

Synthesis of Tertiary Amines by Direct Brønsted Acid Catalyzed Reductive Amination

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General Methods

Reactions, unless otherwise stated, were conducted under a positive pressure of argon in oven-dried glassware. Water for the hydration reactions was deionized water. Commercially available solvents and reagents were used as purchased unless otherwise noted. Analytical thin layer chromatography was performed using aluminium plates precoated with silica gel 60 F₂₅₄ (0.2 mm). Flash chromatography employed 230-400 mesh silica gel. Solvents used for chromatography are quoted as volume/volume ratios.

NMR spectroscopy was performed at 298 K using an Avance III HD 400 (400.1 MHz, ¹H; 100.6 MHz, ¹³C, 376.5 MHz, ¹⁹F) or an Avance III 300 (300 MHz, ¹H; 75 MHz, ¹³C; 282.5 MHz, ¹⁹F). Data is expressed in parts per million (ppm) downfield shift from tetramethylsilane with residual solvent as an internal reference (δ 7.26 ppm for chloroform, 5.27 ppm for dichloromethane) and is reported as position (δ in ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (*J* in Hz) and integration (number of protons). ¹³C NMR spectra were recorded at 298 K with complete proton decoupling. Data is expressed in parts per million (ppm) downfield shift relative to the internal reference (δ 77.2 ppm for the central peak of deuterated chloroform).

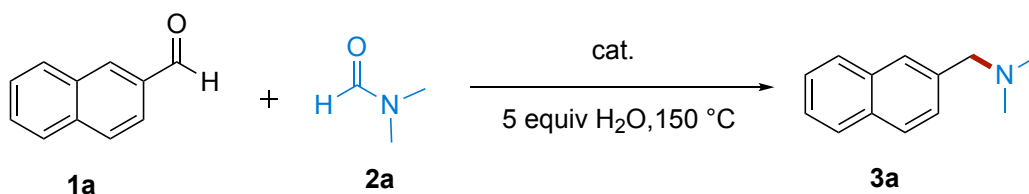
Infrared spectra were obtained on a ThermoNicolet Avatar 370 FT-IR spectrometer and are reported in wavenumbers (cm⁻¹). HRMS were performed at the Bioanalytical Mass Spectrometry Facility within the Mark Wainwright Analytical Centre at the University of New South Wales on an Orbitrap LTQ XL (Thermo Fisher Scientific, San Jose, CA, USA) ion trap mass spectrometer.

Microwave reactions were carried out in 10 mL microwave vials on CEM Discover – SP W/ACTIVENT 909155 or 10 ml vials on Anton Paar Monowave 300.

Optimization Studies

General Procedure for Acid Catalyst Screening (Table S1)

Table S1. Acid catalyzed reductive amination reaction



Entry ^a	Catalyst	Catalyst loading (mol%)	Time ^b (h)	Yield ^c
1	-	-	48	traces
2	Trop.BF ₄	10	48	41%
3	HBF ₄	10	15	53%
4	<i>p</i> TsOH	10	15	59%
4	CH ₃ CO ₂ H	10	15	62%
5	HCO ₂ H	10	15	22%
6	CF ₃ CO ₂ H	10	15	69%
7	CF ₃ SO ₃ H	10	15	82%

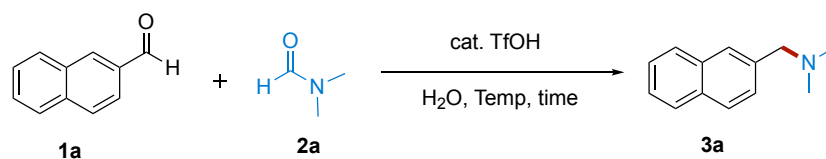
^a Reaction conditions: catalyst (0.1 mmol), aldehyde **1a** (1.0 mmol) and water (5.0 mmol) in DMF (**2a**, 1.0 mL); ^b Time of complete consumption of the starting material as confirmed by ¹H NMR;

^c Yield of isolated product.

An oven-dried 4 mL reaction vessel was charged with 2-naphthaldehyde **1a** (1.0 mmol, 1.0 equiv), acid catalyst (0.1 equiv), H₂O (5.0 equiv) and DMF **2a** (1.0 mL, ~ 13 equiv). The reaction vessel was closed and heated to 150 °C. When the starting material **1a** was completely consumed (monitored by TLC or ¹H NMR), the reaction was cooled to rt. Brine (10 mL) was added to the reaction mixture, followed by the extraction of the products with ether (3 x 10 mL). The organic layers were combined, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residues were then purified by column chromatography (SiO₂, dichloromethane/methanol 20 : 1 to 10 : 1) to obtain *N,N*-dimethyl-1-(naphthalen-2-yl)methanimine (**3a**) as the product.

General Procedure for Optimization Studies in DMF (Table S2)

Table S2. Optimization studies of Brønsted acid catalysed reductive amination reaction



Entry ^a	Catalyst loading	Water (equiv)	Temp	Time (h)	Yield ^b
1	20 mol%	5	150 °C	15	74%
2	10 mol%	5	150 °C	15	82%
3	10 mol%	2	150 °C	8	89%
4	5 mol%	2	150 °C	8	90%
5	2 mol%	2	150 °C	15	82%
6	1 mol%	2	150 °C	15	61%
7 ^c	5 mol%	2	150 °C	1	40%
8	5 mol%	2	100 °C	15	84%
9	5 mol%	2	80 °C	15	57%

^a Reaction conditions (entries 1-9): catalyst TfOH, aldehyde **1a** (1.0 mmol) and water in DMF (**2a**, 1.0 mL) in a closed 4 mL reaction vial; ^b Yield of isolated product; ^c Reaction was carried out in a pressurized MW reactor.

An oven-dried 4 mL reaction vessel was charged with 2-naphthaldehyde **1a** (1.0 mmol, 1.0 equiv), TfOH catalyst (indicated amount), H₂O (2.0 equiv) and DMF **2a** (1.0 mL ~ 13 equiv). The reaction vessel was closed and heated to 150 °C. When the starting material **1a** was completely consumed (monitored by TLC or ¹H NMR), the reaction was cooled to rt. Brine (10 mL) was added to the reaction mixture, followed by the extraction of the products with ether (3 x 10 mL). The organic layers were combined, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residues were then purified by column chromatography (SiO₂, dichloromethane/methanol 20 : 1 to 10 : 1) to obtain *N,N*-dimethyl-1-(naphthalen-2-yl)methanamine (**3a**) as the product.

General Procedure for Optimization Studies in Other Solvents (Table S3)

Table S3. Optimization studies on reaction solvent other than DMF

Reaction scheme: 2-naphthaldehyde (**1a**) + DMF (**2a**) $\xrightarrow[\text{H}_2\text{O (2 equiv), Temp, time}]{\text{cat. TfOH (5 mol\%)}}$ 2-(dimethylamino)naphthalene (**3a**)

Entry ^a	Solvent	DMF (equiv)	Temp	Time (h)	Yield ^b
1	no solvent	2	150 °C	8	39%
2	no solvent	5	150 °C	8	51%
3	Toluene	5	120 °C	8	19%
4	DCE	5	100 °C	8	41%
5	MeCN	5	100 °C	8	37%
6	EtOH	5	100 °C	8	34%
7	TFE	5	100 °C	8	62%
8	HFIP	5	60 °C	8	67%
9	[bmim]PF ₆	5	150 °C	8	64%
10	HFIP	5	60 °C	24	86%
11	HFIP	5	60 °C	12	91%
12	HFIP	5	40 °C	24	40%
13	HFIP	5	25 °C	24	21%
14	HFIP	5	25 °C	96	63%

^a Reaction conditions: catalyst TfOH (0.05 mmol), aldehyde **1a** (1.0 mmol) and water (2.0 mmol), DMF (**2a**) in solvent (0.5 mL) in a closed 4 mL reaction vial; ^b Yield of isolated product.

An oven-dried 4 mL reaction vessel was charged with 2-naphthaldehyde **1a** (1.0 mmol, 1.0 equiv), TfOH catalyst (indicated amount), H₂O (2.0 equiv), DMF **2a** (indicated

amount) and reaction solvent (~0.5 mL). The reaction vessel was closed and heated to 150 °C. When the starting material **1a** was completely consumed (monitored by TLC or ¹H NMR), the reaction was cooled to rt. Brine (10 mL) was added to the reaction mixture, followed by the extraction of the products with ether (3 x 10 mL). The organic layers were combined, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residues were then purified by column chromatography (SiO₂, dichloromethane/methanol 20 : 1 to 10 : 1) to obtain *N,N*-dimethyl-1-(naphthalen-2-yl)methylamine (**3a**) as the product.

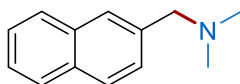
General Procedures for Substrate Scope Studies

Procedure A: An oven-dried 4 mL reaction vessel was charged with carbonyl compound **1** (1.0 mmol, 1.0 equiv), TfOH catalyst (5 mol%), H₂O (2.0 equiv) and formamide **2** (1.0 mL). The reaction vessel was closed and heated to 150 °C for 8 h then cooled to rt. Brine (10 mL) was added to the reaction mixture, followed by the extraction of the products with ether (3 x 10 mL). The organic layers were combined, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residues were then purified by column chromatography (SiO₂, dichloromethane/methanol 20 : 1 to 10 : 1) to obtain product **3**.

Procedure B: An oven-dried 4 mL reaction vessel was charged with carbonyl compound **1** (1.0 mmol, 1.0 equiv), TfOH catalyst (5 mol%), H₂O (2.0 equiv), formamide **2** (5.0 equiv) and HFIP (0.5 mL). The reaction vessel was closed and heated to 60 °C for 12 h then cooled to rt. Brine (10 mL) was added to the reaction mixture, followed by the extraction of the products with ether (3 x 10 mL). The organic layers were combined, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residues were then purified by column chromatography (SiO₂, dichloromethane/methanol 20 : 1 to 10 : 1) to obtain product **3**.

Characterization Data of Products in Scheme 2 (Procedure A Yields)

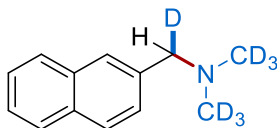
***N,N*-dimethyl-1-(naphthalen-2-yl) methylamine¹** (compound number **3a**): Prepared using the general procedure from 2-naphthaldehyde and DMF to give the title compound as a light-yellow liquid (145 mg, 90% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.91 (s, 1H), 7.86-7.81 (m, 3H), 7.54-7.47 (m, 3H), 4.24 (s, 2H), 2.77 (s, 6H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 133.8, 133.3, 130.7, 129.5, 128.4, 127.9, 127.8, 127.5, 127.1, 127.0, 62.5, 43.4 ppm.

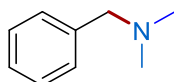
***N*-(Methyl-d₃)-*N*-(naphthalen-2-ylmethyl-d)methanamine-d₃¹** (compound number ***d*₇-3a**): Prepared using the general procedure from 2-naphthaldehyde and DMF-*d*⁷ to give the title compound as a light yellow liquid (180 mg, 93% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.87-7.81 (m, 3H), 7.75 (s, 1H), 7.51-7.45 (m, 3H), 3.57 (s, 1H), ppm;

¹³C NMR (100 MHz, CDCl₃) δ 136.4, 133.5, 132.9, 128.1, 127.8, 127.7, 127.6, 127.5, 126.1, 125.7, 64.2, 64.1, 63.9 ppm.

***N,N*-Dimethylbenzylamine²** (compound number **3b**): Prepared using the general procedure from benzaldehyde and DMF to give the title compound as a colorless liquid (131 mg, 96% yield).



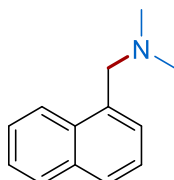
¹ L. Yang, J. Lin, L. Kang, W. Zhou, D. Y. Ma, *Adv. Synth. Catal.* **2018**, 360, 485-490.

² C. Kelly, R. McDonald, O. L. Sydora, M. Stradiotto, L. Turculet, *Angew. Chem. Int. Ed.* **2017**, 56, 15901-15904.

¹H NMR (400 MHz, CDCl₃) δ 7.35-7.23 (m, 5H), 3.43 (s, 2H), 2.25 (s, 6H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 138.9, 129.1, 128.2, 127.1, 64.4, 45.4 ppm.

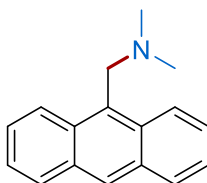
***N,N*-Dimethyl-1-(naphthalen-1-yl) methylamine¹** (compound number **3c**): Prepared using the general procedure from 1-naphthaldehyde and DMF to give the title compound as a light yellow liquid (130.5 mg, 71% yield).



¹H NMR (400 MHz, CDCl₃) δ 8.29 (d, J = 8.4 Hz, 1H), 7.89-7.81 (m, 2H), 7.58-7.49 (m, 2H) 7.47-7.42 (m, 2H), 3.89 (s, 2H), 2.36 (s, 6H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 134.4, 134.0, 132.6, 128.6, 128.3, 127.8, 126.2, 125.7, 125.2, 124.5, 62.4, 45.6 ppm.

9-(*N,N*-Dimethylaminomethyl)anthracene³ (compound number **3d**): Prepared using the general procedure from 9-anthraldehyde and DMF to give the title compound as a yellow solid (195 mg, 91% yield).

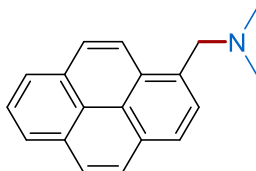


¹H NMR (400 MHz, CDCl₃) δ 8.47 (s, 1H), 8.42 (d, J = 9.7 Hz, 2H), 7.99 (d, J = 8.5 Hz, 2H), 7.53 (ddd, J = 1.3 Hz, 2H), 7.48 (ddd, J = 1.3 Hz, 2H), 4.40 (s, 2H), 2.39 (s, 6H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 131.6, 131.4, 129.2, 127.7, 127.1, 126.0, 125.0, 124.8, 55.4, 45.7 ppm.

***N,N*-Dimethyl-1-(pyren-1-yl)methanamine** (compound number **3e**): Prepared using the general procedure from 1-pyrenecarboxaldehyde and DMF to give the title compound as a colorless oil (225.3 mg, 86% yield).

³ M. Horiguchi, Y. Ito, *J. Org. Chem.* **2006**, *71*, 3608-3611.



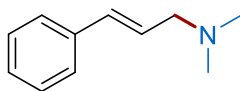
¹H NMR (400 MHz, CDCl₃) δ 8.50 (d, J = 9.2 Hz, 1H), 8.20-8.12 (m, 4H), 8.05 (s, 2H), 8.02 -7.97 (m, 4H), 4.14 (s, 2H), 2.38 (s, 6H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 131.4, 131.2, 131.0, 130.1, 128.6, 127.8, 127.6, 127.5, 126.1, 125.3, 125.1, 124.9, 124.6, 123.7, 61.9, 45.4 ppm

IR (KBr) 3044, 2931, 2856, 2815, 2763, 1674, 1599 cm⁻¹;

HRMS (ESI+) (m/z) Anal. Calcd. for [C₁₉H₁₇N₁+H] 260.1439, found 260.1432.

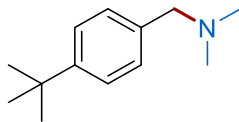
(*E*)-*N,N*-Dimethyl-3-phenylprop-2-en-1-amine¹ (compound number **3f**): Prepared using the general procedure from cinnamaldehyde and DMF to give the title compound as a light yellow liquid (130 mg, 81% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.46-7.42 (m, 2H), 7.38-7.33 (m, 3H), 6.78 (d, J = 15.8 Hz, 1H), 6.43 (dt, J = 7.6, 7.3 Hz, 1H), 3.76 (dd, J = 5.2, 4.8 Hz, 2H), 2.80 (s, 6H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 140.8, 134.7, 128.9, 127.6, 116.3, 60.1, 42.1 ppm.

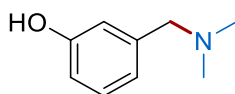
1-(4-(*tert*-Butyl)phenyl)-*N,N*-dimethylmethanamine¹ (compound number **3g**): Prepared using the general procedure from 4-*tert*-butylbenzaldehyde and DMF to give the title compound as a light yellow liquid (150 mg, 79% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.59 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 4.11 (s, 2H), 2.74 (s, 6H), 1.62 (s, 9H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 130.79, 129.7, 126.3, 125.1, 61.2, 42.4, 34.8, 31.3 ppm.

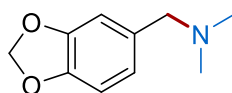
3-((Dimethylamino)methyl)phenol⁴ (compound number **3h**): Prepared using the general procedure from 3-hydroxybenzaldehyde and DMF to give the title compound as a white powder (122.5 mg, 81% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.21-7.10 (m, 2H), 6.85-6.78 (m, 2H), 3.68 (s, 2H), 2.47 (s, 6H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 157.3, 130.1, 121.6, 116.8, 116.6, 63.0, 43.9 ppm.

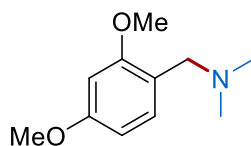
1-(Benzo[d][1,3]dioxol-5-yl)-N,N-dimethylmethanamine⁵ (compound number **3i**): Prepared using the general procedure from piperonal and DMF to give the title compound as a brown liquid (129.3 mg, 73% yield).



¹H NMR (400 MHz, CDCl₃) δ 6.84-6.75 (m, 3H), 5.94 (s, 2H), 3.39 (s, 2H), 2.26 (s, 6H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 147.8, 146.9, 122.6, 109.7, 108.1, 101.1, 63.9, 45.0 ppm.

1-(2,4-Dimethoxyphenyl)-N,N-dimethylmethanamine¹ (compound number **3j**): Prepared using the general procedure from 2,4-dimethoxybenzaldehyde and DMF to give the title compound as a light yellow liquid (165 mg, 84% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.49 (d, J = 8.4 Hz, 1H), 6.55 (dd, J = 2.3 Hz, 1H), 6.48 (d, J = 2.2 Hz, 1H), 4.15 (d, J = 4.7 Hz, 2H), 3.85 (s, 3H), 3.82 (s, 3H), 2.70 (m, 6H) ppm;

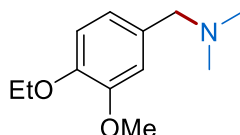
¹³C NMR (100 MHz, CDCl₃) δ 162.9, 159.5, 134.5, 109.1, 105.3, 98.9, 55.8, 55.7, 54.7, 41.9 ppm.

⁴ D. M. Spasyuk, D. Zargarian, A. v. d. Est, *Organometallics* **2009**, 28, 6531-6540.

⁵ X. Cui, X. Dai, Y. Deng, F. Shi, *Chem. Eur. J.* **2013**, 19, 3665-3675.

1-(4-Ethoxy-3-methoxyphenyl)-*N,N*-dimethylmethanamine (compound number **3k**):

Prepared using the general procedure from 4-ethoxy-3-methoxybenzaldehyde and DMF to give the title compound as a yellow oil (165 mg, 78% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.44 (d, J = 1.7 Hz, 1H), 6.92 (dd, J = 1.9, 1.7 Hz, 1H), 6.85 (d, J = 8.1 Hz, 1H), 4.11 (q, J = 7.0 Hz, 2H), 4.06 (s, 2H), 3.96 (s, 3H), 2.74 (s, 6H), 1.47 (t, J = 7.0 Hz, 3H) ppm;

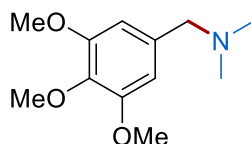
¹³C NMR (100 MHz, CDCl₃) δ 150.1, 149.6, 123.1, 122.8, 113.4, 112.4, 64.5, 62.5, 56.4, 43.1, 14.8 ppm;

IR (KBr) 3378, 2977, 1608, 1518, 1469 cm⁻¹;

HRMS (ESI⁺) (m/z) Anal. Calcd. for [C₁₂H₁₉N₁O₂+H] 210.1494, found 210.1487.

***N,N*-dimethyl-1-(3,4,5-trimethoxyphenyl)methanamine¹** (compound number **3l**):

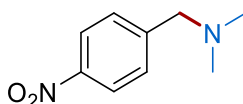
Prepared using the general procedure from 3,4,5-trimethoxybenzaldehyde and DMF to give the title compound as a light yellow liquid (196.2, 87% yield).



¹H NMR (400 MHz, CDCl₃) δ 6.55 (s, 2H), 3.85 (s, 6H), 3.82 (s, 3H), 3.38 (s, 2H), 2.26 (s, 6H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 153.2, 137.2, 134.2, 105.9, 64.7, 60.9, 56.2, 45.3 ppm.

***N,N*-Dimethyl-1-(4-nitrophenyl) methenamine⁶** (compound number **3m**): Prepared using the general procedure from 4-nitrobenzaldehyde and DMF to give the title compound as a yellow oil (145.9 mg, 82% yield).

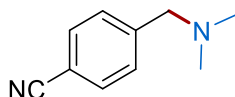


⁶A. Chardon, T. M. E. Dine, R. Legay, M. D. Paolis, J. Rouden, J. Blanchet, *Chem. Eur. J.* **2017**, 23, 2005-2009.

¹H NMR (400 MHz, CDCl₃) δ 8.19 (d, J = 8.6 Hz, 2H), 7.52 (d, J = 8.6 Hz, 2H), 3.54 (s, 2H), 2.28 (s, 6H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 147.4, 146.4, 129.8, 123.7, 63.5, 45.5 ppm.

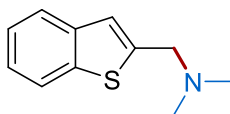
4-((Dimethyl amino)methyl)benzonitrile¹ (compound number **3n**): Prepared using the general procedure from 4-formylbenzonitrile and DMF to give the title compound as a light yellow liquid (140.3 mg, 89% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.65 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 3.53 (s, 2H), 2.30 (s, 6H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 144.0, 132.3, 129.8, 119.0, 111.3, 63.7, 45.4 ppm.

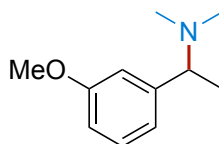
1-(Benzo[b]thiophen-2-yl)-*N,N*-dimethylmethanamine⁷ (compound number **3o**): Prepared using the general procedure from benzo[b]thiophene-2-carboxaldehyde and DMF to give the title compound as a yellow oil (155 mg, 81% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.82-7.79 (m, 1H), 7.71-7.68 (m, 1H), 7.35-7.26 (m, 2H), 7.14 (d, J = 0.7 Hz, 1H), 3.73 (d, J = 0.6 Hz, 2H), 2.33 (s, 6H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 143.9, 140.2, 139.7, 124.1, 123.9, 123.2, 122.4, 122.2, 59.3, 45.4 ppm.

2-(3-Methoxyphenyl)-*N,N*-dimethylpropan-1-amine (compound number **3p**): Prepared using the general procedure from 3'-methoxyacetophenone and DMF to give the title compound as a light yellow liquid (115.3 mg, 60% yield).



⁷ L. L. Liao, G. M. Cao, J. H. Ye, G. Q. Sun, W. J. Zhou, Y. Y. Gui, S. S. Yan, G. Shen, D. G. Yu, *J. Am. Chem. Soc.* **2018**, *140*, 17338-17342.

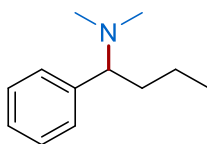
¹H NMR (400 MHz, CDCl₃) δ 7.36 (t, J = 8.0 Hz, 1H), 7.11 (s, 1H) 7.01-6.96 (m, 2H), 4.15 (p, J = 6.5 Hz, 1H), 3.86 (s, 3H), 2.84 (d, J = 5.0 Hz, 3H), 2.65 (d, J = 5.0 Hz, 3H), 1.83 (d, J = 8.4 Hz, 3H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 160.6, 135.2, 130.7, 120.8, 116.1, 114.0, 67.3, 55.8, 42.2, 40.4, 17.5 ppm;

IR (KBr) 3044, 2931, 2856, 2763, 1674, 1599, 1458 cm⁻¹;

HRMS (ESI+) (m/z) Anal. Calcl. for [C₁₂H₁₉N₁O₁+H] 180.1388, found 180.1383.

***N,N*-Dimethyl-1-phenylbutan-1-amine** (compound number **3q**): Prepared using the general procedure from butyrophenone and DMF to give the title compound as a yellowish oil (110 mg, 57% yield).



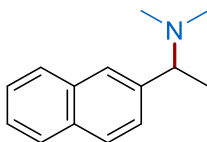
¹H NMR (400 MHz, CDCl₃) δ 7.51-7.43 (m, 5H), 4.07-4.02 (m, 1H), 2.81(d, J = 5.0 Hz, 3H), 2.64 (d, J = 5.0 Hz, 3H), 2.33-2.19 (m, 2H), 1.35-1.11(m, 2H), 0.92 (t, J = 7.2 Hz, 3H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 131.3, 130.6, 129.6, 129.7, 71.5, 42.8, 39.2, 32.5, 19.6, 13.6 ppm

IR (KBr) 2961, 2873, 2677, 1733, 1636, 1459 cm⁻¹;

HRMS (ESI+) (m/z) Anal. Calcl. for [C₁₃H₂₁N₁+H] 178.1596, found 178.1585.

***N,N*-Dimethyl-1-phenylbutan-1-amine**⁸ (compound number **3r**): Prepared using the general procedure from 2-acetonaphthone and DMF to give the title compound as a colorless oil (196.5 mg, 71% yield).

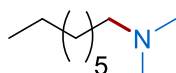


¹H NMR (400 MHz, CDCl₃) δ 7.97-7.87 (m, 4H), 7.60-7.55 (m, 3H), 2.81 (m, 1H), 2.93 (d, J = 5.0 Hz, 3H), 2.71 (d, J = 5.0 Hz, 3H), 1.91 (d, J = 6.9 Hz, 3H) ppm;

⁸ P. Maity, D. M. S. McAtee, G. P. A. Yap, E. R. Sirianni, M. P. Watson, *J. Am. Chem. Soc.* **2013**, *135*, 280-285.

¹³C NMR (100 MHz, CDCl₃) δ 134.0, 133.2, 130.5, 130.0, 129.0, 128.4, 128.0, 127.8, 127.5, 124.7, 67.6, 42.4, 40.6, 17.4 ppm

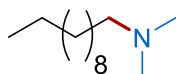
***N,N*-Dimethyloctan-1-amine⁹** (compound number **3s**): Prepared using the general procedure from octanal and DMF to give the title compound as a yellow liquid (120 mg, 77% yield).



¹H NMR (400 MHz, CDCl₃) δ 3.03-2.96 (m, 2H), 2.85 (d, J = 5.0 Hz, 6H), 1.85-1.77 (m, 2H), 1.33-1.25 (m, 10H), 0.87 (t, J = 7.0 Hz, 3H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 58.5, 43.2, 31.7, 29.0, 26.6, 24.4, 22.6, 14.1 ppm.

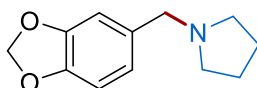
***N,N*-Dimethylundecan-1-amine¹⁰** (compound number **3t**): Prepared using the general procedure from undecanal and DMF to give the title compound as a yellow liquid (140 mg, 70% yield).



¹H NMR (400 MHz, CDCl₃) δ 2.98-2.92 (m, 2H), 2.78 (d, J = 5.0 Hz, 6H), 1.88-1.80 (m, 2H), 1.33-1.25 (m, 16H), 0.87 (t, J = 6.6, 7.0 Hz, 3H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 58.2, 42.9, 31.9, 29.6, 29.5, 29.4, 29.4, 29.1, 26.7, 24.3, 22.8, 14.2 ppm.

1-(Benzo[d][1,3]dioxol-5-ylmethyl)pyrrolidine¹¹ (compound number **4a**): Prepared using the general procedure from piperonal and 1-formylpyrrolidine to give the title compound as a colorless oil (191 mg, 90% yield).



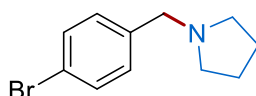
⁹ T. Mitsudome, K. Miyagawa, Z. Maeno, T. Mizugaki, K. Jitsukawa, J. Yamasaki, Y. Kitagawa, K. Kaneda, *Angew. Chem. Int. Ed.* **2017**, 56, 9381-9385.

