# SUPPORTING INFORMATION

## Rhodium-catalyzed asymmetric transfer hydrogenation of 4-quinolone derivatives

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## I. General information

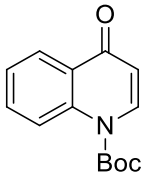
All air and/or water sensitive reactions were carried out under an argon atmosphere. THF, $Et_2O$, $CH_2Cl_2$, DMF and toluene were dried over alumina columns in a solvent purification apparatus (Innovative technology). Reactions were monitored by thin layer chromatography carried out on precoated silica gel plates (Merck 60 F254) and revealed with either a ultra-violet lamp ($\lambda$ = 254 nm) or a potassium permanganate solution. Proton nuclear magnetic resonance ($^1$H NMR) spectra were recorded using a Bruker AC 400 (400 MHz). The chemical shifts are expressed in parts per million (ppm) referenced to residual chloroform (7.26 ppm). Data are reported as follows: chemical shifts ($\delta$), multiplicity (recorded as s, singlet; d, doublet; t, triplet; q, quadruplet; quint, quintuplet; sext, sextuplet; hept, heptuplet; m, multiplet; and br, broad), coupling constants and integration. Carbon-13 nuclear magnetic resonance ($^{13}$C NMR) spectra were recorded using a Bruker AC 400 (100 MHz). The chemical shifts are expressed in parts per million (ppm) relative to the centre line of the triplet at 77.16 ppm for $CDCl_3$. Melting points (m.p.) were determined on a Kofler melting point apparatus. Optical rotations were measured on a Jasco P-1010 polarimeter. HRMS analyses were measured on a LTQ-Orbitrap (Thermo Fisher Scientific) apparatus at Sorbonne Université.

## II. General procedure for the preparation of compounds 1a–1m[1]

A 100 mL round-bottom flask was charged with quinoline (3 mmol), $Boc_2O$ (4.5 mmol, 1.5 equiv), DMAP (0.3 mmol, 0.1 equiv), $Et_3N$ (4.5 mmol, 1.5 equiv), THF (15 mL). The mixture was stirred at room temperature for 2 h. The mixture was concentrated, and the residue was solubilized with ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate. The solvent was evaporated, and the crude product was purified by chromatography on silica gel column (PE/EA = 2:1 as eluent).

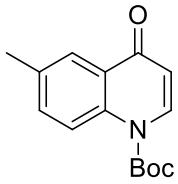
## III. Analytical data for compounds 1a–1m

**_tert_-Butyl 4-oxoquinoline-1(4H)-carboxylate (1a)**



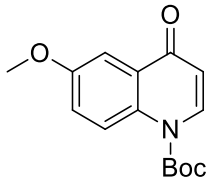

White solid, 7.5g, 76% yield, m.p. 80 °C. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 8.8 Hz, 1H), 8.37 (dd, *J* = 8.0, 1.5 Hz, 1H), 8.30 (d, *J* = 8.5 Hz, 1H), 7.65 (ddd, *J* = 8.9, 7.1, 1.8 Hz, 1H), 7.42 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 6.25 (d, *J* = 8.5 Hz, 1H), 1.67 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 179.1, 150.0, 138.8, 138.6, 132.7 126.7, 126.5, 125.2, 120.0, 111.9, 86.6, 28.0.

***tert*-Butyl 6-methyl-4-oxoquinoline-1(4H)-carboxylate (1b)**



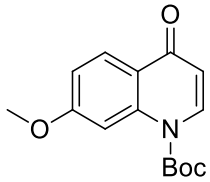

White solid, 563mg, 72% yield, m.p. 124 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 9.0 Hz, 1H), 8.29 (d, *J* = 8.5 Hz, 1H), 8.17 (dd, *J* = 1.6, 0.7 Hz, 1H), 7.47 (ddd, *J* = 8.9, 2.3, 0.7 Hz, 1H), 6.24 (d, *J* = 8.5 Hz, 1H), 2.46 (s, 3H), 1.67 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 179.3, 150.1, 138.6, 136.6, 135.2, 134.0, 126.6, 126.1, 120.0, 111.8, 86.5, 28.1, 20.9.

***tert*-Butyl 6-methoxy-4-oxoquinoline-1(4H)-carboxylate (1c)**



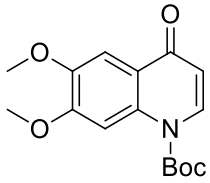

White solid, 1330 mg, 80% yield, m.p. 114 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 9.5 Hz, 1H), 8.29 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 3.1 Hz, 1H), 7.25 (dd, *J* = 9.6, 3.2 Hz, 1H), 6.25 (d, *J* = 8.4 Hz, 1H), 3.92 (s, 3H), 1.67 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 178.7, 156.8, 149.9, 138.1, 132.9, 128.0, 122.4, 121.8, 111.0, 106.0, 86.4, 55.7, 28.0.

***tert*-Butyl 7-methoxy-4-oxoquinoline-1(4H)-carboxylate (1d)**



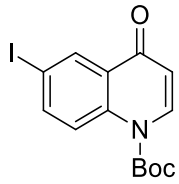

White solid, 1300 mg, 80% yield, m.p. 123 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 9.0 Hz, 1H), 8.26 (d, *J* = 8.5 Hz, 1H), 8.17 (d, *J* = 2.4 Hz, 1H), 7.00 (dd, *J* = 8.9, 2.4 Hz, 1H), 6.20 (d, *J* = 8.6 Hz, 1H), 3.91 (s, 3H), 1.68 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 178.6, 163.2, 150.1, 140.4, 138.5, 128.3, 120.8, 113.8, 112.0, 103.2, 86.5, 55.7, 28.0.

***tert*-Butyl 6,7-dimethoxy-4-oxoquinoline-1(4H)-carboxylate (1e)**



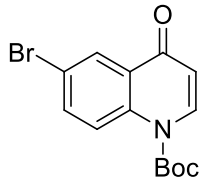

White solid, 1030 mg, 78% yield, m.p. 154 °C.$^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 8.28 (d, *J* = 8.5 Hz, 1H), 7.75 (s, 1H), 6.23 (d, *J* = 8.4 Hz, 1H), 4.00 (br, 6H), 1.68 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 178.1, 153.1, 150.1, 147.4, 137.8, 134.2, 121.1, 111.6, 105.9, 102.3, 86.5, 56.3, 56.2, 28.1.

***tert*-Butyl 6-iodo-4-oxoquinoline-1(4H)-carboxylate (1f)**



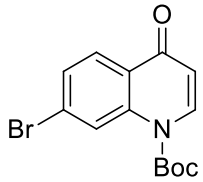

White solid, 890 mg, 80% yield, m.p. 178 °C.$^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.68 (t, *J* = 2.2 Hz, 1H), 8.37 (dd, *J* = 9.3, 1.3 Hz, 1H), 8.30 (dd, *J* = 8.5, 0.9 Hz, 1H), 7.90 (dt, *J* = 9.2, 2.0 Hz, 1H), 6.26 (dd, *J* = 8.6, 1.6 Hz, 1H), 1.67 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 177.6, 149.6, 141.2, 139.0, 138.1, 135.4, 128.2, 122.2, 112.2, 90.1, 87.2, 28.1.

***tert*-Butyl 6-bromo-4-oxoquinoline-1(4H)-carboxylate (1g)**



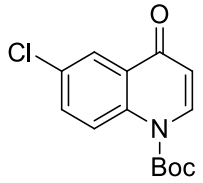

White solid, 1630 mg, 84% yield, m.p. 166 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 9.3 Hz, 1H), 8.49 (d, *J* = 2.5 Hz, 1H), 8.30 (d, *J* = 8.5 Hz, 1H), 7.72 (dd, *J* = 9.3, 2.6 Hz, 1H), 6.26 (d, *J* = 8.5 Hz, 1H), 1.67 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 177.8, 149.7, 139.0, 137.5, 135.6, 129.2, 128.2, 122.2, 119.3, 112.2, 87.2, 28.1.

***tert*-Butyl 7-bromo-4-oxoquinoline-1(4H)-carboxylate (1h)**



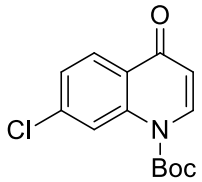

Colourless solid, 800 mg, 83% yield, m.p. 148 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.87 (d, *J* = 1.8 Hz, 1H), 8.29 (d, *J* = 8.5 Hz, 1H), 8.22 (d, *J* = 8.5 Hz, 1H), 7.54 (dd, *J* = 8.6, 1.7 Hz, 1H), 6.25 (d, *J* = 8.6 Hz, 1H), 1.69 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 178.4, 149.6, 139.2, 138.9, 128.7, 128.1, 127.8, 125.4, 123.15, 112.3, 87.3, 28.0.

***tert*-Butyl 6-chloro-4-oxoquinoline-1(4H)-carboxylate (1i)**



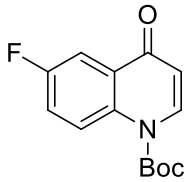

White solid, 640 mg, 76% yield, m.p. 160 °C.$^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 9.5 Hz, 1H), 8.33 (d, *J* = 2.6 Hz, 1H), 8.31 (d, *J* = 8.6 Hz, 1H), 7.59 (dd, *J* = 9.4, 2.7 Hz, 1H), 6.26 (d, *J* = 8.6 Hz, 1H), 1.68 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 177.8, 149.6, 139.0, 137.0, 132.7, 131.4, 127.9, 125.9, 122.0, 112.0, 87.2, 28.0.

***tert*-Butyl 7-chloro-4-oxoquinoline-1(4H)-carboxylate (1j)**



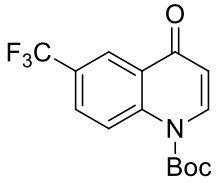

Colourless, 1000 mg, 60% yield, m.p. 126 °C.$^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 1.9 Hz, 1H), 8.26 (d, *J* = 7.2 Hz, 1H), 8.24 (d, *J* = 7.1 Hz, 1H), 7.34 (dd, *J* = 8.6, 1.9 Hz, 1H), 6.20 (d, *J* = 8.5 Hz, 1H), 1.66 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 178.2, 149.5, 139.2, 139.1, 138. 9, 128.0, 125.8, 125.0, 120.1, 112.2, 87.2, 28.0.

***tert*-Butyl 6-fluoro-4-oxoquinoline-1(4H)-carboxylate (1k)**



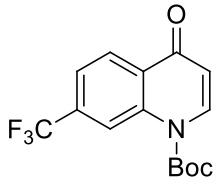

White solid, 400 mg, 51% yield, m.p. 100 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.67 (dd, *J* = 9.6, 4.6 Hz, 1H), 8.32 (d, *J* = 8.5 Hz, 1H), 8.01 (dd, *J* = 8.6, 3.4 Hz, 1H), 7.37 (ddd, *J* = 10.0, 7.3, 3.1 Hz, 1H), 6.24 (d, *J* = 8.4 Hz, 1H), 1.68 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 178.1, 159.7 (d, *J* = 247.8 Hz), 149.7, 138.9, 135.0, 128.5 (d, *J* = 6.8 Hz), 122.8 (d, *J* = 7.4 Hz), 120.6 (d, *J* = 23.9 Hz), 111.3 (d, *J* = 22.9 Hz), 111.2, 87.0, 28.0. $^{19}$F NMR (376 MHz, $CDCl_3$) δ –115.56 (q, *J* = 7.0 Hz).

***tert*-Butyl 4-oxo-6-(trifluoromethyl)quinoline-1(4H)-carboxylate (1l)**




White solid, 640 mg, 68% yield, m.p. 158 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 9.2 Hz, 1H), 8.67 (br s, 1H), 8.34 (d, *J* = 8.5 Hz, 1H), 7.85 (dd, *J* = 9.3, 2.4 Hz, 1H), 6.31 (d, *J* = 8.6 Hz, 1H), 1.69 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 178.1, 149.6, 140.7, 139.4, 128.8 (d, *J* = 3.7 Hz), 127.4 (q, *J* = 33.7 Hz), 126.5, 124.4 (d, *J* = 4.3 Hz), 123.8 (q, *J* = 272.2 Hz), 121.2, 112.6, 87.6, 28.0. $^{19}$F NMR (376 MHz, $CDCl_3$) δ –62.52.

***tert*-Butyl 4-oxo-7-(trifluoromethyl)quinoline-1(4H)-carboxylate (1m)**




Colourless solid, 640 mg, 68% yield, m.p.138°C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.98 (br s, 1H), 8.49 (d, *J* = 8.4 Hz, 1H), 8.40 (d, *J* = 8.5 Hz, 1H), 7.65 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.32 (d, *J* = 8.5 Hz, 1H), 1.70 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 178.1, 149.6, 139.5, 138.4, 134.1 (q, *J* = 32.6 Hz), 128.6,

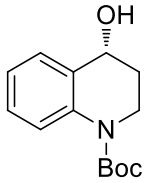
127.8, 123.7 (q, $J$ = 273.2 Hz), 121.4 (d, $J$ = 3.8 Hz), 118.2 (q, $J$ = 4.4 Hz), 112.6, 87.8, 28.0. $^{19}$F NMR (376 MHz, $CDCl_3$) δ –62.95.

## IV. General procedure for the synthesis of diols 2a–2m by ATH of compounds 1a–1m

In a round-bottom tube charged with complex (*R*,*R*)-**3a** (5.0 $\mu$mol, 0.01 equiv) was added under argon a solution of the ketone **1** (0.50 mmol, 1.0 equiv) in anhydrous $CH_2Cl_2$ (0.5 mL), then $HCO_2H/NEt_3$ (5:2) azeotropic mixture (170 $\mu$L, 2.0 mmol, 4.0 equiv) was added dropwise. The mixture was stirred under argon at 30 °C for 16 h, then quenched with water (5.0 mL) and extracted with $CH_2Cl_2$ (3*15 mL). The combined organic phases were washed with brine, dried with $MgSO_4$, filtered and concentrated under vacuum. Purification of the residue by flash column chromatography (petroleum ether/ethyl acetate 2:1) afforded compound **2** and the enantiomeric excess was determined by SFC analysis.

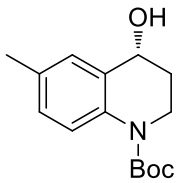
## V. Analytical data for compounds 2a–2m

**(*R*)-*tert*-Butyl 4-hydroxy-3,4-dihydroquinoline-1(2H)-carboxylate (2a)**[2]



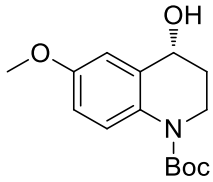

White solid, 103 mg, 83% yield, *ee* > 99%, m.p. 85°C, $[\alpha]_D^{25}$ = +33.0 (*c* 0.96, $CHCl_3$), lit.[2] $[\alpha]_D^{25}$ = − 27.7 (*c* 1.04, $CHCl_3$) for the (*S*)-enantiomer. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, $J$ = 8.4 Hz, 1H), 7.38 (dd, $J$ = 7.6, 1.6 Hz, 1H), 7.25 (ddd, $J$ = 8.6, 7.3, 1.7 Hz, 1H), 7.07 (td, $J$ = 7.5, 1.2 Hz, 1H), 4.76 (q, $J$ = 4.8 Hz, 1H), 4.04 (ddd, $J$ = 13.1, 5.5, 4.7 Hz, 1H), 3.59 (ddd, $J$ = 13.4, 9.8, 4.0 Hz, 1H), 2.14 – 1.97 (m, 2H), 1.79 (d, $J$ = 5.1 Hz, 1H), 1.53 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 153.7, 137.9, 130.7, 128.3, 128.1, 123.8, 123.6, 81.3, 66.0, 40.6, 32.1, 28.5.
SFC: Chiralpak AS-H, *sc*$CO_2$/ MeOH 98/2, 3.0 mL/min, P = 100 bar, λ = 254 nm, $t_S$ = 5.30 min, $t_R$ = 6.31 min.

**(*R*)-*tert*-Butyl 4-hydroxy-6-methyl-3,4-dihydroquinoline-1(2H)-carboxylate (2b)**




White solid, 104 mg, 79% yield, *ee* > 99%, m.p. 111 °C, $[\alpha]_D^{25}$ = +20.9 (*c* 0.96, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, $J$ = 8.5 Hz, 1H), 7.18 (br, 1H), 7.05 (dd, $J$ = 8.5, 2.1 Hz, 1H), 4.73 (q, $J$ = 4.8 Hz, 1H), 4.04 (dt, $J$ = 13.1, 5.0 Hz, 1H), 3.56 (ddd, $J$ = 13.4, 9.9, 3.9 Hz, 1H), 2.31 (s, 3H), 2.10 – 1.94 (m, 2H), 1.80 (d, $J$ = 5.2 Hz, 1H), 1.52 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 153.7, 135.3, 133.1, 130.5, 128.8, 128.7, 123.6, 81.1, 66.0, 40.6, 32.2, 28.5, 20.8.
HRMS (ESI/ion trap): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{21}NNaO_3$ 286.1419, found 286.1415.
SFC: Chiralpak AS-H, *sc*$CO_2$/ MeOH 95/5, 2.0 mL/min, P = 100 bar, λ = 254 nm, $t_S$ =3.91 min, $t_R$ = 4.61 min.

**(*R*)-*tert*-Butyl 4-hydroxy-6-methoxy-3,4-dihydroquinoline-1(2H)-carboxylate (2c)**

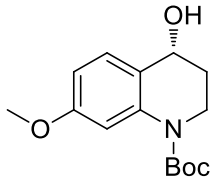



Light yellow oil, 105 mg, 75% yield, *ee* > 99%, $[\alpha]_D^{25}$ = +18.8 (*c* 1.17, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 9.1 Hz, 1H), 6.92 (d, *J* = 3.0 Hz, 1H), 6.80 (dd, *J* = 9.1, 3.0 Hz, 1H), 4.72 (q, *J* = 5.0 Hz, 1H), 3.99 (ddd, *J* = 13.1, 6.3, 4.3 Hz, 1H), 3.79 (s, 3H), 3.56 (ddd, *J* = 13.2, 9.5, 3.8 Hz, 1H), 2.09 (ddt, *J* = 14.0, 9.3, 4.5 Hz, 1H), 2.00 – 1.92 (m, 2H), 1.51 (s, 9H). $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 155.8, 153.8, 132.1, 131.1, 125.2, 114.2, 112.2, 81.1, 66.2, 55.6, 40.8, 32.5, 28.5.

HRMS (ESI/ion trap): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{21}NNaO_4$ 302.1368, found 302.1364.

SFC: Chiralpak AS-H, *sc*$CO_2$/ MeOH 95/5, 2.0 mL/min, P = 100 bar, λ = 254 nm, $t_S$ =4.66 min, $t_R$ = 5.73 min.

**(*R*)-*tert*-Butyl 4-hydroxy-7-methoxy-3,4-dihydroquinoline-1(2H)-carboxylate (2d)**

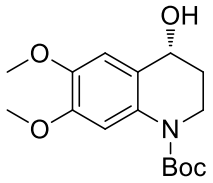



Light yellow solide, 70 mg, 50% yield, *ee* = 99%, m.p. 95°C, $[\alpha]_D^{25}$ = + 9.3 (*c* 1.02, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 2.5 Hz, 1H), 7.26 (d, *J* = 8.5 Hz, 1H), 6.65 (dd, *J* = 8.5, 2.6 Hz, 1H), 4.73 (q, *J* = 4.4 Hz, 1H), 4.08 (dt, *J* = 13.0, 4.8 Hz, 1H), 3.80 (s, 3H), 3.55 (ddd, *J* = 13.2, 7.9, 6.3 Hz, 1H), 2.03 – 1.98 (m, 2H), 1.76 (d, *J* = 4.6 Hz, 1H), 1.54 (s, 9H). $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 159.3, 153.6, 139.1, 129.6, 123.0, 110.3, 108.4, 81.4, 65.6, 55.5, 40.5, 32.0, 28.5.

HRMS (ESI/ion trap): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{21}NNaO_4$ 302.1368, found 302.1363.

SFC: Chiralpak IF, *sc*$CO_2$/ MeOH 90/10, 2.0 mL/min, P = 100 bar, λ = 254 nm, $t_R$ =7.45 min, $t_S$ = 9.38 min.

**(*R*)-*tert*-Butyl 4-hydroxy-6,7-dimethoxy-3,4-dihydroquinoline-1(2H)-carboxylate (2e)**

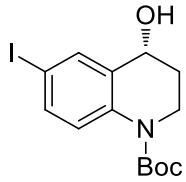



White solid, 36 mg, 23% yield, *ee* = 97%, m.p. 94°C, $[\alpha]_D^{25}$ = +30.7 (*c* 0.57, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.40 (s, 1H), 6.86 (s, 1H), 4.70 (br, 1H), 4.06 (ddd, *J* = 13.1, 5.6, 3.9 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.52 (ddd, *J* = 13.4, 10.3, 3.4 Hz, 1H), 2.11 – 1.93 (m, 2H), 1.84 (br s, 1H), 1.53 (s, 9H). $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 153.6, 148.3, 145.6, 131.6, 122.4, 110.8, 107.5, 81.2, 65.8, 56.2, 56.1, 40.7, 32.6, 28.6.

HRMS (ESI/ion trap): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{23}NNaO_5$ 332.1474, found 332.1469.

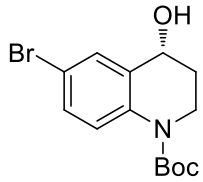
SFC: Chiralpak AS-H, *sc*$CO_2$/ MeOH 97/3, 3.0 mL/min, P = 100 bar, λ = 254 nm, $t_S$ = 5.09 min, $t_R$ = 6.55 min.

**(*R*)-*tert*-Butyl 4-hydroxy-6-iodo-3,4-dihydroquinoline-1(2H)-carboxylate (2f)**



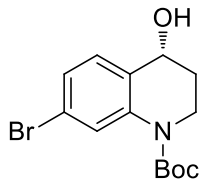

White solid, 120 mg, 64% yield, *ee* > 99%, m.p. 150°C, $[\alpha]_D^{25}$ = +4.7 (*c* 0.94, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 1.9 Hz, 1H), 7.58 (d, *J* = 8.8 Hz, 1H), 7.51 (dd, *J* = 8.9, 2.2 Hz, 1H), 4.70 (q, *J* = 5.1 Hz, 1H), 3.99 (ddd, *J* = 13.1, 6.2, 4.5 Hz, 1H), 3.59 (ddd, *J* = 13.3, 9.5, 4.0 Hz, 1H), 2.10 – 2.01 (m, 1H), 1.99 – 1.92 (m, 1H), 1.87 (d, *J* = 5.4 Hz, 1H), 1.52 (s, 9H). $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 153.4, 137.6, 136.8, 136.8, 133.1, 125.6, 86.8, 81.8, 65.6, 40.7, 31.9, 28.4.
HRMS (ESI/ion trap): *m/z* $[M + Na]^+$ calcd for $C_{14}H_{18}INNaO_3$ 398.0229, found 398.0224.
SFC: Chiralpak AS-H, *sc*$CO_2$/ MeOH 97/3, 3.0 mL/min, P = 100 bar, λ = 254 nm, $t_S$ = 8.23 min, $t_R$ = 9.72 min.

**(*R*)-*tert*-Butyl 6-bromo-4-hydroxy-3,4-dihydroquinoline-1(2H)-carboxylate (2g)**[3]



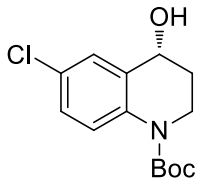

White solid, 120 mg, 73% yield, *ee* > 99%, m.p. 131°C, $[\alpha]_D^{25}$ = +12.0 (*c* 1.2, $CHCl_3$), lit.[3] $[\alpha]_D^{25}$ = – 11.2 (*c* 0.64, $CHCl_3$) for the (*S*)-enantiomer. $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.9 Hz, 1H), 7.52 (dd, *J* = 2.3, 0.5 Hz, 1H), 7.33 (dd, *J* = 8.9, 2.3 Hz, 1H), 4.71 (q, *J* = 5.1 Hz, 1H), 3.98 (ddd, *J* = 13.0, 6.4, 4.5 Hz, 1H), 3.59 (ddd, *J* = 13.2, 9.4, 4.0 Hz, 1H), 2.07 (ddt, *J* = 13.8, 9.1, 4.5 Hz, 1H), 2.00 – 1.91 (m, 2H), 1.52 (s, 9H). $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 153.5, 136.8, 133.0, 130.8, 130.7, 125.3, 116.2, 81.7, 65.6, 40.8, 32.0, 28.4.
SFC: Chiralpak AS-H, *sc*$CO_2$/ MeOH 98/2, 2.0 mL/min, P = 100 bar, λ = 254 nm, $t_R$ = 17.79 min, $t_S$ = 21.42 min.

**(*R*)-*tert*-Butyl 7-bromo-4-hydroxy-3,4-dihydroquinoline-1(2H)-carboxylate (2h)**



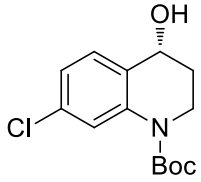

White solid, 110 mg, 67% yield, *ee* > 99%, m.p. 114°C, $[\alpha]_D^{25}$ = +5.7 (*c* 1.04, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 1.9 Hz, 1H), 7.24 (d, *J* = 8.2 Hz, 1H), 7.18 (dd, *J* = 8.2, 1.9 Hz, 1H), 4.71 (q, *J* = 4.8 Hz, 1H), 4.01 (ddd, *J* = 13.1, 5.9, 4.5 Hz, 1H), 3.59 (ddd, *J* = 13.4, 9.6, 4.1 Hz, 1H), 2.10 – 1.93 (m, 2H), 1.83 (d, *J* = 5.2 Hz, 1H), 1.54 (s, 9H). $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 153.3, 139.0, 129.6, 129.4, 126.3, 126.3, 121.6, 81.9, 65.6, 40.6, 31.7, 28.4.
HRMS (ESI/ion trap): *m/z* $[M + Na]^+$ calcd for $C_{14}H_{18}BrNNaO_3$ 350.0368, found 350.0362.
SFC: Chiralpak IF, *sc*$CO_2$/ MeOH 90/10, 2.0 mL/min, P = 100 bar, λ = 254 nm, $t_R$ = 8.35 min, $t_s$ = 8.95 min.

**(*R*)-*tert*-Butyl 6-chloro-4-hydroxy-3,4-dihydroquinoline-1(2H)-carboxylate (2i)**[3]



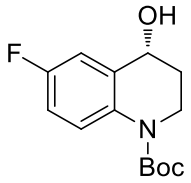

White solid, 95 mg, 67% yield, *ee* > 99%, m.p. 104°C, $[\alpha]_D^{25}$ = +19.5 (*c* 1.06, $CHCl_3$), lit.[3] $[\alpha]_D^{25}$ = –17.2 (*c* 0.71, $CHCl_3$) for the (*S*)-enantiomer. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.9 Hz, 1H), 7.35 (d, *J* = 2.5 Hz, 1H), 7.16 (dd, *J* = 9.0, 2.6 Hz, 1H), 4.65 (q, *J* = 5.1 Hz, 1H), 3.93 (ddd, *J* = 13.0, 6.6, 4.5 Hz, 1H), 3.56 (ddd, *J* = 13.1, 9.2, 4.0 Hz, 1H), 2.49 (d, *J* = 5.1 Hz, 1H), 2.08 – 2.00 (m, 1H), 1.94 – 1.87 (m, 1H), 1.51 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 153.6, 136.2, 132.6, 128.5, 127.8, 127.7, 125.0, 81.7, 65.6, 40.8, 32.0, 28.4.
SFC: Chiralpak AD-H, *sc*$CO_2$/ MeOH 80/20, 2.0 mL/min, P = 100 bar, λ = 254 nm, $t_S$ = 3.77 min, $t_R$ = 5.75 min.

**(*R*)-*tert*-Butyl 7-chloro-4-hydroxy-3,4-dihydroquinoline-1(2H)-carboxylate (2j)**[4]




White solid, 94 mg, 66% yield, *ee* > 99%, m.p. 94°C, $[\alpha]_D^{25}$ = +12.0 (*c* 0.94, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 2.1 Hz, 1H), 7.28 (d, *J* = 8.3 Hz, 1H), 7.01 (dd, *J* = 8.2, 2.1 Hz, 1H), 4.69 (br, 1H), 3.98 (ddd, *J* = 13.1, 5.9, 4.5 Hz, 1H), 3.57 (ddd, *J* = 13.4, 9.7, 4.1 Hz, 1H), 2.19 (br s, 1H), 2.06 – 1.91 (m, 2H), 1.53 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 153.4, 138.8, 133.6, 129.4, 128.9, 123.4, 123.4, 81.9, 65.5, 40.6, 31.7, 28.4.
SFC: Chiralpak IF, *sc*$CO_2$/ MeOH 90/10, 2.0 mL/min, P = 100 bar, λ = 254 nm, $t_R$ = 7.97 min, $t_s$ = 8.85 min.

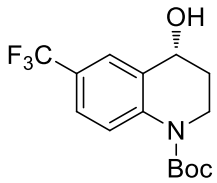
**(*R*)-*tert*-Butyl 6-fluoro-4-hydroxy-3,4-dihydroquinoline-1(2H)-carboxylate (2k)**




White solid, 97 mg, 73% yield, *ee* > 99%, m.p. 100°C, $[\alpha]_D^{25}$ = +26.5 (*c* 0.99, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 9.2, 5.1 Hz, 1H), 7.11 (dd, *J* = 8.8, 3.1 Hz, 1H), 6.94 (td, *J* = 8.6, 3.0 Hz, 1H), 4.72 (q, *J* = 5.4 Hz, 1H), 3.98 (ddd, *J* = 12.9, 6.6, 4.6 Hz, 1H), 3.59 (ddd, *J* = 13.0, 9.1, 4.0 Hz, 1H), 2.11 (ddt, *J* = 13.7, 9.2, 4.6 Hz, 1H), 2.00 – 1.90 (m, 2H), 1.52 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 158.9 (d, *J* = 243.4 Hz), 153.8, 133.7 (d, *J* = 2.8 Hz), 133.1 (d, *J* = 6.7 Hz), 125.5 (d, *J* = 7.8 Hz), 114.7 (d, *J* = 22.3 Hz), 114.0 (d, *J* = 22.6 Hz), 81.4, 65.8, 40.9, 32.4, 28.4. $^{19}$F NMR (376 MHz, $CDCl_3$) δ –119.37 (q, *J* = 7.4 Hz).
HRMS (ESI/ion trap): *m/z* $[M + Na]^+$ calcd for $C_{14}H_{18}FNNaO_3$ 290.1168, found 290.1166.

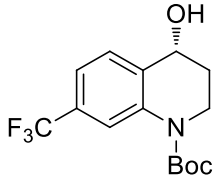
SFC: Chiralpak AD-H, *sc*$CO_2$/ MeOH 80/20, 2.0 mL/min, P = 100 bar, λ = 254 nm, $t_S$ = 2.55 min, $t_R$ = 3.38 min.

**(*R*)-*tert*-Butyl 4-hydroxy-6-(trifluoromethyl)-3,4-dihydroquinoline-1(2H)-carboxylate (2l)**



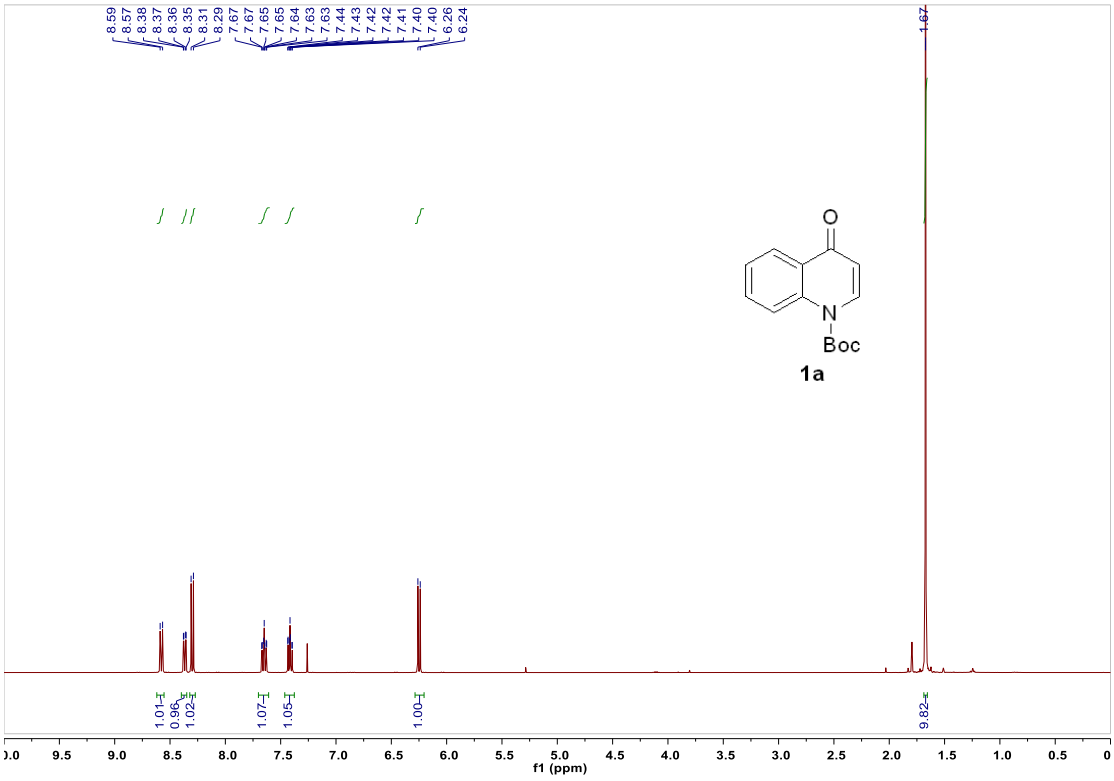

White solid, 105 mg, 66% yield, *ee* > 99%, m.p. 93°C, $[\alpha]_D^{25}$ = +36.1 (*c* 1.18, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.8 Hz, 1H), 7.66 (br d, *J* = 1.8 Hz, 1H), 7.48 (dd, *J* = 8.9, 2.2 Hz, 1H), 4.79 (q, *J* = 5.2 Hz, 1H), 4.02 (ddd, *J* = 13.1, 6.4, 4.6 Hz, 1H), 3.66 (ddd, *J* = 13.2, 9.4, 4.1 Hz, 1H), 2.11 (ddt, *J* = 13.8, 9.2, 4.4 Hz, 1H), 2.05 – 1.96 (m, 1H), 1.91 (d, *J* = 5.4 Hz, 1H), 1.54 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 153.5, 140.8, 130.9, 125.2 (d, *J* = 4.1 Hz), 124.9 (d, *J* = 4.3 Hz), 124.3 (q, *J* = 271.4 Hz), 123.5, 82.1, 65.8, 40.9, 31.8, 28.4. $^{19}$F NMR (376 MHz, $CDCl_3$) δ –62.10.
HRMS (ESI/ion trap): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{18}F_3NNaO_3$ 340.1136, found 340.1131.
SFC: Chiralpak AD-H, *sc*$CO_2$/ MeOH 80/20, 2.0 mL/min, P = 100 bar, λ = 254 nm, $t_S$ = 2.46 min, $t_R$ = 3.13 min.

