Modified ToxT inhibitor reduces *Vibrio cholerae* virulence *in vivo*

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SUPPORTING INFORMATION

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Figure S1. TcpA western blot

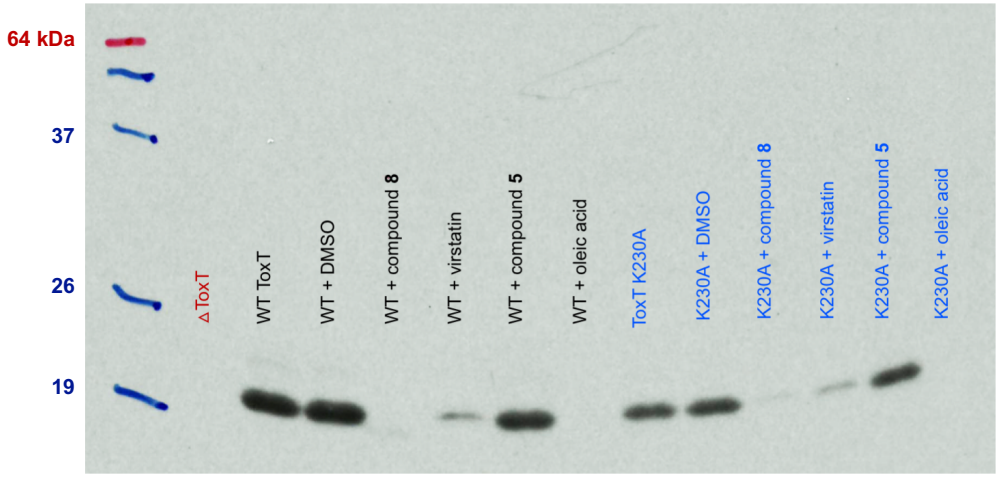


Figure S1. Western blot showing TcpA production in 3 backgrounds: *ΔtoxT* (lane 1; strain MBN017), WT *toxT* (lanes 2-7; strain O395 Sm), and *toxT K230A* (lanes 8-13; strain AW46). Compound **8**, virstatin, and compound **5** were added to a final concentration of 5 μM. The concentration of oleic acid was 708 μM (0.02%). The ladder used was the BenchMark Pre-Stained Protein Ladder from Invitrogen (molecular weights labeled on left). The molecular weight of TcpA is 20.5 kDa.

Table S1. Oligonucleotides used in this study

Designation	Sequence (5' – 3')
ToxT F Sap	GATCGGCTCTTCAATGATTGGGAAAAAATCTTTTCAAAC
TcpJ R Not	GAATAGCGGCCGCAGAGCTTTCAACTGTTAATG
TcpF F Xba	GGCCGTCTAGACAGAAACAGGAGTTATCTATG
ToxT R Sap	GATCGGCTCTTCACATTGCGTTCTACTCTGAAG

Table S2. Colonization Index (CI) data

Group	Mouse	Raw Data	Log2 Transform	Box Cox Transform
ΔToxT	1	0.0196	-5.6695	-0.2748
	2	0.0012	-9.7313	-0.3875
	3	0.0151	-6.0532	-0.2878
	4	0.0179	-5.8053	-0.2795
DMSO	1	0.5184	-0.9480	-0.0590
	2	0.1408	-2.8281	-0.1589
	3	0.5143	-0.9594	-0.0597
	4	0.3531	-1.5020	-0.0907
virstatin	1	0.0520	-4.2642	-0.2221
	2	0.0331	-4.9187	-0.2477
	3	0.0655	-3.9321	-0.2084
	4	0.2469	-2.0178	-0.1184
compound **4**	1	0.6551	-0.6102	-0.0387
	2	0.2551	-1.9709	-0.1160
	3	0.0939	-3.4131	-0.1859
	4	0.2959	-1.7567	-0.1046
	5	0.0551	-4.1818	-0.2188
compound **8**	1	0.0420	-4.5721	-0.2344
	2	0.0561	-4.1553	-0.2177
	3	0.0037	-8.0886	-0.3480
	4	0.0041	-7.9366	-0.3440

Figure S2. Histograms and boxplot of the Colonization Index (CI) data.

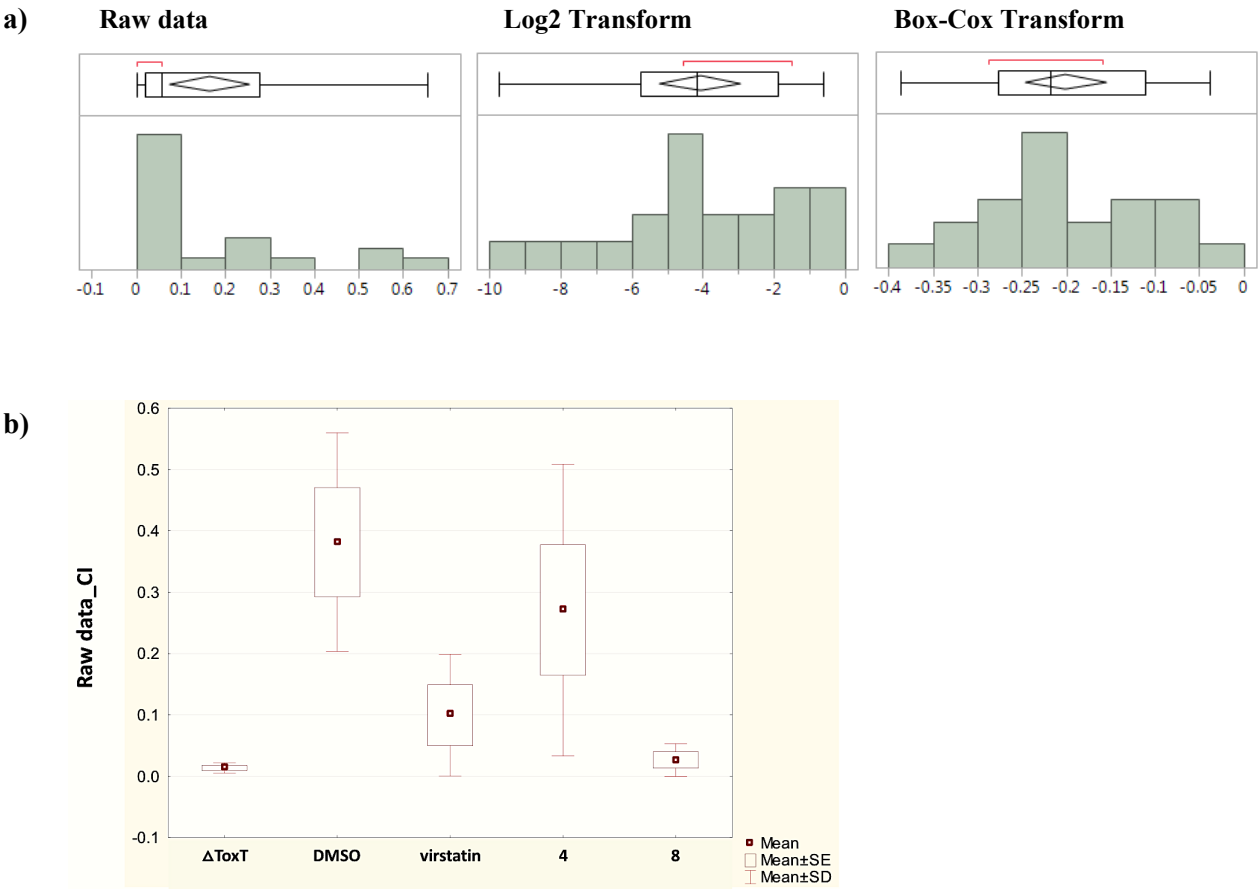
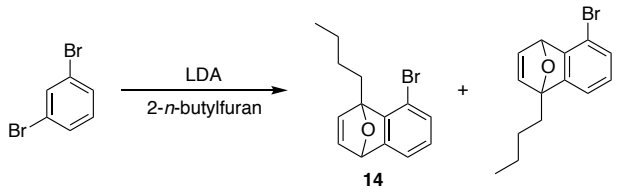


Figure S2. a) Histograms of CI data distributions: untransformed (raw) data, Log2 transformed raw data, and Box-Cox transformed raw data. The Box-Cox transformation results in the most normal distribution of the data. **b)** Boxplot of the raw data. A Kruskal-Wallis H test using the raw data showed a statistically significant difference in CI between the different drug treatments, $\chi^2(4) = 14.9428$, $p = 0.0048$, with a mean rank CI score of 4.00 for ΔToxT, 17.75 for DMSO, 10.75 for virstatin, 15.4 for compound **4** and 6.00 for compound **8**.

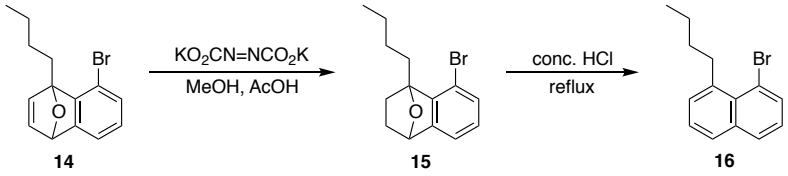
Chemical synthesis: general experimental methods

All reactions were conducted in oven-dried glassware under a balloon of nitrogen gas (N_2). All solvents and reagents were obtained commercially as reagent grade and, unless otherwise noted, used without further purification. Reactions were monitored by TLC on silica gel 60 F_{254} glass-backed plates and visualized by UV light and *p*-anisaldehyde staining. Column chromatography was performed using silica gel (60 Å, 40-63 μm particle size). ^{1}H NMR data were recorded on a Bruker Avance III 500 MHz spectrometer (TBI probe) and a Bruker Avance III 600 MHz spectrometer (BBFO probe) with calibration of spectra to $CDCl_3$ (7.26 ppm) or CD_2Cl_2 (5.32 ppm). ^{13}C NMR data were recorded at 150 MHz on the 600 MHz spectrometer with calibration of spectra to the central line of $CDCl_3$ (77.16 ppm) or CD_2Cl_2 (53.84 ppm). Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, mutiplet; br, broad. High-resolution mass spectra (HRMS) analyses were obtained at the Mass Spectrometry Laboratory of the University of Illinois at Urbana-Champaign using electron ionization (EI) or electrospray (ESI).

Synthesis of compounds



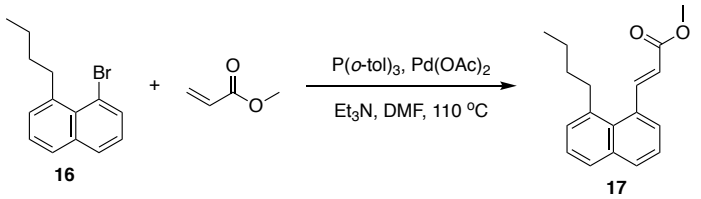
8-Bromo-1-butyl-1,4-dihydro-1,4-epoxynaphthalene (14). To a solution of 1,3-dibromobenzene (5 g, 21.20 mmol) in Et_2O (25 mL) at −78 °C was added LDA (2 M in THF; 11.1 mL, 22.26 mmol) dropwise. The mixture was stirred for 1 h at −78 °C, treated dropwise with 2-*n*-butylfuran (6.7 mL, 47.49 mmol), and allowed to warm to room temperature overnight. The cooled reaction mixture was quenched with ice water and extracted twice with Et_2O. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to yield orange oil. The crude mixture was purified via silica gel chromatography (60:1 hexanes/EtOAc) to afford **14** and the 1,5 isomer (5-bromo-1-butyl-1,4-dihydro-1,4-epoxynaphthalene) (1.54 g, 26%). The isomers were further separated by crystallization from hexanes to yield **14** as a white solid. R_f = 0.33 (15:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.12 (d, J = 7.0 Hz, 1H), 7.08 (d, J = 7.9, 1H), 7.01 (dd, J = 5.5, 1.7 Hz, 1H), 6.85 – 6.78 (m, 2H), 5.63 (d, J = 1.7 Hz, 1H), 2.63 (ddd, J = 14.3, 11.1, 4.7 Hz, 1H), 2.46 (ddd, J = 14.6, 11.4, 4.4 Hz, 1H), 1.70 – 1.45 (m, 4H), 1.00 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 154.1, 149.0, 144.9, 144.5, 130.0, 127.0, 118.7, 114.8, 95.2, 81.5, 30.1, 27.2, 23.2, 14.1 ppm; HRMS (EI): *m/z* calcd for $C_{14}H_{15}OBr$ $[M]^+$ 278.03063, found 278.03132.



8-Bromo-1-butyl-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (15) and **1-bromo-8-butylnaphthalene (16).** To a solution of **14** (460 mg, 1.65 mmol) in MeOH (10 mL) was added potassium azodicarboxylate (970 mg, 4.99 mmol). The mixture was stirred at room temperature while a solution of glacial acetic acid (0.5 mL) in MeOH (7.5 mL) was added dropwise. The mixture was stirred until TLC showed no remaining SM (~15 min). The crude mixture was treated with water and extracted three times with EtOAc. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford **15** as a pale-yellow solid in quantitative yield, which was used in the next step without further purification. R_f = 0.55 (15:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 (d, J = 8.1 Hz, 1H), 7.13 (d, J = 7.2, 1H), 6.99 (t, J = 7.6 Hz, 1H), 5.31 (d, J = 5.0 Hz, 1H), 2.81 – 2.70

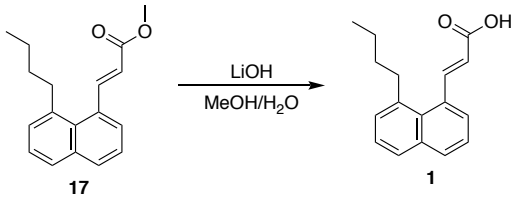
(m, 1H), 2.22 – 2.11 (m, 1H), 2.09 – 1.99 (m, 1H), 1.79 (td, J = 11.0, 3.7 Hz, 1H), 1.62 – 1.52 (m, 2H), 1.52 – 1.42 (m, 3H), 1.36 (ddd, J = 11.6, 8.8, 3.7 Hz, 1H), 0.97 (t, J = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 149.5, 144.3, 131.1, 128.3, 117.6, 114.2, 91.0, 77.7, 32.4, 31.1, 29.0, 27.3, 23.2, 14.1 ppm.

Crude **15** was refluxed with concentrated hydrochloric acid (5 mL) overnight at 80 °C. The cooled reaction mixture was quenched with ice water and extracted three times with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford **16** as yellow oil. Purification via silica gel chromatography (100% hexanes) gave the pure product as pale-yellow oil (350 mg, 81%). R_f = 0.79 (15:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.84 (dd, J = 7.3, 1.3 Hz, 1H), 7.79 (dd, J = 8.0, 1.3 Hz, 1H), 7.71 (dd, J = 7.2, 2.4 Hz, 1H), 7.41 – 7.36 (m, 2H), 7.21 (t, J = 7.7 Hz, 1H), 3.53 – 3.48 (m, 2H), 1.75 – 1.67 (m, 2H), 1.47 (app sextet, J = 7.4 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 140.2, 137.0, 133.9, 130.7, 130.5, 129.8, 128.3, 126.0, 125.5, 119.3, 36.4, 36.0, 22.9, 14.2 ppm; HRMS (EI): *m/z* calcd for $C_{14}H_{15}Br$ $[M]^+$ 262.03571, found 262.03505.



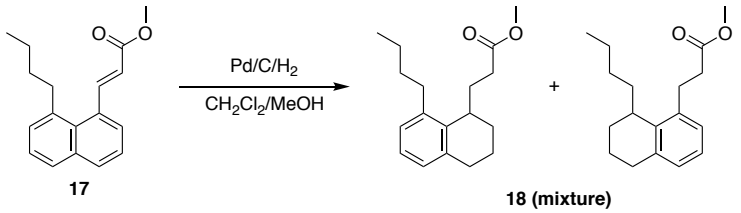
16 **17**

Methyl (*E*)-3-(8-butylnaphthalen-1-yl)acrylate (17). To a solution of 1-bromo-8-butylnaphthalene (**16**) (100 mg, 0.38 mmol), palladium(II) acetate (8.5 mg, 0.038 mmol), tri-*o*-tolylphosphine (23.1 mg, 0.076 mmol), and triethylamine (0.53 mL, 3.80 mmol) in DMF (0.1 M; 3 mL) was added methyl acrylate (0.12 mL, 1.33 mmol) dropwise. The reaction mixture was refluxed overnight at 110 °C. The mixture was then cooled to room temperature and quenched with water. The organic layer was extracted three times with EtOAc, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to yield brown oil. The crude mixture was purified via silica gel chromatography (20:1 hexanes/EtOAc) to afford **17** as colorless oil (100 mg, 98%). R_f = 0.74 (3:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.62 (d, J = 15.4 Hz, 1H), 7.86 (d, J = 8.1 Hz, 1H), 7.73 (dd, J = 7.9, 1.3 Hz, 1H), 7.49 – 7.38 (m, 4H), 6.27 (d, J = 15.4 Hz, 1H), 3.88 (s, 3H), 3.16 – 3.11 (m, 2H), 1.76 – 1.68 (m, 2H), 1.54 (app sextet, J = 7.4 Hz, 2H), 1.02 (t, J = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 167.2, 149.2, 139.8, 135.1, 133.9, 131.3, 130.6, 129.5, 128.1, 127.6, 125.8, 124.7, 119.5, 51.7, 36.6, 35.5, 22.7, 14.1 ppm; HRMS (EI): *m/z* calcd for $C_{18}H_{20}O_2$ $[M]^+$ 268.14633, found 268.14609.



