Supporting Information

Asymmetric formal synthesis of (+)-cycloclavine

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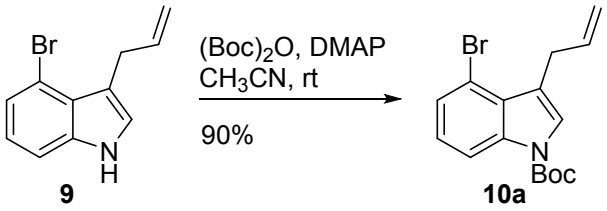
Contents:

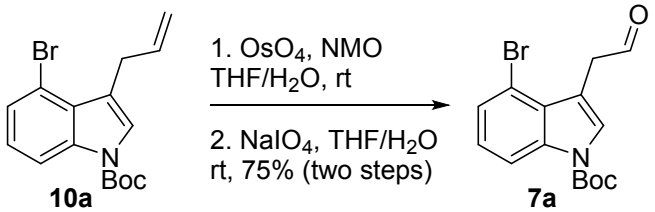
1. General procedures

All reagents and commercially available starting materials were used without further purification unless otherwise noted. All the solvents used were dried and dealed with according to the standard methods. Petroleum ether (PE) used had a boiling range of 60–90 °C. Air- or moisture-sensitive reagents or intermediates were carried out under an inert atmosphere of argon in glassware. Elevated temperatures were maintained using thermostat-controlled silicone oil baths. All reactions were monitored by thin-layer chromatography analysis (TLC). Flash chromatography was conducted on silica gel (200–300 mesh) with relevant solvents. ^{1}H and ^{13}C NMR spectra were recorded on a 400 or 600 MHz and 100 or 150 MHz, respectively. Chemical shifts (δ) are reported in parts per million, coupling constants (J) are reported in Hz. The splitting abbreviations were used: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad, dd = doublet of doublets, q = quartet. High-resolution mass spectrometry (HRMS) were performed by an FTMS mass spectrometer (ESI). Infrared spectra (IR) were recorded as FT-IR spectra and reported in terms of frequency of absorption (v, cm^{-1}). Optical rotations were measured using a 0.1 mL cell with a 1 cm path length on automatic polarimeter and concentrations (c) were reported in mg/mL. The X-ray single-crystal determination was performed with a diffractometer working with graphite monochromated Mo Kα radiation. Melting points were determined by using of a microscope apparatus and are uncorrected. Compounds **9**[10,11] and **7b**[5e] were synthesized as previously reported, and **7a** was afforded by a modified protocol. Compounds (±)-**6a**, (±)-**4a**, (±)-**13a**, (±)-**14a**, (±)-**3a** and Szántay's amine (±)-**2** were prepared as the similar procedure of (+)-**6a**, (+)-**4a**, (–)-**13a**, (–)-**14a**, (–)-**3a** and Szántay's amine (+)-**2** respectively.

2. Experimental and spectral data

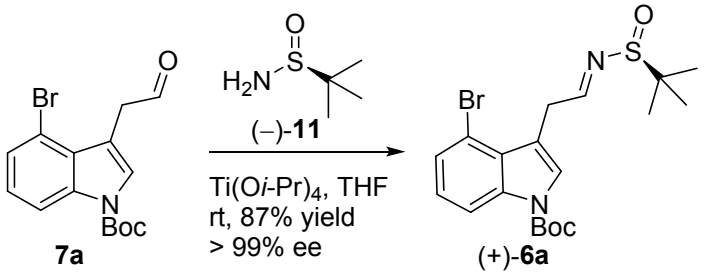


***tert*-Butyl 3-allyl-4-bromo-1*H*-indole-1-carboxylate (10a).** To a solution of 3-allyl indole **9** (5.8 g, 24.7 mmol, 1.0 equiv) in dry acetonitrile (100 mL) was added DMAP (6.0 g, 49.4 mmol, 2.0 equiv) at room temperature. The mixture was stirred for 5 min and $(Boc)_2O$ (8.1 g, 37.0 mmol, 1.5 equiv) was added. Until the starting material was consumed completely for about 6 hours, the reaction mixture was added into a saturated aqueous NH_4Cl solution. The organic solvent was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with water and brine respectively, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 20/1) to give the *N*-Boc indole **10a** as a colurless liquid (7.4 g, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.2 Hz, 1H), 7.41 – 7.39 (m, 2H), 7.14 (t, J = 8.1 Hz, 1H), 6.21 – 6.11 (m, 1H), 5.18 – 5.12 (m, 2H), 3.78 (dd, J = 6.4, 1.2 Hz, 2H), 1.69 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 137.1, 136.6, 128.4, 127.1, 125.1, 124.7, 119.8, 116.2, 114.4, 114.2, 84.0, 30.9, 28.2; IR ν_{max}: 3448, 2979, 2930, 1737, 1421, 1370, 1255, 1158, 1090, 1054, 917, 850, 773; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{19}BrNO_2$ 336.0594, found 336.0589.



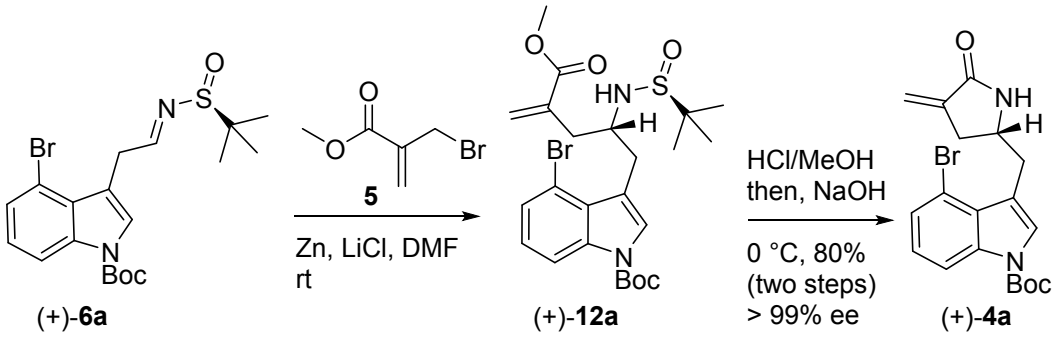
***tert*-Butyl 4-bromo-3-(2-oxoethyl)-1*H*-indole-1-carboxylate (7a).** To a stirred mixture of **10a** (7.3 g, 21.7 mmol, 1.0 equiv) and NMO (4.6 g, 39.1 mmol, 1.8 equiv) in THF/H_2O (150 mL, 3:1) was added OsO_4 (2.5 wt % *t*-BuOH, 11.0 mL, 1.1 mmol) at 0 °C. The mixture was stirred for overnight at room temperature and quenched with saturated Na_2SO_3. After stirring for 30 min, the reaction mixture was extracted with

ethyl acetate. The extract was washed with H_2O and brine and dried over anhydrous Na_2SO_4. The filtrate was concentrated under reduced pressure to give a crude diol, which was used next step without further purification. To a stirred solution of the above crude product diol in THF/H_2O (150 mL, 3/1) was added $NaIO_4$ (18.6 g 86.8 mmol, 4.0 equiv,) at room temperature. After stirring for 4 h at this temperature, the mixture was diluted with ethyl acetate. The organic phase was separated, washed with H_2O and brine, and dried over anhydrous Na_2SO_4. The filtrate was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5/1) to give the *N*-Boc aldehyde **7a** as a colorless oil (5.5 g, 75% yield, two steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.92 (t, J = 1.6 Hz, 1H), 8.20 (d, J = 8.4 Hz, 1H), 7.57 (s, 1H), 7.37 (dd, J = 7.6, 0.4 Hz, 1H), 7.15 (t, J = 8.4 Hz, 1H), 4.06 (s, 2H), 1.68 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 148.9, 137.0, 128.0, 127.1, 126.9, 125.5, 114.7, 113.8, 111.9, 84.4, 40.9, 28.1; IR ν_{max}: 3435, 2979, 2933, 1734, 1423, 1371, 1281, 1256, 1156, 1097, 1054, 848, 774, 744; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{17}BrNO_3$ 338.0386, found 338.0383.



***tert*-Butyl (*S*)-4-bromo-3-(2-((*tert*-butylsulfinyl)imino)ethyl)-1*H*-indole-1-carboxylate [(+)-6a].** To a solution of *N*-Boc aldehyde **7a** (1.5 g, 4.4 mmol, 1.0 equiv) in anhydrous THF (50 mL) was added Ti(O*i*-Pr)$_4$ (2.5 g, 8.8 mmol, 2.0 equiv) at room temperature. The mixture was stirred for 5 min and (*S*)-2-methylpropane-2-sulfinamide [(–)-**11** (0.75 g, 6.2 mmol, 1.4 equiv)] was added. After completion of the reaction monitored by TLC, water and ethyl acetate were added, and the white solid was filtered by Celite. The filtrate was extracted by ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4 and then purified by silica gel column chromatography (petroleum ether/ethyl acetate = 30/1) to give the (*S*)-*N*-*tert*-butanesulfinyl imine (+)-**6a** as a foamy white solid (1.7 g, 87% yield). The enantiomeric excess was determined using a chiral HPLC (AD-H column, *n*-hexane/*i*-PrOH = 95/5, 1 mL/min) to be more than 99% ee, t_R (major) = 6.945 min; m.p. = 75–

77 °C; $[\alpha]_D^{29}$ = +55.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (t, *J* = 4.4 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.52 (s, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.16 (t, *J* = 8.0 Hz, 1H), 4.25 (d, *J* = 4.4 Hz, 2H), 1.67 (s, 9H), 1.20 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4 (CH), 148.9 (C), 136.9 (C), 127.9 (C), 127.2 (CH), 125.9 (CH), 125.5 (CH), 114.7 (C), 114.6 (CH), 114.0 (C), 84.4 (C), 57.0 (C), 33.2 (CH_2), 28.1 (CH_3), 22.5 (CH_3); IR ν_{max}: 3340, 2977, 2928, 1738, 1422, 1369, 1295, 1256, 1156, 1097, 849, 778; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{26}BrN_2O_3S$ 441.0842, found 441.0844.

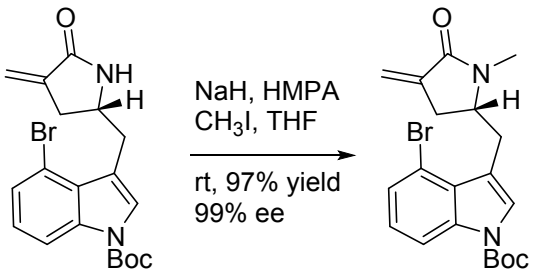


***tert*-Butyl (*R*)-4-bromo-3-((4-methylene-5-oxopyrrolidin-2-yl)methyl)-1*H*-indole-1-carboxylate [(+)-4a].** To a solution of (*S*)-*N*-*tert*-butanesulfinyl imine **6a** (1.8 g, 4.1 mmol, 1.0 equiv) in anhydrous DMF (100 mL) at room temperature was added actived zinc power (0.8 g, 12.3 mmol, 3.0 equiv), anhydrous LiCl (0.86 g, 20.5 mmol, 5.0 equiv), successively. The mixture was stirred for 10 min and methyl 2-(bromomethyl)but-2-enoate (**5**) (2.2 g, 12.3 mmol, 3.0 equiv) was added. After completion of the reaction monitored by TLC, the reaction was quenched with water, and extracted with ethyl acetate, dried over anhydrous Na_2SO_4, concentrated and the residue (+)-**12a** was used next step without further purification or purified by flash column chromatography to characterize by NMR and HRMS. The above crude product (+)-**12a** was dissolved in CH_2Cl_2, which was added 4 N HCl/MeOH (4 mL) and stirred for 30 min at 0 °C. Saturated $NaHCO_3$ was added, and extracted by ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was dissolved in anhydrous methanol and NaOH (0.65 g, 16.4mmol, 4.0 equiv) was added and stirred for another 1 h. The reaction mixture was quenched with saturated NH_4Cl and extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4, concentrated under reduced pressure. The crude product was purified by flash column

chromatography (petroleum ether/ethyl acetate = 1/1) to afford the lactam (+)-**4a** as a foamy white solid (1.32 g, 80% yield, over two steps).

(+)-12a: Foamy white solid; m.p. = 135–141 °C; $[\alpha]_D^{29}$ = +78.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.4 Hz, 1H), 7.60 (s, 1H), 7.37 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.11 (t, *J* = 8.0 Hz, 1H), 6.25 (d, *J* = 1.6 Hz, 1H), 5.65 (s, 1H), 3.96 – 3.91 (m, 1H), 3.68 (s, 3H), 3.53 – 3.48 (m, 2H), 3.21 (dd, *J* = 14.8, 7.2 Hz, 1H), 2.69 – 2.52 (m, 2H), 1.65 (s, 9H), 1.16 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5 (C), 149.0 (C), 137.4 (C), 137.1 (C), 128.4 (CH_2), 128.3 (C), 127.4 (CH), 126.5 (CH), 125.2 (CH), 116.8 (C), 114.5 (CH), 114.1 (C), 84.2 (C), 56.1 (C), 56.0 (CH_3), 51.9 (CH), 38.0 (CH_2), 32.9 (CH_2), 28.1 (CH_3), 22.6 (CH_3); IR ν_{max}: 3427, 3281, 2953, 2927, 1736, 1422, 1370, 1282, 1256, 1157, 1097, 1055, 849, 816, 780; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{34}BrN_2O_5S$ 541.1366, found 541.1369.

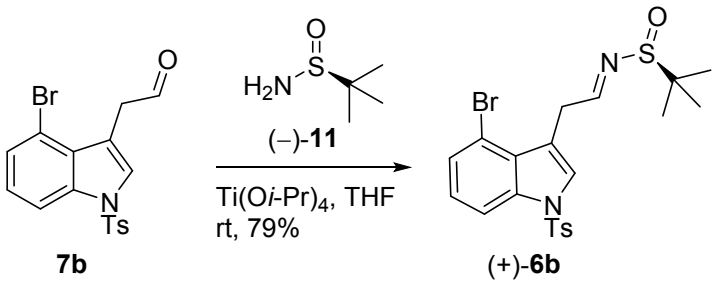
(+)-4a: The enantiomeric excess was determined using a chiral HPLC (AD-H column, *n*-hexane/*i*-PrOH = 95/5, 1 mL/min) to be more than 99% ee, t_R (major) = 11.261 min; m.p. = 95–97 °C; $[\alpha]_D^{18}$ = +33.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.2 Hz, 1H), 7.48 (s, 1H), 7.42 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.18 (t, *J* = 8.1 Hz, 1H), 6.20 (s, 1H), 6.04 (t, *J* = 2.6 Hz, 1H), 5.41 (s, 1H), 4.19 – 4.13 (m, 1H), 3.38 (dd, *J* = 14.2, 4.8 Hz, 1H), 3.13 – 3.06 (m, 1H), 2.91 (dd, *J* = 14.4, 8.4 Hz, 1H), 2.68 – 2.62 (m, 1H), 1.70 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0 (C), 148.9 (C), 139.0 (C), 137.3 (C), 127.8 (C), 127.4 (CH), 125.7 (CH), 125.5 (CH), 116.6 (CH_2), 116.5 (C), 114.8 (CH), 114.0 (C), 84.6 (C), 51.6 (CH), 34.2 (CH_2), 33.0 (CH_2), 28.2 (CH_3); IR ν_{max}: 3363, 2975, 2926, 1735, 1700, 1659, 1421, 1370, 1294, 1281, 1256, 1156, 1097, 848, 777, 744; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{22}BrN_2O_3$ 405.0808, found 405.0808.