¹⁰ E. Karakhanov, A. Maksimov, Y. Kardasheva, E. Runova, R. Zakharov, M. Terenina, C. Kenneally, V. Arredondo, *Catal. Sci. Technol.* **2014**, 4, 540-54.

¹¹ G. Wuitschik, M. R. Evans, A. Buckl, M. Bernasconi, M. Märki, T. Godel, H. Fischer, B. Wagner, I. Parrilla, F. Schuler, J. Schneider, A. Alker, W. B. Schweizer, K. Müller, E. M. Carreira, *Angew. Chem. Int. Ed.* **2008**, 47, 4512-4515.

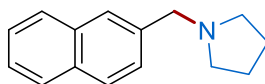
¹H NMR (400 MHz, CDCl₃) δ 6.99 (d, J = 1.3 Hz, 1H), 6.87 (dd, J = 1.6, 1.3 Hz, 1H), 6.77 (d, J = 7.9 Hz, 1H), 5.94 (s, 2H), 3.78 (s, 2H), 2.82 (m, 4H), 1.92 (m, 4H) ppm;
¹³C NMR (100 MHz, CDCl₃) δ 148.1, 147.8, 128.7, 123.5, 110.2, 108.5, 101.4, 59.5, 53.5, 23.5 ppm.

1-(4-Bromobenzyl)pyrrolidine¹² (compound number **4b**): Prepared using the general procedure from 4-bromobenzaldehyde and 1-formylpyrrolidine to give the title compound as a yellow liquid (180 mg, 75% yield).



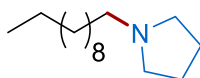
¹H NMR (400 MHz, CDCl₃) δ 7.52 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 8.3 Hz, 2H), 3.92 (s, 2H), 2.94 (m, 4H), 2.00 (m, 4H) ppm;
¹³C NMR (100 MHz, CDCl₃) δ 132.4, 132.1, 131.6, 130.9, 58.5, 53.4, 23.2 ppm.

N-(1-Naphthylmethyl)pyrrolidine¹³ (compound number **4c**): Prepared using the general procedure from 2-naphthaldehyde and 1-formylpyrrolidine to give the title compound as a yellow oil (215 mg, 95% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.87-7.81 (m, 4H), 7.66 (dd, J = 1.7, 1.3 Hz, 1H), 7.50-7.46 (m, 2H), 4.03 (s, 2H), 2.87 (m, 4H), 1.96-1.93 (m, 4H) ppm;
¹³C NMR (100 MHz, CDCl₃) δ 133.2, 133.1, 128.6, 128.5, 127.9, 127.7, 127.2, 126.4, 126.3, 59.8, 53.7, 23.3 ppm.

1-Undecylpyrrolidine¹⁴ (compound number **4d**): Prepared using the general procedure from undecanal and 1-formylpyrrolidine to give the title compound as a yellow liquid (165 mg, 73% yield).



¹H NMR (400 MHz, CDCl₃) δ 3.74-3.70 (m, 2H), 3.05-2.99 (m, 2H), 2.89-2.82 (m, 2H), 2.18-2.04 (m, 4H), 1.81-1.75 (m, 2H), 1.33-1.21 (m, 16H), 0.84 (t, J = 7.0 Hz, 3H) ppm;

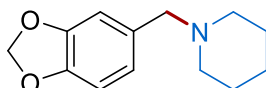
¹² S. Lu, C. Li, J. Wang, Y. Pan, X. Cao, H. Gu, *Chem. Commun.* **2014**, 50, 11110-11113.

¹³ R. Ueno, Y. Ikeda, E. Shirakawa, *Eur. J. Org. Chem.* **2017**, 4188-4193.

¹⁴ M. Janjetovic, A. M. Träff, G. Hilmersson, *Chem. Eur. J.* **2015**, 21, 3772-3777.

^{13}C NMR (100 MHz, CDCl_3) δ 55.8, 53.9, 31.9, 29.6, 29.5, 29.4, 29.3, 29.1, 26.7, 25.8, 23.3, 22.7, 14.2 ppm.

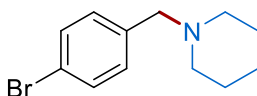
1-(Benzo[d][1,3]dioxol-5-ylmethyl)piperidine⁹ (compound number **5a**): Prepared using the general procedure from piperonal and 1-formylpiperidine to give the title compound as a colorless oil (190 mg, 87% yield).



^1H NMR (400 MHz, CDCl_3) δ 7.01 (s, 1H), 6.89 (d, J = 8.0 Hz, 1H), 6.78 (d, J = 8.6 Hz, 1H), 5.95 (s, 2H), 3.71 (s, 2H), 2.67 (m, 4H), 1.81 (m, 4H), 1.51 (m, 2H) ppm;

^{13}C NMR (100 MHz, CDCl_3) δ 148.1, 147.9, 124.1, 110.7, 108.4, 101.4, 62.2, 53.5, 24.3, 23.3 ppm.

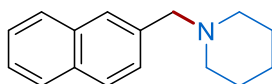
1-(4-Bromobenzyl) piperidine¹¹ (compound number **5b**): Prepared using the general procedure from 4-bromobenzaldehyde and 1-formylpiperidine to give the title compound as a yellow liquid (200 mg, 79% yield).



^1H NMR (400 MHz, CDCl_3) δ 7.49 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.3 Hz, 2H), 3.76 (s, 2H), 2.69 (m, 4H), 1.79 (m, 4H), 1.52 (m, 2H) ppm;

^{13}C NMR (100 MHz, CDCl_3) δ 132.0, 131.8, 131.2, 131.0, 61.4, 53.4, 24.1, 23.1 ppm.

N-(1-Naphthylmethyl)pyrrolidine¹⁵ (compound number **5c**): Prepared using the general procedure from 2-naphthaldehyde and 1-formylpyrrolidine to give the title compound as a yellow oil (215 mg, 90% yield).

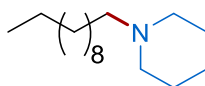


^1H NMR (400 MHz, CDCl_3) δ 7.87-7.81 (m, 4H), 7.66 (dd, J = 1.7, 1.3 Hz, 1H), 7.50-7.46 (m, 2H), 4.03 (s, 2H), 2.87 (m, 4H), 1.96-1.93 (m, 4H), 1.52 (m, 2H) ppm;

¹⁵ R. Ueno, Y. Ikeda, E. Shirakawa, *Eur. J. Org. Chem.* **2017**, 4188-4193.

^{13}C NMR (100 MHz, CDCl_3) δ 133.2, 133.1, 128.6, 128.5, 127.9, 127.7, 127.2, 126.4, 126.3, 59.8, 53.7, 23.3 ppm.

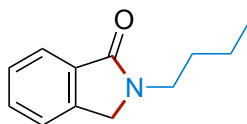
1-Undecylpiperidine¹⁶ (compound number **5d**): Prepared using the general procedure from undecanal and 1-formylpiperidine to give the title compound as a yellow liquid (159 mg, 66% yield).



^1H NMR (400 MHz, CDCl_3) δ 3.81-3.74 (m, 2H), 3.00-2.95 (m, 2H), 2.76-2.70 (m, 2H), 2.26-2.21 (m, 2H), 2.07-2.01 (m, 2H), 1.89-1.75 (m, 4H), 1.31-1.24 (m, 16H), 0.87 (t, J = 7.0 Hz, 3H) ppm;

^{13}C NMR (100 MHz, CDCl_3) δ 57.7, 53.3, 31.9, 29.6, 29.5, 29.4, 29.3, 29.1, 26.9, 23.7, 22.8, 22.7, 22.1, 14.2 ppm.

2-Butylisoindolin-1-one¹⁷ (compound number **6a**): Prepared using the general procedure from phthalaldehyde and *N*-butylformamide to give the title compound as a yellowish oil (149 mg, 79% yield).



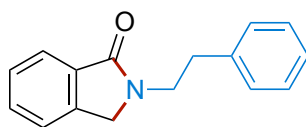
^1H NMR (400 MHz, CDCl_3) δ 7.85 (d, J = 7.4 Hz, 1H), 7.53-7.42 (m, 3H), 4.37 (s, 2H), 3.62 (t, J = 7.3 Hz, 2H), 1.65 (p, J = 7.4 Hz, 2H), 1.43-1.33 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H) ppm;

^{13}C NMR (100 MHz, CDCl_3) δ 168.5, 141.2, 133.2, 131.1, 128.1, 123.7, 122.7, 49.9, 42.2, 30.6, 20.2, 13.9 ppm.

2-phenethylisoindolin-1-one¹⁷ (compound number **6b**): Prepared using the general procedure A from phthalaldehyde and *N*-phenethylformamide to give the title compound as an orange-brown solid (205 mg, 78% yield).

¹⁶ S. Güllak, L. Wu, Q. Liu, R. Franke, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2014**, 53, 7320-7323.

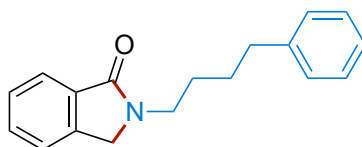
¹⁷ S. Das, D. Addis, L. R. Knäpke, U. Bentrup, K. Junge, A. Brückner, M. Beller, *Angew. Chem. Int. Ed.* **2011**, 50, 9180-9184.



¹H NMR (300 MHz, CDCl₃) δ 7.87 – 7.30 (m, 4H), 7.29 – 7.22 (m, 5H), 4.21 (s, 2H), 3.88 (t, J = 7.5 Hz, 2H), 3.01 (t, J = 7.5 Hz, 2H) ppm;

¹³C NMR (75 MHz, CDCl₃) δ 168.7, 141.4, 139.0, 133.1, 131.4, 129.0, 128.9, 128.1, 126.8, 123.9, 122.8, 50.8, 44.3, 35.1 ppm.

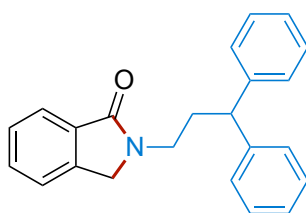
2-(4-Phenyl-butyl)-2,3-dihydro-isoindol-1-one¹⁷ (compound number **6c**): Prepared using the general procedure from phthalaldehyde and *N*-(4-phenylbutyl)formamide to give the title compound as a yellow oil (185 mg, 70% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.85 (d, J = 7.5 Hz, 1H), 7.53-7.41(m, 3H), 7.28-7.24 (m, 2H), 7.18-7.15 (m, 3H), 4.32 (s, 2H), 3.64 (t, J = 6.7 Hz, 2H), 2.66 (t, J = 7.0 Hz, 2H), 1.69 (m, 4H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 168.6, 142.1, 142.2, 133.1, 131.2, 128.5, 128.4, 128.1, 125.9, 123.7, 122.7, 49.6, 42.2, 35.5, 28.6, 27.9 ppm.

2-(3,3-Diphenylpropyl)isoindolin-1-one (compound number **6d**): Prepared using the general procedure A from phthalaldehyde and *N*-(3,3-diphenylpropyl)formamide to give the title compound as a white solid (315 mg, 77% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.85– 7.15 (m, 14H), 4.30 (s, 2H), 4.30 (s, 2H), 4.02 (t, J = 8.0 Hz, 1H), 3.60 (t, J = 8.0 Hz, 2H), 2.42 – 2.48 (m, 2H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 168.4, 144.0, 141.0, 132.8, 131.0, 128.4, 127.8, 127.6, 126.2, 123.5, 122.4, 50.0, 48.8, 41.3, 34.0 ppm.

IR (KBr) 3027, 2928, 2035, 1673, 1618, 1454 cm⁻¹;

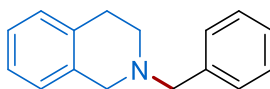
HRMS (ESI+) m/z : [M+Na]⁺ Calcd. for C₂₃H₂₁NO+Na 350.1515; Found 350.1519.

General Procedures for the Direct Reductive Amination in Ethyl Formate

A screw-cap high pressure reaction vessel was charged with tetrahydroisoquinoline **7** (1.0 mmol, 1.0 equiv); carbonyl compound **9** (1.2 equiv), TfOH catalyst (10 mol%), H₂O (2.0 equiv) and ethyl formate (4.0 mL). The reaction vessel was sealed carefully and heated to 100 °C for 24 h. The reaction was cooled to rt. Brine (10 mL) was added to the reaction mixture, followed by the extraction of the products with ether (3 x 10 mL). The organic layers were combined, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residues were then purified by column chromatography (SiO₂, dichloromethane/methanol 20 : 1 to 10 : 1) to obtain product **10**.

Characterization Data of Products in Scheme 3 and Scheme 4

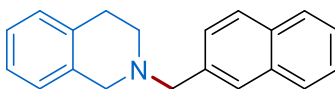
2-Benzyl-1,2,3,4-tetrahydroisoquinoline¹⁸ (compound number **10a**): Prepared using the general procedure from benzaldehyde and tetrahydroisoquinoline **7** to give the title compound as a yellowish oil (185 mg, 83% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.45 (d, J = 7.3 Hz, 2H), 7.35 (t, J = 7.5 Hz, 2H), 7.31–7.22 (m, 1H), 7.19–7.10 (m, 3H), 6.99 (d, J = 7.0 Hz, 1H), 3.78 (s, 2H), 3.72 (s, 2H), 2.95 (t, J = 5.7 Hz, 2H), 2.85 (t, J = 5.1 Hz, 2H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 131.1, 130.7, 129.8, 129.4, 129.0, 128.3, 127.3, 127.1, 67.6, 59.3, 52.7, 49.1, 25.2 ppm.

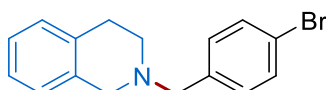
2-(Naphthalen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline¹⁸ (compound number **10b**): Prepared using the general procedure from 2-naphthaldehyde and tetrahydroisoquinoline **7** to give the title compound as a white solid (205.4 mg, 75% yield).



¹H NMR (400 MHz, CDCl₃) δ 7.84 (t, J = 7.0 Hz, 4H), 7.60 (d, J = 8.5 Hz, 1H), 7.50–7.45 (m, 2H), 7.16–7.08 (m, 3H), 6.99 (d, J = 6.9 Hz, 1H), 3.87 (s, 2H), 3.71 (s, 4H), 2.94 (t, J = 5.7 Hz, 2H), 2.83 (p, J = 5.7, 5.9 Hz, 2H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 135.7, 134.6, 134.3, 133.0, 128.8, 128.2, 128.0, 127.8, 127.7, 127.5, 127.2, 126.8, 126.4, 126.1, 125.8, 62.8, 56.1, 50.7, 29.0 ppm.

2-(4-Bromobenzyl)-1,2,3,4-tetrahydroisoquinoline¹⁸ (compound number **10c**): Prepared using the general procedure from 4-bromobenzaldehyde and tetrahydroisoquinoline **7** to give the title compound as a white solid (184 mg, 61% yield).



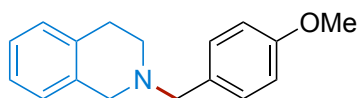
¹⁸ G. Oss, S. D. de Vos, K. N. H. Luc, J. H. Harper, T. V. Nguyen, *J. Org. Chem.* **2018**, 83, 1000-1010

¹H NMR (400 MHz, CDCl₃) δ 7.47-6.97 (m, 8H), 3.66 (t, J = 5.8 Hz, 4H), 2.91 (t, J = 5.8 Hz, 2H), 2.76 (t, J = 5.8 Hz, 2H) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 137.2, 134.2, 131.6 (2C), 130.9 (2C), 128.8, 126.7, 126.4, 125.8, 121.2, 61.9, 55.9, 50.6, 29.0 ppm.

2-(4-methoxybenzyl)-1,2,3,4-tetrahydroisoquinoline¹⁸ (compound number **10d**):

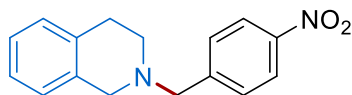
Prepared using the general procedure from 4-methoxybenzaldehyde and tetrahydroisoquinoline **6.9a** to give the title compound as an orange oil (152 mg, 60% yield).



¹H NMR (300 MHz, CDCl₃) δ 7.57 – 6.57 (m, 8H), 3.85 (s, 3H), 3.66 (s, 4H), 2.93 (t, J = 5.9 Hz, 2H), 2.77 (t, J = 5.9 Hz, 2H) ppm;

¹³C NMR (75 MHz, CDCl₃) δ 158.8, 135.0, 134.4, 130.4, 130.3 (2C), 128.7, 126.6, 126.1, 125.5, 113.7 (2C), 62.2, 56.1, 55.3, 50.5, 29.2 ppm.

2-(4-Nitrobenzyl)-1,2,3,4-tetrahydroisoquinoline¹⁸ (compound number **10e**): Prepared using the general procedure from 4-nitrobenzaldehyde and tetrahydroisoquinoline **7** to give the title compound as a yellow oil (208 mg, 78% yield).

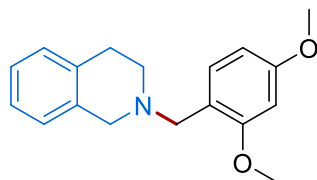


¹H NMR (300 MHz, CDCl₃) δ 8.20 (d, J = 6.0 Hz, 2H), 7.59 (d, J = 6.0 Hz, 2H), 7.20 - 6.98 (m, 4H), 3.79 (s, 2H), 3.66 (s, 2H), 2.92 – 2.96 (t, J = 6.0 Hz, 2H), 2.76 – 2.80 (t, J = 6.0 Hz, 2H) ppm;

¹³C NMR (75 MHz, CDCl₃) δ 147.2, 146.5, 140.1, 134.4, 134.1, 129.4, 128.7, 126.5, 126.3, 125.7, 123.6, 61.9, 56.1, 50.8, 29.1 ppm.

2-(2,4-dimethoxybenzyl)-1,2,3,4-tetrahydroisoquinoline¹⁸ (compound number **10f**):

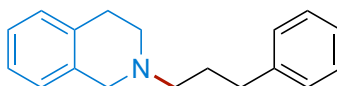
Prepared using the general procedure from 2,4-dimethoxybenzaldehyde and tetrahydroisoquinoline **7** to give the title compound as a yellowish liquid (156 mg, 55% yield).



^1H NMR (400 MHz, CDCl_3) δ 7.80 (d, $J = 8.1$ Hz, 1H), 7.29-7.17 (m, 3H), 7.05 (d, $J = 7.3$ Hz, 1H), 6.54 (dd, $J = 2.1, 2.3$ Hz, 2H), 4.23 (s, 4H), 3.87 (s, 3H), 3.83 (s, 3H), 3.45 (s, 2H), 3.18 (s, 2H) ppm;

^{13}C NMR (100 MHz, CDCl_3) δ 162.8, 159.4, 133.7, 128.8, 128.4, 127.3, 127.0, 105.2, 98.7, 55.7, 55.5, 52.7, 51.4, 48.4, 24.1 ppm.

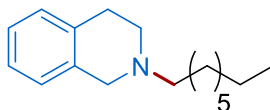
3-Phenylpropyl-1,2,3,4-tetrahydroisoquinoline¹⁸ (compound number **10g**): Prepared using the general procedure from phenylpropanaldehyde and tetrahydroisoquinoline **7** to give the title compound as a yellow oil (148 mg, 59% yield).



^1H NMR (400 MHz, CDCl_3) δ 7.40 – 7.30 (m, 2H), 7.30 – 7.10 (m, 6H), 7.10 – 7.00 (m, 1H), 3.70 – 3.62 (m, 2H), 2.96 (t, $J = 5.9$ Hz, 2H), 2.82 – 2.69 (m, 4H), 2.66 – 2.50 (m, 2H), 2.08 – 1.90 (m, 2H) ppm;

^{13}C NMR (100 MHz, CDCl_3) δ 142.3, 134.9, 134.4, 128.7, 128.5, 128.4 (2C), 126.6, 126.1, 125.8, 125.6, 57.8, 56.2, 51.0, 33.7, 29.2, 28.9 ppm.

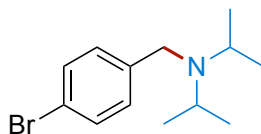
2-Octyl-1,2,3,4-tetrahydroisoquinoline¹⁸ (compound number **10h**): Prepared using the general procedure from octanal and tetrahydroisoquinoline **7** to give the title compound as a as yellow oil (169.4 mg, 70% yield).



^1H NMR (400 MHz, CDCl_3) δ 7.21-7.03 (m, 4H), 3.94 (s, 2H), 3.06 (s, 4H), 2.75 (t, $J = 7.9$ Hz, 2H), 1.77 (p, $J = 7.4$ Hz, 2H), 1.32-1.26 (m, 10H), 0.87 (t, $J = 7.0$ Hz, 3H) ppm;

^{13}C NMR (100 MHz, CDCl_3) δ 128.9, 127.3, 126.8, 126.6, 56.9, 54.3, 49.9, 31.9, 29.4, 29.3, 27.4, 26.8, 25.8, 22.7, 14.2 ppm.

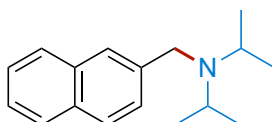
***N*-(4-bromobenzyl)-*N*-isopropylpropan-2-amine¹⁹** (compound number **13a**): Prepared using the general procedure from diisopropylamine and 4-bromobenzaldehyde in ethyl formate to give the title compound as a yellow oil (103 mg, 38% yield).



¹H NMR (300 MHz, CDCl₃) δ 7.42 – 7.29 (m, 4H), 3.60 (s, 2H), 3.03 (sep, J = 6.5 Hz, 2H), 1.03 (d, J = 6.5 Hz, 12H) ppm;

¹³C NMR (75 MHz, CDCl₃) δ 141.9, 131.2 (2H), 129.8 (2H), 119.9, 48.6, 48.4, 20.8 ppm.

***N*-Isopropyl-*N*-(naphthalen-2-ylmethyl)propan-2-amine** (compound number **13b**): Prepared using the general procedure from diisopropylamine and 2-naphthaldehyde in ethyl formate to give the title compound as a white solid (151 mg, 63% yield).



¹H NMR (300 MHz, CDCl₃) δ 7.88 – 7.81 (m, 4H), 7.62 (d, J = 9.0 Hz, 1H), 7.43 – 7.52 (m, 2H), 3.90 (s, 2H), 3.12 – 3.25 (sep, J = 6.5 Hz, 2H), 1.13 – 1.15 (d, J = 6.5 Hz, 12H) ppm;

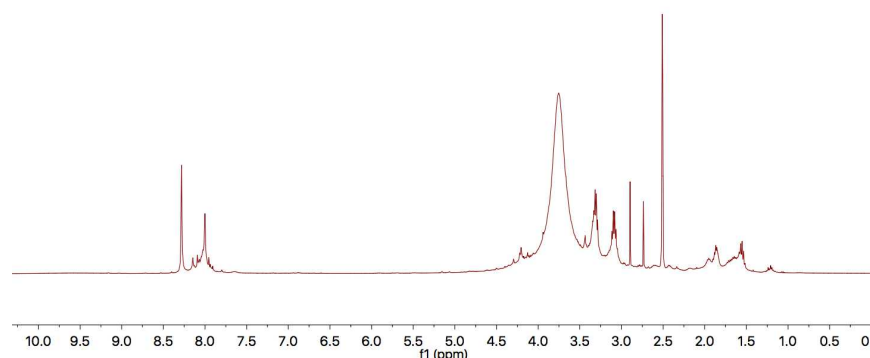
¹³C NMR (75 MHz, CDCl₃) δ 139.5, 133.5, 132.8, 127.8, 127.7, 127.7, 126.9, 126.7, 125.9, 125.4, 49.4, 48.6, 20.7 ppm;

IR (KBr) 3053, 2961, 2869, 2602, 1699, 1631, 1601, 1508 cm⁻¹;

HRMS (ESI⁺) *m/z*: [M+H]⁺ Calcd. for C₁₇H₂₁N₁+H 243.1937; Found 243.1935.

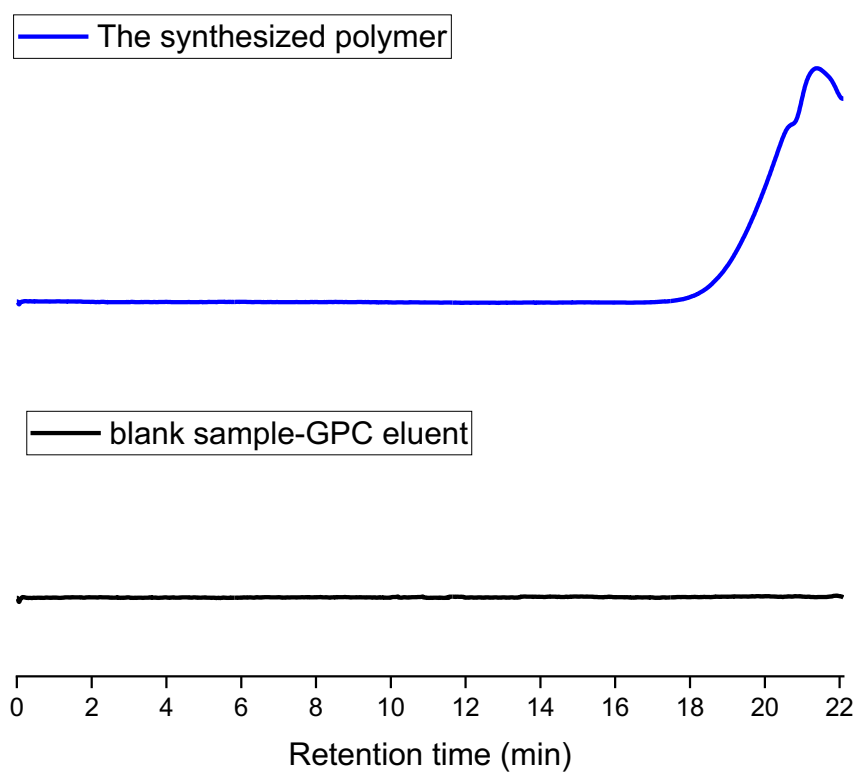
¹⁹ J. C. Bottaro, *Synth. Commun.* **1985**, 15, 195-199

Synthesis of polyamines 16: Glurataldehyde **14** (50 wt. % in water, 20 mmol) and 1,3-diaminopropane **15** (20 mmol) and TfOH (2 mmol) was dissolved in ethyl formate (5 mL) in a screw-cap high pressure tube. The reaction mixture was heated to 100 °C for 48 h. Water and excess ethyl formate were removed under reduced pressure. Mass balance and ^1H NMR spectrum of the crude residues suggested that ~80% of the monomers have been converted to a range of polyamines (**16**).



