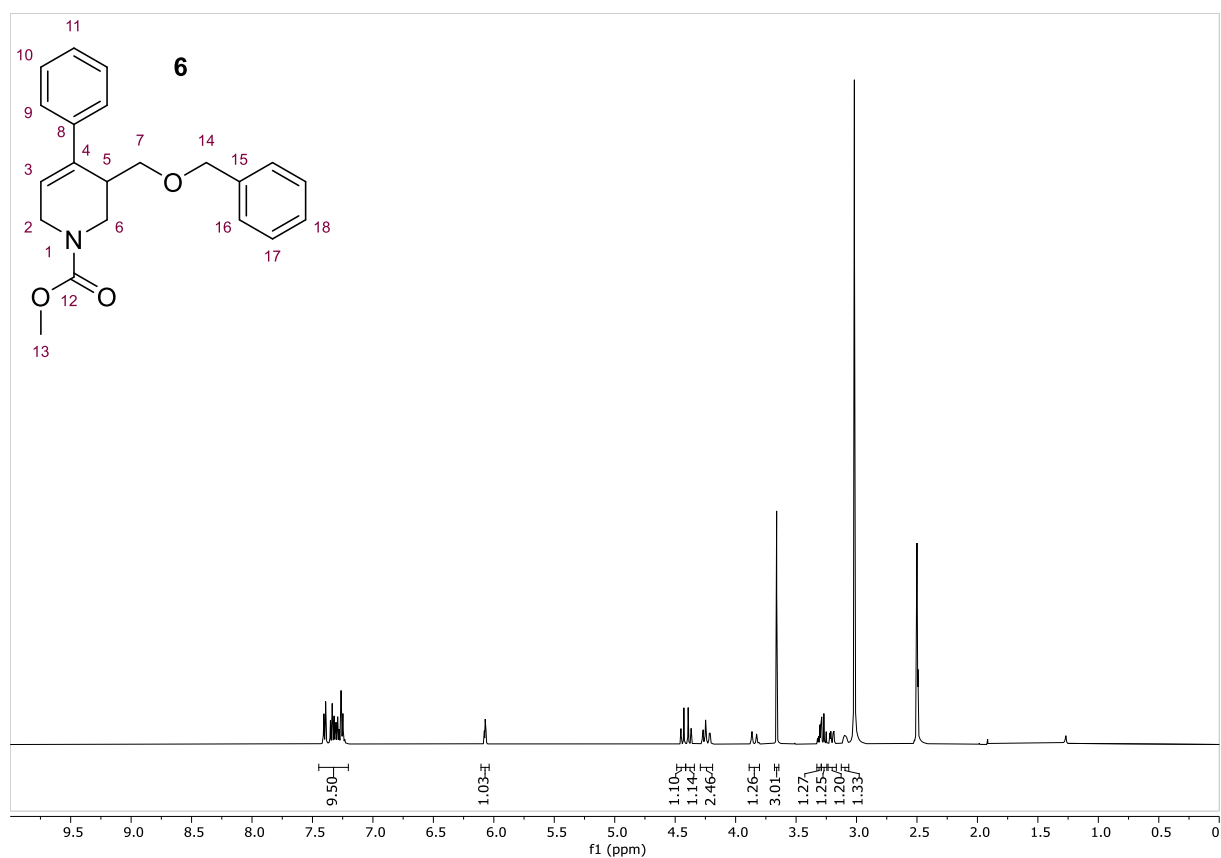


