

Enantioselective Metal/Organo-Catalyzed Aerobic Oxidative sp^3 C-H Olefination of Tertiary Amines Using Molecular Oxygen as the Sole Oxidant

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Supporting information

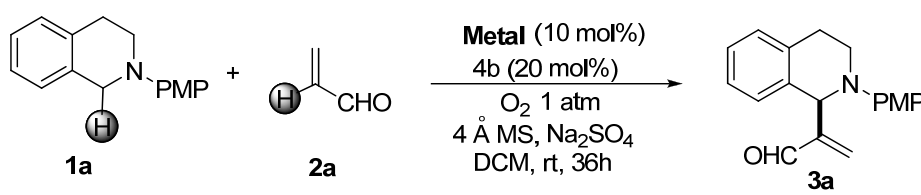
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1.0 General Methods

All reactions were carried out under an argon atmosphere condition unless otherwise noted and solvents were dried according to established procedures. Reactions were monitored by thin layer chromatography (TLC), column chromatography purifications were carried out using silica gel GF254. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on Bruker 300 MHz spectrometer in CDCl_3 unless otherwise noted and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Bruker 300 MHz spectrometer in CDCl_3 using tetramethylsilane (TMS) as internal standard unless otherwise noted. Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, cm = complex multiplet) and coupling constant in Hertz (Hz). Infrared (IR) spectra were recorded on a FT-IR spectrometer. Optical rotations were recorded on a Perkin-Elmer 341 polarimeter. HR-MS was measured with an APEX II 47e mass spectrometer. Melting points were measured on an XT-4 melting point apparatus and were uncorrected. The ee values determination was carried out using chiral high-performance liquid chromatography (HPLC) with Daicel Chiracel AD-H or OD-H column on Waters with a 2996 UV-detector. *N*-aryl tetrahydroisoquinolin, and organocatalysts **4h-n** were prepared according to the previous reported procedures.^{[1], [2], [3], [4], [5]}

2.0. The Metal, Solvent and *N*-Protecting Group Optimization Results

Table S1. The metal optimization results^[a]

			
Entry	Metal	Yield [%] ^[b]	Ee [%] ^[c]
1	AgOTf	55	-47
2	Yb(OTf) ₃	68	59
3	CuOTf	51	43
4	Cu(OTf)₂	70	91
5	Cu(OAc) ₂	45	24
6	CuBr	53	-19
7	CuBr ₂	38	-13
8	CuCl	41	-27
9	Pd(OAc) ₂	36	24
10	Mg(OTf) ₂	62	52

11	Zn(OTf) ₂	57	55
12	Sc(OTf) ₃	60	43

[a] Unless otherwise specified, the reaction was carried out with **1a** (0.1 mmol) and **2a** (0.2 mmol) in the presence of metal salts (0.01 mmol) and **4b** (0.02 mmol), 4 Å molecular sieve (100 mg), anhydrous Na₂SO₄ (0.3 mmol), and DCM (1.0 mL) under 1 atm molecular oxygen at room temperature for 36 h. [b] Isolated yield. [c] Determined by HPLC on chiral stationary phase.

Table S2. The Solvent optimization results ^[a]

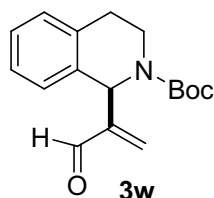
Entry	Solvent	Yield [%] ^[b]	Ee [%] ^[c]
1	Tol	69	71
2	THF	<10	n.d. ^[d]
3	MeCN	76	69
4	DCM	71	90
5	EtOH	<10	n.d. ^[d]
6	CHCl ₃	63	70
7	Xylene	58	67
8	Dioxane	<10	n.d. ^[d]
9	DMF	<10	n.d. ^[d]
10	Et ₂ O	<10	n.d. ^[d]

[a] Unless otherwise specified, the reaction was carried out with **1a** (0.1 mmol) and **2a** (0.2 mmol) in the presence of Cu(OTf)₂ (0.01 mmol) and **4b** (0.02 mmol), 4 Å molecular sieve (100 mg), anhydrous Na₂SO₄ (0.3 mmol), and solvent (1.0 mL) at under 1 atm molecular oxygen at room temperature for 36 h. [b] Isolated yield. [c] Determined HPLC on chiral stationary phase. [d] Not determined.

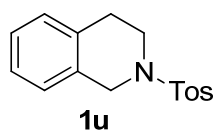
Table S3. The optimization of *N*-protecting groups of tetrahydroisoquinolines ^[a]

Entry	Pg	Yield [%] ^[b]	Ee [%] ^[c]
1	1s /H	n.d. ^[d]	n.d. ^[d]
2	1t /Boc	3w /56	50
3	1u /Tos	<10	n.d. ^[d]
4	1a / PMP	70	90
5	1v /allyl	<10	n.d. ^[d]
6	1w /Me	<10	n.d. ^[d]
7	1x /Bn	<10	n.d. ^[d]

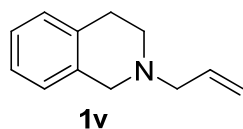
[a] Unless otherwise specified, the reaction was carried out with **1** (0.1 mmol) and **2a** (0.2 mmol) in the presence of Cu(OTf)₂ (0.01 mmol) and **4b** (0.02 mmol), 4 Å molecular sieve (100 mg), anhydrous Na₂SO₄ (0.3 mmol), and DCM (1.0 mL) at under 1 atm molecular oxygen at room temperature for 36 h. [b] Isolated yield. [c] Determined by HPLC on chiral stationary phase. [d] Not determined.



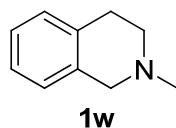
(S)-tert-butyl 1-(3-oxoprop-1-en-2-yl)-3,4-dihydroisoquinoline-2(1H)-carboxylate: yellow oil, 56%, 50% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 6.61$ min, $t_{\text{minor}} = 9.45$ min); $[\alpha]_{\text{D}}^{20} = +16$ ($c=1.0$, CHCl₃); **¹H NMR** (300 MHz, CDCl₃): δ 9.60 (s, 1 H), 7.16-7.20 (m, 4 H), 6.17 (s, 1 H), 6.11 (s, 1 H), 6.05 (s, 1 H), 3.80-3.89 (m, 1 H), 3.50-3.58 (m, 1 H), 2.83-2.89 (m, 2 H), 1.46 (s, 9 H) ppm; **¹³C NMR** (75 MHz, CDCl₃): δ 192.6, 154.6, 135.1, 134.2, 128.6, 127.7, 127.1, 126.4, 80.4, 76.6, 52.7, 28.7, 28.4 ppm; **HRMS** (ESI): C₁₇H₂₁NO₃ [M+Na]⁺ calcd: 310.1414, found: 310.1428.



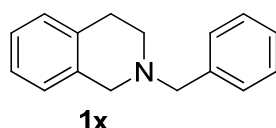
2-tosyl-1,2,3,4-tetrahydroisoquinoline (known compounds): white solid, **¹H NMR** (300 MHz, CDCl₃): δ 7.71-7.74 (d, $J = 8.4$ Hz, 2 H), 7.31-7.33 (d, $J = 7.8$ Hz, 2 H), 7.00-7.15 (m, 4 H), 4.23 (s, 2 H), 3.32-3.40 (t, $J = 6.0$ Hz, 2 H), 2.90-2.94 (t, $J = 6.0$ Hz, 2 H), 2.42 (s, 3 H) ppm; **¹³C NMR** (75 MHz, CDCl₃): δ 143.7, 133.1, 133.0, 131.6, 129.7, 128.8, 17.7, 126.7, 126.4, 126.3, 47.6, 43.7, 28.9, 21.6 ppm.



2-allyl-1,2,3,4-tetrahydroisoquinoline (known compounds): colorless oil, **¹H NMR** (300 MHz, CDCl₃): δ 7.07-7.09 (m, 3 H), 6.98-6.99 (m, 1 H), 5.90-5.99 (m, 1 H), 5.16-5.27 (m, 2 H), 3.60 (s, 2 H), 3.14-3.16 (d, $J = 6.6$ Hz, 2 H), 3.87-3.90 (t, $J = 6.0$ Hz, 2 H), 2.67-2.70 (t, $J = 6.0$ Hz, 2 H) ppm; **¹³C NMR** (75 MHz, CDCl₃): δ 135.4, 134.2, 134.1, 128.7, 126.7, 126.2, 125.4, 117.3, 61.5, 56.0, 50.6 ppm.

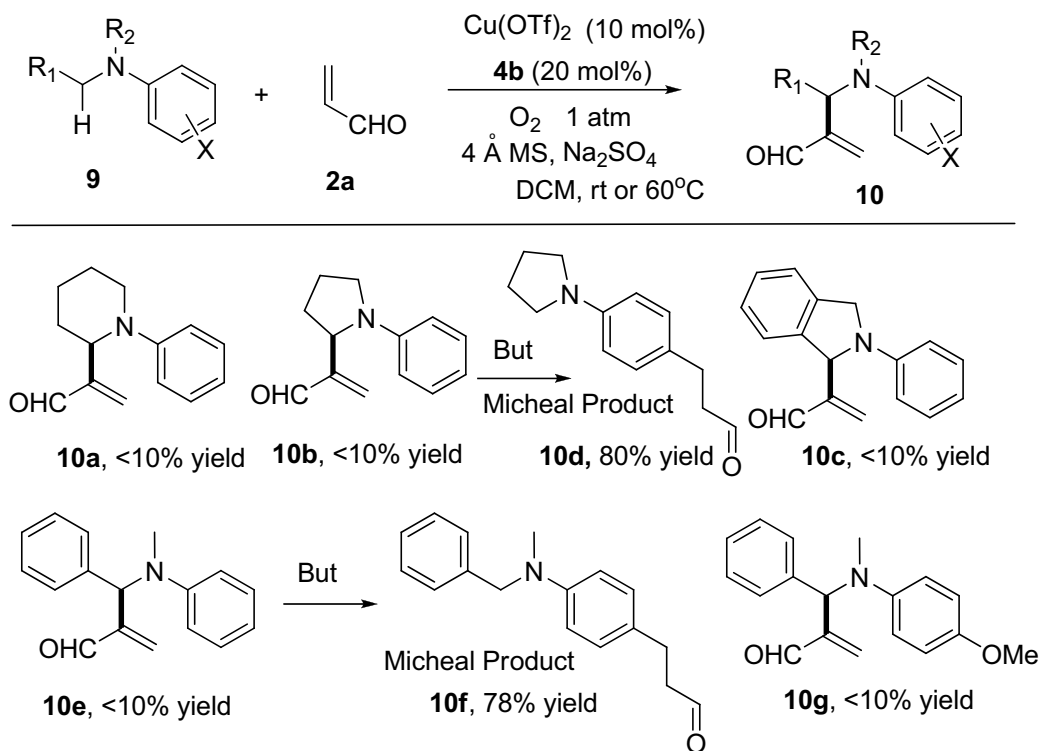


2-methyl-1,2,3,4-tetrahydroisoquinoline (known compounds): colorless oil, ^1H NMR (300 MHz, CDCl_3): δ 7.14-7.28 (m, 3 H), 7.02-7.17 (m, 1 H), 4.22-4.27 (d, J = 16.2 Hz, 1 H), 3.83-4.88 (d, J = 16.2 Hz, 1 H), 3.17-3.27 (m, 2 H), 2.99-3.03 (m, 2 H), 2.63 (s, 3 H) ppm; ^{13}C NMR (75 MHz, CDCl_3): δ 130.8, 130.2, 128.7, 127.4, 126.9, 126.8, 61.5, 56.5, 53.5, 24.4 ppm.

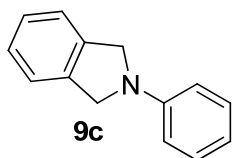


2-benzyl-1,2,3,4-tetrahydroisoquinoline (known compounds): colorless oil, ^1H NMR (300 MHz, CDCl_3): δ 7.29-7.41 (m, 5 H), 7.08-7.11 (m, 3 H), 6.17 (s, 1 H), 3.68 (s, 2 H), 3.63 (s, 2 H), 2.88-2.92 (t, J = 6.0 Hz, 2 H), 2.72-2.76 (t, J = 6.0 Hz, 2 H) ppm; ^{13}C NMR (75 MHz, CDCl_3): δ 138.4, 134.9, 134.4, 129.2, 128.7, 128.3, 127.1, 126.6, 126.1, 125.6, 62.8, 56.1, 50.4, 29.2 ppm.

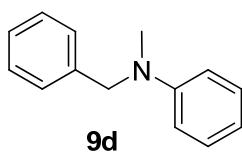
3. 0 Other Unsuccessful Examples for Asymmetric Oxidative sp^3 C-H Olefination



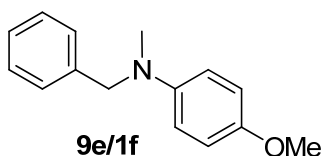
Scheme S1. Unsuccessful examples.



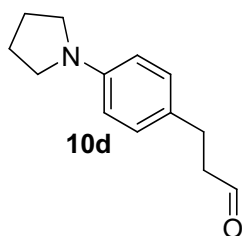
2-phenylisoindoline (known compounds): white solid, ^1H NMR (300 MHz, CDCl_3): δ 7.27-7.35 (m, 6 H), 6.72-6.77 (t, $J = 6.0$ Hz, 1 H), 6.66-6.68 (d, $J = 6.0$ Hz, 2 H), 4.68 (s, 4 H) ppm; ^{13}C NMR (75 MHz, CDCl_3): δ 147.2, 137.3, 129.4, 127.1, 122.6, 116.2, 111.6, 53.8 ppm.



N-benzyl-N-methylaniline (known compounds): colorless oil, ^1H NMR (300 MHz, CDCl_3): δ 7.25-7.31 (m, 2 H), 7.19-7.23 (m, 5 H), 6.71-6.76 (m, 3 H), 4.53 (s, 2 H), 3.01 (s, 3 H) ppm; ^{13}C NMR (75 MHz, CDCl_3): δ 138.5, 135.0, 134.5, 129.3, 128.8, 128.4, 127.2, 126.8, 126.2, 125.7, 62.9, 50.7 ppm.

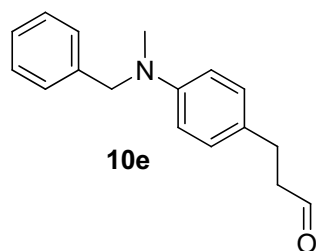


N-benzyl-4-methoxy-N-methylaniline (known compounds): colorless oil, ^1H NMR (300 MHz, CDCl_3): δ 7.25-7.31 (m, 3 H), 7.22-7.24 (m, 2 H), 6.81-6.854 (d, $J = 9.3$ Hz, 2 H), 6.72-6.75 (d, $J = 9.0$ Hz, 2 H), 4.43 (s, 2 H), 3.75 (s, 3 H), 2.91 (s, 3 H) ppm; ^{13}C NMR (75 MHz, CDCl_3): δ 151.7, 144.8, 139.2, 128.4, 127.1, 126.9, 114.7, 114.5, 58.0, 55.7, 39.1 ppm.



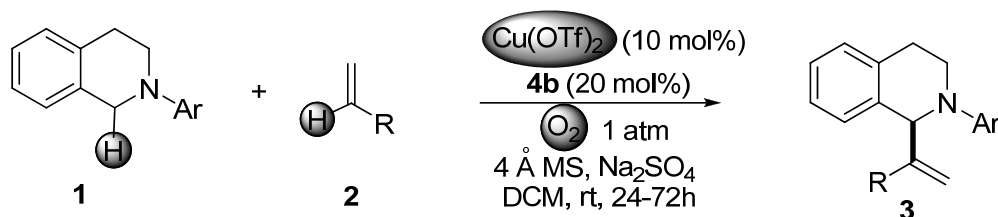
2-(4-(pyrrolidin-1-yl)phenyl)acetaldehyde (known compounds): colorless oil, ^1H NMR (300 MHz, CDCl_3): δ 9.81 (s, 1 H), 7.04-7.07 (d, $J = 6.6$ Hz, 2 H), 6.50-6.52 (d, $J = 6.6$ Hz, 2 H), 3.23-3.27 (t, $J = 6.6$ Hz, 4 H), 2.84-2.89 (t, $J = 6.6$ Hz, 2 H), 2.69-2.74 (t, $J = 6.9$ Hz, 2 H), 1.96-2.01 (t, $J = 6.9$ Hz, 4 H) ppm; ^{13}C NMR (75 MHz, CDCl_3): δ 202.5, 146.6, 129.0, 126.7,

111.8, 47.7, 45.9, 27.3, 25.4 ppm.

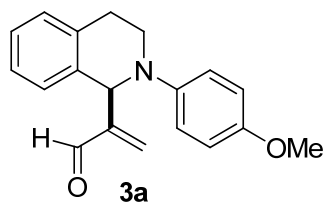


2-(4-(benzyl(methyl)amino)phenyl)acetaldehyde (known compounds): colorless oil, ^1H NMR (300 MHz, CDCl_3): δ 9.81 (s, 1 H), 7.26-7.31 (m, 6 H), 7.03-7.07 (d, J = 11.7 Hz, 2 H), 6.67-6.70 (d, J = 11.7 Hz, 2 H), 4.50 (s, 2 H), 3.00 (s, 3 H), 2.84-2.89 (t, J = 7.5 Hz, 1 H), 2.70-2.74 (t, J = 7.5 Hz, 1 H) ppm.

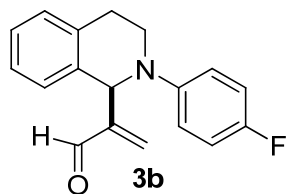
4.0 General Procedure for the Preparation of Optically Active C₁-alkene Tetrahydroisoquinolins



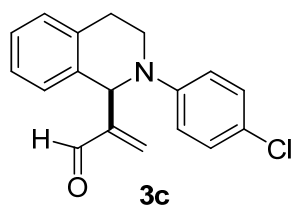
Typical experimental procedure: Under O_2 , a solution of $\text{Cu}(\text{OTf})_2$ (0.01 mmol) and chiral ligand **4b** (0.012 mmol) in anhydrous DCM (0.4 mL) was stirred at room temperature for 0.5 h, and then the mixture was added to a Schlenk tube which were charged with aryl-substituted 1,2,3,4-tetrahydroisoquinolin **1** (0.1 mmol), 4 Å molecular sieve (100 mg), anhydrous Na_2SO_4 (0.3 mmol), anhydrous DCM (0.4 mL) and O_2 (1 atm). Finally, a solution of unsaturated carbonyl compounds **2** (0.1 mol) in anhydrous DCM (0.2 mL) was slowly added to the mixture above prepared and the resultant reaction mixture was stirred at room temperature for the appropriate time. After the reaction was completed (monitored by TLC), the resulting mixture was concentrated under reduced pressure and the residue was purified through column chromatography on silica gel (eluent, ethyl acetate / hexane 1:7). After filtration and the solvent was removed at reduced pressure to give the pure products.



(S)-2-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow solid, 72% yield; 90% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 11.96$ min, $t_{\text{minor}} = 16.89$ min); $[\alpha]_{\text{D}}^{20} = +24$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.61 (s, 1 H), 7.16-7.20 (m, 4 H), 6.82-6.90 (dd, $J = 9.3$, 12.0 Hz, 4 H), 6.09-6.10 (d, $J = 3.3$ Hz, 2 H), 5.72 (s, 1 H), 3.76 (s, 3 H), 3.58-3.66 (m, 1 H), 3.41-3.49 (m, 1 H), 3.00-3.06 (m, 1 H), 2.88-2.98 (m, 1 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 193.4, 153.0, 151.4, 143.3, 135.6, 135.1, 134.7, 128.4, 128.1, 127.0, 126.2, 117.2, 114.6, 57.3, 55.6, 44.1, 27.6 ppm; **IR** (neat): 3363, 3051, 2923, 2833, 1687, 1511, 1458, 1244, 1036, 944, 754 cm^{-1} ; **HRMS** (ESI): $\text{C}_{19}\text{H}_{20}\text{NO}_2$ $[\text{M}+\text{H}]^+$ calcd: 294.1489, found: 294.1481.