(+)-**4a** (–)-**13a**

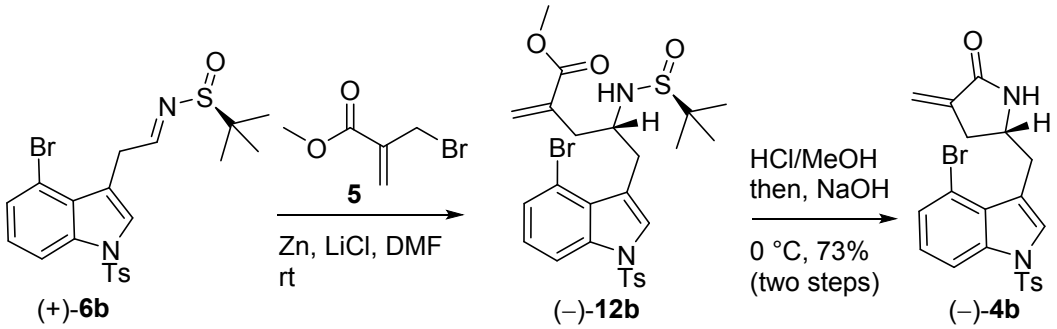
***tert*-Butyl (*R*)-4-bromo-3-((1-methyl-4-methylene-5-oxopyrrolidin-2-yl)methyl)-1*H*-indole-1-carboxylate [(–)-13a].** To a solution of lactam (+)-**4a** (20.0 mg, 0.05

mmol, 1.0 equiv) in anhydrous THF (10 mL) was added 60% NaH (10.0 mg, 0.25 mmol, 5.0 equiv) at ice water. The mixture was stirred for 10 min at this temperature and an excess of iodomethane (35.5 mg, 0.25 mmol, 5.0 equiv) was added. Warmed to room temperature and the starting material was consumed after stirring for 30 min. After completion of the reaction monitored by TLC, the reaction mixture was quenched with water at ice water and added ethyl acetate. The organic solvent was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with water and brine respectively, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate = 5/1) to afford *N*-Boc lactam (–)-**13a** as a foamy white solid (20.0 mg, 97% yield). The enantiomeric excess was determined using a chiral HPLC (AD-H column, *n*-hexane/*i*-PrOH = 95/5, 1 mL/min) to be 99% ee, t_R (minor) = 11.465 min, t_R (major) = 13.414 min; m.p. = 119–121 °C; $[\alpha]_D^{18}$ = –25.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.2 Hz, 1H), 7.46 (s, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.18 (t, *J* = 8.1 Hz, 1H), 6.02 (t, *J* = 2.6 Hz, 1H), 5.33 (s, 1H), 4.09 – 4.04 (m, 1H), 3.78 (dd, *J* = 14.1, 3.6 Hz, 1H), 3.09 (s, 3H), 2.80 – 2.72 (m, 1H), 2.64 – 2.56 (m, 2H), 1.70 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2 (C), 149.0 (C), 138.9 (C), 137.1 (C), 128.1 (CH), 127.4 (CH), 125.9 (CH), 125.4 (C), 116.0 (CH_2), 115.5 (CH), 114.7 (C), 113.9 (C), 84.6 (C), 57.1 (CH), 30.6 (CH_2), 30.4 (CH_2), 28.7 (CH_3), 28.2 (CH_3); IR ν_{max}: 3384, 2922, 2373, 1735, 1595, 1421, 1382, 1262, 1116, 780, 738; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{24}BrN_2O_3$ 419.0965, found 419.0961.



(*S*)-*N*-(2-(4-Bromo-1-tosyl-1*H*-indol-3-yl)ethylidene)-2-methylpropane-2-sulfinamide [(+)-6b]. To a solution of *N*-Ts aldehyde **7b** (3.0 g, 7.6 mmol, 1.0 equiv) in anhydrous THF (100 mL) was added Ti(O*i*-Pr)$_4$ (4.3 g, 15.3 mmol, 2.0 equiv) at room temperature. The mixture was stirred for 5 min and (*S*)-2-methylpropane-2-sulfinamide [(–)-**11** (1.3 g, 10.6 mmol, 1.4 equiv)] was added. After completion of the

reaction monitored by TLC, water and ethyl acetate were added, and the white solid was filtered by Celite. The filtrate was extracted by ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4 and then purified by silica gel column chromatography (petroleum ether/ethyl acetate = 30/1) to give the (*S*)-*N*-*tert*-butanesulfinyl imine (+)-**6b** as a foamy pale yellow solid (3.0 g, 79% yield). m.p. = 71–74 °C; $[\alpha]_D^{29}$ = +232.5 (*c* 0.4, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (t, *J* = 4.4 Hz, 1H), 7.98 (dd, *J* = 8.3, 0.6 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.53 (s, 1H), 7.35 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.14 (t, *J* = 8.0 Hz, 1H), 4.20 (d, *J* = 4.0 Hz, 2H), 2.34 (s, 3H), 1.14 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 145.4, 136.3, 134.8, 130.1, 128.3, 127.8, 126.8, 126.1, 125.8, 116.7, 114.3, 112.9, 57.0, 33.1, 22.4, 21.6; IR ν_{max}: 3423, 2960, 2924, 1622, 1597, 1413, 1373, 1190, 1174, 1088, 983, 668, 574; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{25}BrN_2O_3S_2$ 495.0406, found 495.0401.

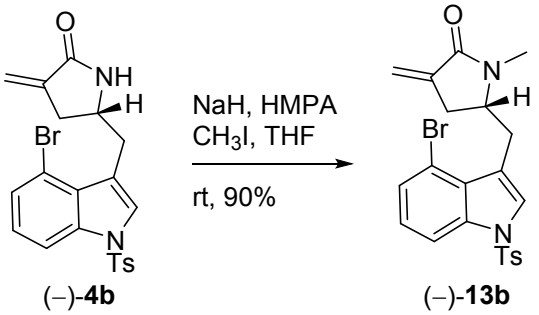


(*R*)-5-((4-Bromo-1-tosyl-1*H*-indol-3-yl)methyl)-3-methylenepyrrolidin-2-one [(–)-4b]. To a solution of (*S*)-*N*-*tert*-butanesulfinyl imine **(+)-6b** (1.8 g, 3.6 mmol, 1.0 equiv) in anhydrous DMF (100 mL) at room temperature was added actived zinc power (0.7 g, 10.8 mmol, 3.0 equiv), anhydrous LiCl (0.8 g, 18.0 mmol, 5.0 equiv), successively. The mixture was stirred for 10 min and methyl 2-(bromomethyl)but-2-enoate (**5**) (1.9 g, 10.8 mmol, 3.0 equiv) was added. After completion of the reaction monitored by TLC, the reaction was quenched with water, and extracted with ethyl acetate, dried over anhydrous Na_2SO_4, concentrated and the residue was used next step without further purification or purified by flash column chromatography to characterize the structure of (–)-**12b** by NMR and HRMS. The above crude product was dissolved in CH_2Cl_2, which was added 4 N HCl/MeOH (3 mL) and stirred for 30 min at 0 °C. Saturated $NaHCO_3$ was added, and extracted by ethyl acetate. Concentrated and the crude product was dissolved in anhydrous methanol. Then

NaOH (1.4 g, 36.0 mmol, 10.0 equiv) was added and stirred for another 2 h. The reaction mixture was quenched with water and extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4, concentrated under reduced pressure. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate = 1/1) to afford the lactam (–)-**4b** (1.22 g, 73% yield, two steps).

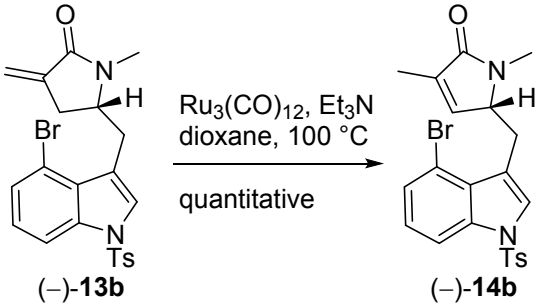
(–)-12b: Foamy white solid; m.p. = 75–78 °C; $[\alpha]_D^{18}$ = –54.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.64 (s, 1H), 7.40 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.13 (t, *J* = 8.1 Hz, 1H), 6.28 (d, *J* = 1.3 Hz, 1H), 5.64 (s, 1H), 3.94 – 3.87 (m, 1H), 3.68 (s, 3H), 3.50 (dd, *J* = 15.1, 6.4 Hz, 1H), 3.37 (d, *J* = 7.1 Hz, 1H), 3.22 (dd, *J* = 14.9, 7.1 Hz, 1H), 2.6 5 – 2.50 (m, 2H), 2.36 (s, 3H), 1.18 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4 (C), 145.2 (C), 137.3 (C), 136.5 (C), 134.9 (C), 129.9 (CH), 128.7 (C), 128.5 (CH_2), 128.0 (CH), 127.0 (CH), 126.7 (CH), 125.5 (CH), 118.7 (C), 114.4 (C), 112.9 (CH), 56.2 (C), 56.1 (CH), 51.9 (CH_3), 38.0 (CH_2), 33.1 (CH_2), 22.6 (CH_3), 21.5 (CH_3); IR ν_{max}: 3423, 2951, 2925, 1720, 1630, 1596, 1412, 1373, 1307, 1192, 1174, 1059, 983, 672, 573; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{32}BrN_2O_5S_2$ 595.0931, found 595.0931.

(–)-4b: Foamy white solid; m.p. = 100–102 °C; $[\alpha]_D^{18}$ = –93.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.98 (d, *J* = 8.3 Hz, 1H), 7.77 (d, *J* = 7.9 Hz, 2H), 7.53 (s, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.16 – 7.12 (m, 2H), 6.01 (s, 1H), 5.35 (s, 1H), 4.14 – 4.07 (m, 1H), 3.23 – 3.11 (m, 2H), 2.98 (dd, *J* = 17.0, 7.6 Hz, 1H), 2.59 (dd, *J* = 17.1, 2.0 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 170.4 (C), 145.4 (C), 139.1 (C), 136.6 (C), 134.7 (C), 130.1 (CH), 128.4 (C), 128.0 (CH), 126.9 (CH), 126.1 (CH), 125.7 (CH), 118.4 (C), 116.4 (CH_2), 114.4 (C), 113.1 (CH), 51.4 (CH), 33.6 (CH_2), 32.6 (CH_2), 21.6 (CH_3); IR ν_{max}: 3394, 2920, 2852, 2372, 1686, 1657, 1602, 1458, 1420, 1274, 1124, 1080, 772, 737, 667; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{20}BrN_2O_3S$ 458.0373, found 459.0384.



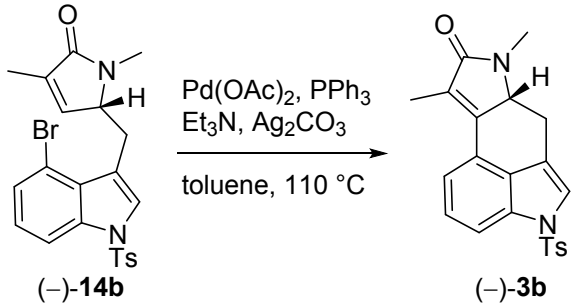
(–)-**4b** (–)-**13b**

(*R*)-5-((4-Bromo-1-tosyl-1*H*-indol-3-yl)methyl)-1-methyl-3-methylenepyrrolidin-2-one [(–)-13b]. To a solution of lactam (–)-**4b** (0.68 g, 1.5 mmol, 1.0 equiv) in anhydrous THF (50 mL) was treated with 60% NaH (0.3 g, 7.5mmol, 5.0 equiv) at ice water. The mixture was stirred for 10 min at this temperature and an excess of iodomethane (1.1 g, 7.5 mmol, 5.0 equiv) was added. Warmed to room temperature and the starting material was consumed after stirring for 30 min. After completion of the reaction monitored by TLC, the reaction mixture was quenched with water at ice water and added ethyl acetate. The organic solvent was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with water and brine respectively, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate = 5/1) to afford *N*-Ts lactam (–)-**13b** as a foamy white solid (0.63 g, 90% yield). m.p. = 183–185 °C; $[\alpha]_D^{18}$ = –44.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.3 Hz, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.45 (s, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.27 (d, J = 8.2 Hz, 2H), 7.17 (t, J = 8.1 Hz, 1H), 5.97 (t, J = 2.3 Hz, 1H), 5.28 (s, 1H), 4.00 – 3.95 (m, 1H), 3.74 (dd, J = 14.2, 3.6 Hz, 1H), 3.04 (s, 3H), 2.72 – 2.49 (m, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1 (C), 145.5 (C), 138.6 (C), 136.5 (C), 134.7 (C), 130.1 (CH), 128.4 (C), 128.1 (CH), 126.9 (CH), 126.1 (CH), 125.8 (CH), 118.0 (C), 115.6 (CH_2), 114.2 (C), 113.1 (CH), 56.9 (CH), 30.3 (CH_2), 30.2 (CH_2), 28.7 (CH_3), 21.6 (CH_3); IR ν_{max}: 3371, 2924, 1689, 1663, 1596, 1373, 1301, 1174, 1099, 981, 774, 740, 672, 616; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{22}BrN_2O_3S$ 473.0529, found 473.0529.



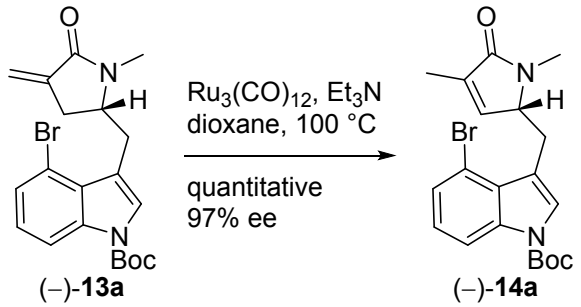
(–)-**13b** (–)-**14b**

(*R*)-5-((4-bromo-1-tosyl-1*H*-indol-3-yl)methyl)-1,3-dimethyl-1,5-dihydro-2*H*-pyrrol-2-one [(–)-14b]. To a solution of *N*-Ts lactam (–)-**13b** (0.1 g, 0.2 mmol, 1.0 equiv) in dioxane (10 mL) was added $Ru_3(CO)_{12}$ (12.8 mg, 0.02 mmol, 0.1 equiv) and Et_3N (31 μL, 0.2 mmol, 1.0 equiv) at room temperature. The mixture was allowed to warm to stir at 100 °C for 2 h. Concentrated the organic solvent under reduced pressure and the crude product was detected by NMR. The starting material was consumed completely, and the exocyclic double bond of lactam (–)-**13b** was isomerized to intra-annular. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate = 1/2) to afford lactam (–)-**14b** as a colorless liquid at a quantitative yield. m.p. = 146–149 °C; $[\alpha]_D^{29}$ = –410.0 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.44 (s, 1H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.18 (t, *J* = 8.1 Hz, 1H), 6.52 (s, 1H), 4.26 – 4.25 (m, 1H), 3.78 (dd, *J* = 14.0, 4.6 Hz, 1H), 3.06 (s, 3H), 2.62 (dd, *J* = 14.0, 9.8 Hz, 1H), 2.37 (s, 3H), 1.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9 (C), 145.5 (C), 139.3 (CH), 136.4 (C), 135.6 (C), 134.6 (C), 130.1 (CH), 128.3 (C), 128.1 (CH), 126.8 (CH), 126.4 (CH), 125.8 (CH), 117.8 (C), 114.1 (C), 113.2 (CH), 62.1 (CH), 28.0 (CH_2), 27.7 (CH_3), 21.6 (CH_3), 11.3 (CH_3); IR ν_{max}: 3368, 2924, 2855, 1686, 1596, 1412, 1375, 1294, 1248, 1174, 983, 815, 775, 670; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{22}BrN_2O_3S$ 473.0529, found 473.0531.