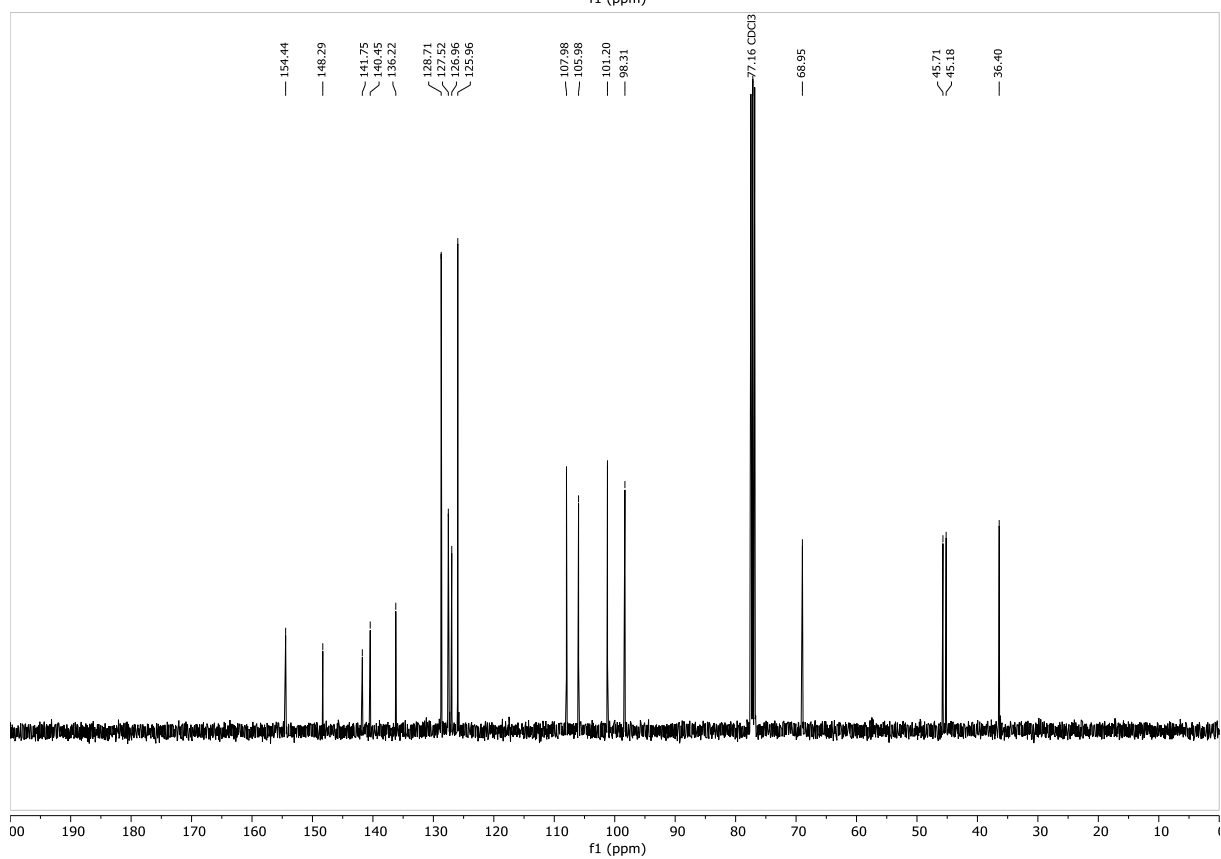
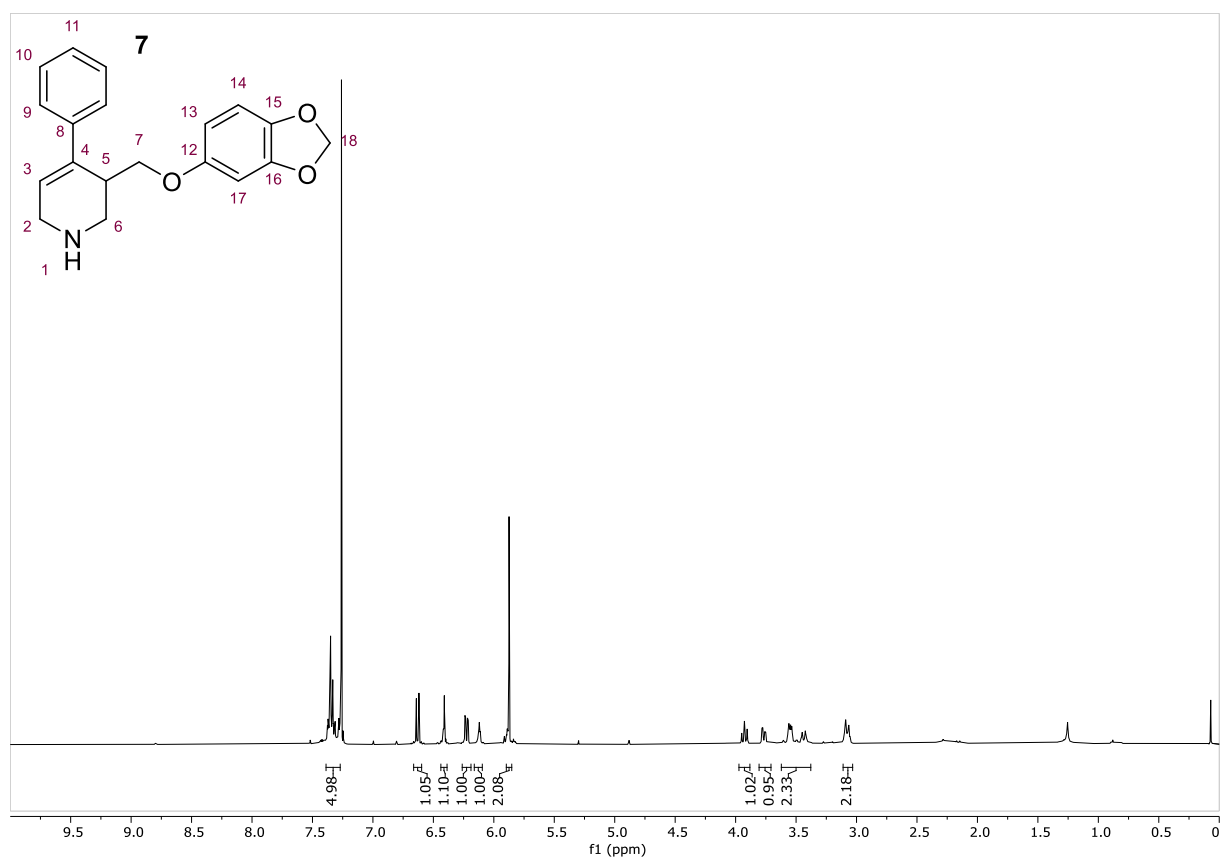


