BINOL derivatives-catalyzsed enantioselective allylboration of isatins: application to the synthesis of (*R*)-chimonamidine

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Supporting information

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1. General information

Molecular sieves were activated by flame heating under Ar and vacuum. TLC analyses were performed using precoated Merck TLC Silica Gel 60 F254 plates. Purifications by column chromatography on silica gel were performed with an Interchim Puriflash 450 apparatus using packed columns (30 µm granulometry). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 instrument. Chemical shifts (δ) are reported in part per million (ppm) relatively to TMS and residual solvent as internal standard.[1] The following abbreviations are used for multiplicities: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; td, triplet of doublets; m, multiplet and bs (broad singlet). Coupling constants (*J*) are reported in Hertz (Hz). HRMS analyses were obtained on a Bruker Maxis 4G instrument. X-ray crystallographic data were collected on a D8 VENTURE Bruker AXS diffractometer. Optical rotations (α) were recorded on a Perkin Elmer Model 341 polarimeter at 589 nm, in a 1 dm cell and at temperature T (°C). Specific rotations $[\alpha]_D^T$ were determined from the following formula $[\alpha]_D^T = \alpha \times 100 / c$ (c concentration, g/100 mL). Melting points were obtained on a hot bench. HPLC analysis were performed on a Shimadzu Prominence system, using Daicel chiral columns (CHIRALPAK® IB, IC or ID (5 µm)).

Reagents **7a**, **7b**, **9e**, **9f**, **9i** and catalysts (*R*)-**8a**, (*S*)-**8a**, (*R*)-**8c** were commercially available (enantiomeric ratios were greater than 98:2).

Isatins **9a** (or **9g**),[2] **9b** (or **9h**),[3] **9c**,[4] **9d**,[4] **9j**,[5] **9k**,[6] **9l**,[7] **9m**[8], **9n**,[9] **9o**,[8] **9p**,[10] **9q**,[11] **9r**[8], **9s**[12], allylboronate reagents **7c**,[13] **7d**,[13] **7e**[14]and catalysts (*R*)-**8b**,[15] (*R*)-**8d**,[16] (*R*)-**8e**,[17] (*R*)-**8f**[18] were prepared according to known procedures. All spectra of known compounds were in agreement with reported data.

Abbreviations: DCM dichloromethane, IPA *iso*-propyl alcohol, MS molecular sieves, LC liquid chromatography.

2. General Procedure for the asymmetric allylboration of isatins 9 and indanone

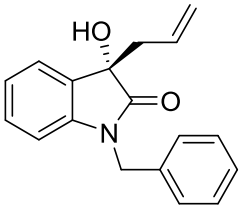
To a dried tube (5 mL) flushed with Ar, were successively added activated 5 Å molecular sieves (400 mg/mmol), toluene (0.7 mL), enantiopure (*R*)-**8a** (4.5 mg, 0.01 mmol, 0.05 eq) *t*-BuOH (93 µL, 5 eq) and allylboronate **7c** (1 M solution in toluene, 0.3 mL, 0.3 mmol, 1.5 eq). The resulting mixture was stirred at room temperature for 5 minutes, then cooled to -10 °C and stirred for 15 min before the isatin derivative **9** or indanone (0.2 mmol) was added. After stirring for 24 h (except starting from **9f**), the reaction mixture was quenched at -10°C with aqueous HCl (1 M solution, 1 mL). After stirring at room temperature for 15 min, distilled water (1 mL) and of DCM (3 mL) were added. The organic layer was separated and the aqueous phase was extracted with DCM (3 x 2 mL). The combined organic phases were washed with distilled water (2 mL), dried over MgSO4 and concentrated under vacuum. A purification was performed *via* preparative liquid chromatography over silica gel (100% DCM to 80% DCM, 20% acetone). The pure fractions were collected and the solvent was evaporated until dryness to give the expected enantio-enriched 3-allyl-3-hydroxy-2-oxindole **10** or 1-allylindan-1-ol **11**.

3. General procedure for the preparation of racemic 3-allyl-3-hydroxy-2-oxindoles.

To a 5 mL round-bottom flask equipped with a stirring bar and flushed with argon was added isatin **9** (0.2 mmol) and toluene (1.0 mL). The mixture was stirred under Ar at room temperature for 15 minutes. Allyl-dioxaborolane **7 c** (1 M solution in toluene, 0.6mL, 0.6 mmol, 3 eq) was added at once. The reaction mixture was stirred at room temperature for 24 h and quenched with an aqueous HCl solution (1 M, 1.0 mL). The biphasic mixture was stirred at room temperature for 15 minutes. The organic layer was separated, dried over $MgSO_4$ and concentrated under vacuum. The purification was performed *via* preparative liquid chromatography over silica gel (100 % DCM to 80 % DCM, 20% acetone). The pure fractions were collected and the solvent was evaporated until dryness to give the expected racemic 3-allyl-3-hydroxy-2-oxindole **10** as a white solid.

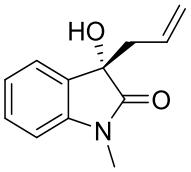
4. Analytical data of compounds 10 and 11

(*S*)-3-Allyl-1-benzyl-3-hydroxyindolin-2-one (10a)[10],[19]



Yield: 56 mg (99%), White solid, mp: 64-66 °C, $[\alpha]_D^{20}$ = -15.2 (c 1.00, $CHCl_3$)
The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 7.15 min, $t_{(S)}$ = 11.48 min (for the chromatogram refer to page S14), e.r.: 3:97.
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.45 – 7.36 (m, 1H), 7.35 – 7.24 (m, 5H), 7.24 – 7.16 (m, 1H), 7.11 – 7.00 (m, 1H), 6.73 – 6.65 (m, 1H), 5.73 – 5.54 (m, 1H), 5.22 – 5.06 (m, 2H), 5.02 (d, *J* = 15.7 Hz, 1H), 4.72 (d, *J* = 15.7 Hz, 1H), 3.11 (bs, 1H), 2.88 – 2.61 (m, 2H)
^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 177.9, 142.6, 135.5, 130.6, 129.8, 129.7, 128.9, 127.8, 127.4, 124.3, 123.2, 120.8, 109.6, 76.0, 44.0, 43.2

(*S*)-3-Allyl-3-hydroxy-1-methylindolin-2-one (10b)[20],[21]

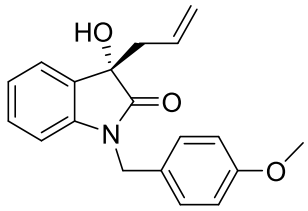


Yield: 39 mg (98%), white solid, mp: 119-121 °C ; $[\alpha]_D^{20}$ = -40.3 (c 1.00, $CHCl_3$)
The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 9.02 min, $t_{(S)}$ = 11.15 min ((for the chromatogram refer to page S15), e.r.: 3.5:96.5.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.42 – 7.35 (m, 1H), 7.35 – 7.28 (m, 1H), 7.13 – 7.05 (m, 1H), 6.85 – 6.78 (m, 1H), 5.73 – 5.53 (m, 1H), 5.14 – 5.03 (m, 2H), 3.28 (bs, 1H), 3.15 (s, 3H), 2.79 – 2.57 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 177.8, 143.4, 130.6, 129.8, 129.8, 124.2, 123.2, 120.6, 108.5, 76.0, 43.0, 26.3

(*S*)-3-Allyl-3-hydroxy-1-(4-methoxybenzyl)indolin-2-one (10c)[22]



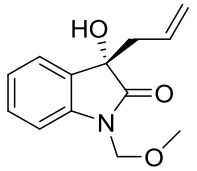
Yield = 54mg (94%), colorless syrup, $[\alpha]_D^{20}$ = -13.9 (c 0.92, $CHCl_3$)

The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 10.90 min, $t_{(S)}$ = 18.85 min (for the chromatogram refer to page S16, e.r.: 3:97.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.43 – 7.35 (m, 1H), 7.25 – 7.16 (m, 3H), 7.09 – 7.01 (m, 1H), 6.87 – 6.78 (m, 2H), 6.76 – 6.67 (m, 1H), 5.70 – 5.52 (m, 1H), 5.18 – 5.06 (m, 2H), 4.94 (d, *J* = 15.4 Hz, 1H), 4.66 (d, *J* = 15.4 Hz, 1H), 3.76 (s, 3H), 3.26 (bs, 1H), 2.88 – 2.63 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 177.9, 159.2, 142.6, 130.7, 129.8, 129.7, 128.8, 127.6, 124.2, 123.1, 120.7, 114.2, 109.6, 76.0, 55.4, 43.4, 43.2

(*S*)-3-Allyl-3-hydroxy-1-(methoxymethyl)indolin-2-one (10d)



Yield: 45 mg (96%), colourless syrup, $[\alpha]_D^{20}$ = -36.9 (c 1.01, $CHCl_3$)

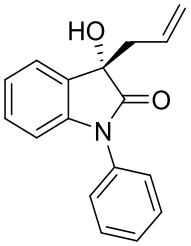
The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 6.91 min, $t_{(S)}$ = 8.87 min (for the chromatogram refer to page S17), e.r.: 4.5:95.5.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.45 – 7.38 (m, 1H), 7.37 – 7.28 (m, 1H), 7.18 – 7.08 (m, 1H), 7.07 – 6.96 (m, 1H), 5.68 – 5.52 (m, 1H), 5.17 – 5.01 (m, 4H), 3.31 (s, 3H), 2.99 (bs, 1H), 2.82 – 2.59 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 178.3, 141.7, 130.5, 130.0, 129.2, 124.3, 123.7, 120.8, 110.0, 76.4, 71.7, 56.5, 43.2

HRMS (ESI) m/z. calcd. for $C_{13}H_{15}NO_3Na$ $[M+Na]^+$ 256.0944; found 256.0946.

(*S*)-3-Allyl-3-hydroxy-1-phenylindolin-2-one (10e)[23]



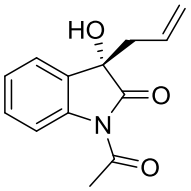
Yield: 49 mg (92%), coloruless syrup, $[\alpha]_D^{20}$ = -50.1 (c 0.94, $CHCl_3$)

The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IB column, heptane/IPA = 95/5, flow rate = 0.7 mL/min, 254 nm, $t_{(R)}$ = 17.11 min, $t_{(S)}$ = 19.08 min (for the chromatogram refer to page S18), e.r.: 4.5:95.5.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.57 – 7.37 (m, 6H), 7.30 – 7.24 (m, 1H), 7.19 – 7.12 (m, 1H), 6.84 – 6.79 (m, 1H), 5.76 – 5.61 (m, 1H), 5.23 – 5.12 (m, 2H), 3.37 (bs, 1H), 2.92 – 2.70 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 177.3, 143.4, 134.1, 130.5, 129.8, 129.7, 129.4, 128.3, 126.6, 124.5, 123.6, 120.7, 109.8, 76.2, 43.6

(*S*)-1-Acetyl-3-allyl-3-hydroxyindolin-2-one (10f)



Reaction time: 6 days at -10 °C, Yield: 39 mg (84%), white solid, mp: 94-98 °C, $[\alpha]_D^{20}$ = -8.5 (c 1.00, $CHCl_3$)

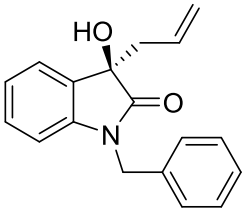
The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 90/10, flow rate = 1.0 mL/min, 235 nm, $t_{(R)}$ = 6.95 min, $t_{(S)}$ = 7.51 min (for the chromatogram refer to page S19), e.r.: 42.5:57.5.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.26 – 8.13 (m, 1H), 7.45 – 7.35 (m, 2H), 7.31 – 7.19 (m, 1H), 5.61 – 5.46 (m, 1H), 5.16 – 5.09 (m, 2H), 3.04 (bs, 1H), 2.79 – 2.64 (m, 2H), 2.63 (s, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 178.6, 170.7, 139.7, 130.3, 129.8, 128.9, 125.8, 123.85, 121.4, 116.9, 76.0, 43.9, 26.6

HRMS (ESI) m/z. calcd. for $C_{13}H_{13}NO_3Na$ $[M+Na]^+$ 254.0788; found 254.0792.

(*R*)-3-Allyl-1-benzyl-3-hydroxyindolin-2-one (10g) [10, 19]



Prepared using commercially available **(*S*)-8a**.

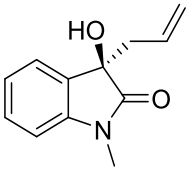
Yield: 56 mg (99%), white solid, mp: 65-68 °C, $[\alpha]_D^{20}$ = +14.8 (c 1.00, $CHCl_3$)

The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 7.53 min, $t_{(S)}$ = 12.58 min (for the chromatogram refer to page S20), e.r.: 97:3.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.45 – 7.36 (m, 1H), 7.35 – 7.24 (m, 5H), 7.24 – 7.16 (m, 1H), 7.11 – 7.00 (m, 1H), 6.73 – 6.65 (m, 1H), 5.73 – 5.54 (m, 1H), 5.22 – 5.06 (m, 2H), 5.02 (d, *J* = 15.7 Hz, 1H), 4.72 (d, *J* = 15.7 Hz, 1H), 3.11 (bs, 1H), 2.88 – 2.61 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 177.9, 142.6, 135.5, 130.6, 129.8, 129.7, 128.9, 127.8, 127.4, 124.3, 123.2, 120.8, 109.6, 76.0, 44.0, 43.2

(*R*)-3-Allyl-3-hydroxy-1-methylindolin-2-one (10h) [21]



Prepared using commercially available **(*S*)-8a**.

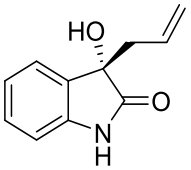
Yield: 1.30 g (98%), white solid, mp: 120-122 °C, $[\alpha]_D^{20}$ = +39.8 (c 1.00, $CHCl_3$)

The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 8.70 min, $t_{(S)}$ = 10.79 min (for the chromatogram refer to page S21), e.r.: 97:3.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.42 – 7.35 (m, 1H), 7.35 – 7.28 (m, 1H), 7.13 – 7.05 (m, 1H), 6.85 – 6.78 (m, 1H), 5.73 – 5.53 (m, 1H), 5.14 – 5.03 (m, 2H), 3.28 (bs, 1H), 3.15 (s, 3H), 2.79 – 2.57 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 177.8, 143.4, 130.6, 129.8, 129.8, 124.2, 123.2, 120.6, 108.5, 76.0, 43.0, 26.3

(*S*)-3-Allyl-3-hydroxyindolin-2-one (10i)[24]



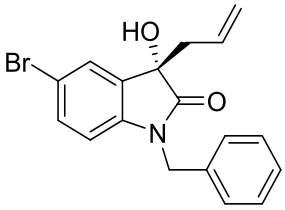
Reaction time: 6 days at -10 °C. Yield : 33 mg (87%), white solid, mp : 164-166 °C, $[\alpha]_D^{20}$ = -51.6 (c 0.50, $CHCl_3$).

The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column heptane/IPA = 90/10, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 16.09 min, $t_{(S)}$ = 17.92 min (for the chromatogram refer to page S22), e.r.: 3:97.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.95 (bs, 1H), 7.41 – 7.34 (m, 1H), 7.31 – 7.22 (m, 1H), 7.12 – 7.04 (m, 1H), 6.91 – 6.84 (m, 1H), 5.76 – 5.62 (m, 1H), 5.18 – 5.08 (m, 2H), 3.07 (bs, 1H), 2.79 – 2.53 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 179.7, 140.3, 130.4, 130.2, 129.9, 124.7, 123.2, 120.8, 110.3, 76.2, 43.0

(*S*)-3-Allyl-1-benzyl-5-bromo-3-hydroxyindolin-2-one (10j) [10]



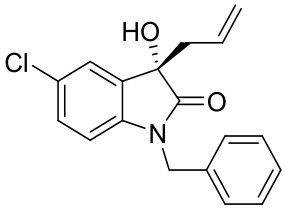
Yield: 71 mg (99%), white solid, mp: 97-99 °C, $[\alpha]_D^{20}$ = -15.0 (c 1.00, $CHCl_3$)

The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 6.04 min, $t_{(S)}$ = 9.56 (for the chromatogram refer to page S23), e.r.: 2.5:97.5.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.52 (d, *J* = 2.0 Hz, 1H), 7.36 – 7.21 (m, 6H), 6.55 (d, *J* = 8.3 Hz, 1H), 5.69 – 5.54 (m, 1H), 5.21 – 5.11 (m, 2H), 4.98 (d, *J* = 15.7 Hz, 1H), 4.69 (d, *J* = 15.7 Hz, 1H), 3.50 (bs, 1H), 2.85 – 2.67 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 177.5, 141.5, 135.0, 132.5, 131.8, 130.1, 129.0, 128.0, 127.6, 127.3, 121.3, 116.0, 111.1, 76.0, 44.0, 43.1

(*S*)-3-Allyl-1-benzyl-5-chloro-3-hydroxyindolin-2-one (10k)[21]



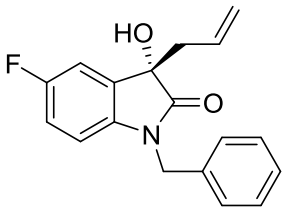
Yield: 62 mg (99%), colourless syrup, $[\alpha]_D^{20}$ = -6.5 (c 0.97, $CHCl_3$)

The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 6.15 min, $t_{(S)}$ = 8.88 min (for the chromatogram refer to page S24), e.r.: 2:98.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.38 (d, *J* = 2.1 Hz, 1H), 7.35 – 7.21 (m, 5H), 7.19 – 7.14 (m, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 5.70 – 5.56 (m, 1H), 5.20 – 5.11 (m, 2H), 4.99 (d, *J* = 15.7 Hz, 1H), 4.71 (d, *J* = 15.7 Hz, 1H), 3.16 (bs, 1H), 2.83 – 2.64 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 177.5, 141.1, 135.1, 131.4, 130.1, 129.7, 129.0, 128.8, 128.0, 127.4, 124.9, 121.3, 110.7, 76.0, 44.1, 43.2

(*S*)-3-Allyl-1-benzyl-5-fluoro-3-hydroxyindolin-2-one (10l)[23]

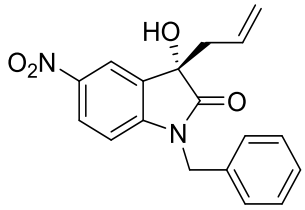


Yield: 56 mg (94%), white solid, mp: 104-106 °C, $[\alpha]_D^{20}$ = -19.2 (c 1.00, $CHCl_3$)

The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 6.22 min, $t_{(S)}$ = 8.73 min (for the chromatogram refer to page S25), e.r.: 3:97.

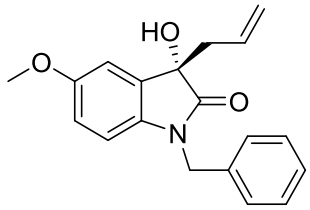
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.35 – 7.21 (m, 5H), 7.19 – 7.10 (m, 1H), 6.95 – 6.82 (m, 1H), 6.65 – 6.54 (m, 1H), 5.74 – 5.51 (m, 1H), 5.20 – 5.08 (m, 2H), 4.99 (d, *J* = 15.7 Hz, 1H), 4.70 (d, *J* = 15.7 Hz, 1H), 3.44 (bs, 1H), 2.85 – 2.63 (m, 2H)
^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 177.9 (d, *J* = 1.1 Hz), 159.6 (d, *J* = 242.2 Hz), 138.4 (d, *J* = 2.1 Hz), 135.2, 131.4 (d, *J* = 7.8 Hz), 130.2, 129.0, 128.0, 127.44, 121.1, 115.9 (d, *J* = 23.5 Hz), 112.5 (d, *J* = 24.9 Hz), 110.3 (d, *J* = 8.0 Hz), 76.3 (d, *J* = 1.7 Hz), 44.1, 43.2

(*S*)-3-Allyl-1-benzyl-3-hydroxy-5-nitroindolin-2-one (10m)[23]



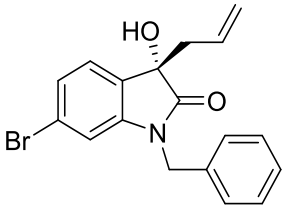
Yield: 60 mg (93%), colourless syrup, $[\alpha]_D^{20}$ = -14.8 (c 1.08, $CHCl_3$)
The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 13.09 min, $t_{(S)}$ = 16.01 min (for the chromatogram refer to page S26), e.r.: 4:96.
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.31 – 8.25 (m, 1H), 8.21 – 8.12 (m, 1H), 7.38 – 7.21 (m, 5H), 6.82 – 6.75 (m, 1H), 5.69 – 5.54 (m, 1H), 5.22 – 5.12 (m, 2H), 5.03 (d, *J* = 15.7 Hz, 1H), 4.79 (d, *J* = 15.7 Hz, 1H), 3.47 (bs, 1H), 2.92 – 2.68 (m, 2H)
^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 178.2, 148.1, 143.9, 134.4, 130.7, 129.4, 129.2, 128.3, 127.4, 126.7, 121.9, 120.3, 109.4, 75.7, 44.3, 43.0

(*S*)-3-Allyl-1-benzyl-3-hydroxy-5-methoxyindolin-2-one (10n)[10]



Yield: 60 mg (97%), colouless syrup, $[\alpha]_D^{20}$ = -8.6 (c 0.98, $CHCl_3$).
The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 10.32 min, $t_{(S)}$ = 18.26 min (for the chromatogram refer to page S27), e.r.: 3:97.
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.37 – 7.19 (m, 5H), 7.08 – 6.96 (m, 1H), 6.80 – 6.67 (m, 1H), 6.64 – 6.53 (m, 1H), 5.74 – 5.51 (m, 1H), 5.23 – 5.05 (m, 2H), 4.99 (d, *J* = 15.7 Hz, 1H), 4.69 (d, *J* = 15.7 Hz, 1H), 3.76 (s, 3H), 3.52 (bs, 1H), 2.89 – 2.64 (m, 2H)
^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 177.8, 156.4, 135.8, 135.6, 131.0, 130.6, 128.9, 127.8, 127.4, 120.7, 114.2, 111.3, 110.1, 76.4, 55.9, 44.0, 43.3

(*S*)-3-Allyl-1-benzyl-6-bromo-3-hydroxyindolin-2-one (10o)[10]



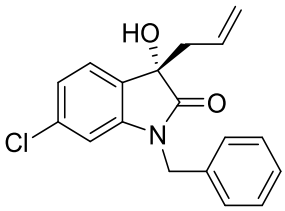
Yield: 70 mg (98%), colourless syrup, $[\alpha]_D^{20}$ = -6.5 (c 0.89, $CHCl_3$)

The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 5.76 min, $t_{(S)}$ = 7.88 min (for the chromatogram refer to page S28), e.r.: 2:98.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.37 – 7.18 (m, 7H), 6.84 (d, *J* = 1.6 Hz, 1H), 5.67 – 5.52 (m, 1H), 5.18 – 5.08 (m, 2H), 4.98 (d, *J* = 15.8 Hz, 1H), 4.66 (d, *J* = 15.8 Hz, 1H), 3.41 (bs, 1H), 2.84 – 2.61 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 177.9, 143.9, 134.9, 130.2, 129.0, 128.7, 128.0, 127.3, 126.1, 125.6, 123.4, 121.1, 113.0, 75.8, 44.0, 43.0

(*S*)-3-Allyl-1-benzyl-6-chloro-3-hydroxyindolin-2-one (10p)[10]



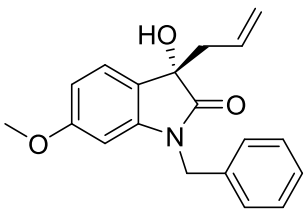
Yield 59 mg (94%), colorless syrup, $[\alpha]_D^{20}$ = -24.7 (c 1.01, $CHCl_3$).

The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 6.90 min, $t_{(S)}$ = 9.70 min (for the chromatogram refer to page S29), e.r.: 2.5:97.5.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.37 – 7.23 (m, 6H), 7.07 – 7.00 (m, 1H), 6.69 (d, *J* = 1.8 Hz, 1H), 5.70 – 5.50 (m, 1H), 5.18 – 5.07 (m, 2H), 4.99 (d, *J* = 15.8 Hz, 1H), 4.67 (d, *J* = 15.8 Hz, 1H), 3.42 (bs, 1H), 2.85 – 2.58 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 177.9, 143.8, 135.6, 135.0, 130.2, 129.1, 128.1, 127.4, 125.3, 123.2, 121.1, 110.3, 75.7, 44.1, 43.1

(*S*)-3-Allyl-1-benzyl-3-hydroxy-6-methoxyindolin-2-one (10q)

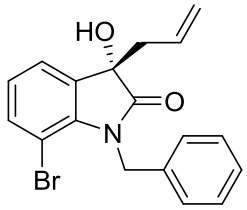


Colorless syrup, Yield: 61 mg (99%), colourless syrup, $[\alpha]_D^{20}$ = -17.7 (c 1.02, $CHCl_3$)

The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 9.65 min, $t_{(S)}$ = 19.72 min (for the chromatogram refer to page S30), e.r.: 3.5:96.5.

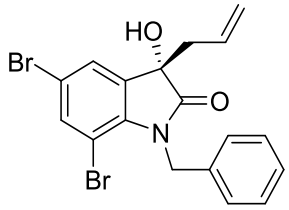
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.40 – 7.02 (m, 6H), 6.53 (dd, *J* = 8.2, 2.2 Hz, 1H), 6.27 (d, *J* = 2.2 Hz, 1H), 5.70 – 5.47 (m, 1H), 5.17 – 5.03 (m, 2H), 4.97 (d, *J* = 15.7 Hz, 1H), 4.65 (d, *J* = 15.7 Hz, 1H), 3.70 (s, 3H), 3.66 (bs, 1H), 2.86 – 2.63 (m, 2H)
^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 178.5, 161.1, 143.9, 135.5, 130.9, 128.8, 127.7, 127.4, 125.0, 121.8, 120.4, 106.5, 97.8, 75.8, 55.5, 43.9, 43.1
HRMS (ESI) m/z. calcd. for $C_{19}H_{19}NO_3Na$ $[M+Na]^+$ 332.1257; found 332.1255.

(*S*)-3-Allyl-1-benzyl-7-bromo-3-hydroxyindolin-2-one (10r)[21]



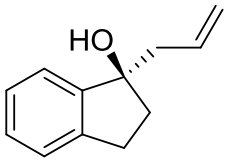
Yield: 71 mg (99%), white solid, mp: 113-115 °C, $[\alpha]_D^{20}$ = -1.9 (c 1.00, $CHCl_3$).
The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 6.38 min, $t_{(S)}$ = 13.81 min (for the chromatogram refer to page S31), e.r.: 5:95.
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.42 – 7.37 (m, 1H), 7.37 – 7.35 (m, 1H), 7.00 – 6.91 (m, 1H), 5.71 – 5.53 (m, 1H), 5.34 (s, 2H), 5.16 – 5.07 (m, 2H), 3.54 (bs, 1H), 2.85 – 2.64 (m, 2H)
^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 178.9, 140.1, 137.1, 135.6, 133.1, 130.2, 128.6, 127.2, 126.5, 124.6, 123.5, 121.2, 102.9, 75.3, 44.7, 43.4

(*S*)-3-Allyl-1-benzyl-5,7-dibromo-3-hydroxyindolin-2-one (10s)



Yield: 87 mg (99%), white solid, mp: 138-140 °C, $[\alpha]_D^{20}$ = -31.0 (c 1.00, $CHCl_3$)
The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 5.18 min, $t_{(S)}$ = 8.50 min (for the chromatogram refer to page S32), e.r.: 4.5:95.5.
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.58 – 7.52 (m, 1H), 7.51 – 7.46 (m, 1H), 7.34 – 7.20 (m, 3H), 7.19 – 7.13 (m, 2H), 5.67 – 5.52 (m, 1H), 5.30 (s, 2H), 5.19 – 5.10 (m, 2H), 3.63 (bs, 1H), 2.81 – 2.65 (m, 2H).
^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 178.5, 139.3, 137.4, 136.7, 134.7, 129.6, 128.7, 127.4, 126.8, 126.4, 121.7, 116.4, 103.4, 75.4, 44.7, 43.4
HRMS (ESI): m/z. calcd. for $C_{18}H_{15}NO_2Br_2Na$ $[M+Na]^+$ 457.9362; found 457.9366.

(*R*)-1-Allyl-2,3-dihydro-1H-inden-1-one (11)[25]



The reaction was performed at room temperature instead of -10 °C. The crude product was purified by flash chromatography with elution by 5-10% AcOEt in cyclohexane.
Yield: 35 mg (80%), colorless oil, $[\alpha]_D^{20}$ = + 8.1 (c 1.0, $CHCl_3$).
The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® IC column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(R)}$ = 8.39 min, $t_{(S)}$ = 9.79 min (for the chromatogram refer to page S33), e.r.: 99.3:0.7.
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.41 – 7.21 (m, 4H), 6.01 – 5.73 (m, 1H), 5.30 – 5.09 (m, 2H), 3.11 – 2.94 (m, 1H), 2.93 – 2.76 (m, 1H), 2.74 – 2.60 (m, 1H), 2.60 – 2.49 (m, 1H), 2.42 (bs, 1H), 2.40 – 2.28 (m, 1H), 2.18 – 1.96 (m, 1H)
^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 147.2, 143.1, 133.9, 128.4, 126.8, 125.1, 123.0, 119.0, 82.9, 45.1, 39.8, 29.6

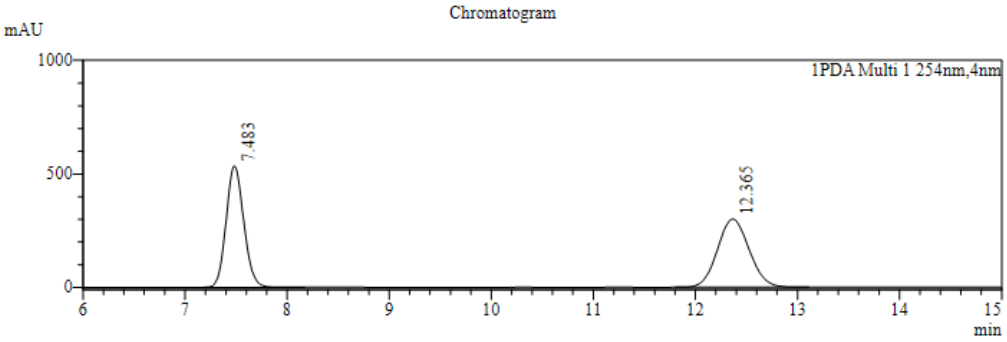
5. HPLC chromatograms of compounds 10 and 11

The chromatogram of the racemic reference compound is followed by that of the enantioenriched **10** and **11**.

(*S*)-3-Allyl-1-benzyl-3-hydroxyindolin-2-one (10a)

Sample Information

Sample Name : jbr_25_p_01_IC_80_20_1mL_20deg
Date Acquired : 07/11/2018 16:06:30
Method File : IC hept-IPA 80-20.lcm



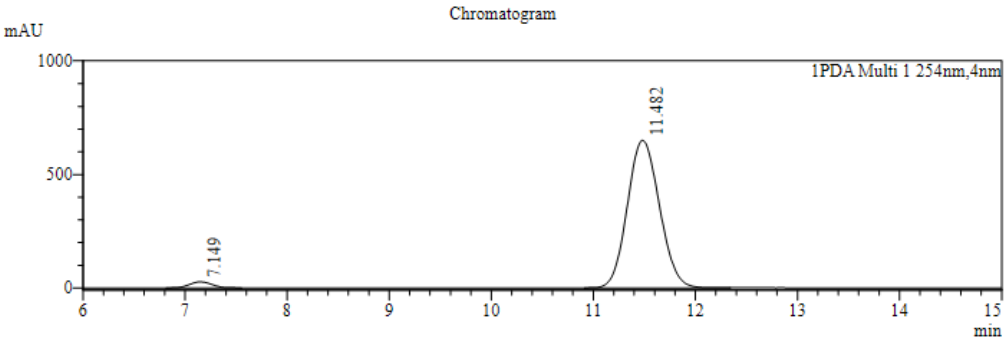
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	7.483	533064	6443800	49.781
2	12.365	300185	6500479	50.219
Total		833249	12944279	100.000

Sample Information

Sample Name : jbr_334_p_01_IC_80_20_1mL_25deg
Date Acquired : 27/02/2019 11:28:38
Method File : IC hept-IPA 80-20.lcm



Peak Table

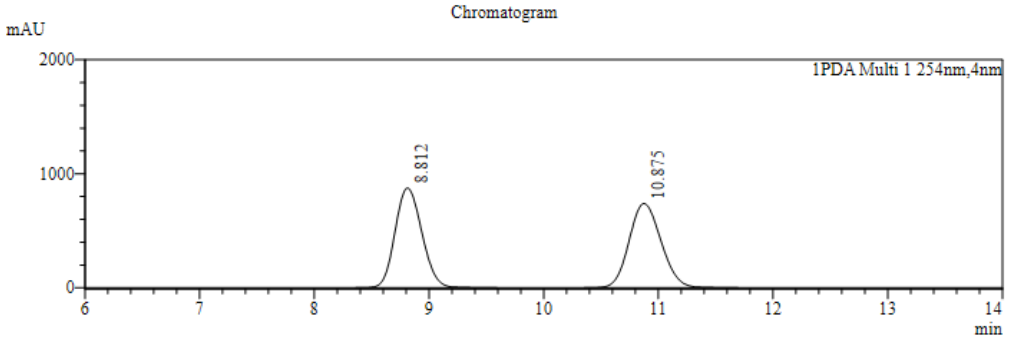
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	7.149	26604	412201	2.814
2	11.482	649884	14235467	97.186
Total		676488	14647668	100.000

(*S*)-3-Allyl-3-hydroxy-1-methylindolin-2-one (10b)

Sample Information

Sample Name : jbr_246_p_01_IC_80_20_1mL_19deg
Date Acquired : 07/12/2018 10:32:28
Method File : IC hept-IPA 80-20.lcm



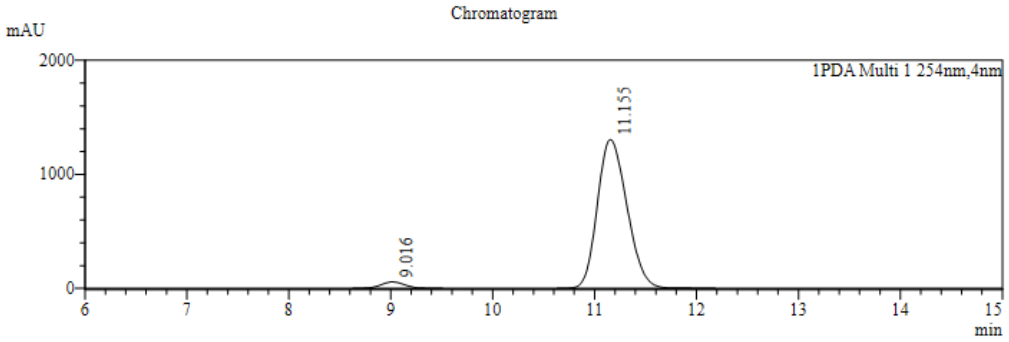
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	8.812	874647	14217692	49.829
2	10.875	738661	14315543	50.171
Total		1613307	28533235	100.000

Sample Information

Sample Name : jbr_352_p_01_IC_80_20_1mL_20deg
Date Acquired : 13/03/2019 15:37:55
Method File : IC hept-IPA 80-20.lcm