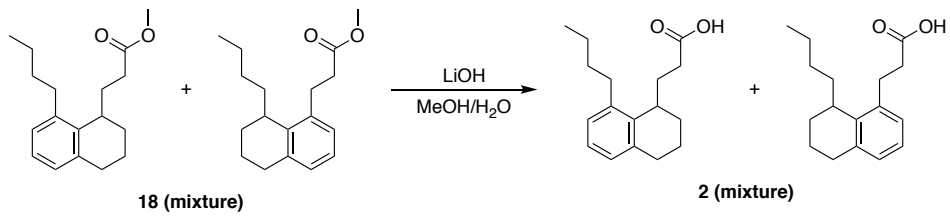
17 1

(*E*)-3-(8-Butylnaphthalen-1-yl)acrylic acid (1). To a solution of **17** (40 mg, 0.15 mmol) in MeOH/$H_2$0 (3:1; 4 mL) was added LiOH (18.8 mg, 0.45 mmol). The mixture was stirred overnight at room temperature. The solution was partially concentrated *in vacuo.* Water and EtOAc were added, and the first organic layer was separated and set aside. The remaining aqueous layer was treated with 1 M HCl and the organic layer was extracted twice with EtOAc, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to yield **1** as a white solid (35.5 mg, 94%). R_f = 0.40 (3:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74 (d, *J* = 15.4 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.74 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.53 – 7.40 (m, 4H), 6.29 (d, *J* = 15.4 Hz, 1H), 3.17 – 3.11 (m, 2H), 1.76 – 1.68 (m, 2H), 1.53 (app sextet, *J* = 7.4 Hz, 2H), 1.00 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.6, 151.6, 139.9, 135.2, 133.7, 131.8, 130.7, 129.7, 128.4, 127.7, 126.0, 124.9, 119.0, 36.8, 35.5, 22.7, 14.1 ppm; HRMS (ESI): *m/z* calcd for $C_{17}H_{17}O_2$ $[M - H]^-$ 253.1229, found 253.1231.



17 18 (mixture)

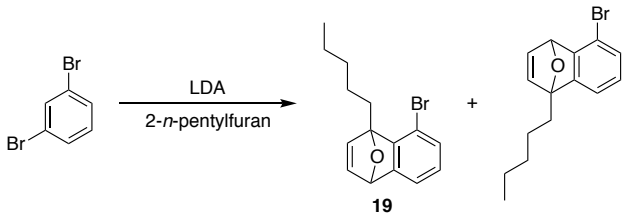
Mixture of methyl 3-(8-butyl-1,2,3,4-tetrahydronaphthalen-1-yl)propanoate and **methyl 3-(8-butyl-5,6,7,8-tetrahydronaphthalen-1-yl)propanoate (18).** To a solution of **17** (58 mg, 0.216 mmol) in CH_2Cl_2/MeOH (1:1; 2 mL) was added 10% Pd/C (22.6 mg, 0.0216 mmol) at room temperature. The mixture was stirred vigorously under H_2 overnight. The mixture was filtered through Celite and concentrated *in vacuo* to yield **18** as colorless oil (55 mg, 93%). R_f = 0.80 (3:1 hexanes/EtOAc); HRMS (EI): *m/z* calcd for $C_{18}H_{26}O_2$ $[M]^+$ 274.19328, found 274.19280.



18 (mixture) 2 (mixture)

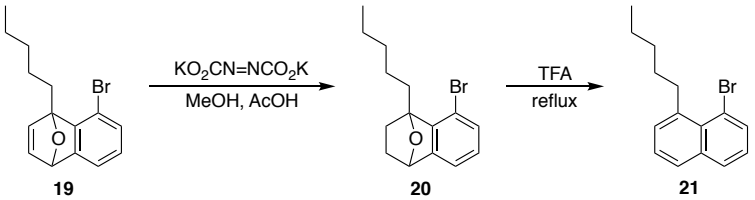
Mixture of 3-(8-butyl-1,2,3,4-tetrahydronaphthalen-1-yl)propanoic acid and **3-(8-butyl-5,6,7,8-tetrahydronaphthalen-1-yl)propanoic acid (2).** To a solution of **18** (15.5 mg, 0.057 mmol) in

MeOH/H_20 (3:1; 1.5 mL) was added LiOH (7.1 mg, 0.17 mmol). The mixture was stirred overnight at room temperature. The solution was partially concentrated *in vacuo.* Water and EtOAc were added, and the first organic layer was separated and set aside. The remaining aqueous layer was treated with 1 M HCl and the organic layer was extracted twice with EtOAc, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to yield **2** as yellow oil (11 mg, 75%). R_f = 0.42 (3:1 hexanes/EtOAc); HRMS (ESI): *m/z* calcd for $C_{17}H_{23}O_2$ $[M - H]^-$ 259.1698, found 259.1700.



19

8-Bromo-1-pentyl-1,4-dihydro-1,4-epoxynaphthalene (19). To a solution of 1,3-dibromobenzene (2.47 g, 10.49 mmol) in Et_2O (12 mL) at −78 °C was added LDA (1.3 M in THF; 8.5 mL, 11.01 mmol) dropwise. The mixture was stirred for 1 h at −78 °C, treated dropwise with 2-*n*-pentylfuran (3.3 mL, 20.98 mmol), allowed to warm to room temperature overnight. The cooled reaction mixture was quenched with ice water and extracted three times with Et_2O. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to yield orange oil. The crude mixture was purified via silica gel chromatography (60:1 hexanes:EtOAc) to afford **19** and the 1,5 isomer (5-bromo-1-pentyl-1,4-dihydro-1,4-epoxynaphthalene) (1.21 g, 39%). Re-crystallization from hexanes gave the pure product **19** as a white solid. R_f = 0.35 (15:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.11 (d, *J* = 7.0 Hz, 1H), 7.07 (d, *J* = 7.9, 1H), 7.00 (dd, *J* = 5.5, 1.5 Hz, 1H), 6.83 – 6.78 (m, 2H), 5.62 (d, *J* = 1.5 Hz, 1H), 2.59 (ddd, *J* = 14.7, 11.5, 4.6 Hz, 1H), 2.42 (ddd, *J* = 14.6, 11.6, 4.9 Hz, 1H), 1.67 – 1.48 (m, 2H), 1.48 – 1.33 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 154.2, 149.0, 145.0, 144.6, 130.1, 127.1, 118.8, 114.9, 95.3, 81.6, 32.4, 30.5, 24.8, 22.8, 14.2 ppm; HRMS (EI): *m/z* calcd for $C_{15}H_{17}OBr$ $[M]^+$ 292.04628, found 292.04550.

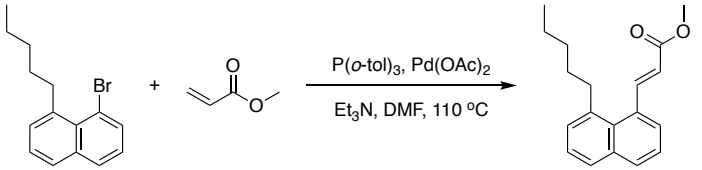


19 **20** **21**

8-Bromo-1-pentyl-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (20) and **1-bromo-8-pentylnaphthalene (21).** To a solution of **19** (360 mg, 1.23 mmol) in MeOH (7 mL) was added potassium azodicarboxylate (723 mg, 3.72 mmol). The mixture was stirred at room temperature while a solution of glacial acetic acid

(0.4 mL) in MeOH (6 mL) was added dropwise. The mixture stirred until TLC showed no remaining SM (~15 min). The crude mixture was treated with water and extracted three times with ethyl acetate. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford **20** as orange oil in quantitative yield, which was used in the next step without further purification. R_f = 0.45 (15:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (d, *J* = 7.9 Hz, 1H), 7.14 (d, *J* = 7.0, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 5.31 (d, *J* = 5.0 Hz, 1H), 2.78 – 2.68 (m, 1H), 2.22 – 2.11 (m, 1H), 2.08 – 1.97 (m, 1H), 1.78 (td, *J* = 11.0, 3.7 Hz, 1H), 1.62 – 1.50 (m, 2H), 1.50 – 1.32 (m, 6H), 0.92 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 149.6, 144.4, 131.2, 128.4, 117.7, 114.3, 91.2, 77.8, 32.8, 32.5, 31.2, 29.1, 24.9, 22.7, 14.2 ppm.

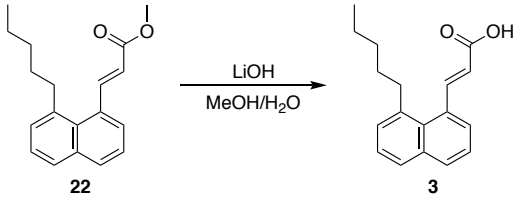
Crude **20** was refluxed with concentrated trifluoroacetic acid (2 mL) overnight at 80 °C. The cooled reaction mixture was quenched with ice water and extracted three times with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford **21** as brown oil (330 mg, 97%). R_f = 0.80 (15:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, *J* = 7.3 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.72 (dd, *J* = 6.7, 2.7 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.21 (t, *J* = 7.8 Hz, 1H), 3.52 – 3.45 (m, 2H), 1.77 – 1.67 (m, 2H), 1.48 – 1.33 (m, 4H), 0.91 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 140.2, 137.0, 133.9, 130.7, 130.5, 129.8, 128.3, 126.0, 125.5, 119.3, 36.7, 33.6, 32.0, 22.8, 14.3 ppm; HRMS (EI): *m/z* calcd for $C_{15}H_{17}Br$ $[M]^+$ 276.05136, found 276.05119.



21 **22**

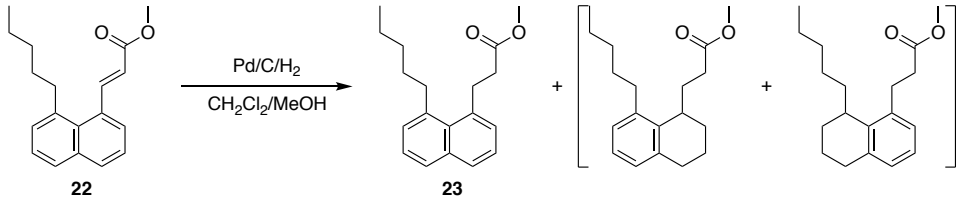
Methyl (*E*)-3-(8-pentylnaphthalen-1-yl)acrylate (22). To a solution of 1-bromo-8-pentylnaphthalene (**21**) (100 mg, 0.361 mmol), palladium(II) acetate (8.1 mg, 0.0361 mmol), tri-*o*-tolylphosphine (22.0 mg, 0.0721 mmol), and triethylamine (0.50 mL, 3.61 mmol) in DMF (0.1 M; 3 mL) was added methyl acrylate (0.11 mL, 1.26 mmol) dropwise. The reaction mixture was refluxed overnight at 110 °C. The mixture was then cooled to room temperature and quenched with water. The organic layer was extracted three times with EtOAc, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to yield brown oil. The crude mixture was purified via silica gel chromatography (40:1 hexanes/EtOAc) to afford **22** as colorless oil (80 mg, 79%). R_f = 0.77 (3:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.60 (d, *J* = 15.4 Hz, 1H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.73 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.48 – 7.37 (m, 4H), 6.26 (d, *J* = 15.4 Hz, 1H), 3.87 (s, 3H), 3.14 – 3.09 (m, 2H), 1.76 – 1.66 (m, 2H), 1.52 – 1.44 (m, 2H), 1.40 (app sextet, *J* = 7.2 Hz, 2H), 0.95 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz,

$CDCl_3$): δ 167.3, 149.2, 139.9, 135.2, 134.0, 131.3, 130.7, 129.5, 128.2, 127.7, 125.9, 124.8, 119.7, 51.7, 36.9, 33.1, 31.8, 22.7, 14.2 ppm; HRMS (EI): *m/z* calcd for $C_{19}H_{22}O_2$ $[M]^+$ 282.16198, found 282.16253.



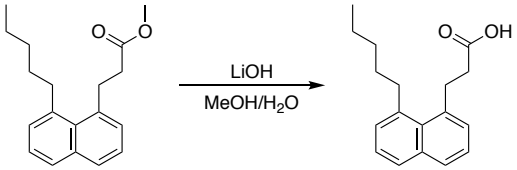
22 3

(*E*)-3-(8-Pentylnaphthalen-1-yl)acrylic acid (3). To a solution of **22** (29 mg, 0.103 mmol) in MeOH/$H_2$0 (3:1; 2.5 mL) was added LiOH (12.9 mg, 0.308 mmol). The mixture was stirred overnight at room temperature. The solution was partially concentrated *in vacuo.* Water and EtOAc were added, and the mixture was treated with 1 M HCl. The organic layer was extracted three times with EtOAc, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo.* The product was triturated with cold hexanes to yield **3** as a white solid (23 mg, 83%). R_f = 0.37 (3:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.72 (d, *J* = 15.4 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.74 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.53 – 7.40 (m, 4H), 6.29 (d, *J* = 15.4 Hz, 1H), 3.15 – 3.10 (m, 2H), 1.76 – 1.68 (m, 2H), 1.52 – 1.45 (m, 2H), 1.39 (sextet, *J* = 7.3 Hz, 2H), 0.94 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.4, 151.6, 139.9, 135.3, 133.7, 131.8, 130.7, 129.7, 128.4, 127.7, 126.0, 124.9, 119.0, 37.1, 33.1, 31.8, 22.8, 14.2 ppm; HRMS (ESI): *m/z* calcd for $C_{18}H_{19}O_2$ $[M - H]^-$ 267.1385, found 267.1385.



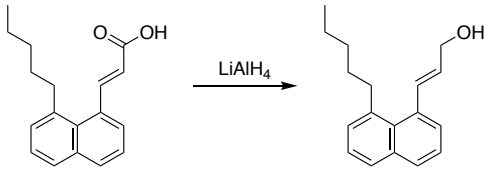
22 23

Methyl 3-(8-pentylnaphthalen-1-yl)propanoate (23). To a solution of **22** (40 mg, 0.142 mmol) in CH_2Cl_2/MeOH (1:1; 2 mL) was added 10% Pd/C (14.8 mg, 0.0142 mmol) at room temperature. The mixture was stirred vigorously under H_2 for 30 min, then filtered through Celite and concentrated *in vacuo.* The crude mixture was purified using a preparative TLC plate (30:1 hexanes/EtOAc) to yield **23** as colorless oil (30 mg, 74%). R_f = 0.65 (3:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.77 – 7.71 (m, 2H), 7.39 – 7.32 (m, 4H), 3.71 (s, 3H), 3.56 – 3.49 (m, 2H), 3.18 – 3.11 (m, 2H), 2.69 – 2.62 (m, 2H), 1.70 – 1.62 (m, 2H), 1.47 – 1.33 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 173.3, 139.3, 137.2, 136.2, 130.7, 129.8, 129.4, 129.2, 128.6, 125.2, 125.0, 51.7, 37.6, 37.3, 33.1, 32.5, 31.9, 22.7, 14.2 ppm; HRMS (EI): *m/z* calcd for $C_{19}H_{24}O_2$ $[M]^+$ 284.17763, found 284.17757.



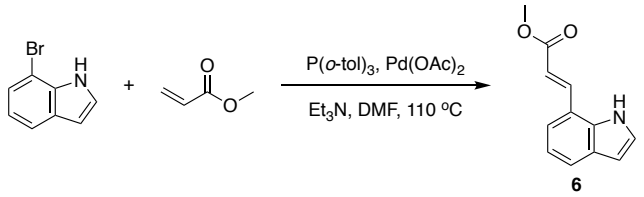
23 4

3-(8-Pentylnaphthalen-1-yl)propanoic acid (4). To a solution of **23** (30 mg, 0.105 mmol) in MeOH/H_20 (3:1; 2 mL) was added LiOH (13.3 mg, 0.316 mmol). The mixture was stirred overnight at room temperature. The solution was partially concentrated *in vacuo.* Water and EtOAc were added, and the mixture was treated with 1 M HCl. The organic layer was extracted three times with EtOAc, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to yield **4** as a white solid (28 mg, 99%). R_f = 0.37 (3:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.80 – 7.71 (m, 2H), 7.41 – 7.34 (m, 4H), 3.59 – 3.52 (m, 2H), 3.19 – 3.12 (m, 2H), 2.76 – 2.69 (m, 2H), 1.71 – 1.63 (m, 2H), 1.48 – 1.33 (m, 4H), 0.92 (t, J = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 179.3, 139.3, 136.8, 136.2, 130.7, 129.9, 129.4, 129.3, 128.6, 125.3, 125.1, 37.6, 37.2, 33.1, 32.2, 31.9, 22.7, 14.2 ppm; HRMS (ESI): *m/z* calcd for $C_{18}H_{21}O_2$ $[M - H]^-$ 269.1542, found 269.1547.



