Supplementary Information

Site-Selective Amination and/or Nitrilation *via* Metal-Free, C(sp^2)–C(sp^3) Cleavage of Benzylic and Allylic Alcohols

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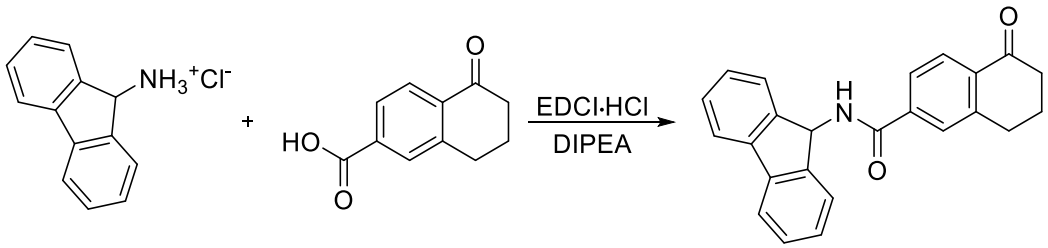
Materials and Methods

Proton and carbon nuclear magnetic resonance (^{1}H and ^{13}C NMR) spectra were obtained on a Varian Inova 400 spectrometer at 400 MHz and 101 MHz, respectively, or a Varian Inova 500 at 500 MHz and 126 MHz, respectively, in $CDCl_3$, unless otherwise stated. The ^{1}H and ^{13}C NMR chemical shifts were measured relative to residual $CHCl_3$ as the internal reference (^{1}H: δ = 7.26 ppm; ^{13}C: δ = 77.00 ppm), unless otherwise stated. ^{1}H NMR data are reported as chemical shift (ppm), multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, app q = apparent quartet, p = pentet, app p = apparent pentet, m = multiplet), and coupling constant (Hz). High resolution mass spectra (HRMS) were obtained using a TripleTOF®6600 Quadrupole mass spectrometer. Melting points were measured using an OptiMelt (Stanford Research Systems) and are uncorrected. Analytical thin layer chromatography (TLC) used EMD Chemicals TLC silica gel 60 F_{254} plates (0.040-0.063 mm) with visualization by UV light and/or $KMNO_4$, phosphomolybdic acid (PMA) and/or ninhydrin solution(s) followed by heating. Chromatographic purifications utilized flash chromatography using pre-packed SiO_2 columns on a medium pressure, automated chromatograph equipped with a UV detector. Unless otherwise noted, yields refer to isolated, purified material whose spectral data were consistent with assigned structures or, if known, were in agreement with literature values. All reactions were conducted under an argon atmosphere in oven-dried glassware with magnetic stirring, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification. Reaction solvents were purified via passage through activated, neutral alumina columns and stored under argon. Hydroxylamine-*O*-sulfonic acid (HOSA) was purchased from Aldrich Chem. Co. while 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) was purchased from Oakwood Chemicals and used without purification.

Experimental Procedures and Analytical Data

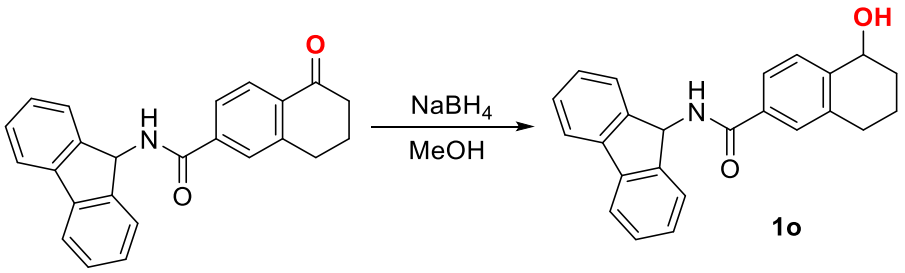
General Procedure for Ketone Reductions

To a stirring, 0 °C solution of ketone (1 equiv) in MeOH (0.5 M) or mixture of THF/MeOH was slowly added $NaBH_4$ (2 equiv) portionwise. After 10 min, the reaction mixture was warmed to rt and maintained until all ketone was consumed (2-16 h). All volatiles were removed *in vacuo* and the residue was purified using a commercial pre-packed SiO_2 column on a medium pressure, automated chromatograph using EtOAc/hexanes to furnish the benzyl alcohol in the indicated yield.

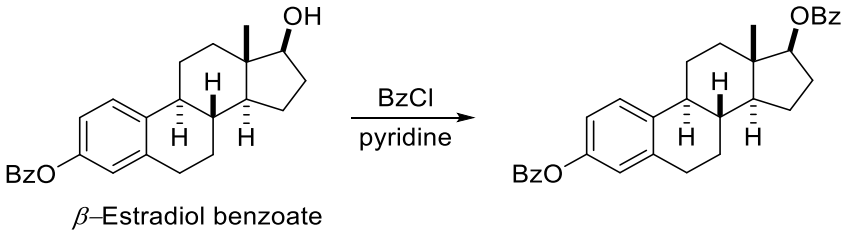


***N*-(9*H*-Fluoren-9-yl)-5-oxo-5,6,7,8-tetrahydronaphthalene-2-carboxamide:** EDCI hydrochloride (241 mg, 1.263 mmol) was added to a 0 °C solution of 6-amino-3,4-dihydronaphthalen-1(2H)-one hydrochloride (274 mg, 1.263 mmol) and 5-oxo-5,6,7,8-tetrahydronaphthalene-2-carboxylic acid (200 mg, 5.357 mmol) in CH_2Cl_2 (5 mL) followed by DIPEA (548 µL, 3.156 mmol). After stirring at rt for 16 h, the reaction mixture was concentrated in *vacuo* and the residue was purified chromatographically using 40% EtOAc/hexanes to give *N*-

(9*H*-fluoren-9-yl)-5-oxo-5,6,7,8-tetrahydronaphthalene-2-carboxamide (267 mg, 72%) as a white solid, mp 119-121 °C. TLC: $R_f \approx 0.7$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.1 Hz, 1H), 7.80–7.58 (m, 5H), 7.43 (td, *J* = 7.6, 1.2 Hz, 2H), 7.33 (td, *J* = 7.4, 1.2 Hz, 2H), 6.44–6.38 (m, 2H), 3.01 (t, *J* = 6.1 Hz, 2H), 2.67 (dd, *J* = 7.3, 5.7 Hz, 2H), 2.15 (p, *J* = 6.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.79, 167.50, 145.01, 144.19, 140.87, 138.24, 134.88, 129.08, 128.18, 128.06, 127.81, 125.39, 124.91, 120.28, 55.35, 39.22, 29.81, 23.18. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{24}H_{21}NO_2^+$ 356.1645; found, 356.1642.

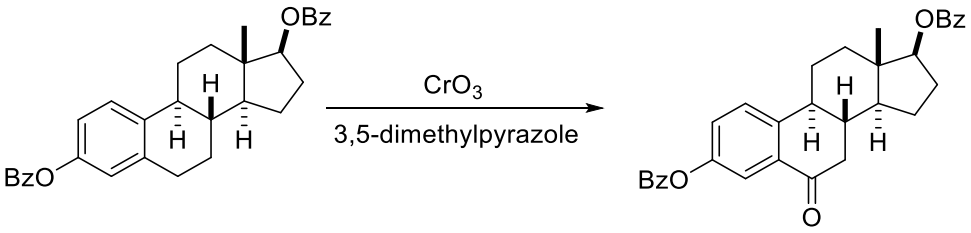


***N*-(9*H*-Fluoren-9-yl)-5-hydroxy-5,6,7,8-tetrahydronaphthalene-2-carboxamide (1o):** Following the general benzyl alcohol procedure, *N*-(9*H*-fluoren-9-yl)-5-oxo-5,6,7,8-tetrahydronaphthalene-2-carboxamide (100 mg, 0.141 mmol), $NaBH_4$ (10 mg, 0.283 mmol) were stirred at 0 ºC to rt in 2:1 mixture of MeOH : THF (4 mL) for 4 h. Chromatographic purification of the crude product afforded *N*-(9*H*-fluoren-9-yl)-5-hydroxy-5,6,7,8-tetrahydronaphthalene-2-carboxamide **(1o)** (80 mg, 80%) as a viscous oil TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 2H), 7.66 – 7.56 (m, 4H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.32 (td, *J* = 7.5, 1.1 Hz, 2H), 6.46 (d, *J* = 8.9 Hz, 1H), 6.35 (d, *J* = 8.9 Hz, 1H), 4.79 (t, *J* = 5.3 Hz, 1H), 2.91 – 2.69 (m, 2H), 2.10–1.73 (m, 4H), 1.63 (br s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.07, 144.51, 142.78, 140.83, 137.80, 133.24, 128.95, 128.91, 128.02, 128.01, 125.42, 124.70, 120.21, 68.15, 55.23, 32.36, 29.34, 19.03. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{24}H_{19}NO_2^+$ 354.1489; found, 354.1488.

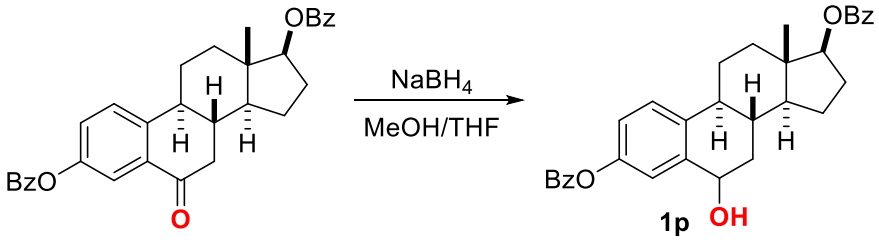


β–Estradiol benzoate

8*R*,9*S*,13*S*,14*S*,17*S*)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthrene-3,17-diyl dibenzoate (*β*-estradiol dibenzoate): To a stirring solution of *β*-estradiol benzoate (300 mg, 0.797 mmol; Aldrich Chem. Co.) in pyridine (5 mL) was slowly added benzoyl chloride (138 µL, 1.195 mmol) at 0 °C. After stirring at rt for 4 h, the reaction mixture was concentrated in *vacuo*, the residue was purified chromatographically using a gradient of 7-10% EtOAc/hexanes as eluent to give (8*R*,9*S*,13*S*,14*S*,17*S*)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*- cyclopenta[a]phenanthrene-3,17-diyl dibenzoate (310 mg, 81%) as a white solid, mp 134-135 °C (lit.[1] 134-135 °C), whose spectral data were in agreement with literature values.[2] TLC: $R_f \approx 0.6$ (10% EtOAc/hexanes).

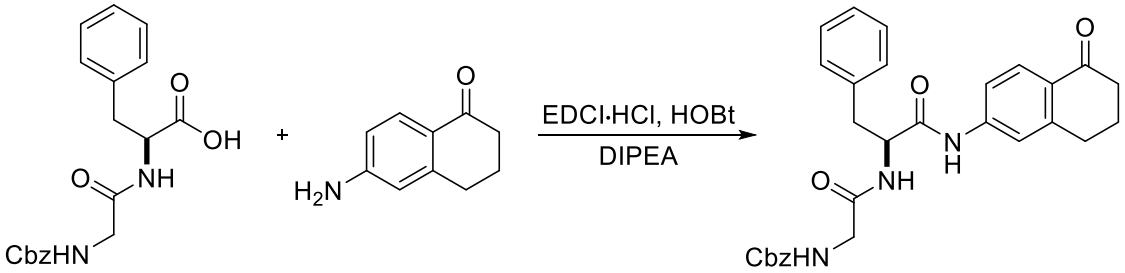


(8*R*,9*S*,13*S*,14*S*,17*S*)-13-methyl-6-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthrene-3,17-diyl dibenzoate: To a stirring solution of chromic anhydride (416 mg, 4.166 mmol) in CH_2Cl_2 (10 mL) was added 3,5-dimethylpyrazole (399 mg, 4.166 mmol) at rt.[3] After 15 min, the reaction mixture was cooled to 0 ºC and a solution of 8*R*,9*S*,13*S*,14*S*,17*S*)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthrene-3,17-diyl dibenzoate (estradiol dibenzoate) (200 mg, 0.416 mmol) in CH_2Cl_2 (5 mL) was added. After stirring at rt for 12 h, the reaction mixture was concentrated in *vacuo* and the residue was purified chromatographically using a gradient of 30-40% EtOAc/hexanes as eluent to give (8*R*,9*S*,13*S*,14*S*,17*S*)-13-methyl-6-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene-3,17-diyl dibenzoate (86 mg, 42%) as a white solid, mp 157-159 °C, and unreacted estradiol dibenzoate (41 mg, 20%). TLC: $R_f \approx 0.5$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.4 Hz, 2H), 8.06 (d, *J* = 7.3 Hz, 2H), 7.90 (d, *J* = 2.6 Hz, 1H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.61–7.36 (m, 7H), 4.99 (t, *J* = 8.4 Hz, 1H), 2.82 (dd, *J* = 16.9, 3.3 Hz, 1H), 2.62 (td, *J* = 11.1, 4.5 Hz, 1H), 2.49–2.24 (m, 3H), 2.15–1.98 (m, 2H), 1.90–1.39 (m, 6H), 1.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.93, 166.59, 165.25, 149.78, 144.43, 133.89, 133.87, 133.04, 130.67, 130.34, 129.68, 129.36, 128.75, 128.51, 127.26, 126.93, 120.24, 82.78, 49.95, 44.01, 43.30, 43.19, 39.72, 36.69, 27.73, 25.52, 23.27, 12.31. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{32}H_{30}O_5^+$ 495.2166; found, 495.2167.

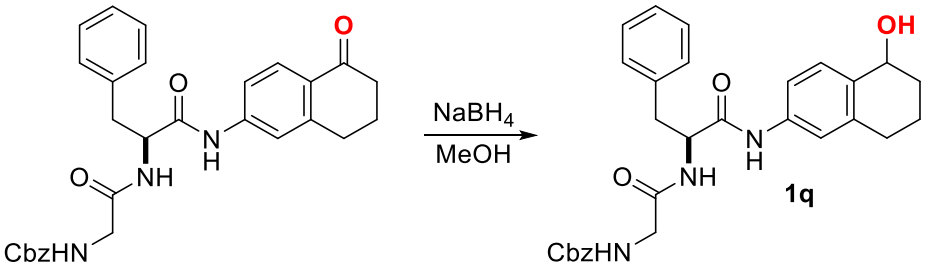


(8*R*,9*S*,13*S*,14*S*,17*S*)-6-hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthrene-3,17-diyl dibenzoate (1p): Following the general ketone reduction procedure, (8*R*,9*S*,13*S*,14*S*,17*S*)-13-methyl-6-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthrene-3,17-diyl dibenzoate (40 mg, 0.080 mmol) and $NaBH_4$ (3.6 mg, 0.097 mmol) were stirred at rt in a mixture of MeOH/THF (2 mL, 1:1) for 2 h. Chromatographic purification of the crude product afforded (8*R*,9*S*,13*S*,14*S*,17*S*)-6-hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H* cyclopenta[a]phenanthrene-3,17-diyl dibenzoate (36 mg, 91%, mixture of diasteremers) **(1p)** as a viscous oil. TLC: $R_f \approx 0.5$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.7 Hz, 2H), 8.06 (d, *J* = 7.7 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.60–7.40 (m, 6H), 7.35 (d, *J* = 8.6 Hz, 1H), 7.14–7.02 (m, 1H), 5.05–4.79 (m, 2H), 2.50–2.25 (m, 4H), 2.08–1.94 (m, 1H), 1.90–1.63 (m, 4H), 1.61–1.34 (m, 5H), 1.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.65, 165.56, 149.48, 141.29, 137.66, 133.71, 132.98, 130.73, 130.29, 129.67, 128.68, 128.48, 126.64, 120.80, 120.41, 83.11, 69.86, 49.35, 44.59, 43.39, 38.09, 37.86,

37.01, 36.15, 34.79, 32.77, 31.72, 29.19, 27.82, 26.16, 25.41, 23.48, 20.84, 14.27, 12.44. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{32}H_{32}O_5^+$ 519.2142; found, 519.2143.

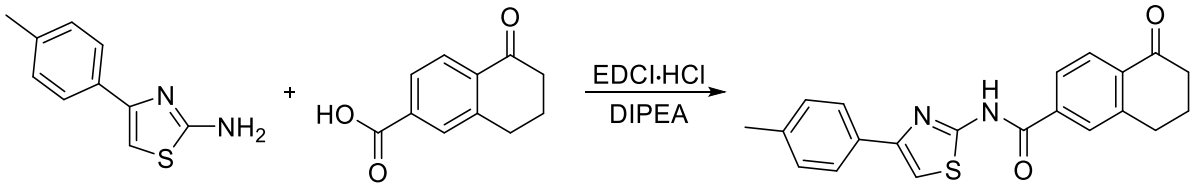


Benzyl (S)-(2-oxo-2-((1-oxo-1-((5-oxo-5,6,7,8-tetrahydronaphthalen-2-yl)amino)-3-phenylpropan-2-yl)amino)ethyl)carbamate(1s): EDCI hydrochloride (284 mg, 1.490 mmol) and hydroxybenzotriazole (HOBt) (201 mg, 1.490 mmol) were added to a 0 °C solution of 6-amino-3,4-dihydronaphthalen-1(2*H*)-one (274 mg, 1.263 mmol) and ((benzyloxy)carbonyl)glycyl-*L*-phenylalanine (530 mg, 1.490 mmol) in CH_2Cl_2 (5 mL) followed by DIPEA (647 µL, 3.726 mmol). After stirring at rt for 24 h, the reaction mixture was concentrated in *vacuo* and the residue was purified chromatographically using EtOAc to give benzyl (*S*)-(2-oxo-2-((1-oxo-1-((5-oxo-5,6,7,8-tetrahydronaphthalen-2-yl)amino)-3-phenylpropan-2-yl)amino)ethyl)carbamate as a viscous oil (440 mg, 71%). TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 28.4 Hz, 1H), 7.92 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.56 (s, 1H), 7.43–7.07 (m, 10H), 7.02–6.98 (m, 1H), 5.51 (t, *J* = 5.5 Hz, 1H), 5.08 (s, 2H), 4.90–4.78 (m, 1H), 3.84 (d, *J* = 5.5 Hz, 2H), 3.21–3.06 (m, 2H), 2.86 (t, *J* = 6.0 Hz, 2H), 2.59 (t, *J* = 6.4 Hz, 2H), 2.07 (p, *J* = 6.4 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.56, 169.66, 169.44, 157.06, 146.17, 141.98, 136.13, 136.11, 135.87, 129.34, 129.03, 128.99, 128.95, 128.77, 128.58, 128.25, 127.43, 127.39, 118.96, 118.03, 67.67, 55.33, 44.92, 39.06, 37.94, 30.06, 23.34. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{29}H_{29}N_3O_5^+$ 500.2180; found, 500.2190.

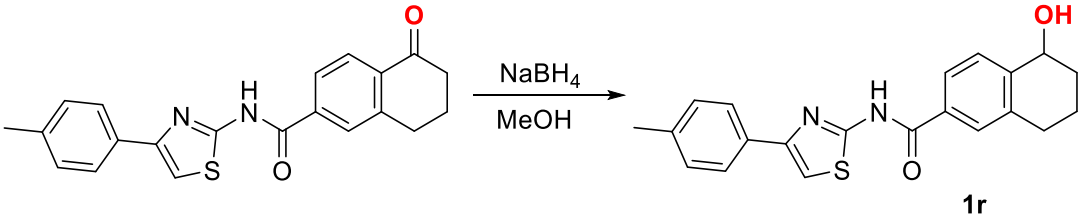


Benzyl (2-(2*S*)-1-((5-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethyl)carbamate (1q): Following the general ketone reduction procedure, benzyl (*S*)-(2-oxo-2-((1-oxo-1-((5-oxo-5,6,7,8-tetrahydronaphthalen-2-yl)amino)-3-phenylpropan-2-yl)amino)ethyl)carbamate (60 mg, 0.120 mmol) and $NaBH_4$ (8.8 mg, 0.240 mmol) were stirred in MeOH (2 mL). After 4 h, all volatiles were removed *in vacuo* and the residue was purified chromatographically to afford benzyl (2-(2*S*)-1-((5-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethyl)carbamate **(1q)** (46 mg, 78%, mixture of distereomers) as an oil. TLC: $R_f \approx 0.6$ (pure EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 11.9 Hz, 1H), 7.41–6.92 (m, 13H), 5.63–5.55 (m, 1H), 5.06 (s, 2H), 4.82 (q, *J* = 7.3 Hz, 1H), 4.67 (t, *J* = 4.4 Hz, 1H), 3.88–3.72 (m, 2H), 3.10 (t, *J* = 6.5 Hz, 1H),

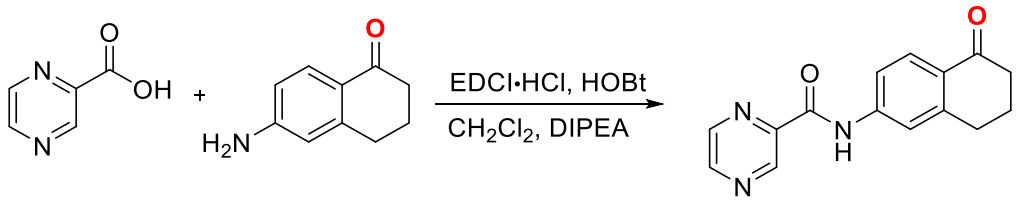
2.76–2.49 (m, 2H), 1.97–1.57 (m, 5H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.57, 169.16, 156.90, 138.06, 136.48, 136.38, 136.04, 135.36, 129.43, 128.90, 128.88, 128.72, 128.47, 128.27, 127.29, 120.45, 120.41, 118.43, 118.41, 118.39, 67.79, 67.50, 55.28, 44.72, 38.36, 32.34, 29.49, 29.46, 18.80, 18.77. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{29}H_{31}N_3O_5^+$ 502.2337; found, 502.2332.



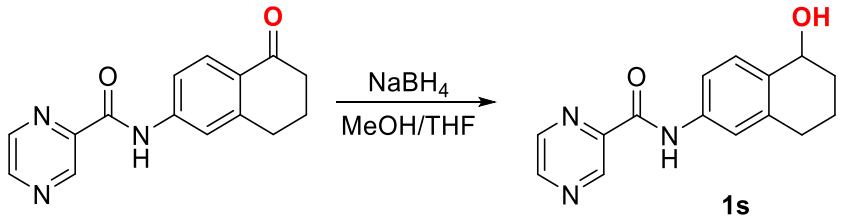
5-Oxo-*N*-(4-(p-tolyl)thiazol-2-yl)-5,6,7,8-tetrahydronaphthalene-2-carboxamide: EDCI hydrochloride (241 mg, 1.262 mmol) was added to a 0 °C solution of 4-(*p*-tolyl)thiazol-2-amine (299 mg, 1.578 mmol) and 5-oxo-5,6,7,8-tetrahydronaphthalene-2-carboxylic acid (200 mg, 1.052 mmol) in CH_2Cl_2 (5 mL) followed by DIPEA (365 µL, 0.357 mmol). After stirring at rt for 18 h, the reaction mixture was concentrated in *vacuo* and the residue was purified chromatographically using 40% EtOAc/hexanes to give 5-oxo-*N*-(4-(*p*-tolyl)thiazol-2-yl)-5,6,7,8-tetrahydronaphthalene-2-carboxamide (241 mg, 66%) as a yellow solid, mp 224-226 °C. TLC: R_f ≈ 0.4 (60% EtOAc/hexanes). ^{1}H NMR (400 MHz, CD_3OD + $CDCl_3$ 2:1) δ 8.09 (d, *J* = 8.1 Hz, 1H), 7.96–7.93 (m, 1H), 7.91 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 2H), 7.23 (s, 1H), 7.19 (d, *J* = 8.1 Hz, 2H), 3.08 (t, *J* = 6.0 Hz, 2H), 2.70 (t, *J* = 6.0 Hz, 2H), 2.35 (s, 3H), 2.23–2.13 (m, 2H); ^{13}C NMR (151 MHz, CD_3OD + $CDCl_3$ 2:1) δ 199.51, 146.00, 138.49, 137.34, 135.72, 132.39, 129.92, 129.44, 128.06, 126.59, 126.40, 107.96, 39.62, 30.14, 23.66, 21.34. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{21}H_{18}N_2O_2S^+$ 363.1162; found, 363.1162.



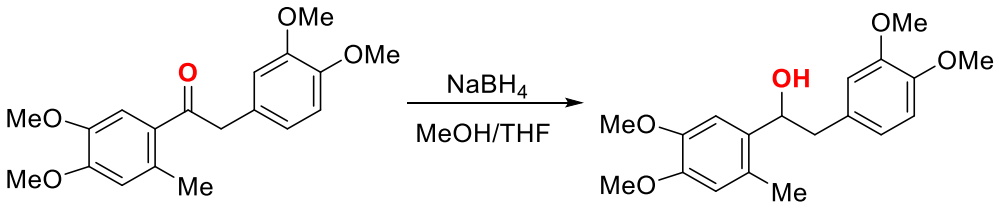
5-Hydroxy-*N*-(4-(p-tolyl)thiazol-2-yl)-5,6,7,8-tetrahydronaphthalene-2-carboxamide (1r): Following the general ketone reduction procedure, 5-oxo-*N*-(4-(*p*-tolyl)thiazol-2-yl)-5,6,7,8-tetrahydronaphthalene-2-carboxamide (100 mg, 0.287 mmol) and $NaBH_4$ (15 mg, 0.431 mmol) were stirred in MeOH (4 mL). After 2 h, all volatiles were removed *in vacuo* and the residue was purified chromatographically to afford 5-hydroxy-*N*-(4-(*p*-tolyl)thiazol-2-yl)-5,6,7,8-tetrahydronaphthalene-2-carboxamide **(1r)** (76 mg, 77%) as an yellow oil. TLC: R_f ≈ 0.4 (80% EtOAc/hexanes).^{1}H NMR (400 MHz, CD_3OD) δ 7.85–7.79 (m, 3H), 7.78–7.75 (m, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.33 (s, 1H), 7.21 (d, *J* = 7.9 Hz, 1H), 4.76 (dd, *J* = 6.8, 4.1 Hz, 1H), 2.95–2.75 (m, 2H), 2.10–1.96 (m, 2H), 1.92–1.75 (m, 2H); ^{13}C NMR (151 MHz, CD_3OD) δ 167.57, 159.88, 151.54, 145.47, 139.04, 138.83, 133.31, 132.39, 130.26, 130.04, 129.51, 127.05, 126.32, 108.10, 68.59, 33.21, 30.25, 21.26, 20.26. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{21}H_{20}N_2O_2^+$ 365.1318; found, 365.1318.



***N*-(5-Oxo-5,6,7,8-tetrahydronaphthalen-2-yl)pyrazine-2-carboxamide:** EDCI hydrochloride (284 mg, 1.490 mmol) and HOBt (201 mg, 3.726 mmol) were added to a 0 °C solution of 6-amino-3,4-dihydronaphthalen-1(2H)-one (200 mg, 1.242 mmol) and pyrazine-2-carboxylic acid (205 mg, 1.490 mmol) in CH_2Cl_2 (5 mL) followed by DIPEA (647 µL, 3.726 mmol). After stirring at rt for 18 h, the reaction mixture was concentrated in *vacuo* and the residue was purified chromatographically using a gradient of 50-70% EtOAc/hexanes as eluent to give *N*-(5-oxo-5,6,7,8-tetrahydronaphthalen-2-yl)pyrazine-2-carboxamide as a viscous oil (1.1 g, 82%). TLC: R_f ≈ 0.4 (60% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (br s, 1H), 9.51 (d, *J* = 1.5 Hz, 1H), 8.84 (d, *J* = 2.5 Hz, 1H), 8.64–8.56 (m, 1H), 8.07 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 1.5 Hz, 1H), 7.51 (dd, *J* = 8.5, 2.2 Hz, 1H), 3.00 (t, *J* = 6.1 Hz, 2H), 2.65 (t, *J* = 6.5 Hz, 2H), 2.15 (p, *J* = 6.3 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.43, 161.04, 148.04, 146.50, 144.90, 144.03, 142.57, 141.52, 129.37, 128.93, 118.82, 117.90, 39.09, 30.15, 23.37. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{15}H_{13}N_3O_2^+$ 268.1103; found, 268.1081.

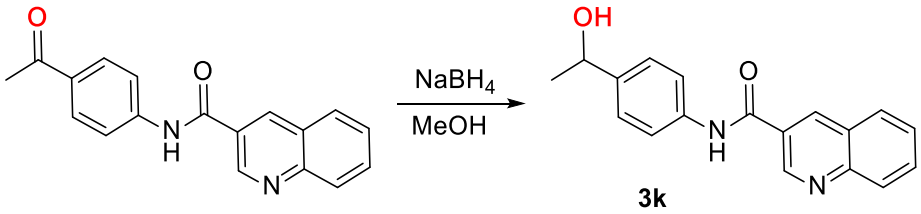


***N*-(5-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)pyrazine-2-carboxamide (1s):** Following the general ketone reduction procedure, *N*-(5-oxo-5,6,7,8-tetrahydronaphthalen-2-yl)pyrazine-2-carboxamide[4] (100 mg, 0.374 mmol) and $NaBH_4$ (27 mg, 0.748 mmol) were stirred at rt in MeOH/THF (4 mL, 1:1). After 2 h, all volatiles were removed *in vacuo* and the residue was purified chromatographically using EtOAc as eluant to afford *N*-(5-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)pyrazine-2-carboxamide (**1s**) (75 mg, 75%) as a yellow solid, mp 150-152 °C. TLC: R_f ≈ 0.4 (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, CD_3OD) δ 9.32 (s, 1H), 8.81 (d, *J* = 2.5 Hz, 1H), 8.73–8.71 (m, 1H), 7.62–7.52 (m, 2H), 7.42 (d, *J* = 8.3 Hz, 1H), 4.70 (dd, *J* = 6.2, 3.7 Hz, 1H), 2.91–2.66 (m, 2H), 2.06–1.70 (m, 4H); ^{13}C NMR (101 MHz, CD_3OD) δ 163.09, 148.57, 146.51, 145.03, 144.58, 139.11, 137.76, 137.00, 130.47, 121.54, 119.53, 68.38, 33.47, 30.50, 20.09. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{15}H_{15}N_3O_2^+$ 270.1237; found, 270.1241.



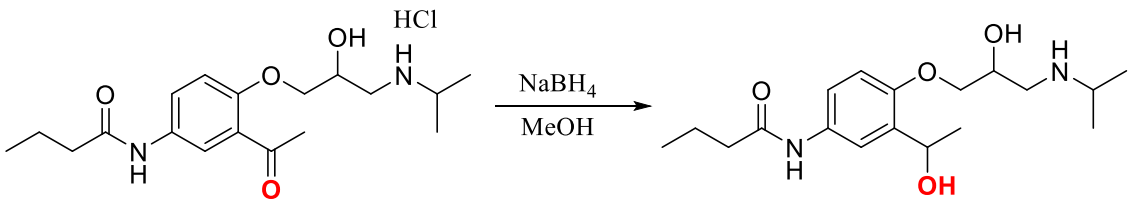
3e

1-(4,5-Dimethoxy-2-methylphenyl)-2-(3,4-dimethoxyphenyl)ethan-1-ol (3e): Following the general ketone reduction procedure, 1-(4,5-dimethoxy-2-methylphenyl)-2-(3,4-dimethoxyphenyl)ethan-1-one[5] (100 mg, 0.316 mmol) and $NaBH_4$ (17 mg, 0.474 mmol) were stirred at rt in a mixture of MeOH/THF (4 mL, 3:1) for 2 h. Chromatographic purification of the crude product afforded methylphenyl)-2-(3,4-dimethoxyphenyl)ethan-1-ol **(3e)** (72 mg, 72%) as a viscous oil. TLC: $R_f \approx 0.5$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (s, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.72 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.62–6.57 (m, 2H), 5.02 (dd, *J* = 7.7, 5.2 Hz, 1H), 3.86 (s, 3H), 3.84 (s, 6H), 3.78 (s, 3H), 2.93–2.81 (m, 2H), 2.13 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.87, 147.87, 147.81, 147.45, 134.05, 130.74, 126.62, 121.53, 113.39, 112.86, 111.33, 108.91, 71.59, 56.09, 55.98, 55.96, 55.85, 44.80, 18.46. HRMS (ESI, *m/z*): calcd. for $[M+Na]^+$, $C_{19}H_{24}O_5^+$ 355.1516; found, 356.1513.



3k

***N*-(4-(1-Hydroxyethyl)phenyl)quinoline-3-carboxamide (3k):** Following the general ketone reduction procedure, *N*-(4-acetylphenyl)quinoline-3-carboxamide (100 mg, 0.344 mmol) and $NaBH_4$ (19 mg, 0.517 mmol) were stirred in MeOH (2 mL). After 4 h, all volatiles were removed *in vacuo* and the residue was purified chromatographically to afford *N*-(4-(1-hydroxyethyl)phenyl)quinoline-3-carboxamide (**3k**) (80 mg, 80%) as a solid, mp 202-204 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 9.33 (d, *J* = 2.3 Hz, 1H), 8.93 (d, *J* = 2.3 Hz, 1H), 8.12 (dd, *J* = 8.3, 5.0 Hz, 2H), 7.91 (t, *J* = 7.7 Hz, 1H), 7.77–7.69 (m, 3H), 7.41 (d, *J* = 8.2 Hz, 2H), 4.88–4.81 (m, 1H), 1.46 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (151 MHz, CD_3OD) δ 166.40, 149.97, 149.75, 144.21, 138.60, 137.94, 133.03, 130.40, 129.33, 129.23, 129.05, 128.48, 127.05, 122.11, 70.48, 25.56. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{18}H_{16}N_2O_2^+$ 293.1285; found, 293.1289.

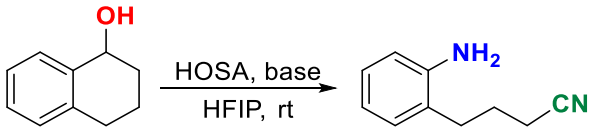


Acebutolol hydrochloride

3o

***N*-(4-(2-Hydroxy-3-(isopropylamino)propoxy)-3-(1-hydroxyethyl)phenyl)butyramide (3o):** Following the general ketone reduction procedure, Acebutolol hydrochloride (100 mg, 0.268 mmol) and $NaBH_4$ (14 mg, 0.402 mmol) were stirred at rt in a mixture of MeOH (2 mL) for 4 h. Chromatographic purification of the crude product afforded *N*-(4-(2-hydroxy-3-(isopropylamino)propoxy)-3-(1-hydroxyethyl)phenyl)butyramide **(3o)** (1:1 dr by ^{13}C NMR, 83 mg, 83%) as a viscous oil whose spectral data were in agreement with literature values.[6] TLC: $R_f \approx 0.4$ (20% MeOH/CH_2Cl_2). ^1H NMR (400 MHz, CD_3OD) δ 7.53 (d, *J* = 2.6 Hz, 1H), 7.46 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.89 (d, *J* = 8.8 Hz, 1H), 5.18 (q, *J* = 6.4 Hz, 1H), 4.12–4.07 (m, 1H), 4.02–3.91 (m, 2H), 3.35 (s, 1H), 2.92–2.80 (m, 2H), 2.74–2.65 (m, 1H), 2.32 (t, *J* = 7.4 Hz, 2H) 1.72 (q, *J* = 7.4 Hz, 2H), 1.42 (d, *J* = 6.5 Hz, 3H), 1.19 (s, 1H), 1.11 (d, *J* = 4.2 Hz, 6H), 1.00 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 174.31, 153.32, 136.26, 136.25, 133.19, 121.40, 119.80, 119.78, 112.91, 112.87, 72.41, 72.40, 69.85, 69.80, 65.31, 65.26, 51.01, 50.98, 49.92, 49.91, 49.85, 39.74, 30.91, 24.01, 23.97, 22.60, 22.58, 22.43, 22.40, 20.41, 14.02.

Optimization Experiments

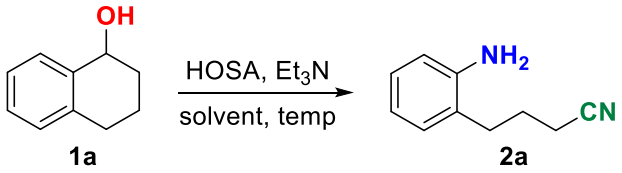


1a **2a**

Base Screening General Procedure: To a stirring, 0 °C solution of HOSA (0.8 mmol, 2.5 equiv) in HFIP (2 mL) was added the indicated base (0.8 mmol, 2.5 equiv) under an argon atmosphere. After 15 min, **1a** (0.3 mmol, 1 equiv) was added and the reaction was continued at rt until complete consumption of **1a** (4-24 h, monitored by TLC). The reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with saturated aq. Na_2CO_3 (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified chromatographically using MeOH/CH_2Cl_2 or EtOAc/hexanes as eluent to furnish **2a** in the indicated yield (Table S2).

Table S2. Base Screening.

Entry	Base	Time (h)	Isolated Yield (%)
1	**Et_3N**	**14**	**92**
2	$^iPr_2NEt$	14	83
3	**CsOH**	**14**	**94**
4	Cs_2CO_3	24	0 + ~90%SM
5	pyridine	14	79%
6	DABCO	14	83
7	DMAP	14	85
8	NaOH	14	84
9	-	14	0 + mixture of non-polar products



Solvent Screening General Procedure: To a stirring, 0 °C solution of HOSA (0.7 mmol, 2.2 equiv) in the indicated solvent (2 mL) was added Et_3N (0.7 mmol, 2.2 equiv) under an argon atmosphere. After 15 min, **1a** (0.3 mmol, 1 equiv) was added and the reaction was continued until complete consumption of **1a** (monitored by TLC). The reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with saturated aq. Na_2CO_3 (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified chromatographically using MeOH/CH_2Cl_2 or EtOAc/hexanes as eluent to furnish **2a** in the indicated yield (Table S3).

Table S3. Solvent Screen.

Entry	Solvent	Temp (˚C)/Time (h)	Isolated Yield (%)
1	**HFIP**	**23/14**	**92**
2	CH_2Cl_2	23-60/24	<5
3	MeOH	23-60/24	<5
4	hexane	23-60/24	0
5	TFE[a]	23-60/2	42
6	CH_3CN	23-60/14	0
7	THF	23-60/14	0
8	$CHCl_3$	23-60/14	<5
9	DMF	23-60/14	0

[a]2,2,2-Trifluoroethanol

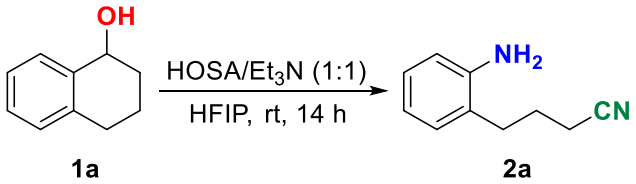
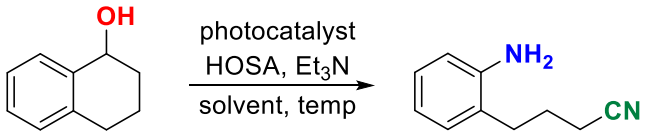


Table S4. HOSA Stoichiometry Optimization.

Entry	HOSA (equiv)	TEA (equiv)	Isoalted Yield (%)
1	2	2	83
2	**2.2**	**2.2**	**92**
3	2.5	2.5	92

Control Experiments



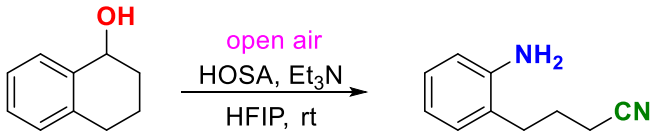
1a **2a**

General Photocatalysis Procedure: To a stirring, 0 °C solution of HOSA (0.7 mmol, 2.5 equiv) in the indicated solvent (2 mL) was added Et_3N (0.7 mmol, 2.5 equiv) under an argon atmosphere. After 15 min, **1a** (0.3 mmol, 1 equiv) and photocatalyst were added and the mixture exposed to blue LED light (260 nm) at rt, unless otherwise stated, until complete consumption of **1a** (4-24 h, monitored by TLC). The reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with saturated aq. Na_2CO_3 (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified chromatographically using MeOH/CH_2Cl_2 or EtOAc/hexanes as eluent to furnish **2a** in the indicated yield (Table S1).

Table S1. Photocatalysis.

Entry	Catalyst	LED light 470 nm	Time (h)	Solvent	Isolated Yield (%)
1	Eosin-Y	+	1	HFIP	70
2	[Ir{dF(CF$_3$)ppy}$_2$(dtbpy)]PF$_6$	+	1	HFIP	72
3	**-**	**-**	**14**	**HFIP**	**92**
4	-	-	1[a]	HFIP	66
5	[Ir{dF(CF$_3$)ppy}$_2$(dtbpy)]PF$_6$	+	12	HFIP/H_2O (4:1)	29
6	[Ir{dF(CF$_3$)ppy}$_2$(dtbpy)]PF$_6$	+	24	CH_2Cl_2	0

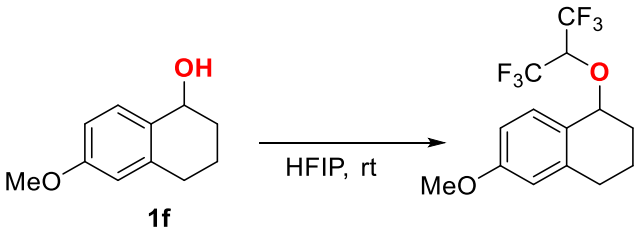
[a]60 °C. [Ir{dF(CF$_3$)ppy}$_2$(dtbpy)]PF$_6$ = [4,4′-bis(1,1-dimethylethyl)-2,2′-bipyridine-N^1,$N^{1'}$]bis[3,5-difluoro-2-[5-(trifluoromethyl)-2-pyridinyl-N]phenyl-C]iridium(III) hexafluorophosphate



1a **2a**

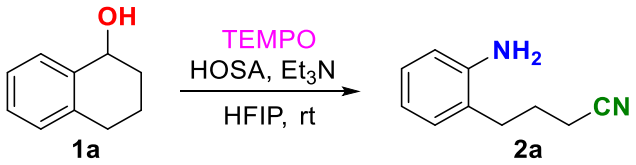
Following the general bis-functionalization procedure, **1** (50 mg, 0.337 mmol), Et_3N (103 µL, 0.743 mmol), and HOSA (84 mg, 0.743 mmol) were stirred at rt in HFIP (2 mL) open to the atmosphere for 14 h. Chromatographic purification of the crude product afforded **2a** (44 mg, 81%) as an oil.

Carbocation confirmation:



1f

6-Methoxy-1,2,3,4-tetrahydronaphthalen-1-ol **1f** (50 mg, 0.280 mmol) was dissolved in HFIP (1.8 mL, 0.15M), stirred at rt for 12 h under an argon atmosphere. The reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with saturated aq. Na_2CO_3 (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified chromatographically using 3% EtOAc/hexanes as eluent to furnish 1-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-6-methoxy-1,2,3,4-tetrahydronaphthalene (72 mg, 79%). in the indicated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.4 Hz, 1H), 6.78 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.67 (s, 1H), 4.77 (t, *J* = 3.5 Hz, 1H), 4.28 (p, *J* = 6.0 Hz, 1H), 3.80 (s, 3H), 2.93–2.62 (m, 2H), 2.22 – 1.95 (m, 2H), 1.90 – 1.67 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.90, 139.81, 131.61, 125.85, 113.76, 112.48, 79.14, 73.94, 73.62, 73.30, 72.98, 72.67, 55.35, 29.17, 27.99, 17.44.

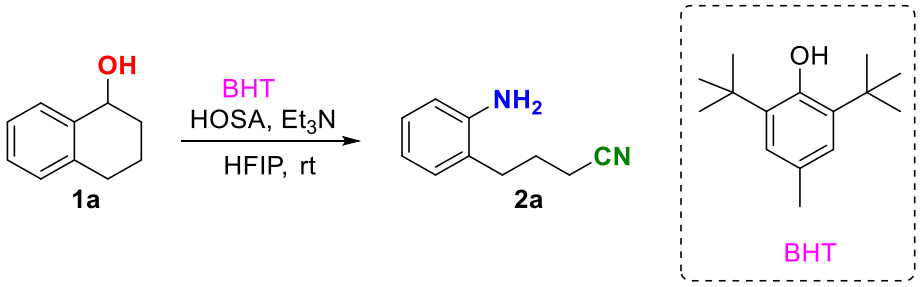


1a **2a**

Following the general bis-functionalization procedure, **1** (50 mg, 0.337 mmol), Et_3N (103 µL, 0.743 mmol), HOSA (84 mg, 0.743 mmol) and TEMPO (52 mg, 0.337 mmol, 1 equiv) were stirred at rt in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **2a** (3 mg, 5%) as an oil and recovered **1** (45 mg, 90%).

Note: The decrease in yield caused by TEMPO is attributed to decomposition of the HOSA aminating agent induced by TEMPO and probably not due to radical trapping.

In a control experiment, aminating agent MsONHMe (50 mg, 0.218 mmol 1 equiv) and TEMPO (51 mg, 0.327 mmol, 1.5 equiv) were stirred at rt in HFIP (2 mL) for 14 h. Decomposition of the closely related aminating agent MsONHMe was observed by TLC. HOSA could not be observed by TLC, therefore we used MsONHMe.

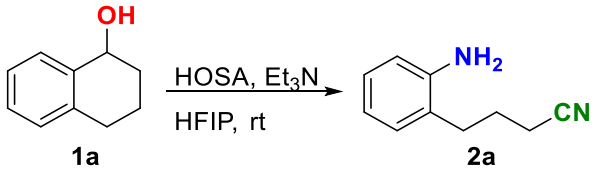


1a **2a**

Following the general bis-functionalization procedure, **1a** (50 mg, 0.337 mmol), Et_3N (103 µL, 0.743 mmol), HOSA (84 mg, 0.743 mmol) and BHT (74 mg, 0.337 mmol, 1 equiv) were stirred at rt in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **2a** (50 mg, 92%) as an oil. TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes).

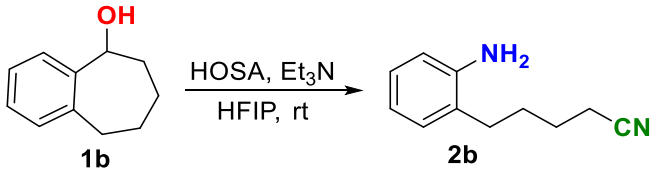
Table 1 Experimental Procedures and Analytical Data

General procedure for bis-functionalization of cyclic benzylic alcohol: Cyclic benzylic alcohol (1 equiv) was added to a stirring equimolar solution of HOSA and Et_3N (2.2 equiv) at 0 °C in HFIP (0.15 M) under an argon atmosphere. After 15 min, the reaction mixture was warmed to rt-50 ºC. After complete consumption (monitored via TLC), the rt reaction mixture was diluted with CH_2Cl_2 (equal vol), washed with saturated aq. Na_2CO_3, brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude residue was purified chromatographically using MeOH/CH_2Cl_2 or EtOAc/hexanes as eluent to furnish the anilino-nitrile. Variations in reaction conditions are noted in the Table 1 legends for select substrates.



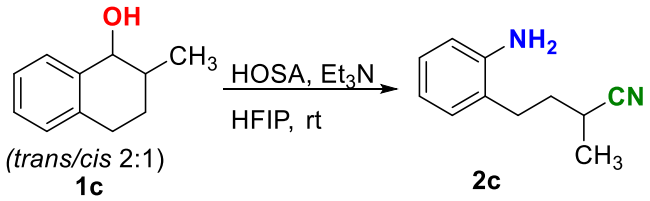
4-(2-Aminophenyl)butanenitrile (2a): Following the general benzyl alcohol bis-functionalization procedure, 1,2,3,4-tetrahydronaphthalen-1-ol (**1**) (50 mg, 0.337 mmol), Et_3N (103 µL, 0.743 mmol), and HOSA (84 mg, 0.743 mmol) were stirred at rt in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **2a** (50 mg, 92%) as an oil. TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (td, *J* = 7.7, 1.5 Hz, 1H), 7.03 (dd, *J* = 7.5, 1.2 Hz, 1H), 6.75 (td, *J* = 7.4, 1.2 Hz, 1H), 6.70 (dd, *J* = 7.9, 1.0 Hz, 1H), 3.63 (br s, 2H), 2.67 (t, *J* = 7.4 Hz, 2H), 2.37 (t, *J* = 7.0 Hz, 2H), 2.00 (p, *J* = 7.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.30, 129.80, 127.82, 123.89, 119.79, 119.03, 116.05, 29.97, 24.38, 16.74. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{10}H_{12}N_2^+$ 161.1073; found, 161.1081.

5 mmol scale: 1a (800 mg, 5.405 mmol), HOSA (1.34 g, 11.891 mmol), and Et_3N (1.65 mL, 11.891 mmol) were stirred at rt in HFIP (32 mL) for 14 h. The residue was purified chromatographically using a gradient of 70-90% EtOAc/hexane to give **2a** (778 mg, 90%) as an oil.

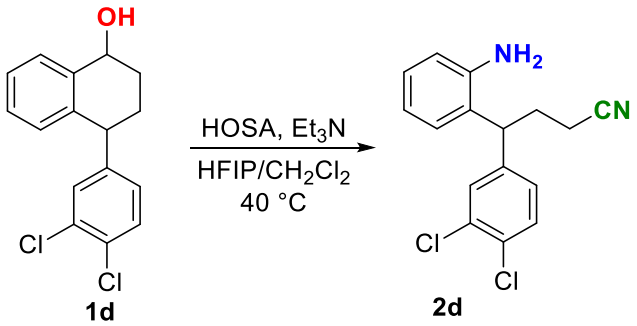


5-(2-Aminophenyl)pentanenitrile (2b): Following the general benzyl alcohol bis-functionalization procedure, 6,7,8,9-tetrahydro-5*H*-benzo[7]annulen-5-ol (50 mg, 0.308 mmol), Et_3N (94 µL, 0.679 mmol), and HOSA (76 mg, 0.679 mmol) were stirred at rt in HFIP (2 mL) for 12 h. Chromatographic purification of the crude product afforded **2b** (47 mg, 87%) as an oil. TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09–6.97 (m, 2H), 6.74 (td, *J* = 7.4, 1.2 Hz, 1H), 6.69 (dd, *J* = 8.0, 1.2 Hz, 1H), 3.62 (br s, 2H), 2.54 (t, *J* = 7.2 Hz, 2H), 2.37 (t, *J* = 6.8 Hz, 2H), 1.86–1.62 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.15, 129.56, 127.38, 125.36,

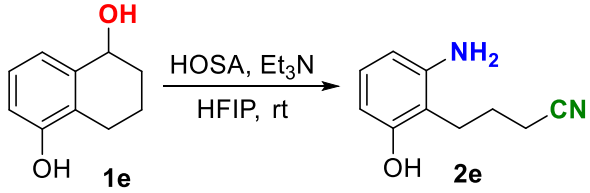
119.76, 118.91, 115.86, 30.47, 27.59, 25.15, 17.16. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{11}H_{14}N_2^+$ 175.1230; found, 175.1236.



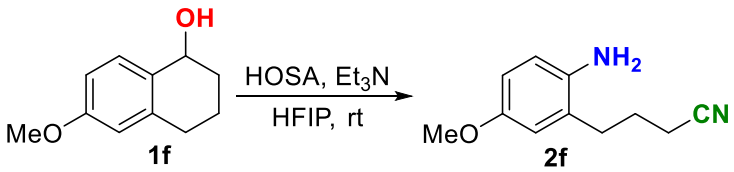
4-(2-Aminophenyl)-2-methylbutanenitrile (2c): Following the general benzyl alcohol bis-functionalization procedure, 2-methyl-1,2,3,4-tetrahydronaphthalen-1(*S*)-ol[7] (50 mg, 0.308 mmol; 2:1 *trans*/*cis*-mixture), Et_3N (94 µL, 0.308 mmol), and HOSA (76 mg, 0.308 mmol) were stirred at rt in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **2c** (40 mg, 75%) as an oil. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10–7.01 (m, 2H), 6.75 (td, *J* = 7.4, 1.2 Hz, 1H), 6.69 (dd, *J* = 7.8, 1.2 Hz, 1H), 3.64 (br s, 2H), 2.79–2.72 (m, 1H), 2.69–2.58 (m, 2H), 1.99–1.82 (m, 2H), 1.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.26, 129.71, 127.76, 124.34, 123.06, 119.07, 116.04, 33.21, 28.87, 25.34, 18.13. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{11}H_{14}N_2^+$ 175.1230; found 175.1240.



4-(2-Aminophenyl)-4-(3,4-dichlorophenyl)butanenitrile (2d): Following the general benzyl alcohol bis-functionalization procedure, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydronaphthalen-1-ol[8] (50 mg, 0.179 mmol), Et_3N (55 µL, 0.179 mmol), and HOSA (44 mg, 0.179 mmol) were stirred at 40 ºC in a mixture (2 mL, 4:1) of HFIP (1.6 mL) and CH_2Cl_2 for 12 h. Chromatographic purification of the crude product afforded **2d** (37 mg, 71%) as an oil. TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.3 Hz, 1H), 7.23 (d, *J* = 2.2 Hz, 1H), 7.12–6.96 (m, 3H), 6.79 (td, *J* = 7.5, 1.3 Hz, 1H), 6.63 (d, *J* = 8.1 Hz, 1H), 3.96 (t, *J* = 7.5 Hz, 1H), 3.54 (br s, 2H), 2.46–2.31 (m, 1H), 2.30–2.14 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.26, 142.41, 131.03, 129.80, 128.49, 127.40, 127.08, 125.63, 119.66, 119.28, 117.53, 43.67, 30.21, 15.86. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{16}H_{14}Cl_2N_2O^+$ 305.0608; found, 305.0613.

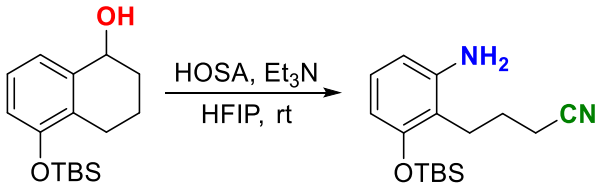


4-(2-Amino-6-hydroxyphenyl)butanenitrile (2e): Following the general benzyl alcohol bis-functionalization procedure, 1,2,3,4-tetrahydronaphthalen-1,5-diol (50 mg, 0.304 mmol), Et_3N (93 µL, 0.670 mmol), and HOSA (75 mg, 0.670 mmol) were stirred at rt in HFIP (2 mL) for 10 h. Chromatographic purification of the crude product afforded **2e** (38 mg, 71%) as a solid, mp 94-96 °C. TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (t, *J* = 8.0 Hz, 1H), 6.29 (d, *J* = 8.0 Hz, 1H), 6.20 (d, *J* = 7.9 Hz, 1H), 5.72 (br s, 1H), 3.71 (br s, 2H), 2.69 (t, *J* = 7.3 Hz, 2H), 2.37 (t, *J* = 7.2 Hz, 2H), 1.92 (p, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.85, 145.72, 127.76, 120.48, 111.54, 108.75, 106.03, 24.14, 22.86, 16.81. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{10}H_{12}N_2O^+$ 177.1022; found, 177.1027.



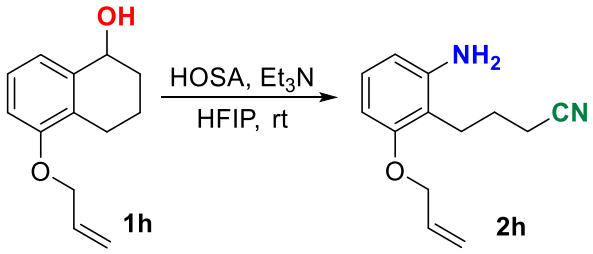
1f **2f**

4-(2-Amino-5-methoxyphenyl)butanenitrile (2f): Following the general benzyl alcohol bis-functionalization procedure, 6-methoxy-1,2,3,4-tetrahydronaphthalen-1-ol (50 mg, 0.284 mmol), Et_3N (87 µL, 0.624 mmol), and HOSA (70 mg, 0.624 mmol) were stirred at rt in HFIP (2 mL) for 7 h. Chromatographic purification of the crude product afforded **2f** (32 mg, 61%) as an oil. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67–6.60 (m, 3H), 3.74 (s, 3H), 3.37 (br s, 2H), 2.66 (t, *J* = 7.4 Hz, 2H), 2.38 (t, *J* = 7.0 Hz, 2H), 1.99 (p, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.06, 137.86, 125.74, 119.78, 117.36, 115.71, 112.97, 55.83, 30.33, 24.50, 16.80. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{11}H_{14}N_2O^+$ 191.1179; found, 191.1182.

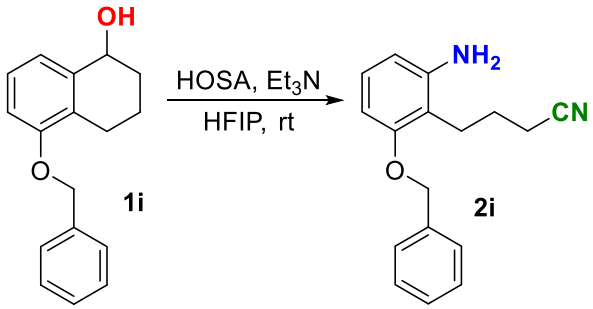


1g **2g**

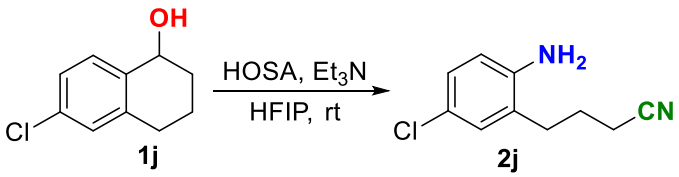
4-(2-Amino-6-((tert-butyldimethylsilyl)oxy)phenyl)butanenitrile (2g): Following the general benzyl alcohol bis-functionalization procedure, 5-((*tert*-butyldimethylsilyl)oxy)-1,2,3,4-tetrahydronaphthalen-1-ol[9] (50 mg, 0.179 mmol), Et_3N (55 µL, 0.179 mmol), and HOSA (44 mg, 0.179 mmol) were stirred at rt in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **2g** (40 mg, 78%) as an oil. TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (t, *J* = 8.0 Hz, 1H), 6.30 (dd, *J* = 18.3, 8.0 Hz, 2H), 3.66 (br s, 2H), 2.67 (t, *J* = 7.5 Hz, 2H), 2.37 (t, *J* = 7.2 Hz, 2H), 1.91 (p, *J* = 7.3 Hz, 2H), 1.01 (s, 9H), 0.25 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.58, 145.95, 127.47, 115.31, 109.16, 109.07, 25.96, 24.37, 23.63, 18.37, 16.97, -3.98. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{16}H_{26}N_2OSi^+$ 291.1887; found 291.1889.



4-(2-(Allyloxy)-6-aminophenyl)butanenitrile (2h): Following the general benzyl alcohol bis-functionalization procedure, 5-(allyloxy)-1,2,3,4-tetrahydronaphthalen-1-ol[10] (**1h**) (50 mg, 0.179 mmol), Et_3N (75 µL, 0.539 mmol), and HOSA (60 mg, 0.539 mmol) were stirred at rt in HFIP (2 mL) for 12 h. Chromatographic purification of the crude product afforded **2h** (41 mg, 78%) as a green solid, mp 79-81 °C. TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (t, *J* = 8.1 Hz, 1H), 6.34 (dd, *J* = 11.1, 8.1 Hz, 2H), 6.13–5.98 (m, 1H), 5.40 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.29–5.25 (m, 1H), 4.51 (dt, *J* = 5.0, 1.4 Hz, 2H), 3.67 (br s, 2H), 2.73 (t, *J* = 7.3 Hz, 2H), 2.36 (t, *J* = 7.2 Hz, 2H), 1.93 (p, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.37, 145.57, 133.65, 127.72, 120.36, 117.05, 112.78, 109.23, 102.33, 68.88, 24.29, 22.91, 16.93. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{13}H_{16}N_2O^+$ 217.1335; found, 217.1341.

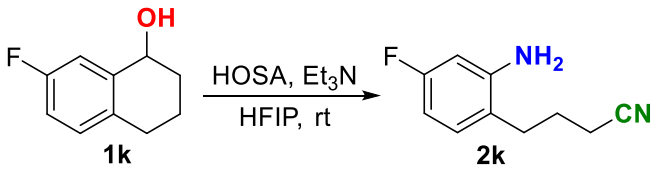


4-(2-Amino-6-(benzyloxy)phenyl)butanenitrile (2i): Following the general benzyl alcohol bis-functionalization procedure, 5-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-1-ol[11] **(1i)** (50 mg, 0.196 mmol), Et_3N (49 µL, 0.433 mmol), and HOSA (60 mg, 0.433 mmol) were stirred at rt in HFIP (2 mL) for 12 h. Chromatographic purification of the crude product afforded **2i** (44 mg, 85%) as an oil. TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.28 (m, 5H), 7.01 (t, *J* = 8.1 Hz, 1H), 6.40 (dd, *J* = 16.0, 8.1 Hz, 2H), 5.06 (s, 2H), 3.70 (br s, 2H), 2.76 (t, *J* = 7.3 Hz, 2H), 2.35 (t, *J* = 7.2 Hz, 2H), 1.93 (p, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.52, 145.62, 137.41, 128.66, 127.92, 127.78, 127.23, 120.32, 112.84, 109.36, 102.47, 70.10, 24.31, 23.05, 16.96. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{17}H_{18}N_2O^+$ 267.1492; found, 267.1506.

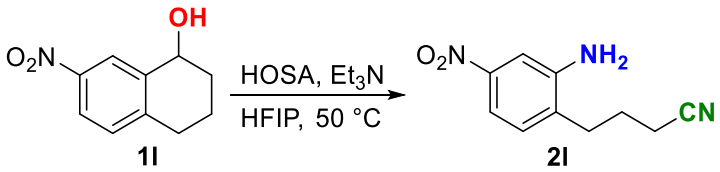


4-(2-Amino-5-chlorophenyl)butanenitrile (2*J*): Following the general benzyl alcohol bis-functionalization procedure, 6-chloro-1,2,3,4-tetrahydronaphthalen-1-ol (**1*J***) (50 mg, 0.274

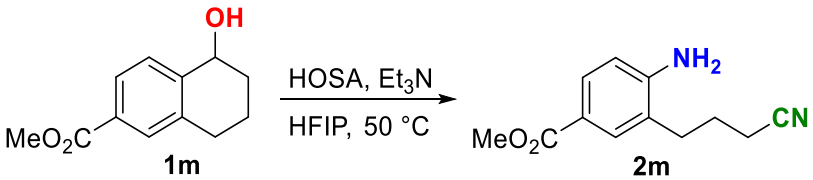
mmol), Et_3N (84 µL, 0.604 mmol), and HOSA (68 mg, 0.604 mmol) were stirred at rt in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **2*J*** (46 mg, 86%) as an oil. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05–6.94 (m, 2H), 6.62 (d, *J* = 8.3 Hz, 1H), 3.63 (br s, 2H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.39 (t, *J* = 6.9 Hz, 2H), 1.98 (p, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.92, 129.30, 127.62, 125.54, 123.46, 119.60, 117.14, 29.83, 24.23, 16.84. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{10}H_{11}ClN_2^+$ 195.0684; found, 195.0685.



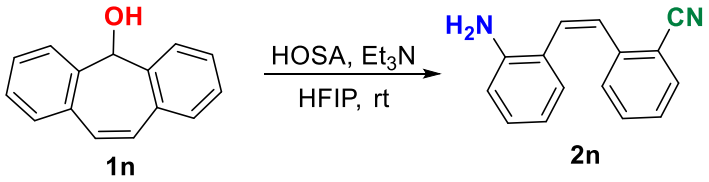
4-(2-Amino-4-fluorophenyl)butanenitrile (2k): Following the general benzyl alcohol bis-functionalization procedure, 7-fluoro-1,2,3,4-tetrahydronaphthalen-1-ol (**1k**) (50 mg, 0.301 mmol), Et_3N (92 µL, 0.662 mmol), and HOSA (74 mg, 0.662 mmol) were stirred at rt in HFIP (2 mL) for 16 h. Chromatographic purification of the crude product afforded **2k** (38 mg, 72%) as an oil. TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (dd, *J* = 8.2, 6.4 Hz, 1H), 6.50–6.19 (m, 2H), 3.74 (s, 2H), 2.62 (t, *J* = 7.5 Hz, 2H), 2.36 (t, *J* = 7.0 Hz, 2H), 1.96 (q, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.78, 161.37, 145.77, 145.67, 130.83, 130.74, 119.62, 119.32, 119.30, 105.35, 105.14, 102.68, 102.43, 29.27, 24.35, 16.61. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{10}H_{11}FN_2^+$ 179.0979; found, 179.0994.



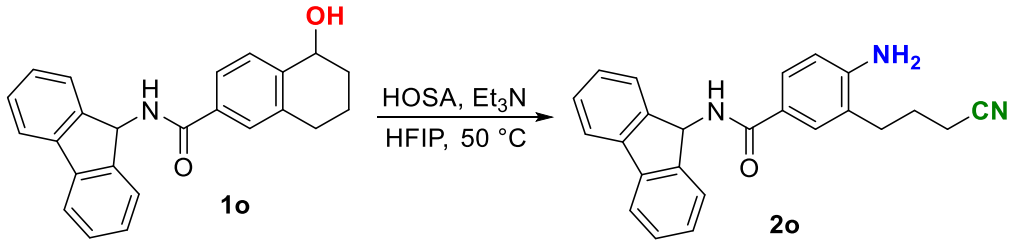
4-(2-Amino-5-nitrophenyl)butanenitrile (2l): Following the general benzyl alcohol bis-functionalization procedure, 7-nitro-1,2,3,4-tetrahydronaphthalen-1-ol (**1l**) (50 mg, 0.259 mmol), Et_3N (115 µL, 0.828 mmol), and HOSA (128 mg, 1.139 mmol) were stirred at 50 ºC in HFIP (2 mL) for 24 h. Chromatographic purification of the crude product afforded **2l** (34 mg, 64%) as an oil. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.53 (d, *J* = 2.3 Hz, 1H), 7.16 (d, *J* = 8.3 Hz, 1H), 3.94 (s, 2H), 2.79–2.67 (m, 2H), 2.43 (t, *J* = 6.9 Hz, 2H), 2.03 (dd, *J* = 8.0, 6.8 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.90, 145.10, 130.70, 130.21, 119.33, 113.72, 110.06, 29.94, 23.81, 16.96. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{10}H_{11}N_3O_2^+$ 206.0924; found, 206.0927.



Methyl 4-amino-3-(3-cyanopropyl)benzoate (2m): Following the general benzyl alcohol bis-functionalization procedure, methyl 5-hydroxy-5,6,7,8-tetrahydronaphthalene-2-carboxylate **(1m)** (50 mg, 0.242 mmol), Et_3N (74 µL, 0.533 mmol), and HOSA (60 mg, 0.533 mmol) were stirred at 50 ºC in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **2m** (32 mg, 84%) as a brown solid, mp 97-99 °C. TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79–7.71 (m, 2H), 6.67 (d, *J* = 8.3 Hz, 1H), 4.15 (br s, 2H), 3.86 (s, 3H), 2.67 (t, *J* = 7.4 Hz, 2H), 2.41 (t, *J* = 7.0 Hz, 2H), 2.01 (p, *J* = 7.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.24, 148.63, 131.52, 130.02, 122.82, 120.32, 119.65, 115.01, 51.83, 29.69, 24.32, 16.93. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{12}H_{14}N_2O_2^+$ 219.1128; found, 219.1133.

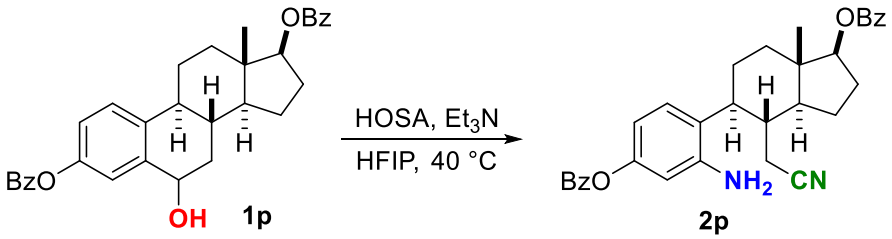


(*E*)-2-(2-Aminostyryl)benzonitrile (2n): Following the general benzyl alcohol bis-functionalization procedure, 5*H*-dibenzo[a,d][7]annulen-5-ol (**1n**) (50 mg, 0.240 mmol), Et_3N (73 µL, 0.528 mmol), and HOSA (59 mg, 0.528 mmol) were stirred at rt in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **2n** (23 mg, 45%, *cis*-isomer determined by coupling constants) as a yellow solid, mp 90-92 °C. TLC: $R_f \approx 0.5$ (30% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.36–7.30 (m, 2H), 7.29–7.22 (m, 1H), 7.11–7.05 (m, 1H), 6.92 (d, *J* = 11.9 Hz, 1H), 6.90–6.87 (m, 1H), 6.79 (d, *J* = 11.9 Hz, 1H), 6.70 (dd, *J* = 8.1, 1.1 Hz, 1H), 6.60 (td, *J* = 7.5, 1.1 Hz, 1H), 3.75 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.19, 140.65, 132.91, 132.31, 131.09, 129.64, 129.29, 129.22, 127.61, 127.46, 121.95, 118.55, 118.11, 115.90, 112.19. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{15}H_{12}N_2^+$ 221.1073; found, 221.1078.
Note: Isomerition of product observed in presence of light after 24 h.

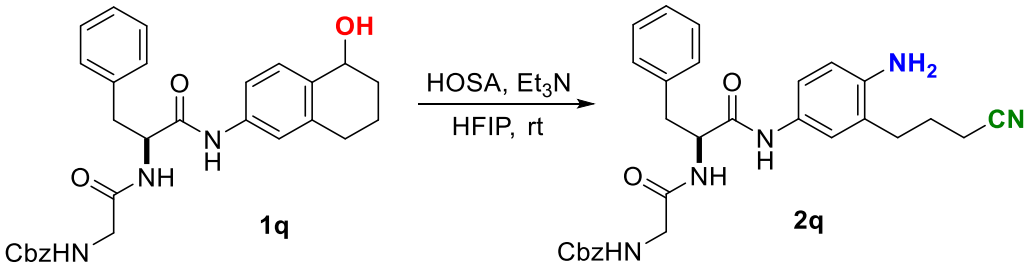


4-Amino-3-(3-cyanopropyl)-*N*-(9*H*-fluoren-9-yl)benzamide (2o): Following the general benzyl alcohol bis-functionalization procedure, *N*-(9*H*-fluoren-9-yl)-5-hydroxy-5,6,7,8-tetrahydronaphthalene-2-carboxamide (**1o**) (50 mg, 0.140 mmol), Et_3N (43 µL, 0.309 mmol), and HOSA (35 mg, 0.309 mmol) were stirred at 50 ºC in HFIP (2 mL) for 10 h. Chromatographic purification of the crude product afforded **2o** (36 mg, 70%) as a viscous oil. TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, CD_3OD) δ 7.78 (d, *J* = 7.7 Hz, 2H), 7.63–7.51 (m, 4H), 7.45–7.35 (m, 2H), 7.31 (td, *J* = 7.5, 1.2 Hz, 2H), 6.72 (d, *J* = 8.3 Hz, 1H), 6.33 (s, 1H), 2.65 (t, *J* = 8.1 Hz, 2H), 2.46 (t, *J* = 7.2 Hz, 2H), 1.94 (p, *J* = 7.4 Hz, 2H); ^{13}C NMR (101 MHz, CD_3OD) δ 171.22, 150.43, 146.18, 142.04, 130.58, 129.53, 128.69, 128.53, 125.94, 124.58, 123.65, 121.16,

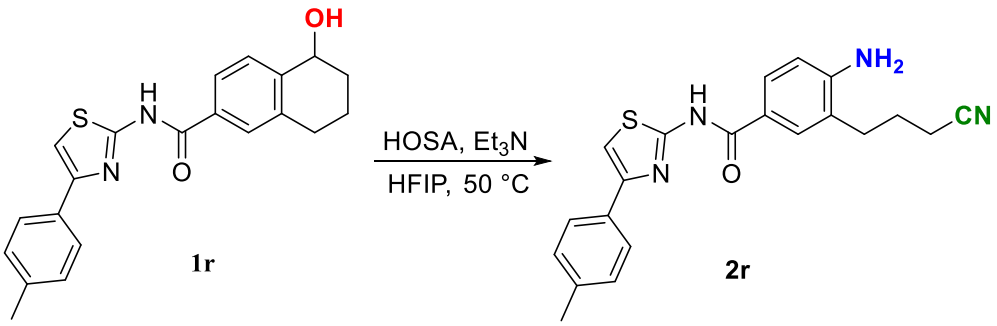
120.98, 115.79, 56.30, 31.01, 25.63, 16.98. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{24}H_{21}N_3O_2^+$ 368.1757; found, 368.1749.