(^1H NMR, 298K, d_6 -DMSO)

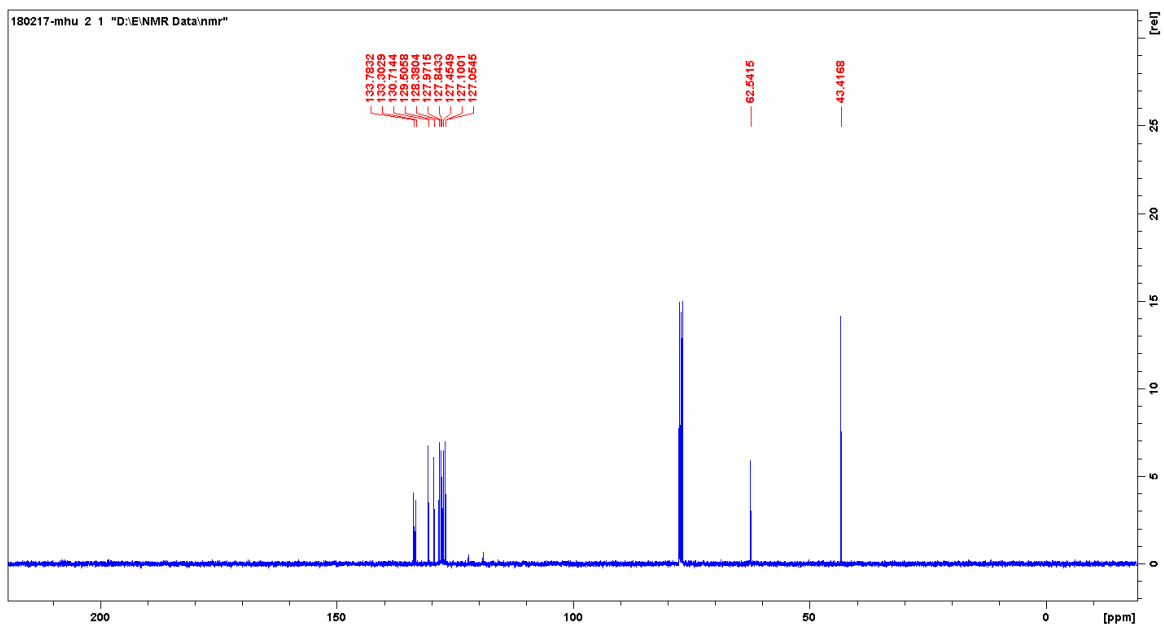
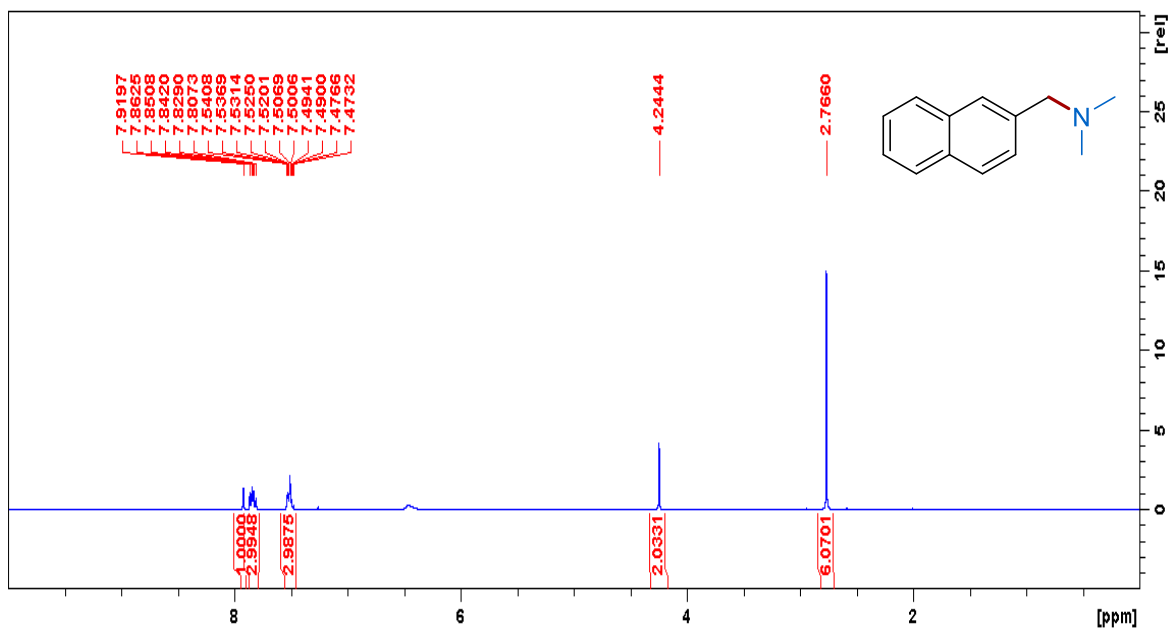
Gel permeation chromatography (GPC) was employed to measure the molecular weights and dispersities of the synthesised polymers. GPC was carried out using UFLC Shimadzu Prominence system comprising a DGU-20A degasser, a LC-20AD pump, a SIL-20A HT automatic injector, a CTO-20A column oven, a RID-10A refractive index detector, a RF-20A fluorescence detector and a SPD-M20A Diode array detector Shimadzu UV/vis detector. A 50 x 7.8 mm guard column and two 300 x 7.8 mm linear columns (10^4 and 10^5 Å pore size, 5 µm particle size) were used for the analyses. *N,N'*-dimethylacetamide (DMAc) (HPLC grade, including 0.05% w/v of 2,6-dibutyl-4-methylphenol (BHT) and 0.03% w/v of LiBr) with a flow rate of 1 mL min $^{-1}$ and a constant temperature of 50 °C was used as the mobile phase. The unit was calibrated using commercially available linear poly(methyl methacrylate) standards (0.5- 1000 kDa, Polymer Laboratories). The samples (4 mg mL $^{-1}$) were dissolved in DMAc and filtered through 0.45 µm PTFE filters prior to injection of 25 µL.



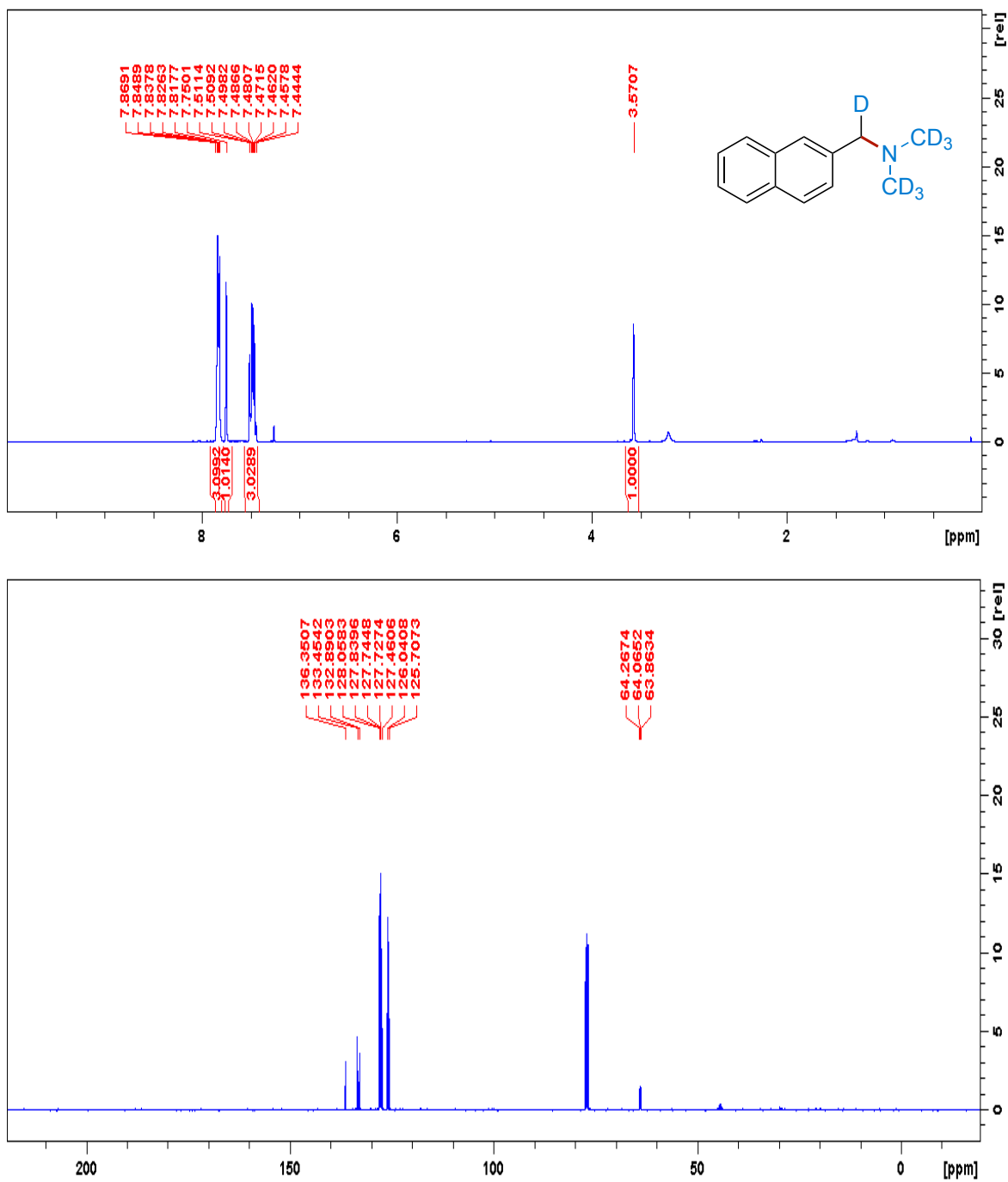
GPC data suggested that the synthesized polymer had an average molecular weight of 2400 g/mol with a dispersity (\bar{D}) of around 1.6 (see above graph at retention time \sim 18-22 min). It should be noted that the whole GPC peak of the polymer was not able to be observed due to overlapping with GPC solvent peaks.

NMR Spectra

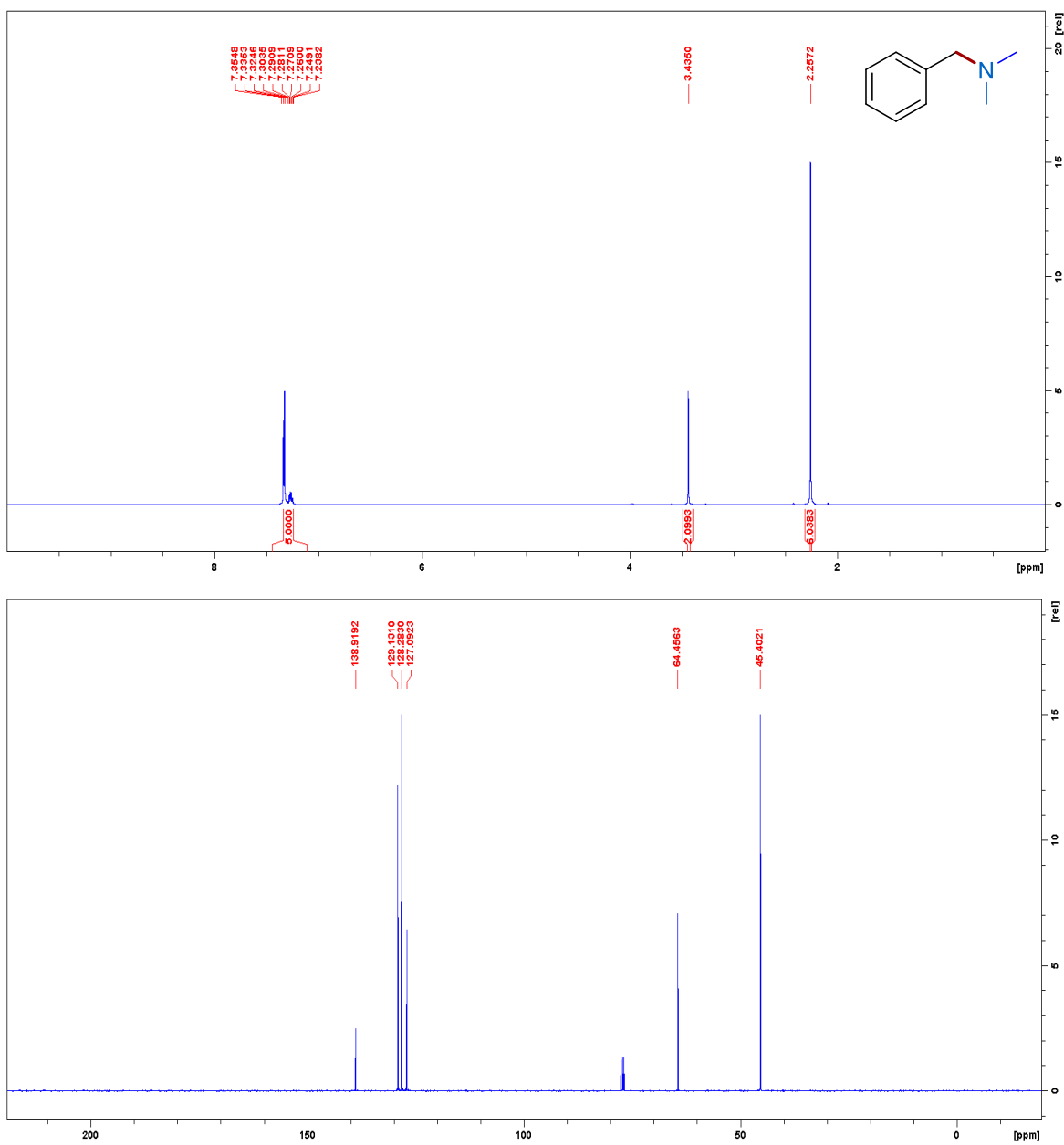
N,N-dimethyl-1-(naphthalen-2-yl) methenamine (**3a**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



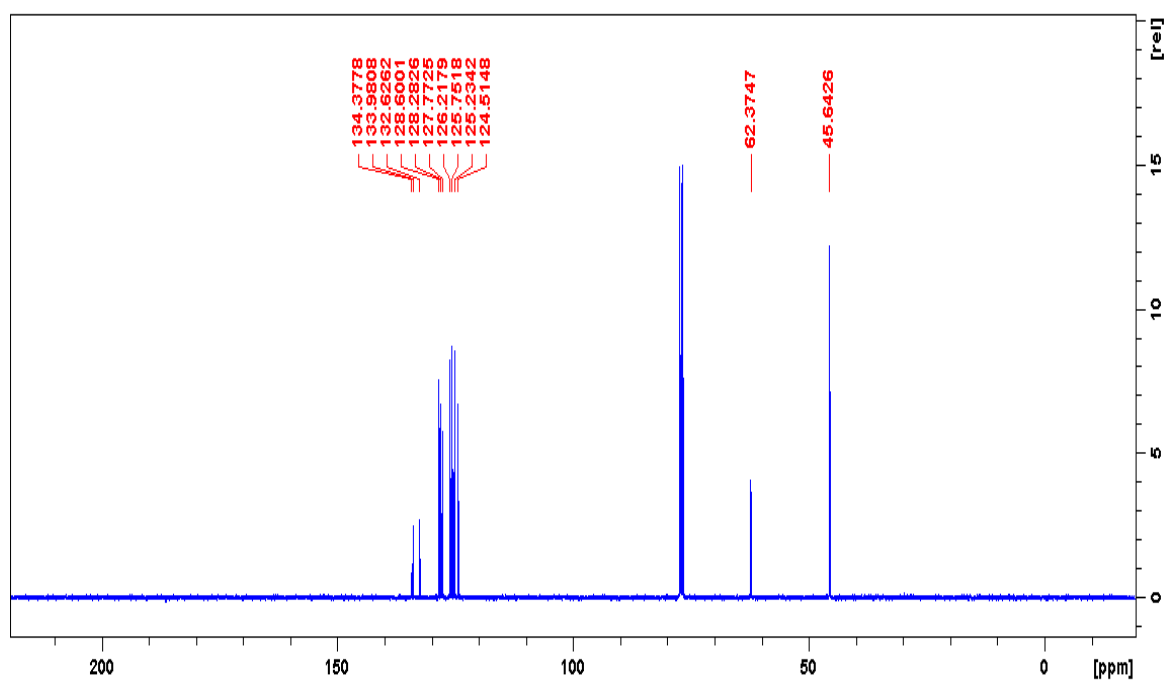
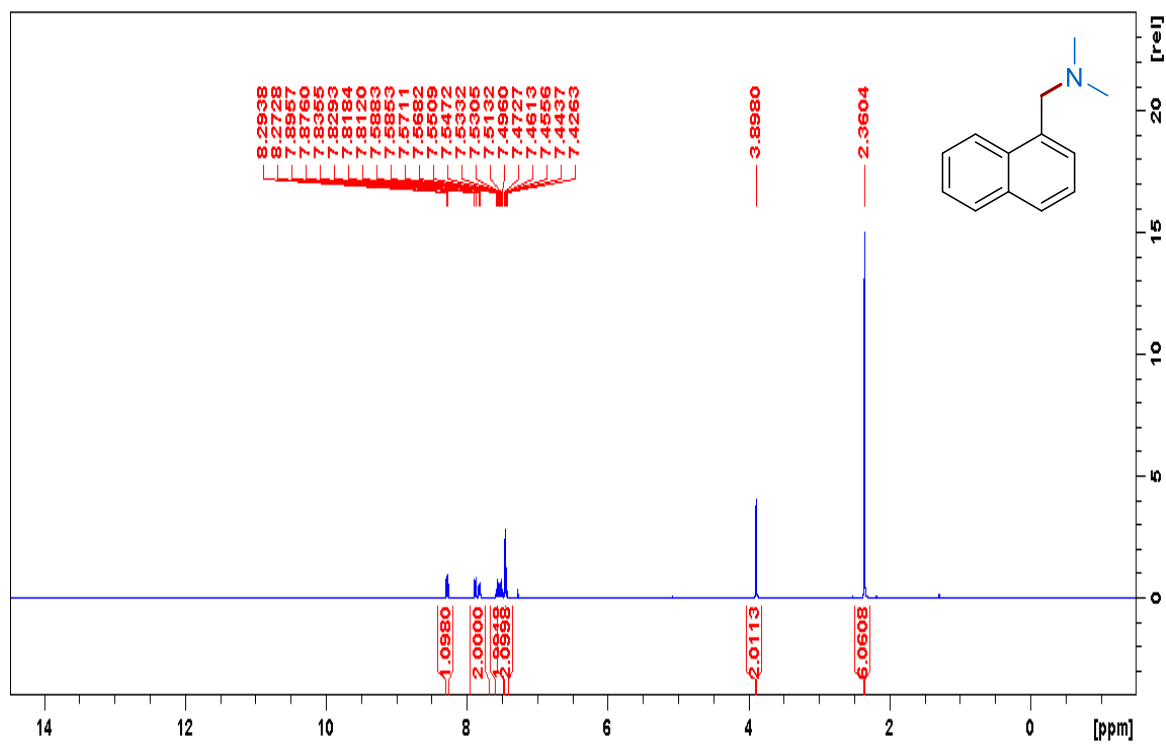
N-(Methyl-d₃)-*N*-(naphthalen-2-ylmethyl-d) methanamine-d₃ (*d*₇-**3a**); ¹H NMR (400 MHz, CDCl₃), ¹³C NMR (100 MHz, CDCl₃).



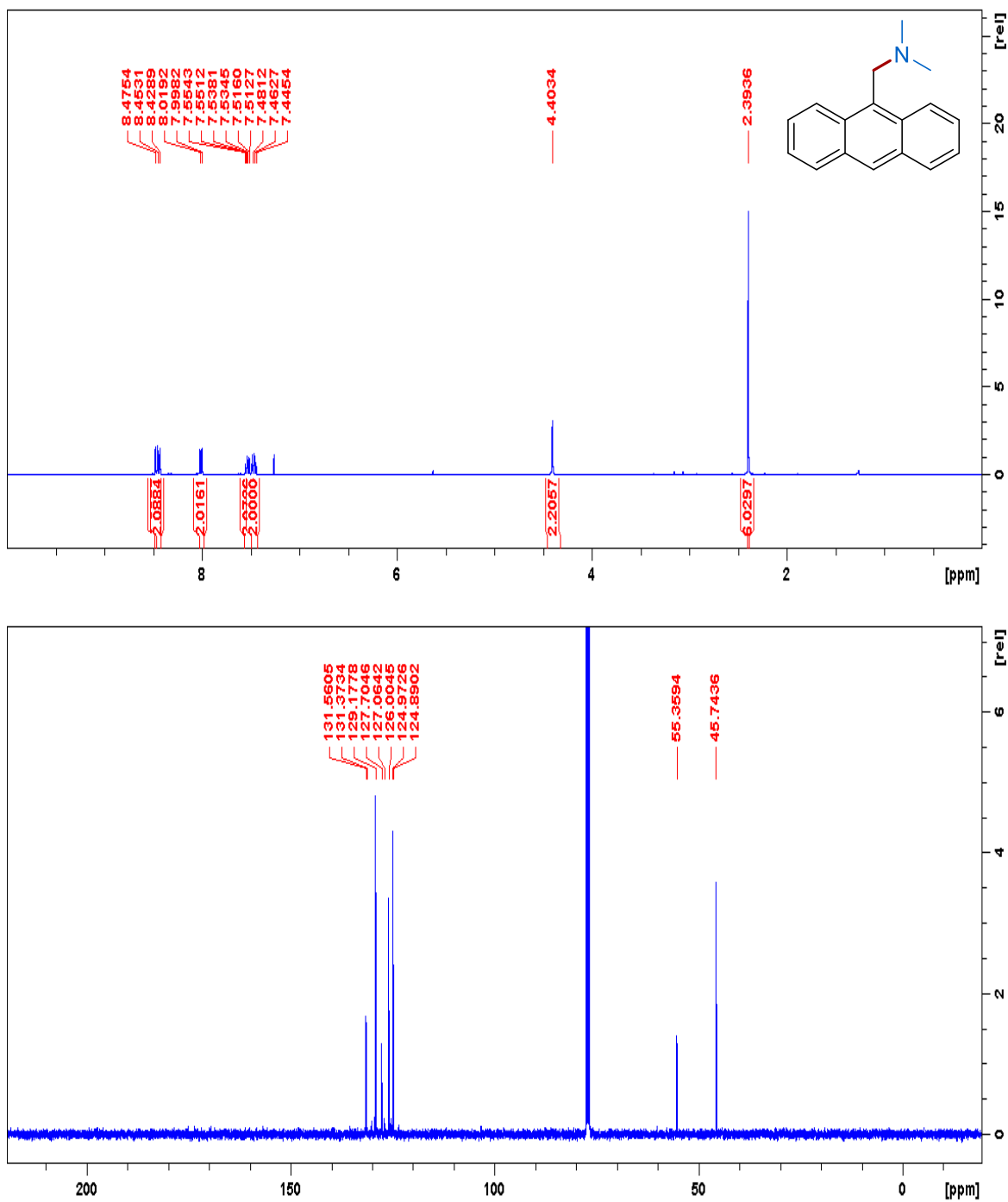
N,N-dimethylbenzylamine (**3b**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



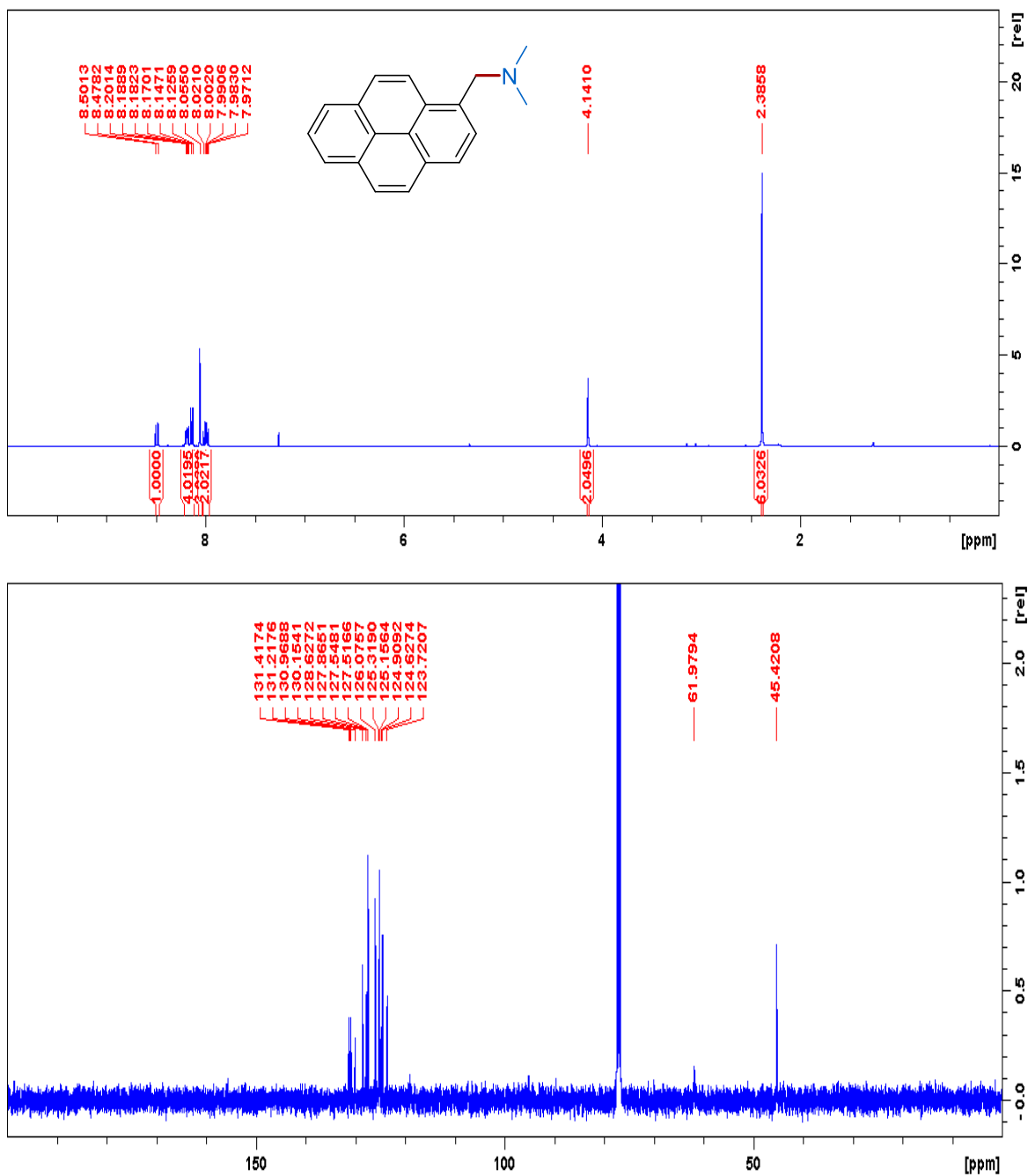
N,N-dimethyl-1-(naphthalen-1-yl) methenamine (**3c**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



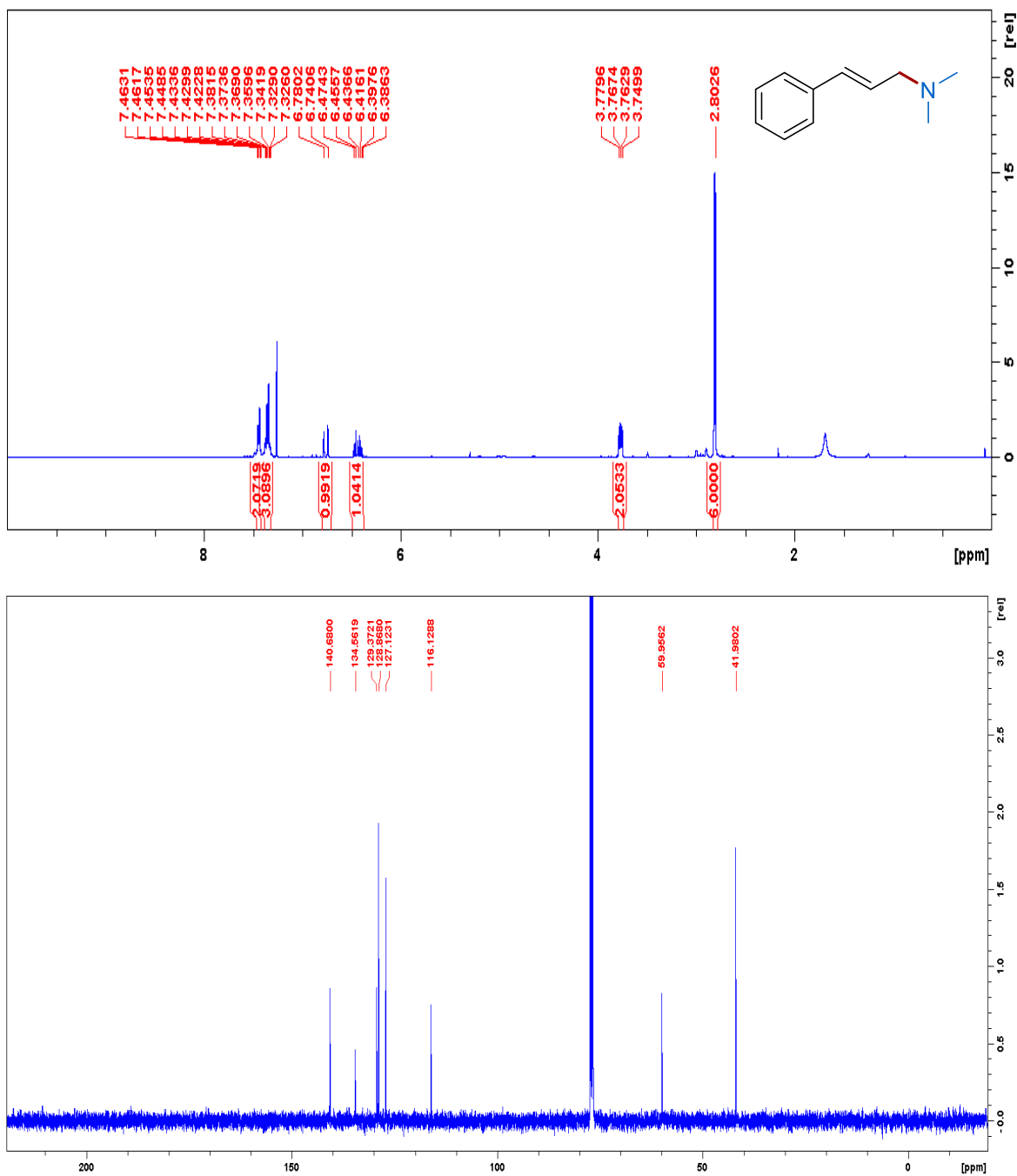
9-(*N,N*-Dimethylaminomethyl) anthracene (**3d**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