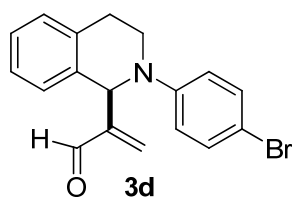


(S)-2-(2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 56% yield; 85% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 6.03$ min, $t_{\text{minor}} = 6.66$ min); $[\alpha]_{\text{D}}^{20} = +16$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.62 (s, 1 H), 7.16-7.20 (m, 4 H), 6.90-6.93 (m, 2 H), 6.80-6.82 (m, 2 H), 6.13 (s, 1 H), 6.09 (s, 1 H), 5.72 (s, 1 H), 3.60-3.64 (m, 1 H), 3.45-3.49 (m, 1 H), 2.99-3.02 (m, 1 H), 2.91-2.95 (m, 1 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 193.3, 154.8, 151.2, 145.3, 135.5, 134.8, 128.3, 128.2, 127.2, 126.4, 116.1, 116.0, 115.7, 115.4, 57.1, 43.7, 27.5 ppm; **IR** (neat): 3369, 3057, 2919, 2846, 1690, 1510, 1385, 1230, 1112, 946, 756 cm^{-1} ; **HRMS** (ESI): $\text{C}_{18}\text{H}_{17}\text{FNO}$ $[\text{M}+\text{H}]^+$ calcd: 282.1289, found: 282.1286.

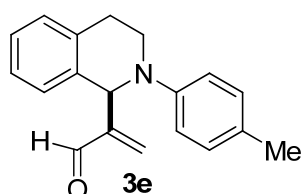


(S)-2-(2-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 51%

yield; 91% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 7.75$ min, $t_{\text{minor}} = 10.81$ min); $[\alpha]_{\text{D}}^{20} = +65$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.63 (s, 1 H), 7.27-7.28 (m, 1 H), 7.15-7.20 (m, 5 H), 6.73-6.76 (d, $J = 9.0$ Hz, 2 H), 6.18 (s, 1 H), 6.08 (s, 1 H), 5.75 (s, 1 H), 3.67-3.73 (m, 1 H), 3.43-3.52 (m, 1 H), 2.94-3.02 (m, 2 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 193.3, 150.9, 147.0, 135.4, 134.7, 129.0, 128.3, 127.4, 126.5, 122.7, 115.0, 56.8, 43.3, 27.6 ppm; **IR** (neat): 3667, 3645, 2916, 2840, 1690, 1594, 1496, 1384, 1330, 943, 751 cm^{-1} ; **HRMS** (ESI): $\text{C}_{18}\text{H}_{17}\text{ClNO}$ $[\text{M}+\text{H}]^+$ calcd: 298.0993, found: 298.0988.

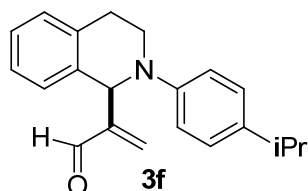


(S)-2-(2-(4-bromophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 47% yield; 88% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 9.59$ min, $t_{\text{minor}} = 8.30$ min); $[\alpha]_{\text{D}}^{20} = +17$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.63 (s, 1 H), 7.28-7.31 (m, 3 H), 7.16-7.18 (m, 3 H), 6.68-6.71 (d, $J = 8.7$ Hz, 2 H), 6.19 (s, 1 H), 6.08 (s, 1 H), 5.74 (s, 1 H), 3.65-3.71 (m, 1 H), 3.47-3.49 (m, 1 H), 2.94-3.02 (m, 2 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 193.3, 150.8, 147.4, 135.4, 134.6, 134.5, 131.8, 128.3, 128.1, 127.4, 126.5, 115.4, 109.9, 56.7, 43.3, 27.6 ppm; **IR** (neat): 3360, 2923, 3068, 2852, 1689, 1588, 1493, 1329, 1230, 1077, 751 cm^{-1} ; **HRMS** (ESI): $\text{C}_{18}\text{H}_{17}\text{BrNO}$ $[\text{M}+\text{H}]^+$ calcd: 342.0488, found: 342.0481.

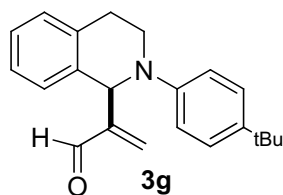


(S)-2-(2-(p-tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 64% yield; 91% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 5.60$ min, $t_{\text{minor}} = 7.30$ min); $[\alpha]_{\text{D}}^{20} = +15$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.63 (s, 1 H), 7.28-7.31 (m, 1 H), 7.16-7.22 (m, 3 H), 7.06-7.09 (d, $J = 8.4$ Hz, 2 H), 6.77-6.80 (d, $J = 8.4$ Hz, 2 H), 6.20 (s, 1 H), 6.08 (s, 1 H), 5.79 (s, 1 H), 3.70-3.74 (m, 1

H), 3.50-3.52 (m, 1 H), 2.95-3.04 (m, 2 H), 2.27 (s, 3 H) ppm; ^{13}C NMR (75 MHz, CDCl_3): δ 193.4, 151.4, 146.4, 135.7, 135.1, 134.4, 129.7, 128.3, 128.1, 127.4, 127.1, 126.3, 114.4, 56.9, 43.5, 27.8, 20.3 ppm; **IR** (neat): 3359, 3026, 2919, 2852, 1670, 1616, 1517, 1384, 1324, 946, 754 cm^{-1} ; **HRMS** (ESI): $\text{C}_{19}\text{H}_{20}\text{NO}$ $[\text{M}+\text{H}]^+$ calcd: 278.1539, found: 278.1531.



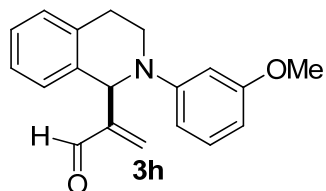
(S)-2-(2-(4-isopropylphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 69% yield; 99% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 4.72$ min, $t_{\text{minor}} = 5.74$ min); $[\alpha]_{\text{D}}^{20} = +25$ ($c=0.5$, CHCl_3); ^1H NMR (300 MHz, CDCl_3): δ 9.64 (s, 1 H), 7.27-7.29 (m, 1 H), 7.09-7.19 (m, 5 H), 6.77-6.80 (d, $J = 8.7$ Hz, 2 H), 6.23 (s, 1 H), 6.06 (s, 1 H), 5.77 (s, 1 H), 3.70-3.74 (m, 1 H), 3.47-3.49 (m, 1 H), 2.90-3.08 (m, 2 H), 2.74-2.85 (m, 1 H), 1.19-1.21 (d, $J = 6.9$ Hz, 6 H) ppm; ^{13}C NMR (75 MHz, CDCl_3): δ 193.4, 151.5, 146.6, 138.3, 135.7, 135.0, 134.3, 128.2, 128.0, 127.1, 127.0, 126.3, 113.9, 57.0, 43.4, 33.0, 27.8, 24.2 ppm; **IR** (neat): 3364, 2956, 2923, 2860, 1689, 1613, 1516, 1383, 1323, 1062, 750 cm^{-1} ; **HRMS** (ESI): $\text{C}_{21}\text{H}_{24}\text{NO}$ $[\text{M}+\text{H}]^+$ calcd: 306.1852, found: 306.1842.



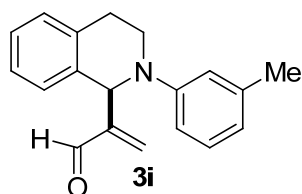
(S)-2-(2-(4-tert-butylphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 60% yield; 90% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 4.76$ min, $t_{\text{minor}} = 5.63$ min); $[\alpha]_{\text{D}}^{20} = +20$ ($c=1.0$, CHCl_3); ^1H NMR (300 MHz, CDCl_3): δ 9.64 (s, 1 H), 7.25-7.28 (m, 3 H), 7.14-7.17 (m, 3 H), 6.77-6.80 (d, $J = 8.7$ Hz, 2 H), 6.24 (s, 1 H), 6.06 (s, 1 H), 5.77 (s, 1 H), 3.69-3.75 (m, 1 H), 3.47-3.50 (m, 1 H), 2.96-3.02 (m, 2 H), 1.28 (s, 9 H) ppm; ^{13}C NMR (75 MHz, CDCl_3): δ 193.5, 151.5, 146.2, 140.5, 135.8, 135.1, 134.4, 128.3, 128.0, 127.1, 126.3, 126.0, 113.4, 57.0, 43.3, 33.8,

31.5, 27.9 ppm; **IR** (neat): 3037, 2959, 2904, 2865, 1691, 1517, 1385, 1360, 1263, 1228, 733 cm^{-1} ;

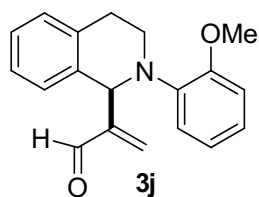
HRMS (ESI): $\text{C}_{22}\text{H}_{26}\text{NO}$ $[\text{M}+\text{H}]^+$ calcd: 320.2009, found: 320.2016.



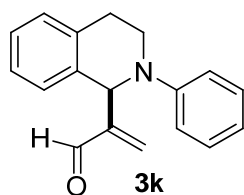
(S)-2-(2-(3-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 70% yield; 90% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 17.58$ min, $t_{\text{minor}} = 26.74$ min); $[\alpha]_{\text{D}}^{20} = -21$ ($c=1.0$, CHCl_3); **^1H NMR** (300 MHz, CDCl_3): δ 9.63 (s, 1 H), 7.30-7.33 (m, 1 H), 7.14-7.18 (m, 4 H), 6.32-6.45 (m, 3 H), 6.24 (s, 1 H), 6.06 (s, 1 H), 5.80 (s, 1 H), 3.78 (s, 3 H), 3.72-3.76 (m, 1 H), 3.44-3.53 (m, 1 H), 2.95-3.03 (m, 2 H) ppm; **^{13}C NMR** (75 MHz, CDCl_3): δ 193.3, 160.6, 151.2, 149.8, 135.7, 134.9, 134.3, 129.8, 128.3, 127.9, 127.2, 126.4, 106.7, 102.6, 100.3, 56.9, 55.1, 43.5, 27.9 ppm; **IR** (neat): 3363, 2922, 2839, 1688, 1606, 1495, 1457, 1211, 1167, 1053, 753 cm^{-1} ; **HRMS** (ESI): $\text{C}_{19}\text{H}_{20}\text{NO}_2$ $[\text{M}+\text{H}]^+$ calcd: 294.1489, found: 294.1481.



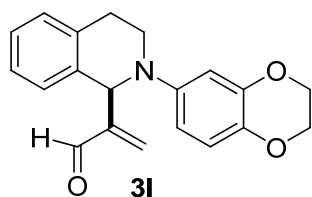
(S)-2-(2-(3-methylphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 67% yield; 90% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 7.03$ min, $t_{\text{minor}} = 6.32$ min); $[\alpha]_{\text{D}}^{20} = +11$ ($c=1.0$, CHCl_3); **^1H NMR** (300 MHz, CDCl_3): δ 9.63 (s, 1 H), 7.30-7.33 (m, 1 H), 7.10-7.19 (m, 4 H), 6.58-6.64 (m, 3 H), 6.23 (s, 1 H), 6.06 (s, 1 H), 5.79 (s, 1 H), 3.70-3.79 (m, 1 H), 3.44-3.54 (m, 1 H), 2.95-3.02 (m, 2 H), 2.30 (s, 3 H) ppm; **^{13}C NMR** (75 MHz, CDCl_3): δ 193.4, 151.2, 148.4, 138.8, 135.7, 134.9, 134.3, 129.0, 128.3, 127.9, 127.1, 126.3, 118.8, 114.4, 110.9, 56.8, 43.4, 27.9, 21.9 ppm; **IR** (neat): 3362, 3034, 2918, 2849, 1689, 1601, 1494, 1382, 1264, 1036, 756 cm^{-1} ; **HRMS** (ESI): $\text{C}_{19}\text{H}_{20}\text{NO}$ $[\text{M}+\text{H}]^+$ calcd: 278.1539, found: 278.1531.



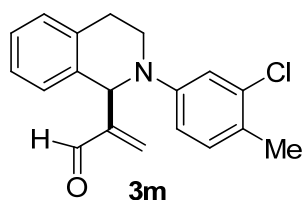
(S)-2-(2-(2-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 73% yield; 94% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 10.02$ min, $t_{\text{minor}} = 14.13$ min); $[\alpha]_{\text{D}}^{20} = +12$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.36 (s, 1 H), 7.13-7.18 (m, 3 H), 6.93-6.99 (m, 2 H), 6.85-6.88 (m, 1 H), 6.79-6.81 (m, 2 H), 6.06 (s, 1 H), 5.90 (s, 1 H), 5.77 (s, 1 H), 3.88 (s, 3 H), 3.34-3.39 (m, 2 H), 2.91-3.14 (m, 1 H), 2.75-2.88 (m, 1 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 192.9, 153.6, 150.3, 139.5, 135.8, 135.4, 135.1, 128.9, 127.8, 126.5, 125.9, 123.7, 121.5, 120.7, 111.8, 55.6, 43.6, 28.4 ppm; **IR** (neat): 3371, 3062, 2924, 2853, 2253, 1694, 1498, 1458, 1241, 1028, 742 cm^{-1} ; **HRMS** (ESI): $\text{C}_{19}\text{H}_{20}\text{NO}_2$ $[\text{M}+\text{H}]^+$ calcd: 294.1489, found: 294.1483.



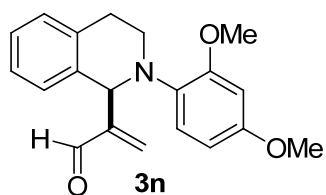
(S)-2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 63% yield; 91% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 6.06$ min, $t_{\text{minor}} = 5.32$ min); $[\alpha]_{\text{D}}^{20} = -11$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.64 (s, 1 H), 7.27-7.31 (m, 2 H), 7.16-7.24 (s, 4 H), 6.81-6.84 (m, 3 H), 6.24 (s, 1 H), 6.07 (s, 1 H), 5.80 (s, 1 H), 3.72-3.77 (m, 1 H), 3.49-3.54 (m, 1 H), 2.99-3.04 (m, 2 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 192.3, 150.2, 147.4, 134.7, 133.9, 133.3, 128.1, 127.3, 126.9, 126.2, 125.4, 116.8, 112.7, 55.8, 42.4, 26.9 ppm; **IR** (neat): 3395, 3058, 2923, 2853, 1686, 1593, 1499, 1311, 1069, 1024, 749 cm^{-1} ; **HRMS** (ESI): $\text{C}_{18}\text{H}_{18}\text{NO}$ $[\text{M}+\text{H}]^+$ calcd: 264.1383, found: 264.1379.



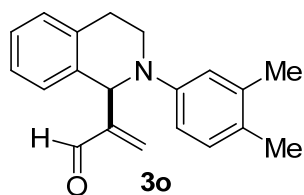
(S)-2-(2-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 81% yield; 90% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, t_{major} = 10.39 min, t_{minor} = 18.03 min); $[\alpha]_{\text{D}}^{20}$ = +18 (c =1.0, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.61 (s, 1 H), 7.12-7.22 (m, 4 H), 6.76-6.73 (d, J = 9.6 Hz, 1 H), 6.40-6.42 (d, J = 6.6 Hz, 2 H), 6.12 (s, 1 H), 6.07 (s, 1 H), 5.67 (s, 1 H), 4.17-4.22 (m, 4 H), 3.56-3.64 (m, 1 H), 3.36-3.45 (m, 1 H), 2.79-3.17 (m, 2 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 193.3, 151.3, 143.9, 143.7, 136.4, 135.6, 134.9, 134.5, 128.2, 127.0, 126.3, 117.4, 108.7, 104.1, 64.7, 64.2, 57.2, 43.8, 27.5 ppm; **IR** (neat): 3365, 3031, 2924, 2872, 1689, 1509, 1281, 1248, 1070, 951, 756 cm^{-1} ; **HRMS** (ESI): $\text{C}_{20}\text{H}_{20}\text{NO}_3$ $[\text{M}+\text{H}]^+$ calcd: 322.1438, found: 322.1429.



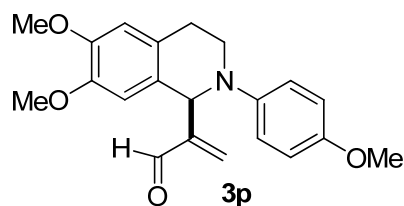
(S)-2-(2-(3-chloro-4-methylphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow solid, 54% yield; 93% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, t_{major} = 5.85 min, t_{minor} = 7.02 min); $[\alpha]_{\text{D}}^{20}$ = +35 (c =1.0, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.63 (s, 1 H), 7.27-7.29 (m, 1 H), 7.15-7.19 (m, 3 H), 7.03-7.06 (d, J = 8.4 Hz, 1 H), 6.83 (s, 1 H), 6.63-6.66 (d, J = 8.4 Hz, 1 H), 6.17 (s, 1 H), 6.08 (s, 1 H), 5.73 (s, 1 H), 3.64-3.72 (m, 1 H), 3.420-3.50 (m, 1 H), 2.92-3.02 (m, 2 H), 2.25 (s, 3 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 193.2, 150.9, 147.5, 135.4, 134.8, 134.5, 131.1, 128.3, 128.0, 127.3, 126.4, 124.8, 114.3, 112.5, 56.7, 43.3, 27.5, 18.8 ppm; **IR** (neat): 3366, 3027, 2920, 2850, 1689, 1611, 1502, 1384, 1328, 1040, 948 cm^{-1} ; **HRMS** (ESI): $\text{C}_{19}\text{H}_{19}\text{ClNO}$ $[\text{M}+\text{H}]^+$ calcd: 312.1150, found: 312.1135.



(S)-2-(2-(2,4-dimethoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 56% yield; 80% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 15.95$ min, $t_{\text{minor}} = 13.77$ min); $[\alpha]_{\text{D}}^{20} = +17$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.36 (s, 1 H), 7.06-7.14 (s, 3 H), 6.90-6.93 (d, $J = 8.4$ Hz, 1 H), 6.72-6.74 (d, $J = 8.4$ Hz, 1 H), 6.32 (s, 1 H), 6.25-6.28 (d, $J = 8.4$ Hz, 1 H), 6.04 (s, 1 H), 5.74 (s, 2 H), 3.84 (s, 3 H), 3.75 (s, 3 H), 3.24-3.33 (m, 2 H), 2.89-2.96 (m, 2 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 192.9, 156.7, 154.9, 150.2, 136.0, 135.3, 134.3, 133.0, 128.8, 127.7, 126.3, 125.8, 122.6, 103.4, 99.8, 56.7, 55.5, 55.3, 44.7, 28.7 ppm; **IR** (neat): 3368, 2999, 2929, 2833, 1693, 1507, 1459, 1288, 1207, 1037, 742 cm^{-1} ; **HRMS** (ESI): $\text{C}_{20}\text{H}_{22}\text{NO}_3$ $[\text{M}+\text{H}]^+$ calcd: 324.1594 found: 324.1587.

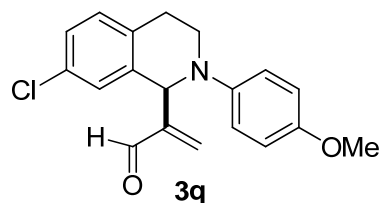


(S)-2-(2-(3,4-dimethylphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde: yellow oil, 49% yield; 90% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 5.55$ min, $t_{\text{minor}} = 6.66$ min); $[\alpha]_{\text{D}}^{20} = +15$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.62 (s, 1 H), 7.67-7.28 (d, $J = 5.1$ Hz, 1 H), 7.13-7.18 (m, 3 H), 6.97-7.00 (d, $J = 8.4$ Hz, 1 H), 6.66 (s, 1 H), 6.57-6.61 (d, $J = 8.4$ Hz, 1 H), 6.18 (s, 1 H), 6.05 (s, 1 H), 5.76 (s, 1 H), 3.65-3.71 (m, 1 H), 3.42-3.50 (m, 1 H), 2.92-3.00 (m, 2 H), 2.22 (s, 3 H), 2.15 (s, 1 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 193.5, 151.5, 146.8, 137.2, 135.8, 135.1, 134.4, 130.2, 128.3, 128.1, 127.1, 126.3, 126.2, 115.9, 111.8, 56.8, 43.6, 27.9, 20.4, 18.7 ppm; **IR** (neat): 3361, 3061, 2918, 2854, 1689, 1613, 1508, 1383, 1262, 1111, 753 cm^{-1} ; **HRMS** (ESI): $\text{C}_{20}\text{H}_{22}\text{NO}$ $[\text{M}+\text{H}]^+$ calcd: 292.1696, found: 292.1690.