Peak Table

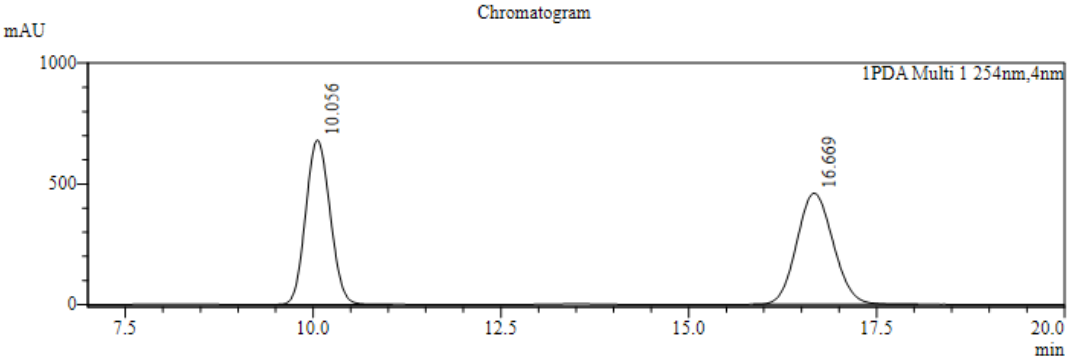
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	9.016	56542	911219	3.341
2	11.155	1305435	26363275	96.659
Total		1361977	27274494	100.000

(*S*)-3-Allyl-3-hydroxy-1-(4-methoxybenzyl)indolin-2-one (10c)

Sample Information

Sample Name : jbr_219_p_01_IC_80_20_1mL_20deg
Date Acquired : 15/03/2019 14:51:55
Method File : IC hept-IPA 80-20.lcm



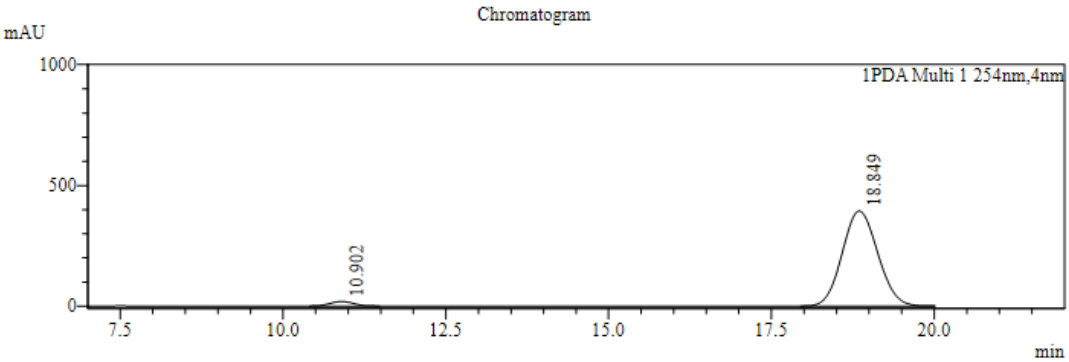
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	10.056	680389	15368607	49.586
2	16.669	460772	15625011	50.414
Total		1141162	30993618	100.000

Sample Information

Sample Name : jbr_354_p_01_IC_80_20_1mL_20deg
Date Acquired : 20/03/2019 15:13:28
Method File : IC hept-IPA 80-20.lcm



Peak Table

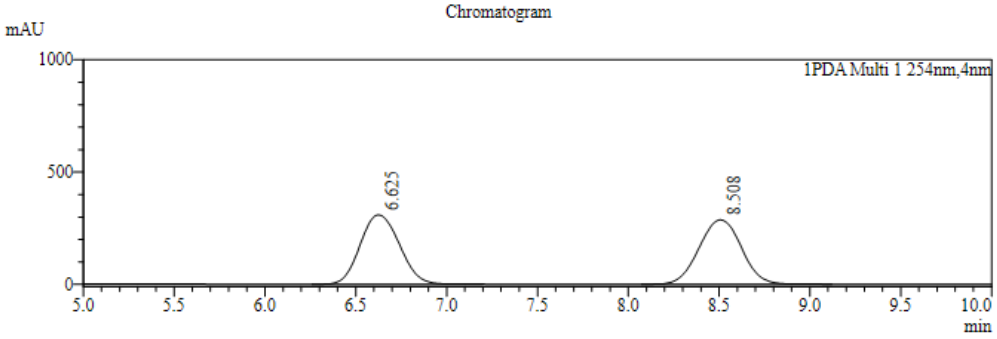
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	10.902	18885	481109	3.109
2	18.849	394109	14992537	96.891
Total		412994	15473645	100.000

(*S*)-3-Allyl-3-hydroxy-1-(methoxymethyl)indolin-2-one (10d)

Sample Information

Sample Name : jbr_213_p_01_IC_80_20_1mL_20deg
Date Acquired : 15/03/2019 14:21:28
Method File : IC hept-IPA 80-20.lcm



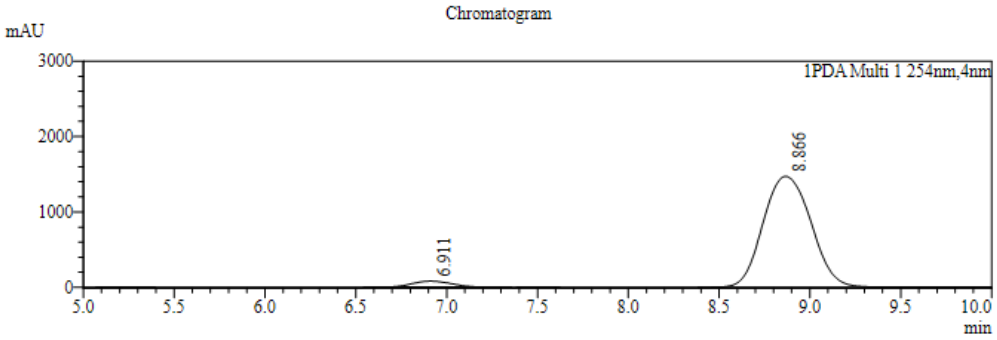
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	6.625	309263	4657414	49.895
2	8.508	287130	4676953	50.105
Total		596393	9334367	100.000

Sample Information

Sample Name : jbr_353_p_01_IC_80_20_1mL_20deg
Date Acquired : 13/03/2019 18:32:56
Method File : IC hept-IPA 80-20.lcm



Peak Table

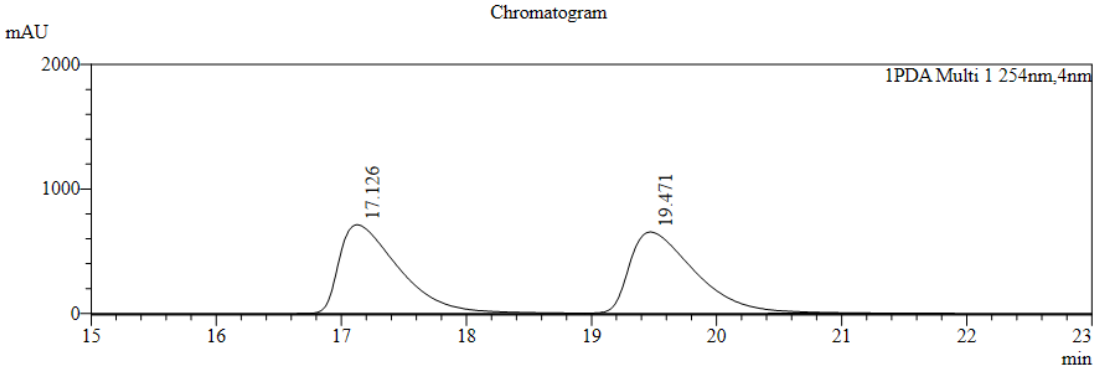
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	6.911	80169	1243051	4.390
2	8.866	1471861	27074542	95.610
Total		1552030	28317593	100.000

(*S*)-3-Allyl-3-hydroxy-1-phenylindolin-2-one (10e)

Sample Information

Sample Name : jbr_253_p_01_IB_95_5_0.7mL_20deg
Date Acquired : 29/11/2018 14:43:30
Method File : IB hept-IPA 95-5 0.7mL.lcm



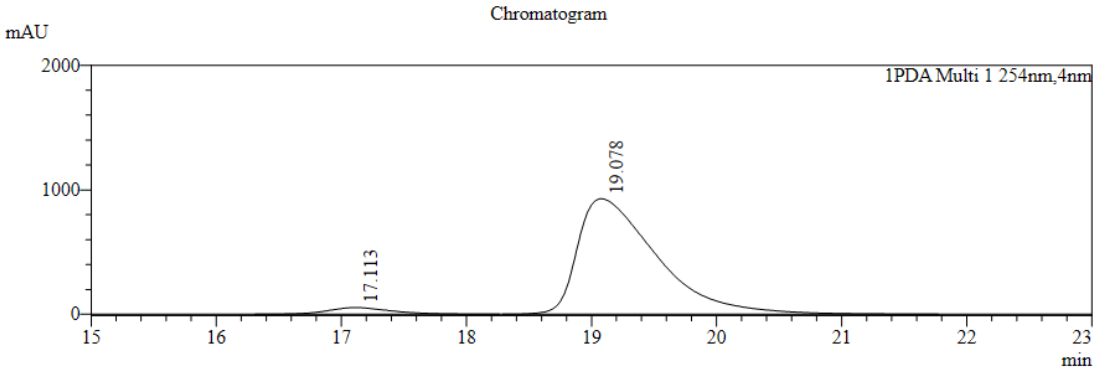
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	17.126	712352	23681917	49.795
2	19.471	653289	23876815	50.205
Total		1365641	47558732	100.000

Sample Information

Sample Name : jbr_371_p_01_IB_95_5_0.7mL_21deg
Date Acquired : 05/04/2019 16:33:06
Method File : IB hept-IPA 95-5 0.7mL.lcm



Peak Table

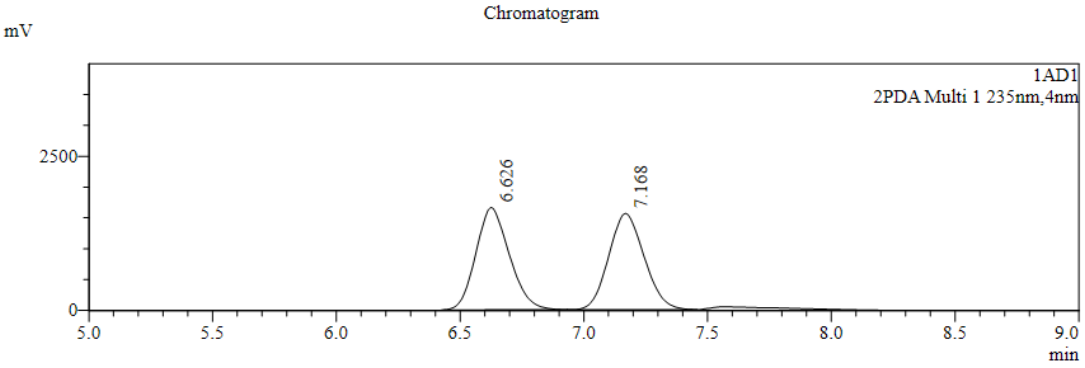
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	17.113	52601	1876688	4.399
2	19.078	927101	40787053	95.601
Total		979703	42663741	100.000

(*S*)-1-Acetyl-3-allyl-3-hydroxyindolin-2-one (10f)

Sample Information

Sample Name : jbr_373_p_01_IC_90_10_1mL_20deg
Date Acquired : 05/04/2019 15:33:13
Method File : IC hept-IPA 90-10.lcm



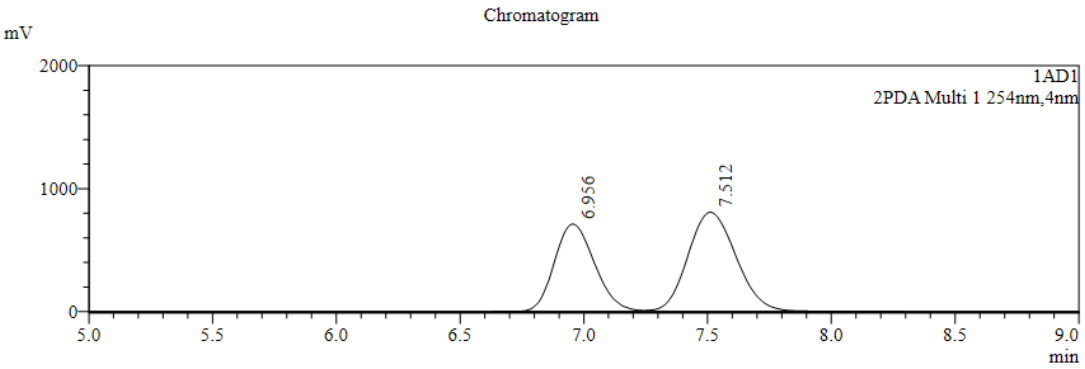
Peak Table

PDA Ch1 235nm

Peak#	Ret. Time	Height	Area	Area%
1	6.626	1665432	15673657	50.127
2	7.168	1564317	15594151	49.873
Total		3229749	31267808	100.000

Sample Information

Sample Name : jbr_379_p_01_IC_90_10_1mL_24deg
Date Acquired : 19/06/2019 15:03:52
Method File : IC hept-IPA 90-10.lcm



Peak Table

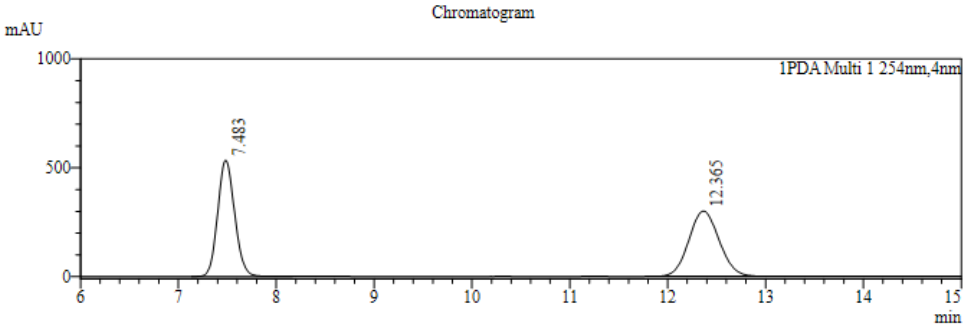
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	6.956	713171	8096626	42.476
2	7.512	808711	10964849	57.524
Total		1521882	19061474	100.000

(*R*)-3-Allyl-1-benzyl-3-hydroxyindolin-2-one (10g)

Sample Information

Sample Name : jbr_25_p_01_IC_80_20_1mL_20deg
Date Acquired : 07/11/2018 16:06:30
Method File : IC hept-IPA 80-20.lcm



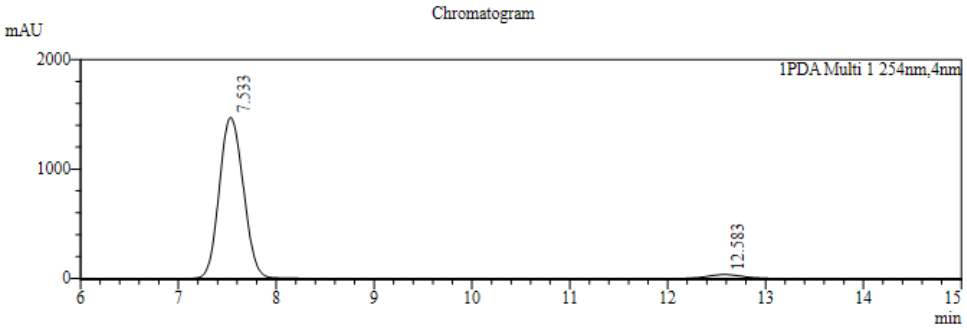
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	7.483	533064	6443800	49.781
2	12.365	300185	6500479	50.219
Total		833249	12944279	100.000

Sample Information

Sample Name : jbr_407_p_01_IC_80_20_1mL_20 deg
Date Acquired : 29/08/2019 18:25:06
Method File : IC hept-IPA 80-20.lcm



Peak Table

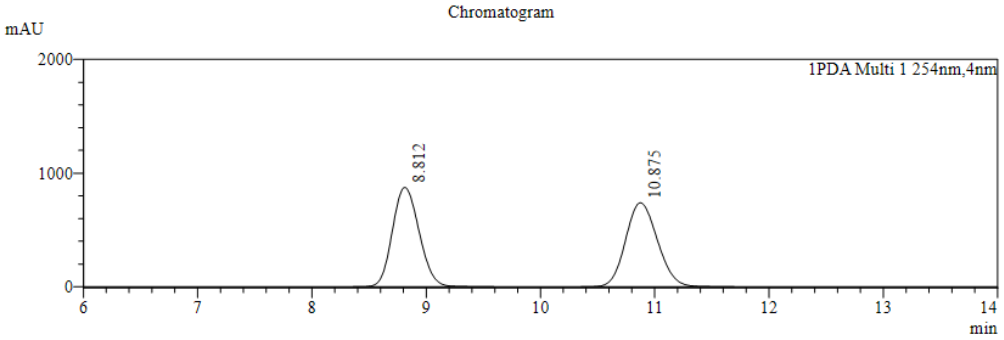
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	7.533	1470858	25156483	96.815
2	12.583	34570	827711	3.185
Total		1505428	25984193	100.000

(*R*)-3-Allyl-3-hydroxy-1-methylindolin-2-one (10h)

Sample Information

Sample Name : jbr_246_p_01_IC_80_20_1mL_19deg
Date Acquired : 07/12/2018 10:32:28
Method File : IC hept-IPA 80-20.lcm



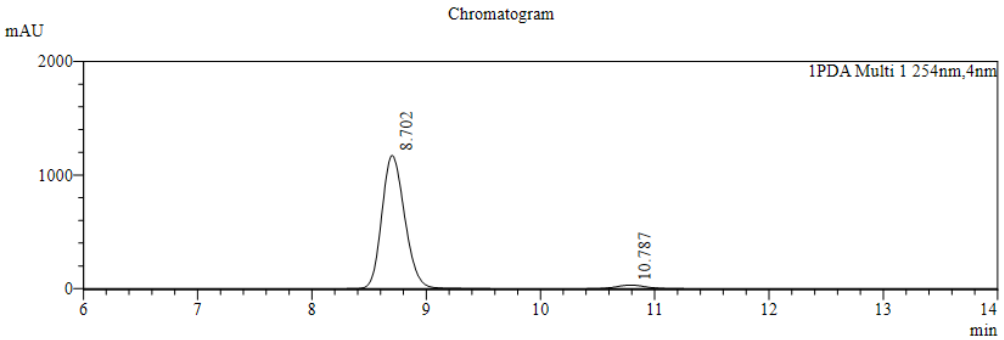
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	8.812	874647	14217692	49.829
2	10.875	738661	14315543	50.171
Total		1613307	28533235	100.000

Sample Information

Sample Name : jbr_406_p_01_IC_80_20_1mL_20 deg
Date Acquired : 29/08/2019 18:54:44
Method File : IC hept-IPA 80-20.lcm



Peak Table

PDA Ch1 254nm

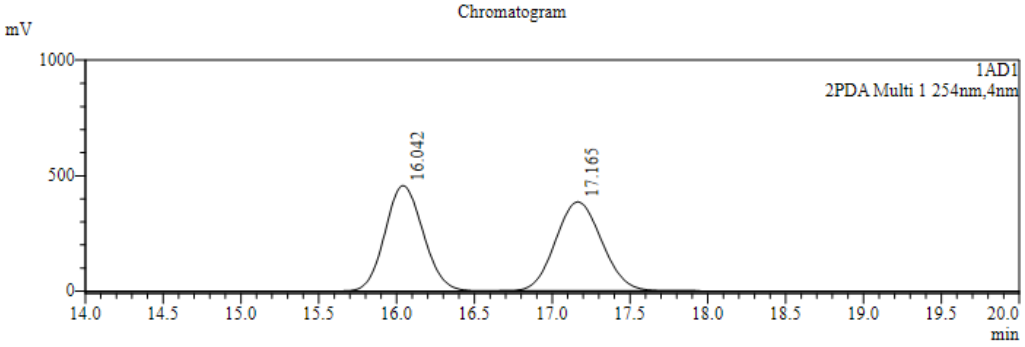
Peak#	Ret. Time	Height	Area	Area%
1	8.702	1171787	16296579	96.859
2	10.787	31157	528561	3.141
Total		1202944	16825140	100.000

(*S*)-3-Allyl-3-hydroxyindolin-2-one (10i)

Sample Information

Sample Name : jbr_14_p_01_IC_90_10_1mL_24deg
Date Acquired : 19/06/2019 14:18:33
Method File : IC hept-IPA 90-10.lcm

Chromatogram



Peak Table

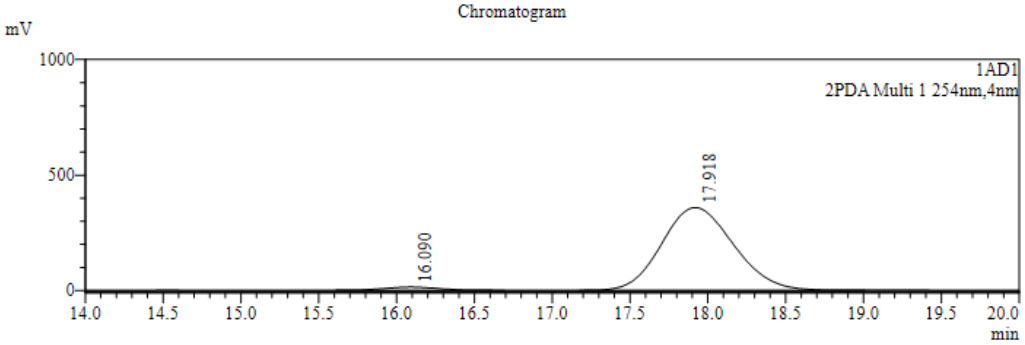
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	16.042	456693	7821146	49.376
2	17.165	385806	8018862	50.624
Total		842499	15840009	100.000

Sample Information

Sample Name : jbr_380_p_01_IC_90_10_1mL_24deg
Date Acquired : 19/06/2019 15:34:20
Method File : IC hept-IPA 90-10.lcm

Chromatogram



Peak Table

PDA Ch1 254nm

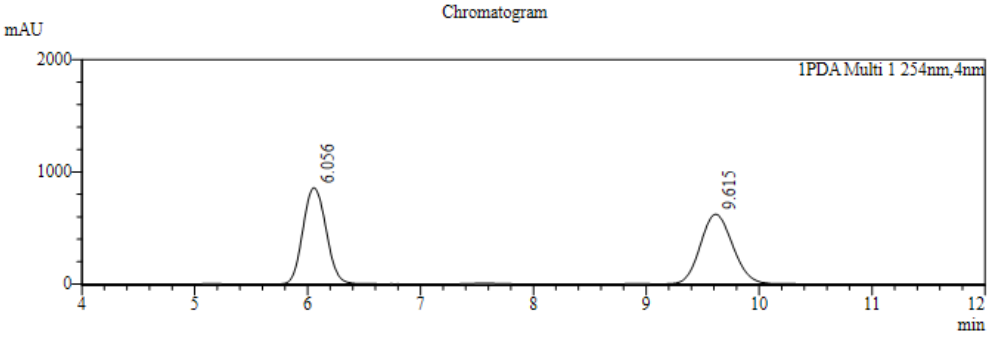
Peak#	Ret. Time	Height	Area	Area%
1	16.090	14082	359937	3.014
2	17.918	358863	11582345	96.986
Total		372945	11942282	100.000

(*S*)-3-Allyl-1-benzyl-5-bromo-3-hydroxyindolin-2-one (10j)

Sample Information

Sample Name : jbr_367_p_01_IC_80_20_1mL_20deg
Date Acquired : 03/04/2019 15:23:13
Method File : IC hept-IPA 80-20.lcm

Chromatogram



Peak Table

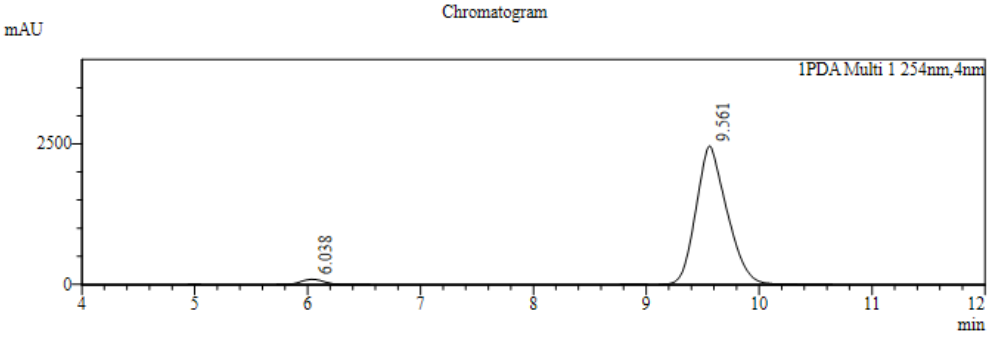
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	6.056	857156	12242835	49.663
2	9.615	621314	12409159	50.337
Total		1478469	24651993	100.000

Sample Information

Sample Name : jbr_369_p_01_IC_80_20_1mL_20deg
Date Acquired : 03/04/2019 16:25:49
Method File : IC hept-IPA 80-20.lcm

Chromatogram



Peak Table

PDA Ch1 254nm

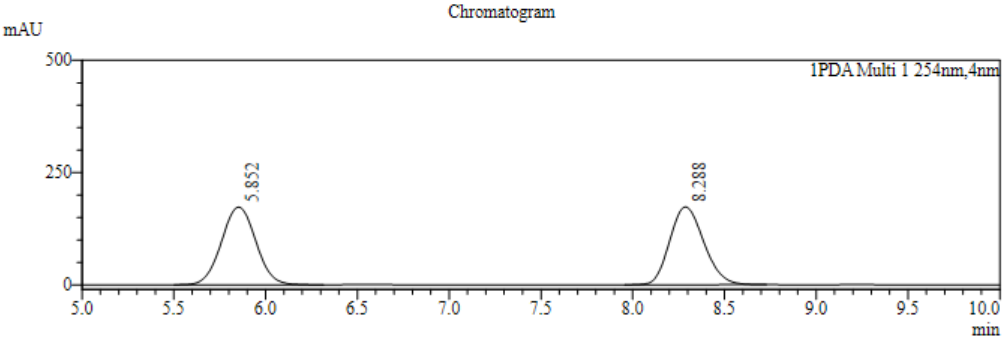
Peak#	Ret. Time	Height	Area	Area%
1	6.038	91794	1280110	2.661
2	9.561	2460159	46822341	97.339
Total		2551954	48102451	100.000

(*S*)-3-Allyl-1-benzyl-5-chloro-3-hydroxyindolin-2-one (10k)

Sample Information

Sample Name : jbr_374_p_01_IC_80_20_1mL_24deg
Date Acquired : 18/07/2019 17:55:30
Method File : IC hept-IPA 80-20.lcm

Chromatogram



Peak Table

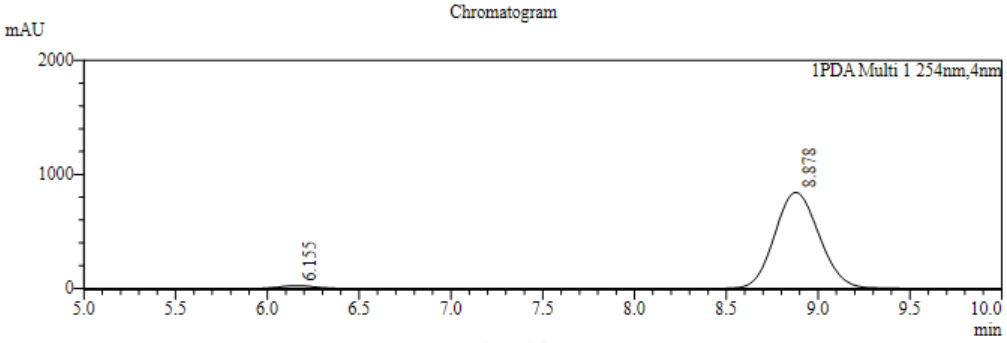
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	5.852	173036	2261806	50.199
2	8.288	173734	2243848	49.801
Total		346770	4505654	100.000

Sample Information

Sample Name : jbr_378_p_01_IC_80_20_1mL_24deg
Date Acquired : 19/06/2019 16:07:19
Method File : IC hept-IPA 80-20.lcm

Chromatogram



Peak Table

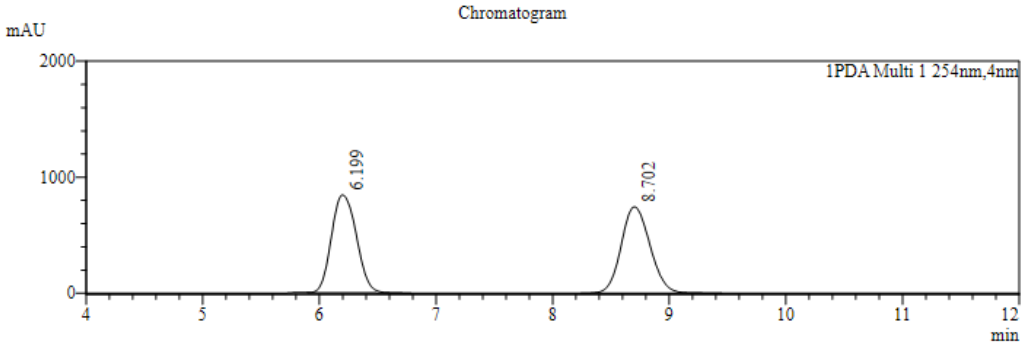
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	6.155	24194	323875	2.232
2	8.878	841241	14186679	97.768
Total		865435	14510555	100.000

(*S*)-3-Allyl-1-benzyl-5-fluoro-3-hydroxyindolin-2-one (10l)

Sample Information

Sample Name : jbr_28_p_01_IC_80_20_1mL_20deg
Date Acquired : 15/03/2019 15:45:40
Method File : IC hept-IPA 80-20.lcm



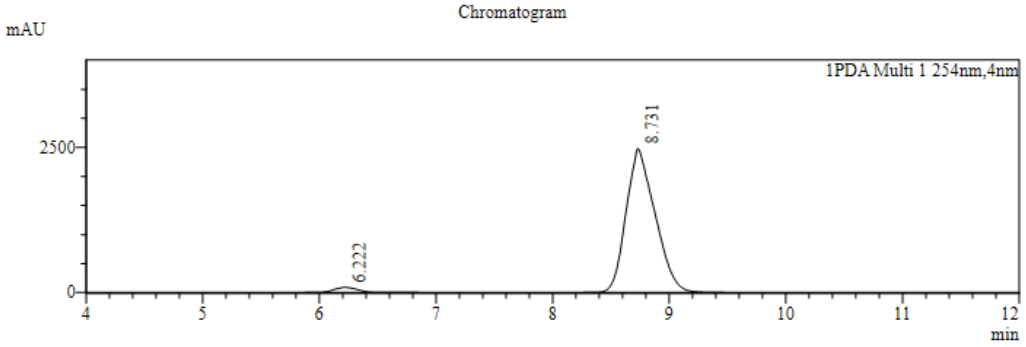
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	6.199	845016	12607357	49.611
2	8.702	744690	12804925	50.389
Total		1589706	25412282	100.000

Sample Information

Sample Name : jbr_370_p_01_IC_80_20_1mL_20deg
Date Acquired : 03/04/2019 16:46:17
Method File : IC hept-IPA 80-20.lcm



Peak Table

PDA Ch1 254nm

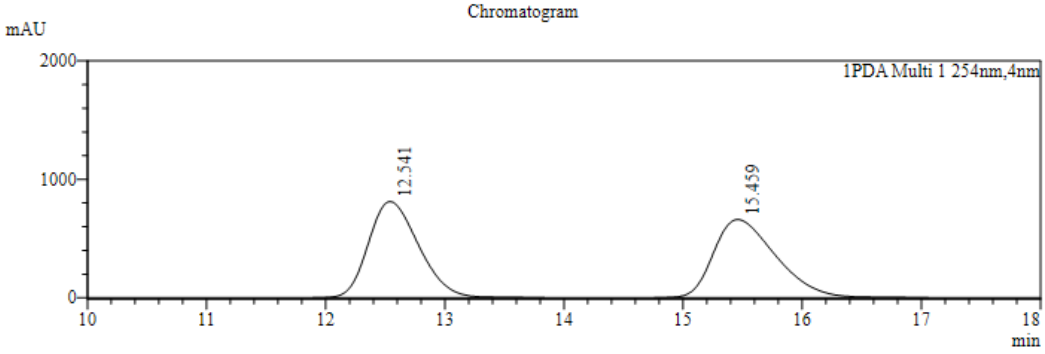
Peak#	Ret. Time	Height	Area	Area%
1	6.222	89404	1335566	3.022
2	8.731	2476475	42865352	96.978
Total		2565879	44200917	100.000

(*S*)-3-Allyl-1-benzyl-3-hydroxy-5-nitroindolin-2-one (10m)

Sample Information

Sample Name : jbr_351_p_01_IC_80_20_1mL_20deg
Date Acquired : 13/03/2019 12:21:01
Method File : IC hept-IPA 80-20.lcm

Chromatogram



Peak Table

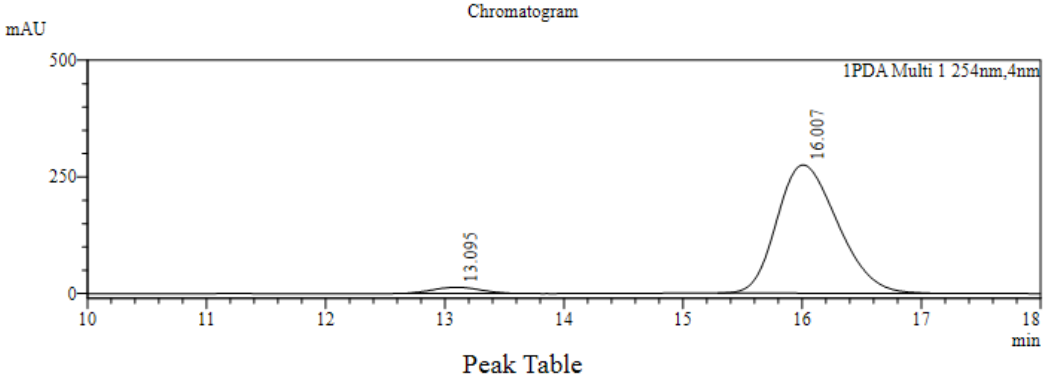
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	12.541	812471	23782714	49.868
2	15.459	659964	23908455	50.132
Total		1472435	47691169	100.000

Sample Information

Sample Name : jbr_361_p_01_IC_80_20_1mL_20deg
Date Acquired : 20/03/2019 16:07:07
Method File : IC hept-IPA 80-20.lcm

Chromatogram



Peak Table

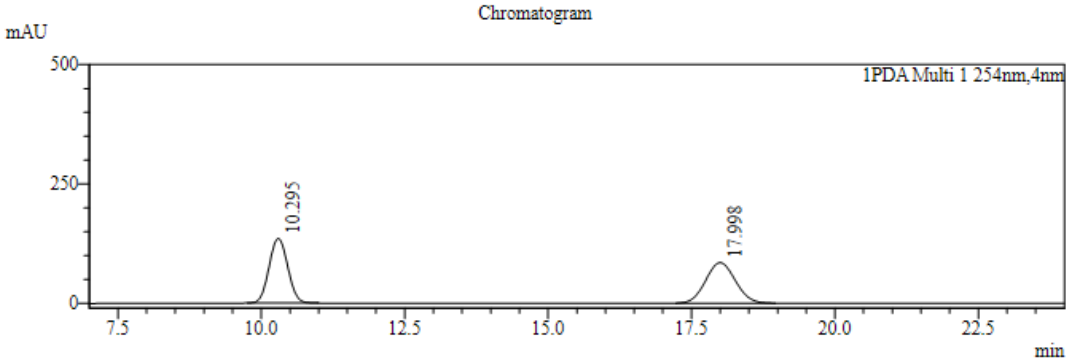
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	13.095	13681	396062	3.895
2	16.007	274957	9771225	96.105
Total		288638	10167287	100.000

(*S*)-3-Allyl-1-benzyl-3-hydroxy-5-methoxyindolin-2-one (10n)

Sample Information

Sample Name : jbr_193_p_01_IC_80_20_1mL_20deg
Date Acquired : 20/02/2019 13:53:09
Method File : IC hept-IPA 80-20.lcm