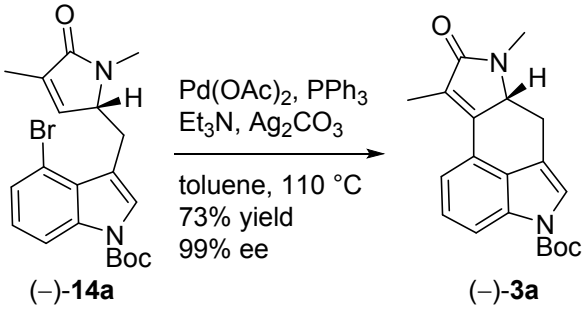
(–)-**14b** (–)-**3b**

***tert*-Butyl (*R*)-7,9-dimethyl-8-oxo-6,6a,7,8-tetrahydro-4*H*-indolo[6,5,4-*cd*]indole-4-carboxylate [(–)-3b].** To a suspension of $Pd(OAc)_2$ (3.0 mg, 0.01 mmol, 0.1 equiv), PPh_3 (19.0 mg, 0.07 mmol, 0.6 equiv), and Ag_2CO_3 (66.0 mg, 0.24 mmol, 2.0 equiv) in dry toluene (10 mL) and Et_3N (10 mL) at room temperature was added a solution of lactam (–)-**14b** (15.0 mg, 0.12 mmol, 1.0 equiv) in dry toluene (10 mL) and dry Et_3N (10 mL). The reaction mixture was degassed (three freeze-pump-thaw cycles) and then heated to 110 °C for 13 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate = 5/1) to obtain both lactam (–)-**3b** and triphenylphosphine oxide as a mixture which was difficult to separate.



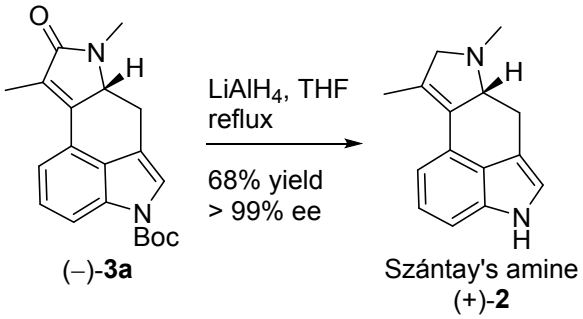
***tert*-Butyl (*R*)-4-bromo-3-((1,4-dimethyl-5-oxo-2,5-dihydro-1*H*-pyrrol-2-yl)methyl)-1*H*-indole-1-carboxylate [(–)-14a].** To a solution of *N*-Boc lactam **13a** (0.25 g, 0.6 mmol, 1.0 equiv) in dioxane (15 mL) was added $Ru_3(CO)_{12}$ (38.4 mg, 0.06 mmol, 0.1 equiv) and Et_3N (86 μL, 0.6 mmol, 1.0 equiv) at room temperature. The mixture was allowed to warm to stir at 100 °C for 2 h. Concentrated the organic solvent under reduced pressure and the crude product was purified by flash column chromatography (petroleum ether/ethyl acetate = 1/2) to afford lactam (–)-**14a** as a colorless liquid at a quantitative yield. The enantiomeric excess was determined using a chiral HPLC (AD-H column, *n*-hexane/*i*-PrOH = 95/5, 1 mL/min) to be 97% ee, t_R (minor) = 10.009 min, t_R (major) = 10.746 min; m.p. = 58–60 °C; $[\alpha]_D^{18}$ = –53.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 8.2 Hz, 1H), 7.45 (s, 1H), 7.41 (d, J = 7.8 Hz, 1H), 7.16 (t, J = 8.1 Hz, 1H), 6.64 (s, 1H), 4.32 (d, J = 7.4 Hz, 1H), 3.78 (dd, J = 13.9, 4.6 Hz, 1H), 3.09 (s, 3H), 2.58 (dd, J = 13.8, 10.4 Hz, 1H), 1.90 (s, 3H), 1.69 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9 (C), 149.0 (C), 139.7 (CH), 137.0 (C), 135.3 (C), 128.0 (C), 127.4 (CH), 126.3 (CH), 125.4 (CH), 116.0 (C),

114.7 (CH), 113.8 (C), 84.6 (C), 62.4 (CH), 28.3 (CH_2), 28.2 (CH_3), 27.7 (CH_3), 11.3 (CH_3); IR ν_{max}: 3373, 2924, 1736, 1688, 1421, 1280, 1257, 1149, 1095, 847, 776; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{24}BrN_2O_3$ 419.0965, found 419.0966.



(–)-**14a** (–)-**3a**

***tert*-Butyl (*R*)-7,9-dimethyl-8-oxo-6,6a,7,8-tetrahydro-4*H*-indolo[6,5,4-*cd*]indole-4-carboxylate [(–)-3a].** To a suspension of $Pd(OAc)_2$ (15.0 mg, 0.07 mmol, 0.1 equiv), PPh_3 (0.1 g, 0.38 mmol, 0.6 equiv), and Ag_2CO_3 (0.37 g, 1.34 mmol, 2.0 equiv) in dry toluene (10 mL) and Et_3N (10 mL) at room temperature was added a solution of lactam (–)-**14a** (0.28 g, 0.38 mmol, 1.0 equiv) in dry toluene (10 mL) and dry Et_3N (10 mL). The reaction mixture was degassed (three freeze-pump-thaw cycles) and then heated to 110 °C for 13 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate = 5/1) to obtain the lactam **(–)-3a** as a light yellow solid (0.165 g, 73% yield). The enantiomeric excess was determined using a chiral HPLC (AD-H column, *n*-hexane/*i*-PrOH = 95/5, 1 mL/min) to be 99% ee, t_R (minor) = 22.083 min, t_R (major) = 23.878 min; m.p. = 192–194 °C; $[\alpha]_D^{18}$ = –20.0 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.45–7.37 (m, 3H), 4.16 (dd, *J* = 12.1, 6.1 Hz, 1H), 3.52 (dd, *J* = 14.6, 6.3 Hz, 1H), 3.12 (s, 3H), 2.55 (t, *J* = 14.0 Hz, 1H), 2.23 (s, 3H), 1.69 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5 (C), 149.8 (C), 144.9 (C), 133.5 (C), 129.7 (C), 128.1 (C), 125.6 (CH), 124.3 (C), 121.3 (CH), 119.1 (CH), 115.7 (CH), 114.2 (C), 84.0 (C), 60.8 (CH), 28.2 (CH_3), 27.4 (CH_3), 26.6 (CH_2), 10.1 (CH_3); IR (KBr) ν_{max}: 3428, 2969, 2925, 1681, 1630, 1383, 1260, 1097, 1021, 953, 799, 587; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{23}N_2O_3$ 339.1702, found 339.1703.



(–)-**3a** Szántay's amine (+)-**2**

(*R*)-7,9-dimethyl-6,6a,7,8-tetrahydro-4*H*-indolo[6,5,4-*cd*]indole [(+)-2]. The Lactam (–)-**3a** (60.0 mg, 0.18 mmol, 1.0 equiv) was dissolved in anhydrous THF (10 mL) and the solution was added dropwise to $LiAlH_4$ (2.5 M solution in THF, 1.4 mL, 3.6 mmol) in THF (10 mL). The mixture was heated under reflux overnight, and then cooled. Water, sodium hydroxide solution (10%) and water (v/v/v=1/2/3) were slowly added dropwise with vigorous stirring, respectively. The mixture was filtered with celite, washed with ethyl acetate, and dried over anhydrous Na_2SO_4, filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography ($CHCl_3$/MeOH = 10/1) to give the chiral Szántay's amine (+)-**2** as a offwhite solid (27.0 mg, 68% yield). The enantiomeric excess was determined using a chiral HPLC (AD-H column, *n*-hexane/*i*-PrOH = 97:3, 1 mL/min) to be 72% after purification by flash column chromatography, t_R (major) = 41.788 min, t_R (minor) = 50.203 min; Interestingly, when this reduction reaction was proceeded at reflux for only 2 hours, the enantiomeric excess of Szántay's amine (+)-**2** was determined using a chiral HPLC (AD-H column, *n*-hexane/*i*-PrOH = 92/8, 1 mL/min) to be more than 99% and without loss yield after purification by flash column chromatography, t_R (major) = 11.371 min; $[\alpha]_D^{29}$ = +14.0 (*c* 0.5, CH_2Cl_2); m.p. = 71–74 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (br, 1H), 7.26–7.19 (m, 3H), 6.90 (t, *J* = 1.8 Hz, 1H), 3.93 (dd, *J* = 13.2, 3.0 Hz, 1H), 3.72–3.68 (m, 1H), 3.54–3.51 (m, 1H), 3.34 (dd, *J* = 14.4, 6.0 Hz, 1H), 2.72 (t, *J* = 12.6 Hz, 1H), 2.60 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 134.1 (C), 130.4 (C), 130.1 (C), 127.3 (C), 125.8 (C), 123.0 (CH), 118.3 (CH), 114.8 (CH), 112.1 (C), 109.3 (CH), 72.4 (CH), 68.2 (CH_2), 40.5 (CH_3), 29.2 (CH_2), 13.6 (CH_3); IR (KBr) ν_{max}: 3434, 2922, 2853, 1629, 1462, 1384, 1249, 1122, 1050, 590; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{17}N_2$ 225.1386, found 225.1385.

3. Comparison ^{1}H NMR data of the racemic Szántay's amine (reported in 2008) and the enantiomerically pure Szántay's amine (+)-**2** (this work):

Szántay's amine (*rac*, 2008) (400 MHz, $CDCl_3$) δ (ppm)	Szántay's amine (+)-**2** (this work) (600 MHz, $CDCl_3$) δ (ppm)
8.0 (s, 1H)	8.00 (br, 1H)
7.25 (dd, *J* = 7.6*,* 7.2 Hz, 1H)	
7.18–7.21 (m, 2H)	7.26–7.19 (m, 3H)
6.91 (s, 1H)	6.90 (t, *J* = 1.8 Hz, 1H)
3.94 (dd, *J* = 14*,* 3.8 Hz, 1H)	3.93 (dd, *J* = 13.2, 3.0 Hz, 1H)
3.71 (m, 1H)	3.72–3.68 (m, 1H)
3.52 (dd, *J* = 14*,* 4.1 Hz, 1H)	3.54–3.51 (m, 1H)
3.34 (dd, *J* = 14.5*,* 6.0 Hz, 1H)	3.34 (dd, *J* = 14.4, 6.0 Hz, 1H)
2.72 (dd, *J* = 15*,* 14.5 Hz, 1H)	2.72 (t, *J* = 12.6 Hz, 1H)
2.60 (s, 3H)	2.60 (s, 3H)
2.14 (s, 3H)	2.14 (s, 3H)

4. Comparison ^{13}C NMR data of the racemic Szántay's amine (reported in 2008) and the enantiomerically pure Szántay's amine (+)-**2** (this work):

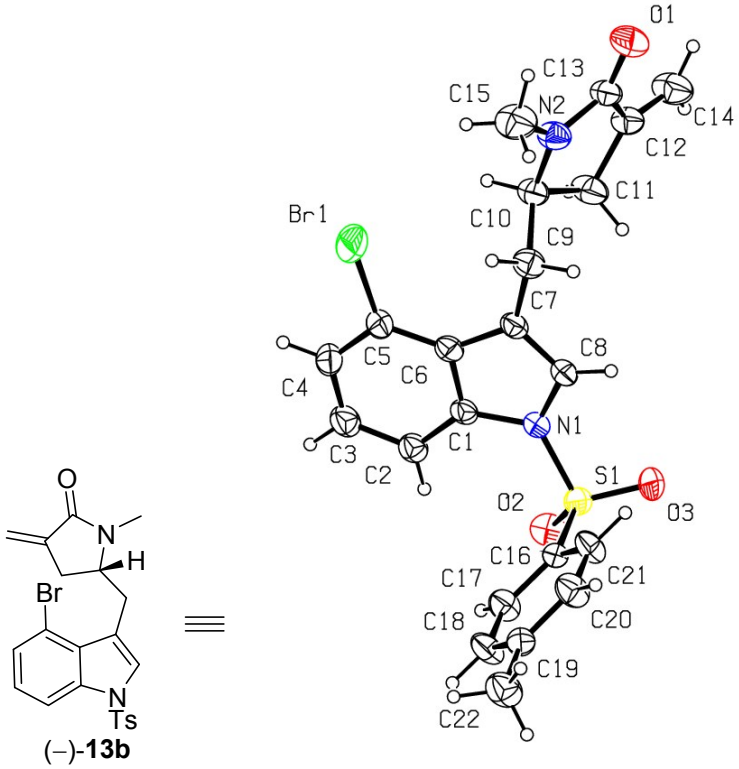
Szántay's amine (*rac*, 2018) (100 MHz, $CDCl_3$) δ (ppm)	Szántay's amine (+)-**2** (this work) (150 MHz, $CDCl_3$) δ (ppm)	$\Delta\delta$ (ppm)
134.1 (C)	134.1 (C)	0.0
130.6 (C)	130.4 (C)	0.2
130.2 (C)	130.1 (C)	0.1
127.4 (C)	127.3 (C)	0.1
125.9 (C)	125.8 (C)	0.1
123.1 (CH)	123.0 (CH)	0.1
118.3 (CH)	118.3 (CH)	0.0
114.8 (CH)	114.8 (CH)	0.0
112.2 (C)	112.1 (C)	0.1
109.3 (CH)	109.3 (CH)	0.0
72.5 (CH)	72.4 (CH)	0.1
68.3 (CH_2)	68.2 (CH_2)	0.1
40.6 (CH_3)	40.5 (CH_3)	0.1
29.3 (CH_2)	29.2 (CH_2)	0.1
13.6 (CH_3)	13.6 (CH_3)	0.0