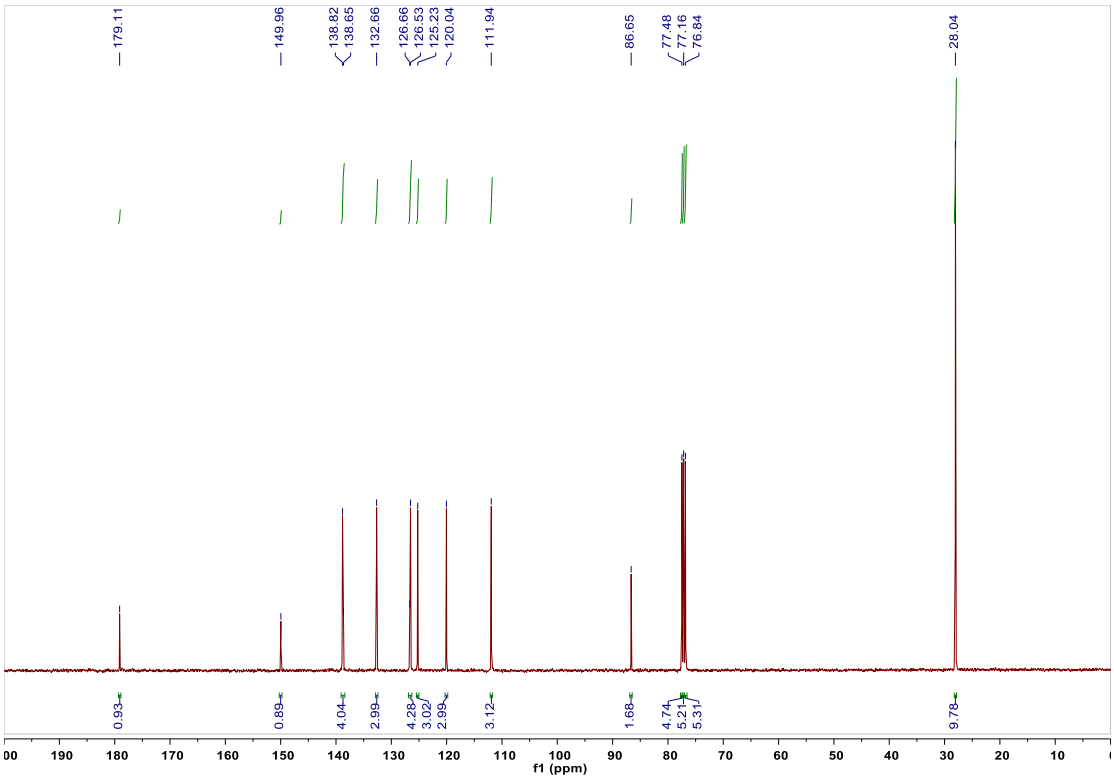
**(*R*)-*tert*-Butyl 4-hydroxy-7-(trifluoromethyl)-3,4-dihydroquinoline-1(2H)-carboxylate (2m)**

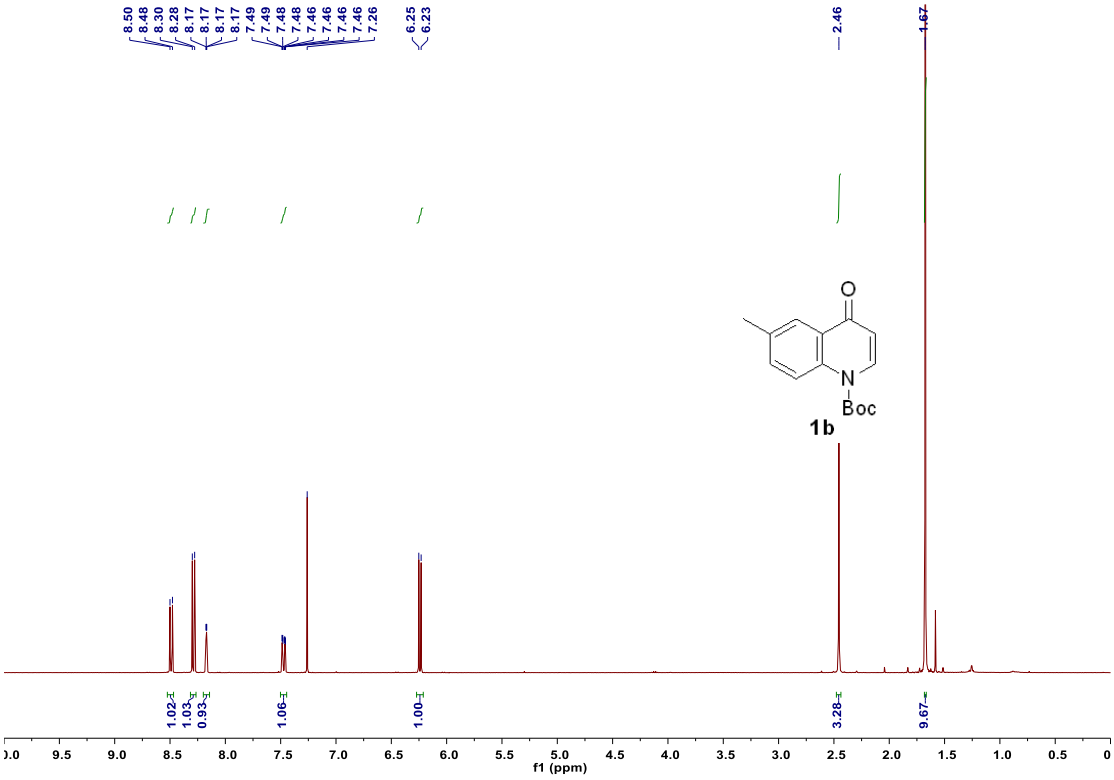


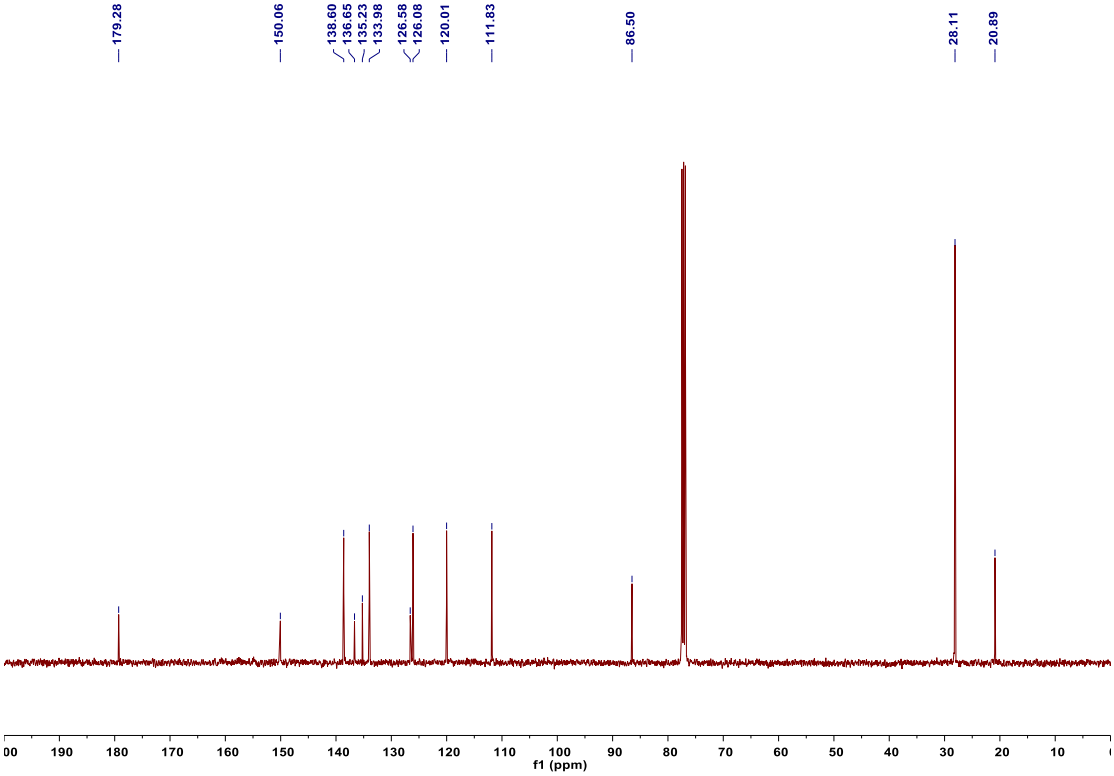

White solid, 106 mg, 67% yield, *ee* > 99%, m.p. 114°C, $[\alpha]_D^{25}$ = +31.7 (*c* 1.0, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.31 (ddd, *J* = 8.0, 1.8, 0.8 Hz, 1H), 4.79 (q, *J* = 5.2 Hz, 1H), 4.03 (ddd, *J* = 13.1, 6.6, 4.5 Hz, 1H), 3.64 (ddd, *J* = 13.2, 9.3, 4.0 Hz, 1H), 2.12 (ddt, *J* = 13.7, 9.1, 4.5 Hz, 1H), 2.00 (dddd, *J* = 13.7, 6.6, 5.6, 4.0 Hz, 1H), 1.88 (d, *J* = 5.4 Hz, 1H), 1.54 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 153.4, 138.1, 134.1, 130.16 (q, *J* = 32.1 Hz), 128.5, 124.1 (q, *J* = 272.2 Hz), 120.8 (d, *J* = 4.5 Hz), 119.7 (d, *J* = 4.1 Hz), 82.2, 65.8, 40.7, 31.9, 28.4. $^{19}$F NMR (376 MHz, $CDCl_3$) δ –62.74.
HRMS (ESI/ion trap): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{18}F_3NNaO_3$ 340.1136, found 340.1131.
SFC: Chiralpak IF, *sc*$CO_2$/ $^i$PrOH 97/3, 2.0 mL/min, P = 100 bar, λ = 254 nm, $t_R$ =13.7 min, $t_s$ = 14.7 min.

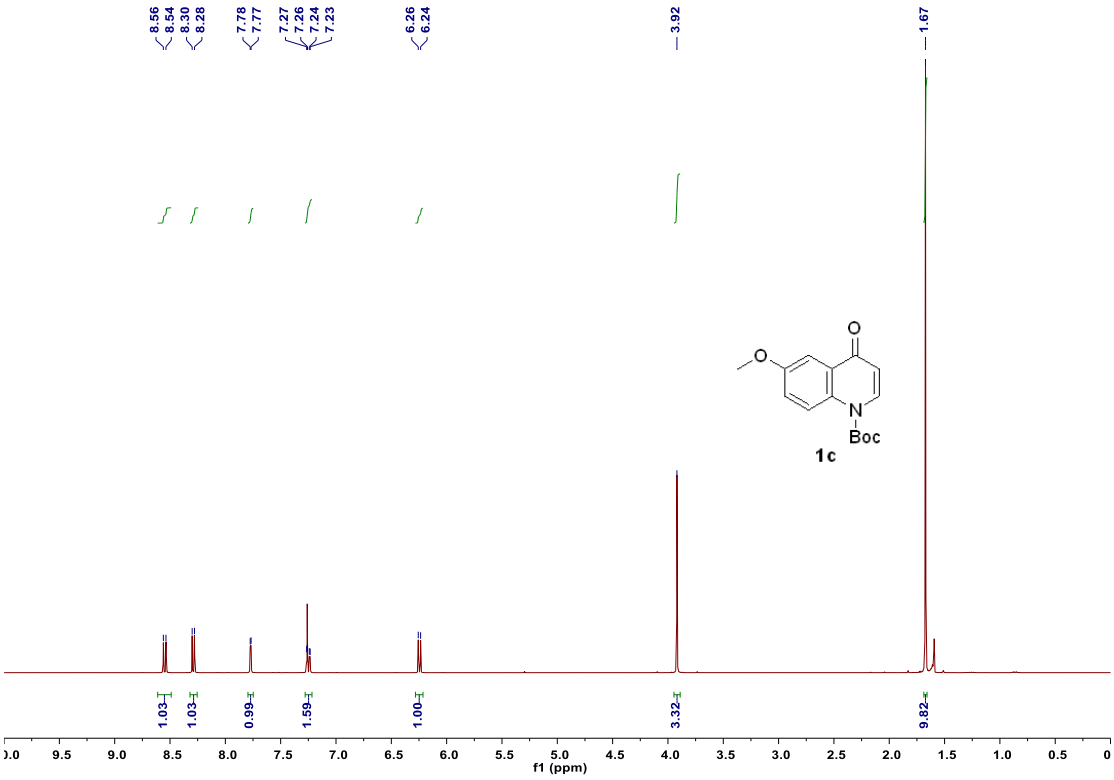
## VI. NMR spectra of compounds 1a–1m

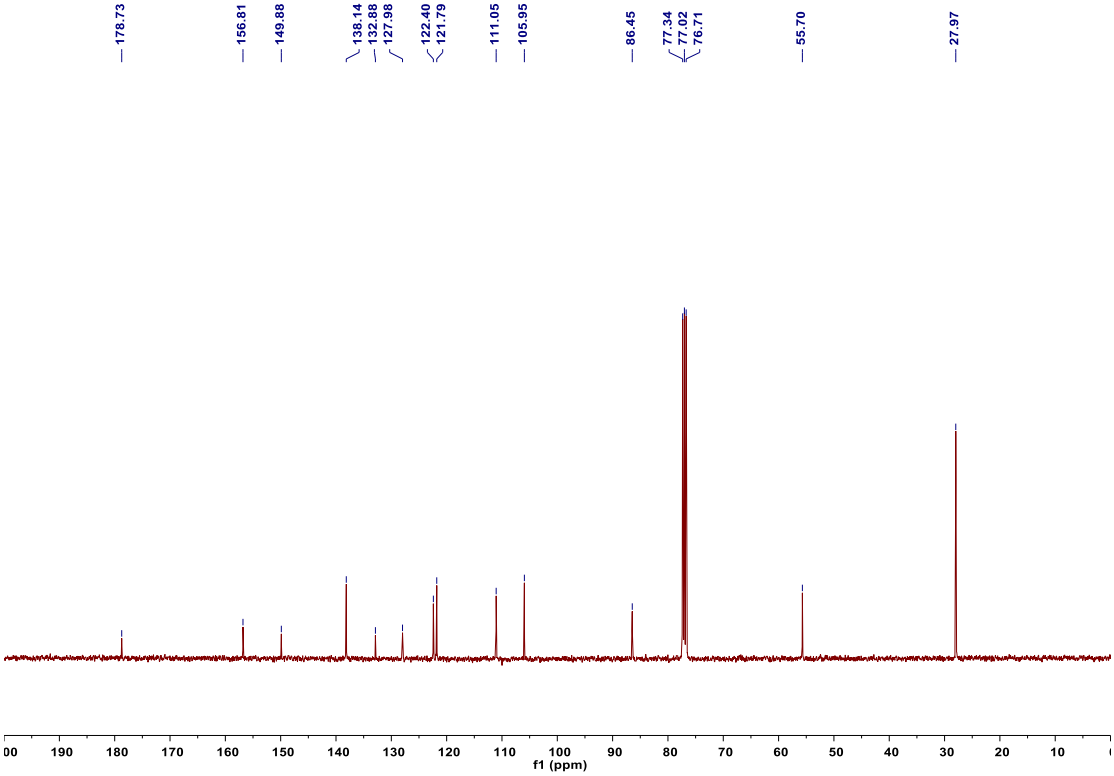


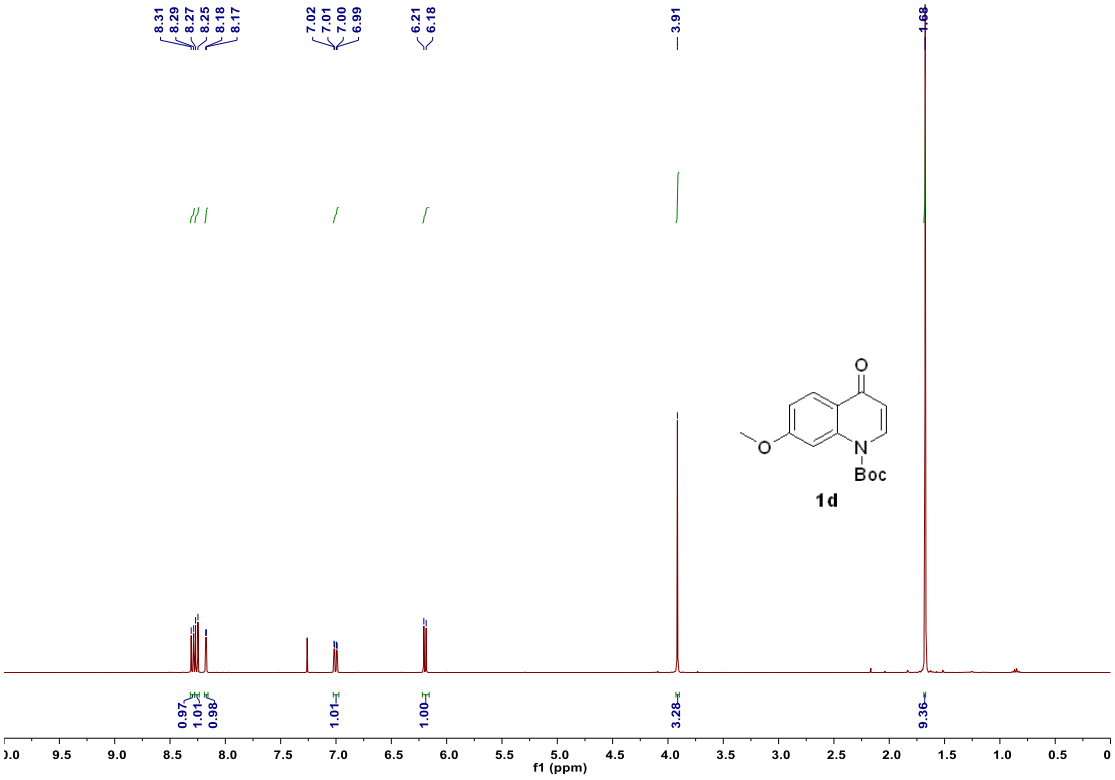



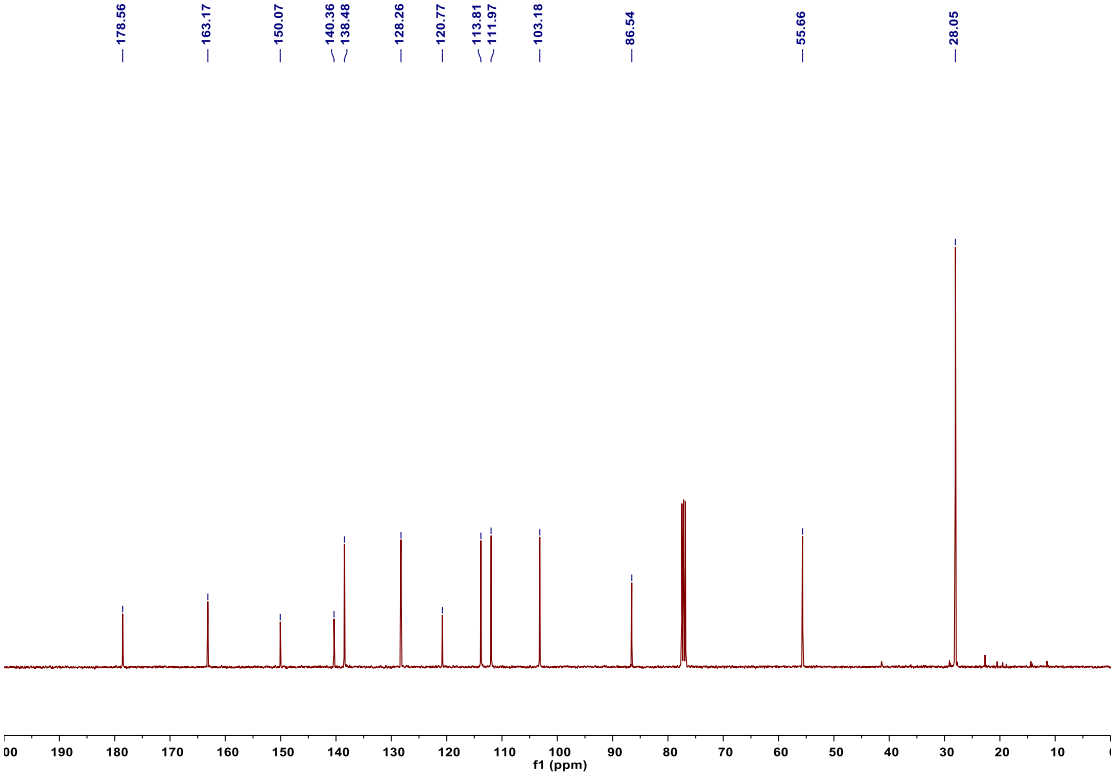

8.50
8.48
8.30
8.28
8.17
8.17
8.17
8.17
7.49
7.49
7.48
7.48
7.46
7.46
7.46
7.46
7.26
6.25
6.23
2.46
1.67
O
N
Boc
1b
1.02
1.03
0.93
1.06
1.00
3.28
9.67
f1 (ppm)

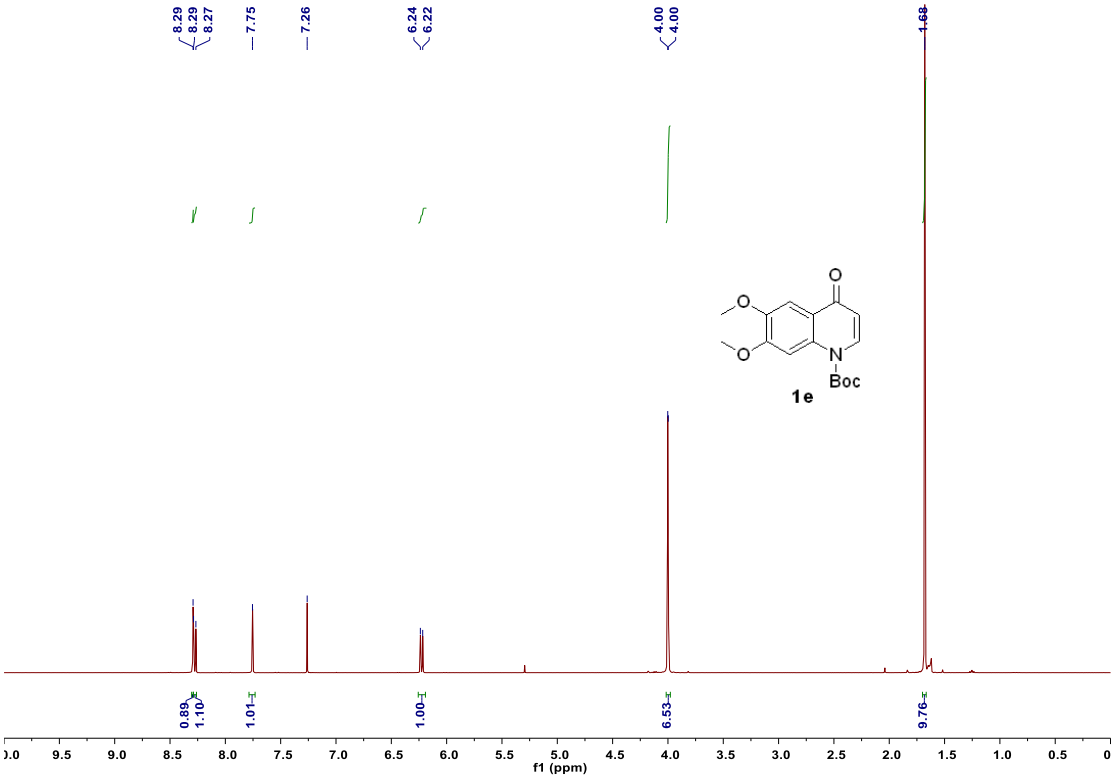

179.28
150.06
138.60
136.65
135.23
133.98
126.58
126.08
120.01
111.83
86.50
28.11
20.89
f1 (ppm)

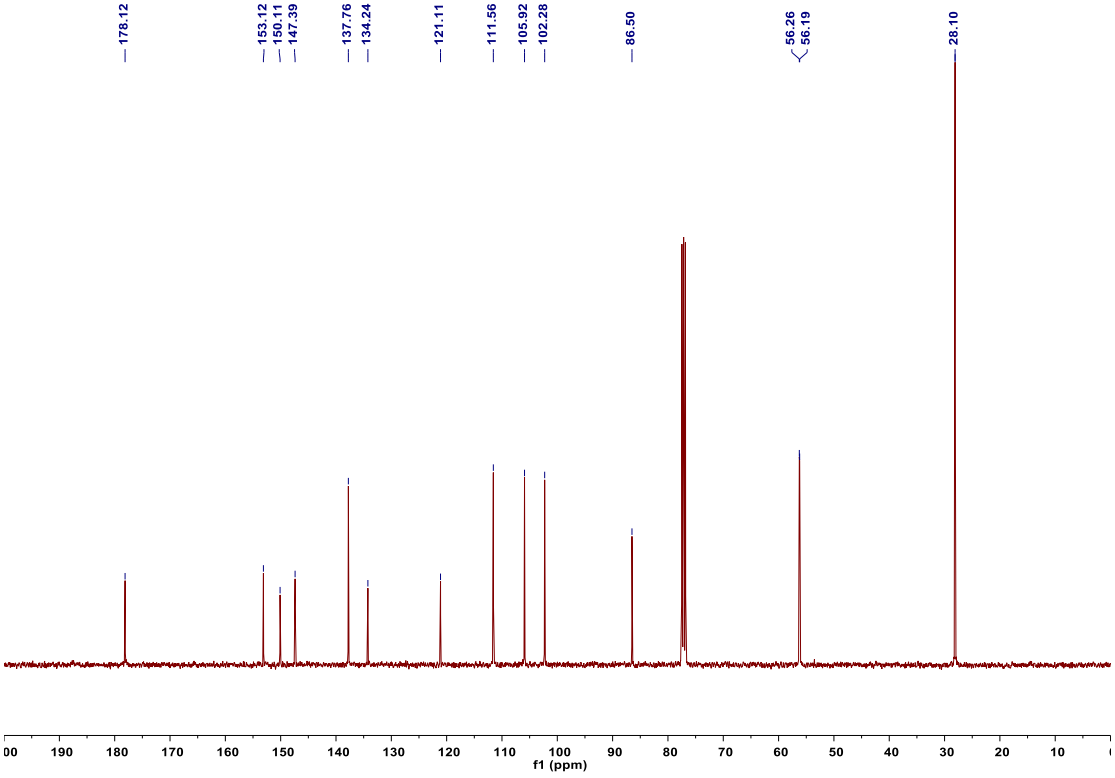

8.56
8.54
8.30
8.28
7.78
7.77
7.27
7.26
7.24
7.23
6.26
6.24
3.92
1.67
O
O
N
Boc
1c
1.03
1.03
0.99
1.59
1.00
3.32
9.82
f1 (ppm)

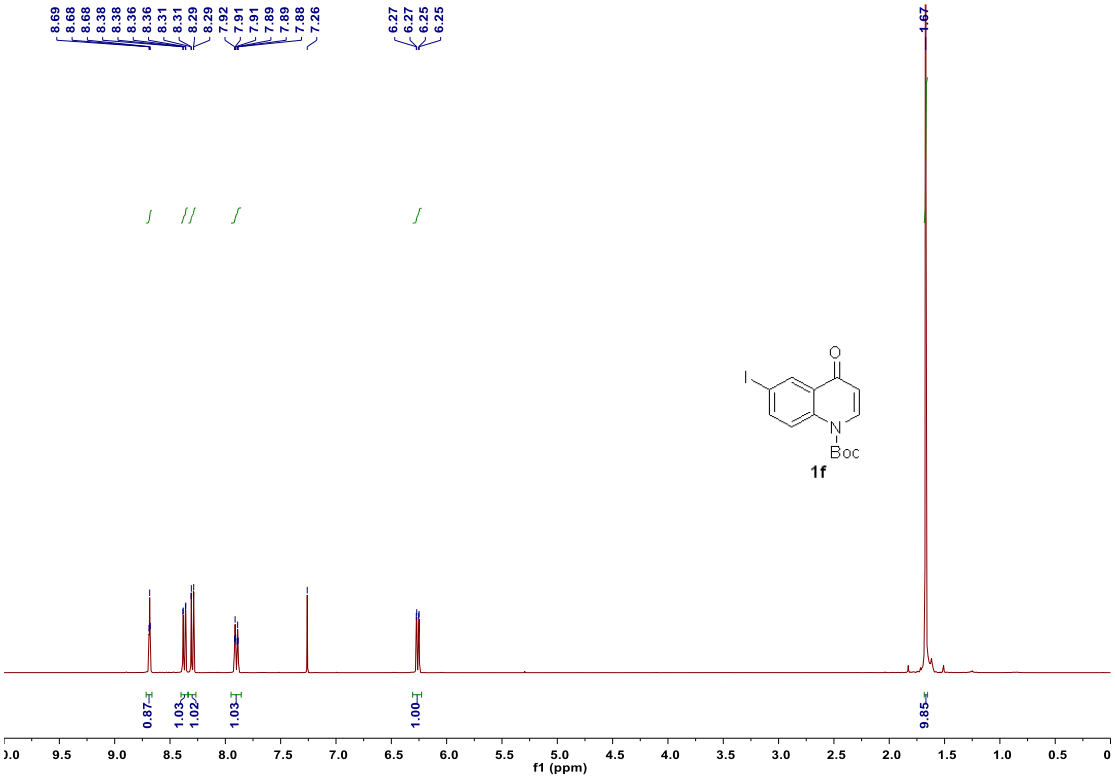

178.73
156.81
149.88
138.14
132.88
127.98
122.40
121.79
111.05
105.95
86.45
77.34
77.02
76.71
55.70
27.97
f1 (ppm)

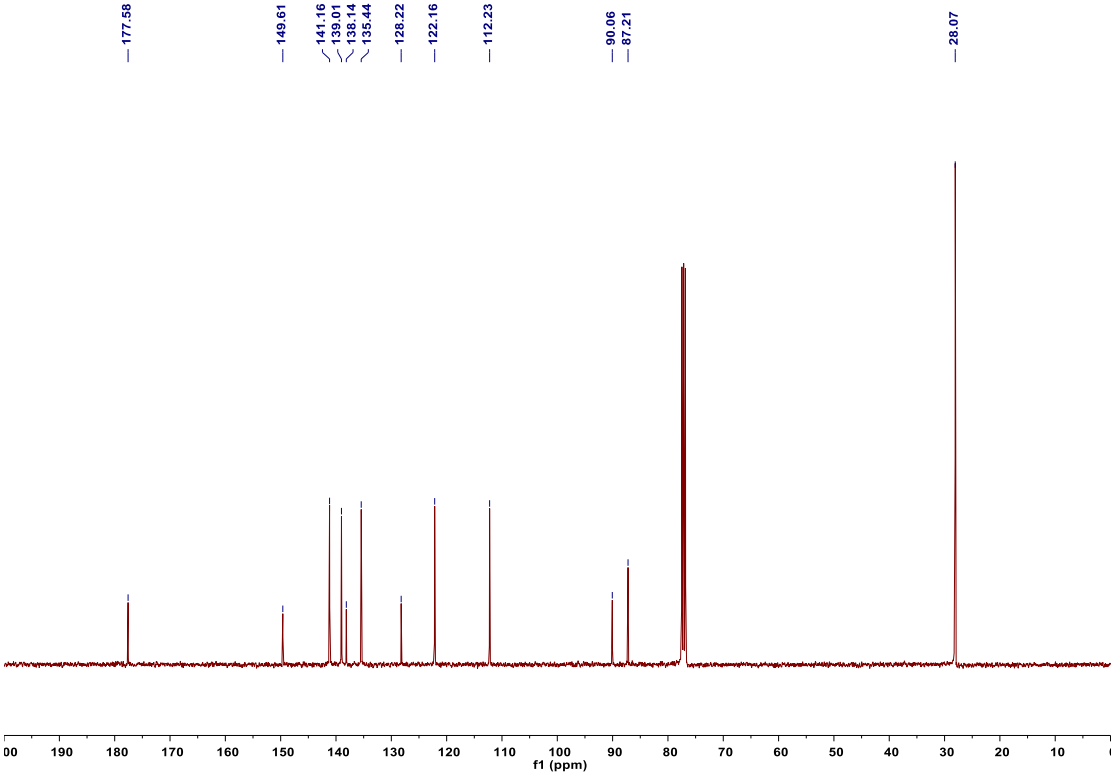

8.31
8.29
8.27
8.25
8.18
8.17
7.02
7.01
7.00
6.99
6.21
6.18
3.91
1.68
O
O
N
Boc
1d
0.97
1.01
0.98
1.01
1.00
3.28
9.36
f1 (ppm)

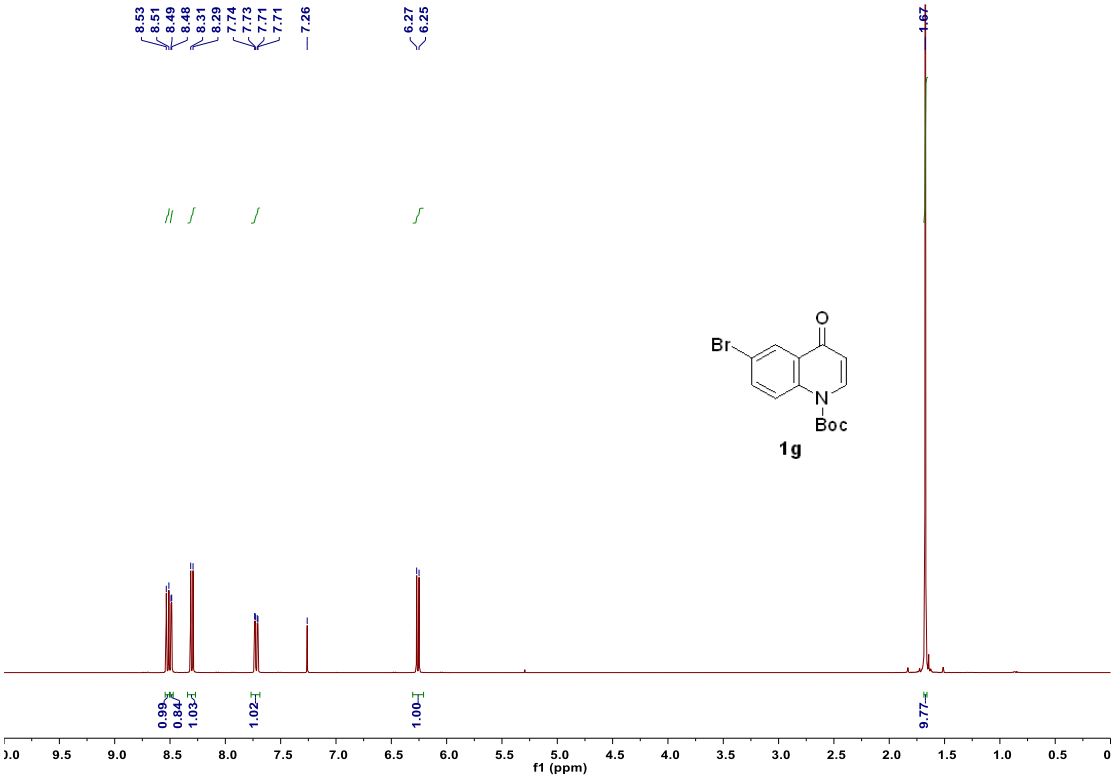

178.56
163.17
150.07
140.36
138.48
128.26
120.77
113.81
111.97
103.18
86.54
55.66
28.05
f1 (ppm)

