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Supporting Information: Cu-Catalyzed Coupling of Aliphatic Amines with Alkylboronic Esters

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1. General Information

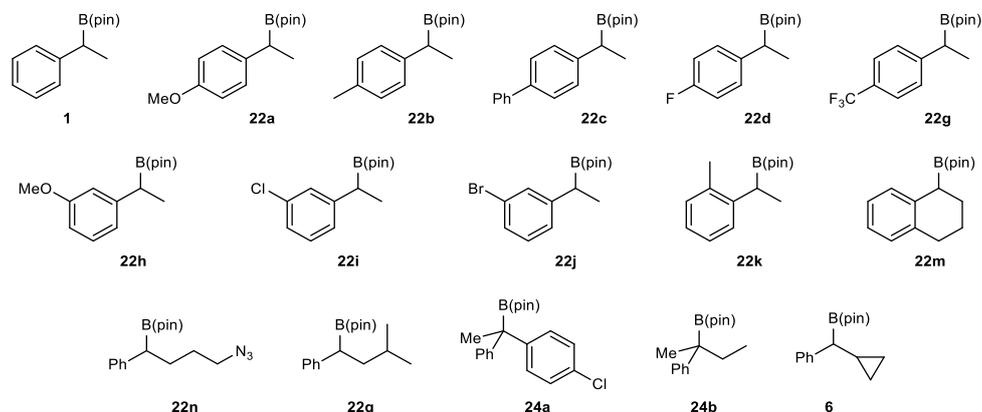
All reagents and solvents used were supplied by commercial sources without further purification unless specified. CuBr_2 was typically used as supplied. However, over time the efficiency of the reaction decreases, presumably because CuBr_2 is hygroscopic and so water content affects the true loading of the Cu salt. More consistent results can be obtained if the CuBr_2 has been dried over P_2O_5 .

All air-sensitive reactions were carried out under a nitrogen or argon atmosphere using oven-dried apparatus. Anhydrous Et_2O , THF and toluene were dried and purified by passage through activated alumina columns using a solvent purification system. All petroleum ether used was 40-60 °C petroleum ether. Thin layer chromatography (TLC) was performed on aluminium-backed plates pre-coated with silica. Compounds were visualised by exposure to UV light or by dipping the plates into solutions of phosphomolybdic acid, ninhydrin, vanillin or KMnO_4 followed by heating. All flash chromatography was carried out using silica gel mesh 40-63. It should be noted that the time taken for chromatography of boronic esters should be kept to minimum to avoid extensive decomposition and reduced yields.

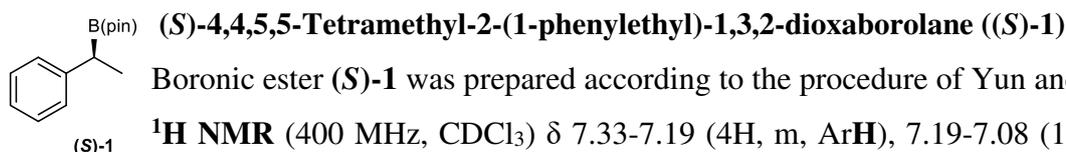
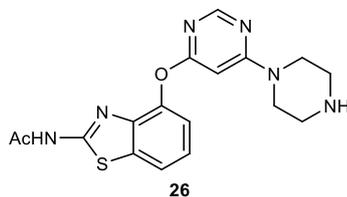
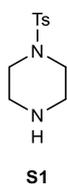
Infra-red spectra were recorded on a Perkin Elmer 100 FT instrument on the neat compound. NMR spectra were recorded on Bruker Advance 400 and 500 instruments at the indicated 101, 128, 126, 377, 400 and 500 MHz as dilute solutions in the indicated deuterated solvent. NMR spectra were recorded at ambient temperature unless otherwise stated. All chemical shifts (δ) reported in parts per million (ppm) relative to residual protio solvent (δH : $\text{CHCl}_3 = 7.27$ ppm, DMSO = 2.50 ppm or $\text{CH}_3\text{CN} = 1.94$ ppm) or the solvent itself (δC : $\text{CDCl}_3 = 77.0$ ppm, DMSO = 39.5 ppm or $\text{CH}_3\text{CN} = 1.32, 118.3$ ppm). All multiplets are designated by the following abbreviations: s = singlet, br s = broad singlet, d = doublet, dt = doublet triplet, td = triplet doublet, ddd = doublet of doublets of doublets, q = quartet, br q = broad quartet, m = multiplet. All coupling constants (J) are reported in Hertz (Hz). ^{13}C NMR data were acquired as DEPT-Q experiments as standard. For samples where quaternary carbons were not observed by DEPT-Q, ^{13}C NMR spectra were acquired as decoupled spectra. ^{19}F NMR spectra acquired as decoupled spectra. High-resolution mass spectra were recorded using either electrospray ionization (ESI) or electron ionisation (EI) by the Chemistry Mass Spectrometry Facility in the Faculty of Science, University of Sheffield. HPLC analysis was performed using an Agilent 1260 Infinity II LC system. Melting points were measured using Linkam HF91 heating stage, used in conjunction with a TC92 controller and are uncorrected.

2. Substrate synthesis

Boronic esters (**1**, **6**, **22a-d**, **22g-22k**, **22m-q**)¹ and boronic esters (**24a**, **24b**)² were prepared by literature methods.



Amines **S1**³ and amine **26**⁴ were prepared by literature methods.



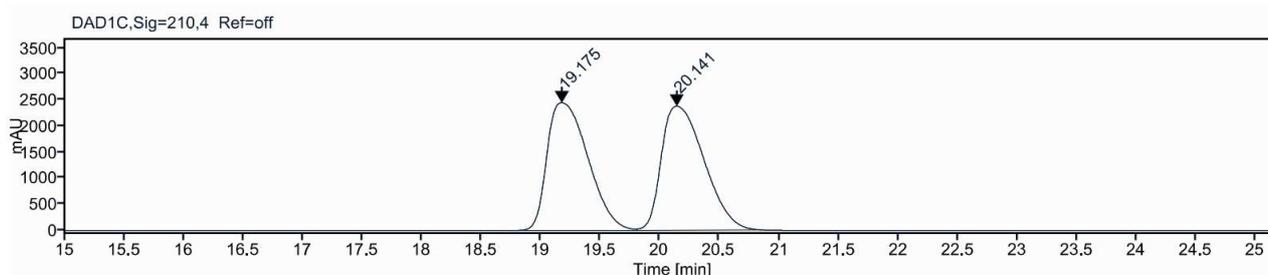
Boronic ester **(S)-1** was prepared according to the procedure of Yun and co-workers.⁵

¹H NMR (400 MHz, CDCl₃) δ 7.33-7.19 (4H, m, ArH), 7.19-7.08 (1H, m, ArH), 2.45 (1H, q, *J* = 7.5 Hz, CH), 1.34 (3H, d, *J* = 7.5 Hz, CHCH₃), 1.22 (6H, s, 2 × CCH₃), 1.21 (6H, s, 2 × CCH₃).

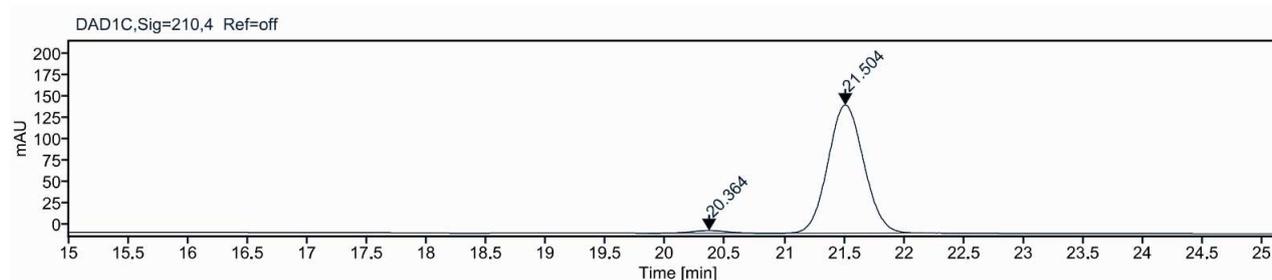
¹³C NMR (101 MHz, CDCl₃) δ 144.9 (C), 128.3 (2 × CH), 127.8 (2 × CH), 125.1 (CH), 83.3 (2 × C), 24.6 (2 × CH₃), 24.6 (2 × CH₃), 17.0 (CH₃).

¹¹B NMR (128 MHz, CDCl₃) δ 33.5.

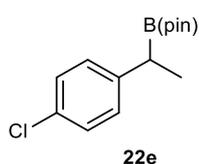
e.r. = 2:98, measured through chiral HPLC analysis of the corresponding alcohol obtained after oxidation. Chiralpak ID column (250 × 4.6 mm), IPA:hexane = 1:99, 0.7 mL/min, column temperature = 22 °C, (*R*)-isomer *t_r* = 20.4 min and (*S*)-isomer *t_r* = 21.5 min.



RT [min]	Type	Width [min]	Area	Height	Area%
19.175	MM m	0.3804	58438.0569	2449.1135	49.6661
20.141	MM m	0.3945	59223.8120	2378.5002	50.3339
Sum			117661.8689		



RT [min]	Type	Width [min]	Area	Height	Area%
20.364	BB	1.0200	57.8583	2.8559	1.8127
21.504	MM m	0.3253	3133.9778	150.2871	98.1873
Sum			3191.8361		



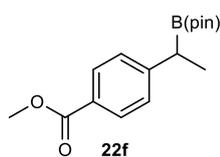
(±)-2-[1-(4-Chlorophenyl)ethyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (22e)

Using a modification of the procedure of Yun and co-workers,⁶ an oven-dried flask was charged with CuCl (0.045 g, 0.45 mmol), tBuOK (0.121 g, 1.08 mmol) and dppBz (0.200 g, 0.45 mmol) and purged with N₂. Anhydrous toluene (16 mL) was added, and the mixture was stirred at room temperature for 10 min. Pinacolborane (3.13 mL, 21.6 mmol) was added and the mixture was stirred for 10 min. 4-Chlorostyrene (2.16 mL, 18.0 mmol) was added, and the mixture heated to 60 °C for 16 h. The mixture was cooled to room temperature, passed through a plug of Celite eluting with EtOAc (10 mL), and concentrated *in vacuo*. Flash chromatography (2% EtOAc/petroleum ether) of the crude material gave boronic ester **22e** (1.41 g, 81%) as a white solid. The data were consistent with the literature.⁶

¹H NMR (400 MHz, CDCl₃) 7.25-7.22 (2H, m, ArH), 7.17-7.14 (2H, m, ArH), 2.41 (1H, q, *J* = 7.5 Hz, CH), 1.31 (3H, d, *J* = 7.5 Hz, CH₃), 1.21 (6H, s, 2 × CCH₃), 1.20 (6H, s, 2 × CCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 143.5 (C), 130.7 (C), 129.1 (2 × CH), 128.3 (2 × CH), 83.4 (2 × C), 24.6 (2 × CH₃), 24.6 (2 × CH₃), 16.9 (CH₃).

¹¹B NMR (128 MHz, CDCl₃) δ 33.3.



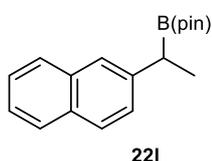
(±)-Methyl 4-[1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]benzoate
(**22f**)

Using a modification of the procedure of Yun and co-workers,⁶ an oven-dried flask was charged with CuCl (0.0147 g, 0.148 mmol), tBuOK (0.0400 g, 0.356 mmol) and dppBz (0.0661 g, 0.148 mmol) and purged with N₂. Anhydrous toluene (3 mL) was added, and the mixture was stirred at room temperature for 10 min. Pinacolborane (1.0 mL, 7.1 mmol) was added and the mixture was stirred for 10 min. A solution of methyl 4-vinylbenzoate (0.963 g, 5.94 mmol) in toluene (4 mL) was added, and the mixture heated to 60 °C for 16 h. The mixture was cooled to room temperature, passed through a plug of Celite eluting with EtOAc (10 mL), and concentrated *in vacuo*. Flash chromatography (100% hexane/0% Et₂O → 90% hexane/10% Et₂O) of the crude material gave boronic ester **22f** (0.756 g, 44%) as a white solid. The data were consistent with the literature.⁷

¹H NMR (400 MHz, CDCl₃) δ 7.95-7.91 (m, 2H), 7.30-7.26 (m, 2H), 3.89 (s, 3H), 2.51 (q, *J* = 7.5 Hz, 1H), 1.35 (d, *J* = 7.4 Hz, 4H), 1.20 (s, 7H), 1.19 (s, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 167.3 (C), 150.8 (C), 129.7 (2 × CH), 127.7 (2 × CH), 127.1 (C), 83.5 (C), 51.9 (CH₃), 24.6 (2 × CH₃), 24.5 (2 × CH₃), 16.4 (CH₃).

¹¹B NMR (128 MHz, CDCl₃) δ 33.5.



(±)-4,4,5,5-Tetramethyl-2-[1-(2-naphthalen-1-yl)ethyl]-1,3,2-dioxaborolane (**22l**).

Using a modification of the procedure of Yun and co-workers,⁶ an oven-dried flask was charged with CuCl (0.064 g, 0.65 mmol), tBuOK (0.174 g, 1.55 mmol) and dppBz (0.290 g, 0.650 mmol) and purged with N₂. Anhydrous toluene (16 mL) was added, and the mixture was stirred at room temperature for 10 min. Pinacolborane (4.5 mL, 31 mmol) was added and the mixture was stirred for 10 min. 2-Vinylnaphthalene (4.00 g, 26.0 mmol) was added, and the mixture heated to 60 °C for 16 h. The mixture was cooled to room temperature, passed through a plug of Celite eluting with EtOAc (10 mL), and concentrated *in vacuo*. Flash chromatography (4% EtOAc/petroleum ether) of the crude material gave boronic ester **22l** (6.20 g, 84%) as a white solid. The data were consistent with the literature.⁸

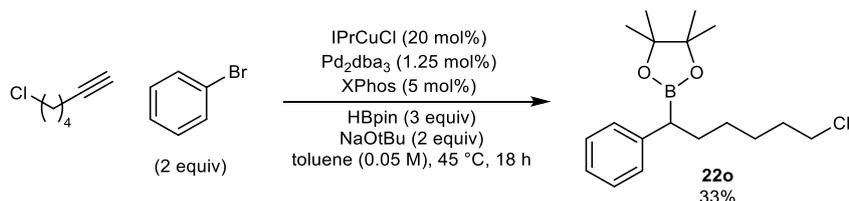
m.p 80-81 °C (EtOAc); literature = 61-63 °C (not specified).⁹

¹H NMR (400 MHz, CDCl₃) δ 7.80-7.74 (3H, m, ArH), 7.65 (1H, s, ArH), 7.45-7.37 (3H, m, ArH), 2.62 (1H, q, *J* = 7.5 Hz, CH), 1.43 (3H, d, *J* = 7.5 Hz, CHCH₃), 1.22 (6H, s, 2 × CCH₃), 1.21 (6H, s, 2 × CCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 142.6 (C), 133.8 (C), 131.7 (C), 127.6 (CH), 127.5 (CH), 127.5 (CH), 127.2 (CH), 125.6 (CH), 125.2 (CH), 124.7 (CH), 83.4 (2 × C), 24.6 (2 × CH₃), 24.6 (2 × CH₃), 16.8 (CH₃).

^{11}B NMR (128 MHz, CDCl_3) δ 34.0.

2-[6-Chloro-1-(phenyl)hexyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (22o)



Using a modification of the procedure by Lalic and Armstrong,¹⁰ a Schlenk flask containing NaO^tBu (0.384 g, 4.00 mmol, 2.0 equiv), IPrCuCl (0.195 g, 0.400 mmol, 0.20 equiv), was backfilled with nitrogen three times. HBpin (0.767 g, 6.00 mmol, 3.0 equiv), anhydrous toluene (40 mL, 0.05 M) and 6-chloro-1-hexyne (0.233 g, 2.00 mmol, 1.0 equiv) were added, and the mixture was stirred at 45 °C until the yellow colour disappeared (~5 mins). Pd₂dba₃ (22.9 mg, 0.025 mmol, 0.0125 equiv), XPhos (47.2 mg, 0.1 mmol, 0.025 equiv) and bromobenzene (0.628 g, 4.00 mmol, 2.0 equiv) were added, and the mixture was vigorously stirred at 45 °C for 18 h. The mixture was cooled to room temperature, diluted with Et₂O (20 mL), and washed with 1 M HCl (20 mL) and brine (20 mL). The organic phase was dried (Na₂SO₄), filtered through a pad a silica gel eluting with Et₂O, and concentrated *in vacuo*. Flash chromatography (100% hexane → 100% CH₂Cl₂) of the crude material gave *boronic ester 22o* (0.215 g, 33%) as a colourless oil.

IR 2978, 2932, 1371, 1321, 1142 cm⁻¹.

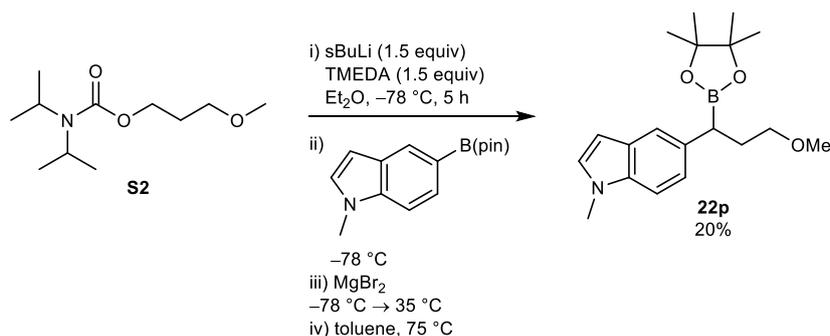
¹H NMR (400 MHz, CDCl_3) δ 7.28-7.17 (4H, m, ArH), 7.15-7.10 (1H, m, ArH), 3.49 (2H, t, J = 6.8 Hz, CH₂Cl), 2.29 (1H, t, J = 7.9 Hz, CH), 1.90-1.80 (1H, m, CH_AH_B), 1.78-1.69 (2H, m, CH₂CH₂Cl), 1.69-1.60 (1H, m, CH_AH_B), 1.48-1.38 (2H, m, CH₂), 1.33-1.28 (2H, m, CH₂), 1.21 (6H, s, 2 × CCH₃), 1.18 (6H, s, 2 × CCH₃).

¹³C NMR (101 MHz, CDCl_3) δ 143.2 (C), 128.3 (2 × CH), 128.3 (2 × CH), 125.2 (CH), 83.3 (2 × OC), 45.1 (CH₂), 32.5 (CH₂), 32.3 (CH₂), 28.4 (CH₂), 26.8 (CH₂), 24.6 (2 × CH₃), 24.6 (2 × CH₃).

¹¹B NMR (128 MHz, CDCl_3) δ 33.4.

HRMS (QTOF) Exact mass calcd for [C₁₈H₂₈¹¹B³⁵ClO₂]⁺ [M+H]⁺: 323.1994, found: 323.1959.

(±)-5-[3-Methoxy-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl]-1-methylindole (**22p**)



Using a modification of the procedure by Aggarwal and co-workers,¹¹ a Schlenck flask containing carbamate **S2**¹² (3.14 g, 14.6 mmol) was backfilled with nitrogen three times. TMEDA (2.18 mL, 14.6 mmol) and anhydrous Et_2O (40 mL) were added, and the mixture was cooled to $-78\text{ }^\circ\text{C}$. $s\text{-BuLi}$ (1.3 M in cyclohexane, 10.4 mL, 14.6 mmol) was added dropwise and the mixture was stirred at $-78\text{ }^\circ\text{C}$ for 5 h. A solution of 1-methylindole-5-boronic acid pinacol ester (2.49 g, 9.68 mmol) in Et_2O (10 mL) was added dropwise and the mixture was stirred at $-78\text{ }^\circ\text{C}$ for 1 h. A solution of MgBr_2 in Et_2O ¹ (2.67 g, 14.6 mmol, 1 M) was added dropwise and the mixture was stirred at $34\text{ }^\circ\text{C}$ for 18 h. Toluene (30 mL) was added and mixture heated to $75\text{ }^\circ\text{C}$ for 18 h. H_2O (60 mL) was added, and the mixture extracted with Et_2O ($3 \times 60\text{ mL}$). The combined organic layers were dried (MgSO_4), filtered, and concentrated *in vacuo*. The crude material was purified by column chromatography (5% $\text{EtOAc}/45\%$ hexane/ 50% CH_2Cl_2) to give boronic ester **22p** (0.633 g, 20%) as an off white solid.

m.p. = $91\text{-}93\text{ }^\circ\text{C}$ (CH_2Cl_2), no literature data available.

IR 2926, 2890, 1668, 1607, 1447, 1336, 1111 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 7.45 (1H, s, ArH), 7.22 (1H, d, $J = 8.4\text{ Hz}$, ArH), 7.12 (1H, d, $J = 8.4\text{ Hz}$, ArH), 7.00 (1H, d, $J = 3.1\text{ Hz}$, ArH), 6.41 (1H, d, $J = 3.1\text{ Hz}$, ArH), 3.76 (3H, s, OCH_3), 3.40-3.32 (2H, m, OCH_2), 3.31 (3H, s, NCH_3), 2.50 (1H, t, $J = 8.6\text{ Hz}$, CH), 2.23-2.17 (1H, m, CHCH_AH_B), 1.98-1.89 (1H, m, CHCH_AH_B), 1.21 (6H, s, $2 \times \text{CCH}_3$), 1.19 (6H, s, $2 \times \text{CCH}_3$).

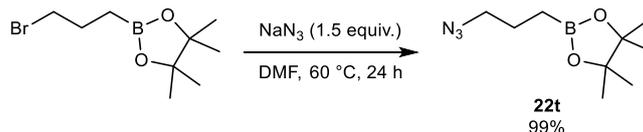
^{13}C NMR (101 MHz, CDCl_3) δ 135.2 (C), 133.4 (C), 128.7 (C), 128.5 (CH), 122.7 (CH), 120.0 (CH), 108.9 (CH), 100.4 (CH), 83.1 ($2 \times \text{C}$), 72.2 (CH_2), 58.4 (CH_3), 33.0 (CH_2), 32.8 (CH_3), 24.6 ($2 \times \text{CH}_3$), 24.6 ($2 \times \text{CH}_3$).

^{11}B NMR (128 MHz, CDCl_3) δ 33.7.

HRMS (QTOF) Exact mass calcd for $[\text{C}_{19}\text{H}_{28}^{11}\text{BNNaO}_3]^+$ $[\text{M}+\text{Na}]^+$: 352.2054. Found: 352.2066.

¹ Freshly prepared before use, by the following procedure: A flask was charged with Mg turnings (1.1 equiv.) and purged with N_2 . Et_2O (3 mL) followed by 1,2-dibromoethane (1 equiv.) were added, and the mixture was stirred at room temperature for 2 h.

2-(3-Azidopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**22t**)



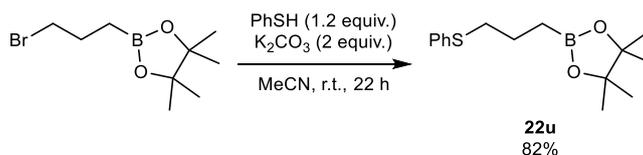
NaN_3 (0.488 g, 7.51 mmol) was added to a solution of 2-(3-bromopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.25 g, 5.00 mmol) in DMF (3.30 ml) and the mixture was stirred at $60\text{ }^\circ\text{C}$ for 24 h. H_2O (50 mL) was added, and the mixture extracted with Et_2O ($3 \times 50\text{ mL}$). The combined organic layers were washed with brine (100 ml), dried (MgSO_4), filtered, and concentrated *in vacuo* to give the azide **22t** as a colourless oil (1.05 g, 99%). The data were consistent with the literature.¹³

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 3.24 (2H, t, $J = 7.0\text{ Hz}$, CH_2N_3), 1.71 (2H, tt, $J = 7.7, 7.0\text{ Hz}$, $\text{N}_3\text{CH}_2\text{CH}_2$), 1.24 (12H, s, $3 \times \text{CH}_3$), 0.83 (2H, t, $J = 7.7\text{ Hz}$, CH_2B).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 83.2 ($2 \times \text{C}$), 53.4 (CH_2), 24.8 ($4 \times \text{CH}_3$), 23.5 (CH_2).

$^{11}\text{B NMR}$ (128 MHz, CDCl_3) δ 33.8.

4,4,5,5-Tetramethyl-2-[3-(phenylsulfanyl)propyl]-1,3,2-dioxaborolane (**22u**)



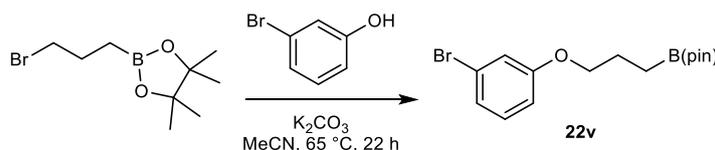
Thiophenol (0.61 ml, 5.98 mmol) was added to a stirring solution of 2-(3-bromopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.25 g, 5.01 mmol) and K_2CO_3 (1.38 g, 10.0 mmol) in MeCN (10.0 ml) and stirred at r.t. for 22 h. H_2O (50 mL) was added, and the mixture extracted with Et_2O ($3 \times 50\text{ mL}$). The combined organic layers were dried (MgSO_4), filtered, and concentrated *in vacuo*. Flash column chromatography (99% hexane/1% Et_3N to 89% hexane/10% Et_2O /1% Et_3N) of the crude material gave thioether **22u** (1.21 g, 87%) as a yellow oil. The data were consistent with the literature.¹⁴

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.39-7.30 (2H, m, ArH), 7.29-7.22 (2H, m, ArH), 7.18-7.09 (1H, m, ArH), 2.93 (t, $J = 7.5\text{ Hz}$, CH_2S), 1.78 (2H, tt, $J = 7.7, 7.5\text{ Hz}$, CCH_2C), 1.24 (12H, s, $3 \times \text{CH}_3$), 0.92 (2H, t, $J = 7.7\text{ Hz}$, CH_2B).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 137.1 (C), 128.7 ($2 \times \text{CH}$), 128.5 ($2 \times \text{CH}$), 125.4 (CH), 83.1 ($2 \times \text{C}$), 35.5 (CH_2), 24.8 ($4 \times \text{CH}_3$), 23.9 (CH_2).

$^{11}\text{B NMR}$ (128 MHz, CDCl_3) δ 33.8.

2-[3-(3-Bromophenoxy)propyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (22v)



3-Bromophenol (0.981 g, 5.67 mmol) was added to a stirring solution of 2-(3-bromopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.90 ml, 4.3 mmol) and K_2CO_3 (1.63 g, 11.8 mmol) in MeCN (10 ml) and stirred at 65 °C for 22 h. The mixture was cooled to room temperature, and saturated aqueous K_2CO_3 (15 mL) and H_2O (10 mL) were added. The mixture was extracted with EtOAc (3 × 50 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Flash column chromatography (100% hexane/0% Et_2O → 100% Et_2O) of the crude material gave *ether* **22v** (0.507 g, 55%) as a colourless oil.

IR 2977, 2933, 1589, 1468, 1371, 1143, 845 cm^{-1} .

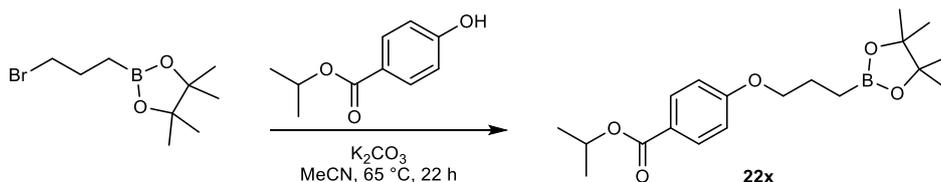
1H NMR (400 MHz, $CDCl_3$) δ 7.15-7.07 (1H, m, ArH), 7.08-7.01 (2H, m, ArH), 6.82 (1H, ddd, $J = 8.2, 2.3, 1.2$ Hz, ArH), 3.92 (2H, t, $J = 6.7$ Hz, OCH_2), 1.88 (2H, tt, $J = 7.8, 6.7$ Hz, OCH_2CH_2), 1.25 (12H, s, 4 × CH_3), 0.91 (2H, t, $J = 7.8$ Hz, BCH_2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0 (C), 130.4 (CH), 123.5 (CH), 122.7 (C), 117.7 (CH), 113.7 (CH), 83.2 (2 × C), 69.8 (CH_2), 24.8 (4 × CH_3), 23.6 (CH_2).

^{11}B NMR (128 MHz, $CDCl_3$) δ 33.5.

HRMS (QTOF) Exact mass calcd for $[C_{15}H_{22}^{11}B^{79}BrNaO_3]^+ [M+Na]^+$: 363.0743 found 363.0738.

Propan-2-yl 4-[3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propoxy]benzoate (22x)



Isopropyl 4-hydroxybenzoate (1.02 g, 5.67 mmol) was added to a stirring solution of 2-(3-bromopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.0 ml, 4.7 mmol) and K_2CO_3 (1.63 g, 11.8 mmol) in MeCN (10 ml) and stirred at 65 °C for 20 h. The mixture was cooled to room temperature, and H_2O (10 mL) was added. The mixture was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Flash column chromatography (100% hexane → 10% EtOAc/90% hexane) of the crude material gave *ether* **22x** (0.510 g, 31%) as a colourless oil.

IR 2978, 2938, 1708, 1606, 1372, 1250, 1099, 771 cm^{-1} .

¹H NMR (400 MHz, CDCl₃) δ 7.99-7.94 (2H, m, ArH), 6.92-6.87 (1H, m, ArH), 5.22 (1H, hept, *J* = 6.2 Hz, CH), 3.99 (2H, t, *J* = 6.7 Hz, OCH₂), 1.95-1.86 (2H, m, OCH₂CH₂), 1.35 (6H, d, *J* = 6.3 Hz, 2 × CHCH₃), 1.25 (12H, s, 4 × CCH₃), 0.92 (2H, t, *J* = 7.8 Hz, BCH₂).

¹³C NMR (101 MHz, CDCl₃) δ 166.0 (C), 162.8 (C), 131.4 (2 × CH), 123.0 (C), 114.0 (2 × CH), 83.2 (2 × C), 69.7 (CH₂), 67.8 (CH), 24.8 (4 × CH₃), 23.6 (CH₂), 22.0 (2 × CH₃).

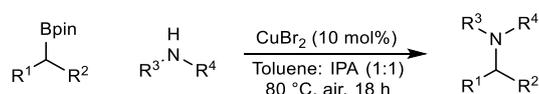
¹¹B NMR (128 MHz, CDCl₃) δ 34.4.

HRMS (QTOF) Exact mass calcd for [C₁₉H₂₉¹¹BO₅]⁺ [M]⁺: 348.2217. Found: 348.2228.

3. Cu-catalysed Amination of Alkylboronic Esters

3.1. General Procedures

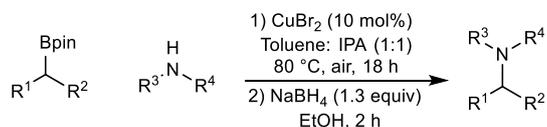
General Procedure 1 (GP1): Preparative scale Cu-catalysed amination of alkylboronic esters



Isopropyl alcohol (0.38 mL) and toluene (0.38 mL) were added to a flask containing the corresponding boronic ester (0.50 mmol, 1 equiv.), amine (1.75 mmol, 3.5 equiv.) and CuBr₂ (0.05 mmol, 10 mol%), and the mixture was stirred under air at 80 °C until the reaction was complete (as determined by TLC). The mixture was cooled to room temperature, passed through a plug of silica eluting with Et₂O, and concentrated *in vacuo*. The crude material was purified by column chromatography.

A video guide to help readers see how we set up our reaction, including some tips for problem solving, can be found here: https://digitalmedia.sheffield.ac.uk/id/1_isl6hrng.

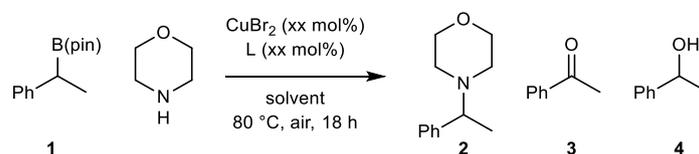
General Procedure 2 (GP2): Preparative scale Cu-catalysed amination of alkylboronic esters with reductive workup.



Isopropyl alcohol (0.38 mL) and toluene (0.38 mL) were added to a flask containing the corresponding boronic ester (0.50 mmol, 1 equiv.), amine (1.75 mmol, 3.5 equiv.) and CuBr₂ (0.05 mmol, 10 mol%), and the mixture was stirred under air at 80 °C until the reaction was complete (as determined by TLC). The mixture was cooled to room temperature, passed through a plug of silica eluting with Et₂O, and concentrated *in vacuo*. EtOH (1 mL) and NaBH₄ (0.025 g, 0.65 mmol) were added, and the mixture stirred at RT for 2 h. The mixture was diluted with EtOAc (10 mL) and H₂O (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by column chromatography.

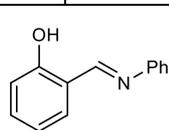
3.2. Optimisation of Reaction Conditions

Reactions conducted as part of the optimisation process were typically conducted on 0.5 mmol scale with respect to boronic ester **1**. It was found that smaller scale reactions (e.g. 0.05 mmol scale) did work but showed lower reproducibility, presumably due to inefficient gas transfer from air to solution limiting catalyst turnover which can be harder to control on smaller scale.

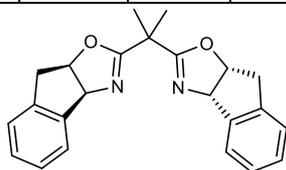


Entry	Cu Source	Cu mol%	L (mol%)	Amine equiv	solvent	T (°C)	Time	Conc.	Yield			
									1	2	3	4
1 ^b	Cu(OAc) ₂	200	-	4	toluene/pyr	80	16 h	0.1 M	53%	0%	2%	-
2 ^b	CuBr ₂	200	-	4	toluene/pyr	80	16 h	0.1 M	51%	46%	-	-
3 ^b	CuBr	200	-	4	toluene/pyr	80	16 h	0.1 M	36%	51%	0%	-
4 ^b	CuCl	200	-	4	toluene/pyr	80	16 h	0.1 M	43%	5%	3%	-
5 ^b	CuI	200	-	4	toluene/pyr	80	16 h	0.1 M	84%	0%	0%	-
6 ^b	CuCl ₂	200	-	4	toluene/pyr	80	16 h	0.1 M	42%	22%	2%	-
7 ^b	CuBr ₂	200	-	4	toluene/pyr	50	16 h	0.1 M	50%	25%	-	-
8 ^b	CuBr ₂	200	-	4	toluene/pyr	50	64 h	0.1 M	-	63%	-	-
9 ^{b,c}	CuBr ₂	200	-	4	toluene/pyr	80	16 h	0.1 M	51%	26%	0%	-
10 ^{b,d}	CuBr ₂	200	-	4	toluene/pyr	80	16 h	0.1 M	32%	30%	0%	-
11 ^{b,e}	CuBr ₂	200	-	4	toluene/pyr	80	16 h	0.1 M	0%	35%	0%	-
12 ^b	CuBr ₂	100	-	4	toluene/pyr	80	16 h	0.16 M	33%	68%	-	-
13 ^b	CuBr ₂	50	-	4	toluene/pyr	80	16 h	0.16 M	45%	34%	-	-
14 ^b	CuBr ₂	100	-	40	-	80	16 h	0.025 M	<5%	>95%	<5%	-
15 ^b	CuBr ₂	50	L1 (100)	4	toluene/pyr	80	16 h	0.16 M	52%	49%	-	--
16 ^b	CuBr ₂	50	L4 (100)	4	toluene/pyr	80	16 h	0.16 M	63%	22%	-	-
17 ^b	CuBr ₂	50	L5 (100)	4	toluene/pyr	80	16 h	0.16 M	65%	32%	-	-
18 ^b	CuBr ₂	50	L6 (100)	4	toluene/pyr	80	16 h	0.16 M	67%	23%	-	-
19 ^b	CuBr ₂	25	L1 (25)	4	toluene	80	16 h	0.16 M	91%	7%	0%	-
20	CuBr ₂	25	L2 (25)	40	-	40	18 h	0.025 M	<5%	95%	-	-
21	CuBr ₂	25	L7 (25)	40	-	40	18 h	0.025 M	<5%	84%	-	-
22	CuBr ₂	25	L3 (25)	40	-	40	18 h	0.025 M	<5%	67%	-	-
23 ^f	CuBr ₂	50	L1 (25)	4	toluene	80	16 h	0.16 M	<5%	30%	34%	-
24 ^g	CuBr ₂	50	L1 (25)	4	toluene	80	16 h	0.16 M	<5%	54%	13%	-
25 ^h	CuBr ₂	50	L1 (25)	4	toluene	80	16 h	0.16 M	<5%	40%	11%	-
26	CuBr ₂	50	-	4	toluene	80	16 h	0.16 M	<5%	45%	13%	-
27	CuBr ₂	25	-	4	toluene	80	16 h	0.16 M	<5%	25%	9%	-
28	CuBr ₂	25	L1 (25)	4	toluene	60	18 h	0.3 M	<5%	81%	9%	10%
29	CuBr ₂	25	L1 (25)	4	IPA	60	18 h	0.3 M	<5%	95%	<5%	3%
30	CuBr ₂	25	L1 (25)	4	dioxane	60	18 h	0.3 M	<5%	88%	10%	2%
31	CuBr ₂	25	L1 (25)	4	PrOAc	60	18 h	0.3 M	<5%	91%	6%	3%
32	CuBr ₂	25	L1 (25)	4	tol/IPA (1:1)	60	18 h	0.3 M	<5%	95%	<5%	2%
33	CuBr ₂	25	L1 (25)	4	tol/IPA (3:1)	60	18 h	0.3 M	<5%	95%	<5%	3%
34	CuBr ₂	25	L1 (25)	4	tol/IPA (1:1)	80	18 h	0.3 M	28%	57%	-	-
35	CuBr ₂	25	L1 (25)	4	tol/IPA (3:1)	80	18 h	0.6 M	<5%	95%	-	-
36	CuBr ₂	25	L1 (25)	4	tol/IPA (3:1)	80	18 h	0.6 M	<5%	95%	-	-
37	CuBr ₂	15	L1 (15)	4	tol/IPA (1:1)	80	18 h	0.6 M	<5%	80%	<5%	-

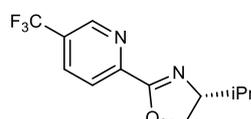
Entry	Cu Source	Cu mol%	L (mol%)	Amine equiv	solvent	T (°C)	Time	Conc.	Yield			
									1	2	3	4
38	CuBr ₂	15	L1 (15)	4	tol/IPA (3:1)	80	18 h	0.6 M	<5%	94%	6%	-
39	CuBr ₂	15	L1 (15)	3	tol/IPA (1:1)	80	18 h	0.6 M	<5%	84%	9%	-
40	CuBr ₂	15	L1 (15)	3.5	tol/IPA (1:1)	80	18 h	0.6 M	<5%	93%	5%	-
41	CuBr ₂	15	L1 (15)	2	tol/IPA (1:1)	80	18 h	0.6 M	<5%	77%	7%	-
42	CuBr ₂	10	L1 (10)	4	tol/IPA (1:1)	80	18 h	0.6 M	<5%	95%	3%	-
43	CuBr ₂	10	L1 (10)	4	tol/IPA (3:1)	80	18 h	0.6 M	<5%	81%	19%	-
44	CuBr ₂	10	L1 (10)	3	tol/IPA (1:1)	80	18 h	0.6 M	<5%	79%	6%	-
45	CuBr ₂	10	-	3.5	tol/IPA (1:1)	80	18 h	0.6 M	<5%	95%	0%	-
46	CuBr ₂	5	-	3.5	tol/IPA (1:1)	80	18 h	0.6 M	<5%	78%	7%	-
47	CuBr ₂	10	-	3.5	MeCN	80	18 h	0.6 M	<5%	78%	8%	5%
48	CuBr ₂	10	-	3.5	MeCN/IPA (1:1)	80	18 h	0.6 M	<5%	77%	7%	6%
49	CuBr ₂	10	-	3.5	tol/IPA (1:1)	80	4h	0.6 M	44%	55%	-	-
50	CuBr ₂	10	-	3.5	tol/IPA (1:1)	RT	18 h	0.6 M	51%	13%	6%	30%
51	-	0	-	3.5	tol/IPA (1:1)	80	18 h	0.6 M	<5%	<5%	4%	58%
52 ^b	CuBr ₂	10	-	3.5	tol/IPA (1:1)	80	18 h	0.6 M	93%	3%	0%	0%
53	S2	100	-	4	toluene	80	16 h	0.16 M	n.d.	0%	-	-
54 ⁱ	CuBr ₂	10	-	1	tol/IPA (1:1)	80	18 h	0.6 M	20% ^j	46%	35% ^j	12% ^j



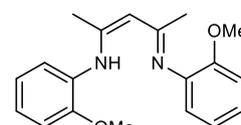
L1



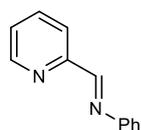
L2



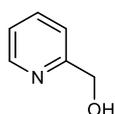
L3



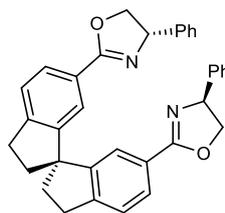
L4



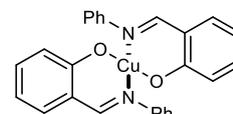
L5



L6



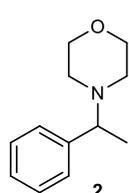
L7



S2

a) Reactions performed using 0.5 mmol of boronic ester **1** unless otherwise stated. Yields determined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard; b) reaction carried out under an inert atmosphere (either N₂ or Ar); c) using CsF (2 equiv); d) using Na₂CO₃ (2 equiv); e) using KOtBu (2 equiv); f) using Cs₂CO₃ (0.5 equiv); g) using Na₂CO₃ (0.5 equiv); h) using KOtBu (0.5 equiv); i) reaction using morpholine as the limiting reagent and 3.5 equivalents of boronic ester **1**; j) yield based on boronic ester **1**; pyr = pyridine; tol = toluene; n.d. = not determined

3.3. Scope of Reaction Using Cyclic Amines

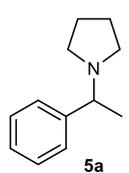


(±)-*N*-(1-Phenylethyl)morpholine (**2**)

Isopropyl alcohol (2.75 mL) and toluene (2.75 mL) were added to a flask containing boronic ester **1** (1.00 g, 4.31 mmol), morpholine (1.31 g, 15.1 mmol) and CuBr₂ (96.3 mg, 0.43 mmol), and the mixture was stirred under air at 80 °C for 18 h. The mixture was cooled to room temperature, passed through a plug of silica eluting with Et₂O and EtOAc, and concentrated in vacuo. Flash column chromatography (69% hexane/30% EtOAc/1% Et₃N) of the crude material gave amine **2** (720 mg, 87%) as a colourless oil. The data were consistent with the literature.¹⁵

¹H NMR (400 MHz, CDCl₃) δ 7.31-7.23 (4 H, m, ArH), 7.22-7.16 (1H, m, ArH), 3.68-3.58 (4H, m, 2 × OCH₂), 3.24 (1H, q, *J* = 6.6 Hz, CH), 2.49-2.38 (2H, m, NCH₂), 2.36-2.27 (2H, m, NCH₂), 1.30 (3H, d, *J* = 6.6 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 143.9 (C), 128.3 (2 × CH), 127.6 (2 × CH), 127.0 (CH), 67.2 (2 × CH₂), 65.4 (CH), 51.3 (2 × CH₂), 19.8 (CH₃).



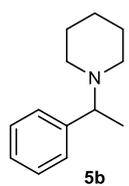
(±)-*N*-(1-Phenylethyl)pyrrolidine (**5a**)

The title compound was prepared according to **GPI** using boronic ester **1** (0.118 g, 0.508 mmol) and pyrrolidine (124.8 mg, 1.75 mmol), heating for 18 h. Flash column chromatography (99% EtOAc/1% Et₃N) of the crude material gave amine **5a** (60.6 mg, 68%) as a colourless oil. The data were consistent with the literature.¹⁶

¹H NMR (400 MHz, CDCl₃) δ 7.37-7.27 (4H, m, ArH), 7.25-7.19 (1H, m, ArH) 3.18 (1H, q, *J* = 6.6 Hz, CH), 2.61-2.50 (2H, m, NCH₂), 2.42-2.32 (2H, m, NCH₂), 1.82-1.70 (4H, m, 2 × CH₂), 1.41 (3H, d, *J* = 6.6 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 145.6 (C), 128.2 (2 × CH), 127.2 (2 × CH), 126.8 (CH), 66.0 (CH), 53.0 (2 × CH₂), 23.4 (2 × CH₂), 23.1 (CH₃).

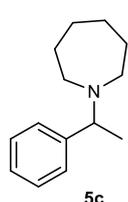
(±)-*N*-(1-Phenylethyl)piperidine (**5b**)



The title compound was prepared according to **GPI** using boronic ester **1** (0.117 g, 0.504 mmol) and piperidine (0.150 g, 1.76 mmol), heating for 18 h. Flash column chromatography (69% hexane/30% EtOAc/1% Et₃N) of the crude material gave amine **5b** (73.8 mg, 77%) as a colourless oil. The data were consistent with the literature.¹⁷

¹H NMR (400 MHz, CDCl₃) δ 7.32-7.27 (4H, m, ArH), 7.27-7.18 (1H, m, ArH), 3.38 (1H, q, *J* = 6.7 Hz, CH), 2.45-2.37 (4H, m, 2 × NCH₂), 1.55-1.50 (4H, m, 2 × NCH₂CH₂), 1.39-1.34 (5H, m, CH₃ and NCH₂CH₂CH₂).

^{13}C NMR (101 MHz, CDCl_3) δ 143.7 (C), 128.0 (2 \times CH), 127.8 (2 \times CH), 126.7 (CH), 65.2 (CH), 51.5 (2 \times CH_2), 26.2 (2 \times CH_2), 24.5 (CH_2), 19.4 (CH_3).

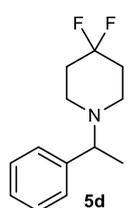


(±)-1-(1-Phenylethyl)azepane (5c)

The title compound was prepared according to **GP1** using boronic ester **1** (0.118 g, 0.508 mmol) and 1-acetylpiperazine (0.202 μL , 1.79 mmol), heating for 18 h. The crude was concentrated under vacuo, dissolved in 5 mL EtOAc and extracted with aqueous HCl (1 M, 3 \times 3 mL). The aqueous phases were combined and basified to pH > 10 with a solution of sat Na_2CO_3 and extracted with EtOAc (3 \times 10 mL). The organic phase was dried over MgSO_4 and concentrated under vacuo. Flash column chromatography (100% CH_2Cl_2 to 50% CH_2Cl_2 /50% EtOAc /1% Et_3N) of the crude material gave amine **5c** (62.9 mg, 61%) as a yellow oil. The data were consistent with the literature.¹⁸

^1H NMR (400 MHz, CDCl_3) δ 7.41-7.36 (2H, m, ArH), 7.35-7.29 (2H, m, ArH), 7.26-7.21 (1H, m, ArH), 3.79 (1H, q, J = 6.7 Hz, CH), 2.66 (4H, br s, 2 \times CH_2N), 1.60 (8H, br s, 2 \times $\text{NCH}_2\text{CH}_2\text{CH}_2$), 1.38 (3H, d, J = 6.7 Hz, CH_3).

^{13}C NMR (101 MHz, CDCl_3) δ 144.8 (C), 127.9 (2 \times CH), 127.6 (2 \times CH), 126.5 (CH), 63.2 (CH), 52.0 (2 \times CH_2), 28.9 (2 \times CH_2), 27.0 (2 \times CH_2), 18.2 (CH_3).



(±)-4,4-Difluoro-1-(1-phenylethyl)piperidine (5d)

The title compound was prepared according to **GP1** using boronic ester **1** (0.116 g, 0.500 mmol) and (0.214 g, 1.77 mmol), heating for 18 h. Flash column chromatography (100% CH_2Cl_2 to 5% Et_2O /95% CH_2Cl_2) of the crude material gave amine **5d** (61.5 mg, 55%) as a pale-yellow oil.

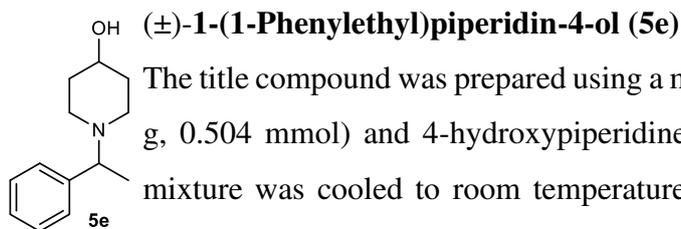
IR 2973, 2813, 1453, 1363, 1098, 927 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 7.35-7.29 (4H, m, ArH), 7.29-7.22 (1H, m, ArH), 3.52 (1H, q, J = 6.7 Hz, CH), 2.59 (dt, J = 11.6, 5.6 Hz, 2H, 2 \times NCH_ACH_B), 2.51 (dt, J = 11.6, 5.6 Hz, 2H, 2 \times NCH_ACH_B), 2.04-1.88 (4H, m, 2 \times CH_2), 1.38 (3H, d, J = 6.7 Hz, CHCH_3).

^{13}C NMR (101 MHz, CDCl_3) δ 143.7 (C), 128.3 (2 \times CH), 127.4 (2 \times CH), 127.0 (CH), 122.2 (t, $J_{\text{C-F}}$ = 241.6 Hz, CF_2), 63.7 (CH), 47.0 (t, $J_{\text{C-F}}$ = 5.4 Hz, 2 \times CH_2), 34.2 (t, $J_{\text{C-F}}$ = 22.7 Hz, 2 \times CH_2), 19.3 (CH_3).

^{19}F NMR (377 MHz, CDCl_3) δ -97.9.

HRMS (Q-TOF) Exact mass calcd for $[\text{C}_{13}\text{H}_{18}\text{F}_2\text{N}]^+$ $[\text{M}+\text{H}]^+$: 226.1402, found: 226.1413.

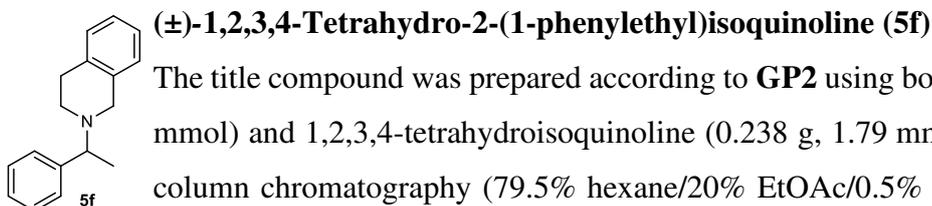


The title compound was prepared using a modification of **GP1** using boronic ester **1** (0.117 g, 0.504 mmol) and 4-hydroxypiperidine (0.181 g, 1.79 mmol), heating for 18 h. The mixture was cooled to room temperature and concentrated *in vacuo*. The mixture was dissolved in EtOAc (5 mL) and extracted with aqueous HCl (1 M, 3 × 5 mL). The combined aqueous phases were basified using aqueous NaOH (2 M, 3 × 5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by column chromatography (99% EtOAc/ 1% TEA) to give amine **5e** (61.5 mg, 60%) as an off-white solid. The data were consistent with the literature.¹⁹

m.p. = 100-102 °C (EtOAc), no literature data available.

¹H NMR (400 MHz, CDCl₃) δ 7.34-7.27 (4H, m, ArH), 7.26-7.19 (1H, m, ArH), 3.60 (1H, tt, *J* = 8.9, 4.2 Hz, CHOH), 3.43 (1H, q, *J* = 6.8 Hz, NCH), 2.91-2.80 (1H, m, NCH_AH_B), 2.75-2.66 (1H, m, NCH_AH_B), 2.24 (1H, br s, OH), 2.16-2.02 (2H, m, NCH₂), 1.93-1.78 (2H, m, OCHCH_AH_B), 1.64-1.46 (2H, m, OCHCH_AH_B), 1.37 (3H, d, *J* = 6.8 Hz, CH₃).

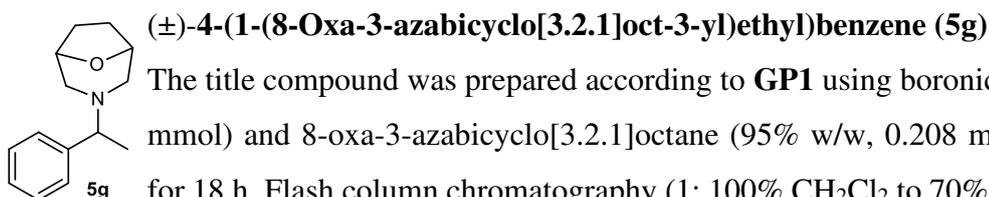
¹³C NMR (101 MHz, CDCl₃) δ 143.6 (C), 128.1 (2 × CH), 127.6 (2 × CH), 126.8 (CH), 68.1 (CH), 64.4 (CH), 48.1 (CH₂), 48.1 (CH₂), 34.7 (CH₂), 34.6 (CH₂), 19.5 (CH₃).



The title compound was prepared according to **GP2** using boronic ester **1** (0.118 g, 0.506 mmol) and 1,2,3,4-tetrahydroisoquinoline (0.238 g, 1.79 mmol), heating for 18 h. Flash column chromatography (79.5% hexane/20% EtOAc/0.5% Et₃N) of the crude material gave amine **5f** (78.1 mg, 65%) as a yellow oil. The data were consistent with the literature.¹⁵

¹H NMR (400 MHz, CDCl₃) δ 7.41-7.38 (2H, m, ArH), 7.36-7.32 (2H, m, ArH), 7.29-7.25 (1H, m, ArH), 7.14-7.08 (3H, m, ArH), 7.02-6.99 (1H, m, ArH), 3.83 (1H, d, *J* = 14.8 Hz, ArCH_ACH_BN), 3.62-3.54 (2H, m, CH and ArCH_ACH_BN), 2.96-2.77 (3H, m, CH₂ and CH_CCH_D), 2.67-2.60 (1H, m, CH_CCH_D), 1.49 (3H, d, *J* = 6.7 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 144.3 (C), 135.2 (C), 134.6 (C), 128.6 (CH), 128.3 (2 × CH), 127.6 (2 × CH), 126.9 (CH), 126.8 (CH), 126.0 (CH), 125.5 (CH), 64.4 (CH), 53.6 (CH₂), 48.0 (CH₂), 29.3 (CH₂), 20.1 (CH₃).



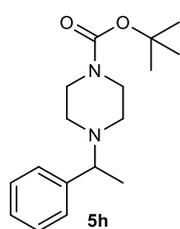
The title compound was prepared according to **GP1** using boronic ester **1** (0.116 g, 0.500 mmol) and 8-oxa-3-azabicyclo[3.2.1]octane (95% w/w, 0.208 mg, 1.75 mmol), heating for 18 h. Flash column chromatography (1: 100% CH₂Cl₂ to 70% hexane/30% EtOAc; 2: 80% hexane/20% Et₂O) of the crude material gave amine **5g** (38.3 mg, 35%) as a yellow oil.

IR 2950, 2800, 1451, 1142, 997, 878 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 7.36-7.27 (4H, m, ArH), 7.25-7.17 (1H, m, ArH), 4.35-4.29 (1H, m, OCH), 4.20-4.14 (1H, m, OCH), 3.29 (1H, q, $J = 6.7$ Hz, CHCH₃), 2.75 (1H, dt, $J = 10.8, 1.8$ Hz, NCH_AH_B), 2.40-2.31 (2H, m, NCH_CH_D, NCH_AH_B), 2.19 (dd, $J = 11.2, 1.5$ Hz, 1H, NCH_CH_D), 2.09-1.98 (1H, m, CH_AH_BCH₂), 1.94-1.73 (3H, m, CH_AH_BCH₂), 1.27 (3H, d, $J = 6.7$ Hz, CH₃).

^{13}C NMR (101 MHz, CDCl_3) δ 145.1 (C), 128.2 (2 \times CH), 127.3 (2 \times CH), 126.8 (CH), 74.9 (2 \times CH), 64.3 (CH), 57.0 (CH₂), 55.2 (CH₂), 28.6 (CH₂), 28.5 (CH₂), 20.0 (CH₃).

HRMS (QTOF) Exact mass calcd for $[\text{C}_{14}\text{H}_{20}\text{NO}]^+ [\text{M}+\text{H}]^+$: 218.1539, found: 218.1539.



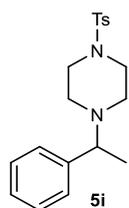
(±)-1-Piperazinecarboxylic acid, 4-(1-phenylethyl)-, 1,1-dimethylethyl ester (5h)

The title compound was prepared according to **GP1** using boronic ester **1** (0.116 g, 0.502 mmol) and *N*-Bocpiperazine (0.326 g, 1.75 mmol), heating for 18 h. Flash column chromatography (69% hexane/30% EtOAc/1% Et₃N) of the crude material gave amine **5h** (0.112 g, 77%) as a colourless oil. The data were consistent with the

literature.¹⁵

^1H NMR (400 MHz, CDCl_3) δ 7.35-7.29 (4H, m, ArH), 7.28-7.23 (1H, m, ArH), 3.45-3.35 (5H, m, 2 \times CH₂ and CH), 2.50-2.40 (2H, m, CH₂), 2.38-2.30 (2H, m, CH₂), 1.45 (9H, s, 3 \times CCH₃), 1.38 (3H, d, $J = 6.7$ Hz, CHCH₃).

^{13}C NMR (101 MHz, CDCl_3) δ 154.7 (C), 143.6 (C), 128.2 (2 \times CH), 127.6 (2 \times CH), 126.9 (CH), 79.4 (C), 64.7 (CH), 50.2 (4 \times CH₂), 28.4 (3 \times CH₃), 19.6 (CH₃).



(±)-1-[(4-Methylphenyl)sulfonyl]-4-(1-phenylethyl)piperazine (5i)

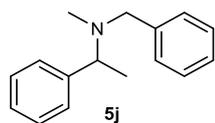
The title compound was prepared according to **GP1** using boronic ester **1** (0.116 g, 0.500 mmol) and *N*-tosylpiperazine (0.420 g, 1.75 mmol), heating for 18 h. Flash column chromatography (99% hexane/1% Et₃N \rightarrow 99% Et₂O /1% Et₃N) of the crude material gave amine **5i** (84.6 mg, 49%) as a white solid. The data were consistent with the literature.²⁰

m.p. 148-149 °C (XX). No literature value available.

^1H NMR (400 MHz, CDCl_3) δ 7.66-7.59 (2H, m, ArH), 7.35-7.18 (7H, m, ArH), 3.36 (1H, q, $J = 6.6$ Hz, CH), 3.03-2.92 (4H, m, 4 \times CH₂), 2.62-2.52 (2H, m, CH₂), 2.50-2.40 (5H, m, CH₂ and ArCH₃), 1.32 (3H, d, $J = 6.6$ Hz, CHCH₃).

^{13}C NMR (101 MHz, CDCl_3) δ 143.6 (C), 143.3 (C), 132.4 (C), 129.6 (2 \times CH), 128.3 (2 \times CH), 127.9 (2 \times CH), 127.5 (2 \times CH), 127.1 (CH), 64.4 (CH), 49.5 (2 \times CH₂), 46.3 (2 \times CH₂), 21.5 (CH₃), 19.5 (CH₃).

3.4. Scope of Reaction Using Acyclic Secondary Amines



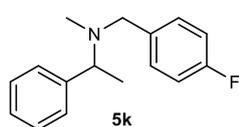
(±)-*N*- α -Dimethyl-*N*-(phenylmethyl)benzenemethanamine (**5j**)

The title compound was prepared according to **GP1** using boronic ester **1** (0.116 g, 0.503 mmol) and *N*-methylbenzylamine (0.214 g, 1.77 mmol), heating for 18 h.

Flash column chromatography (94% hexane/5% EtOAc/1% Et₃N) of the crude material gave amine **5j** (71.2 mg, 63%) as a colourless oil. The data were consistent with the literature.²¹

¹H NMR (400 MHz, CDCl₃) δ 7.44-7.41 (2H, m, ArH), 7.37-7.31 (6H, m, ArH), 7.28-7.22 (2H, m, ArH), 3.66 (1H, q, J = 6.8 Hz, CH), 3.60 (1H, d, J = 13.3 Hz, CH_AH_B), 3.32 (1H, d, J = 13.3 Hz, CH_AH_B), 2.15 (3H, s, NCH₃), 1.44 (3H, d, J = 6.8 Hz, CHCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 144.2 (C), 140.1 (C), 128.7 (2 \times CH), 128.2 (2 \times CH), 128.1 (2 \times CH), 127.7 (2 \times CH), 126.8 (CH), 126.7 (CH), 63.2 (CH), 58.9 (CH₂), 38.3 (CH₃), 18.4 (CH₃).



(±)-[(4-Fluorophenyl)methyl](methyl)(1-phenylethyl)amine (**5k**)

The title compound was prepared according to **GP1** using boronic ester **1** (0.116 g, 0.503 mmol) and *N*-methyl-4-fluorobenzylamine (0.245 g, 1.76 mmol), heating

for 18 h. Flash column chromatography (94% hexane/5% EtOAc/1% Et₃N) of the crude material gave amine **5k** (64.4 mg, 53%) as a colourless oil.

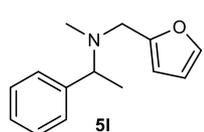
IR 2981, 2790, 1604, 1506, 1453, 1125 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.44-7.34 (4H, m, ArH), 7.31-7.24 (3H, m, ArH), 7.04-7.96 (2H, m, ArH), 3.65 (1H, q, J = 6.7 Hz, CH), 3.55 (1H, d, J = 13.3 Hz, CH_AH_B), 3.28 (2H, d, J = 13.3 Hz, CH_AH_B), 2.14 (3H, s, NCH₃), 1.44 (3H, d, J = 6.7 Hz, CHCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 161.9 (C, d, J_F = 245.5 Hz), 144.1 (C), 135.7 (C), 130.1 (2 \times CH, d, J_F = 8.4 Hz), 128.2 (2 \times CH), 127.6 (2 \times CH), 126.8 (CH), 114.9 (2 \times CH, d, J_F = 20.5 Hz), 63.2 (CH), 58.1 (CH₂), 38.2 (CH₃), 18.4 (CH₃).

¹⁹F NMR (377 MHz, CDCl₃) δ -116.5.

HRMS (Q-TOF) Exact mass calcd for [C₁₆H₁₈FN]⁺ [M+H]⁺: 244.1496, found: 244.1508.



(±)-*N*-Methyl-*N*-(furan-2-ylmethyl)-1-phenylethanamine (**5l**)

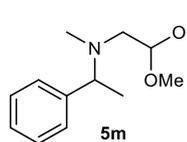
The title compound was prepared according to **GP1** using boronic ester **1** (0.117 g, 0.504 mmol) and *N*-methylfurfurylamine (0.196 g, 1.76 mmol), heating for 18 h.

Flash column chromatography (94% hexane/5% EtOAc/1% Et₃N) of the crude material gave amine **5l** (69.6 mg, 64%) as a colourless oil. The data were consistent with the literature.²²

¹H NMR (400 MHz, CDCl₃) δ 7.41-7.32 (5H, m, ArH), 7.29-7.24 (1H, m, ArH), 6.33 (1H, dd, J = 3.1, 1.9 Hz, ArH), 6.17 (1H, d, J = 3.1 Hz, ArH), 3.67 (d, J = 14.4 Hz, CH_ACH_B), 3.58 (1H, q, J =

6.7 Hz, CH), 3.44 (1H, d, $J = 14.4$ Hz, CH_ACH_B), 2.23 (3H, s, NCH₃), 1.44 (3H, t, $J = 6.7$ Hz, CHCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 152.9 (C), 143.8 (C), 141.9 (CH), 128.2 (2 × CH), 127.7 (2 × CH), 126.9 (CH), 109.9 (CH), 108.3 (CH), 62.7 (CH), 51.0 (CH₂), 38.9 (CH₃), 19.6 (CH₃).



(±)-*N*-(2,2-Dimethoxyethyl)-*N*, α -dimethylbenzenemethanamine (**5m**)

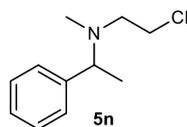
The title compound was prepared according to **GP1** using boronic ester **1** (0.118 g, 0.508 mmol) and 2,2-dimethoxy-*N*-methylethylamine (0.223 g, 1.78 mmol), heating for 18 h. Flash column chromatography (79% hexane / 20% EtOAc / 1% Et₃N) of the crude material gave amine **5m** (86.0 mg, 76%) as a green oil.

IR: 2830, 1451, 1124, 1071 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.35-7.27 (4H, m, ArH), 7.26-7.20 (1H, m, ArH), 4.43 (1H, dd, $J = 5.5, 5.1$ Hz, CHO), 3.65 (1H, q, $J = 6.8$ Hz, CH₃CH), 3.30 (3H, s, OCH₃), 3.28 (3H, s, OCH₃), 2.60 (1H, dd, $J = 13.4, 5.3$ Hz, CH_ACH_B), 2.42 (1H, dd, $J = 13.4, 5.3$ Hz, CH_ACH_B), 2.28 (3H, s, NCH₃), 1.38 (d, $J = 6.8$ Hz, 1H, CHCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 143.1 (C), 128.0 (2 × CH), 127.8 (2 × CH), 126.8 (CH), 103.3 (CH), 63.8 (CH), 55.3 (CH₂), 53.3 (CH₃), 53.0 (CH₃), 39.7 (CH₃), 17.7 (CH₃).

HRMS (QTOF) Exact mass calcd for [C₁₃H₂₂NO₂]⁺ [M+H]⁺: 224.1645, found: 224.1654.



(±)-3-(Methyl-(1-phenylethyl)amine)propanenitrile (**5n**)

The title compound was prepared according to **GP1** using boronic ester **1** (0.116 g, 0.500 mmol) and *N*-(methylamino)propionitrile (0.143 g, 1.70 mmol), heating for 18 h. Flash column chromatography (60% hexane/40% Et₂O) of the crude material gave amine **5n** (65.5 mg, 70%) as a colorless oil.

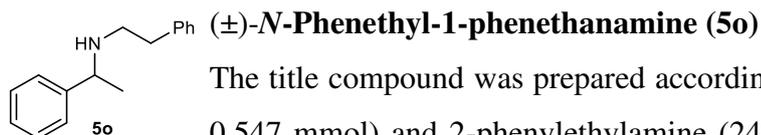
IR 2974, 2799, 2238, 1251, 1371, 1070, 958 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.35-7.30 (4H, m, ArH), 7.27-7.24 (1H, m, ArH), 3.62 (1H, q, $J = 6.7$ Hz, NCH), 2.77 (1H, dt, $J = 12.9, 7.2$ Hz, NCH_AH_B), 2.62 (1H, dt, $J = 12.9, 6.8$ Hz, NCH_AH_B), 2.42 (2H, dd, $J = 7.2, 6.8$ Hz, CH₂CN), 2.26 (3H, s, NCH₃), 1.37 (3H, d, $J = 6.7$ Hz, CHCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 143.3 (C), 128.4 (2 × CH), 127.5 (2 × CH), 127.2 (CH), 118.9 (C), 63.3 (CH), 49.7 (CH₂), 38.4 (CH₃), 18.4 (CH₃), 16.5 (CH₂).

HRMS (Q-TOF) Exact mass calcd for [C₁₂H₁₇N₂]⁺ [M+H]⁺: 189.1386, found: 189.1393.

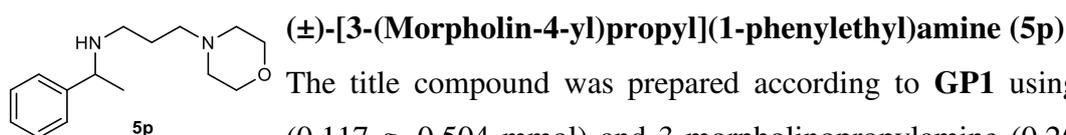
3.5. Scope of Reaction Using Primary amines



The title compound was prepared according to **GP1** using boronic ester **1** (0.127 g, 0.547 mmol) and 2-phenylethylamine (240 μ L, 1.90 mmol), heating for 18 h. The crude was concentrated under vacuo, dissolved in 5 mL EtOAc and extracted with aqueous HCl (1 M, 3 \times 3 mL). The aqueous phases were combined, basified to pH > 10 with a solution of saturated aqueous Na₂CO₃, and extracted with EtOAc (3 \times 10 mL). The organic phase was dried over MgSO₄ and concentrated *in vacuo*. Flash column chromatography (75% hexane/25% EtOAc \rightarrow 100% EtOAc) of the crude material gave amine **5o** (68.3 mg, 55%) as a yellow oil. The data were consistent with the literature.²³

¹H NMR (400 MHz, CDCl₃) δ 7.38-7.16 (10H, m, ArH), 3.81 (1H, q, J = 6.6 Hz, CH), 2.87-2.69 (4H, m, 2 \times CH₂), 1.45 (1H, br s, NH), 1.37 (d, J = 6.6 Hz, 3H, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 145.5 (C), 140.0 (C), 128.6 (2 \times CH), 128.3 (4 \times CH), 126.8 (CH), 126.5 (2 \times CH), 126.0 (CH), 58.1 (CH), 48.9 (CH₂), 36.4 (CH₂), 24.3 (CH₃).



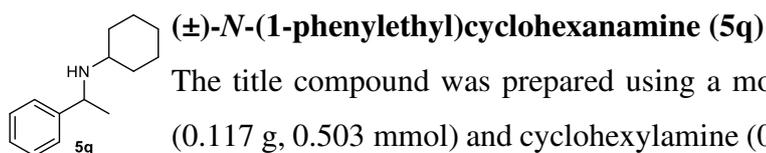
The title compound was prepared according to **GP1** using boronic ester **1** (0.117 g, 0.504 mmol) and 3-morpholinopropylamine (0.253 g, 1.78 mmol), heating for 18 h. Flash column chromatography (97% CH₂Cl₂/2% MeOH/1% Et₃N) of the crude material gave amine **5p** (61.7 mg, 49%) as a yellow oil.

IR 2960, 2810, 1675, 1455, 1275, 1118 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.36-7.30 (4H, m, ArH), 7.27-7.22 (1H, m, ArH), 3.77 (1H, q, J = 6.6 Hz, CH), 3.68 (4H, t, J = 4.7 Hz, 2 \times OCH₂), 2.65-2.57 (1H, m, CHNCH_ACH_B), 2.54-2.32 (7H, m, CHNCH_ACH_B, CH₂N(CH₂)₂ and 2 \times NCH₂CH₂O), 1.76-1.63 (2H, m, NCH₂CH₂CH₂), 1.39 (3H, d, J = 6.6 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 145.1 (C), 128.4 (2 \times CH), 127.0 (CH), 126.5 (2 \times CH), 66.9 (2 \times CH₂), 58.4 (CH), 57.5 (CH₂), 53.7 (2 \times CH₂), 46.5 (CH₂), 26.3 (CH₂), 24.0 (CH₃).

HRMS (Q-TOF) Exact mass calcd for [C₁₅H₂₅N₂O]⁺ [M+H]⁺: 249.1961, found: 249.1970

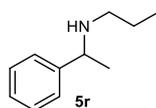
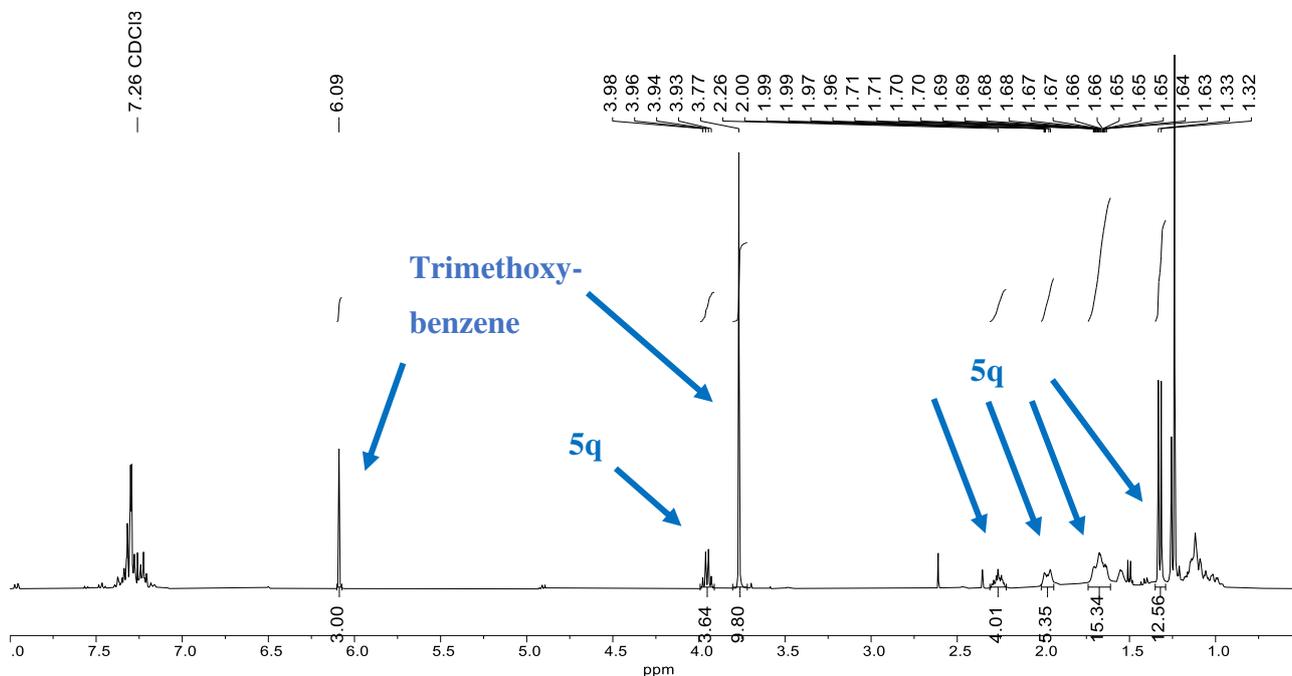


The title compound was prepared using a modification of **GP1** using boronic ester **1** (0.117 g, 0.503 mmol) and cyclohexylamine (0.20 mL, 1.7 mmol), heating for 18 h. The mixture was filtered through a silica plug, eluting with Et₂O (10 mL). 1,3,5-Trimethoxybenzene (16.5 mg, 0.0981 mmol) was added to the filtrate, and the mixture was concentrated *in vacuo*. The

mixture was analysed by ^1H NMR, which indicated amine **5q** was formed in 63% yield (average of two reactions). The data matched the literature.²⁴

Characteristic peaks for **5q**.

^1H NMR (400 MHz, CDCl_3): 3.95 (1H, q, $J = 6.6$ Hz, CH), 2.31-2.21 (1H, m, CH_2), 2.01-1.94 (1H, m, CH_2), 1.75-1.61 (3H, m, CH_2), 1.32 (3H, d, $J = 6.6$ Hz, CH_3).

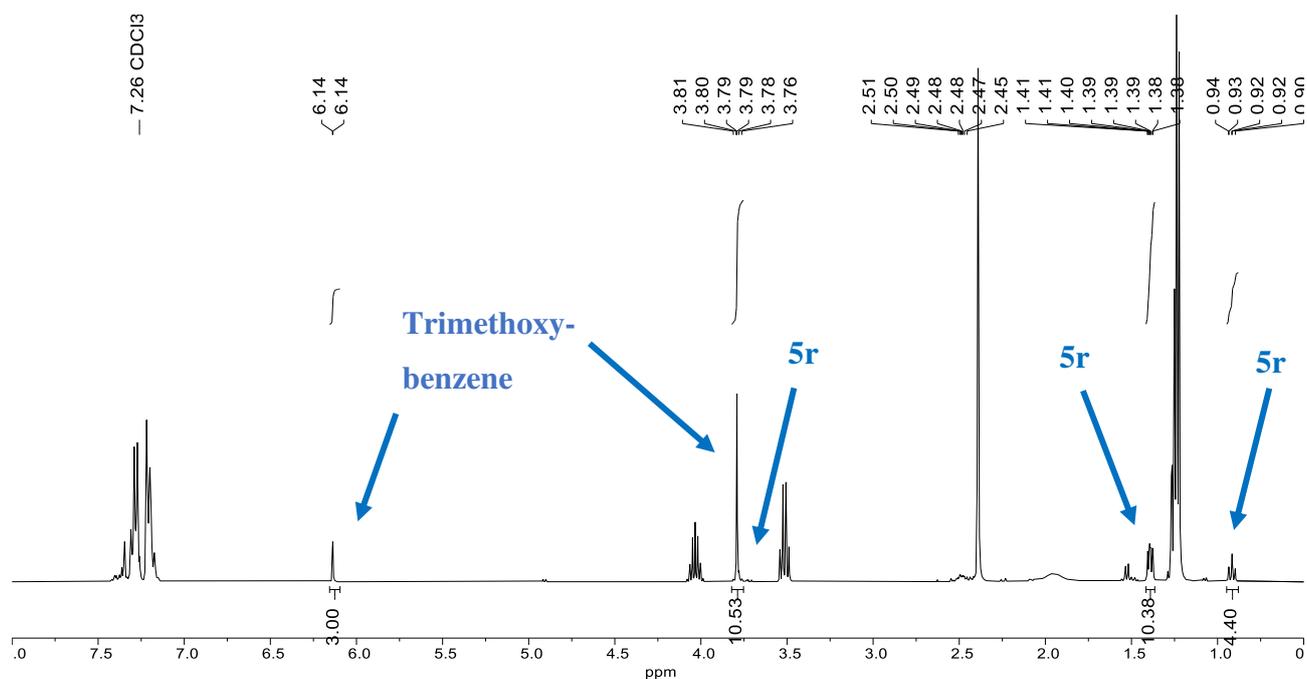


(\pm)-*N*-(1-phenylethyl)propan-1-amine (5r**)**

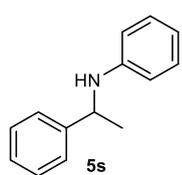
The title compound was prepared using a modification of **GPI** using boronic ester **1** (0.117 g, 0.502 mmol) and propylamine (0.15 mL, 1.8 mmol), heating for 18 h. The mixture was filtered through a silica plug, eluting with Et_2O (10 mL). 1,3,5-Trimethoxybenzene (20.4 mg, 0.121 mmol) was added to the filtrate, and the mixture was concentrated *in vacuo*. The mixture was analysed by ^1H NMR, which indicated amine **5r** was formed in 45% yield (average of two reactions). The data matched the literature.²⁵

Characteristic peaks for **5r**.

^1H NMR (400 MHz, CDCl_3) δ 3.79 (1H, q, $J = 6.5$ Hz, CH), 1.41-1.37 (5H, m, $\text{CH}_2\text{CH}_3 + \text{CHCH}_3$), 0.92 (3H, t, $J = 7.4$ Hz, CH_2CH_3).



(±)-*N*-(1-Phenylethyl)aniline (**5s**)

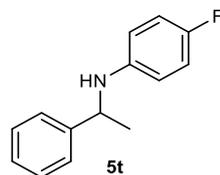


The title compound was prepared according to **GP1** using boronic ester **1** (0.117 g, 0.505 mmol) and aniline (0.163 mg, 1.75 mmol), heating for 18 h. Flash column chromatography (98% hexane/2% EtOAc) of the crude material gave amine **5s** (44.3 mg, 45%) as an orange oil. The data were consistent with the literature.²⁶

¹H NMR (400 MHz, CDCl₃) δ 7.42-7.38 (2H, m, ArH), 7.37-7.32 (2H, m, ArH), 7.27-7.23 (1H, m, ArH), 7.15-7.09 (2H, m, ArH), 6.70-6.65 (1H, m, ArH), 6.56-6.52 (2H, m, ArH), 4.51 (1H, q, *J* = 6.7 Hz, CH), 4.16 (1H, br s, NH), 1.55 (3H, d, *J* = 6.7 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 147.1 (C), 145.1 (C), 129.1 (2 × CH), 128.6 (2 × CH), 126.9 (CH), 125.8 (2 × CH), 117.3 (CH), 113.4 (2 × CH), 53.5 (CH), 25.0 (CH₃).

(±)-4-Fluoro-*N*-(1-phenylethyl)aniline (**5t**)

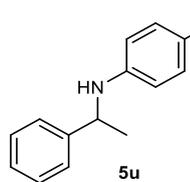


The title compound was prepared according to **GP1** using boronic ester **1** (0.116 g, 0.500 mmol) and 4-fluoroaniline (0.196 g, 1.76 mmol), heating for 18 h. Flash column chromatography (98% hexane/2% EtOAc) of the crude material gave amine **5t** (53.0 mg, 49%) as an orange oil. The data were consistent with the literature.²⁶

¹H NMR (400 MHz, CDCl₃) δ 7.40-7.33 (4H, m, ArH), 7.27-7.23 (1H, m, ArH), 6.85-6.78 (2H, m, ArH), 6.48-6.43 (2H, m, ArH), 4.44 (1H, q, *J* = 6.7 Hz, CH), 4.04 (1H, br s, NH), 1.53 (3H, d, *J* = 6.7 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 155.7 (C, d, *J_F* = 234.6 Hz), 144.9 (C), 143.5 (C), 128.7 (2 × CH), 127.0 (CH), 125.8 (2 × CH), 115.5 (2 × CH, d, *J_F* = 22.3 Hz), 114.1 (2 × CH, d, *J_F* = 7.1 Hz), 54.1 (CH), 25.0 (CH₃).

^{19}F NMR (377 MHz, CDCl_3) δ -128.2.



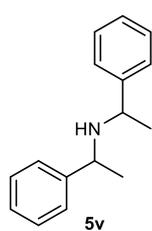
(±)-4-Methoxy-N-(1-phenylethyl)aniline (5u)

The title compound was prepared according to **GP1** using boronic ester **1** (0.117 g, 0.505 mmol) and *p*-anisidine (0.217 g, 1.76 mmol), heating for 18 h. Flash column chromatography (96% hexane/4% EtOAc) of the crude material gave amine **5u** (31.6 mg, 28%) as an orange oil. The data were consistent with the literature.²⁶

^1H NMR (400 MHz, CDCl_3) δ 7.41-7.37 (2H, m, ArH), 7.36-7.32 (2H, m, ArH), 7.31-7.21 (1H, m, ArH), 6.75-6.69 (2H, m, ArH), 6.53-6.47 (2H, m, ArH), 4.44 (1H, q, $J = 6.7$ Hz, CH), 3.72 (3H, s, OCH₃), 1.52 (3H, d, $J = 6.7$ Hz, CH₃).

^{13}C NMR (101 MHz, CDCl_3) δ 151.9 (C), 145.4 (C), 141.5 (C), 128.6 (2 × CH), 126.8 (CH), 125.9 (2 × CH), 114.7 (2 × CH), 114.6 (2 × CH), 55.7 (CH₃), 54.3 (CH), 25.1 (CH₃).

3.6. Diastereomeric Compounds



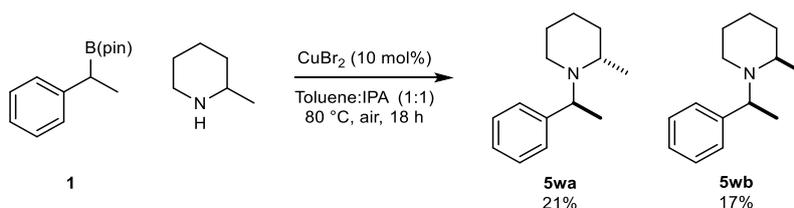
(±)-Bis(1-phenylethyl)amine (mixture of diastereoisomers) (5v)

The title compound was prepared according to **GP1** using boronic ester **1** (0.116 g, 0.500 mmol) and (*R*)-methylbenzylamine (212 mg, 1.75 mmol), heating for 18 h. Flash column chromatography (dichloromethane to 69% hexane/ 30% EtOAc/ 1% Et₃N) of the crude material gave amine **5v** (63.6 mg, 56%, *dl/meso* = 1:0.98) as a yellow oil. The data were consistent with the literature.²⁹

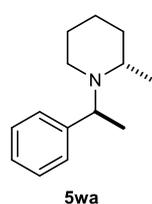
^1H NMR (400 MHz, CDCl_3) δ 7.42-7.22 (20H, m, ArH, *dl* and *meso* isomers), 3.81 (2H, q, $J = 6.5$ Hz, CH, *dl* isomer), 3.55 (2H, q, $J = 6.7$ Hz, CH, *meso* isomer), 1.66 (2H, br s, NH, *dl* and *meso* isomers), 1.40 (6H, d, $J = 6.6$ Hz, CH₃, *dl* isomer), 1.32 (6H, d, $J = 6.7$ Hz, CH₃, *meso* isomer).

^{13}C NMR (101 MHz, CDCl_3) δ 145.8 (4 × C, *dl* and *meso* isomers), 128.4 (8 × CH, *dl* and *meso* isomers), 126.8 (4 × CH, *dl* and *meso* isomers), 126.6 (4 × CH, *dl* and *meso* isomers), 126.5 (4 × CH, *dl* and *meso* isomers), 55.1 (2 × CH, *meso*), 54.8 (2 × CH, *dl*), 24.9 (2 × CH₃, *meso*), 23.1 (2 × CH₃, *dl*).

(±)-2-Methyl-1-(1-phenylethyl)piperidine (**5w**)



The title compound was prepared according to **GP1** using boronic ester **1** (0.117 g, 0.502 mmol) and 2-methyl piperidine (0.175 g, 1.76 mmol), heating for 18 h. Flash column chromatography (69% hexane/30% EtOAc/1% Et_3N) of the crude material gave amine **5wa** (21.0 mg, 21%) as a yellow oil and amine **5wb** (17.3 mg, 17%) as a yellow oil. The data for **5wa**²⁷ and **5wb**²⁸ were consistent with the literature.