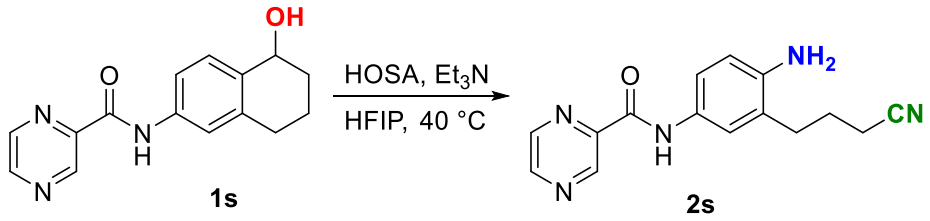
3-Amino-4-((1*S*,3a*S*,4*R*,5*S*,7a*S*)-1-(benzoyloxy)-4-(cyanomethyl)-7a-methyloctahydro-1*H*-inden-5-yl)phenyl benzoate (2p): Following the general benzyl alcohol bis-functionalization procedure, (8*R*,9*S*,13*S*,14*S*,17*S*)-6-hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthrene-3,17-diyl dibenzoate (**1p**) (22 mg, 0.044 mmol), Et_3N (13 µL, 0.097 mmol), and HOSA (11 mg, 0.097 mmol) were stirred at 40 ºC in HFIP (1 mL) for 21 h. Chromatographic purification of the crude product afforded **2p** (17 mg, 81%) as a viscous oil. TLC: $R_f \approx 0.5$ (30% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 7.6 Hz, 2H), 8.05 (d, *J* = 7.5 Hz, 2H), 7.66–7.41 (m, 6H), 6.77–6.49 (m, 2H), 4.99 (t, *J* = 7.51, 1H), 3.97 (br s, 2H), 2.66–2.53 (m, 1H), 2.51–2.23 (m, 3H), 2.17–2.06 (m, 1H), 2.00–1.83 (m, 3H), 1.82–1.67 (m, 3H), 1.61–1.46 (m, 3H), 1.13 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.49, 165.31, 150.16, 145.85, 133.72, 133.08, 130.58, 130.28, 129.72, 129.68, 128.70, 128.52, 127.32, 125.07, 118.69, 112.48, 109.64, 82.76, 47.92, 43.71, 40.97, 38.41, 36.90, 29.95, 27.63, 23.93, 19.29, 12.58. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{32}H_{32}N_2O_4^+$ 509.2435; found 509.2431.



Benzyl (S)-(2-((1-((4-amino-3-(3-cyanopropyl)phenyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethyl)carbamate (2q): Following the general benzyl alcohol bis-functionalization procedure, benzyl (2-(2*S*)-1-((5-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethyl)carbamate (**1q**) (30 mg, 0.0598 mmol), Et_3N (18 µL, 0.1317 mmol), and HOSA (14 mg, 0.1317 mmol) were stirred at rt in HFIP (1.5 mL) for 10 h. Chromatographic purification of the crude product afforded **2q** (23 mg, 76%) as a solid, mp 123-125 °C. TLC: $R_f \approx 0.5$ (10% MeOH/CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96–7.88 (m, 1H), 7.43–6.86 (m, 12H), 6.56 (dd, *J* = 8.3, 2.0 Hz, 1H), 5.59–5.46 (m, 1H), 5.08 (s, 2H), 4.79 (q, *J* = 7.2 Hz, 1H), 4.02–3.42 (m, 4H), 3.10 (t, *J* = 7.3 Hz, 2H), 2.55 (td, *J* = 7.5, 3.2 Hz, 2H), 2.30 (t, *J* = 7.0 Hz, 2H), 1.91 (q, *J* = 7.3 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.43, 168.78, 156.89, 141.39, 136.51, 136.09, 129.45, 129.03, 128.87, 128.83, 128.72, 128.46, 128.28, 127.25, 127.21, 124.41, 122.40, 122.37, 120.58, 120.54, 119.83, 116.28, 67.46, 55.23, 44.71, 38.51, 29.94, 24.28, 16.75. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{29}H_{31}N_5O_4^+$ 514.2449; found 514.2451.



4-Amino-3-(3-cyanopropyl)-N-(4-(*p*-tolyl)thiazol-2-yl)benzamide (2r): Following the general benzyl alcohol bis-functionalization procedure, 5-hydroxy-*N*-(4-(*p*-tolyl)thiazol-2-yl)-5,6,7,8-tetrahydronaphthalene-2-carboxamide (**1r**) (50 mg, 0.142 mmol), Et_3N (43 µL, 0.314 mmol), and HOSA (35 mg, 0.314 mmol) were stirred at 50 ºC in HFIP (2 mL) for 16 h. Chromatographic purification of the crude product afforded 4-amino-3-(3-cyanopropyl)-*N*-(4-(*p*-tolyl)thiazol-2-yl)benzamide **2r** (38 mg, 72%) as an oil. TLC: $R_f \approx 0.5$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, CD_3OD + $CDCl_3$ 3:1) δ 7.80–7.65 (m, 4H), 7.24–7.15 (m, 3H), 6.76 (d, *J* = 9.0 Hz, 1H), 2.73–2.66 (m, 2H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.35 (s, 3H), 2.06–1.94 (m, 2H); ^{13}C NMR (151 MHz, CD_3OD + $CDCl_3$ 3:1) δ 167.09, 151.69, 151.01, 138.52, 132.99, 130.79, 130.08, 128.86, 126.78, 124.00, 120.88, 120.71, 115.38, 107.58, 30.77, 25.18, 21.31, 16.96. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{21}H_{20}N_4OS^+$ 377.1431; found, 377.1435.

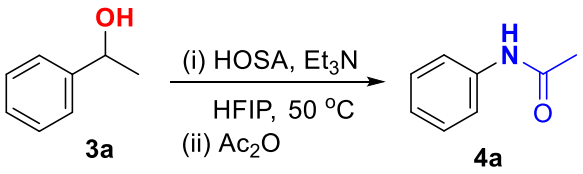


N-(4-Amino-3-(3-cyanopropyl)phenyl)pyrazine-2-carboxamide (2s): Following the general benzyl alcohol bis-functionalization procedure, *N*-(5-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)pyrazine-2-carboxamide (**1s**) (50 mg, 0.185 mmol), Et_3N (56 µL, 0.408 mmol), and HOSA (46 mg, 0.408 mmol) were stirred at 40 ºC in HFIP (2 mL) for 3 h. Chromatographic purification of the crude product afforded **2s** (45 mg, 88%) as a yellow solid, mp 137-139 °C. TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55–9.42 (m, 2H), 8.78 (d, *J* = 2.5 Hz, 1H), 8.60–8.51 (m, 1H), 7.49 (d, *J* = 2.5 Hz, 1H), 7.42 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.71 (d, *J* = 8.5 Hz, 1H), 3.65 (br s, 2H), 2.69 (t, *J* = 7.5 Hz, 2H), 2.41 (t, *J* = 7.0 Hz, 2H), 2.03 (p, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.36, 147.43, 144.72, 144.61, 142.45, 141.64, 129.11, 124.58, 121.81, 120.00, 119.74, 116.47, 30.07, 24.39, 16.82. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{15}H_{15}N_5O^+$ 282.1349; found, 282.1355.

Table 2 Experimental Procedures and Analytical Data

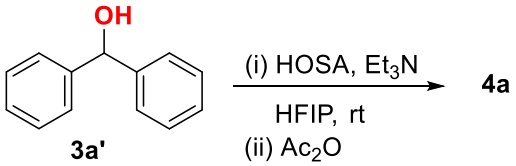
General procedure for benzyl alcohol amination: Acyclic benzylic alcohol (1 equiv) was added to a stirring equimolar solution of HOSA and Et_3N (1.5 equiv) at 0 °C in HFIP (0.15 M) under an argon atmosphere. After 15 min, the reaction mixture was warmed to rt-50 ºC. After complete

consumption (monitored via TLC), the rt reaction mixture was diluted with CH_2Cl_2 (equal vol), washed with saturated aq. Na_2CO_3, brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude residue was purified chromatographically using MeOH/CH_2Cl_2 or EtOAc/hexanes as eluent to furnish the anilines. Variations in reaction conditions are noted in the Table 2 legends for select substrates.



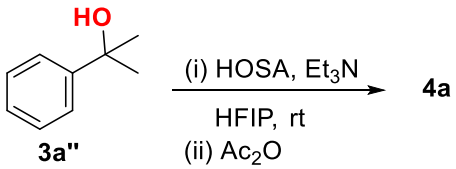
(*i*) ***N*-Phenylacetamide (4a):** Following the general benzyl alcohol amination procedure, 1-phenylethan-1-ol (**3a**) (50 mg, 0.409 mmol), Et_3N (85 µL, 0.614 mmol), and HOSA (69 mg, 0.614 mmol) were stirred at 50 ºC in HFIP (2 mL) for 6 h. After extractive isolation using CH_2Cl_2 (3 × 10 mL) and concentration *in vacuo*, the residue (56 mg) was acetylated (*vide infra*) to facilitate isolation and identification.

Acetic anhydride (0.28 mL, 3.010 mmol) was added to a stirring, rt solution of the above residue (56 mg, 0.602 mmol) in dry CH_2Cl_2 (5 mL). After 15 h, all volatiles were removed *in vacuo* and the crude residue was purified chromatographically using 70-80% EtOAc/hexanes as eluent to furnish **4a** (39 mg, 71%) as a colorless solid whose spectral data were in agreement with literature values.[12] mp 113-115 °C (lit.[12] 113-115 °C), TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (br s, 1H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.29 (t, *J* = 7.8 Hz, 2H), 7.09 (t, *J* = 7.4 Hz, 1H), 2.15 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.98, 138.10, 129.00, 124.37, 120.19, 24.53.



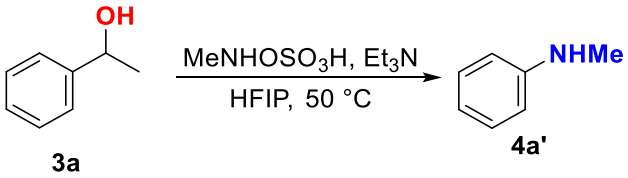
(*ii*) ***N*-Phenylacetamide (4a):** Following the general benzyl alcohol amination procedure, diphenylmethanol (**3a′**) (50 mg, 0.271 mmol), Et_3N (56 µL, 0.407 mmol), and HOSA (46 mg, 0.407 mmol) were stirred at rt in HFIP (2 mL) for 4 h. After extractive isolation using CH_2Cl_2 (3 × 10 mL) and concentration *in vacuo*, the residue (58 mg) was acetylated (*vide infra*) to facilitate isolation and identification.

Acetic anhydride (0.29 mL, 3.115 mmol) was added to stirring solution of the above crude (58 mg, 0.623 mmol) in dry CH_2Cl_2 (5 mL). After 15 h, all volatiles were removed *in vacuo* and the crude residue was purified chromatographically using 70-80% EtOAc/hexane to furnish **4a** (27 mg, 76%) as a solid identical to an authentic sample (*vide supra) and* benzaldehyde (10 mg, 36%), benzonitrile (5 mg, 18%).

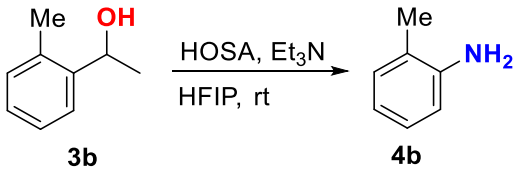


(*iii*) ***N*-Phenylacetamide (4a):** Following the general benzyl alcohol amination procedure, 2-phenylpropan-2-ol (**3a′′**) (50 mg, 0.367 mmol), Et_3N (76 µL, 0.551 mmol), and HOSA (62 mg, 0.551 mmol) were stirred at rt in HFIP (2 mL) for 4 h. After isolation, the residue (55 mg) was acetylated (*vide infra*) to facilitate isolation and identification.

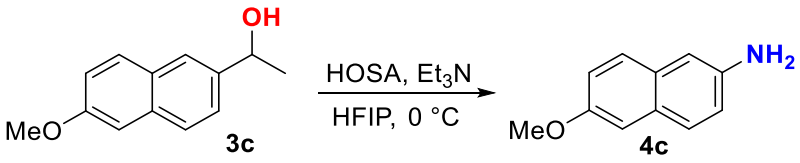
Acetic anhydride (0.27 mL, 2.956 mmol) was added to stirring solution of the above crude residue (55 mg, 0.591 mmol) in dry CH_2Cl_2 (5 mL). After 15 h, all volatiles were removed *in vacuo* and the crude residue was purified chromatographically using 70-80% EtOAc/hexane to furnish **4a** (33 mg, 68%) as a solid identical to an authentic sample (*vide supra*).



***N*-Methylaniline (4a′):** In a modification of the the general benzyl alcohol amination procedure, 1-phenylethan-1-ol (**3a**) (50 mg, 0.409 mmol), Et_3N (85 µL, 0.614 mmol), and $MeNHOSO_3H$[13] (136 mg, 1.227 mmol) were stirred at 50 ºC in HFIP (2 mL) for 1 h. Chromatographic purification of the crude product afforded **4a′** (31 mg, 72%) as an yellow oil whose spectral data were in agreement with literature values.[14] TLC: $R_f \approx 0.4$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.15 (m, 2H), 6.73 (tt, *J* = 7.4, 1.1 Hz, 1H), 6.66–6.61 (m, 2H), 3.71 (br s, 1H), 2.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.44, 129.31, 117.34, 112.52, 30.83.

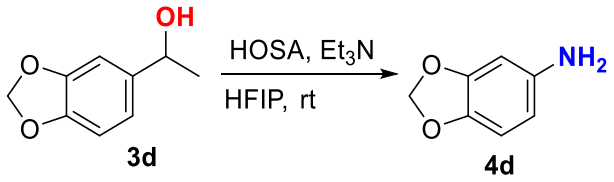


***o*-Toluidine (4b):** Following the general benzyl alcohol amination procedure, 1-(*o*-tolyl)ethan-1-ol (**3b**) (50 mg, 0.367 mmol), Et_3N (76 µL, 0.551 mmol), and HOSA (44 mg, 0.551 mmol) were stirred at rt in HFIP (2 mL) for 5 h. Chromatographic purification of the crude product afforded **4b** (34 mg, 88%) as an yellow oil whose spectral data were in agreement with literature values.[15] TLC: $R_f \approx 0.5$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10–7.03 (m, 2H), 6.78–6.67 (m, 2H), 3.57 (br s, 2H), 2.20 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.59, 130.55, 127.06, 122.46, 118.77, 115.06, 17.45.

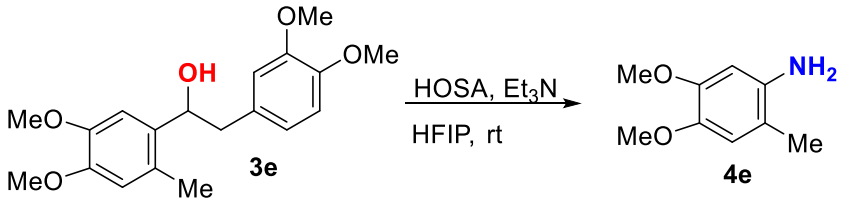


6-Methoxynaphthalen-2-amine (4d): Following the general benzyl alcohol amination procedure, 1-(6-methoxynaphthalen-2-yl)ethan-1-ol (**3c**) (50 mg, 0.247 mmol), Et_3N (51 µL, 0.371 mmol), and HOSA (41 mg, 0.371 mmol) were stirred at 0 ºC in HFIP (2 mL) for 2 h. Chromatographic purification of the crude product afforded **4c** (30 mg, 73%) as a white solid whose spectral data

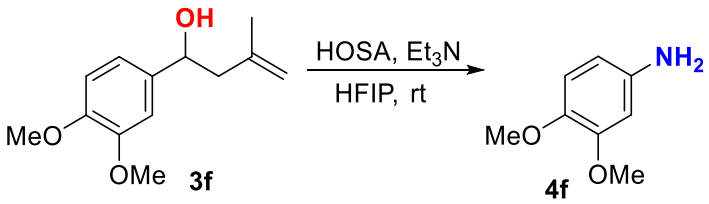
were in agreement with literature values.[16] TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 23.2, 8.7 Hz, 2H), 7.14–6.86 (m, 4H), 3.89 (s, 3H), 3.73 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.42, 142.35, 130.23, 128.70, 127.94, 127.35, 119.00, 118.76, 109.26, 106.12, 55.31.



Benzo[d][1,3]dioxol-5-amine (4d): Following the general benzyl alcohol amination procedure, 1-(benzo[d][1,3]dioxol-5-yl)ethan-1-ol (**3d**) (50 mg, 0.301 mmol), Et_3N (62 µL, 0.451 mmol), and HOSA (51 mg, 0.451 mmol) were stirred at rt in HFIP (2 mL) for 3 h. Chromatographic purification of the crude product afforded **4d** (27 mg, 66%) as a yellow solid whose spectral data were in agreement with literature values.[17] TLC: $R_f \approx 0.5$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.62 (dd, *J* = 8.2, 1.7 Hz, 1H), 6.29 (t, *J* = 2.0 Hz, 1H), 6.13 (dt, *J* = 8.3, 2.0 Hz, 1H), 5.86 (s, 2H), 3.37 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.34, 141.53, 140.49, 108.70, 106.99, 100.78, 98.19.

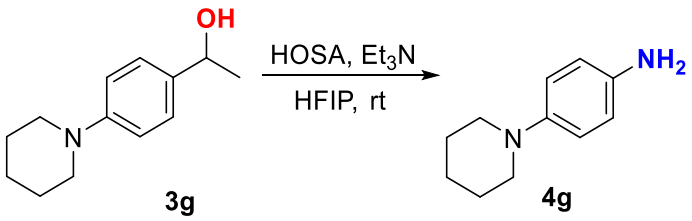


4,5-Dimethoxy-2-methylaniline (4e): Following the general benzyl alcohol amination procedure, 1-(4,5-dimethoxy-2-methylphenyl)-2-(3,4-dimethoxyphenyl)ethan-1-ol (**3e**) (50 mg, 0.157 mmol), Et_3N (32 µL, 0.235 mmol), and HOSA (26 mg, 0.235 mmol) were stirred at rt in HFIP (2 mL) for 12 h. Chromatographic purification of the crude product afforded **4e** (21 mg, 80%) as a solid whose spectral data were in agreement with literature values. mp 106-108 °C (lit.[18] 106-107 °C), TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, CD_3OD) δ 6.62 (s, 1H), 6.30 (s, 1H), 3.81 (s, 3H), 3.80 (br s, 3H), 2.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.24, 142.02, 138.20, 115.37, 113.82, 100.97, 56.92, 56.12, 16.96.

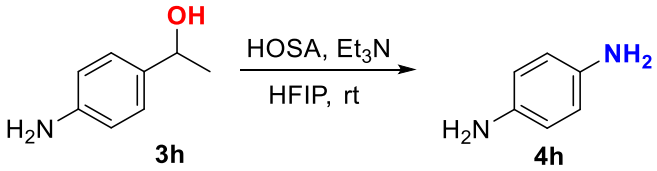


3,4-Dimethoxyaniline (4f): Following the general benzyl alcohol amination procedure, 1-(3,4-dimethoxyphenyl)-3-methylbut-3-en-1-ol[19] (**3f**) (50 mg, 0.225 mmol), Et_3N (47 µL, 0.337 mmol), and HOSA (38 mg, 0.337 mmol) were stirred at rt in HFIP (2 mL) for 16 h. Chromatographic

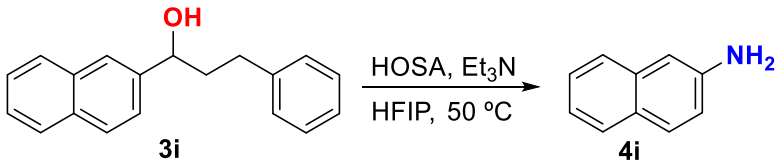
purification of the crude product afforded **4f** (27 mg, 81%) as an oil whose spectral data were in agreement with literature values.[20] TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.70 (d, *J* = 8.4 Hz, 1H), 6.32 (d, *J* = 2.5 Hz, 1H), 6.25 (dd, *J* = 8.4, 2.6 Hz, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.20 (br s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.95, 142.32, 140.66, 113.10, 106.50, 100.82, 56.71, 55.85.



4-(Piperidin-1-yl)aniline (4h): Following the general benzyl alcohol amination procedure, 1-(4-(piperidin-1-yl)phenyl)ethan-1-ol (**3g**) (50 mg, 0.243 mmol), Et_3N (51 µL, 0.365 mmol), and HOSA (41 mg, 0.365 mmol) were stirred at rt in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **4g** (27 mg, 65%) a brown solid mp 38-40 °C (lit.[21] 41 °C), whose spectral data were in agreement with literature values.[21] TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (d, *J* = 8.8 Hz, 2H), 6.64 (d, *J* = 8.7 Hz, 2H), 3.41 (br s, 2H), 3.00–2.95 (m, 4H), 1.71 (p, *J* = 5.7 Hz, 4H), 1.58–1.47 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.93, 139.94, 119.28, 116.29, 52.74, 26.33, 24.33.

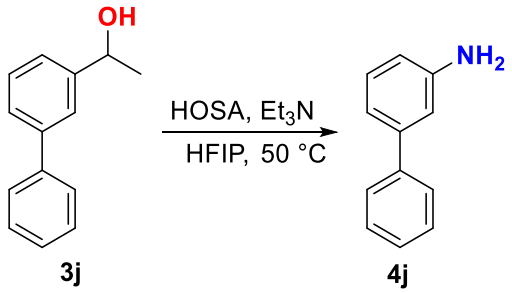


Benzene-1,4-diamine (4h): Following the general benzyl alcohol amination procedure, 1-(4-aminophenyl)ethan-1-ol ol (**3h**) (50 mg, 0.364 mmol), Et_3N (76 µL, 0.547 mmol), and HOSA (61 mg, 0.547 mmol) were stirred at rt in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **4h** (30 mg, 78%) as a brown solid whose spectral data were in agreement with literature values.[22] TLC: $R_f \approx 0.5$ (10% MeOH/CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57 (s, 4H), 3.21 (br s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.70, 116.85.

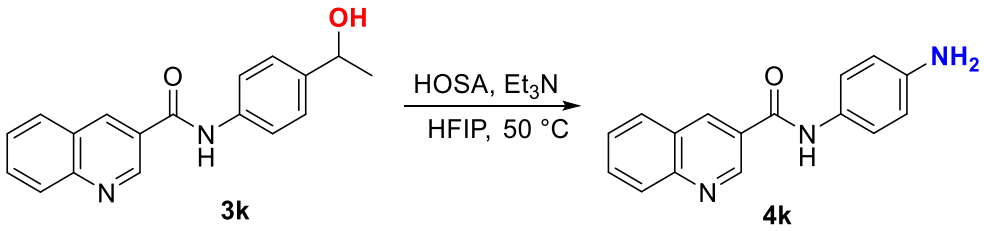


2-Naphthylamine (4i): Following the general benzyl alcohol amination procedure, 1-(naphthalen-2-yl)-3-phenylpropan-1-ol[23] (50 mg, 0.190 mmol), Et_3N (40 µL, 0.286 mmol), and HOSA (32 mg, 0.286 mmol) were stirred at 50 ºC in HFIP (2 mL) for 10 h. Chromatographic purification of the crude product afforded **4i** (19 mg, 70%) as an off white solid whose spectral data were in agreement with literature values.[24] TLC: $R_f \approx 0.4$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 13.9, 8.4 Hz, 2H), 7.60 (d, *J* = 8.3 Hz, 1H), 7.38 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.26–7.20

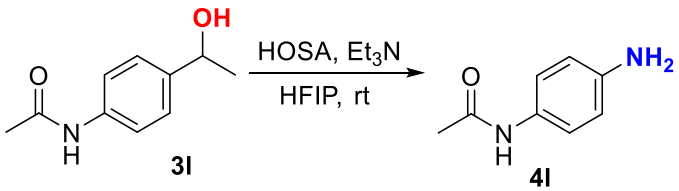
(m, 1H), 6.99 (d, *J* = 2.3 Hz, 1H), 6.95 (dd, *J* = 8.6, 2.3 Hz, 1H), 3.82 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.22, 135.04, 129.34, 128.10, 127.84, 126.47, 125.92, 122.60, 118.35, 108.72.



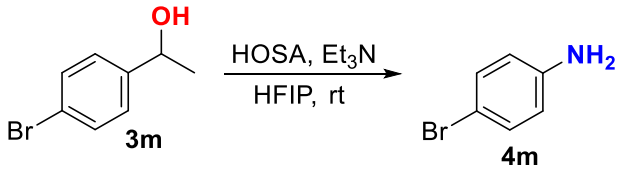
[1,1'-Biphenyl]-3-amine (4*J*): Following the general benzyl alcohol amination procedure, 1-(1,1'-biphenyl]-3-yl)ethan-1-ol (50 mg, 0.252 mmol), Et_3N (52 µL, 0.378 mmol), and HOSA (42 mg, 0.378 mmol) were stirred at 50 ºC in HFIP (2 mL) for 5 h. Chromatographic purification of the crude product afforded **4*J*** (31 mg, 73%) as a yellow solid whose spectral data were in agreement with literature values.[25] TLC: $R_f \approx 0.5$ (30% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61–7.53 (m, 2H), 7.47–7.39 (m, 2H), 7.38–7.31 (m, 1H), 7.28–7.20 (m, 1H), 7.01 (dt, *J* = 7.7, 1.3 Hz, 1H), 6.92 (t, *J* = 2.0 Hz, 1H), 6.70 (ddd, *J* = 8.0, 2.3, 1.0 Hz, 1H), 3.53 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.69, 142.59, 141.50, 129.81, 128.76, 127.35, 127.24, 117.92, 114.30, 114.12.



***N*-(4-Aminophenyl)quinoline-3-carboxamide (4k):** Following the general benzyl alcohol amination procedure, *N*-(4-(1-hydroxyethyl)phenyl)quinoline-3-carboxamide (50 mg, 0.171 mmol), Et_3N (35 µL, 0.256 mmol), and HOSA (28 mg, 0.256 mmol) were stirred at 50 ºC in HFIP (2 mL) for 12 h. Chromatographic purification of the crude product afforded **4k** (37 mg, 83%) as an yellow solid (decomposes at 179 °C) whose spectral data were in agreement with literature values.[26] TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, CD_3OD) δ 9.31 (d, *J* = 2.2 Hz, 1H), 8.89 (d, *J* = 2.2 Hz, 1H), 8.14–8.05 (m, 2H), 7.89 (ddd, *J* = 8.5, 7.0, 1.4 Hz, 1H), 7.72 (ddd, *J* = 8.0, 6.9, 1.2 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 2H), 6.77 (d, *J* = 8.7 Hz, 2H), 3.34 (br s, 1H). ^{13}C NMR (151 MHz, 2 :1 CD_3OD : $CDCl_3$) δ 165.48, 149.39, 149.07, 144.54, 137.39, 132.43, 130.27, 129.79, 128.79, 128.73, 128.50, 127.94, 123.61, 116.63.



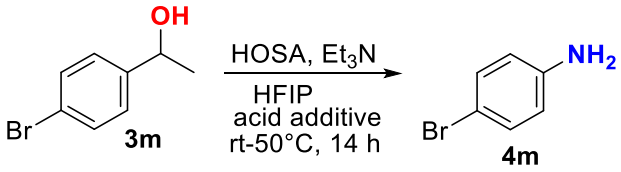
***N*-(4-Aminophenyl)acetamide (4l)**: Following the general benzyl alcohol amination procedure, *N*-(4-(1-hydroxyethyl)phenyl)acetamide (50 mg, 0.279 mmol), Et_3N (58 µL, 0.418 mmol), and HOSA (47 mg, 0.418 mmol) were stirred at rt in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **4l** (33 mg, 81%) as a solid mp 160-163 °C (lit.[27] 165-167 °C), whose spectral data were in agreement with literature values.[27] TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (d, *J* = 8.7 Hz, 2H), 6.68 (d, *J* = 8.7 Hz, 2H), 2.06 (br s, 2H); ^{13}C NMR (101 MHz, CD_3OD) δ 171.26, 145.55, 130.70, 123.18, 116.67, 23.46.

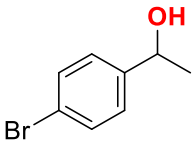
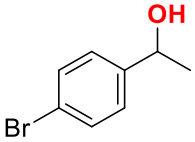
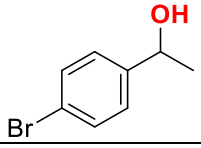


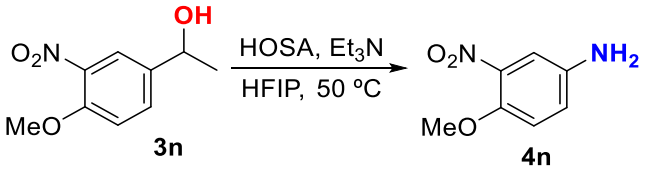
4-Bromoaniline (4m): Following the general benzyl alcohol amination procedure, 1-(4-bromophenyl)ethan-1-ol (50 mg, 0.251 mmol), Et_3N (105 µL, 0.753 mmol), and HOSA (85 mg, 0.753 mmol) were stirred at rt in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **4m** (30 mg, 72%) as a brown solid mp 59-61 °C (lit.[28] 60-61 °C), whose spectral data were in agreement with literature values.[28] TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.6 Hz, 2H), 6.58 (d, *J* = 8.7 Hz, 2H), 3.67 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.53, 132.10, 116.81, 110.27.

Note: 1.5 equiv of each HOSA and TEA at 50 °C for 14 h gave **4m** in 33% (14 mg) yield and unreacted starting material 51% (25 mg).

Screening with acid additives:

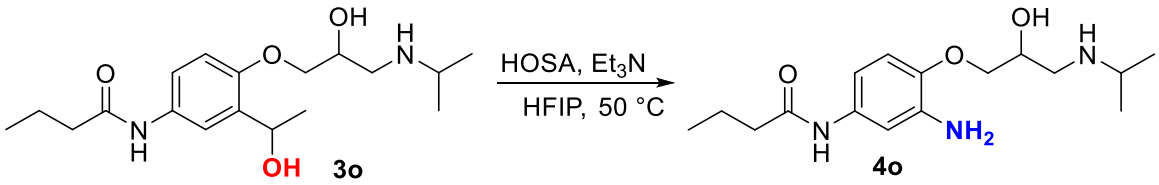


Starting material **3m**	HOSA(equiv)	TEA(equiv)	Additive (equiv)	Yield of **4m**	Yield of **3m**
	1.5	1.5	-	33%	51%
	1.5	1.5	Triflouroacetic acid (1)	14%	63%
	1.5	1.5	Methanesulphonic acid (1)	16%	66%



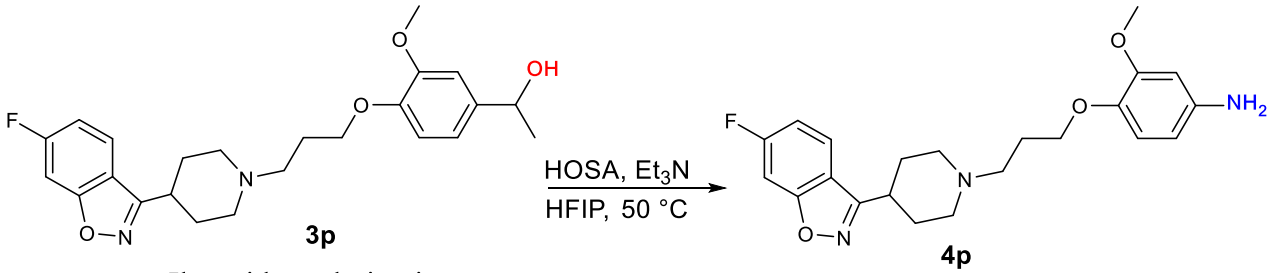
4-Methoxy-3-nitroaniline (4n): Following the general benzyl alcohol amination procedure, 1-(4-methoxy-3-nitrophenyl)ethan-1-ol (50 mg, 0.253 mmol), Et_3N (105 µL, 0.759 mmol), and HOSA (85 mg, 0.759 mmol) were stirred at 50 ºC in HFIP (2 mL) for 6 h. Chromatographic purification of the crude product afforded **4n** (28 mg, 73%) as a pale yellow solid mp 50-52 °C (lit.[29] 51-53 °C), whose spectral data were in agreement with literature values.[29] TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, *J* = 2.8 Hz, 1H), 6.95–6.83 (m, 2H), 3.87 (s, 3H), 3.61 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.09, 140.13, 121.15, 115.67, 111.69, 57.32.

Note: 1.5 equiv of each HOSA and TEA at 50 °C for 12 h gave **4n** in 21% (8 mg) yield and unreacted starting material 68% (34 mg).



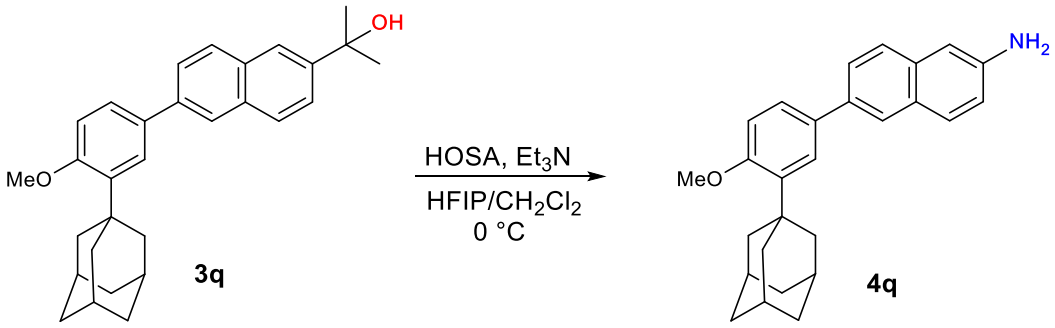
Acebutolol derivative

***N*-(3-Amino-4-(2-hydroxy-3-(isopropylamino)propoxy)phenyl)butyramide (4o):** Following the general benzyl alcohol amination procedure, *N*-(4-(2-hydroxy-3-(isopropylamino)propoxy)-3-(1-hydroxyethyl)phenyl)butyramide(30 mg, 0.080 mmol), Et_3N (33 µL, 0.240 mmol), and HOSA (27 mg, 0.240 mmol) were stirred at 50 ºC in HFIP (2 mL) for 5 h. Chromatographic purification of the crude product afforded **4o** (17 mg, 72%) as an yellow oil. TLC: $R_f \approx 0.5$ (20% MeOH/CH_2Cl_2). ^{1}H NMR (400 MHz, CD_3OD) δ 7.04 (d, *J* = 2.2 Hz, 1H), 6.82 – 6.74 (m, 2H), 4.13– 4.06 (m, 1H), 4.01 – 3.88 (m, 2H), 3.02 – 2.90 (m, 2H), 2.79 (dd, *J* = 12.2, 8.8 Hz, 1H), 2.29 (t, *J* = 7.4 Hz, 2H), 1.69 (q, *J* = 7.4 Hz, 2H), 1.16 (dd, *J* = 6.4, 2.7 Hz, 6H), 0.98 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 174.23, 144.89, 138.38, 133.81, 113.23, 111.60, 109.77, 72.58, 69.31, 50.44, 50.13, 39.79, 21.71, 21.66, 20.42, 14.00. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{16}H_{27}N_3O_3^+$ 310.2125; found 310.2130.



Iloperidone derivative

4-(3-(4-(6-Fluorobenzo[d]isoxazol-3-yl)piperidin-1-yl)propoxy)-3-methoxyaniline (4p): Following the general benzyl alcohol amination procedure, 1-(4-(3-(4-(6-fluorobenzo[d]isoxazol-3-yl)piperidin-1-yl)propoxy)-3-methoxyphenyl)ethan-1-ol[30] (30 mg, 0.070 mmol), Et_3N (7 µL, 0.105 mmol), and HOSA (11 mg, 0.105 mmol) were stirred at 50 ºC in HFIP (2 mL) for 1 h. Chromatographic purification of the crude product afforded **4p** (24 mg, 86%) as an yellow oil whose spectral data were in agreement with literature values.[31] TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.7, 5.1 Hz, 1H), 7.23 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.05 (td, *J* = 8.9, 2.1 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 6.30 (d, *J* = 2.5 Hz, 1H), 6.22 (dd, *J* = 8.4, 2.6 Hz, 1H), 4.01 (t, *J* = 6.6 Hz, 2H), 3.81 (s, 3H), 3.45 (br s, 2H), 3.14–3.00 (m, 3H), 2.59 (t, *J* = 7.4 Hz, 2H), 2.26–1.89 (m, 8H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.03, 164.03, 163.94, 163.37, 161.27, 150.79, 141.43, 141.24, 122.83, 122.76, 117.41, 117.40, 116.24, 112.52, 112.36, 106.68, 101.01, 97.64, 97.46, 68.89, 55.92, 55.58, 53.65, 34.72, 30.62, 27.05.

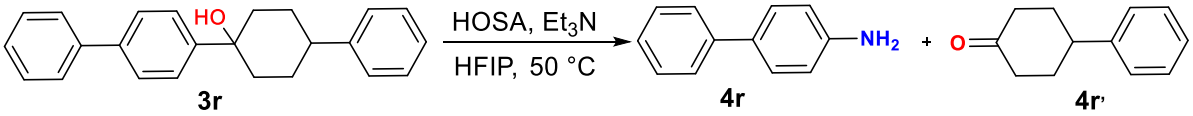


Adapalene derivative

6-(3-((3r,5r,7r)-Adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-amine (4q): Following the general benzyl alcohol amination procedure, 2-(6-(3-((3r,5r,7r)-adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-yl)propan-2-ol (30 mg, 0.070 mmol), Et_3N (29 µL, 0.210 mmol), and HOSA (23 mg, 0.210 mmol) were stirred at 0 ºC in a mixture of HFIP/CH_2Cl_2 (1.5 mL, 2:1) for 3 h. Chromatographic purification of the crude product afforded **4q** (21 mg, 80%) as a white solid mp 250-252 °C (lit.[31] 250-252 °C), whose spectral data were in agreement with literature values.[31] TLC: $R_f \approx 0.5$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 1.5 Hz, 1H), 7.72 (d, *J* = 8.7 Hz, 1H), 7.67–7.59 (m, 2H), 7.55 (d, *J* = 2.3 Hz, 1H), 7.49 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.04 (d, *J* = 2.3 Hz, 1H), 7.01–6.95 (m, 2H), 3.89 (s, 3H), 2.23–2.14 (m, 6H), 2.13–2.06 (m, 3H), 1.85–1.74 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.33, 143.47, 138.86, 135.98,

133.76, 133.63, 129.57, 128.56, 126.35, 125.80, 125.39, 125.13, 118.75, 112.17, 109.02, 55.31, 40.75, 37.29, 29.26.

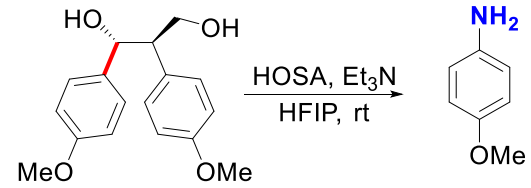
Test for Identification of byproduct and confirmation for imine hydrolysis:



[1,1'-Biphenyl]-4-amine (4r): Following the general benzyl alcohol amination procedure, 1-([1,1'-biphenyl]-4-yl)-4-phenylcyclohexan-1-ol[32] (50 mg, 0.152 mmol), Et_3N (29 µL, 0.152 mmol), and HOSA (17 mg, 0.152 mmol) were stirred at 50 ºC in HFIP (1.5 mL) for 2 h. Chromatographic purification of the crude product afforded **4r** (11 mg, 45%) as a solid[31] and **4r'** (10 mg, 38%) as a white solid[32] whose spectral data were in agreement with literature values.

[1,1'-Biphenyl]-4-amine (4r): TLC: $R_f \approx 0.5$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.52 (m, 2H), 7.46–7.36 (m, 4H), 7.28 (d, *J* = 7.4 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 2H), 3.73 (br s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.96, 141.29, 131.73, 128.79, 128.15, 126.54, 126.39, 115.52.

Note: Using HOSA (1.5 equiv) and Et_3N (1.5 equiv) provided **4r** (17 mg, 67%) and **4r'** (11 mg, 45%).

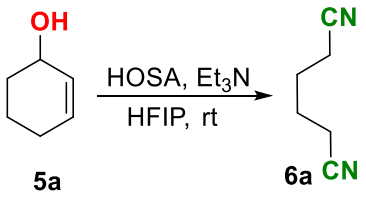


4-Methoxyaniline (4s): Following the general benzyl alcohol amination procedure, 1,2-bis(4-methoxyphenyl)propane-1,3-diol[33] (50 mg, 0.173 mmol), Et_3N (36 µL, 0.260 mmol), and HOSA (29 mg, 0.260 mmol) were stirred at rt in HFIP (1.2 mL) for 5 h. Chromatographic purification of the crude product afforded 4-methoxyaniline **4s** (13 mg, 63%) as a solid whose spectral data were in agreement with literature values.[31] TLC: $R_f \approx 0.5$ (30% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.75 (d, *J* = 8.7 Hz, 2H), 6.65 (d, *J* = 8.8 Hz, 2H), 3.75 (s, 3H), 3.44 (br s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.93, 139.99, 116.55, 114.91, 55.83.

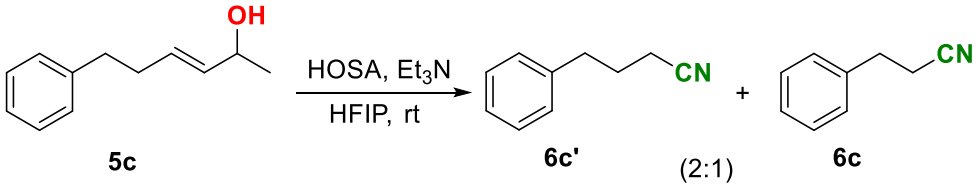
Table 3 Experimental Procedures and Analytical Data

General procedure for allyl alcohol nitrilation: Allylic alcohol (1 equiv) was added to a stirring equimolar solution of HOSA and Et_3N (4 equiv) at 0 °C in HFIP (0.15 M) under an argon atmosphere. After 15 min, the reaction mixture was warmed to rt-50 ºC. After complete consumption (monitored via TLC), the rt reaction mixture was diluted with CH_2Cl_2 (equal vol), washed with saturated aq. Na_2CO_3, brine, dried over anhydrous Na_2SO_4, and concentrated in

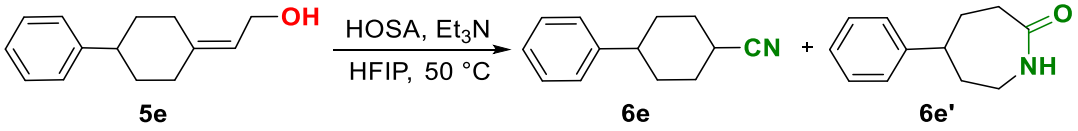
vacuo. The crude residue was purified chromatographically using MeOH/CH_2Cl_2 or EtOAc/hexanes as eluent to furnish the niriles. Variations in reaction conditions are noted in the Table 3 legends for select substrates.



Adiponitrile (6a): Following the general allyl alcohol nitrilation procedure, cyclohex-2-en-1-ol **(5a)** (50 mg, 0.510 mmol), Et_3N (284 µL, 2.040 mmol), and HOSA (230 mg, 2.040 mmol) were stirred at rt in HFIP (3 mL) for 24 h. Chromatographic purification of the crude product afforded **6a** (41 mg, 75%) as an oil whose spectral data were in agreement with literature values.[34] TLC: $R_f \approx 0.5$ (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, CD_3Cl_3) δ 2.49–2.35 (m, 4H), 1.90–1.73 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 118.79, 24.36, 16.75.



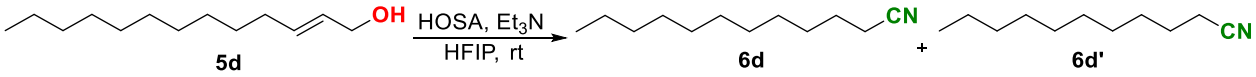
Mixture of 4-Phenylbutanenitrile (6c) and 3-phenylpropanenitrile (6c′): Following the general allyl alcohol nitrilation procedure, (*E*)-6-phenylhex-3-en-2-ol **(5c)** (50 mg, 0.179 mmol)[35], Et_3N (55 µL, 0.179 mmol), and HOSA (44 mg, 0.179 mmol) were stirred at rt in HFIP (2 mL) for 24 h. Chromatographic purification of the crude product afforded **6c′** and **6c** (33 mg, 82%, 2:1 as determined by ^{1}H NMR) as an inseparable oil whose spectral data were in agreement with literature values.[34] TLC: $R_f \approx 0.5$ (5% EtOAc/hexanes). **6c′**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.08 (m, 5H), 2.79 (t, *J* = 7.4 Hz, 2H), 2.32 (t, *J* = 7.1 Hz, 2H), 1.99 (p, *J* = 7.2 Hz, 2H). **6c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.08 (m, 5H), 2.96 (t, *J* = 7.4 Hz, 2H), 2.62 (t, *J* = 7.4 Hz, 2H).



4-Phenylcyclohexane-1-carbonitrile (6e) and 5-Phenylazepan-2-one (6e′): Following the general allyl alcohol nitrilation procedure, 2-(4-phenylcyclohexylidene)ethan-1-ol[37](50 mg, 0.247 mmol), Et_3N (138 µL, 0.990 mmol), and HOSA (111 mg, 0.990 mmol) were stirred at 50 ºC in HFIP (3 mL) for 14 h. Chromatographic purification of the crude product afforded **6e** (9 mg, 21%) as an oil and **6e′** (28 mg, 61%) as a creamy solid . Spectral data for both were in agreement with literature values[38,39].

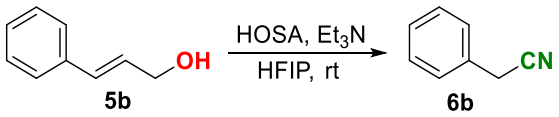
6e[38] (85:15 dr by ^{13}C NMR): TLC: $R_f \approx 0.5$ (10% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.28 (m, 2H), 7.27–7.15 (m, 3H), 3.10–2.95 (m, 1H), 2.58–2.47 (m, 1H), 2.31–1.99 (m, 2H),

1.94–1.83 (m, 3H), 1.77–1.63 (m, 2H), 1.57–1.41 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.16, 145.92, 128.67, 128.65, 126.92, 126.75, 126.57, 126.51, 122.78, 122.13, 43.72, 42.97, 32.82, 30.31, 30.04, 29.84, 28.88, 28.13, 26.85.
6e′[39]: mp 137-139 °C (lit.[37] 138-140 °C), TLC: $R_f \approx 0.5$ (10% MeOH/CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 2H), 7.25–7.14 (m, 3H), 6.49 (br s, 1H), 3.45–3.24 (m, 2H), 2.76 (tt, *J* = 12.1, 3.5 Hz, 1H), 2.68–2.51 (m, 2H), 2.07–1.92 (m, 2H), 1.88–1.63 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.57, 146.46, 128.77, 126.77, 126.66, 48.97, 42.26, 37.51, 35.96, 30.66.



Mixture of Dodecanenitrile (6d) and Undecanenitrile (6d′): Following the general allyl alcohol nitrilation procedure, (*E*)-tridec-2-en-1-ol **(5d)** (50 mg, 0.252 mmol), Et_3N (140 µL, 1.010 mmol), and HOSA (114 mg, 0.1.010 mmol) were stirred at rt in HFIP (3 mL) for 24 h. Chromatographic purification of the crude product afforded a mixture of **6d** and **6d′** (32 mg, 71%, 1.3:1 via mass spec analysis LC-HRMS) as an inseparable oil whose spectral data were in agreement with literature values.[38,39] TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (t, *J* = 7.1 Hz, 2H), 1.65 (p, *J* = 7.2 Hz, 2H), 1.51–1.39 (m, 2H), 1.35–1.21 (m, 14H), 0.88 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 120.05, 32.03, 31.99, 31.94, 29.85, 29.69, 29.65, 29.60, 29.44, 29.40, 29.31, 28.91, 28.81, 25.51, 22.82, 22.81, 22.78, 17.28, 14.27, 14.26, 14.24.

Index	Sample Name	Formula	Adduct / Charge	Precursor Mass	Found At Mass	Expected RT	Area	Mass Error (p...
1	RG-V-49-11C	C12H23N	[M+H]+	182.190	182.1901	2.97	7.544e5	-1.5
2	RG-V-49-11C	C11H21N	[M+H]+	168.175	168.1746	2.92	5.762e5	-0.2

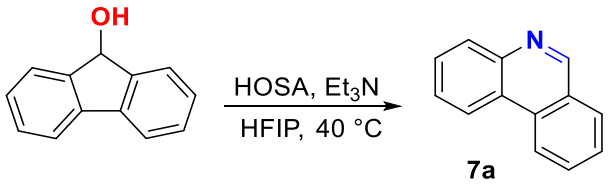


2-Phenylacetonitrile (6b): Following the general allyl alcohol nitrilation procedure, (*E*)-3-phenylprop-2-en-1-ol (**5b**) (50 mg, 0.337mmol), Et_3N (188 µL, 1.351 mmol), and HOSA (152 mg, 0.1.351 mmol) were stirred at rt in HFIP (3 mL) for 16 h. Chromatographic purification of the crude product afforded **6b** (30 mg, 76%) as an oil whose spectral data were in agreement with literature values.[40] TLC: $R_f \approx 0.5$ (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.29 (m, 5H), 3.76 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 130.01, 129.22, 128.13, 128.00, 117.98, 23.68.

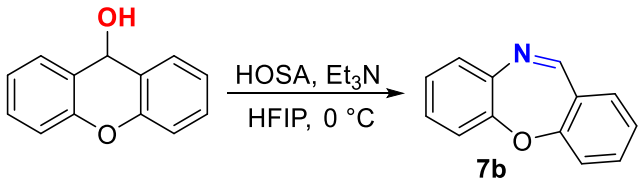
Table 4 Experimental Procedures and Analytical Data

General procedure for *N*-heterocyclic synthesis: Cyclic benzylic alcohol (1 equiv) was added to a stirring equimolar solution of HOSA and Et_3N (2.2 equiv) at 0 °C in HFIP (0.15 M) under an argon atmosphere. After 15 min, the reaction mixture was warmed to rt-40 ºC. After complete consumption (monitored via TLC), the rt reaction mixture was diluted with CH_2Cl_2 (equal vol), washed with saturated aq. Na_2CO_3, brine, dried over anhydrous Na_2SO_4, and concentrated in

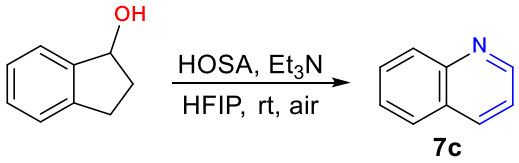
vacuo. The crude residue was purified chromatographically using MeOH/CH_2Cl_2 or EtOAc/hexanes as eluent to furnish the *N*-heterocycles. Variations in reaction conditions are noted in the Table 4 legends for select substrates.



Phenanthridine (7a): Following the general *N*-heterocyclic synthesis procedure, 9*H*-fluoren-9-ol (50 mg, 0.274 mmol), Et_3N (84 µL, 0.604 mmol), and HOSA (68 mg, 0.604 mmol) were stirred at 40 ºC in HFIP (2 mL) for 14 h. Chromatographic purification of the crude product afforded **7a** (37 mg, 75%) as a white solid mp 107-109 °C (lit.[39] 106-108 °C), whose spectral data were in agreement with literature values.[41] TLC: $R_f \approx 0.5$ (5% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 8.65–8.50 (m, 2H), 8.20 (dd, *J* = 8.1, 1.5 Hz, 1H), 8.04 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.85 (ddd, *J* = 8.4, 7.0, 1.4 Hz, 1H), 7.80–7.61 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.66, 144.54, 132.67, 131.14, 130.23, 128.89, 128.81, 127.61, 127.21, 126.49, 124.22, 122.33, 121.98.

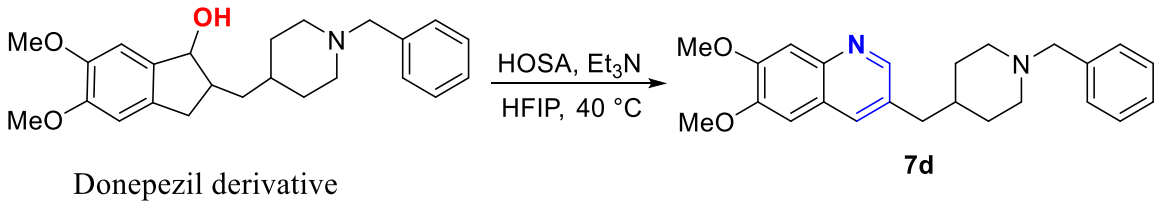


Dibenzo[b,f][1,4]oxazepine (7b): Following the general *N*-heterocyclic synthesis procedure, 9*H*-xanthen-9-ol (50 mg, 0.252 mmol), Et_3N (42 µL, 0.303 mmol), and HOSA (34 mg, 0.303 mmol) were stirred at 0 ºC in HFIP (2 mL) for 5 h. Chromatographic purification of the crude product afforded **7b** (34 mg, 70%) a yellow solid mp 75-77 °C (lit.[42] 74-77 °C), whose spectral data were in agreement with literature values.[42] TLC: $R_f \approx 0.5$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.46 (td, *J* = 8.1, 1.7 Hz, 1H), 7.36 (td, *J* = 7.0, 1.8 Hz, 2H), 7.25–7.08 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.72, 160.57, 152.83, 140.63, 133.44, 130.22, 129.35, 128.90, 127.47, 125.81, 125.18, 121.48, 120.83.



Quinoline (7c): Following the general *N*-heterocyclic synthesis procedure, 2,3-dihydro-1*H*-inden-1-ol (50 mg, 0.373 mmol), Et_3N (114 µL, 0.820 mmol), and HOSA (92 mg, 0.820 mmol) were stirred at rt in HFIP (2 mL) open to the atmosphere for 6 h. Chromatographic purification of the crude product afforded **7c** (32 mg, 68%) as an oil whose spectral data were in agreement with literature values.[43] TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (dd,

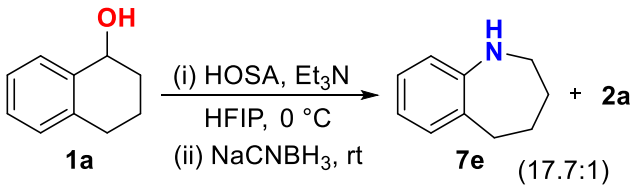
J = 4.2, 1.7 Hz, 1H), 8.19–8.05 (m, 2H), 7.85–7.79 (m, 1H), 7.72 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.55 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.40 (dd, *J* = 8.3, 4.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.52, 148.39, 136.21, 129.60, 129.57, 128.42, 127.91, 126.68, 121.20.



Donepezil derivative

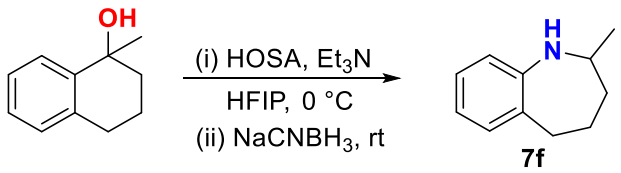
7d

3-((1-Benzylpiperidin-4-yl)methyl)-6,7-dimethoxyquinoline (7d): Following the general *N*-heterocyclic synthesis procedure, 2-((1-benzylpiperidin-4-yl)methyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-ol[44] (50 mg, 0.119 mmol), Et_3N (36 µL, 0.263 mmol), and HOSA (29 mg, 0.263 mmol) were stirred at 40 ºC in HFIP (2 mL) for 5 h. Chromatographic purification of the crude product afforded **7d** (34 mg, 76%) as an oil. TLC: $R_f \approx 0.5$ (20% MeOH/CH_2Cl_2).^{1}H NMR (400 MHz, CD_3OD) δ 8.44 (d, *J* = 2.1 Hz, 1H), 7.95 (d, *J* = 2.1 Hz, 1H), 7.35–7.23 (m, 6H), 7.21 (s, 1H), 3.97 (s, 3H), 3.96 (s, 3H), 3.50 (s, 2H), 2.94–2.85 (m, 2H), 2.70 (d, *J* = 6.6 Hz, 2H), 1.99 (td, *J* = 12.1, 2.4 Hz, 2H), 1.71–1.57 (m, 3H), 1.45–1.28 (m, 2H); ^{13}C NMR (151 MHz, CD_3OD) δ 152.54, 150.25, 148.51, 142.82, 136.70, 134.60, 131.59, 129.53, 127.90, 127.09, 124.12, 105.70, 104.92, 62.84, 55.04, 54.99, 53.16, 39.36, 37.45, 31.11. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{24}H_{28}N_2O_2^+$ 377.2224; found 377.2238.

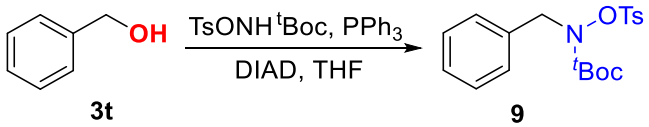


1a **7e** (17.7:1)

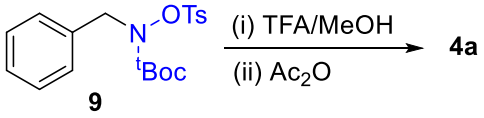
Mixture of 2,3,4,5-Tetrahydro-1*H*-benzazepine (7e) and 2a: To a stirring, 0 °C solution of HOSA (45 mg, 0.404 mmol) in HFIP (2 mL) was added Et_3N (56 µL mg, 0.404 mmol) under an argon atmosphere. After 15 min, **1a** (50 mg, 0.337 mmol) was added and stirred at 0 ºC. After 3 h (monitored by TLC), $NaCNBH_3$ (41 mg, 0.674 mmol) was added and then the reaction mixture was stirred at rt. After 4 h, the reaction mixture was diluted with H_2O (10 mL) and CH_2Cl_2 (10 mL), washed with saturated aq. Na_2CO_3 (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified chromatographically using a gradient of 20-30% EtOAc/hexanes to give **7e** (35 mg, 71%) as a pale yellow solid whose spectral data were in agreement with literature values.[45] mp 30-32 °C (lit.[45] 30-32 °C), and **2a** (4 mg, 4%) as an oil. **7e:** TLC: $R_f \approx 0.5$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.04 (td, *J* = 7.6, 1.6 Hz, 1H), 6.83 (td, *J* = 7.4, 1.2 Hz, 1H), 6.74 (dd, *J* = 7.8, 1.2 Hz, 1H), 3.65 (br s, 1H), 3.08–3.01 (m, 2H), 2.82–2.72 (m, 2H), 1.87–1.74 (m, 2H), 1.70–1.60 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.34, 133.89, 130.86, 126.67, 121.03, 119.50, 49.00, 36.14, 32.05, 27.00.



2-Methyl-2,3,4,5-tetrahydro-1*H*-benzo[b]azepine (7f): To a stirring, 0 °C solution of HOSA (41 mg, 0.369 mmol) in HFIP (2 mL) was added Et_3N (51 µL, 0.369 mmol) under an argon atmosphere. After 15 min, the 1-methyl-1,2,3,4-tetrahydronaphthalen-1-ol (50 mg, 0.308 mmol) was added and stirred at 0 ºC. After 30 min (monitored by TLC), $NaCNBH_3$ (38 µL, 0.616 mmol) was added and then the reaction mixture was stirred at rt. After 4 h, the reaction mixture was diluted with H_2O (10 mL) and CH_2Cl_2 (10 mL), washed with saturated aqueous Na_2CO_3 (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified chromatographically using a gradient of 20-30% EtOAc/hexanes to give **7f** (45 mg, 91%) as a white solid whose spectral data were in agreement with literature values.[46] mp 57-59 °C (lit.[44] 57-60 °C), TLC: $R_f \approx 0.5$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 7.5 Hz, 1H), 7.06 (td, *J* = 7.8, 1.6 Hz, 1H), 6.86 (td, *J* = 7.4, 1.3 Hz, 1H), 6.75 (d, *J* = 7.2 Hz, 1H), 3.39 (br s, 1H), 3.00–3.89 (m, 1H), 2.90–2.63 (m, 2H), 2.02–1.76 (m, 2H), 1.59–1.34 (m, 2H), 1.27 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.02, 133.95, 130.64, 126.67, 121.06, 119.92, 53.85, 39.43, 35.65, 26.39, 24.21.



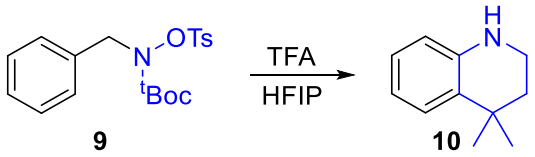
***tert*-Butyl benzyl(tosyloxy)carbamate (9):** Diisopropyl azodicarboxylate (DIAD) (109 µL, 0.462 mmol) was added to a stirring, 0 °C solution of PPh_3 (145 mg, 0.555 mmol) in dry THF under an argon atmosphere. A white precipitate developed after stirring for about 10 min. After 30 min total, a solution of benzyl alcohol **(3t)** (50 mg, 0.462 mmol) in dry THF and neat *N*-*tert*-butyl tosyloxycarbamate (TsONH*t*Boc) (150 mg, 0.555 mmol) were added successively. The ice bath was removed after 1 h and the reaction mixture was stirred at rt. After 2 h, all volatiles were removed *in vacuo* and the residue was purified chromatographyically using a gradient of 10-15% EtOAc/hexanes as eluent to furnish adduct **9** (160 mg, 91%) as a solid, mp 88-90 °C. TLC: $R_f \approx 0.5$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.9 Hz, 2H), 7.40–7.20 (m, 7H), 4.76 (s, 2H), 2.45 (s, 3H), 1.19 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.31, 145.86, 134.97, 131.38, 129.83, 129.68, 129.05, 128.62, 128.17, 83.63, 56.40, 27.69, 21.84. HRMS (ESI, *m/z*): calcd. for $[M+H]^+$, $C_{19}H_{23}NO_5S^+$ 378.1370; found 378.1374.



(*iv*) ***N*-phenylacetamide (4a):** To a stirring, 0 °C solution of **9** (100 mg, 0.265 mmol) in MeOH (3 mL, 1:2) was added trifluoroacetic acid (TFA) under an argon atmosphere. After stirring for 5

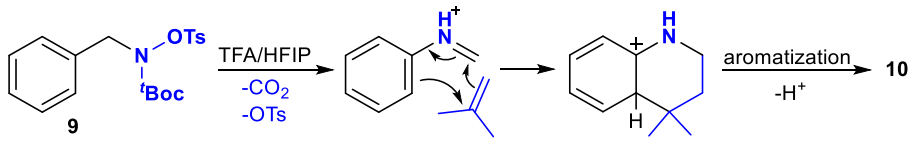
h, the reaction mixture was diluted with H_2O (10 mL) and CH_2Cl_2 (10 mL), washed with saturated aqueous Na_2CO_3 (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue (65 mg) was acetylated without purification (*vide infra*).

Acetic anhydride (0.32 mL, 3.464 mmol) was added to stirring, rt solution of the above crude material (65 mg, 0.698 mmol) in dry CH_2Cl_2 (5 mL). After 15 h, all volatiles were removed *in vacuo* and the crude residue was purified chromatographically using 70-80% EtOAc/hexanes as eluemt to furnish **4a** (30 mg, 63%) as a solid whose spectral data were in agreement with literature values (*vide supra*).



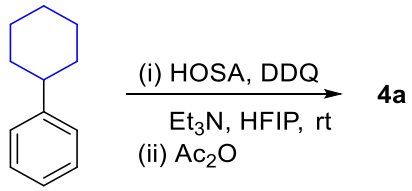
9 **10**

Plausible mechanism



9

4,4-Dimethyl-1,2,3,4-tetrahydroquinoline (10): To a stirring, 0 °C solution of adduct **9** (100 mg, 0.265 mmol) in HFIP (2 mL) was added trifluoroacetic acid (TFA) (101 µL, 1.326 mmol, 5 equiv) under an argon atmosphere. After 30 min, the reaction mixture was diluted with H_2O (10 mL) and CH_2Cl_2 (10 mL), washed with saturated aqueous Na_2CO_3 (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified chromatographically to give **10** (45 mg, 78%) as an oil whose spectral data were in agreement with literature values.[47] TLC: $R_f \approx 0.6$ (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (dd, J = 7.8, 1.5 Hz, 1H), 6.96 (ddd, J = 8.0, 7.2, 1.5 Hz, 1H), 6.70–6.63 (m, 1H), 6.50 (dd, J = 8.0, 1.3 Hz, 1H), 3.39–3.13 (m, 2H), 1.82–1.69 (m, 2H), 1.30 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.21, 130.55, 126.60, 126.51, 117.40, 114.51, 38.52, 37.30, 31.73, 31.05.



(*i*) ***N*-Phenylacetamide (4a):** Following the general benzyl alcohol amination procedure, cyclohexyl benzene (50 mg, 0.312 mmol), Et_3N (65 µL, 0.468 mmol), HOSA (52 mg, 0.468 mmol) and DDQ (70 mg, 0.312 mmol), were stirred at rt in HFIP (2 mL) for 6 h. After extractive isolation using CH_2Cl_2 (3 × 10 mL) and concentration *in vacuo*, the residue (56 mg) was acetylated (*vide infra*) to facilitate isolation and identification.

Acetic anhydride (0.30 mL, 3.279 mmol) was added to a stirring, rt solution of the above residue (61 mg, 0.655 mmol) in dry CH_2Cl_2 (5 mL). After 15 h, all volatiles were removed *in vacuo* and the crude residue was purified chromatographically using 70-80% EtOAc/hexanes as eluent to

furnish **4a** (28 mg, 67%) as a solid whose spectral data were in agreement with literature values (*vide supra*).