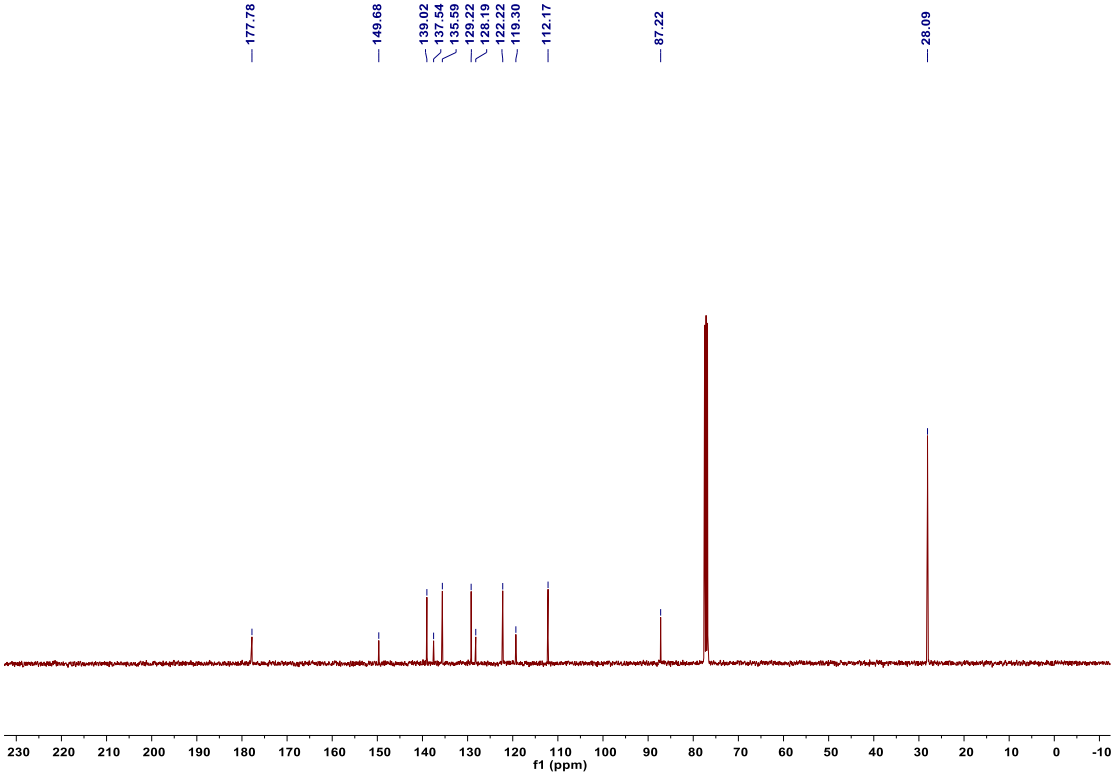

8.29
8.29
8.27
7.75
7.26
6.24
6.22
4.00
4.00
1.68
O
O
O
N
Boc
1e
0.89
1.10
1.01
1.00
6.53
9.76
f1 (ppm)

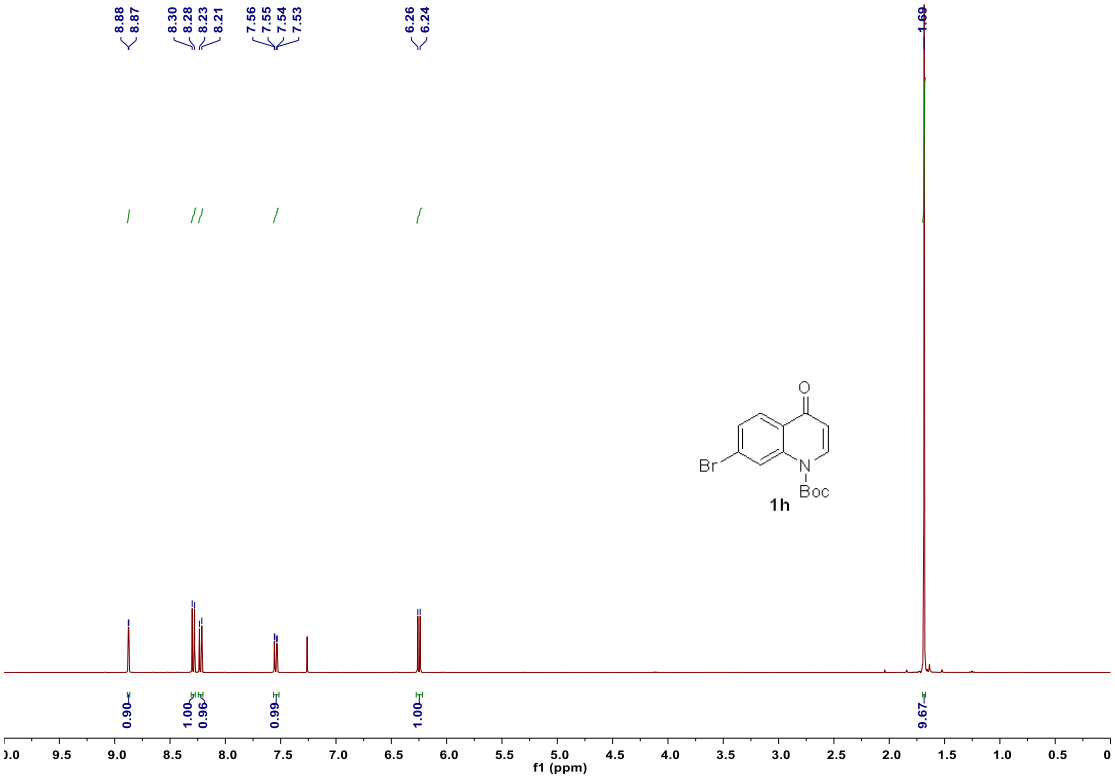

178.12
153.12
150.11
147.39
137.76
134.24
121.11
111.56
105.92
102.28
86.50
56.26
56.19
28.10
f1 (ppm)

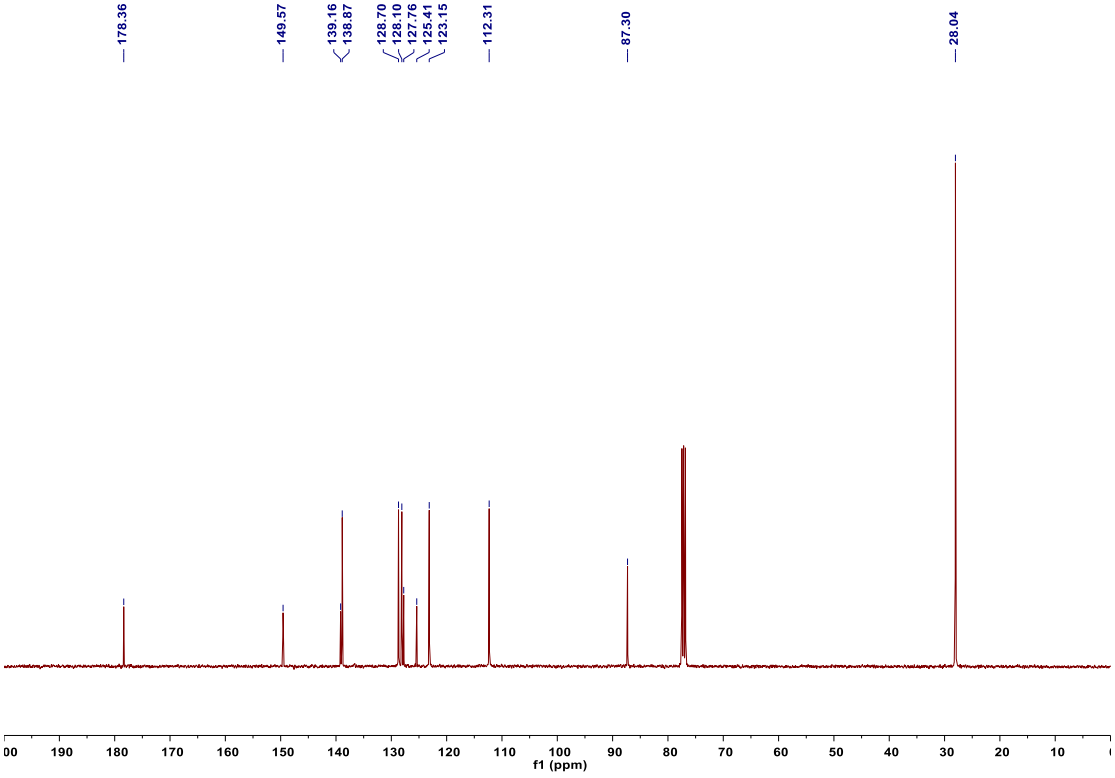

8.69
8.68
8.68
8.38
8.38
8.36
8.36
8.31
8.31
8.29
8.29
7.92
7.91
7.91
7.89
7.89
7.88
7.26
6.27
6.27
6.25
6.25
1.67
0.87
1.03
1.02
1.03
1.00
9.85
f1 (ppm)
O
I
N
Boc
1f

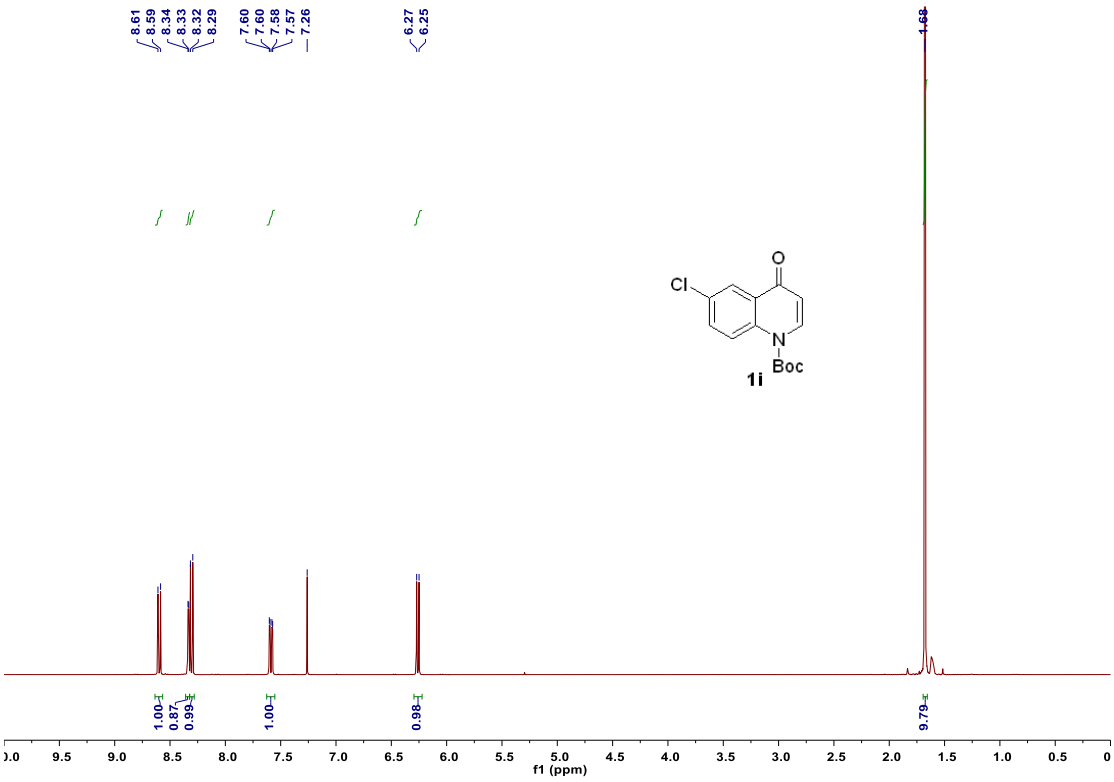

177.58
149.61
141.16
139.01
138.14
135.44
128.22
122.16
112.23
90.06
87.21
28.07
f1 (ppm)

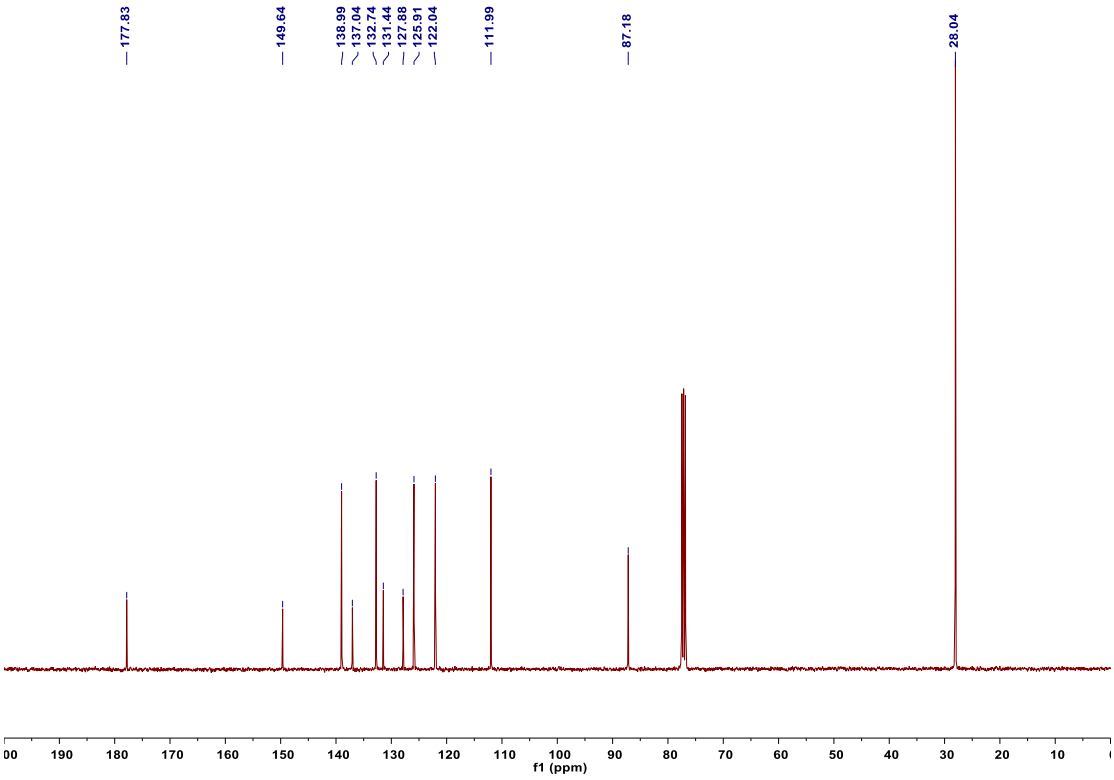

8.53
8.51
8.49
8.48
8.31
8.29
7.74
7.73
7.71
7.71
7.26
6.27
6.25
1.67
Br
O
N
Boc
1g
0.99
0.84
1.03
1.02
1.00
9.77
f1 (ppm)

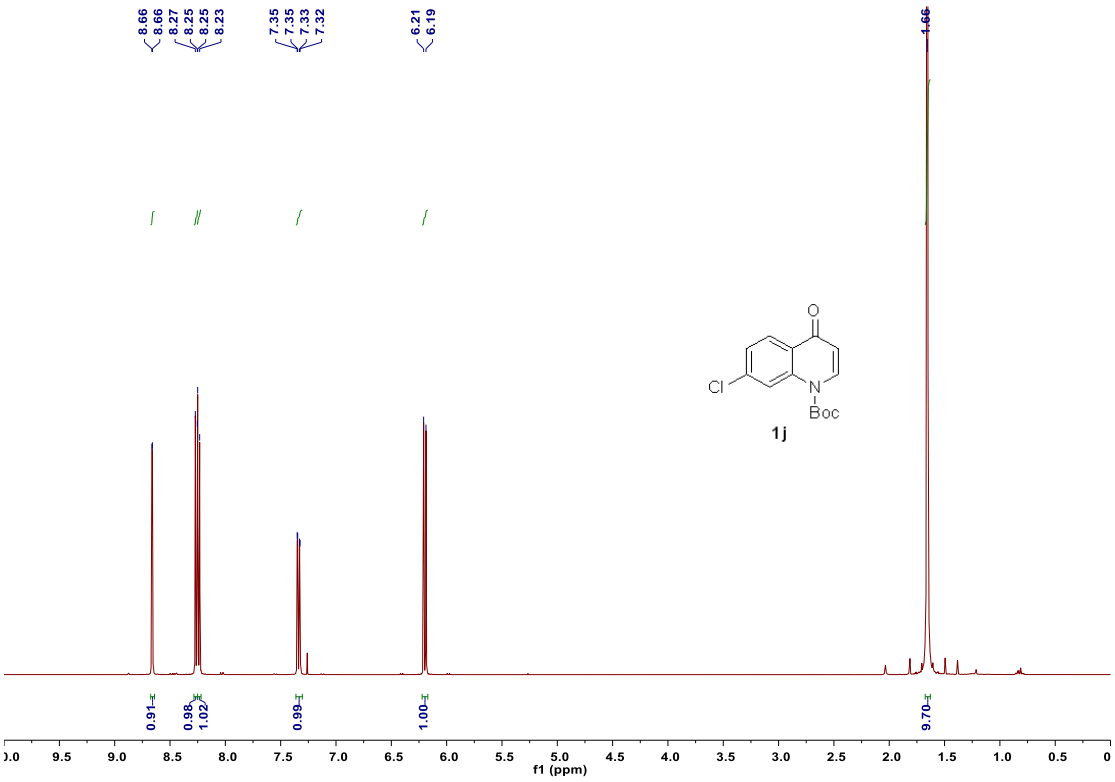

177.78
149.68
139.02
137.54
135.59
129.22
128.19
122.22
119.30
112.17
87.22
28.09
f1 (ppm)

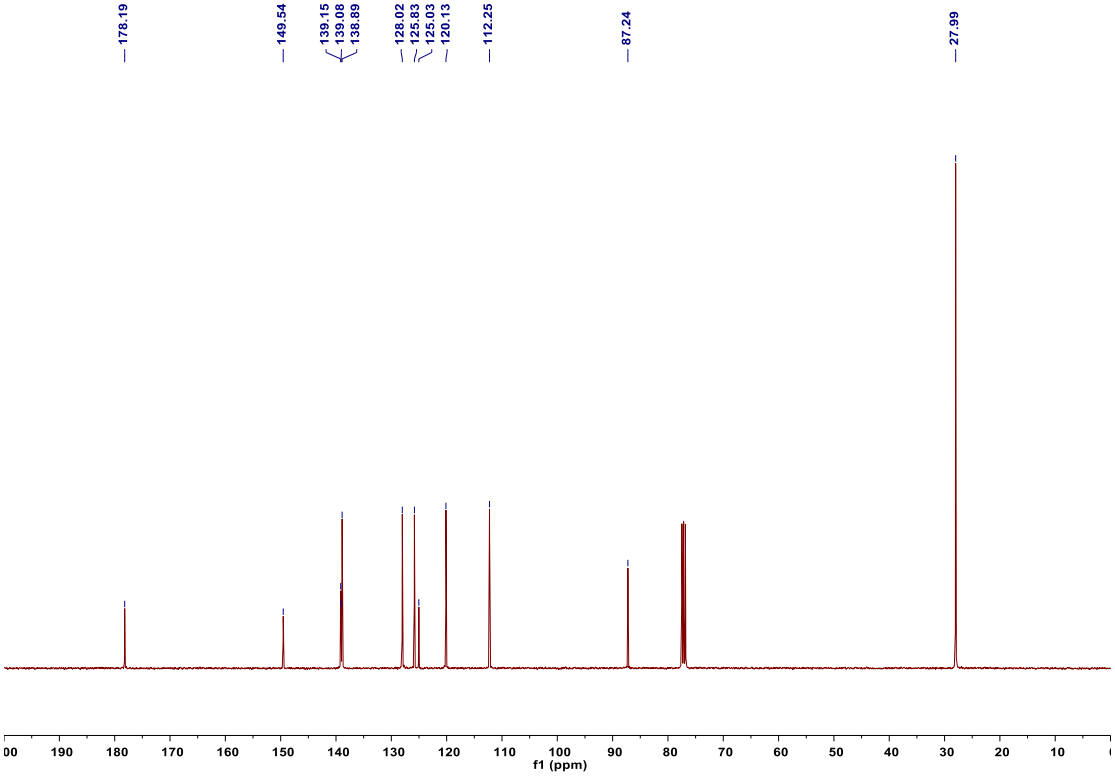

8.88
8.87
8.30
8.28
8.23
8.21
7.56
7.55
7.54
7.53
6.26
6.24
1.69
O
Br
N
Boc
1h
0.90
1.00
0.96
0.99
1.00
9.67
f1 (ppm)

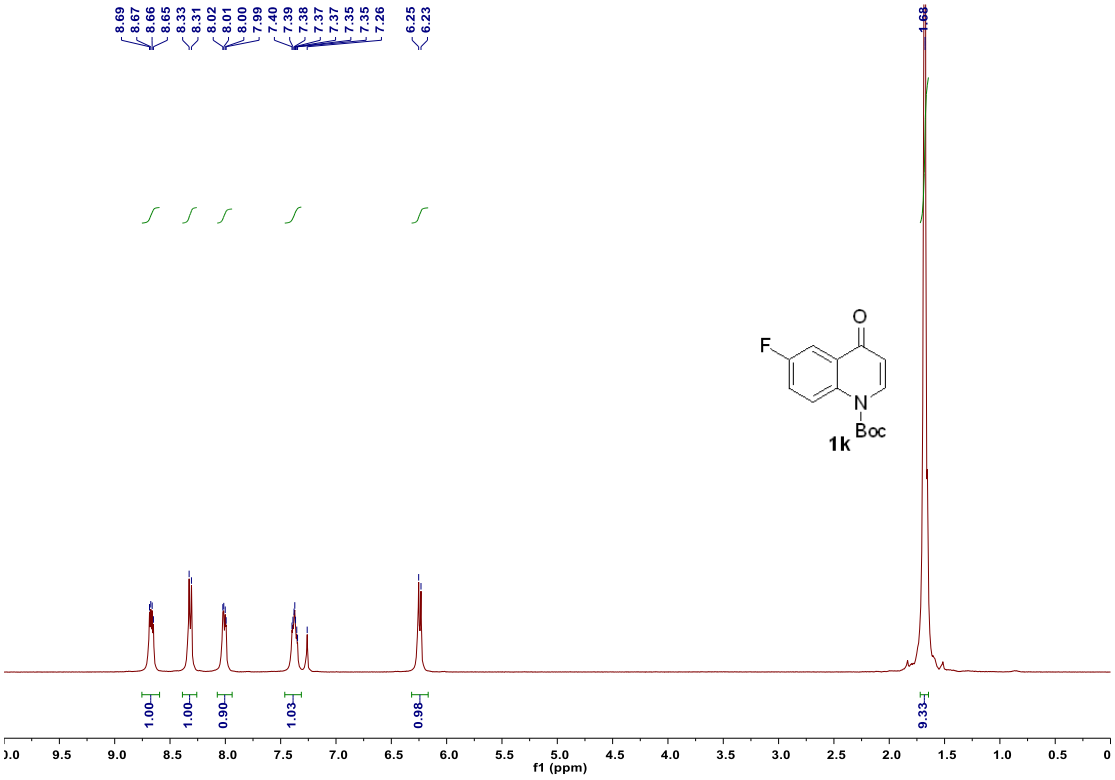

178.36
149.57
139.16
138.87
128.70
128.10
127.76
125.41
123.15
112.31
87.30
28.04
f1 (ppm)

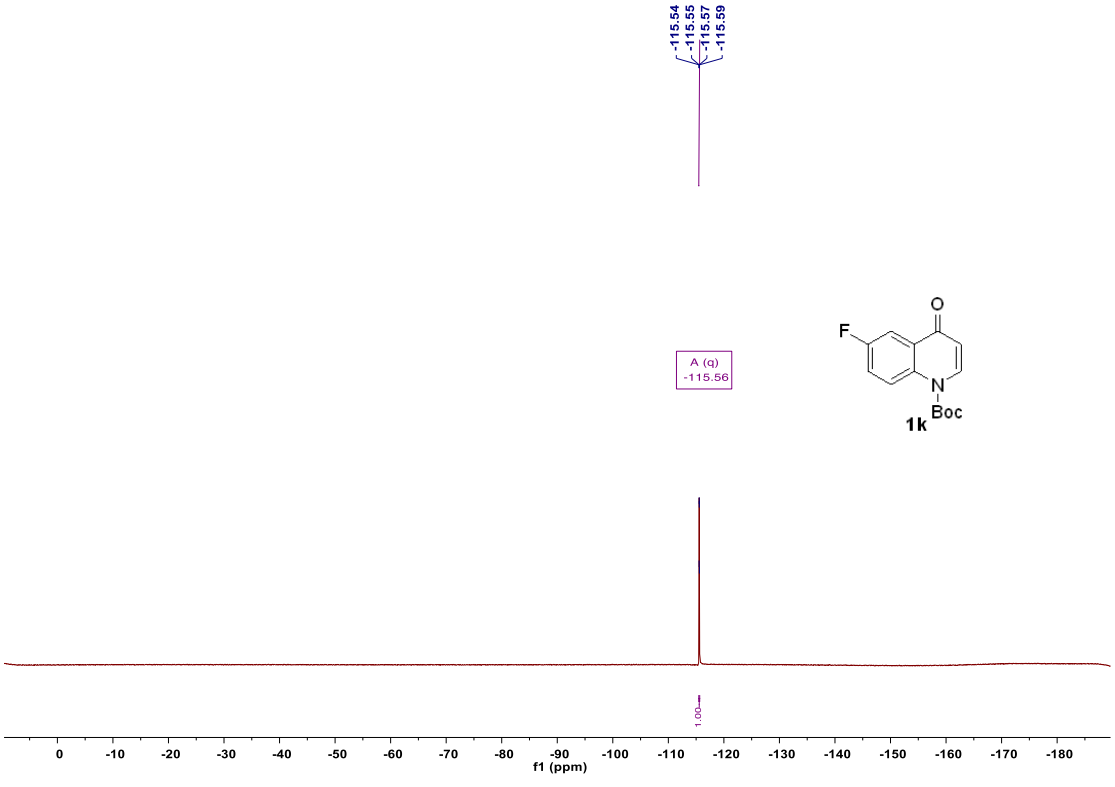

8.61
8.59
8.34
8.33
8.32
8.29
7.60
7.60
7.58
7.57
7.26
6.27
6.25
1.68
Cl
O
N
Boc
1i
1.00
0.87
0.99
1.00
0.98
9.79
f1 (ppm)

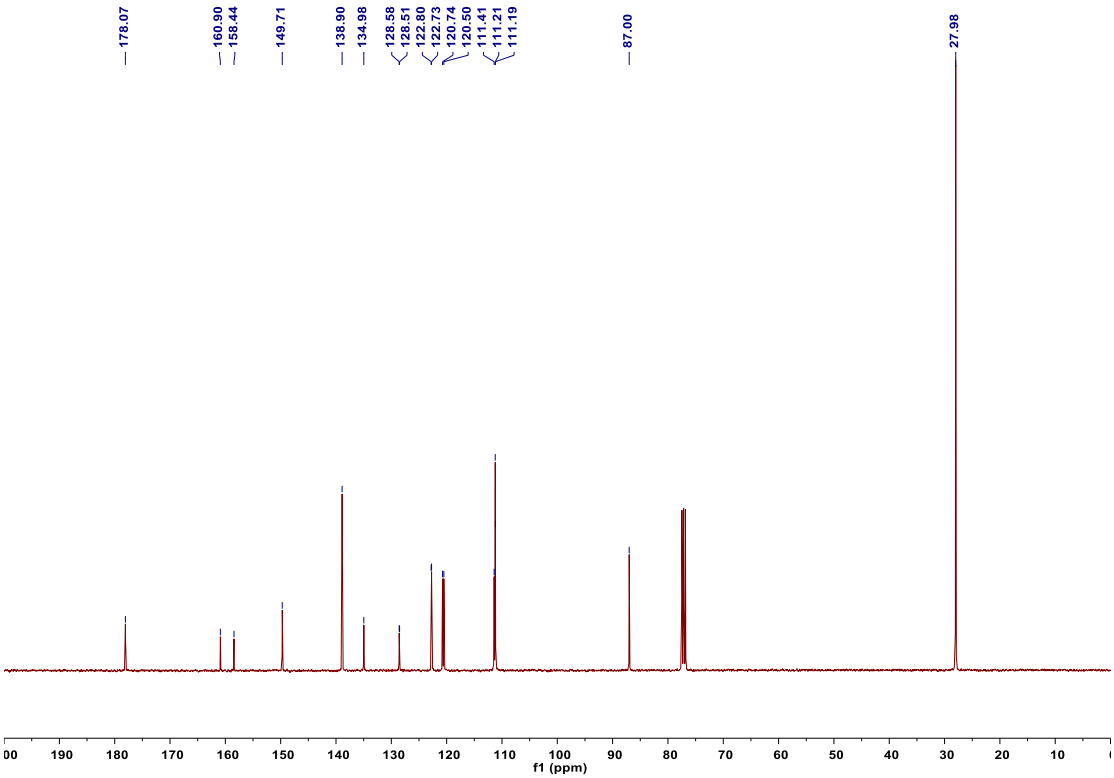

177.83
149.64
138.99
137.04
132.74
131.44
127.88
125.91
122.04
111.99
87.18
28.04
f1 (ppm)

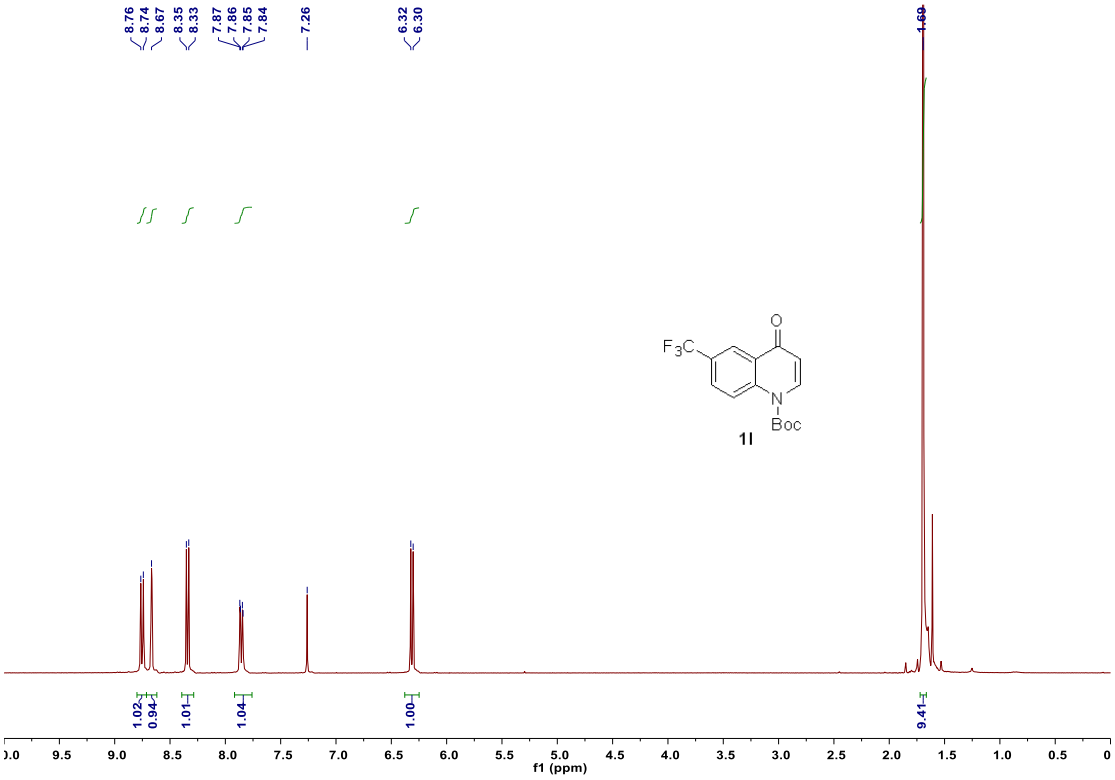

8.66
8.66
8.27
8.25
8.25
8.23
7.35
7.35
7.33
7.32
6.21
6.19
1.66
O
Cl
N
Boc
1j
0.91
0.98
1.02
0.99
1.00
9.70
f1 (ppm)

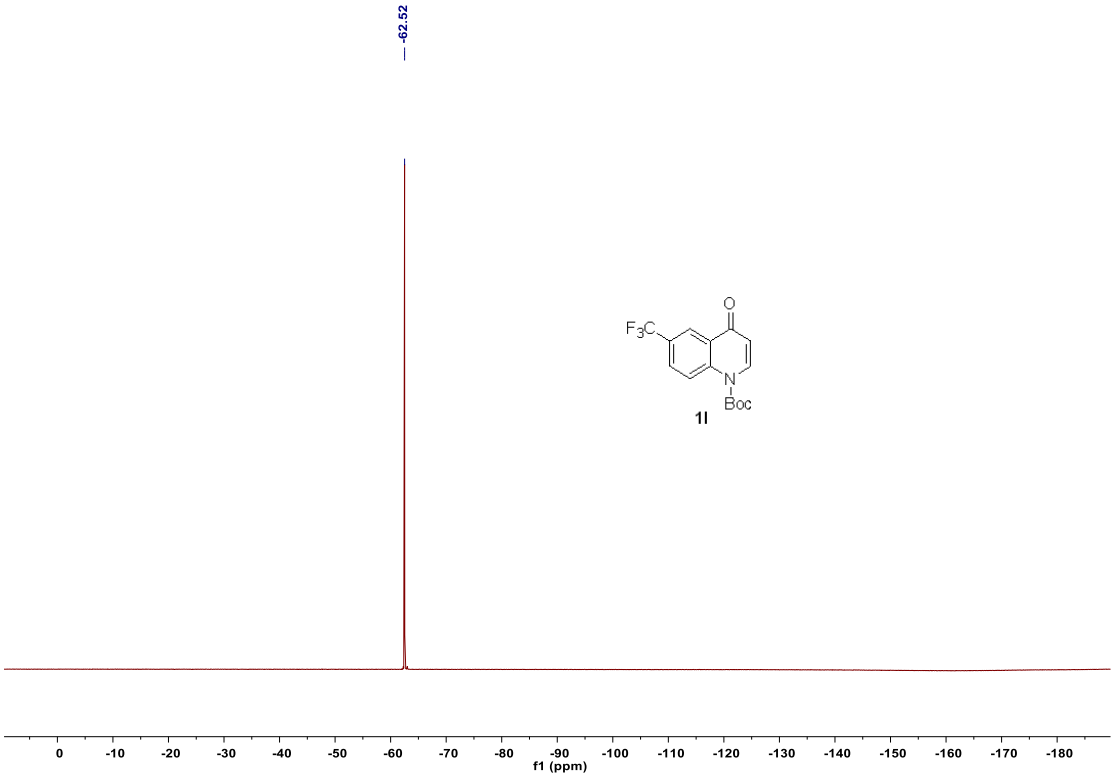

178.19
149.54
139.15
139.08
138.89
128.02
125.83
125.03
120.13
112.25
87.24
27.99
f1 (ppm)