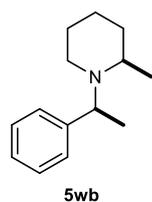
(±)-(S,S)-2-Methyl-1-(1-phenylethyl)piperidine (**5wa**)

IR 2930, 2793, 1447, 1373, 1279, 1066 cm^{-1} .

¹H NMR (400 MHz, CDCl_3) δ 7.47-7.42 (2H, m, ArH), 7.35-7.29 (2H, m, ArH), 7.24-7.20 (1H, m, ArH), 4.07 (1H, q, $J = 6.7$ Hz, ArCH), 2.87-2.80 (1H, m, NCH CH_2), 2.40-2.33 (1H, m, CH ACH_B), 2.20-2.12 (1H, m, CH ACH_B), 1.75-1.68 (1H, m, CH $_2$), 1.67-1.59 (1H, m, CH $_2$), 1.47-1.31 (4H, m, 2 \times CH $_2$), 1.27 (3H, d, $J = 6.7$ Hz, ArCHCH $_3$), 1.14 (3H, d, $J = 6.3$ Hz, CH $_2$ CHCH $_3$).

¹³C NMR (101 MHz, CDCl_3) δ 145.8 (C), 127.9 (2 \times CH), 127.7 (2 \times CH), 126.2 (CH), 56.6 (CH), 52.0 (CH), 44.9 (CH $_2$), 34.7 (CH $_2$), 26.4 (CH $_2$), 23.4 (CH $_2$), 17.0 (CH $_3$), 12.5 (CH $_3$).

HRMS (QTOF) Exact mass calcd for $[\text{C}_{14}\text{H}_{21}\text{N}]^+$ $[\text{M}+\text{H}]^+$: 204.1747, found: 204.1751.



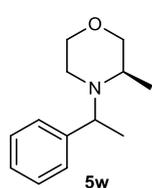
(±)-(R,S)-2-Methyl-1-(1-phenylethyl)piperidine (**5wb**)

IR 2940, 2523, 1455, 1205, 1064 cm^{-1} .

¹H NMR (400 MHz, CDCl_3) δ 7.35-7.22 (5H, m, ArH), 4.10 (1H, q, $J = 6.9$ Hz, ArCH), 2.89-2.83 (1H, m, NCH AH_B), 2.39-2.32 (1H, m, NCH CH_2), 2.18-2.09 (1H, m, NCH AH_B), 1.64-1.50 (4H, m, 2 \times CH $_2$), 1.42 (3H, d, $J = 6.9$ Hz, ArCHCH $_3$), 1.39-1.29 (1H, m, CH $_2$), 1.25-1.17 (1H, m, CH $_2$), 1.14 (3H, d, $J = 6.2$ Hz, CH $_2$ CHCH $_3$).

¹³C NMR (101 MHz, CDCl_3) δ 141.8 (C), 128.1 (2 \times CH), 127.8 (2 \times CH), 126.6 (CH), 57.4 (CH), 52.4 (CH), 44.8 (CH $_2$), 34.7 (CH $_2$), 26.5 (CH $_2$), 22.9 (CH $_2$), 20.1 (CH $_3$), 17.3 (CH $_3$).

HRMS (QTOF) Exact mass calcd for $[\text{C}_{14}\text{H}_{21}\text{N}]^+$ $[\text{M}+\text{H}]^+$: 204.1747, found: 204.1754.



(±)-3-Methyl-4-(1-phenylethyl)morpholine (**5x**)

The title compound was prepared according to **GP1** using boronic ester **1** (0.116 g, 0.498 mmol) and (*R*)-3-methylmorpholine (182 mg, 1.80 mmol), heating for 18 h. The mixture was concentrated *in vacuo*, dissolved in 5 mL EtOAc and extracted with aqueous HCl (1

M, 3 × 3 mL). The combined aqueous phases were and basified to pH > 10 using saturated aqueous Na₂CO₃, and extracted with CH₂Cl₂ (3 × 10 mL). Flash column chromatography (75% hexane/25% EtOAc to 50% hexane/50% EtOAc) of the crude material gave two diastereoisomers, *amine 5xa* (23.5 mg, 23%) as a colourless oil and *amine 5xb* (23.2 mg, 23%) as a colourless oil.

Mixture of diastereomers:

HRMS (Q-TOF) Exact mass calcd for [C₁₃H₂₀NO]⁺ [M+H]⁺: 206.1539, found: 206.1547.

Data for 5xa:

IR 2965, 2848, 1446, 1138, 1125, 1076 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.44-7.38 (2H, m, ArH), 7.34-7.28 (2H, m, ArH), 7.25-7.19 (1H, m, ArH), 3.98 (1H, q, *J* = 6.8 Hz, ArCH), 3.75 (dd, *J* = 10.9, 3.0 Hz, 1H, CHCH_ACH_B), 3.60 (dt, *J* = 10.8, 4.4 Hz, 1H, CH₂CH_ACH_B), 3.52 (dd, *J* = 10.8, 5.2, 5.0 Hz, 1H, CH₂CH_ACH_B), 3.43 (dd, *J* = 10.9, 6.7 Hz, 1H, CHCH_ACH_B), 2.97 (1H, dqd, *J* = 6.7, 6.5, 3.0 Hz, NCHCH₃), 2.33-2.25 (2H, m, NCH₂), 1.29 (3H, d, *J* = 6.8 Hz, ArCHCH₃), 1.11 (3H, d, *J* = 6.5 Hz, CH₂CHCH₃).

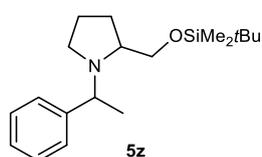
¹³C NMR (101 MHz, CDCl₃) δ 144.6 (C), 128.1 (2 x CH), 127.7 (2 x CH), 126.6 (CH), 73.3 (CH₂), 67.8 (CH₂), 56.9 (CH), 51.0 (CH), 44.3 (CH₂), 13.4 (CH₃), 12.0 (CH₃).

Data for 5xb:

IR 2965, 2848, 1452, 1136, 1125, 969 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.37-7.20 (5H, m,), 3.97 (1H, q, *J* = 6.9 Hz, ArCH), 3.80-3.67 (2H, m, OCH₂), 3.61 (1H, dd, *J* = 10.9, 3.1 Hz, OCH_AH_BCH), 3.33 (1H, dd, *J* = 10.9, 6.5 Hz, OCH_AH_BCH), 2.82-2.72 (1H, m,), 2.50-2.37 (2H, m, NCH₂), 1.39 (3H, d, *J* = 6.9 Hz, ArCHCH₃), 1.04 (3H, d, *J* = 6.4 Hz, CH₂CHCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 141.4 (C), 128.1 (2 x CH), 128.0 (2 x CH), 126.9 (CH), 73.2 (CH₂), 67.8 (CH₂), 57.8 (CH), 51.2 (CH), 44.2 (CH₂), 19.9 (CH₃), 12.0 (CH₃).



(±)-2-((*tert*-Butyldimethylsilyloxy)methyl)-1-(1-phenylethyl)pyrrolidine
(5y)

The title compound was prepared according to **GP1** using boronic ester **1** (0.116 g, 0.501 mmol) and 2-((*tert*-butyldimethylsilyloxy)methyl)pyrrolidine (378 mg, 1.75 mmol), heating for 18 h. Flash column chromatography (100% CH₂Cl₂ → 69% CH₂Cl₂/30% Et₂O/1% Et₃N) of the crude material gave *amine 5y* (103 mg, 64%, dr: 1.03:1) as a yellow oil. Upon further purification one of the diastereoisomers (**5ya**) was isolated for further characterisation.

Mixture of diastereoisomers (5ya and 5yb):

IR 2928, 1453, 1252, 1092, 833, 774 cm⁻¹.

¹H NMR (400 MHz, CD₃CN) δ 7.39-7.34 (2H, m, ArH, **5yb**), 7.34-7.26 (m, 6H, ArH, **5ya** + **5yb**), 7.25-7.19 (m, 2H, ArH, **5ya** + **5yb**), 3.83-3.70 (m, 2H, ArCH, **5ya** + **5yb**), 3.60 (dd, *J* = 10.0, 4.4 Hz,

1H, OCH_AH_B, **5ya**), 3.35 (dd, *J* = 10.0, 8.2 Hz, 1H, OCH_AH_B, **5ya**), 3.15 (1H, dd, *J* = 9.9, 4.8 Hz, OCH_AH_B, **5yb**) 3.10 (1H, dd, *J* = 9.9, 8.3 Hz, OCH_AH_B, **5yb**), 2.93-2.78 (3H, m, CH₂CH, **5ya** + **5yb**; NCH_AH_B, **5yb**), 2.77-2.69 (m, 1H, NCH_AH_B, **5ya**), 2.50 (td, *J* = 9.1, 6.8 Hz, 1H, NCH_AH_B, **5yb**), 2.39-2.29 (1H, m, NCH_AH_B, **5ya**), 1.78-1.54 (m, 8H, CHCH₂CH₂, **5ya** + **5yb**), 1.36 (3H, d, *J* = 6.7 Hz, CHCH₃, **5ya**), 1.33 (3H, d, *J* = 6.7 Hz, CHCH₃, **5yb**), 0.91 (9H, s, 3 × CCH₃, **5ya**), 0.80 (9H, s, 3 × CCH₃, **5yb**), 0.07 (3H, s, SiCH₃, **5ya**), 0.06 (3H, s, SiCH₃, **5ya**), -0.11 (3H, s, SiCH₃, **5yb**), -0.13 (3H, s, **5yb**).

¹³C NMR (101 MHz, CD₃CN) δ 147.1 (C), 145.8 (C), 129.0 (4 × CH), 128.7 (2 × CH), 128.6 (2 × CH), 127.8 (CH), 127.6 (CH), 67.7 (CH₂), 67.0 (CH₂), 63.8 (CH), 63.2 (CH), 63.0 (CH), 62.1 (CH), 52.8 (CH₂), 51.9 (CH₂), 29.0 (CH₂), 28.6 (CH₂), 26.3 (3 × CH₃), 26.3 (3 × CH₃), 26.1 (CH₃), 24.3 (CH₂), 24.2 (CH₂), 23.2 (CH₃), 19.8 (CH), 18.9 (C), 18.8 (C), -5.0 (CH₃), -5.1 (CH₃), -5.1 (CH₃), -5.2 (CH₃).

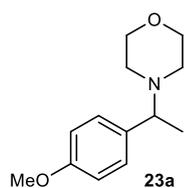
HRMS (QTOF) Exact mass calcd for [C₁₉H₃₄NOSi]⁺ [M+H]⁺: 320.2404, found: 320.2414.

Diastereoisomer 5ya:

¹H NMR (400 MHz, CD₃CN) δ 7.37-7.26 (4H, m, ArH), 7.25-7.19 (1H, m, ArH), 3.81 (1H q, *J* = 6.7 Hz, ArCH), 3.60 (1H, dd, *J* = 10.0, 4.4 Hz, OCH_AH_B), 3.35 (1H, dd, *J* = 10.0, 8.1 Hz, OCH_AH_B), 2.88 (1H, tt, *J* = 8.1, 4.5 Hz, NHCH₂), 2.77-2.69 (1H, m, NCH_AH_B), 2.39-2.29 (1H, m, NCH_AH_B), 1.77-1.51 (4H, m, CHCH₂CH₂), 1.37 (3H, d, *J* = 6.7 Hz, CHCH₃), 0.90 (9H, s, 3 × CCH₃), 0.07 (3H, s, SiCH₃), 0.06 (3H, s, SiCH₃).

¹³C NMR (101 MHz, CD₃CN) δ 145.4 (C), 129.1 (2 × CH), 128.7 (2 × CH), 127.7 (CH), 67.6 (CH₂), 63.1 (CH), 62.3 (CH), 52.8 (CH₂), 29.0 (CH₂), 26.3 (3 × CH₃), 24.1 (CH₂), 23.1 (CH₃), 18.9 (C), -5.0 (CH₃), -5.1 (CH₃).

3.7. Scope of Reaction Using Benzylic Boronic Esters

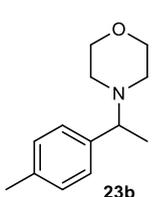


(±)-*N*-[1-(4-Methoxyphenyl)ethyl]morpholine (**23a**)

The title compound was prepared according to **GP1** using boronic ester **22a** (0.131 g, 0.500 mmol) and morpholine (0.152 g, 1.75 mmol), heating for 18 h. Flash column chromatography (99% hexane/1% Et₃N → 49.5% hexane/49.5% Et₂O/1% Et₃N) of the crude material gave amine **23a** (72.7 mg, 66%) as a colourless oil. The data were consistent with the literature.¹⁵

¹H NMR (400 MHz, CDCl₃) δ 7.22 (2H, d, *J* = 8.7 Hz, ArH), 6.85 (2H, d, *J* = 8.7 Hz, ArH), 3.80 (3H, s, OCH₃), 3.69-3.67 (4H, m, 2 × OCH₂), 3.26 (1H, q, *J* = 6.7 Hz, CH), 2.49-2.44 (2H, m, NCH₂), 2.37-2.32 (2H, m, NCH₂), 1.33 (3H, d, *J* = 6.7 Hz, CHCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 158.6 (C), 135.8 (C), 128.6 (2 × CH), 113.6 (2 × CH), 67.2 (2 × CH₂), 64.6 (CH), 55.2 (CH₃), 51.2 (2 × CH₂), 19.7 (CH₃).

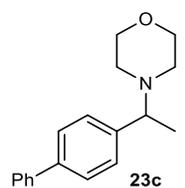


(±)-*N*-[1-(4-Methylphenyl)ethyl]morpholine (**23b**)

The title compound was prepared according to **GP1** using boronic ester **22b** (0.124 g, 0.504 mmol) and morpholine (0.153 g, 1.76 mmol), heating for 18 h. Flash column chromatography (70% hexane/30% EtOAc) of the crude material gave amine **23b** (75.0 mg, 73%) as a colourless oil. The data were consistent with the literature.³⁰

¹H NMR (400 MHz, CDCl₃) δ 7.20 (2H, d, *J* = 7.9 Hz, ArH), 7.13 (2H, d, *J* = 7.9 Hz, ArH), 3.72-3.64 (4H, m, 2 × OCH₂), 3.27 (1H, q, *J* = 6.5 Hz, CH), 2.47 (2H, br s, NCH₂), 2.39-2.34 (2H, m, NCH₂), 2.33 (3H, s, ArCH₃), 1.35 (3H, d, *J* = 6.5 Hz, CHCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 140.7 (C), 136.6 (C), 129.0 (2 × CH), 127.6 (2 × CH), 67.2 (2 × CH₂), 65.1 (CH), 51.3 (2 × CH₂), 21.0 (CH₃), 19.8 (CH₃).

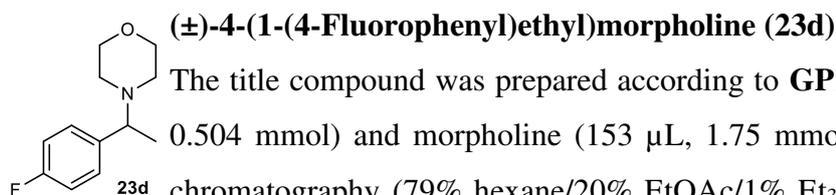


(±)-*N*-[1-([1,1'-Biphenyl]-4-yl)ethyl]morpholine (**23c**)

The title compound was prepared according to **GP1** using boronic ester **22c** (0.155 g, 0.503 mmol) and morpholine (0.156 g, 1.79 mmol), heating for 18 h. Flash column chromatography (59% hexane/40% EtOAc/1% Et₃N) of the crude material gave amine **23c** (99.6 mg, 74%) as a colourless oil. The data were consistent with the literature.³⁰

¹H NMR (400 MHz, CDCl₃) δ 7.64-7.53 (4H, m, ArH), 7.48-7.37 (4H, m, ArH), 7.37-7.29 (1H, m, ArH), 3.76-3.66 (4H, m, 2 × OCH₂), 3.37 (1H, q, *J* = 6.6 Hz, CH), 2.60-2.49 (2H, m, NCH₂), 2.47-2.36 (2H, m, NCH₂), 1.40 (3H, d, *J* = 6.6 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 143.0 (C), 140.9 (C), 139.9 (C), 128.7 (2 × CH), 128.0 (2 × CH), 127.1 (CH), 127.0 (4 × CH), 67.2 (2 × CH), 65.1 (CH), 51.3 (2 × CH), 19.7 (CH₃).

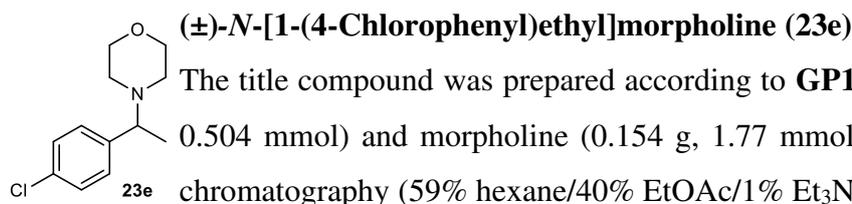


The title compound was prepared according to **GP1** using boronic ester **22d** (0.126 g, 0.504 mmol) and morpholine (153 μ L, 1.75 mmol), heating for 18 h. Flash column chromatography (79% hexane/20% EtOAc/1% Et₃N to 99% EtOAc/1% Et₃N) of the crude material gave amine **23d** (76.9 mg, 73%) as a colourless oil. The data were consistent with the literature.³¹

¹H NMR (400 MHz, CDCl₃) δ 7.30-7.23 (2H, m, ArH), 7.02-6.94 (2H, m, ArH), 3.74-3.60 (4H, m, 2 \times OCH₂), 3.28 (1H, q, J = 6.7 Hz, CH), 2.55-2.40 (2H, m, 2 \times NCH_AH_B), 2.37-2.27 (2H, m, 2 \times NCH_AH_B), 1.31 (3H, d, J = 6.7 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 161.8 (d, J_{C-F} = 244.7 Hz, C), 139.7 (d, J_{C-F} = 3.2 Hz, C), 128.9 (d, J_{C-F} = 7.8 Hz, 2 \times CH), 115.0 (d, J_{C-F} = 21.0 Hz, 2 \times CH), 67.1 (2 \times CH₂), 64.5 (CH), 51.1 (2 \times CH₂), 19.8 (CH₃).

¹⁹F NMR (377 MHz, CDCl₃) δ -116.0.



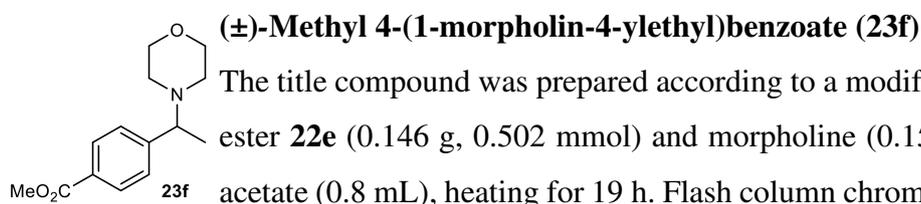
The title compound was prepared according to **GP1** using boronic ester **22e** (0.134 g, 0.504 mmol) and morpholine (0.154 g, 1.77 mmol), heating for 19 h. Flash column chromatography (59% hexane/40% EtOAc/1% Et₃N) of the crude material gave amine **23e** (88.0 mg, 78%) as a colourless oil.

IR 2960, 2854, 2907, 1490, 1272, 1116 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.32-7.22 (4H, m, ArH), 3.73-3.62 (4H, m, 2 \times OCH₂), 3.28 (1H, q, J = 6.7 Hz, CH), 2.52-2.42 (2H, m, NCH₂), 2.38-2.29 (2H, m, NCH₂), 1.31 (3H, d, J = 6.7 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 142.7 (C), 132.5 (C), 128.9 (2 \times CH), 128.5 (2 \times CH), 67.2 (2 \times CH₂), 64.7 (CH), 51.2 (2 \times CH₂), 19.8 (CH₃).

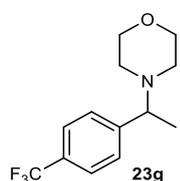
HRMS (Q-TOF) Exact mass calcd for [C₁₂H₁₆³⁵ClNO]⁺ [M+H]⁺: 226.0993, found: 226.1004.



The title compound was prepared according to a modification of **GP1** using boronic ester **22e** (0.146 g, 0.502 mmol) and morpholine (0.154 g, 1.77 mmol) and propyl acetate (0.8 mL), heating for 19 h. Flash column chromatography (20% EtOAc/80% CH₂Cl₂) of the crude material gave amine **23f** (63.0 mg, 50%) as a colourless oil. The data were consistent with the literature.³⁰

¹H NMR (400 MHz, CDCl₃) 8.02-7.91 (2H, m, ArH), 7.44-7.35 (2H, m), 3.90 (3H, s, OCH₃), 3.74-3.62 (4H, m, 2 \times OCH₂), 3.35 (1H, q, J = 6.7 Hz, CH), 2.54-2.43 (2H, m, NCH₂), 2.38-2.28 (2H, m, NCH₂), 1.33 (3H, d, J = 6.7 Hz, CHCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 167.0 (CH), 149.6 (CH), 129.7 (2 × CH), 128.9 (C), 127.5 (2 × CH), 67.1 (2 × CH₂), 65.1 (CH₃), 52.0 (CH), 51.3 (2 × CH₂), 19.7 (CH₃).



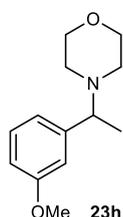
(±)-N-[1-[4-(Trifluoromethyl)phenyl]ethyl]morpholine (23g)

The title compound was prepared according to **GP1** using boronic ester **22g** (0.154 g, 0.514 mmol) and morpholine (159 μL, 1.82 mmol), heating for 18 h. Flash column chromatography (89% hexane/10% EtOAc/1% Et₃N → 79% hexane/20% EtOAc/1% Et₃N) of the crude material gave amine **23g** (82.5 mg, 62%) as a colourless oil. The data were consistent with the literature.¹⁵

¹H NMR (400 MHz, CDCl₃) δ 7.61-7.54 (2H, m, ArH), 7.51-7.40 (2H, m, ArH), 3.69 (4H, br s, 2 × OCH₂), 3.42-3.29 (1H, m, CH), 2.58-2.43 (2H, m, 2 × NCH_AH_B), 2.40-2.27 (2H, m, 2 × NCH_AH_B), 1.34 (3H, d, *J* = 4.0 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 148.4 (C), 129.3 (C, q, *J*_{C-F} = 31.7 Hz), 127.9 (2 × CH), 125.3 (2 × CH, q, *J*_{C-F} = 4.4 Hz), 124.4 (C, q, *J*_{C-F} = 271.0 Hz), 67.1 (2 × CH₂), 65.1 (CH), 51.2 (2 × CH₂), 19.7 (CH₃).

¹⁹F NMR (377 MHz, CDCl₃) δ -62.4.



(±)-N-[1-(3-Methoxyphenyl)ethyl]morpholine (23h)

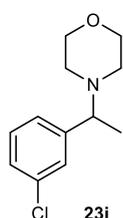
The title compound was prepared according to **GP1** using boronic ester **22h** (0.131 g, 0.500 mmol) and morpholine (0.154 g, 1.77 mmol), heating for 18 h. Flash column chromatography (69% hexane/30% EtOAc/1% Et₃N) of the crude material gave amine **23h** (88.0 mg, 80%) as a colourless oil.

IR 2958, 2853, 1585, 1264, 1116 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.25-7.20 (1H, m, ArH), 6.93-6.87 (2H, m, ArH), 6.78 (1H, dd, *J* = 7.8, 2.1 Hz, ArH), 3.81 (3H, s, OCH₃), 3.74-3.64 (4H, m, 2 × OCH₂), 3.31-3.21 (1H, m, CH), 2.56-2.43 (2H, m, NCH₂), 2.42-2.32 (2H, m, NCH₂), 1.34 (3H, d, *J* = 6.4 Hz, CHCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 159.6 (C), 145.8 (C), 129.2 (CH), 120.0 (CH), 113.3 (CH), 112.1 (CH), 67.2 (2 × CH₂), 65.4 (CH), 55.2 (2 × CH₂), 51.3 (CH₃), 19.9 (CH₃).

HRMS (QTOF) Exact mass calcd for [C₁₃H₁₉NO₂]⁺ [M]⁺: 221.1410, found: 221.1417.



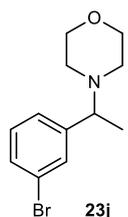
(±)-N-[1-(3-Chlorophenyl)ethyl]morpholine (23i)

The title compound was prepared according to **GP1** using boronic ester **22i** (0.135 g, 0.509 mmol) and morpholine (158 μL, 1.81 mmol), heating for 18 h. Flash column

chromatography (59% hexane/40% EtOAc/1% Et₃N) of the crude material gave amine **23i** (79.4 mg, 69%) as a pale-yellow oil. The data were consistent with the literature.¹⁸

¹H NMR (400 MHz, CDCl₃) δ 7.34 (1H, t, *J* = 1.8 Hz, ArH), 7.26-7.15 (3H, m, ArH), 3.73-3.62 (4H, m, 2 × OCH₂), 3.27 (1H, q, *J* = 6.7 Hz, CH), 2.53-2.42 (2H, m, 2 × NCH_AH_B), 2.39-2.29 (2H, m, 2 × NCH_AH_B), 1.31 (3H, d, *J* = 6.7 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 146.3 (C), 134.2 (C), 129.5 (CH), 127.5 (CH), 127.1 (CH), 125.7 (CH), 67.1 (2 × CH₂), 64.9 (CH), 51.1 (2 × CH₂), 19.7 (CH₃).

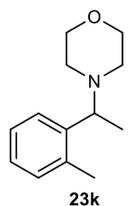


(±)-4-(1-(3-Bromophenyl)ethyl)morpholine (23j)

The title compound was prepared according to **GP1** using boronic ester **22j** (0.156 g, 0.502 mmol) and morpholine (155 μL, 1.77 mmol), heating for 18 h. Flash column chromatography (90% hexane/ 10% EtOAc to 100% EtOAc) of the material gave amine **23j** (88.2 mg, 65%) as a colourless oil. The data were consistent with the literature.³⁰

¹H NMR (400 MHz, CDCl₃) δ 7.48 (1H, t, *J* = 1.8 Hz, ArH), 7.39-7.33 (1H, m, ArH), 7.25-7.21 (1H, m, ArH), 7.17 (1H, t, *J* = 7.7 Hz, ArH), 3.74-3.62 (4H, m, 2 × OCH₂), 3.26 (1H, q, *J* = 6.7 Hz, CH), 2.52-2.42 (2H, m, 2 × NCH_AH_B), 2.39-2.30 (2H, m, 2 × NCH_AH_B), 1.31 (3H, d, *J* = 6.7 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 146.6 (C), 130.4 (CH), 130.0 (CH), 129.9 (CH), 126.2 (CH), 122.5 (C), 67.1 (CH₂), 64.9 (CH), 51.2 (CH₂), 19.7 (CH₃).



(±)-N-[1-(2-Methylphenyl)ethyl]morpholine (23k)

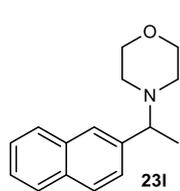
The title compound was prepared according to **GP1** using boronic ester **22k** (0.124 g, 0.505 mmol) and morpholine (0.153 g, 1.76 mmol), heating for 19 h. Flash column chromatography (69% hexane/30% EtOAc/1% Et₃N) of the crude material gave amine **23k** (87.7 mg, 85%) as a colourless oil.

IR 2958, 2852, 1454, 1261, 1116 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.45 (1H, d, *J* = 7.5 Hz, ArH), 7.21-7.14 (1H, m, ArH), 7.12 (2H, d, *J* = 3.9 Hz, ArH), 3.74-3.63 (4H, m, 2 × OCH₂), 3.53 (1H, q, *J* = 6.6 Hz, CH), 2.56-2.45 (2H, m, NCH₂), 2.42-2.36 (2H, m, NCH₂), 2.36 (3H, s, ArCH₃), 1.28 (3H, d, *J* = 6.6 Hz, CHCH₃).

¹³C NMR (101 MHz, CDCl₃) δ 142.6 (C), 135.8 (C), 130.4 (CH), 126.8 (CH), 126.4 (CH), 126.0 (CH), 67.3 (2 × CH₂), 60.8 (CH), 51.3 (2 × CH₂), 19.5 (CH₃), 18.6 (CH₃).

HRMS (Q-TOF) Exact mass calcd for [C₁₃H₁₉NO]⁺ [M+H]⁺: 206.1539, found: 206.1549.

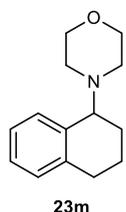


(±)-N-[1-(2-Naphthalenyl)ethyl]morpholine (23l)

The title compound was prepared according to **GP1** using boronic ester **22l** (0.142 g, 0.503 mmol) and morpholine (0.155 mg, 1.78 mmol), for 18 h. Flash column chromatography (69% hexane/30% EtOAc/1% Et₃N) of the crude material gave amine **23l** (86.3 mg, 71%) as a colourless oil. The data were consistent with the literature.¹⁵

¹H NMR (400 MHz, CDCl₃) δ 7.85-7.78 (3H, m, ArH), 7.72 (1H, s, ArH), 7.55-7.42 (3H, m, ArH), 3.76-3.65 (4H, m, 2 × OCH₂), 3.46 (1H, q, *J* = 6.5 Hz, CH), 2.60-2.51 (2H, m, NCH₂), 2.45-2.35 (2H, m, NCH₂), 1.44 (3H, d, *J* = 6.5 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 141.7 (C), 133.3 (C), 132.8 (C), 128.1 (CH), 127.7 (CH), 127.6 (CH), 126.2 (CH), 126.0 (CH), 125.8 (CH), 125.6 (CH), 67.2 (2 × CH₂), 65.6 (CH), 51.5 (2 × CH₂), 19.8 (CH₃).

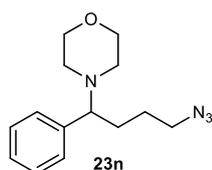


(±)-4-(1,2,3,4-Tetrahydro-1-naphthalenyl)morpholine (23m)

The title compound was prepared according to modification of **GP1** using boronic ester **22m** (0.134 g, 0.519 mmol) and morpholine (158 μL, 1.81 mmol), heating for 18 h. The crude was concentrated under vacuo, dissolved in EtOAc (5 mL) and extracted with aqueous HCl (1 M, 3 × 3 mL). The aqueous phases were combined, basified to pH > 10 with saturated aqueous Na₂CO₃, and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried (MgSO₄), and concentrated *in vacuo*. Flash column chromatography (90% hexane/ 10% Et₂O → 100% Et₂O) of the crude material gave amine **23m** (77.5 mg, 69%) as a colourless oil. The data were consistent with the literature.³²

¹H NMR (400 MHz, CDCl₃) δ 7.72 (1H, dd, *J* = 7.1, 1.3 Hz, ArH), 7.23-7.11 (2H, m, ArH), 7.11-7.05 (1H, m, ArH), 3.86-3.67 (5H, m, CH and 2 × OCH₂), 2.89-2.69 (2H, m, ArCH₂), 2.69-2.59 (2H, m, 2 × NCH_AH_B), 2.56-2.45 (2H, m, 2 × NCH_AH_B), 2.08-1.91 (2H, m, CHCH_AH_B and ArCH₂CH_AH_B), 1.82-1.63 (2H, m, CHCH_AH_B and ArCH₂CH_AH_B).

¹³C NMR (101 MHz, CDCl₃) δ 138.3 (C), 137.6 (C), 128.8 (CH), 128.1 (CH), 126.3 (CH), 125.6 (CH), 67.6 (2 × CH₂), 63.0 (CH), 48.9 (2 × CH₂), 29.6 (CH₂), 21.5 (CH₂), 21.5 (CH₂).



(±)-4-(4-Azido-1-phenylbutyl)morpholine (23n)

The title compound was prepared according to **GP1** using boronic ester **22n** (154 mg, 0.514 mmol) and morpholine (87.0 mg, 0.99 mmol), for 18 h. Flash column chromatography (69% hexane/30% EtOAc/1% Et₃N) of the crude material gave

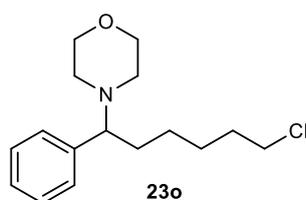
amine **23n** (94.9 mg, 71%) as a colourless oil.

IR 2954, 2853, 2092, 1450, 1731, 1116.

¹H NMR (400 MHz, CDCl₃) δ 7.39-7.19 (5H, m, ArH), 3.68 (4H, t, *J* = 4.7 Hz, 2 × OCH₂), 3.26 (1H, dd, *J* = 8.9, 5.2 Hz, CH), 3.21 (2H, t, *J* = 6.8 Hz, CH₂N₃), 2.52-2.33 (4H, m, 2 × CH₂CH₂O), 2.06-1.94 (1H, m, CHCH_AH_B), 1.85-1.70 (1H, m, CHCH_AH_B), 1.55-1.31 (2H, m, CH₂CH₂N₃).

¹³C NMR (101 MHz, CDCl₃) δ 139.6 (C), 128.4 (2 × CH), 128.2 (2 × CH), 127.3 (CH), 69.9 (CH), 67.0 (2 × CH₂), 51.4 (CH₂), 50.9 (2 × CH₂), 29.4 (CH₂), 25.5 (CH₂).

HRMS (Q-TOF) Exact mass calcd for [C₁₄H₂₁N₄O]⁺ [M+H]⁺: 261.1715, found: 261.1722.



(±)-N-(6-Chloro-1-phenylhexyl)morpholine (23o)

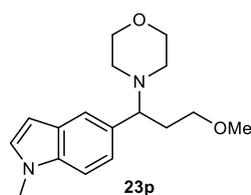
The title compound was prepared according to **GP1** using boronic ester **22o** (89.8 mg, 0.28 mmol) and morpholine (87.0 mg, 0.99 mmol), for 18 h. Flash column chromatography (69% hexane/30% EtOAc/1% Et₃N) of the crude material gave *amine* **23o** (31.5 mg, 40%, ~90% purity) as a colourless oil.

IR 2935, 2856, 1450, 1683, 1273, 1116.

¹H NMR (400 MHz, CDCl₃) δ 7.36-7.30 (2H, m, ArH), 7.28-7.21 (3H, m, ArH), 3.72-3.65 (4H, m, 2 × OCH₂), 3.46 (2H, t, *J* = 6.7 Hz, CH₂Cl), 3.24-3.20 (1H, m, CH), 50-2.32 (4H, m, 2 × NCH₂), 1.96-1.87 (1H, m, CH_ACH_B), 1.76-1.64 (3H, m, CH_ACH_B and CH₂), 1.44-1.34 (2H, m, CH₂), 1.20-1.02 (2H, m, CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 145.7 (C), 128.6 (2 × CH), 128.1 (2 × CH), 127.2 (CH), 70.5 (CH), 67.2 (2 × CH₂), 51.1 (2 × CH₂), 45.0 (CH₂), 32.4 (2 × CH₂), 26.9 (CH₂), 25.4 (CH₂).

HRMS (Q-TOF) Exact mass calcd for [C₁₆H₂₄³⁵ClNO]⁺ [M+H]⁺: 282.1619 found: 282.1631.



(±)-3-[3-Methoxy-1-(morpholinyl)propyl]-1-methyl-indole (23p)

The title compound was prepared according to **GP1** using boronic ester **22p** (0.165 g, 0.501 mmol) and morpholine (155 μL, 1.75 mmol), heating for 18 h.

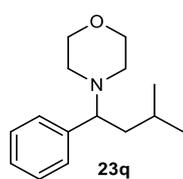
Flash column chromatography (1: 95% CH₂Cl₂/5% MeOH; 2: 50% hexane/50% isopropanol) gave *amine* **23p** (80.1 mg, 55%) as a brown oil.

IR 2924 (CH), 1447, 1115 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.47 (1H, s, ArH), 7.28 (1H, d, *J* = 8.5 Hz, ArH), 7.14 (1H, dd, *J* = 8.5, 1.3 Hz, ArH), 7.05 (1H, d, *J* = 3.1 Hz, ArH), 6.46 (1H, d, *J* = 3.1 Hz, ArH), 3.79 (3H, s, NCH₃), 3.67 (4H, t, *J* = 4.7 Hz, (CH₂)₂O), 3.45 (1H, dd, *J* = 9.9, 4.9 Hz, NCH), 3.27-3.19 (4H, m, OCH₃ and CH_AH_BOCH₃), 3.14 (1H, dt, *J* = 9.3, 7.3 Hz, CH_AH_BOCH₃), 2.57-2.44 (2H, m, 2 × NCH_AH_B), 2.44-2.36 (2H, m, 2 × NCH_AH_B), 2.36-2.26 (1H, m, CHCH_ACH_B), 2.03-1.89 (1H, m, CHCH_AH_B).

¹³C NMR (101 MHz, CDCl₃) δ 136.2 (C), 130.8 (C), 129.0 (CH), 128.2 (C), 122.2 (CH), 120.8 (CH), 108.9 (CH), 100.8 (CH), 70.3 (CH₂), 67.8 (CH), 67.3 (2 × CH₂), 58.6 (CH₃), 51.3 (2 × CH₂), 32.9 (CH₂), 32.9 (CH₃).

HRMS (Q-TOF) Exact mass calcd for $[C_{17}H_{25}N_2O_2]^+$ $[MH]^+$ calcd. 289.1922, found 289.1927.



(±)-4-(2-Phenylbutan-2-yl)morpholine (23q)

The title compound was prepared according to **GP1** using boronic ester **22q** (0.137 g, 0.501 mmol) and morpholine (153 mg, 1.76 mmol), for 18 h. Flash column chromatography (79% hexane/20% EtOAc/1% Et₃N) of the crude material gave *amine*

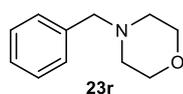
23q (19.8 mg, 17%) as a colourless oil.

IR 2955, 2854, 1451, 1270, 1117 cm^{-1} .

¹H NMR (400 MHz, CDCl₃) δ 7.35-7.27 (2H, m, ArH), 7.27-7.19 (3H, m, ArH), 3.71-3.59 (4H, m, 2 \times OCH₂), 3.32 (1H, dd, $J = 9.4, 5.6$ Hz, ArCH), 2.48-2.39 (2H, m, NCH₂), 2.39-2.30 (2H, m, NCH₂), 1.77-1.62 (2H, m, CHCH₂), 1.32-1.25 (1H, m, CHCH₃), 0.86 (3H, d, $J = 6.6$ Hz, CH₃), 0.83 (3H, d, $J = 6.6$ Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 140.1 (C), 128.7 (2 \times CH), 128.0 (2 \times CH), 127.1 (CH), 68.5 (CH), 67.3 (2 \times CH₂), 50.9 (2 \times CH₂), 41.3 (CH₂), 25.0 (CH₃), 23.7 (CH), 21.9 (CH₃).

HRMS (Q-TOF) Exact mass calcd for $[C_{15}H_{24}NO]^+$ $[M+H]^+$: 234.1852 found: 234.1862.



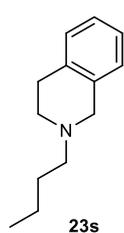
N-Benzylmorpholine (23r)

The title compound was prepared according to **GP1** using boronic ester **22r** (0.109 g, 0.500 mmol) and morpholine (0.152 mg, 1.74 mmol), for 18 h. Flash column chromatography (99% hexane/1% Et₃N to 99% Et₂O/1% Et₃N) of the crude material gave *amine* **23r** (66.3 mg, 75%) as a colourless oil. The data were consistent with the literature.²³

¹H NMR (400 MHz, CDCl₃) δ 7.34-7.29 (4H, m, ArH), 7.27-7.23 (1H, m, ArH), 3.72-3.70 (4H, m, 2 \times OCH₂), 3.50 (2H, s, ArCH₂), 2.46-2.43 (4H, m, 2 \times NCH₂CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 137.8 (C), 129.2 (2 \times CH), 128.2 (2 \times CH), 127.1 (CH), 67.0 (2 \times CH₂), 63.5 (CH₂), 53.6 (2 \times CH₂).

3.8. Scope of Reaction Using Aliphatic Boronic Esters

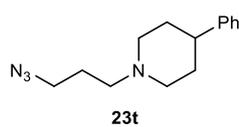


2-Butyl-1,2,3,4-tetrahydroisoquinoline (23s)

The title compound was prepared according to **GP1** using *n*-butyl pinacol boronic ester (0.103 g, 0.560 mmol) and 1,2,3,4-tetrahydroisoquinoline (253 μ L, 2.02 mmol), heating for 18 h. Flash column chromatography (70% hexane/ 29% EtOAc/ 1% Et₃N) of the material gave amine **23s** (36.6 mg, 35%) as an orange oil. The data were consistent with the literature.³³

¹H NMR (400 MHz, CDCl₃) δ 7.15-7.06 (3H, m, ArH), 7.05-6.98 (1H, m, ArH), 3.63 (2H, s, NCH₂Ar), 2.92 (2H, t, *J* = 5.9 Hz, NCH₂CH₂Ar), 2.74 (2H, t, *J* = 5.9 Hz, ArCH₂CH₂), 2.55-2.46 (2H, m, NCH₂CH₂CH₂), 1.65-1.54 (2H, m, CH₂CH₂CH₃), 1.46-1.32 (2H, m, CH₂CH₃), 0.96 (3H, t, *J* = 7.3 Hz, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 134.9 (C), 134.3 (C), 128.6 (CH), 126.6 (CH), 126.0 (CH), 125.5 (CH), 58.3 (CH₂), 56.2 (CH₂), 51.0 (CH₂), 29.3 (CH₂), 29.21 (CH₂), 20.8 (CH₂), 14.1 (CH₃).



1-(3-Azidopropyl)-4-phenylpiperidine (23t)

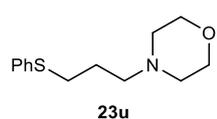
The title compound was prepared according to **GP1** using boronic ester **22t** (0.106 g, 0.502 mmol) and 4-phenylpiperidine (0.282 g, 1.75 mmol), heating for 18 h. Flash column chromatography (59% hexane/40% Et₂O/1% Et₃N) of the material gave amine **23t** (74.8 mg, 61%) as a colourless oil.

IR 2932, 2093, 1452, 1253, 1131 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.30 (2H, dd, *J* = 8.0, 7.7 Hz, ArH), 7.23 (2H, d, *J* = 7.7 Hz, ArH), 7.21 (1H, t, *J* = 8.0 Hz, ArH), 3.38 (2H, t, *J* = 6.7 Hz, CH₂N₃), 3.08 (2H, d, *J* = 11.9 Hz, 2 \times NCH_AH_BCH₂CH), 2.56-2.48 (3H, m, NCH₂CH₂CH₂ + CH), 2.15-2.09 (2H, m, CH₂CH₂N₃), 1.89-1.82 (6H, m, NCH_AH_BCH₂CH + 2 \times CH₂CH).

¹³C NMR (101 MHz, CDCl₃) δ 146.1 (C), 128.4 (2 \times CH), 126.8 (2 \times CH), 126.2 (CH), 55.7 (CH₂), 54.3 (2 \times CH₂), 49.7 (2 \times CH₂), 42.6 (CH), 33.3 (CH₂), 26.4 (CH₂).

HRMS (Q-TOF) Exact mass calcd for C₁₄H₂₁N₄⁺ [M+H]⁺: 245.1761 found: 245.1764.



4-[3-(Phenylsulfanyl)propyl]morpholine (23u)

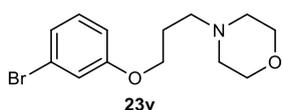
The title compound was prepared according to **GP1** using boronic ester **22u** (0.139 g, 0.500 mmol) and morpholine (0.152 g, 1.74 mmol), heating for 18 h. Flash column chromatography (99% hexane/1% Et₃N \rightarrow 49.5% hexane/49.5% Et₂O/1% Et₃N) of the material gave amine **23u** (72.5 mg, 61%) as a colourless oil.

IR 2853, 1584, 1439, 1259, 1116 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.34 (2H, d, *J* = 8.1 Hz, ArH), 7.27 (1H, dd, *J* = 8.1, 7.2 Hz, ArH), 7.17 (1H, t, *J* = 7.2 Hz, ArH), 3.71 (4H, t, *J* = 4.6 Hz, OCH₂), 2.97 (2H, t, *J* = 7.2 Hz, SCH₂), 2.58-2.25 (6H, m, CH₂CH₂CH₂N + 2 × OCH₂CH₂N), 1.83 (2H, p, *J* = 7.2 Hz, SCH₂CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 136.5 (C), 129.1 (2 × CH), 128.9 (2 × CH), 125.9 (CH), 66.9 (CH₂), 57.5 (CH₂), 53.6 (2 × CH₂), 31.4 (2 × CH₂), 26.0 (CH₂).

HRMS (Q-TOF) Exact mass calcd for [C₁₃H₂₀NOS]⁺ [M+H]⁺: 238.1260 found: 238.1268.



4-[3-(3-Bromophenoxy)propyl]morpholine (**23v**)

The title compound was prepared according to **GP1** using boronic ester **22v** (0.169 g, 0.496 mmol) and morpholine (0.152 g, 1.74 mmol), heating for 18 h.

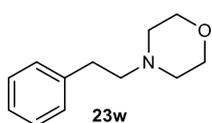
Flash column chromatography (40% EtOAc/59% hexane/1% Et₃N) of the material gave *amine 23v* (96.6 mg, 65%) as a pale yellow oil.

IR 2954, 2810, 1588, 1467, 1229, 1116, 860 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.16-7.09 (1H, m, ArH), 7.09-7.02 (2H, m, ArH), 6.86-6.78 (1H, m, ArH), 4.00 (2H, t, *J* = 6.3 Hz, ArOCH₂), 3.72 (4H, t, *J* = 4.6, Hz, OCH₂CH₂N), 2.50 (2H t, *J* = 7.2, Hz, CH₂CH₂CH₂N), 2.48-2.44 (4H, m, OCH₂CH₂N), 1.95 (2H, tt, *J* = 7.2, 6.3 Hz, ArOCH₂CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 159.8 (C), 130.5 (CH), 123.7 (CH), 122.8 (C), 117.7 (CH), 113.6 (CH), 67.0 (2 × CH₂), 66.3 (CH₂), 55.4 (CH₂), 53.7 (2 × CH₂), 26.3 (CH₂).

HRMS (Q-TOF) Exact mass calcd for [C₁₃H₁₉⁷⁹BrNO₂]⁺ [M+H]⁺: 300.0594 found: 300.0599.

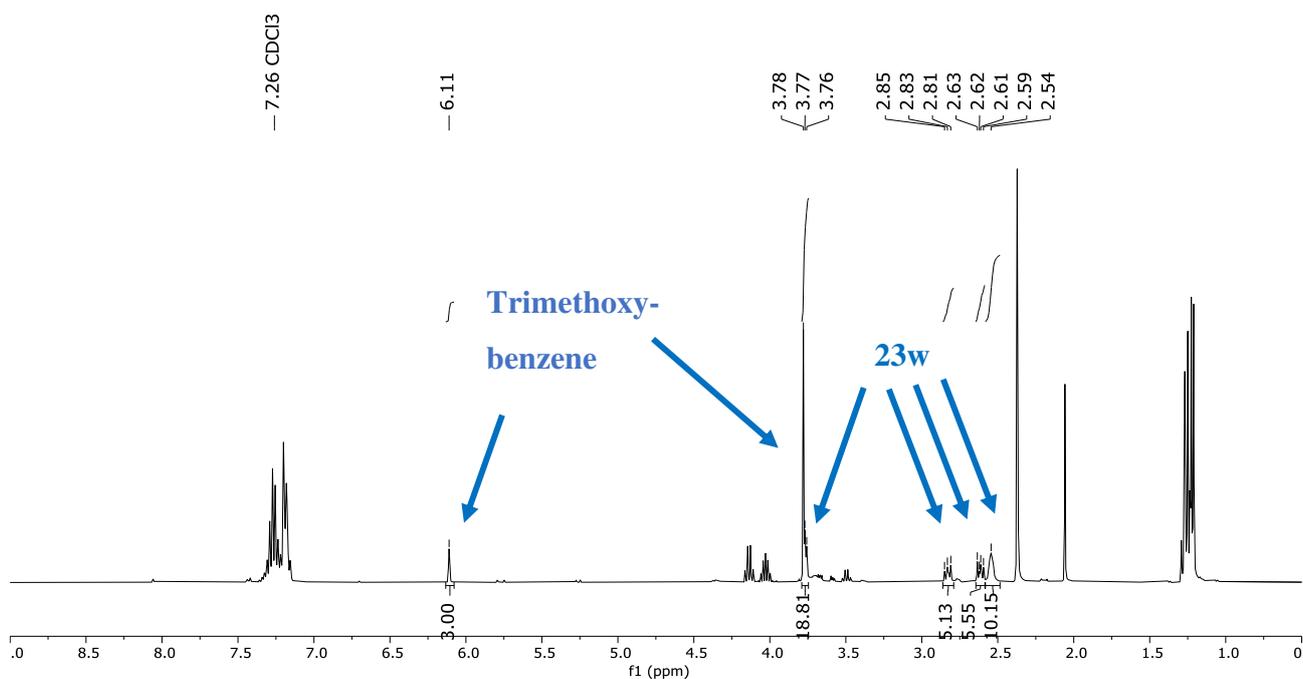


4-(2-Phenylethyl)morpholine (**23w**)

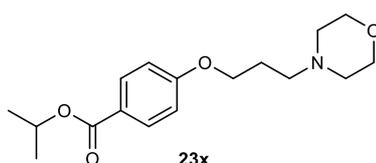
The title compound was prepared using a modification of **GP1** using 4,4,5,5-tetramethyl-2-phenethyl-1,3,2-dioxaborolane (0.117 g, 0.503 mmol) and morpholine (0.16 mL, 1.8 mmol), heating for 18 h. The mixture was filtered through a silica plug, eluting with EtOAc (10 mL). 1,3,5-Trimethoxybenzene (21.1 mg, 0.125 mmol) was added to the filtrate, and the mixture was concentrated *in vacuo*. The mixture was analysed by ¹H NMR, which indicated *amine 23w* was formed in 72% yield (average of two reactions). The data matched the literature.³⁴

Characteristic peaks for **23w**.

¹H NMR (400 MHz, CDCl₃): δ 3.77-3.75 (4H, m, 2 × OCH₂), 2.86-2.80 (2H, m, NCH₂), 2.64-2.58 (2H, m, PhCH₂), 2.54 (4H, s, 2 × NCH₂).



HRMS (Q-TOF) Exact mass calcd for $[C_{12}H_{18}NO]^+$ $[M+H]^+$: 192.1383 found: 192.1388.



Propan-2-yl 4-(3-morpholin-4-ylpropoxy)benzoate (23x)

The title compound was prepared according to **GP1** using boronic ester **22x** (0.174 g, 0.500 mmol) and morpholine (0.16 mL, 1.8 mmol), heating for 18 h. Flash column chromatography (1: 100% EtOAc, 2:

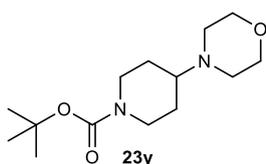
2% EtOH/98% CH_2Cl_2) of the material gave *amine* **23x** (86.0 mg, 56%) as a pale yellow oil.

IR 2956, 2854, 1705, 1605, 1251, 1099, 771 cm^{-1} .

1H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.94 (2H, m, ArH), 6.93 – 6.87 (2H, m, ArH), 5.22 (1H, hept, $J = 6.3$ Hz, CH), 4.08 (2H t, $J = 6.3$ Hz, $ArOCH_2$), 3.77 – 3.69 (4H, m, $2 \times OCH_2CH_2N$), 2.58 – 2.41 (6H, m, $3 \times NCH_2$), 1.99 (1H, tt, $J = 6.4, 6.3$ Hz, $ArOCH_2CH_2$), 1.35 (6H, d, $J = 6.3$ Hz, $2 \times CH_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9 (C), 162.6 (C), 131.5 ($2 \times CH$), 123.3 (C), 113.9 ($2 \times CH$), 67.9 (CH), 67.0 ($2 \times CH_2$), 66.2 (CH_2), 55.4 (CH_2), 53.7 ($2 \times CH_2$), 26.3 (CH_2), 22.0 ($2 \times CH_3$).

HRMS (Q-TOF) Exact mass calcd for $[C_{17}H_{26}NO_4]^+$ $[M+H]^+$: 308.1866 found: 308.1856.

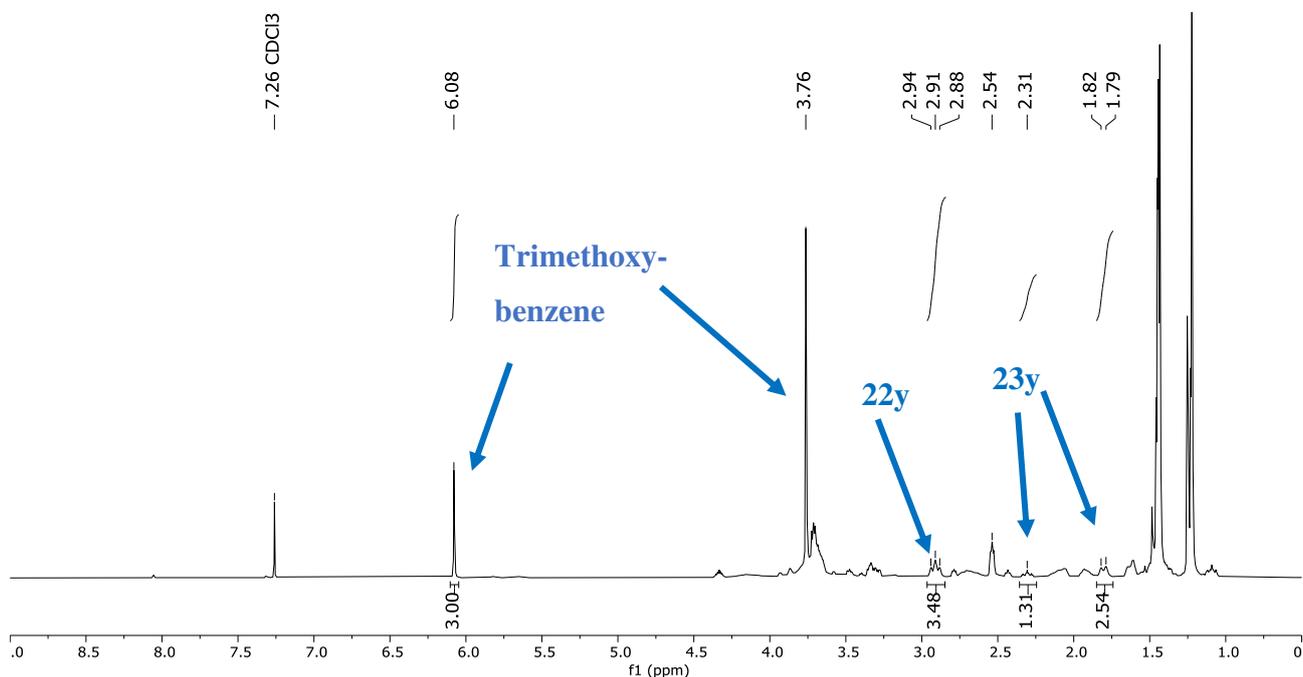


tert-Butyl 4-morpholinopiperidine-1-carboxylate (23y)

The title compound was prepared using a modification of **GP1** using *N*-Boc-piperidine-4-boronic acid pinacol ester **22y** (0.156 g, 0.503 mmol) and morpholine (0.16 mL, 1.8 mmol), heating for 18 h. The mixture was filtered through a silica plug, eluting with EtOAc (10 mL). 1,3,5-Trimethoxybenzene (18.9 mg, 0.112 mmol) was added to the filtrate, and the mixture was concentrated *in vacuo*. The mixture was analysed by 1H NMR, which indicated *amine* **23y** was formed in 29% yield (average of two reactions). The data matched the literature.³⁵

Characteristic peaks for **10y**.

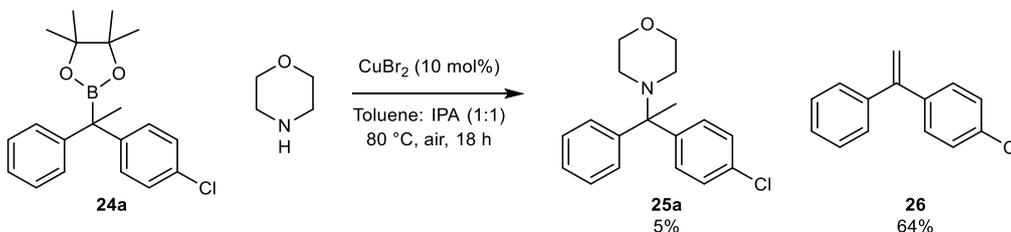
$^1\text{H NMR}$ (400 MHz, CDCl_3): δ 2.36-2.25 (1H, m, **CH**), 1.80 (2H, d, $J = 13.0$ Hz, **CH**₂).



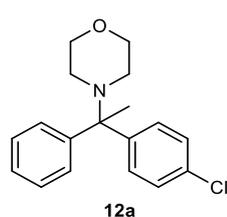
HRMS (Q-TOF) Exact mass calcd for $[\text{C}_{14}\text{H}_{27}\text{N}_2\text{O}_3]^+$ $[\text{M}+\text{H}]^+$: 271.2016 found: 271.2020.

3.9. Coupling of Tertiary Boronic Esters

4-[1-(4-Chlorophenyl)-1-phenylethyl]morpholine (**25a**)



The title compounds were prepared according to **GP1** using boronic ester **23a** (0.171 g, 0.502 mmol) and morpholine (0.153 g, 1.76 mmol). Flash chromatography (89% hexane/10% EtOAc/1% Et₃N) of the crude material gave *amine* **25a** (8.0 mg, 5%) as a colourless oil and alkene **26** (68.5 mg, 64%) as a colourless oil.



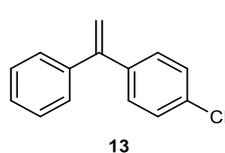
4-[1-(4-Chlorophenyl)-1-phenylethyl]morpholine (**25a**)

IR 2958, 2851, 1488, 1267, 1114 cm^{-1} .

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.47-7.39 (4H, m, **ArH**), 7.31-7.21 (4H, m, **ArH**), 7.21-7.14 (1H, m, **ArH**), 3.81-3.67 (4H, m, 2 \times **OCH**₂), 2.47-2.32 (4H, m, 2 \times **NCH**₂), 1.76 (3H, s, **CH**₃).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 144.8 (C), 144.2 (C), 132.0 (C), 128.9 (2 \times CH), 128.1 (4 \times CH), 127.4 (2 \times CH), 126.5 (CH), 67.7 (2 \times **CH**₂), 66.4 (C), 47.7 (2 \times **CH**₂), 18.9 (**CH**₃).

HRMS (Q-TOF) Exact mass calcd for $[C_{18}H_{20}^{35}ClNO]^+ [M]^+$: 301.1228 found: 301.1220.



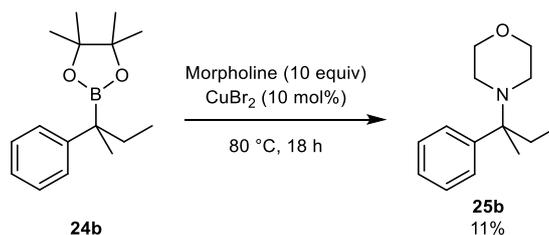
1-(4-Chlorophenyl)-1-phenylethylene (**26**)

The data were consistent with the literature.³⁶

¹H NMR (400 MHz, CDCl₃) δ 7.37-7.25 (9H, m, ArH), 5.48-5.44 (2H, m, CH₂)

¹³C NMR (101 MHz, CDCl₃) δ 149.0 (C), 141.0 (C), 139.9 (C), 133.6 (C), 129.5 (2 \times CH), 128.3 (2 \times CH), 128.3 (2 \times CH), 128.2 (2 \times CH), 127.9 (CH), 114.7 (CH₂).

(\pm)-4-(3-Methyl-1-phenylbutyl)morpholine (**25b**)



Morpholine (0.218 g, 2.5 mmol) was added to a flask containing boronic ester **24b** (0.065 g, 0.25 mmol) and CuBr₂ (5.6 mg, 0.025 mmol), and the mixture was stirred under air at 80 °C for 18 h. The mixture was cooled to room temperature, passed through a plug of silica eluting with Et₂O, and concentrated *in vacuo*. Flash chromatography (89% hexane/10% EtOAc/1% Et₃N) of the crude material gave and amine **25b** (5.8 mg, 11%) as a colourless oil.

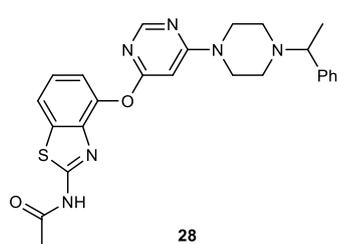
IR 2966, 2851, 1493, 1446, 1273, 1118 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 7.49-7.44 (2H, m, ArH), 7.33-7.27 (2H, m, ArH), 7.22-7.17 (1H, m, ArH), 3.74-3.63 (4H, m, 2 \times OCH₂), 2.59-2.50 (2H, m, 2 \times NCH_AH_B), 2.43-2.36 (2H, m, 2 \times NCH_AH_B), 1.81-1.71 (1H, m, CCH_AH_B), 1.66-1.56 (1H, m, CCH_AH_B), 1.33 (3H, s, CCH₃), 0.57 (3H, t, J = 7.4 Hz, CH₂CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 145.8 (C), 127.7 (2 \times CH), 127.3 (2 \times CH), 126.1 (CH), 67.9 (2 \times CH₂), 62.8 (C), 46.8 (2 \times CH₂), 33.8 (CH₂), 15.7 (CH₃), 8.7 (CH₃).

HRMS (Q-TOF) Exact mass calcd for $[C_{14}H_{22}NO]^+ [M+H]^+$: 220.1696 found: 220.1703.

3.10. Synthesis of a TRVP1 Inhibitor



(\pm)-N-[5-[6-[4-(1-Phenylethyl)piperazin-1-yl]pyrimidin-4-yl]oxy-1,3-benzothiazol-2-yl]acetamide (**28**)

The title compound was prepared using a modification of the **GP1** using boronic ester **1** (0.117 g, 0.504 mmol), CuBr₂ (22.6 mg, 0.100 mmol) and amine **27** (0.324 g, 1.75 mmol) in DMSO (0.75 mL) heating for 18 h. The mixture was diluted in CH₂Cl₂, filtered, and the filtrate concentrated *in vacuo*. Flash column

chromatography (100% EtOAc) of the crude material gave amine **28** (88.4 mg, 37%) as an off-white solid. The data were consistent with the literature.⁴

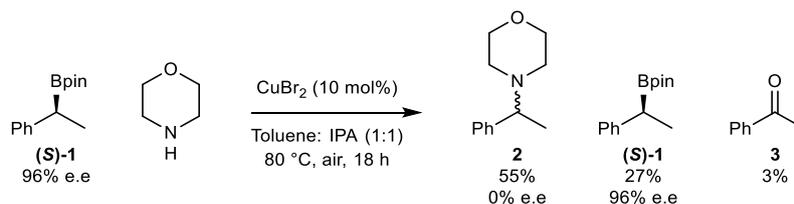
m.p. 175-178 °C (DMSO). Literature 132-135 °C (Not reported).⁴

¹H NMR (400 MHz, DMSO-*d*⁶) δ 12.41 (1H, br s, NH), 8.05 (1H, s, ArH), 7.84 (1H, dd, *J* = 7.9, 1.1 Hz, ArH), 7.36-7.23 (6H, m, ArH), 7.18 (1H, d, *J* = 7.9, 1.1 Hz, ArH), 6.31 (1H, s, ArH), 3.59-3.56 (4H, m, 2 \times ArNCH₂), 3.45 (1H, q, *J* = 6.7 Hz, CHCH₃), 2.49-2.43 (2H, m, 2 \times CHNCH_AH_B), 2.38-2.32 (2H, m, 2 \times CHNCH_AH_B), 2.15 (3H, s, COCH₃), 1.32 (3H, d, *J* = 6.7 Hz, CHCH₃).

¹³C NMR (101 MHz, DMSO-*d*⁶) δ 169.9 (C), 169.5 (C), 163.6 (C), 158.0 (C), 157.3 (CH), 144.2 (C), 143.1 (C), 141.8 (C), 133.4 (C), 128.2 (2 \times CH), 127.5 (2 \times CH), 127.0 (CH), 124.0 (CH), 119.2 (CH), 118.9 (CH), 85.7 (CH), 63.7 (CH), 49.5 (2 \times CH₂), 43.9 (2 \times CH₂), 22.6 (CH₃), 19.3 (CH₃).

3.11. Mechanistic Studies

Reaction With Enantiomerically Enriched Boronic Ester

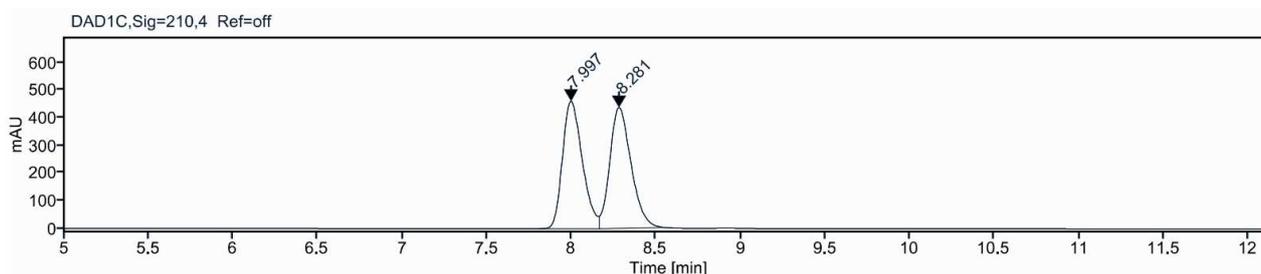


IPA (0.38 mL) and toluene (0.38 mL) were added to a flask containing boronic ester (**(S)-1**) (0.117 g, 0.503 mmol), morpholine (0.155 μ l, 1.75 mmol) and CuBr_2 (11.3 mg, 0.05 mmol), and the mixture was stirred under air at 80 °C for 1.5 h. The mixture was cooled to room temperature, passed through a plug of silica eluting with Et_2O , and concentrated *in vacuo*. The crude material was purified by column chromatography (5% $\text{EtOAc}/95\%$ hexane then 1% $\text{Et}_3\text{N}/30\%$ $\text{EtOAc}/69\%$ hexane) to give amine **2** (53.2 mg, 55%), boronic ester **1** (31 mg, 27%), and acetophenone (2.0 mg, 3%).

(±)-*N*-(1-Phenylethyl)morpholine (**2**).

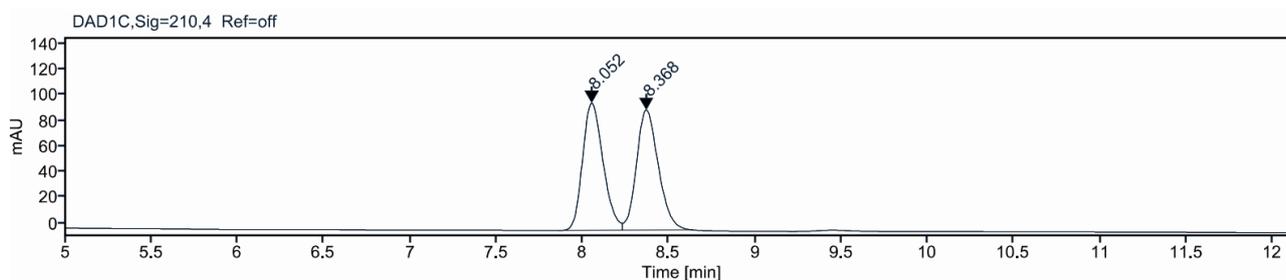
See above for data.
e.r. = 50:50, Chiralpak ID column (250 \times 4.6 mm), IPA:hexane = 1:99, 0.7 mL/min, column temperature = 22 °C, t_r = 8.1 min and t_r = 8.4 min.

Racemate



RT [min]	Type	Width [min]	Area	Height	Area%
7.997	BM m	0.1270	3765.7788	462.3245	49.5545
8.281	MM m	0.1339	3833.4956	438.8471	50.4455
Sum			7599.2744		

Reaction:



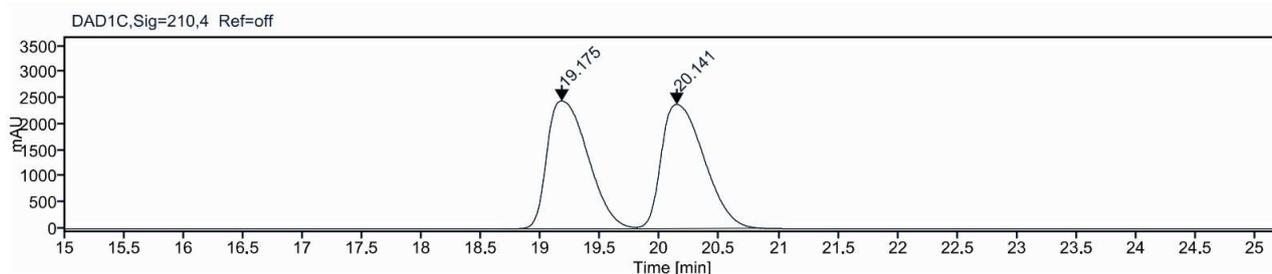
RT [min]	Type	Width [min]	Area	Height	Area%
8.052	MM m	0.1281	822.2641	99.8313	49.7669
8.368	MM m	0.1369	829.9678	94.1140	50.2331
Sum			1652.2318		

(S)-4,4,5,5-Tetramethyl-2-(1-phenylethyl)-1,3,2-dioxaborolane ((S)-1)

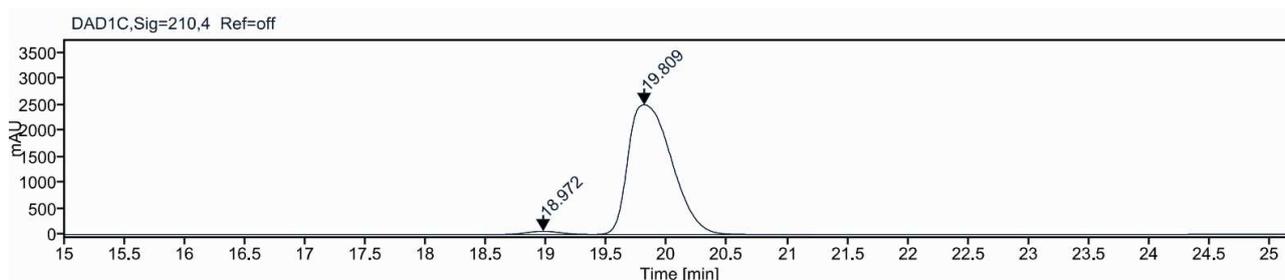
See above for data.

(S)-1

96% e.e. *e.r.* = 2:98, measured through chiral HPLC analysis of the corresponding alcohol obtained after oxidation. Chiralpak ID column (250 × 4.6 mm), IPA:hexane = 1:99, 0.7 mL/min, column temperature = 22 °C, (*R*)- isomer *t_r* = 19.0 min and (*S*)-isomer *t_r* = 19.8 min.

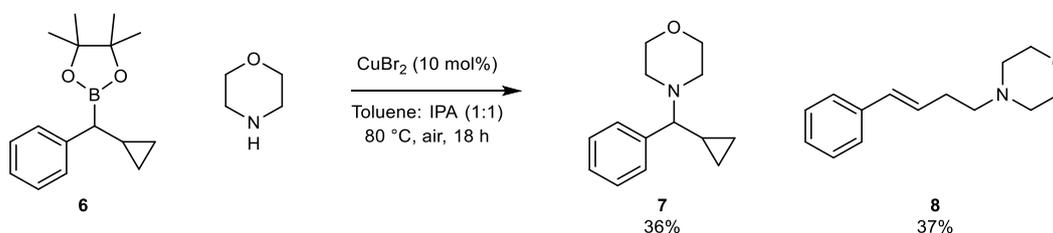


RT [min]	Type	Width [min]	Area	Height	Area%
19.175	MM m	0.3804	58438.0569	2449.1135	49.6661
20.141	MM m	0.3945	59223.8120	2378.5002	50.3339
Sum			117661.8689		

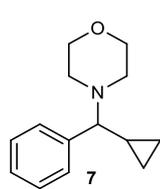


RT [min]	Type	Width [min]	Area	Height	Area%
18.972	MM m	0.3057	1260.7191	64.0195	1.9641
19.809	MB m	0.3995	62926.0405	2501.1997	98.0359
Sum			64186.7596		

(±)-N-[Cyclopropyl(phenyl)methyl]morpholine (6) and (±)-N-[(3E)-4-Phenylbut-3-en-1-yl]morpholine (8)



The title compounds were prepared according to **GP1** using boronic ester **6** (0.129 g, 0.501 mmol) and morpholine (0.154 mg, 1.78 mmol), heating for 18 h. Flash column chromatography (69% hexane/30% EtOAc/1% Et₃N) of the crude material gave *amine* **7** (39.6 mg, 36%, ~94% purity) as a colourless oil and *amine* **8** (40.3 mg, 37%) as a pale yellow oil.



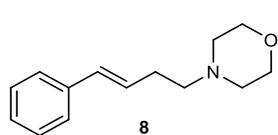
(±)-N-[Cyclopropyl(phenyl)methyl]morpholine (7)

IR 2959, 2804, 1451, 1278, 1117 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 7.35-7.28 (4H, m, ArH), 7.27-7.22 (1H, m, ArH), 3.77-3.63 (4H, m, $2 \times \text{OCH}_2$), 2.81-2.64 (2H, m, NCH_2), 2.41-2.30 (2H, m, NCH_2), 2.23 (1H, d, $J = 9.2$ Hz, NCH), 1.09-0.94 (1H, m, CHCH_2), 0.80-0.70 (1H, m, CHCH_AH_B), 0.47-0.39 (1H, m, CHCH_AH_B), 0.39-0.30 (1H, m, CHCH_CH_D), 0.06--0.03 (1H, m, CHCH_CH_D).

^{13}C NMR (101 MHz, CDCl_3) δ 143.3 (C), 128.2 ($2 \times \text{CH}$), 127.9 ($2 \times \text{CH}$), 126.9 (CH), 76.6 (CH), 67.2 ($2 \times \text{CH}_2$), 52.4 ($2 \times \text{CH}_2$), 15.5 (CH), 8.6 (CH_2), 2.00 (CH_2).

HRMS (Q-TOF) Exact mass calcd for $[\text{C}_{14}\text{H}_{20}\text{NO}]^+$ $[\text{M}+\text{H}]^+$: 218.1539 found: 218.1549.



N-[(3E)-4-Phenylbut-3-en-1-yl]morpholine (8)

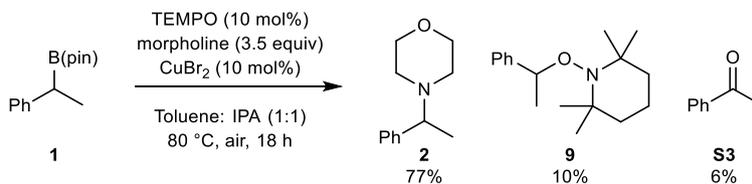
IR 2956, 2854, 2806, 1698, 1447, 1271, 1116 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 7.38-7.28 (4H, m, ArH), 7.24-7.18 (1H, m, ArH), 6.45 (1H, d, $J = 15.9$ Hz, CH), 6.22 (1H, dt, $J = 15.9, 6.1$ Hz, CHCH_2), 3.79-3.71 (4H, m, $2 \times \text{OCH}_2$), 2.59-2.48 (6H, m, $3 \times \text{NCH}_2$), 2.47-2.39 (2H, m, $\text{C}=\text{CCH}_2$).

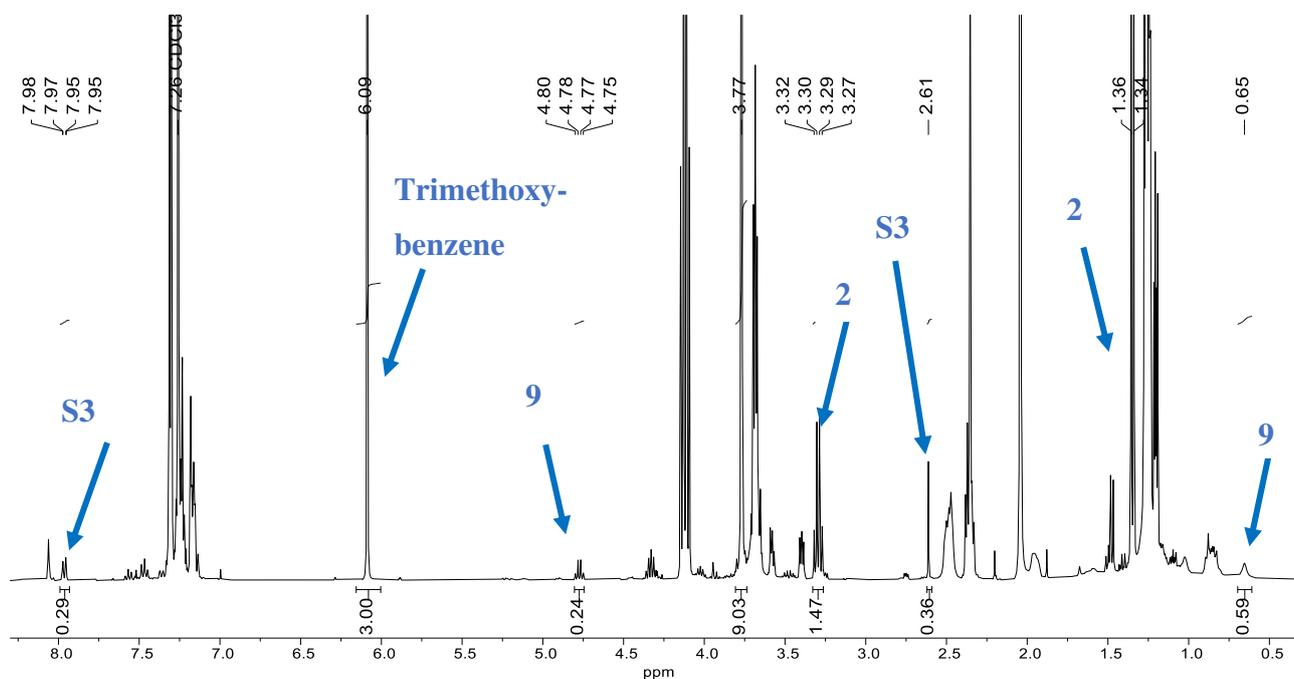
^{13}C NMR (101 MHz, CDCl_3) δ 137.5 (C), 131.1 (CH), 128.5 ($2 \times \text{CH}$), 128.0 (CH), 127.0 (CH), 126.0 ($2 \times \text{CH}$), 66.9 ($2 \times \text{CH}_2$), 58.6 (CH_2), 53.6 ($2 \times \text{CH}_2$), 30.3 (CH_2).

HRMS (Q-TOF) Exact mass calcd for $[\text{C}_{14}\text{H}_{20}\text{NO}]^+$ $[\text{M}+\text{H}]^+$: 218.1539 found: 218.1541.

Trapping Experiments with TEMPO



Using a modification of **GPI** using boronic ester **1** (0.116 g, 0.500 mmol) and morpholine (0.15 mL) and TEMPO (7.8 mg, 0.050 mmol), the mixture was heated at 80 °C for 18 h, cooled to RT and filtered through Celite eluting with EtOAc. The filtrate was concentrated and analysed by ^1H NMR using 1,3,5-trimethoxybenzene (0.0441 g, 0.26 mmol) as an internal standard.



Characteristic peaks for (\pm)-*N*-(1-Phenylethyl)morpholine (**2**):

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 3.29 (q, $J = 6.7$ Hz, 1H), 1.35 (d, $J = 6.7$ Hz, 3H). See earlier for full characterisation data.

Characteristic peaks for 2,2,6,6-tetramethyl-1-(1-phenylethoxy)piperidine (**9**):

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 4.78 (q, $J = 6.7$ Hz, 1H), 0.66 (s, 3H).

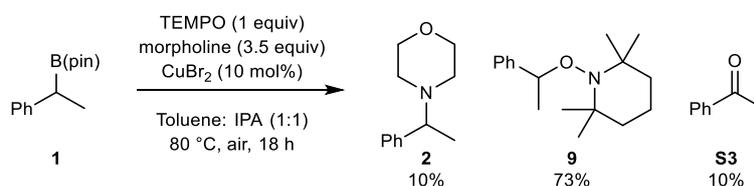
HRMS (Q-TOF) Exact mass calcd for $[\text{C}_{17}\text{H}_{28}\text{NO}]^+$ $[\text{M}+\text{H}]^+$: 262.2171 found: 262.2167.

The data was consistent with the literature.³⁷

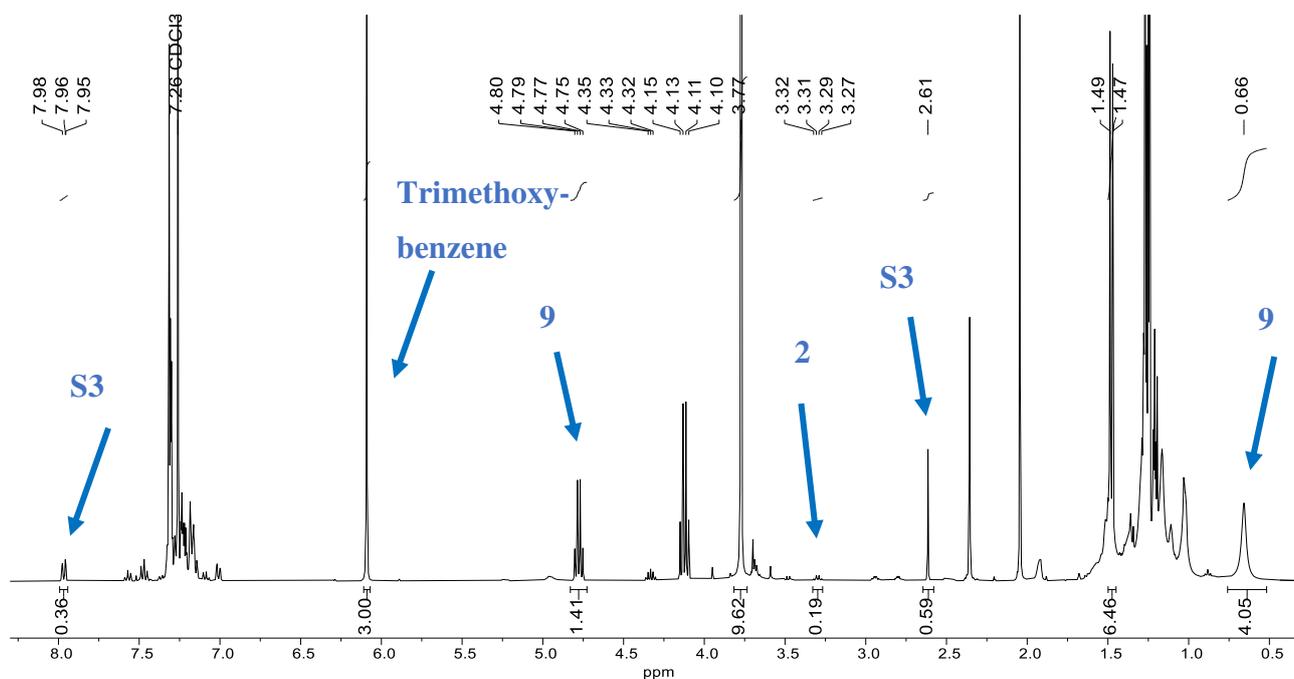
Characteristic peaks for acetophenone (**S3**):

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.99–7.94 (m, 2H), 2.61 (s, 3H).

The data was consistent with the literature.¹



Using a modification of **GPI** using boronic ester **1** (0.116 g, 0.500 mmol) and morpholine (0.15 mL) and TEMPO (7.8 mg, 0.050 mmol), the mixture was heated at 80 °C for 18 h, cooled to RT and filtered through Celite eluting with EtOAc. The filtrate was concentrated and analysed by $^1\text{H NMR}$ using 1,3,5-trimethoxybenzene (0.0441 g, 0.26 mmol) as an internal standard.



Characteristic peaks for (\pm)-*N*-(1-Phenylethyl)morpholine (**2**):

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 3.30 (q, $J = 6.7$ Hz, 1H). See earlier for full characterisation data.

Characteristic peaks for 2,2,6,6-tetramethyl-1-(1-phenylethoxy)piperidine (**9**):

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 4.78 (q, $J = 6.7$ Hz, 1H), 0.66 (s, 3H).

HRMS (Q-TOF) Exact mass calcd for $[\text{C}_{17}\text{H}_{28}\text{NO}]^+$ $[\text{M}+\text{H}]^+$: 262.2171 found: 262.2170.

The data was consistent with the literature.³⁷

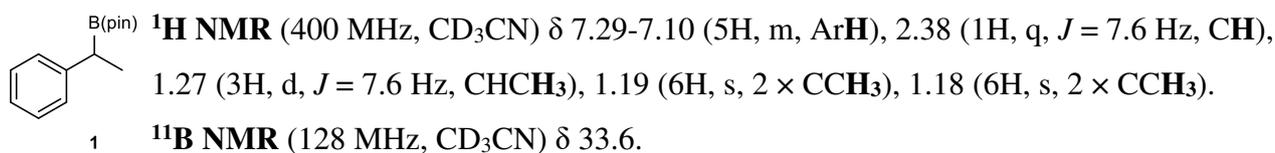
Characteristic peaks for acetophenone (**S3**):

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.99–7.94 (m, 2H), 2.61 (s, 3H).

The data was consistent with the literature.¹

NMR studies: Boronic ester **1** in the presence of morpholine

An NMR tube was charged with **1** (34.8 g, 0.150 mmol) dissolved in CD_3CN (0.7 mL) and $^1\text{H NMR}$ and $^{11}\text{B NMR}$ spectra were recorded. Morpholine (53 μL , 0.60 mmol) was added by microsyringe and $^1\text{H NMR}$ and $^{11}\text{B NMR}$ spectra were recorded after homogenization.