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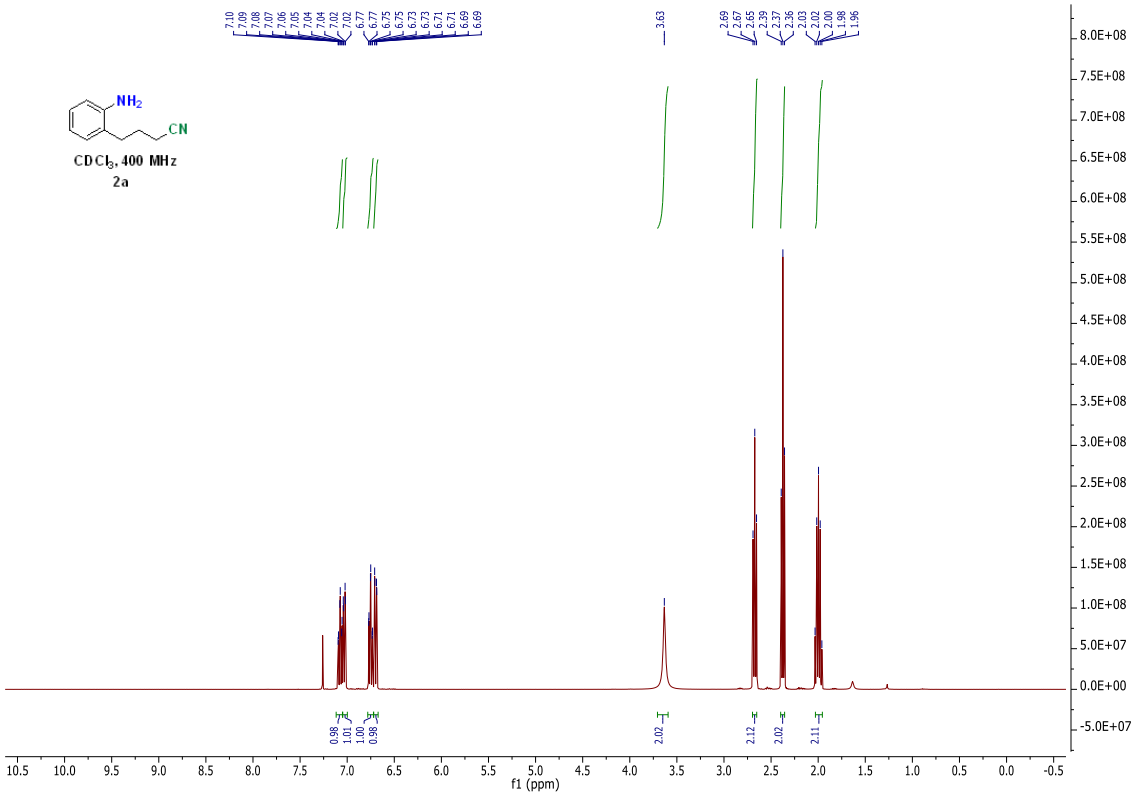
^{1}H/^{13}C NMR Spectra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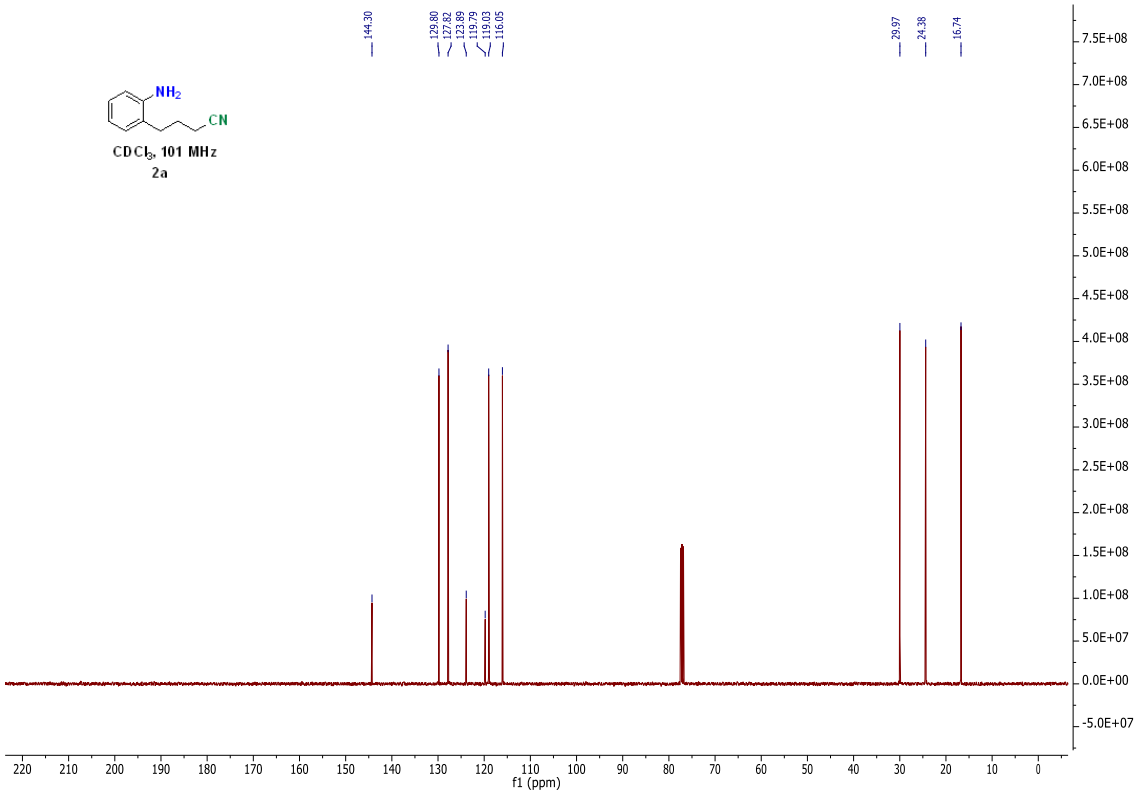
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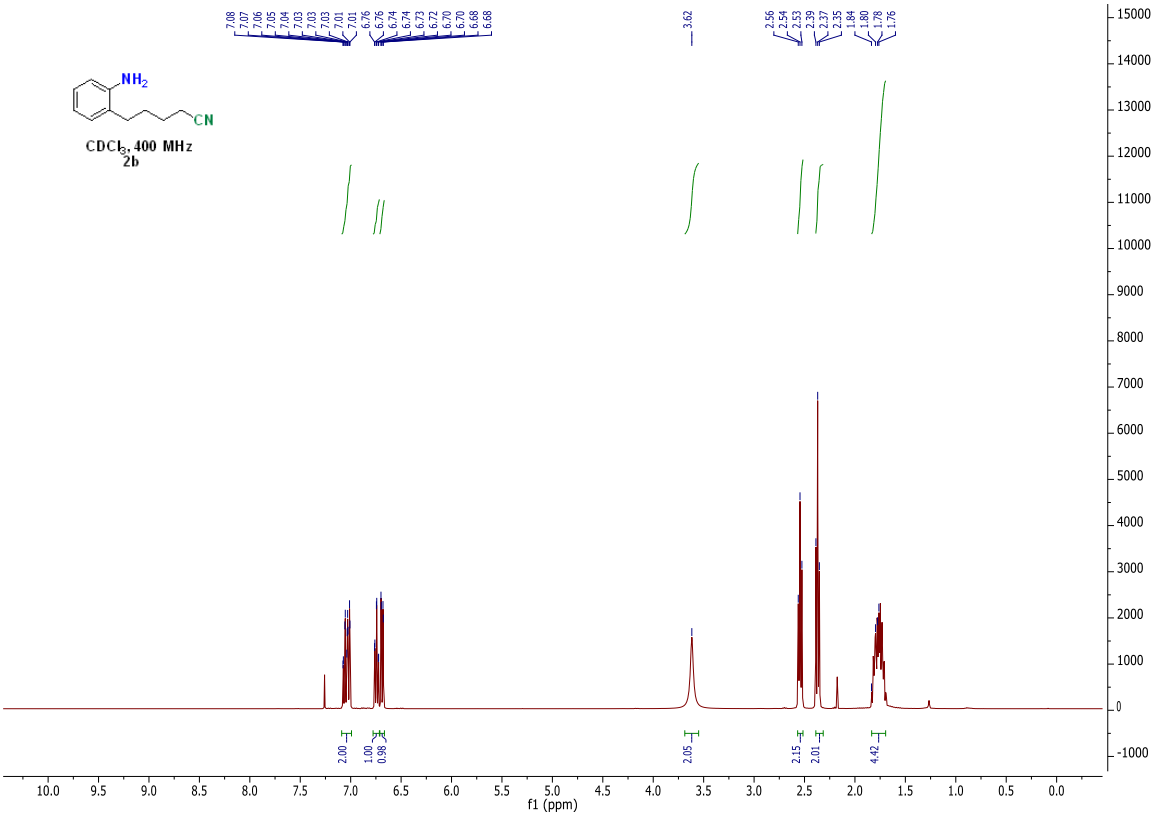
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7.07
7.06
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7.04
7.03
7.03
7.03
7.01
7.01
6.76
6.76
6.74
6.74
6.73
6.72
6.70
6.70
6.68
6.68
3.62
2.56
2.54
2.53
2.39
2.37
2.35
1.84
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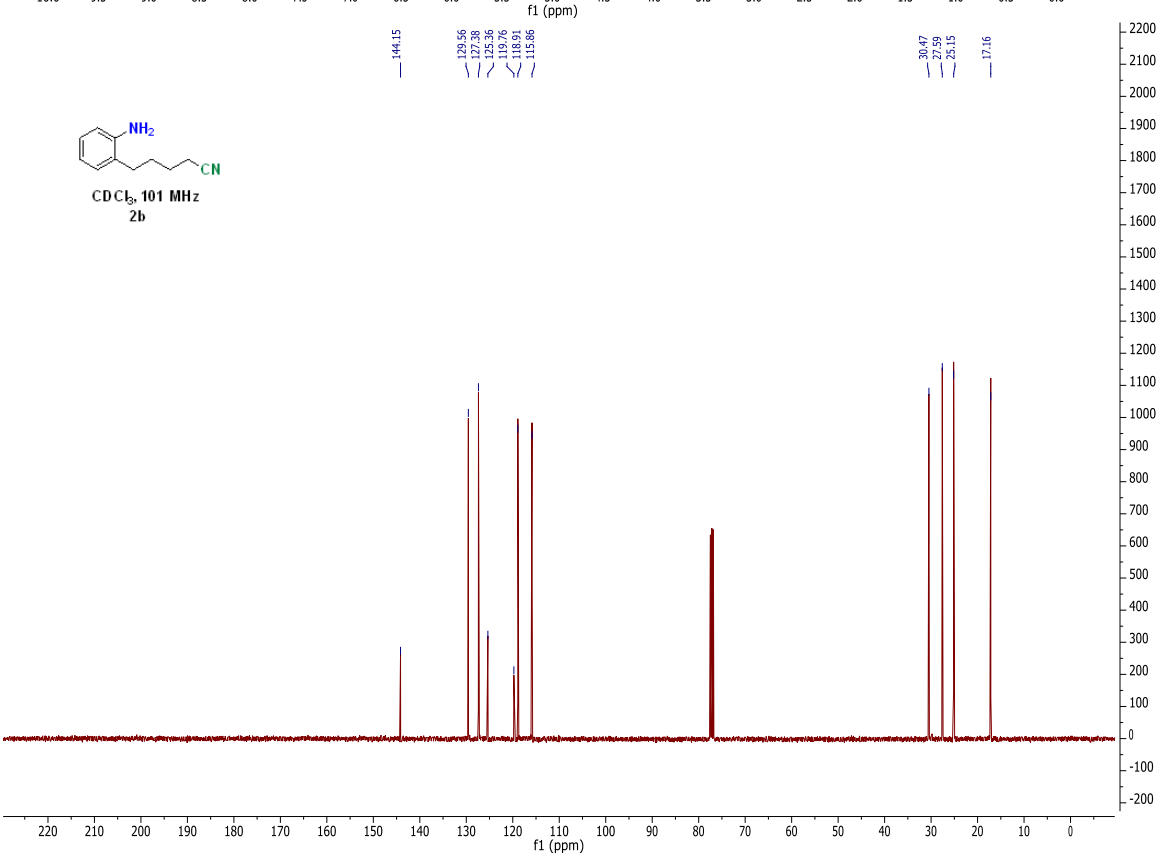
1.76
2.00
1.00
0.98
2.05
2.15
2.01
4.42
f1 (ppm)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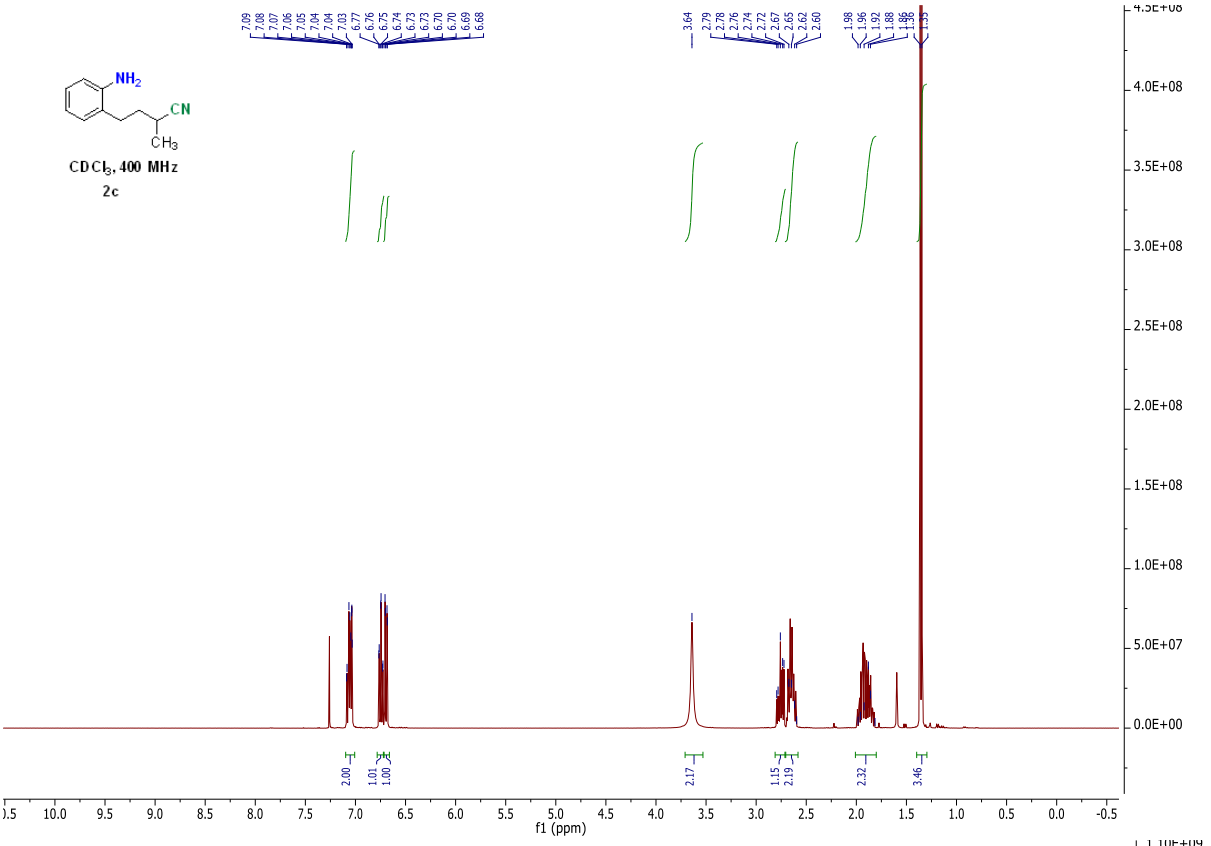
27.59
25.15
17.16
f1 (ppm)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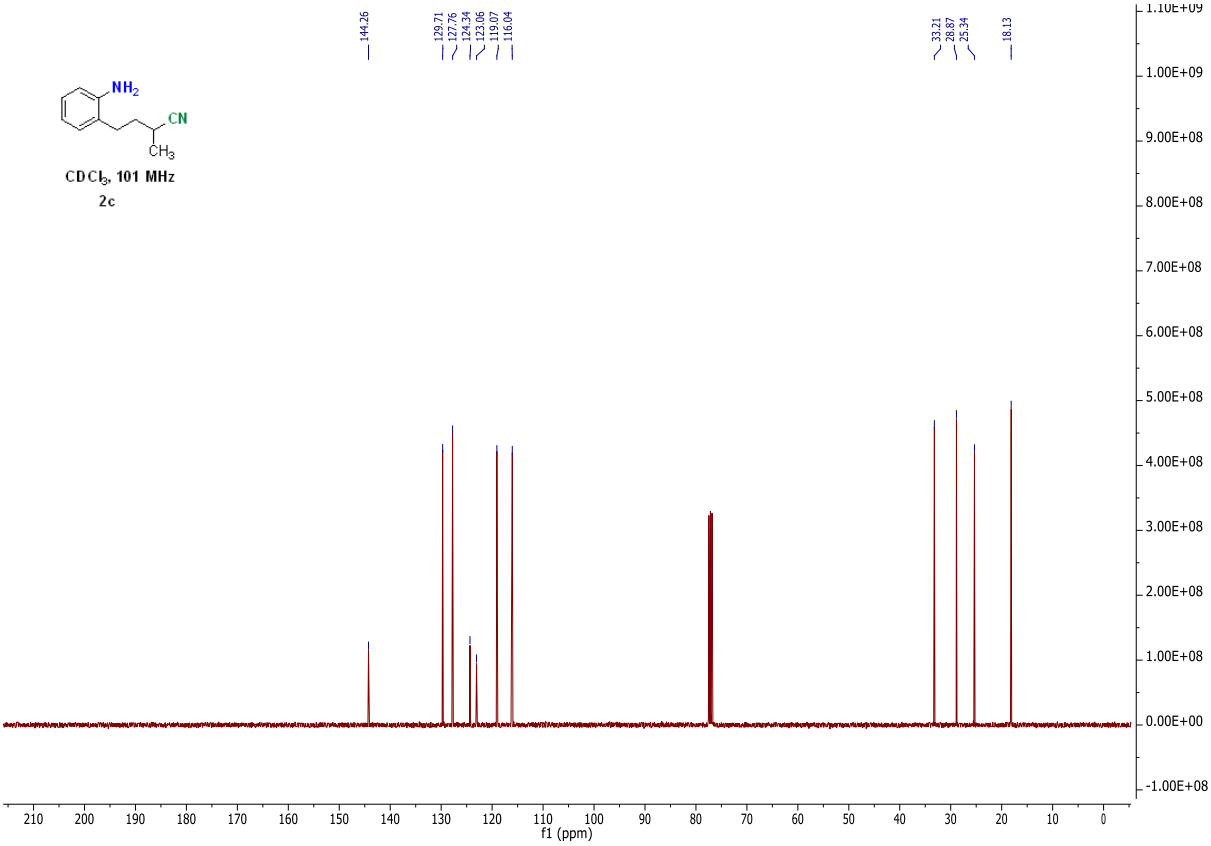
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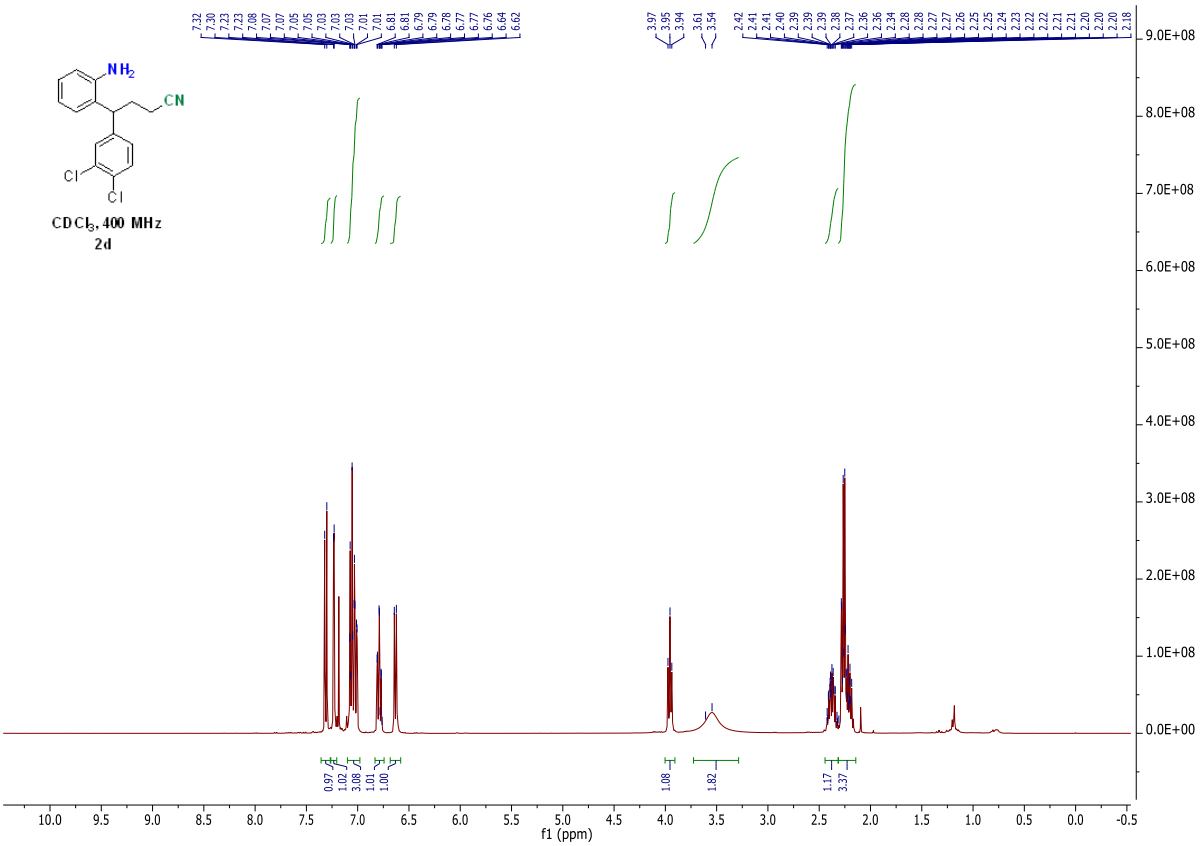
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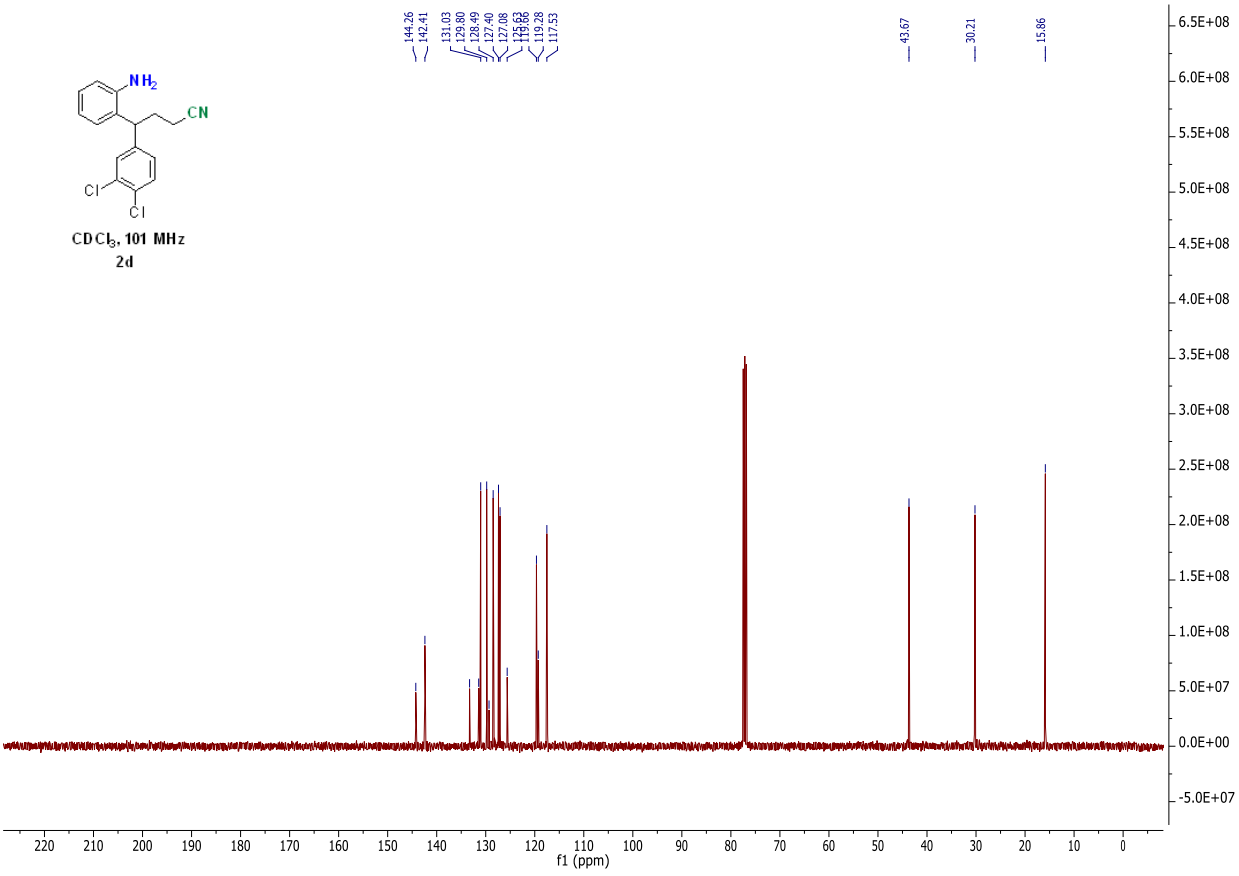
2d
f1 (ppm)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Cl
Cl
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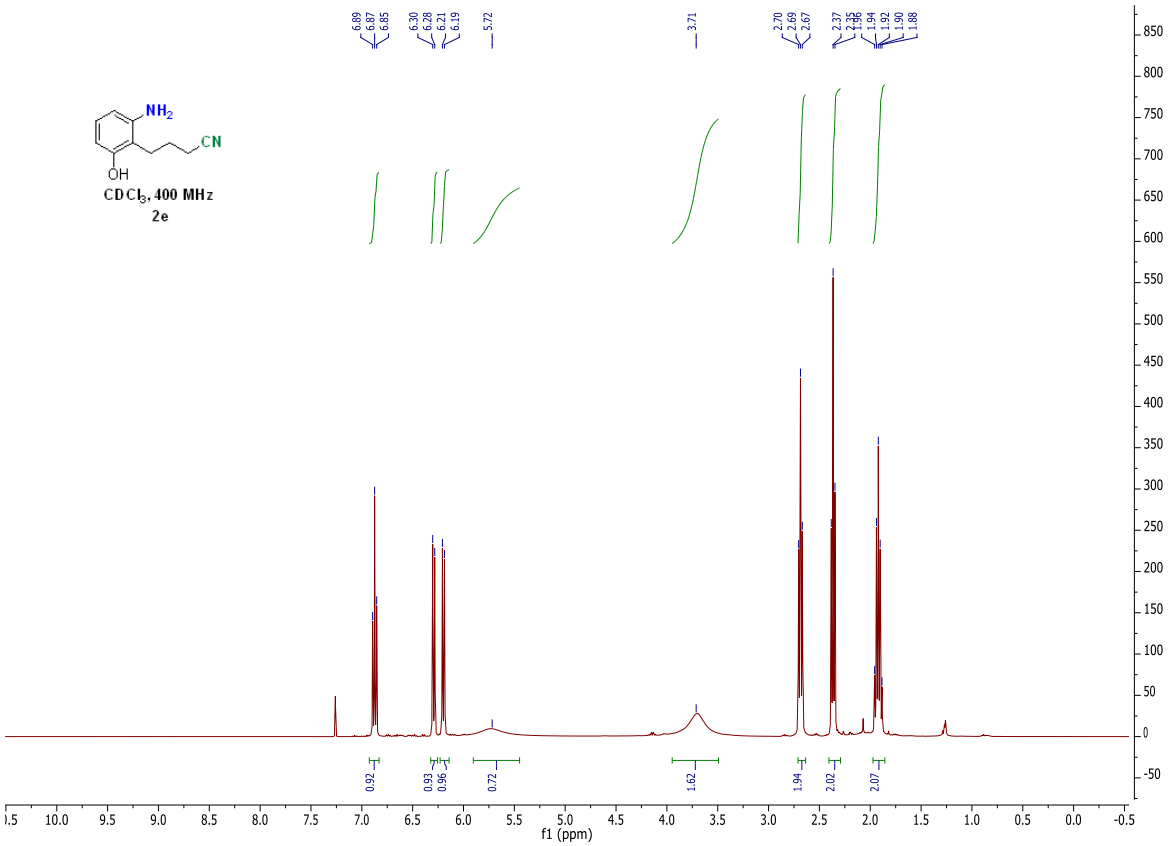
2d
f1 (ppm)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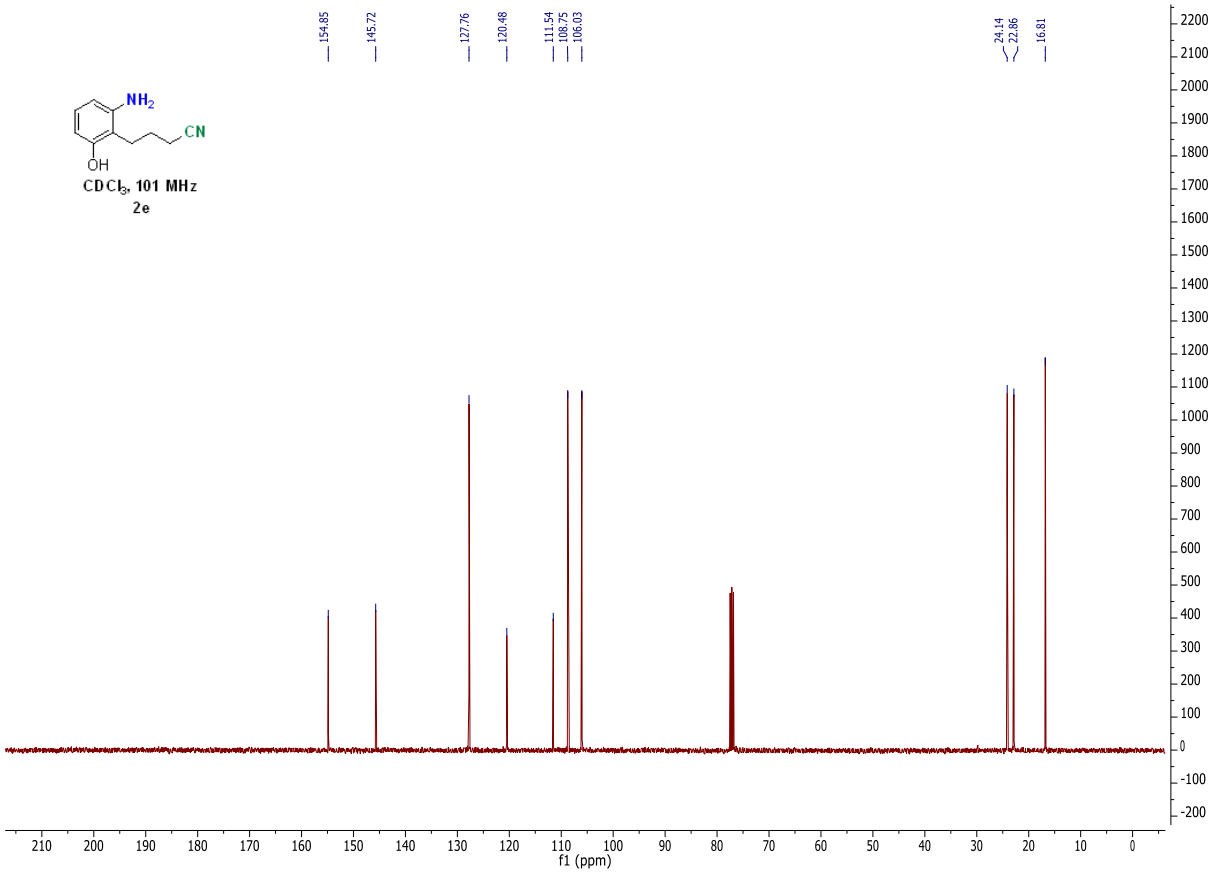
3.71
2.70
2.69
2.67
2.37
2.35
2.33
1.94
1.92
1.90
1.88
0.92
0.93
0.96
0.72
1.62
1.94
2.02
2.07
f1 (ppm)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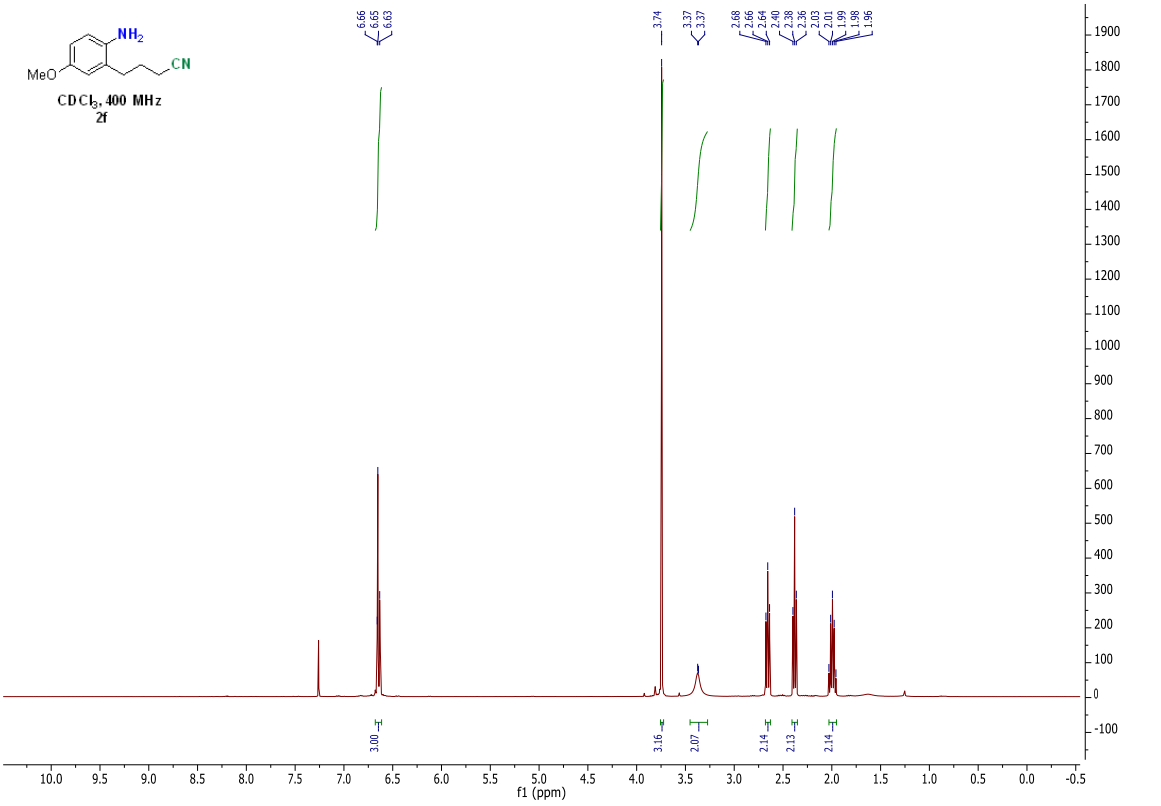
16.81
f1 (ppm)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3.37
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2.64
2.40
2.38
2.36
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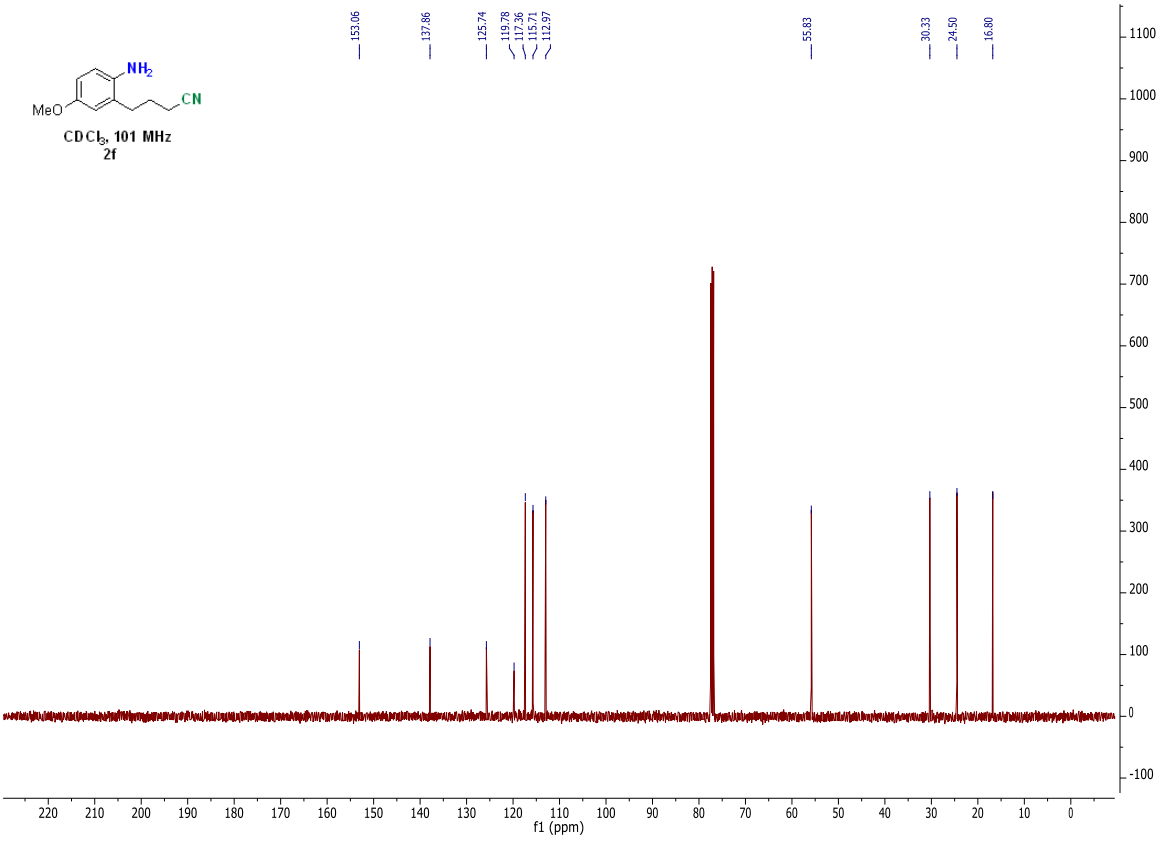
2.07
2.14
2.13
2.14
f1 (ppm)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CN
CDCl3, 101 MHz
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30.33
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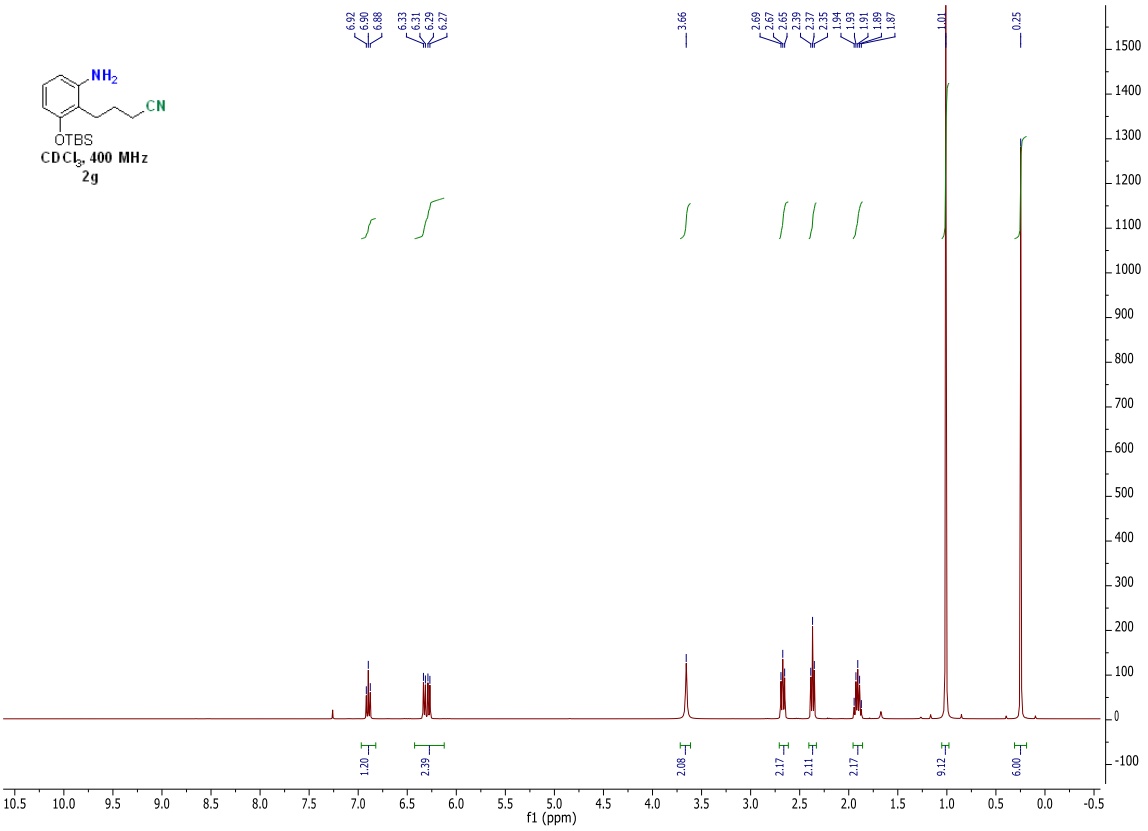
f1 (ppm)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CN
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6.88
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6.31
6.29
6.27
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2.69
2.67
2.65
2.39
2.37
2.35
1.94
1.93
1.91
1.89
1.87
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2.08
2.17
2.11
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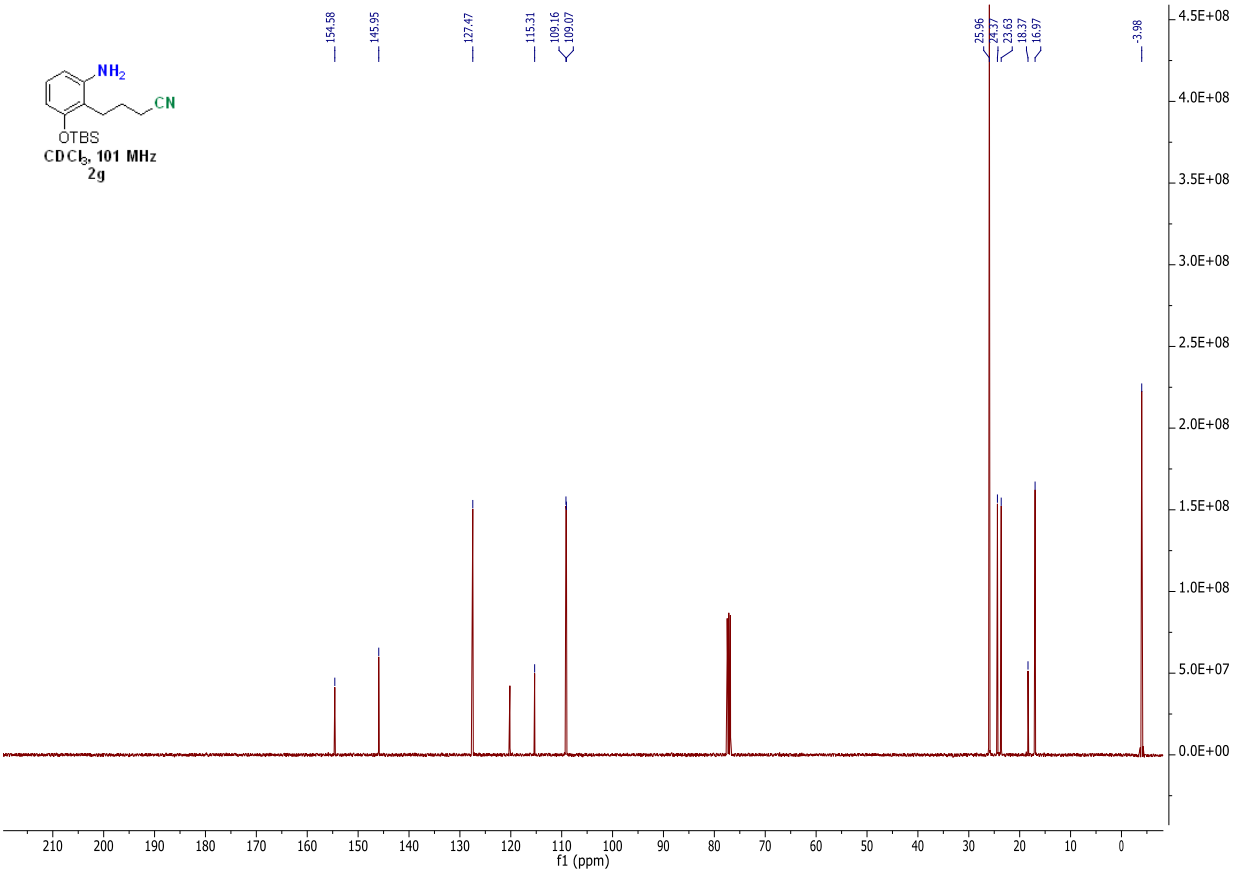
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23.63
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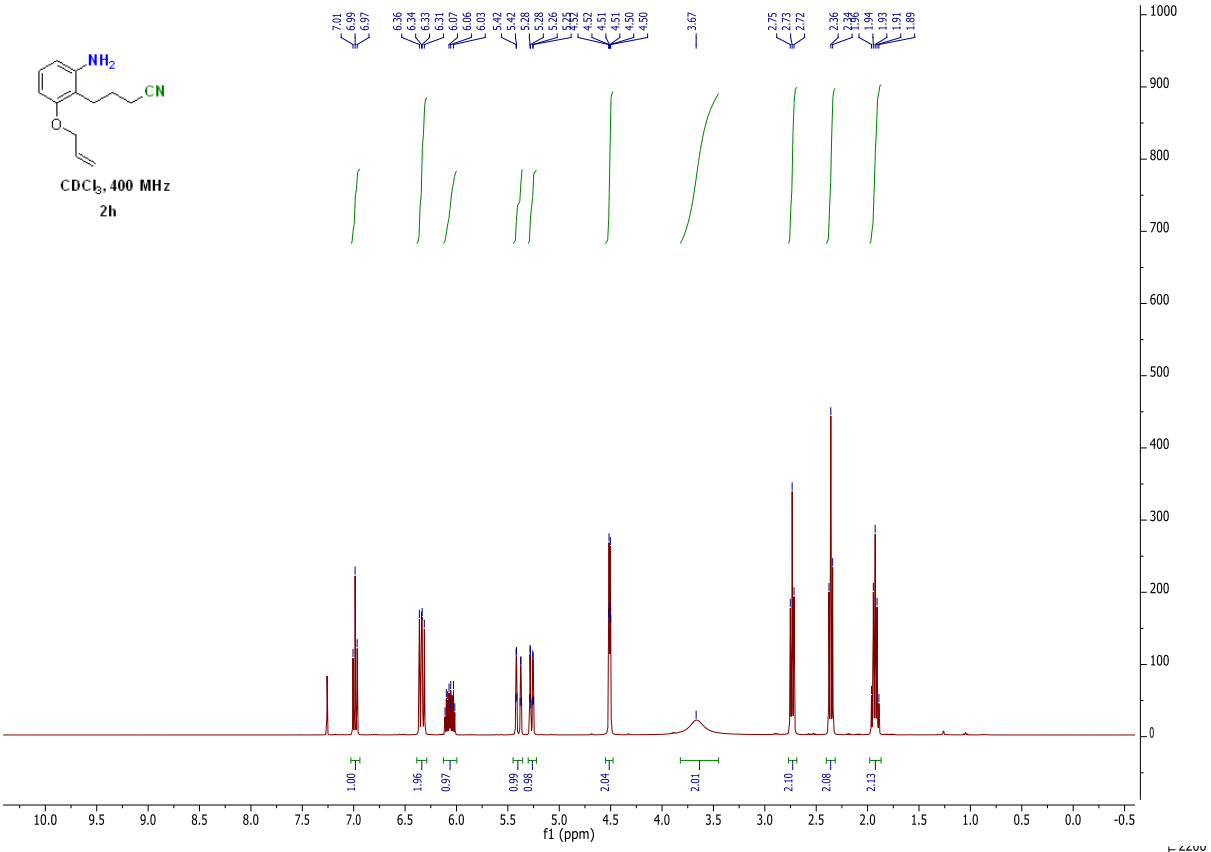
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O
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6.34
6.33
6.31
6.07
6.06
6.03
5.42
5.42
5.28
5.28
5.26
5.26
4.52
4.52
4.51
4.51
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2.72
2.36
2.34
2.34
2.32
1.94
1.93
1.91
1.89
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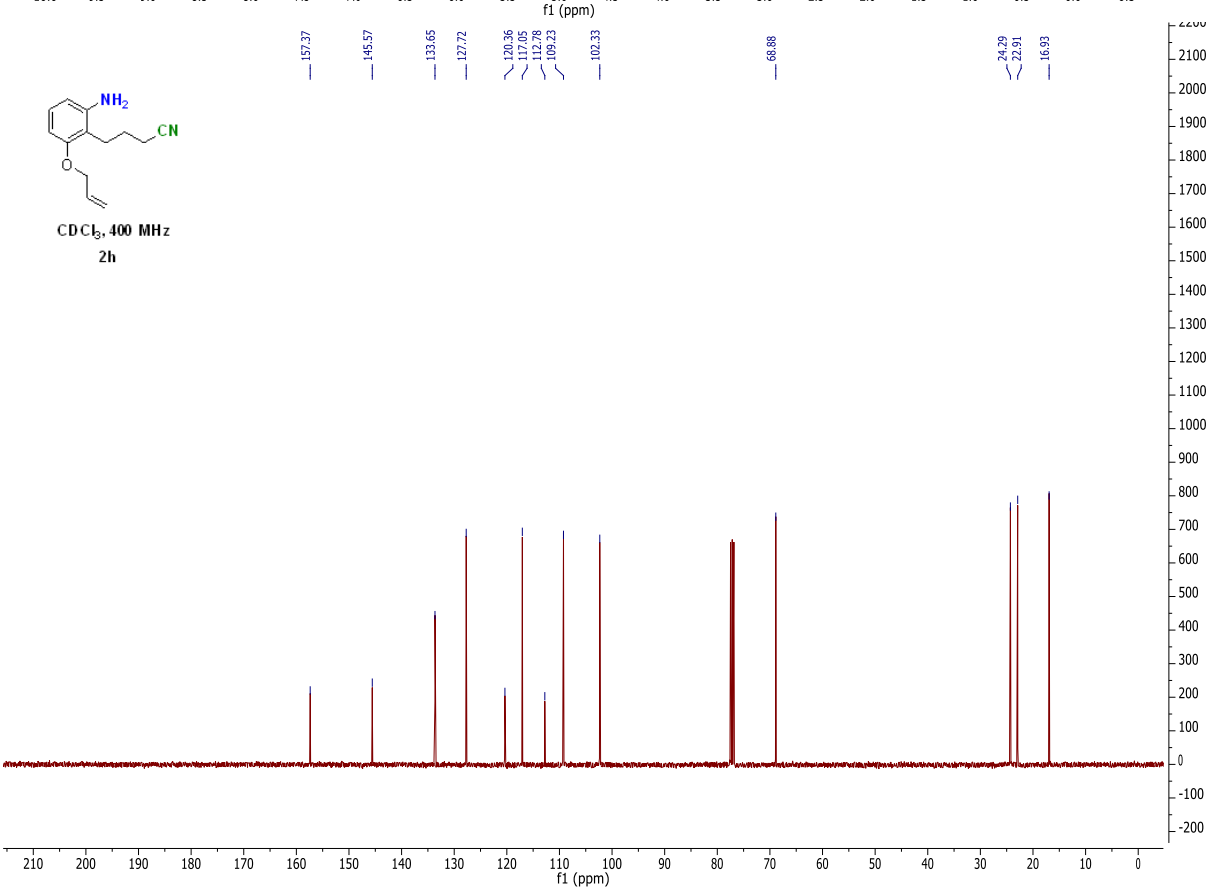
0.99
0.98
2.04
2.01
2.10
2.08
2.13
f1 (ppm)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O
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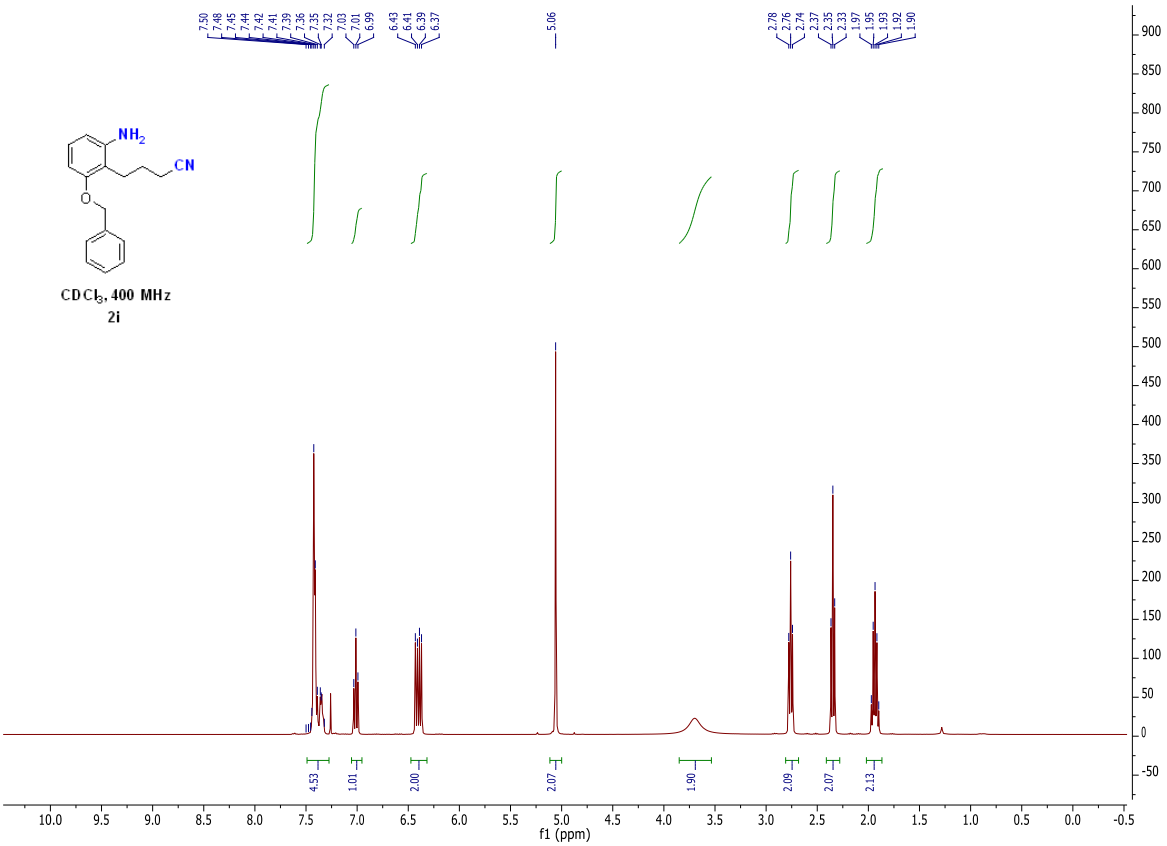
109.23
102.33
68.88
24.29
22.91
16.93
f1 (ppm)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O
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7.36
7.35
7.32
7.03
7.01
6.99
6.43
6.41
6.39
6.37
5.06
2.78
2.76
2.74
2.37
2.35
2.33
1.97
1.95
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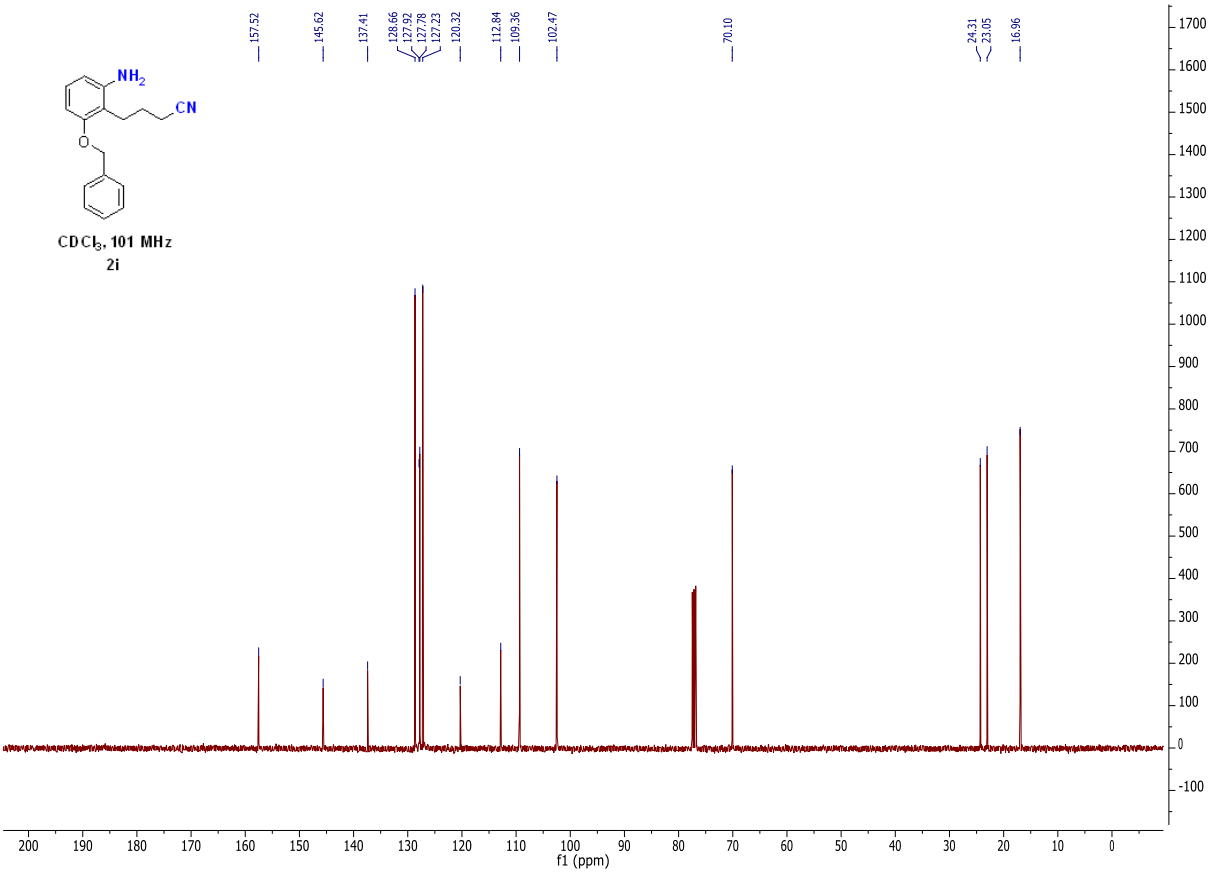
2.09
2.07
2.13
f1 (ppm)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O
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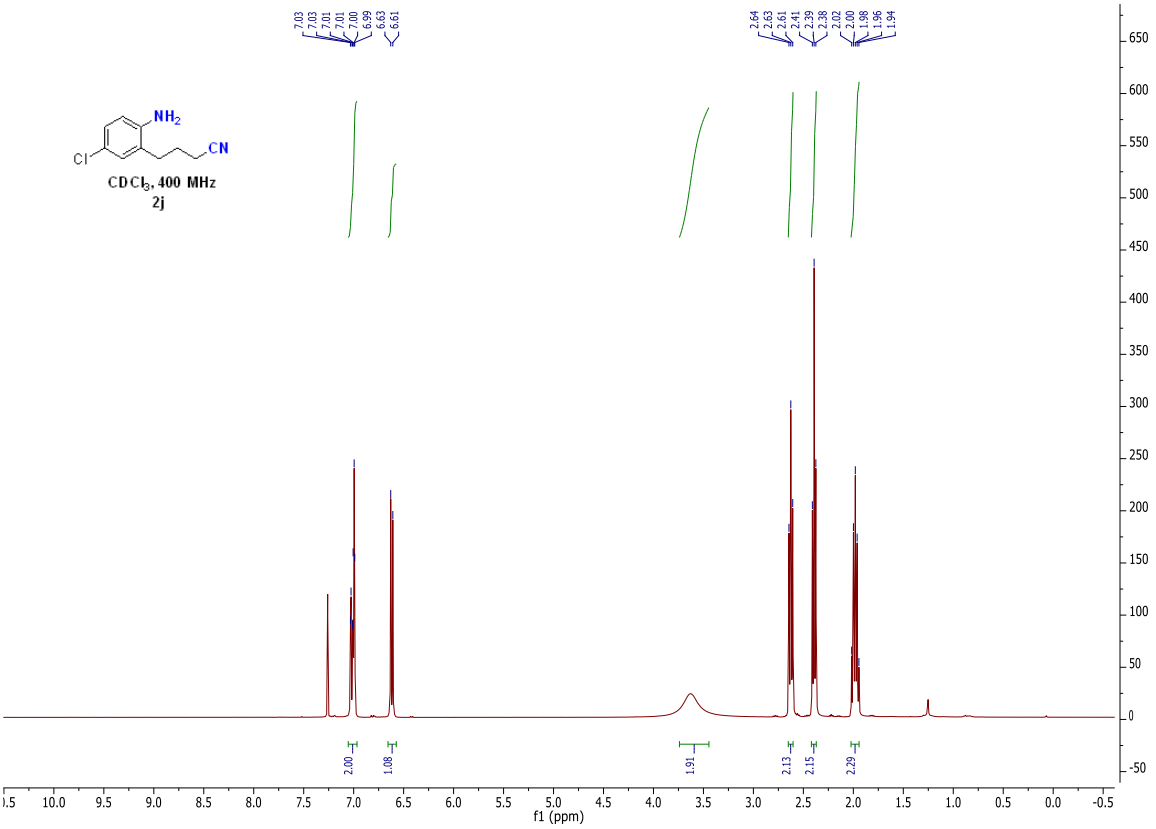
23.05
16.96
f1 (ppm)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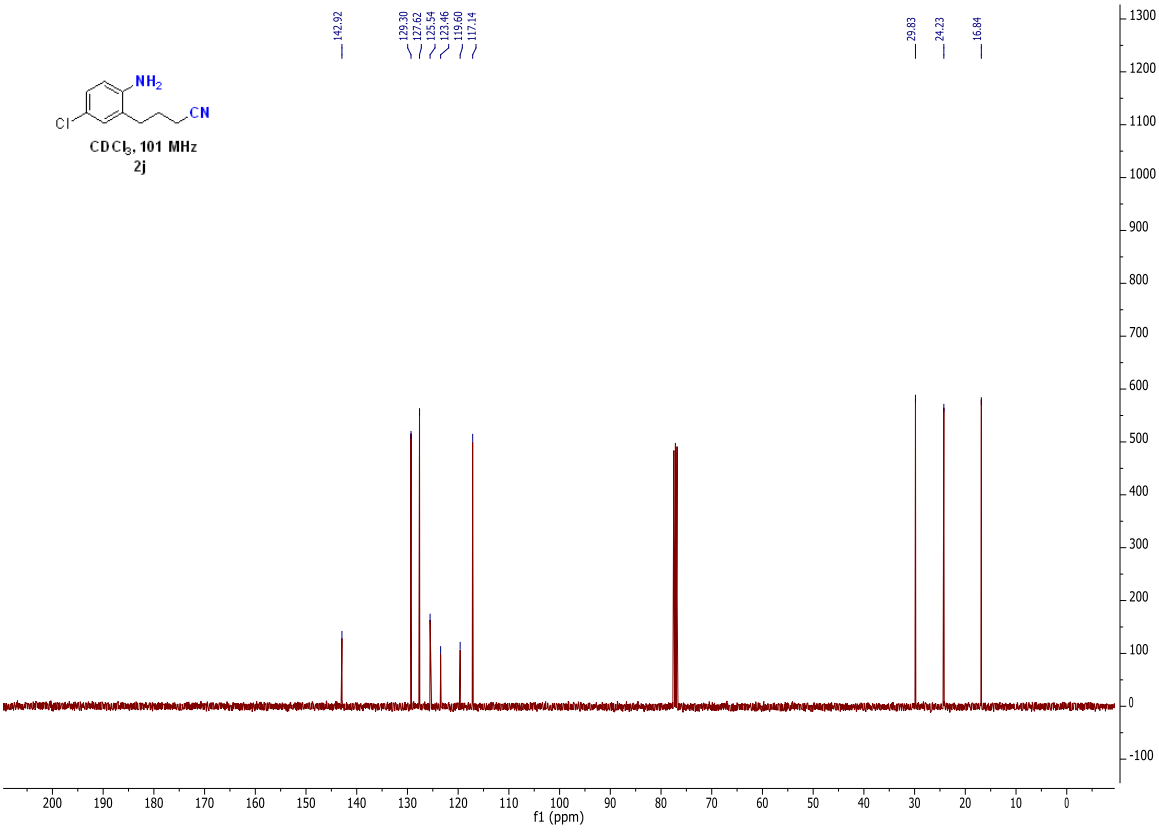
2.39
2.38
2.02
2.00
1.98
1.96
1.94
NH2
Cl
CN
CDCl3, 400 MHz
2j
2.00
1.08
1.91
2.13
2.15
2.29
f1 (ppm)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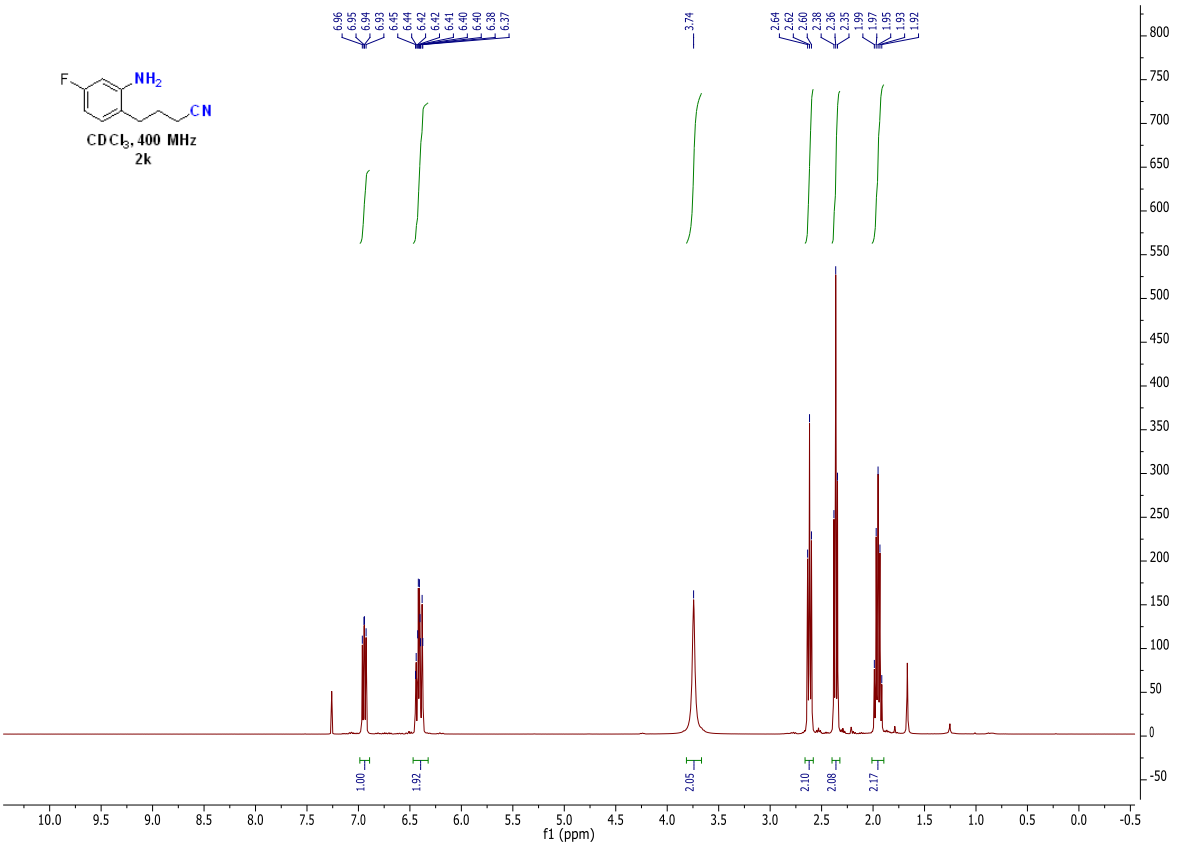
Cl
CN
CDCl3, 101 MHz
2j
f1 (ppm)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CN
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6.40
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6.38
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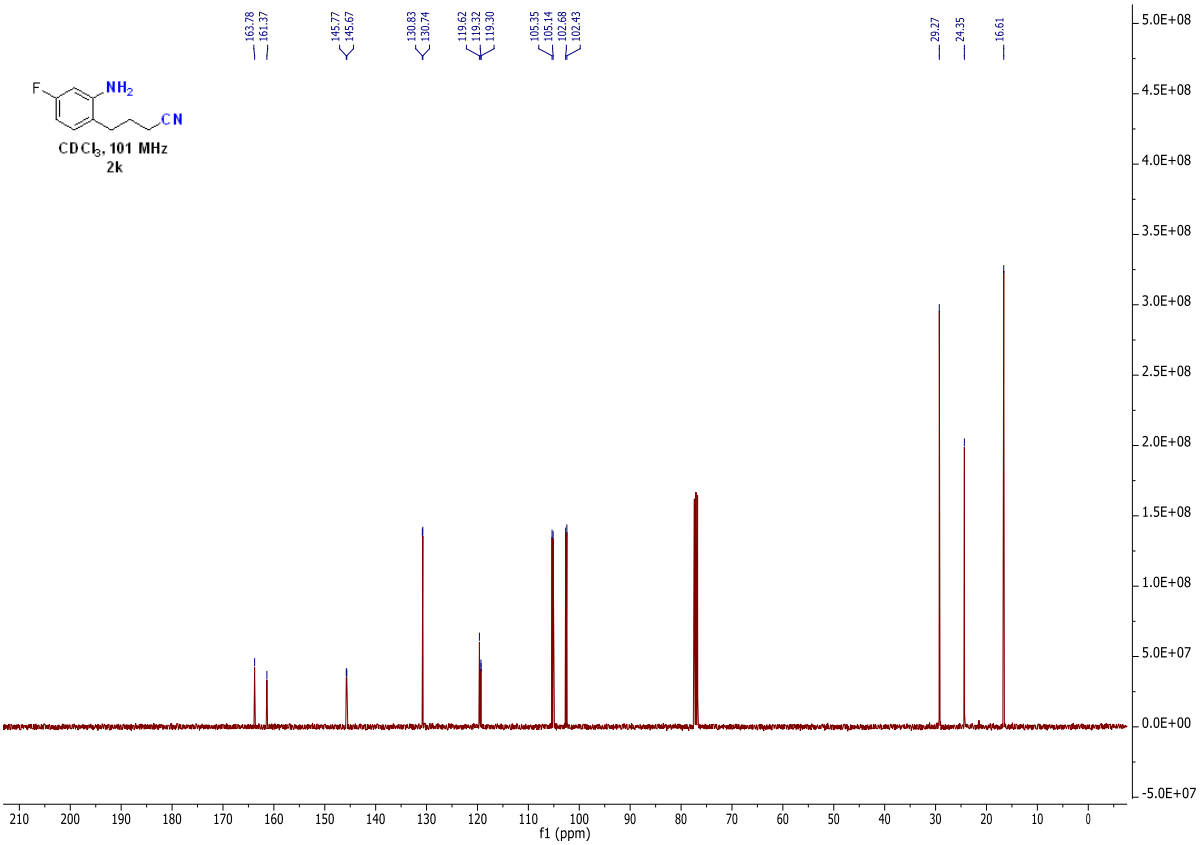
2.05
2.10
2.08
2.17
f1 (ppm)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102.43
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24.35
16.61
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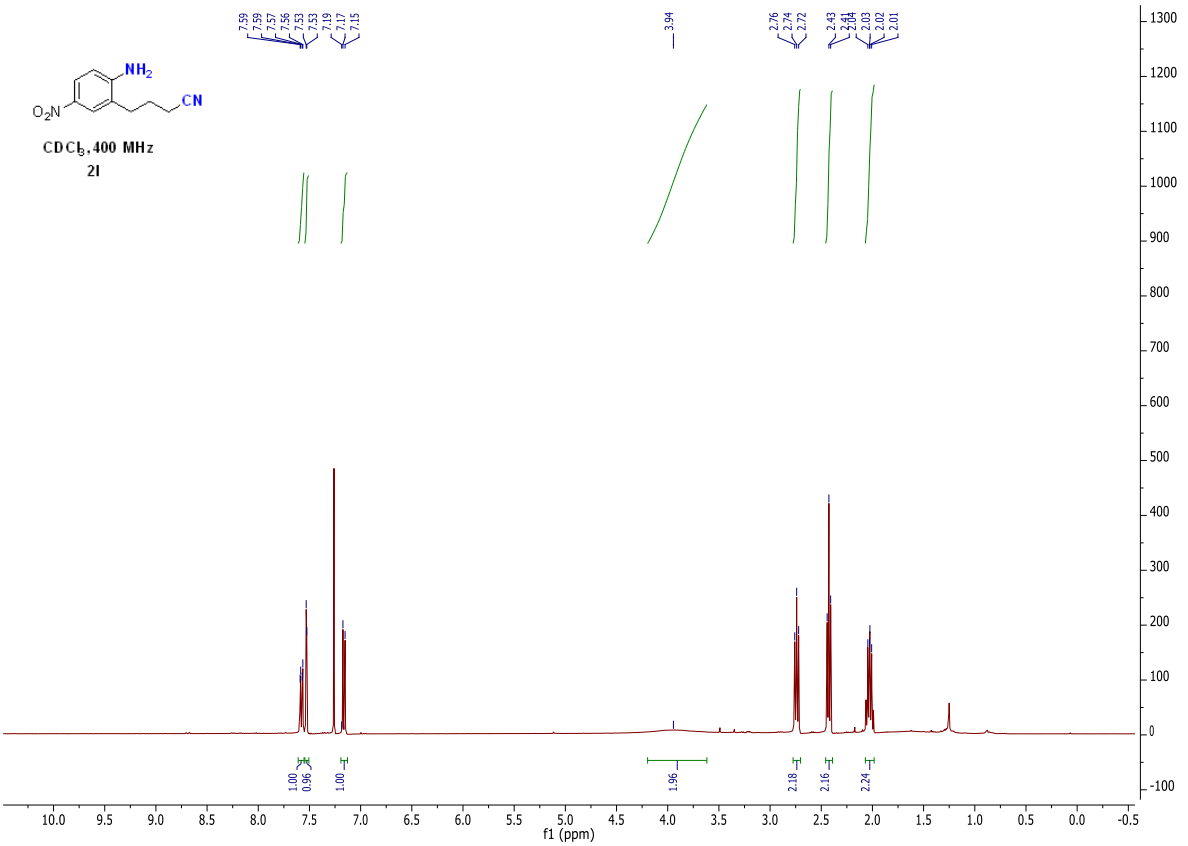
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7.15
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2.76
2.74
2.72
2.43
2.41
2.04
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2.01
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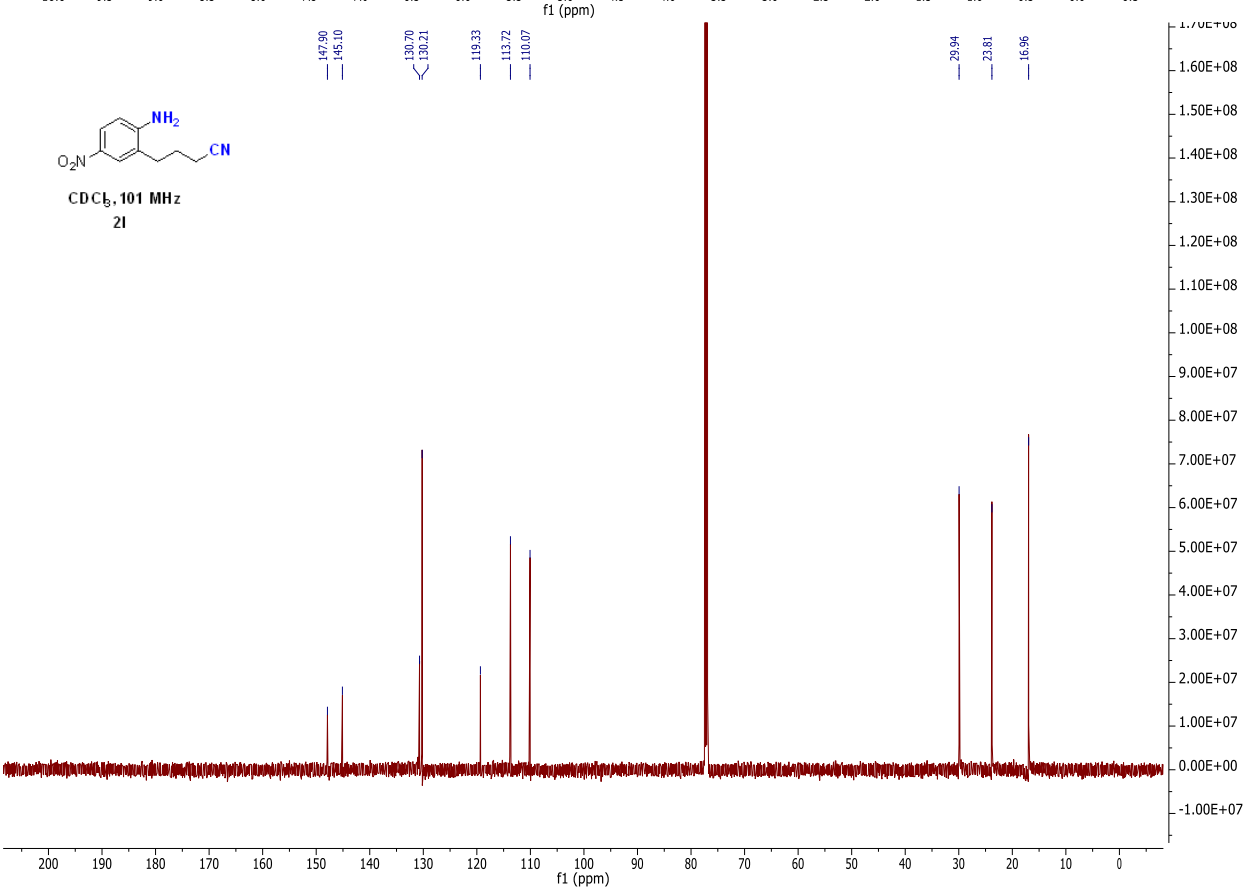
1.00
1.96
2.18
2.16
2.24
f1 (ppm)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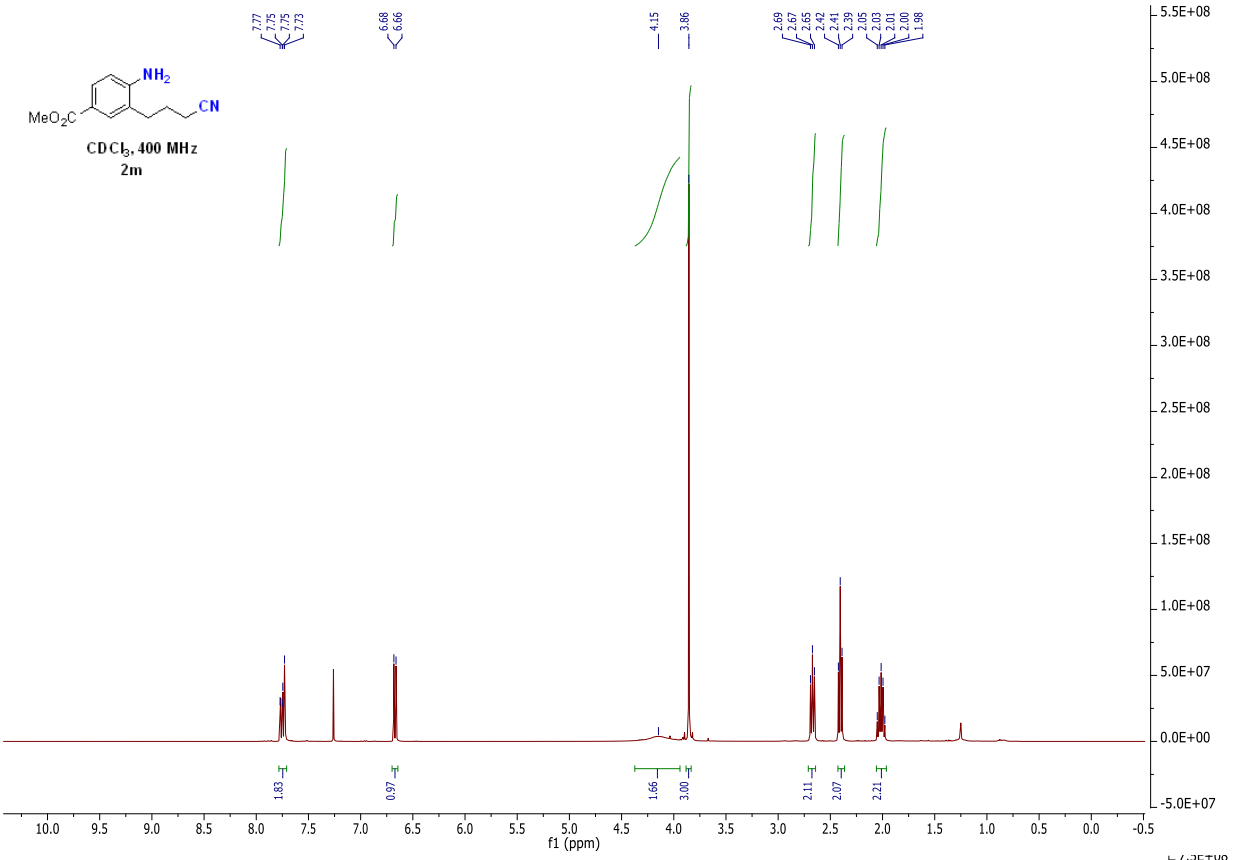
16.96
f1 (ppm)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2.69
2.67
2.65
2.42
2.41
2.39
2.05
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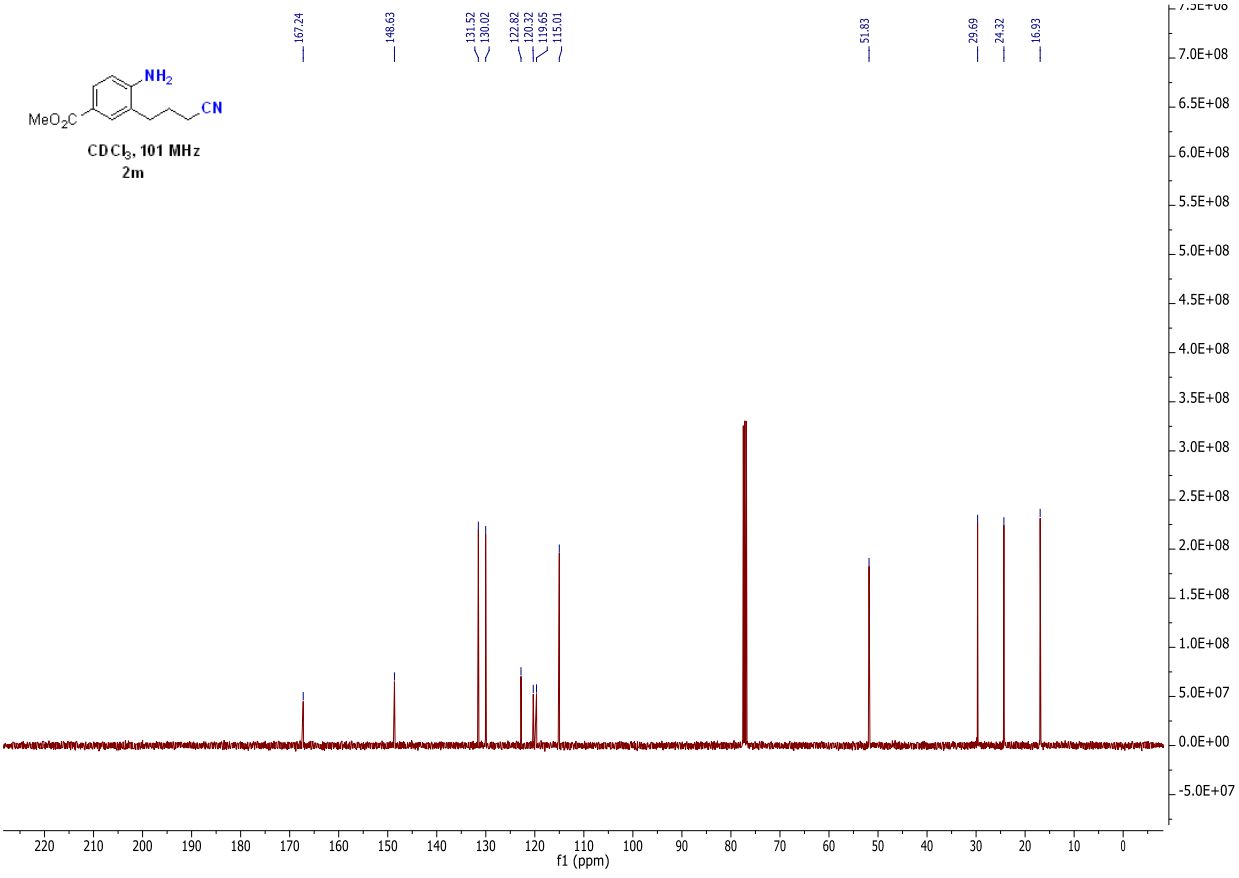
2.21
f1 (ppm)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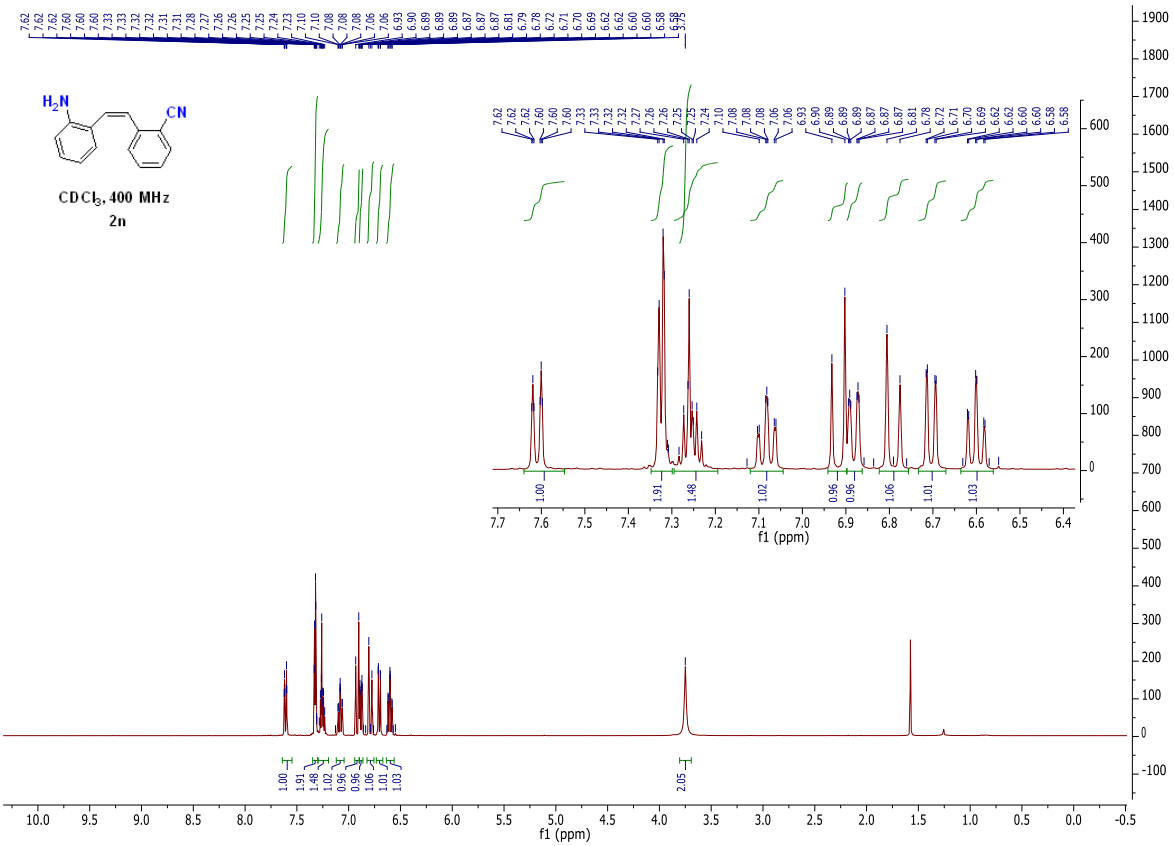
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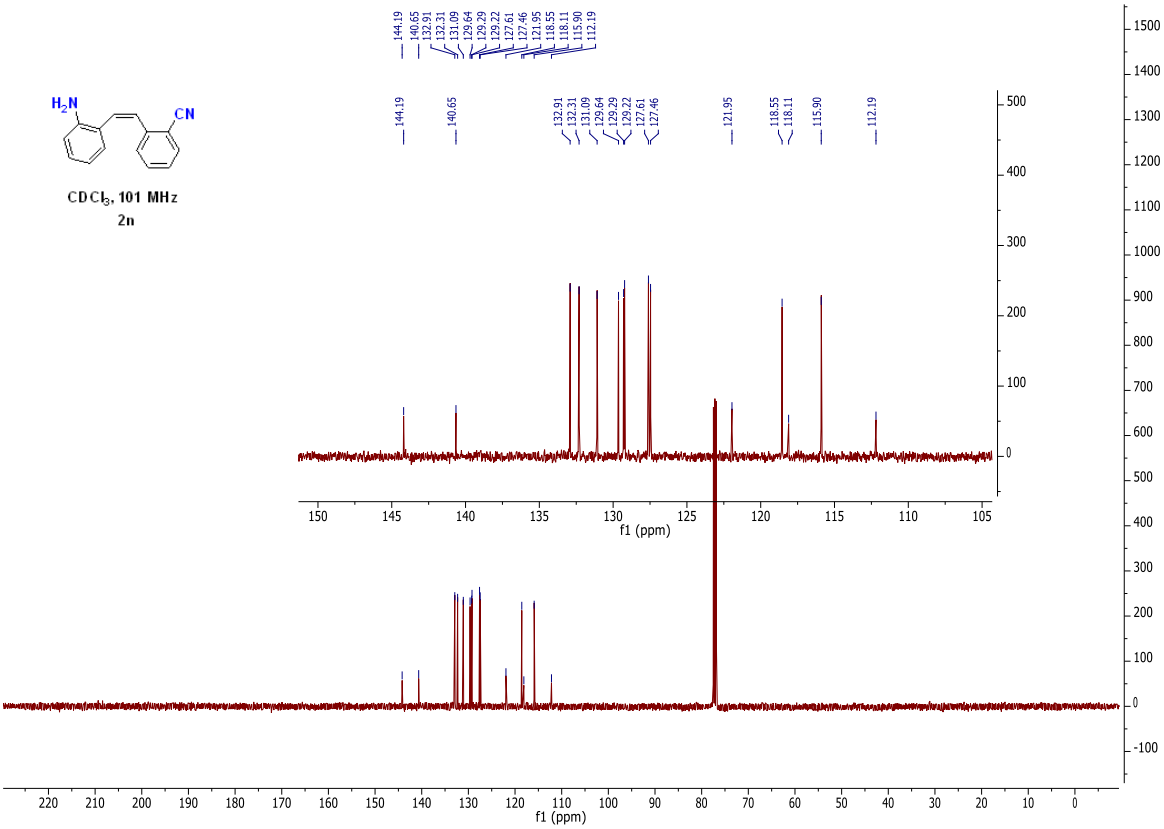
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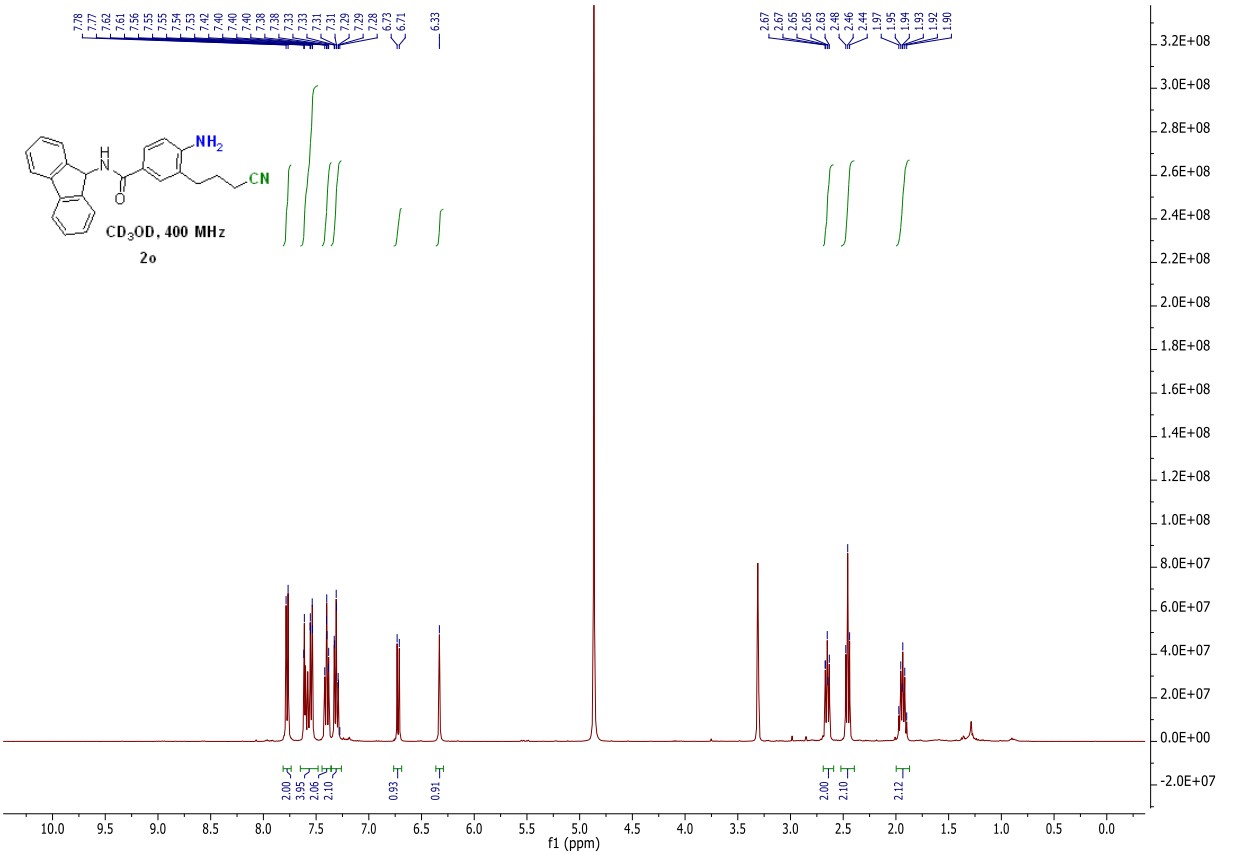
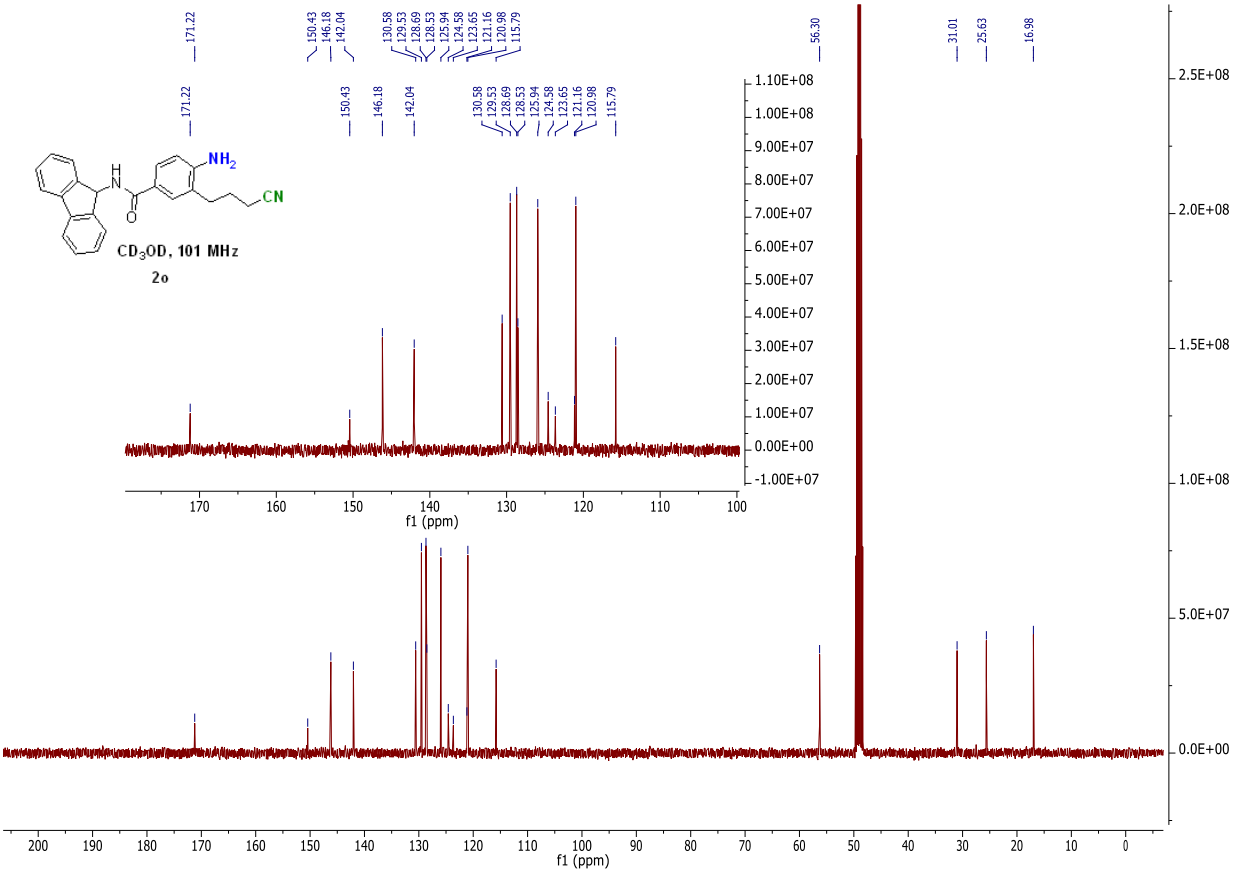
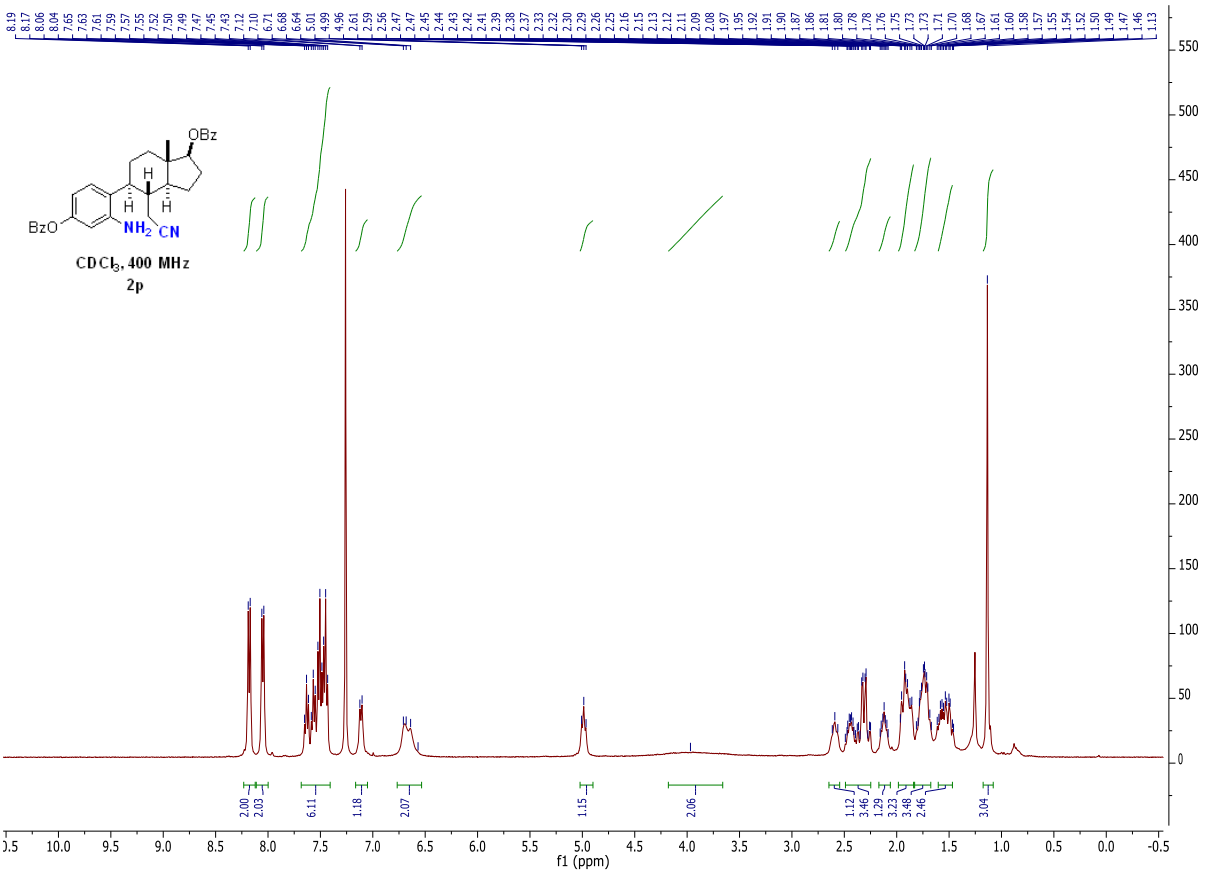
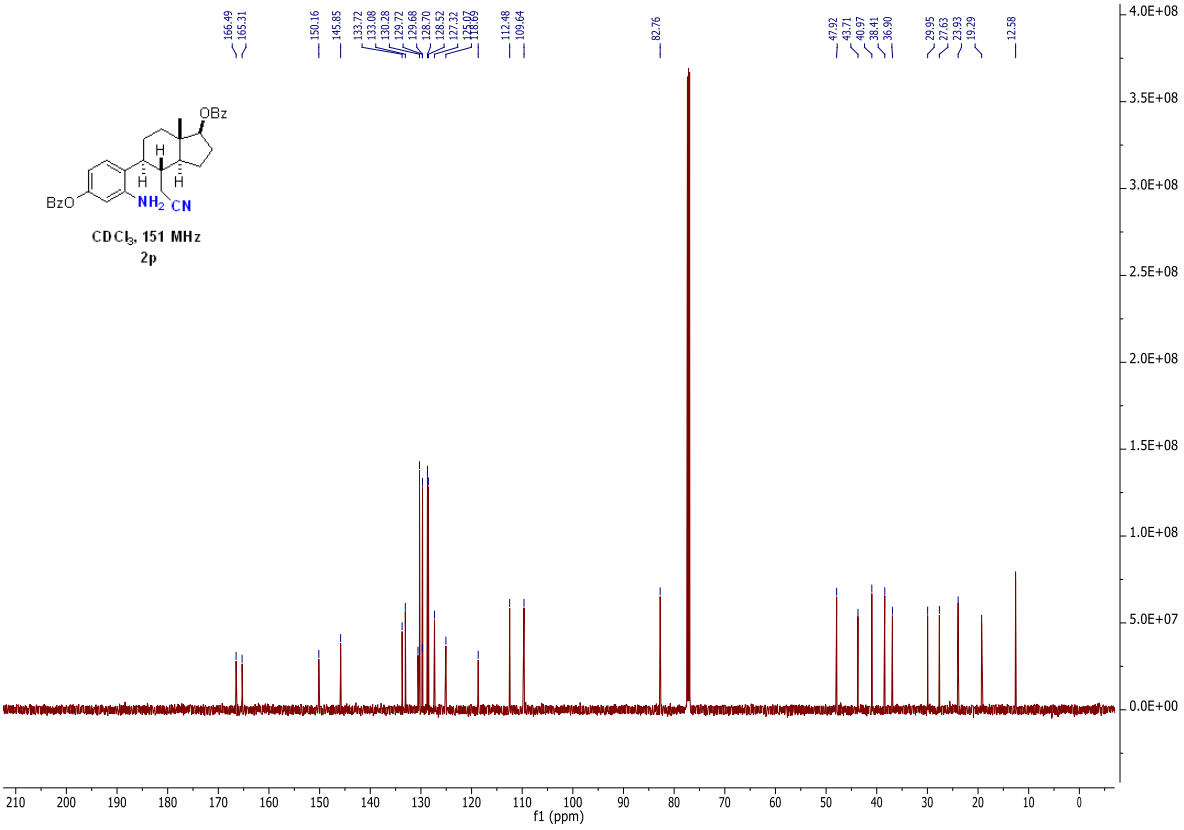
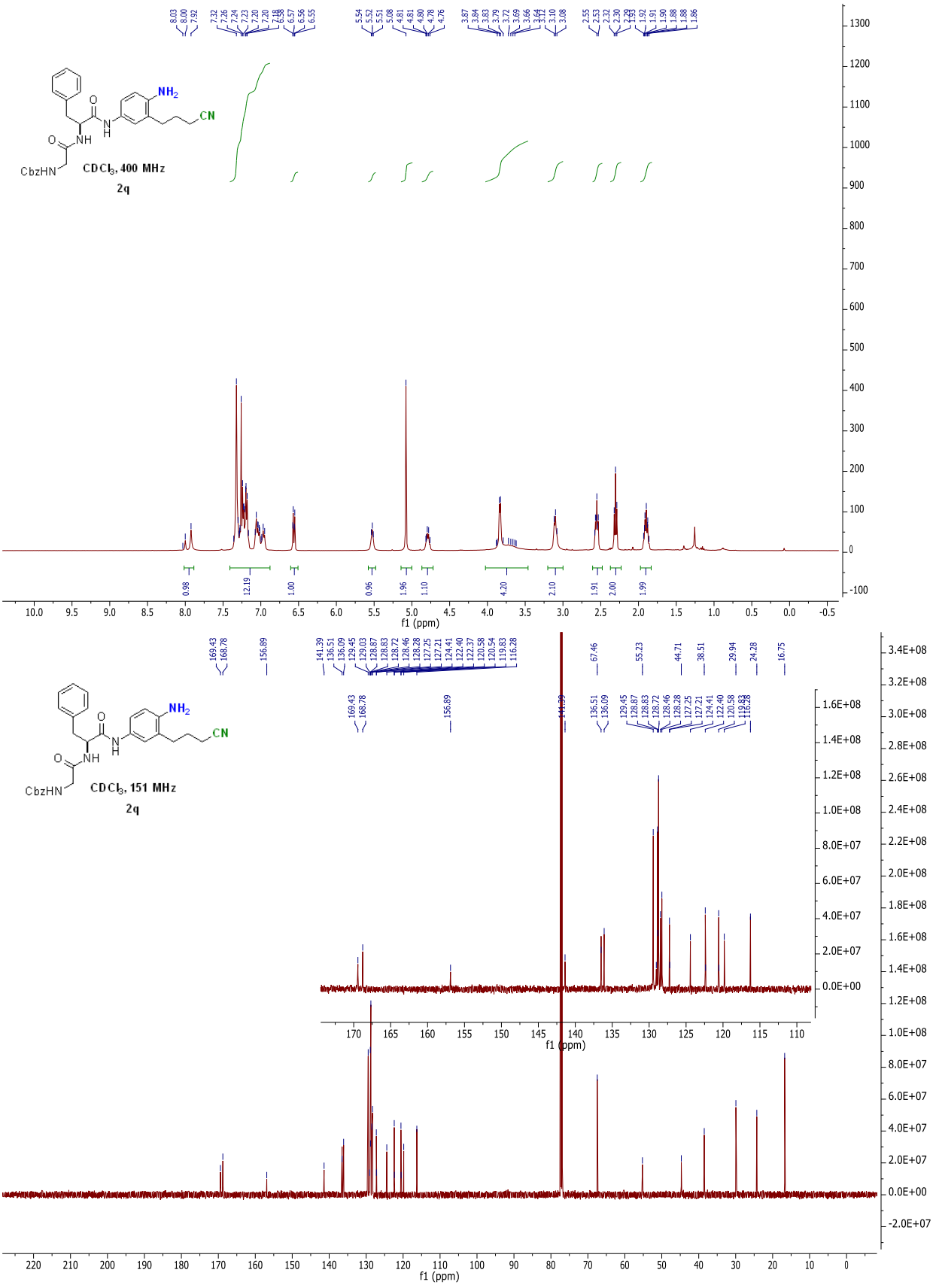
2n
f1 (ppm)