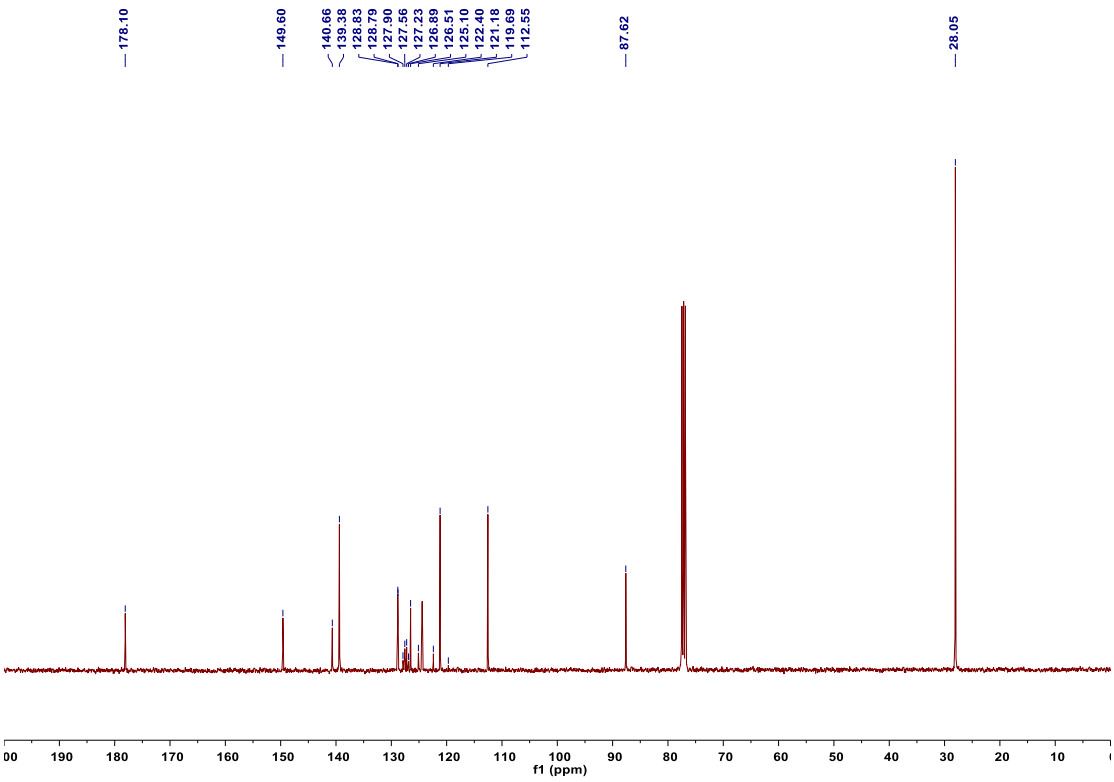

8.69
8.67
8.66
8.65
8.33
8.31
8.02
8.01
8.00
7.99
7.40
7.39
7.38
7.37
7.37
7.35
7.35
7.26
6.25
6.23
1.68
1.00
1.00
0.90
1.03
0.98
9.33
f1 (ppm)
F
O
N
Boc
1k

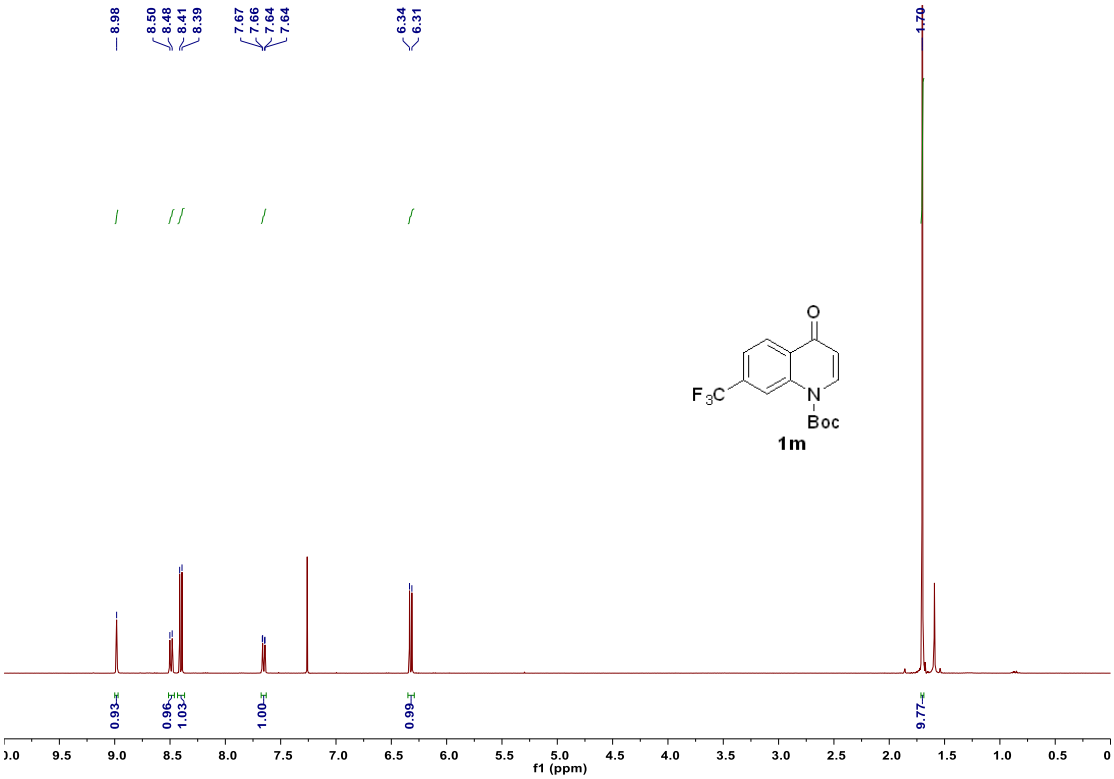

-115.54
-115.55
-115.57
-115.59
A (q)
-115.56
1.00
f1 (ppm)
F
O
N
Boc
1k

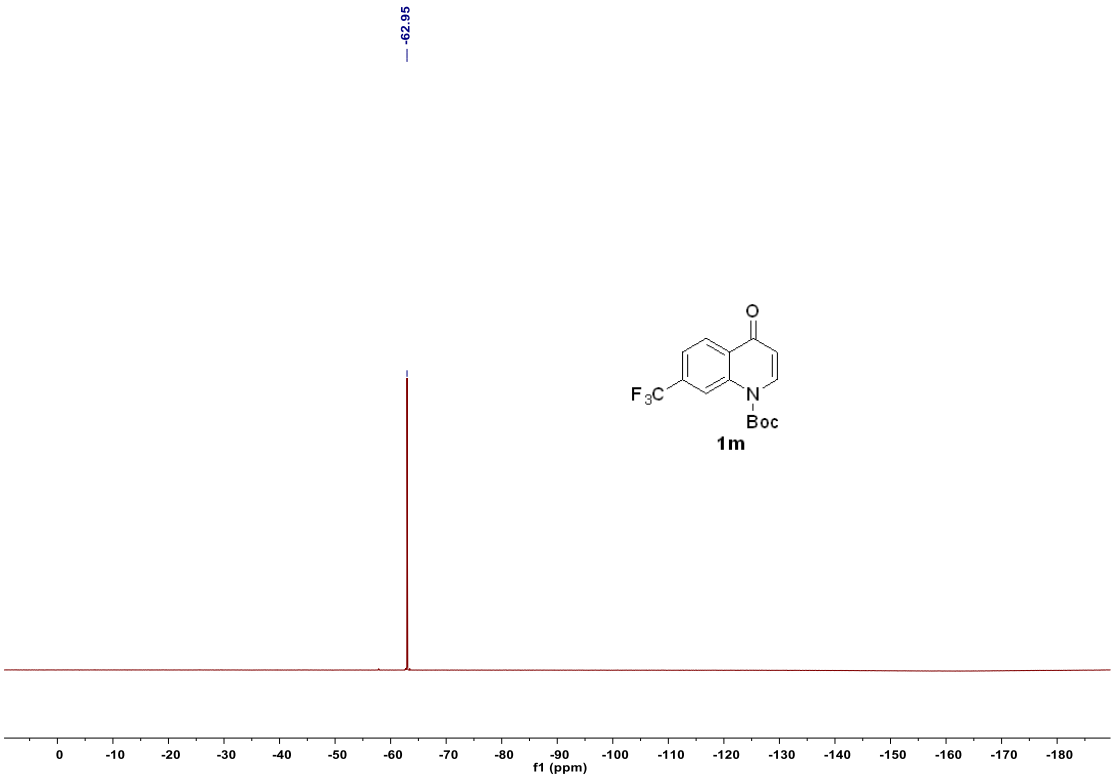

178.07
160.90
158.44
149.71
138.90
134.98
128.58
128.51
122.80
122.73
120.74
120.50
111.41
111.21
111.19
87.00
27.98
f1 (ppm)

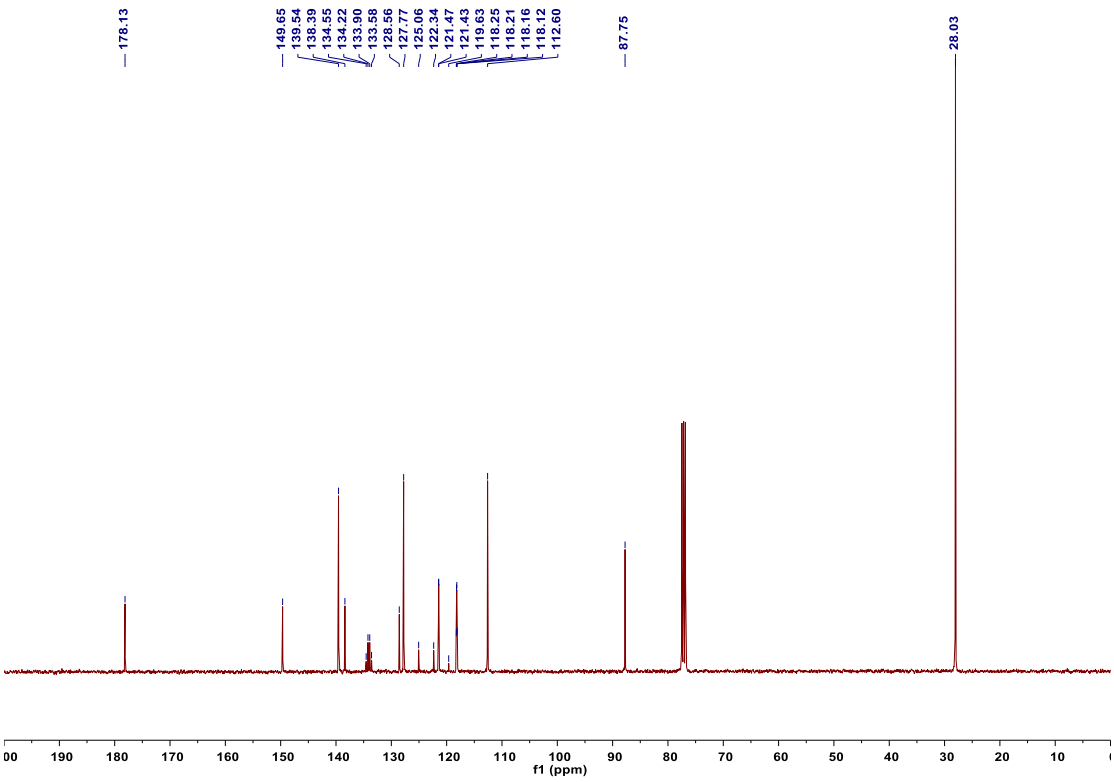

8.76
8.74
8.67
8.35
8.33
7.87
7.86
7.85
7.84
7.26
6.32
6.30
1.69
1.02
0.94
1.01
1.04
1.00
9.41
f1 (ppm)
F3C
O
N
Boc
1l


-62.52
f1 (ppm)
F3C
O
N
Boc
1l

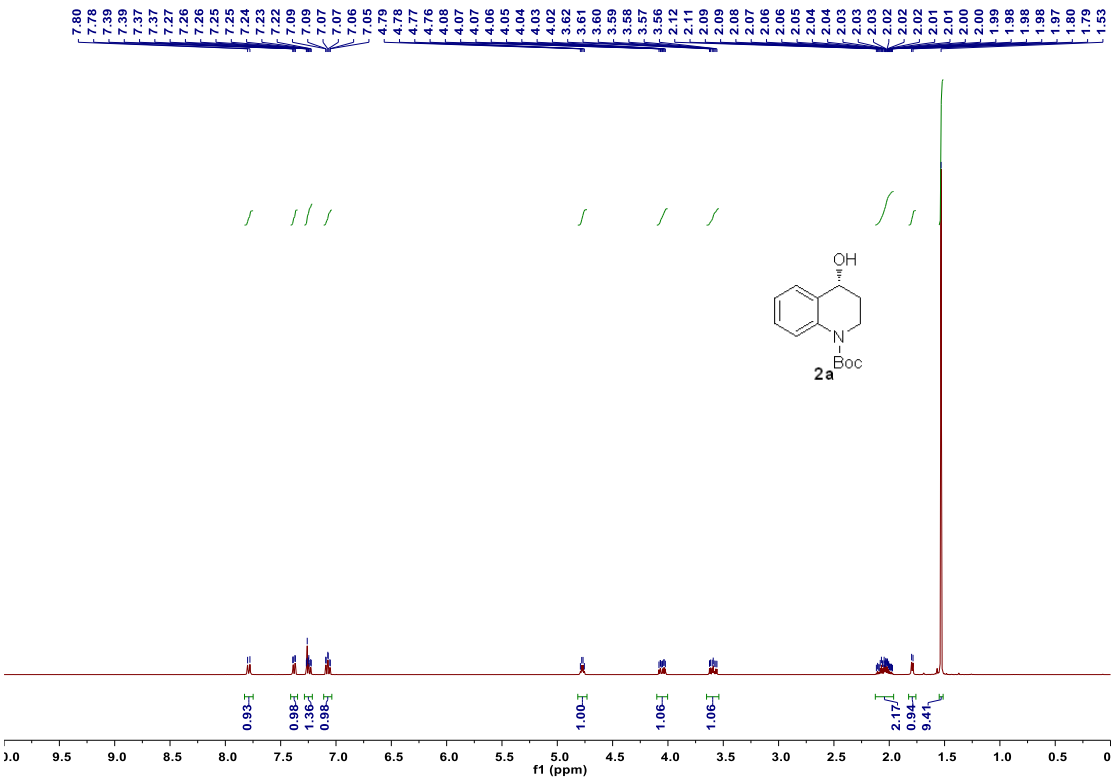

178.10
149.60
140.66
139.38
128.83
128.79
127.90
127.56
127.23
126.89
126.51
125.10
122.40
121.18
119.69
112.55
87.62
28.05
f1 (ppm)

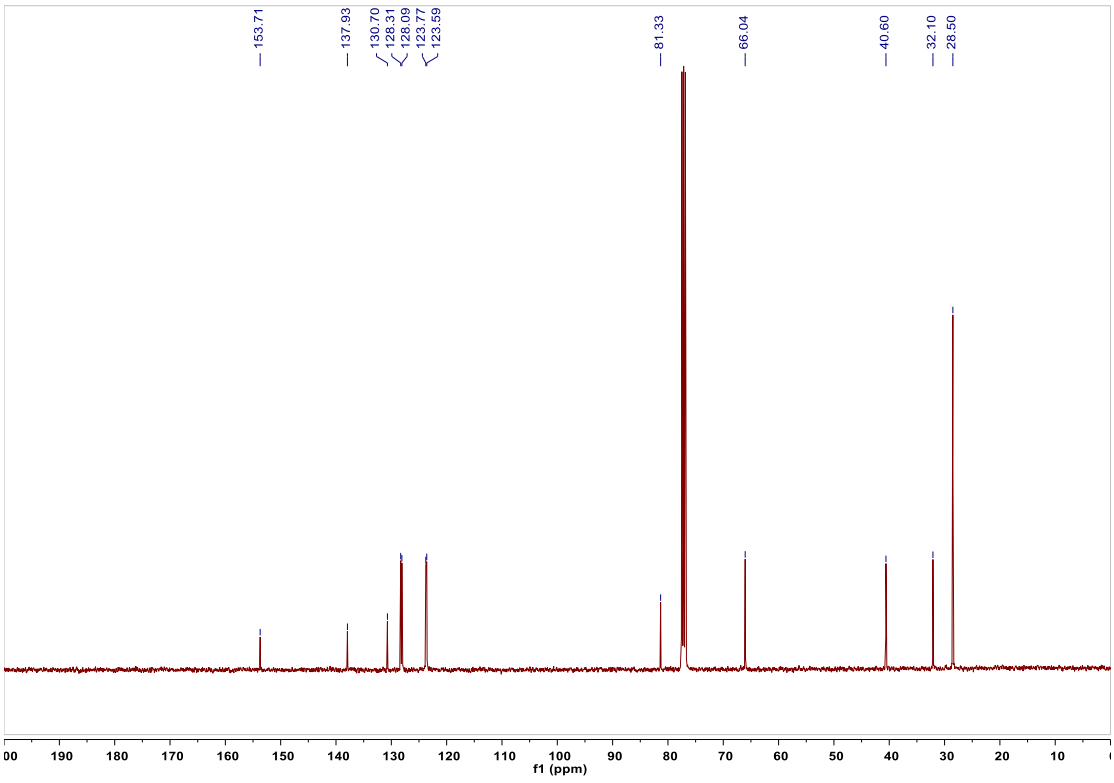

8.98
8.50
8.48
8.41
8.39
7.67
7.66
7.64
7.64
6.34
6.31
1.70
0.93
0.96
1.03
1.00
0.99
9.77
f1 (ppm)
O
F3C
N
Boc
1m


-62.95
f1 (ppm)
O
F3C
N
Boc
1m


178.13
149.65
139.54
138.39
134.55
134.22
133.90
133.58
128.56
127.77
125.06
122.34
121.47
121.43
119.63
118.25
118.21
118.16
118.12
112.60
87.75
28.03
f1 (ppm)

## VII. NMR spectra and SFC chromatograms for compounds 2a–2m

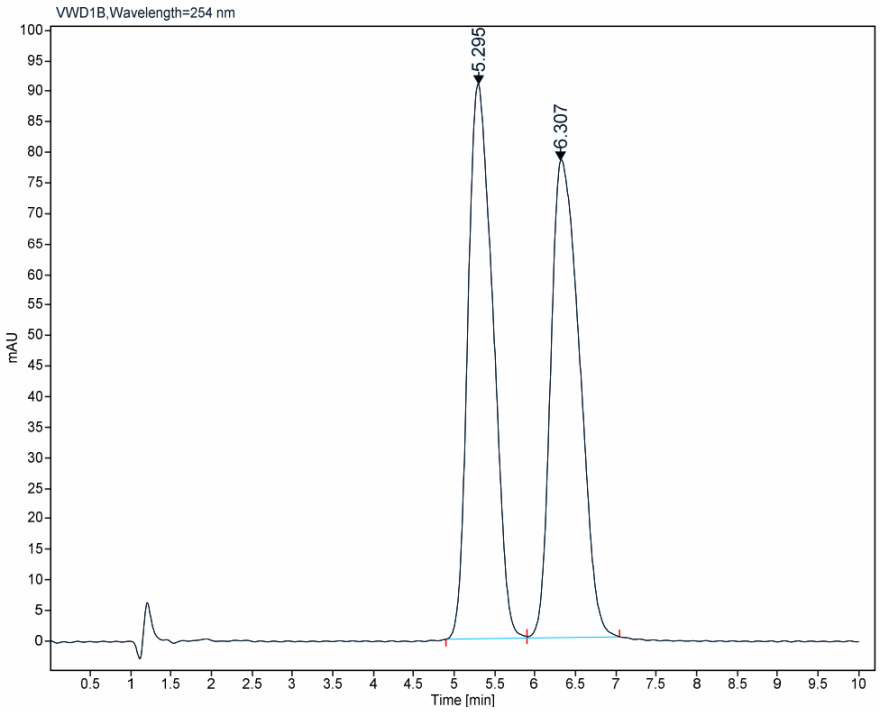


Injection Acq Method Name ASH - 100 bars - 3 mL.min-1 - 2% MeOH.amx

Injection Acquired Date 2019-04-24 16:52:55+02:00

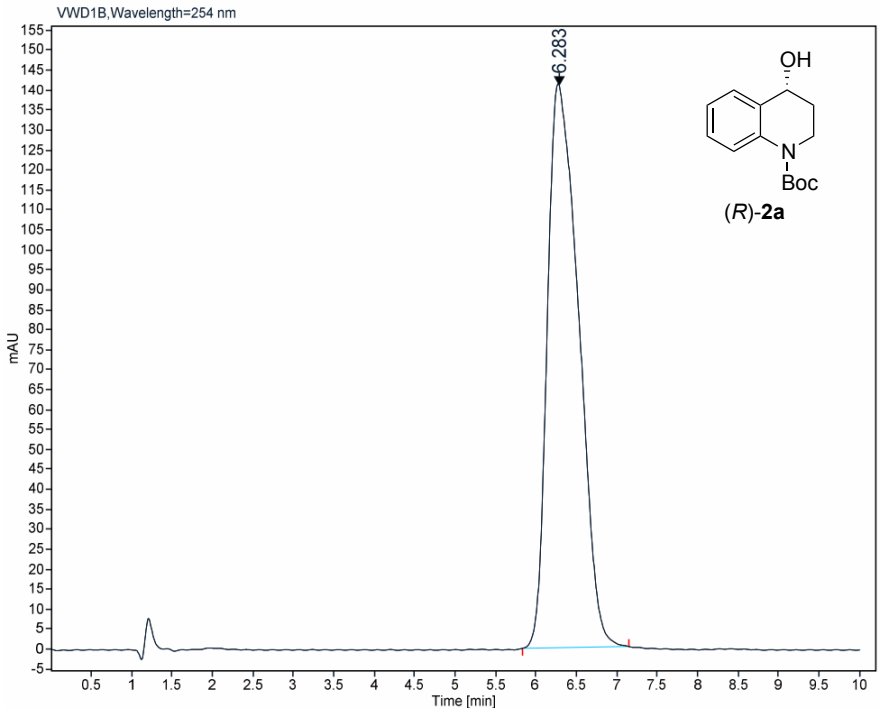
| *RT* | *Peak Area %* |
|---|---|
| 5.295 | 50.13 |
| 6.307 | 49.87 |




Injection Acq Method Name ASH - 100 bars - 3 mL.min-1 - 2% MeOH.amx

Injection Acquired Date 2019-04-24 17:03:38+02:00

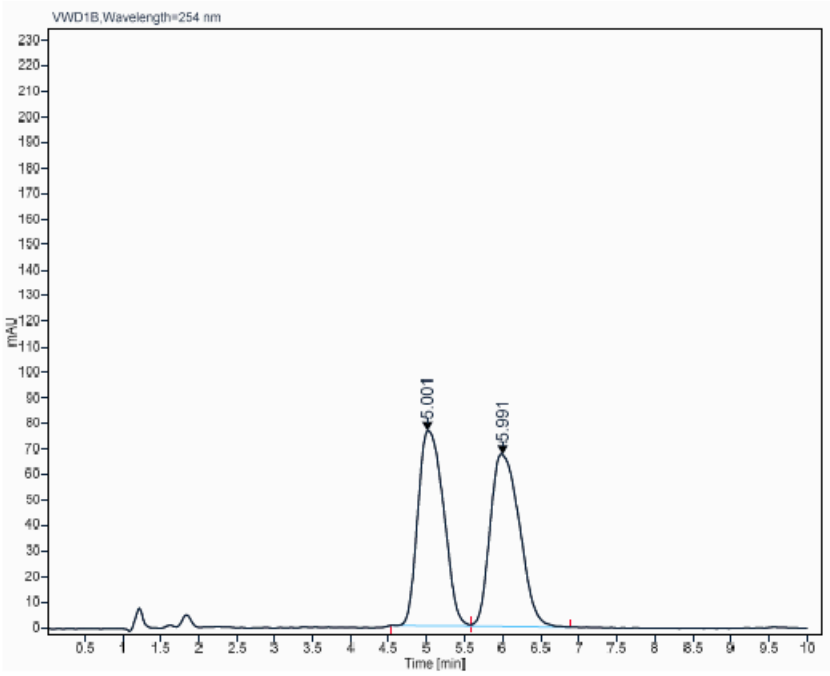
| *RT* | *Peak Area %* |
|---|---|
| 6.283 | 100.00 |



Injection Acq Method Name ASH - 100 bars - 3 mL.min-1 - 2% MeOH.amx

Injection Acquired Date 2019-11-06 10:21:58+01:00

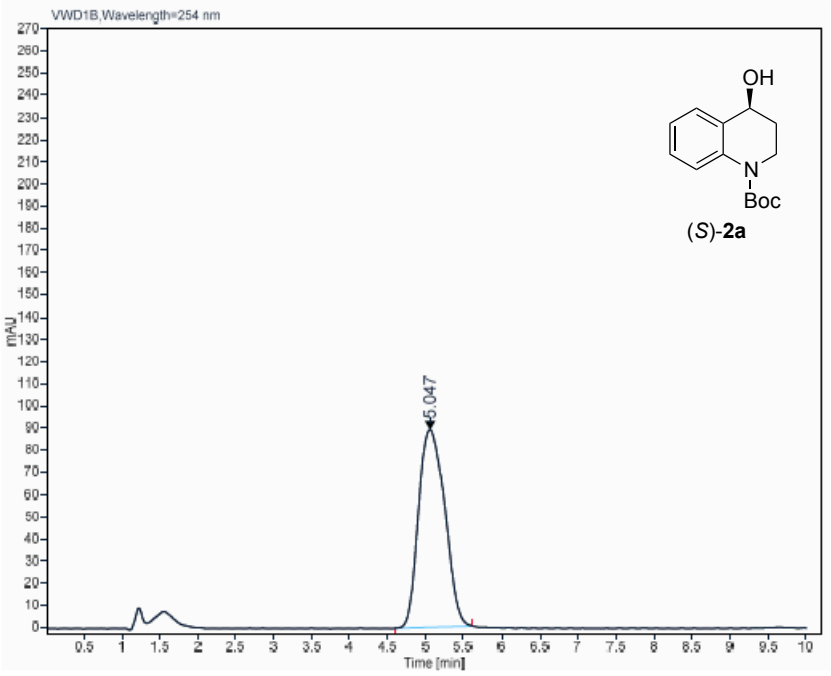
| *RT* | *Peak Area %* |
|---|---|
| 5.001 | 49.78 |
| 5.991 | 50.22 |



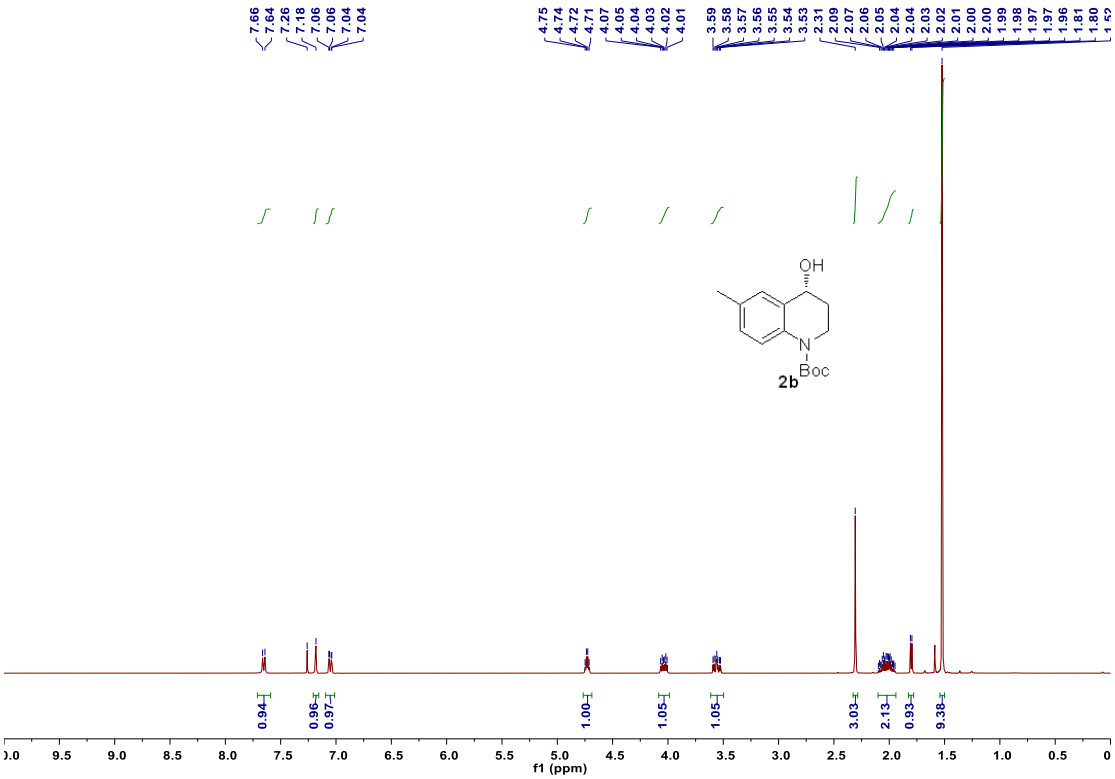

Injection Acq Method Name ASH - 100 bars - 3 mL.min-1 - 2% MeOH.amx

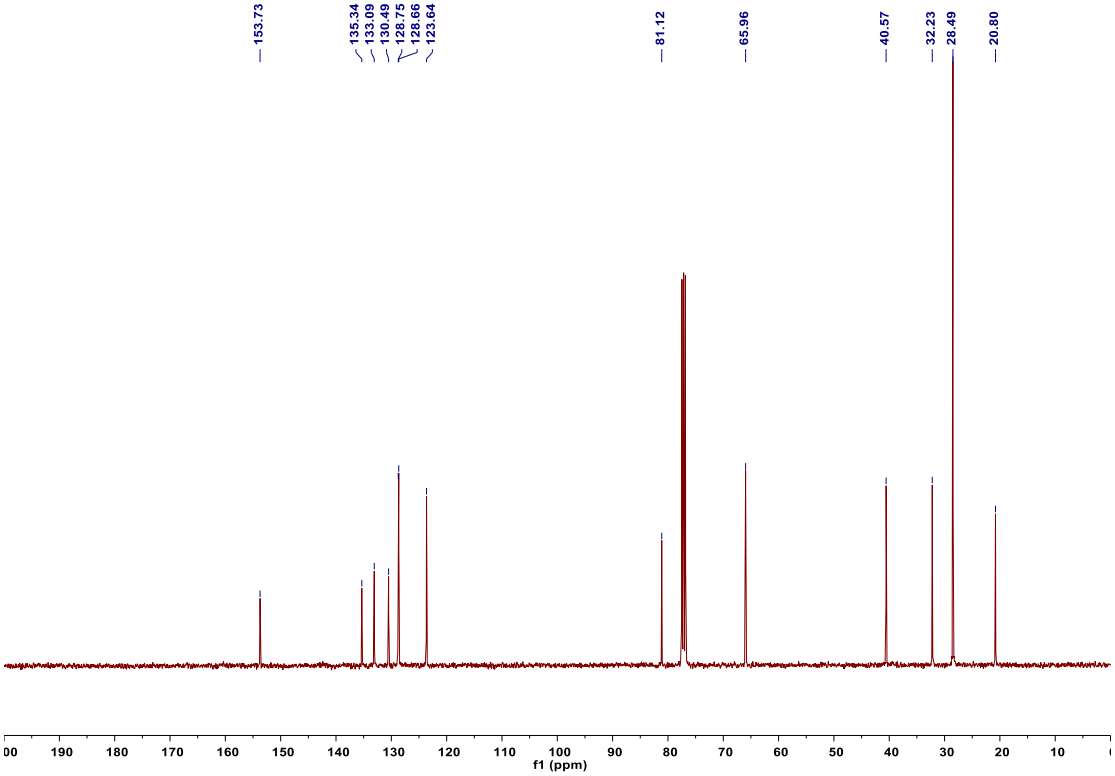
Injection Acquired Date 2019-11-06 10:32:44+01:00

| *RT* | *Peak Area %* |
|---|---|
| 5.047 | 100.00 |




(*S*)-**2a**

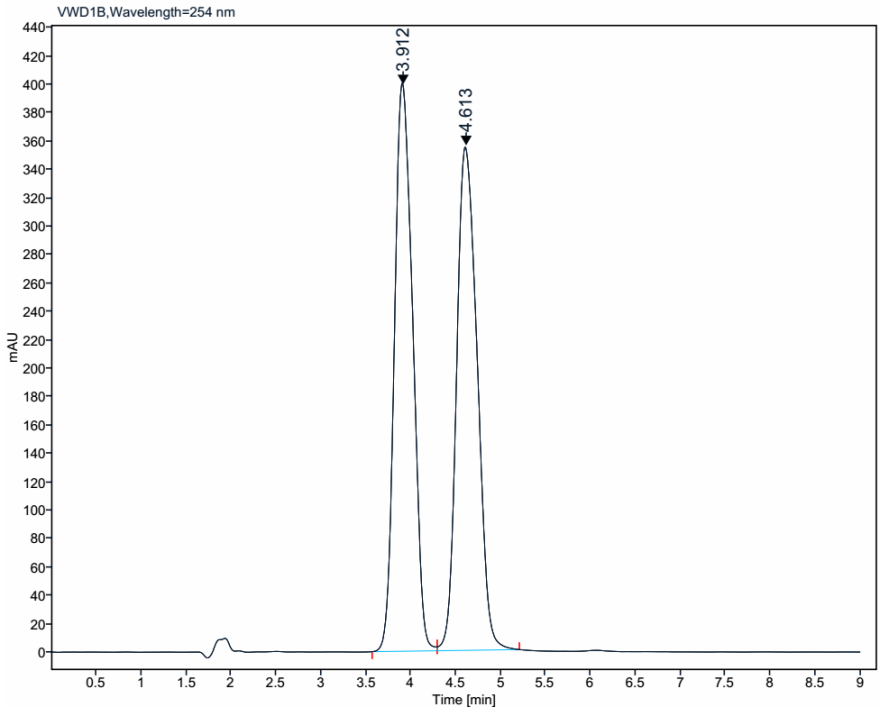

7.66
7.64
7.26
7.18
7.06
7.06
7.04
7.04
4.75
4.74
4.72
4.71
4.07
4.05
4.04
4.03
4.02
4.01
3.59
3.58
3.57
3.56
3.55
3.54
3.53
2.31
2.09
2.07
2.06
2.05
2.04
2.04
2.03
2.02
2.01
2.00
2.00
1.99
1.98
1.97
1.97
1.96
1.81
1.80
OH
N
Boc
2b
0.94
0.96
0.97
1.00
1.05
1.05
3.03
2.13
0.93
9.38
f1 (ppm)


153.73
135.34
133.09
130.49
128.75
128.66
123.64
81.12
65.96
40.57
32.23
28.49
20.80
f1 (ppm)

Injection Acq Method Name ASH - 100 bars - 2 mL.min-1 - 5% MeOH.amx

Injection Acquired Date 2019-04-24 11:49:28+02:00

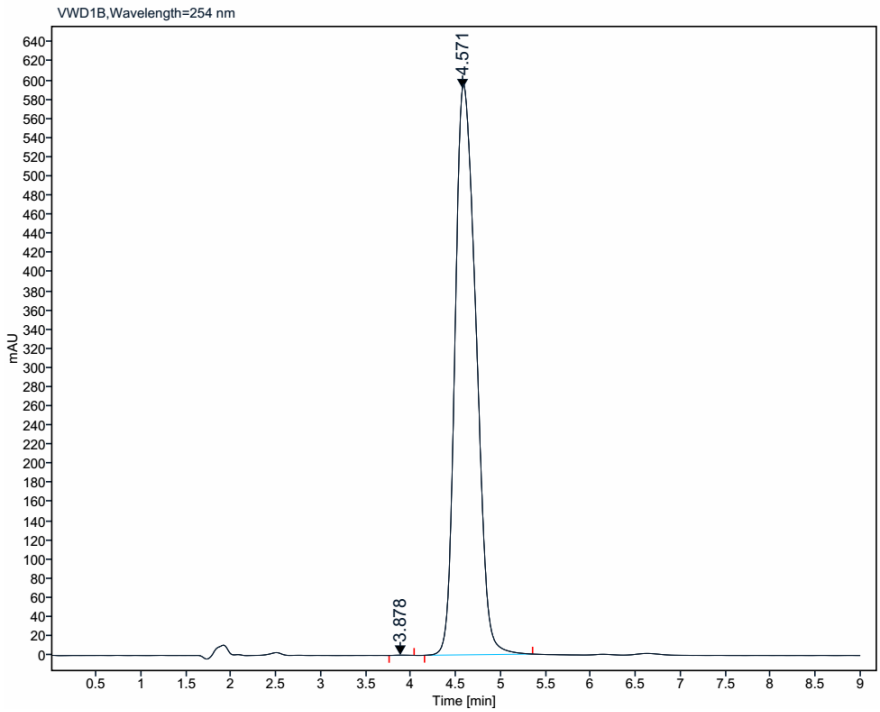
| RT | Peak Area % |
|---|---|
| 3.912 | 49.99 |
| 4.613 | 50.01 |