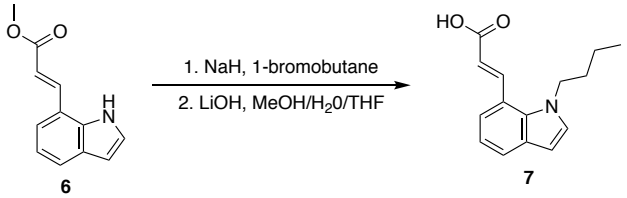
3 5

(*E*)-3-(8-Pentylnaphthalen-1-yl)prop-2-en-1-ol (5). To a solution of **3** (12 mg, 0.045 mmol) in Et_2O (2 mL) at 0 °C was added lithium aluminum hydride (4 M in Et_2O; 0.1 mL) dropwise. The mixture was stirred for 2 h at 0 °C. The reaction mixture was quenched with a saturated solution of potassium sodium tartrate tetrahydrate in H_20, then filtered through Celite. The organic layer was extracted three times with EtOAc, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Removal of solvent grease and trace impurities using a preparative TLC plate gave the pure product **5** as a white, waxy substance (10 mg, 88% yield). R_f = 0.49 (3:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.80 – 7.74 (m, 1H), 7.70 (dd, J = 7.9, 1.5 Hz, 1H), 7.45 – 7.31 (m, 5H), 6.07 (dt, J = 15.3, 5.5 Hz, 1H), 4.40 (dd, J = 5.8, 1.5 Hz, 2H), 3.19 – 3.13 (m, 2H), 1.69 – 1.60 (m, 2H), 1.45 – 1.31 (m, 4H), 0.91 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CD_2Cl_2): δ 140.7, 137.1, 135.6, 134.7, 131.0, 130.6, 129.6, 129.2, 128.5, 127.8, 125.7, 125.3, 64.0, 37.0, 33.3, 32.3, 23.1, 14.3 ppm; HRMS (EI): *m/z* calcd for $C_{18}H_{22}O$ $[M]^+$ 254.16707, found 254.16749.



6

Methyl (*E*)-3-(1*H*-indol-7-yl)acrylate (6). To a solution of 7-bromoindole (200 mg, 1.02 mmol), palladium(II) acetate (22.9 mg, 0.102 mmol), tri-*o*-tolylphosphine (93.2 mg, 0.306 mmol), and triethylamine (1.42 mL, 10.20 mmol) in DMF (0.1 M; 10 mL) was added methyl acrylate (0.14 mL, 1.53 mmol) dropwise. The reaction mixture was refluxed overnight at 110 °C. The mixture was then cooled to room temperature and quenched with water. The organic layer was extracted three times with EtOAc, rinsed twice with water (to remove DMF), washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to yield brown oil. The crude mixture was purified via silica gel chromatography (5:1 hexanes/EtOAc) to afford **6** as a bright yellow solid (180 mg, 88%). R_f = 0.47 (3:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.59 (br s, 1H), 8.04 (d, J = 16.0 Hz, 1H), 7.71 (d, J = 7.7 Hz, 1H), 7.42 (d, J = 7.3 Hz, 1H), 7.29 – 7.27 (m, 1H), 7.16 (t, J = 7.7 Hz, 1H), 6.62 (dd, J = 3.3, 2.2 Hz, 1H), 6.52 (d, J = 16.0 Hz, 1H), 3.85 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.2, 141.6, 134.5, 129.0, 125.1, 123.5, 122.1, 120.1, 118.3, 117.4, 103.2, 51.9 ppm; HRMS (EI): *m/z* calcd for $C_{12}H_{11}NO_2$ $[M]^+$ 201.07898, found 201.07870.

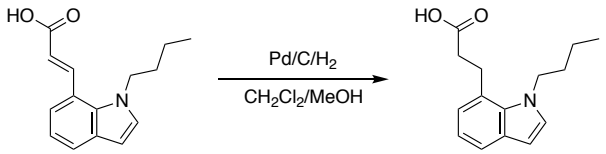


6 **7**

(*E*)-3-(1-Butyl-1*H*-indol-7-yl)acrylic acid (7). Sodium hydride (60% in mineral oil; 27.5 mg, 0.688 mmol) was rinsed three times with hexanes, resuspended in DMF (5 mL), and cooled to 0 °C. **6** (83 mg, 0.412 mmol) in DMF (8 mL) was added dropwise. The ice bath was removed, and the mixture was stirred for 15 min. Bromobutane (0.05 mL, 0.438 mmol) was added at 0 °C dropwise. The ice bath was again removed, and the mixture was stirred at room temperature overnight. Water and CH_2Cl_2 were added, and the mixture was treated with 1 M HCl. The organic layer was extracted three times with CH_2Cl_2, rinsed twice with water (to remove DMF), washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo.* The crude product was used in the next step without further purification.

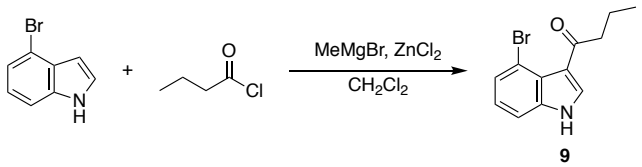
To a solution of crude material in MeOH/$H_2$0/THF (3:1:1; 4 mL) was added LiOH (56 mg, 1.34 mmol). The mixture was stirred overnight at room temperature. The solution was partially concentrated *in vacuo.* Water and EtOAc were added, and the mixture was treated with 1 M HCl. The organic layer was extracted three times with EtOAc, washed with brine, dried over anhydrous $MgSO_4$, filtered, and

concentrated *in vacuo.* The crude mixture was purified via silica gel chromatography (5:1 hexanes/EtOAc) to afford **7** as a pale yellow solid (94 mg, 94%). R_f = 0.55 (10:1 CH_2Cl_2/MeOH); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.56 (d, *J* = 15.4 Hz, 1H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.42 (d, *J* = 7.3 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 2.9 Hz, 1H), 6.51 (d, *J* = 2.9 Hz, 1H), 6.42 (d, *J* = 15.4 Hz, 1H), 4.30 (t, *J* = 7.3 Hz, 2H), 1.92 – 1.81 (m, 2H), 1.43 (app sextet, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CD_2Cl_2): δ 172.6, 145.2, 133.8, 131.2, 131.1, 124.1, 122.1, 119.9, 119.8, 118.6, 101.8, 50.0, 33.8, 20.4, 13.9 ppm; HRMS (EI): *m/z* calcd for $C_{15}H_{17}NO_2$ $[M]^+$ 243.12593, found 243.12566.



7 **8**

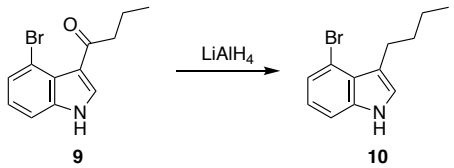
3-(1-Butyl-1*H*-indol-7-yl)propanoic acid (8). To a solution of **7** (7 mg, 0.03 mmol) in CH_2Cl_2/MeOH (1:1; 1 mL) was added 10% Pd/C (3 mg, 0.003 mmol) at room temperature. The mixture was stirred vigorously under H_2 for 30 min, filtered through Celite, and concentrated *in vacuo* to yield a yellow oil. Purification via silica gel chromatography (20:1 CH_2Cl_2/MeOH) gave **8** as a pure white solid (7 mg, 97%). R_f = 0.55 (10:1 CH_2Cl_2/MeOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.07 – 6.96 (m, 3H), 6.49 (d, *J* = 3.1 Hz, 1H), 4.27 (t, *J* = 7.4 Hz, 2H), 3.40 – 3.34 (m, 2H), 2.81 – 2.75 (m, 2H), 1.83 – 1.74 (m, 2H), 1.37 (app sextet, *J* = 7.5 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 178.4, 133.6, 130.6, 130.2, 123.3, 123.1, 120.0, 119.7, 101.8, 49.1, 35.9, 34.5, 27.9, 20.1, 13.9 ppm; HRMS (EI): *m/z* calcd for $C_{15}H_{19}NO_2$ $[M]^+$ 245.14158, found 245.14143.



9

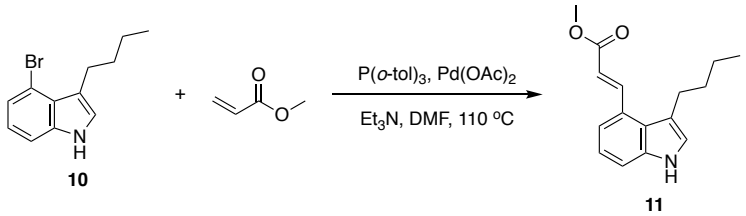
1-(4-Bromo-1*H*-indol-3-yl)butan-1-one (9). To a solution of 4-bromoindole (0.06 mL, 0.485 mmol) in anhydrous CH_2Cl_2 (1 mL) was added MeMgBr (3 M in Et_2O; 0.17 mL, 0.509 mmol) dropwise. The solution was stirred at room temperature for 10 min. $ZnCl_2$ (1 M in Et_2O; 1.46 mL, 1.455 mmol) was added dropwise and the reaction mixture was stirred for an additional 30 min. Butyryl chloride (0.053 mL, 0.509 mmol) was added dropwise, upon which the solution changed from an opaque pink color to a clear ruby red color. The mixture stirred until TLC showed no remaining SM (~3.5 h). The reaction mixture was quenched with a saturated solution of NH_4Cl and stirred for 15 min. The organic layer was extracted three times with CH_2Cl_2, washed with brine, dried over anhydrous $MgSO_4$, filtered, and

concentrated *in vacuo* to yield a pink solid. The crude product was re-crystallized from Et_2O to yield **9** as a white solid (117 mg, 91%). R_f = 0.17 (3:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.80 (br s, 1H), 7.72 (d, *J* = 2.9 Hz, 1H), 7.47 (dd, *J* = 7.7, 0.7 Hz, 1H), 7.35 (dd, *J* = 8.1, 0.7 Hz, 1H), 7.10 (t, *J* = 7.9 Hz, 1H), 2.88 (t, *J* = 7.3 Hz, 2H), 1.81 (app sextet, *J* = 7.3 Hz, 2H), 1.02 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 197.4, 138.4, 131.6, 127.4, 124.8, 124.5, 119.4, 114.7, 111.2, 44.4, 18.8, 14.0 ppm; HRMS (EI): *m/z* calcd for $C_{12}H_{12}NOBr$ $[M]^+$ 265.01022, found 265.01050.



9 **10**

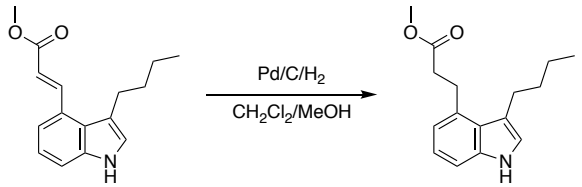
4-Bromo-3-butyl-1*H*-indole (10). To a solution of **9** (55 mg, 0.207 mmol) in THF (5 mL) was added $LiAlH_4$ (4 M in Et_2O; 0.10 mL, 0.414 mmol) dropwise. The mixture was stirred for 3 h at reflux. The reaction mixture was cooled to 0 °C and quenched with a saturated solution of potassium sodium tartrate tetrahydrate in H_20. After stirring for several minutes at room temperature, the crude mixture was filtered through Celite. The organic layer was extracted three times with CH_2Cl_2, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo.* The crude mixture was purified via silica gel chromatography (20:1 hexanes/EtOAc) to yield **10** as colorless oil (44 mg, 84%). R_f = 0.59 (3:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, CD_2Cl_2): δ 8.16 (br s, 1H), 7.31 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.24 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.06 – 7.03 (m, 1H), 6.98 (t, *J* = 7.8 Hz, 1H), 3.02 – 2.96 (m, 2H), 1.75 – 1.66 (m, 2H), 1.46 (app sextet, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CD_2Cl_2): δ 138.2, 125.9, 124.0, 123.5, 122.9, 118.3, 114.6, 110.9, 34.3, 26.3, 23.0, 14.2 ppm; HRMS (EI): *m/z* calcd for $C_{12}H_{14}NBr$ $[M]^+$ 251.03095, found 251.03068.



10 **11**

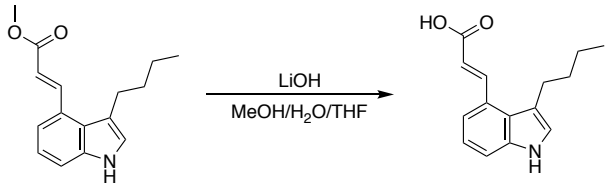
Methyl (*E*)-3-(3-butyl-1*H*-indol-4-yl)acrylate (11). To a solution of **10** (45 mg, 0.178 mmol), palladium(II) acetate (4.0 mg, 0.0178 mmol), tri-*o*-tolylphosphine (10.8 mg, 0.036 mmol), and triethylamine (0.25 mL, 1.78 mmol) in DMF (0.1 M; 2 mL) was added methyl acrylate (0.02 mL, 0.267 mmol) dropwise. The reaction mixture was refluxed overnight at 110 °C. The mixture was then cooled to room temperature and quenched with water. The organic layer was extracted three times with CH_2Cl_2, rinsed twice with water (to remove DMF), washed with brine, dried over anhydrous $MgSO_4$, filtered, and

concentrated *in vacuo* to yield brown oil. The crude mixture was purified via silica gel chromatography (20:1 hexanes/EtOAc) to afford **11** as a yellow solid (38 mg, 83%). R_f= 0.46 (3:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, CD_2Cl_2): δ 8.48 (d, *J* = 15.7 Hz, 1H), 8.22 (br s, 1H), 7.43 – 7.38 (m, 2H), 7.16 (t, *J* = 7.8 Hz, 1H), 7.11 – 7.07 (m, 1H), 6.45 (d, *J* = 15.7 Hz, 1H), 3.80 (s, 3H), 2.95 – 2.88 (m, 2H), 1.74 – 1.65 (m, 2H), 1.49 (app sextet, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CD_2Cl_2): δ 167.8, 144.0, 137.8, 128.3, 126.1, 124.0, 122.2, 118.2, 118.2, 117.8, 113.5, 51.8, 33.4, 27.7, 23.1, 14.1 ppm; HRMS (EI): *m/z* calcd for $C_{16}H_{19}NO_2$ $[M]^+$ 257.14158, found 257.14106.



11 **24**

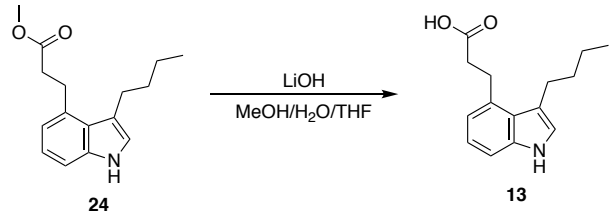
Methyl 3-(3-butyl-1*H*-indol-4-yl)propanoate (24). To a solution of **11** (18 mg, 0.07 mmol) in CH_2Cl_2/MeOH (1:1; 2 mL) was added 10% Pd/C (7.3 mg, 0.007 mmol) at room temperature. The mixture was stirred vigorously under H_2 for 30 min, then filtered through Celite and concentrated *in vacuo.* Purification via silica gel chromatography (30:1 hexanes/EtOAc) gave **24** as colorless oil (16.5 mg, 91%). R_f= 0.54 (3:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, CD_2Cl_2): δ 8.09 (br s, 1H), 7.21 (d, *J* = 8.1, 1H), 7.05 (t, *J* = 7.6, Hz, 1H), 7.00 – 6.97 (m, 1H), 6.84 (d, *J* = 7.1 Hz, 1H), 3.67 (s, 3H), 3.37 – 3.30 (m, 2H), 2.92 – 2.84 (m, 2H), 2.72 – 2.65 (m, 2H), 1.74 – 1.66 (m, 2H), 1.48 (app sextet, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CD_2Cl_2): δ 173.7, 137.5, 134.0, 125.4, 122.1, 122.1, 119.8, 117.5, 109.9, 51.8, 36.7, 33.7, 28.9, 27.3, 23.1, 14.2 ppm; HRMS (EI): *m/z* calcd for $C_{16}H_{21}NO_2$ $[M]^+$ 259.15723, found 259.15706.



11 **12**

(*E*)-3-(3-Butyl-1*H*-indol-4-yl)acrylic acid (12). To a solution of **11** (8 mg, 0.031 mmol) in MeOH/$H_2$0/THF (3:1:1; 1.5 mL) was added LiOH (3.9 mg, 0.093 mmol). The mixture was stirred overnight at room temperature. The solution was partially concentrated *in vacuo,* then treated with 1 M HCl. Water and EtOAc were added, and the organic layer was extracted with EtOAc. Solid NaCl was added to the remaining aqueous layer (until the solution was supersaturated), and the organic layer was extracted again with EtOAc. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered,

and concentrated *in vacuo.* The crude product was purified via silica gel chromatography (10:1 to 2:1 hexanes/EtOAc) to yield **12** as a yellow solid (7 mg, 93%). R_f= 0.17 (3:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, CD_2Cl_2): δ 8.61 (d, *J* = 15.6 Hz, 1H), 8.20 (br s, 1H), 7.45 (dd, *J* = 12.3, 7.9 Hz, 2H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.13 – 7.10 (m, 1H), 6.47 (d, *J* = 15.8 Hz, 1H), 2.97 – 2.91 (m, 2H), 1.75 – 1.68 (m, 2H), 1.50 (app sextet, *J* = 7.4 Hz, 2H), 0.99 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CD_2Cl_2): δ 171.5, 146.3, 137.8, 127.9, 126.3, 124.2, 122.2, 118.6, 117.8, 117.2, 113.9, 33.2, 27.8, 23.1, 14.1 ppm; HRMS (EI): *m/z* calcd for $C_{15}H_{17}NO_2$ $[M]^+$ 243.12593, found 243.12628.