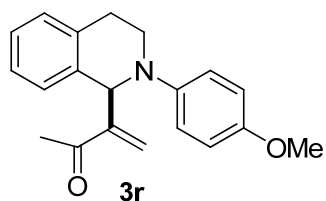
(S)-2-(6,7-dimethoxy-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde:

yellow oil, 57% yield; 70% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, t_{major} = 10.75 min, t_{minor} = 13.42 min); $[\alpha]_{\text{D}}^{20}$ = +23 (c =1.0, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.62 (s, 1 H), 6.82-6.86 (dd, J = 11.1, 15.3 Hz, 4 H), 6.62-6.65 (d, J = 7.5 Hz, 2 H), 6.09 (s, 1 H), 6.06 (s, 1 H), 5.61 (s, 1 H), 3.86 (s, 3 H), 3.82 (s, 3 H), 3.75 (s, 3 H), 3.51-3.55 (m, 1 H), 3.42-3.45 (m, 1 H), 2.88-2.96 (m, 1 H), 2.72-2.80 (m, 1 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 193.6, 153.0, 151.4, 147.9, 147.3, 143.4, 134.7, 127.7, 126.7, 117.4, 114.5, 110.9, 110.7, 56.8, 55.9, 55.8, 55.6, 43.7, 26.7 ppm; **IR** (neat): 2933, 2833, 2695, 2253, 1690, 1511, 1463, 1249, 1115, 1035, 731 cm^{-1} ; **HRMS** (ESI): $\text{C}_{21}\text{H}_{24}\text{NO}_4$ $[\text{M}+\text{H}]^+$ calcd: 354.1700, found: 354.1708.

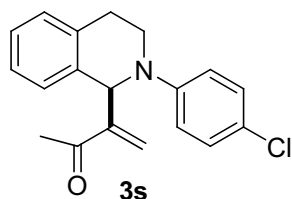


(S)-2-(7-chloro-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylaldehyde:

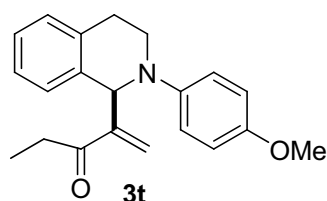
yellow solid, 82% yield; 85% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, t_{major} = 7.48 min, t_{minor} = 10.00 min); $[\alpha]_{\text{D}}^{20}$ = +29 (c =1.0, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 9.60 (s, 1 H), 7.13-7.17 (m, 2 H), 6.06-6.09 (d, J = 7.8 Hz, 1 H), 6.79-6.88 (dd, J = 6.8, 21.0 Hz, 4 H), 6.13 (s, 1 H), 6.05 (s, 1 H), 5.65 (s, 1 H), 3.75 (s, 3 H), 3.50-3.75 (m, 1 H), 3.39-3.47 (m, 1 H), 2.91-3.01 (m, 1 H), 2.77-2.86 (m, 1 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 193.0, 153.4, 150.8, 143.1, 136.9, 135.2, 134.0, 131.7, 129.9, 127.9, 127.1, 117.9, 114.5, 57.0, 55.6, 43.8, 26.8 ppm; **IR** (neat): 3666, 3351, 2916, 2833, 1690, 1511, 1460, 1244, 1035, 943, 751 cm^{-1} ; **HRMS** (ESI): $\text{C}_{19}\text{H}_{18}\text{ClNO}_2$ $[\text{M}+\text{H}]^+$ calcd: 328.1099, found: 328.1095.



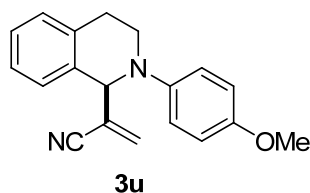
(S)-3-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)but-3-en-2-one: yellow solid, 77% yield; 95% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 8.04$ min, $t_{\text{minor}} = 6.68$ min); $[\alpha]_{\text{D}}^{20} = +14$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.11-7.19 (m, 4 H), 6.78-6.91 (dd, $J = 9.3, 12.8$ Hz, 4 H), 6.03 (s, 1 H), 5.83 (s, 1 H), 5.53 (s, 1 H), 3.78 (s, 3 H), 3.74-3.78 (m, 1 H), 3.58-3.66 (m, 1 H), 2.93-3.03 (m, 1 H), 2.81-2.93 (m, 1 H), 2.28 (s, 3 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 200.1, 152.7, 151.1, 143.3, 135.7, 135.5, 128.3, 128.2, 126.8, 126.1, 125.2, 116.9, 114.5, 58.7, 55.7, 43.5, 27.2, 27.0 ppm; **IR** (neat): 2924, 2853, 2495, 2119, 1679, 1611, 1503, 1384, 1040, 945, 752 cm^{-1} ; **HRMS** (ESI): $\text{C}_{20}\text{H}_{22}\text{NO}_2$ $[\text{M}+\text{H}]^+$ calcd: 308.1645, found: 308.1649.



(S)-3-(2-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)but-3-en-2-one: yellow oil, 54% yield; 93% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 6.70$ min, $t_{\text{minor}} = 5.88$ min); $[\alpha]_{\text{D}}^{20} = +12$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.15-7.23 (m, 6 H), 6.75-6.78 (d, $J = 9.0, 2$ H), 6.03 (s, 1 H), 5.90 (s, 1 H), 5.65 (s, 1 H), 3.67-3.74 (m, 1 H), 3.43-3.51 (m, 1 H), 2.89-3.04 (m, 2 H), 2.31 (s, 3 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 199.9, 150.3, 147.0, 135.5, 135.0, 128.9, 128.4, 128.0, 127.2, 126.4, 124.9, 122.4, 114.9, 58.2, 43.1, 27.4, 27.1 ppm; **IR** (neat): 2921, 2851, 2354, 1677, 1594, 1496, 1385, 1359, 1263, 1101, 750 cm^{-1} ; **HRMS** (ESI): $\text{C}_{19}\text{H}_{19}\text{ClNO}$ $[\text{M}+\text{H}]^+$ calcd: 312.1150, found: 312.1153.

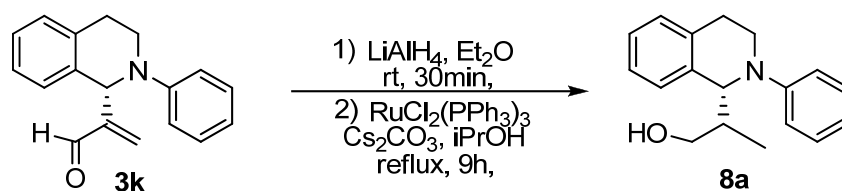


(S)-2-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)pent-1-en-3-one: yellow oil, 48% yield; 69% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 5.38$ min, $t_{\text{minor}} = 5.83$ min); $[\alpha]_{\text{D}}^{20} = +13$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.13-7.15 (m, 4 H), 6.79-6.88 (dd, $J = 9.3, 12.8$ Hz, 4 H), 5.96 (s, 1 H), 5.85 (s, 1 H), 5.45 (s, 1 H), 3.74 (s, 3 H), 3.58-3.66 (m, 1 H), 3.40-3.48 (m, 1 H), 2.94-3.04 (m, 1 H), 2.79-2.88 (m, 1 H), 2.57-2.64 (dd, $J = 7.5, 14.4$ Hz, 2 H), 0.98-1.03 (t, $J = 7.2$, Hz, 3 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 203.2, 152.6, 150.9, 143.3, 135.7, 135.5, 128.3, 128.2, 126.8, 126.1, 123.5, 116.7, 114.5, 59.1, 55.7, 43.3, 32.3, 27.1, 8.1 ppm; **IR** (neat): 2993, 2924, 2833, 1677, 1511, 1462, 1385, 1245, 1185, 1038, 755 cm^{-1} ; **HRMS** (ESI): $\text{C}_{21}\text{H}_{24}\text{NO}_2$ $[\text{M}+\text{H}]^+$ calcd: 322.1802, found: 322.1810.

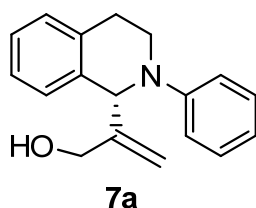


(S)-2-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylonitrile: yellow oil, 71% yield; 99% *ee* determined by HPLC on a Chiralpak OD-H column (hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, 254nm, $t_{\text{major}} = 7.26$ min, $t_{\text{minor}} = 7.56$ min); $[\alpha]_{\text{D}}^{20} = +22$ ($c=1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.16-7.20 (m, 4 H), 6.80-6.93 (dd, $J = 9.3, 12.8$ Hz, 4 H), 5.96 (s, 1 H), 5.75 (s, 1 H), 5.14 (s, 1 H), 3.77 (s, 3 H), 3.63-3.67 (m, 1 H), 3.43-3.55 (m, 1 H), 2.93-2.97 (t, d, $J = 5.7$ Hz, 2 H) ppm; $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 153.7, 143.1, 135.8, 132.6, 131.1, 128.7, 127.9, 126.5, 125.7, 118.4, 114.6, 63.8, 55.6, 44.8, 28.0 ppm; **IR** (neat): 2924, 2853, 2222, 1958, 1580, 1511, 1460, 1245, 1036, 946, 735 cm^{-1} ; **HRMS** (ESI): $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ calcd: 291.1492, found: 291.1494.

5.0 Transformation of 3k to 8a ^{[6], [7]}

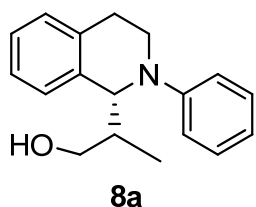


A mixture of **3a** (0.2 mmol) and LiAlH₄ (0.6 mmol) in the solution of ether (5.0 ml) was stirred at room temperature for 30 min. After the reaction completed, 5 ml water was slowly added to the mixture at 0°C, then the mixture was extracted with ether (5 ml ×3). The combined organic extracts were washed with brine, and then dried over Na₂SO₃, and concentrated to give yellow oil. The residue was used without further purified. To the mixture of the residue in anhydrous propan-2-ol was added the solution of RuCl₂(PPh₃)₃ (1.0 % mol) and Cs₂CO₃ (2.0 % mol) in anhydrous propan-2-ol, and the mixture was stirred at 82°C for 9h. After the reaction completed, the mixture was concentrated under reduced pressure, and the residue was purified through column chromatography on silica gel (eluent, ethyl acetate / hexane 1:5). After filtration and the solvent was removed at reduced pressure to give the pure products **8a** as colorless oil (over all yield: 86%).



(S)-2-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)prop-2-en-1-ol: yellow oil,

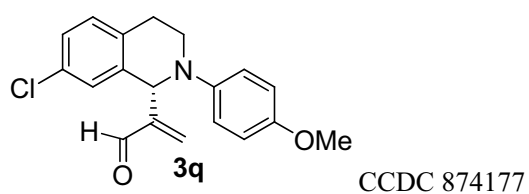
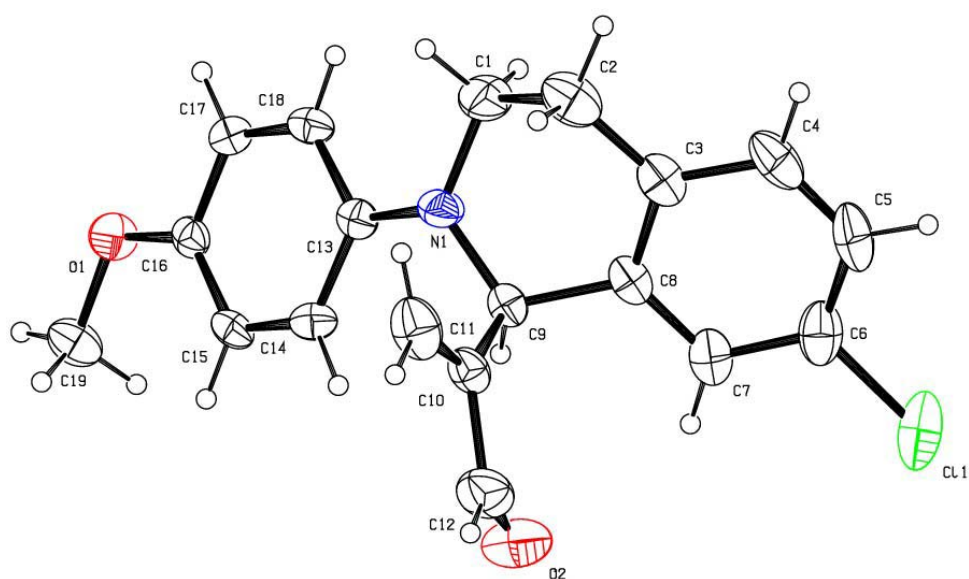
¹H NMR (300 MHz, CDCl₃): δ 7.10-7.27 (m, 6 H), 6.92-6.95 (d, *J* = 8.1 Hz, 2 H), 6.77-6.82 (t, *J* = 7.5 Hz, 1 H), 5.33 (s, 1 H), 5.25 (s, 1 H), 4.83 (s, 1 H), 4.16 (s, 2 H), 3.62-3.67 (m, 1 H), 3.51-3.57 (m, 1 H), 2.86-2.92 (m, 2 H), 2.50 (br, 1 H) ppm.



2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-1-ol: colorless oil, ¹H NMR (300 MHz, CDCl₃): The *syn*-isomer: δ 7.15-7.25 (m, 6 H), 6.78-6.81 (d, *J* = 8.1 Hz, 2 H), 6.81-6.83 (t, *J* = 7.2 Hz, 1 H), 4.83-4.85 (d, *J* = 7.5 Hz, 1 H), 3.82-3.88 (m, 1 H), 3.68-3.70 (d, *J* = 6.0 Hz, 2 H), 1.65 (br, 1 H), 1.10-1.12 (d, *J* = 7.2 Hz, 3 H) ppm; The *anti*-isomer: δ 7.10-7.20 (m, 6 H),

6.96-6.99 (d, $J = 8.1\text{Hz}$, 2 H), 6.73-6.76 (t, $J = 7.2\text{Hz}$, 1 H), 4.52-4.53 (d, $J = 9.2\text{ Hz}$, 1 H), 3.72-3.74 (d, $J = 6.0\text{ Hz}$, 2 H), 3.56-3.59 (m, 1 H), 3.30 (br, 1 H), 0.93-0.96 (d, $J = 6.9\text{ Hz}$, 3 H) ppm.

6.0 X-ray Structure of 3q



Bond precision:	C-C = 0.0087 Å	Wavelength=0.71073
Cell:	a=6.634(19) b=7.46(2) c=16.24(4)	
	alpha=90 beta=91.67(3) gamma=90	
Temperature: 296 K		
	Calculated	Reported
Volume	803(4)	803(4)
Space group	P 21	P2(1)
Hall group	P 2yb	?
Moiety formula	C19 H18 Cl N O2	?

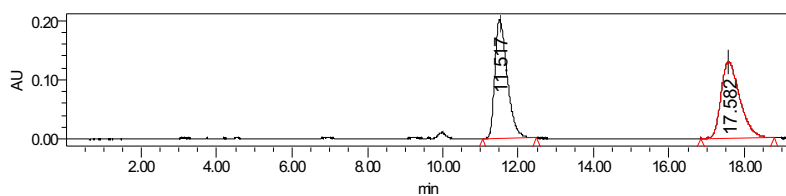
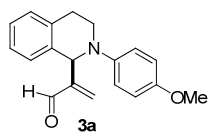
Sum formula	C19 H18 Cl N O2	C19 H18 Cl N O2
Mr	327.79	327.79
Dx,g cm-3	1.356	1.356
Z	2	2
Mu (mm-1)	0.247	0.247
F000	344.0	344.0
F000'	344.43	
h,k,lmax	8,9,19	8,9,19
Nref	1607[2966]	2363
Tmin,Tmax	0.938,0.961	0.938,0.961
Tmin'	0.938	
Correction method= MULTI-SCAN		
Data completeness= 1.47/0.80	Theta(max)= 25.490	
R(reflections)= 0.0573(1500)	wR2(reflections)= 0.1458(2363)	
S = 1.010	Npar= 209	

7.0 References

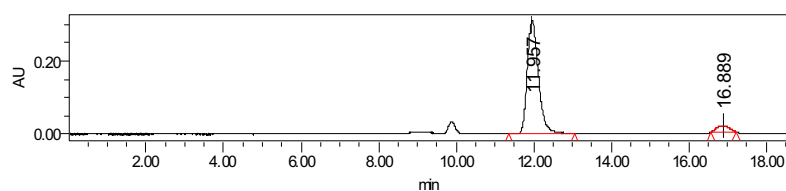
- [1] X.-Z. Shu, X.-F. Xia, Y.-F. Yang, K.-G. Ji, X.-Y. Liu, Y.-M. Liang, *J. Org. Chem.* **2009**, *74*, 7464-7469.
- [2] Z. Li, C.-J. Li, *J. Am. Chem. Soc.* **2005**, *127*, 6968-6969.
- [3] M. Shi, L.-H. Chen, C.-Q. Li, *J. Am. Chem. Soc.* **2005**, *127*, 3790-3800.
- [4] K. Matsui, S. Takizawa, H. Sasai, *J. Am. Chem. Soc.* **2005**, *127*, 3680-3681.
- [5] A. J. Bojarski, M. J. Mokrosz, S. C. Minol, A. Koziol, A. Wesolowska, E. Tatarczynska, A. Klodzinskab, E. Chojnacka-Woojcik, *Bioorg. Med. Chem.* **2010**, *10*, 87-95.
- [6] G. Zhang, Y. Zhang, R. Wang, *Angew. Chem.* **2011**, *123*, 10613-10616; *Angew. Chem. Int. Ed.* **2011**, *50*, 10429-10432.
- [7] V. Cadierno, P. Crochet, J. Francos, S. E. Garéa-Garrido, J. Gimeno, N. Nebra, *Green Chem.*, **2009**, *11*, 1992–2000.

8.0 Copies of HPLC spectra of racemic /chiral products

HPLC using an OD (*n*-Hexane/*i*PrOH= 90/10, flow rate 1.0 mL/min)

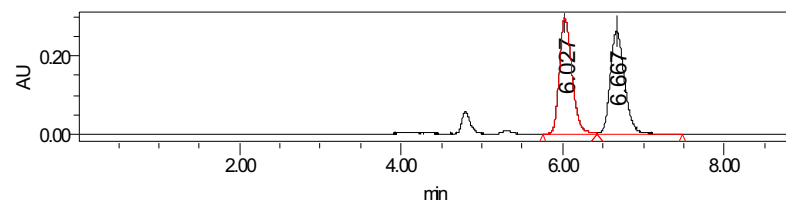
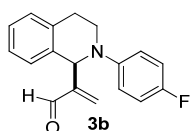


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	11.517	4582716	50.65	199752	bb	Unknown
2	17.582	4465206	49.35	128700	bb	Unknown

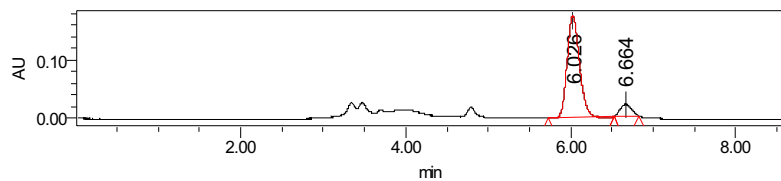


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	11.957	6142443	94.84	309119	bb	Unknown
2	16.889	334059	5.16	16105	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

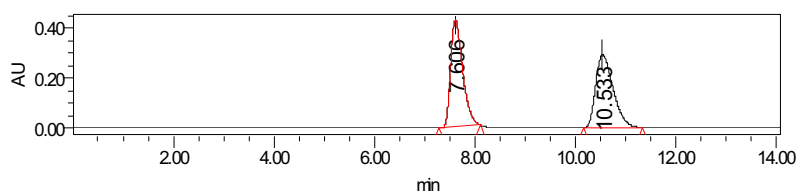
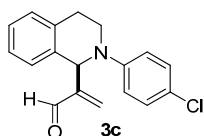


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	6.027	3221658	49.78	296841	BV	Unknown
2	6.667	3250577	50.22	263767	VB	Unknown

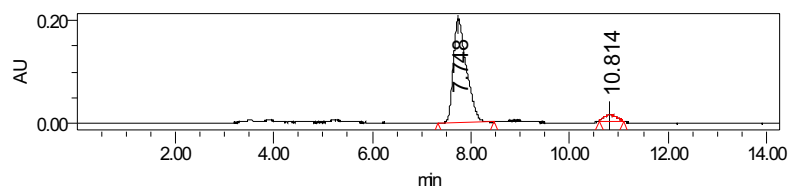


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	6.026	1827899	92.34	175177	bb	Unknown
2	6.664	151614	7.66	17654	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 80/20, flow rate 1.0 mL/min)