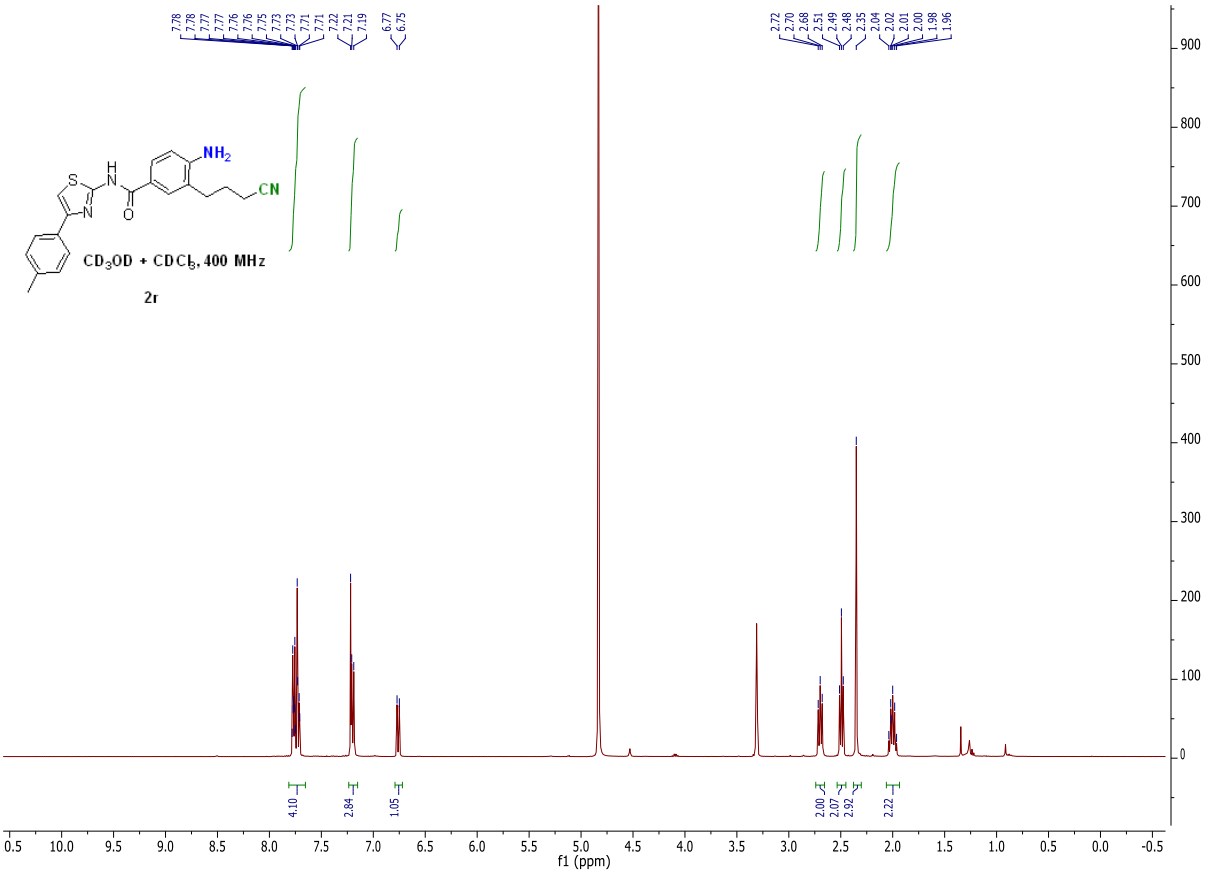

NH2
CN
CD3OD, 400 MHz
2o
f1 (ppm)

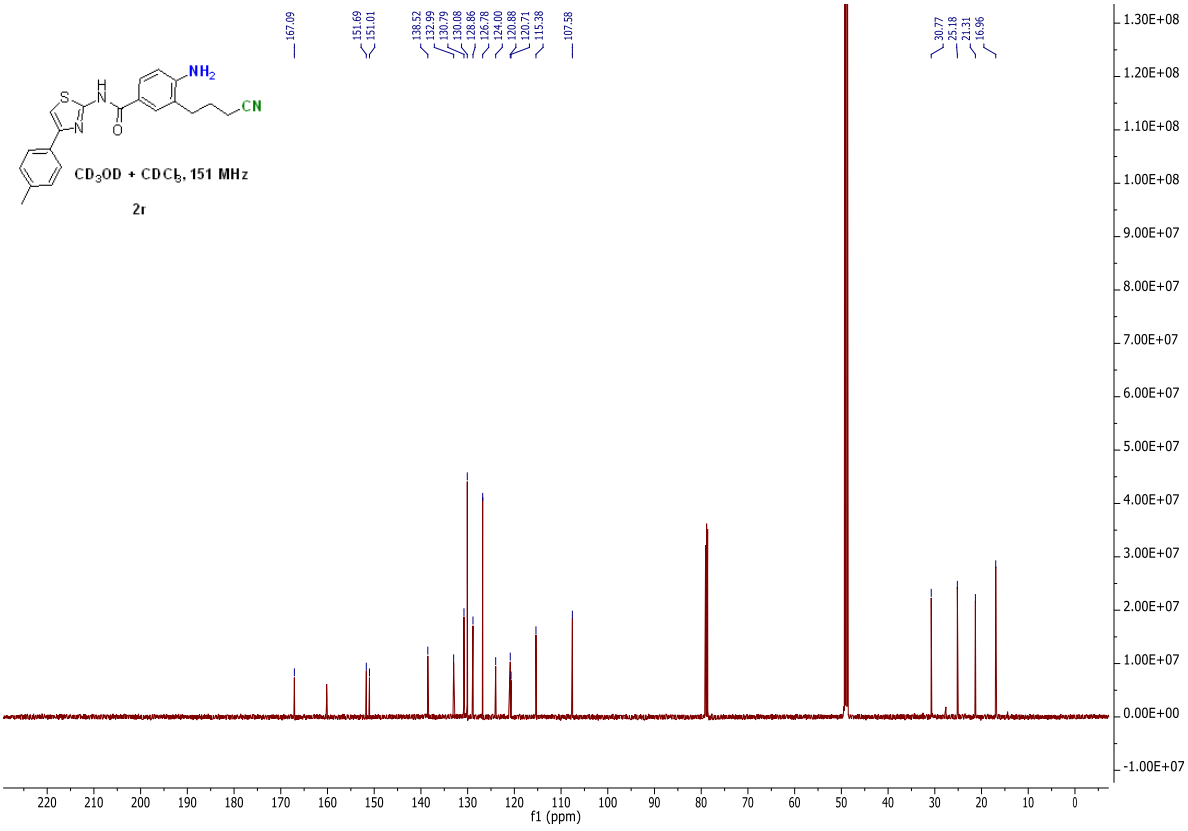

NH2
CN
CD3OD, 101 MHz
2o
f1 (ppm)

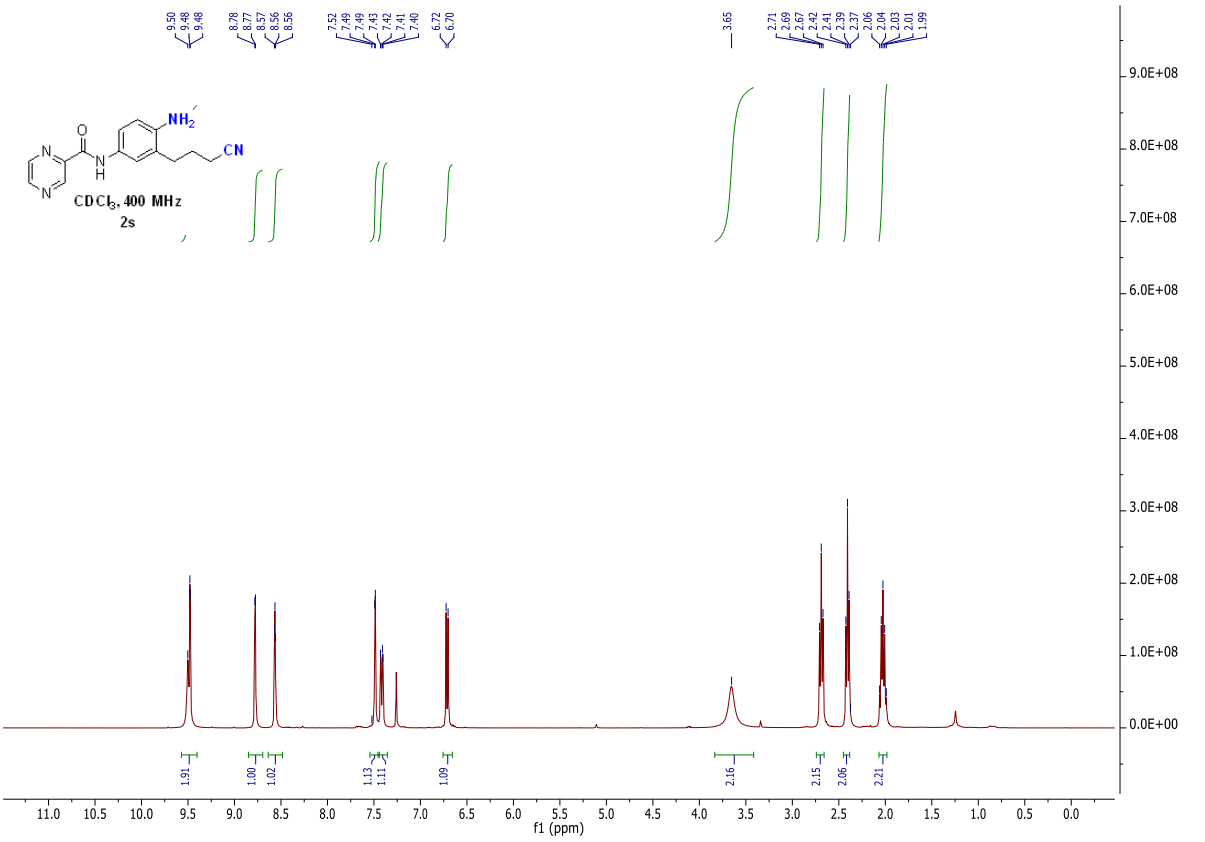

OBz
H
H
H
BzO
NH2 CN
CDCl3, 400 MHz
2p
f1 (ppm)

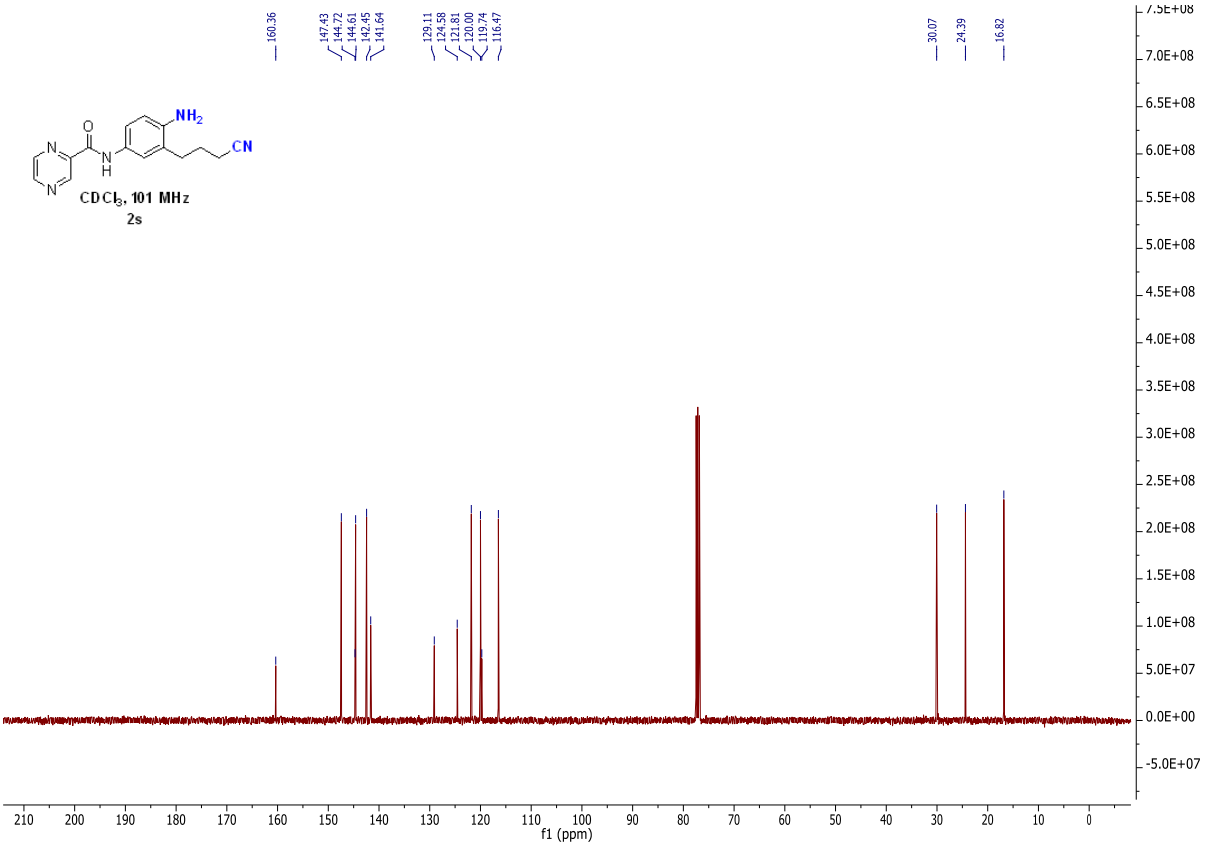

OBz
H
H
H
BzO
NH2 CN
CDCl3, 151 MHz
2p
f1 (ppm)

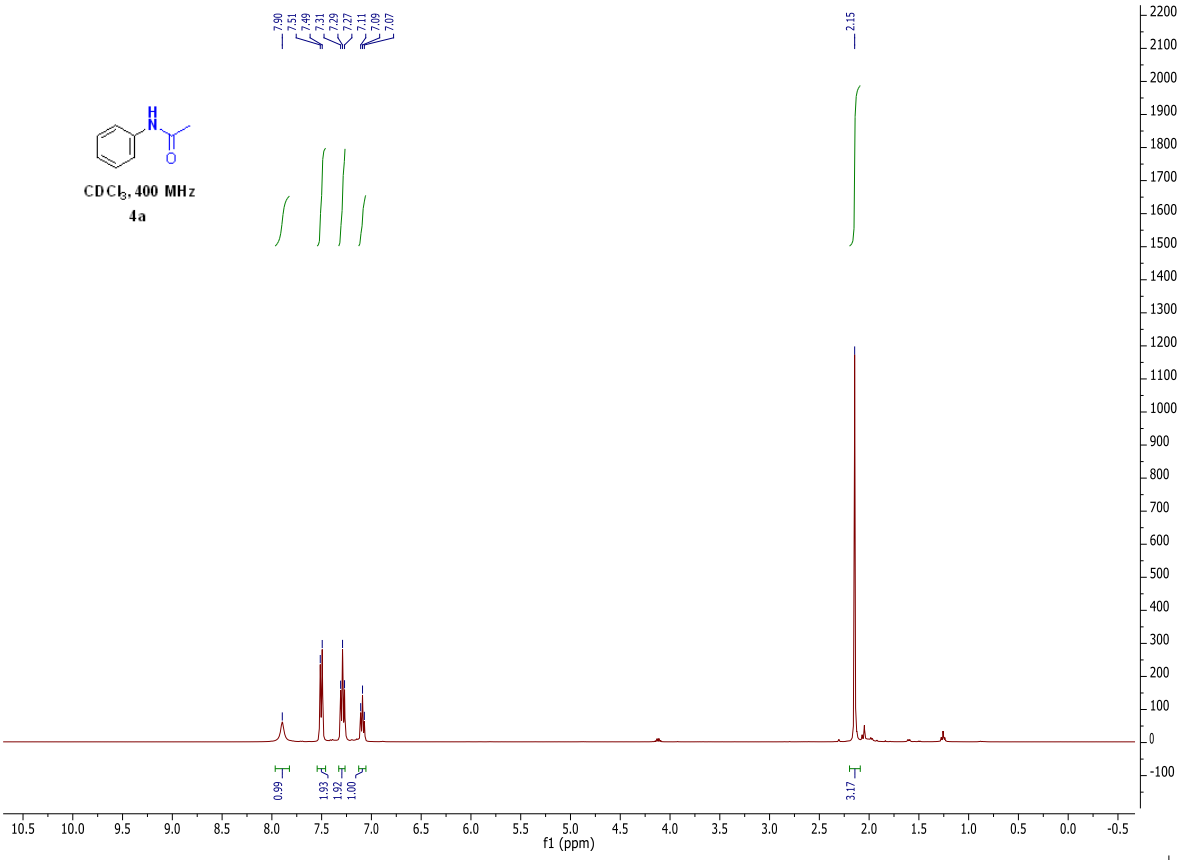

CDCl3, 400 MHz
2q
CDCl3, 151 MHz
2q
f1 (ppm)

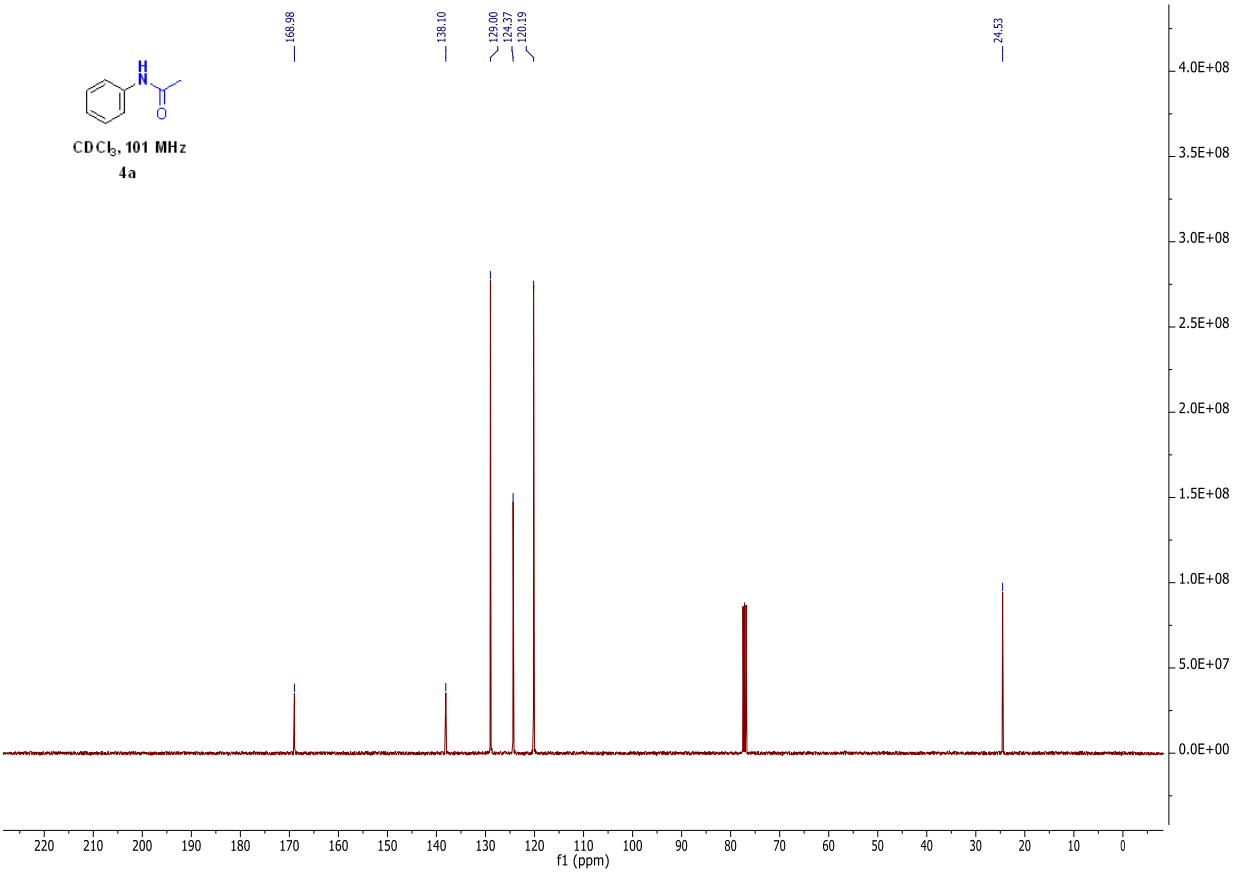

7.78
7.78
7.77
7.77
7.77
7.76
7.76
7.75
7.73
7.73
7.71
7.71
7.22
7.21
7.19
6.77
6.75
2.72
2.70
2.68
2.51
2.49
2.48
2.35
2.04
2.02
2.01
2.00
1.98
1.96
NH2
CN
CD3OD + CDCl3, 400 MHz
2r
4.10
2.84
1.05
2.00
2.07
2.92
2.22
f1 (ppm)

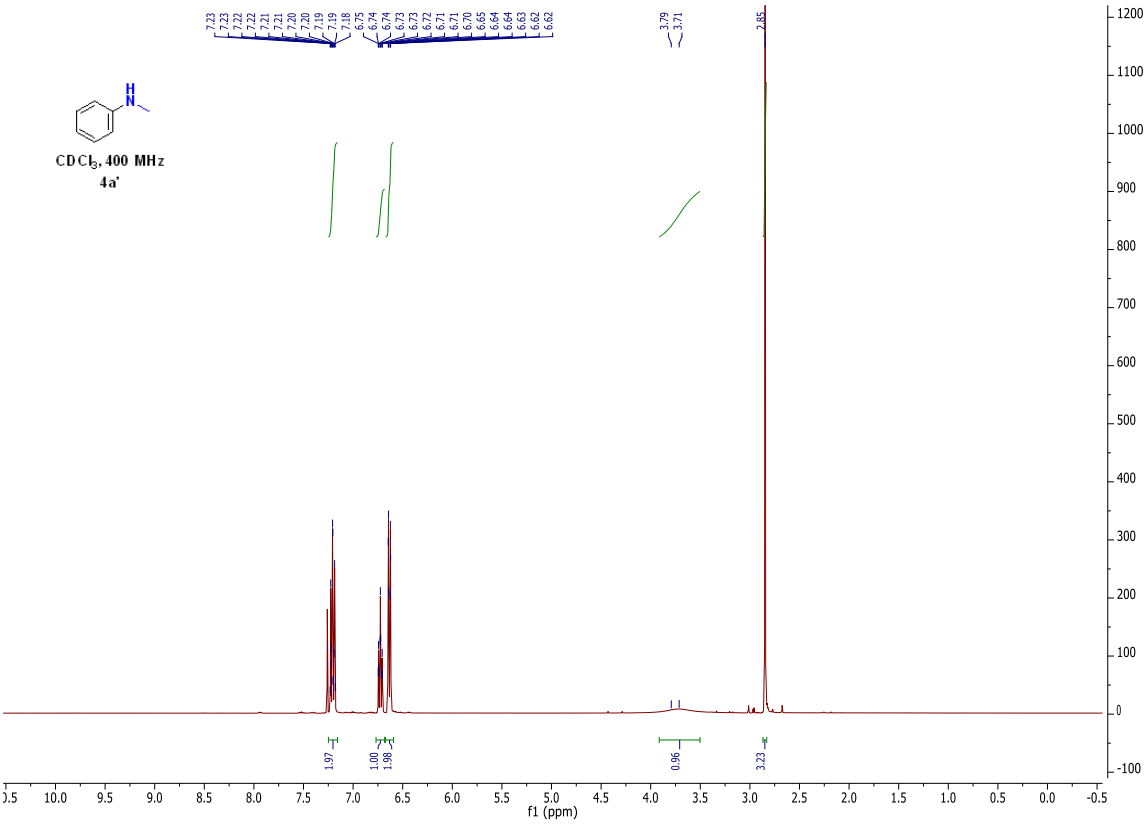

167.09
151.69
151.01
138.52
132.99
130.79
130.08
128.86
126.78
124.00
120.88
120.71
115.38
107.58
30.77
25.18
21.31
16.96
NH2
CN
CD3OD + CDCl3, 151 MHz
2r
f1 (ppm)

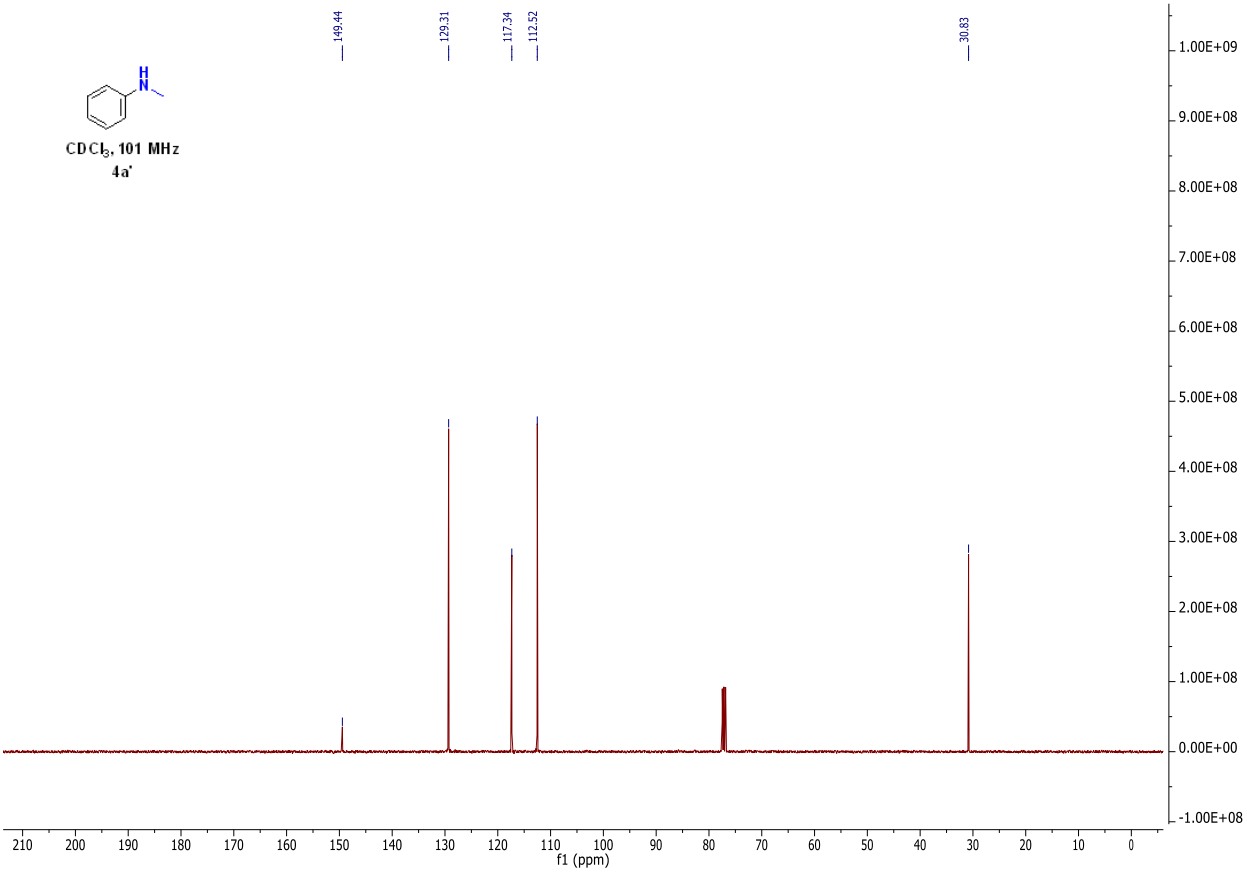

9.50
9.48
9.48
8.78
8.77
8.57
8.56
8.56
7.52
7.49
7.49
7.43
7.42
7.41
7.40
6.72
6.70
3.65
2.71
2.69
2.67
2.42
2.41
2.39
2.37
2.06
2.04
2.03
2.01
1.99
NH2
O
N
H
N
CN
CDCl3, 400 MHz
2s
9.0E+08
8.0E+08
7.0E+08
6.0E+08
5.0E+08
4.0E+08
3.0E+08
2.0E+08
1.0E+08
0.0E+00
1.91
1.00
1.02
1.13
1.11
1.09
2.16
2.15
2.06
2.21
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

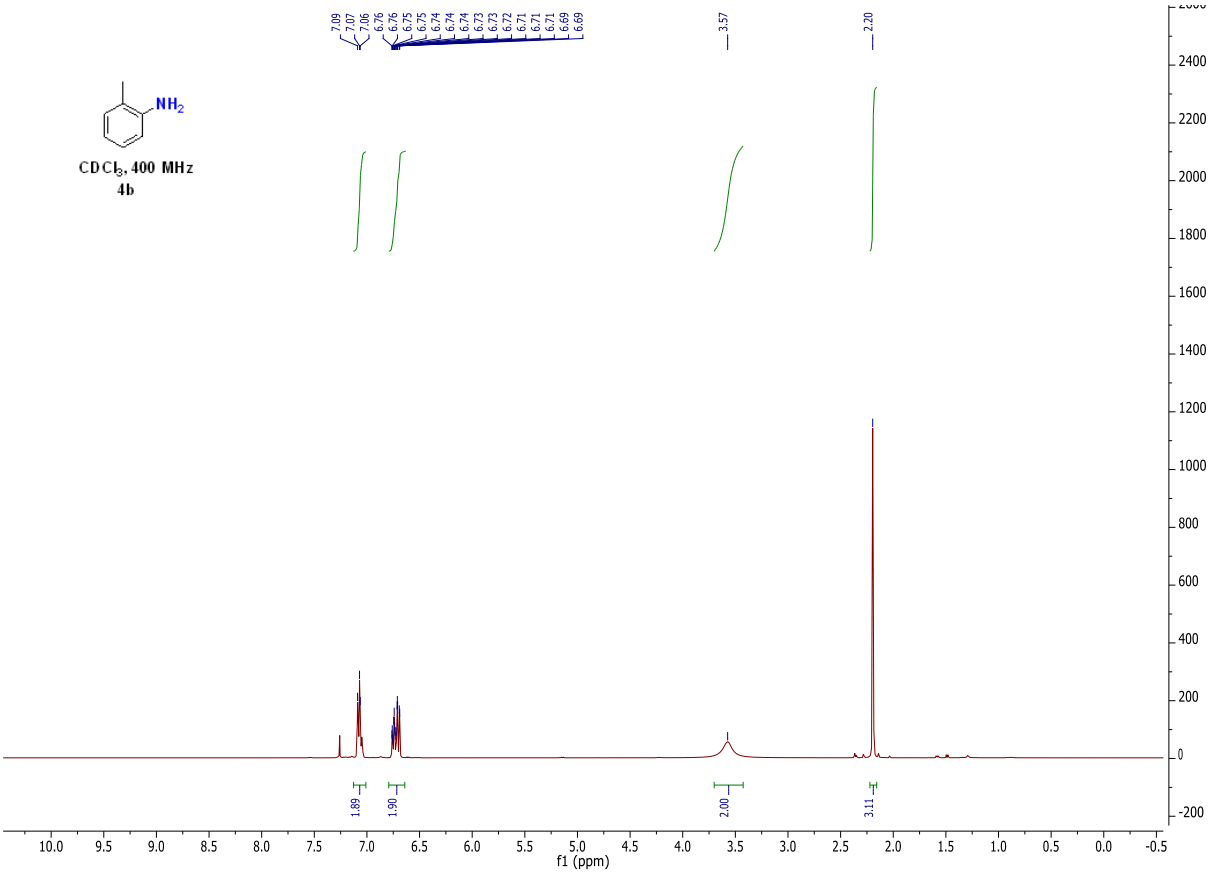

160.36
147.43
144.72
144.61
142.45
141.64
129.11
124.58
121.81
120.00
119.74
116.47
30.07
24.39
16.82
NH2
O
N
H
N
CN
CDCl3, 101 MHz
2s
7.5E+08
7.0E+08
6.5E+08
6.0E+08
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

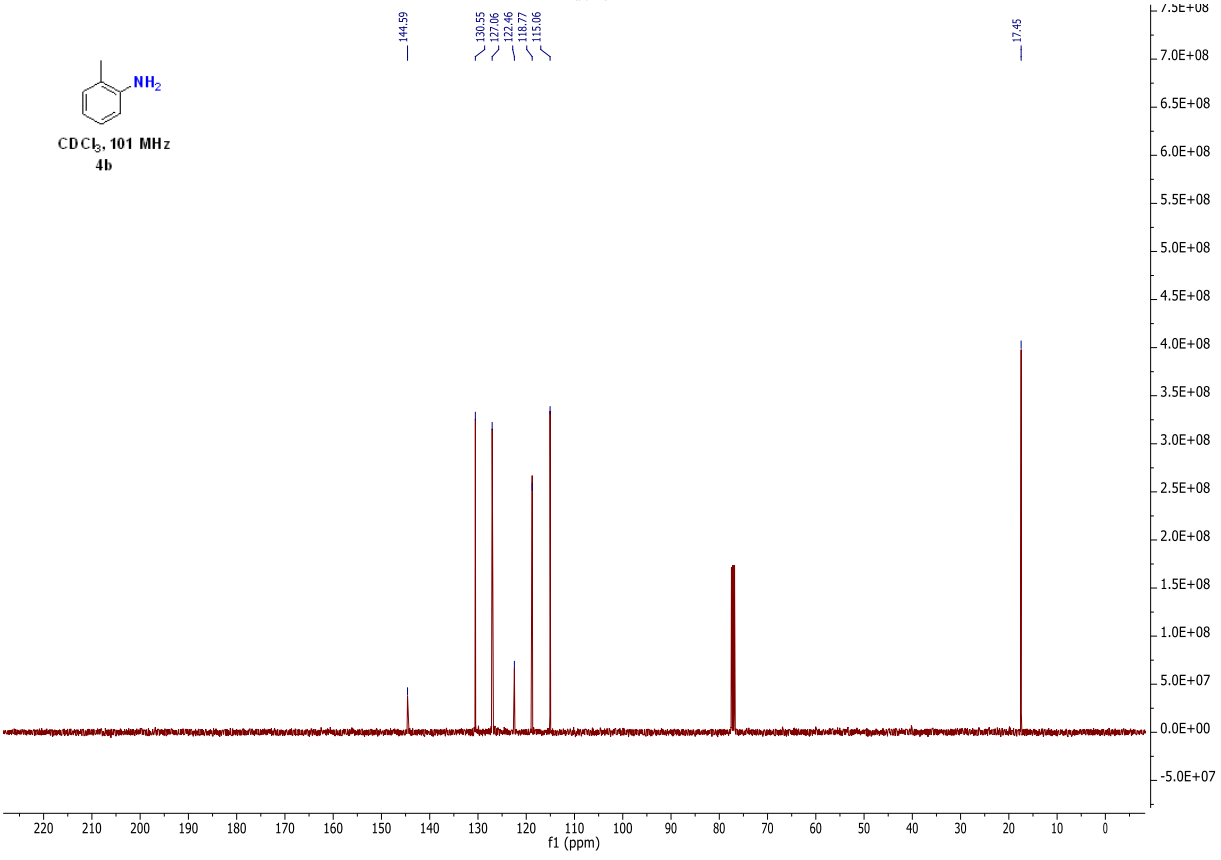

7.90
7.51
7.49
7.31
7.29
7.27
7.11
7.09
7.07
2.15
CDCl3, 400 MHz
4a
0.99
1.93
1.92
1.00
3.17
f1 (ppm)

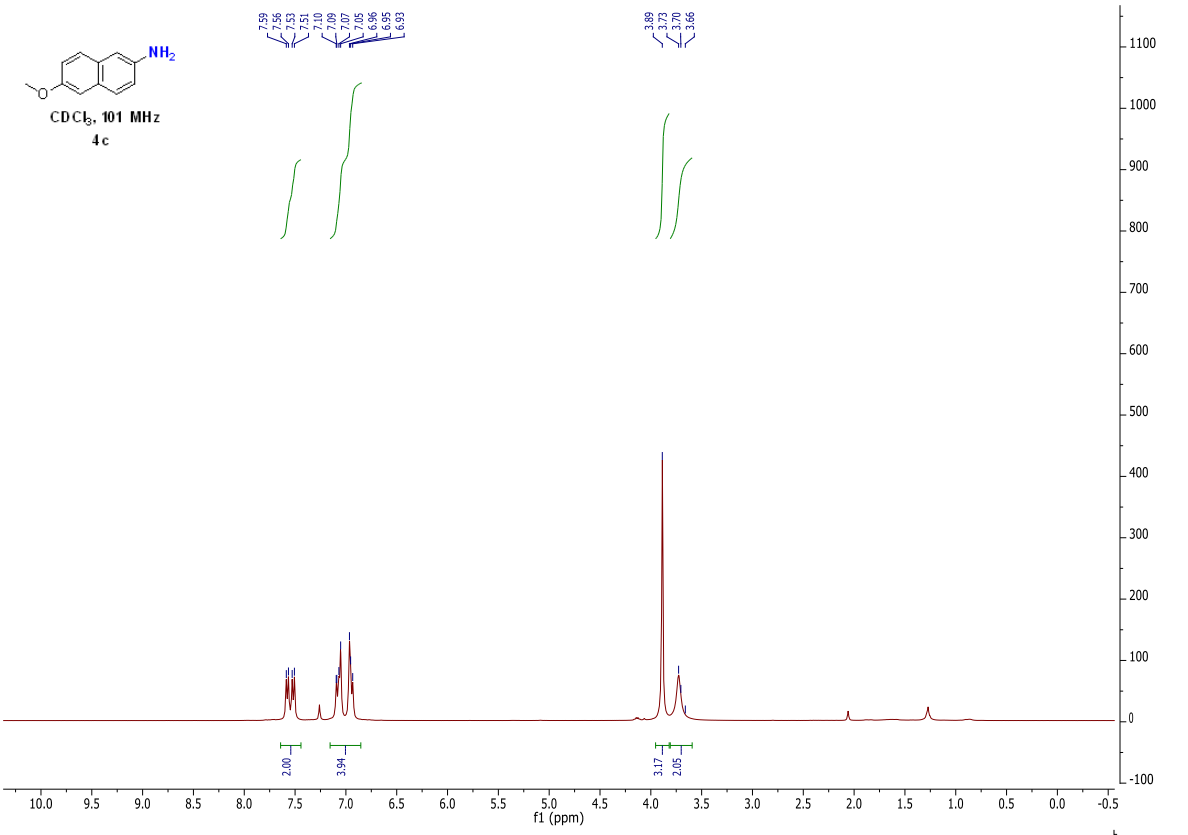

168.98
138.10
129.00
124.37
120.19
24.53
CDCl3, 101 MHz
4a
f1 (ppm)

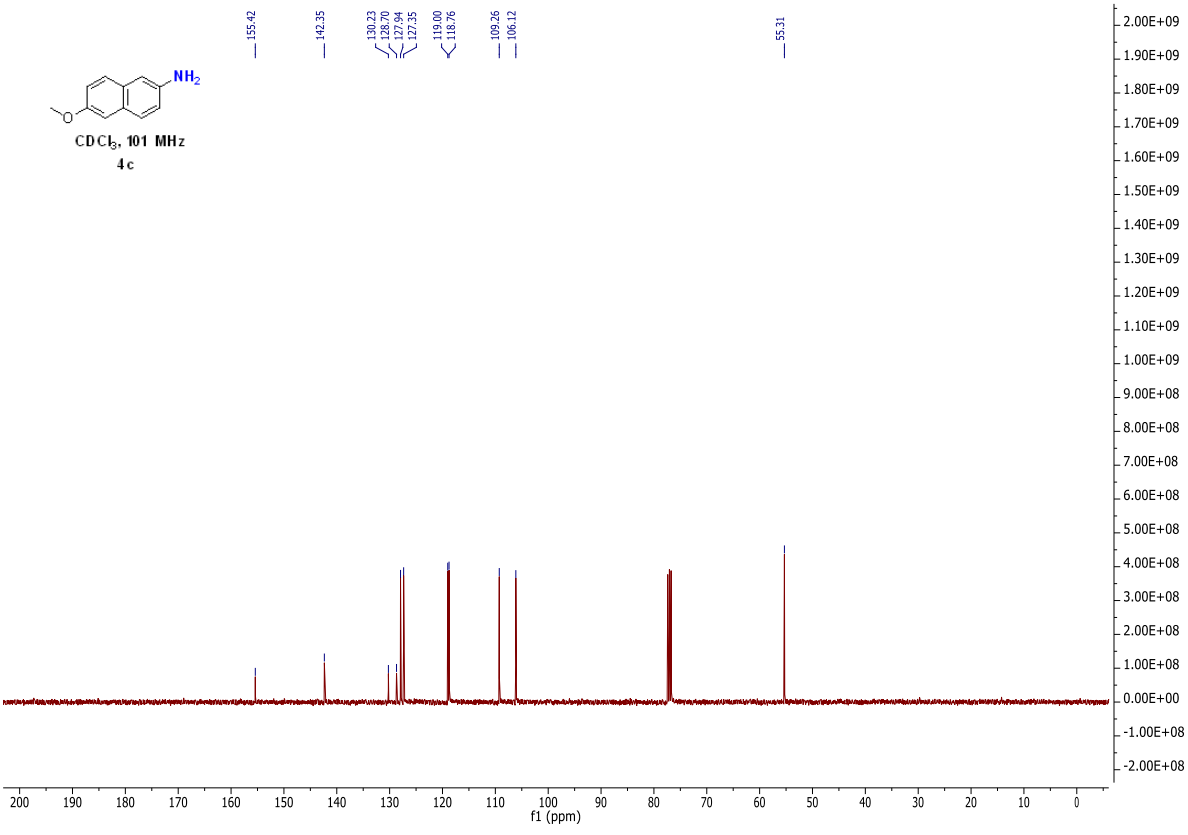

CDCl3, 400 MHz
4a'
f1 (ppm)

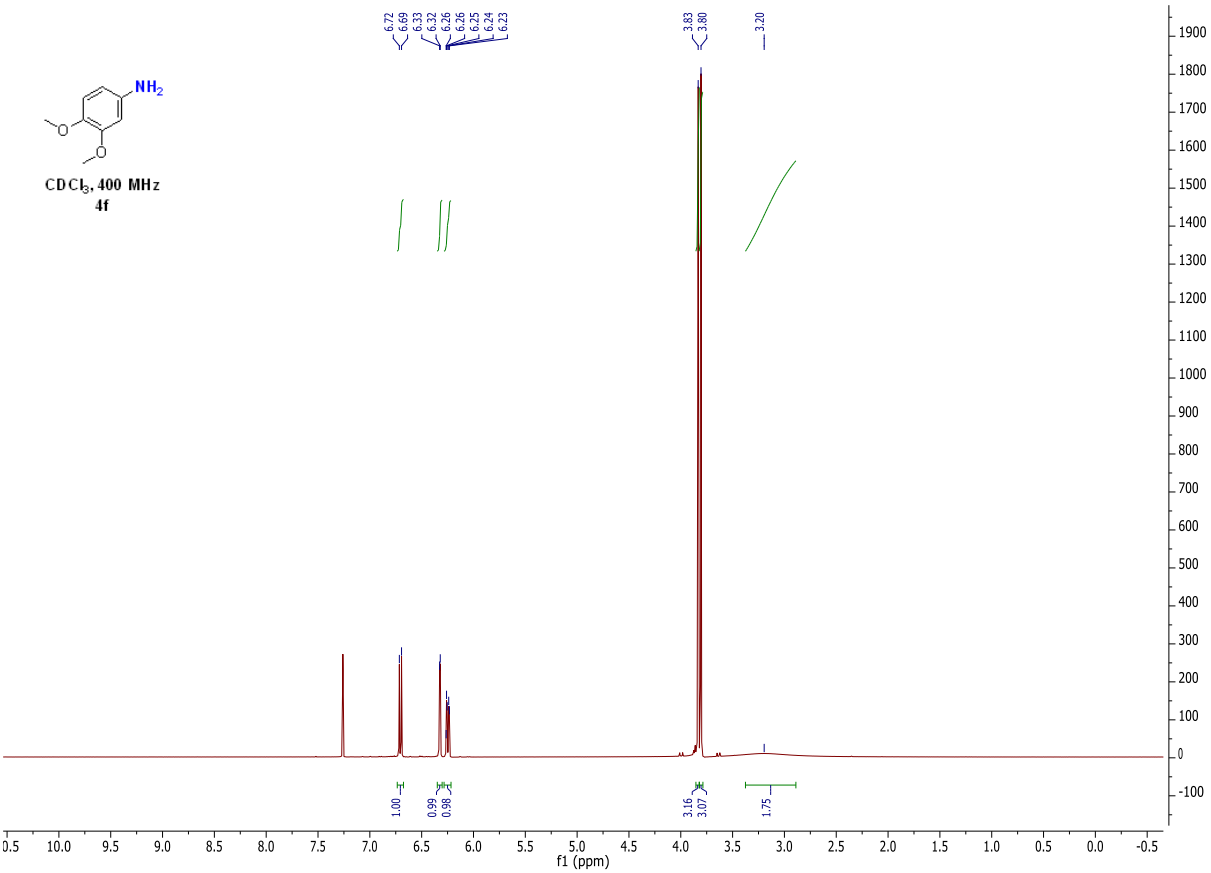

CDCl3, 101 MHz
4a'
f1 (ppm)