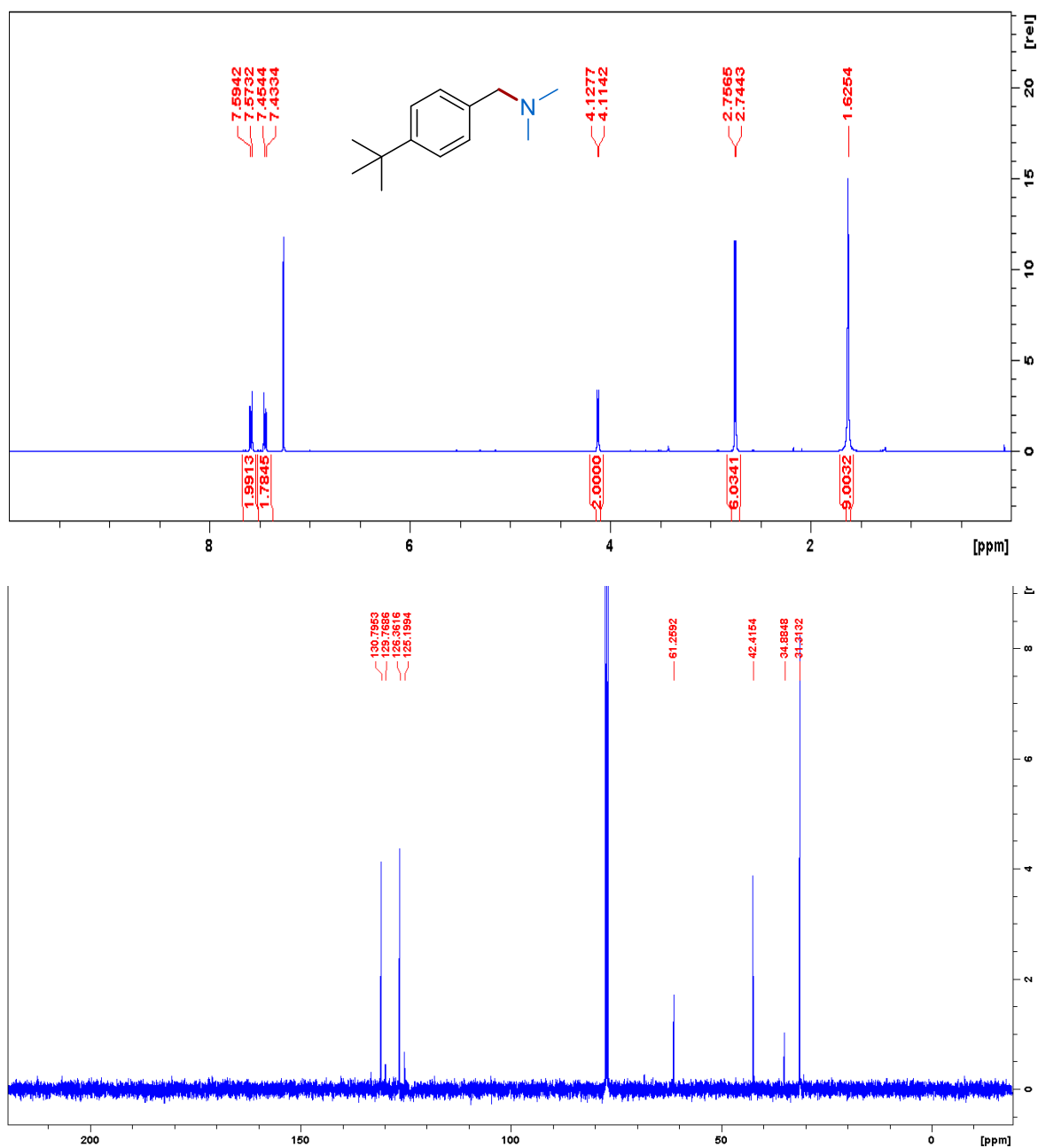
N,N-dimethyl-1-(pyren-1-yl)methanamine (**3e**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



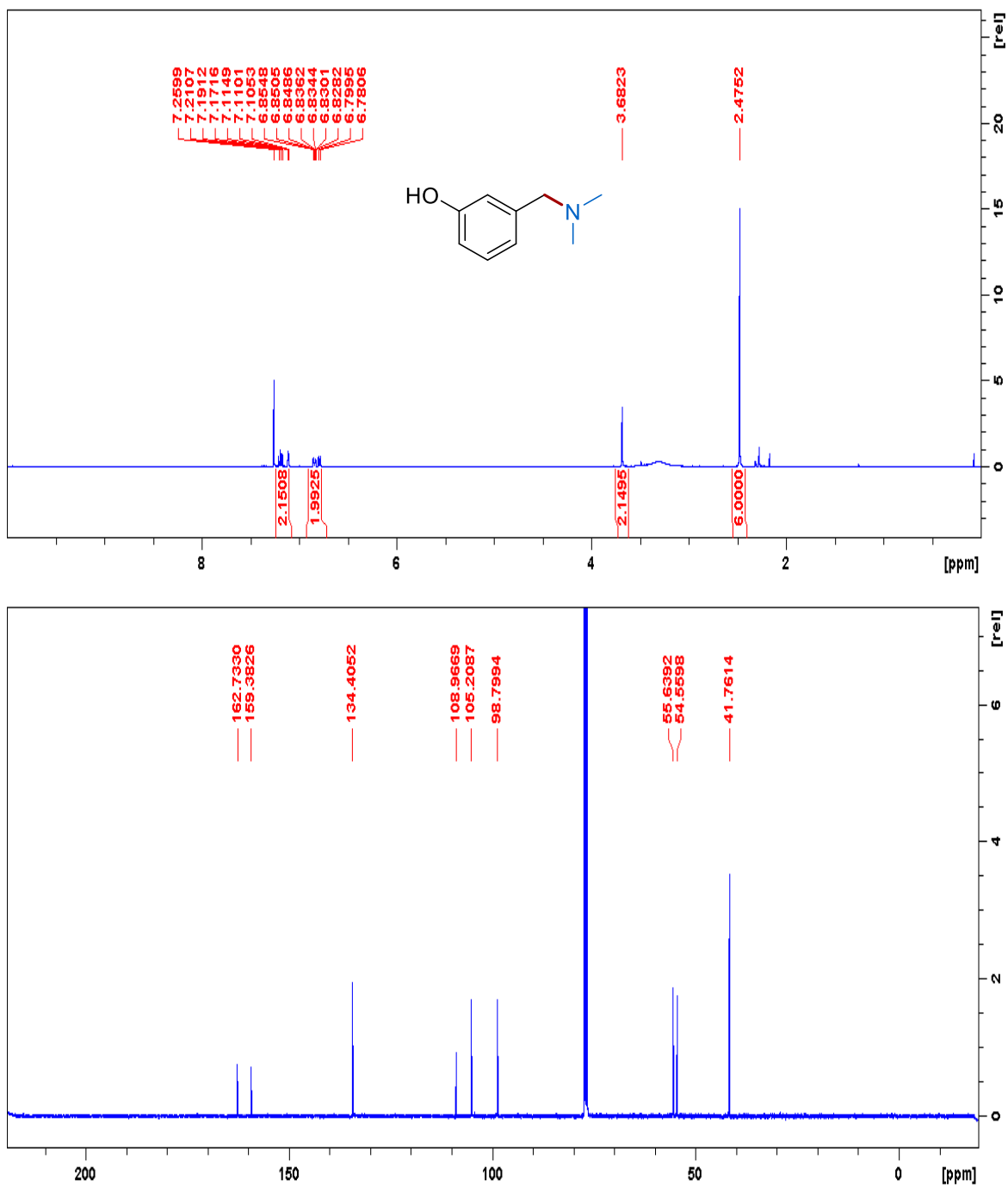
(*E*)-*N,N*-dimethyl-3-phenylprop-2-en-1-amine (**3f**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



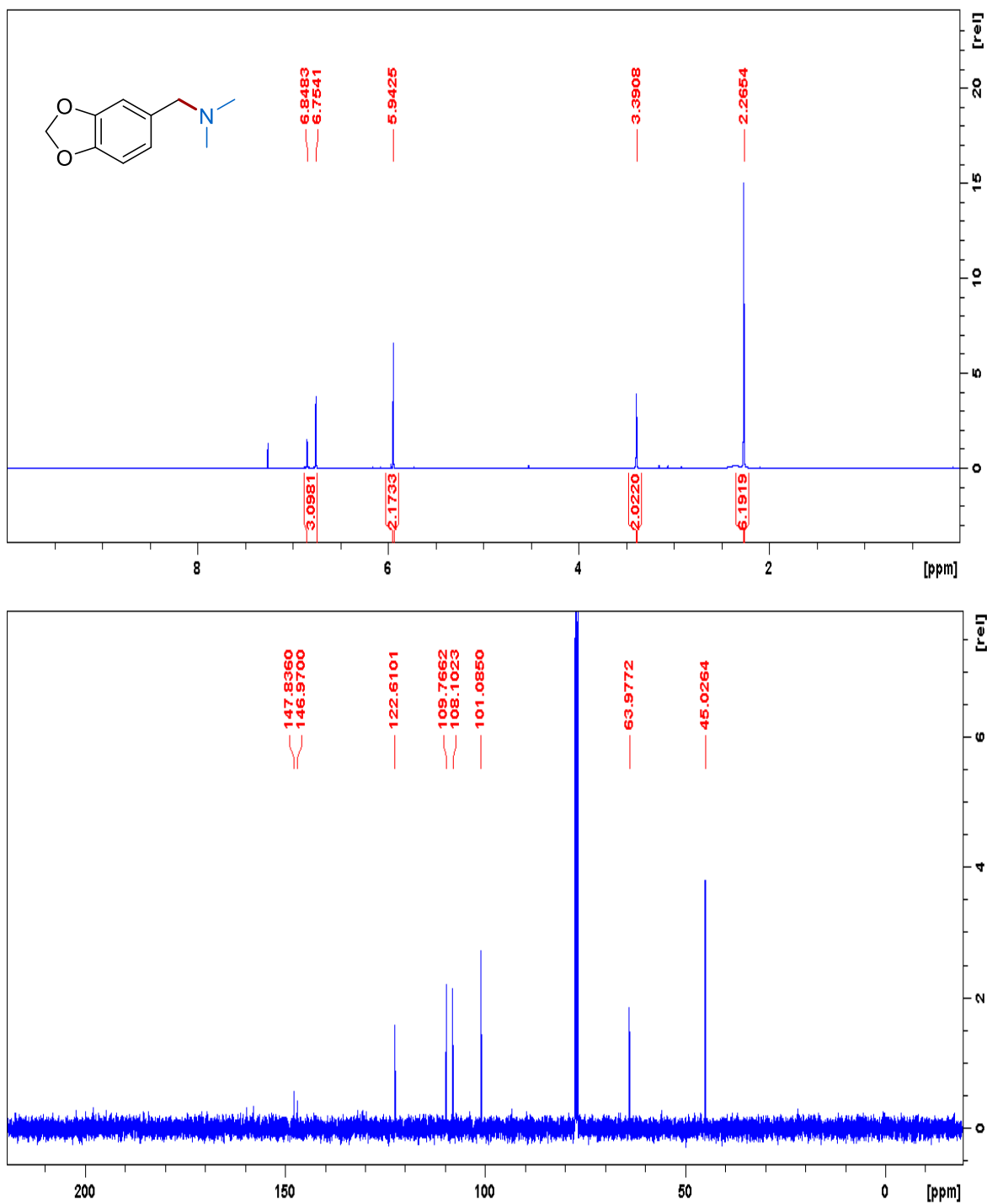
1-(4-(tert-butyl) phenyl)-*N,N*-dimethylmethanamine (**3g**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



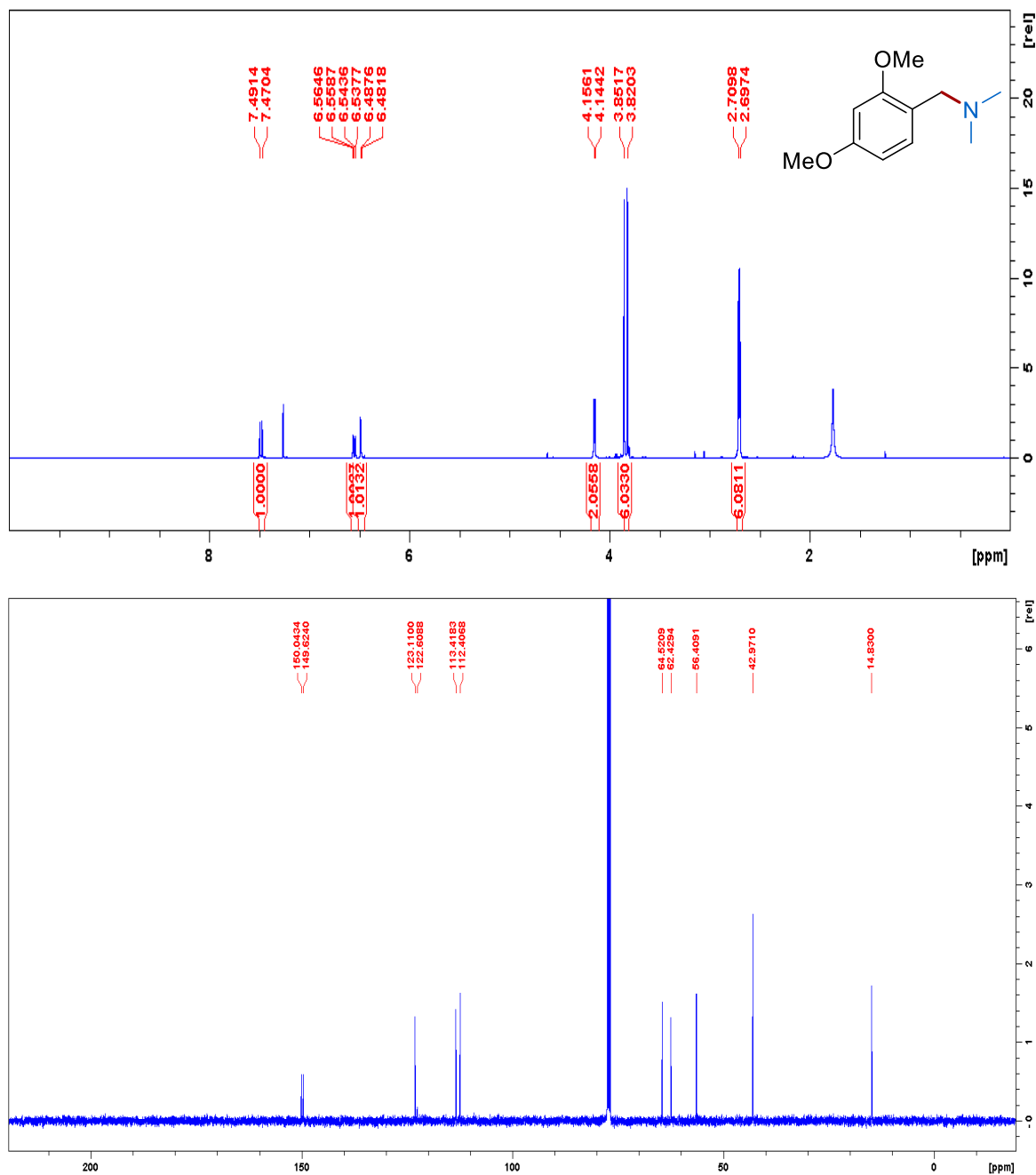
3-((Dimethylamino)methyl)phenol (**3h**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



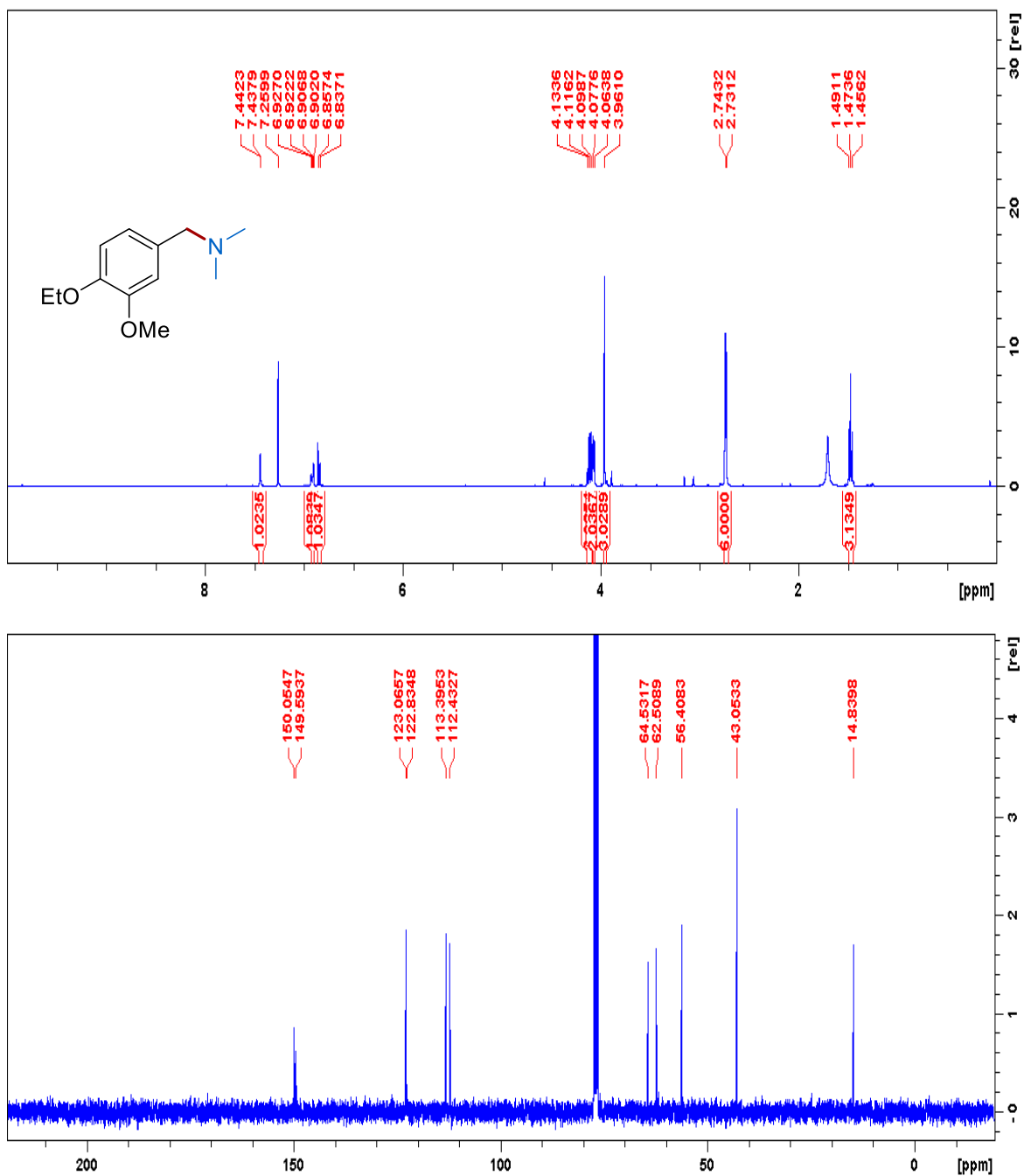
1-(benzo[d][1,3]dioxol-5-yl)-*N,N*-dimethylmethanamine (**3i**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



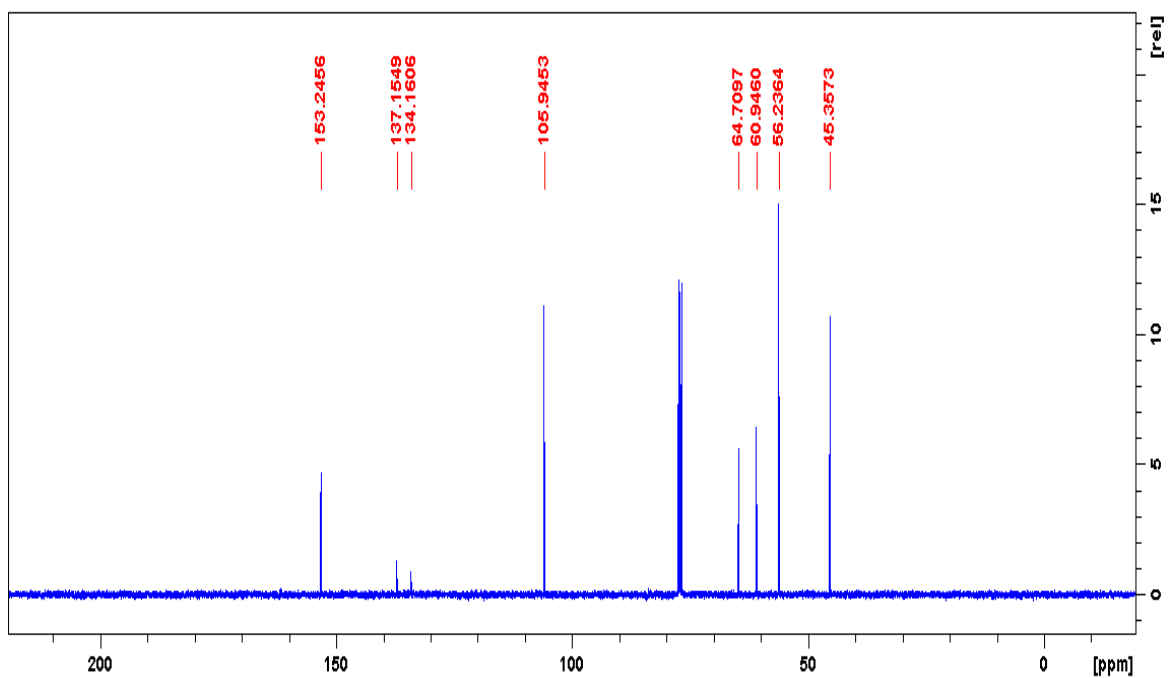
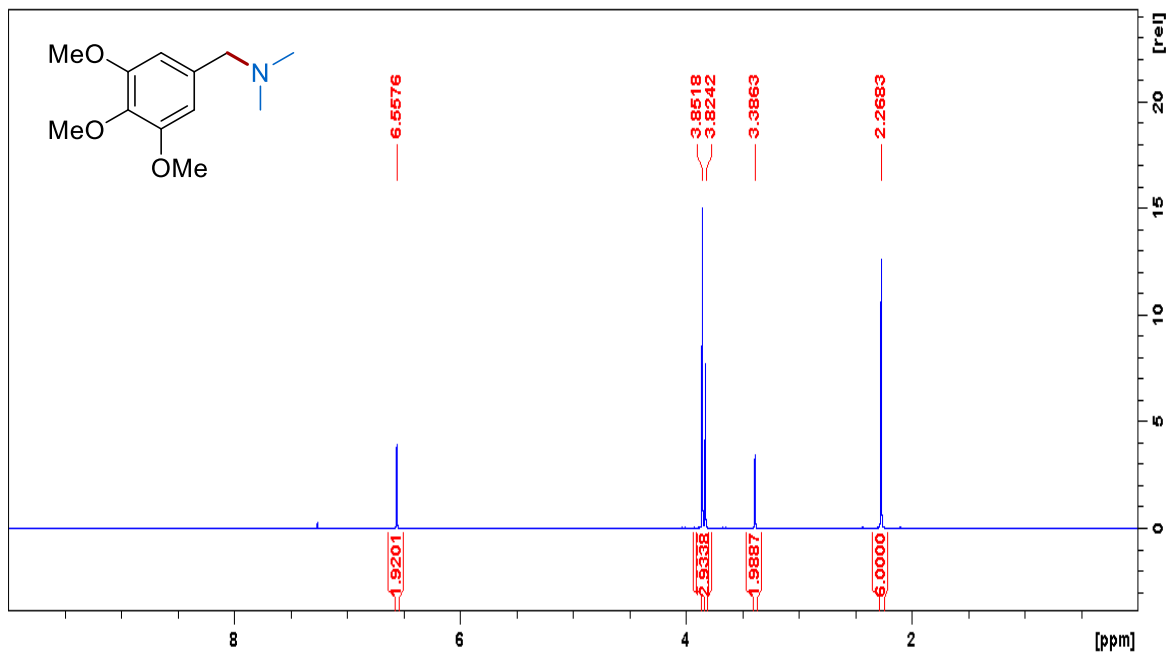
1-(2,4-Dimethoxyphenyl)-*N,N*-dimethylmethanamine (**3j**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



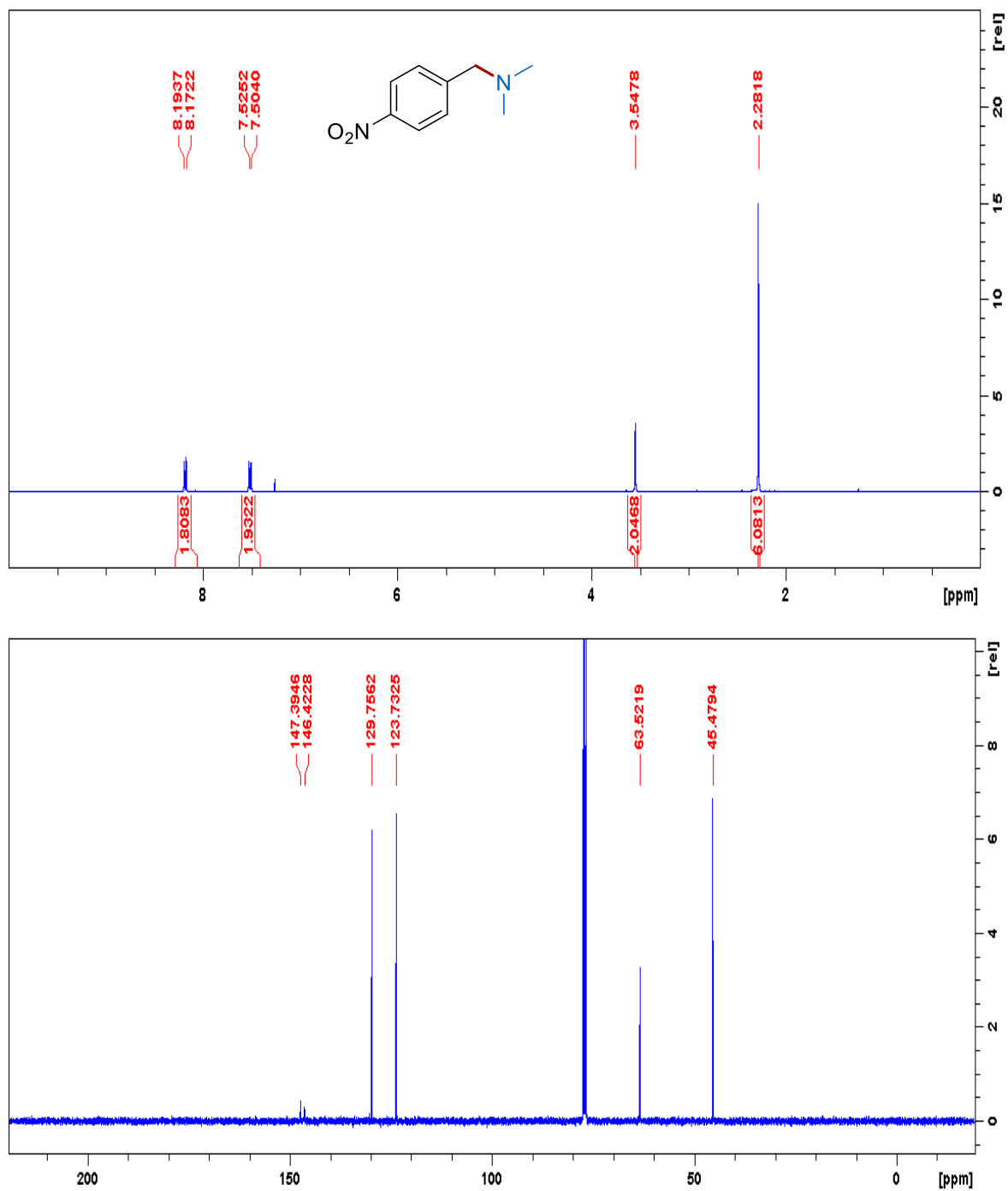
1-(4-ethoxy-3-methoxyphenyl)-*N,N*-dimethylmethanamine (**3k**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



