Practical Asymmetric Synthesis of Bioactive Aminotetralins from a Racemic Precursor using Regiodivergent Resolution

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General Experimental Remarks

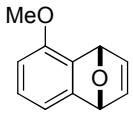
Melting points were recorded using a Fisher-Johns melting point apparatus. NMR spectra were recorded as dilute solutions in deuterated solvent on a BrukerAvance III 400 MHz, Varian Mercury 400MHz or Varian Mercury 300 MHz spectrometer using the deuterated solvent as the internal deuterium lock. ^{1}H chemical shift data are given in units δ relative to the residual protic solvent where $\delta(CDCl_3)$ = 7.26 ppm, s. ^{13}C chemical shift data were recorded with broadband proton decoupling and are given in units δ relative to the solvent where $\delta(CDCl_3)$ = 77.0 ppm, t. IR spectra were recorded as thin films on NaCl plates using a Shimadzu FTIR-8400S spectrometer, selected frequencies (ν_{max}) are reported. High resolution mass spectra were recorded using a Micromass 70S-250 spectrometer (EI) or an ABI/SciexQstar mass spectrometer (ESI). Optical rotation was measured using a Rudolph Research Analytical Autopol IV spectrometer, a concentration of c = 1.0 represents 10 mg per mL of solvent. Enantiomeric excess was determined using an Agilent 1200 series HPLC using a Diode Array Detector. Where appropriate, reactions were performed in oven-dried glassware under an argon atmosphere. Purification was performed using Silicycle Ultra-Pure 230-400 mesh silica gel. Toluene, dioxane and tetrahydrofuran (THF) were distilled under nitrogen from Na/benzophenone immediately prior to use. Triethylamine was distilled from KOH immediately before use. Dichloromethane was passed through a column of activated alumina under nitrogen. All reagents were used as received from Sigma-Aldrich, all metal catalysts were used as received from Strem Chemicals. We thank Solvias AG for the generous gift of Josiphos ligands: (R,S_p)-**2** and (S,R_p)-**2**.

Many of the products indicated were isolated as a white solid / colourless oil but became significantly darker upon standing at ambient conditions either neat or in solution. Analysis of the darker compounds revealed significant decomposition.

The NMR spectra of these compounds are included in a separate data file.

Application of the Regiodivergent Reaction to the Synthesis of Biologically Active Products

1,4-Epoxy-5-methoxy-1,4-dihydronaphthalene (±1)



(±)-**1**

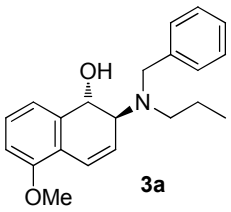
A solution of 3-chloro-methoxybenzene (25.2 g, 177 mmol), diisopropylamine (2.5 mL, 6.2 mmol) and furan (70 mL) in THF (600 mL) was cooled to −10 °C and a solution of *n*-BuLi (74 mL, 65 mmol, 2.5M in hexanes) was added by syringe pump over a period of four hours.After the addition was complete, the reaction was quenched with saturated aqueous ammonium chloride and extracted with diethyl ether (3 × 200 mL).The organic layers were separated, dried (Na_2SO_4) and concentrated to afford crude (±)-**1**. The crude product was filtered over a short pad of silica gel, eluting with 10% ethyl acetate in pentane.The semi-purified product was concentrated and recrystallized from pentane/diethyl ether to yield the title compound (13.7 g, 46%) as a white solid. The analytical data were in agreement with those reported previously.[11] **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.08 (dd, 1H, *J* = 1.7, 5.5 Hz), 7.03 (dd, 1H, *J* = 1.8, 5.5 Hz), 6.96 (m, 2H), 6.59 (dd, 1H, *J* = 1.3, 7.7 Hz), 5.96 (s, 1H), 5.70 (s, 1H), 3.83 (s, 3H) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ =143.0, 142.8, 126.9, 113.6, 110.3, 82.5, 80.0, 55.7.

General Procedure 1

A solution of rhodium(I) salt, ligand and additive in THF was stirred at ambient temperature for 10 minutes. A solution of the nucleophile and bicyclic alkene in THF was added and the resulting mixture was stirred at the stated temperature for the stated time. After the reaction was deemed complete (TLC analysis) the reaction mixture was cooled to ambient temperature, concentrated and purified directly by flash column chromatography.

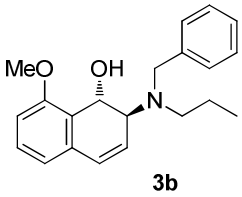
trans-2-(Benzyl(propyl)amino)-5-methoxy-1,2-dihydronaphthalen-1-ol (3a) and *trans*-2-(benzyl-(propyl)amino)-8-methoxy-1,2-dihydronaphthalen-1-ol (3b)

Prepared according to **General Procedure 1** using [Rh(cod)$_2$OTf] (1 mol%), (*S,R*)-PPF-P*t*-Bu$_2$ (1.5 mol%), NH_4BF_4 (1.0 equiv.), *N*-propyl-benzylamine (1.5 equiv.) and (±)-**1** (5.0 g, 1 equiv.) in THF (20 mL) at 60 °C for 5 days.The crude mixture was purified by flash chromatography (gradient from 3 to 15% ethyl acetate in pentane) to give **3a** (4.64 g, 50% yield, 93% ee) as an oil that solidified on standing and **3b** (4.08 g, 44% yield, 98% ee) as a white solid.



3a

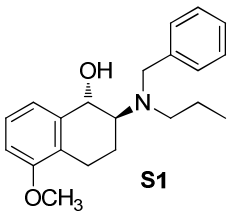
M.P. (ethyl acetate) = 99-100 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.31 (m, 4H), 7.21 (m, 3H), 6.91 (dd, 1H, *J* = 2.7, 10.2 Hz), 6.77 (d, 1H, *J* = 7.5 Hz), 6.10 (dd, 1H, *J* = 2.1, 10.2 Hz), 4.86 (d, 1H, *J* = 12.7 Hz), 3.99 (d, 1H, *J* =13.8 Hz), 3.83 (s, 3H), 3.63 (m, 1H) overlapping 3.58 (d, 1H, *J* = 13.9 Hz), 3.44 (s, 1H), 2.69 (m, 1H), 2.59 (ddd, 1H, *J* = 4.7, 8.4, 13.0 Hz), 1.54 (m, 2H), 0.88 (t, 3H) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 154.59, 139.56, 138.52, 128.79, 128.62, 128.43, 127.09, 125.01, 123.44, 120.42, 116.81, 109.61, 69.11, 63.38, 55.56, 55.43, 52.85, 21.61, 11.72 ppm; **IR** (neat): ν_{max} = 3472 (broad), 3028, 2959, 1574, 1474, 1261, 1045 cm^{-1}; **HRMS** *m/z* (ESI): 324.1970 (calculated for M + H^+: 324.1958); **$[\alpha]_D^{28}$** = +203 (c = 1.1, $CHCl_3$, 93% ee); **HPLC** (AD-H Chiralpak, 1 mL/min, 3% isopropanol/hexane) retention times: 11.9 min (major enantiomer), 15.4 min (minor enantiomer).



3b

M.P. (ethyl acetate) = 64-65 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.26 (m, 6H), 6.83 (d,1H, *J* = 8.1 Hz), 6.78 (d,1H, *J* = 7.5 Hz), 6.65 (d,1H, *J* = 9.6 Hz), 6.02 (dd,1H, *J* = 4.8, 9.6 Hz), 5.34 (s, 1H), 3.90 (s, 3H), 3.70 (s, 1H), 3.57 (d, 1H, *J* = 14.0 Hz), 3.40 (d, 1H, *J* = 13.8 Hz), 2.42 (m, 2H), 2.25 (s, 1H), 1.47 (m, 2H), 0.81 (t, 3H, *J* = 7.3 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 156.89, 140.91, 133.15, 129.16, 128.48, 128.16, 127.99, 127.55, 126.50, 123.59, 119.18, 110.15, 62.76, 60.11, 55.53, 54.16, 52.02, 21.53, 11.64 ppm; **IR** (neat): ν_{max} = 3441 (broad), 3028, 2959, 2870, 1578, 1466, 1370, 1076 cm^{-1}; **HRMS** *m/z* (ESI): 324.1970 (calculated for M + H^+: 324.1958); **$[\alpha]_D^{28}$** = +336 (c = 1.2, $CHCl_3$, 98% ee); **HPLC** (AD-H Chiralpak, 1 mL/min, 10% isopropanol/hexane) retention times: 7.6 min (minor enantiomer), 11.0 min (major enantiomer).

(1*S*,2*S*)-2-(Benzyl(propyl)amino)-5-methoxy-1,2,3,4-tetrahydronaphthalen-1-ol (S1)

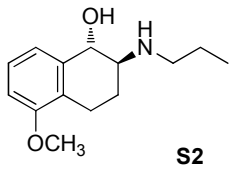


S1

To a solution of **3a** (3.95 g, 12.2 mmol) and toluenesulfonylhydrazide (11.4 g, 61.1 mmol) in THF (160 mL) was added H_2O (160 mL) followed by NaOAc (10.0 g, 122.2 mmol) at room temperature.The mixture was stirred vigorously at 80 °C (external) in a flask fitted with a reflux condenser open to the atmosphere.After the reaction was complete, saturated aqueous K_2CO_3 (10 mL) was added, the organic layer was separated, and the aqueous layer was extracted with diethyl ether (3 x 50 mL).The combined organics were dried (Na_2SO_4) and concentrated to give crude **S1**.The crude product was filtered through a plug of silica gel (eluting with 10% ethyl acetate in pentane) to give the title compound (3.97 g, quant.) as an oil that solidified in the freezer.

M.P. (ethyl acetate) = 110-111 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ =7.34 (m, 4H), 7.24 (m, 3H), 6.73 (dd, 1H, *J* = 2.2, 7.0 Hz), 4.67 (d, 1H, *J* = 9.9 Hz), 3.95 (d, 1H, *J* = 13.6 Hz), 3.88 (s, 1H), 3.82 (s, 3H) 3.46 (d, 1H, *J* = 13.6 Hz), 3.02 (ddd, 1H, *J* = 1.4, 5.8, 17.7 H), 2.79 (ddd, 1H, *J* = 2.6, 10.0, 12.6 Hz), 2.54 (m, 3H), 2.15 (tdd, 1H, *J* = 2.0, 6.0, 10.5 Hz), 1.58 (m, 3H), 0.89 (t, 3H, *J* = 7.4 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 156.56, 139.81, 139.70, 128.76, 128.40, 127.02, 126.79, 123.69, 118.70, 107.93, 68.23, 62.21, 55.22, 54.05, 51.31, 23.66, 21.64, 18.84, 11.72 ppm; **IR** (neat): ν_{max} = 3457, 2932, 2835, 1586, 1474, 1262, 1045 cm^{-1}; **$[\alpha]_D^{28}$** = +54 (c = 0.9, $CHCl_3$); **HRMS** *m/z* (ESI): calculated for M + H^+: 326.2114, found: 326.2118.

(1*S*,2*S*)-5-Methoxy-2-(propylamino)-1,2,3,4-tetrahydronaphthalen-1-ol (S2)

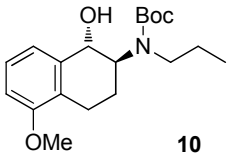


S2

To a solution of **S1** (2.0 g, 6.15 mmol) in ethyl acetate (20 mL), purged with Ar, was added 10% palladium on carbon (300 mg).The reaction was fitted with a balloon containing H_2 and backfilled three times with H_2/aspirator vacuum.When the reaction was deemed complete (TLC, 6 hours), the reaction vessel was evacuated using aspirator pressure for 10 minutes, and the suspension was filtered over a pad of Celite, washing liberally with ethyl acetate.Concentration of the collected solvent afforded the title compound (1.34 g, 93%) as a white solid which was analytically pure without further purification.

M.P. (ethyl acetate) = 125-126 °C; **^{1}H-NMR** (CD_3OD, 400 MHz): δ = 7.16 (t, 1H, *J* = 7.9 Hz), 7.10 (d, 1H, *J* = 7.8 Hz), 6.77 (d, 1H, *J* = 7.8 Hz), 4.40 (d, 1H, *J* = 8.4 Hz), 3.78 (s, 3H) 2.76 (m, 3H), 2.54 (m, 2H), 2.16 (m, 1H), 1.53 (m, 3H), 0.96 (t, 3H, *J* = 7.4 Hz) ppm; **^{13}C-NMR** (CD_3OD, 100 MHz): δ =158.04, 140.79, 127.81, 126.00, 120.52, 109.37, 73.49, 61.41, 55.81, 49.86, 25.92, 23.86, 22.82, 12.08 ppm; **IR** (neat): ν_{max} = 3275, 3187 (broad), 2951, 2932, 1586, 1466, 1258, 1042 cm^{-1}; **$[\alpha]_D^{28}$** = −2.2 (c = 0.8, CH_3OH); **HRMS** *m/z* (ESI): 236.1645 (calculated for M + H^+: 236.1645).

***tert*-Butyl [(1S,2S)-1-hydroxy-5-methoxy-1,2,3,4-tetrahydronaphthalen-2-yl]-propyl-carbamate (10)**



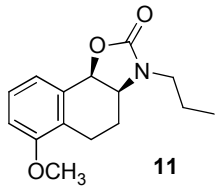
10

A solution of di-*tert*-butyl-dicarbonate (983 mg, 4.51 mmol) in THF (4 mL) was added to a room temperature solution of **S2** (1.95 g) in THF (20 mL).The resulting mixture was heated to 70 °C overnight then concentrated to give the title compound **10** (1.44 g, quant.) as a colourless oil which was analytically pure without further purification.

^{1}H-NMR ($CDCl_3$, 400 MHz, line broadening observed due to hindered rotation of *tert*-butyl carbamate): δ = 7.23 (m, 2H), 6.73 (d, 1H, *J* = 1.5, 7.2 Hz), 4.80 (br. s, 1H), 4.15 (br. s, 1H), 3.82 (s, 3H), 3.17 (m, 2H),

2.98 (m, 1H), 2.66 (m, 1H), 2.44 (br. s, 1H), 1.98 (m, 2H), 1.64 (m, 2H), 1.48 (s, 9H), 0.90 (t, 3H, *J* = 7.4 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 157.5, 156.5, 140.5, 126.9, 124.2, 119.1, 108.2, 79.9, 71.3, 58.9, 55.3, 45.7, 28.5, 26.2, 24.1, 23.7, 11.5 ppm; **IR** (neat): ν_{max} = 3426 (broad), 2967, 2932, 1670, 1586, 1470, 1367, 1261 cm^{-1}; **$[\alpha]_D^{28}$** = −44 (c = 0.2, $CHCl_3$); **HRMS** *m/z* (ESI): 358.1992 (calculated for M + Na^+: 358.1988).

(3a*S*,9b*R*)-6-Methoxy-3-propyl-3,3a,4,5-tetrahydronaphtho[2,1-*d*]oxazol-2(9b*H*)-one (11)

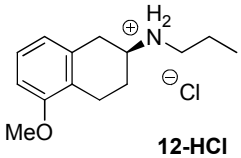


11

Compound **10** (780 mg, 2.33 mmol, 1.0 equiv) was dissolved in DCM (20 mL) and $FeCl_3 \cdot 6H_2O$ (189 mg, 0.70 mmol) was added. The reaction mixture was stirred at room temperature until the reaction was deemed complete (TLC) then quenched with saturated aqueous sodium bicarbonate solution (5 mL).The organic layer was separated and the aqueous layer was extracted with DCM (3 × 20 mL).The organic layers were dried (Na_2SO_4), concentrated *in vacuo* and filtered through a silica gel plug (eluting 50% ethyl acetate in pentane).Concentration of the eluent gave the title compound**11**(600 mg, 99%) as a colourless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.23 (dd, 1H, *J* = 8.0/8.0 Hz), 7.06 (d, 1H, *J* = 7.7 Hz), 6.82 (d, 1H, *J* = 8.0 Hz), 5.43 (d, 1H, *J* = 8.2 Hz), 4.10 (m, 1H), 3.83 (s, 3H), 3.48 (ddd, 1H, *J* = 7.3, 8.8, 14.0 Hz), 3.06 (ddd, 1H, *J* = 5.2, 8.6, 13.9 Hz), 2.74 (ddd, 1H, *J* = 4.2, 8.4, 16.8 Hz), 2.59 (ddd, 1H, *J* = 4.3, 7.6, 16.9 Hz), 1.97 (tdd, 1H, *J* = 4.2, 8.4, 16.9 Hz), 1.83 (dtd, 1H, *J* = 4.3, 7.3, 11.5 Hz), 1.65 (m, 2H), 0.97 (t, 3H, *J* = 7.4 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 157.9, 156.2, 132.4, 132.4, 127.3, 126.6, 122.3, 110.0, 72.5, 55.5, 54.1, 43.5, 24.1, 20.8, 17.7, 11.2 ppm; **IR** (neat): ν_{max} = 2963, 2932, 1740, 1589, 1474, 1265 cm^{-1}; **$[\alpha]_D^{28}$** = +158 (c = 0.8, $CHCl_3$); **HRMS** *m/z* (ESI): 262.1428 (calculated for M + H^+: 262.1437).

(*S*)-5-Methoxy-*N*-propyl-1,2,3,4-tetrahydronaphthalen-2-amine hydrochloride salt (12-HCl)



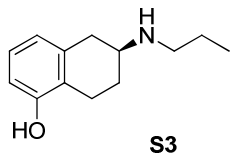
12-HCl

A mixture of **11**(147 mg, 0.6 mmol), 10% palladium on carbon (30 mg), 2N HCl (0.3 mL) in EtOH (6 mL) was hydrogenated at 35 psi overnight. After filtration and evaporation of the solvent, then recrystallization from diethyl ether/ethanol, the product **12-HCl**was obtained as a white solid (140 mg, 97%).

^{1}H-NMR (CD_3OD,400 MHz): δ = 7.12 (dd, 1H, *J* = 8.0, 8.0 Hz), 6.77 (d, 1H, *J* = 8.2 Hz), 6.73 (d, 1H, *J* = 7.8 Hz), 3.80 (s, 3H), 3.47 (ddt, 1H, *J* = 3.1, 5.0, 11.1 Hz), 3.23 (ddd, 1H, *J* = 1.6, 4.9, 15.9 Hz), 3.09 (m, 2H), 3.00 (ddd, 1H, *J* = 3.4, 5.8, 17.8 Hz), 2.87 (dd, 1H, *J* = 10.6, 15.7 Hz), 2.64 (m, 1H), 2.46 (m, 1H), 1.78 (m, 3H), 1.06 (t, 3H, *J* = 6.5 Hz) ppm; **^{13}C-NMR** (CD_3OD,100 MHz): δ = 158.6 134.4, 128.2, 124.7, 122.3, 109.1,

55.8, 55.7, 47.9, 33.2, 26.7, 22.7, 21.0, 11.4 ppm; $[\alpha]_D^{30}$ = −65 (c = 1.1, CH_3OH); **HRMS***m/z* (ESI): 220.1690 (calculated for M^+: 220.1695).

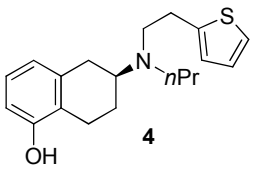
(*S*)-5-Hydroxy-*N*-propyl-1,2,3,4-tetrahydronaphthalen-2-amine(S3)


S3

To a solution of **12**(free-base, 109 mg, 0.50 mmol) in DCM (5 mL) at −40 °C was added BBr_3(1.2 mL, 1.2 mmol, 1.0M in DCM) dropwise*via* syringe. The reaction was stirred for 2 h at this temperature, and warmed to room temperature stirring overnight. After careful quenching with saturated aqueous sodium bicarbonate, the mixture was extracted with DCM (3×), dried over anhydrous sodium sulphate, filtered and concentrated to give the title compound **S3** (99 mg, 97%) as a yellow film.

^{1}H-NMR (CD_3OD, 400 MHz): δ = 6.95 (dd, 1H, *J* = 7.8/7.8 Hz), 6.61 (d, 1H, *J* = 8.0 Hz), .45 (m, 1H), 3.20 (dd, 1H, *J* = 3.5, 15.8 Hz), 3.08 (m, 2H), 2.99 (ddd, 1H, *J* = 3.4, 5.7, 17.7 Hz), 2.86 (dd, 1H, *J* = 10.4, 15.7 Hz), 2.64 (ddd, 1H, *J* = 6.2, 11.2, 17.5 Hz), 2.34 (m, 1H), 1.79 (m, 3H), 1.05 (t, 3H, *J* = 7.4 Hz) ppm; **^{13}C-NMR** (CD_3OD, 100 MHz): δ = 156.2, 134.4, 128.0, 123.1, 121.2, 113.5, 55.9, 47.9, 33.2, 26.8, 22.7, 21.0, 11.4 ppm; **HRMS** *m/z* (EI): 206.1542 (calculated for M+ H^+: 206.1545).

Rotigotine (4)

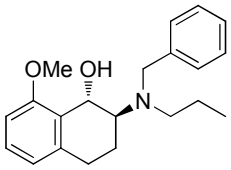

4

A mixture of amine **S3** (90 mg, 0.44 mmol), 2-(thiophen-2-yl)ethyl 4-methylbenzenesulfonate (618 mg, 2.19 mmol), Na_2CO_3 (anhydrous, 28 mg, 0.26 mmol) and xylenes (5 mL) was heated to 140 °C for 24 h. The reaction was cooled to room temperature, diluted with diethyl ether and extracted with 0.5N HCl (3 × 20 mL). The aqueous layer was neutralized with solid sodium bicarbonate, then extracted with ether (1×) and DCM (3×). The organics were dried over anhydrous sodium sulphate and then filtered. Concentration of the organics gave a brown oil that was filtered over a plug of silica (eluting with 20% ethyl acetate in pentane) to give the product **4**as a colourless oil (128 mg, 92%). Alternatively, the crude product could be purified by conversion to the HCl salt followed by recrystallization.

4(free base): **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.13 (dd, 1H, J = 1.1, 5.1 Hz), 6.99 (dd, 1H, J = 7.8/7.8 Hz), 6.93 (dd, 1H, *J* = 3.4, 5.1 Hz), 6.83 (d, 1H, *J* = 2.7 Hz), 6.68 (d, 1H, *J*= 7.6 Hz), 6.61 (d, 1H, *J* = 7.8 Hz), 5.03 (br. s. 1H), 3.01 (br. s, 3H), 2.91 (m, 3H), 2.77 (m, 1H), 2.57 (m, 3H), 2.13 (m, 1H), 1.62 (m, 3H), 0.92 (t, 3H, *J* = 7.3 Hz) ppm.

4-HCl (HCl salt): **^{1}H-NMR** (CD_3OD, 400 MHz): δ = 7.32 (ddd, 1H, *J* = 1.1, 2.3, 5.0 Hz), 7.04 (d, 1H, *J* = 3.4 Hz), 6.98 (m, 2H), 6.63 (dd, 1H, *J* = 7.9, 11.8 Hz), 3.78 (m, 1H), 3.60 (m, 1H), 3.48 (m, 1H), 3.37 (m, 3H), 3.24 (m, 1H), 3.10 (m, 3H), 2.64 (m, 1H), 2.35 (m, 1H), 1.86 (m, 3H), 1.05 (t, 3H, *J* = 7.3 Hz) ppm; **^{13}C-NMR** (CD_3OD, 100 MHz): δ = 156.2, 139., 134.7, 128.4, 128.1, 127.6, 126.0, 123.1, 121.3, 113.5, 62.2 (app. d, *J* = 4.3 Hz), 54.0 (app. d, *J* = 21.8 Hz), 53.5 (app. d, *J* = 23.9 Hz), 30.8 (app. d, *J* = 8.5 Hz), 26.5 (app. d, *J* = 15.2 Hz), 24.9 (app. d, *J* = 14.0 Hz), 23.7, 19.9 (app. d, *J* = 14.0 Hz), 11.3 (app. d, *J* = 1.8 Hz) ppm. The aliphatic carbon signals appear to be doublets aliphatic signals appear as doublets, presumably due to the central chirality of the quarternized nitrogen atom; $[\alpha]_D^{30}$ = −53 (c = 1.0, CH_3OH, HCl salt), lit.[#] $[\alpha]_{578}^{25}$ = −55.79 (c = 0.99, CH_3OH, HCl salt, >99% ee); **HRMS** *m/z* (EI): 314.1570 (calculated for M^+-H: 314.1579).

(1*S*,2*S*)-2-(*N*-Benzyl-*N*-propylamino)-8-methoxy-1,2,3,4-tetrahydronaphthalen-1-ol (S4)

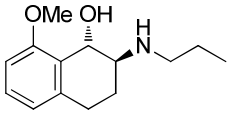


S4

Prepared in a similar manner to **S1** with **3b** (3.50 g, 10.8 mmol), toluenesulfonylhydrazide (10.08 g, 54.2 mmol), NaOAc (8.89 g, 108.4 mmol), THF (160 mL) and H_2O (160 mL).Filtration of the crude product over a plug of silica gel (20% ethyl acetate in pentane) gave the title compound (3.52 g, quant.) as a colourless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.42 (m, 2H), 7.30 (m, 7.4), 7.21 (m, 1H), 7.14 (m, 1H), 6.72 (m, 2H), 5.06 (d, 1H, *J* = 8.2 Hz), 3.96 (d, 1H, *J* = 14.2 Hz), 3.88 (s, 3H), 3.62 (m, 2H), 3.02 (m, 1H), 2.81 (m, 2H), 2.64 (td, 1H, *J* = 7.6, 12.9 Hz), 2.54 (m, 1H), 2.03 (qd, 1H, *J* = 3.4, 12.3 Hz), 1.63 (ddd, 1H, 1H *J* = 6.3, 12.5, 18.7 Hz), 1.52 (m, 2H), 0.87 (t, 3H, *J* = 7.4 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 158.6, 141.1, 139.2, 128.5, 128.1, 129.0, 127.2, 126.6, 121.1, 108.1, 67.5, 63.6, 55.4, 55.1, 52.7, 30.1, 22.8, 21.8, 11.8 ppm; **IR** (neat): ν_{max} = 3565 (broad), 3063, 3024, 2932, 1586, 1474, 1458, 1250, 1076 cm^{-1}; $[\alpha]_D^{28}$ = −51 (c = 0.9, $CHCl_3$); **HRMS** *m/z* (EI): 326.2129 (calculated for M + H^+: 326.2114).

(1*S*,2*S*)-8-Methoxy-2-(propylamino)-1,2,3,4-tetrahydronaphthalen-1-ol (S5)

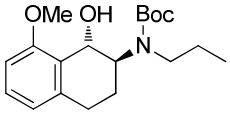


S5

Prepared in a similar manner to **S2** with **S4** (2.6 g, 7.98 mmol) and 10% palladium on carbon (350 mg) in ethyl acetate (20 mL).Evaporation of the organics after filtration gave the title compound (1.80 g, 96%) as a white solid which was analytically pure without further purification.

M.P. (ethyl acetate) = 82-83 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.14 (dd, 1H, *J* = 7.9/7.9 Hz), 6.72 (m, 2H), 4.80 (d, 1H, *J* = 6.8 Hz), 3.86 (s, 3H), 2.95 (ddd, 1H, *J* = 3.1, 6.8, 9.9 Hz), 2.76 (m, 3H), 2.62 (ddd, 1H, *J* = 6.4, 8.1, 11.2 Hz), 2.09 (dtd, 1H, *J* = 3.1, 5.2, 13.3 Hz), 1.57 (m, 3H), 0.94 (t, 3H, *J* = 7.4 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 158.31, 138.65, 128.00, 126.26, 121.46, 107.88, 70.00, 59.76, 55.39, 49.38, 27.46, 25.19, 23.42, 11.81 ppm; **IR** (neat): ν_{max} = 3333 (broad), 2932, 2835, 1636, 1586, 1466, 1254, 1018 cm^{-1}; **$[\alpha]_D^{28}$** = +13 (c = 1.0, CH_3OH); **HRMS** *m/z* (ESI): 236.1654 (calculated for M + H^+:236.1645).

