

Evolution of the dearomative functionalization of activated quinolines and isoquinolines: expansion of the electrophile scope

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Electronic Supplementary information

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General Experimental Techniques

Chemicals and solvents

Unless stated otherwise, all chemicals were purchased from commercial suppliers (Sigma-Aldrich, Fluorochem, Alfa Aesar, TCI) and used without further purification. Formic acid/triethylamine 5:2 complex was purchased from Sigma-Aldrich and used without further purification. Rh-catalyst stock solutions were prepared in a 25-mL volumetric flask by dissolving 2 mg $[\text{RhCp}^*\text{Cl}_2]_2$ in acetonitrile. All solvents used were HPLC grade or p.a. unless stated otherwise. Pentamethylphenyl vinyl ketone was prepared according to a published procedure.¹

Glassware and reaction conditions

Reactions were carried out in flasks, oven-dried microwave vials, or fresh GC vials under an atmosphere of air unless otherwise stated.

Analytical techniques

^1H , and ^{13}C NMR spectra were recorded on a Bruker AVIII400 Spectrometer (^1H : 400 MHz and ^{13}C : 101 MHz), Bruker AVII500 (^1H : 500 MHz and ^{13}C : 126 MHz) or a Bruker AvanceIV600 (^1H : 600 MHz and ^{13}C : 151 MHz) in CDCl_3 , $\text{DMSO}-d_6$ or C_6D_6 and referenced to residual solvent peaks. Chemical shifts δ are quoted in parts per million (ppm) to the nearest 0.01 for ^1H and 0.1 for ^{13}C , coupling constants J are quoted in Hz to the nearest 0.1 and splitting are recorded as singlet (s), doublet (d), triplet (t), quartet (q), pentet (p), hexet (h), heptet (hept), and multiplet (m). Assignments were based upon COSY, HSQC and HMBC experiments. Where unambiguous assignments could not be made the candidate positions are indicated by solidus “/”. Low temperature² single crystal X-ray diffraction data were collected using a (Rigaku) Oxford Diffraction SuperNova diffractometer for **2m·HCl**, **8a·HCl** and **8e** and data were collected for **5m·HCl** at , Beamline I19-1, Diamond Light Source.³ Raw frame data were reduced using

¹ Keumi, T., Inagaki, T., Nakayama, N., Taniguchi, M., Morita, T., Kitajima, H., *J. Org. Chem.* **1989**, 17, 54, 4034 – 4038

² Cosier J.; Glazer, A. M. *J. Appl. Cryst.* **1986**, 19, 105-107.

³ Allan, D. R. et al. *Crystals*. **2017**, 7(11), 336-358.

CrysAlisPro and the structures were solved using 'Superflip'⁴ before refinement with CRYSTALS.⁵ The structures were then modified, improved and optimised by full-matrix least squares on F^2 as per the SI (CIF). Infrared spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer fitted with an Attenuated Total Reflectance (ATR) sampling accessory. Absorption maxima are quoted in wavenumbers (cm^{-1}). High resolution mass spectra were recorded on a Bruker MicroTOF (resolution = 10000 FWHM). Melting points (m.p.) were obtained using a Lecia VMGT heated-stage microscope and are uncorrected.

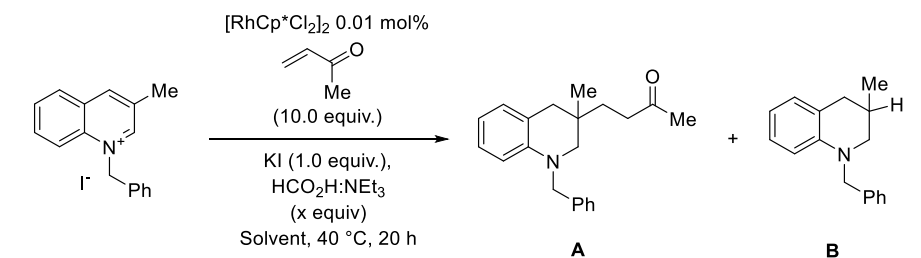
Chromatography

Analytical thin layer chromatography was performed on pre-coated silica gel aluminium sheets from Merck (TLC Silica Gel 60 F₂₅₄). Spots were visualized either by the quenching of UV fluorescence or by staining with phosphomolybdic acid/cerium sulfate, potassium permanganate or vanillin solutions. Preparative flash column chromatography was carried out using Geduran Silica Gel 60 (40 μm – 63 μm) from Merck.

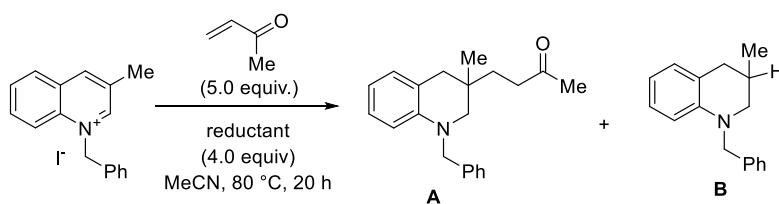
⁴ Palatinus L.; Chapuis, G. *J. Appl. Cryst.* **2007**, *40*, 786-790.

⁵ (a) Parois, P.; Cooper, R. I.; Thompson, A. L. *Chem. Cent. J.* **2015**, *9*, 30. (b) Cooper, R. I.; Thompson, A. L.; Watkin, D. J. *J. Appl. Cryst.* **2010**, *43*, 1100-1107.

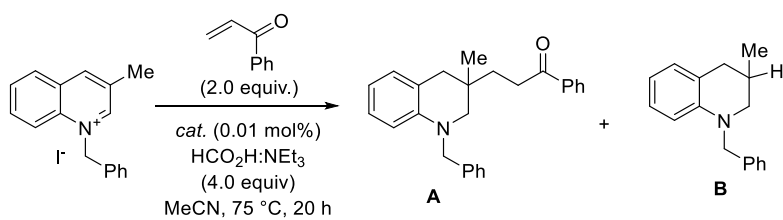
Optimisation of reaction conditions



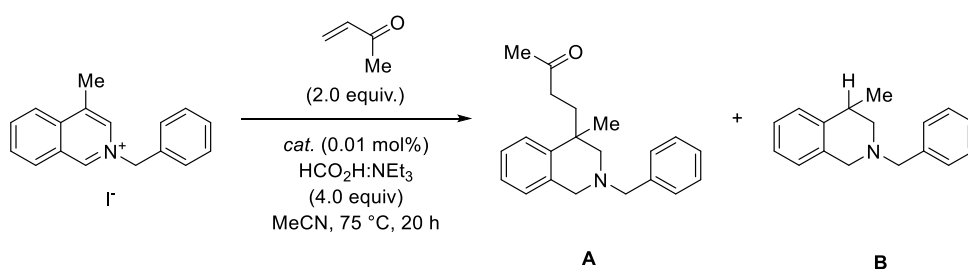
entry	solvent	conc.	equiv. of $^o\text{H}^-$	Yield A	Yield B
1	neat	0.13 M	100	59%	5%
2	CH_2Cl_2	0.1 M	10	66% (63%)	/
3	DCE	0.1 M	10	46%	/
4	CCl_3H	0.1 M	10	10%	/
5	THF	0.1 M	10	/	/
6	MeCN	0.1 M	10	41%	12%
7	MeOH	0.1 M	10	Complex mixtures	
8	<i>i</i> -PrOH	0.1 M	10	Messy	
9	TFE	0.1 M	10	Sm only	
10	HFIP	0.1 M	10	Sm only	
11	H_2O	0.1 M	10	Complex mixtures	
12	PhMe	0.1 M	10	7%	/



entry	Reductant	$^o\text{H}^-$	Yield A	Yield B
1	$\text{HCO}_2\text{H}:\text{NEt}_3$ 5:2	4	86%	<5%
2	HCO_2H	4	0%	0%
3	$\text{HCO}_2\text{H}:\text{NEt}_3$ 1:1	4	86%	<5%
4	$\text{HCO}_2\text{H}:\text{NEt}_3$ 2:5	4	67%	24%
5	NaHCO_2	4	0%	0%
6	NH_4HCO_2	4	0%	0%



entry	Catalyst	Yield A	Yield B
1	[RhCp*Cl ₂] ₂	83%	0%
2	[Ru(<i>p</i> -cymene)Cl ₂] ₂	85%	0%
3	[IrCp*Cl ₂] ₂	83%	0%



entry	Catalyst	Yield A	Yield B
1	[RhCp*Cl ₂] ₂	94%	0%
2	[Ru(<i>p</i> -cymene)Cl ₂] ₂	77%	0%
3	[IrCp*Cl ₂] ₂	80%	0%

Unsuccessful electrophiles

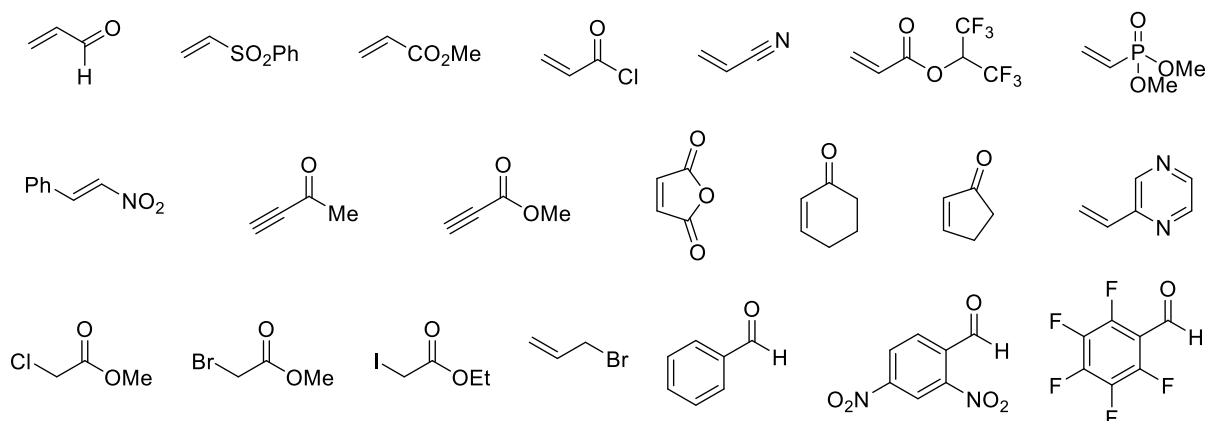


Figure 1: Electrophiles that were unsuccessful in the reaction with quinoline **1a**

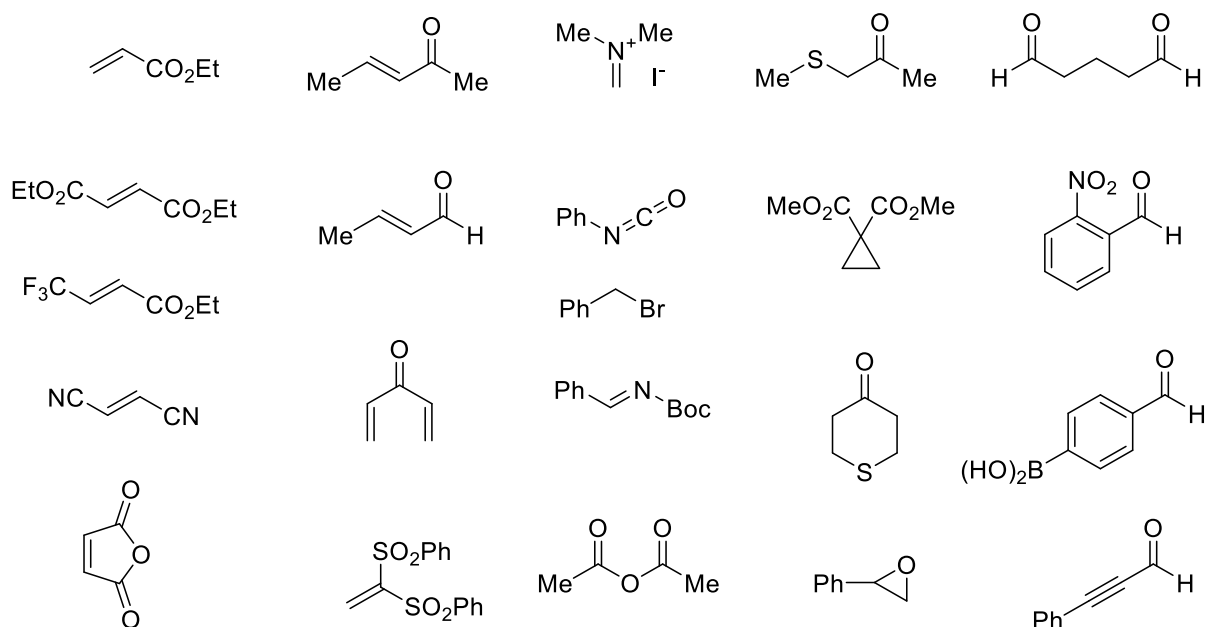


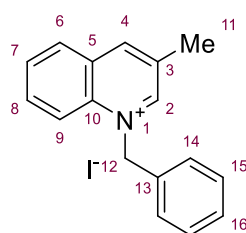
Figure 2: Electrophiles that were unsuccessful in the reaction with isoquinoline **4a**

Synthesis of quinolinium salts

General procedure A: Preparation of quinolinium salts

A mixture of the corresponding quinoline (1.0 equiv.) and benzyl iodide (2.0 equiv.) in acetone (0.5 M) was stirred in the dark at room temperature for 20 – 48 hours. Addition of diethyl ether (10 mL) resulted in precipitation and the resulting suspension was sonicated (15 min). The solids were collected by filtration, washed with diethyl ether and dried under vacuum to give the benzyl quinolinium iodide salts as crystalline solids.

***N*-Benzyl-3-methylquinolinium iodide (1a)**



The title compound was prepared according to General Procedure **A** using 3-methylquinoline (716 mg, 5.00 mmol) and benzyl iodide (1.25 mL, 10.0 mmol) in acetone (10 mL) to give salt **1a** as a yellow solid (1.44 g, 80%). Spectroscopic data was consistent with that reported in the literature.⁶

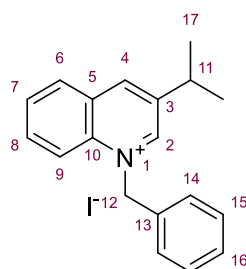
HRMS (ESI): Exact mass calculated for C₁₇H₁₆N [M+H]⁺: 234.1277, found: 234.1279.

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.77 (d, *J* = 1.9 Hz, 1H, C²H), 9.20 (d, *J* = 2.1 Hz, 1H, C⁴H), 8.43 (dd, *J* = 9.0, 1.0 Hz, 1H, C⁹H), 8.38 (dd, *J* = 8.2, 1.5 Hz, 1H, C⁶H), 8.12 (ddd, *J* = 8.8, 7.0, 1.5 Hz, 1H, C⁸H), 7.97 (ddd, *J* = 8.0, 7.0, 0.9 Hz, 1H, C⁷H), 7.45 – 7.30 (m, 5H, 2 x C¹⁴H + 2 x C¹⁵H + C¹⁶H), 6.33 (s, 2H, C¹²H₂), 2.71 (s, 3H, C¹¹H₃).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 151.5 (C²H), 146.8 (C⁴H), 135.9 (C¹⁰), 134.6 (C⁸H), 133.9 (C¹³), 132.6 (C³), 130.0 (C⁶H), 129.9 (C⁷H), 129.6 (C⁵), 129.0 (2 x C¹⁴H/C¹⁵H), 128.7 (C¹⁶H), 127.2 (2 x C¹⁴H/C¹⁵H), 119.0 (C⁹H), 59.9 (C¹²H₂), 18.1 (C¹¹H₃).

IR (neat) (cm⁻¹): 2981, 2160, 2034, 2009, 1978, 1523, 1362, 771, 753, 738.

***N*-Benzyl-3-isopropylquinolinium iodide (1b)**



The title compound was prepared according to General Procedure **A** using 3-isopropylquinoline (514 mg, 3.00 mmol) and benzyl iodide (0.75 mL, 6.00 mmol) to give salt **1b** as a yellow solid (746 mg, 65%).

m.p. (acetone): 196 – 198 °C

HRMS (ESI): Exact mass calculated for C₁₉H₂₀N [M+H]⁺: 262.1590, found: 262.1591.

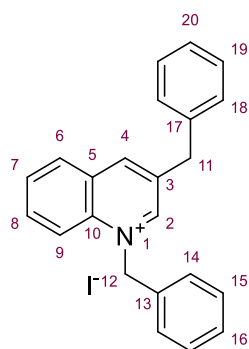
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.85 (d, *J* = 2.0 Hz, 1H, C²H), 9.30 (d, *J* = 2.0 Hz, 1H, C⁴H), 8.43 (dd, *J* = 8.2, 1.6 Hz, 2H, C⁶H + C⁹H), 8.13 (ddd, *J* = 8.9, 7.0, 1.5 Hz, 1H, C⁷H/C⁸H), 7.98 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H, C⁷H/C⁸H), 7.44 – 7.30 (m, 5H, 5 x C^{Ar}H), 6.37 (s, 2H, C¹²H₂), 3.45 – 3.34 (m, 1H, C¹¹H), 1.46 (d, *J* = 6.9 Hz, 6H, 2 x C¹⁷H₃).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.3 (C²H), 144.6 (C⁴H), 142.5 (C^{Ar}), 136.2 (C^{Ar}), 134.8 (C⁸H), 134.0 (C^{Ar}), 130.3 (C⁶H), 129.90 (C^{Ar}/C⁷H), 129.88 (C^{Ar}/C⁷H), 129.1 (2 x C¹⁴H/C¹⁵H), 128.7 (C¹⁶H), 127.0 (2 x C¹⁴H/C¹⁵H), 119.0 (C⁹H), 60.0 (C¹²H₂), 31.3 (C¹¹H), 22.9 (2 x C¹⁷H₃).

IR (neat) (cm⁻¹): 2981, 2528, 2160, 2031, 1977, 1602, 1509, 770, 751, 733.

⁶ Grozavu, A.; Hepburn, H. B.; Smith, P. J.; Potukuchi, H. K.; Lindsay-Scott, P. J.; Donohoe, T. J.; *Nat. Chem.* **2019**, *11*, 242–247

***N*-Benzyl-3-benzylquinolinium iodide (1c)**



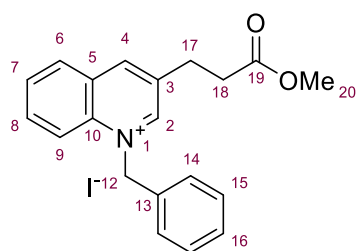
The title compound was prepared according to General Procedure **A** using 3-benzylquinoline (170 mg, 0.78 mmol) and benzyl iodide (0.19 mL, 1.55 mmol) in acetone (1 mL) to give salt **1c** as a yellow solid (275 mg, 81%). Spectroscopic data was consistent with that reported in the literature.²

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.83 (s, 1H, C²H), 9.22 (s, 1H, C⁴H), 8.46 (d, *J* = 9.0 Hz, 1H, C⁹H), 8.42 (dd, *J* = 8.3, 1.4 Hz, 1H, C⁶H), 8.14 (ddd, *J* = 8.8, 7.0, 1.5 Hz, 1H, C⁸H), 7.97 (ddd, *J* = 8.1, 7.0, 0.9 Hz, 1H, C⁷H), 7.49 – 7.21 (m, 10H, 10 x

C^{Ar}H), 6.35 (s, 2H, C¹²H₂), 4.43 (s, 2H, C¹¹H₂).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 151.1 (C²H), 146.8 (C⁴H), 138.7 (C^{Ar}), 136.3 (C^{Ar}), 135.9 (C^{Ar}), 135.1 (C⁸H), 133.9 (C^{Ar}), 130.4 (C⁶H), 130.0 (C^{Ar}), 129.8 (C⁷H), 129.03 (2 x C^{Ar}H), 128.99 (2 x C^{Ar}H), 128.9 (2 x C^{Ar}H), 128.7 (C¹⁶H/C²⁰H), 127.2 (2 x C^{Ar}H), 126.9 (C¹⁶H/C²⁰H), 119.1 (C⁹H), 60.0 (C¹²H₂), 37.5 (C¹¹H₂).

***N*-Benzyl-3-(3-methoxy-3-oxopropyl)quinolinium iodide (1d)**

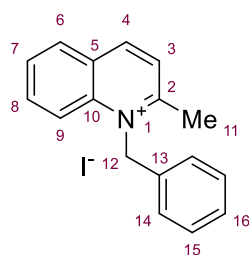


The title compound was prepared according to General Procedure **A** using 3-methylquinoline (538 mg, 2.50 mmol) and benzyl iodide (0.63 mL, 5.00 mmol) to give salt **1d** as a yellow solid (983 mg, 91%). Spectroscopic data was consistent with that reported in the literature.²

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.82 (d, *J* = 1.9 Hz, 1H, C²H), 9.27 (s, 1H, C⁴H), 8.45 (dd, *J* = 9.0, 1.0 Hz, 1H, C⁹H), 8.39 (dd, *J* = 8.2, 1.4 Hz, 1H, C⁶H), 8.14 (ddd, *J* = 8.8, 7.0, 1.5 Hz, 1H, C⁸H), 7.98 (ddd, *J* = 8.0, 7.0, 0.9 Hz, 1H, C⁷H), 7.48 – 7.23 (m, 5H, 5 x C^{Ar}H), 6.34 (s, 2H, C¹²H₂), 3.61 (s, 3H, C²⁰H₃), 3.28 (t, *J* = 7.3 Hz, 2H, C¹⁸H₂), 2.98 (t, *J* = 7.3 Hz, 2H, C¹⁷H₂).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 172.2 (C¹⁹O), 151.3 (C²H), 146.7 (C⁴H), 136.1 (C^{Ar}), 135.3 (C^{Ar}), 135.0 (C⁸H), 133.8 (C^{Ar}), 130.3 (C⁶H), 130.0 (C⁷H), 129.6 (C^{Ar}), 129.0 (2 x C¹⁴H/C¹⁵H), 128.8 (C¹⁶H), 127.2 (2 x C¹⁴H/C¹⁵H), 119.0 (C⁹H), 60.0 (C¹²H₂), 51.6 (C²⁰H₂), 33.2 (C¹⁸H₂), 27.1 (C¹⁷H₂).

***N*-Benzyl-2-methylquinolinium iodide (1e)**



The title compound was prepared according to a modified General Procedure **A**. A solution of 3-methylquinoline (0.7 mL, 5.0 mmol) and benzyl iodide (1.25 mL, 10.0 mmol) in 1,4-dioxane (10 mL) was heated to 90 °C for 16^h. The reaction mixture was cooled to room temperature, addition of Et₂O (20 mL) resulted in formation of the precipitate which was filtered and washed with Et₂O to give salt **1e** as a brown solid (768 mg, 43%).

m.p. (EtOAc): 200 – 204 °C

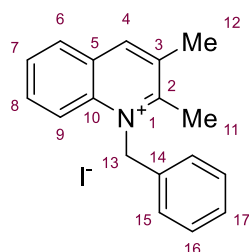
HRMS (ESI): Exact mass calculated for C₁₇H₁₆N [M+H]⁺: 234.1277, found: 234.1279.

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.24 (d, *J* = 8.5 Hz, 1H, C⁴H), 8.46 (dd, *J* = 8.2, 1.5 Hz, 1H, C⁶H), 8.39 (d, *J* = 9.0 Hz, 1H, C⁹H), 8.25 (d, *J* = 8.6 Hz, 1H, C³H), 8.15 (ddd, *J* = 8.9, 7.0, 1.6 Hz, 1H, C⁸H), 7.98 (dd, *J* = 8.0, 7.0 Hz, 1H, C⁷H), 7.42 – 7.29 (m, 3H, 3 x C^{Ar}H), 7.18 – 7.08 (m, 2H, 2 x C^{Ar}H), 6.33 (s, 2H, C¹²H₂), 3.08 (s, 3H, C¹¹H₃).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 161.7 (C²), 146.7 (C⁴H), 138.9 (C^{Ar}), 135.5 (C⁸H), 133.2 (C^{Ar}), 130.7 (C⁶H), 129.22 (C⁷H), 129.20 (2 x C¹⁵H), 128.4 (C^{Ar}/C¹⁶H), 128.2 (C^{Ar}/C¹⁶H), 125.9 (2 x C¹⁴H), 125.8 (C³H), 119.2 (C⁹H), 54.4 (C¹²H₂), 22.8 (C¹¹H₃).

IR (neat) (cm⁻¹): 2961, 2530, 2160, 2029, 1977, 1602, 1523, 1350, 827, 771.

***N*-Benzyl-2,3-dimethylquinolinium iodide (1f)**



The title compound was prepared according to a modified General Procedure **A**. A solution of 3,4-dimethylquinoline (555 mg, 3.5 mmol) and benzyl iodide (0.88 mL, 7.0 mmol) in 1,4-dioxane (7.0 mL) was heated to 90 °C for 16^h. The reaction mixture was cooled to room temperature, addition of Et₂O (20 mL) resulted in formation of the precipitate which was filtered and washed with Et₂O to give salt **1f** as a yellow solid (433 mg, 33%).

m.p. (EtOAc): 200 – 202 °C

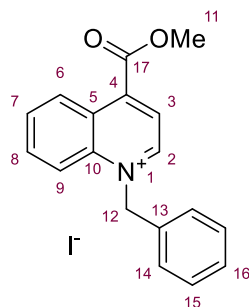
HRMS (ESI): Exact mass calculated for C₁₈H₁₈N [M+H]⁺: 248.1434, found: 248.1436.

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.10 (s, 1H, C⁴H), 8.33 (dd, *J* = 8.2, 1.8 Hz, 2H, C⁶H + C⁹H), 8.07 (ddd, *J* = 8.9, 7.0, 1.6 Hz, 1H, C⁷H/C⁸H), 7.94 (dd, *J* = 7.7, 7.7 Hz, 1H, C⁷H/C⁸H), 7.43 – 7.29 (m, 3H), 7.15 (dd, *J* = 7.7, 1.7 Hz, 2H, 2 x C¹⁵H), 6.37 (s, 2H, C¹³H₂), 2.97 (s, 3H, C¹¹H₃), 2.68 (2, 3H, C¹²H₃).

¹³C NMR (101 MHz, CDCl₃) δ 162.3 (C²), 145.4 (C⁴H), 137.8 (C^{Ar}), 134.4 (C⁷H/C⁸H), 133.7 (C^{Ar}), 133.3 (C^{Ar}), 129.7 (C⁷H/C⁸H), 129.2 (C⁴H), 129.1 (2 x C¹⁶H), 128.1 (C^{Ar}/C¹⁷H), 127.8 (C^{Ar}/C¹⁷H), 125.9 (2 x C¹⁵H), 119.2 (C⁹H), 55.0 (C¹³H₂), 20.1 (C¹¹H₃), 19.7 (C¹²H₃).

IR (neat) (cm⁻¹): 2956, 2529, 2160, 2032, 1977, 1509, 771, 751, 734, 692.

***N*-Benzyl-4-(methoxycarbonyl)quinolinium iodide (1g)**

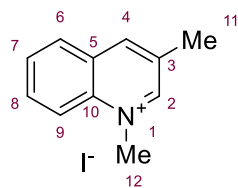


The title compound was prepared according to a modified General Procedure **A**. Methyl quinoline-4-carboxylate (710 mg, 3.79 mmol) and benzyl iodide (0.96 mL, 7.60 mmol) in acetone (9 mL) were stirred at rt in the dark for 24 hours to give salt **1g** as a red solid (650 mg, 42%). Spectroscopic data was consistent with that reported in the literature.²

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.87 (d, *J* = 6.0 Hz, 1H, C²H), 8.79 (dd, *J* = 8.6, 1.4 Hz, 1H, C⁶H), 8.63 – 8.56 (m, 2H, C³H + C⁹H), 8.27 (ddd, *J* = 8.9, 7.0, 1.5 Hz, 1H, C⁸H), 8.11 (ddd, *J* = 8.1, 7.0, 1.0 Hz, 1H, C⁷H), 7.45 – 7.33 (m, 5H, 5 C^{Ar}H), 6.44 (s, 2H, C¹²H₂), 4.11 (s, 3H, C¹¹H₃).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 164.1 (C¹⁷O), 151.0 (C²H), 145.0 (C^{Ar}), 138.3 (C^{Ar}), 135.7 (C⁸H), 133.4 (C^{Ar}), 131.1 (C⁷H), 129.1 (2 x C¹⁴H/C¹⁵H), 128.9 (C¹⁶H), 127.8 (C³H), 127.5 (2 x C¹⁴H/C¹⁵H), 126.5 (C^{Ar}), 122.8 (C³H), 119.9 (C⁹H), 60.7 (C¹²H₂), 54.1 (C¹¹H₃).

1,3-Dimethylquinolinium iodide (1h)



The title compound was prepared according to a modified General Procedure **A**. A mixture of 3-methylquinoline (573 mg, 4.00 mmol) and iodomethane (1.24 mL, 20.0 mmol) in 1,4-dioxane (0.4 M) was heated in a sealed pressure resistant flask at 90 °C for 16 hours. The mixture was allowed to cool to room

temperature, the solid was collected by filtration, washed with diethyl ether and dried under vacuum for one hour to give title compound **1h** as a yellow solid (1.10 g, 97%).

m.p. (EtOAc): 203 – 205 °C

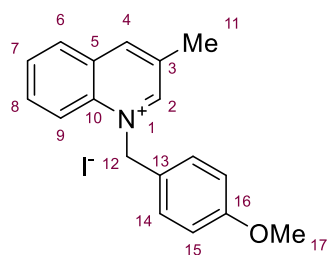
HRMS (ESI): Exact mass calculated for C₁₁H₁₂N [M+H]⁺: 158.0964, found 158.0965.

¹H NMR (400 MHz, CDCl₃) δ 9.50 (d, *J* = 1.9 Hz, 1H, C²H), 9.09 (s, 1H, C⁴H), 8.46 (dd, *J* = 8.9, 1.0 Hz, 1H, C⁹H), 8.36 (dd, *J* = 8.3, 1.4 Hz, 1H, C⁶H), 8.21 (ddd, *J* = 8.7, 7.0, 1.1 Hz, 1H, C⁸H), 8.02 (ddd, *J* = 8.1, 7.0, 1.0 Hz, 1H, C⁷H), 4.61 (s, 3H, C¹²H₃), 2.64 (s, 3H, C¹¹H₃).

¹³C NMR (101 MHz, CDCl₃) δ 151.3 (C²H), 145.5 (C⁴H), 136.7 (C^{Ar}), 134.3 (C⁸H), 132.0 (C^{Ar}), 129.9 (C⁷H), 129.5 (C⁶H), 128.9 (C), 118.8 (C⁹H), 45.2 (C¹²H₃), 17.9 (C¹¹H₃).

IR (neat) (cm⁻¹): 2516, 2160, 2029, 1592, 1521, 1230, 868, 773, 748, 608.

***N*-(4-Methoxybenzyl)-3-methylquinolinium iodide (1i)**



The title compound was prepared according to General Procedure **A** using 3-methylquinoline (0.27 mL, 2.0 mmol) and 4-methoxybenzyl iodide (975 mg, 3.9 mmol) in acetone (4 mL) to give salt **1i** as a yellow solid (782 mg, 99%).

m.p. (EtOAc): 190 – 192 °C

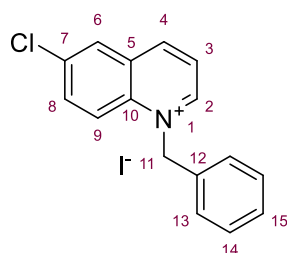
HRMS (ESI): Exact mass calculated for C₁₈H₁₈NO [M+H]⁺: 264.1383, found: 264.1385.

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.72 (d, *J* = 1.9 Hz, 1H, C²H), 9.16 (s, 1H, C⁴H), 8.55 – 8.48 (m, 1H, C⁹H), 8.36 (dd, *J* = 8.2, 1.5 Hz, 1H, C⁶H), 8.13 (ddd, *J* = 8.8, 7.0, 1.5 Hz, 1H, C⁸H), 7.97 (ddd, *J* = 8.0, 7.0, 0.9 Hz, 1H, C⁷H), 7.43 (d, *J* = 8.8 Hz, 2H, 2 x C¹⁴H), 6.94 (d, *J* = 8.8 Hz, 1H, 2 x C¹⁵H), 6.23 (s, 2H, C¹²H₂), 3.72 (s, 3H, C¹⁷H₃), 2.70 (s, 3H, C¹¹H₃).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 159.5 (C¹⁶), 151.0 (C²H), 146.6 (C⁴H), 135.8 (C^{Ar}), 134.5 (C⁸H), 132.6 (C), 130.0 (C⁶H), 129.9 (C⁷H), 129.6 (C^{Ar}), 129.1 (2 x C¹⁴H), 125.6 (C^{Ar}), 119.1 (C⁹H), 114.4 (2 x C¹⁵H), 59.6 (C¹⁷H₃), 55.2 (C¹²H₂), 18.1 (C¹¹H₃).

IR (neat) (cm⁻¹): 2956, 2160, 2030, 1977, 1516, 1243, 1180, 1019, 832, 805.

***N*-Benzyl-6-chloroquinolinium iodide (1k)**

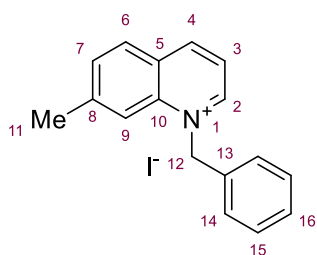


The title compound was prepared according to General Procedure **A** using 6-chloroquinoline (650 mg, 4.00 mmol) and benzyl iodide (1.00 mL, 8.00 mmol) to give salt **1k** as an orange solid (1.37 g, 90%). Spectroscopic data was consistent with that reported in the literature.²

¹H NMR (400 MHz, CDCl₃) δ 9.75 (dd, *J* = 5.8, 1.4 Hz, 1H, C²H), 9.30 (dt, *J* = 8.5, 1.1 Hz, 1H, C⁴H), 8.70 (d, *J* = 2.4 Hz, 1H, C⁶H), 8.54 (d, *J* = 9.5 Hz, 1H, C⁹H), 8.35 (dd, *J* = 8.5, 5.8 Hz, 1H, C³H), 8.26 (dd, *J* = 9.4, 2.4 Hz, 1H, C⁸H), 7.46 – 7.32 (m, 5H, 5 x C^{Ar}H), 6.39 (s, 2H, C¹¹H₂).

¹³C NMR (101 MHz, CDCl₃) δ 150.8 (C²H), 147.4 (C⁴H), 136.3 (C^{Ar}), 135.6 (C⁸H), 134.5 (C^{Ar}), 133.6 (C^{Ar}), 130.8 (C^{Ar}), 129.3 (C⁶H), 129.1 (2 x C¹⁴H), 128.8 (C¹⁵H), 127.3 (2 x C¹³H), 123.7 (C³H), 121.6 (C⁹H), 60.2 (C¹¹H₂).

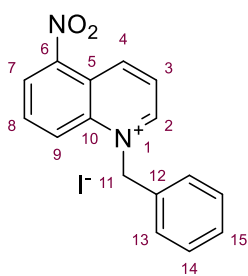
***N*-Benzyl-7-methylquinolinium iodide (1l)**



The title compound was prepared according to General Procedure **A** using 7-methylquinoline (573 mg, 4.00 mmol) and benzyl iodide (1.00 mL, 8.00 mmol) to give salt **1m** as a yellow solid (1.29 g, 91%). Spectroscopic data was consistent with that reported in the literature.²

¹H NMR (400 MHz, CDCl₃) δ 9.64 (dd, *J* = 5.9, 1.5 Hz, 1H, C²H), 9.31 (dt, *J* = 8.3, 1.2 Hz, 1H, C⁴H), 8.44 – 8.36 (m, 2H, C⁶H + C⁹H), 8.20 (dd, *J* = 8.3, 5.9 Hz, 1H, C³H), 7.88 (dd, *J* = 8.4, 1.4 Hz, 1H, C⁷H), 7.46 – 7.32 (m, 5H, 5 x C^{Ar}H), 6.33 (s, 2H, C¹²H₂), 2.63 (d, *J* = 0.9 Hz, 3H, C¹¹H₃).
¹³C NMR (101 MHz, CDCl₃) δ 149.7 (C²H), 147.6 (C⁴H), 137.9 (C^{Ar}), 133.8 (C^{Ar}), 132.0 (C⁷H), 130.4 (C⁶H), 129.1 (2 x C¹⁵H), 128.8 (C^{Ar}/C¹⁶H), 128.3 (C^{Ar}/C¹⁶H), 127.4 (2 x C¹⁴H), 121.4 (C³H), 118.0 (C⁹H), 59.5 (C¹²H₂), 22.3 (C¹¹H₃).

***N*-Benzyl-5-nitroquinolinium iodide (1m)**



The title compound was prepared according to a modified General Procedure **A**. 5-Nitroquinoline (522 mg, 3.00 mmol) and benzyl iodide (0.75 mL, 6.00 mmol) in acetone (6.00 mL) were stirred at rt in the dark for 2 days to give salt **1k** as an orange solid (471 mg, 40%).

m.p. (acetone): 189 – 191 °C

HRMS (ESI): Exact mass calculated for C₁₆H₁₃N₂O₂ [M+H]⁺: 265.0972, found: 265.0973.

¹H NMR (400 MHz, CDCl₃) δ 9.90 (dd, *J* = 5.8, 1.3 Hz, 1H, C²H), 9.61 (dt, *J* = 9.0, 1.2 Hz, 1H, C⁴H), 8.90 (dt, *J* = 9.2, 1.0 Hz, 1H, C⁷H), 8.74 (dd, *J* = 7.8, 0.8 Hz, 1H, C⁹H), 8.50 (dd, *J* = 9.0, 5.8 Hz, 1H, C³H), 8.37 (dd, *J* = 9.1, 7.8 Hz, 1H, C⁸H), 7.45 – 7.35 (m, 5H, 5 x C^{Ar}H), 6.48 (s, 2H, C¹¹H₂).

¹³C NMR (101 MHz, CDCl₃) δ 152.0 (C²H), 146.6 (C⁴H), 137.6 (C^{Ar}), 134.2 (C^{Ar}), 133.4 (C⁸H), 129.1 (2 x C¹⁴H), 128.9 (C¹⁵H), 127.4 (2 x C¹³H), 127.1 (C⁹H), 125.2 (C⁷H), 125.0 (C³H), 122.6 (C^{Ar}), 61.1 (C¹¹H₂), C⁶ missing.

IR (neat) (cm⁻¹): 2981, 2523, 2160, 2030, 1977, 1525, 1385, 1365, 1244, 746.

Synthesis of Tetrahydroquinolines

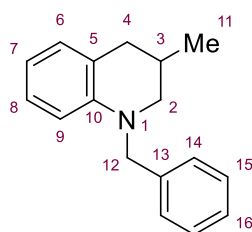
General Procedure B: Preparation of Tetrahydroquinolines

Quinolinium salt (0.125 mmol, 1.00 equiv.) and electrophile (1.00 to 5.00 equiv.) were dissolved in MeCN (0.10 mL, 1.25 M). Upon addition of HCO₂H:NEt₃ 5:2 complex (42 μ L, 4.00 equiv.) the reaction mixture was heated to 80 °C for 16 hours. The reaction was diluted with CH₂Cl₂ (10 mL) and quenched with an aqueous solution of K₂CO₃ (10 mL, 0.1 M). The phases were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL). The organic layers were combined, dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography to furnish the corresponding amines.

General Procedure C: Metal Catalysed Preparation of Tetrahydroquinolines

Quinolinium salt (1.00 equiv.), and [RhCp*Cl₂]₂ (0.01 mol%) were added to a microwave vial. MeCN (1.25 M), electrophile (1.0 – 5.0 equiv.) and HCO₂H:NEt₃ (5:2, 4.0 equiv.) were added and the solution heated at 80 °C for 20 hours. The reaction was diluted with CH₂Cl₂ (10 mL) and quenched with an aqueous solution of K₂CO₃ (10 mL, 0.1 M). The phases were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL). The organic layers were combined, dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography to furnish the corresponding amines.

N-Benzyl-3-methyl-1,2,3,4-tetrahydroquinoline (**3a**)



The title compound was prepared according to General Procedure **B** using salt **1a** (45 mg, 0.125 mmol) in the absence of electrophile. Purification by column chromatography (0%-2% EtOAc in pentane) gave *amine 3a* (23 mg, 77%) as a clear oil. Spectroscopic data was consistent with that reported in the literature.⁷

HRMS (ESI): Exact mass calculated for C₁₇H₂₀N [M+H]⁺: 238.1590, found: 238.1589.

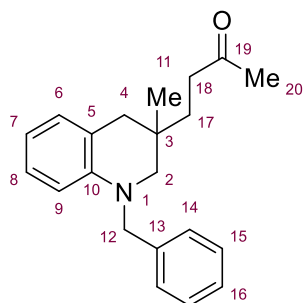
¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.22 (m, 5H, 2 x C¹⁴H + 2 x C¹⁵H + C¹⁶H), 7.05 – 6.96 (m, 2H, C⁶H + C⁸H), 6.61 (td, *J* = 7.3, 1.1 Hz, 1H, C⁷H), 6.57 – 6.47 (m, 1H, C⁹H), 4.51 (s, 2H, C¹²H₂), 3.31 (ddd, *J* = 11.2, 4.0, 2.2 Hz, 1H, C²H₂), 3.06 (dd, *J* = 11.2, 9.6 Hz, 1H, C²H₂), 2.85 (ddd, *J* = 15.6, 4.6, 2.2 Hz, 1H, C⁴H₂), 2.53 (dd, *J* = 15.6, 10.5 Hz, 1H, C⁴H₂), 2.28 – 2.13 (m, 1H, C³H), 1.08 (d, *J* = 6.6 Hz, 3H, C¹¹H₃).

⁷Kaga, A.; Hayashi, H; Hakamata, H; Oi, M.; Uchiyama, M.; Takita, R.; Chiba, S.; *Angew.Chem. Int.Ed.* **2017**, 56,11807 –11811

^{13}C NMR (101 MHz, CDCl_3) δ 145.3 (C^{10}), 139.2 (C^{13}), 129.3 ($\text{C}^6\text{H}/\text{C}^8\text{H}$), 128.7 (2 x $\text{C}^{14}\text{H}/\text{C}^{15}\text{H}$), 127.3 ($\text{C}^6\text{H}/\text{C}^8\text{H}$), 126.9 (C^{16}H), 126.7 (2 x $\text{C}^{14}\text{H}/\text{C}^{15}\text{H}$), 122.0 (C^5), 116.0 (C^7H), 110.9 (C^9H), 57.0 (C^2H_2), 55.3 (C^{12}H_2), 36.6 (C^4H_2), 27.5 (C^3H), 19.2 (C^{11}H_3).

IR (neat) (cm^{-1}): 2953, 2922, 1602, 1506, 1494, 1452, 1359, 1349, 1283, 1245.

4-(*N*-Benzyl-3-methyl-1,2,3,4-tetrahydroquinolin-3-yl)butan-2-one (**2a**)



The title compound was prepared according to General Procedure **B** using salt **1a** (45 mg, 0.125 mmol) and methyl vinyl ketone (50 μL , 0.63 mmol) as electrophile. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine 2a* (30 mg, 78%) as a clear oil.

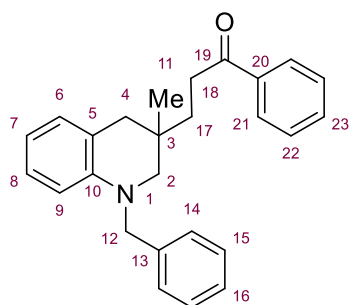
HRMS (ESI): Exact mass calculated for $\text{C}_{21}\text{H}_{26}\text{NO}$ $[\text{M}+\text{H}]^+$: 308.2009, found: 308.2009.

^1H NMR (400 MHz, CDCl_3) δ 7.36 – 7.20 (m, 5H, 2 x C^{14}H + 2 x C^{15}H + C^{16}H), 7.04 – 6.93 (m, 2H, C^6H + C^8H), 6.61 (t, J = 7.3 Hz, 1H, C^7H), 6.56 (d, J = 8.2 Hz, 1H, C^9H), 4.48 (d, J = 3.3 Hz, 2H, C^2H_2), 3.08 – 2.96 (m, 2H, C^4H_2), 2.59 (s, 2H, C^{12}H_2), 2.50 – 2.31 (m, 2H, C^{18}H_2), 2.11 (s, 3H, C^{20}H_3), 1.71 – 1.53 (m, 2H, C^{17}H_2), 0.97 (s, 3H, C^{11}H_3).

^{13}C NMR (101 MHz, CDCl_3) δ 208.9 (C^{19}), 144.7 (C^{10}), 139.2 (C^{13}), 129.9 ($\text{C}^6\text{H}/\text{C}^8\text{H}$), 128.7 (2 x $\text{C}^{14}\text{H}/\text{C}^{15}\text{H}$), 127.3 ($\text{C}^6\text{H}/\text{C}^8\text{H}$), 127.0 (C^{16}H), 126.8 (2 x $\text{C}^{14}\text{H}/\text{C}^{15}\text{H}$), 120.6 (C^5), 116.5 (C^7H), 110.9 (C^9H), 59.8 (C^2H_2), 55.5 (C^{12}H_2), 40.7 (C^4H_2), 38.4 (C^{18}H_2), 32.5 (C^{17}H_2), 30.8 (C^3), 30.1 (C^{20}H_3), 23.5 (C^{11}H_3).

IR (neat) (cm^{-1}): 2919, 2834, 1714, 1602, 1504, 1497, 1451, 1352, 1282, 1249.

3-(*N*-Benzyl-3-methyl-1,2,3,4-tetrahydroquinolin-3-yl)-1-phenylpropan-1-one (**2b**)



The title compound was prepared according to General Procedure **B** using salt **1a** (45 mg, 0.125 mmol) and phenyl vinyl ketone (33 mg, 0.25 mmol) as electrophile. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine 2b* (37 mg, 77%) as a clear oil.

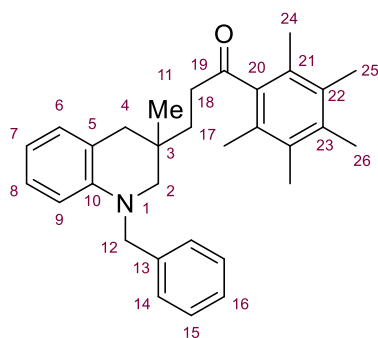
HRMS (ESI): Exact mass calculated for $\text{C}_{26}\text{H}_{28}\text{NO}$ $[\text{M}+\text{H}]^+$: 370.2165, found: 360.2168.

^1H NMR (400 MHz, CDCl_3) δ 7.92 – 7.82 (m, 2H, 2 x C^{21}H), 7.60 – 7.48 (m, 1H, C^{23}H), 7.42 (dd, J = 8.4, 7.1 Hz, 2H, 2 x C^{22}H), 7.32 – 7.16 (m, 5H, 2 x C^{14}H + 2 x C^{15}H + C^{16}H), 7.04 – 6.96 (m, 2H, C^6H + C^8H), 6.61 (t, J = 1.1 Hz, 1H, C^7H), 6.56 (d, J = 8.1 Hz, 1H, C^9H), 4.55 – 4.42 (m, 2H, C^{12}H_2), 3.15 – 3.03 (m, 2H, C^2H_2), 3.03 – 2.82 (m, 2H, C^{18}H_2), 2.73 – 2.57 (m, 2H, C^4H_2), 1.79 (t, J = 8.2 Hz, 2H, C^{17}H_2), 1.05 (s, 3H, C^{11}H_3).

¹³C NMR (101 MHz, CDCl₃) δ 200.5 (C¹⁹), 144.8 (C¹⁰), 139.2 (C¹³), 137.1 (C²⁰), 133.1 (C²³H), 129.9 (C⁶H/C⁸H), 128.72 (2 x C¹⁵H/C²²H), 128.69 (2 x C¹⁵H/C²²H), 128.2 (2 x C²¹H), 127.4 (C⁶H/C⁸H), 127.0 (C¹⁶), 126.9 (2 x C¹⁴H), 120.7 (C⁵), 116.5 (C⁷H), 111.0 (C⁹H), 60.0 (C²H₃), 55.6 (C¹²H₃), 40.7 (C⁴H₃), 33.33 (C¹⁷H₂/C¹⁸H₂), 33.31 (C¹⁷H₂/C¹⁸H₂), 31.1 (C³), 23.6 (C¹¹H₃).

IR (neat) (cm⁻¹): 2981, 2895, 1683, 1601, 1505, 1450, 1283, 1249, 743, 692.

3-(*N*-Benzyl-3-methyl-1,2,3,4-tetrahydroquinolin-3-yl)-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one (2c)



The title compound was prepared according to General Procedure **B** using salt **1a** (45 mg, 0.125 mmol) and 2,3,4,5,6-pentamethylphenyl vinyl ketone (51 mg, 0.25 mmol) as electrophile. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine 2c* (35 mg, 65%) as a white solid.

m.p. (EtOAc): 112 – 114 °C

HRMS (ESI): Exact mass calculated for C₃₁H₃₈NO [M+H]⁺: 440.2948,

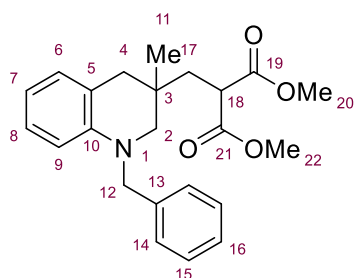
found: 440.2942.

¹H NMR (400 MHz, CDCl₃) δ 7.35 – 7.21 (m, 5H, 2 x C¹⁴H + 2 x C¹⁵H + C¹⁶H), 7.05 – 6.98 (m, 1H, C⁸H), 6.96 (dd, *J* = 7.4, 1.6 Hz, 1H, C⁶H), 6.61 (td, *J* = 7.3, 1.1 Hz, 1H, C⁷H), 6.55 (dd, *J* = 8.2, 1.1 Hz, 1H, C⁹H), 4.58 – 4.37 (m, 2H, C¹²H₂), 3.13 – 2.99 (m, 2H, C²H₂), 2.76 – 2.55 (m, 4H, C⁴H₂ + C¹⁸H₂), 2.24 (s, 3H, C²⁶H₃), 2.19 (s, 6H, 2 x C²⁴H₃/C²⁵H₃), 2.07 (s, 6H, 2 x C²⁴H₃/C²⁵H₃), 1.88 – 1.74 (m, 2H, C¹⁷H₂), 1.01 (s, 3H, C¹¹H₃).

¹³C NMR (101 MHz, CDCl₃) δ 212.1 (C¹⁹), 144.8 (C¹⁰), 141.1 (C^{Ar}), 139.2 (C^{Ar}), 135.6 (C^{Ar}), 133.2 (2 x C^{Ar}), 129.8 (C⁶H), 128.7 (2 x C¹⁴H/C¹⁵H), 127.4 (C⁸H), 127.3 (2 x C^{Ar}), 127.0 (C¹⁶H), 126.7 (2 x C¹⁴H/C¹⁵H), 120.6 (C⁵), 116.5 (C⁷H), 111.0 (C⁹H), 60.2 (C²H₂), 55.7 (C¹²H₂), 40.6 (C⁴H₂/C¹⁸H₂), 40.3 (C⁴H₂/C¹⁸H₂), 32.4 (C¹⁷H₂), 30.9 (C³), 23.3 (C¹¹H₃), 17.4 (2 x C²⁴H₃/C²⁵H₃), 16.8 (C²⁶H₃), 16.1 (2 x C²⁴H₃/C²⁵H₃).

IR (neat) (cm⁻¹): 2922, 1700, 1603, 1506, 1497, 1452, 1357, 1317, 1283, 1249, 745.

Dimethyl 2-((*N*-benzyl-3-methyl-1,2,3,4-tetrahydroquinolin-3-yl)methyl)malonate (2d)



The title compound was prepared according to a modified General Procedure **B** using salt **1a** (45 mg, 0.125 mmol) and dimethyl 2-methylenemalonate (90 mg, 0.625 mmol) as electrophile. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine 2d* (15 mg, 32%) as a clear oil.

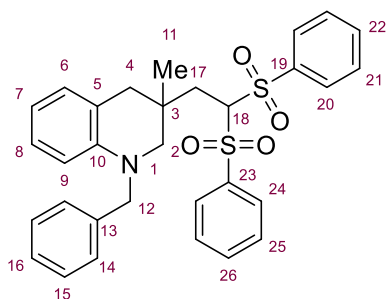
HRMS (ESI): Exact mass calculated for $C_{23}H_{28}NO_4$ $[M+H]^+$: 382.2013, found: 382.2013.

1H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.09 (m, 5H, 5 x $C^{Ar}H$), 6.92 (ddd, J = 8.2, 7.3, 1.7 Hz, 1H, C^8H), 6.87 (dd, J = 7.4, 1.6 Hz, 1H, C^6H), 6.52 (ddd, J = 7.3, 7.3, 1.1 Hz, 1H, C^7H), 6.48 (dd, J = 8.2, 1.1 Hz, 1H, C^9H), 4.40 (dd, J = 16.9, 16.9 Hz, 2H, $C^{12}H_2$), 3.63 (s, 6H, $C^{20}H_3 + C^{22}H_3$), 3.40 (t, J = 6.5 Hz, 1H, $C^{18}H$), 3.08 – 2.82 (m, 2H, C^4H_2), 2.66 – 2.39 (m, 2H, C^2H_2), 2.07 – 1.93 (m, 2H, $C^{17}H_2$), 0.89 (s, 3H, $C^{11}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.49 ($C^{19}O/C^{21}O$), 170.45 ($C^{19}O/C^{21}O$), 144.5 (C^{Ar}), 139.0 (C^{Ar}), 129.9 (C^6H), 128.7 (2 x $C^{14}H/C^{15}H$), 127.4 (C^8H), 127.0 ($C^{16}H$), 126.8 (2 x $C^{14}H/C^{15}H$), 120.2 (C^{Ar}), 116.6 (C^7H), 111.1 (C^9H), 59.8 (C^2H_2), 55.6 ($C^{12}H_2$), 52.82 ($C^{20}H_3/C^{22}H_3$), 52.81 ($C^{20}H_3/C^{22}H_3$), 47.8 ($C^{18}H$), 40.3 (C^4H_2), 37.8 ($C^{17}H$), 31.3 (C^3), 23.1 ($C^{11}H_3$).

IR (neat) (cm^{-1}): 2953, 1753, 1735, 1603, 1576, 1502, 1452, 1436, 1379, 1352.

***N*-Benzyl-3-(2,2-bis(phenylsulfonyl)ethyl)-3-methyl-1,2,3,4-tetrahydroquinoline (2e)**



The title compound was prepared according to a modified General Procedure **B** using salt **1a** (45 mg, 0.125 mmol) and 1,1-bis(phenylsulfonyl)ethylene (154 mg, 0.5 mmol) as electrophile and $HCO_2H:NEt_3$ 5:2 (84 μ L, 1.0 mmol) as the terminal reductant. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine 2e* (42 mg, 62%) as a white solid.

m.p. (EtOAc): 169 – 171 $^{\circ}C$

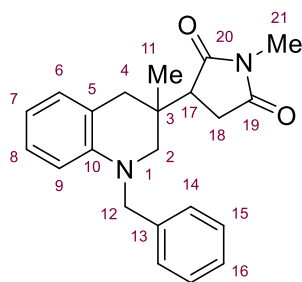
HRMS (ESI): Exact mass calculated for $C_{31}H_{32}NO_4S_2$ $[M+H]^+$: 546.1767, found: 546.1768.

1H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.87 (m, 2H, 2 x $C^{Ar}H$), 7.74 – 7.59 (m, 4H, 4 x $C^{Ar}H$), 7.58 – 7.51 (m, 2H, 2 x $C^{Ar}H$), 7.49 – 7.39 (m, 2H, 2 x $C^{Ar}H$), 7.30 – 7.19 (m, 3H, 3 x $C^{Ar}H$), 7.16 – 6.99 (m, 4H, 2 x $C^{Ar}H + C^6H + C^8H$), 6.69 (td, J = 7.4, 1.1 Hz, 1H, C^7H), 6.59 (dd, J = 8.3, 1.1 Hz, 1H, C^9H), 4.59 (t, J = 4.0 Hz, 1H, $C^{18}H$), 4.46 (q, J = 17.0 Hz, 2H, $C^{12}H_2$), 3.14 (dd, J = 11.7, 1.2 Hz, 1H, C^2H_2), 3.03 (dd, J = 11.6, 2.1 Hz, 1H, C^2H_2), 2.81 (dd, J = 16.1, 2.1 Hz, 1H, C^4H_2), 2.57 (d, J = 16.1 Hz, 1H, C^4H_2), 2.35 – 2.18 (m, 2H, $C^{17}H_2$), 1.12 (s, 3H, $C^{11}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.3 (C^{10}), 138.8 (C^{Ar}), 138.3 (C^{Ar}), 136.7 (C^{Ar}), 134.6 ($C^{Ar}H$), 134.5 ($C^{Ar}H$), 130.8 ($C^{Ar}H$), 130.5 (2 x $C^{Ar}H$), 129.9 (2 x $C^{Ar}H$), 129.2 (2 x $C^{Ar}H$), 129.0 (2 x $C^{Ar}H$), 128.7 (2 x $C^{Ar}H$), 127.5 ($C^{Ar}H$), 127.0 ($C^{Ar}H$), 126.7 (2 x $C^{Ar}H$), 119.9 (C^{Ar}), 116.9 (C^7H), 111.1 (C^9H), 81.1 ($C^{18}H$), 60.3 (C^2H_2), 55.3 ($C^{12}H_2$), 39.2 (C^4H_2), 32.2 (C^3), 31.8 ($C^{17}H_2$), 24.2 ($C^{11}H_3$).

IR (neat) (cm^{-1}): 3063, 2924, 1669, 1602, 1500, 1448, 1329, 1287, 1249, 1194.

3-(*N*-Benzyl-3-methyl-1,2,3,4-tetrahydroquinolin-3-yl)-*N*-methylpyrrolidine-2,5-dione (**2f**)



The title compound was prepared according to General Procedure **B** using salt **1a** (45 mg, 0.125 mmol) and *N*-methylmaleimide (28 mg, 0.25 mmol) as electrophile. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine* **2f** as an inseparable 2:1 diastereomeric mixture (36 mg, 82%) as a clear oil.

HRMS (ESI): Exact mass calculated for C₂₂H₂₅N₂O₂ [M+H]⁺: 349.1911, found:

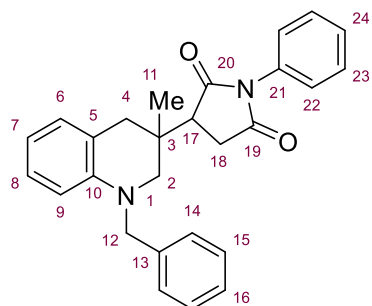
349.1912

¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.15 (m, 10H, 5 x C^{Ar}H, A + B), 7.09 – 6.82 (m, 4H, C⁸H, A+B, C⁸H, A+B), 6.72 – 6.53 (m, 4H, C⁹H, A+B, C⁷H, A+B), 4.75 – 4.62 (m, 1H, C¹²H₂, B), 4.57 – 4.47 (m, 2H, C¹²H₂, A+B), 4.39 (d, *J* = 16.6 Hz, 1H, C¹²H₂, A), 3.86 (dd, *J* = 11.9, 2.2 Hz, 1H, C²H₂, B), 3.54 – 3.42 (m, 2H, C⁴H₂, A, C²H₂, B), 3.12 – 2.99 (m, 3H, C¹⁷H, B, C²H₂, A), 3.00 – 2.91 (m, 7H, C²¹H₃, A+B, C¹⁷H, A), 2.84 (d, *J* = 16.1 Hz, 1H, C⁴H₂, A), 2.82 – 2.59 (m, 2H, C⁴H₂, B), 2.58 – 2.48 (m, 2H, C¹⁸H₂, A+B), 2.45 – 2.30 (m, 2H, C¹⁸H₂, A+B), 0.95 (s, 3H, C¹¹H₃, B), 0.94 (s, 3H, C¹¹H₃, A).

¹³C NMR (101 MHz, CDCl₃) δ 178.8 (C¹⁹O/C²⁰O, B), 178.6 (C¹⁹O/C²⁰O, A), 176.5 (C¹⁹O/C²⁰O, B), 176.4 (C¹⁹O/C²⁰O, A), 145.7 (C¹⁰, B), 144.8 (C¹⁰, A), 139.0 (C¹³, B), 138.7 (C¹³, A), 130.5 (C⁸H, A), 129.8 (C⁸H, B), 128.9 (2 x C^{Ar}H, A/B), 128.8 (C^{Ar}H, A/B), 128.7 (C^{Ar}H, A/B), 128.4 (C^{Ar}H, A/B), 127.9 (C^{Ar}H, A/B), 127.6 (C^{Ar}H, A/B), 127.4 (C^{Ar}H, A/B), 127.0 (2 x C^{Ar}H, A/B), 120.5 (C⁵, A), 120.2 (C⁸H, B), 118.7 (C⁵, B), 117.5 (C⁷H, A), 116.6 (C⁷H, B), 114.8 (C⁸H, B), 111.2 (C⁹H, B), 111.1 (C⁹H, A), 64.3, 58.7 (C²H₂, A), 58.3 (C²H₂, B), 55.6 (C¹²H₂, B), 55.3 (C¹²H₂, A), 44.0 (C¹⁷H, A), 43.8 (C¹⁷H, B), 40.3 (C⁴H₂, B), 38.8 (C⁴H₂, A), 34.3 (C³, A), 33.9 (C³, B), 30.9 (C¹⁸H₂, A), 30.7 (C¹⁸H₂, B), 24.83 (C²¹H₃, B), 24.80 (C²¹H₃, A), 19.5 (C¹¹H₃, A), 19.2 (C¹¹H₃, B).

IR (neat) (cm⁻¹): 2956, 1771, 1694, 1602, 1498, 1435, 1382, 1355, 1281, 1123.

3-(*N*-Benzyl-3-methyl-1,2,3,4-tetrahydroquinolin-3-yl)-*N*-phenylpyrrolidine-2,5-dione (**2g**)



The title compound was prepared according to General Procedure **B** using salt **1a** (45 mg, 0.125 mmol) and *N*-phenylmaleimide (43 mg, 0.25 mmol) as electrophile. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine* **2g** as an inseparable 1.5:1 diastereomeric mixture (38 mg, 73%) as a white wax.

HRMS (ESI): Exact mass calculated for C₂₇H₂₇N₂O₂ [M+H]⁺: 411.2067,

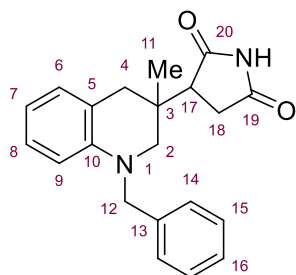
found: 411.2067.

¹H NMR (400 MHz, CDCl₃, A = major diastereomer) δ 7.54 – 7.20 (m, 20H, 20 x C^{Ar}H, A + B), 7.13 – 7.01 (m, 3H, C⁶H + C⁸H, A, C⁶H/C⁸H, B), 6.98 (dd, *J* = 7.4, 1.6 Hz, 1H, C⁶H/C⁸H, B), 6.70 (t, *J* = 7.2 Hz, 2H, C⁷H,

A + B), 6.66 – 6.58 (m, 2H, C⁹H, A + B), 4.74 (d, *J* = 17.1 Hz, 1H, C¹²H₂, B), 4.61 – 4.36 (m, 3H, C¹²H₂, A + B), 3.92 (dd, *J* = 12.0, 2.3 Hz, 1H, C²H₂, B), 3.57 (dd, *J* = 16.2, 2.3 Hz, 1H, C⁴H₂, A), 3.50 (d, *J* = 11.9 Hz, 1H, C²H₂, B), 3.22 (dd, *J* = 8.9, 5.8 Hz, 1H, C¹⁷H, B), 3.18 – 3.06 (m, 3H, C²H₂, A, C¹⁷H, A), 2.94 – 2.63 (m, 6H, C⁴H₂, A + B, C¹⁸H₂, A + B), 2.61 – 2.52 (m, 1H, C¹⁸H₂, A), 1.09 (s, 3H, C¹¹H₃, B), 1.07 (s, 3H, C¹¹H₃, A).
¹³C NMR (101 MHz, CDCl₃) δ 177.8 (C¹⁹/C²⁰, B), 177.5 (C¹⁹/C²⁰, A), 175.4 (C¹⁹/C²⁰, B), 175.4 (C¹⁹/C²⁰, A), 144.9 (C¹⁰, B), 144.8 (C¹⁰, A), 139.0 (C¹³, B), 138.7 (C¹³, A), 134.3 (C²¹, B), 132.0 (C²¹, A), 130.6 (C⁶H/C⁸H, A), 129.8 (C⁶H/C⁸H, B), 129.31 (C^{Ar}H, A/B), 129.26 (C^{Ar}H, A/B), 128.9 (C^{Ar}H, A/B), 128.8 (C^{Ar}H, A/B), 128.74 (C^{Ar}H, A/B), 128.69 (C^{Ar}H, A/B), 128.0 (C^{Ar}H, A/B), 127.6 (C^{Ar}H, A/B), 127.4 (C^{Ar}H, A/B), 127.0 (C^{Ar}H, A/B), 126.9 (C^{Ar}H, A/B), 126.8 (C^{Ar}H, A/B), 126.6 (C^{Ar}H, A/B), 120.2 (C⁵, A), 118.6 (C⁵, B), 117.53 (C⁷H, A), 116.65 (C⁷H, B), 111.2 (C⁹H, A), 111.1 (C⁹H, B), 58.8 (C²H₂, A), 58.2 (C²H₂, B), 55.4 (C¹²H₂, B), 55.3 (C¹²H₂, A), 43.7 (C¹⁷H, A), 43.5 (C¹⁷H, B), 40.4 (C⁴H₂, B), 38.8 (C⁴H₂, A), 34.7 (C³, A), 34.2 (C³, B), 31.1 (C¹⁸H₂, A), 31.0 (C¹⁸H₂, B), 19.5 (C¹¹H₃, A), 19.2 (C¹¹H₃, B).

IR (neat) (cm⁻¹): 2929, 1774, 1707, 1600, 1499, 1453, 1381, 1286, 1180, 1028.

3-(*N*-Benzyl-3-methyl-1,2,3,4-tetrahydroquinolin-3-yl)pyrrolidine-2,5-dione (2h)



The title compound was prepared according to General Procedure **B** using salt **1a** (45 mg, 0.125 mmol) and maleimide (24 mg, 0.25 mmol) as electrophile. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine 2h* as an inseparable 1.7:1 diastereomeric mixture (28 mg, 67%) as a clear oil.

HRMS (ESI): Exact mass calculated for C₂₁H₂₃N₂O₂ [M+H]⁺: 335.1754, found:

335.1754.

¹H NMR (400 MHz, CDCl₃) δ 8.44 – 8.14 (m, 2H, NH, A + B), 7.34 – 7.07 (m, 10H, 10 x C^{Ar}H, A + B), 7.04 – 6.74 (m, 4H, C⁶H + C⁸H, A + B), 6.63 – 6.45 (m, 4H, C⁷H + C⁹H, A + B), 4.68 – 4.23 (m, 4H, C¹²H₂, A + B), 3.75 (dd, *J* = 11.9, 2.3 Hz, 1H, C⁴H₂, B), 3.43 – 3.31 (m, 2H, C²H₂, A, C⁴H₂, B), 3.04 – 2.98 (m, 1H, C¹⁷H, B), 2.98 – 2.89 (m, 3H, C⁴H₂ + C¹⁷H, A), 2.75 (d, *J* = 16.2 Hz, 1H, C²H₂, A), 2.70 – 2.41 (m, 4H, C²H₂, B, C¹⁸H₂, A + B), 2.39 – 2.29 (m, 1H, C¹⁸H₂, A), 0.95 (s, 3H, C¹¹H₃, B), 0.93 (s, 3H, C¹¹H₃, A).

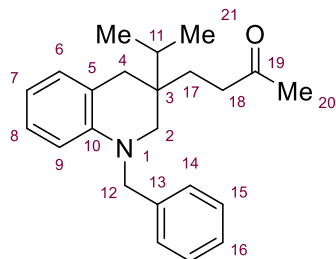
Major diastereoisomer A: ¹³C NMR (101 MHz, CDCl₃) δ 178.9 (C¹⁹O/ C²⁰O), 176.45 (C¹⁹O/ C²⁰O), 144.79 (C¹⁰), 138.6 (C¹³), 130.6 (C⁸H), 128.9 (2 x C¹⁴H/C¹⁵H), 127.6 (C⁶H), 127.4 (C¹⁶H), 127.02 (2 x C¹⁴H/C¹⁵H), 120.2 (C⁵), 117.5 (C⁷H), 111.17 (C⁹H), 58.6 (C²H₂), 55.3 (C¹²H₂), 45.2 (C¹⁷H), 38.7 (C⁴H₂), 34.3 (C³), 32.0 (C¹⁸H₂), 19.5 (C¹¹H₃).

Minor diastereoisomer B: ¹³C NMR (101 MHz, CDCl₃) δ 179.0 (C¹⁹O/ C²⁰O), 176.50 (C¹⁹O/ C²⁰O), 144.83 (C¹⁰), 139.0 (C¹³), 129.8 (C⁸H), 128.7 (2 x C¹⁴H/C¹⁵H), 127.9 (C⁶H), 126.95 (C¹⁶H), 126.8 (2 x C¹⁴H/C¹⁵H),

118.6 (C⁵), 116.7 (C⁷H), 111.21 (C⁹H), 58.1 (C²H₂), 55.5 (C¹²H), 44.9 (C¹⁷H), 40.2 (C⁴H₂), 33.9 (C³), 31.9 (C¹⁸H₂), 19.3 (C¹¹H₃).

IR (neat) (cm⁻¹): 3221, 1776, 1701, 1600, 1497, 1453, 1350, 1179, 908, 727.

4-(*N*-Benzyl-3-isopropyl-1,2,3,4-tetrahydroquinolin-3-yl)butan-2-one (**2i**)



The title compound was prepared according to General Procedure **B** using salt **1b** (45 mg, 0.125 mmol) and methyl vinyl ketone (50 μ L, 0.63 mmol) as electrophile. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine 2i* (25 mg, 60%) as a yellow oil.

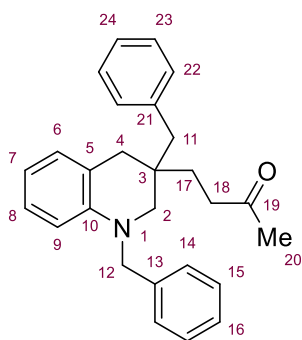
HRMS (ESI): Exact mass calculated for C₂₃H₃₀NO [M+H]⁺: 336.2322, found: 336.2320.

¹H NMR (400 MHz, CDCl₃) δ 7.36 – 7.20 (m, 5H, 2 x C¹⁴H + 2 x C¹⁵H + C¹⁶H), 7.04 – 6.96 (m, 2H, C⁶H + C⁸H), 6.61 (td, *J* = 7.3, 1.1 Hz, 1H, C⁷H), 6.57 (dd, *J* = 8.7, 1.1 Hz, 1H, C⁹H), 4.52 (d, *J* = 16.8 Hz, 1H, C¹²H₂), 4.42 (d, *J* = 16.8 Hz, 1H, C¹²H₂), 3.19 (dd, *J* = 11.6, 1.0 Hz, 1H, C²H₂), 2.93 (dd, *J* = 11.6, 2.1 Hz, 1H, C¹¹H₂), 2.79 (d, *J* = 15.9 Hz, 1H, C⁴H₂), 2.48 (dd, *J* = 16.0, 2.1 Hz, 1H, C⁴H₂), 2.42 – 2.22 (m, 2H, C¹⁸H₂), 2.05 (s, 3H, C²⁰H₃), 1.80 – 1.53 (m, 3H, C¹¹H + C¹⁷H₂), 0.90 (dd, *J* = 6.9, 2.0 Hz, 6H, 2 x C²¹H₃).

¹³C NMR (101 MHz, CDCl₃) δ 209.0 (C¹⁹), 145.2 (C¹⁰), 139.2 (C¹³), 130.0 (C⁶H/C⁸H), 128.7 (2 x C¹⁴H/C¹⁵H), 127.1 (C⁶H/C⁸H/C¹⁵H), 127.01 (C⁶H/C⁸H/C¹⁵H), 126.97 (2 x C¹⁴H/C¹⁵H), 121.2 (C⁵), 116.7 (C⁷H), 111.0 (C⁹H), 55.7 (C²H₂/C¹²H₂), 55.6 (C²H₂/C¹²H₂), 38.4 (C⁴H₂), 35.4 (C³ + C¹⁸H₂), 35.2 (C³ + C¹⁸H₂), 31.4 (C¹¹H), 30.0 (C²⁰H₃), 26.2 (C¹⁷H₂), 17.3 (C²¹H₃), 17.0 (C²¹H₃).

IR (neat) (cm⁻¹): 3027, 2959, 1715, 1602, 1576, 1506, 1452, 1387, 1354, 1280.

4-(*N*-Benzyl-3-benzyl-1,2,3,4-tetrahydroquinolin-3-yl)butan-2-one (**2j**)



The title compound was prepared according to General Procedure **B** using salt **1c** (45 mg, 0.125 mmol) and methyl vinyl ketone (50 μ L, 0.63 mmol) as electrophile. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine 2j* (43 mg, 90%) as a yellow oil.

HRMS (ESI): Exact mass calculated for C₂₇H₃₀NO [M+H]⁺: 384.2322, found: 384.2322.

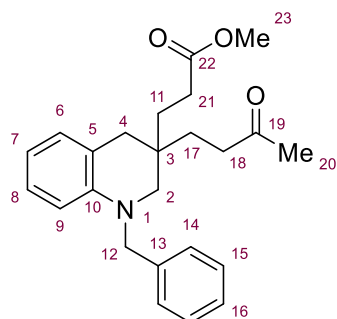
¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.18 (m, 8H, 8 x C^{Ar}H), 7.12 – 6.96 (m, 4H, 4 x C^{Ar}H), 6.68 – 6.59 (m, 2H, C⁷H + C⁹H), 4.60 (d, *J* = 16.9 Hz, 1H, C¹²H₂), 4.42 (d, *J* = 16.9 Hz, 1H, C¹²H₂), 3.07 (brs, *J* = 1.5 Hz, 2H, C²H₂), 2.74 – 2.54 (m, 4H, C⁴H₂ + C¹¹H₂), 2.54 – 2.32 (m, 2H, C¹⁸H₂), 2.09 (s, 3H, C²⁰H₃), 1.73 – 1.48 (m, 2H, C¹⁷H₂).

¹³C NMR (101 MHz, CDCl₃) δ 208.6 (C¹⁹), 144.6 (C¹⁰), 138.9 (C¹³), 137.7 (C^{Ar}), 130.6 (2 x C^{Ar}H), 130.1 (C^{Ar}H), 128.7 (2 x C^{Ar}H), 128.2 (2 x C^{Ar}H), 127.4 (C^{Ar}H), 127.04 (C^{Ar}H), 126.99 (2 x C^{Ar}H), 126.5 (C^{Ar}H),

120.3 (C⁵), 116.7 (C⁷H/C⁹H), 111.1 (C⁷H/C⁹H), 57.8 (C²H₂), 55.5 (C¹²H₂), 41.7 (C⁴H₂/C¹¹H₂), 38.3 (C⁴H₂/C¹¹H₂), 38.1 (C¹⁸H₂), 34.6 (C³), 30.1 (C²⁰H₃), 29.0 (C¹⁷H₂).

IR (neat) (cm⁻¹): 3061, 3027, 2920, 1714, 1602, 1576, 1499, 1452, 1354, 1286.

Methyl 3-(*N*-benzyl-3-(3-oxobutyl)-1,2,3,4-tetrahydroquinolin-3-yl)propanoate (**2k**)



The title compound was prepared according to General Procedure **B** using salt **1d** (45 mg, 0.125 mmol) and methyl vinyl ketone (50 μL, 0.63 mmol) as electrophile. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine 2k* (39 mg, 82%) as a clear oil.

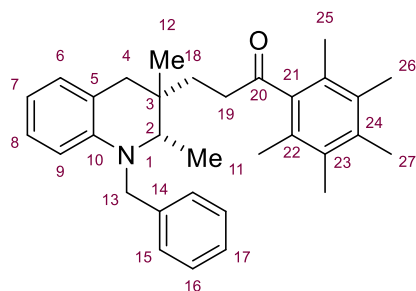
HRMS (ESI): Exact mass calculated for C₂₄H₃₀NO₃ [M+H]⁺: 380.2220, found: 380.2219.

¹H NMR (400 MHz, CDCl₃) δ 7.36 – 7.20 (m, 5H, 2 x C¹⁴H + 2 x C¹⁵H + C¹⁶H), 7.05 – 6.93 (m, 2H, C⁶H + C⁸H), 6.66 – 6.56 (m, 2H, C⁷H + C⁹H), 4.57 – 4.34 (m, 2H, C¹²H₂), 3.65 (s, 3H, C²³H₃), 3.01 (s, 2H, C⁴H₂), 2.62 (s, 2H, C⁴H₂), 2.48 – 2.15 (m, 4H, C¹⁸H₂ + C²¹H₂), 2.10 (s, 3H, C²⁰H₃), 1.79 – 1.47 (m, 4H, C¹¹H₂ + C¹⁷H₂).

¹³C NMR (101 MHz, CDCl₃) δ 208.4 (C¹⁹O), 174.2 (C²⁰O), 144.8 (C¹⁰), 138.9 (C⁵), 130.0 (C⁶H/C⁸H), 128.7 (2 x C¹⁴H/C¹⁵H), 127.4 (C⁶H/C⁸H), 127.1 (C¹⁶H), 126.9 (2 x C¹⁴H/C¹⁵H), 120.0 (C¹³), 116.8 (C⁷H/C⁹H), 111.1 (C⁷H/C⁹H), 57.6 (C²H₂), 55.4 (C¹²H₂), 51.8 (C²³H₃), 39.0 (C⁴H₂), 37.6 (C¹⁸H₂/C²¹H₂), 32.9 (C³), 30.1 (C²⁰H₃), 29.9 (C¹¹H₂/C¹⁷H₂), 28.4 (C¹⁸H₂/C²¹H₂), 28.3 (C¹¹H₂/C¹⁷H₂).

IR (neat) (cm⁻¹): 3027, 2925, 1734, 1715, 1602, 1502, 1452, 1436, 1354, 1320.

3-(*N*-Benzyl-2,3-dimethyl-1,2,3,4-tetrahydroquinolin-3-yl)-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one (**2l**)



The title compound was prepared according to General Procedure **C** using salt **1f** (45 mg, 0.125 mmol) and 2,3,4,5,6-pentamethylphenyl vinyl ketone (51 mg, 0.25 mmol) as electrophile. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine 2l* (22 mg, 32%) as an inseparable 2:1 diastereomeric mixture as a white wax.

The title compound could not be prepared according to General procedure **B** and only starting material was recovered from the reaction.

HRMS (ESI): Exact mass calculated for C₃₂H₄₄NO [M+H]⁺: 545.3104, found: 545.3102.

¹H NMR (400 MHz, CDCl₃) δ 7.35 – 7.17 (m, 10H, 2 x C¹⁵H + 2 x C¹⁶H + C¹⁷H, A + B), 7.04 – 6.91 (m, 3H, C⁶H + C⁸H, A + B), 6.66 – 6.55 (m, 2H, C⁷H, A + B), 6.46 (dd, J = 8.3, 1.1 Hz, 1H, C⁹H, A), 6.40 (d, J = 8.1 Hz, 1H, C⁹H, B), 4.73 (d, J = 16.7 Hz, 1H, C¹³H₂, B), 4.58 – 4.34 (m, 3H, C¹³H₂, A + B), 3.27 – 3.20 (m, 1H,

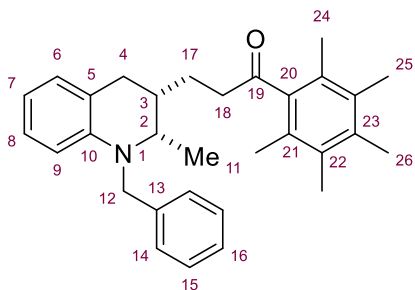
C^2H , B), 3.12 – 2.99 (m, 1H, C^2H_2 , A), 2.84 (dd, J = 16.4, 3.7 Hz, 2H, C^4H_2 , A + B), 2.80 – 2.53 (m, 4H, $C^{19}H_2$, A + B), 2.51 – 2.37 (m, 2H, C^4H_2 , A + $C^{13}H_2$, B), 2.29 – 1.94 (m, 30H, 2 x $C^{25}H_3$ + 2 x $C^{26}H_3$ + $C^{27}H_3$, A + B), 1.94 – 1.67 (m, 4H, $C^{18}H_2$, A + B), 1.12 – 1.04 (m, 6H, $C^{11}H_3$, A + B), 1.03 (s, 3H, $C^{12}H_3$, A), 0.99 (s, 3H, $C^{12}H_3$, B).

Major diastereoisomer A: ^{13}C NMR (151 MHz, $CDCl_3$) δ 212.0 ($C^{20}O$), 143.5 (C^{10}), 141.0 (C^{21}), 139.8 (C^{14}), 135.6 (C^{Ar}), 133.3 (2 x C^{Ar}), 129.8 (C^6H/C^8H), 128.6 (2 x $C^{15}H/C^{16}H$), 127.3 (2 x C^{Ar} + C^6H/C^8H), 127.14 ($C^{17}H$), 126.8 (2 x $C^{15}H/C^{16}H$), 120.0 (C^5), 116.2 (C^7H), 111.9 (C^9H), 62.0 (C^2H), 54.8 ($C^{12}H_2$), 40.0 ($C^{19}H_2$), 36.74 (C^4H_2), 33.7 (C^3), 33.1 ($C^{18}H_2$), 23.83 ($C^{12}H_3$), 17.4 (2 x $C^{25}H_3/C^{26}H_3$), 16.81 ($C^{27}H_3$), 16.09 (2 x $C^{25}H_3/C^{26}H_3$), 13.9 ($C^{11}H_3$).

Minor diastereoisomer B: ^{13}C NMR (151 MHz, $CDCl_3$) δ 212.1 ($C^{20}O$), 143.6 (C^{10}), 141.1 (C^{21}), 139.7 (C^{14}), 135.4 (C^{Ar}), 133.1 (2 x C^{Ar}), 129.5 (C^6H/C^8H), 128.7 (2 x $C^{15}H/C^{16}H$), 127.4 (2 x C^{Ar} + C^6H/C^8H), 127.11 ($C^{17}H$), 126.9 (2 x $C^{15}H/C^{16}H$), 120.2 (C^5), 116.4 (C^7H), 112.2 (C^9H), 61.6 (C^2H), 55.0 ($C^{13}H_2$), 40.3 ($C^{19}H_2$), 36.69 (C^4H_2), 33.8 (C^3), 31.8 ($C^{18}H_2$), 23.77 ($C^{12}H_3$), 17.3 (2 x $C^{25}H_3/C^{26}H_3$), 16.78 ($C^{27}H_3$), 16.07 (2 x $C^{25}H_3/C^{26}H_3$), 14.3 ($C^{11}H_3$).

IR (neat) (cm^{-1}): 3029, 2923, 1698, 1602, 1497, 1451, 1315, 1116, 1027, 909.

3-(*N*-Benzyl-2-methyl-1,2,3,4-tetrahydroquinolin-3-yl)-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one (2m)



The title compound was prepared according to General Procedure C using salt **1e** (45 mg, 0.125 mmol) and 2,3,4,5,6-pentamethylphenyl vinyl ketone (37 mg, 0.19 mmol) as electrophile. Purification by column chromatography (0%-5% EtOAc in pentane) gave *amine 2m* (18 mg, 33%) as an inseparable 5:1 diastereomeric ratio as a white wax.

The title compound could not be prepared according to General procedure B and only starting material was recovered from the reaction.

HRMS (ESI): Exact mass calculated for $C_{31}H_{38}NO$ $[M+H]^+$: 440.2948, found: 440.2946.

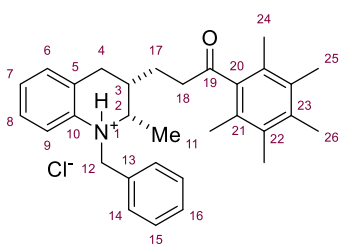
1H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.18 (m, 10H, 5 x $C^{Ar}H$, A + B), 7.05 – 6.89 (m, 4H, C^6H , A + B, C^8H , A + B), 6.64 – 6.54 (m, 2H, C^7H/C^9H , A + B), 6.45 – 6.37 (m, 2H, C^7H/C^9H , A + B), 4.58 – 4.39 (m, 4H, $C^{12}H_2$, A + B), 3.51 – 3.41 (m, 1H, C^2H , A), 3.39 – 3.29 (q, 1H, C^2H , B), 2.94 – 2.61 (m, 8H, C^4H_2 , A + B, $C^{18}H_2$, A + B), 2.28 – 2.00 (m, 32H, C^3H , A + B, 2 x $C^{23}H_3$, A + B, 2 x $C^{24}H_3$, A + B, $C^{26}H_3$, A + B), 1.87 – 1.73 (m, 4H, $C^{17}H_2$, A + B), 1.19 (d, J = 6.5 Hz, 3H, $C^{11}H_3$, B) 1.07 (d, J = 6.5 Hz, 3H, $C^{11}H_3$, A).