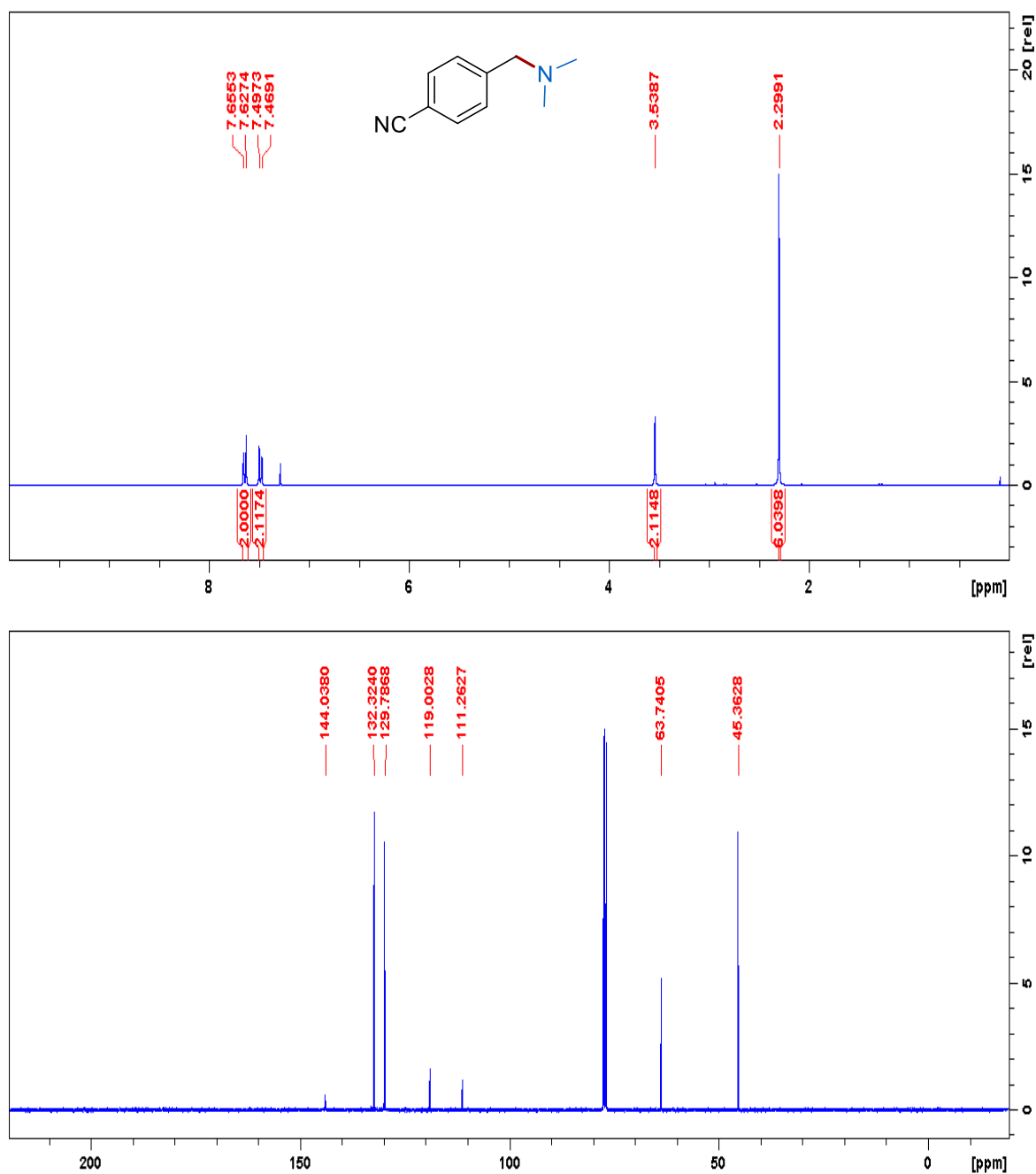
N,N-Dimethyl-1-(3,4,5-trimethoxyphenyl)methanamine (**3**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



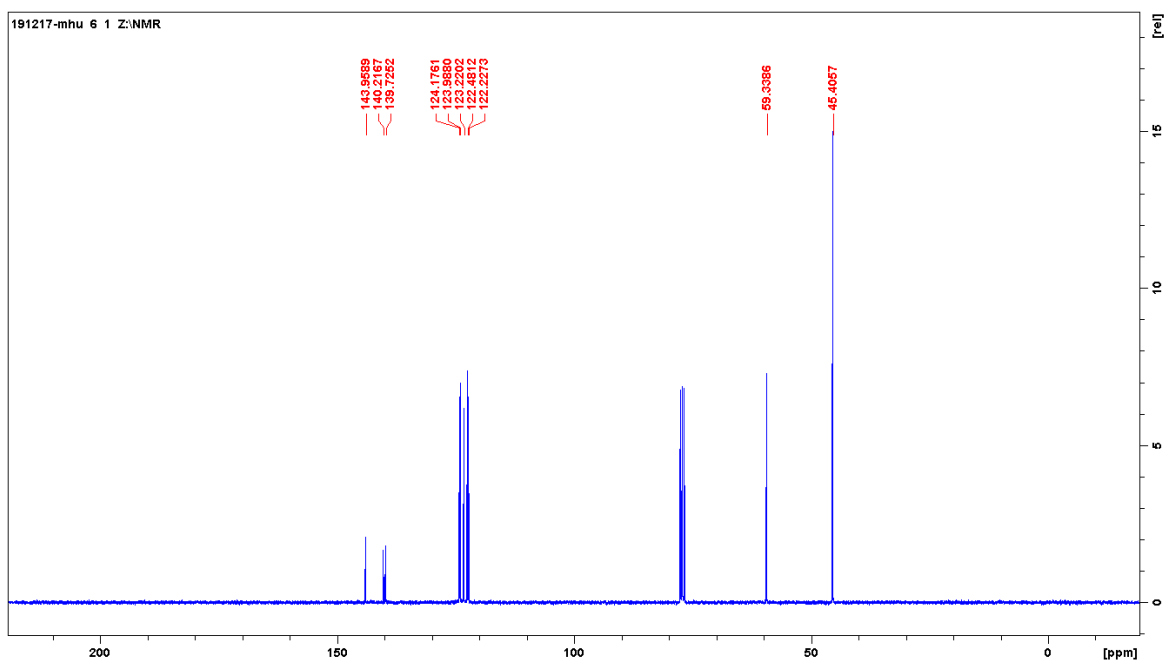
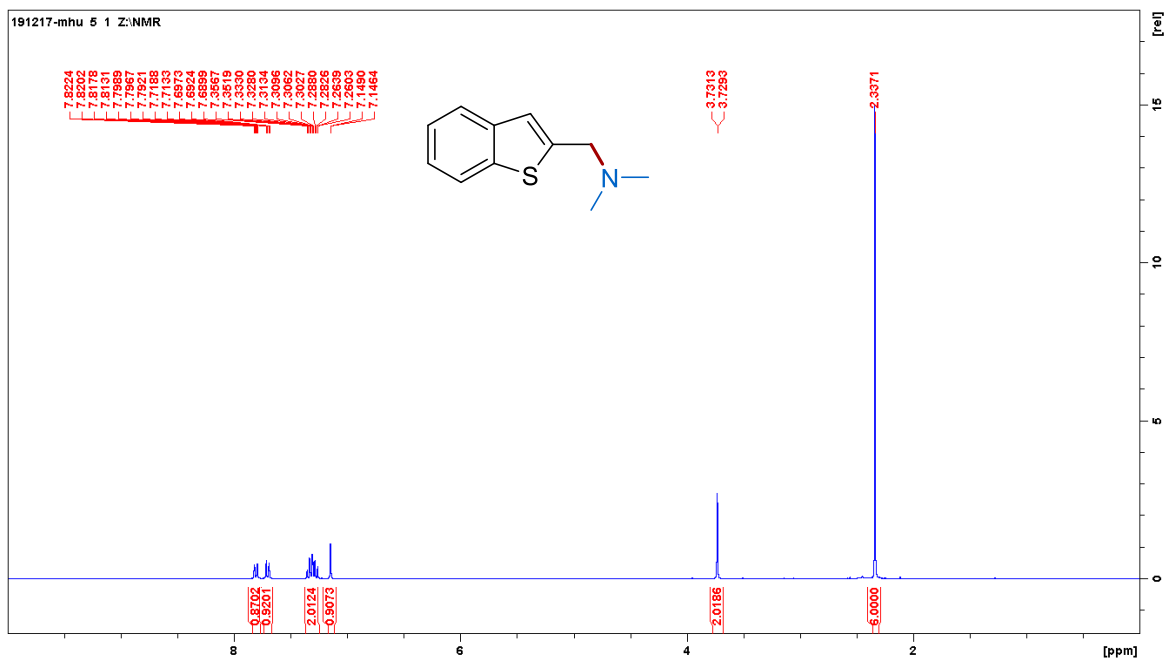
N,N-Dimethyl-1-(4-nitrophenyl) methenamine (**3m**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3)



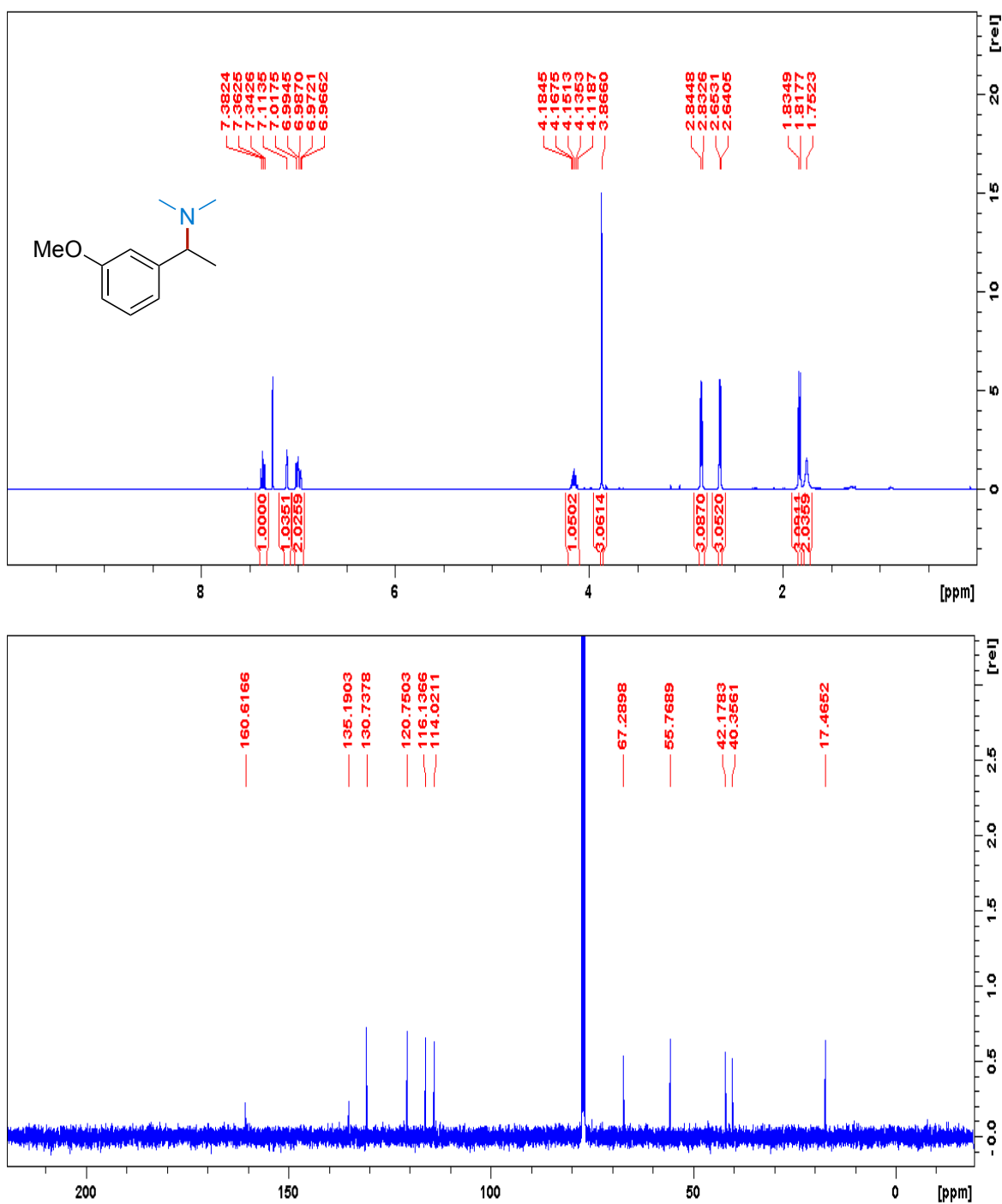
4-((Dimethylamino)methyl) benzonitrile (**3n**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



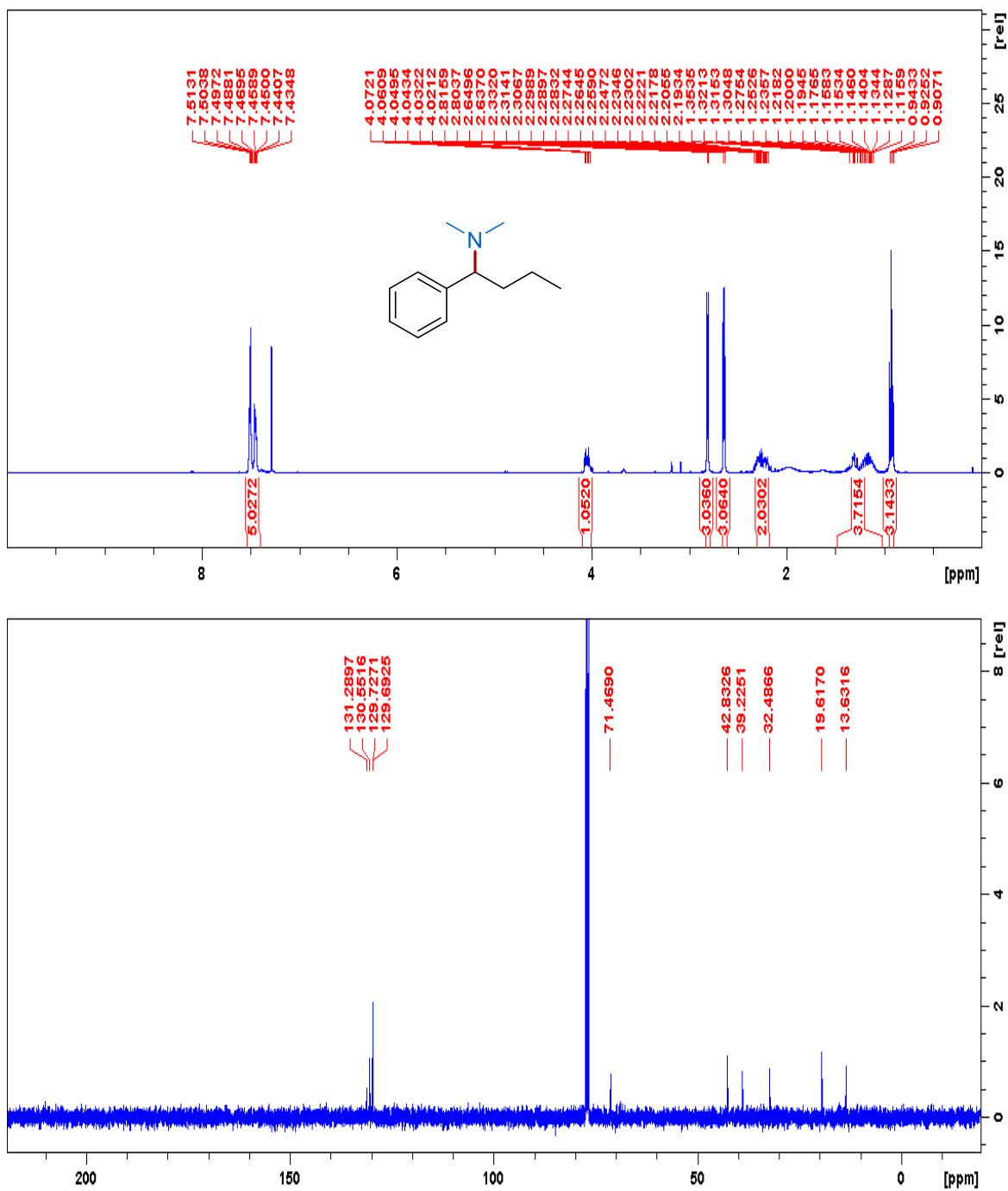
1-(Benzo[b]thiophen-2-yl)-*N,N*-dimethylmethanamine (**3o**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



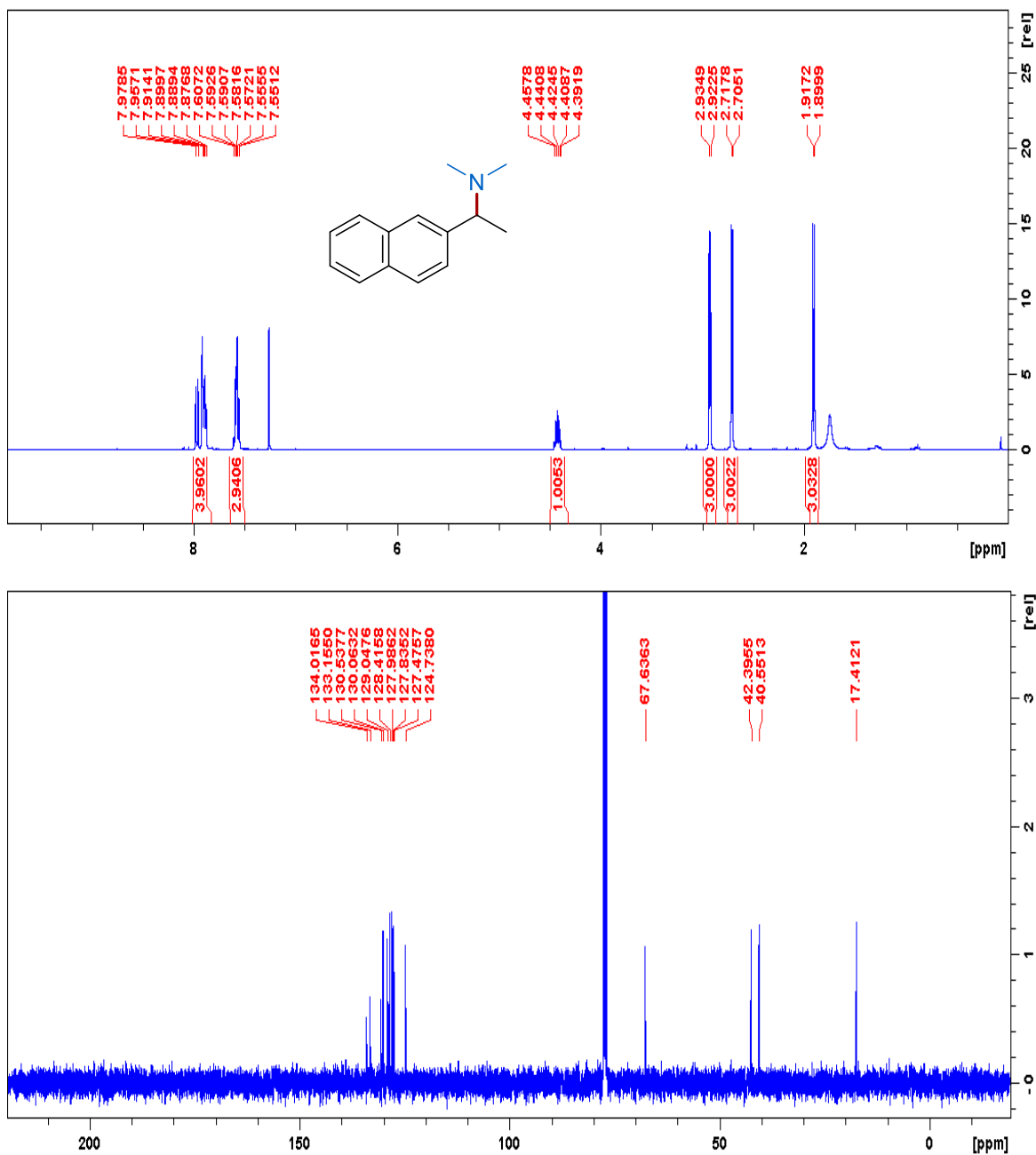
2-(3-Methoxyphenyl)-*N,N*-dimethylpropan-1-amine (**3p**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



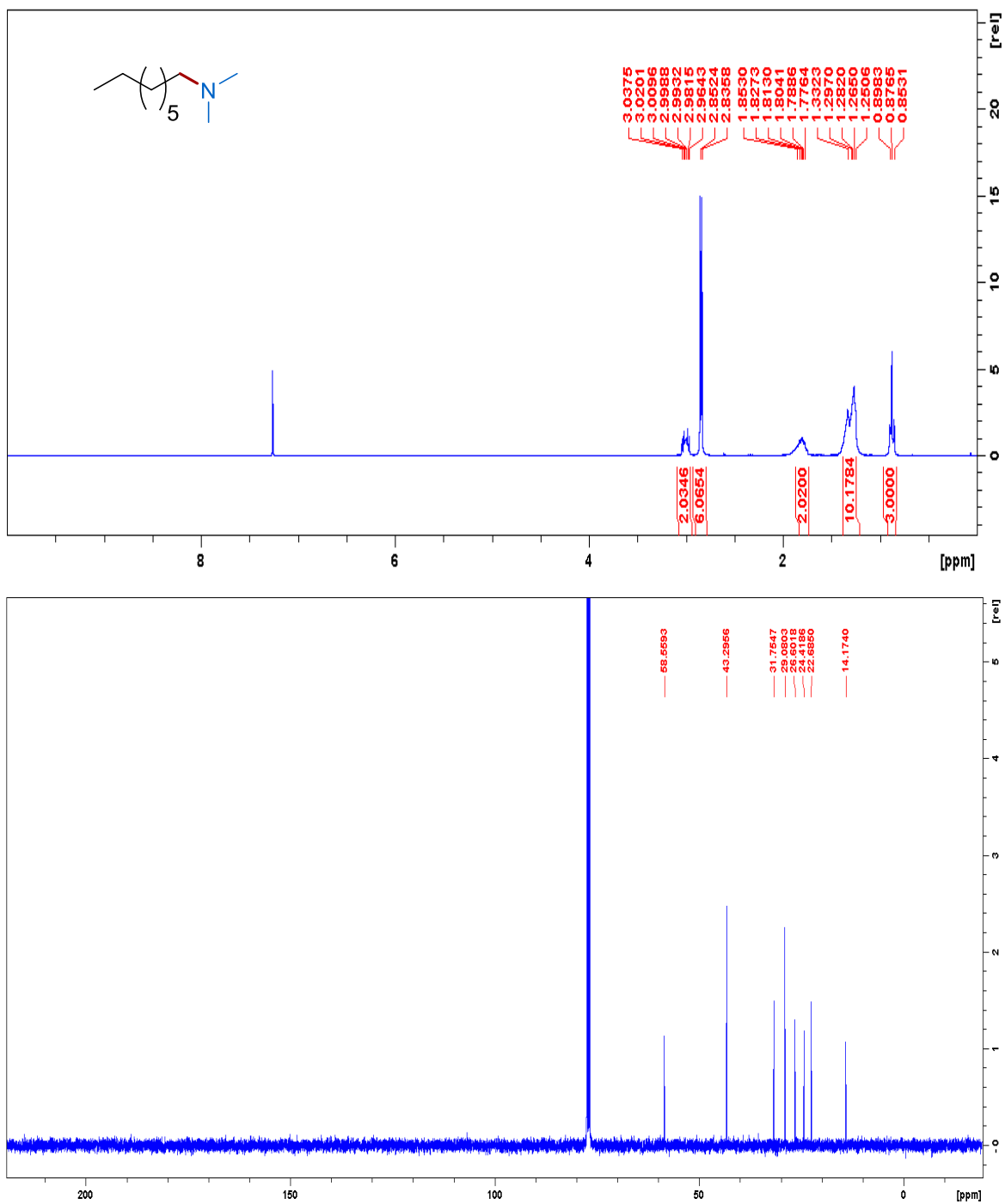
N,N-dimethyl-1-phenylbutan-1-amine (**3q**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



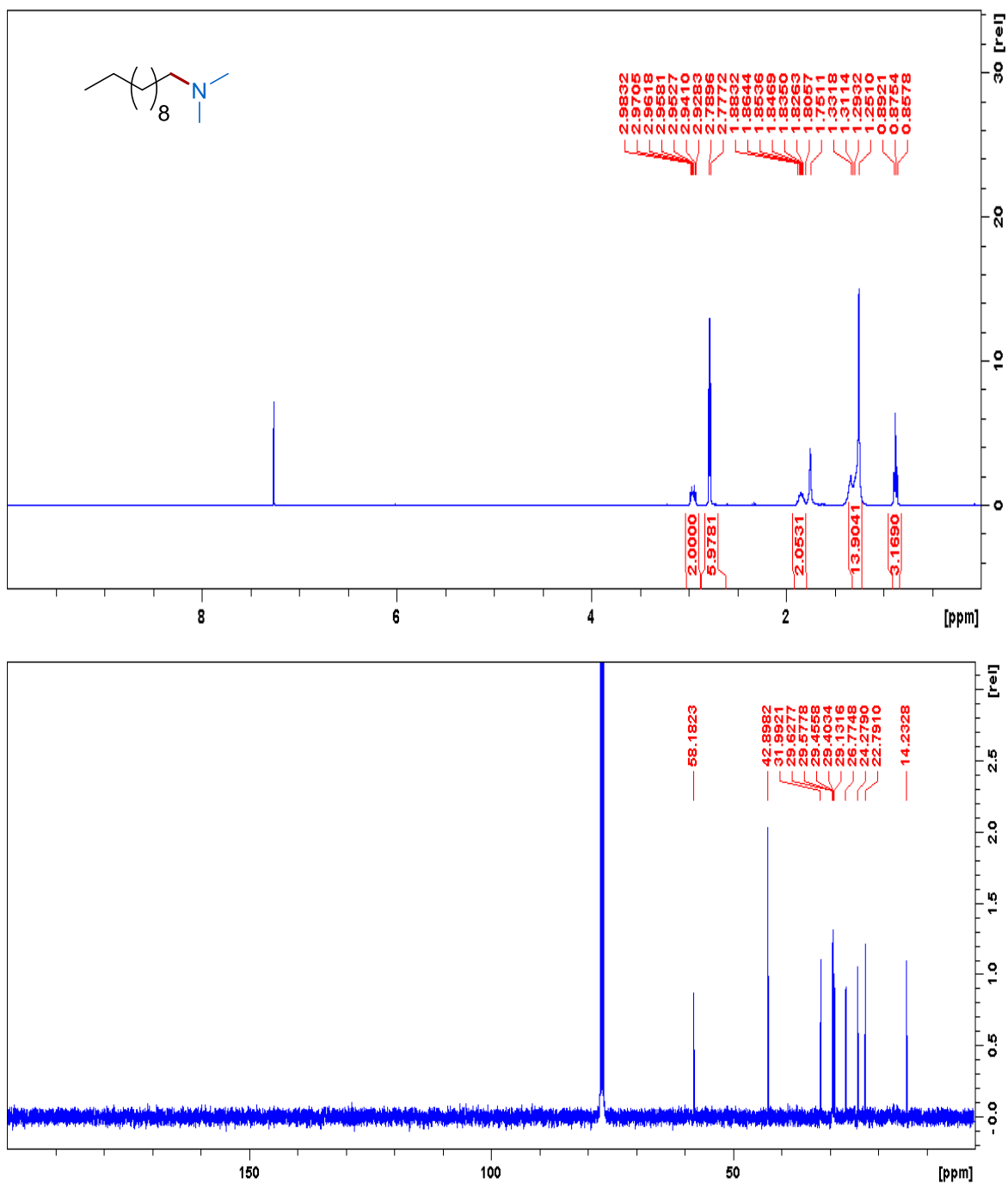
N,N-dimethyl-1-(naphthalen-2-yl)ethan-1-amine (**3r**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