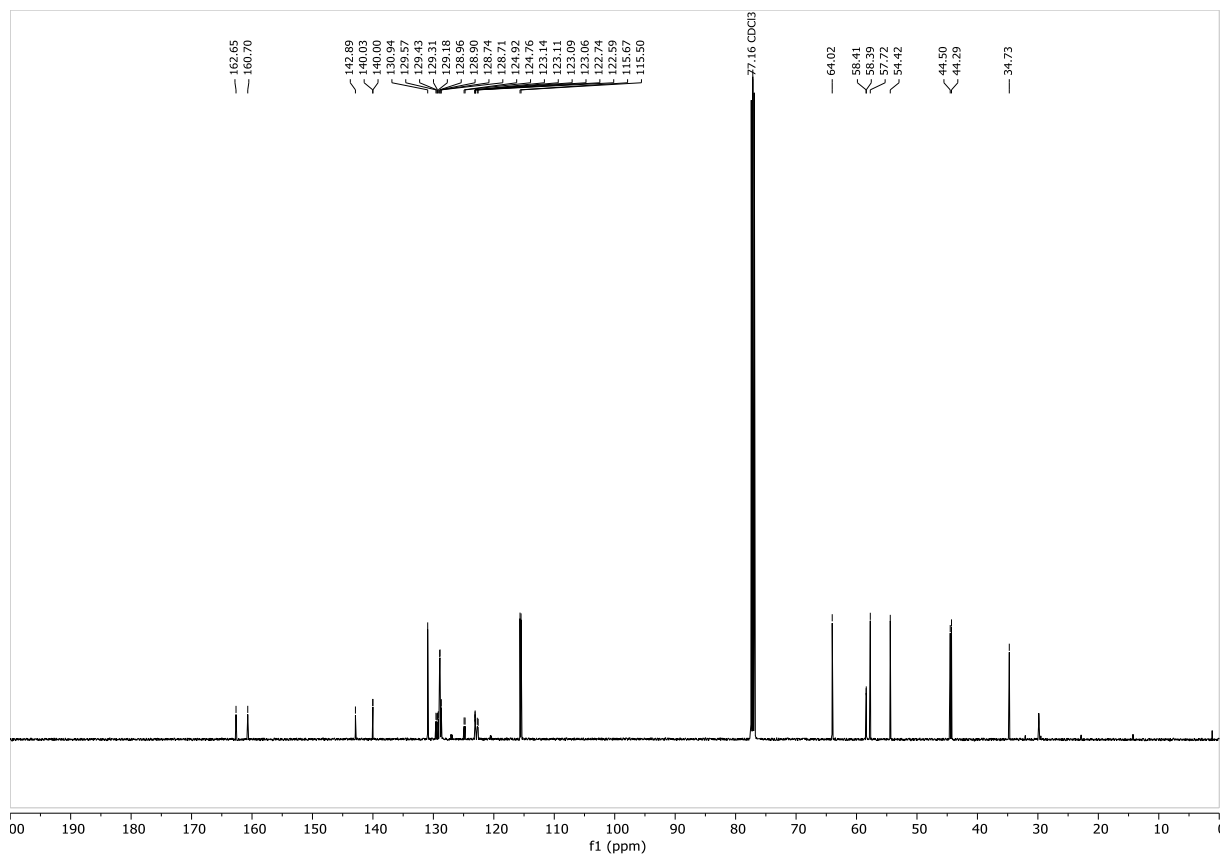