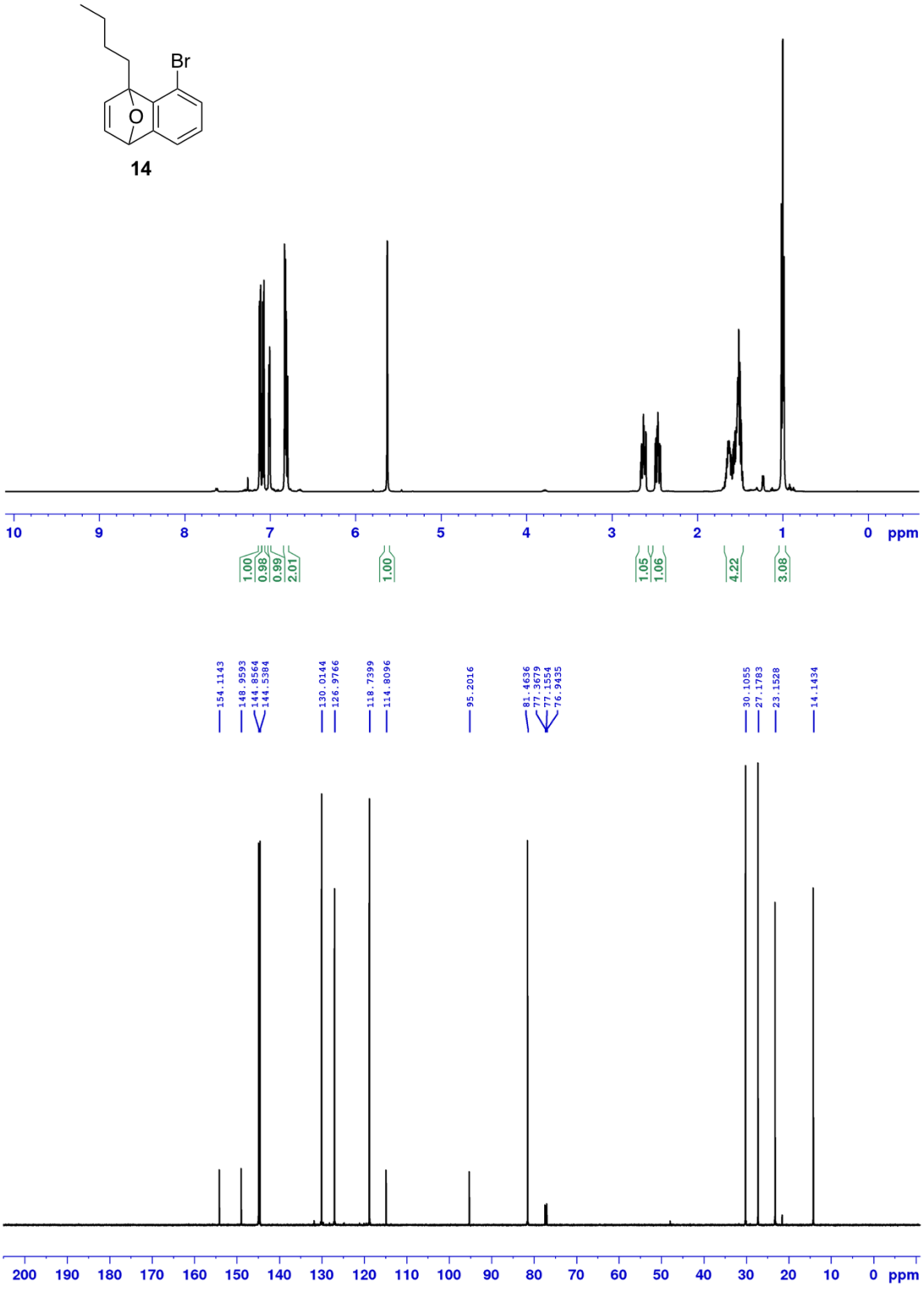


24 **13**

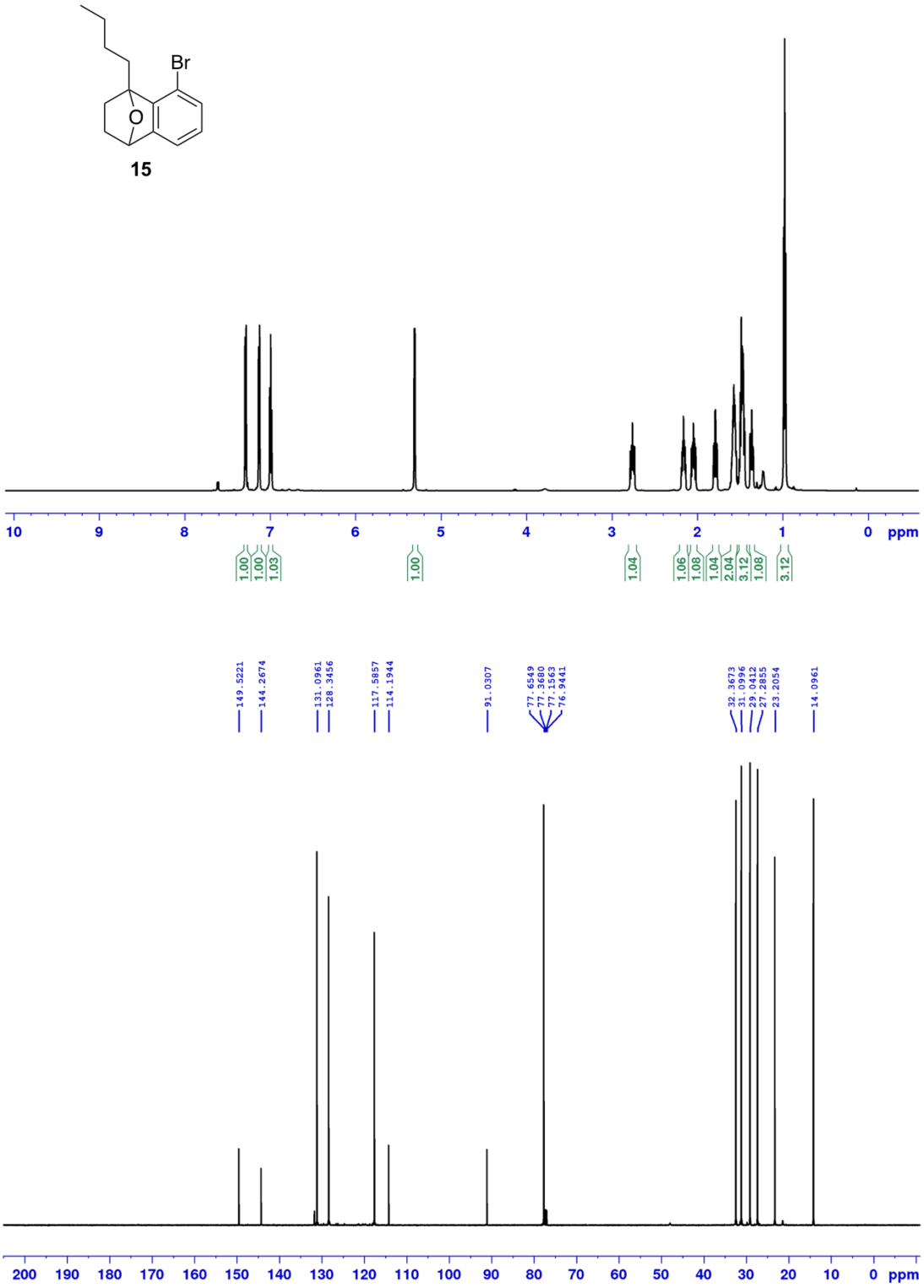
3-(3-Butyl-1*H*-indol-4-yl)propanoic acid (13). To a solution of **24** (13 mg, 0.05 mmol) in MeOH/$H_2$0/THF (3:1:1; 1.5 mL) was added LiOH (6.3 mg, 0.15 mmol). The mixture was stirred overnight at room temperature. The solution was partially concentrated *in vacuo,* then treated with 1 M HCl. Water and EtOAc were added, and the organic layer was extracted with EtOAc. Solid NaCl was added to the remaining aqueous layer (until the solution was supersaturated), and the organic layer was extracted again with EtOAc. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to yield **13** as a white solid (11.7 mg, 95%). R_f= 0.15 (3:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, CD_2Cl_2): δ 8.09 (br s, 1H), 7.23 (d, *J* = 8.1, 1H), 7.07 (t, *J* = 7.7, Hz, 1H), 7.03 – 6.98 (m, 1H), 6.88 (d, *J* = 7.2 Hz, 1H), 3.41 – 3.34 (m, 2H), 2.93 – 2.86 (m, 2H), 2.80 – 2.73 (m, 2H), 1.76 – 1.66 (m, 2H), 1.49 (app sextet, *J* = 7.4 Hz, 2H), 0.99 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CD_2Cl_2): δ 179.1, 137.5, 133.6, 125.4, 122.2, 122.2, 119.8, 117.5, 110.0, 36.4, 33.7, 28.6, 27.4, 23.1, 14.2 ppm; HRMS (EI): *m/z* calcd for $C_{15}H_{19}NO_2$ $[M]^+$ 245.14158, found 245.14144.

Experimental spectra of synthesized compounds

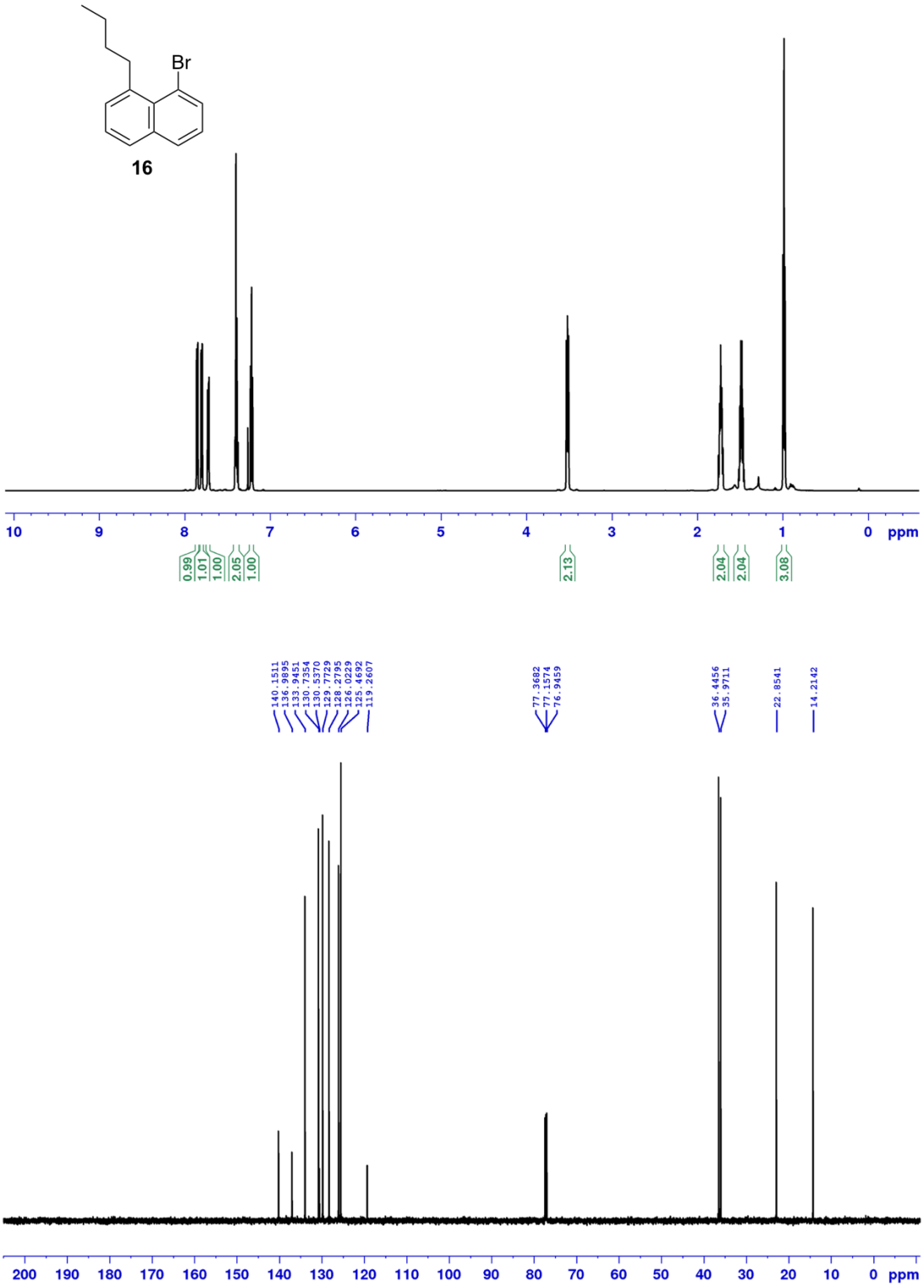
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **14.**



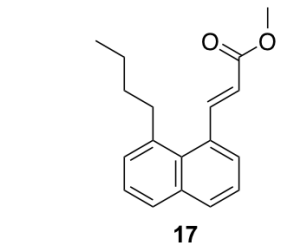
^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **15.**



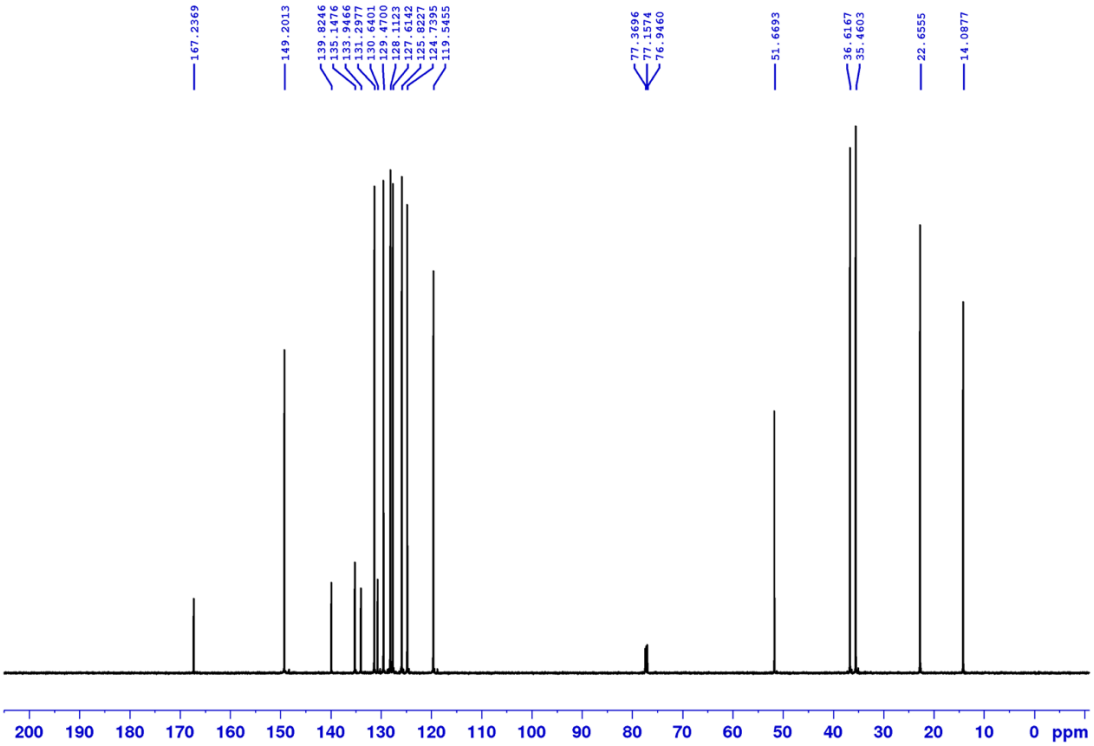
^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **16.**



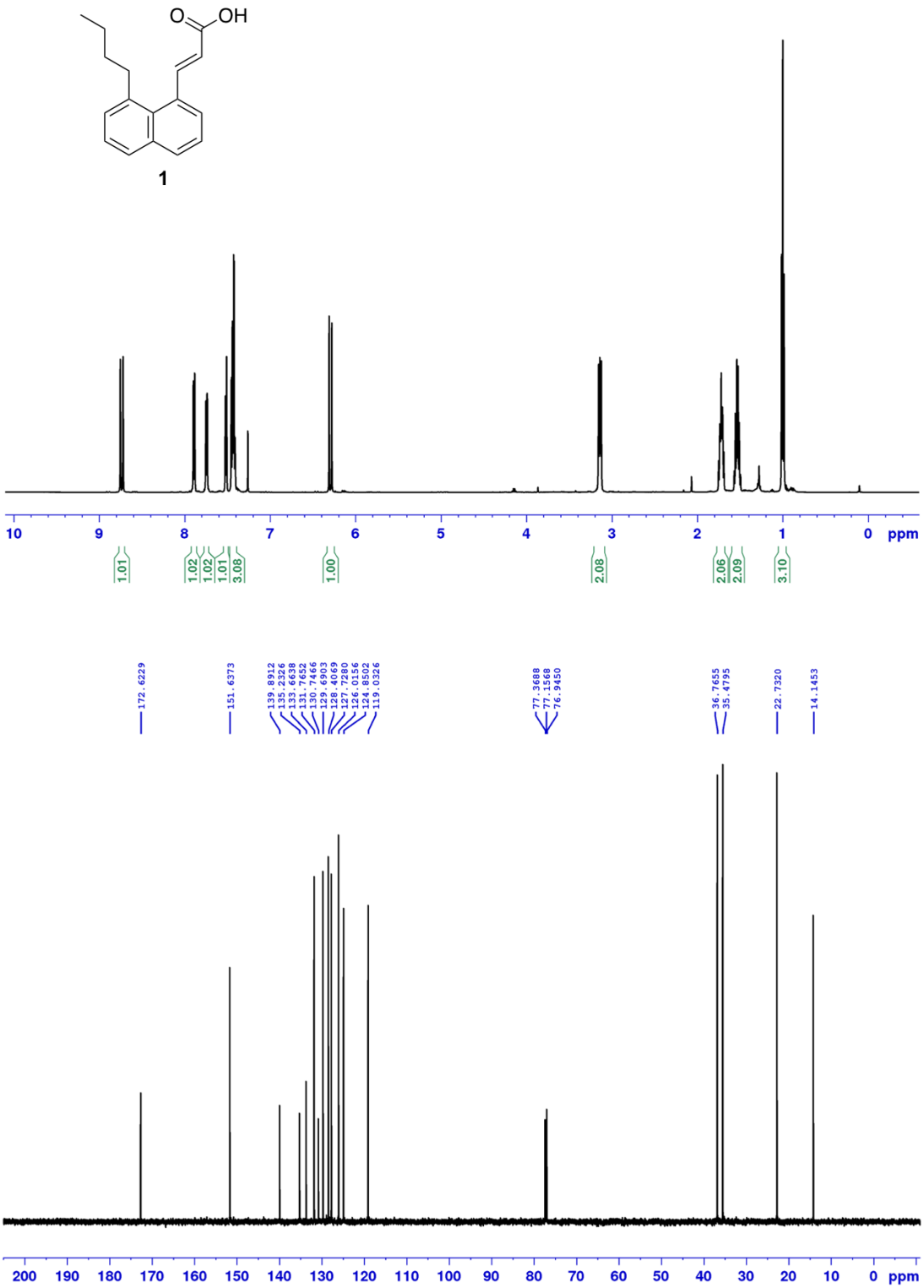
^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **17.**