***tert*-Butyl [(1S,2S)-1-hydroxy-8-methoxy-1,2,3,4-tetrahydronaphthalen-2-yl]-propyl-carbamate(13)**

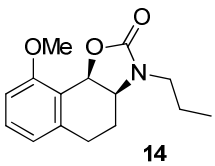


13

Prepared in a similar manner to **10** using **S5** (1.65 g, 7.01 mmol) and di-*tert*-butyl-dicarbonate (1.61 g, 7.36 mmol) in THF (40 mL).The title compound (2.35 g, quant.) was isolated as a colourless oil which was analytically pure without further purification.

^{1}H-NMR ($CDCl_3$, 400 MHz, line broadening observed due to hindered rotation of *tert*-butyl carbamate): δ = 7.14 (dd, 1H, *J* = 7.9/7.9 Hz), 6.72 (m, 2H), 5.22 (d, 1H, J = 6.6 Hz), 3.90 (br. m, 2H), overlapping 3.87 (s, 3H), 3.22 (br. s, 2H), 2.93 (m, 1H), 2.75 (m, 1H), 2.09 (br. s, 1H), 1.87 (tdd, 1H, *J* = 3.2, 4.4, 12.5 Hz) 1.64 (m, 2H), 1.47 (s, 9H), 0.89 (t, 3H, *J* = 7.4 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 158.2, 155.8, 138.4, 128.0, 127.1, 121.2, 108.0, 79.1, 68.2, 61.0, 55.3, 48.0, 30.1, 28.5, 27.4, 23.4, 11.4 ppm; **IR** (neat): ν_{max} = 3572 (broad), 2967, 2932, 2874, 1678, 1586, 1474, 1366, 1250 cm^{-1}; **$[\alpha]_D^{28}$** = −51 (c = 0.7, $CHCl_3$); **HRMS** *m/z* (EI): 317.1991 (calculated for $M^+ - H_2O$: 317.1991).

(3a*S*,9b*R*)-9-Methoxy-3-propyl-3,3a,4,5-tetrahydronaphtho[2,1-*d*]oxazol-2(9b*H*)-one (14)



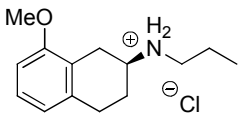
14

Prepared in a similar manner to **11**with **13**(1.00 g, 2.98 mmol) and $FeCl_3 \cdot 6H_2O$ (80 mg, 0.29 mmol) in DCM (30 mL).The reaction was finished in 30 minutes at room temperature.Aqueous work-up with sodium bicarbonate gave the title compound (782 mg, quant.) as a colourless oil which was analytically pure without the need for further purification.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.22 (dd, 1H, *J* = 7.9/7.9 Hz), 6.73 (m, 2H), 5.8 (d, 1H, *J* = 8.3 Hz), 4.13 (td, 1H, *J* = 4.4, 8.4 Hz), 3.83 (s, 3H), 3.49 (td, 1H, *J* = 8.0, 14.2 Hz), 3.02 (ddd, 1H, *J* = 5.1, 8.5, 13.8 Hz), 2.78 (m, 1H), 2.55 (m, 1H), 1.98 (ddd, 1H, *J* = 5.3, 9.4, 14.4 Hz), 1.83 (m, 1H), 1.61 (m, 2H), 0.95 (t, 3H, *J* = 7.4 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 159.10, 158.33, 139.74, 129.80, 120.34, 119.93, 108.60, 68.38, 55.56, 53.48, 43.28, 27.28, 24.42, 24.38, 20.55, 11.11ppm; **IR** (neat): ν_{max} = 2963, 2936, 1740, 1589,

1474, 1420, 1265 cm^{-1}; $[\alpha]_D^{28}$ = +309 (c = 0.5, $CHCl_3$); **HRMS** *m/z* (EI): 261.1365 (calculated for M^+: 261.1365).

(*S*)-8-Methoxy-*N*-propyl-1,2,3,4-tetrahydronaphthalen-2-amine hydrochloride salt (15-HCl)

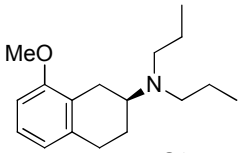


15-HCl

Prepared in a similar manner to **12-HCl** with **14** (670 mg, 2.56 mmol), 10% palladium on carbon (140 mg), 2M HCl (1.4 mL) in EtOH (30 mL). The mixture was hydrogenated at 35 psig overnight. After filtration and evaporation of the solvent, and recrystallization from diethyl ether/ethanol, the product was obtained as a white solid (650 mg, 98%).

M.P. (ethanol) = 203-205 °C; **^{1}H-NMR** (CD_3OD400 MHz): δ = 7.12 (dd, 1H, *J* = 7.9/7.9 Hz), 6.76 (d, 1H, J = 8.1 Hz), 6.72 (d, 1H, *J* = 7.7 Hz), 3.81 (s, 3H), 3.47 (m, 1H), 3.09 (m, 2H), 2.92 (m, 2H), 2.56 (dd, 1H, *J* = 10.3, 16.7 Hz), 2.30 (d, 1H, *J* = 14.0 Hz), 1.78 (m, 3H), 1.06 (t, 3H), *J* = 7.4 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 158.7, 137.3, 128.4, 121.8, 108.6, 55.1, 55.9, 47.9, 28.6, 27.5, 26.8, 21.1, 11.4 ppm; **HRMS** *m/z* (EI): 219.1629 (calculated for M^+: 219.1693).

(*S*)-*N,N*-Dipropyl-8-methoxy-1,2,3,4-tetrahydronaphthalen-2-amine(S6)

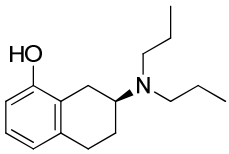


S6

Compound **15-HCl** (600 mg, 2.3 mmol) was suspended in 1,2-DCE (20 mL) and Et_3N (0.7 mL) was added, followed by propionaldehyde (270 mg, 4.7 mmol) and $NaBH(OAc)_3$ (1.0 g, 4.7 mmol). The reaction stirred at room temperature overnight and was quenched by the addition of saturated aqueous NH_4Cl. The mixture was extracted (DCM) and the organic layer was dried (sodium sulphate), filtered and concentrated to give the title compound **S6** (606 mg, 99%) as a viscous yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.08 (dd, 1H, *J* = 7.9/7.9 Hz), 6.71 (d, 1H, *J* = 7.6 Hz), 6.66 (d, 1H, *J*= 8.1 Hz), 3.82 (s, 3H), 2.93 (m, 2H), 2.84 (m, 2H), 2.46 (m, 5H), 1.98 (d, 1H, *J* = 11.1 Hz), 1.61 (m, 1H), 1.47 (m, 4H), 0.89 (t, 3H, *J* = 7.3 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 157.5, 137.7, 126.0, 125.0, 120.8, 106.8, 57.1, 55.2, 52.5, 30.1, 25.8, 25.0, 21.7, 11.9 ppm; **HRMS** *m/z* (EI): 261.2088 (calculated for M^+: 261.2093).

(*S*)-8-Hydroxy-*N*,*N*-dipropyl-2-aminotetralin [(*S*)-*8-OH-DPAT*](5)



5

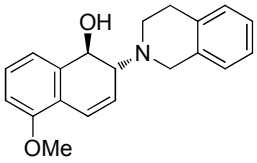
Prepared in a similar manner to **4**with **S6**(535 mg, 2.05 mmol). To a solution of **S6** in DCM (6 mL) at −40 °C was added BBr_3(4.5 mL, 4.5 mmol, 1.0 M in DCM) dropwise*via* syringe. The reaction was stirred for 2 h at this temperature, and warmed to room temperature stirring overnight. After careful quenching with saturated aqueous sodium bicarbonate, the mixture was extracted with DCM (3×), dried (sodium sulphate), filtered and concentrated to give the title compound (505 mg, 99%) as a viscous yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.08 (dd, 1H, *J* = 7.9/7.9 Hz), 6.71 (d, 1H, *J* = 7.6 Hz), 6.66 (d, 1H, *J*= 8.1 Hz), 3.82 (s, 3H), 2.93 (m, 2H), 2.84 (m, 2H), 2.46 (m, 5H), 1.98 (d, 1H, *J* = 11.1 Hz), 1.61 (m, 1H), 1.47 (m, 4H), 0.89 (t, 3H, *J* = 7.3 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 157.5, 137.7, 126.0, 125.0, 120.8, 106.8, 57.1, 55.2, 52.5, 30.1, 25.8, 25.0, 21.7, 11.9 ppm; **$[\alpha]_D^{28}$** = -67 (freebase, c = 0.6, $CHCl_3$); **HRMS** *m/z* (EI): 247.1933 (calculated for M^+ $C_{16}H_{25}NO$: 247.1936).

Regiodivergent Asymmetric Ring Opening Reaction: Scope

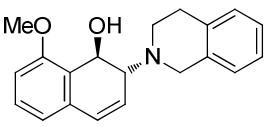
trans-2-(3,4-Dihydroisoquinolin-2(1*H*)-yl)-5-methoxy-1,2-dihydronaphthalen-1-ol (16a) and *trans*-2-(3,4-dihydroisoquinolin-2(1*H*)-yl)-8-methoxy-1,2-dihydronaphthalen-1-ol (16b)

Prepared according to **General Procedure 1** using [Rh(cod)$_2$OTf] (5 mol%), (*R*,*S*)-PPF-P*t*-Bu$_2$ (6 mol%), NH_4BF_4 (1.0 equiv.), tetrahydroisoquinoline(1.3 equiv.) and (±)-**1**(80mg, 1 equiv.) in THF (3.3 mL) at 60 °C for 3 hrs.The crude mixture was purified by flash chromatography (50% ethyl acetate in pentane) to give **16a** (57mg, 40% yield, 94% ee) as a colourless oil; followed by **16b** (60mg, 43% yield, 97% ee) as a white solid.



16a

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.30–7.24 (2 H, m), 7.21–7.13 (3 H, m), 7.09–7.05 (1 H, m), 6.99 (1 H, dd, *J* = 10.2, 2.6 Hz), 6.83 (1 H, dd, *J* = 7.2, 1.9 Hz), 6.16 (1 H, dd, *J* = 10.2, 2.5 Hz), 4.98 (1 H, d, *J* = 12.2 Hz), 4.04 (1 H, d, *J* = 14.9 Hz), 3.87 (3 H, s), 3.83 (1 H, d, *J* = 14.9 Hz), 3.65 (1 H, ddd, *J* = 12.2, 2.6, 2.5 Hz), 3.20–3.12 (1 H, m), 3.02–2.89 (2 H, m), 2.86–2.78 (1 H, m) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 154.70, 138.60, 134.80, 134.40, 128.70, 128.70, 126.60, 126.10, 125.60, 123.50, 123.20, 120.40, 116.90, 109.70, 68.20, 67.20, 55.50, 51.90, 46.80, 29.90 ppm; **IR** ν_{max} 3425 (O-H), 3065 (C-H), 2932 (C-H), 2838 (C-H), 1600, 1575, 1496, 1473, 1439, 1307, 1264, 1191, 1104, 1045 cm^{-1}; **HRMS** *m*/*z* (ESI) 308.1649 (M^+ + H. $C_{20}H_{22}NO_2$ requires 308.1651); **HPLC** (AD-H Chiralpak, 1 mL/min, 30% isopropanol/hexane, 262 nm) retention times: 7.0 min (minor enantiomer), 8.2 min (major enantiomer).

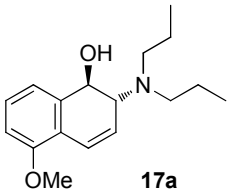


16b

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.29 (1 H, dd, *J* = 8.1, 7.7 Hz), 7.10–7.03 (3 H, m), 6.95–6.91 (1 H, m), 6.87–6.82 (2 H, m), 6.72 (1 H, dd, *J* = 9.8, 1.3 Hz), 6.05 (1 H, dd, *J* = 9.8, 1.3 Hz), 5.39 (1 H, br), 3.92 (1 H, d, *J* = 14.9 Hz), 3.88 (3 H, s), 3.75 (1 H, dt, *J* = 4.9, 1.6 Hz), 3.64 (1 H, d, *J* = 14.9 Hz), 2.93–2.78 (3 H, m), 2.67–2.59 (1 H, m) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 156.70, 135.10, 134.20, 132.90, 129.30, 128.90, 128.70, 126.60, 125.80, 125.70, 125.30, 123.60, 120.00, 110.30, 64.20, 61.40, 55.50, 50.90, 46.20, 29.80 ppm; **IR** ν_{max} 3425 (O-H), 3065 (C-H), 3033 (C-H), 2930 (C-H), 2839 (C-H), 1600, 1575, 1496, 1470, 1458, 1343, 1301, 1262, 1190, 1151, 1099, 1079, 1054 cm^{-1}; **HRMS** *m*/*z* (ESI) 308.1643 (M^+ + H. $C_{20}H_{22}NO_2$ requires 308.1651); **HPLC** (OD-H Chiralpak, 1 mL/min, 30% isopropanol/hexane, 262 nm) retention times: 6.2 min (major enantiomer), 11.1 min (minor enantiomer).

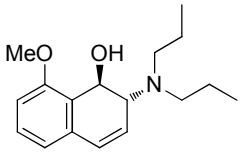
trans-2-(Di-*n*-propylamino)-5-methoxy-1,2-dihydronaphthalen-1-ol (17a) and *trans*-2-(di-*n*-propylamino)-8-methoxy-1,2-dihydronaphthalen-1-ol (17b)

Prepared according to **General Procedure 1** using [Rh(cod)$_2$OTf] (5 mol%), (*R*,*S*)-PPF-P*t*-Bu$_2$ (6 mol%), NH_4BF_4 (1.0 equiv.), di-*n*-propylamine(1.3 equiv.) and (±)-**1**(80mg, 1 equiv.) in THF (3.3 mL) at 60 °C for 3 hrs.The crude mixture was purified by flash chromatography (gradient from 10 to 40% ethyl acetate in pentane) to give **17a** (57 mg, 45% yield, 97% ee) as a colourless oil; followed by **17b** (42 mg, 33% yield, >98% ee) as a white solid.



17a

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.25–7.20 (2 H, m), 6.86 (1 H, dd, *J* = 10.2, 2.7 Hz), 6.80–6.76 (1 H, m), 6.05 (1 H, dd, *J* = 10.2, 2.7 Hz), 4.76 (1 H, d, *J* = 13.1 Hz), 3.82 (3 H, s), 3.55 (1 H, ddd, *J* = 13.1, 2.7, 2.7 Hz), 2.65 (2 H, ddd, *J* = 13.0, 8.6, 7.5 Hz), 2.52 (2 H, ddd, *J* = 13.0, 8.4, 4.8 Hz), 1.61–1.38 (4 H, m), 0.91 (6 H, t, *J* = 7.4 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 154.55, 138.68, 128.55, 125.88, 123.24, 120.44, 116.56, 109.55, 69.19, 64.41, 55.53, 53.41 (2 x C), 21.99 (2 x C), 11.74 (2 x C) ppm; **IR**ν_{max} 3472 (O-H), 2959 (C-H), 2933 (C-H), 2872 (C-H), 2836 (C-H), 1620, 1597, 1574, 1473, 1378, 1263, 1227, 1162, 1093, 1048 cm^{-1}; **HRMS** *m*/*z* (ESI) 276.1947 (M^+ + H. $C_{17}H_{26}NO_2$ requires 276.1964); **[α]$_D^{28}$** = −214 (c = 1.9, $CHCl_3$, 97% ee); **HPLC** (AD-H Chiralpak, 1 mL/min, 10% isopropanol/hexane, 262 nm) retention times: 4.3 min (minor enantiomer), 5.6 min (major enantiomer).

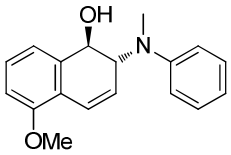


17b

M.P. (EtOAc) = 82-83 °C;**^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.23 (1 H, dd, *J* = 8.2, 7.7 Hz), 6.82 (1 H, dd, *J* = 8.3, 0.7 Hz), 6.77 (1 H, d, *J* = 7.5 Hz), 6.59 (1 H, dd, *J* = 9.8, 1.6 Hz), 5.97 (1 H, ddd, *J* = 9.8, 4.8, 0.7 Hz), 5.23 (1 H, br d, *J* = 1.9 Hz), 3.89 (3 H, s), 3.64 (1 H, ddd, *J* = 4.6, 2.0, 2.0 Hz), 2.35–2.29 (4 H, m), 1.48–1.38 (4 H, m), 0.81 (6 H, t, *J* = 7.4 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 156.89, 133.24, 129.04, 127.92, 127.88, 123.72, 119.92, 110.08, 63.07, 61.24, 55.54, 52.44 (2 x C), 22.01 (2 x C), 11.69 (2 x C) ppm; **IR**ν_{max} 3441 (O-H), 3034 (C-H), 2958 (C-H), 2932 (C-H), 2871 (C-H), 1597, 1576, 1469, 1377, 1259, 1187, 1099, 1080 cm^{-1}; **HRMS** *m*/*z* (ESI) 276.1962 (M^+ + H. $C_{17}H_{26}NO_2$ requires 276.1964);**[α]$_D^{28}$** = −363 (c = 0.1, $CHCl_3$, >98% ee); **HPLC** (AD-H Chiralpak, 1 mL/min, 10% isopropanol/hexane, 262 nm) retention times: 4.5 min (minor enantiomer), 8.1 min (major enantiomer).

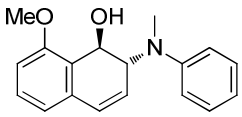
trans-5-Methoxy-2-(methyl(phenyl)amino)-1,2-dihydronaphthalen-1-ol (18a) and trans-8-methoxy-2-(methyl(phenyl)amino)-1,2-dihydronaphthalen-1-ol (18b)

Prepared according to **General Procedure 1** using [Rh(cod)$_2$OTf] (5 mol%), (*R*,*S*)-PPF-P*t*-Bu$_2$ (6 mol%), NH_4BF_4 (1.0 equiv.), *N*-methyl-aniline(1.3 equiv.) and (±)-**1**(80 mg, 1 equiv.) in THF (3.3 mL) at 60 °C for 3 hrs.The crude mixture was purified by flash chromatography (gradient from 10 to 40% ethyl acetate in pentane) to give **18a** (37g, 29% yield, 96% ee) as a colourlessoil; followed by **18b** (34 mg, 26% yield, >98% ee) as a white solid.



18a

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.26–7.21 (3 H, m), 7.15 (1 H, d, *J* = 7.5 Hz), 6.98 (1 H, dd, *J* = 10.0, 2.5 Hz), 6.94 (2 H, d, *J* = 8.1 Hz), 6.82 (1 H, d, *J* = 8.3 Hz), 6.78 (1 H, t, *J* = 7.3 Hz), 5.90 (1 H, dd, *J* = 10.0, 3.0 Hz), 5.03 (1 H, d, *J* = 9.8 Hz), 4.70 (1 H, ddd, *J* = 9.8, 3.0, 2.5 Hz), 3.83 (3 H, s), 2.82 (3 H, s), 2.36 (1 H, br) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 154.84, 150.25, 137.98, 129.19 (2 x C), 128.87, 126.36, 123.58, 120.61, 117.95, 117.90, 114.56 (2 x C), 110.21, 70.13, 62.96, 55.59, 33.24 ppm; **IR**ν_{max} 3426 (O-H), 3060 (C-H), 3001 (C-H), 2934 (C-H), 2836 (C-H), 1597, 1575, 1503, 1473, 1366, 1306, 1265, 1211, 1105, 1041 cm^{-1}; **$[\alpha]_D^{28}$** = −15 (*c* = 1.9, $CHCl_3$, 96%ee); **HRMS** *m*/*z* (EI) 281.1411 (M^+. $C_{18}H_{19}NO_2$ requires 281.1416); **HPLC**(AD-H Chiralpak, 1 mL/min, 3% isopropanol/hexane, 262 nm) retention times: 26.8 min (major enantiomer), 31.7 min (minor enantiomer).

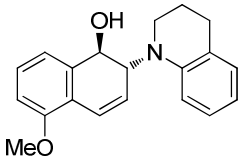


18b

M.P. (EtOAc) = 111–113 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.30–7.24 (3 H, m), 6.97 (2 H, d, *J* = 8.2 Hz), 6.86–6.81 (2 H, m), 6.77 (1 H, t, *J* = 7.3 Hz), 6.73 (1 H, dd, *J* = 9.8, 1.5 Hz), 5.96 (1 H, dd, *J* = 9.7, 5.1 Hz), 5.19 (1 H, unresolved), 4.72–4.69 (1 H, m), 3.83 (3 H, s), 2.54 (3 H, s), 2.42 (1 H, br) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 157.01, 149.30, 132.79, 129.48, 129.24, 129.23 (2 x C), 126.11, 123.33, 120.15, 117.19, 113.76 (2 x C), 110.45, 64.67, 59.10, 55.47, 32.62 ppm; **IR**ν_{max} 3426 (O-H), 3035 (C-H), 2932 (C-H), 2838 (C-H), 1597, 1575, 1504, 1472, 1361, 1263, 1207, 1100, 1077, 1033 cm^{-1}; **HRMS** *m*/*z* (EI) 281.1413 (M^+. $C_{18}H_{19}NO_2$ requires 281.1416); **$[\alpha]_D^{28}$** = −229 (*c* = 1.8, $CHCl_3$, >98%ee); **HPLC** (AD-H Chiralpak, 1 mL/min, 3% isopropanol/hexane, 262 nm) retention times: 37.2 min (major enantiomer), 41.4 min (minor enantiomer).

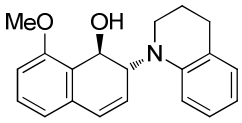
trans-2-(3,4-Dihydroquinolin-1(2H)-yl)-5-methoxy-1,2-dihydronaphthalen-1-ol (19a) and *trans*-2-(3,4-dihydroquinolin-1(2H)-yl)-8-methoxy-1,2-dihydronaphthalen-1-ol (19b)

Prepared according to **General Procedure 1** using [$Rh(cod)_2OTf$] (5 mol%), (*R*,*S*)-PPF-P*t*-Bu_2 (6 mol%), NH_4BF_4 (1.0 equiv.), tetrahydroquinoline(1.3 equiv.) and (±)-**1** (80 mg, 1 equiv.) in THF (3.3 mL) at 60 °C for 3 hrs.The crude mixture was purified by flash chromatography (gradient from 10 to 20% ethyl acetate in pentane) to give **19a** (66 mg, 47% yield, 97% ee) as a colourless oil; followed by **19b** (68 mg, 48% yield, 95% ee) as a white solid.



19a

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.23 (1 H, t, *J* = 7.9 Hz), 7.12 (1 H, d, *J* = 7.5 Hz), 7.07–7.00 (2 H, m), 6.99 (1 H, d, *J* = 7.2 Hz), 6.90 (1 H, d, *J* = 8.3 Hz), 6.83 (1 H, d, *J* = 8.2 Hz), 6.63 (1 H, t, *J* = 7.3 Hz), 5.91 (1 H, dd, *J* = 10.0, 3.3 Hz), 5.04 (1 H, 8.9), 4.72 (1 H, ddd, *J* = 8.9, 3.3, 2.8 Hz), 3.85 (3 H, s), 3.26 (1 H, ddd, *J* = 11.2, 5.5, 5.5 Hz), 3.08 (1 H, ddd, *J* = 11.2, 5.9, 5.9 Hz), 2.82–2.70 (2 H, m), 2.76 (1 H, br), 1.93–1.85 (2 H, m) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 154.90, 145.20, 138.00, 129.50, 128.80, 127.00, 126.50, 124.00, 123.70, 120.60, 118.20, 116.70, 112.10, 110.20, 69.60, 55.60, 43.90, 28.10, 22.50 ppm; **IR**ν_{max} 3445 (O-H), 2929 (C-H), 2836 (C-H), 1597, 1575, 1473, 1263, 1102, 1046 cm^{-1}; **HRMS** *m*/*z* (ESI) 306.1487 ($M^+ + H - H_2$. $C_{20}H_{20}NO_2$ requires 306.1494); **HPLC** (AD-H Chiralpak, 1 mL/min, 10% isopropanol/hexane, 262 nm) retention times: 11.9 (minor enantiomer), 14.4 min (major enantiomer).

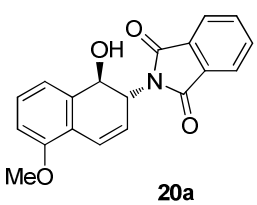


19b

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.27 (1 H, t, *J* = 7.9 Hz), 7.11 (1 H, td, *J* = 7.7, 1.1 Hz), 7.04 (1 H, d, *J* = 8.2 Hz), 6.97 (1 H, d, *J* = 7.2 Hz), 6.84–6.80 (2 H, m), 6.74 (1 H, dd, *J* = 9.6, 1.5 Hz), 6.63 (1 H, t, *J* = 6.7 Hz), 5.94 (1 H, dd, *J* = 9.6, 5.1 Hz), 5.22 (1 H, br), 4.70 (1 H, d, *J* = 5.1 Hz), 3.82 (3 H, s), 3.10 (1 H, ddd, *J* = 11.1, 6.3, 4.3 Hz), 2.72–2.62 (3 H, m), 2.40 (1 H, br), 1.79–1.67 (2 H, m) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 156.90, 144.82, 132.87, 129.44, 129.41, 129.39, 127.07, 125.79, 123.73, 123.38, 120.07, 116.37, 111.63, 110.33, 64.29, 57.41, 55.41, 42.95, 28.11, 22.51 ppm; **IR**ν_{max} 3441 (O-H), 3034 (C-H), 2931 (C-H), 2839 (C-H), 1600, 1575, 1496, 1470, 1457, 1343, 1261, 1190, 1151, 1098, 1079 cm^{-1}; **HRMS** *m*/*z* (ESI) 290.1538 ($M^+ + H - H_2O$. $C_{20}H_{20}NO$ requires 290.1545); **HPLC** (AD-H Chiralpak, 1 mL/min, 10% isopropanol/hexane, 220 nm) retention times: 12.4 min (major enantiomer), 13.2 min (minor enantiomer).

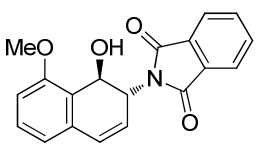
2-(*trans*-1-Hydroxy-5-methoxy-1,2-dihydronaphthalen-2-yl)isoindoline-1,3-dione (20a) and 2-(*trans*-1-hydroxy-8-methoxy-1,2-dihydronaphthalen-2-yl)isoindoline-1,3-dione (20b)

Prepared according to **General Procedure 1** using [Rh(cod)$_2$OTf] (5 mol%), (*R*,*S*)-PPF-P*t*-Bu$_2$ (6 mol%), *n*Bu$_4$I(0.2 equiv.), phthalimide(0.99 equiv.) and (±)-**1**(80 mg, 1 equiv.) in THF (0.5 mL) and DMF (1 mL) at 95 °C for 3 hrs.The crude mixture was purified by flash chromatography (gradient from 10 to 30% ethyl acetate in pentane) to give **20a** (67 mg, 45% yield, >98% ee) as a whitesolid; followed by **20b** (62 mg, 42% yield, 98% ee) as a white solid.