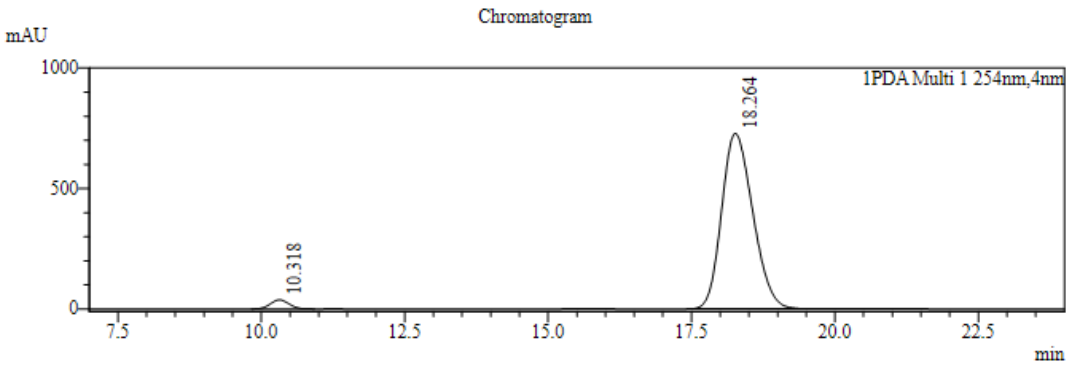
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	10.295	135195	3067433	49.999
2	17.998	84862	3067570	50.001
Total		220057	6135003	100.000

Sample Information

Sample Name : jbr_355_p_01_IC_80_20_1mL_19deg
Date Acquired : 13/03/2019 16:19:36
Method File : IC hept-IPA 80-20.lcm



Peak Table

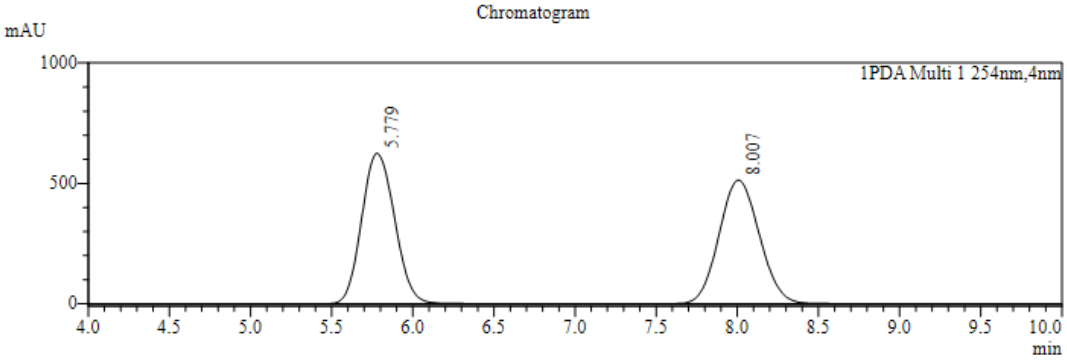
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	10.318	37436	855451	3.011
2	18.264	727214	27555170	96.989
Total		764649	28410621	100.000

(*S*)-3-Allyl-1-benzyl-6-bromo-3-hydroxyindolin-2-one (10o)

Sample Information

Sample Name : jbr_343_p_01_IC_80_20_1mL_21deg
Date Acquired : 06/03/2019 14:39:36
Method File : IC hept-IPA 80-20.lcm



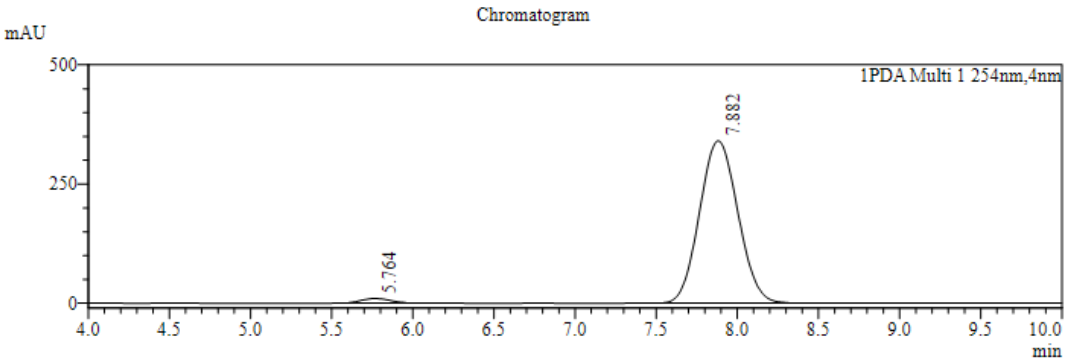
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	5.779	625250	8860217	49.923
2	8.007	513070	8887495	50.077
Total		1138320	17747712	100.000

Sample Information

Sample Name : jbr_360_p_02_IC_80_20_1mL_20deg
Date Acquired : 07/06/2019 13:00:17
Method File : IC hept-IPA 80-20.lcm



Peak Table

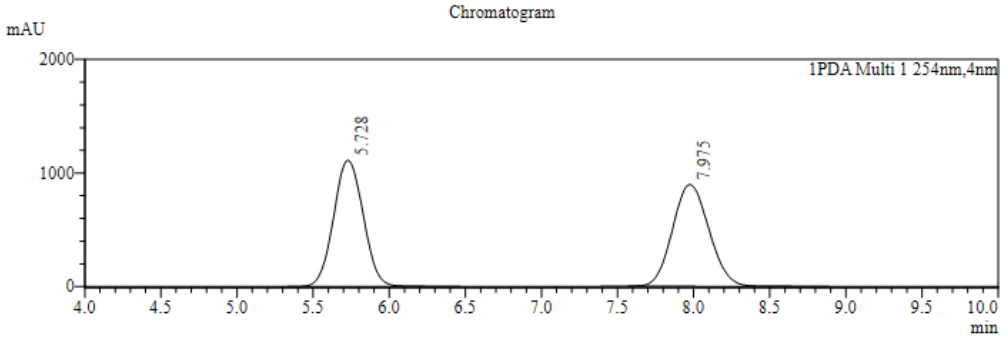
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	5.764	9905	127178	2.213
2	7.882	340939	5619727	97.787
Total		350844	5746905	100.000

(*S*)-3-Allyl-1-benzyl-6-chloro-3-hydroxyindolin-2-one (10p)

Sample Information

Sample Name : jbr_252_p_01_IC_80_20_1mL_22deg
Date Acquired : 05/12/2018 14:53:11
Method File : IC hept-IPA 80-20.lcm



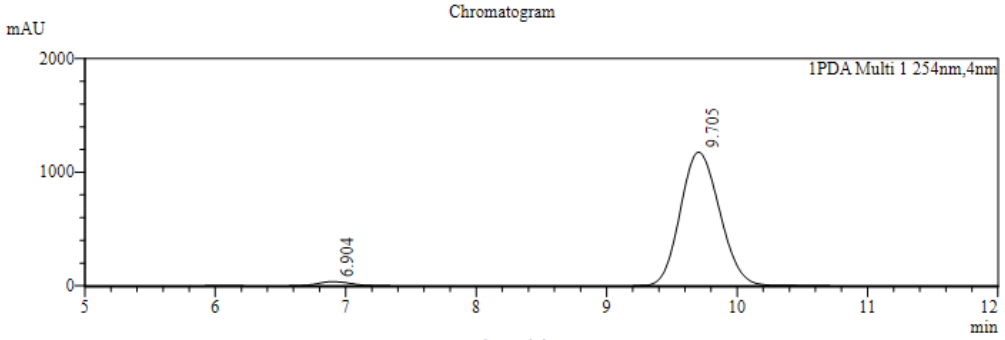
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	5.728	1112996	15089154	50.185
2	7.975	896525	14977747	49.815
Total		2009522	30066900	100.000

Sample Information

Sample Name : jbr_359_p_01_IC_80_20_1mL_20deg
Date Acquired : 20/03/2019 15:33:55
Method File : IC hept-IPA 80-20.lcm



Peak Table

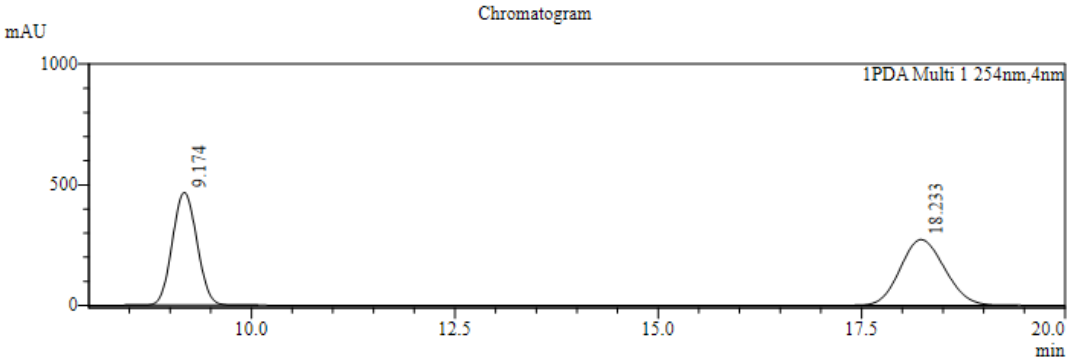
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	6.904	35403	599425	2.371
2	9.705	1175925	24679863	97.629
Total		1211328	25279288	100.000

(*S*)-3-Allyl-1-benzyl-3-hydroxy-6-methoxyindolin-2-one (10q)

Sample Information

Sample Name : jbr_251_p_01_IC_80_20_1mL_22deg
Date Acquired : 05/12/2018 14:07:43
Method File : IC hept-IPA 80-20.lcm



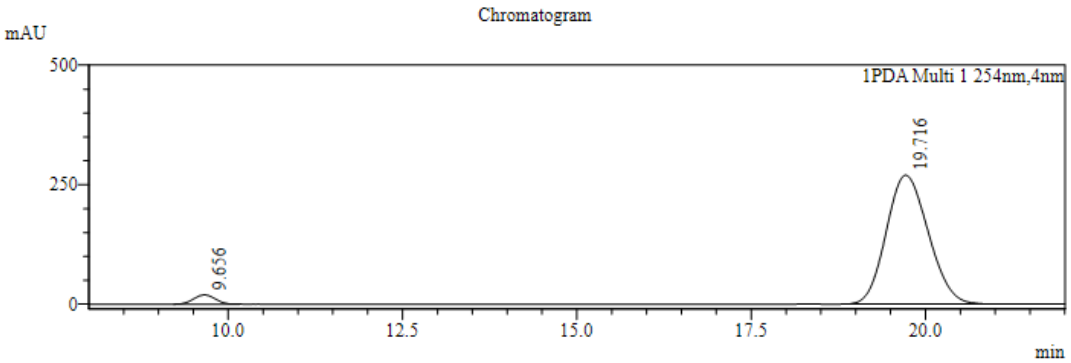
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	9.174	467270	9905037	48.827
2	18.233	272545	10381128	51.173
Total		739815	20286166	100.000

Sample Information

Sample Name : jbr_251_p_01_IC_80_20_1mL_22deg
Date Acquired : 05/12/2018 14:07:43
Method File : IC hept-IPA 80-20.lcm



Peak Table

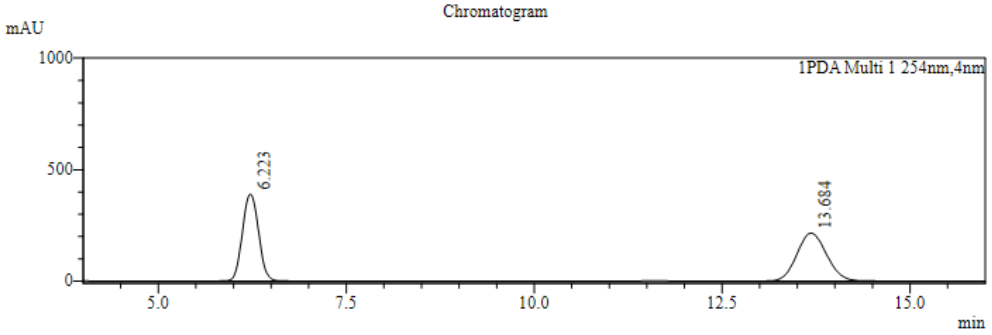
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	9.656	19502	428018	3.642
2	19.716	269820	11322788	96.358
Total		289322	11750807	100.000

(*S*)-3-Allyl-1-benzyl-7-bromo-3-hydroxyindolin-2-one (10r)

Sample Information

Sample Name : jbr_357_p_01_IC_80_20_1mL_20deg
Date Acquired : 13/03/2019 13:30:07
Method File : IC hept-IPA 80-20.lcm



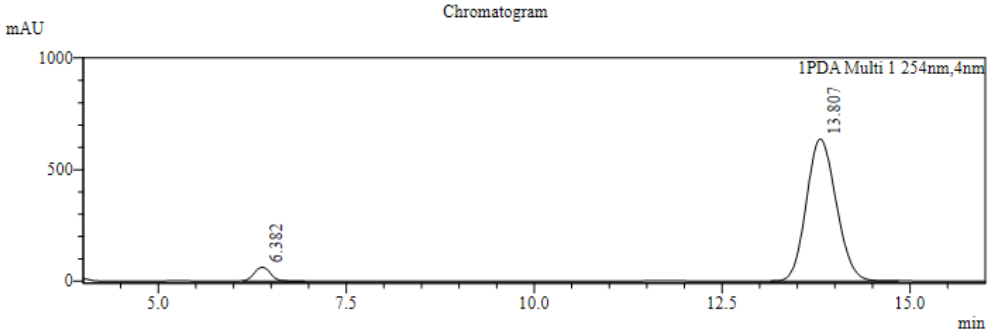
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	6.223	388688	5846896	49.687
2	13.684	215069	5920463	50.313
Total		603757	11767359	100.000

Sample Information

Sample Name : jbr_362_p_01_IC_80_20_1mL_20deg
Date Acquired : 20/03/2019 16:27:33
Method File : IC hept-IPA 80-20.lcm



Peak Table

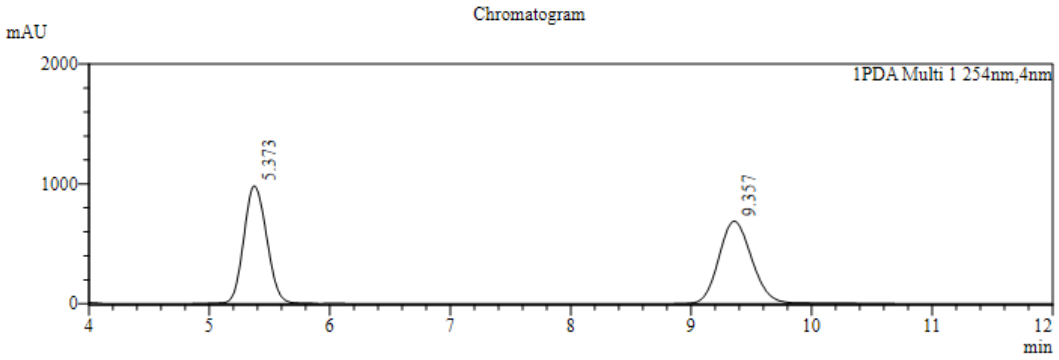
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	6.382	61372	908879	4.909
2	13.807	636719	17607471	95.091
Total		698092	18516350	100.000

(*S*)-3-Allyl-1-benzyl-5,7-dibromo-3-hydroxyindolin-2-one (10s)

Sample Information

Sample Name : jbr_358_p_01_IC_80_20_1mL_20deg
Date Acquired : 13/03/2019 14:00:34
Method File : IC hept-IPA 80-20.lcm



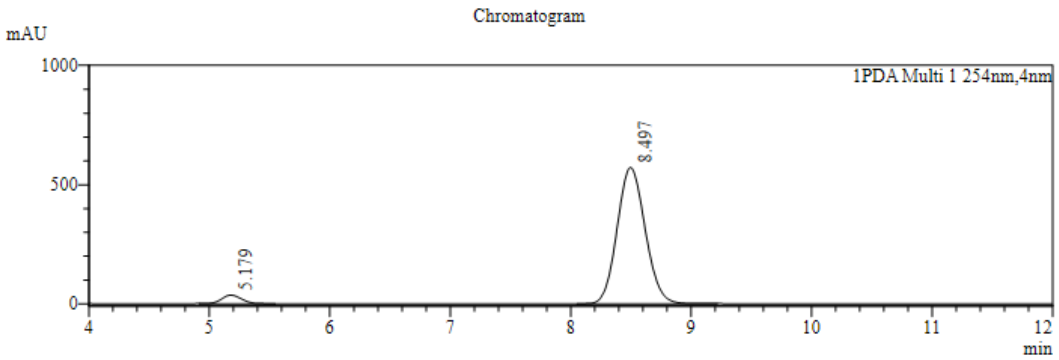
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	5.373	982703	13007066	49.678
2	9.357	689163	13175846	50.322
Total		1671866	26182912	100.000

Sample Information

Sample Name : jbr_363_p_01_IC_80_20_1mL_24deg
Date Acquired : 19/06/2019 13:12:14
Method File : IC hept-IPA 80-20.lcm



Peak Table

PDA Ch1 254nm

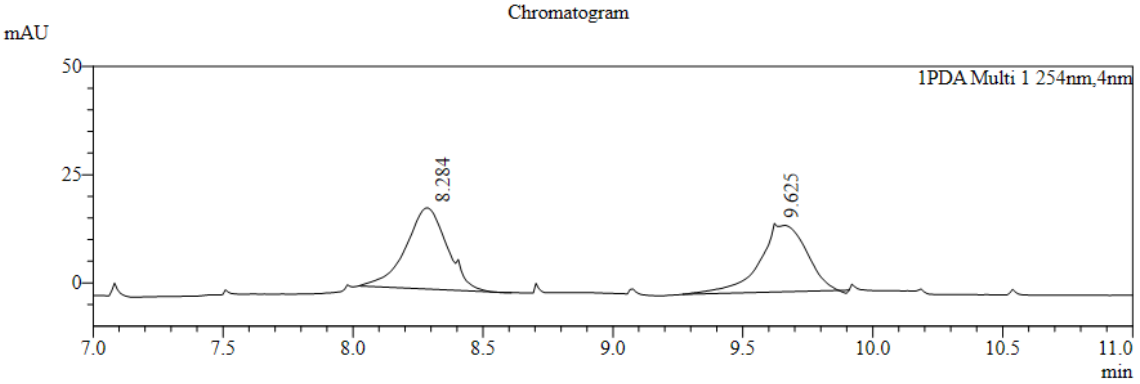
Peak#	Ret. Time	Height	Area	Area%
1	5.179	35986	419052	4.322
2	8.497	571746	9277150	95.678
Total		607732	9696202	100.000

(*R*)-1-Allyl-2,3-dihydro-1H-inden-1-ol (11)

Sample Information

Sample Name : jbr_417_p_01_IB_98_2_1mL_27deg
Date Acquired : 13/09/2019 15:50:24
Method File : IB hept-IPA 98-2.lcm

Chromatogram



Peak Table

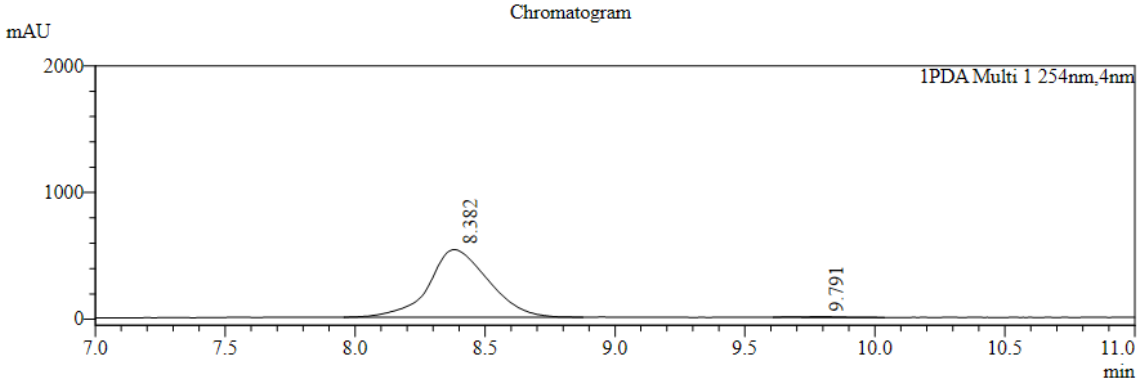
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	8.284	18779	208895	51.731
2	9.625	15883	194918	48.269
Total		34662	403813	100.000

Sample Information

Sample Name : jbr_418_p_01_IB_98_2_1mL_27deg
Date Acquired : 13/09/2019 16:33:21
Method File : IB hept-IPA 98-2.lcm

Chromatogram



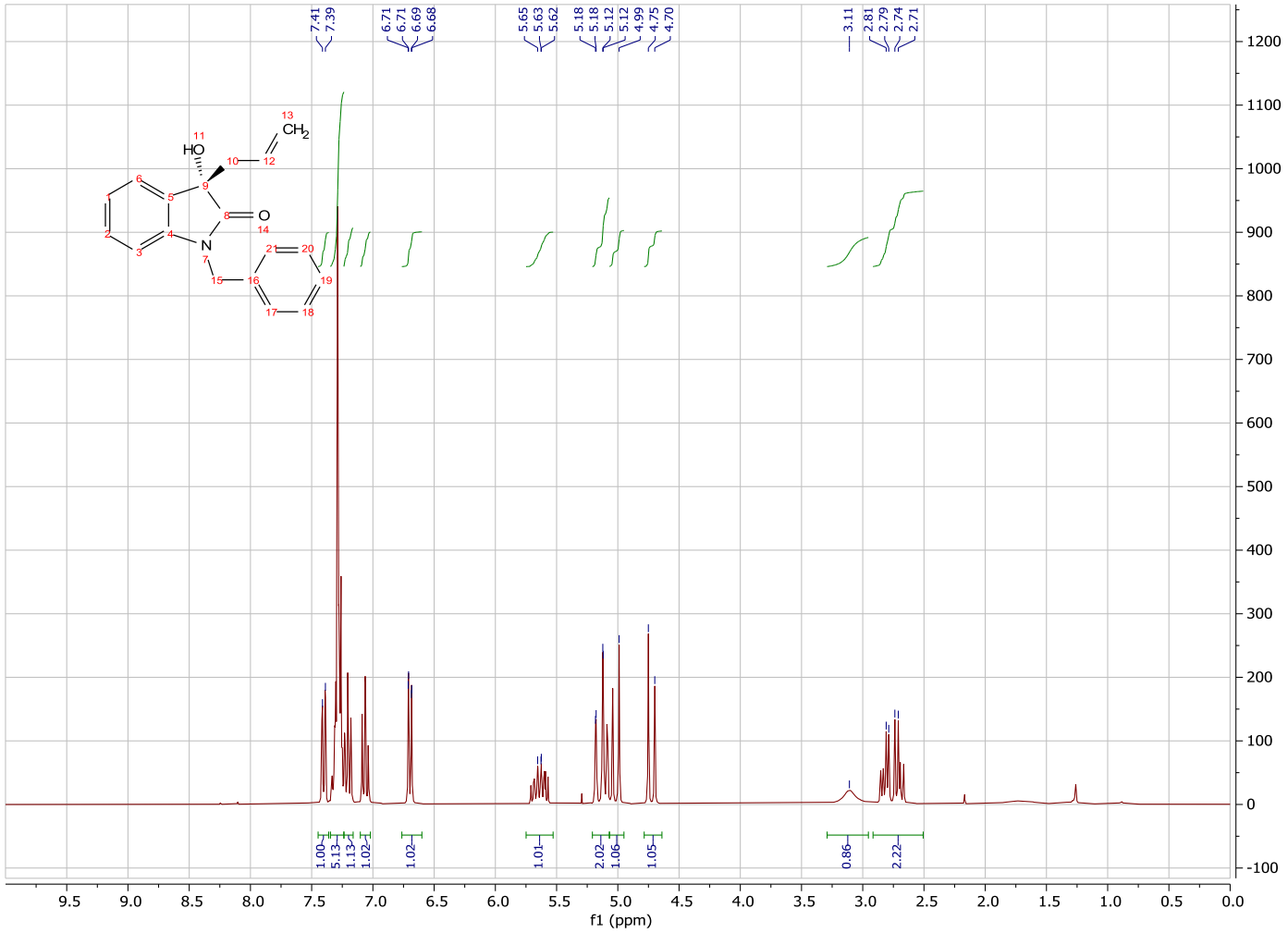
Peak Table

PDA Ch1 254nm

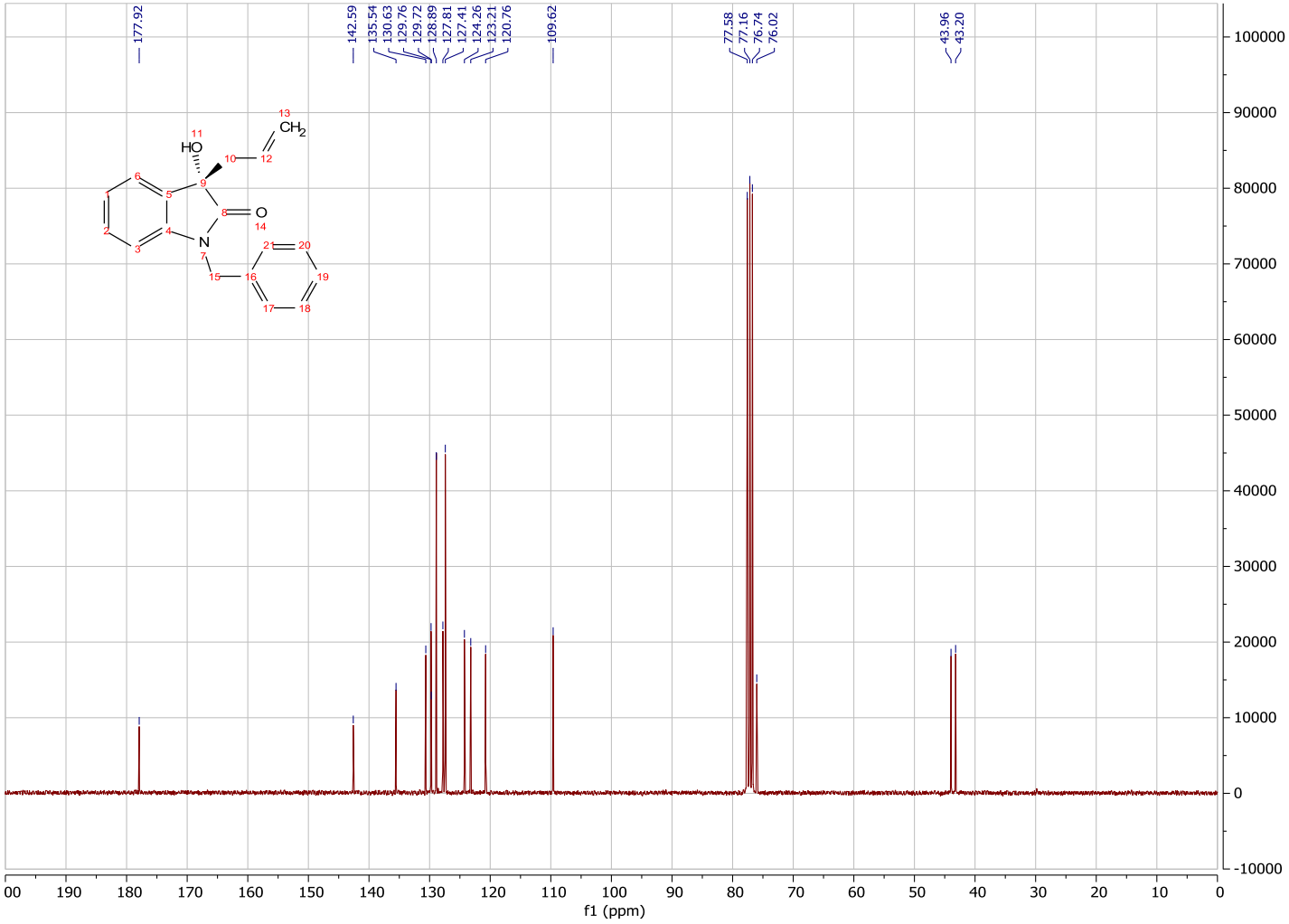
Peak#	Ret. Time	Height	Area	Area%
1	8.382	534064	8511747	99.345
2	9.791	4497	56093	0.655
Total		538561	8567839	100.000

6. Copies of NMR Spectra of compounds 10

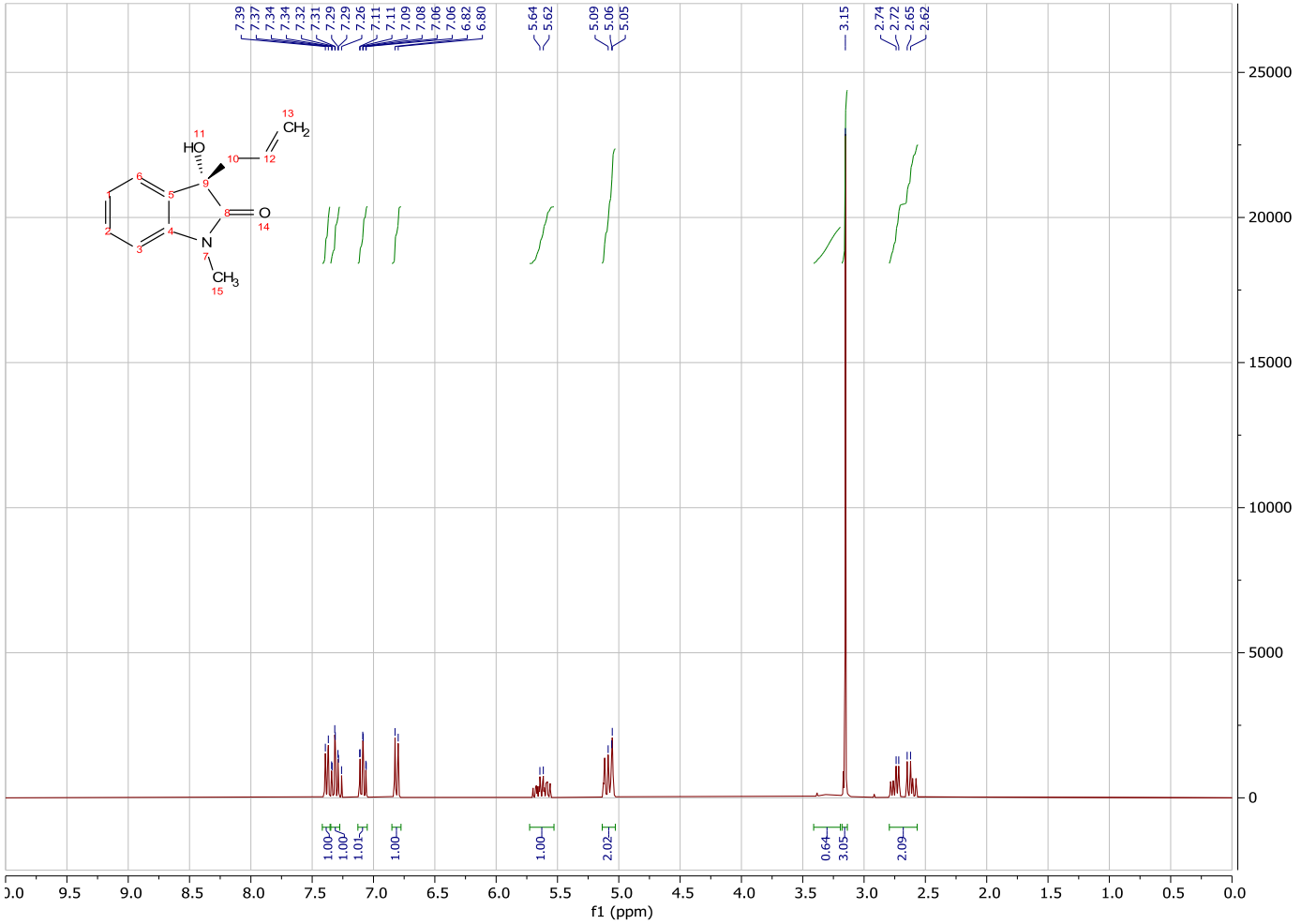
(S)-3-Allyl-1-benzyl-3-hydroxyindolin-2-one (10a) (^{1}H NMR, 300 MHz, $CDCl_3$)



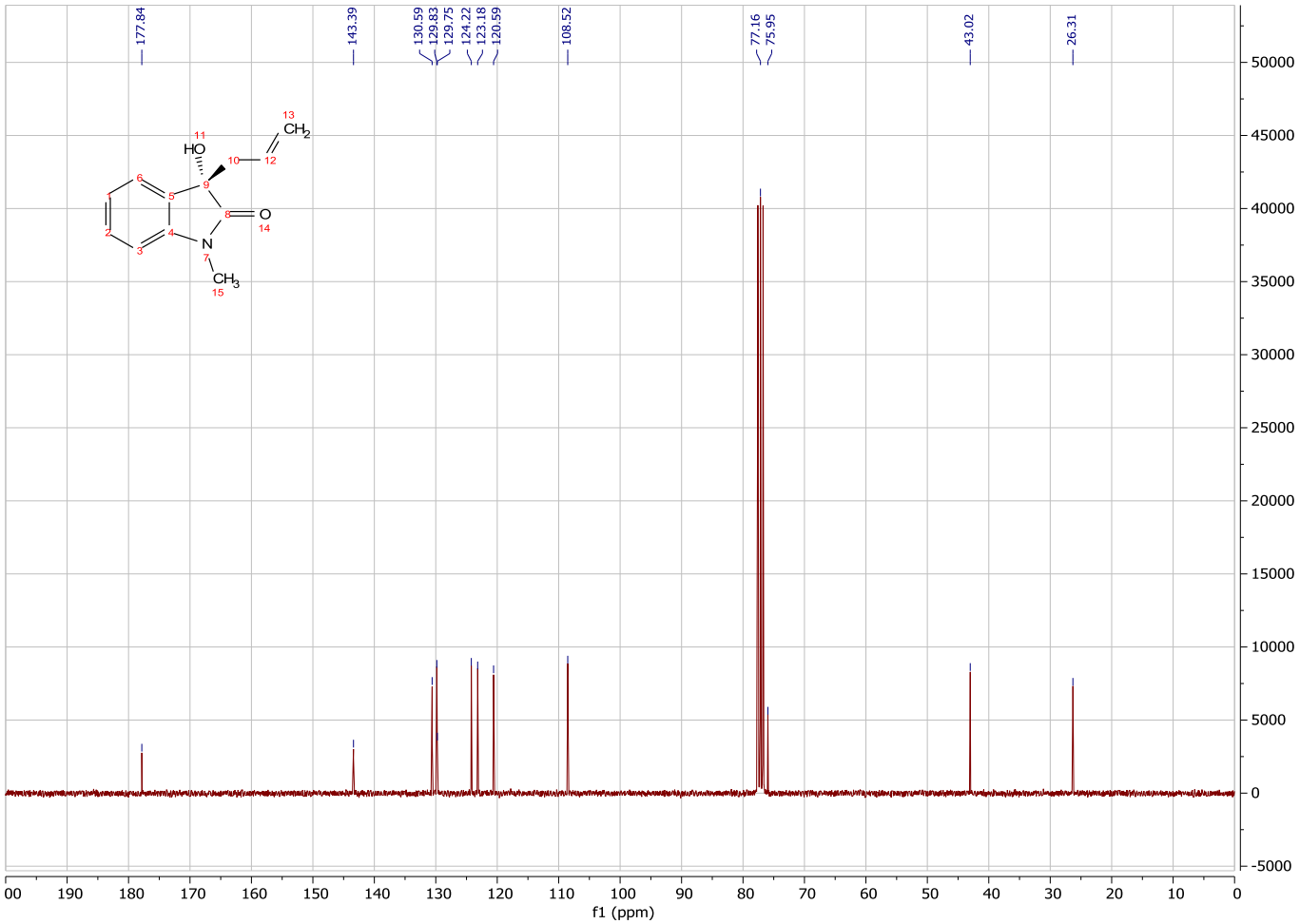
(S)-3-Allyl-1-benzyl-3-hydroxyindolin-2-one (10a) (^{13}C NMR, 75 MHz, $CDCl_3$)