5. Tabulated summary of synthesis of Szántay's amine **2** and cycloclavine (**1**)

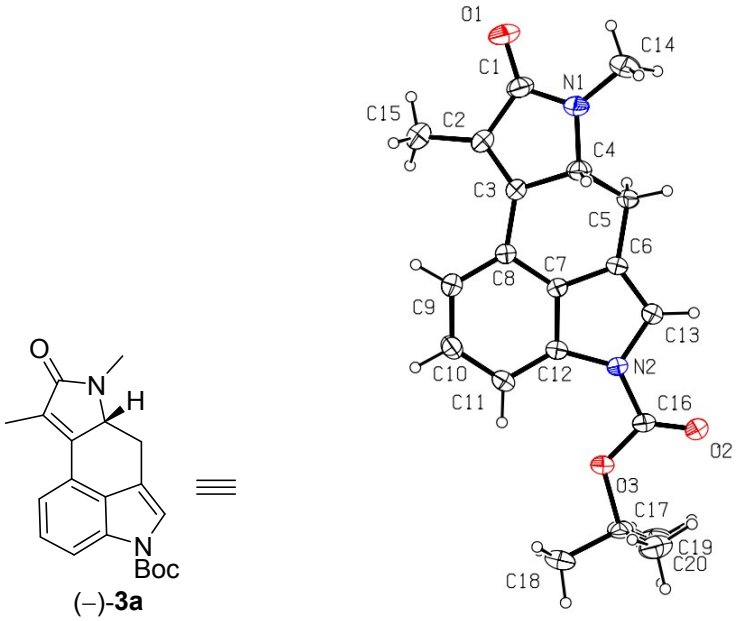
main author (year)	starting material and key features	optical rotation	Szántay's amine **2**	cycloclavine (**1**)	ref.
Szántay (2008)	[a]Uhle's ketone derivative [b]first total synthesis, [b]cyclopropanation with diazomethane	(±)	seven steps, 3.3% overall yield (eleven steps, 1.2% overall yield from 3-indolepropionic acid)	eight steps, 1.1% overall yield (twelve steps, 0.4% overall yield from 3-indolepropionic acid)	5a
Wipf (2011)	[a]*β*-methallyl alcohol [b]total synthesis, [b]intramolecular Diels-Alder furan cycloaddition	(±)		fourteen steps, 1.2% overall yield	5b
Brewer (2014)	[a]Uhle's ketone [b]total synthesis, [b]ring fragmentation, [b]1,3-dipolar cycloaddition	(±)		fourteen steps, 1.1% overall yield (seventeen steps, 0.5% overall yield from 3-indolepropionic acid)	5c
Cao (2014)	[a]indole aldehyde [b]aza-Cope–Mannich cyclization, [b]intramolecular Heck coupling, [b]radical-alkene cyclization	(±)	seven steps, 27.4% overall yield (eleven steps, 19.7% overall yield from 4-bromoindole)	(In Szántay method, from **2** to **1**, 32% yield, ref 5a)	5e
Opatz (2016)	[a]4-bromoindole [b]intramolecular Heck coupling	(±)	seven steps, 16.8% overall yield	(In Szántay method, from **2** to **1**, 32% yield, ref 5a)	5d
Wipf (2017)	[a]unsubstituted allene [b]total synthesis, [b]first asymmetric cyclopropanation, [b]intramolecular [4+2] cycloaddition	(−)		eight steps, 7.1% overall yield	4e
Cao (this work)	[a]4-bromoindole [b]first asymmetric formal synthesis, [b]asymmetric induction by Ellman's sulfinimine, [b]rhodium-catalyzed isomerization of C=C bond	(+)	eleven steps, 19.7% overall yield	(In Szántay method, from **2** to **1**, 32% yield, ref 5a)	

[a]starting material: known compound or commercially available. [b]key features.

6. X-ray structure of compound (–)-**13b** (CCDC 1536641)

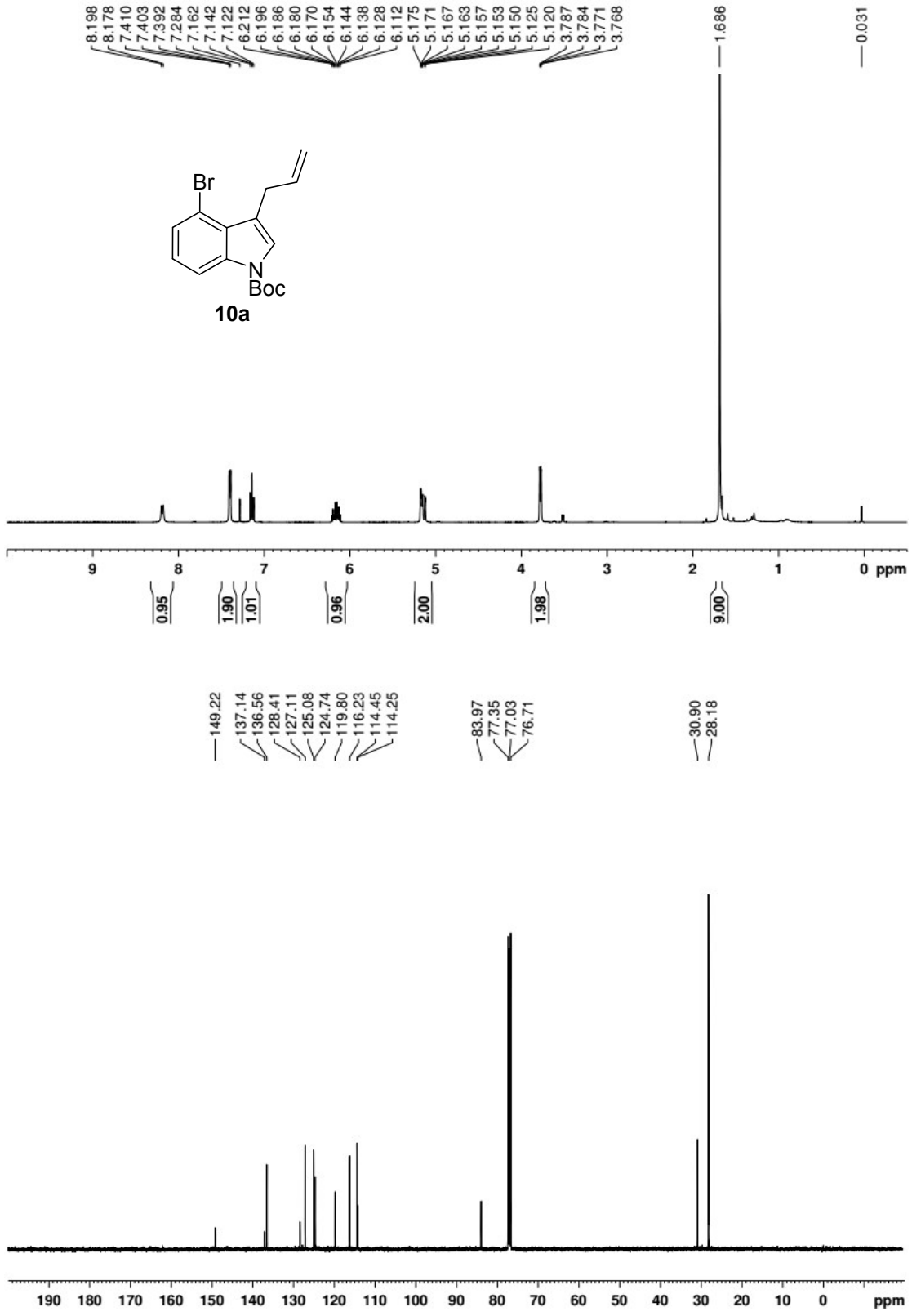


X-ray structure of compound (–)-**3a** (CCDC 1559337)

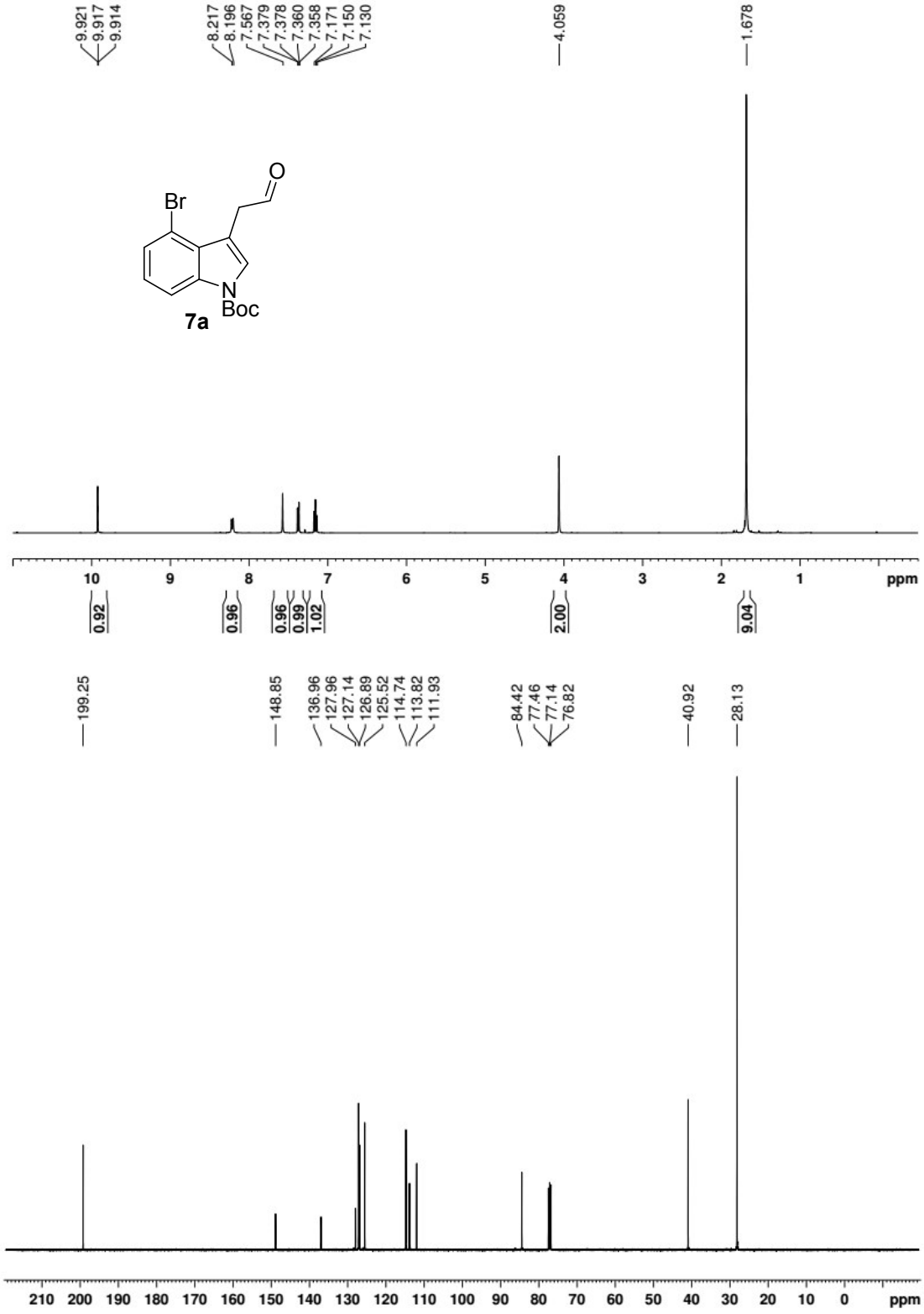


7. NMR spectra of compounds: **10a**, **7a**, (+)-**6a**, (+)-**12a**, (+)-**4a**, (–)-**13a**, (+)-**6b**, (–)-**12b**, (–)-**4b**, (–)-**13b**, (–)-**14b**, (–)-**14a**, (–)-**3a** and Szántay's amine (+)-**2**

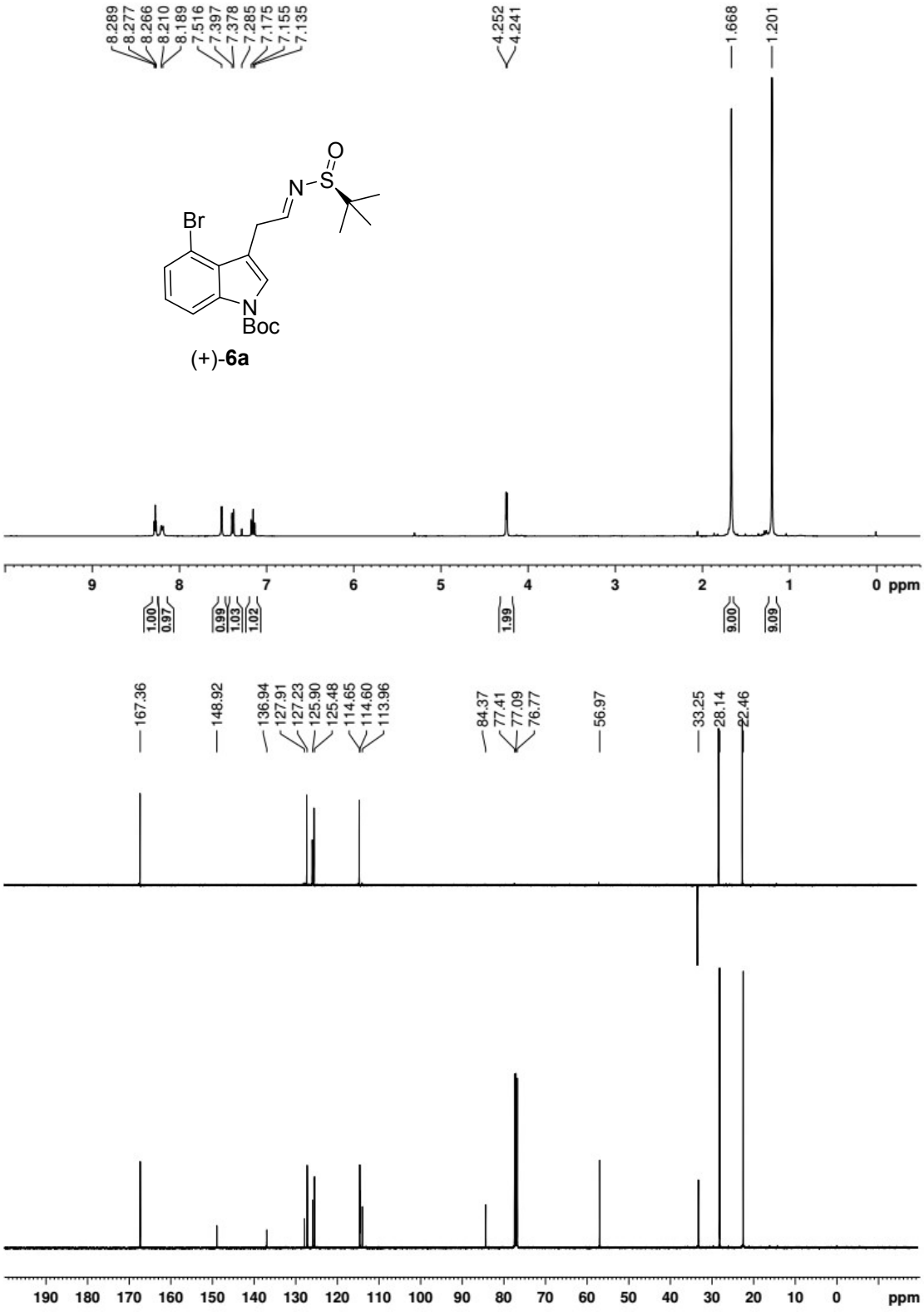
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of **10a**