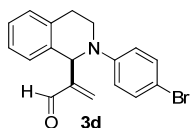


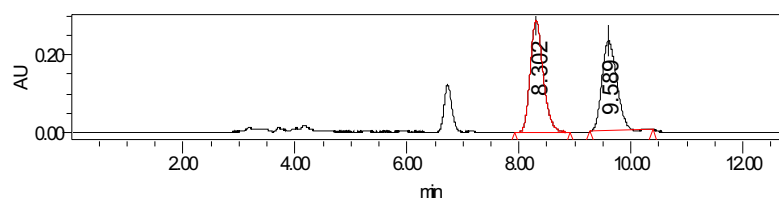
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	7.606	7045530	50.14	425898	bb	Unknown
2	10.533	7006508	49.86	292182	bb	Unknown



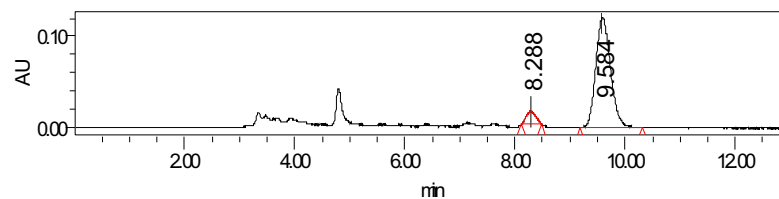
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	7.748	3749771	95.76	202460	bb	Unknown
2	10.814	165949	4.24	10688	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)



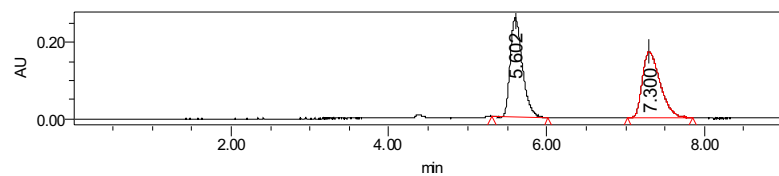
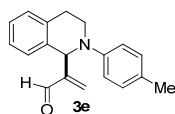


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	8.302	4642221	51.82	287752	bb	Unknown
2	9.589	4316973	48.18	232607	bb	Unknown

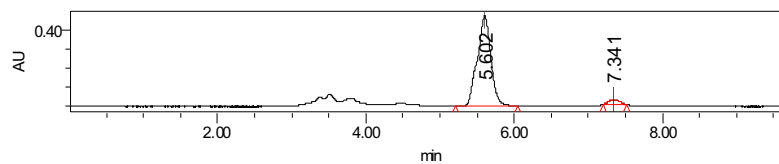


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	8.288	92843	5.91	8248	bb	Unknown
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HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

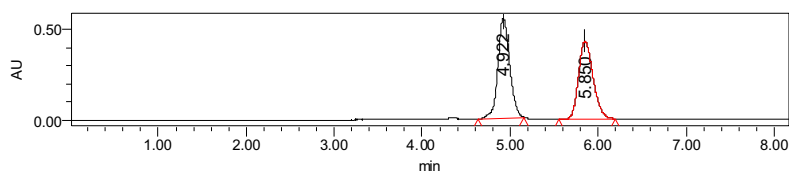
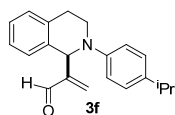


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	5.602	2763794	50.56	259018	bb	Unknown
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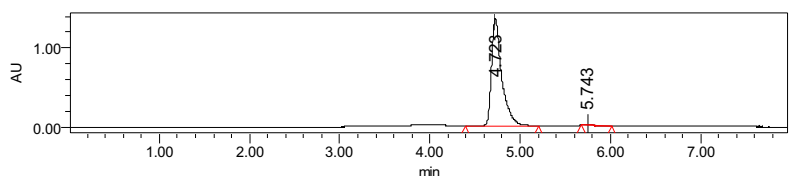


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	5.602	5888800	95.58	469526	bb	Unknown
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HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

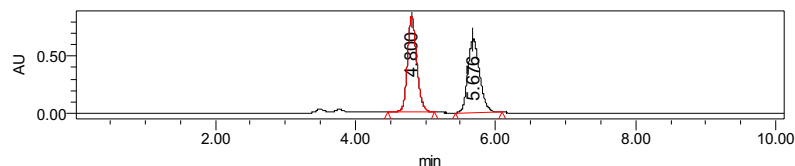
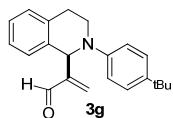


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	4.922	5112210	50.83	550871	bb	Unknown
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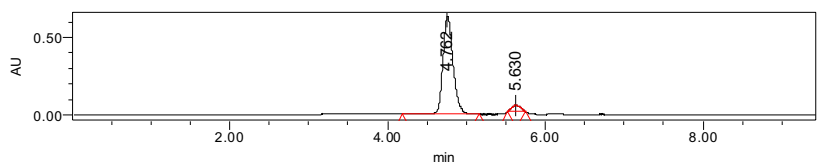


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	4.723	10644337	99.61	1355011	bb	Unknown
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HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

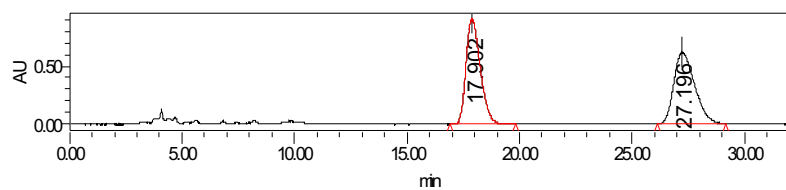
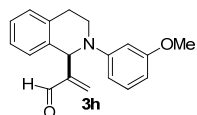


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	4.800	7788221	50.98	840920	bb	Unknown
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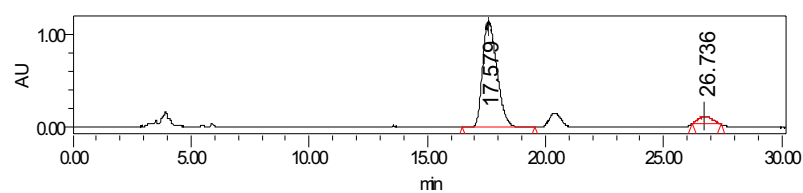


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	4.762	5661556	95.02	629838	bb	Unknown
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HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

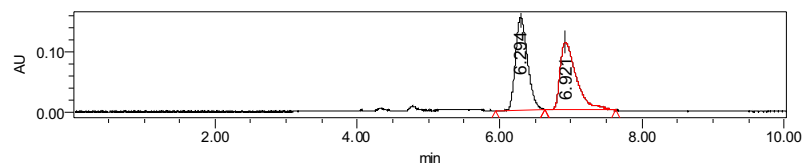
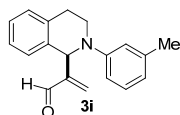


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	17.902	40285620	50.24	905277	bb	Unknown
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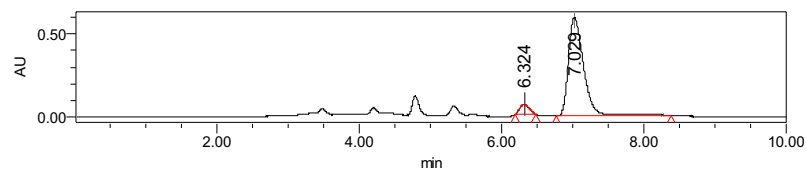


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	17.579	47732337	94.83	1134593	bb	Unknown
2	26.736	2604773	5.17	68105	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

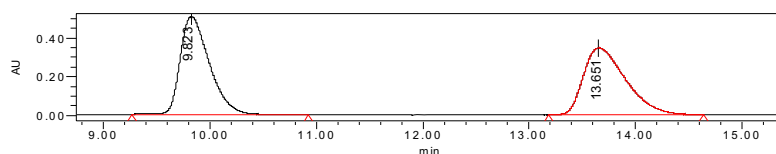
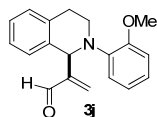


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	6.294	1824646	50.37	155301	bb	Unknown
2	6.921	1797585	49.63	112882	bb	Unknown

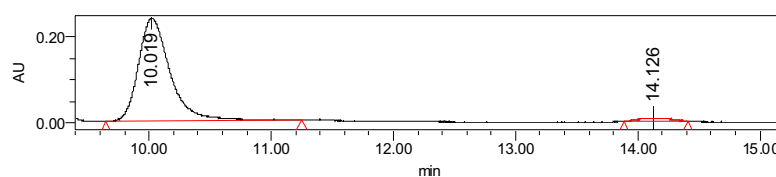


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	6.324	501091	5.22	57039	bb	Unknown
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HPLC using an OD (*n*-Hexane/*i*PrOH= 90/10, flow rate 1.0 mL/min)

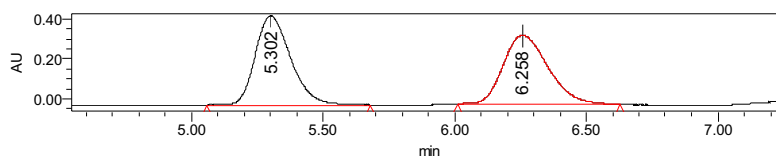
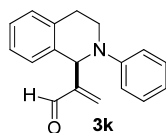


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	9.823	9772006	50.41	509119	bb	Unknown
2	13.651	9613930	49.59	347603	bb	Unknown

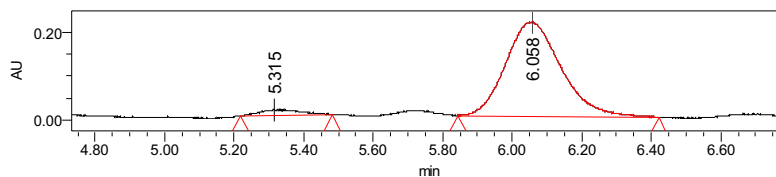


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	10.019	4253469	96.98	238608	bb	Unknown
2	14.126	132428	3.02	7434	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

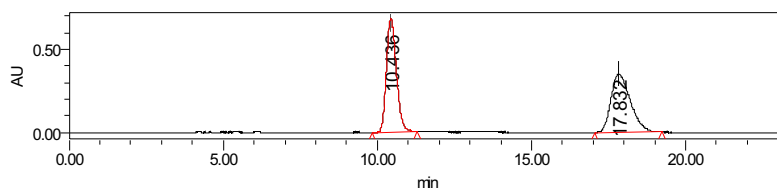
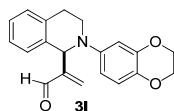


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	5.302	4165687	50.47	447810	bb	Unknown
2	6.258	4087368	49.53	344842	bb	Unknown

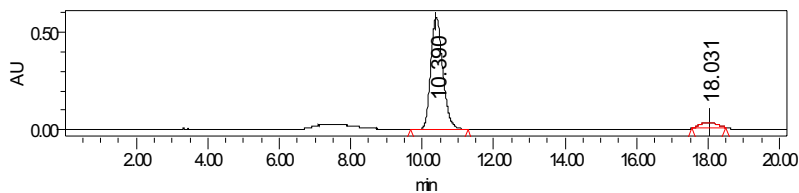


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	5.315	113148	4.60	12880	bb	Unknown
2	6.058	2348678	95.40	213460	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

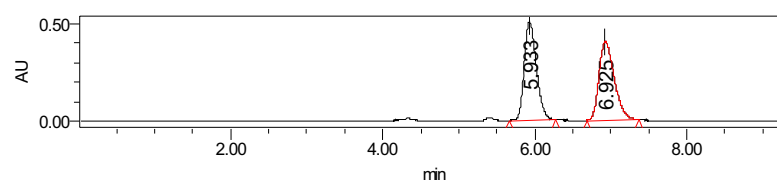
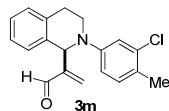


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	10.436	15178648	49.86	681600	bb	Unknown
2	17.832	15261948	50.14	349405	bb	Unknown

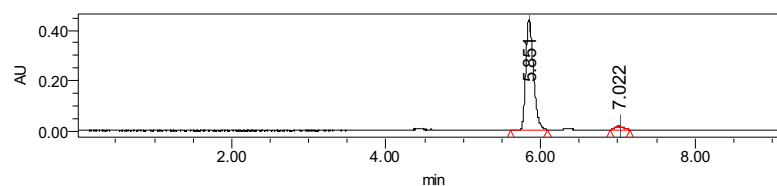


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	10.390	13406212	95.14	578279	bb	Unknown
2	18.031	684249	4.86	24707	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

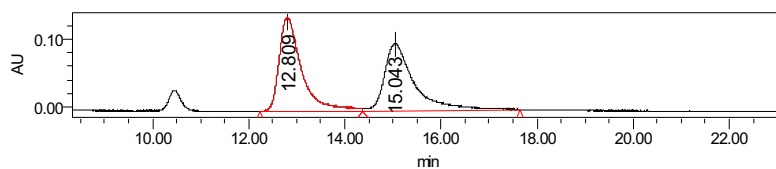
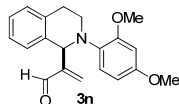


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	5.933	5561912	49.87	504615	bb	Unknown
2	6.925	5591252	50.13	399944	bb	Unknown

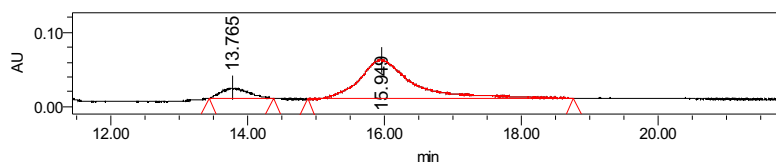


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	5.851	2984746	96.64	439205	bb	Unknown
2	7.022	103693	3.36	12605	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 90/10, flow rate 1.0 mL/min)

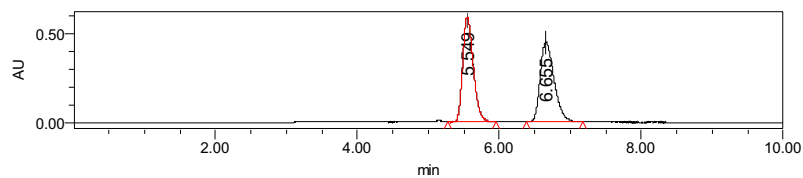
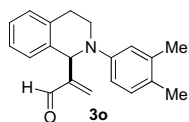


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	12.810	4903433	51.32	150176	BV	Unknown
2	15.027	4651962	48.68	106727	Vb	Unknown

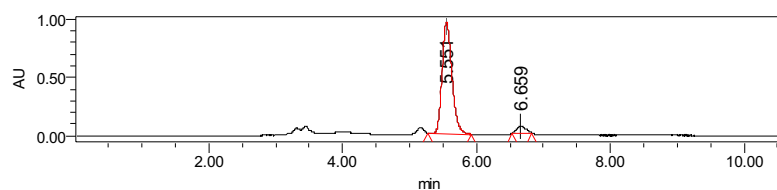


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	13.765	371405	10.19	14032	bb	Unknown
2	15.949	3272030	89.81	59376	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

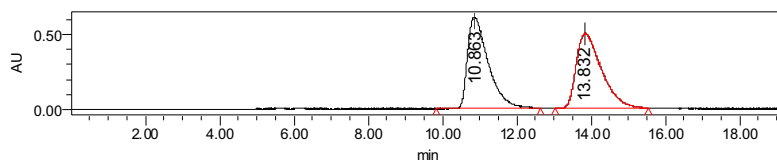
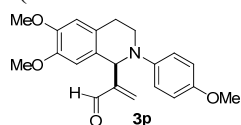


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	5.549	6117432	49.83	592006	bb	Unknown
2	6.655	6159698	50.17	450566	bb	Unknown

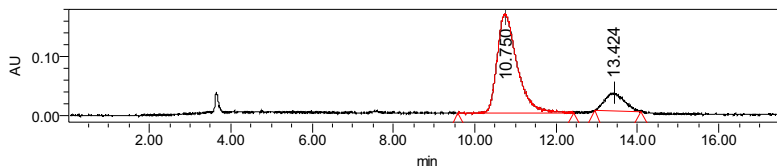


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	5.551	9594090	95.67	929929	Vb	Unknown
2	6.659	434089	4.33	48260	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

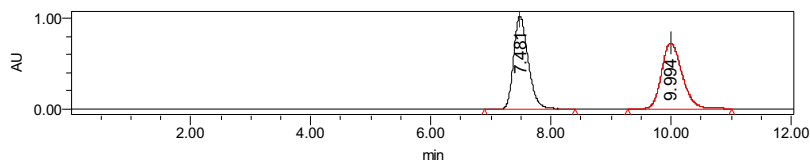
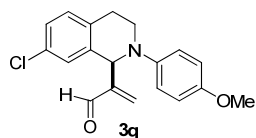


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	10.863	23561111	50.01	614077	bb	Unknown
2	13.832	23552054	49.99	498127	bb	Unknown

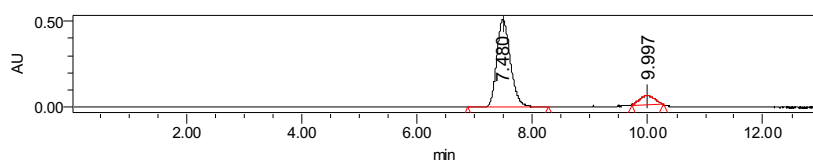


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	10.750	5655550	85.09	168177	bb	Unknown
2	13.424	990793	14.91	29426	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

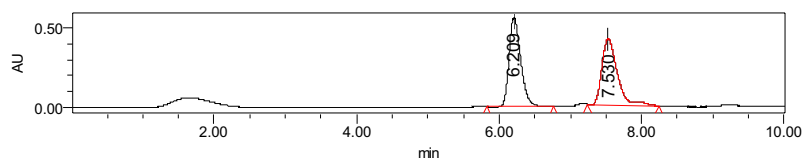
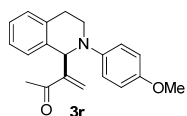


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	7.481	17170026	49.83	1021570	7.481	Unknown
2	9.994	17286080	50.17	725458	9.994	Unknown

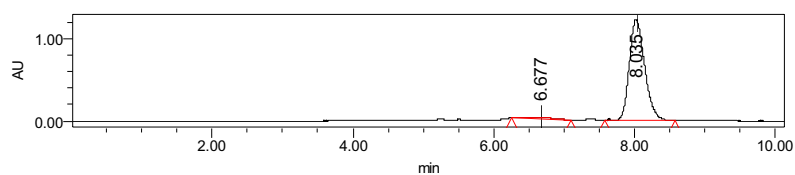


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	7.480	8350144	92.40	507550	bb	Unknown
2	9.997	687101	7.60	43053	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)

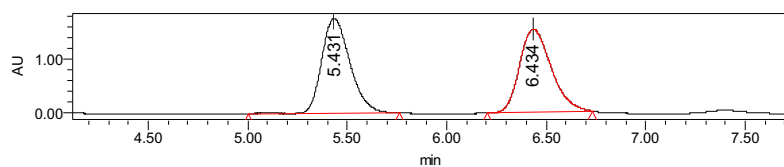
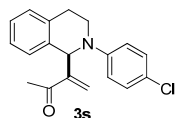


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	6.209	6332197	50.66	554694	bb	Unknown
2	7.530	6168252	49.34	411074	bb	Unknown



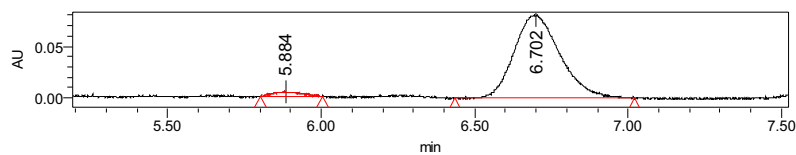
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	6.677	473486	2.49	17707	bb	Unknown
2	8.035	18579450	97.51	1218085	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 80/20, flow rate 1.0 mL/min)



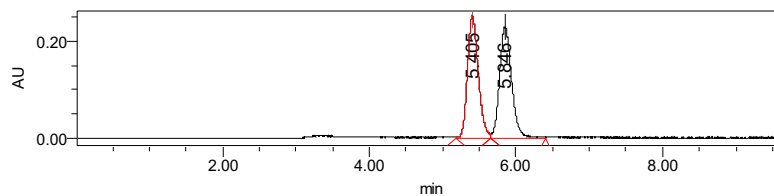
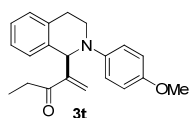
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	5.431	17250722	50.41	1750499	bb	Unknown

2	6.434	16969820	49.59	1535756	bb	Unknown
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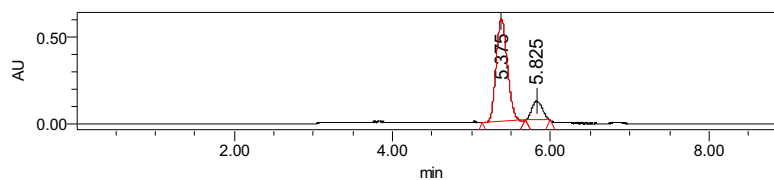