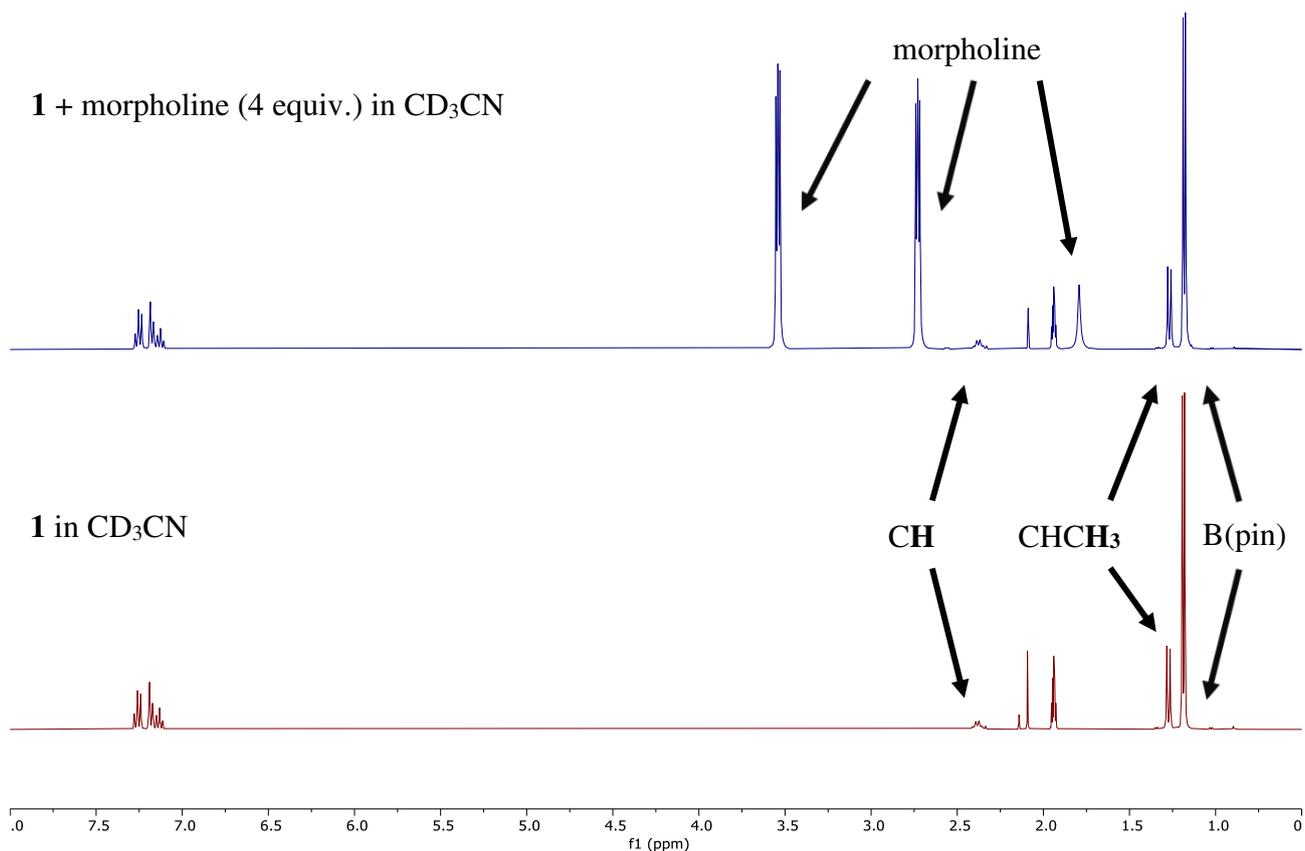


Figure S1: ^1H NMR spectra of boronic ester **1** in CD_3CN the absence and presence of morpholine.

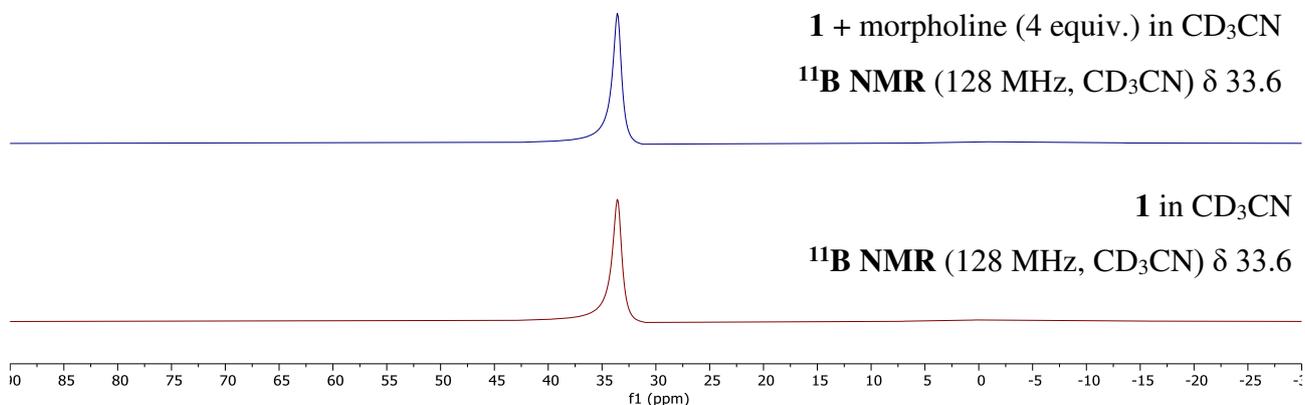


Figure S2: ^{11}B NMR spectra of boronic ester **1** in CD_3CN in the absence and presence of morpholine.

NMR studies: Boronic ester **1** in the presence of IPA and morpholine

An NMR tube was charged with a solution of boronic ester **1** (0.023 g, 0.10 mmol) in 0.5 mL CD_3CN and an ^{11}B NMR spectrum was recorded. Isopropanol (0.5 mL) was added, and an ^{11}B NMR spectrum was recorded after homogenization. Morpholine (44 μL , 0.50 mmol,) was added, and an ^{11}B NMR spectrum was recorded after homogenization.

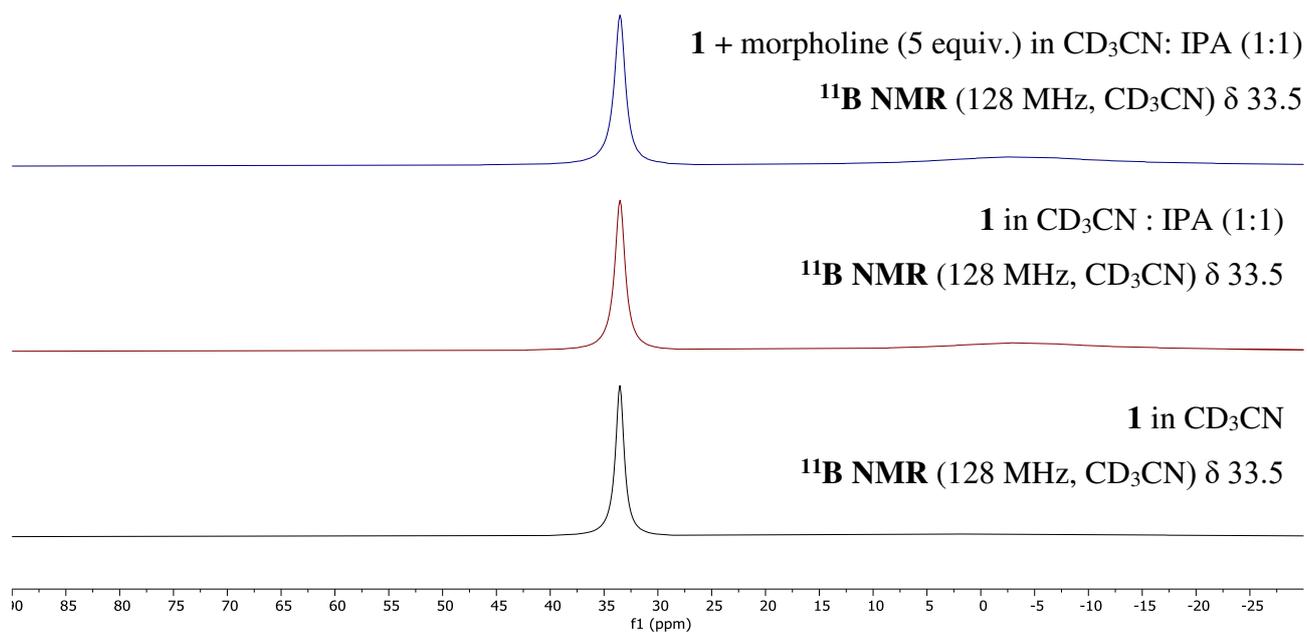


Figure S3: ¹¹B NMR spectra of **1** in in CD₃CN in the absence and presence of IPA, and IPA and morpholine.

Cyclic Voltammetry Studies

All cyclic voltammetric measurements were performed at room temperature, using an Autolab® PGSTAT100 potentiostat in a conventional three-electrode cell configuration with a glassy carbon (GC) as working electrode (3 mm diameter), a platinum electrode (2 mm diameter) as counter electrode and Ag/AgCl (KCl 3M) as reference. The cell was purged with N₂ for 10 min before each measurement, and the GC working electrode was polished with alumina before each experiment. Redox potentials were calculated against the Fc⁺/Fc⁰ couple as an internal reference. (Ferrocene was added in the last experiment of a series, or separately just after an experiment. It was considered that in this period of time, the reference electrode's composition would not change and would be kept constant.) All the experiments were carried out at 100 mV/s.

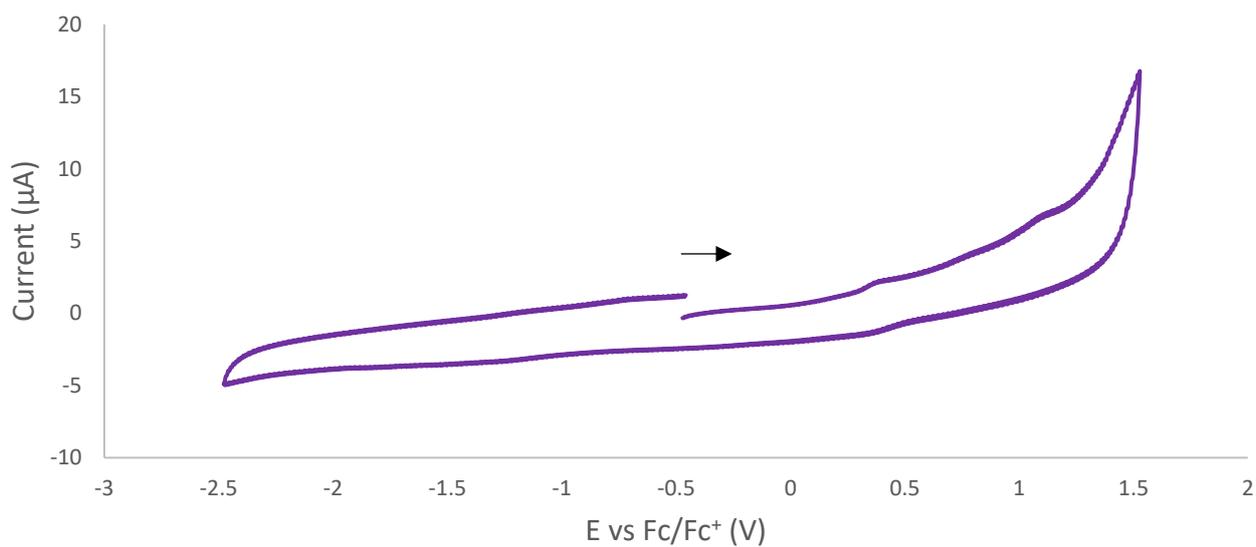


Figure S4. CV trace for MeCN ($n\text{Bu}_4\text{NPF}_6$ 0.1 M), 100 mV/s.

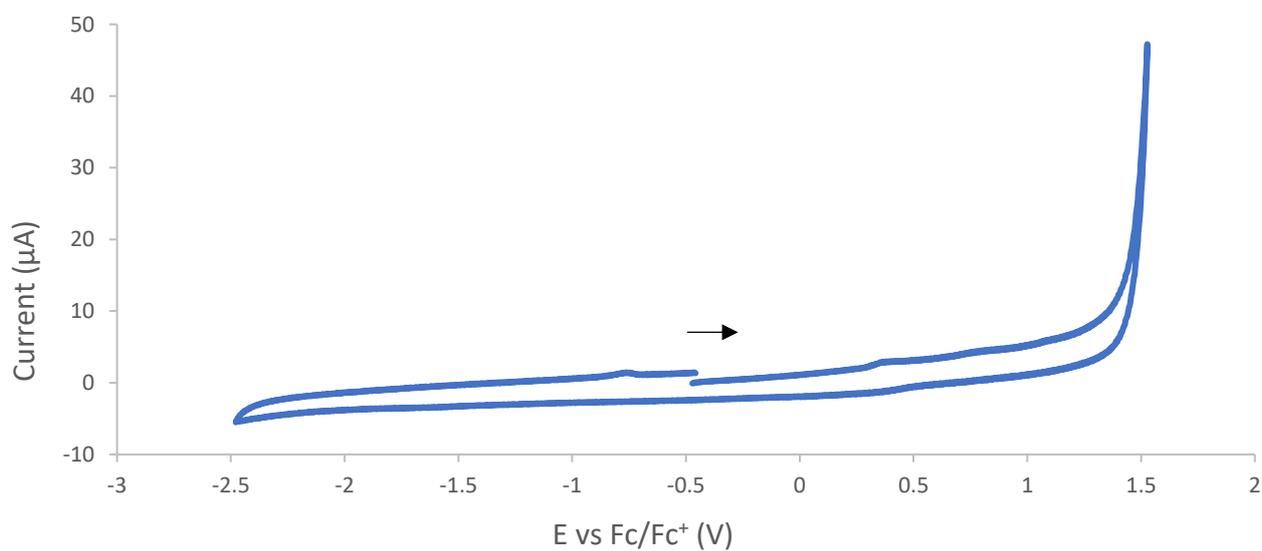


Figure S5. CV trace for boronic ester **1** (3 mM) in MeCN ($n\text{Bu}_4\text{NPF}_6$ 0.1 M), 100 mV/s.

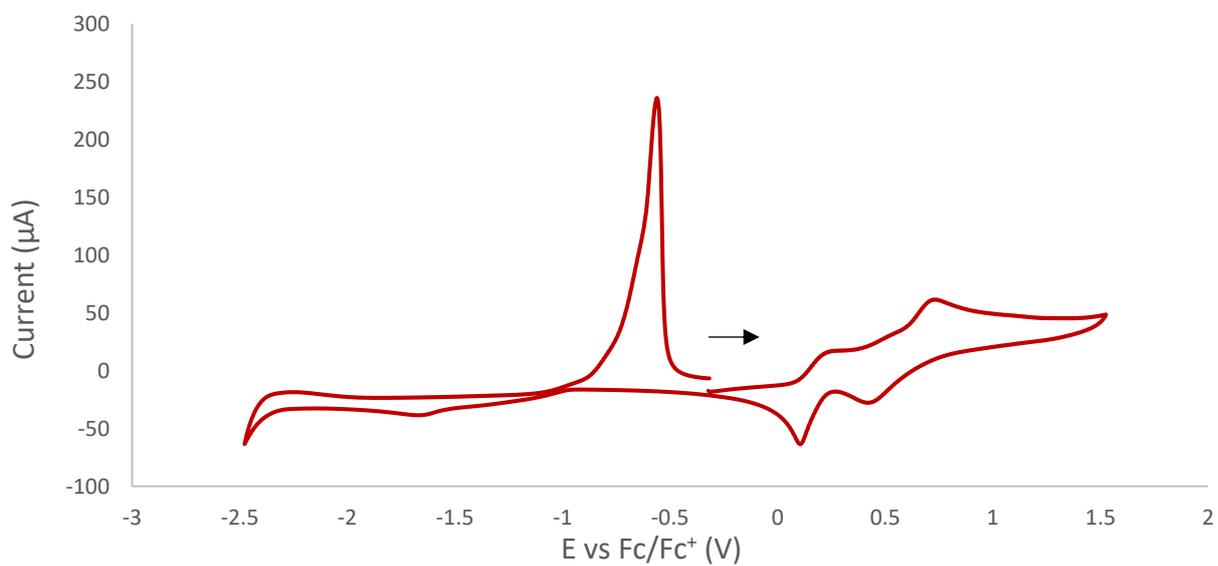


Figure S6. CV trace for CuBr₂ (3 mM) in MeCN (*n*Bu₄NPF₆ 0.1 M), 100 mV/s.

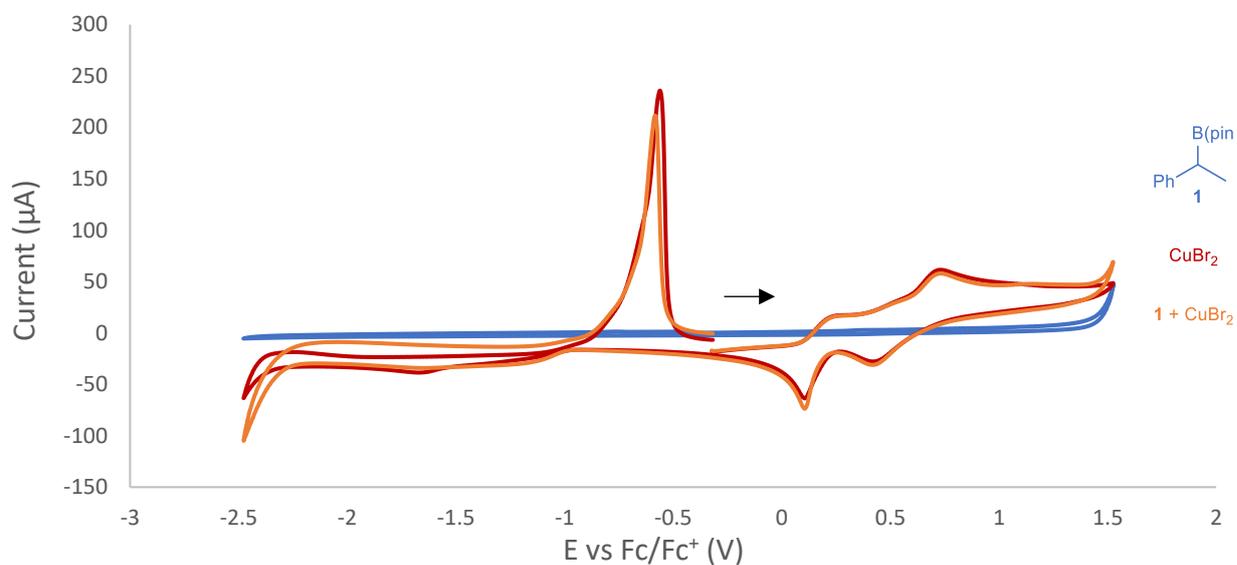


Figure S7. Individual traces of boronic ester **1** (3 mM), CuBr₂ (3 mM) and a mixture 1:1 of both (3 mM each) in MeCN (*n*Bu₄NPF₆ 0.1 M), 100 mV/s.

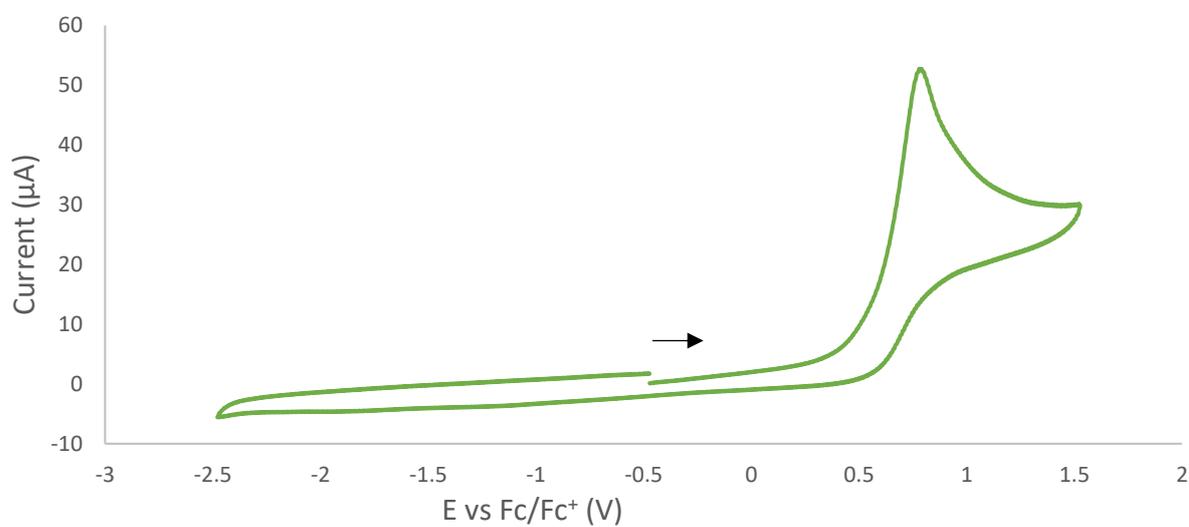


Figure S8. CV trace for morpholine (3 mM) in MeCN (*n*Bu₄NPF₆ 0.1 M), 100 mV/s.

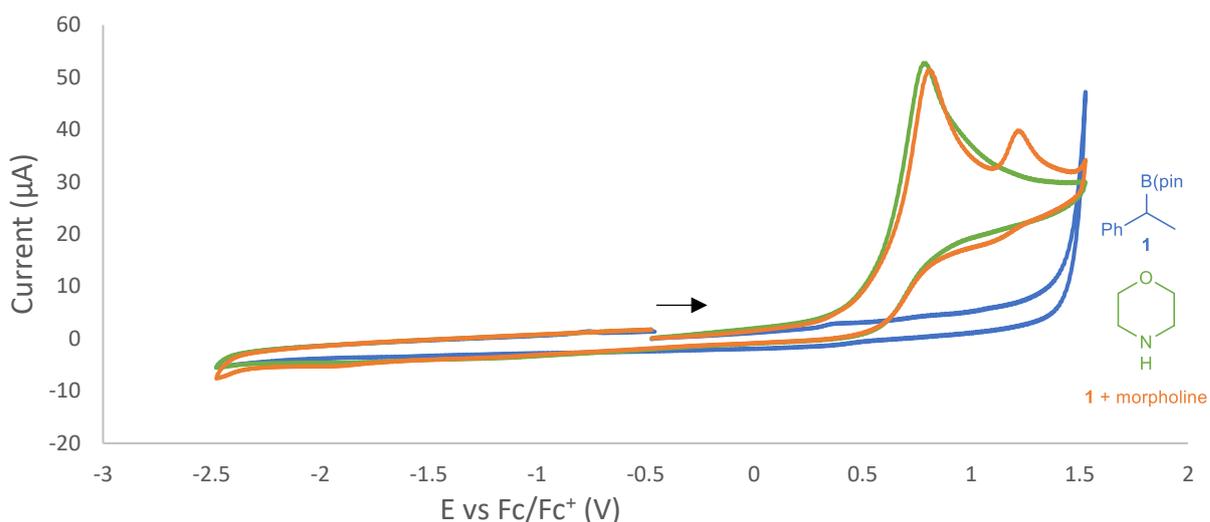


Figure S9. Individual traces of boronic ester **1** (3 mM), morpholine (3 mM) and a mixture 1:1 (3 mM each) in MeCN (nBu_4NPF_6 0.1 M), 100 mV/s.

3.12. EPR Experiments

EPR Methods:

All EPR samples were prepared aerobically in 1:1 toluene/isopropyl alcohol solvent mixture. For the spin-trapping EPR experiments, the concentrations of the individual reactants in the reaction mixture were: boronic ester **1** (300 mM), $CuBr_2$ (30 mM), morpholine (1050 mM) and 5,5-dimethyl-1-pyrroline N-oxide (DMPO; 400 mM). Samples were loaded into a 1.3 mm outer diameter/1 mm inner diameter glass capillary EPR tubes (sample \sim 40 mm in height) and inserted into a 4 mm outer diameter/3 mm inner diameter quartz tube (Wilmad LabGlass). The position of the sample inside the active-resonator was optimised by measuring a TEMPO standard. Spectra were measured on a Bruker EMXmicro EPR spectrometer equipped with a Bruker ER 4112SHQ X-band resonator, with a ER4131VT variable temperature unit. The optimum spectrometer conditions were: microwave power 23 dB (1 mW), modulation amplitude 0.5 G, time constant 82 ms, conversion time 1 ms, sweep time 30 s, receiver gain 30 dB. The average microwave frequency was 9.462 GHz. All EPR spectra were measured as a fluid solution at 80 °C. Analysis of the spectra and simulations were performed using the EasySpin toolbox (5.2.35) for the Matlab program package.³⁸ The extracted spin-Hamiltonian parameters are consistent with previously reported values for DMPO-amine and DMPO-R adducts.³⁹

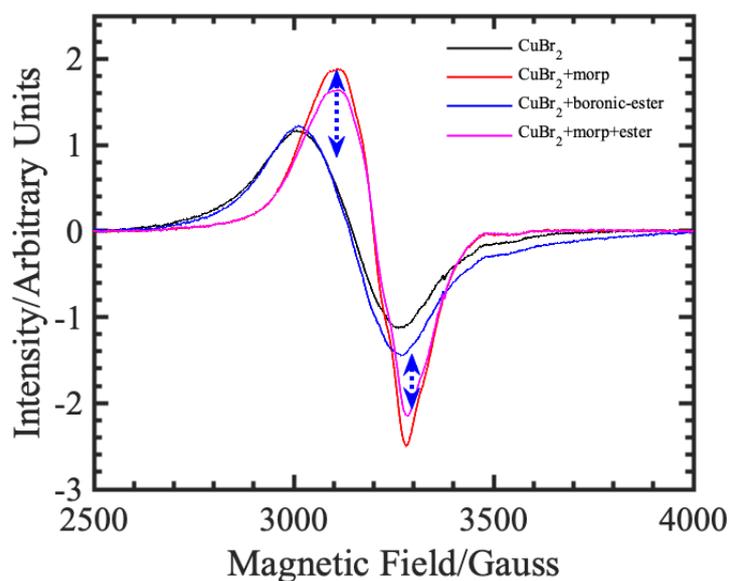


Figure S10: cw-EPR spectra of CuBr₂ in the absence (black trace) and presence of boronic ester **1** (blue trace) or morpholine (red trace), or both (magenta trace) measured at 80° C. The shift in the spectra in the presence of morpholine shows that the latter is interacting with the Cu(II). Experimental conditions as described in the EPR methods section.

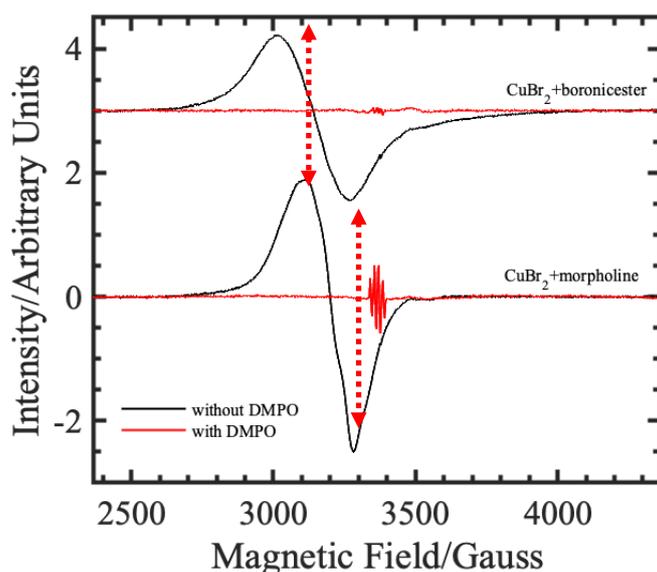


Figure S11: cw-EPR spectra of CuBr₂ with morpholine, and of CuBr₂ with boronic-ester, in the absence (black traces) and presence (red traces) of DMPO, measured at 80° C. The disappearance of the Cu(II) signals could imply that Cu(II) gets reduced to EPR-silent Cu(I). However, it was noted that Cu(II) signal was regenerated slowly during the catalysis reaction. Experimental conditions as described in the EPR methods section.

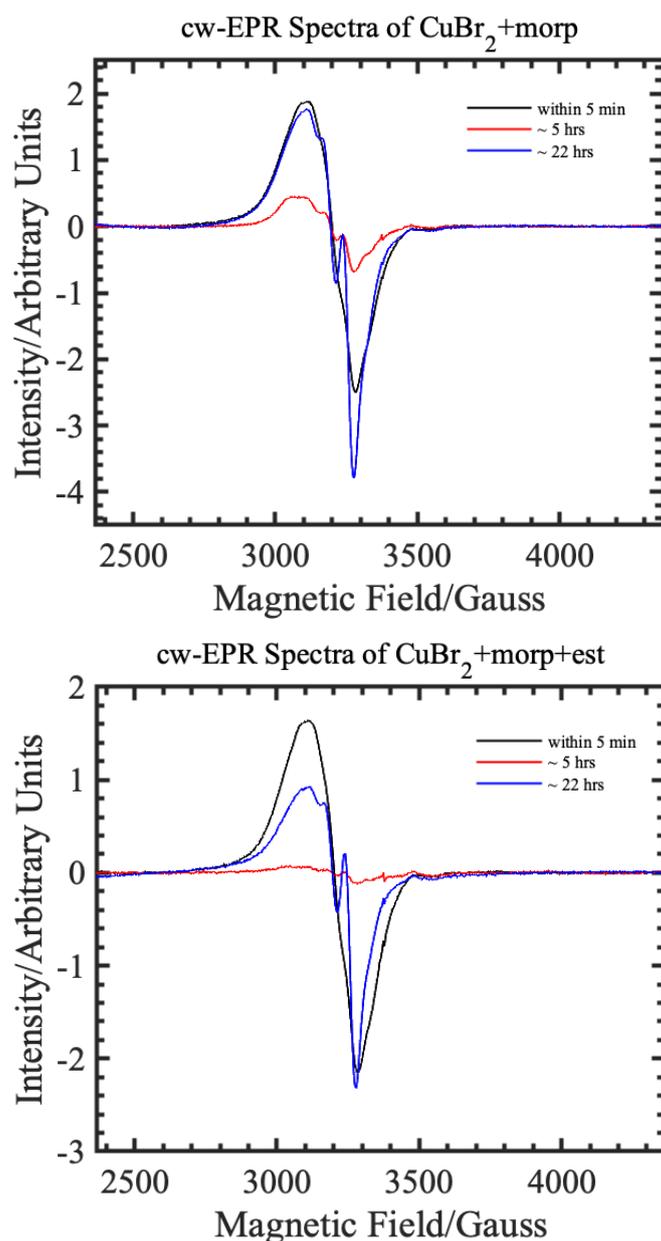


Figure S12: cw-EPR spectra of CuBr_2 with morpholine (top panel), and of CuBr_2 with morpholine and boronic-ester (bottom panel), in the absence of DMPO, measured at 80°C . The disappearance of the Cu(II) signals could imply that Cu(II) gets reduced to EPR-silent Cu(I) (red traces). However, these signals were regenerated slowly during the catalysis reaction (blue traces). Experimental conditions as described in the EPR methods section.

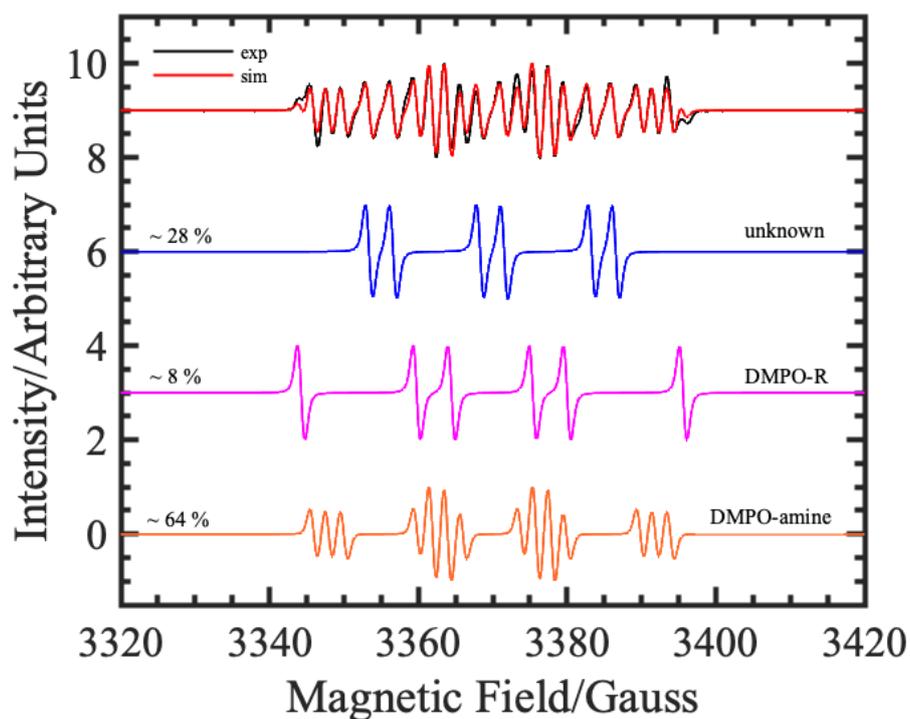
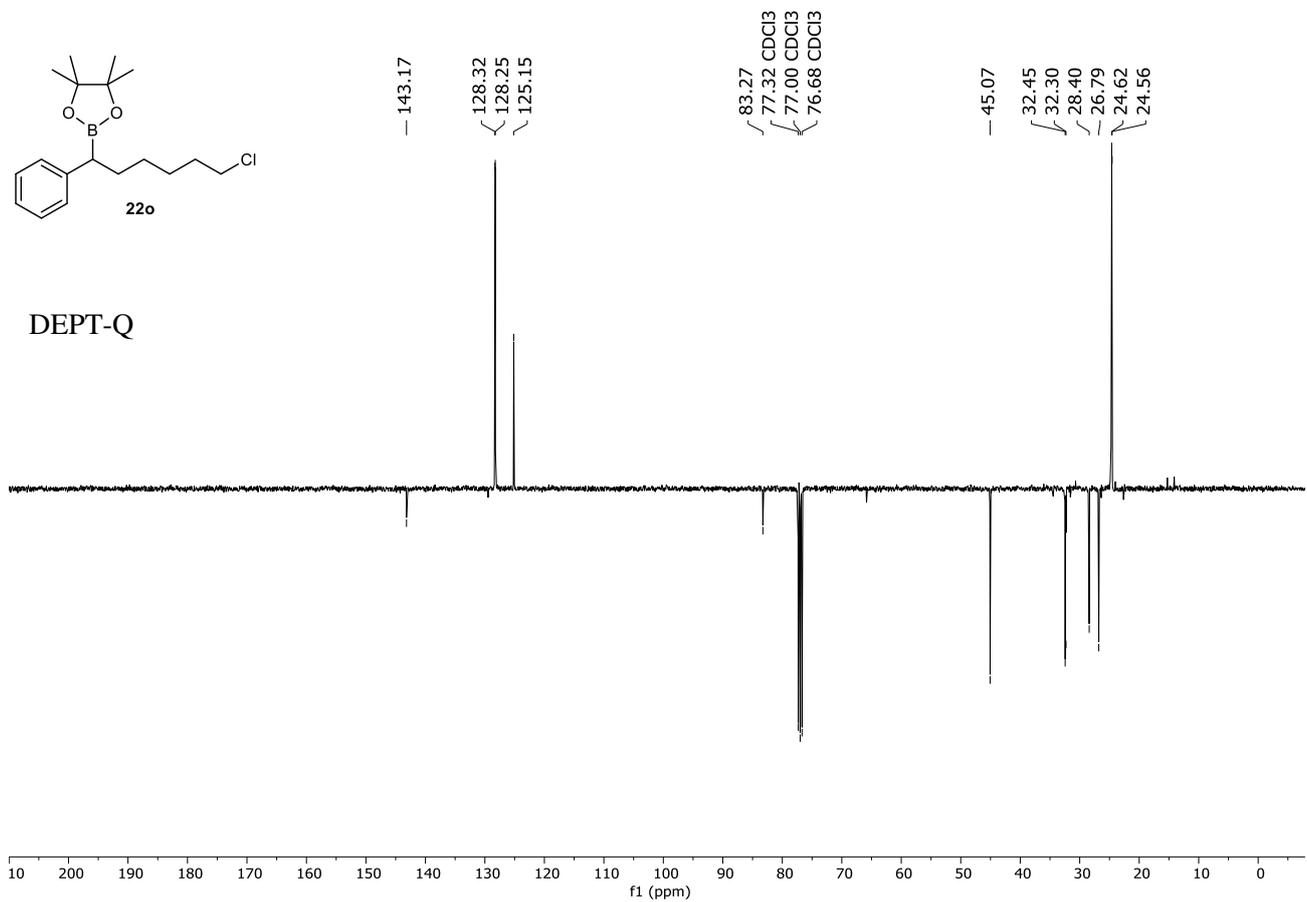
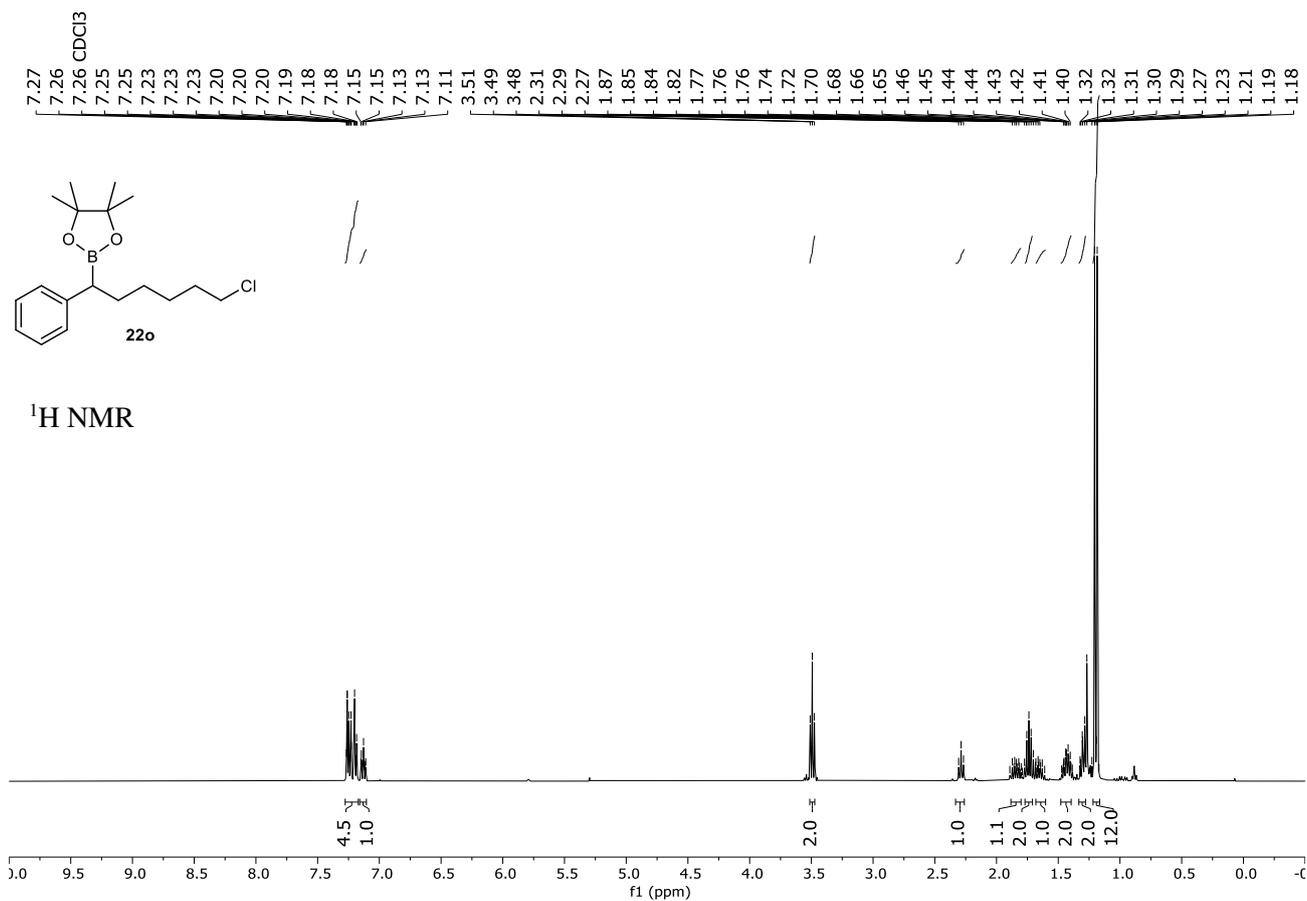
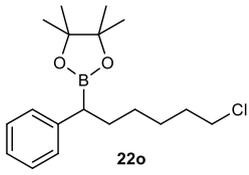


Figure S13: Experimental (black) and simulated (red) cw-EPR spectra of the CuBr_2 , morpholine and boronic ester mixture with DMPO, measured at 80°C . It was necessary to include three DMPO-adducts to reproduce the experimental spectra (see main text for more details). The spin-Hamiltonian parameters used were (relative weights are given in the figure): *DMPO-amine* - $g_{\text{iso}} = 2.0059$, $a_{\text{iso}}(^{14}\text{N}) = 39.1 \text{ MHz}$, $a_{\text{iso}}(^1\text{H}) = 45.0 \text{ MHz}$ and $a_{\text{iso}}(^{14}\text{N}) = 5.7 \text{ MHz}$; *DMPO-R* - $g_{\text{iso}} = 2.0058$, $a_{\text{iso}}(^{14}\text{N}) = 43.7 \text{ MHz}$ and $a_{\text{iso}}(^1\text{H}) = 56.7 \text{ MHz}$; *DMPO-unknown* - $g_{\text{iso}} = 2.0059$, $a_{\text{iso}}(^{14}\text{N}) = 41.8 \text{ MHz}$ and $a_{\text{iso}}(^1\text{H}) = 9.1 \text{ MHz}$. Experimental conditions as described in the EPR methods section.

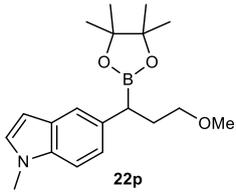
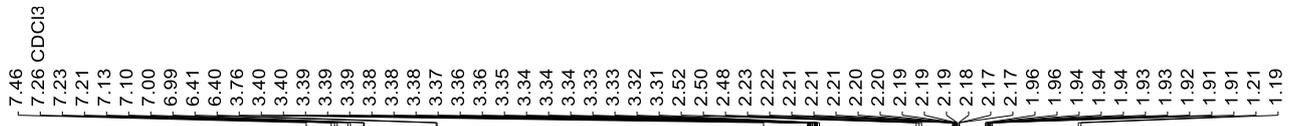
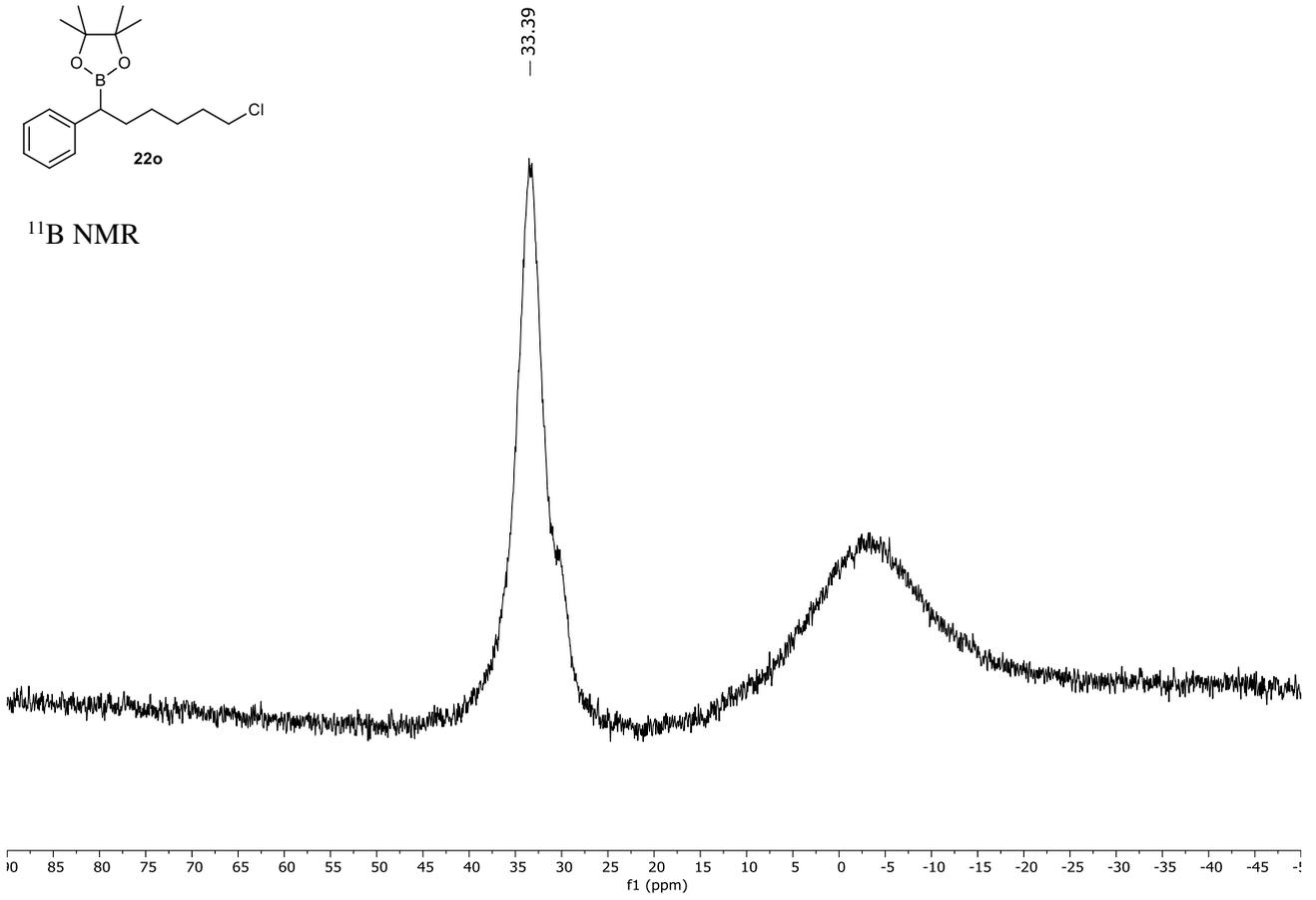
4. NMR Spectra

4.1. Boronic Esters

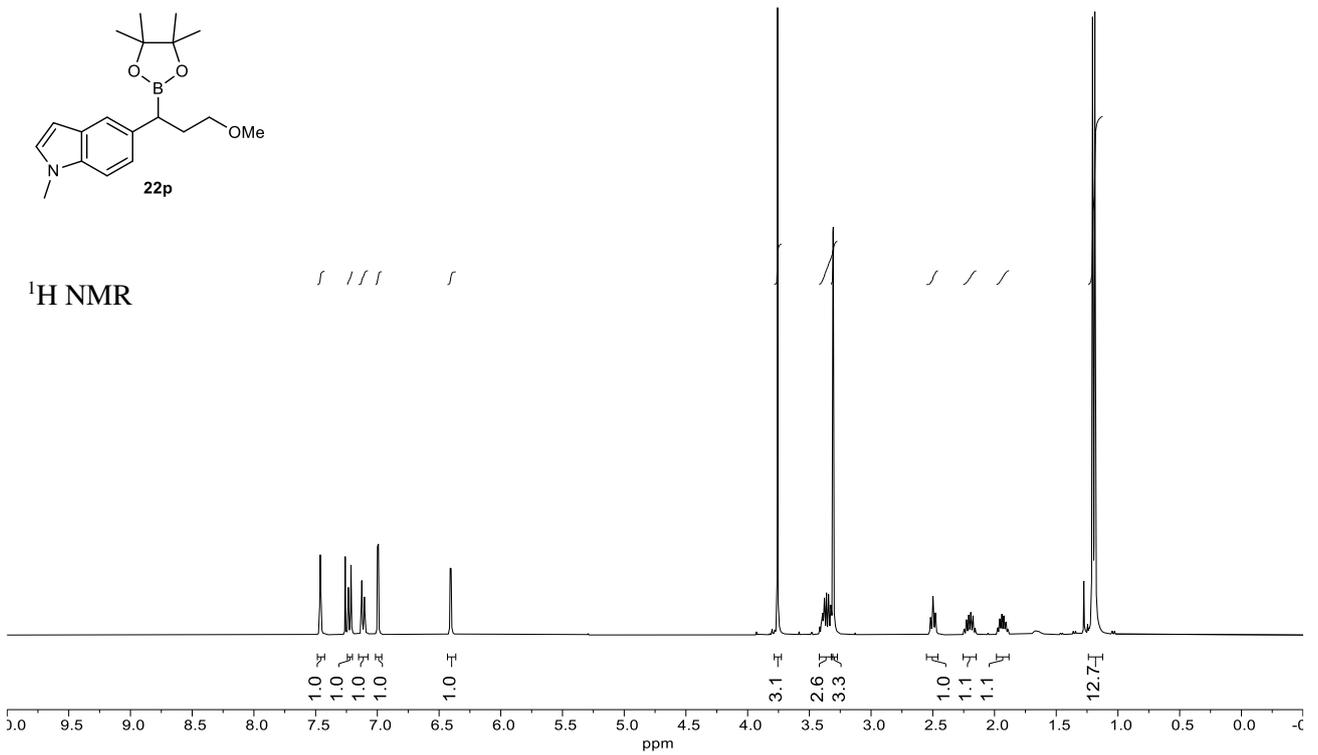


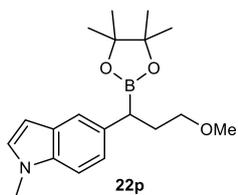


¹¹B NMR



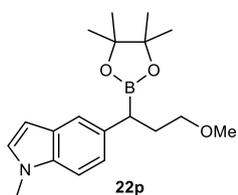
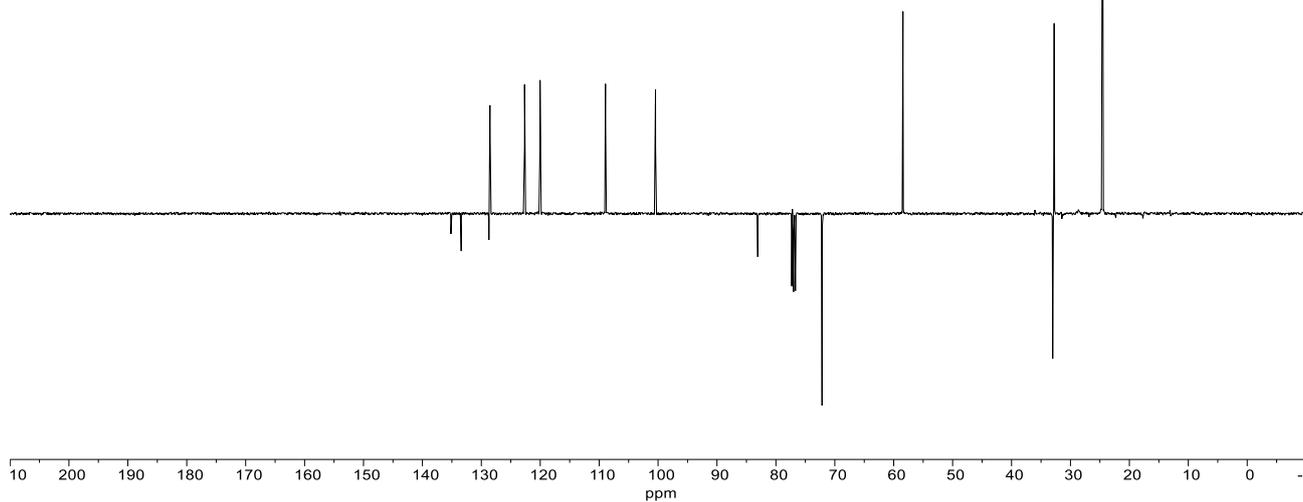
¹H NMR





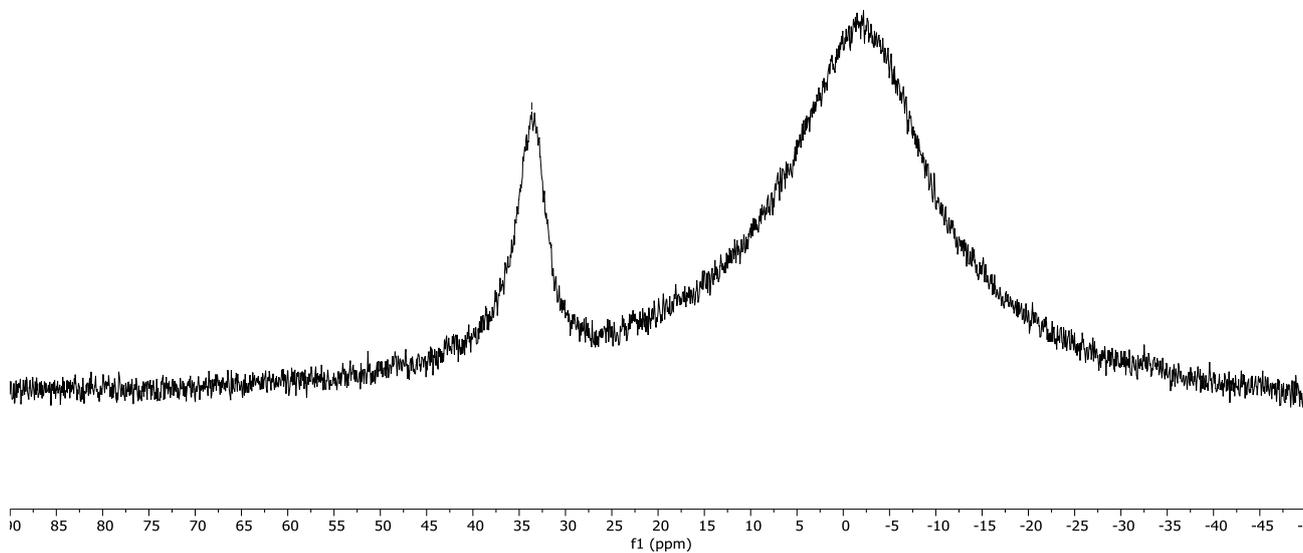
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 133.42
 128.71
 128.53
 122.66
 120.03
 - 108.92
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 - 58.44
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 24.56

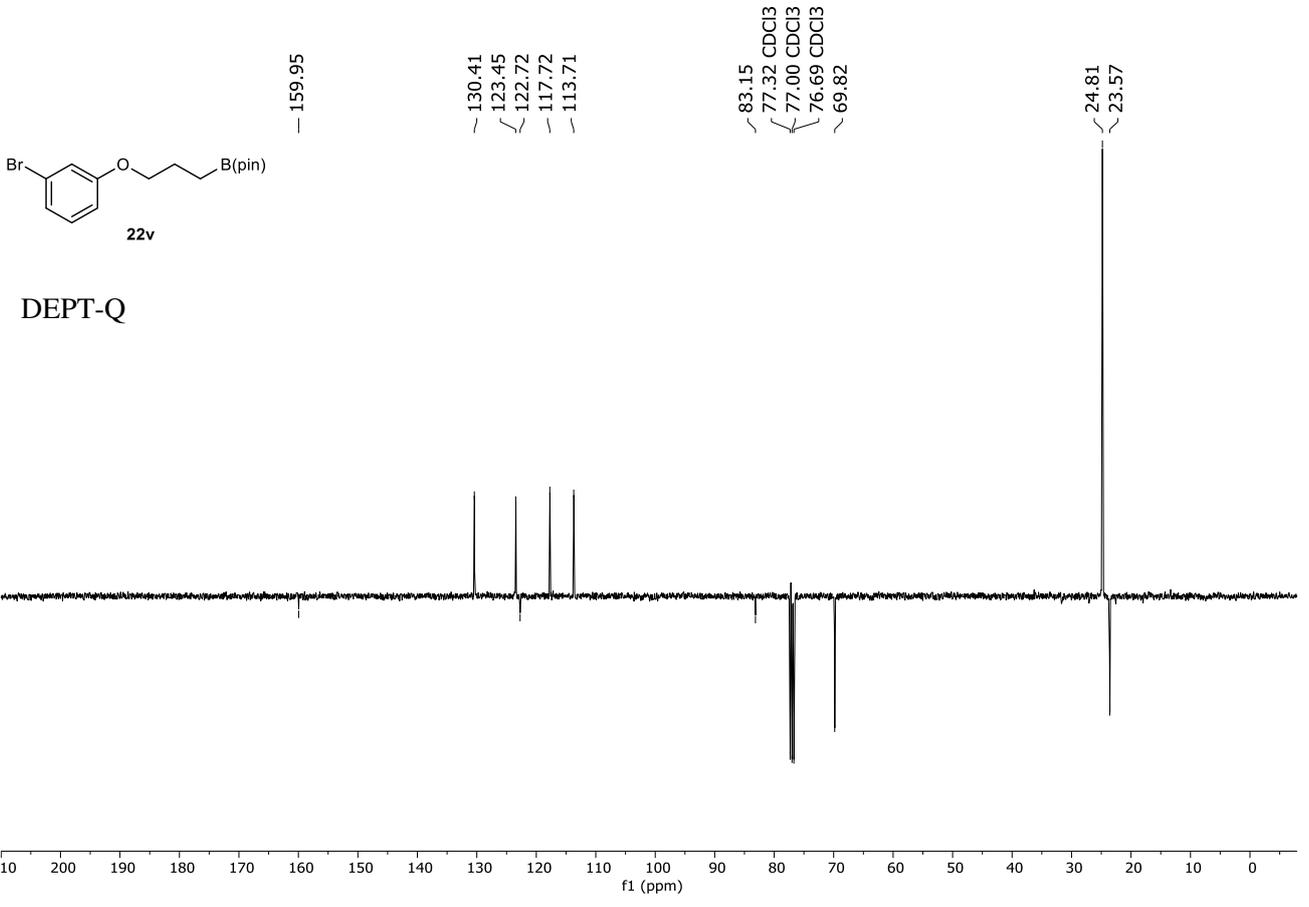
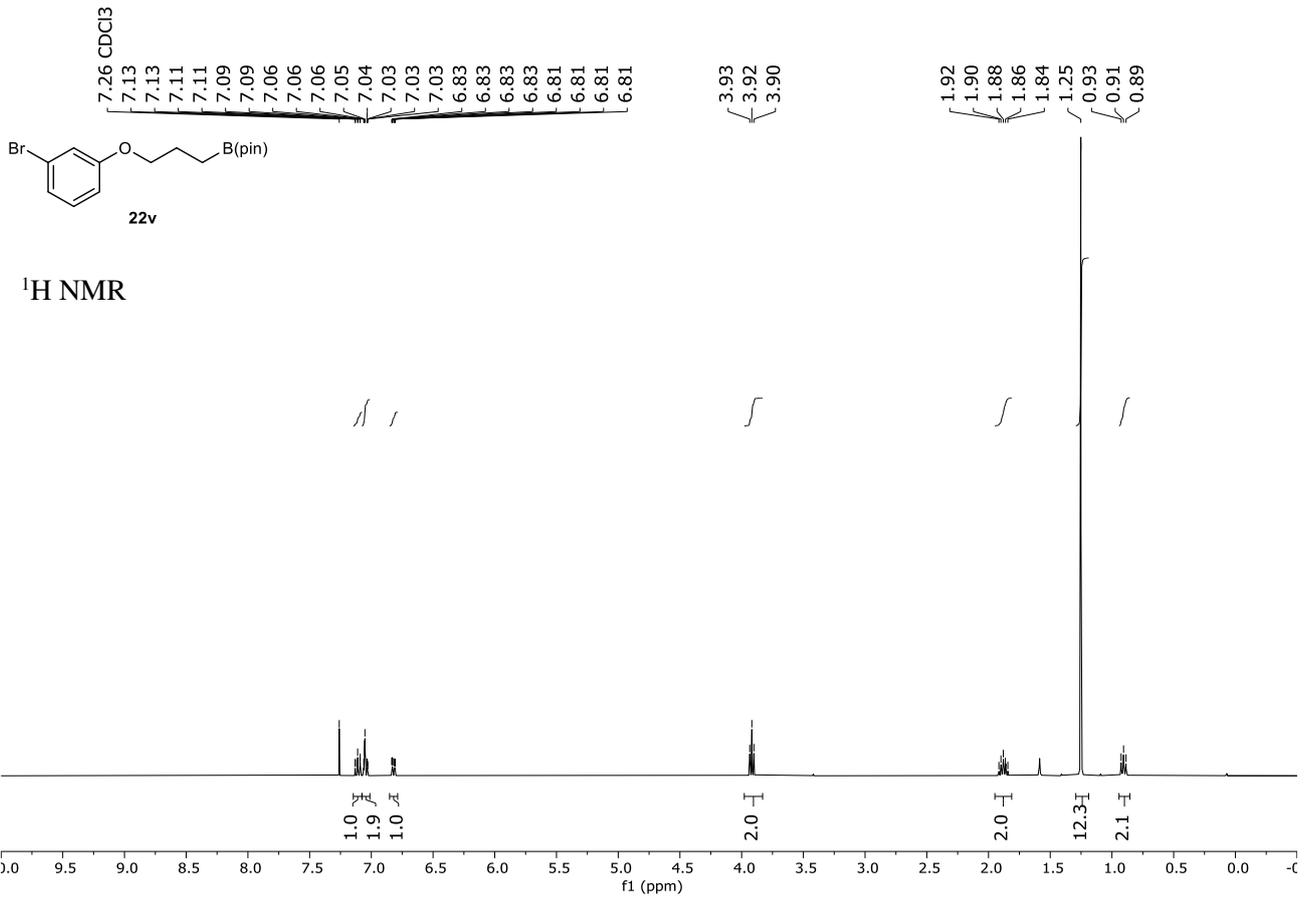
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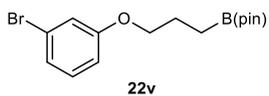


- 33.65

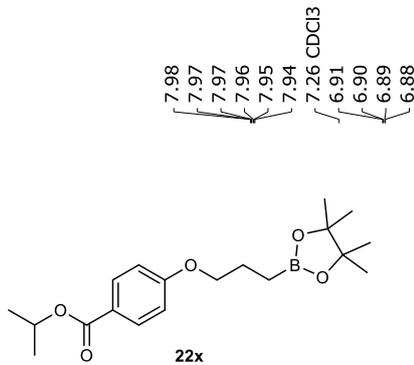
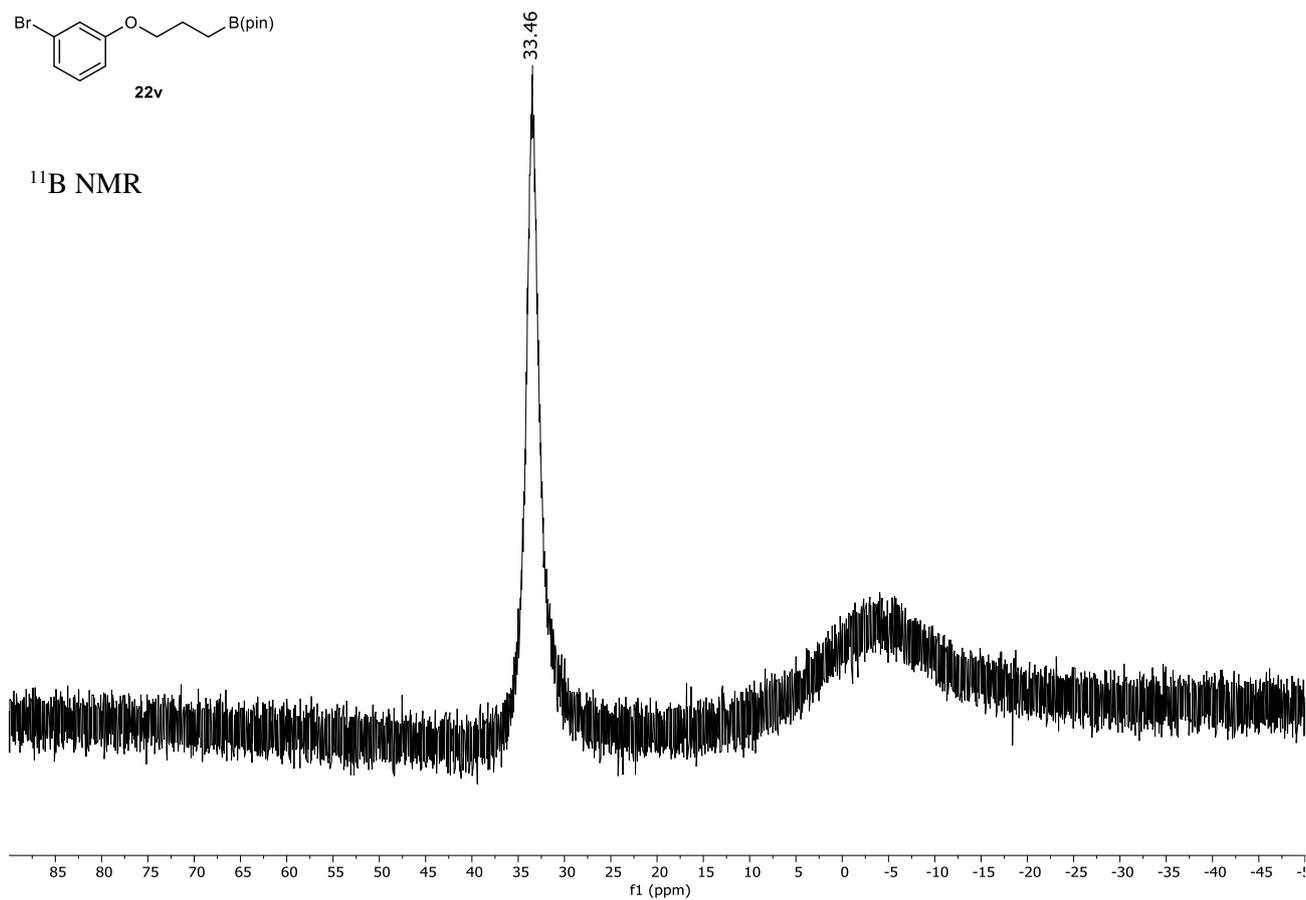
¹¹B NMR



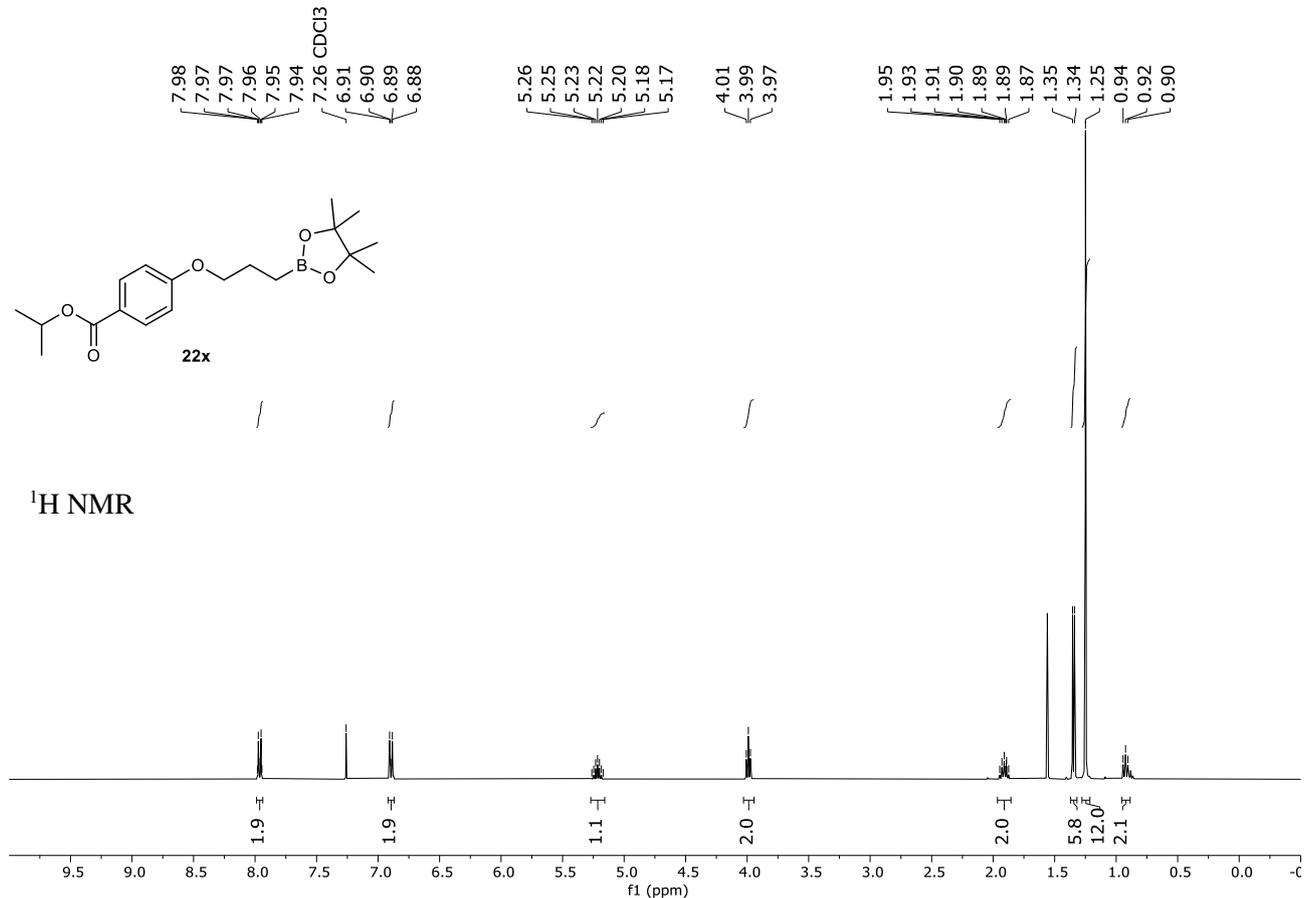


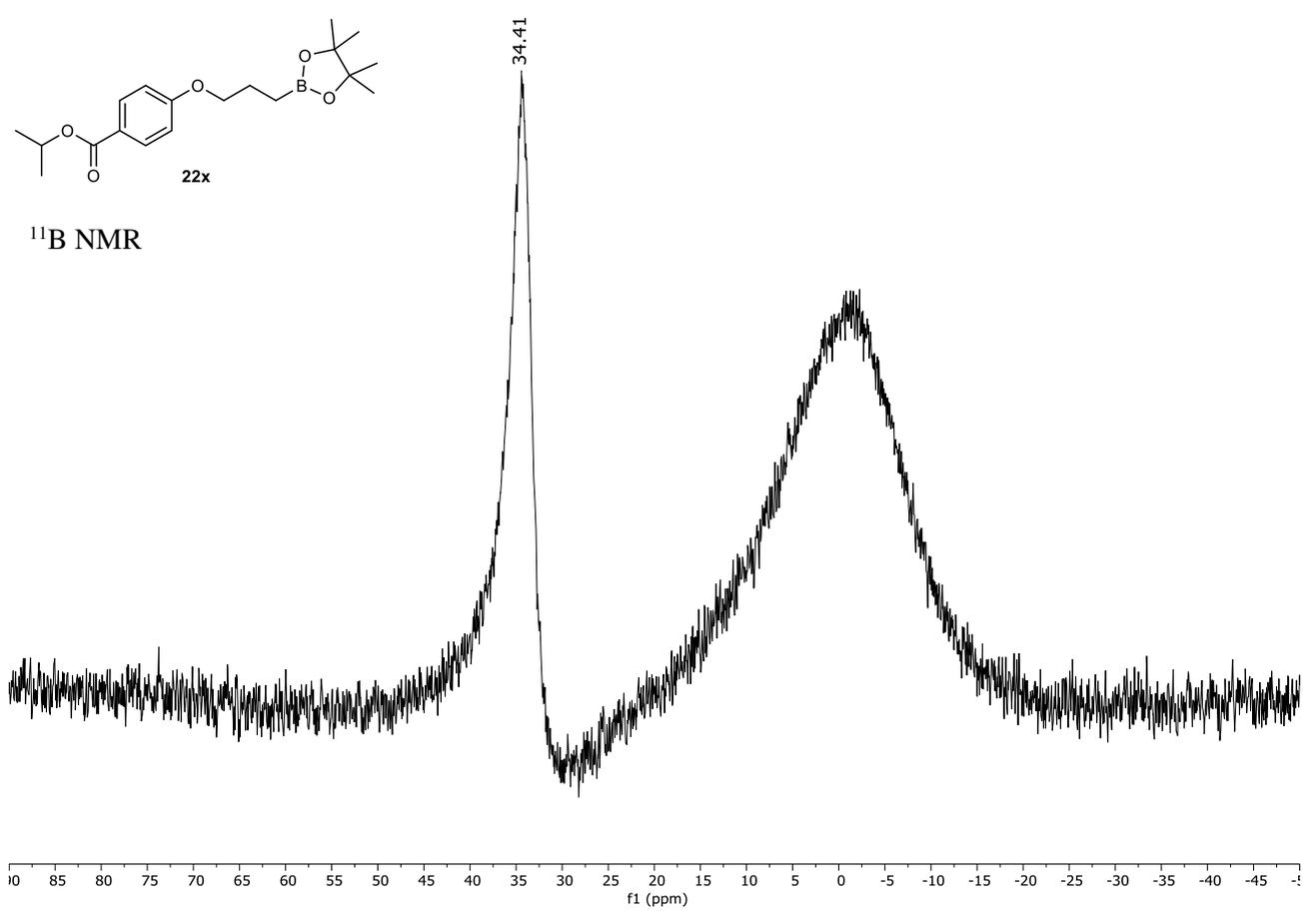
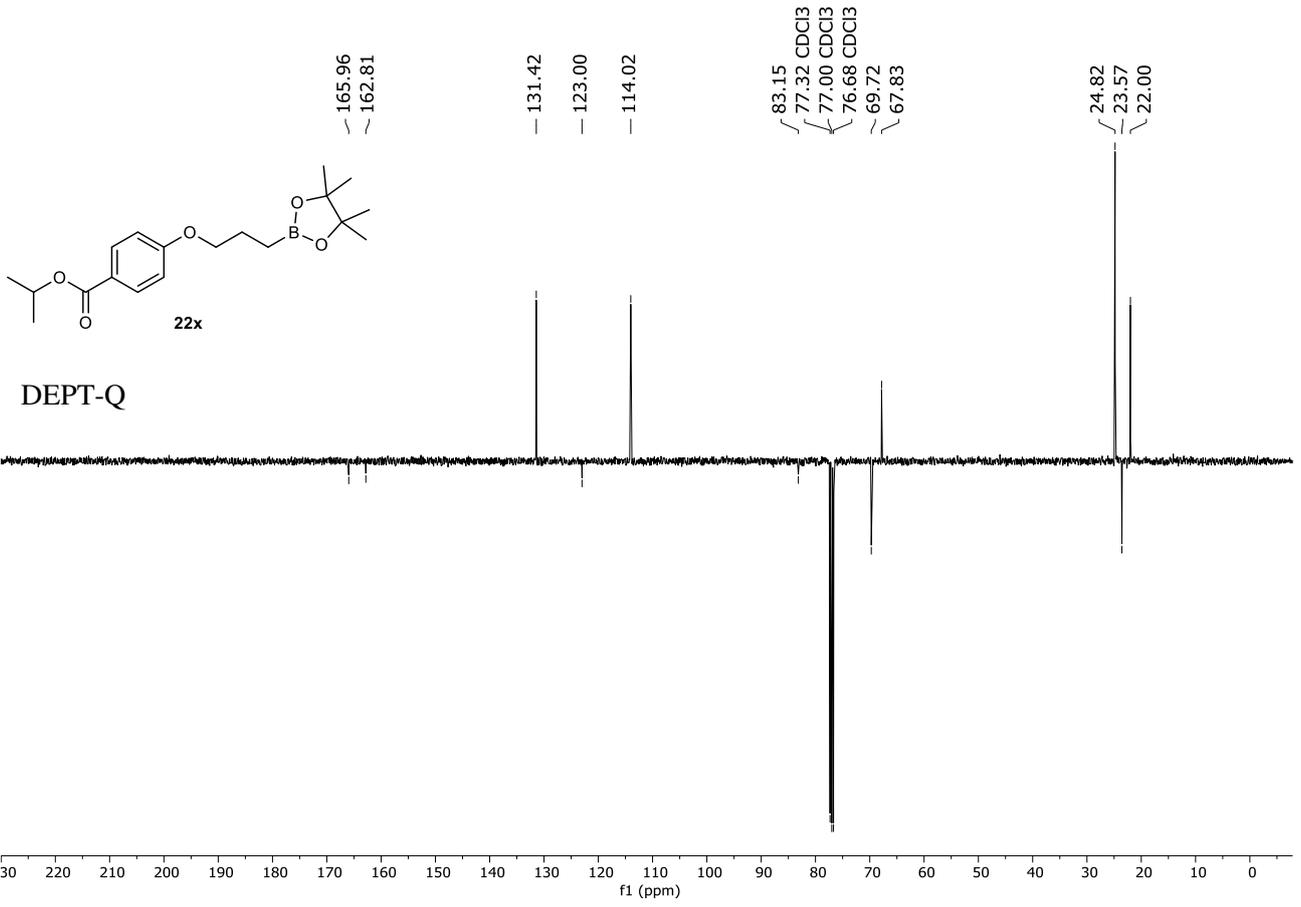


^{11}B NMR

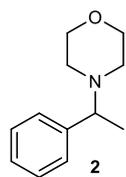


^1H NMR

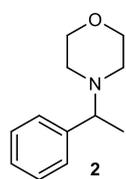
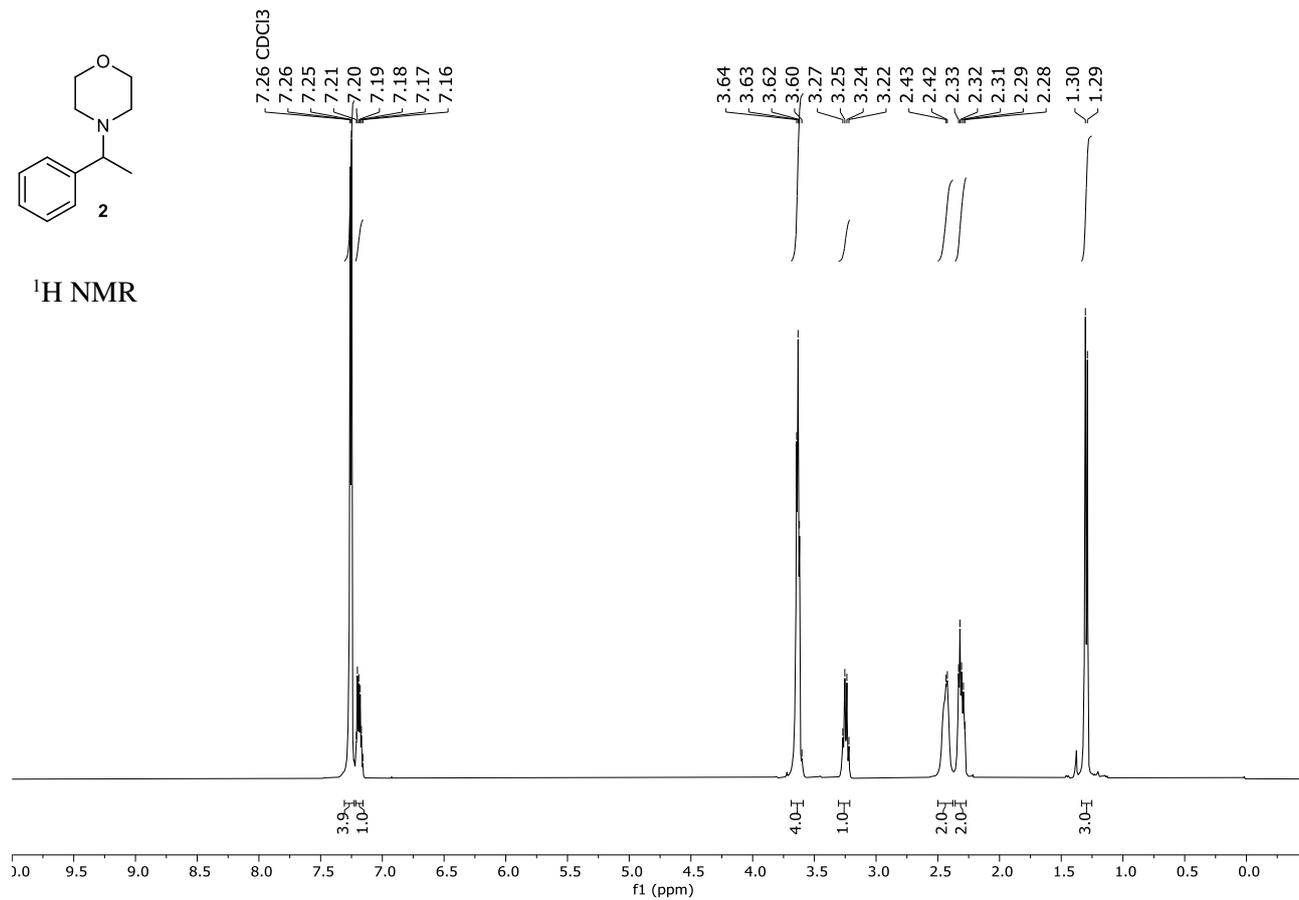