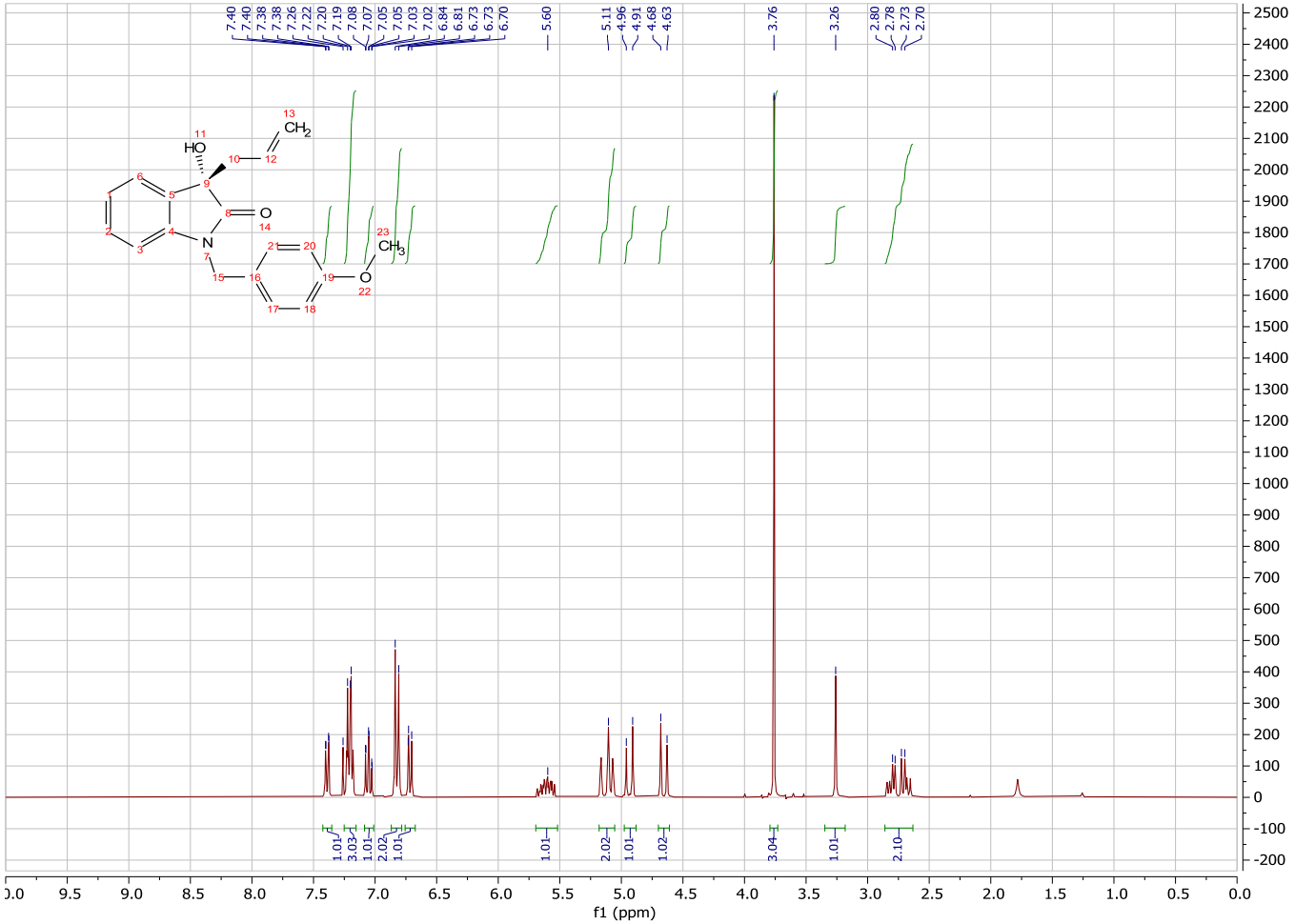
(*S*)-3-Allyl-3-hydroxy-1-methylindolin-2-one (10b) (^{1}H NMR, 300 MHz, $CDCl_3$)



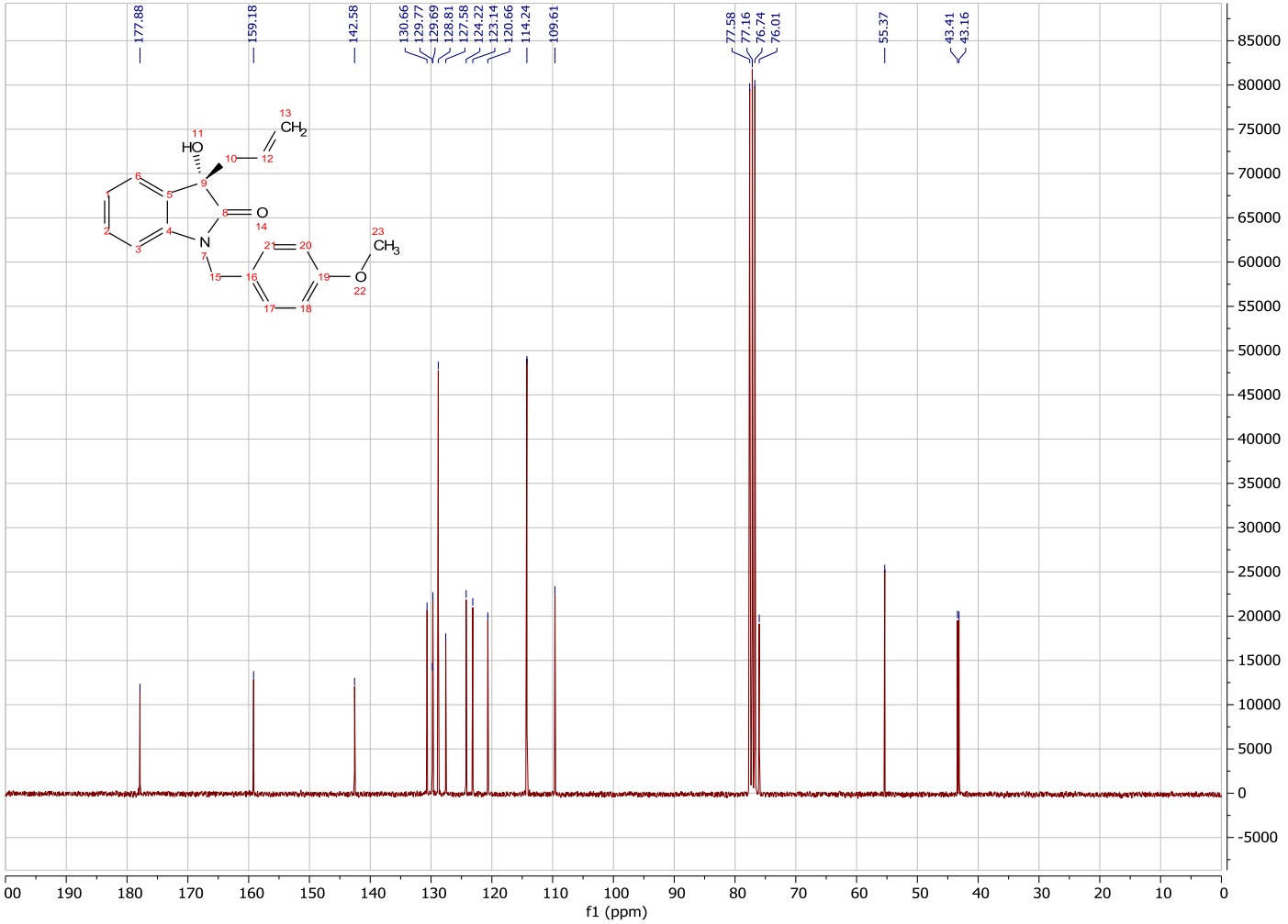
(*S*)-3-Allyl-3-hydroxy-1-methylindolin-2-one (10b) (^{13}C NMR, 75 MHz, $CDCl_3$)



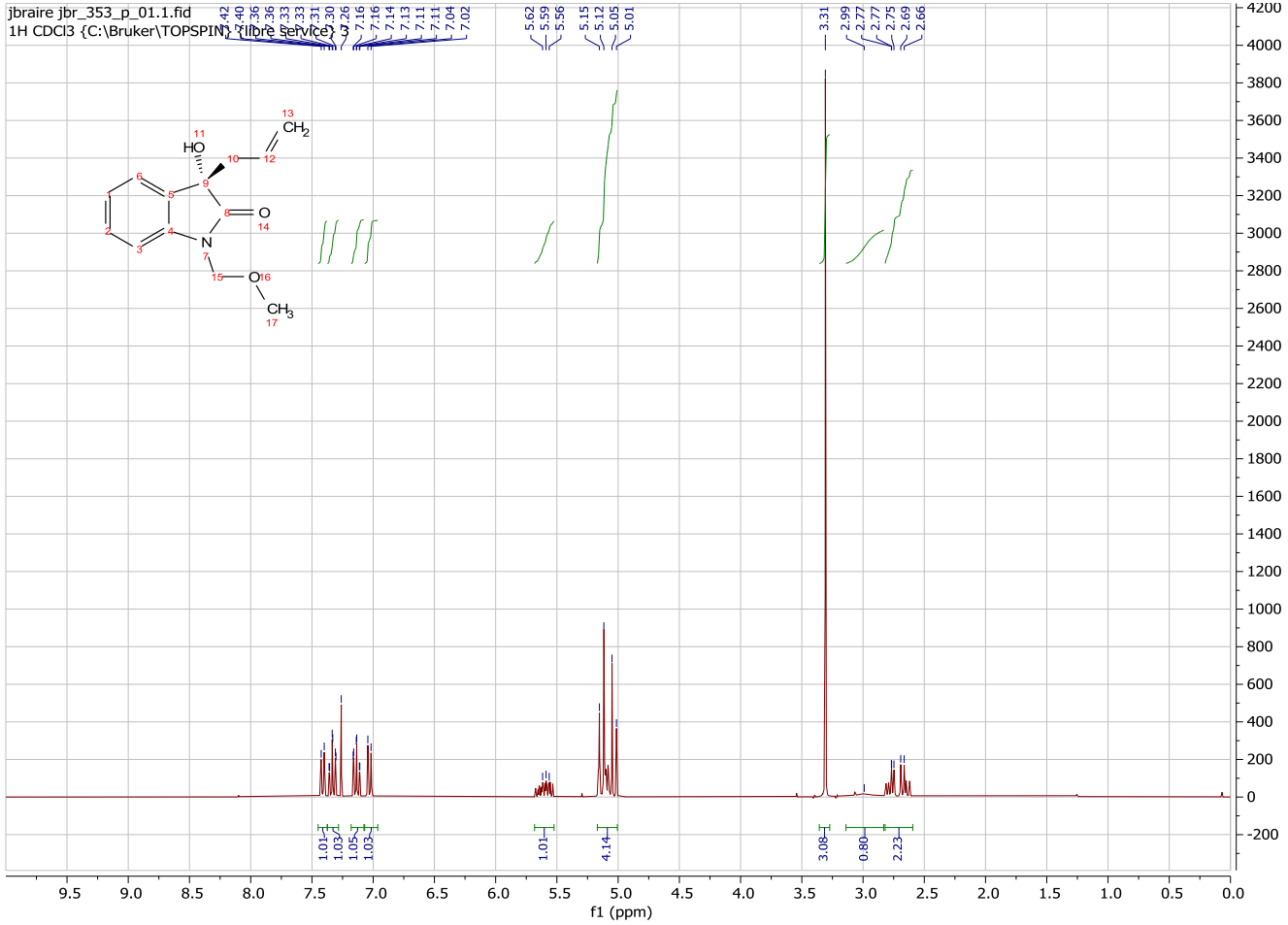
(*S*)-3-Allyl-3-hydroxy-1-(4-methoxybenzyl)indolin-2-one 10c (^{1}H NMR, 300 MHz, $CDCl_3$)



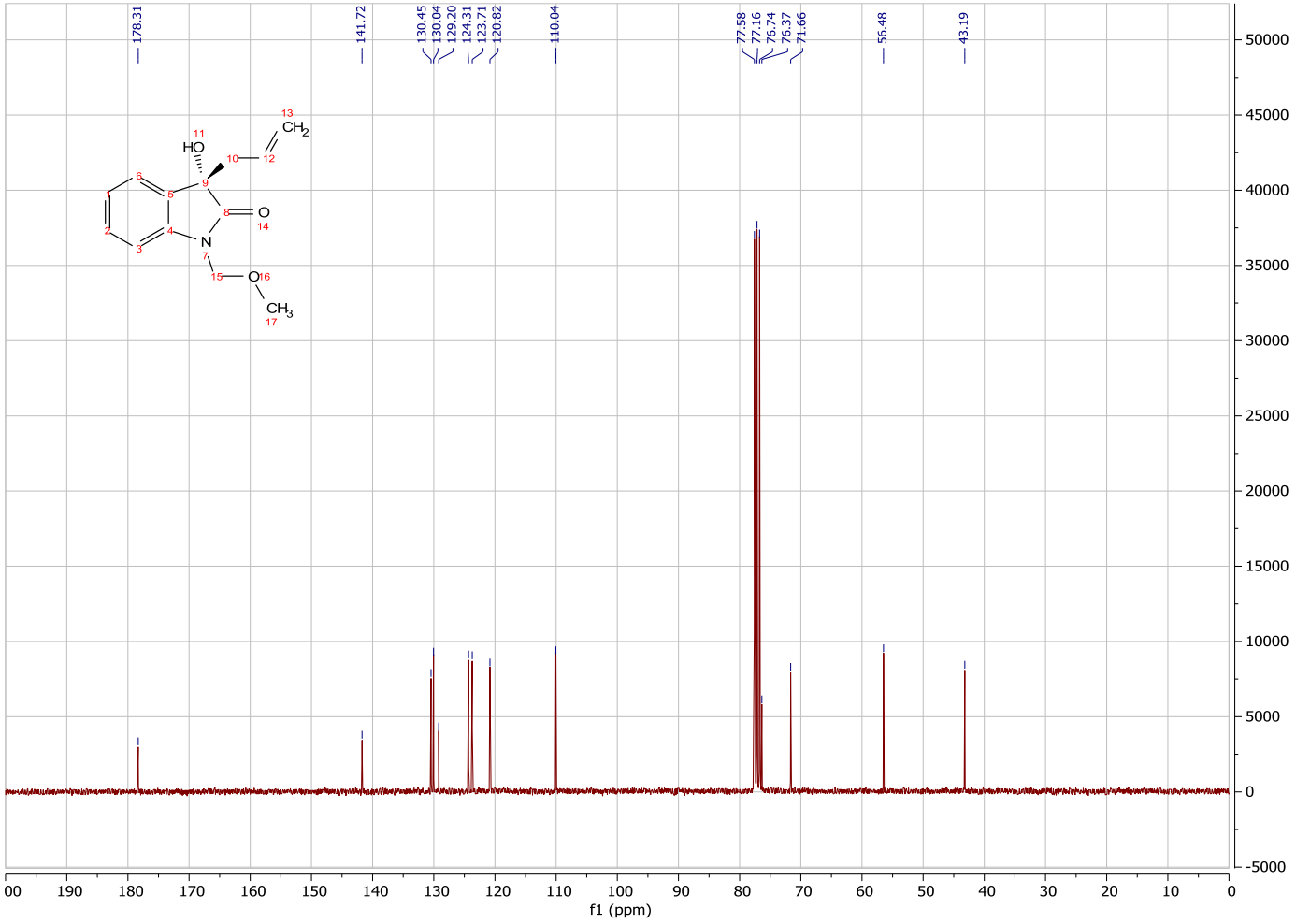
(*S*)-3-Allyl-3-hydroxy-1-(4-methoxybenzyl)indolin-2-one 10c (^{13}C NMR, 75 MHz, $CDCl_3$)



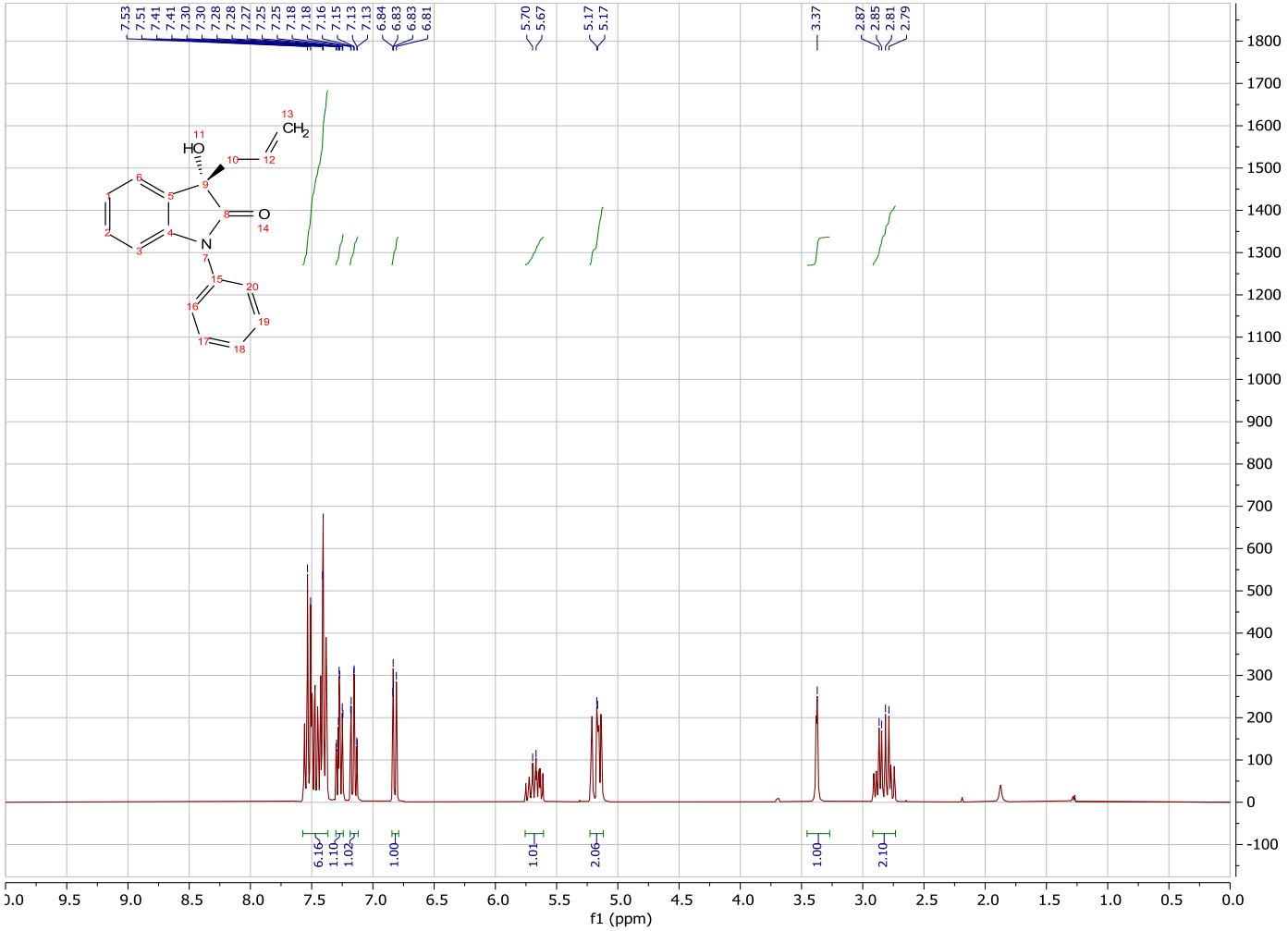
(*S*)-3-Allyl-3-hydroxy-1-(methoxymethyl)indolin-2-one (10d) (^{1}H NMR, 300 MHz, $CDCl_3$)



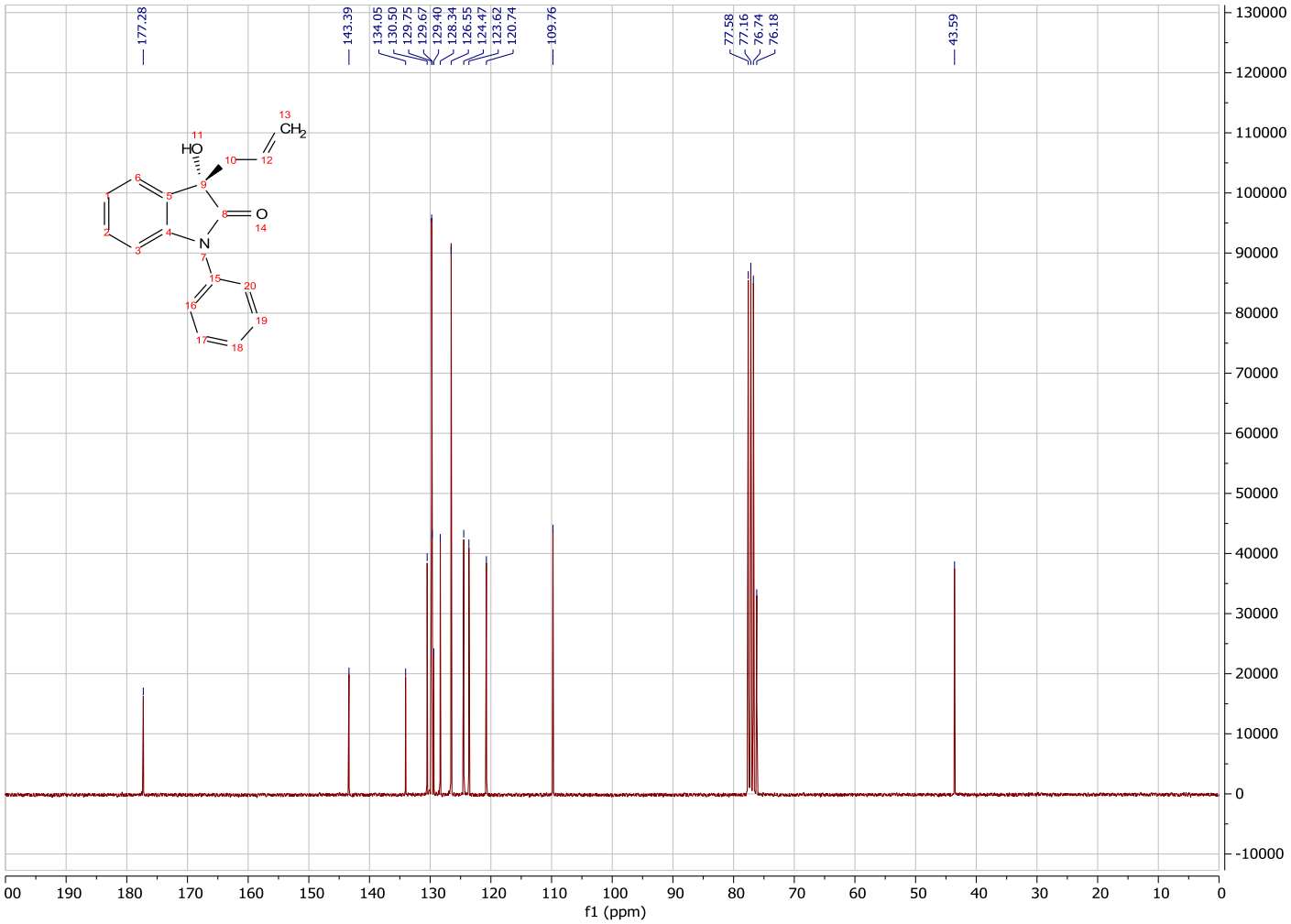
(*S*)-3-Allyl-3-hydroxy-1-(methoxymethyl)indolin-2-one (10d) (^{13}C NMR, 75 MHz, $CDCl_3$)



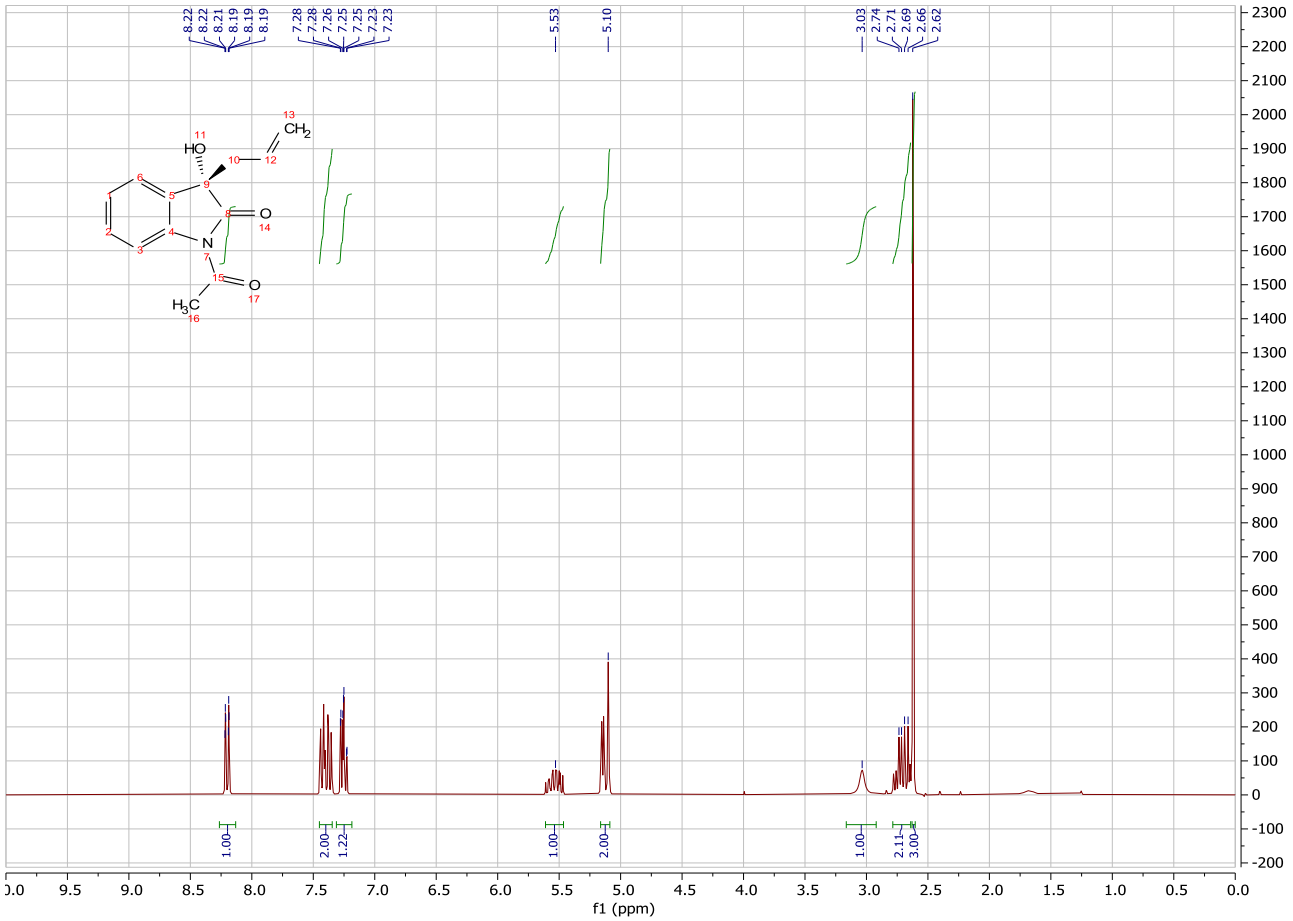
(*S*)-3-Allyl-3-hydroxy-1-phenylindolin-2-one (10e) (^{1}H NMR, 300 MHz, $CDCl_3$)



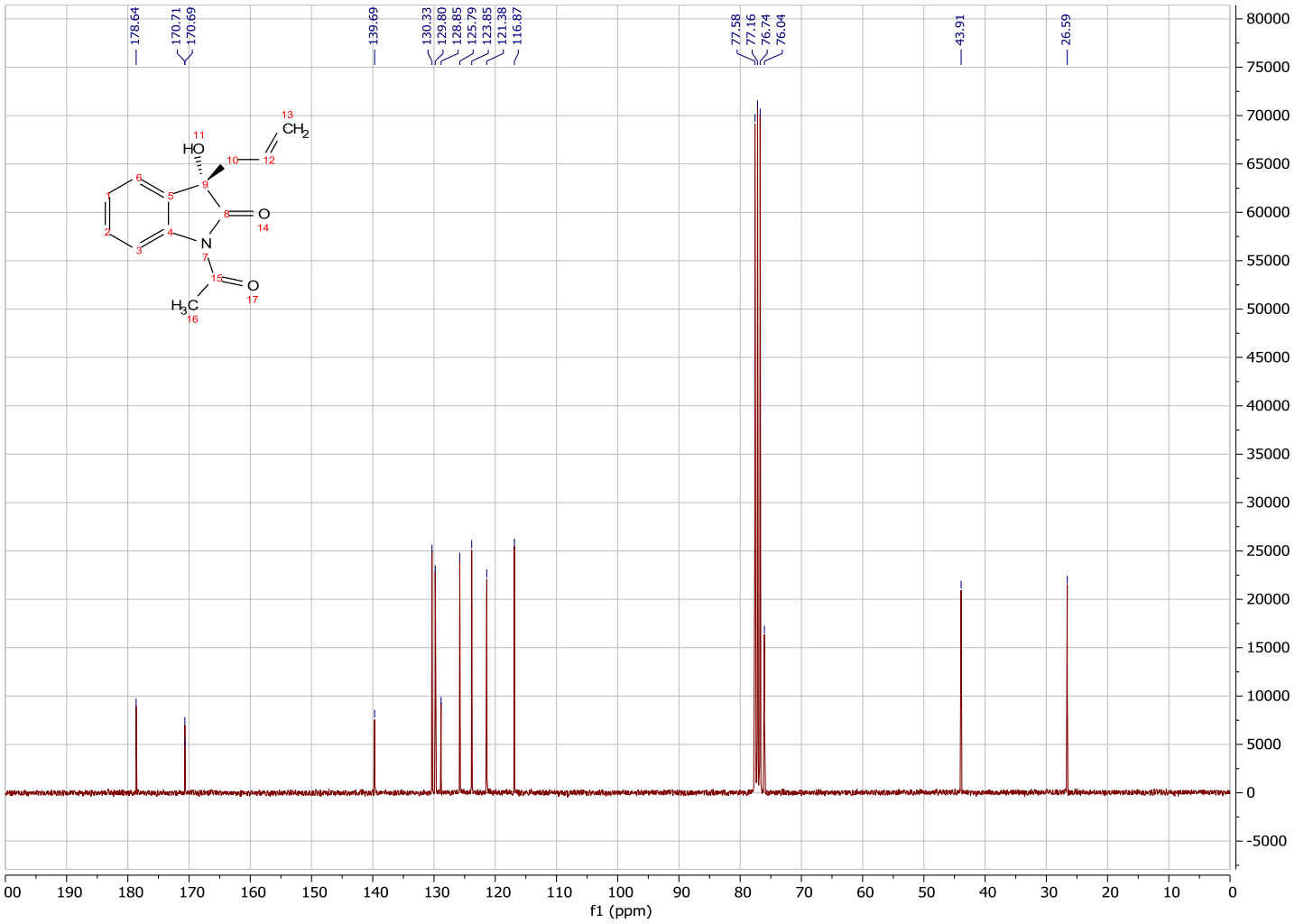
(*S*)-3-Allyl-3-hydroxy-1-phenylindolin-2-one (10e) (^{13}C NMR, 75 MHz, $CDCl_3$)



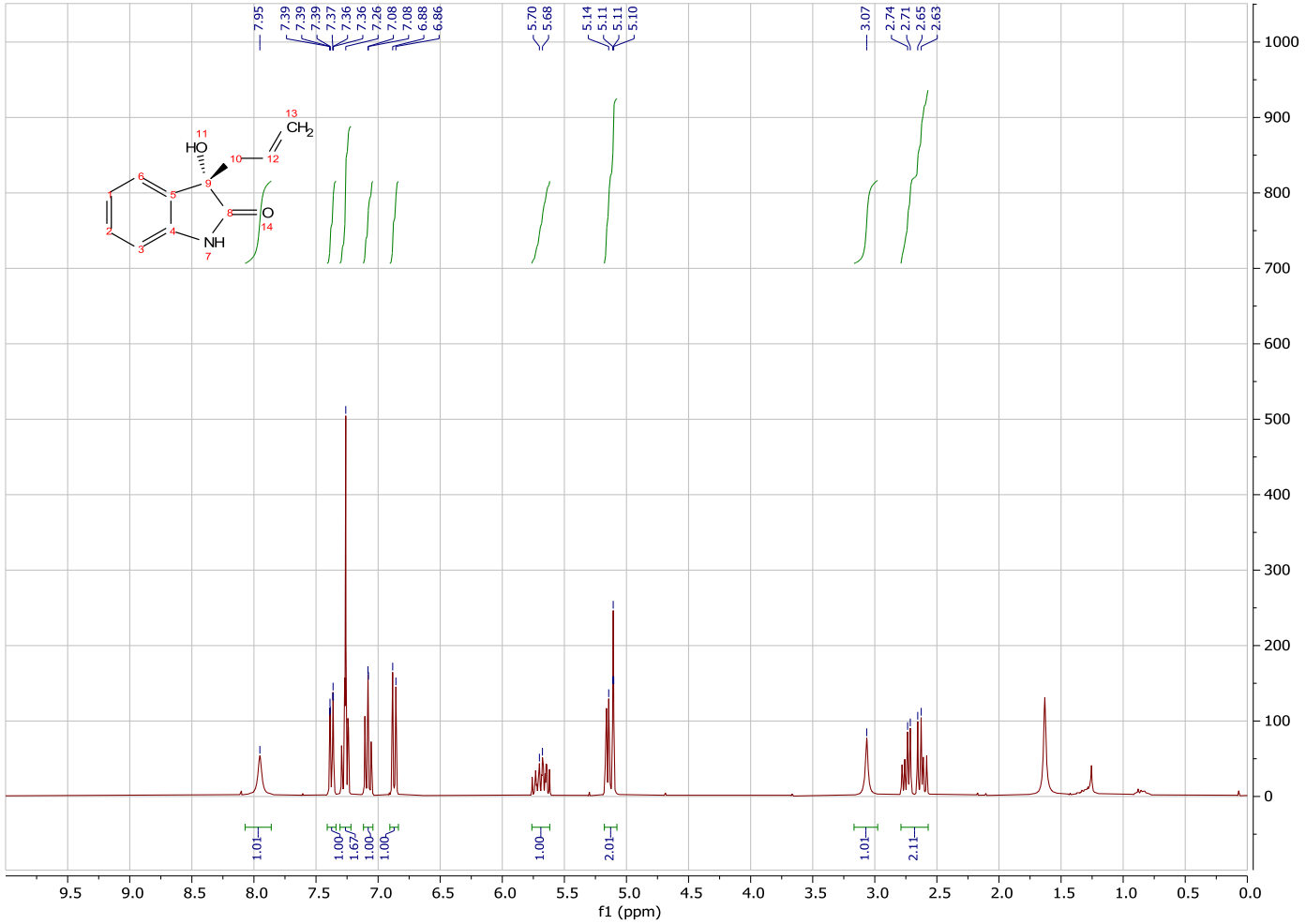
(*S*)-1-Acetyl-3-allyl-3-hydroxyindolin-2-one (10f) (^{1}H NMR, 300 MHz, $CDCl_3$)