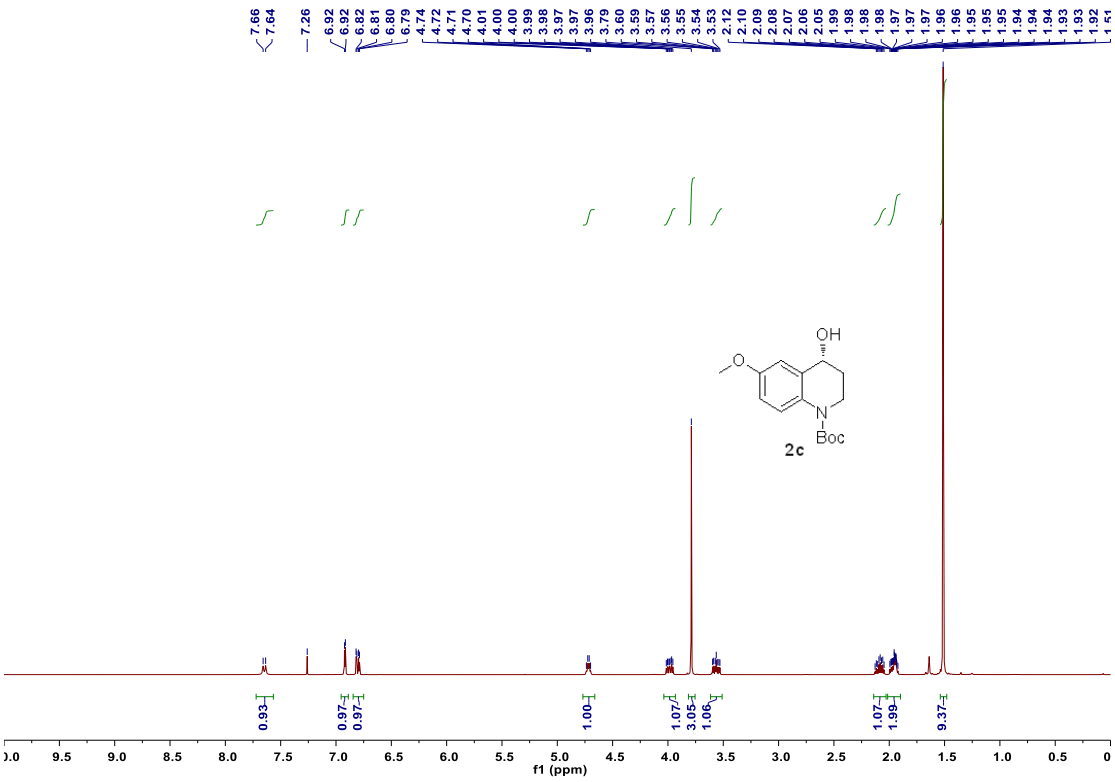


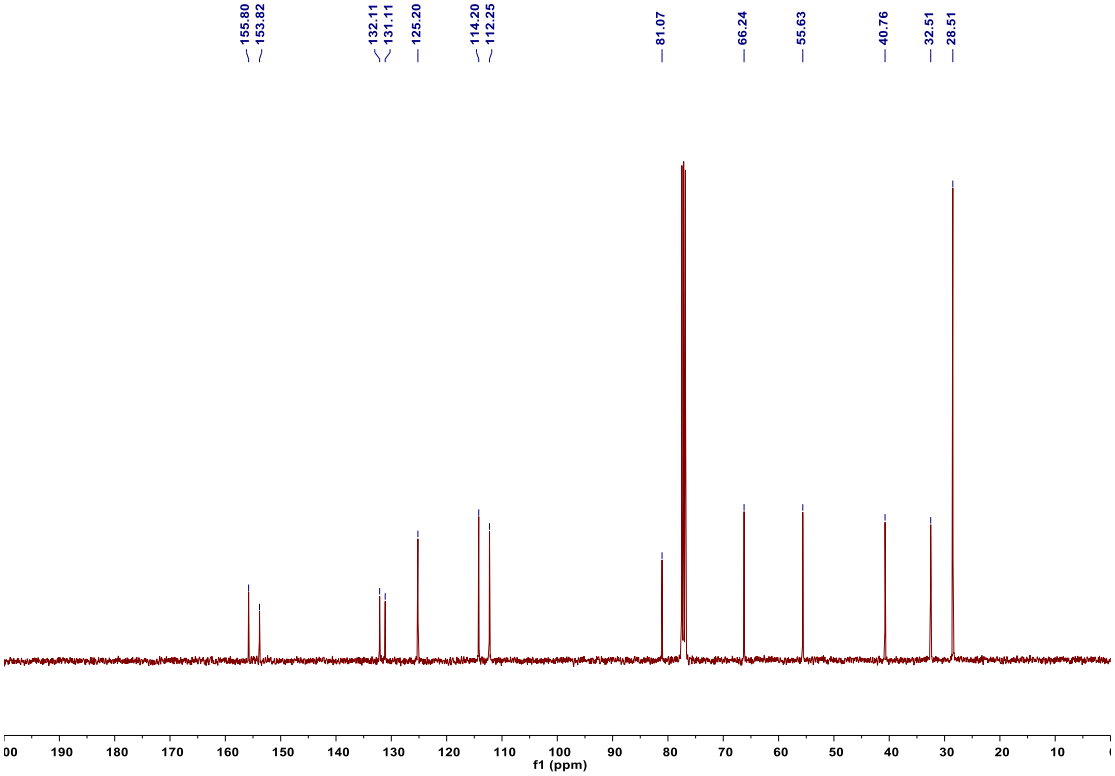

Injection Acq Method Name ASH - 100 bars - 2 mL.min-1 - 5% MeOH.amx

Injection Acquired Date 2019-04-24 11:59:14+02:00

| RT | Peak Area % |
|---|---|
| 3.878 | 0.03 |
| 4.571 | 99.97 |



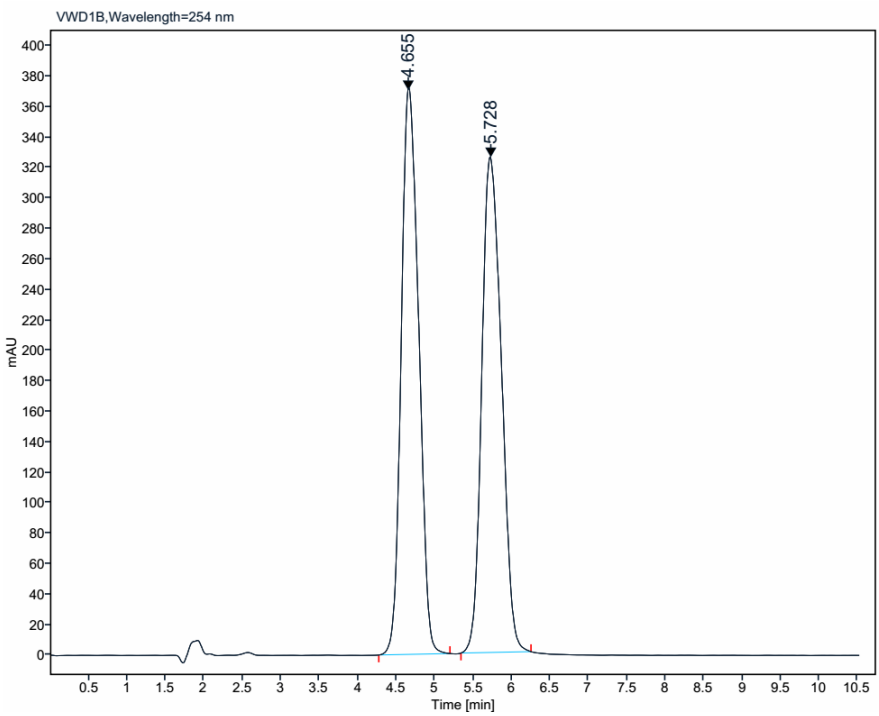

7.66
7.64
7.26
6.92
6.92
6.82
6.81
6.80
6.79
4.74
4.72
4.71
4.70
4.01
4.00
4.00
3.99
3.98
3.97
3.97
3.96
3.79
3.60
3.59
3.57
3.56
3.55
3.54
3.53
2.12
2.10
2.09
2.08
2.07
2.06
2.05
1.99
1.98
1.98
1.97
1.97
1.97
1.96
1.96
1.95
1.95
1.95
1.94
1.94
1.94
1.93
1.93
1.92
OH
O
N
Boc
2c
0.93
0.97
0.97
1.00
1.07
3.05
1.06
1.07
1.99
9.37
f1 (ppm)


155.80
153.82
132.11
131.11
125.20
114.20
112.25
81.07
66.24
55.63
40.76
32.51
28.51
f1 (ppm)

Injection Acq Method Name ASH - 100 bars - 2 mL.min-1 - 5% MeOH.amx

Injection Acquired Date 2019-04-24 11:11:52+02:00

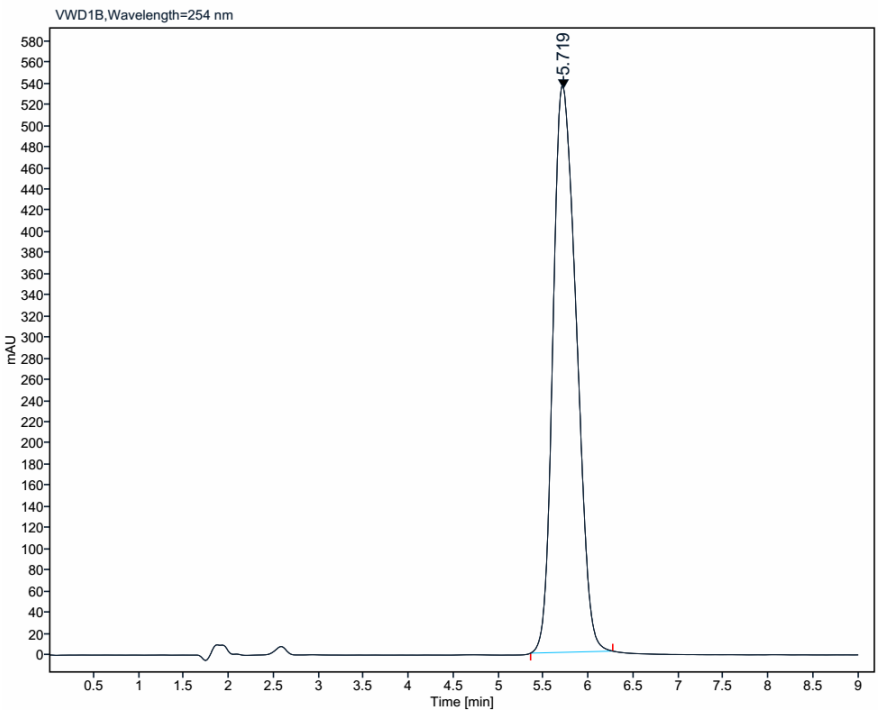
| *RT* | *Peak Area %* |
|---|---|
| 4.655 | 50.33 |
| 5.728 | 49.67 |

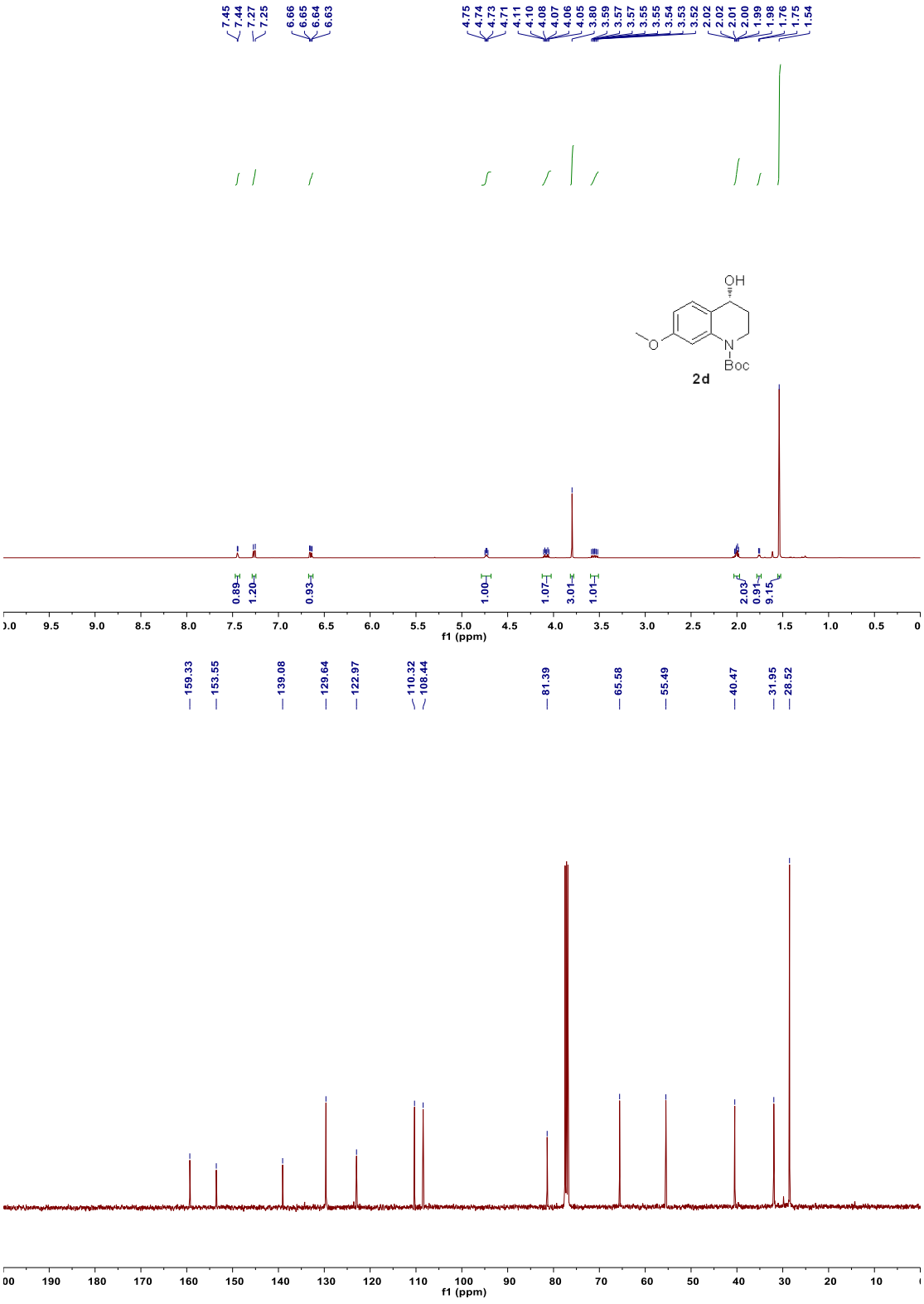



Injection Acq Method Name ASH - 100 bars - 2 mL.min-1 - 5% MeOH.amx

Injection Acquired Date 2019-04-24 11:24:30+02:00

| *RT* | *Peak Area %* |
|---|---|
| 5.719 | 100.00 |

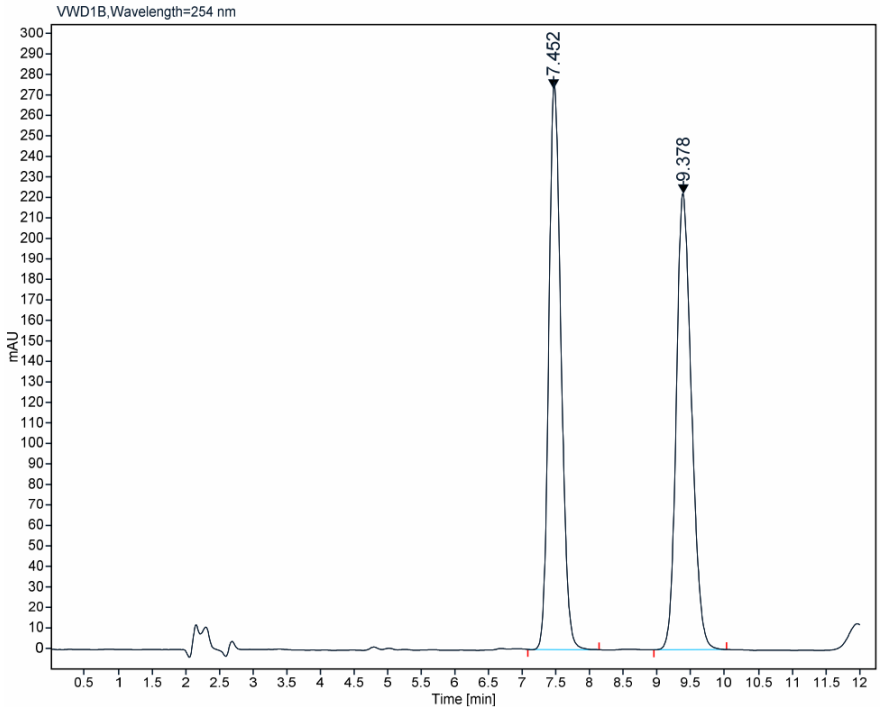



7.45
7.44
7.27
7.25
6.66
6.65
6.64
6.63
4.75
4.74
4.73
4.71
4.11
4.10
4.08
4.07
4.06
4.05
3.80
3.59
3.57
3.57
3.55
3.55
3.54
3.53
3.52
2.02
2.02
2.01
2.00
1.99
1.98
1.76
1.75
1.54
OH
O
N
Boc
2d
0.89
1.20
0.93
1.00
1.07
3.01
1.01
2.03
0.91
9.15
f1 (ppm)
159.33
153.55
139.08
129.64
122.97
110.32
108.44
81.39
65.58
55.49
40.47
31.95
28.52
f1 (ppm)

Injection Acq Method Name IF- 100 bars - 2 mL.min-1 - 10% MeOH.amx

Injection Acquired Date 2019-07-12 13:31:45+02:00

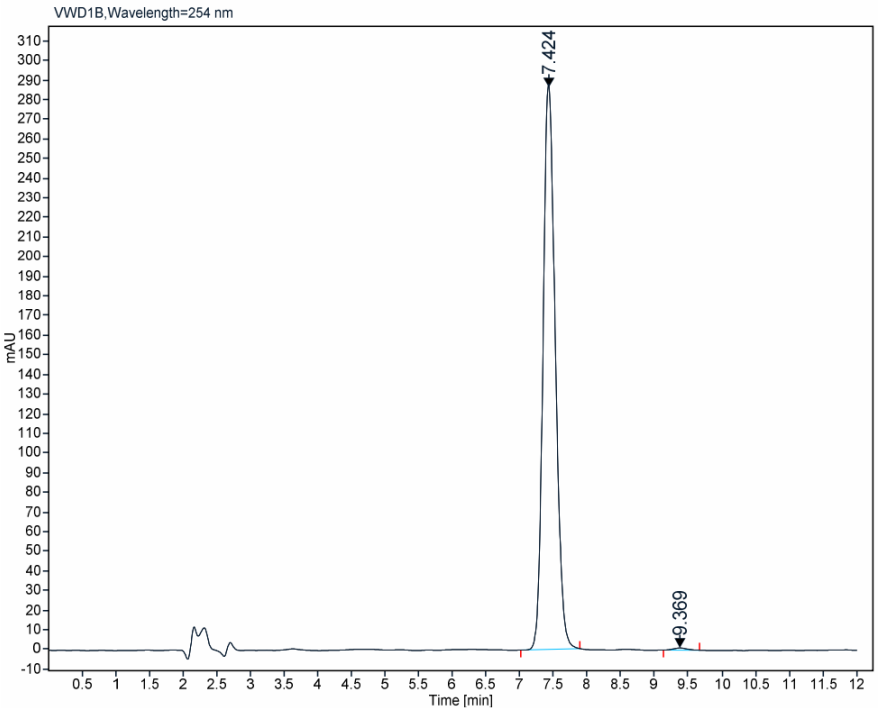
| *RT* | *Peak Area %* |
|---|---|
| 7.452 | 49.95 |
| 9.378 | 50.05 |

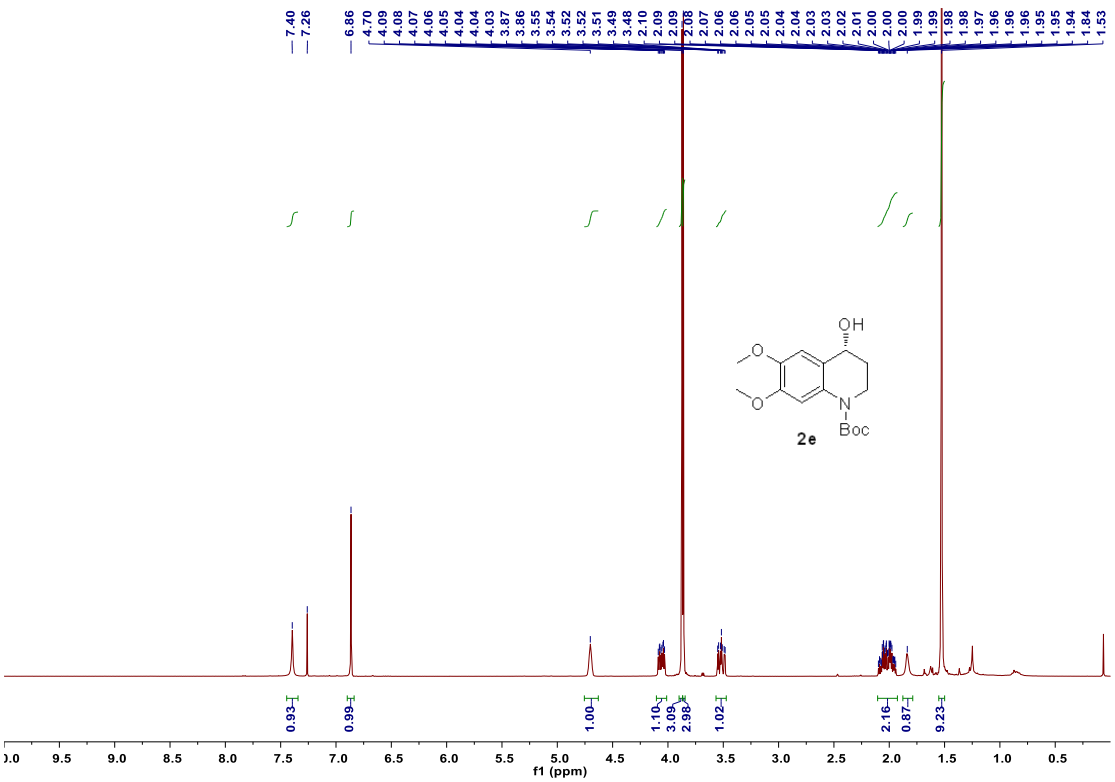


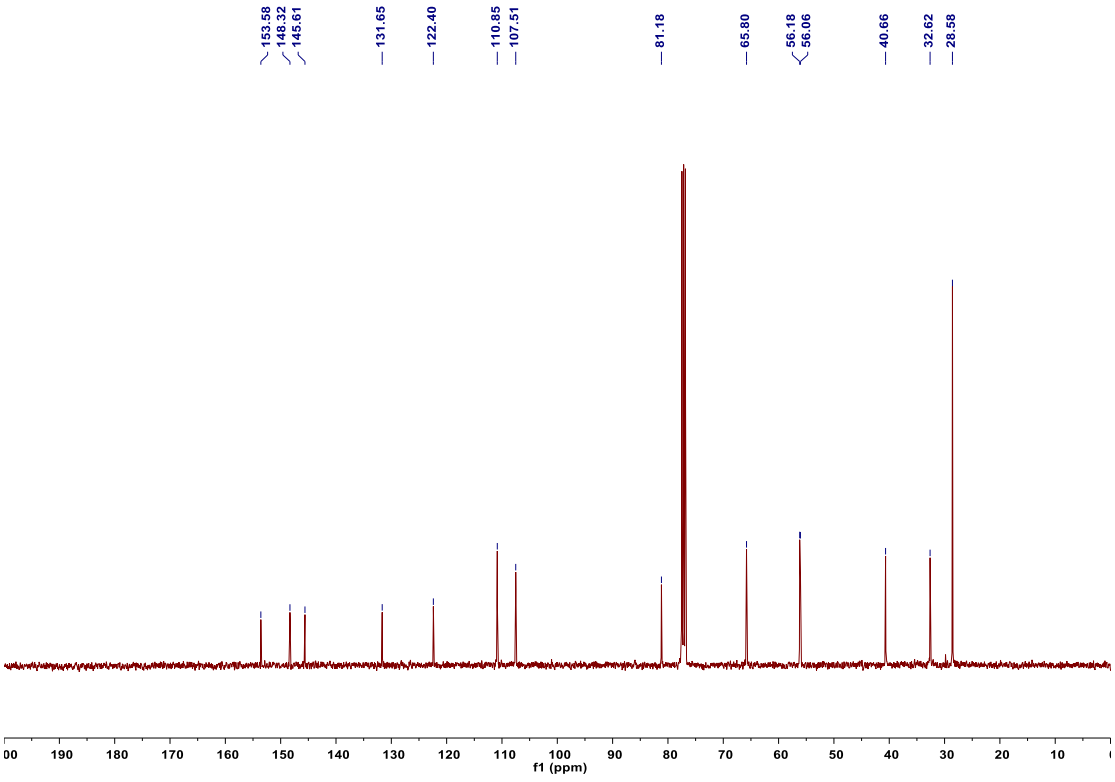

Injection Acq Method Name IF- 100 bars - 2 mL.min-1 - 10% MeOH.amx

Injection Acquired Date 2019-07-12 13:44:30+02:00

| *RT* | *Peak Area %* |
|---|---|
| 7.424 | 99.60 |
| 9.369 | 0.40 |



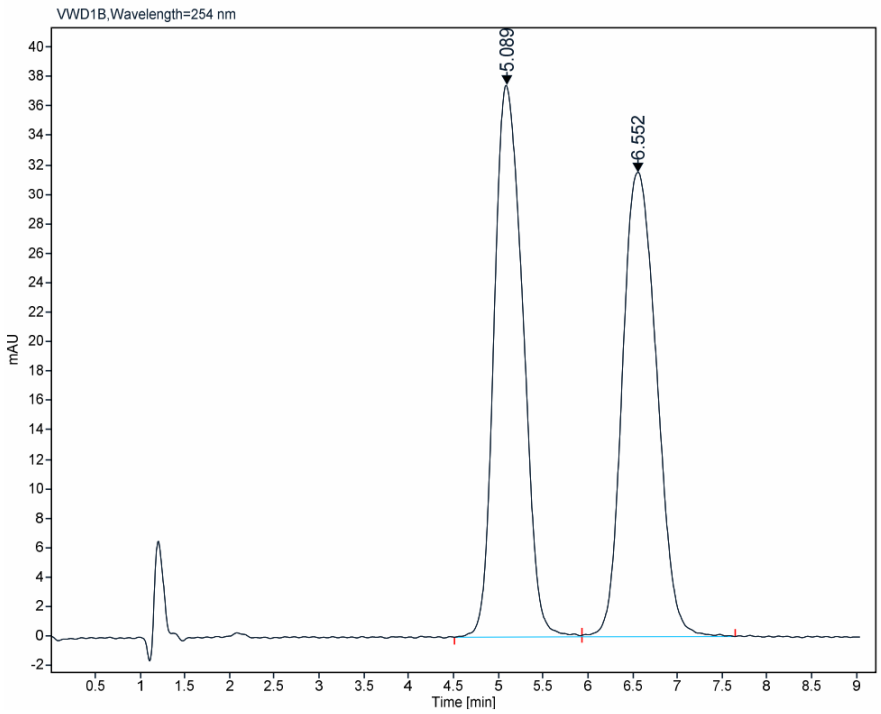

7.40
7.26
6.86
4.70
4.09
4.08
4.07
4.06
4.05
4.04
4.04
4.03
3.87
3.86
3.55
3.54
3.52
3.52
3.51
3.49
3.48
2.10
2.09
2.09
2.08
2.07
2.06
2.06
2.05
2.05
2.04
2.04
2.03
2.03
2.02
2.01
2.00
2.00
1.99
1.99
1.98
1.98
1.97
1.96
1.96
1.95
1.95
1.94
1.84
1.53
OH
O
O
N
Boc
2e
0.93
0.99
1.00
1.10
3.09
2.98
1.02
2.16
0.87
9.23
f1 (ppm)


153.58
148.32
145.61
131.65
122.40
110.85
107.51
81.18
65.80
56.18
56.06
40.66
32.62
28.58
f1 (ppm)

Injection Acq Method Name ASH - 100 bars - 3 mL.min-1 - 3% MeOH.amx

Injection Acquired Date 2019-05-15 09:55:20+02:00

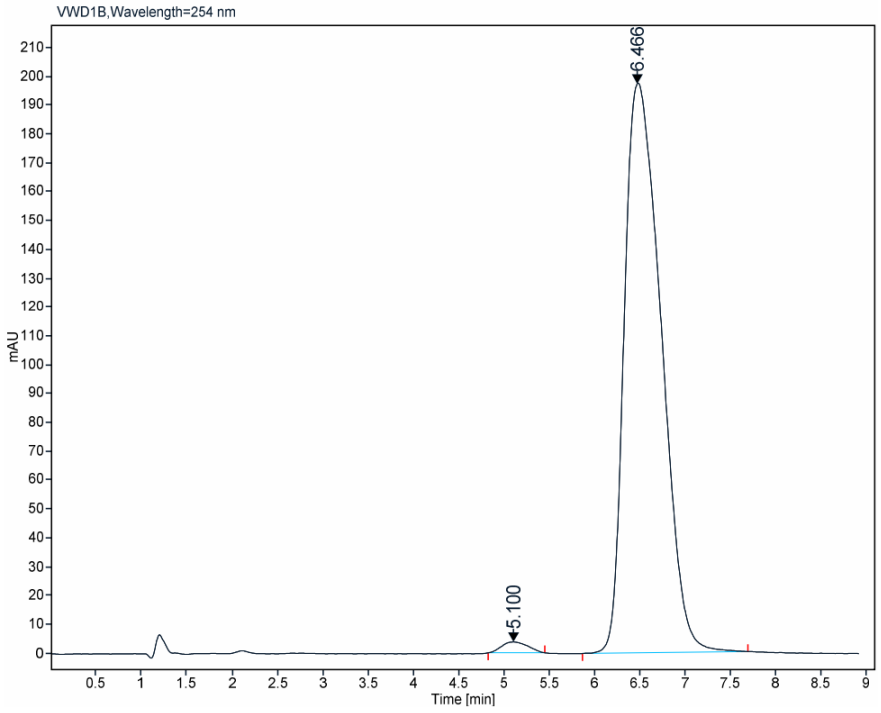
| *RT* | *Peak Area %* |
|---|---|
| 5.089 | 49.97 |
| 6.552 | 50.03 |

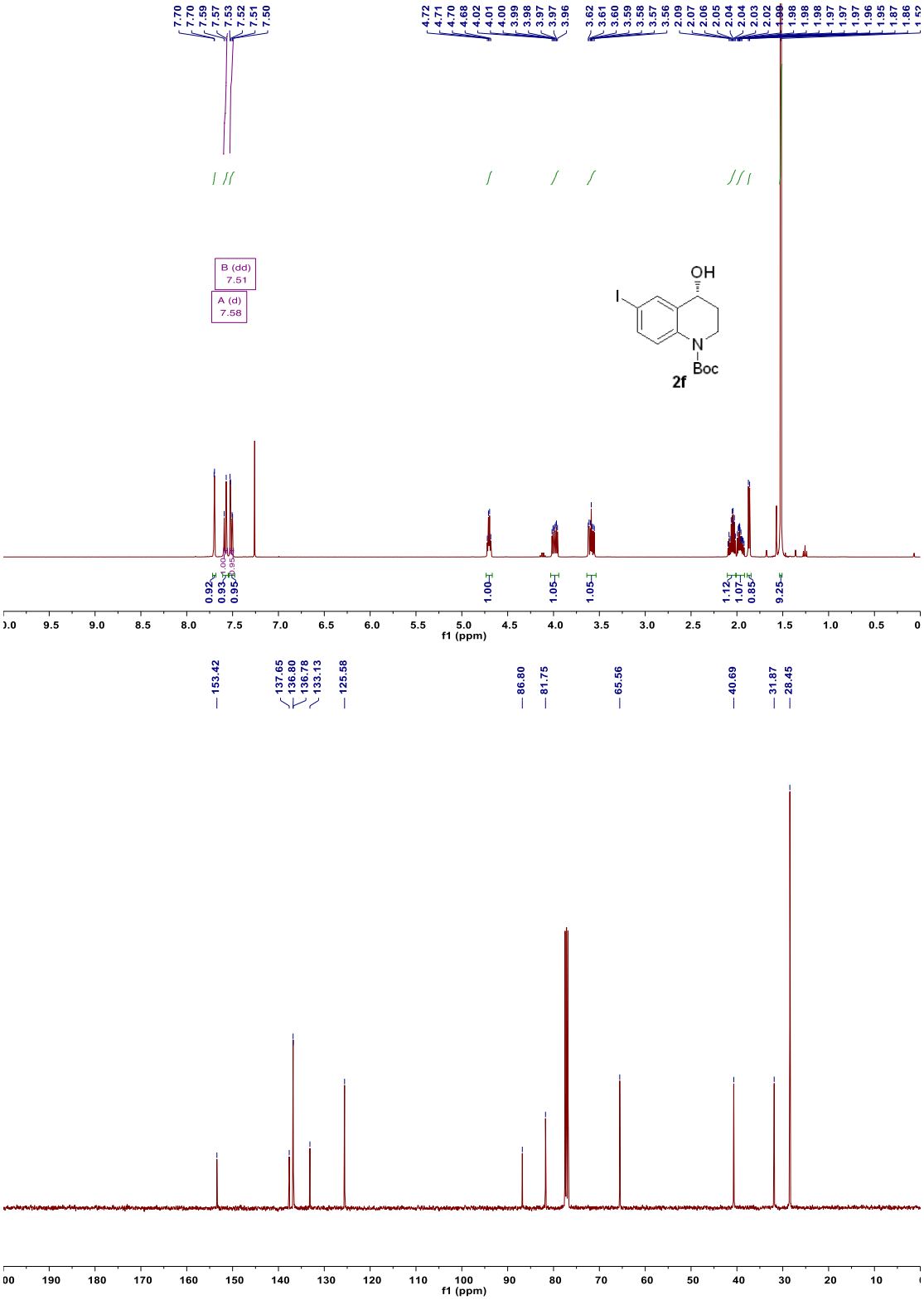



Injection Acq Method Name ASH - 100 bars - 3 mL.min-1 - 3% MeOH.amx

Injection Acquired Date 2019-05-15 10:05:34+02:00

| *RT* | *Peak Area %* |
|---|---|
| 5.100 | 1.34 |
| 6.466 | 98.66 |

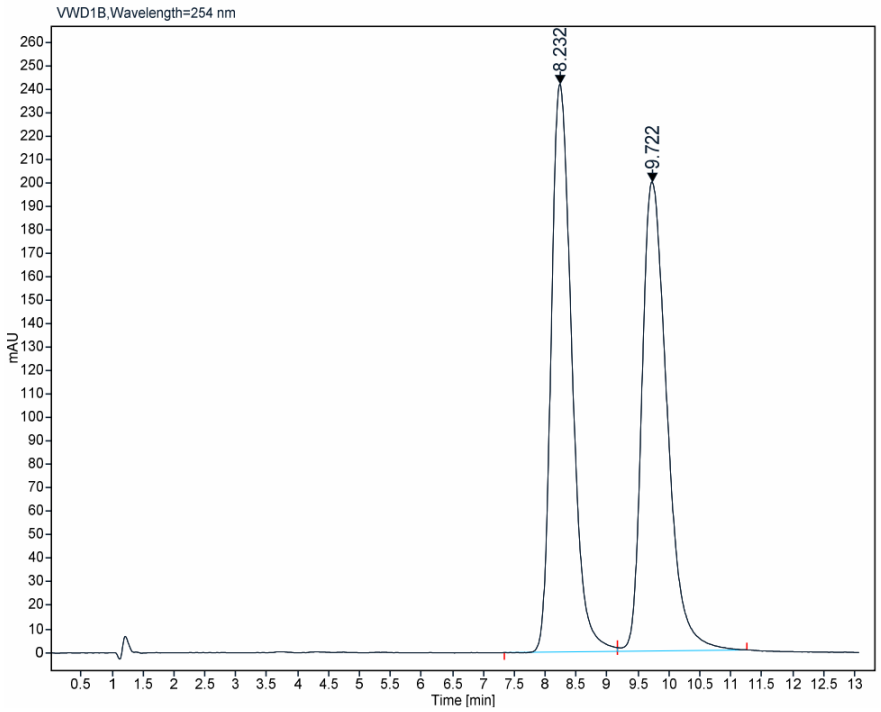



B (dd)
7.51
A (d)
7.58
OH
I
N
Boc
2f
f1 (ppm)
f1 (ppm)