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	5.884	28159	3.27	4199	bb	Unknown
2	6.702	833620	96.73	79846	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 80/20, flow rate 1.0 mL/min)

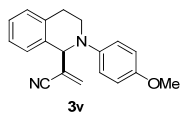


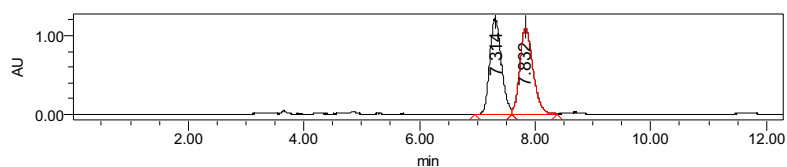
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	5.405	2531262	49.52	248860	VV	Unknown
2	5.846	2580357	50.48	226931	VB	Unknown



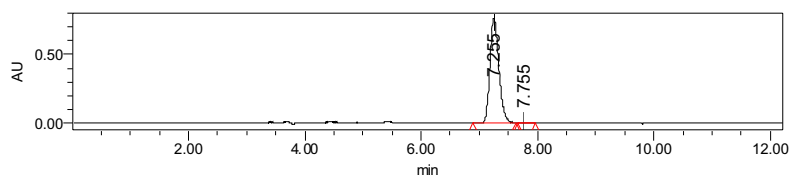
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	5.375	5776553	84.69	593663	bb	Unknown
2	5.825	1044229	15.31	111186	bb	Unknown

HPLC using an OD (*n*-Hexane/*i*PrOH= 60/40, flow rate 1.0 mL/min)



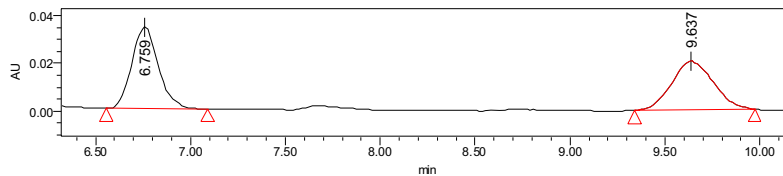
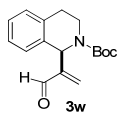


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	7.314	17105166	49.47	1222805	VV	Unknown
2	7.832	17468280	50.53	1101978	VV	Unknown

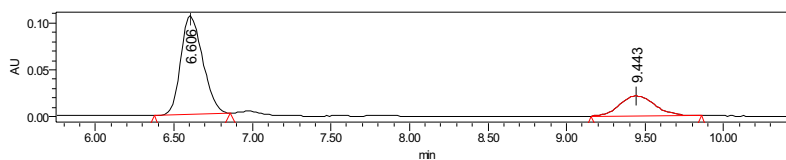


	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	7.255	8162393	99.92	757911	bb	Unknown
2	7.755	6168	0.08	-1301	bb	Unknown

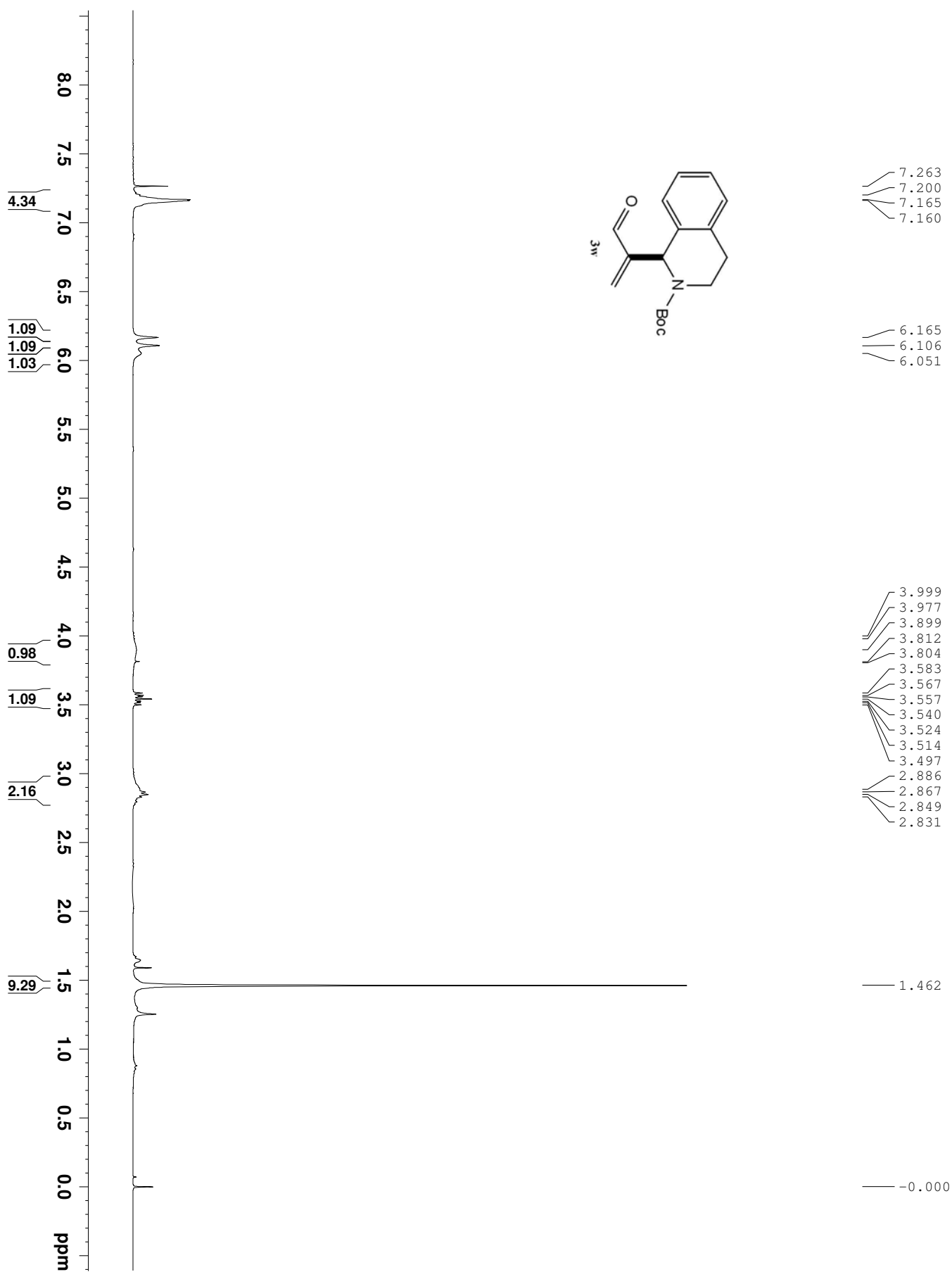
HPLC using an OD (*n*-Hexane/*i*PrOH= 80/20, flow rate 1.0 mL/min)

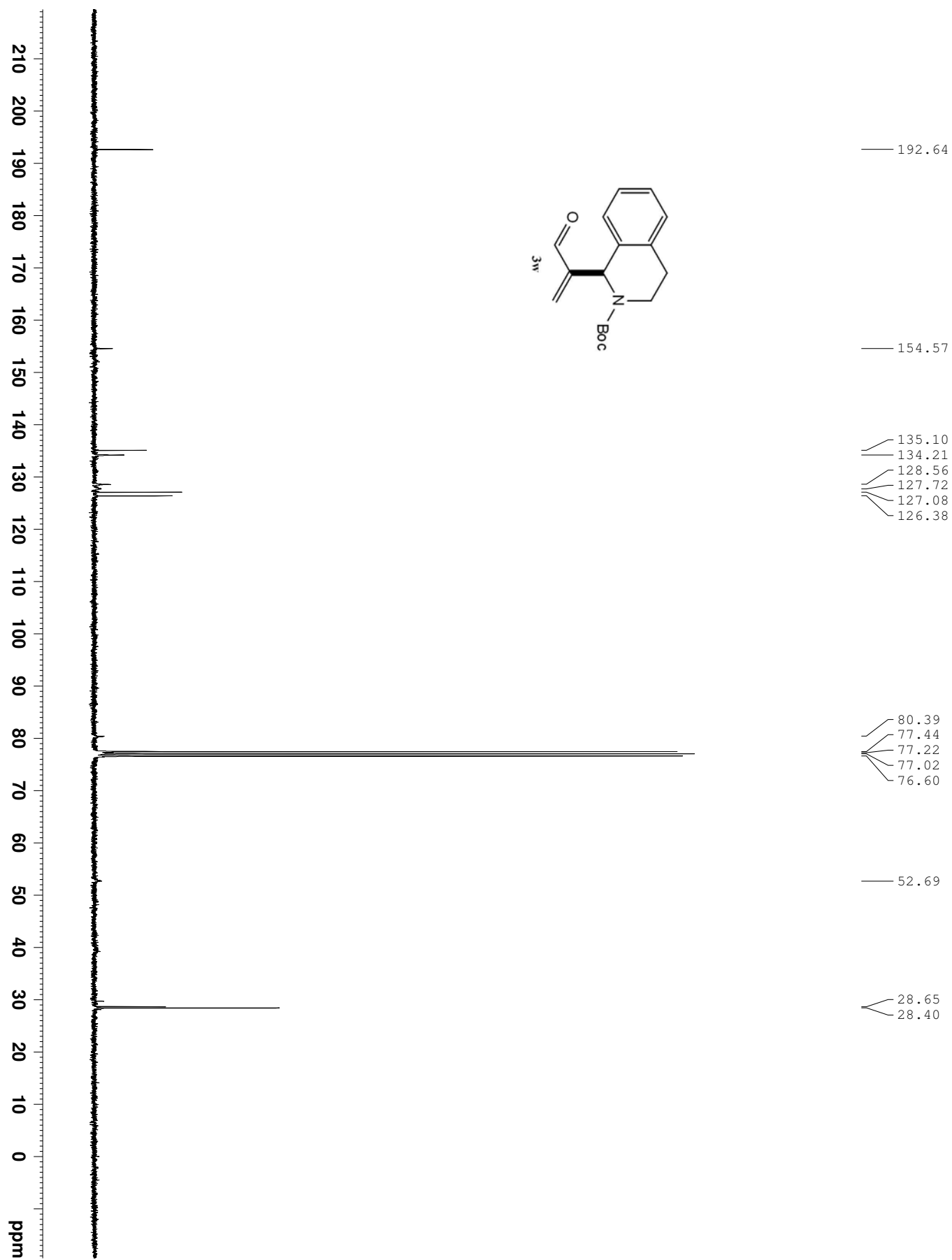


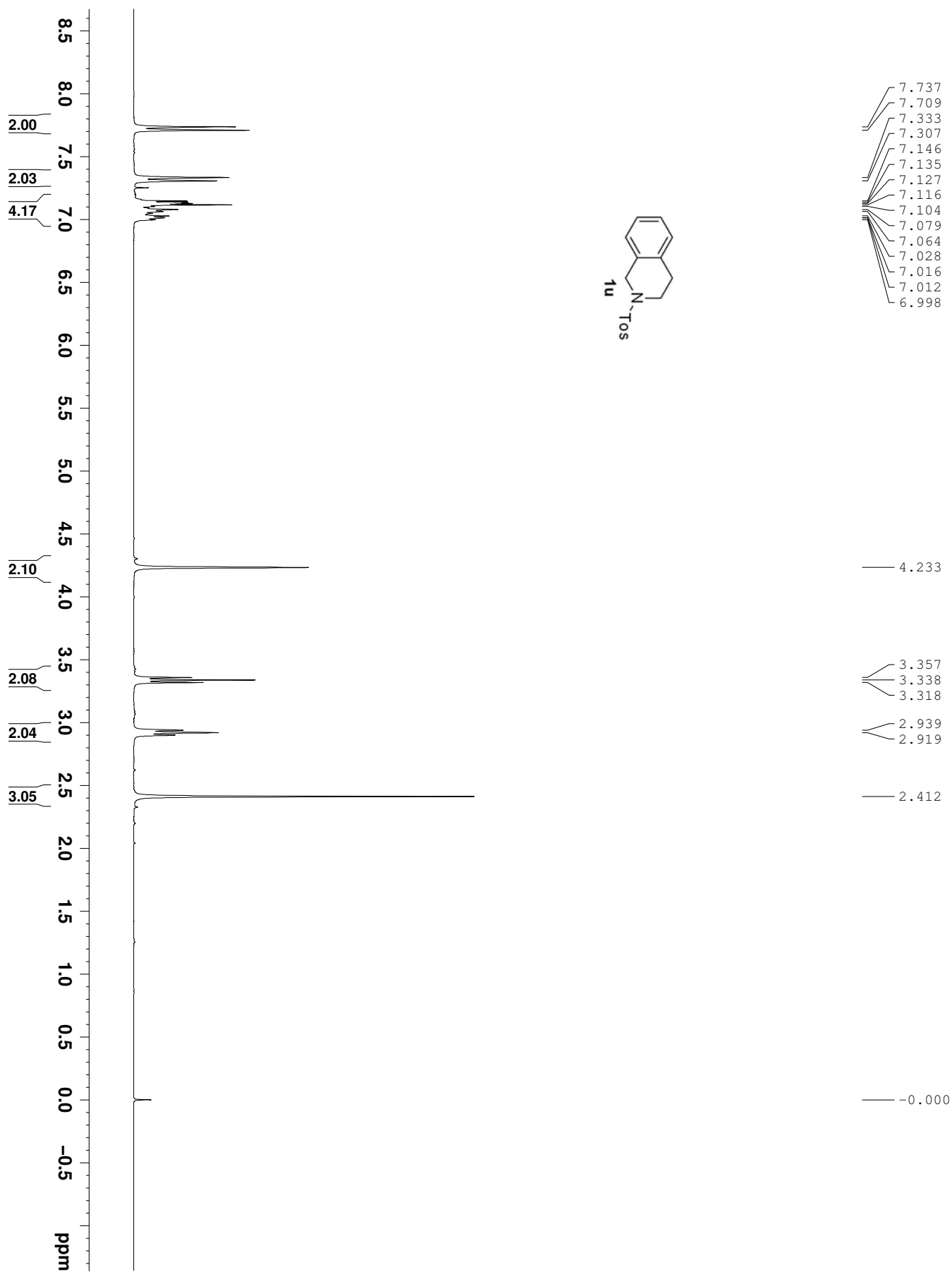
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	6.759	329068	51.43	33891	bb	Unknown
2	9.637	310789	48.57	20381	bb	Unknown

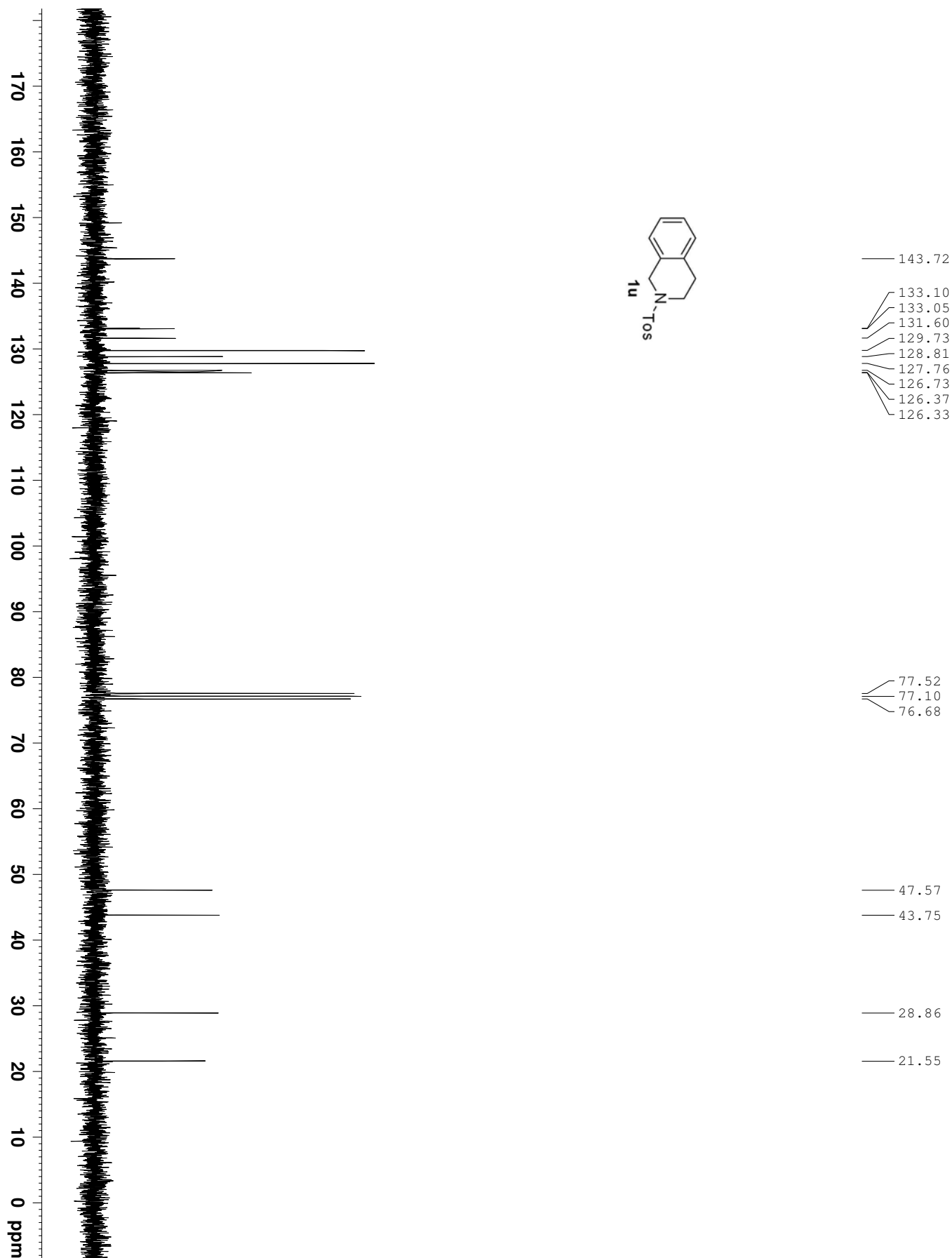


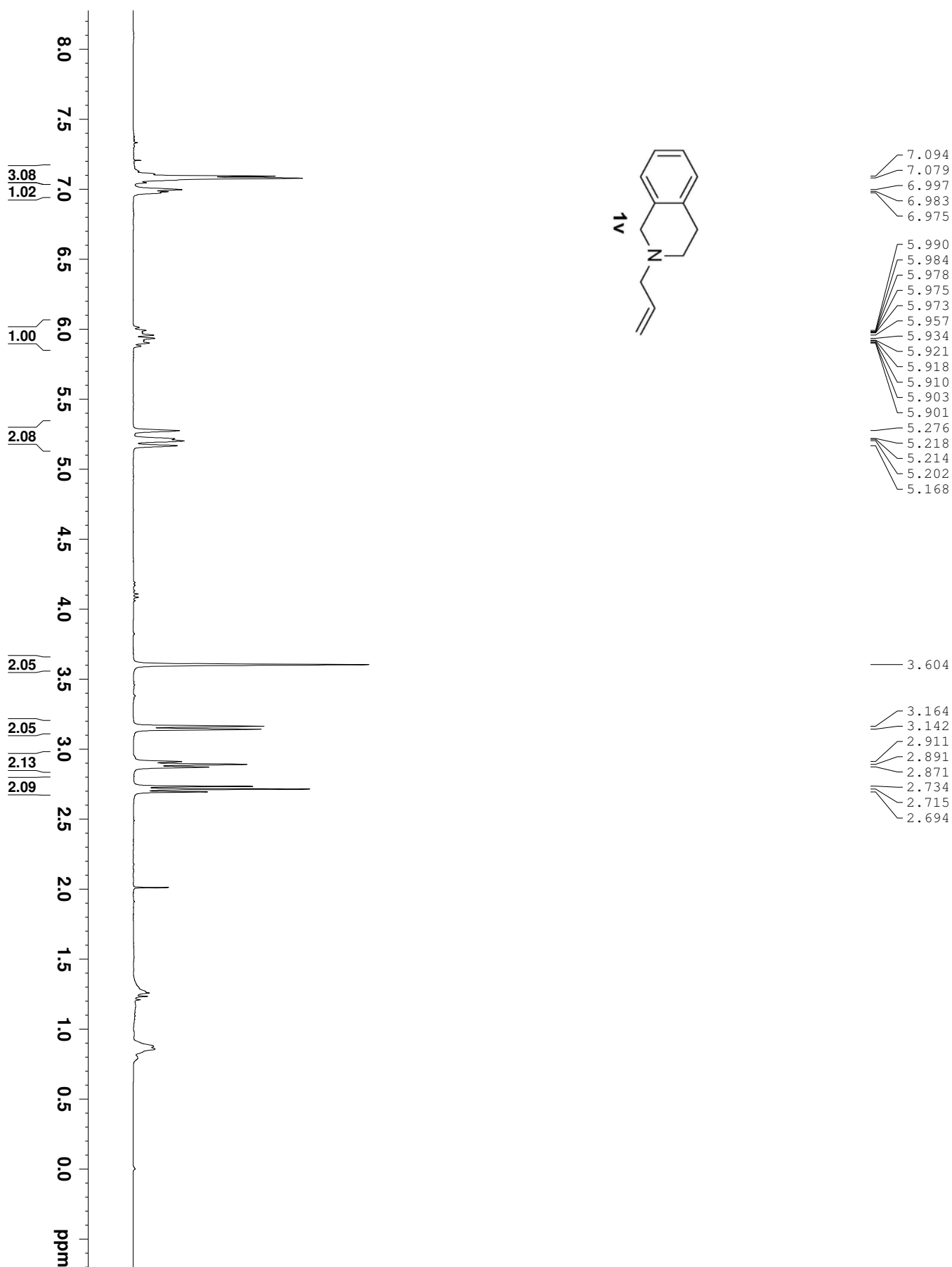
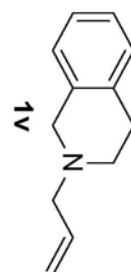
	Retention Time	Area	% Area	Height	Int Type	Peak Type
1	6.606	1024607	75.18	105636	bb	Unknown
2	9.443	338319	24.82	21633	bb	Unknown