^{13}C NMR (151 MHz, $CDCl_3$, only major diastereomer A reported) δ 211.6 ($C^{19}O$), 144.1 (C^{10}), 140.8 (C^{20}), 139.4 (C^{13}), 135.6 (C^{23}), 133.3 (2 x C^{21}/C^{22}), 129.2 (C^6H/C^8H), 128.7 (2 x $C^{14}H/C^{15}H$), 127.4 ($C^6H/C^8H/2$ x

C^{Ar}), 127.3 ($C^6H/C^8H/2 \times C^{Ar}$), 126.9 ($C^{16}H$), 126.5 ($2 \times C^{14}H/C^{15}H$), 120.9 (C^5), 115.8 (C^7H), 111.7 (C^9H), 57.1 (C^2H), 54.0 ($C^{12}H_2$), 43.5 (C^4H_2), 36.0 (C^3H), 29.9 ($C^{18}H_2$), 26.6 ($C^{17}H_2$), 17.4 ($2 \times C^{24}H_3/C^{25}H_3$), 16.8 ($C^{26}H_3$), 16.1 ($2 \times C^{24}H_3/C^{25}H_3$), 12.2 ($C^{11}H_3$).

IR (neat) (cm^{-1}): 2924, 1699. 1602, 1499, 1451, 1377, 1353, 1251. 743, 697.

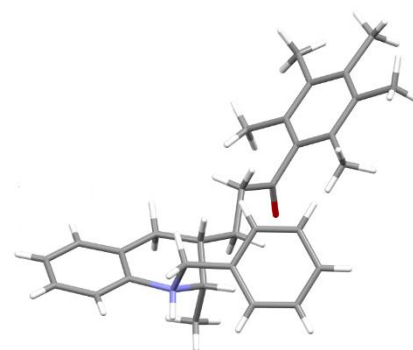
3-(*N*-Benzyl-2-methyl-1,2,3,4-tetrahydroquinolin-3-yl)-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one (2m·HCl)



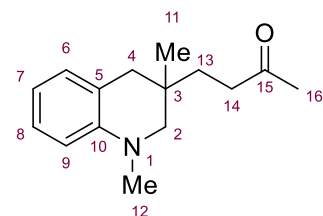
In a 25 mL round bottom flask under argon was charged quinoline product **2m** (35 mg, 0.08 mmol, 1.0 eq.) in dry diethyl ether (1.5 mL). The solution was chilled to 0 °C and 2M HCl in diethyl ether (0.06 mL, 0.12 mmol, 1.5 eq.) was introduced dropwise. After 15 minutes the solids were collected via filtration to give the title compound **2m·HCl** (38 mg, 99%) as a white solid. A single crystal for X-ray diffraction was obtained by slow evaporation from the CH_2Cl_2 /heptane solvent system.

1H NMR (400 MHz, $CDCl_3$, major diastereomer) δ 7.92 (dd, $J = 8.1, 1.4$ Hz, 1H), 7.78 – 7.74 (m, 2H), 7.42 – 7.38 (m, 2H), 7.34 (dd, $J = 7.5, 1.4$ Hz, 1H), 7.30 (dd, $J = 7.8, 1.7$ Hz, 1H), 7.26 – 7.21 (m, 2H), 4.80 (d, $J = 13.0$ Hz, 1H), 4.35 (d, $J = 13.1$ Hz, 1H), 3.67 (dd, $J = 6.8, 3.0$ Hz, 1H), 3.02 (dd, $J = 16.6, 4.9$ Hz, 1H), 2.94 (t, $J = 7.5$ Hz, 1H), 2.73 – 2.49 (m, 2H), 2.25 (s, 3H), 2.20 (s, 6H), 2.14 (d, $J = 7.1$ Hz, 1H), 2.07 (s, 6H), 2.00 (s, 1H), 1.85 (d, $J = 6.6$ Hz, 1H), 1.79 – 1.67 (m, 1H), 1.41 (d, $J = 6.8$ Hz, 3H).

Crystal data $C_{31}H_{38}ClNO = 476.10$, triclinic, $a = 9.2443(4)$, $b = 16.6064(5)$, $c = 18.4379(7)$ Å, $\beta = 97.470(3)^\circ$, $Z = 4$, $T = 300$ K, space group $P-1$, 28854 reflections measured, 11191 unique ($R_{int} = 0.049$), which were used in all calculations.



4-(1,3-Dimethyl-1,2,3,4-tetrahydroquinolin-3-yl)butan-2-one (2n)



The title compound was prepared according to General Procedure **B** using quinolinium salt **1h** (36 mg, 0.125 mmol) and methyl vinyl ketone (50 μ L, 0.63 mmol) as electrophile. Purification by column chromatography (0-10% EtOAc in pentane) furnished *amine* **2n** (23 mg, 78%) as a light-yellow oil.

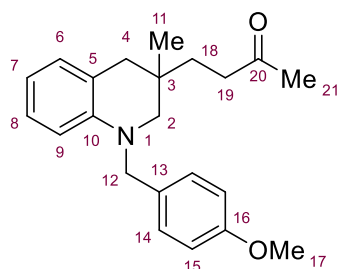
HRMS (ESI): Exact mass calculated for $C_{15}H_{22}NO$ $[M+H]^+$: 232.1696, found: 232.1698.

1H NMR (400 MHz, $CDCl_3$) δ 7.13 – 7.04 (m, 1H, C^8H), 6.93 (d, $J = 1.1$ Hz, 1H, C^6H), 6.66 – 6.56 (m, 2H, $C^7H + C^9H$), 2.95 – 2.83 (m, 5H, $C^2H_2 + C^{12}H_3$), 2.60 – 2.51 (m, 2H, C^4H_2), 2.51 – 2.43 (m, 2H, $C^{14}H_2$), 2.14 (s, 3H, $C^{16}H_3$), 1.69 – 1.52 (m, 2H, $C^{13}H_2$), 0.95 (s, 3H, $C^{11}H_3$).

¹³C NMR (101 MHz, CDCl₃) δ 209.1 (C¹⁵), 145.6 (C¹⁰), 129.6 (C⁶H), 127.2 (C⁸H), 121.1 (C⁵), 116.5 (C⁷H), 110.8 (C⁹H), 61.4 (C²H₂), 40.3 (C⁴H₂), 39.3 (C¹²H₃), 38.6 (C¹⁴H₂), 32.7 (C¹³H₂), 30.9 (C³), 30.0 (C¹⁶H₃), 23.6 (C¹¹H₃).

IR (neat) (cm⁻¹): 3657, 2980, 1714, 1603, 1503, 1461, 1375, 1278, 1160, 747.

4-(*N*-(4-Methoxybenzyl)-3-methyl-1,2,3,4-tetrahydroquinolin-3-yl)butan-2-one (**2o**)



The title compound was prepared according to General Procedure **B** using quinolinium salt **1i** (49 mg, 0.125 mmol) and methyl vinyl ketone (50 μL, 0.63 mmol) as electrophile. Purification by column chromatography (0-10% EtOAc in pentane) furnished *amine 2o* (33 mg, 77%) as a pale yellow oil.

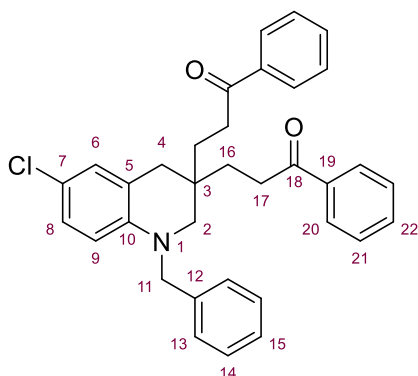
HRMS (ESI): Exact mass calculated for C₂₂H₂₈NO₂ [M+H]⁺: 338.2115, found: 338.2112.

¹H NMR (400 MHz, CDCl₃) δ 7.19 (d, *J* = 8.9 Hz, 2H, 2 x C¹⁴H), 7.01 (ddd, *J* = 8.2, 7.3, 1.7 Hz, 1H, C⁸H), 7.00 – 6.92 (m, 1H, C⁶H), 6.86 (d, *J* = 8.7 Hz, 2H, 2 x C¹⁵H), 6.64 – 6.55 (m, 2H, C⁷H + C⁹H), 4.48 – 4.33 (m, 2H, C¹²H₂), 3.79 (s, 3H, C¹⁷H₃), 3.05 – 2.93 (m, 2H, C⁴H₂), 2.58 (s, 2H, C²H₂), 2.50 – 2.30 (m, 2H, C¹⁹H₂), 2.11 (s, 3H, C²¹H₃), 1.70 – 1.52 (m, 2H, C¹⁸H₂), 0.96 (s, 3H, C⁸H₃).

¹³C NMR (101 MHz, CDCl₃) δ 209.0 (C²⁰O), 158.7 (C¹⁶), 144.8 (C¹⁰), 131.1 (C^{Ar}), 129.9 (C⁶H), 128.0 (2 x C¹⁴H), 127.3 (C⁸H), 120.6 (C^{Ar}), 116.4 (C⁷H/C⁹H), 114.1 (2 x C¹⁵H), 110.9 (C⁷H/C⁹H), 59.5 (C⁴H₂), 55.4 (C¹⁷H₃), 54.8 (C¹²H₂), 40.7 (C²H₂), 38.4 (C¹⁹H₂), 32.5 (C¹⁸H₂), 30.8 (C³), 30.0 (C²¹H₂), 23.5 (C¹¹H₃).

IR (neat) (cm⁻¹): 2980, 1714, 1603, 1509, 1457, 1352, 1282, 1244, 1170, 1034.

3,3'-(*N*-Benzyl-6-chloro-1,2,3,4-tetrahydroquinoline-3,3-diyl)bis(1-phenylpropan-1-one) (**2p**)



The title compound was prepared according to General Procedure **B** using quinolinium salt **1k** (48 mg, 0.125 mmol) and phenyl vinyl ketone (66 mg, 0.50 mmol) as electrophile. Purification by column chromatography (5-20% EtOAc in pentane) gave *amine 2p* (38 mg, 58%) as a pale yellow solid.

m.p. (EtOAc): 148 – 150 °C.

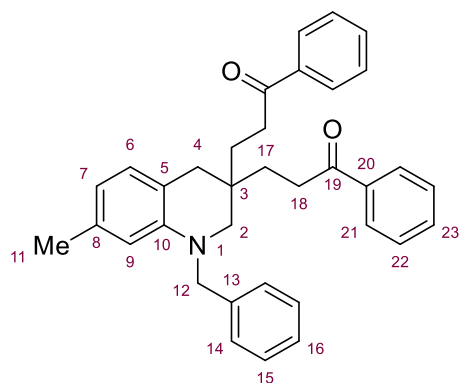
HRMS (ESI): Exact mass calculated for C₃₄H₃₂NO₂Cl [M+H]⁺: 522.2205, found: 522.2196.

¹H NMR (400 MHz, CDCl₃) δ 7.93 – 7.80 (m, 4H, 4 x C²⁰H), 7.60 – 7.51 (m, 2H, 2 x C²²H), 7.46 – 7.37 (m, 4H, 4 x C²¹H), 7.31 – 7.12 (m, 5H, 5 x C^{Ar}H), 7.02 – 6.90 (m, 2H, C⁷H + C⁸H), 6.51 (d, *J* = 8.7 Hz, 1H, C⁹H), 4.45 (s, 2H, C¹¹H₂), 3.13 (s, 2H, C⁴H₂), 3.06 – 2.78 (m, 4H, 2 x C¹⁷H₂), 2.71 (s, 2H, C²H₂), 1.92 – 1.74 (m, 4H, 2 x C¹⁶H₂).

¹³C NMR (101 MHz, CDCl₃) δ 199.6 (2 x C¹⁸O), 151.6 (C⁷Cl), 146.0 (C^{Ar}), 137.6 (2 x C^{Ar}), 136.8 (C^{Ar}), 133.3 (2 x C²²H), 129.0 (2 x C¹³H/C¹⁴H), 128.8 (4 x C²¹H), 128.1 (4 x C²⁰H), 127.5 (C⁶H + C⁸H + C¹⁵H), 126.7 (2 x C¹⁴H/C¹³H), 114.8 (C⁹H), 113.8 (C^{Ar}), 112.2 (C⁶H), 57.5 (C⁴H₂), 56.1 (C¹¹H₂), 35.3 (C²H₂), 32.6 (C³), 32.4 (2 x C¹⁷H₂), 29.0 (2 x C¹⁶H₂).

IR (neat) (cm⁻¹): 3059, 2159, 2028, 1686, 1596, 1503, 1447, 1298, 1278, 1222.

3,3'-(*N*-Benzyl-7-methyl-1,2,3,4-tetrahydroquinoline-3,3-diyl)bis(1-phenylpropan-1-one) (**2q**)



The title compound was prepared according to General Procedure **C** using quinolinium salt **1l** (45 mg, 0.125 mmol) and phenyl vinyl ketone (66 mg, 0.50 mmol) as electrophile. Purification by column chromatography (5-20% EtOAc in pentane) gave *amine 2q* (27 mg, 44%) as a pale brown solid. General procedure **B** afforded the title compound in a significantly reduced yield of 29%.

m.p. (EtOAc): 123 – 125 °C

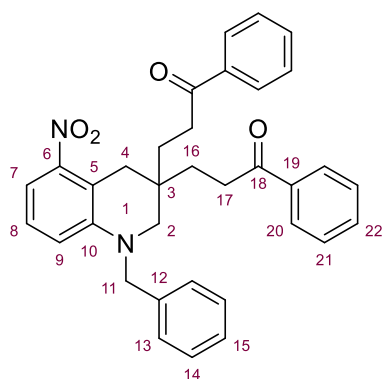
HRMS (ESI): Exact mass calculated for C₃₅H₃₅NO₂ [M+H]⁺: 502.2741, found: 502.2741.

¹H NMR (400 MHz, CDCl₃) δ 7.87 – 7.78 (m, 4H, 4 x C²¹H), 7.55 – 7.45 (m, 2H, 2 x C²³H), 7.43 – 7.34 (m, 4H, 4 x C²²H), 7.29 – 7.08 (m, 5H, 5 x C^{Ar}H), 6.88 (d, *J* = 7.8 Hz, 1H, C⁶H), 6.48 – 6.41 (m, 2H, C⁷H + C⁹H), 4.44 (s, 2H, C¹²H₂), 3.07 (s, 2H, C⁴H₂), 3.00 – 2.78 (m, 4H, 2 x C¹⁸H₂), 2.69 (s, 2H, C²H₂), 2.19 (s, 3H, C¹¹H₃), 1.90 – 1.71 (m, 4H, 2 x C¹⁷H₂).

¹³C NMR (101 MHz, CDCl₃) δ 200.1 (2 x C¹⁹O), 144.9 (C¹⁰), 139.1 (C¹³), 137.1 (C⁸), 137.0 (2 x C²⁰), 133.1 (2 x C²³H), 129.9 (C⁶H), 128.73 (2 x C¹⁴H), 128.67 (4 x C²²H), 128.2 (4 x C²¹H), 127.2 (2 x C¹⁵H), 127.1 (C¹⁶H), 117.8 (C⁷H), 117.3 (C⁵), 111.7 (C⁹H), 57.7 (C⁴H₂), 55.3 (C¹²H₂), 39.1 (C²H₂), 33.3 (C³), 32.7 (2 x C¹⁸H₂), 29.2 (2 x C¹⁷H₂), 21.7 (C¹¹H₃).

IR (neat) (cm⁻¹): 3657, 2980, 2921, 1682, 1512, 1449, 1379, 1251, 1158, 741.

3,3'-(*N*-Benzyl-5-nitro-1,2,3,4-tetrahydroquinoline-3,3-diyl)bis(1-phenylpropan-1-one) (**2r**)



The title compound was prepared according to General Procedure **B** using quinolinium salt **1m** (49 mg, 0.125 mmol) and phenyl vinyl ketone (66 mg, 0.50 mmol) as electrophile. Purification by column chromatography (5-20% EtOAc in pentane) gave *amine 2r* (22 mg, 33%) as an orange solid.

m.p. (EtOAc): 168 – 170 °C

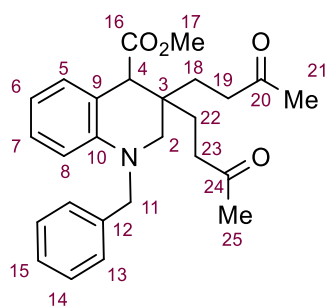
HRMS (ESI): Exact mass calculated for $C_{34}H_{32}N_2O_4$ $[M+H]^+$: 533.446, found: 533.2434.

1H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.77 (m, 4H, 4 x $C^{20}H$), 7.51 – 7.42 (m, 2H, 2 x $C^{22}H$), 7.35 (dd, J = 8.4, 7.0 Hz, 4H, 4 x $C^{21}H$), 7.22 – 7.05 (m, 5H, 5 x $C^{Ar}H$), 7.04 – 6.95 (m, 2H, C^7H + C^8H), 6.69 (dd, J = 6.4, 3.2 Hz, 1H, C^9H), 4.47 (s, 2H, $C^{11}H_2$), 3.15 (s, 2H, C^4H_2), 3.01 – 2.88 (m, 2H, 2 x $C^{17}H_2$), 2.84 – 2.72 (m, 4H, C^2H_2 + 2 x $C^{17}H_2$), 1.86 – 1.65 (m, 4H, 2 x $C^{16}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 199.6 (2 x $C^{18}O$), 151.6 (C^6), 146.0 (C^{10}), 137.6 (2 x C^{Ar}), 136.8 (C^{Ar}), 133.3 (2 x $C^{22}H$), 129.0 (2 x $C^{13}H/C^{14}H$), 128.8 (4 x $C^{20}H/C^{21}H$), 128.1 (4 x $C^{20}H/C^{21}H$), 127.5 (C^8H + C^{15}), 126.7 (2 x $C^{13}H/C^{14}H$), 114.8 (C^9H), 113.8 (C^{Ar}), 112.2 (C^7H), 57.5 (C^4H_2), 56.1 ($C^{11}H_2$), 35.3 (C^2H_2), 32.6 (C^3), 32.4 (2 x $C^{17}H_2$), 29.0 (2 x $C^{16}H_2$).

IR (neat) (cm^{-1}): 3061, 2922, 1680, 1600, 1521, 1496, 1449, 1350, 1288, 1213.

Methyl 1-benzyl-3,3-bis(3-oxobutyl)-1,2,3,4-tetrahydroquinoline-4-carboxylate (**2s**)



The title compound was prepared according to General Procedure **B** using quinolinium salt **1g** (50 mg, 0.12 mmol) and methyl vinyl ketone (33 mg, 0.43 mmol) as electrophile. Purification by column chromatography (3-25% EtOAc in pentane) furnished *amine 2s* (36 mg, 69%) as a light-yellow oil.

HRMS (ESI): Exact mass calculated for $C_{26}H_{32}NO_4$ $[M+H]^+$: 422.2326 found: 422.2325;

1H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 2H, $C^{13}H$), 7.27 – 7.20 (m, 3H, $C^{14}H$ + $C^{15}H$), 7.11 – 6.98 (m, 2H, C^5H + C^6H), 6.65 (dd, J = 8.4, 1.1 Hz, 1H, C^8H), 6.60 (td, J = 7.3, 1.1 Hz, 1H, C^7H), 4.60 (d, J = 16.9 Hz, 1H, $C^{11}H_a$), 4.47 (d, J = 16.9 Hz, 1H, $C^{11}H_b$), 3.66 (s, 3H, $C^{17}H_3$), 3.63 – 3.70 (d, J = 12.0, 1H, C^2H_a), 3.50 (d, J = 2.1 Hz, 1H, C^4H), 2.78 (dd, J = 12.0, 2.1 Hz, 1H, C^2H_b), 2.62 (ddd, J = 17.4, 10.9, 5.0 Hz, 1H, $C^{19}H_a$), 2.41 (ddd, J = 17.1, 10.9, 5.5 Hz, 1H, $C^{19}H_b$), 2.27 – 2.10 (m, 5H, $C^{23}H_2$ + $C^{21}H_3$), 2.00 (s, 3H, $C^{25}H_3$), 1.69 – 1.37 (m, 4H, $C^{18}H_2$ + $C^{22}H_2$).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.0 ($C^{20}O$), 207.8 ($C^{24}O$), 173.6 ($C^{16}O$), 144.1 (C^{10}), 138.6 (C^{12}), 130.3 (C^5H), 129.0 (C^7H), 128.8 (2 x $C^{14}H$), 127.1 ($C^{15}H$), 126.9 (2 x $C^{13}H$), 116.5 (C^9), 116.4 (C^6H), 111.4 (C^8H), 54.8 ($C^{11}H_2$), 52.8 (C^2H_2), 52.3 (C^4H), 52.1 ($C^{17}H_3$), 37.2 ($C^{19}H_2$), 36.9 ($C^{23}H_2$), 34.6 (C^3), 30.22 ($C^{21}H_3$), 30.17 ($C^{25}H_3$), 26.6 ($C^{18}H_2$), 26.4 ($C^{22}H_2$).

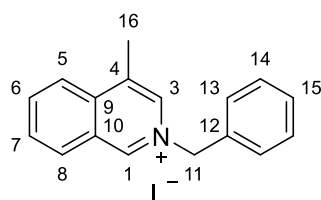
IR (neat) (cm^{-1}): 2947, 2925, 1713, 1602, 1507, 1355, 1244, 1159, 746.

Synthesis of isoquinolinium salts

General Procedure D: Preparation of isoquinolinium salts

A mixture of the corresponding isoquinoline (1.00 equiv.) and benzyl iodide (2.00 equiv.) in acetone (0.5 M) was stirred in the dark at room temperature for 20 hours. Addition of diethyl ether (10 mL) resulted in precipitation and the resulting suspension was sonicated (15 min). The solids were collected by filtration, washed with diethyl ether, and dried under vacuum to give the benzyl quinolinium iodide salts as crystalline solids. Where necessary additional purification by column chromatography was performed.

N-Benzyl-4-methylisoquinolinium iodide (**4a**)



The title compound was prepared according to the General Procedure **D** using 4-methylisoquinoline (858 mg, 6.00 mmol, 1.0 equiv.) and benzyl iodide (1.13 mL, 9.00 mmol) in acetone (0.5 M). The resultant solid was washed with diethyl ether and dried under vacuum. Further drying under high vacuum at 70 °C for 10 hours gave the salt **4a** (2.09 g, 97%) as a yellow solid.

m.p. (acetone): 126 – 128 °C

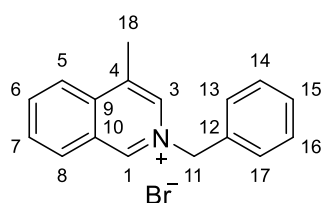
HRMS (ESI): Exact mass calculated for C₁₇H₁₆N [M]⁺: 234.1277, found 234.1278

¹H NMR (400 MHz, DMSO-*d*₆) δ 10.20 (s, 1H, C¹H), 8.80 (s, 1H, C³H), 8.54 (dd, *J* = 8.3, 1.1 Hz, 1H, C^{5/8}H), 8.36 (dd, *J* = 8.6, 1.1 Hz, 1H, C^{5/8}H), 8.30 (dd, *J* = 6.9, 1.4 Hz, 1H, C^{6/7}H), 8.09 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H, C^{6/7}H), 7.66 – 7.57 (m, 2H, 2 x C¹⁴H), 7.50 – 7.37 (m, 3H, 2 x C¹³H + C¹⁵H), 5.94 (s, 2H, C¹¹H₂), 2.76 (s, 3H, C¹⁶H₃)

¹³C NMR (101 MHz, DMSO-*d*₆) δ 148.3 (C¹H), 137.0 (C^{Ar}H), 136.6 (C^Q), 135.2 (C^Q), 134.2 (C^Q), 133.3 (C³H), 131.1 (2 x C^{Ar}H), 129.3 (C¹⁵H), 129.2 (2 x C¹³H), 128.8 (2 x C¹⁴H), 126.9 (C^Q), 124.4 (C^{Ar}), 63.2 (C¹¹H₂), 15.8 (C¹⁶H₃)

IR (neat) (cm⁻¹): 3672, 2999, 2886, 1474, 1460, 1380, 1252, 1152, 1072, 954.

N-Benzyl-4-methylisoquinolinium bromide (**4a'**)



The title compound was prepared according to a modified General Procedure **D**. A mixture of 4-methylisoquinoline (500 mg, 3.49 mmol, 1.0 eq.) and benzyl bromide (0.50 mL, 4.19 mmol, 1.2 eq.) in dioxane (10 mL) was stirred at 90 °C for 24 h. The reaction mixture was filtered.

The resultant solid was sonicated in Et₂O (10 mL) for 5 min and washed with ether (50 mL) then dried under vacuum to give isoquinolinium bromide **4a'** (1.01 g, 92%) as an off-white solid.

m.p. (acetone): 197 °C

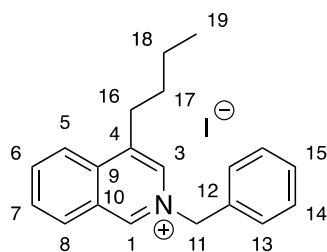
HRMS (ESI): Exact mass calculated for $C_{17}H_{16}N$ $[M]^+$: 234.1277, found: 234.1279;

1H NMR (400 MHz, $DMSO-d_6$) δ 10.24 (s, 1H, C^1H), 8.82 (t, $J = 1.3$ Hz, 1H, C^3H), 8.54 (dt, $J = 8.2, 1.1$ Hz, 1H, $C^{5/8H}$), 8.37 (dd, $J = 8.6, 1.1$ Hz, 1H, $C^{5/8H}$), 8.30 (ddd, $J = 8.5, 6.9, 1.3$ Hz, 1H, $C^{6/7H}$), 8.09 (ddd, $J = 8.2, 6.9, 1.2$ Hz, 1H, $C^{6/7H}$), 7.64 – 7.59 (m, 2H, 2 x C^{ArH}), 7.48 – 7.41 (m, 3H, 3 x C^{ArH}), 5.94 (s, 2H, $C^{11}H_2$), 2.276 (s, 1H, $C^{18}H_3$);

^{13}C NMR (101 MHz, $DMSO-d_6$) δ 148.4 (C^1H), 137.0 ($C^{5/8H}$), 136.6 (C^{Ar}), 135.2 (C^{Ar}), 134.3 (C^{Ar}), 133.3 (C^3H), 131.2 (C^{ArH}), 131.1 (C^{ArH}), 129.3 (C^{ArH}), 129.2 (2 x C^{ArH}), 128.8 (2 x C^{ArH}), 127.0 (C^{Ar}), 124.4 ($C^{5/8H}$), 63.2 ($C^{11}H_2$), 15.7 ($C^{18}H_3$);

IR (neat) (cm^{-1}): 3418, 3006, 2164, 2032, 1978, 1642, 1399, 1170, 1116, 871, 744, 699.

***N*-Benzyl-4-butylisoquinolinium iodide (4b)**



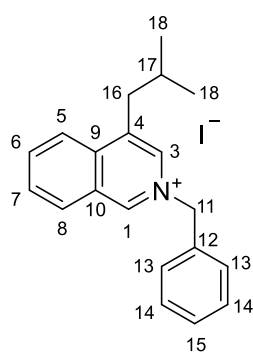
The title compound was prepared according to the General Procedure **D** using 4-butylisoquinoline (930 mg, 5.00 mmol) and benzyl iodide (1.20 mL, 10.0 mmol) in acetone (0.5 M). The resultant solid was washed with diethyl ether and dried under vacuum to give salt **4b** (1.95 g, 97%) as a yellow solid. Spectroscopic data was consistent with that reported in the literature.⁸

1H NMR (400 MHz, $DMSO-d_6$) δ 10.16 (s, 1H, C^1H), 8.78 (s, 1H, C^3H), 8.53 (d, $J = 7.8$ Hz, 1H, $C^{5/8H}$), 8.45 (dd, $J = 8.6, 1.0$ Hz, 1H, $C^{5/8H}$), 8.29 (ddd, $J = 8.4, 7.0, 1.3$ Hz, 1H, $C^{6/7H}$), 8.08 (ddd, $J = 8.1, 7.0, 1.0$ Hz, 1H, $C^{6/7H}$), 7.63 – 7.55 (m, 2H, 2 x C^{14H}), 7.50 – 7.37 (m, 3H, 2 x $C^{13H} + C^{15H}$), 5.94 (s, 2H, $C^{11}H_2$), 3.22 – 3.14 (m, 2H, $C^{16}H_2$), 1.73 – 1.61 (m, 2H, $C^{17}H_2$), 1.38 (m, 2H, $C^{18}H_2$), 0.91 (t, $J = 7.3$ Hz, 3H, $C^{19}H_3$).

^{13}C NMR (101 MHz, $DMSO-d_6$) δ 148.4 (C^1H), 139.2 (C^Q), 137.1 ($C^{6/7H}$), 136.1 (C^Q), 134.4 (C^Q), 133.3 (C^3H), 131.4 ($C^{5/8H}$), 131.1 ($C^{6/7H}$), 129.3 (C^{15H}), 129.2 (2 x C^{13H}), 128.7 (2 x C^{14H}), 127.4 (C^Q), 124.2 ($C^{5/8H}$), 63.3 ($C^{11}H_2$), 31.7 ($C^{17}H_2$), 28.8 ($C^{16}H_2$), 21.9 ($C^{18}H_2$), 13.7 ($C^{19}H_3$).

⁸ Reeves, B. M.; Hepburn, H. B.; Grozavu, A.; Lindsay-Scott, P. J.; Donohoe, T. J.; *Angew. Chem.* **2019**, *58*, 15697–15701.

***N*-Benzyl-4-isobutylisoquinolinium iodide (4c)**

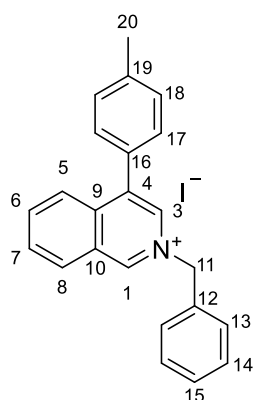


The title compound was prepared according to a modified General Procedure **D**. A mixture of 4-isobutylisoquinoline (758 mg, 4.09 mmol, 1.0 eq.) and benzyl iodide (0.50 mL, 4.91 mmol, 1.2 eq.) in acetone (5 mL) was stirred for 24 hours. The resultant precipitate was dried under vacuum to give isoquinolinium iodide **4c** (1.21 g, 99%) as a yellow solid. Spectroscopic data was consistent with that reported in the literature.⁴

¹H NMR (400 MHz, CDCl₃) δ 10.93 (d, *J* = 1.4 Hz, 1H, C¹H), 8.67 (d, *J* = 8.3 Hz, 1H, C⁵H), 8.60 (d, *J* = 1.5 Hz, 1H, C³H), 8.15 – 8.05 (m, 2H, C⁸H + C⁷H), 7.88 (ddd, *J* = 8.1, 6.4, 1.6 Hz, 1H, C⁶H), 7.75 – 7.67 (m, 2H C¹³H), 7.31 (dd, *J* = 5.0, 1.9 Hz, 3H, C¹⁴H + C¹⁵H), 6.28 (s, 2H, C¹¹H₂), 2.98 (d, *J* = 7.2 Hz, 2H, C¹⁶H₂), 2.01 (hept, *J* = 6.7 Hz, 1H, C¹⁷H), 0.90 (d, *J* = 6.6 Hz, 6H, C¹⁸H₃).

¹³C NMR (101 MHz, CDCl₃) δ 147.8 (C¹H), 138.7 (C¹²), 137.3 (C⁹), 136.9 (C⁷H), 133.3 (C^{Ar}), 133.2 (C³H), 132.0 (C⁵H), 130.9 (C⁶H), 129.9 (C¹⁵H), 129.6 (2 x C¹³H), 129.5 (2 x C¹⁴H), 127.9 (C¹⁰), 123.8 (C⁸H), 63.4 (C¹¹H₂), 39.0 (C¹⁶H₂), 29.5 (C¹⁷H), 22.6 (2 x C¹⁸H₃).

***N*-Benzyl-4-toluyloisoquinolinium iodide (4d)**

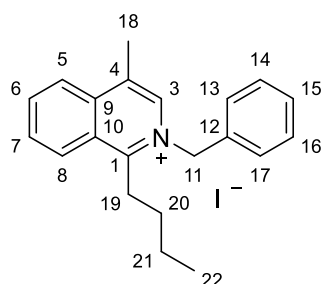


The title compound was prepared according to General Procedure **D** using 4-(*p*-tolyl)isoquinoline (1.05 g, 4.79 mmol) and benzyl iodide (0.72 mL, 5.75 mmol) to give salt **4d** (1.60 g, 77 %) as a brown solid. Spectroscopic data was consistent with that reported in the literature.⁴

¹H NMR (400 MHz, CDCl₃) δ 11.15 (s, 1H, C¹H), 8.79 (d, *J* = 8.3 Hz, 1H, C⁵H), 8.33 (d, *J* = 1.5 Hz, 1H, C³H), 8.11 – 7.99 (m, 2H, C⁸H + C⁷H), 7.94 (ddd, *J* = 8.2, 6.5, 1.6 Hz, 1H, C⁶H), 7.71 – 7.65 (m, 2H, C¹³H), 7.47 – 7.40 (m, 2H, C¹⁷H), 7.39 – 7.32 (m, 5H, C¹⁴H + C¹⁵H + C¹⁸H), 6.35 (s, 2H, C¹¹H₂), 2.45 (s, 3H, C²⁰H₃).

¹³C NMR (101 MHz, CDCl₃) δ 148.6 (C¹H), 140.4 (C⁹), 140.0 (C¹⁶), 137.3 (C⁷H), 136.7 (C¹²), 132.8 (C⁴), 132.4 (C³H), 131.9 (C⁵H), 131.3 (C⁶H), 130.16 (C^{Ar}), 130.06 (C^{Ar}), 129.9 (C^{Ar}), 129.8 (C^{Ar}), 129.7 (4x C^{Ar}), 128.2 (C^{Ar}), 125.7 (C⁸H), 64.2 (C¹¹H₂), 21.5 (C²⁰H₃).

***N*-Benzyl-1-butyl-4-methylisoquinolinium iodide (4e)**



The title compound was prepared according to General Procedure **D** using 1-butyl-4-methylisoquinoline (199 mg, 1.0 mmol, 1.0 eq.) and benzyl iodide (0.19 mL, 1.5 mmol 1.5 eq.) in acetone (2.5 mL) to give salt **4e** (402 mg, 96%) as a cream-colored solid.

m.p. (acetone): 234 °C

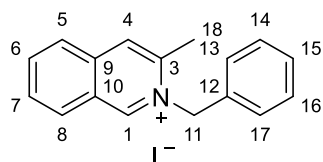
HRMS (ESI): Exact mass calculated for $C_{21}H_{24}N [M]^+$: 290.1903, found: 290.1905;

1H NMR (400 MHz, $DMSO-d_6$) δ 8.81 (d, $J = 1.1$ Hz, 1H, C^3H), 8.72 (dt, $J = 8.7, 0.9$ Hz, 1H, $C^{5/8}H$), 8.40 (dd, $J = 8.4, 1.2$ Hz, 1H, $C^{5/8}H$), 8.30 (ddd, $J = 8.3, 7.0, 1.1$ Hz, 1H, $C^{6/7}H$), 8.09 (ddd, $J = 8.3, 6.9, 1.2$ Hz, 1H, $C^{6/7}H$), 7.48 – 7.38 (m, 3H, 3 x $C^{Ar}H$), 7.33 (dd, $J = 7.9, 1.8$ Hz, 2H, 2 x $C^{Ar}H$), 6.07 (s, 2H, $C^{11}H_2$), 3.66 – 3.53 (m, 2H, $C^{19}H$), 2.77 (s, 3H, $C^{18}H_3$), 1.56 – 1.32 (m, 4H, $C^{20}H_2 + C^{21}H_2$), 0.83 (t, $J = 7.1$ Hz, 3H, $C^{22}H_3$);

^{13}C NMR (101 MHz, $DMSO-d_6$) δ 161.1 (C^1), 136.8 (C^{Ar}), 136.2 ($C^{6/7}H$), 135.4 (C^9H), 134.5 (C^{Ar}), 132.7 (C^{Ar}), 131.1 ($C^{6/7}H$), 129.1 (2 x $C^{Ar}H$), 129.1 ($C^{5/8}H$), 128.6 (C^{Ar}), 127.0 (2 x $C^{Ar}H$), 126.7 (C^A), 125.0 ($C^{5/8}H$), 60.8 ($C^{11}H_2$), 31.6 ($C^{21}H_2$), 29.1 ($C^{19}H_2$), 22.2 ($C^{20}H_2$), 15.7 ($C^{18}H_3$), 13.5 ($C^{22}H_3$);

IR (neat) (cm^{-1}): 2961, 2938, 2161, 2033, 2034, 1978, 1493, 1413, 782, 741, 725, 699, 686.

2-Benzyl-3-methylisoquinolin-2-ium iodide (4f)



The title compound was prepared according to General Procedure **D** using 3-methylisoquinoline (430 mg, 3.00 mmol, 1.0 eq.) and benzyl iodide (0.56 mL, 4.5 mmol 1.5 eq.) in acetone (6 mL) to give salt **4f** (907 mg, 84%) as a yellow solid.

m.p. (acetone): 201 °C

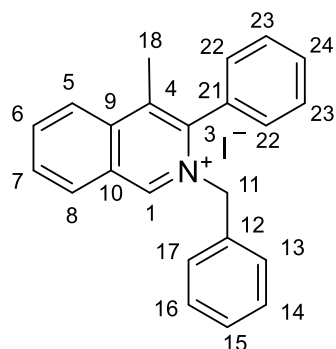
HRMS (ESI): Exact mass calculated for $C_{17}H_{16}N [M]^+$: 234.1277, found: 234.1277;

1H NMR (400 MHz, $DMSO-d_6$) δ 10.29 (s, 1H, C^1H), 8.54 (s, 1H, C^4H), 8.50 (d, $J = 8.4$ Hz, 1H, $C^{5/8}H$), 8.28 – 8.22 (m, 2H, $C^{6/7}H + C^{5/8}H$), 8.03 (dt, $J = 8.2, 4.0$ Hz, 1H, $C^{6/7}H$), 7.48 – 7.38 (m, 3H, 3 x $C^{Ar}H$), 7.36 – 7.30 (m, 2H, 2 x $C^{Ar}H$), 6.09 (s, 2H, $C^{11}H_2$), 2.76 (s, 3H, $C^{18}H_3$);

^{13}C NMR (101 MHz, $DMSO-d_6$) δ 151.5 (C^1H), 144.3 (C^{Ar}), 138.0 (C^{Ar}), 137.2 (C^8), 133.3 (C^{Ar}), 130.5 ($C^{6/7}$), 130.2 ($C^{5/8}H$), 129.2 (2 x $C^{Ar}H$), 128.7 ($C^{Ar}H$), 127.5 (2 x $C^{Ar}H$), 126.6 (C^4H), 126.3 ($C^{6/7}H$), 126.1 (C^{Ar}), 60.6 ($C^{11}H_2$), 19.2 ($C^{18}H_3$);

IR (neat) (cm^{-1}): 2982, 2162, 1645, 1439, 1400, 1344, 913, 747, 740, 706.

N-Benzyl-4-methyl-3-phenylisoquinolinium iodide (4g)



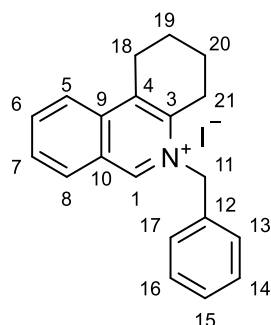
The title compound was prepared according to General Procedure **D** using 3-phenyl-4-butylisoquinoline (318 mg, 1.45 mmol) and benzyl iodide (0.26 mL, 2.00 mmol). Purification by flash column chromatography (0-6% MeOH in CH_2Cl_2) gave salt **4g** (511 mg, 81%) as a yellow solid. Spectroscopic data was consistent with that reported in the literature.⁴

1H NMR (400 MHz, $CDCl_3$) δ 10.99 (s, 1H, C^1H), 8.83 – 8.75 (d, $J = 8.2$, 1H, C^5H), 8.27 – 8.10 (m, 2H, $C^8H + C^7H$), 7.95 (ddd, $J = 8.2, 6.5, 1.6$ Hz, 1H, C^6H), 7.63 – 7.54 (m, 1H,

$C^{15}H$), 7.54 – 7.45 (m, 2H, $C^{23}H$), 7.32 – 7.15 (m, 5H, $C^{24}H + C^{22}H + C^{14}H + C^{16}H$), 7.00 – 6.88 (m, 2H, $C^{13}H + C^{17}H$), 5.93 (s, 2H, $C^{11}H_2$), 2.44 (s, 3H, $C^{18}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 150.1 (C^1H), 143.8 (C^9), 138.0 (C^4), 137.6 (C^7H), 134.3 (C^{12}), 133.2 (C^{21}), 132.4 ($C^5H + C^{Ar}$), 131.0 ($C^{Ar}H$), 130.9 (C^7H), 130.2 (2 x $C^{Ar}H$), 129.6 (2 x $C^{23}H$), 129.3 (2 x $C^{Ar}H$), 129.2 (C^{Ar}), 128.3 ($C^{13} + C^{17}$), 126.7 (C^{10}), 124.3 (C^8H), 62.9 ($C^{11}H_2$), 16.5 ($C^{18}H_3$).

***N*-Benzyl-1,2,3,4-tetrahydrophenanthridinium iodide (4h)**



The title compound was prepared according to General Procedure **D** using 1,2,3,4-tetrahydrophenanthridine⁹ (110 mg, 0.6 mmol, 1.0 eq.), benzyl iodide (0.13 mL, 1.0 mmol, 1.7 eq.) and acetone (2 mL). After precipitation with diethyl ether the product **4h** was obtained as light-yellow powder (179 mg, 74% yield).

m.p. (acetone): 231 °C

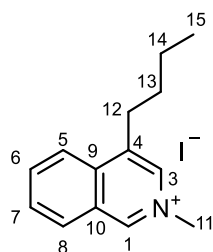
HRMS (ESI): Exact mass calculated for $C_{20}H_{20}N$ $[M]^+$: 274.1590, found: 274.1591.

1H NMR (400 MHz, $DMSO-d_6$) δ 10.13 (s, 1H, C^1H), 8.48 (d, J = 8.2 Hz, 1H, C^5H), 8.36 (d, J = 8.6 Hz, 1H, C^8H), 8.28 (ddd, J = 8.4, 6.8, 1.3 Hz, 1H, C^7H), 8.04 (t, J = 7.3 Hz, 1H, C^6H), 7.47 – 7.37 (m, 3H, $C^{13}H + C^{15}H + C^{17}H$), 7.34 – 7.21 (m, 2H, $C^{14}H + C^{16}H$), 6.05 (s, 2H, $C^{11}H_2$), 3.30 – 3.23 (m, 2H, $C^{21}H_2$), 3.09 – 2.93 (m, 2H, $C^{18}H_2$), 1.99 – 1.78 (m, 4H, $C^{19}H_2 + C^{20}H_2$).

^{13}C NMR (101 MHz, $DMSO-d_6$) δ 150.1 (C^3), 142.6 (C^1H), 137.2 (C^7H), 136.9 (C^{12}), 133.8 (C^9), 133.6 (C^4), 131.1 (C^5H), 130.3 (C^6H), 129.3 ($C^{13} + C^{17}$), 128.7 ($C^{15}H$), 127.2 ($C^{14} + C^{16}$), 125.2 (C^{10}), 123.2 (C^8H), 60.3 ($C^{11}H_2$), 26.2 ($C^{18}H_2$), 24.9 ($C^{21}H_2$), 21.1 ($C^{19}H_2$), 20.3 ($C^{20}H_2$).

IR (neat) (cm^{-1}): 3026, 2943, 2869, 1634, 1601, 1508, 1455, 1424, 1367, 1030.

***N*-Methyl-4-butylisoquinolin-ium iodide (4i)**



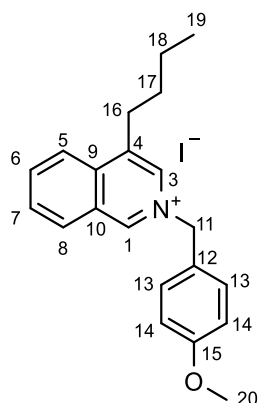
The title compound was prepared according to General Procedure **D** using 4-butylisoquinoline (556 mg, 3.00 mmol) to give salt **4i** (1.09 g, 99 %) as a yellow solid. Spectroscopic data was consistent with that reported in the literature.⁴

1H NMR (400 MHz, $CDCl_3$) δ 10.65 (s, 1H, C^1H), 8.65 (d, J = 8.3 Hz, 1H, C^5H), 8.54 – 8.48 (m, 1H, C^3H), 8.19 (dd, J = 8.5, 1.1 Hz, 1H, C^8H), 8.12 (ddd, J = 8.5, 6.9, 1.3 Hz, 1H, C^7H), 7.93 (ddd, J = 8.1, 6.8, 1.2 Hz, 1H, C^6H), 4.76 (s, 3H, $C^{11}H_3$), 3.29 – 3.01 (m, 2H, $C^{12}H_2$), 1.83 – 1.72 (m, 2H, $C^{13}H_2$), 1.48 (h, J = 7.3 Hz, 2H, $C^{14}H_2$), 0.97 (t, J = 7.3 Hz, 3H, $C^{15}H_3$).

⁹Prepared according to: Pandey, G., Balakrishnan, M., *J. Org. Chem.* **2008**, 73, 20, 8128 – 8131.

¹³C NMR (101 MHz, CDCl₃) δ 148.6 (C¹H), 139.7 (C⁹), 136.87 (C⁴), 136.84 (C⁷H), 133.7 (C³H), 131.8 (C⁵H), 131.1 (C⁶H), 127.8 (C¹⁰), 123.6 (C⁸H), 48.8 (C¹¹H₃), 32.2 (C¹³H₂), 29.9 (C¹²H₂), 22.8 (C¹⁴H₄), 13.9 (C¹⁵H₂).

***N*-(4-Methoxybenzyl)-4-butyloisoquinolin-2-ium iodide (4j)**



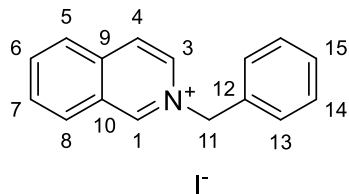
The title compound was prepared according to General Procedure **D** using 4-butyloisoquinoline (371 mg, 2.00 mmol) and 4-methoxybenzyl iodide (0.34 mL, 2.40 mmol) to give salt **4j** (986 mg, 99 %) as a white solid. Spectroscopic data was consistent with that reported in the literature.⁴

¹H NMR (400 MHz, CDCl₃) δ 10.86 (s, 1H, C¹H), 8.67 (d, *J* = 8.2 Hz, 1H, C⁵H), 8.52 – 8.39 (m, 1H, C³H), 8.18 – 8.02 (m, 2H, C⁸H + C⁷H), 7.90 (ddd, *J* = 8.1, 6.5, 1.4 Hz, 1H, C⁶H), 7.66 (d, *J* = 8.7 Hz, 2H, C¹³H₂), 6.86 (d, *J* = 8.7 Hz, 2H, C¹⁴H₂), 6.17 (s, 2H, C¹¹H₂), 3.76 (s, 3H, C²⁰H₃), 3.25 – 2.96 (m, 2H, C¹⁶H₂), 1.79 – 1.68

(m, 2H, C¹⁸H₂), 1.43 (h, *J* = 7.4 Hz, 2H, C¹⁷H₂), 0.95 (t, *J* = 7.3 Hz, 3H, C¹⁹H₃).

¹³C NMR (101 MHz, CDCl₃) δ 160.8 (C¹⁵), 147.8 (C¹H), 139.8 (C⁹), 137.0 (C⁴), 136.9 (C⁷H), 132.2 (C⁵H + C³H), 131.4 (2 x C¹³H), 131.0 (C⁶H), 127.9 (C¹⁰), 124.9 (C¹²), 123.6 (C⁸H), 115.0 (2 x C¹⁴H), 63.4 (C¹¹H₂), 55.5 (C²⁰H₃), 32.1 (C¹⁶H₂), 30.1 (C¹⁷H₂), 22.8 (C¹⁸H₂), 13.9 (C¹⁹H₃).

***N*-Benzylisoquinolinium iodide (4k)**

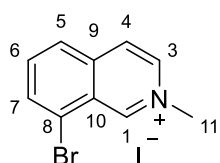


The title compound was prepared according to General Procedure **D** using isoquinoline (1.00 g, 7.74 mmol) and benzyl iodide (1.9 mL, 15.48 mmol) to give salt **4k** (2.6 g, 97%) as a light yellow solid. Spectroscopic data was consistent with that reported in the literature.⁴

¹H NMR (400 MHz, DMSO-*d*₆) δ 10.28 (s, 1H, C¹H), 8.83 (dd, *J* = 6.8, 1.5 Hz, 1H C³H), 8.61 (d, *J* = 6.8 Hz, 1H, C⁴H), 8.54 (d, *J* = 8.47 Hz, 1H, C⁵H), 8.36 (dd, *J* = 8.3, 1.1 Hz, 1H, C⁸H), 8.28 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H, C⁷H), 8.10 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H, C⁶H), 7.62 – 7.55 (m, 2H, 2 x C^{Ar}H), 7.50 – 7.38 (m, 3H, 3 x C^{Ar}H), 5.98 (s, 2H, C¹¹H₂).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.2 (C¹H), 137.2 (C⁷H), 137.1 (C^{Ar}), 134.8 (C³H), 134.3 (C^{Ar}), 131.4 (C⁶H), 130.6 (C⁵H), 129.3 (C¹⁵H), 129.2 (2 x C^{Ar}H), 128.8 (2 x C^{Ar}H), 127.4 (C⁸H), 127.3 (C^{Ar}), 126.3 (C⁴H), 63.4 (C¹¹H₂).

8-Bromo-*N*-methylisoquinolinium iodide (4l)



A mixture of the 8-Bromisoquinoline (624 mg, 3.0 mmol, 1.0 eq.) and methyl iodide (0.37 mL, 6.0 mmol, 2.0 eq.) in CH₂Cl₂ (7.5 mL) was stirred at 40 °C for 12 h.

The reaction mixture was filtered under reduced pressure. The resulting solid was

washed with ether (50 mL) then dried under vacuum to give isoquinolinium iodide **4l** (439 mg, 42%) as a yellow solid.

m.p. (CH₂Cl₂): 296 °C

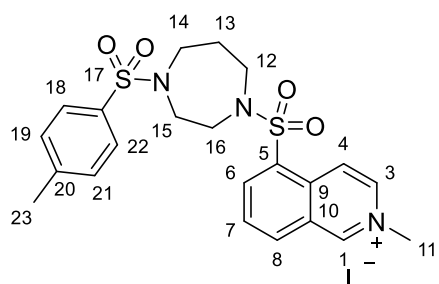
HRMS (ESI): Exact mass calculated for C₁₀H₉BrN⁺ [M]⁺: 221.9913, found: 290.1915.

¹H NMR (400 MHz, DMSO-*d*₆): 9.96 (s, 1H, C¹H), 8.81 (dd, *J* = 6.7, 1.3 Hz, 1H, C³H), 8.64 (d, *J* = 6.7 Hz, 1H, C⁴H), 8.40 (dd, *J* = 7.6, 0.9 Hz, 1H, C⁷H), 8.36 (d, *J* = 8.4, 1.0 Hz, 1H, C⁵H), 8.12 (dd, *J* = 8.3, 7.5 Hz, 1H, C⁶H), 4.57 (s, 3H, C¹¹H₃);

¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.0 (C¹H), 138.8 (C^{Ar}), 137.2 (C³H + C⁶H), 135.3 (C⁷H), 127.3 (C⁵H), 126.4 (C^{Ar}), 126.0 (C⁴H), 123.2 (C^{Ar}), 48.4 (C¹¹H₃);

IR (neat) (cm⁻¹): 3043, 3002, 1646, 1558, 1359, 1337, 1185, 851, 790, 745, 671.

***N*-Methyl-5-((4-tosyl-1,4-diazepan-1-yl)sulfonyl)isoquinolinium iodide (4m)**



A mixture of Fasudil (560 mg, 1.9 mmol, 1.0 eq.), *N,N*-diisopropylethylamine (0.1 mL, 3.8 mmol, 2.0 eq.) and *p*-toluenesulfonyl chloride (544 mg, 2.85 mmol, 1.5 eq.) in CH₂Cl₂ (20 mL) was stirred at room temperature overnight. After the addition of H₂O (10 mL) the aqueous phase was extracted with CH₂Cl₂ (3 x 10 mL). Removal of the solvent and flash column

chromatography (10% EtOAc in pentane → 100% EtOAc) delivered the tosylated isoquinoline **4m'** (450 mg, 53%) as a white solid. Subsequently **4m'** (446 mg, 1.0 mmol, 1.0 eq.) was directly used in General Procedure **D** with methyl iodide (0.12 mL, 2.0 mmol, 2.0 eq.) in CH₂Cl₂ (2.0 mL) to give salt **4m** (394 mg, 67%) as a yellow solid.

m.p. (CH₂Cl₂): 210 °C

HRMS (ESI): Exact mass calculated for C₂₂H₂₆N₃O₄S₂ [M]⁺: 460.1359, found: 460.1356.

¹H NMR (400 MHz, DMSO-*d*₆) δ 10.20 (s, 1H, C¹H), 8.92 (d, *J* = 7.1 Hz, 1H, C³H), 8.84 (dd, *J* = 7.2, 1.5 Hz, 1H, C⁴H), 8.76 (d, *J* = 8.4 Hz, 1H, C^{6/8}H), 8.71 (dd, *J* = 7.5, 1.2 Hz, 1H, C^{6/8}H), 8.19 (t, *J* = 8.4, 1H, C⁷H), 7.66 (d, *J* = 8.3 Hz, 2H, C¹⁸H + C²²H), 7.42 (d, *J* = 7.7 Hz, 2H, C¹⁹H + C²¹H), 4.52 (s, 3H, C¹¹H₃), 3.61 – 3.55 (m, 2H, C^{12/14/15/16}H₂), 3.50 (t, *J* = 5.9 Hz, 2H, C^{12/14/15/16}H₂), 3.25 (t, *J* = 5.9 Hz, 2H, C^{12/14/15/16}H₂), 2.40 (s, 3H, C²³H₃), 1.88 – 1.77 (m, 2H (C¹³H₂)).; **N.B.** one C^{12/14/15/16}H₂ under the DMSO signal.

¹³C NMR (101 MHz, DMSO-*d*₆) δ 151.7 (C¹H), 143.4 (C^{Ar}), 138.0 (C⁴H), 137.3 (C^{6/8}H), 135.7 (C^{6/8}H), 135.5 (C^{Ar}), 134.8 (C^{Ar}), 132.4 (C^{Ar}), 130.5 (C⁷H), 130.0 (C¹⁹H + C²¹H), 128.5 (C^{Ar}), 126.7 (C¹⁸H + C²²H), 122.2 (C¹⁰H), 49.2 (C^{12/14/15/16}H₂), 49.1 (C^{12/14/15/16}H₂), 48.1 (C¹¹H₃), 46.8 (C^{12/14/15/16}H₂), 46.8 (C^{12/14/15/16}H₂), 29.3 (C¹³H₂), 21.0 (C²³H₃);

IR (neat) (cm⁻¹): 2930, 2154, 2033, 1315, 1148, 1131, 978, 905, 813, 807, 701.

Synthesis of tetrahydroisoquinolines

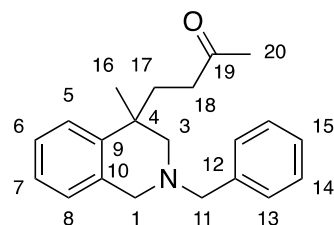
General procedure E: Synthesis of tetrahydroisoquinolines

Isoquinolinium salt (0.125 mmol, 1.00 equiv.) and electrophile (1.00 to 5.00 equiv.) were dissolved in MeCN (0.10 mL, 1.25 M). Upon addition of HCO₂H:NEt₃ 5:2 complex (42 μ L, 4.00 equiv.) the reaction mixture was heated to 80 °C for 18 hours. The reaction was diluted with CH₂Cl₂ (10 mL) and quenched with an aqueous solution of K₂CO₃ (10 mL, 0.1 M). The solution was separated, and the aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL). The organic layers were combined, dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography to furnish the respective amines

General procedure F: Rhodium catalysed synthesis of tetrahydroisoquinolines

Isoquinolinium salt (1.00 equiv.), and [RhCp*Cl₂]₂ (0.01 mol%) was added to a microwave vial. MeCN (1.25 M), electrophile (1.0-2.0 equiv.) and HCO₂H:NEt₃ (5:2, 4.0 equiv.) were added and the solution heated at 75 °C for 18 hours. The reaction was diluted with CH₂Cl₂ (10 mL) and quenched with an aqueous solution of K₂CO₃ (10 mL, 0.1 M). The solution was separated, and the aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL). The organic layers were combined, dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography to furnish the respective amines.

N-Benzyl-4-(butan-2-one)-4-methyl-1,2,3,4-tetrahydroisoquinoline (5a)



The title compound was prepared by General Procedure E using *N*-benzyl-4-methylisoquinolinium iodide **4a** (45 mg, 0.125 mmol) and methyl vinyl ketone (21 μ L, 0.250 mmol). Purification by column chromatography (5% EtOAc in pentane) gave amine **5a** (33 mg, 86%) as a yellow oil.

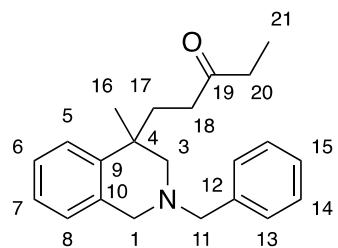
HRMS (ESI): Exact mass calculated for C₂₁H₂₆ON [M+H]⁺: 308.2009, found 308.2011.

¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.21 (m, 6H, 6 x C^{Ar}H), 7.21 – 7.14 (m, 1H, C^{Ar}H), 7.10 (td, *J* = 7.3, 1.5 Hz, 1H, C^{Ar}H), 6.99 (ddd, *J* = 7.6, 1.6, 0.7 Hz, 1H, C^{Ar}H), 3.74 – 3.49 (m, 2H, C^{1/11}H₂), 3.61 (q, *J* = 13.0 Hz, 2H, C^{1/11}H₂), 2.57 (dd, *J* = 11.5, 1.3 Hz, 1H, C³H₂), 2.45 (ddd, *J* = 16.1, 11.7, 4.9 Hz, 1H, C¹⁸H₂), 2.30 (dd, *J* = 11.4, 0.8 Hz, 1H, C³H₂), 2.12 – 1.99 (m, 2H, C¹⁷H₂ + C¹⁸H₂), 2.02 (s, 3H, C²⁰H₃), 1.80 (ddd, *J* = 15.1, 11.8, 4.9 Hz, 1H, C¹⁷H₂), 1.24 (s, 3H, C¹⁶H₃)

¹³C NMR (101 MHz, CDCl₃) δ 209.3 (C¹⁹O), 142.2 (C^Q), 138.7 (C^Q), 134.9 (C^Q), 129.2 (2 x C^{Ar}), 128.4 (2 x C^{Ar}), 127.3 (C^{Ar}), 126.7 (C^{Ar}), 126.5 (C^{Ar}), 126.2 (C^{Ar}), 125.8 (C^{Ar}), 63.0 (C^{1/11}H₂), 61.8 (C³H₂), 57.6 (C^{1/11}H₂), 39.7 (C¹⁸H₂), 37.8 (C⁴), 36.1 (C¹⁷H₂), 30.1 (C²⁰H₃), 27.8 (C¹⁶H₃)

IR (neat) (cm⁻¹): 2927, 2799, 1714, 1493, 1452, 1162, 1096, 914, 760, 700.

***N*-Benzyl-4-methyl-4-(pentan-3-one)-1,2,3,4-tetrahydroisoquinoline (5b)**



The title compound was prepared by General Procedure E using *N*-benzyl-4-methylisoquinolinium iodide **4a** (45 mg, 0.125 mmol) and ethyl vinyl ketone (25 μ L, 0.250 mmol). Purification by flash column chromatography (5% EtOAc in pentane) gave amine **5b** (37 mg, 92%) as a yellow oil.

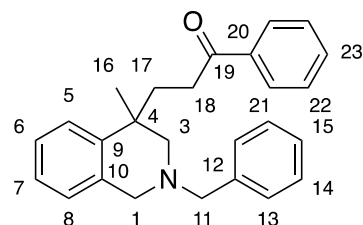
HRMS (ESI): Exact mass calculated for $C_{22}H_{28}ON$ $[M+H]^+$: 322.2165, found 322.2165.

1H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.40 (m, 2H, 2 x $C^{Ar}H$), 7.40 – 7.33 (m, 2H, 2 x $C^{Ar}H$), 7.33 – 7.24 (m, 2H, 2 x $C^{Ar}H$), 7.21 (td, J = 7.5, 1.5 Hz, 1H, $C^{Ar}H$), 7.14 (td, J = 7.4, 1.4 Hz, 1H, $C^{Ar}H$), 7.02 (dd, J = 7.6, 1.4 Hz, 1H, $C^{Ar}H$), 3.80 – 3.49 (m, 4H, C^1H_2 + $C^{11}H_2$), 2.61 (dd, J = 11.4, 1.2 Hz, 1H, C^3H_2), 2.45 (ddd, J = 16.3, 12.3, 4.9 Hz, 1H, $C^{18}H_2$), 2.38 – 2.27 (m, 3H, C^3H_2 + $C^{20}H_2$), 2.16 – 2.02 (m, 2H, $C^{18}H_2$ + $C^{17}H_2$), 1.84 (ddd, J = 15.9, 12.2, 4.9 Hz, 1H, $C^{17}H_2$), 1.28 (s, 3H, $C^{16}H_3$), 1.02 (t, J = 7.3 Hz, 3H, $C^{21}H_3$)

^{13}C NMR (126 MHz, $CDCl_3$) δ 211.9 ($C^{19}O$), 142.2 (C^Q), 138.7 (C^Q), 134.9 (C^Q), 129.2 (2 x C^{Ar}), 128.4 (2 x C^{Ar}), 127.2 (C^{Ar}), 126.6 (C^{Ar}), 126.5 (C^{Ar}), 126.2 (C^{Ar}), 125.7 (C^{Ar}), 63.0 ($C^{1/11}H_2$), 61.8 (C^3H_2), 57.6 ($C^{1/11}H_2$), 38.3 ($C^{18}H_2$), 37.8 (C^4), 36.1 ($C^{17}H_2$), 35.9 ($C^{20}H_2$), 27.9 ($C^{16}H_3$), 8.0 ($C^{21}H_3$)

IR (neat) (cm^{-1}): 2932, 2798, 1713, 1493, 1453, 1368, 1346, 1097, 759, 700.

***N*-Benzyl-4-methyl-4-(1-phenylpropan-1-one)-1,2,3,4-tetra-hydroisoquinoline (5c)**



The title compound was prepared by General Procedure E using *N*-benzyl-4-methylisoquinolinium iodide **4a** (45 mg, 0.125 mmol) and phenyl vinyl ketone (33 mg, 0.250 mmol). Purification by flash column chromatography (2.5% EtOAc in pentane) gave amine **5c** (40 mg, 87%) as a yellow oil.

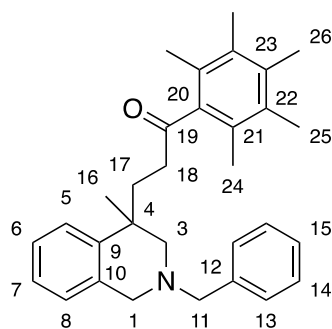
HRMS (ESI): Exact mass calculated for $C_{26}H_{28}ON$ $[M+H]^+$: 370.2165, found 370.2165.

1H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.69 (m, 2H, 2 x $C^{Ar}H$), 7.48 – 7.39 (m, 1H, $C^{Ar}H$), 7.37 – 7.24 (m, 4H, 4 x $C^{Ar}H$), 7.24 – 7.13 (m, 4H, 4 x $C^{Ar}H$), 7.13 – 7.07 (m, 1H, $C^{Ar}H$), 7.03 (td, J = 7.4, 1.4 Hz, 1H, $C^{Ar}H$), 6.94 – 6.88 (m, 1H, $C^{Ar}H$), 3.64 (d, J = 14.6 Hz, 1H, C^1H_2), 3.53 (s, 2H, $C^{11}H_2$), 3.43 (d, J = 14.6 Hz, 1H, C^1H_2), 2.98 (ddd, J = 16.4, 11.3, 4.9 Hz, 1H, $C^{18}H_2$), 2.63 (d, J = 11.3, 1H, C^3H_2), 2.52 (ddd, J = 16.8, 11.2, 4.8 Hz, 1H, $C^{18}H_2$), 2.29 (d, J = 11.5 Hz, 1H, C^3H_2), 2.16 (ddd, J = 14.1, 11.3, 4.8 Hz, 1H, $C^{17}H_2$), 2.01 – 1.85 (m, 1H, $C^{17}H_2$), 1.23 (s, 3H, $C^{16}H_3$)

^{13}C NMR (101 MHz, $CDCl_3$) δ 200.8 ($C^{19}O$), 142.2 (C^Q), 138.6 (C^Q), 137.2 (C^Q), 135.0 (C^Q), 132.9 (C^{Ar}), 129.2 (2 x C^{Ar}), 128.6 (2 x C^{Ar}), 128.4 (2 x C^{Ar}), 128.1 (2 x C^{Ar}), 127.3 (C^{Ar}), 126.7 (C^{Ar}), 126.6 (C^{Ar}), 126.2 (C^{Ar}), 125.8 (C^{Ar}), 63.1 ($C^{11}H_2$), 62.3 (C^3H_2), 57.5 (C^1H_2), 38.0 (C^4), 37.0 ($C^{17}H_2$), 34.8 ($C^{18}H_2$), 28.1 ($C^{16}H_3$)

IR (neat) (cm^{-1}): 2925, 2854, 1681, 1597, 1449, 1273, 1240, 1113, 760, 700.

***N*-Benzyl-4-methyl-4-(1-pentamethylphenylpropan-1-one)-1,2,3,4-tetra-hydroisoquinoline (5d)**



The title compound was prepared by General Procedure **E** using *N*-benzyl-4-methylisoquinolinium iodide **4a** (45 mg, 0.125 mmol) and pentamethylphenyl vinyl ketone (51 mg, 0.250 mmol). Purification by flash column chromatography (CH₂Cl₂) gave amine **5d** (51 mg, 92%) as a yellow oil.

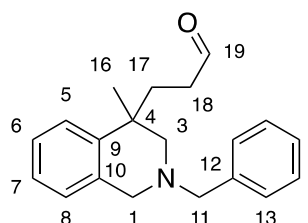
HRMS (ESI): Exact mass calculated for C₃₁H₃₈ON [M+H]⁺: 440.2948, found 440.2952.

¹H NMR (400 MHz, CDCl₃) δ 7.30 – 7.14 (m, 6H, 6 x C^{Ar}H), 7.08 (td, *J* = 7.6, 1.5 Hz, 1H, C^{Ar}H), 6.99 (td, *J* = 7.4, 1.3 Hz, 1H, C^{Ar}H), 6.86 (dd, *J* = 7.6, 1.4 Hz, 1H, C^{Ar}H), 3.58 – 3.39 (m, 4H, C¹H₂ + C¹¹H₂), 2.76 – 2.63 (m, 1H, C¹⁸H₂), 2.46 (d, *J* = 11.3 Hz, 1H, C³H₂), 2.32 (d, *J* = 11.3 Hz, 1H, C³H₂), 2.35 – 2.06 (m, 2H, C¹⁷H₂ + C¹⁸H₂), 2.12 (s, 3H, C²⁶H₃), 2.06 (s, 6H, 2 x C²⁴H₃), 1.90 (s, 6H, 2 x C²⁵H₃), 1.99 – 1.77 (m, 1H, C¹⁷H₂), 1.24 (s, 3H, C¹⁶H₃)

¹³C NMR (101 MHz, CDCl₃) δ 212.4 (C¹⁹), 141.8 (C^Q), 141.2 (C^Q), 138.6 (C^Q), 135.4 (C^Q), 135.0 (C^Q), 133.1 (2 x C^Q), 129.0 (2 x C^{Ar}), 128.4 (2 x C^{Ar}), 127.4 (2 x C^Q), 127.2 (C^{Ar}), 126.7 (C^{Ar}), 126.6 (C^{Ar}), 126.1 (C^{Ar}), 125.8 (C^{Ar}), 63.3 (C¹¹H₂), 62.6 (C³H₂), 57.5 (C¹H₂), 41.9 (C¹⁸H₂), 37.9 (C⁴), 35.5 (C¹⁷H₂), 28.9 (C¹⁶H₃), 17.3 (2 x C^{24/25}H₃), 16.8 (C²⁶H₃), 16.0 (2 x C^{24/25}H₃)

IR (neat) (cm⁻¹): 2926, 2800, 1698, 1493, 1452, 1311, 910, 759, 730, 700.

***N*-Benzyl-4-methyl-4-propanal-1,2,3,4-tetra-hydroisoquinoline (5e)**



The title compound was prepared by General Procedure **F** using *N*-benzyl-4-methylisoquinolinium iodide **4a** (45 mg, 0.125 mmol), acrolein (17 μL, 0.250 mmol), HCO₂H:NEt₃ (5:2) (42 μL, 0.500 mmol), and 0.1 mL of the catalyst stock solution (corresponding to 0.01 mol% of [RhCp*Cl₂]₂) was added to a sealed vial and the solution was heated at

47 °C for 20 hours. The reaction mixture was diluted with dichloromethane (10 mL) and quenched with potassium carbonate (10 mL, 0.1 M). The phases were separated, and the aqueous layer was extracted with dichloromethane (3 x 10 mL). The combined organic layers were concentrated *in vacuo*. The crude material was purified by flash column chromatography (15-20% EtOAc in pentane) to give amine **5e** (29 mg, 79%) as a yellow oil.

The title compound could not be prepared according to General procedure **E** and only starting material was recovered from the reaction.

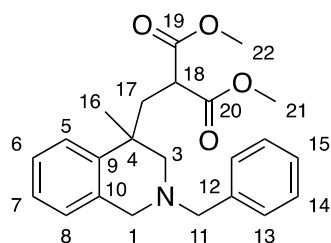
HRMS (ESI): Exact mass calculated for C₂₀H₂₄ON [M+H]⁺: 294.1852, found 294.1853.

¹H NMR (400 MHz, CDCl₃) δ 9.53 (t, *J* = 1.6 Hz, 1H, C¹⁹H), 7.33 – 7.13 (m, 6H, 6 x C^{Ar}H), 7.10 (dddd, *J* = 8.5, 7.8, 1.5, 0.7 Hz, 1H, C^{Ar}H), 7.03 (td, *J* = 7.3, 1.5 Hz, 1H, C^{Ar}H), 6.91 (ddt, *J* = 7.5, 1.5, 0.7 Hz, 1H, C^{Ar}H), 3.65 (d, *J* = 14.7 Hz, 1H, C¹H_a), 3.52 (s, 2H, C¹¹H₂), 3.42 (d, *J* = 14.7 Hz, 1H, C¹H_b), 2.53 (d, *J* = 11.5, 1H, C³H_a), 2.45 – 2.31 (m, 1H, C¹⁸H₂), 2.23 (d, *J* = 11.5 Hz, 1H, C³H_b), 2.09 – 1.94 (m, 2H, C¹⁷H_a + C¹⁸H₂), 1.88 – 1.76 (m, 1H, C¹⁷H_b), 1.17 (s, 3H, C¹⁶H₃)

¹³C NMR (101 MHz, CDCl₃) δ 202.2 (C¹⁹O), 141.8 (C^Q), 138.4 (C^Q), 134.9 (C^Q), 129.3 (2 x C^{Ar}), 128.4 (2 x C^{Ar}), 127.3 (C^{Ar}), 126.7 (C^{Ar}), 126.6 (C^{Ar}), 126.1 (C^{Ar}), 126.0 (C^{Ar}), 63.0 (C¹¹H₂), 62.0 (C³H₂), 57.3 (C¹H₂), 40.1 (C¹⁸H₂), 37.7 (C⁴), 34.6 (C¹⁷H₂), 27.5 (C¹⁶H₃)

IR (neat) (cm⁻¹): 2926, 1721, 1683, 1493, 1453, 1369, 910, 760, 731, 700.

***N*-Benzyl-4-methyl-4-(dimethyl methylenmalonate)-1,2,3,4-tetra-hydroisoquinoline (5f)**



The title compound was prepared by General Procedure E using *N*-benzyl-4-methylisoquinolinium iodide **4a** (45 mg, 0.125 mmol) and dimethyl 2-methylenemalonate (36 mg, 0.25 mmol). Purification by column chromatography (4-6% EtOAc in pentane) gave *amine 5f* (15 mg, 34%) as a yellow oil. General procedure E afforded the title compound

in a significantly reduced yield of 11%.

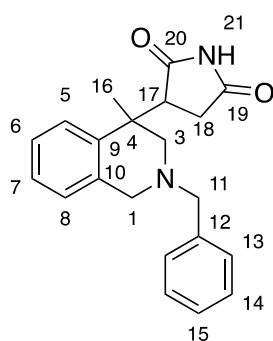
HRMS (ESI): Exact mass calculated for C₂₃H₂₈O₄N [M+H]⁺: 382.2013, found 382.2011.

¹H NMR (500 MHz, CDCl₃) δ 7.42 – 7.26 (m, 6H, 6 x C^{Ar}H), 7.23 – 7.16 (m, 1H, C^{Ar}H), 7.11 (td, *J* = 7.4, 1.3 Hz, 1H, C^{Ar}H), 7.00 – 6.95 (m, 1H, C^{Ar}H), 3.87 (t, *J* = 6.1 Hz, 1H, C¹⁸H), 3.82 – 3.72 (m, 1H, C^{1/11}H₂), 3.69 (s, 3H, C^{21/22}H₃), 3.72 – 3.64 (m, 1H, C^{1/11}H₂), 3.62 – 3.53 (m, 1H, C^{1/11}H₂), 3.48 (s, 3H, C^{21/22}H₃), 3.40 (d, *J* = 14.7 Hz, 1H, C^{1/11}H₂), 2.79 – 2.72 (m, 1H, C³H₂), 2.49 (dd, *J* = 14.5, 6.2 Hz, 1H, C¹⁷H₂), 2.42 – 2.33 (m, 2H, C³H₂ + C¹⁷H₂), 1.27 (s, 3H, C¹⁶H₃)

¹³C NMR (126 MHz, CDCl₃) δ 170.68 (C¹⁹O/C²⁰O), 170.65 (C¹⁹O/C²⁰O), 140.4 (C^Q), 138.2 (C^Q), 135.2 (C^Q), 129.1 (2 x C^{Ar}), 128.4 (2 x C^{Ar}), 127.2 (C^Q), 126.8 (C^{Ar}), 126.6 (C^{Ar}), 126.5 (C^{Ar}), 126.1 (C^{Ar}), 62.97 (C³H₂/C^{1/11}H₂), 62.95 (C³H₂/C^{1/11}H₂), 56.9 (C^{1/11}H₂), 52.7 (C^{21/22}H₃), 52.5 (C^{21/22}H₃), 48.7 (C¹⁸H), 41.7 (C¹⁷H₂), 37.9 (C⁴), 28.1 (C¹⁶H₃)

IR (neat) (cm⁻¹): 2952, 2925, 1735, 1494, 1435, 1266, 1150, 1028, 762, 701.

N-Benzyl-4-methyl-4-(2,5-dioxopyrrolidin-3-yl)-1,2,3,4-tetrahydroisoquinoline (5g)



The title compound was prepared by General Procedure E using *N*-benzyl-4-methylisoquinolinium iodide **4a** (45 mg, 0.125 mmol) and maleimide (24 mg, 0.25 mmol). Purification by column chromatography (10-33% EtOAc in pentane) gave *amine* **5g** (25 mg, 59%) as an inseparable 2:1 diastereomeric mixture as a yellow oil.

HRMS (ESI): Exact mass calculated for C₂₁H₂₃O₂N₂ [M+H]⁺: 335.1754 found 335.1753.

Major diastereomer: ¹H NMR (600 MHz, CDCl₃) δ 7.91 (d, *J* = 7.4 Hz, 1H, N²¹H), 7.42 – 6.98 (m, 9H, 9 x C^{Ar}H), 3.79 (d, *J* = 14.7 Hz, 1H, C^{1/11}H₂), 3.61 (d, *J* = 12.6 Hz, 1H, C^{1/11}H₂), 3.48 (d, *J* = 7.2 Hz, 1H, C^{1/11}H₂), 3.46 (d, *J* = 5.0 Hz, 1H, C^{1/11}H₂), 3.20 (dd, *J* = 9.6, 4.9 Hz, 1H, C¹⁷H), 3.03 – 2.96 (m, 1H, C¹⁸H₂), 2.93 (d, *J* = 12.2 Hz, 1H, C³H₂), 2.40 (d, *J* = 13.5 Hz, 1H, C³H₂), 2.30 – 2.23 (m, 1H, C¹⁸H₂), 1.64 (s, 3H, C¹⁶H₃)

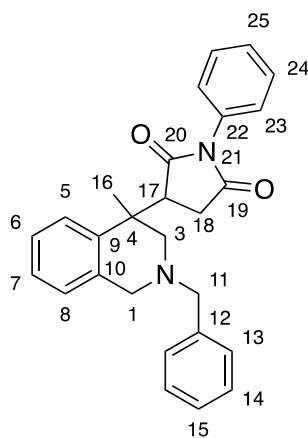
¹³C NMR (151 MHz, CDCl₃) δ 178.5 (C^{19/20}O), 176.9 (C^{19/20}O), 140.2 (C^Q), 137.7 (C^Q), 134.8 (C^Q), 129.6 (2 x C^{Ar}), 128.5 (2 x C^{Ar}), 127.5 (C^{Ar}), 127.3 (C^{Ar}), 126.9 (C^{Ar}), 126.7 (C^{Ar}), 125.8 (C^{Ar}), 63.2 (C^{1/11}H₂), 59.7 (C³H₂), 57.4 (C^{1/11}H₂), 51.8 (C¹⁷H), 40.0 (C⁴), 35.4 (C¹⁸H₂), 27.0 (C¹⁶H₃).

Minor diastereomer: ¹H NMR (600 MHz, CDCl₃) δ 8.22 (s, 1H, N²¹H), 7.42 – 6.98 (m, 9H, 9 x C^{Ar}H), 3.87 (d, *J* = 15.0 Hz, 1H, C^{1/11}H₂), 3.76 (d, *J* = 12.9 Hz, 1H, C^{1/11}H₂), 3.60 (d, *J* = 12.9 Hz, 1H, C^{1/11}H₂), 3.45 – 3.39 (m, 2H, C^{1/11}H₂ + C¹⁷H), 3.26 (d, *J* = 11.7 Hz, 1H, C³H₂), 2.90 – 2.83 (m, 1H, C¹⁸H₂), 2.63 – 2.55 (m, 1H, C¹⁸H₂), 2.40 (d, *J* = 11.7 Hz, 1H, C³H₂), 1.45 (s, 3H, C¹⁶H₃)

¹³C NMR (151 MHz, CDCl₃) δ 178.5 (C^{19/20}O), 176.8 (C^{19/20}O), 138.6 (C^Q), 138.0 (C^Q), 135.4 (C^Q), 129.3 (C^{Ar}), 129.2 (C^{Ar}), 128.4 (C^{Ar}), 127.4 (C^{Ar}), 127.0 (C^{Ar}), 126.9 (C^{Ar}), 126.6 (C^{Ar}), 126.2 (C^{Ar}), 125.4 (C^{Ar}), 63.0 (C^{1/11}H₂), 61.8 (C³H₂), 56.7 (C^{1/11}H₂), 50.0 (C¹⁷H), 40.8 (C⁴), 33.6 (C¹⁸H₂), 22.9 (C¹⁶H₃).

IR (neat) (cm⁻¹): 3213, 2805, 1778, 1701, 1494, 1349, 1182, 910, 730, 700.

N-Benzyl-4-methyl-4-(*N*-phenyl-2,5-dioxopyrrolidin-3-yl)-1,2,3,4-tetrahydroisoquinoline (5h)



The title compound was prepared by General Procedure E using *N*-benzyl-4-methylisoquinolinium iodide **4a** (45 mg, 0.125 mmol) and *N*-phenylmaleimide (43 mg, 0.25 mmol). Purification by column chromatography (CH₂Cl₂) gave *amine* **5h** (31 mg, 60%) as an inseparable 2:1 diastereomeric mixture as a yellow oil.

HRMS (ESI): Exact mass calculated for C₂₇H₂₇O₂N₂ [M+H]⁺: 411.2067, found 411.2066.

Major diastereomer: ¹H NMR (600 MHz, CDCl₃) δ 7.53 – 7.00 (m, 14H, 14 x C^{Ar}H), 3.76 (t, *J* = 14.1 Hz, 1H, C^{1/11}H₂), 3.67 (d, *J* = 12.9 Hz, 1H, C^{1/11}H₂),

3.55 (d, $J = 12.8$ Hz, 1H, C^{1/11}H₂), 3.45 (d, $J = 14.7$ Hz, 1H, C^{1/11}H₂), 3.39 (dd, $J = 9.7, 4.7$ Hz, 1H, C¹⁷H), 3.19 – 3.11 (m, 1H, C¹⁸H₂), 2.97 (d, $J = 12.1$, 1H, C³H₂), 2.54 (d, $J = 12.1$ Hz, 1H, C³H₂), 2.51 – 2.43 (m, 1H, C¹⁸H₂), 1.72 (s, 3H, C¹⁶H₃)

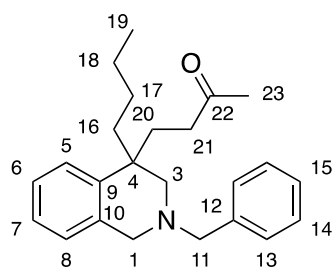
¹³C NMR (101 MHz, CDCl₃) δ 177.4 (C^{19/20}O), 175.9 (C^{19/20}O), 140.2 (C^Q), 137.6 (C^Q), 134.8 (C^Q), 132.1 (C^Q), 129.2 (2 x C^{Ar}), 129.2 (2 x C^{Ar}), 128.7 (2 x C^{Ar}), 128.6 (C^{Ar}), 128.5 (C^{Ar}), 127.6 (C^{Ar}), 127.0 (C^{Ar}), 126.7 (C^{Ar}), 126.6 (2 x C^{Ar}), 125.9 (C^{Ar}), 63.6 (C^{1/11}H₂), 60.3 (C³H₂), 56.9 (C^{1/11}H₂), 50.4 (C¹⁷H), 40.6 (C⁴), 34.3 (C¹⁸H₂), 27.2 (C¹⁶H₃).

Minor diastereomer: **¹H NMR** (600 MHz, CDCl₃) δ 7.53 – 7.00 (m, 14H, 14 x C^{Ar}H), 3.90 (d, $J = 14.9$ Hz, 1H, C^{1/11}H₂), 3.76 (t, $J = 14.1$ Hz, 1H, C^{1/11}H₂), 3.67 (d, $J = 12.9$ Hz, 1H, C^{1/11}H₂), 3.46 (dd, $J = 15.1, 6.6$ Hz, 2H, C^{1/11}H₂ + C¹⁷H), 3.31 – 3.24 (m, 1H, C³H₂), 3.19 – 3.11 (m, 1H, C¹⁸H₂), 2.79 – 2.71 (m, 1H, C¹⁸H₂), 2.51 – 2.43 (m, 1H, C³H₂), 1.54 (s, 3H, C¹⁶H₃)

¹³C NMR (101 MHz, CDCl₃) δ 177.4 (C^{19/20}O), 175.9 (C^{19/20}O), 138.3 (C^Q), 137.9 (C^Q), 135.6 (C^Q), 132.2 (C^Q), 129.4 (2 x C^{Ar}), 129.2 (4 x C^{Ar}), 128.6 (C^{Ar}), 127.5 (C^{Ar}), 127.3 (2 x C^{Ar}), 127.1 (2 x C^{Ar}), 126.6 (C^{Ar}), 126.3 (C^{Ar}), 63.0 (C^{1/11}H₂), 62.7 (C³H₂), 56.7 (C^{1/11}H₂), 49.1 (C¹⁷H), 41.1 (C⁴), 32.7 (C¹⁸H₂), 23.3 (C¹⁶H₃).

IR (neat) (cm⁻¹): 2926, 1774, 1707, 1499, 1380, 1180, 911, 733, 698, 623.

***N*-Benzyl-4-(butan-2-one)-4-butyl-1,2,3,4-tetrahydroisoquinoline (5i)**



The title compound was prepared by General Procedure **E** using *N*-benzyl-4-butyloisoquinolinium iodide **4b** (50 mg, 0.125 mmol) and methyl vinyl ketone (21 μ L, 0.25 mmol). Purification by column chromatography (5% EtOAc in pentane) gave *amine 5i* (33 mg, 76%) as a yellow oil.

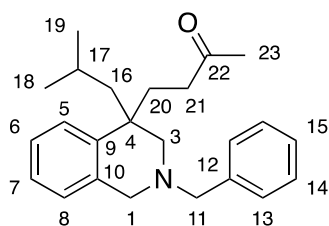
HRMS (ESI): Exact mass calculated for C₂₄H₃₂ON [M+H]⁺: 350.2478, found 350.2478.