Injection Acq Method Name ASH - 100 bars - 3 mL.min-1 - 3% MeOH.amx

Injection Acquired Date 2019-05-14 14:26:47+02:00

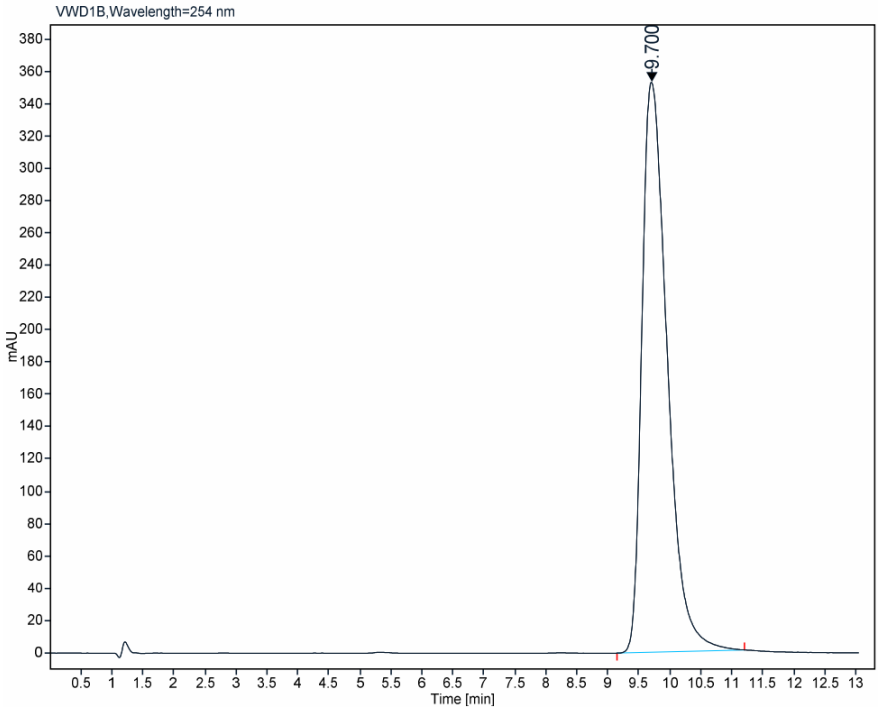
| RT | Peak Area % |
|---|---|
| 8.232 | 49.89 |
| 9.722 | 50.11 |

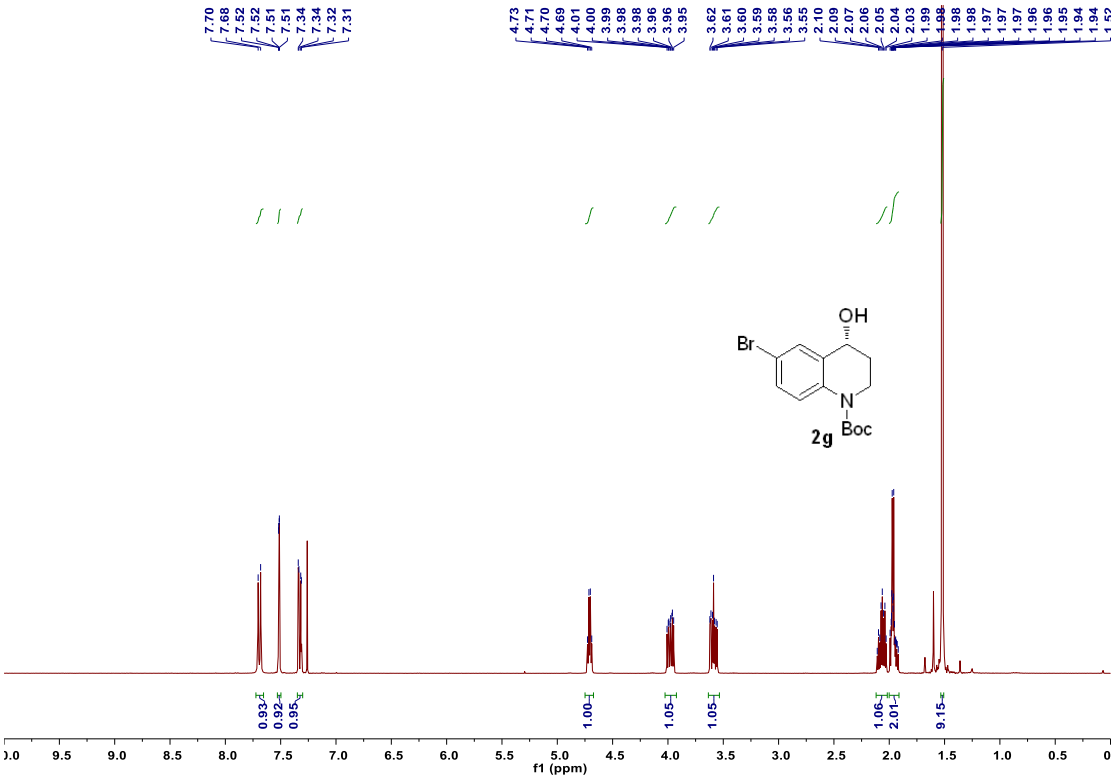


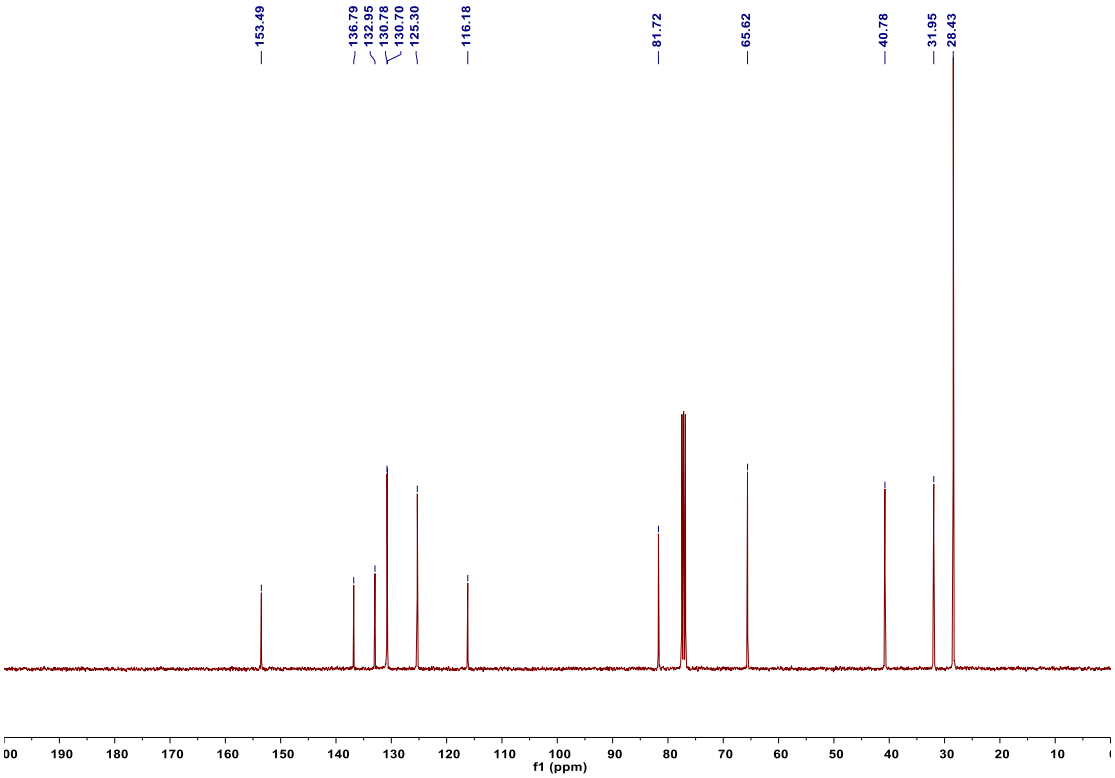

Injection Acq Method Name ASH - 100 bars - 3 mL.min-1 - 3% MeOH.amx

Injection Acquired Date 2019-05-14 14:41:04+02:00

| RT | Peak Area % |
|---|---|
| 9.700 | 100.00 |



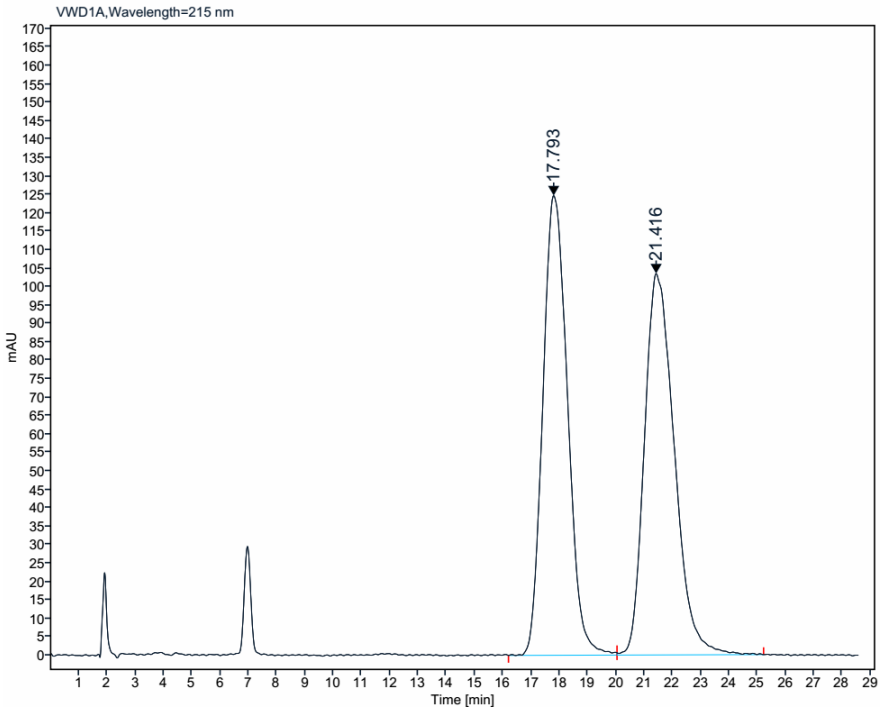

7.70
7.68
7.52
7.52
7.51
7.51
7.34
7.34
7.32
7.31
4.73
4.71
4.70
4.69
4.01
4.00
3.99
3.98
3.98
3.96
3.96
3.95
3.62
3.61
3.60
3.59
3.58
3.56
3.55
2.10
2.09
2.07
2.06
2.05
2.04
2.03
1.99
1.98
1.98
1.98
1.97
1.97
1.97
1.96
1.96
1.95
1.94
1.94
OH
Br
N
Boc
2g
0.93
0.92
0.95
1.00
1.05
1.05
1.06
2.01
9.15
f1 (ppm)


153.49
136.79
132.95
130.78
130.70
125.30
116.18
81.72
65.62
40.78
31.95
28.43
f1 (ppm)

Injection Acq Method Name ASH - 100 bars - 2 mL.min-1 - 2% MeOH.amx

Injection Acquired Date 2019-04-11 13:47:39+02:00

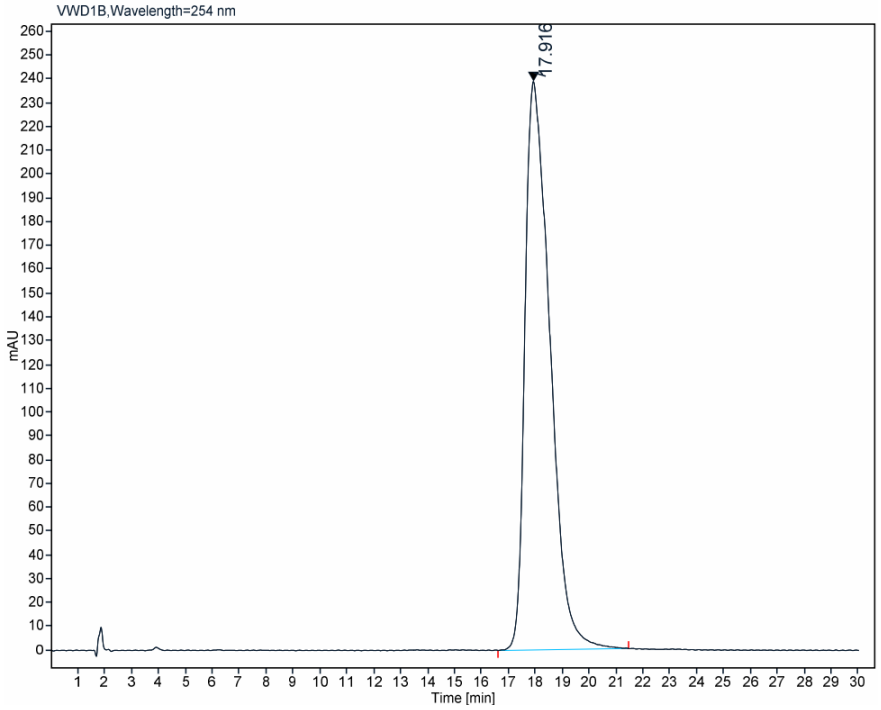
| RT | Peak Area % |
|---|---|
| 17.793 | 49.93 |
| 21.416 | 50.07 |

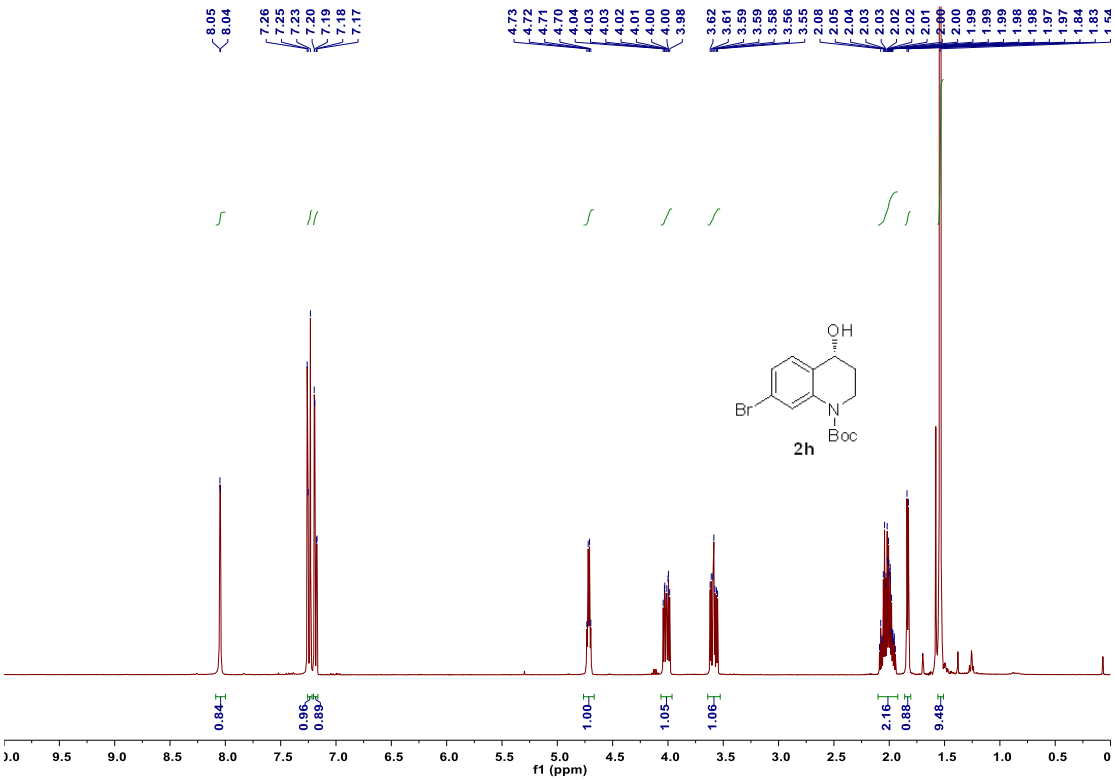


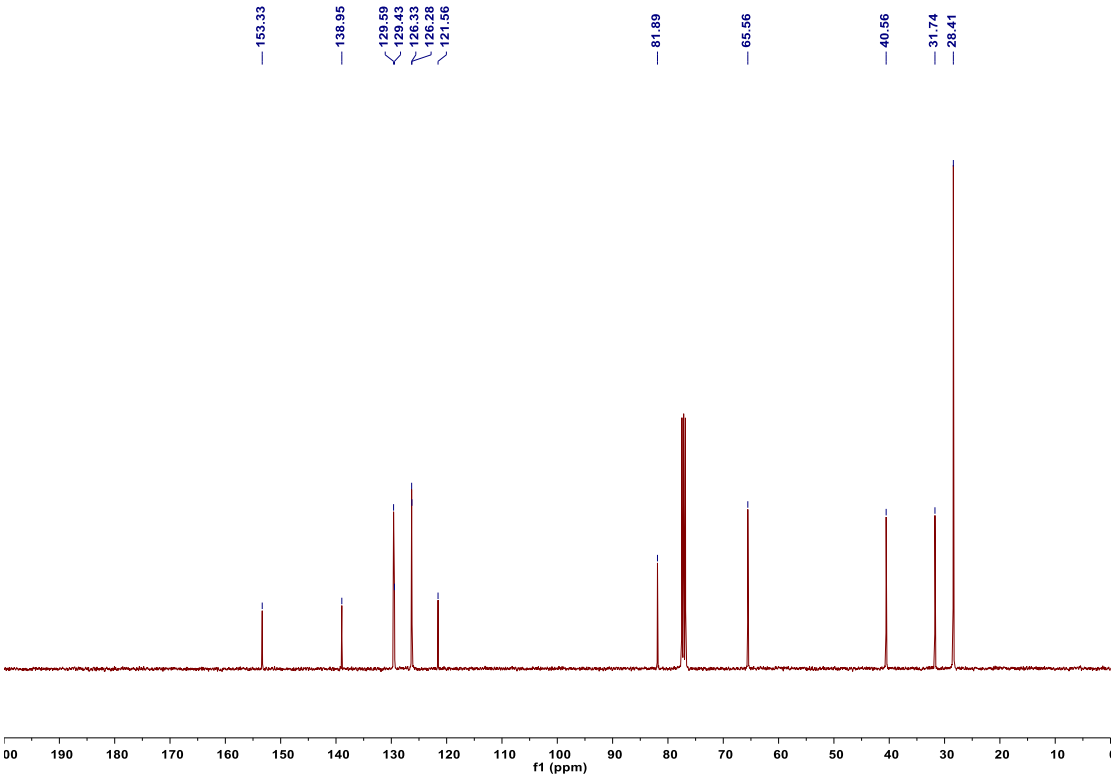

Injection Acq Method Name ASH - 100 bars - 2 mL.min-1 - 2% MeOH.amx

Injection Acquired Date 2019-04-24 14:30:14+02:00

| RT | Peak Area % |
|---|---|
| 17.916 | 100.00 |



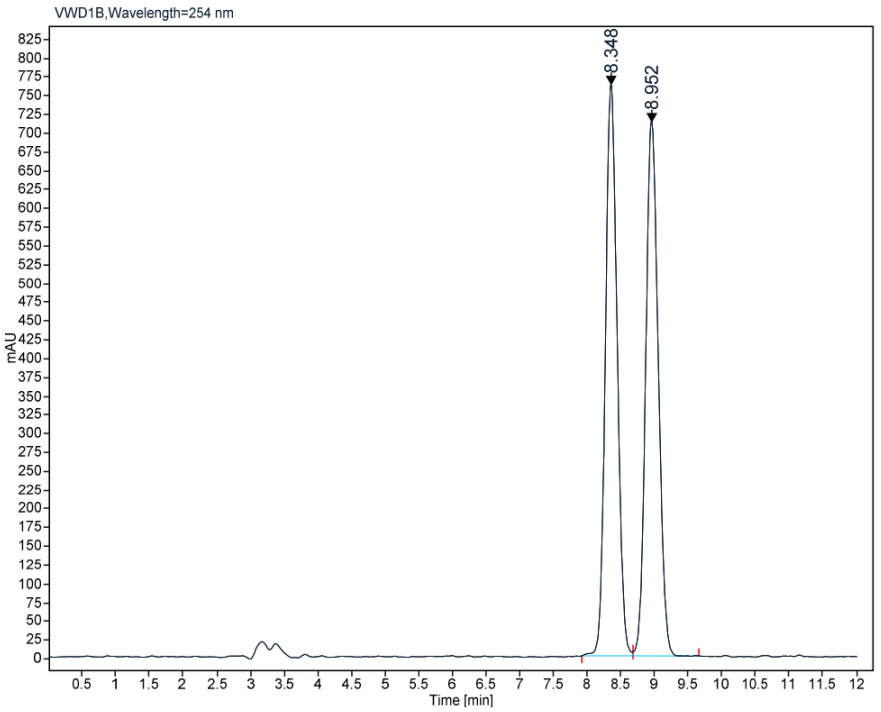

8.05
8.04
7.26
7.25
7.23
7.20
7.19
7.18
7.17
4.73
4.72
4.71
4.70
4.04
4.03
4.02
4.01
4.00
3.98
3.62
3.61
3.59
3.59
3.58
3.56
3.55
2.08
2.05
2.04
2.03
2.02
2.02
2.01
2.00
2.00
1.99
1.99
1.99
1.98
1.98
1.97
1.97
1.84
1.83
OH
Br
N
Boc
2h
0.84
0.96
0.89
1.00
1.05
1.06
2.16
0.88
9.48
f1 (ppm)


153.33
138.95
129.59
129.43
126.33
126.28
121.56
81.89
65.56
40.56
31.74
28.41
f1 (ppm)

Injection Acq Method Name IF- 100 bars - 2 mL.min-1 - 10% MeOH.amx

Injection Acquired Date 2019-06-26 17:25:33+02:00

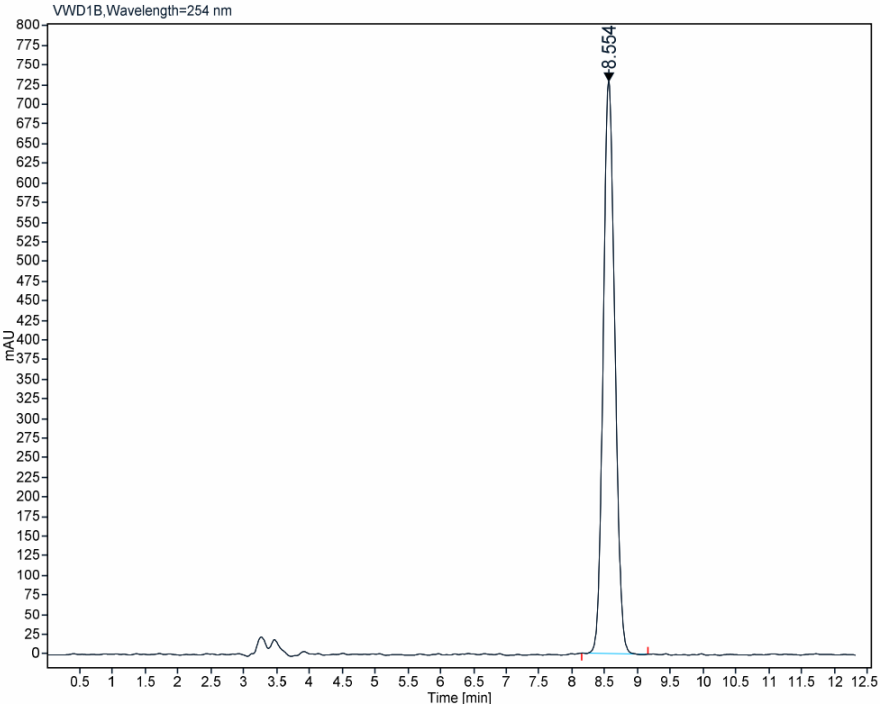
| *RT* | *Peak Area %* |
|---|---|
| 8.348 | 49.97 |
| 8.952 | 50.03 |

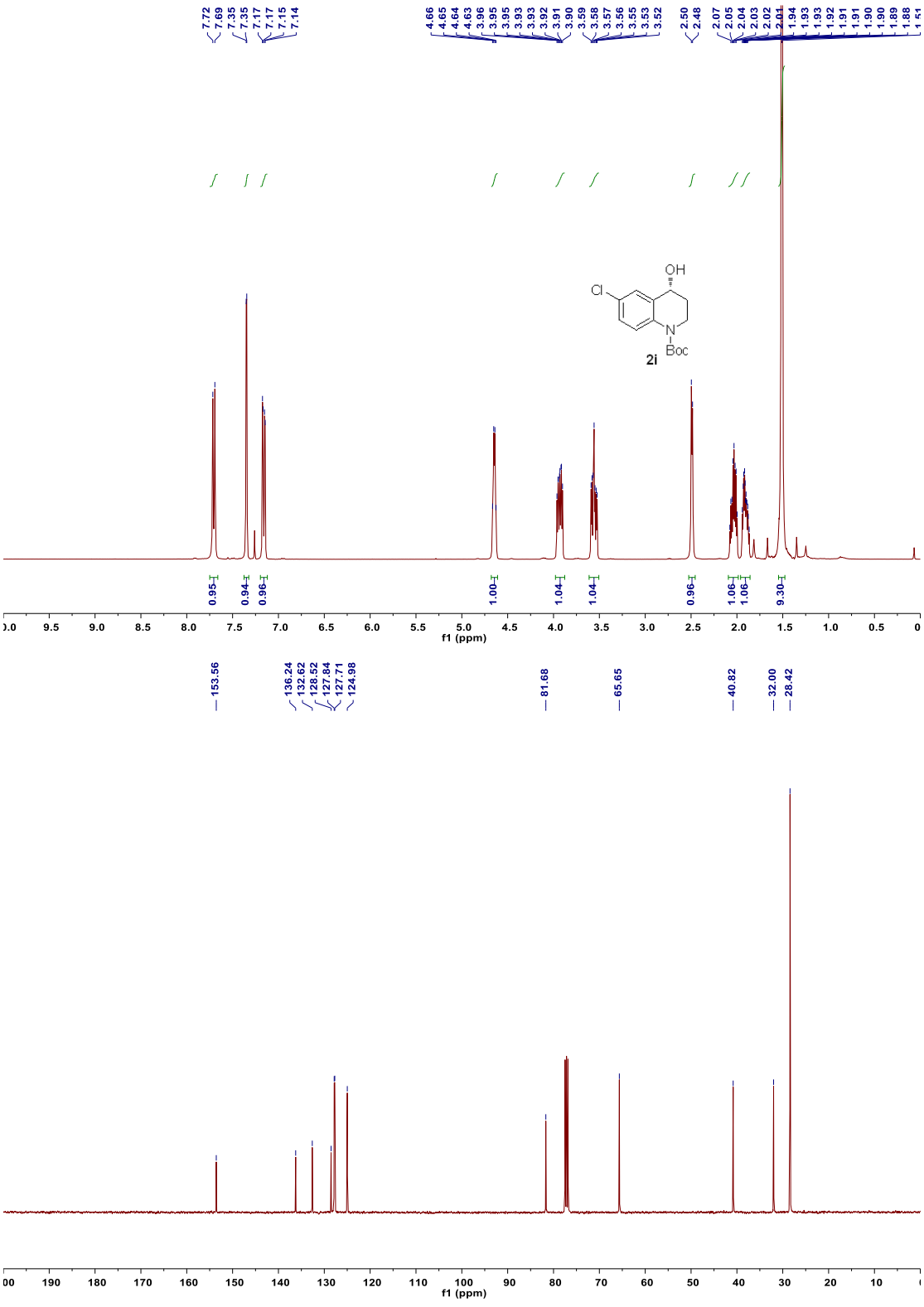



Injection Acq Method Name IF- 100 bars - 2 mL.min-1 - 10% MeOH.amx

Injection Acquired Date 2019-06-26 17:10:24+02:00

| *RT* | *Peak Area %* |
|---|---|
| 8.554 | 100.00 |

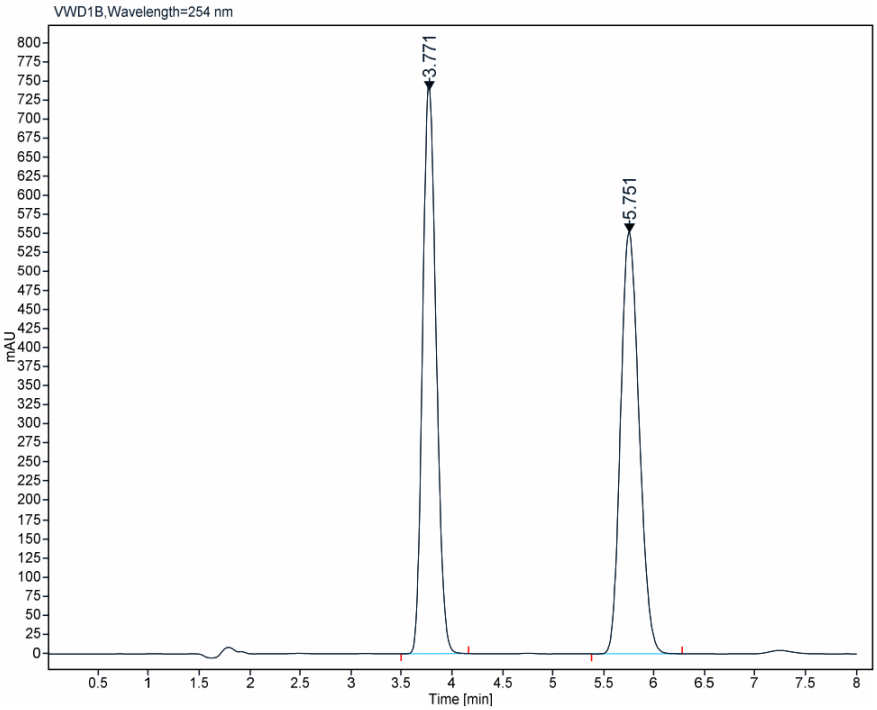



7.72
7.69
7.35
7.35
7.17
7.17
7.15
7.14
4.66
4.65
4.64
4.63
3.96
3.95
3.95
3.93
3.93
3.92
3.91
3.90
3.59
3.58
3.57
3.56
3.55
3.53
3.52
2.50
2.48
2.07
2.05
2.04
2.03
2.02
2.01
1.94
1.93
1.93
1.92
1.91
1.91
1.90
1.90
1.89
1.88
OH
Cl
N
Boc
2i
0.95
0.94
0.96
1.00
1.04
1.04
0.96
1.06
1.06
9.30
f1 (ppm)
153.56
136.24
132.62
128.52
127.84
127.71
124.98
81.68
65.65
40.82
32.00
28.42
f1 (ppm)

Injection Acq Method Name ADH - 100 bars - 2 mL.min-1 - 20% MeOH.amx

Injection Acquired Date 2019-05-14 13:11:03+02:00

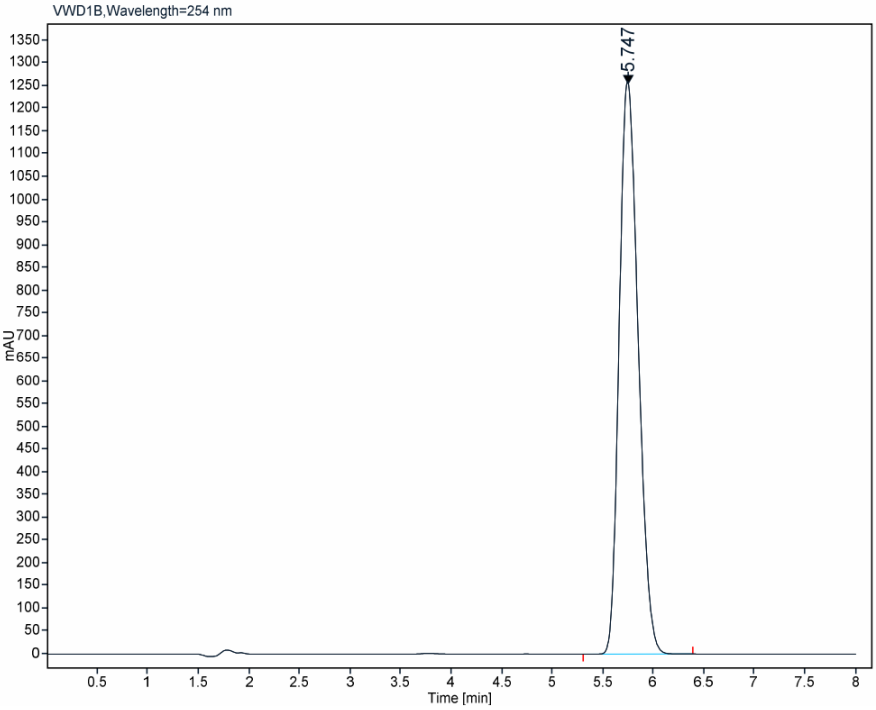
| RT | Peak Area % |
|---|---|
| 3.771 | 49.84 |
| 5.751 | 50.16 |