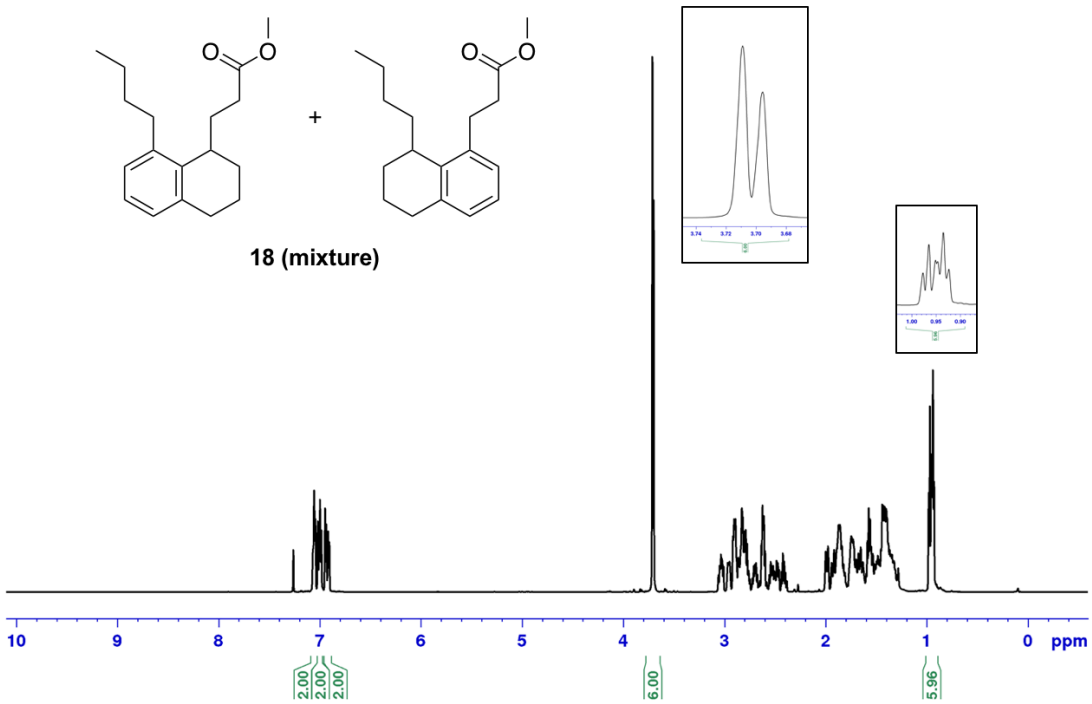
17



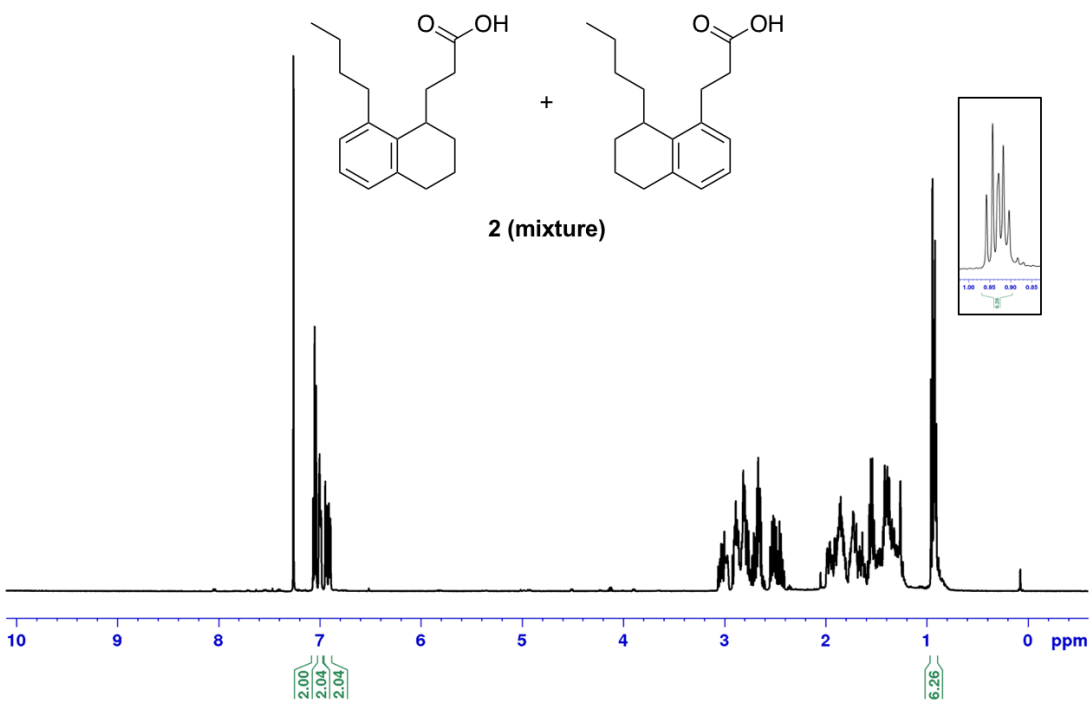
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **1.**



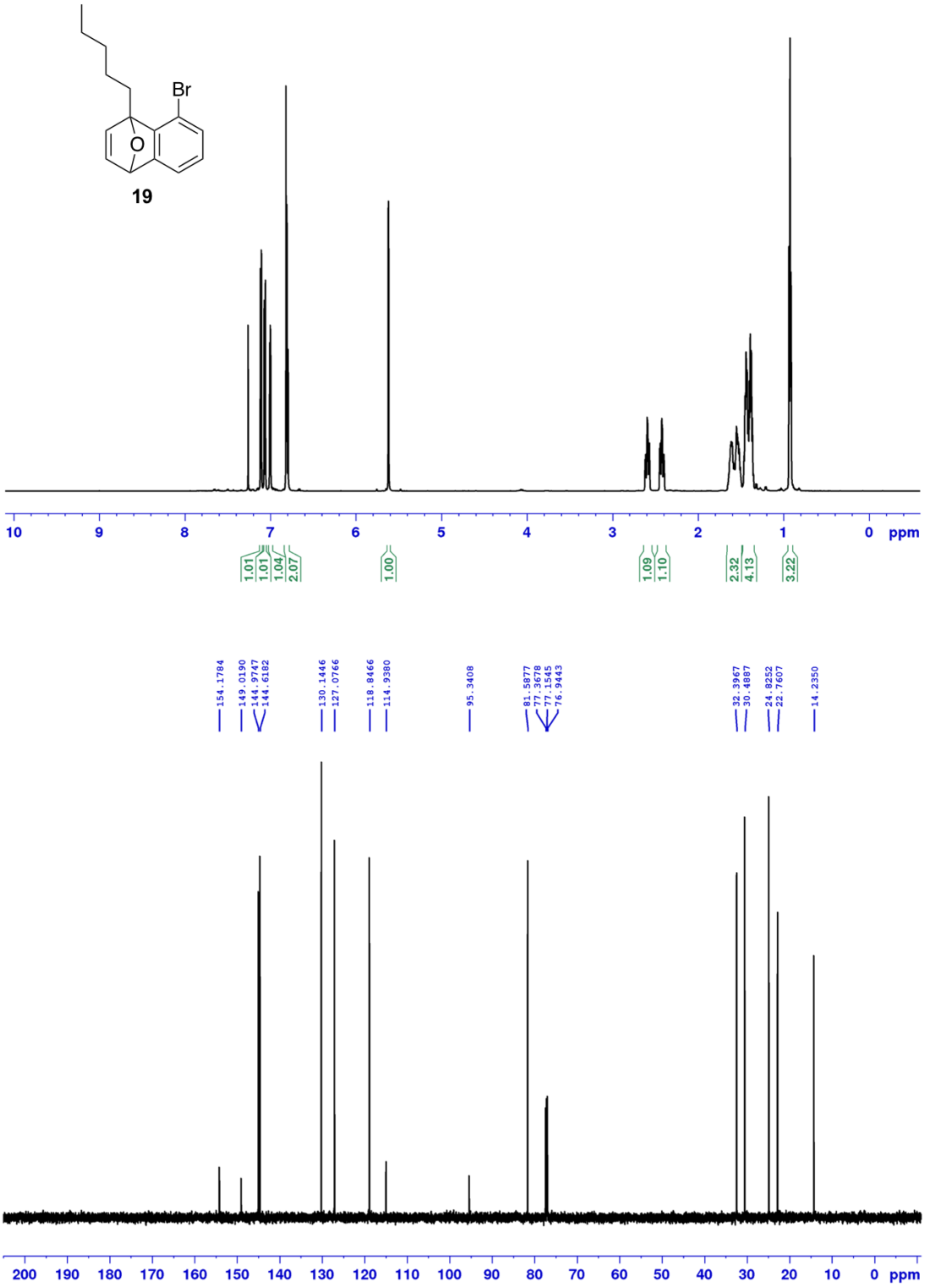
^{1}H NMR (600 MHz, $CDCl_3$) of **18.**



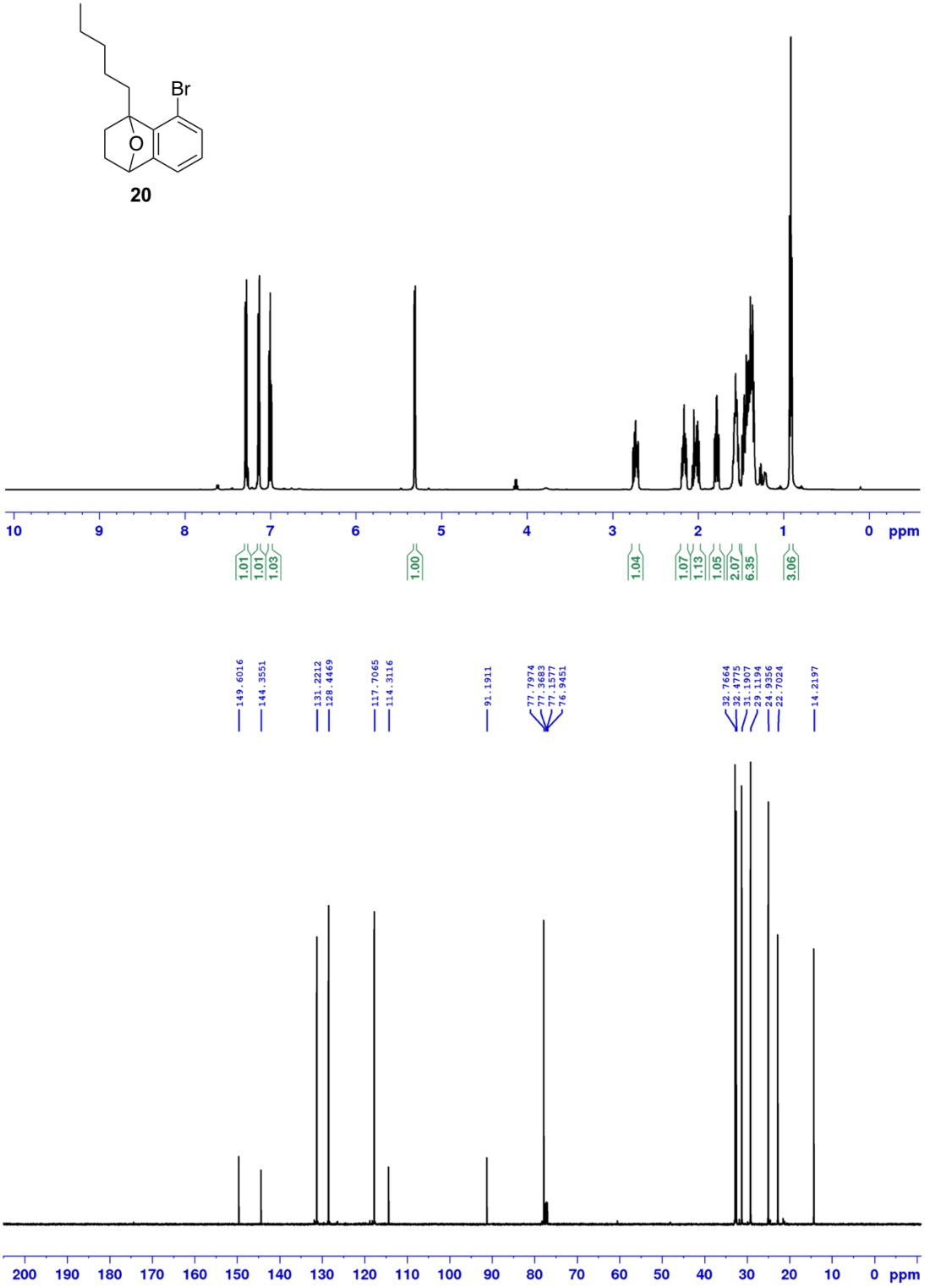
^{1}H NMR (500 MHz, $CDCl_3$) of **2.**



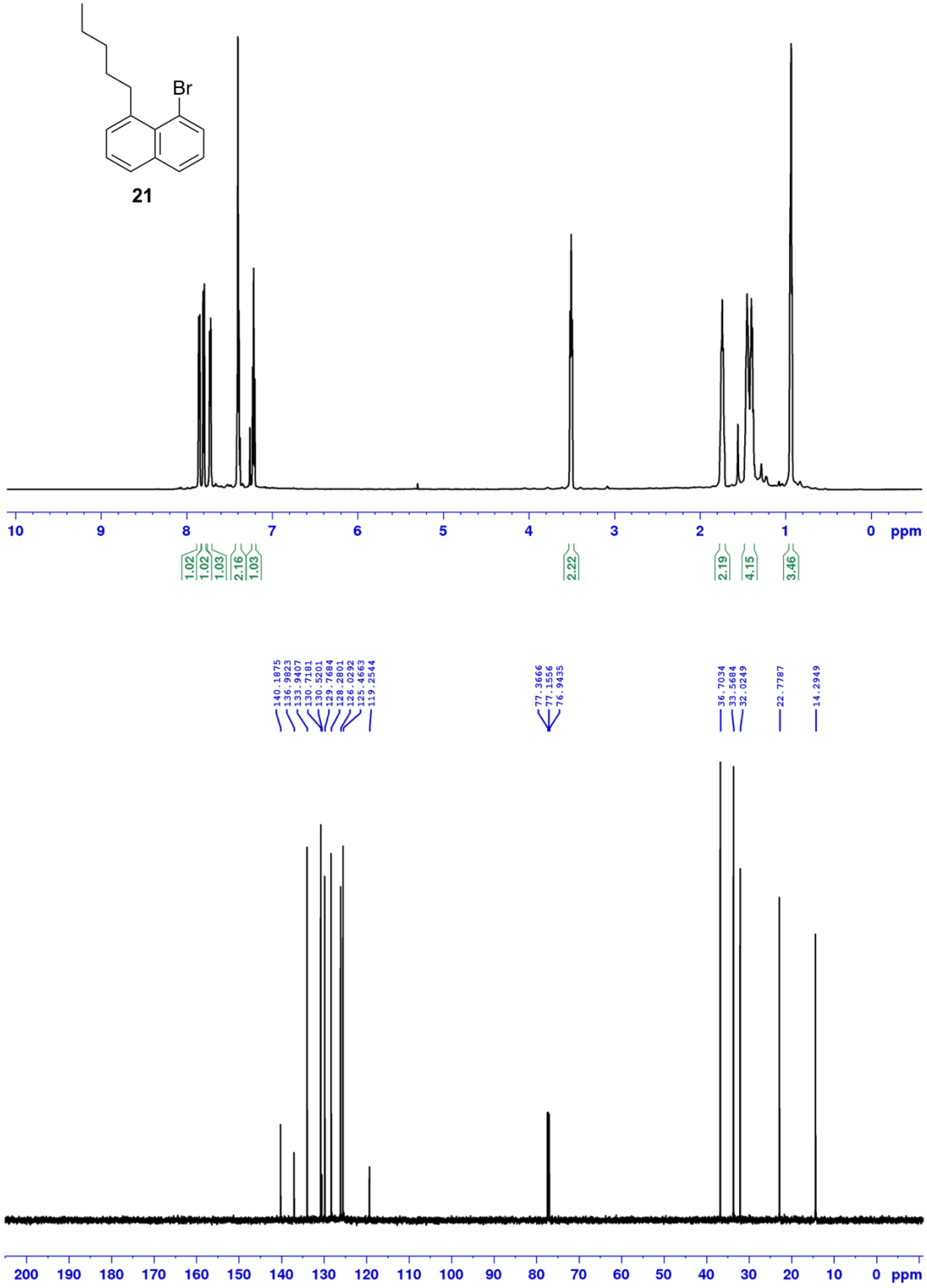
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **19.**