¹H NMR (500 MHz, CDCl₃) δ 7.45 – 7.33 (m, 4H, 4 x C^{Ar}H), 7.33 – 7.26 (m, 1H, C^{Ar}H), 7.23 – 7.16 (m, 2H, 2 x C^{Ar}H), 7.16 – 7.08 (m, 1H, C^{Ar}H), 7.01 (d, $J = 7.6$ Hz, 1H, C^{Ar}H), 3.75 – 3.45 (m, 4H, C¹H₂ + C¹¹H₂), 2.58 – 2.46 (m, 3H, C³H₂ + C²¹H₂), 2.22 – 1.99 (m, 2H, C²⁰H₂ + C²¹H₂), 2.03 (s, 3H, C²³H₃), 1.83 (ddd, $J = 14.0, 11.7, 4.9$ Hz, 1H, C²⁰H₂), 1.80 – 1.70 (m, 1H, C¹⁶H₂), 1.53 (ddd, $J = 13.8, 12.2, 3.8$ Hz, 1H, C¹⁶H₂), 1.27 – 1.18 (m, 3H, C¹⁷H₂ + C¹⁸H₂), 1.00 – 0.89 (m, 1H, C¹⁷H₂), 0.85 (t, $J = 7.1$ Hz, 3H, C¹⁹H₃)

¹³C NMR (126 MHz, CDCl₃) δ 209.5 (C²²O), 140.9 (C^Q), 138.7 (C^Q), 135.7 (C^Q), 129.3 (2 x C^{Ar}), 128.4 (2 x C^{Ar}), 127.3 (C^{Ar}), 126.6 (C^{Ar}), 126.6 (C^{Ar}), 126.4 (C^{Ar}), 125.6 (C^{Ar}), 63.2 (C^{1/11}H₂), 59.4 (C³H₂), 57.6 (C^{1/11}H₂), 41.4 (C¹⁶H₂), 40.7 (C⁴), 39.8 (C²¹H₂), 35.0 (C²⁰H₂), 30.1 (C²³H₃), 26.5 (C¹⁷H₂), 23.6 (C¹⁸H₂), 14.2 (C¹⁹H₃)

IR (neat) (cm⁻¹): 2930, 1715, 1493, 1453, 1352, 1161, 1093, 919, 757, 700.

***N*-Benzyl-4-(butan-2-one)-4-isobutyl-1,2,3,4-tetrahydroisoquinoline (5j)**



The title compound was prepared by General Procedure **E** using *N*-benzyl-4-isobutylisoquinolinium iodide **4c** (50 mg, 0.125 mmol) and methyl vinyl ketone (21 μ L, 0.25 mmol). Purification by column chromatography (3% EtOAc in pentane) gave *amine 5j* (26.5 mg, 61%) as a yellow oil.

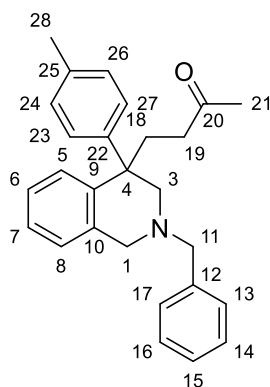
HRMS (ESI): Exact mass calculated for $C_{24}H_{32}ON$ $[M+H]^+$: 350.2478, found 350.2484.

1H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.15 (m, 5H, 5 x $C^{Ar}H$), 7.15 – 7.04 (m, 2H, 2 x $C^{Ar}H$), 7.00 (td, J = 7.3, 1.6 Hz, 1H, $C^{Ar}H$), 6.88 (dd, J = 7.5, 1.4 Hz, 1H, $C^{Ar}H$), 3.67 – 3.35 (m, 4H, C^1H_2 + $C^{11}H_2$), 2.57 – 2.40 (m, 2H, C^3H_2), 2.48 – 2.34 (m, 1H, $C^{21}H_2$), 2.05 – 1.93 (m, 1H, $C^{21}H_2$), 1.92 (s, 3H, $C^{23}H_3$), 1.97 – 1.86 (m, 1H, $C^{20}H_2$), 1.72 (ddd, J = 13.8, 11.7, 4.9 Hz, 1H, $C^{20}H_2$), 1.65 (dd, J = 13.8, 5.7 Hz, 1H, $C^{16}H_2$), 1.62 – 1.53 (m, 1H, $C^{17}H$), 1.38 (dd, J = 13.8, 4.7 Hz, 1H, $C^{16}H_2$), 0.78 (d, J = 6.5 Hz, 3H, $C^{18/19}H_3$), 0.56 (d, J = 6.5 Hz, 3H, $C^{18/19}H_3$)

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.5 (C^{22}), 140.7 (C^Q), 138.6 (C^Q), 135.7, (C^Q) 129.3 (2 x C^{Ar}), 128.4 (2 x C^{Ar}), 127.3 (C^{Ar}), 126.7 (C^{Ar}), 126.6 (C^{Ar}), 126.4 (C^{Ar}), 125.6 (C^{Ar}), 63.4 ($C^{1/11}H_2$), 60.1 (C^3H_2), 57.4 ($C^{1/11}H_2$), 50.4 ($C^{16}H_2$), 41.4 (C^4), 39.8 ($C^{21}H_2$), 36.4 ($C^{20}H_2$), 30.1 ($C^{23}H_3$), 25.9 ($C^{18/19}H_3$), 24.9 ($C^{18/19}H_3$), 24.6 ($C^{17}H$)

IR (neat) (cm^{-1}): 3028, 2953, 2807, 1715, 1453, 1365, 1162, 918, 756, 700.

4-(*N*-Benzyl-4-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinolin-4-yl)butan-2-one (5k)



The title compound was prepared according to General Procedure **E** using isoquinolinium salt **4d** (55 mg, 0.125 mmol), methyl vinyl ketone (20 μ L, 0.250 mmol), 5:2 $HCO_2H:Et_3N$ (42 μ L, 0.500 mmol) in MeCN (0.1 mL) and was purified by column chromatography (4% EtOAc in pentane) to furnish tetrahydroisoquinoline **5k** (24 mg, 50%) as a colourless oil.

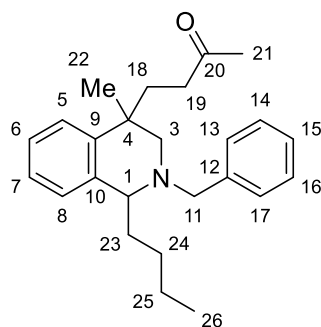
HRMS (ESI): Exact mass calculated for $C_{27}H_{30}NO$ $[M+H]^+$: 384.2322, found: 384.2303.

1H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.14 (m, 5H, 5 x $C^{Ar}H$), 7.09 – 6.96 (m, 7H, 7 x $C^{Ar}H$), 6.80 (dd, J = 7.7, 1.5 Hz, 1H, $C^{Ar}H$), 3.72 (d, J = 14.7 Hz, 1H, C^1H_2), 3.56 – 3.48 (m, 3H, C^1H_2 + $C^{11}H_2$), 2.69 (dd, J = 11.6, 1.3 Hz, 1H, C^3H_2), 2.60 (d, J = 11.8 Hz, 1H, C^3H_2), 2.57 – 2.43 (m, 2H, $C^{19}H_2$ + $C^{18}H_2$), 2.35 – 2.27 (m, 1H, $C^{18}H_2$), 2.23 (s, 3H, $C^{21}H_3$), 2.18 – 2.09 (m, 1H, $C^{19}H_2$), 1.95 (s, 3H, $C^{28}H_3$)

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.1 (C^{20}), 144.1 (C^{Ar}), 140.6 (C^{Ar}), 138.3 (C^{Ar}), 135.9 (C^{Ar}), 135.7 ($C^{Ar}H$), 129.1 (2 x $C^{Ar}H$), 129.1 ($C^{Ar}H$), 128.8 (2 x $C^{Ar}H$), 128.3 (2 x $C^{Ar}H$), 128.0 (2 x $C^{Ar}H$), 127.2 ($C^{Ar}H$), 126.6 ($C^{Ar}H$), 126.4 ($C^{Ar}H$), 126.1 ($C^{Ar}H$), 65.1 (C^3H_2), 62.8 ($C^{11}H_2$), 57.3 (C^1H_2), 46.6 (C^4), 40.3 ($C^{19}H_2$), 33.5 ($C^{18}H_2$), 30.7 ($C^{28}H_3$), 21.0 ($C^{21}H_3$)

IR (neat) (cm⁻¹): 2925, 2797, 1712, 1602, 1854, 1493, 1239, 1159, 1095, 1071.

4-(2-Benzyl-1-butyl-4-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)butan-2-one (5I)



The title compound was prepared according to General Procedure **F** using isoquinolinium salt **4e** (52 mg, 0.125 mmol), methyl vinyl ketone (20 μ L, 0.250 mmol), in MeCN (0.2 mL) at 55 °C and was purified by column chromatography (3% EtOAc in pentane) to furnish tetrahydroisoquinoline **5I** (25 mg, 55%) as an inseparable 4.5:1 diastereomeric mixture as a colourless oil.

The title compound could not be prepared according to General procedure **E** and only starting material was recovered from the reaction.

Data for major **both diastereomers A and B** (from the mixture):

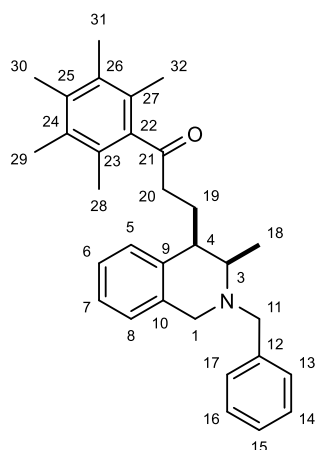
HRMS (ESI): Exact mass calculated for C₂₅H₃₄NO [M+H]⁺: 364.2635, found: 364.2632.

¹H NMR (400 MHz, CDCl₃) δ 7.32 – 7.21 (m, 4H, C^{Ar}H), 7.20 – 7.03 (m, 5H, C^{Ar}H), 4.04 (d, J = 13.3 Hz, 0.2H, C¹¹H_{2B}), 3.87 (d, J = 13.4 Hz, 0.8H, C¹¹H_{2A}), 3.72 – 3.64 (m, 1H, C¹H), 3.43 (d, J = 13.3 Hz, 0.8H, C¹¹H_{2A}), 3.19 (d, J = 13.3 Hz, 0.2H, C¹¹H_{2B}), 2.60 (d, J = 11.9 Hz, 0.2H, C³H_{2B}), 2.54 (d, J = 11.8 Hz, 0.8H, C³H_{2B}), 2.27 – 2.06 (m, 2H, C³H₂, C¹⁹H₂), 2.00 – 1.71 (m, 7H, C¹⁹H₂, C¹⁸H₂, C²¹H₃, C²³H₂), 1.55 (ddd, J = 13.9, 11.4, 4.7 Hz, 1H, C¹⁸H₂), 1.49 – 1.35 (m, 1H, C²⁴H₂), 1.25 – 1.01 (m, 6H, C²²H₃, C²⁴H₂, C²⁵H₂), 1.03 (s, 3H, C²⁶H₃)

¹³C NMR (101 MHz, CDCl₃) δ 209.2 (C²⁰_B), 209.2 (C²⁰_A), 143.7 (C^{Ar}_B), 142.5 (C^{Ar}_A), 139.8 (C^{Ar}_B), 139.7 (C^{Ar}_A), 139.1 (C^{Ar}_B), 138.2 (C^{Ar}_A), 129.1 (2 x C^{Ar}H_B), 129.0 (2 x C^{Ar}H_A), 128.2 (2 x C^{Ar}H_{A+B}), 127.0 (C^{Ar}H_B), 126.9 (C^{Ar}H_A), 126.7 (C^{Ar}H_A), 126.5 (C^{Ar}H_B), 126.2 (C^{Ar}H_A), 125.9 (C^{Ar}H_B), 125.8 (C^{Ar}H_B), 125.8 (C^{Ar}H_A), 125.7 (C^{Ar}H_B), 125.3 (C^{Ar}H_A), 63.0 (C¹H_B), 62.8 (C¹H_A), 59.0 (C¹¹H_{2B}), 58.9 (C¹¹H_{2A}), 57.5 (C³H_{2B}), 56.1 (C³H_{2A}), 39.3 (C¹⁹H_{2B}), 39.2 (C¹⁹H_{2A}), 36.9 (C⁴_A), 36.7 (C⁴_B), 35.6 (C¹⁸H_{2A}), 34.9 (C¹⁸H_{2A}), 32.6 (C²³H_{2B}), 30.9 (C²³H_{2A}), 29.9 (C²¹H_{3A}), 29.8 (C²¹H_{3B}), 28.4 (C²²H_{3A}), 27.8 (C²⁴H_{2A}), 26.8 (C²⁴H_{2B}), 25.8 (C²²H_{3B}), 23.2 (C²⁵H_{2A}), 23.1 (C²⁵H_{2B}), 14.1 (C²⁶H_{3A+B})

IR (neat) (cm⁻¹): 2955, 2932, 1714, 1491, 1453, 1356, 1162, 910, 731, 699.

3-(*N*-Benzyl-3-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one (5m)



The title compound was prepared according to General Procedure **F** using isoquinolinium salt **4f** (43 mg, 0.125 mmol), 1-(2,3,4,5,6-pentamethylphenyl)prop-2-en-1-one (28 mg, 0.125 mmol), 5:2 HCO₂H:Et₃N (42 μL, 0.50 mmol) in MeCN (0.1 mL) and was purified by column chromatography (3-5% EtOAc in pentane) to furnish tetrahydroisoquinoline **5m** (50 mg, 91%) as an inseparable 12:1 diastereomeric mixture as a colourless oil. The major diastereomer was found to be *cis*-**5o** (see crystal structure of the corresponding HCl salt below; NOESY inconclusive).

The title compound could not be prepared according to General procedure **E**.

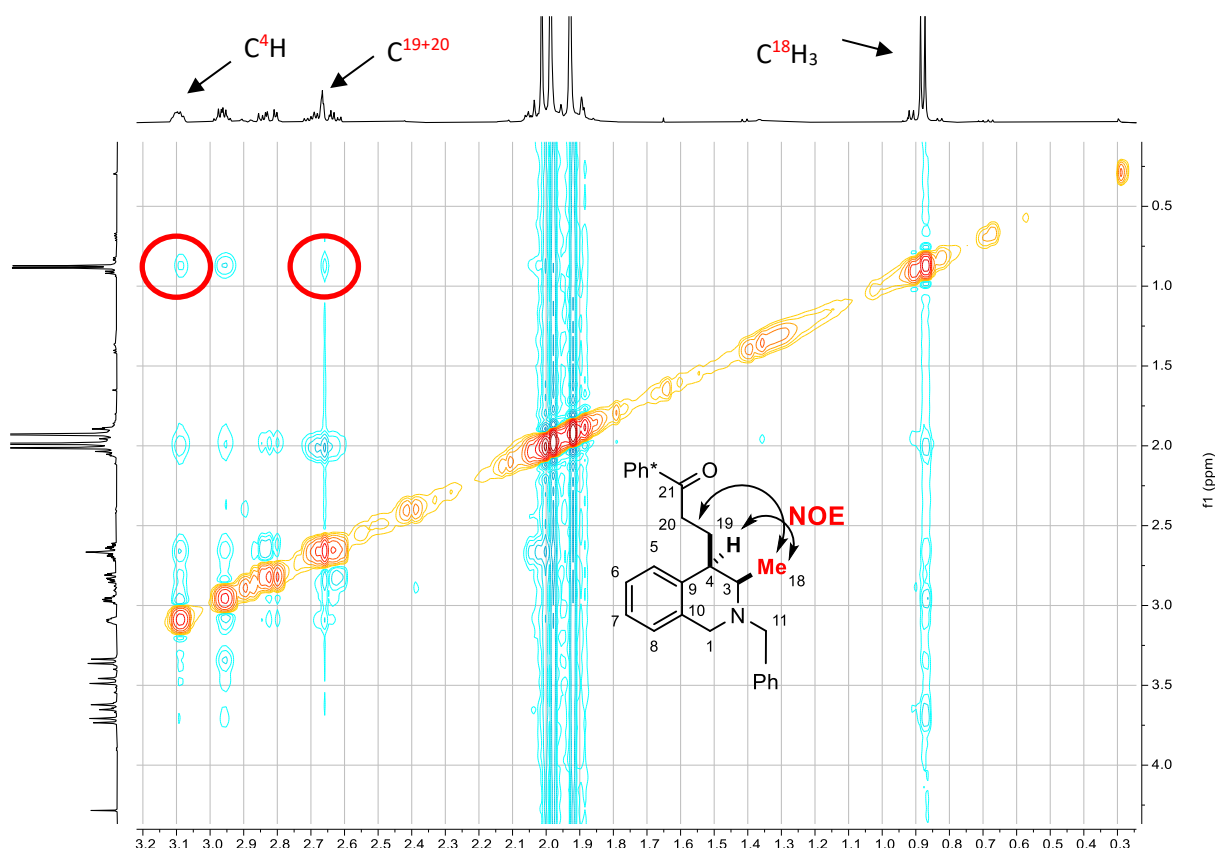
HRMS (ESI): Exact mass calculated for C₃₁H₃₈NO [M+H]⁺: 440.2948, found: 440.2950.

Major diastereomer: **¹H NMR** (500 MHz, C₆D₆) δ 7.39 – 7.35 (m, 2H, 2 x C^{Ar}H), 7.31 (d, *J* = 7.7 Hz, 1H, C^{Ar}H), 7.24 – 7.15 (m, 2H, 2 x C^{Ar}H), 7.12 – 7.05 (m, 2H, 2 x C^{Ar}H), 7.02 – 6.96 (m, 1H, C^{Ar}H), 6.70 (dd, *J* = 7.7, 1.4 Hz, 1H, C^{Ar}H), 3.72 (d, *J* = 13.4 Hz, 1H, C¹H₂), 3.64 (d, *J* = 15.7 Hz, 1H, C¹¹H₂), 3.47 (d, *J* = 15.7 Hz, 1H, C¹¹H₂), 3.35 (d, *J* = 13.3 Hz, 1H, C¹H₂), 3.14 – 3.05 (m, 1H, C⁴H), 2.96 (dt, *J* = 6.6, 3.3 Hz, 1H, C³H), 2.87 – 2.79 (m, 1H, C²⁰H₂), 2.75 – 2.60 (m, 2H, C²⁰H₂ + C¹⁹H₂), 2.07 – 2.02 (m, 1H, C¹⁹H₂), 2.01 (s, 3H, C³⁰H₃), 1.99 (s, 6H, C²⁸H₃ + C³²H₃), 1.93 (s, 6H, C²⁹H₃ + C³¹H₃), 0.88 (d, *J* = 6.6 Hz, 3H, C¹⁸H₃)

¹³C NMR (126 MHz, C₆D₆) δ 210.4 (C²¹), 141.9 (C^{Ar}), 140.1 (C^{Ar}), 137.9 (C^{Ar}), 135.3 (C^{Ar}), 134.8 (C^{Ar}), 132.9 (2 x C^{Ar}), 128.8 (2 x C^{Ar}H), 128.7 (2 x C^{Ar}H), 127.5 (2 x C^{Ar}), 127.4 (C^{Ar}H), 127.2 (C^{Ar}H), 126.6 (C^{Ar}H), 126.5 (C^{Ar}H), 126.0 (C^{Ar}H), 59.4 (C¹H₂), 55.6 (C³H), 52.7 (C¹¹H₂), 43.4 (C²⁰H₂), 42.4 (C⁴H), 24.2 (C¹⁹H₂), 17.3 (C²⁹H₃ + C³¹H₃), 16.6 (C³⁰H₃), 15.9 (C²⁸H₃ + C³²H₃), 10.2 (C¹⁸H₃)

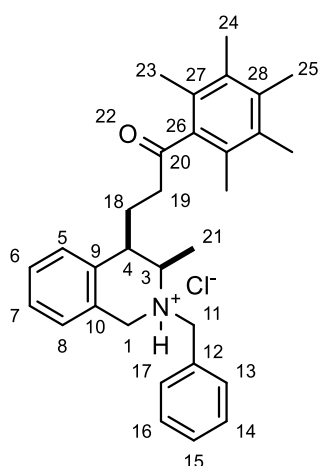
IR (neat) (cm⁻¹): 2964, 1698, 1452, 1377, 1315, 1262, 1116, 1027, 909, 799.

Relative stereochemistry could not be unambiguously assigned by NOESY correlations:



Crystal structure of the corresponding HCl salt:

***N*-Benzyl-3-methyl-4-(3-oxo-3-(2,3,4,5,6-pentamethylphenyl)propyl)-1,2,3,4-tetrahydroisoquinolinium chloride (5m·HCl)**



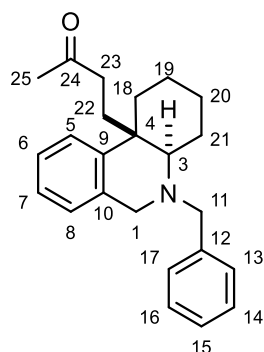
In a 25 mL round bottom flask under argon was charged isoquinoline product **5m** (140 mg, 0.32 mmol) in dry diethyl ether (5 mL). The solution was chilled to 0 °C and 2M HCl in diethyl ether (0.19 mL, 0.38 mmol) was introduced dropwise. After 15 minutes the solids were collected via filtration to give the title compound **5m·HCl** (148 mg, 98%, two diastereomers ca. 55:45) as a white solid. A single crystal for X-ray diffraction was obtained from slow evaporation from the CH₂Cl₂/hexane/MTBE solvent system.

m.p. (Et₂O): 186 – 188 °C

¹H NMR (400 MHz, CDCl₃) δ 12.90 (s, 1H), 12.81 (s, 1H), 7.89 (d, *J* = 5.4 Hz, 2H), 7.82 – 7.72 (m, 2H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.48 – 7.27 (m, 9H), 7.20 (t, *J* = 8.4 Hz, 1H), 7.01 (d, *J* = 7.3 Hz, 1H), 4.73 (d, *J* = 15.8 Hz, 1H), 4.45 (d, *J* = 10.8 Hz, 2H), 4.25 (s, 1H), 4.18 – 4.05 (m, 1H), 4.00 (d, *J* = 16.3 Hz, 1H), 3.91 (s, 0H), 3.68 (s, 1H), 3.60 (s, 1H), 3.38 (s, 1H), 2.93 (ddd, *J* = 15.0, 11.0, 3.8 Hz, 1H), 2.78 – 2.67 (m, 1H), 2.67 – 2.56 (m, 3H), 2.56 – 2.40 (m, 1H), 2.23 (s, 6H), 2.18 (s, 12H), 2.07 (s, 6H), 2.02 (s, 6H), 1.88 – 1.76 (m, 2H), 1.70 (s, 2H), 1.42 (d, *J* = 6.5 Hz, 3H), 1.16 (d, *J* = 6.2 Hz, 2H).

Crystal data C₃₁H₃₈ClNO, M = 476.10, monoclinic, a = 20.6290(8), b = 7.2107(3), c = 17.2803(6) Å, β = 91.754°, Z = 4, T = 35 K, space group *Pc*, 24211 reflections measured, 11639 unique (R_{int} = 0.120), which were used in all calculations.

4-((4a*R*,10b*R*)-5-Benzyl-2,3,4a,5,6-hexahydrophenanthridin-10b(1*H*)-yl)butan-2-one (5n)



The title compound was prepared according to General Procedure **F** using isoquinolinium salt **4h** (48 mg, 0.12 mmol), methyl vinyl ketone (20 μL, 0.24 mmol), 5:2 HCO₂H:Et₃N (50 μL, 0.6 mmol), [RhCp*Cl]₂ (7 μg, 0.005 mmol, 0.01 mol%) in MeCN (0.15 mL) and was purified by column chromatography (2.5-5% EtOAc in pentane) to furnish tetrahydroisoquinoline **5n** (28 mg, 67%, d.r. > 25:1) as a colourless oil.

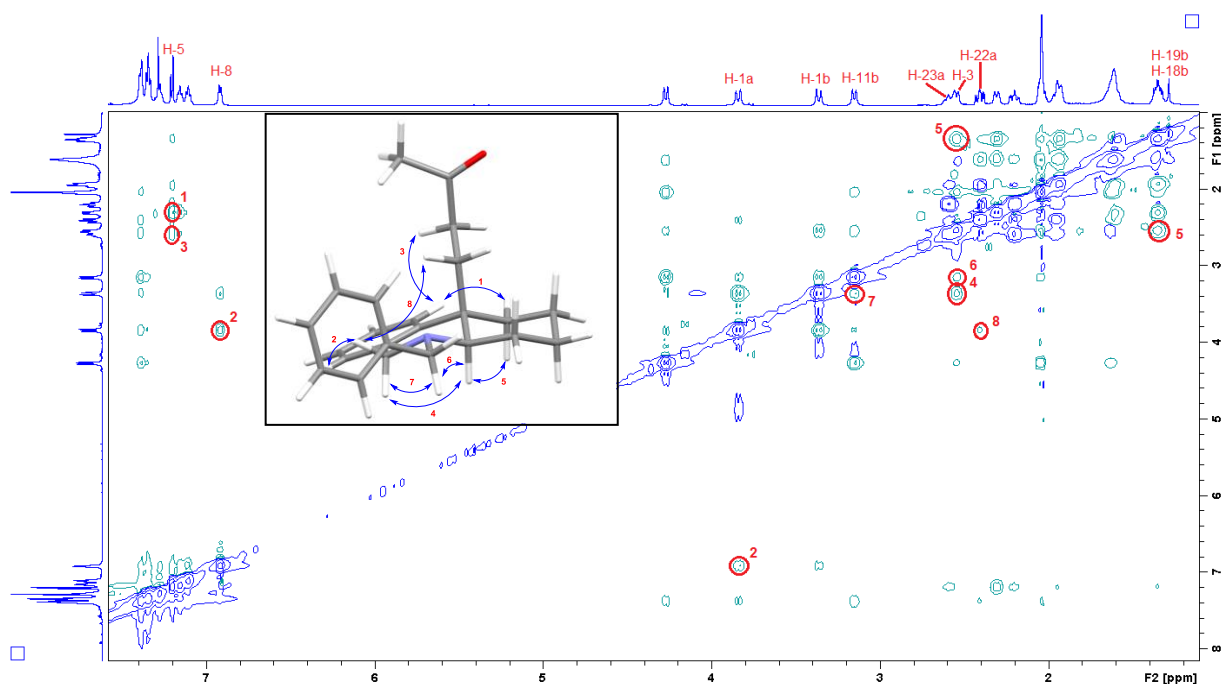
HRMS (ESI): Exact mass calculated for C₂₄H₃₀NO [M+H]⁺: 348.2322, found: 348.2322.

¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.29 (m, 4H, C^{Ar}H), 7.27 – 7.23 (m, 1H, C^{Ar}H), 7.18 (dd, *J* = 7.7, 1.6 Hz, 1H, C⁵H), 7.13 (td, *J* = 7.5, 1.5 Hz, 1H, C⁶H), 7.08 (td, *J* = 7.3, 1.6 Hz, 1H, C⁷H), 6.89 (dd, *J* = 7.4, 1.5 Hz, 1H, C⁸H), 4.25 (d, *J* = 12.9 Hz, 1H, C¹¹H_a), 3.82 (d, *J* = 15.6 Hz, 1H, C¹H_a), 3.34 (d, *J* = 15.6 Hz, 1H, C¹H_b), 3.13 (d, *J* = 12.9 Hz, 1H, C¹¹H_b), 2.63 – 2.47 (m, 2H, C²³H_a + C³H), 2.38 (ddd, *J* = 14.1, 11.9, 4.7 Hz, 1H, C²²H_a), 2.28 (m, 1H, C¹⁸H_a), 2.18 (ddd, *J* = 16.5, 12.0, 4.4 Hz, 1H, C²³H_b), 2.02 (s, 3H, C²⁵H₃), 1.99 – 2.05 (m, 1H, C²¹H_a), 1.92 (m, 2H, C¹⁹H_a + C²²H_b), 1.58 (m, 3H, C²⁰H₂ + C²¹H_b), 1.42 – 1.27 (m, 2H, C¹⁹H_b + C¹⁸H_b)

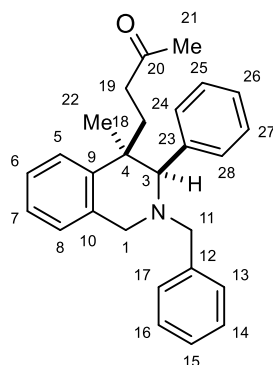
¹³C NMR (101 MHz, CDCl₃) δ 210.1 (C²⁴), 142.8 (C⁹), 140.5 (C¹²), 134.9 (C¹⁰), 128.8 (C¹³ + C¹⁷), 128.4 (C¹⁴ + C¹⁶), 126.9 (C¹⁵), 126.6 (C⁸), 125.8 (C⁷), 125.6 (C⁶), 125.5 (C⁵), 67.2 (C³), 57.3 (C¹¹), 57.1 (C¹), 40.8 (C⁴), 40.0 (C²³), 34.2 (C¹⁸), 30.1 (C²⁵), 27.6 (C²²), 25.6 (C¹⁹), 25.1 (C²¹), 20.9 (C²⁰)

IR (neat) (cm⁻¹): 2928, 2855, 2782, 1711, 1492, 1451, 1355, 1160, 1116, 760.

Relative stereochemistry was assigned by the following observed NOESY correlations:



4-(*N*-Benzyl-4-methyl-3-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)butan-2-one (**5o**)



The title compound was prepared according to General Procedure **E** using isoquinolinium salt **4g** (55 mg, 0.125 mmol), methyl vinyl ketone (20 μ L, 0.250 mmol), 5:2 $\text{HCO}_2\text{H}:\text{Et}_3\text{N}$ (42 μ L, 0.50 mmol) in MeCN (0.1 mL) and was purified by column chromatography (10% EtOAc in pentane) to furnish tetrahydroisoquinoline **5o** (46 mg, 96%, dr > 25:1) as a colourless oil. The relative stereochemistry was assigned by NOESY. General procedure **E** gave the title compound in a significantly reduced yield of 72%.

HRMS (ESI): Exact mass calculated for $\text{C}_{27}\text{H}_{30}\text{NO}$ $[\text{M}+\text{H}]^+$: 384.2322, found: 384.2303.

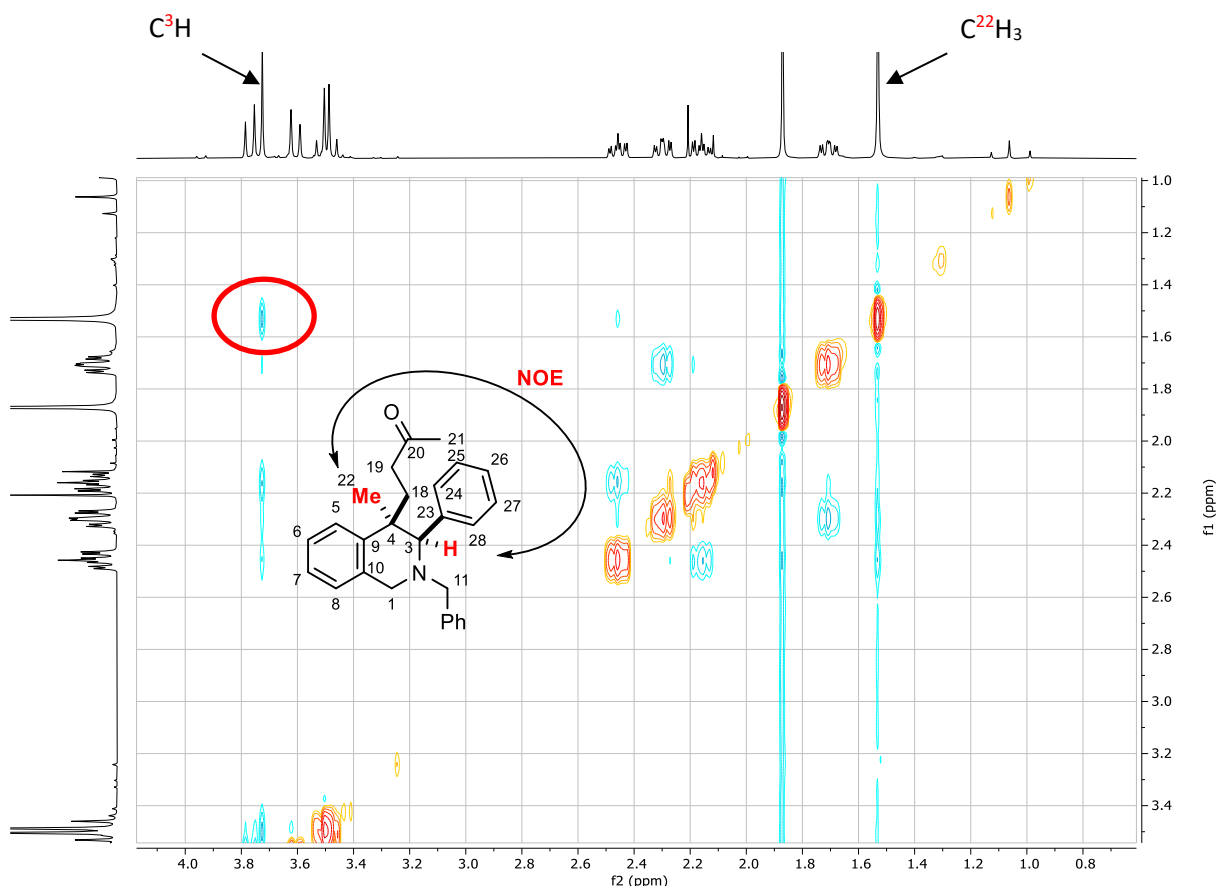
Data for major diastereomer **5o** from the mixture.

^1H NMR (500 MHz, CDCl_3) δ 7.46 – 7.36 (m, 5H, 5 x $\text{C}^{\text{Ar}}\text{H}$), 7.34 – 7.26 (m, 5H, 5 x $\text{C}^{\text{Ar}}\text{H}$), 7.23 – 7.19 (m, 1H, $\text{C}^{\text{Ar}}\text{H}$), 7.06 – 7.01 (m, 3H, 3 x $\text{C}^{\text{Ar}}\text{H}$), 3.77 (d, $J = 16.0$ Hz, 1H, C^1H_2), 3.73 (s, 1H, C^3H), 3.61 (d, $J = 16.0$ Hz, 1H, C^1H_2), 3.54 – 3.45 (m, 2H, C^{11}H_2), 2.46 (ddd, $J = 16.1, 11.9, 4.2$ Hz, 1H, C^{19}H_2), 2.30 (ddd, $J = 13.8, 11.7, 4.2$ Hz, 1H, C^{18}H_2), 2.16 (ddd, $J = 16.2, 11.8, 4.4$ Hz, 1H, C^{19}H_2), 1.87 (s, 3H, C^{21}H_3), 1.71 (ddd, $J = 13.8, 11.9, 4.5$ Hz, 1H, C^{18}H_2), 1.53 (s, 3H, C^{22}H_3)

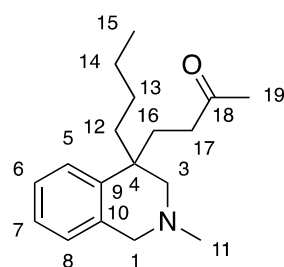
^{13}C NMR (126 MHz, CDCl_3) δ 209.2 (C^{20}), 143.0 (C^{Ar}), 139.3 (C^{Ar}), 135.1 (C^{Ar}), 134.4 (C^{Ar}), 130.1 (2 x $\text{C}^{\text{Ar}}\text{H}$), 128.8 (2 x $\text{C}^{\text{Ar}}\text{H}$), 128.4 (2 x $\text{C}^{\text{Ar}}\text{H}$), 128.0 (2 x $\text{C}^{\text{Ar}}\text{H}$), 127.5 ($\text{C}^{\text{Ar}}\text{H}$), 127.1 ($\text{C}^{\text{Ar}}\text{H}$), 126.8 ($\text{C}^{\text{Ar}}\text{H}$), 126.3 ($\text{C}^{\text{Ar}}\text{H}$), 125.8 ($\text{C}^{\text{Ar}}\text{H}$), 125.7 ($\text{C}^{\text{Ar}}\text{H}$), 70.7 (C^3H), 59.7 (C^{11}H_2), 52.4 (C^1H_2), 40.6 (C^4), 38.8 (C^{19}H_2), 31.4 (C^{18}H_2), 30.2 (C^{21}H_3), 29.7 (C^{22}H_3)

IR (neat) (cm^{-1}): 2959, 1714, 1492, 1451, 1355, 1279, 1240, 1162, 1072, 1028, 909.

Relative stereochemistry was assigned by the following observed NOESY correlations:



***N*-Methyl-4-(butan-2-one)-4-butyl-1,2,3,4-tetrahydroisoquinoline (5p)**



The title compound was prepared by General Procedure **E** using *N*-methyl-4-butylisoquinolinium iodide **4i** (41 mg, 0.125 mmol) and methyl vinyl ketone (21 μ L, 0.25 mmol). Purification by column chromatography (20% EtOAc in pentane) gave *amine* **5p** (21 mg, 62%) as a yellow oil.

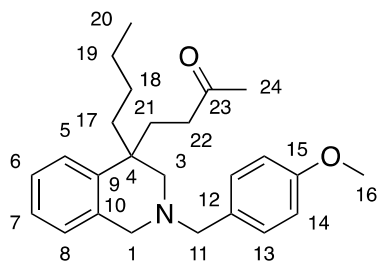
HRMS (ESI): Exact mass calculated for $C_{18}H_{28}ON$ $[M+H]^+$: 274.2165, found 274.2165.

1H NMR (400 MHz, $CDCl_3$) δ 7.10 (s, 2H, 2 x $C^{Ar}H$), 7.09 – 7.00 (m, 1H, $C^{Ar}H$), 6.94 (dt, J = 7.5, 1.0 Hz, 1H, $C^{Ar}H$), 3.49 (d, J = 14.6 Hz, 1H, C^1H_2), 3.28 (d, J = 14.6 Hz, 1H, C^1H_2), 2.50 – 2.35 (m, 1H, $C^{17}H_2$), 2.40 (dd, J = 11.5, 1H, C^3H_2), 2.27 (d, J = 11.6 Hz, 1H, C^3H_2), 2.20 (s, 3H, $C^{11}H_3$), 2.08 – 1.90 (m, 2H, $C^{16}H_2$ + $C^{17}H_2$), 1.93 (s, 3H, $C^{19}H_3$), 1.85 – 1.72 (m, 1H, $C^{16}H_2$), 1.61 (ddd, J = 13.8, 11.9, 4.4 Hz, 1H, $C^{12}H_2$), 1.67 – 1.55 (m, 1H, $C^{12}H_2$), 1.27 – 1.08 (m, 3H, $C^{13}H_2$ + $C^{14}H_2$), 1.02 – 0.89 (m, 1H, $C^{13}H_2$), 0.77 (t, J = 7.1 Hz, 3H, $C^{15}H_3$)

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.7 ($C^{18}O$), 140.1 (C^Q), 135.9 (C^Q), 126.6 (C^{Ar}), 126.3 (2 x C^{Ar}), 125.6 (C^{Ar}), 62.5 (C^3H_2), 59.1 (C^1H_2), 46.0 ($C^{11}H_3$), 41.7 ($C^{12}H_2$), 40.7 (C^4), 39.9 ($C^{17}H_2$), 35.9 ($C^{16}H_2$), 30.1 ($C^{19}H_3$), 26.5 ($C^{13}H_2$), 23.6 ($C^{14}H_2$), 14.2 ($C^{15}H_3$)

IR (neat) (cm^{-1}): 2931, 2860, 1714, 1492, 1464, 1450, 1253, 1161, 908, 763.

***N*-(4-Methoxybenzyl)-4-(butan-2-one)-4-butyl-1,2,3,4-tetrahydroisoquinoline (5q)**



The title compound was prepared by General Procedure E using *N*-(4-methoxybenzyl)-4-butylisoquinolinium iodide **4j** (54 mg, 0.125 mmol) and methyl vinyl ketone (21 μ L, 0.25 mmol). Purification by flash column chromatography (6% EtOAc in pentane) gave *amine* **5q** (27 mg, 57%) as a yellow oil.

HRMS (ESI): Exact mass calculated for $C_{25}H_{34}O_2N$ $[M+H]^+$: 380.2584,

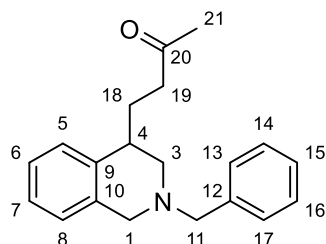
found 380.2584.

1H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.15 (m, 2H, 2 x $C^{Ar}H$), 7.13 – 7.04 (m, 2H, 2 x $C^{Ar}H$), 7.07 – 6.96 (m, 1H, $C^{Ar}H$), 6.90 (dt, J = 7.6, 1.0 Hz, 1H, $C^{Ar}H$), 6.83 – 6.75 (m, 2H, 2 x $C^{Ar}H$), 3.73 (s, 3H, $C^{16}H_3$), 3.56 – 3.37 (m, 4H, $C^1H_2 + C^{11}H_2$), 2.48 – 2.32 (m, 1H, $C^{22}H_2$), 2.38 (d, J = 5.5 Hz, 2H, C^3H_2), 2.06 – 1.85 (m, 2H, $C^{21}H_2 + C^{22}H_2$), 1.93 (s, 3H, $C^{24}H_3$), 1.79 – 1.66 (m, 1H, $C^{21}H_2$), 1.70 – 1.59 (m, 1H, $C^{17}H_2$), 1.48 – 1.36 (m, 1H, $C^{17}H_2$), 1.12 (m, 3H, $C^{18}H_2 + C^{19}H_2$), 0.84 (m, 1H, $C^{18}H_2$), 0.74 (t, J = 7.1 Hz, 3H, $C^{20}H_3$)

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.5 ($C^{23}O$), 158.9 (C^Q), 140.9 (C^Q), 135.8 (C^Q), 130.7 (C^Q), 130.4 (2 x C^{Ar}), 126.6 (2 x C^{Ar}), 126.5 (C^{Ar}), 126.4 (C^{Ar}), 125.6 (C^{Ar}), 113.7 (C^{Ar}), 62.5 ($C^{1/11}H_2$), 59.2 (C^3H_2), 57.5 ($C^{1/11}H_2$), 55.4 ($C^{16}H_3$), 41.4 ($C^{17}H_2$), 40.7 (C^4), 39.9 ($C^{22}H_2$), 35.0 ($C^{21}H_2$), 30.1 ($C^{24}H_3$), 26.5 ($C^{18}H_2$), 23.6 ($C^{19}H_2$), 14.2 ($C^{20}H_3$)

IR (neat) (cm^{-1}): 2931, 1714, 1612, 1512, 1302, 1246, 1171, 1036, 830, 762.

4-(*N*-Benzyl-1,2,3,4-tetrahydroisoquinolin-4-yl)butan-2-one (5r)



The title compound was prepared according to General Procedure E using isoquinolinium salt **4k** (43 mg, 0.125 mmol), methyl vinyl ketone (10 μ L, 0.125 mmol), 5:2 $HCO_2H:Et_3N$ (42 μ L, 0.50 mmol) in MeCN (0.1 mL) and was purified by flash column chromatography (6-10% EtOAc in pentane) to furnish tetrahydroisoquinoline **5r** (23 mg, 63%) as a colourless oil.

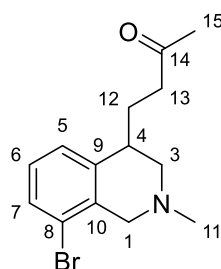
HRMS (ESI): Exact mass calculated for $C_{20}H_{24}NO$ $[M+H]^+$: 294.1852, found: 294.1850.

1H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.16 (m, 5H, 5 x $C^{Ar}H$), 7.13 – 7.01 (m, 3H, 3 x $C^{Ar}H$), 6.92 (d, J = 6.7 Hz, 1H, $C^{Ar}H$), 3.73 (d, J = 14.8 Hz, 1H, C^1H_2), 3.67 (d, J = 13.0 Hz, 1H, $C^{11}H_2$), 3.47 (d, J = 13.0 Hz, 1H, $C^{11}H_2$), 3.40 (d, J = 14.8 Hz, 1H, C^1H_2), 2.76 – 2.66 (m, 1H, C^4H), 2.61 (ddd, J = 11.6, 3.6, 1.2 Hz, 1H, C^3H_2), 2.45 (dd, J = 11.6, 4.3 Hz, 1H, C^3H_2), 2.31 (ddd, J = 16.2, 9.2, 6.6 Hz, 1H, $C^{19}H_2$), 2.19 (ddd, J = 16.8, 9.4, 5.6 Hz, 1H, $C^{19}H_2$), 1.99 (s, 3H, $C^{21}H_3$), 1.98 – 1.87 (m, 2H, 2 x $C^{18}H_2$)

¹³C NMR (101 MHz, CDCl₃) δ 209.1 (C²⁰O), 138.8 (C^{Ar}), 138.4 (C^{Ar}), 135.2 (C^{Ar}), 129.2 (2 x C^{Ar}H), 128.5 (2 x C^{Ar}H), 128.4 (C^{Ar}H), 127.3 (C^{Ar}H), 126.6 (C^{Ar}H), 126.3 (C^{Ar}H), 126.0 (C^{Ar}H), 62.9 (C¹¹H₂), 56.9 (C¹H₂), 53.9 (C³H₂), 41.4 (C¹⁹H₂), 38.0 (C⁴H), 30.0 (C²¹H₃), 30.0 (C¹⁸H₂)

IR (neat) (cm⁻¹): 2925, 2797, 1712, 1493, 1452, 1366, 1159, 1095, 740, 700.

4-(6-Bromo-*N*-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)butan-2-one (5s)



The title compound was prepared according to General Procedure **E** using isoquinolinium salt **4l** (44 mg, 0.125 mmol), methyl vinyl ketone (10 μL, 0.125 mmol), 5:2 HCO₂H:Et₃N (42 μL, 0.50 mmol) in MeCN (0.1 mL) and was purified by flash column chromatography (6-10% EtOAc in pentane) to furnish tetrahydroisoquinoline **5s** (16 mg, 43%) as a colourless oil.

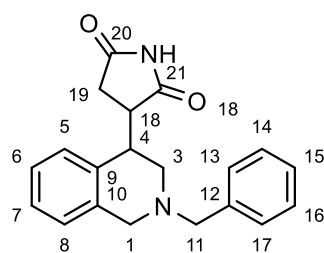
HRMS (ESI): Exact mass calculated for C₁₄H₁₉BrNO [M+H]⁺: 296.0645, found: 296.0645.

¹H NMR (400 MHz, CDCl₃) δ 7.38 (dd, *J* = 7.8, 1.2 Hz, 1H, C⁷H), 7.19 – 7.14 (m, 1H, C⁵H), 7.09 – 7.01 (m, 1H, C⁶H), 3.74 (d, *J* = 16.0 Hz, 1H, C¹H₂), 3.27 (d, *J* = 16.0 Hz, 1H, C¹H₂), 2.86 (dt, *J* = 8.5, 4.2 Hz, 1H, C⁴H), 2.61 – 2.54 (m, 1H, C³H₂), 2.54 – 2.48 (m, 2H, C³H₂ + C¹³H₂), 2.45 – 2.36 (m, 4H, C¹¹H₃ + C¹³H₂), 2.13 (s, 3H, C¹⁵H₃), 2.11 – 2.05 (m, 1H, C¹²H₂), 1.95 (dtd, *J* = 14.1, 8.2, 5.9 Hz, 1H, C¹²H₂);

¹³C NMR (101 MHz, CDCl₃) δ 208.5 (C¹⁴O), 140.5 (C^{9/10}), 134.6 (C^{9/10}), 130.1 (C⁷H), 127.6 (C^{5/6}H), 127.6 (C^{5/6}H), 122.7 (C⁸), 58.9 (C¹H₂), 56.4 (C³H₂), 46.1 (C¹¹H₃), 41.0 (C¹³H₂), 38.2 (C⁴H), 30.1 (C¹⁵H₃), 29.8 (C¹²H₂)

IR (neat) (cm⁻¹): 2938, 2780, 1713, 1564, 1461, 1445, 1377, 1367, 1356, 1161, 1113, 776, 715.

3-(*N*-Benzyl-1,2,3,4-tetrahydroisoquinolin-4-yl)pyrrolidine-2,5-dione (5t)



The title compound was prepared according to General Procedure **E** using isoquinolinium salt **4k** (43 mg, 0.125 mmol), methyl vinyl ketone (12 mg, 0.125 mmol), 5:2 HCO₂H:Et₃N (42 μL, 0.50 mmol) in MeCN (0.1 mL) and was purified by flash column chromatography (6-10% EtOAc in pentane) to furnish tetrahydroisoquinoline **5t** (26 mg, 65%) as

an inseparable 2:1 diastereomeric mixture as a colourless oil.

Data for **both diastereomers A and B** (from the mixture):

HRMS (ESI): Exact mass calculated for C₂₀H₂₁N₂O₂ [M+H]⁺: 321.1598, found: 321.1593.

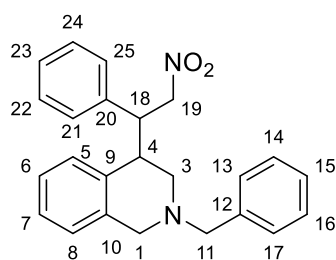
¹H NMR (400 MHz, CDCl₃) δ 8.20 (s, 0.48H, NH_A), 8.09 – 7.91 (m, 0.45H, NH_B), 7.34 – 7.17 (m, 5H, C^{Ar}H_{A/B}), 7.15 – 6.92 (m, 4H, C^{Ar}H_{A/B}), 3.88 – 3.76 (m, 1H, C¹H_{2A+B}), 3.69 – 3.52 (m, 2H, C¹⁸H_{A/B} + C¹¹H_{2A+B} + C¹⁹H_{2A/B}), 3.52 – 3.44 (m, 1H, C¹⁸H_{A/B}), 3.37 – 3.22 (m, 2H, C¹H_{2A+B} + C⁴H_{A+B} + C¹¹H_{2A+B}), 2.98 (ddd, *J* = 8.7, 5.8, 2.4 Hz, 0.52H, C⁴H_{A/B}), 2.89 – 2.77 (m, 1H, C¹H_{2A+B} + C³H_{2A+B}), 2.71 (dd, *J* = 19.0, 9.2 Hz, 0.57H,

$C^{19}H_{A/B}$), 2.62 (dd, $J = 11.6, 3.9$ Hz, 0.52H, $C^1H_{2A/B}$), 2.58 – 2.43 (m, 1H, C^3H_{2A+B}), 2.23 (dd, $J = 18.7, 9.5$ Hz, 0.49H, $C^{19}H_{2A/B}$)

^{13}C NMR (101 MHz, $CDCl_3$) δ 180.4 (C^{21}_A), 179.4 (C^{21}_B), 177.7 (C^{20}_A), 177.5 (C^{20}_B), 138.2(C^{Ar}_B), 137.6 (C^{Ar}_A), 136.1 (C^{Ar}_B), 135.7 (C^{Ar}_A), 134.5 (C^{Ar}_B), 132.7 (C^{Ar}_A), 129.6 (2 x $C^{Ar}H_B$), 129.1(2 x $C^{Ar}H_A$), 128.6 (2 x $C^{Ar}H_B$), 128.6 (2 x $C^{Ar}H_A$), 128.2 ($C^{Ar}H_A$), 127.9 ($C^{Ar}H_B$), 127.5 ($C^{Ar}H_B$), 127.5 ($C^{Ar}H_A$), 127.4 ($C^{Ar}H_B$), 127.0 (4 x $C^{Ar}H_{A/B}$), 126.8 ($C^{Ar}H_A$), 63.2 ($C^{11}H_{2B}$), 63.1 ($C^{11}H_{2A}$), 56.9 (C^1H_{2B}), 56.5 ($C^1H_{2A} + C^3H_{2A/B}$), 52.3 (C^3H_{2A+B}), 49.0 (C^4H_A), 48.4 (C^4H_B), 38.0 ($C^{18}H_A$), 36.5 ($C^{18}H_A$), 33.8 ($C^{19}H_{2A}$), 33.2($C^{19}H_{2A}$)

IR (neat) (cm^{-1}): 3204, 3064, 2804, 2762, 1700, 1348, 1268, 1180, 1092, 910.

***N*-Benzyl-4-(2-nitro-1-phenylethyl)-1,2,3,4-tetrahydroisoquinoline (5u)**



The title compound was prepared according to General Procedure E using isoquinolinium salt **4k** (43 mg, 0.125 mmol), (*E*)-(2-nitrovinyl)benzene (19 mg, 0.125 mmol), 5:2 $HCO_2H:Et_3N$ (42 μ L, 0.50 mmol) in MeCN (0.1 mL) and was purified by column chromatography (4% EtOAc in pentane) to furnish the diastereomeric tetrahydroisoquinolines **5uA** (19 mg, 41%) and **5uB** (9 mg, 19%) as colourless oils.

Data for **major diastereomer 5uA**:

HRMS (ESI): Exact mass calculated for $C_{24}H_{25}N_2O_2$ $[M+H]^+$: 373.1911, found: 373.1901.

1H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.24 (m, 5H, 5 x $C^{Ar}H$), 7.21 – 7.04 (m, 7H, 7 x $C^{Ar}H$), 6.98 (dd, $J = 7.6, 1.5$ Hz, 1H, $C^{Ar}H$), 6.90 (dd, $J = 7.6, 1.5$ Hz, 1H, $C^{Ar}H$), 4.64 – 4.59 (m, 2H, $C^{19}H_2$), 4.03 (td, $J = 9.5, 6.8$ Hz, 1H, $C^{18}H$), 3.94 (d, $J = 15.4$ Hz, 1H, C^1H_2), 3.47 (s, 2H, $C^{11}H_2$), 3.26 (d, $J = 15.5$ Hz, 1H, C^1H_2), 2.93 (dt, $J = 9.3, 2.5$ Hz, 1H, C^4H), 2.67 (dt, $J = 11.5, 1.6$ Hz, 1H, C^3H_2), 2.32 (dd, $J = 11.6, 3.2$ Hz, 1H, C^3H_2)

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4 (C^{Ar}), 138.1 (C^{Ar}), 135.8 (C^{Ar}), 134.2 (C^{Ar}), 129.7 ($C^{Ar}H$), 129.3 (2 x $C^{Ar}H$), 128.8 (2 x $C^{Ar}H$), 128.5 (2 x $C^{Ar}H$), 128.1 (2 x $C^{Ar}H$), 127.4 ($C^{Ar}H$), 127.3 ($C^{Ar}H$), 127.3 ($C^{Ar}H$), 127.1 ($C^{Ar}H$), 125.7 ($C^{Ar}H$), 79.9 ($C^{19}H$), 63.0 ($C^{11}H_2$), 55.9 (C^1H_2), 53.4 (C^3H_2), 48.3 ($C^{18}H$), 43.8 (C^4H)

IR (neat) (cm^{-1}): 3029, 2921, 2805, 1551, 1495, 1454, 1378, 1089, 911, 757, 735, 701.

Data for **minor diastereomer 5uB**:

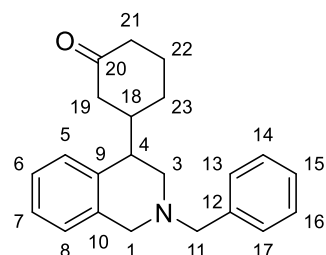
HRMS (ESI): Exact mass calculated for $C_{24}H_{25}N_2O_2$ $[M+H]^+$: 373.1911, found: 373.1904.

1H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.40 (m, 5H, 5 x $C^{Ar}H$), 7.37 – 7.30 (m, 1H, $C^{Ar}H$), 7.26 – 7.06 (m, 6H, 6 x $C^{Ar}H$), 6.81 – 6.74 (m, 2H, 2 x $C^{Ar}H$), 5.19 (dd, $J = 14.1, 12.2$ Hz, 1H, $C^{19}H_2$), 4.18 (dd, $J = 14.1, 3.8$ Hz, 1H, $C^{19}H_2$), 4.08 – 3.96 (m, 2H, $C^{18}H + C^1H_2$), 3.83 (d, $J = 12.2$ Hz, 1H, $C^{11}H_2$), 3.41 (d, $J = 14.9$ Hz, 1H, C^1H_2), 3.31 (d, $J = 12.3$ Hz, 1H, $C^{11}H_2$), 3.01 (t, $J = 4.6$ Hz, 1H, C^4H), 2.91 (d, $J = 12.3$ Hz, 1H, C^3H_2), 2.07 (dd, $J = 12.4, 4.3$ Hz, 1H, C^3H_2)

¹³C NMR (101 MHz, CDCl₃) δ 138.9 (C^{Ar}), 138.0 (C^{Ar}), 136.5 (C^{Ar}), 135.1 (C^{Ar}), 130.3 (2 x C^{Ar}H), 128.9 (2 x C^{Ar}H), 128.8 (2 x C^{Ar}H), 128.6 (C^{Ar}H), 127.8 (2 x C^{Ar}H), 127.8 (C^{Ar}H), 127.2 (C^{Ar}H), 127.1 (C^{Ar}H), 127.0 (C^{Ar}H), 126.7 (C^{Ar}H), 75.4 (C¹⁹H₂), 63.1 (C¹¹H₂), 57.4 (C¹H₂), 50.4 (C¹⁸H), 49.2 (C³H₂), 43.8 (C⁴H)

IR (neat) (cm⁻¹): 3029, 2804, 1547, 1495, 1453, 1380, 1088, 756, 738, 700.

3-(*N*-Benzyl-1,2,3,4-tetrahydroisoquinolin-4-yl)cyclohexan-1-one (**5w**)



The title compound was prepared according to General Procedure **E** using isoquinolinium salt **4k** (43 mg, 0.125 mmol), cyclohex-2-en-1-one (12 mg, 0.125 mmol), 5:2 HCO₂H:Et₃N (42 μL, 0.50 mmol) in MeCN (0.1 mL) and was purified by flash column chromatography (6-10% EtOAc in pentane) to furnish tetrahydroisoquinoline **5w** (12 mg, 30%) as an inseparable 1:1 diastereomeric mixture as a colourless oil.

Data for **both diastereomers A and B** (from the mixture):

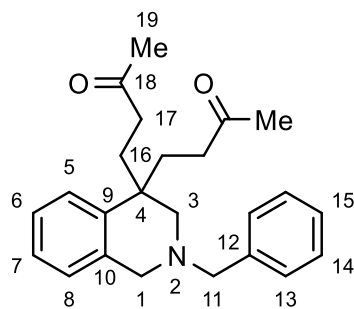
HRMS (ESI): Exact mass calculated for C₂₂H₂₆NO [M+H]⁺: 320.2009, found: 320.2009.

¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.24 (m, 5H, 5 x C^{Ar}H_{A+B}), 7.18 – 7.07 (m, 3H, 3 x C^{Ar}H_{A+B}), 7.04 – 6.96 (m, 1H, C^{Ar}H_{A+B}), 7.04 – 6.96 (m, 1H, C¹H_{2A+B}), 3.76 – 3.66 (m, 1H, C¹¹H_{2A+B}), 3.59 – 3.51 (m, 1H, C¹¹H_{2A+B}), 3.47 – 3.34 (m, 1H, C¹H_{2A+B}), 3.47 – 3.34 (m, 1H, C³H_{2A+B}), 2.79 (q, *J* = 4.2 Hz, 0.5H, C⁴H_{A/B}), 2.66 (q, *J* = 4.0 Hz, 0.5H, C⁴H_{A/B}), 2.54 – 2.44 (m, 1H, C³H_{2A+B}), 2.42 – 1.93 (m, 6H, C¹⁸H_{A+B} + C¹⁹H_{2A+B} + C²¹H_{2A+B} + C²²H_{2A/B}), 1.87 – 1.79 (m, 0.5H, C²³H_{A/B}), 1.65 – 1.42 (m, 2H, C²³H_{2A/B} + C²²H_{2A/B}), 1.41 – 1.29 (m, 0.5H, C²³H_{2A/B})

¹³C NMR (151 MHz, CDCl₃) δ 212.6 (C²⁰_{A/B}), 212.3 (C²⁰_{A/B}), 138.6 (C^{Ar}_{A/B}), 138.4 (C^{Ar}_{A/B}), 136.2 (C^{Ar}_{A/B}), 136.2 (C^{Ar}_{A/B}), 135.7 (C^{Ar}_{A/B}), 135.7 (C^{Ar}_{A/B}), 129.4 (2 x C^{Ar}H_{A/B}), 129.3 (2 x C^{Ar}H_{A/B}), 128.9 (C^{Ar}H_{A/B}), 128.6 (C^{Ar}H_{A/B}), 128.5 (2 x C^{Ar}H_{A/B}), 128.4 (2 x C^{Ar}H_{A/B}), 127.4 (C^{Ar}H_{A/B}), 127.4 (C^{Ar}H_{A/B}), 126.7 (C^{Ar}H_{A/B}), 126.6 (C^{Ar}H_{A/B}), 126.2 (C^{Ar}H_{A/B}), 126.2 (2 x C^{Ar}H_{A/B}), 126.0 (C^{Ar}H_{A/B}), 63.2 (C¹¹H_{2A/B}), 63.0 (C¹¹H_{2A/B}), 56.7 (C¹H_{2A/B}), 56.6 (C¹H_{2A/B}), 52.0 (C³H_{2A/B}), 51.7 (C³H_{2A/B}), 47.2 (C¹⁹H_{2A/B}), 45.3 (C¹⁹H_{2A/B}), 44.1 (C⁴H_{A/B}), 44.0 (C⁴H_{A/B}), 43.4 (C¹⁸H_{A/B}), 42.9 (C¹⁸H_{A/B}), 41.6 (C²¹H_{A/B}), 41.6 (C²¹H_{A/B}), 30.1 (C²³H_{2A/B}), 28.7 (C²³H_{2A/B}), 25.8 (C²²H_{2A/B}), 25.6 (C²²H_{2A/B})

IR (neat) (cm⁻¹): 3027, 2926, 2864, 2799, 2757, 1708, 1494, 1345, 1312, 1093.

4,4'-(2-Benzyl-1,2,3,4-tetrahydroisoquinoline-4,4-diyl)bis(butan-2-one) (5x)



The title compound was prepared according to modified General Procedure **F** using isoquinolinium salt **4k** (43 mg, 0.125 mmol), methyl vinyl ketone (50 μ L, 0.61 mmol), 5:2 HCO₂H:Et₃N (42 μ L, 0.50 mmol) in MeCN (0.1 mL) and was purified by flash column chromatography (2% MeCN in 1:1 pentane:CH₂Cl₂) to furnish tetrahydroisoquinoline **5x** (20 mg, 44%) as a colourless oil.

General procedure **E** gave the title compound in comparable yield of 45%, however this procedure resulted in formation of an impurity that made purification significantly more challenging and a clean sample of **5x** could not be obtained without significant losses in yield.

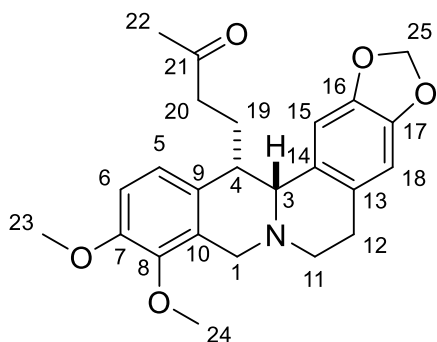
HRMS (ESI): Exact mass calculated for C₂₄H₃₀NO₂ [M+H]⁺: 364.2271, found: 364.2274.

¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.24 (m, 5H, 5 x C^{Ar}H), 7.24 – 7.08 (m, 3H, 3 x C^{Ar}H), 7.00 (dd, J = 7.5, 1.4 Hz, 1H, C^{Ar}H), 3.60 – 3.53 (m, 4H, C¹H₂ + C¹¹H₂), 2.51 – 2.37 (m, 4H, C³H₂ + C¹⁷H₂), 2.12 – 1.96 (m, 10H, C¹⁶H₂ + C¹⁷H₂ + 2 x C⁹H₃), 1.84 – 1.74 (m, 2H, C¹⁶H₂)

¹³C NMR (101 MHz, CDCl₃) δ 208.9 (C¹⁸), 139.5 (C^{Ar}), 138.3 (C^{Ar}), 135.9 (C^{Ar}), 129.4 (2 x C¹³H/C¹⁴H), 128.4 (2 x C¹³H/C¹⁴H), 127.4 (C^{Ar}H), 126.9 (C^{Ar}H), 126.7 (C^{Ar}H), 126.3 (C^{Ar}H), 126.0 (C^{Ar}H), 63.1 (C¹¹H₂), 59.4 (C¹H₂), 57.4 (C³H₂), 40.2 (C¹⁷H₂), 39.5 (C⁴H), 35.0 (C¹⁹H₃), 30.1 (C¹⁶H₂)

IR (neat) (cm⁻¹): 2925, 2797, 1712, 1493, 1452, 1366, 1159, 1095, 740, 700.

4-(9,10-Dimethoxy-5,8,13,13a-tetrahydro-6H-[1,3]dioxolo[4,5-g]isoquinolino[3,2-a]isoquinolin-13-yl)butan-2-one (5y)



The title compound was prepared according to General Procedure **E** using berberine chloride (47 mg, 0.125 mmol), methyl vinyl ketone (10 μ L, 0.125 mmol), 5:2 HCO₂H:Et₃N (42 μ L, 0.50 mmol) in MeCN (0.3 mL) and was purified by flash column chromatography (0.5% MeOH in CH₂Cl₂) to furnish tetrahydroisoquinoline **5y** (44 mg, 86%, d.r. > 25:1) as a colourless oil.

HRMS (ESI): Exact mass calculated for C₂₄H₂₈NO₅ [M+H]⁺: 410.1962, found: 410.1963.

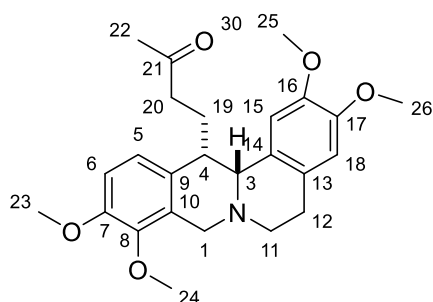
¹H NMR (400 MHz, CDCl₃) δ 6.84 (d, J = 8.4 Hz, 1H, C^{5/6}H), 6.79 (d, J = 8.4 Hz, 1H, C^{5/6}H), 6.67 (s, 1H, C^{15/18}H), 6.57 (s, 1H, C^{15/18}H), 5.92 (d, J = 1.4 Hz, 1H, C²⁵H₂), 5.90 (d, J = 1.4 Hz, 1H, C²⁵H₂), 4.21 (d, J = 16.1 Hz, 1H, C¹H₂), 3.86 (s, 3H, C^{23/24}H₃), 3.86 (s, 3H, C^{23/24}H₃), 3.68 (d, J = 2.9 Hz, 1H, C³H), 3.48 (d, J = 16.1 Hz, 1H, C¹H₂), 3.16 – 2.99 (m, 3H, C⁴H + C¹¹H₂, C¹²H₂), 2.63 – 2.49 (m, 2H, C¹¹H₂, C¹²H₂), 2.49 – 2.34 (m, 1H, C²⁰H₂), 2.26 – 2.13 (m, 1H, C²⁰H₂), 1.95 (s, 3H, C²²H₂), 1.76 – 1.60 (m, 2H, C¹⁹H₂)

¹³C NMR (101 MHz, CDCl₃) δ 209.7 (C²¹), 149.6 (C^{Ar}), 146.4 (C^{Ar}), 145.8 (C^{Ar}), 145.1 (C^{Ar}), 132.2 (C^{Ar}), 129.4 (C^{Ar}), 129.2 (C^{Ar}), 128.9 (C^{Ar}), 124.5 (C^{5/6}H), 110.3 (C^{5/6}H), 108.4 (C^{15/18}H), 105.6 (C^{15/18}H), 100.8 (C²⁵H₂), 63.4 (C³H), 60.1 (C^{23/24}H₃), 55.8 (C^{23/24}H₃), 54.2 (C¹H₂), 50.5 (C¹¹H₂), 43.3 (C⁴H), 41.7 (C²⁰H₂), 29.8 (C¹²H₂), 29.7 (C²²H₃), 26.1 (C¹⁹H₂)

IR (neat) (cm⁻¹): 2905, 1709, 1484, 1278, 1245, 1221, 1163, 1087, 1070, 1037, 859, 808, 730.

Relative stereochemistry was assigned based on the *J*_{H3–H4} coupling constant (2.9 Hz observed, calculated¹⁰ for *cis*: 3.6 Hz)

4-(2,3,9,10-Tetramethoxy-5,8,13,13a-tetrahydro-6H-isoquinolino[3,2-a]isoquinolin-13-yl)butan-2-one (5z)



The title compound was prepared according to General Procedure E using palmatine chloride (48 mg, 0.125 mmol), methyl vinyl ketone (10 μL, 0.125 mmol), 5:2 HCO₂H:Et₃N (42 μL, 0.50 mmol) in MeCN (0.2 mL) and was purified by column chromatography (0.4–0.5% MeOH in CH₂Cl₂) to furnish tetrahydroisoquinoline **5y** (40 mg, 75%, d.r. > 25:1) as a

colourless oil.

HRMS (ESI): Exact mass calculated for C₂₅H₃₂NO₅ [M+H]⁺: 426.2280, found: 426.2279.

¹H NMR (400 MHz, CDCl₃) δ 6.85 (d, *J* = 8.4 Hz, 1H, C^{5/6}H), 6.79 (d, *J* = 8.4 Hz, 1H, C^{5/6}H), 6.70 (s, 1H, C^{15/18}H), 6.60 (s, 1H, C^{15/18}H), 4.21 (d, *J* = 16.1 Hz, 1H, C¹H₂), 3.89 (s, 3H, C^{23/24/25/26}H₃), 3.87 (s, 3H, C^{23/24/25/26}H₃), 3.86 (s, 3H, C^{23/24/25/26}H₃), 3.86 (s, 4H, C^{23/24/25/26}H₃), 3.74 – 3.66 (d, *J* = 3.0 Hz, 1H, C³H), 3.49 (d, *J* = 16.1 Hz, 1H, C¹H₂), 3.20 – 3.04 (m, 3H, C⁴H + C¹¹H₂, C¹²H₂), 2.64 – 2.52 (m, 2H, C¹¹H₂, C¹²H₂), 2.42 – 2.31 (m, 1H, C²⁰H₂), 2.28 – 2.16 (m, 1H, C²⁰H₂), 1.93 (s, 3H, C²²H₃), 1.72 – 1.63 (m, 2H, C¹⁹H₂)

¹³C NMR (101 MHz, CDCl₃) δ 209.9 (C²¹), 150.6 (C^{Ar}), 147.7 (C^{Ar}), 147.4 (C^{Ar}), 145.3 (C^{Ar}), 132.4 (C^{Ar}), 129.0 (C^{Ar}), 128.4 (C^{Ar}), 128.2 (C^{Ar}), 125.1 (C^{5/6}H), 111.4 (C^{15/18}H), 110.4 (C^{5/6}H), 108.8 (C^{15/18}H), 63.1 (C³H), 60.2 (C^{23/24/25/26}H₃), 56.1 (C^{23/24/25/26}H₃), 55.9 (C^{23/24/25/26}H₃), 55.9 (C^{23/24/25/26}H₃), 54.4 (C¹H₂), 51.5 (C¹¹H₂), 42.0 (C⁴H), 41.6 (C²⁰H₂), 29.8 (C²⁰H₂), 29.4 (C¹²H₂), 26.4 (C¹⁹H₂)

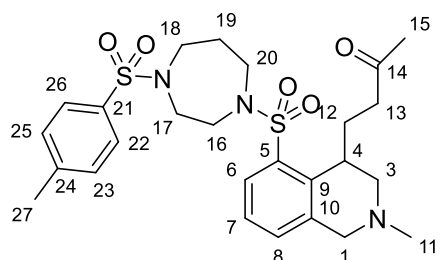
IR (neat) (cm⁻¹): 2937, 2834, 1710, 1610, 1517, 1456, 1279, 1231, 1144, 1110, 913.

Relative stereochemistry was assigned based on the *J*_{H3–H4} coupling constant (3.0 Hz observed, calculated¹¹ for *cis*: 3.6 Hz)

¹⁰ <https://www.nmrdb.org/> (accessed 07.10.2021)

¹¹ <https://www.nmrdb.org/> (accessed 07.10.2021)

**4-(2-Methyl-5-((4-tosyl-1,4-diazepan-1-yl)sulfonyl)-1,2,3,4-tetrahydroisoquinolin-4-yl)butan-2-one
(5aa)**



The title compound was prepared according to General Procedure E using isoquinolinium salt **4m** (83 mg, 0.141 mmol), methyl vinyl ketone (12 μ L, 0.141 mmol), 5:2 HCO₂H:Et₃N (42 μ L, 0.50 mmol) in MeCN (0.3 mL) and was purified by flash column chromatography (1% MeOH in CH₂Cl₂)

to furnish tetrahydroisoquinoline **5aa** (71 mg, 95%) as a colourless oil.

HRMS (ESI): Exact mass calculated for C₂₆H₃₆N₃O₅S₂ [M+H]⁺: 534.2091, found: 534.2090.

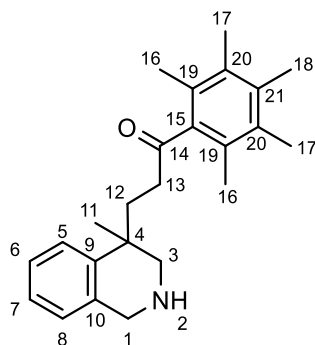
¹H NMR (400 MHz, CDCl₃) δ 7.59 (d, J = 8.3 Hz, 2H, 2 x C^{Ar}H), 7.37 (dd, J = 7.5, 1.7 Hz, 1H, C^{Ar}H), 7.24 (d, J = 7.9 Hz, 2H, 2 x C^{Ar}H), 7.20 – 7.10 (m, 2H, 2 x C^{Ar}H), 3.92 (d, J = 15.6 Hz, 1H, C¹H₂), 3.51 – 3.28 (m, 9H, C¹⁶H₂ + C¹⁷H₂ + C¹⁸H₂ + C²⁰H₂ + C⁴H), 3.19 (d, J = 15.6 Hz, 1H, C¹H₂), 2.79 (dt, J = 11.7, 1.9 Hz, 1H, C³H₂), 2.55 – 2.44 (m, 1H, C¹³H₂), 2.45 – 2.35 (m, 1H, C¹³H₂), 2.35 (s, 3H, C²⁷H₃), 2.30 (s, 3H, C¹¹H₃), 2.25 (dd, J = 11.4, 3.2 Hz, 1H, C³H₂), 2.13 – 1.99 (m, 5H, C¹⁵H₃ + C¹²H₂), 1.94 (td, J = 6.3, 2.1 Hz, 2H, C¹⁹H₂)

¹³C NMR (101 MHz, CDCl₃) δ 210.1 (C¹⁴), 143.6 (C^{Ar}), 138.6 (C^{Ar}), 137.7 (C^{Ar}), 137.6 (C^{Ar}), 136.2 (C^{Ar}), 131.3 (C^{Ar}H), 129.9 (2 x C^{Ar}H), 126.9 (2 x C^{Ar}H), 126.2 (C^{Ar}H), 126.1 (C^{Ar}H), 57.6 (C¹H₂), 54.3 (C³H₂), 51.8 (C^{16/17/18/20}H₂), 51.6 (C^{16/17/18/20}H₂), 47.7 (C^{16/17/18/20}H₂), 47.7 (C^{16/17/18/20}H₂), 46.0 (C¹¹H₃), 43.0 (C¹³H₂), 36.3 (C⁴H), 30.2 (C¹²H₂), 29.7 (C¹⁵H₃), 29.6 (C¹⁹H₂), 21.6 (C²⁷H₃)

IR (neat) (cm⁻¹): 2947, 2784, 1709, 1321, 1290, 1228, 1090, 1057, 983, 906.

Derivatisations of tetrahydroisoquinolines

3-(4-Methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one (6a)



In a microwave vial tetrahydroisoquinoline **5d** (60 mg, 0.13 mmol) was charged and dissolved in MeOH (5 mL). To the solution was added Pd(OH)₂/C (20% wt, 7.7 mg, 11 μmol, 8 mol%) and ammonium formate (86.0 mg, 1.36 mmol). The reaction mixture was then heated to 65 °C and stirred for 16 h. After cooling to room temperature, the reaction was poured onto 1M NaOH and extracted with CH₂Cl₂ (3 × 10 mL). After drying over MgSO₄ and evaporating the solvent the crude product was

purified by silica gel chromatography (2% MeOH in CH₂Cl₂) to give amine **6a** (37 mg, 78%) as a colourless oil.

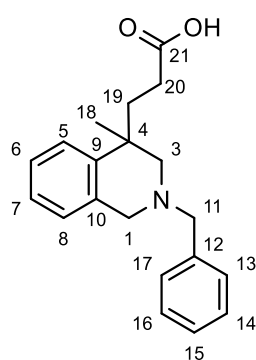
HRMS (ESI): Exact mass calculated for C₂₄H₃₂NO [M+H]⁺: 350.2478, found: 350.2479.

¹H NMR (400 MHz, CDCl₃) δ 7.28 (dd, *J* = 7.8, 1.4 Hz, 1H, C⁵H), 7.21 – 7.14 (m, 1H, C⁶H), 7.09 (td, *J* = 7.4, 1.4 Hz, 1H, C⁷H), 6.97 (dd, *J* = 7.6, 1.4 Hz, 1H, C⁸H), 3.97 (s, 2H, C¹H₂), 2.97 (d, *J* = 13.0 Hz, 1H, C³H_a), 2.85 (d, *J* = 13.0 Hz, 1H, C³H_b), 2.75 – 2.59 (m, 1H, C¹³H_a), 2.54 – 2.40 (m, 1H, C¹³H_b), 2.30 (ddd, *J* = 14.4, 11.6, 4.1 Hz, 1H, C¹²H_a), 2.21 (s, 3H, C¹⁸H), 2.16 (s, 6H, C¹⁶H), 2.12 (s, 1H, N²H), 2.01 (s, 6H, C¹⁷H), 1.97 (dd, *J* = 10.4, 4.1 Hz, 1H, C¹²H_b), 1.33 (s, 3H, C¹¹H).

¹³C NMR (151 MHz, CDCl₃) δ 211.9 (C¹⁴), 141.9 (C⁹), 140.9 (C¹⁵), 135.6 (C¹⁰), 135.5 (C²¹), 133.1 (2 × C¹⁹), 127.3 (2 × C²⁰), 126.7 (C⁷), 126.6 (C⁶), 126.2 (C⁸H), 125.8 (C⁷H), 55.0 (C³), 49.3 (C¹), 41.4 (C¹³), 35.6 (C⁴), 33.9 (C¹²), 28.7 (C¹¹), 17.2 (2 × C¹⁷), 16.7 (C¹⁸), 16.0 (2 × C¹⁶).

IR (neat) (cm⁻¹): 2923, 2865, 1698, 1489, 1446, 1407, 1381, 1311, 1118, 930.

3-(2-Benzyl-4-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)propanoic acid (6b)



In a microwave vial tetrahydroisoquinoline **5d** (140 mg, 0.32 mmol) was charged and dissolved in HFIP (1.7 mL). To the solution was added concentrated hydrochloric acid (37%, 0.42 mL, 5.1 mmol) and the reaction mixture was heated to 65 °C and stirred for 19 hours. The reaction was allowed to cool to room temperature and diluted with water (10 mL) and CH₂Cl₂ (20 mL). The phases were separated, the aqueous phase was extracted once more with 20 mL CH₂Cl₂ and the combined organic phases dried over

MgSO₄. After evaporation of the solvent the crude product was purified by silica gel chromatography (3% MeOH in CH₂Cl₂) to give carboxylic acid **6b** (85 mg, 86%) as a colourless oil.

HRMS (ESI): Exact mass calculated for C₂₀H₂₄NO₂ [M+H]⁺: 310.1802, found: 310.1802.

¹H NMR (400 MHz, CDCl₃) δ 8.82 (br s, 1H, C²¹OH), 7.42 – 7.38 (m, 2H, C⁸ⁿH), 7.34 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 2H, C⁸ⁿH), 7.31 – 7.27 (m, 1H, C⁸ⁿH), 7.26 – 7.23 (m, 1H, C⁵H), 7.19 (td, *J* = 7.5, 1.5 Hz, 1H, C⁷H), 7.11 (td, *J* = 7.4, 1.5 Hz, 1H, C⁶H), 6.98 (dd, *J* = 7.6, 1.3 Hz, 1H, C⁸H), 3.74 (d, *J* = 14.7 Hz, 1H, C¹H_a), 3.72 – 3.61 (m, 2H, C¹¹H), 3.54 (d, *J* = 14.7 Hz, 1H, C¹H_b), 2.68 (dd, *J* = 11.6, 1.3 Hz, 1H, C³H_a), 2.42 – 2.30 (m, 2H, C³H_b + C¹⁹H_a), 2.14 (ddd, *J* = 13.1, 10.2, 5.4 Hz, 1H, C²⁰H_a), 2.05 (ddd, *J* = 15.6, 10.1, 5.4 Hz, 1H, C¹⁹H_b), 1.89 (ddd, *J* = 13.1, 10.1, 5.4 Hz, 1H, C²⁰H_b), 1.27 (s, 3H, C¹⁸H)

¹³C NMR (101 MHz, CDCl₃) δ 179.5 (C²¹), 141.5 (C⁹), 137.7 (C¹⁰), 134.4 (C¹²), 129.4 (C¹³ + C¹⁷), 128.5 (C¹⁴ + C¹⁶), 127.5 (C¹⁵), 126.9 (C⁸), 126.6 (C⁷), 126.1 (C⁶), 126.0 (C⁵), 62.9 (C¹¹), 61.8 (C¹), 57.0 (C³), 37.8 (C⁴), 37.4 (C²⁰), 30.4 (C¹⁹), 27.8 (C¹⁸)

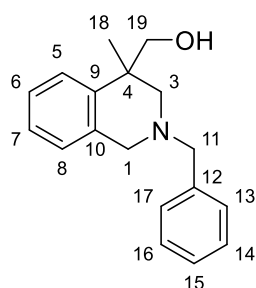
IR (neat) (cm⁻¹): 2924, 2799, 1708, 1558, 1493, 1395, 1304, 1211, 1074, 1028, 912.

Alkylation of isoquinolinium salts

General procedure G: Alkylation of isoquinolinium salts with aldehydes

Isoquinolinium salt (0.125 mmol, 1.0 equiv.) and aldehyde (1.0 to 4.0 equiv.) are dissolved in MeCN (0.10 mL \pm 1.25 M). Upon addition of HCO₂H:NEt₃ 5:2 complex (42 μ L, 4.0 equiv.) the reaction mixture is heated to 80 °C for 18 hours. The reaction was diluted with CH₂Cl₂ (10 mL) and quenched with an aqueous solution of K₂CO₃ (10 mL, 0.1 M). The solution was separated, and the aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL). The organic layers were combined, dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography to furnish the respective amines.

(*N*-Benzyl-4-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)methanol (**7a**)



The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4a** (45 mg, 0.125 mmol), formaldehyde (37 wt. % in H₂O, 19 μ L, 0.25 mmol), 5:2 HCO₂H:Et₃N (42 μ L, 0.50 mmol) in MeCN (0.1 mL) and was purified by flash column chromatography (20% EtOAc in pentane) to furnish tetrahydroisoquinoline **7a** (25 mg, 75%) as a colourless oil.

HRMS (ESI): Exact mass calculated for C₁₉H₂₂NO[M+H]⁺: 268.1696, found:

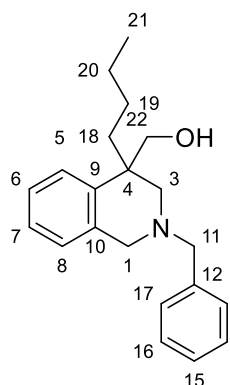
268.1696.

¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.36 (m, 4H, 4 x C^{Ar}H), 7.36 – 7.29 (m, 2H, 2 x C^{Ar}H), 7.25 (t, *J* = 7.4 Hz, 1H, C^{Ar}H), 7.16 (td, *J* = 7.4, 1.3 Hz, 1H, C^{Ar}H), 7.01 (dd, *J* = 7.5, 1.4 Hz, 1H, C^{Ar}H), 3.91 (dd, *J* = 14.9, 1.8 Hz, 1H, C¹H₂), 3.78 (d, *J* = 10.0 Hz, 1H, C¹⁹H₂), 3.73 – 3.61 (m, 3H, 2 x C¹¹H₂ + C¹⁹H₂), 3.39 (d, *J* = 14.8 Hz, 1H, C¹H₂), 3.06 (dd, *J* = 11.4, 1.9 Hz, 1H, C³H₂), 2.48 (dd, *J* = 11.4, 2.6 Hz, 1H, C³H₂), 1.16 (s, 3H, C¹⁸H₃);

¹³C NMR (101 MHz, CDCl₃) δ 139.6 (C^{Ar}), 137.0 (C^{Ar}), 135.0 (C^{Ar}), 129.3 (2 x C^{Ar}H), 128.7 (2 x C^{Ar}H), 127.7 (C^{Ar}H), 127.2 (C^{Ar}H), 126.4 (C^{Ar}H), 126.3 (C^{Ar}H), 125.7 (C^{Ar}H), 76.2 (C¹⁹H₂), 63.7 (C³H₂), 63.1 (C¹¹H₂), 56.9 (C¹H₂), 39.1 (C⁴), 22.5 (C¹⁸H₃).

IR (neat) (cm⁻¹): 3295, 3029, 2833, 1494, 1452, 1092, 1073, 1050, 1028, 762.