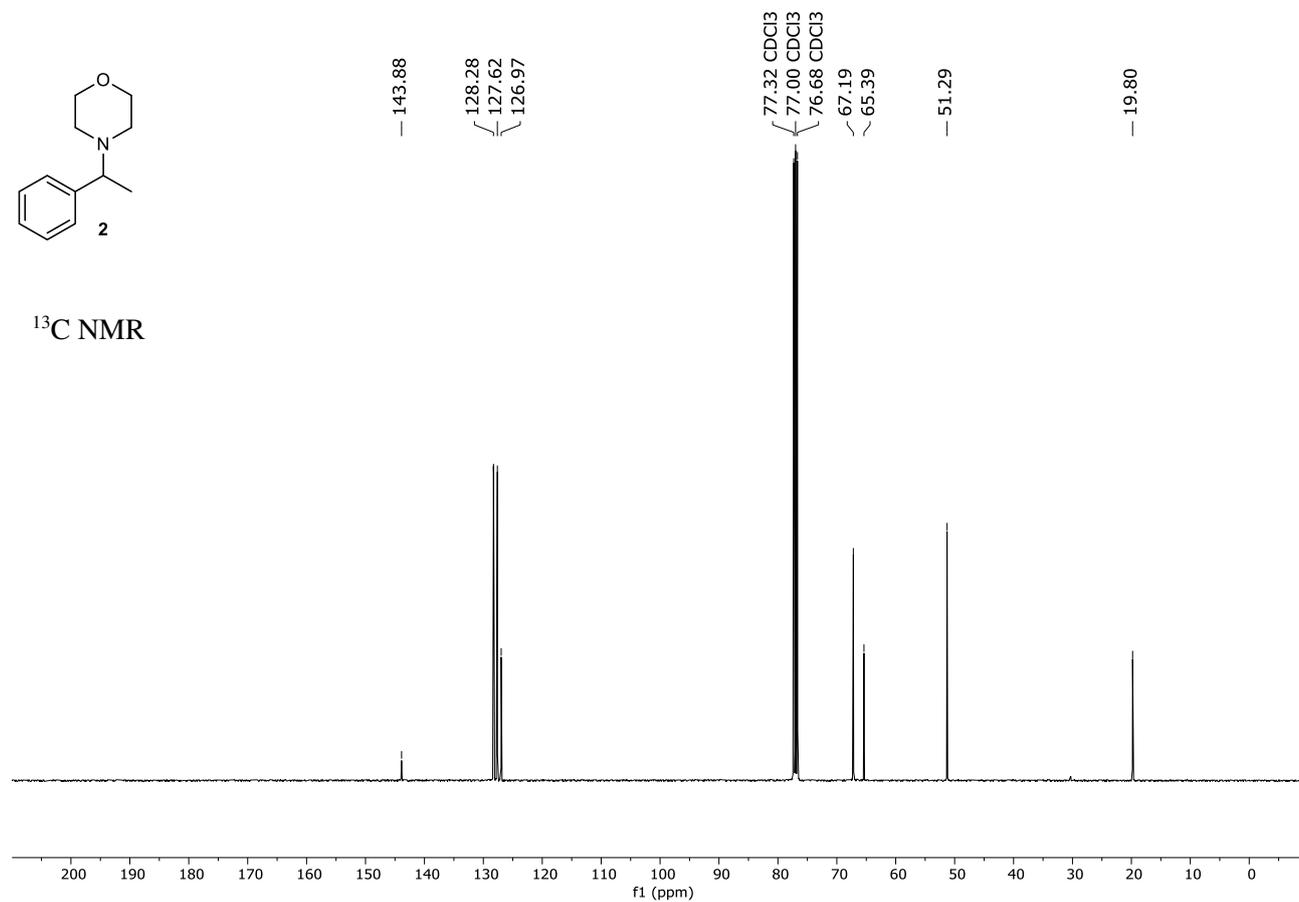
4.2. Coupling of Secondary Amines

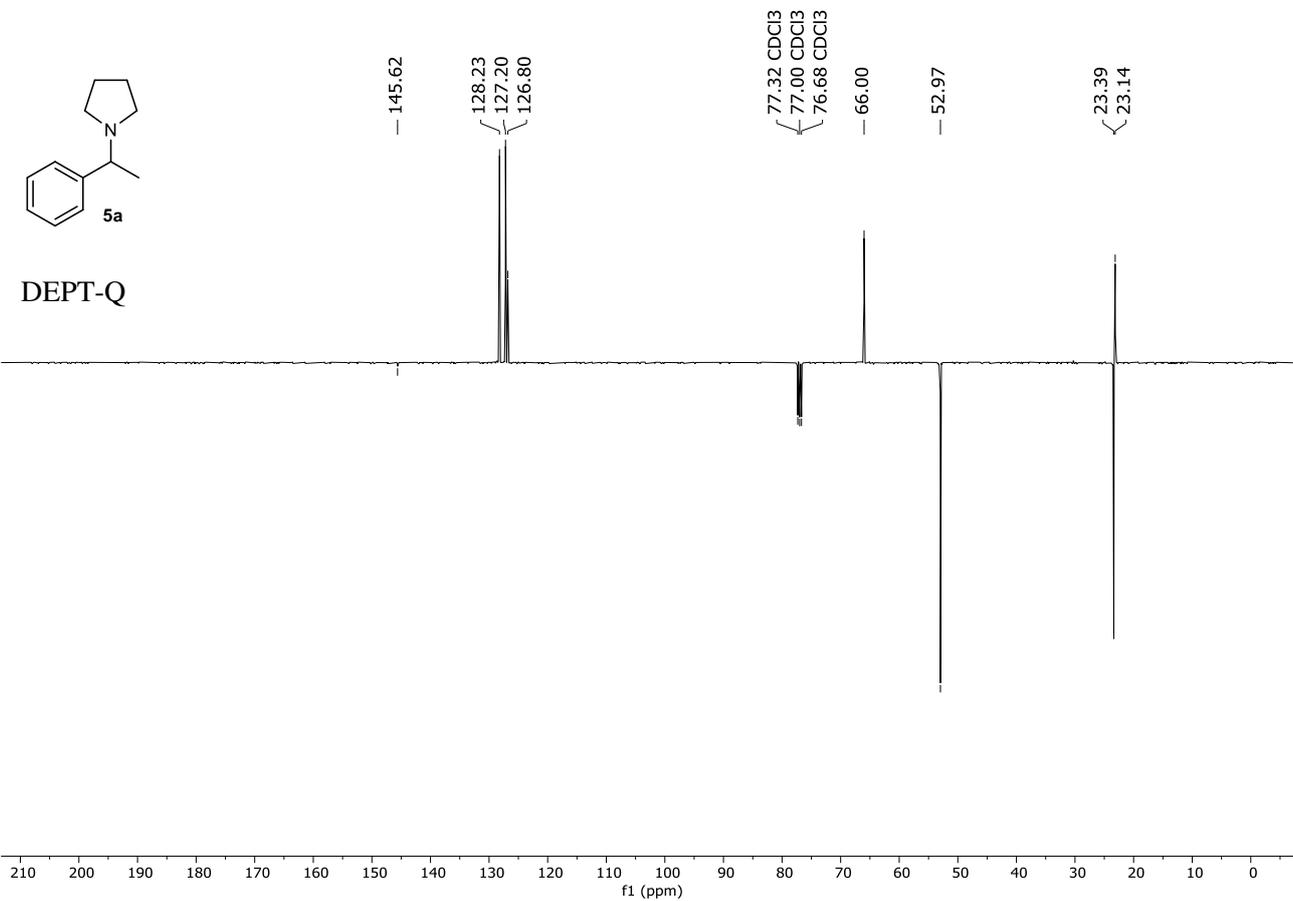
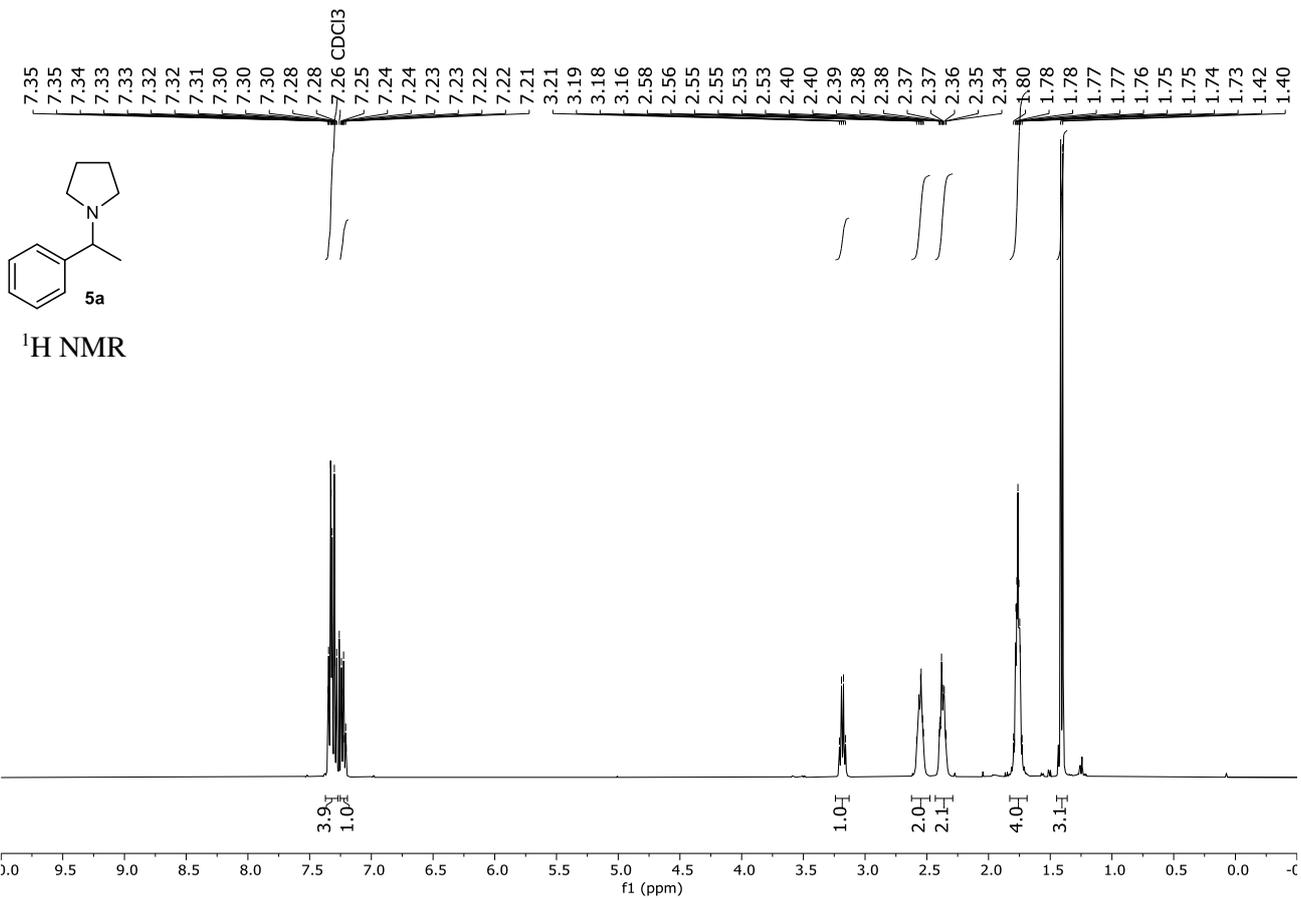


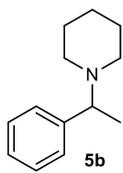
^1H NMR



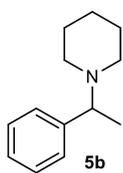
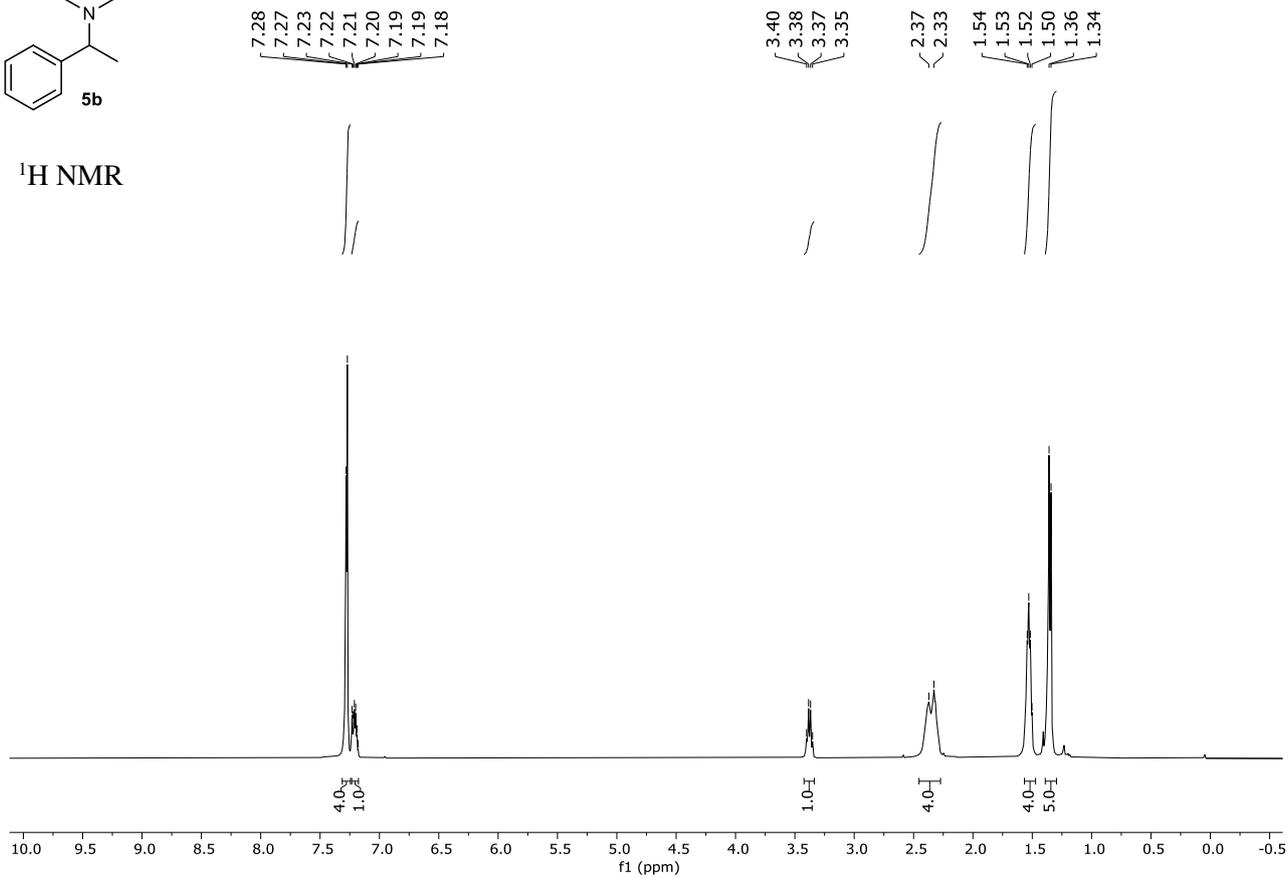
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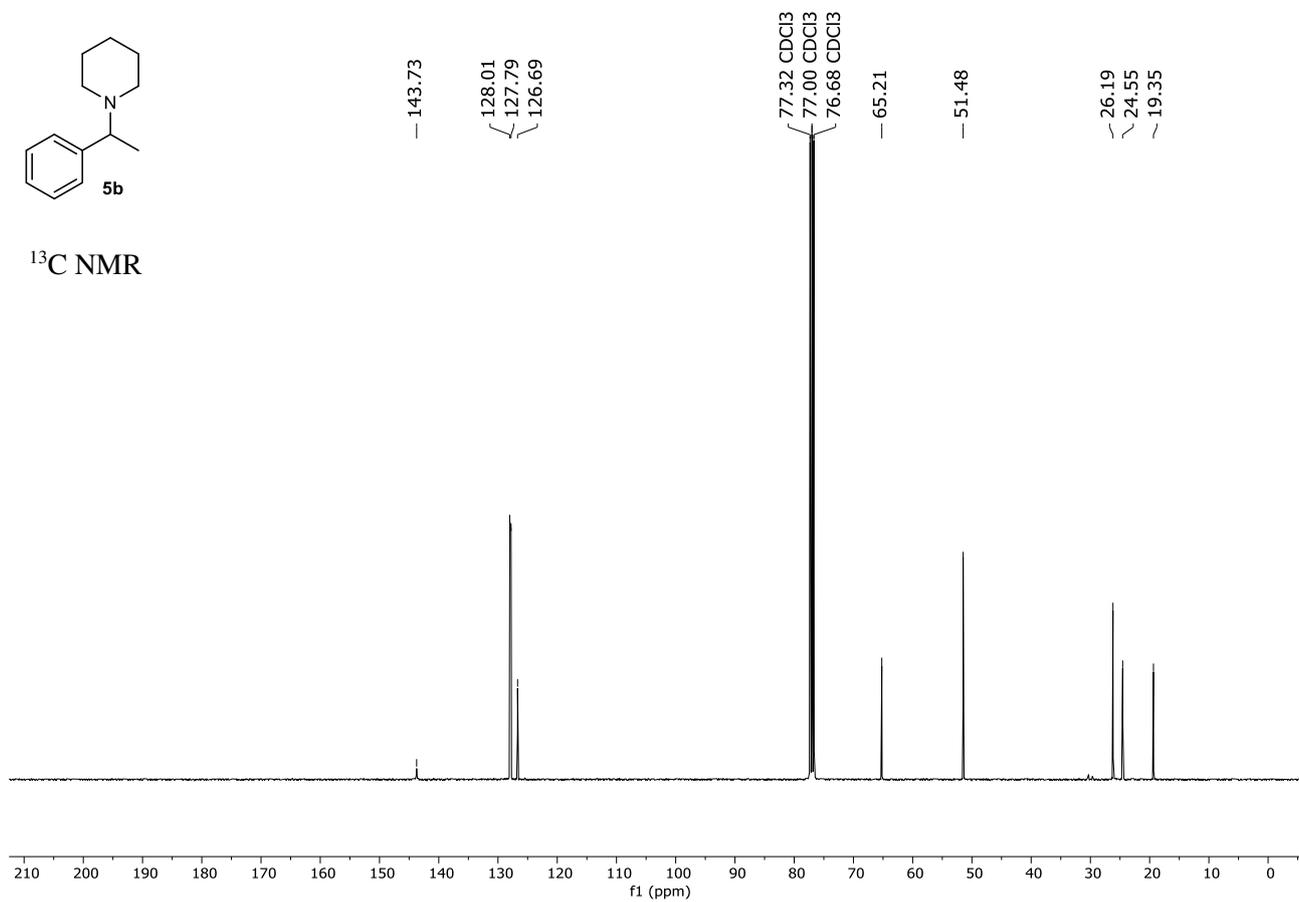


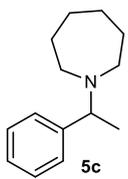


¹H NMR

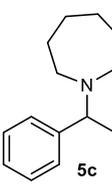
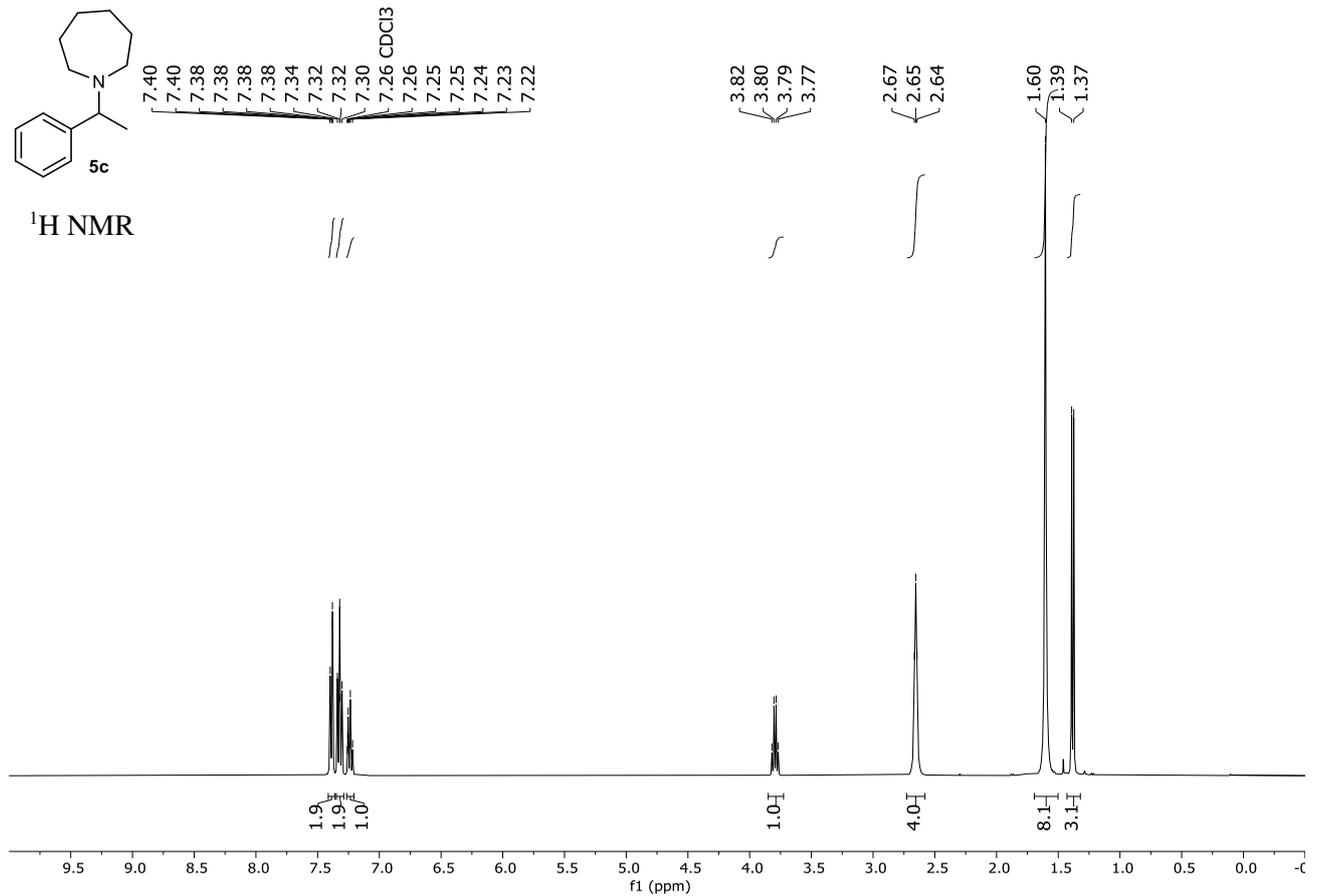


¹³C NMR

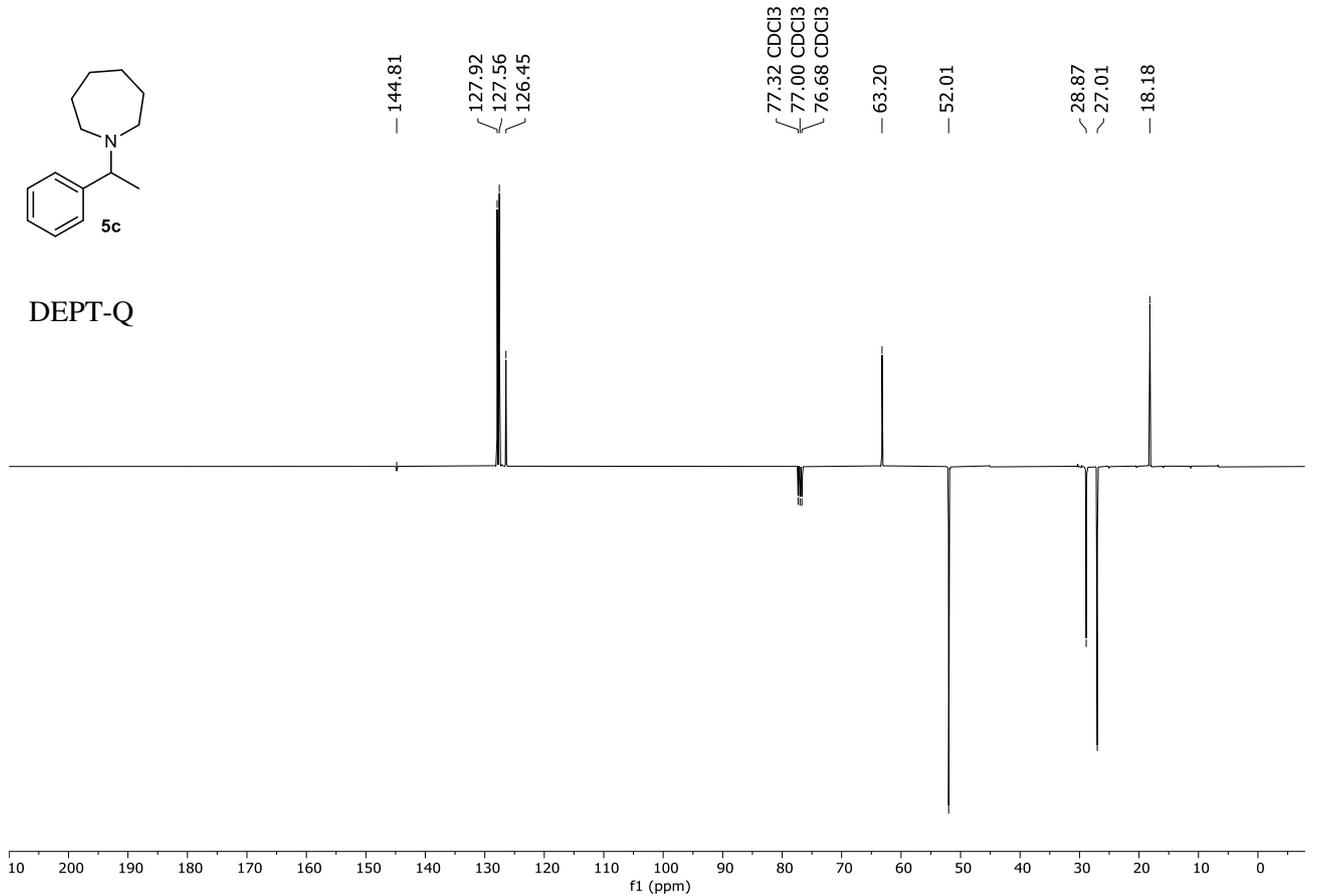


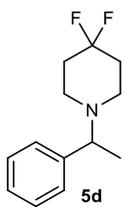


¹H NMR

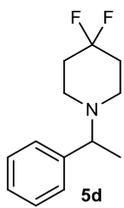
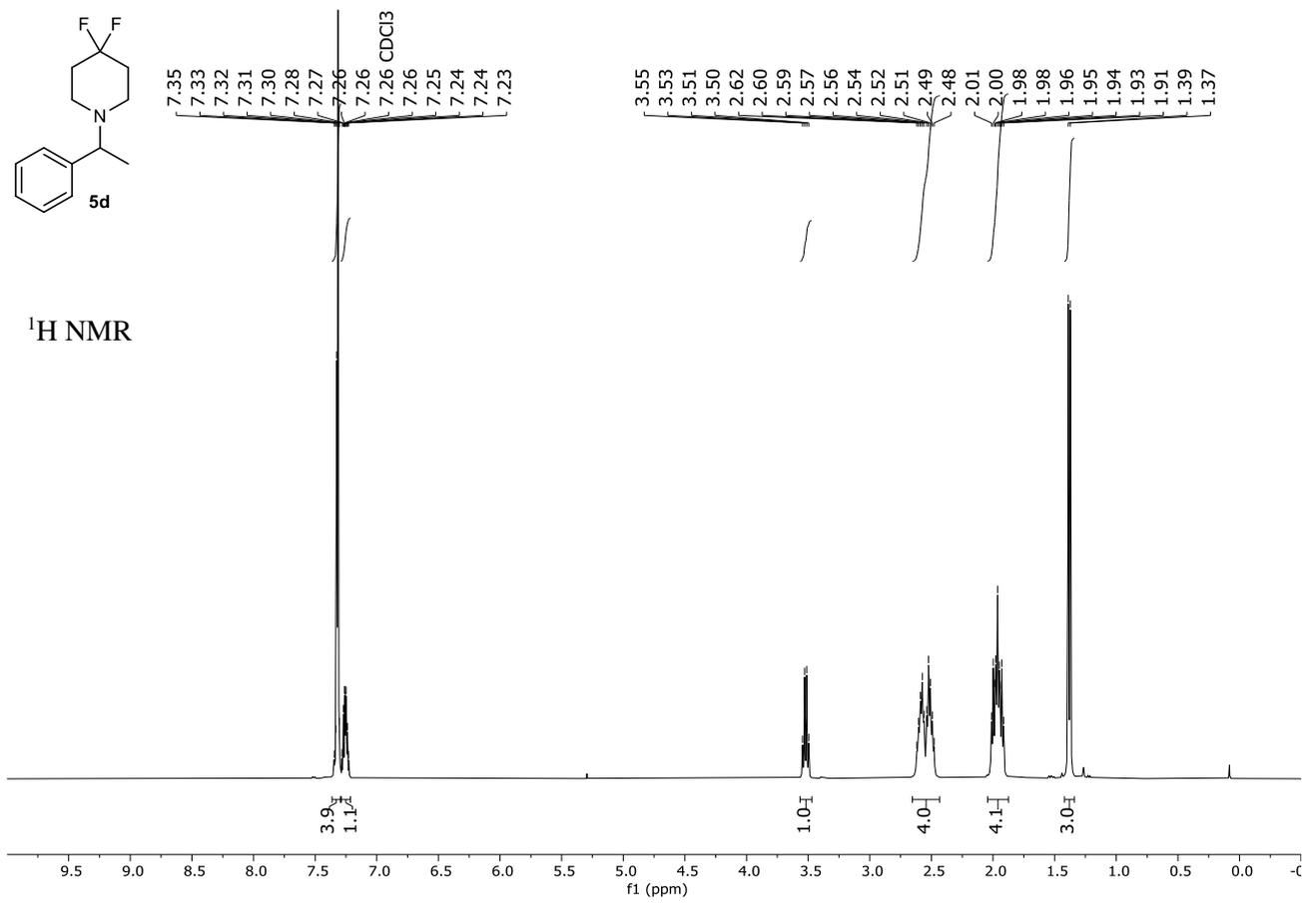


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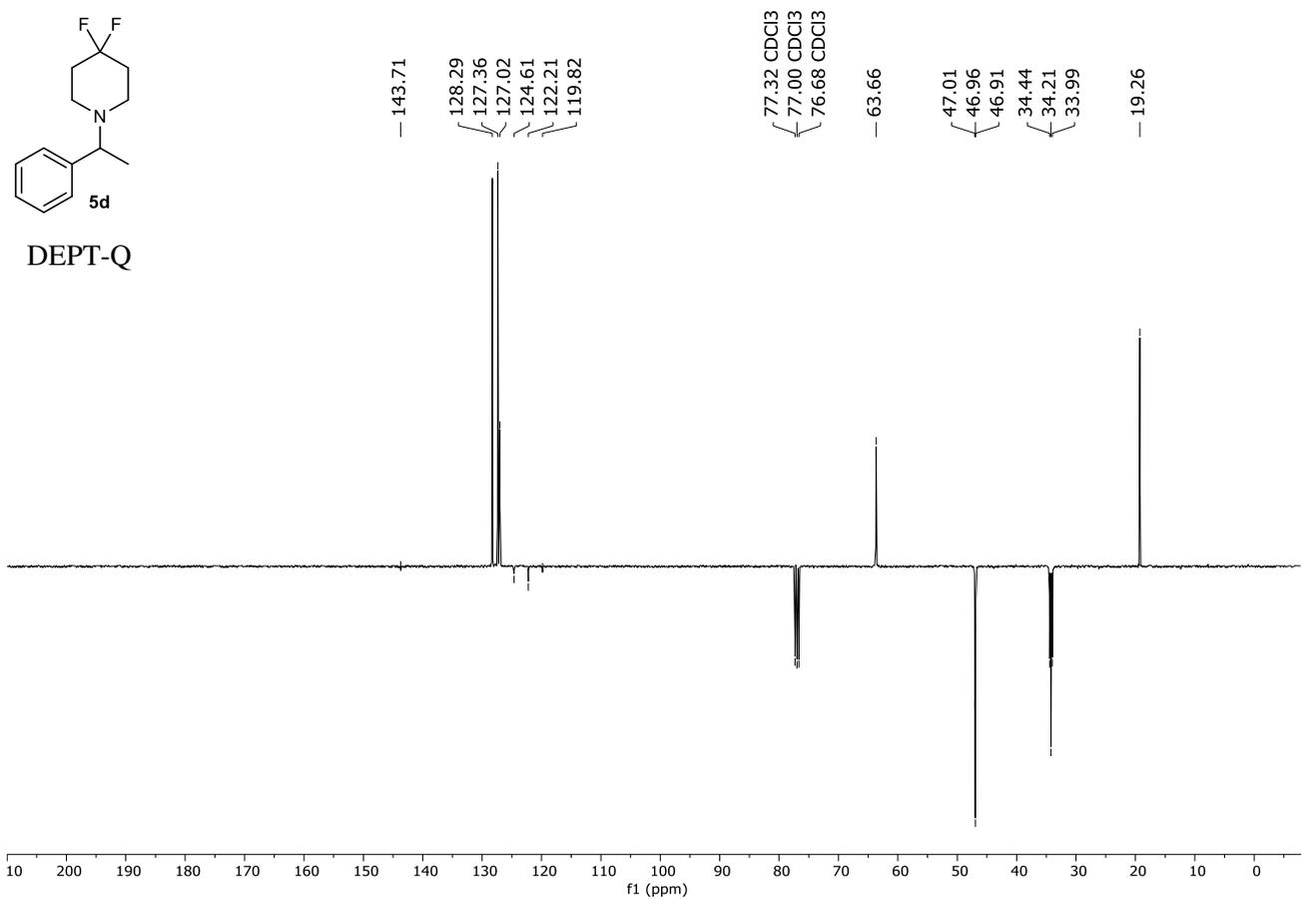


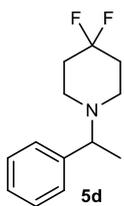


$^1\text{H NMR}$

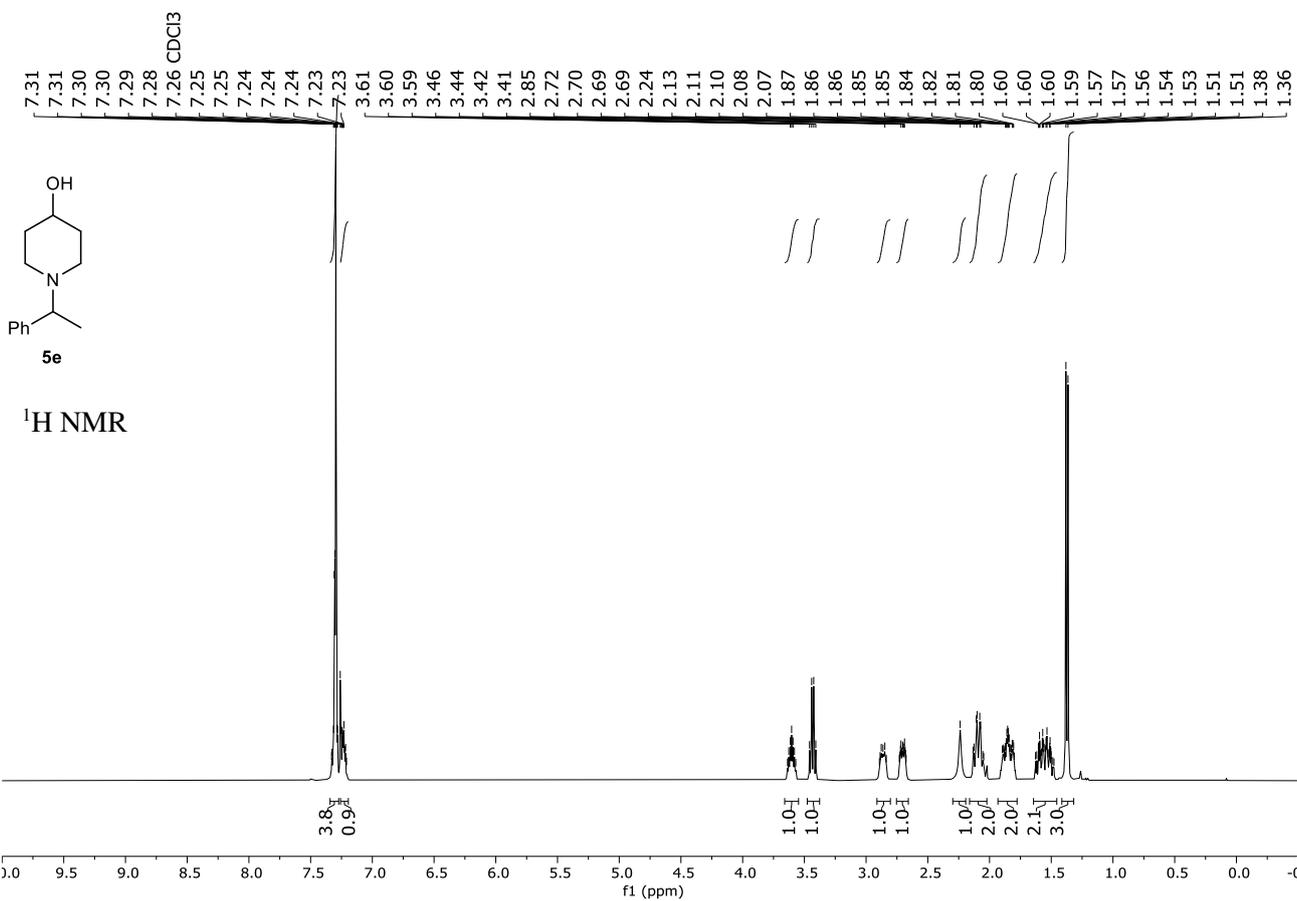
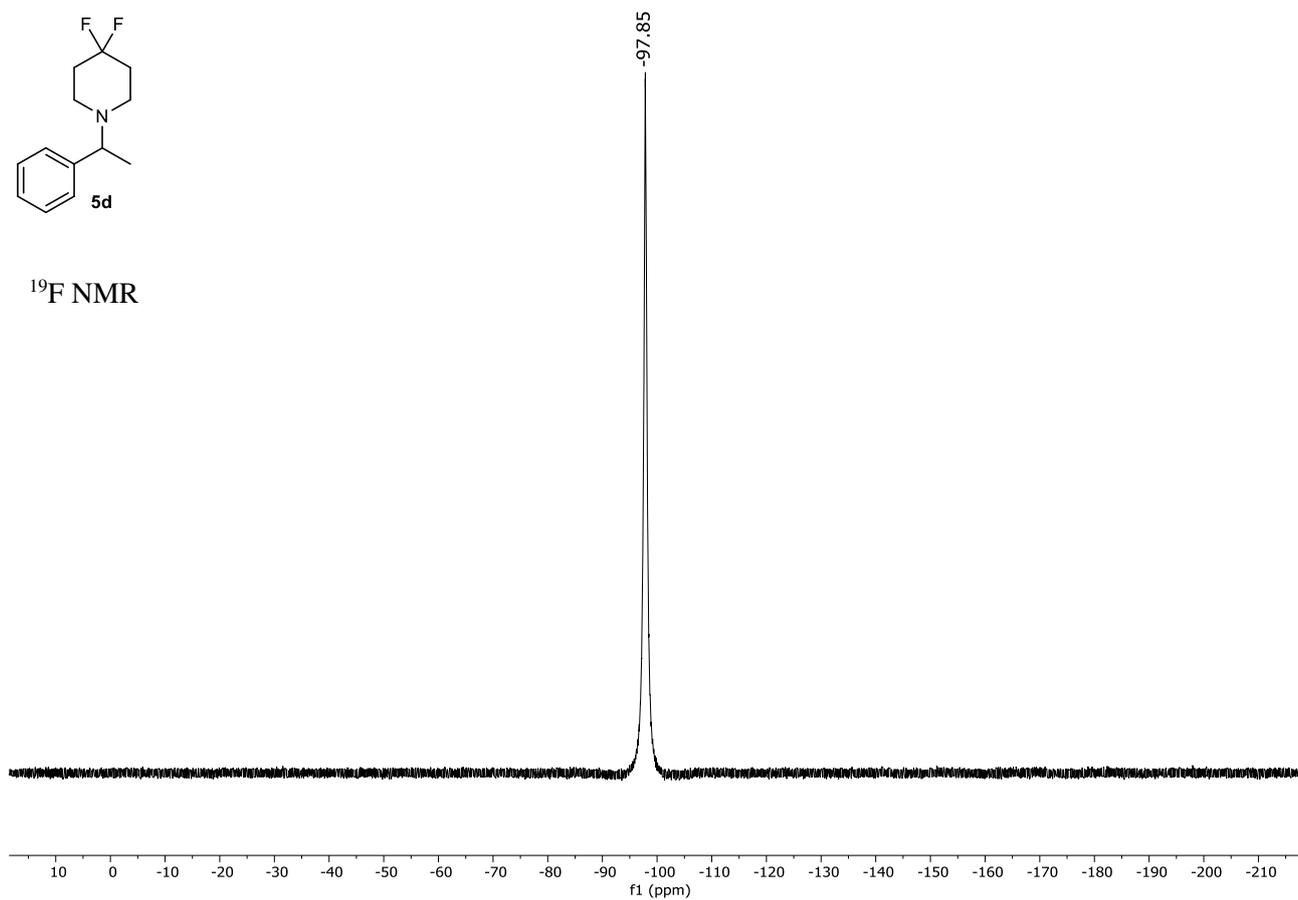


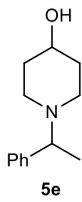
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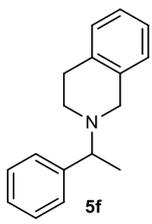
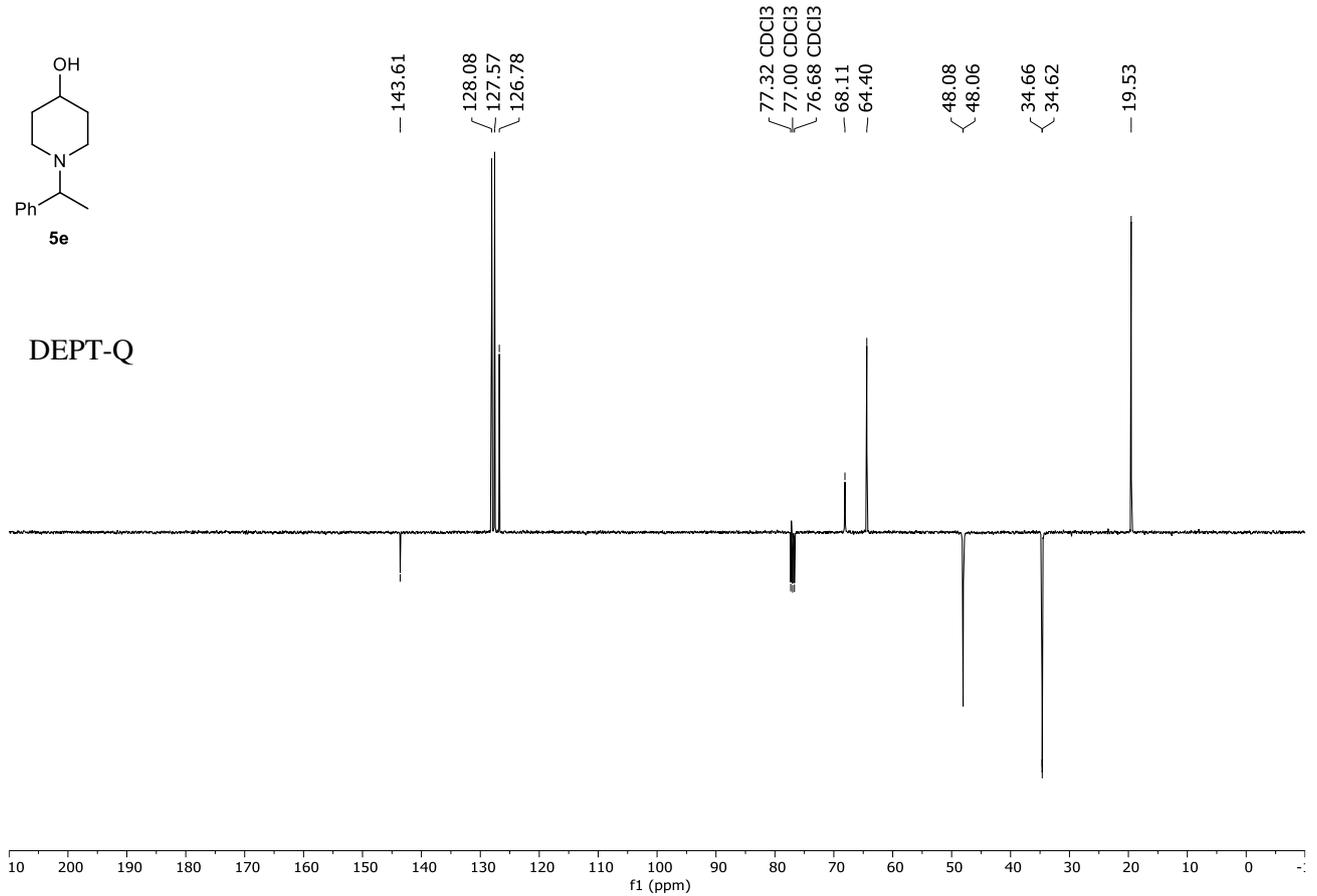


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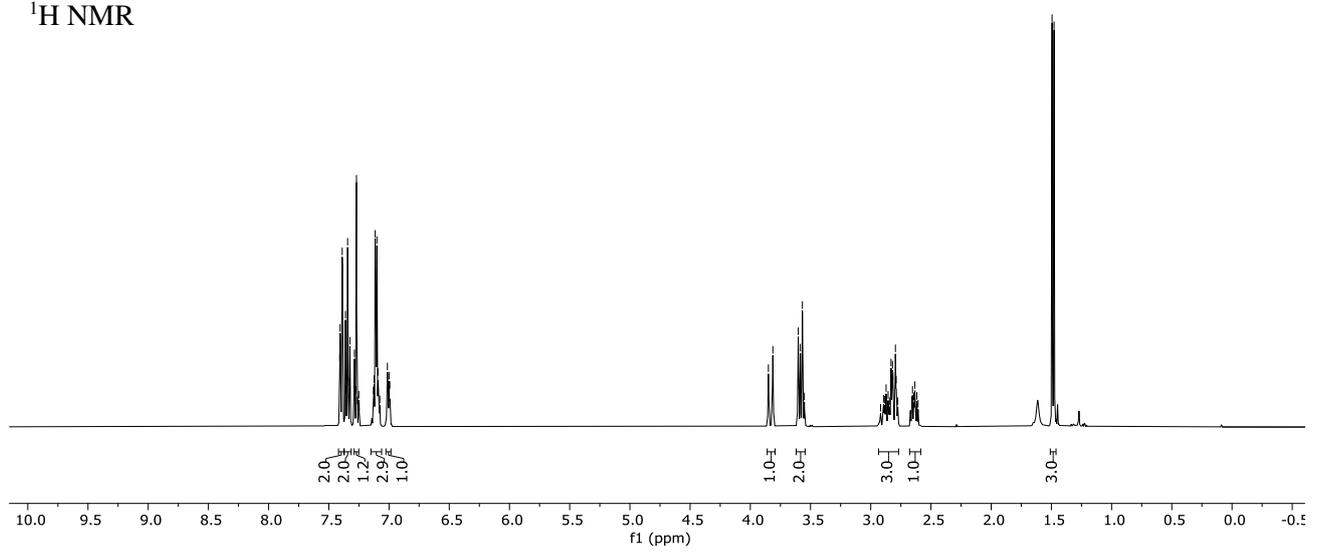


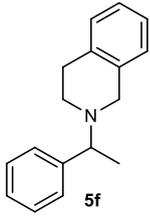


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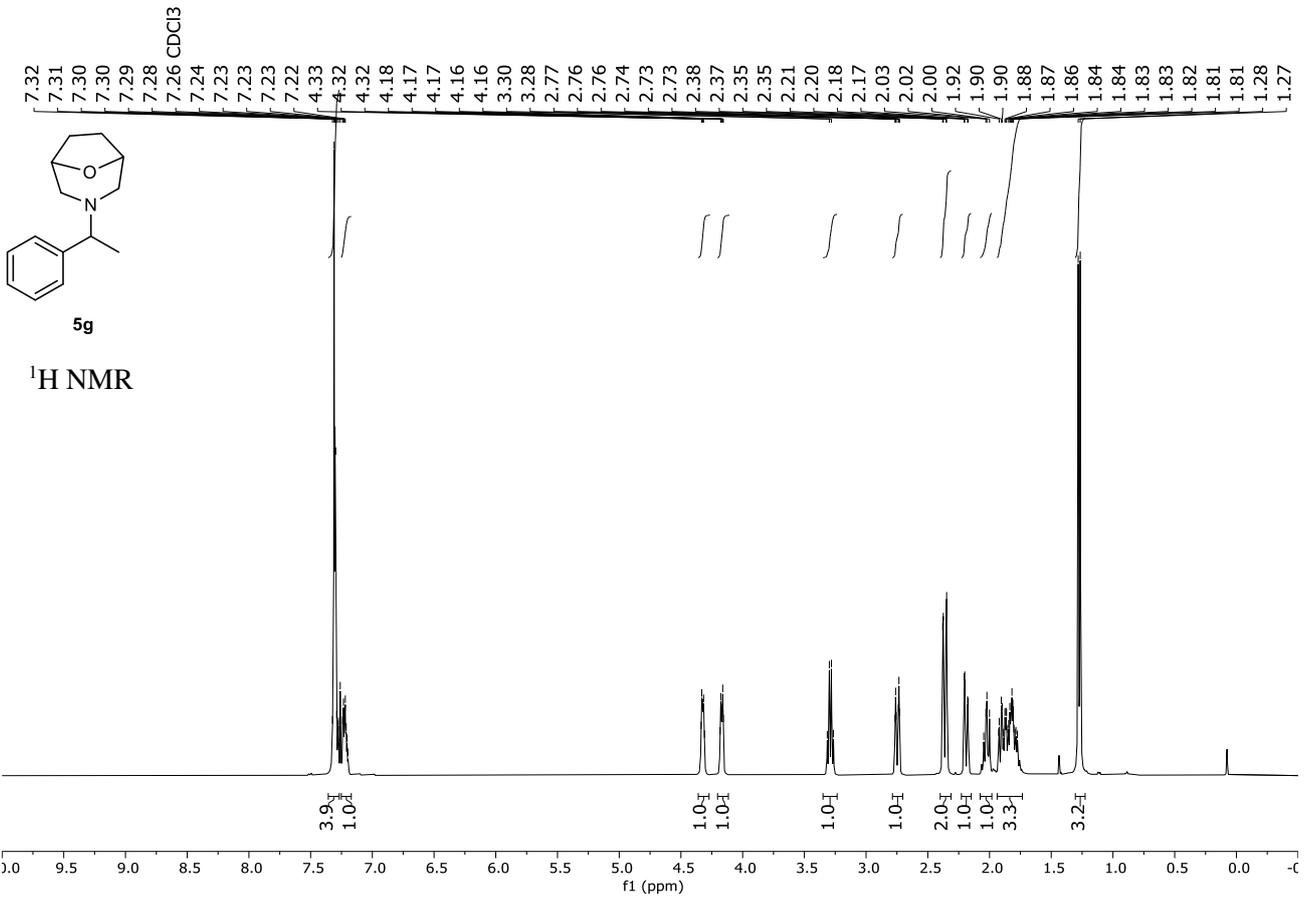
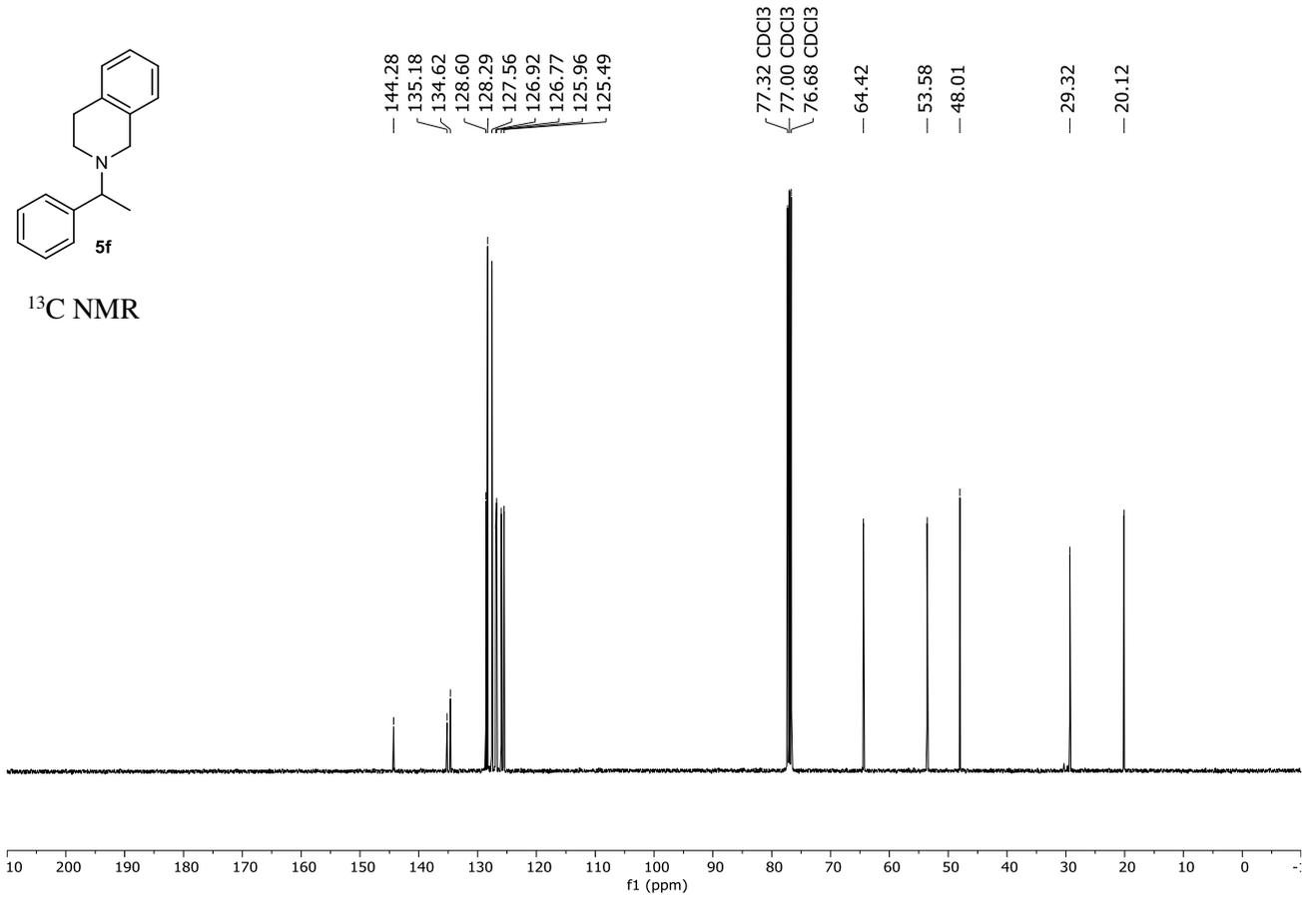


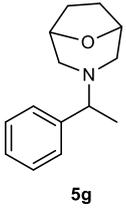
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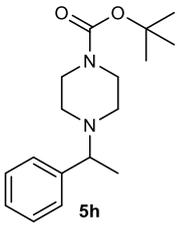
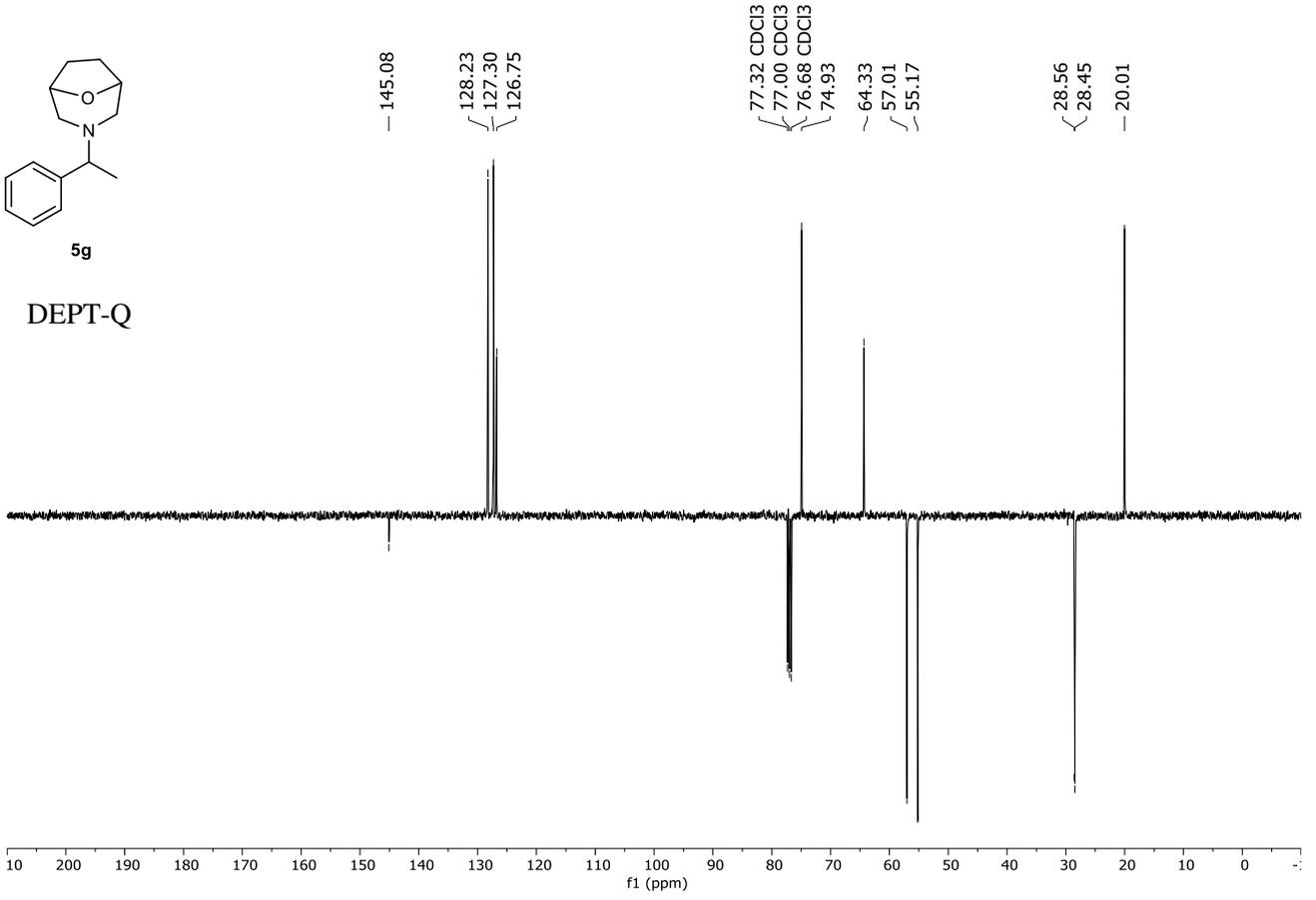


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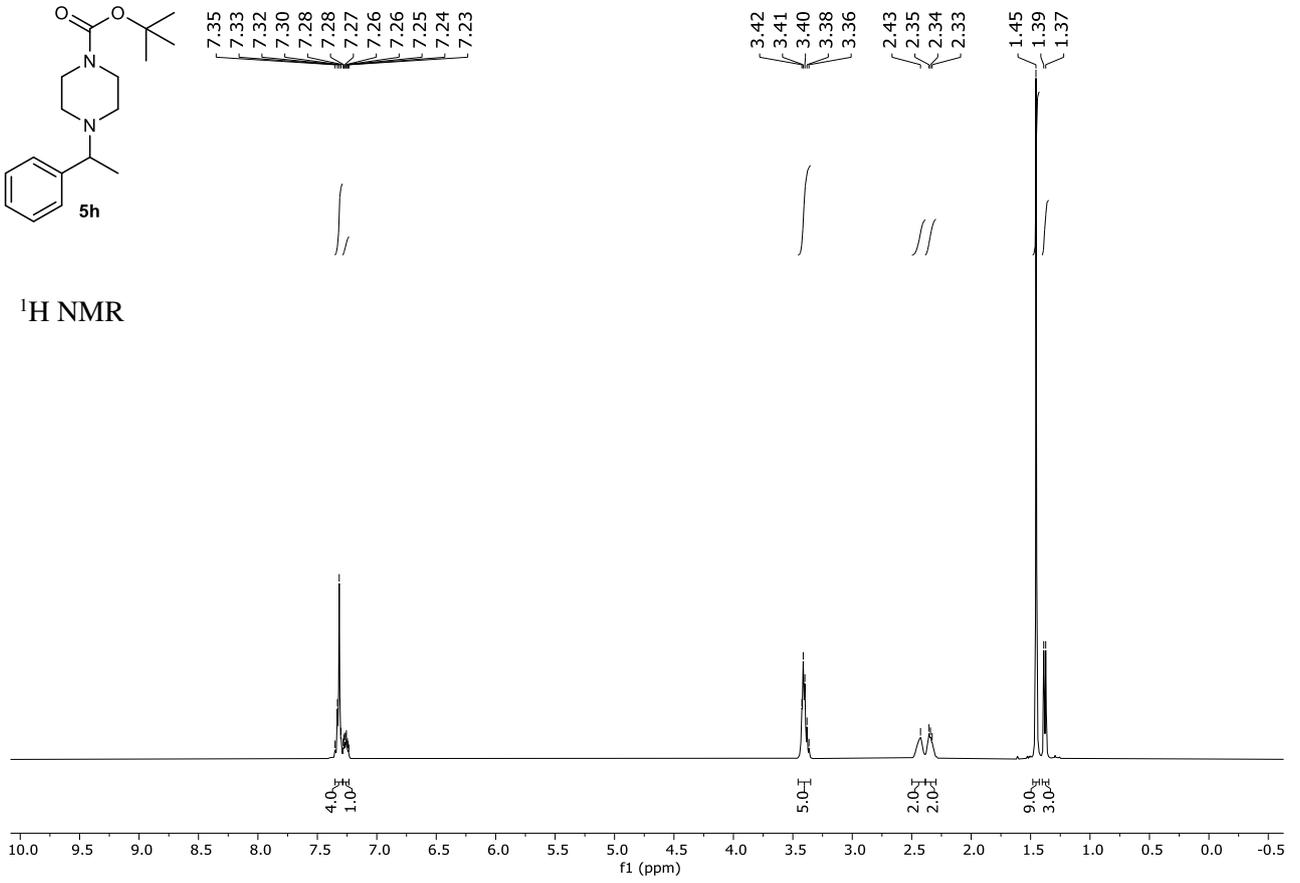


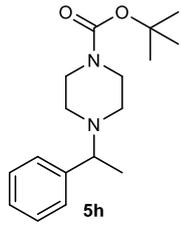


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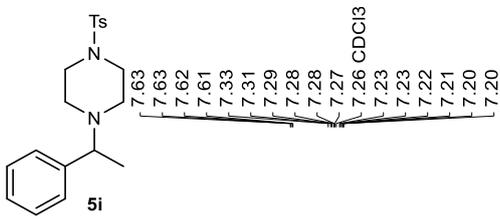
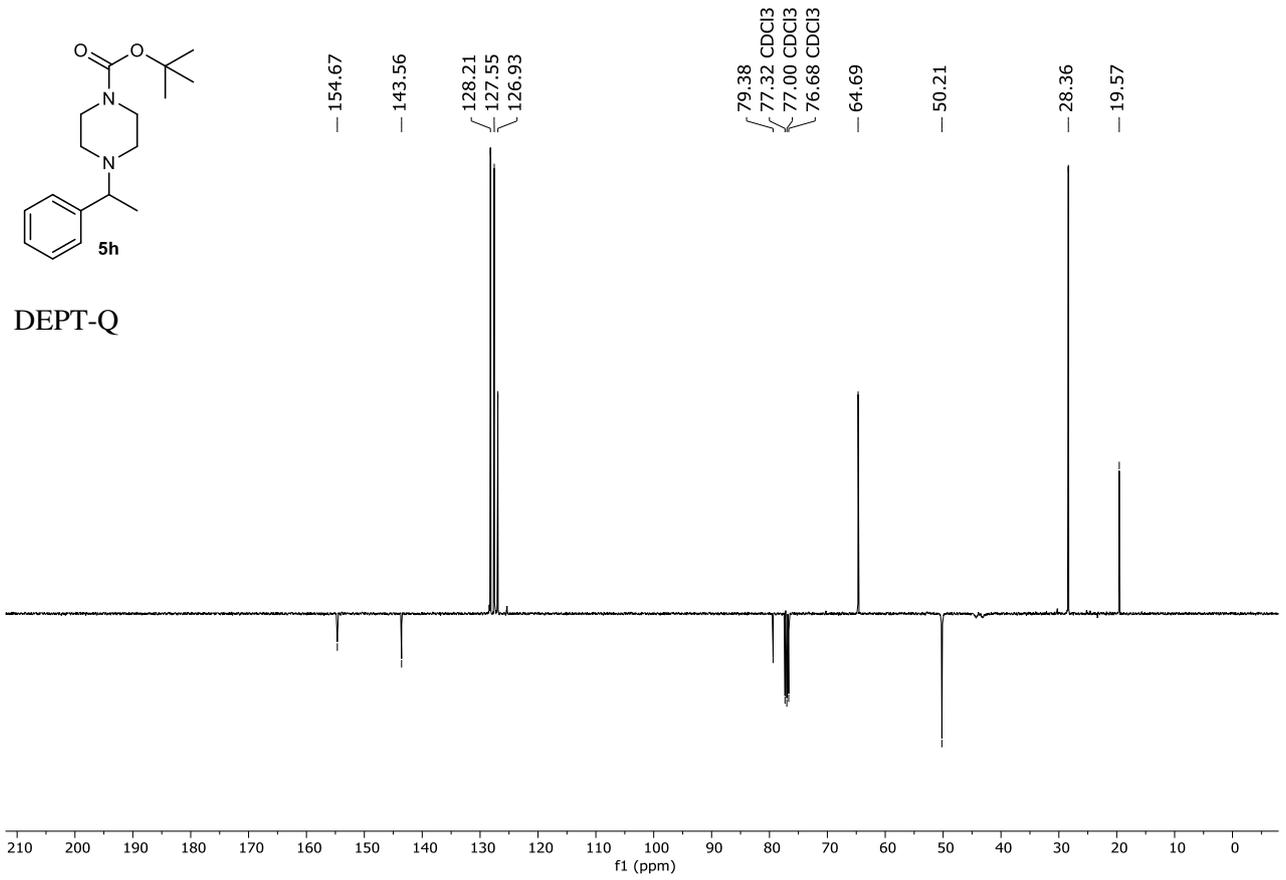


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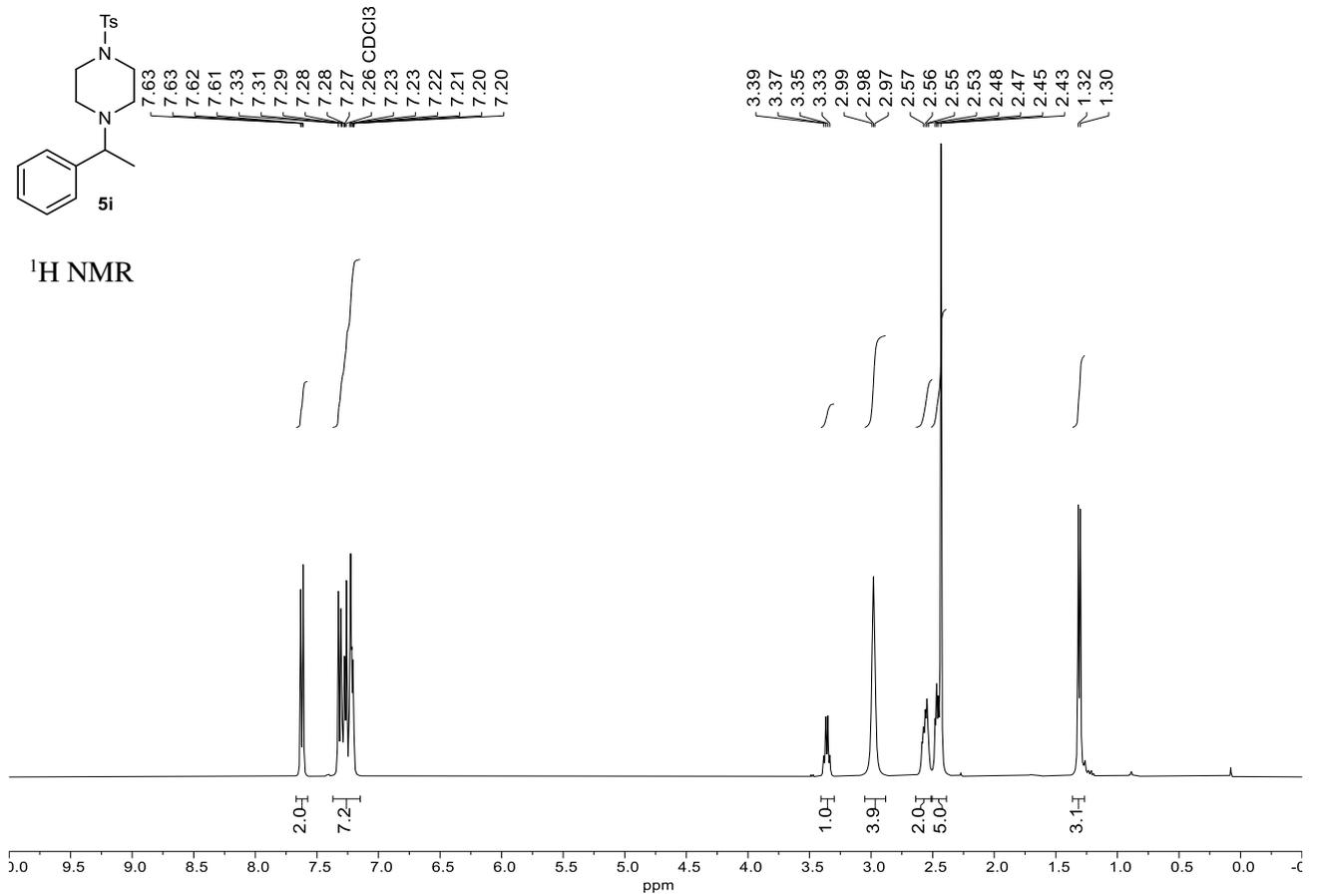


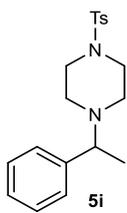


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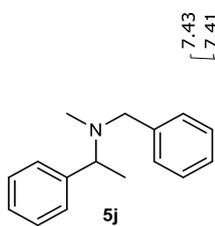
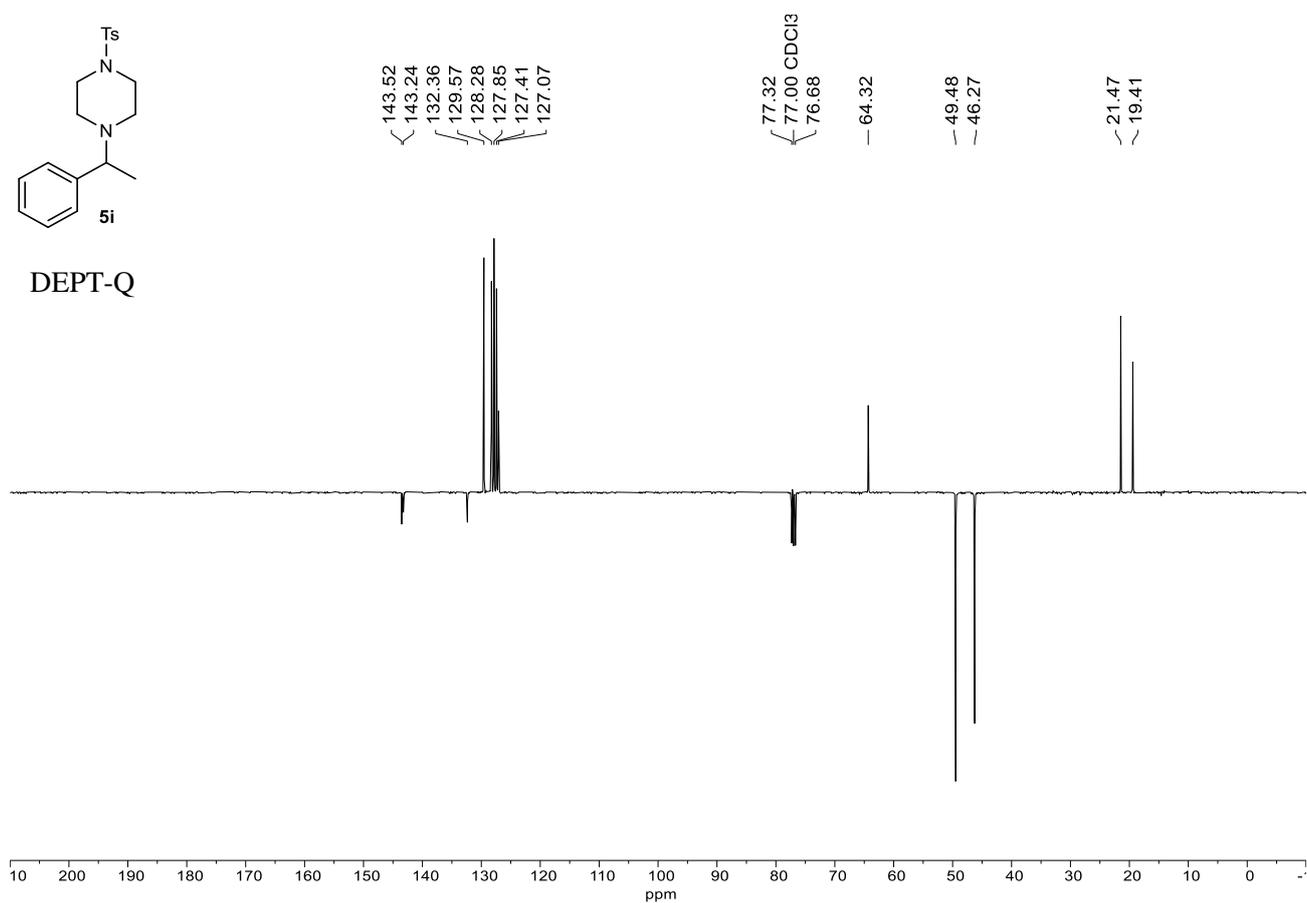


¹H NMR

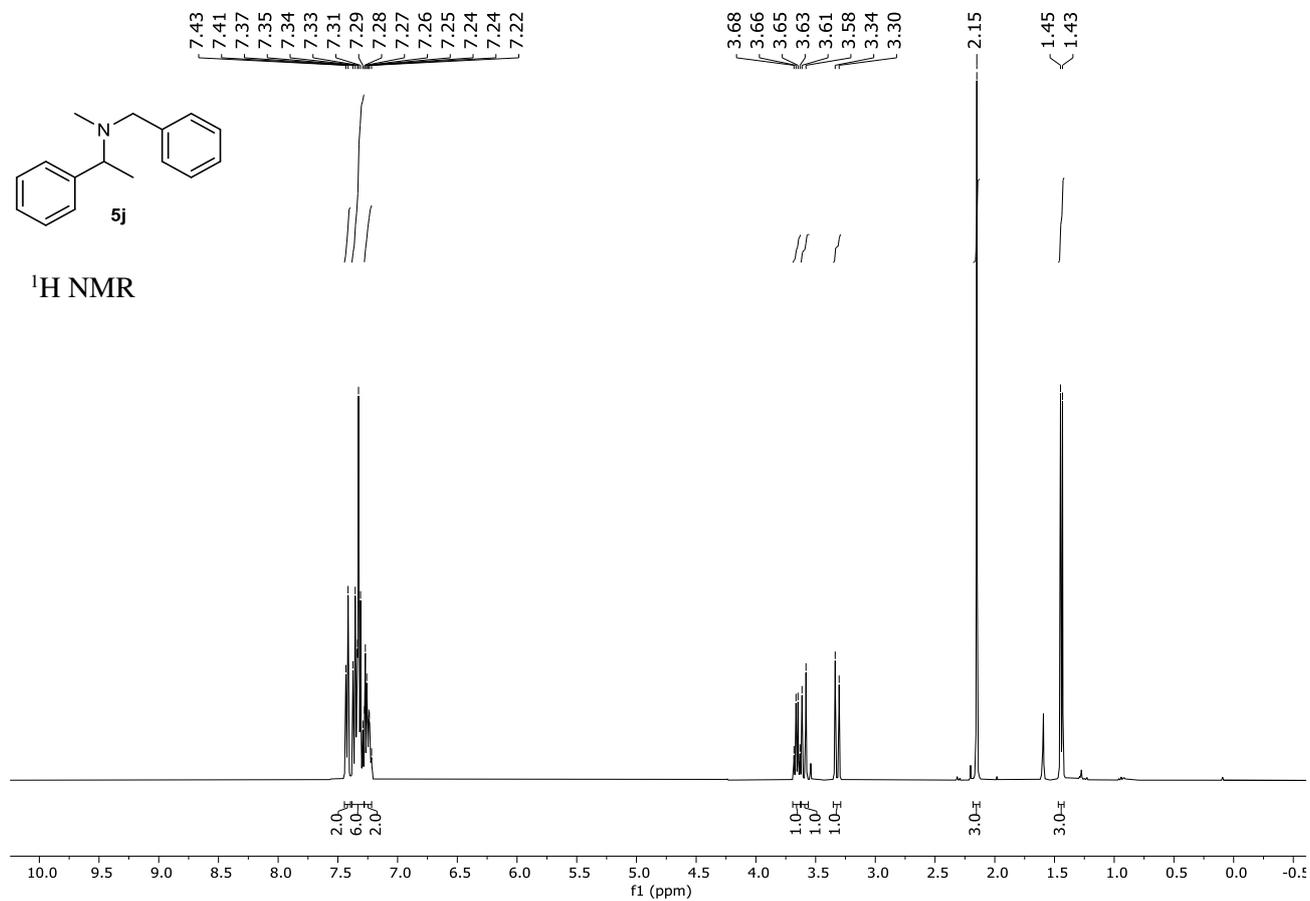


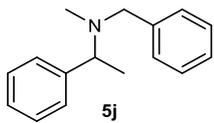


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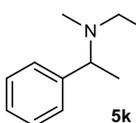
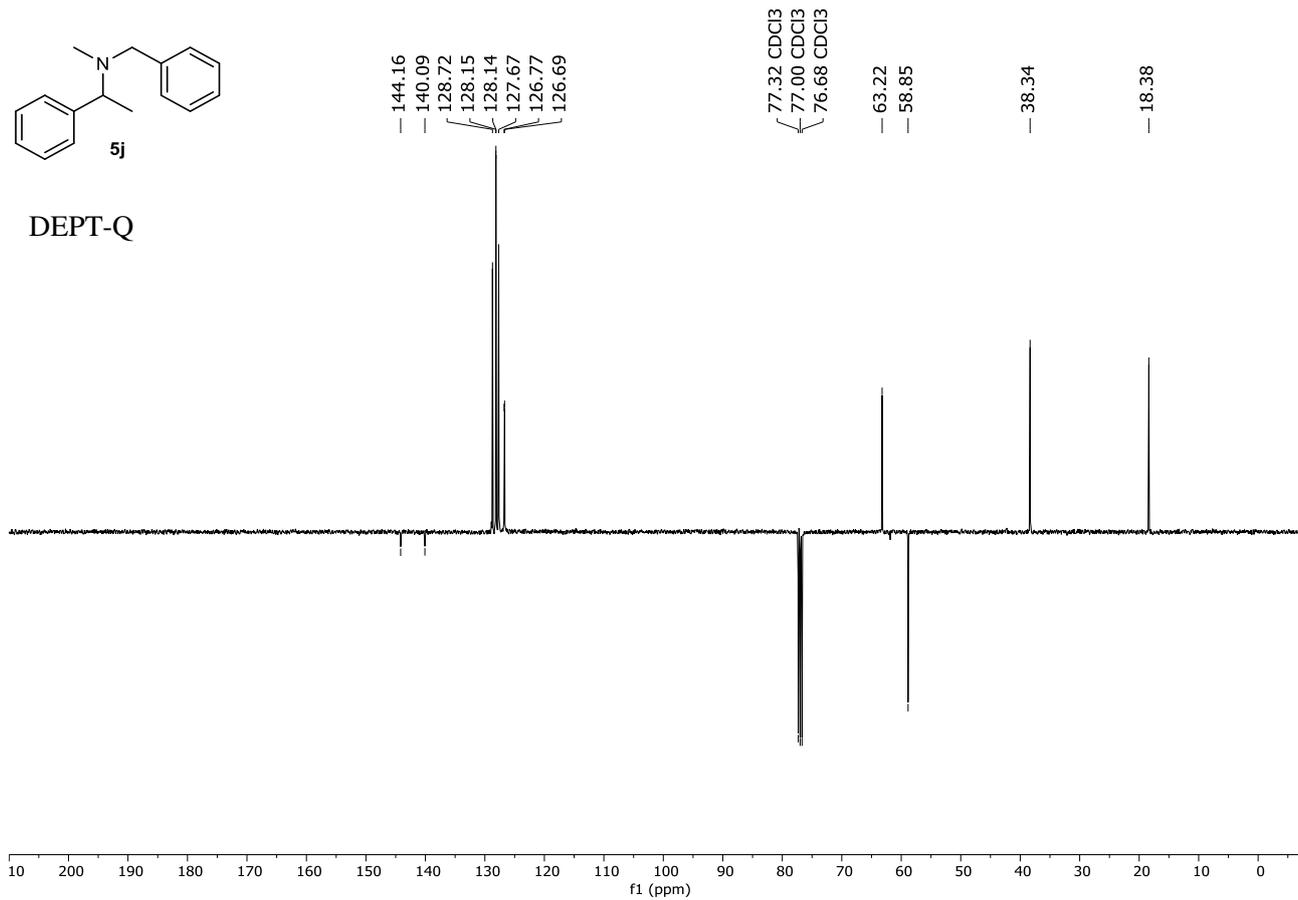


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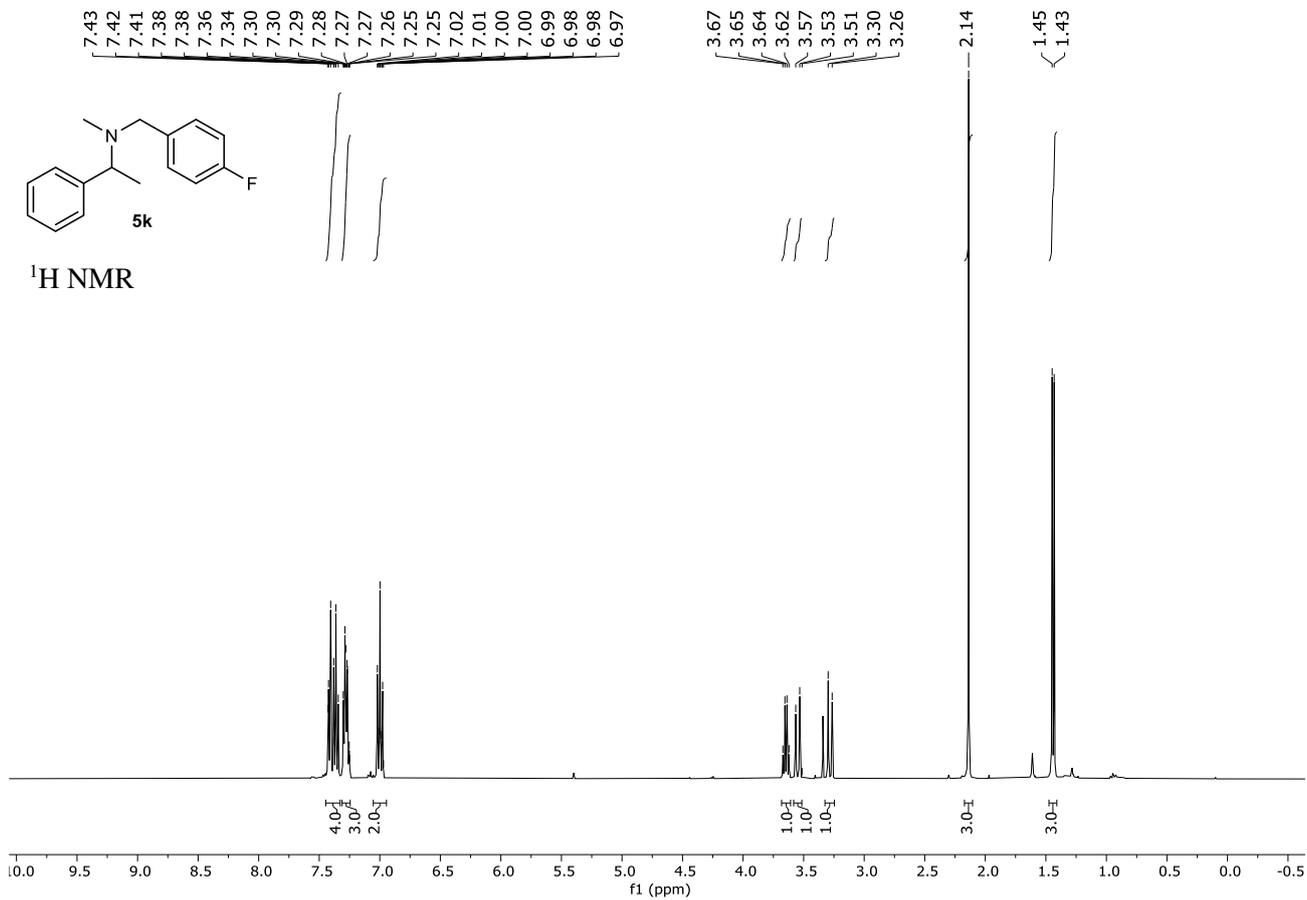


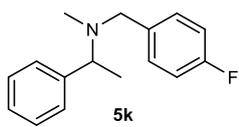


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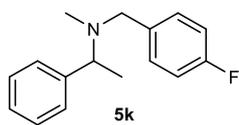
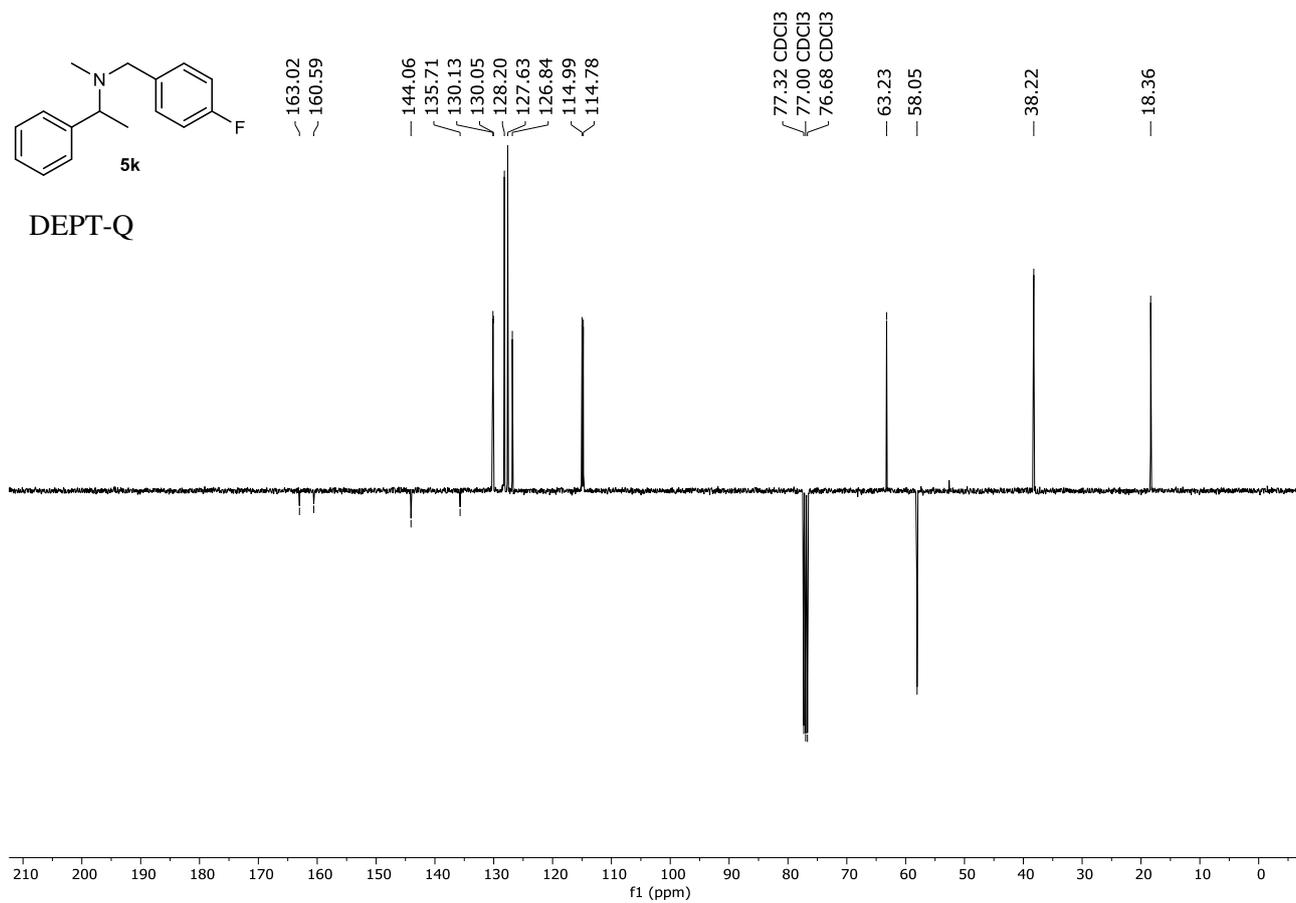