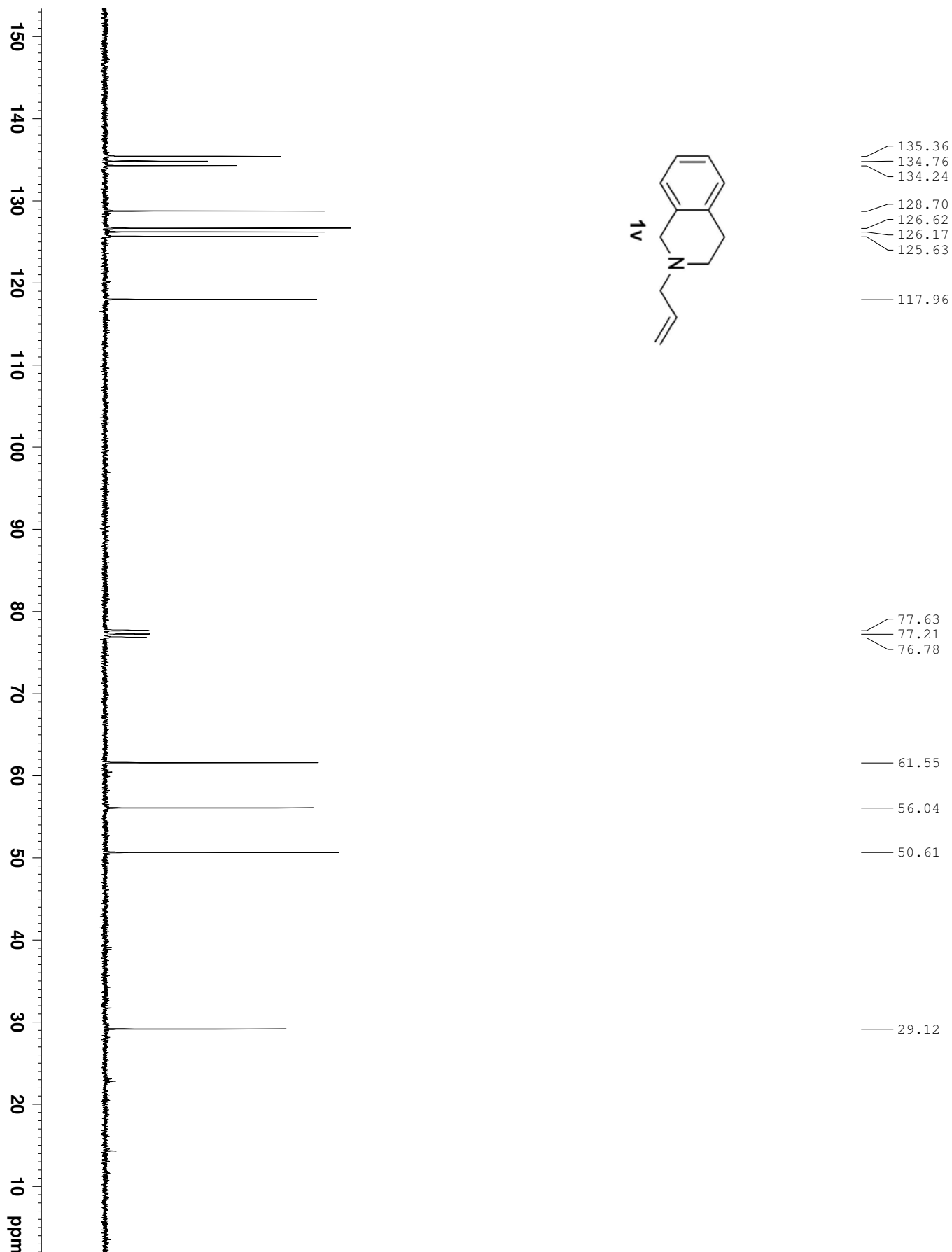
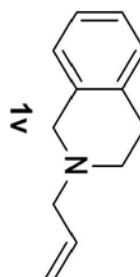