20a

M.P. (EtOAc) = 192–193 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.88–7.85 (2 H, m), 7.75–7.72 (2 H, m), 7.26 (1 H, dd, *J* = 8.2, 7.6 Hz), 7.20 (1 H, d, *J* = 7.6 Hz), 6.95 (1 H, dd, *J* = 10.0, 3.1 Hz), 6.84 (1 H, d, *J* = 8.2 Hz), 5.88 (1 H, dd, *J* = 10.0, 2.3 Hz), 5.47 (1 H, dd, *J* = 12.9, 9.5 Hz), 5.16 (1 H, ddd, *J* = 12.9, 3.1, 2.3 Hz), 3.85 (3 H, s), 2.08 (1 H, d, *J* = 9.5 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 168.4, 154.8, 138.6, 134.0, 131.9, 128.9, 125.4, 123.3, 122.6, 121.1, 116.3, 110.3, 71.0, 55.6, 54.8 ppm; **IR**ν_{max}3465 (O-H), 3065 (C-H), 2933 (C-H), 2839 (C-H), 1716 (C=O), 1709 (C=O), 1701 (C=O), 1577, 1473, 1388, 1264cm^{-1}; **HRMS** *m*/*z* (ESI) 344.0893 (M^+ + Na. $C_{19}H_{15}NNaO_4$ requires 344.0899); **$[\alpha]_D^{25}$** −61.5 (*c* 1.0, $CHCl_3$, >98%ee); **HPLC** (OD-H Chiralcel, 1.5 mL/min, 20% isopropanol/hexane, 210 nm) retention times: 9.2 min (major enantiomer), 11.9 min (minor enantiomer).

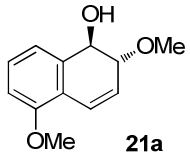


20b

M.P. (EtOAc) = 165–166 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.86–7.83 (2 H, m), 7.73–7.70 (2 H, m), 7.30–7.26 (1 H, m), 6.87 (1 H, d, *J* = 8.3 Hz), 6.84 (1 H, d, *J* = 7.6 Hz), 6.60 (1 H, dd, *J* = 9.7, 2.6 Hz), 5.83 (1 H, dd, *J* = 9.7, 3.4 Hz), 5.60 (1 H, dd, *J* = 7.6, 2.0 Hz), 5.33 (1 H, ddd, *J* = 7.6, 3.4, 2.6 Hz), 3.91 (1 H, d, *J* = 2.0 Hz), 3.87 (3 H, s) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 167.8 (2 x C), 157.0, 134.0 (2 x C), 133.1, 132.0 (2 x C), 129.2, 128.9, 124.6, 123.3 (2 x C), 123.1, 120.6, 111.0, 68.7, 55.7, 52.7 ppm; **IR**ν_{max} 3511 (O-H), 2932 (C-H), 1716 (C=O), 1710 (C=O), 1472, 1385, 1258, 1081 and 1009 cm^{-1}; **HRMS** *m*/*z* (ESI) 344.0893 (M^+ + Na. $C_{19}H_{15}NNaO_4$ requires 344.0899); **$[\alpha]_D^{28}$** = −201.4 (c = 0.35, $CHCl_3$, 98% ee); **HPLC** (AD-H Chiralpak, 1.5 mL/min, 20% isopropanol/hexane, 262 nm) retention times: 13.3 min (minor enantiomer), 17.5 min (major enantiomer).

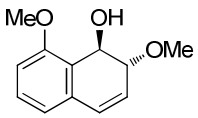
trans-2,5-Dimethoxy-1,2-dihydronaphthalen-1-ol (21a) and *trans*-2,8-dimethoxy-1,2-dihydro-naphthalen-1-ol (21b)

Prepared according to **General Procedure 1** using [Rh(cod)$_2$OTf] (5 mol%), (*R*,*S*)-PPF-P*t*-Bu$_2$ (6 mol%), NH_4BF_4 (1.0 equiv.), methanol (0.3 mL, 1:10 THF, 16 equiv.) and (±)-**1** (80 mg, 1 equiv.) in THF (3.0 mL) at 60 °C for 24 hrs.The crude mixture was purified by flash chromatography (gradient from 20 to 50% ethyl acetate in pentane) to give **21a** (45 mg, 47% yield, 83% ee) as a white solid; followed by **21b** (42mg, 44% yield, 93% ee – measured following reduction) as a white solid.



21a

M.P. (ethyl acetate) = 67–69 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.26–7.18 (2 H, m), 6.86 (1 H, dd, *J* = 10.1, 2.1 Hz), 6.81 (1 H, dd, *J* = 7.5, 0.8 Hz), 6.03 (1 H, dd, *J* = 10.1, 2.3 Hz), 4.85 (1 H, dd, *J* = 10.4, 3.6 Hz), 4.08 (1 H, ddd, *J* = 10.4, 2.3, 2.1 Hz), 3.83 (3 H, s), 3.50 (3 H, s), 2.60 (1 H, d, *J* = 3.6 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 154.80, 137.30, 128.70, 125.40, 122.30, 120.50, 117.30, 110.10, 81.80, 72.50, 56.60, 55.50 ppm; **IR**ν_{max} 3419 (O-H), 2933 (C-H), 2835 (C-H), 1577, 1473, 1387, 1265, 1188, 1108, 1048 cm^{-1}; **$[\alpha]_D^{28}$** = −188 (*c* = 2.1, $CHCl_3$, 83% ee); **HRMS** *m*/*z* (EI) 206.0940 (M^+. $C_{12}H_{14}O_3$ requires 206.0943); **HPLC** (AD-H Chiralpak, 1 mL/min, 10% isopropanol/hexane, 262 nm) retention times: 9.8 min (minor enantiomer), 12.6 min (major enantiomer).

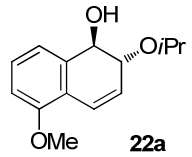


21b

M.P. (EtOAc) = 116–118 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.25 (1 H, dd, *J* = 8.3, 7.5 Hz), 6.84 (1 H, d, *J* = 8.3 Hz), 6.80 (1 H, d, *J* = 7.5 Hz), 6.61 (1 H, d, *J* = 9.7 Hz), 6.12 (1 H, dd, *J* = 9.7, 4.8 Hz), 5.22 (1 H, unresolved), 4.07 (1 H, dd, *J* = 4.8, 3.0 Hz), 3.88 (3 H, s), 3.45 (3 H, s), 2.46 (1 H, br) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 157.40, 132.40, 129.60, 129.40, 125.10, 122.60, 120.20, 110.70, 77.40, 64.70, 56.40, 55.50 ppm; **IR**ν_{max} 3301 (O-H), 2934 (C-H), 2821 (C-H), 1575, 1472, 1433, 1395, 1342, 1269, 1185, 1083, 1021 cm^{-1}; **$[\alpha]_D^{28}$** −301 (*c* 1.5, $CHCl_3$, 93%); **HRMS** *m*/*z* (EI) 206.0941 (M^+. $C_{12}H_{14}O_3$ requires 206.0943); **HPLC** The enantiomers proved inseparable by chiral phase HPLC so the compound was reduced to 2,5-dimethoxy-1,2,3,4-tetrahydronaphthalen-1-ol using *p*-toluenesulfonylhydrazine (5 equiv.) and sodium acetate (10 equiv.) in refluxing THF / water (1:1) for 16 hrs in quantitative yield.For the reduced product the ee was 93%: (AD-H Chiralpak, 1 mL/min, 10% isopropanol/hexane, 220 nm) retention times: 9.9 min (minor enantiomer), 10.9 min (major enantiomer).

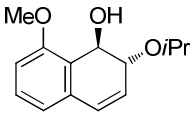
trans-2-isoPropoxy-5-methoxy-1,2-dihydronaphthalen-1-ol (22a) and *trans*-2-isopropoxy-8-methoxy-1,2-dihydronaphthalen-1-ol (22b)

Prepared according to **General Procedure 1** using [Rh(cod)$_2$OTf] (5 mol%), (*R*,*S*)-PPF-P*t*-Bu$_2$ (6 mol%), NH_4BF_4 (1.0 equiv.), isopropanol(0.3 mL, 1:10 THF, 9 equiv.) and (±)-**1** (80 mg, 1 equiv.) in THF (3.0 mL) at 60 °C for 24 hrs.The crude mixture was purified by flash chromatography (gradient from 20 to 50% ethyl acetate in pentane) to give **22a** (51 mg, 47% yield, 95% ee) as a colourless oil; followed by **22b** (42 mg, 39% yield, >98% ee) as a white solid.



22a

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.26–7.20 (2 H, m), 6.82–6.77 (2 H, m), 5.95 (1 H, dd, *J* = 10.1, 2.1 Hz), 4.81 (1 H, dd, *J* = 11.1, 2.8 Hz), 4.23 (1 H, ddd, *J* = 11.1, 2.2, 2.1 Hz), 3.85 (1 H, septet, *J* = 6.1 Hz), 3.82 (3 H, s), 2.68 (1 H, br), 1.26 (3 H, d, *J* = 6.1 Hz), 1.22 (3 H, d, *J* = 6.1 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 154.68, 137.51, 128.59, 128.24, 121.67, 120.75, 117.02, 109.99, 78.45, 72.98, 70.80, 55.55, 23.32, 22.15 ppm; **IR** ν_{max} 3456 (O-H), 2971 (C-H), 2933 (C-H), 2838 (C-H), 1578, 1474, 1440, 1381, 1292, 1265, 1142, 1100, 1072, 1048 cm^{-1}; **HRMS** *m*/*z* (EI) 234.1262 (M^+. $C_{14}H_{18}O_3$ requires 234.1256); **$[\alpha]_D^{28}$** = −199 (*c* = 2.0, $CHCl_3$, 95%ee); **HPLC** (AD-H Chiralpak, 1 mL/min, 10% isopropanol/hexane, 262 nm) retention times: 6.3 min (minor enantiomer), 9.7 min (major enantiomer).

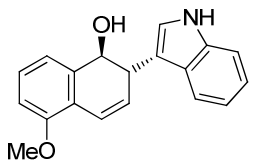


22b

M.P. (ethyl acetate) = 53–55 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.23 (1 H, t, *J* = 7.9 Hz), 6.83 (1 H, d, *J* = 8.3 Hz), 6.78 (1 H, d, *J* = 7.5 Hz), 6.55 (1 H, d, *J* = 9.7 Hz), 6.04 (1 H, dd, *J* = 9.7, 4.8 Hz), 5.15 (1 H, unresolved), 4.20 (1 H, dd, *J* = 4.3, 3.2 Hz), 3.93 (1 H, septet, *J* = 6.1 Hz), 3.88 (3 H, s), 2.47 (1 H, br), 1.20 (6 H, d, *J* = 6.1 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 157.51, 132.56, 129.29, 128.65, 126.55, 122.80, 120.27, 110.59, 74.11, 70.29, 66.24, 55.57, 23.01, 22.53 ppm; **IR**ν_{max} 3348 (O-H), 2964 (C-H), 2934 (C-H), 1577, 1473, 1381, 1265, 1098, 1046, 1018 cm^{-1}; **HRMS** *m*/*z* (EI) 234.1255 (M^+. $C_{14}H_{18}O_3$ requires 234.1256); **$[\alpha]_D^{28}$** = −321 (*c* = 1.8, $CHCl_3$, >98%ee); **HPLC** (AD-H Chiralpak, 1 mL/min, 10% isopropanol/hexane, 215 nm) retention times: 9.1 min (major enantiomer), 10.1 min (minor enantiomer).

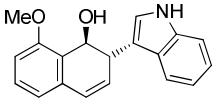
trans-2-(1*H*-Indol-2-yl)-5-methoxy-1,2-dihydronaphthalen-1-ol (23a)

Prepared according to **General Procedure 1** using [$Rh(cod)_2OTf$] (5 mol%), (*R*,*S*)-PPF-P*t*-Bu_2 (6 mol%), NH_4BF_4 (1.0 equiv.), indole(3.0 equiv.) and (±)-**8** (80mg, 1 equiv.) in THF (3.3 mL) at 60 °C for 3 hrs.The crude mixture was purified by flash chromatography (gradient from 5 to 30% ethyl acetate in pentane) to give unreacted indole, followed by the full aromatic compoundand finally **23a** (60 mg, 44% yield, 88% ee) as a colourless oil.

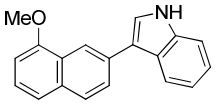


23a

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.03 (1 H, br), 7.78 (1 H, d, *J* = 7.9 Hz), 7.36 (1 H, d, *J* = 8.1 Hz), 7.25–7.19 (2 H, m), 7.15 (1 H, dd, *J* = 7.2, 7.2 Hz), 7.09–7.03 (2 H, m), 6.96 (1 H, d, *J* = 2.3 Hz), 6.86 (1 H, d, *J* = 8.2 Hz), 6.18 (1 H, dd, *J* = 9.8, 3.9 Hz), 5.00 (1 H, dd, *J* = 8.0, 2.8 Hz), 4.08 (1 H, ddd, *J* = 8.0, 3.6, 2.2 Hz), 3.89 (3 H, s), 2.10 (1 H, d, *J* = 3.8 Hz) ppm;**^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 154.7, 137.4, 136.6, 128.9, 128.4, 126.6, 122.5, 122.2, 121.2, 120.9, 119.4, 119.4, 118.9, 114.3, 111.3, 110.3, 72.9, 55.6, 40.7 ppm; **HRMS** *m*/*z* (ESI) 314.1136 (M^+ + Na. $C_{19}H_{17}NNaO_2$ requires 314.1157);**HPLC** (AD-H Chiralpak, 1.0 mL/min, 30% isopropanol/hexane, 262 nm) retention times: 11.9 min (minor enantiomer), 14.5 min (major enantiomer).



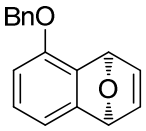
Only a trace of the other regioisomer was detected. **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.84 (1 H, br), 7.76 (1 H, d, *J* = 7.4 Hz), 7.31–7.12 (4 H, m), 6.83 (1 H, d, *J* = 7.4 Hz), 6.75 (1 H, d, *J* = 8.3 Hz), 6.71 (1 H, d, *J* = 2.3 Hz), 6.66 (1 H, d, *J* = 9.5 Hz), 6.23 (1 H, dd, *J* = 9.5, 5.3 Hz), 5.38 (1 H, br), 4.28 (1 H, d, *J* = 5.3 Hz), 3.71 (3 H, s), 2.28 (1 H, br) ppm.



The majority decomposed to the fully aromatic compound:**^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 8.56 (1 H, s), 8.21 (1 H, br s), 7.87-7.80 (2 H, m), 7.46-7.39 (3 H, m), 7.39 (1 H, t, *J* = 7.9 Hz), 7.29-7.20 (2 H, m), 6.83 (1 H, d, *J* = 7.4 Hz), 4.01 (3 H, s) ppm.

Regiodivergent Reactions with an Optically Pure Substrate

(1*S*,4*R*)-5-Benzyloxy-1,4-epoxy-1,4-dihydronaphthalene (24)[3]



(1*S*,4*R*)-**24**

A sample if this compound was generously provided by Solvias AG.

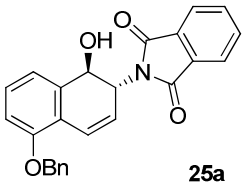
Prepared in a similar manner to **1** using 3-chloro-benzyloxybenzene (8.38 g, 38.3 mmol), diisopropylamine (0.54 mL, 3.83 mmol), furan (14 mL), *n*-BuLi (26.3 mL, 42.1 mmol, 1.6 M in hexanes) and THF (190 mL). The product was purified using flash chromatography (gradient from 5 to 10% ethyl acetate in pentane; required two purifications to be obtained sufficiently pure) to yield the title compound (4.20 g, 44%) as a colourless oil.

Racemic 1,4-epoxy-5-benzyloxy-1,4-dihydronaphthalene was purified to give 237 mg of **24** in >99.5% ee by preparative HLPC (retention time: 18.1 min, 250 x 20 mm CHIRALPAK IA 5 micron, 10% CH_2Cl_2 in heptane, 20 ml/min, 230 nm, 25 °C, other enantiomer: 13.9 min, 200 mg).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.39 (m, 5H), 7.02 (dd, 1H, *J* = 1.7, 5.5 Hz), 7.00 (dd, 1H, *J* = 1.8, 5.5 Hz), 6.95 (m, 2H), 6.65 (m, 1H), 5.96 (s, 1H), 5.71 (dd, 1H, *J* = 1.0, 1.5 Hz), 5.10 (s, 2H) ppm; **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ = 152.1, 151.6, 143.0, 142.8, 137.0, 135.7, 128.6, 128.0, 127.4, 126.9, 114.0, 112.0, 82.5, 80.1, 70.7 ppm; **IR** (neat): ν_{max} =3027, 2925, 1614, 1596, 1474, 1454, 1279, 1179 cm^{-1}; **HRMS**(EI): 250.0991 (calculated for $C_{17}H_{14}O_2$ (M^+) 250.0994).

2-[(*trans*)-8-(Benzyloxy)-1-hydroxy-1,2-dihydronaphthalen-2-yl]isoindoline-1,3-dione (25a) and 2-

A solution of the Rh(I) complex was prepared by addition of Bu_4NI (5.9 mg, 0.0.016 mmol) to a solution of $Rh(cod)_2OTf$ (0.9 mg, 0.002 mmol) and (*R*,*S*)-**2** (2.2 mg, 0.004 mmol) in THF (0.07 mL). After 5 minutes at RT, the solution was transferred by syringe to a solution of **24** (20 mg, 0.08 mmol) and phthalimide (12 mg, 0.08 mmol) in DMF (0.13 mL) and the resulting solution was heated to 95 °C for 6 h. After cooling to RT, the reaction mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed under vacuum. The residue was purified by column chromatography (gradient from 10 to 20% EtOAc in hexane) to give **25a** (27.5 mg, 87%, >99%ee) as a white solid; followed by **25b** (236 mg, 44%, 98%ee) as a white solid.

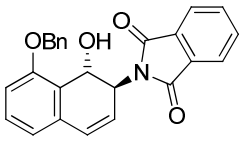


25a

M.P. 212-215 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ =7.87-7.83 (m, 2H), 7.75-7.70 (m, 2H), 7.45-7.31 (m, 5H), 7.26-7.22 (m, 2H), 7.02 (dd, *J* = 10, 3 Hz, 1 H), 6.89 (dd, *J* = 7.5, 2 Hz, 1 H), 5.87 (dd, *J* = 10, 2.5 Hz, 1 H), 5.84 (dd, *J* = 13, 9.5 Hz, 1 H), 5.13 (ddd, *J* = 13, 3, 2 Hz, 1 H), 5.11 (s, 2H), 2.02 (d, *J* = 9.5 Hz, 1 H); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ =168.4, 154.1 , 138.8, 136.9, 134.1 , 132.0, 128.9, 128.6, 127.9, 127.3, 125.6, 123.4, 122.8, 121.6, 116.7, 111.9, 71.1, 70.4, 54.9; **IR**ν_{max} 3440br, 3018, 177O, 1715, 1470, 1389; **HRMS** *m*/*z* (EI) 397.1314 (calculated for $C_{25}H_{19}NO_4$ (M+) 397.1314); **$[\alpha]_D^{26}$** = -63 (c = 2.5, $CHCl_3$, 98% ee);**HPLC** (OD Chiralpak,1.5 mL/min, 10% *i*PrOH in hexane) retention times:25.1 min (minor enantiomer) and 39.2 min (major enantiomer).

[(*trans*)-5-(benzyloxy)-1-hydroxy-1,2-dihydronaphthalen-2-yl]isoindoline-1,3-dione (25b)

A solution of the Rh(I) complex was prepared by addition of Bu_4NI (5.9 mg, 0.0.016 mmol) to a solution of $Rh(cod)_2OTf$ (0.9 mg, 0.002 mmol) and (*S*,*R*)-**2** (2.2 mg, 0.004 mmol) in THF (0.07 mL). After 5 minutes at RT, the solution was transferred by syringe to a solution of **24** (20 mg, 0.08 mmol) and phthalimide (12 mg, 0.08 mmol) in DMF (0.13 mL) and the resulting solution was heated to 95 °C for 6 h. After cooling to RT, the reaction mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed under vacuum. The residue was purified by column chromatography (gradient from 10 to 20% EtOAc in hexane) to give **25b** (25.5 mg, 80%, >99%ee) as a white solid; accompanied by **25a** (1.3 mg, 4%)..



25b

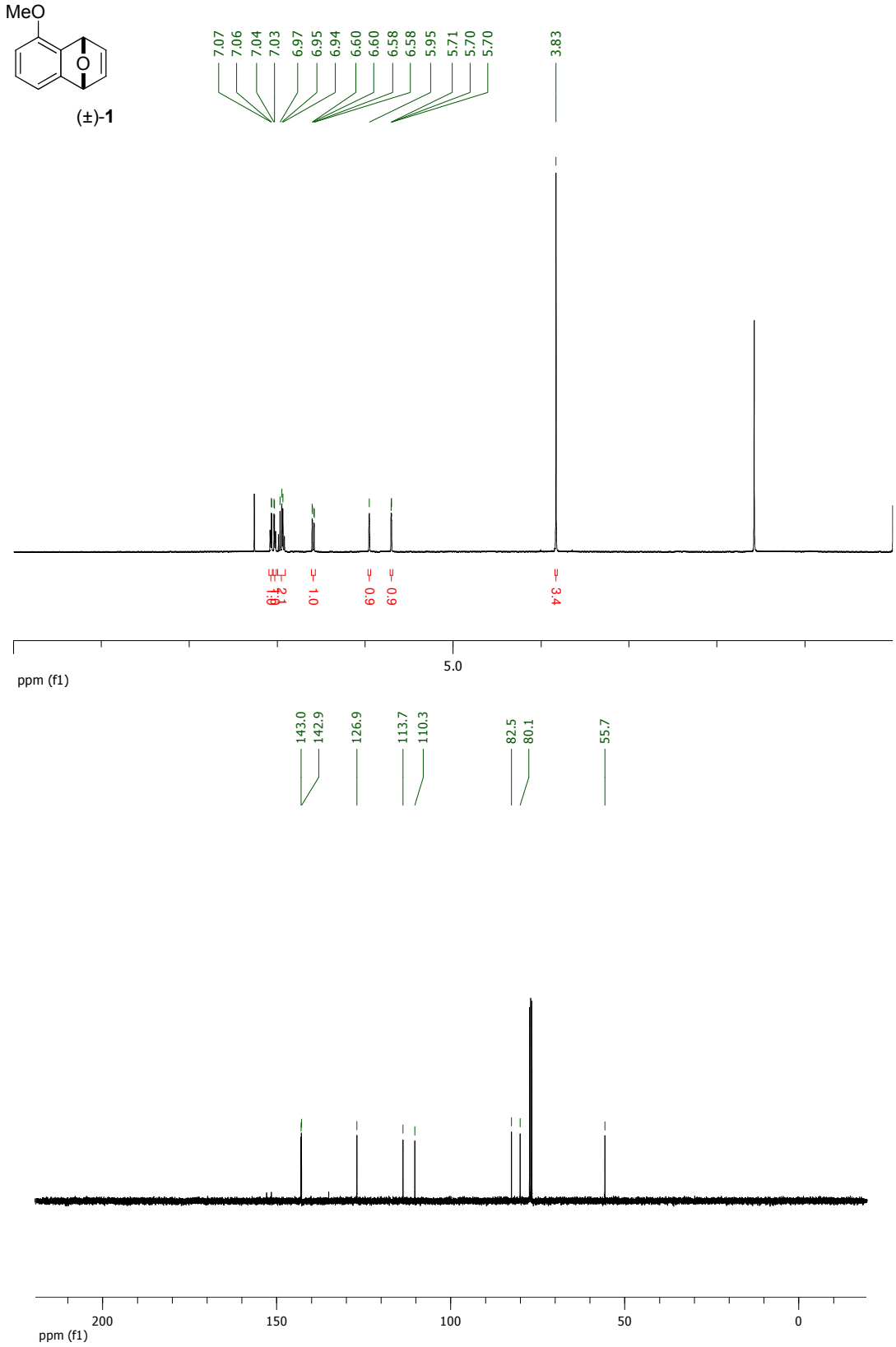
M.P. 130-132 °C;**^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.84-7.80 (m, 2H), 7.72-7.67 (m, 2H), 7.39-7.23 (m, 6H), 6.94 (dd, *J* = 8.0, 0.5 Hz, 1 H), 6.85 (d, *J* = 7.5 Hz, 1 H), 6.58 (dd, *J* = 10.0, 2.5 Hz, 1 H), 5.82 (dd, *J* = 10.0, 3.5 Hz, 1 H), 5.64 (dd, *J* = 8.0, 1.5 Hz, 1 H), 5.33 (ddd, *J* = 8.0, 3.5, 2.5 Hz, 1 H), 5.12 (d, *J* = 11.0 Hz, 1 H), 5.08 (d, *J* = 11.0 Hz, 1 H), 3.95 (d, J = 1.5, 1 H); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ =167.8, 156.3, 136.0, 133.9, 133.2, 132.0, 129.1 , 128.8, 128.7,128.3, 127.7, 124.9, 123.5, 123.3, 120.8, 112.2, 70.7, 68.9, 52.8;**IR**ν_{max} 3531br, 3017, 1772, 1717, 1387 cm^{-1}; **HRMS***m*/*z* (ESI) 420.1203 (calculated for $C_{25}H_{19}NONa$ ($M+Na^+$) 420.1206);**$[\alpha]_D^{24}$** = -230 (c = 2.0, $CHCl_3$, >98% ee);**HPLC** (AD Chiralpak,1.5 mL/min, 8% *i*PrOH in hexane) retention times: 49.0 min (minor enantiomer) and 52.9 min (major enantiomer).

References

1. M. Lautens; G. A. Schmid; A. Chau. *J Org Chem* **2002**, *67*, 8043-8053.
2. F. Gavina; S. V. Luis; A. M. Costero; P. Gil. *Tetrahedron* **1986**, *42*, 155-166.
3. M. J. Fleming; M. Lautens; M. Thommen; D. Spielvogel (Solvias AG) WO2009/109648, **2009**.