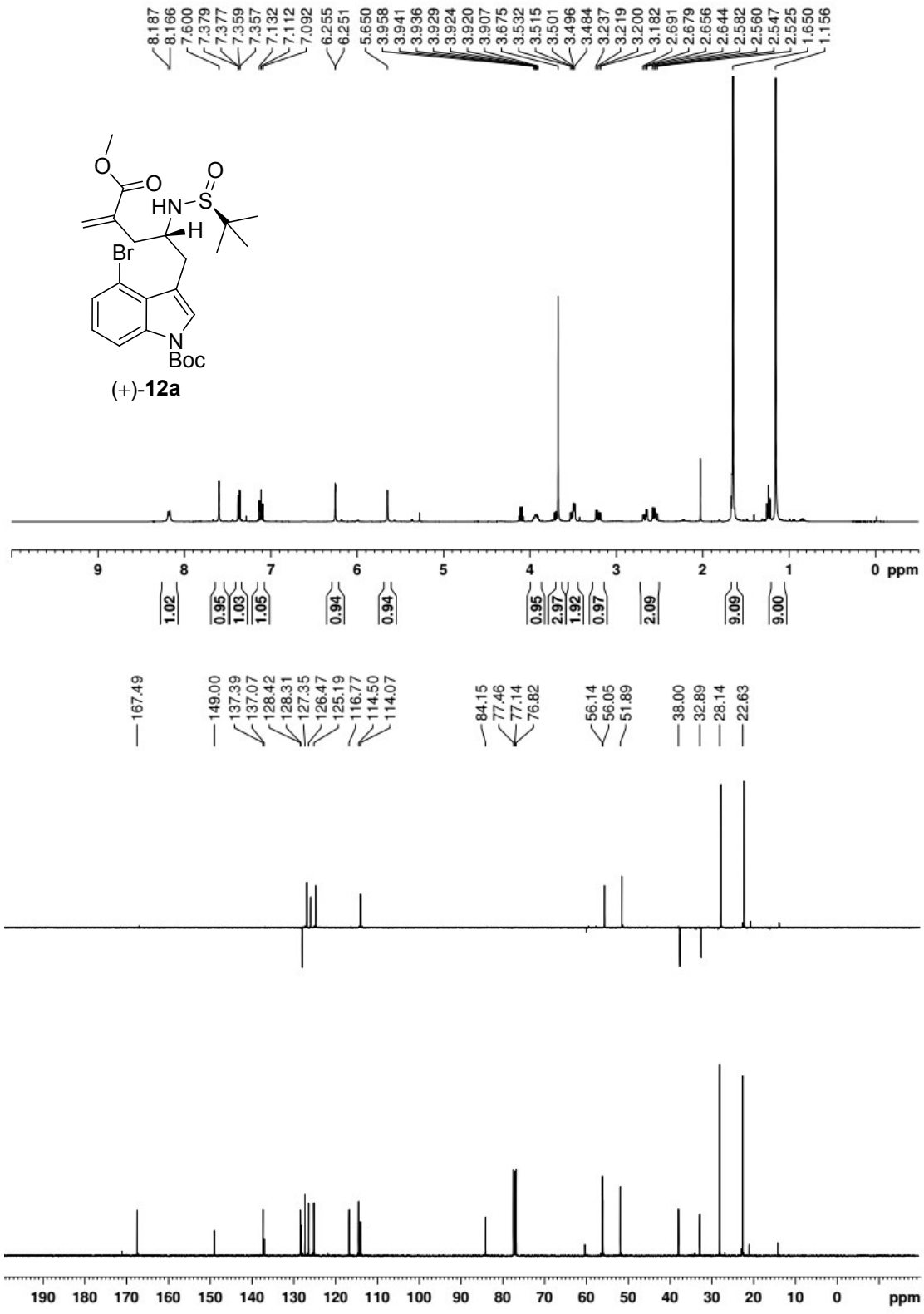
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of **7a**



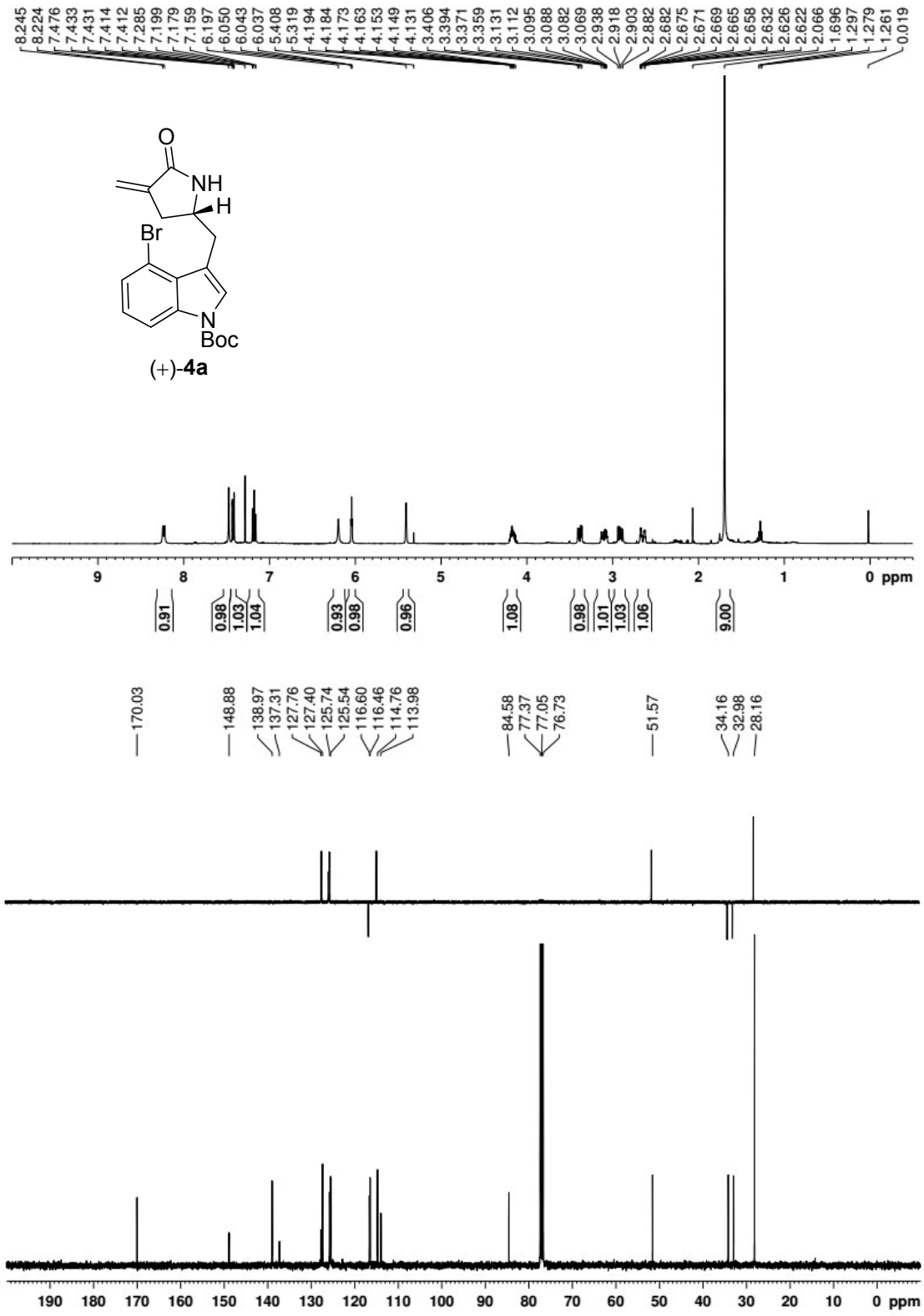
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of (+)-**6a**



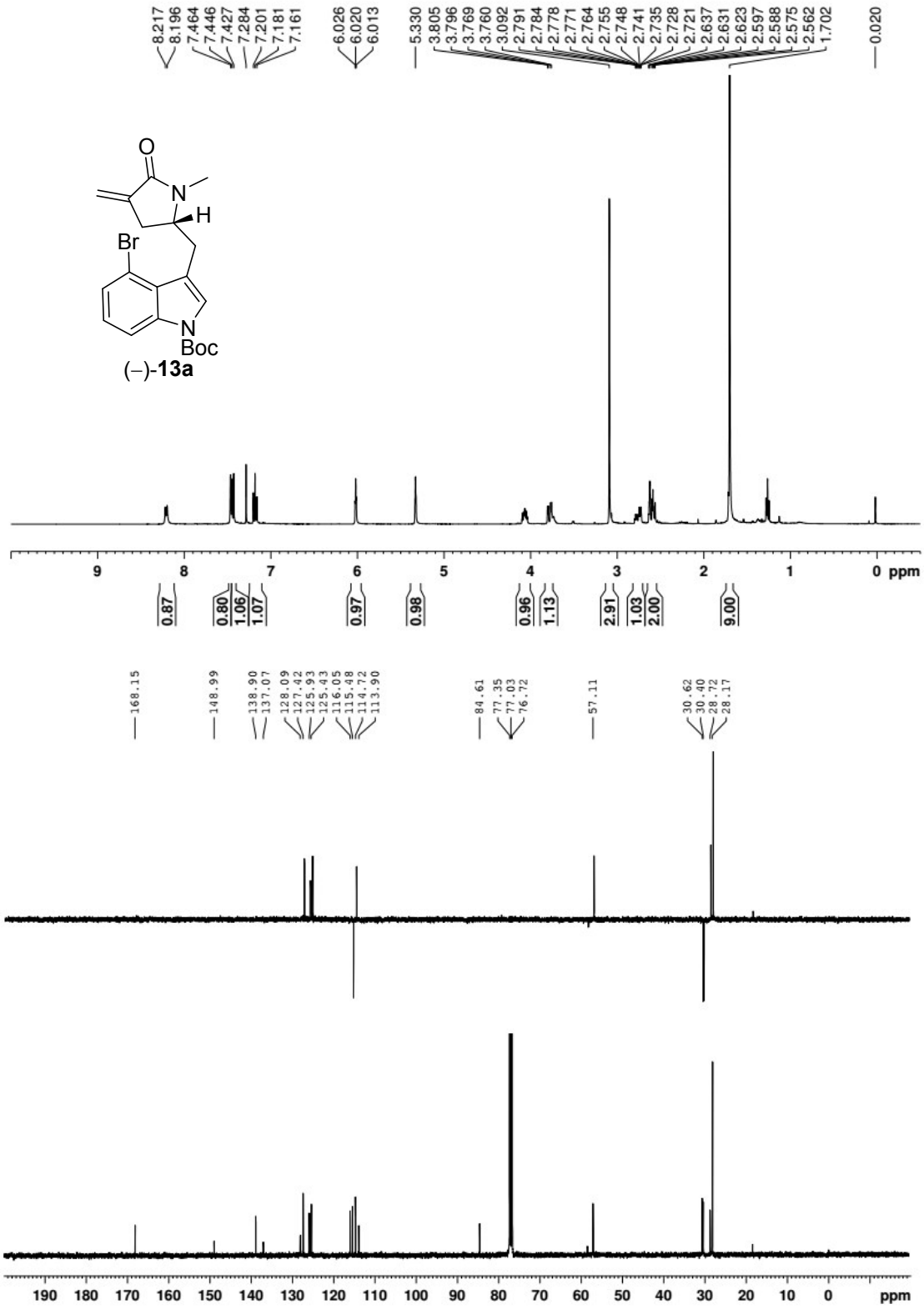
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of (+)-**12a**



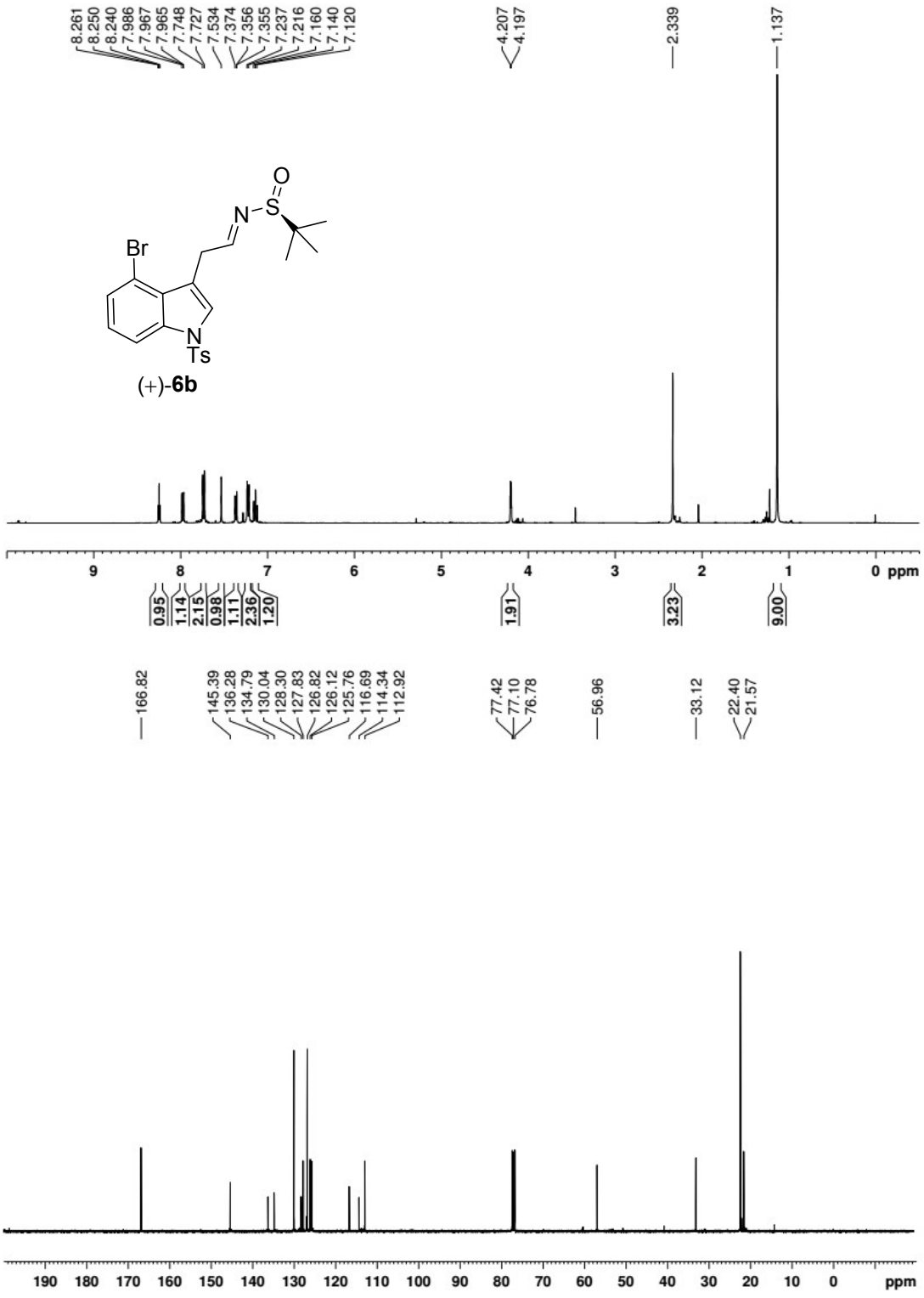
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of (+)-**4a**