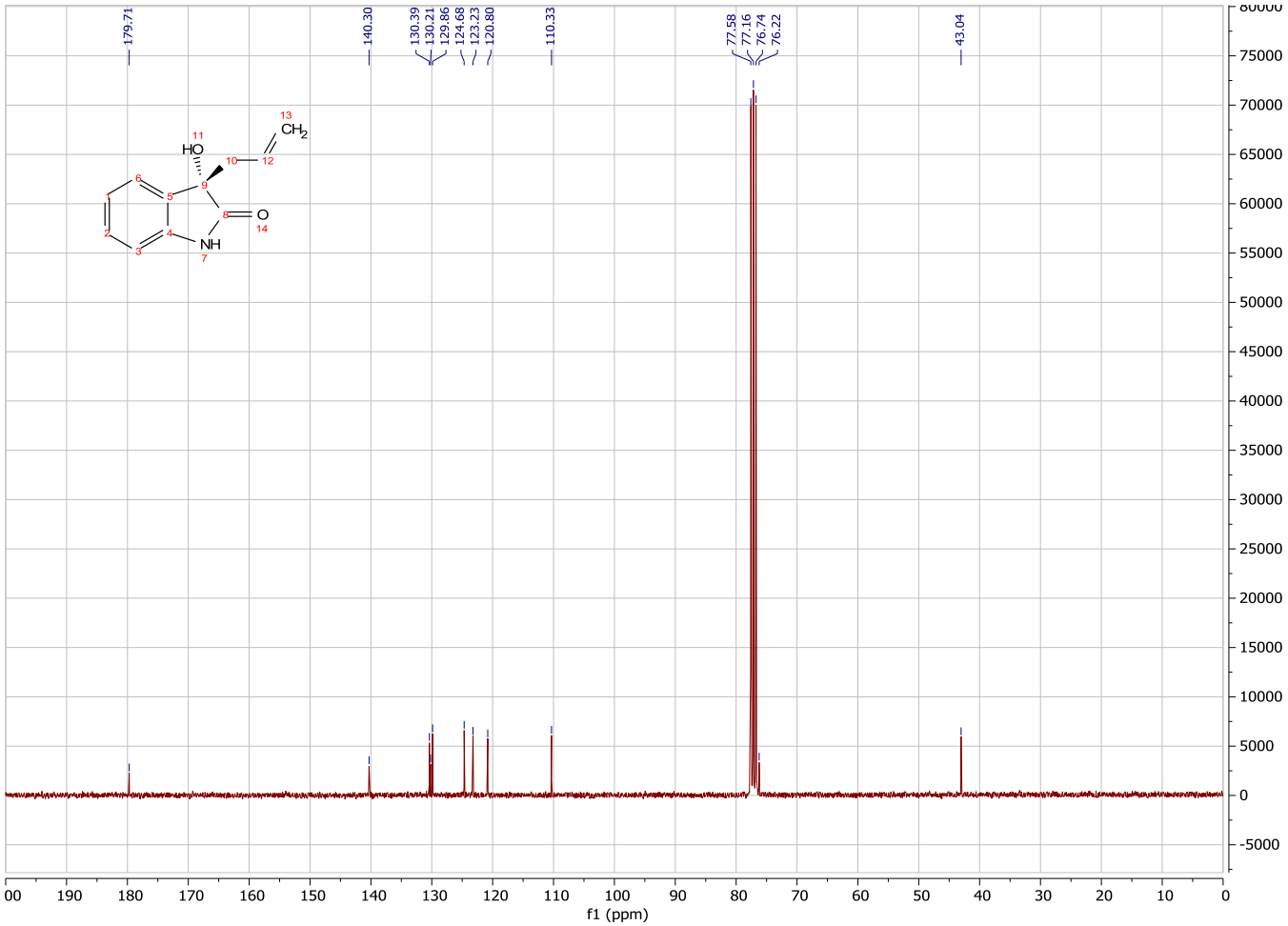
(*S*)-1-Acetyl-3-allyl-3-hydroxyindolin-2-one (10f) (^{13}C NMR, 75 MHz, $CDCl_3$)



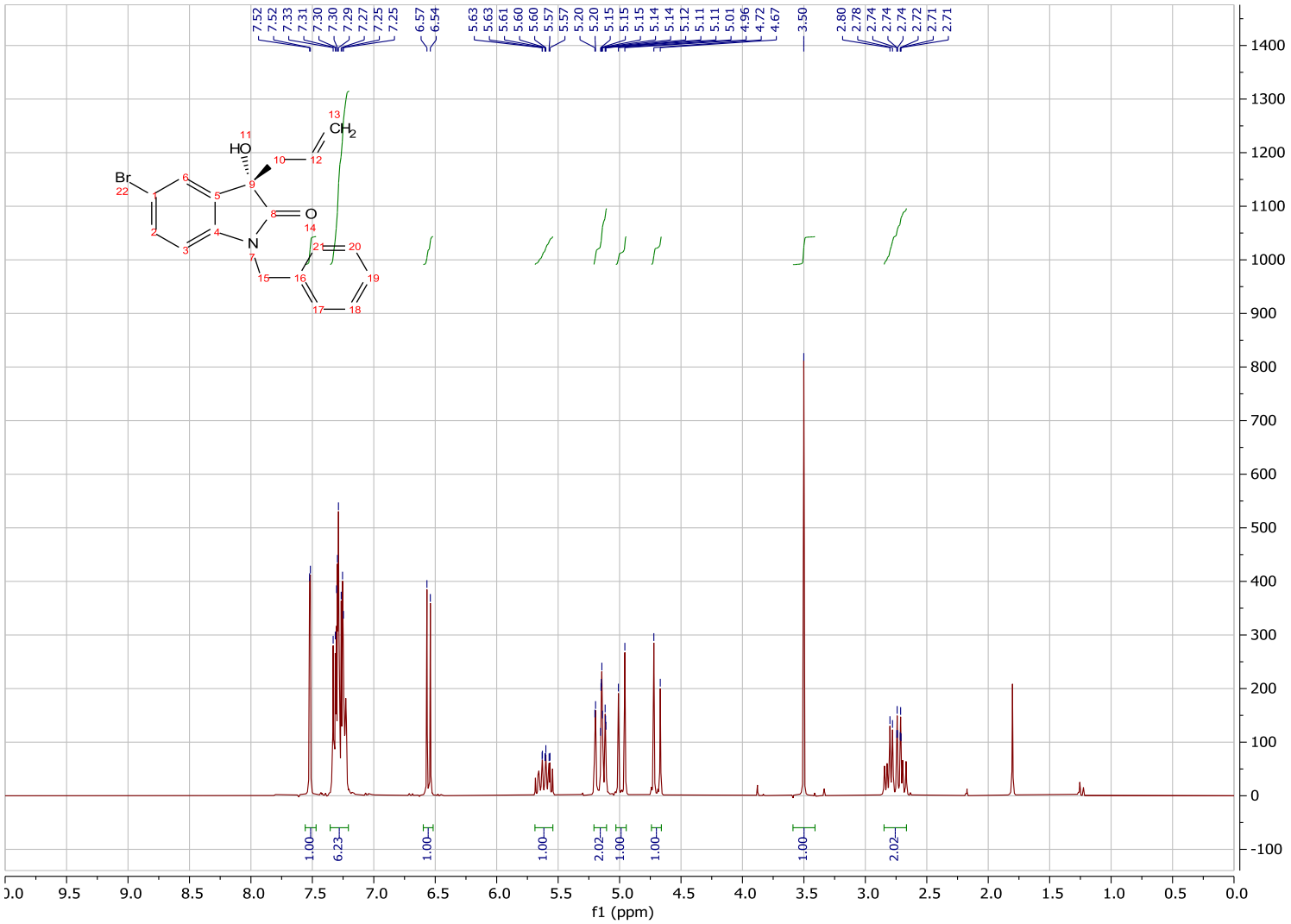
(*S*)-3-Allyl-3-hydroxyindolin-2-one (10i) (^{1}H NMR, 300 MHz, $CDCl_3$)



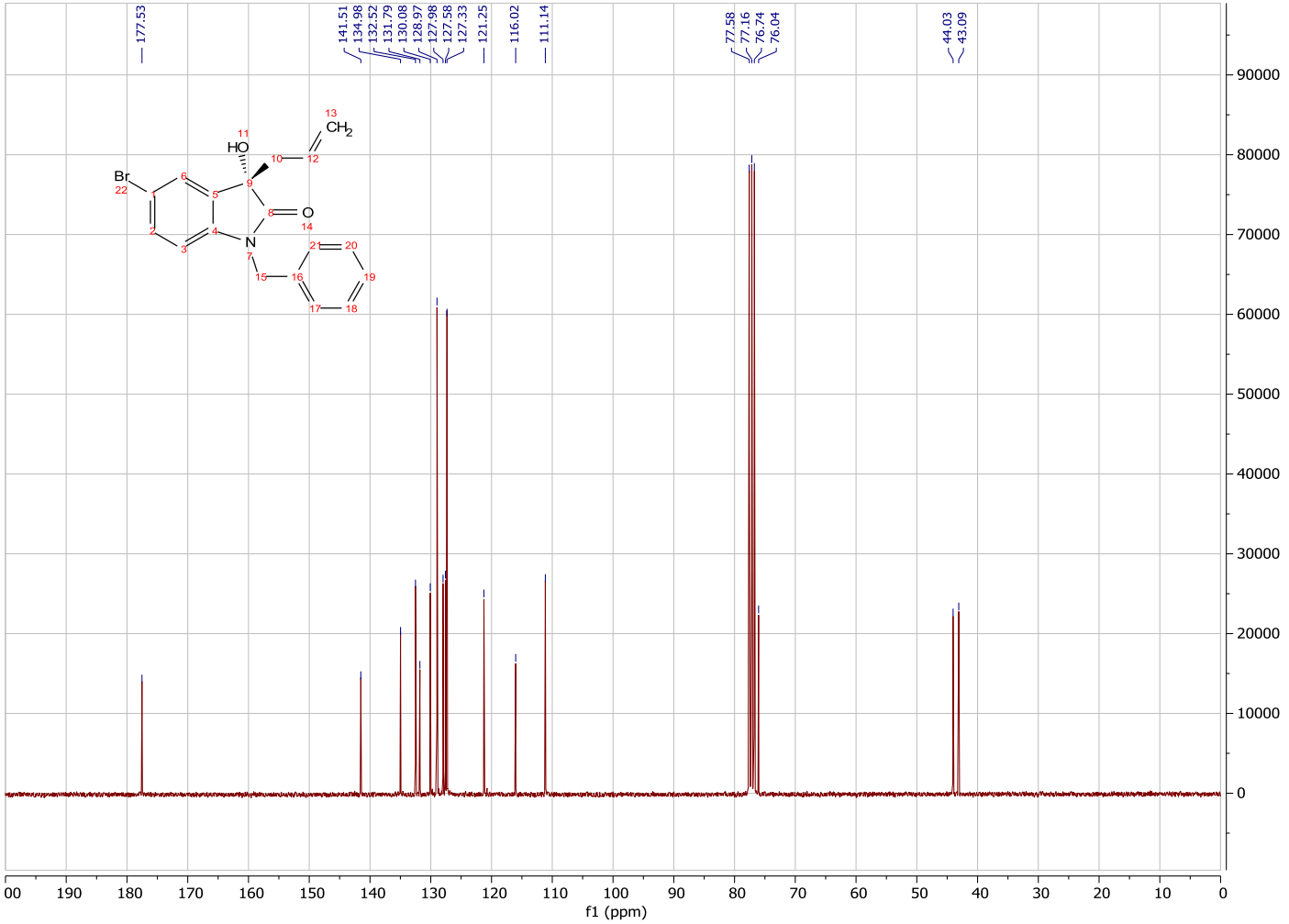
(*S*)-3-Allyl-3-hydroxyindolin-2-one (10i) (^{13}C NMR, 75 MHz, $CDCl_3$)



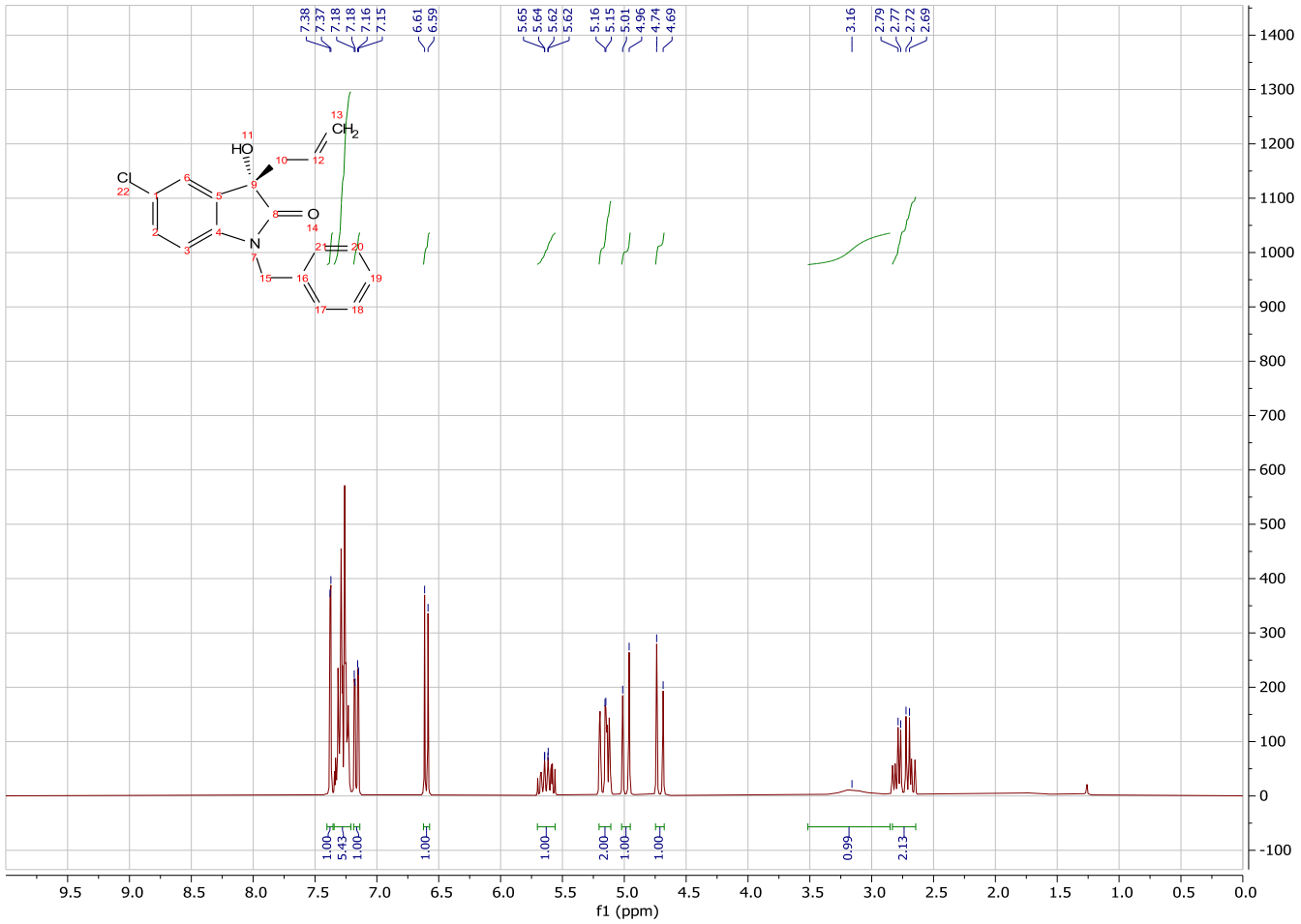
(*S*)-3-Allyl-1-benzyl-5-bromo-3-hydroxyindolin-2-one (10j) (^{1}H NMR, 300 MHz, $CDCl_3$)



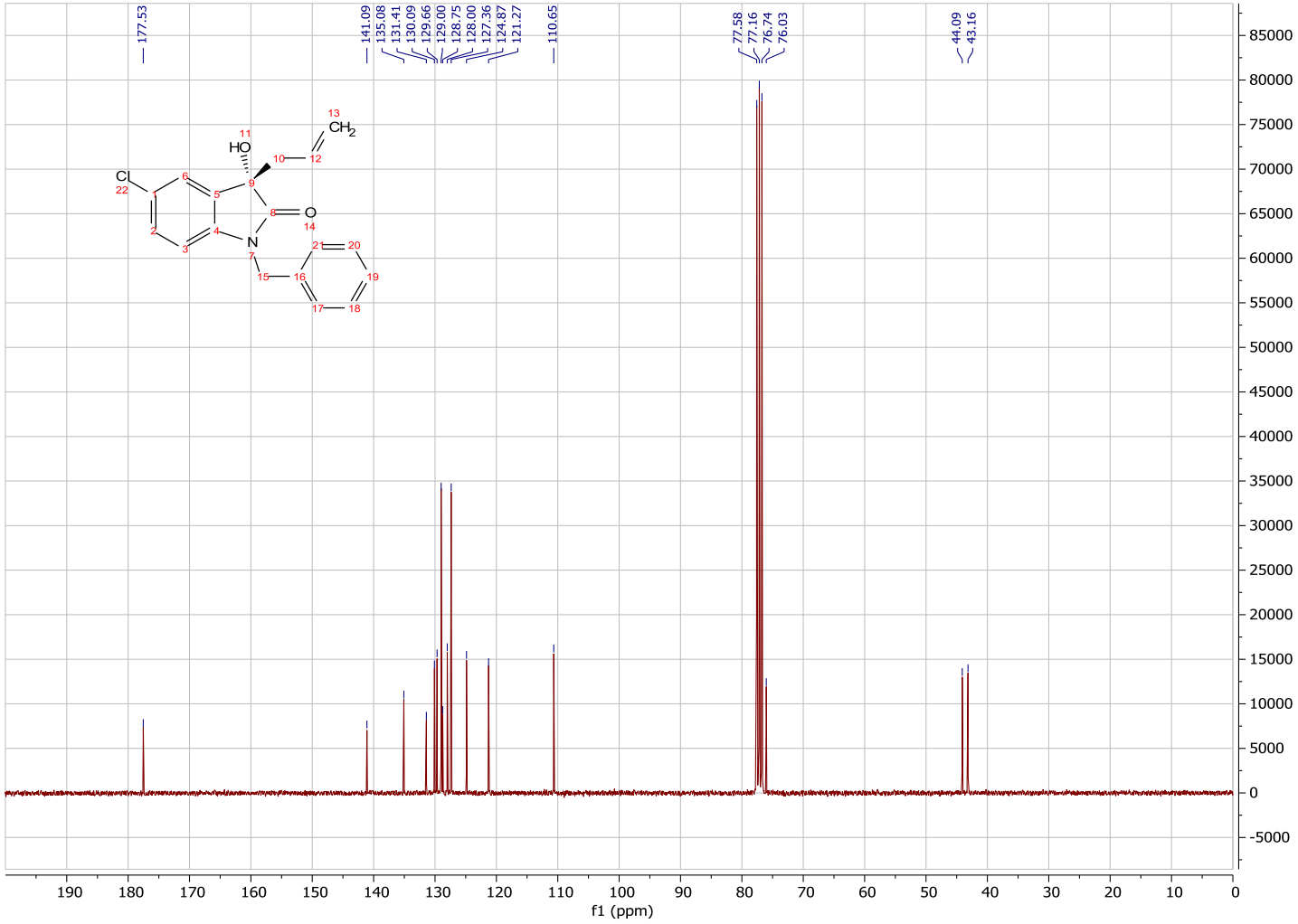
(*S*)-3-Allyl-1-benzyl-5-bromo-3-hydroxyindolin-2-one (10j) (^{13}C NMR, 75 MHz, $CDCl_3$)



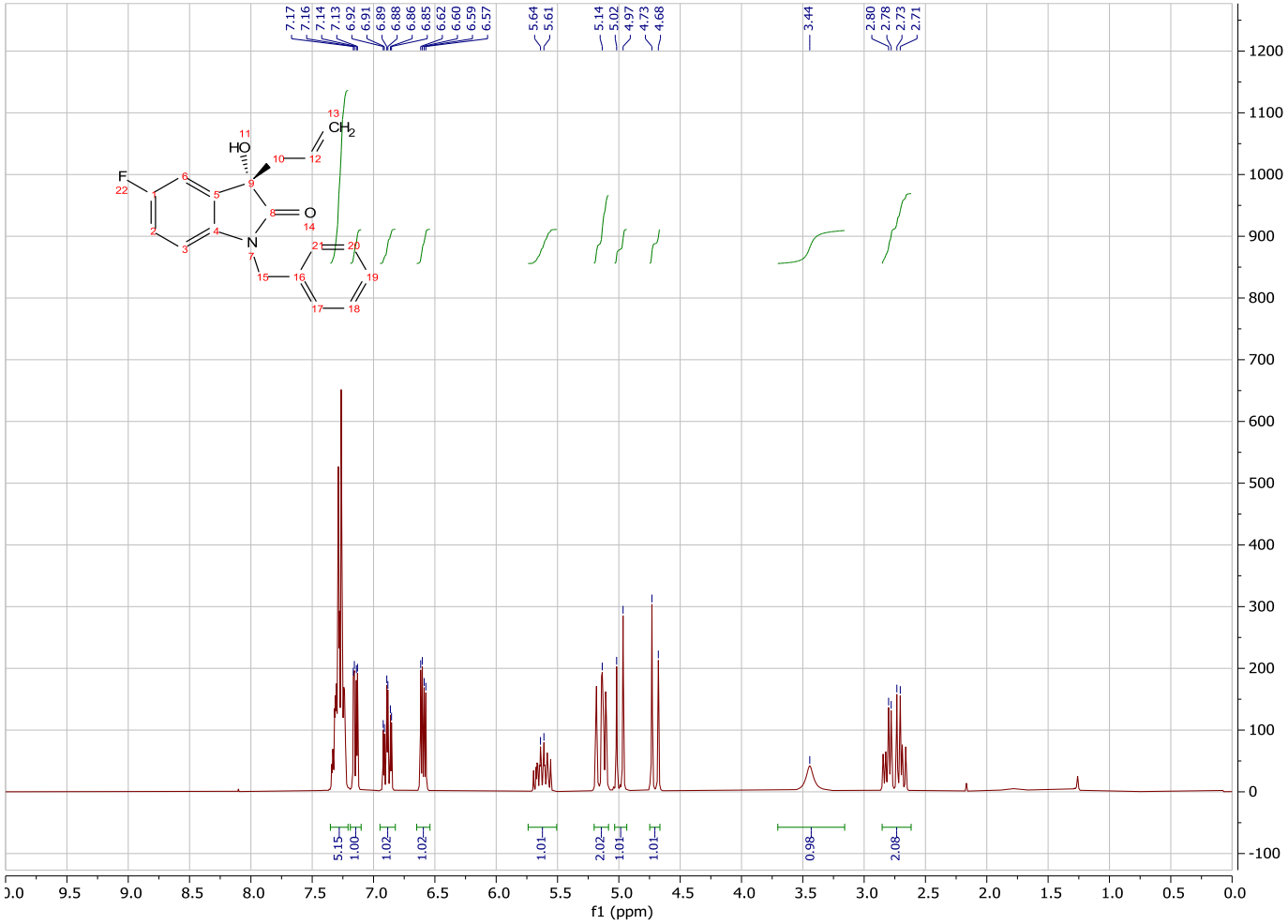
(*S*)-3-Allyl-1-benzyl-5-chloro-3-hydroxyindolin-2-one (10k) (^{1}H NMR, 300 MHz, $CDCl_3$)



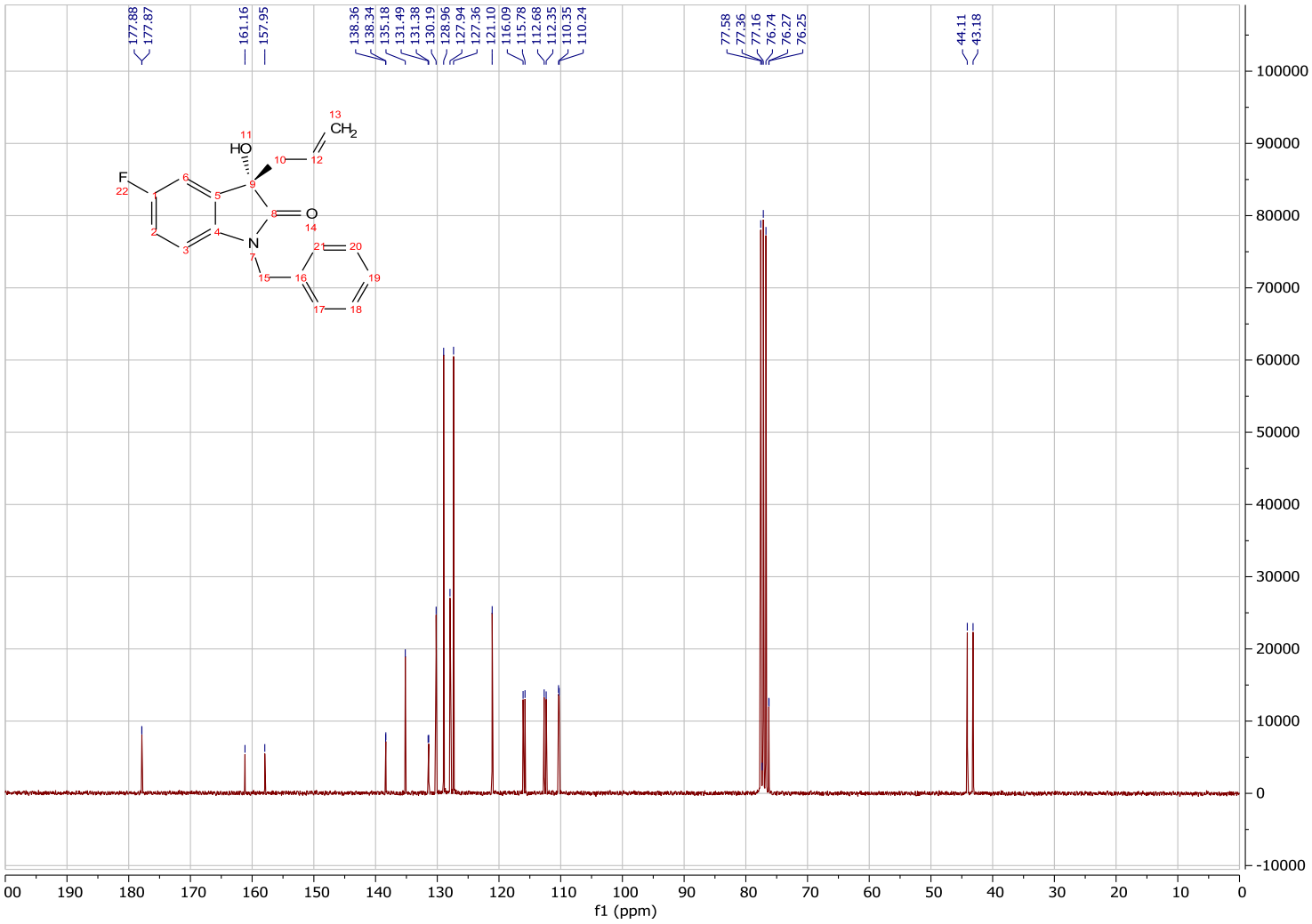
(*S*)-3-Allyl-1-benzyl-5-chloro-3-hydroxyindolin-2-one (10k) (^{13}C NMR, 75 MHz, $CDCl_3$)



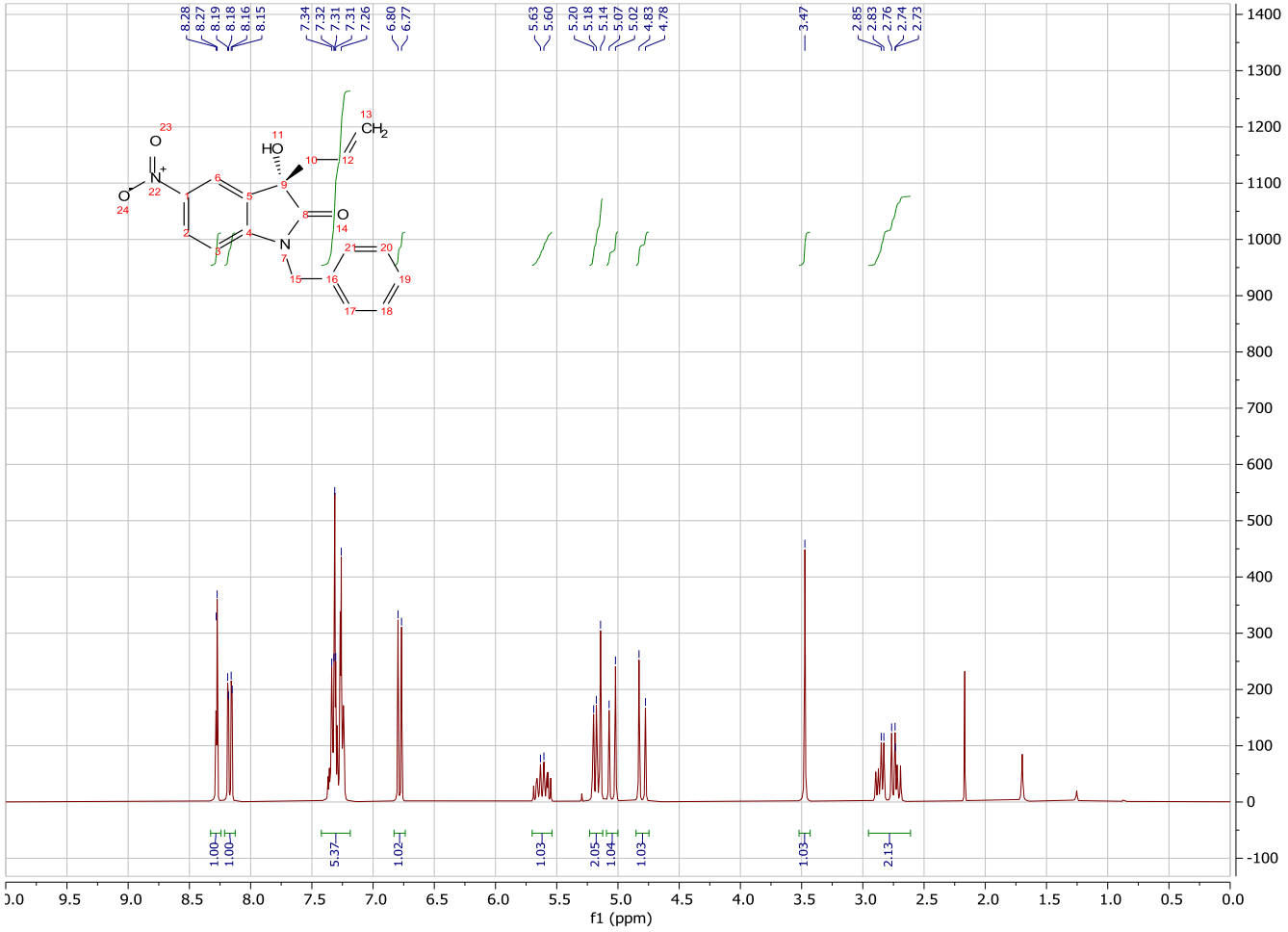
(*S*)-3-Allyl-1-benzyl-5-fluoro-3-hydroxyindolin-2-one (10l) (^{1}H NMR, 300 MHz, $CDCl_3$)



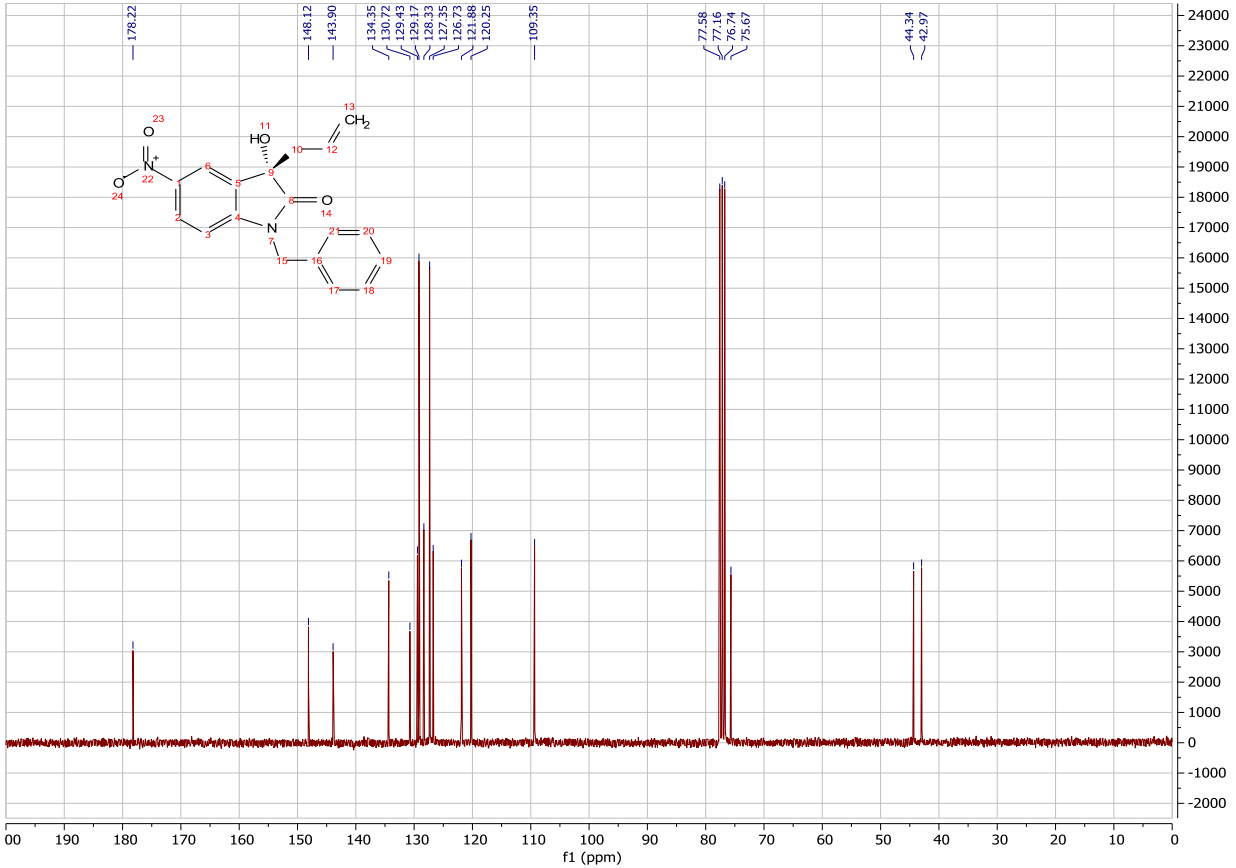
(*S*)-3-Allyl-1-benzyl-5-fluoro-3-hydroxyindolin-2-one (10l) (^{13}C NMR, 75 MHz, $CDCl_3$)



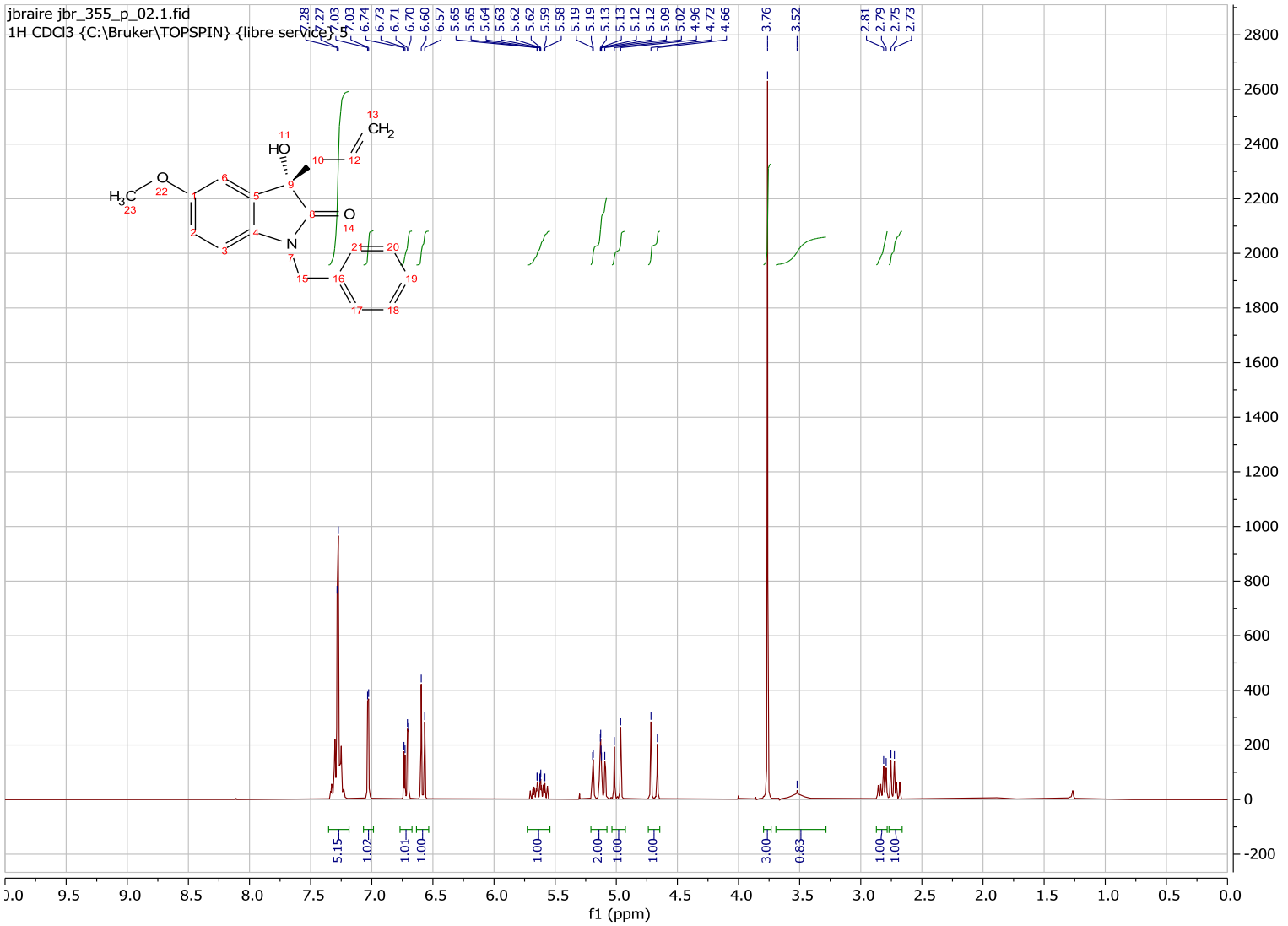
(*S*)-3-Allyl-1-benzyl-3-hydroxy-5-nitroindolin-2-one (10m) (^{1}H NMR, 300 MHz, $CDCl_3$)