SUPPORTING SPECTRA

(±)-1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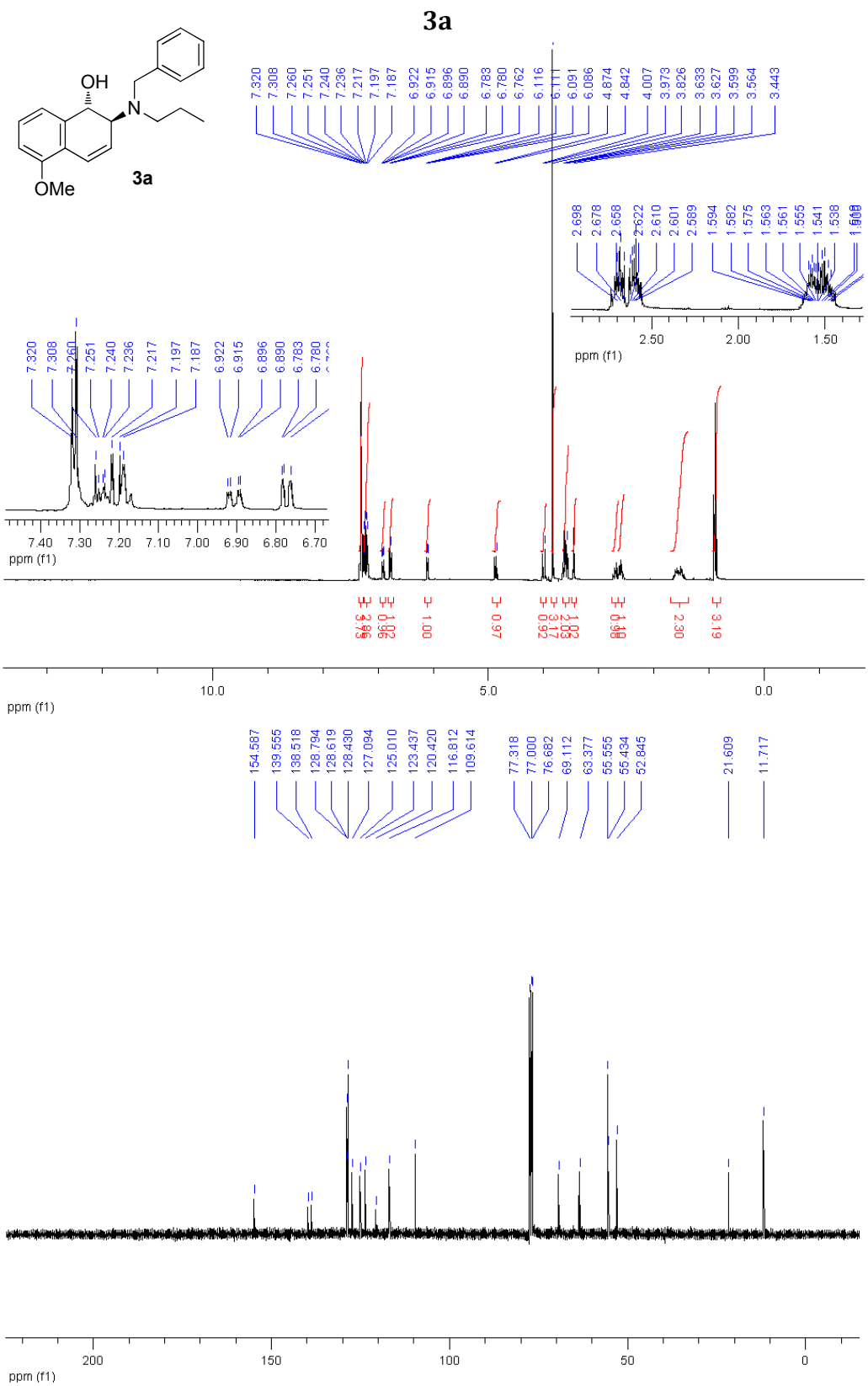
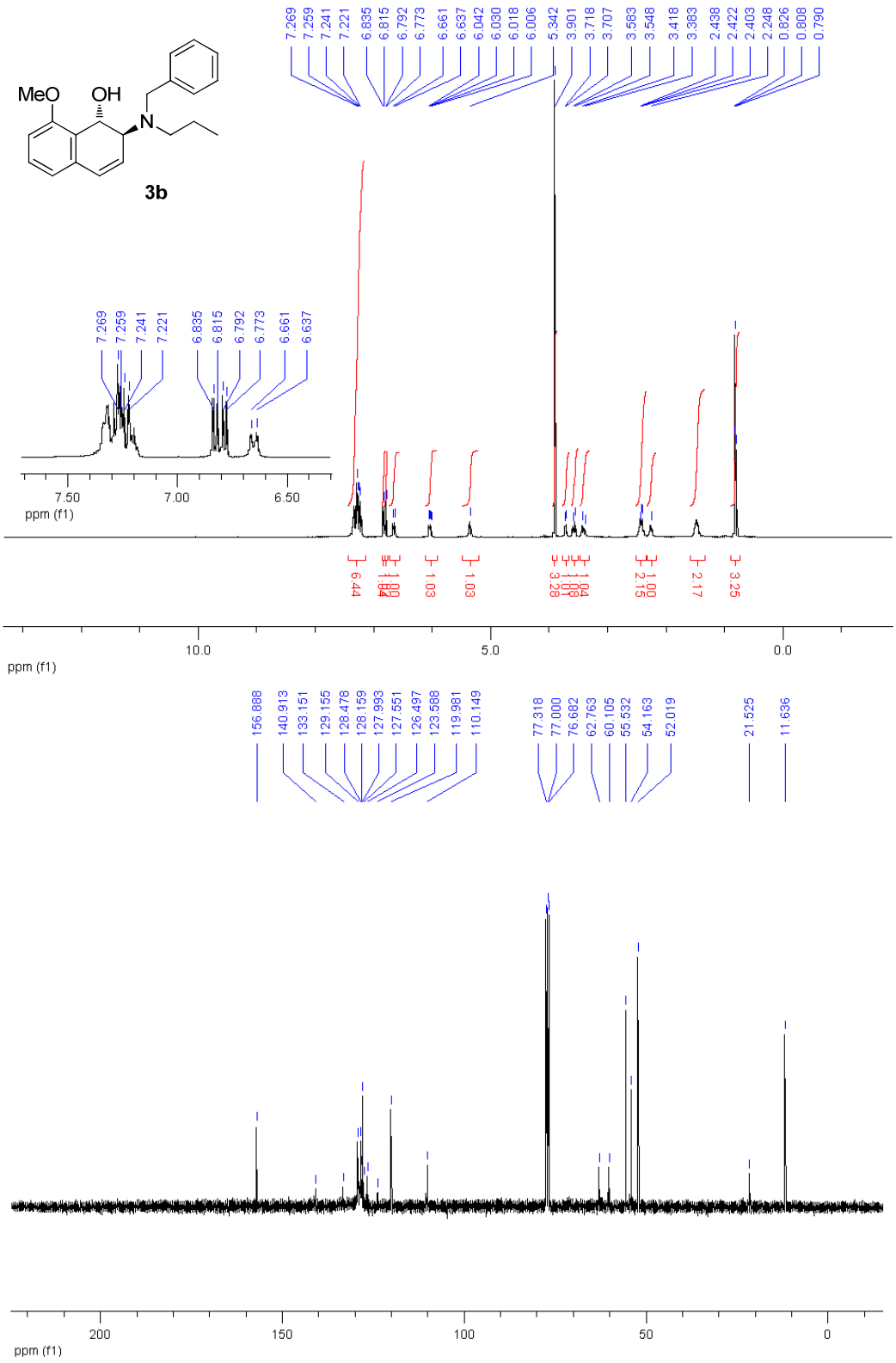
ppm (f1)

3a



3b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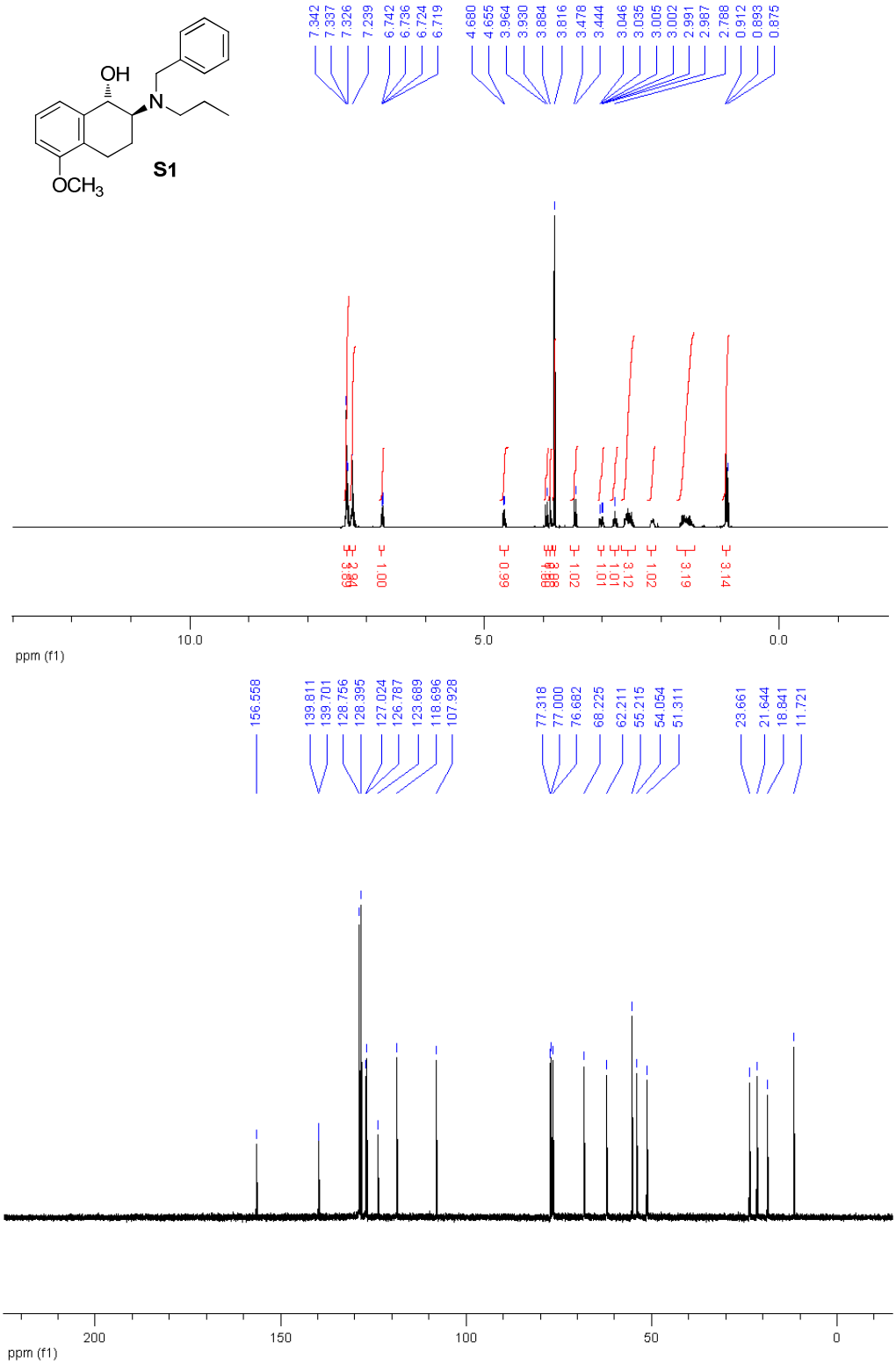
ppm (f1)

S1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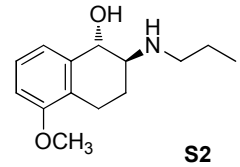
ppm (f1)

S2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0.961
0.942
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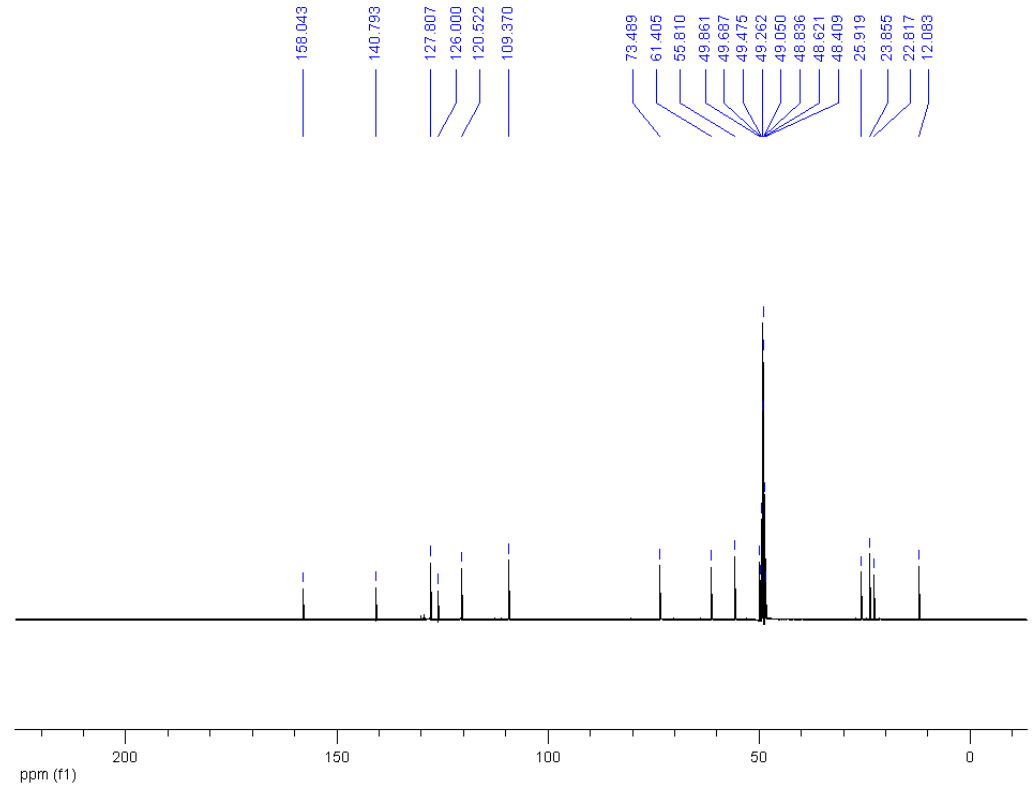
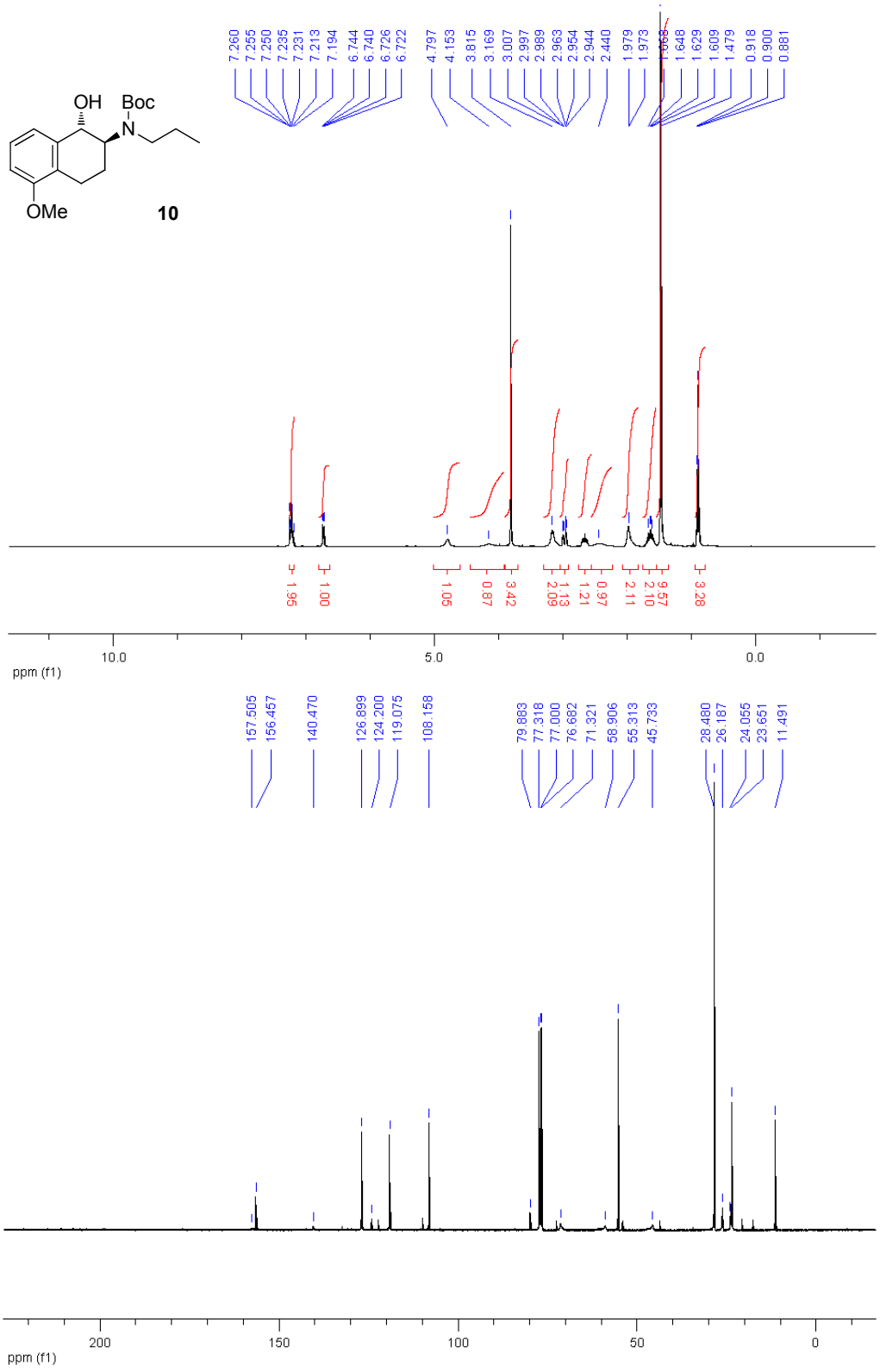
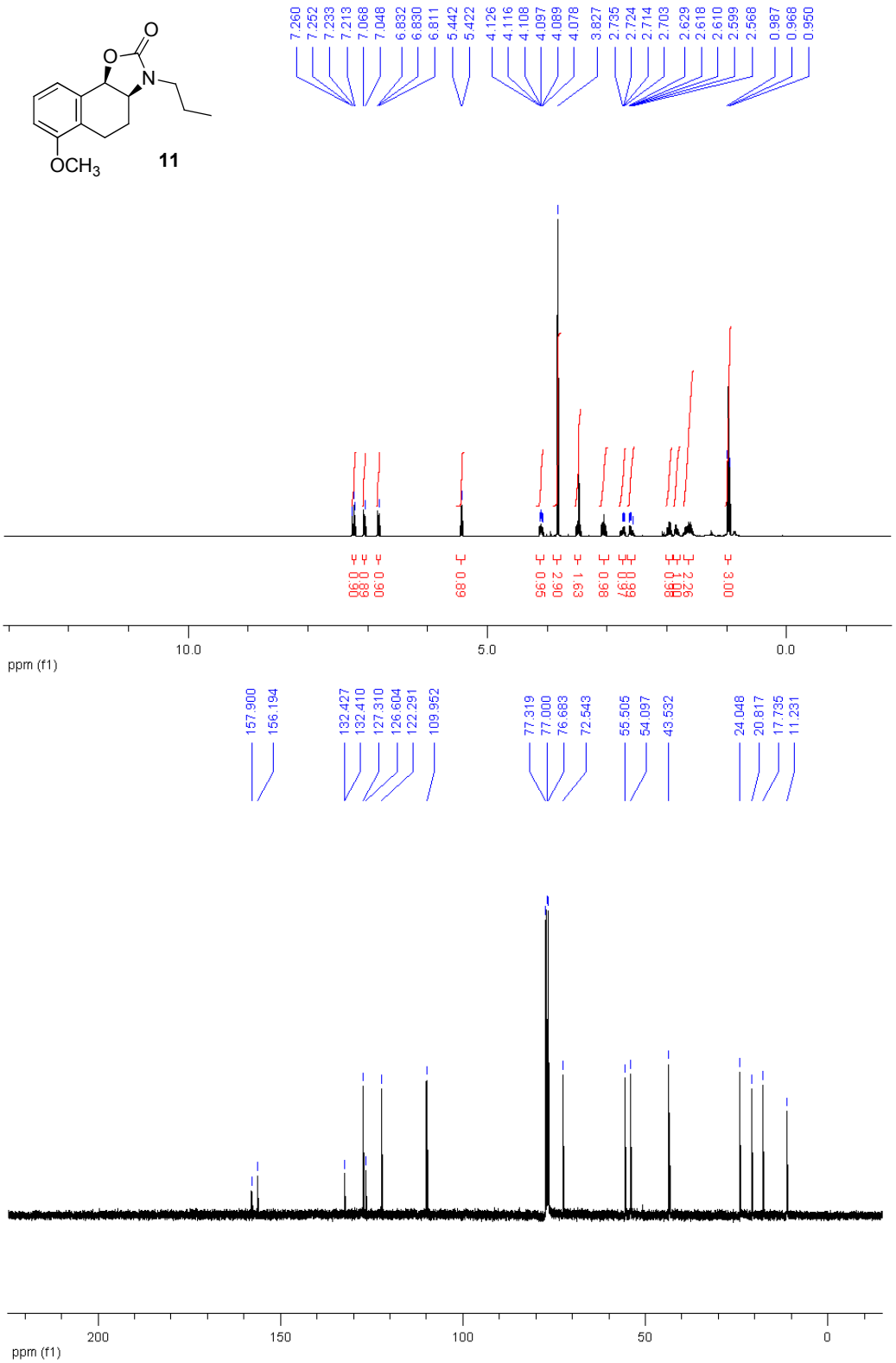
3.10
0.66
3.02
2.08
1.01
3.12
2.92
10.0
5.0
0.0
ppm (f1)


158.043
140.793
127.807
126.000
120.522
109.370
73.489
61.405
55.810
49.861
49.687
49.475
49.262
49.050
48.836
48.621
48.409
25.919
23.855
22.817
12.083
200
150
100
50
0
ppm (f1)

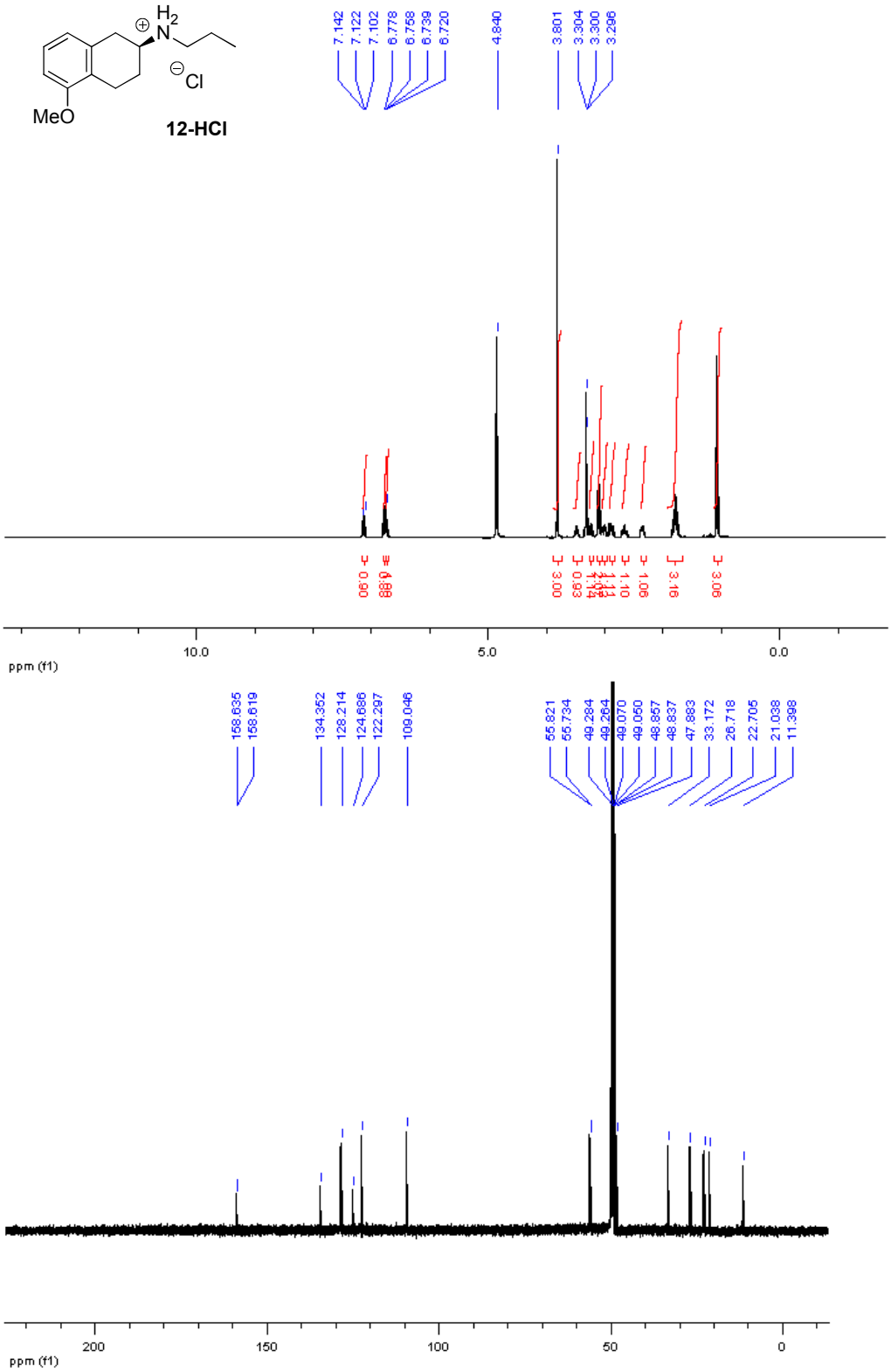
10


OH
Boc
N
OMe
10
7.260
7.255
7.250
7.235
7.231
7.213
7.194
6.744
6.740
6.726
6.722
4.797
4.153
3.815
3.169
3.007
2.997
2.989
2.963
2.954
2.944
2.440
1.979
1.973
1.668
1.648
1.629
1.609
1.479
0.918
0.900
0.881
1.95
1.00
1.05
0.87
3.42
2.09
1.13
1.21
0.97
2.11
9.57
2.10
3.28
10.0
5.0
0.0
ppm (f1)
157.505
156.457
140.470
126.899
124.200
119.075
108.158
79.883
77.318
77.000
76.682
71.321
58.906
55.313
45.733
28.480
26.187
24.055
23.651
11.491
200
150
100
50
0
ppm (f1)

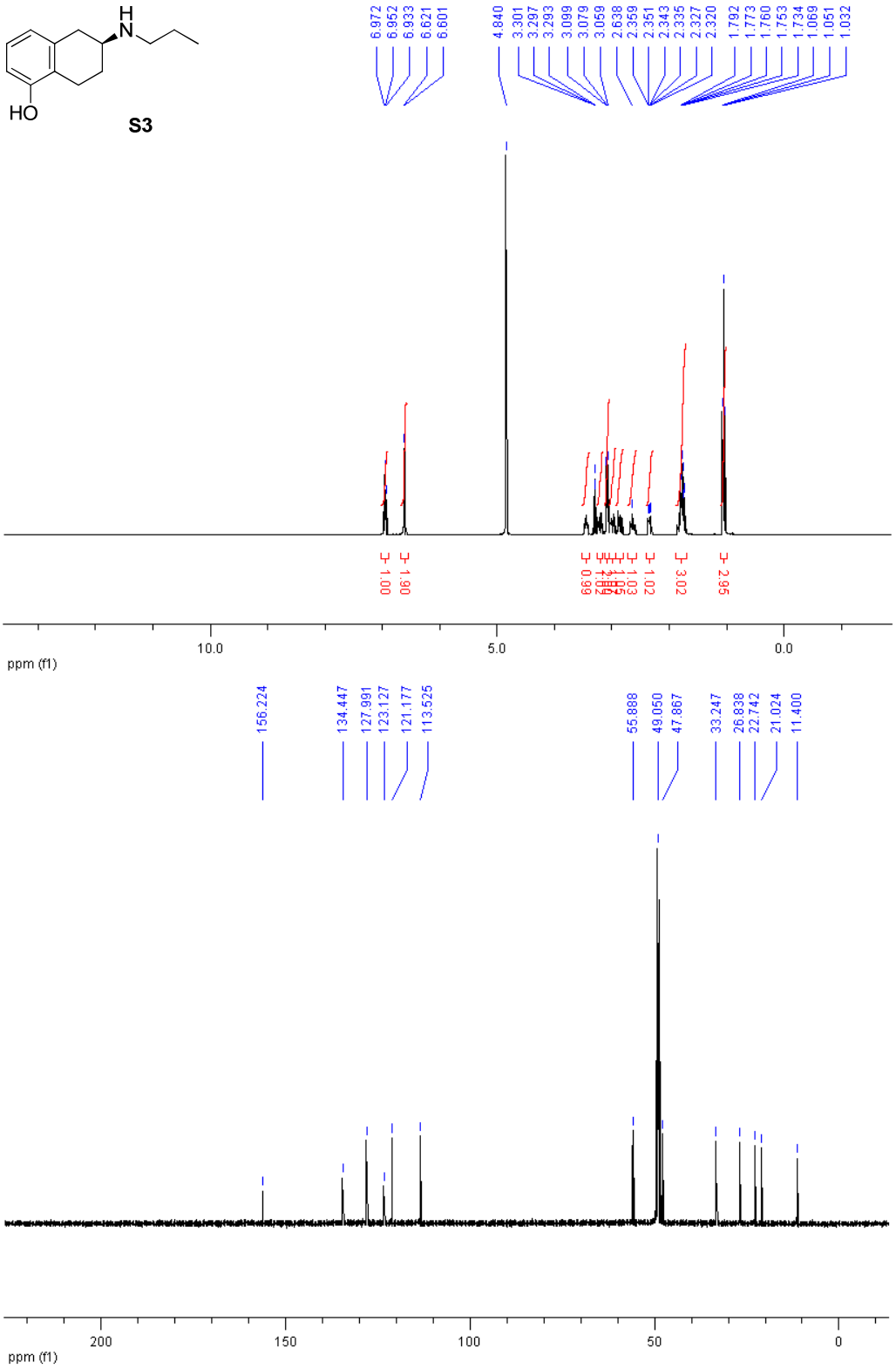
11


11
OCH3
7.260
7.252
7.233
7.213
7.068
7.048
6.832
6.830
6.811
5.442
5.422
4.126
4.116
4.108
4.097
4.089
4.078
3.827
2.735
2.724
2.714
2.703
2.629
2.618
2.610
2.599
2.568
0.987
0.968
0.950
0.90
0.88
0.90
0.89
0.96
2.90
1.63
0.98
0.97
0.89
2.26
3.00
10.0
5.0
0.0
ppm (f1)
157.900
156.194
132.427
132.410
127.310
126.604
122.291
109.952
77.319
77.000
76.683
72.543
55.505
54.097
43.532
24.048
20.817
17.735
11.231
200
150
100
50
0
ppm (f1)