(*N*-Benzyl-4-butyl-1,2,3,4-tetrahydroisoquinolin-4-yl)methanol (**7b**)

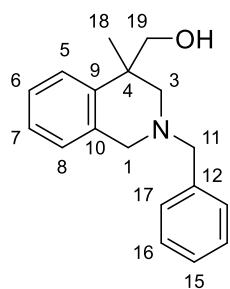


The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4b** (43 mg, 0.125 mmol), formaldehyde (37 wt. % in H₂O, 19 μ L, 0.25 mmol), 5:2 HCO₂H:Et₃N (42 μ L, 0.50 mmol) in MeCN (0.1 mL) and was purified by flash column chromatography (12-20% EtOAc in pentane) to furnish tetrahydroisoquinoline **7b** (28 mg, 72%) as a colourless oil. Spectroscopic data are in accordance with those described in the literature.⁴

¹H NMR (400 MHz, CDCl₃) δ 7.37 (d, J = 4.4 Hz, 4H, 4 x C^{Ar}H), 7.34 – 7.22 (m, 3H, 3 x C^{Ar}H), 7.14 (ddd, J = 8.5, 7.1, 1.6 Hz, 1H, C^{6/7}H), 6.99 (d, J = 7.6 Hz, 1H, C^{5/8}H), 3.85 (dd, J = 14.7, 1.9 Hz, 1H, C¹H₂), 3.79 (d, J = 9.8 Hz, 1H, C²²H₂), 3.71 (d, J = 12.8 Hz, 1H, C¹¹H₂), 3.63 (d, J = 7.3 Hz, 1H, C¹¹H₂), 3.60 (dd, J = 7.1 Hz, 2.7 Hz, 1H, C²²H₂), 3.32 (d, J = 14.6 Hz, 1H, C¹H₂), 2.99 (dd, J = 11.4, 1.9 Hz, 1H, C³H₂), 2.65 (dd, J = 11.4, 2.7 Hz, 1H, C³H₂), 1.68 (ddd, J = 13.9, 12.2, 4.6 Hz, 1H, C¹⁸H₂), 1.40 (ddd, J = 13.9, 12.0, 4.7 Hz, 1H, C¹⁸H₂), 1.31 – 1.20 (m, 2H, C²⁰H₂), 1.17 – 0.97 (m, 2H, C¹⁹H₂), 0.85 (t, J = 7.3 Hz, 3H, C²¹H₃).

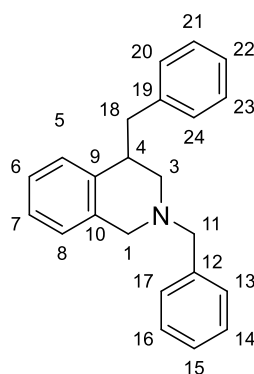
¹³C NMR (101 MHz, CDCl₃) δ 138.2 (C^{Ar}), 137.0 (C^{Ar}), 135.7 (C^{Ar}), 129.3 (2 x C^{Ar}H), 128.7 (2 x C^{Ar}H), 127.7 (C^{Ar}H), 127.2 (C^{Ar}H), 126.3 (C^{Ar}H), 126.1 (C^{Ar}H), 125.8 (C^{Ar}H), 76.3 (C²²H₂), 63.3 (C¹¹H₂), 61.0 (C³H₂), 56.9 (C¹H₂), 42.3 (C⁴), 35.1 (C¹⁸H₂), 26.2 (C¹⁹H₂), 23.6 (C²⁰H₂), 14.0 (C²¹H₃).

(*N*-Benzyl-4-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)methanol (**7a**)



The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4k** (43 mg, 0.125 mmol), formaldehyde (37 wt. % in H₂O, 29 μ L, 0.375 mmol), 5:2 HCO₂H:Et₃N (63 μ L, 0.75 mmol) in MeCN (0.1 mL) and was purified by flash column chromatography (20% EtOAc in pentane) to furnish tetrahydroisoquinoline **7a** (23 mg, 69%) as a colourless oil. For full characterisation data see above.

2,4-Dibenzyl-1,2,3,4-tetrahydroisoquinoline (**7c**)



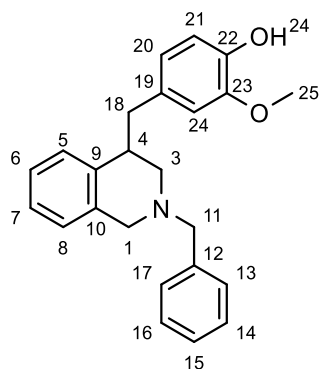
The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4k** (43 mg, 0.125 mmol), benzaldehyde (13 mg, 0.125 mmol), 5:2 HCO₂H:Et₃N (42 μ L, 0.5 mmol) in MeCN (0.1 mL) and was purified by column chromatography (2.5% EtOAc in pentane) to furnish

tetrahydroisoquinoline **7c** (28 mg, 72%) as a colourless oil. Spectroscopic data are in accordance with those described in the literature.¹²

¹H NMR (400 MHz, CDCl₃) δ 7.48 – 7.42 (m, 2H, 2 x C^{Ar}H), 7.42 – 7.31 (m, 3H, 3 x C^{Ar}H), 7.25 – 7.12 (m, 6H, 6 x C^{Ar}H), 7.07 – 7.00 (m, 3H, 3 x C^{Ar}H), 3.90 (d, *J* = 14.8 Hz, 1H, C¹H₂), 3.74 (d, *J* = 12.9 Hz, 1H, C¹¹H₂), 3.56 (d, *J* = 12.8 Hz, 1H, C¹¹H₂), 3.46 (d, *J* = 14.8 Hz, 1H, C¹H₂), 3.07 – 2.97 (m, 3H, C¹⁸H₂ + C⁴H), 2.79 (d, *J* = 11.5 Hz, 1H, C³H₂), 2.39 (d, *J* = 11.6 Hz, 1H, C³H₂);

¹³C NMR (101 MHz, CDCl₃) δ 140.9 (C^{Ar}), 138.7 (C^{Ar}), 138.7 (C^{Ar}), 135.2 (C^{Ar}), 129.6 (2 x C^{Ar}H), 129.5 (2 x C^{Ar}H), 128.8 (C^{Ar}H), 128.5 (2 x C^{Ar}H), 128.4 (2 x C^{Ar}H), 127.3 (C^{Ar}H), 126.6 (C^{Ar}H), 126.3 (C^{Ar}H), 126.0 (2 x C^{Ar}H), 63.1 (C¹¹H₂), 56.8 (C¹H₂), 53.1 (C³H₂), 42.9 (C¹⁸H₂), 41.5 (C⁴H).

4-((2-Benzyl-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)-2-methoxyphenol (**7d**)



The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4k** (40 mg, 0.115 mmol), vanillin (26 mg, 0.17 mmol) and 5:2 HCO₂H:Et₃N (39 μL, 0.46 mmol) in MeCN (0.1 mL) and was purified by column chromatography (10% EtOAc in pentane) to furnish phenol **7d** (30 mg, 72%) as a colourless oil.

HRMS (ESI): Exact mass calculated for C₂₄H₂₆NO₂ [M+H]⁺: 360.1958 found: 360.1957.

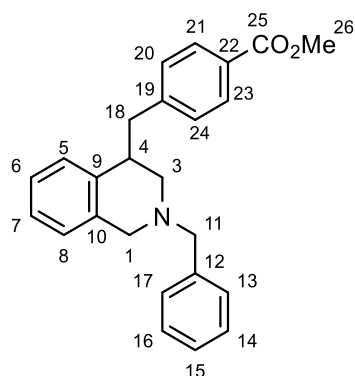
¹H NMR (400 MHz, CDCl₃) δ 7.47 – 7.42 (m, 2H, C¹³H + C¹⁷H), 7.40 – 7.34 (m, 2H, C¹⁴H + C¹⁶H), 7.34 – 7.28 (m, 1H, C¹⁵H), 7.21 – 7.11 (m, 3H, C⁶H – C⁸H), 7.06 – 6.99 (m, 1H, C⁵H), 6.77 (d, *J* = 8.0 Hz, 1H, C²¹H), 6.63 (d, *J* = 1.9 Hz, 1H, C²⁴H), 6.51 (dd, *J* = 8.0, 1.9 Hz, 1H, C²⁰H), 5.52 (br s, 1H, O²⁴H), 3.86 (d, *J* = 14.9 Hz, 1H, C¹H_a), 3.80 (s, 3H, C²⁵H₃), 3.72 (d, *J* = 13.1 Hz, 1H, C¹¹H_a), 3.59 (d, *J* = 13.0 Hz, 1H, C¹¹H_b), 3.45 (d, *J* = 14.9 Hz, 1H, C¹H_b), 2.96 (d, *J* = 5.2 Hz, 3H, C⁴H + C¹⁸H₂), 2.80 (ddd, *J* = 11.1, 1.8 Hz, 1H, C³H_a), 2.45 (dd, *J* = 11.5, 3.3 Hz, 1H, C³H_b).

¹³C NMR (101 MHz, CDCl₃) δ 146.4 (C²²), 143.9 (C²³), 138.8 (C⁹), 138.6 (C¹⁹), 135.1 (C¹²), 133.1 (C¹⁰), 129.3 (C¹³H + C¹⁷H), 128.8 (C⁸H), 128.5 (C¹⁴H + C¹⁶H), 127.3 (C¹⁵H), 126.6 (C⁵H), 126.2 (C⁷H), 125.9 (C⁶H), 122.2 (C²⁰H), 114.3 (C²¹H), 111.9 (C²⁴H), 63.1 (C¹¹H₂), 56.8 (C¹H₂), 56.0 (C²⁵H₃), 53.6 (C³H₂), 42.6 (C¹⁸H₂), 41.6 (C⁴H).

IR (neat) (cm⁻¹): 3531, 3025, 2921, 2798, 1512, 1429, 1268, 1206, 1120, 1033, 856, 821.

¹²B. Sundararaju, M. Achard, G. V. M. Sharma, C. Bruneau, *J. Am. Chem. Soc.* **2011**, 133, 10340–10343.

4-((2-Benzyl-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)benzonitrile (7e)



The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4k** (40 mg, 0.12 mmol), methyl 4-formylbenzoate (19 mg, 0.12 mmol) and 5:2 HCO₂H:Et₃N (39 μ L, 0.46 mmol) in MeCN (0.1 mL) and was purified by column chromatography (5% Et₂O in pentane) to furnish methyl ester **7e** (27 mg, 63%) as a colourless oil.

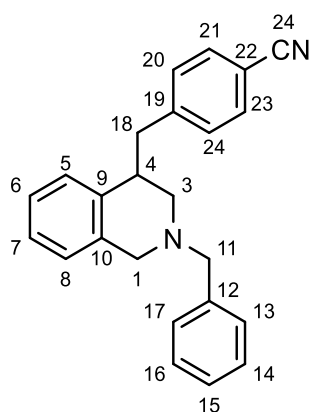
HRMS (ESI): Exact mass calculated for C₂₅H₂₆NO₂ [M+H]⁺: 372.1958 found: 372.1958.

¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, J = 8.2 Hz, 2H, C²¹H + C²³H), 7.46 – 7.33 (m, 5H, C^{Bn}H), 7.21 – 7.12 (m, 3H, C⁵H – C⁷H), 7.04 (dd, J = 7.8, 5.8 Hz, 3H, C²⁰H + C²⁴H + C⁸H), 3.92 (s, 3H, C²⁶H₃), 3.88 – 3.95 (m, 1H, C¹H_a), 3.75 (d, J = 12.7 Hz, 1H, C¹¹H_a), 3.48 (m, 2H, C¹H_b + C¹¹H_b), 3.14 – 2.95 (m, 3H, C¹⁸H₂ + C⁴H), 2.73 (ddd, J = 11.8, 1.9, 1.9 Hz, 1H, C³H_a), 2.35 (dd, J = 11.6, 3.7 Hz, 1H, C³H_b).

¹³C NMR (101 MHz, CDCl₃) δ 167.2 (C²⁵O), 146.6 (C¹⁹), 138.6 (C⁹), 138.2 (C¹²), 135.1 (C²²), 129.6 (C²¹H + C²³H), 129.5 (C¹³H + C¹⁷H), 129.4 (C²⁰H + C²⁴H), 128.7 (C⁶H), 128.4 (C¹⁴H + C¹⁶H), 127.9 (C¹⁰), 127.3 (C¹⁵H), 126.6 (C⁸H), 126.2 (C⁷H), 126.0 (C⁵H), 62.9 (C¹¹H₂), 56.9 (C¹H₂), 52.7 (C³H₂), 52.0 (C²⁶H₃), 42.8 (C¹⁸H₂), 41.3 (C⁴H).

IR (neat) (cm⁻¹): 3027, 2921, 2799, 1718, 1434, 1275, 1177, 1101, 757, 740, 723.

4-((2-Benzyl-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)benzonitrile (7f)



The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4k** (40 mg, 0.115 mmol), 4-cyanobenzaldehyde (23 mg, 0.17 mmol) and 5:2 HCO₂H:Et₃N (39 μ L, 0.46 mmol) in MeCN (0.1 mL) and was purified by column chromatography (10% EtOAc in pentane) to furnish nitrile **7f** (23 mg, 58%) as a colourless solid.

m.p.: 113 °C (CHCl₃)

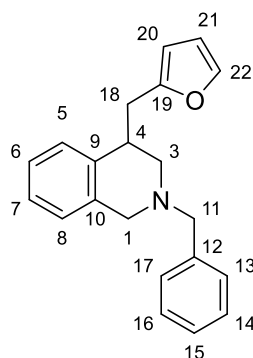
HRMS (ESI): Exact mass calculated for C₂₄H₂₃N₂ [M+H]⁺: 339.1856, found: 339.1855.

¹H NMR (600 MHz, CDCl₃) δ 7.43 (d, J = 8.2 Hz, 2H, C²¹H + C²³H), 7.40 – 7.33 (m, 5H, C^{Bn}H), 7.22 – 7.15 (m, 2H, C⁶H + C⁷H), 7.13 (dd, J = 6.6, 2.6 Hz, 1H, C⁵H), 7.07 – 7.04 (m, 1H, C⁸H), 6.98 (d, J = 7.8 Hz, 2H, C²⁰H + C²⁴H), 3.95 (d, J = 14.9 Hz, 1H, C¹H_a), 3.78 (d, J = 12.7 Hz, 1H, C¹¹H_a), 3.49 (d, J = 14.8 Hz, 1H, C¹H_b), 3.44 (d, J = 12.7 Hz, 1H, C¹¹H_b), 3.19 – 3.01 (m, 1H, C¹⁸H_a), 3.00 – 2.90 (m, 2H, C¹⁸H_b + C⁴H), 2.68 (d, J = 11.6 Hz, 1H, C³H_a), 2.42 – 2.26 (m, 1H, C³H_b).

¹³C NMR (151 MHz, CDCl₃) δ 146.6 (C¹⁹), 138.5 (C¹²), 137.8 (C⁹), 135.1 (C¹⁰), 132.0 (C²⁰H + C²⁴H), 130.1 (C²¹H + C²³H), 129.7 (C¹³H + C¹⁷H), 128.7 (C⁵H), 128.4 (C¹⁴H + C¹⁶H), 127.3 (C¹⁵H), 126.6 (C⁸H), 126.3 (C⁷H), 126.2 (C⁶H), 119.1 (C²²), 109.7 (C²⁴N), 62.8 (C¹¹H₂), 57.1 (C¹H₂), 52.1 (C³H₂), 42.8 (C¹⁸H₂), 41.2 (C⁴H).

IR (neat) (cm⁻¹): 3028, 2922, 2800, 2755, 2226, 1606, 1091, 851, 749, 700.

***N*-Benzyl-4-(furan-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline (7g)**



The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4k** (43 mg, 0.125 mmol), furfural (13 mg, 0.125 mmol), 5:2 HCO₂H:Et₃N (42 μL, 0.5 mmol) in MeCN (0.1 mL) and was purified by column chromatography (2% EtOAc in pentane) to furnish tetrahydroisoquinoline **7g** (33 mg, 87%) as a colourless oil.

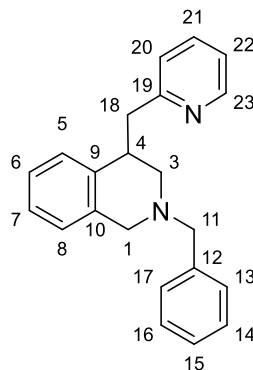
HRMS (ESI): Exact mass calculated for C₂₁H₂₂NO [M+H]⁺: 304.1696, found: 304.1696.

¹H NMR (400 MHz, CDCl₃) δ 7.44 – 7.27 (m, 6H, 6 x C^{Ar}H), 7.18 – 7.10 (m, 3H, 3 x C^{Ar}H), 7.05 – 7.00 (m, 1H,), 6.22 (dd, *J* = 3.2, 1.8 Hz, 1H, C^{20/21}H), 5.70 (d, *J* = 3.0 Hz, 1H, C^{20/21}H), 3.86 (d, *J* = 14.5 Hz, 1H, C¹H), 3.74 (d, *J* = 13.0 Hz, 1H, C¹¹H₂), 3.57 (d, *J* = 13.0 Hz, 1H, C¹¹H₂), 3.46 (d, *J* = 14.8 Hz, 1H, C¹H₂), 3.16 – 3.07 (m, 2H, C⁴H + C¹⁸H₂), 3.02 – 2.90 (m, 1H, C¹⁸H₂), 2.83 – 2.48 (m, 1H, C³H₂), 2.48 (dd, *J* = 11.4, 3.3 Hz, 1H, C³H₂);

¹³C NMR (101 MHz, CDCl₃) δ 154.8 (C¹⁹H), 141.1 (C^{Ar}H), 138.9 (C^{Ar}), 138.1 (C^{Ar}), 135.3 (C^{Ar}), 129.3 (2 x C^{Ar}H), 128.8 (C^{Ar}H), 128.4 (2 x C^{Ar}H), 127.2 (C^{Ar}H), 126.6 (C^{Ar}H), 126.3 (C^{Ar}H), 126.1 (C^{Ar}H), 110.2 (C^{20/21}H), 106.6 (C^{20/21}H), 63.0 (C¹¹H₂), 56.8 (C¹H₂), 53.8 (C³H₂), 38.6 (C⁴H), 35.1 (C¹⁸H₂);

IR (neat) (cm⁻¹): 3026, 2911, 2799, 2756, 1598, 1368, 1145, 1095, 1029, 1010, 922.

***N*-Benzyl-4-(pyridin-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline (7h)**



The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4k** (43 mg, 0.125 mmol), picolinaldehyde (13 mg, 0.125 mmol), 5:2 HCO₂H:Et₃N (42 μL, 0.50 mmol) in MeCN (0.1 mL) and was purified by flash column chromatography (0.5% MeOH in CH₂Cl₂) to furnish tetrahydroisoquinoline **7h** (20 mg, 51%) as a colourless oil.

HRMS (ESI): Exact mass calculated for C₂₂H₂₃N₂ [M+H]⁺: 315.1856, found: 315.1857.

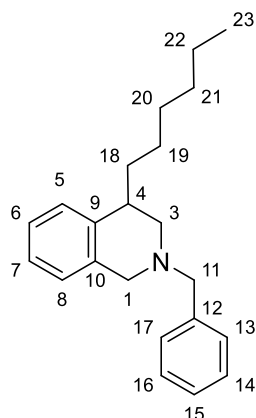
¹H NMR (400 MHz, CDCl₃) δ 8.56 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H, C²³H), 7.44 – 7.27 (m, 6H, 6 x C^{Ar}H), 7.23 – 7.17 (m, 1H, C^{Ar}H), 7.16 – 7.11 (m, 2H, 2 x C^{Ar}H), 7.09 – 7.00 (m, 2H, 2 x C^{Ar}H), 6.67 (dt, *J* = 7.8, 1.1 Hz,

1H, C^{Ar}H), 3.91 (dd, $J = 14.8, 1.3$ Hz, 1H, C¹H₂), 3.73 (d, $J = 12.9$ Hz, 1H, C¹¹H₂), 3.52 – 3.43 (m, 2H, C¹H₂ + C¹¹H₂), 3.41 – 3.31 (m, 1H, C⁴H), 3.21 – 3.09 (m, 2H, C¹⁸H₂), 2.70 (ddd, $J = 11.6, 2.8, 1.4$ Hz, 1H, C³H₂), 2.40 (dd, $J = 11.6, 4.0$ Hz, 1H, C³H₂);

¹³C NMR (101 MHz, CDCl₃) δ 160.7 (C¹⁹), 149.6 (C²³H), 138.8 (C^{Ar}), 138.6 (C^{Ar}), 136.1 (C^{Ar}H), 135.1 (C^{Ar}), 129.5 (2 x C^{Ar}H), 128.9 (C^{Ar}H), 128.4 (2 x C^{Ar}H), 127.2 (C^{Ar}H), 126.6 (C^{Ar}H), 126.3 (C^{Ar}H), 126.0 (C^{Ar}H), 124.4 (C^{Ar}H), 121.1 (C^{Ar}H), 63.0 (C¹¹H₂), 57.0 (C¹H₂), 53.5 (C³H₂), 45.2 (C¹⁸H₂), 39.6 (C⁴H);

IR (neat) (cm⁻¹): 3026, 2798, 2756, 1590, 1568, 1470, 1438, 1145, 1094, 1029, 756, 700.

***N*-Benzyl-4-hexyl-1,2,3,4-tetrahydroisoquinoline (7i)**

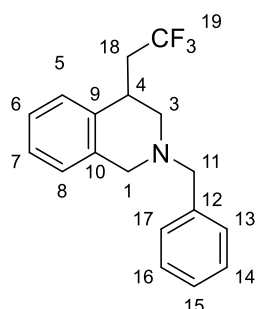


The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4k** (43 mg, 0.125 mmol), hexanal (13 mg, 0.125 mmol), 5:2 HCO₂H:Et₃N (42 μ L, 0.500 mmol) in MeCN (0.1 mL) and was purified by column chromatography (1.5% EtOAc in pentane) to furnish tetrahydroisoquinoline **7i** (27 mg, 70%) as a colourless oil. Spectroscopic data are in accordance with those described in the literature.¹²

¹H NMR (400 MHz, CDCl₃) δ 7.44 – 7.39 (m, 2H, 2 x C^{Ar}H), 7.37 – 7.31 (m, 2H, 2 x C^{Ar}H), 7.30 – 7.25 (m, 1H, C^{Ar}H), 7.22 – 7.13 (m, 2H, 2 x C^{Ar}H), 7.10 (td, $J = 7.2, 1.9$ Hz, 1H, C^{Ar}H), 6.99 (dd, $J = 7.5, 1.4$ Hz, 1H, C^{Ar}H), 3.80 – 3.73 (m, 2H, C¹H₂ + C¹¹H₂), 3.58 (d, $J = 13.2$ Hz, 1H, C¹¹H₂), 3.51 (d, $J = 14.8$ Hz, 1H, C¹H₂), 2.83 – 2.73 (m, 1H, C⁴H), 2.74 – 2.68 (m, 1H, C³H₂), 2.65 – 2.57 (m, 1H, C³H₂), 1.84 – 1.73 (m, 1H, C¹⁸H₂), 1.72 – 1.62 (m, 1H, C¹⁸H₂), 1.33 – 1.20 (m, 8H, C¹⁹H₂ + C²⁰H₂ + C²¹H₂ + C²²H₂), 0.94 – 0.86 (m, 3H, C²³H₃);

¹³C NMR (101 MHz, CDCl₃) δ 139.7 (C^{Ar}), 138.9 (C^{Ar}), 135.0 (C^{Ar}), 129.1 (2 x C^{Ar}H), 128.4, (C^{Ar}H), 128.4 (2 x C^{Ar}H), 127.2 (C^{Ar}H), 126.5 (C^{Ar}H), 126.2 (C^{Ar}H), 125.6 (C^{Ar}H), 63.0 (C¹¹H₂), 56.9 (C¹H₂), 54.4 (C³H₂), 38.9 (C⁴H), 36.2 (C¹⁸H₂), 32.0 (C¹⁹H₂), 29.7 (C²⁰H₂), 27.5 (C²¹H₂), 22.8 (C²²H₂), 14.3 (C²³H₃).

***N*-Benzyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroisoquinoline (7j)**



The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4k** (43 mg, 0.125 mmol), 2,2,2-trifluoroacetaldehyde monohydrate (72% in H₂O) (20 mg, 0.125 mmol), 5:2 HCO₂H:Et₃N (42 μ L, 0.50 mmol) in MeCN (0.1 mL) and was purified by column chromatography (1% EtOAc in pentane) to furnish tetrahydroisoquinoline **7j** (8 mg, 21%) as a colourless oil.

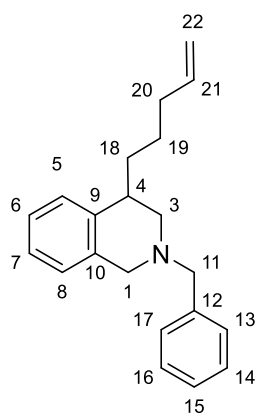
HRMS (ESI): Exact mass calculated for C₁₈H₁₉F₃N+ [M+H]⁺: 306.1464, found: 306.1465.

¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.33 (m, 4H, 4 x C^{Ar}H), 7.31 – 7.26 (m, 1H, C^{Ar}H), 7.21 – 7.12 (m, 3H, 3 x C^{Ar}H), 6.99 (d, *J* = 7.4 Hz, 1H, C^{Ar}H), 3.82 (d, *J* = 15.0 Hz, 1H, C¹H₂), 3.69 (d, *J* = 3.8 Hz, 2H, C¹¹H₂), 3.40 (d, *J* = 15.0 Hz, 1H, C¹H₂), 3.22 – 3.14 (m, 1H, C⁴H₂), 2.98 (d, *J* = 11.7 Hz, 1H, C³H₂), 2.81 (dt, *J* = 15.3, 10.7 Hz, 1H, C¹⁸H₂), 2.62 (d, *J* = 11.8 Hz, 1H, C³H₂), 2.33 (ddd, *J* = 15.2, 11.9, 3.3 Hz, 1H, C¹⁸H₂);

¹³C NMR (101 MHz, CDCl₃) δ 138.3 (C^{Ar}), 137.0 (C^{Ar}), 135.3 (C^{Ar}), 129.2 (2 x C^{Ar}H), 128.7 (C^{Ar}H), 128.5 (2 x C^{Ar}H), 127.4 (C^{Ar}H), 127.1 (q, *J* = 277.4 Hz, C¹⁹F₃), 126.8 (C^{Ar}H), 126.8 (C^{Ar}H), 126.6 (C^{Ar}H), 63.0 (C¹¹H₂), 56.0 (C¹H₂), 54.3 (C³H₂), 40.1 (q, *J* = 26.9 Hz, C¹⁸H₂), 33.9 (C⁴H);

IR (neat) (cm⁻¹): 2806, 2762, 2360, 2341, 1440, 1371, 1129, 1108, 747, 725, 700.

N-Benzyl-4-(pent-4-en-1-yl)-1,2,3,4-tetrahydroisoquinoline (**7k**)



The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4k** (43 mg, 0.125 mmol), pent-4-enal (22 mg, 0.25 mmol), 5:2 HCO₂H:Et₃N (53 μL, 0.625 mmol) in MeCN (0.1 mL) and was purified by column chromatography (CH₂Cl₂) to furnish tetrahydroisoquinoline **7k** (15 mg, 41%) as a colourless oil.

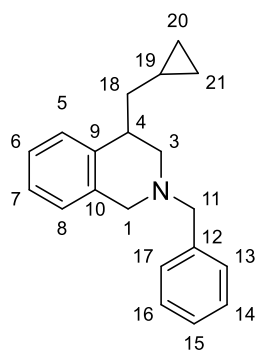
HRMS (ESI): Exact mass calculated for C₂₁H₂₆N [M+H]⁺: 292.2060, found: 292.2060.

¹H NMR (400 MHz, CDCl₃) δ 7.35 – 7.29 (m, 2H, 2 x C^{Ar}H), 7.29 – 7.22 (m, 2H, 2 x C^{Ar}H), 7.22 – 7.16 (m, 1H, 1 x C^{Ar}H), 7.12 – 6.99 (m, 3H, 3 x C^{Ar}H), 6.94 – 6.88 (m, 1H, C^{Ar}H), 5.70 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, C²¹H), 4.96 – 4.82 (m, 2H, C²²H₂), 3.73 – 3.64 (m, 2H, C¹¹H₂ + C¹H₂), 3.49 (d, *J* = 13.1 Hz, 1H, C¹¹H₂), 3.42 (d, *J* = 14.8 Hz, 1H, C¹H₂), 2.75 – 2.65 (m, 1H, C⁴H), 2.63 (ddd, *J* = 11.3, 4.3, 1.1 Hz, 1H, C³H₂), 2.51 (dd, *J* = 11.4, 4.4 Hz, 1H, C³H₂), 2.04 – 1.89 (m, 2H, C²⁰H₂), 1.79 – 1.67 (m, 1H, C¹⁸H₂), 1.65 – 1.54 (m, 1H, C¹⁸H₂), 1.33 – 1.21 (m, 2H, C¹⁹H₂);

¹³C NMR (101 MHz, CDCl₃) δ 139.5 (C^{Ar}), 139.0 (C²¹H), 139.0 (C^{Ar}), 135.0 (C^{Ar}), 129.1 (2 x C^{Ar}H), 128.4 (C^{Ar}), 128.4 (2 x C^{Ar}H), 127.2 (C^{Ar}H), 126.5 (C^{Ar}H), 126.2 (C^{Ar}H), 125.7 (C^{Ar}H), 114.6 (C²²H₂), 63.0 (C¹¹H₂), 56.9 (C¹H₂), 54.3 (C³H₂), 38.7 (C⁴H), 35.7 (C¹⁸H₂), 34.1 (C²⁰H₂), 26.9 (C¹⁹H₂);

IR (neat) (cm⁻¹): 3063, 3026, 2925, 2855, 2795, 1640, 1494, 1096, 1029, 742.

N-Benzyl-4-(cyclopropylmethyl)-1,2,3,4-tetrahydroisoquinoline (**7l**)



The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4k** (43 mg, 0.125 mmol, 1.0 eq.), cyclopropanecarbaldehyde (9 mg, 0.125 mmol, 1.0 eq.), 5:2 HCO₂H:Et₃N (42 μ L, 0.500 mmol, 4.0 eq.) in MeCN (0.1 mL) and was purified by column chromatography (2% EtOAc in pentane) to furnish tetrahydroisoquinoline **7l** (27 mg, 78%) as a colourless oil.

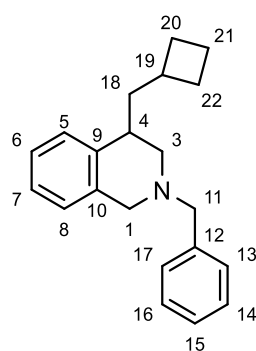
HRMS (ESI): Exact mass calculated for C₂₀H₂₄N [M+H]⁺: 278.1903, found: 278.1904.

¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.37 (m, 2H, 2 x C^{Ar}H), 7.35 – 7.30 (m, 2H, 2 x C^{Ar}H), 7.28 – 7.23 (m, 1H, C^{Ar}H), 7.19 – 7.04 (m, 3H, 3 x C^{Ar}H), 6.99 – 6.93 (m, 1H, C^{Ar}H), 3.78 – 3.68 (m, 2H, C¹H₂ + C¹¹H₂), 3.61 (d, *J* = 13.1 Hz, 1H, C¹¹H₂), 3.45 (d, *J* = 14.8 Hz, 1H, C¹H₂), 2.95 – 2.86 (m, 2H, C⁴H + C³H₂), 2.72 – 2.64 (m, 1H, C³H₂), 1.71 (ddd, *J* = 13.8, 9.4, 7.0 Hz, 1H, C¹⁸H₂), 1.55 (ddd, *J* = 13.8, 6.9, 4.2 Hz, 1H, C¹⁸H₂), 0.69 – 0.60 (m, 1H, C¹⁹H), 0.39 (ddt, *J* = 7.8, 4.8, 1.3 Hz, 2H, C^{20/21}H₂), 0.02 (ddd, *J* = 5.0, 3.2, 1.8 Hz, 2H, C^{20/21}H₂);

¹³C NMR (101 MHz, CDCl₃) δ 139.3 (C^{Ar}), 138.9 (C^{Ar}), 135.0 (C^{Ar}), 129.2 (2 x C^{Ar}H), 128.5 (C^{Ar}H), 128.4 (2 x C^{Ar}H), 127.2 (C^{Ar}H), 126.5 (C^{Ar}H), 126.1 (C^{Ar}H), 125.6 (C^{Ar}H), 63.2 (C¹¹H₂), 56.8 (C¹H₂), 54.8 (C³H₂), 41.3 (C¹⁸H₂), 39.8 (C⁴H), 9.6 (C¹⁹H), 5.5 (C^{20/21}H₂), 4.3 (C^{20/21}H₂);

IR (neat) (cm⁻¹): 3071, 3025, 2912, 2753, 1493, 1454, 1367, 1144, 1095, 1028, 823, 741, 699.

N-Benzyl-4-(cyclobutylmethyl)-1,2,3,4-tetrahydroisoquinoline (**7m**)



The title compound was prepared according to General Procedure **G** using isoquinolinium salt **4k** (40 mg, 0.115 mmol), formylcyclobutane (19 mg, 0.23 mmol) and 5:2 HCO₂H:Et₃N (39 μ L, 0.46 mmol) in MeCN (0.1 mL) and was purified by column chromatography (4% EtOAc in pentane) to furnish tetrahydroisoquinoline **7m** (27 mg, 80%) as a colourless oil.

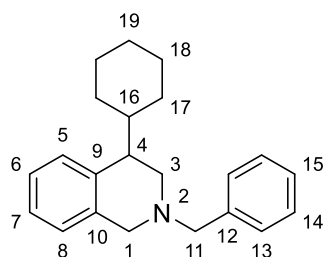
HRMS (ESI): Exact mass calculated for C₂₁H₂₆N [M+H]⁺: 292.2060, found: 292.2062.

¹H NMR (400 MHz, CDCl₃) δ 7.45 – 7.39 (m, 2H, C¹³H + C¹⁷H), 7.35 (tt, *J* = 6.4, 1.0 Hz, 2H, C¹⁴H + C¹⁶H), 7.32 – 7.27 (m, 1H, C¹⁵H), 7.19 – 7.15 (m, 2H, C⁷H + C⁸H), 7.14 – 7.05 (m, 1H, C⁶H), 6.98 (dt, *J* = 7.6, 1.1 Hz, 1H, C⁵H), 3.76 (d, *J* = 12.3 Hz, 1H, C¹H_a), 3.72 (d, *J* = 10.6 Hz, 1H, C¹¹H_a), 3.62 (d, *J* = 13.1 Hz, 1H, C¹¹H_b), 3.48 (d, *J* = 14.8 Hz, 1H, C¹H_b), 2.80 – 2.71 (m, 1H, C⁴H), 2.67 (ddd, *J* = 11.3, 4.3, 1.0 Hz, 1H, C³H_a), 2.60 (dd, *J* = 11.4, 4.5 Hz, 1H, C³H_b), 2.40 – 2.24 (m, 1H, C¹⁹H), 2.08 – 1.97 (m, 2H, C²⁰H_a + C²²H_a), 1.95 – 1.86 (m, 1H, C¹⁸H_a), 1.86 – 1.75 (m, 3H, C¹⁸H_b + C²¹H₂), 1.72 – 1.55 (m, 2H, C²⁰H_b + C²²H_b).

^{13}C NMR (101 MHz, CDCl_3) δ 139.5 (C^9), 138.8 (C^{12}), 135.0 (C^{10}), 129.2 ($\text{C}^{13} + \text{C}^{17}$), 128.42 (C^8), 128.36 ($\text{C}^{14} + \text{C}^{16}$), 127.2 (C^{15}), 126.5 (C^5), 126.2 (C^7), 125.6 (C^6), 63.0 (C^{11}), 56.7 (C^1), 54.8 (C^3), 43.8 (C^{18}), 37.2 (C^4), 34.4 (C^{19}), 29.2 (C^{20}), 28.6 (C^{22}), 18.6 (C^{21}).

IR (neat) (cm^{-1}): 2925, 2863, 2794, 1367, 1143, 1095, 1071, 1028, 914, 739, 698.

***N*-Benzyl-4-cyclohexyl-1,2,3,4-tetrahydroisoquinoline (7n)**



The title compound was prepared according to modified General Procedure **G** using isoquinolinium salt **4k** (40 mg, 0.125 mmol), cyclohexanone (25 mg, 0.25 mmol), 5:2 $\text{HCO}_2\text{H}:\text{Et}_3\text{N}$ (42 μL , 0.50 mmol) and $[\text{RhCp}^*\text{Cl}_2]_2$ (0.01 mol%) in MeCN (0.1 mL) and was purified by column chromatography (4% EtOAc in pentane) to furnish tetrahydroisoquinoline **7n** (10 mg, 26%) as a colourless oil.

The title compound could not be prepared in the absence of a rhodium catalyst.

HRMS (ESI): Exact mass calculated for $\text{C}_{22}\text{H}_{27}\text{N}$ $[\text{M}+\text{H}]^+$: 306.2216, found: 306.2218.

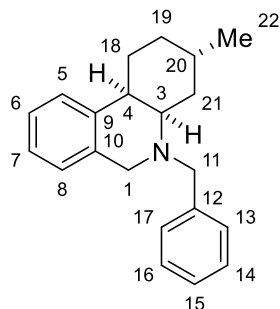
^1H NMR (400 MHz, CDCl_3) δ 7.44 – 7.23 (m, 5H, 5 x $\text{C}^{\text{Ar}}\text{H}$), 7.21 – 7.05 (m, 3H, 3 x $\text{C}^{\text{Ar}}\text{H}$), 7.02 – 6.92 (m, 1H, $\text{C}^{\text{Ar}}\text{H}$), 3.77 – 3.66 (m, 2H, $\text{C}^1\text{H}_2 + \text{C}^{11}\text{H}_2$), 3.58 (d, $J = 13.0$ Hz, 1H, $\text{C}^1\text{H}_2/\text{C}^{11}\text{H}_2$), 3.46 (d, $J = 14.9$ Hz, 1H, $\text{C}^1\text{H}_2/\text{C}^{11}\text{H}_2$), 2.80 (dd, $J = 11.3, 4.8$ Hz, 1H, C^3H_2), 2.67 (td, $J = 5.15, 5.14$ Hz, 1H, C^4H), 2.57 (dd, $J = 11.3, 4.7$ Hz, 1H, C^3H_2), 1.91 – 1.78 (m, 1H, C^{16}H), 1.78 – 1.69 (m, 1H, $\text{C}^{17}\text{H}_2/\text{C}^{18}\text{H}_2/\text{C}^{19}\text{H}_2$), 1.69 – 1.57 (m, 3H, $\text{C}^{17}\text{H}_2/\text{C}^{18}\text{H}_2/\text{C}^{19}\text{H}_2$), 1.51 – 1.39 (m, 1H, $\text{C}^{17}\text{H}_2/\text{C}^{18}\text{H}_2/\text{C}^{19}\text{H}_2$), 1.33 – 1.17 (m, 1H, $\text{C}^{17}\text{H}_2/\text{C}^{18}\text{H}_2/\text{C}^{19}\text{H}_2$), 1.17 – 0.96 (m, 4H, $\text{C}^{17}\text{H}_2/\text{C}^{18}\text{H}_2/\text{C}^{19}\text{H}_2$).

^{13}C NMR (101 MHz, CDCl_3) δ 137.7 (C^{12}), 129.3 (2 x $\text{C}^{13}\text{H}/\text{C}^{14}\text{H}$), 128.9 (C^{15}H), 128.3 (2 x $\text{C}^{13}\text{H}/\text{C}^{14}\text{H}$), 127.2 ($\text{C}^5\text{H}/\text{C}^6\text{H}/\text{C}^7\text{H}/\text{C}^8\text{H}$), 126.5 ($\text{C}^5\text{H}/\text{C}^6\text{H}/\text{C}^7\text{H}/\text{C}^8\text{H}$), 125.7 ($\text{C}^5\text{H}/\text{C}^6\text{H}/\text{C}^7\text{H}/\text{C}^8\text{H}$), 125.6 ($\text{C}^5\text{H}/\text{C}^6\text{H}/\text{C}^7\text{H}/\text{C}^8\text{H}$), 63.2 ($\text{C}^1\text{H}_2/\text{C}^{11}\text{H}_2$), 56.8 ($\text{C}^1\text{H}_2/\text{C}^{11}\text{H}_2$), 52.5 (C^3H), 44.0 (C^4H), 42.4 (C^{16}H), 32.0 ($\text{C}^{\text{Cy}}\text{H}_2$), 29.7 ($\text{C}^{\text{Cy}}\text{H}_2$), 27.2 ($\text{C}^{\text{Cy}}\text{H}_2$), 27.1 ($\text{C}^{\text{Cy}}\text{H}_2$), 26.8 ($\text{C}^{\text{Cy}}\text{H}_2$), C^9 and C^{10} not observed.

IR (neat) (cm^{-1}) 2980, 2920, 2850, 2795, 2754, 1494, 1451, 1368, 1256, 1146.

Annulation reactions

N-Benzyl-3-methyl-1,2,3,4,4a,5,6,10b-octahydrophenanthridine (**8a**)



The title compound was prepared according to General Procedure **F** using isoquinolinium salt **4f** (45 mg, 0.125 mmol), methyl vinyl ketone (10 μ L, 0.125 mmol), 5:2 $\text{HCO}_2\text{H}:\text{Et}_3\text{N}$ (42 μ L, 0.50 mmol), $[\text{RhCp}^*\text{Cl}]_2$ (7.7 μ g, 0.0125 μ mol, 0.01 mol%) in MeCN (0.1 mL) and was purified by flash column chromatography (1-2% EtOAc in pentane) to furnish the annulated tetrahydroisoquinoline **8a** (20 mg, 55%) as a single diastereomer as a colourless oil. A repetition on a 0.625 mmol scale furnished the product **8a** in 53% isolated yield.

The title compound could not be prepared according to General procedure **E**.

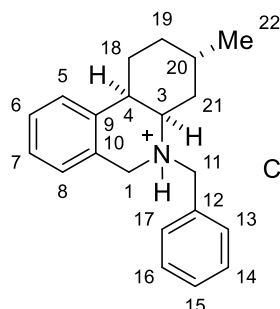
HRMS (ESI): Exact mass calculated for $\text{C}_{21}\text{H}_{26}\text{N}$ $[\text{M}+\text{H}]^+$: 292.2060, found: 292.2054.

^1H NMR (400 MHz, CDCl_3) 7.52 – 7.46 (m, 2H, 2 x $\text{C}^{\text{Ar}}\text{H}$), 7.43 – 7.35 (m, 2H, 2 x $\text{C}^{\text{Ar}}\text{H}$), 7.35 – 7.29 (m, 1H, $\text{C}^{\text{Ar}}\text{H}$), 7.21 – 7.07 (m, 3H, 3 x $\text{C}^{\text{Ar}}\text{H}$), 6.92 (d, $J = 7.5$ Hz, 1H, $\text{C}^{\text{Ar}}\text{H}$), 4.39 (d, $J = 13.0$ Hz, 1H, C^1H_2), 3.86 (d, $J = 15.4$ Hz, 1H, C^{11}H_2), 3.29 (d, $J = 14.7$ Hz, 1H, C^{11}H_2), 3.12 (d, $J = 13.0$ Hz, 1H, C^1H_2), 2.89 (d, $J = 3.2$ Hz, 1H, C^3H), 2.73 (dt, $J = 11.9, 3.5$ Hz, 1H, C^4H), 2.36 – 2.26 (m, 1H, C^{21}H_2), 2.26 – 2.15 (m, 1H, C^{18}H_2), 1.98 – 1.85 (m, 2H, $\text{C}^{19}\text{H} + \text{C}^{20}\text{H}_2$), 1.80 (dq, $J = 13.3, 3.6$ Hz, 1H, C^{18}H_2), 1.35 (ddd, $J = 14.8, 11.9, 3.1$ Hz, 1H, C^{21}H_2), 1.31 – 1.16 (m, 1H, C^{19}H_2), 0.97 (d, $J = 6.5$ Hz, 3H, C^{22}H_3);

^{13}C NMR (101 MHz, CDCl_3) δ 140.8 (C^{Ar}), 140.4 (C^{Ar}), 134.6 (C^{Ar}), 128.7 (2 x $\text{C}^{\text{Ar}}\text{H}$), 128.4 (2 x $\text{C}^{\text{Ar}}\text{H}$), 128.1 ($\text{C}^{\text{Ar}}\text{H}$), 126.9 ($\text{C}^{\text{Ar}}\text{H}$), 126.1 ($\text{C}^{\text{Ar}}\text{H}$), 126.0 ($\text{C}^{\text{Ar}}\text{H}$), 125.6 ($\text{C}^{\text{Ar}}\text{H}$), 58.3 (C^3H), 56.8 (C^1H_2), 56.0 (C^{11}H_2), 42.5 (C^4H), 37.5 (C^{21}H_2), 35.6 (C^{19}H_2), 32.4 (C^{18}H_2), 26.0 (C^{20}H), 22.7 (C^{22}H);

IR (neat) (cm^{-1}): 2946, 2922, 2786, 1379, 1369, 1155, 1069, 966, 744, 699.

N-Benzyl-3-methyl-1,2,3,4,4a,5,6,10b-octahydrophenanthridin-5-ium chloride (**8a**·HCl)



The hydrochloride of **8a** was formed by dissolving **8a** (94 mg, 0.32 mmol) in degassed Et_2O (3 mL) and adding 2M HCl in diethyl ether (0.18 mL, 0.35 mmol) dropwise at 0 °C. After stirring at 0 °C for 20 min the reaction mixture was filtered to give **8a**·HCl (100 mg, 85%) as a colourless solid.

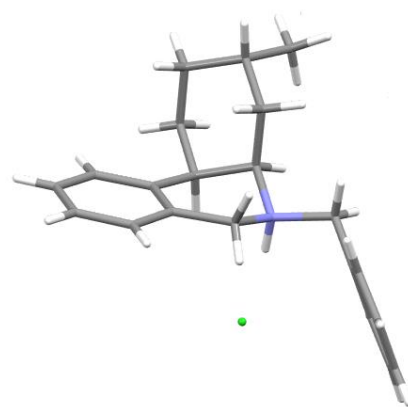
m.p. (CH_2Cl_2): 176 °C.

HRMS (ESI): Exact mass calculated for $\text{C}_{21}\text{H}_{27}\text{N}$ $[\text{M}]^+$: 292.2060, found: 292.2061.

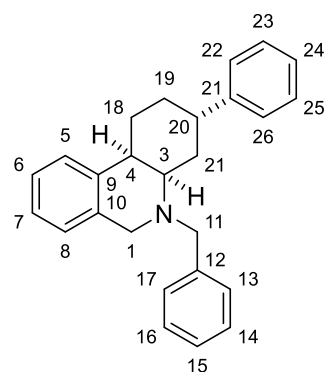
^1H NMR (400 MHz, CDCl_3 , mixture of diastereomers 60:40) δ 12.82 (s, 1H), 12.21 (s, 1H), 7.93 – 7.86 (m, 2H), 7.69 – 7.64 (m, 3H), 7.43 (m, 7H), 7.34 – 7.27 (m, 2H), 7.25 – 7.14 (m, 4H), 7.04 (d, $J = 7.0$ Hz, 1H), 6.99 (dd, $J = 7.8, 1.3$ Hz, 1H), 4.59 (dd, $J = 16.0, 4.2$ Hz, 2H), 4.48 (dd, $J = 13.6, 3.9$ Hz, 2H), 4.46 – 4.38 (m, 2H), 4.30 (dd, $J = 13.5, 5.7$ Hz, 1H), 4.13 (dd, $J = 12.7, 7.0$ Hz, 1H), 3.97 (dd, $J = 15.8, 5.2$ Hz,

4H), 3.07 (dt, $J = 9.1, 4.5$ Hz, 1H), 2.40 (dtd, $J = 14.2, 9.0, 3.4$ Hz, 1H), 2.28 – 2.01 (m, 3H), 1.91 – 1.70 (m, 5H), 1.65 (ddd, $J = 12.4, 4.8$ Hz, 1H), 1.42 (dddd, $J = 13.8, 4.1$ Hz, 1H), 1.24 – 1.11 (m, 3H), 0.94 (d, $J = 6.8$ Hz, 4H), 0.86 (d, $J = 7.3$ Hz, 3H).

Crystal data $C_{21}H_{26}ClN$, $M = 327.90$, orthorhombic, $a = 11.29240(10)$, $b = 13.6629(2)$, $c = 23.2273(2)$ Å, $\beta = 90^\circ$, $Z = 8$, $T = 150$ K, space group $Pna2_1$, 43420 reflections measured, 6973 unique ($R_{\text{int}} = 0.027$), which were used in all calculations.



***N*-Benzyl-3-phenyl-1,2,3,4,4a,5,6,10b-octahydrophenanthridine (8b)**



The title compound was prepared according to General Procedure **F** using isoquinolinium salt **4f** (45 mg, 0.125 mmol), phenyl vinyl ketone (17 mg, 0.125 mmol), 5:2 $\text{HCO}_2\text{H}:\text{Et}_3\text{N}$ (42 μL , 0.50 mmol), $[\text{RhCp}^*\text{Cl}]_2$ (7.7 μg , 0.0125 μmol , 0.01 mol%) in MeCN (0.1 mL) and was purified by column chromatography (0.75-1% EtOAc in pentane) to furnish the annulated tetrahydroisoquinoline **8b** (14 mg, 32%, d.r. > 25:1) as a colourless solid. The title compound could not be prepared according to

General procedure **E**.

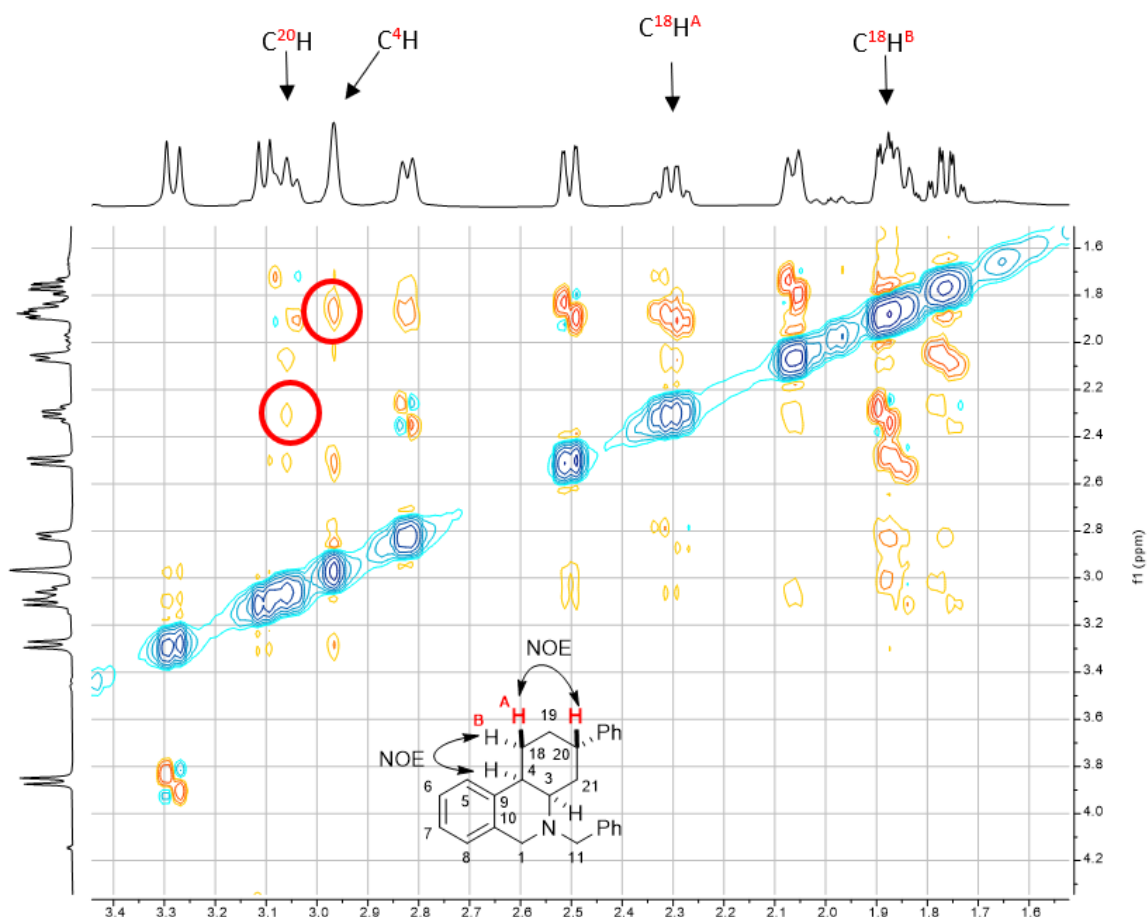
m.p. (CH_2Cl_2): 119 °C.

HRMS (ESI): Exact mass calculated for $\text{C}_{26}\text{H}_{28}\text{N}^+ [\text{M}+\text{H}]^+$: 354.2216, found: 354.2217.

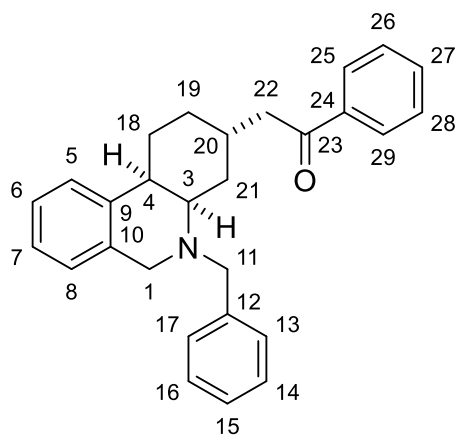
^1H NMR (400 MHz, CDCl_3) δ 7.51 – 7.45 (m, 2H, 2 x $\text{C}^{\text{Ar}}\text{H}$), 7.40 – 7.27 (m, 5H, 5 x $\text{C}^{\text{Ar}}\text{H}$), 7.25 – 7.06 (m, 6H, 6 x $\text{C}^{\text{Ar}}\text{H}$), 6.94 – 6.87 (m, 1H, $\text{C}^{\text{Ar}}\text{H}$), 4.43 (d, $J = 13.0$ Hz, 1H, C^1H_2), 3.86 (d, $J = 15.4$ Hz, 1H, C^{11}H_2), 3.28 (d, $J = 15.4$ Hz, 1H, C^{11}H_2), 3.10 (d, $J = 13.0$ Hz, 1H, C^1H_2), 3.04 (dt, $J = 12.5, 3.2$ Hz, 1H, C^{20}H), 2.97 (q, $J = 3.1$ Hz, 1H, C^3H), 2.82 (dt, $J = 12.1, 3.5$ Hz, 1H, C^4H), 2.51 (dq, $J = 14.6, 2.8$ Hz, 1H, C^{21}H_2), 2.38 – 2.24 (m, 1H, C^{18}H_2), 2.12 – 2.01 (m, 1H, C^{19}H_2), 1.94 – 1.70 (m, 2H, $\text{C}^{21}\text{H}_2 + \text{C}^{18}\text{H}_2$), 1.81 – 1.70 (m, 1H, C^{19}H_2);

^{13}C NMR (101 MHz, CDCl_3) δ 147.2 (C^{Ar}), 140.5 (C^{Ar}), 140.2 (C^{Ar}), 134.5 (C^{Ar}), 128.8 (2 x $\text{C}^{\text{Ar}}\text{H}$), 128.6 (4x $\text{C}^{\text{Ar}}\text{H}$), 128.2 ($\text{C}^{\text{Ar}}\text{H}$), 127.0 ($\text{C}^{\text{Ar}}\text{H}$), 127.0 (2 x $\text{C}^{\text{Ar}}\text{H}$), 126.2 ($\text{C}^{\text{Ar}}\text{H}$), 126.2 ($\text{C}^{\text{Ar}}\text{H}$), 126.1 ($\text{C}^{\text{Ar}}\text{H}$), 125.8 ($\text{C}^{\text{Ar}}\text{H}$), 58.6 (C^3H), 56.9 (C^1H_2), 56.2 (C^{11}H_2), 42.5 (C^4H), 37.4 (C^{20}H), 36.7 (C^{21}H_2), 34.8 (C^{19}H_2), 33.0 (C^{18}H_2);

IR (neat) (cm^{-1}): 2926, 2786, 1138, 1111, 1071, 1028, 957, 745, 698.



2-(*N*-Benzyl-1,2,3,4,4a,5,6,10b-octahydrophenanthridin-3-yl)-1-phenylethan-1-one (**8c**)



The title compound was prepared according to General Procedure E using isoquinolinium salt **4f** (45 mg, 0.125 mmol), (*E*)-1-phenylhexa-3,5-dien-1-one¹³ (20 mg, 0.125 mmol), 5:2 HCO₂H:Et₃N (42 μL, 0.50 mmol) in MeCN (0.1 mL) and was purified by column chromatography (2-3% EtOAc in pentane) to furnish the annulated tetrahydroisoquinoline **8c** (11 mg, 22%, d.r. > 25:1) as a colourless solid.

m.p. (CH₂Cl₂): 121 °C;

HRMS (ESI): Exact mass calculated for C₂₈H₃₀NO [M+H]⁺: 396.2322, found: 396.2321.

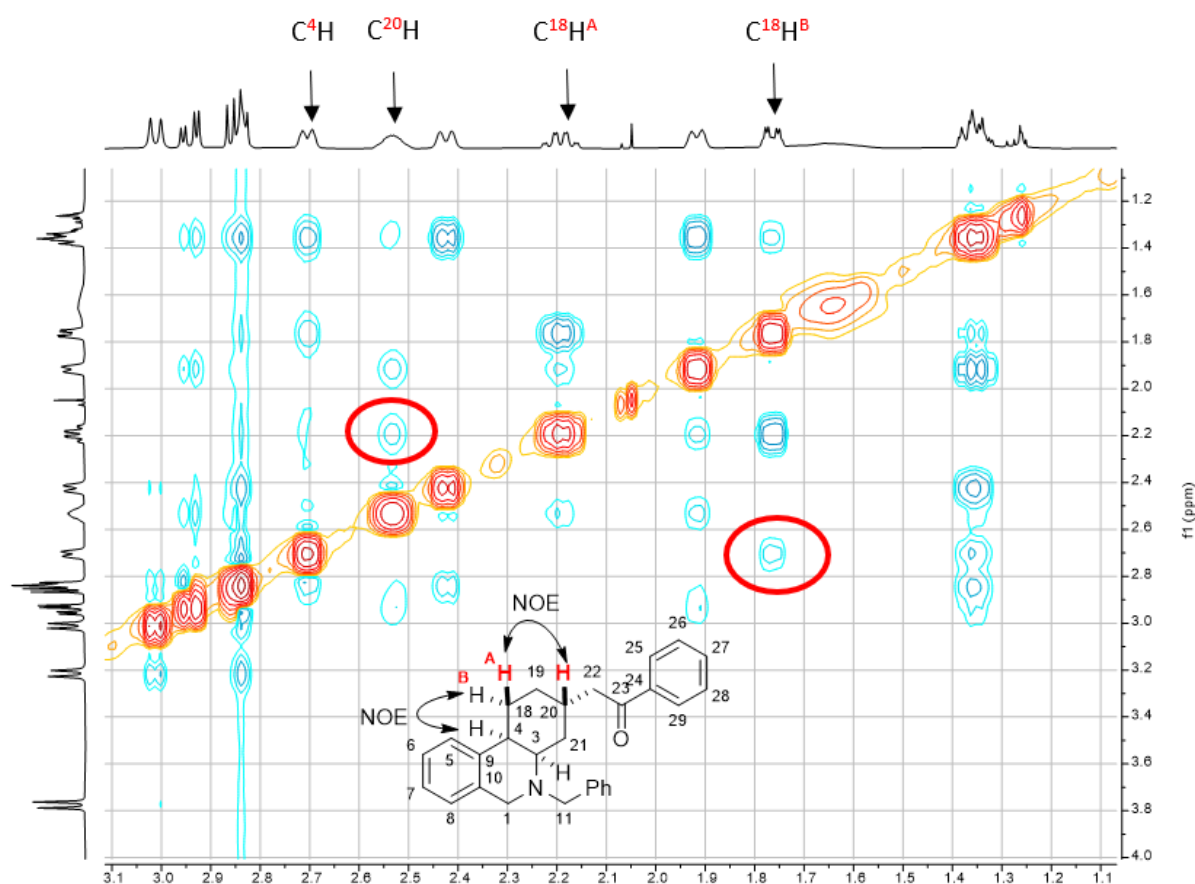
¹H NMR (600 MHz, CDCl₃) δ 7.94 – 7.91 (m, 2H, C²⁵H + C²⁹H), 7.49 (t, *J* = 7.4 Hz, 1H, C²⁷H), 7.43 – 7.35 (m, 4H, 4 x C^{Ar}H), 7.29 (t, *J* = 7.5 Hz, 2H, 2 x C^{Ar}H), 7.24 (t, *J* = 7.3 Hz, 1H, C^{Ar}H), 7.13 – 7.02 (m, 3H, 3 x C^{Ar}H), 6.86 (d, *J* = 7.6 Hz, 1H, C^{Ar}H), 4.44 (d, *J* = 12.7 Hz, 1H, C¹H₂), 3.78 (d, *J* = 15.4 Hz, 1H C¹²H₂), 3.21

¹³ L. Bernardi, J. López-Cantarero, B. Niess, K. A. Jørgensen, *J. Am. Chem. Soc.* **2007**, *129*, 5772–5778.

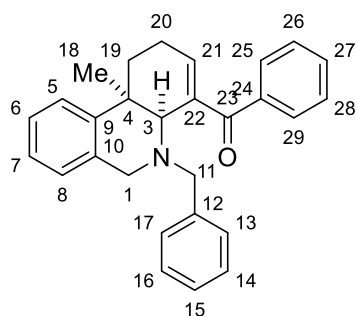
(d, $J = 15.4$ Hz, 1H, $C^{12}H_2$), 3.01 (d, $J = 12.7$ Hz, 1H, C^1H_2), 2.94 (dd, $J = 16.2, 5.5$ Hz, 1H, $C^{22}H_2$), 2.87 – 2.82 (m, 2H, $C^{22}H_2 + C^3H$), 2.74 – 2.67 (m, 1H, C^4H), 2.59 – 2.49 (m, 1H, $C^{20}H$), 2.43 (d, $J = 13.5$ Hz, 1H, $C^{21}H_2$), 2.19 (qd, $J = 13.0, 3.8$ Hz, 1H, $C^{18}H_2$), 1.96 – 1.89 (m, 1H, $C^{19}H_2$), 1.80 – 1.73 (m, 1H, $C^{18}H_2$), 1.40 – 1.31 (m, 2H, $C^{21}H_2 + C^{19}H_2$);

^{13}C NMR (151 MHz, $CDCl_3$) δ 200.0 (C^{23}), 140.4 (C^{Ar}), 140.2 (C^{Ar}), 137.4 (C^{Ar}), 134.6 (C^{Ar}), 133.0 (C^{27}), 129.0 (2 x $C^{Ar}H$), 128.7 (2 x $C^{Ar}H$), 128.3 (2 x $C^{Ar}H$), 128.1 (2 x $C^{Ar}H$), 128.0 ($C^{Ar}H$), 126.8 ($C^{Ar}H$), 126.2 ($C^{Ar}H$), 126.0 ($C^{Ar}H$), 125.7 ($C^{Ar}H$), 58.0 (C^3H), 56.8 (C^1H_2), 55.9 ($C^{11}H_2$), 46.0 ($C^{22}H_2$), 42.6 (C^4H), 35.3 ($C^{21}H_2$), 33.7 ($C^{19}H_2$), 32.2 ($C^{18}H_2$), 27.9 ($C^{20}H$);

IR (neat) (cm^{-1}): 2926, 2787, 1683, 1597, 1448, 1367, 1316, 1068, 1001, 910, 748, 699.



(*N*-Benzyl-10b-methyl-1,2,4a,5,6,10b-hexahydrophenanthridin-4-yl)(phenyl)methanone (8d**)**



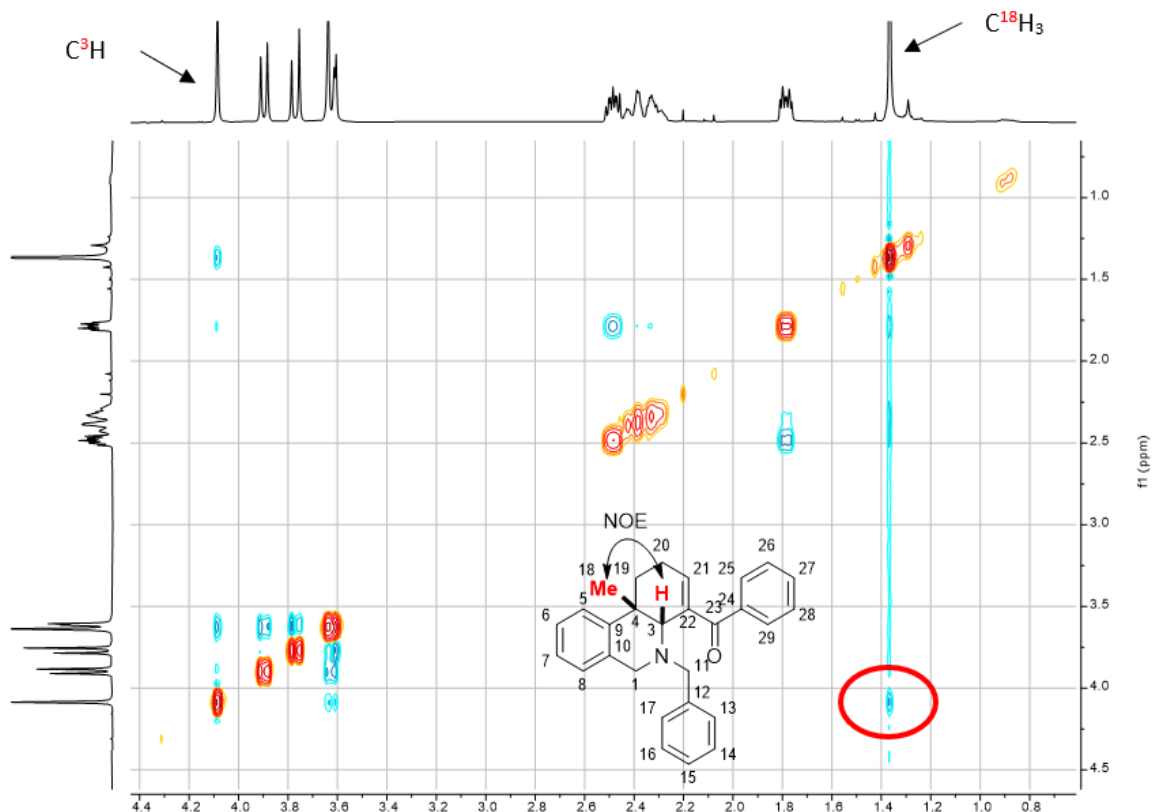
The title compound was prepared according to General Procedure E using isoquinolinium salt **4a** (45 mg, 0.125 mmol), (*E*)-1-phenylhexa-3,5-dien-1-one¹³ (40 mg, 0.250 mmol), 5:2 HCO₂H:Et₃N (42 μ L, 0.500 mmol) in MeCN (0.1 mL) and was purified by flash column chromatography (1-2% EtOAc in pentane) to furnish the annulated tetrahydroisoquinoline **8d** (27 mg, 55%, d.r. > 25:1) as a colourless oil.

The product was found to be the *cis*-diastereomer (confirmed by NOESY).

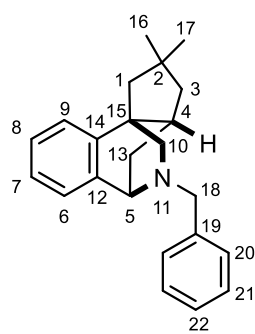
HRMS (ESI): Exact mass calculated for C₂₈H₂₈NO [M+H]⁺: 394.2165, found: 394.2165.

¹H NMR (500 MHz, CDCl₃) δ 7.85 – 7.76 (m, 2H, 2 x C^{Ar}H), 7.61 – 7.53 (m, 1H, C^{Ar}H), 7.45 (t, *J* = 7.7 Hz, 2H, 2 x C^{Ar}H), 7.39 (dd, *J* = 7.9, 1.3 Hz, 1H, 2 x C^{Ar}H), 7.34 – 7.20 (m, 6H, 6 x C^{Ar}H), 7.13 (td, *J* = 7.5, 1.3 Hz, 1H, C^{Ar}H), 6.93 (dd, *J* = 7.6, 1.4 Hz, 1H, C^{Ar}H), 6.70 (t, *J* = 3.8 Hz, 1H C²¹H), 4.09 (s, 1H, C³H), 3.90 (d, *J* = 13.4 Hz, 1H, C¹H₂), 3.77 (d, *J* = 15.6 Hz, 1H, C¹¹H₂), 3.67 – 3.58 (m, 2H, C¹H₂ + C¹¹H₂), 2.49 (ddd, *J* = 13.7, 8.7, 5.8 Hz, 1H, C¹⁹H₂), 2.44 – 2.26 (m, 2H, C²⁰H₂), 1.82 – 1.75 (m, 1H, C¹⁹H₂), 1.37 (s, 3H, C¹⁸H₃); **¹³C NMR** (126 MHz, CDCl₃) δ 197.2 (C²³), 145.0 (C²¹H), 143.5 (C^{Ar}), 140.6 (C^{Ar}), 139.4 (C^{Ar}), 137.7 (C^{Ar}), 134.4 (C^{Ar}), 132.3 (C^{Ar}H), 129.8 (2 x C^{Ar}H), 128.6 (2 x C^{Ar}H), 128.4 (2 x C^{Ar}H), 128.3 (2 x C^{Ar}H), 126.9 (C^{Ar}H), 126.6 (C^{Ar}H), 126.6 (C^{Ar}H), 126.4 (C^{Ar}H), 125.6 (C^{Ar}H), 62.4 (C³H), 58.5 (C¹H₂), 53.7 (C¹¹H₂), 37.7 (C⁴), 32.9 (C¹⁹H₂), 25.6 (br s, C¹⁸H₃), 24.5 (C²⁰H₂);

IR (neat) (cm⁻¹): 2926, 1649, 1597, 1446, 1355, 1365, 1310, 1268, 909, 758.



***N*-benzyl-2,2-dimethyl-1,2,3,3a,4,5-hexahydro-5,9b-(epiminomethano)cyclopenta[*a*]naphthalene (8e)**



The title compound was prepared according to General Procedure **E** using isoquinolinium salt **4k** (80 mg, 0.23 mmol), 2,2-dimethylpent-4-enal (90%, 57 mg, 0.46 mmol) and 5:2 HCO₂H:Et₃N (72 μ L, 0.92 mmol) in MeCN (0.2 mL) and was purified by column chromatography (1% acetone in CH₂Cl₂) to furnish tetracycle **8e** (33 mg, 45%, d.r. > 25:1) as an off-white solid. A single-crystal for X-ray analysis was grown by dissolving in CHCl₃/MTBE and slow evaporation.

The single-crystal corresponded to the HI salt of **8e** and was obtained directly without the need for salt formation in an extra step.

m.p. (MTBE/CHCl₃): 86 – 87 °C.

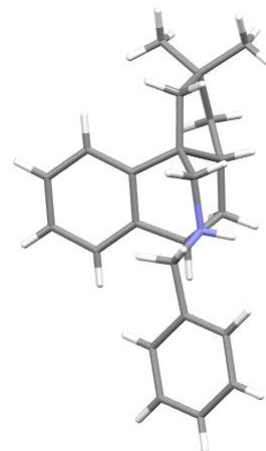
HRMS (ESI): Exact mass calculated for C₂₃H₃₈N [M+H]⁺: 318.2216, found: 318.2216.

¹H NMR (400 MHz, CDCl₃) δ 7.40 (dd, J = 7.5, 1.3 Hz, 1H, C⁹H), 7.38 – 7.27 (m, 5H, C⁸ⁿH + C⁸H), 7.28 – 7.21 (m, 2H, C⁸ⁿH + C⁷H), 7.13 (dd, J = 7.1, 1.5 Hz, 1H, C⁶H), 3.69 (t, J = 2.7 Hz, 1H, C⁵H), 3.39 (d, J = 13.3 Hz, 1H, C¹⁸H_a), 3.23 (d, J = 13.3 Hz, 1H, C¹⁸H_b), 3.07 (d, J = 9.0 Hz, 1H, C¹⁰H_a), 2.45 – 2.37 (m, 1H, C¹³H_a), 2.34 (d, J = 13.8 Hz, 1H, C¹H_a), 2.31 – 2.20 (m, 1H, C⁴H), 1.90 (d, J = 9.0 Hz, 1H, C¹⁰H_b), 1.44 (dd, J = 12.1, 5.8 Hz, 1H, C³H_a), 1.35 (d, J = 13.9 Hz, 1H, C¹H_b), 1.18 (s, 3H, C¹⁶H₃), 1.11 (s, 3H, C¹⁷H₃), 1.00 (ddd, J = 12.0, 6.0, 1.7 Hz, 1H, C¹³H_b), 0.62 (app t, J = 12.5 Hz, 1H, C³H_b).

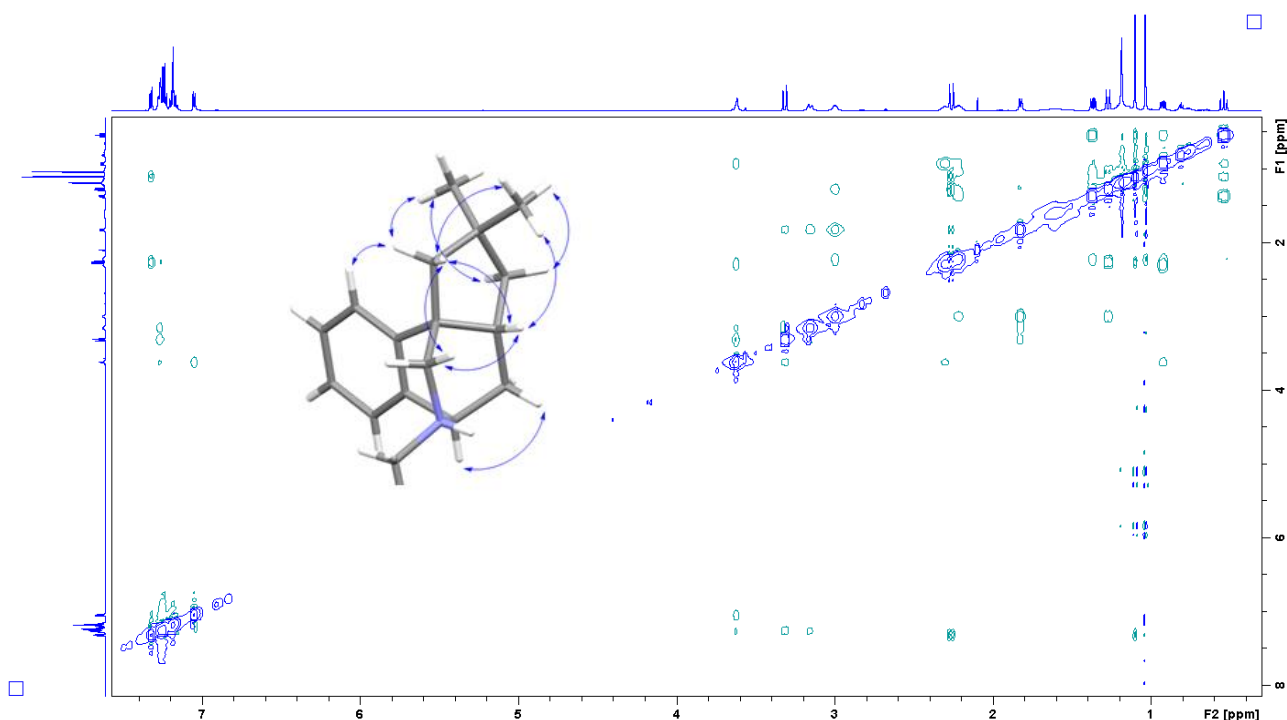
^{13}C NMR (101 MHz, CDCl_3) δ 141.9 (C^{14}), 139.6 ($\text{C}^{12} + \text{C}^{19}$), 129.0 (2 x C^{20}H), 128.3 (2 x C^{21}H), 127.0 (C^{22}H), 126.6 (C^8H), 125.8 (C^7H), 123.8 (C^6H), 123.2 (C^9H), 64.1 (C^{10}H_2), 61.5 (C^{18}H_2), 57.0 (C^5H), 48.8 (C^{15}), 47.9 (C^3H_2), 43.1 (C^1H_2), 40.2 (C^4H), 39.1 (C^2), 33.6 (C^{13}H_2), 33.1 (C^{16}H_3), 31.4 (C^{17}H_3).

IR (neat) (cm^{-1}): 3025, 2946, 2864, 1452, 1120, 1026, 909, 750, 728, 698.

Crystal data $\text{C}_{23}\text{H}_{28}\text{NI}$, $M = 445.39$, monoclinic, $a = 9.2483(3)$, $b = 14.3133(4)$, $c = 16.1073(5)$ Å, $\beta = 106.151(4)^\circ$, $Z = 4$, $T = 150$ K, space group $P2_1/n$, 14033 reflections measured, 4251 unique ($R_{\text{int}} = 0.032$), which were used in all calculations.



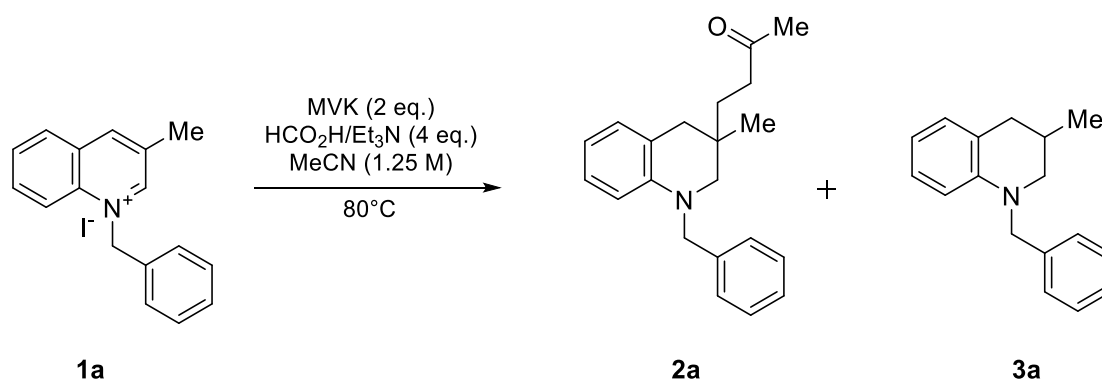
Relative stereochemistry could also be assigned from the following observed NOESY correlations:



Investigation into reaction kinetics

General

Reactions were carried out in GC vials using 20 mg of *N*-Benzyl-3-methylquinolinium iodide (**1a**), and a “Mastermix”, containing aliquots of 8.9 μ L methyl vinyl ketone, 18.7 μ L 5:2 formic acid-triethylamine complex and $[\text{RhCp}^*\text{Cl}_2]_2$ in acetonitrile (45 μ L). The new vials (without magnetic stirring) were placed in an 80 °C oil bath and heated for the time indicated before quenching by dilution in CH_2Cl_2 /0.1 M aqueous K_2CO_3 . Crude mixtures obtained this way were analysed by quantitative ^1H -NMR using trimethoxybenzene (3.1 mg per CDCl_3 aliquot) as an internal standard. Methoxy peaks of TMB (6.09 ppm) and methyl peaks of the product **3a** (0.97 ppm) and reduced side-product **2a** (1.05 ppm) were chosen as diagnostic signals for quantification.



Analysis of kinetic data

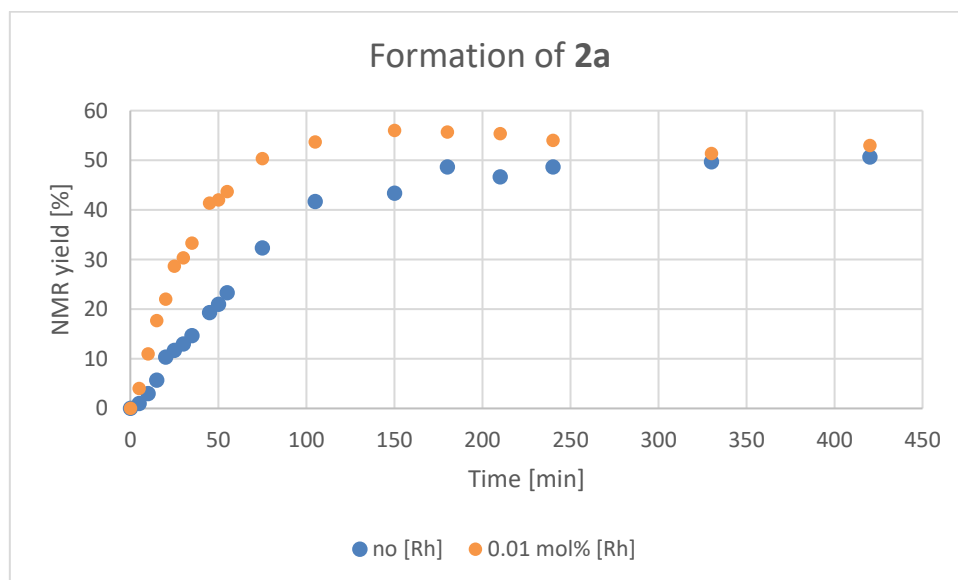


Figure 3: Difference in formation of **3a** in the presence of metal-catalyst

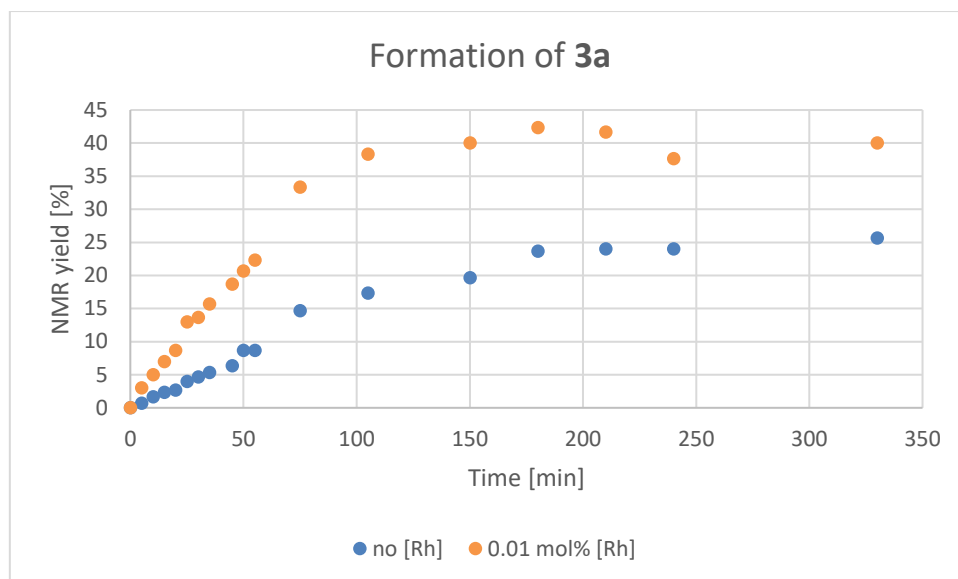
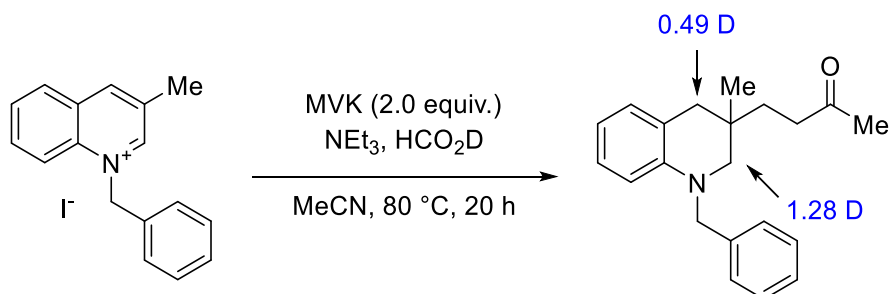


Figure 4: Difference in formation of **2a** in the presence of metal-catalyst

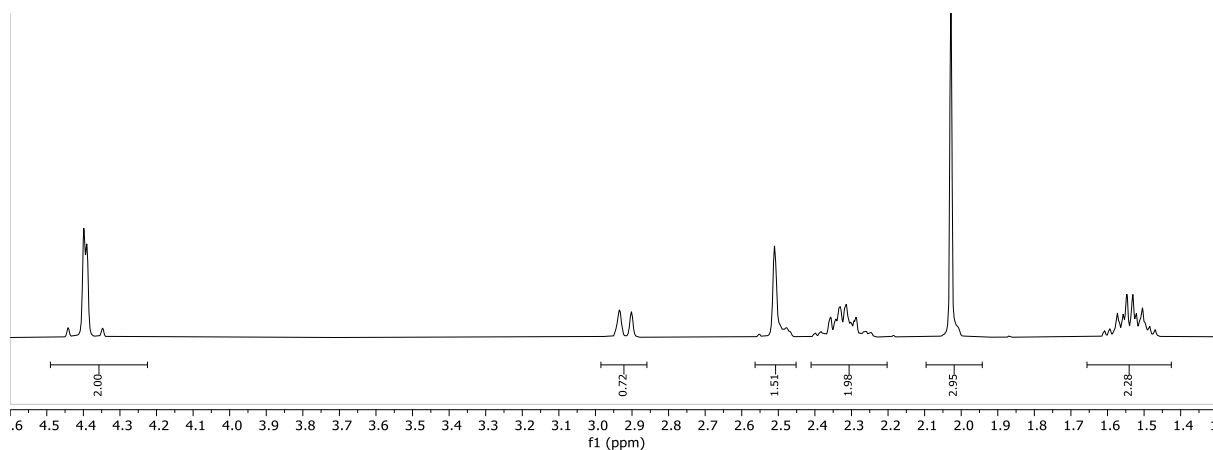
Deuterium labelling experiments

Formic-d acid, formic acid-d and formic acid-d₂ were purchased from Sigma Aldrich and used without further purification. All reactions were performed following General Procedure B or E, using deuterated reagents where specified in the reaction scheme.