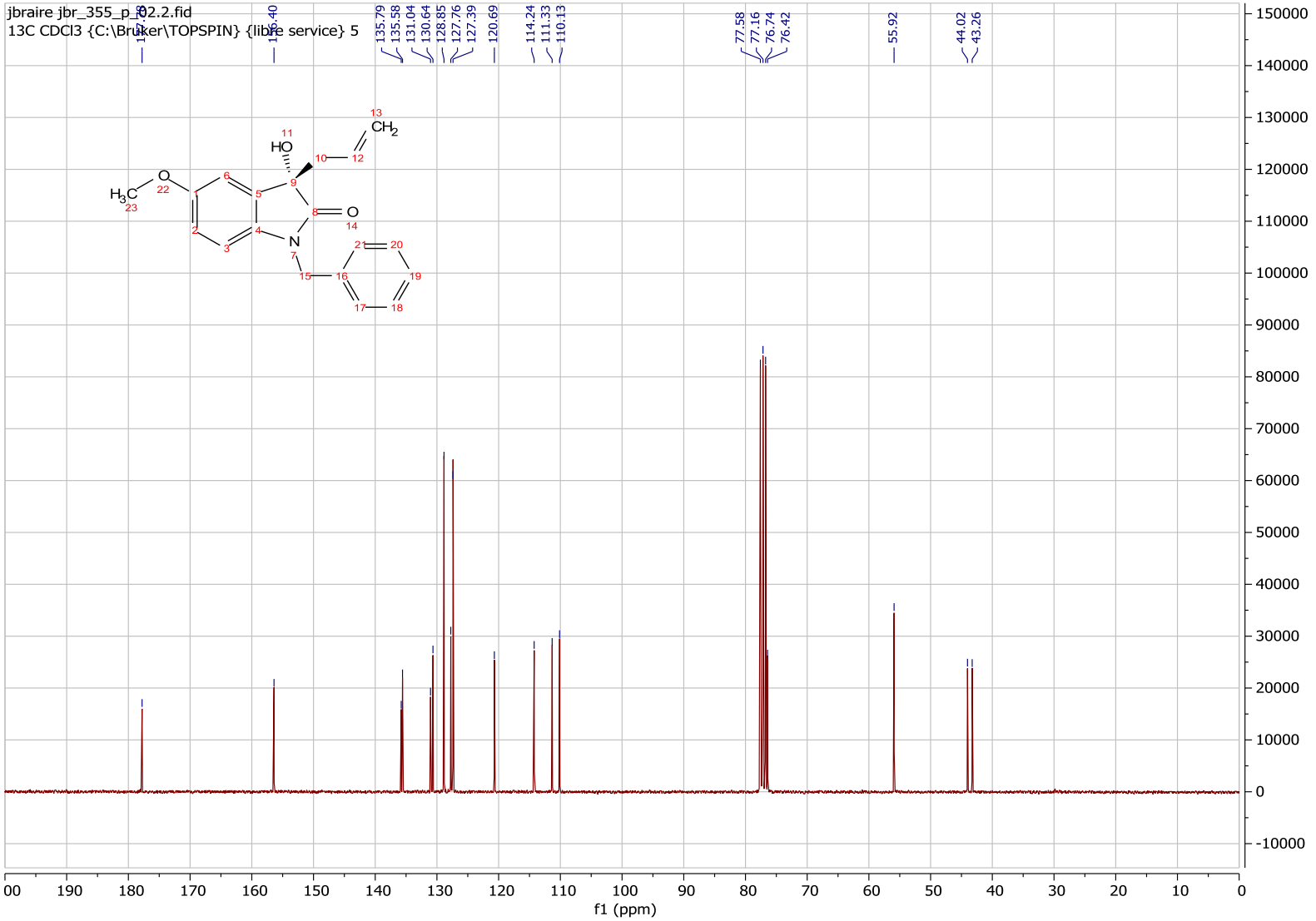
(*S*)-3-Allyl-1-benzyl-3-hydroxy-5-nitroindolin-2-one (10m) (^{13}C NMR, 75 MHz, $CDCl_3$)



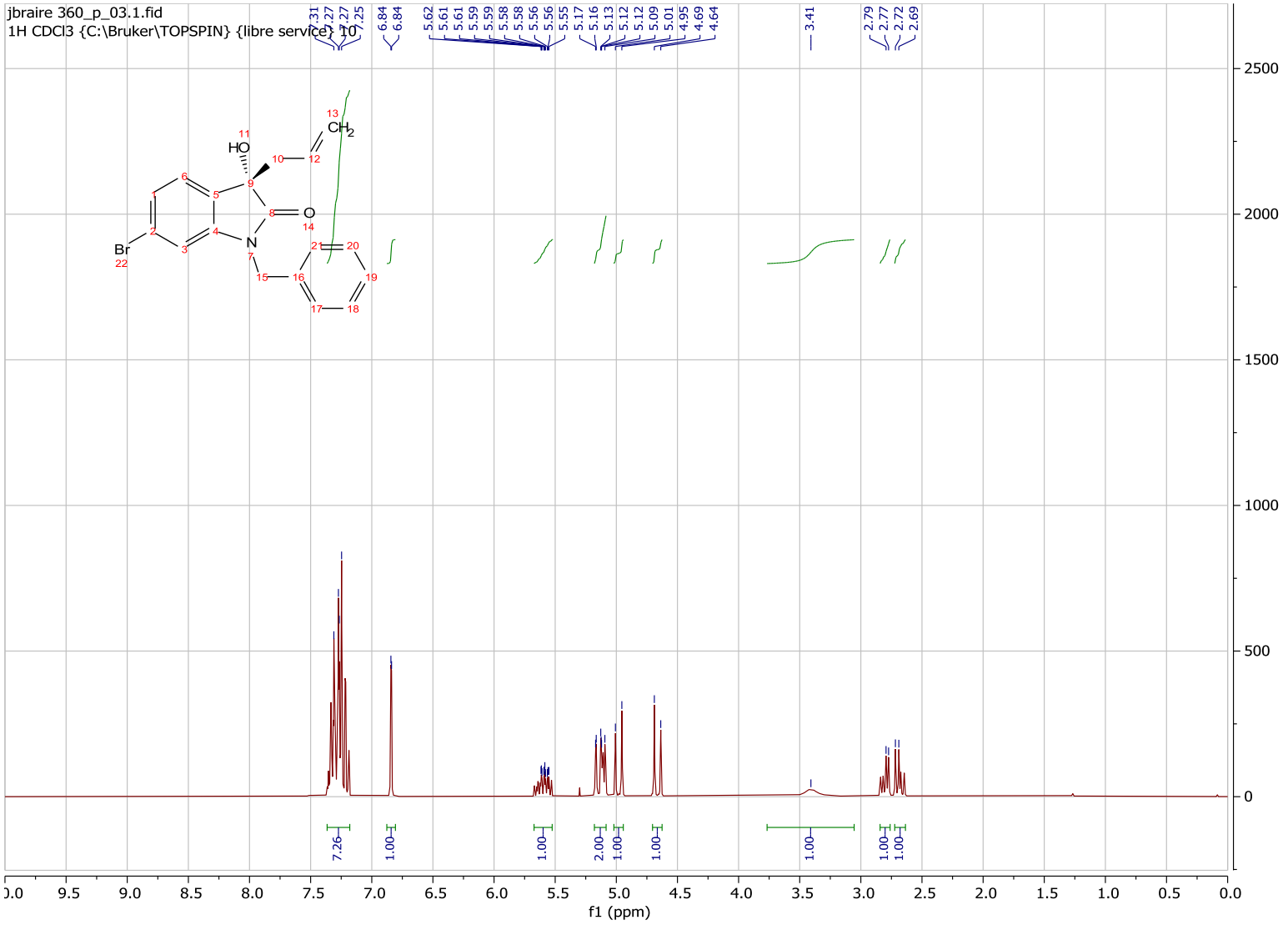
(*S*)-3-Allyl-1-benzyl-3-hydroxy-5-methoxyindolin-2-one (10n) (^{1}H NMR, 300 MHz, $CDCl_3$)



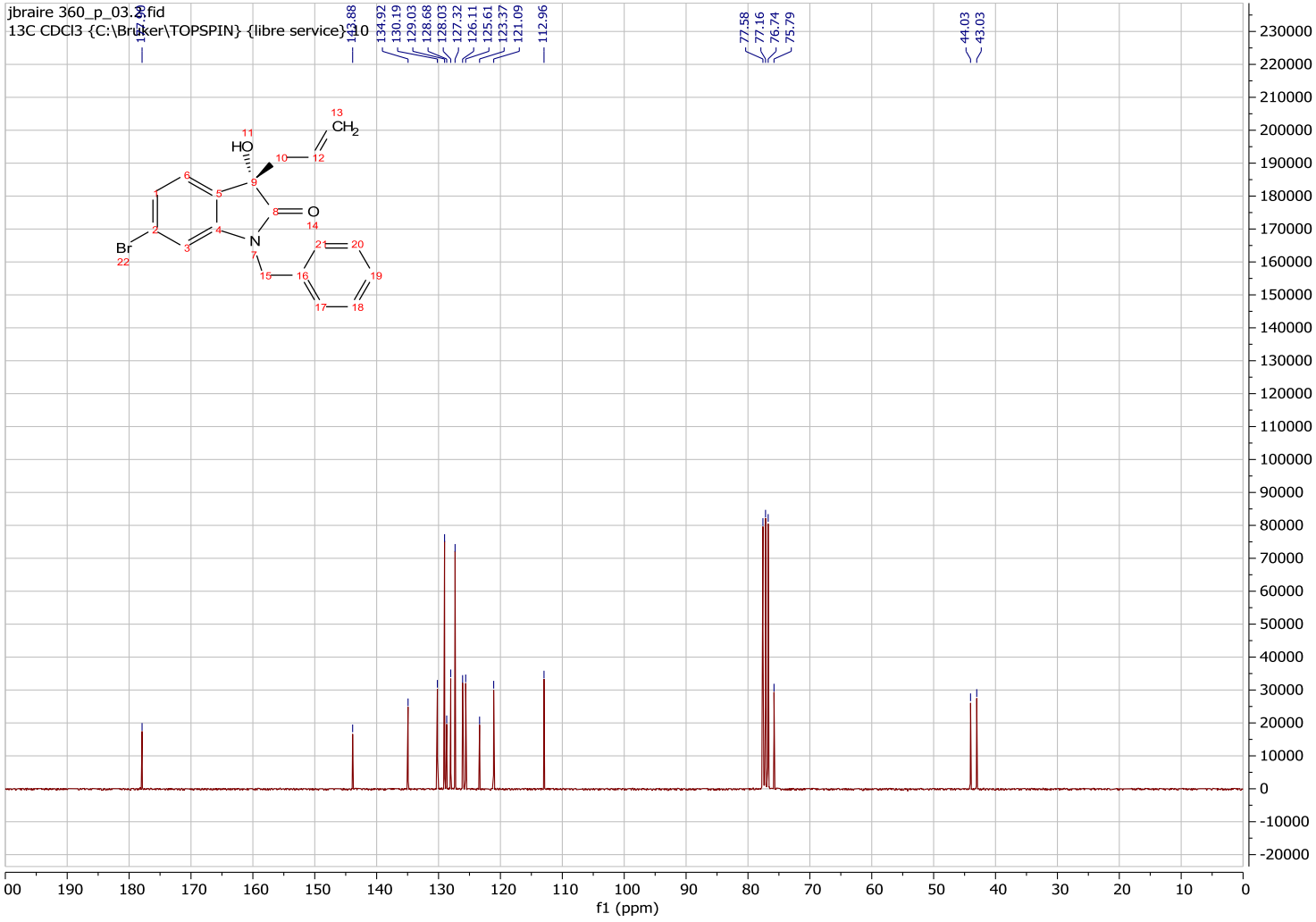
(*S*)-3-Allyl-1-benzyl-3-hydroxy-5-methoxyindolin-2-one (10n) (^{13}C NMR, 75 MHz, $CDCl_3$)



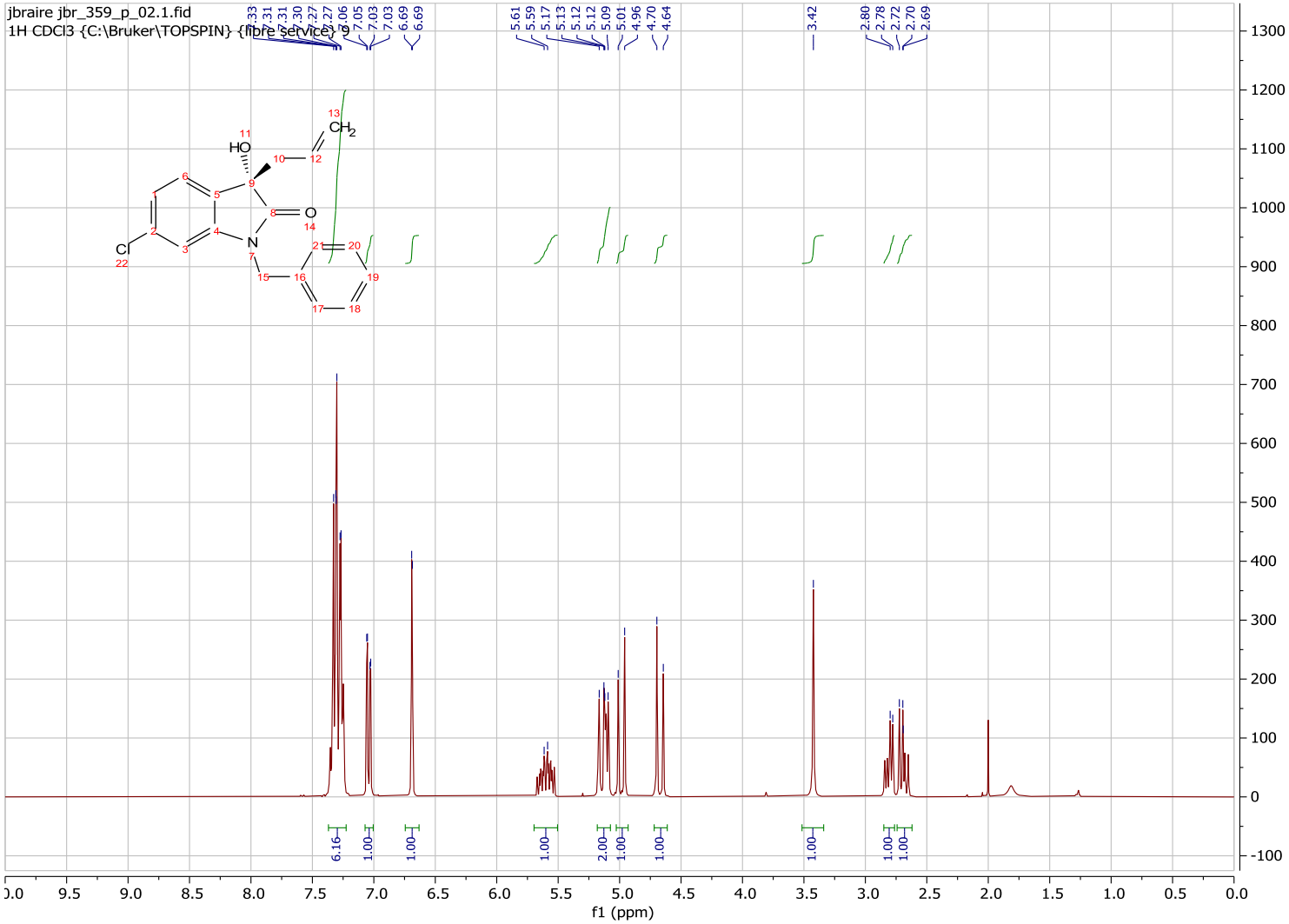
(*S*)-3-Allyl-1-benzyl-6-bromo-3-hydroxyindolin-2-one (10o) (^{1}H NMR, 300 MHz, $CDCl_3$)



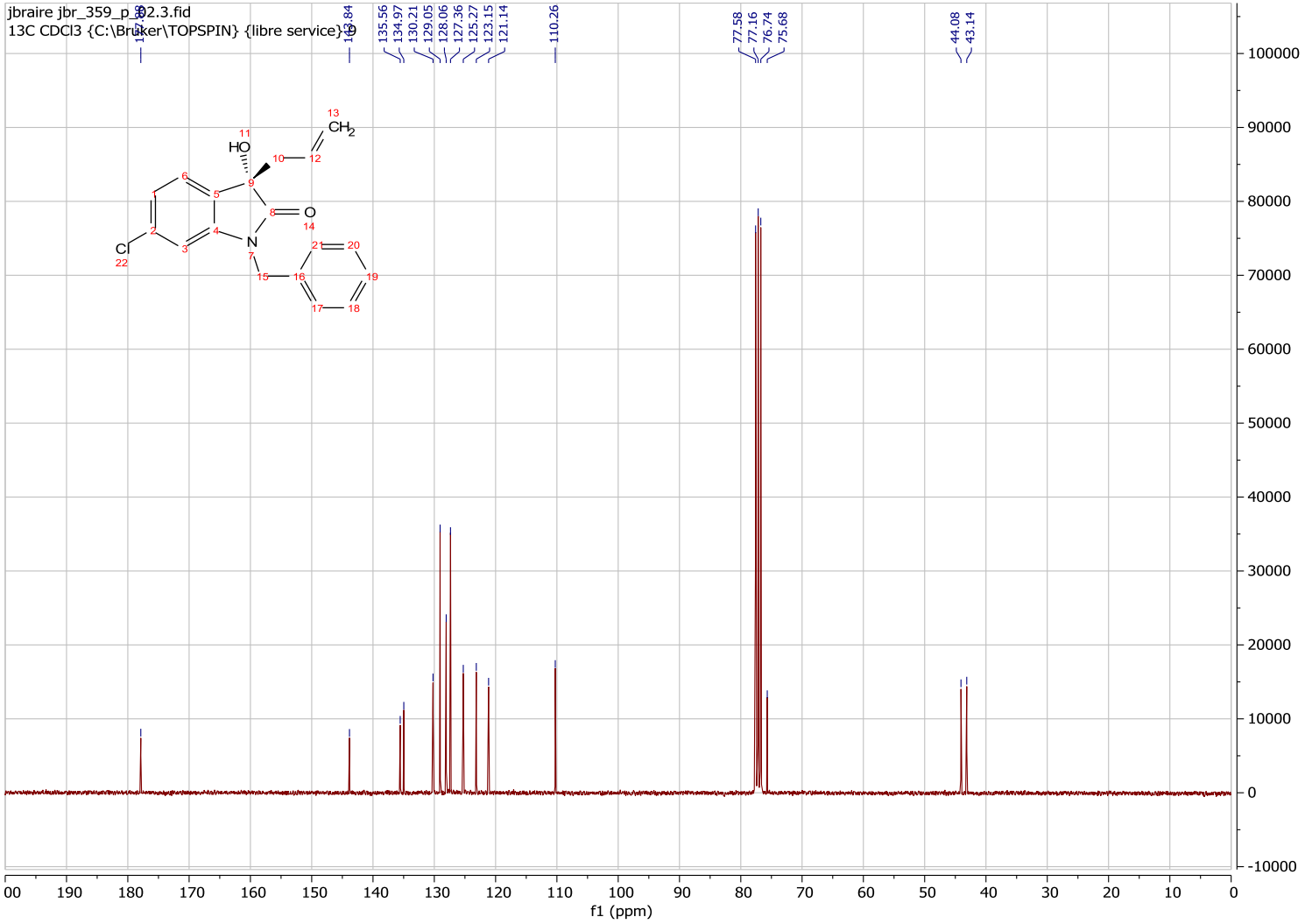
(*S*)-3-Allyl-1-benzyl-6-bromo-3-hydroxyindolin-2-one (10o) (^{13}C NMR, 75 MHz, $CDCl_3$)



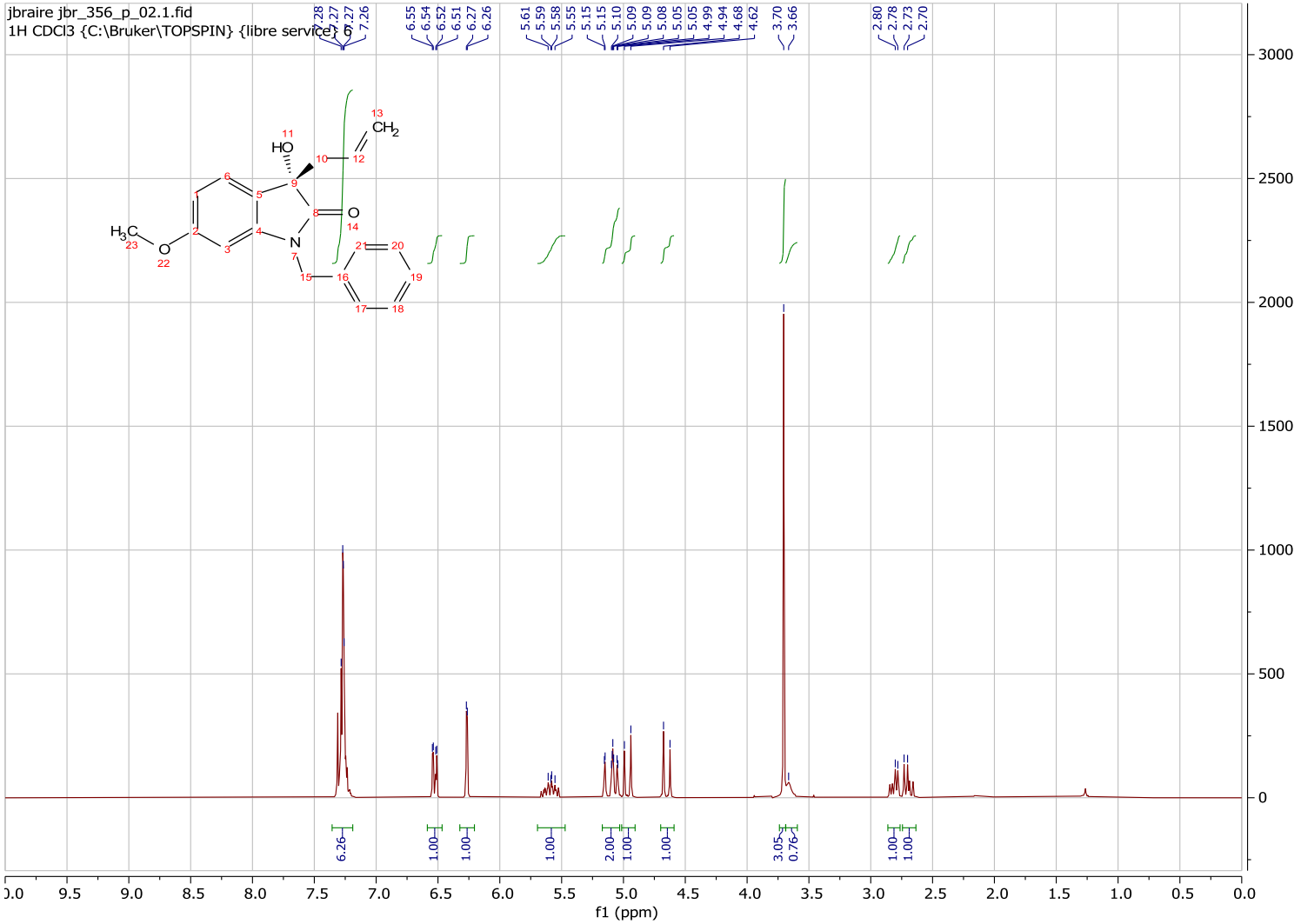
(*S*)-3-Allyl-1-benzyl-6-chloro-3-hydroxyindolin-2-one (10p) (^{1}H NMR, 300 MHz, $CDCl_3$)



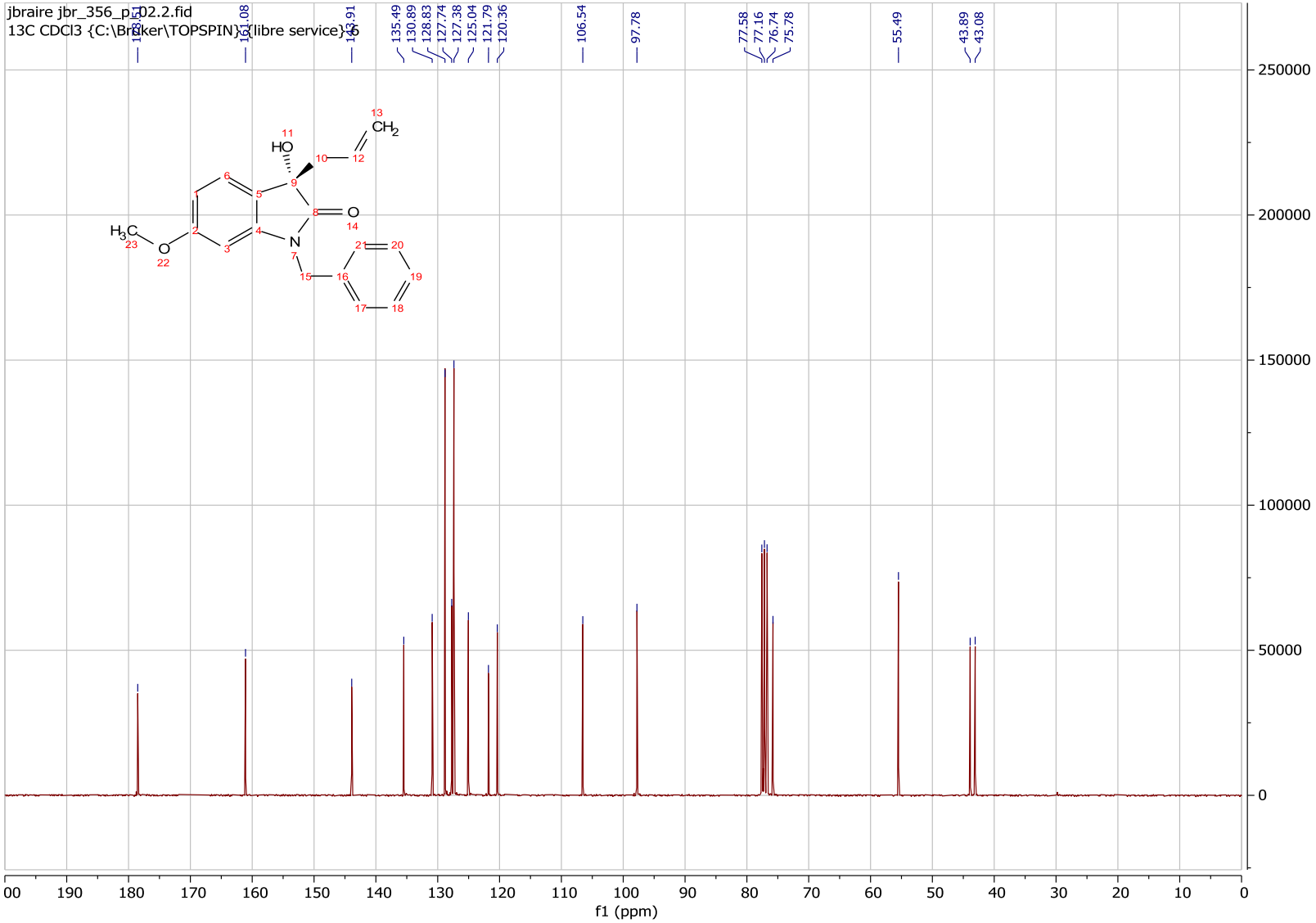
(*S*)-3-Allyl-1-benzyl-6-chloro-3-hydroxyindolin-2-one (10p) (^{13}C NMR, 75 MHz, $CDCl_3$)



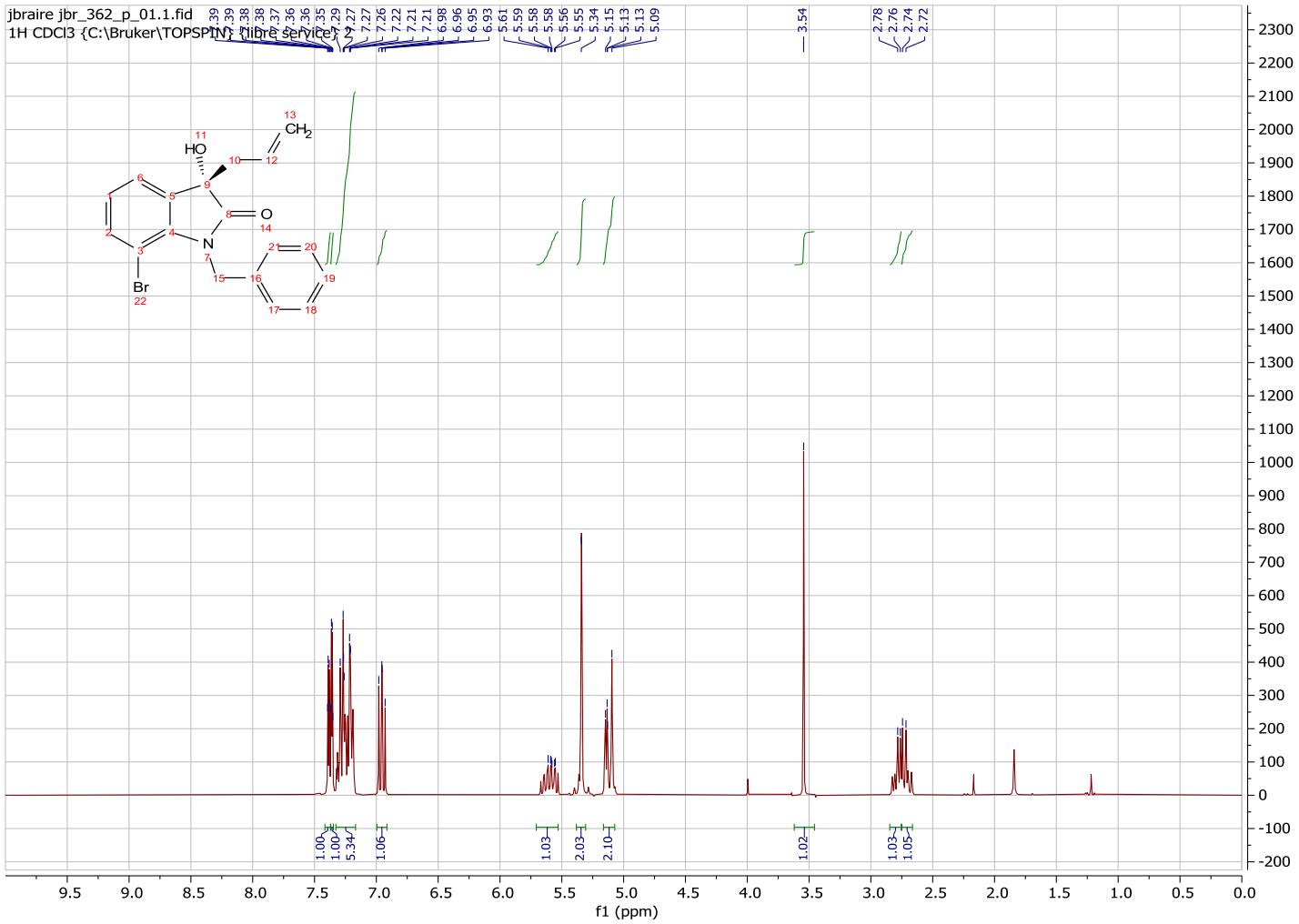
(*S*)-3-Allyl-1-benzyl-3-hydroxy-6-methoxyindolin-2-one (10q) (^{1}H NMR, 300 MHz, $CDCl_3$)



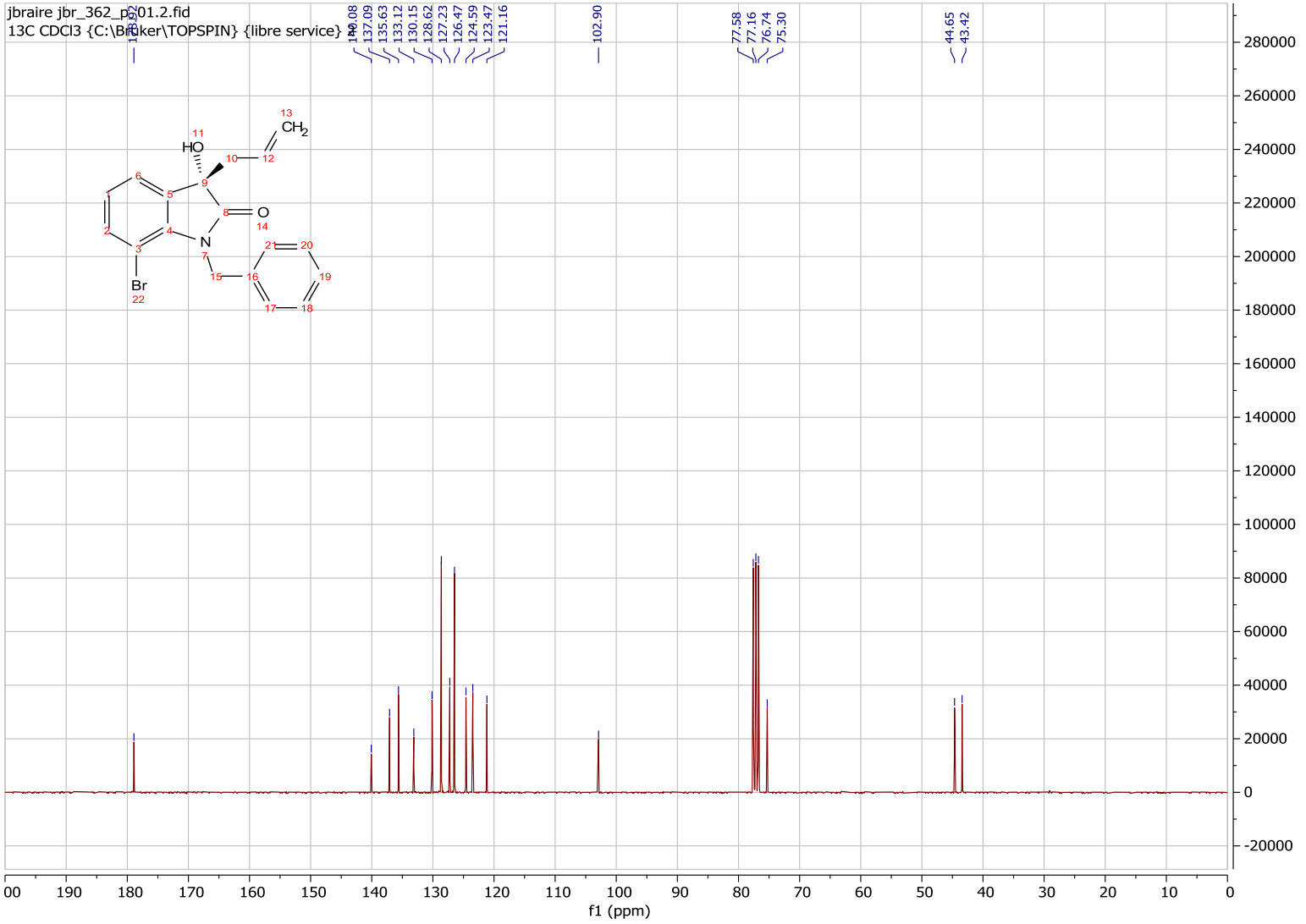
(*S*)-3-Allyl-1-benzyl-3-hydroxy-6-methoxyindolin-2-one (10q) (^{13}C NMR, 75 MHz, $CDCl_3$)