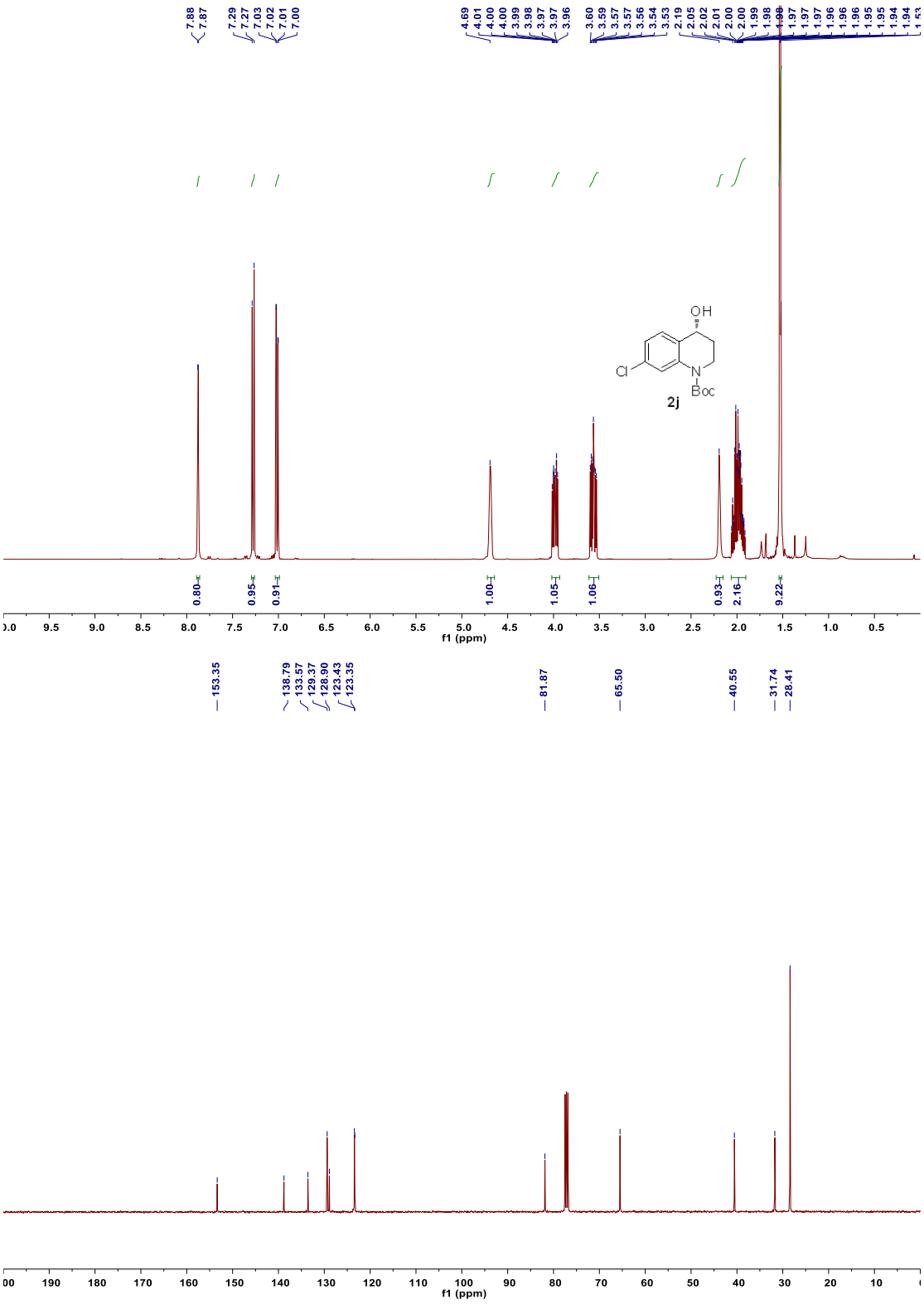



Injection Acq Method Name ADH - 100 bars - 2 mL.min-1 - 20% MeOH.amx

Injection Acquired Date 2019-05-14 13:19:48+02:00

| RT | Peak Area % |
|---|---|
| 5.747 | 100.00 |

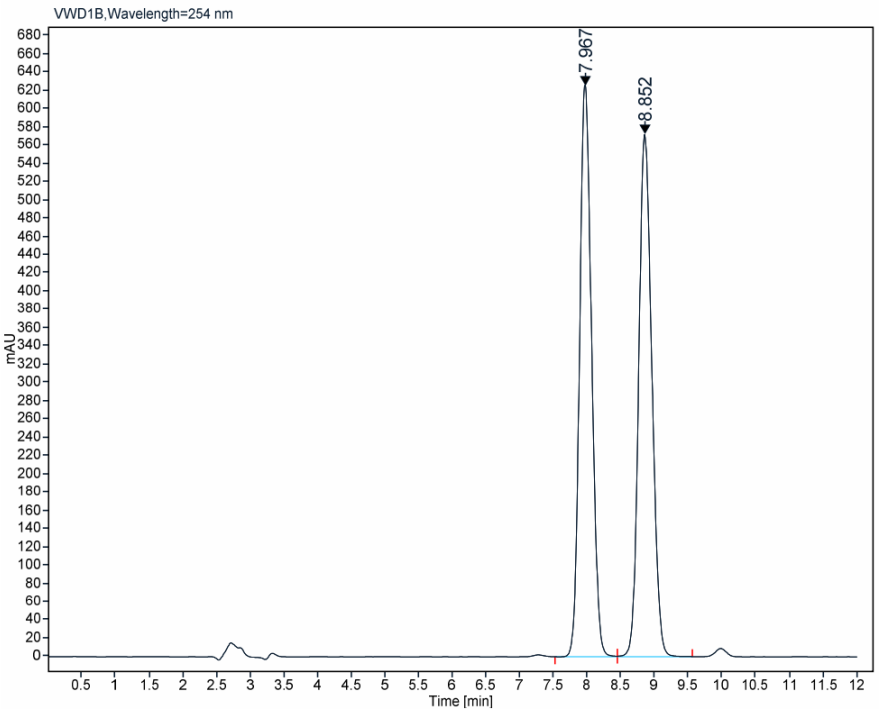



7.88
7.87
7.29
7.27
7.03
7.02
7.01
7.00
4.69
4.01
4.00
4.00
3.99
3.98
3.97
3.97
3.96
3.60
3.59
3.57
3.57
3.56
3.54
3.53
2.19
2.05
2.02
2.01
2.00
2.00
1.99
1.98
1.97
1.97
1.97
1.96
1.96
1.96
1.95
1.95
1.94
1.94
OH
Cl
N
Boc
2j
0.80
0.95
0.91
1.00
1.05
1.06
0.93
2.16
9.22
f1 (ppm)
153.35
138.79
133.57
129.37
128.90
123.43
123.35
81.87
65.50
40.55
31.74
28.41
f1 (ppm)

Injection Acq Method Name IF- 100 bars - 2 mL.min-1 - 10% MeOH.amx

Injection Acquired Date 2019-06-20 09:32:46+02:00

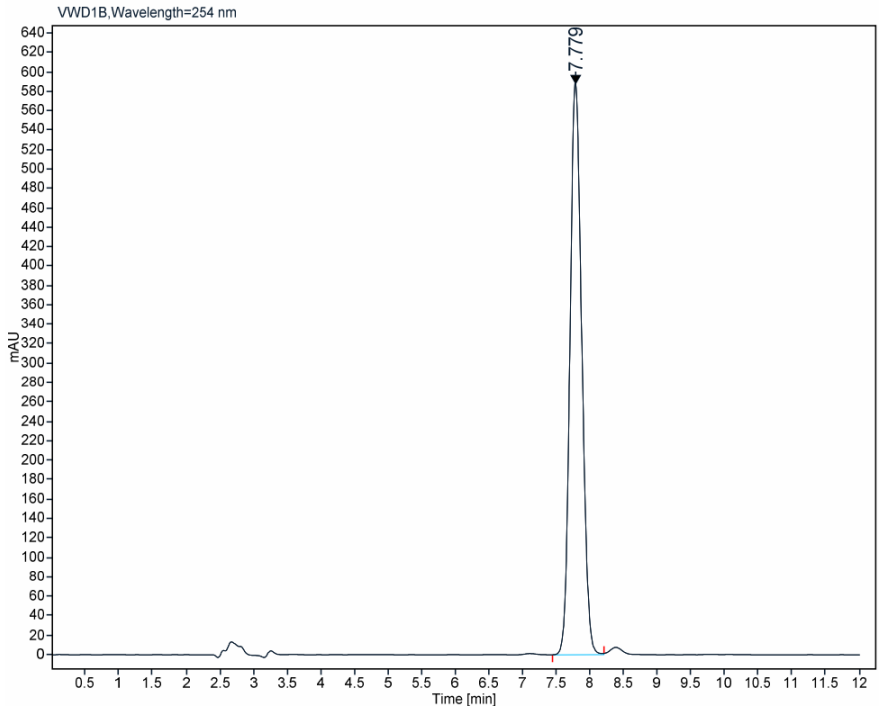
| RT | Peak Area % |
|---|---|
| 7.967 | 49.94 |
| 8.852 | 50.06 |

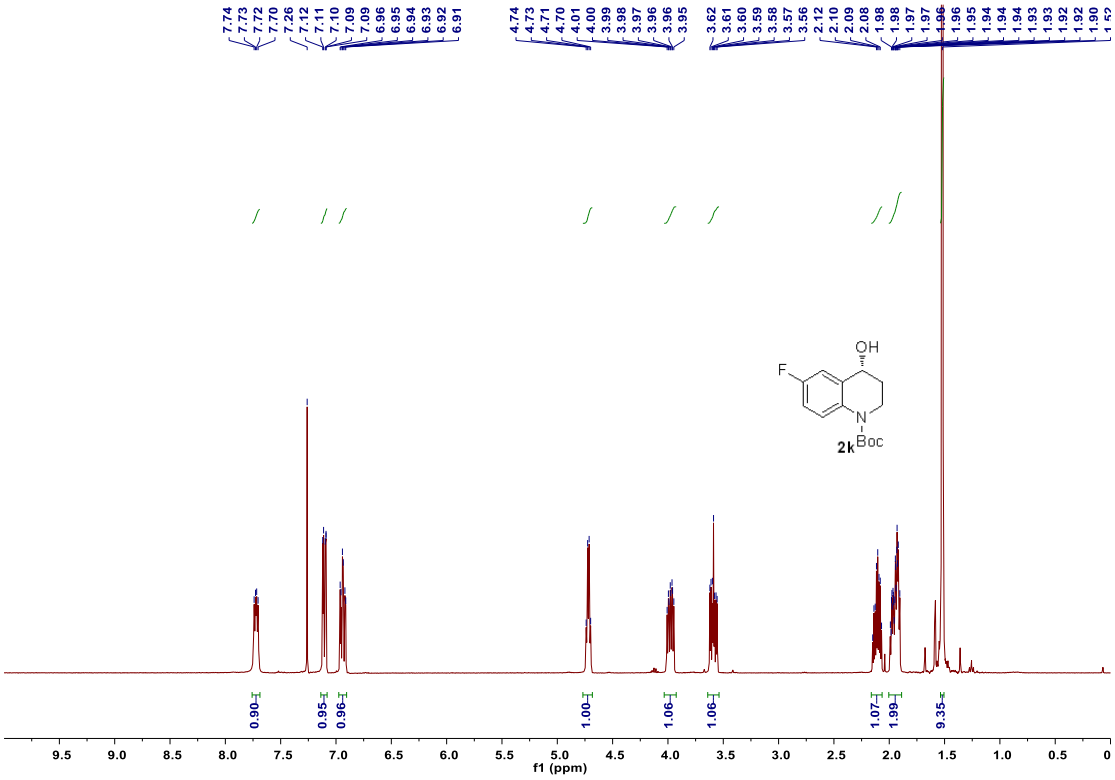


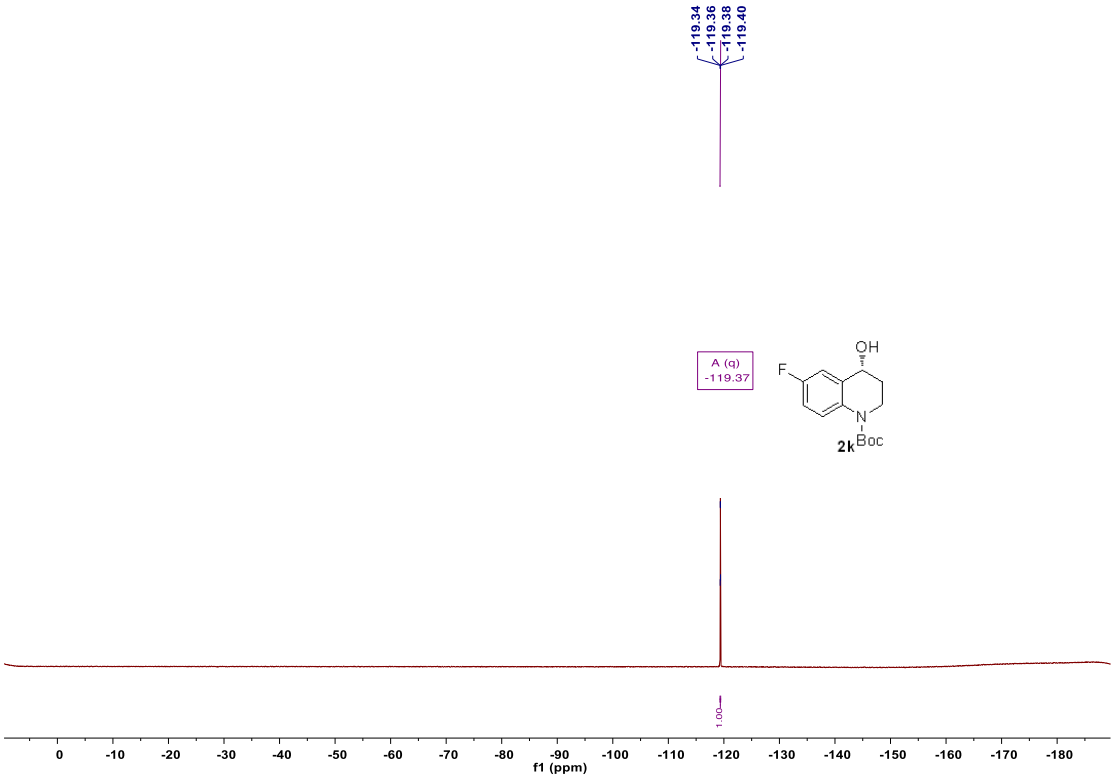

Injection Acq Method Name IF- 100 bars - 2 mL.min-1 - 10% MeOH.amx

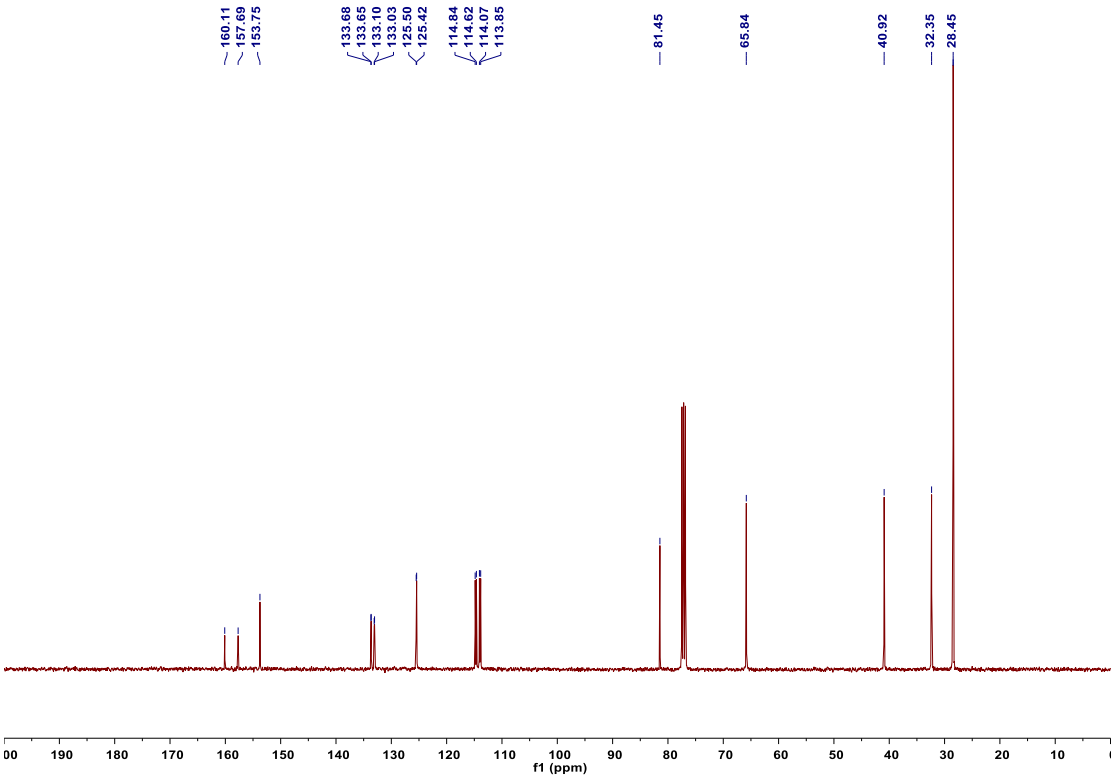
Injection Acquired Date 2019-06-20 09:45:30+02:00

| RT | Peak Area % |
|---|---|
| 7.779 | 100.00 |




7.74
7.73
7.72
7.70
7.26
7.12
7.11
7.10
7.09
7.09
6.96
6.95
6.94
6.93
6.92
6.91
4.74
4.73
4.71
4.70
4.01
4.00
3.99
3.98
3.97
3.96
3.96
3.95
3.62
3.61
3.60
3.59
3.58
3.57
3.56
2.12
2.10
2.09
2.08
1.98
1.98
1.97
1.97
1.96
1.96
1.95
1.94
1.94
1.94
1.93
1.93
1.92
1.92
1.90
OH
F
N
Boc
2k
0.90
0.95
0.96
1.00
1.06
1.06
1.07
1.99
9.35
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
f1 (ppm)


-119.34
-119.36
-119.38
-119.40
A (q)
-119.37
OH
F
N
Boc
2k
1.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
f1 (ppm)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153.75
133.68
133.65
133.10
133.03
125.50
125.42
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114.62
114.07
113.85
81.45
65.84
40.92
32.35
28.45
f1 (ppm)

Injection Acq Method Name ADH - 100 bars - 2 mL.min-1 - 20% MeOH.amx

Injection Acquired Date 2019-05-14 10:37:37+02:00

| *RT* | *Peak Area %* |
|---|---|
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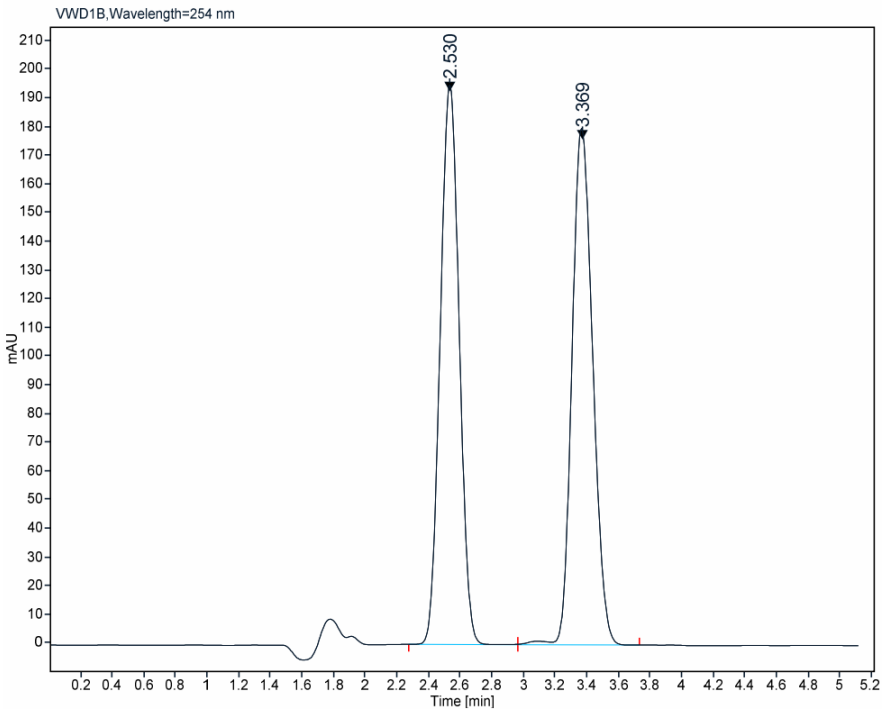
| 3.369 | 50.15 |




Injection Acq Method Name ADH - 100 bars - 2 mL.min-1 - 20% MeOH.amx

Injection Acquired Date 2019-05-14 10:43:45+02:00

| *RT* | *Peak Area %* |
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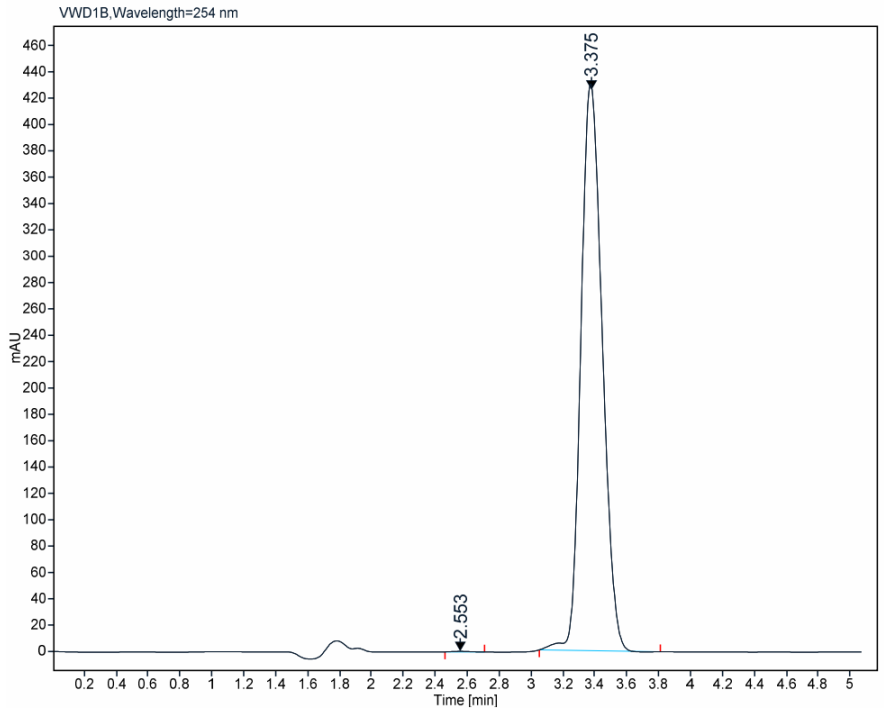
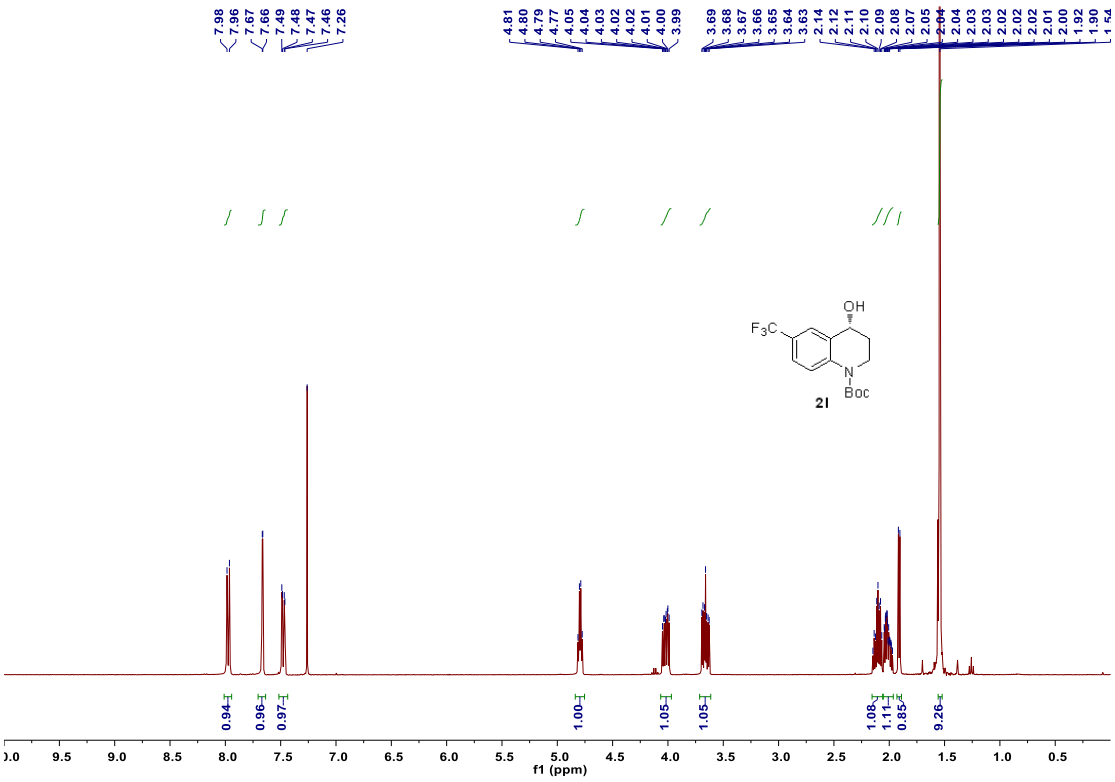
| 2.553 | 0.08 |
| 3.375 | 99.92 |

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7.67
7.66
7.49
7.48
7.47
7.46
7.26
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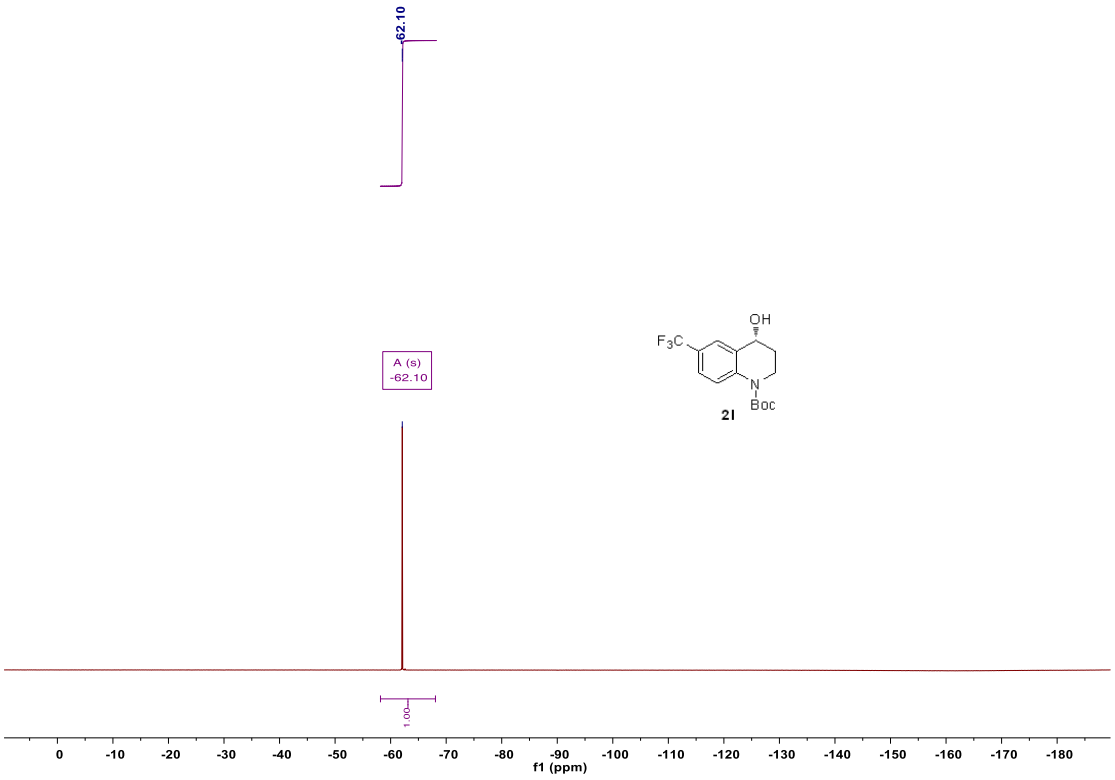
4.80
4.79
4.77
4.05
4.04
4.03
4.02
4.02
4.01
4.00
3.99
3.69
3.68
3.67
3.66
3.65
3.64
3.63
2.14
2.12
2.11
2.10
2.09
2.08
2.07
2.05
2.04
2.04
2.03
2.03
2.02
2.02
2.02
2.01
2.00
1.92
1.90
1.54
OH
F3C
N
Boc
2l
0.94
0.96
0.97
1.00
1.05
1.05
1.08
1.11
0.85
9.26
f1 (ppm)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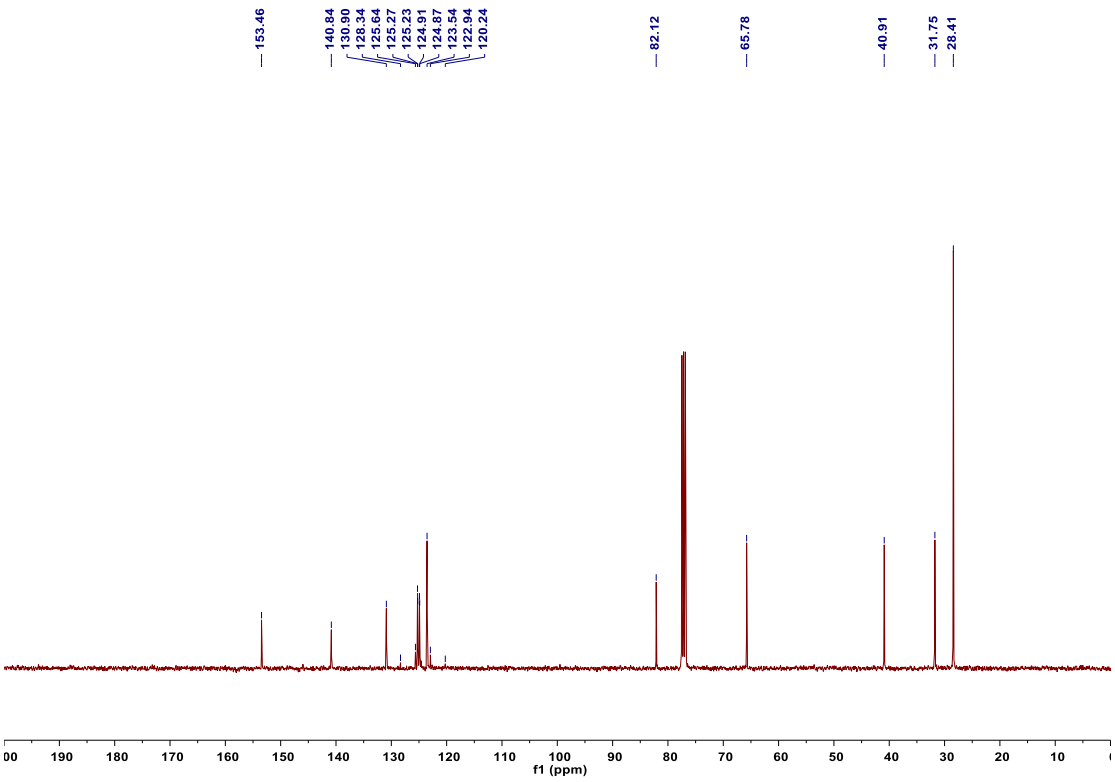
A (s)
-62.10
OH
F3C
N
Boc
2l
1.00
f1 (ppm)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140.84
130.90
128.34
125.64
125.27
125.23
124.91
124.87
123.54
122.94
120.24
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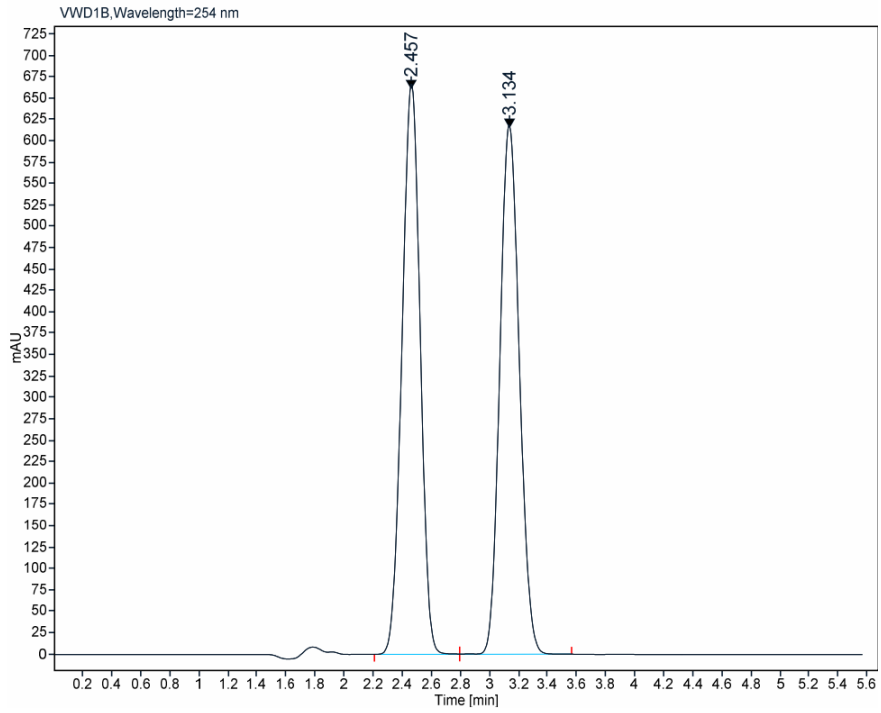
65.78
40.91
31.75
28.41
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Injection Acq Method Name ADH - 100 bars - 2 mL.min-1 - 20% MeOH.amx

Injection Acquired Date 2019-05-14 10:49:52+02:00

| *RT* | *Peak Area %* |
|---|---|
| 2.457 | 49.92 |
| 3.134 | 50.08 |




Injection Acq Method Name ADH - 100 bars - 2 mL.min-1 - 20% MeOH.amx

Injection Acquired Date 2019-05-14 10:56:29+02:00

| *RT* | *Peak Area %* |
|---|---|
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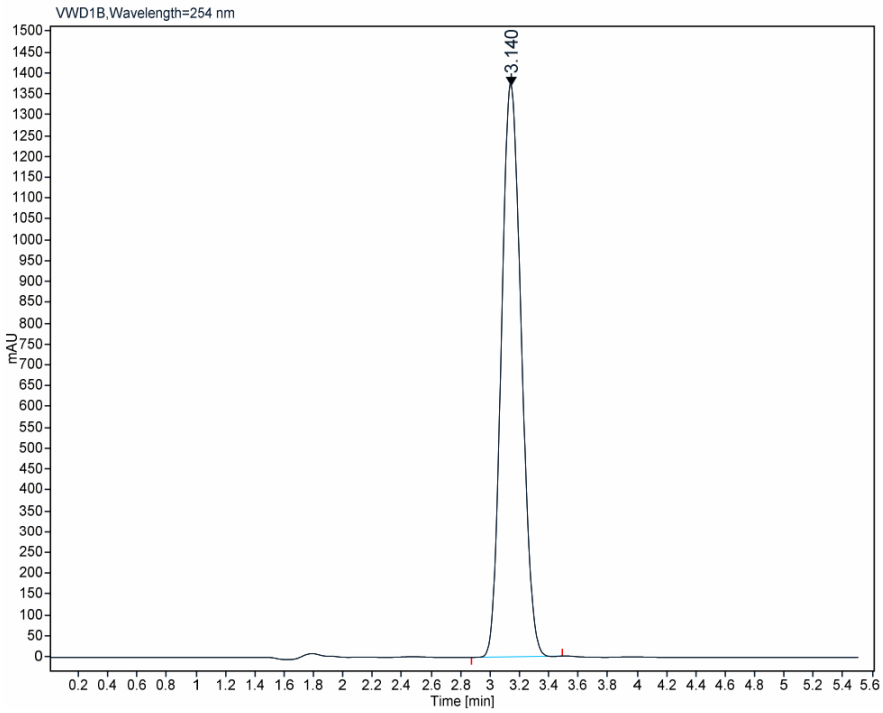