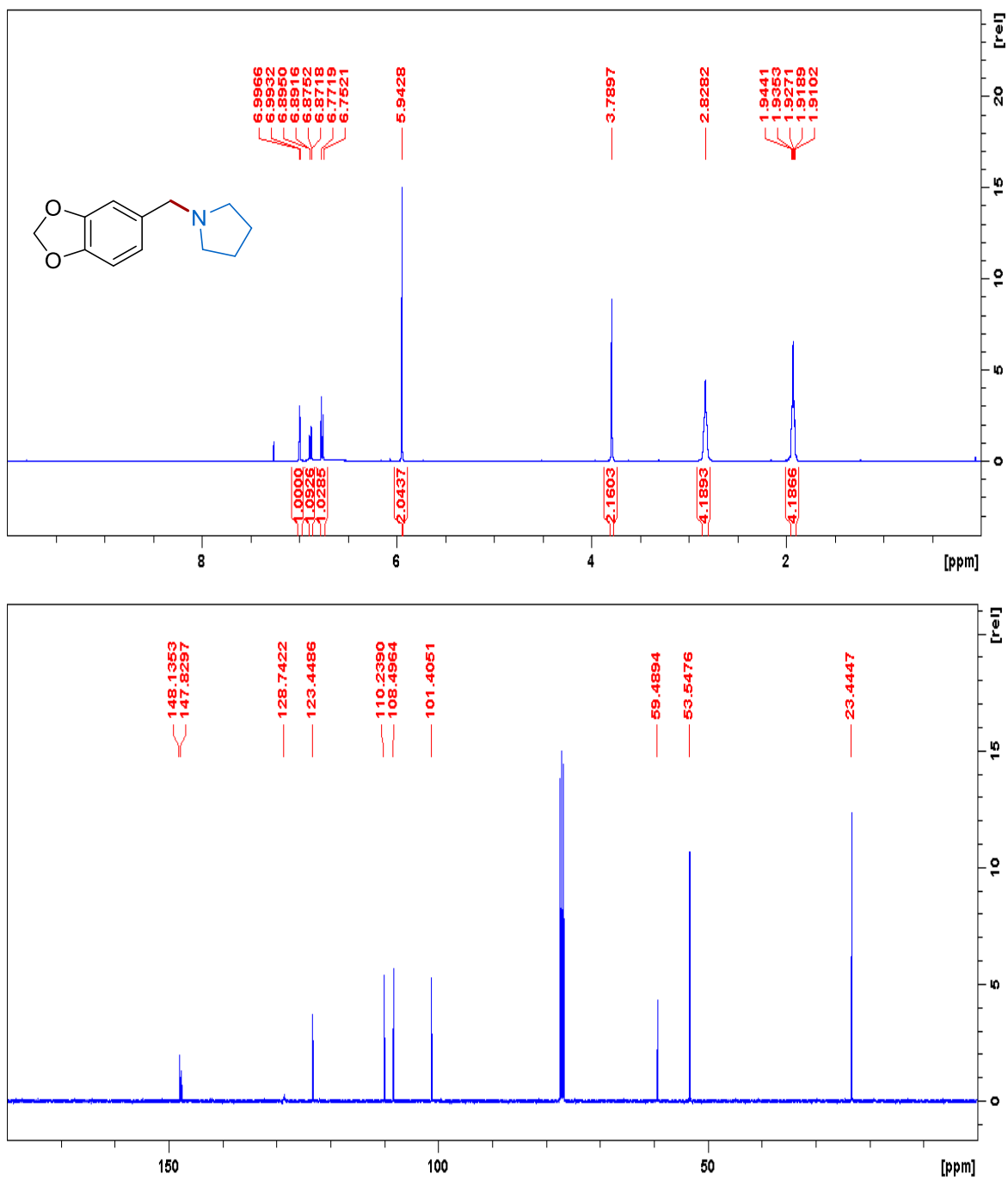
N,N-dimethyloctan-1-amine (**3s**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



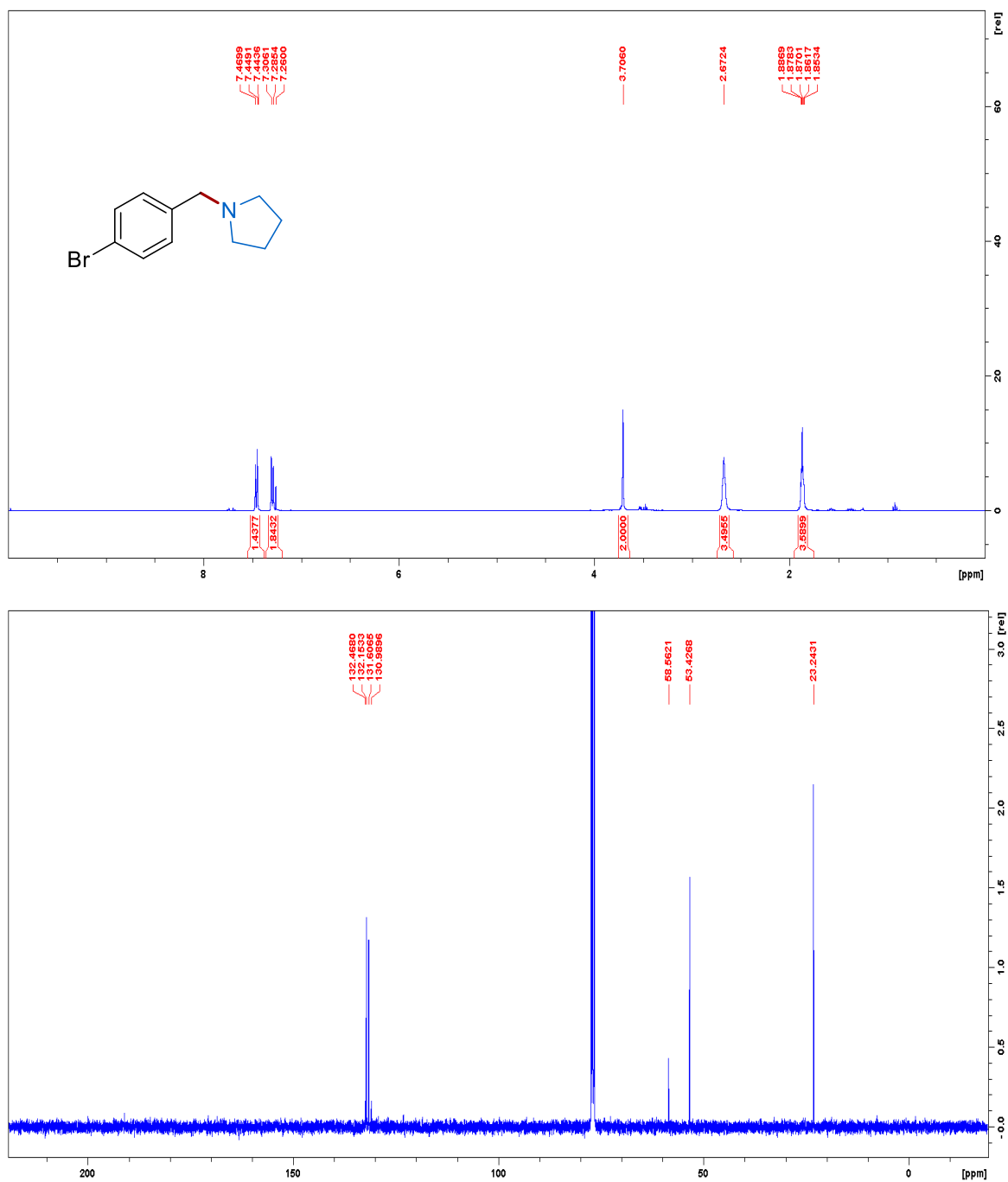
N,N-dimethyldecan-1-amine (**3t**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



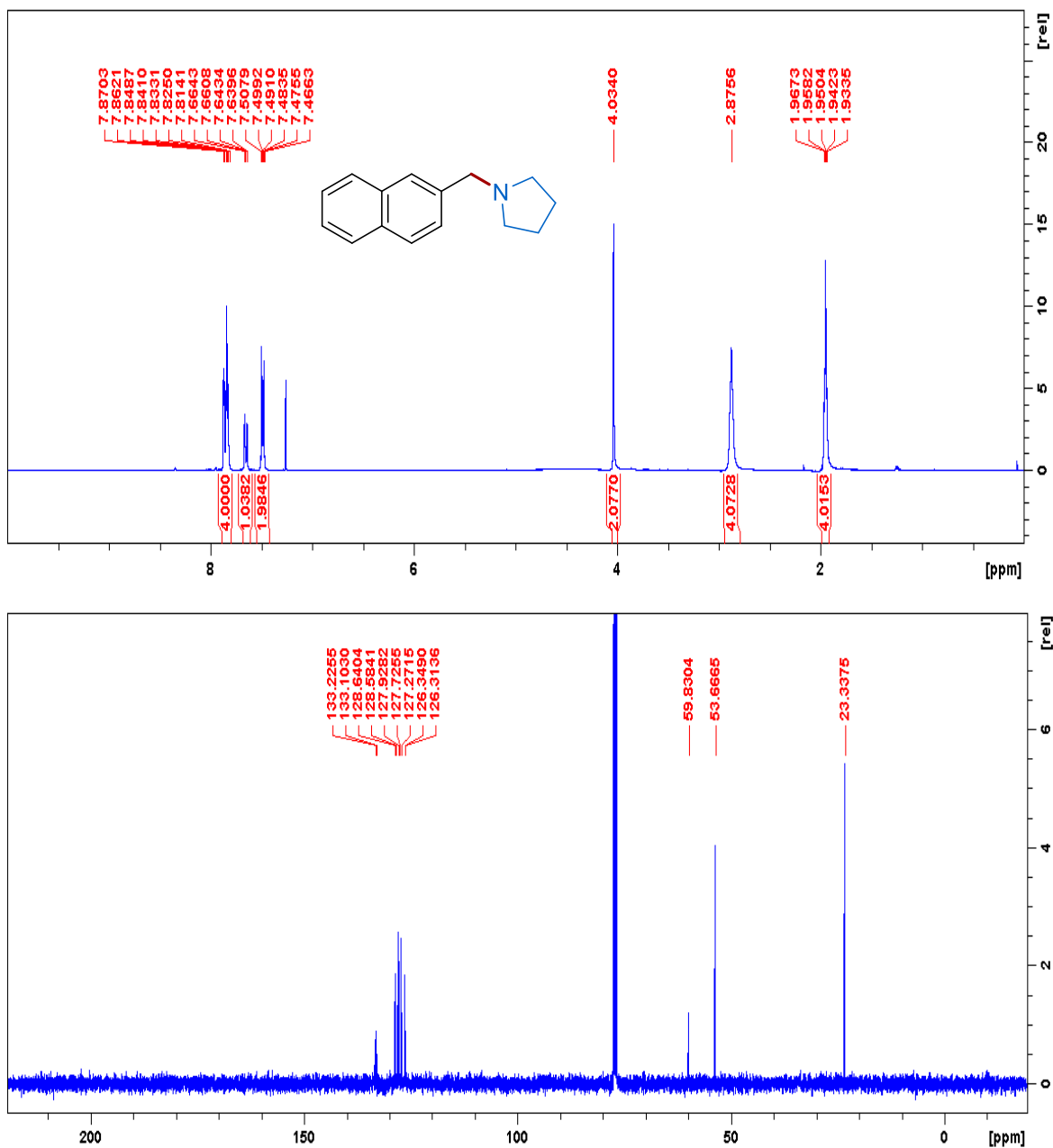
1-(Benzo[d][1,3]dioxol-5-ylmethyl)pyrrolidine (**4a**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



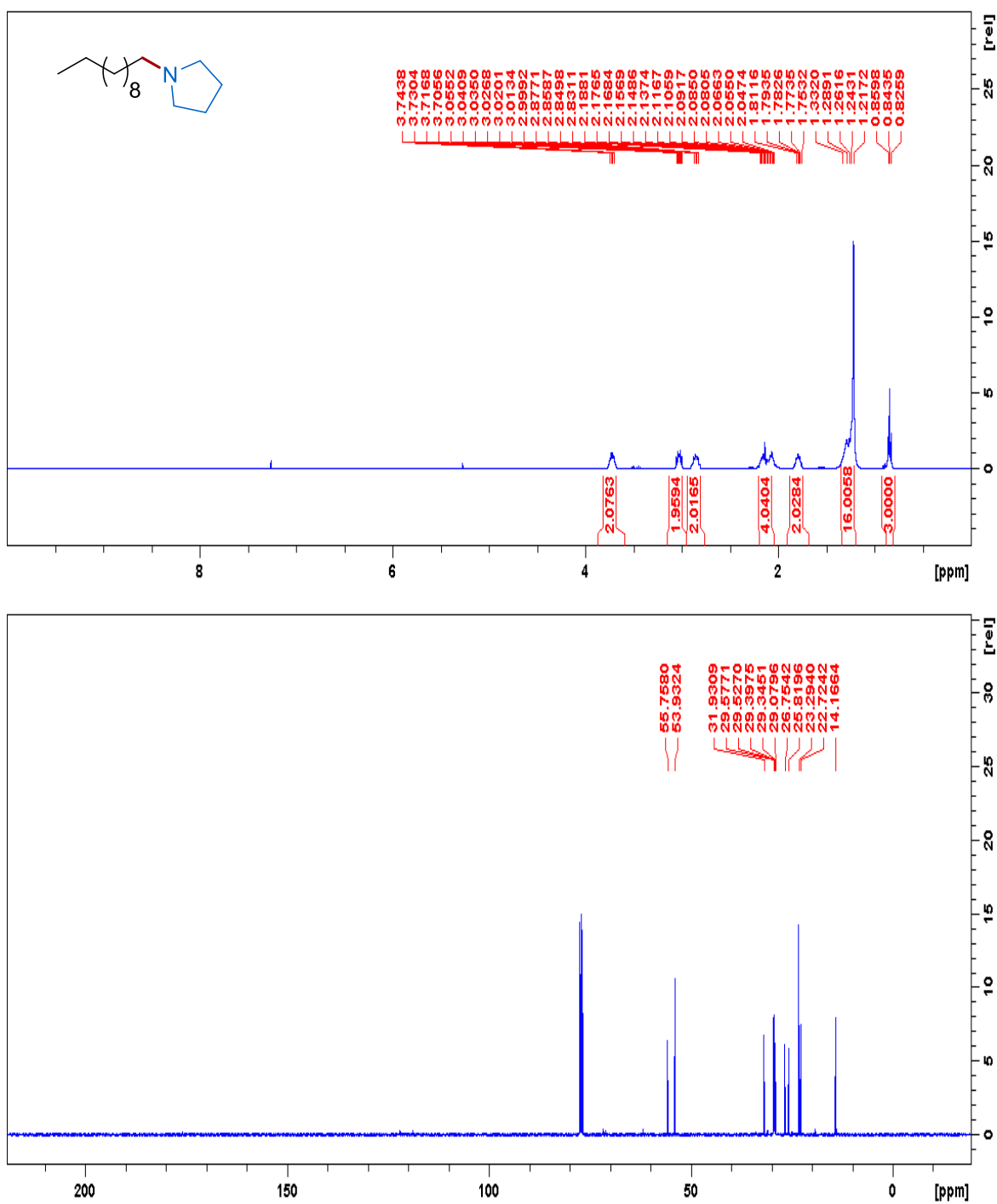
1-(4-Bromobenzyl)pyrrolidine (**4b**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



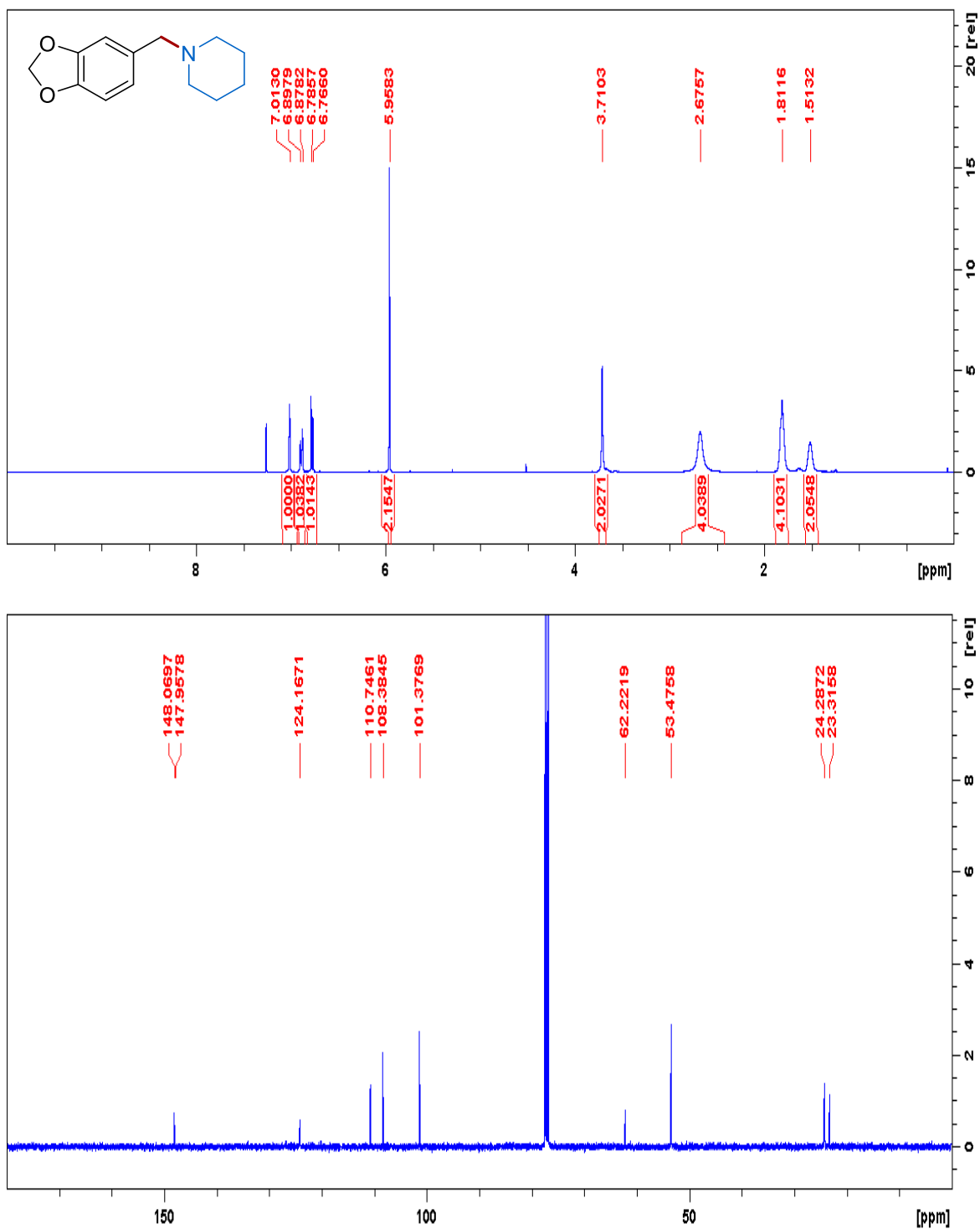
N-(1-Naphthylmethyl)pyrrolidine (**4c**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



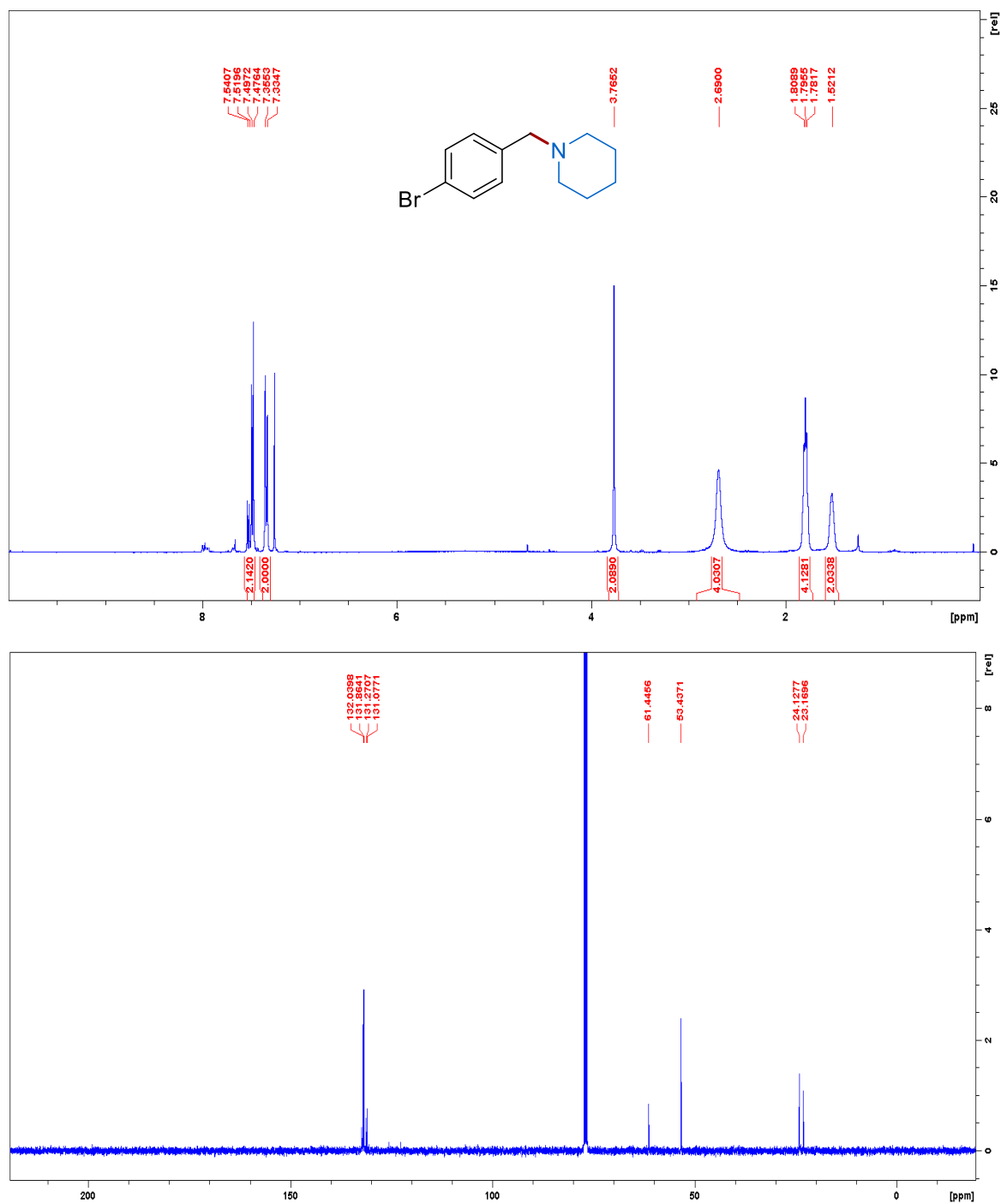
1-Undecylpyrrolidine (**4d**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



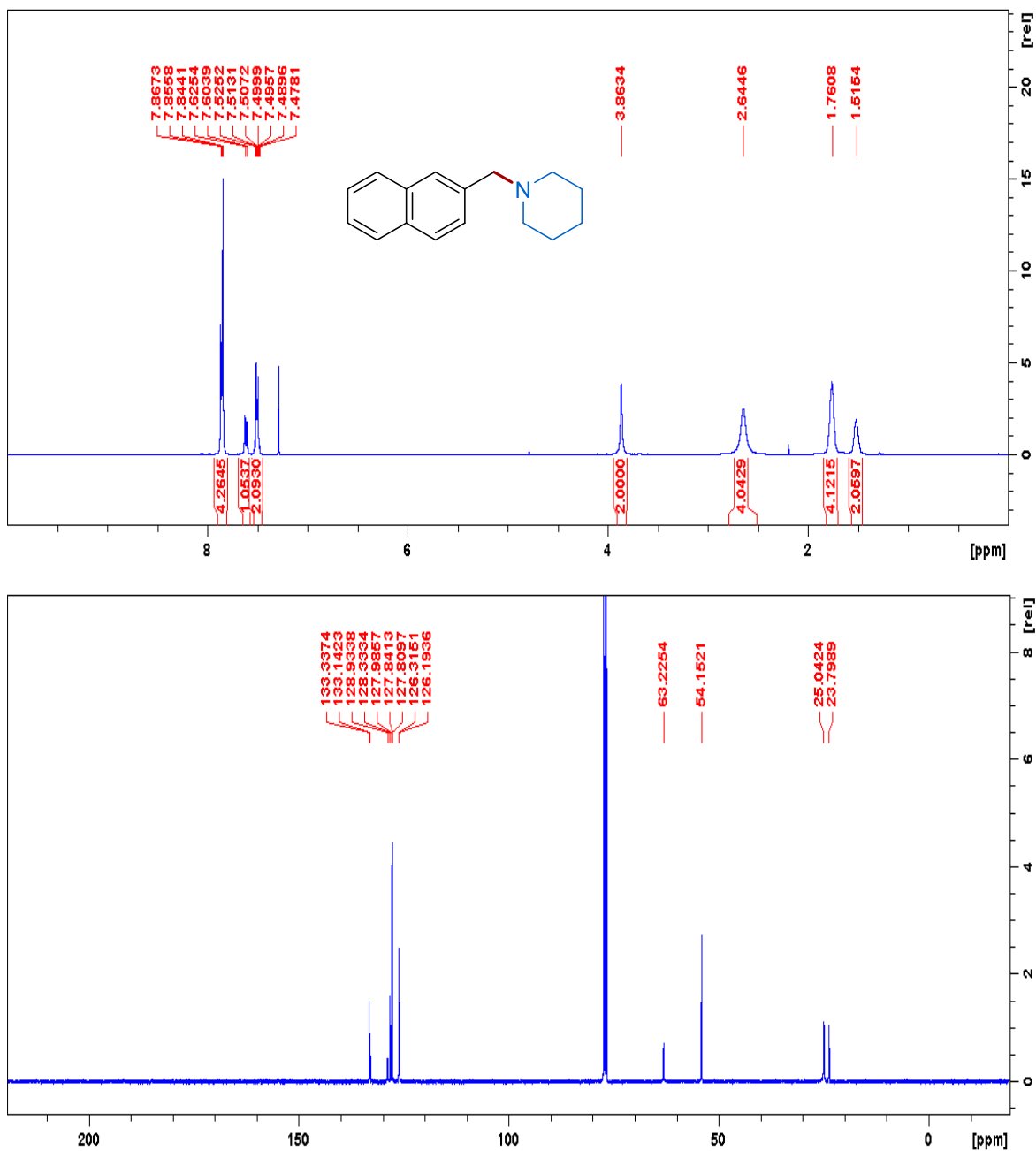
1-(Benzo[d][1,3]dioxol-5-ylmethyl)piperidine (**5a**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