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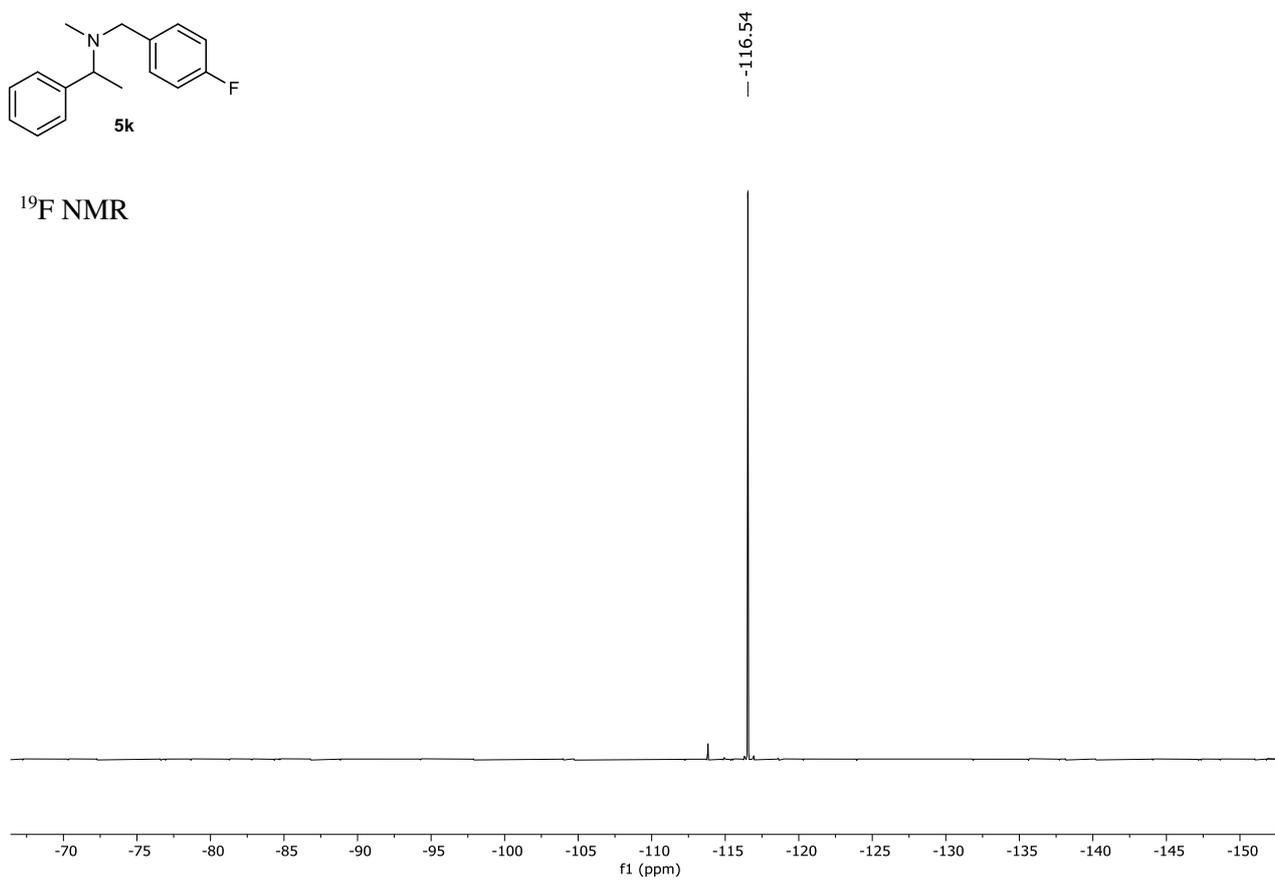


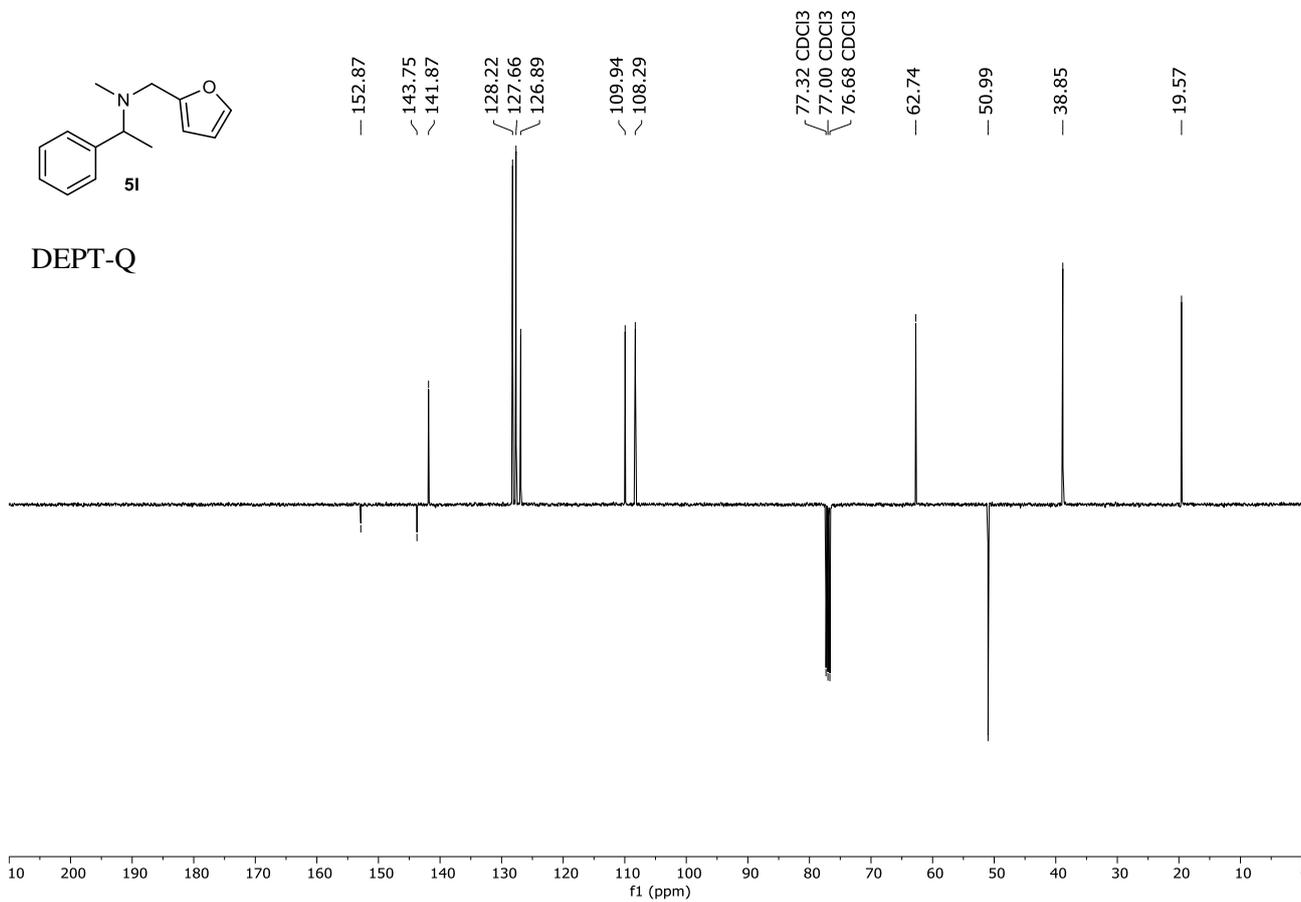
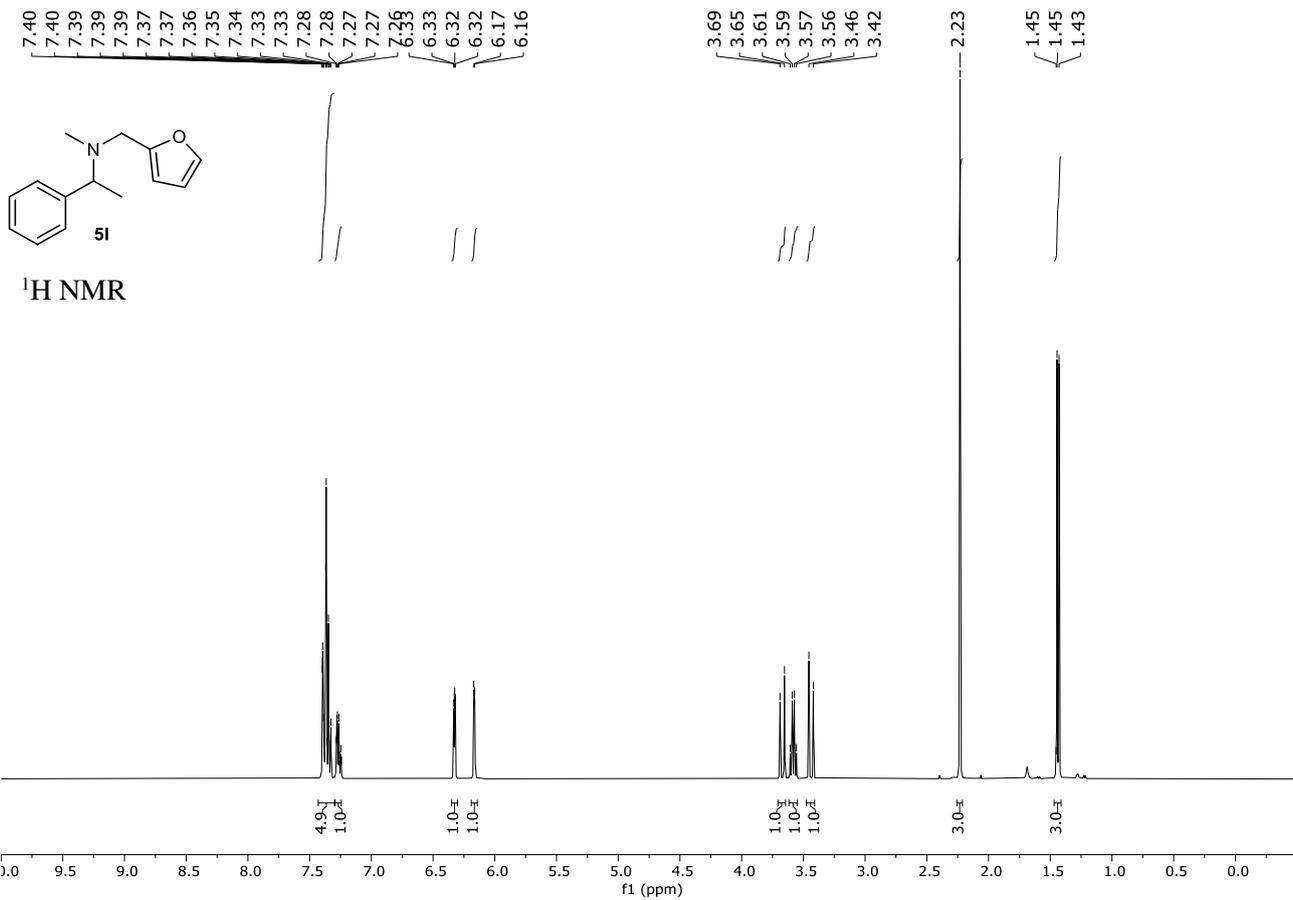


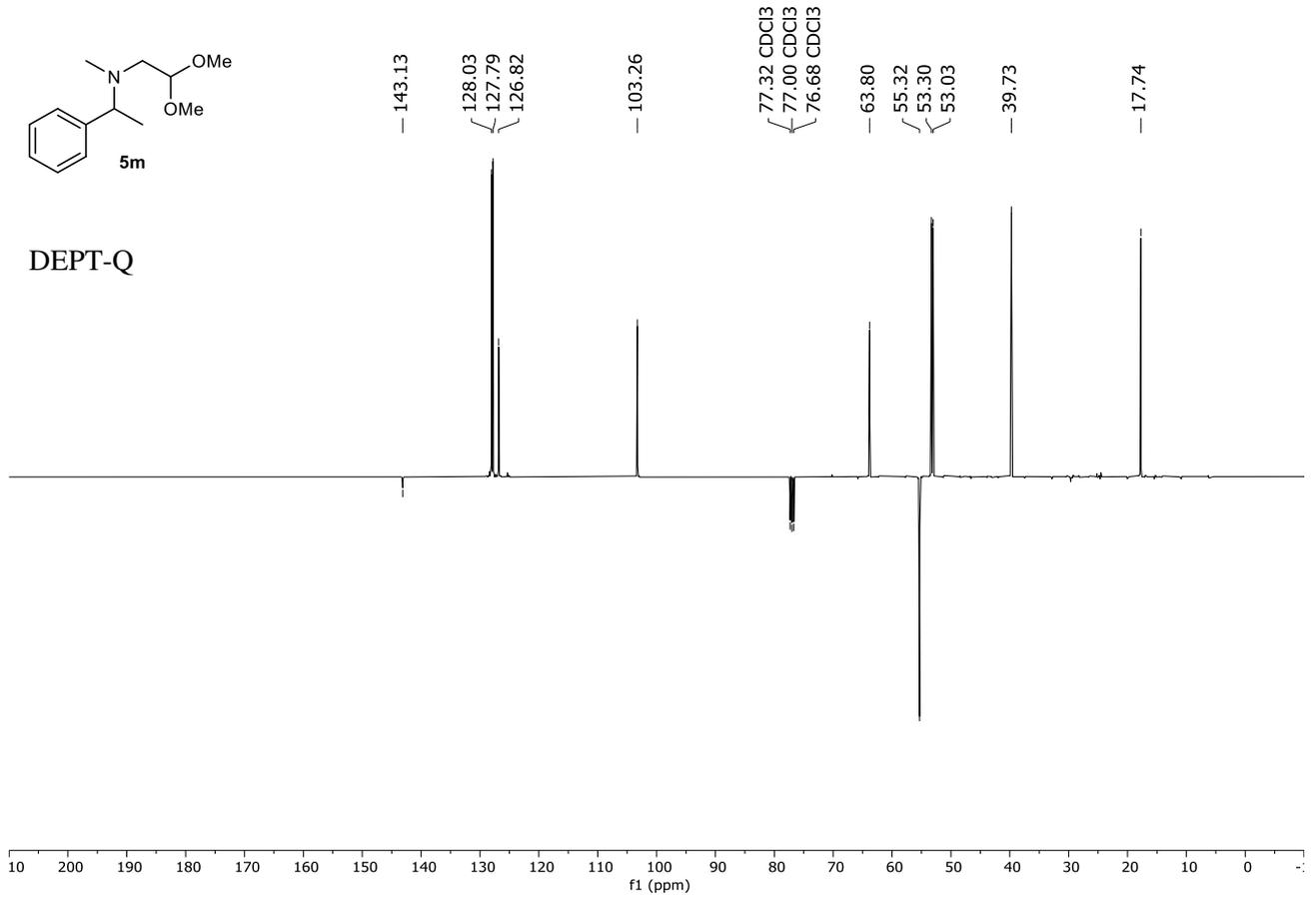
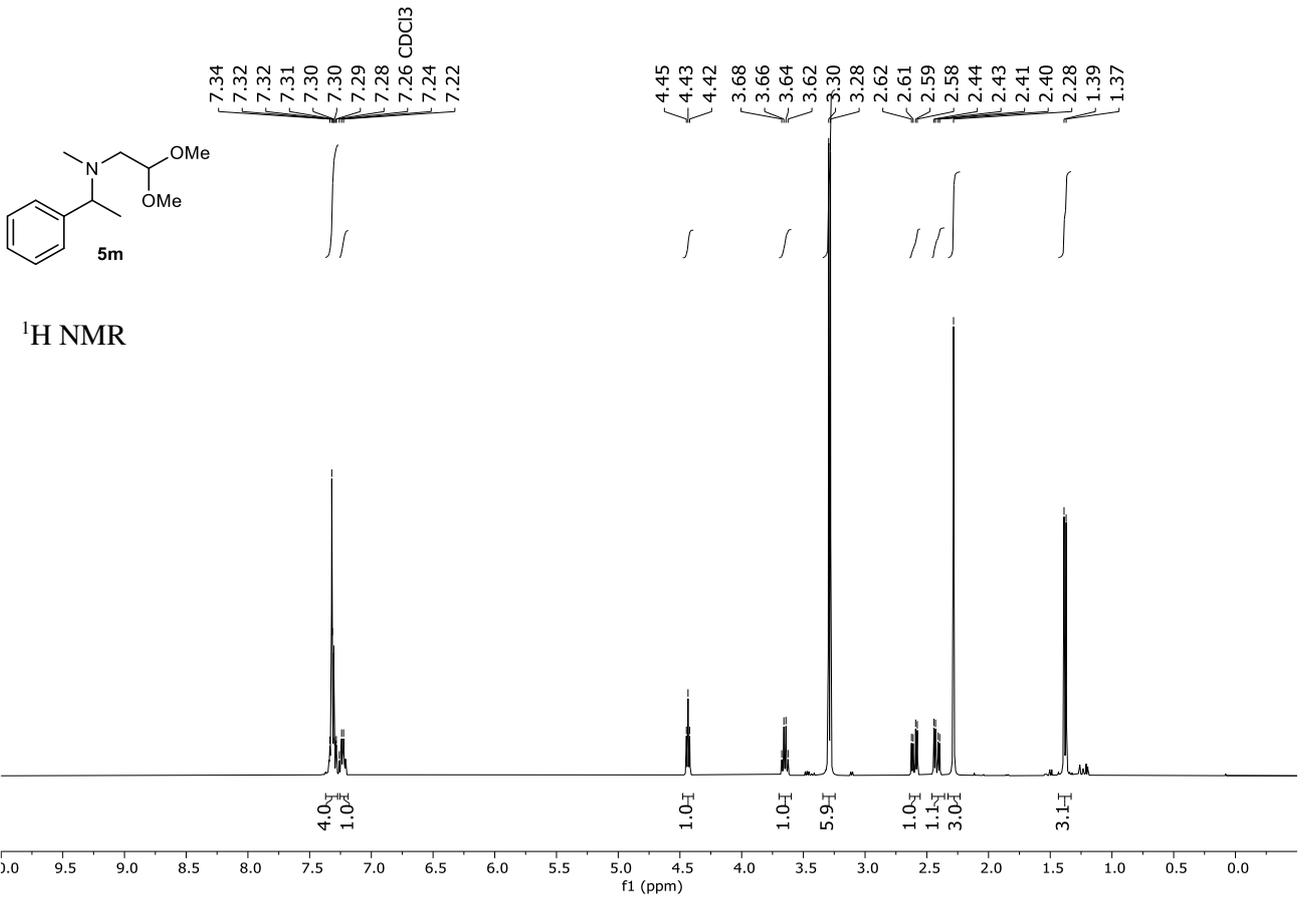
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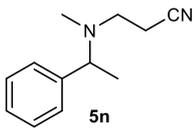


¹⁹F NMR





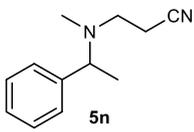
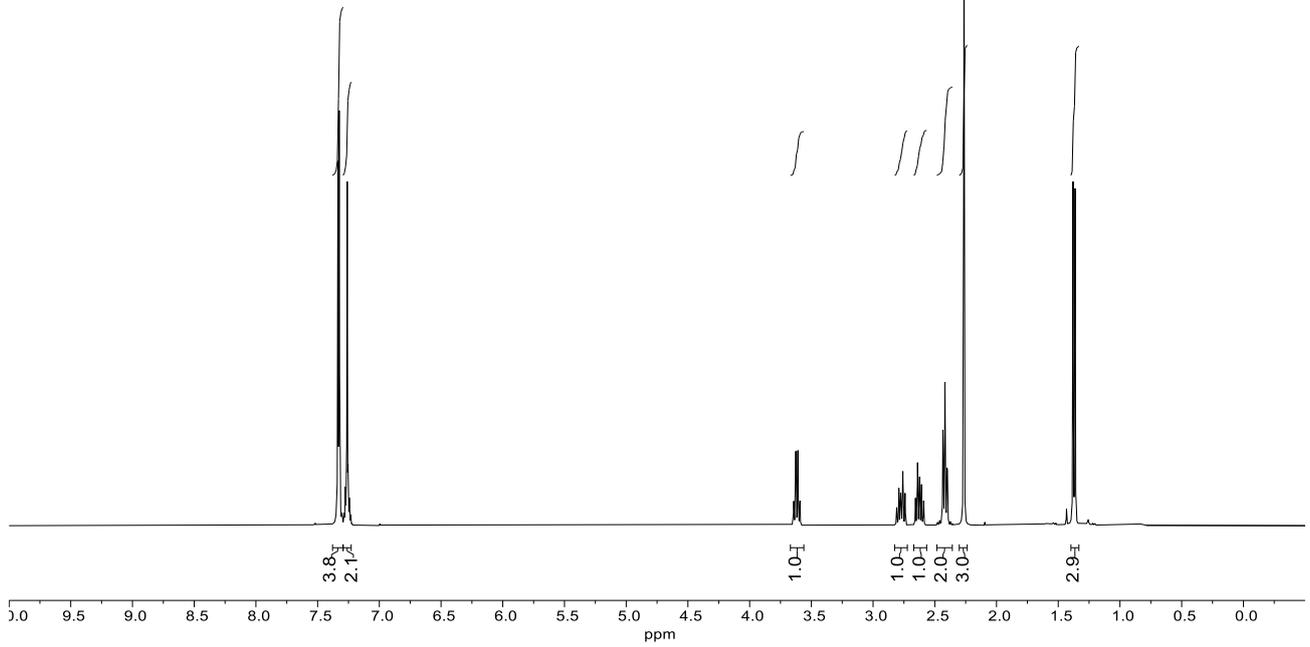




7.34
 7.32
 7.27
 7.26 CDCl₃
 7.25
 7.24
 7.24

3.64
 3.63
 3.61
 3.59
 2.81
 2.79
 2.78
 2.77
 2.76
 2.74
 2.66
 2.64
 2.62
 2.61
 2.59
 2.44
 2.43
 2.42
 2.41
 2.40
 2.40
 2.26
 1.38
 1.36

¹H NMR



143.26
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 127.46
 127.15
 118.94

77.32
 77.00 CDCl₃
 76.68

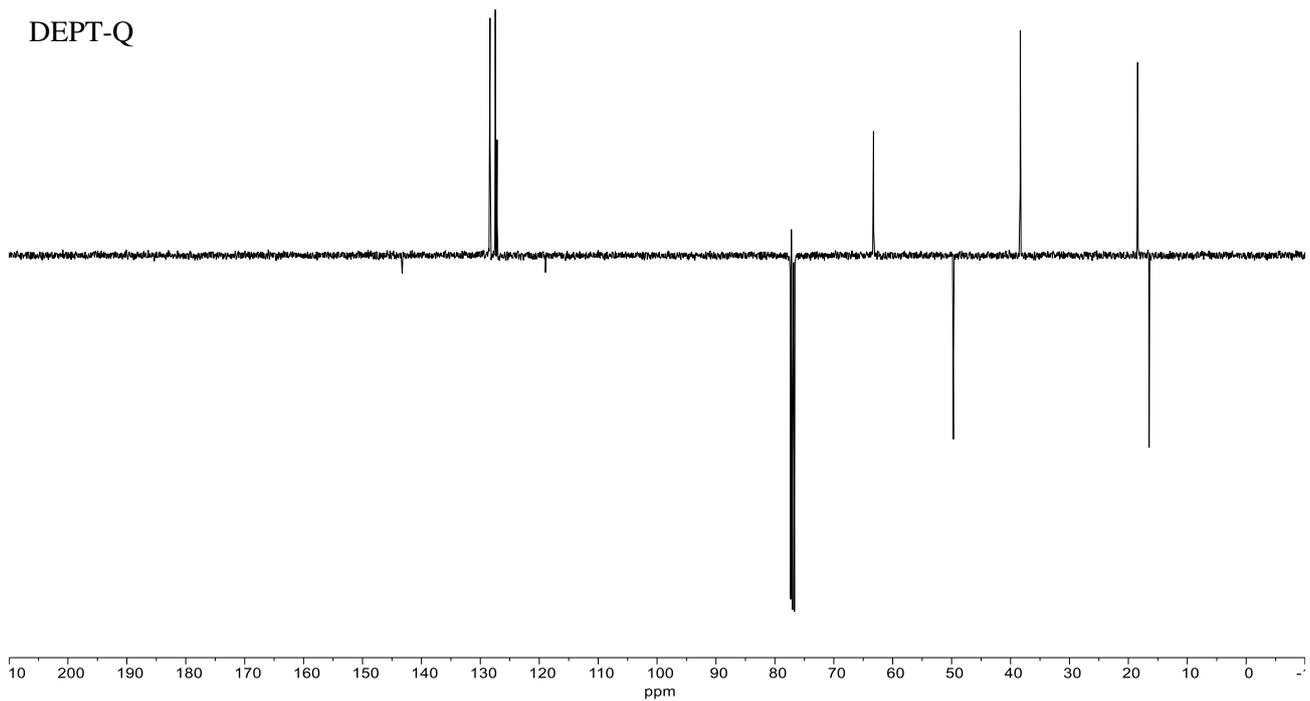
63.26

49.70

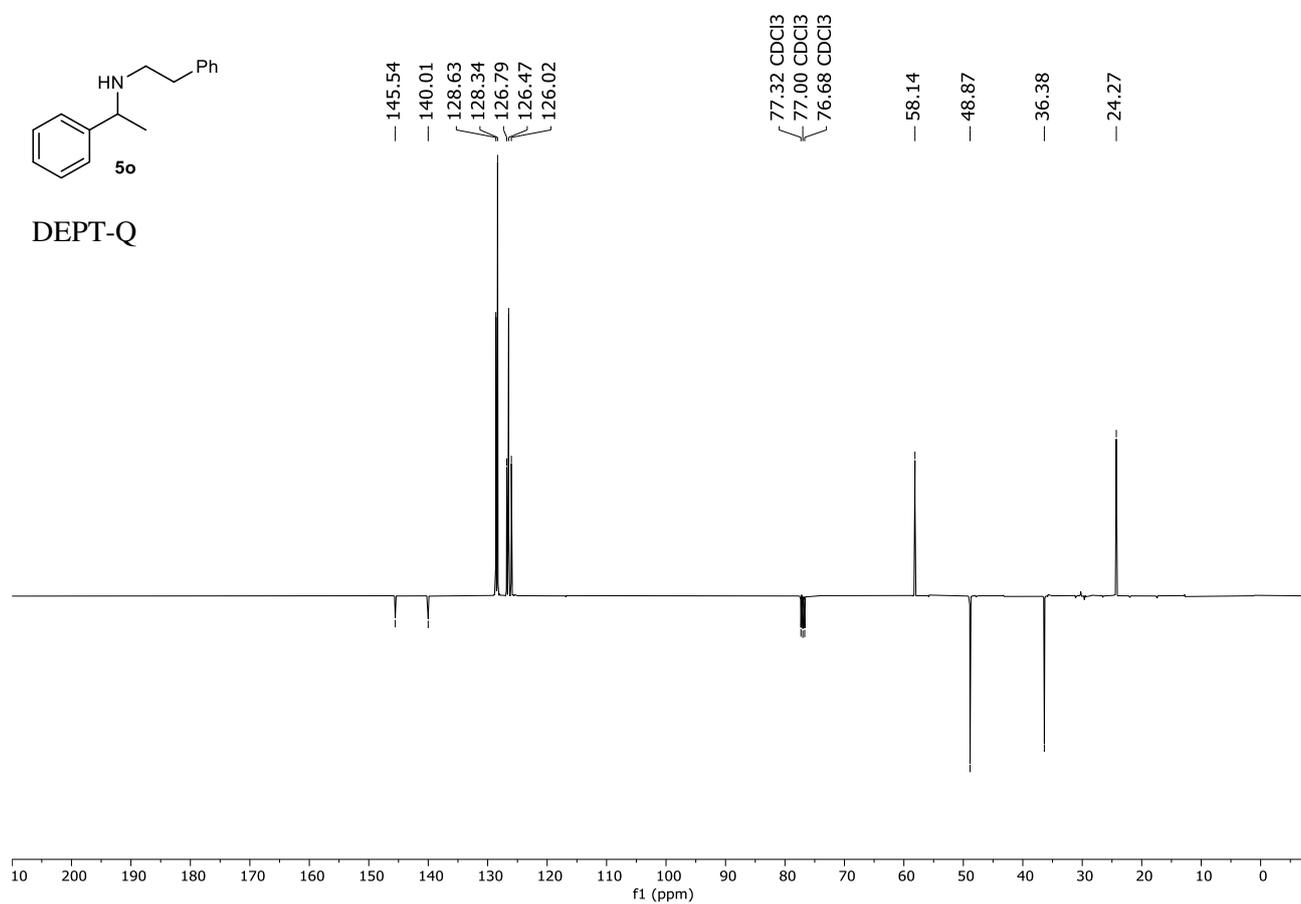
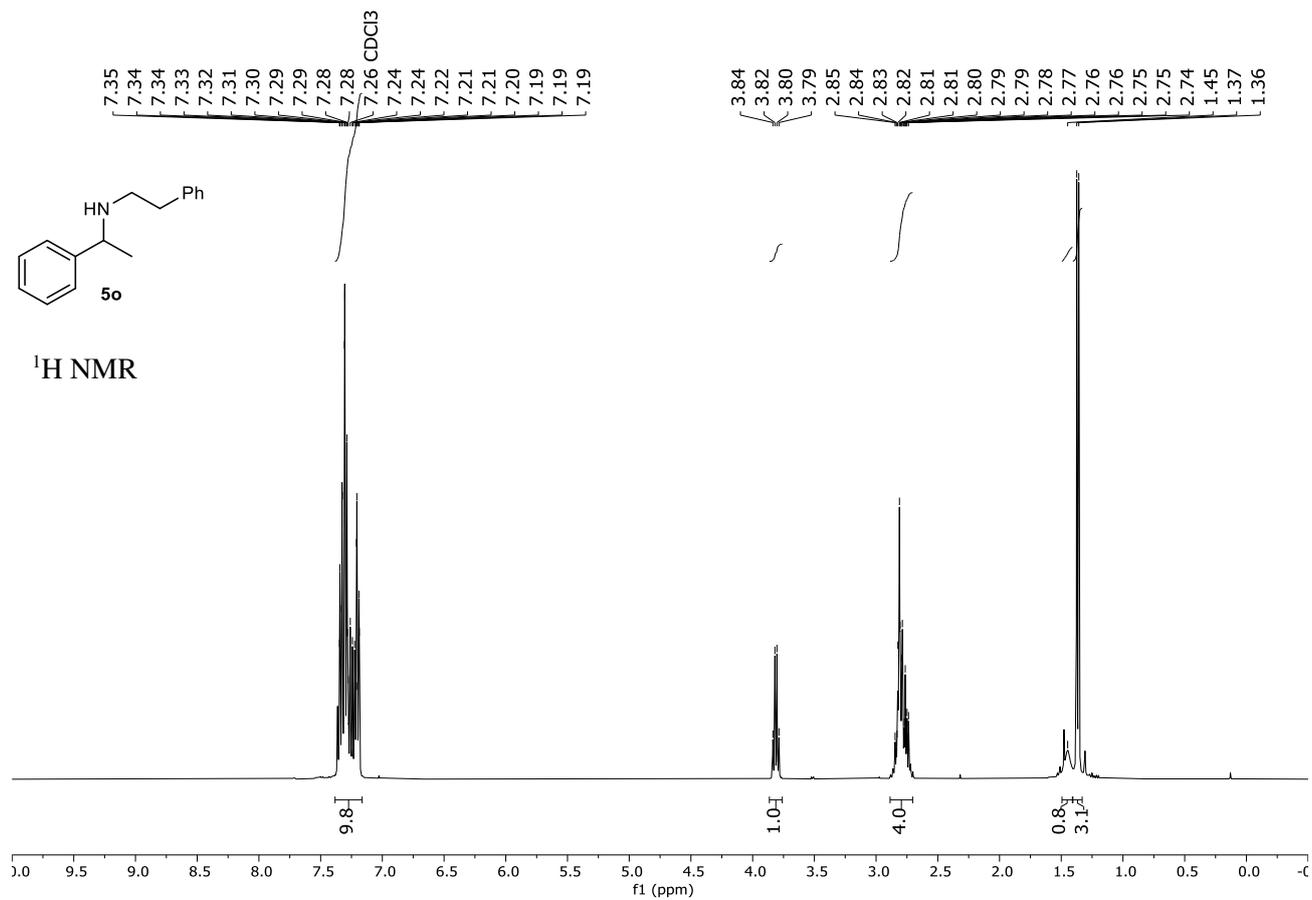
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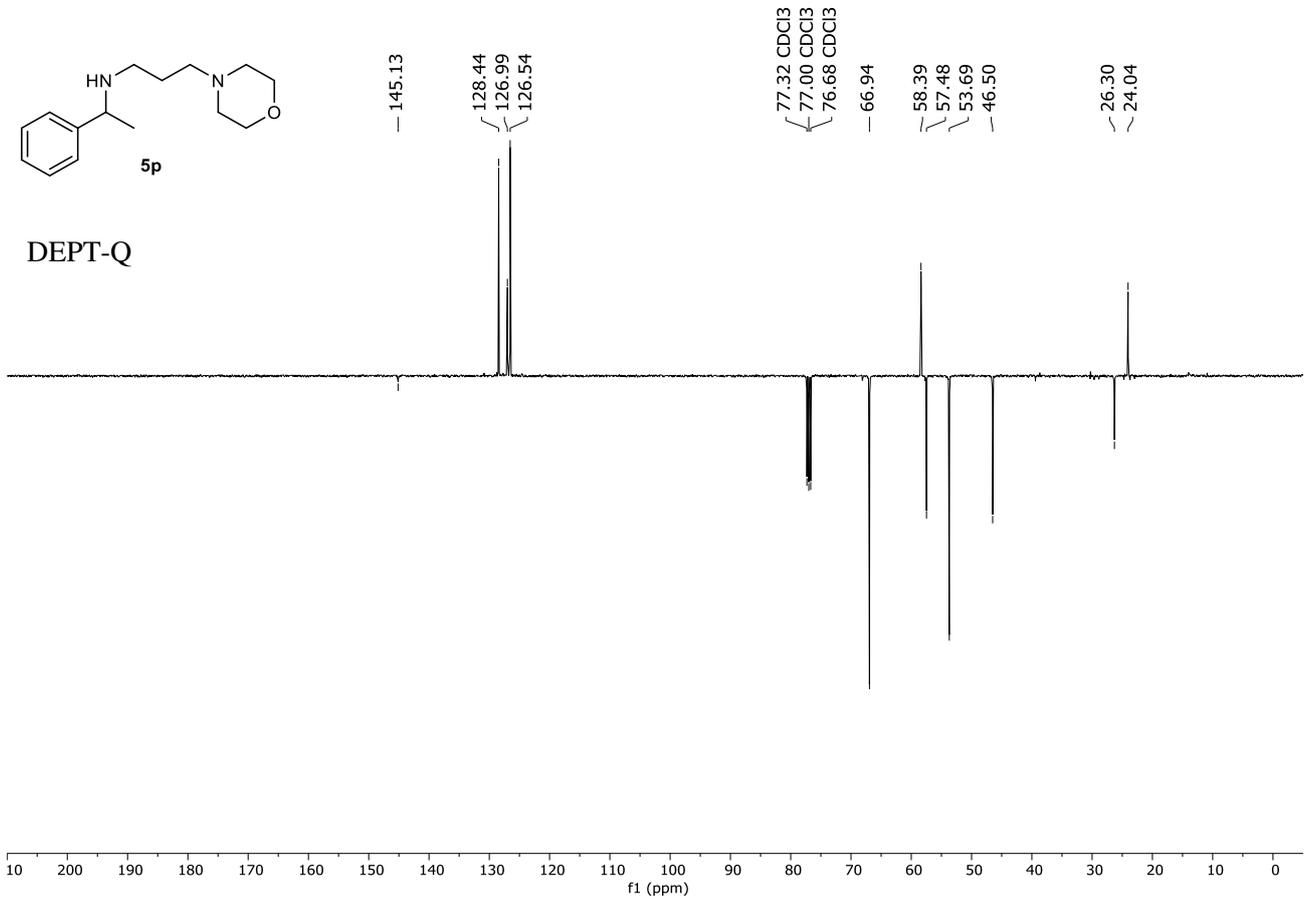
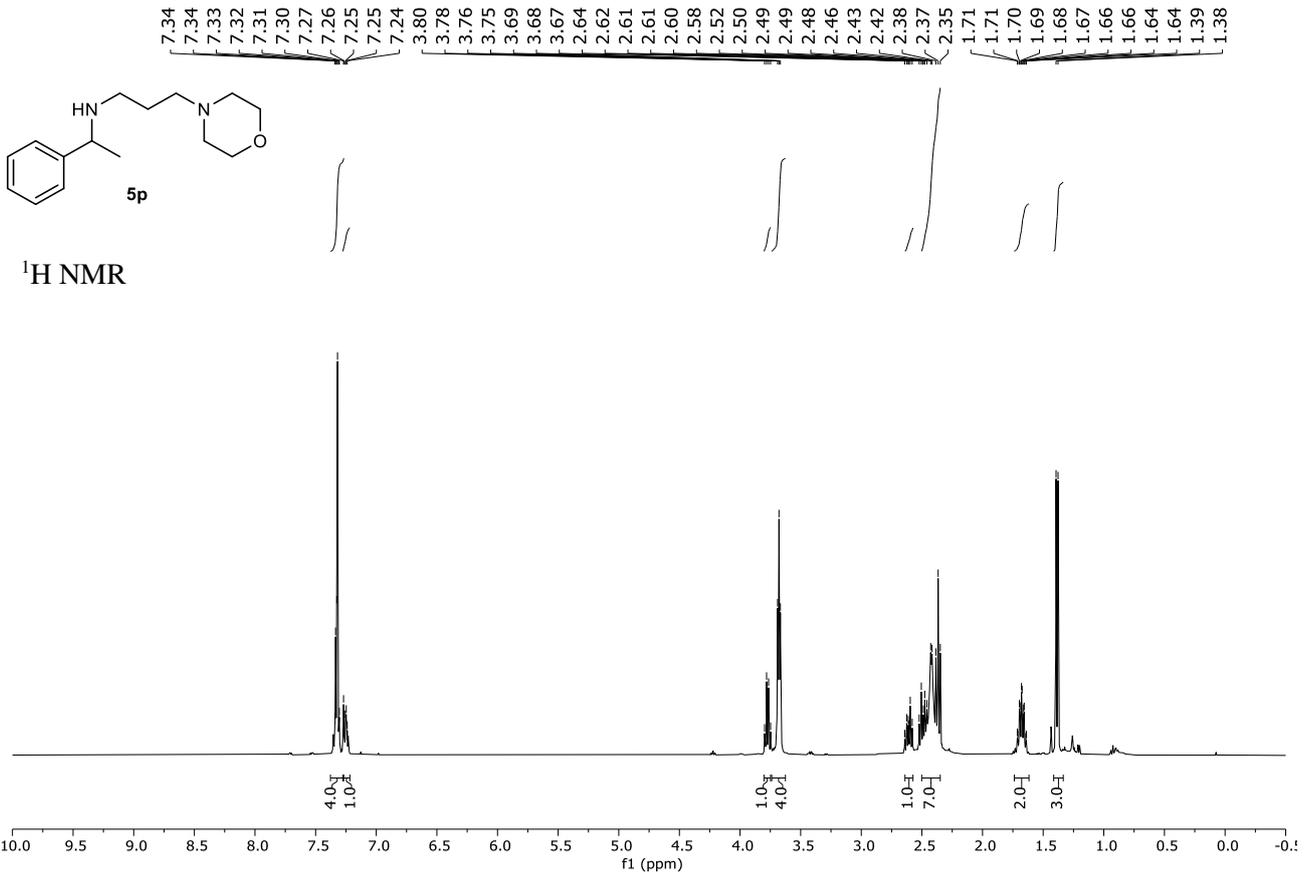
18.43
 16.48

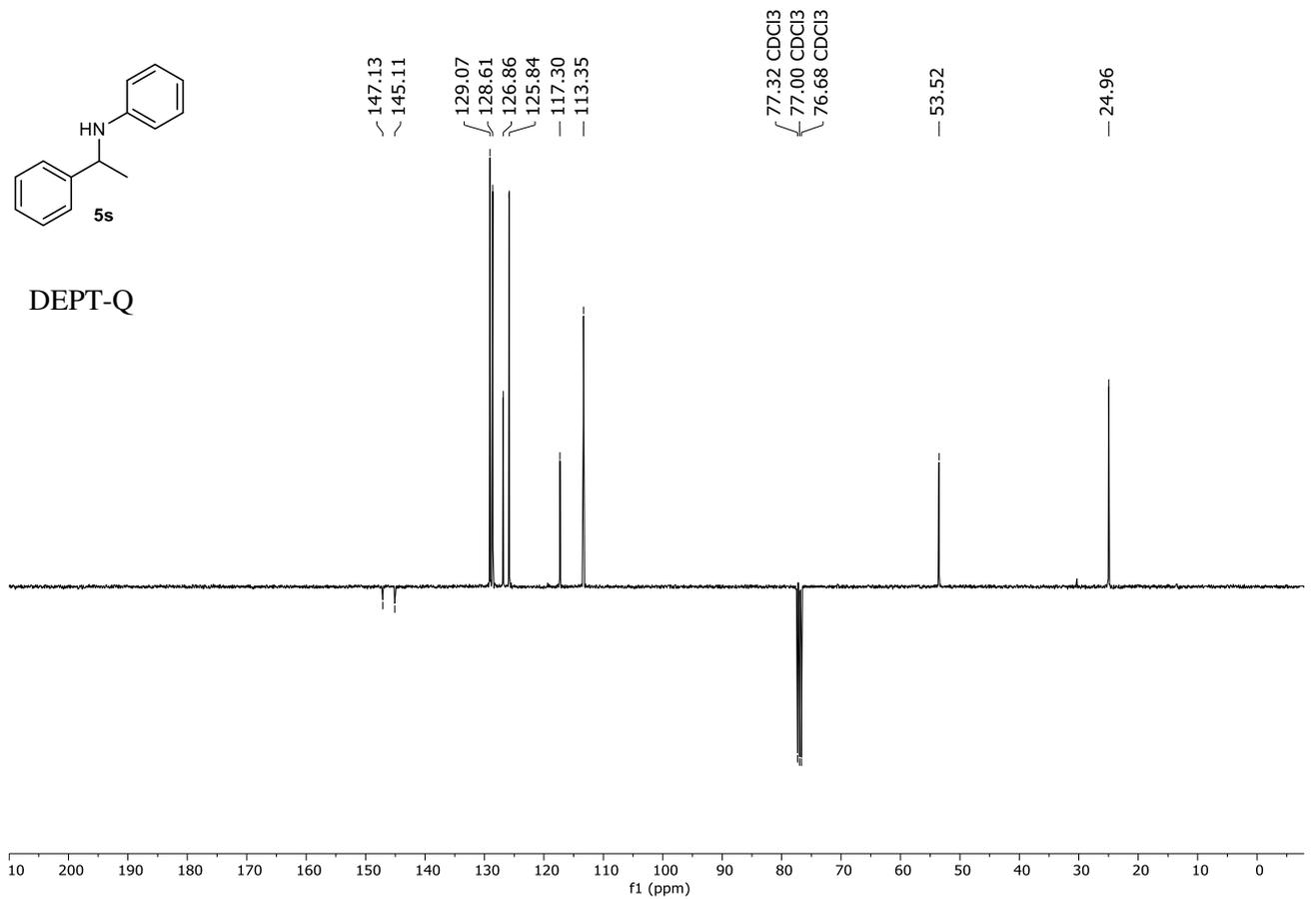
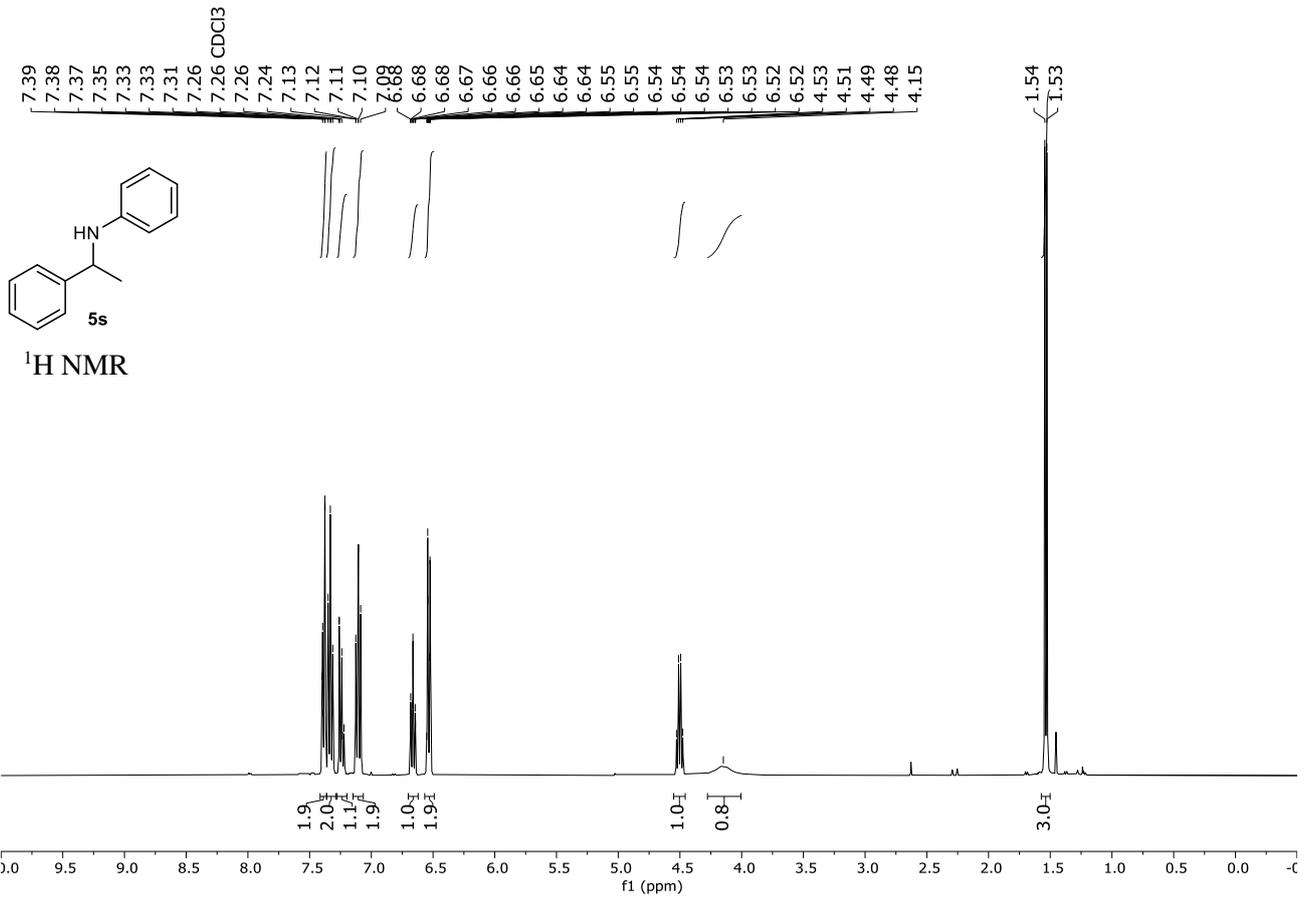
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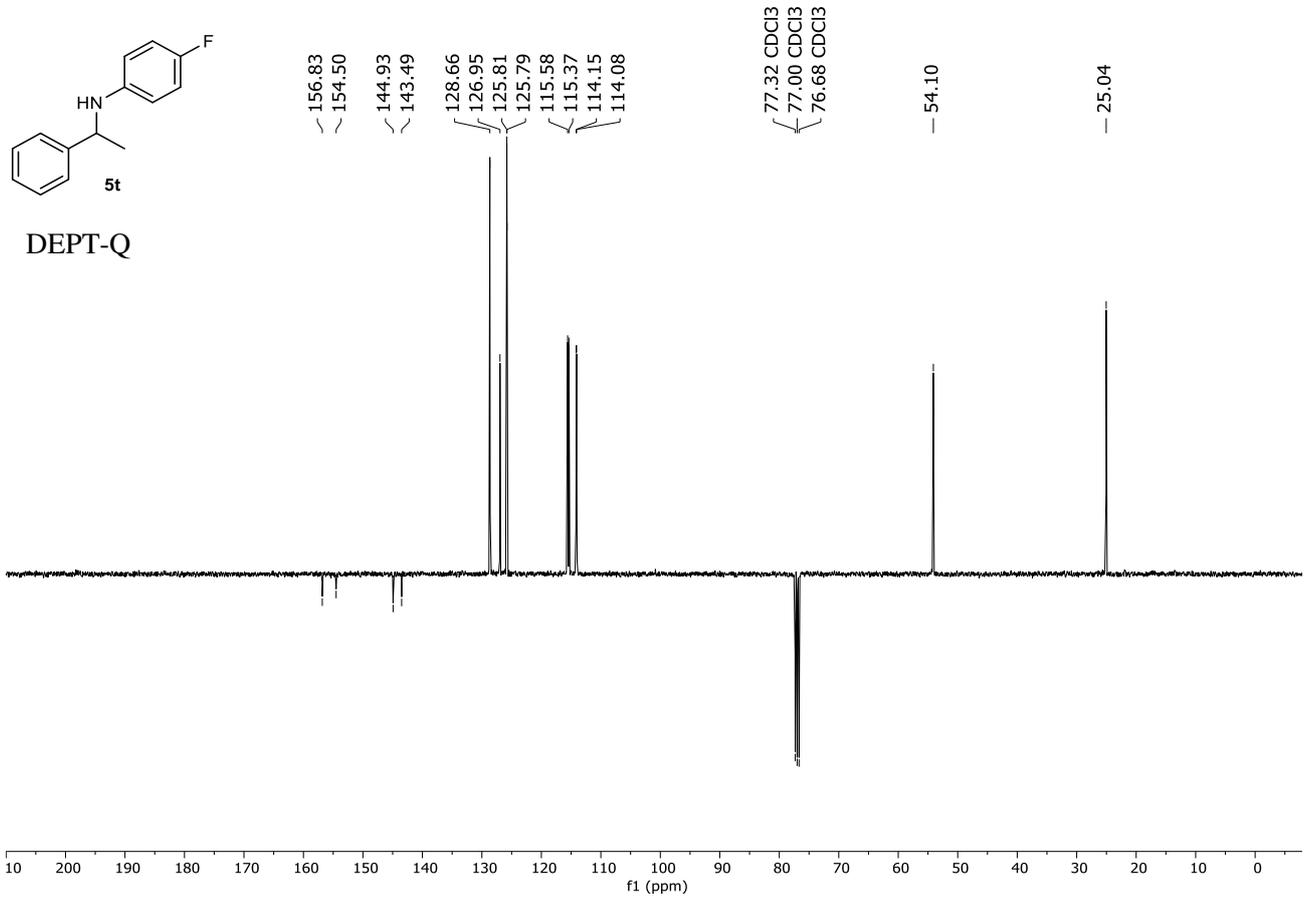
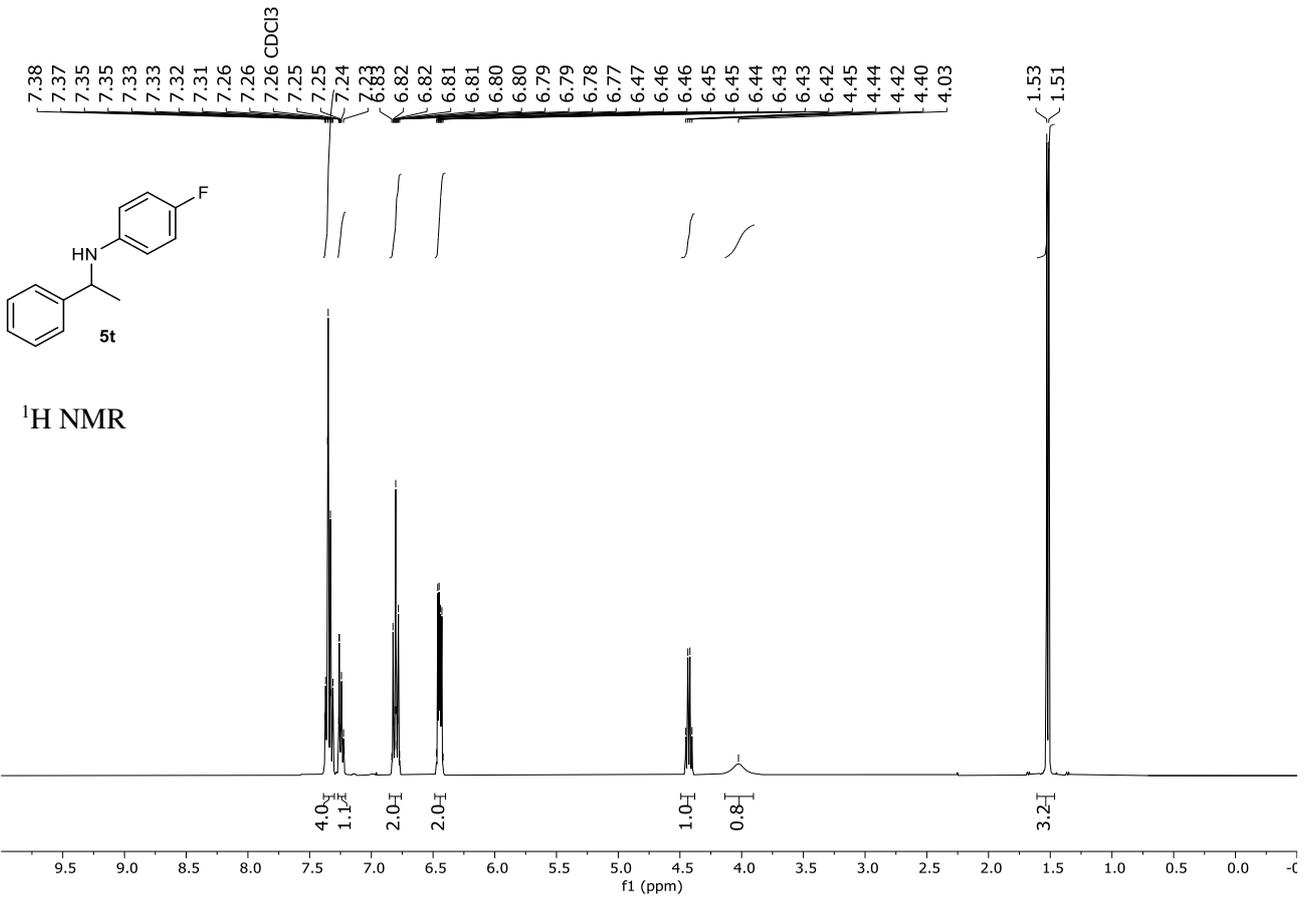


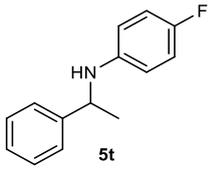
4.3. Coupling of Primary Amines



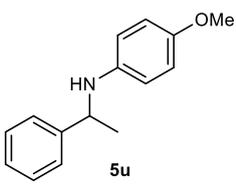
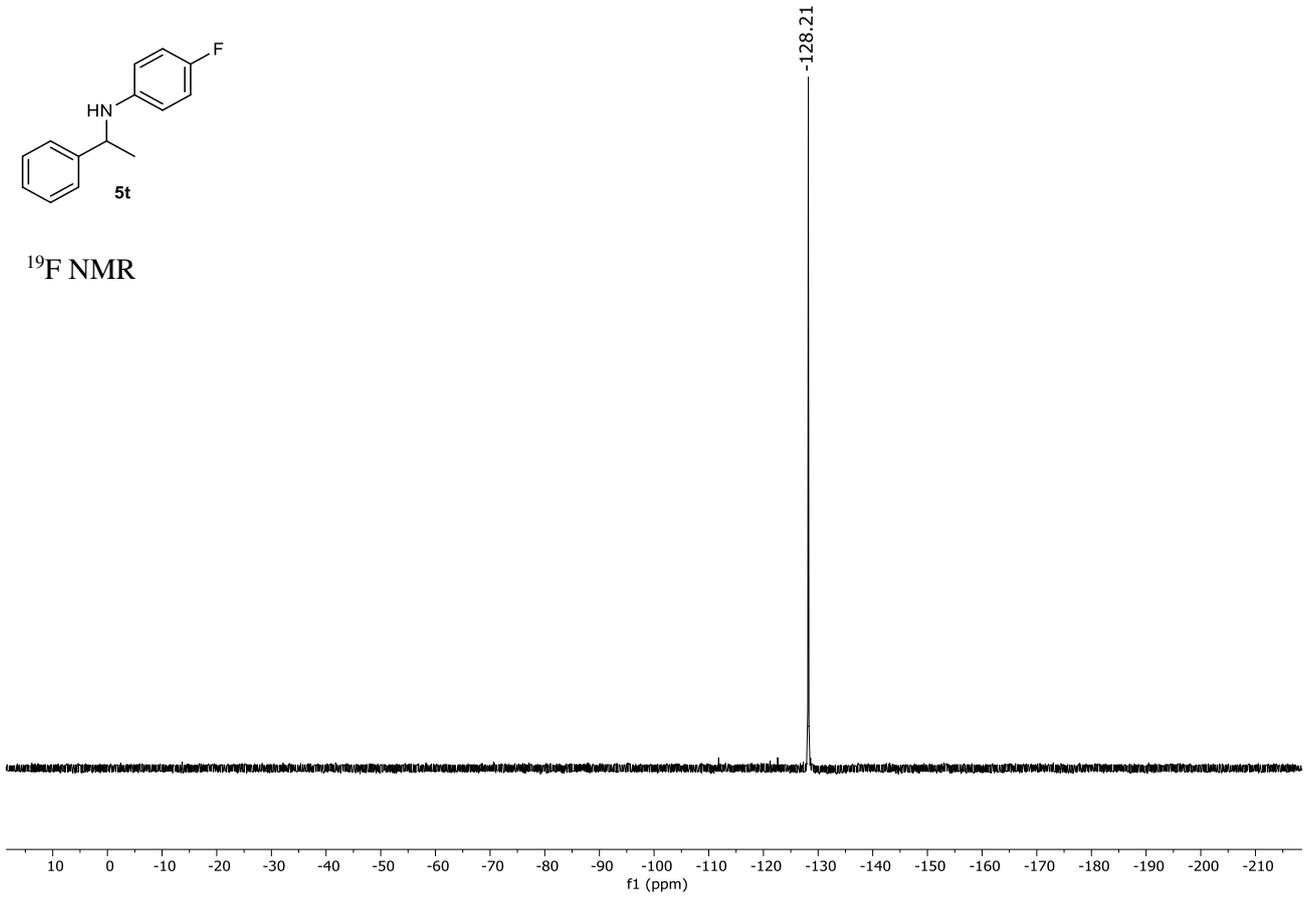




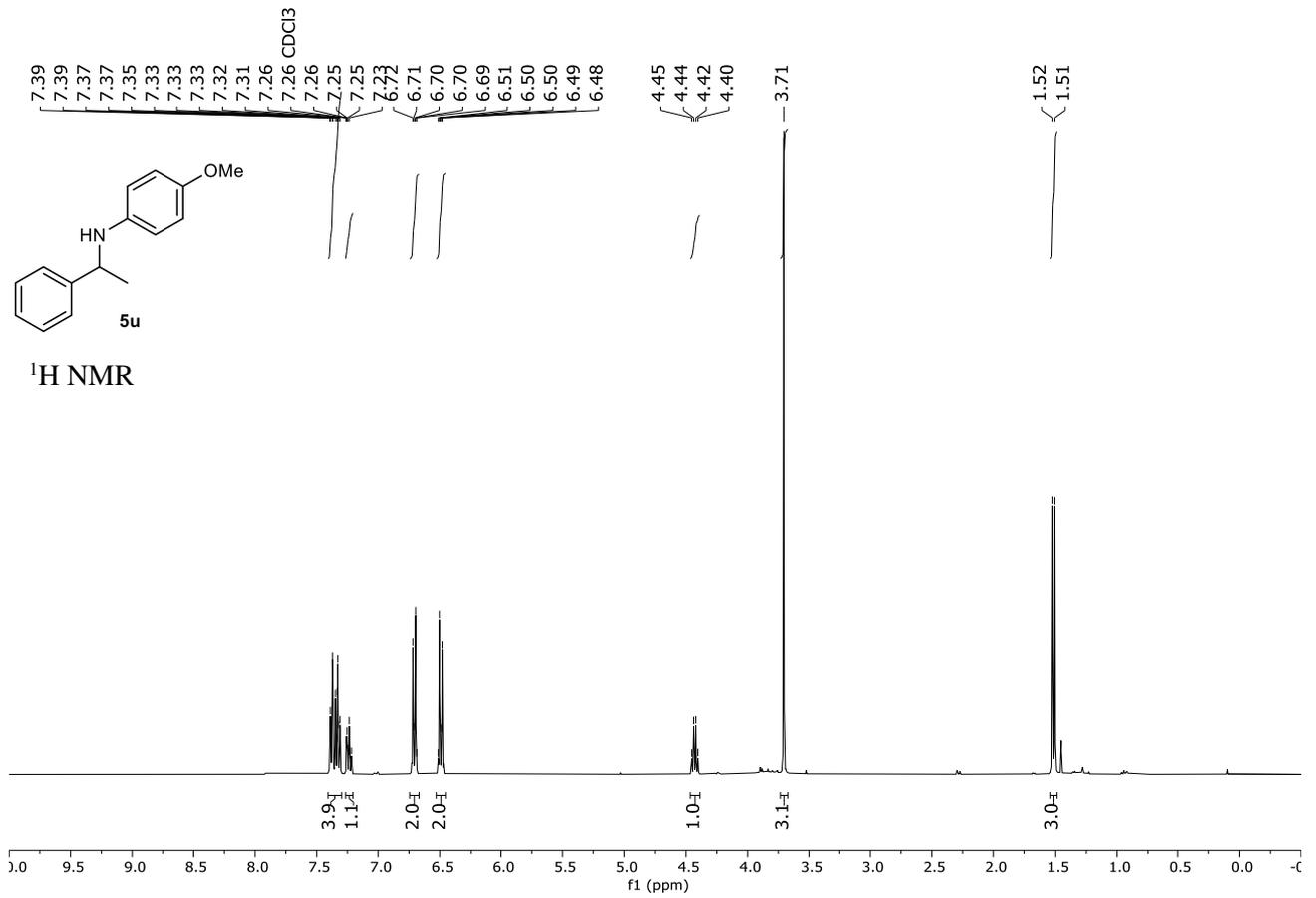


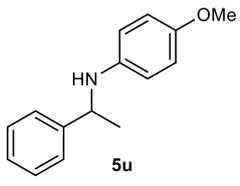


¹⁹F NMR

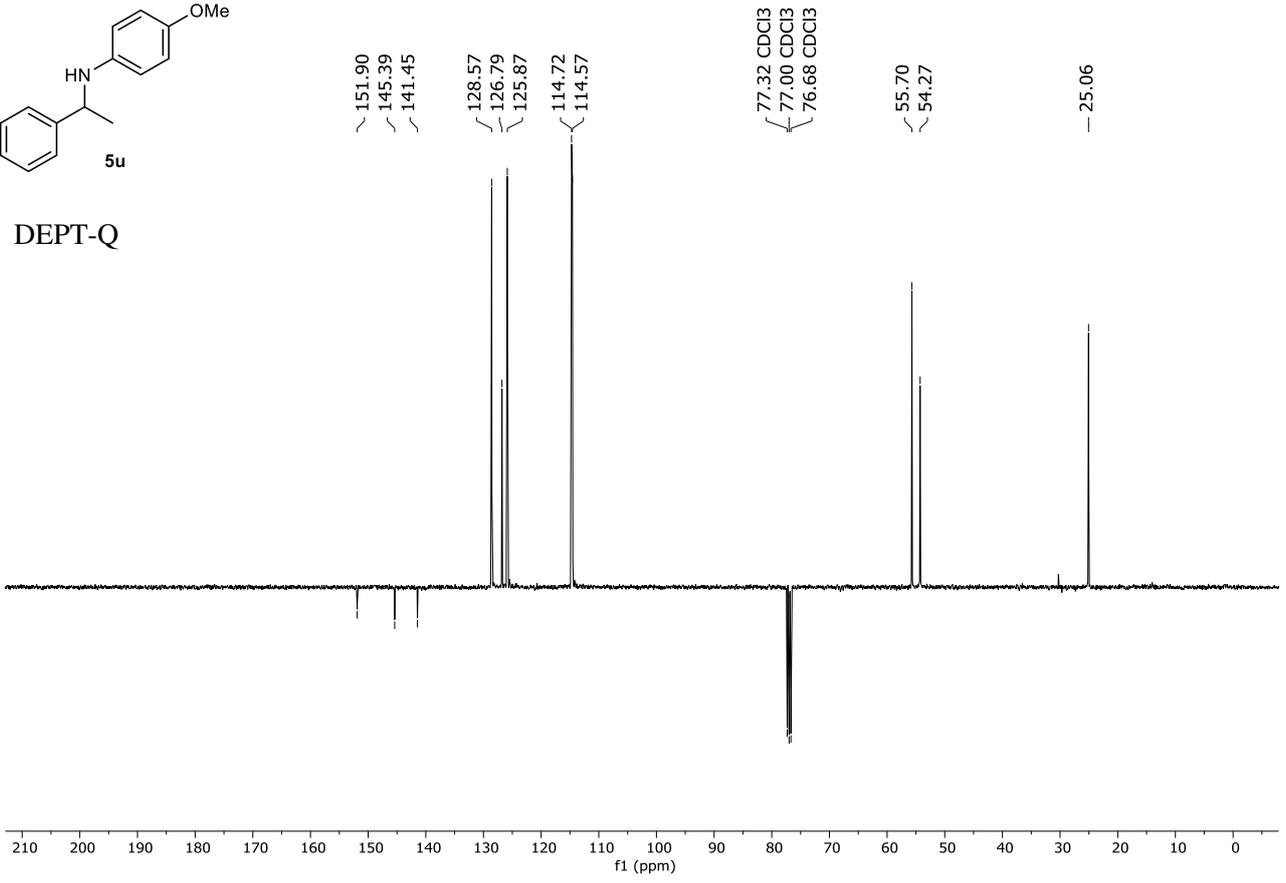


¹H NMR

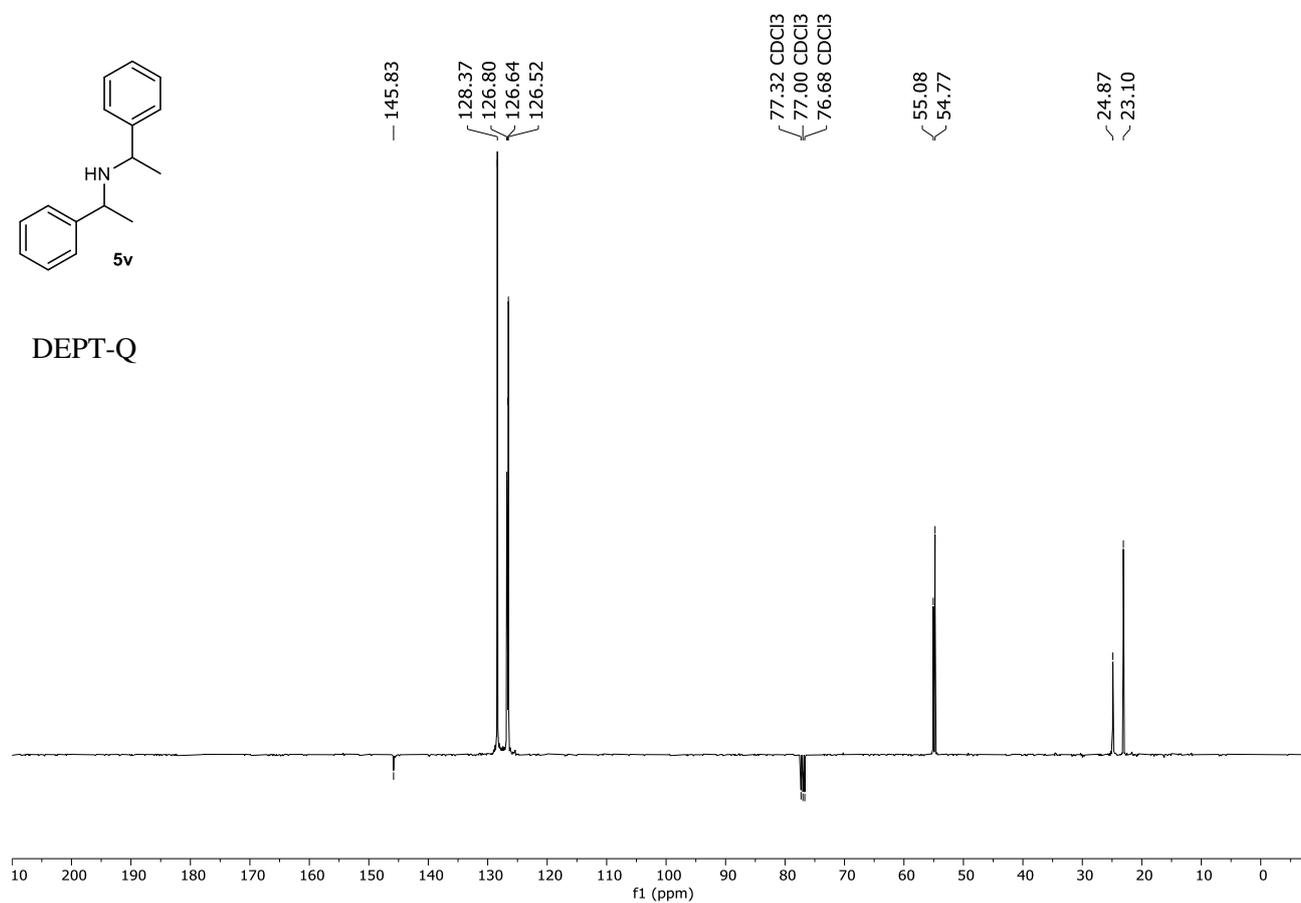
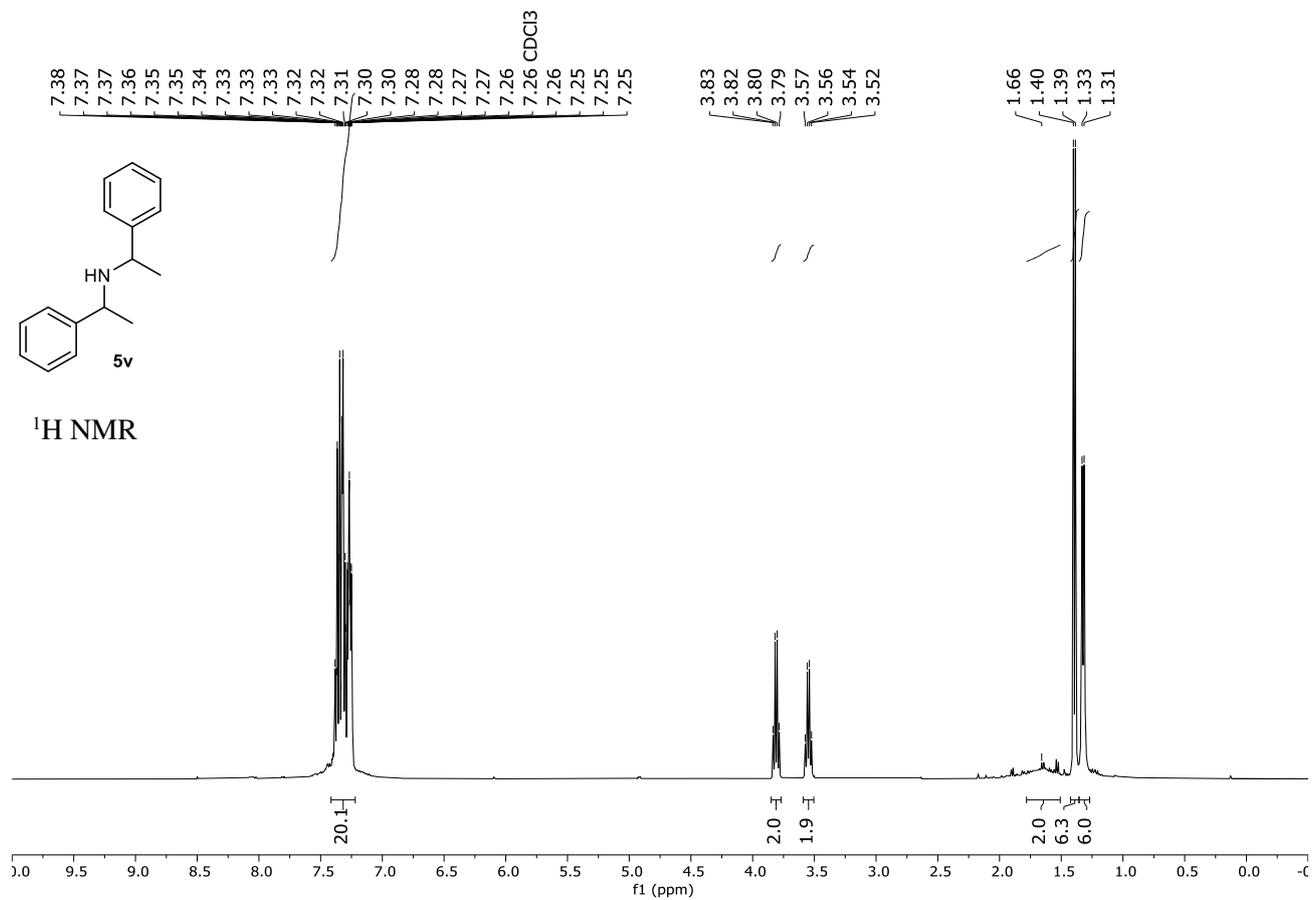


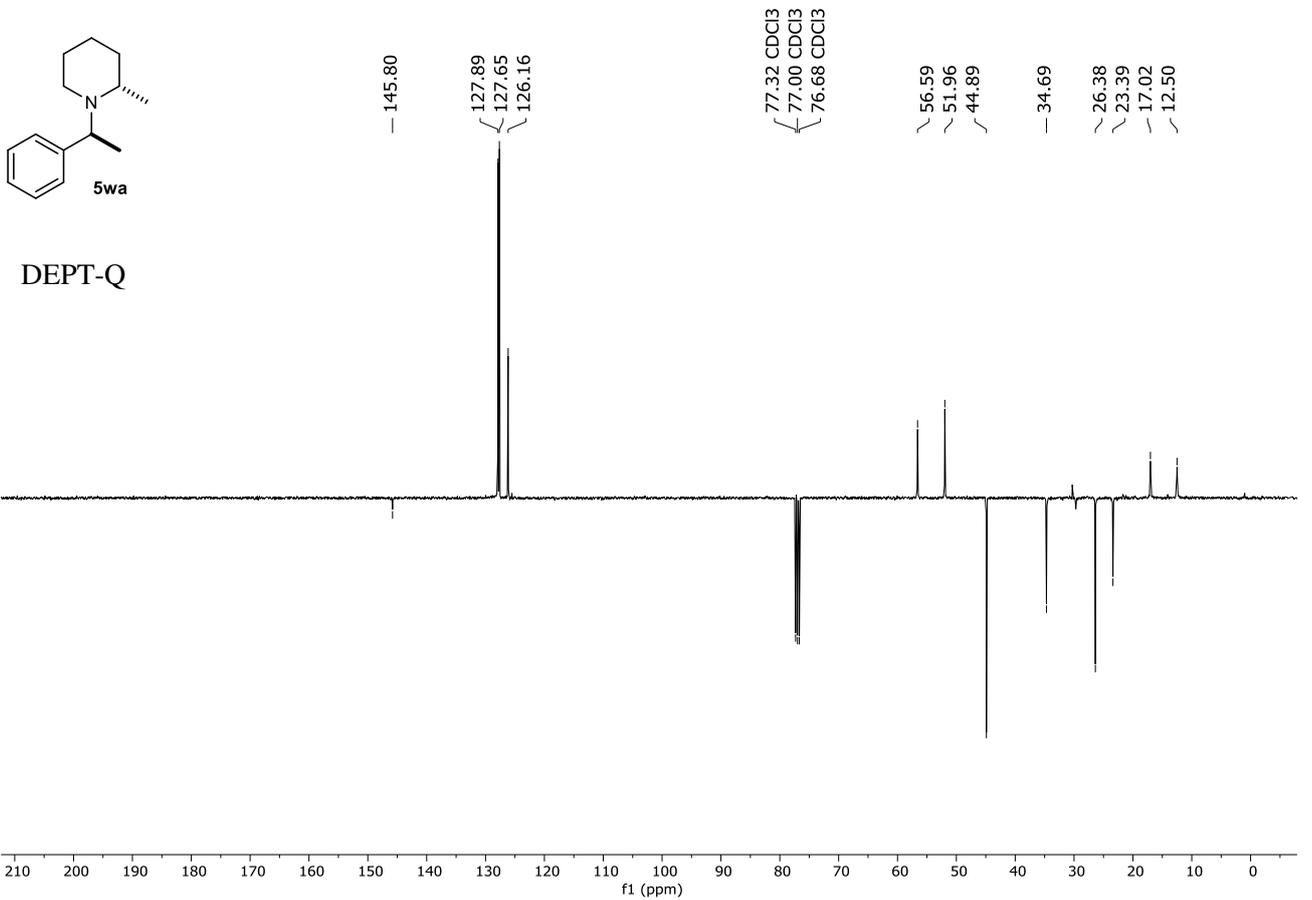
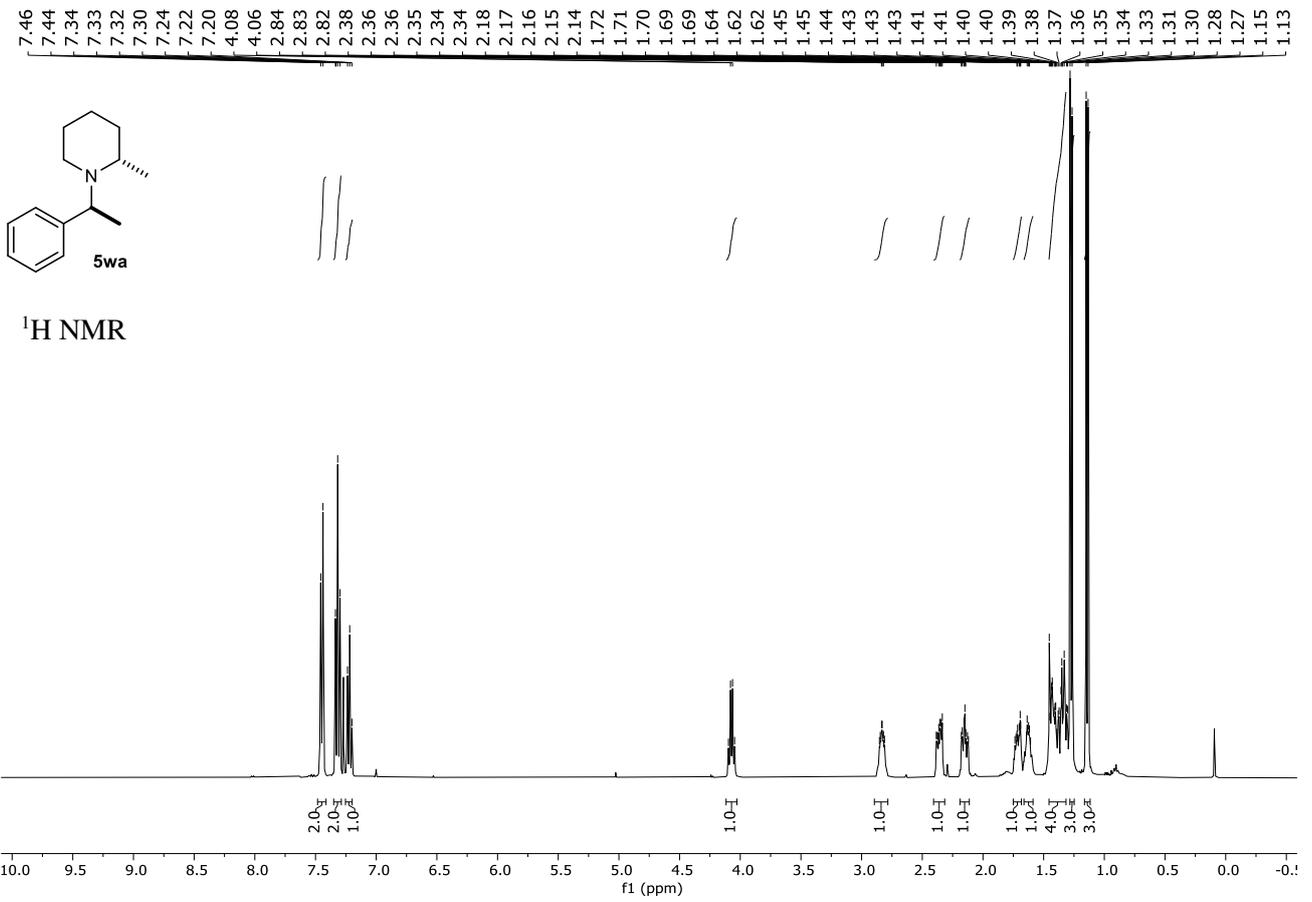