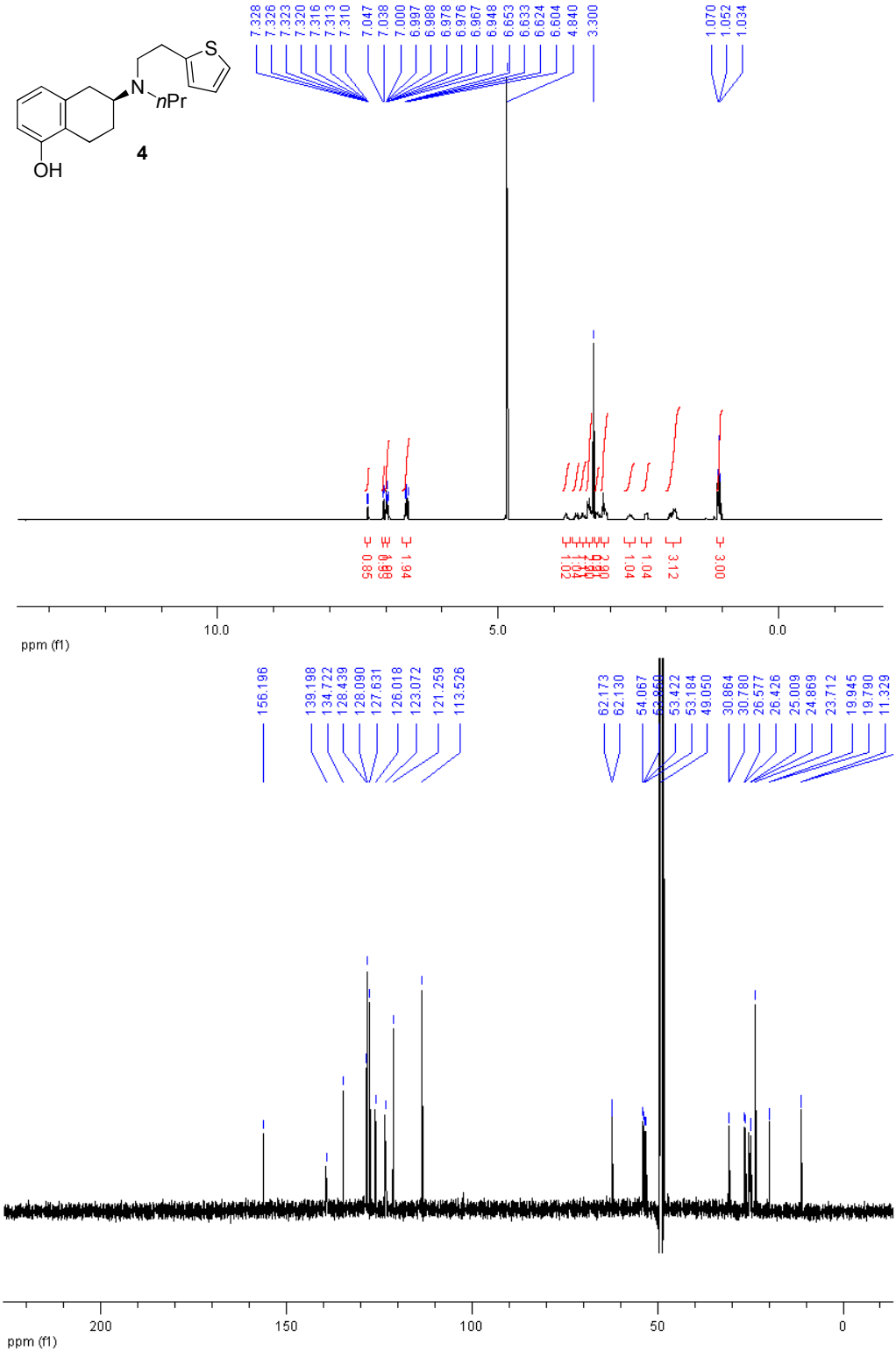
12 (HCl salt)


12-HCl
7.142
7.122
7.102
6.778
6.758
6.739
6.720
4.840
3.801
3.304
3.300
3.296
0.90
4.88
3.00
0.93
1.10
1.06
3.16
3.06
10.0
5.0
0.0
ppm (f1)
158.635
158.619
134.352
128.214
124.686
122.297
109.046
55.821
55.734
49.284
49.264
49.070
49.050
48.857
48.837
47.883
33.172
26.718
22.705
21.038
11.398
200
150
100
50
0
ppm (f1)

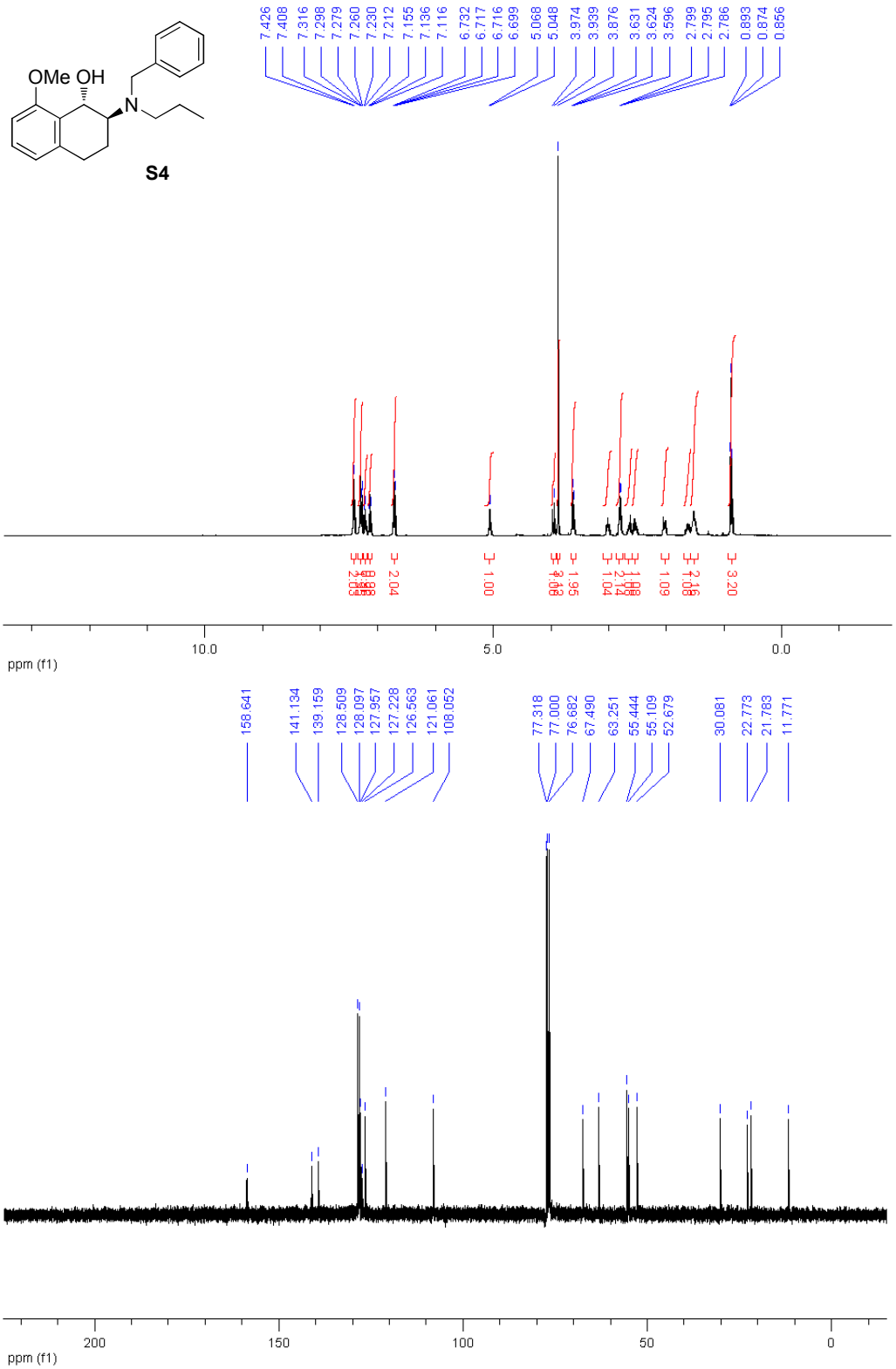
S3


S3
6.972
6.952
6.933
6.621
6.601
4.840
3.301
3.297
3.293
3.099
3.079
3.059
2.638
2.359
2.351
2.343
2.335
2.327
2.320
1.792
1.773
1.760
1.753
1.734
1.069
1.051
1.032
1.00
1.90
0.99
1.03
1.12
3.02
2.95
10.0
5.0
0.0
ppm (f1)
156.224
134.447
127.991
123.127
121.177
113.525
55.888
49.050
47.867
33.247
26.838
22.742
21.024
11.400
200
150
100
50
0
ppm (f1)

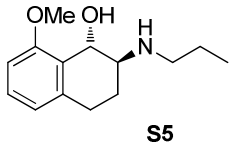
4 (HCl Salt)


7.328
7.326
7.323
7.320
7.316
7.313
7.310
7.047
7.038
7.000
6.997
6.988
6.978
6.976
6.967
6.948
6.653
6.633
6.624
6.604
4.840
3.300
1.070
1.052
1.034
N
nPr
S
OH
4
0.95
0.99
1.94
1.04
1.04
3.12
3.00
10.0
5.0
0.0
ppm (f1)
156.196
139.198
134.722
128.439
128.090
127.631
126.018
123.072
121.259
113.526
62.173
62.130
54.067
53.422
53.184
49.050
30.864
30.780
26.577
26.426
25.009
24.869
23.712
19.945
19.790
11.329
200
150
100
50
0
ppm (f1)

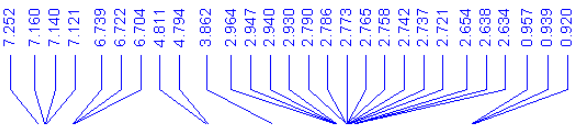
S4

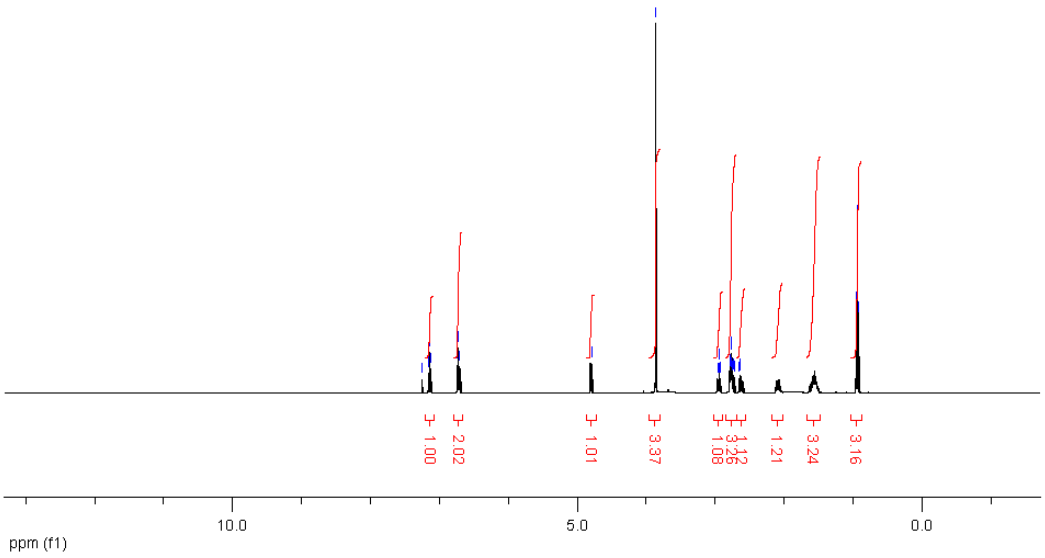

OMe OH
N
S4
7.426
7.408
7.316
7.298
7.279
7.260
7.230
7.212
7.155
7.136
7.116
6.732
6.717
6.716
6.699
5.068
5.048
3.974
3.939
3.876
3.631
3.624
3.596
2.799
2.795
2.786
0.893
0.874
0.856
2.04
1.00
1.95
1.04
1.09
2.16
3.20
10.0
5.0
0.0
ppm (f1)
158.641
141.134
139.159
128.509
128.097
127.957
127.228
126.563
121.061
108.052
77.318
77.000
76.682
67.490
63.251
55.444
55.109
52.679
30.081
22.773
21.783
11.771
200
150
100
50
0
ppm (f1)

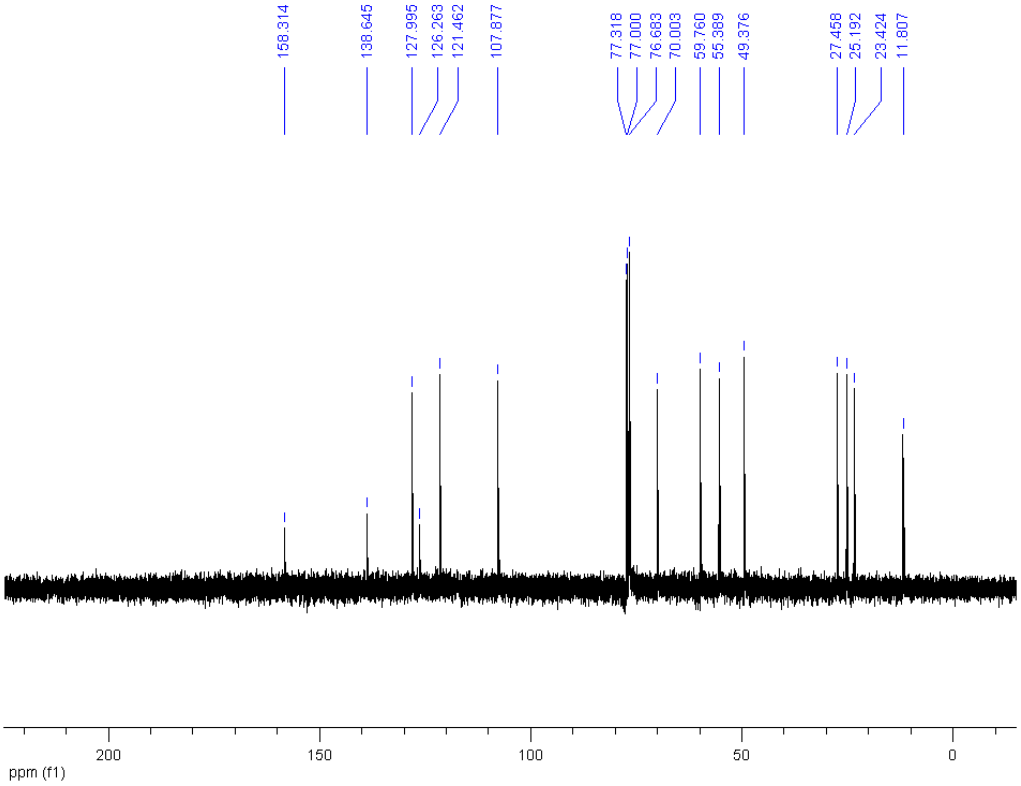
S5


OMe OH
H
N

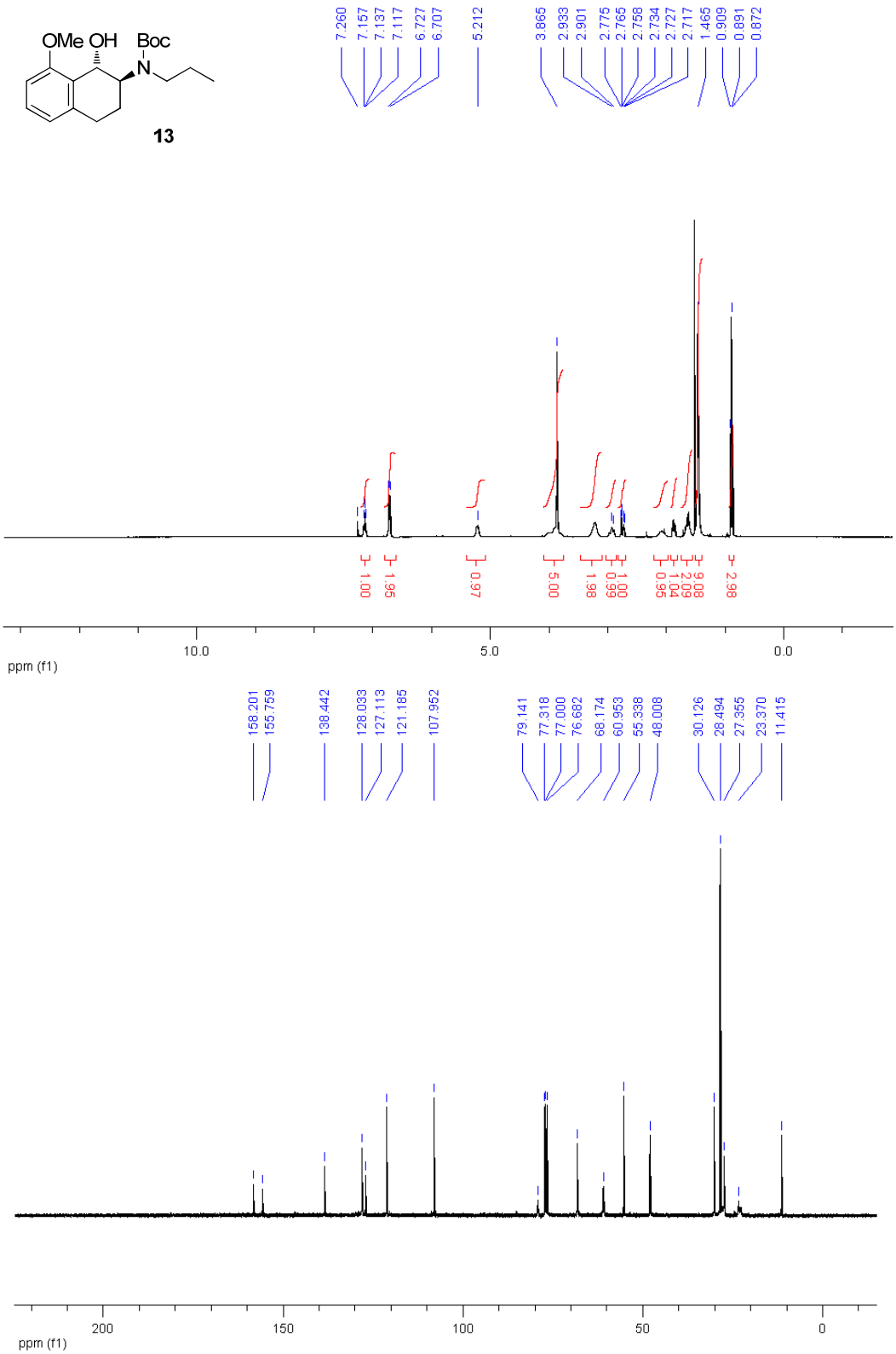
S5


7.252
7.160
7.140
7.121
6.739
6.722
6.704
4.811
4.794
3.862
2.964
2.947
2.940
2.930
2.790
2.786
2.773
2.765
2.758
2.742
2.737
2.721
2.654
2.638
2.634
0.957
0.939
0.920

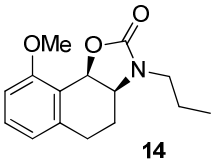

1.00
2.02
1.01
3.37
3.26
1.08
1.21
3.24
3.16
10.0
5.0
0.0
ppm (f1)


158.314
138.645
127.995
126.263
121.462
107.877
77.318
77.000
76.683
70.003
59.760
55.389
49.376
27.458
25.192
23.424
11.807
200
150
100
50
0
ppm (f1)

13


OMe OH Boc
N
13
7.260
7.157
7.137
7.117
6.727
6.707
5.212
3.865
2.933
2.901
2.775
2.765
2.758
2.734
2.727
2.717
1.465
0.909
0.891
0.872
1.00
1.95
0.97
5.00
1.98
1.00
0.99
0.95
1.04
2.09
6.08
2.98
10.0
5.0
0.0
ppm (f1)
158.201
155.759
138.442
128.033
127.113
121.185
107.952
79.141
77.318
77.000
76.682
68.174
60.953
55.338
48.008
30.126
28.494
27.355
23.370
11.415
200
150
100
50
0
ppm (f1)

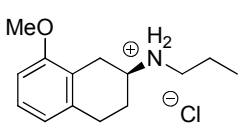
14


OMe
O
O
N

14

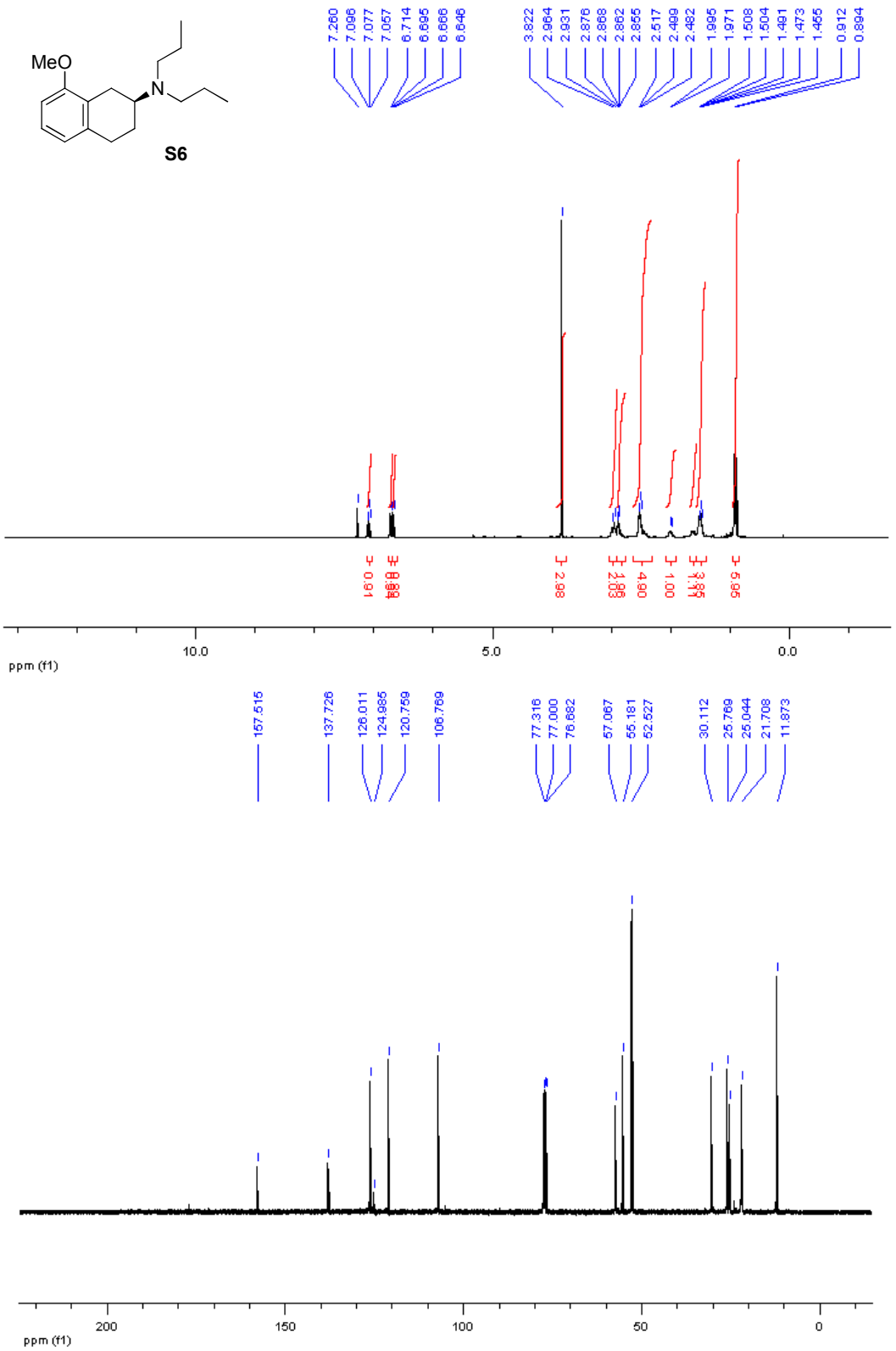
7.260
7.235
7.215
7.195
6.757
6.736
6.723
6.704
5.810
5.789
4.143
4.133
4.123
3.832
3.526
3.507
3.490
3.486
3.471
3.450
2.578
2.568
2.554
2.538
2.527
2.514
0.970
0.951
0.933
0.98
2.01
1.00
1.01
3.06
1.02
1.03
1.02
1.03
2.06
1.07
1.01
3.08
10.0
5.0
0.0
ppm (f1)
159.097
158.327
139.739
129.795
120.340
119.934
108.603
77.318
77.000
76.681
68.381
55.557
53.475
43.276
27.280
24.416
24.380
20.545
11.105
200
150
100
50
0
ppm (f1)

15 (HCl Salt)