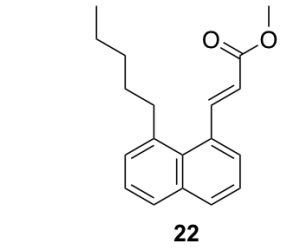
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **20.**



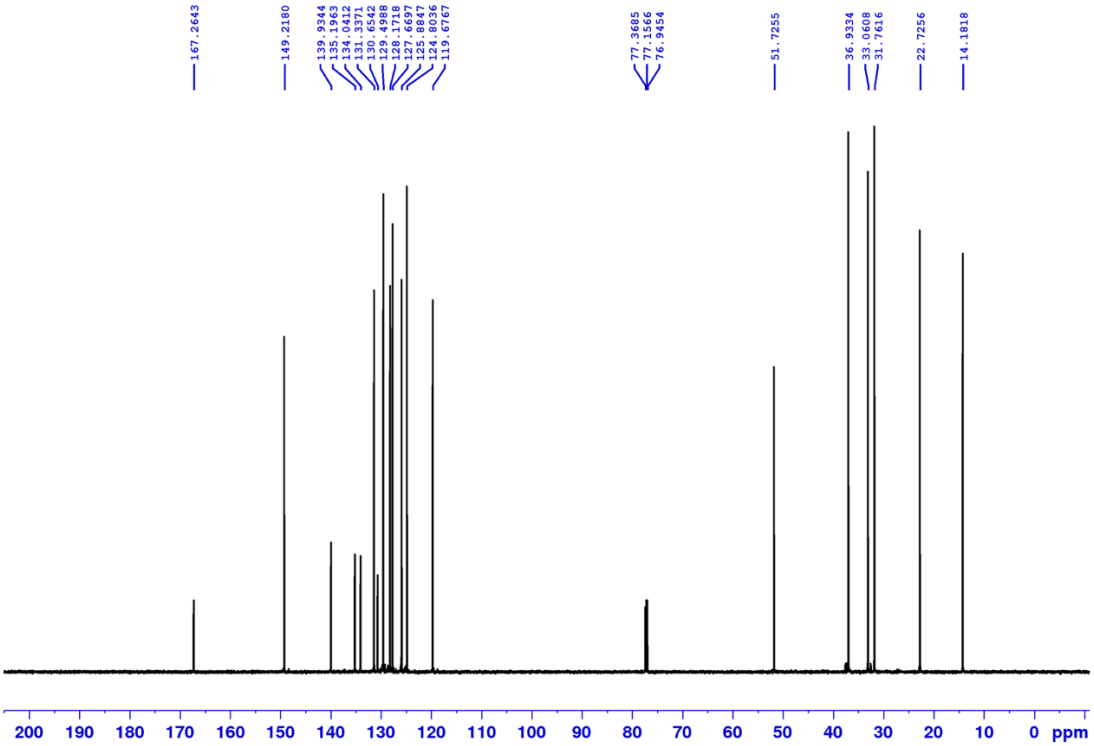
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **21.**



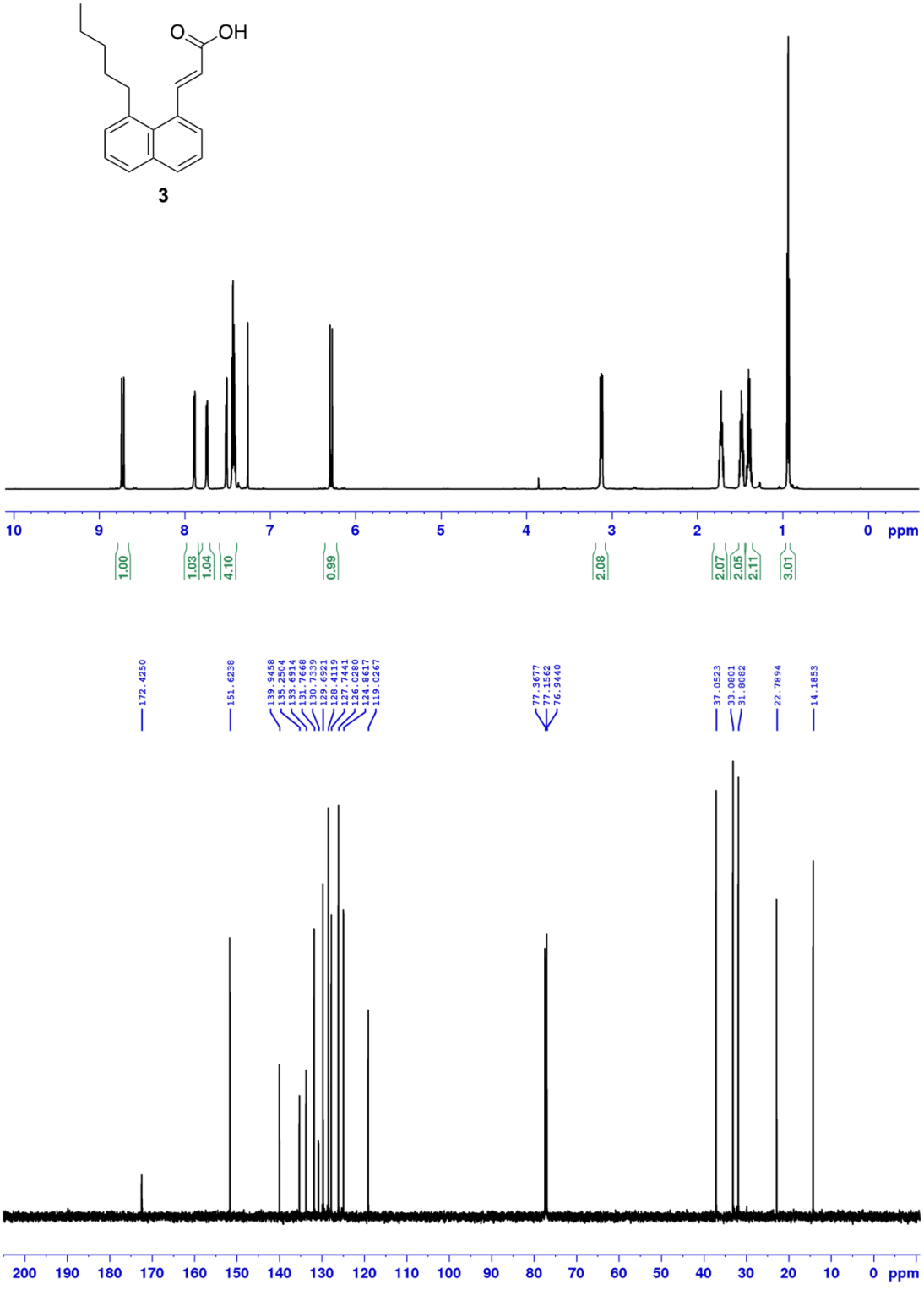
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **22.**



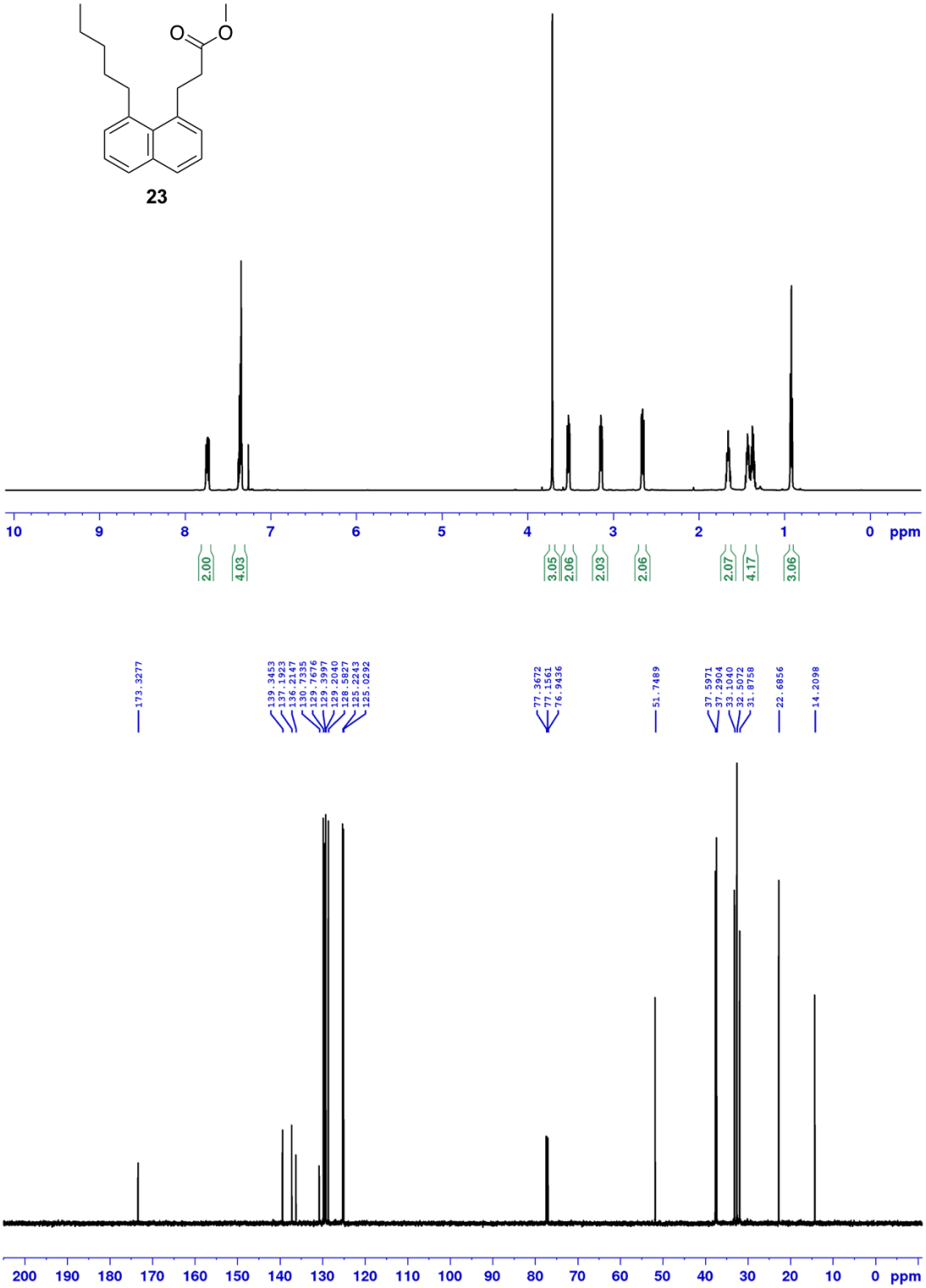
22



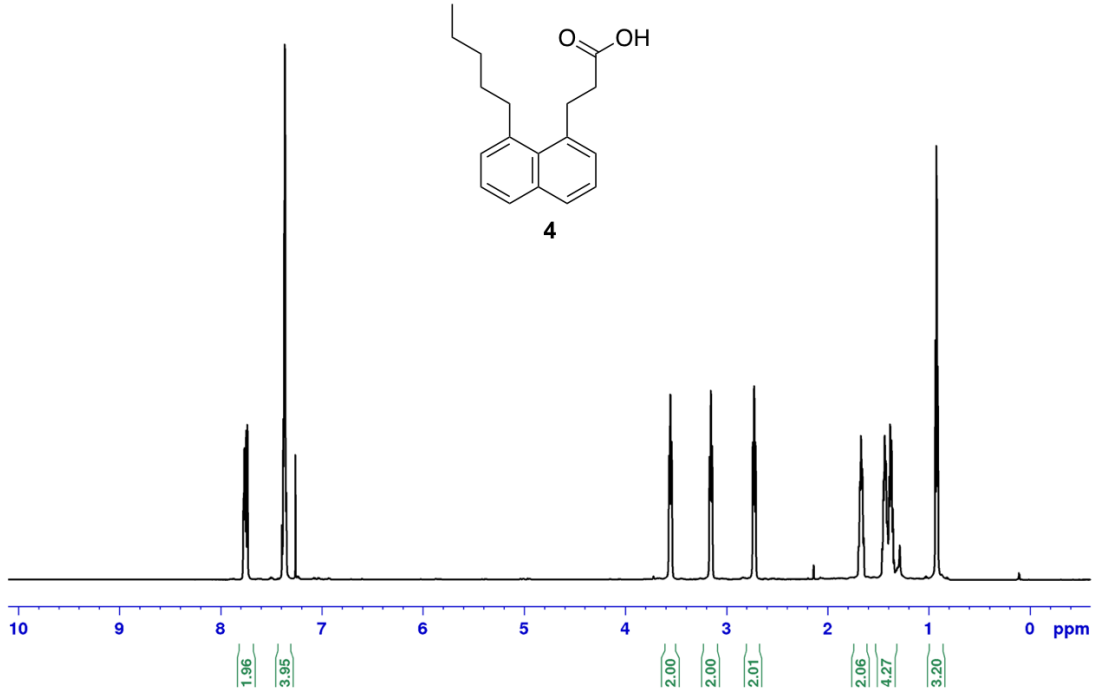
^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **3.**