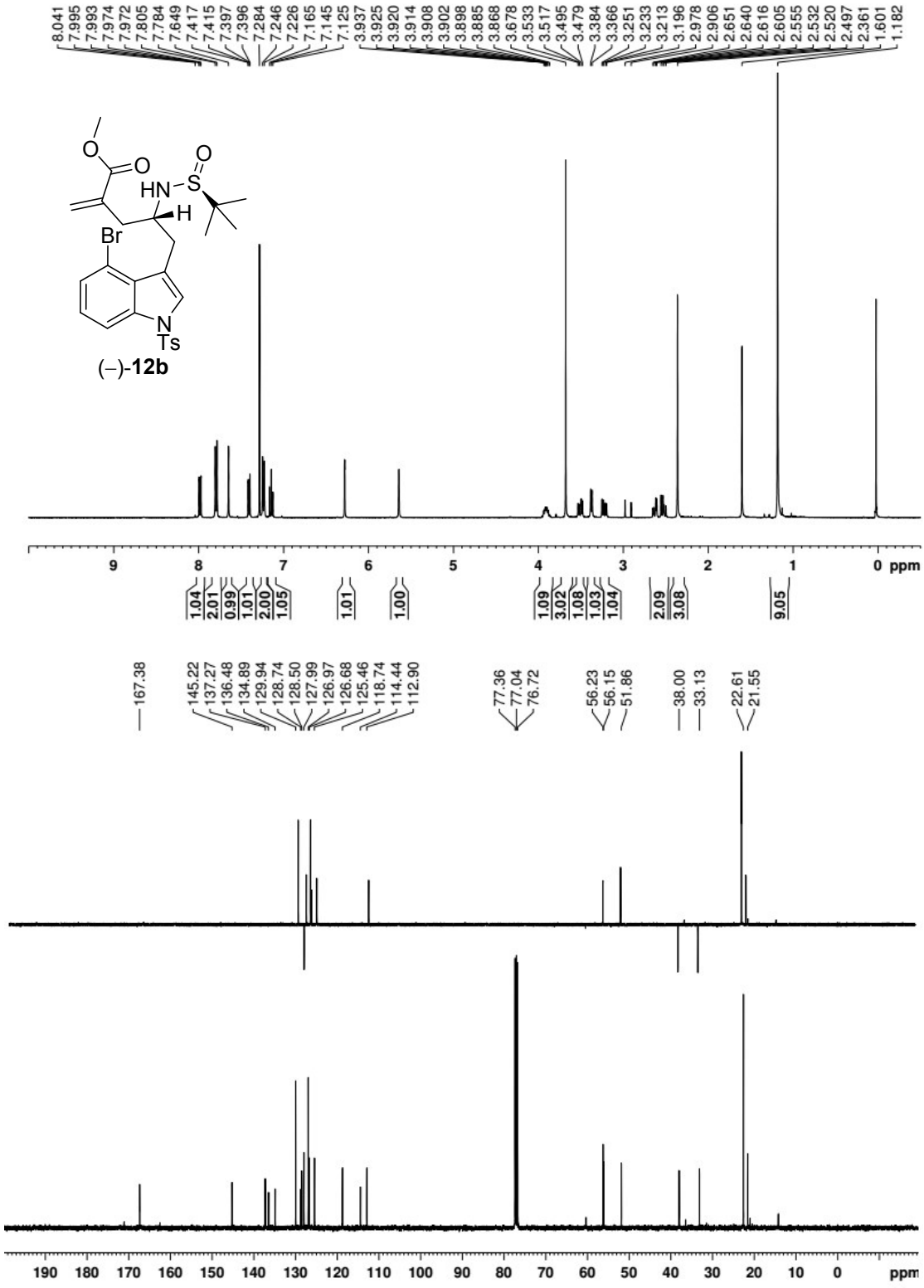
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of (–)-**13a**



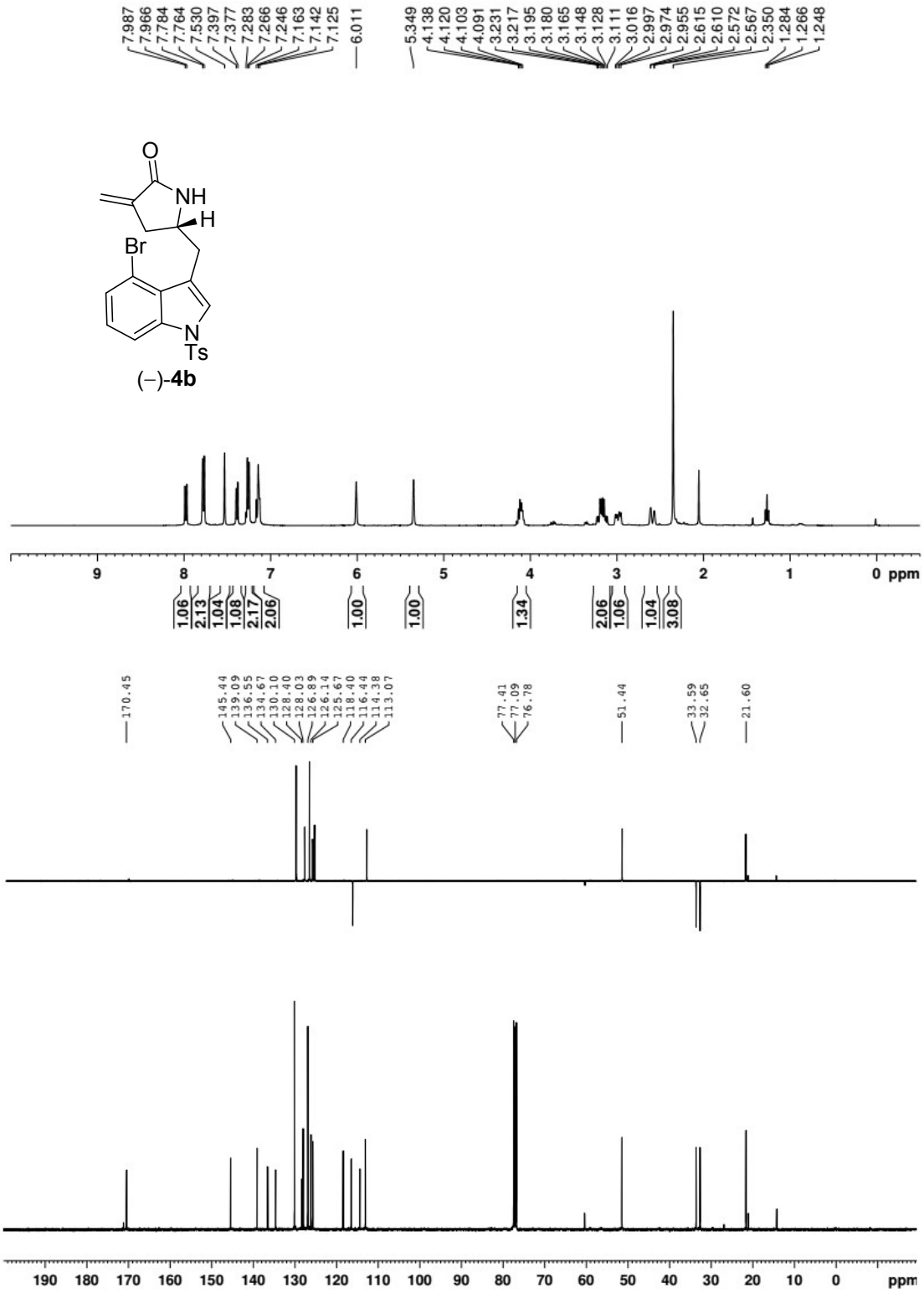
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of (+)-**6b**



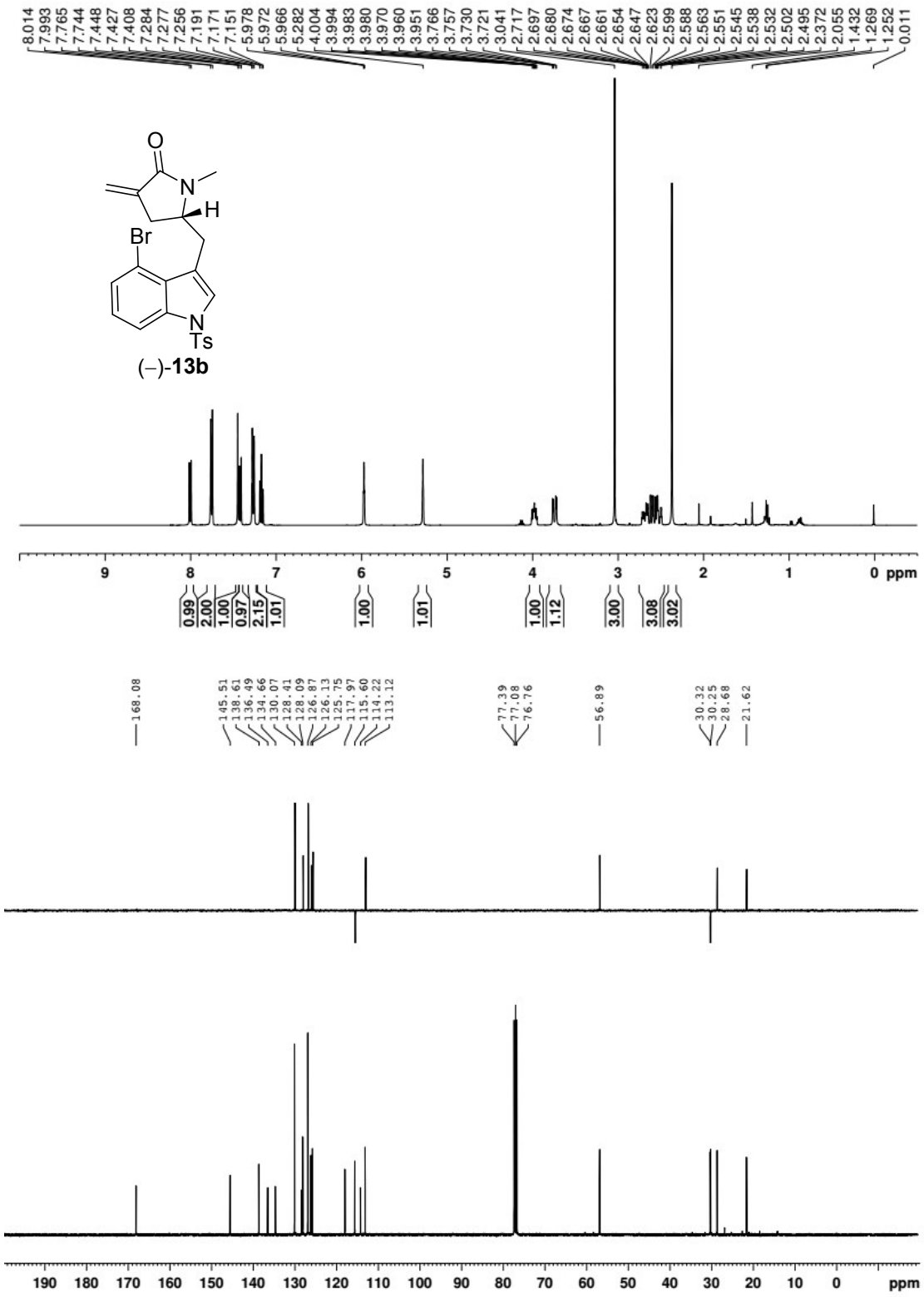
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of (–)-**12b**



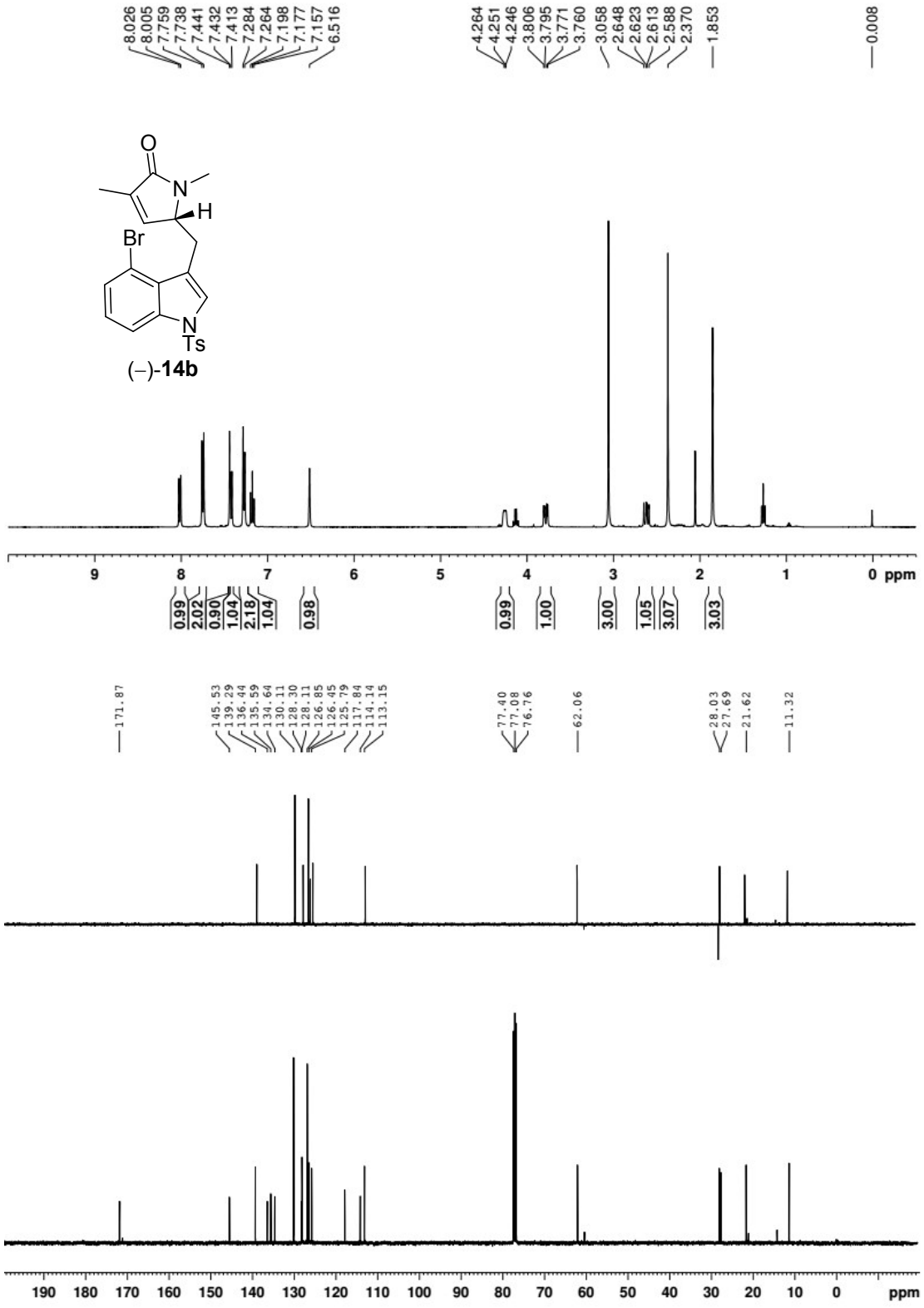
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of (–)-**4b**