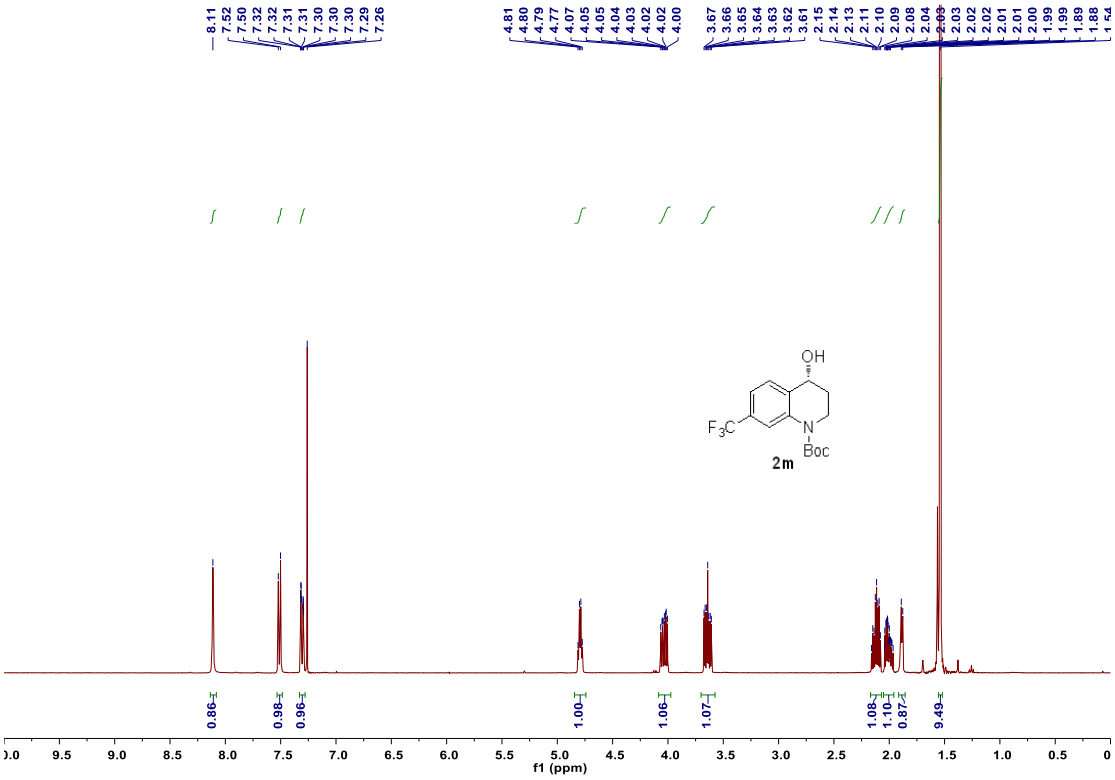
8.11
7.52
7.50
7.32
7.32
7.31
7.31
7.30
7.30
7.30
7.29
7.26
4.81
4.80
4.79
4.77
4.07
4.05
4.05
4.04
4.03
4.02
4.02
4.00
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3.65
3.64
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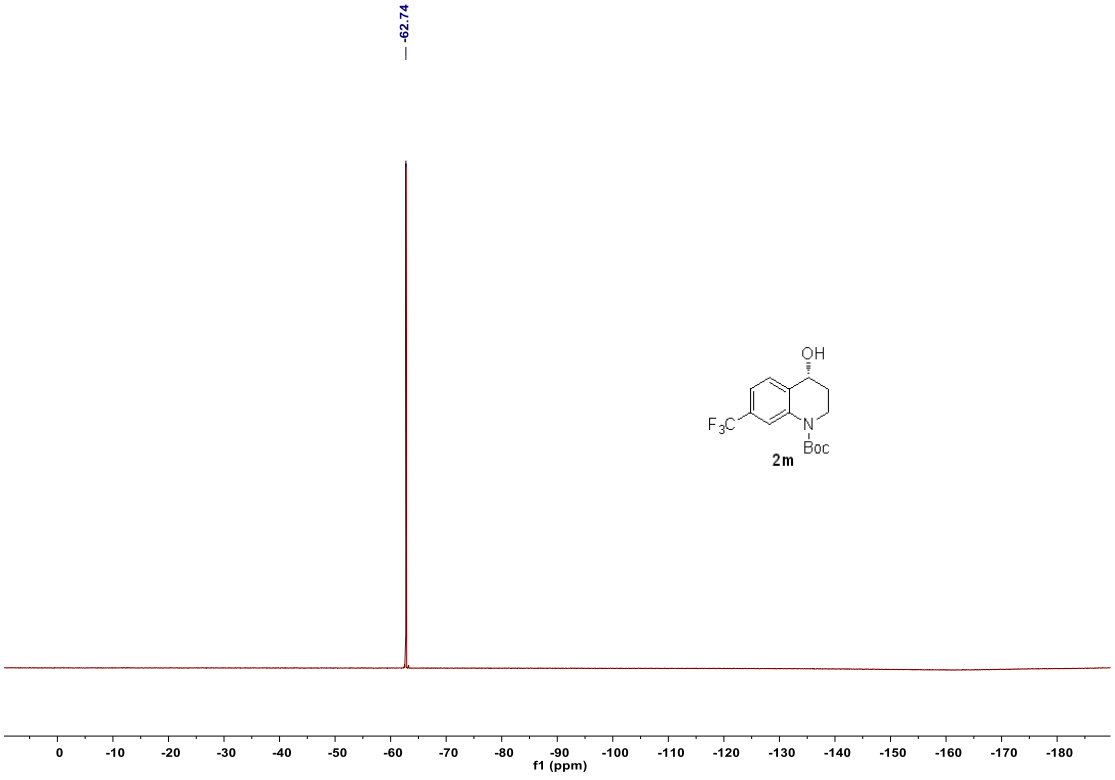
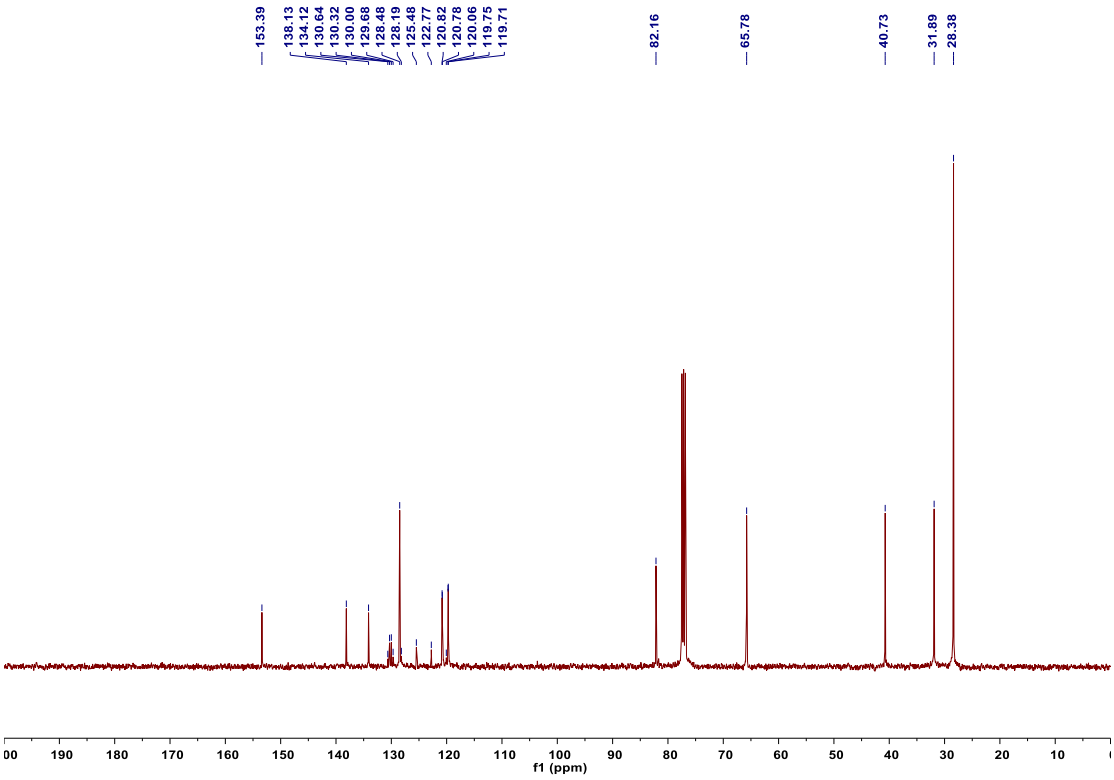
2.01
2.00
1.99
1.99
1.89
1.88
1.54
OH
F3C
N
Boc
2m
0.86
0.98
0.96
1.00
1.06
1.07
1.08
1.10
0.87
9.49
f1 (ppm)

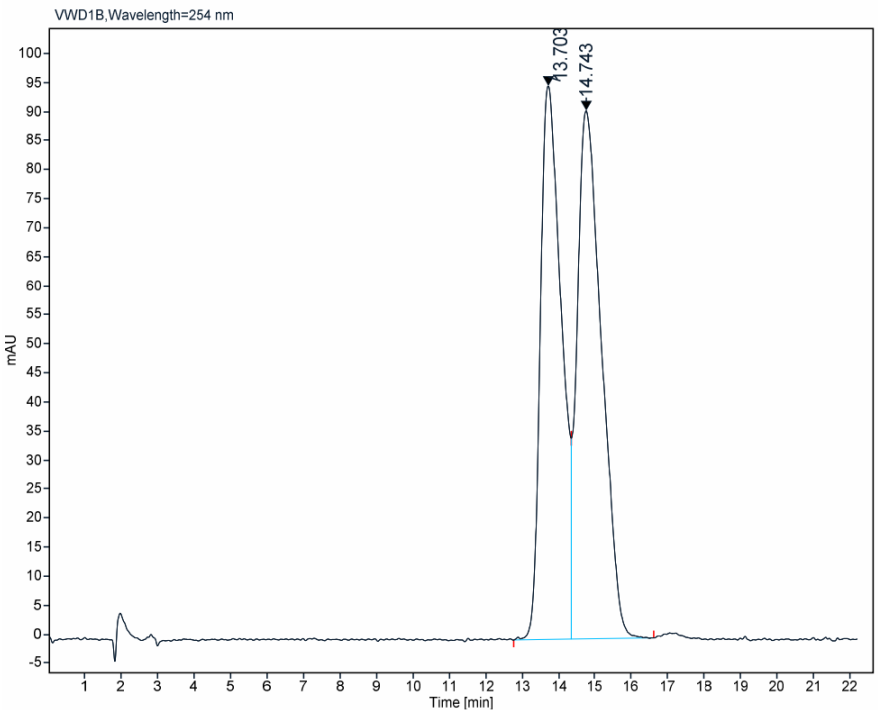

-62.74
OH
F3C
N
Boc
2m
f1 (ppm)


153.39
138.13
134.12
130.64
130.32
130.00
129.68
128.48
128.19
125.48
122.77
120.82
120.78
120.06
119.75
119.71
82.16
65.78
40.73
31.89
28.38
f1 (ppm)

Injection Acq Method Name IF - 100 bars - 3 mL.min-1 - 2% iPrOH.amx

Injection Acquired Date 2019-06-27 17:40:02+02:00

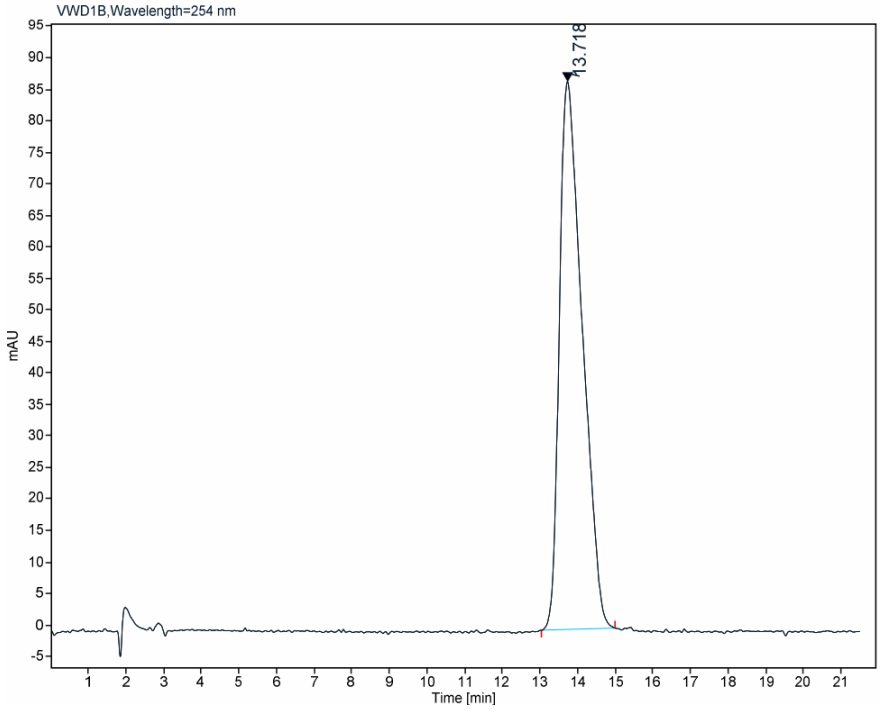
| *RT* | *Peak Area %* |
|---|---|
| 13.703 | 47.29 |
| 14.743 | 52.71 |




Injection Acq Method Name IF - 100 bars - 3 mL.min-1 - 2% iPrOH.amx

Injection Acquired Date 2019-06-27 18:03:25+02:00

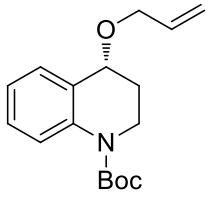
| *RT* | *Peak Area %* |
|---|---|
| 13.718 | 100.00 |



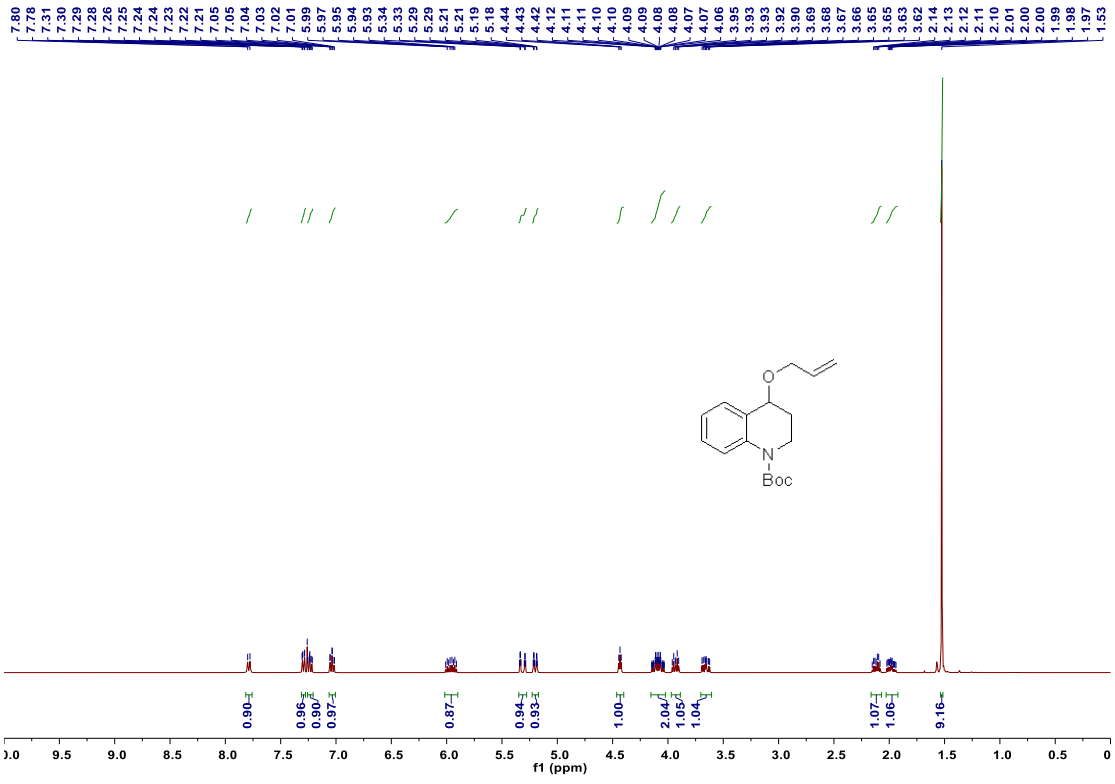
## VIII. Analytical data and procedures for compounds 4–6

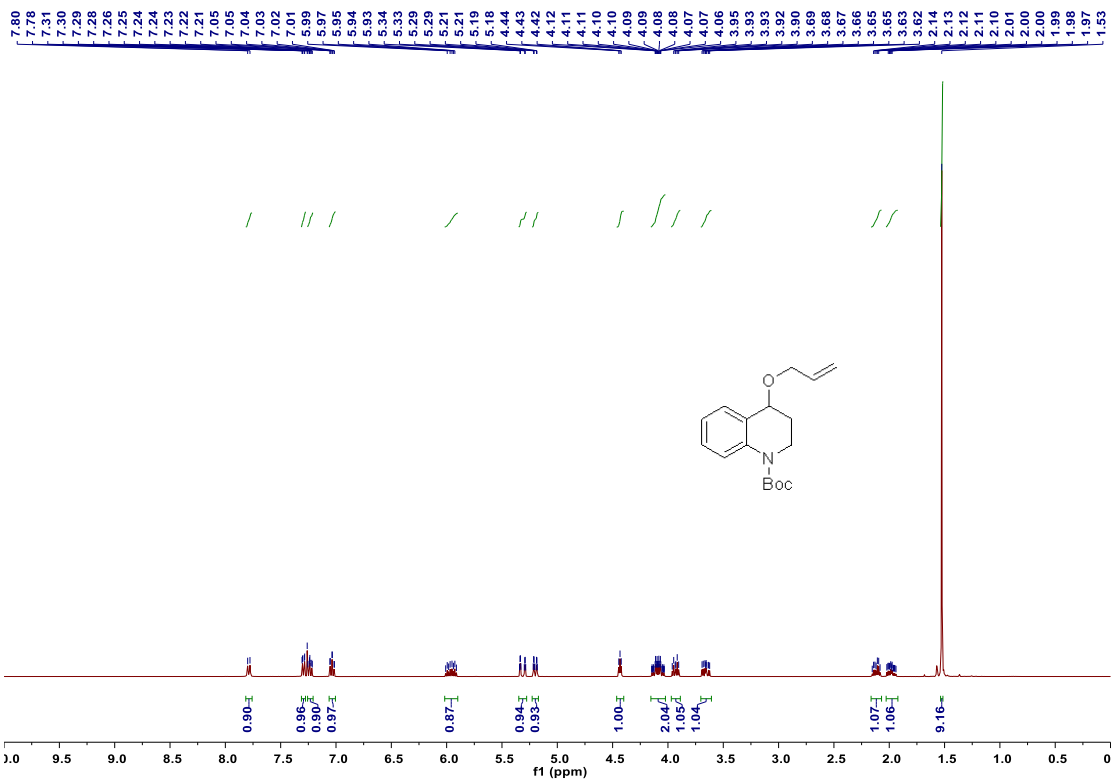
**Compound 4:**[5]

To a solution of (*R*)-*tert*-butyl 4-hydroxy-3,4-dihydroquinoline-1(2H)-carboxylate **2a** (125 mg, 0.5 mmol) in DMF (1.5 mL) was added NaH (60% dispersion in oil, 0.55 mmol, 22 mg) at room temperature. The mixture was stirred at the same temperature for 30 min then allyl bromide (0.55 mmol, 48 μl) was added dropwise. After being stirred for 1 h, the reaction mixture was poured into water and extracted with $CH_2Cl_2$. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA 40:1) to afford pure **4** (111 mg, 77% yield) as a colorless liquid.



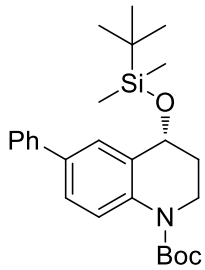

$[\alpha]_D^{25}$ = +39.7 (*c* 0.75, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 1H), 7.29 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.26 – 7.21 (m, 1H), 7.03 (td, *J* = 7.5, 1.1 Hz, 1H), 5.96 (ddd, *J* = 22.8, 10.7, 5.6 Hz, 1H), 5.31 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.20 (dq, *J* = 10.4, 1.5 Hz, 1H), 4.43 (t, *J* = 4.4 Hz, 1H), 4.09 (qdt, *J* = 12.7, 5.6, 1.5 Hz, 2H), 3.93 (dt, *J* = 12.8, 5.2 Hz, 1H), 3.66 (ddd, *J* = 12.7, 10.3, 4.4 Hz, 1H), 2.15 – 2.08 (m, 1H), 2.00 – 1.94 (m, 1H), 1.53 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 153.9, 138.2, 135.1, 128.9, 128.0, 123.7, 123.0, 117.2, 81.1, 72.5, 69.4, 40.9, 28.9, 28.5. HRMS (ESI/ion trap): *m/z* [M + Na]$^+$ calcd for $C_{17}H_{23}NNaO_3$ 312.1576, found 312.1570.





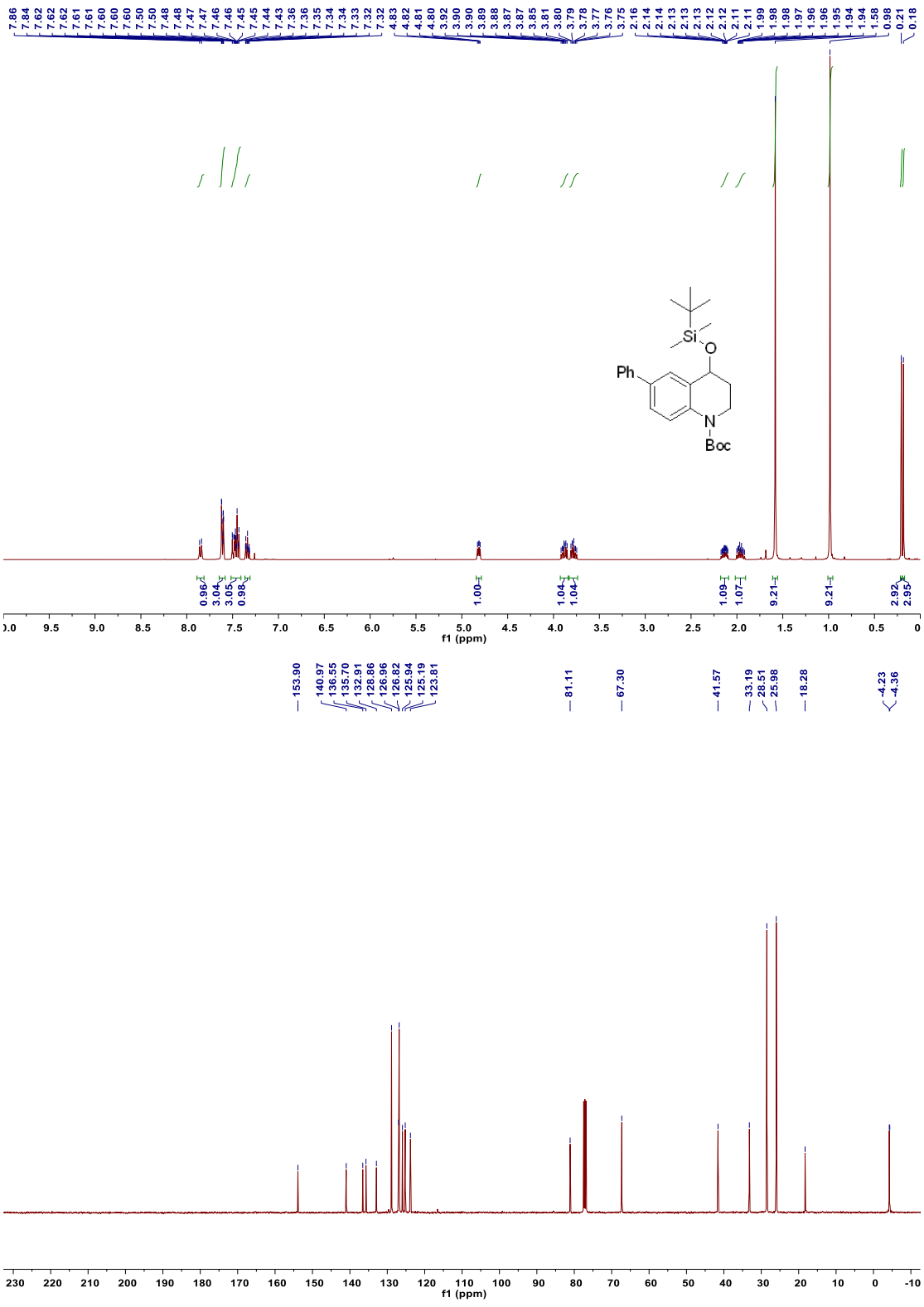

**Compound 5:**[6,7]

A solution of (*R*)-*tert*-butyl 6-bromo-4-hydroxy-3,4-dihydroquinoline-1(2H)-carboxylate **2g** (164 mg, 0.50 mmol) and imidazole (41 mg, 0.6 mmol) in DMF (x mL) was added dropwise to a cooled (0 °C) solution of TBSCl (90 mg, 0.6 mmol) in DMF (0.2 mL) and the mixture stirred at 30 °C for 24 h. Water (10 ml) was added and the mixture was extracted with $Et_2O$ (3 x 20 mL). The organic extracts were combined, dried with $MgSO_4$, and concentrated. The reside was purified by flash column chromatography to give pure (*R*)-tert-butyl-6-bromo-4-((*tert*-butyldimethylsilyl)oxy)-3,4-dihydroquinoline-1(2H)-carboxylate (207 mg, 94% yield). The latter compound (132 mg, 0.3 mmol) was placed in a round-bottom tube, and phenylboronic acid (73 mg, 0.6 mmol), $K_2CO_3$ (124 mg, 0.9 mmol), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol) and cataCXium A (10.7 mg, 0.03 mmol) were added. The tube was purged with argon three times and DMF (1.5 ml) was added. The reaction was heated at 100 °C overnight, quenched with water and extracted by $CH_2Cl_2$ (3 x 5 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel (cyclohexane/EtOAc 20:1) to give pure **5** (129 mg, 98% yield) as a white solid.



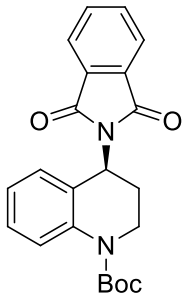

m.p. 85 °C, $[\alpha]_D^{25}$ = +24.1 (*c* 1.19, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.6 Hz, 1H),

7.63 – 7.58 (m, 3H), 7.51 – 7.41 (m, 3H), 7.38 – 7.31 (m, 1H), 4.81 (dd, *J* = 7.4, 4.0 Hz, 1H), 3.94 – 3.85 (m, 1H), 3.82 – 3.72 (m, 1H), 2.20 – 2.07 (m, 1H), 2.03 – 1.89 (m, 1H), 1.58 (s, 9H), 0.98 (s, 9H), 0.21 (s, 3H), 0.18 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 153.9, 141.0, 136.6, 135.7, 132.9, 128.9, 127.0, 126.8, 125.9, 125.2, 123.8, 81.1, 67.3, 41.6, 33.2, 28.5, 26.0, 18.3, –4.2, –4.4. HRMS (ESI/ion trap): *m/z* $[M + Na]^+$ calcd for $C_{26}H_{37}NNaO_3Si$ 462.2440, found 462.2436.

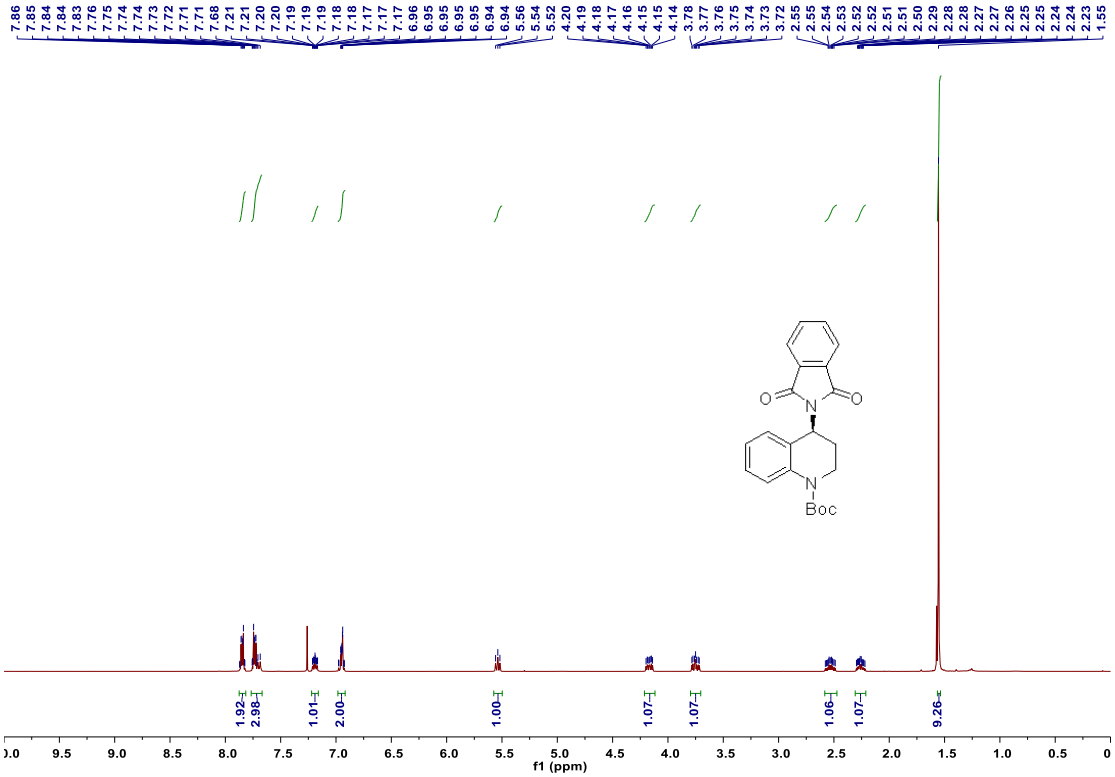


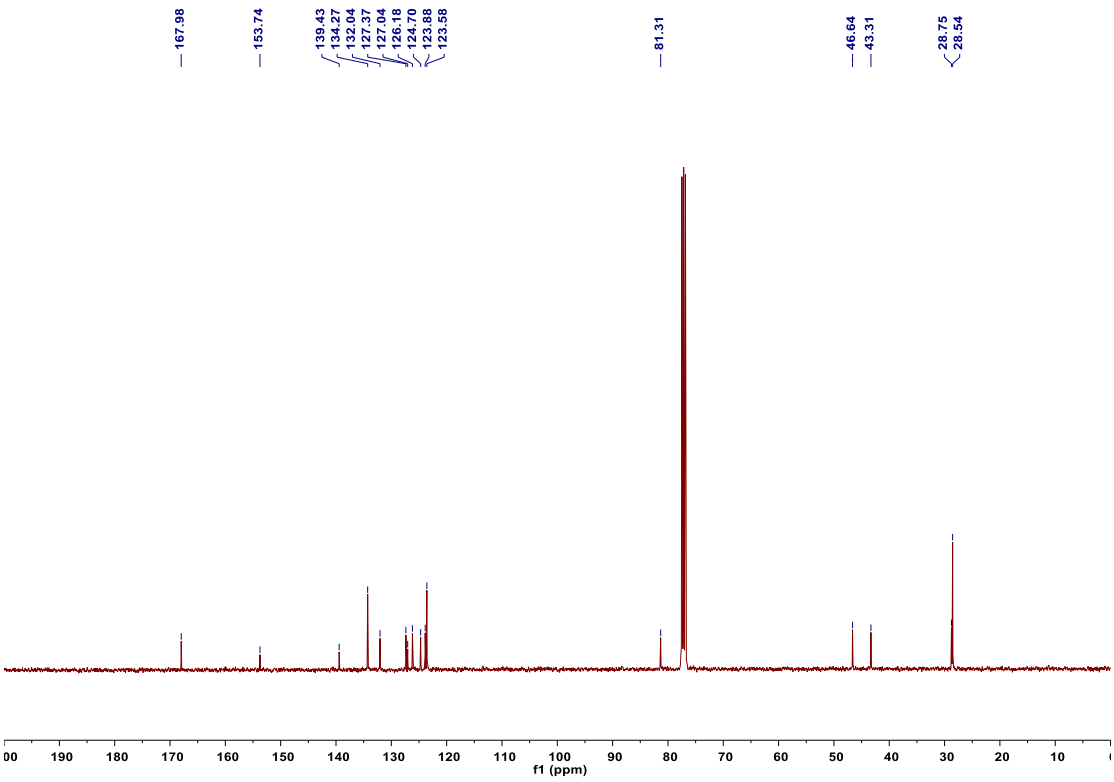
**Compound 6:**[8]

A solution of (*R*)-*tert*-butyl 4-hydroxy-3,4-dihydroquinoline-1(2H)-carboxylate **2a** (125 mg, 0.5 mmol) in THF (2 ml) was added to a mixture of $PPh_3$ (197 mg, 0.75 mmol) and phthalimide (100 mg, 0.75 mmol). The reaction mixture was allowed to stir for 10 min and then cooled to 0 °C. Once cooled, a solution of diisopropyl azodicarboxylate (DIAD) (202 mg, 1.0 mmol) in dry THF (1.0 ml) was added dropwise over a period of 5 min. The mixture was allowed to reach room temperature and stirred for 24 h. The reaction mixture was poured into water and extracted with $CH_2Cl_2$. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column (PE/EA 10:1) to afford pure **6** (100 mg, 53% yield) as a white solid.




m.p. 166 °C, $[\alpha]_D^{25}$ = –97.9 (*c* 1.03, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.82 (m, 2H), 7.76 – 7.68 (m, 3H), 7.21 – 7.16 (m, 1H), 6.99 – 6.91 (m, 2H), 5.54 (t, *J* = 7.8 Hz, 1H), 4.17 (ddd, *J* = 13.1, 6.1, 4.2 Hz, 1H), 3.75 (ddd, *J* = 13.3, 9.7, 3.8 Hz, 1H), 2.58 – 2.49 (m, 1H), 2.30 – 2.22 (m, 1H), 1.55 (s, 9H). $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 168.0, 153.7, 139.4, 134.3, 132.0, 127.4, 127.0, 126.2, 124.7, 123.9, 123.6, 81.3, 46.6, 43.3, 28.8, 28.5. HRMS (ESI/ion trap): *m/z* $[M + K]^+$ calcd for $C_{22}H_{22}N_2KO_4$ 417.1217, found 417.1210.






## IX. References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