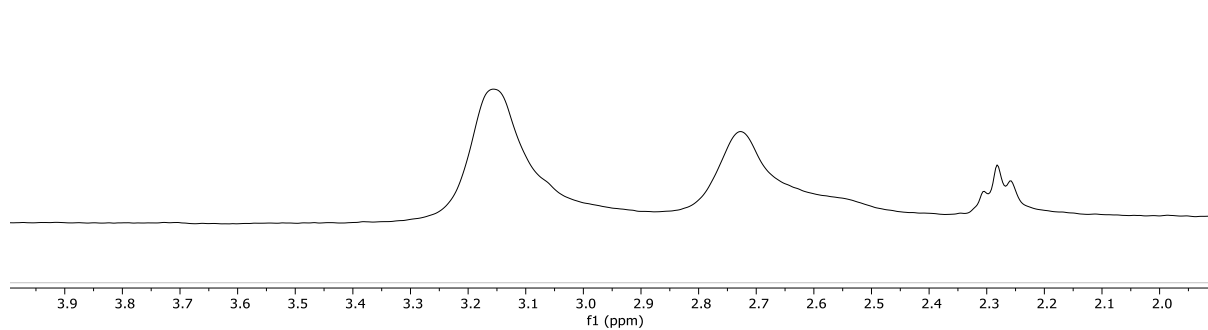
Reaction with formic-d acid (DCO₂H):



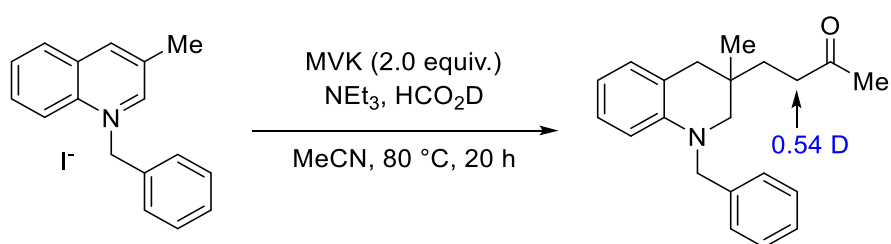
¹H NMR



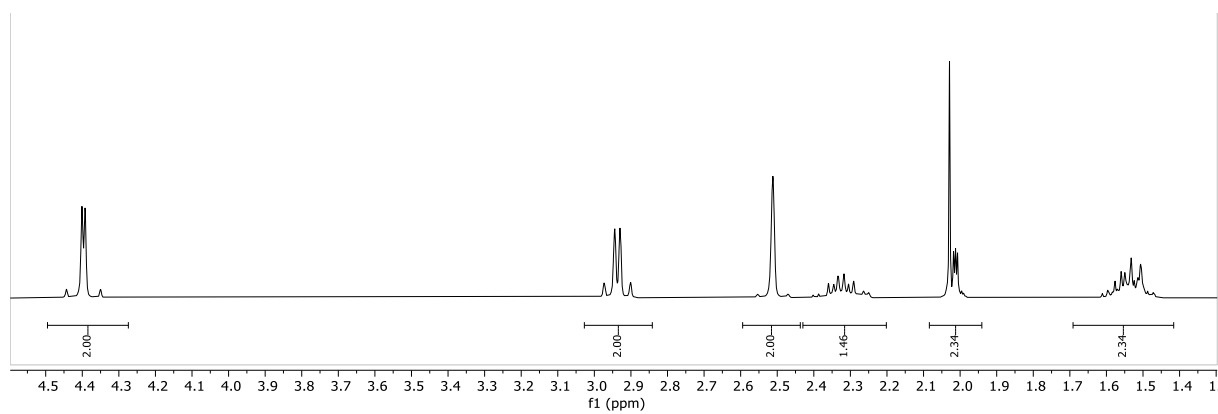
^2H NMR



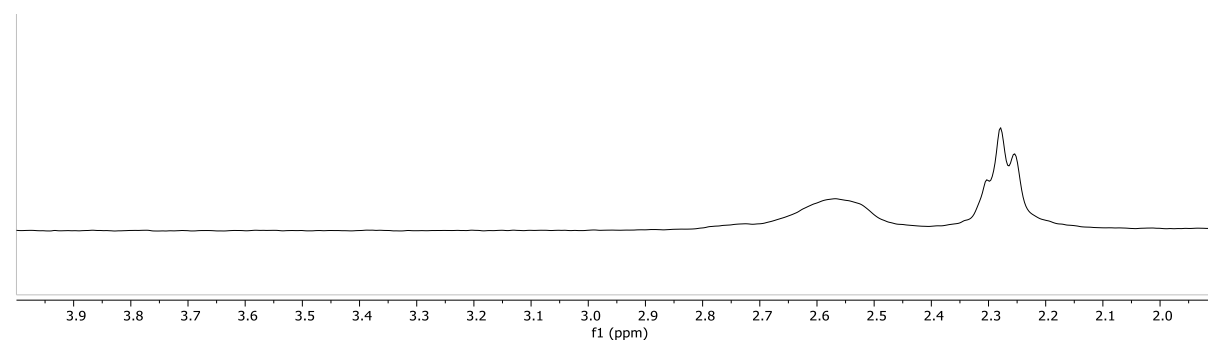
Reaction with formic acid-d (HCO_2D):



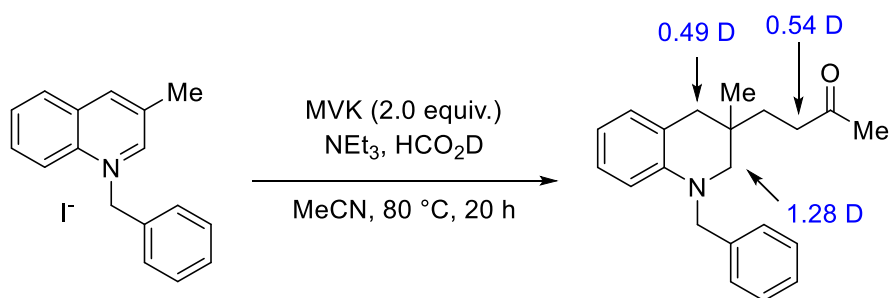
^1H NMR



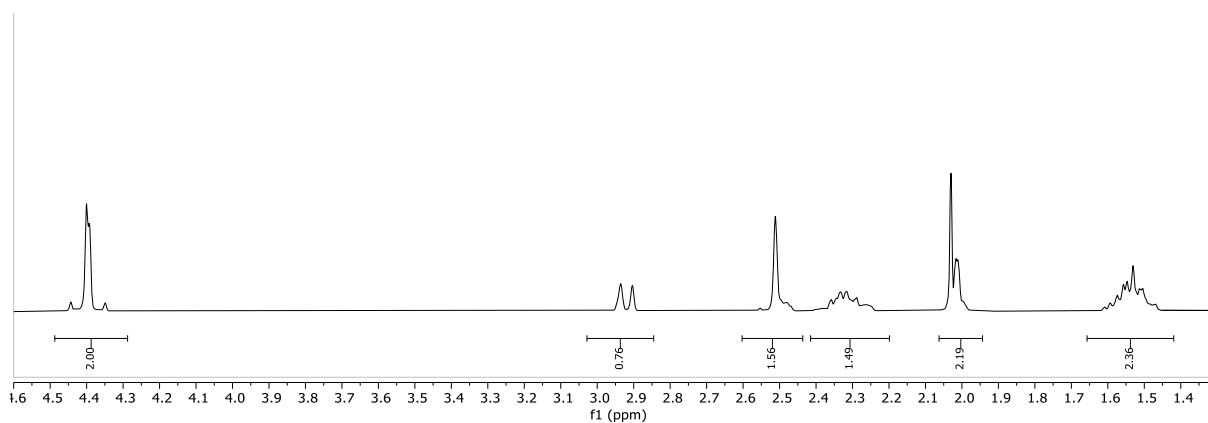
^2H NMR



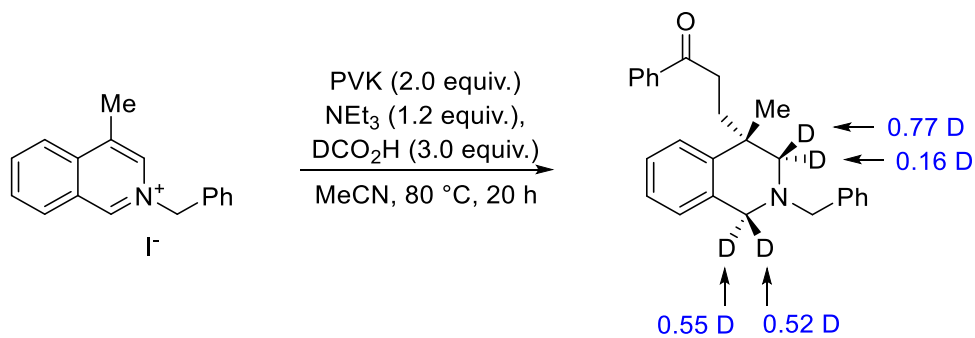
Reaction with formic acid-d₂ (DCO₂D):



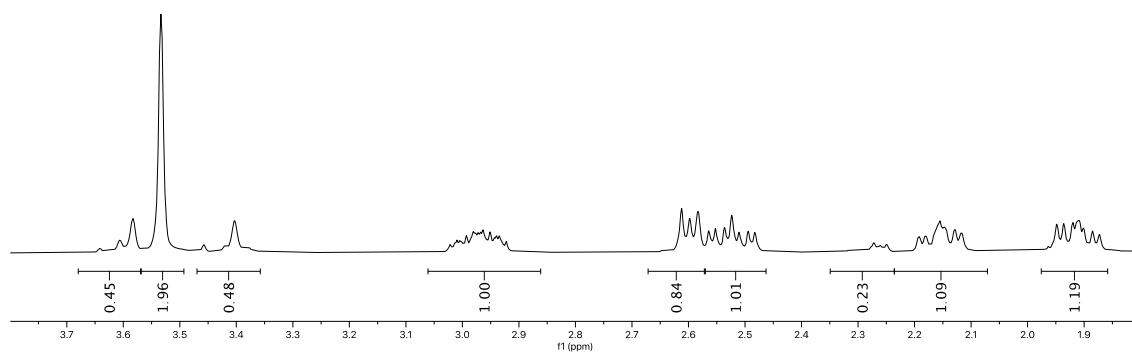
¹H NMR



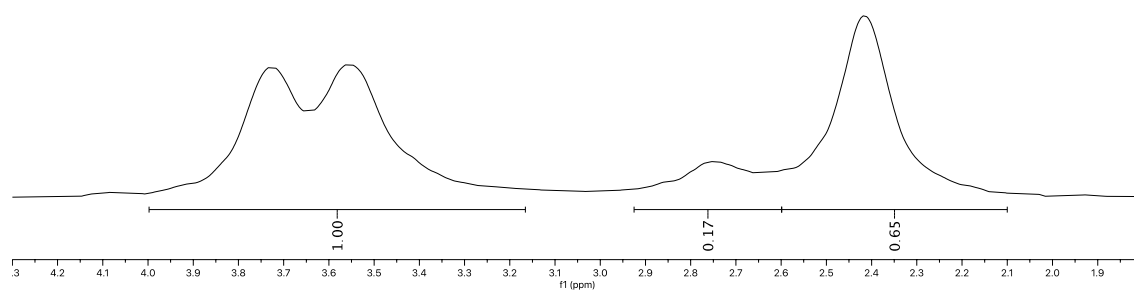
Reaction with formic-d acid (DCO₂H):



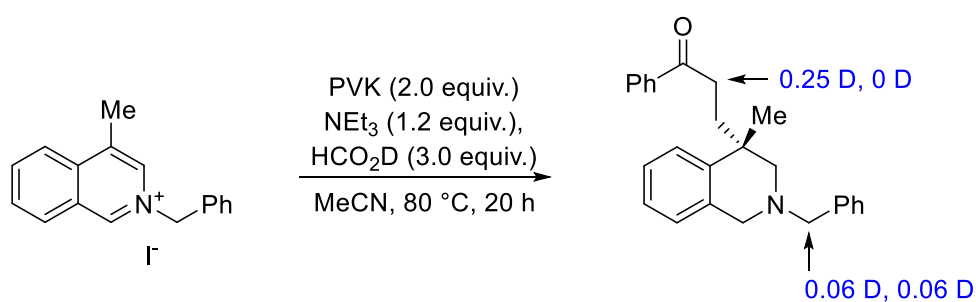
¹H NMR



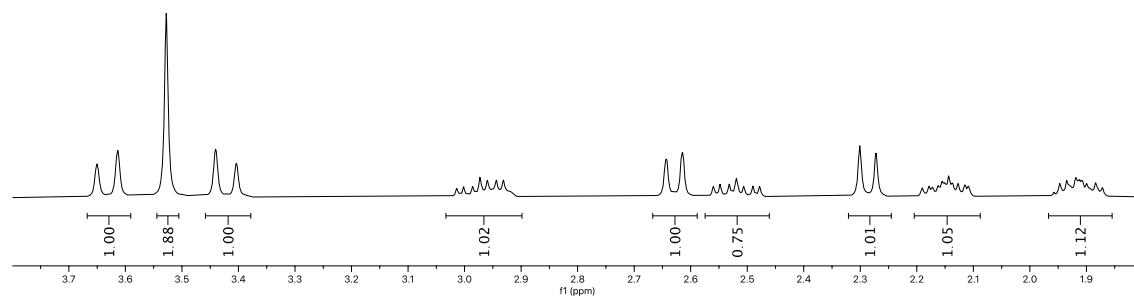
^2H NMR



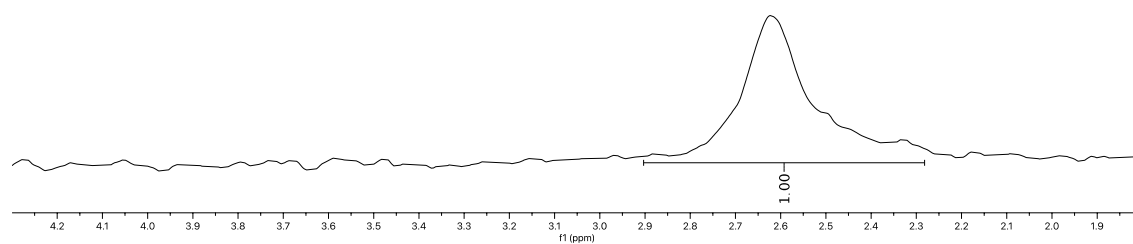
Reaction with formic acid-d (HCO_2D):



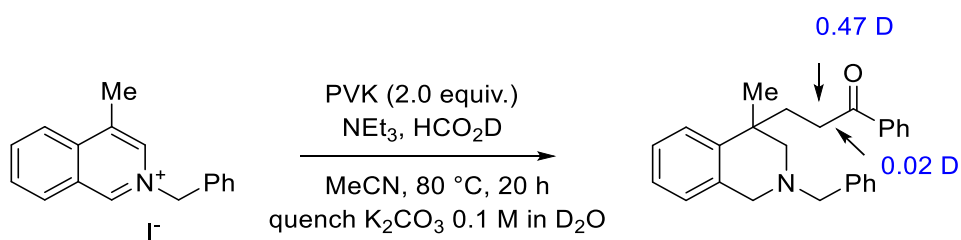
^1H NMR



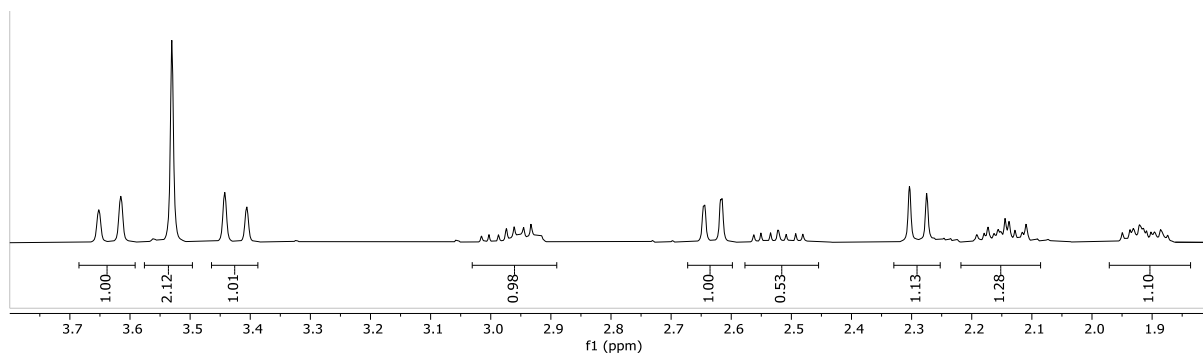
^2H NMR



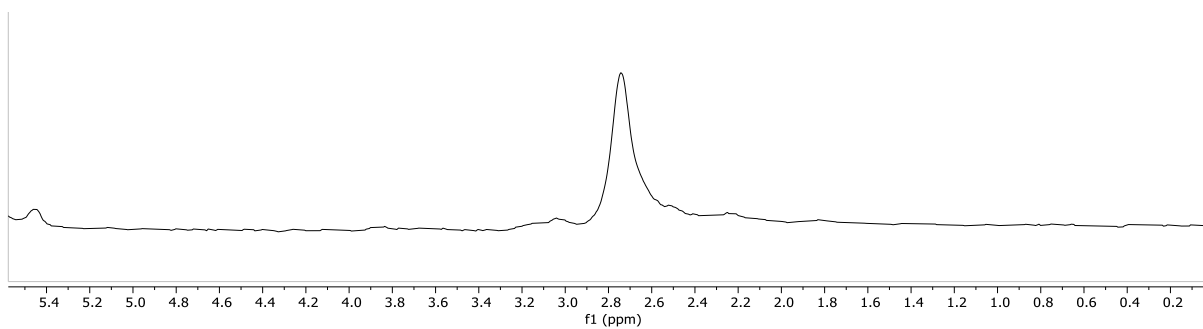
Reaction with formic acid-d (HCO_2D) and quench with 0.1 K_2CO_3 in D_2O :



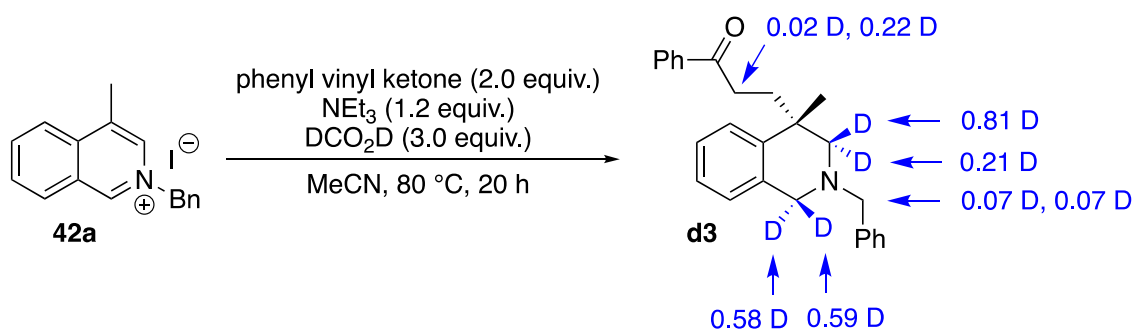
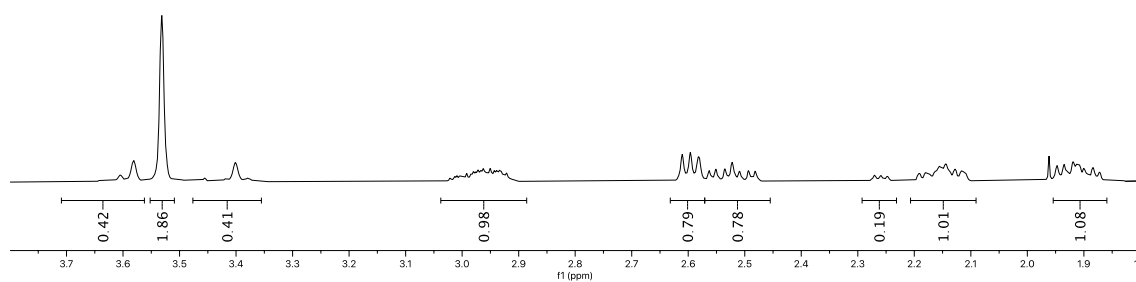
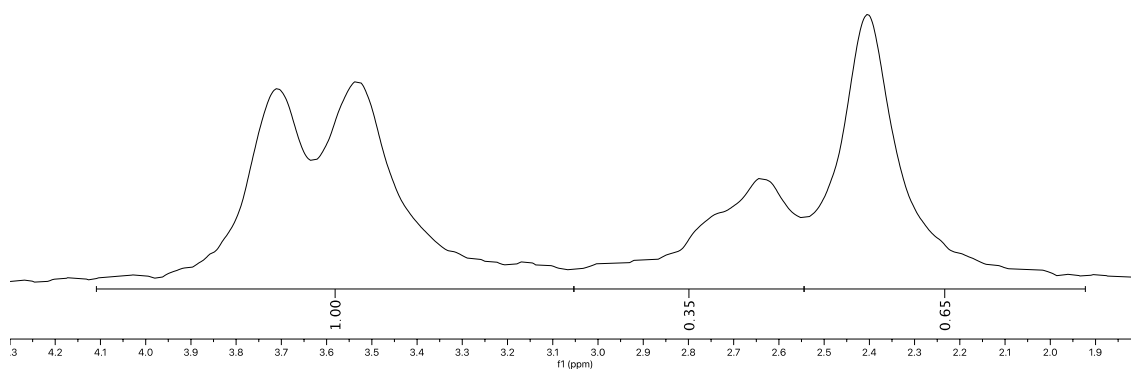
^1H NMR



^2H NMR



Reaction with formic acid-d₂ (DCO₂D):

¹H NMR²H NMR

Proposed mechanism for quinolinium and isoquinolinium salts

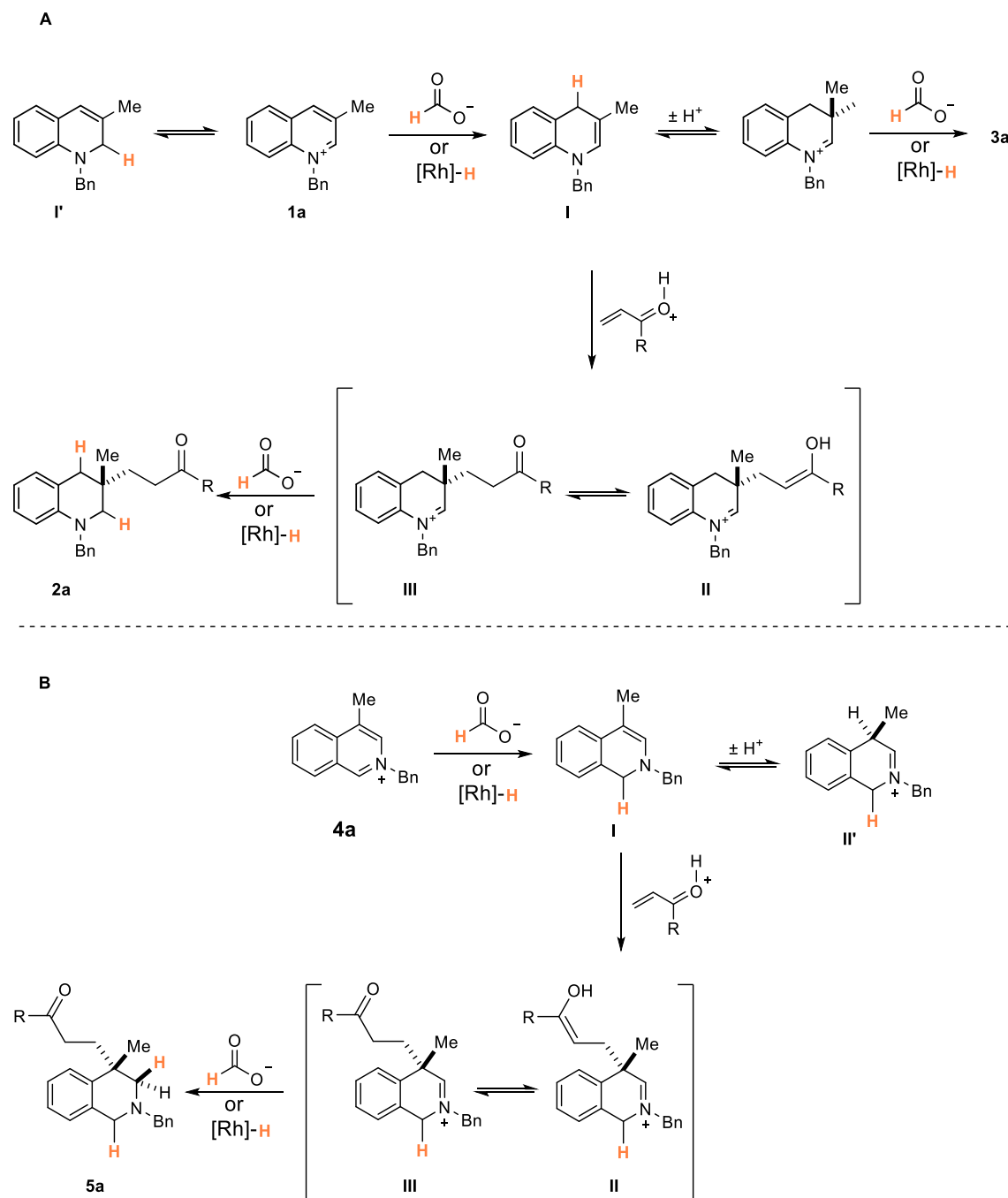


Figure 5: Mechanism of the reaction with activated quinoline (A) and isoquinolines (B)

Crystallographic data

Table 1. Crystal data and structure refinement for **2m**.

Empirical formula	C ₃₁ H ₃₈ Cl N O	
Formula weight	476.10	
Temperature	300 K	
Wavelength	1.54184 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 9.2443(4) Å	α = 90.582(3)°.
	b = 16.6064(5) Å	β = 97.470(3)°.
	c = 18.4379(7) Å	γ = 104.885(3)°.
Volume	2709.49(18) Å ³	
Z	4	
Density (calculated)	1.167 Mg/m ³	
Absorption coefficient	1.407 mm ⁻¹	
F(000)	1023.991	
Crystal size	0.11 x 0.08 x 0.05 mm ³	
Theta range for data collection	3.585 to 76.936°.	
Index ranges	-11 ≤ h ≤ 11, -15 ≤ k ≤ 20, -23 ≤ l ≤ 22	
Reflections collected	28854	
Independent reflections	11191 [R(int) = 0.049]	
Completeness to theta = 73.347°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.93 and 0.73	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	11190 / 0 / 613	
Goodness-of-fit on F ²	1.0231	
Final R indices [I > 2σ(I)]	R1 = 0.0752, wR2 = 0.1996	
R indices (all data)	R1 = 0.1019, wR2 = 0.2419	
Largest diff. peak and hole	0.80 and -0.47 e.Å ⁻³	

Table 2. Crystal data and structure refinement for **5o.Hcl**.

Empirical formula	C ₃₁ H ₃₈ Cl N O	
Formula weight	476.10	
Temperature	35 K	
Wavelength	0.68890 Å	
Crystal system	Monoclinic	
Space group	P c	
Unit cell dimensions	a = 20.6290(8) Å	$\alpha = 90^\circ$.
	b = 7.2107(3) Å	$\beta = 91.754(3)^\circ$.
	c = 17.2803(6) Å	$\gamma = 90^\circ$.
Volume	2569.23(17) Å ³	
Z	4	
Density (calculated)	1.231 Mg/m ³	
Absorption coefficient	0.158 mm ⁻¹	
F(000)	1024.001	
Crystal size	0.15 x 0.05 x 0.01 mm ³	
Theta range for data collection	1.915 to 23.684°.	
Index ranges	-29 ≤ h ≤ 26, -10 ≤ k ≤ 10, -24 ≤ l ≤ 24	
Reflections collected	24211	
Independent reflections	11639 [R(int) = 0.120]	
Completeness to theta = 25.058°	96.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00 and 0.75	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	7483 / 355 / 666	
Goodness-of-fit on F ²	1.0081	
Final R indices [I > 2σ(I)]	R1 = 0.1266, wR2 = 0.3183	
R indices (all data)	R1 = 0.1357, wR2 = 0.3322	
Absolute structure parameter	-0.11(8)	
Largest diff. peak and hole	1.18 and -0.77 e.Å ⁻³	

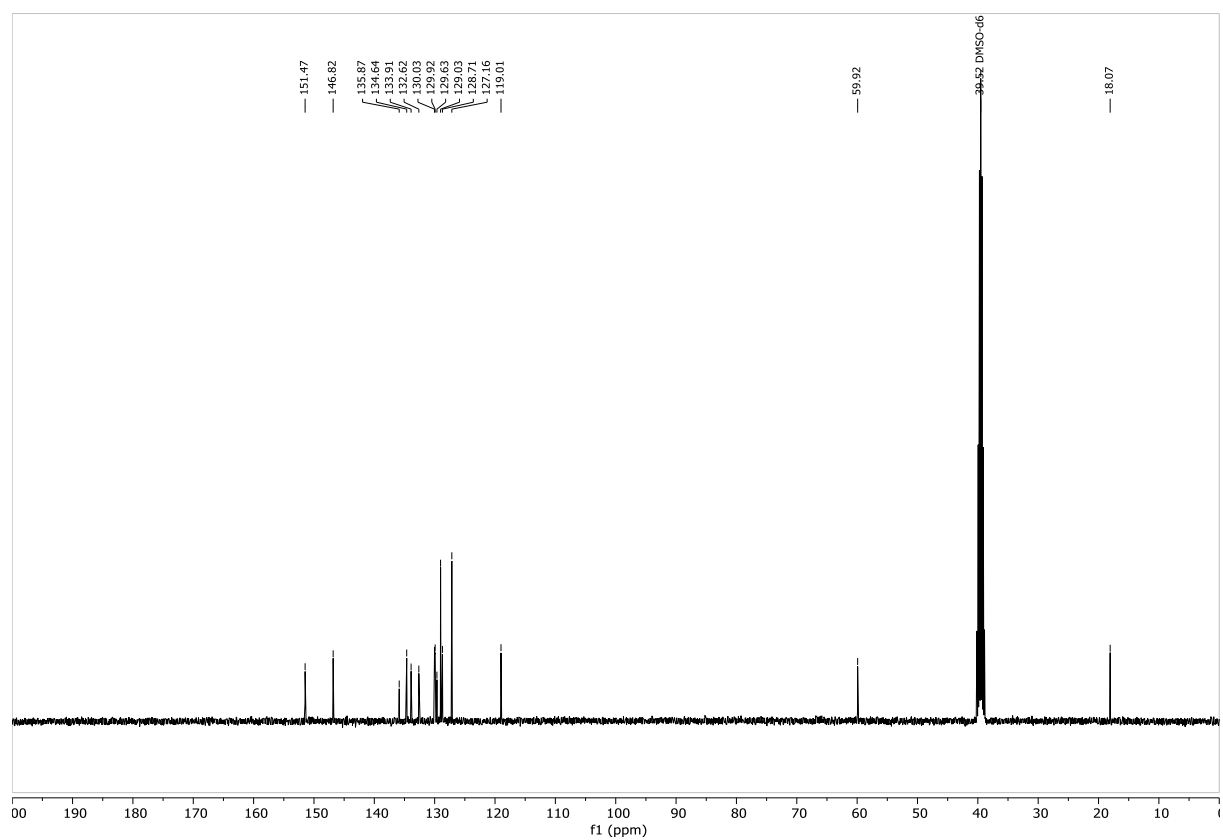
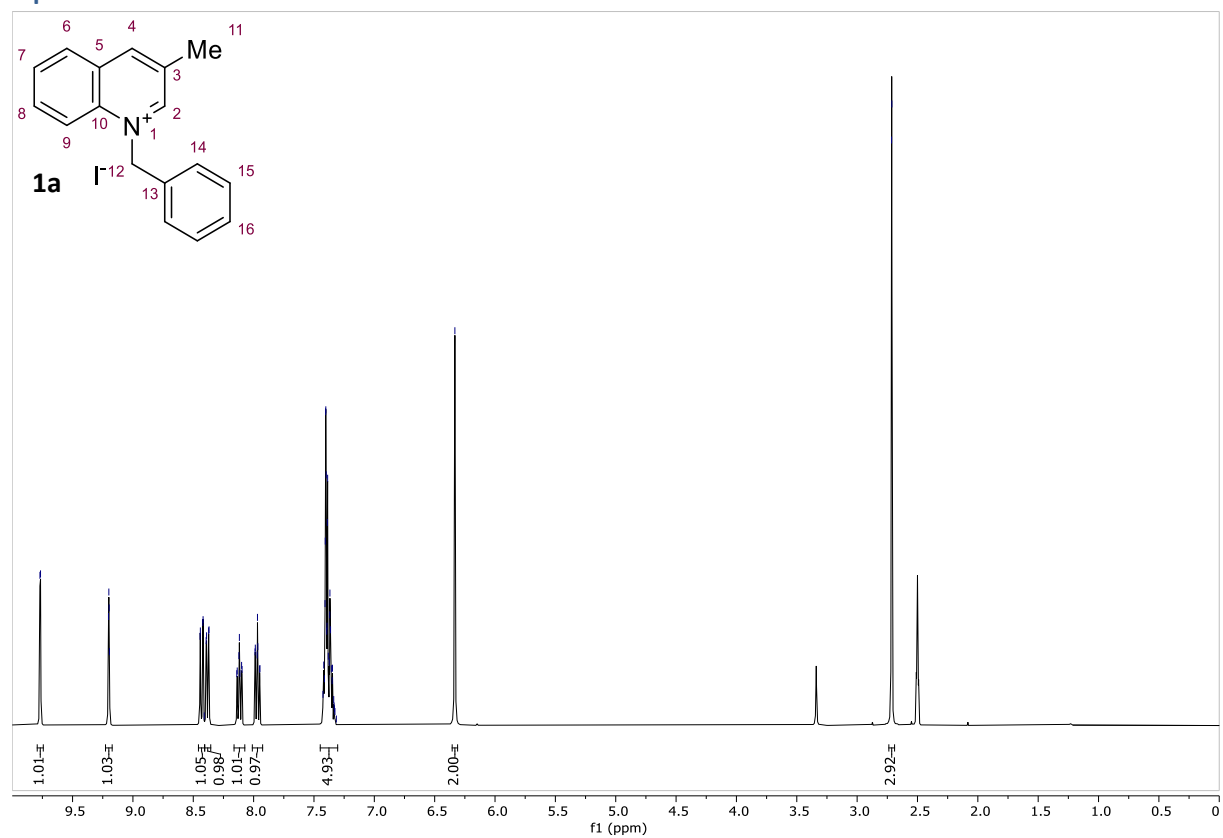
Table 3. Crystal data and structure refinement for **8a**.

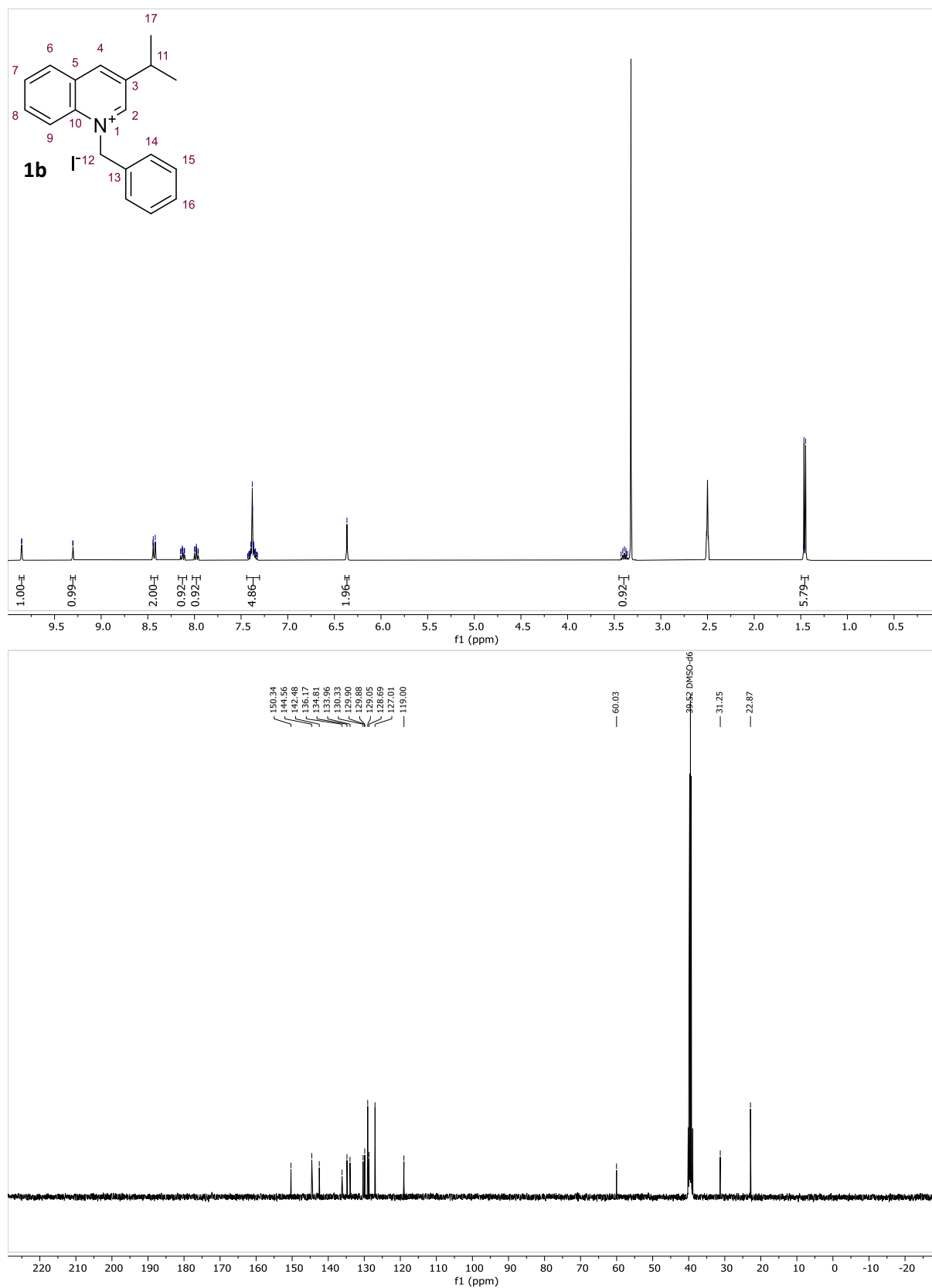
Empirical formula	C ₂₁ H ₂₆ Cl N	
Formula weight	327.90	
Temperature	150 K	
Wavelength	1.54180 Å	
Crystal system	Orthorhombic	
Space group	P n a 2 ₁	
Unit cell dimensions	a = 11.29240(10) Å	α = 90°.
	b = 13.6629(2) Å	β = 90°.
	c = 23.2273(2) Å	γ = 90°.
Volume	3583.67(7) Å ³	
Z	8	
Density (calculated)	1.215 Mg/m ³	
Absorption coefficient	1.857 mm ⁻¹	
F(000)	1408	
Crystal size	0.20 x 0.19 x 0.18 mm ³	
Theta range for data collection	3.753 to 76.284°.	
Index ranges	-13 ≤ h ≤ 14, -16 ≤ k ≤ 17, -27 ≤ l ≤ 29	
Reflections collected	43420	
Independent reflections	6973 [R(int) = 0.027]	
Completeness to theta = 76.284°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.72 and 0.56	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	6973 / 1 / 416	
Goodness-of-fit on F ²	1.0023	
Final R indices [I > 2σ(I)]	R1 = 0.0243, wR2 = 0.0666	
R indices (all data)	R1 = 0.0247, wR2 = 0.0671	
Absolute structure parameter	0.014(4)	
Largest diff. peak and hole	0.06 and -0.07 e.Å ⁻³	

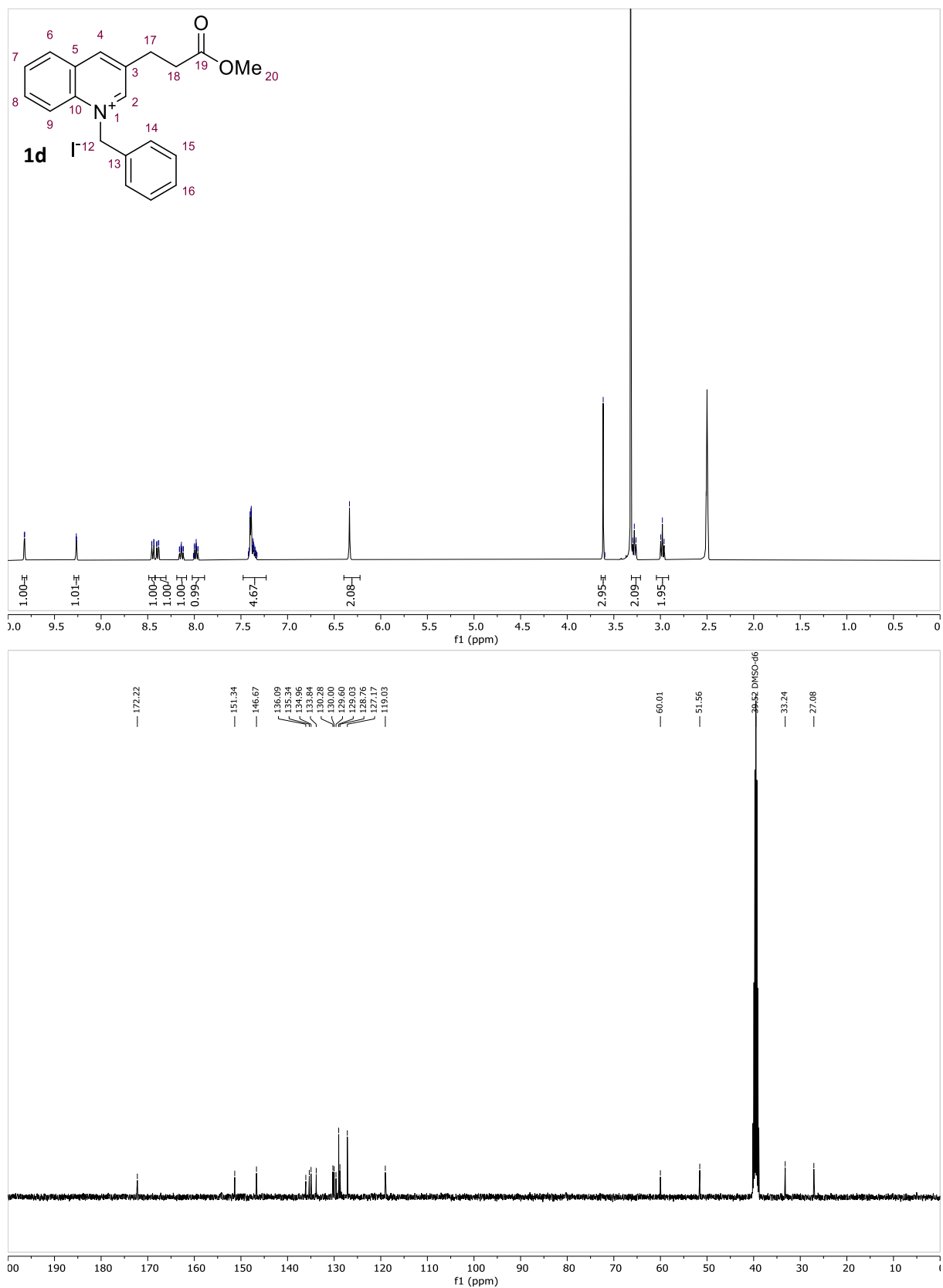
Table 4. Crystal data and structure refinement for **8e**.

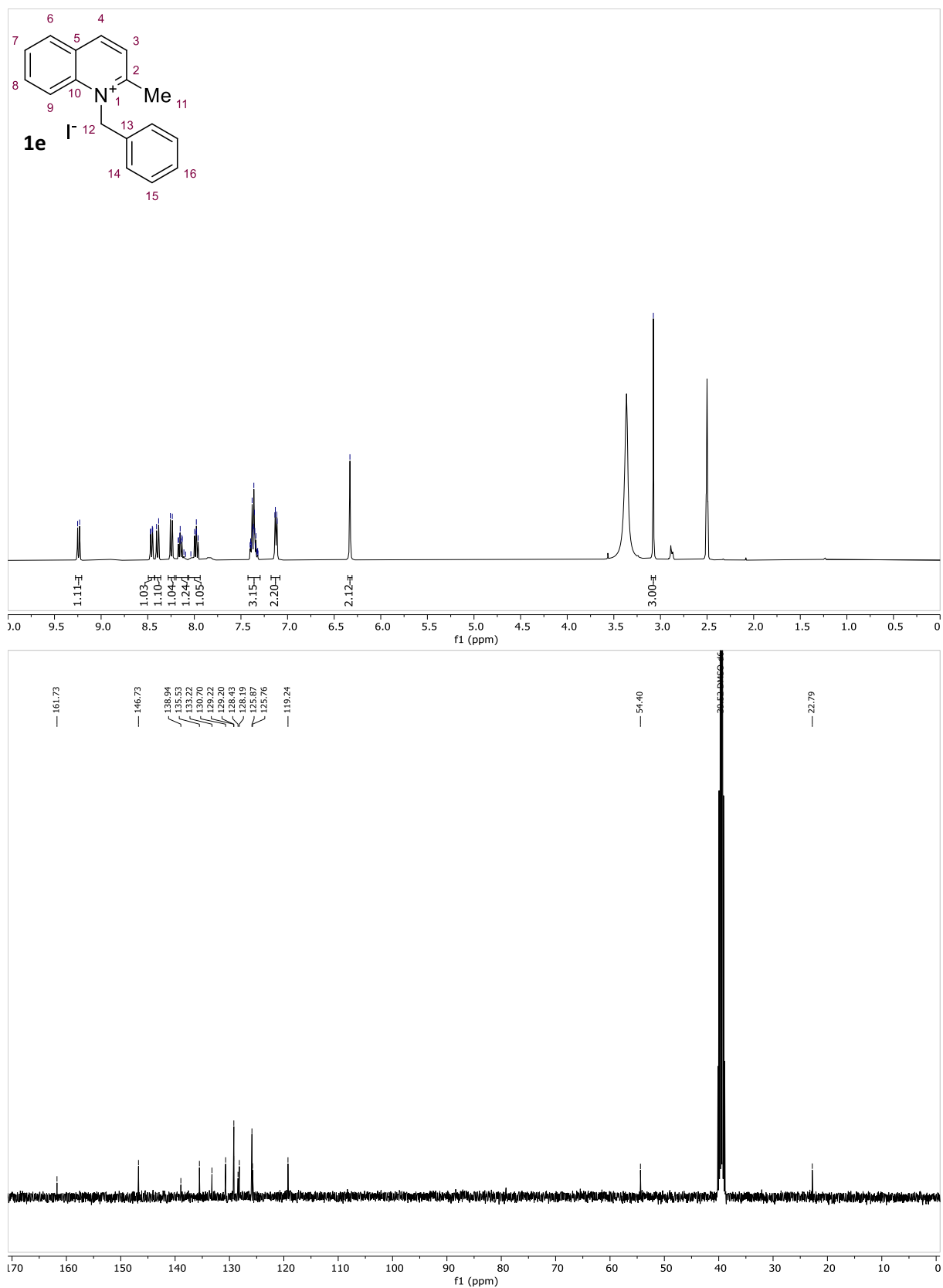
Empirical formula	C ₂₃ H ₂₈ I N	
Formula weight	445.39	
Temperature	150 K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	P 2 ₁ /n	
Unit cell dimensions	a = 9.2483(3) Å	α = 90°.
	b = 14.3133(4) Å	β = 106.151(4)°.
	c = 16.1073(5) Å	γ = 90°.
Volume	2048.03(12) Å ³	
Z	4	
Density (calculated)	1.444 Mg/m ³	
Absorption coefficient	12.297 mm ⁻¹	
F(000)	904	
Crystal size	0.07 x 0.05 x 0.05 mm ³	
Theta range for data collection	4.208 to 76.604°.	
Index ranges	-11 ≤ h ≤ 11, -17 ≤ k ≤ 12, -19 ≤ l ≤ 20	
Reflections collected	14033	
Independent reflections	4251 [R(int) = 0.032]	
Completeness to theta = 74.306°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.54 and 0.05	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	4244 / 0 / 226	
Goodness-of-fit on F ²	1.0544	
Final R indices [I > 2σ(I)]	R1 = 0.0767, wR2 = 0.1713	
R indices (all data)	R1 = 0.0819, wR2 = 0.1815	
Largest diff. peak and hole	2.84 and -0.50 e.Å ⁻³	
Kirsten to add data here for		

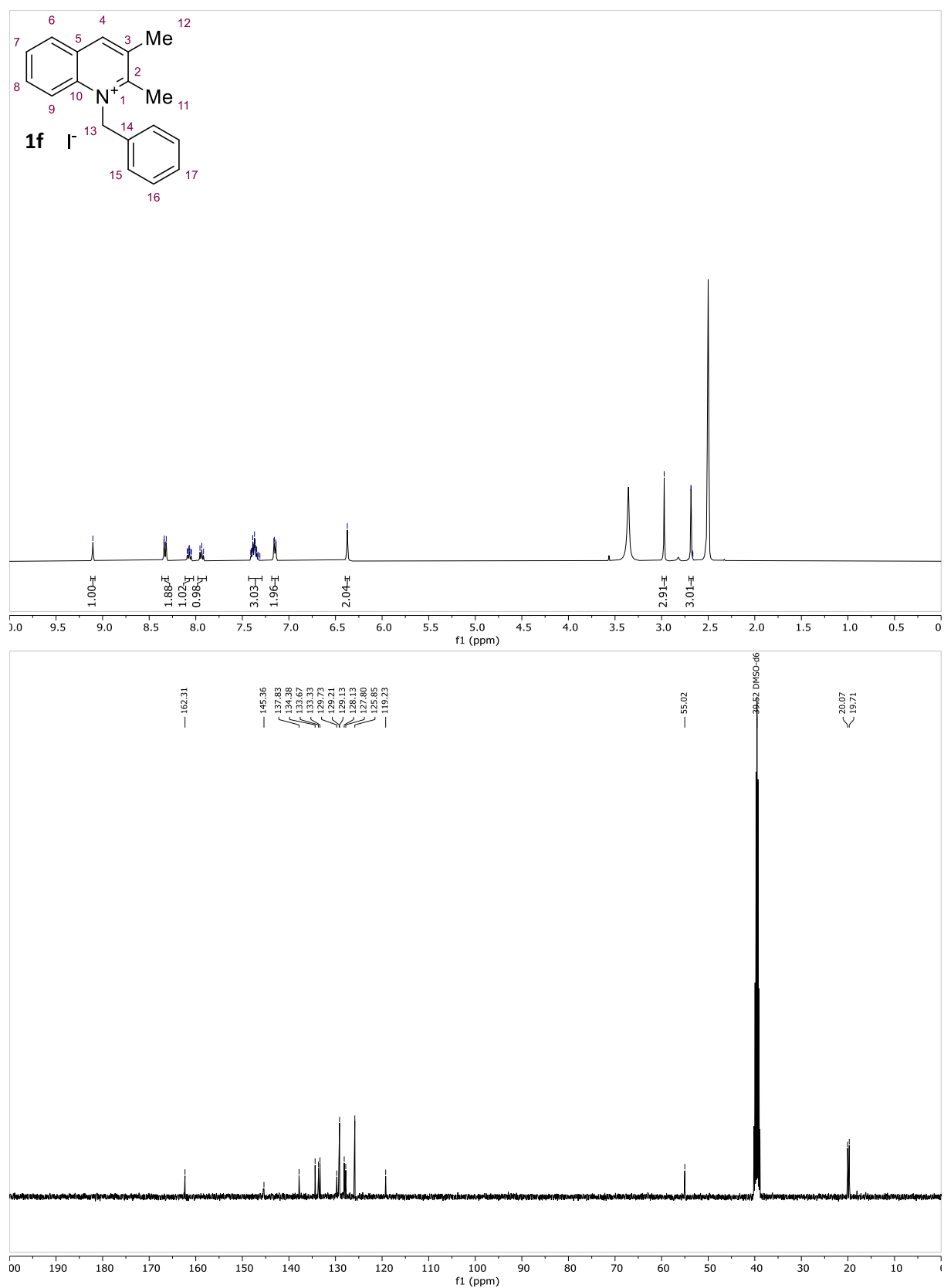
Spectra

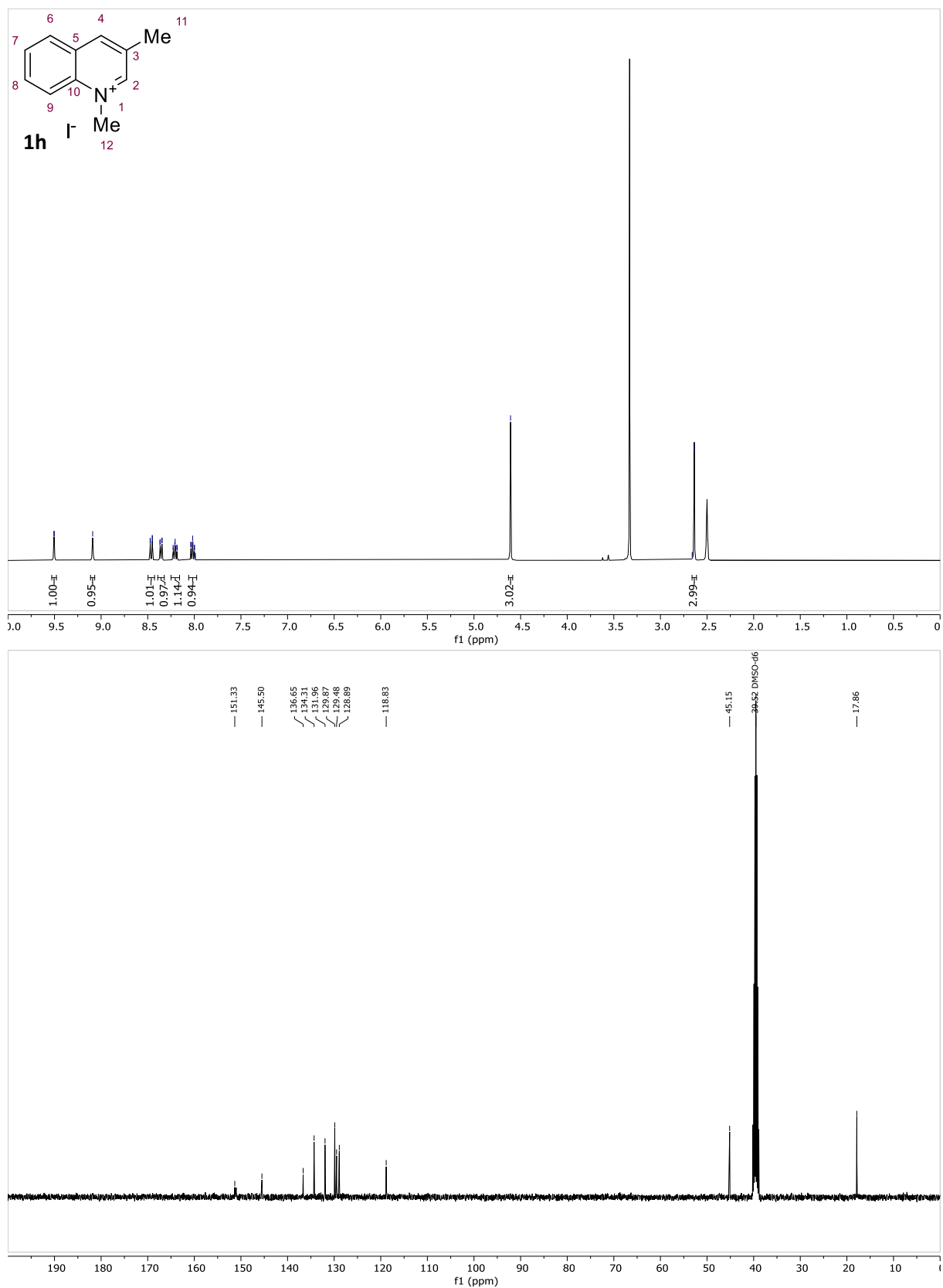


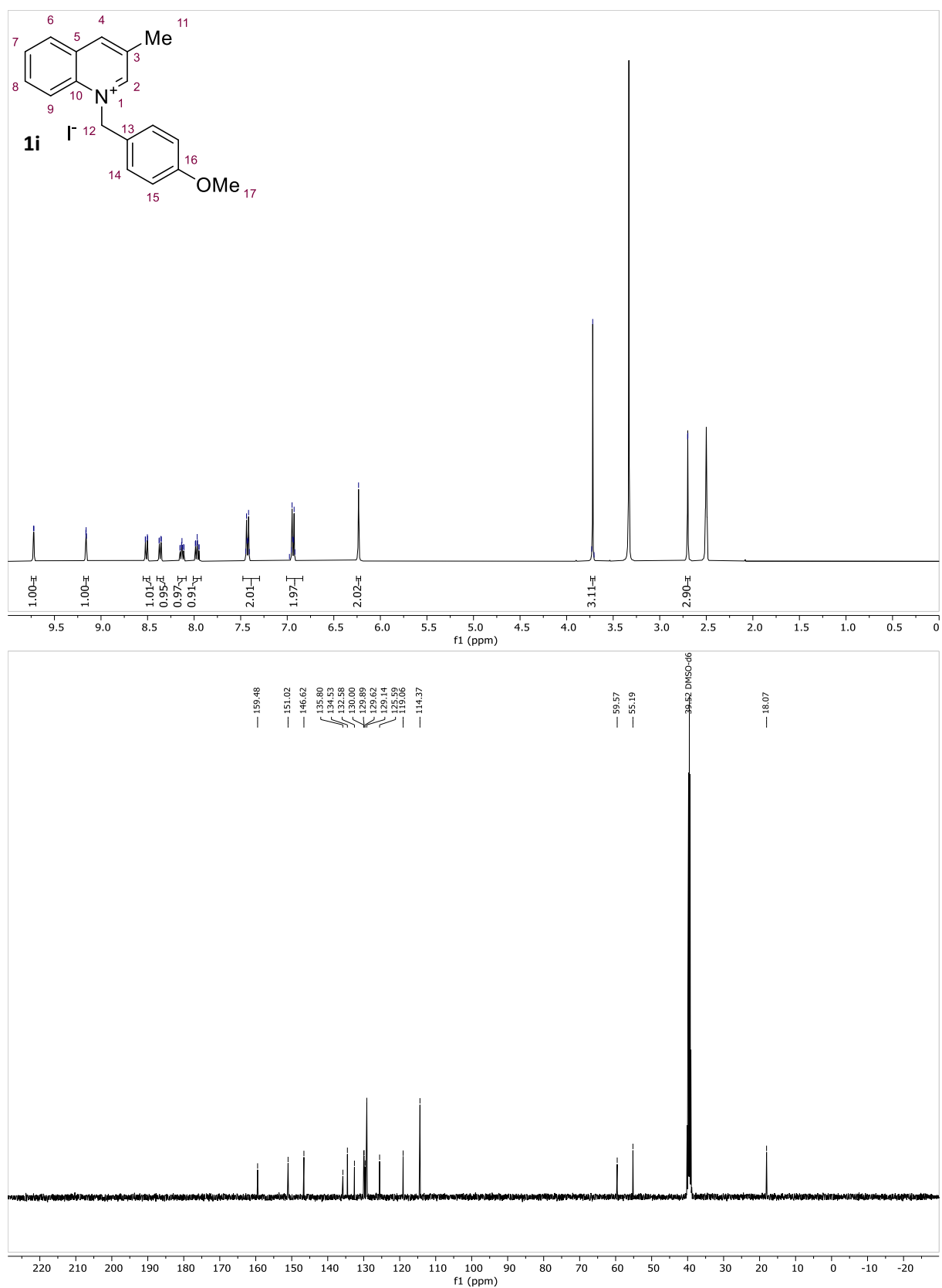


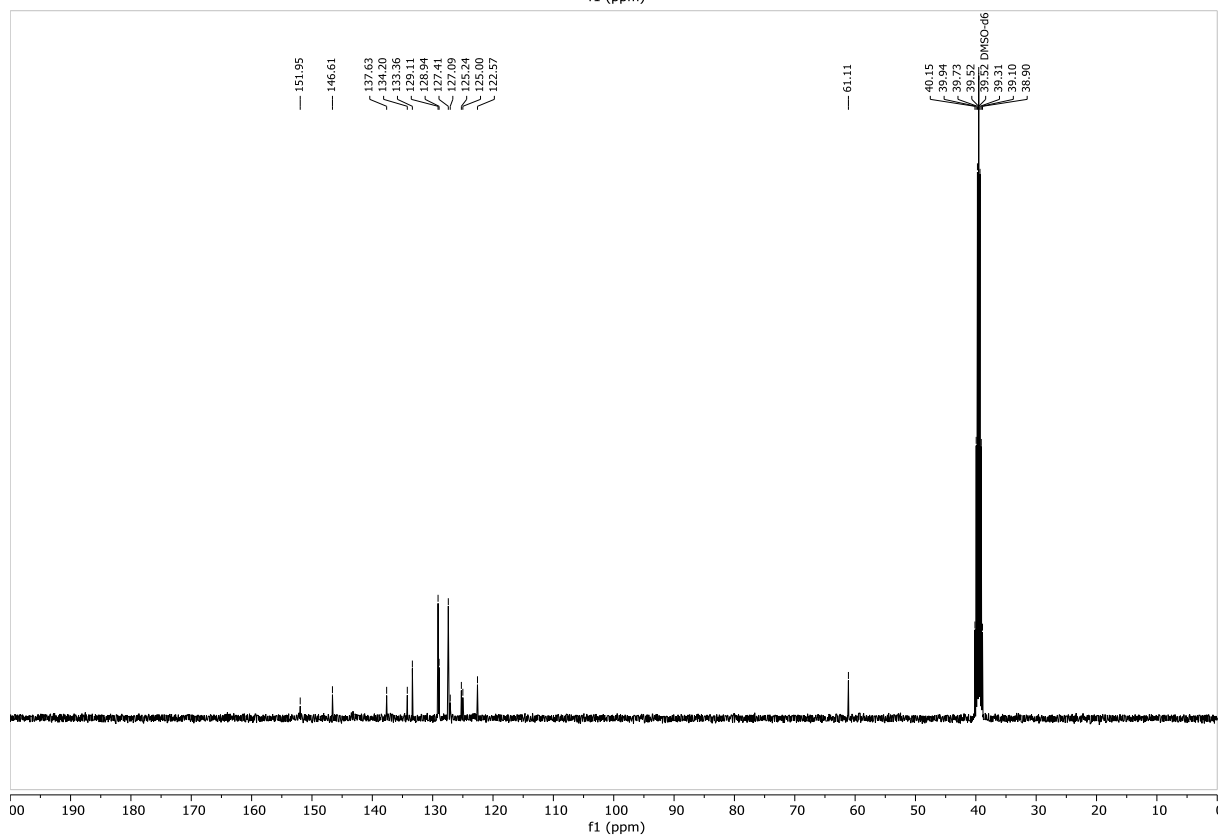
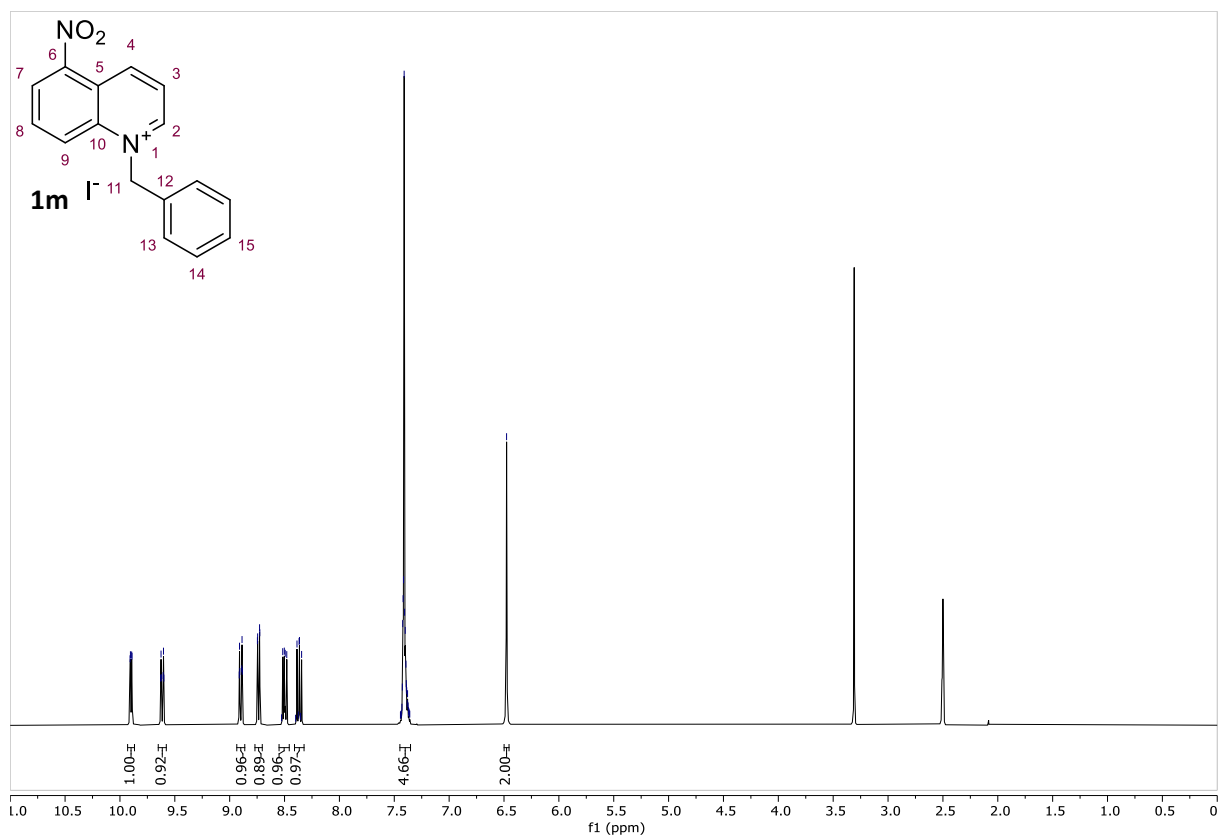