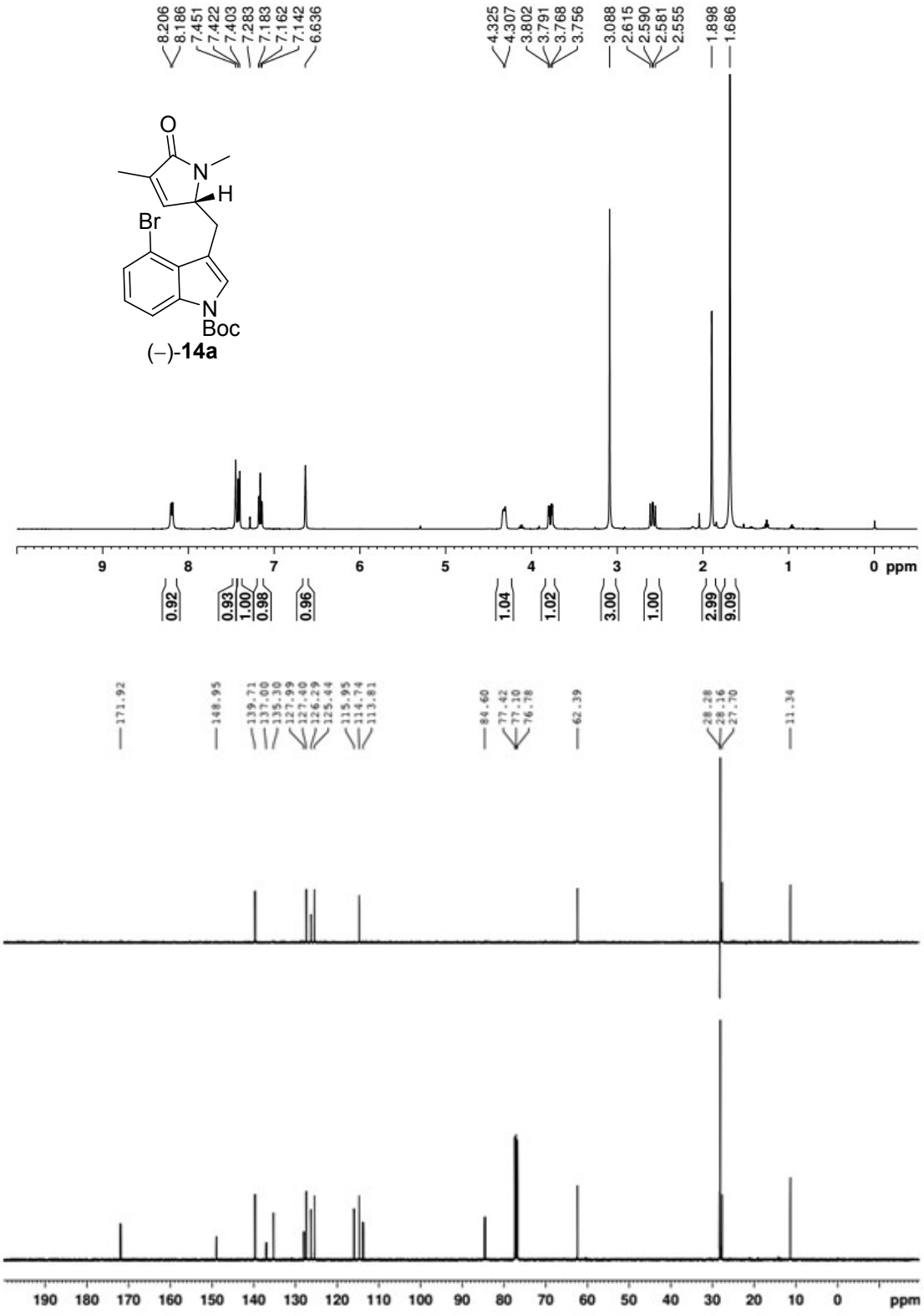
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of (–)-**13b**



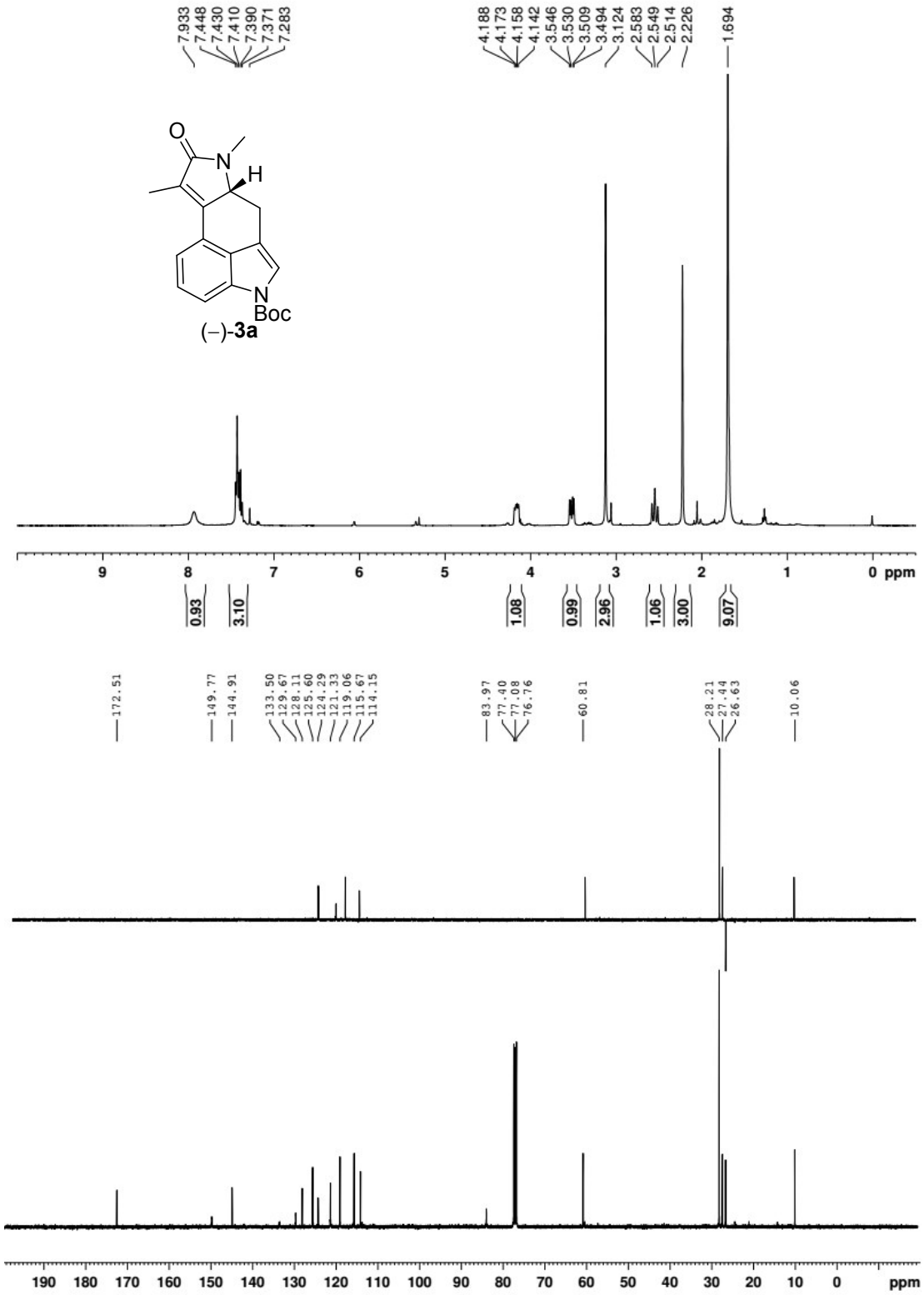
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of (–)-**14b**



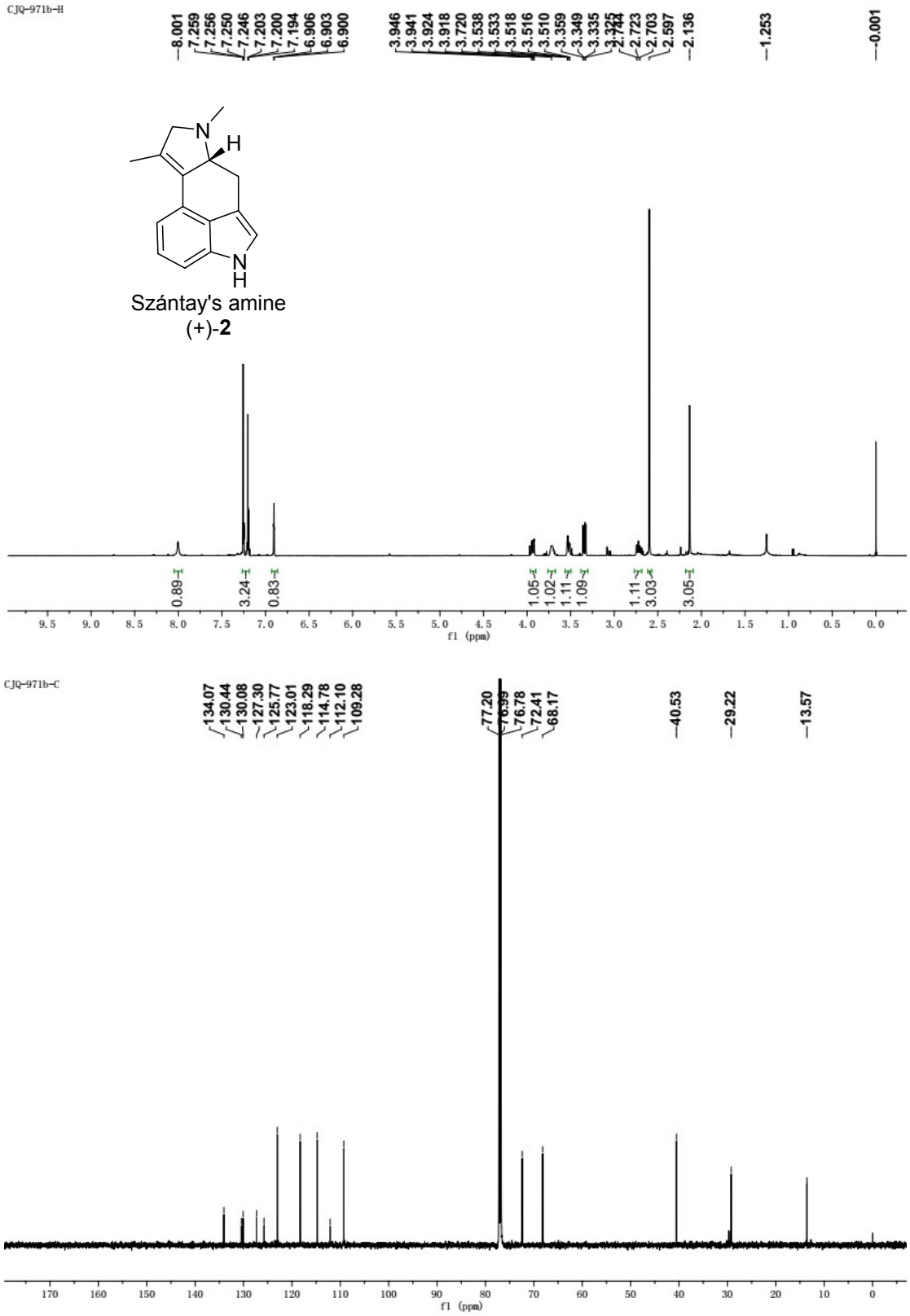
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of (–)-**14a**

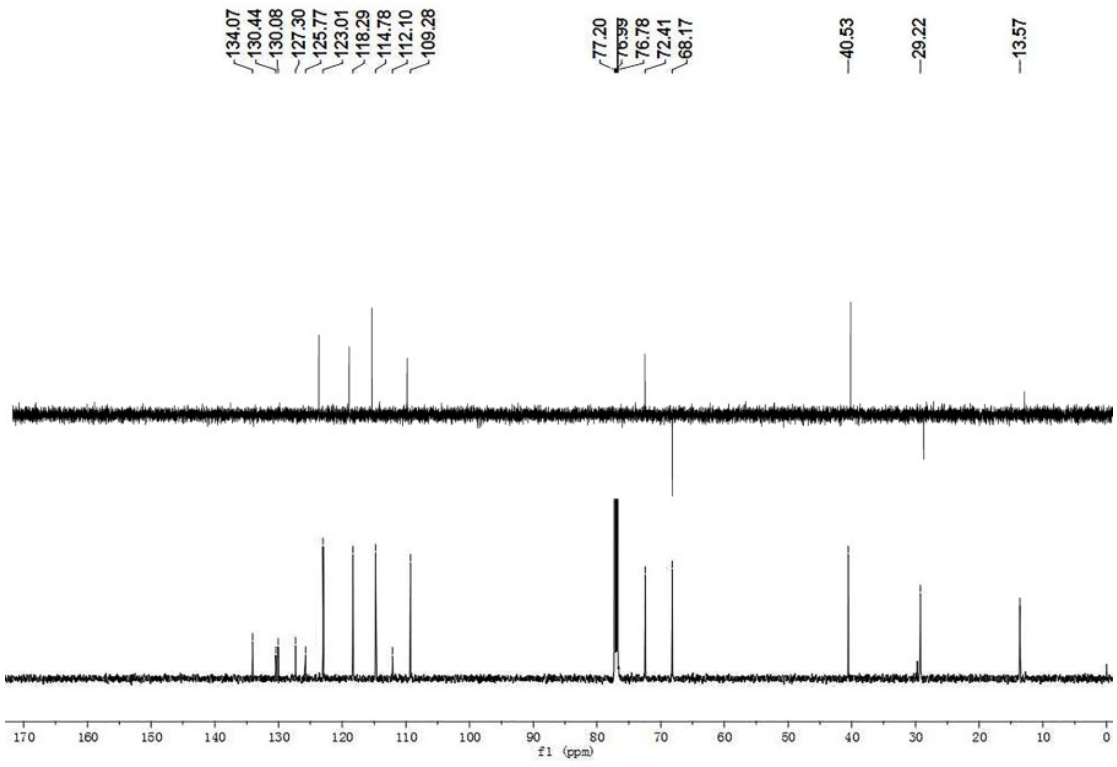


^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of (–)-**3a**



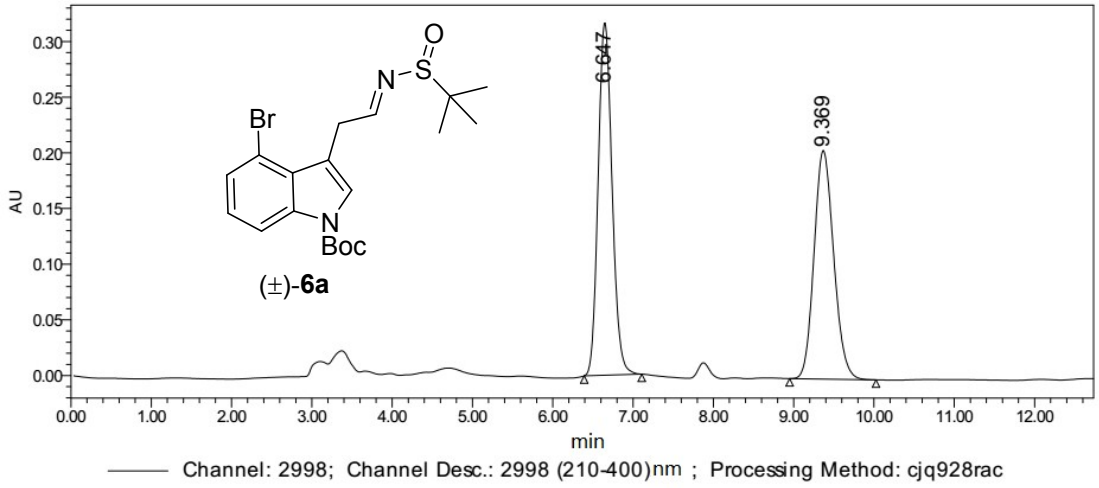
^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) spectra of Szántay's amine (+)-**2**