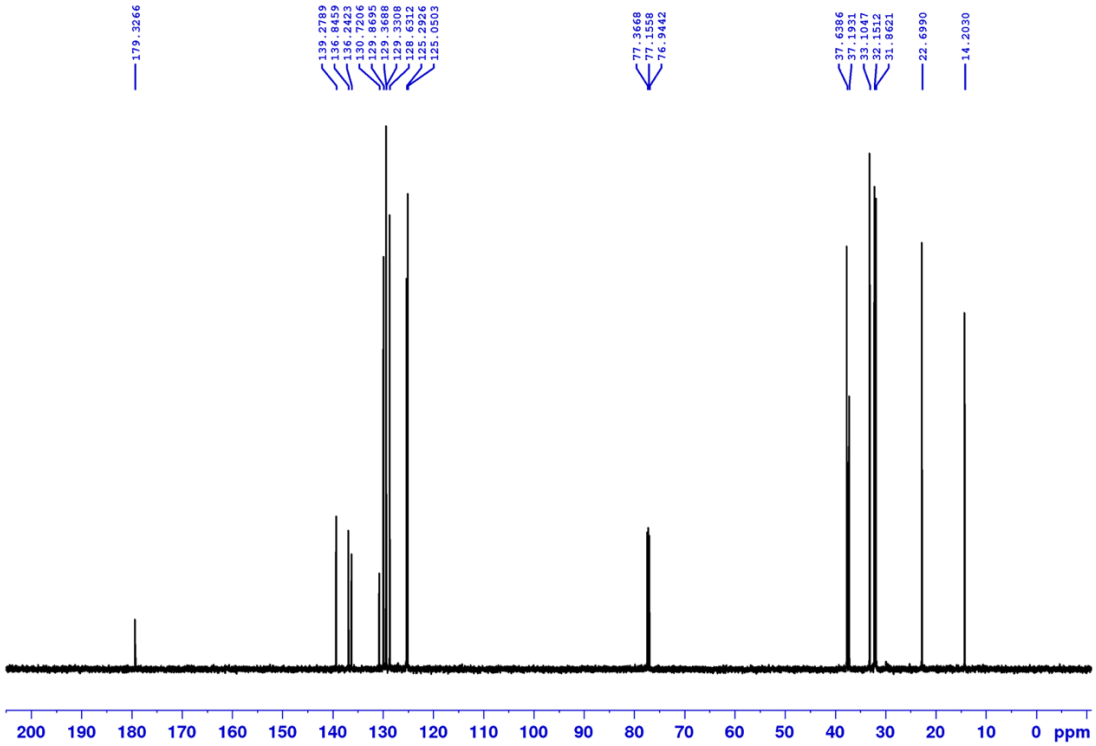


^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **23.**

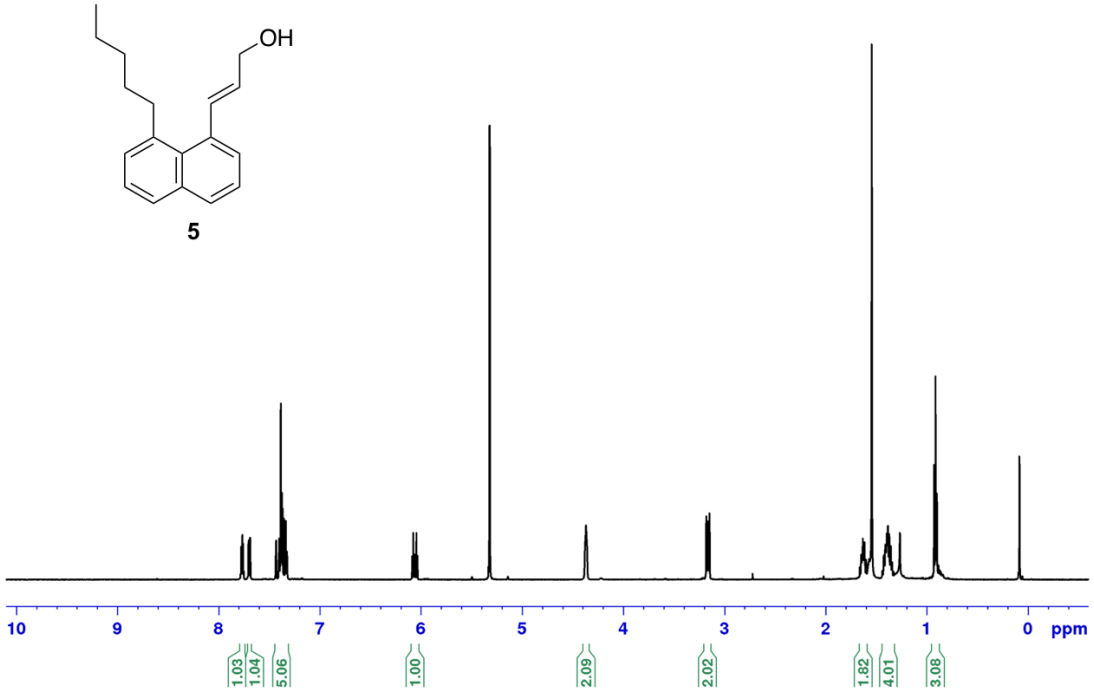


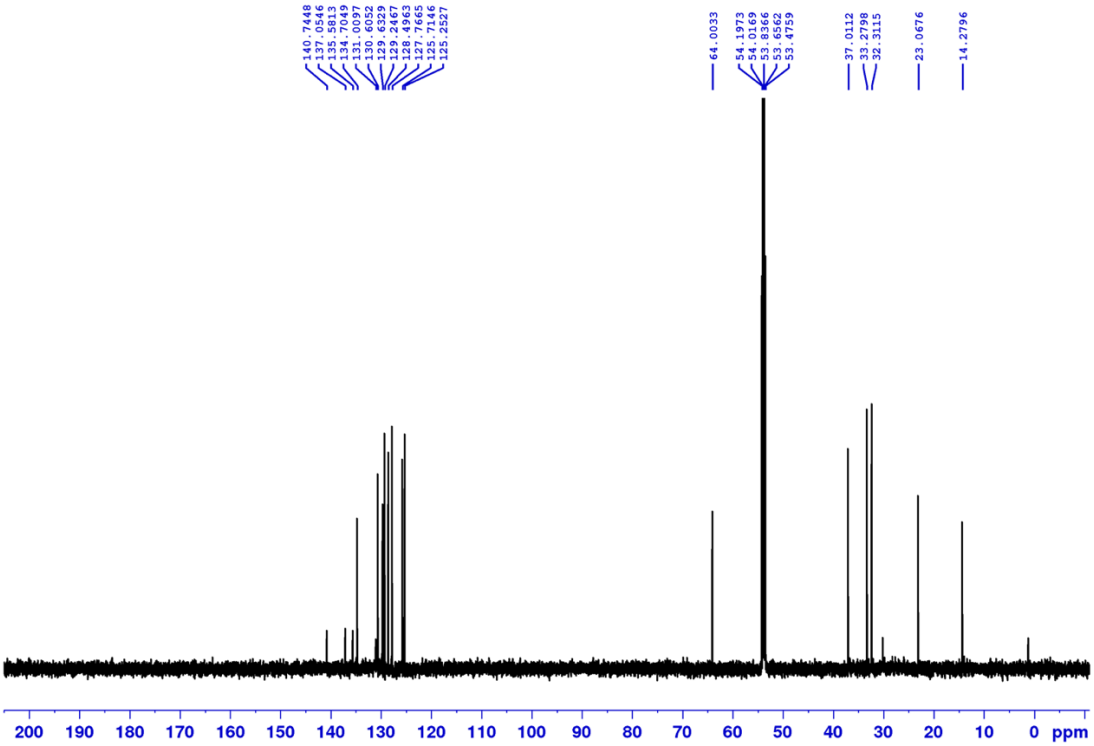
^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **4.**



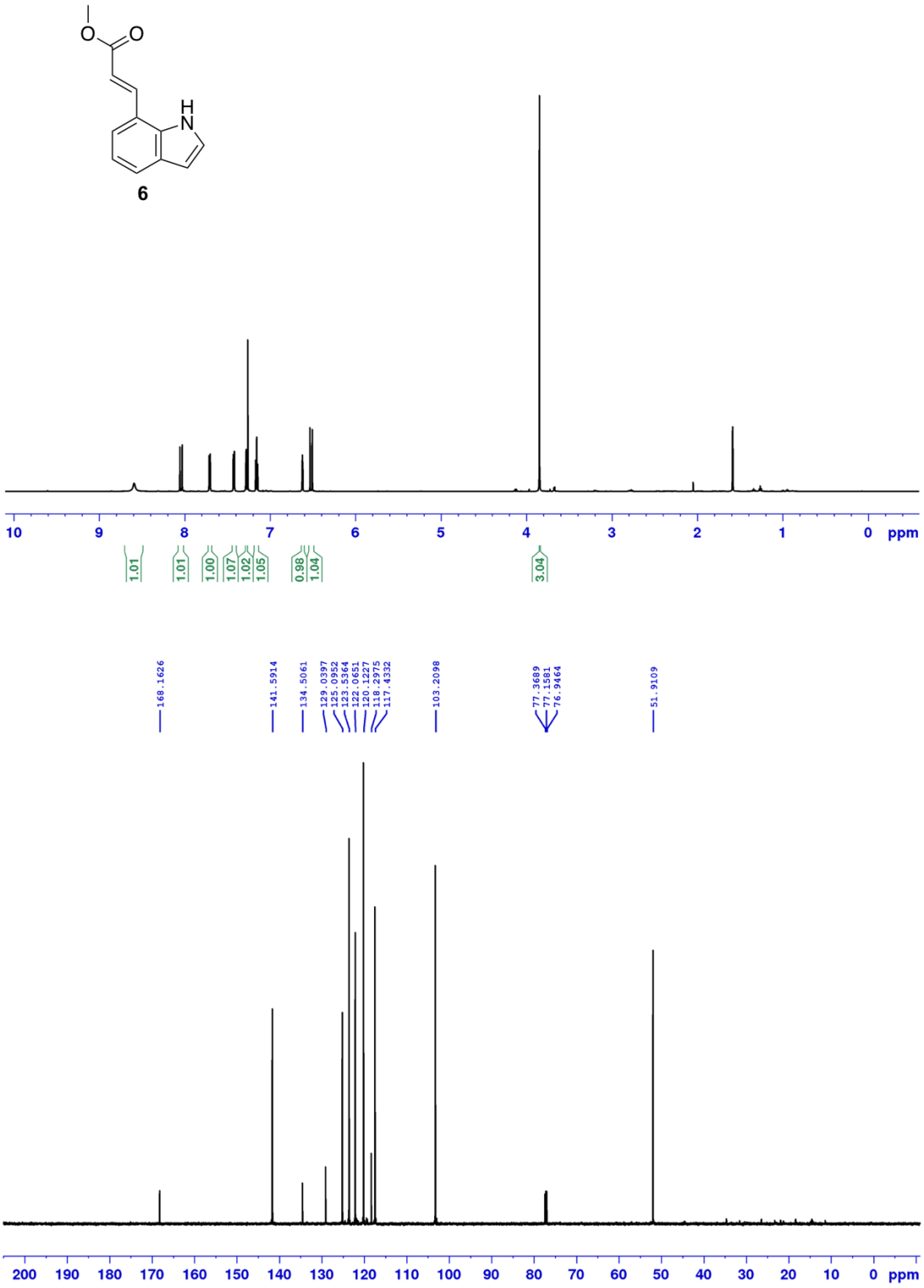


^{1}H NMR (500 MHz, CD_2Cl_2) and ^{13}C NMR (150 MHz, CD_2Cl_2) of **5.**

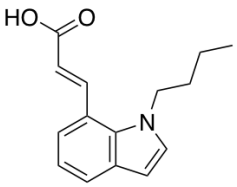




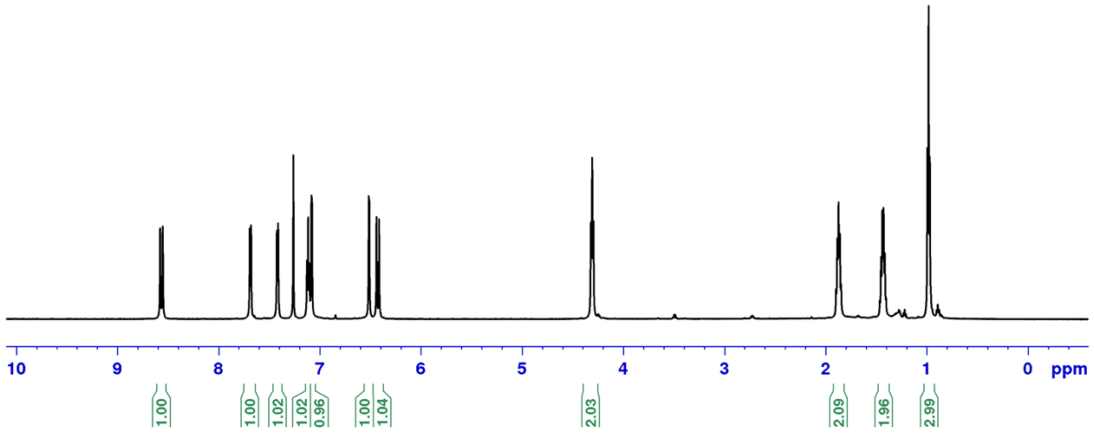
^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **6.**