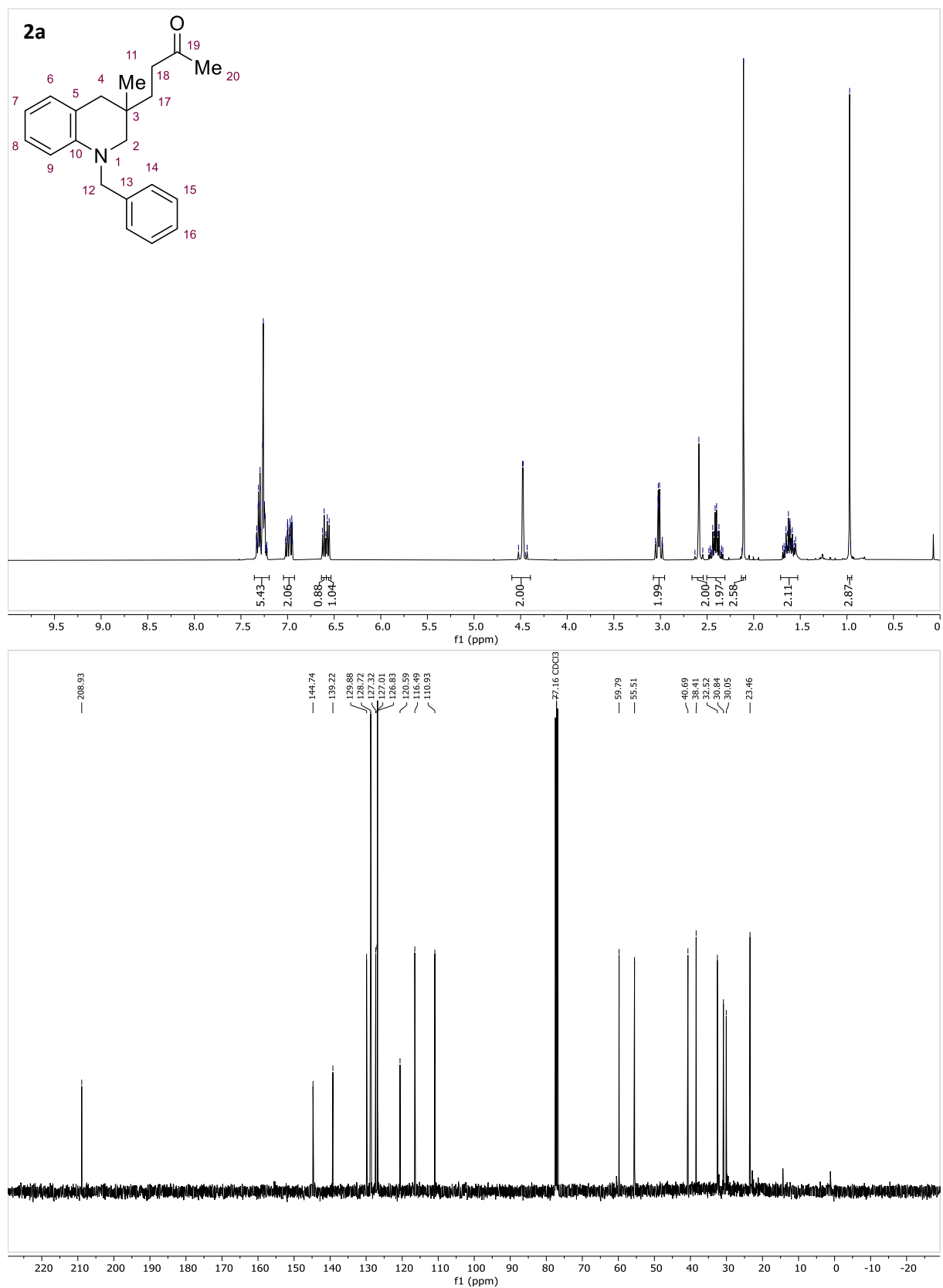


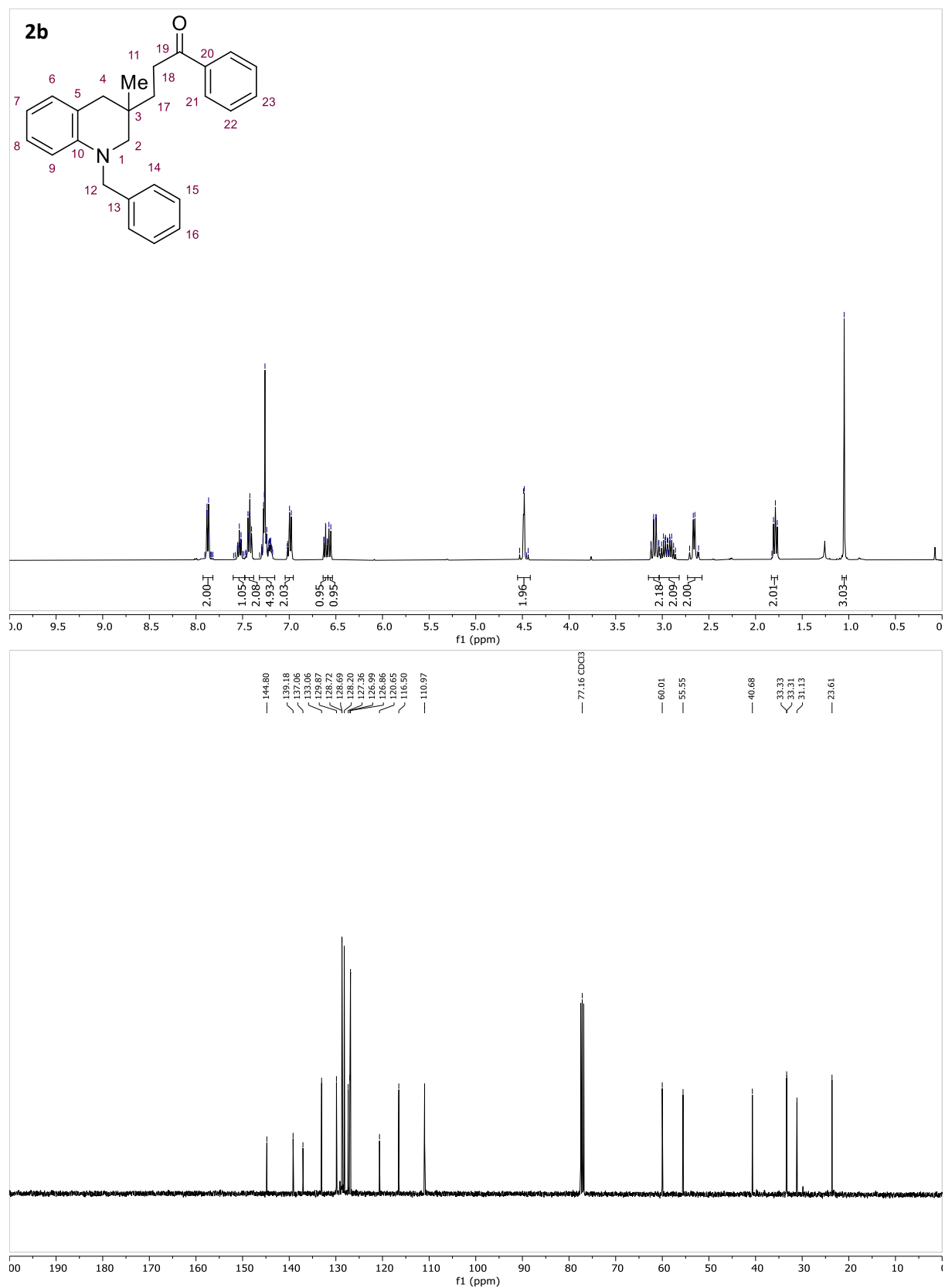


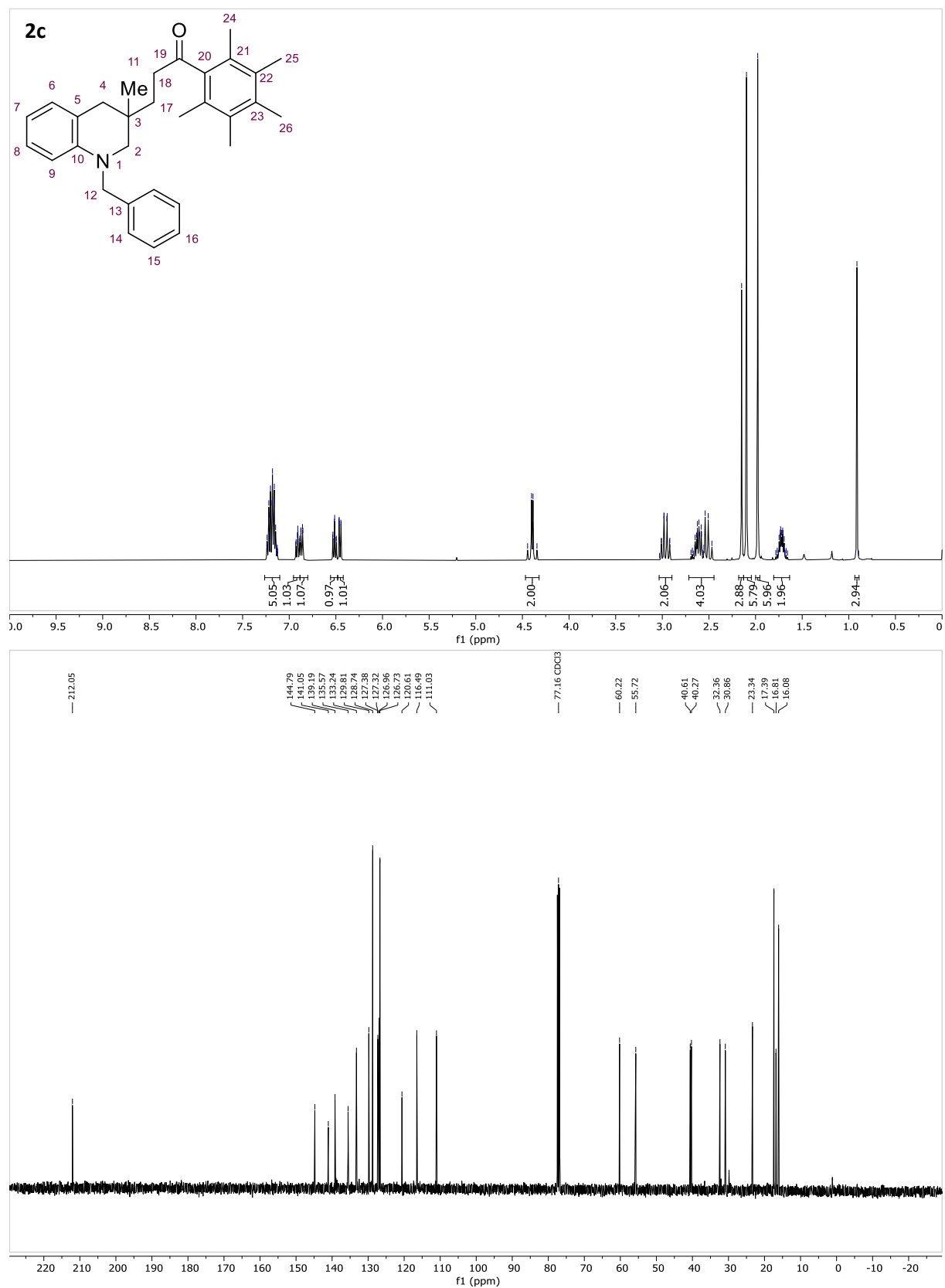


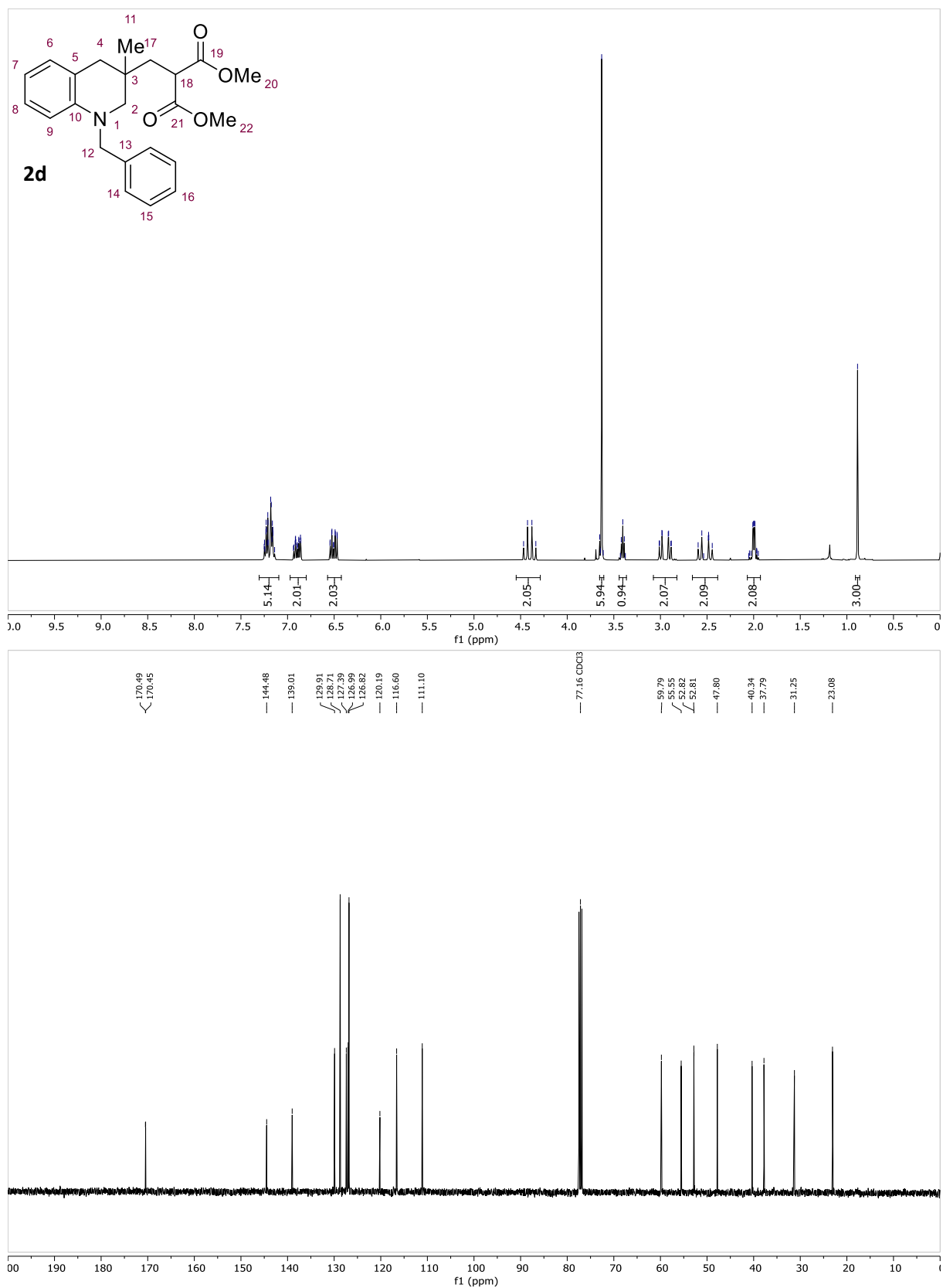


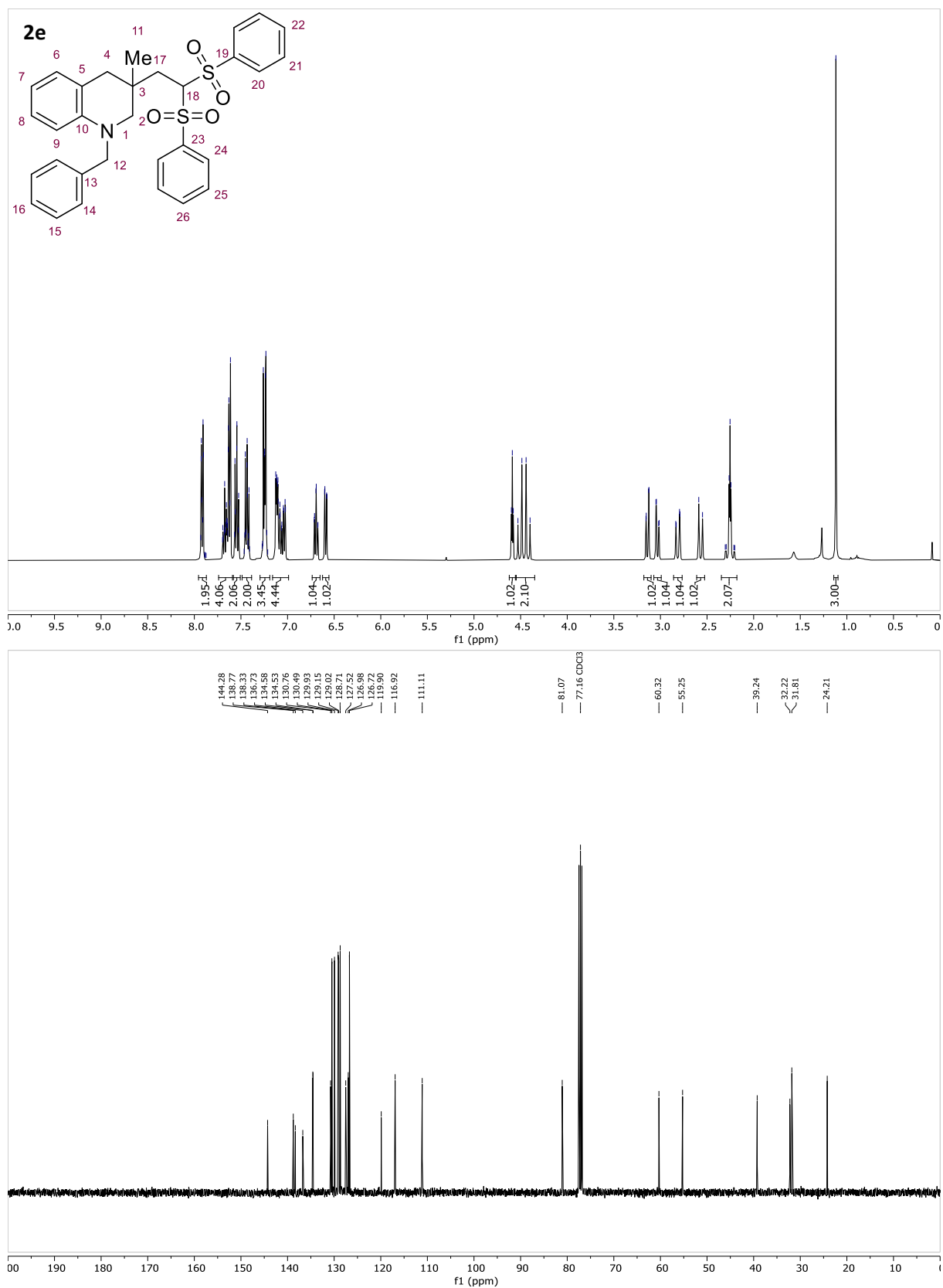


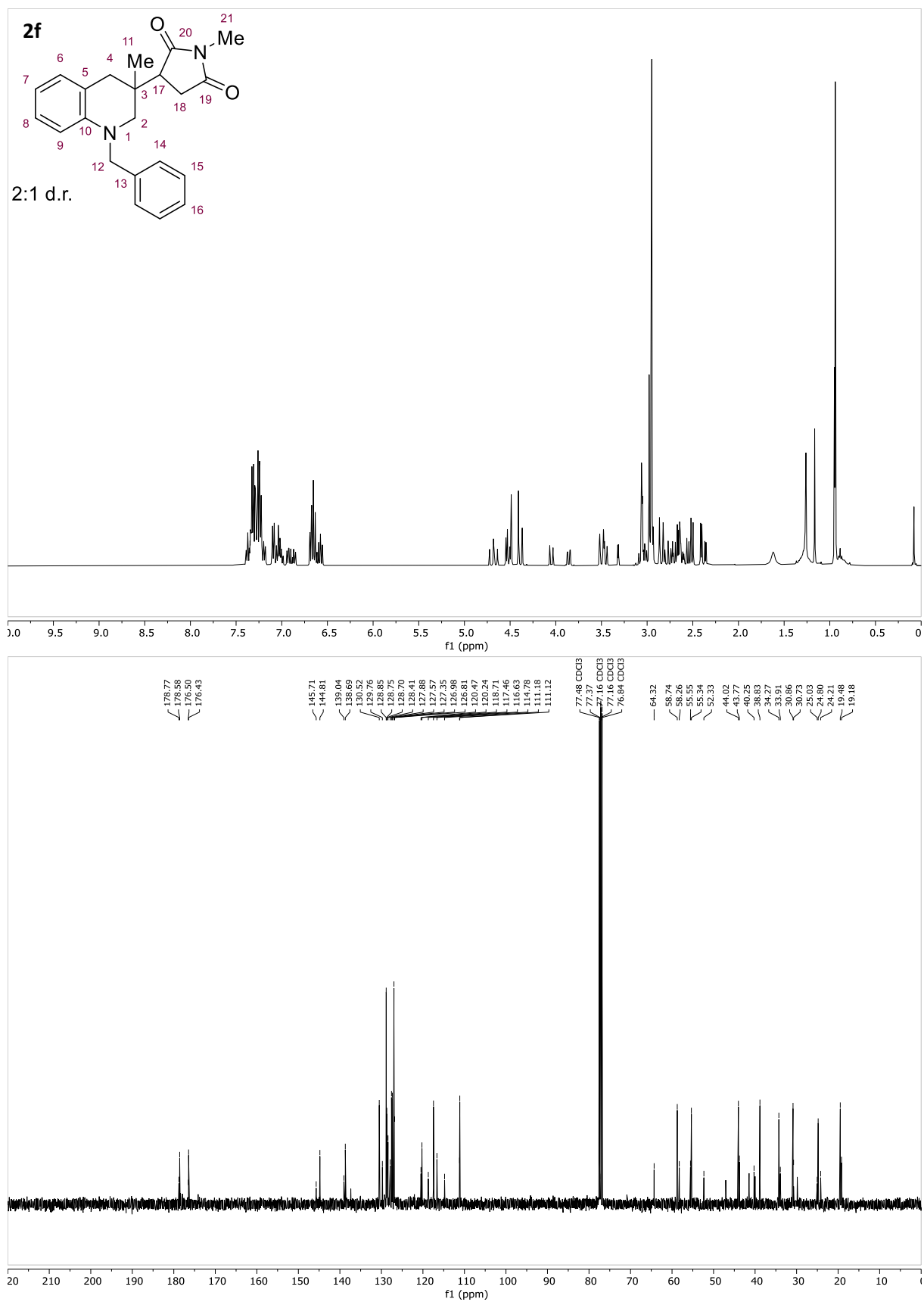


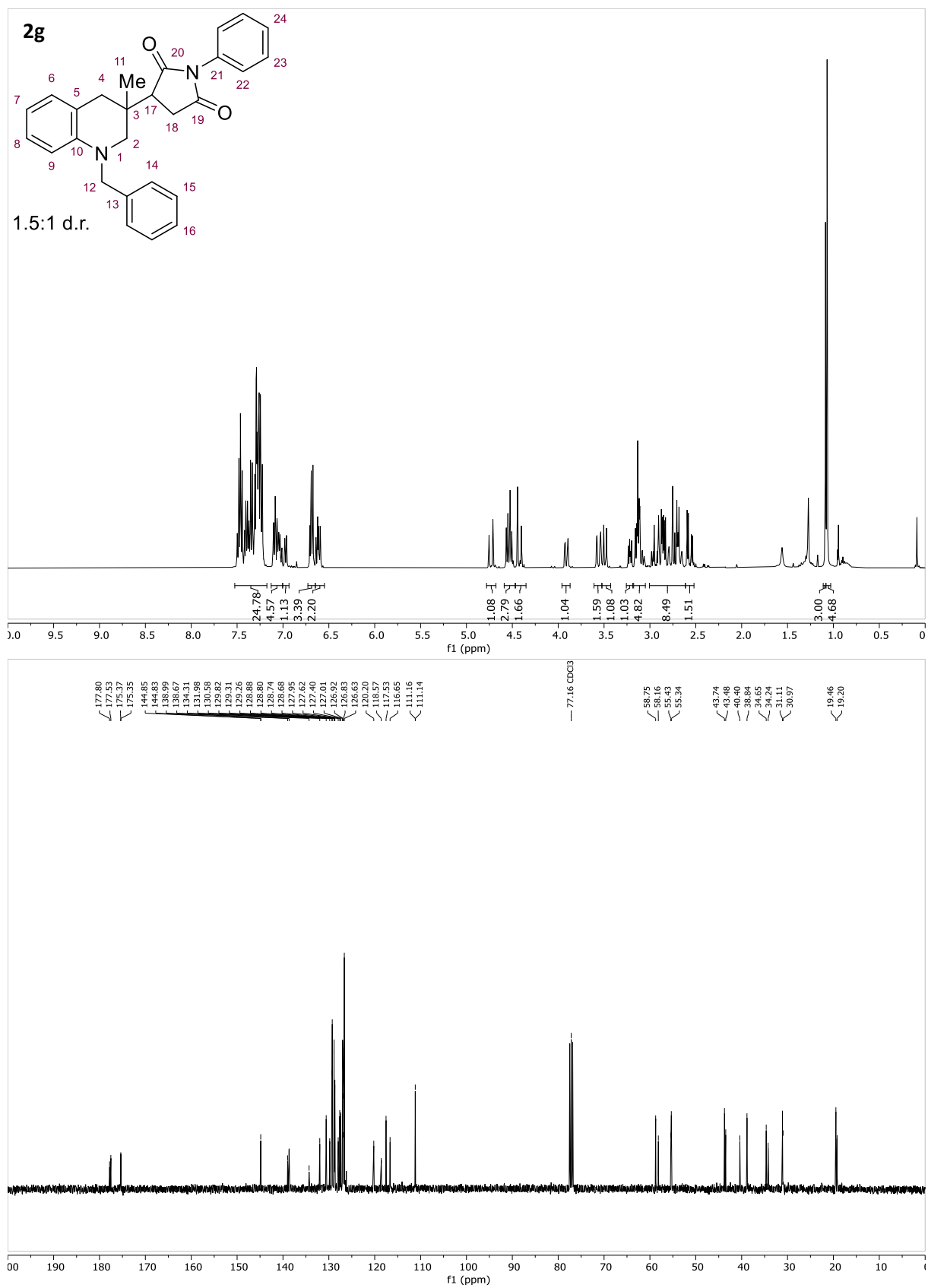


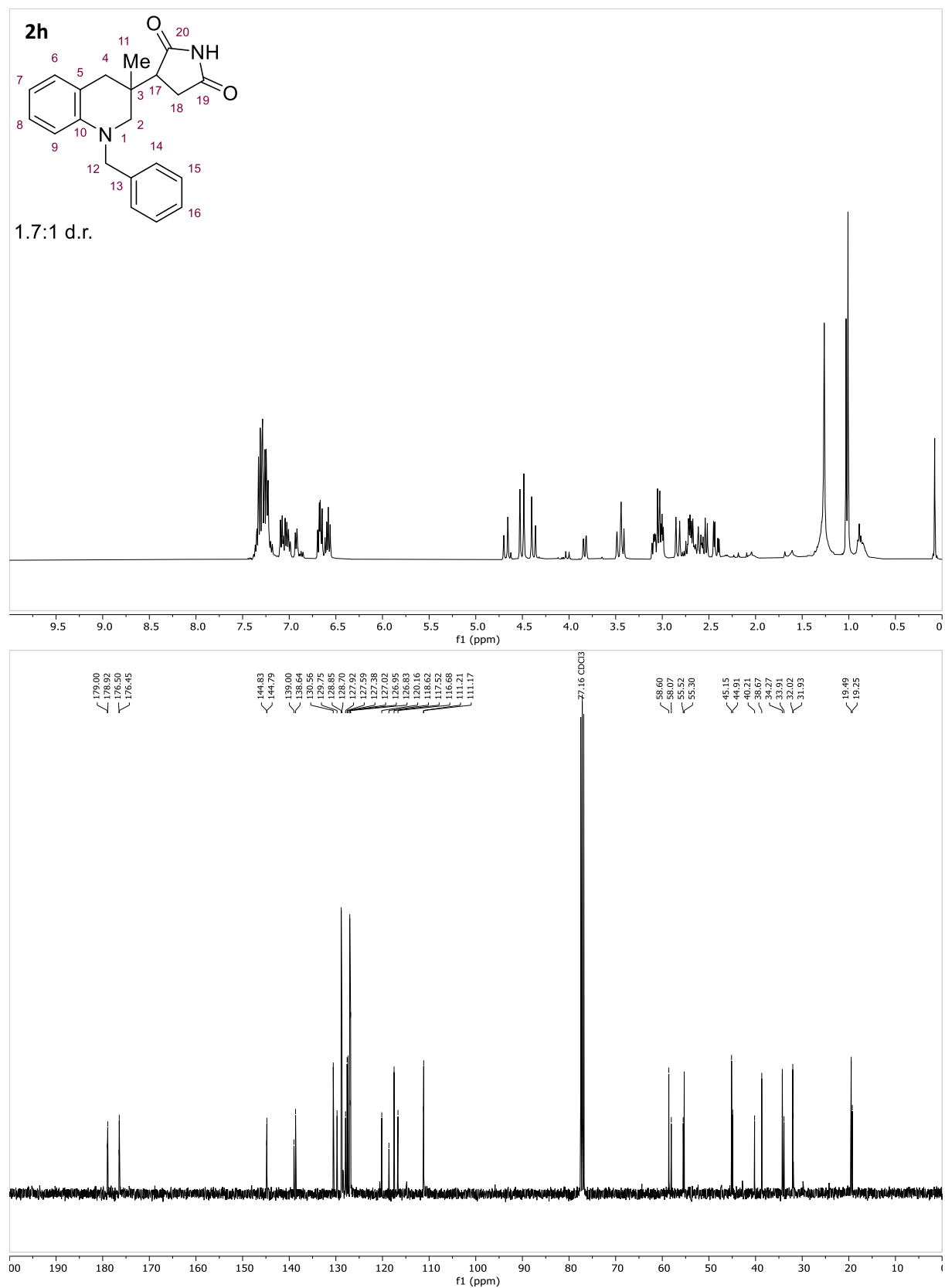


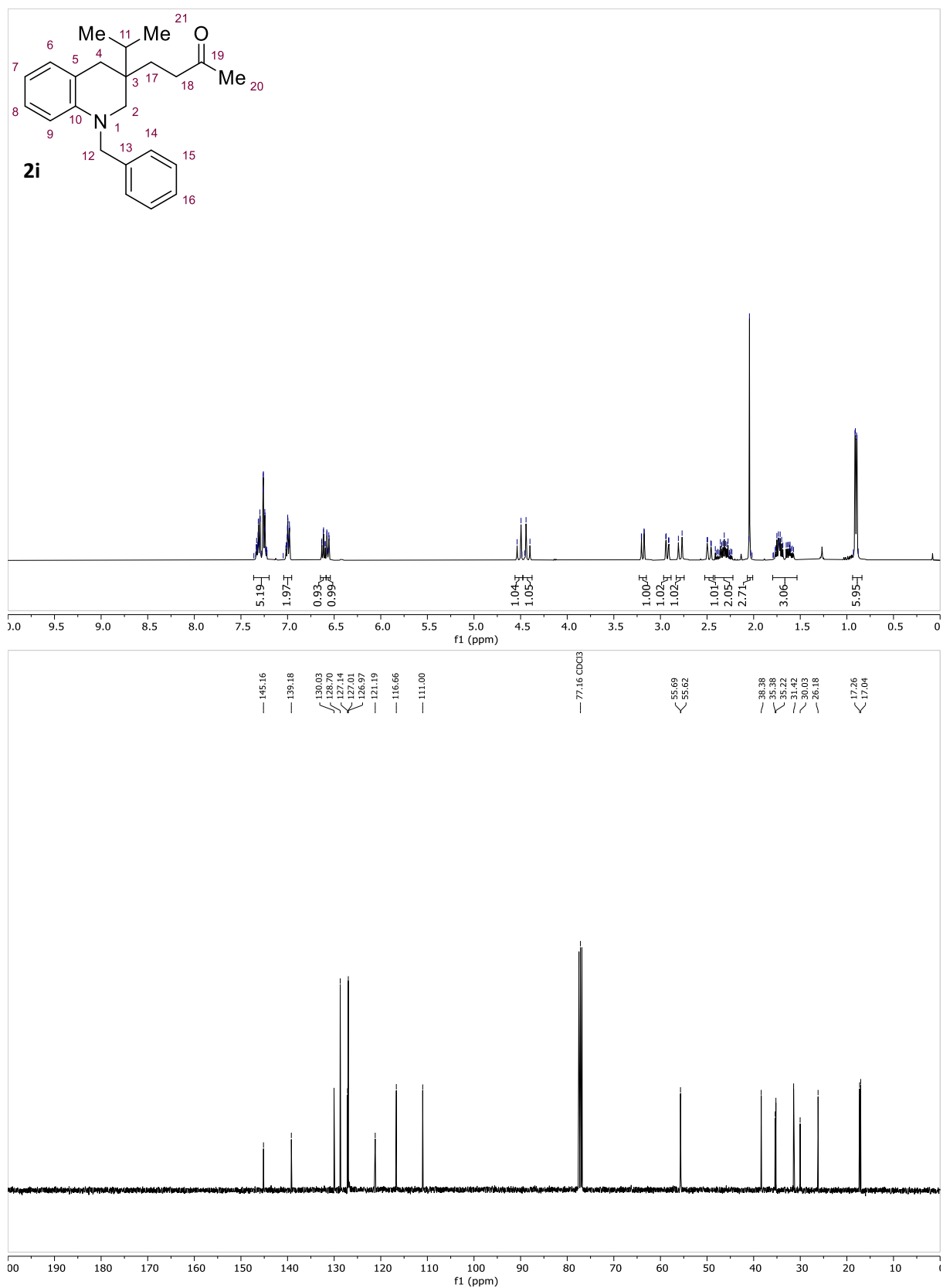


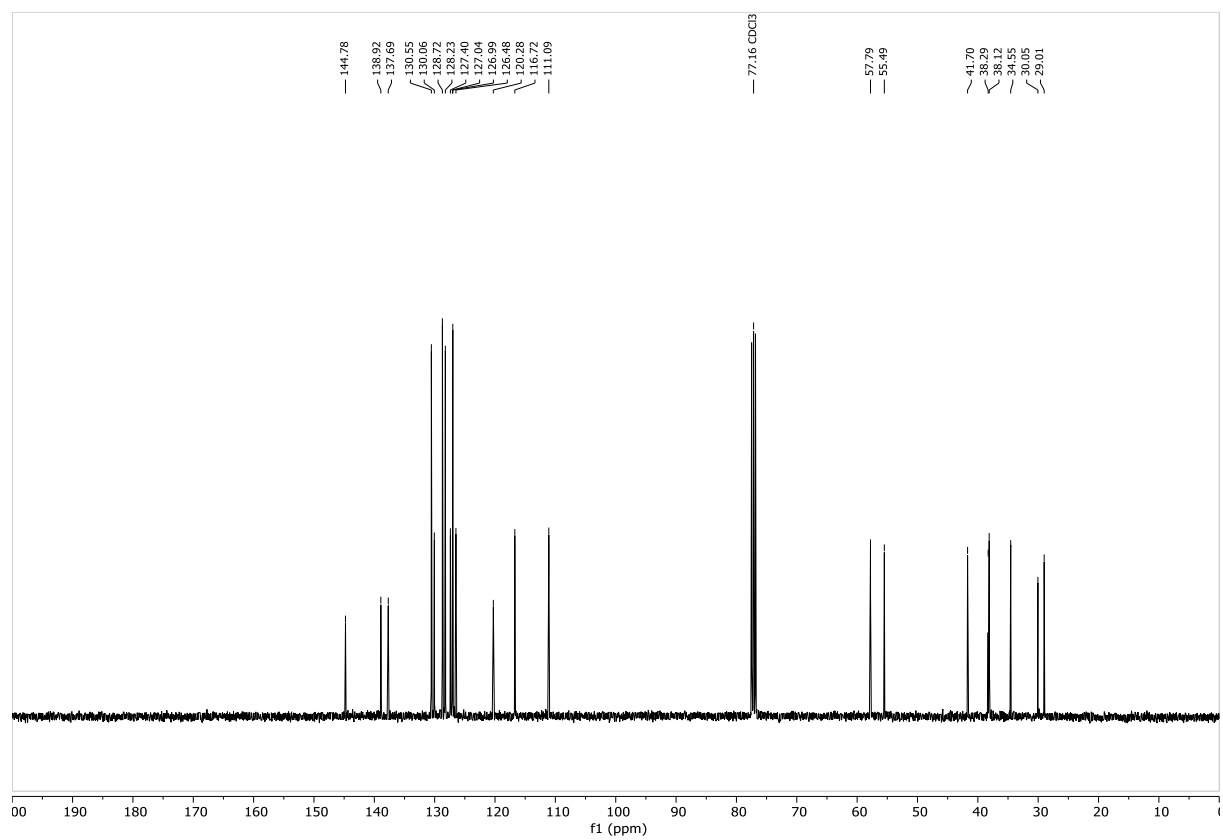
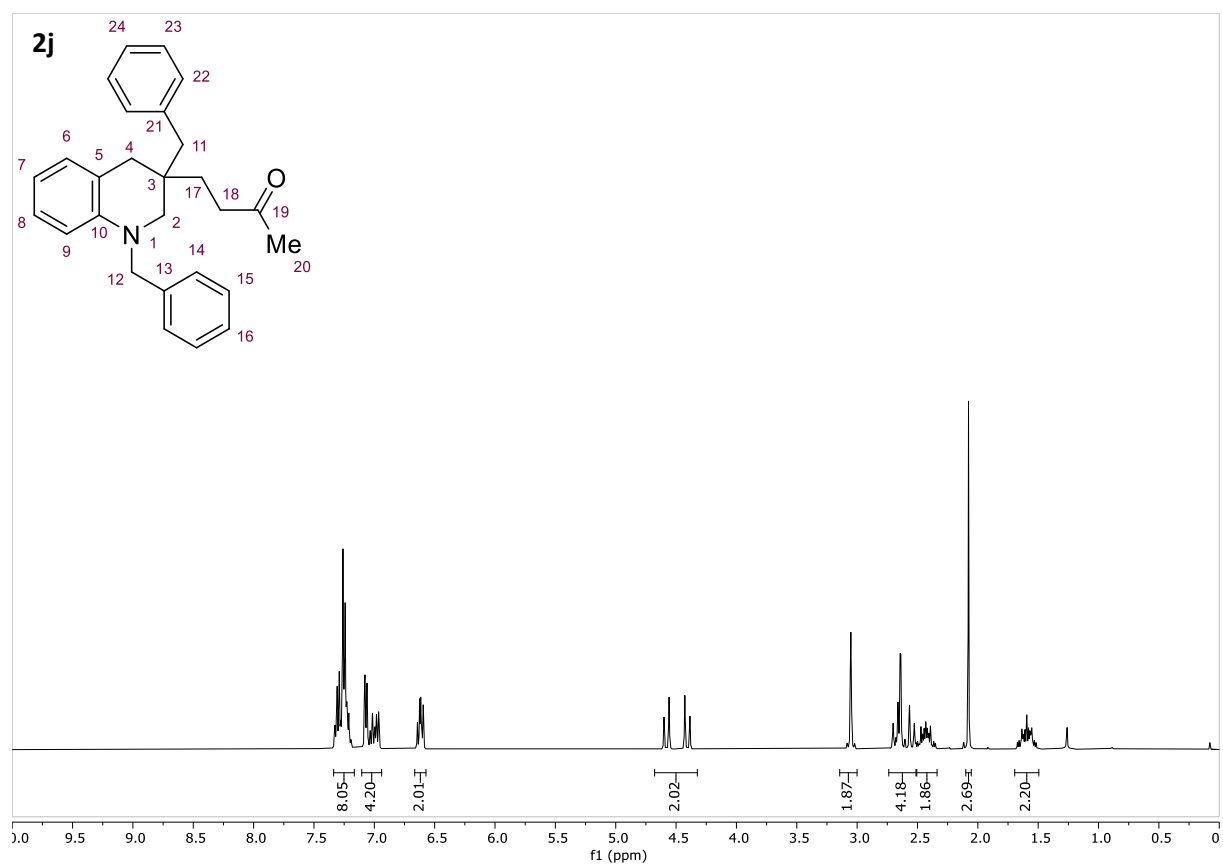


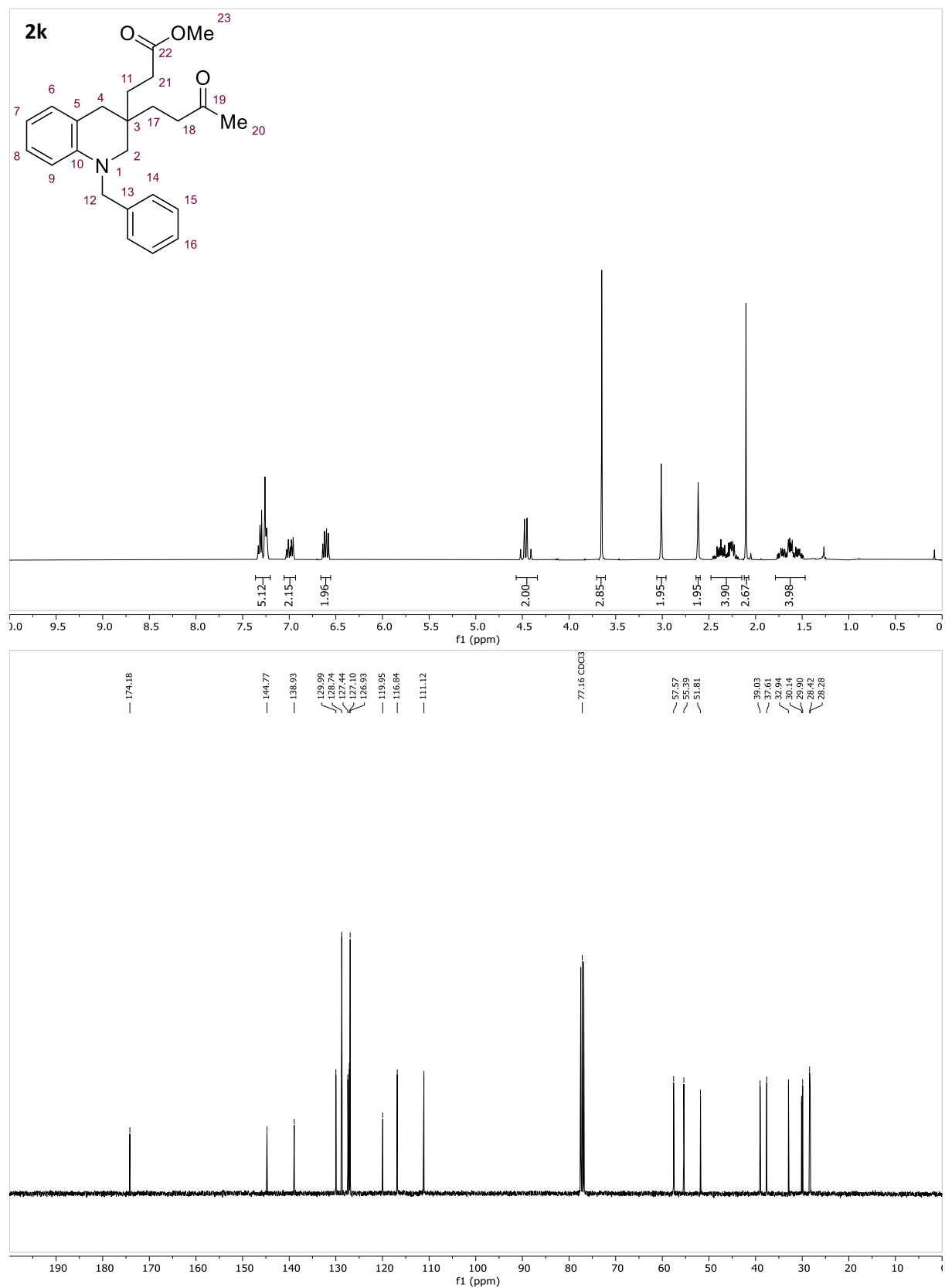


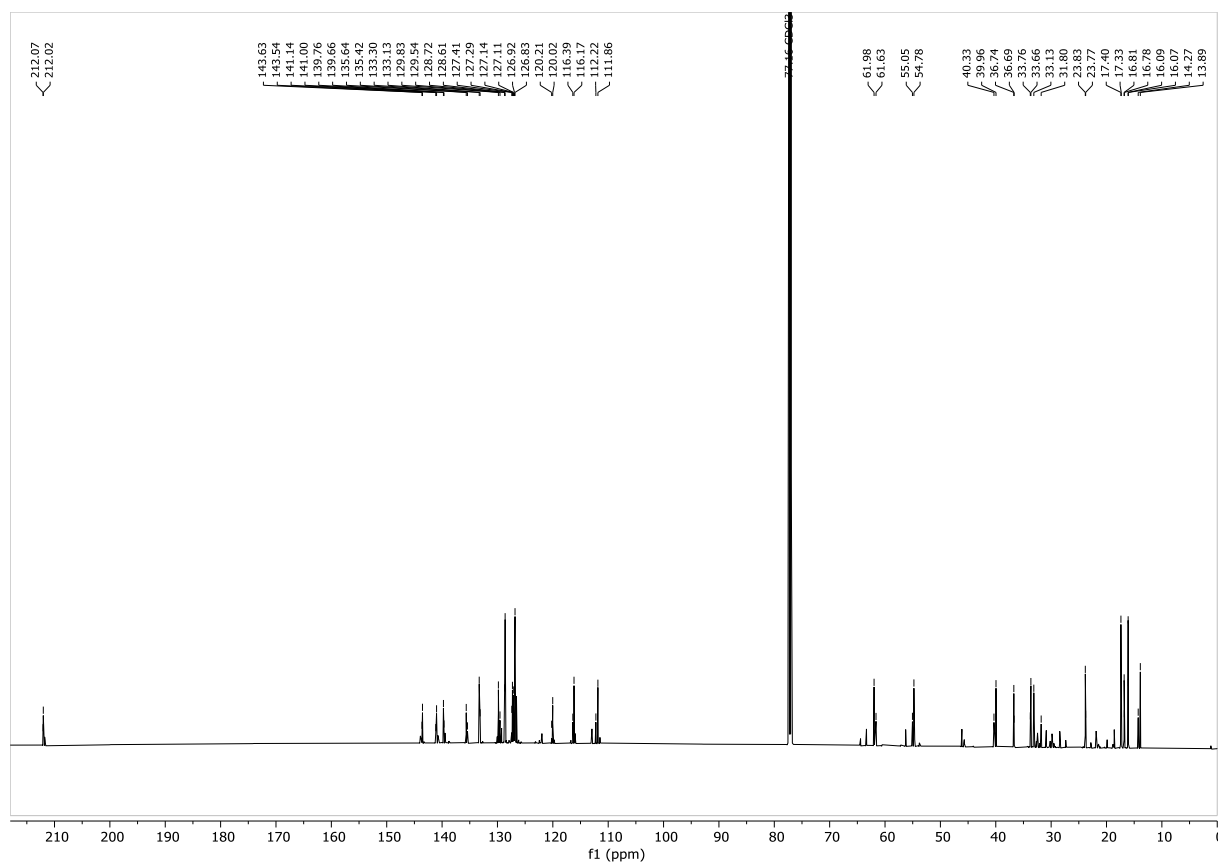
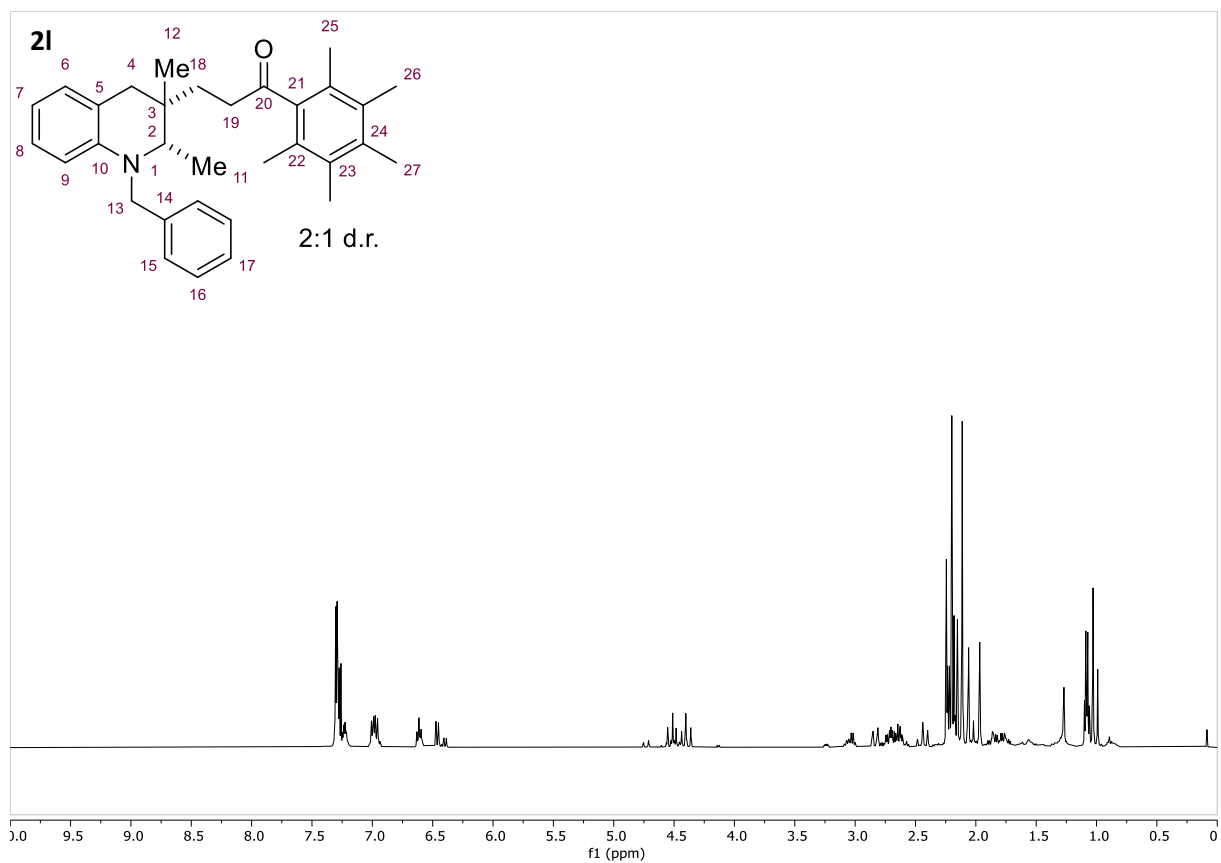


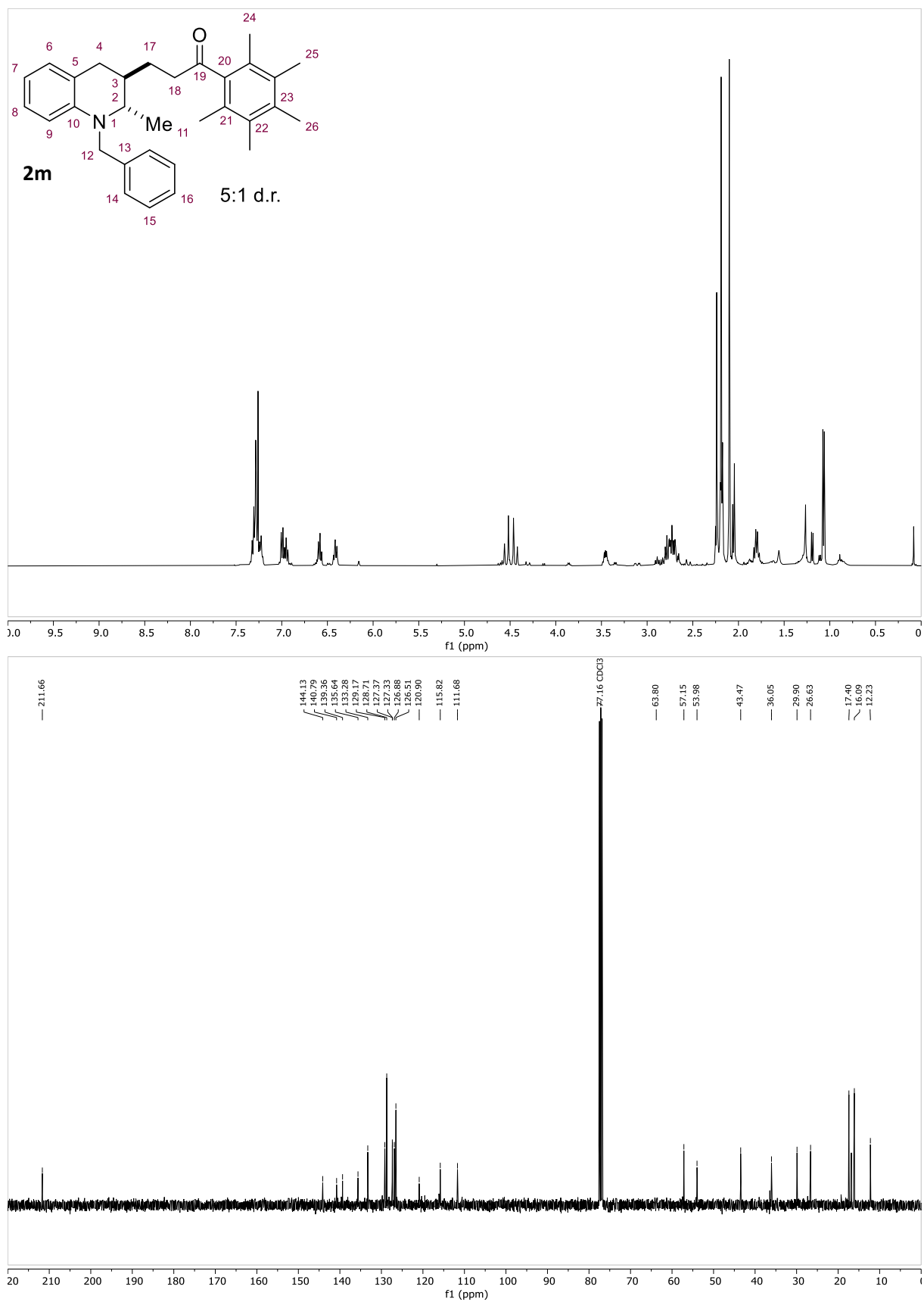


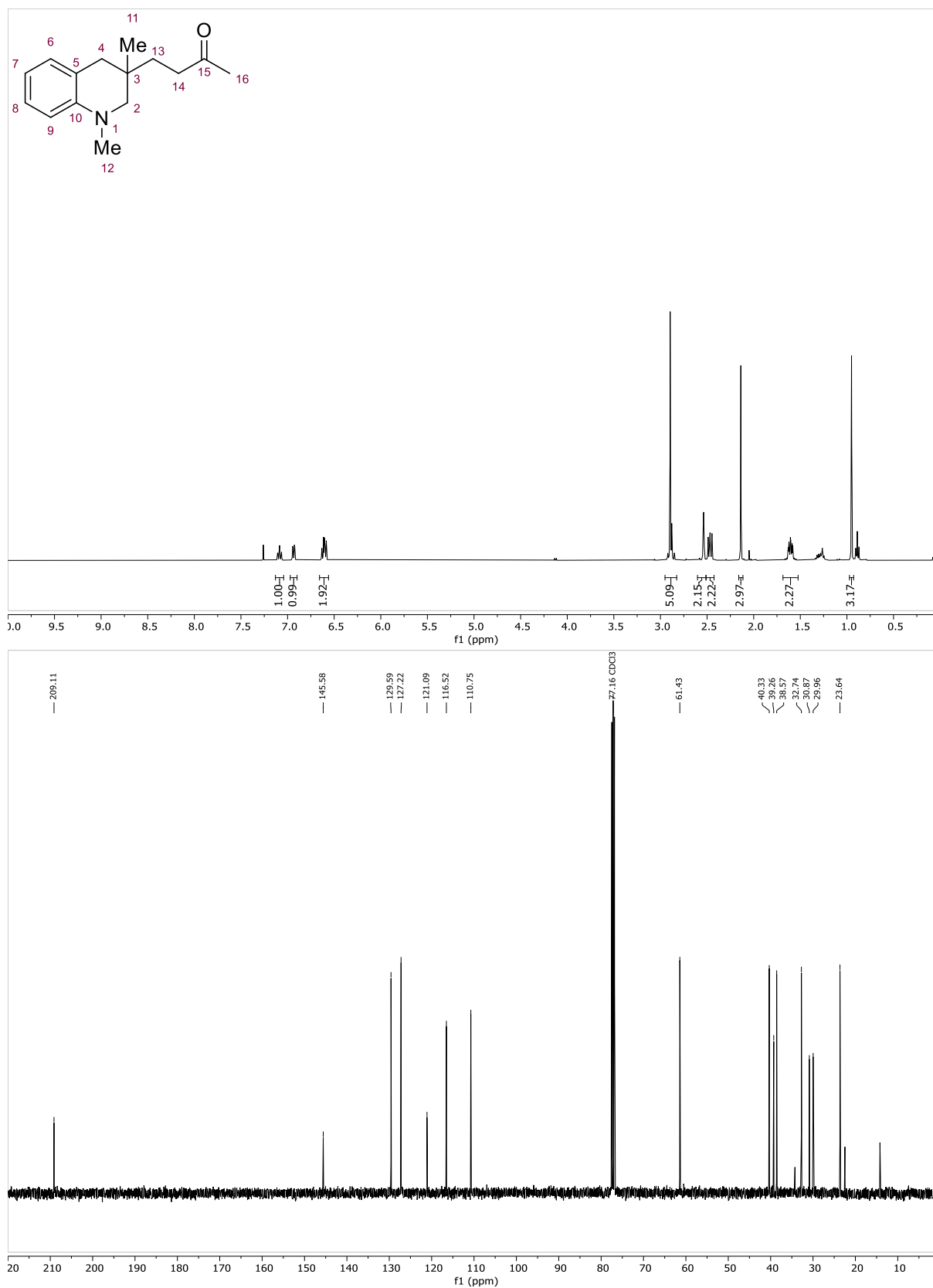


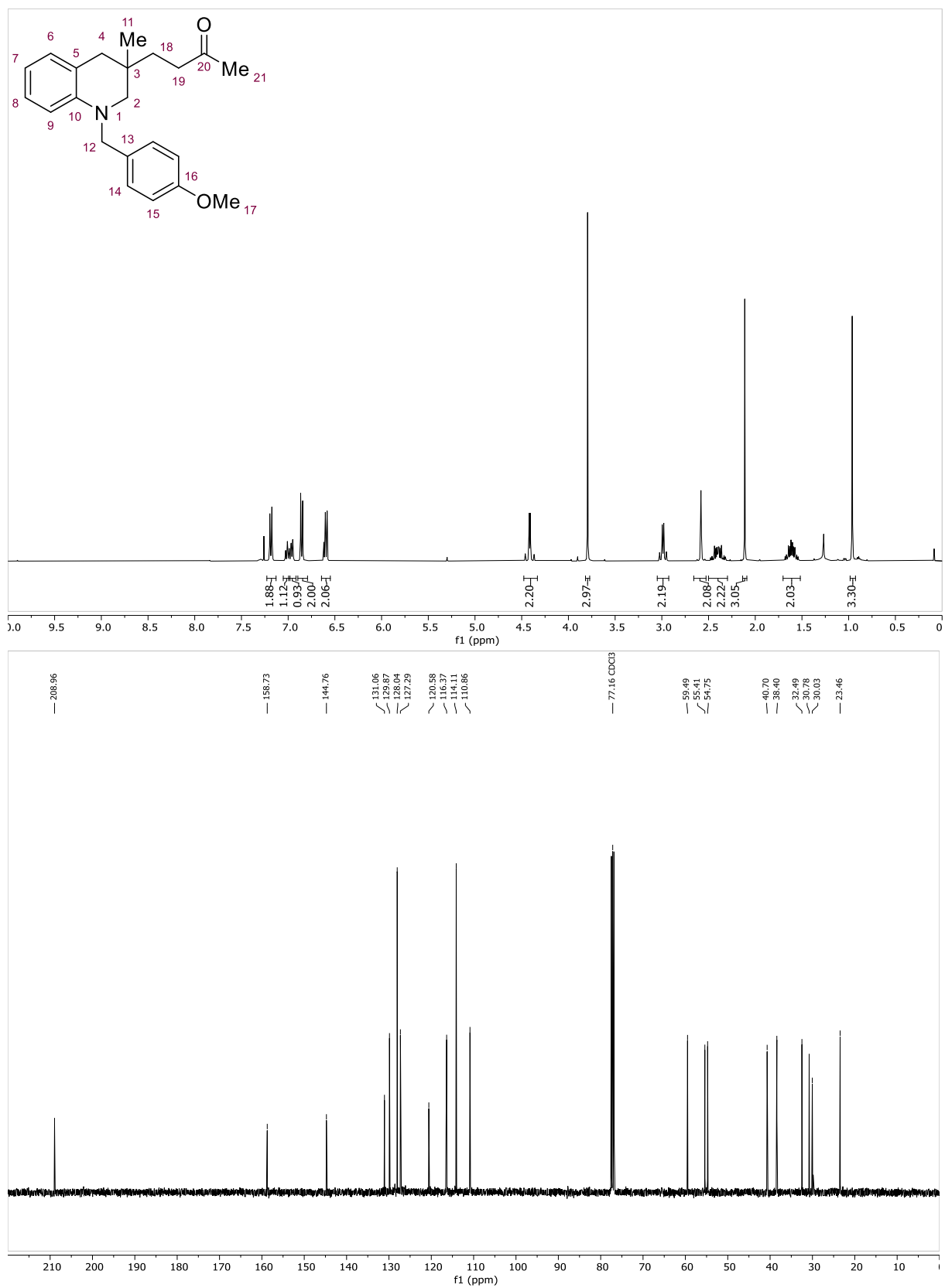


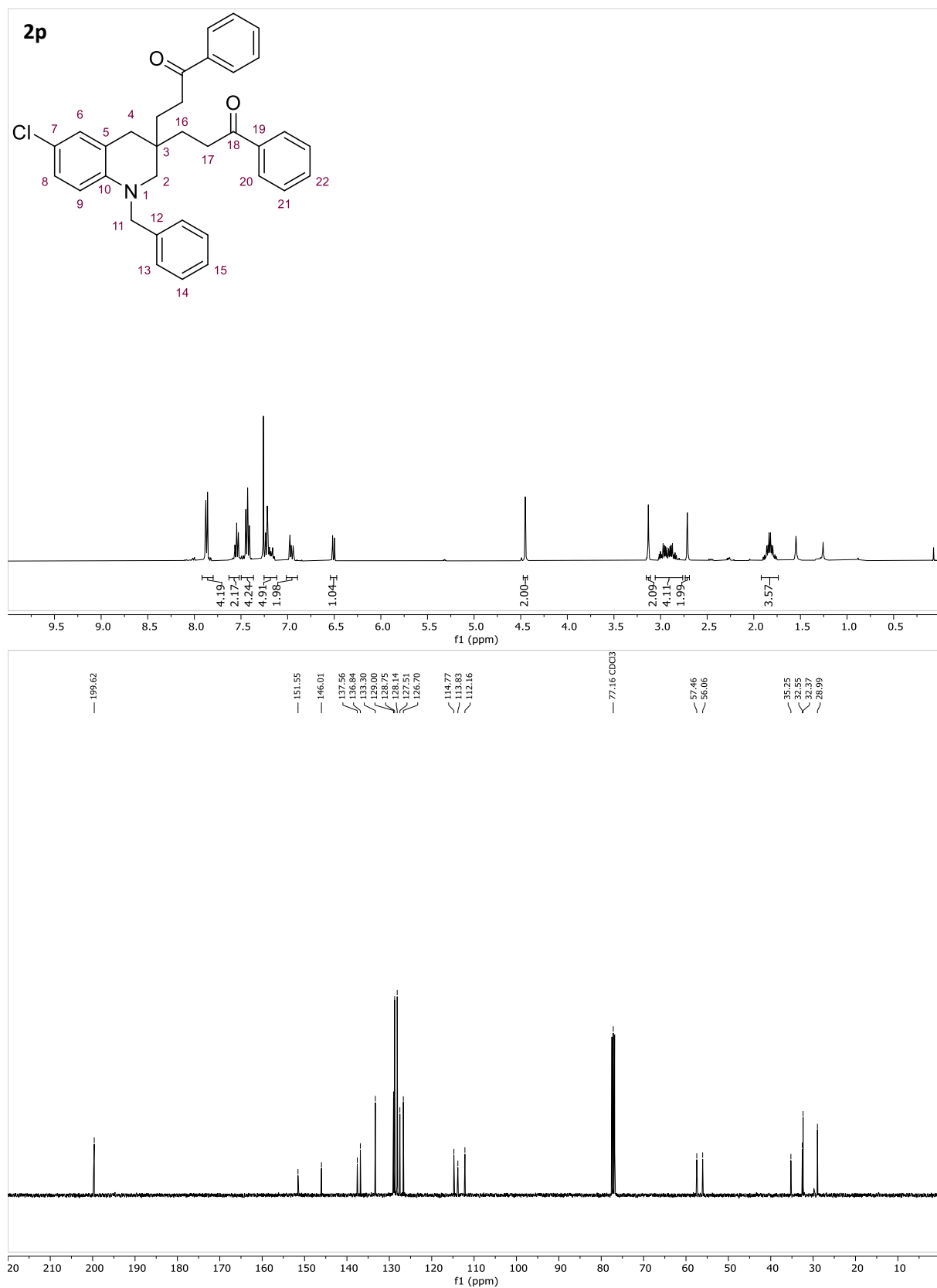


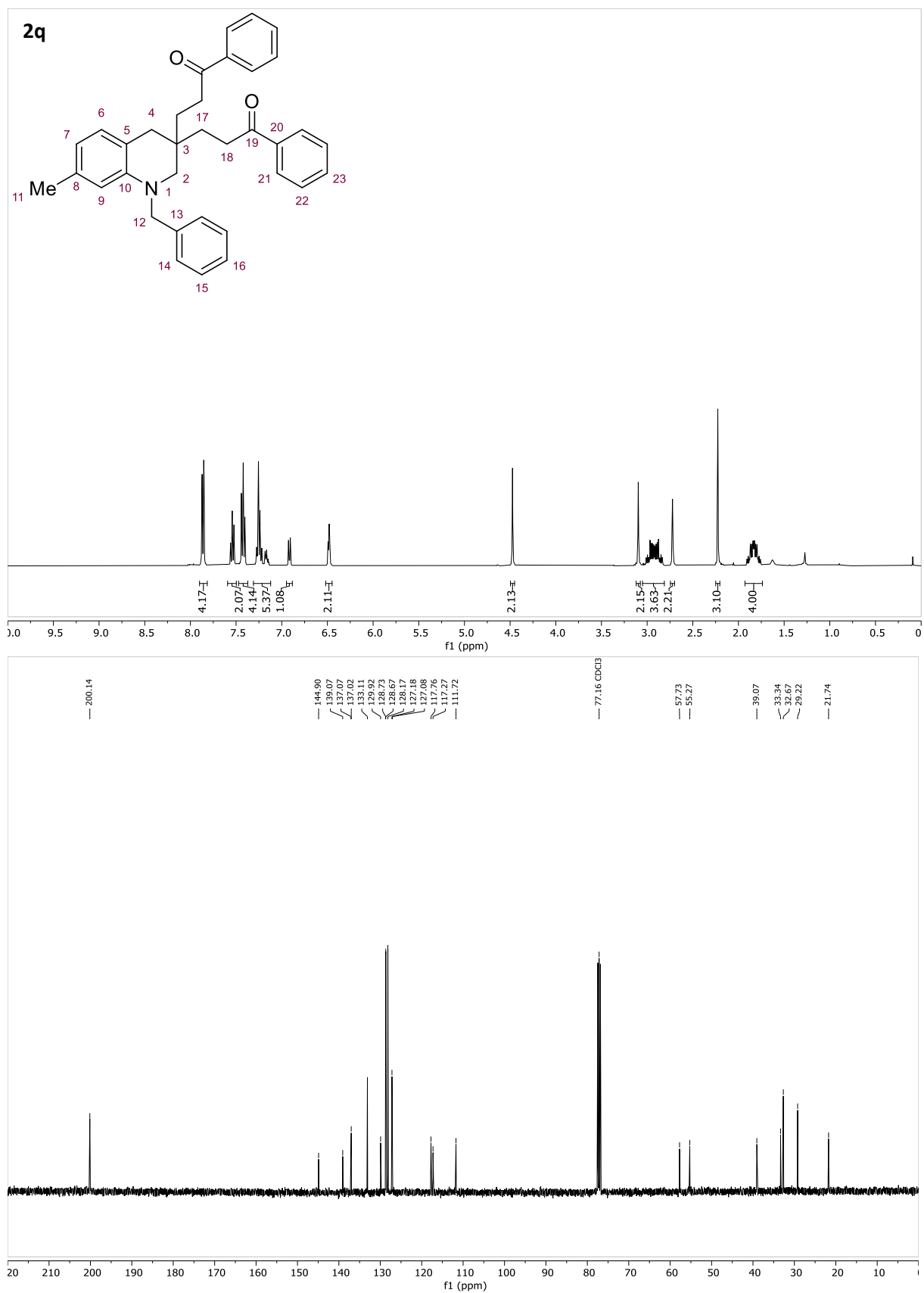


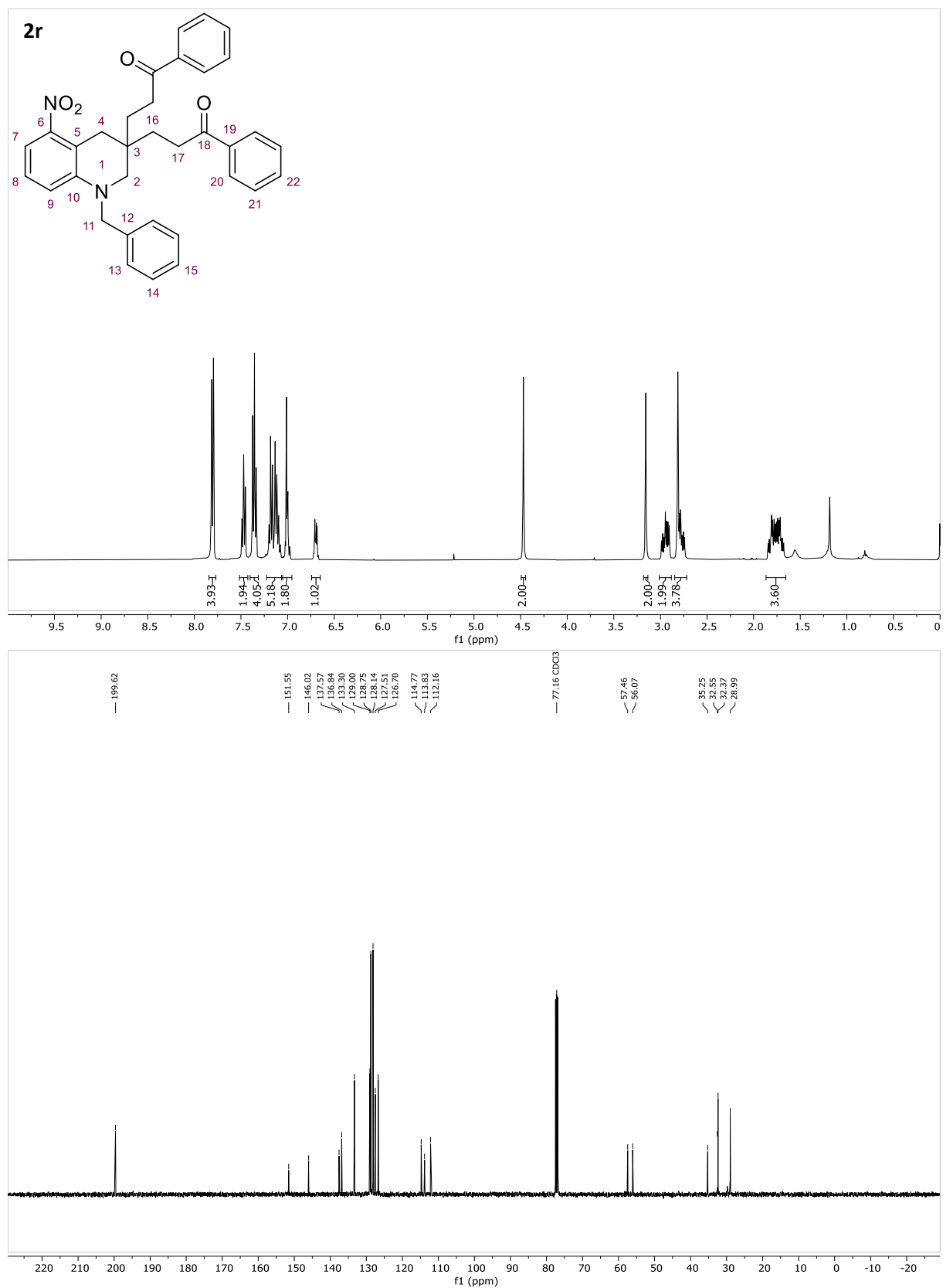


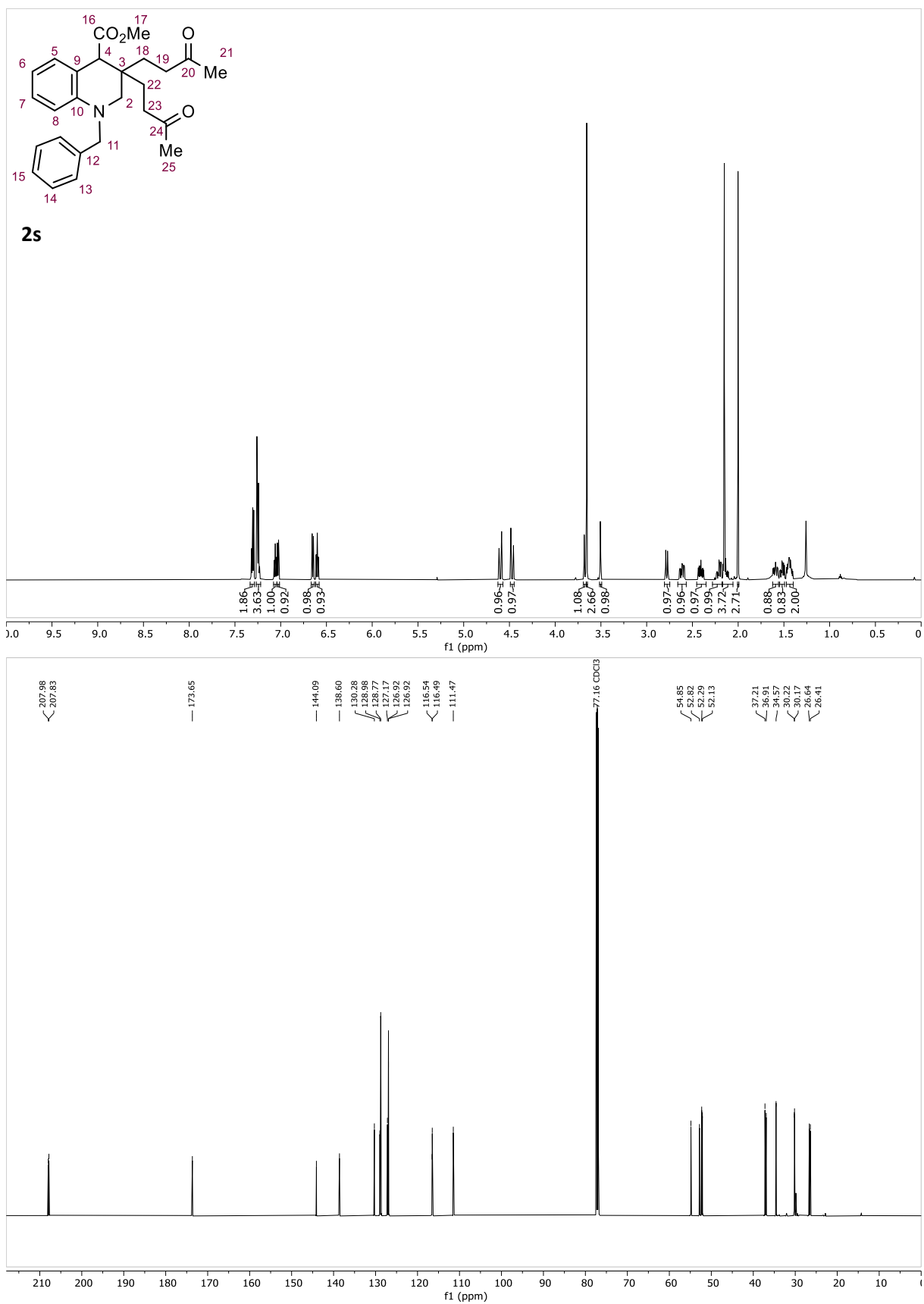


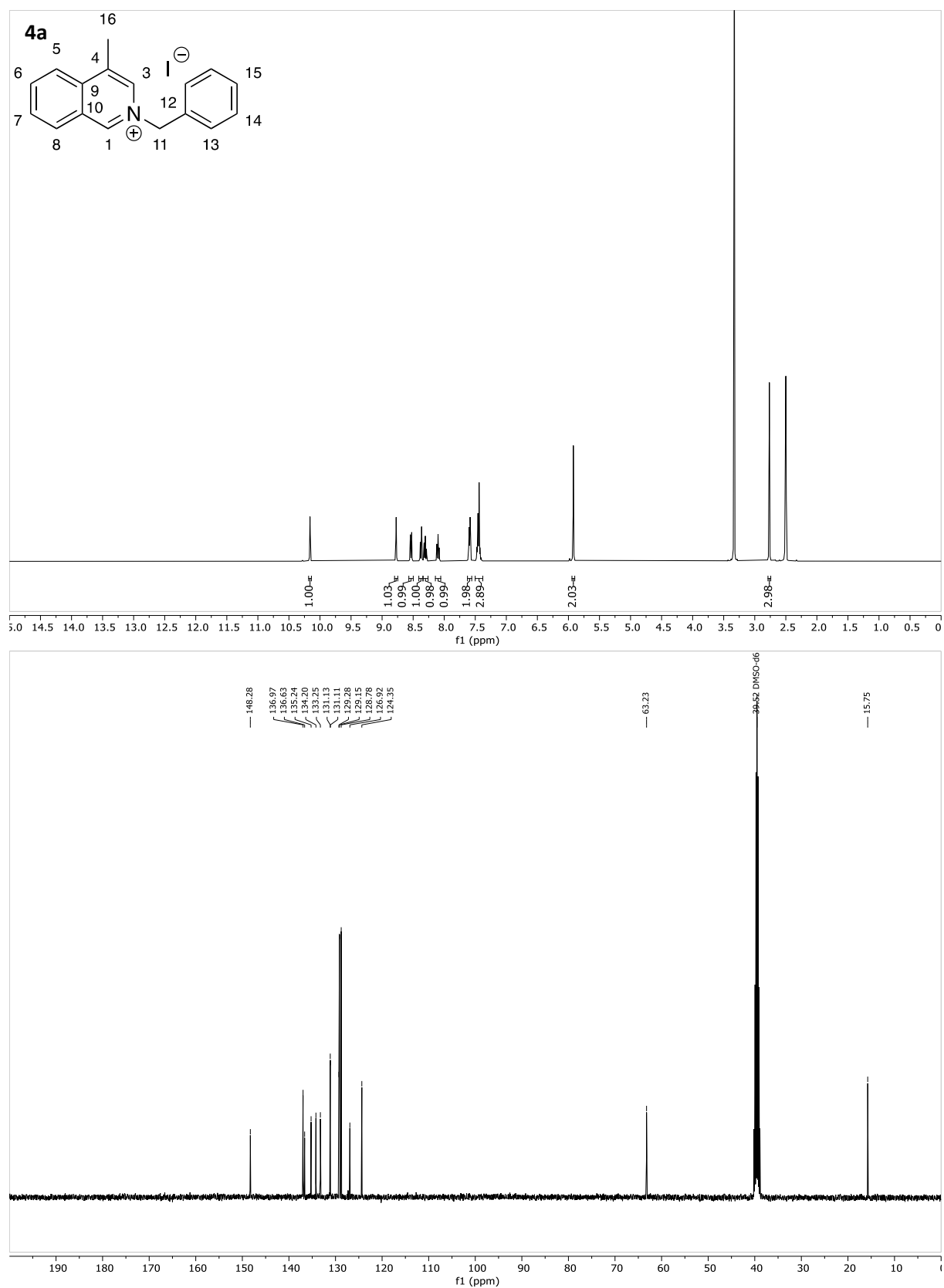


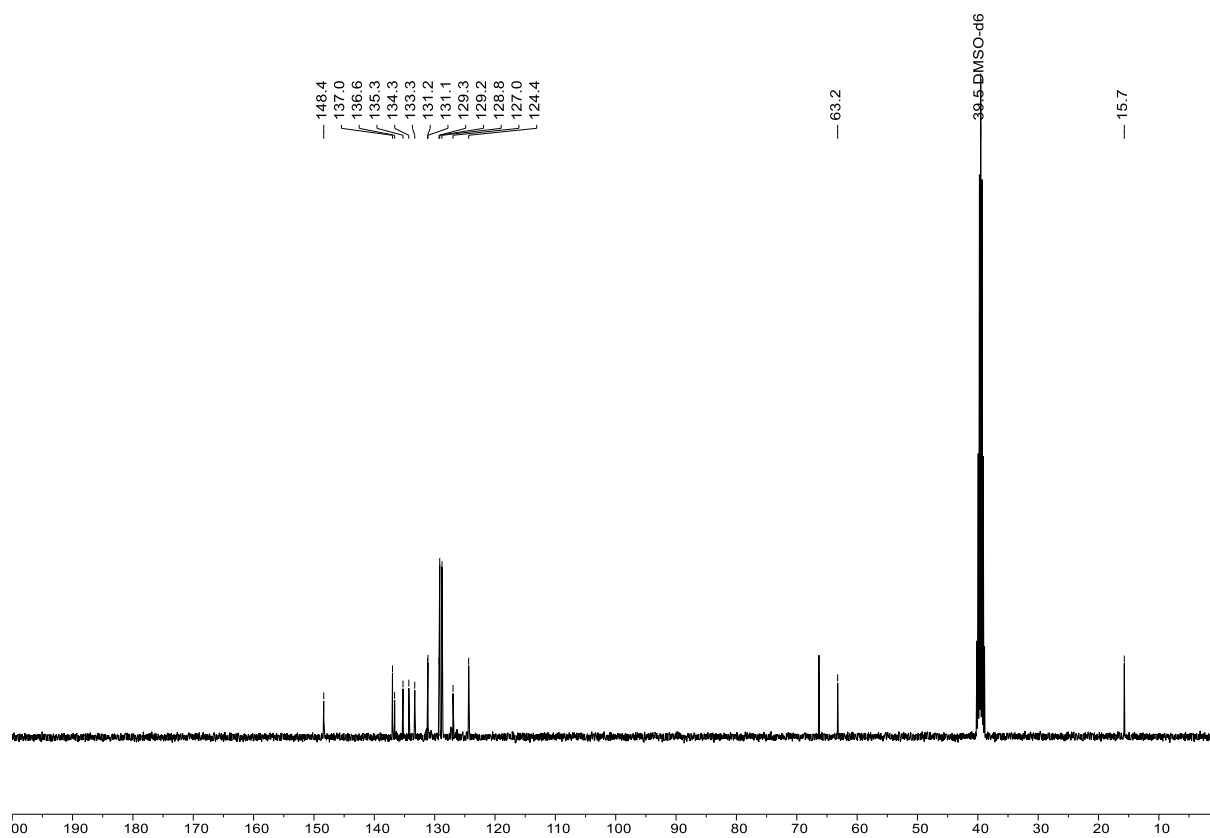
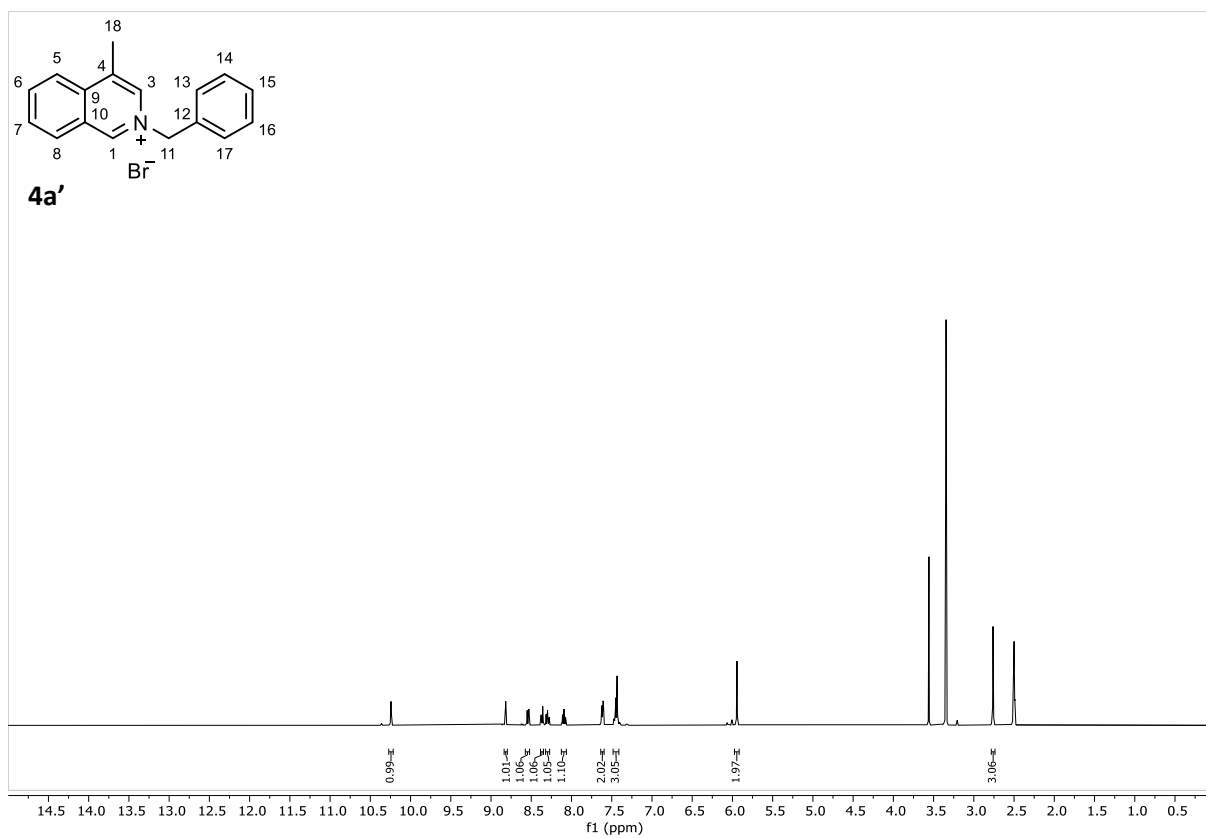


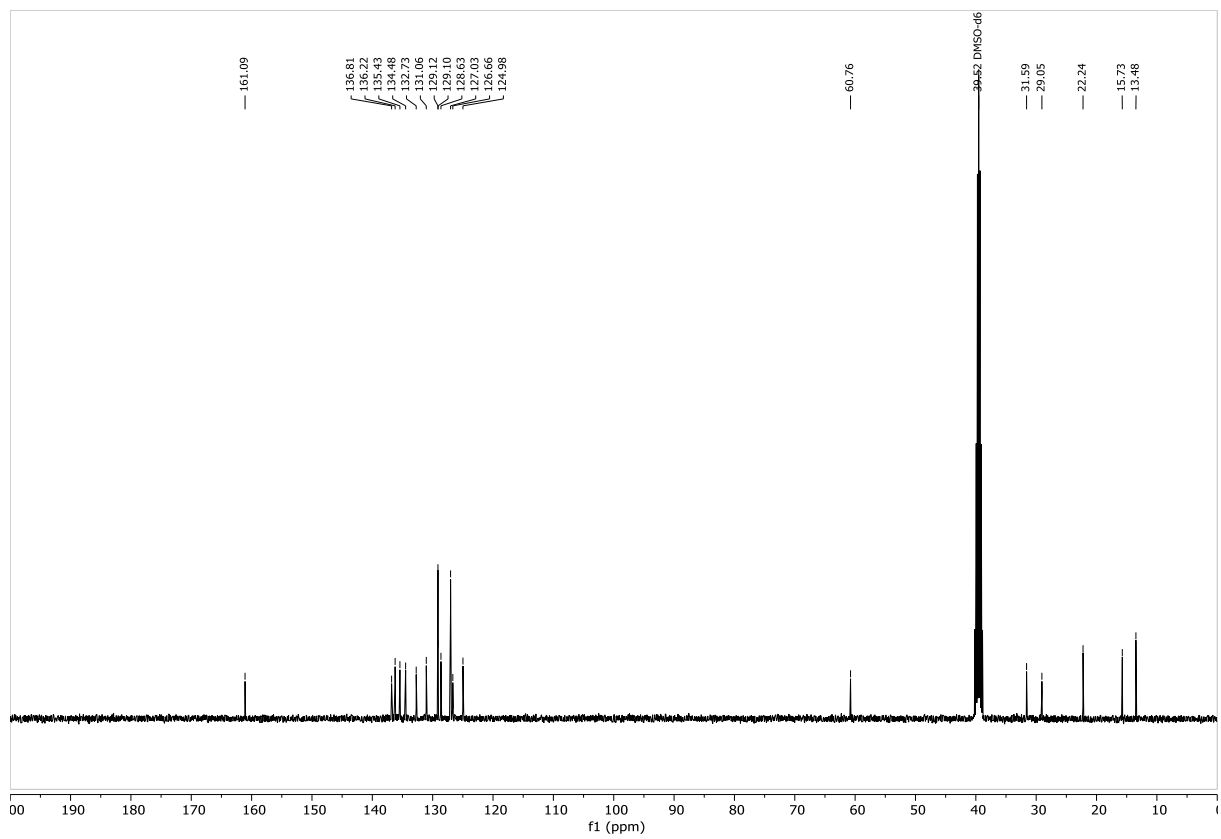
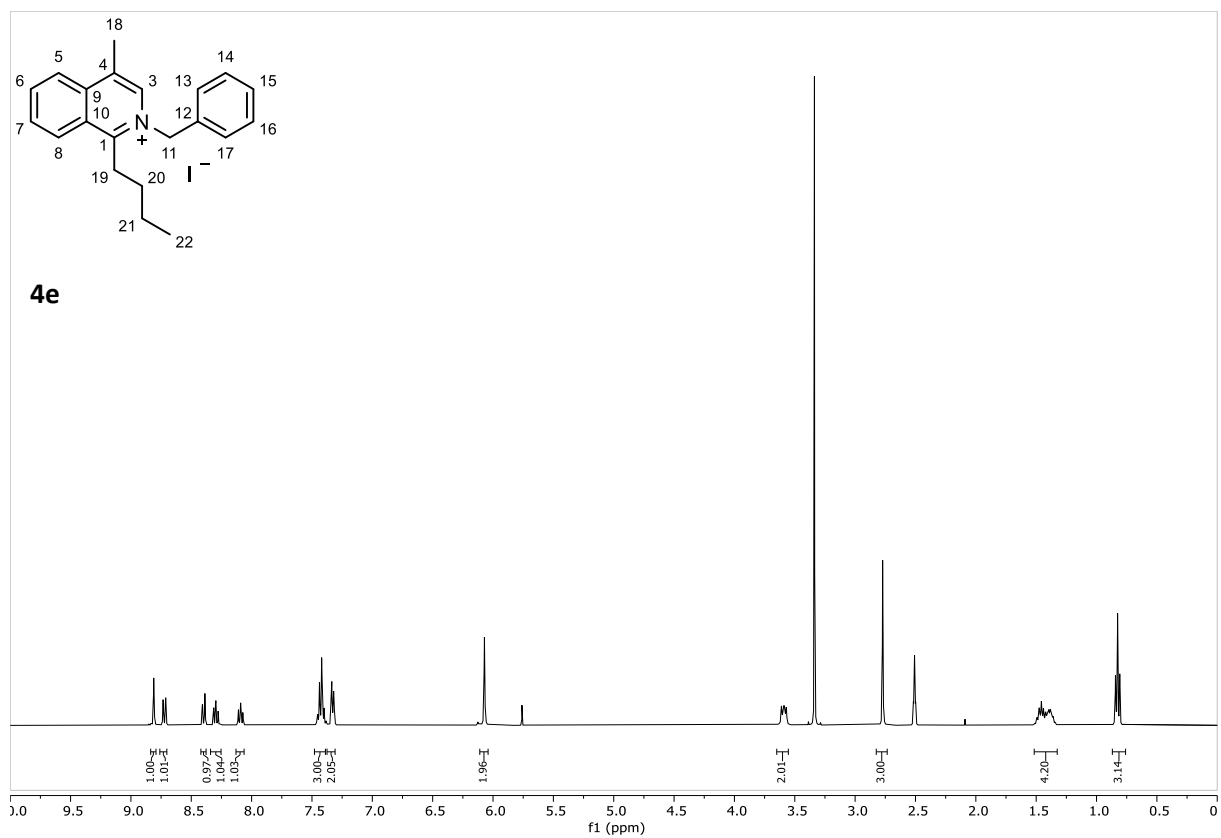