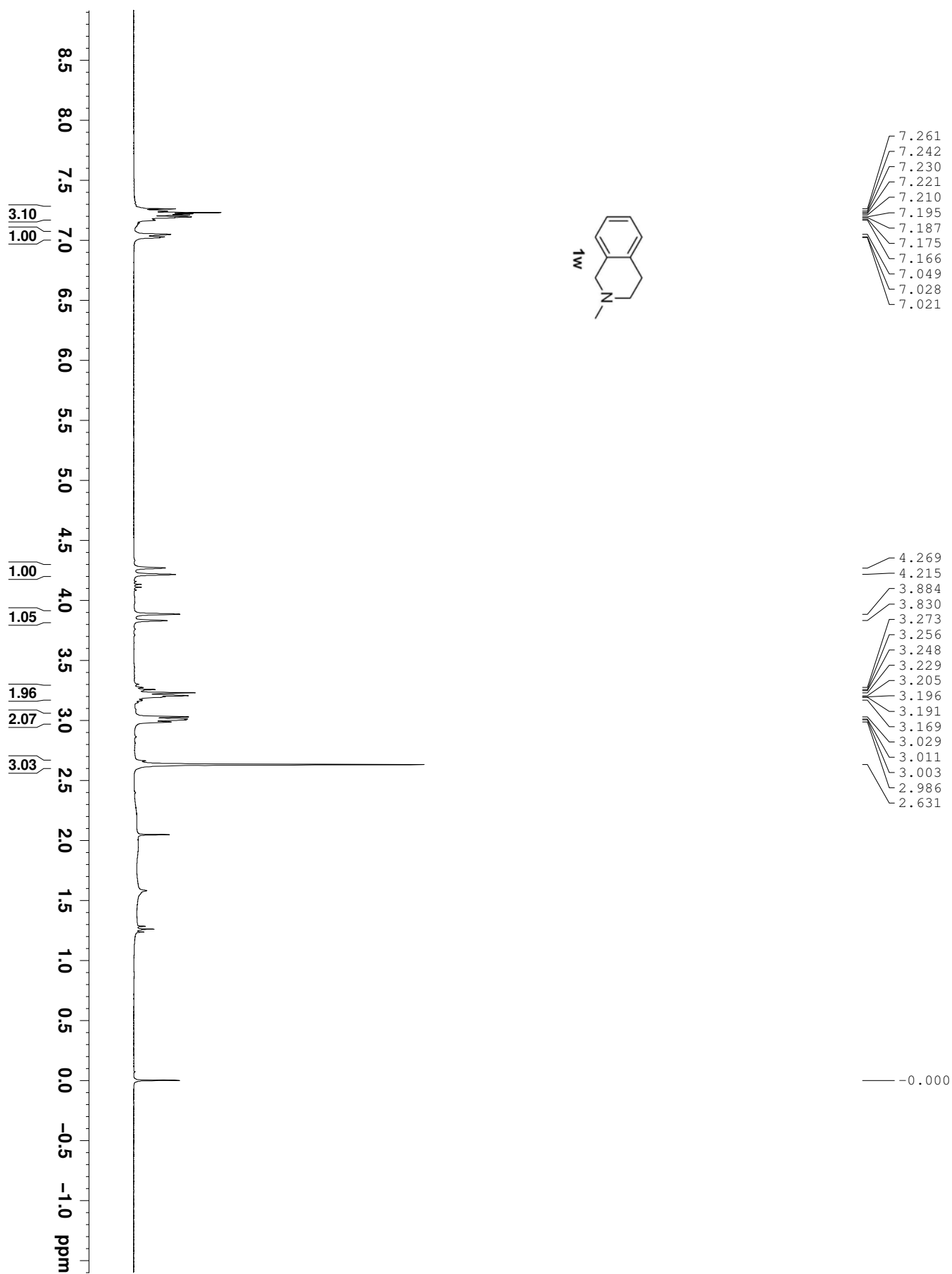


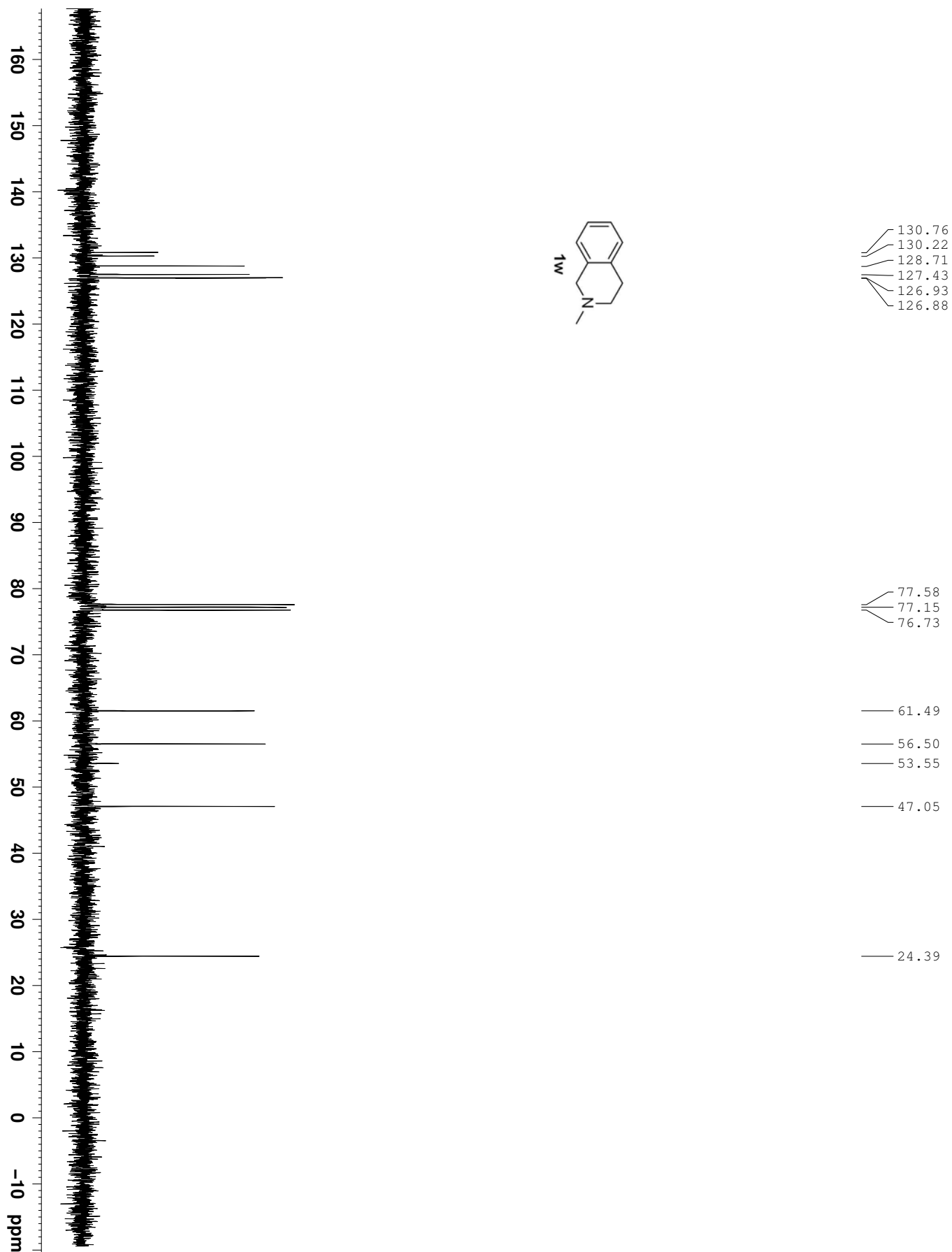


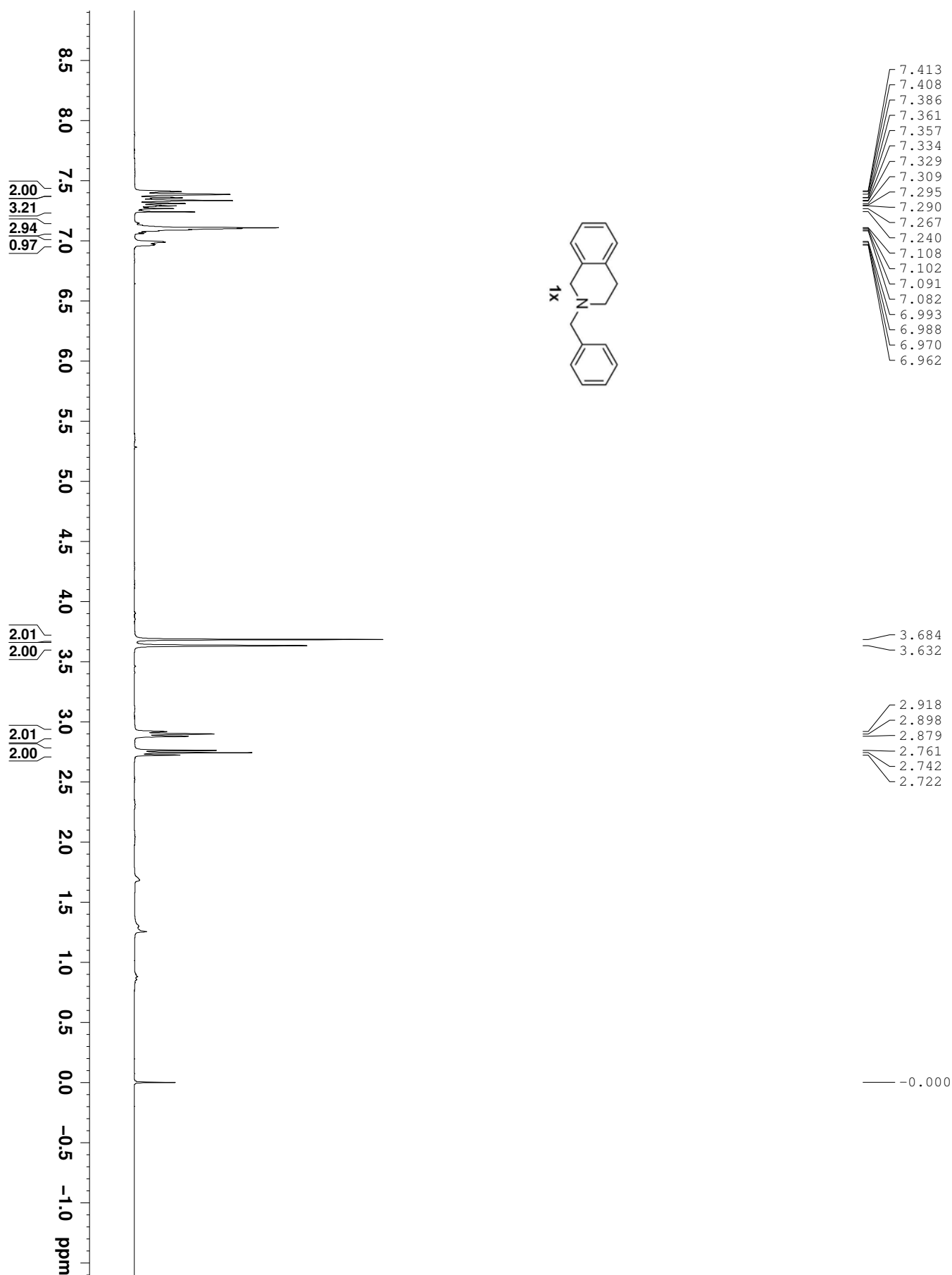


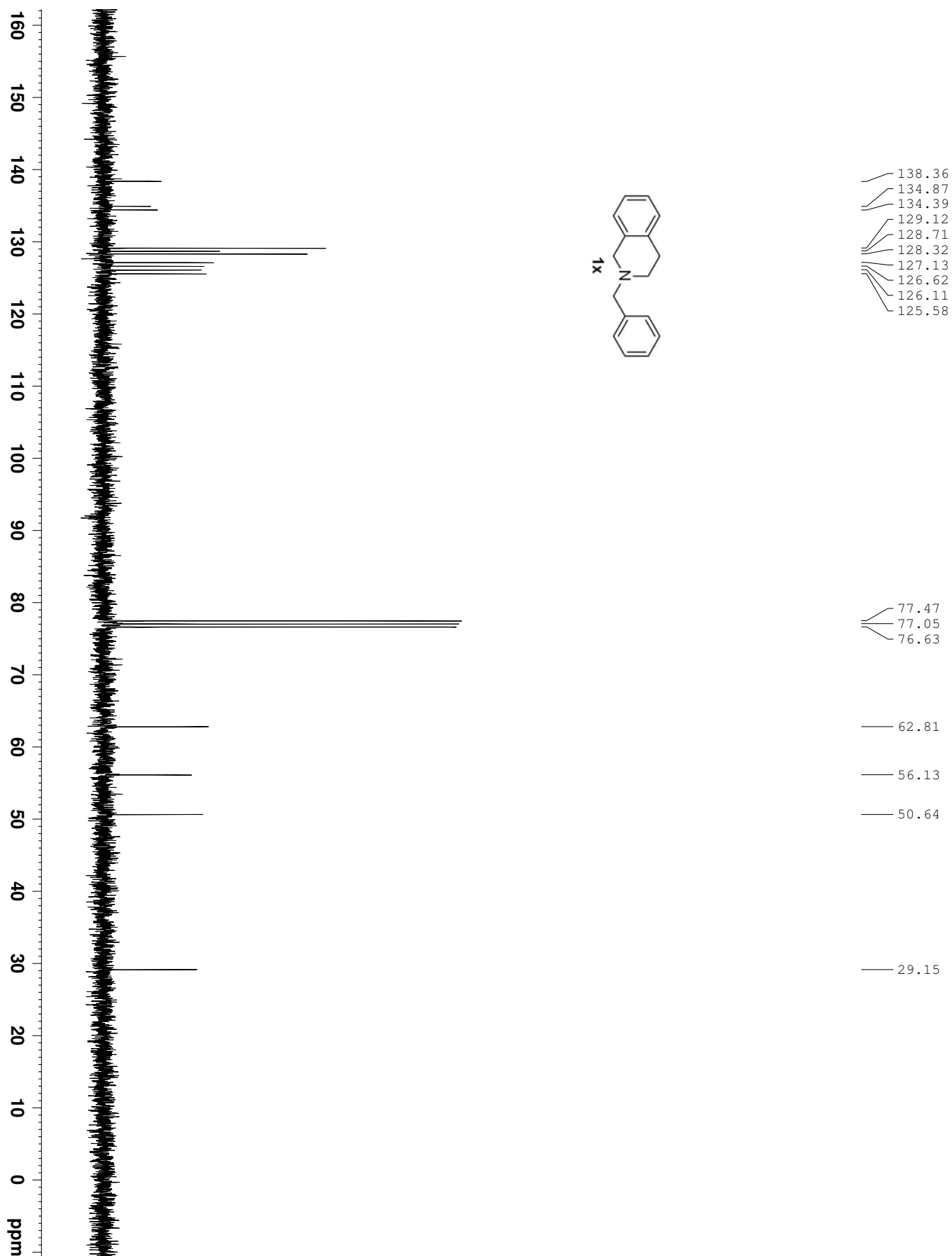


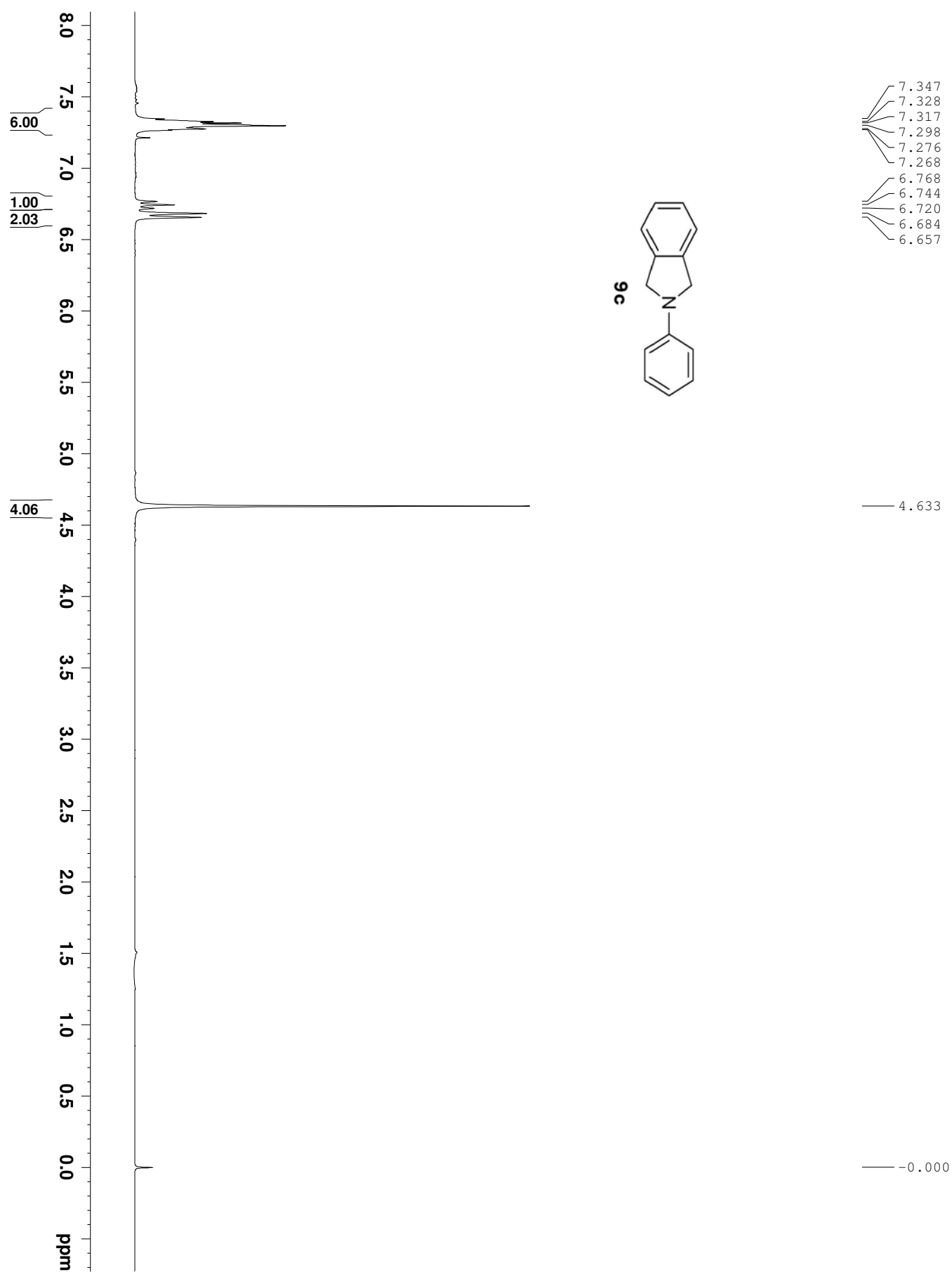
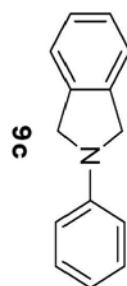


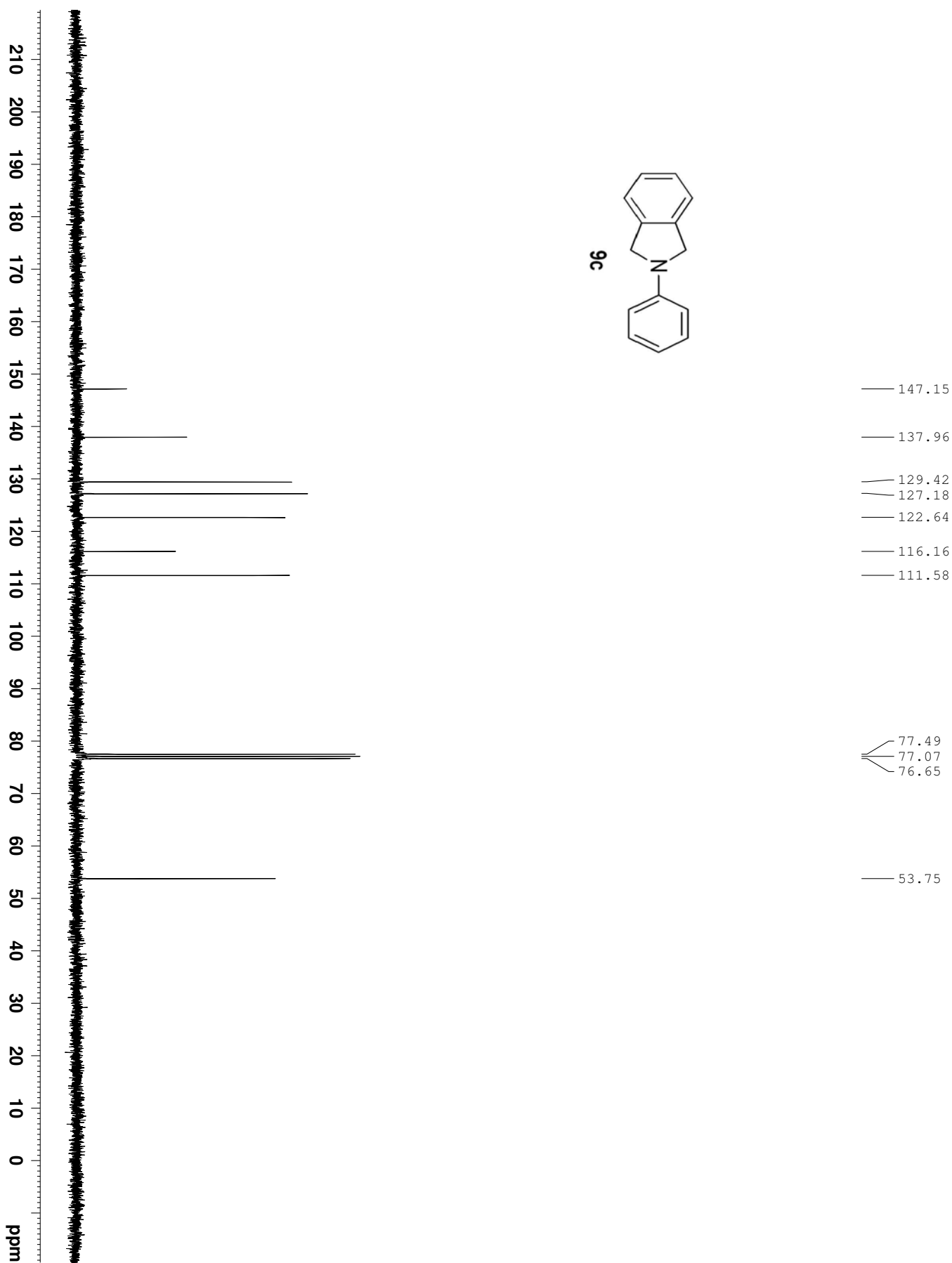


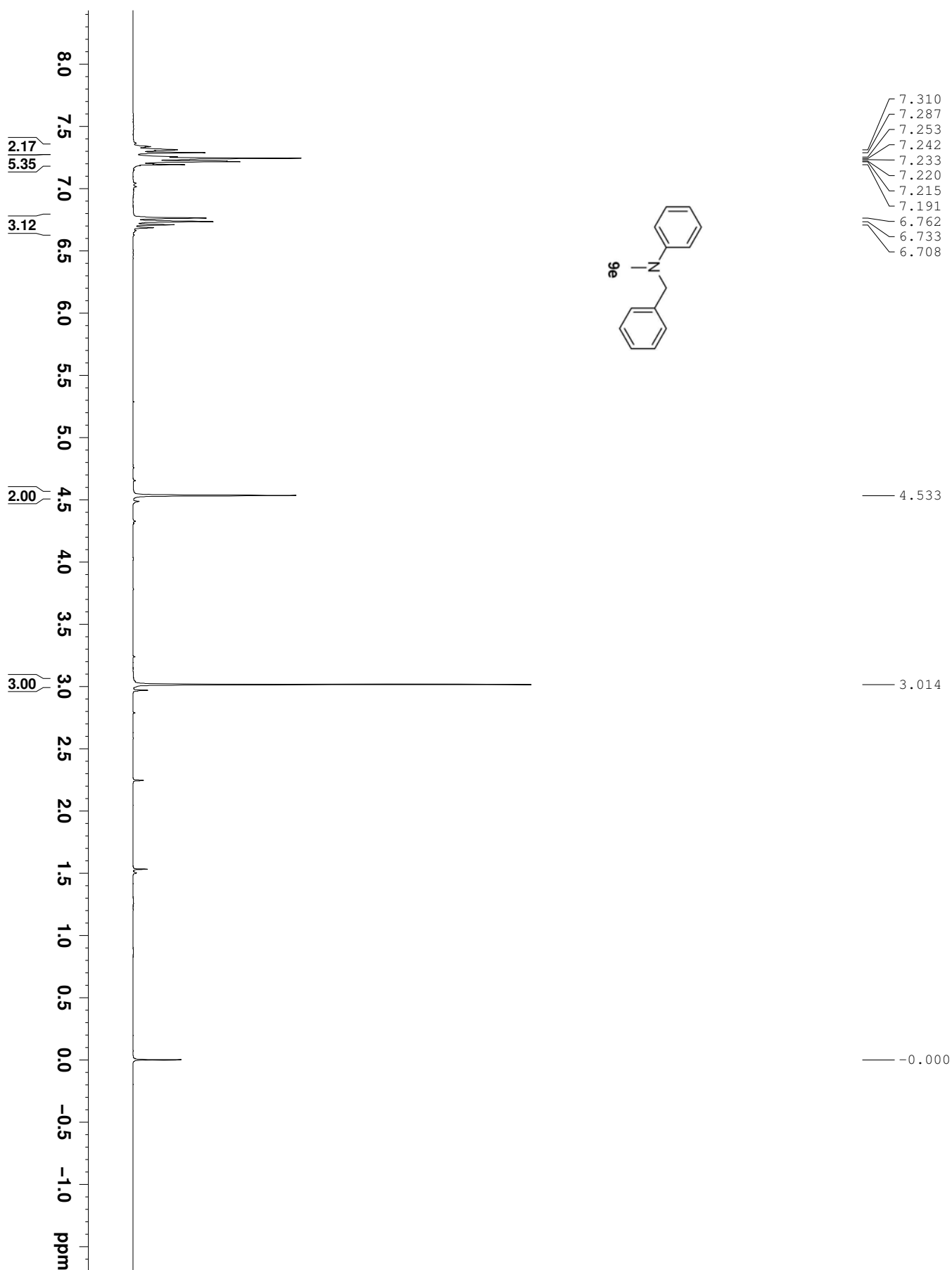
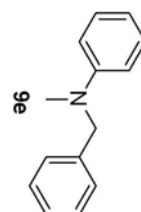


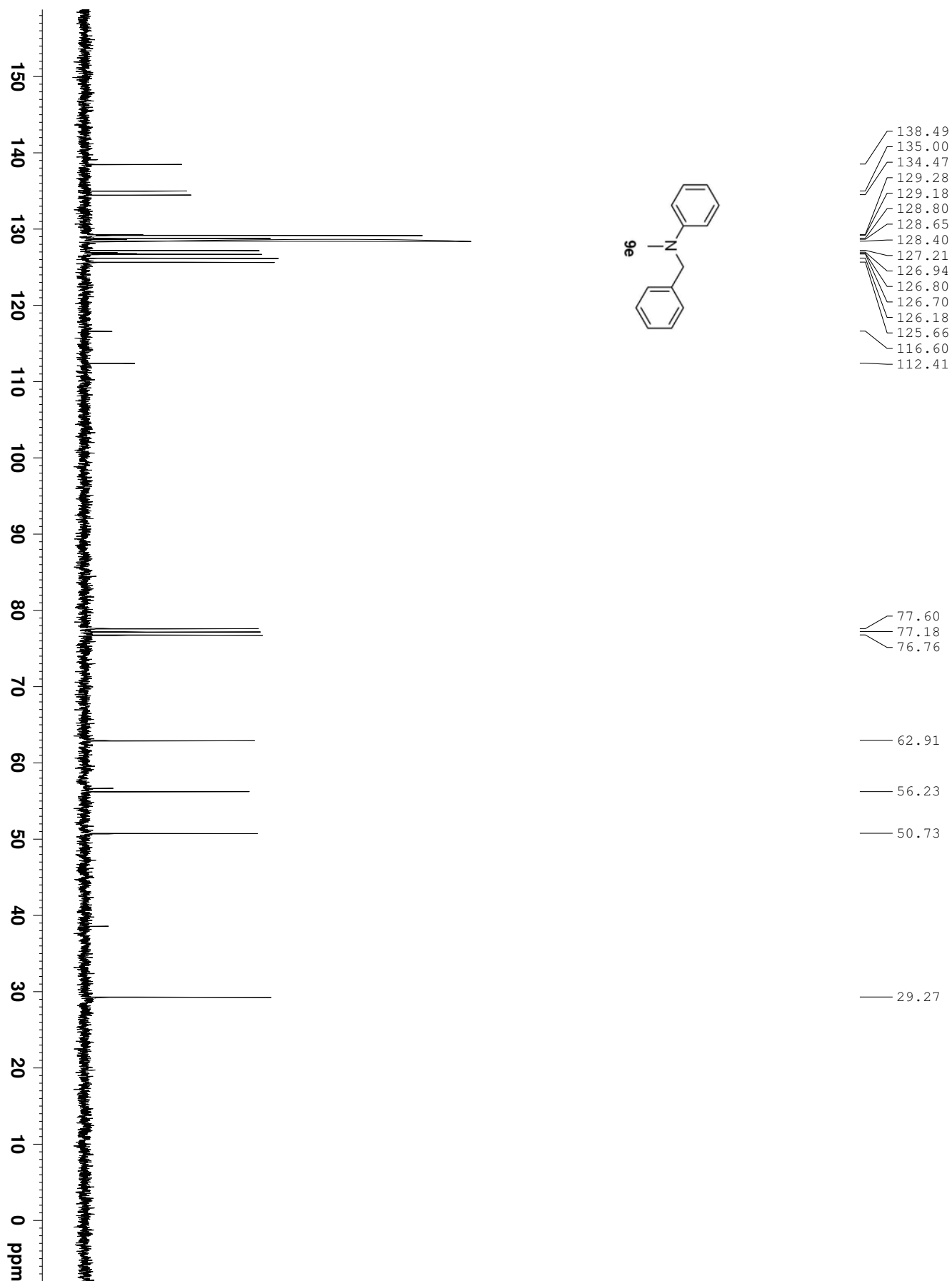
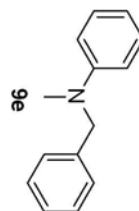


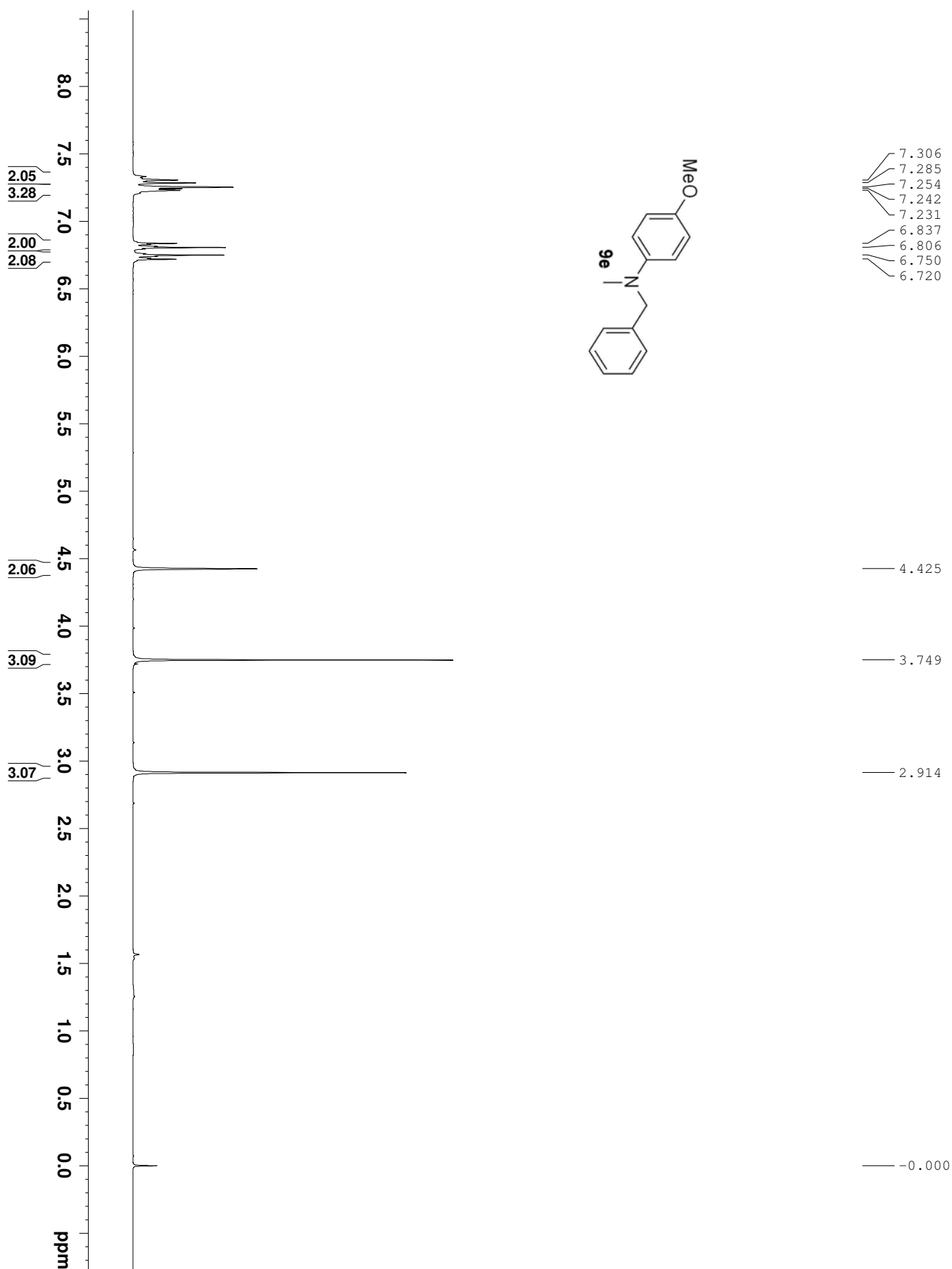
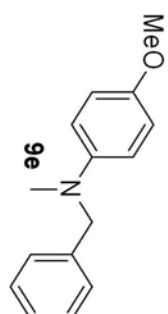