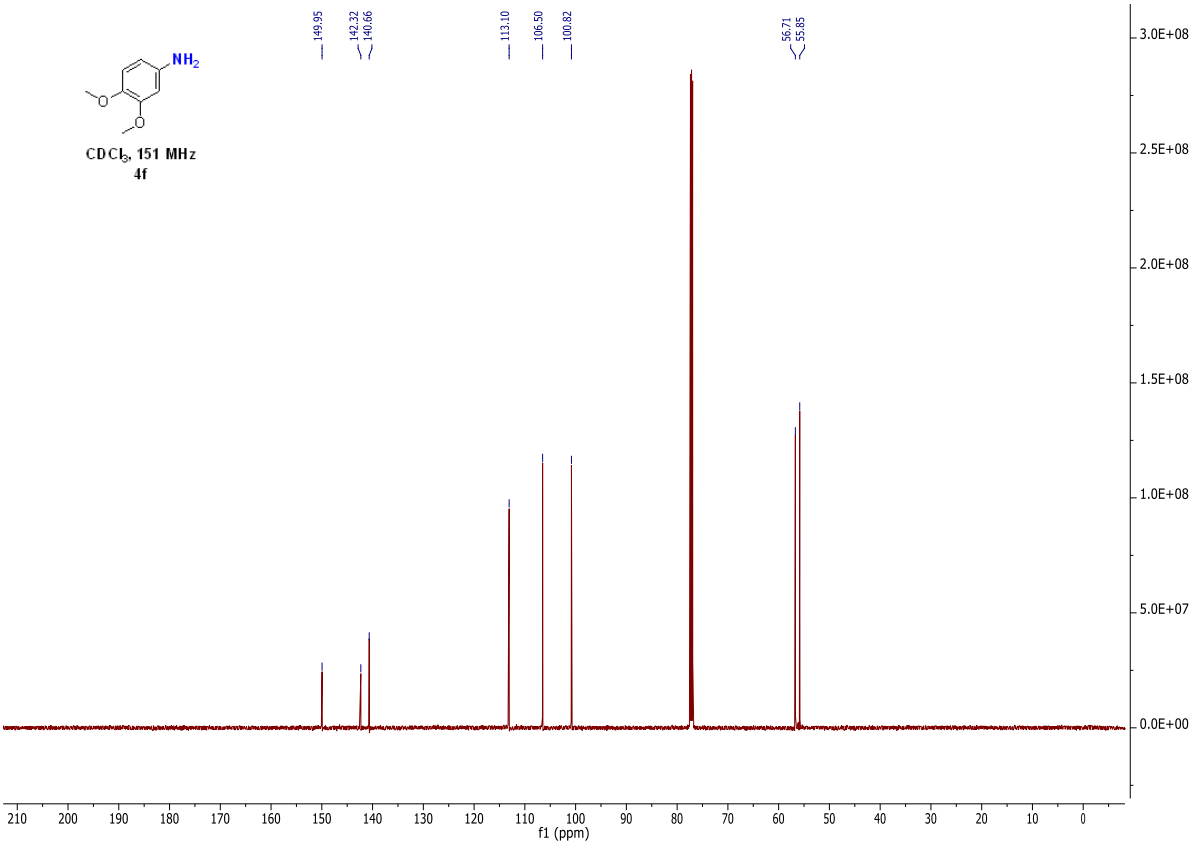

NH2
CDCl3, 400 MHz
4b
7.09
7.07
7.06
6.76
6.76
6.75
6.75
6.74
6.74
6.74
6.73
6.73
6.72
6.71
6.71
6.71
6.69
6.69
3.57
2.20
1.89
1.90
2.00
3.11
f1 (ppm)

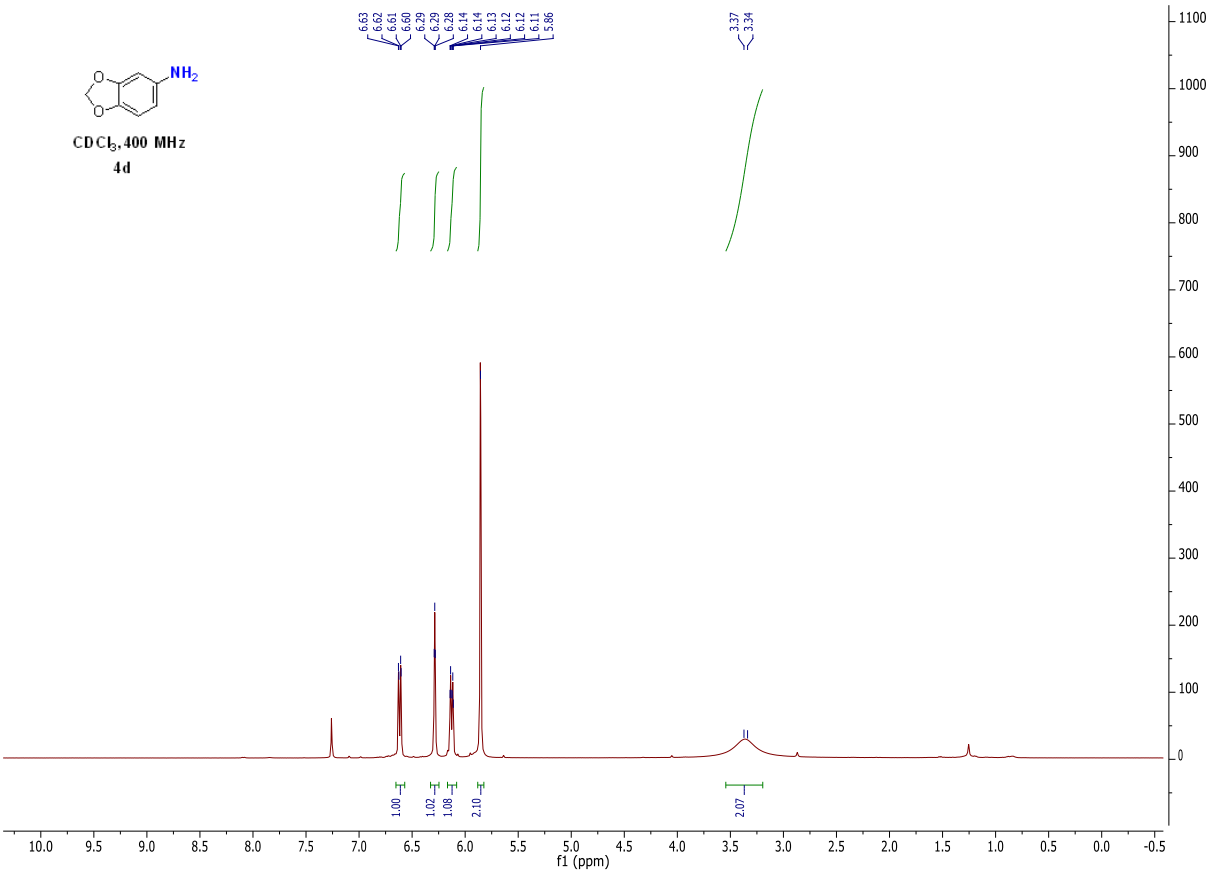

NH2
CDCl3, 101 MHz
4b
144.59
130.55
127.06
122.46
118.77
115.06
17.45
f1 (ppm)

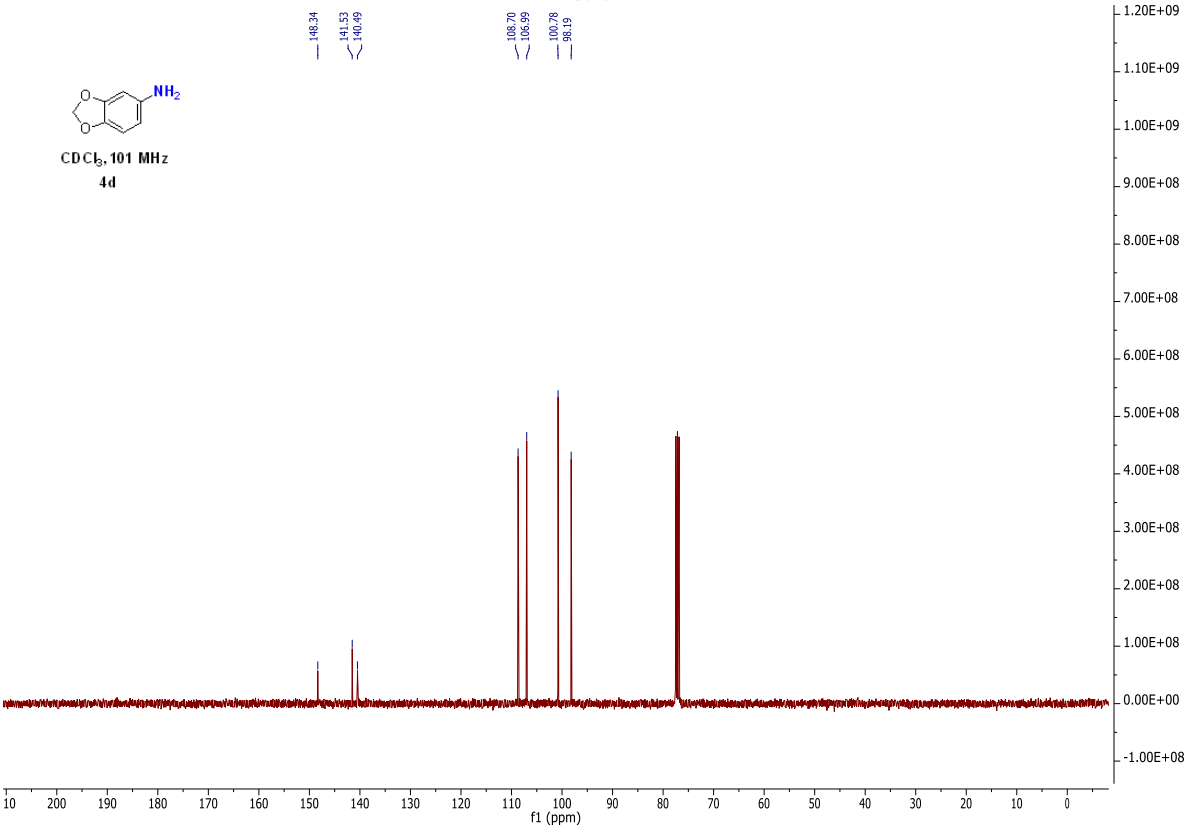

NH2
CDCl3, 101 MHz
4c
7.59
7.56
7.53
7.51
7.10
7.09
7.07
7.05
6.96
6.95
6.93
3.89
3.73
3.70
3.66
2.00
3.94
3.17
2.05
f1 (ppm)

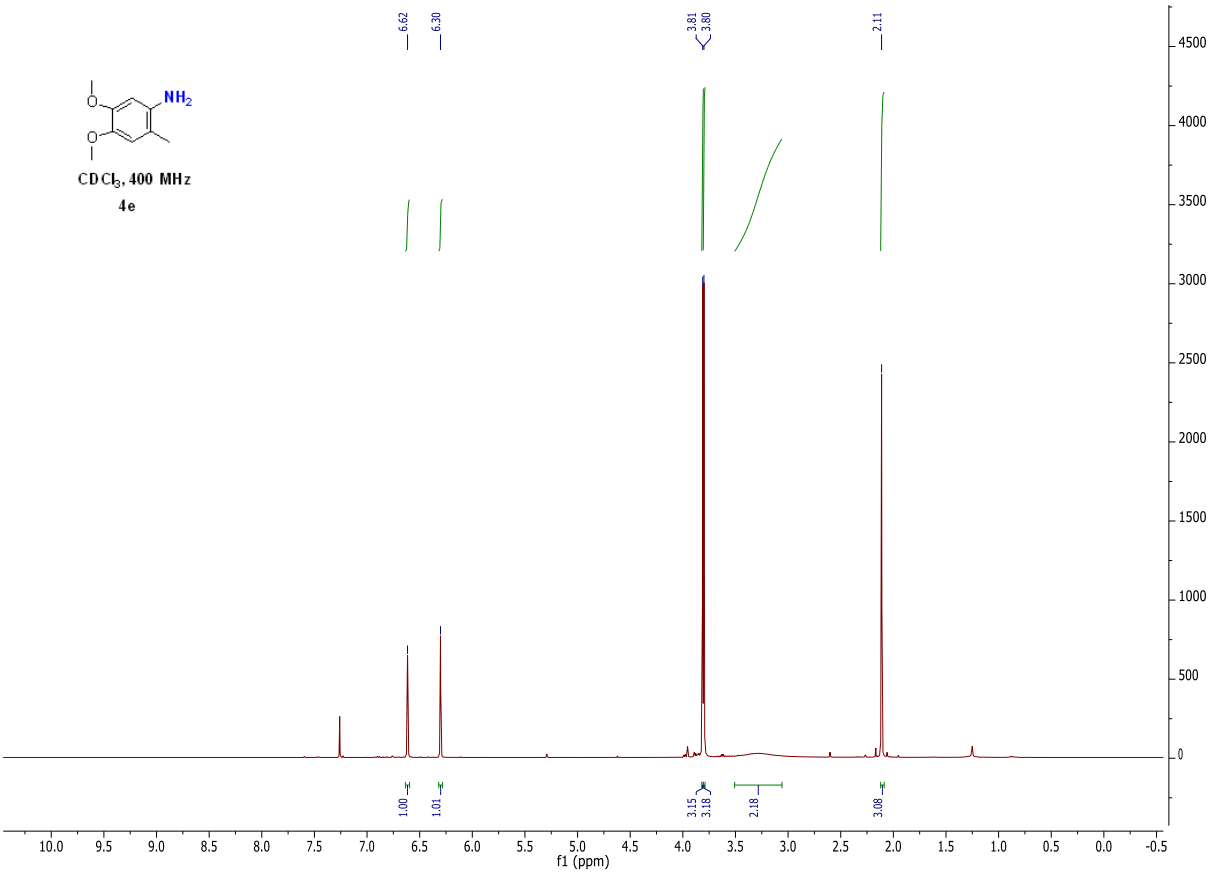

NH2
CDCl3, 101 MHz
4c
155.42
142.35
130.23
128.70
127.94
127.35
119.00
118.76
109.26
106.12
55.31
f1 (ppm)

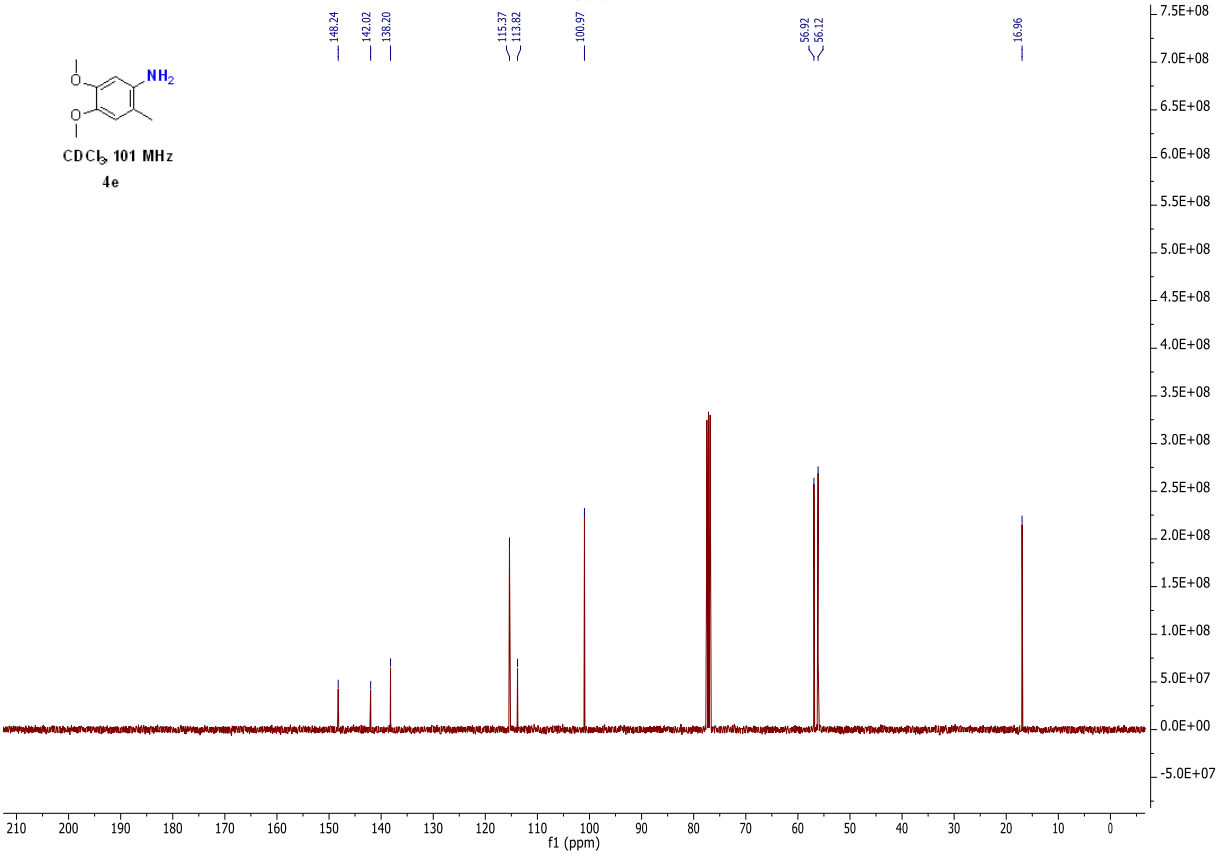

NH2
CDCl3, 400 MHz
4f
6.72
6.69
6.33
6.32
6.26
6.26
6.25
6.24
6.23
3.83
3.80
3.20
1.00
0.99
0.98
3.16
3.07
1.75
f1 (ppm)

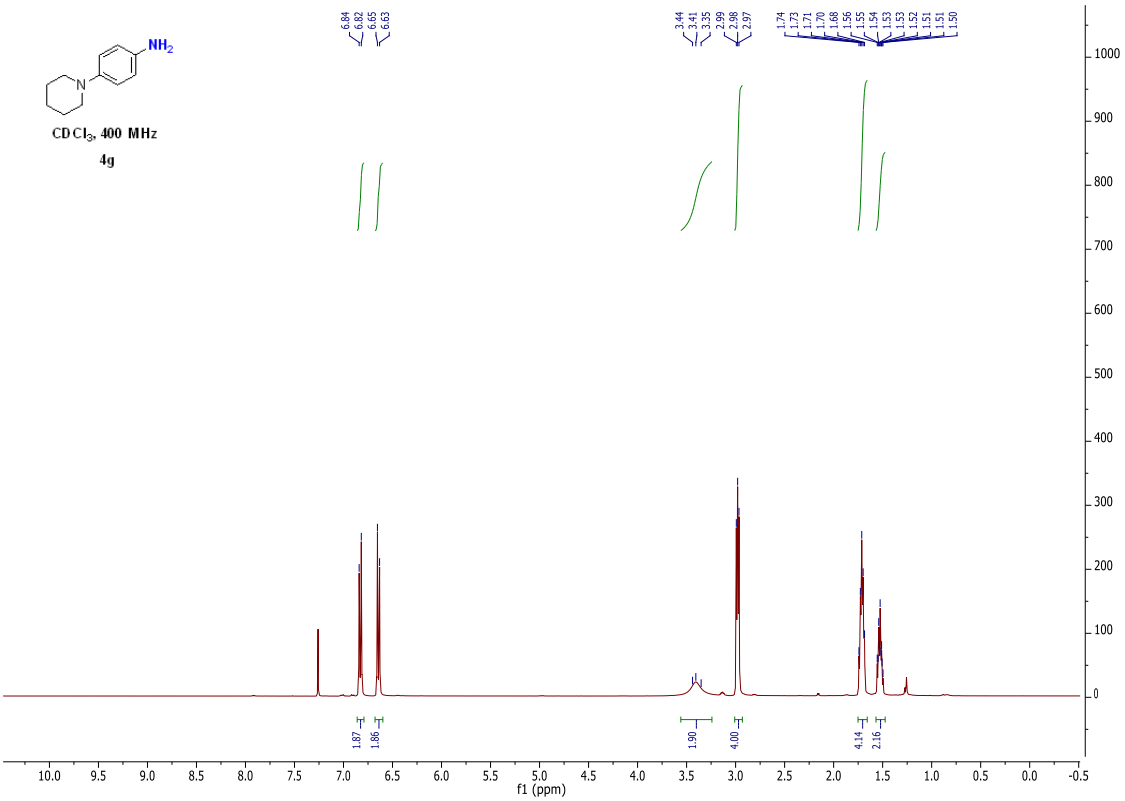

NH2
CDCl3, 151 MHz
4f
149.95
142.32
140.66
113.10
106.50
100.82
56.71
55.85
f1 (ppm)

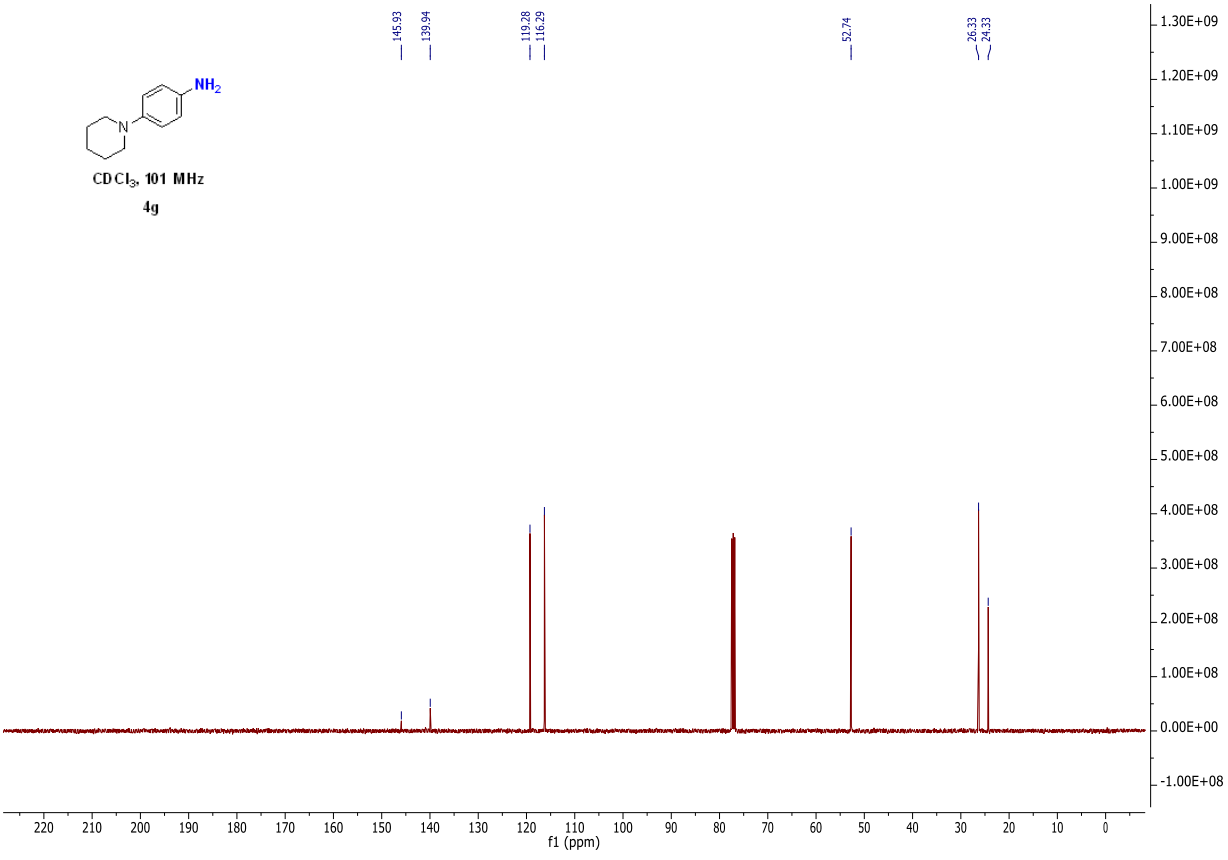

NH2
CDCl3, 400 MHz
4d
6.63
6.62
6.61
6.60
6.29
6.29
6.28
6.14
6.14
6.13
6.12
6.12
6.11
5.86
3.37
3.34
1.00
1.02
1.08
2.10
2.07
f1 (ppm)

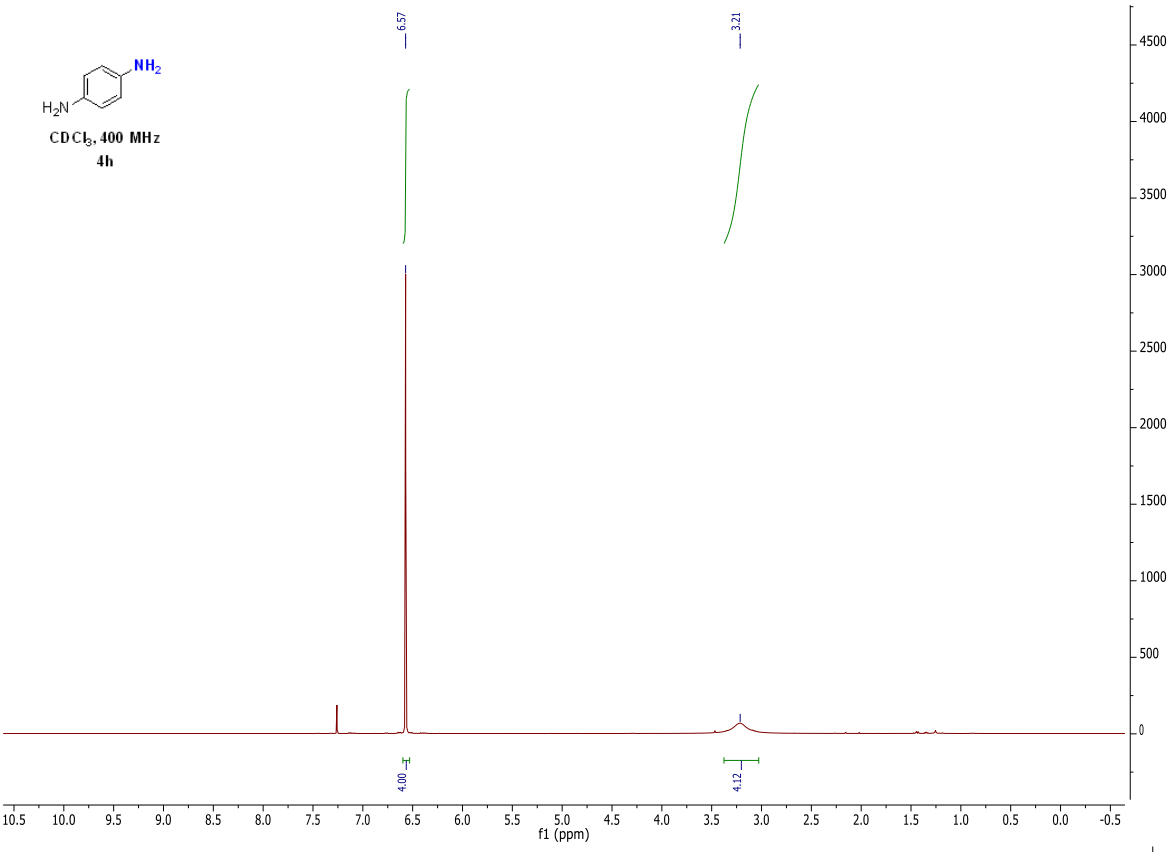

NH2
CDCl3, 101 MHz
4d
148.34
141.53
140.49
108.70
106.99
100.78
98.19
f1 (ppm)

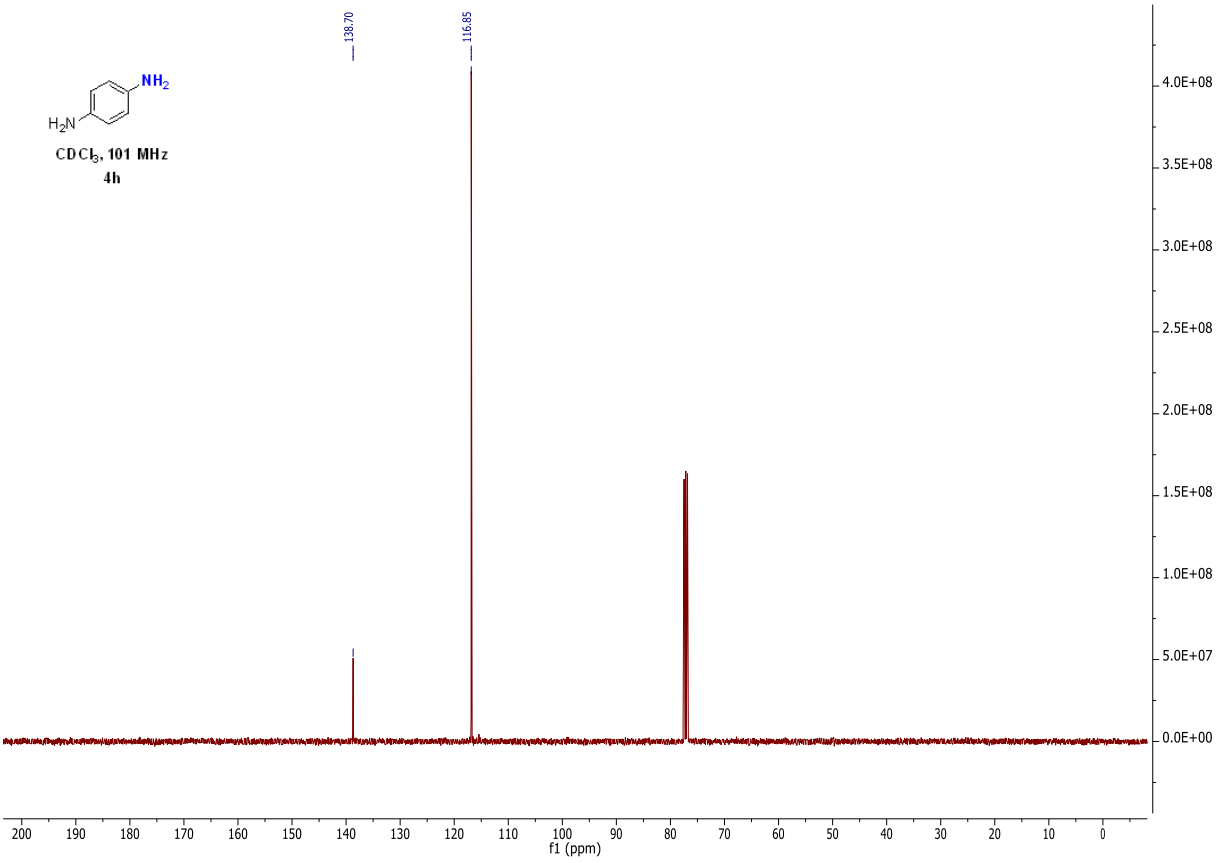

6.62
6.30
3.81
3.80
2.11
NH2
CDCl3, 400 MHz
4e
1.00
1.01
3.15
3.18
2.18
3.08
f1 (ppm)

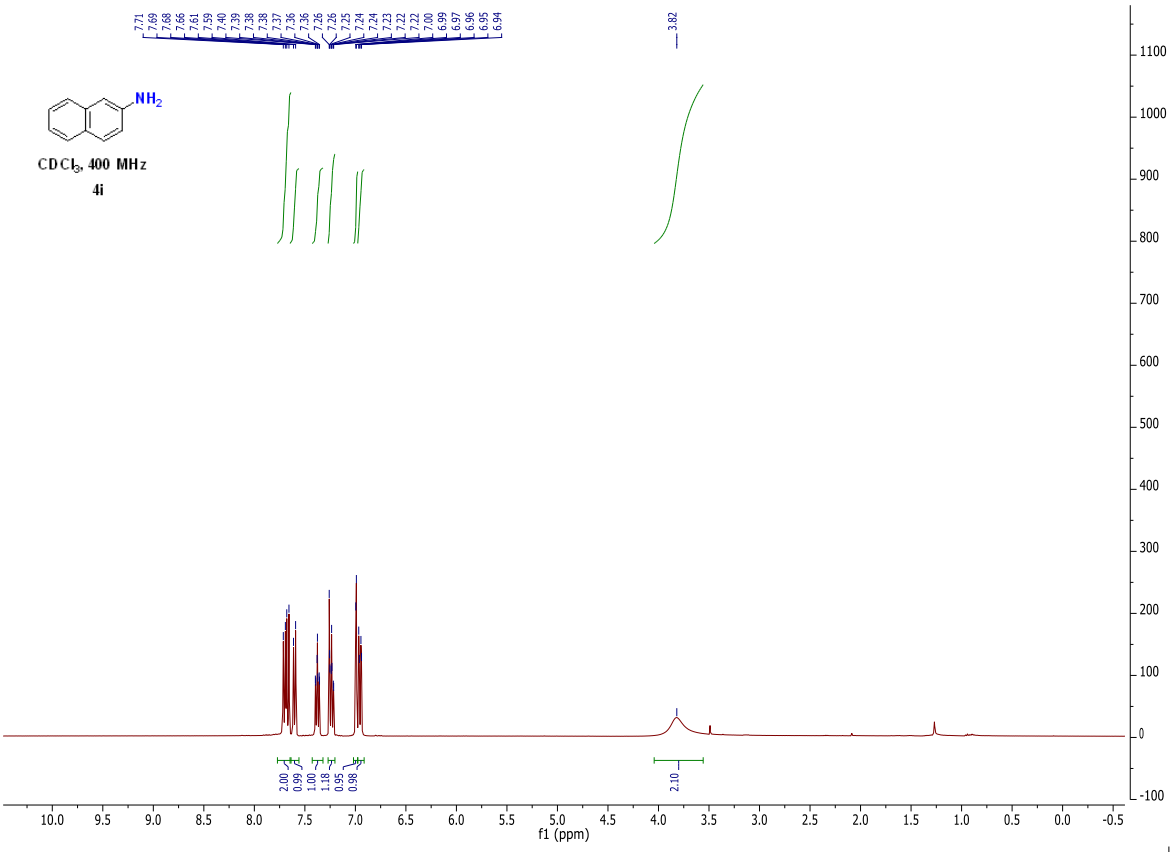

148.24
142.02
138.20
115.37
113.82
100.97
56.92
56.12
16.96
NH2
CDCl3, 101 MHz
4e
f1 (ppm)

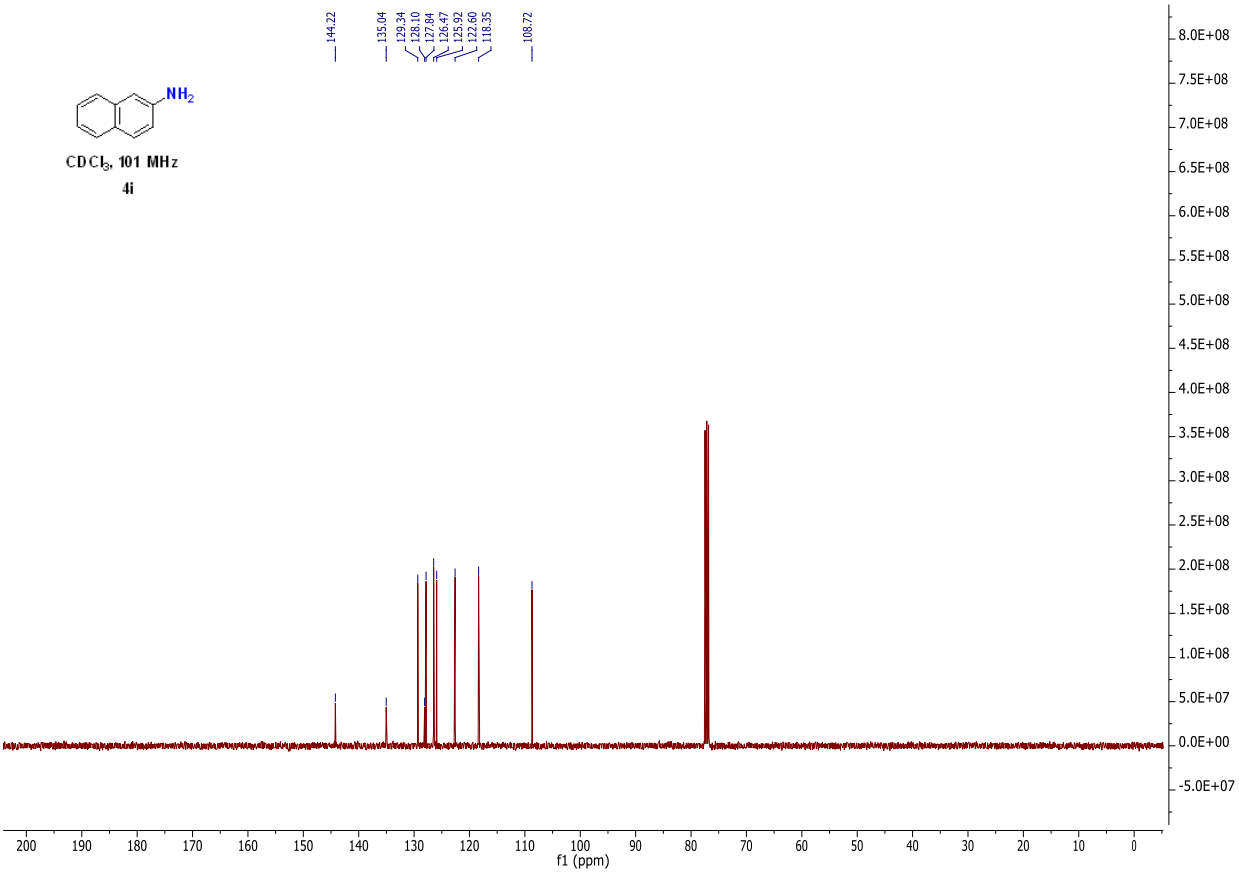

NH2
N
CDCl3, 400 MHz
4g
6.84
6.82
6.65
6.63
3.44
3.41
3.35
2.99
2.98
2.97
1.74
1.73
1.71
1.70
1.68
1.56
1.55
1.54
1.53
1.53
1.52
1.51
1.51
1.50
1.87
1.86
1.90
4.00
4.14
2.16
f1 (ppm)

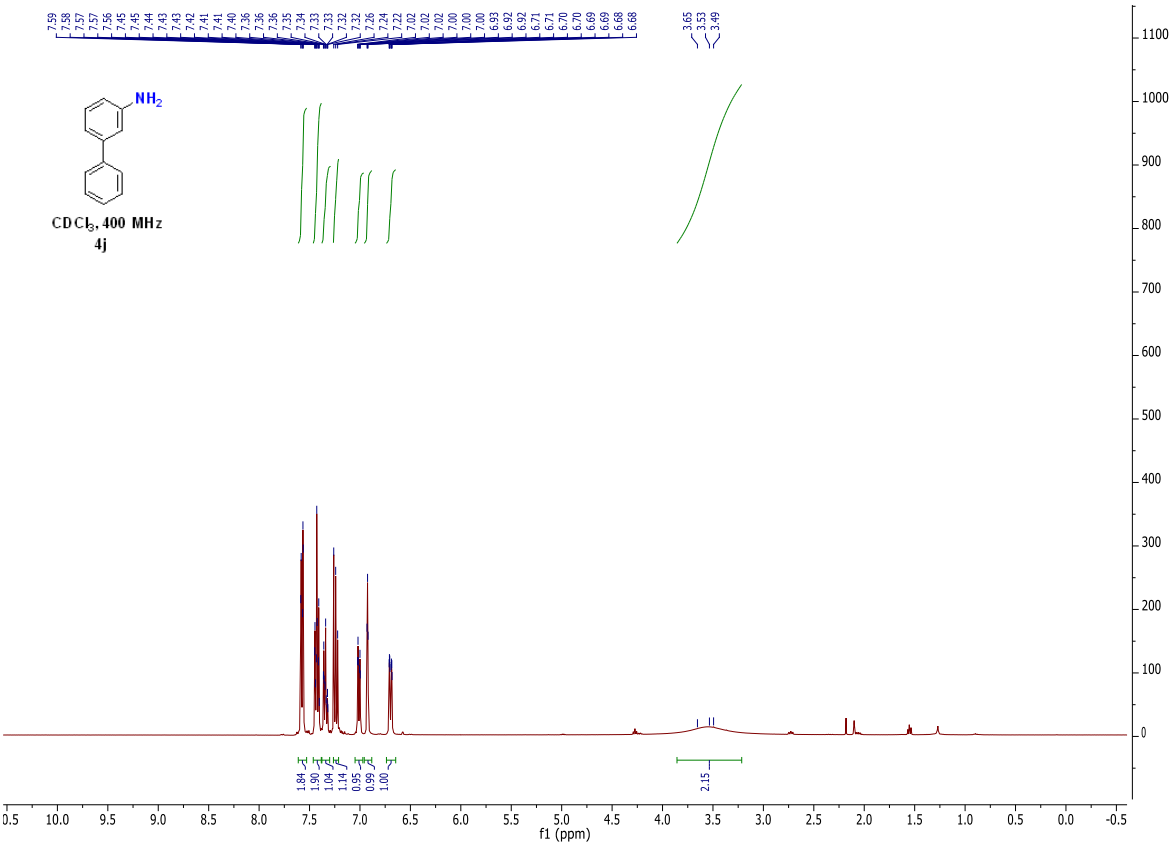

NH2
N
CDCl3, 101 MHz
4g
145.93
139.94
119.28
116.29
52.74
26.33
24.33
f1 (ppm)

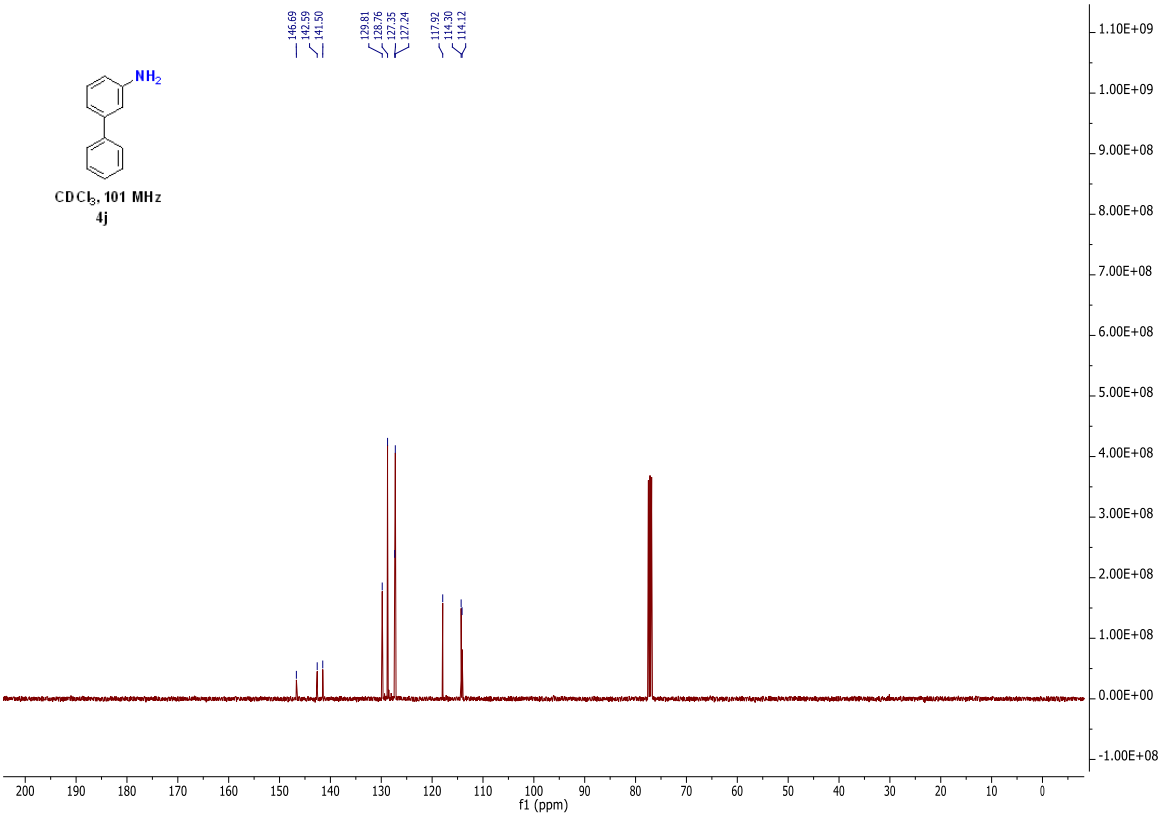

NH2
H2N
CDCl3, 400 MHz
4h
6.57
3.21
4.00
4.12
f1 (ppm)

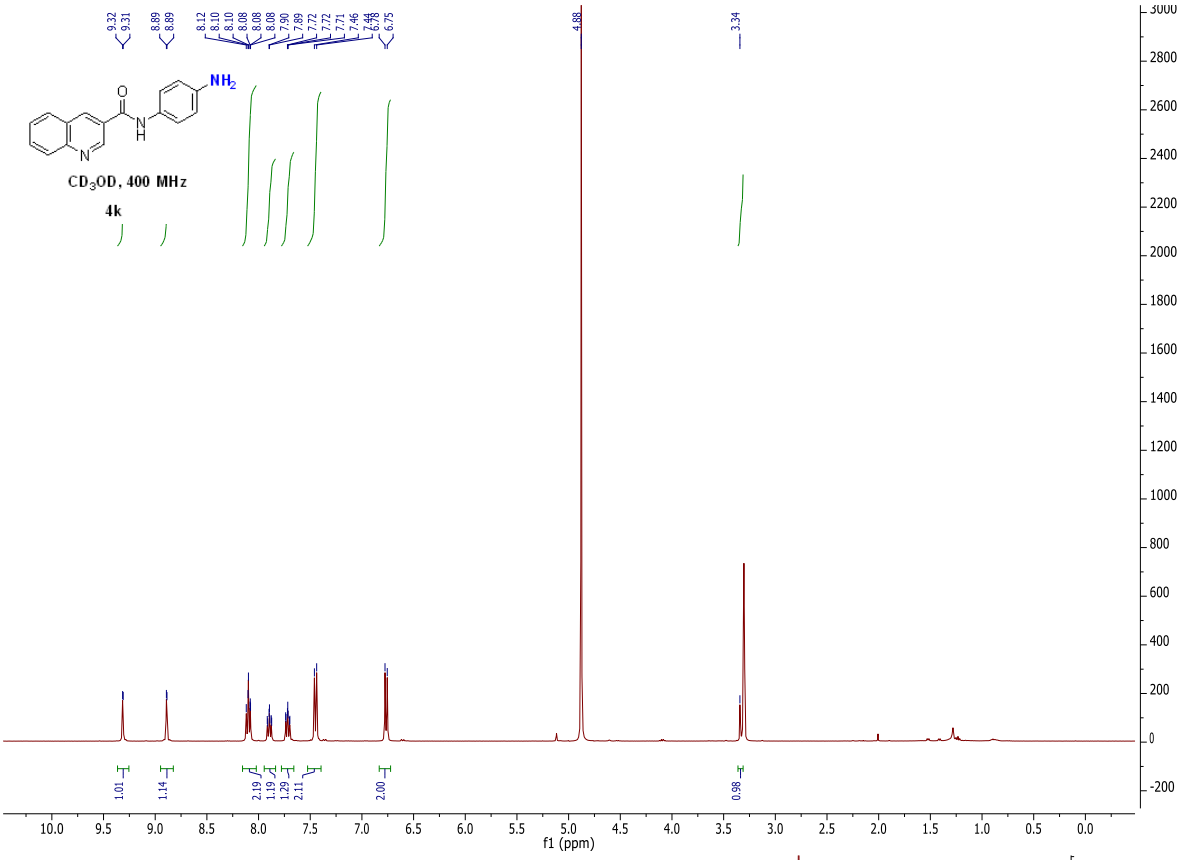

NH2
H2N
CDCl3, 101 MHz
4h
138.70
116.85
f1 (ppm)

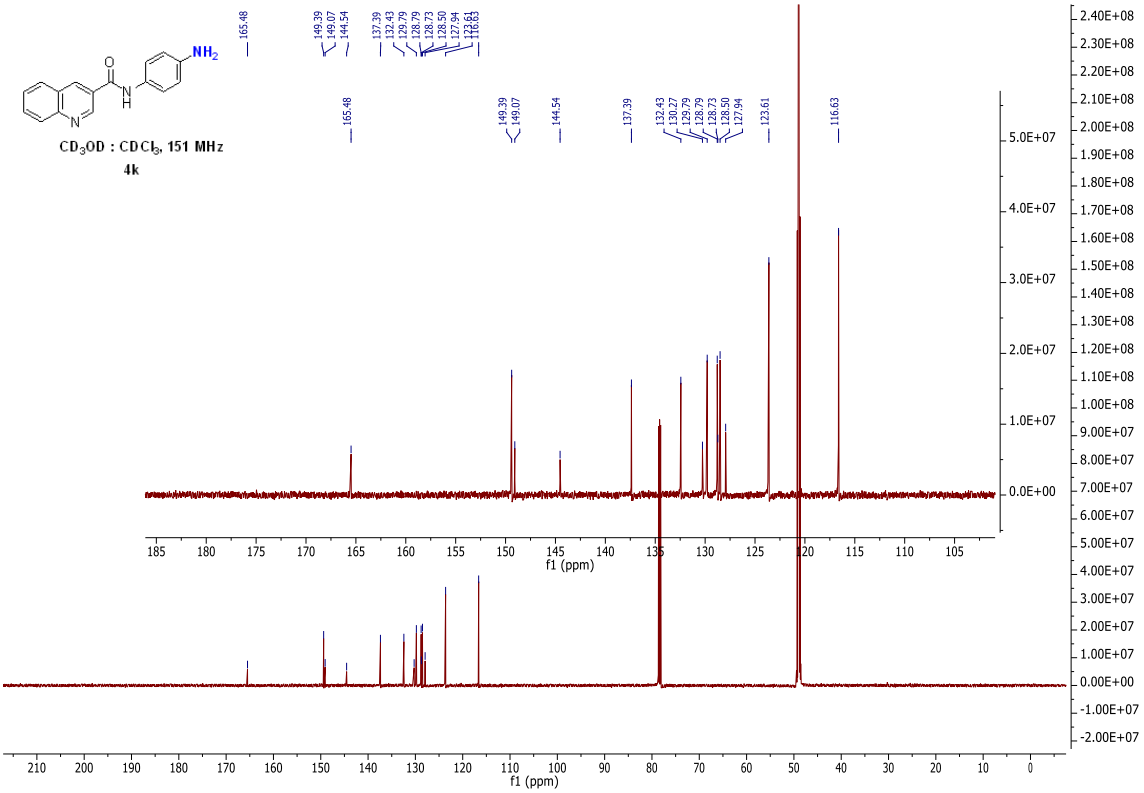

7.71
7.69
7.68
7.66
7.61
7.59
7.40
7.39
7.38
7.38
7.37
7.36
7.36
7.26
7.26
7.25
7.24
7.24
7.23
7.22
7.22
7.00
6.99
6.97
6.96
6.95
6.94
3.82
NH2
CDCl3, 400 MHz
4i
2.00
0.99
1.00
1.18
0.95
0.98
2.10
f1 (ppm)

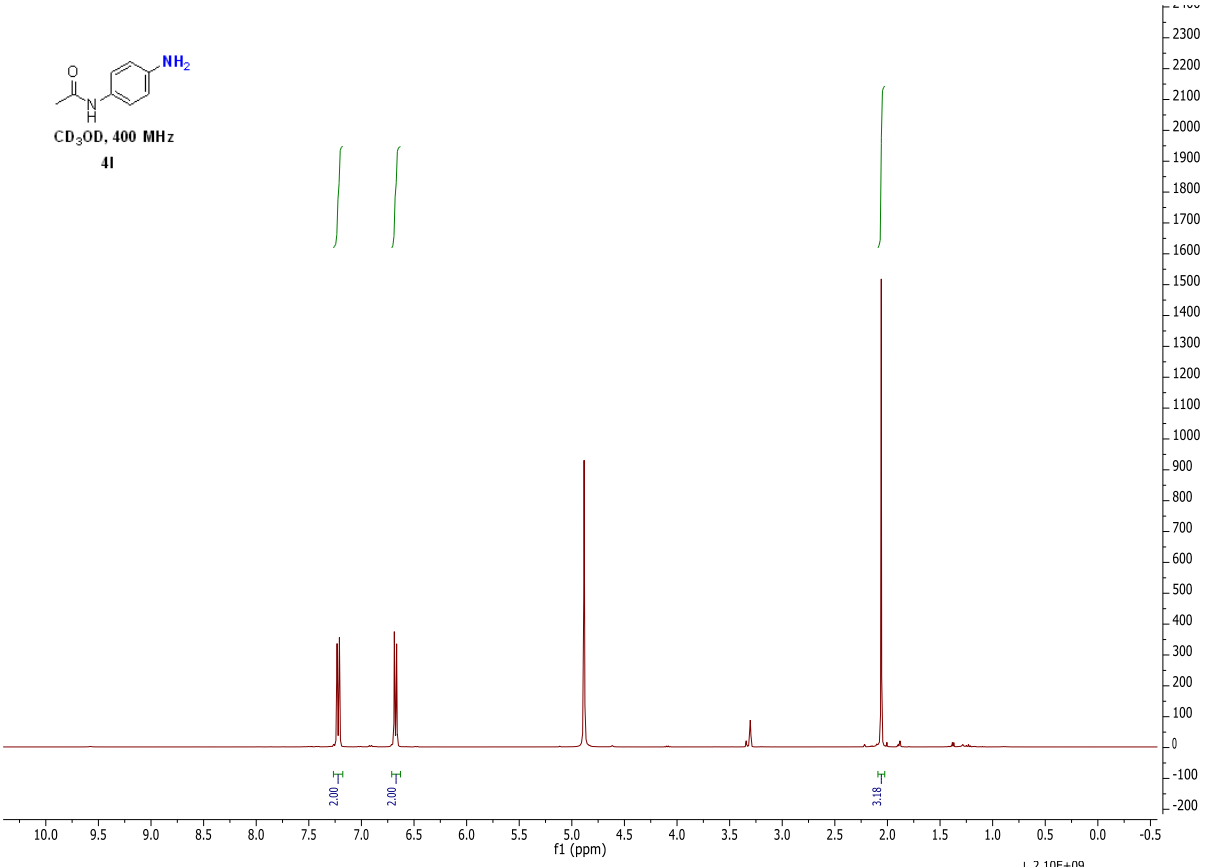

144.22
135.04
129.34
128.10
127.84
126.47
125.92
122.60
118.35
108.72
NH2
CDCl3, 101 MHz
4i
f1 (ppm)

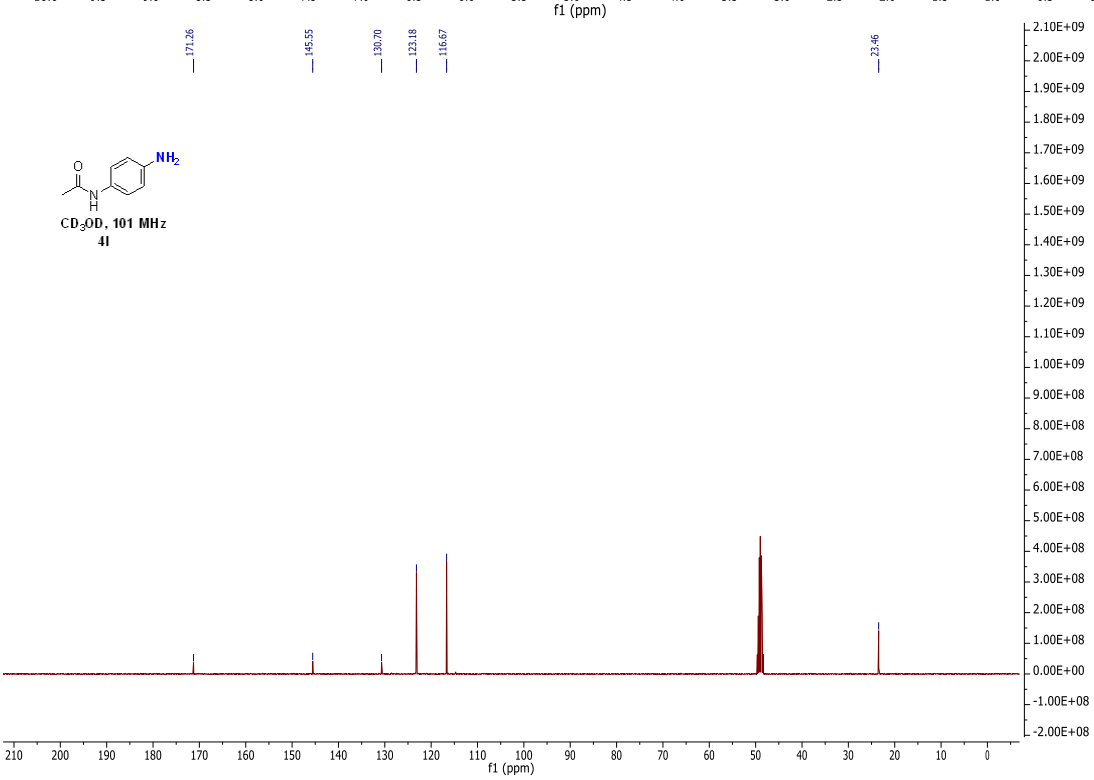

NH2
CDCl3, 400 MHz
4j
f1 (ppm)

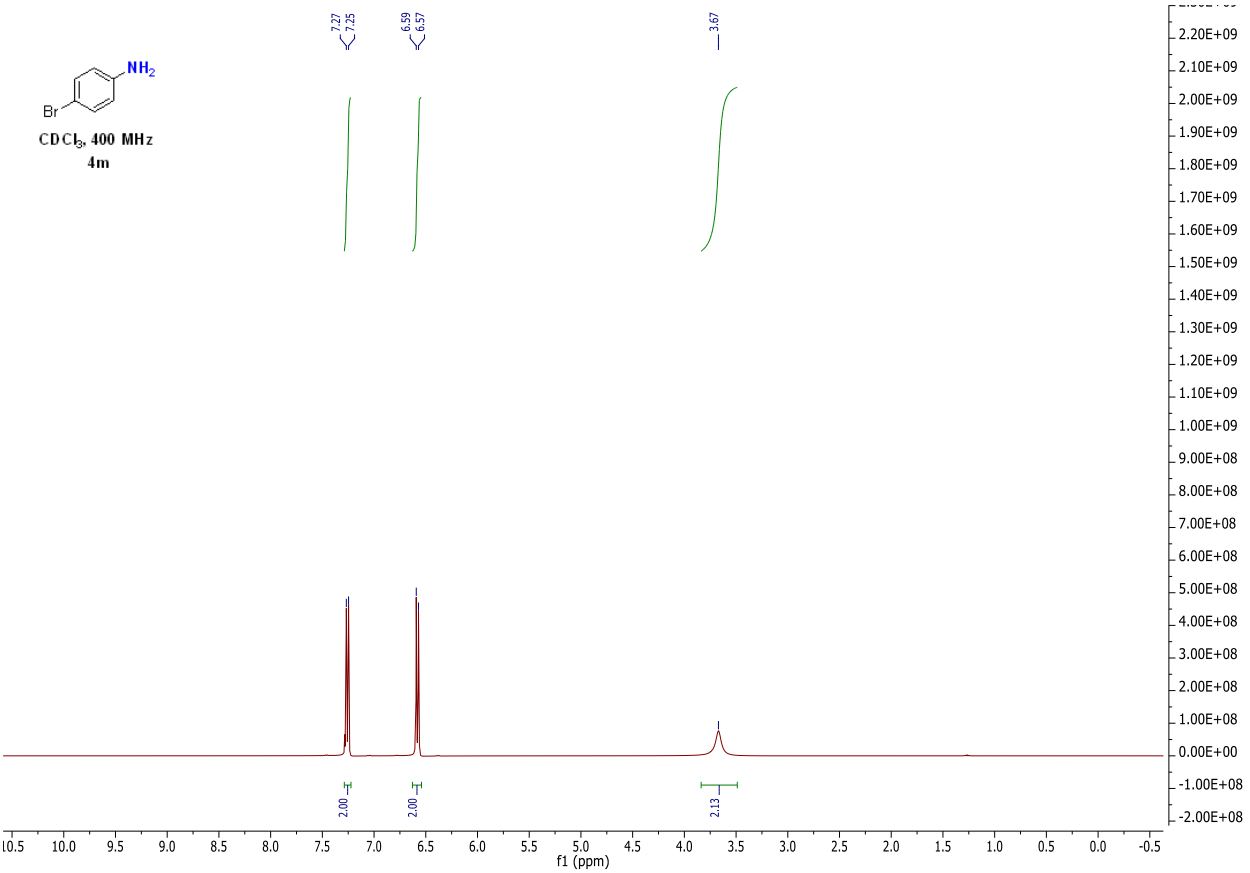

NH2
CDCl3, 101 MHz
4j
f1 (ppm)

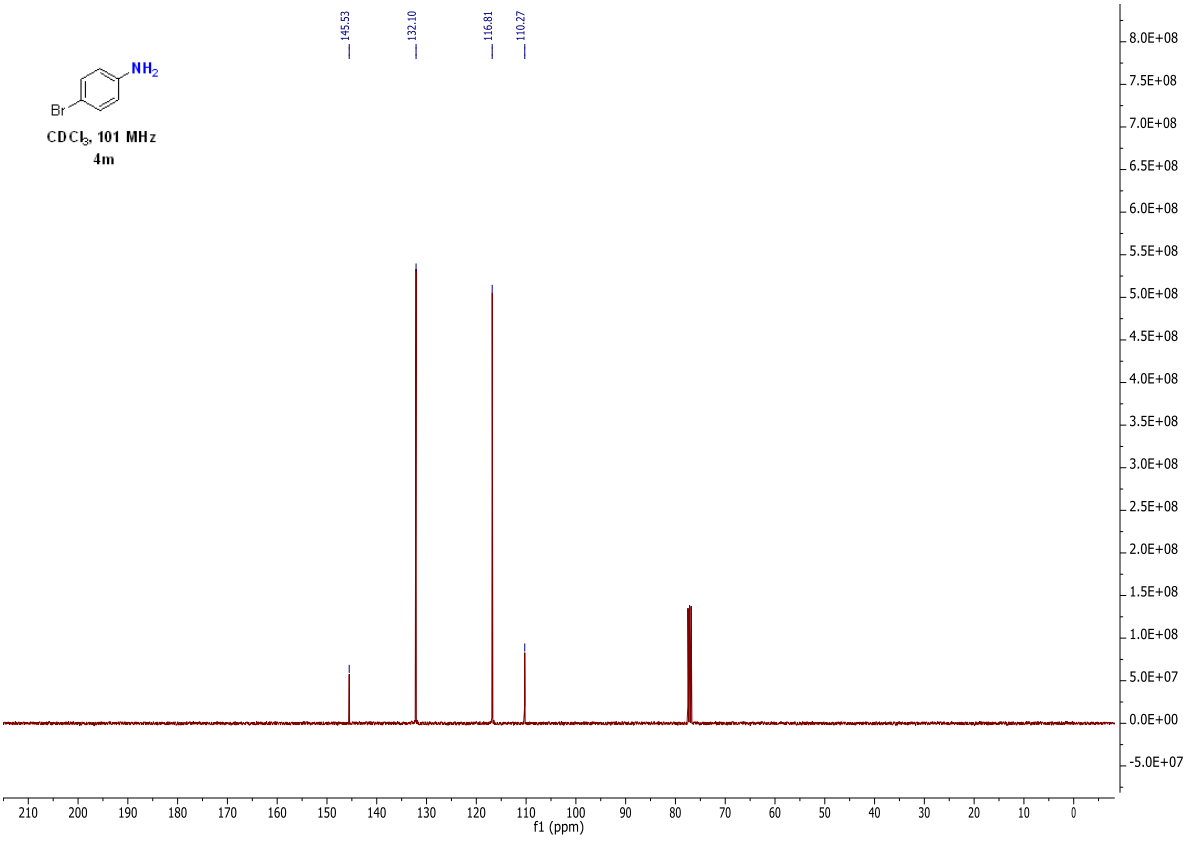

9.32
9.31
8.89
8.89
8.12
8.10
8.10
8.08
8.08
8.08
8.08
7.90
7.89
7.72
7.72
7.71
7.46
7.44
6.78
6.75
4.88
3.34
NH2
O
N
H
N
CD3OD, 400 MHz
4k
1.01
1.14
2.19
1.19
1.29
2.11
2.00
0.98
f1 (ppm)

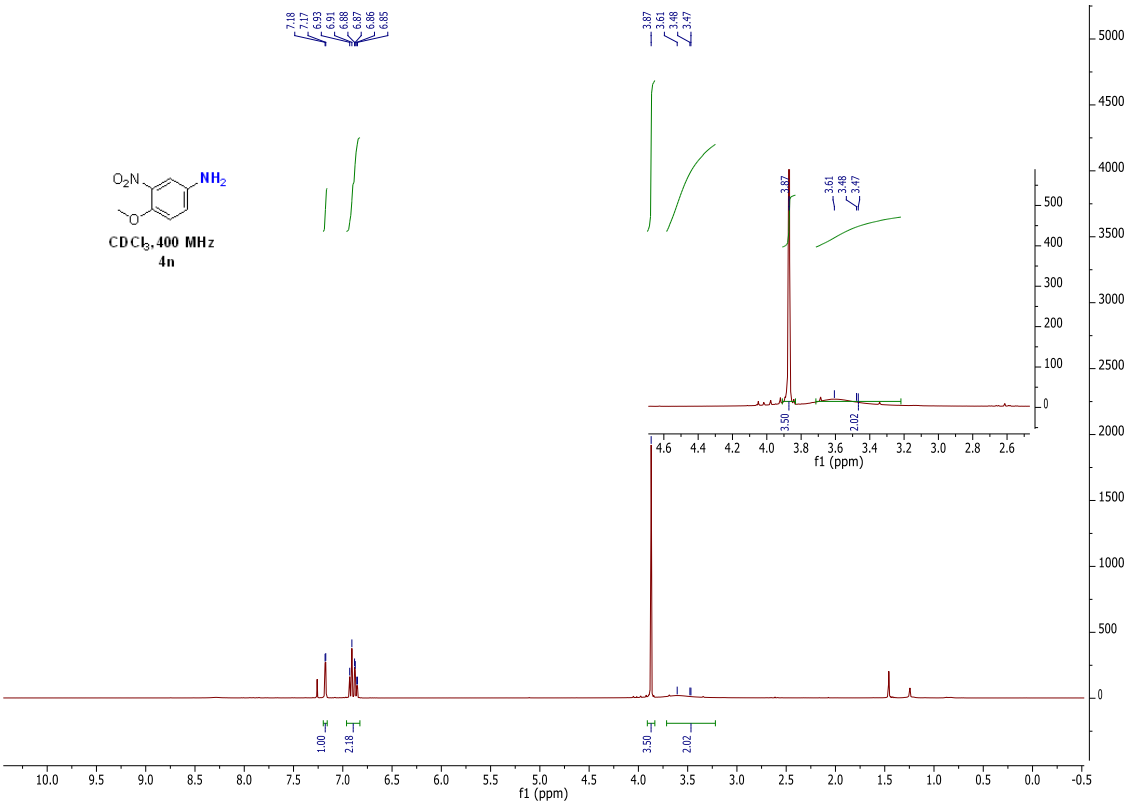

165.48
149.39
149.07
144.54
137.39
132.43
130.27
129.79
128.79
128.73
128.50
127.94
123.61
116.63
NH2
O
N
H
N
CD3OD : CDCl3, 151 MHz
4k
f1 (ppm)
f1 (ppm)

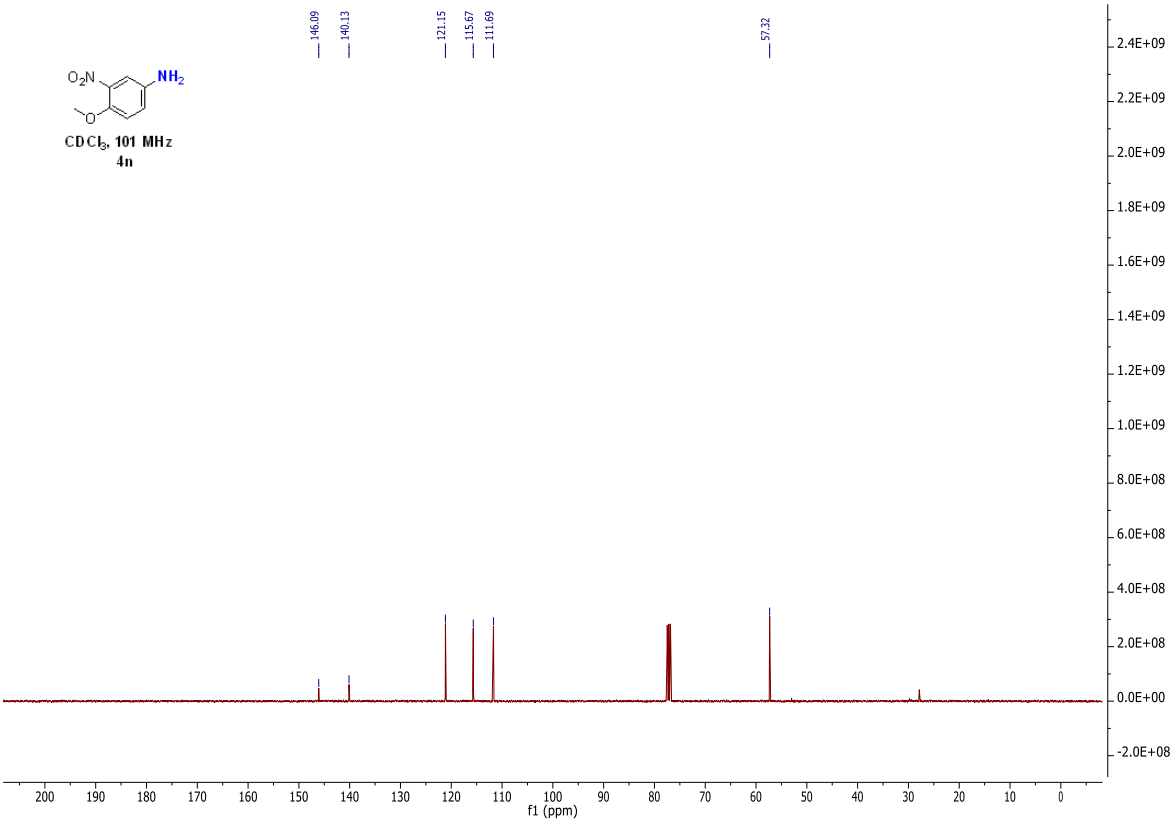

CD3OD, 400 MHz
4l
2.00
2.00
3.18
f1 (ppm)

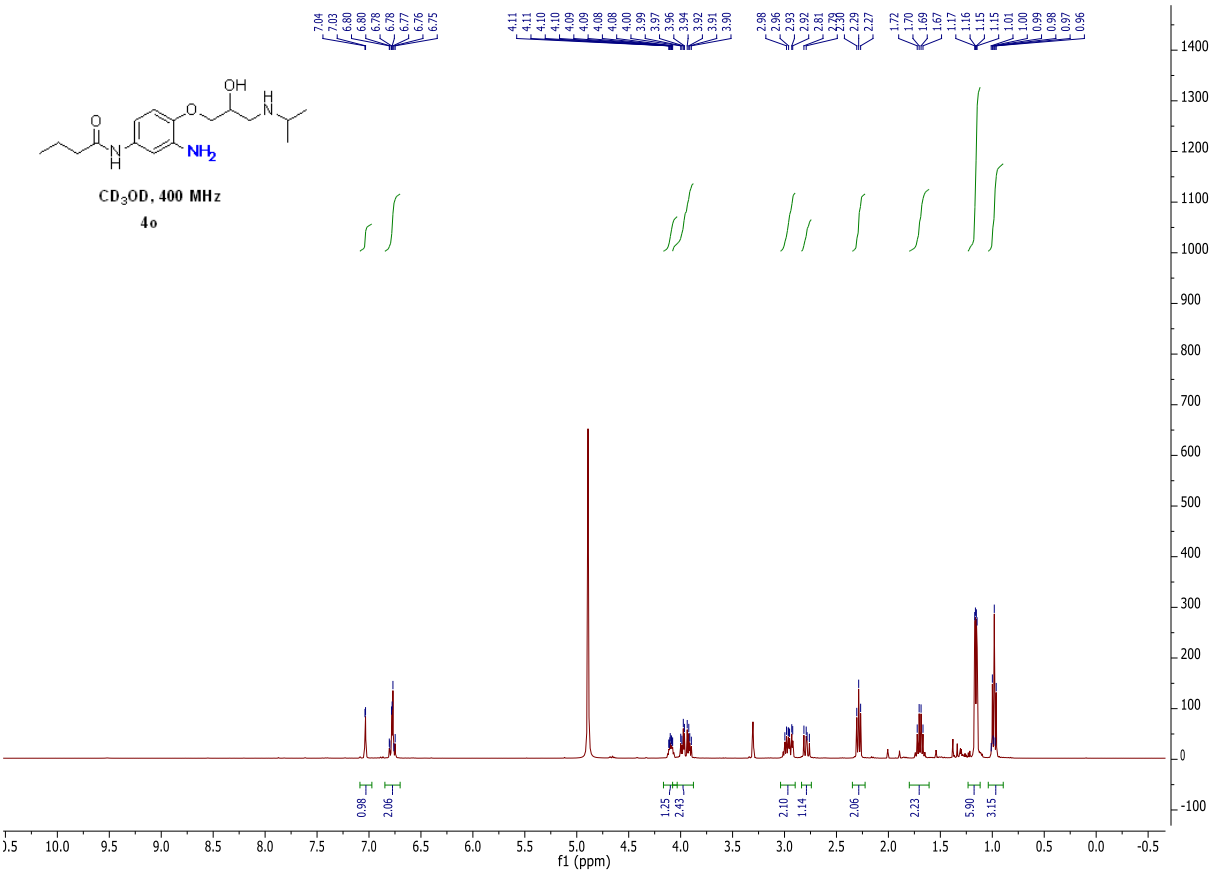

171.26
145.55
130.70
123.18
116.67
23.46
CD3OD, 101 MHz
4l
f1 (ppm)