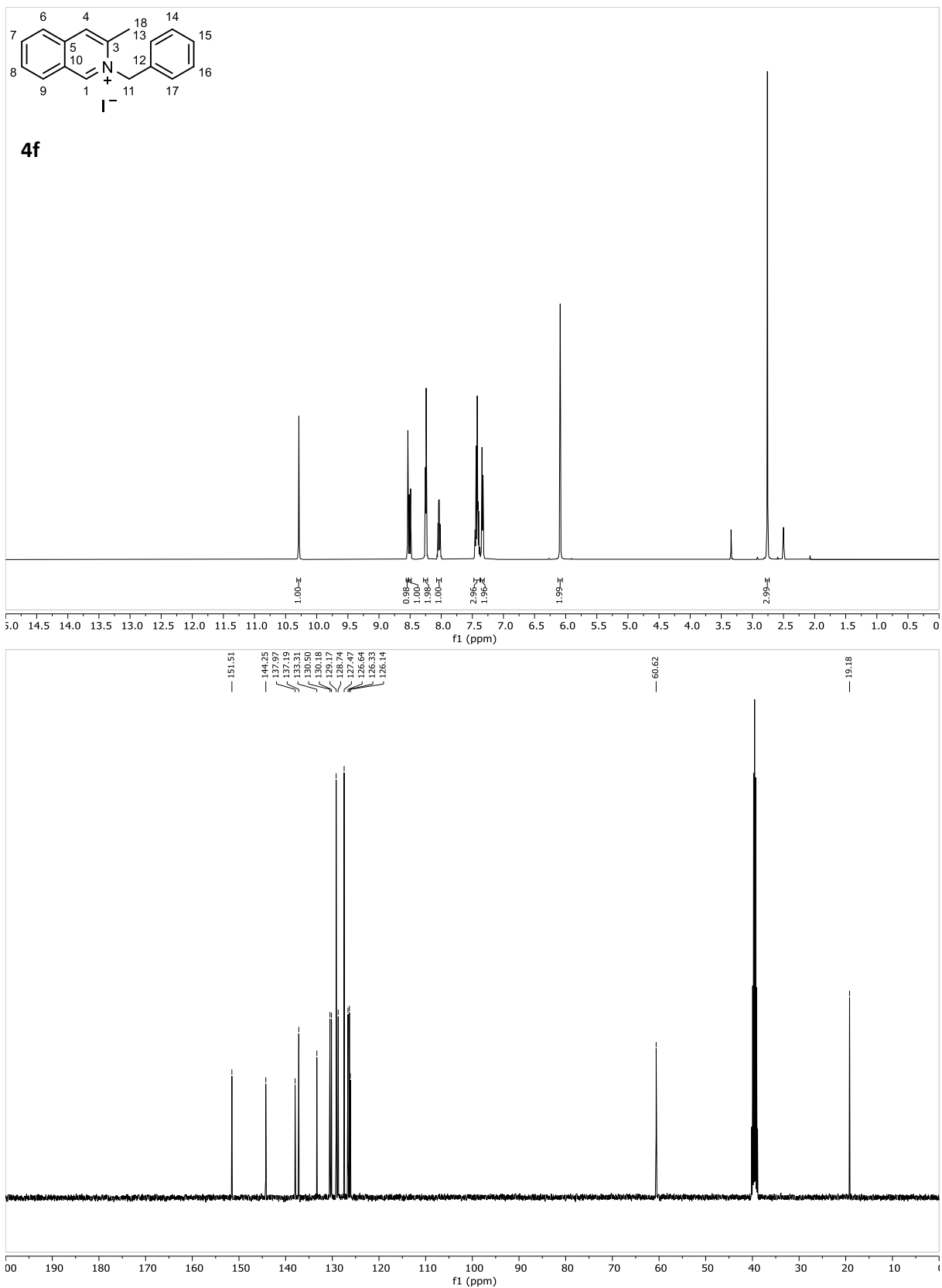


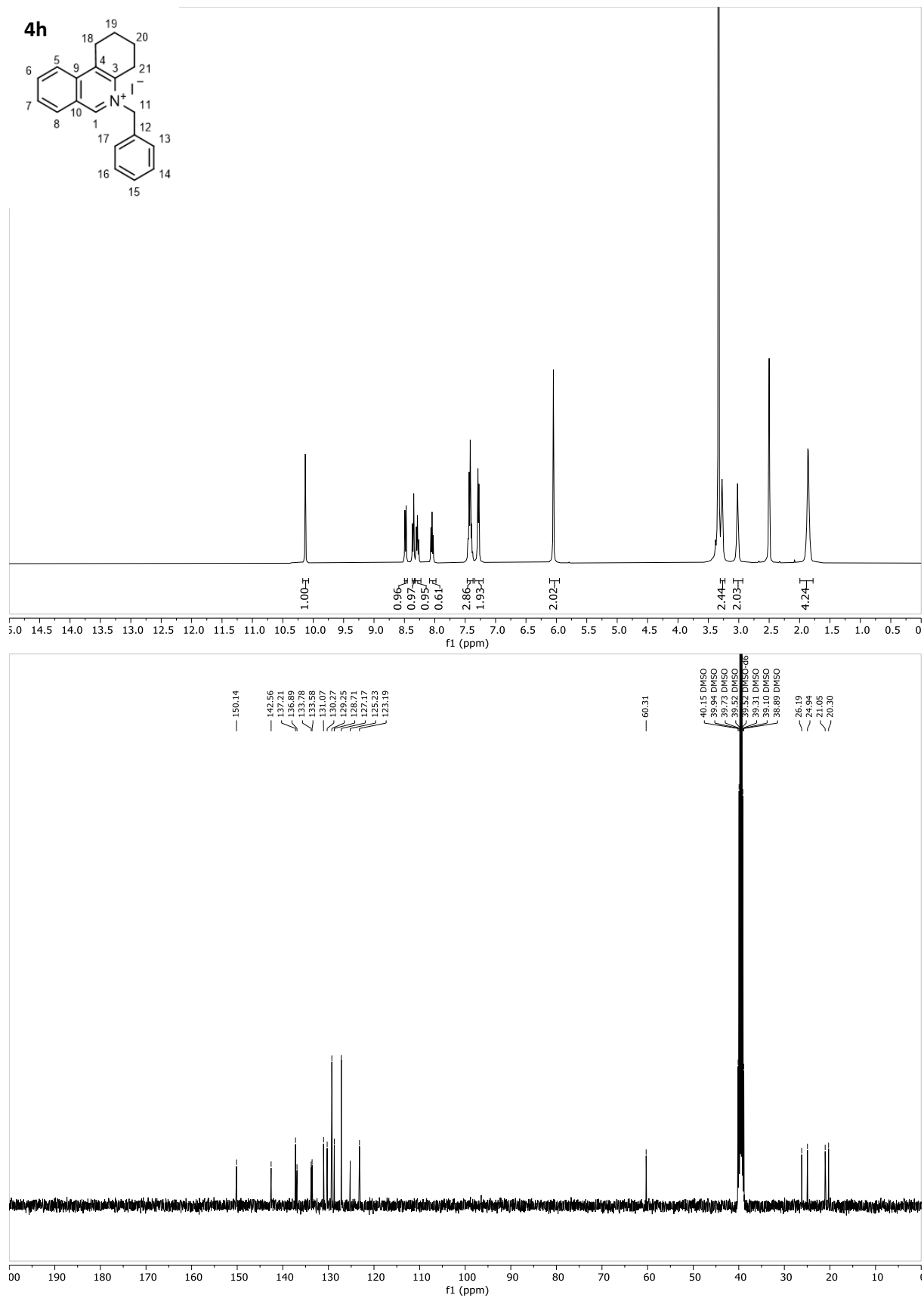


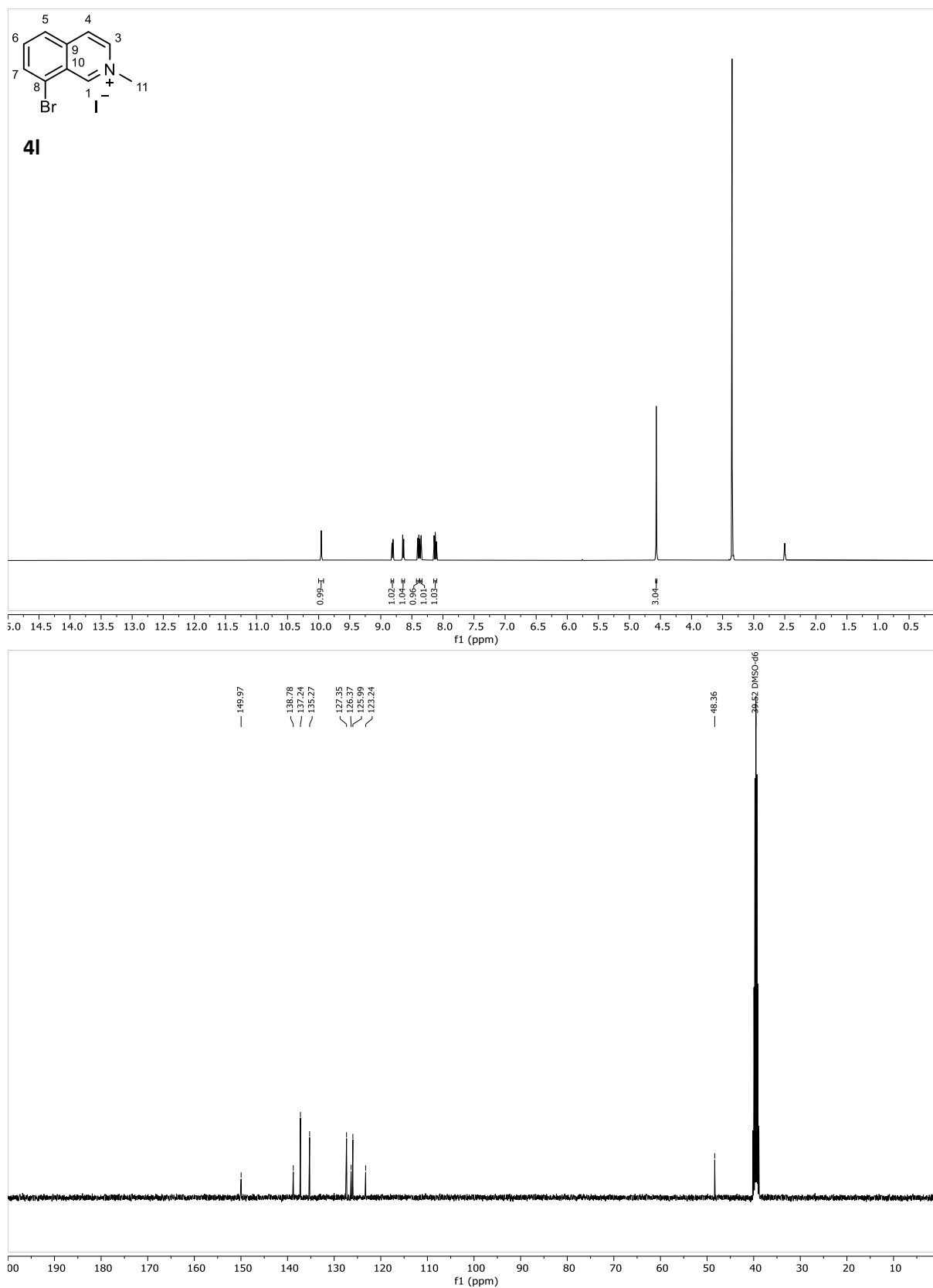


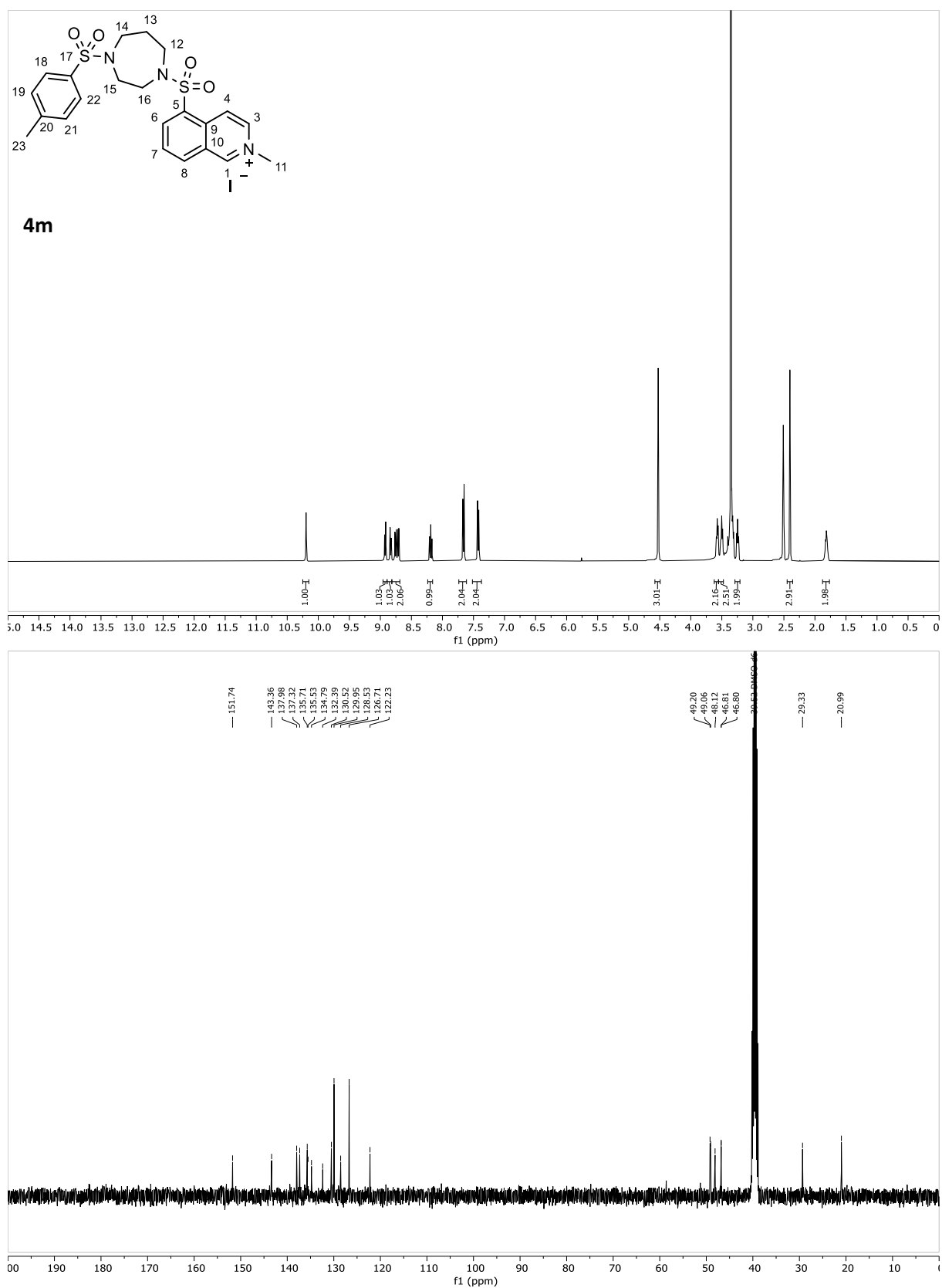


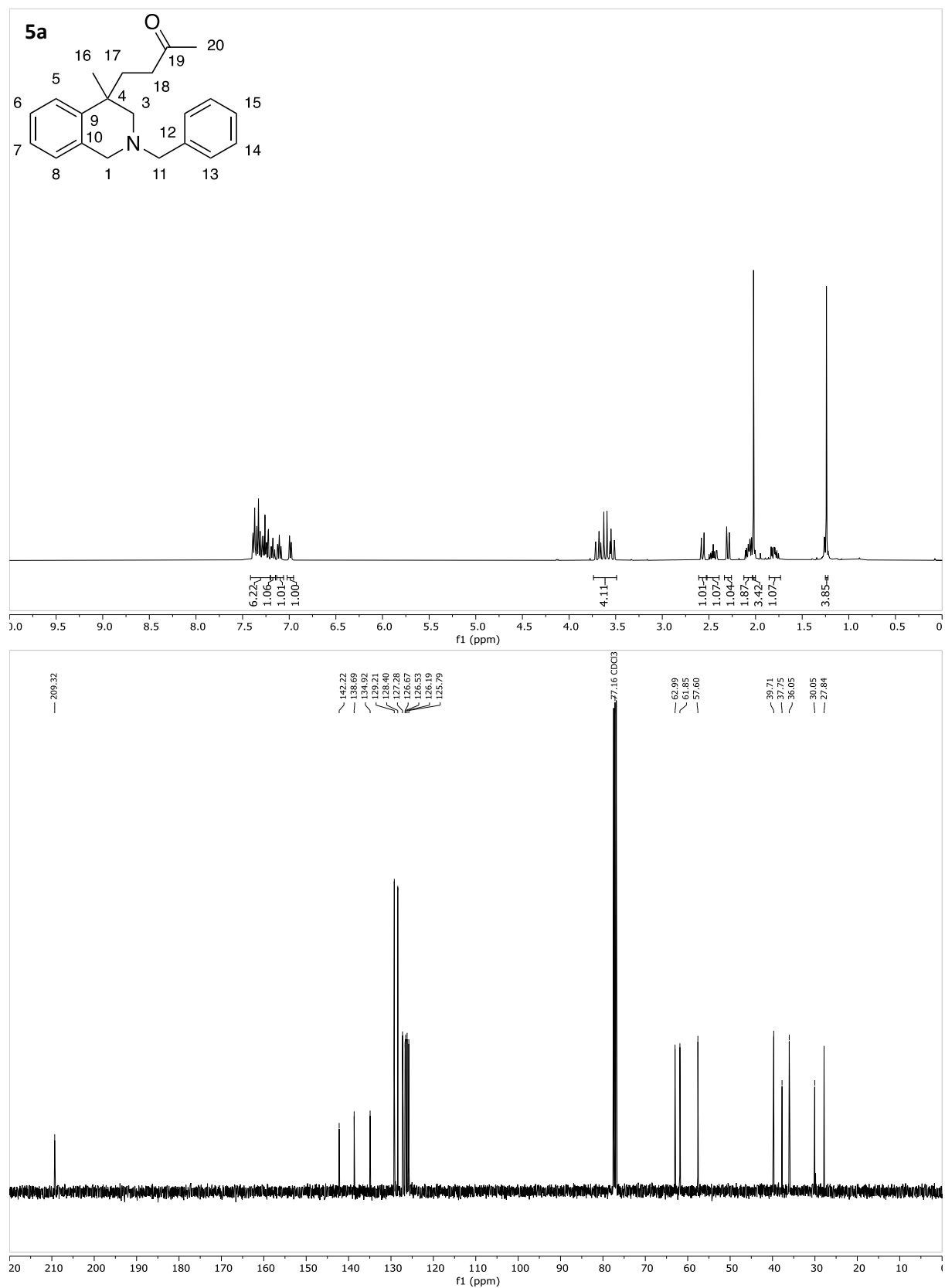


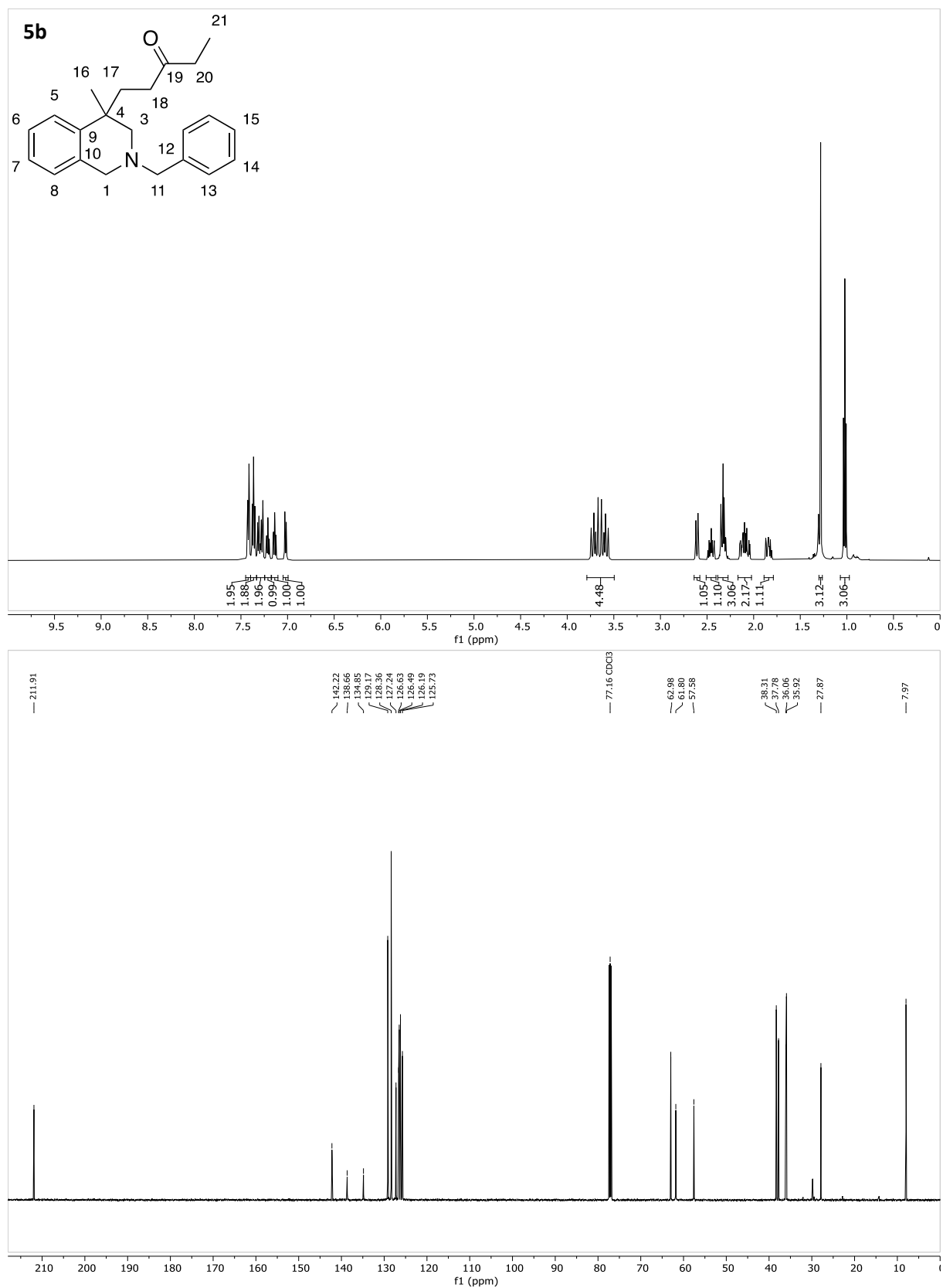


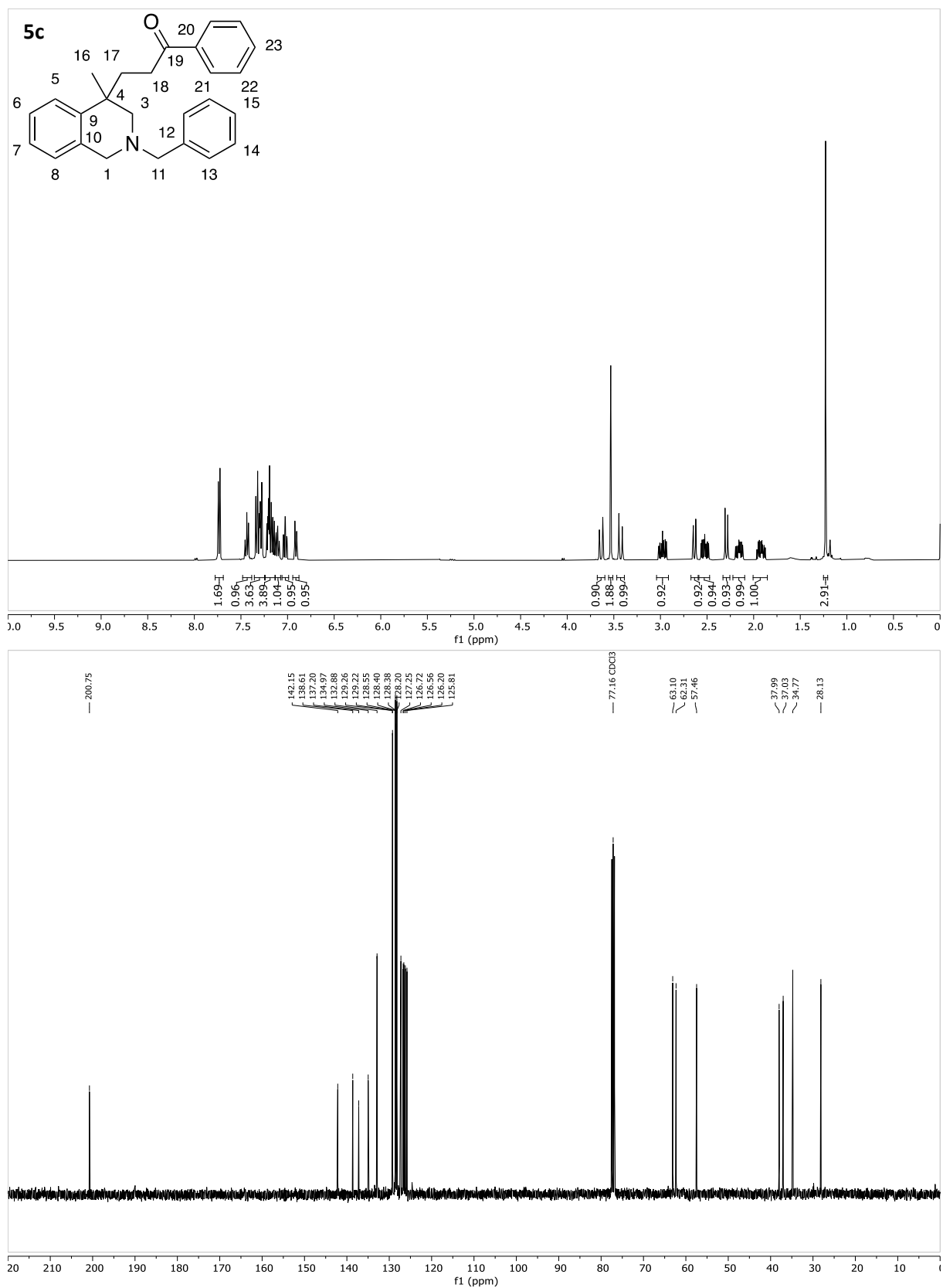


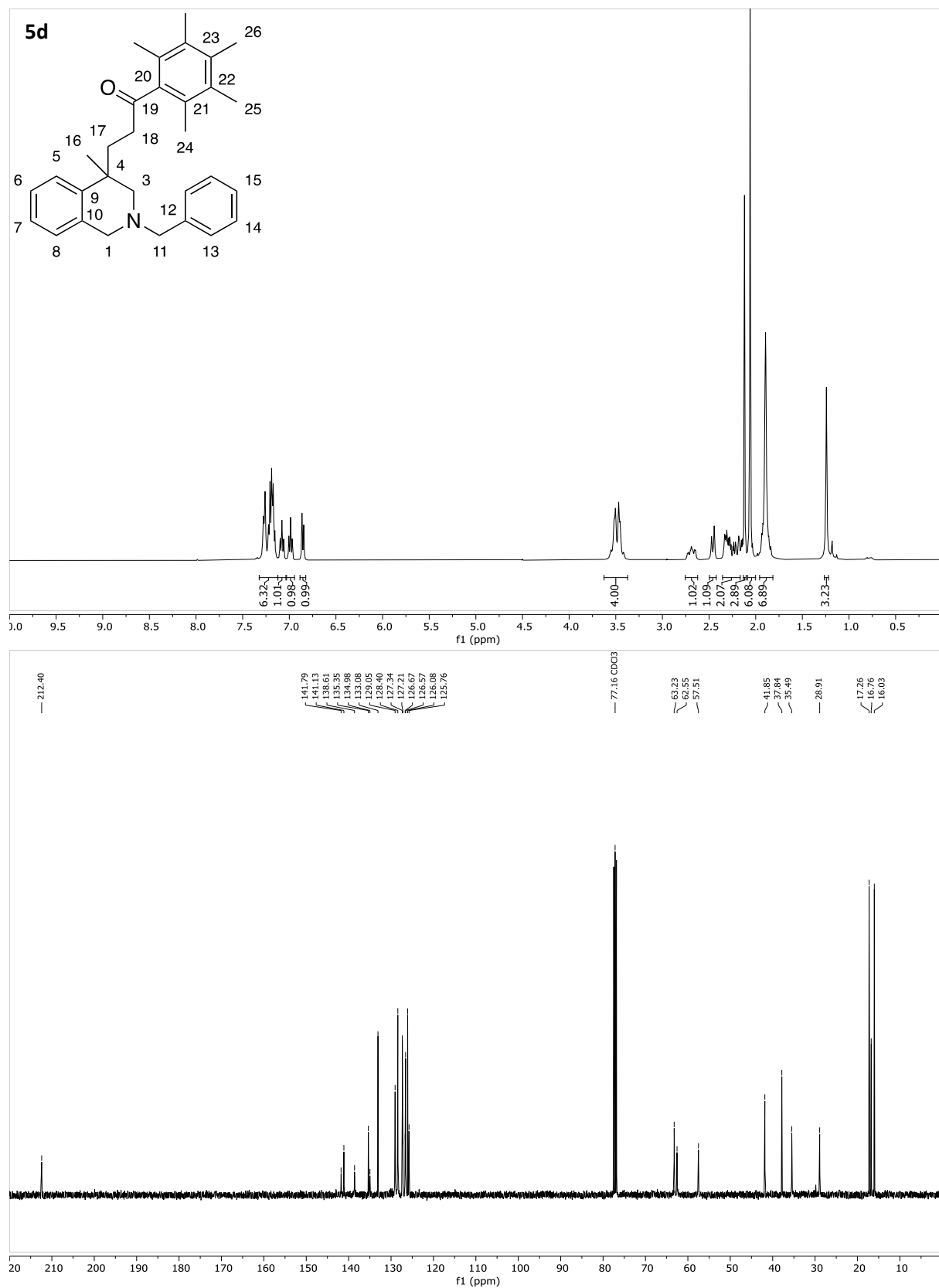


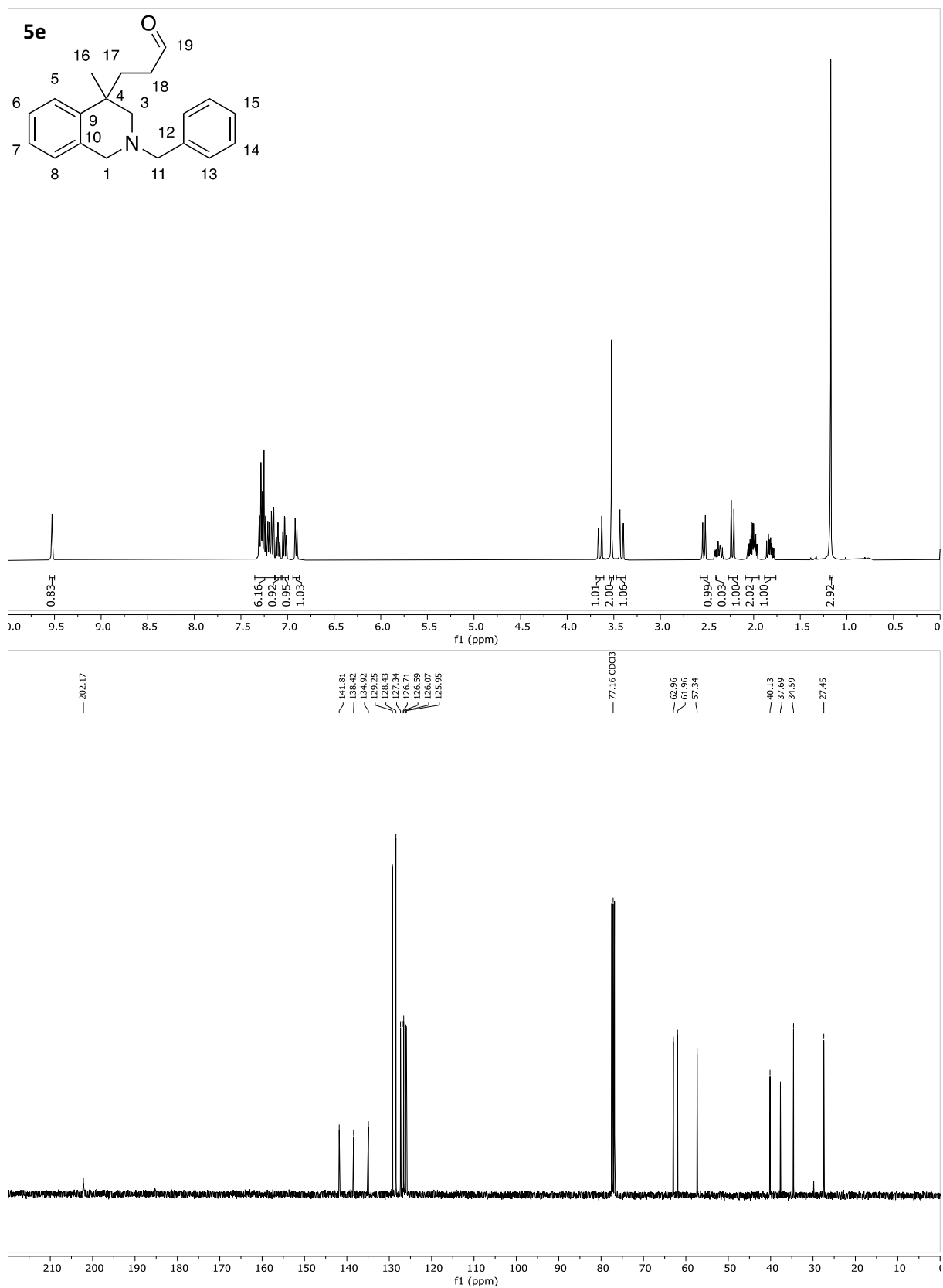


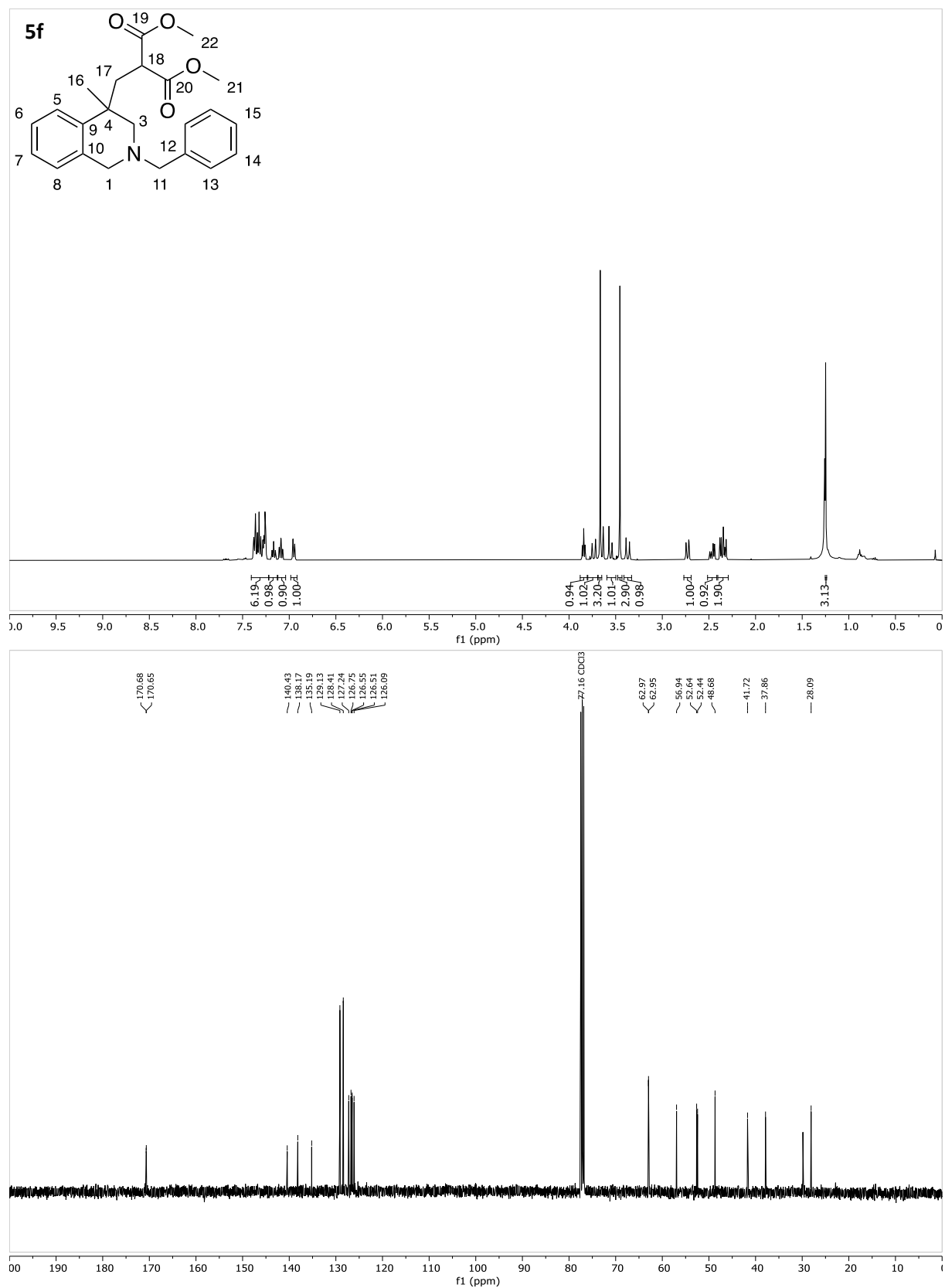


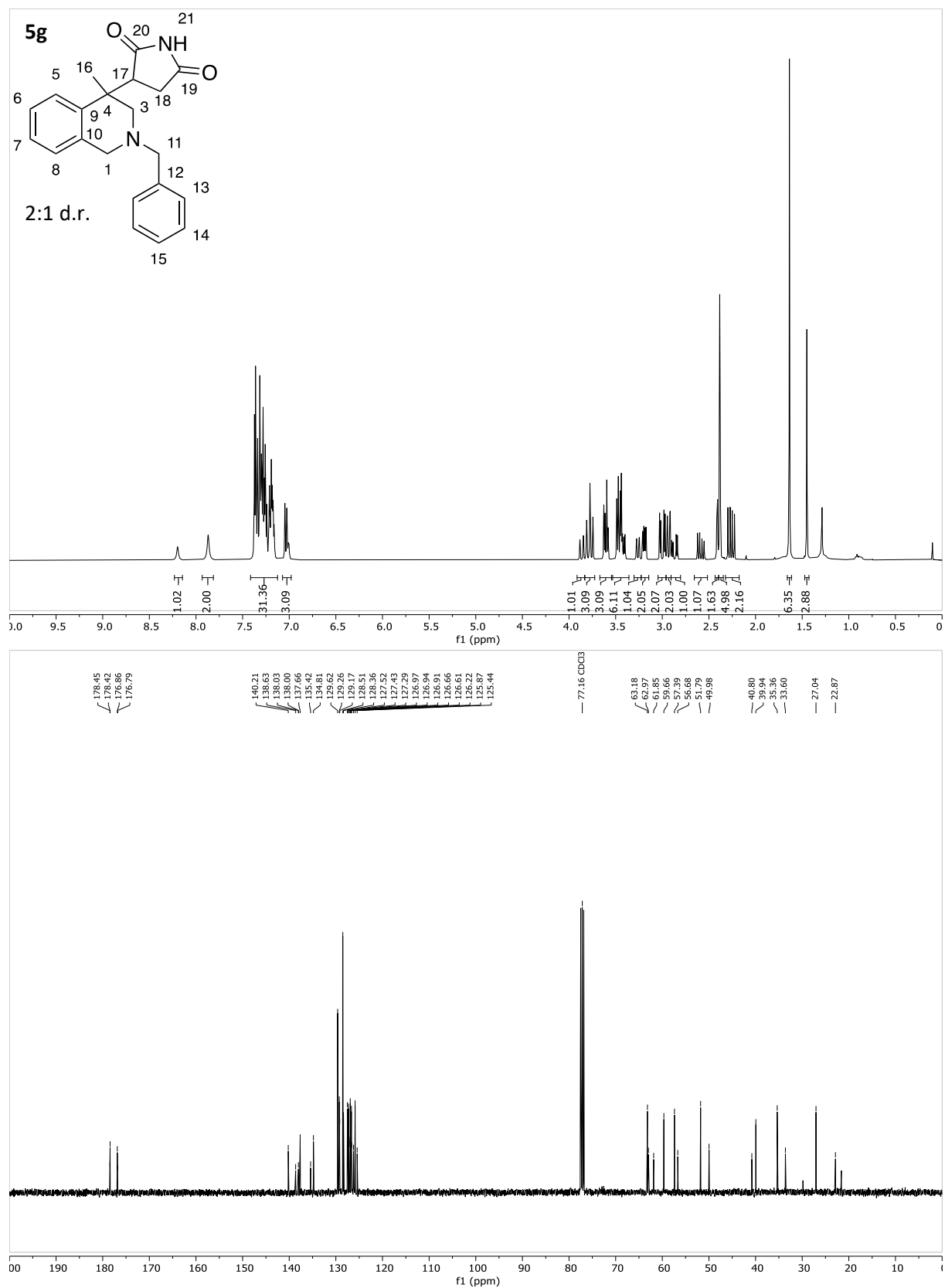


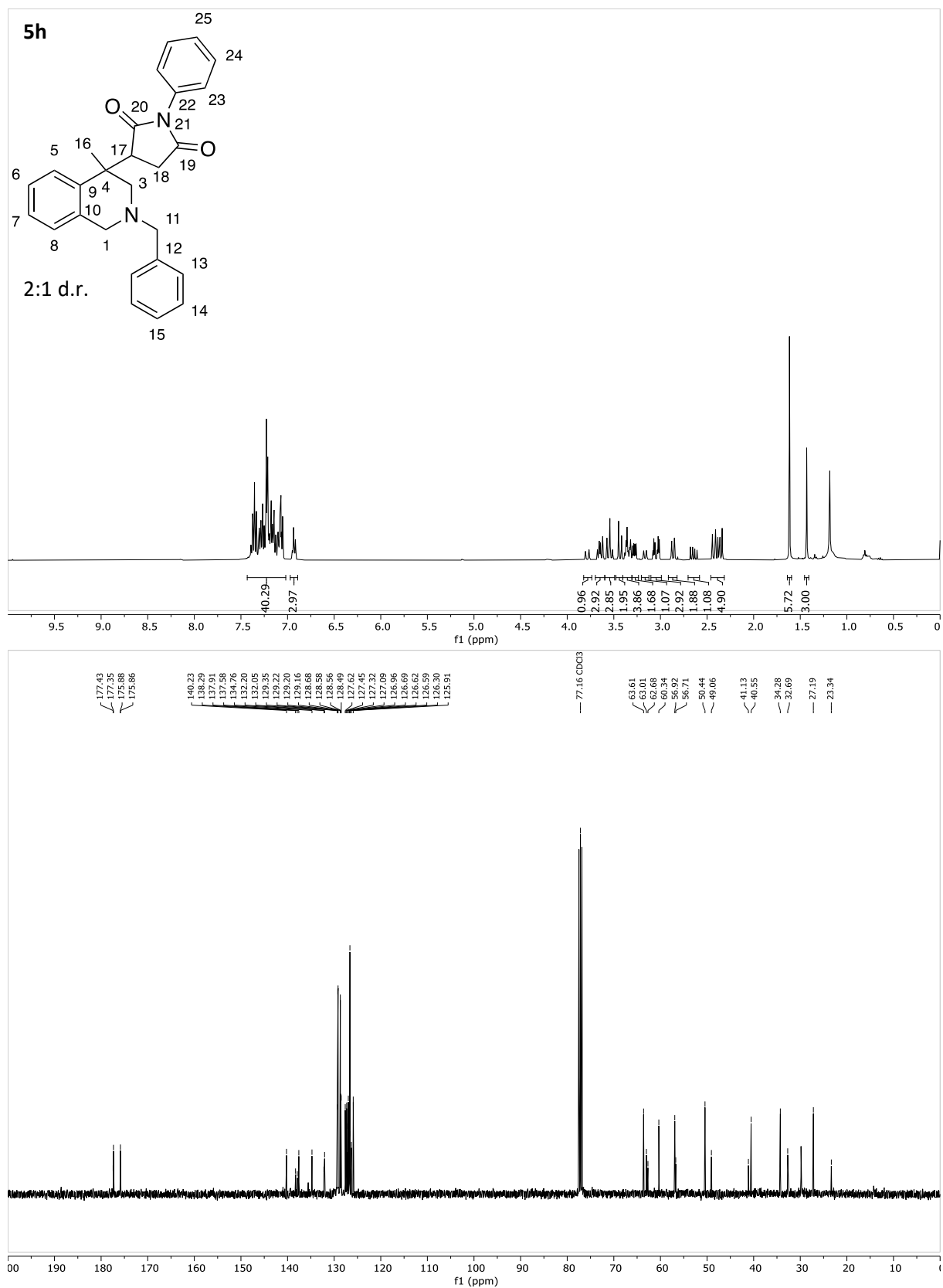


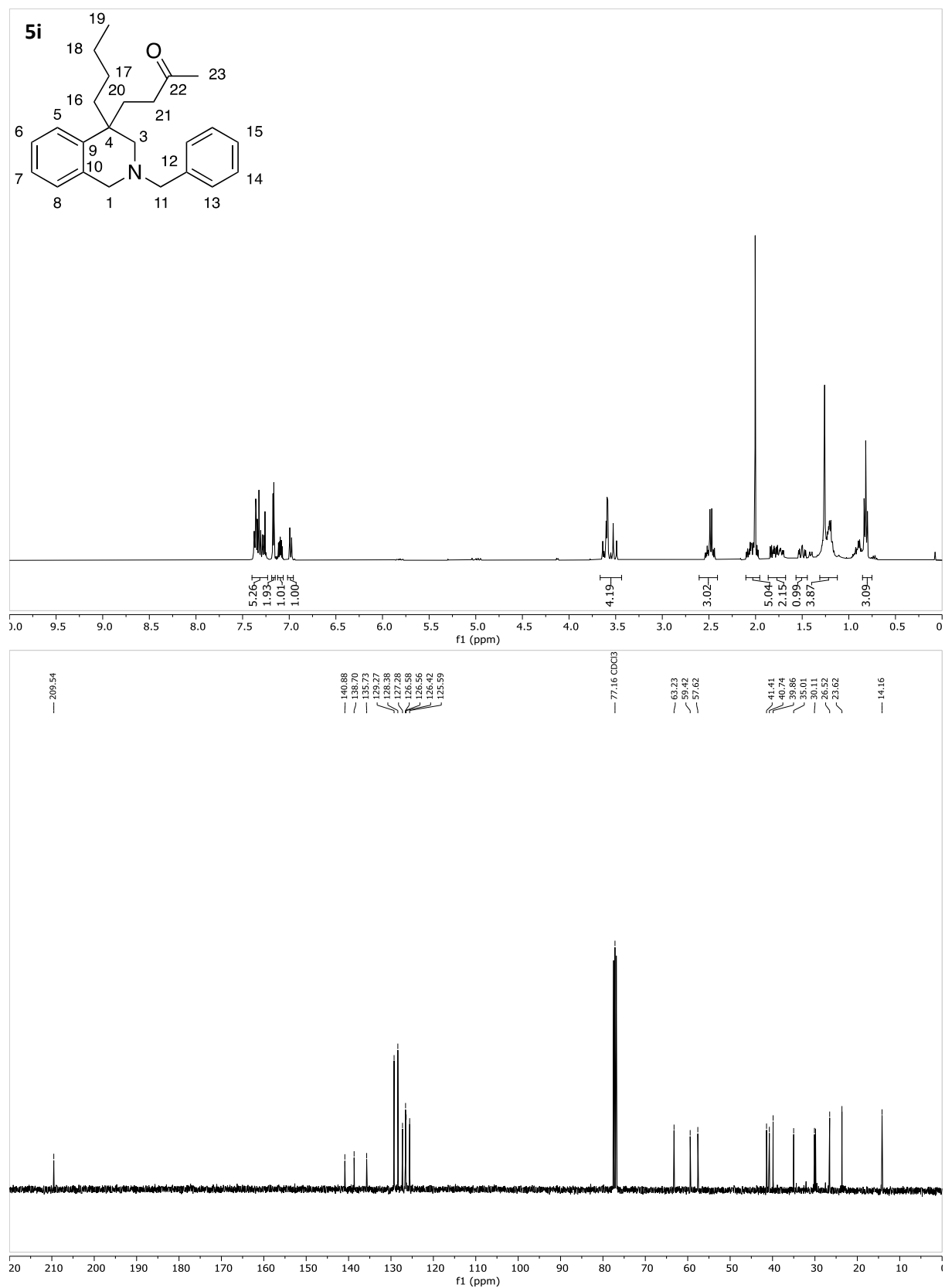


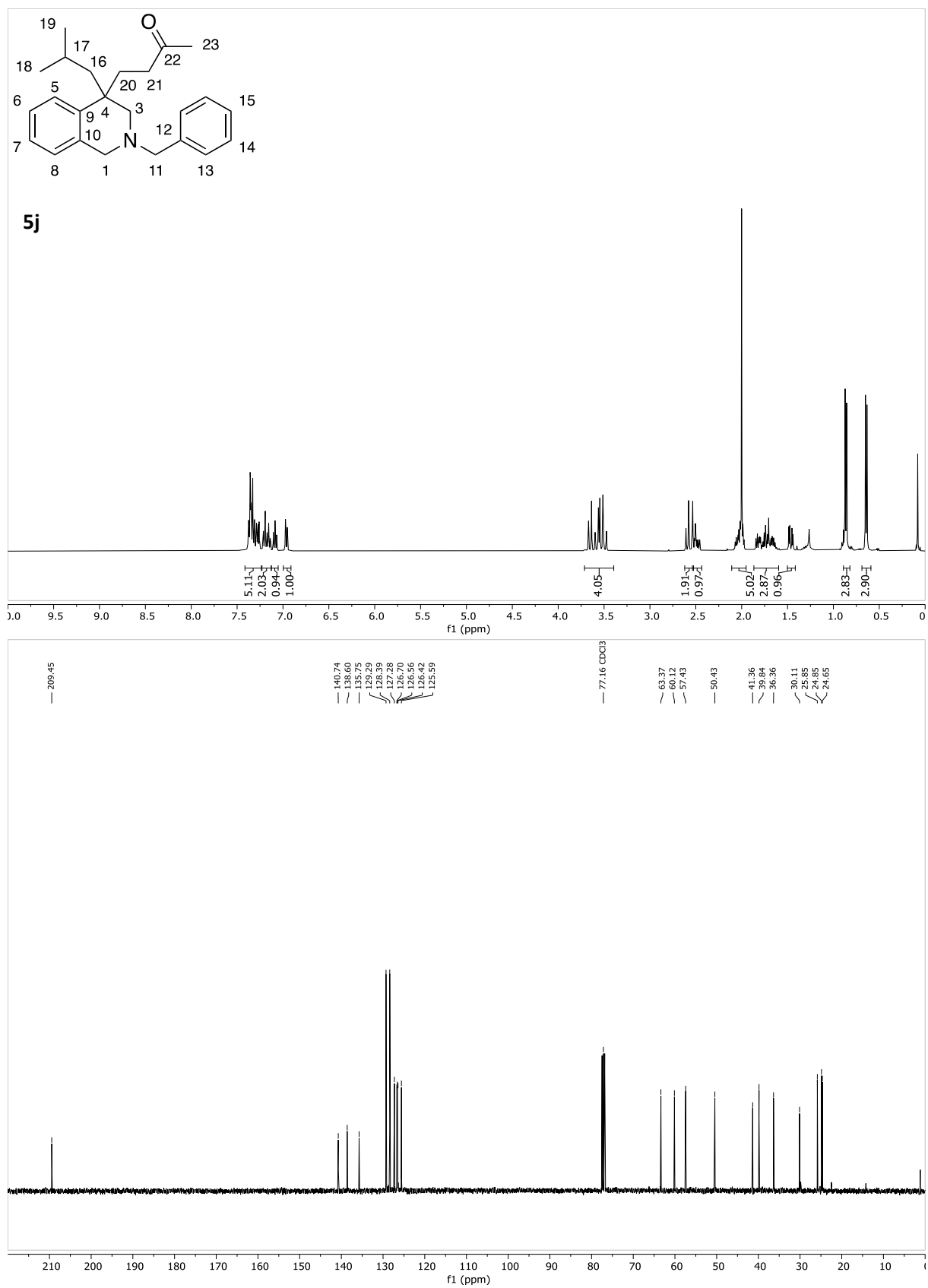


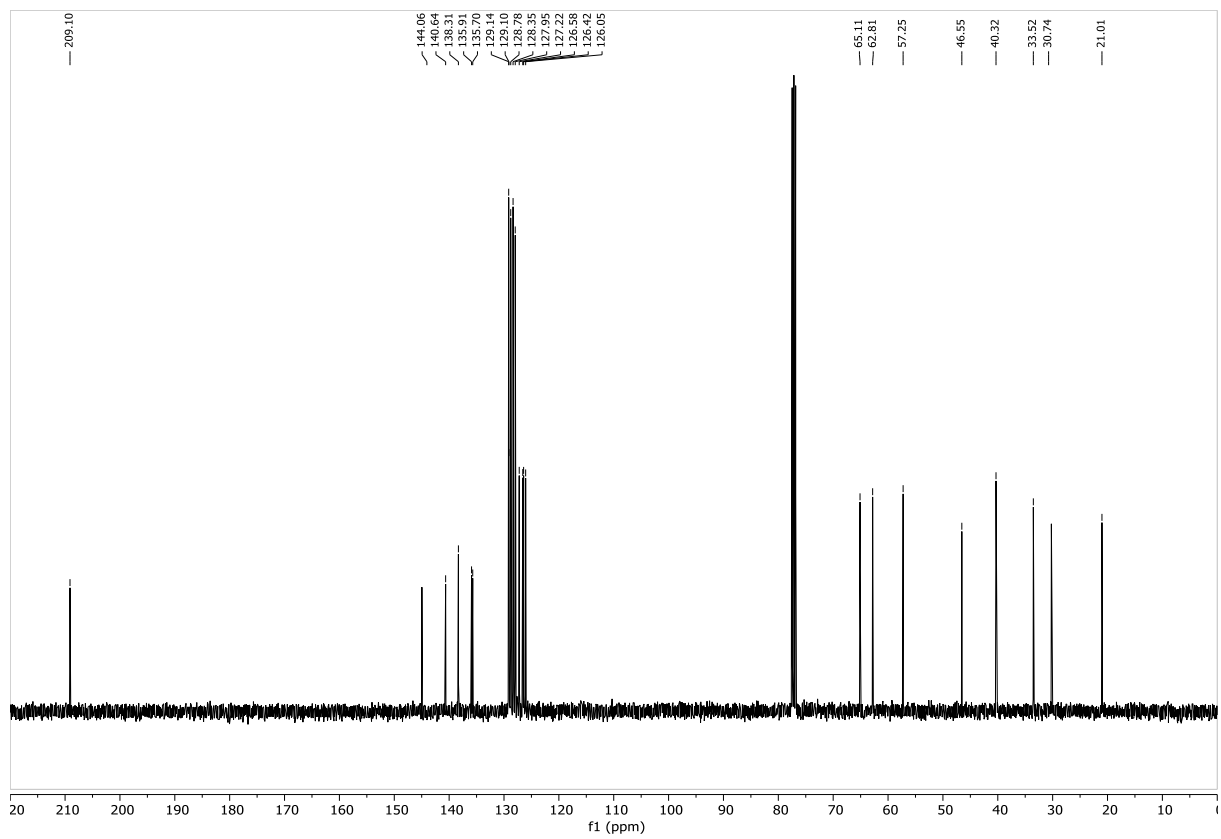
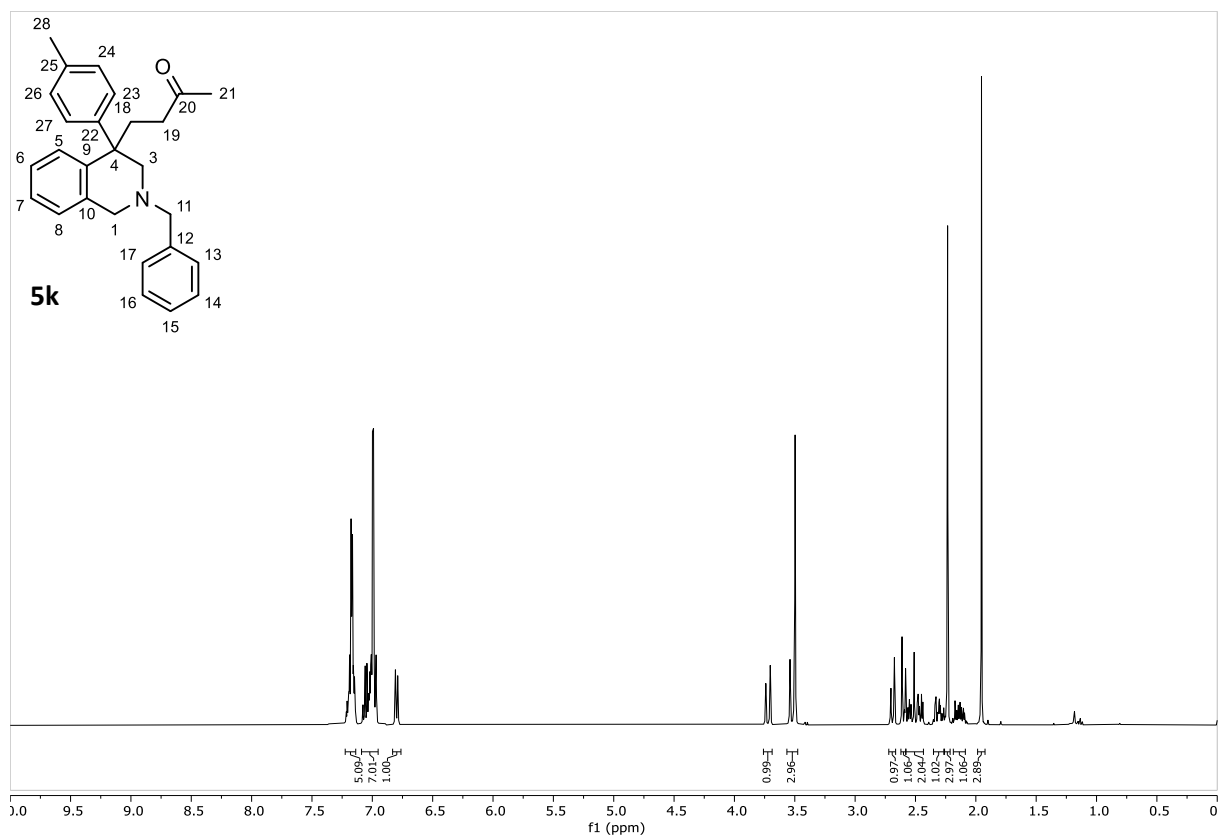


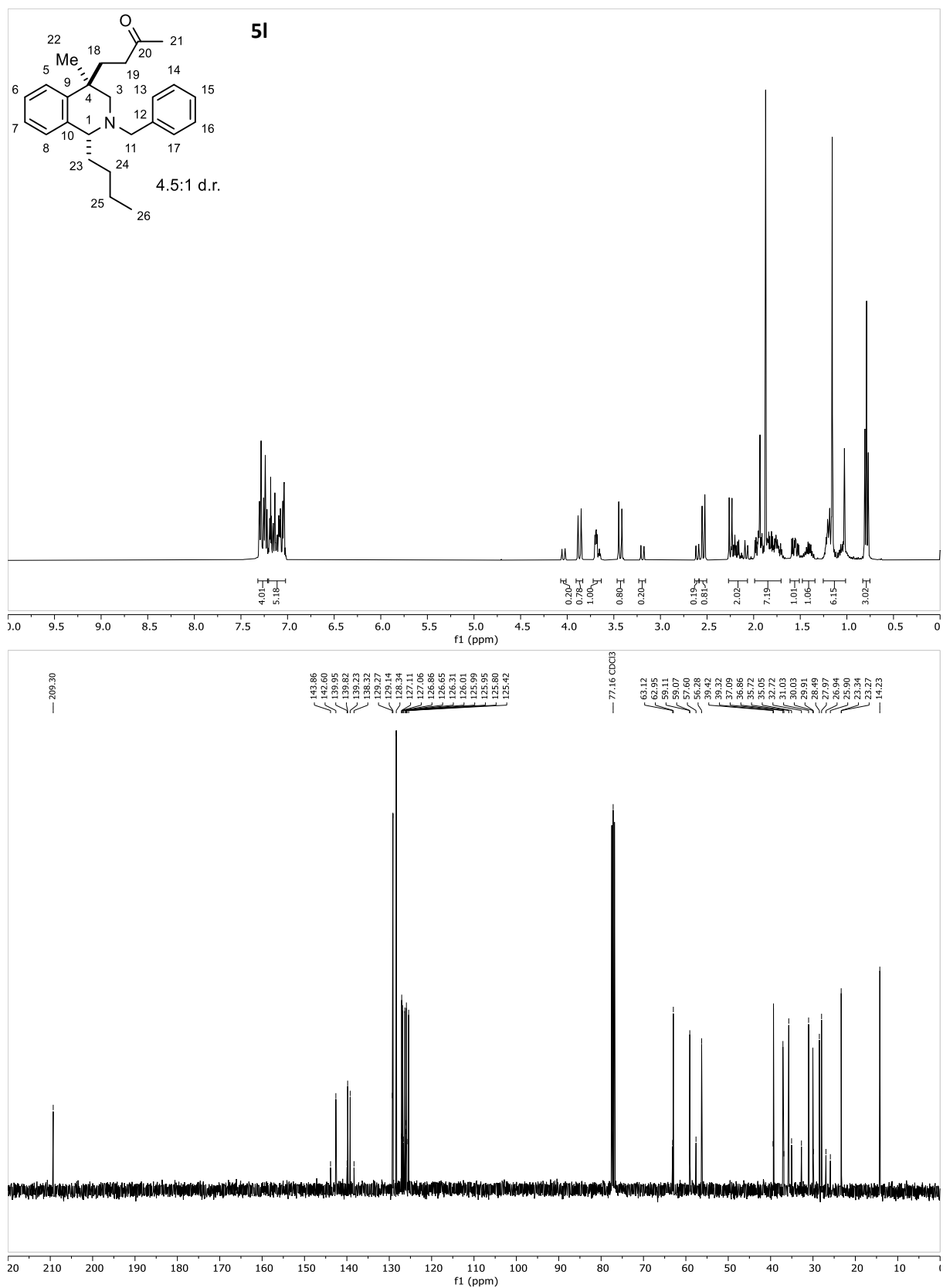


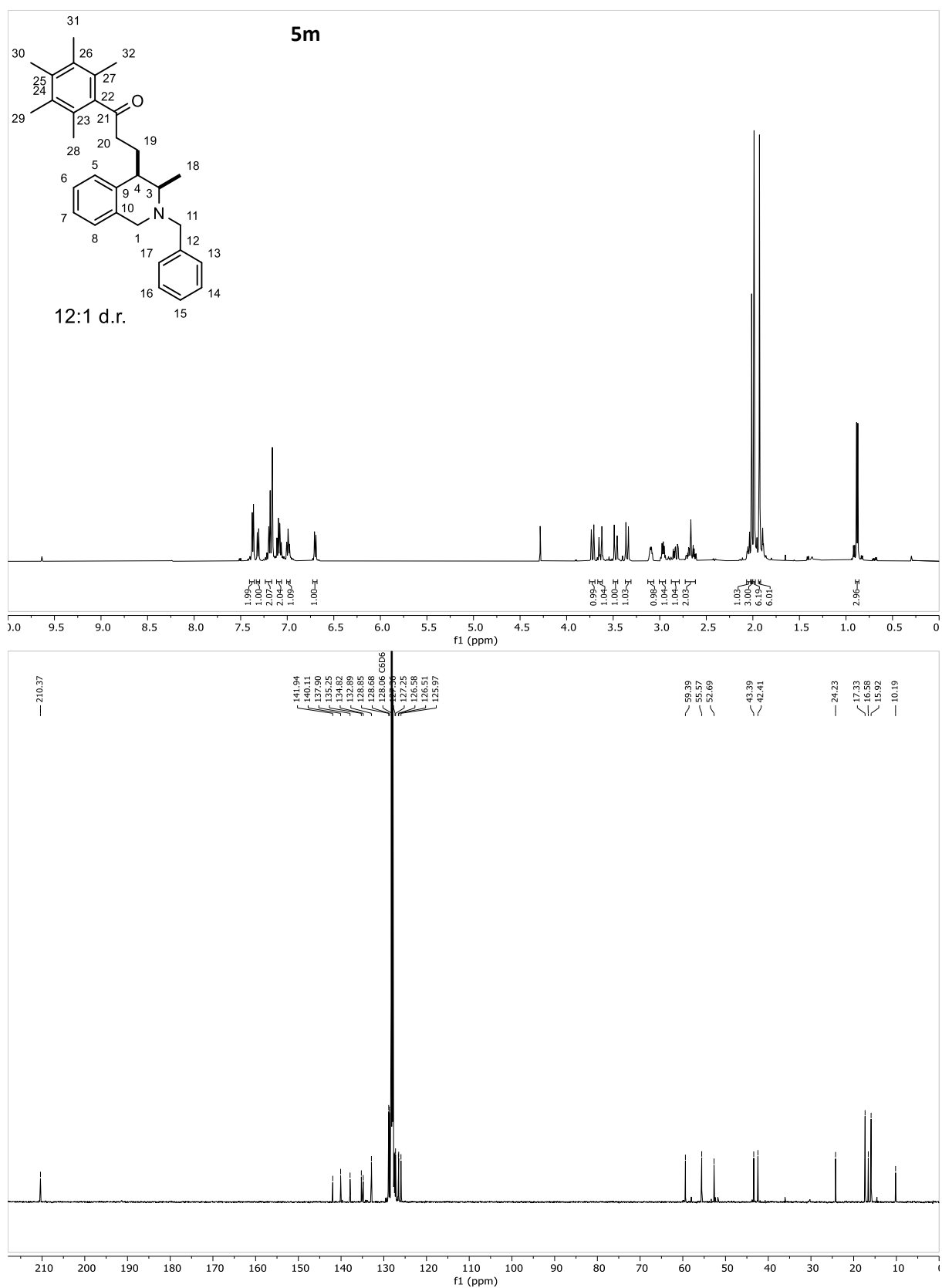


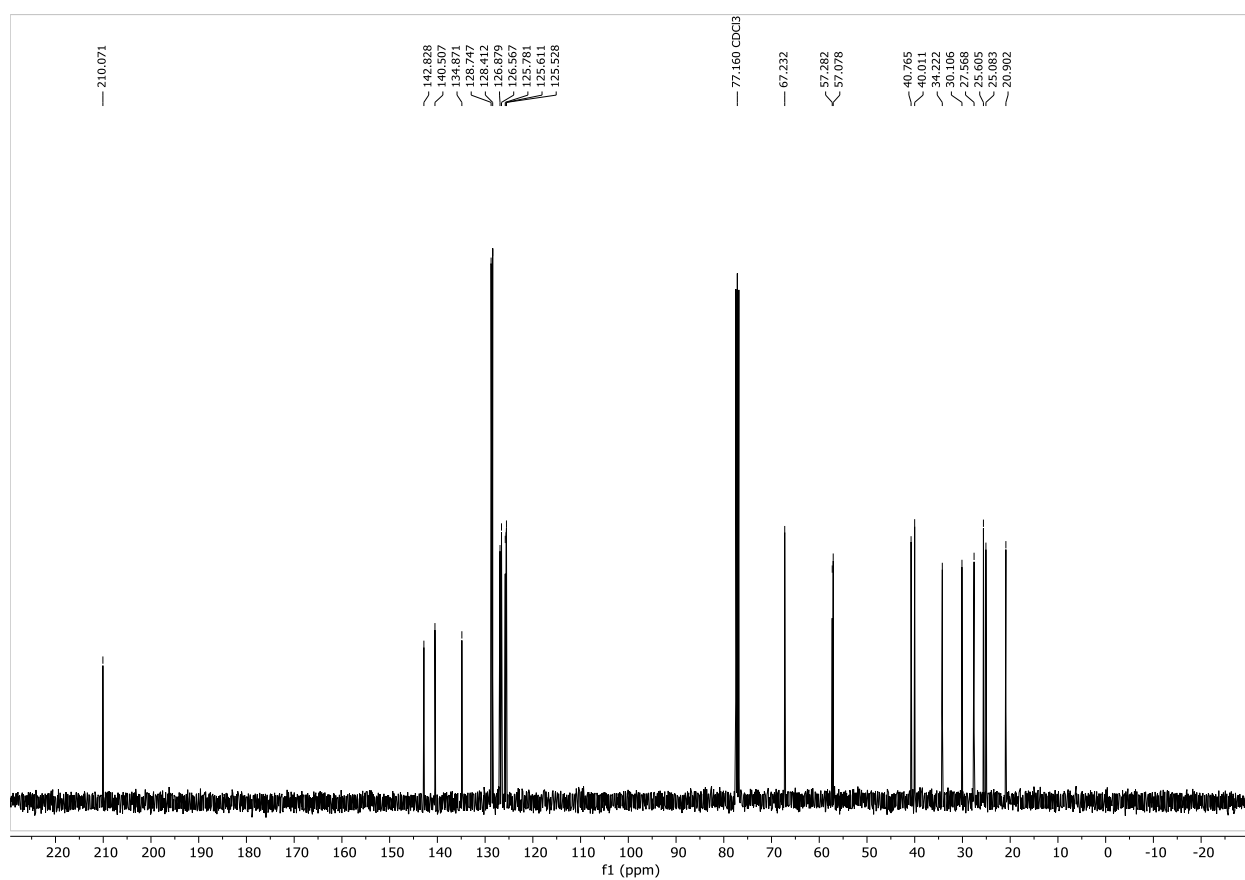
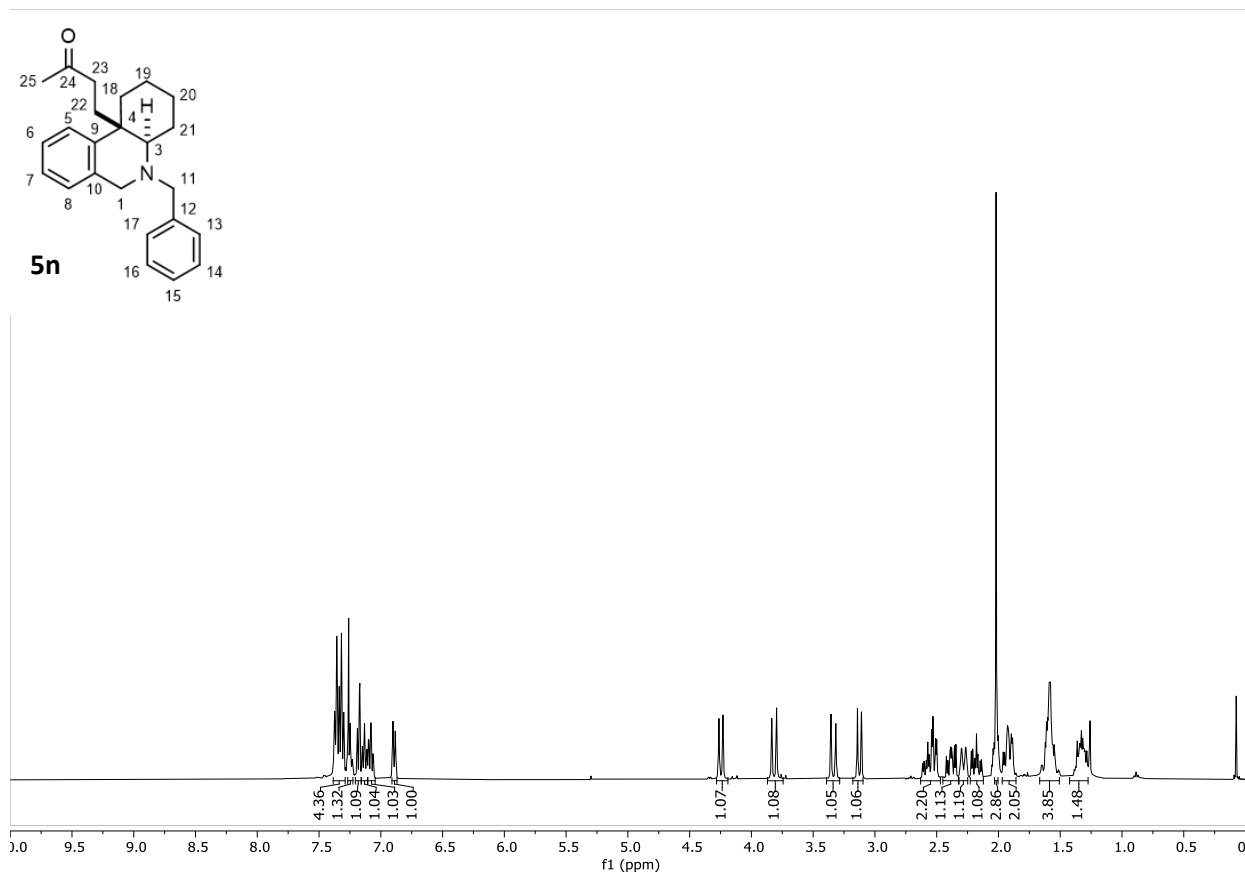


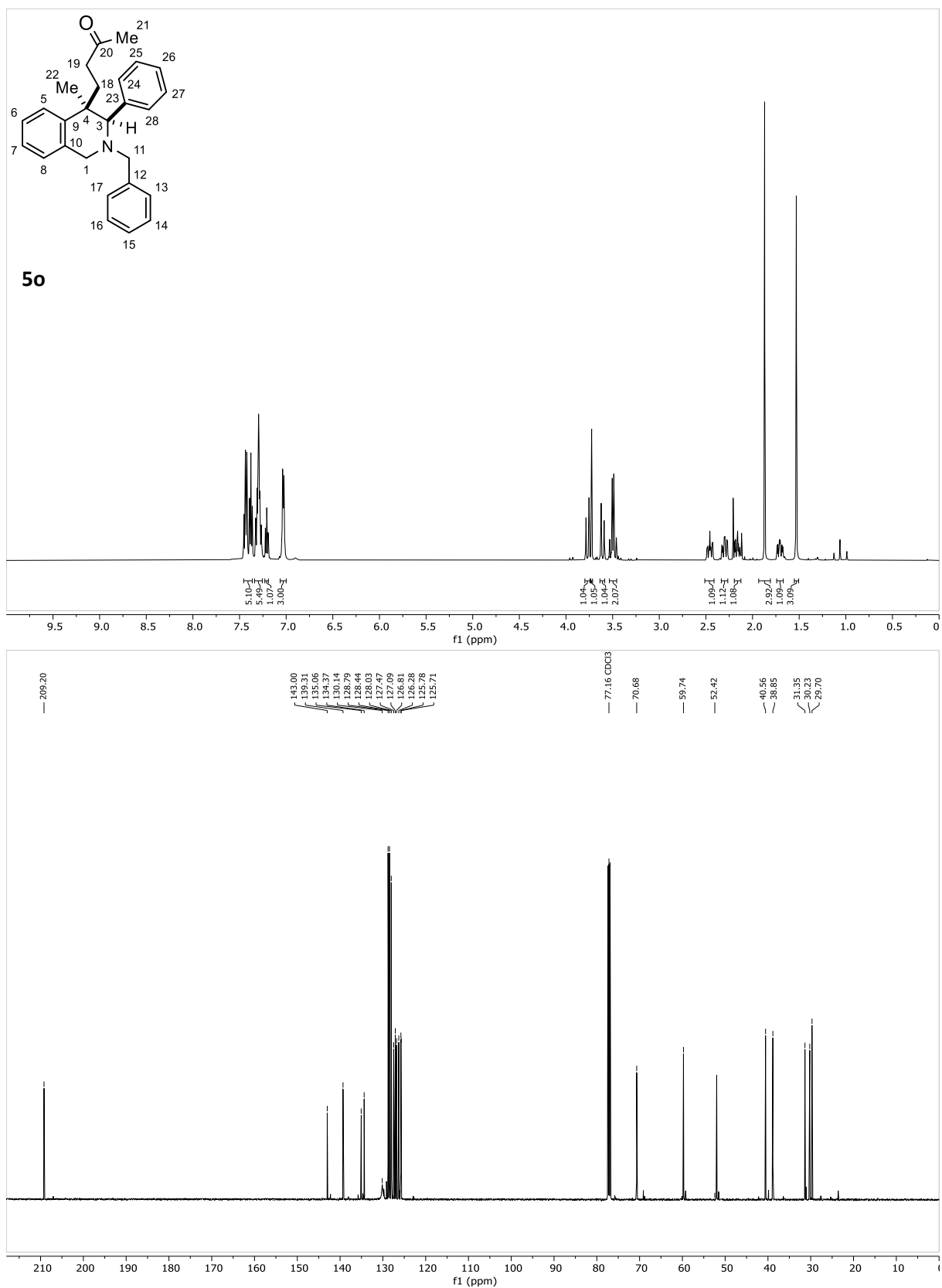


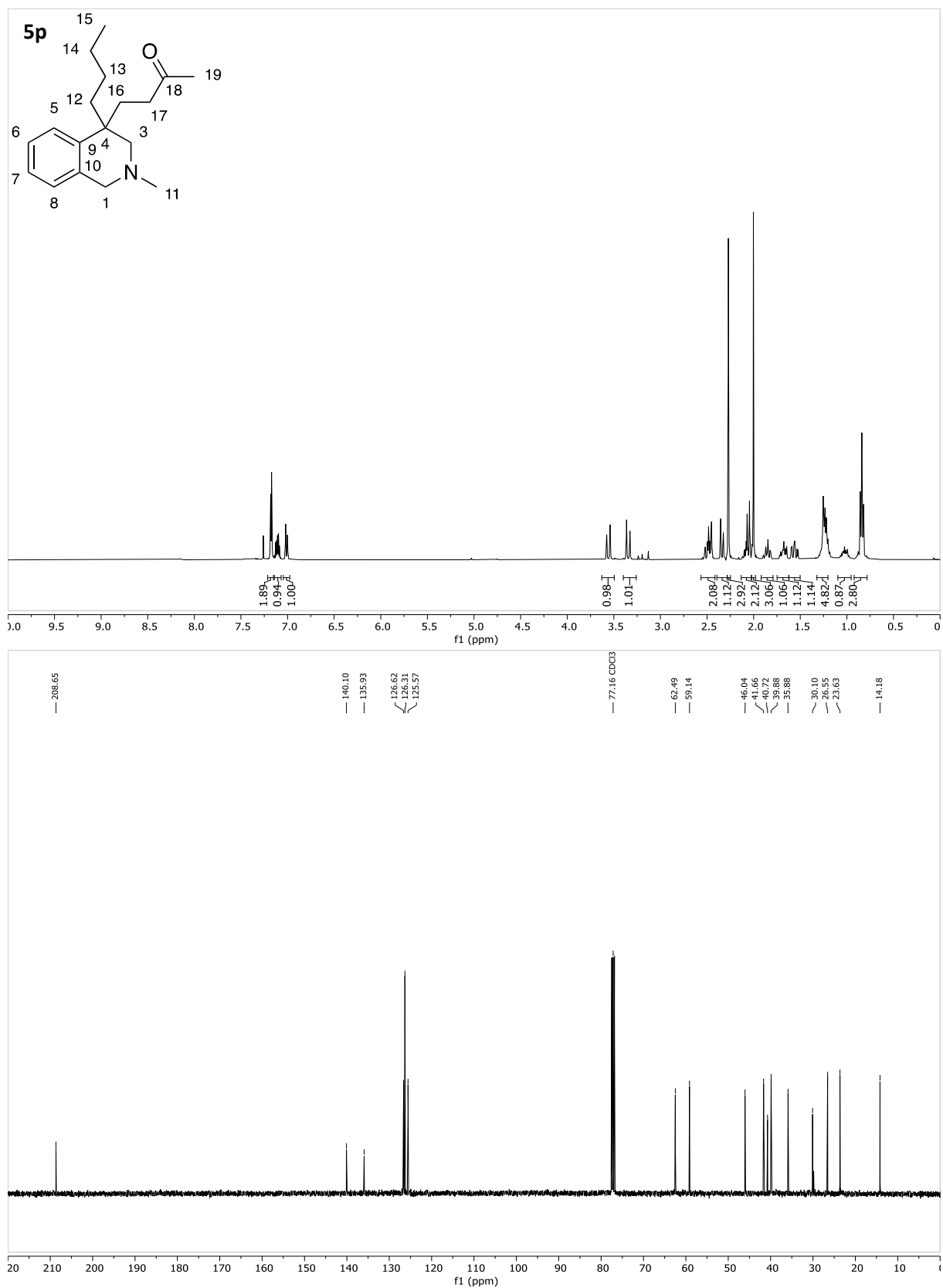


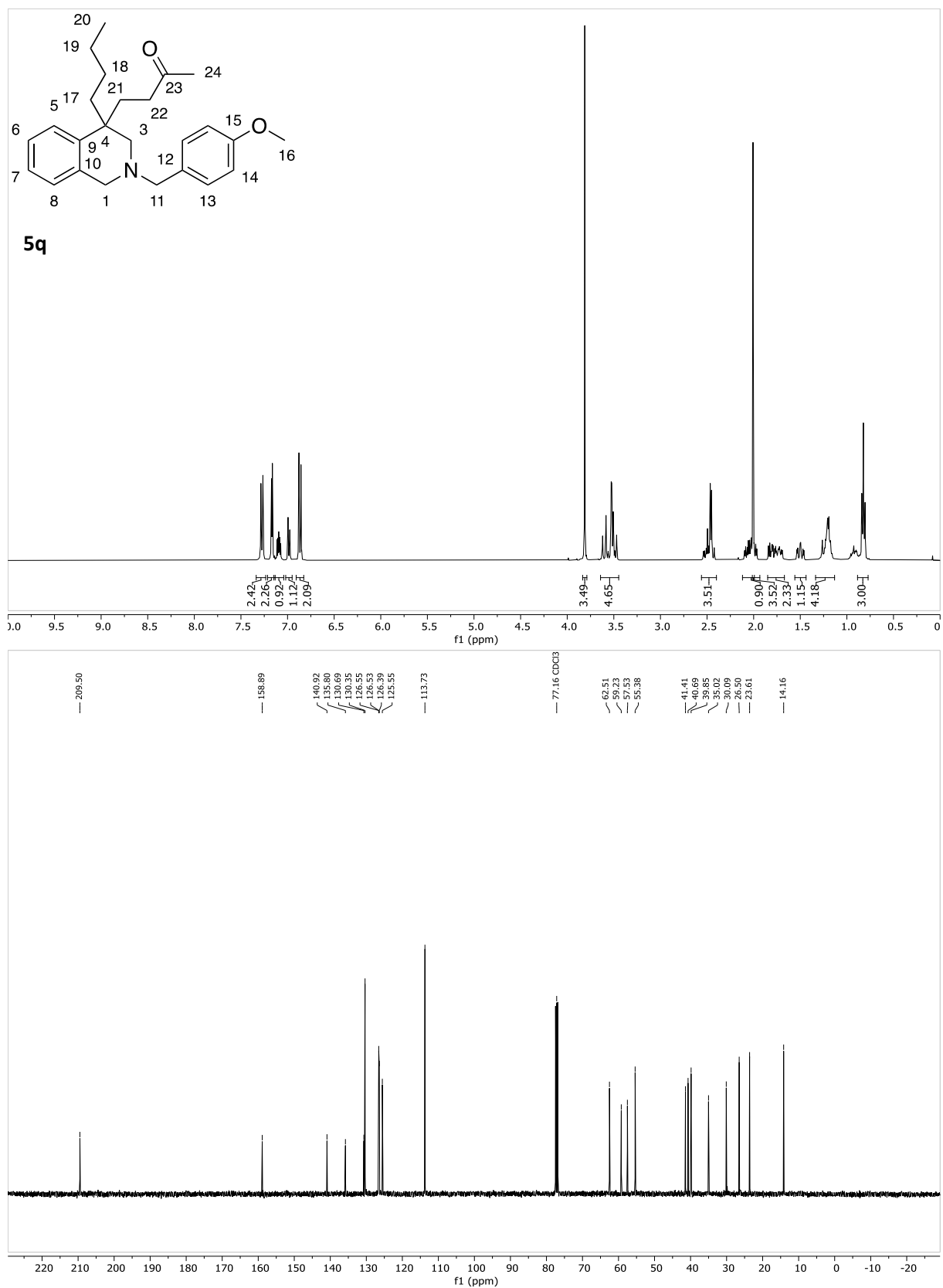


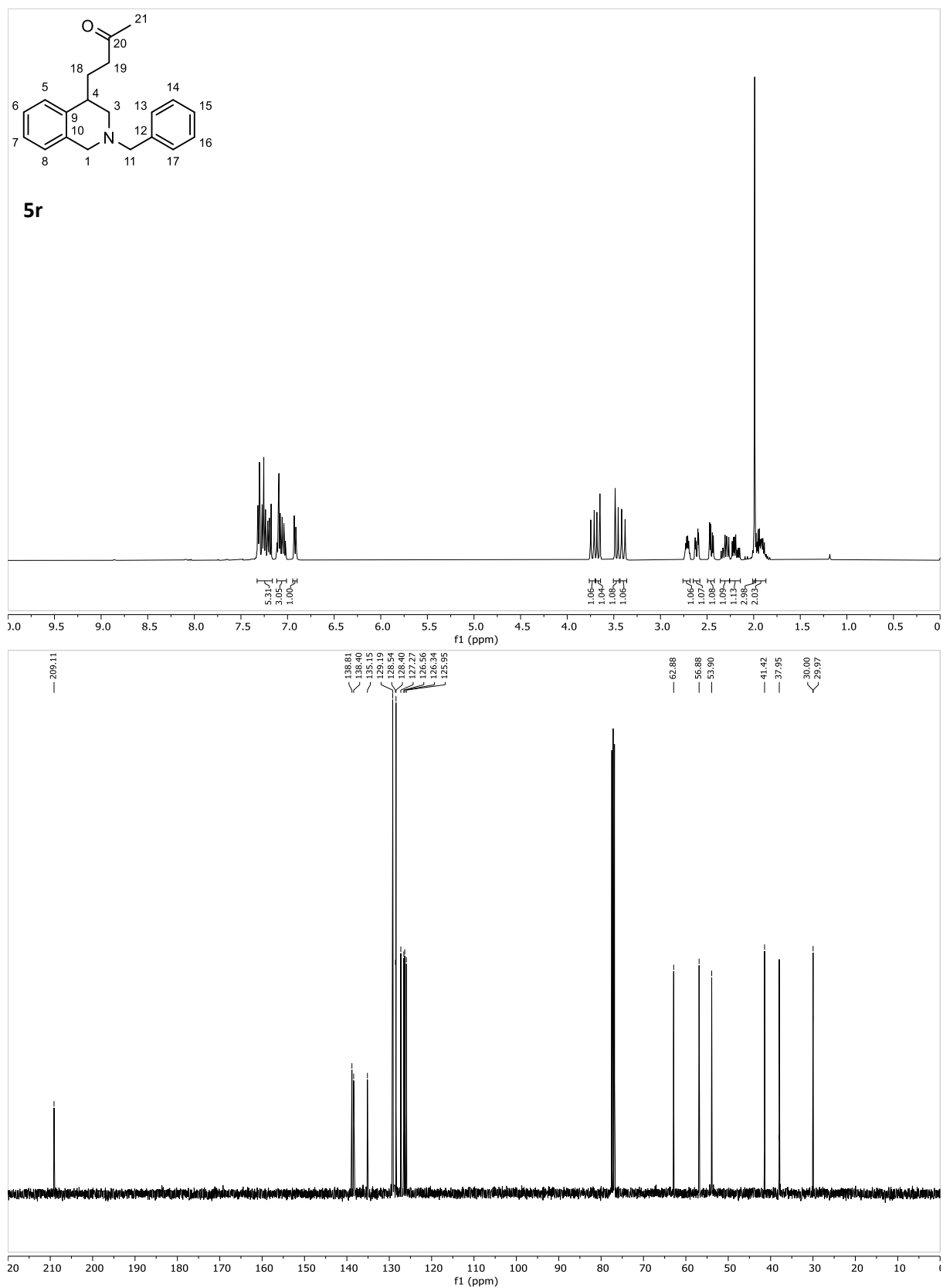


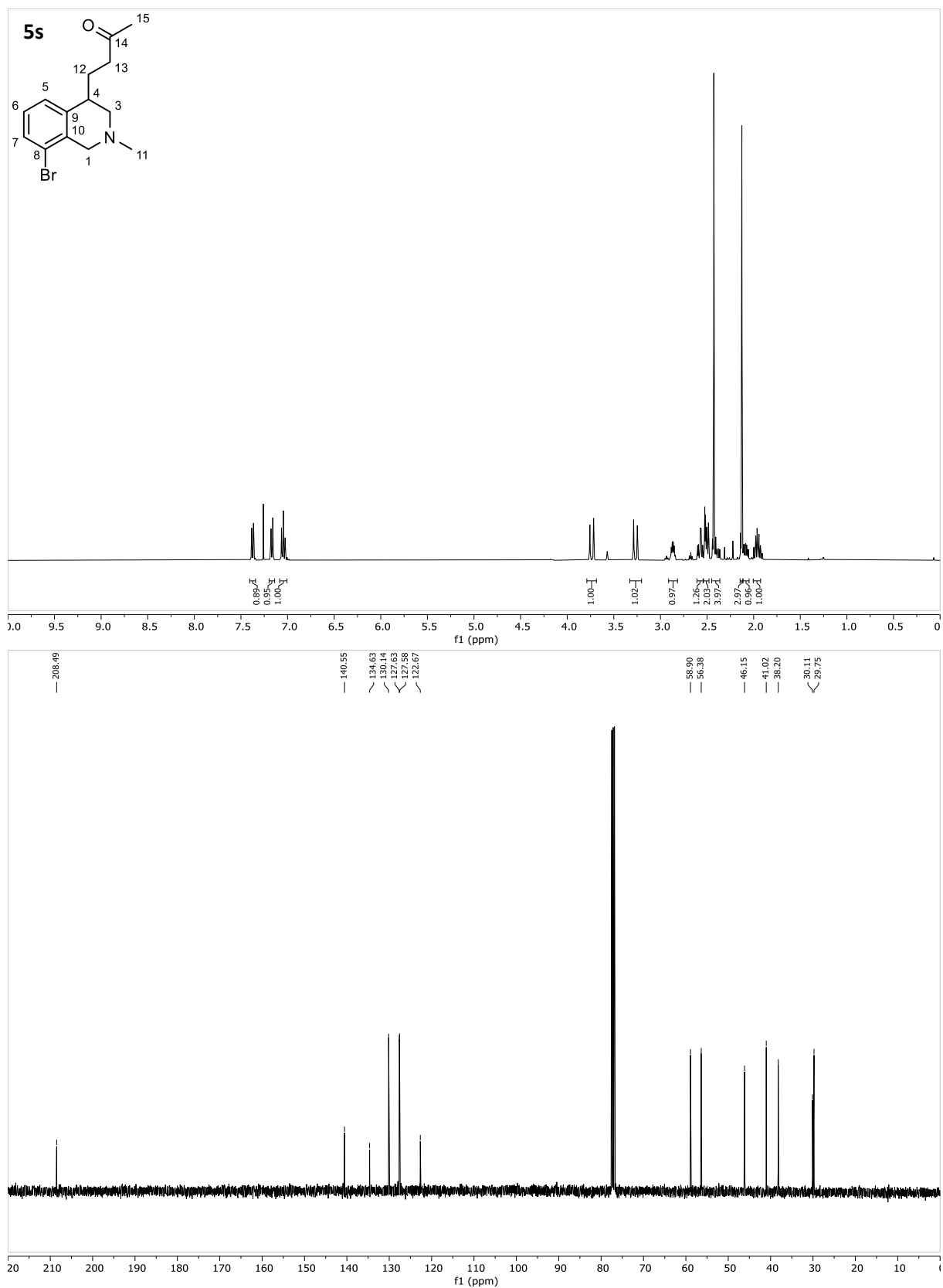


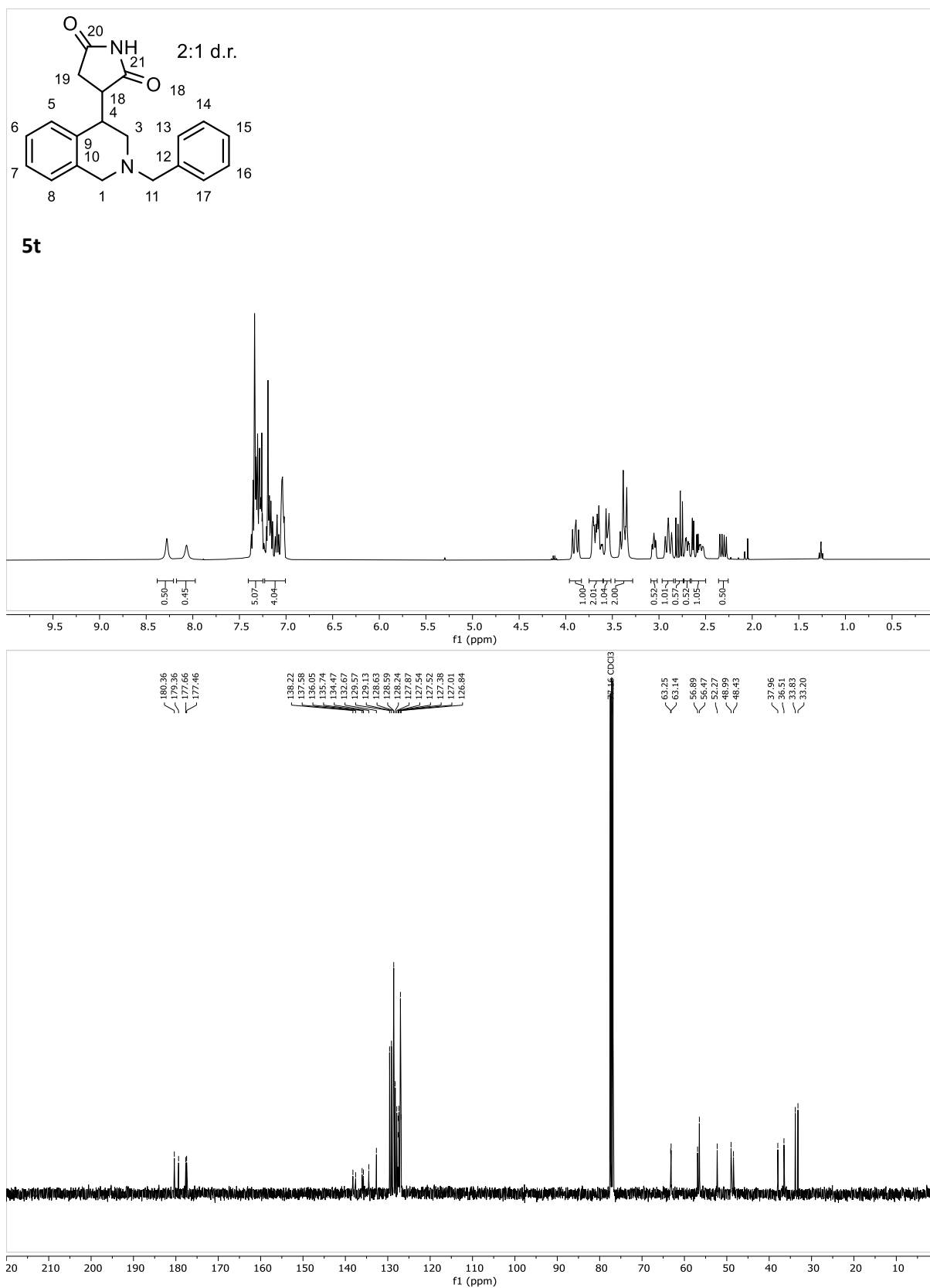


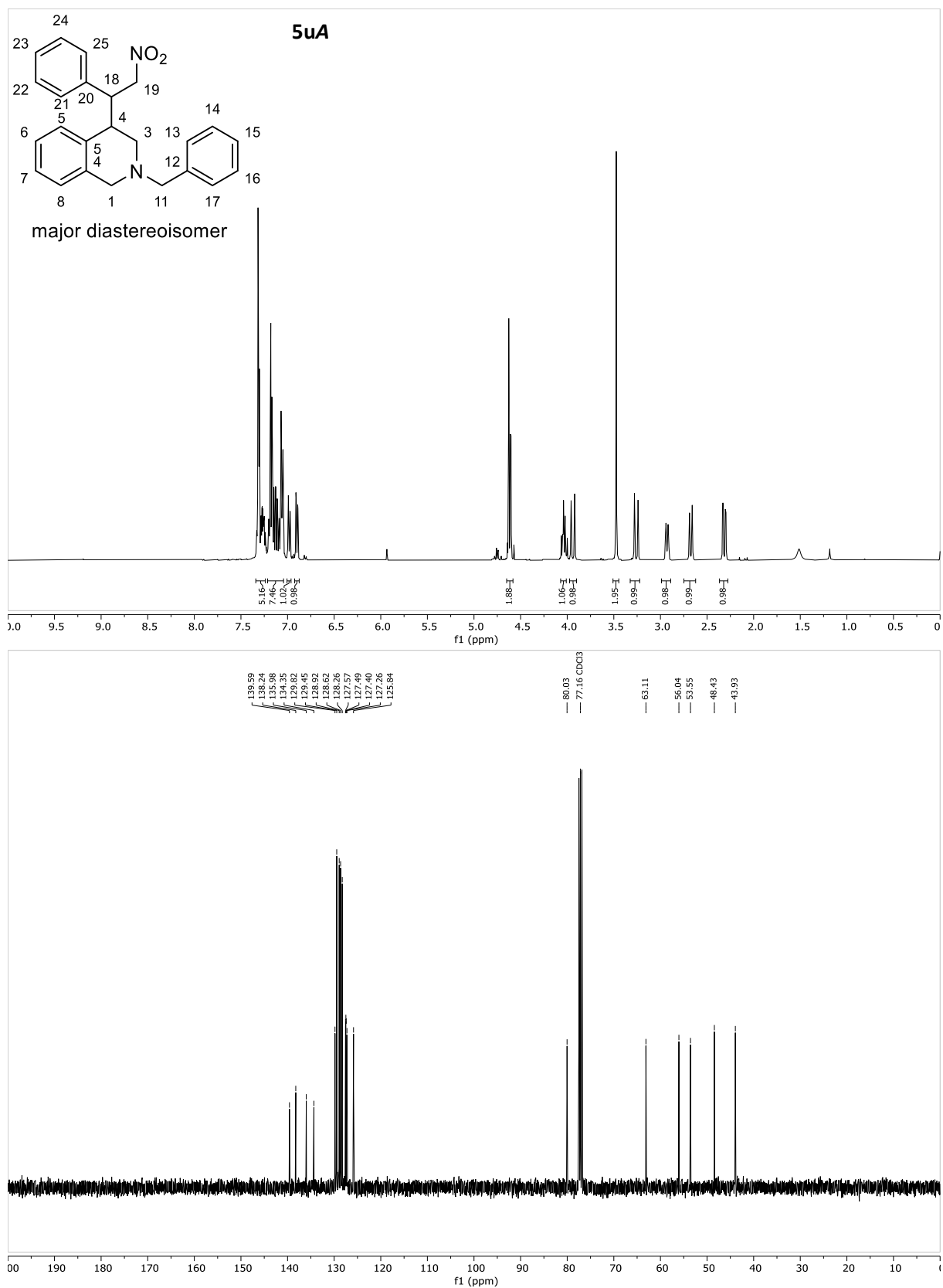


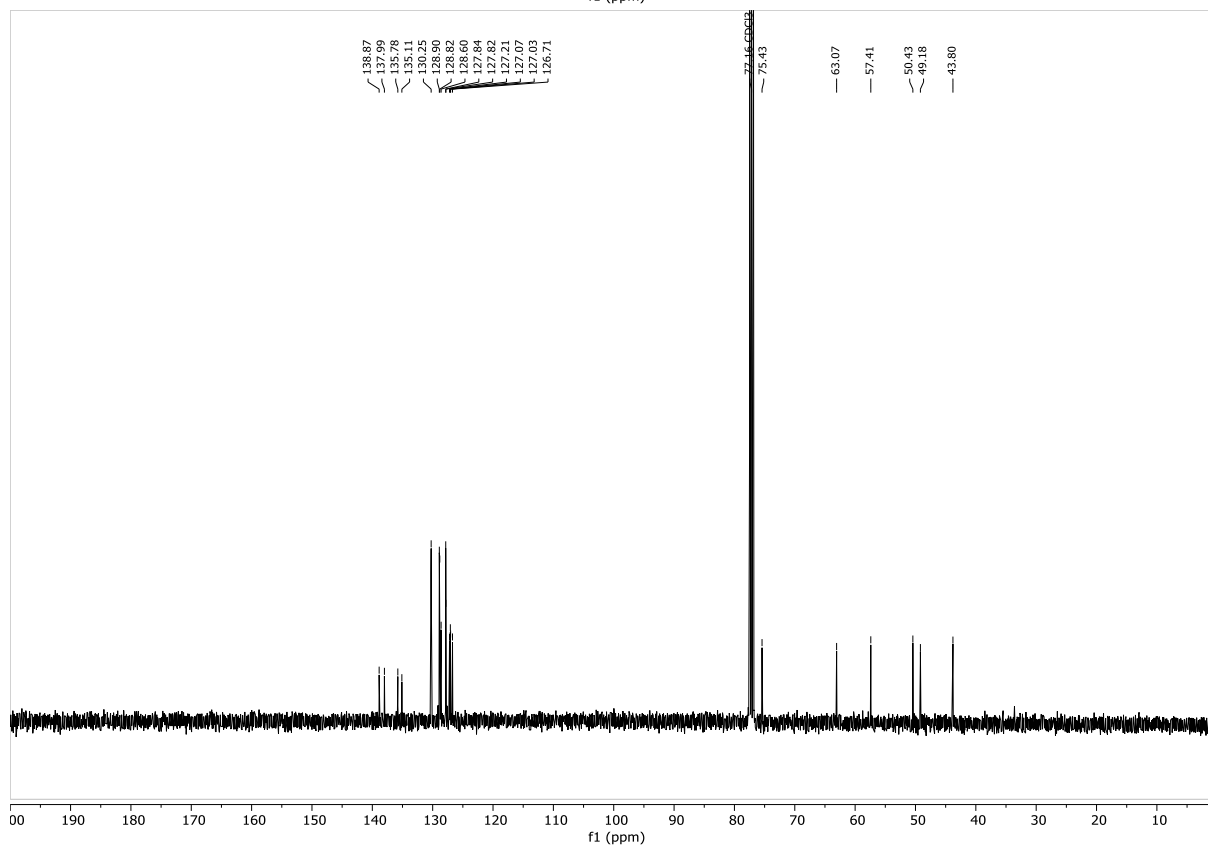
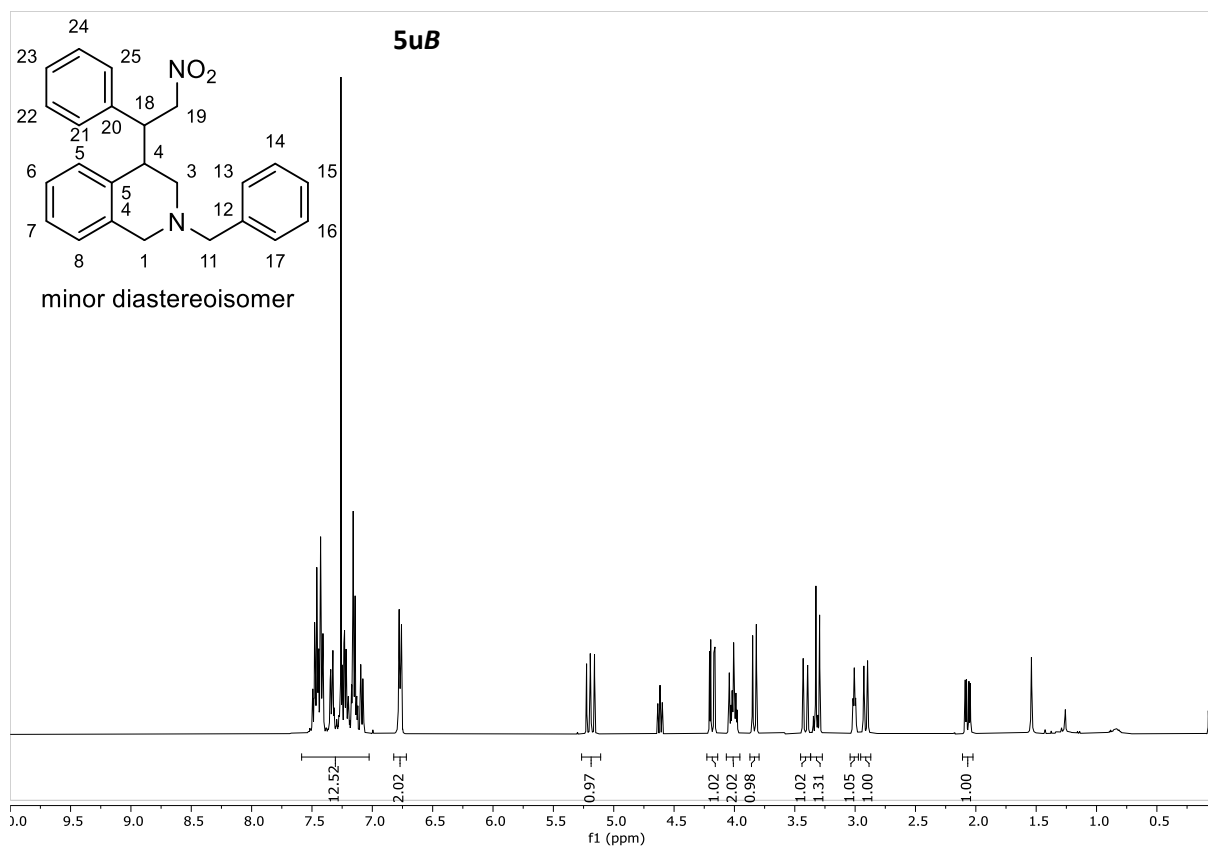