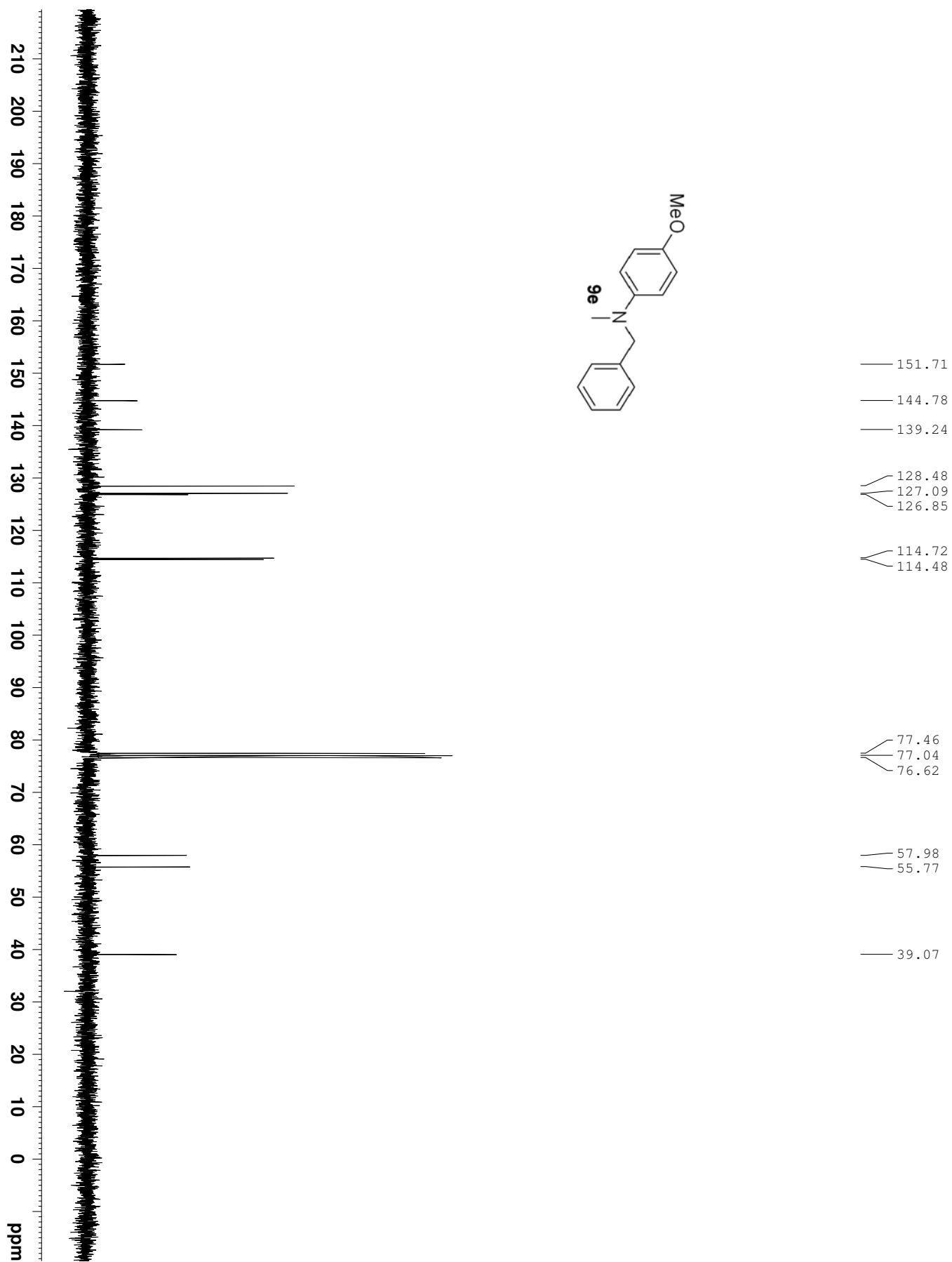


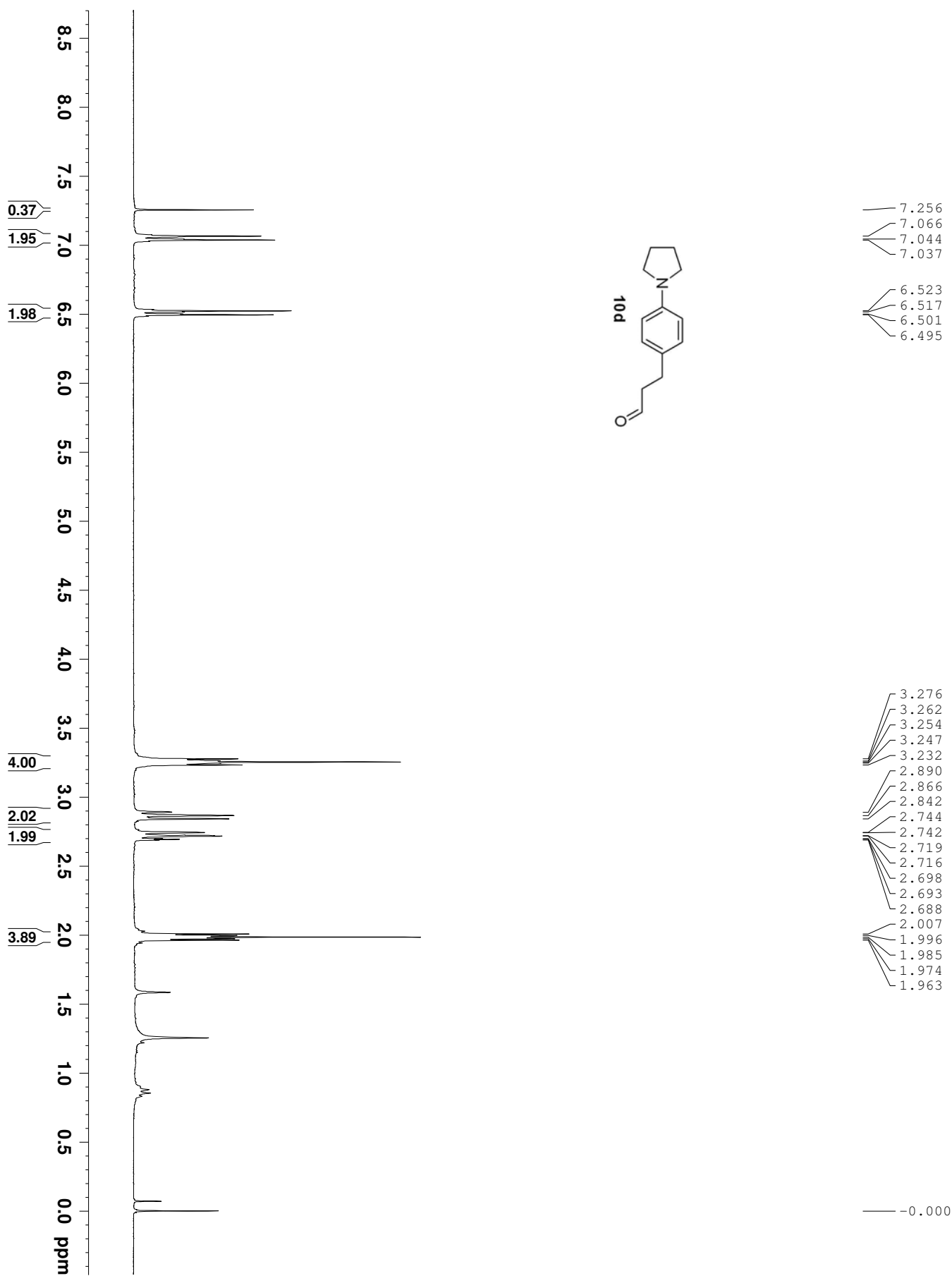
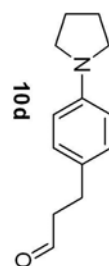


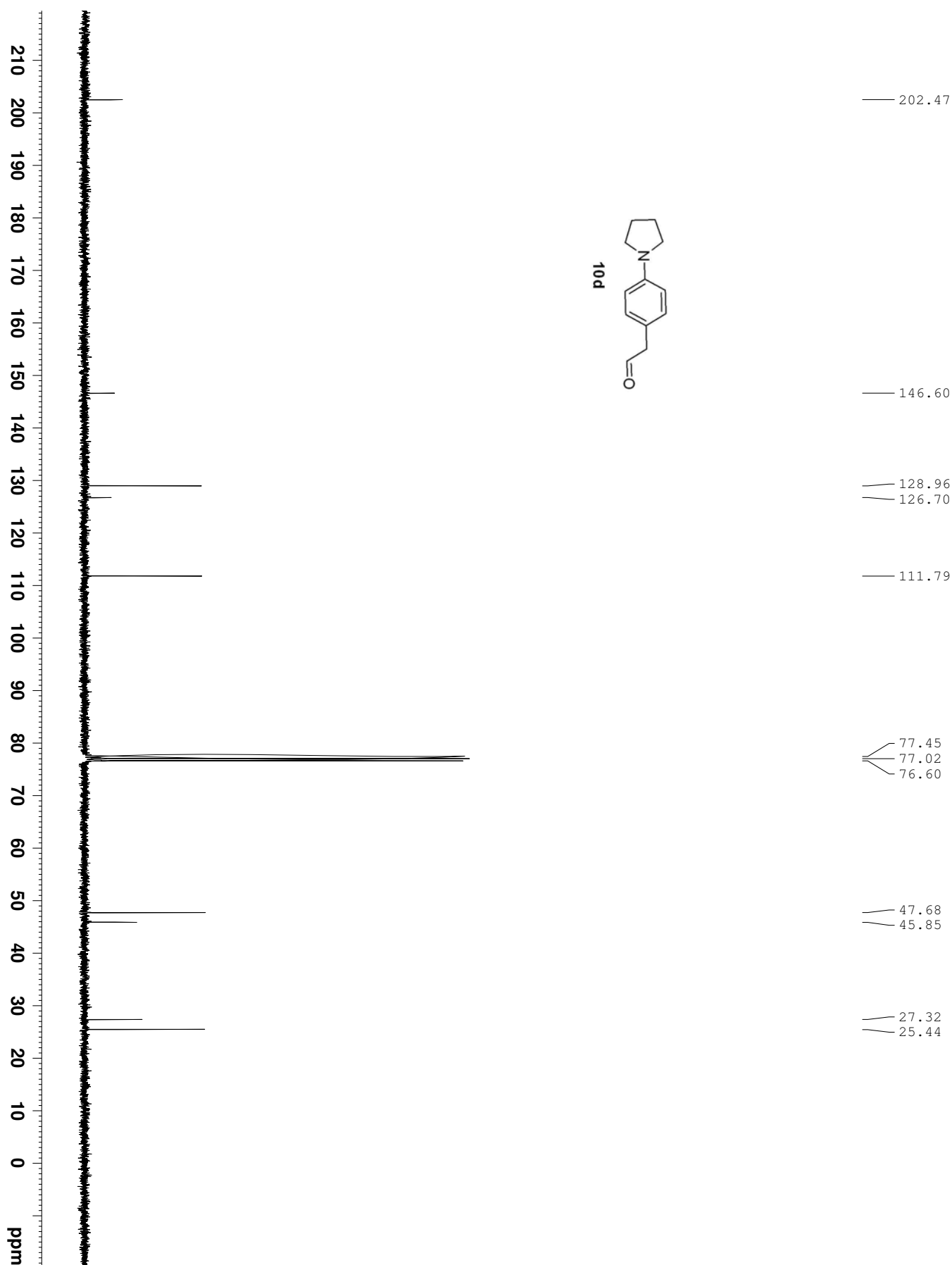


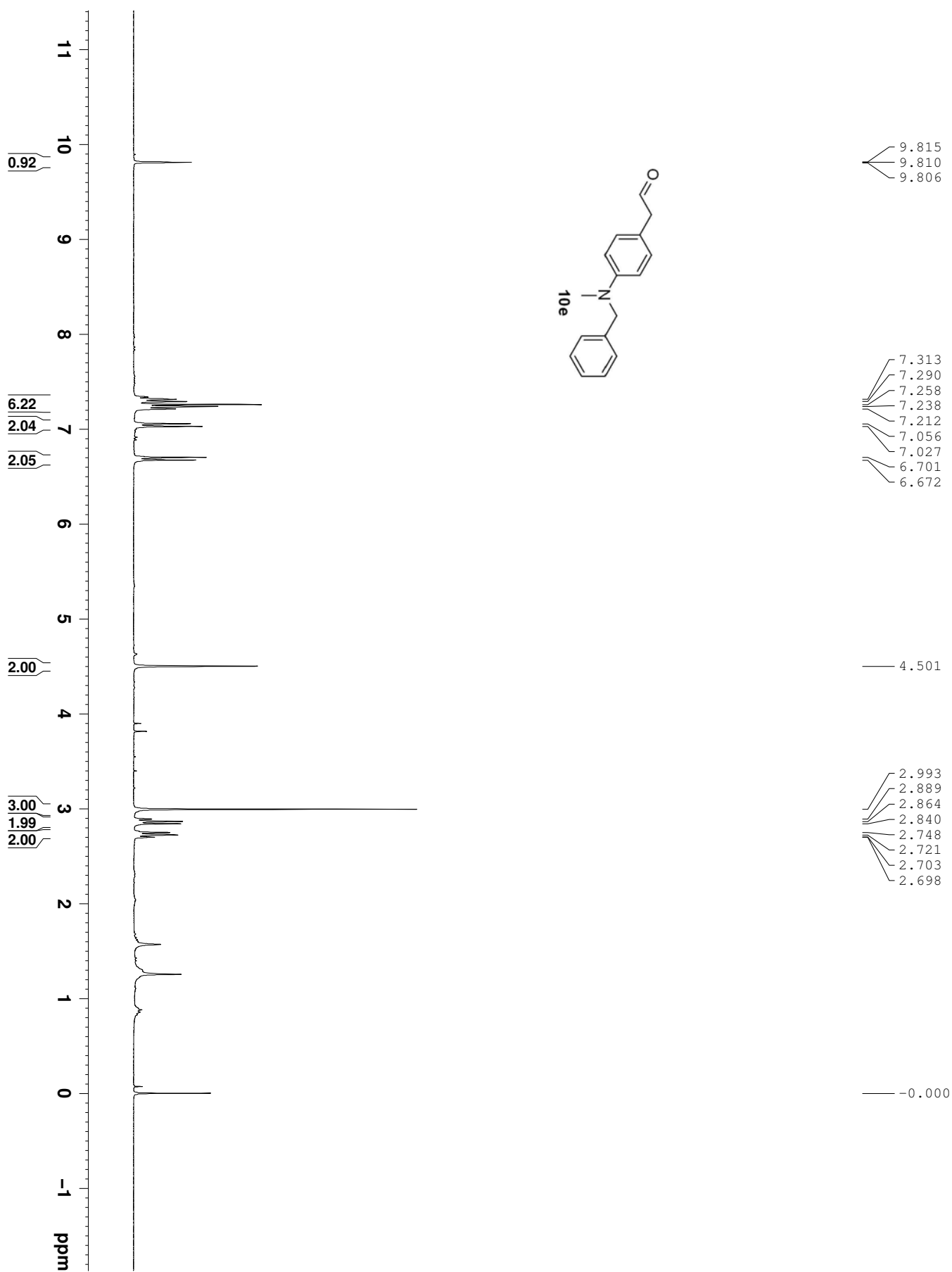


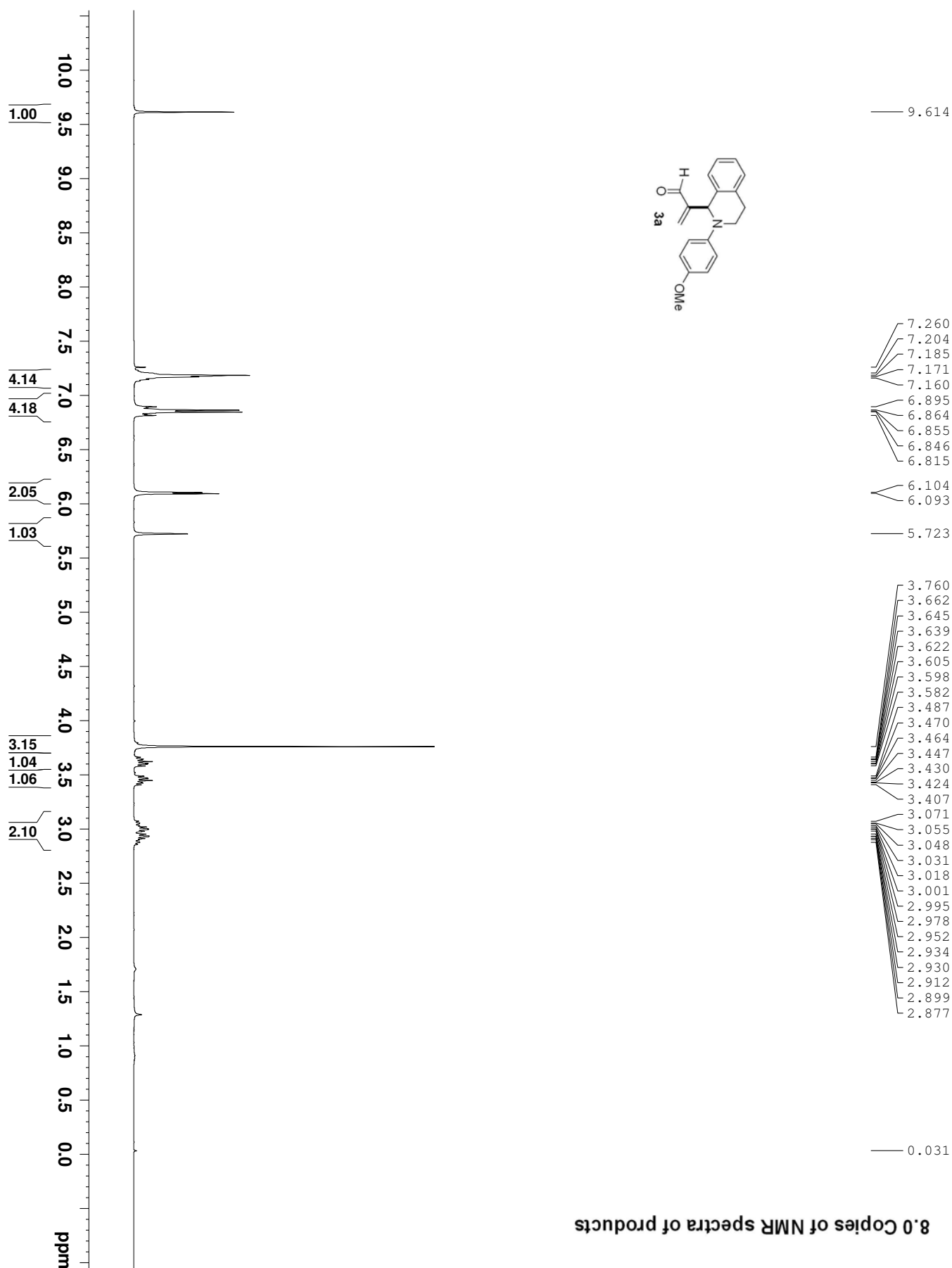


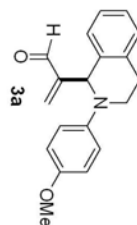
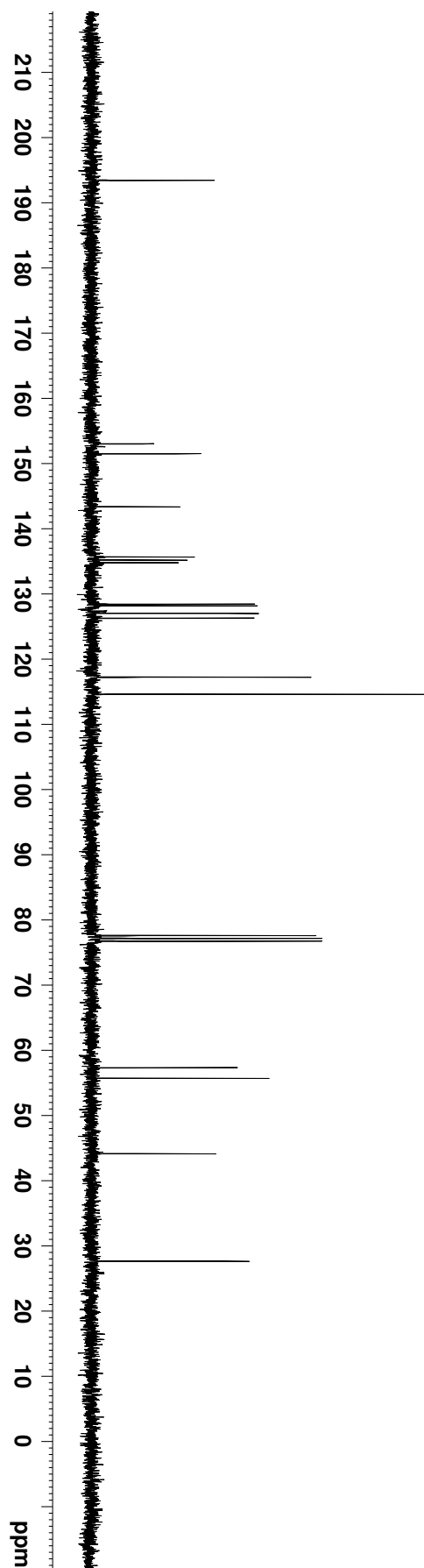












— 193.39

152.97
151.44

— 143.31

135.60
135.14
134.73

128.39
128.13
126.97
126.23

117.17
114.56

77.53
77.11
76.68

57.27
55.64

— 44.08

— 27.60