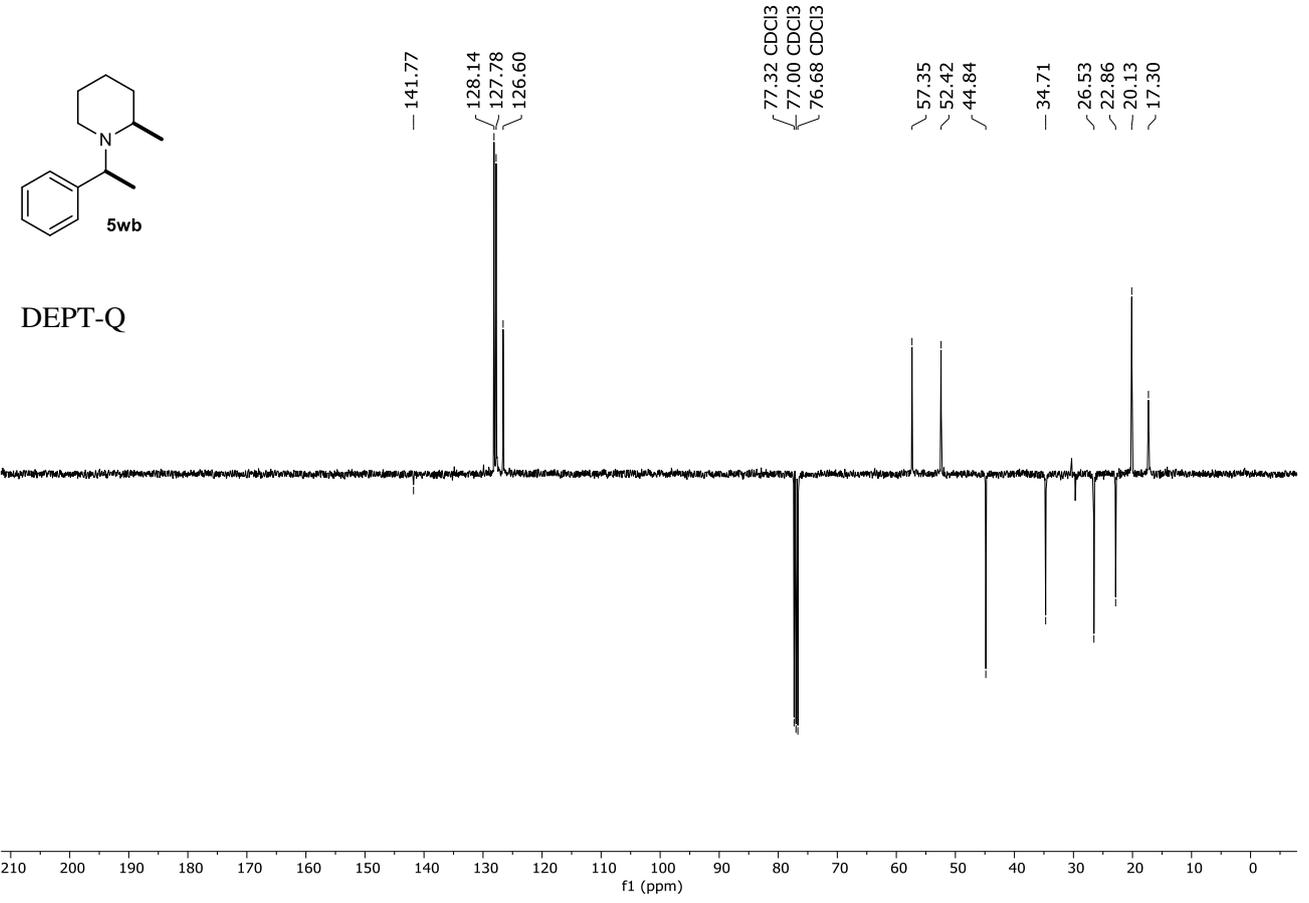
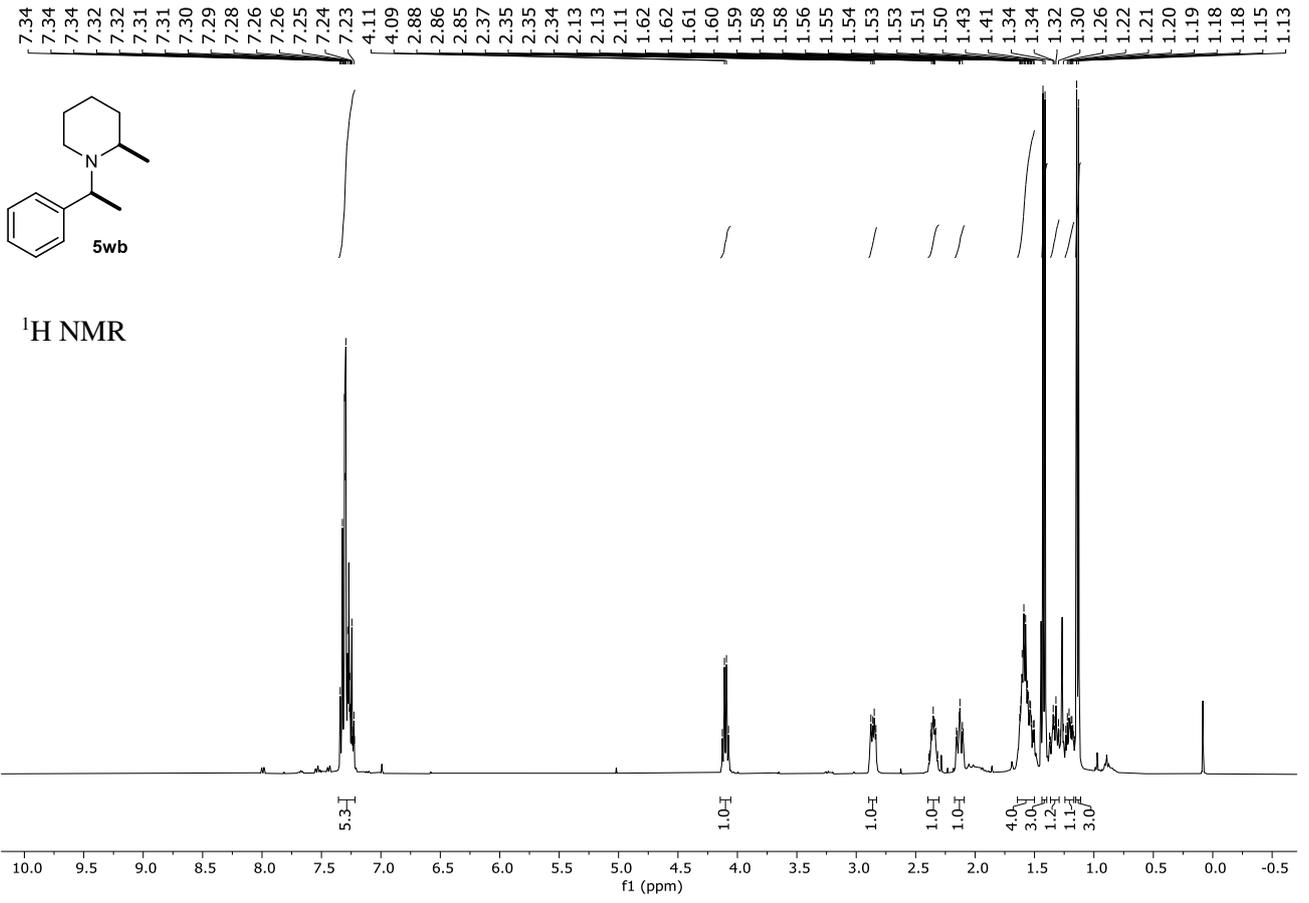
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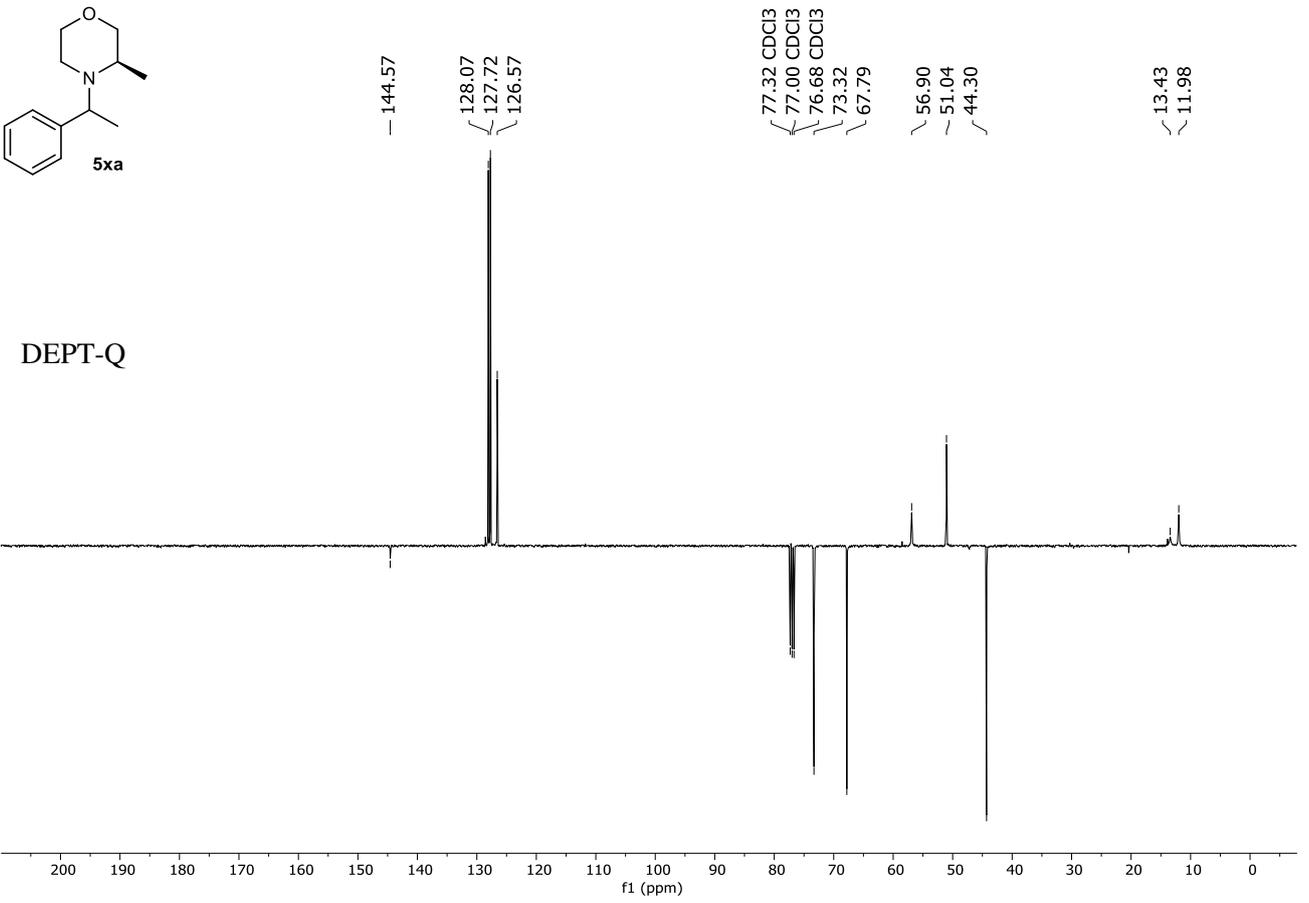
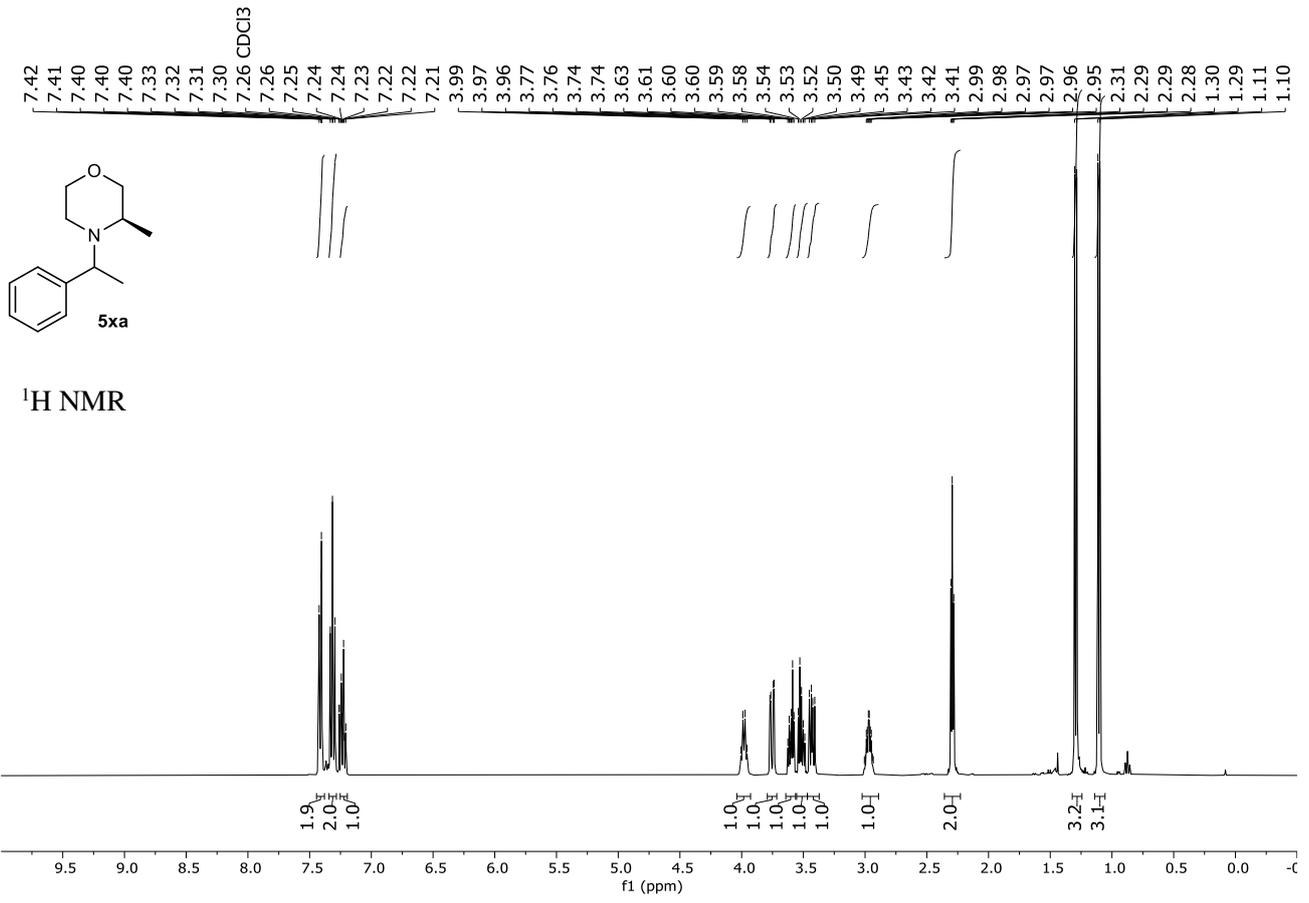


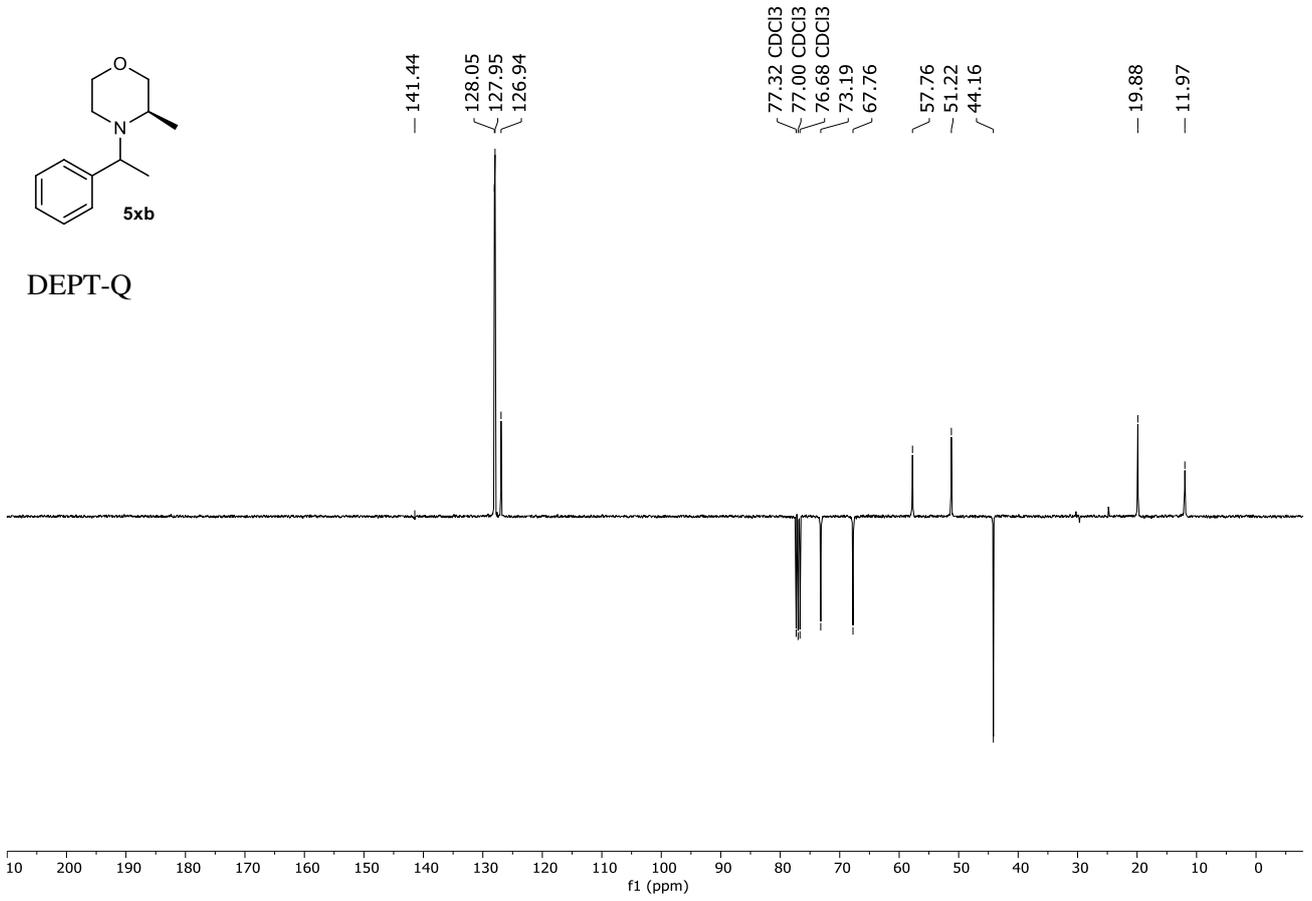
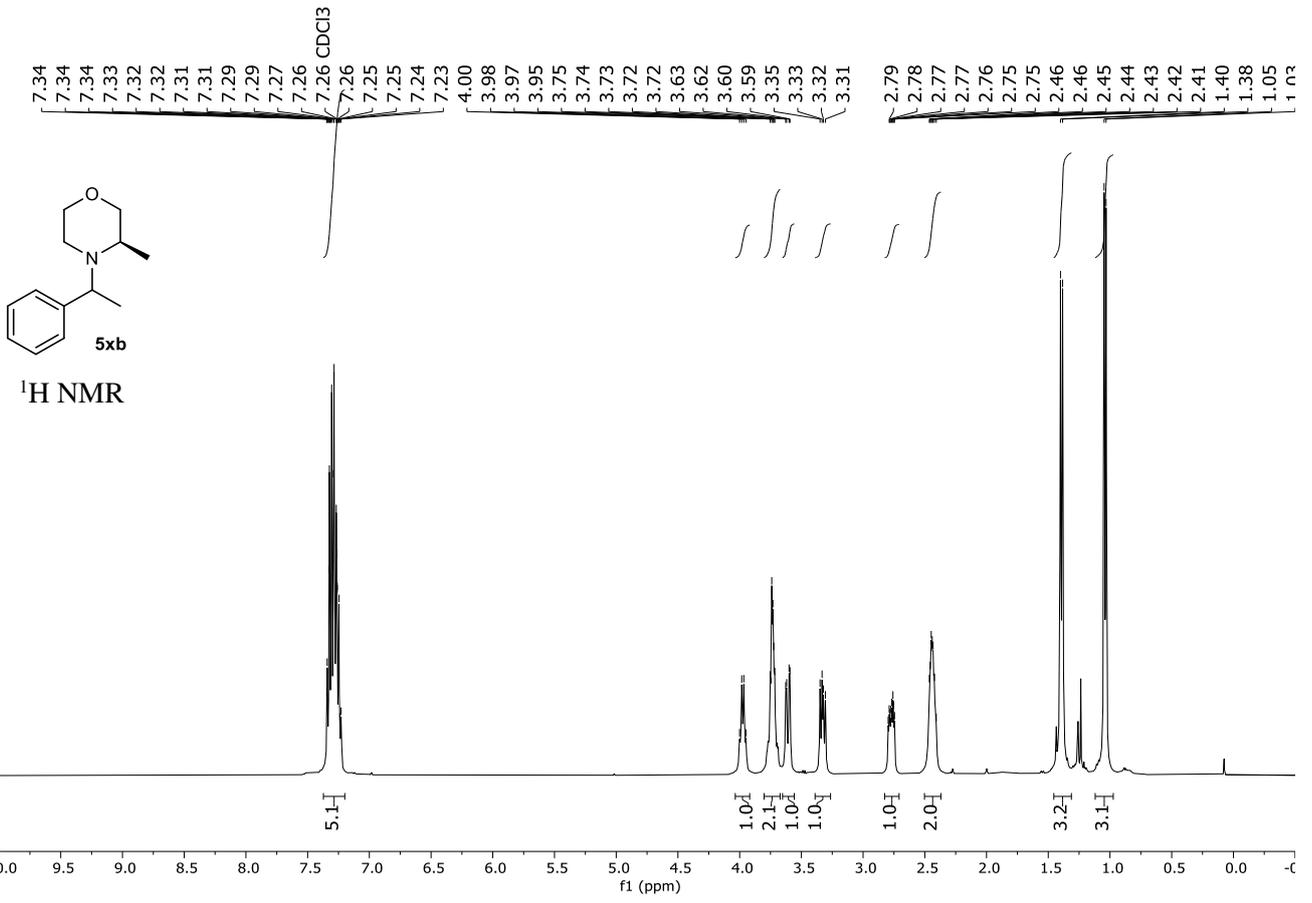
4.4. Diastereomeric Compounds

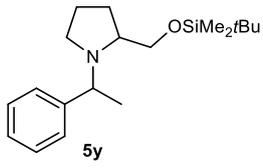




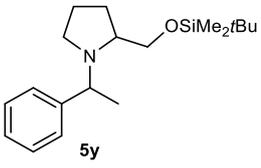
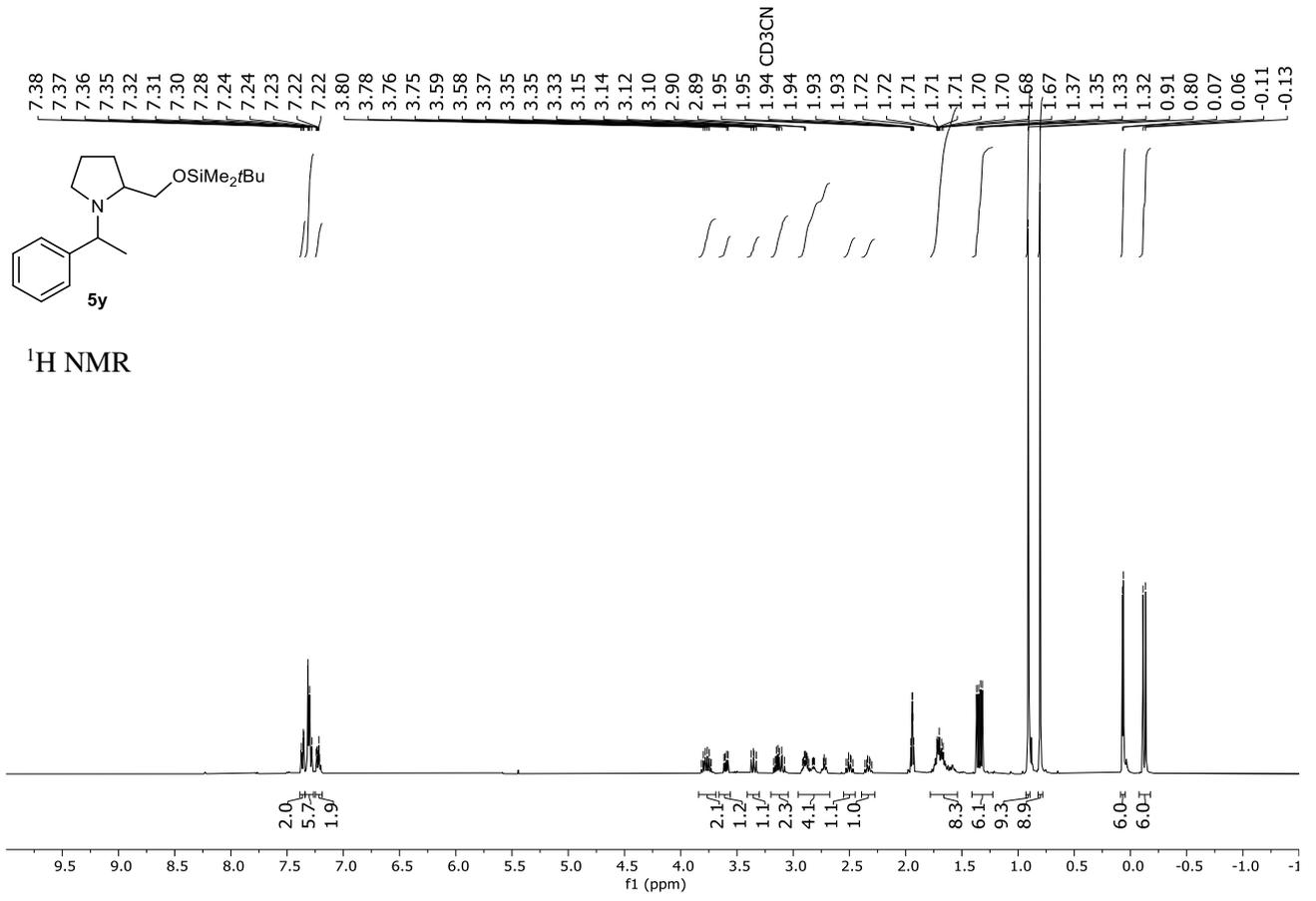




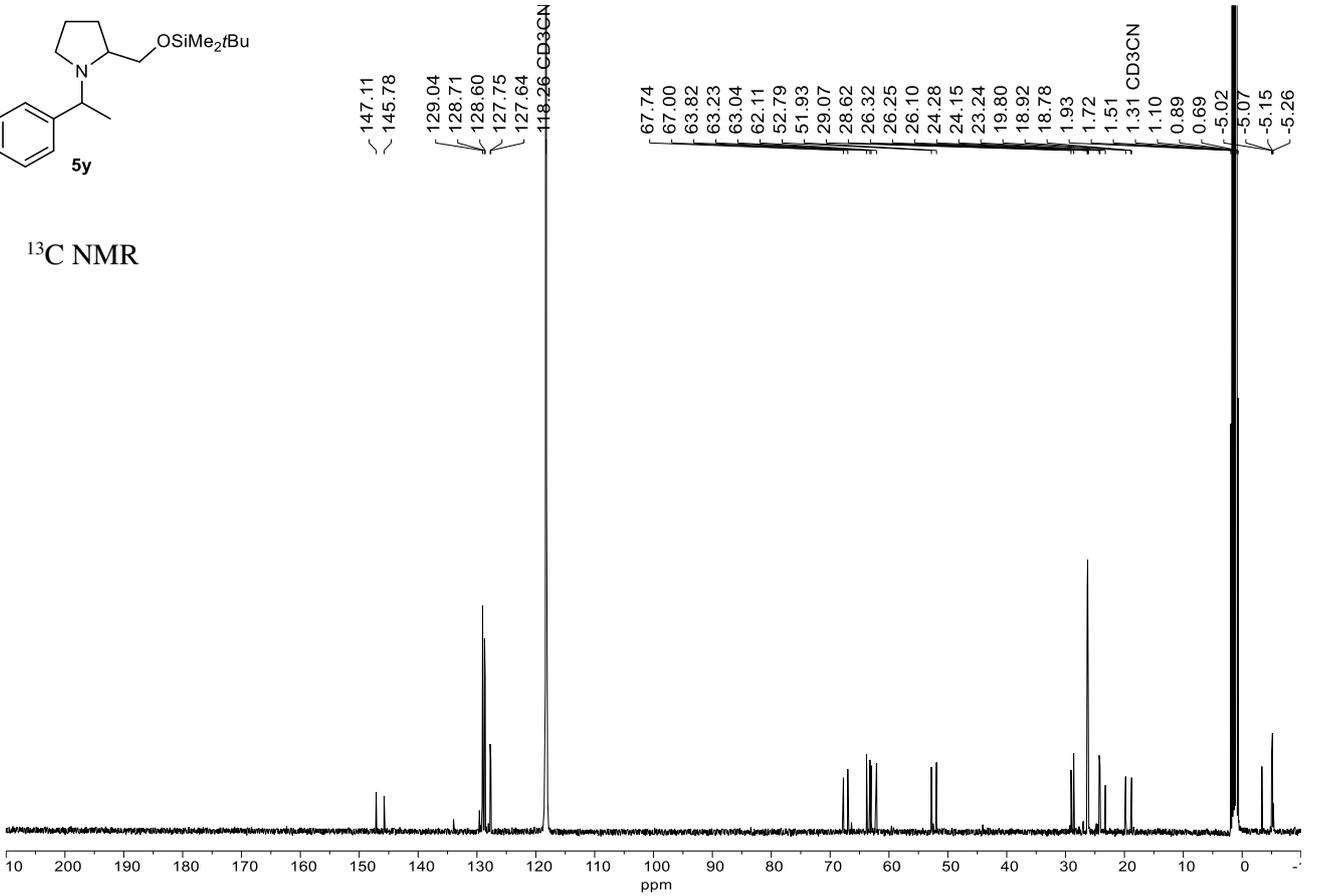


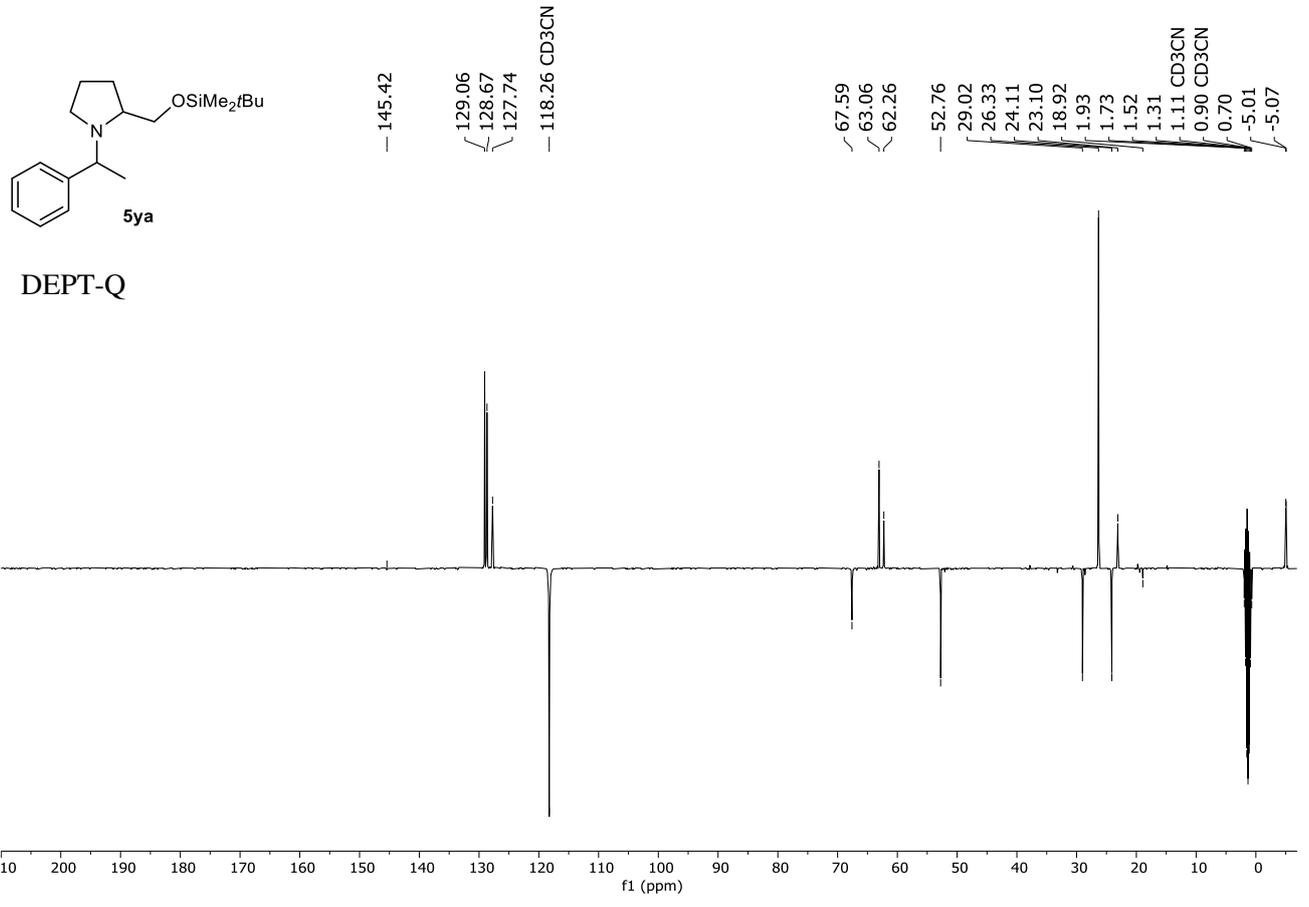
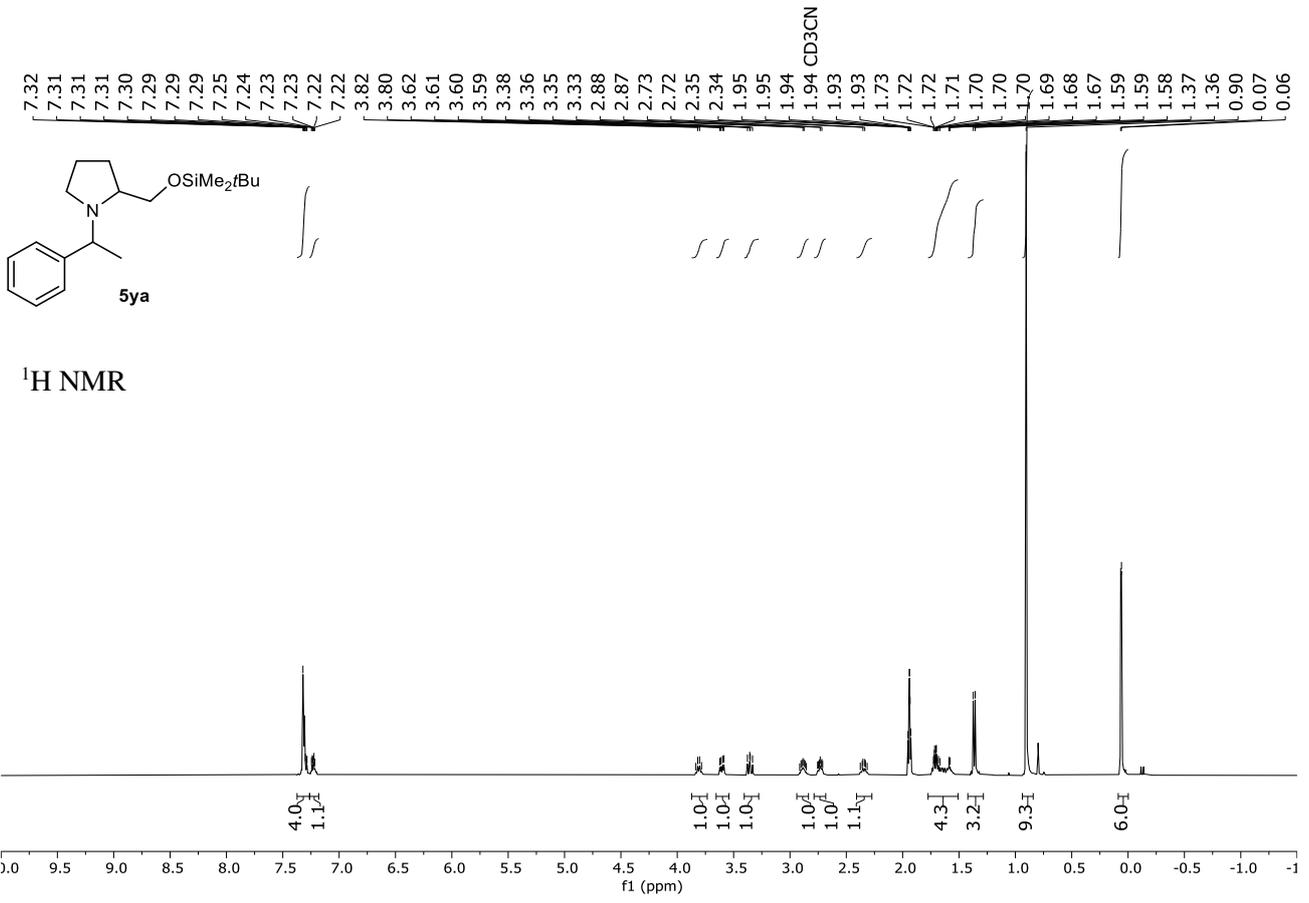


¹H NMR

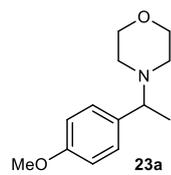


¹³C NMR

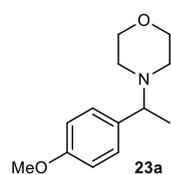
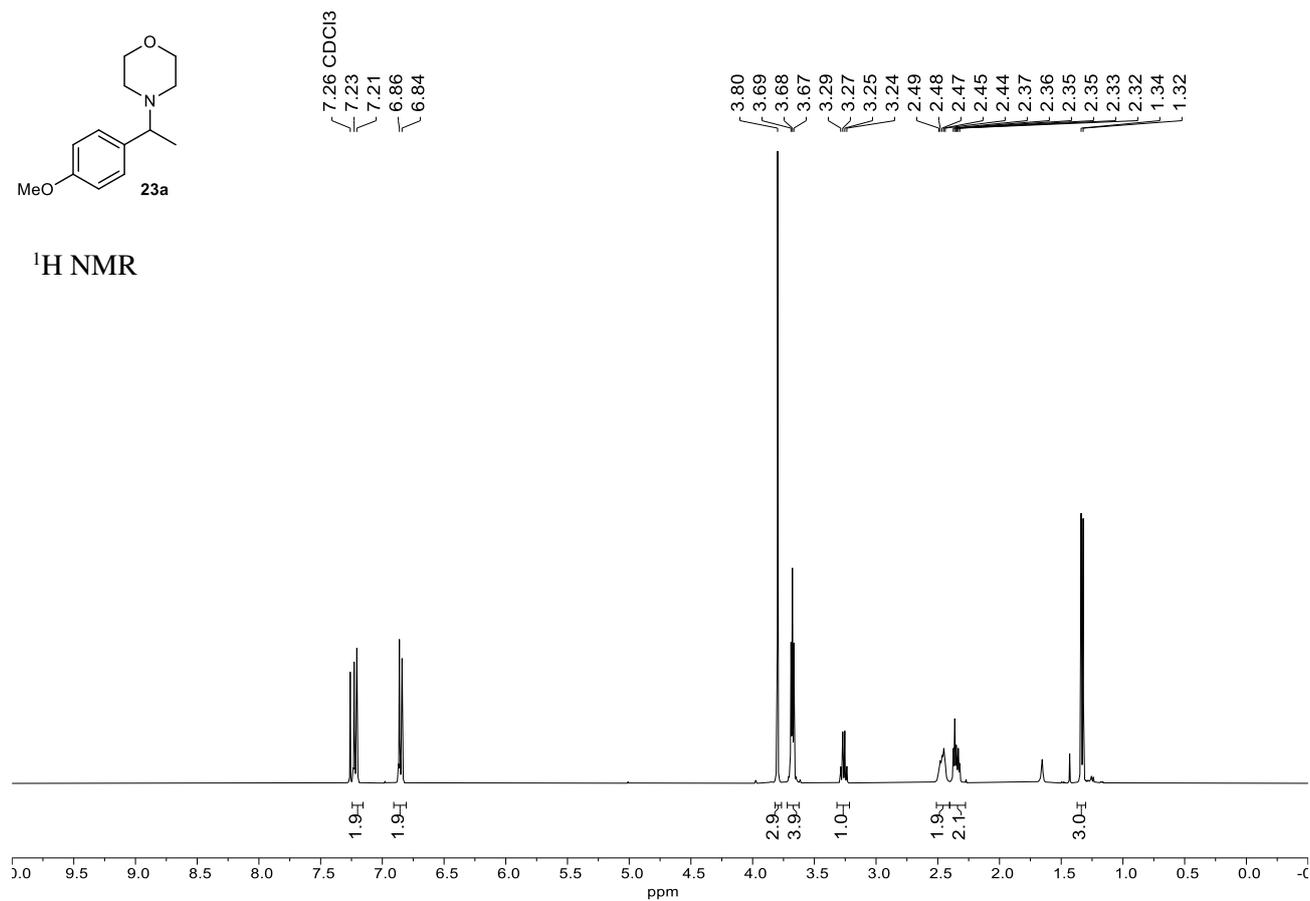




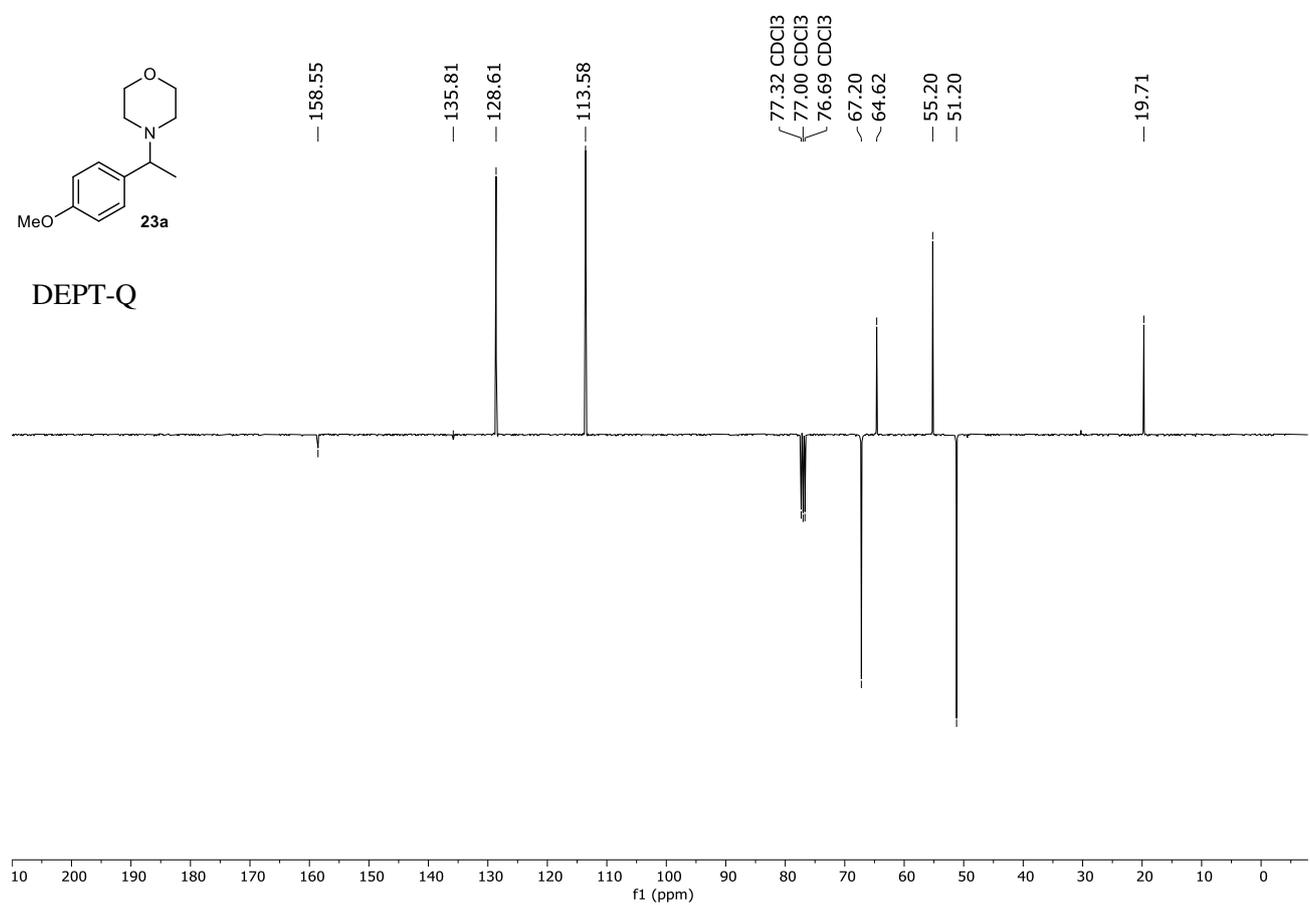
4.5. Coupling of Benzylic Boronic Esters

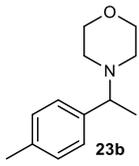


$^1\text{H NMR}$

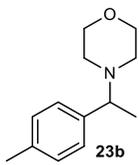
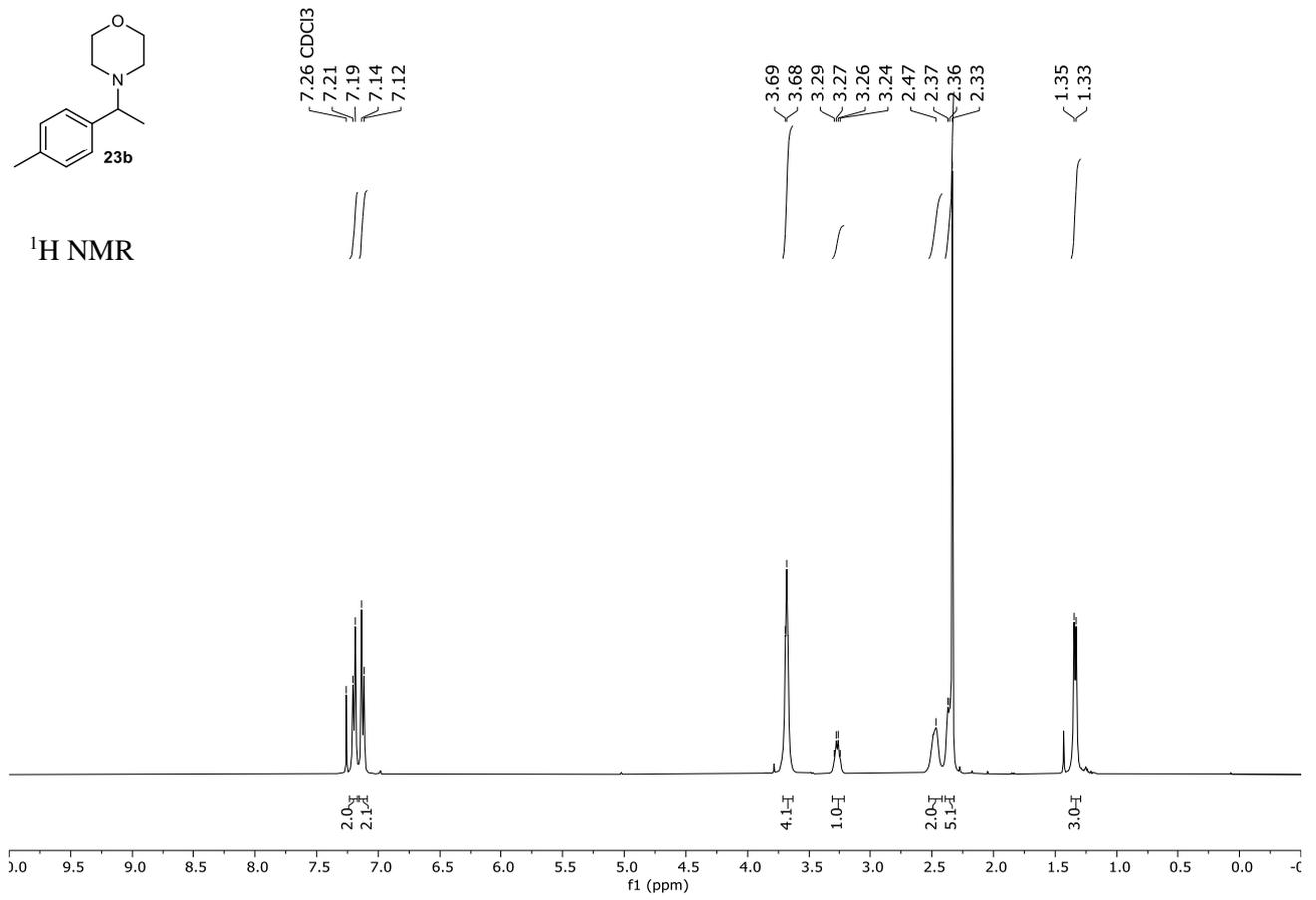


DEPT-Q

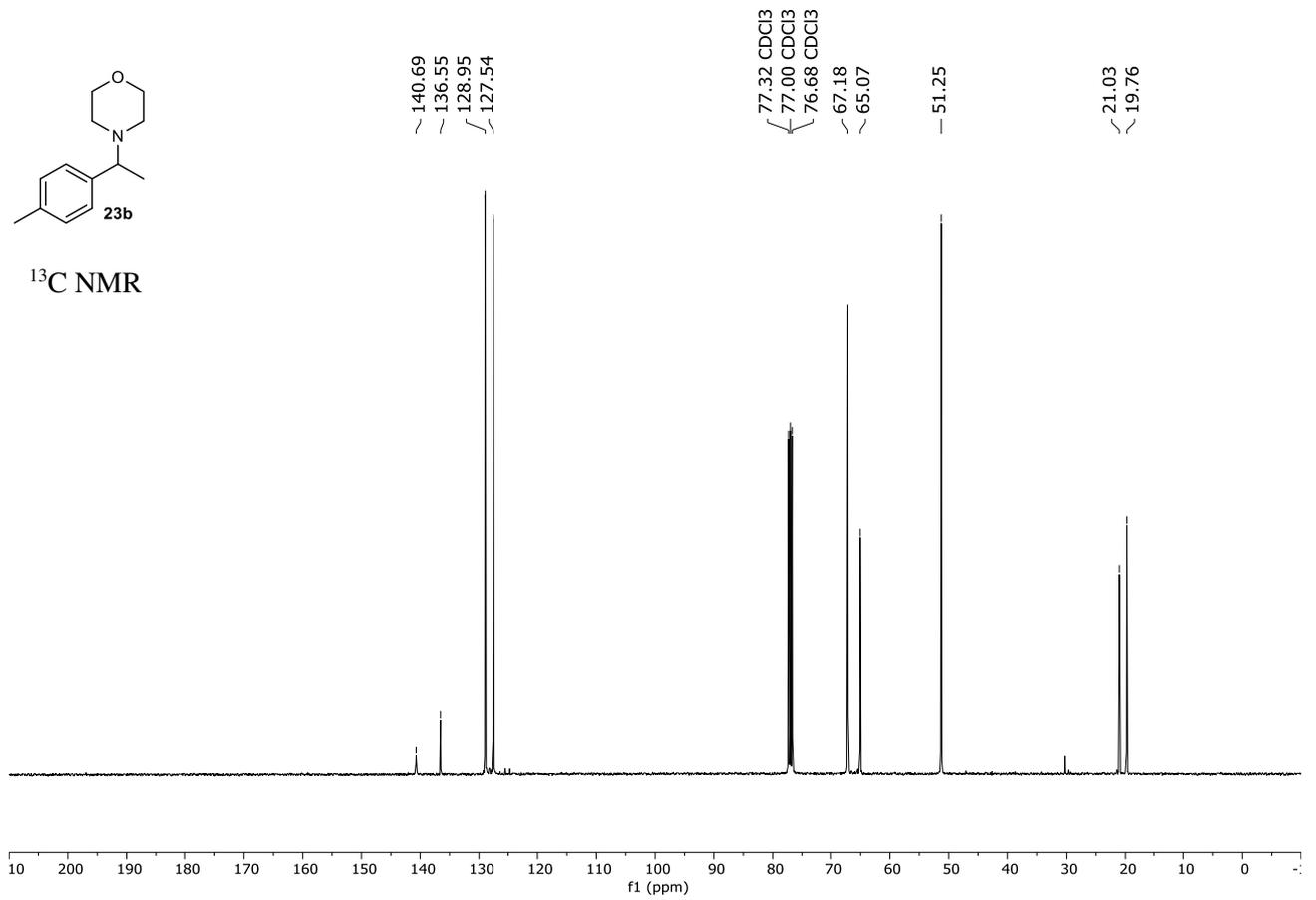


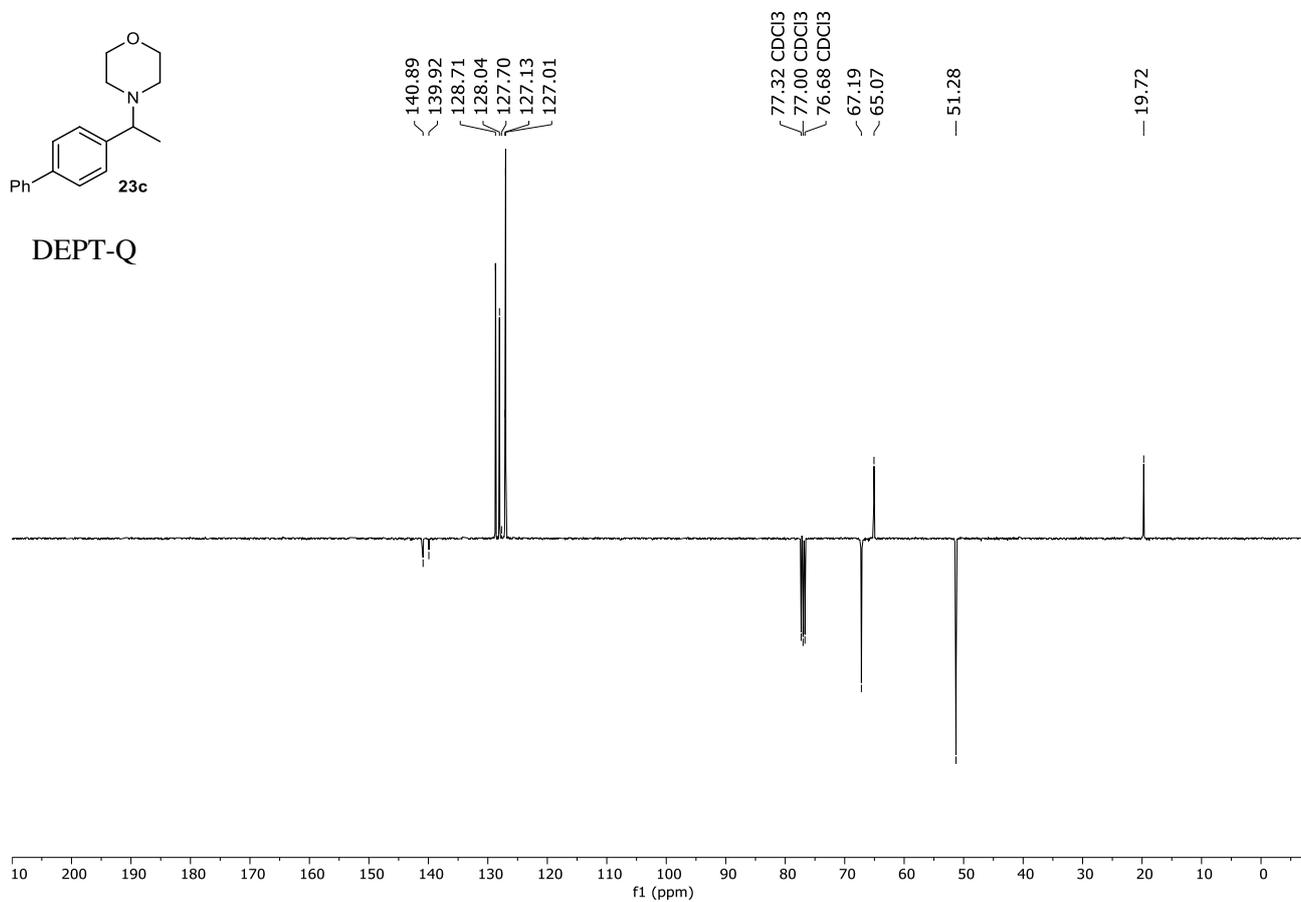
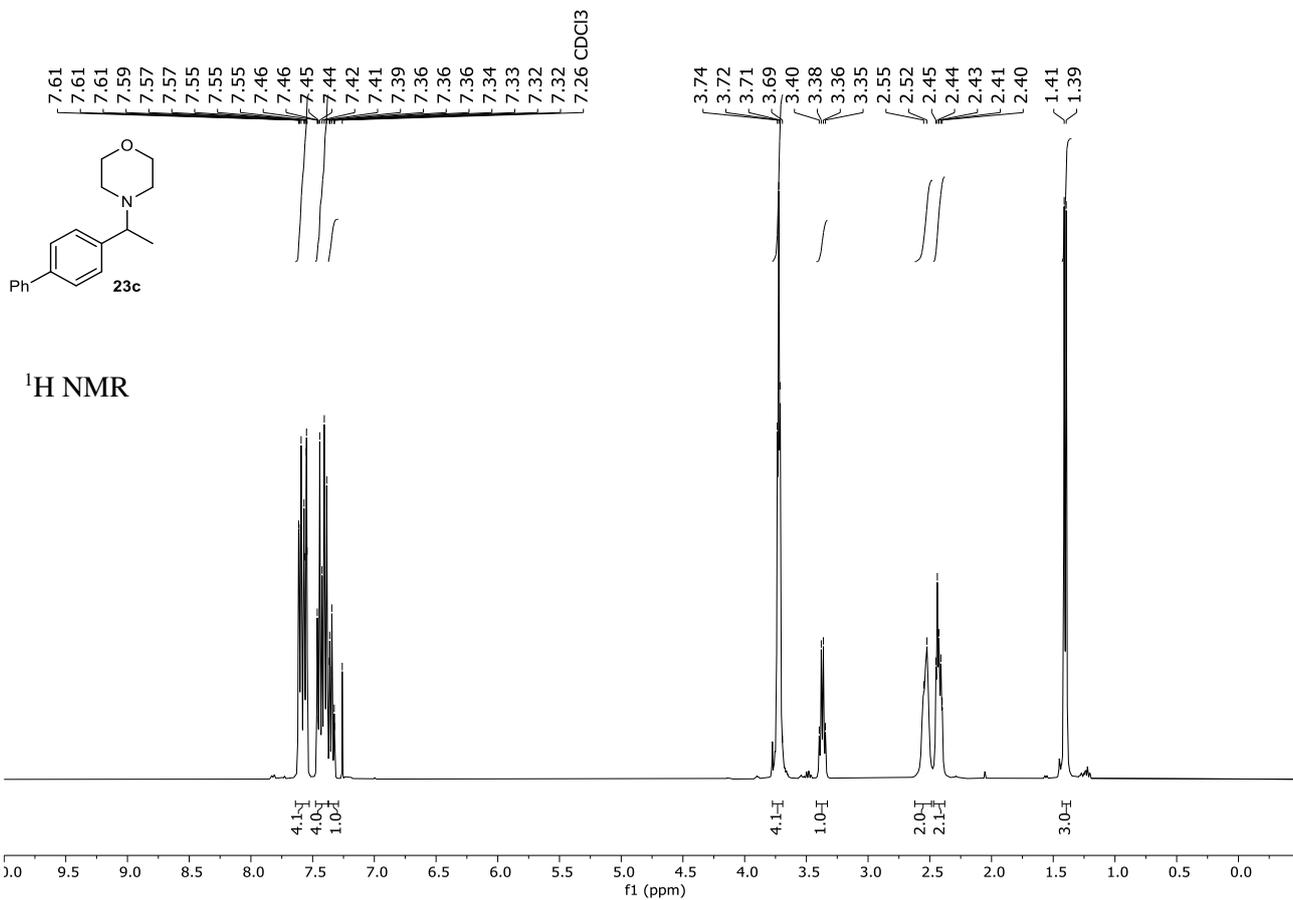


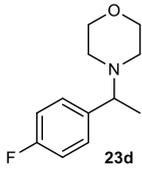
¹H NMR



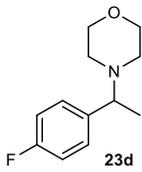
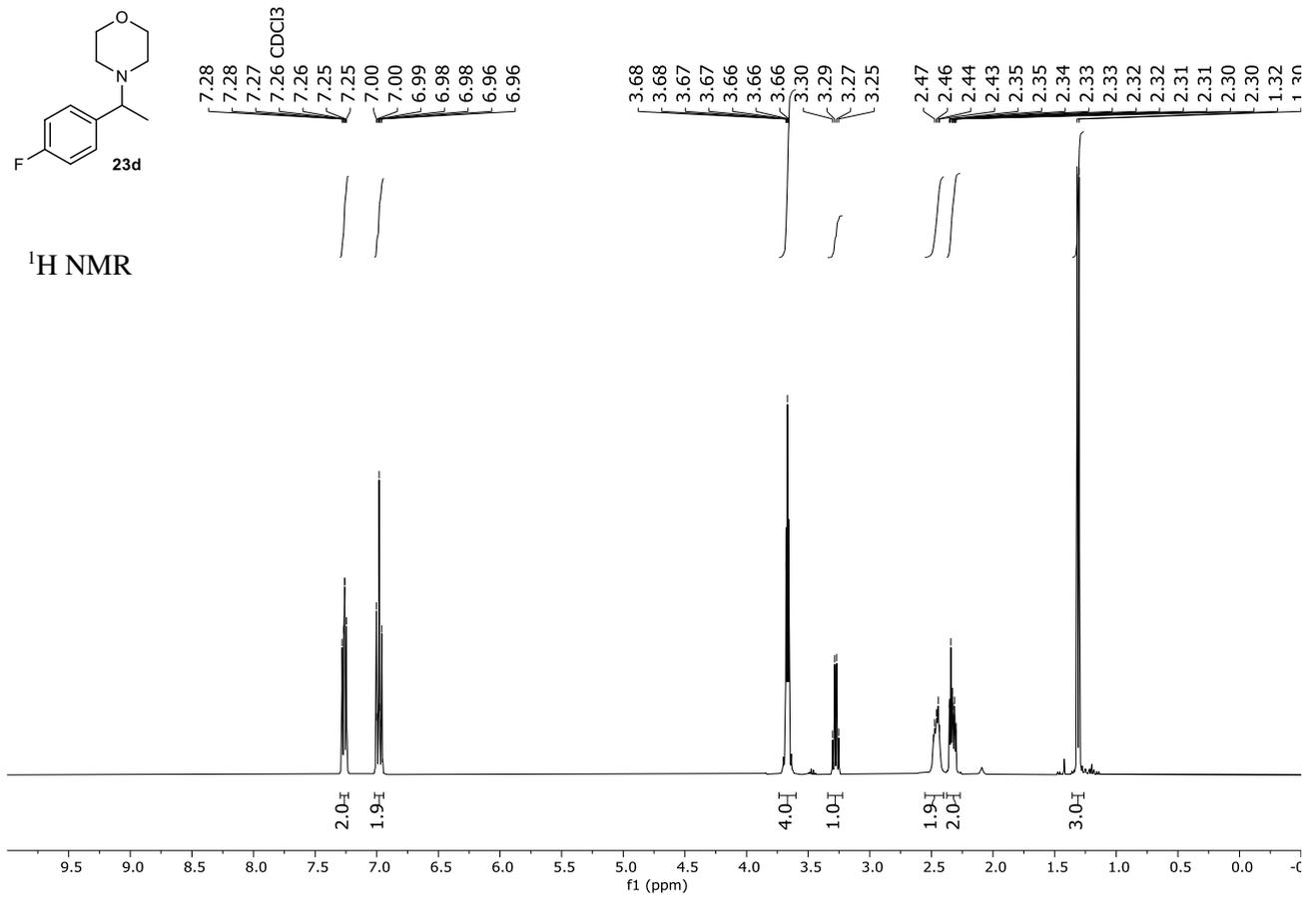
¹³C NMR



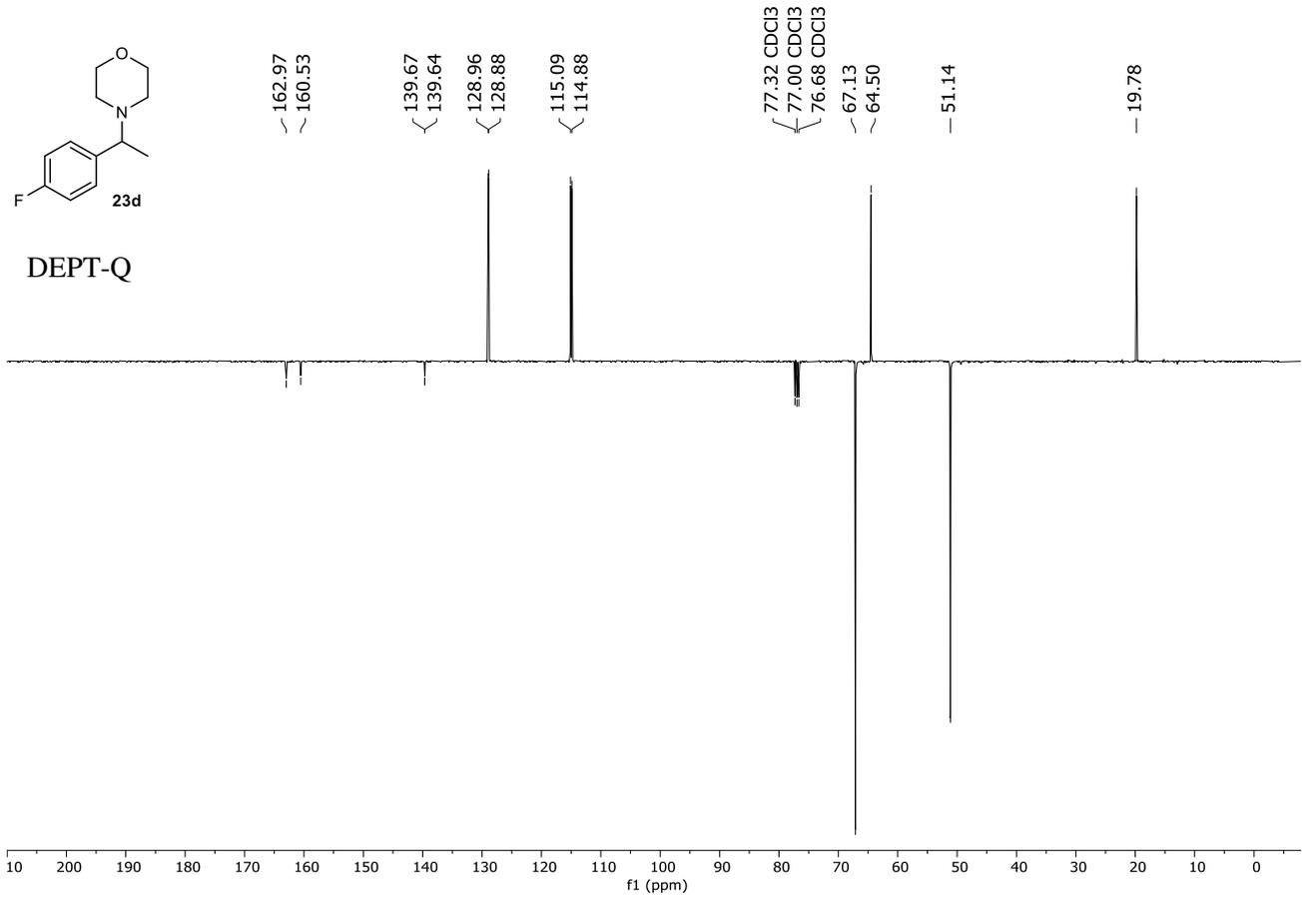


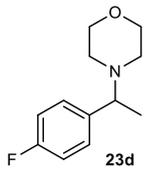


¹H NMR

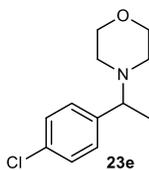
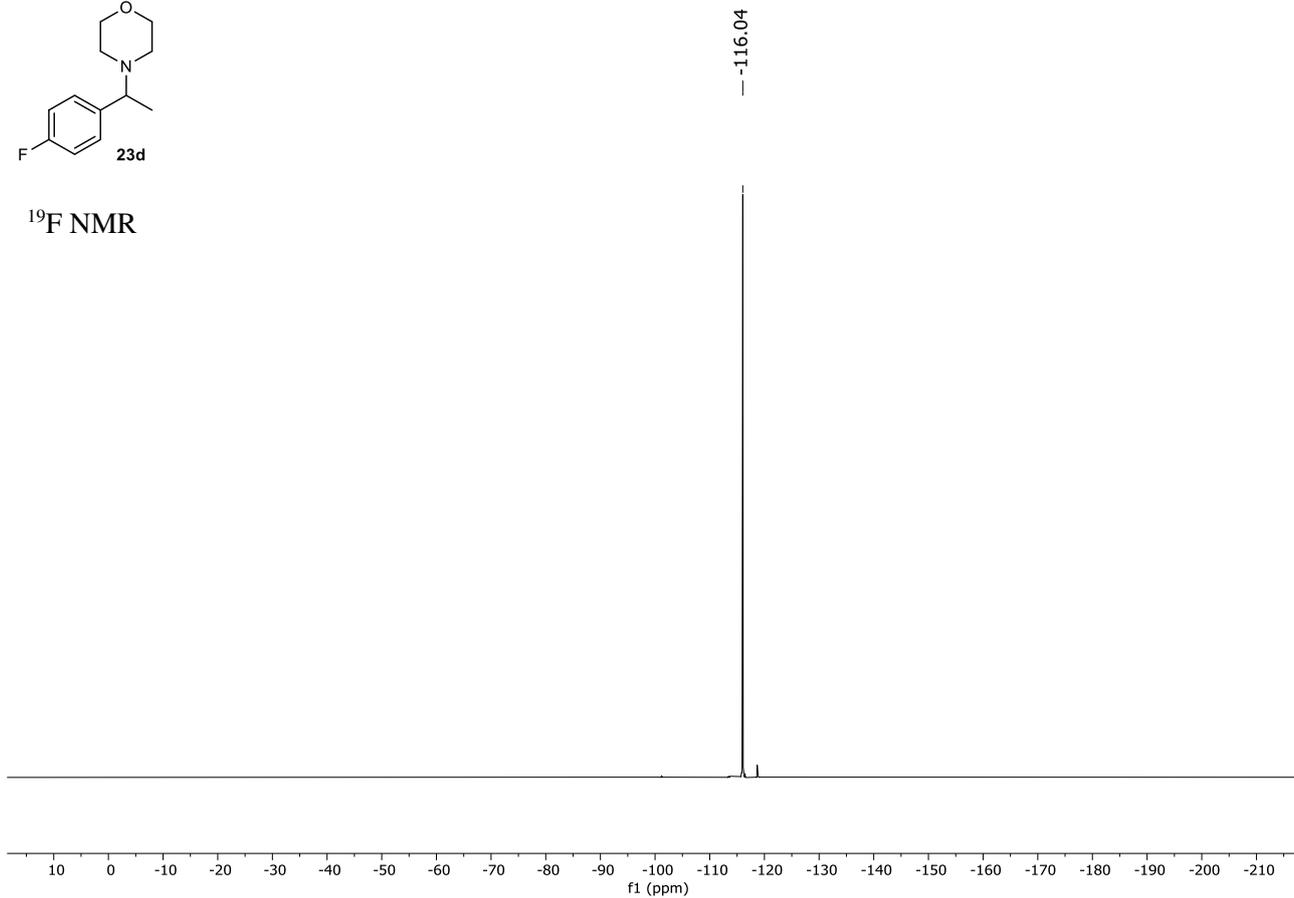


DEPT-Q

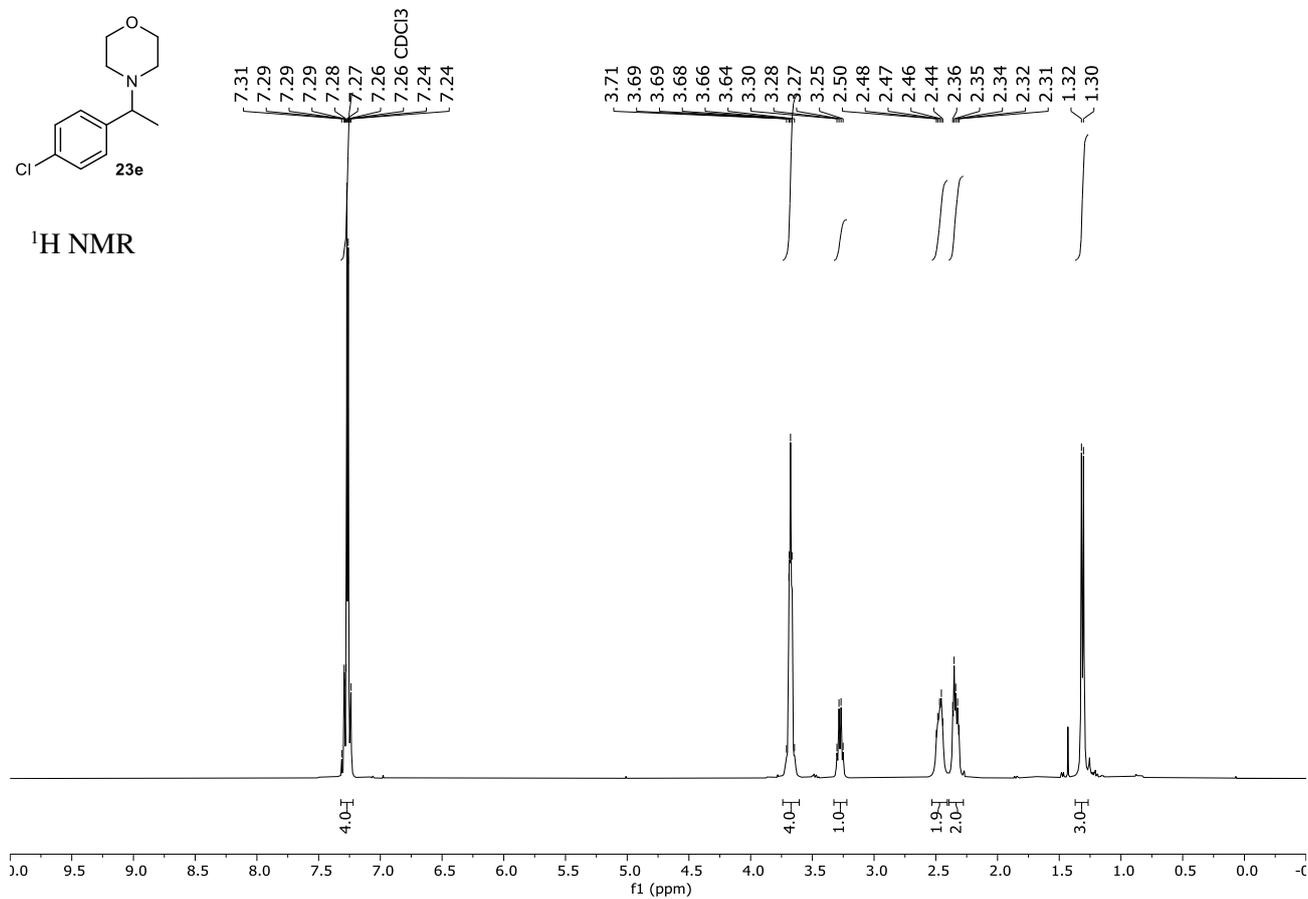


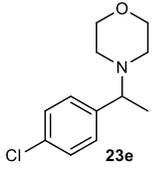


¹⁹F NMR

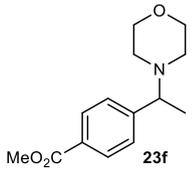
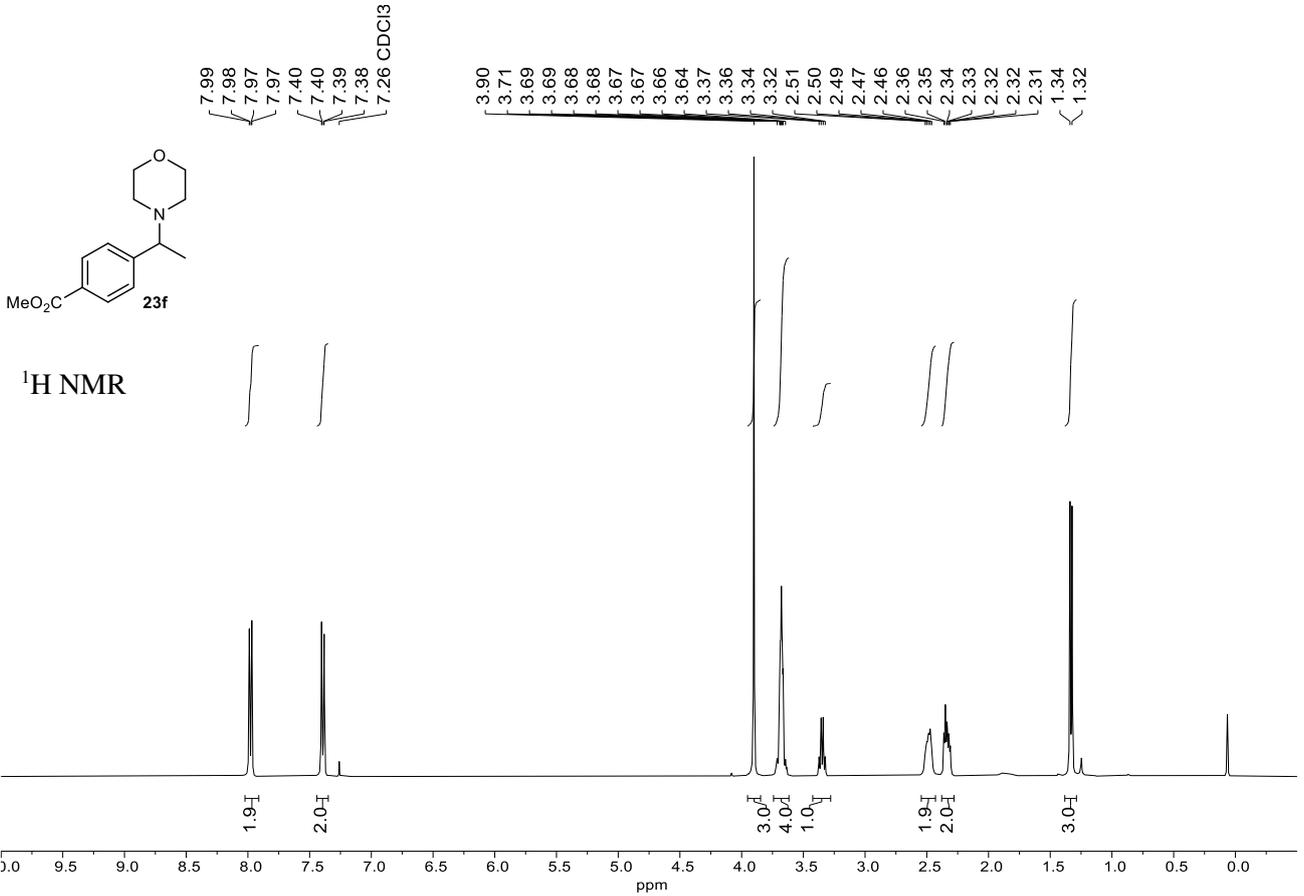
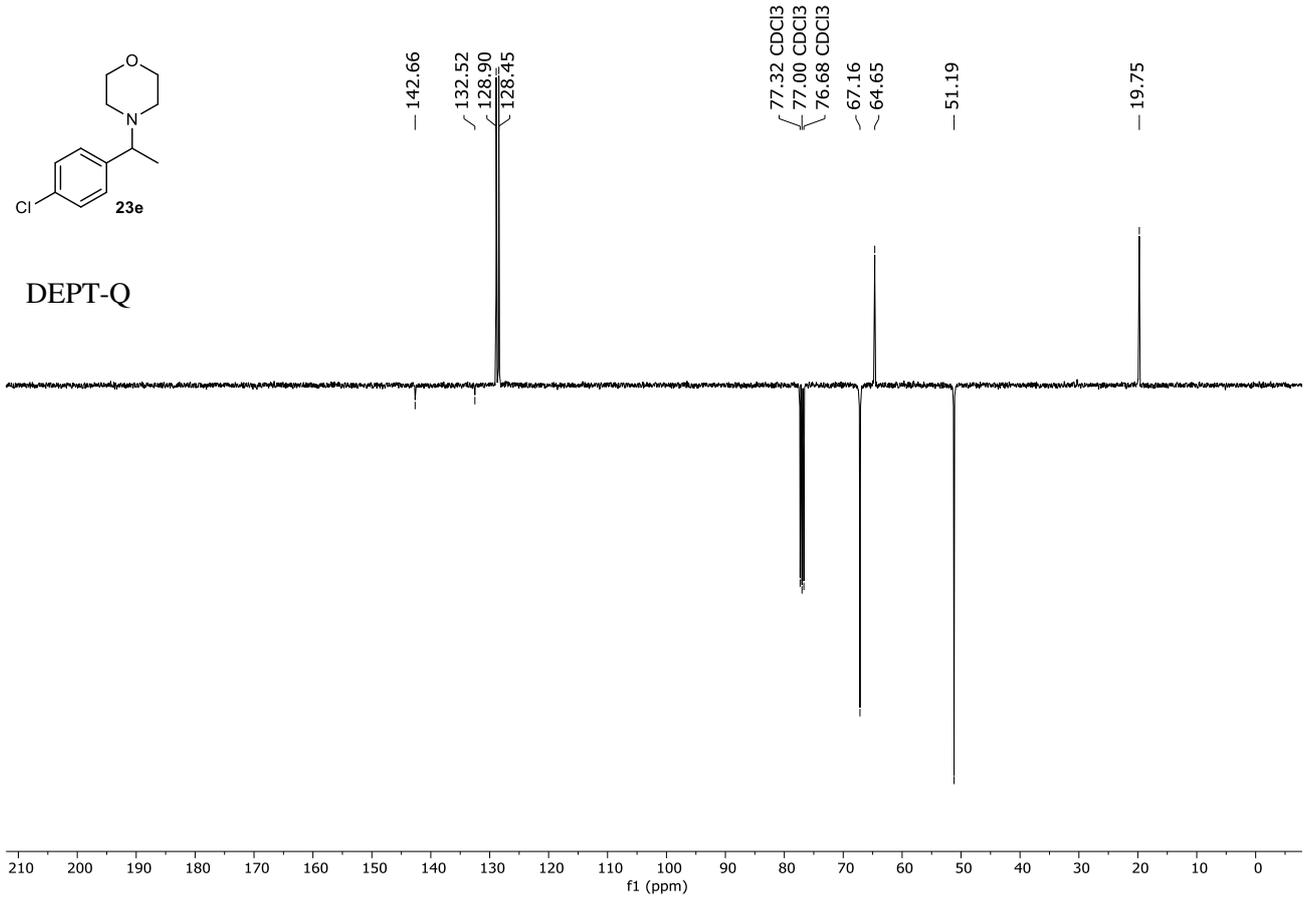


¹H NMR

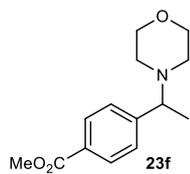




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¹H NMR



— 166.98

— 149.62

{ 129.69
 { 128.92
 { 127.53

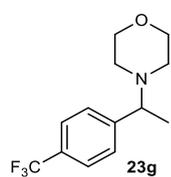
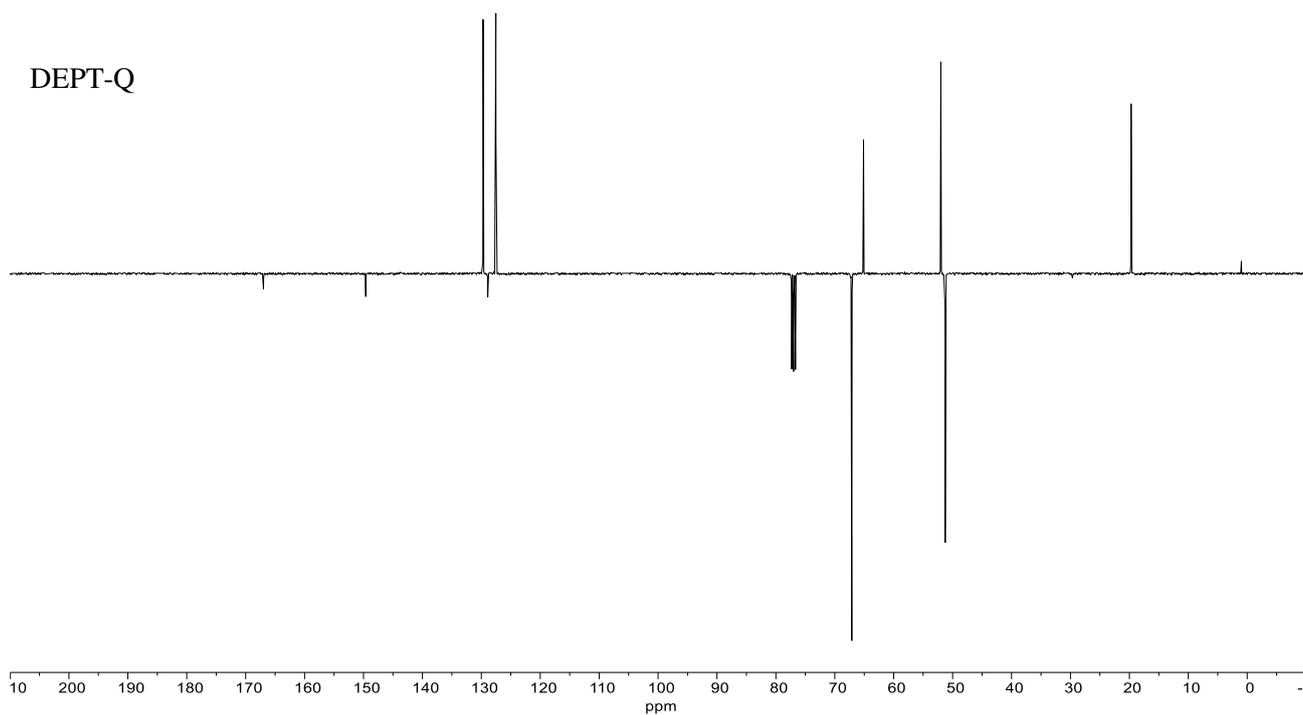
{ 77.32 CDCl3
 { 77.00 CDCl3
 { 76.68 CDCl3