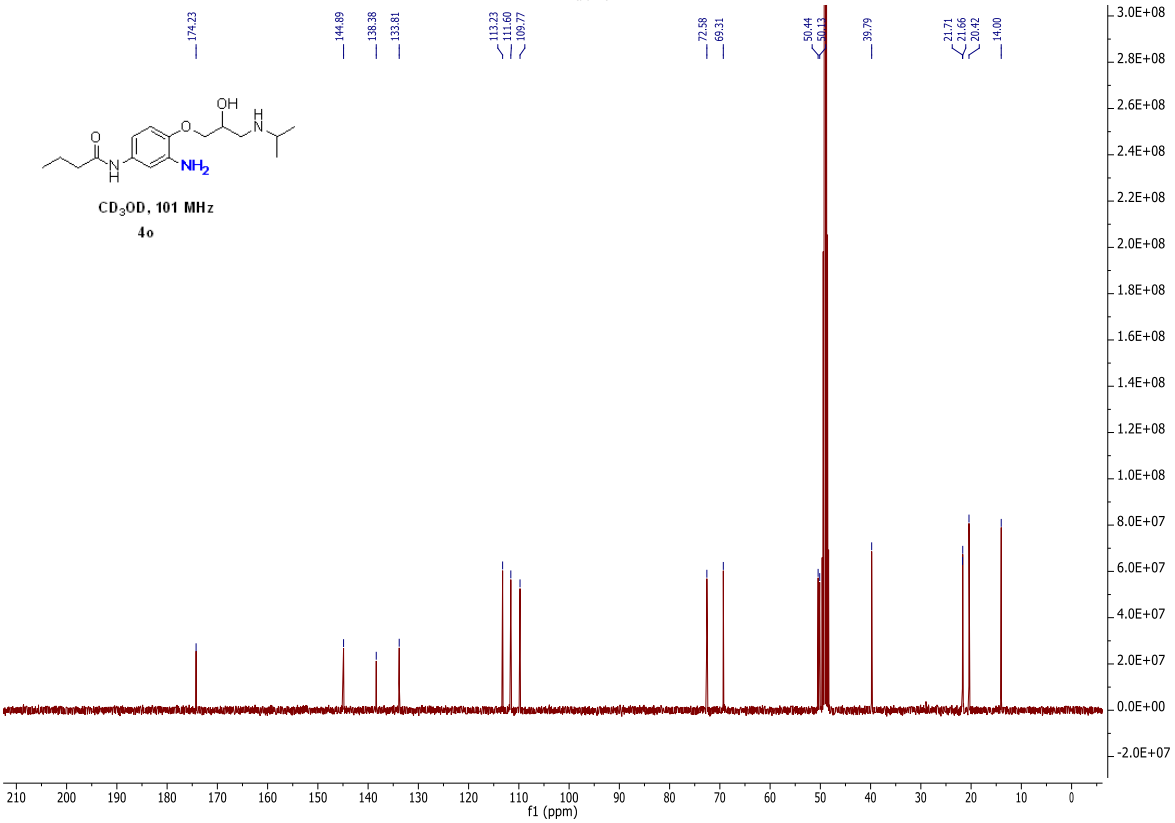

NH2
Br
CDCl3, 400 MHz
4m
7.27
7.25
6.59
6.57
3.67
2.00
2.00
2.13
f1 (ppm)

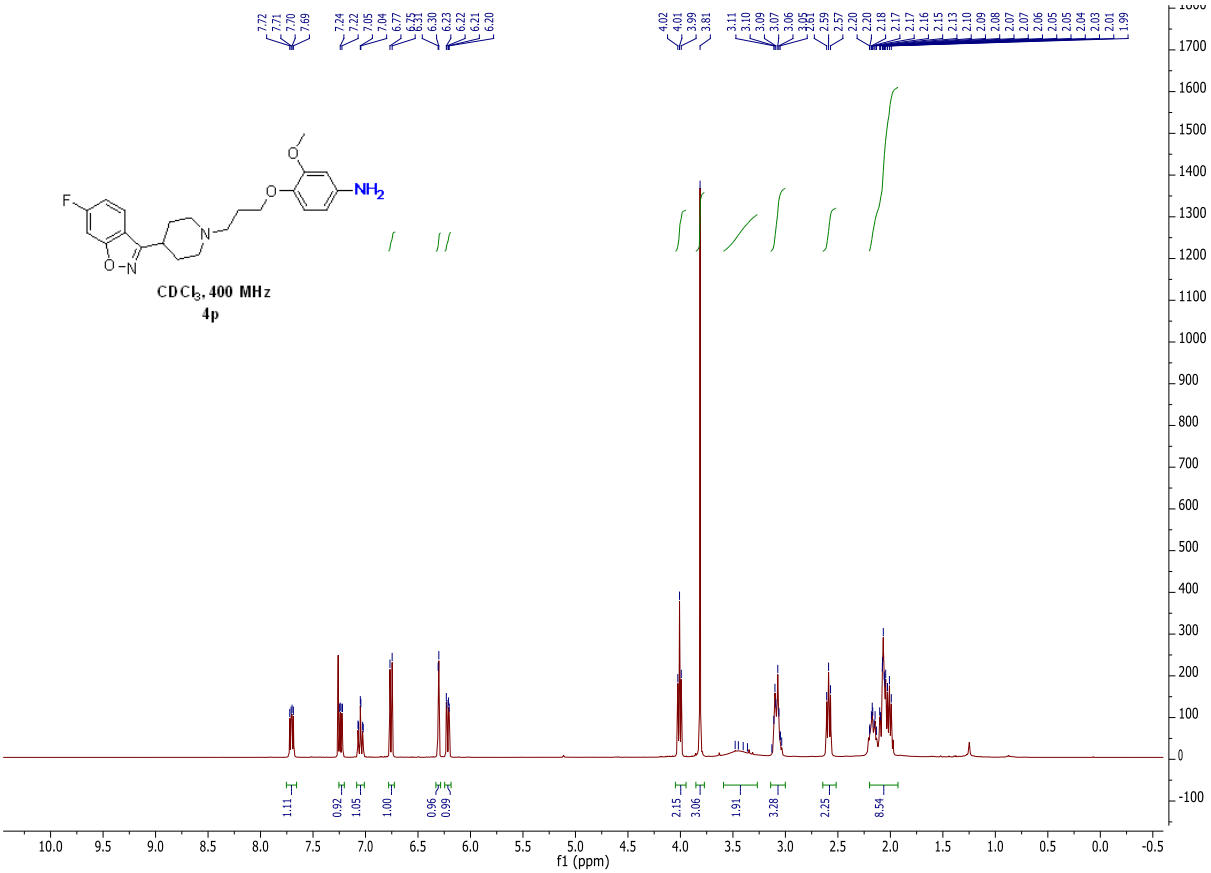

NH2
Br
CDCl3, 101 MHz
4m
145.53
132.10
116.81
110.27
f1 (ppm)

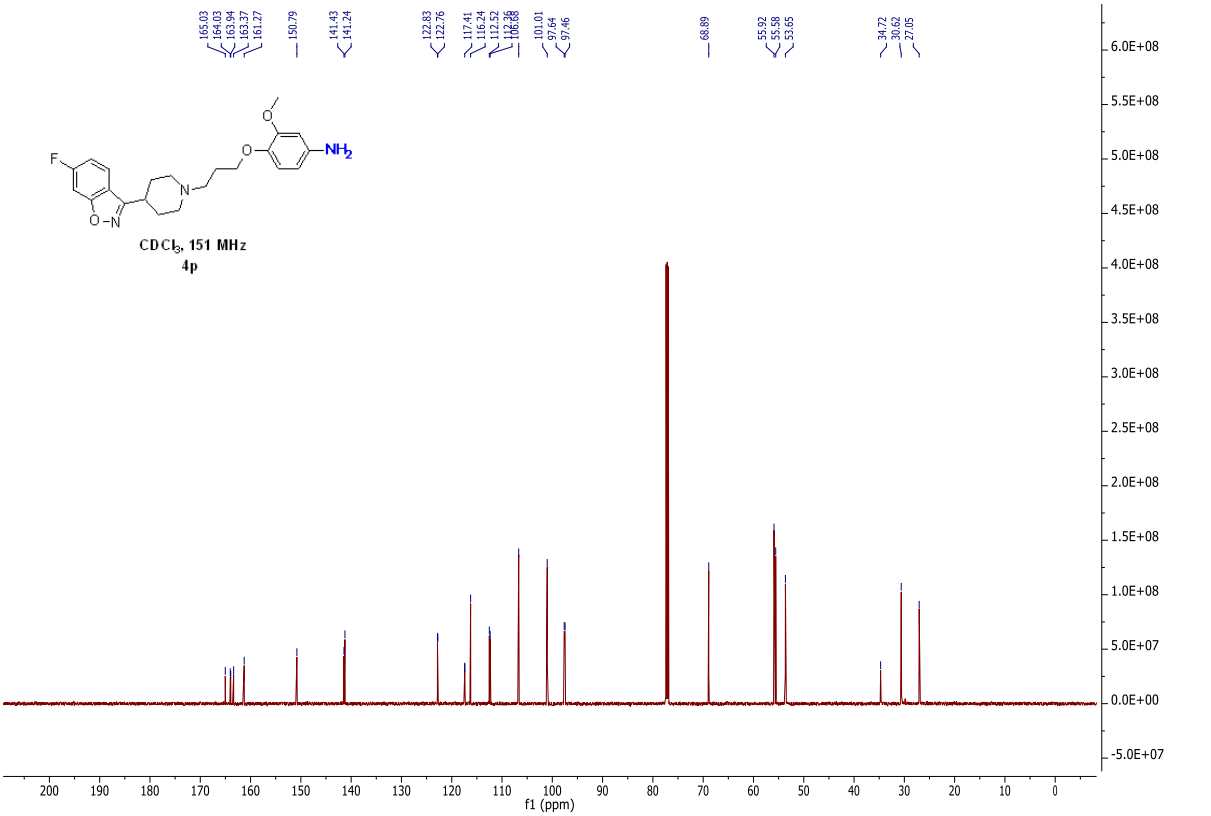

7.18
7.17
6.93
6.91
6.88
6.87
6.86
6.85
3.87
3.61
3.48
3.47
3.62
3.50
2.02
NH2
O2N
CDCl3, 400 MHz
4n
f1 (ppm)

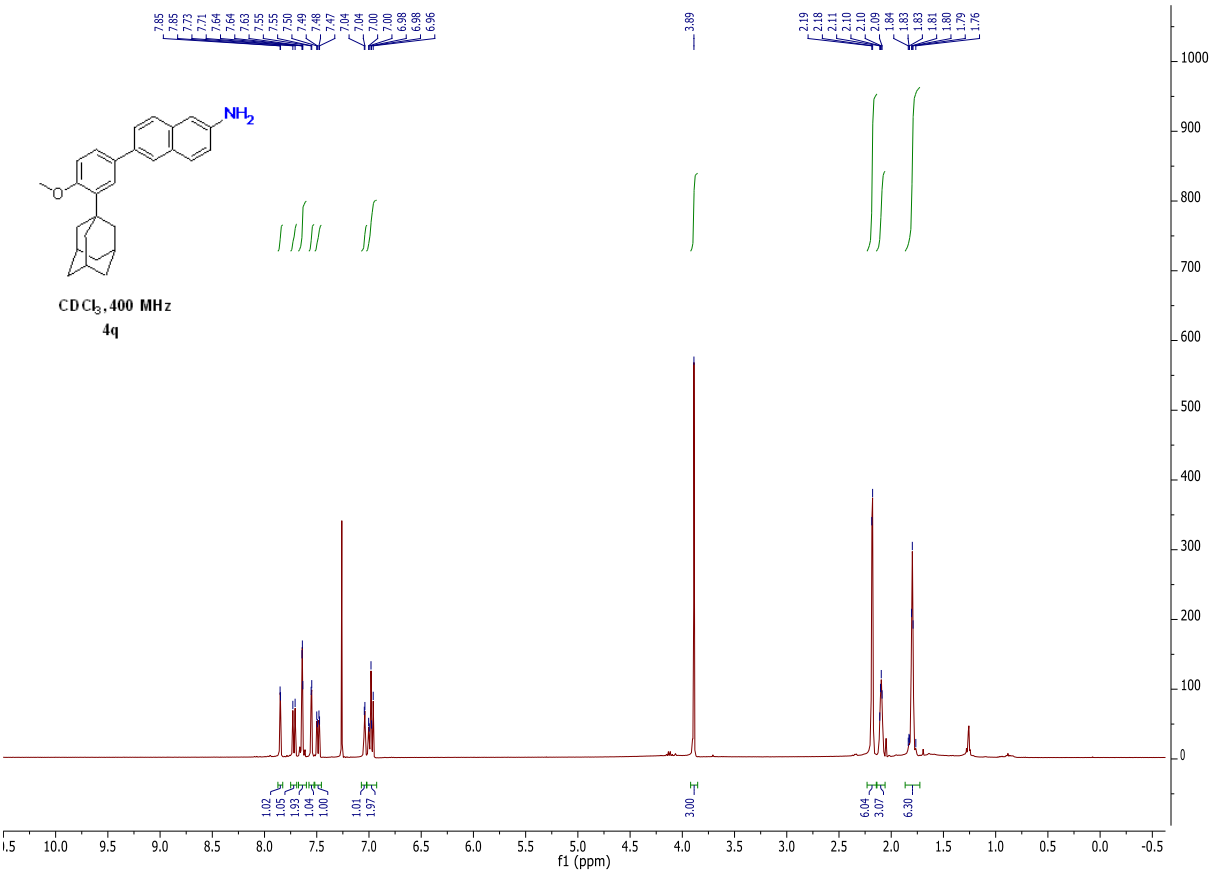

146.09
140.13
121.15
115.67
111.69
57.32
NH2
O2N
CDCl3, 101 MHz
4n
f1 (ppm)

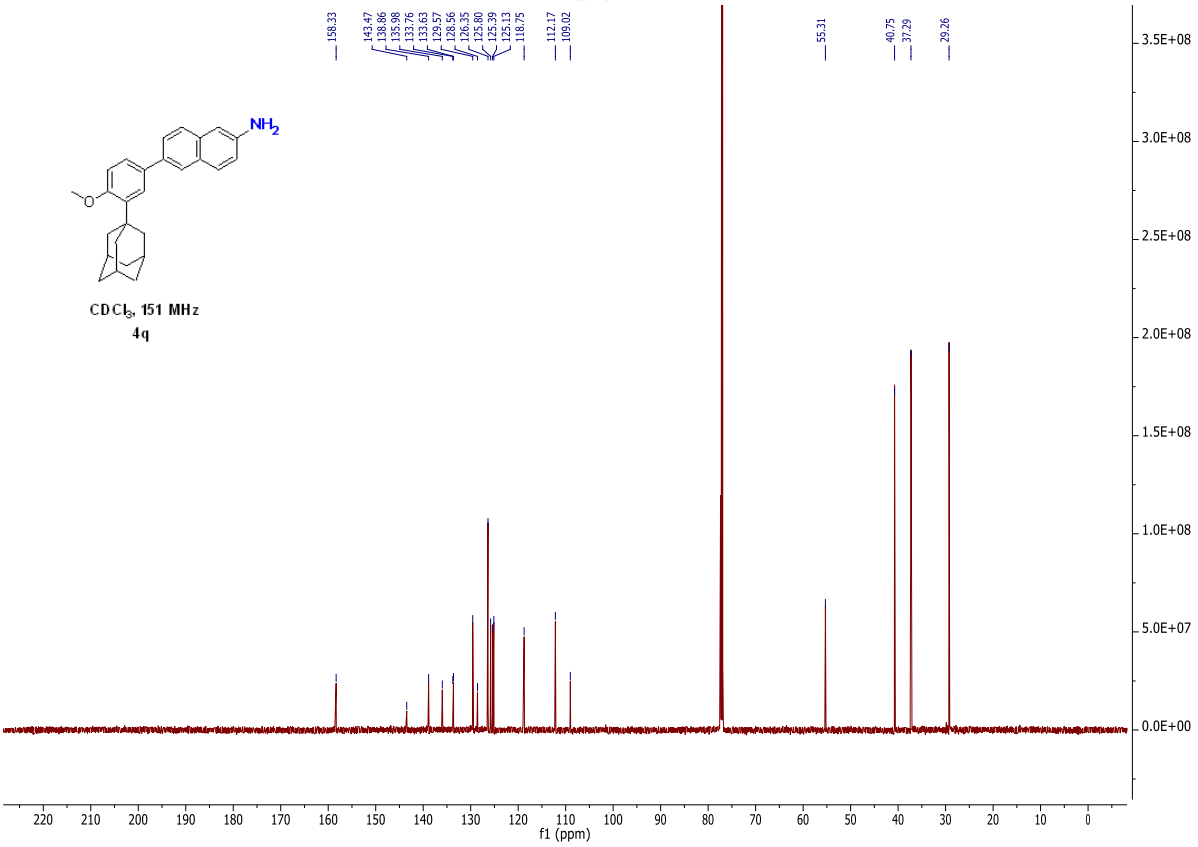

CD3OD, 400 MHz
4o
f1 (ppm)

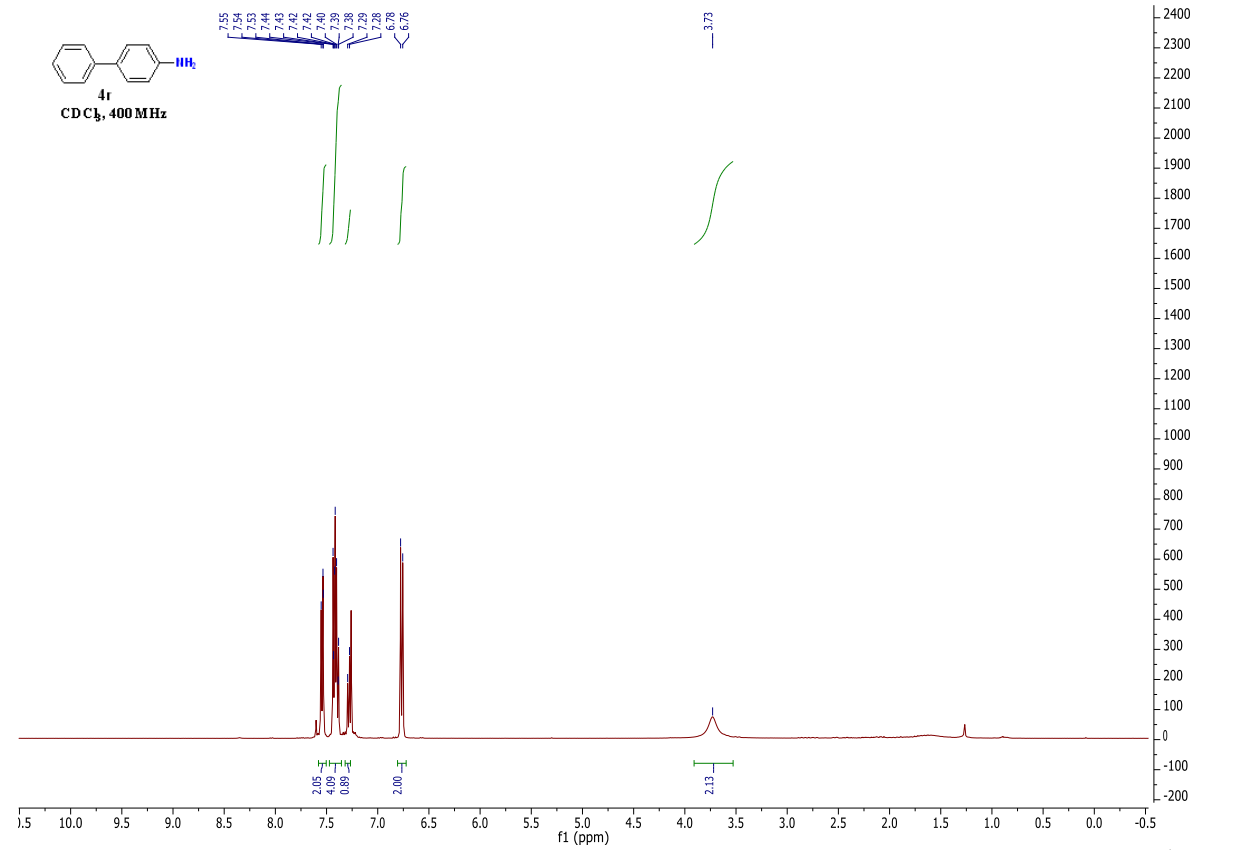

CD3OD, 101 MHz
4o
f1 (ppm)

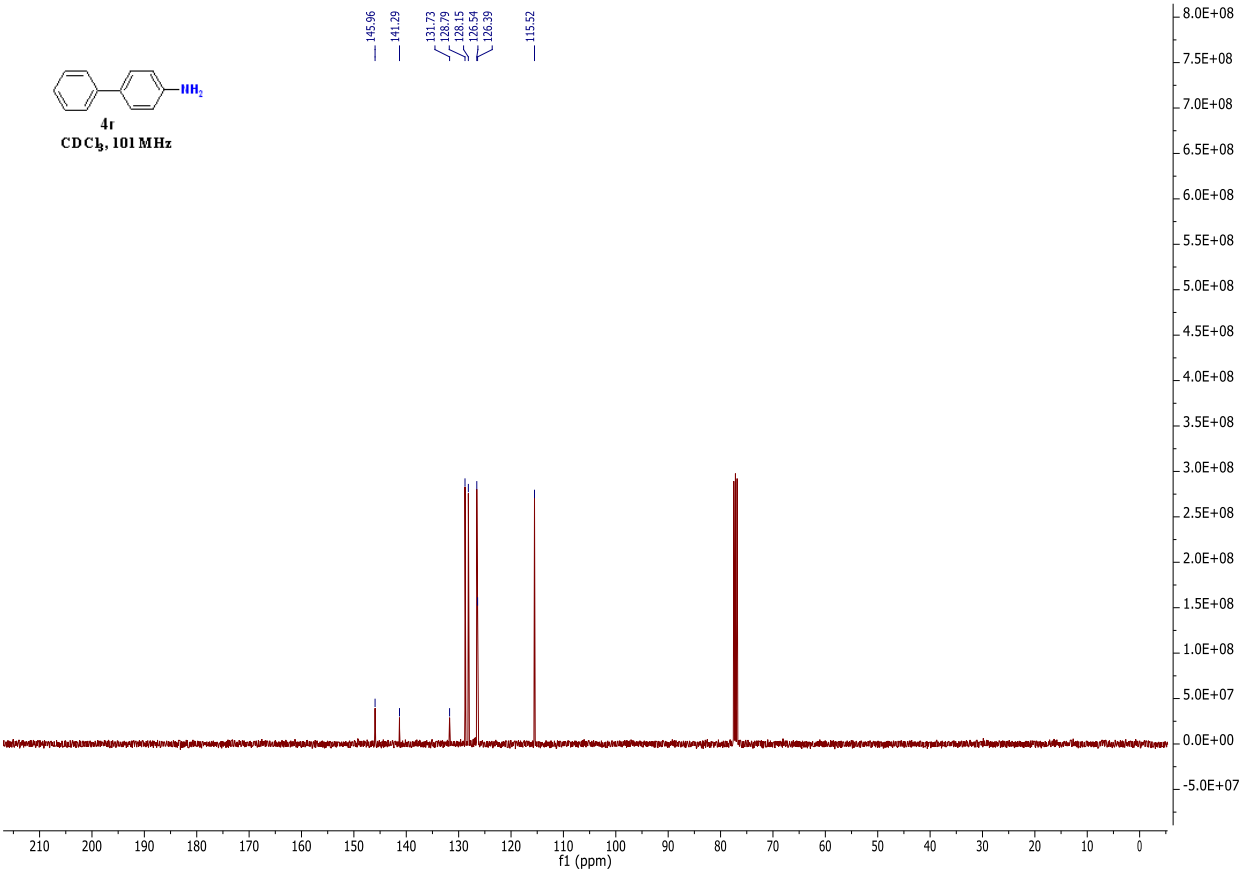

CDCl3, 400 MHz
4p
f1 (ppm)

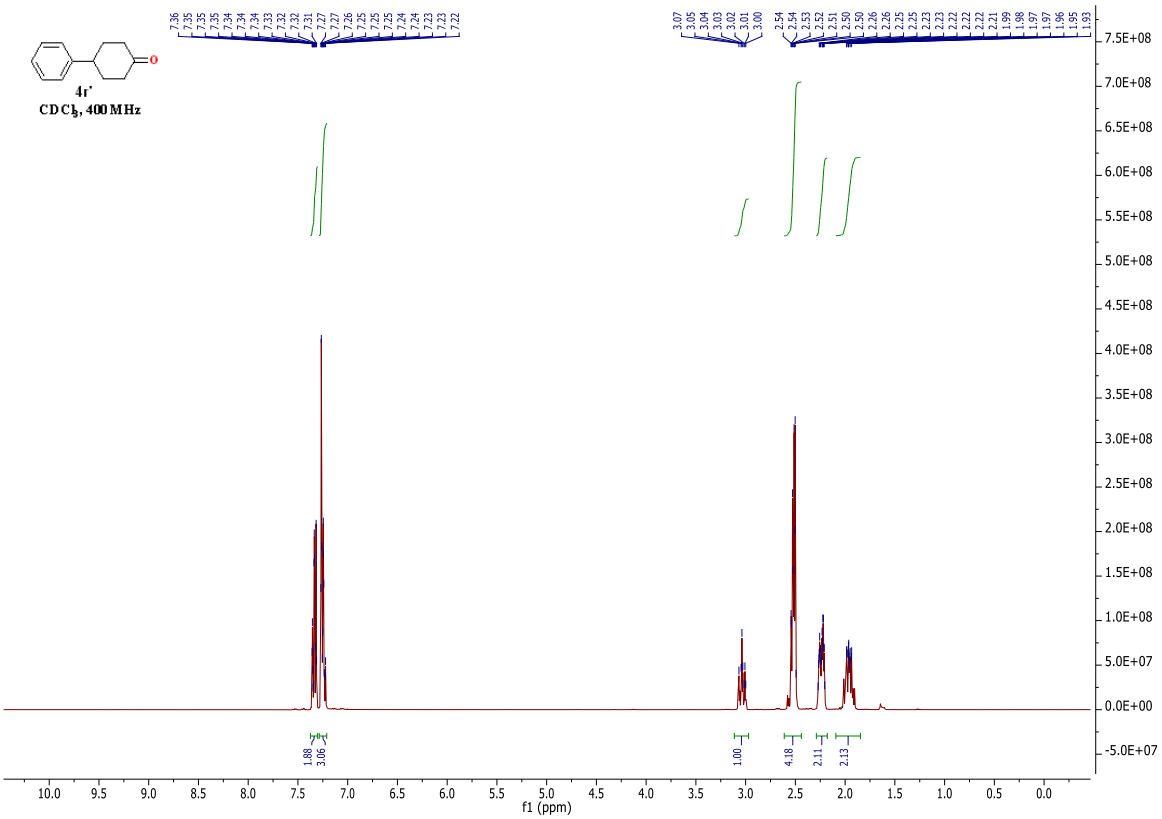

CDCl3, 151 MHz
4p
f1 (ppm)

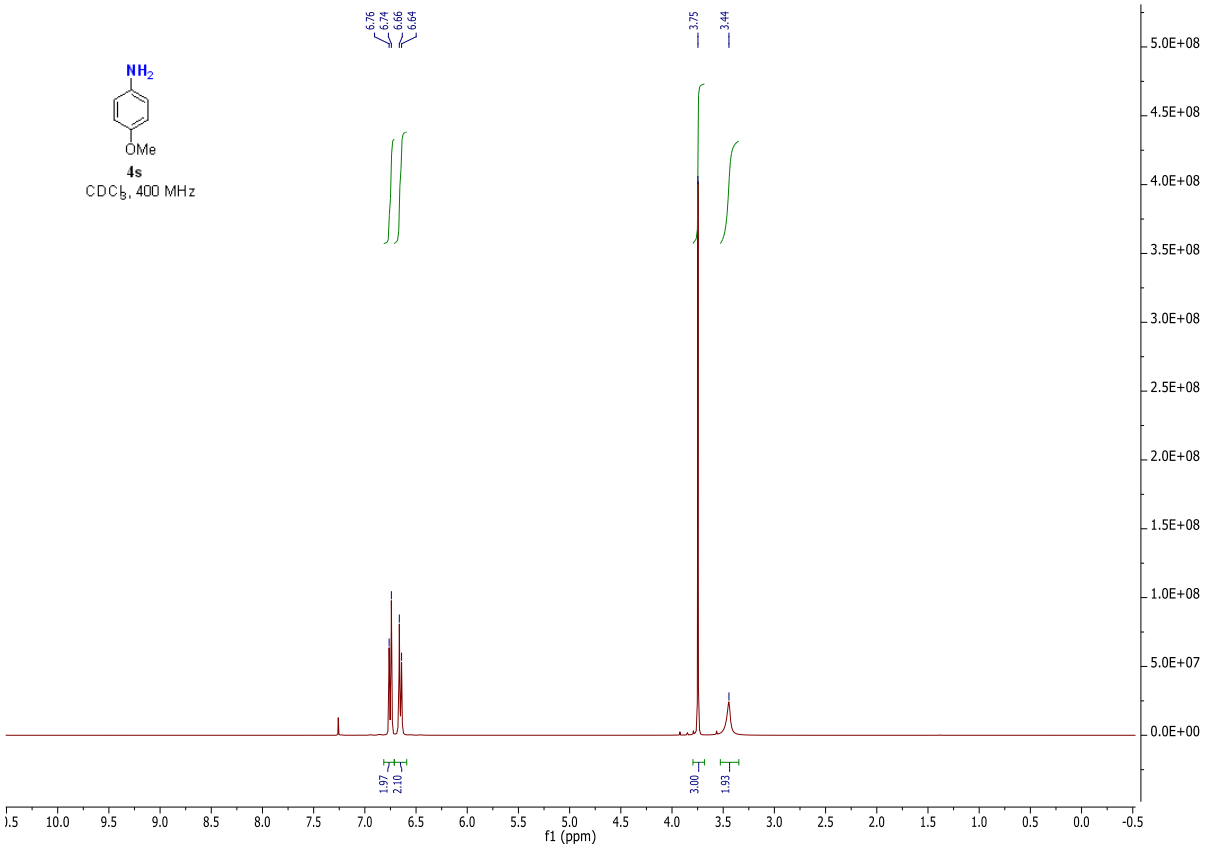

NH2
O
CDCl3, 400 MHz
4q
f1 (ppm)

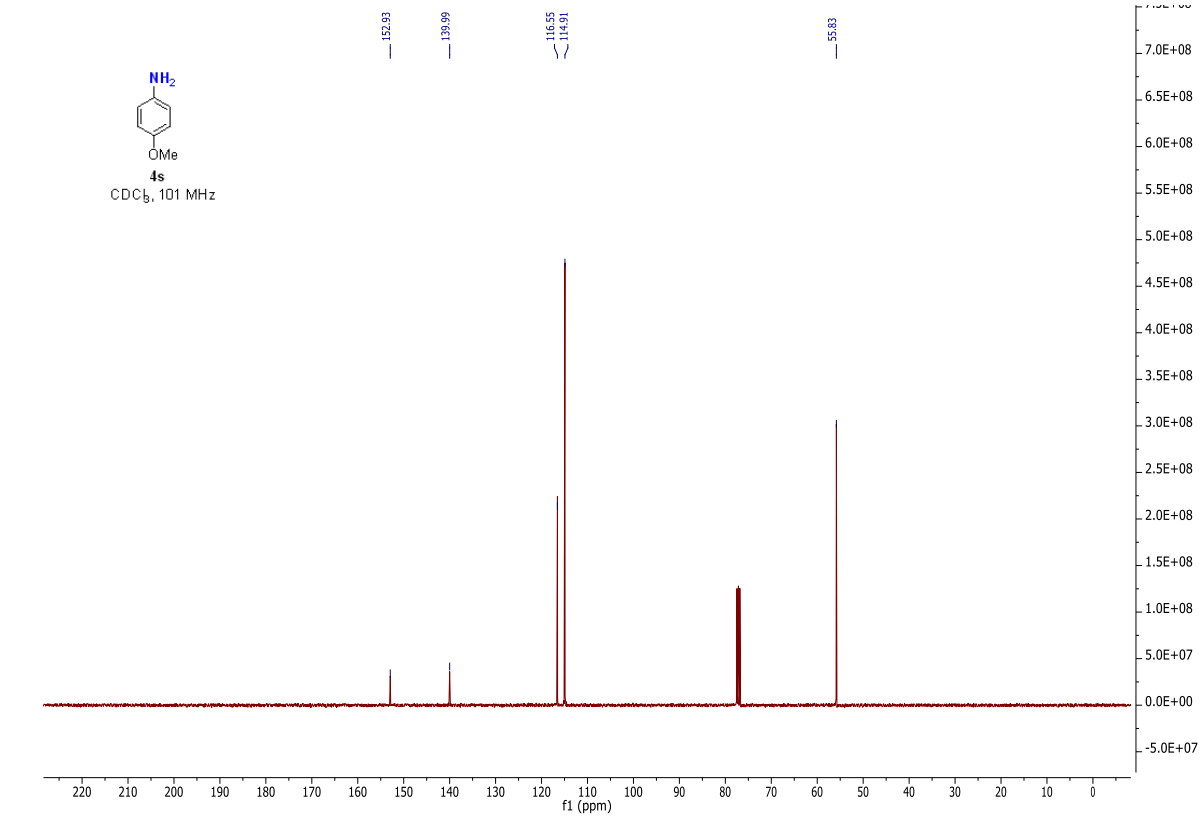

NH2
O
CDCl3, 151 MHz
4q
f1 (ppm)

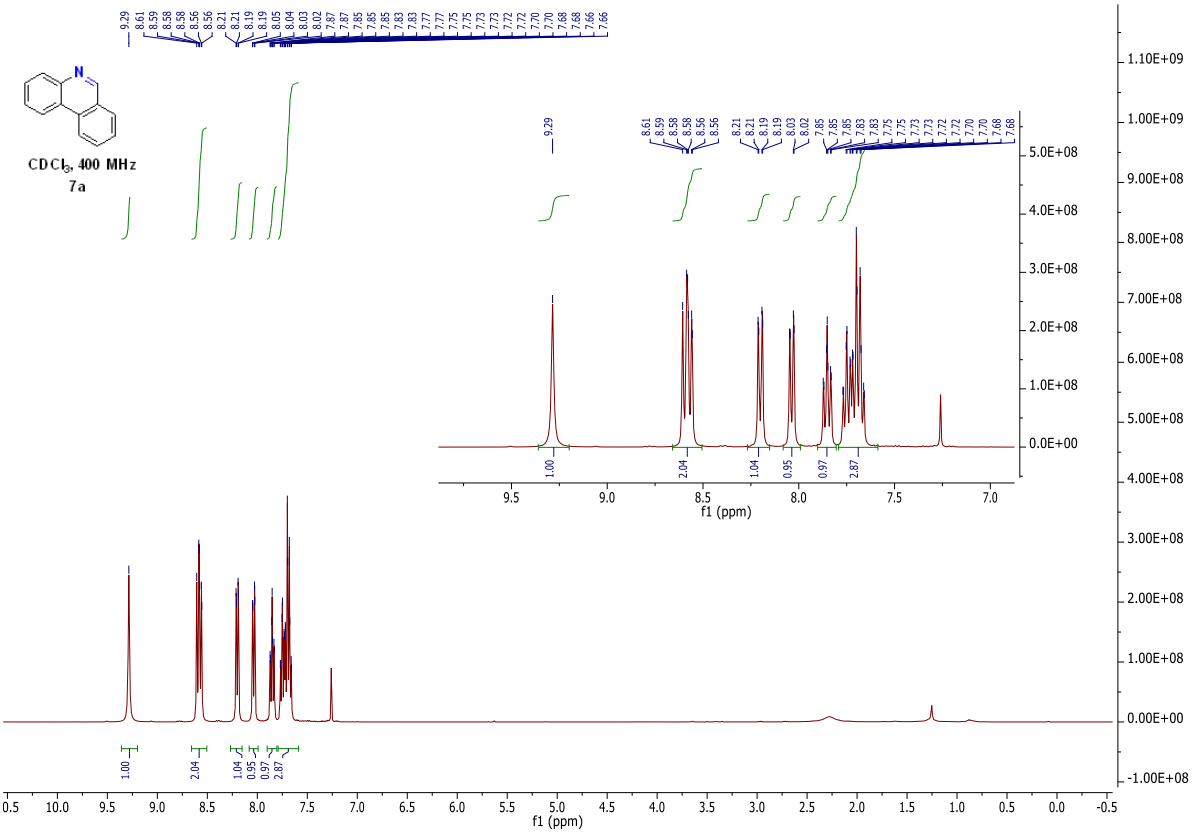

4r
CDCl3, 400 MHz
7.55
7.54
7.53
7.44
7.43
7.42
7.42
7.40
7.39
7.38
7.29
7.28
6.78
6.76
3.73
2.05
4.09
0.89
2.00
2.13
f1 (ppm)

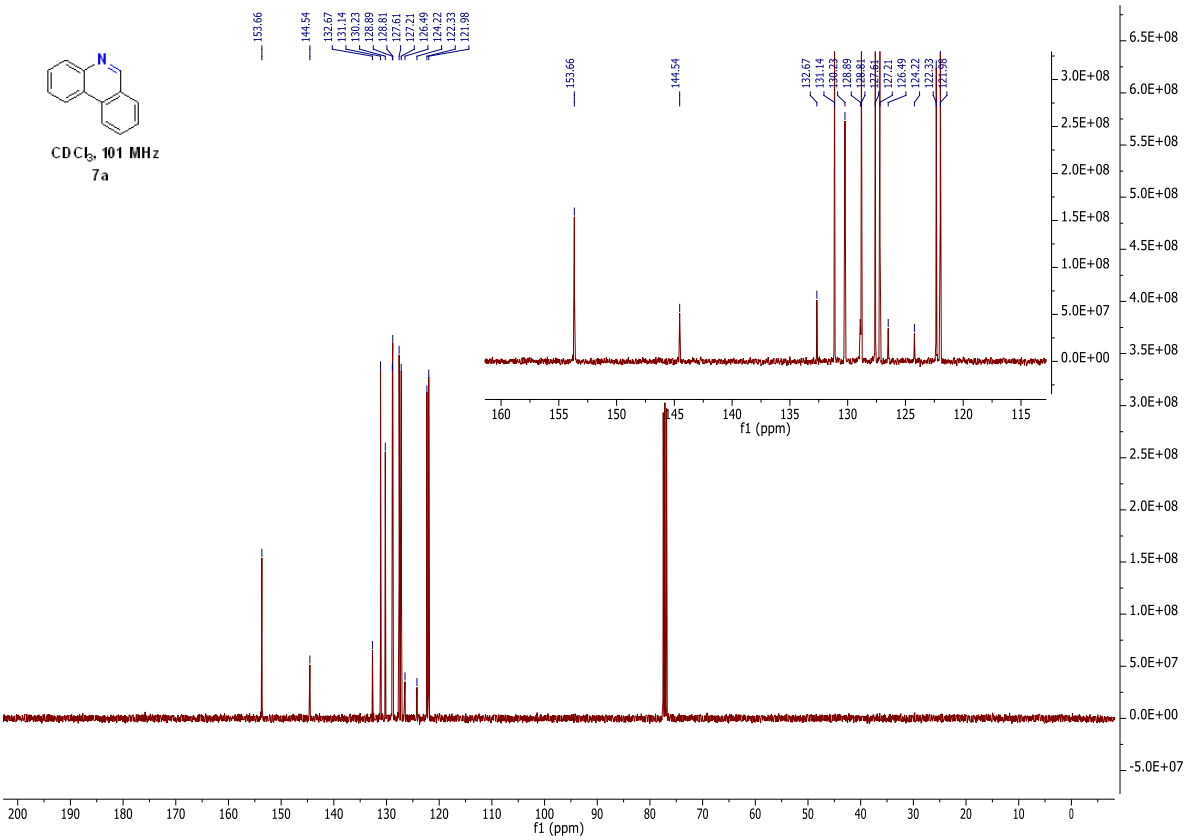

4r
CDCl3, 101 MHz
145.96
141.29
131.73
128.79
128.15
126.54
126.39
115.52
f1 (ppm)

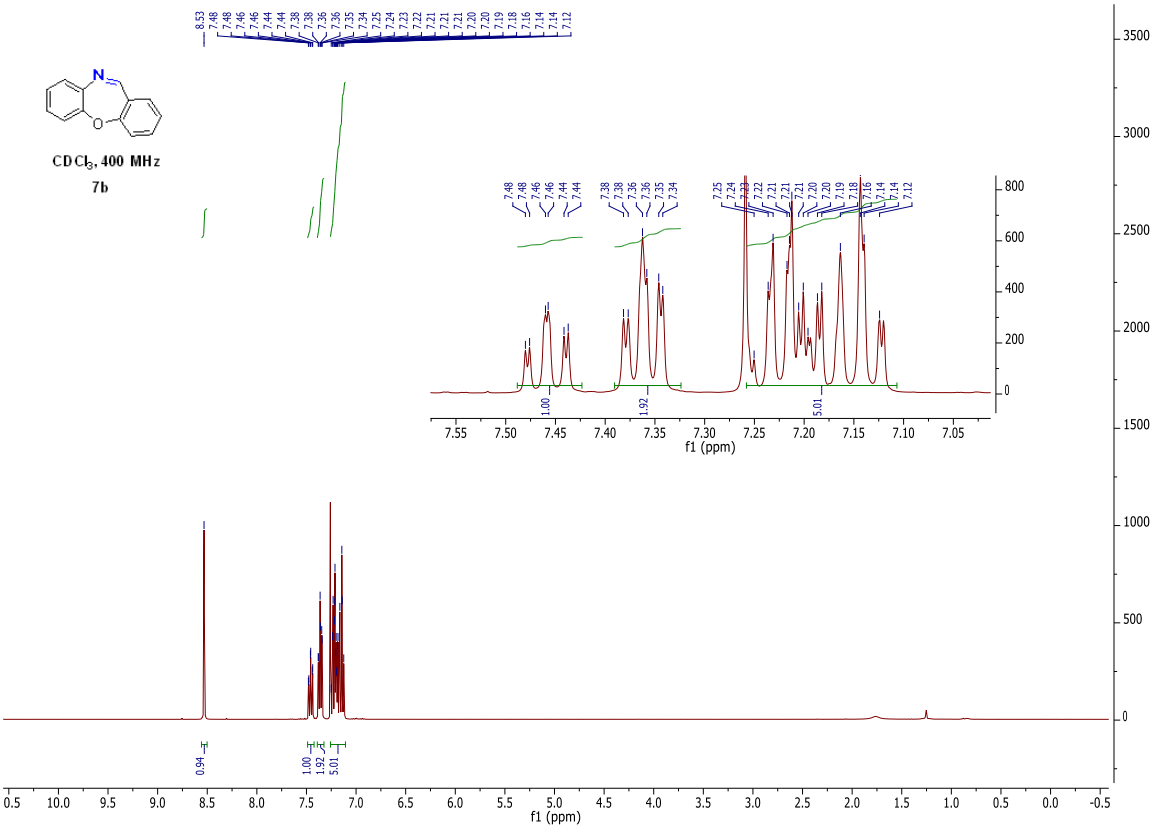

4r'
CDCl3, 400 MHz
f1 (ppm)

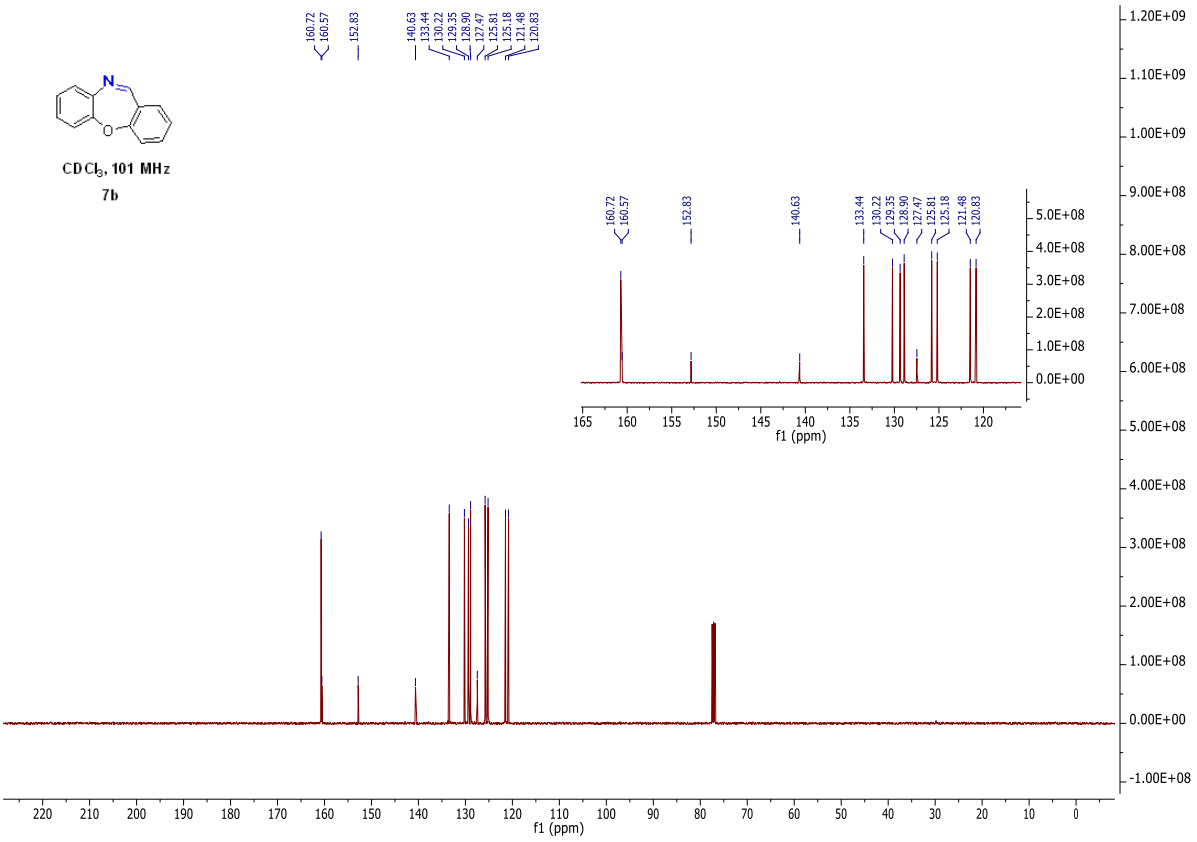

NH2
OMe
4s
CDCl3, 400 MHz
f1 (ppm)

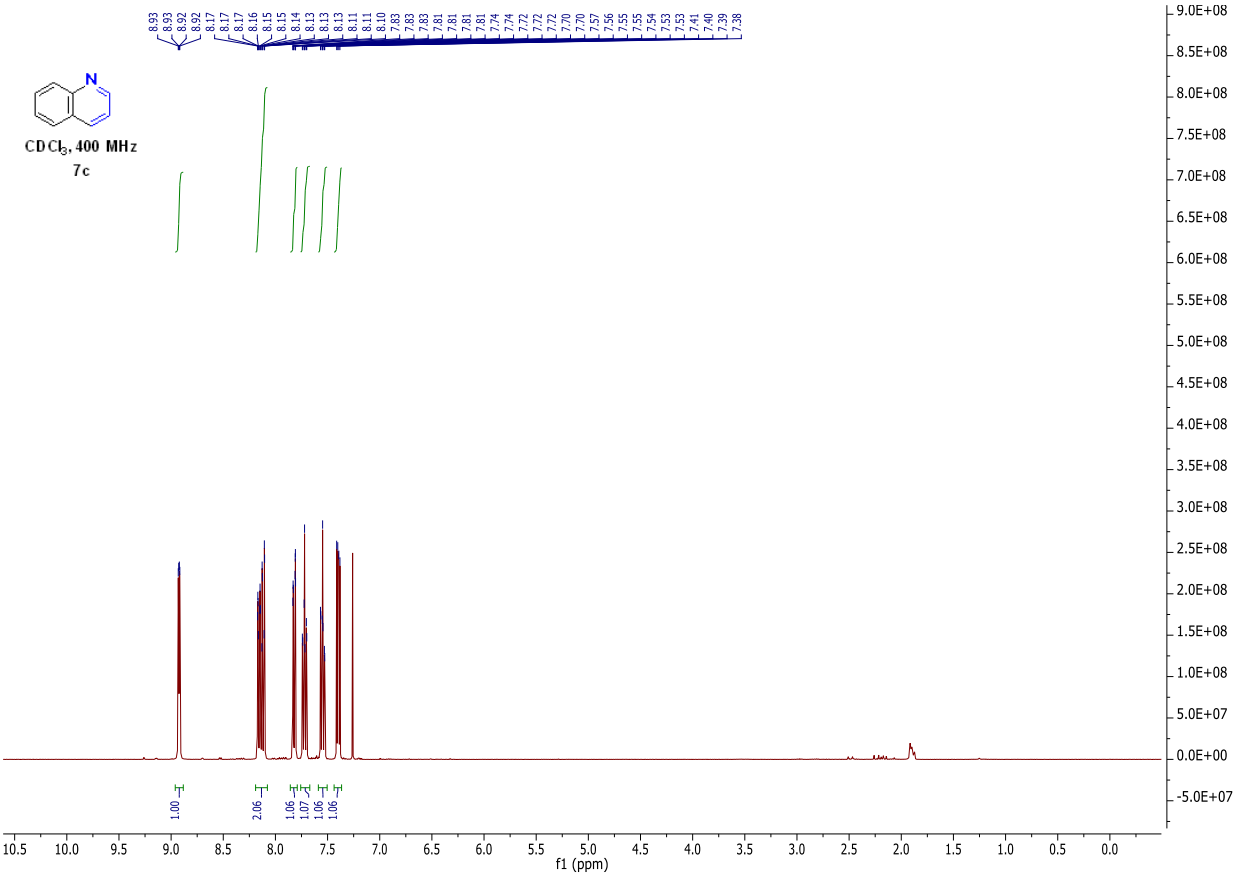

NH2
OMe
4s
CDCl3, 101 MHz
152.93
139.99
116.55
114.91
55.83
f1 (ppm)

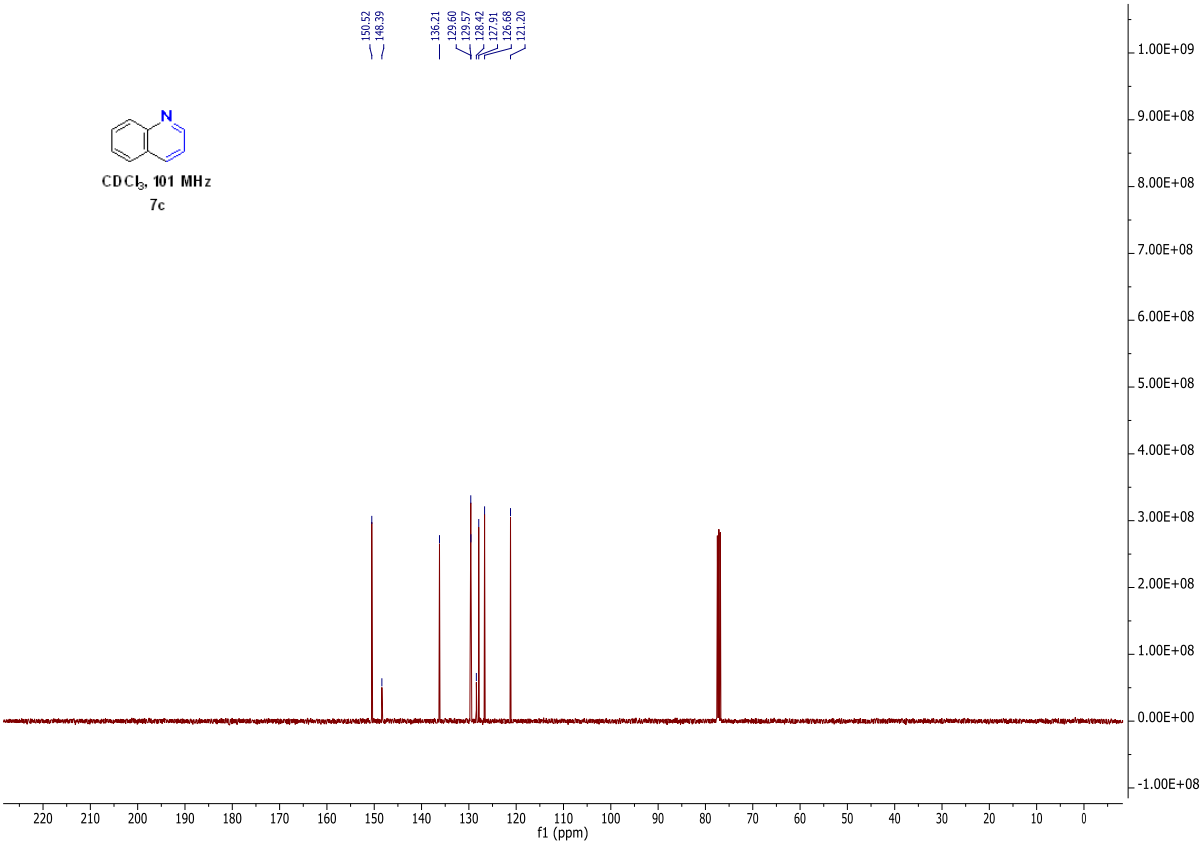

CDCl3, 400 MHz
7a
f1 (ppm)

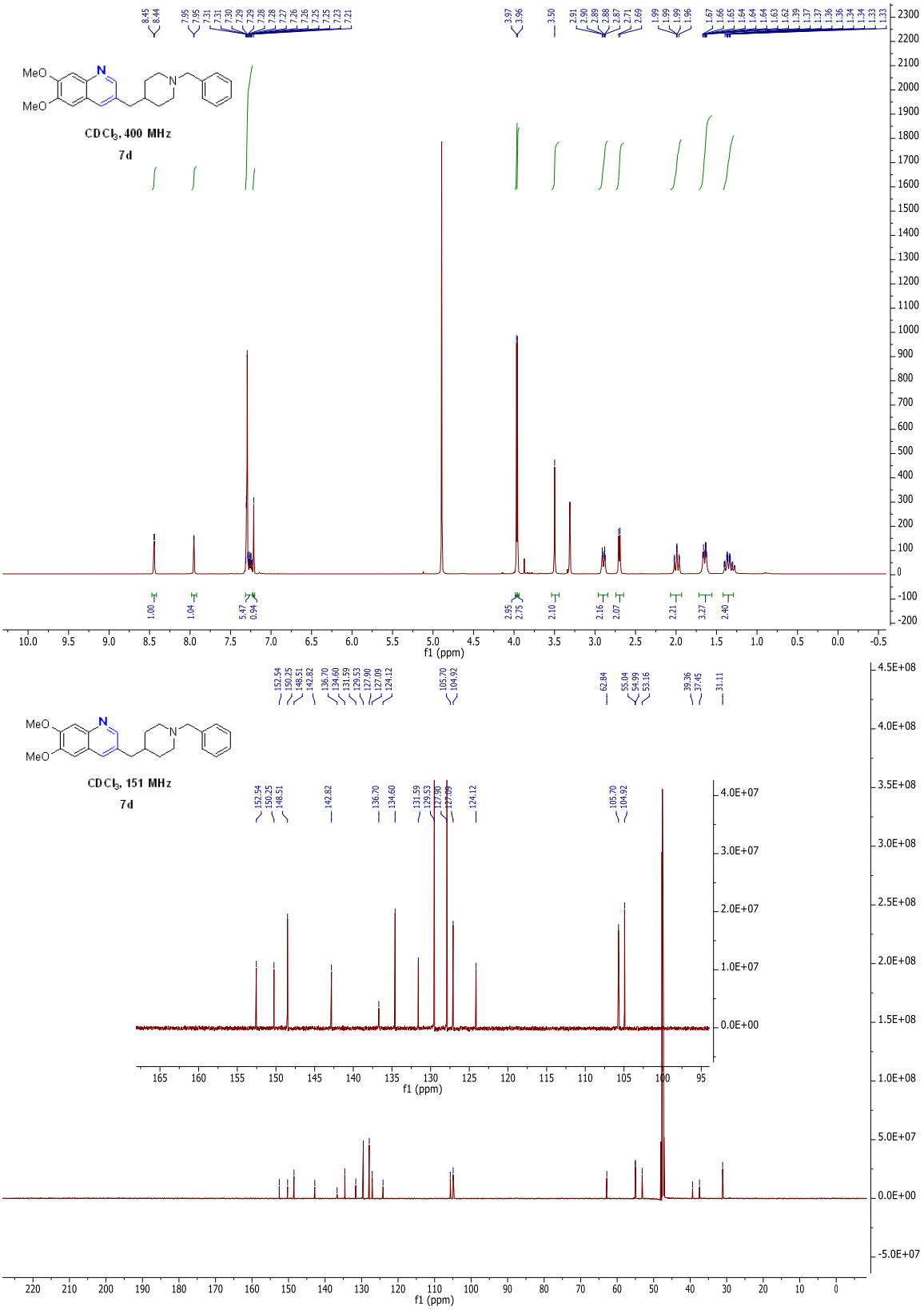

CDCl3, 101 MHz
7a
153.66
144.54
132.67
131.14
130.23
128.89
128.81
127.61
127.21
126.49
124.22
122.33
121.98
f1 (ppm)

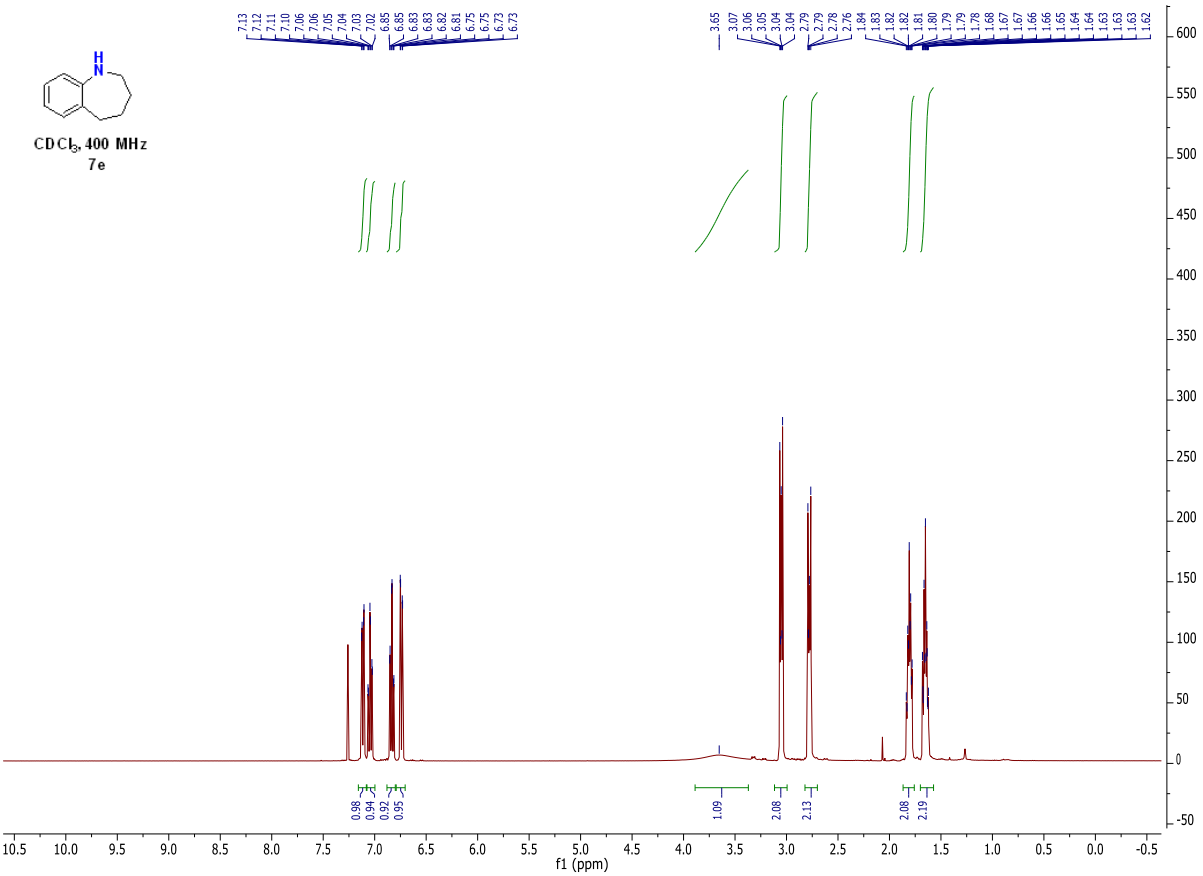

CDCl3, 400 MHz
7b
f1 (ppm)

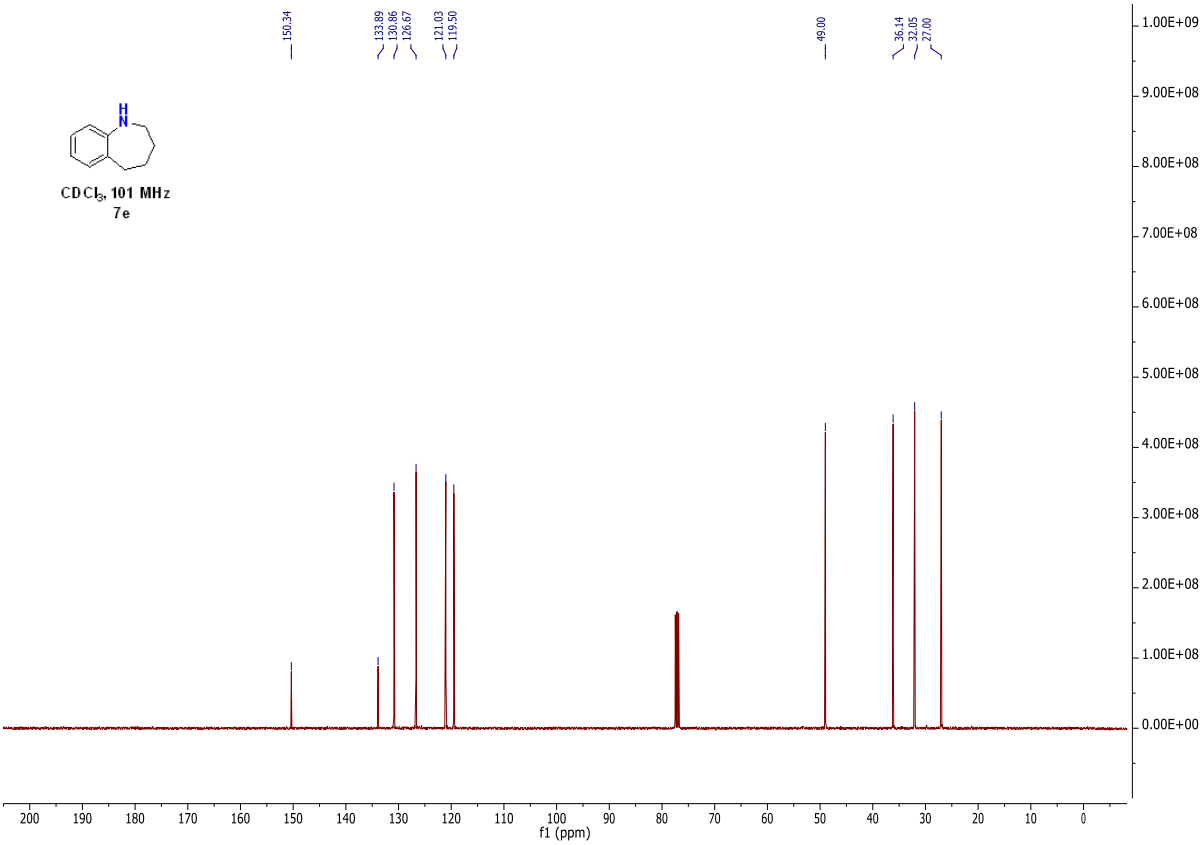

160.72
160.57
152.83
140.63
133.44
130.22
129.35
128.90
127.47
125.81
125.18
121.48
120.83
CDCl3, 101 MHz
7b
f1 (ppm)

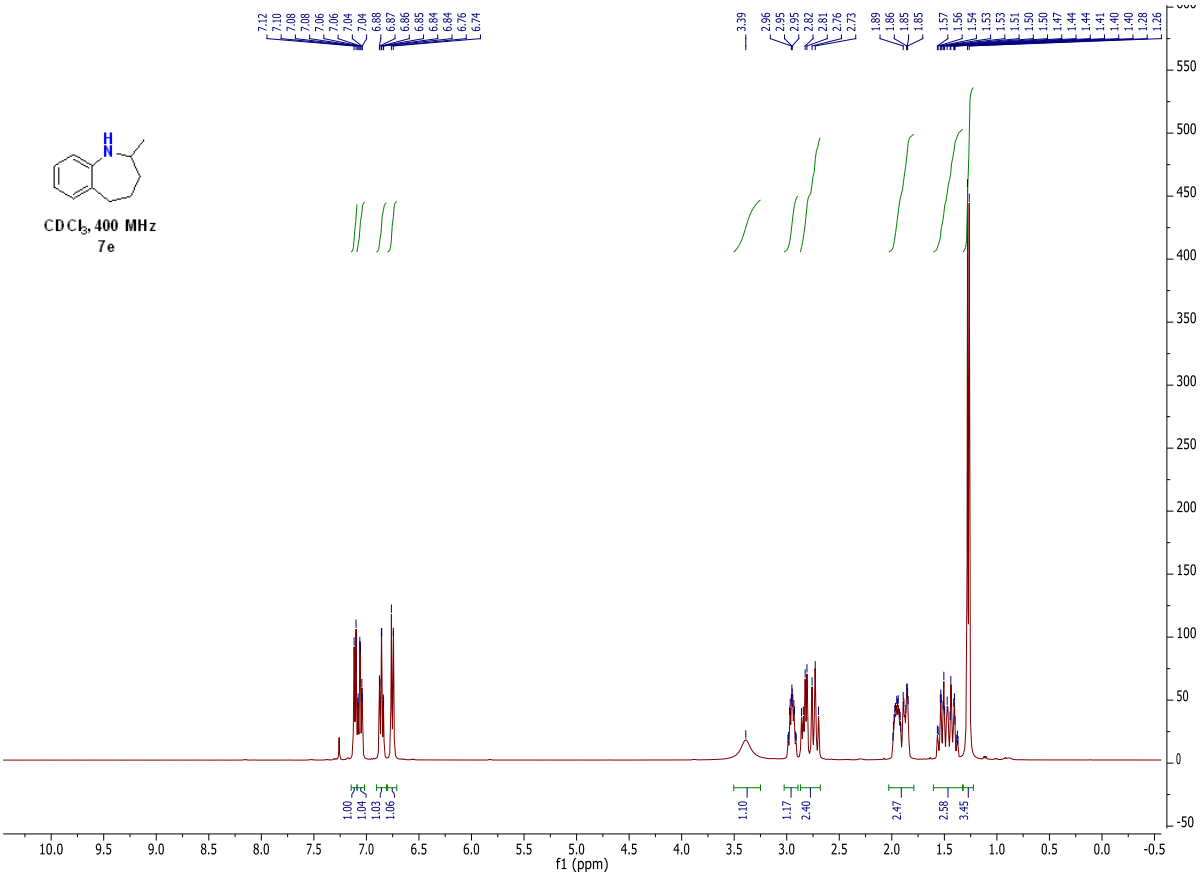

CDCl3, 400 MHz
7c
f1 (ppm)

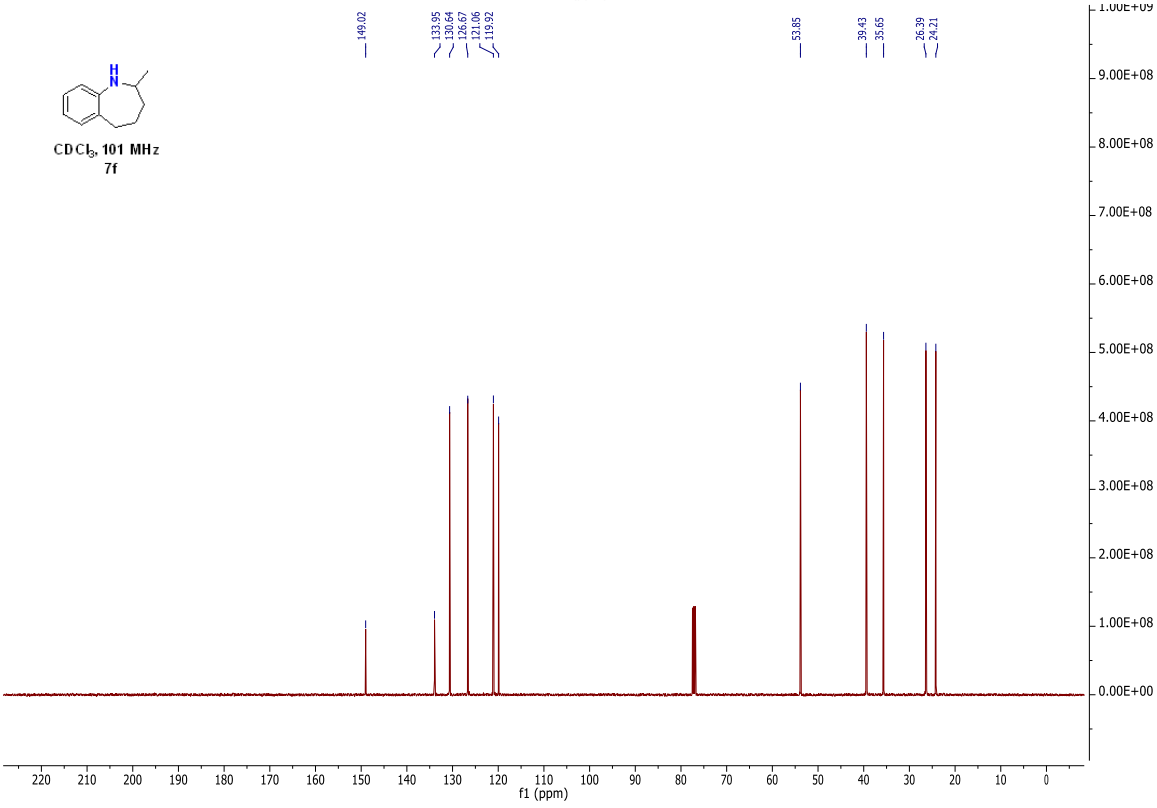

CDCl3, 101 MHz
7c
f1 (ppm)

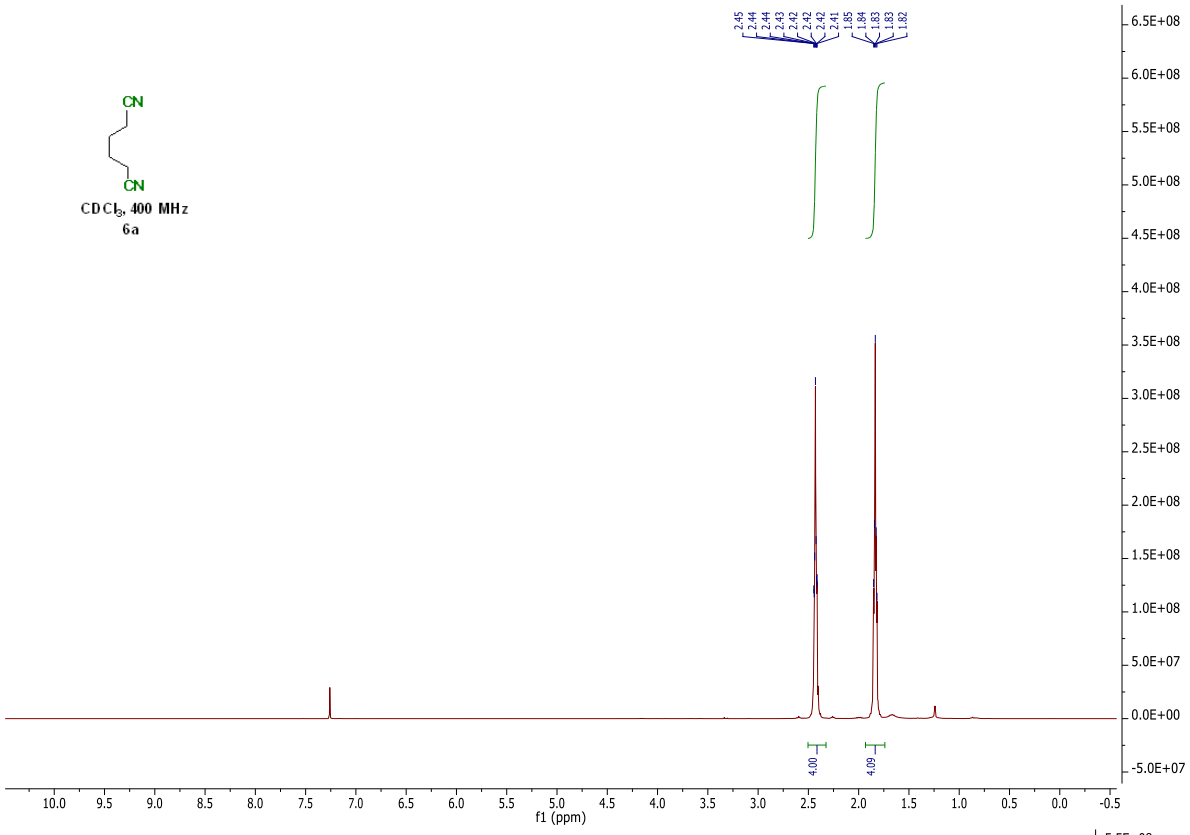

MeO
MeO
N
CDCl3, 400 MHz
7d
f1 (ppm)
CDCl3, 151 MHz
7d
f1 (ppm)