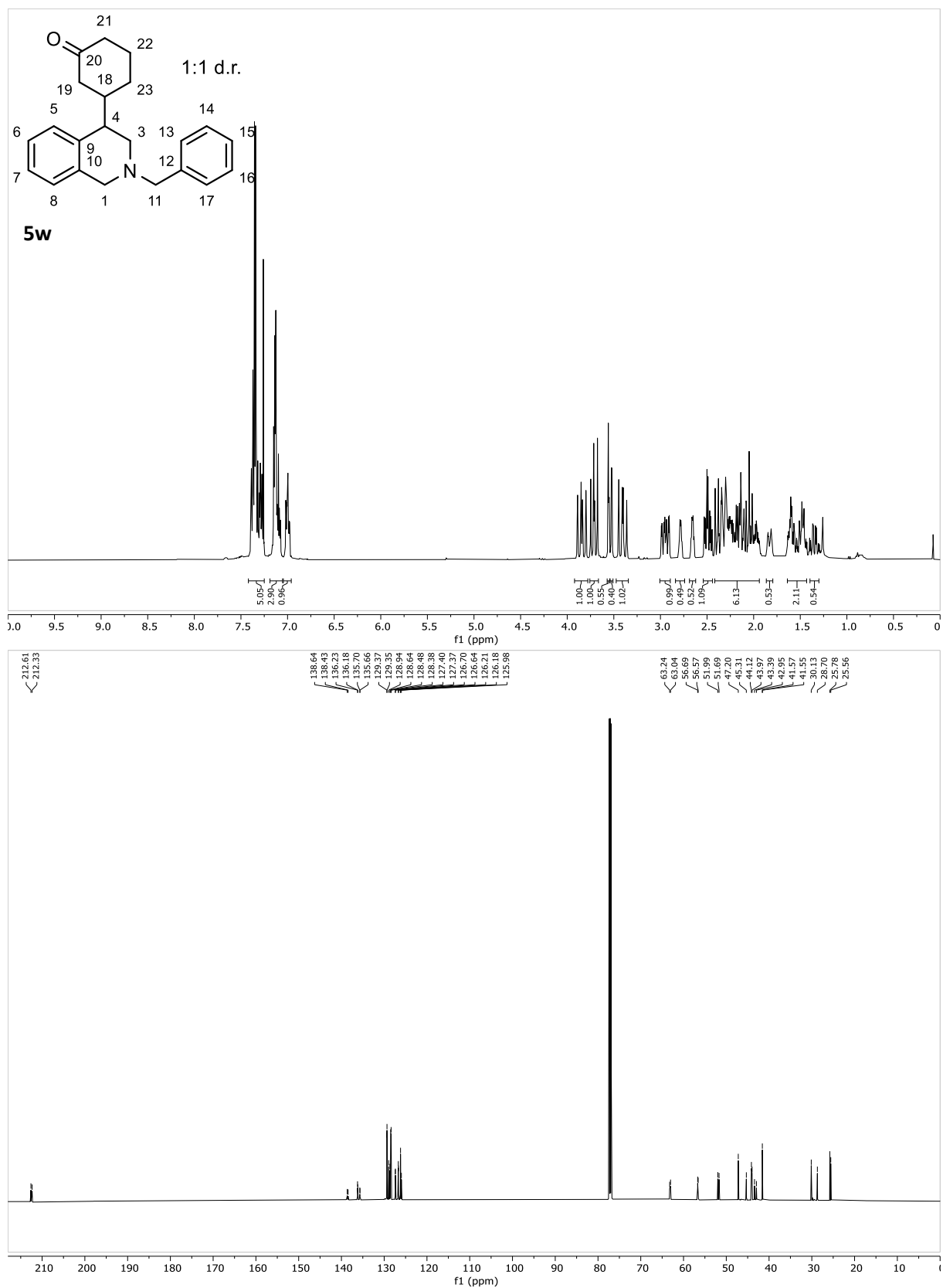


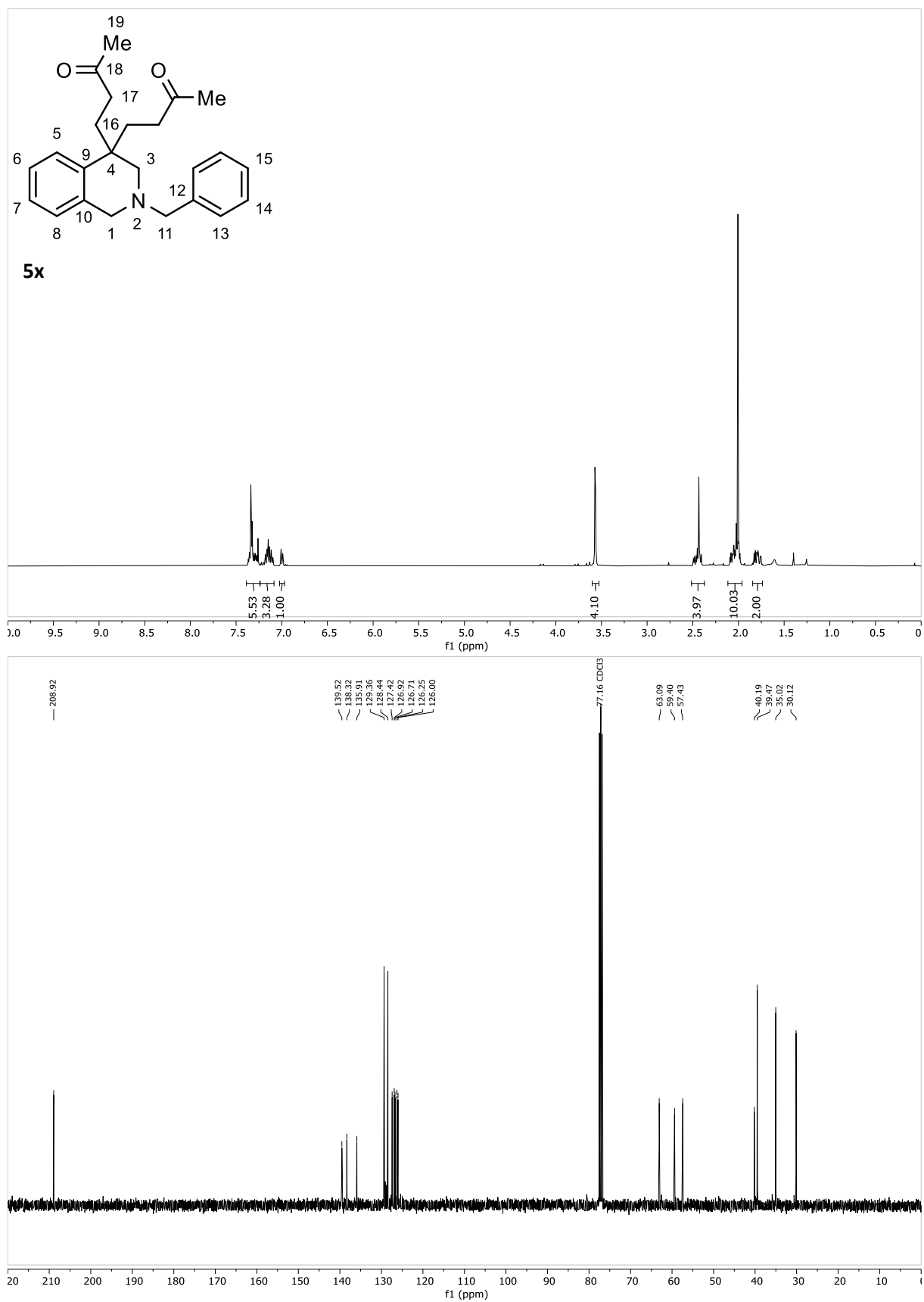


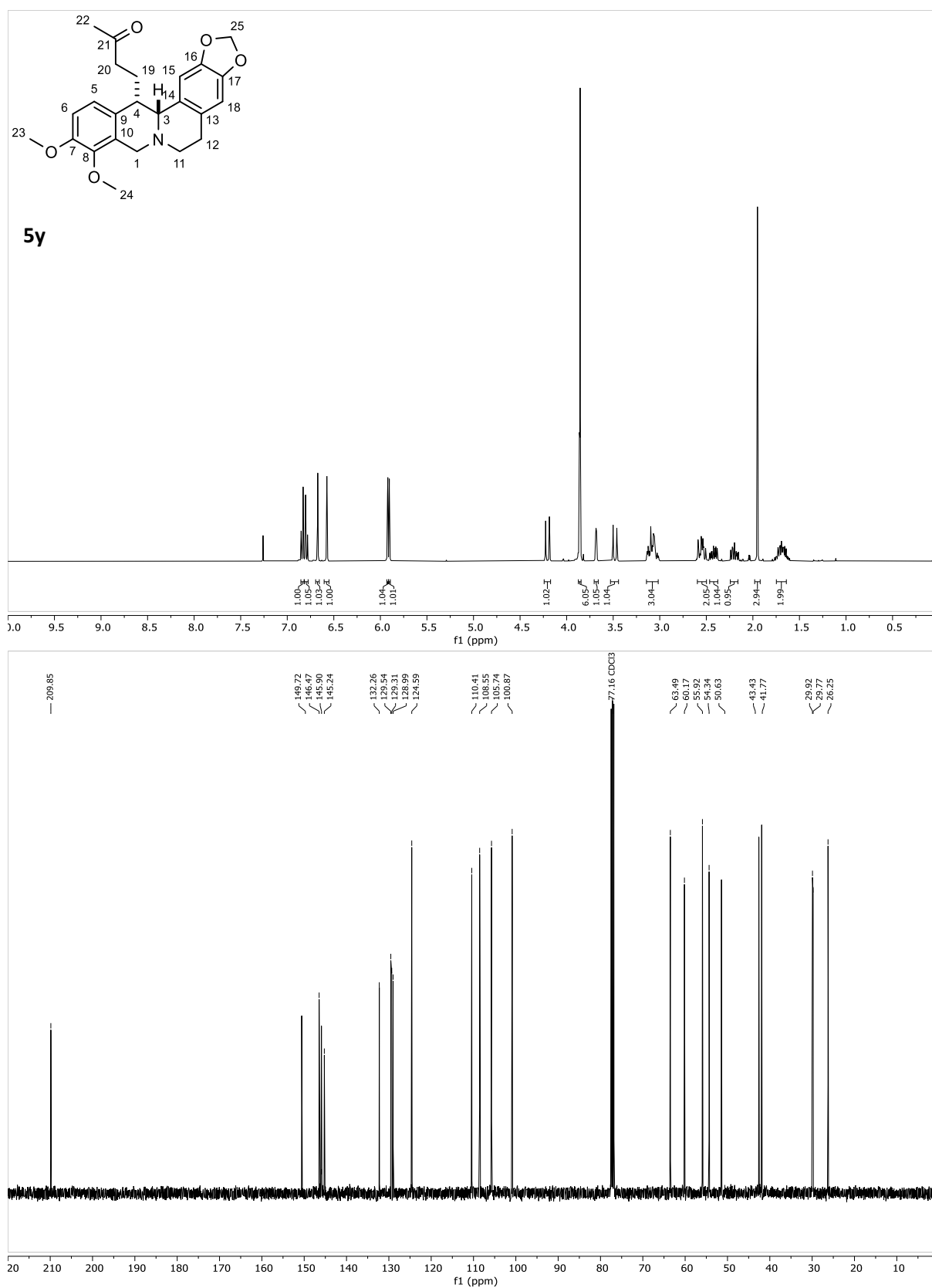


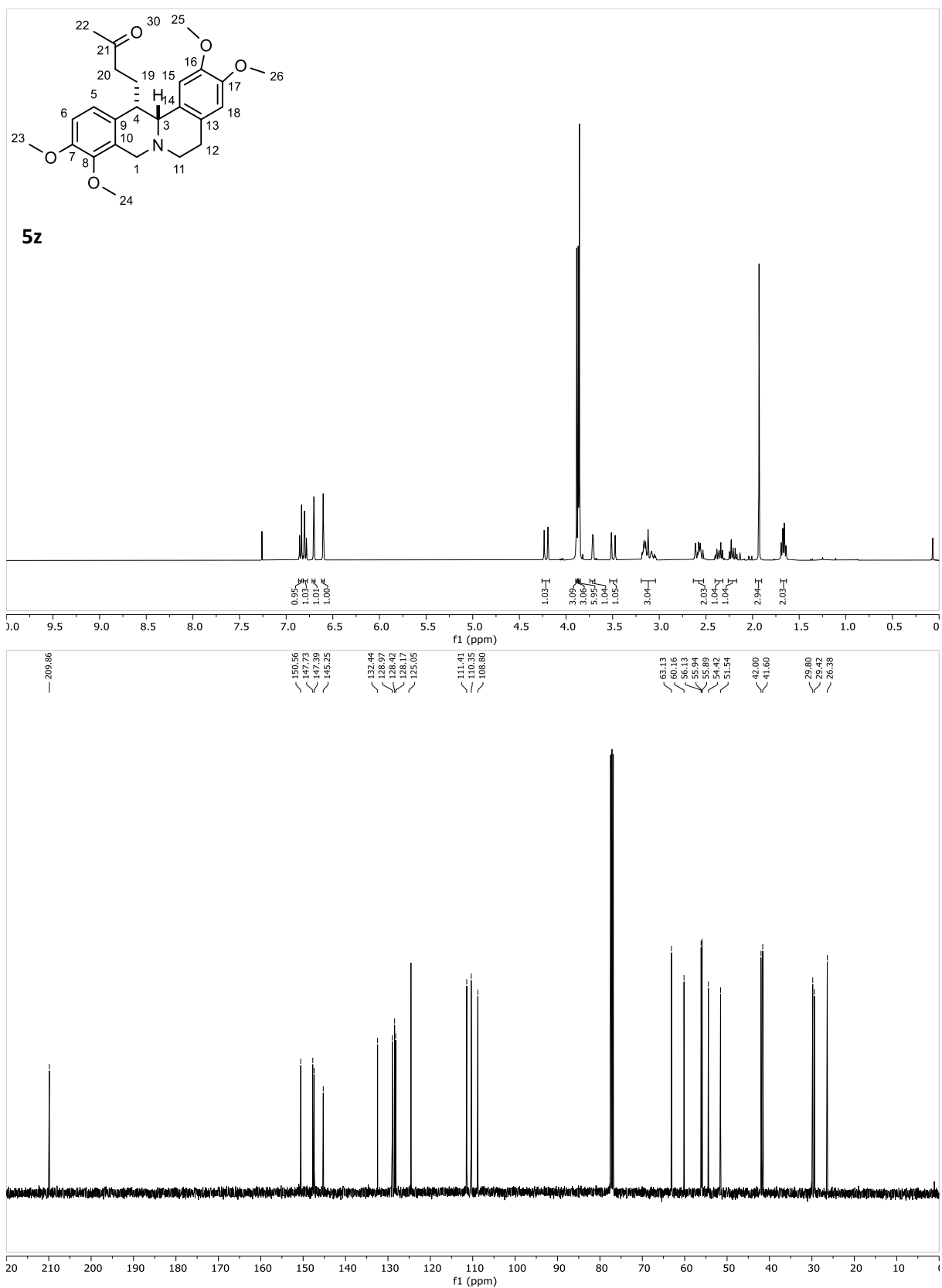


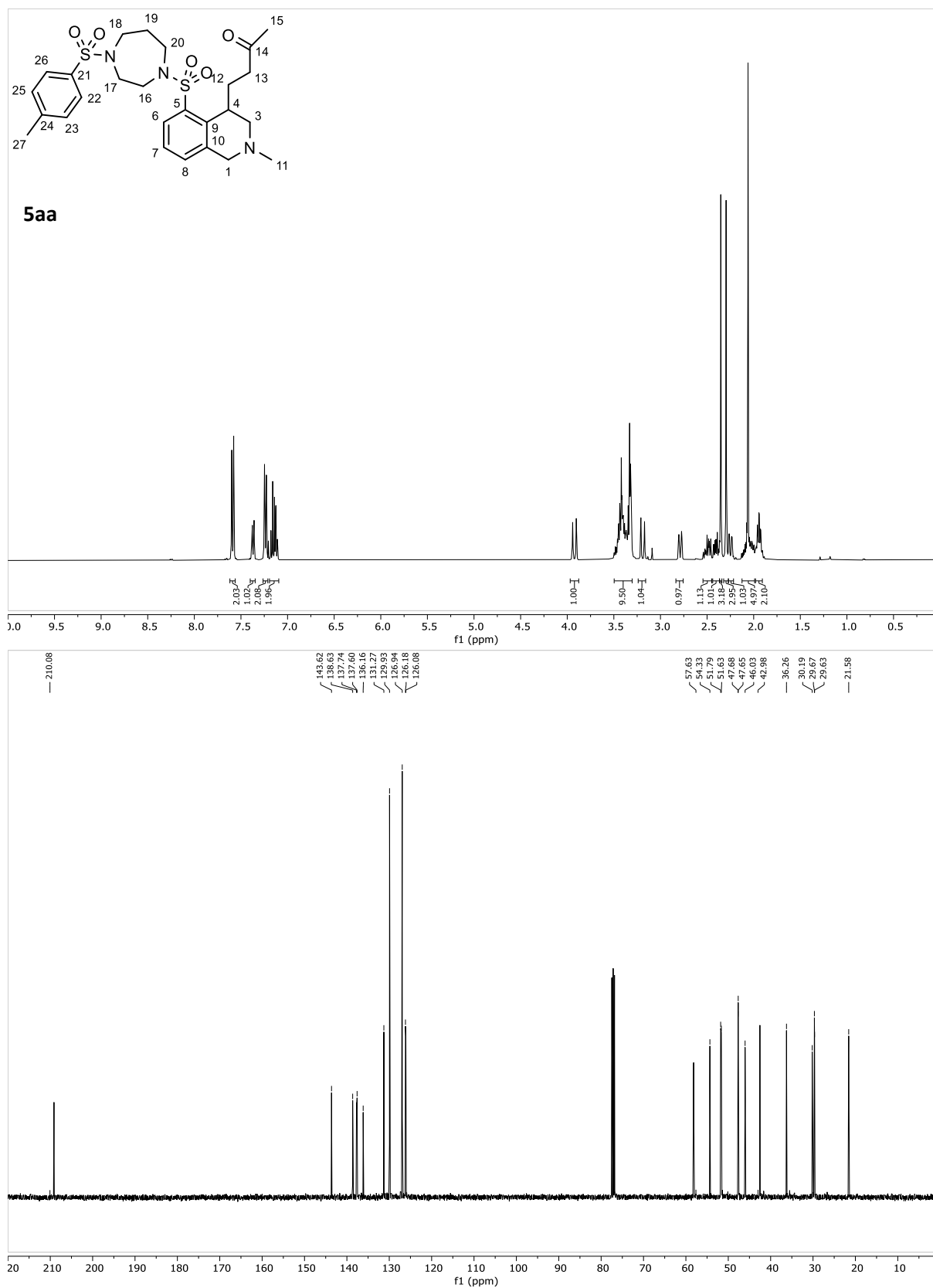




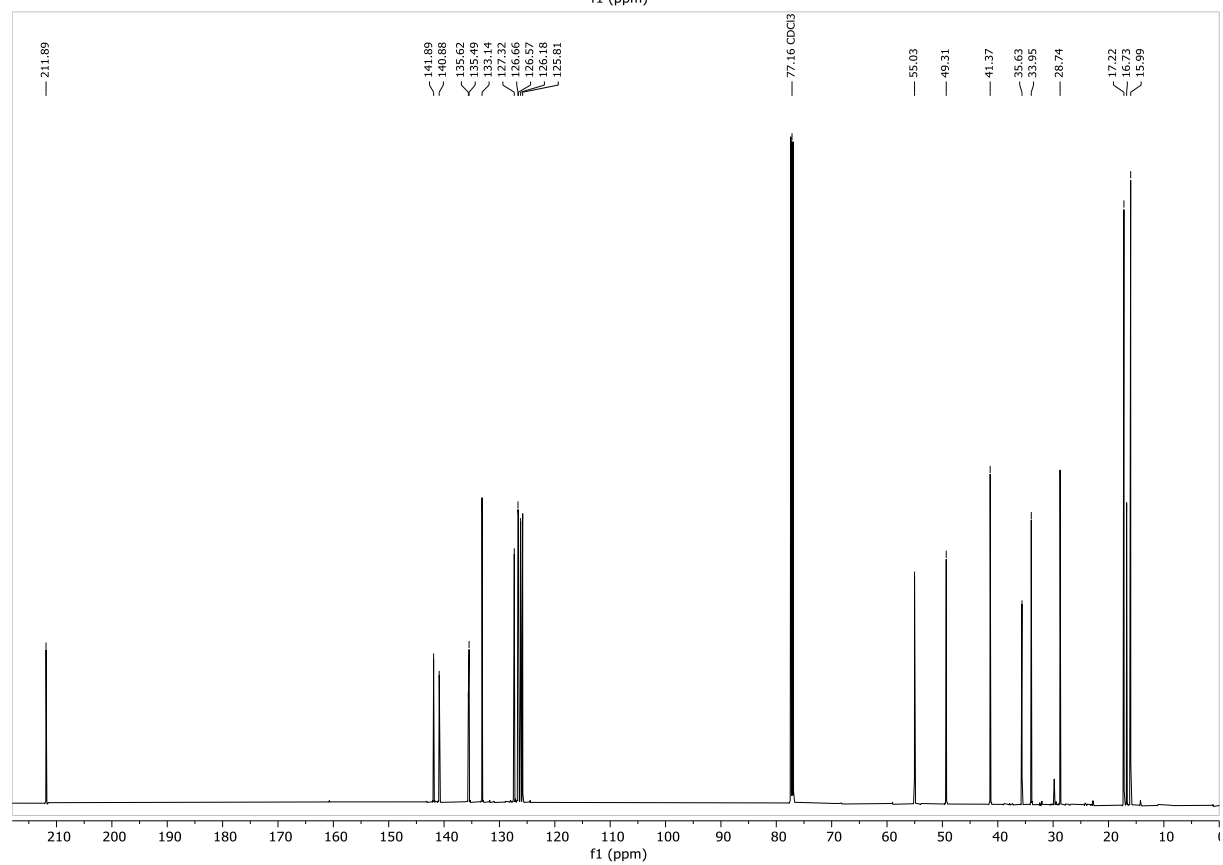
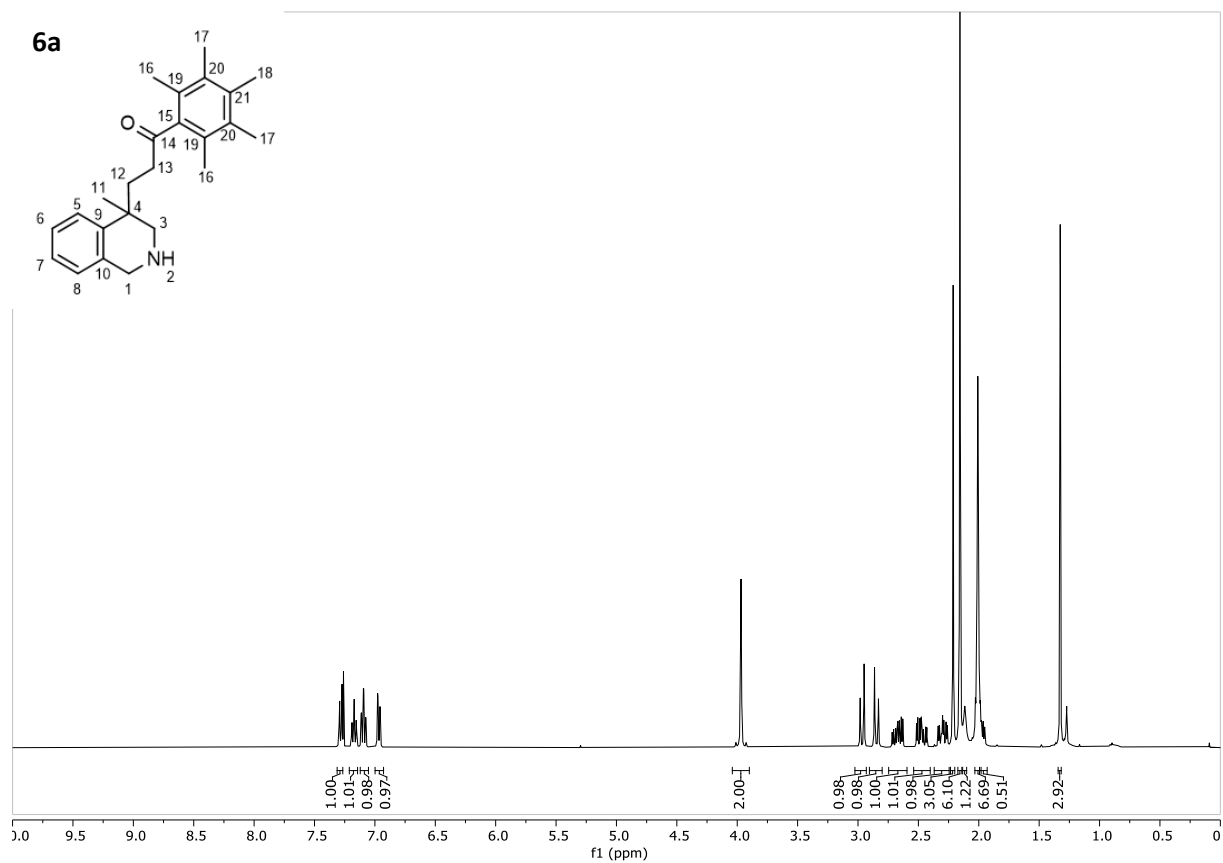
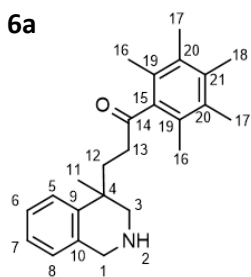


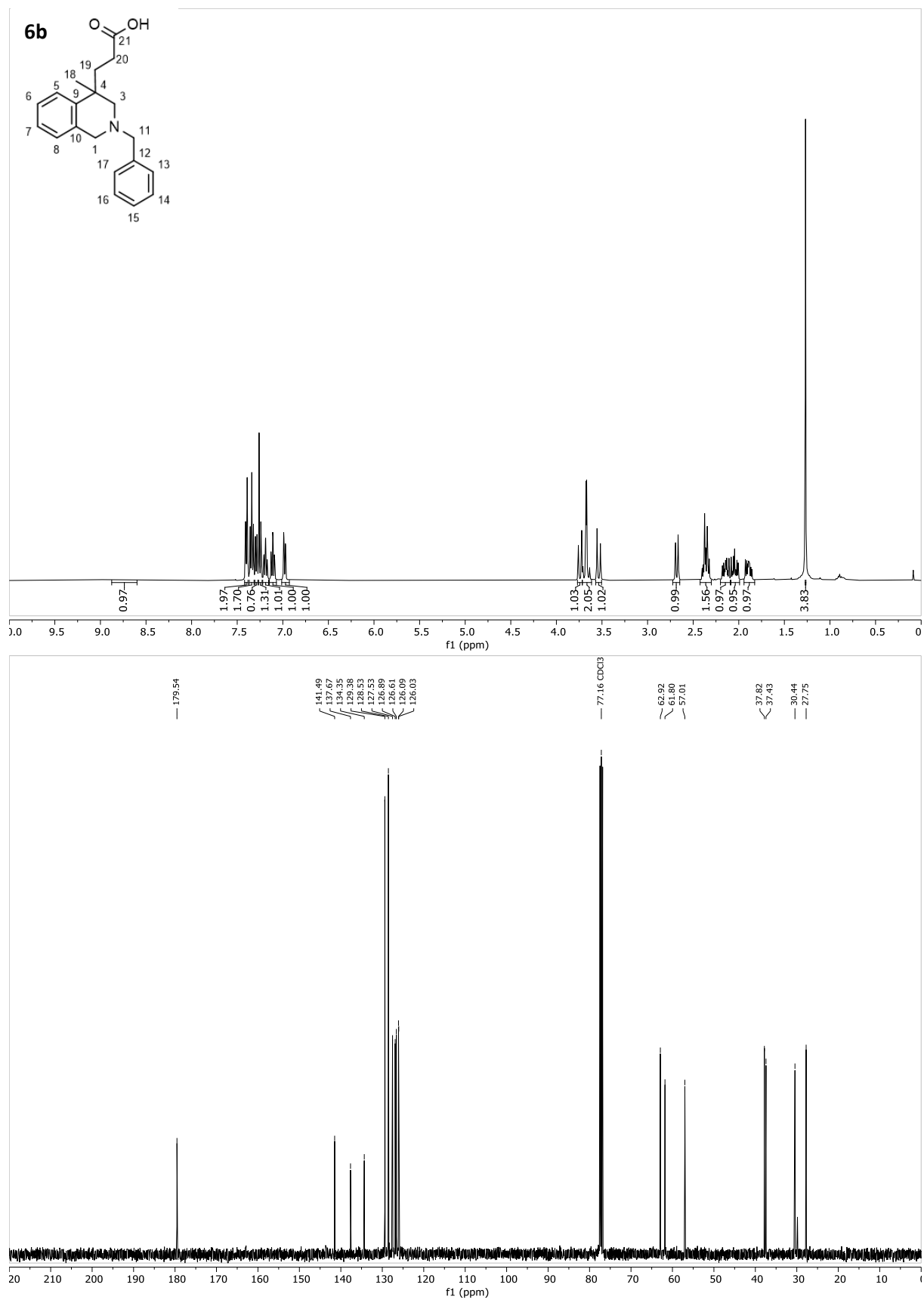


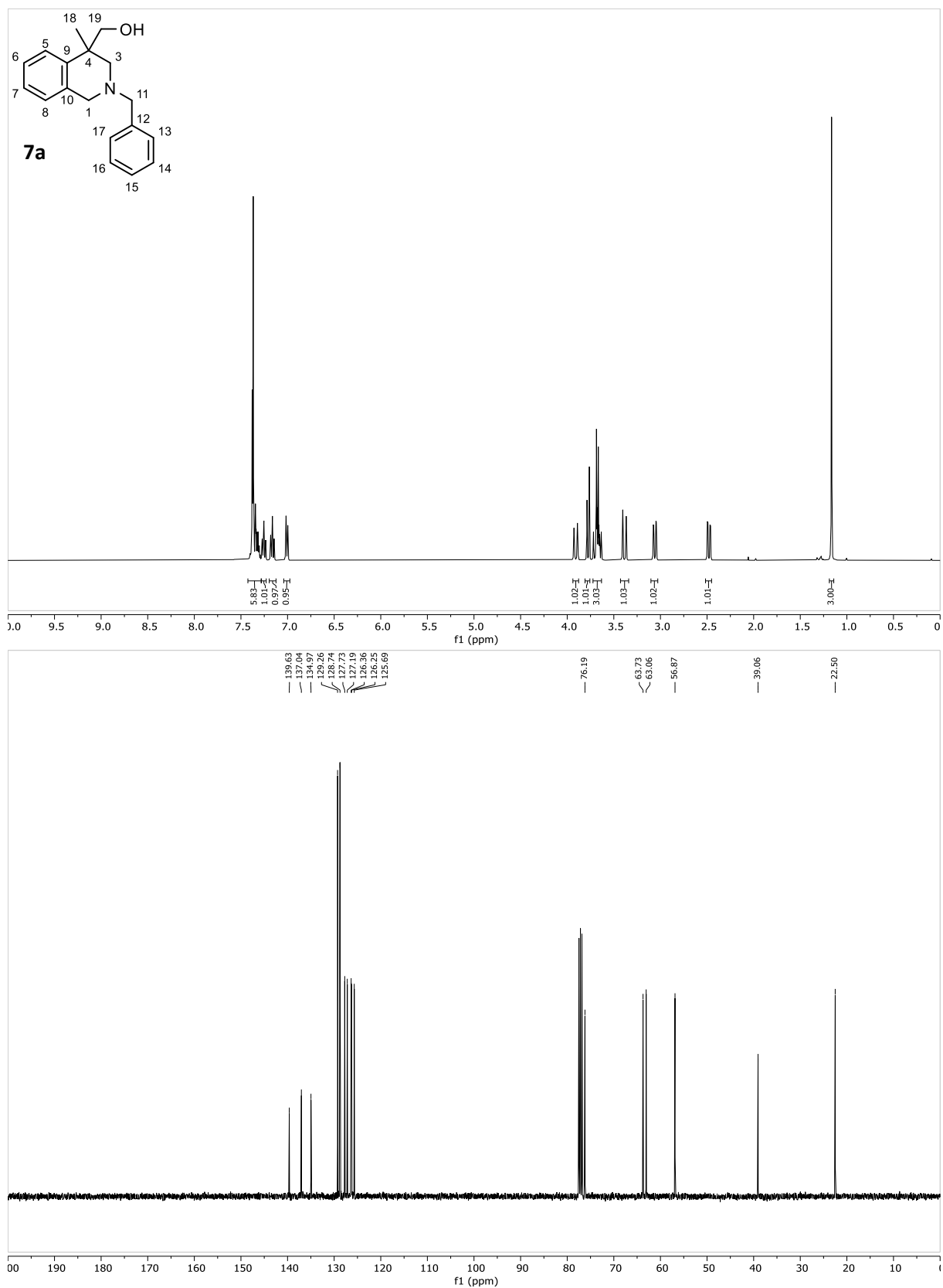


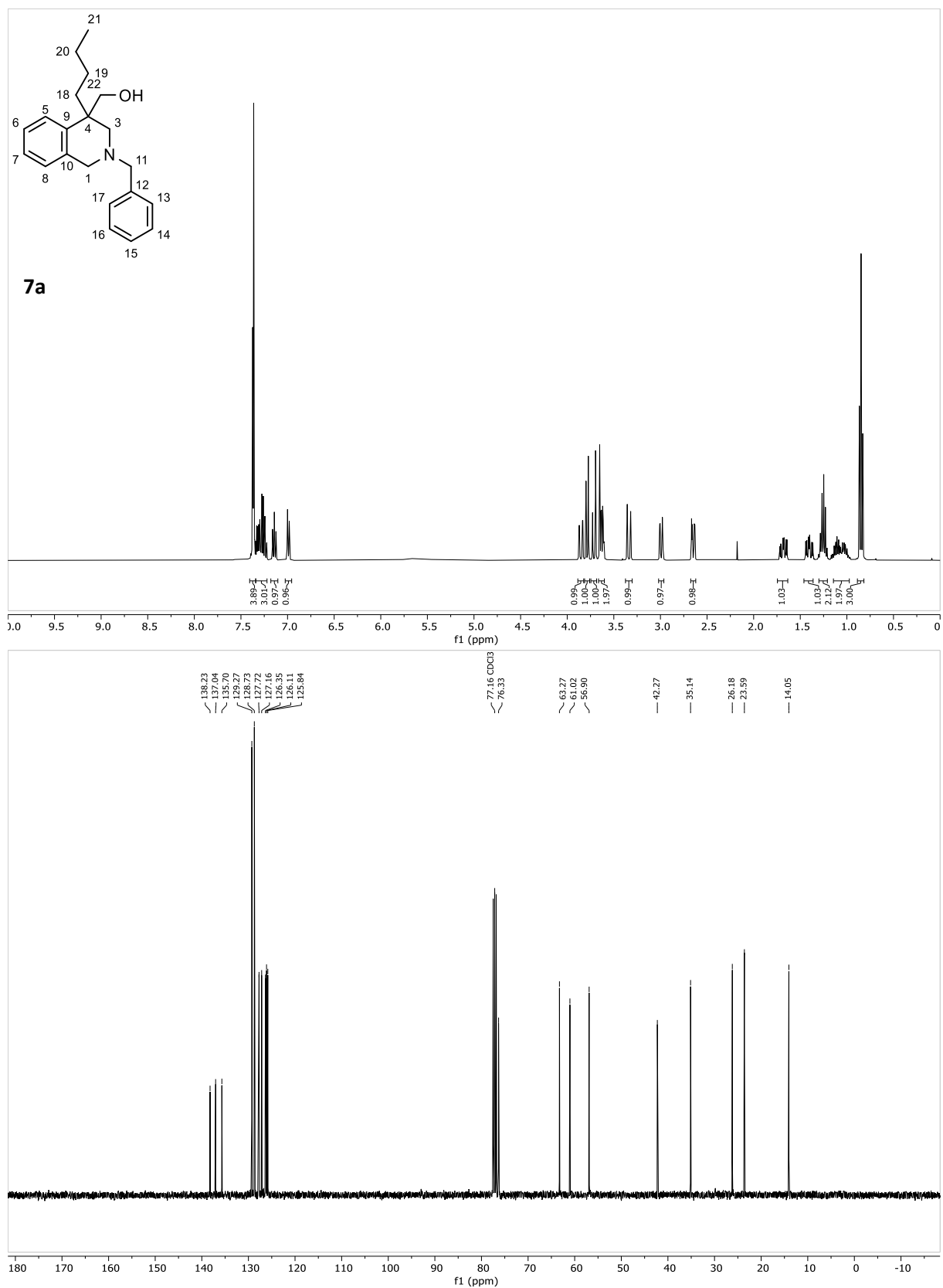


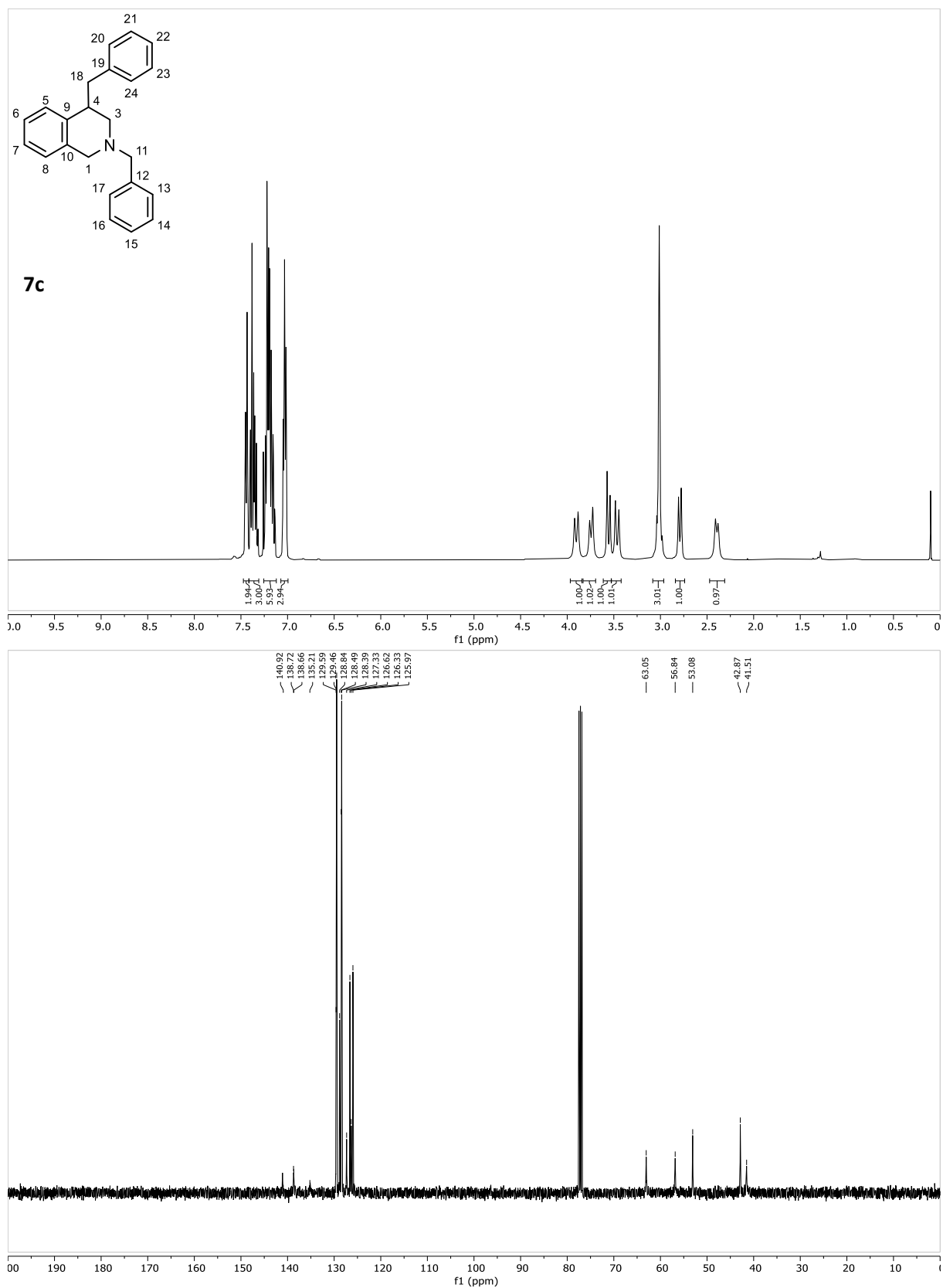
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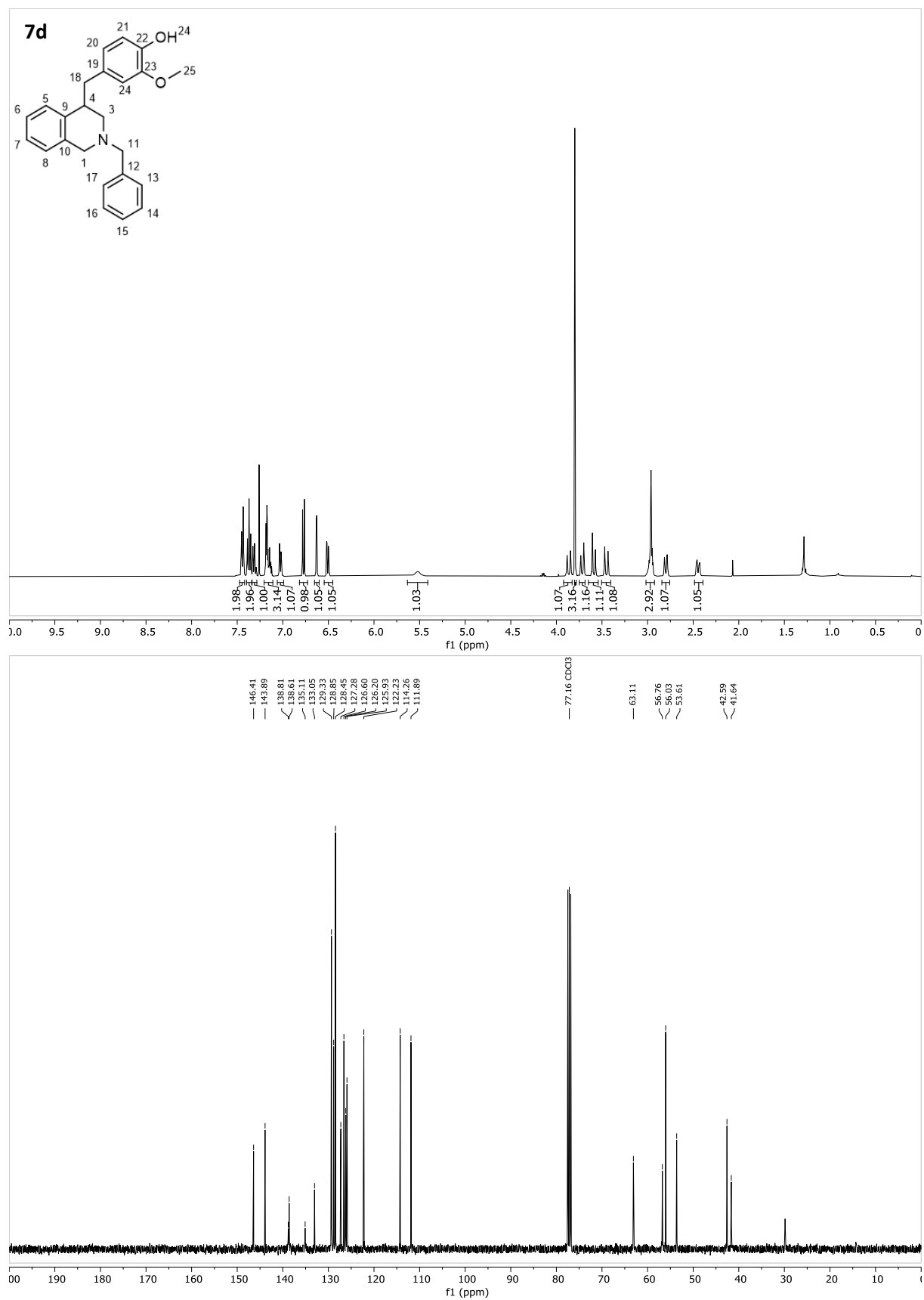


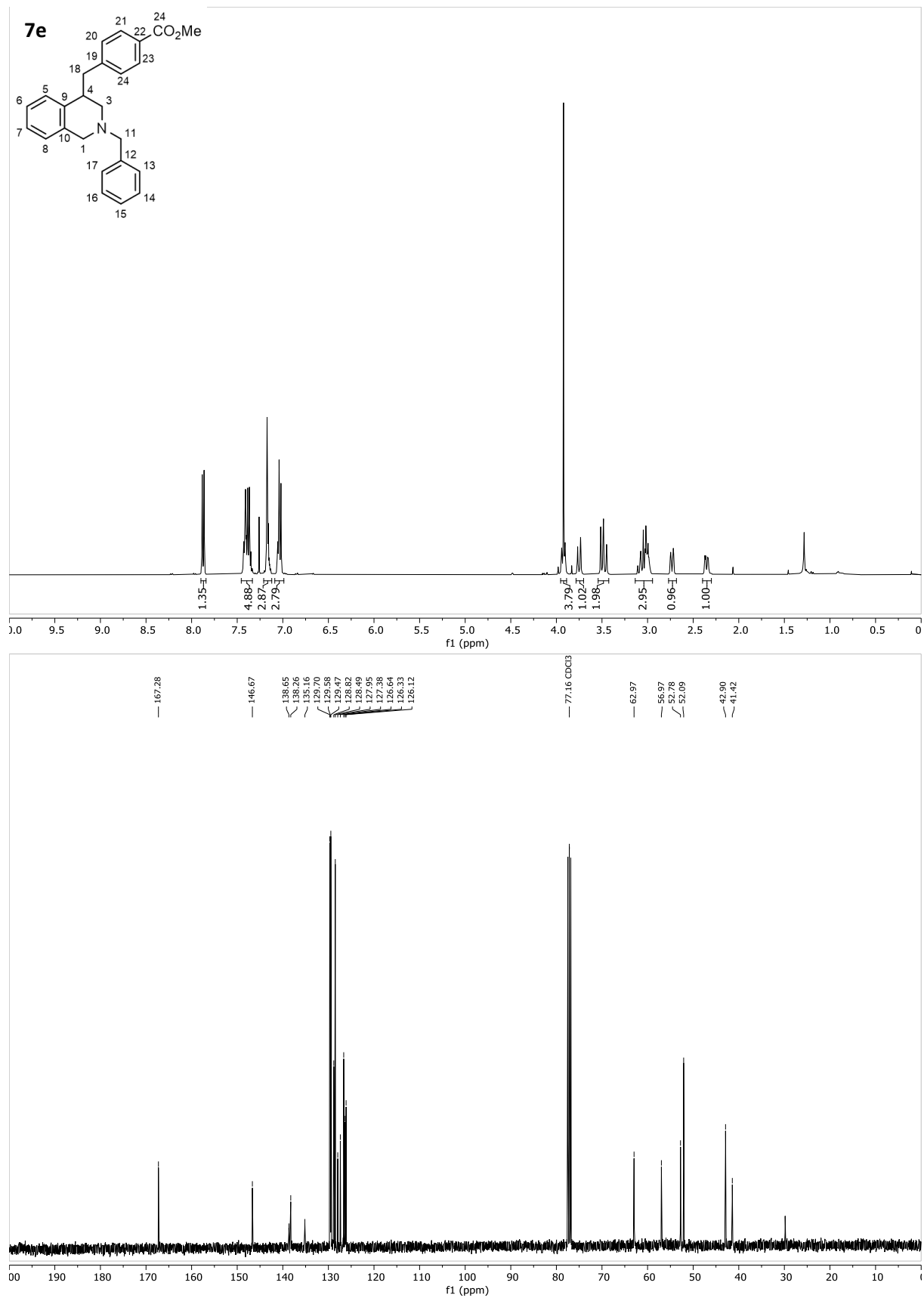


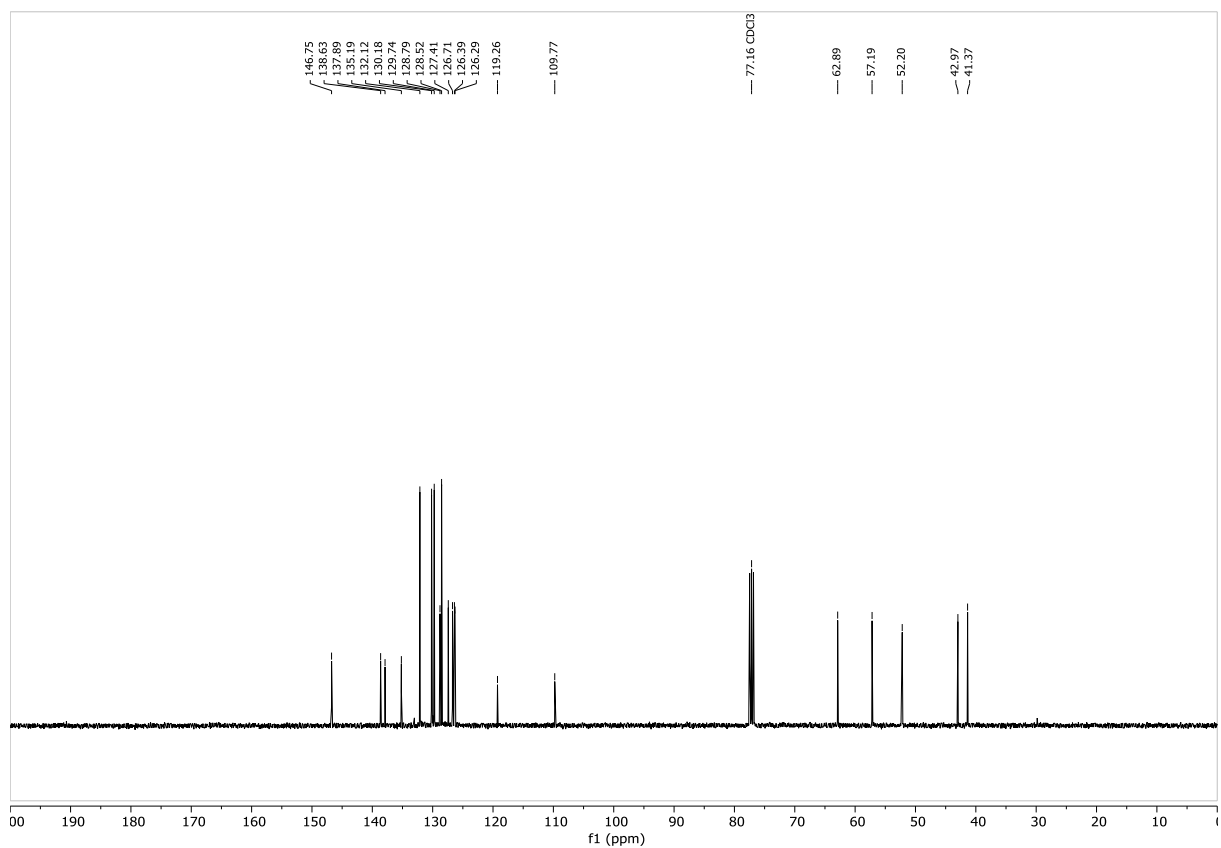
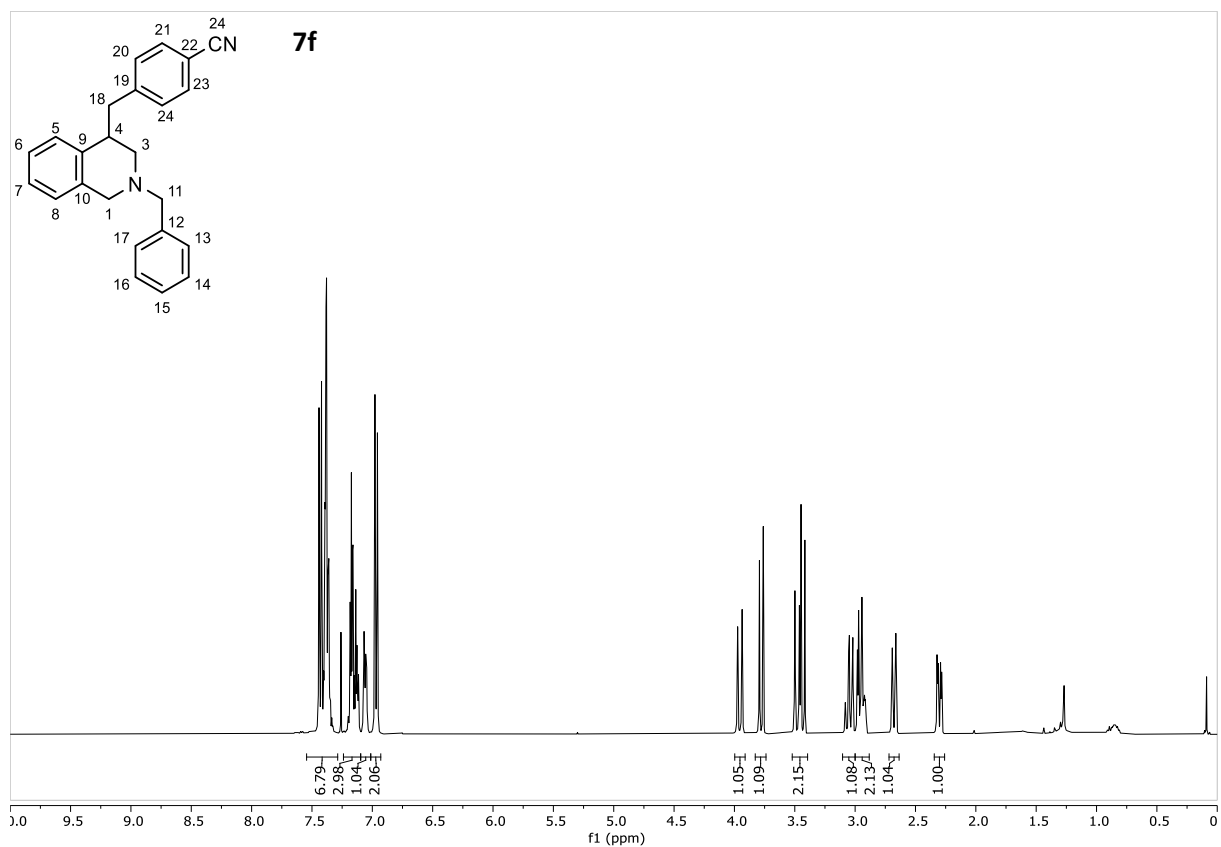


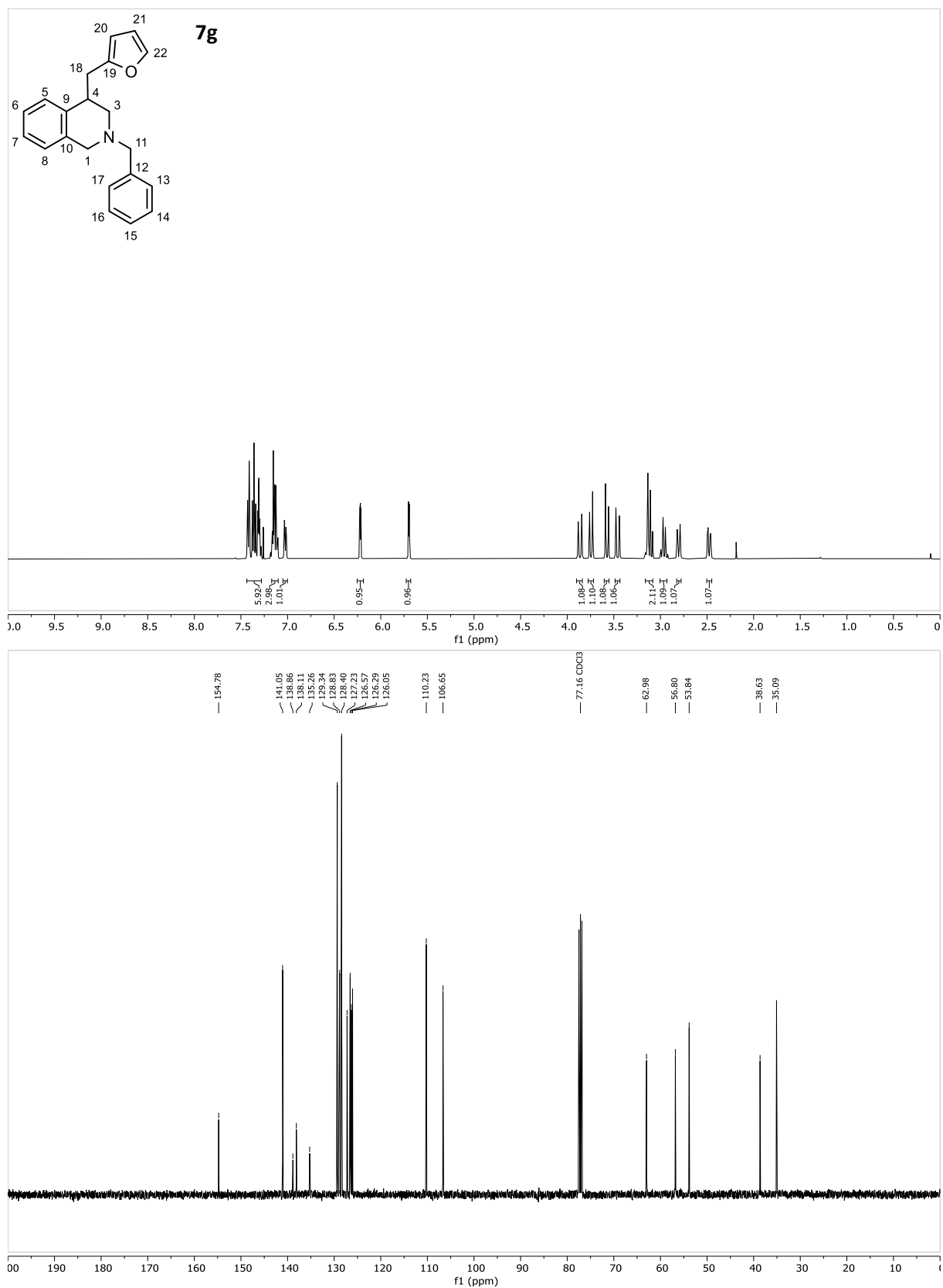


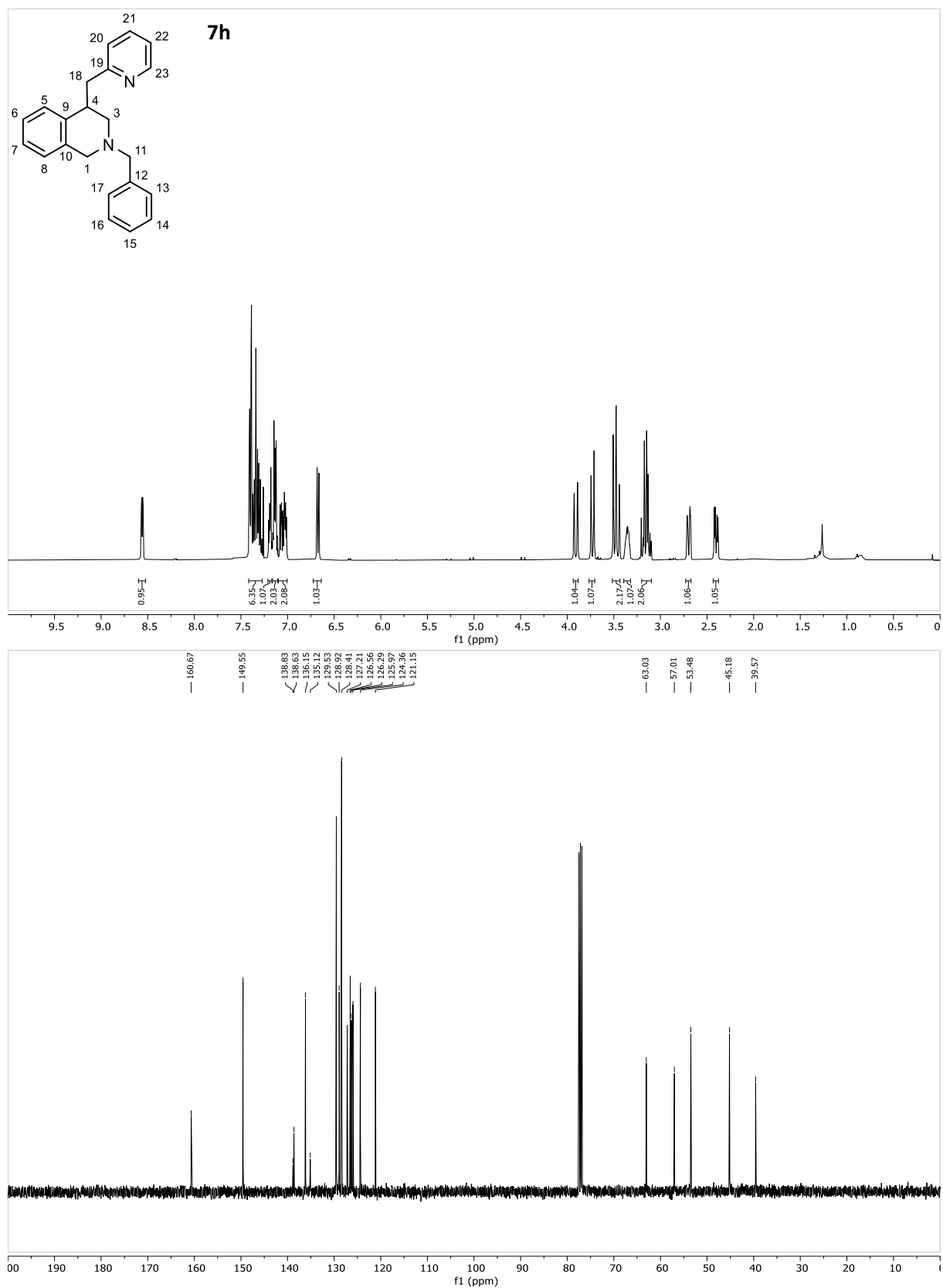


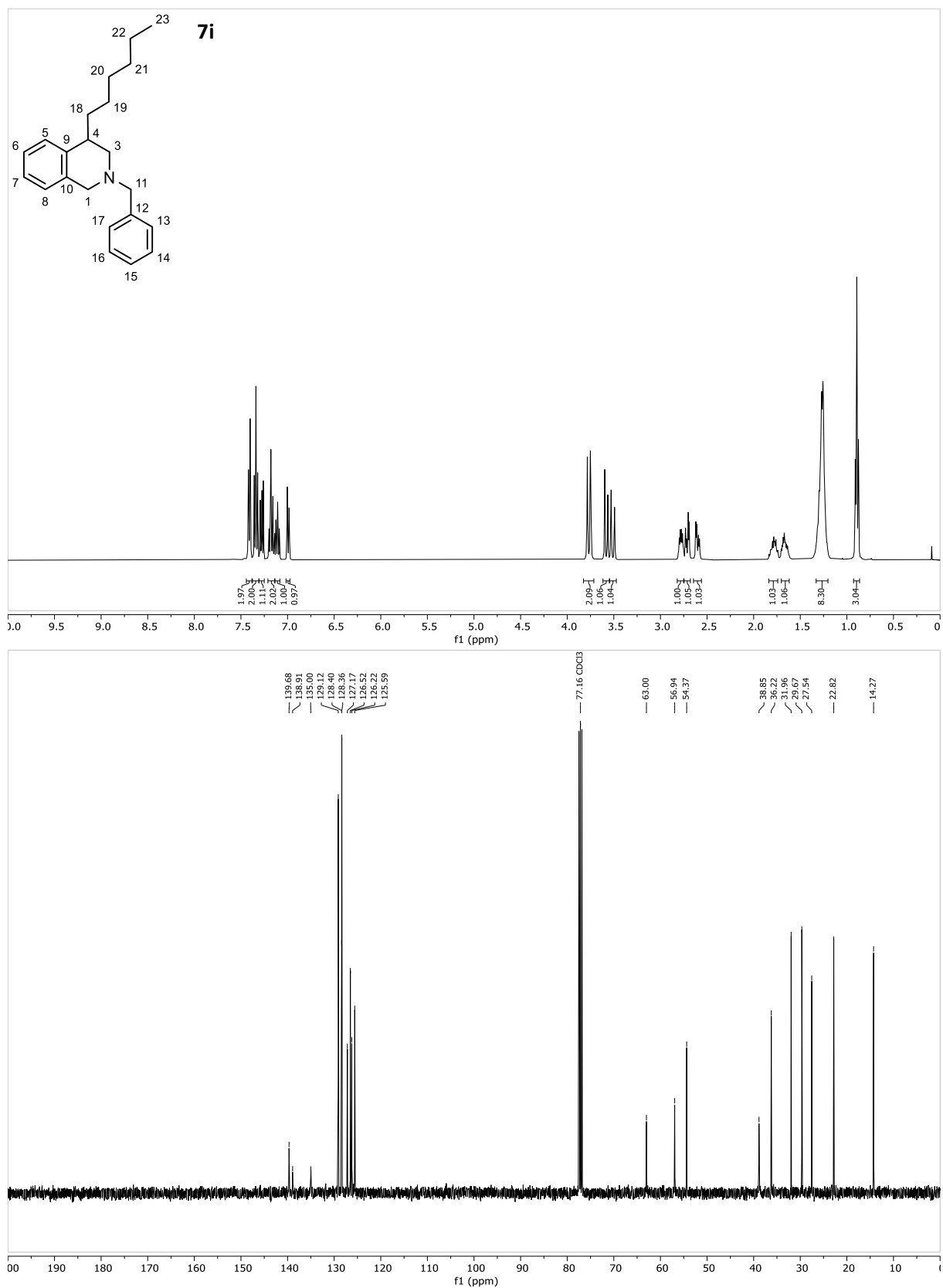


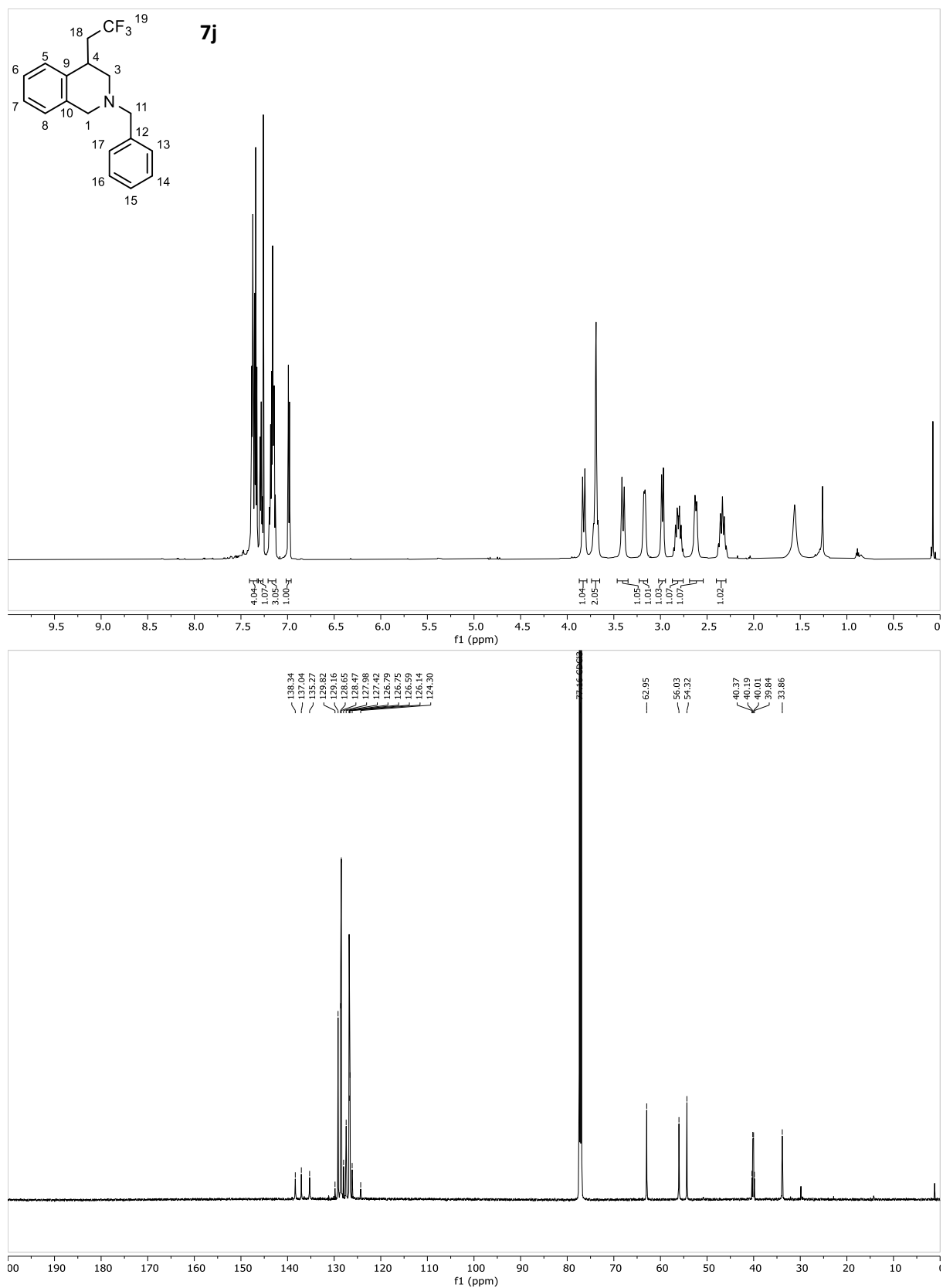


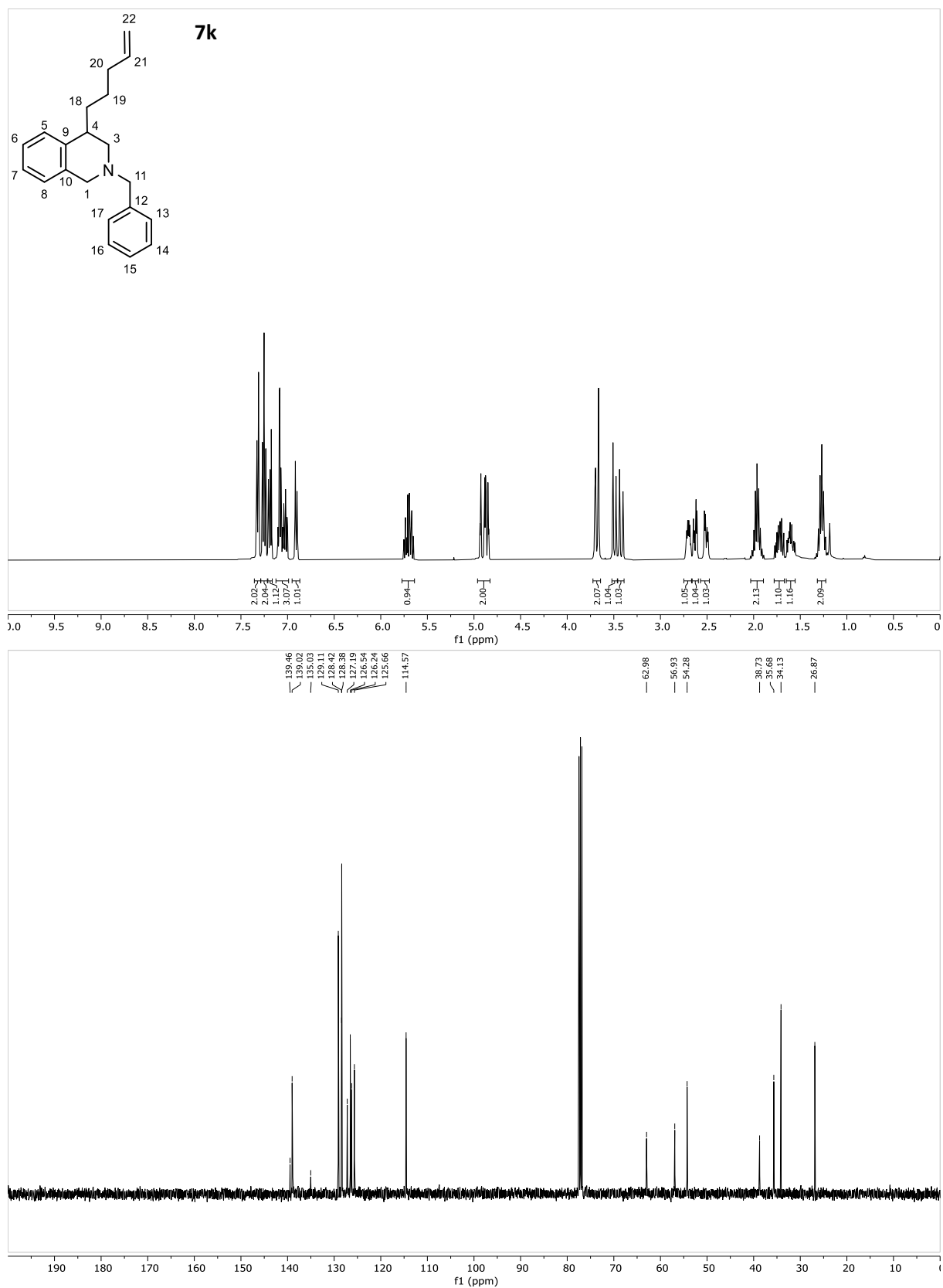


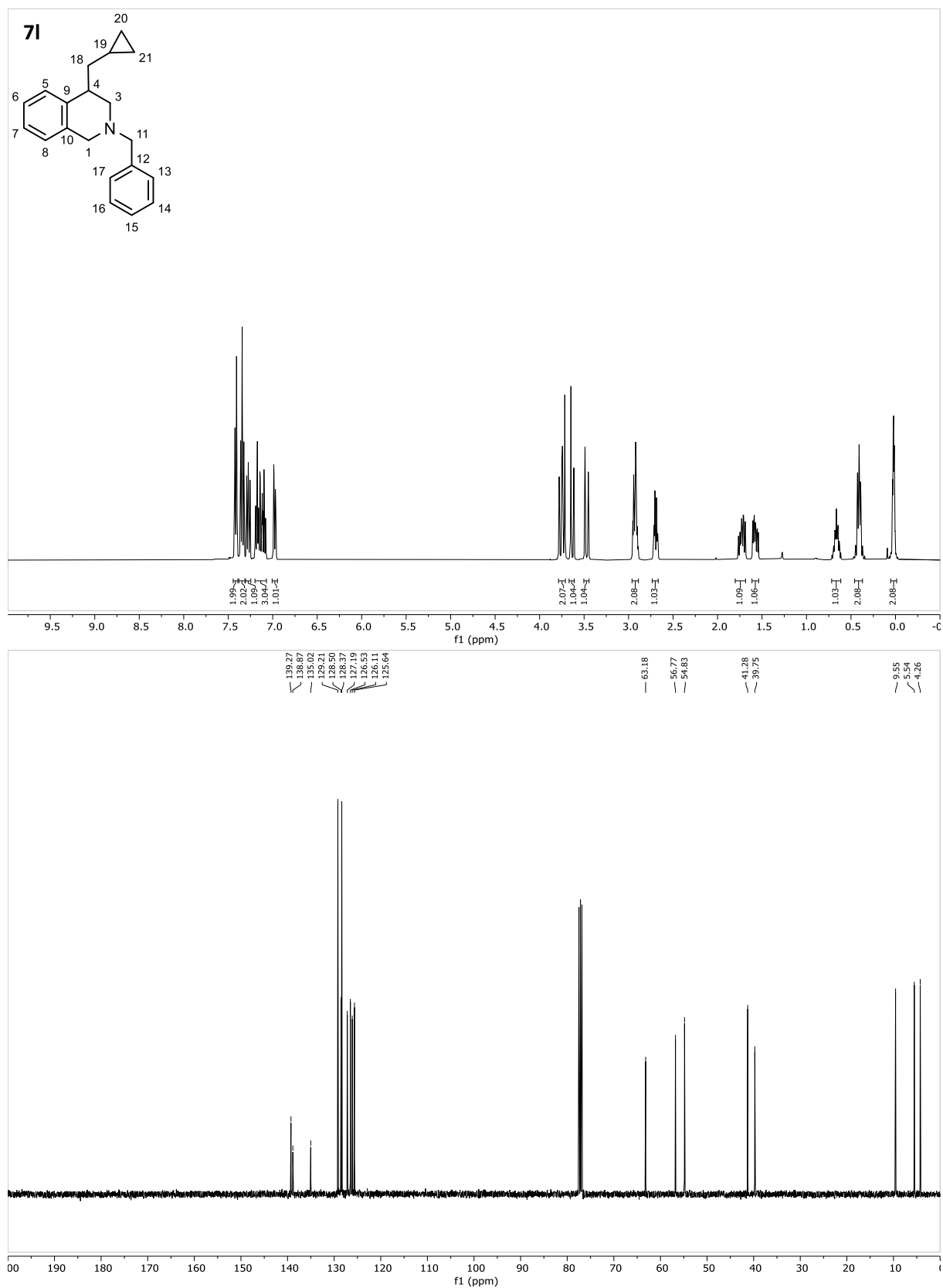












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