{ 67.12
 { 65.12

{ 52.01
 { 51.25

— 19.70

DEPT-Q



{ 7.58
 { 7.56
 { 7.46
 { 7.44
 { 7.25 CDCl3

3.69

— 3.36

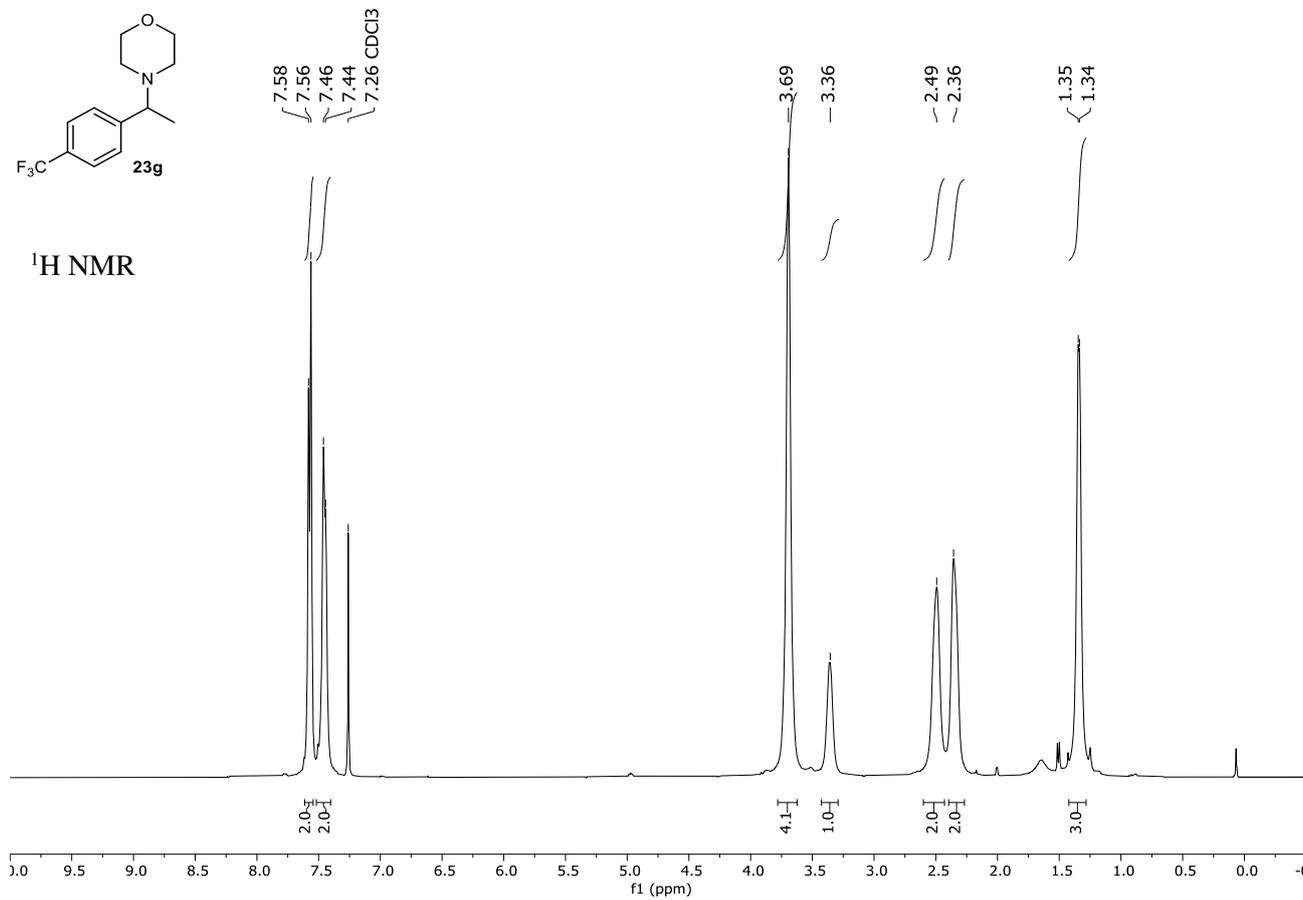
2.49

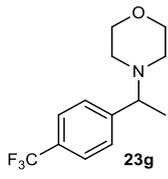
2.36

1.35

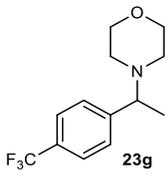
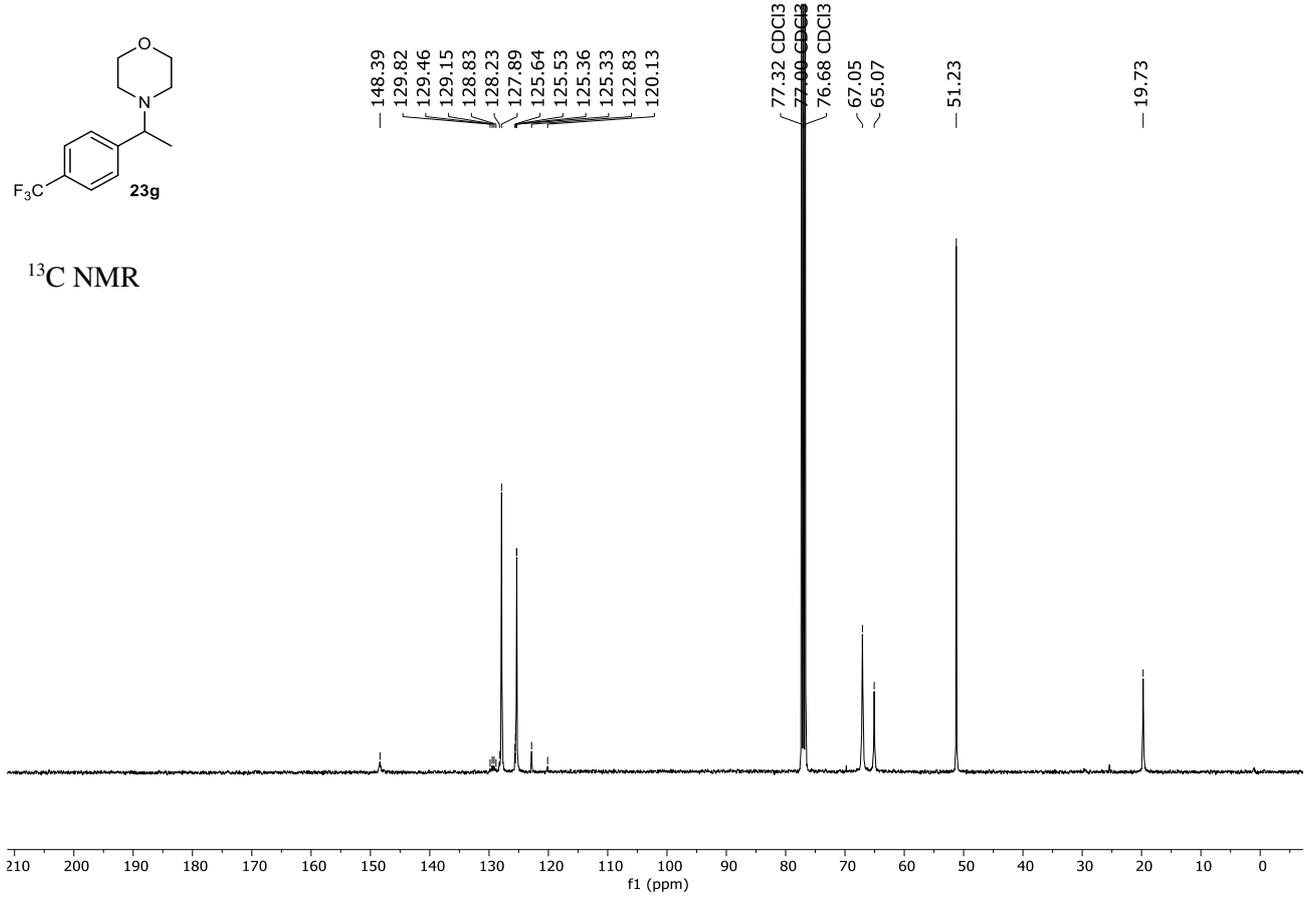
1.34

¹H NMR

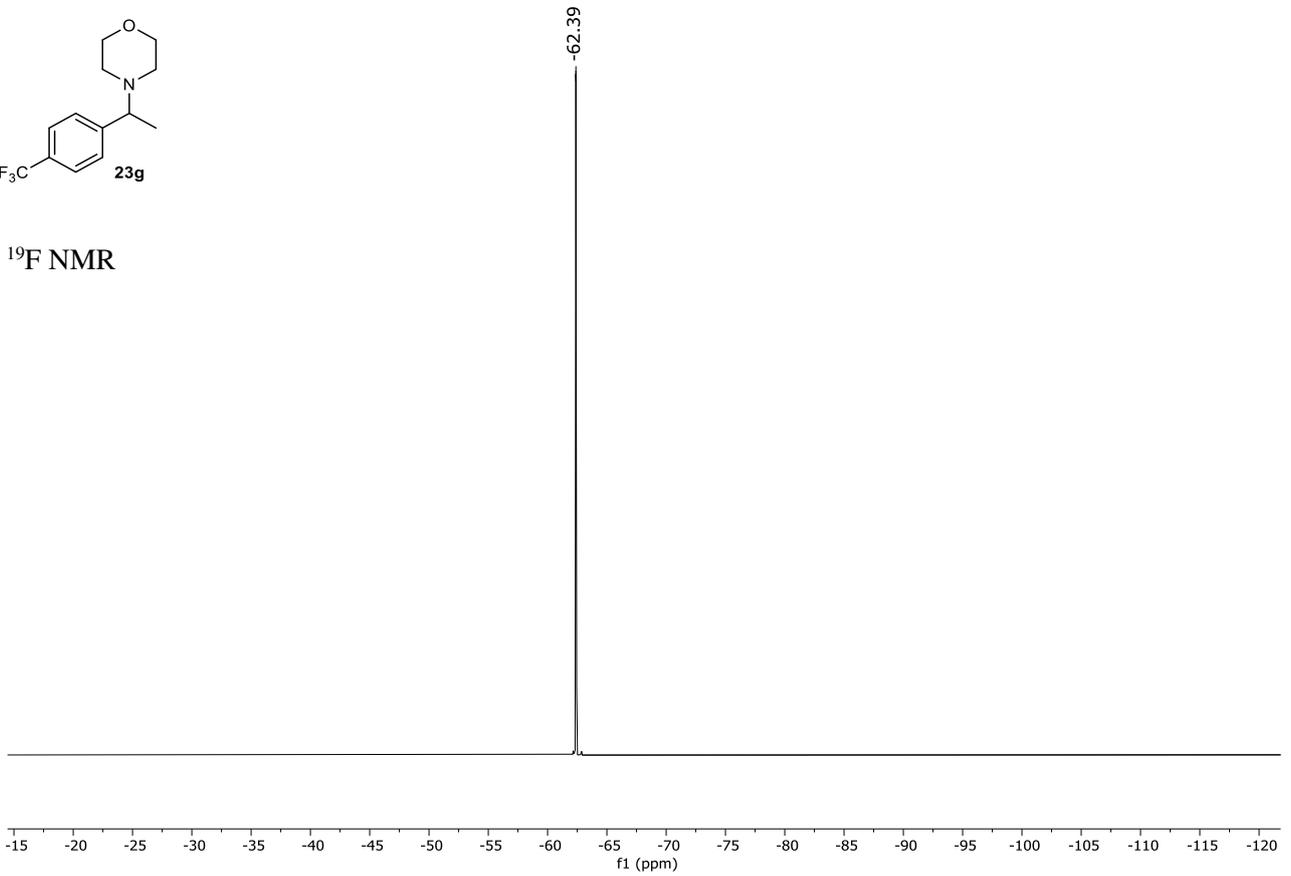


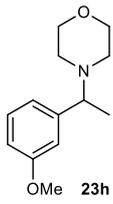


¹³C NMR

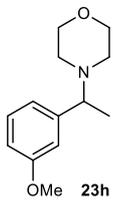
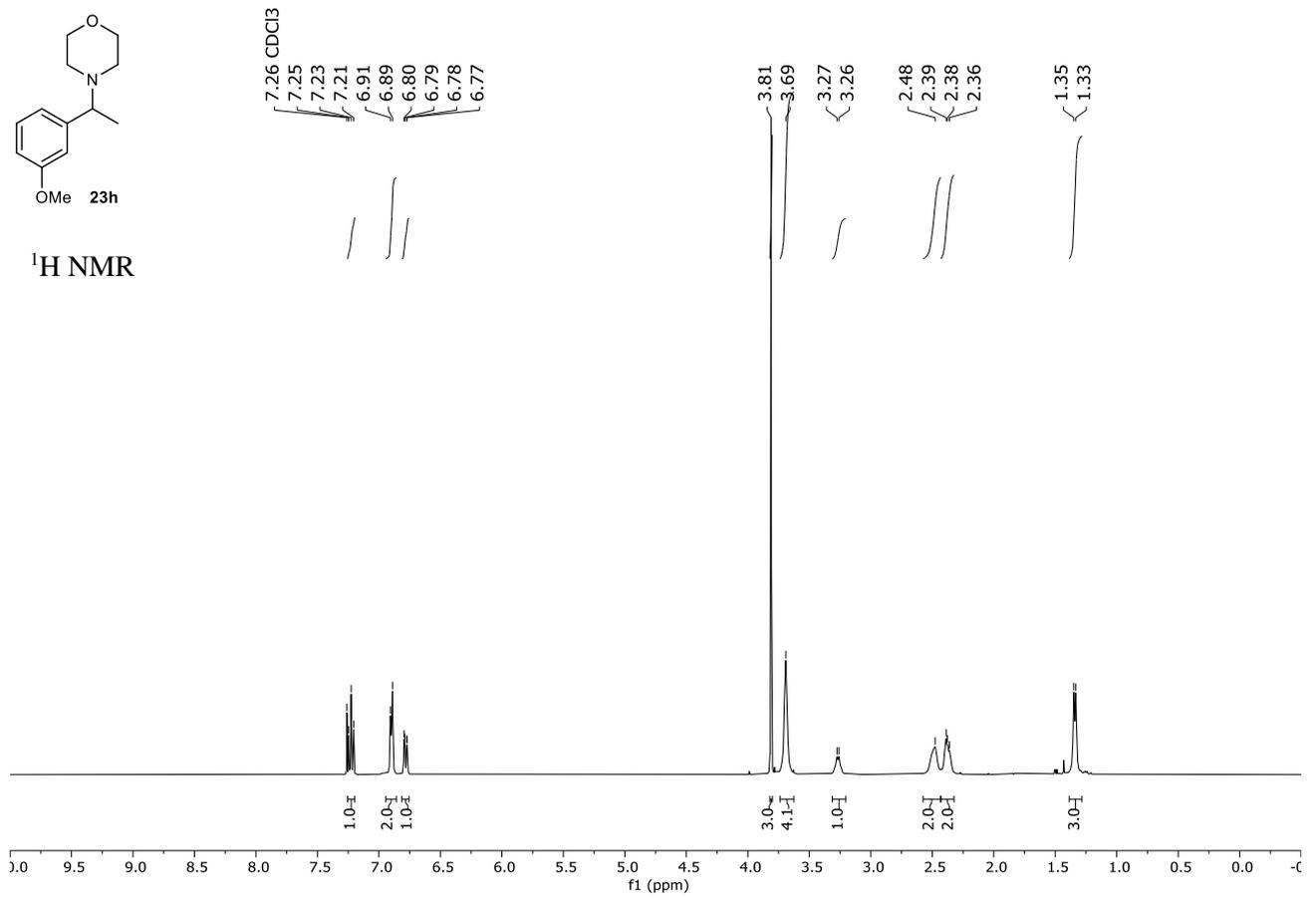


¹⁹F NMR

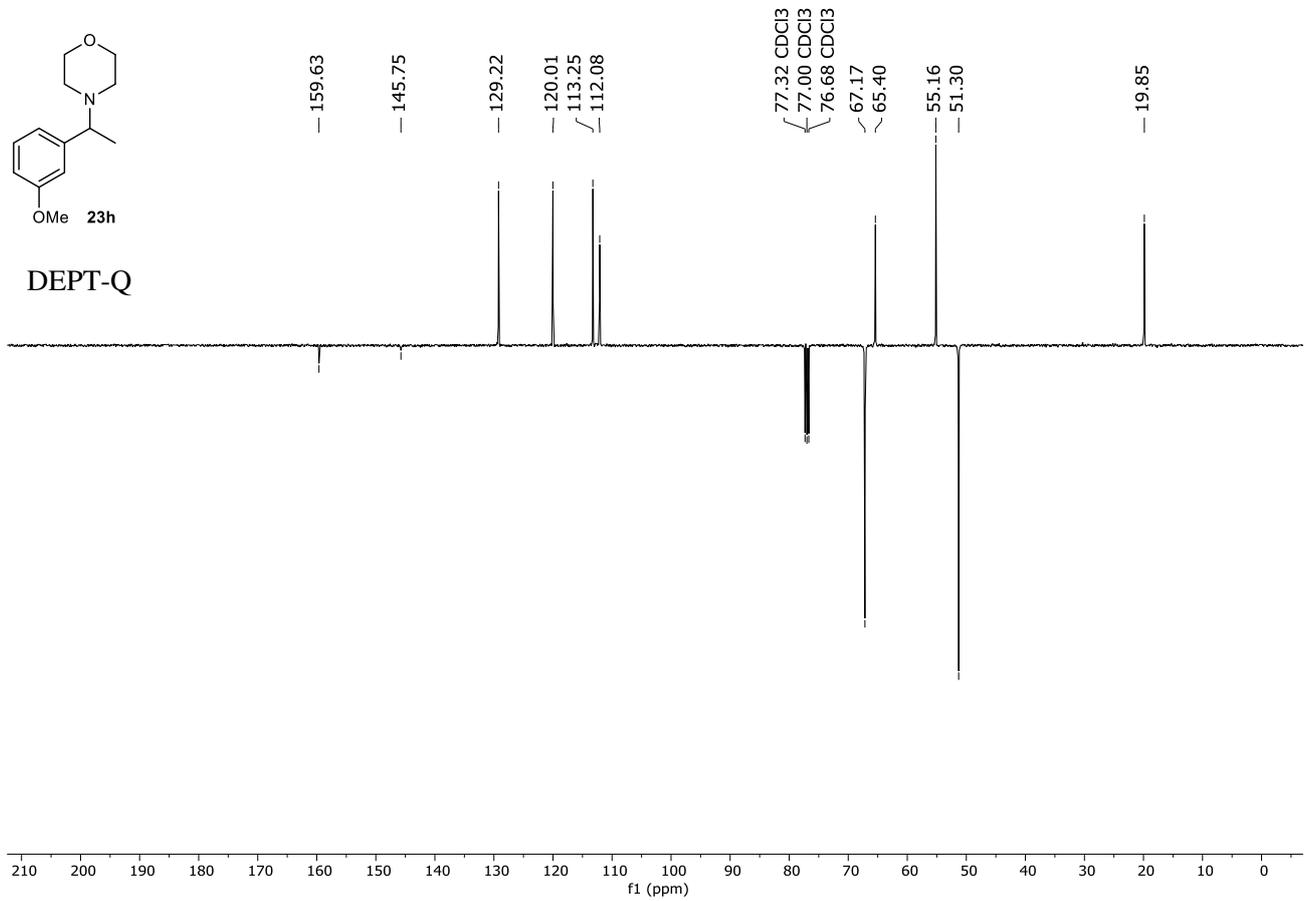


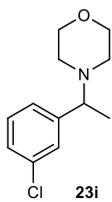


¹H NMR

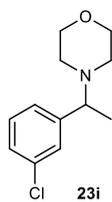
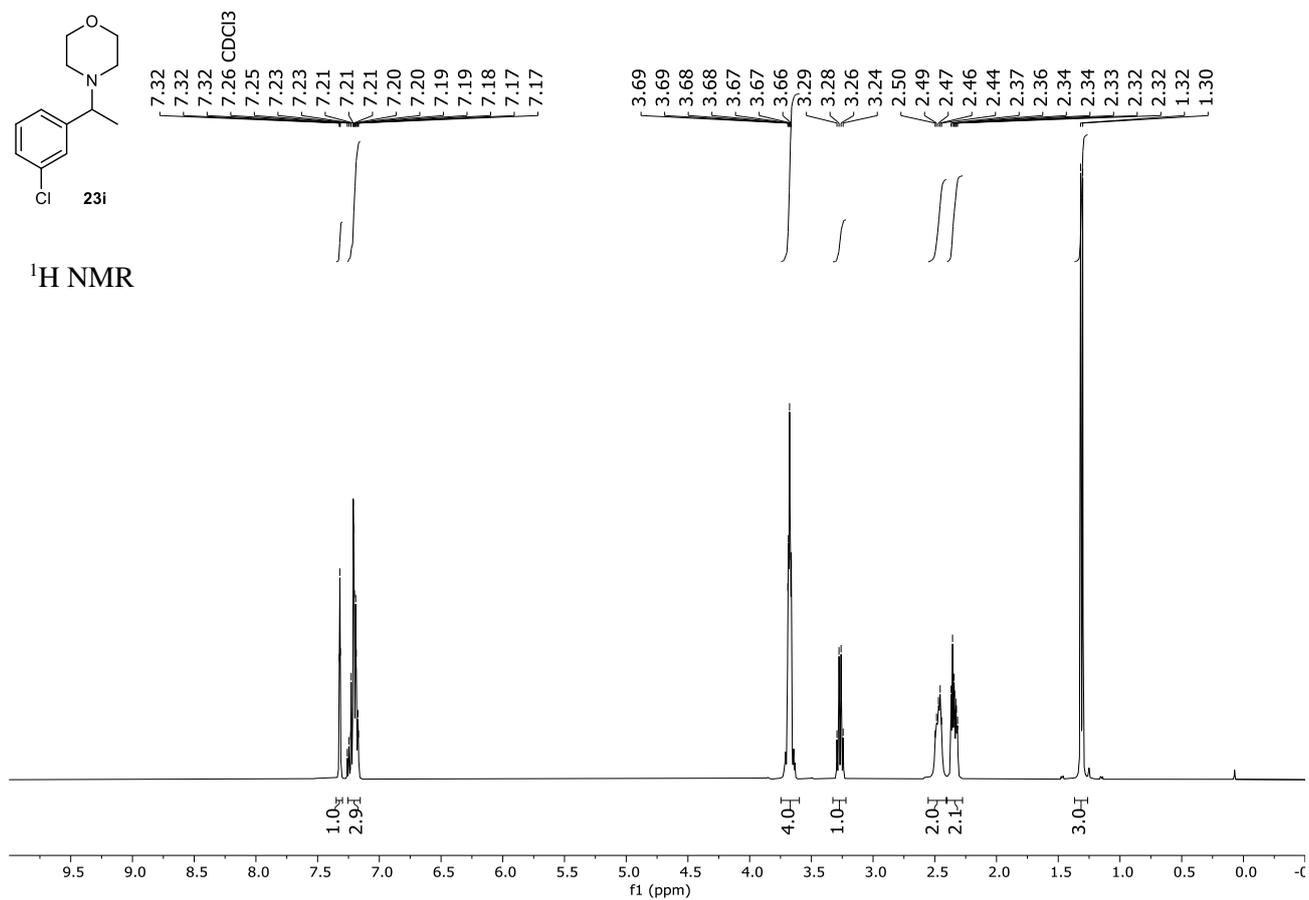


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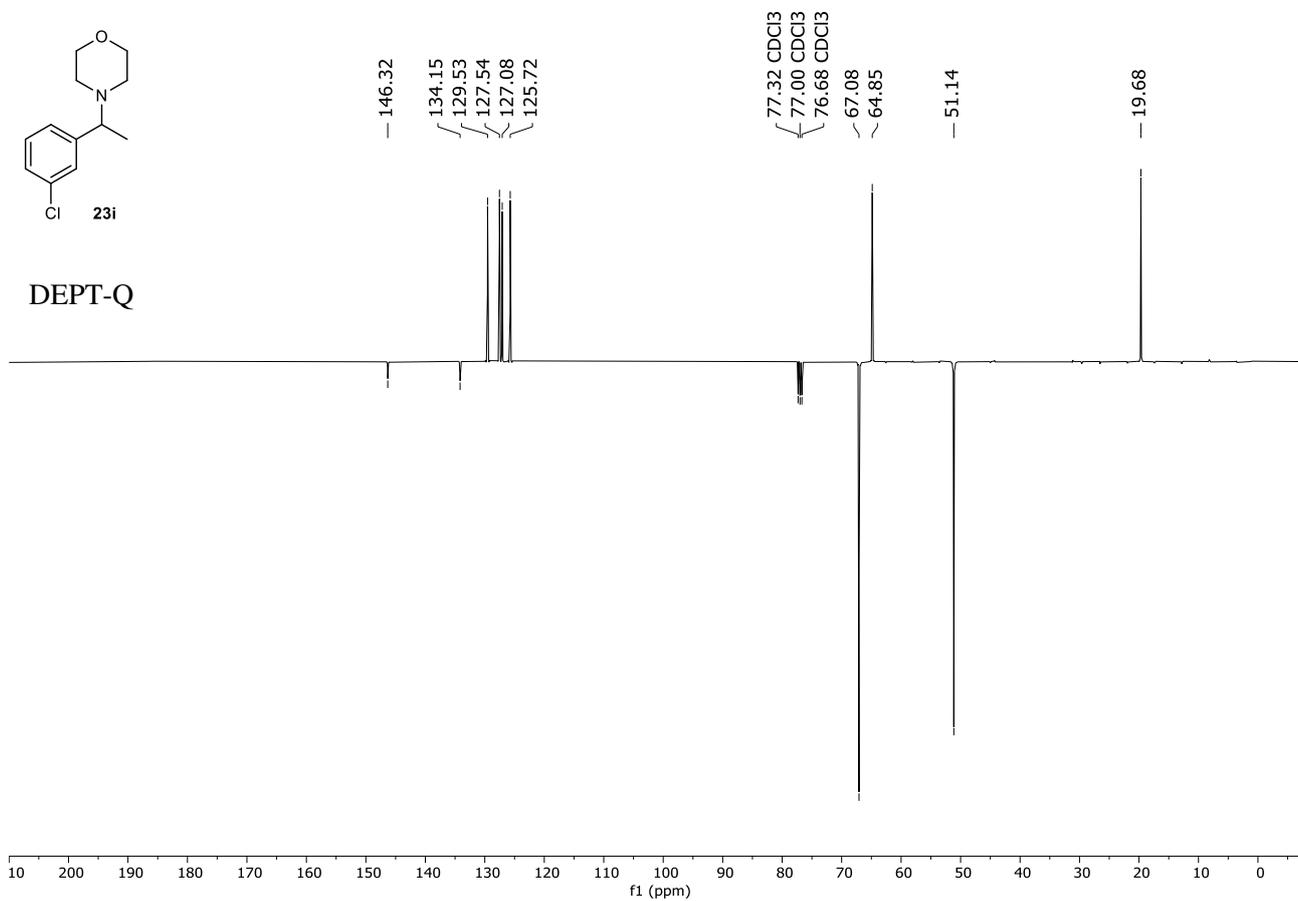


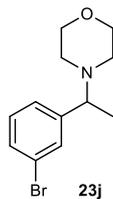


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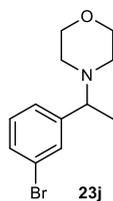
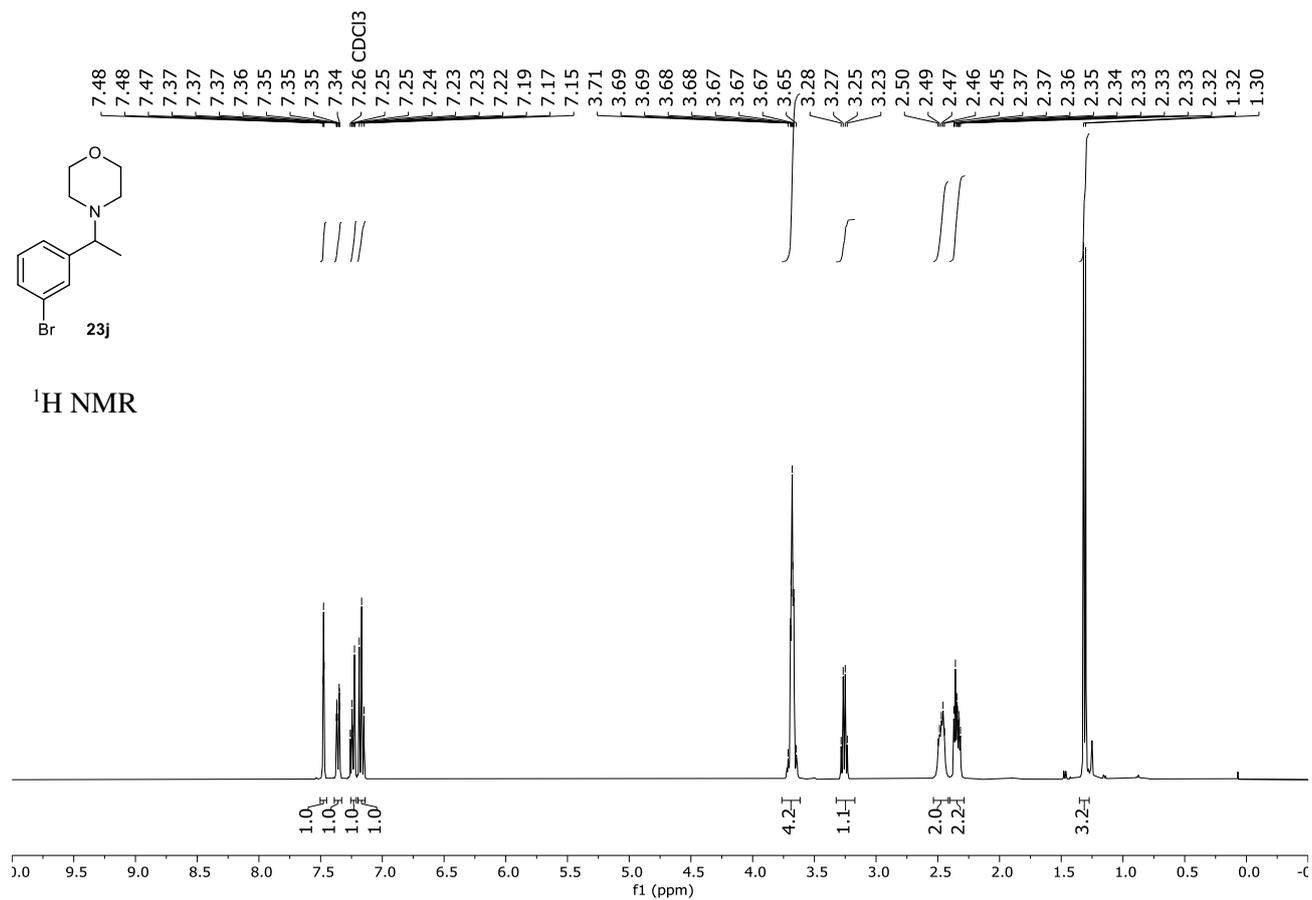


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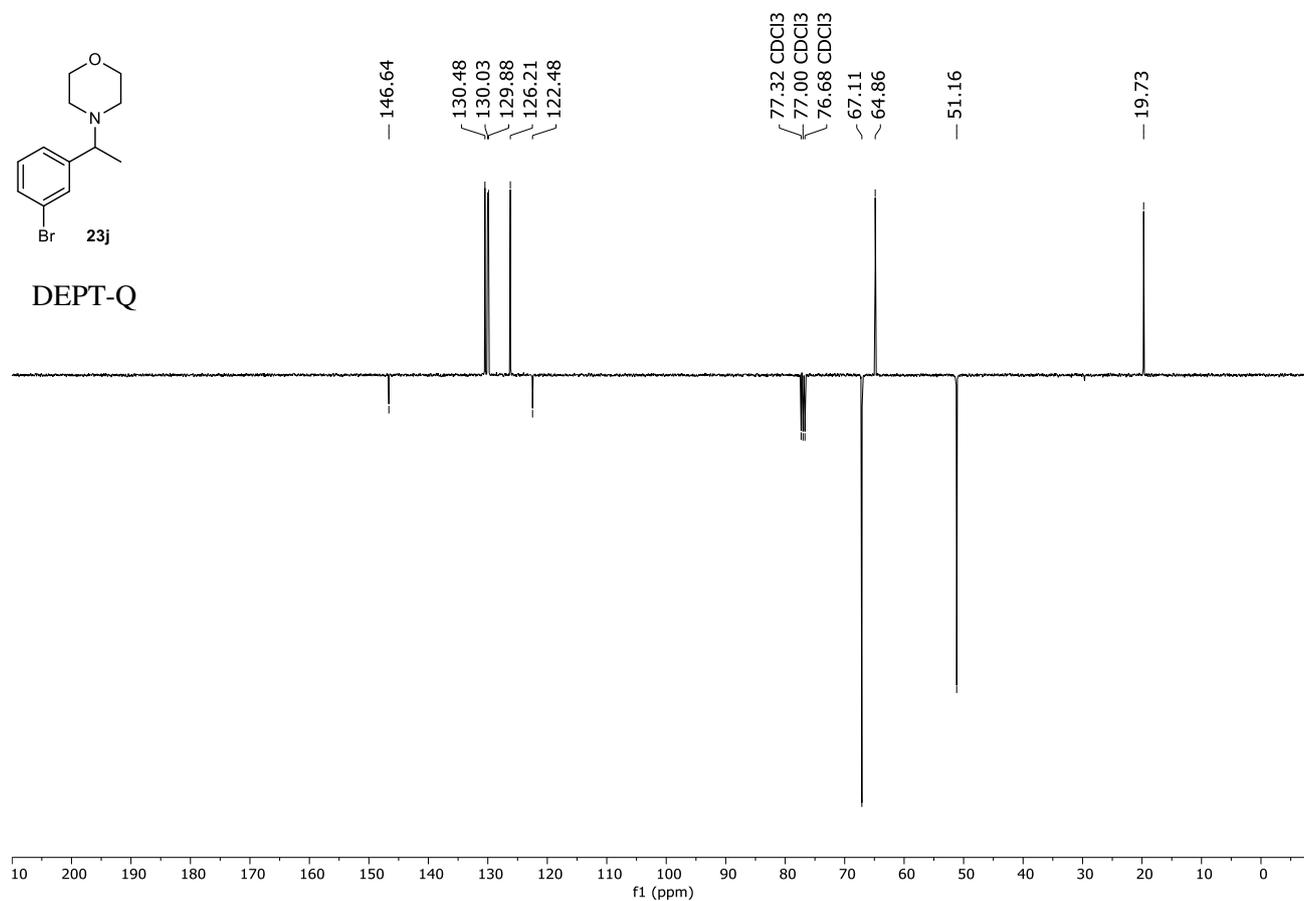


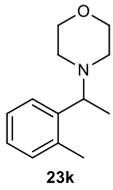


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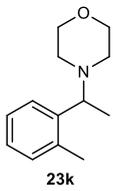
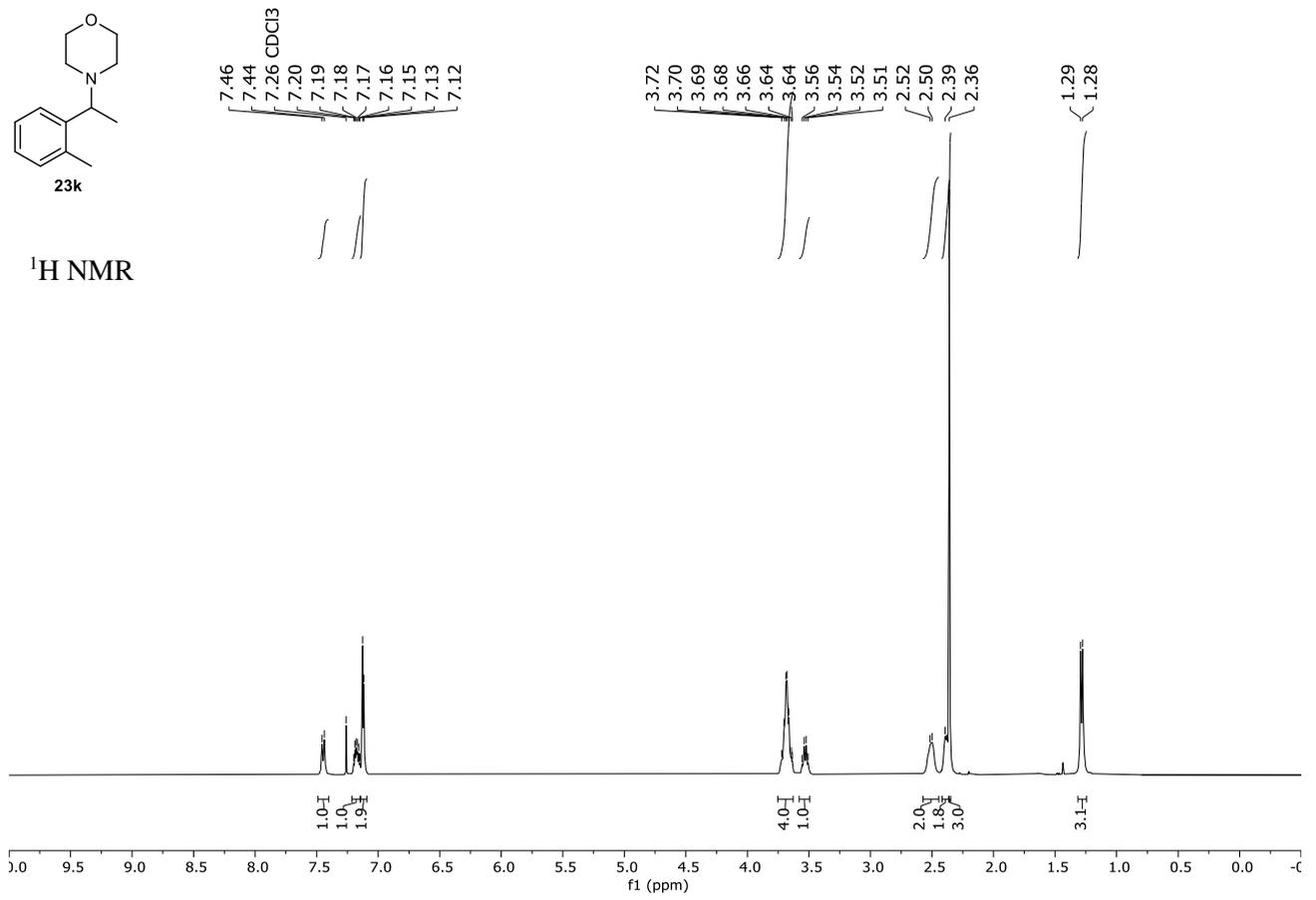


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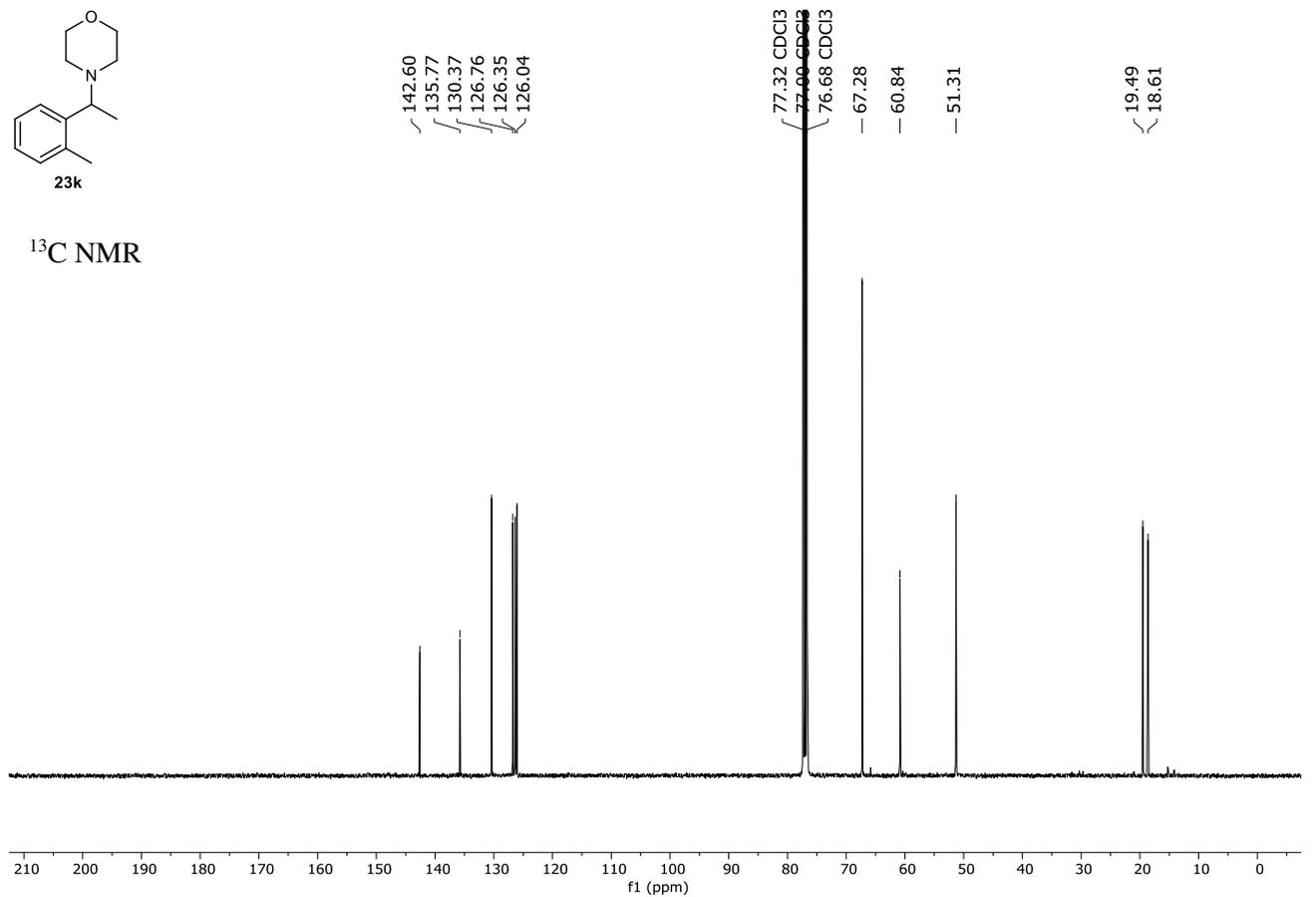


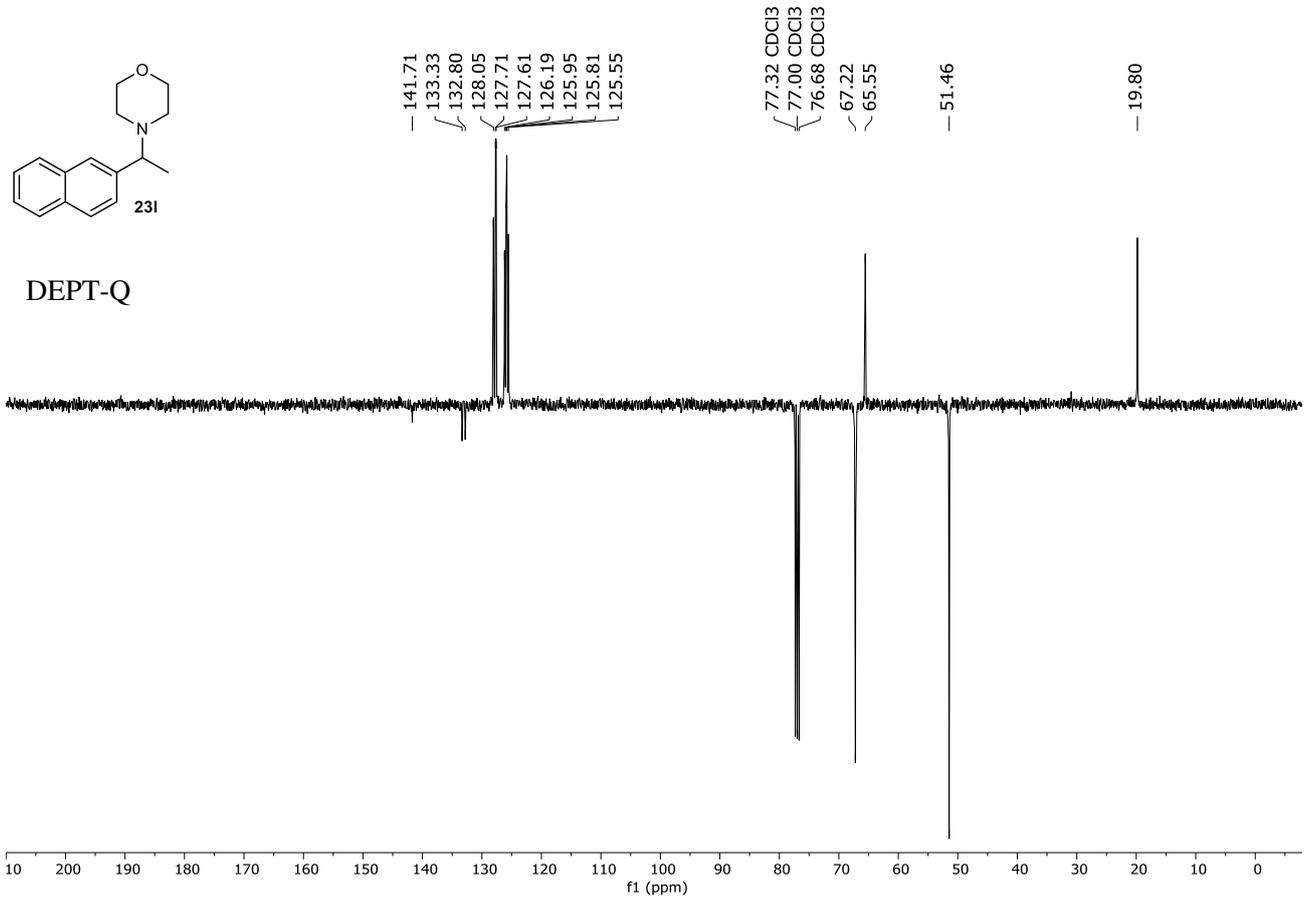
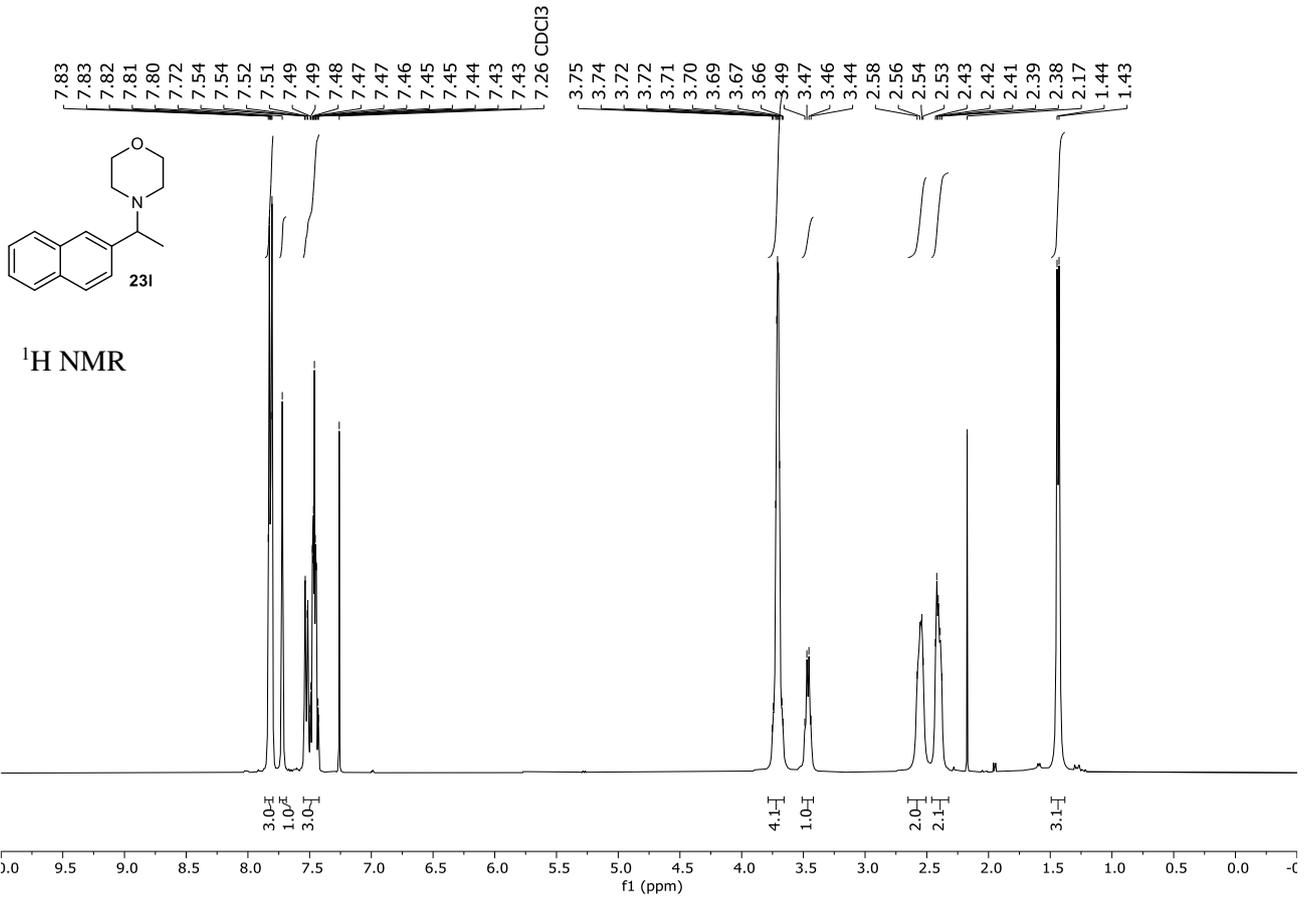


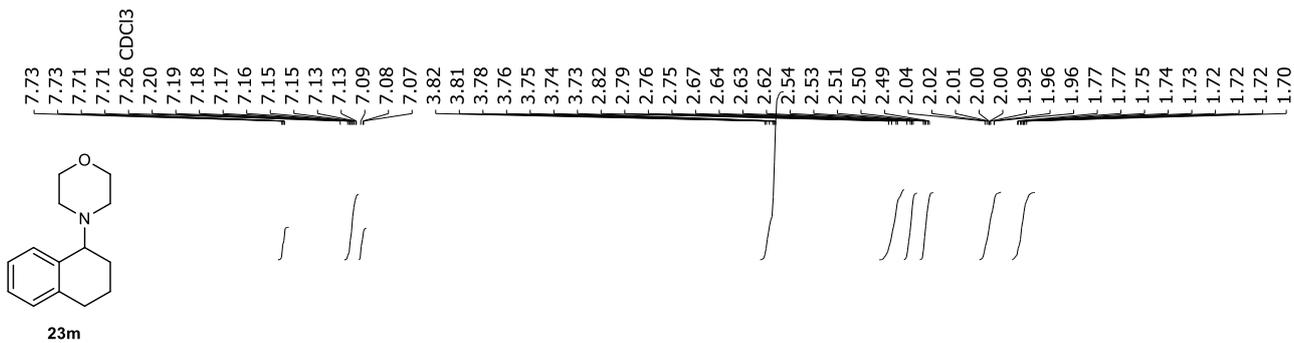
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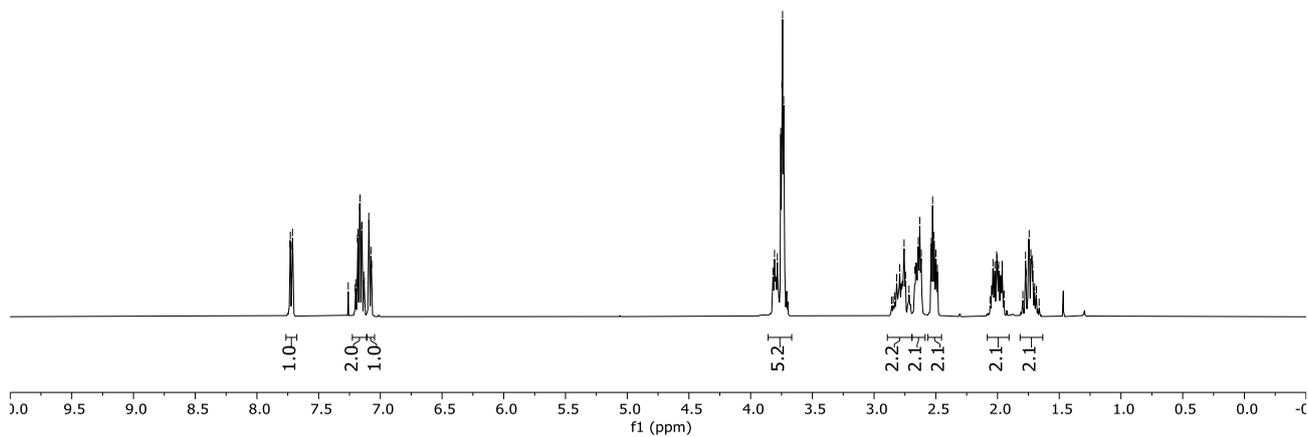
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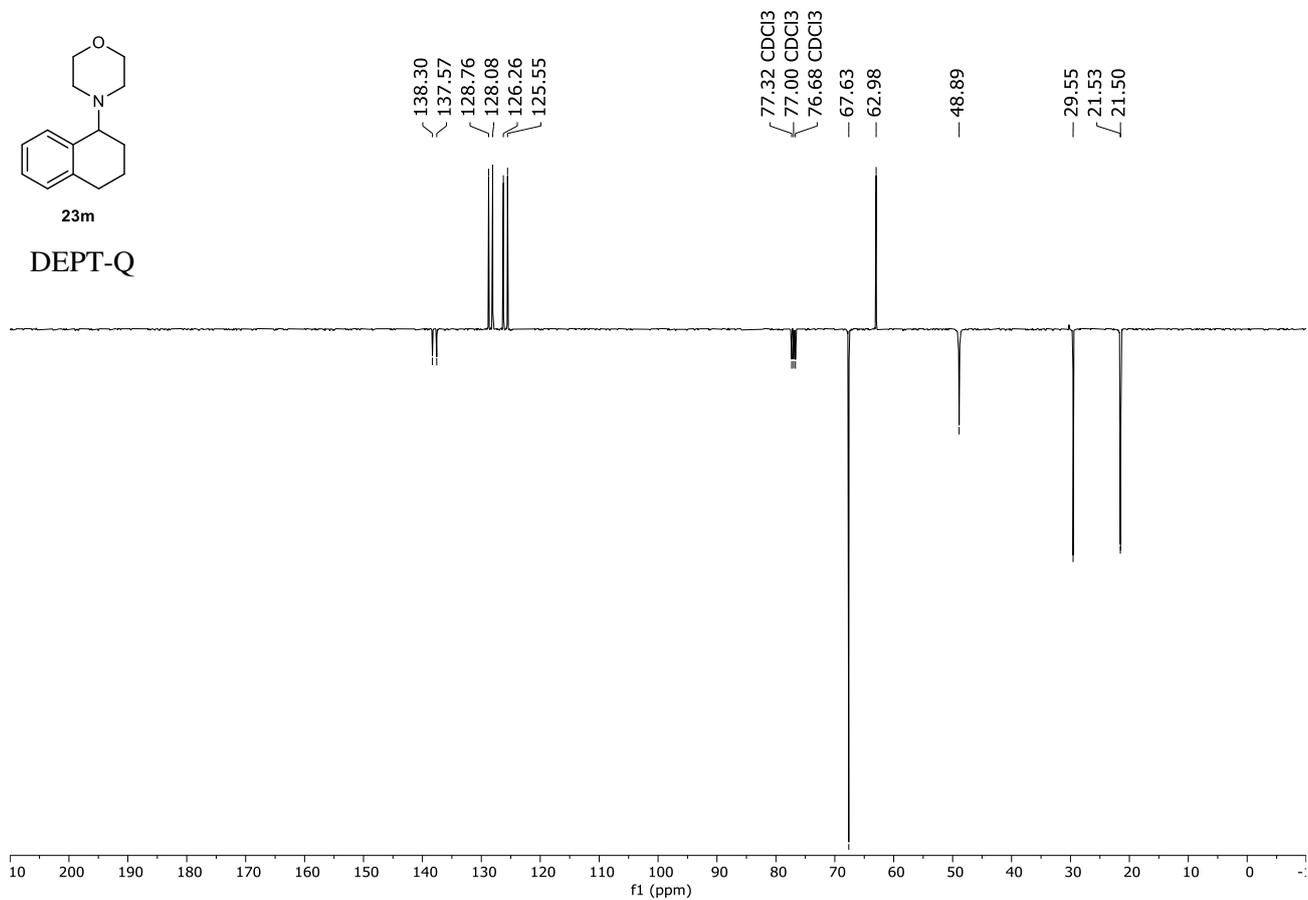


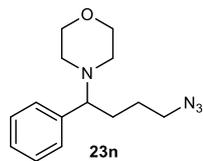


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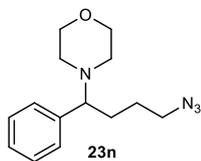
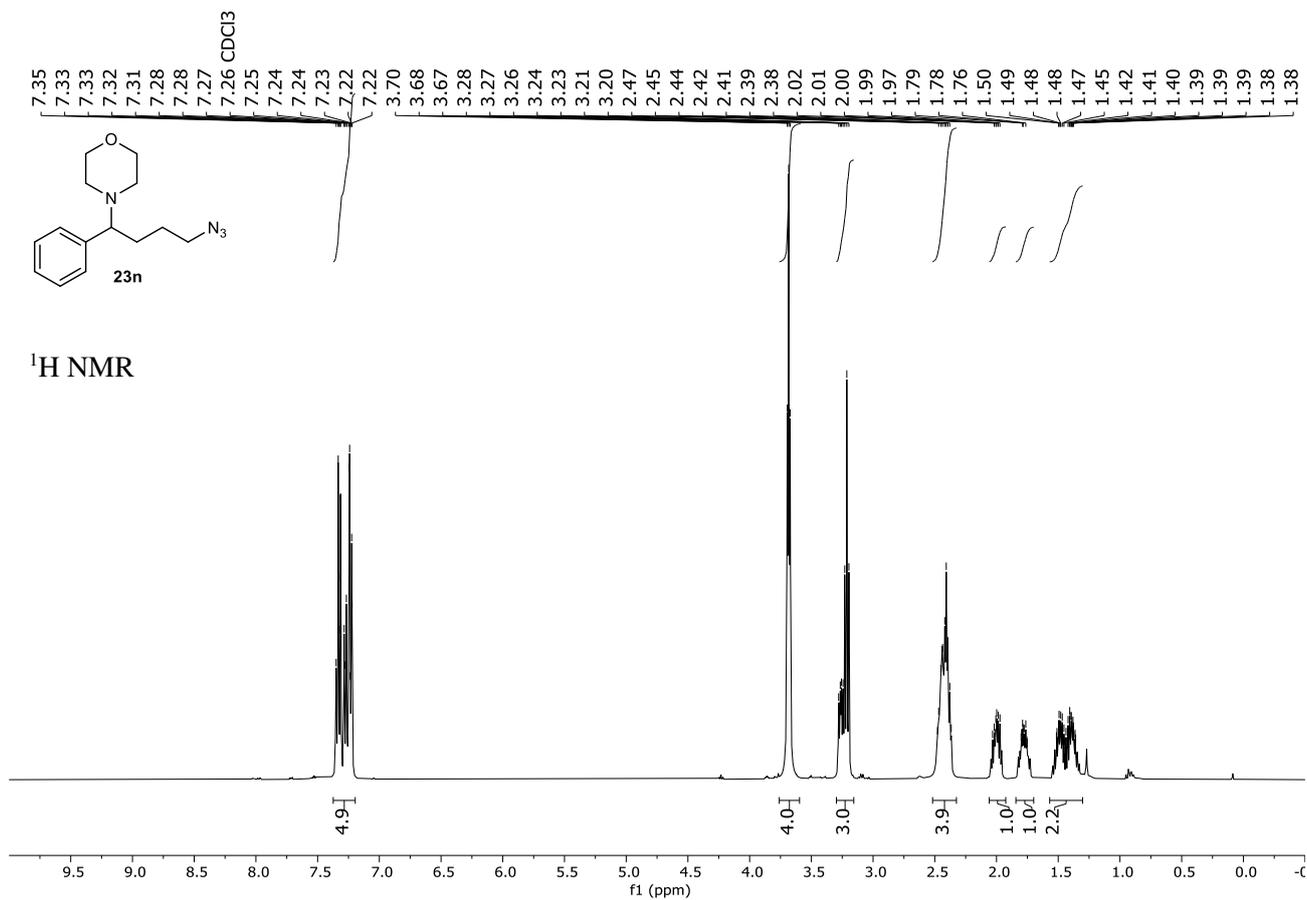


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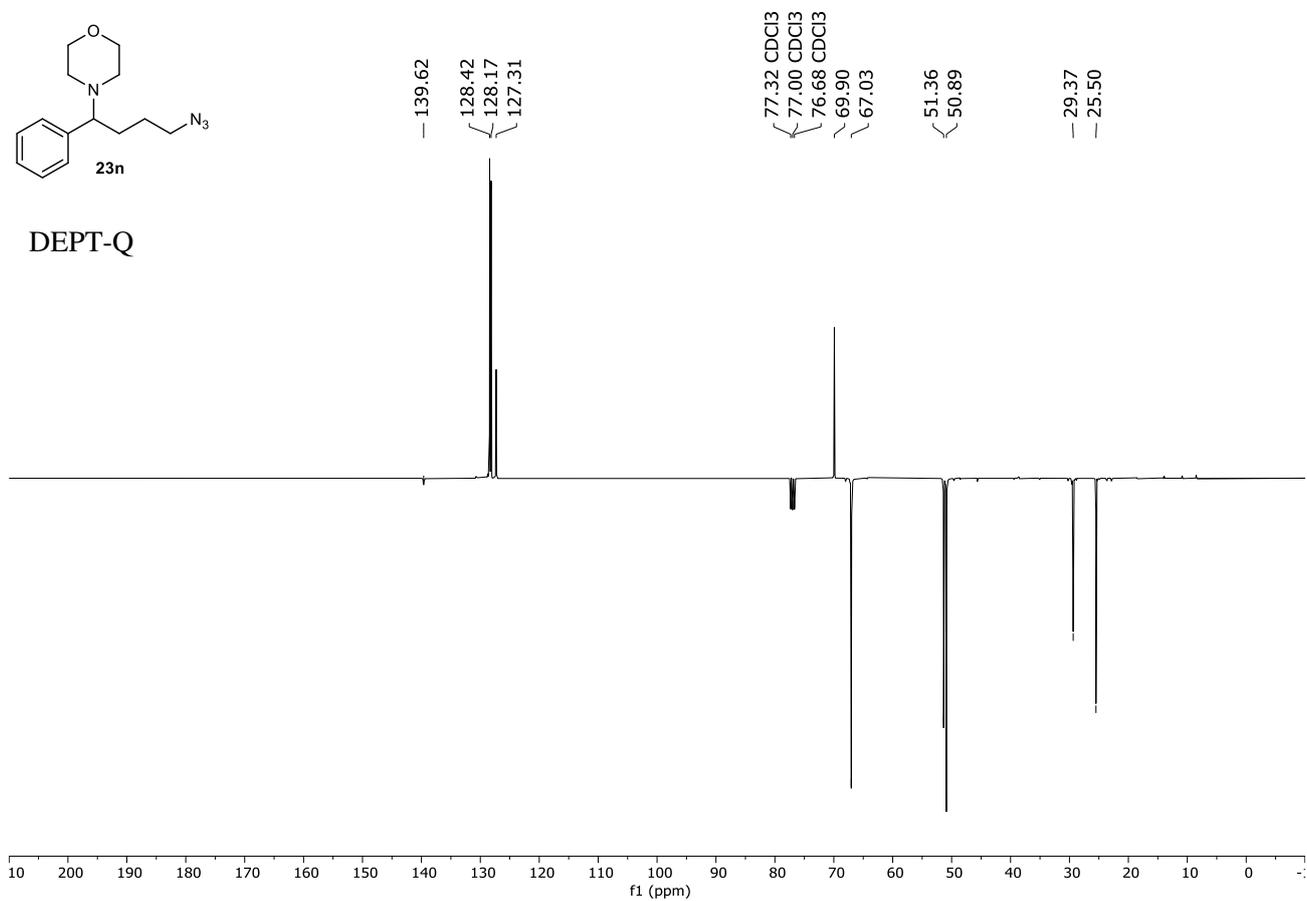


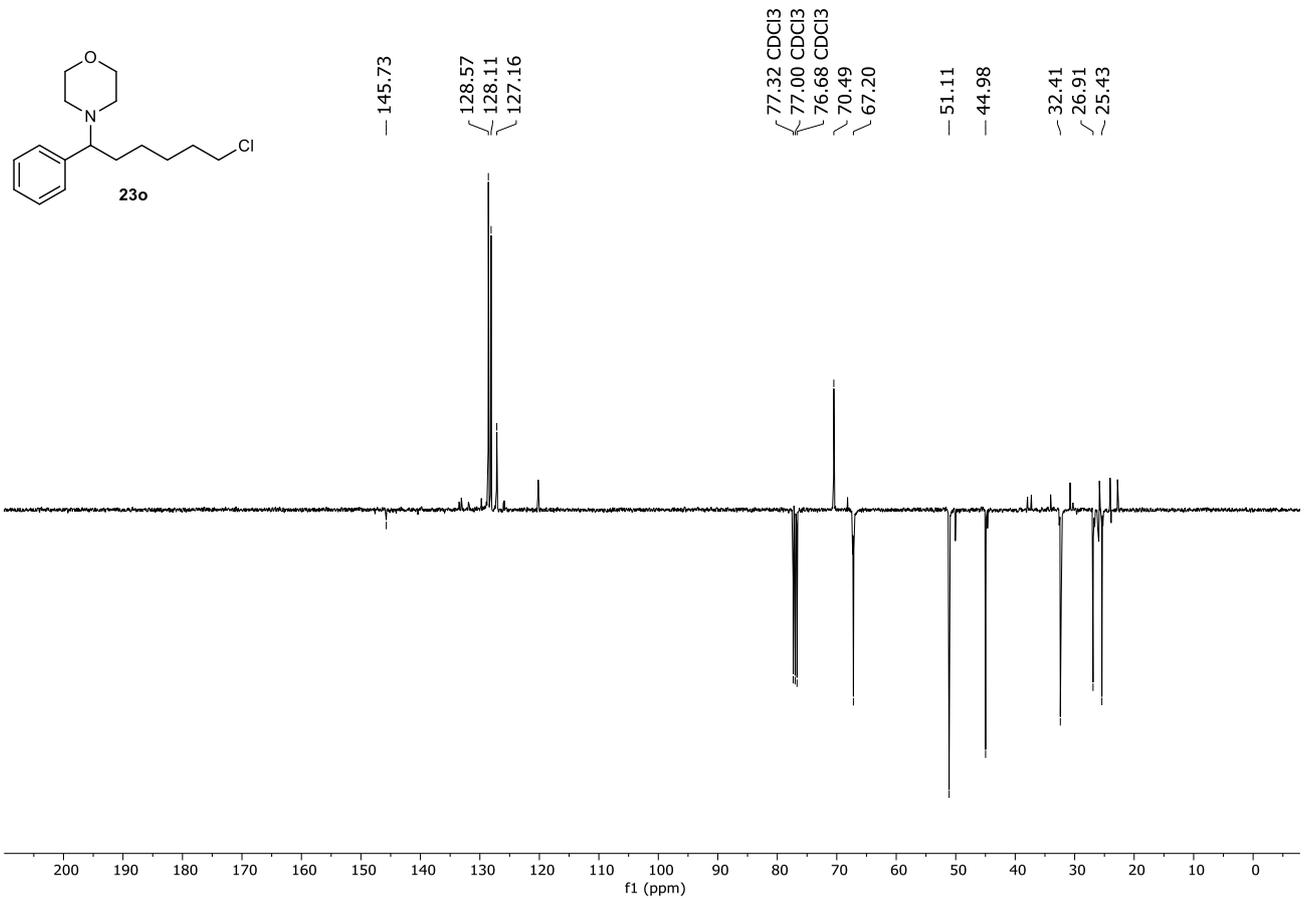
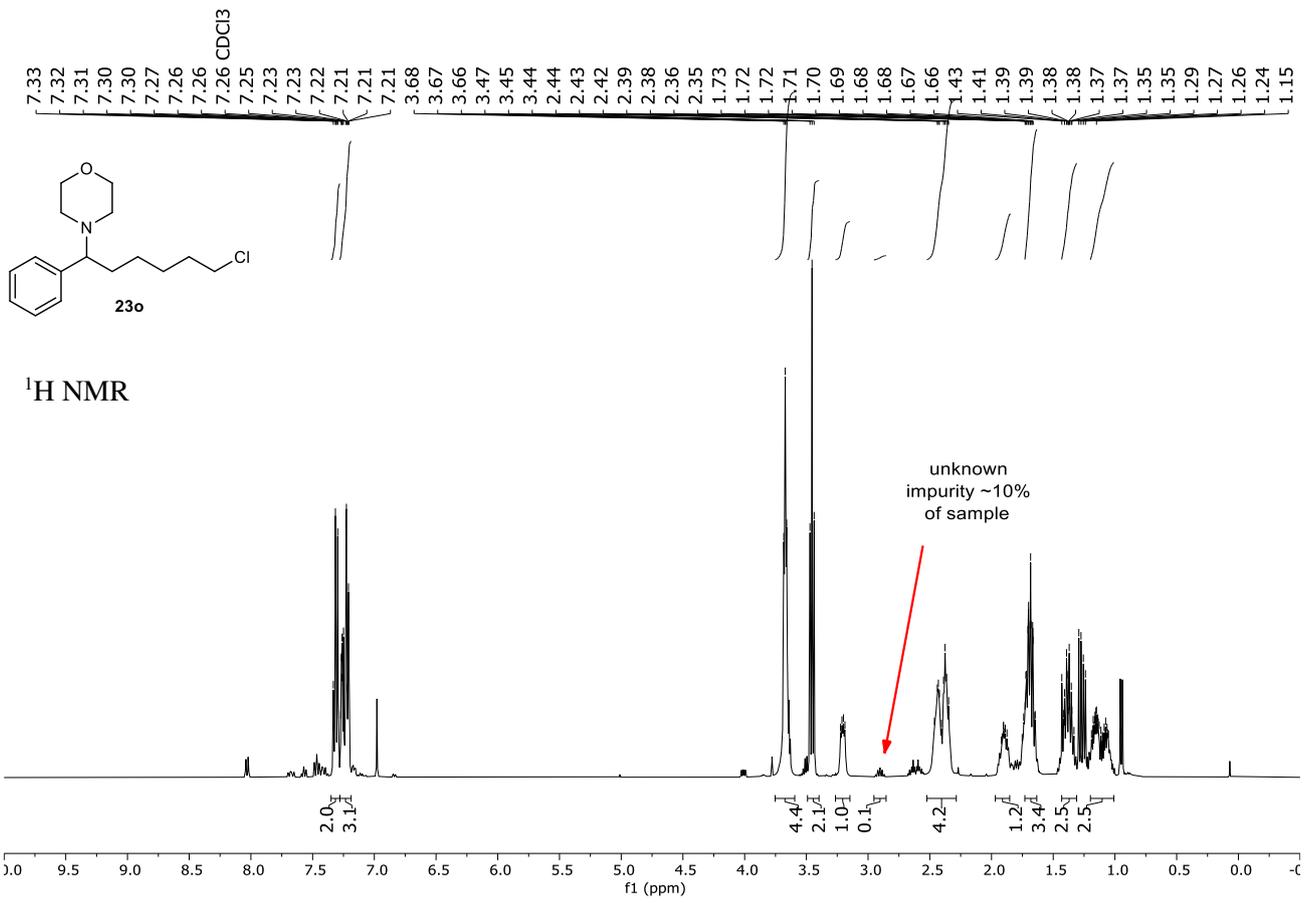


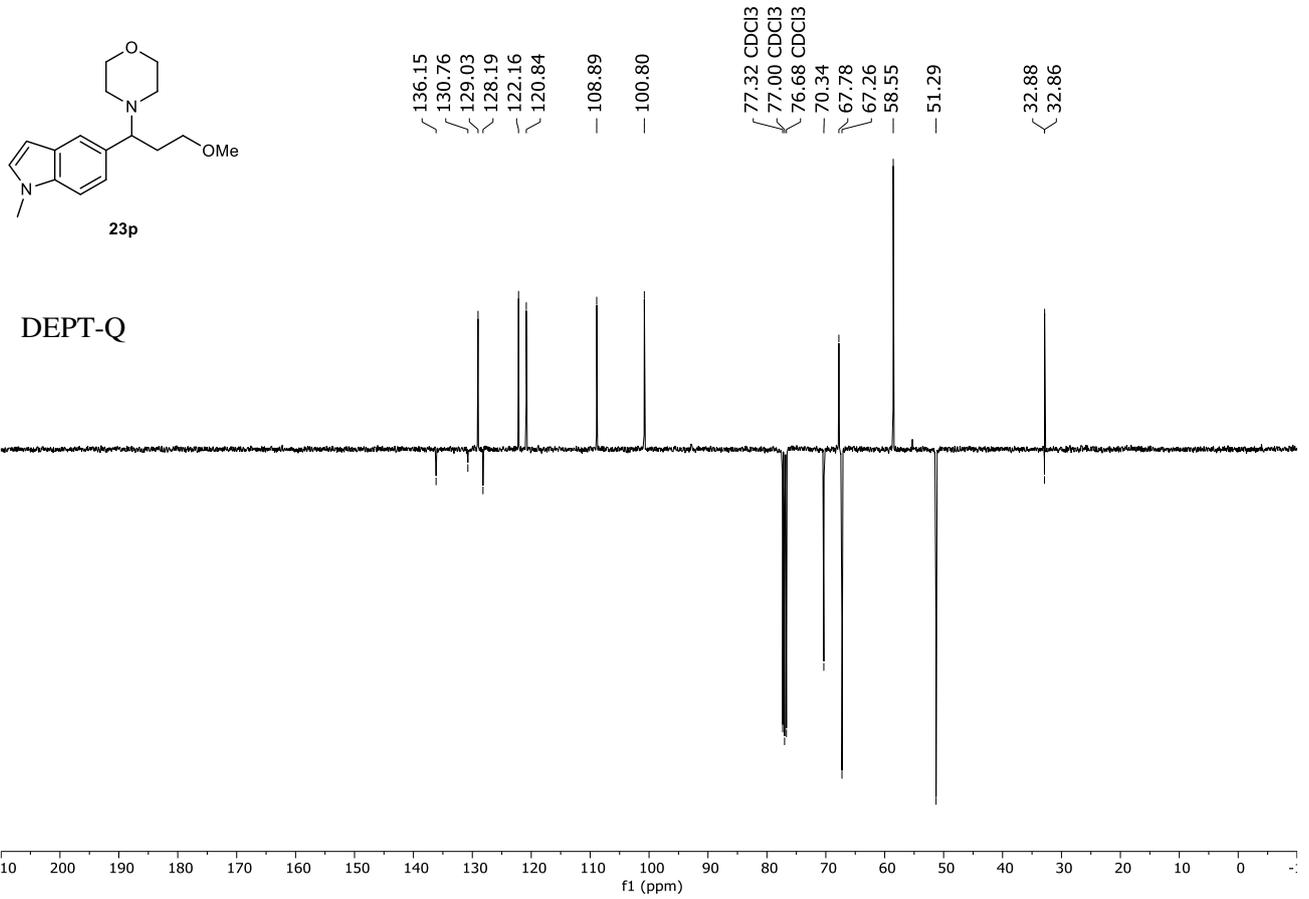
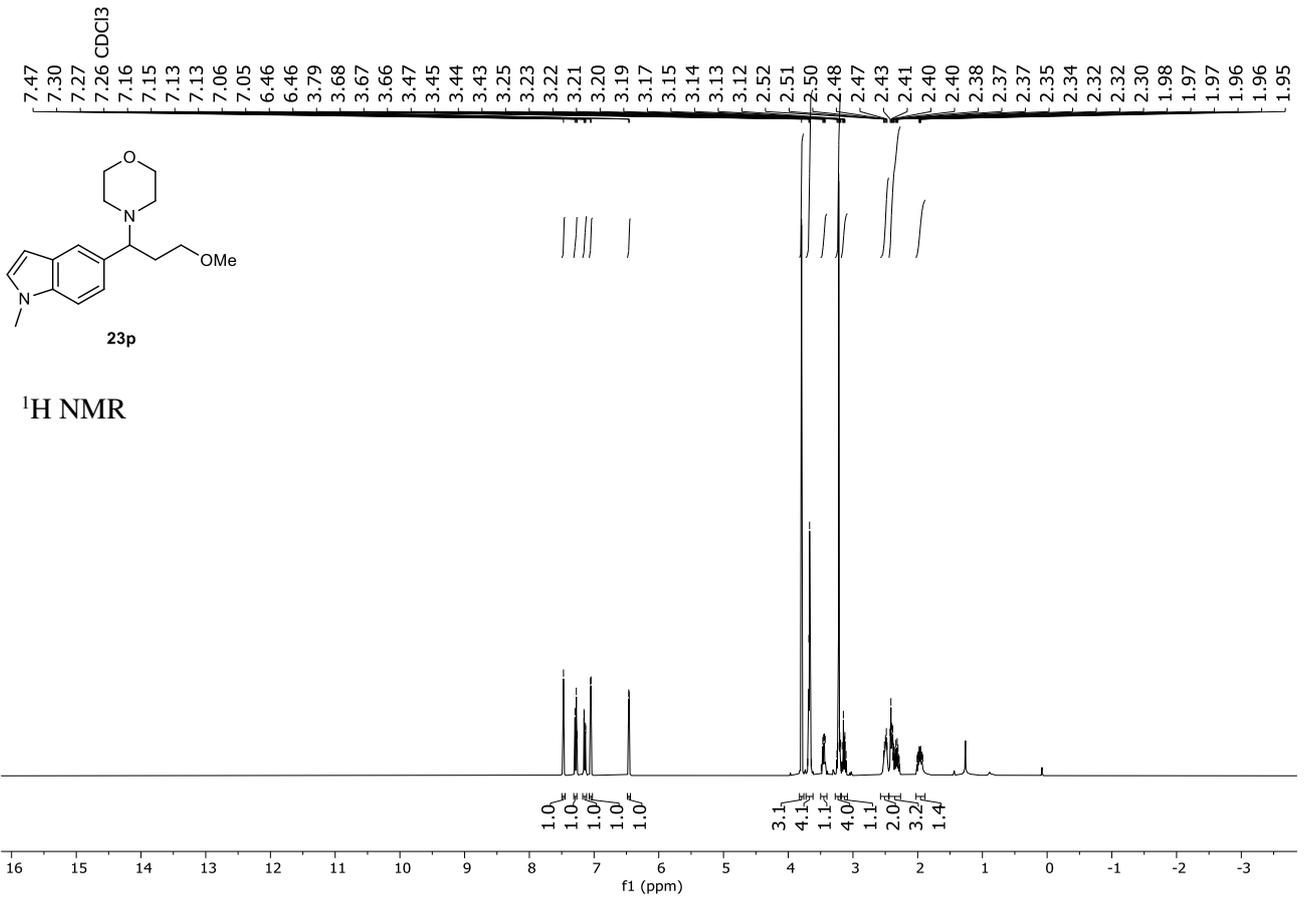
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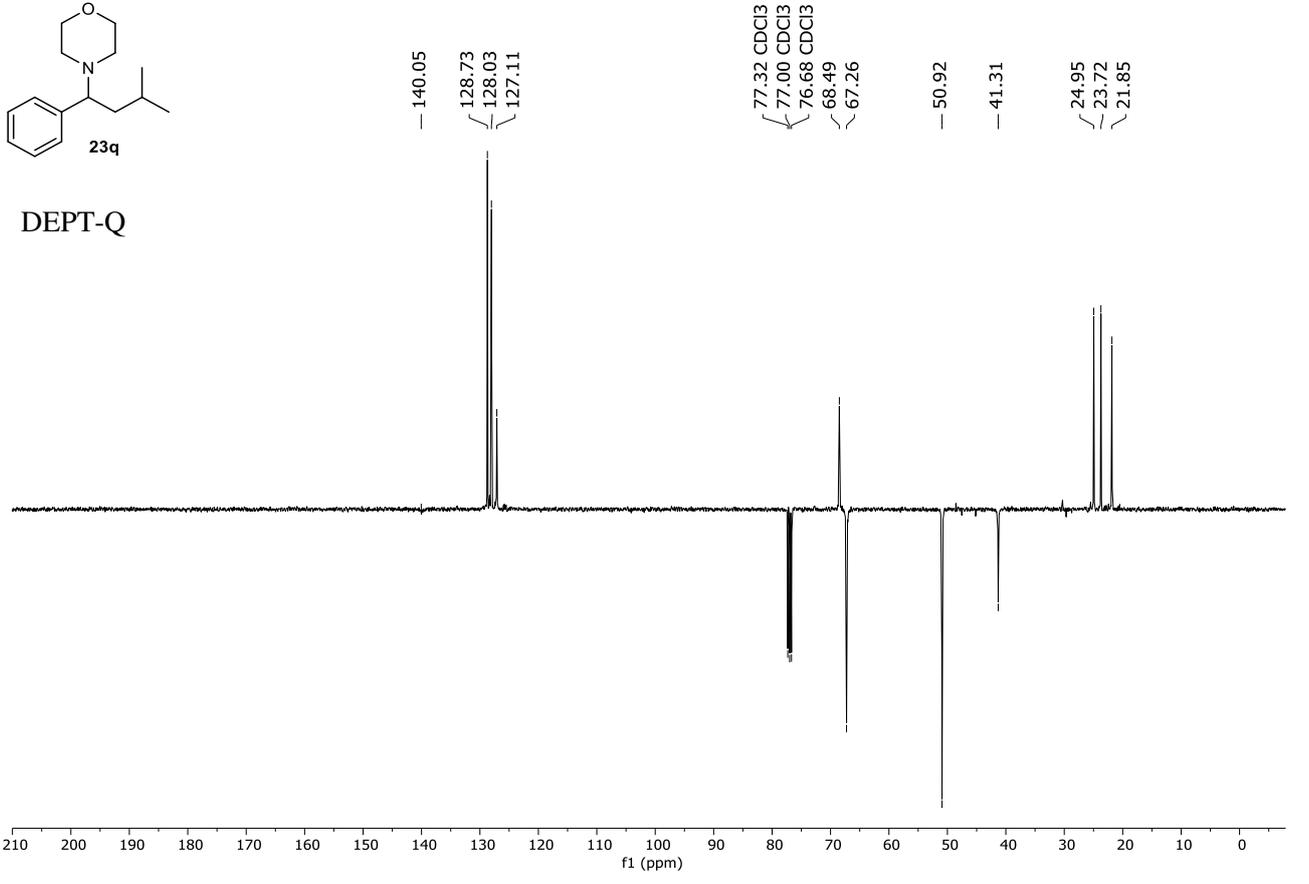
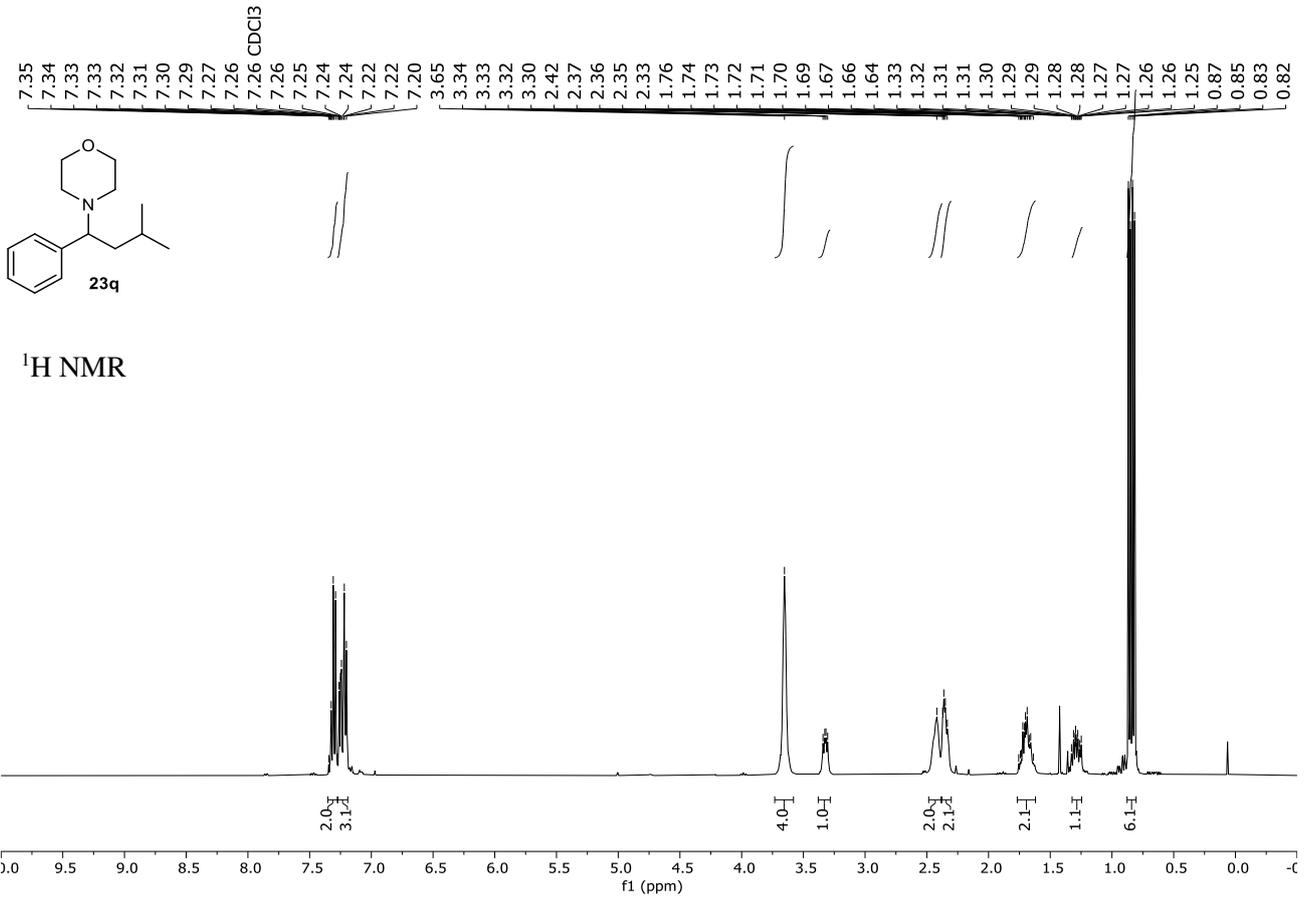


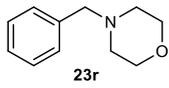
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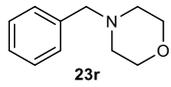
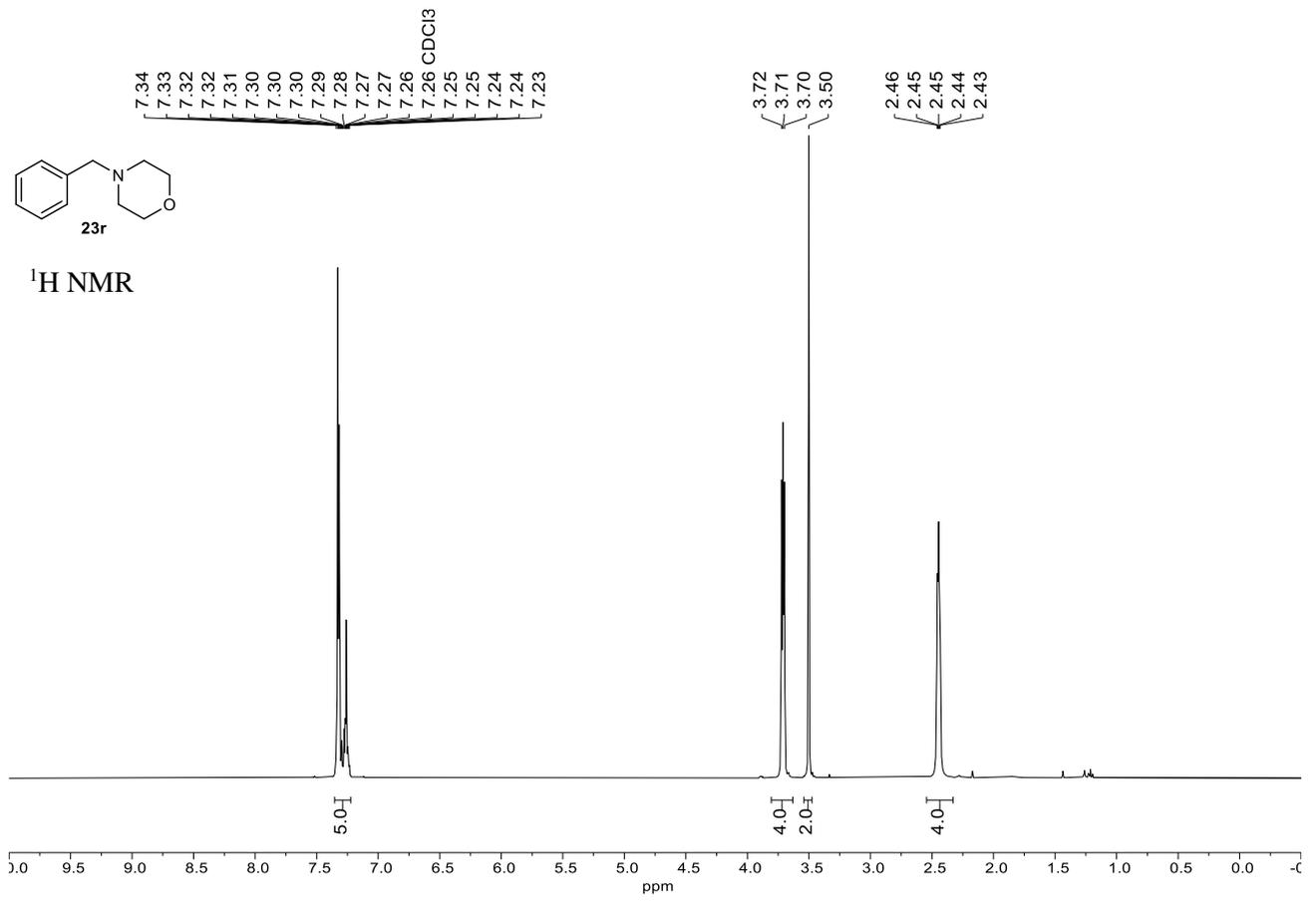