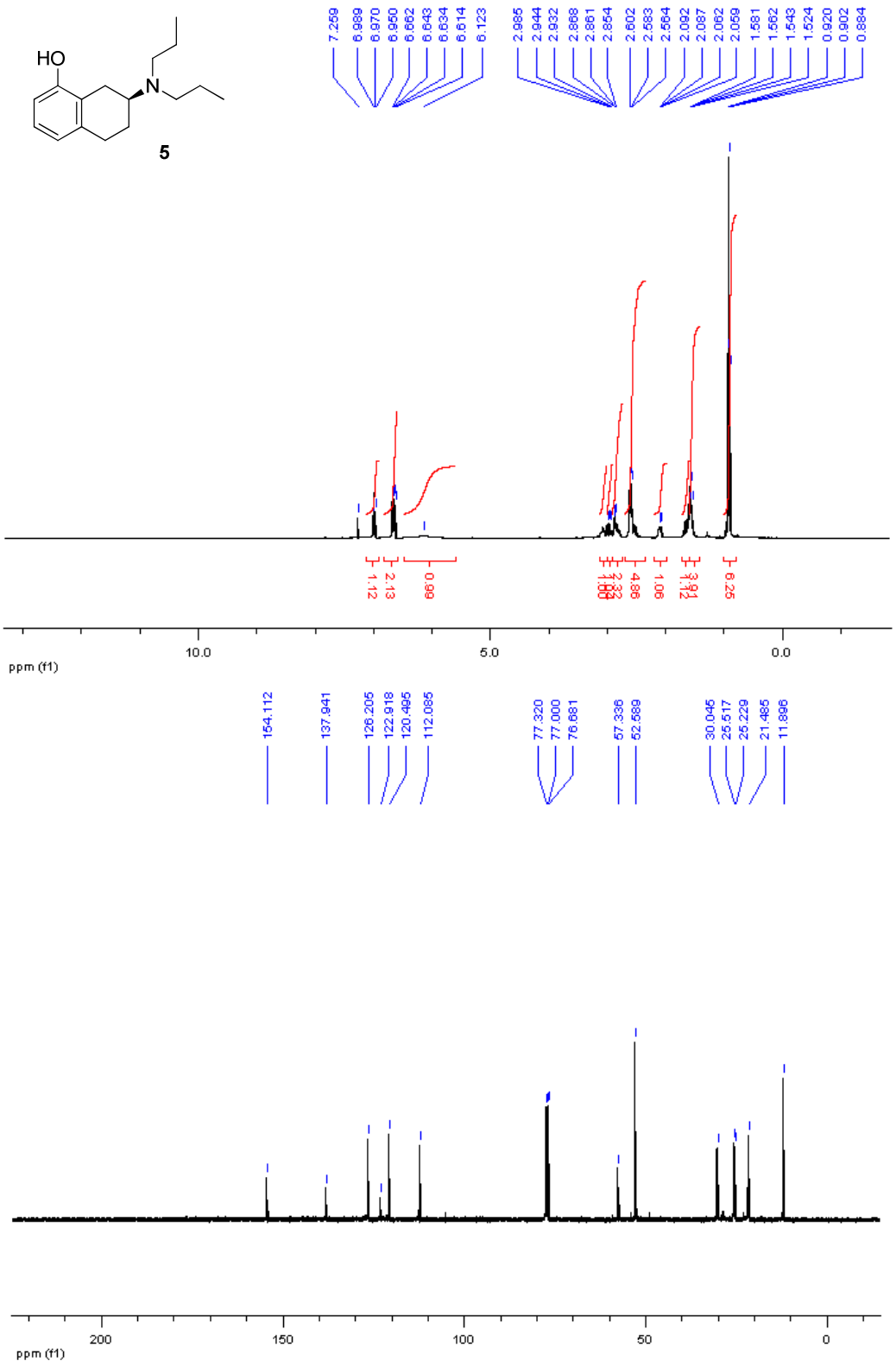


15-HCl

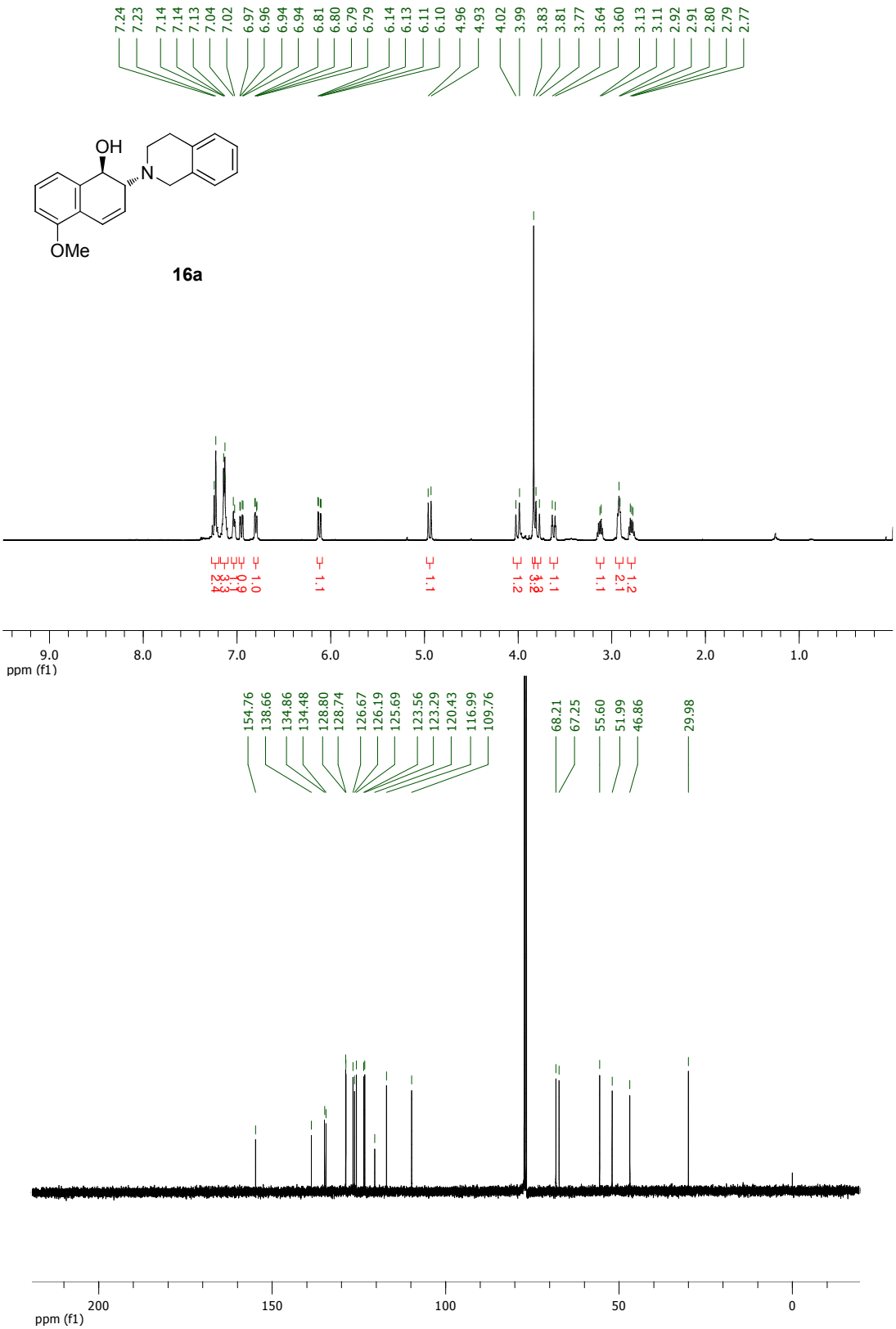
S6


MeO
N
S6
7.260
7.096
7.077
7.057
6.714
6.695
6.666
6.646
3.822
2.964
2.931
2.876
2.868
2.862
2.855
2.517
2.499
2.482
1.995
1.971
1.508
1.504
1.491
1.473
1.455
0.912
0.894
3.00
2.88
4.90
1.00
3.96
ppm (f1)
157.515
137.726
126.011
124.985
120.759
106.769
77.316
77.000
76.682
57.067
55.181
52.527
30.112
25.769
25.044
21.708
11.873
ppm (f1)

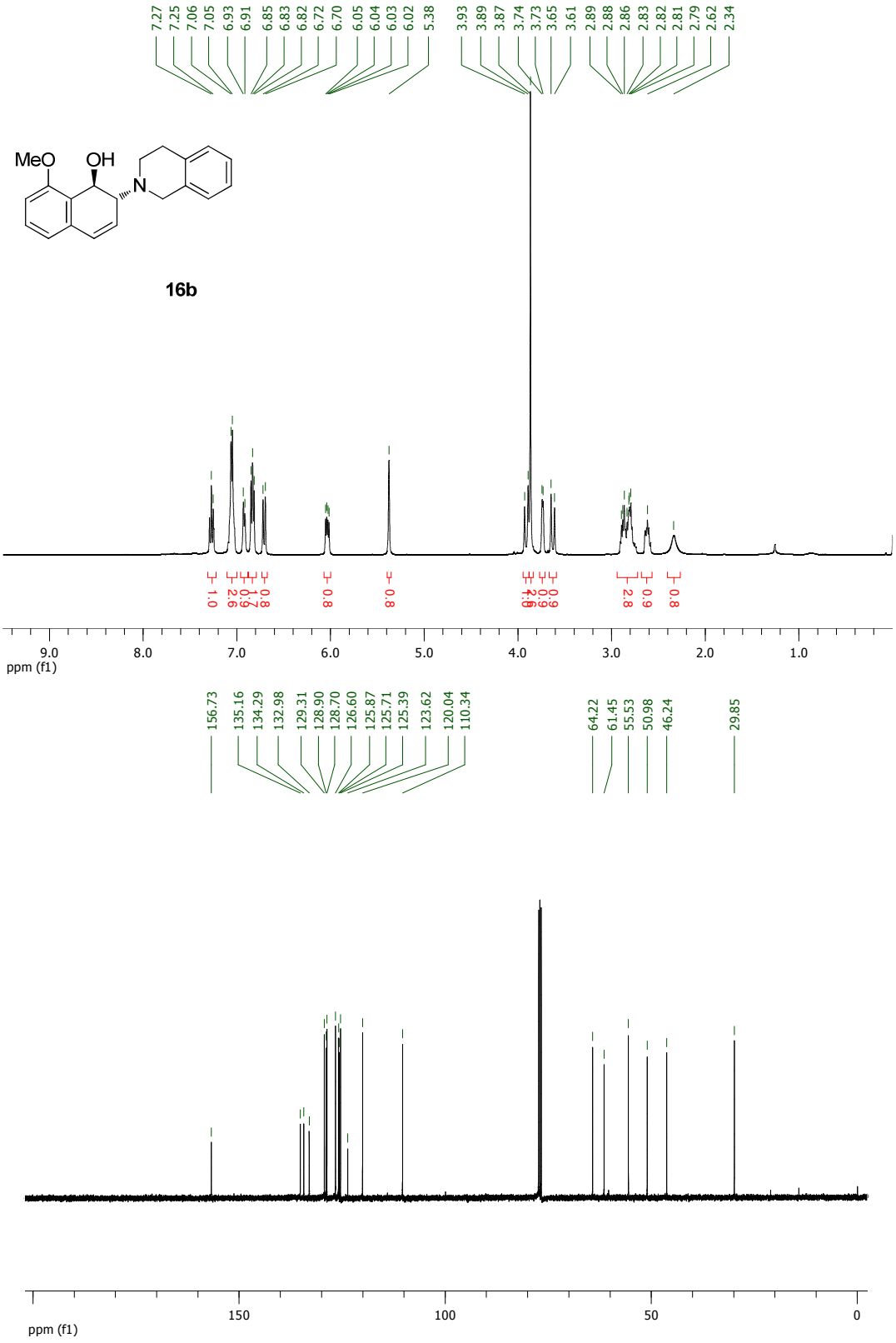
5


HO
N
5
7.259
6.989
6.970
6.950
6.662
6.643
6.634
6.614
6.123
2.985
2.944
2.932
2.868
2.861
2.854
2.602
2.583
2.564
2.092
2.087
2.062
2.059
1.581
1.562
1.543
1.524
0.920
0.902
0.884
1.12
2.13
0.99
4.86
1.06
3.91
6.25
10.0
5.0
0.0
ppm (f1)
154.112
137.941
126.205
122.918
120.495
112.085
77.320
77.000
76.681
57.336
52.589
30.045
25.517
25.229
21.485
11.896
200
150
100
50
0
ppm (f1)

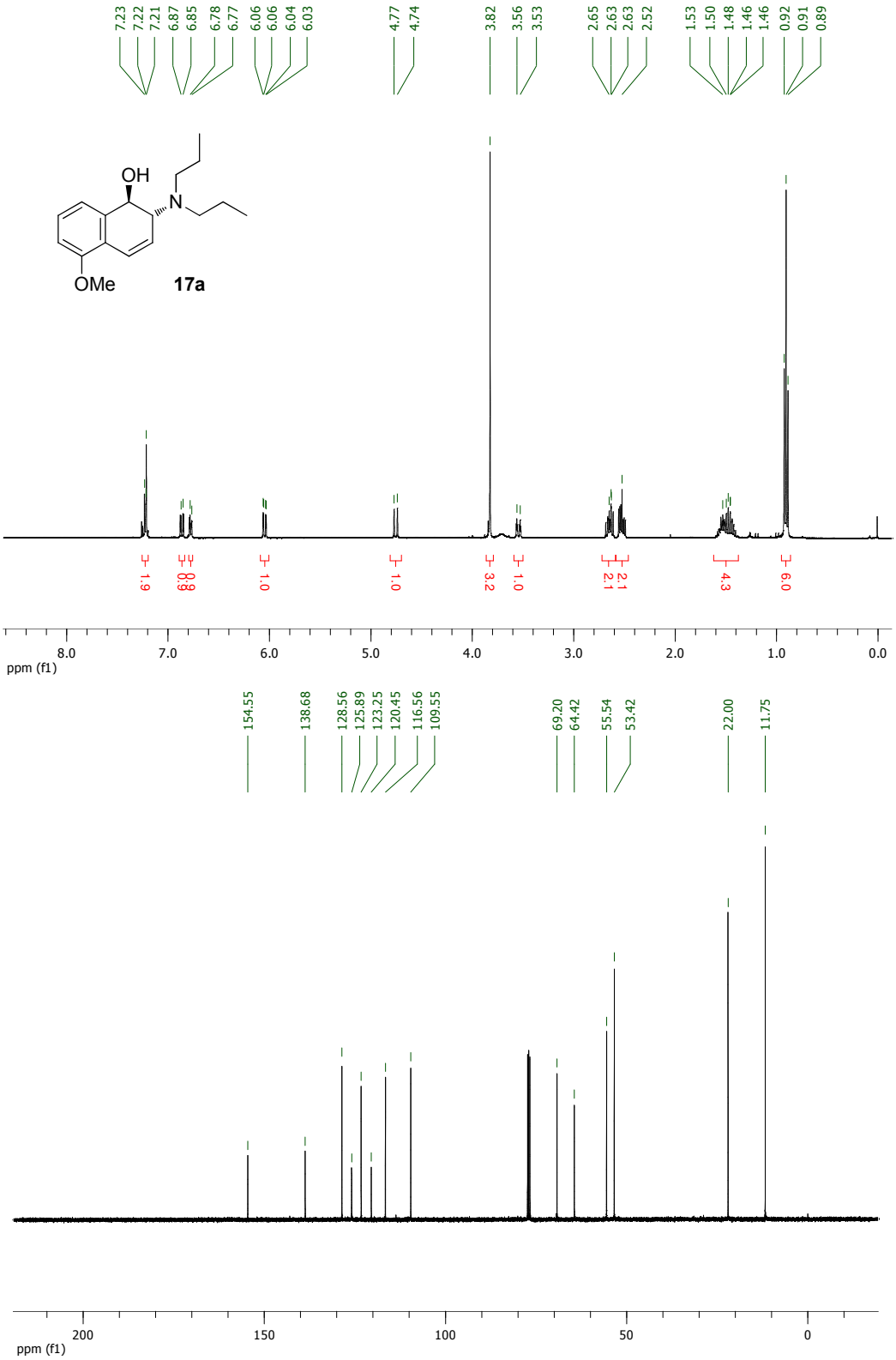
16a


7.24
7.23
7.14
7.14
7.13
7.04
7.02
6.97
6.96
6.94
6.94
6.81
6.80
6.79
6.79
6.14
6.13
6.11
6.10
4.96
4.93
4.02
3.99
3.83
3.81
3.77
3.64
3.60
3.13
3.11
2.92
2.91
2.80
2.79
2.77
OH
N
OMe
16a
1.0
1.1
1.1
1.2
1.1
1.1
2.1
1.2
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)
154.76
138.66
134.86
134.48
128.80
128.74
126.67
126.19
125.69
123.56
123.29
120.43
116.99
109.76
68.21
67.25
55.60
51.99
46.86
29.98
200
150
100
50
0
ppm (f1)

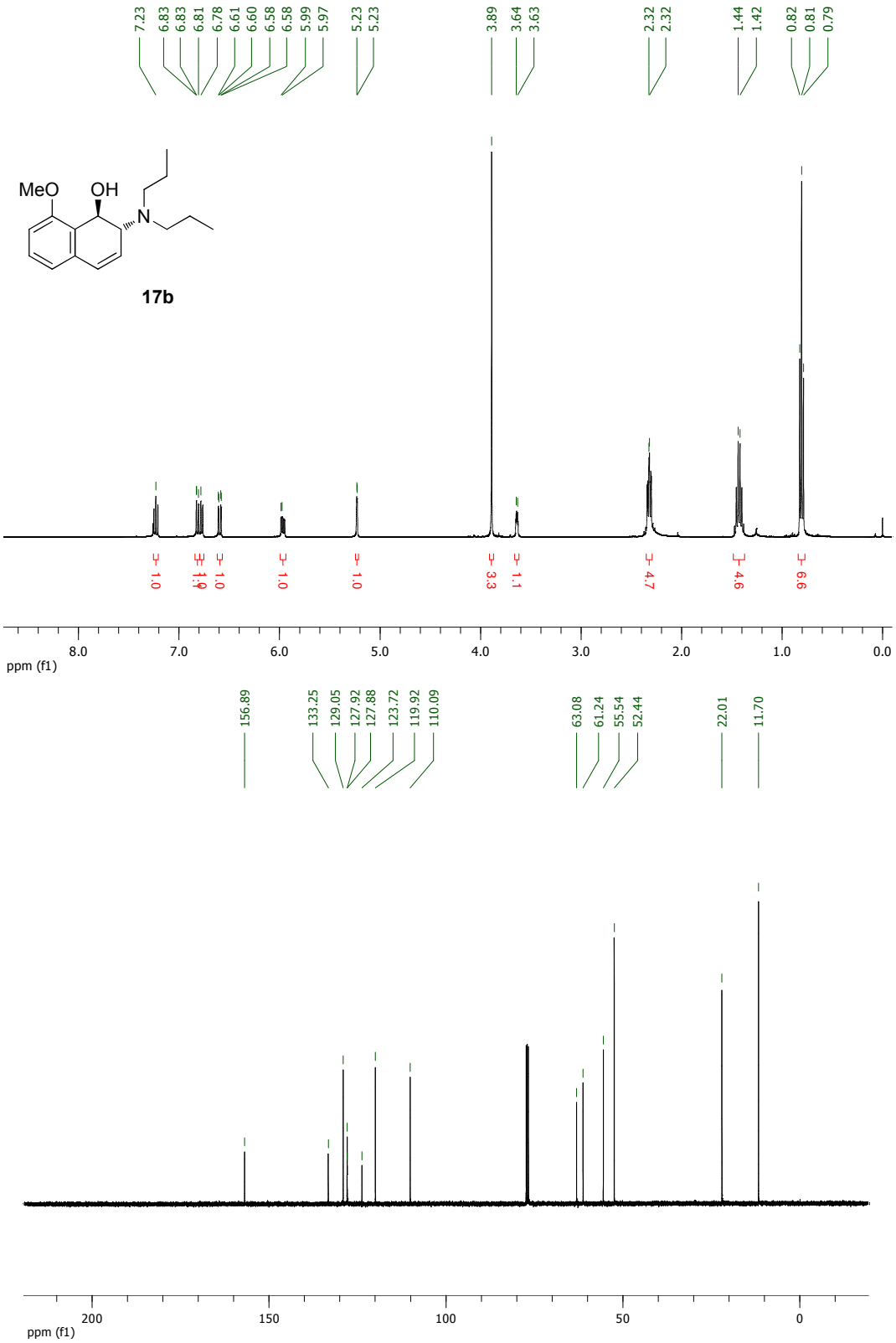
16b


7.27
7.25
7.06
7.05
6.93
6.91
6.85
6.83
6.82
6.72
6.70
6.05
6.04
6.03
6.02
5.38
3.93
3.89
3.87
3.74
3.73
3.65
3.61
2.89
2.88
2.86
2.83
2.82
2.81
2.79
2.62
2.34
MeO
OH
N
16b
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)
156.73
135.16
134.29
132.98
129.31
128.90
128.70
126.60
125.87
125.71
125.39
123.62
120.04
110.34
64.22
61.45
55.53
50.98
46.24
29.85
150
100
50
0
ppm (f1)

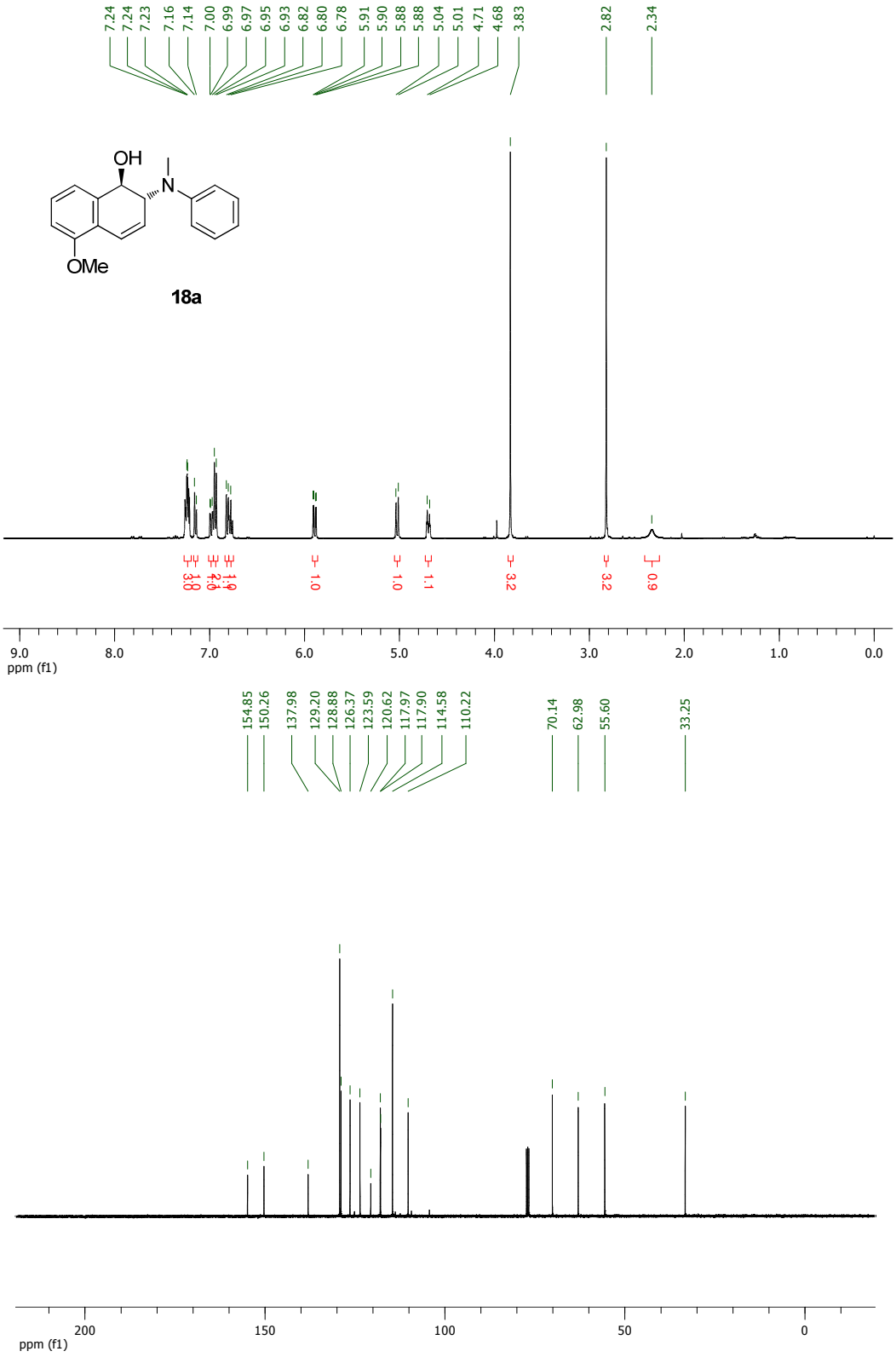
17a


7.23
7.22
7.21
6.87
6.85
6.78
6.77
6.06
6.06
6.04
6.03
4.77
4.74
3.82
3.56
3.53
2.65
2.63
2.63
2.52
1.53
1.50
1.48
1.46
1.46
0.92
0.91
0.89
OH
N
OMe
17a
1.9
0.8
0.9
1.0
1.0
3.2
1.0
2.1
2.1
4.3
6.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)
154.55
138.68
128.56
125.89
123.25
120.45
116.56
109.55
69.20
64.42
55.54
53.42
22.00
11.75
200
150
100
50
0
ppm (f1)

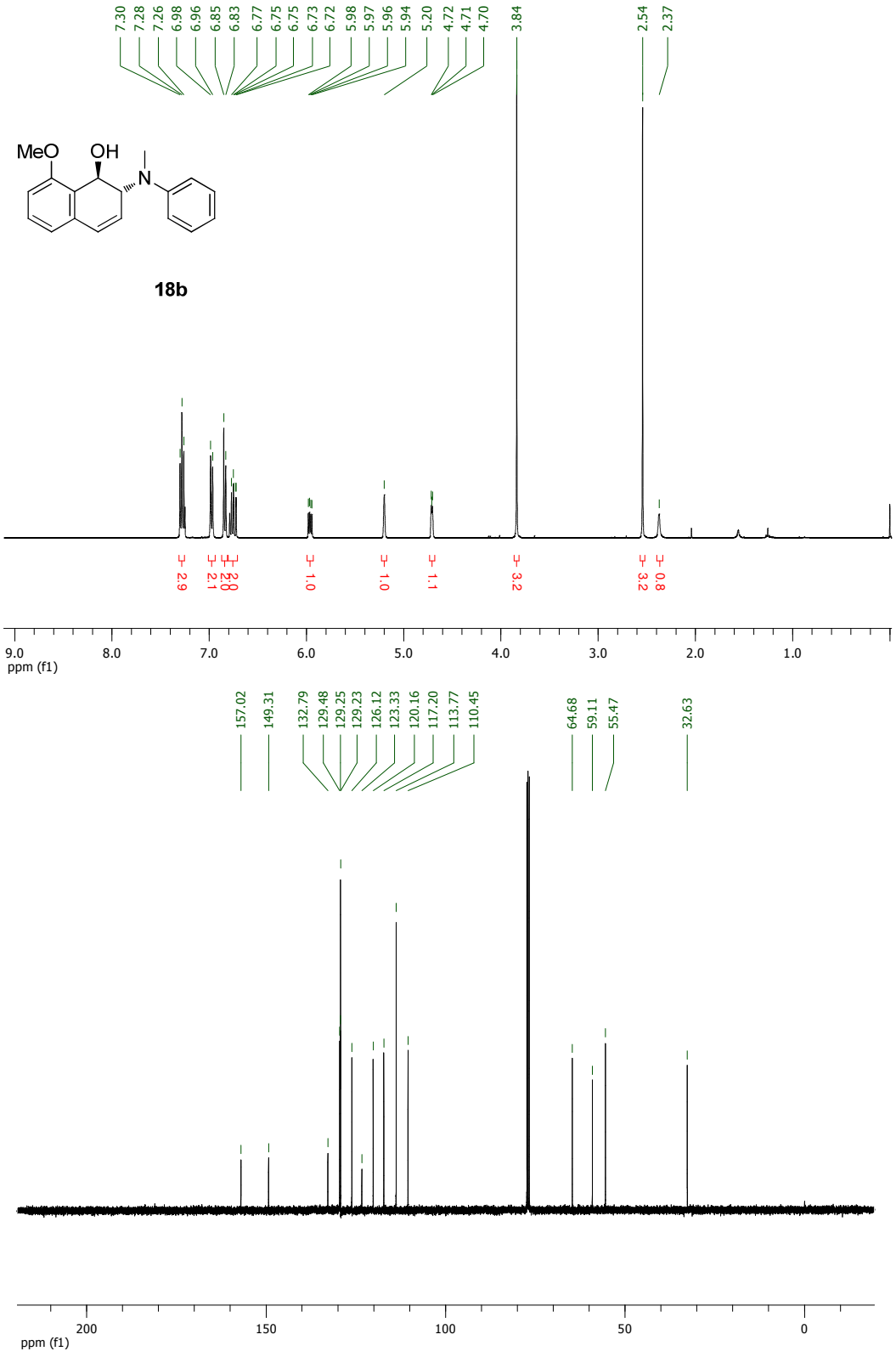
17b


7.23
6.83
6.83
6.81
6.78
6.61
6.60
6.58
6.58
5.99
5.97
5.23
5.23
3.89
3.64
3.63
2.32
2.32
1.44
1.42
0.82
0.81
0.79
MeO
OH
N
17b
1.0
1.9
1.0
1.0
1.0
3.3
1.1
4.7
4.6
6.6
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)
156.89
133.25
129.05
127.92
127.88
123.72
119.92
110.09
63.08
61.24
55.54
52.44
22.01
11.70
200
150
100
50
0
ppm (f1)