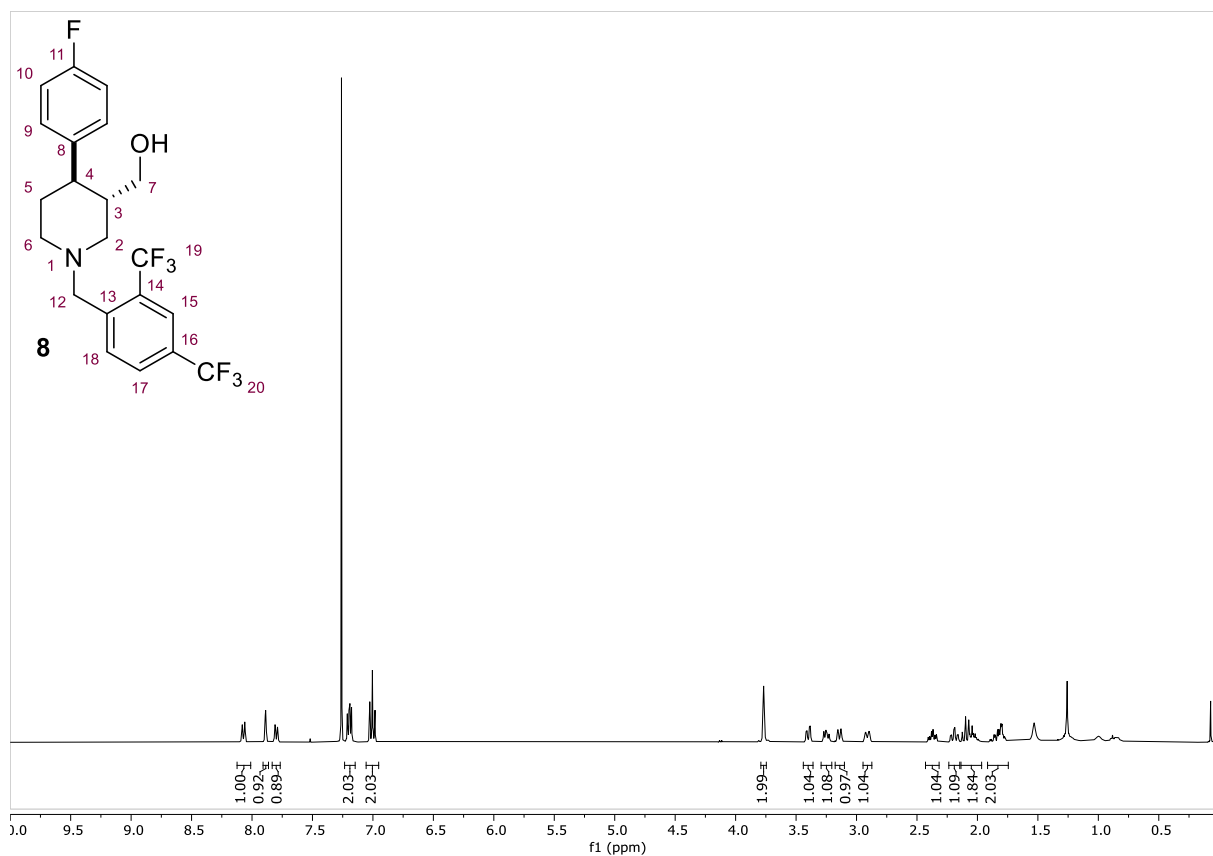


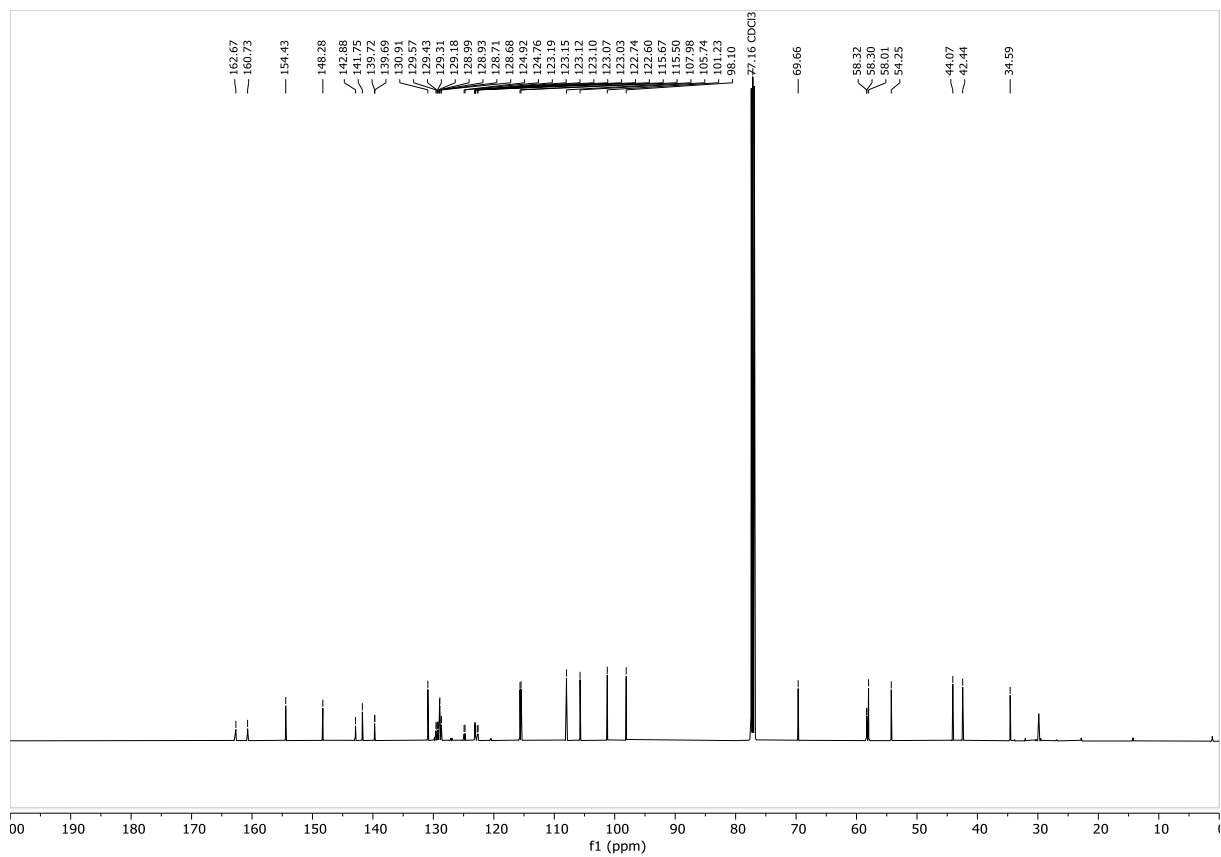