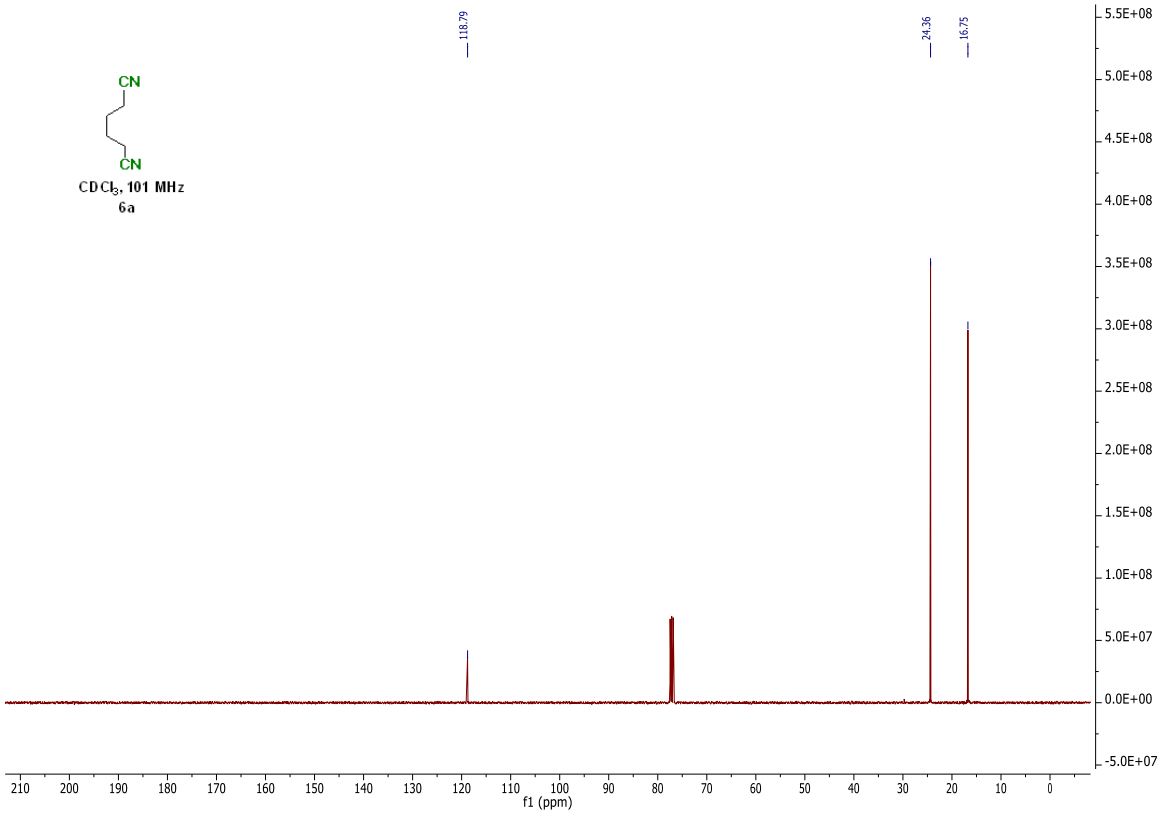

CDCl3, 400 MHz
7e
f1 (ppm)

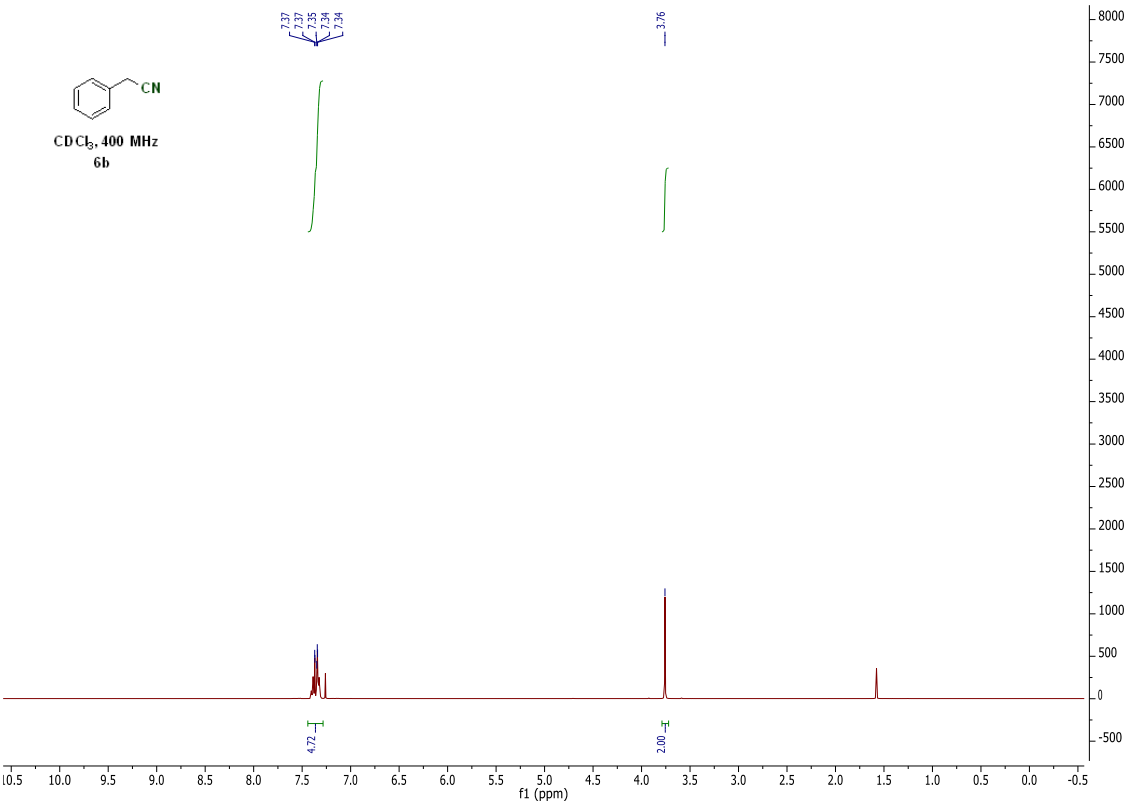

CDCl3, 101 MHz
7e
f1 (ppm)

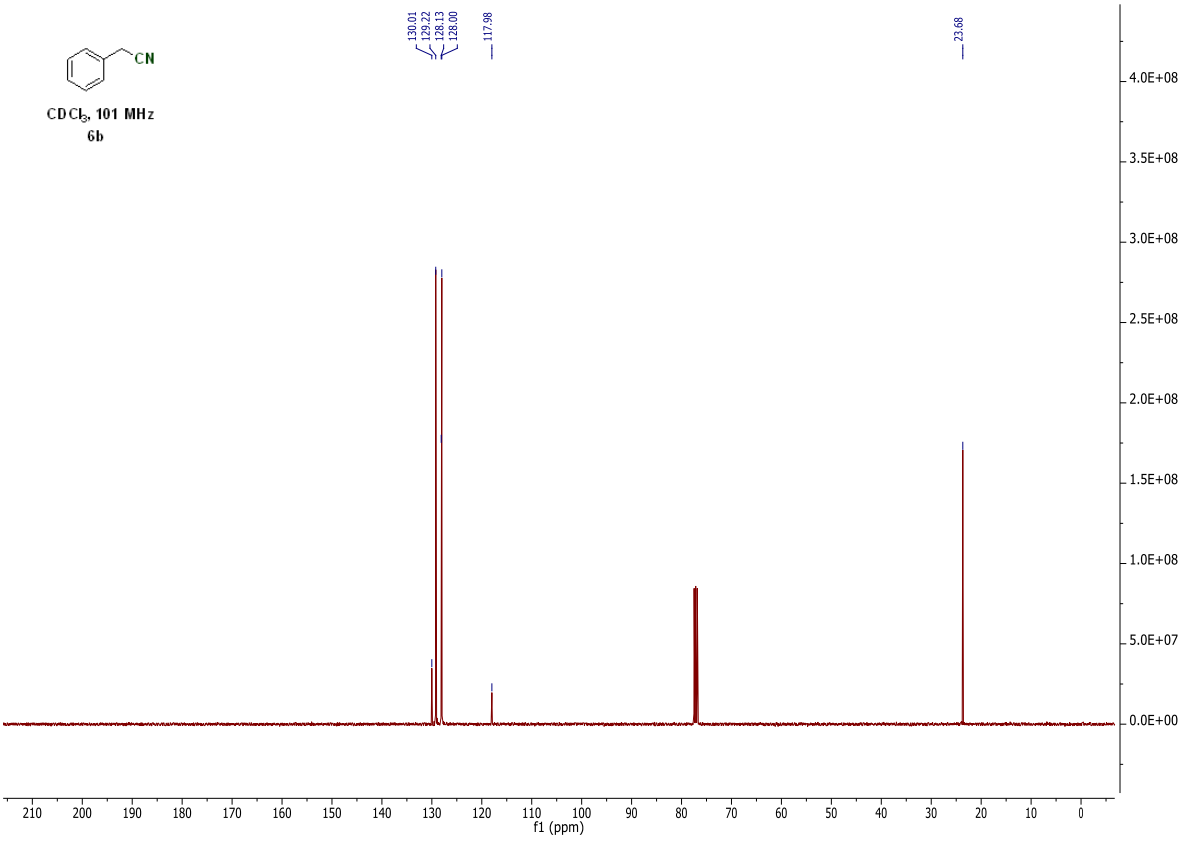

CDCl3, 400 MHz
7e
f1 (ppm)

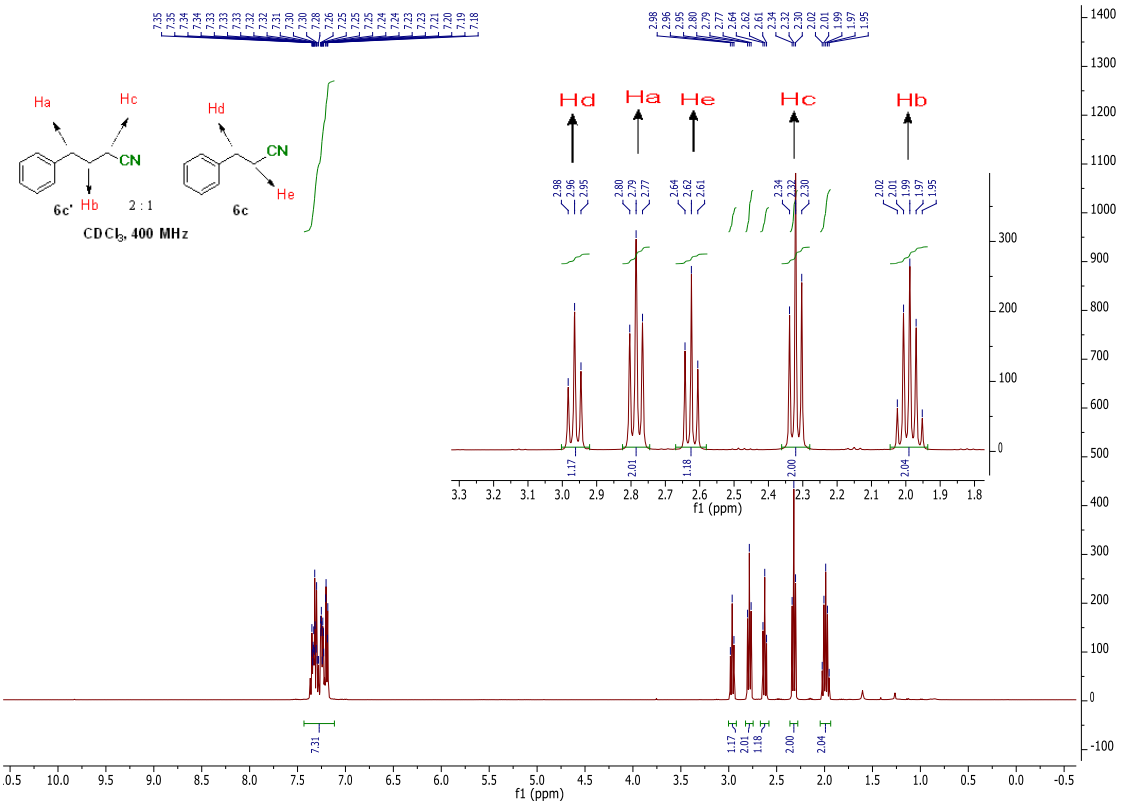

CDCl3, 101 MHz
7f
f1 (ppm)

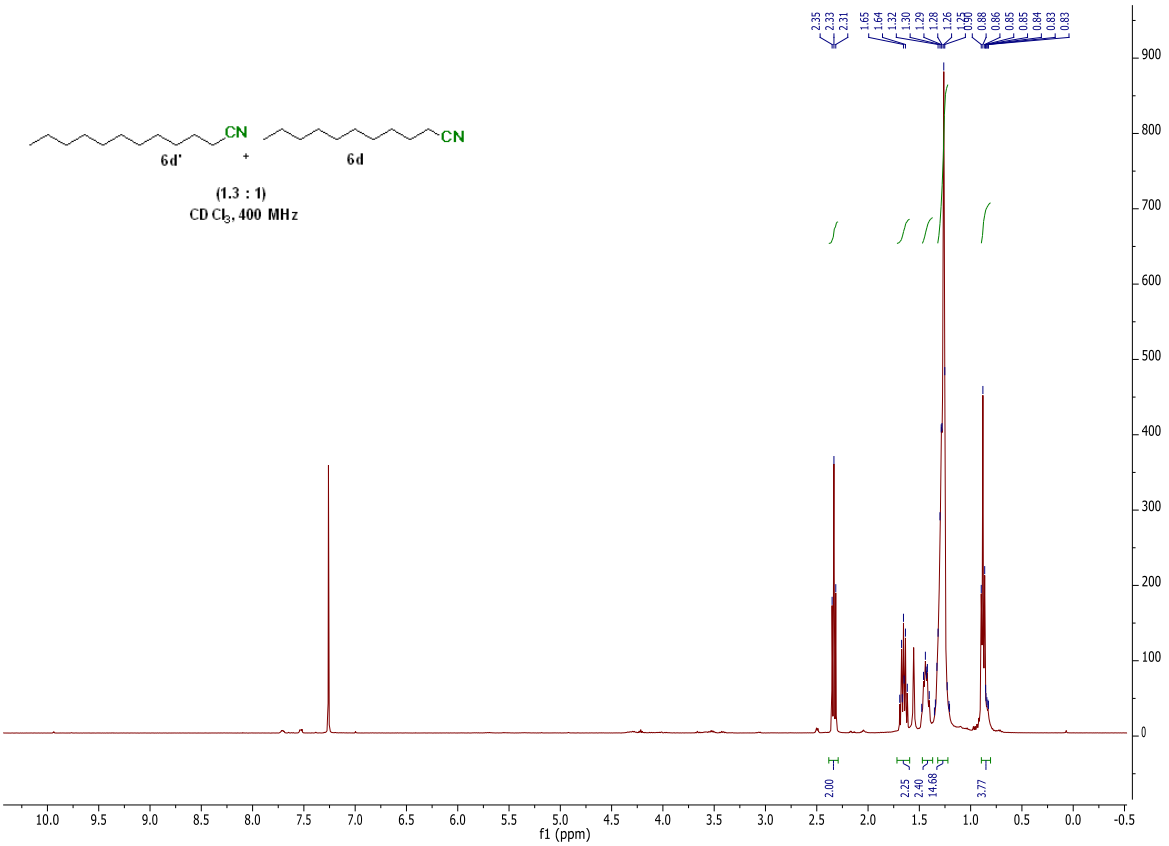

CN
CN
CDCl3, 400 MHz
6a
2.45
2.44
2.44
2.43
2.42
2.42
2.42
2.41
1.85
1.84
1.83
1.83
1.82
4.00
4.09
f1 (ppm)

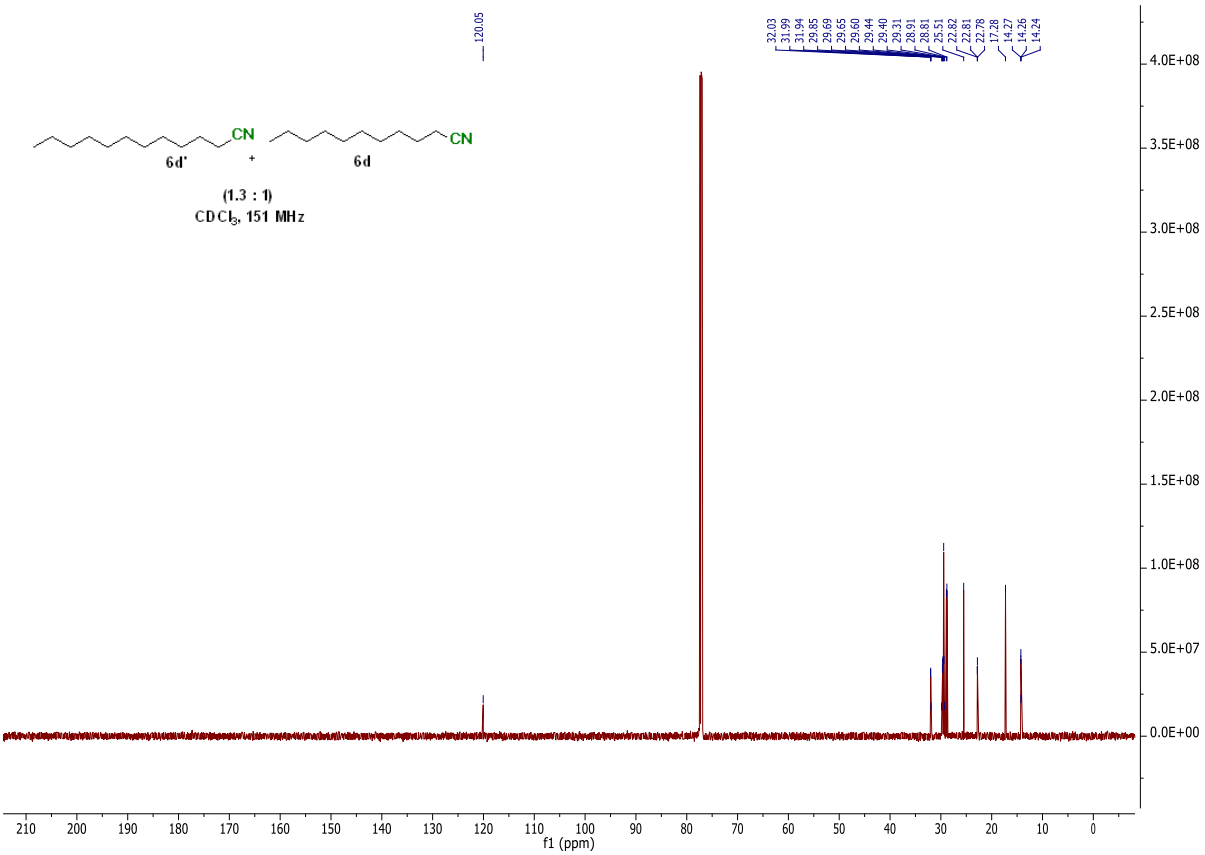

CN
CN
CDCl3, 101 MHz
6a
118.79
24.36
16.75
f1 (ppm)

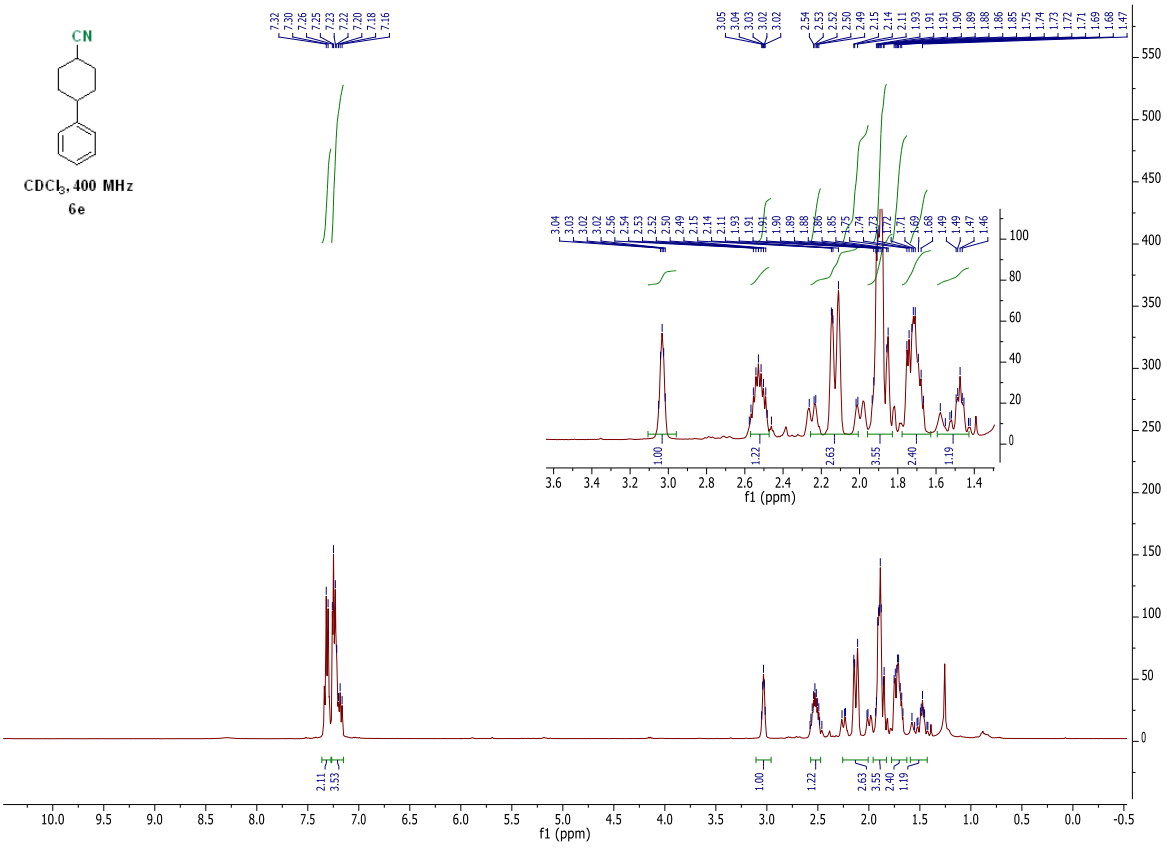

CN
CDCl3, 400 MHz
6b
7.37
7.37
7.35
7.34
7.34
3.76
4.72
2.00
f1 (ppm)

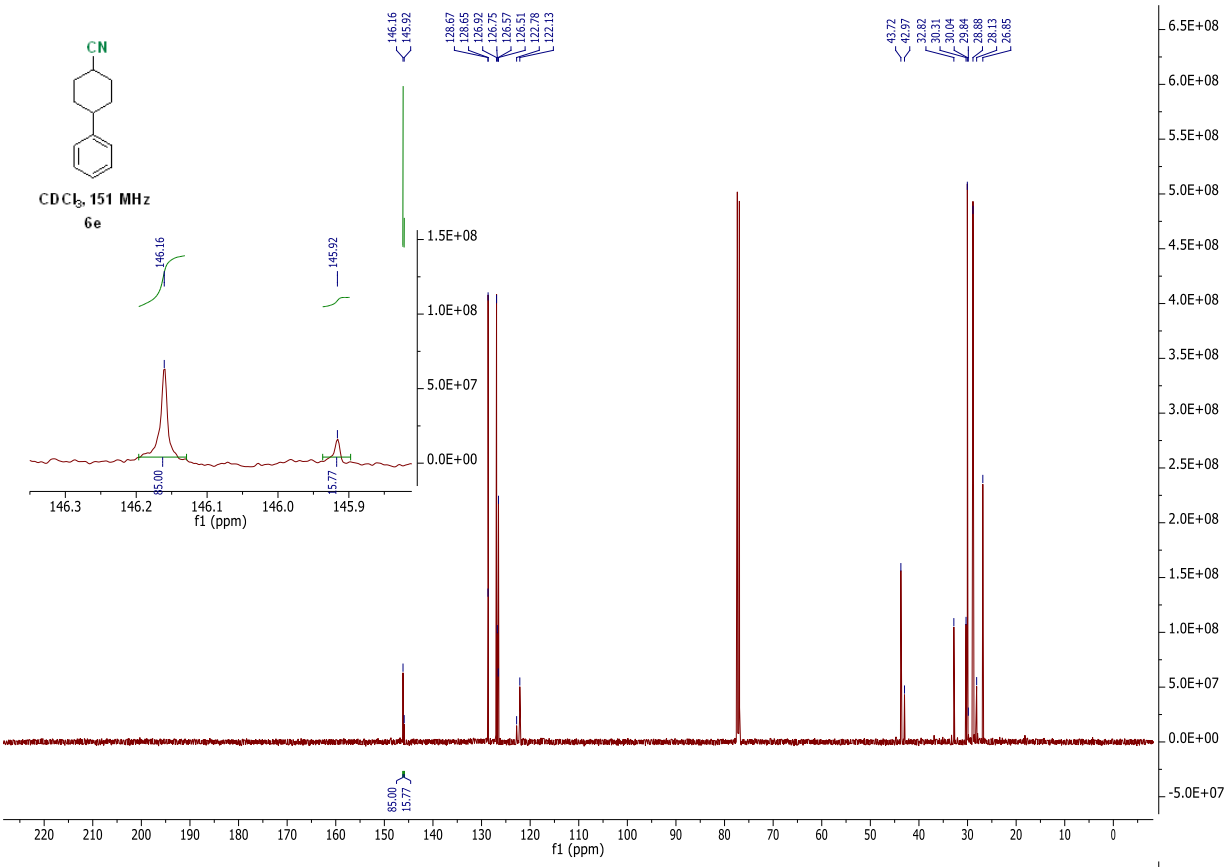

CN
CDCl3, 101 MHz
6b
130.01
129.22
128.13
128.00
117.98
23.68
f1 (ppm)

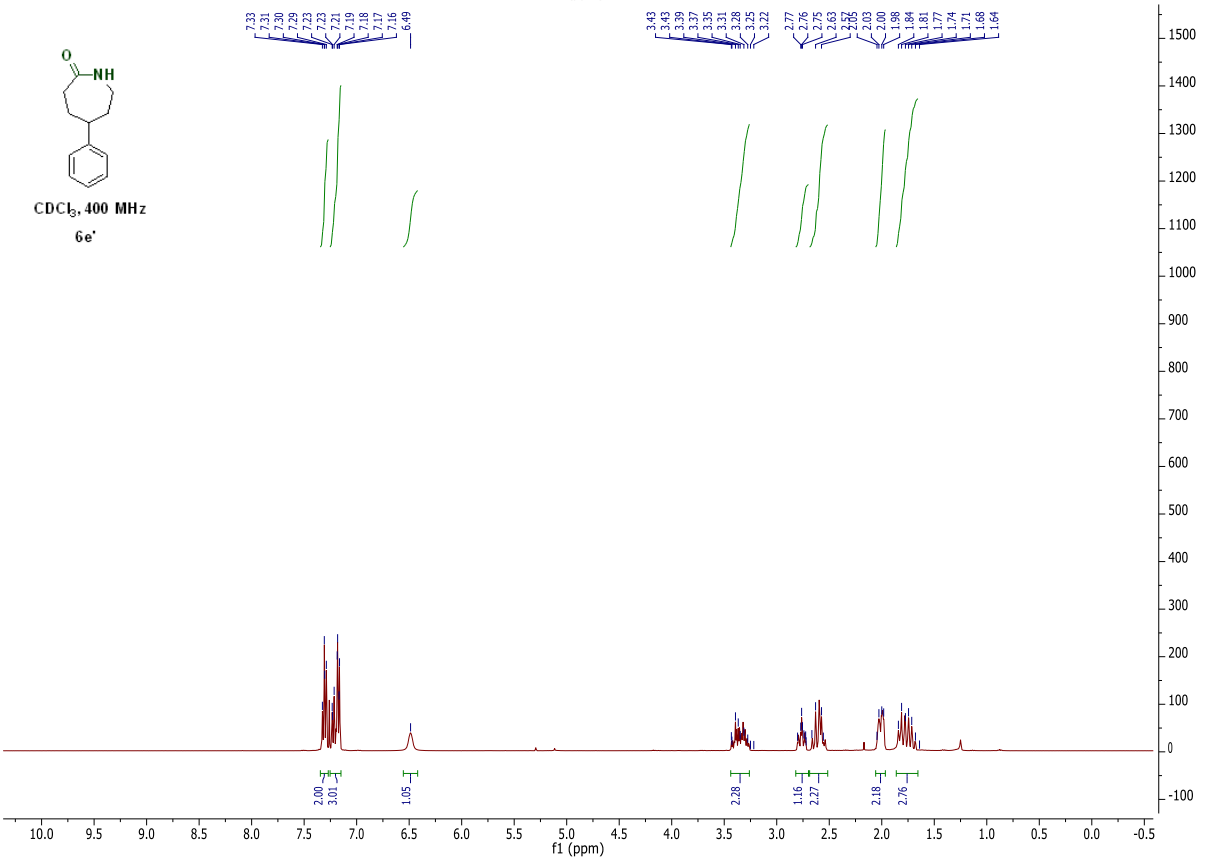

Ha
Hc
CN
Hb
6c'
2 : 1
Hd
CN
He
6c
CDCl3, 400 MHz
Hd
Ha
He
Hc
Hb
f1 (ppm)
f1 (ppm)

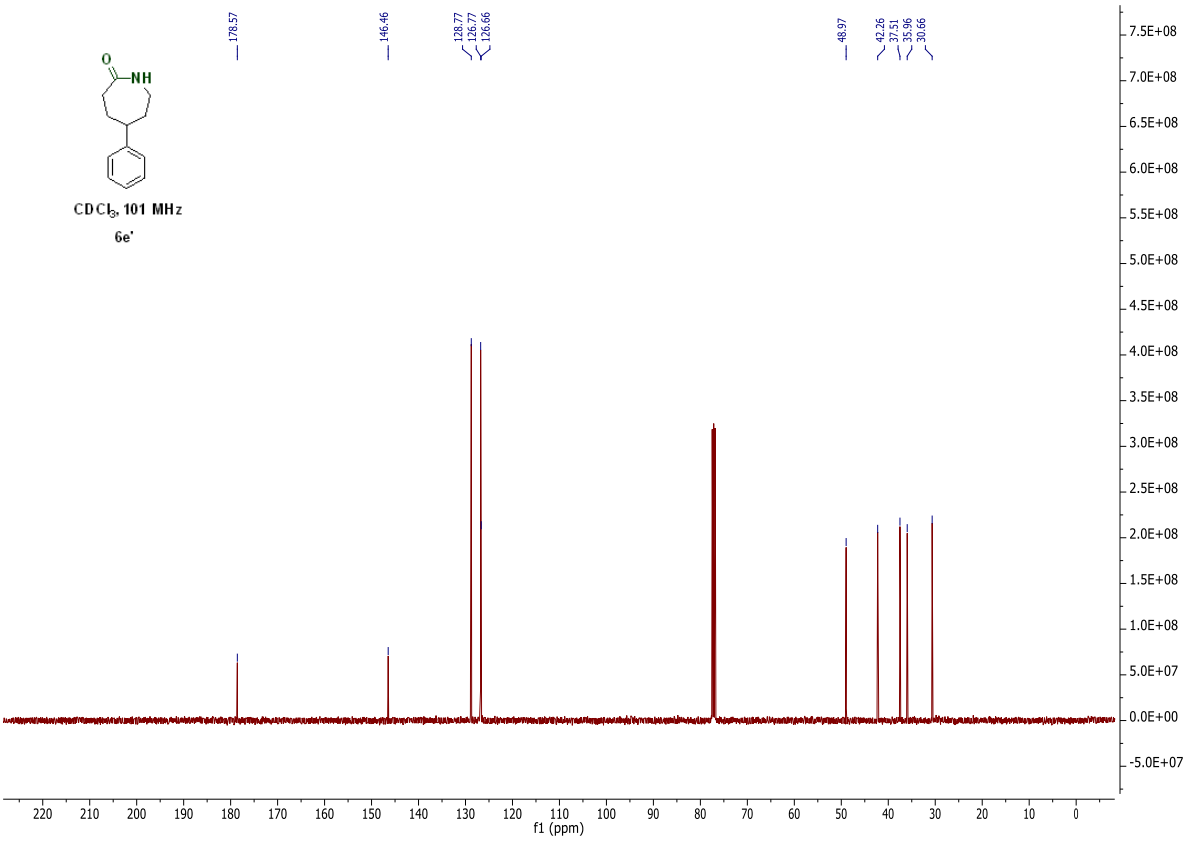

CN
6d'
+
CN
6d
(1.3 : 1)
CDCl3, 400 MHz
f1 (ppm)

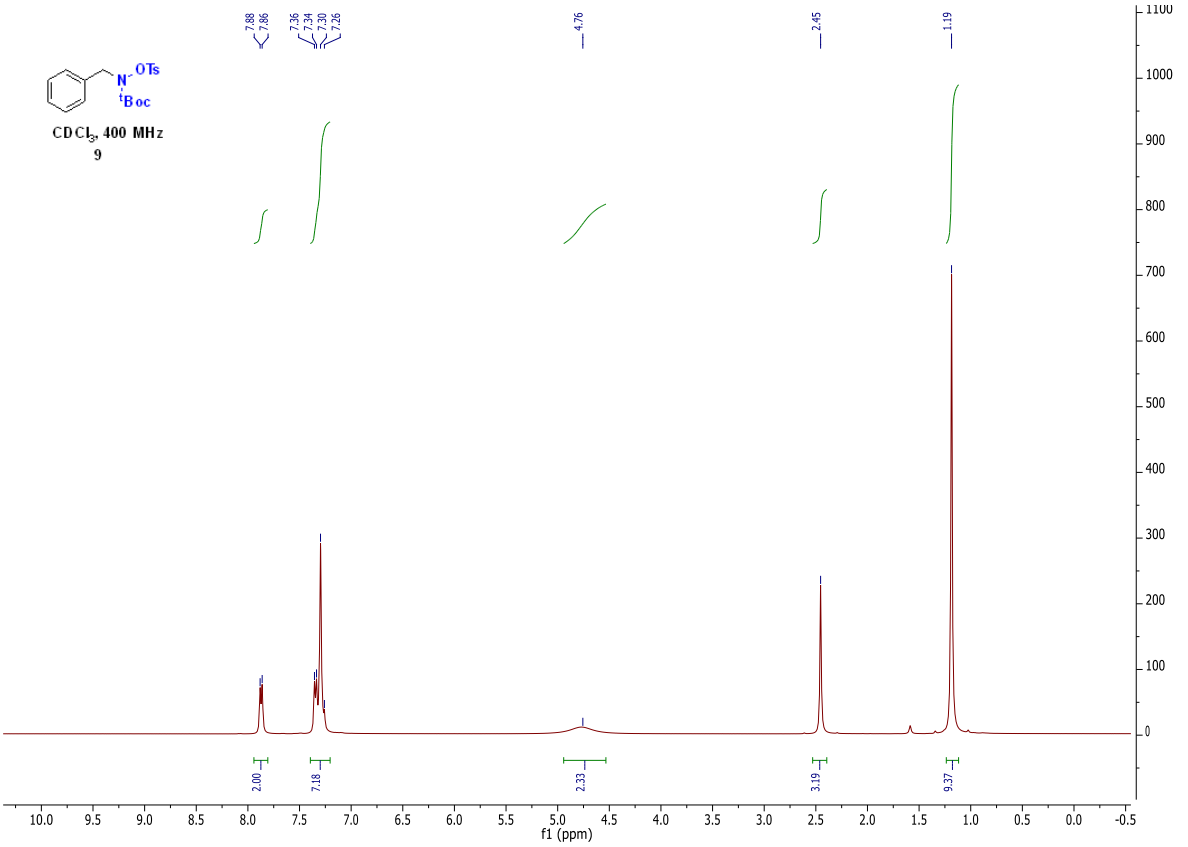

CN
6d'
+
CN
6d
(1.3 : 1)
CDCl3, 151 MHz
f1 (ppm)

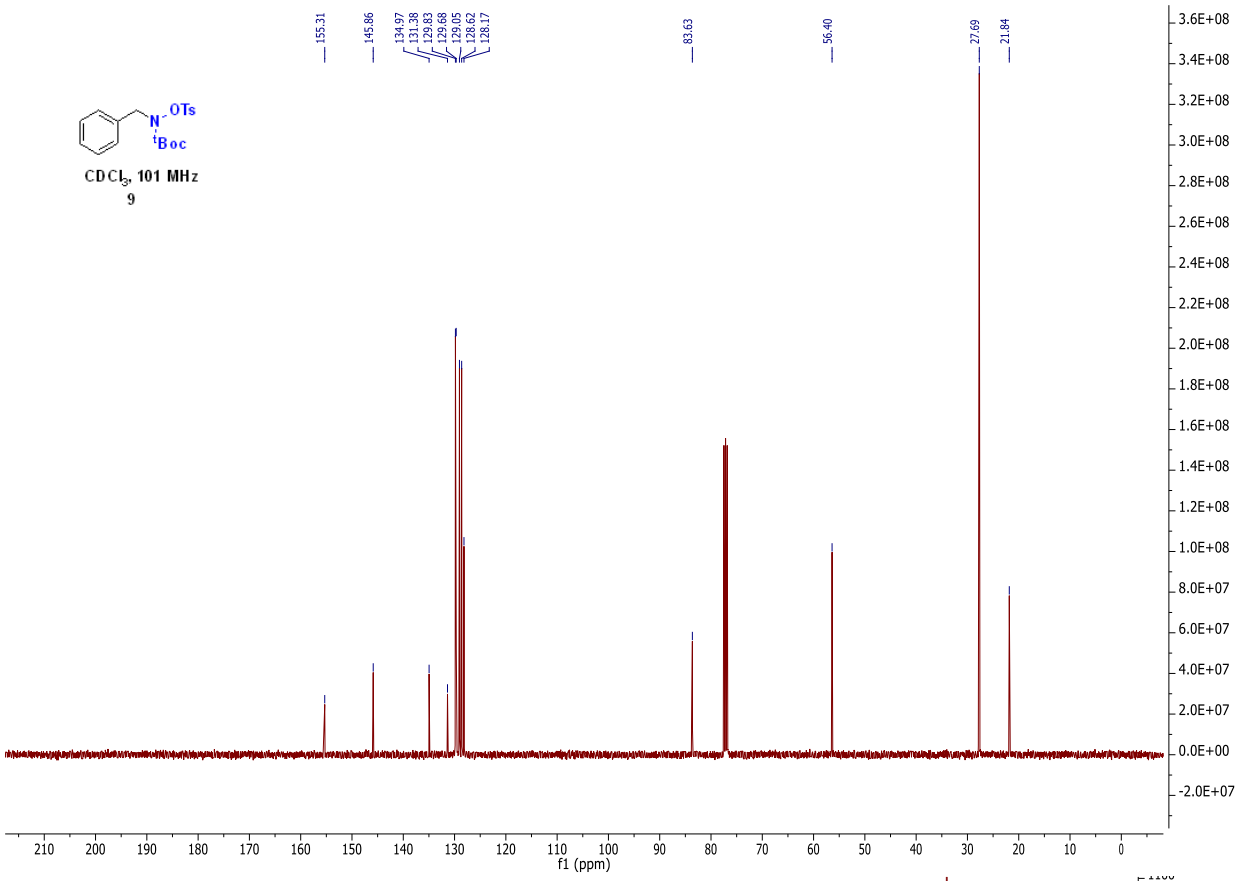

CN
CDCl3, 400 MHz
6e
f1 (ppm)

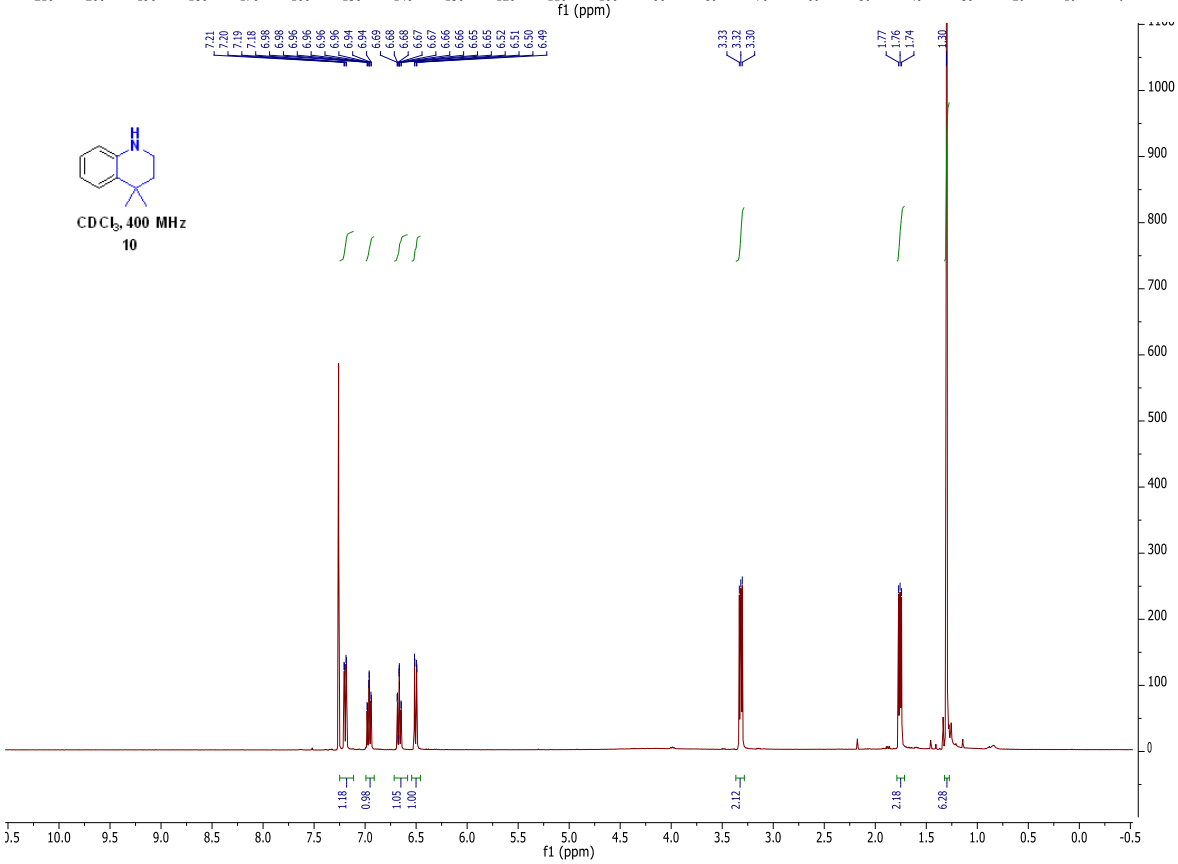

CN
CDCl3, 151 MHz
6e
f1 (ppm)

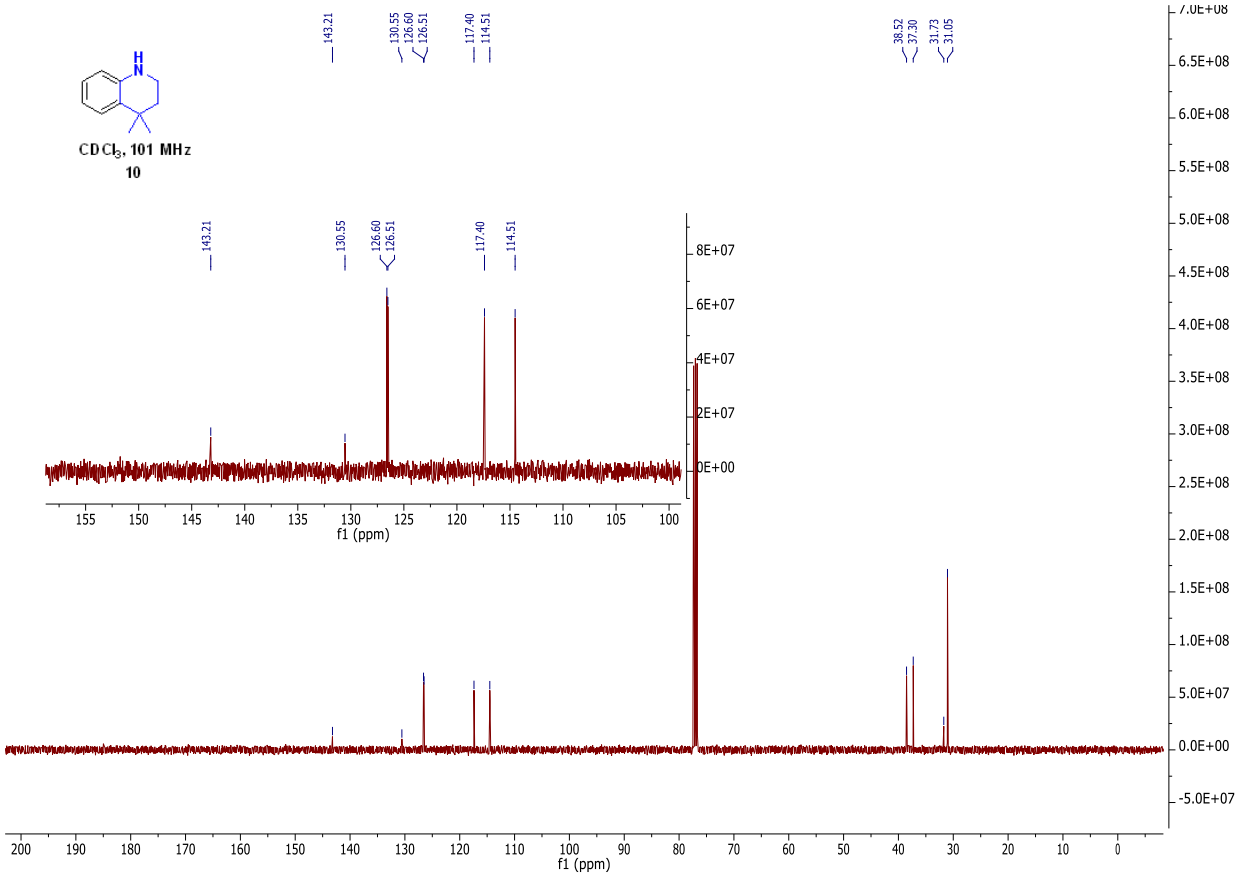

O
NH
CDCl3, 400 MHz
6e'
f1 (ppm)

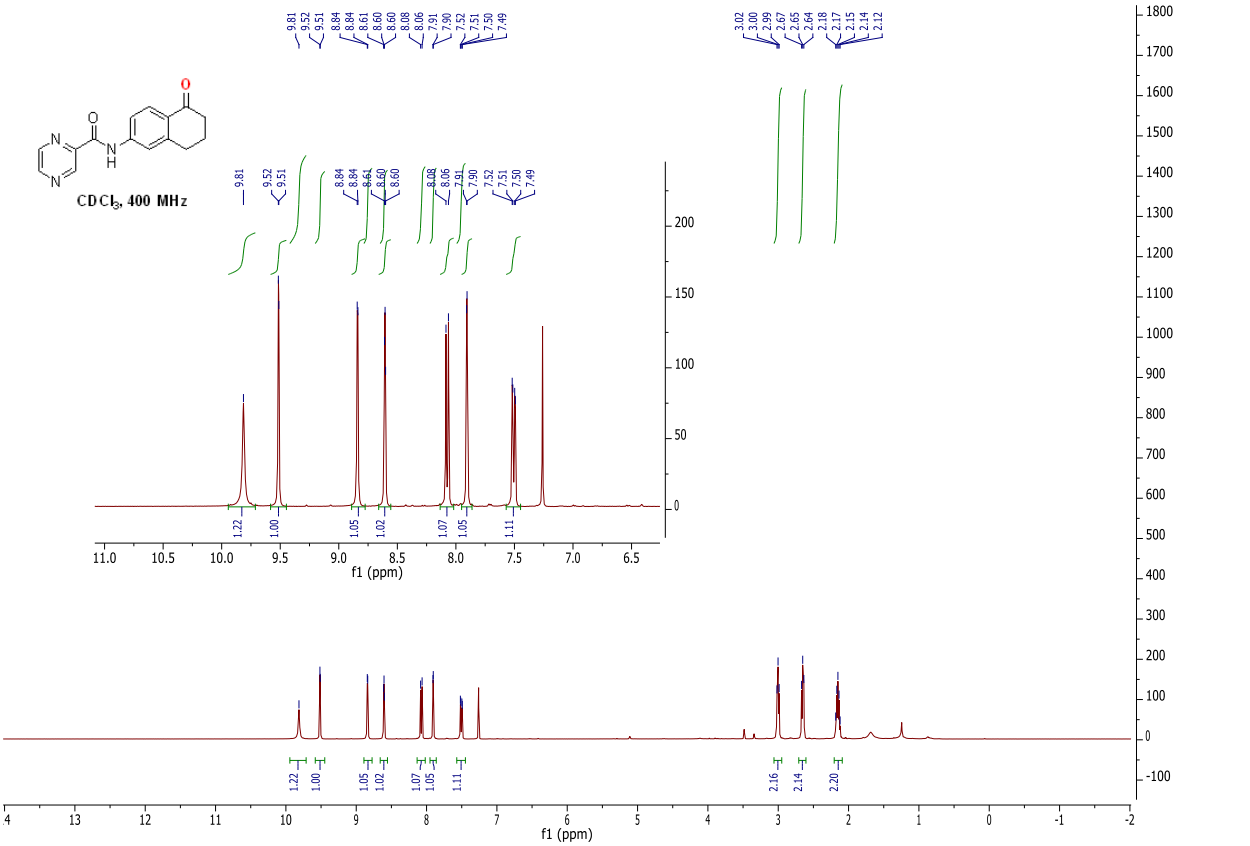

178.57
146.46
128.77
126.77
126.66
48.97
42.26
37.51
35.96
30.66
CDCl3, 101 MHz
6e'
f1 (ppm)

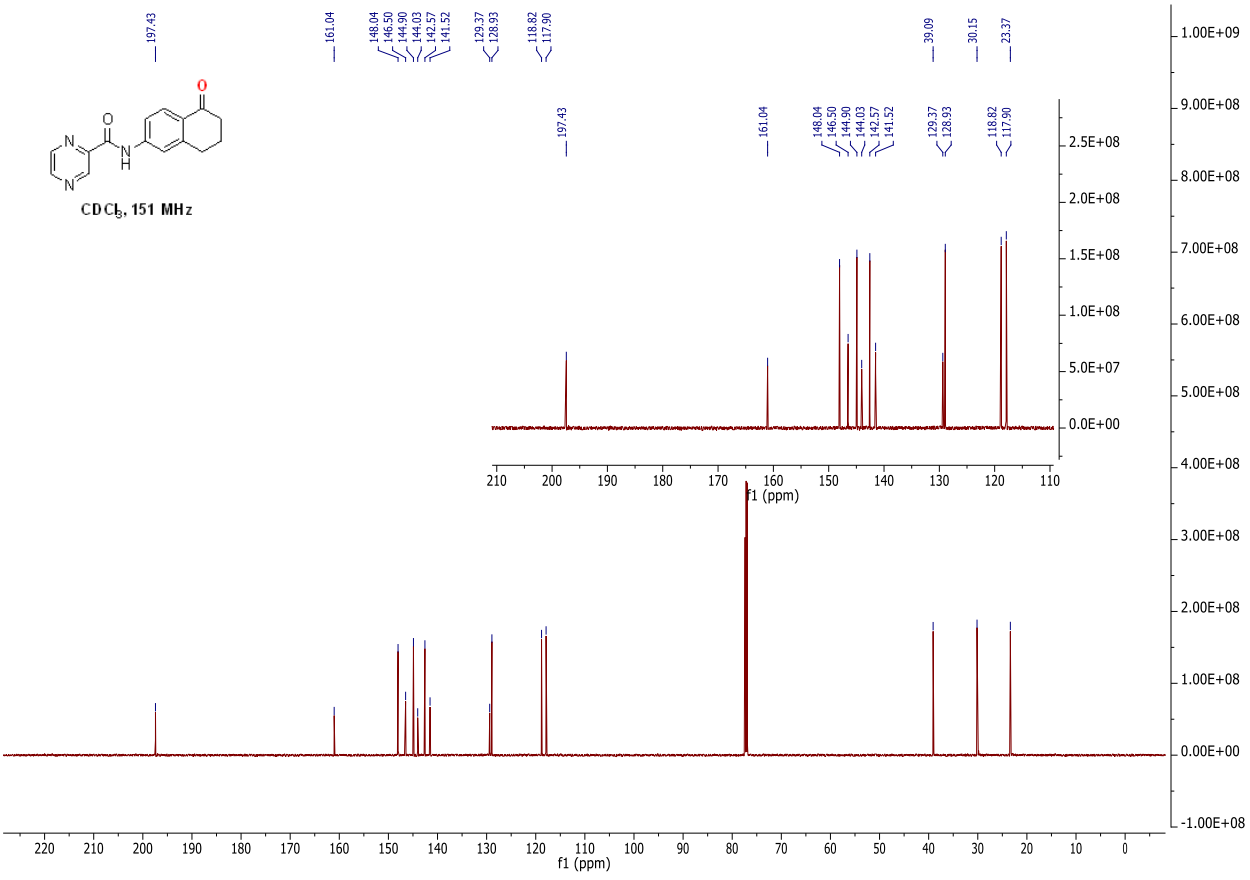

7.88
7.86
7.36
7.34
7.30
7.26
4.76
2.45
1.19
OTs
Boc
CDCl3, 400 MHz
9
2.00
7.18
2.33
3.19
9.37
f1 (ppm)

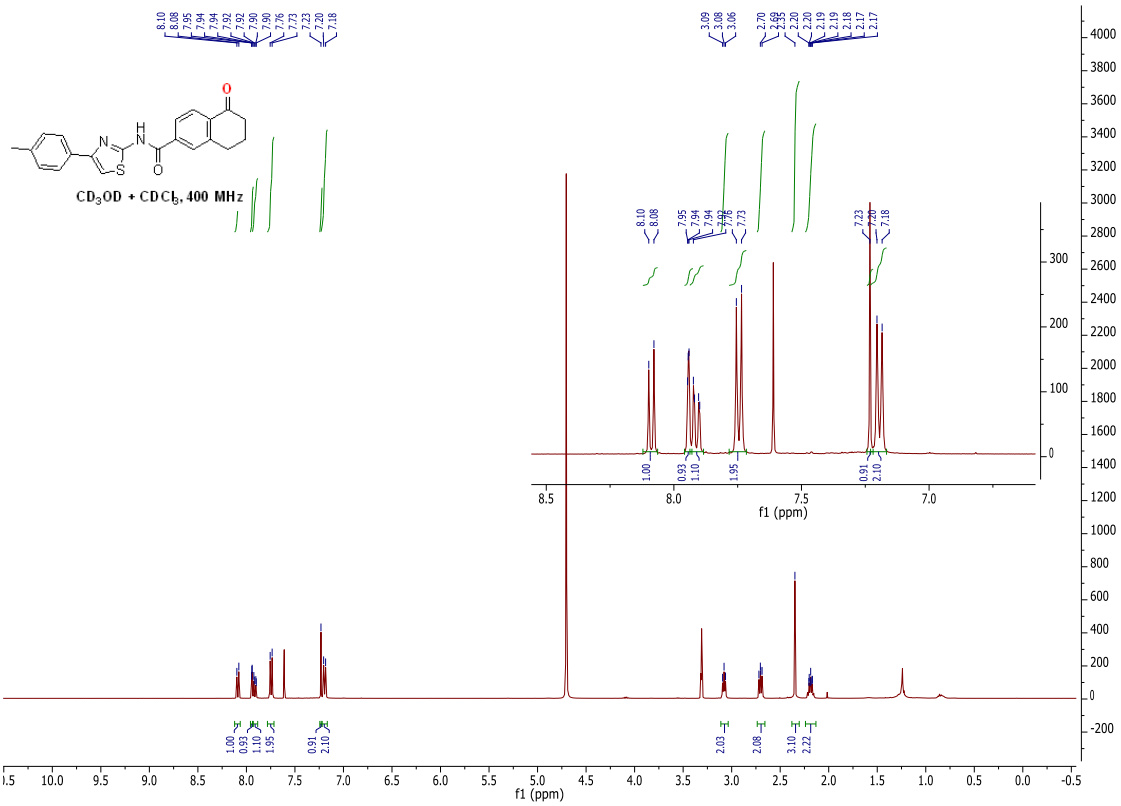

155.31
145.86
134.97
131.38
129.83
129.68
129.05
128.62
128.17
83.63
56.40
27.69
21.84
OTs
N
tBoc
CDCl3, 101 MHz
9
f1 (ppm)

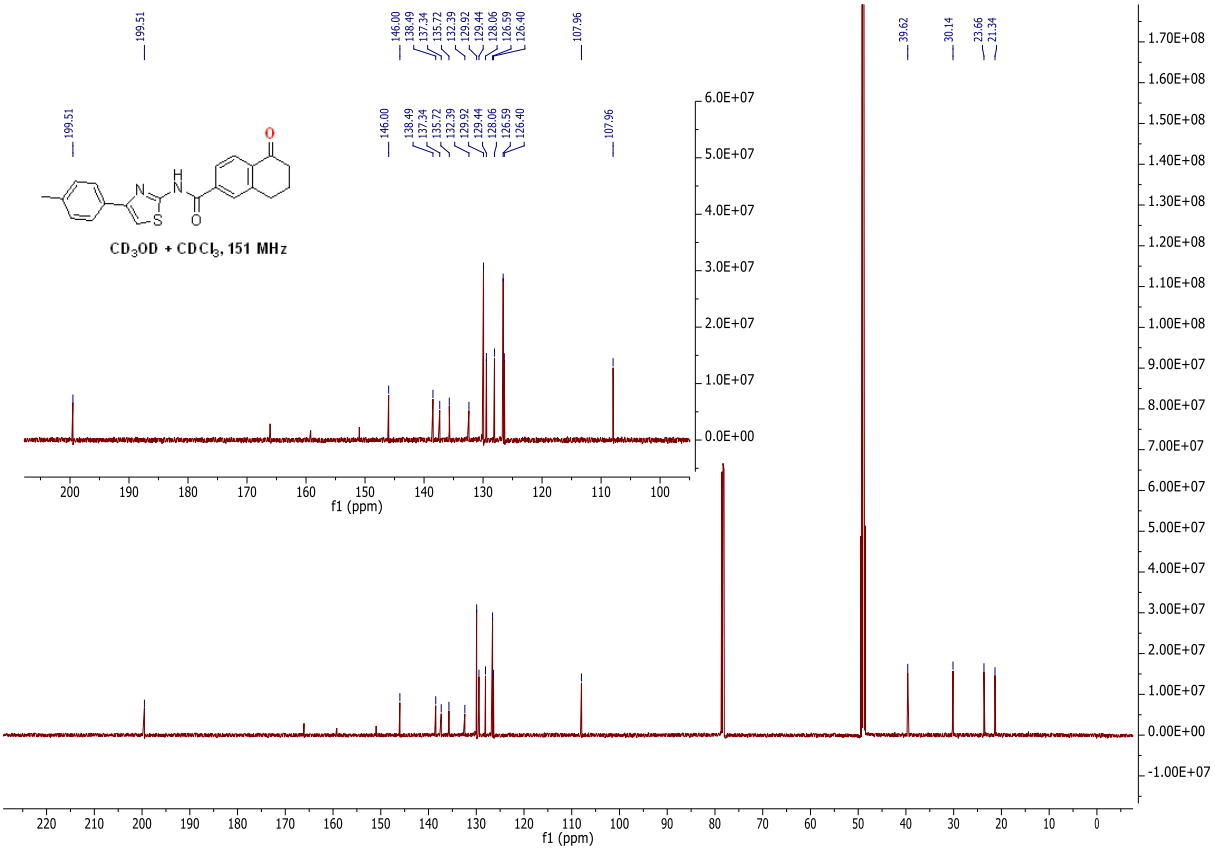

7.21
7.20
7.19
7.18
6.98
6.96
6.94
6.69
6.68
6.67
6.66
6.65
6.52
6.51
6.50
6.49
3.33
3.32
3.30
1.77
1.76
1.74
1.30
H
N
CDCl3, 400 MHz
10
1.18
0.98
1.05
1.00
2.12
2.18
6.28
f1 (ppm)

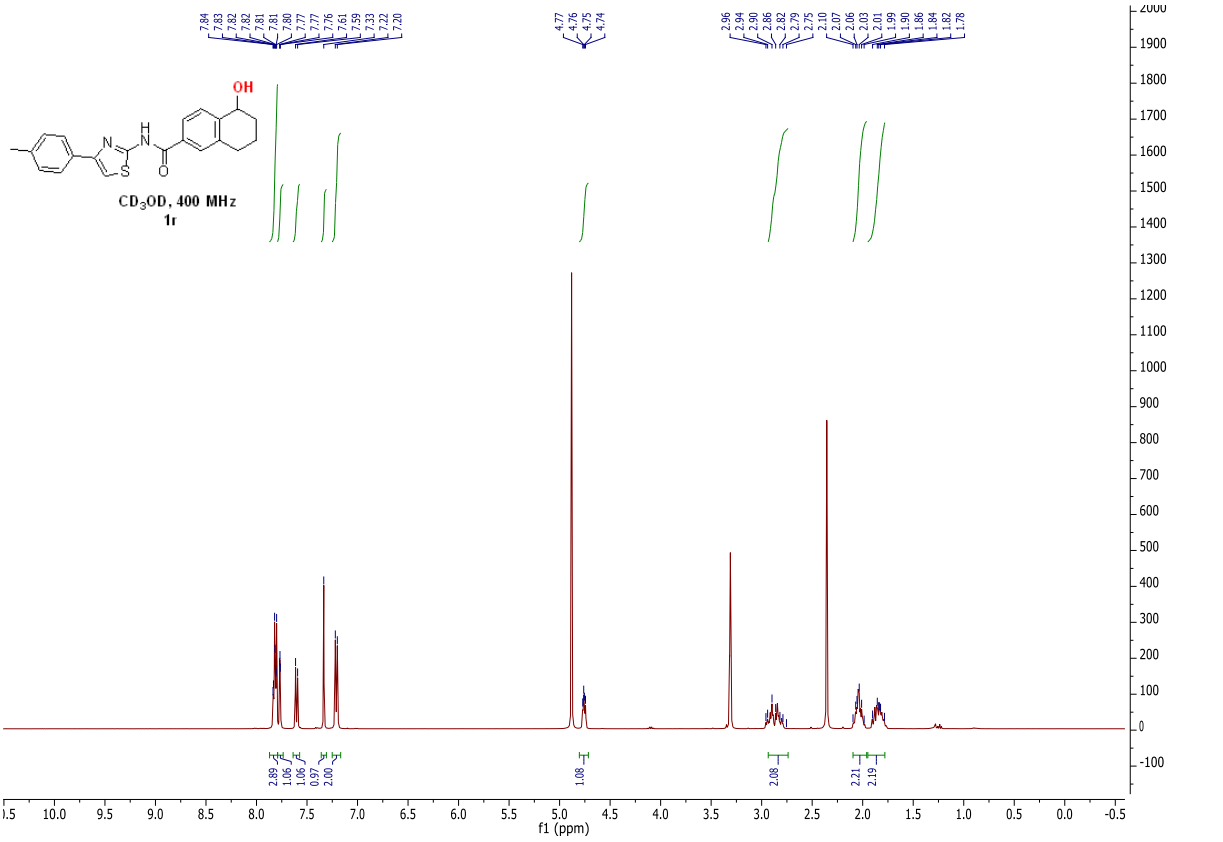

143.21
130.55
126.60
126.51
117.40
114.51
38.52
37.30
31.73
31.05
CDCl3, 101 MHz
10
f1 (ppm)

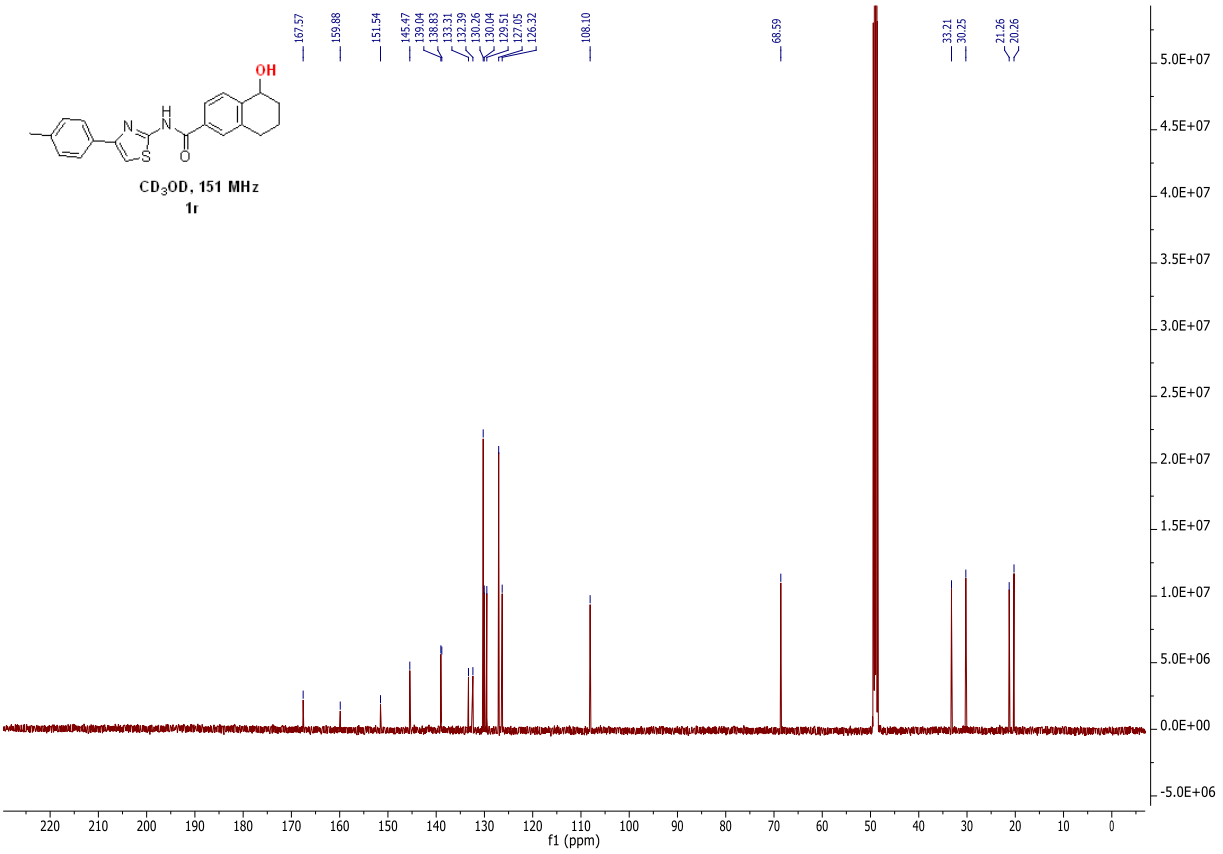

CDCl3, 400 MHz
f1 (ppm)

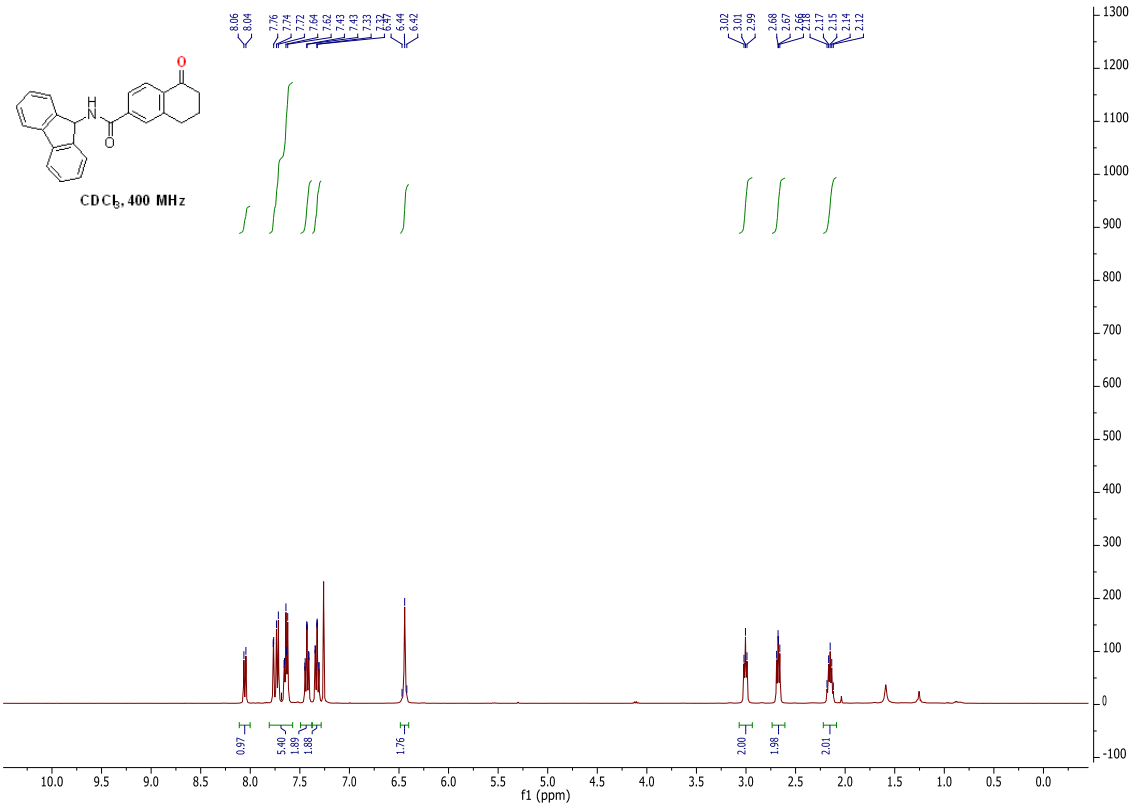

CDCl3, 151 MHz
f1 (ppm)

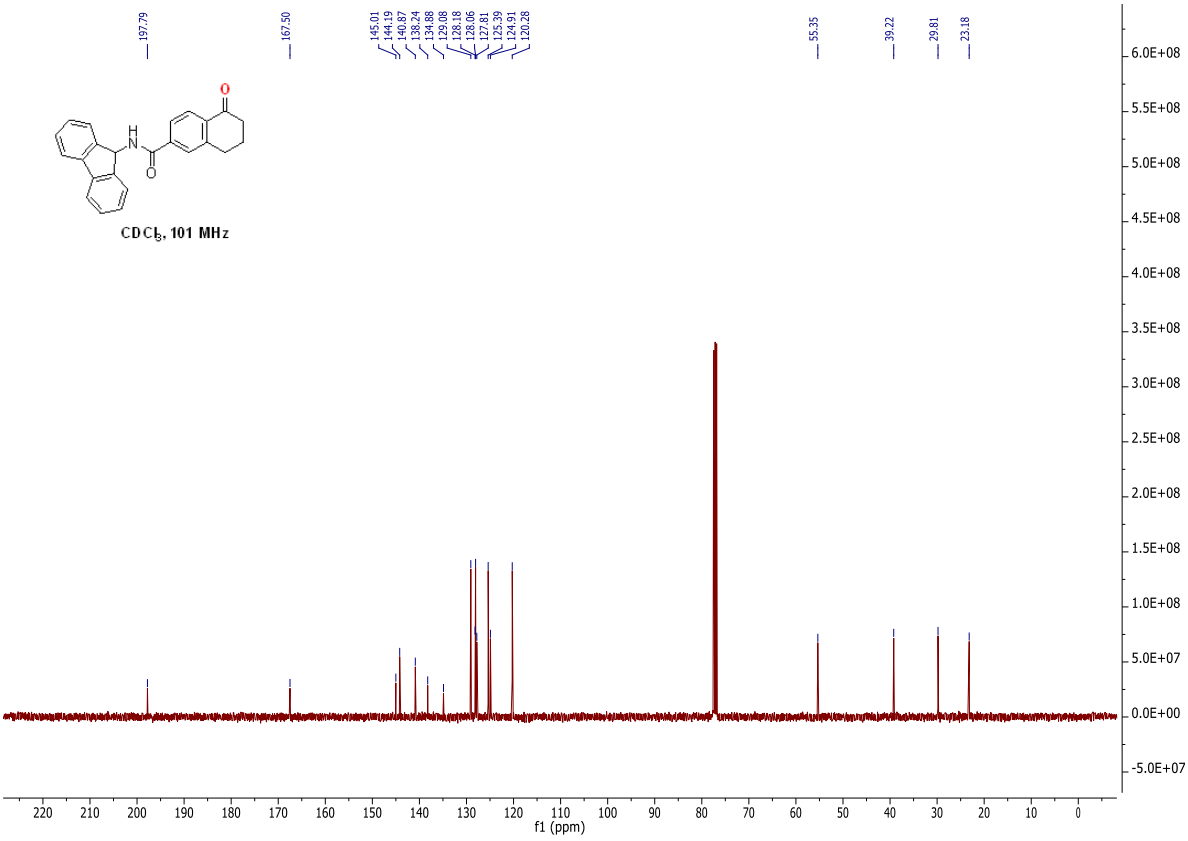

CD3OD + CDCl3, 400 MHz
f1 (ppm)