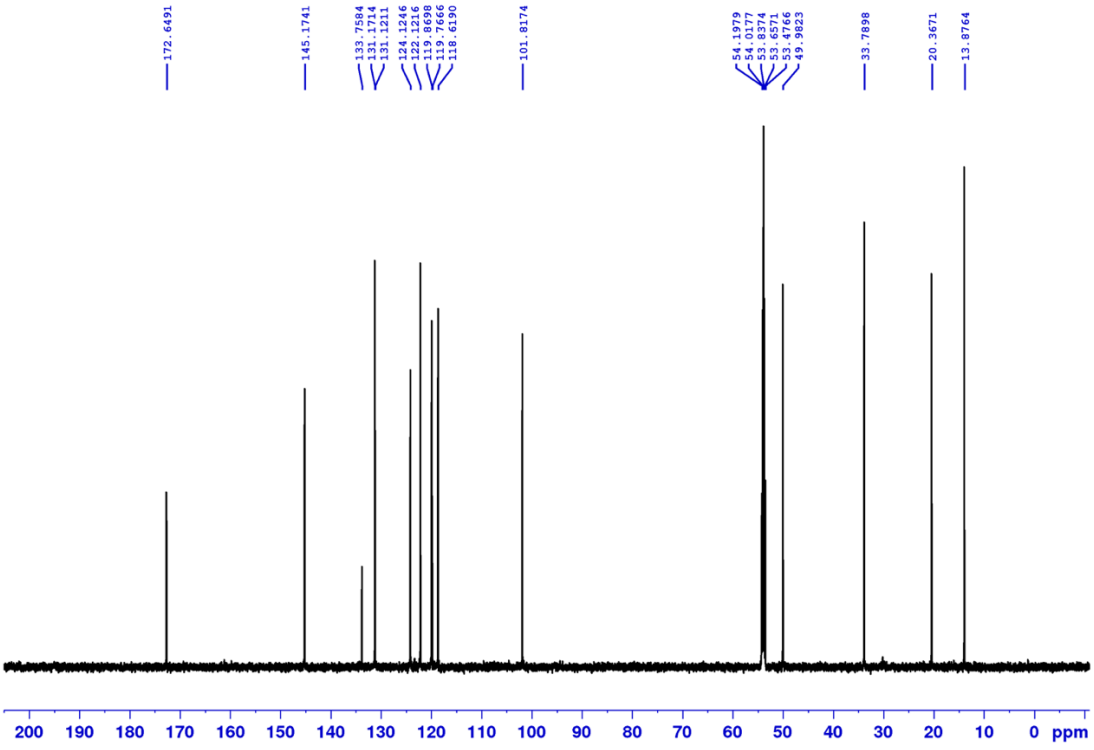


^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, CD_2Cl_2) of **7.**

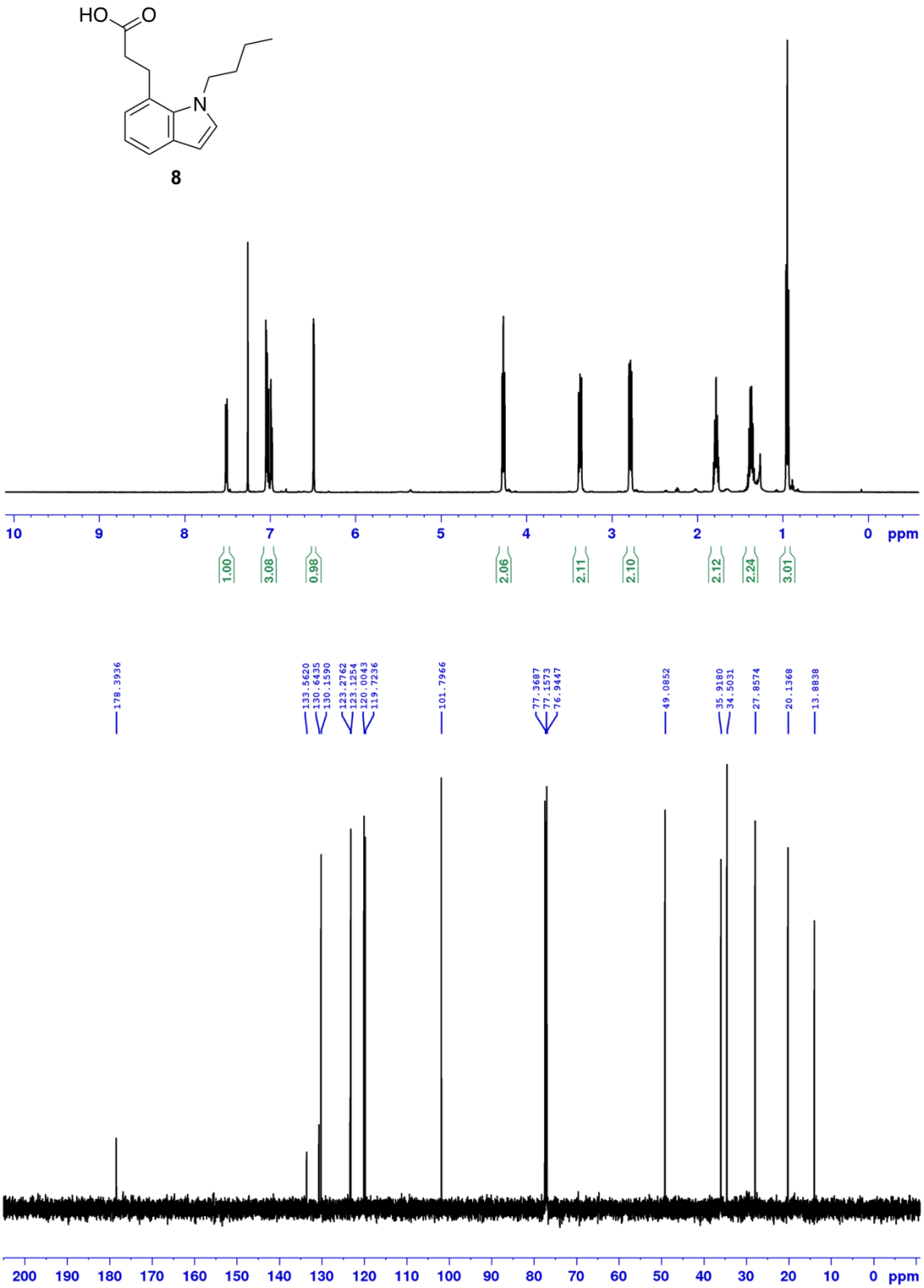


7

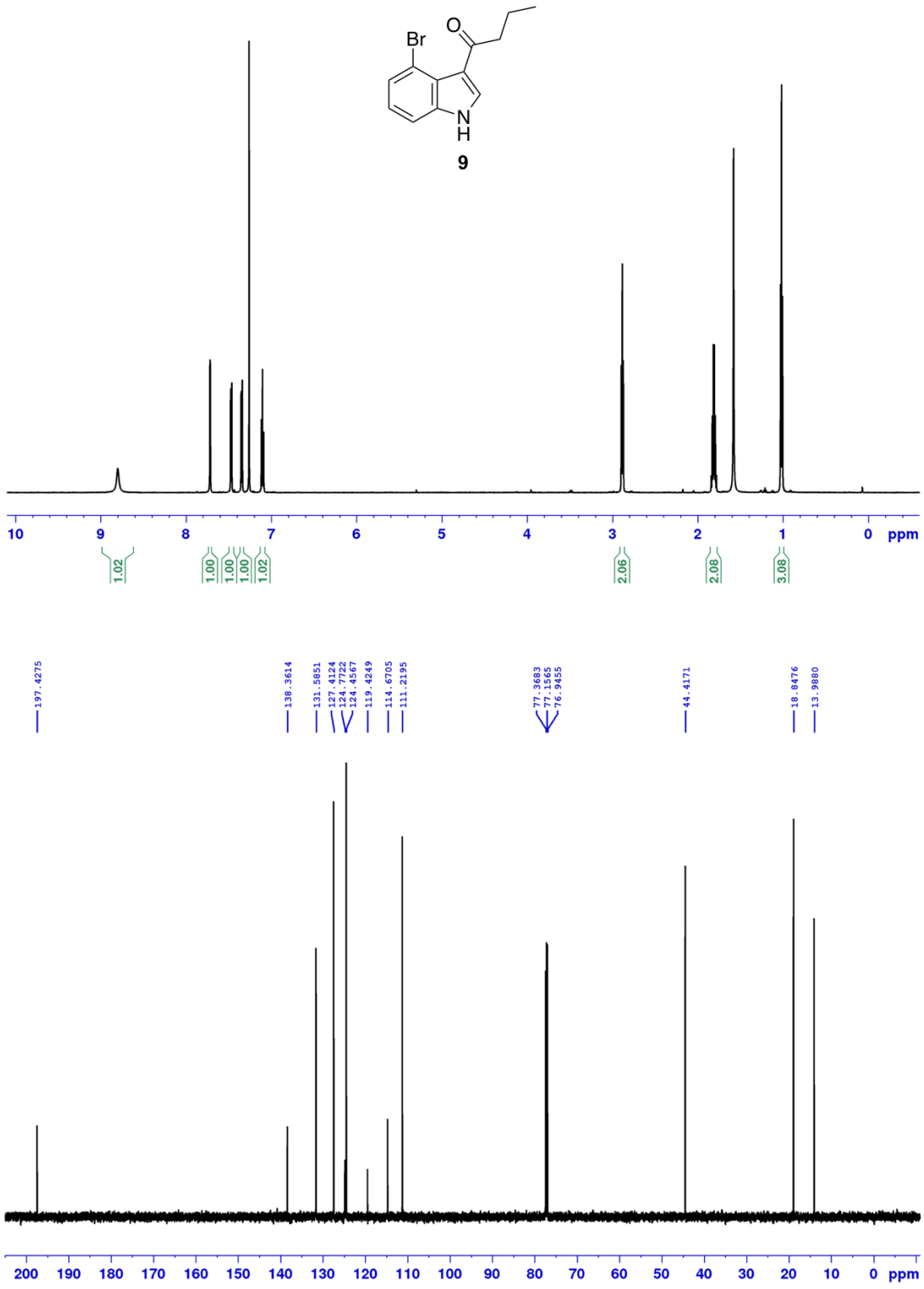




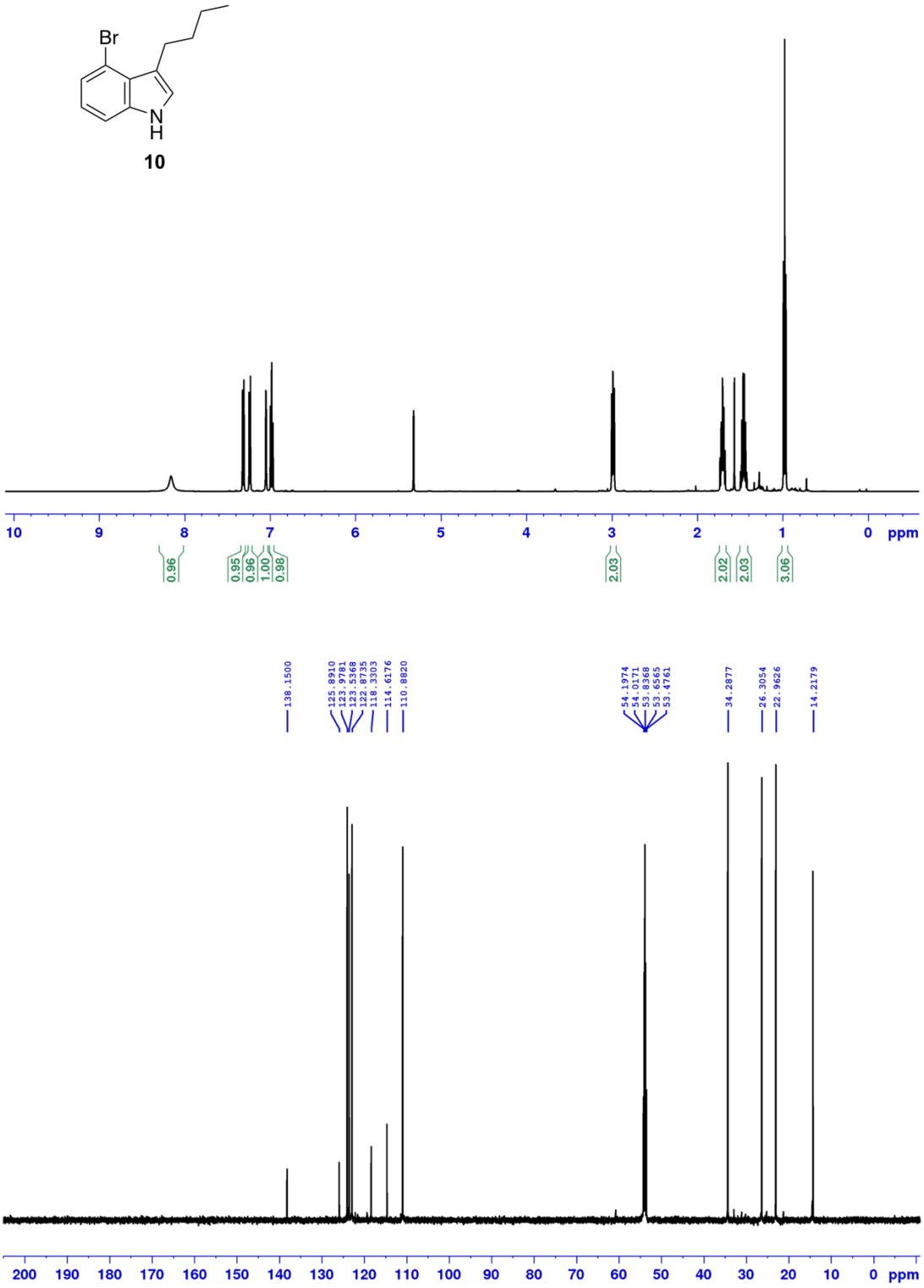
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **8.**



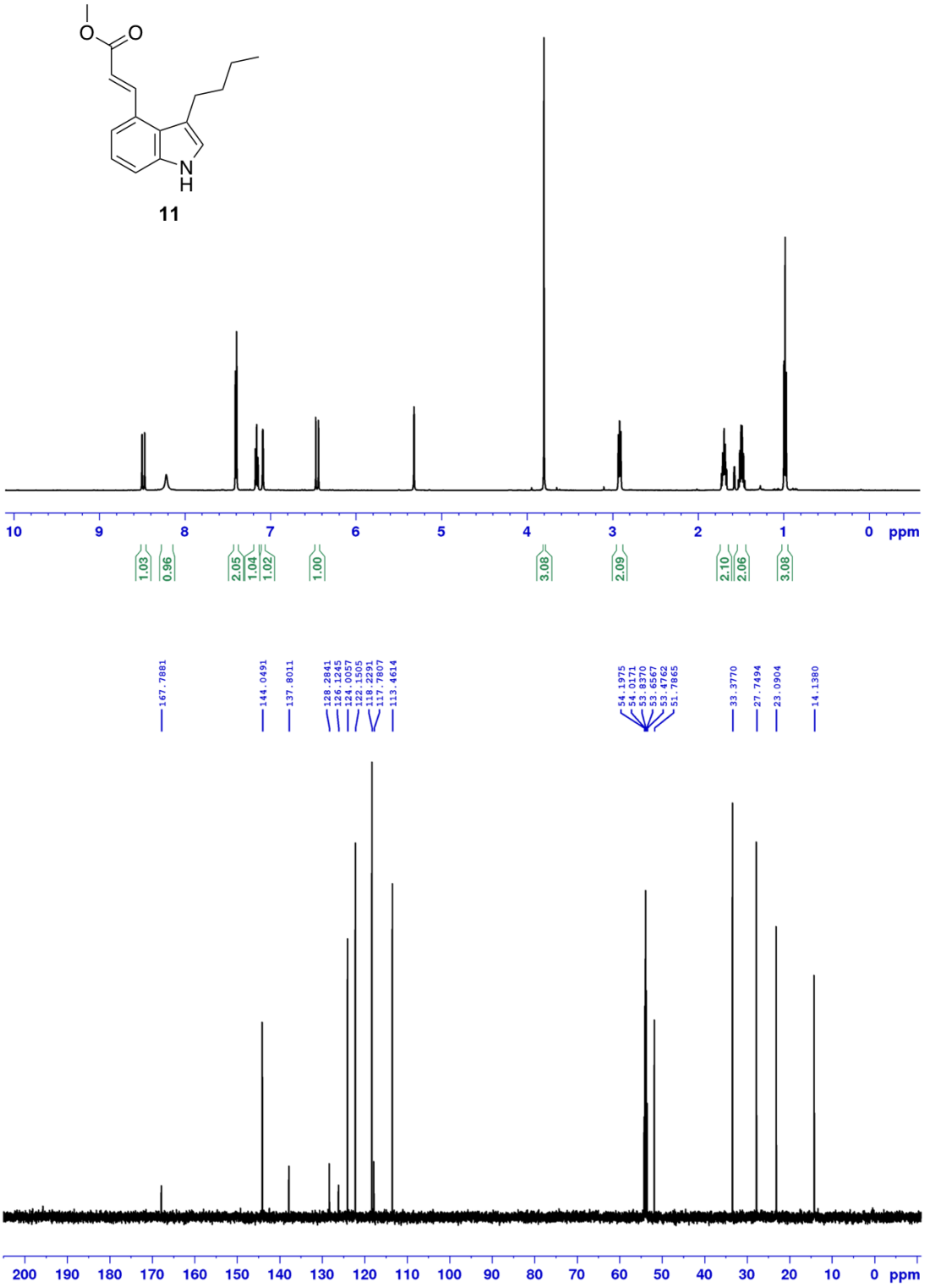
^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **9.**



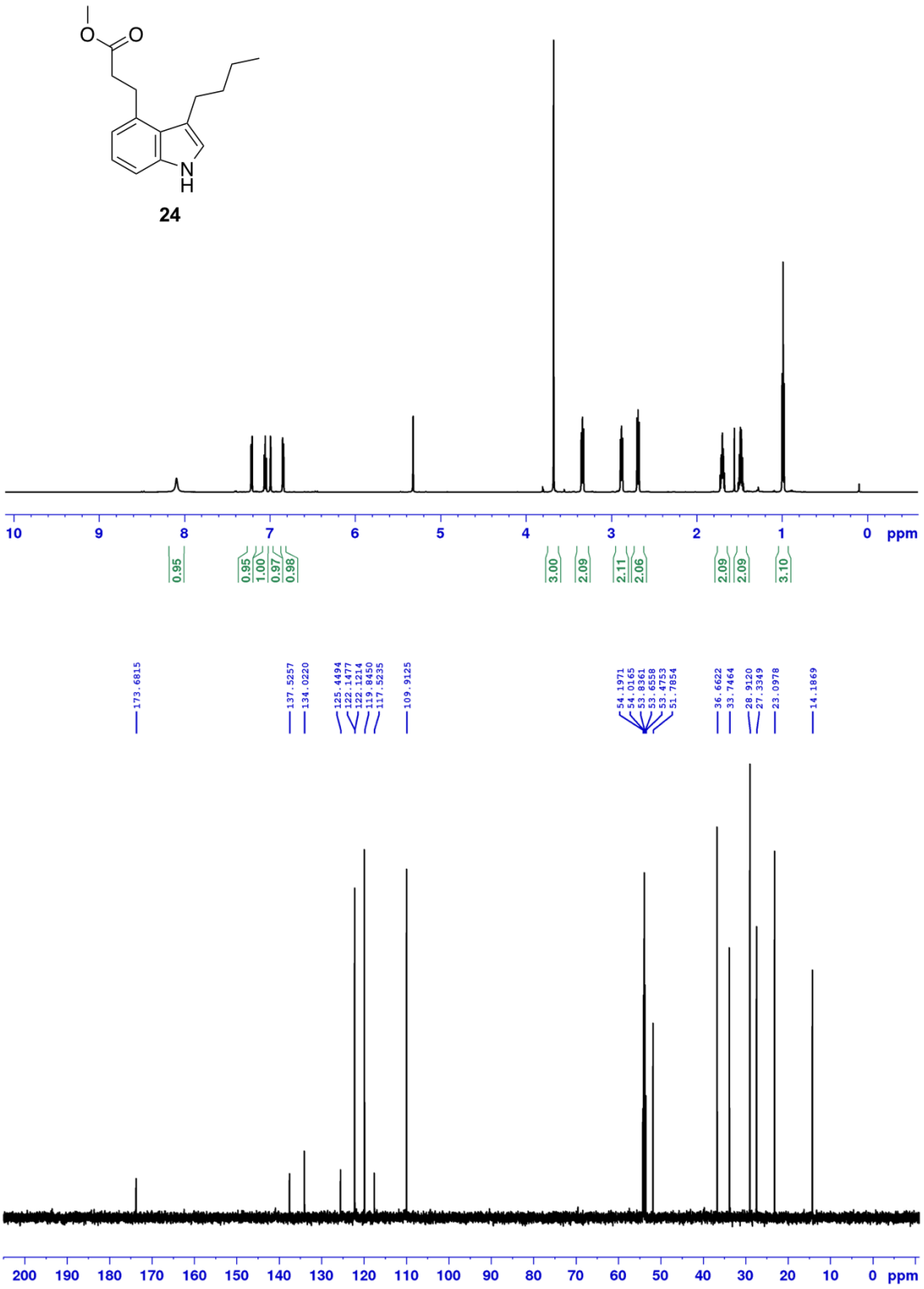
^{1}H NMR (500 MHz, CD_2Cl_2) and ^{13}C NMR (150 MHz, CD_2Cl_2) of **10.**



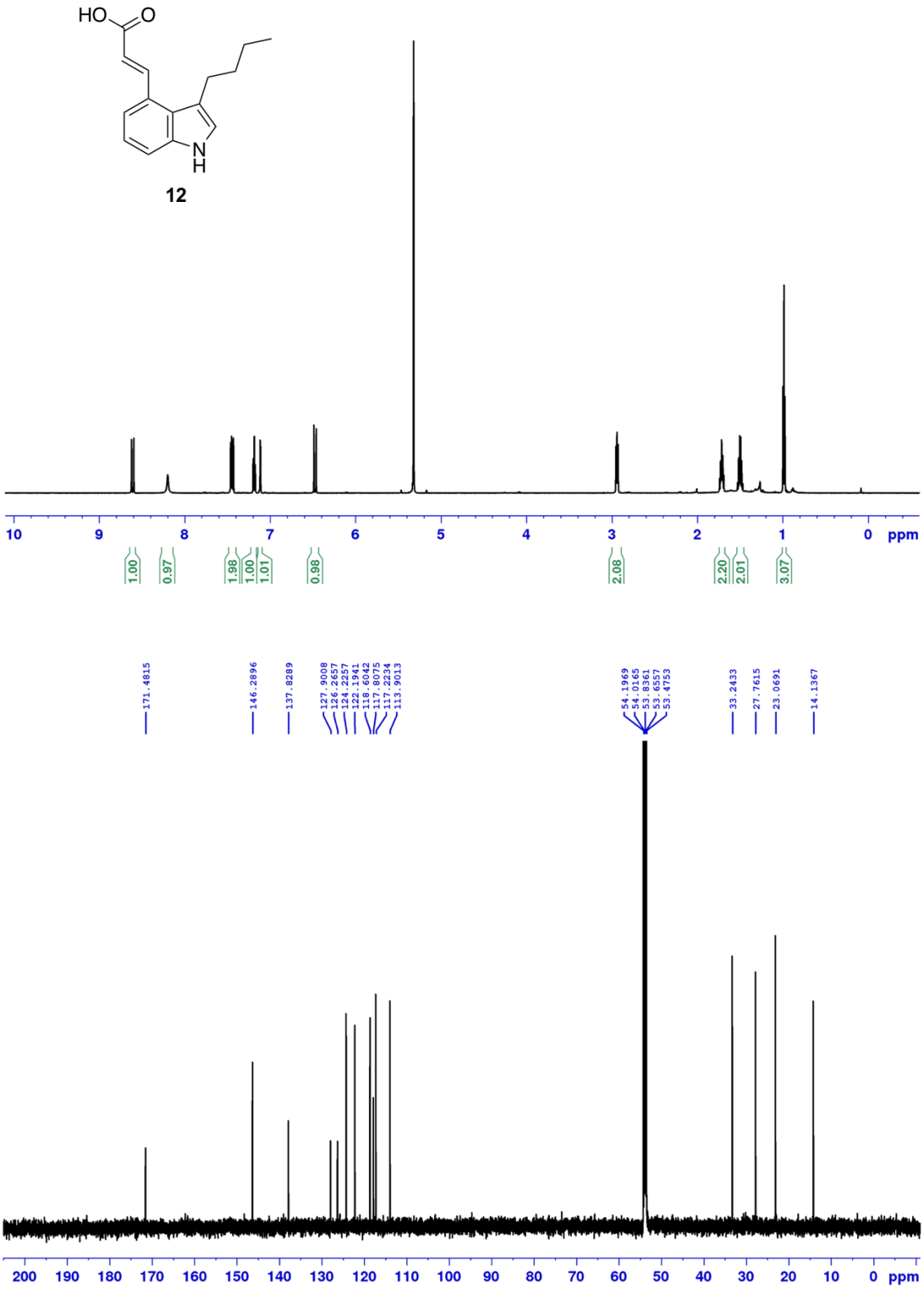
^{1}H NMR (500 MHz, CD_2Cl_2) and ^{13}C NMR (150 MHz, CD_2Cl_2) of **11.**



^{1}H NMR (600 MHz, CD_2Cl_2) and ^{13}C NMR (150 MHz, CD_2Cl_2) of **24.**



^{1}H NMR (600 MHz, CD_2Cl_2) and ^{13}C NMR (150 MHz, CD_2Cl_2) of **12.**



^{1}H NMR (600 MHz, CD_2Cl_2) and ^{13}C NMR (150 MHz, CD_2Cl_2) of **13.**