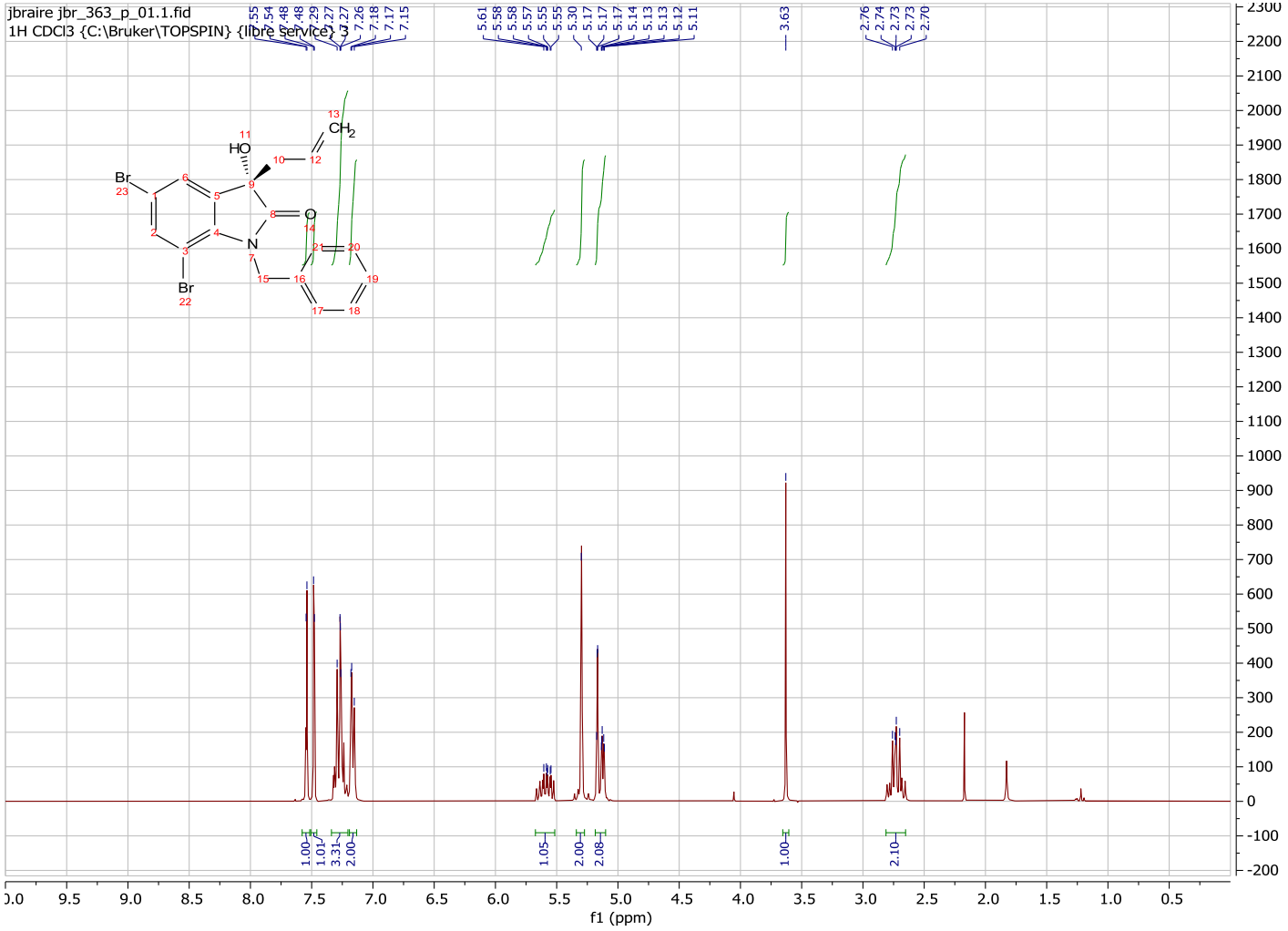
(*S*)-3-Allyl-1-benzyl-7-bromo-3-hydroxyindolin-2-one (10r) (^{1}H NMR, 300 MHz, $CDCl_3$)



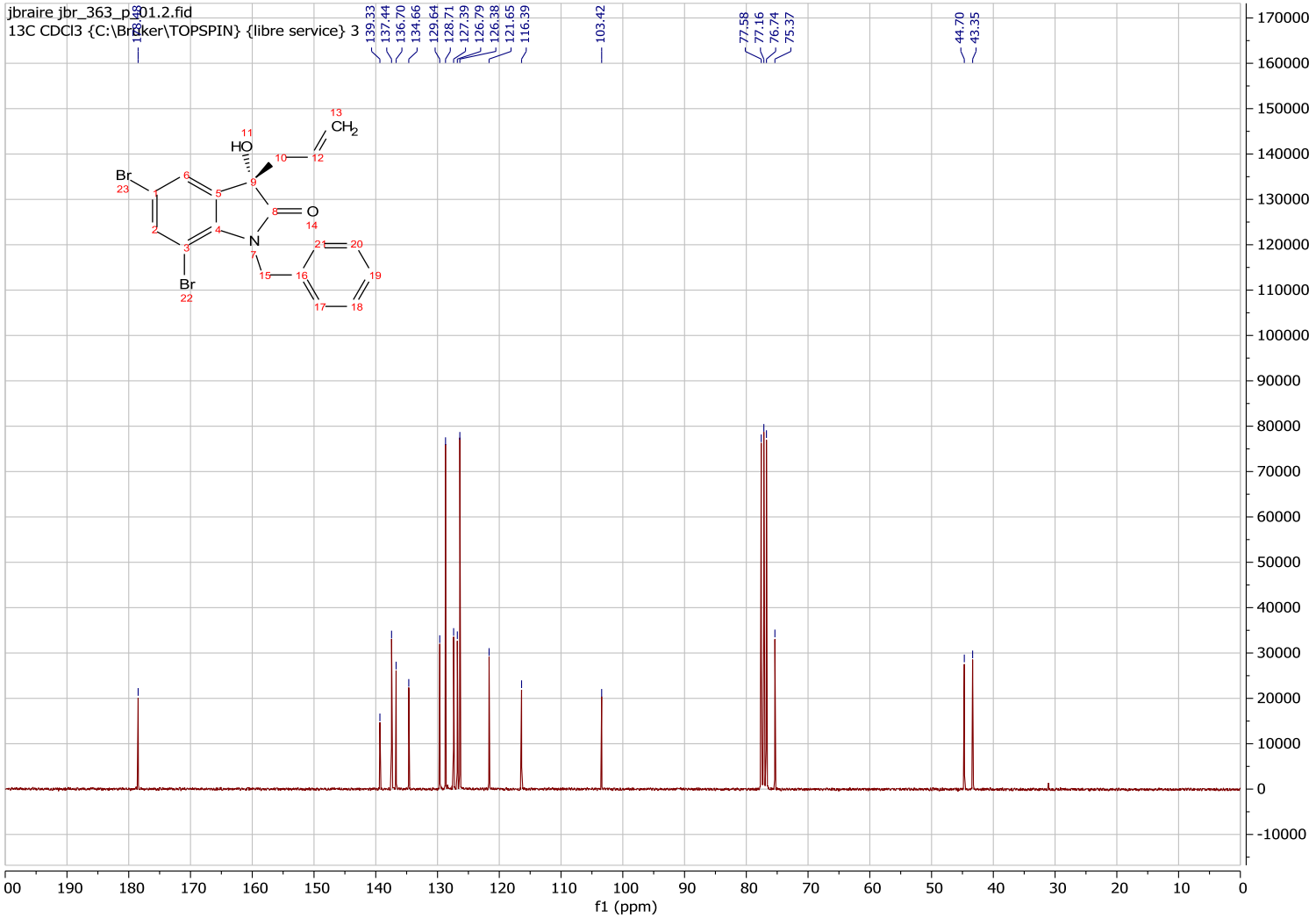
(*S*)-3-Allyl-1-benzyl-7-bromo-3-hydroxyindolin-2-one (10r) (^{13}C NMR, 75 MHz, $CDCl_3$)



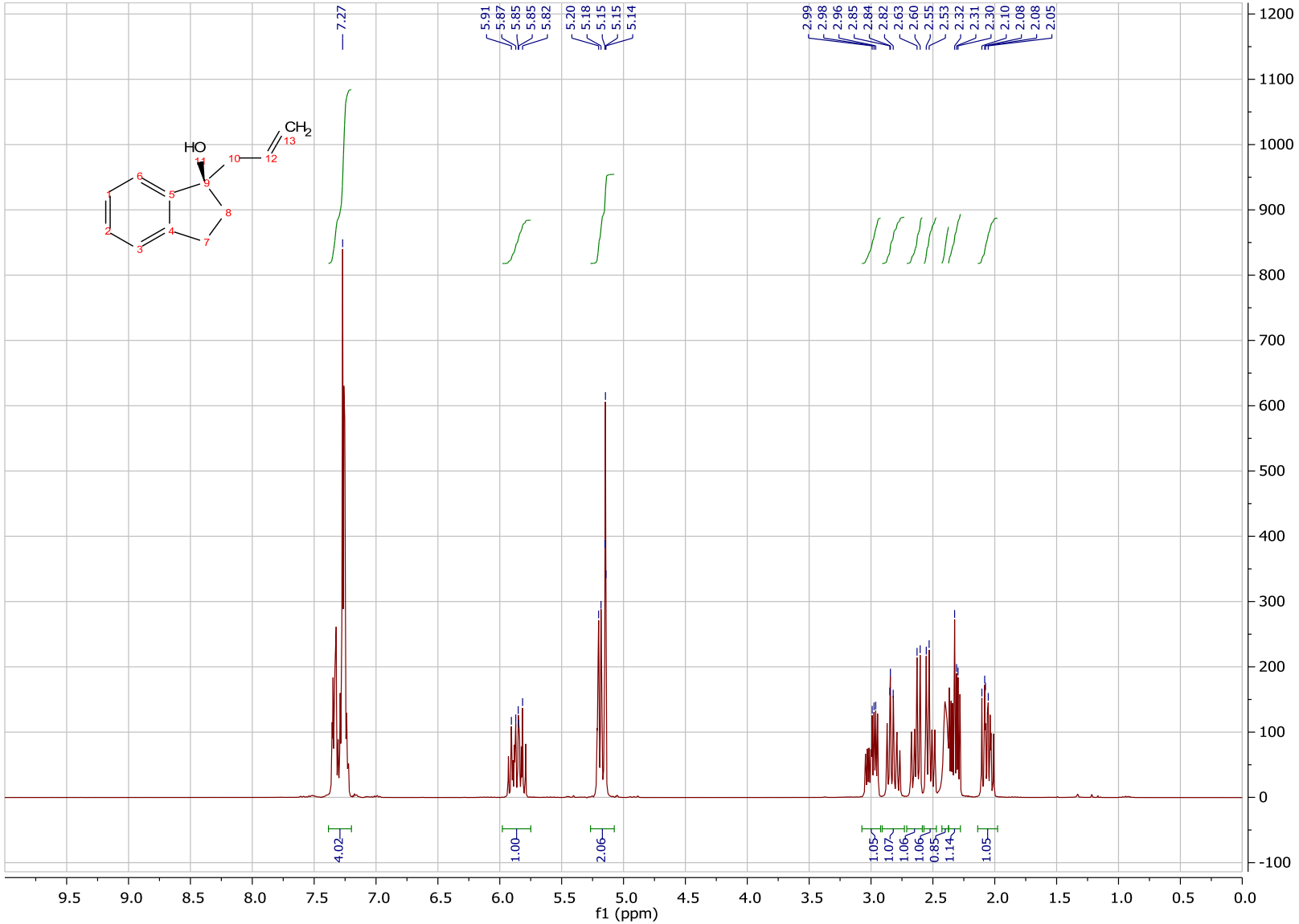
(*S*)-3-Allyl-1-benzyl-5,7-dibromo-3-hydroxyindolin-2-one (10s) (^{1}H NMR, 300 MHz, $CDCl_3$)



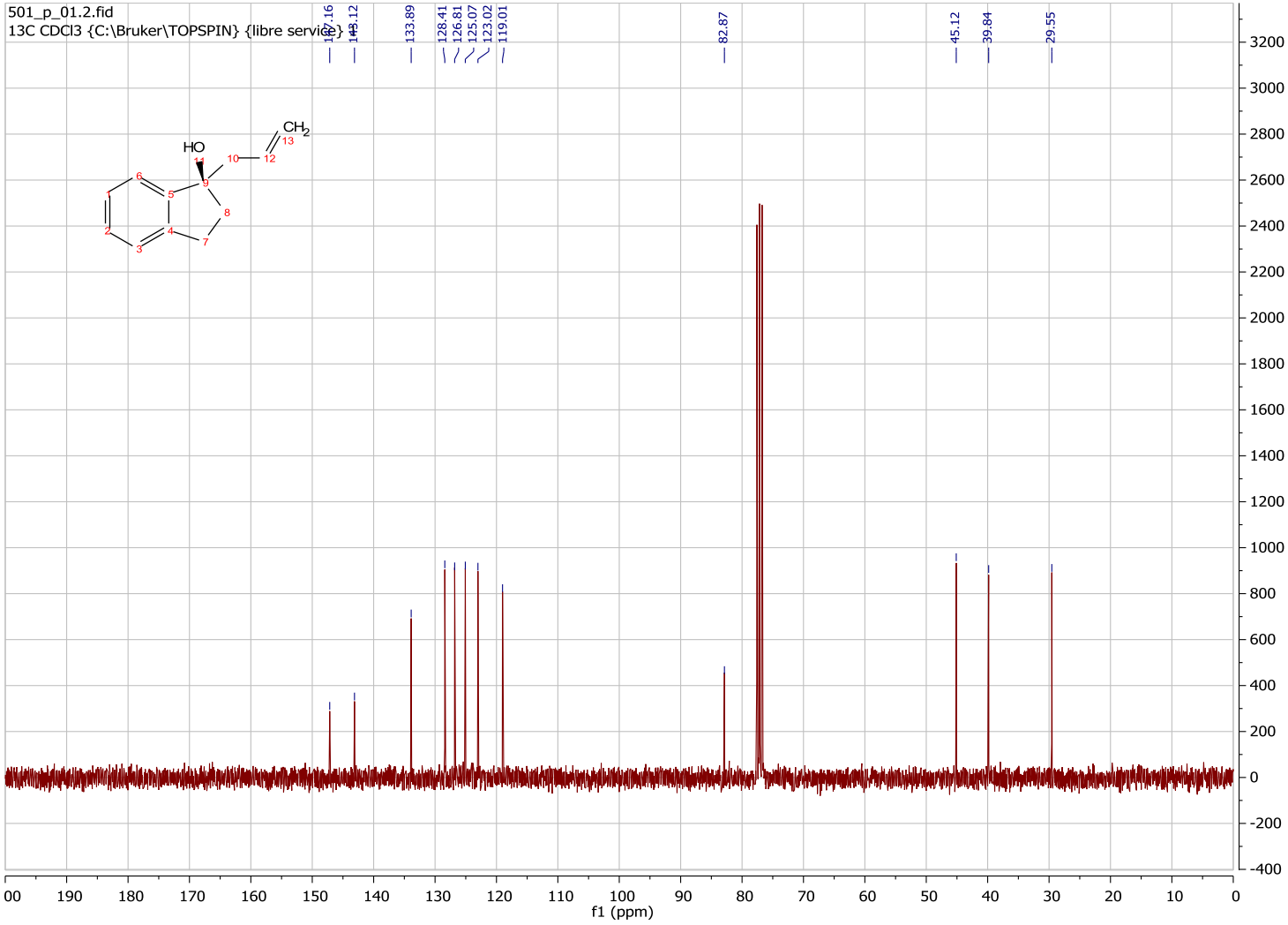
(*S*)-3-Allyl-1-benzyl-5,7-dibromo-3-hydroxyindolin-2-one (10s) (^{13}C NMR, 75 MHz, $CDCl_3$)



(*R*)-1-Allyl-2,3-dihydro-1H-inden-1-ol (11) (^{1}H NMR, 300 MHz, $CDCl_3$)



(*R*)-1-Allyl-2,3-dihydro-1H-inden-1-ol (11) (^{13}C NMR, 75 MHz, $CDCl_3$)



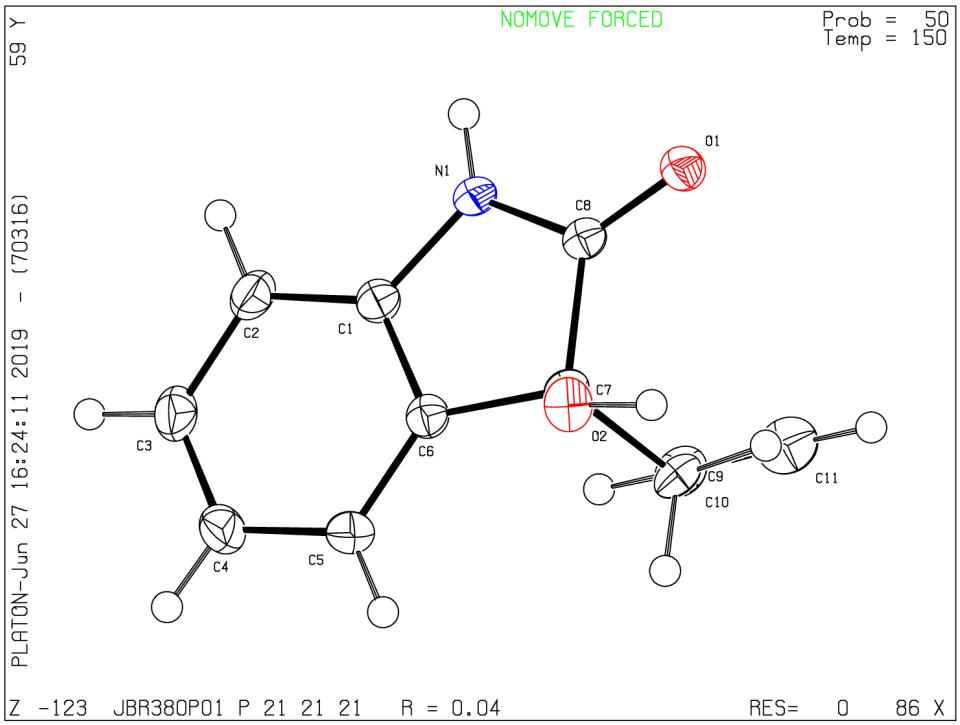
7. X-Ray of 10h and 10i

D8 VENTURE Bruker AXS diffractometer equipped with a (CMOS) PHOTON 100 detector, [*], Cu-Kα radiation (λ = 1.54178 Å, multilayer monochromator), T = 150(2) K; orthorhombic P 21 21 21 (I.T.#19), a = 7.5291(8), b = 7.4902(8), c = 17.0281(19) Å, V = 960.29(18) Å3. Z = 4, d = 1.309 g.cm-3, μ = 0.740 mm-1. The structure was solved by dual-space algorithm using the SHELXT program,[26] and then refined with full-matrix least-squares methods based on F2 (SHELXL).[27] All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. Except H1N and H2O hydrogen atoms that were introduced in the structural model through Fourier difference maps analysis, H atoms were finally included in their calculated positions and treated as riding on their parent atom with constrained thermal parameters.

10i: A final refinement on F2 with 1916 unique intensities and 134 parameters converged at ωRF2 = 0.1034 (RF = 0.0376) for 1865 observed reflections with I > 2σ(I).

10h: A final refinement on F2 with 1990 unique intensities and 139 parameters converged at ωRF2 = 0.2006 (RF = 0.0830) for 1408 observed reflections with I > 2σ(I).

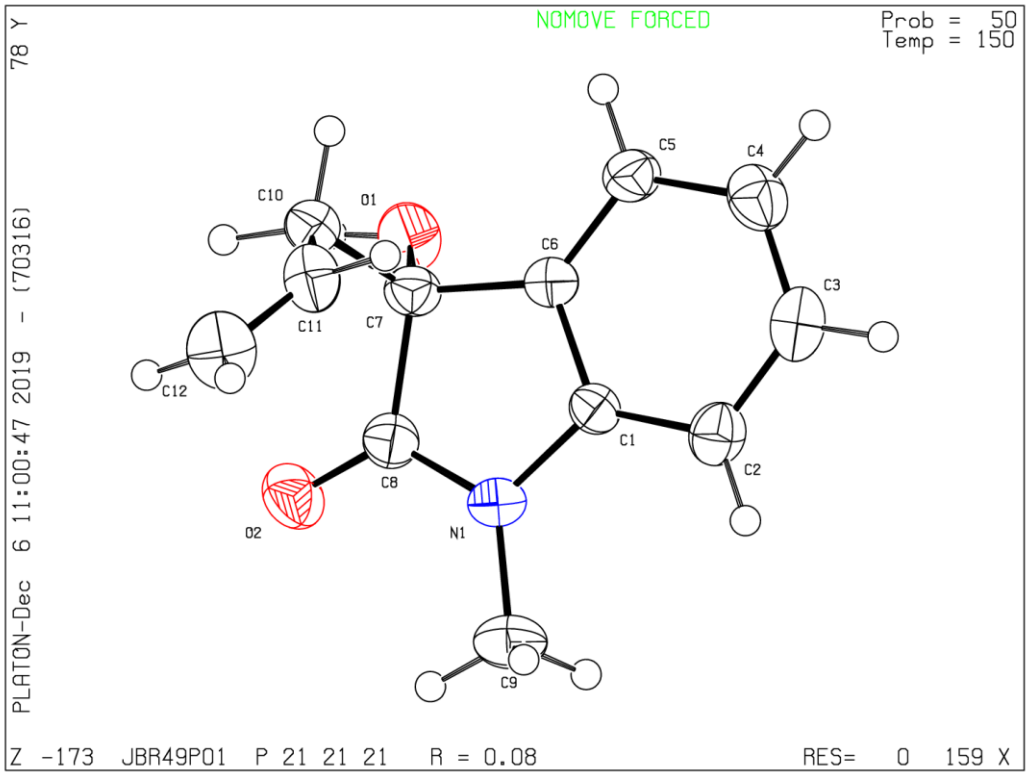
(*S*)-3-Allyl-3-hydroxyindolin-2-one (10i)



Empirical formula	$C_{11}H_{11}NO_2$
Formula weight	189.21 g/mol
Temperature	150(2) K
Wavelength	1.54178 Å
Crystal system, space group	orthorhombic, P 2_1 2_1 2_1

Unit cell dimensions	a = 7.5291(8) Å
	b = 7.4902(8) Å
	c = 17.0281(19) Å
	α = 90 °
	β = 90 °
	γ = 90 °
Volume	960.29(18) Å3
Z, Calculated density	4, 1.309 g.cm-3
Absorption coefficient	0.740 mm-1
F(000)	400
Crystal size	0.600 x 0.270 x 0.200 mm
Crystal color	colourless
Theta range for data collection	6.456 to 74.104 °
h_min, h_max	-9, 9
k_min, k_max	-8, 9
l_min, l_max	-18, 21
Reflections collected / unique	7285 / 1916 [R(int)a = 0.0430]
Reflections [I>2σ]	1865
Completeness to theta_max	0.981
Absorption correction type	multi-scan
Max. and min. transmission	0.862, 0.586
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	1916 / 0 / 134
Flack parameter	0.00(12)
bS (Goodness-of-fit)	1.146
Final R indices [I>2σ]	R1c = 0.0376, wR2d = 0.1034
R indices (all data)	R1c = 0.0385, wR2d = 0.1042
Largest diff. peak and hole	0.298 and -0.320 e-.Å-3

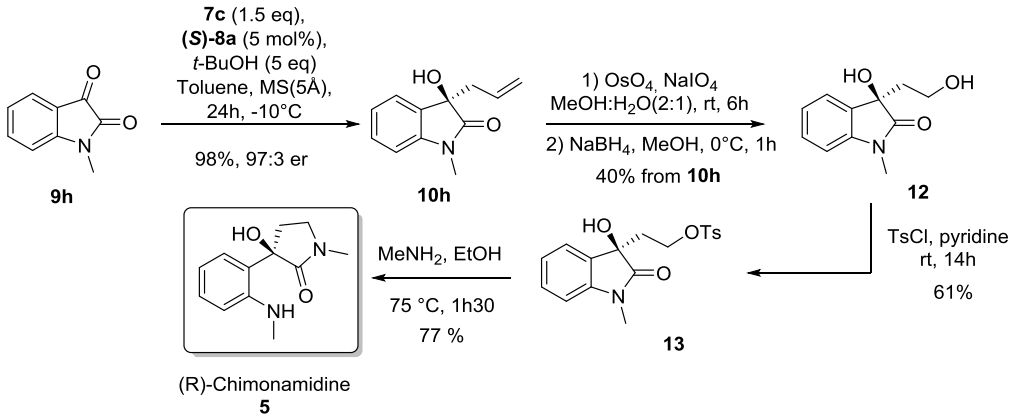
(*R*)-3-Allyl-3-hydroxy-1-methylindolin-2-one (10h)



Empirical formula	$C_{12}H_{13}NO_2$
Formula weight	203.23 g/mol
Temperature	150(2) K
Wavelength	1.54178 Å
Crystal system, space group	orthorhombic, P 2_1 2_1 2_1
Unit cell dimensions	a = 7.3607(8) Å
	b = 8.0406(11) Å
	c = 17.598(2) Å
	α = 90 °
	β = 90 °
	γ = 90 °
Volume	1041.5(2) Å3
Z, Calculated density	4, 1.296 g.cm-3
Absorption coefficient	0.718 mm-1
F(000)	432
Crystal size	0.600 x 0.240 x 0.220 mm
Crystal color	colourless
Crystal description	prism
Theta range for data collection	6.519 to 74.603 °
h_min, h_max	-9, 6
k_min, k_max	-9, 9
l_min, l_max	-18, 22
Reflections collected / unique	4737 / 1990 [R(int)a = 0.0566]

Reflections [I>2σ]	1408
Completeness to theta_max	0.968
Absorption correction type	multi-scan
Max. and min. transmission	0.854, 0.693
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1990 / 0 / 139
Flack parameter	0.0(4)
bS (Goodness-of-fit)	1.015
Final R indices [I>2σ]	R1c = 0.0830, wR2d = 0.2006
R indices (all data)	R1c = 0.1305, wR2d = 0.2428
Largest diff. peak and hole	0.310 and -0.314 e-.Å-3

8. Synthesis of (*R*) chimonamidine 5



(*R*)-3-(2-Hydroxyethyl)-3-hydroxy-1-methylindolin-2-one (12)[28]

(*R*)-3-Allyl-3-hydroxy-1-methylindolin-2-one **(10h)** (81 mg, 0.4 mmol) was dissolved in methanol (2 mL) and water (1 mL) contained in a 10 mL flask. $NaIO_4$ (214 mg, 1.0 mmol) was introduced, followed by osmium tetroxide (30 µL, 2.5 wt. % solution in *tert*-butanol). The reaction mixture was stirred vigorously for 6 h, treated with Celite®, and agitated for an additional 10 minutes prior to filtration. The filtrate was concentrated to 1/3 of its volume under reduced pressure, then extracted with EtOAc (3 × 3 mL). The combined organic phases were washed with brine (2 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude compound was used in the next step without further purification.

To a solution of the above crude compound in MeOH (3 mL) at 0 °C was added $NaBH_4$ (22.4 mg, 2.0 mmol). After stirring for 1h at this temperature, water (3 mL) was added and the major part of methanol was removed under vacuum. The resulting aqueous solution was extracted with EtOAc (3 x 5 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The crude product was purified by flash column chromatography (Eluent 100 DCM to 80/20 DCM/Acetone) to afford (*R*)-3-(2-hydroxyethyl)-3-hydroxy-1-methylindolin-2-one **12 (**33 mg, 40% yield overall yield from **10h**) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 1H), 7.37 – 7.29 (m, 1H), 7.17 – 7.07 (m, 1H), 6.88 – 6.80 (m, 1H), 4.05 – 3.91 (m, 2H), 3.19 (s, 3H), 2.62 - 252 (m, 2H), 2.31 – 2.16 (m, 1H), 2.07 – 1.96 (m, 1H).

(*R*)-2-(3-Hydroxy-1-methyl-2-oxoindolin-3-yl)ethyl 4-methylbenzenesulfonate (13)[28]

To a solution of compound **12** (33 mg, 0.16 mmol) in dry pyridine (2.0 mL) was added p-toluenesulfonyl chloride (46 mg, 0.24 mmol). After stirring for 14 h at room temperature, the reaction mixture was quenched with aqueous HCl solution (1 M solution, 5 mL) and AcOEt (5 mL) was added. After stirring at room temperature for 10 min, the organic layer was separated and the aqueous phase was extracted with EtOAc (3 x 5 mL). The combined organic phases were washed with a saturated aqueous K_2CO_3 solution (5 mL), washed with brine (5 mL), dried over $MgSO_4$ and concentrated under vacuum. The crude product was purified by flash

column chromatography (Eluent 100 DCM to 90/10 DCM/Acetone) to afford (*R*)-2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl)ethyl 4-methylbenzenesulfonate **13** (35 mg, 61% yield) as a colorless oil.[28]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 – 7.61 (m, 2H), 7.39 – 7.24 (m, 4H), 7.13 – 7.01 (m, 1H), 6.88 – 6.76 (m, 1H), 4.15 – 3.98 (m, 2H), 3.11 (s, 3H), 2.41 (s, 3H), 2.41 – 2.18 (m, 2H).

(*R*)-Chimonamidine (5)[28-29]

A mixture of compound **13** (35 mg, 0.10 mmol) and a methylamine solution (2 mL, 33 wt % in absolute ethanol) was stirred at 75 °C for 1h30. After concentration of the mixture under vacuum, the resulting crude product was purified by flash column chromatography (Eluent 100 DCM to 85/15 DCM/Acetone) to afford (*R*)-chimonamidine **5** (16mg, 77% yield) as a white solid.

$[\alpha]_D^{20}$ = -43.3 (c 0.10, $CHCl_3$), $[\alpha]_D^{20}$ = -150.2 (c 0.10, EtOH)

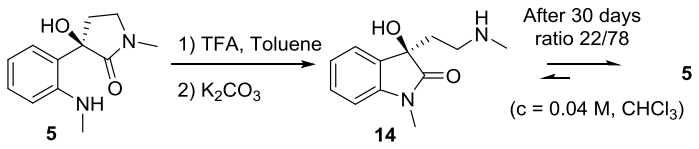
The enantiomeric ratio was determined by HPLC using a Daicel CHIRALPAK® ID column, heptane/IPA = 80/20, flow rate = 1.0 mL/min, 254 nm, $t_{(S)}$ = 15.88 min, $t_{(R)}$ = 17.30 min (for the chromatogram refer to page S80), e.r.: 3:97.

^{1}H NMR (300 MHz, $CHCl_3$) δ 7.22 (td, *J* = 8.3, 1.6 Hz, 1H), 6.82 (dd, *J* = 7.5, 1.6 Hz, 1H), 6.72 (d, *J* = 8.3 Hz, 1H), 6.64 (td, *J* = 7.5, 1.2 Hz, 1H), 5.75 (bs, 1H), 3.33-27 (m, 1H), 3.22 (td, *J* = 9.7, 6.2 Hz, 1H), 2.97 (s, 3H), 2.84 (s, 3H), 2.71 (ddd, *J* = 12.8, 6.1, 1.4 Hz, 1H), 2.40 (dt, *J* = 12.8, 9.2 Hz, 1H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 175.3, 148.4, 129.6, 125.6, 124.7, 116.8, 111.8, 79.9, 45.9, 33.2, 30.4, 30.1

After 95 h at room temperature in $CDCl_3$ (c = 0.04 M), we observed by ^{1}H NMR the apparition of a new defined compound in a 80:20 ratio in favor of **5**. The structure of this compound was unambiguously attributed to **14** by the reaction below.

(*R*)-3-Hydroxy-1-methyl-3-(2-(methylamino)ethyl)indolin-2-one (14)



(*R*)-Chimonamidine (5 mg, 0. 23 mmol) was treated by a solution of TFA in toluene (1 mL, 1 M) for 30 min at room temperature. The reaction mixture was heated to 60 °C for 5 min and concentrated under vacuum at this temperature during 30 min. The reaction mixture is cooled at room temperature and DCM (2 mL) was added followed by an aqueous solution of K_2CO_3 (2 mL, 1 M). The biphasic mixture was stirred at room temperature for 30 min. The organic layer was separated and the aqueous phase was extracted with DCM (3 x 2 mL). The combined organic phases were washed with distilled water (2 mL), dried over $MgSO_4$ and concentrated under vacuum to afford 4.0 mg (80% yield) of **14** as a colorless syrup.

$[\alpha]_D^{20}$ = + 23.2 (c 0.10, EtOH)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.35 (m, 1H), 7.32 – 7.26 (m, 1H), 7.11 – 7.04 (m, 1H), 6.82 – 6.77 (m, 1H), 3.57 – 3.48 (m, 1H), 3.17 (s, 3H), 2.94 – 2.87 (m, 1H), 2.54 (s, 3H), 2.09 – 1.99 (m, 1H), 1.81 – 1.73 (m, 1H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 178.7, 142.9, 132.2, 129.3, 123.7, 123.0, 108.3, 46.8, 36.1, 34.7, 29.9, 26.2

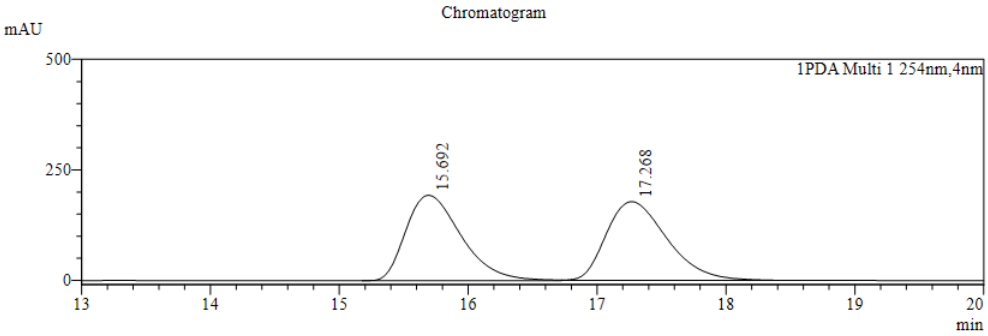
HRMS (ESI): m/z. calcd. for $C_{12}H_{16}N_2O_2Na$ $[M+Na]^+$ 243.1104; found 243.1102

Upon standing for 30 days at room temperature in $CDCl_3$ (c = 0.04M), an equilibrium between **5** and **14** was reached in a 72:28 ratio in favor of **5**.