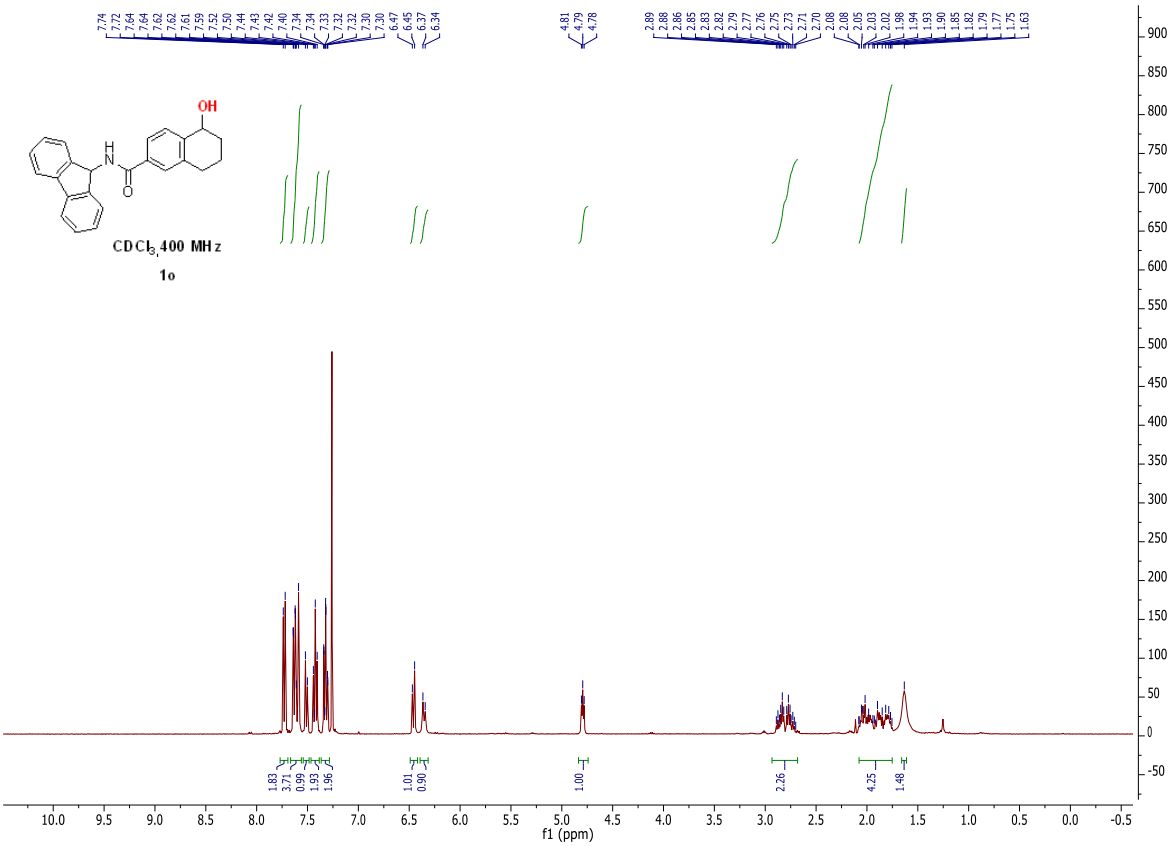

CD3OD + CDCl3, 151 MHz
f1 (ppm)

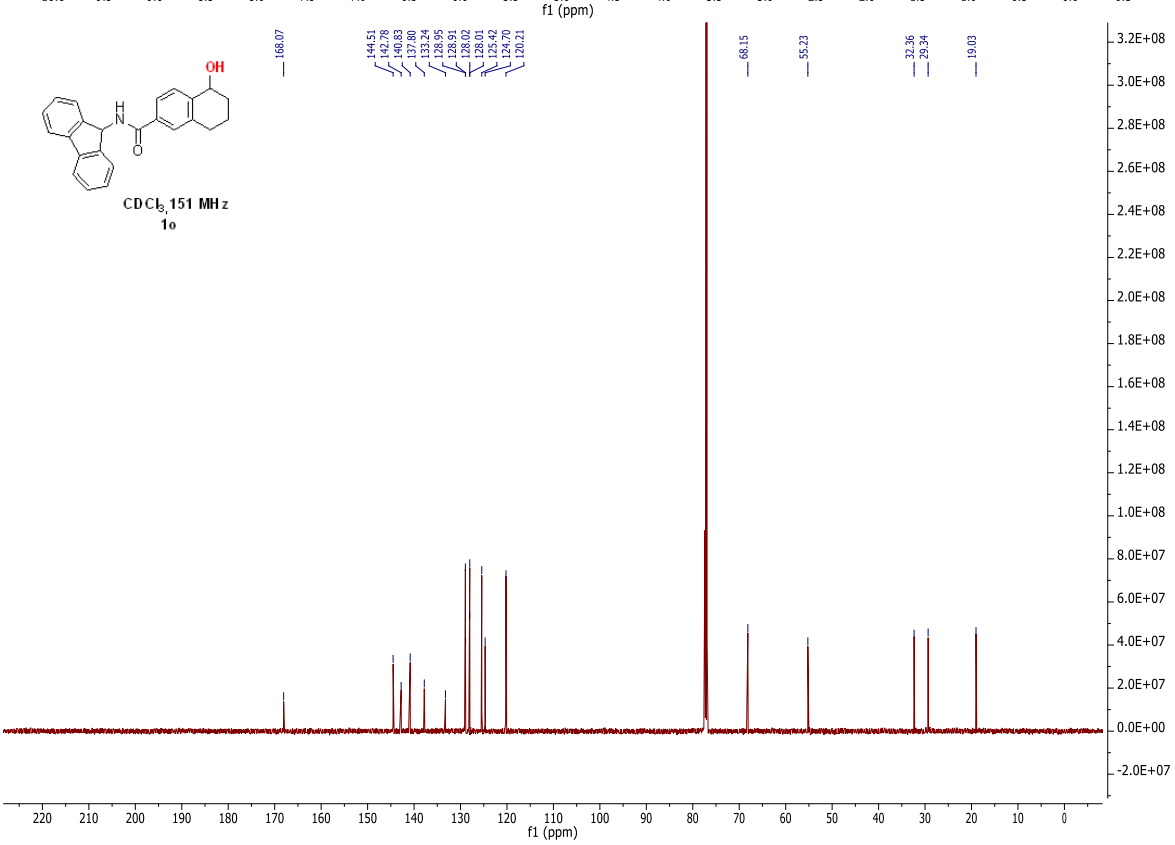

OH
N
H
N
S
O
CD3OD, 400 MHz
1r
7.84
7.83
7.82
7.82
7.81
7.81
7.80
7.77
7.77
7.76
7.61
7.59
7.33
7.22
7.20
4.77
4.76
4.75
4.74
2.96
2.94
2.90
2.86
2.82
2.79
2.75
2.10
2.07
2.06
2.03
2.01
1.99
1.90
1.86
1.84
1.82
1.78
2.89
1.06
1.06
0.97
2.00
1.08
2.08
2.21
2.19
f1 (ppm)

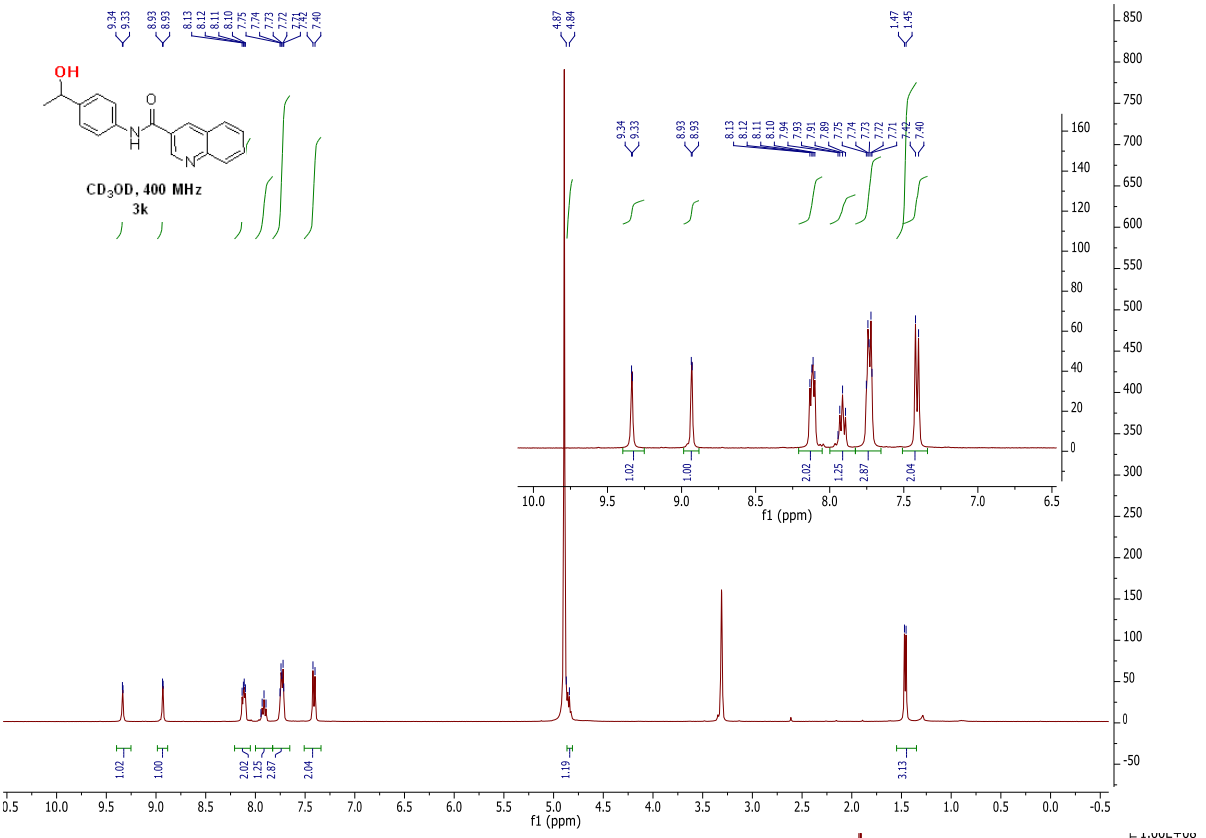

OH
N
H
N
S
O
CD3OD, 151 MHz
1r
167.57
159.88
151.54
145.47
139.04
138.83
133.31
132.39
130.26
130.04
129.51
127.05
126.32
108.10
68.59
33.21
30.25
21.26
20.26
f1 (ppm)

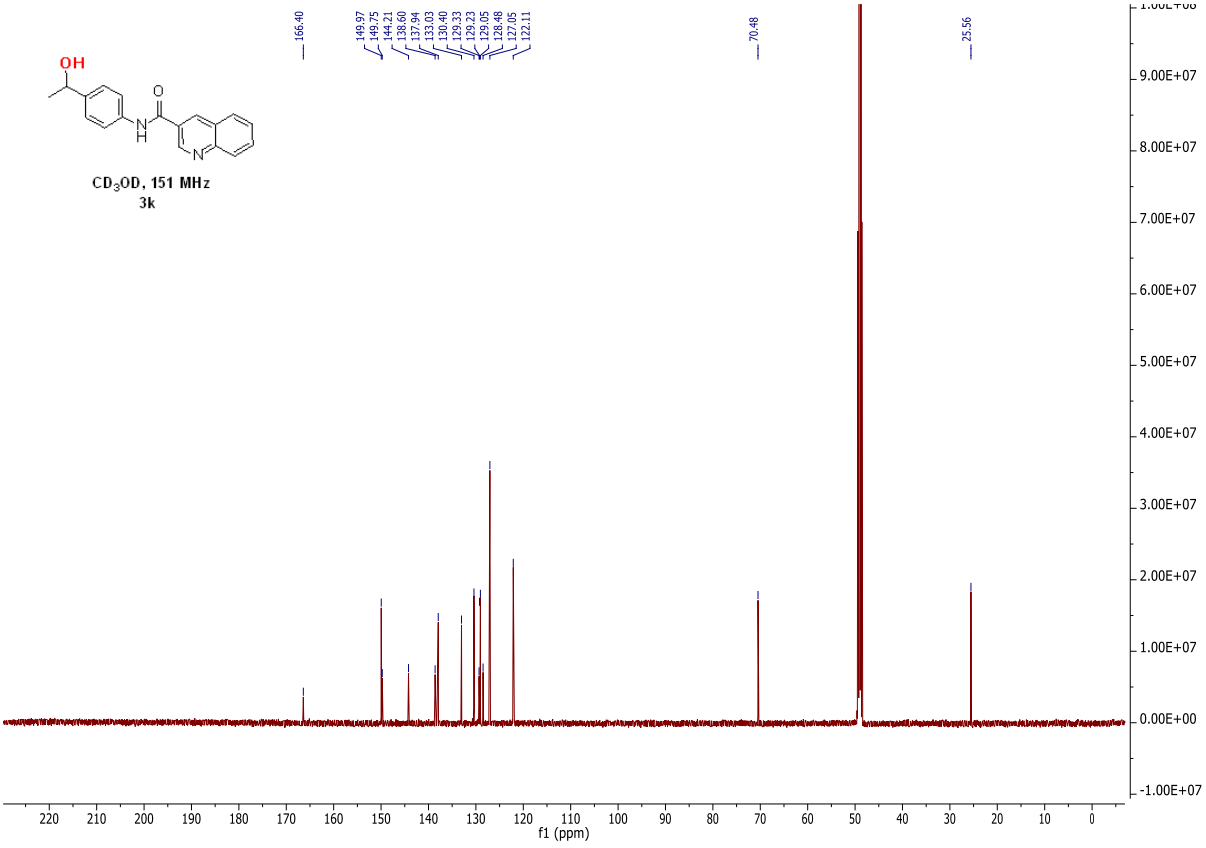

CDCl3, 400 MHz
f1 (ppm)

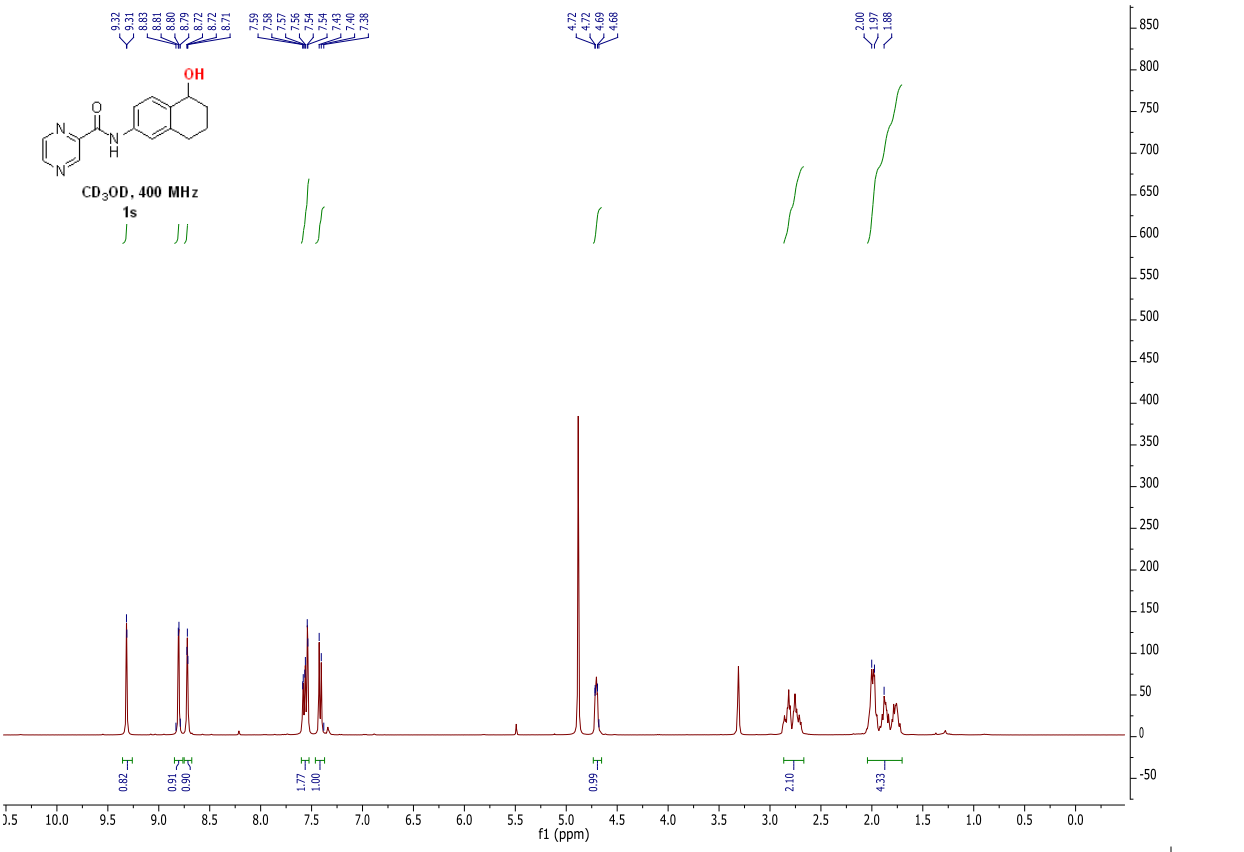

CDCl3, 101 MHz
f1 (ppm)

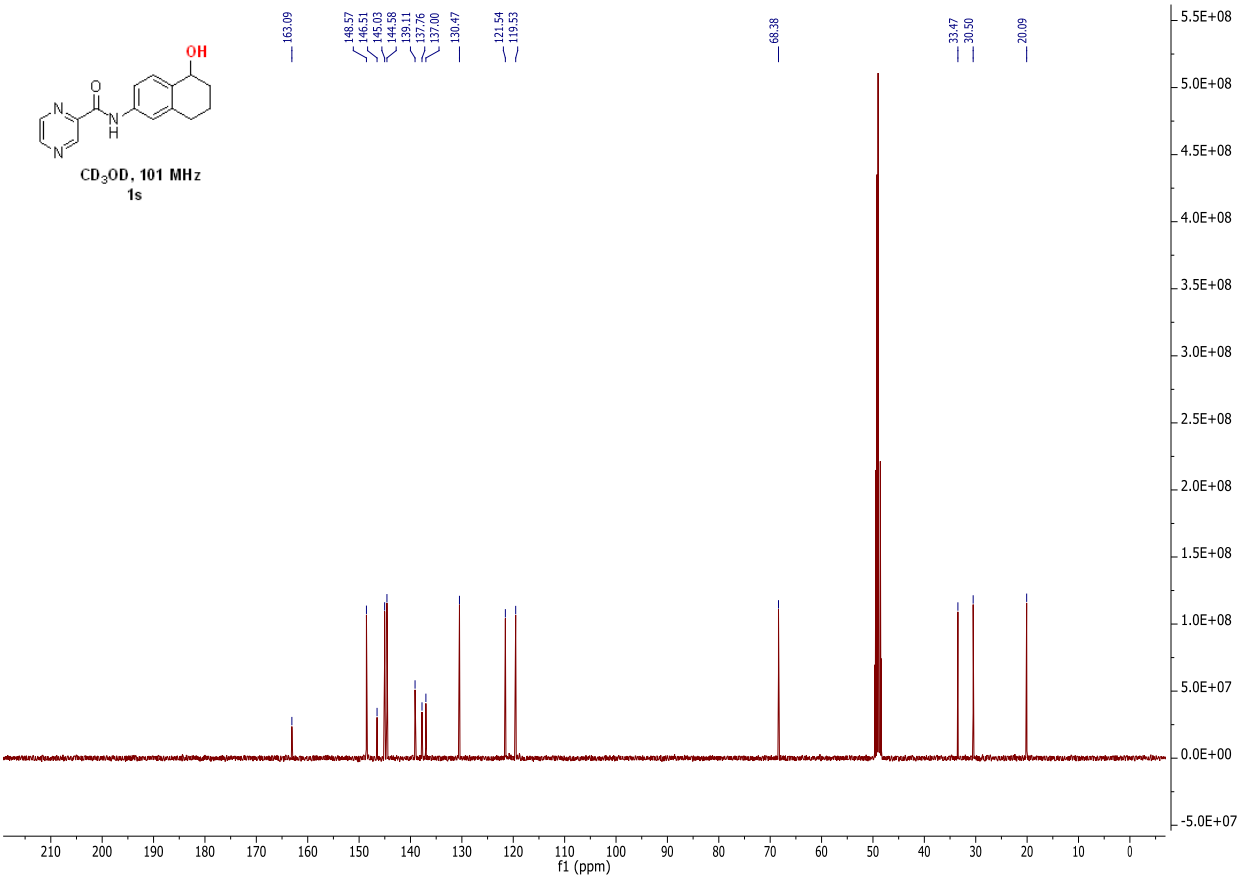

OH
H
N
O
CDCl3, 400 MHz
1o
f1 (ppm)

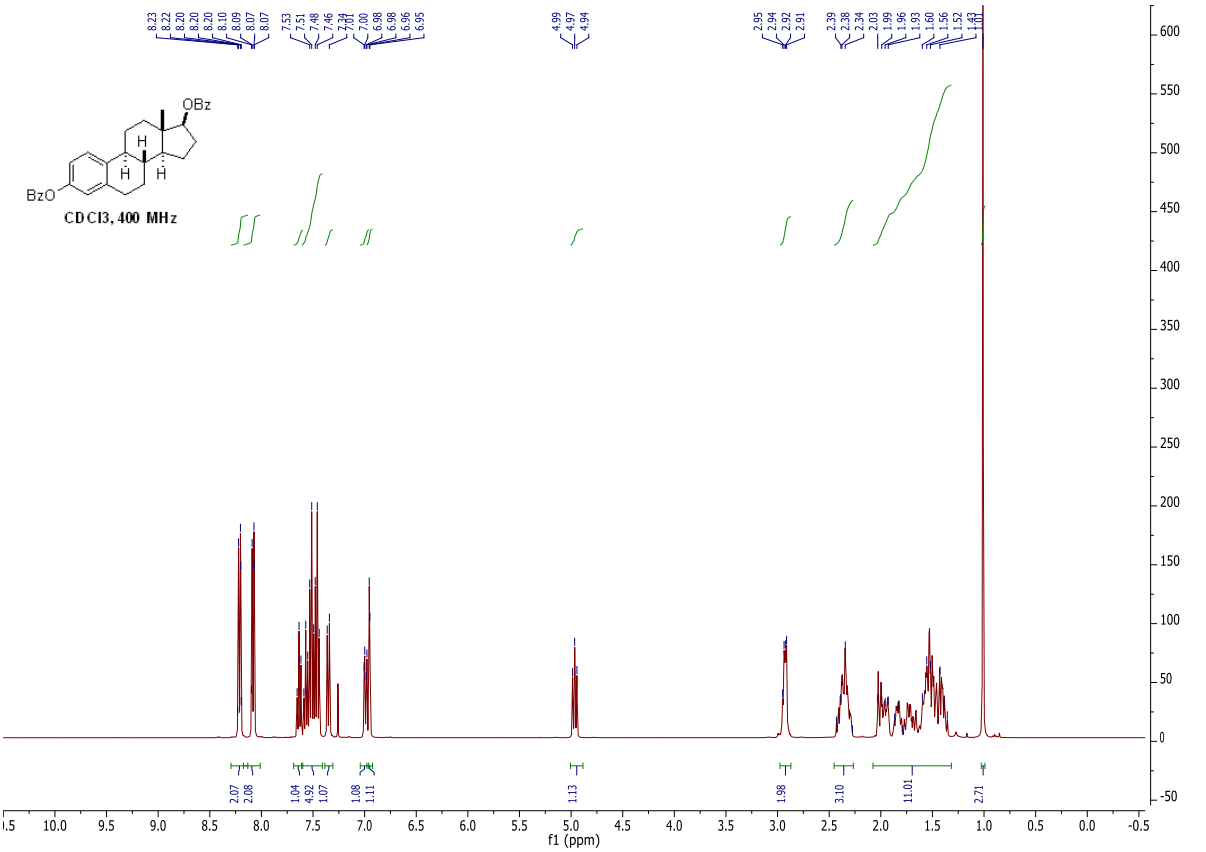

OH
H
N
O
CDCl3, 151 MHz
1o
f1 (ppm)

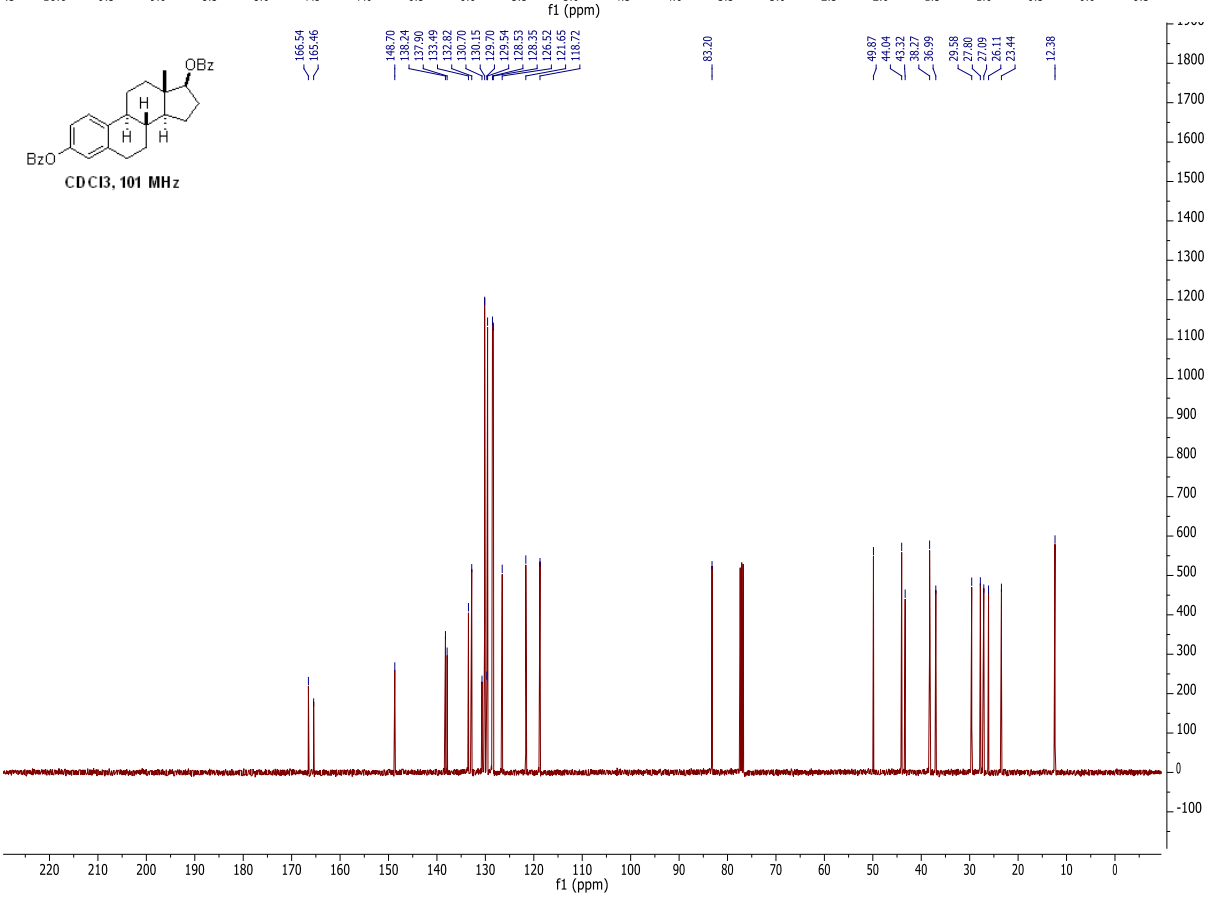

OH
O
N
H
N
CD3OD, 400 MHz
3k
f1 (ppm)

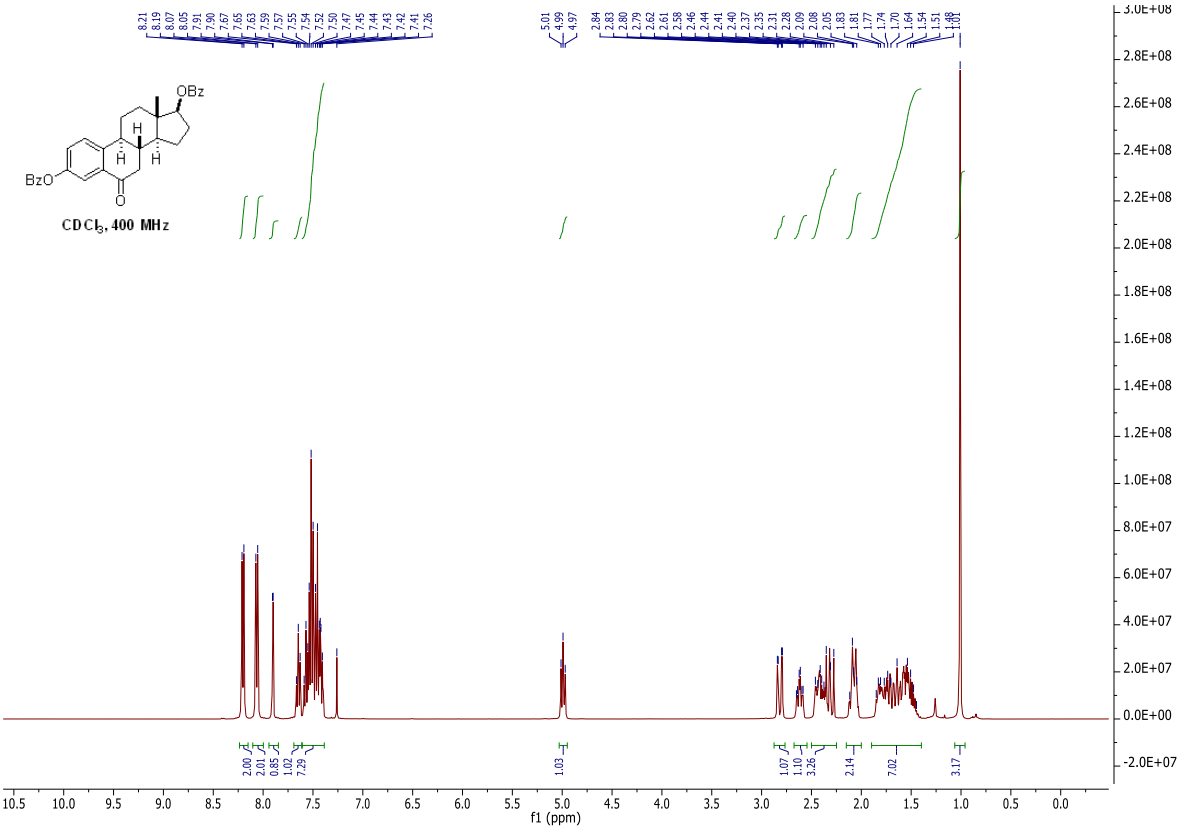

OH
O
N
H
N
CD3OD, 151 MHz
3k
f1 (ppm)

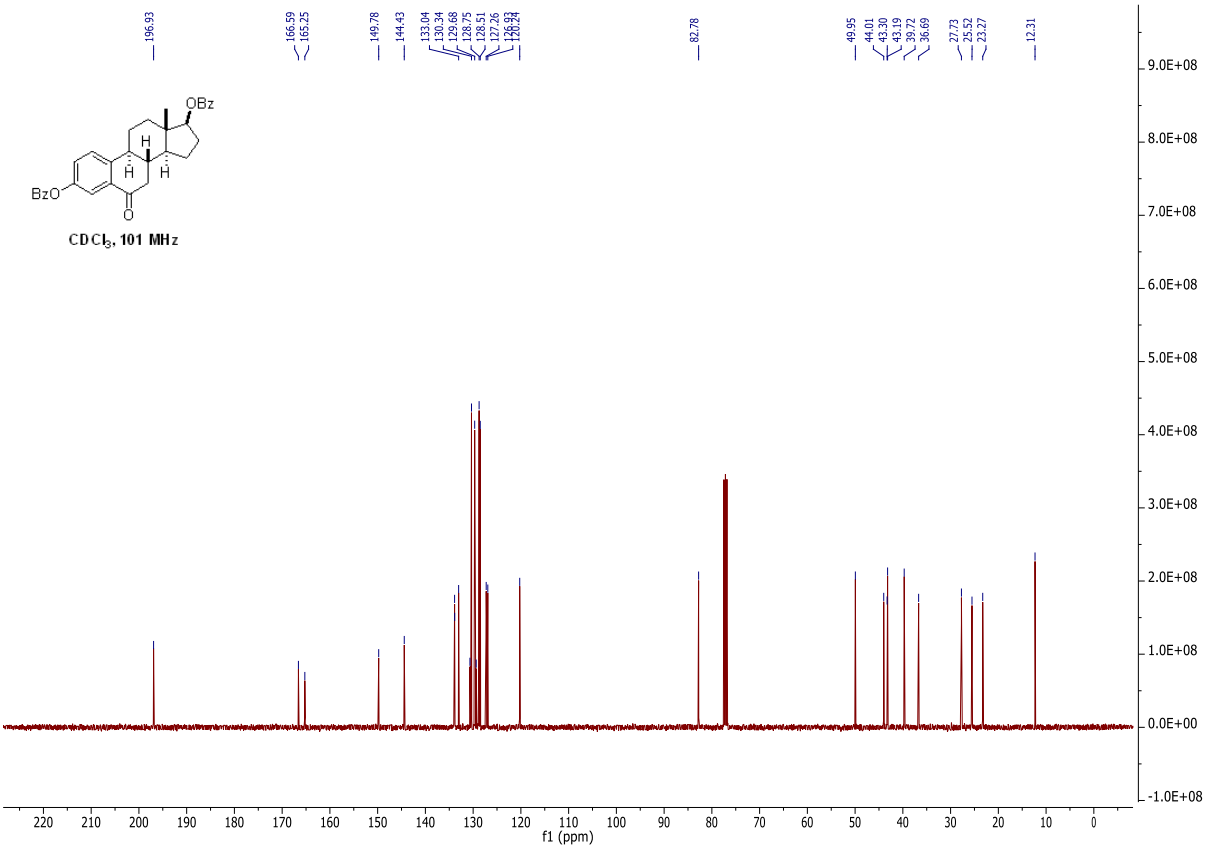

9.32
9.31
8.83
8.81
8.80
8.79
8.72
8.72
8.72
8.71
7.59
7.58
7.57
7.56
7.54
7.54
7.43
7.40
7.38
4.72
4.72
4.69
4.68
2.00
1.97
1.88
OH
N
O
N
H
CD3OD, 400 MHz
1s
0.82
0.91
0.90
1.77
1.00
0.99
2.10
4.33
f1 (ppm)

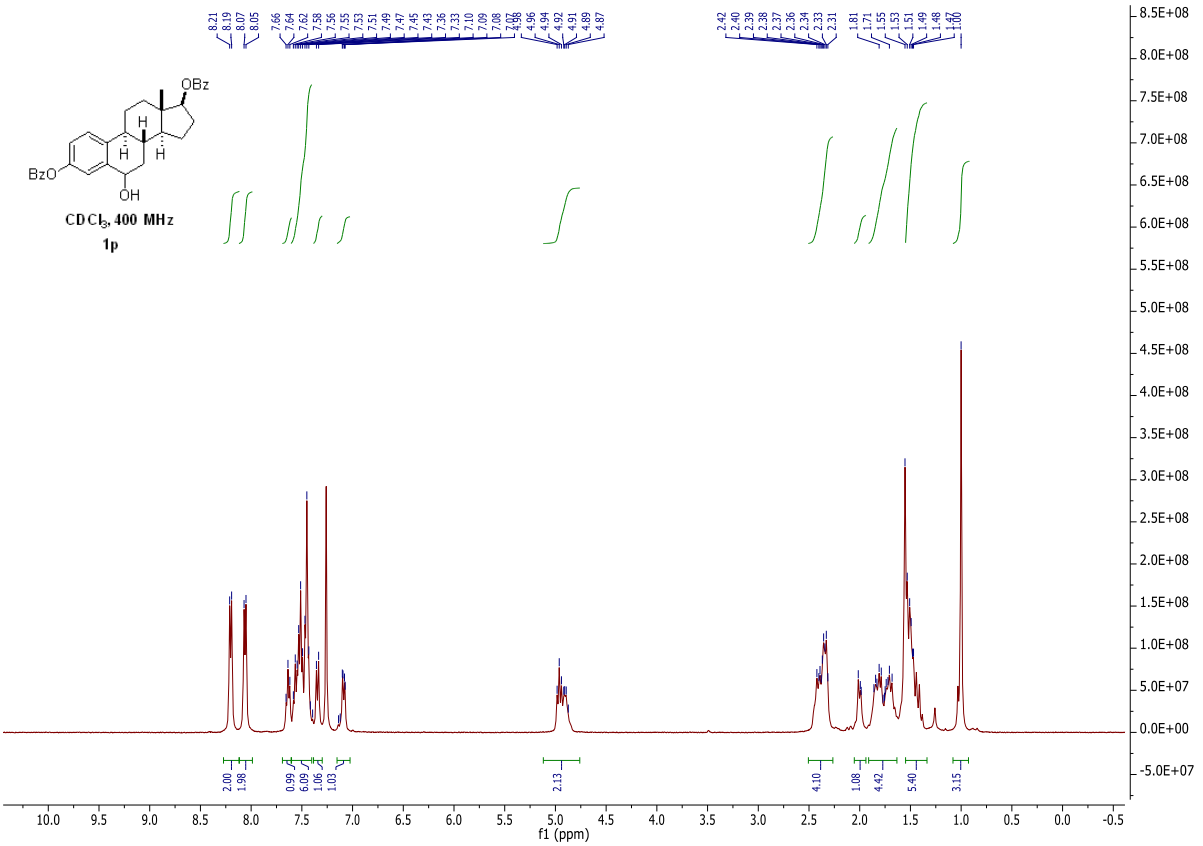

163.09
148.57
146.51
145.03
144.58
139.11
137.76
137.00
130.47
121.54
119.53
68.38
33.47
30.50
20.09
OH
N
O
N
H
CD3OD, 101 MHz
1s
f1 (ppm)

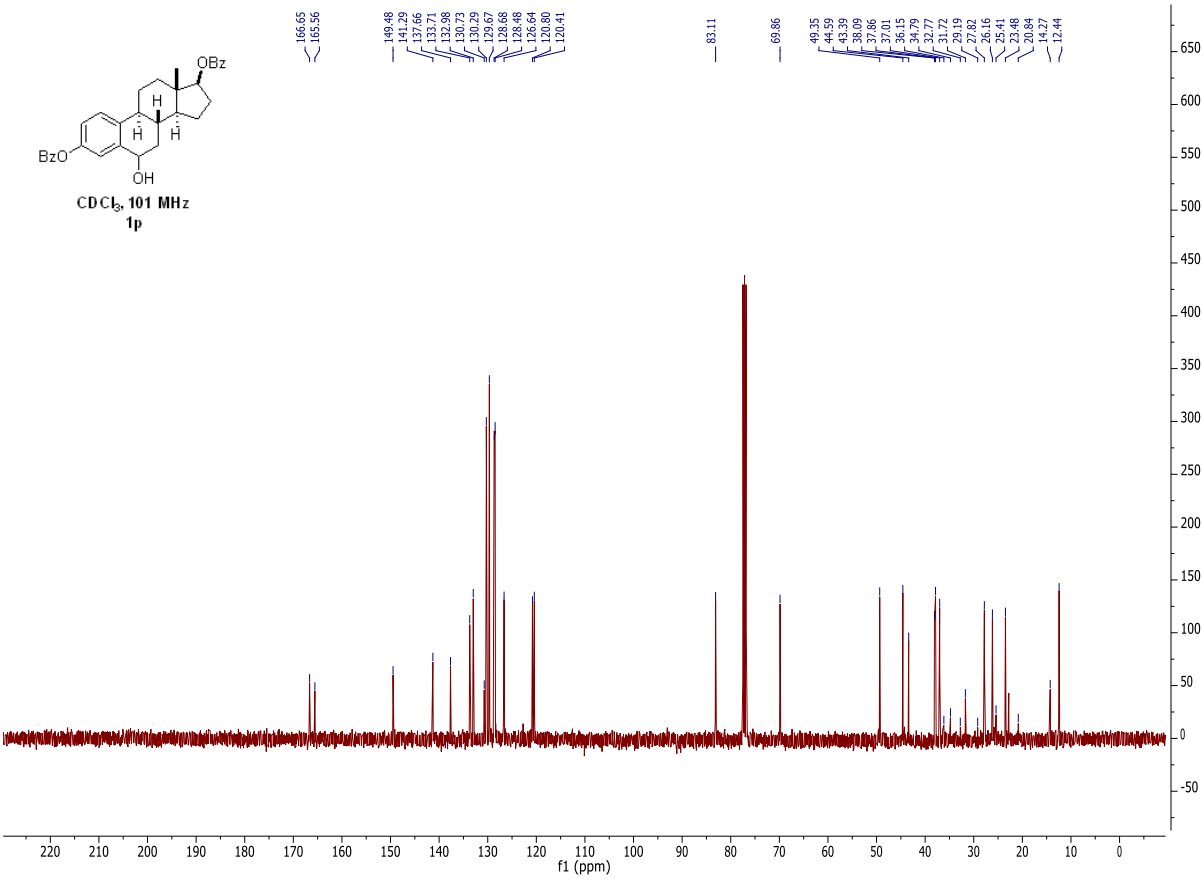

OBz
BzO
CDCl3, 400 MHz
f1 (ppm)

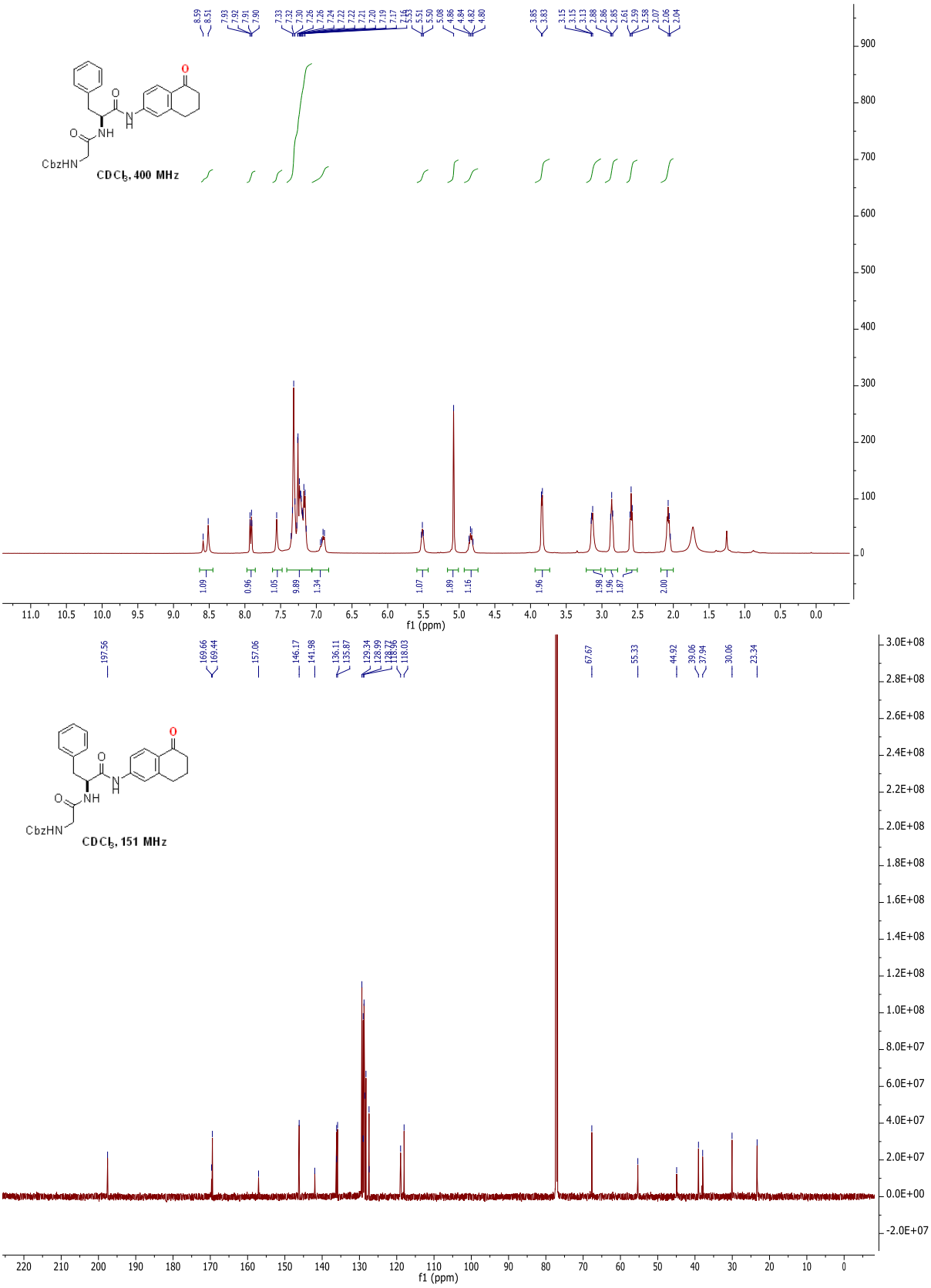

OBz
BzO
CDCl3, 101 MHz
f1 (ppm)

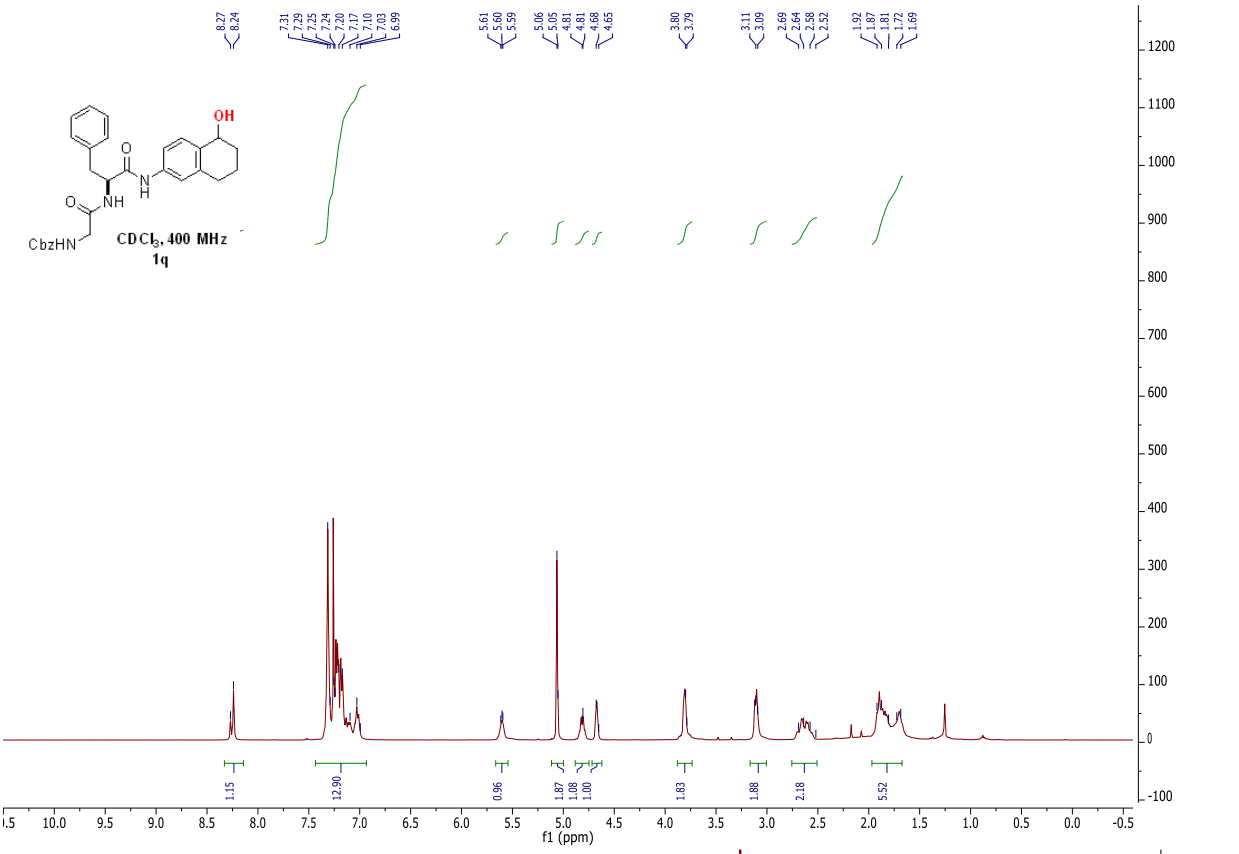

OBz
BzO
H
H
H
O
CDCl3, 400 MHz
f1 (ppm)

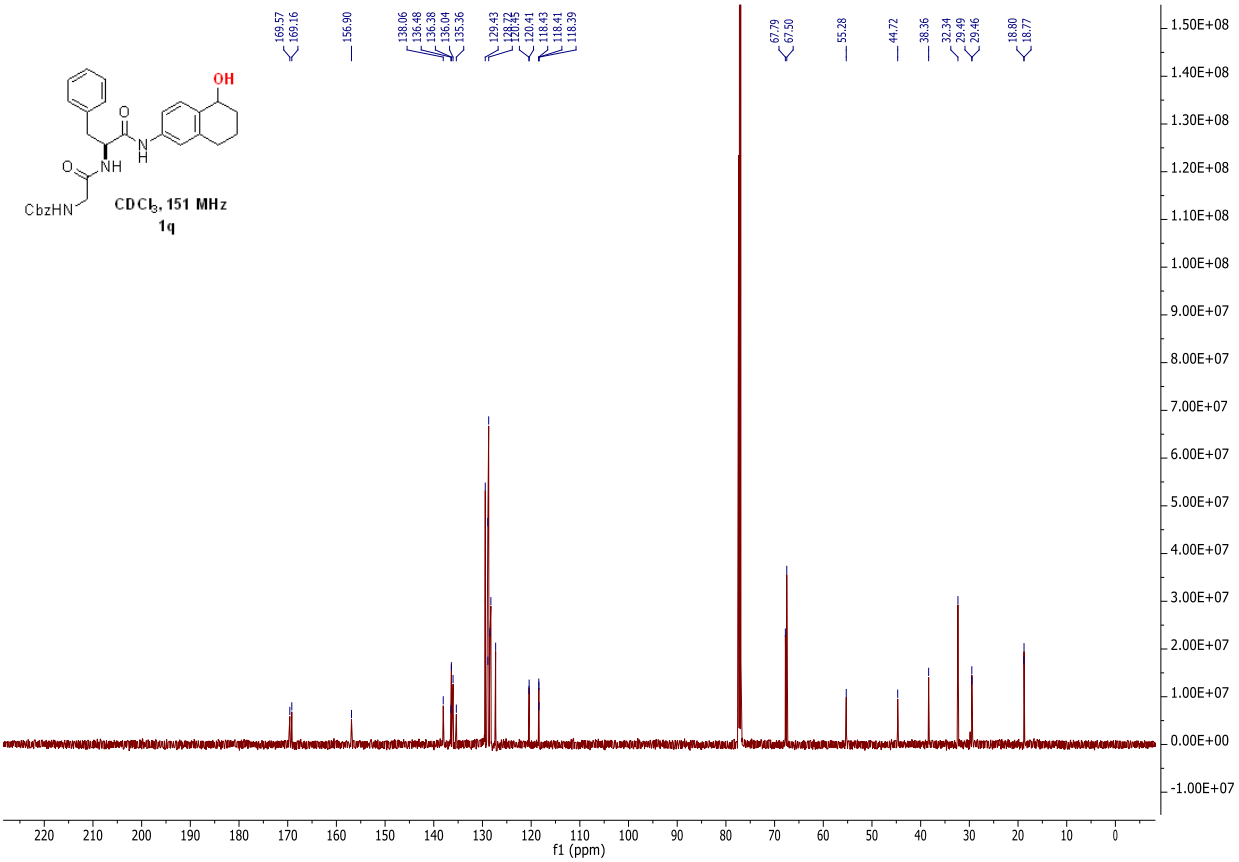

OBz
BzO
H
H
H
O
CDCl3, 101 MHz
f1 (ppm)

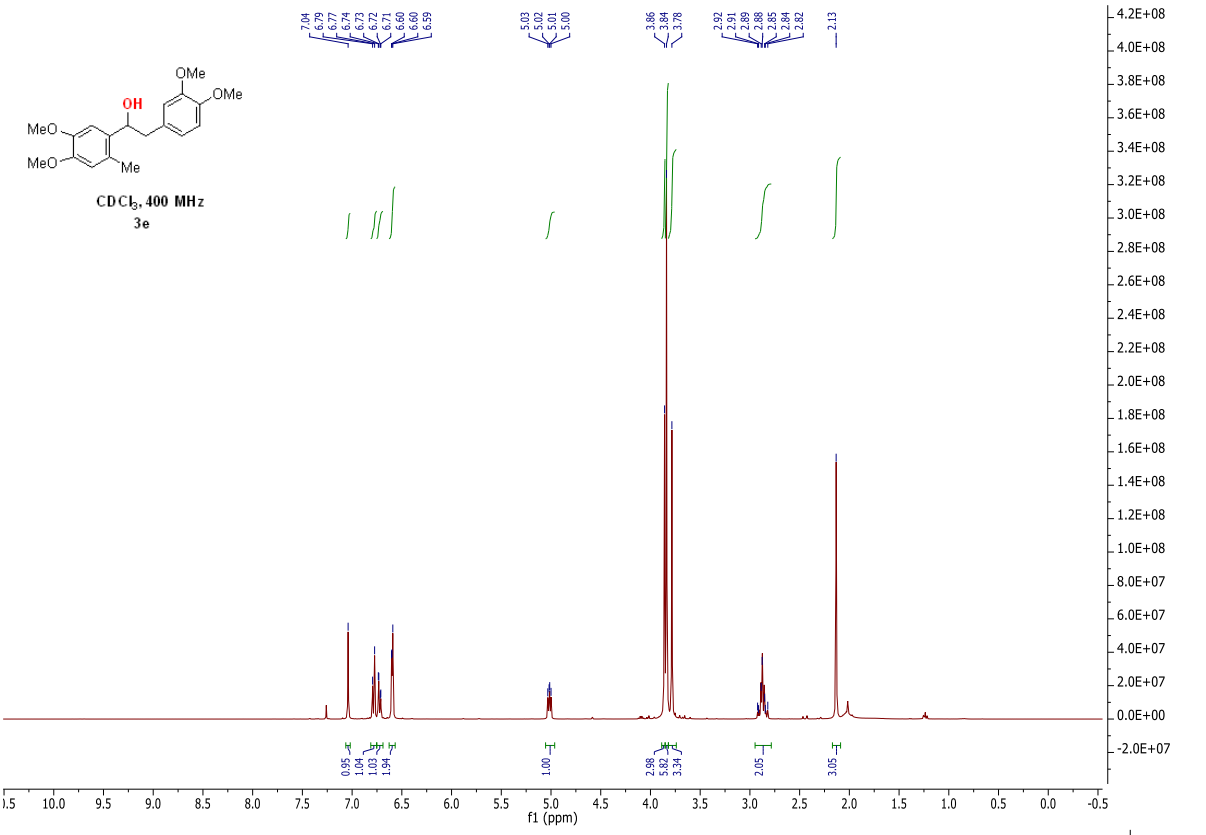

OBz
BzO
OH
H
H
H
CDCl3, 400 MHz
1p
f1 (ppm)

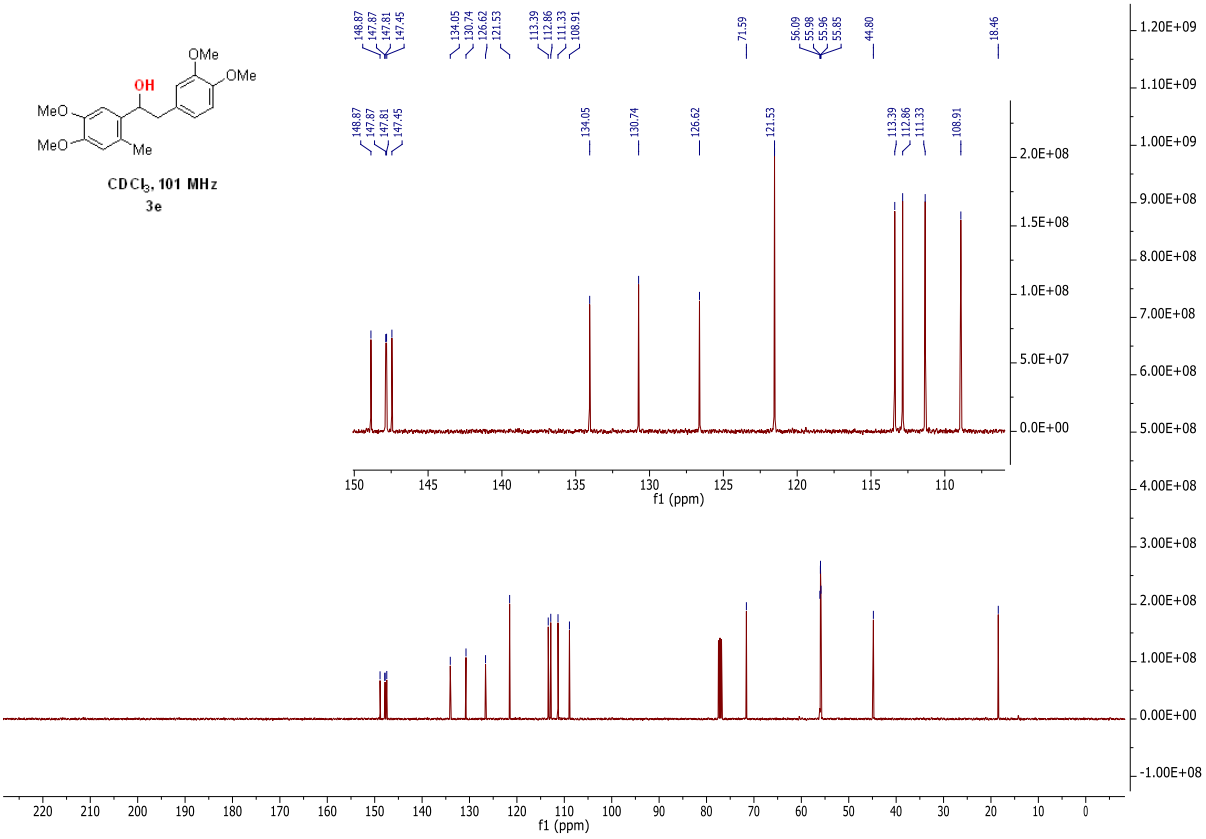

OBz
BzO
OH
H
H
H
CDCl3, 101 MHz
1p
f1 (ppm)

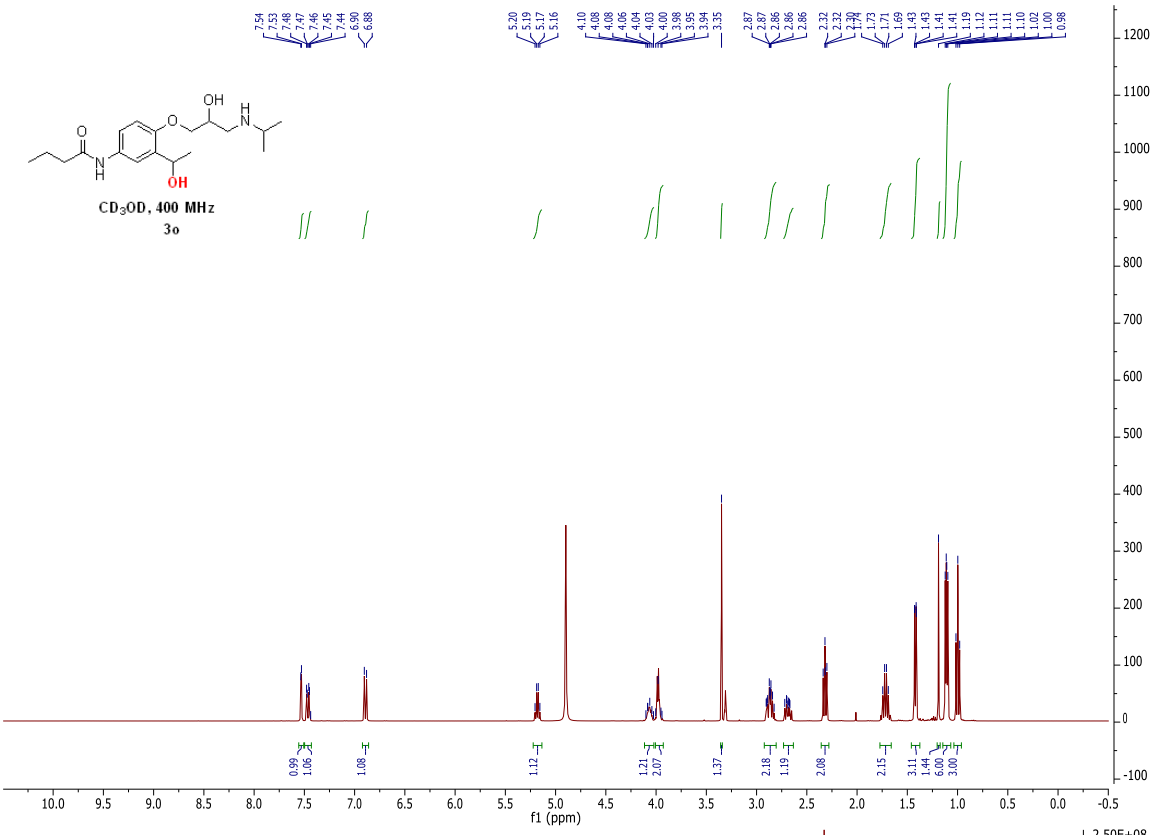

CDCl3, 400 MHz
f1 (ppm)
CDCl3, 151 MHz
f1 (ppm)

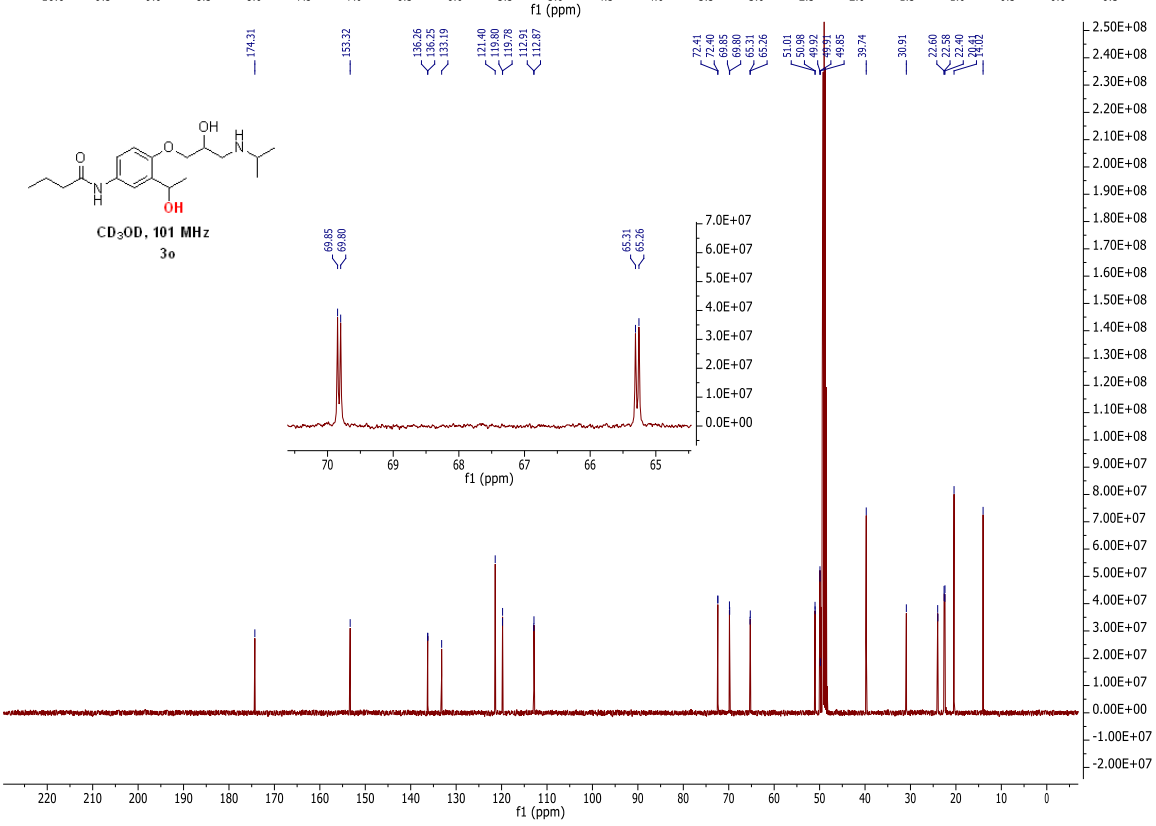

OH
O
N
H
NH
O
CbzHN
CDCl3, 400 MHz
1q
8.27
8.24
7.31
7.29
7.25
7.24
7.20
7.17
7.10
7.03
6.99
5.61
5.60
5.59
5.06
5.05
4.81
4.81
4.68
4.65
3.80
3.79
3.11
3.09
2.69
2.64
2.58
2.52
1.92
1.87
1.81
1.72
1.69
1.15
12.90
0.96
1.87
1.08
1.00
1.83
1.88
2.18
5.52
f1 (ppm)

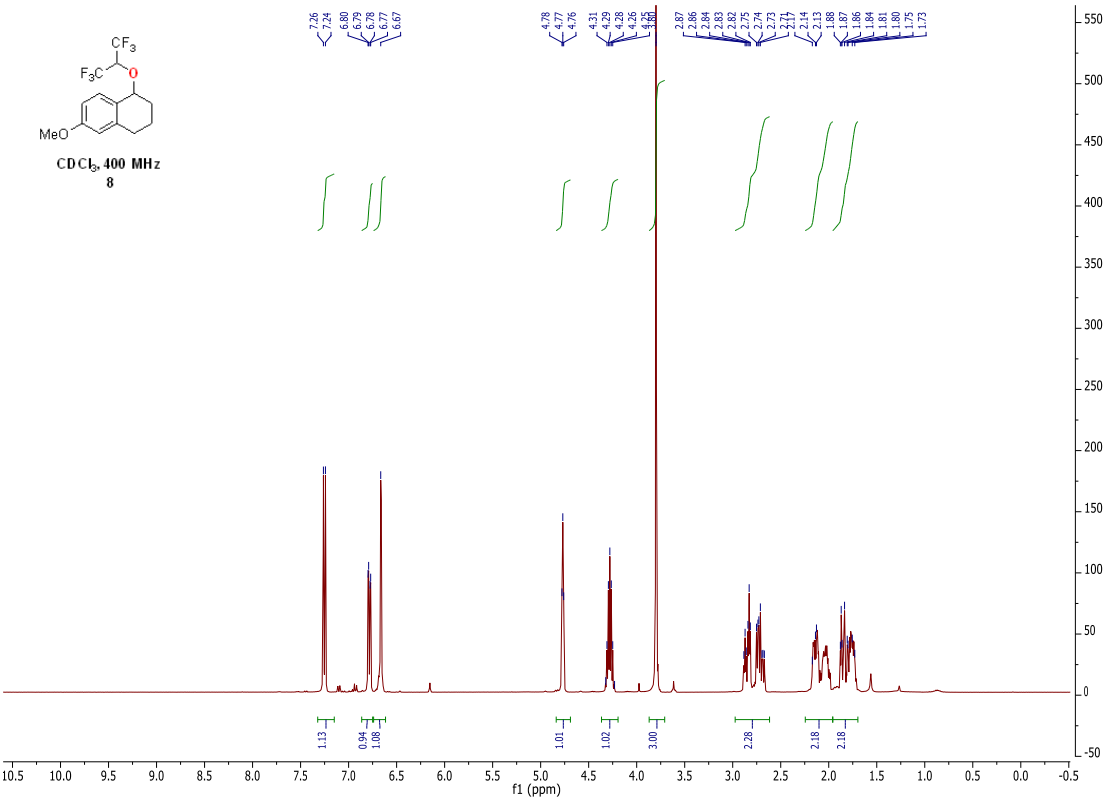

OH
O
N
H
NH
O
CbzHN
CDCl3, 151 MHz
1q
169.57
169.16
156.90
138.06
136.48
136.38
136.04
135.36
129.43
128.72
120.45
120.41
118.43
118.41
118.39
67.79
67.50
55.28
44.72
38.36
32.34
29.49
29.46
18.80
18.77
f1 (ppm)

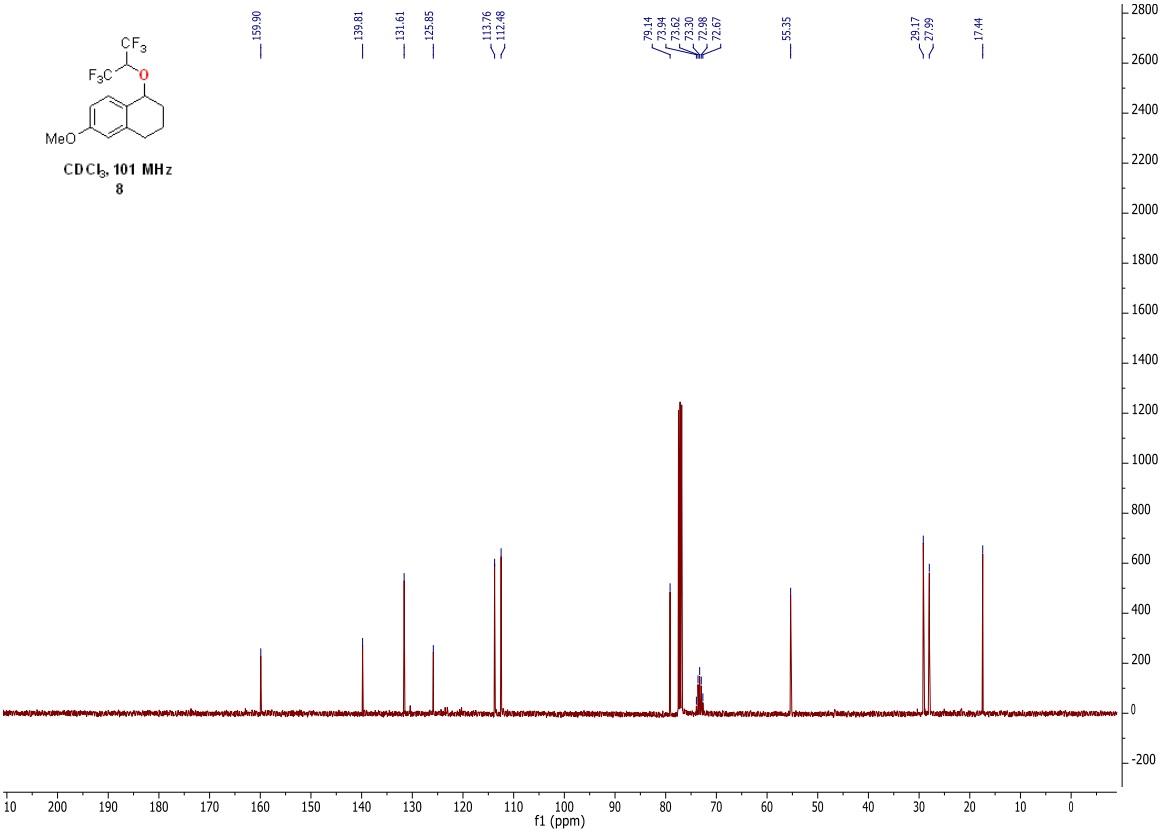

OMe
OMe
OH
MeO
MeO
Me
CDCl3, 400 MHz
3e
f1 (ppm)


OMe
OMe
OH
MeO
MeO
Me
CDCl3, 101 MHz
3e
f1 (ppm)


CD3OD, 400 MHz
3o
f1 (ppm)


CD3OD, 101 MHz
3o
f1 (ppm)


CDCl3, 400 MHz
8
f1 (ppm)


CDCl3, 101 MHz
8
f1 (ppm)