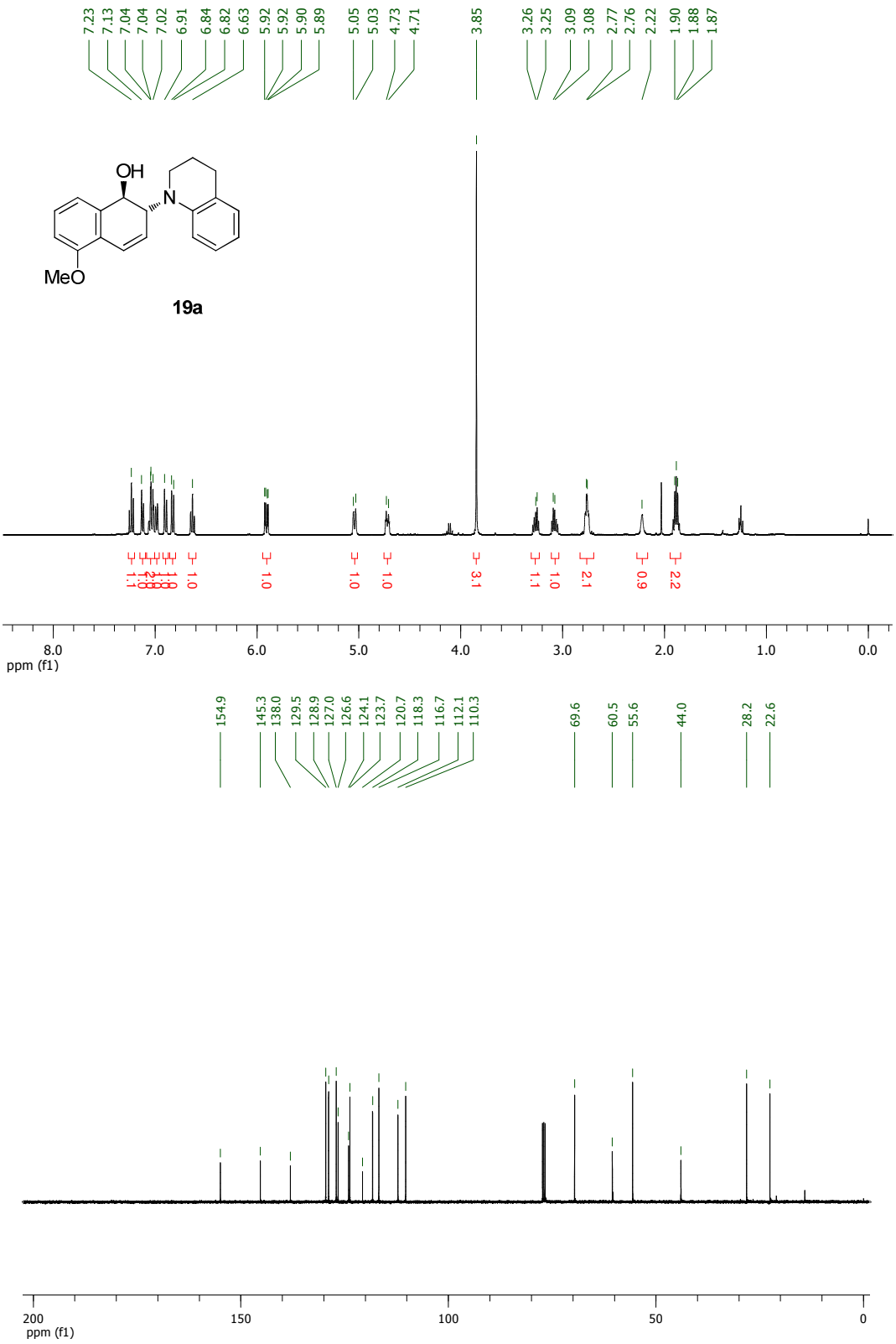
18a


7.24
7.24
7.23
7.16
7.14
7.00
6.99
6.97
6.95
6.93
6.82
6.80
6.78
5.91
5.90
5.88
5.88
5.04
5.01
4.71
4.68
3.83
2.82
2.34
OH
N
OMe
18a
3.0
1.0
4.0
2.1
1.9
1.0
1.0
1.1
3.2
3.2
0.9
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)
154.85
150.26
137.98
129.20
128.88
126.37
123.59
120.62
117.97
117.90
114.58
110.22
70.14
62.98
55.60
33.25
200
150
100
50
0
ppm (f1)

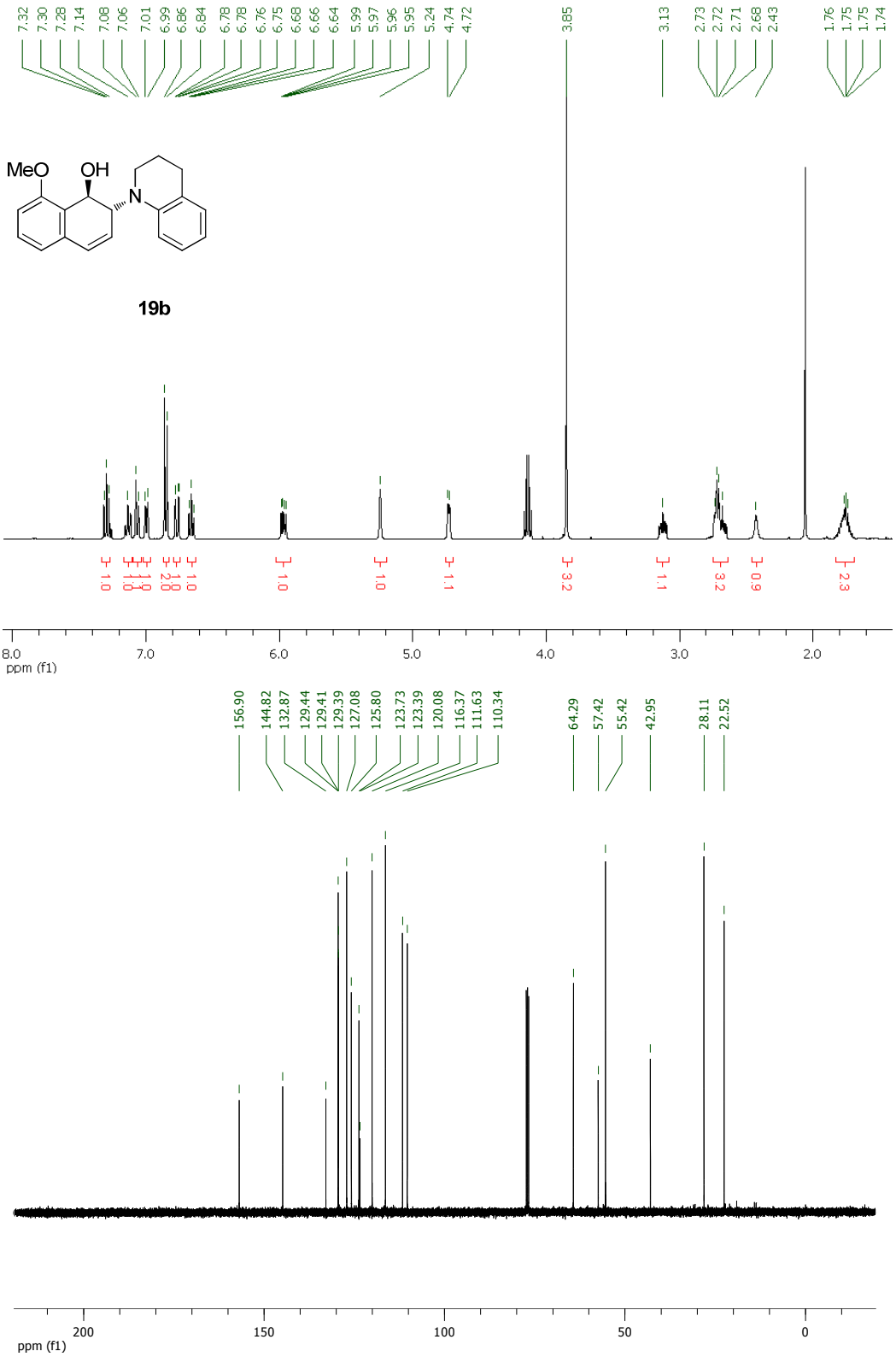
18b


7.30
7.28
7.26
6.98
6.96
6.85
6.83
6.77
6.75
6.75
6.73
6.72
5.98
5.97
5.96
5.94
5.20
4.72
4.71
4.70
3.84
2.54
2.37
MeO
OH
N
18b
2.9
2.1
2.0
1.0
1.0
1.1
3.2
3.2
0.8
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)
157.02
149.31
132.79
129.48
129.25
129.23
126.12
123.33
120.16
117.20
113.77
110.45
64.68
59.11
55.47
32.63
200
150
100
50
0
ppm (f1)

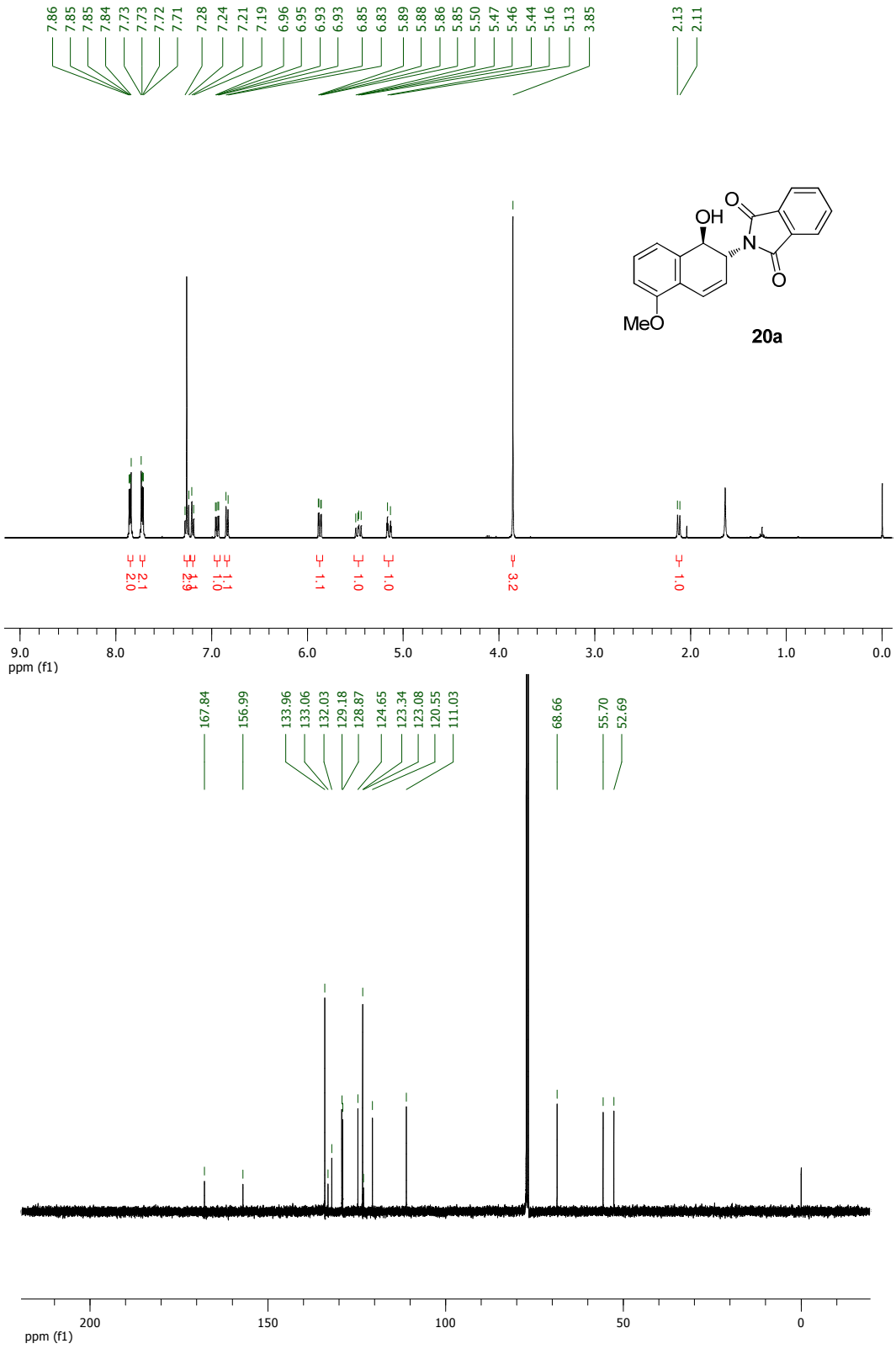
19a


7.23
7.13
7.04
7.04
7.02
6.91
6.84
6.82
6.63
5.92
5.92
5.90
5.89
5.05
5.03
4.73
4.71
3.85
3.26
3.25
3.09
3.08
2.77
2.76
2.22
1.90
1.88
1.87
OH
N
MeO
19a
1.1
1.0
1.0
1.0
3.1
1.1
1.0
2.1
0.9
2.2
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)
154.9
145.3
138.0
129.5
128.9
127.0
126.6
124.1
123.7
120.7
118.3
116.7
112.1
110.3
69.6
60.5
55.6
44.0
28.2
22.6
200
150
100
50
0
ppm (f1)

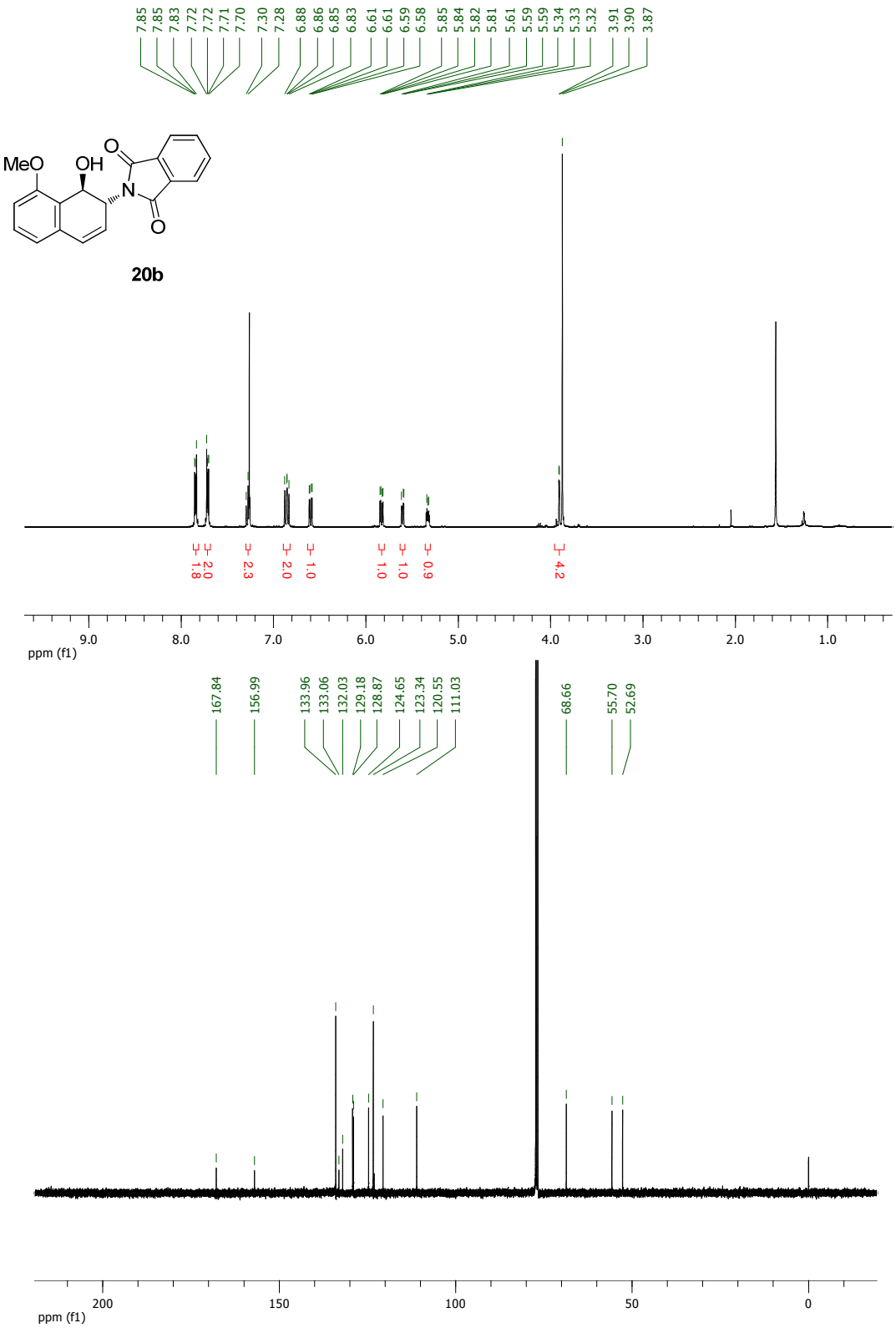
19b


7.32
7.30
7.28
7.14
7.08
7.06
7.01
6.99
6.86
6.84
6.78
6.78
6.76
6.75
6.68
6.66
6.64
5.99
5.97
5.96
5.95
5.24
4.74
4.72
3.85
3.13
2.73
2.72
2.71
2.68
2.43
1.76
1.75
1.75
1.74
MeO
OH
N
19b
1.0
1.0
1.0
1.0
1.0
2.0
1.0
1.0
1.0
1.1
3.2
1.1
3.2
0.9
2.3
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)
156.90
144.82
132.87
129.44
129.41
129.39
127.08
125.80
123.73
123.39
120.08
116.37
111.63
110.34
64.29
57.42
55.42
42.95
28.11
22.52
200
150
100
50
0
ppm (f1)

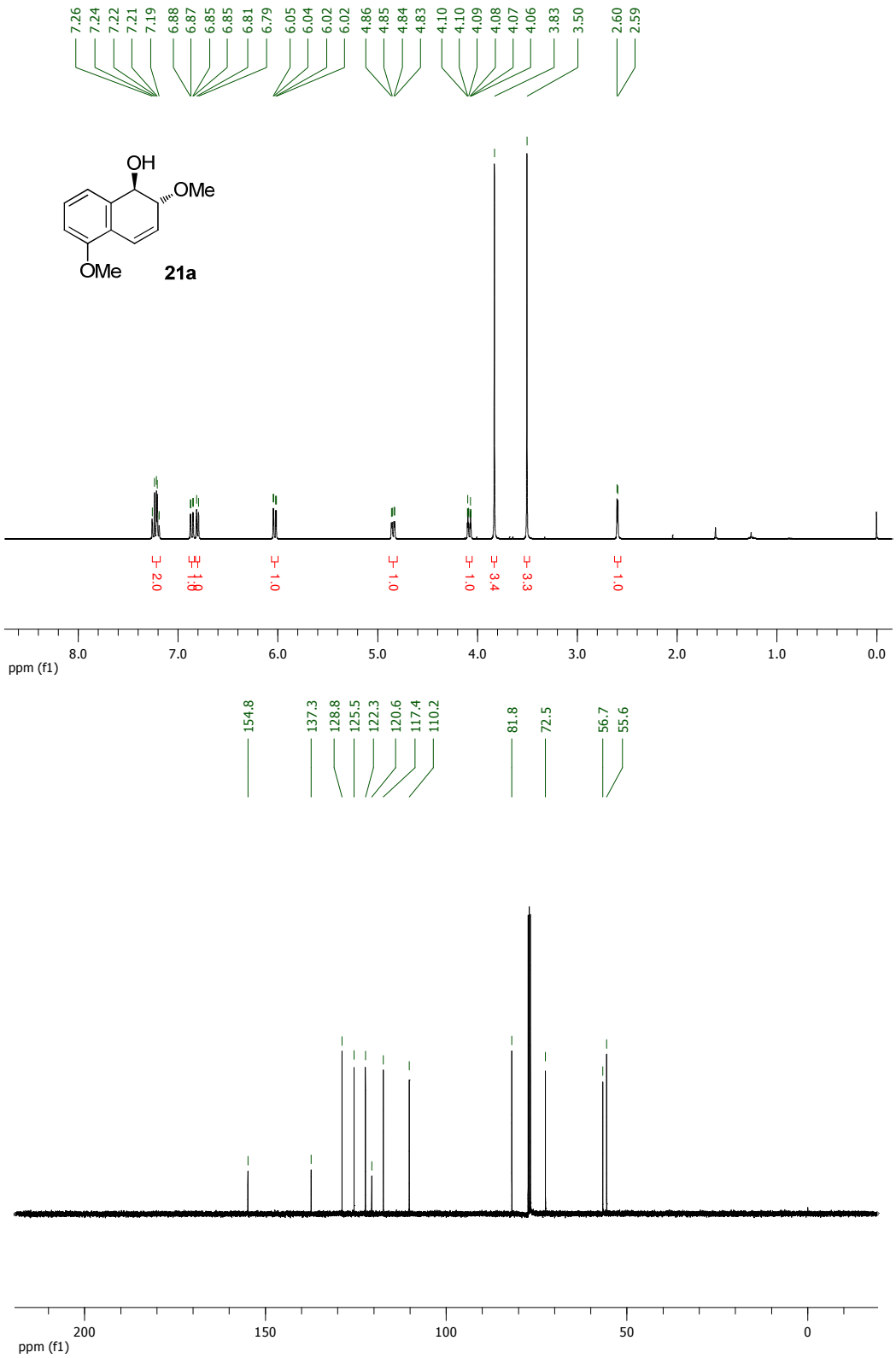
20a


7.86
7.85
7.85
7.84
7.73
7.73
7.72
7.71
7.28
7.24
7.21
7.19
6.96
6.95
6.93
6.93
6.85
6.83
5.89
5.88
5.86
5.85
5.50
5.47
5.46
5.44
5.16
5.13
3.85
2.13
2.11
OH
O
N
O
MeO
20a
2.0
2.1
1.1
1.0
1.1
1.0
1.0
3.2
1.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)
167.84
156.99
133.96
133.06
132.03
129.18
128.87
124.65
123.34
123.08
120.55
111.03
68.66
55.70
52.69
200
150
100
50
0
ppm (f1)

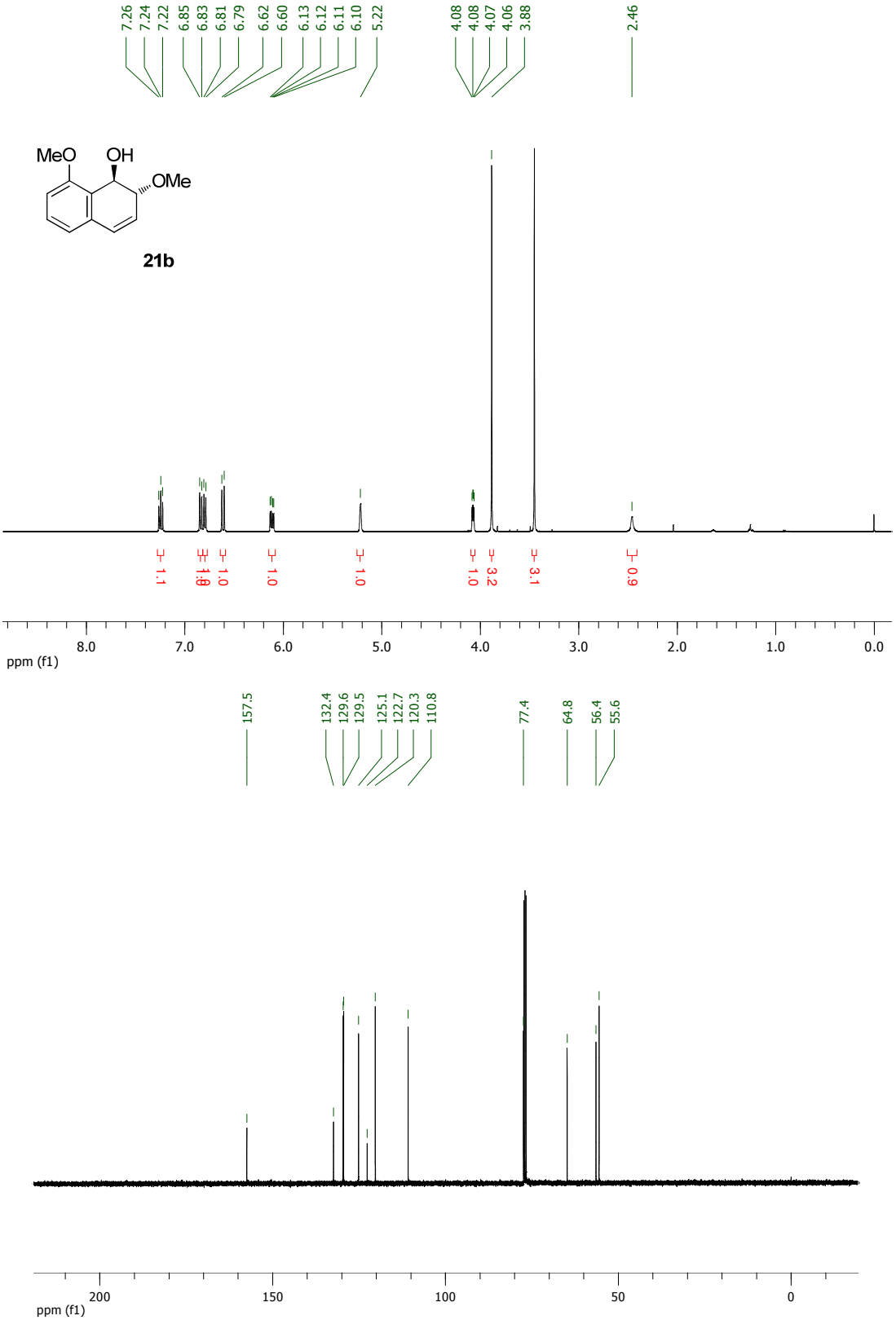
20b


7.85
7.85
7.83
7.72
7.72
7.71
7.70
7.30
7.28
6.88
6.86
6.85
6.83
6.61
6.61
6.59
6.58
5.85
5.84
5.82
5.81
5.61
5.59
5.59
5.34
5.33
5.32
3.91
3.90
3.87
MeO
OH
O
N
O
20b
1.8
2.0
2.3
2.0
1.0
1.0
1.0
0.9
4.2
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)
167.84
156.99
133.96
133.06
132.03
129.18
128.87
124.65
123.34
120.55
111.03
68.66
55.70
52.69
200
150
100
50
0
ppm (f1)