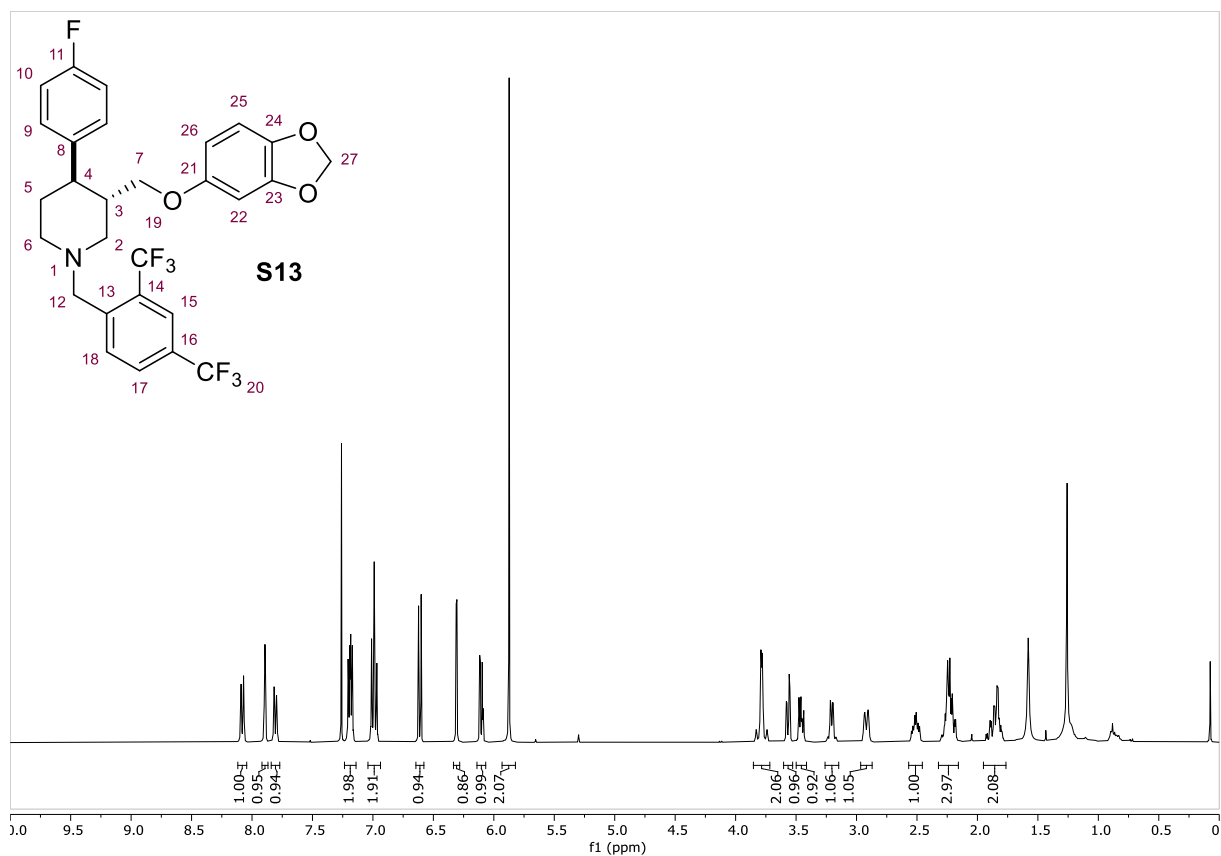












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