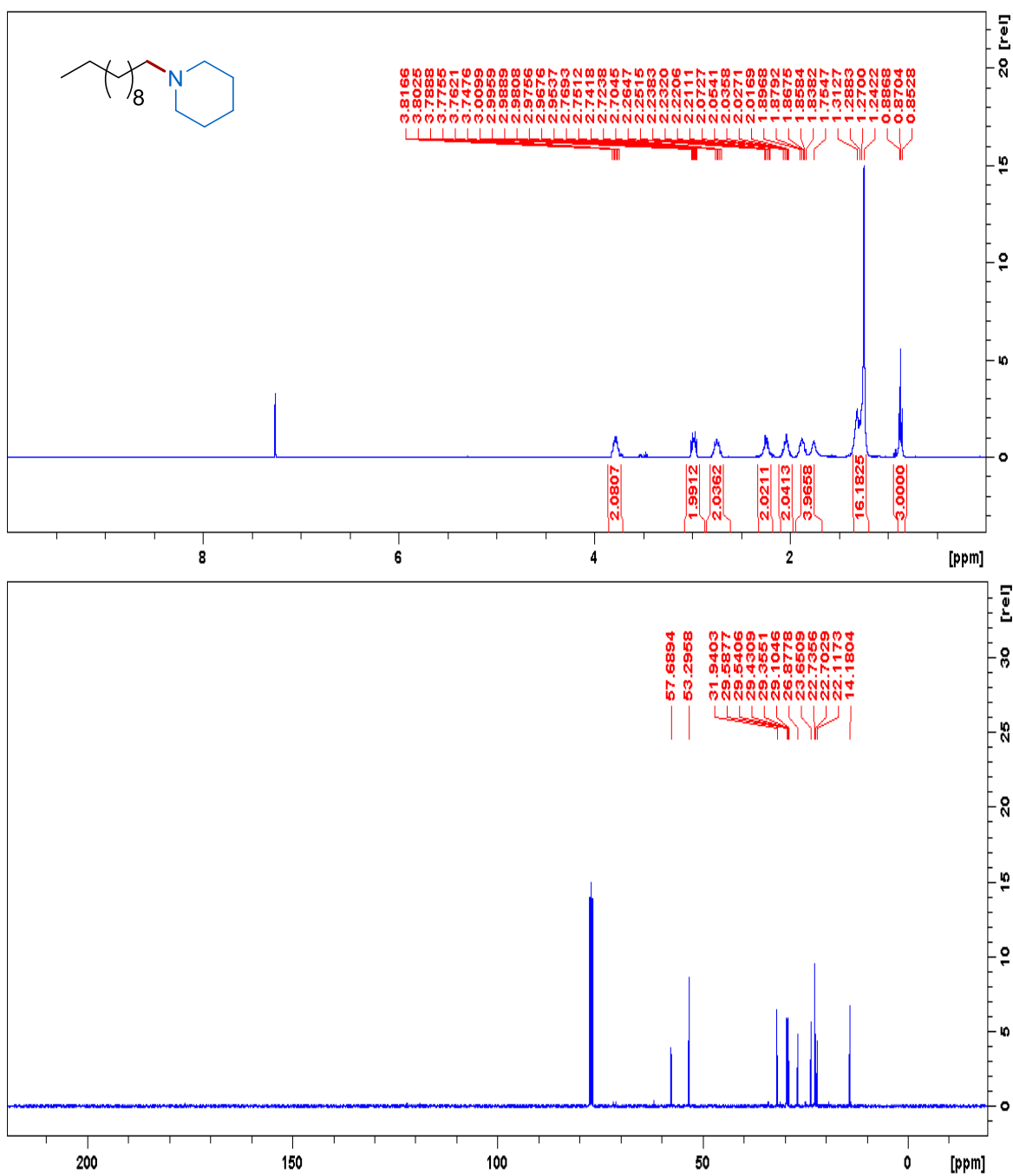
1-(4-Bromobenzyl)piperidine (**5b**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



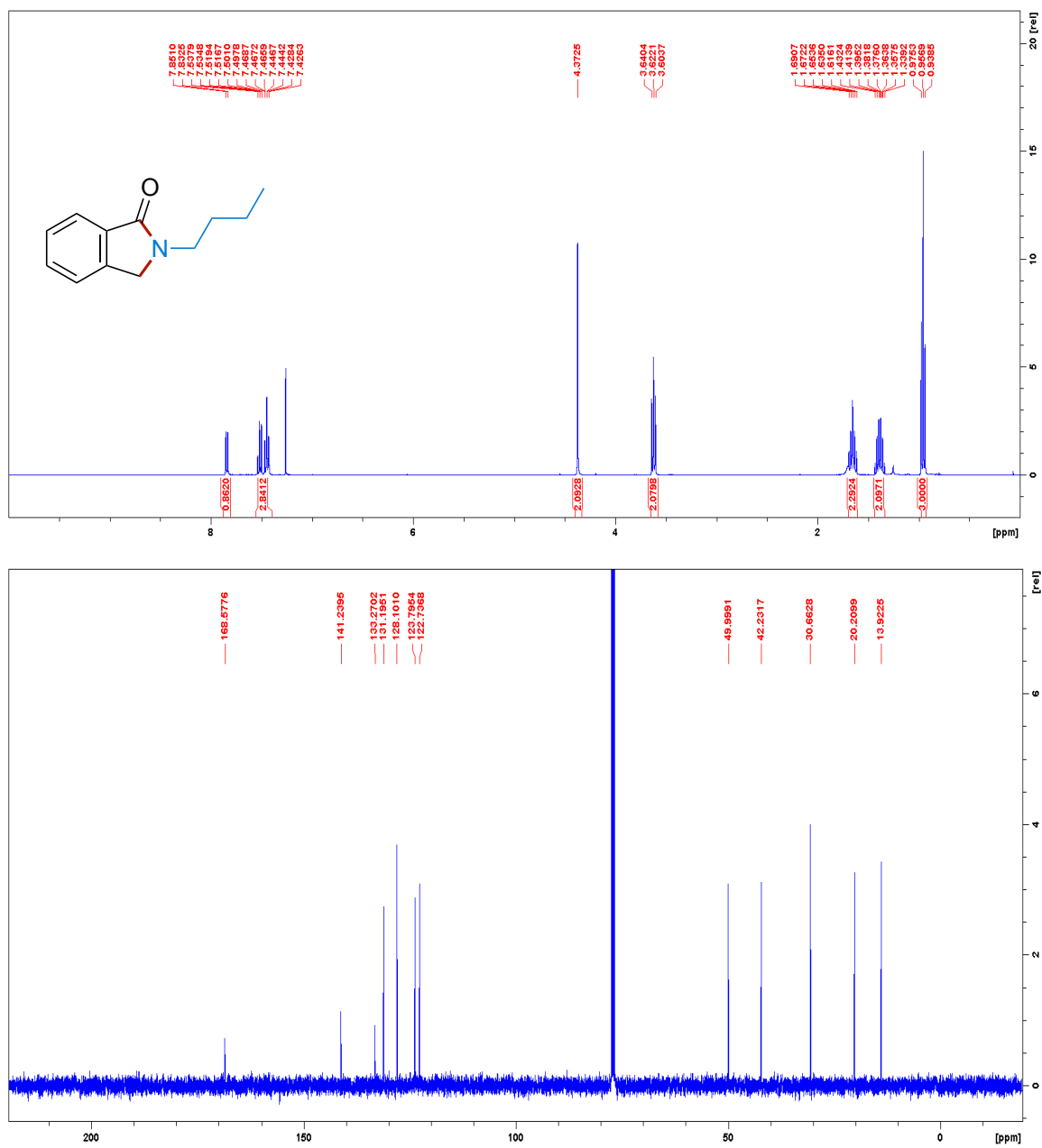
1-(Naphthalen-2-ylmethyl)piperidine (**5c**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



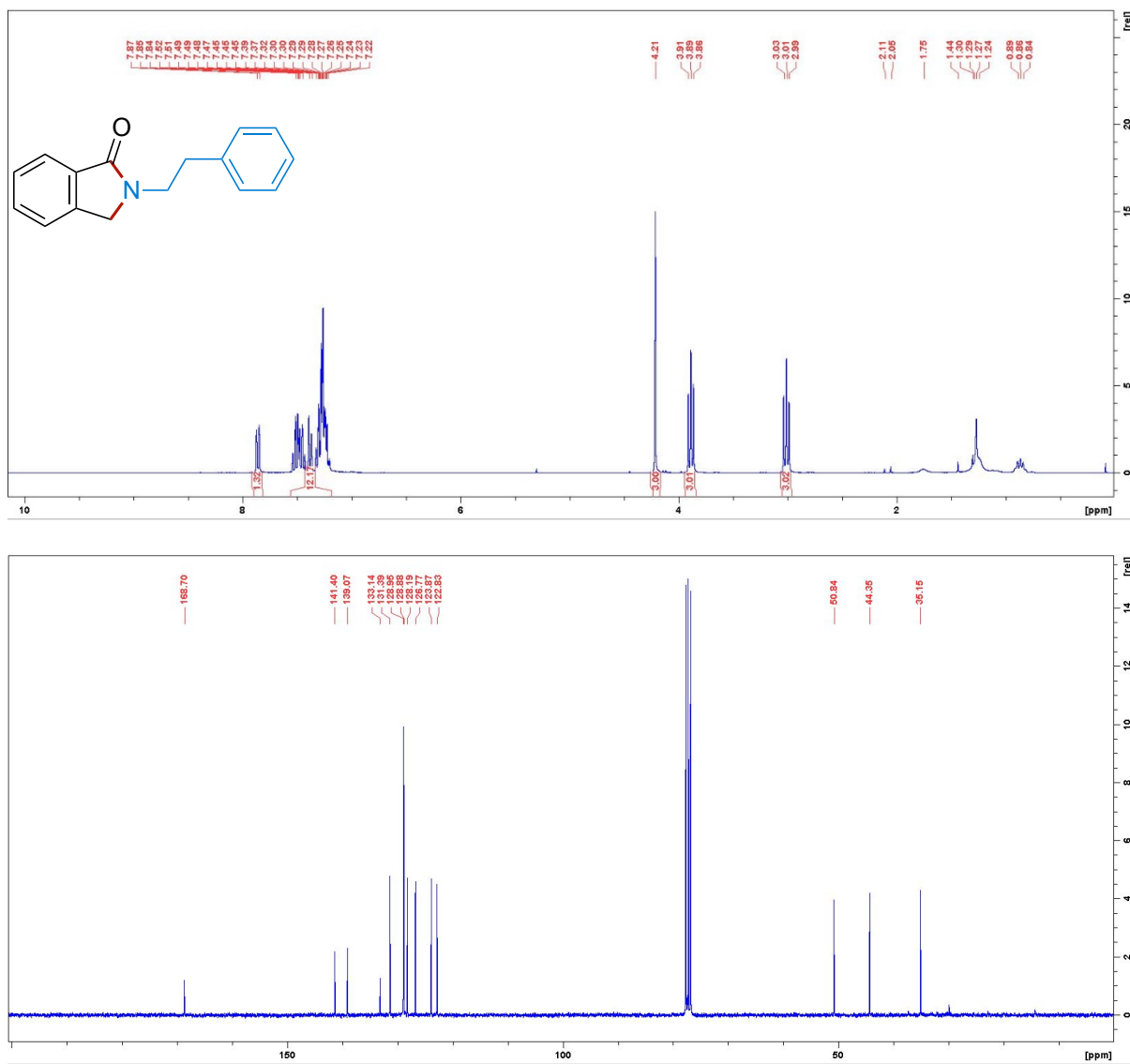
1-Undecylpiperidine (**5d**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



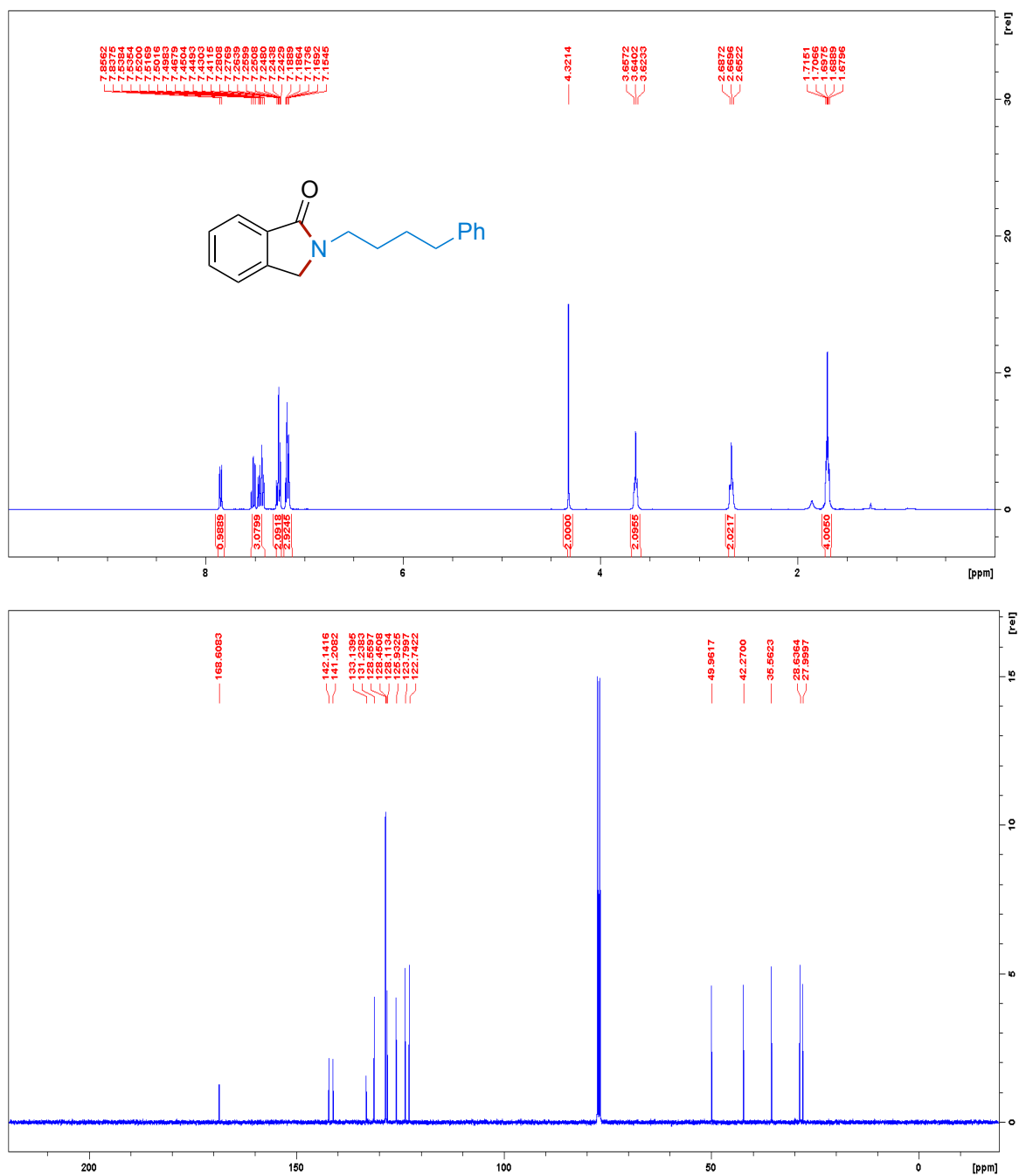
2-Butylisoindolin-1-one (**6a**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



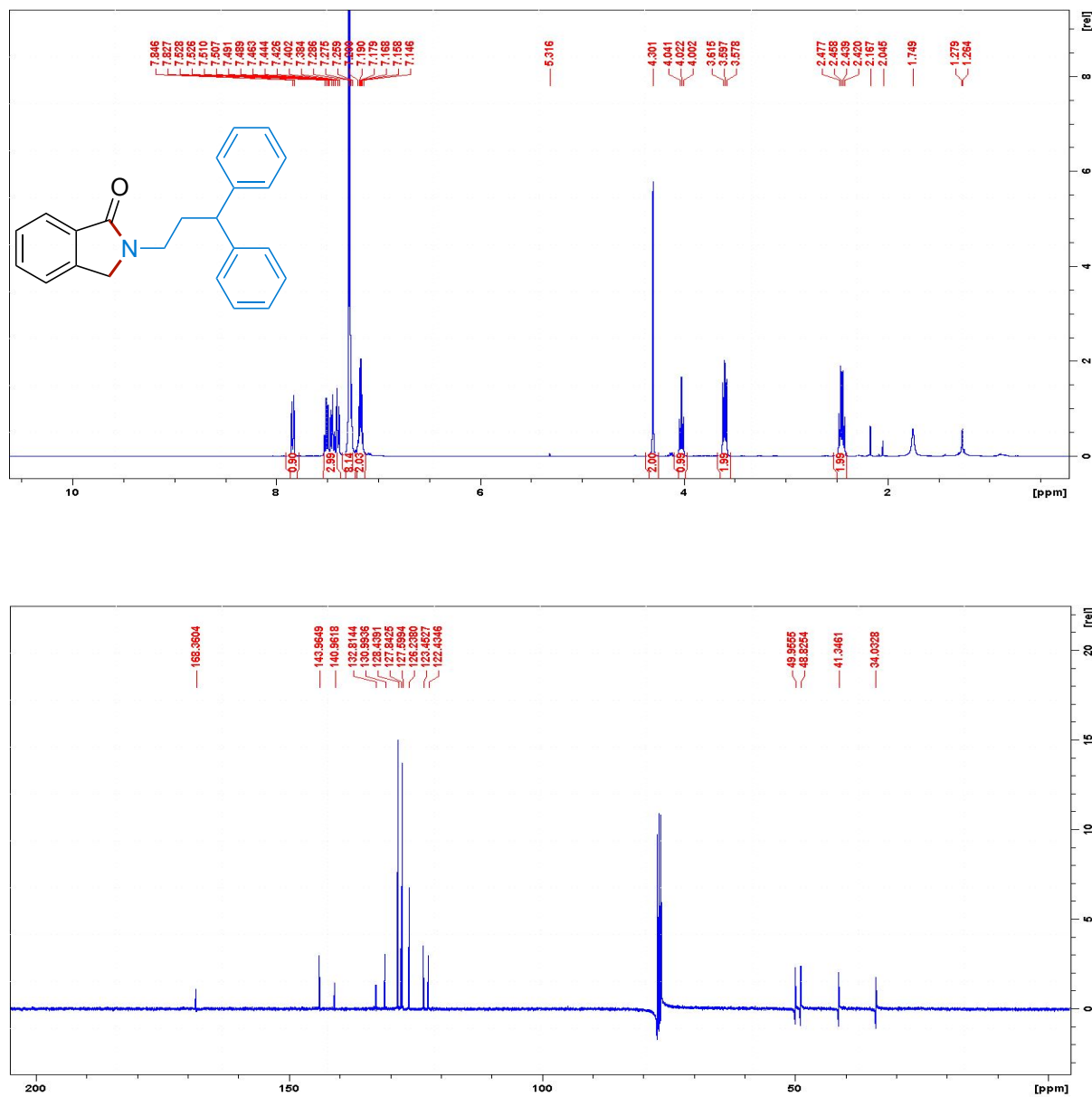
2-(2-Phenethyl)isoindol-1-one (**6b**); ^1H NMR (300 MHz, CDCl_3), ^{13}C NMR (75 MHz, CDCl_3).



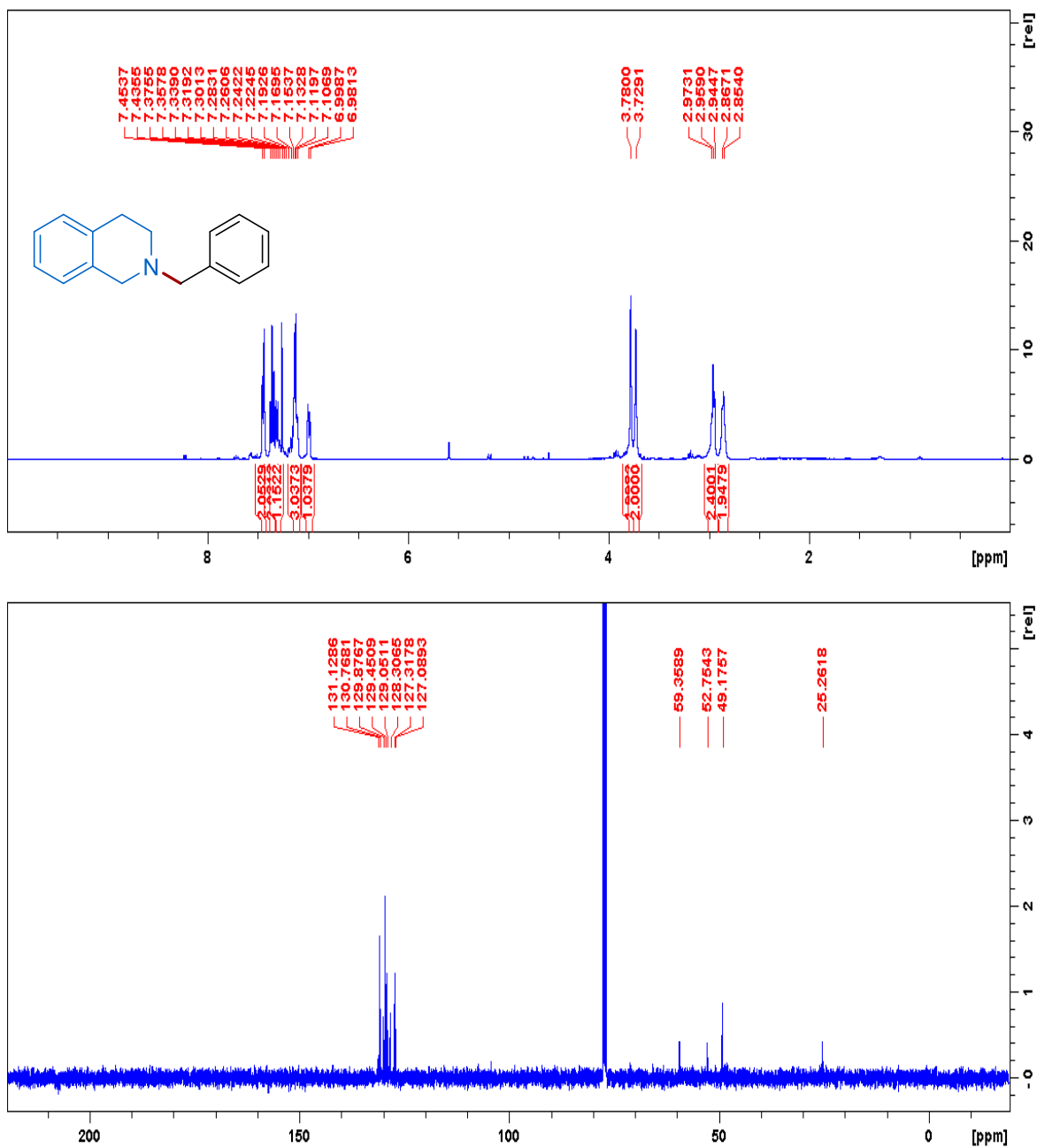
2-(4-Phenyl-butyl)isoindol-1-one (**6c**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



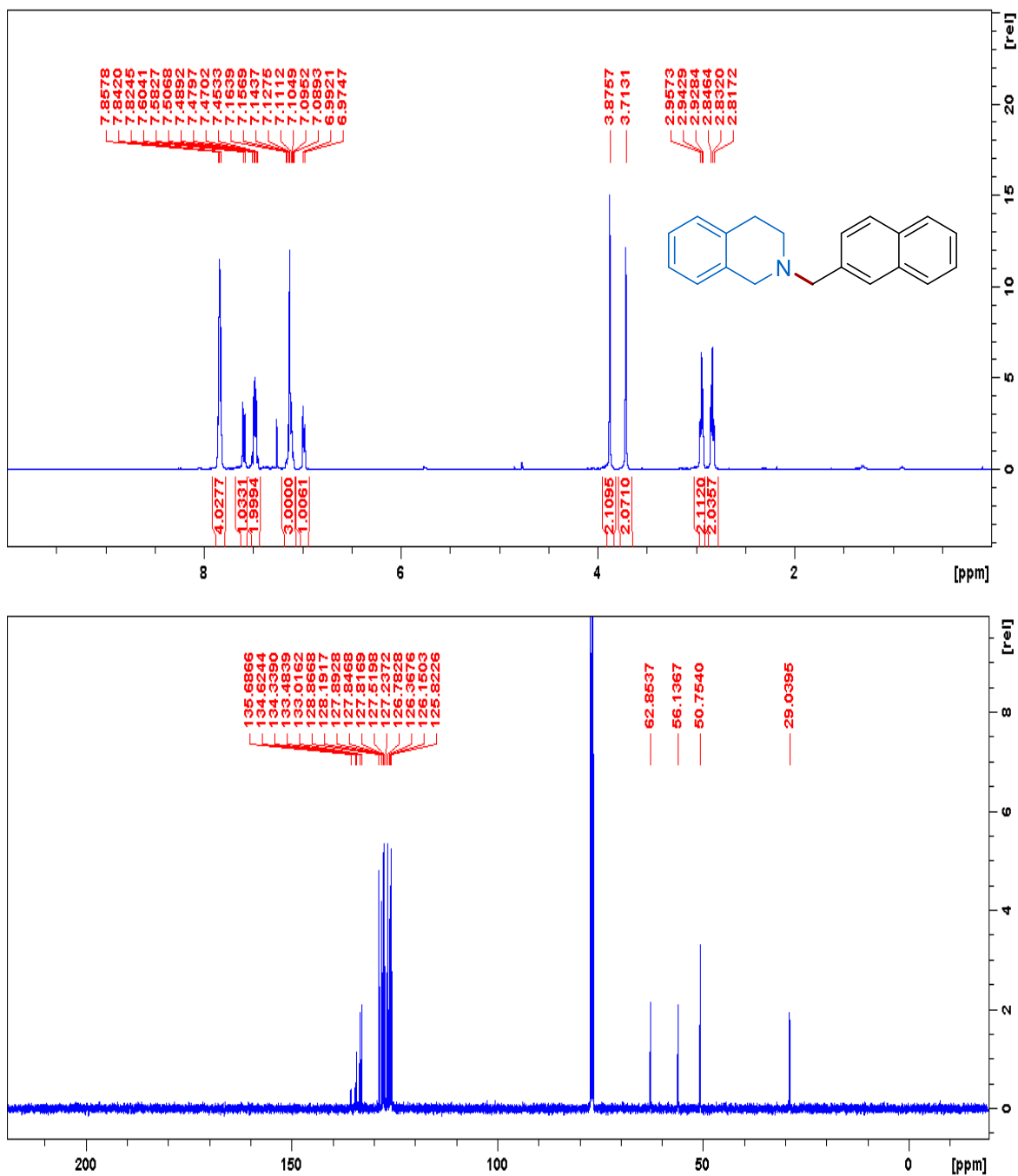
2-(3,3-diphenylpropyl)isoindolin-1-one (**6d**); ^1H NMR (300 MHz, CDCl_3), ^{13}C NMR (75 MHz, CDCl_3).