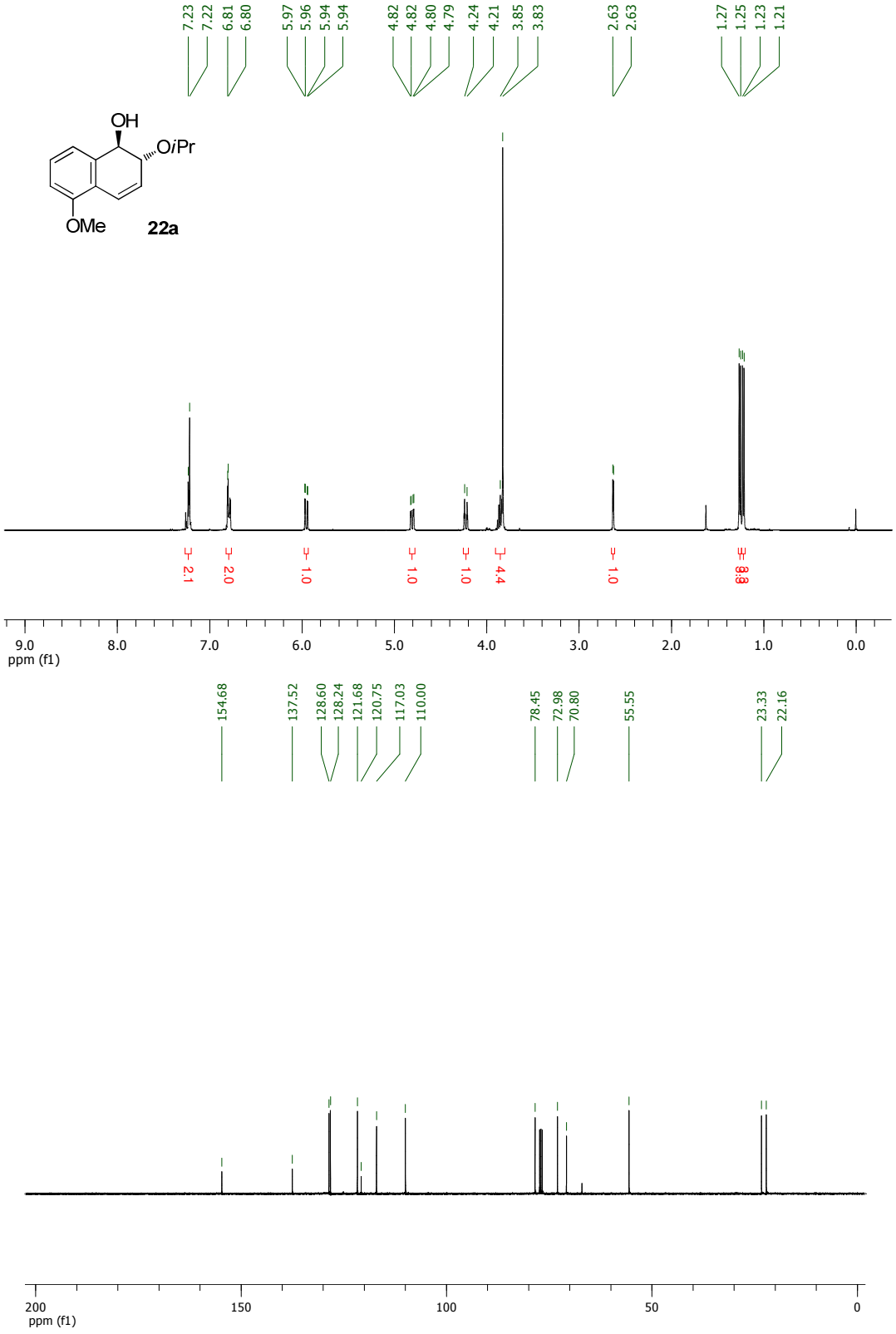
21a


7.26
7.24
7.22
7.21
7.19
6.88
6.87
6.85
6.85
6.81
6.79
6.05
6.04
6.02
6.02
4.86
4.85
4.84
4.83
4.10
4.10
4.09
4.08
4.07
4.06
3.83
3.50
2.60
2.59
OH
OMe
OMe
21a
2.0
1.0
1.0
1.0
3.4
3.3
1.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)
154.8
137.3
128.8
125.5
122.3
120.6
117.4
110.2
81.8
72.5
56.7
55.6
200
150
100
50
0
ppm (f1)

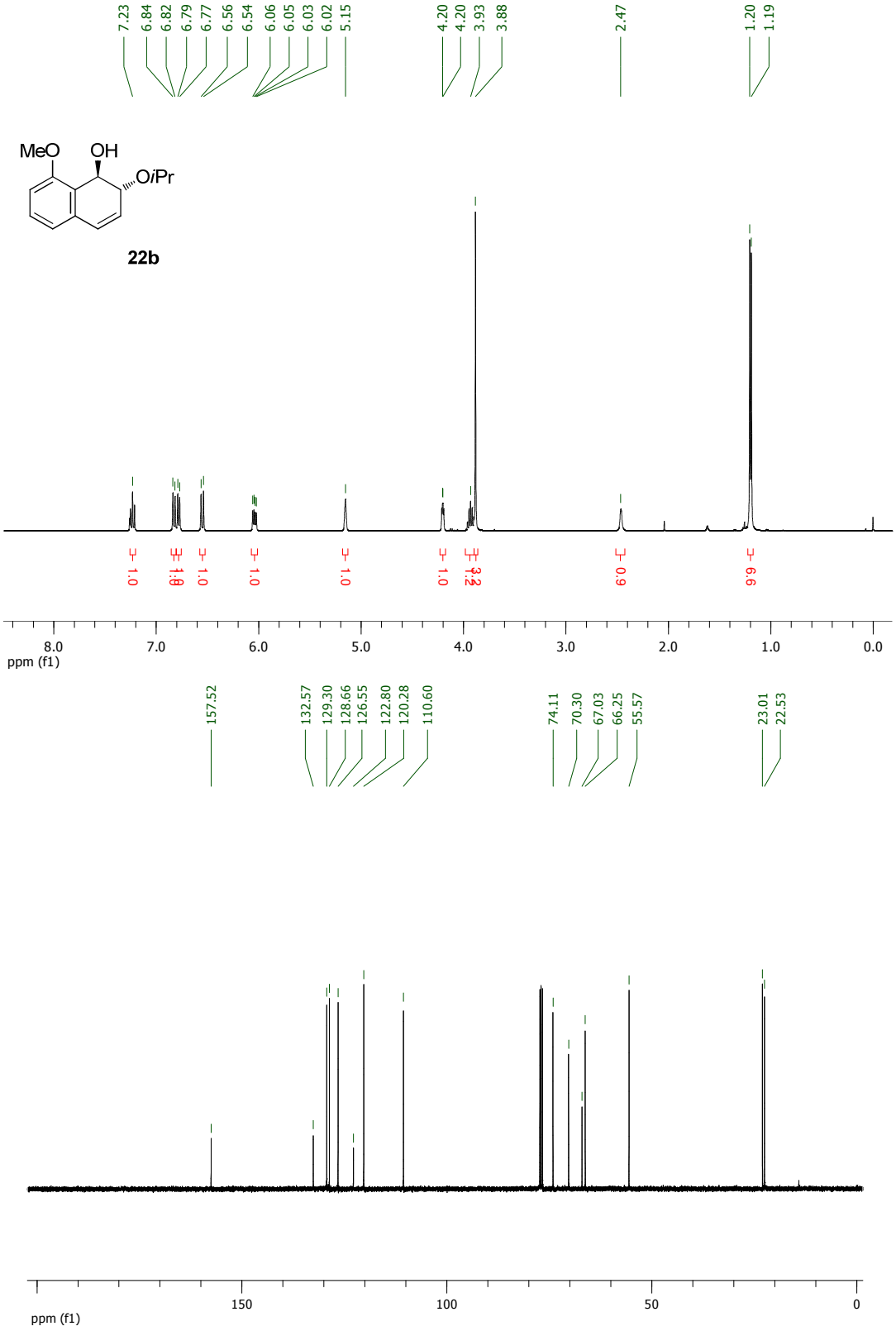
21b


7.26
7.24
7.22
6.85
6.83
6.81
6.79
6.62
6.60
6.13
6.12
6.11
6.10
5.22
4.08
4.08
4.07
4.06
3.88
2.46
MeO
OH
OMe
21b
1.1
1.0
1.0
1.0
1.0
3.2
3.1
0.9
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)
157.5
132.4
129.6
129.5
125.1
122.7
120.3
110.8
77.4
64.8
56.4
55.6
200
150
100
50
0
ppm (f1)

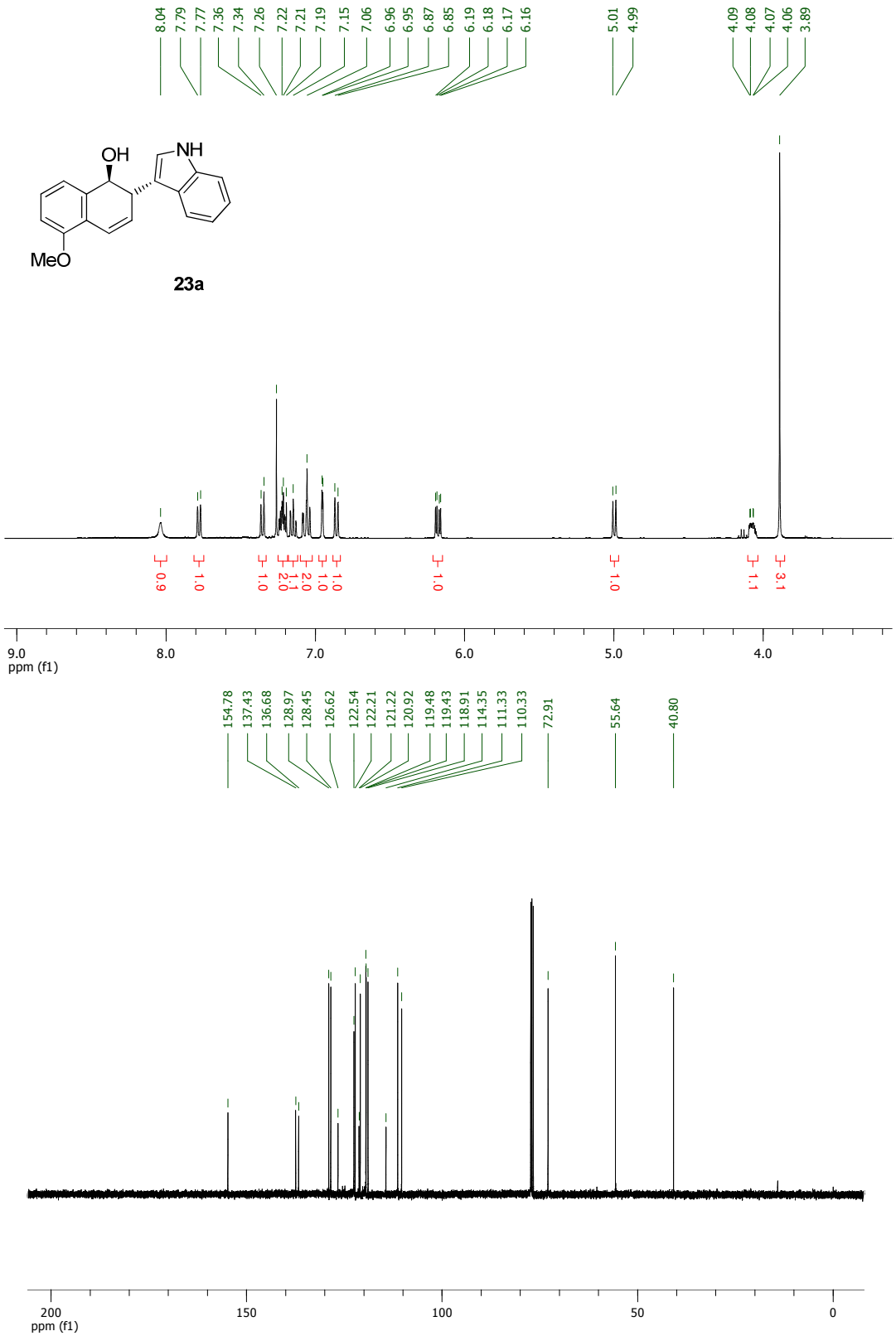
22a


7.23
7.22
6.81
6.80
5.97
5.96
5.94
5.94
4.82
4.82
4.80
4.79
4.24
4.21
3.85
3.83
2.63
2.63
1.27
1.25
1.23
1.21
OH
O*i*Pr
OMe
22a
2.1
2.0
1.0
1.0
1.0
4.4
1.0
8.3
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)
154.68
137.52
128.60
128.24
121.68
120.75
117.03
110.00
78.45
72.98
70.80
55.55
23.33
22.16
200
150
100
50
0
ppm (f1)

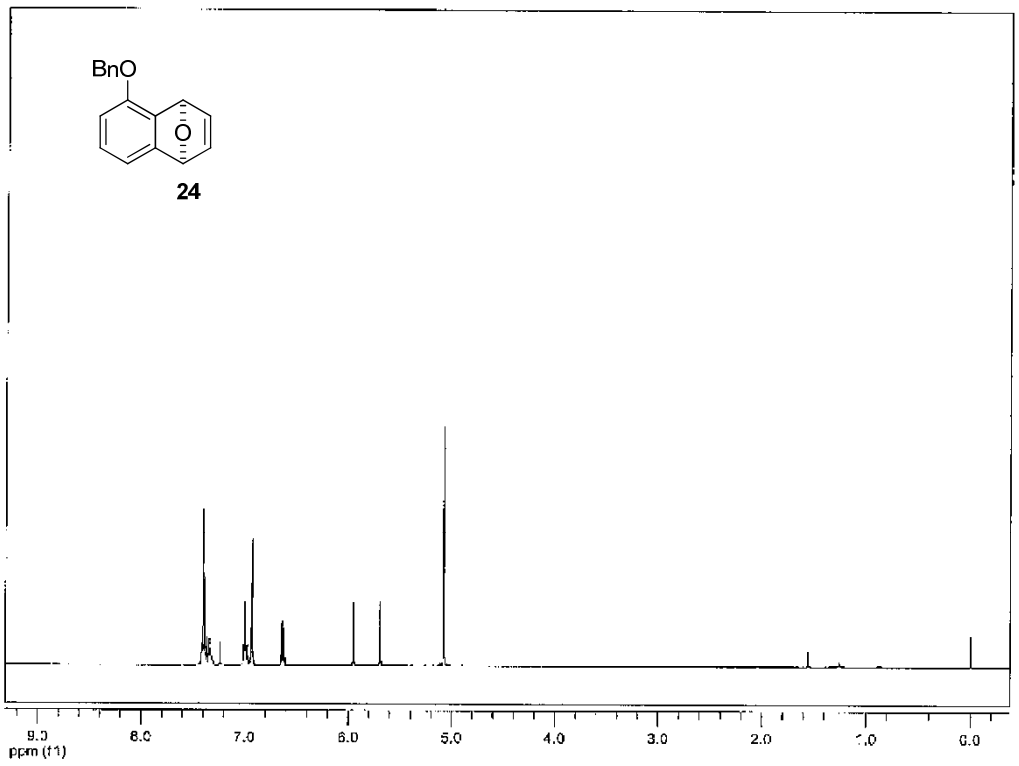
22b

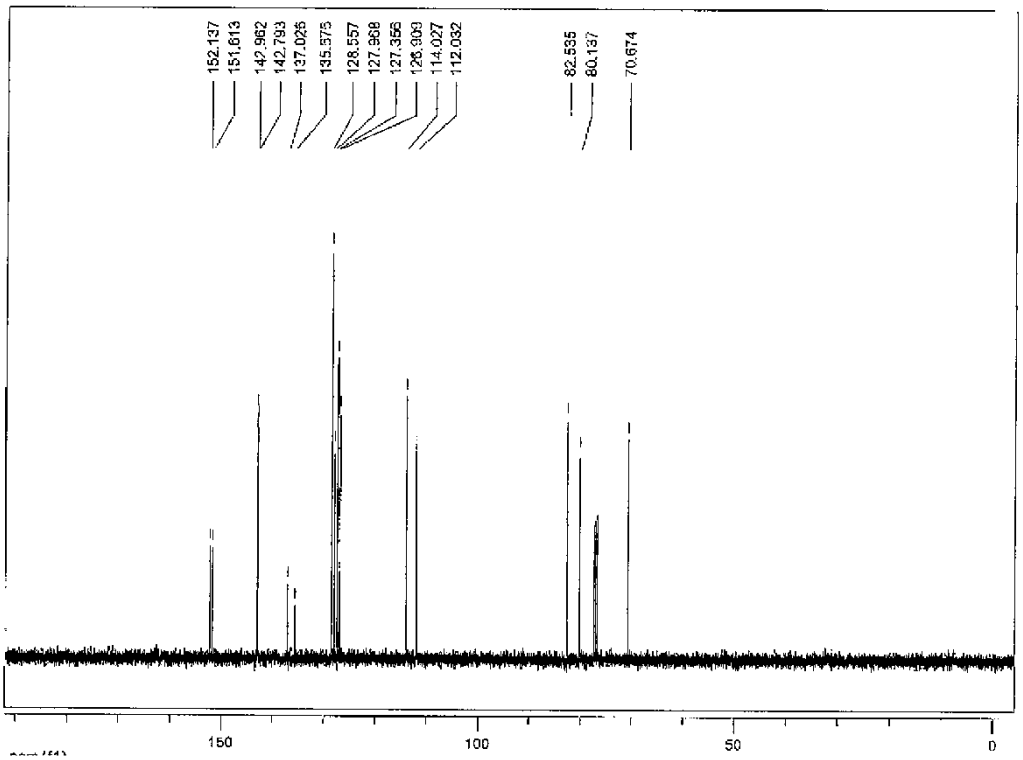

7.23
6.84
6.82
6.79
6.77
6.56
6.54
6.06
6.05
6.03
6.02
5.15
4.20
4.20
3.93
3.88
2.47
1.20
1.19
MeO
OH
OiPr
22b
1.0
1.0
1.0
1.0
1.0
0.9
6.6
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)
157.52
132.57
129.30
128.66
126.55
122.80
120.28
110.60
74.11
70.30
67.03
66.25
55.57
23.01
22.53
150
100
50
0
ppm (f1)

23a

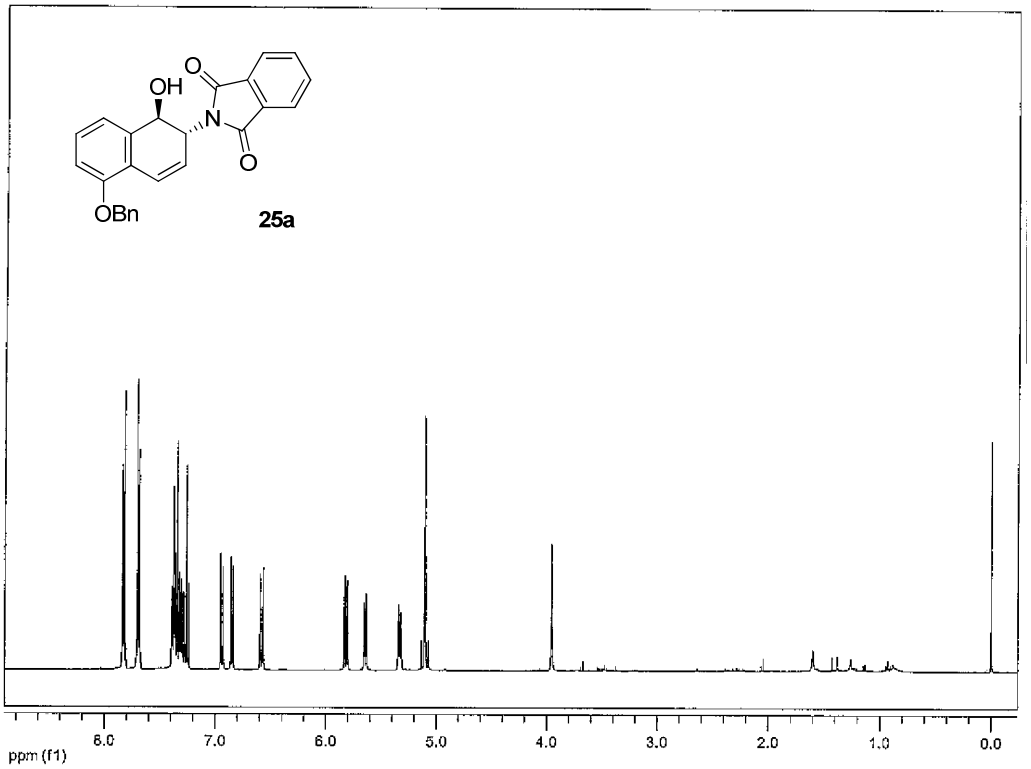

8.04
7.79
7.77
7.36
7.34
7.26
7.22
7.21
7.19
7.15
7.06
6.96
6.95
6.87
6.85
6.19
6.18
6.17
6.16
5.01
4.99
4.09
4.08
4.07
4.06
3.89
OH
NH
MeO
23a
0.9
1.0
1.0
2.0
1.1
1.0
1.0
1.0
1.0
1.1
3.1
9.0
8.0
7.0
6.0
5.0
4.0
ppm (f1)
154.78
137.43
136.68
128.97
128.45
126.62
122.54
122.21
121.22
120.92
119.48
119.43
118.91
114.35
111.33
110.33
72.91
55.64
40.80
200
150
100
50
0
ppm (f1)

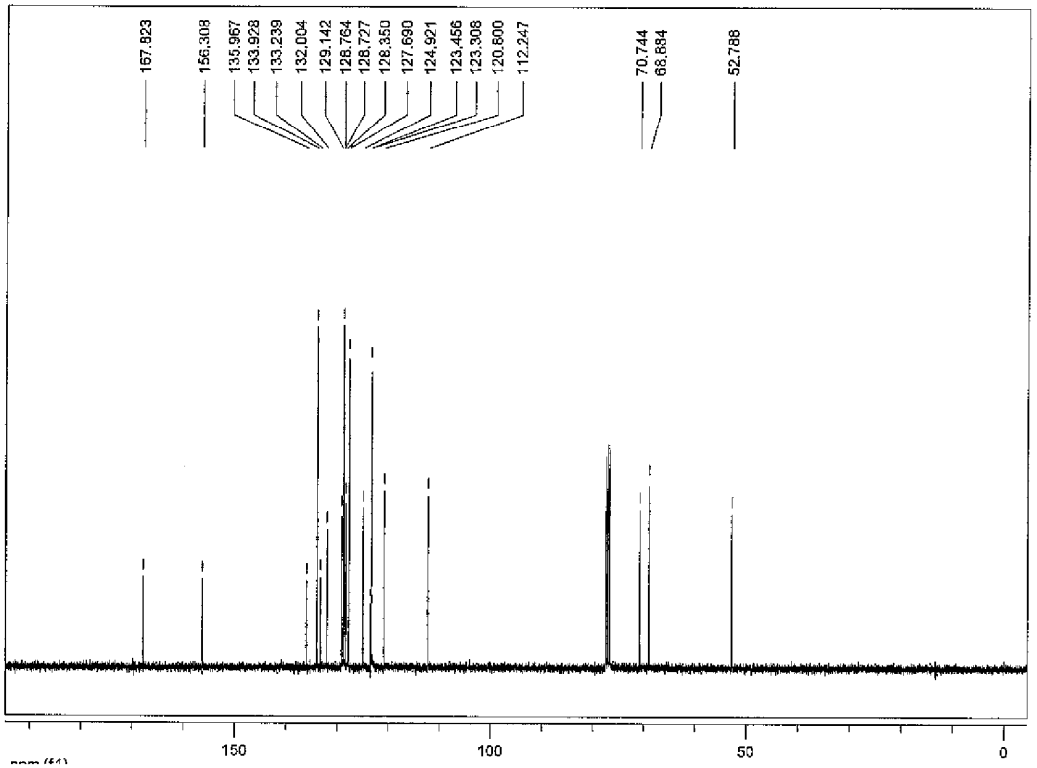
(±)-24


BnO
O
24
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

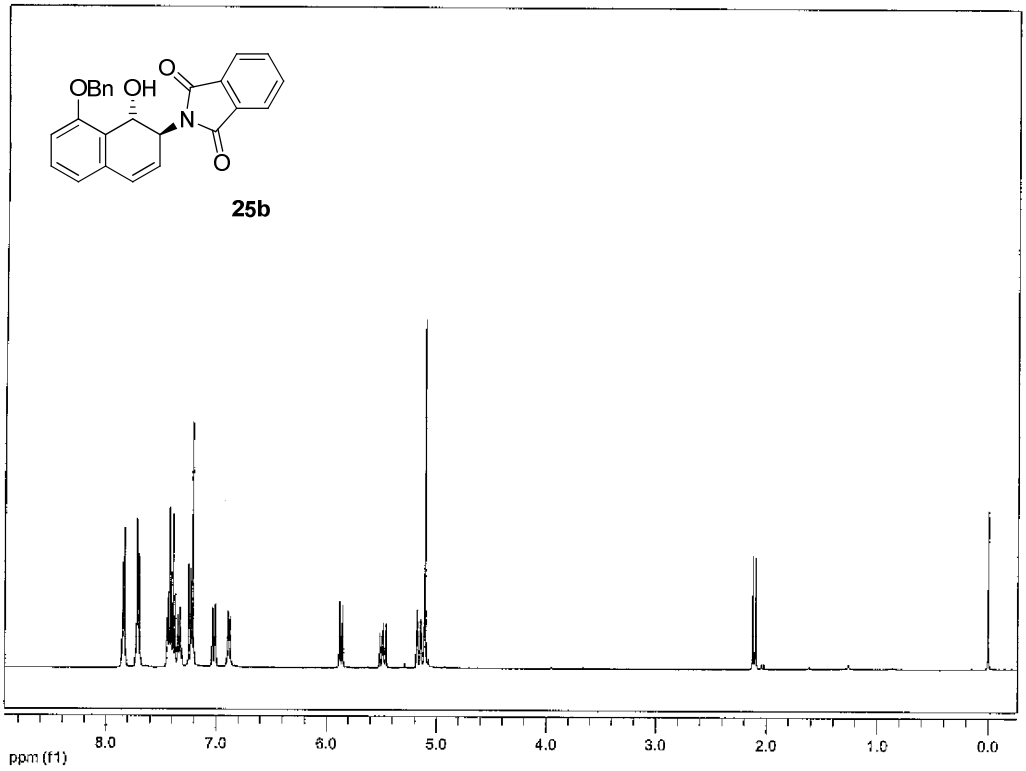

152.137
151.613
142.962
142.793
137.026
135.575
128.557
127.968
127.356
126.909
114.027
112.032
82.535
80.137
70.674
150
100
50
0

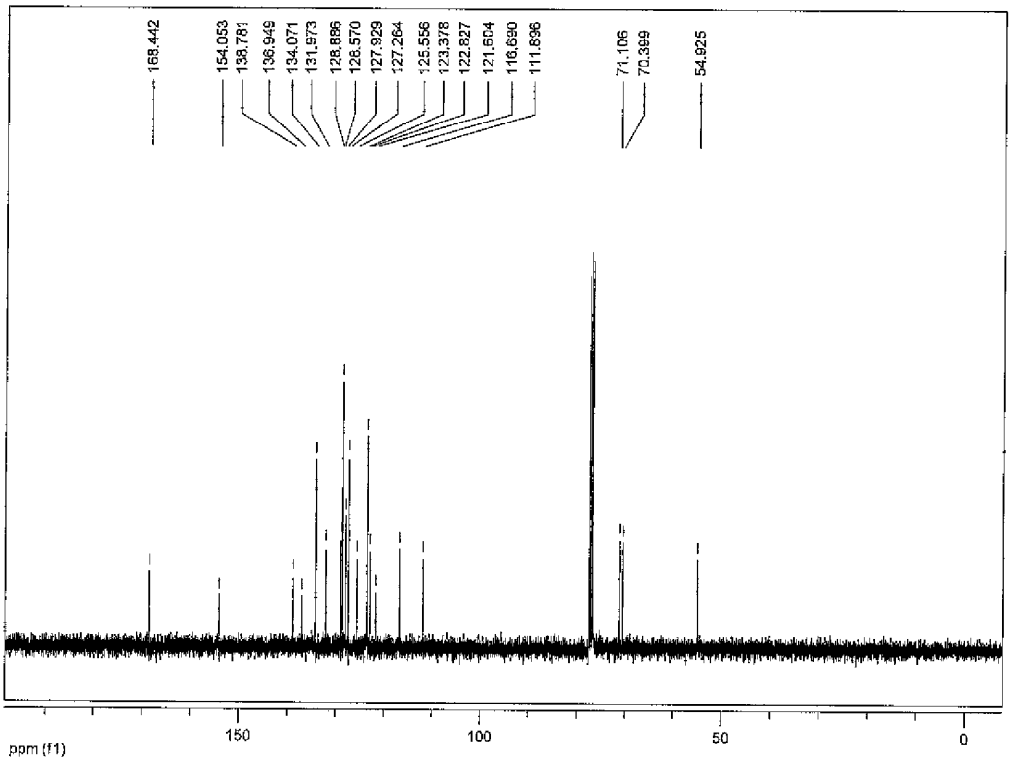
25a


OH
O
N
O
OBn
25a
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


167.823
156.308
135.967
133.928
133.239
132.004
129.142
128.764
128.727
128.350
127.690
124.921
123.456
123.308
120.600
112.247
70.744
68.884
52.788
150
100
50
0

25b


OBn
OH
O
N
O
25b
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


168.442
154.053
138.781
136.949
134.071
131.973
128.886
128.570
127.929
127.264
125.556
123.378
122.827
121.604
116.690
111.696
71.106
70.399
54.925
150
100
50
0
ppm (f1)