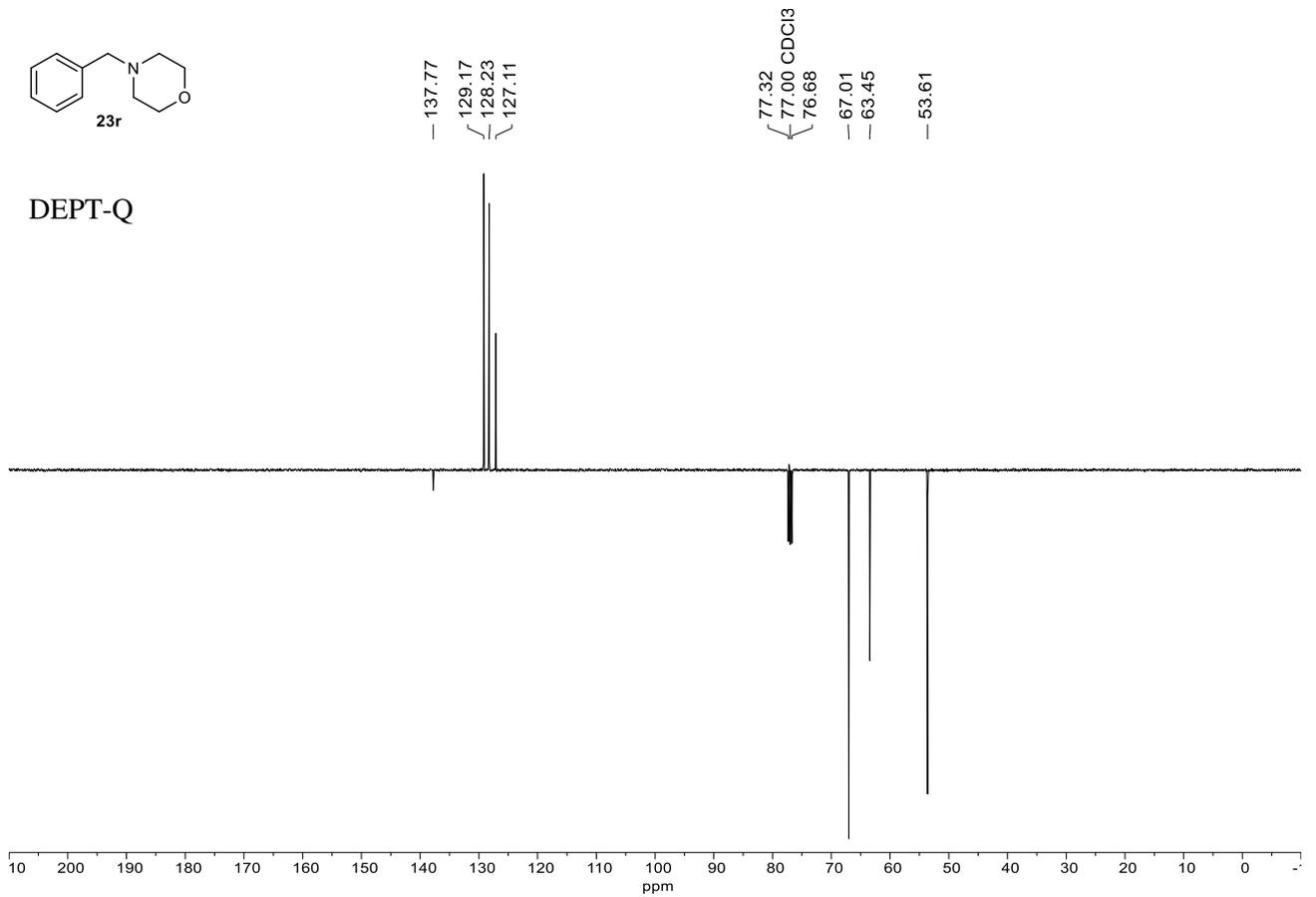




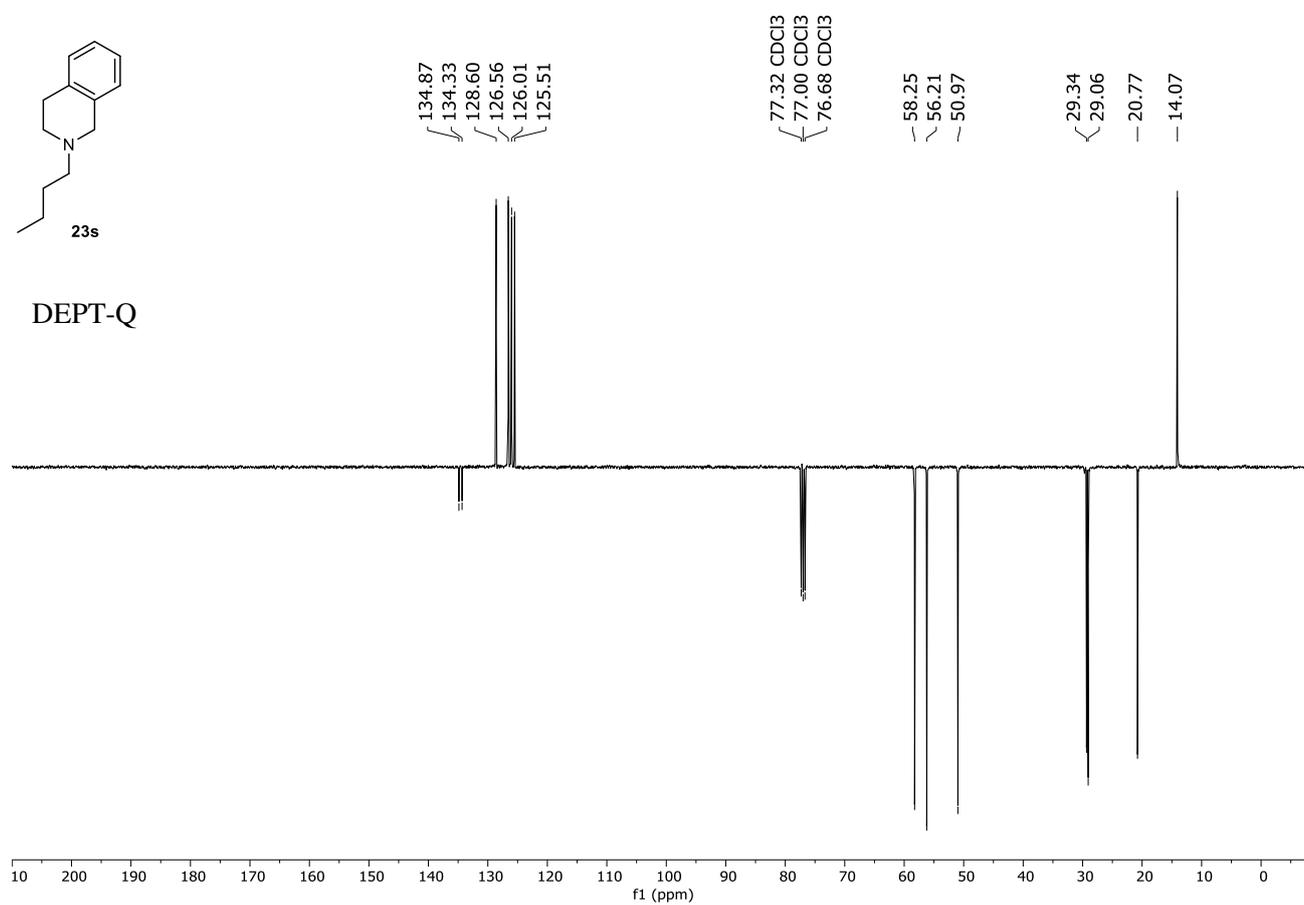
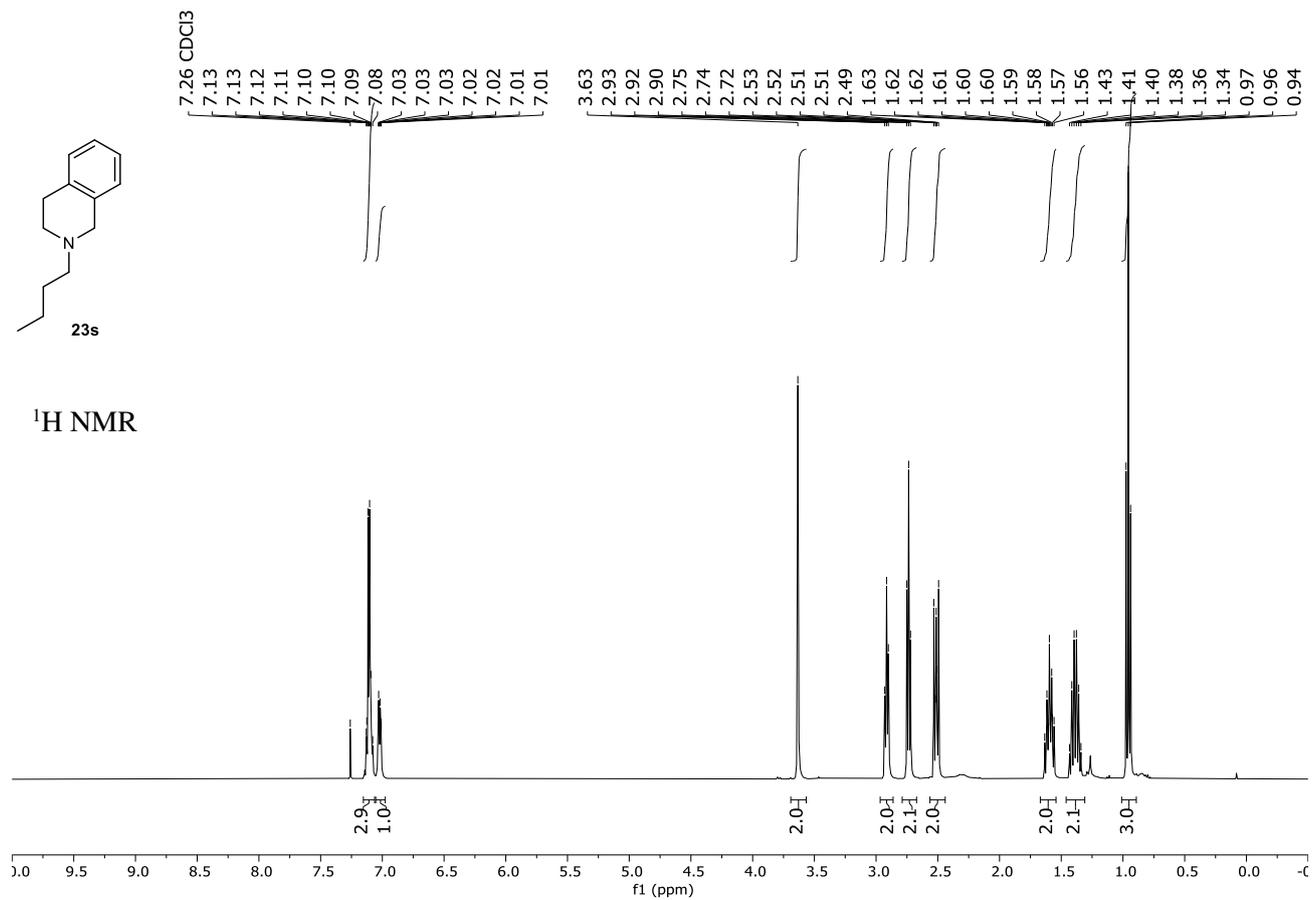
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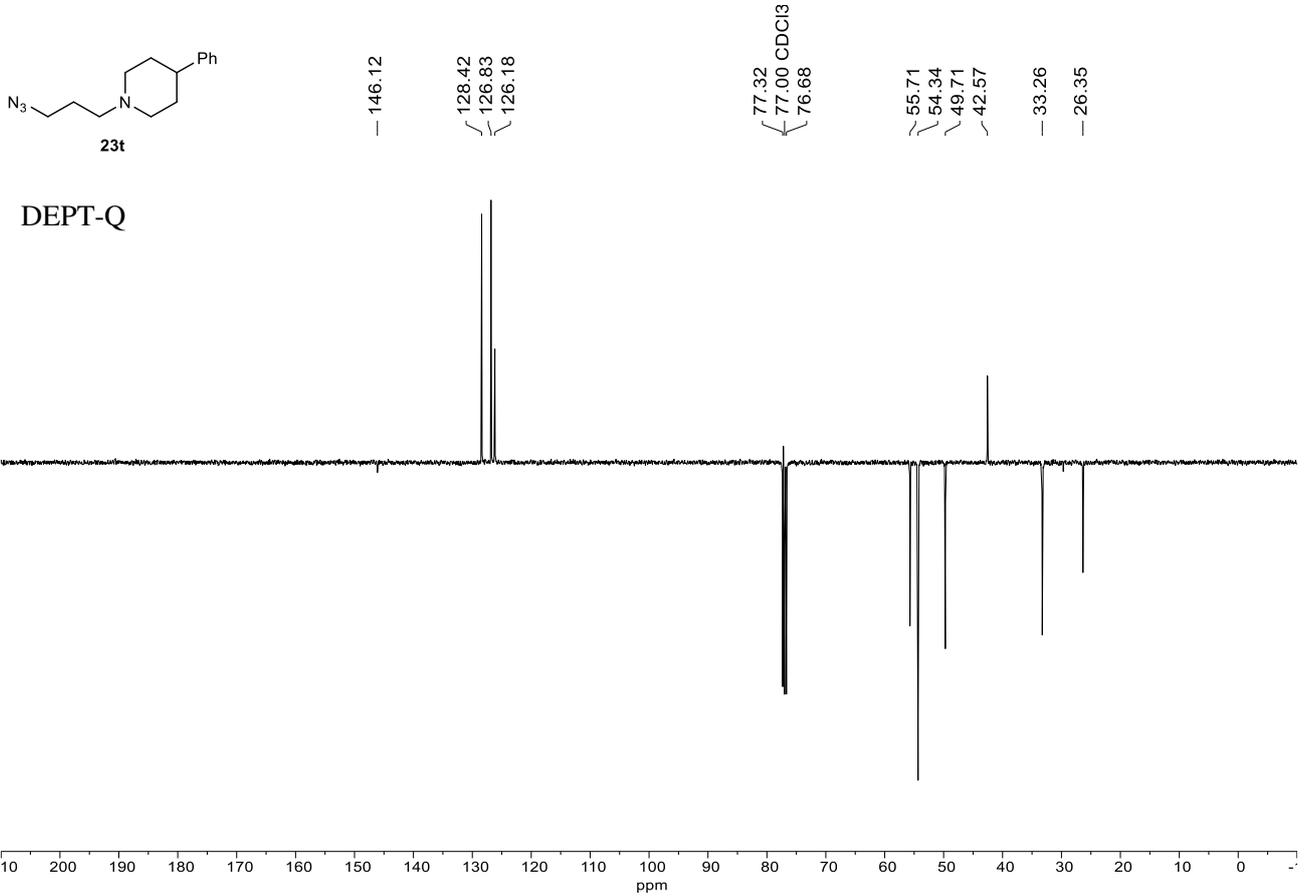
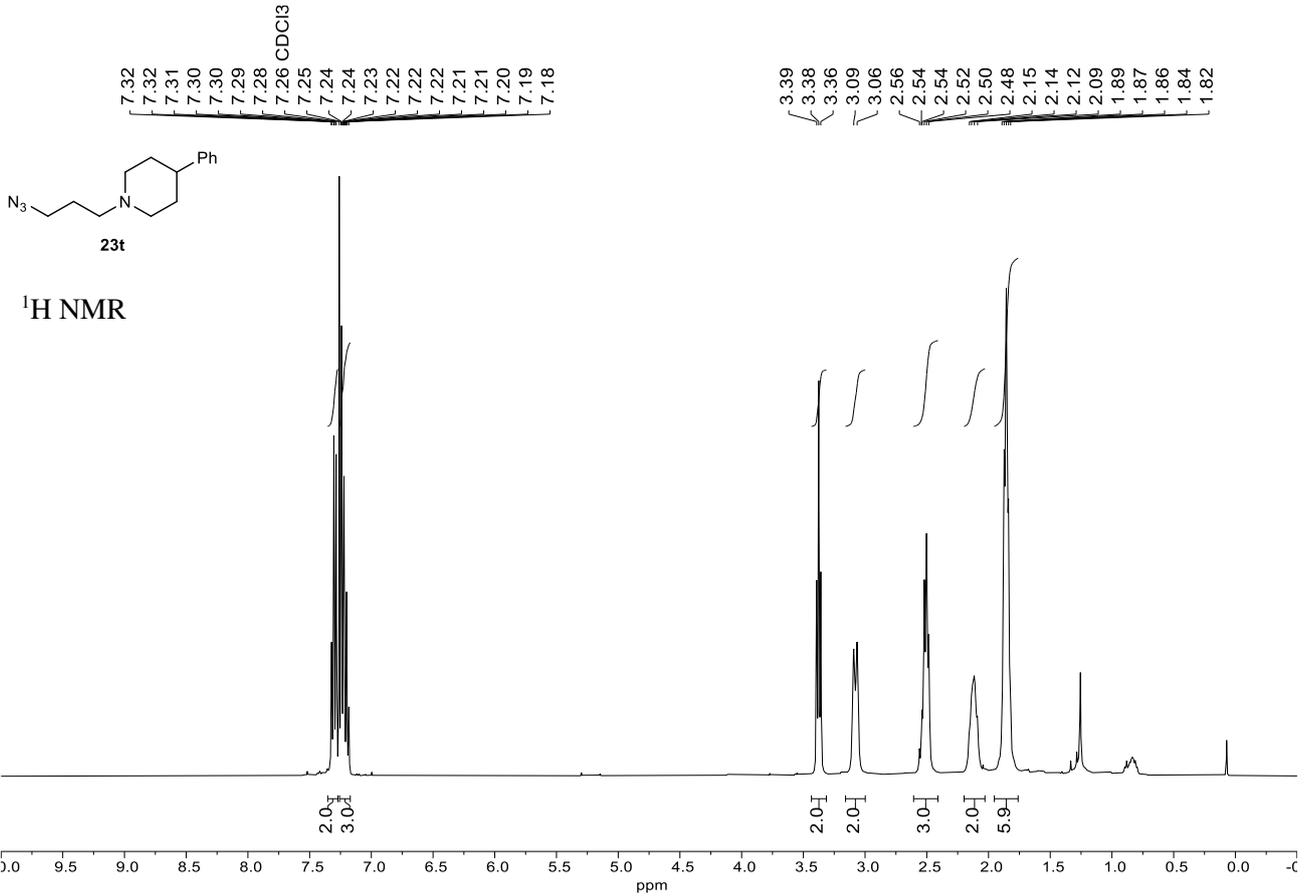


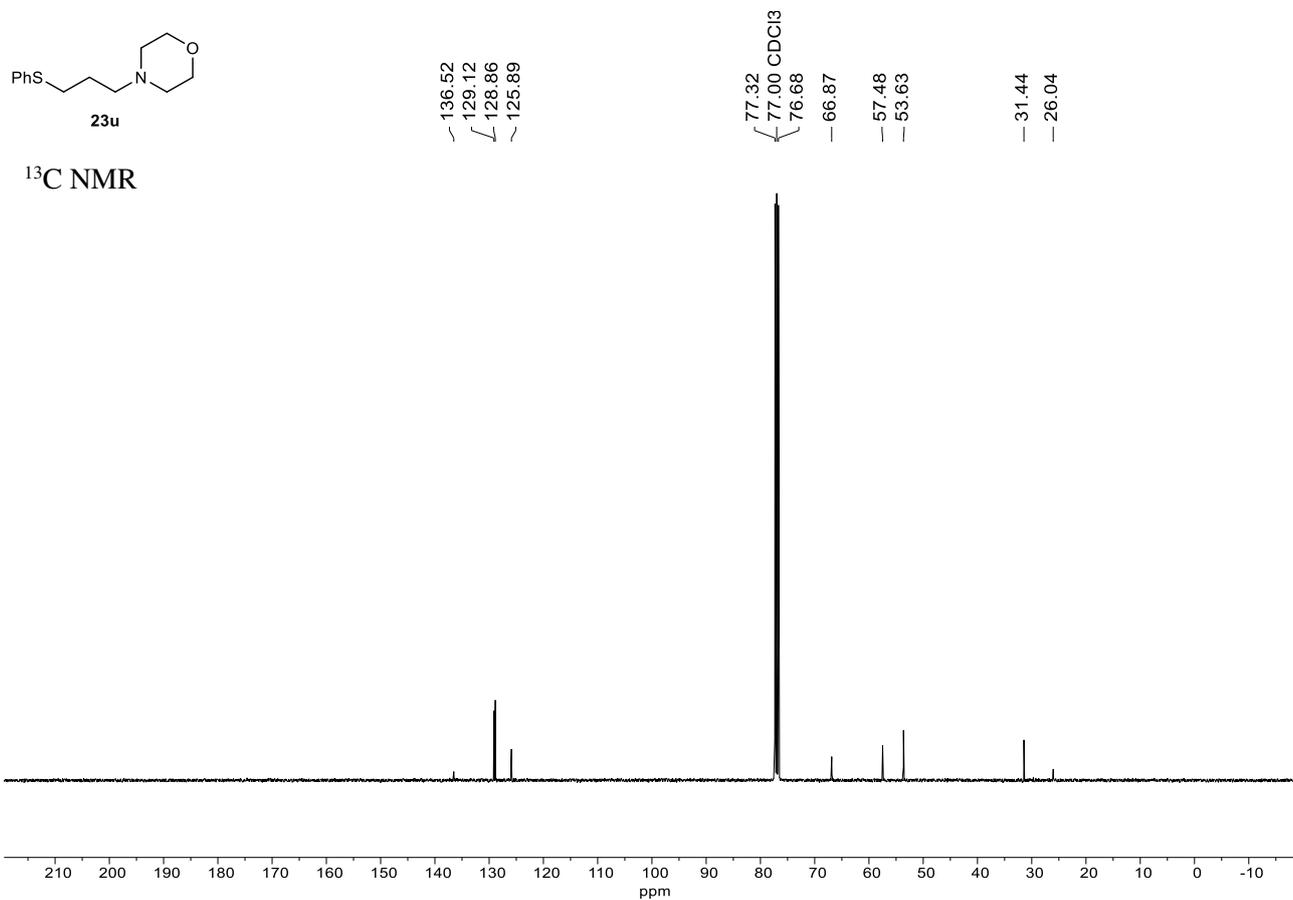
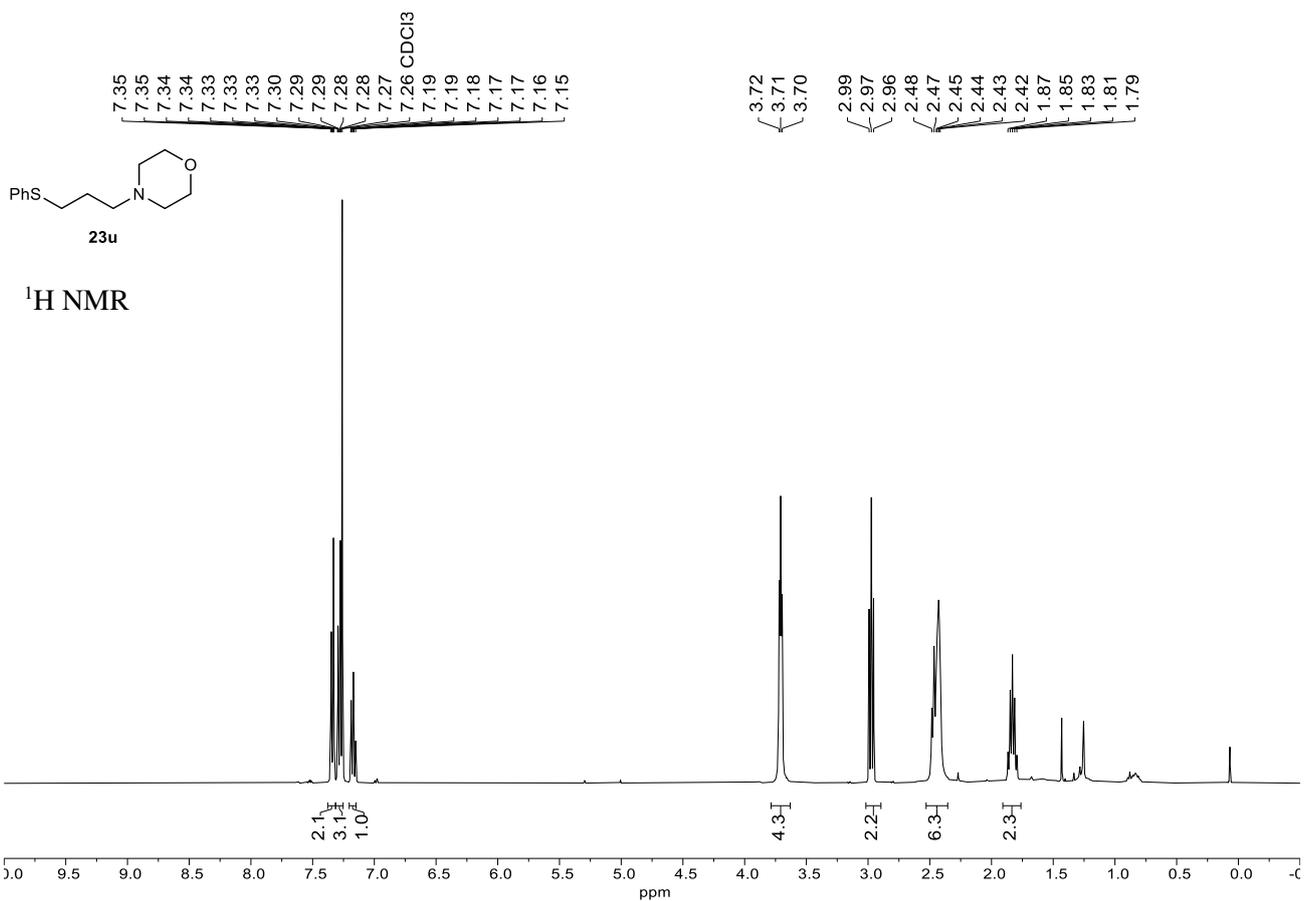
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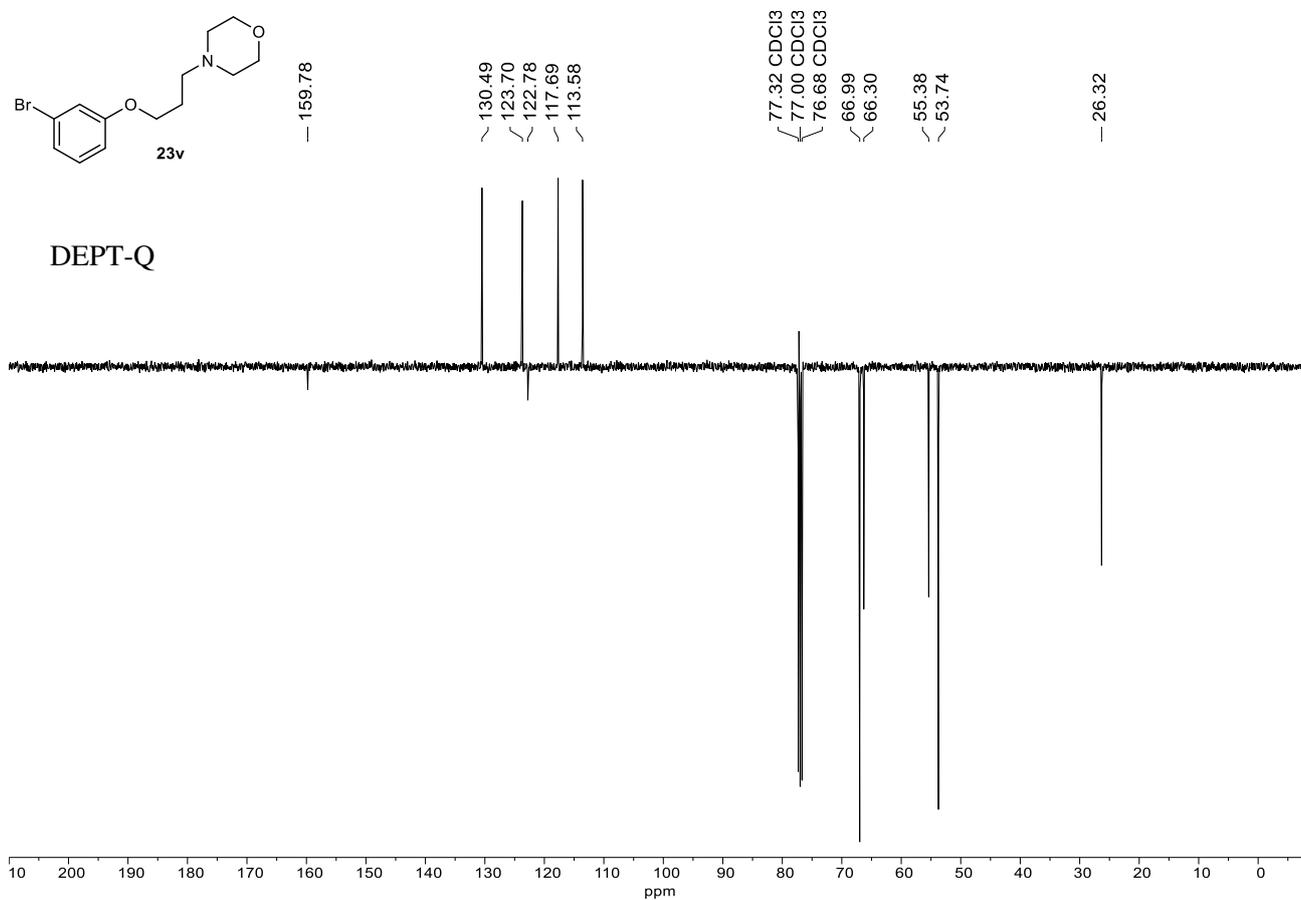
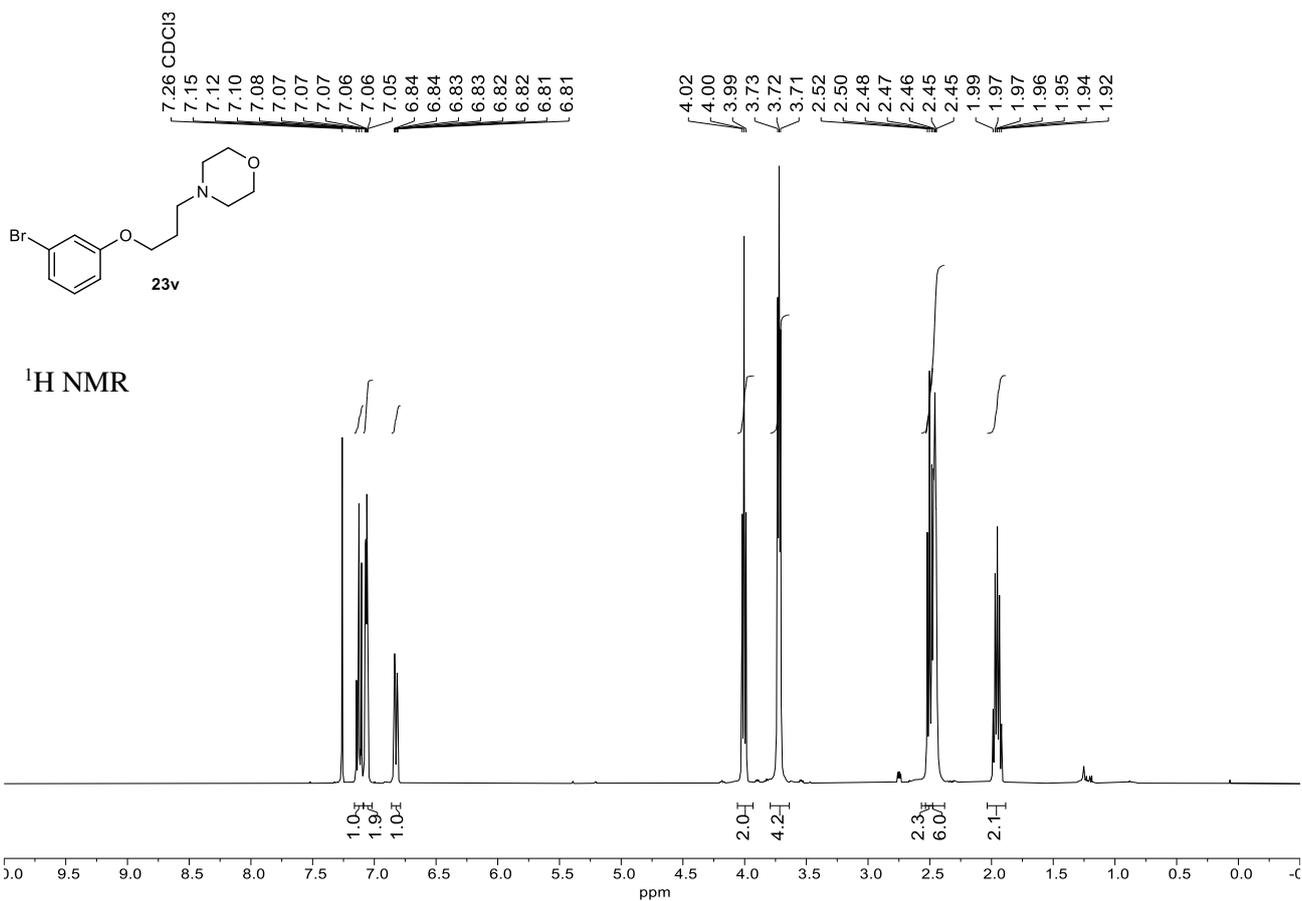


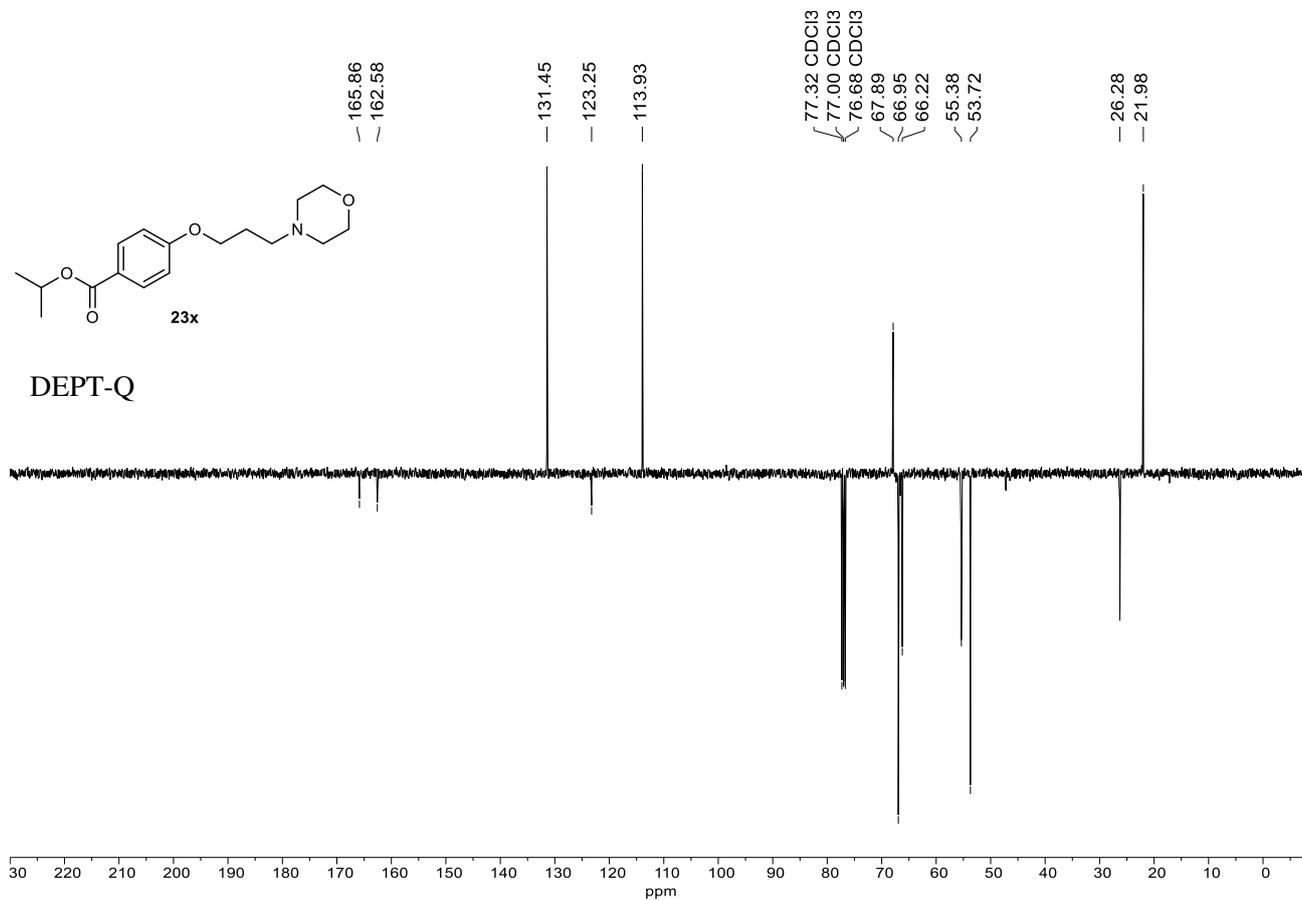
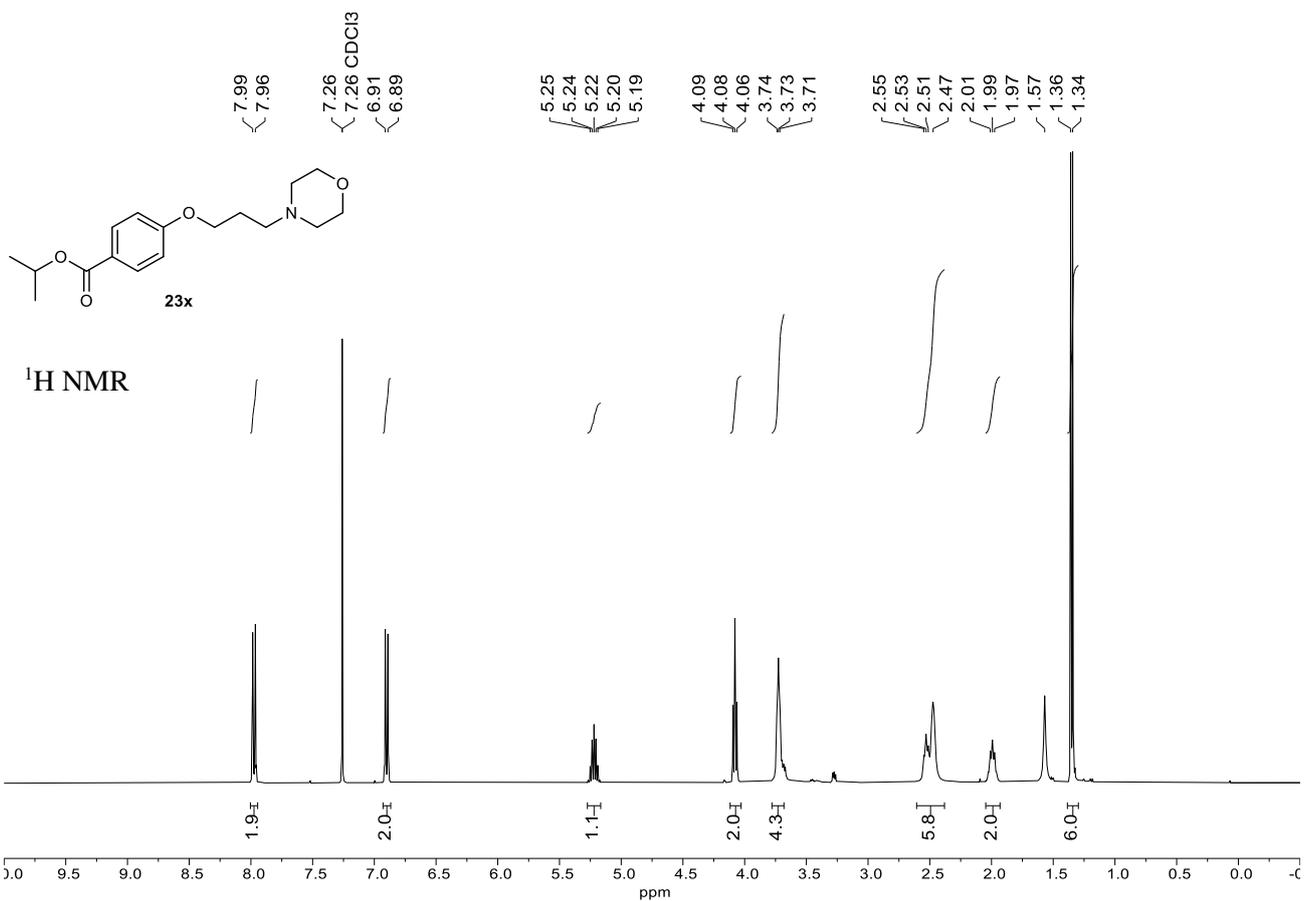
4.6. Coupling of Aliphatic Boronic Esters



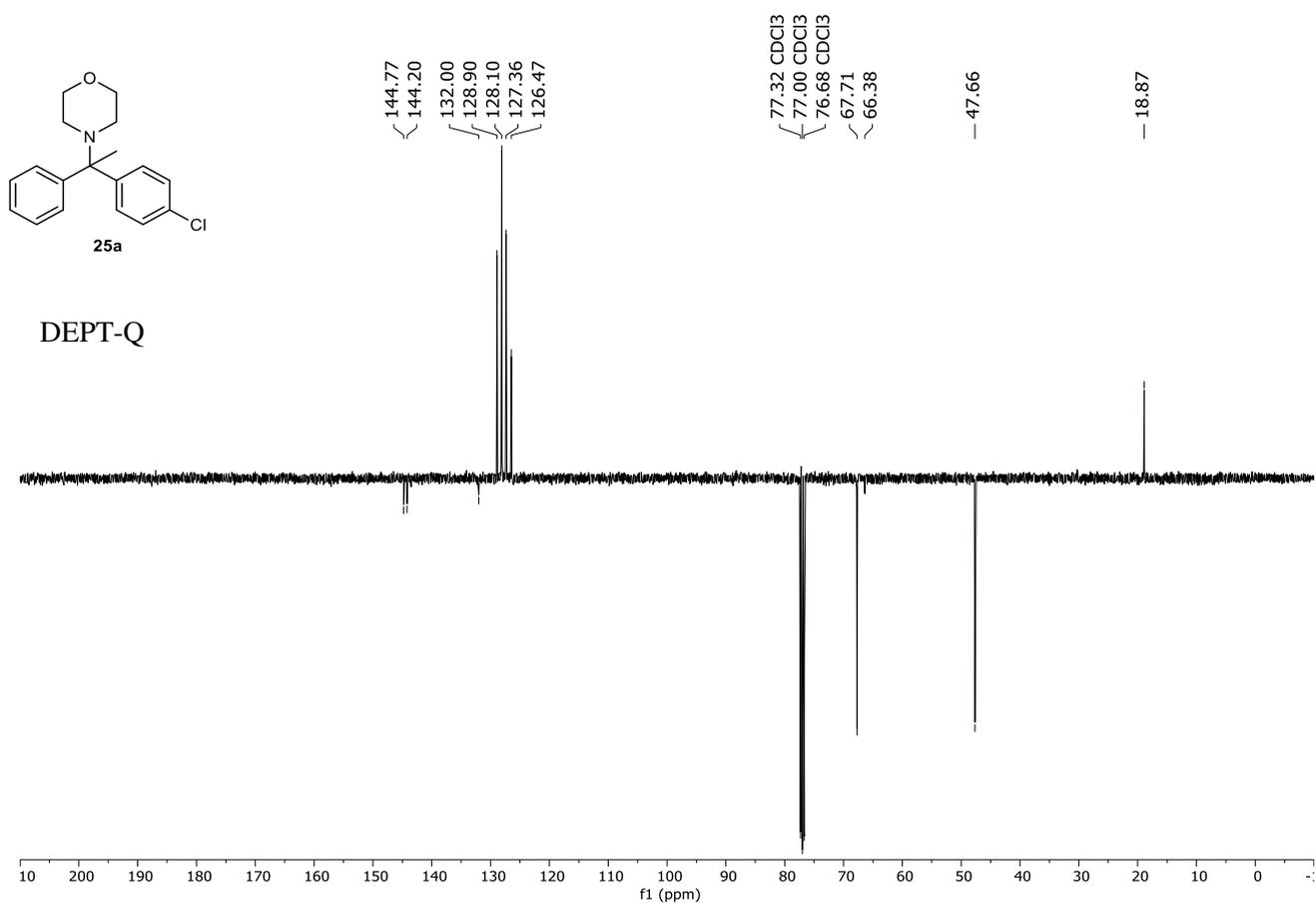
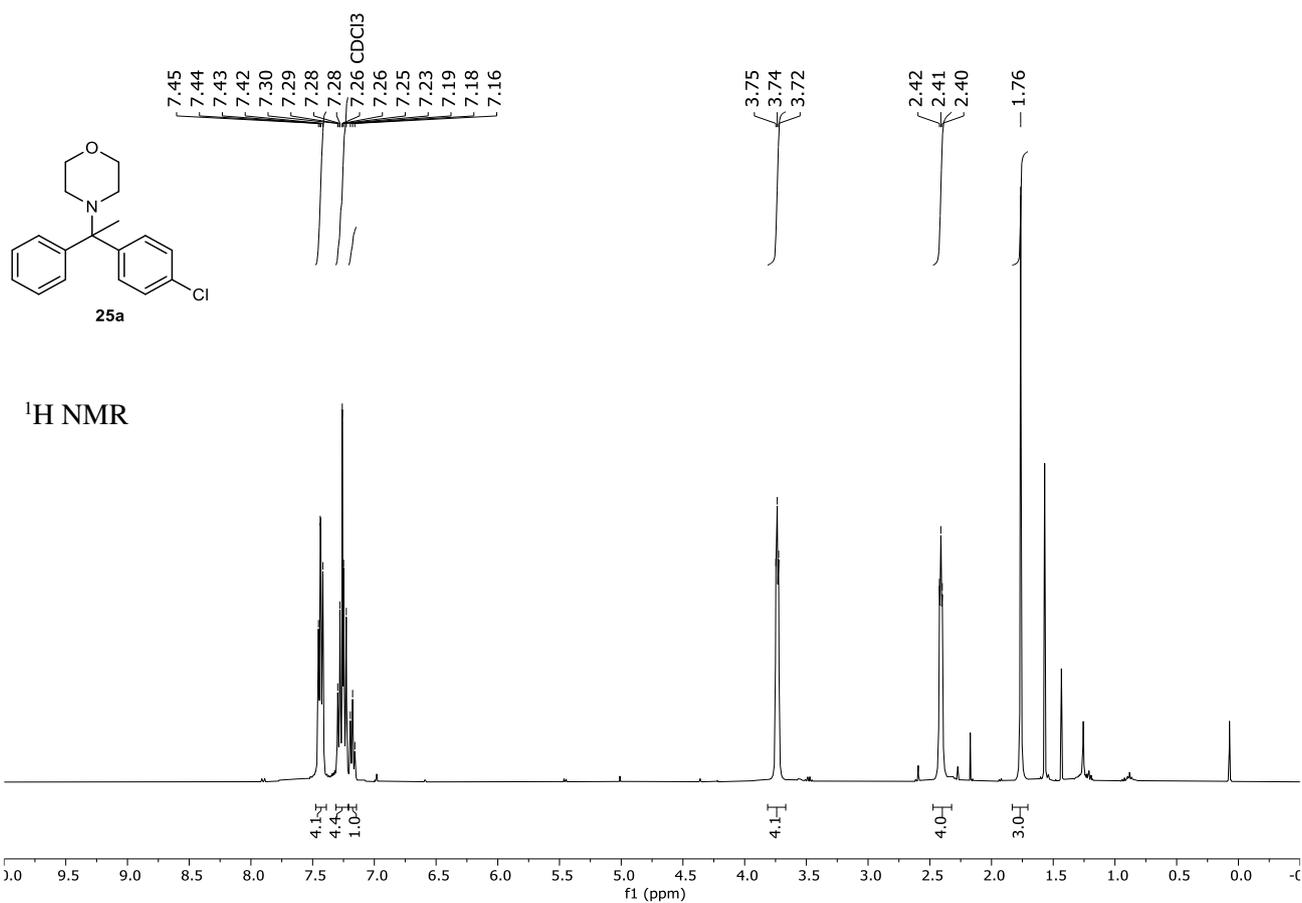


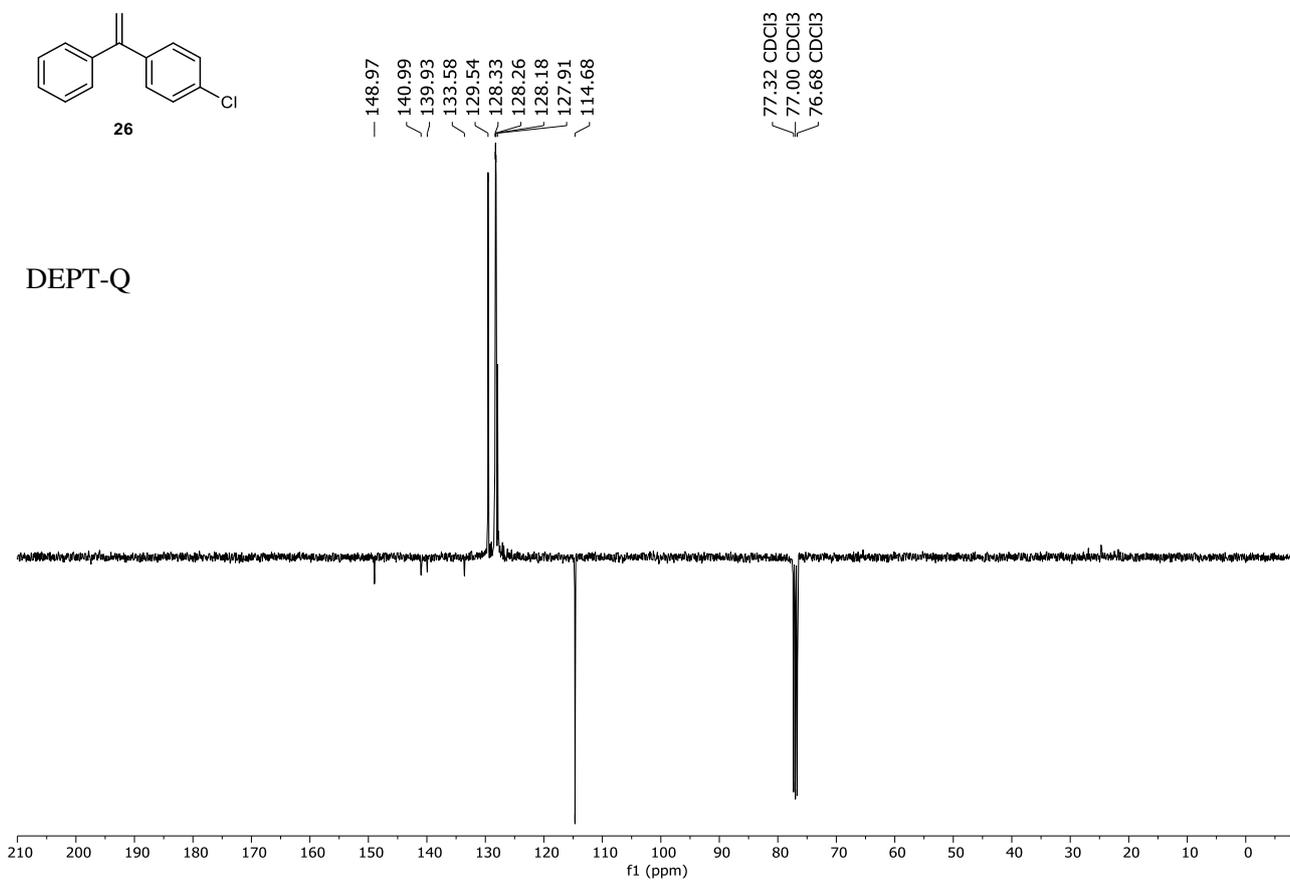
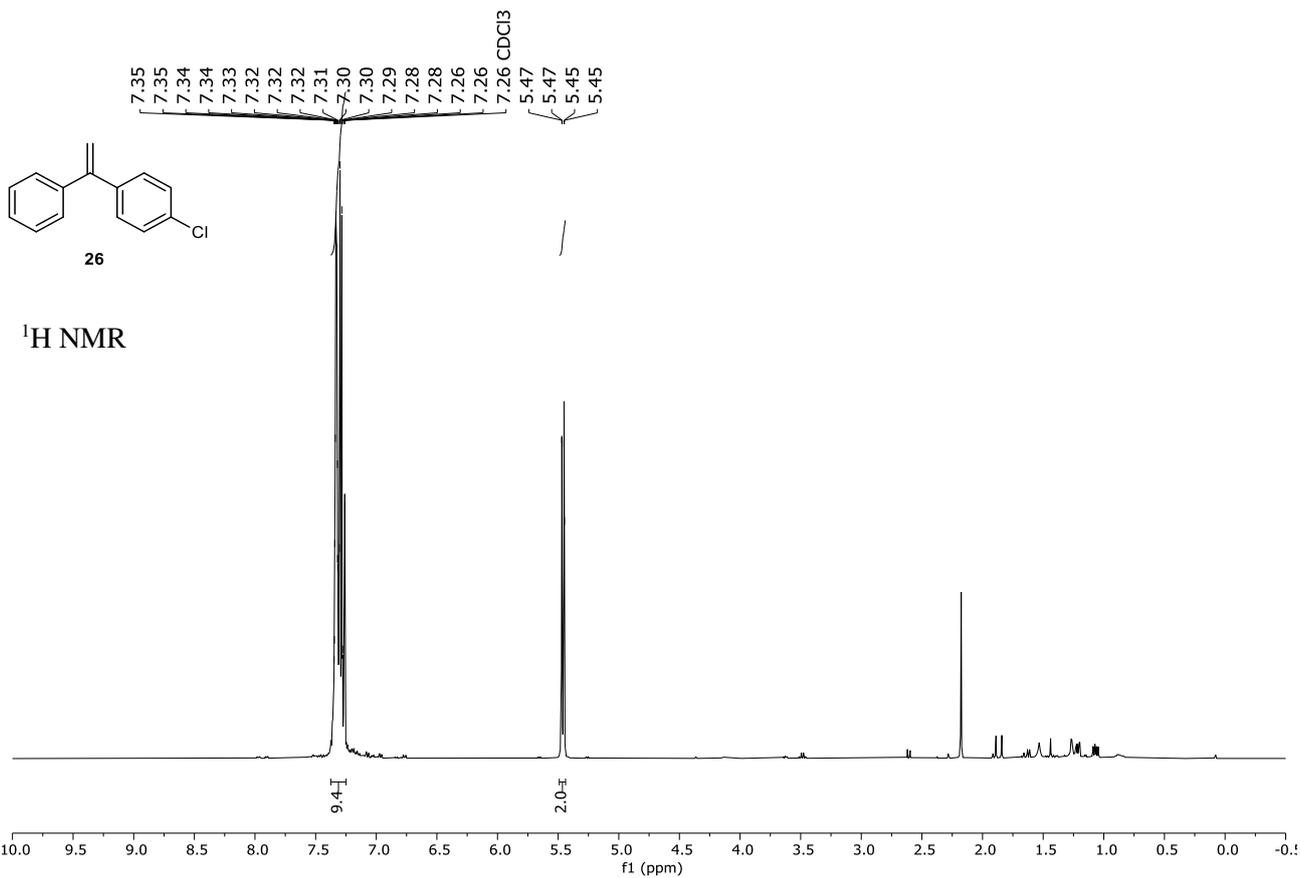


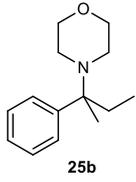




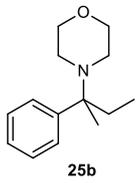
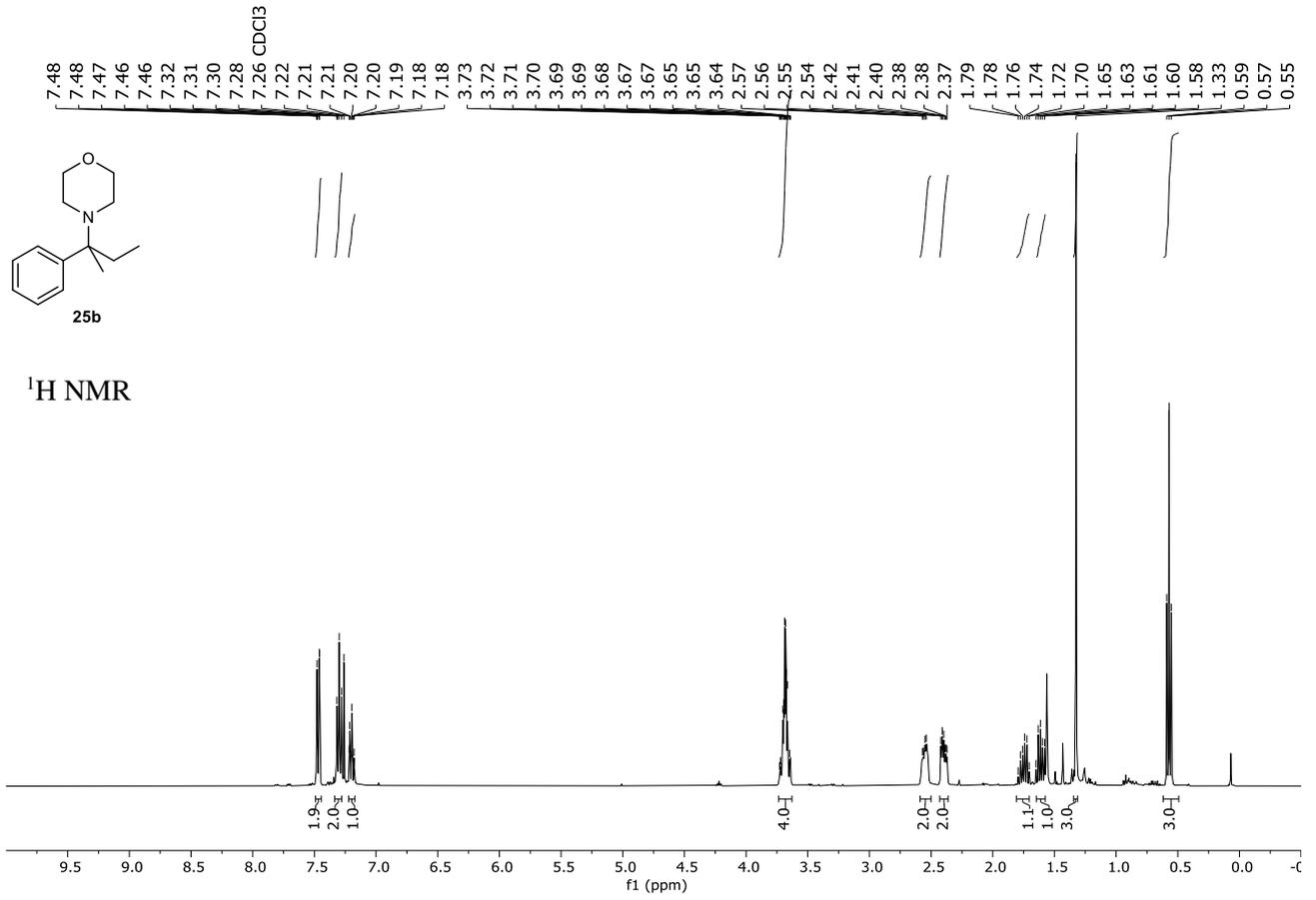
4.7. Coupling of Tertiary Boronic Esters



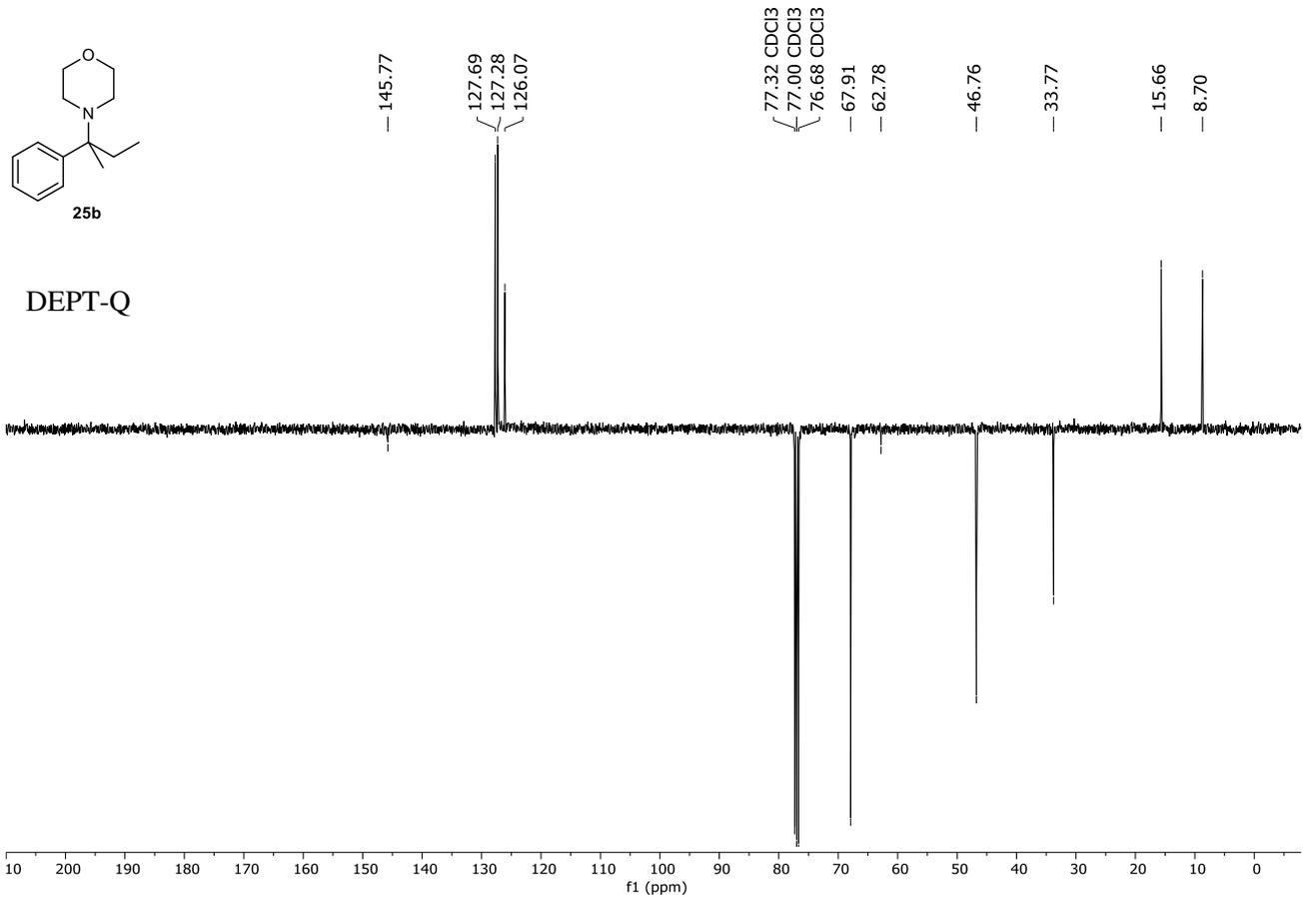




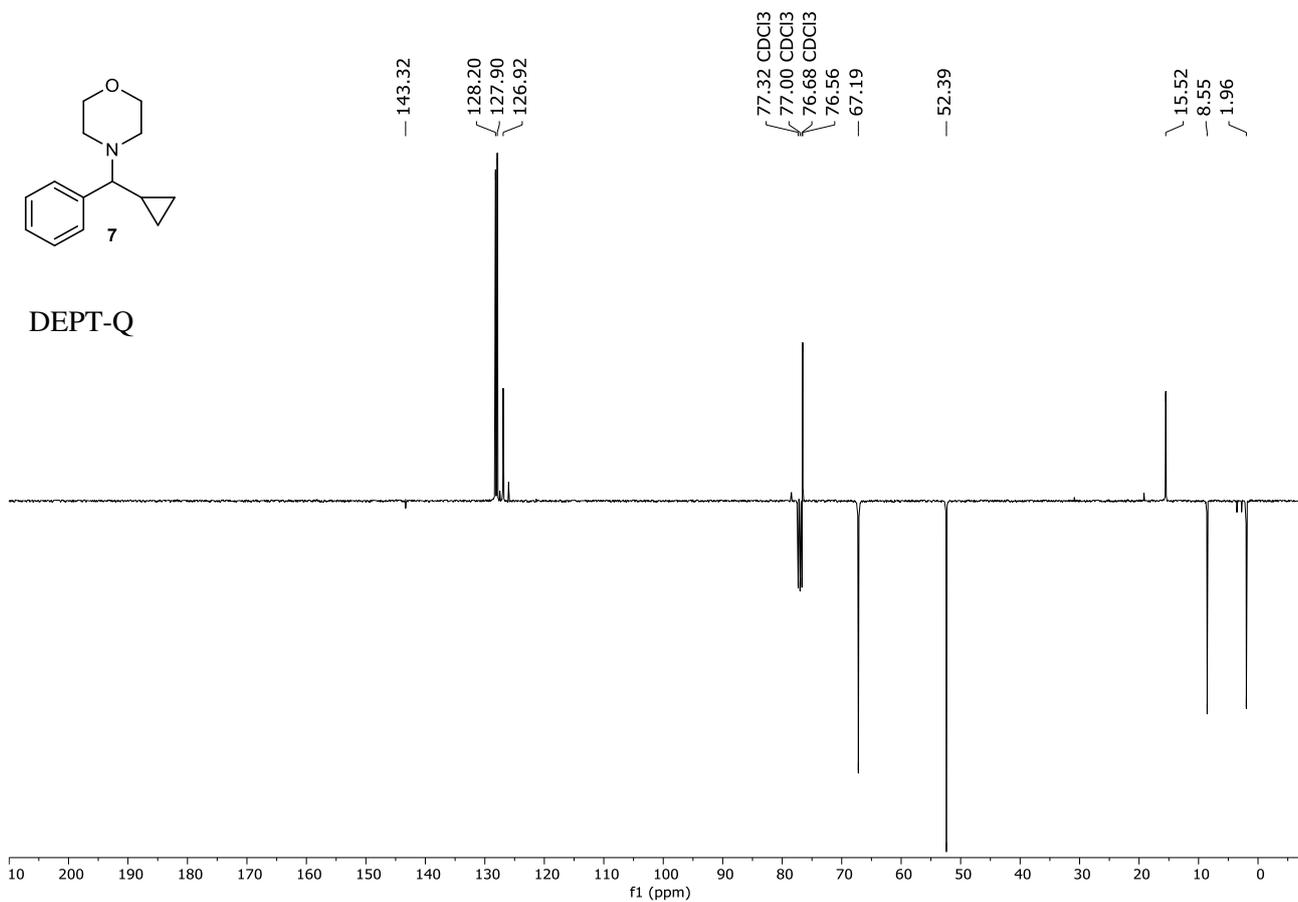
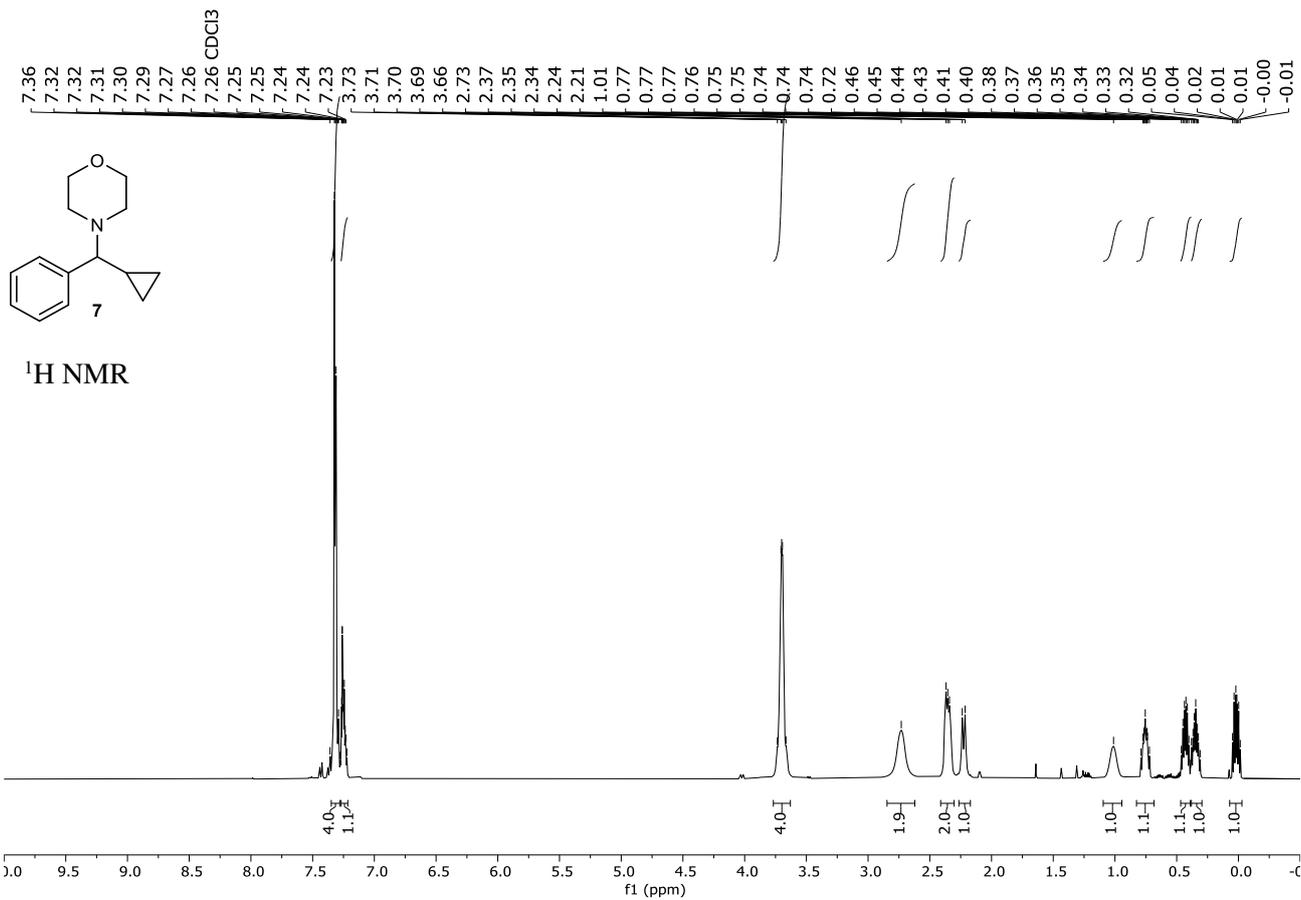
¹H NMR

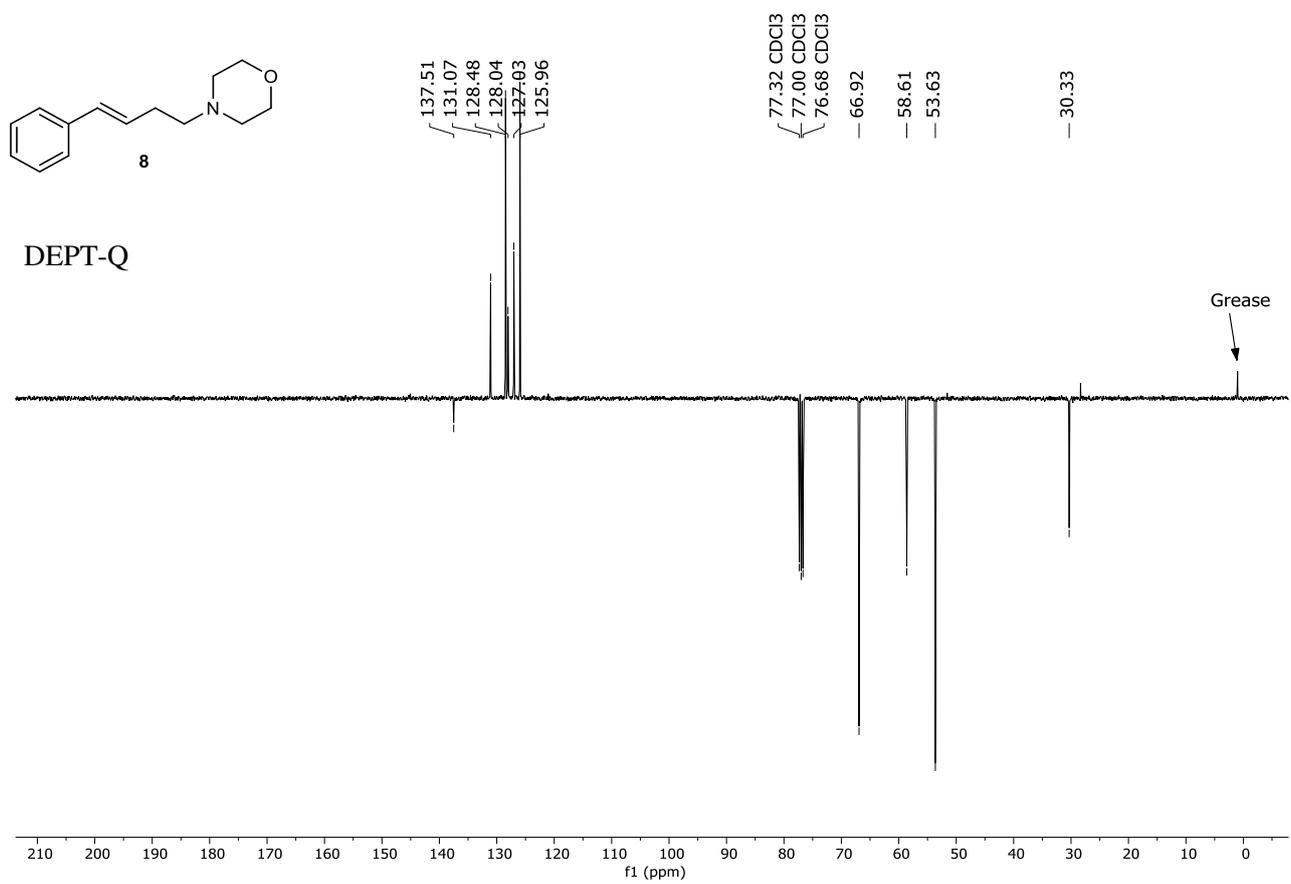
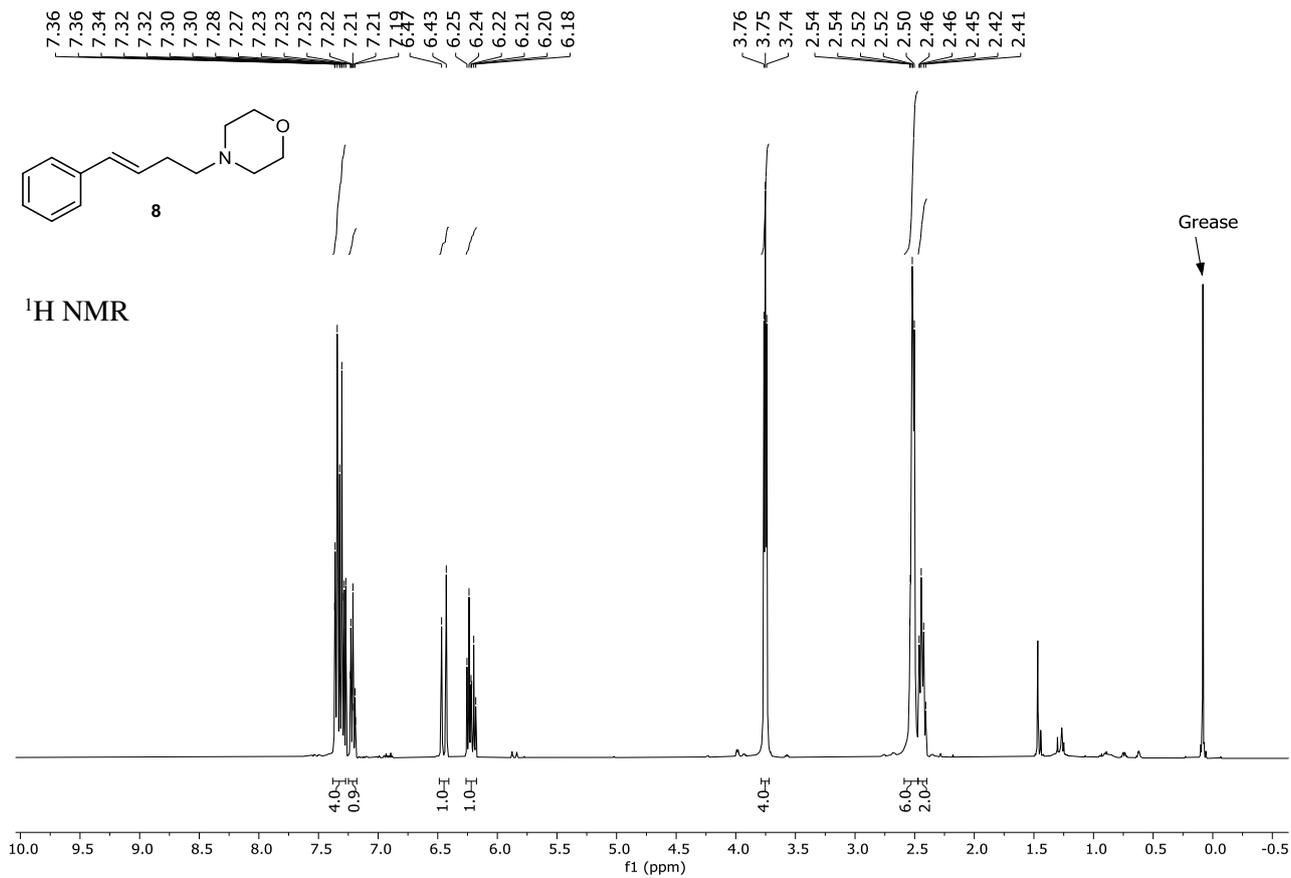


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4.9.Mechanistic Studies





5. References

- 1 J. D. Grayson and B. M. Partridge, *ACS Catal.*, 2019, **9**, 4296–4301.
- 2 J. D. Grayson, F. M. Dennis, C. C. Robertson and B. M. Partridge, *J. Org. Chem.*, 2021, **86**, 9883–9897.
- 3 C. Buathongjan, D. Beukeaw and S. Yotphan, *Eur. J. Org. Chem.*, 2015, **2015**, 1575–1582.
- 4 H.-L. Wang, J. Katon, C. Balan, A. W. Bannon, C. Bernard, E. M. Doherty, C. Dominguez, N. R. Gavva, V. Gore, V. Ma, N. Nishimura, S. Surapaneni, P. Tang, R. Tamir, O. Thiel, J. J. S. Treanor and M. H. Norman, *J. Med. Chem.*, 2007, **50**, 3528–3539.
- 5 D. Noh, S. K. Yoon, J. Won, J. Y. Lee and J. Yun, *Chem. Asian J.*, 2011, **6**, 1967–1969.
- 6 D. Noh, H. Chea, J. Ju and J. Yun, *Angew. Chemie Int. Ed.*, 2009, **48**, 6062–6064.
- 7 R. D. Grigg, J. W. Rigoli, R. Van Hoveln, S. Neale and J. M. Schomaker, *Chem. – A Eur. J.*, 2012, **18**, 9391–9396.
- 8 G. Vijaykumar, M. Bhunia and S. K. Mandal, *Dalt. Trans.*, 2019, **48**, 5779–5784.
- 9 J. Huang, W. Yan, C. Tan, W. Wu and H. Jiang, *Chem. Commun.*, 2018, **54**, 1770–1773.
- 10 M. K. Armstrong and G. Lalic, *J. Am. Chem. Soc.*, 2019, **141**, 6173–6179.
- 11 V. Bagutski, A. Ros and V. K. Aggarwal, *Tetrahedron*, 2009, **65**, 9956–9960.
- 12 J. D. Grayson, F. M. Dennis, C. C. Robertson and B. M. Partridge, *J. Org. Chem.*, 2021, **86**, 9883–9897.
- 13 S. Aichhorn, R. Bigler, E. L. Myers and V. K. Aggarwal, *J. Am. Chem. Soc.*, 2017, **139**, 9519–9522.
- 14 N. W. J. Ang and L. Ackermann, *Chem. – A Eur. J.*, 2021, **27**, 4883–4887.
- 15 M. Utsunomiya and J. F. Hartwig, *J. Am. Chem. Soc.*, 2003, **125**, 14286–14287.
- 16 C. Wang, A. Pettman, J. Basca and J. Xiao, *Angew. Chemie - Int. Ed.*, 2010, **49**, 7548–7552.
- 17 P. Spies, S. Schwendemann, S. Lange, G. Kehr, R. Fröhlich and G. Erker, *Angew. Chemie - Int. Ed.*, 2008, **47**, 7543–7546.
- 18 Y. Miki, K. Hirano, T. Satoh and M. Miura, *Angew. Chemie Int. Ed.*, 2013, **52**, 10830–10834.
- 19 J. L. Nallasivam and R. A. Fernandes, *Eur. J. Org. Chem.*, 2015, **2015**, 2012–2022.
- 20 J. D. Firth, P. O'Brien and L. Ferris, *J. Am. Chem. Soc.*, 2016, **138**, 651–659.
- 21 S. Zhu, N. Niljianskul and S. L. Buchwald, *J. Am. Chem. Soc.*, 2013, **135**, 15746–15749.
- 22 Z. R. Valiullina, S. S. Gataullin, B. Y. Tsirel'son, R. F. Valeev and M. S. Miftakhov, *Russ. J. Org. Chem.*, 2012, **48**, 439–441.
- 23 M. H. S. A. Hamid, C. L. Allen, G. W. Lamb, A. C. Maxwell, H. C. Maytum, A. J. A. Watson and J. M. J. Williams, *J. Am. Chem. Soc.*, 2009, **131**, 1766–1774.
- 24 A. Hamza, K. Sorochkina, B. Kótai, K. Chernichenko, D. Berta, M. Bolte, M. Nieger, T. Repo and I. Pápai, *ACS Catal.*, 2020, **10**, 14290–14301.

- 25 L. C. M. Castro, J.-B. Sortais and C. Darcel, *Chem. Commun.*, 2012, **48**, 151–153.
- 26 Q. Lei, Y. Wei, D. Talwar, C. Wang, D. Xue and J. Xiao, *Chem. Eur. J.*, 2013, **19**, 4021–4029.
- 27 V. H. Vu, L. A. Jouanno, A. Cheignon, T. Roisnel, V. Dorcet, S. Sinbandhit and J. P. Hurvois, *Eur. J. Org. Chem.*, 2013, 5464–5474.
- 28 J. Choi, N. N. Yadav and H. J. Ha, *Asian J. Org. Chem.*, 2017, **6**, 1292–1307.
- 29 R. Kawahara, K. Fujita and R. Yamaguchi, *J. Am. Chem. Soc.*, 2010, **132**, 15108–15111.
- 30 T. Hou, P. Lu and P. Li, *Tetrahedron Lett.*, 2016, **57**, 2273–2276.
- 31 T. Jia, S. Fan, F. Li, X. Ye, W. Zhang, Z. Song and X. Shi, *Org. Lett.*, 2021, **23**, 6019–6023.
- 32 M. C. Willis and G. N. Brace, *Tetrahedron Lett.*, 2002, **43**, 9085–9088.
- 33 C. Xu, Z. Zhu, Y. Wang, Z. Jing, B. Gao, L. Zhao and W.-K. Dong, *J. Org. Chem.*, 2019, **84**, 2234–2242.
- 34 V. Vinayagam, S. K. Sadhukhan, S. K. Karre, R. Srinath, R. K. Maroju, P. R. Karra, H. S. N. B. Bathula, S. Kundrapu and S. R. Surukonti, *Org. Lett.*, 2023, **25**, 4610–4614.
- 35 R. J. Mattson, K. M. Pham, D. J. Leuck and K. A. Cowen, *J. Org. Chem.*, 1990, **55**, 2552–2554.
- 36 Y. Zou, L. Qin, X. Ren, Y. Lu, Y. Li and J. (Steve) Zhou, *Chem. – A Eur. J.*, 2013, **19**, 3504–3511.
- 37 Y.-F. Zhang, X.-Y. Dong, J.-T. Cheng, N.-Y. Yang, L.-L. Wang, F.-L. Wang, C. Luan, J. Liu, Z.-L. Li, Q.-S. Gu and X.-Y. Liu, *J. Am. Chem. Soc.*, 2021, **143**, 15413–15419.
- 38 S. Stoll and A. Schweiger, *J. Magn. Reson.*, 2006, **178**, 42–55.
- 39 G. R. Buettner, *Free Radic. Biol. Med.*, 1987, **3**, 259–303.