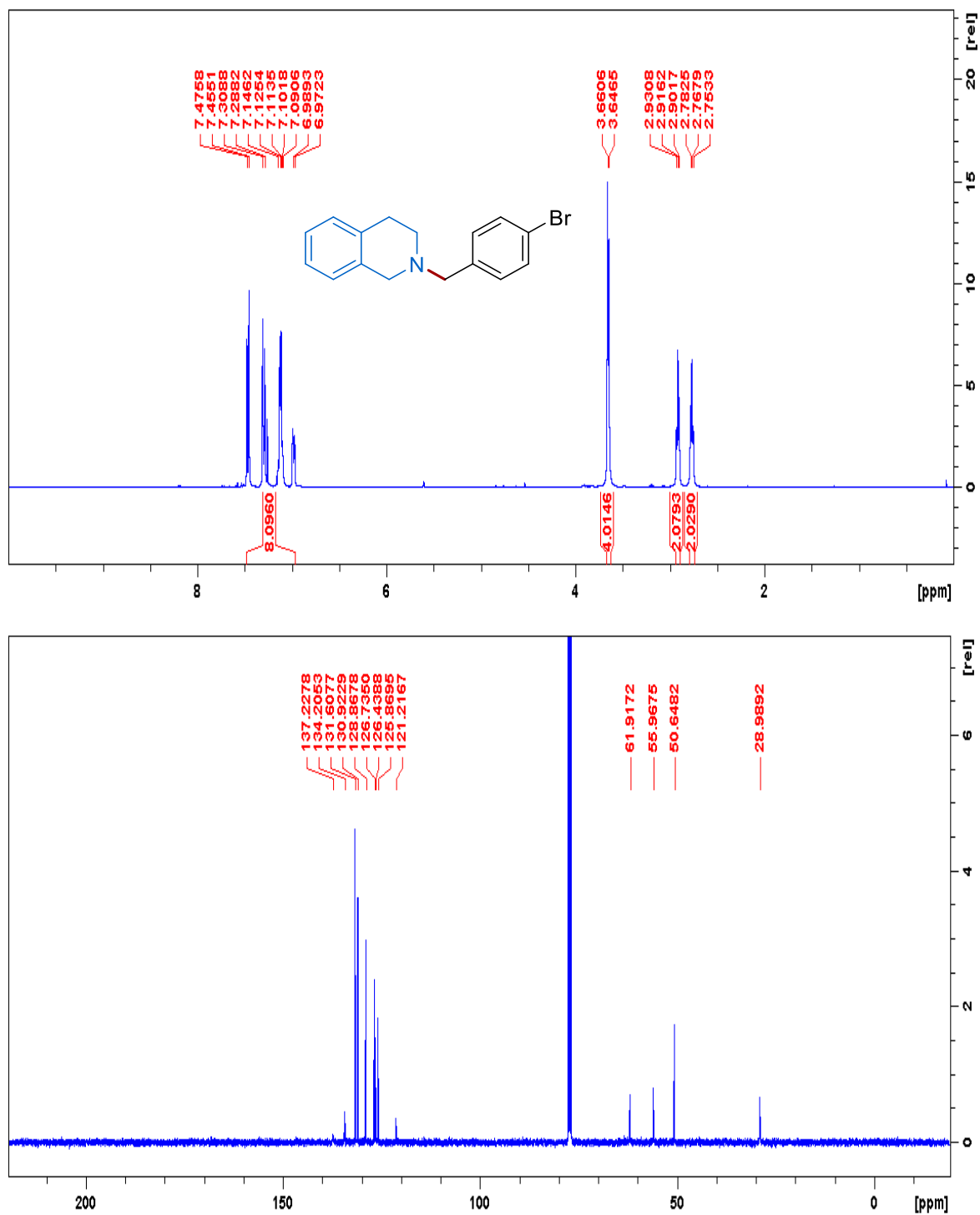
2-Benzyl-1,2,3,4-tetrahydroisoquinoline (**10a**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



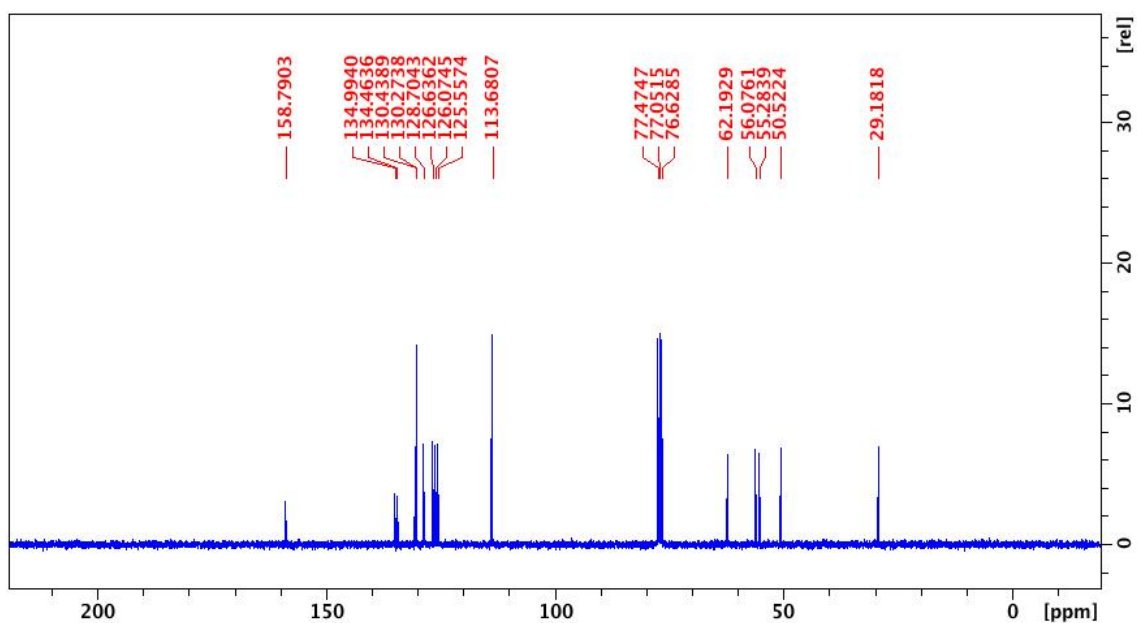
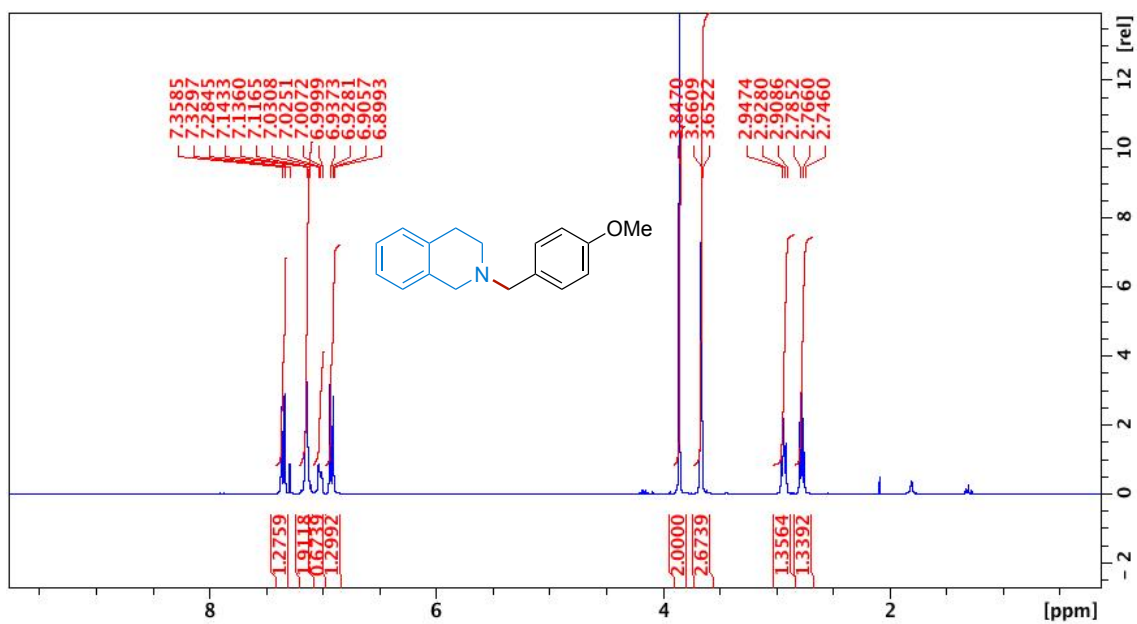
2-(Naphthalen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline (**10b**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



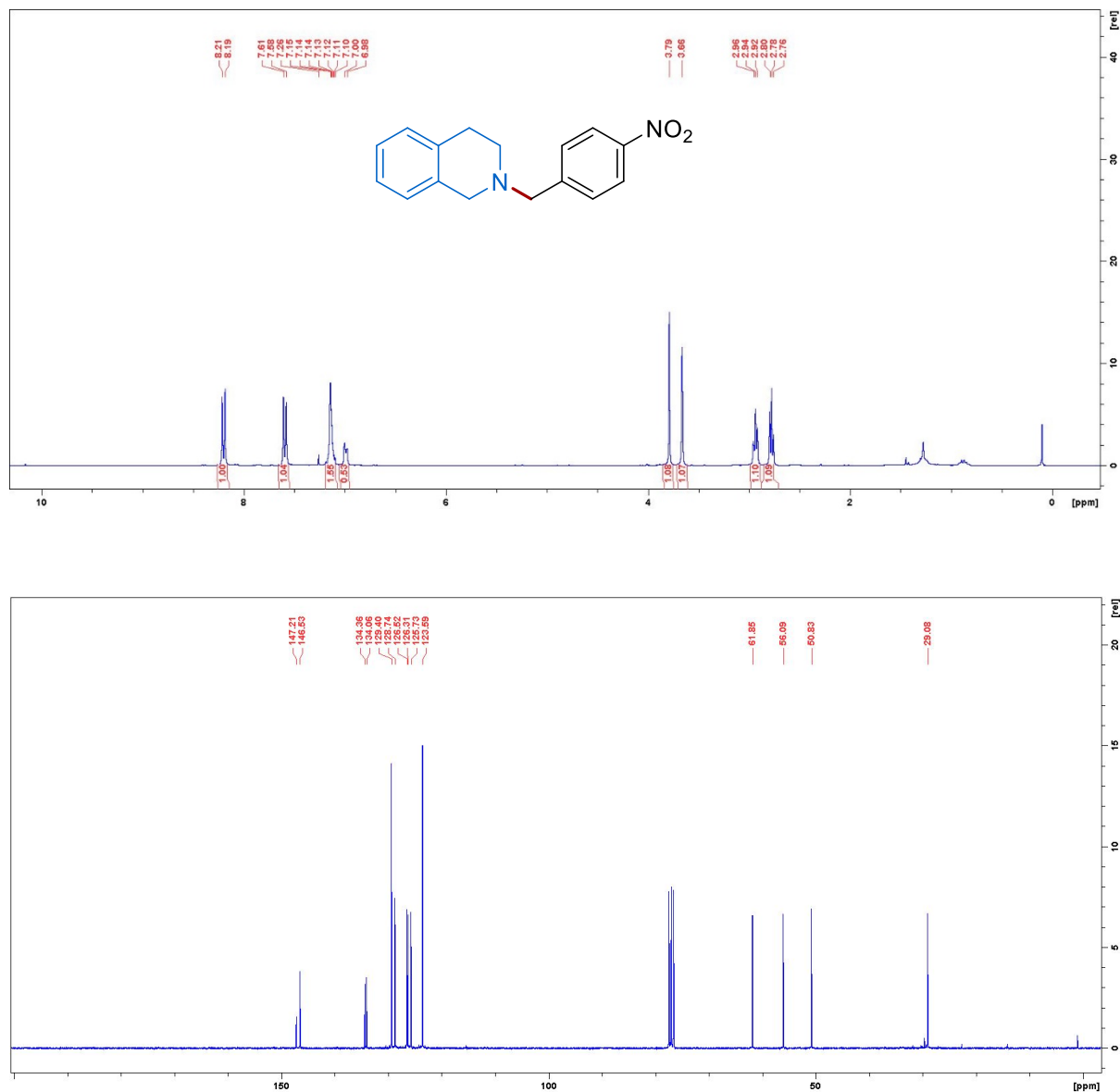
2-(4-Bromobenzyl)-1,2,3,4-tetrahydroisoquinoline (**10c**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



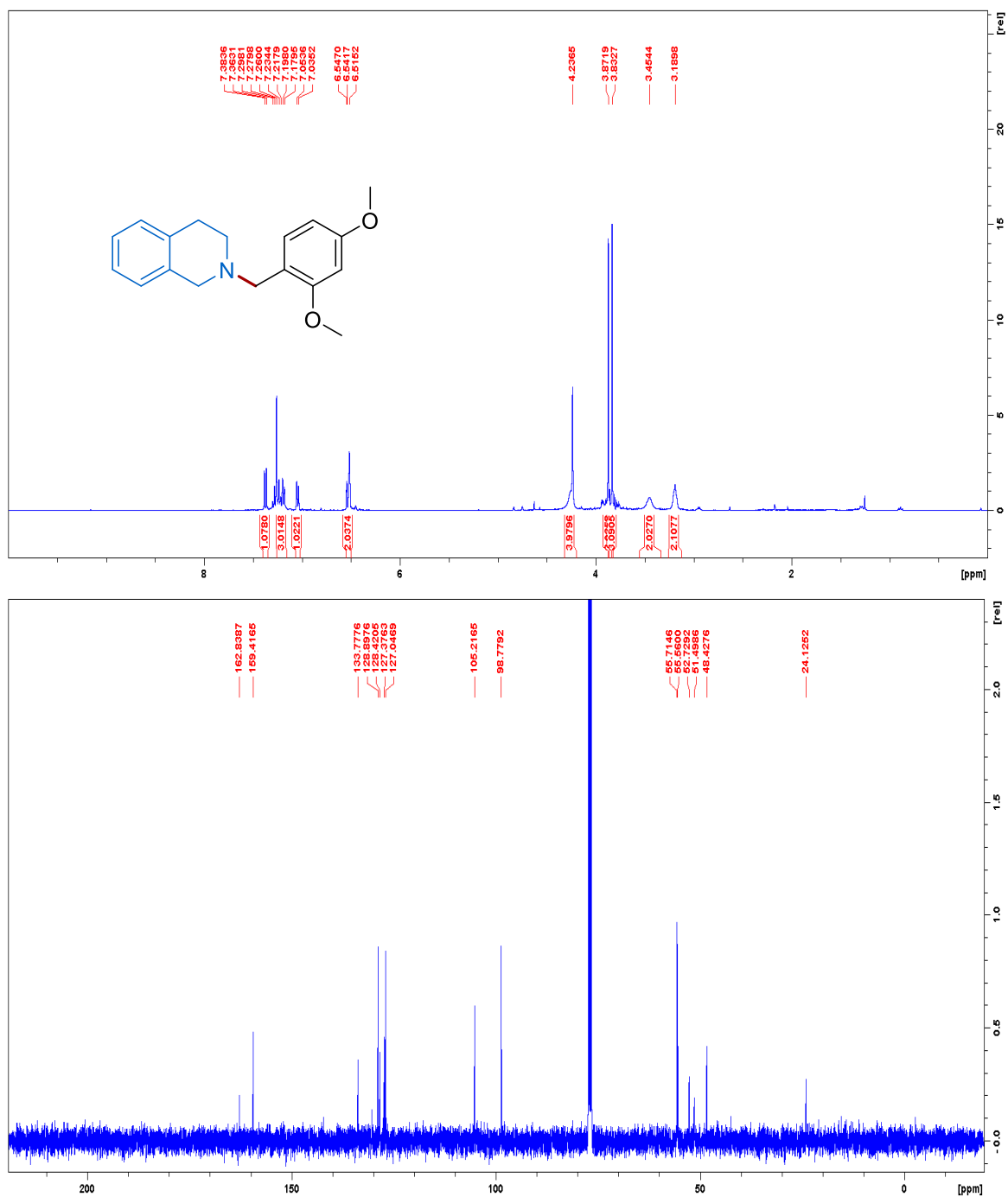
2-(4-methoxybenzyl)-1,2,3,4-tetrahydroisoquinoline (**10d**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



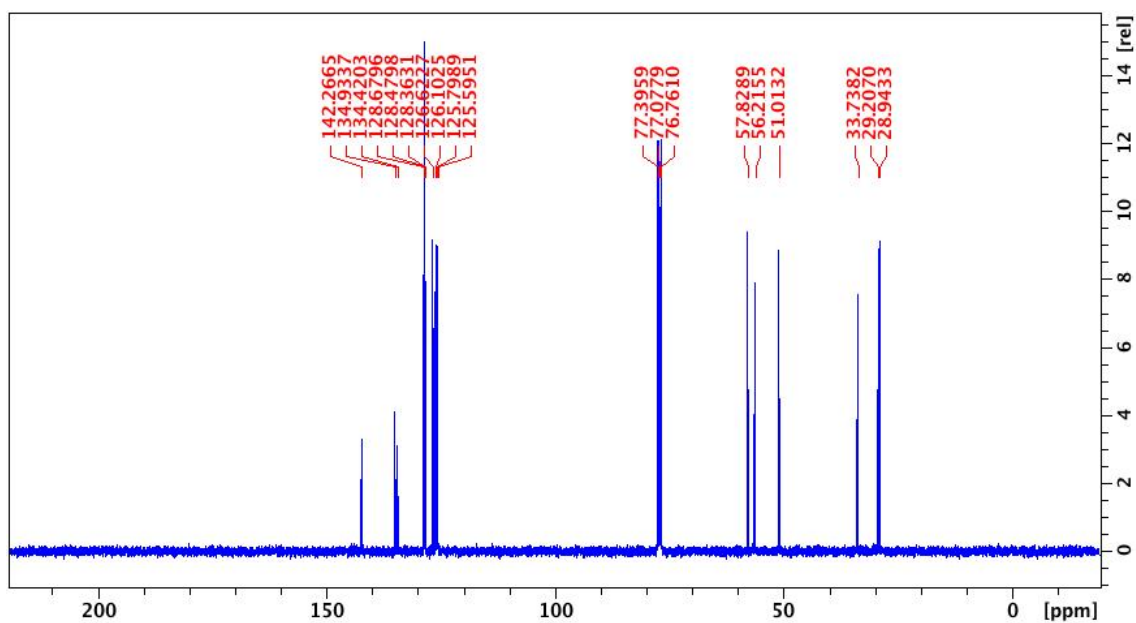
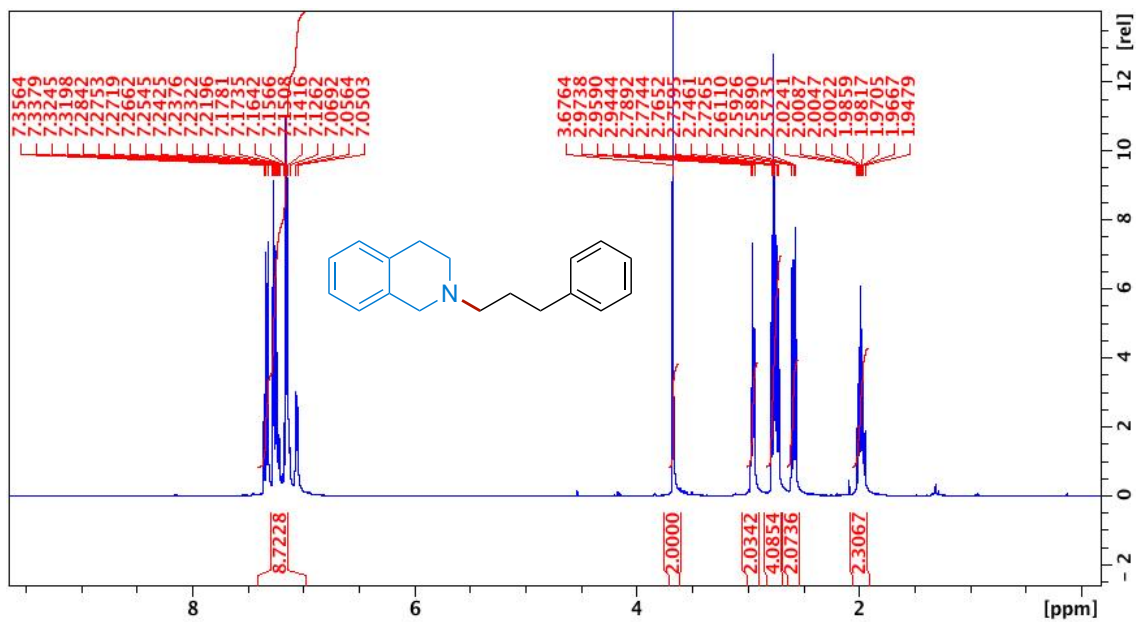
2-(4-Nitrobenzyl)-1,2,3,4-tetrahydroisoquinoline (**10e**); ¹H NMR (300 MHz, CDCl₃), ¹³C NMR (75 MHz, CDCl₃).



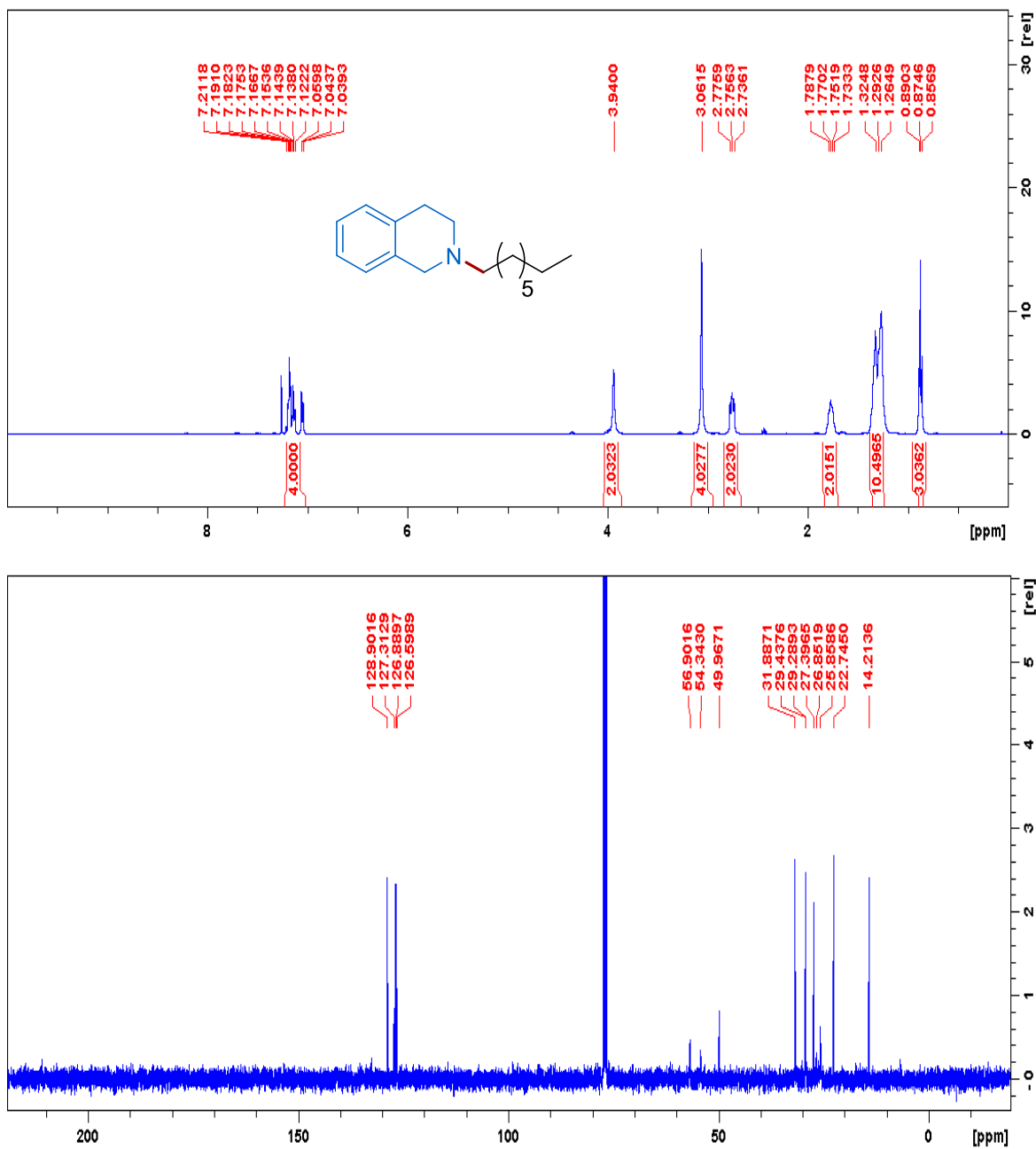
2-(2,4-dimethoxybenzyl)-1,2,3,4-tetrahydroisoquinoline (**10f**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



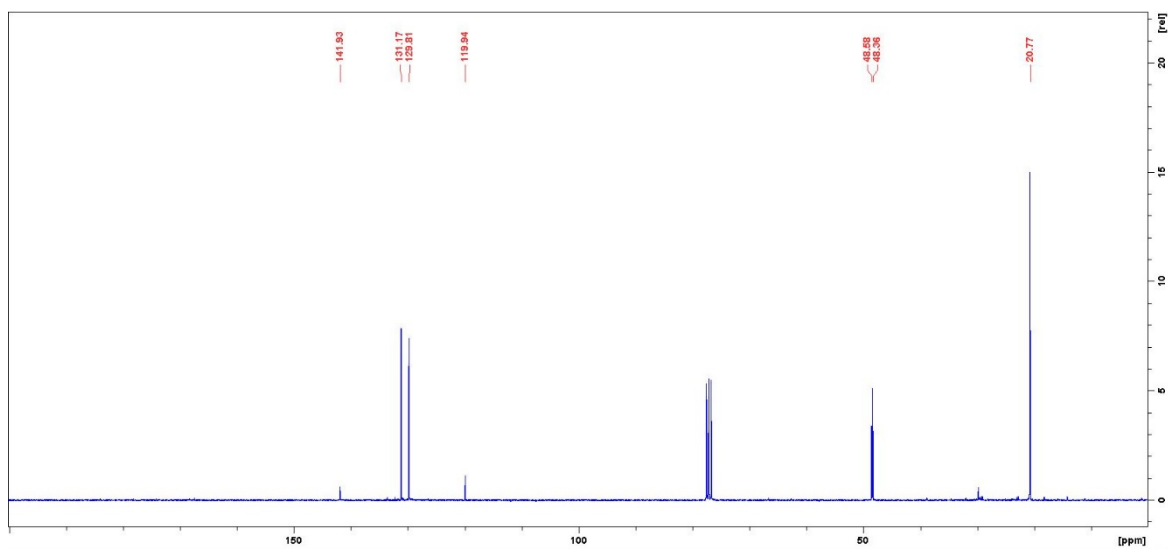
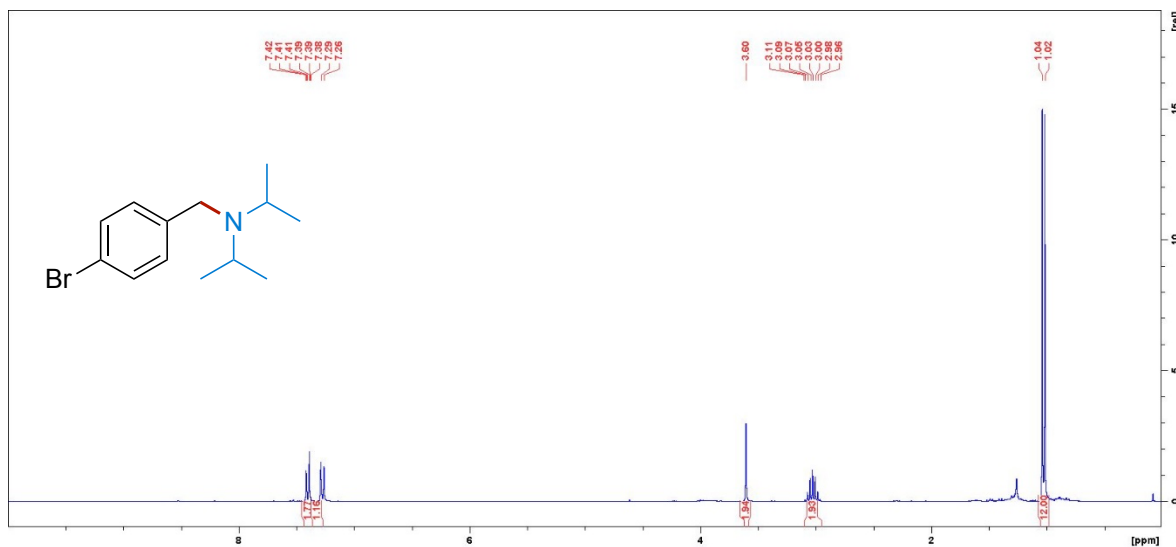
2-(3-phenylpropyl)-1,2,3,4-tetrahydroisoquinoline (**10g**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



2-Octyl-1,2,3,4-tetrahydroisoquinoline (**10h**); ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100 MHz, CDCl_3).



N-(4-bromobenzyl)-*N*-isopropylpropan-2-amine (**13a**); ^1H NMR (300 MHz, CDCl_3), ^{13}C NMR (75 MHz, CDCl_3).



N-isopropyl-*N*-(naphthalen-2-ylmethyl)propan-2-amine (**13b**); ¹H NMR (300 MHz, CDCl₃), ¹³C NMR (75 MHz, CDCl₃).