9. Chiral HPLC chromatogram for (*R*)-chimonamidine

Sample Information

Sample Name : jbr_474_p_01_chimorac_ID_80_20_1mL_21deg
Date Acquired : 06/12/2019 08:53:02
Method File : ID hept-IPA 80-20.lcm



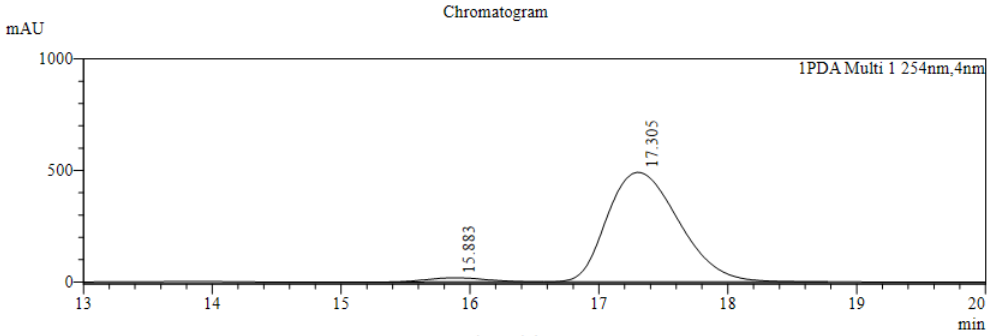
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	15.692	193476	5787619	49.592
2	17.268	178613	5882941	50.408
Total		372089	11670560	100.000

Sample Information

Sample Name : jbr_chimo_ID_80_20_1mL_20deg
Date Acquired : 21/11/2019 15:56:13
Method File : ID hept-IPA 80-20.lcm



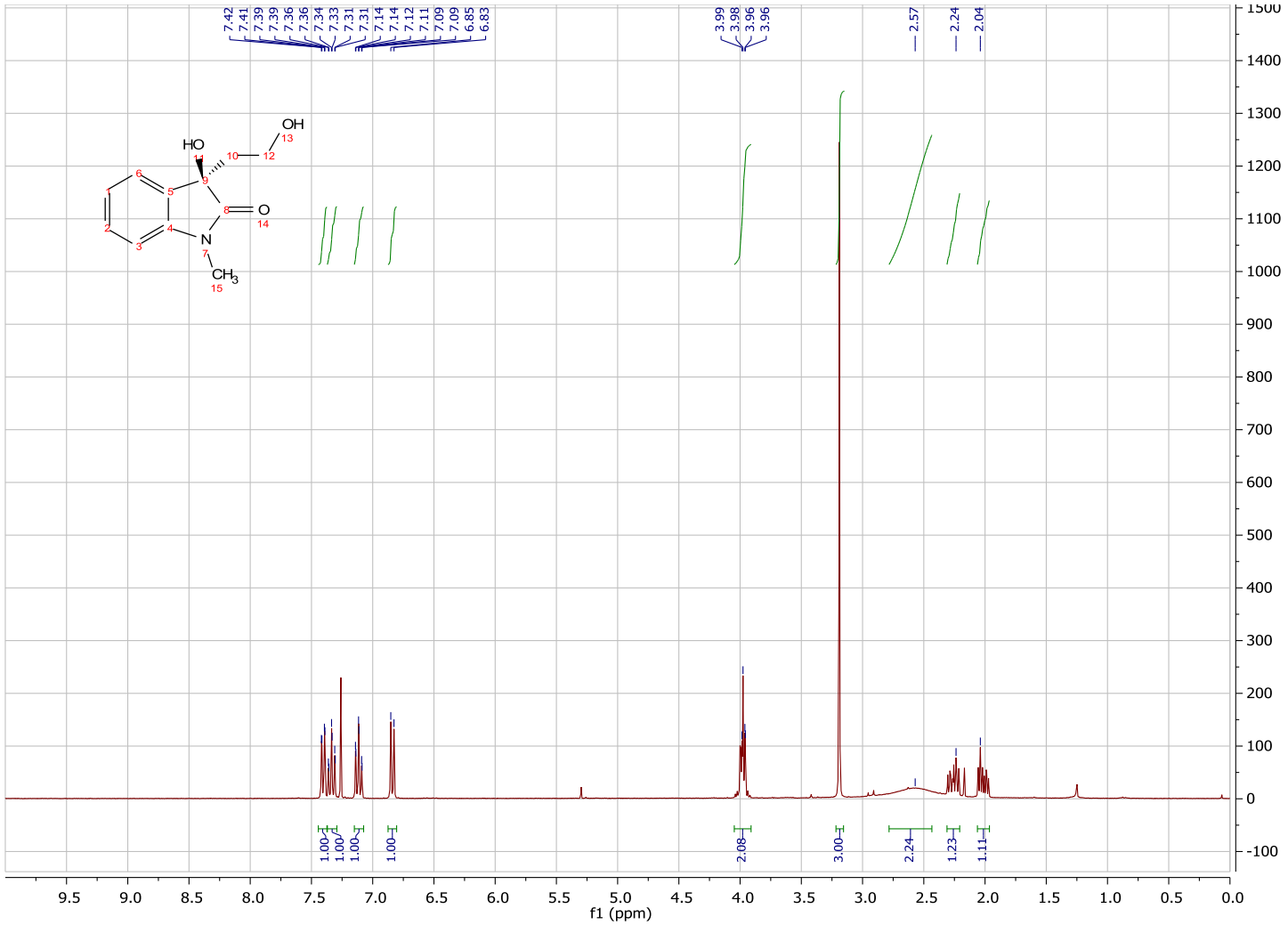
Peak Table

PDA Ch1 254nm

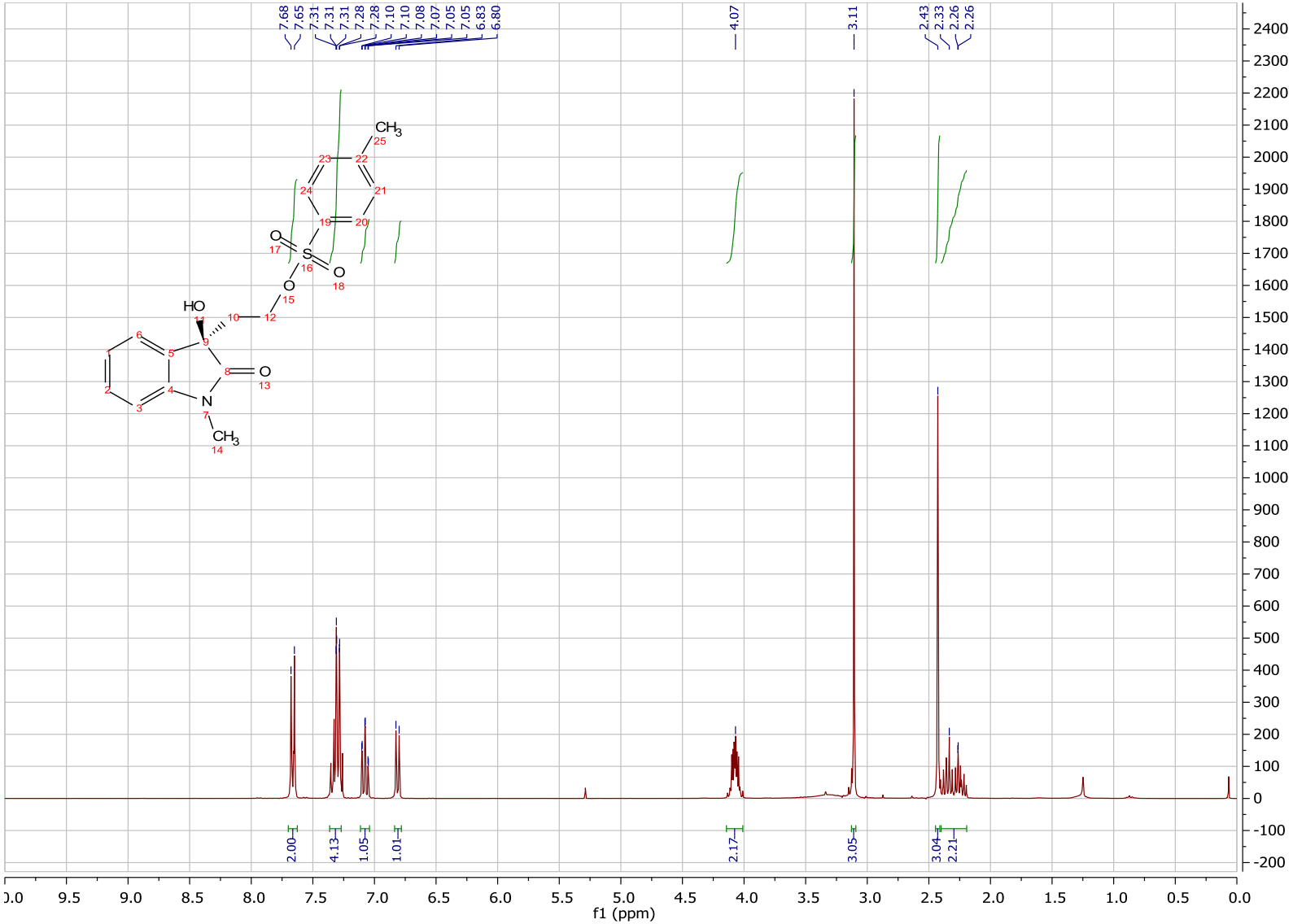
Peak#	Ret. Time	Height	Area	Area%
1	15.883	18391	565834	2.900
2	17.305	490407	18945944	97.100
Total		508798	19511778	100.000

10. Copies of NMR spectra of chimonamidine derivatives

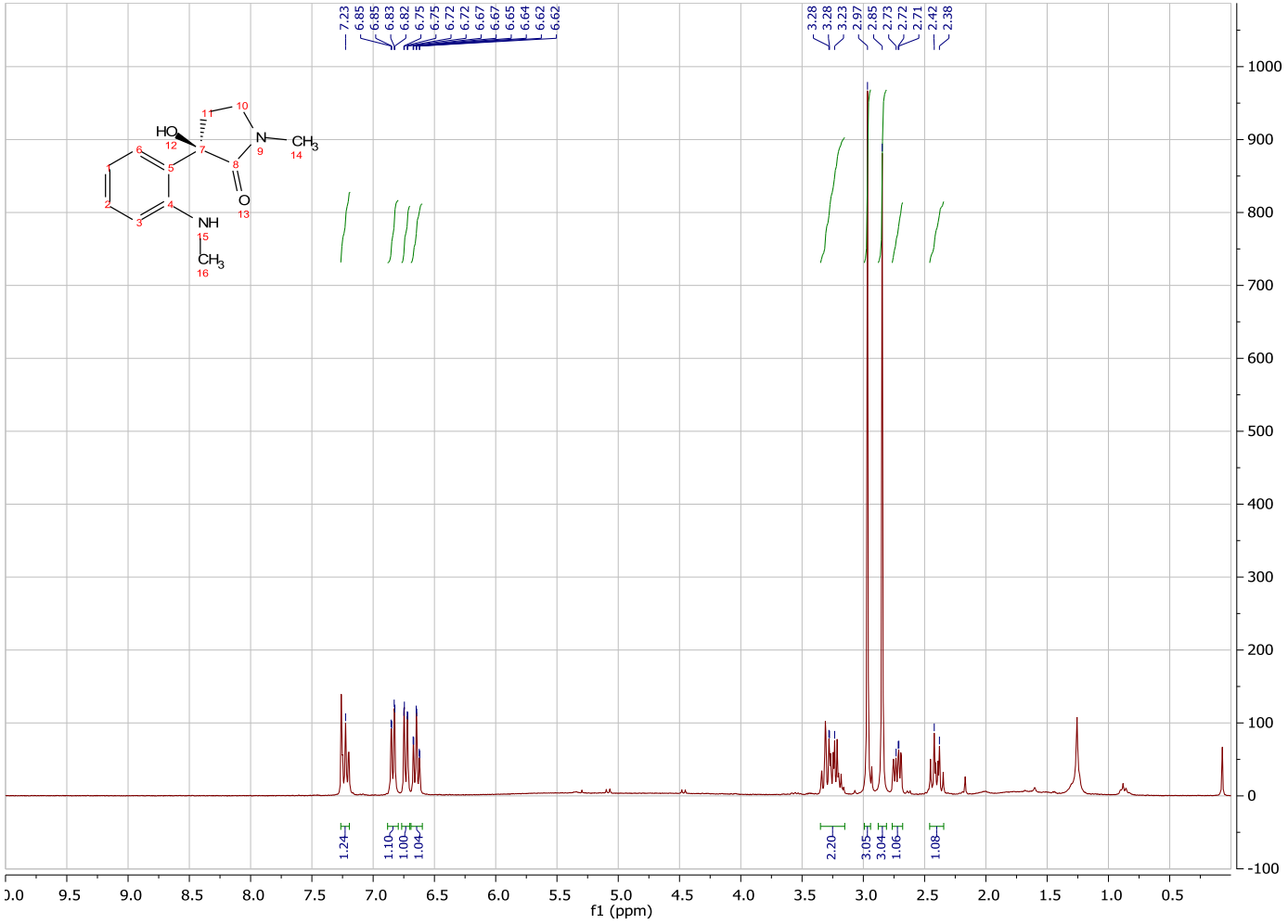
(*R*)-3-hydroxy-3-(2-hydroxyethyl)-1-methylindolin-2-one (12) (^{1}H NMR, 300 MHz, $CDCl_3$)



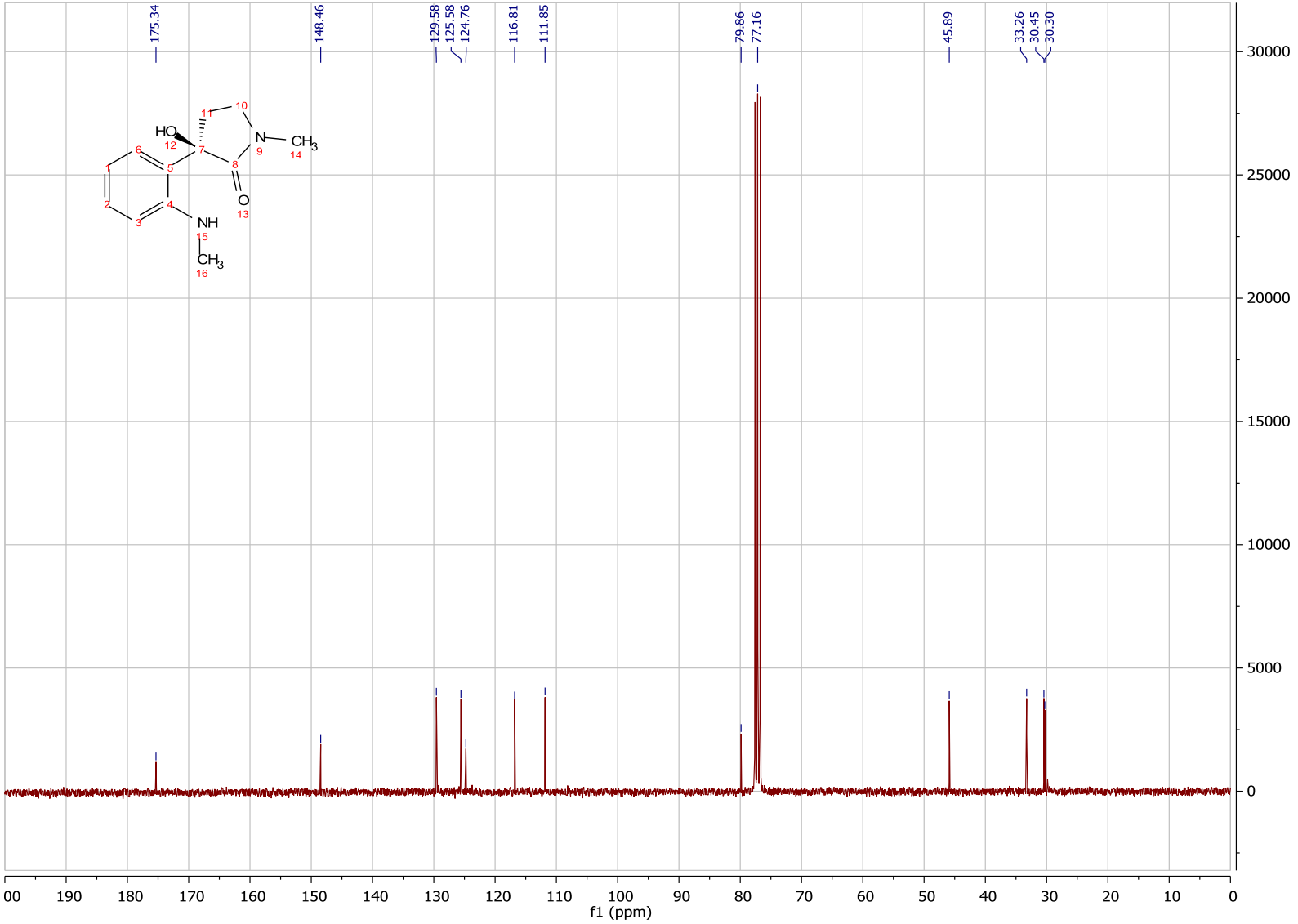
(*R*)-2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl)ethyl 4-methylbenzenesulfonate (13) (^{1}H NMR, 300 MHz, $CDCl_3$)



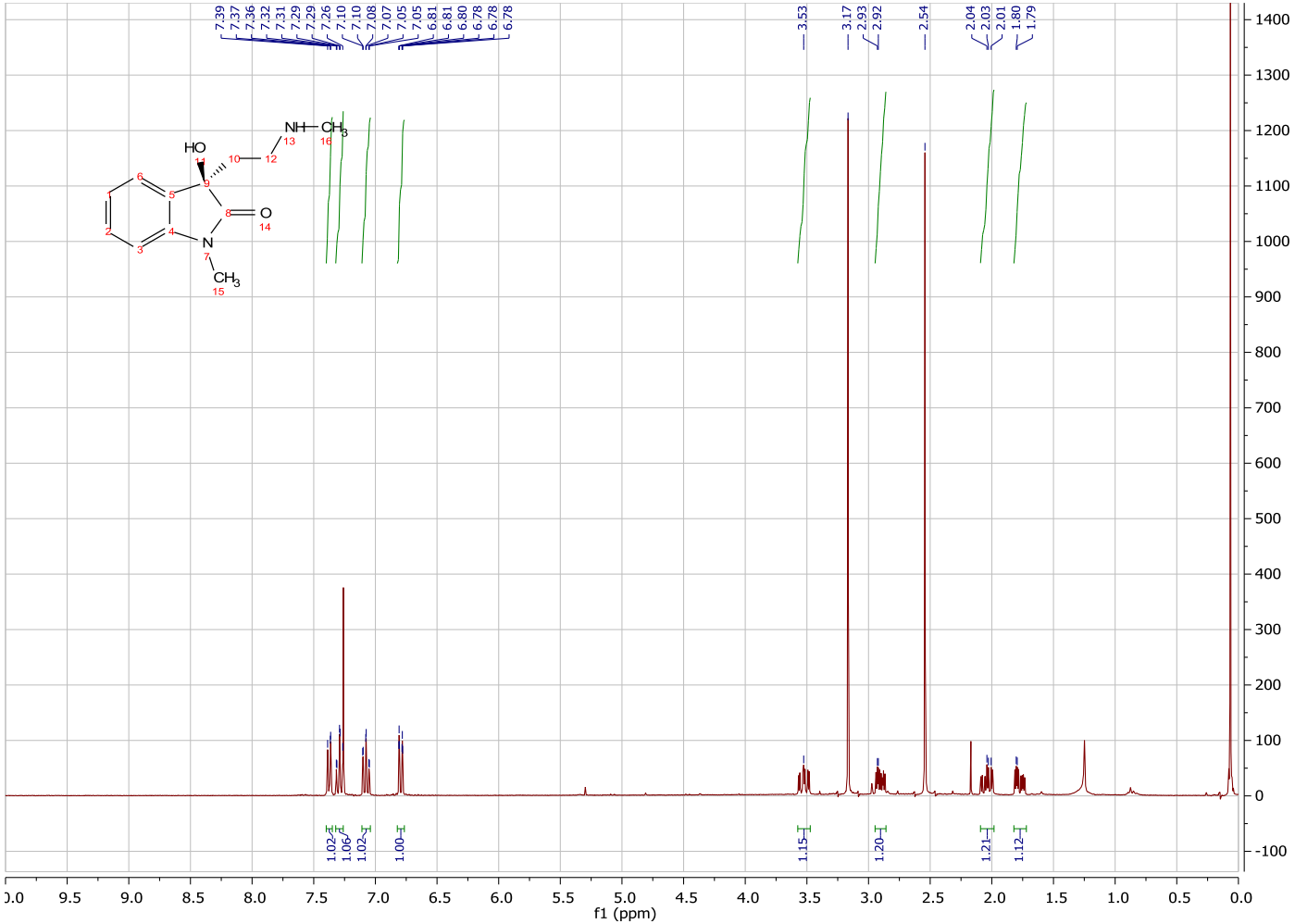
Chimonamidine (5) (^{1}H NMR, 300 MHz, $CDCl_3$)



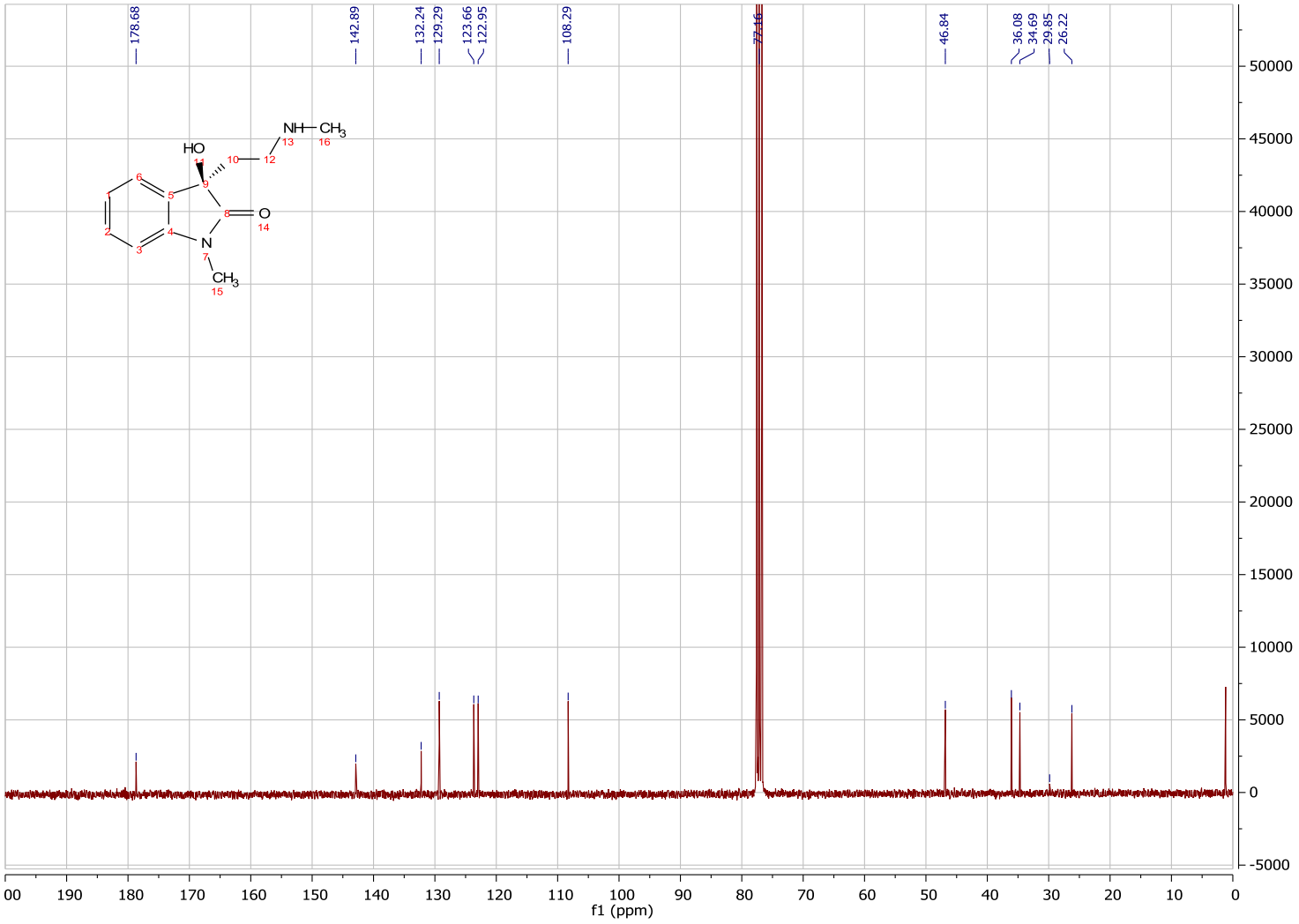
Chimonamidine (5) (^{13}C NMR, 300 MHz, $CDCl_3$)



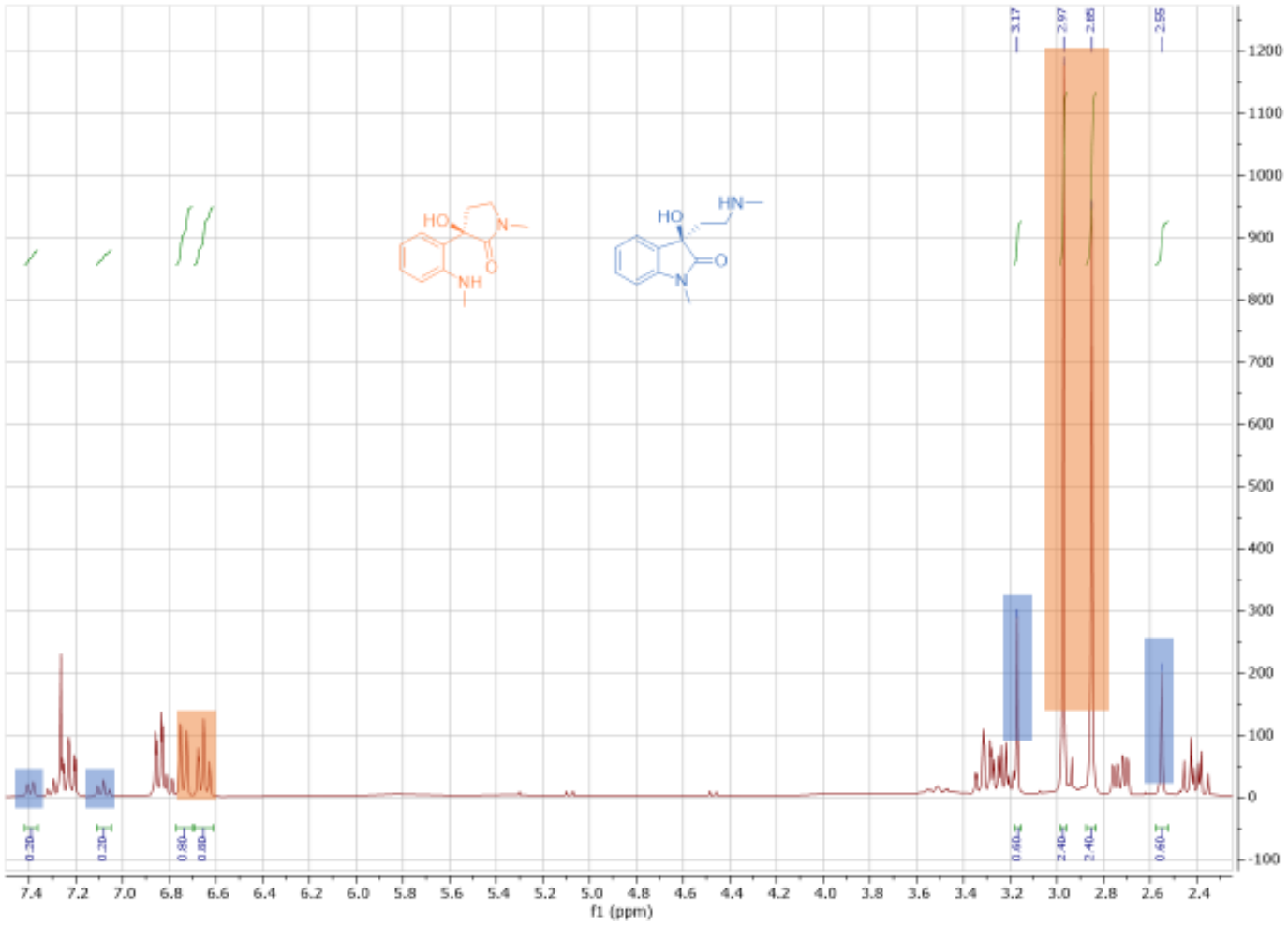
(*R*)-3-hydroxy-1-methyl-3-(2-(methylamino)ethyl)indolin-2-one (14) (^{1}H NMR, 300 MHz, $CDCl_3$)



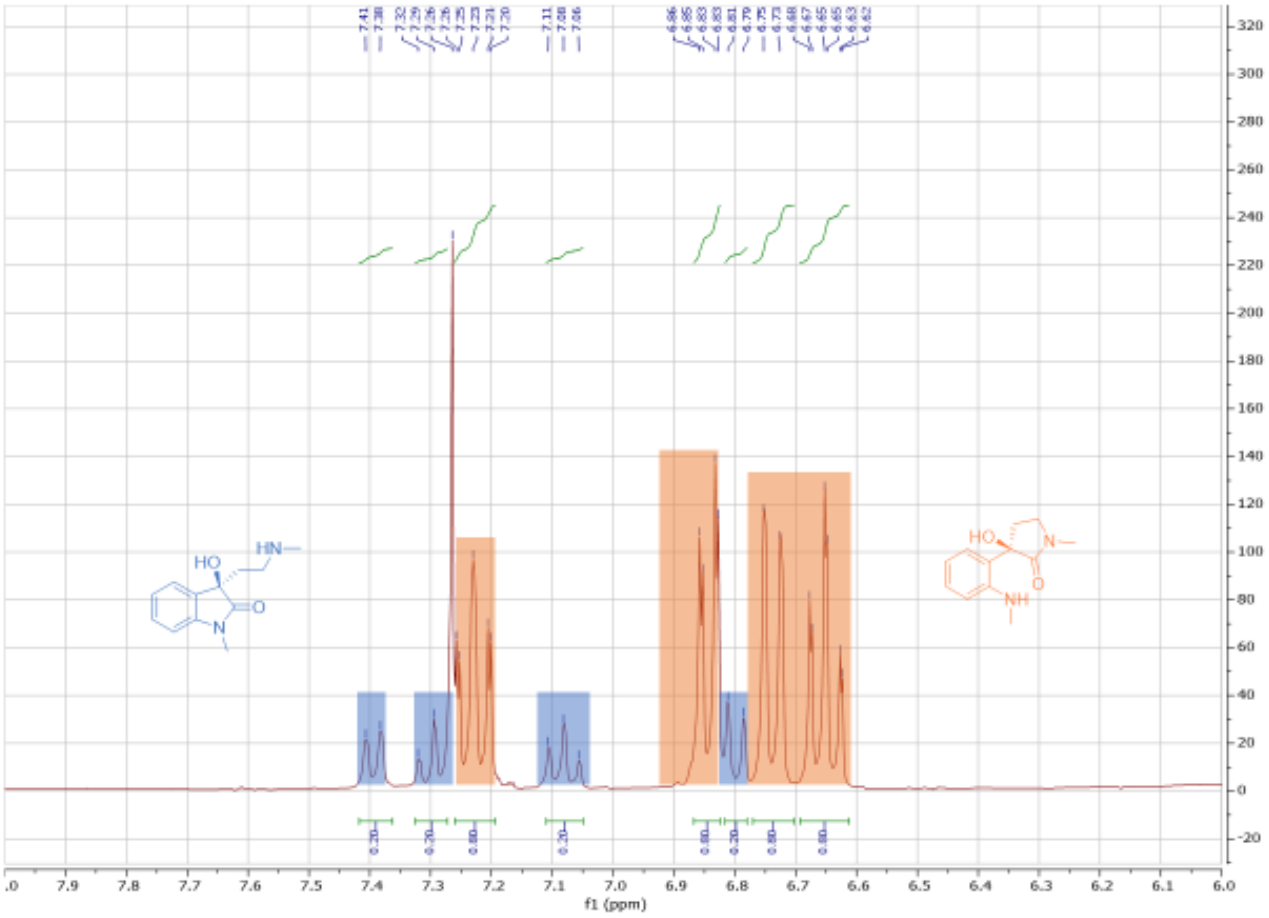
(*R*)-3-hydroxy-1-methyl-3-(2-(methylamino)ethyl)indolin-2-one (14) (^{13}C NMR, 300 MHz, $CDCl_3$)



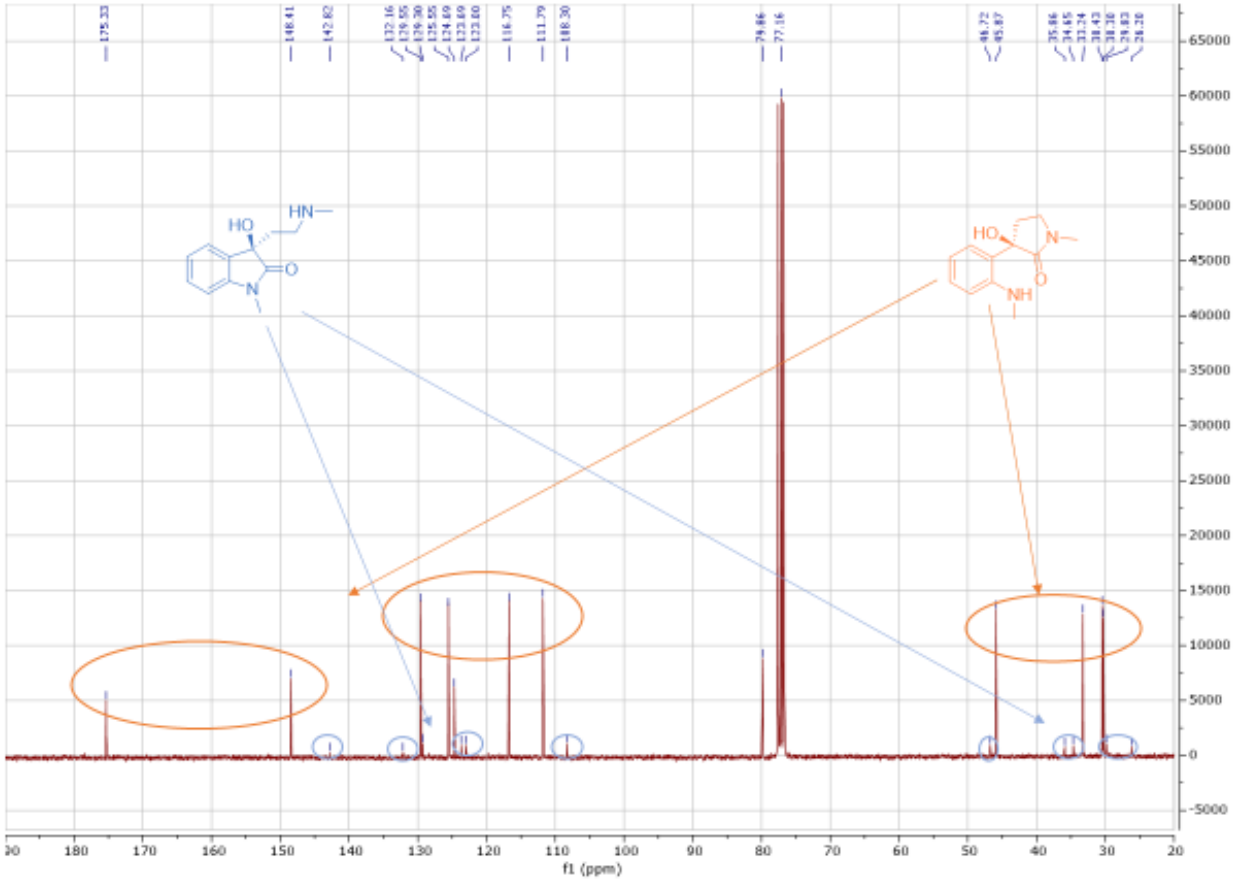
Chimonamidine (5) after 95h at room temperature (c = 0.04 M, $CDCl_3$) (^{1}H NMR, 300 MHz, $CDCl_3$)



Chimonamidine (5) after 95h at room temperature (c = 0.04 M, $CDCl_3$) (^{1}H NMR, 300 MHz, $CDCl_3$)



Chimonamidine (5) after 95h at room temperature (c = 0.04 M, $CDCl_3$) (^{13}C NMR, 300 MHz, $CDCl_3$)



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