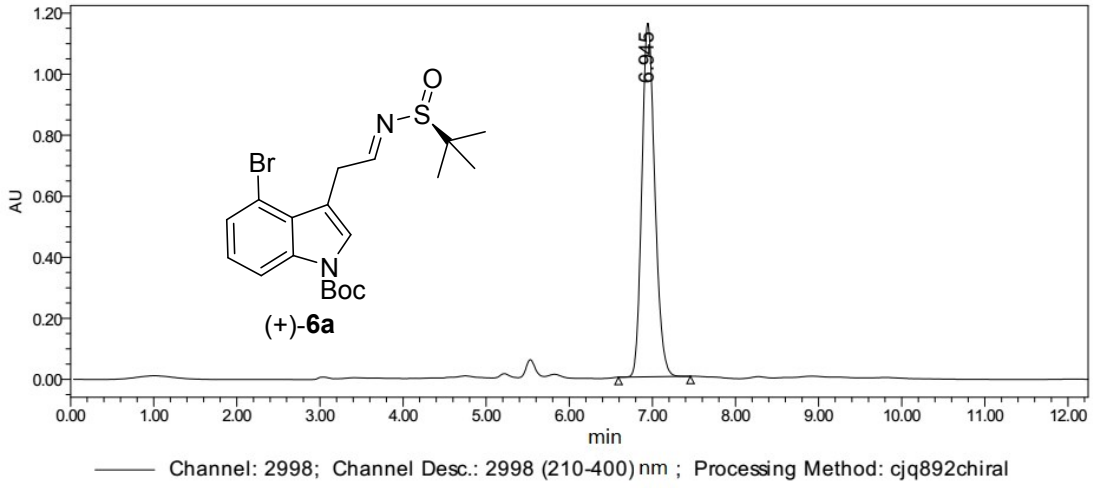

134.07
130.44
130.08
127.30
125.77
123.01
118.29
114.78
112.10
109.28
77.20
76.78
72.41
68.17
40.53
29.22
13.57
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

8. HPLC of compounds: (±)-**6a** and (+)-**6a**, (±)-**4a** and (+)-**4a**, (±)-**13a** and (–)-**13a**, (±)-**14a** and (–)-**14a**, (±)-**3a** and (–)-**3a**, Szántay's amine (±)-**2** and (+)-**2**

HPLC spectra of (±)-**6a** and (+)-**6a**



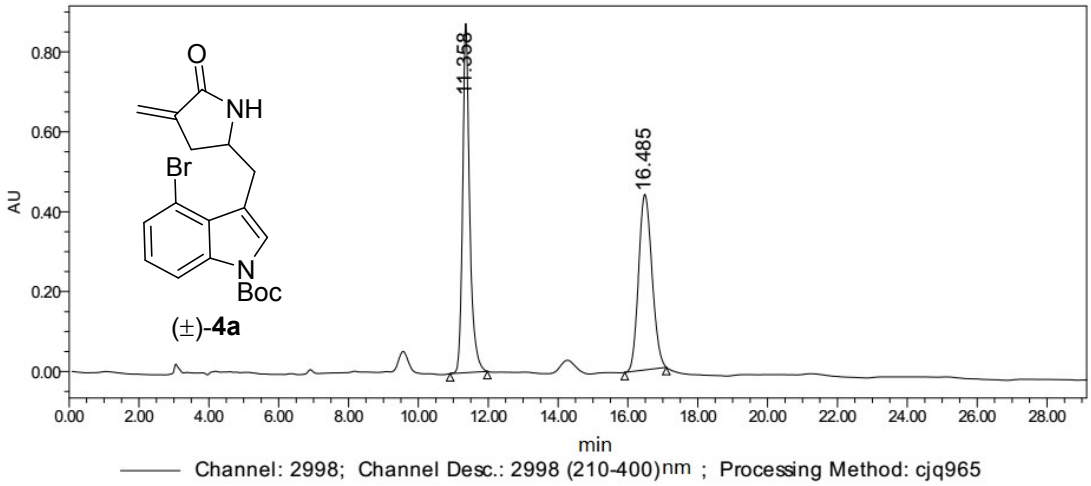
	Channel	Retention time (min)	Area (μv.s)	%Area	Height (μv)
1	2998 (210-400)nm	6.647	3816597	52.26	316422
2	2998 (210-400)nm	9.369	3487056	47.74	205229



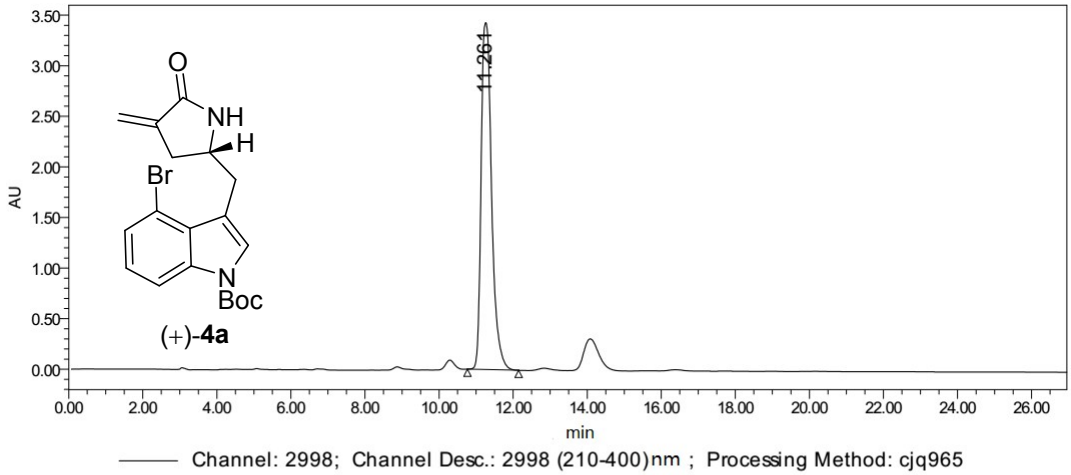
	Channel	Retention time (min)	Area (μv.s)	%Area	Height (μv)
1	2998 (210-400)nm	6.945	12590914	100.00	1159924

Compound (±)-**6a** was prepared as the similar procedure of (+)-**6a**.

HPLC spectra of (±)-**4a** and (+)-**4a**



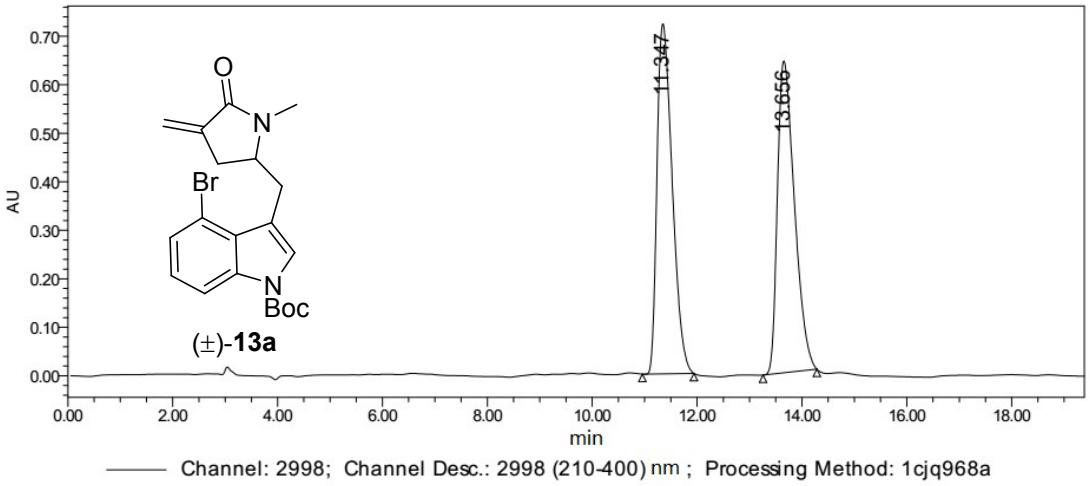
	Channel	Retention time (min)	Area (μv.s)	% Area	Height (μv)
1	2998 (210-400)nm	11.358	12215224	51.04	873285
2	2998 (210-400)nm	16.485	11717677	48.96	439470



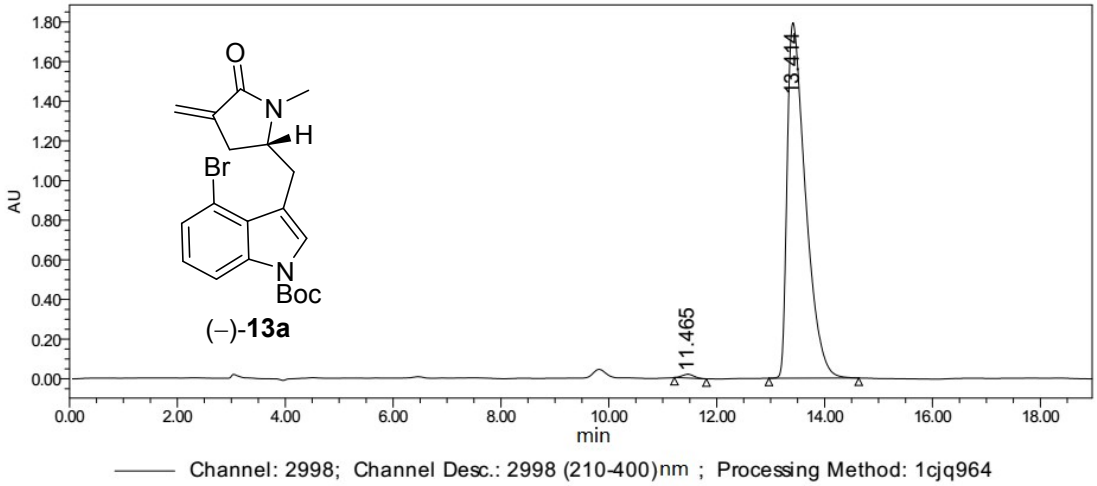
	Channel	Retention time (min)	Area (μv.s)	% Area	Height (μv)
1	2998 (210-400)nm	11.261	67305295	100.00	3429145

Compound (±)-**4a** was prepared as the similar procedure of (+)-**4a**.

HPLC spectra of (±)-**13a** and (–)-**13a**



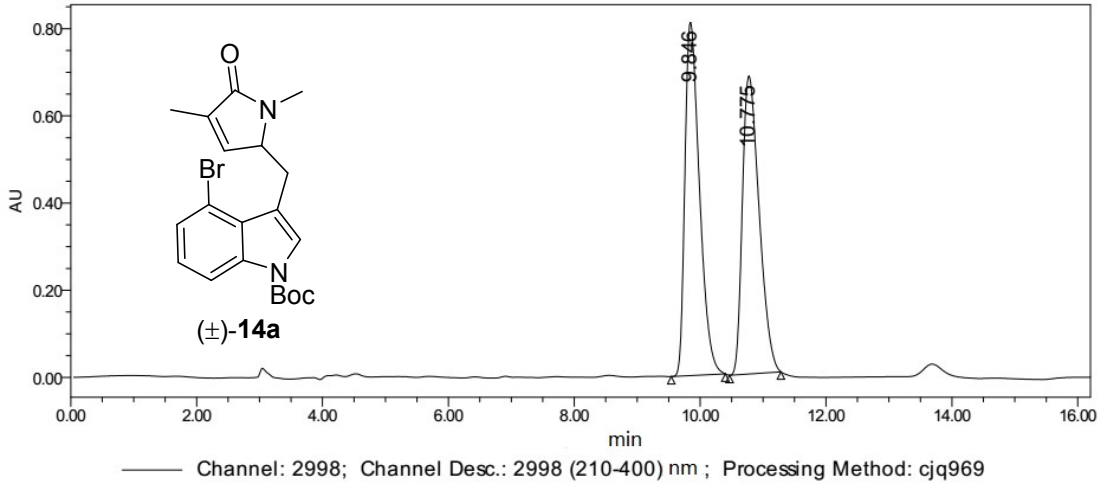
	Channel	Retention time (min)	Area (μv.s)	% Area	Height (μv)
1	2998 (210-400)nm	11.347	14536531	50.13	721865
2	2998 (210-400)nm	13.656	14463236	49.87	642811



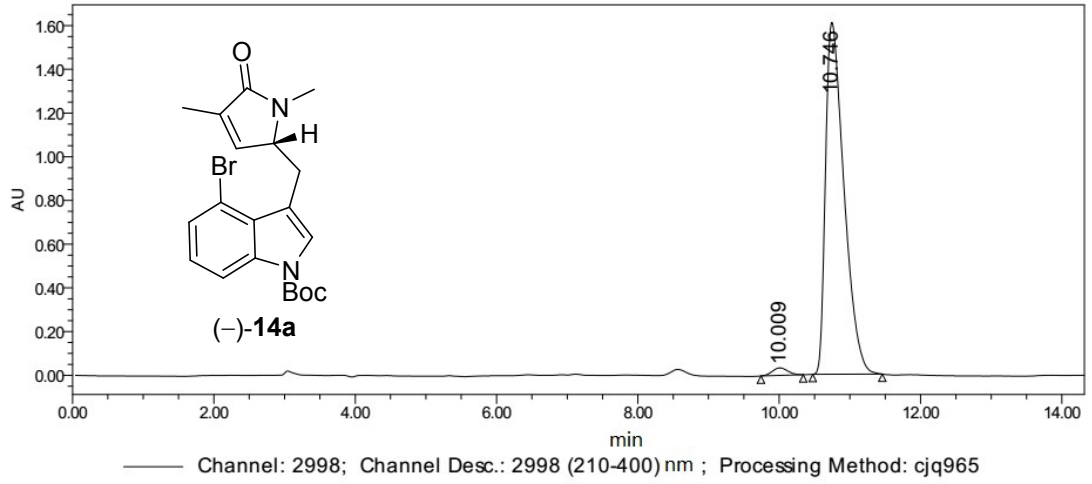
	Channel	Retention time (min)	Area (μv.s)	% Area	Height (μv)
1	2998 (210-400)	11.465	289269	0.68	19253
2	2998 (210-400)	13.414	42468521	99.32	1792717

Compound (±)-**13a** was prepared as the similar procedure of (–)-**13a**.

HPLC spectra of (±)-**14a** and (–)-**14a**



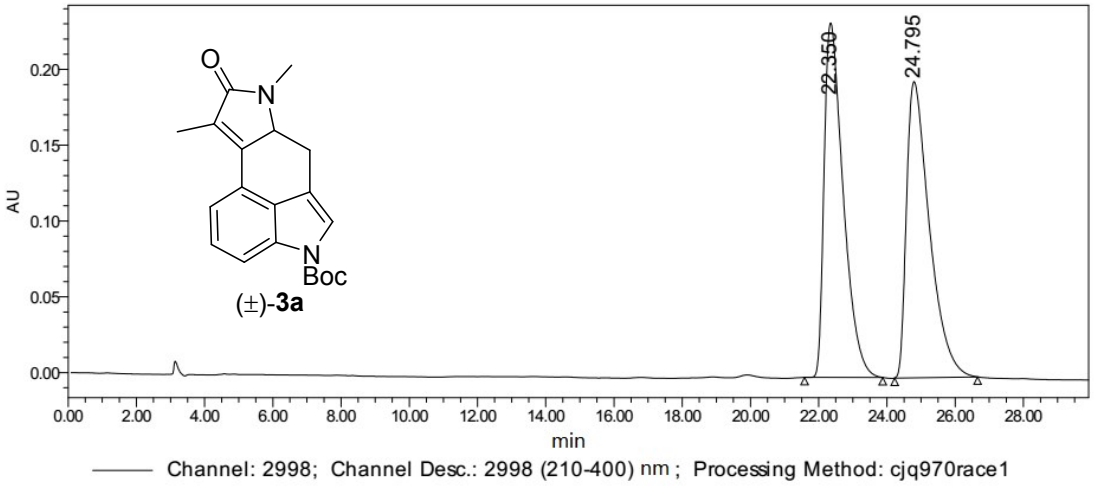
	Channel	Retention time (min)	Area (μv.s)	% Area	Height (μv)
1	2998 (210-400) nm	9.846	13024860	50.75	810568
2	2998 (210-400) nm	10.775	12640637	49.25	683480



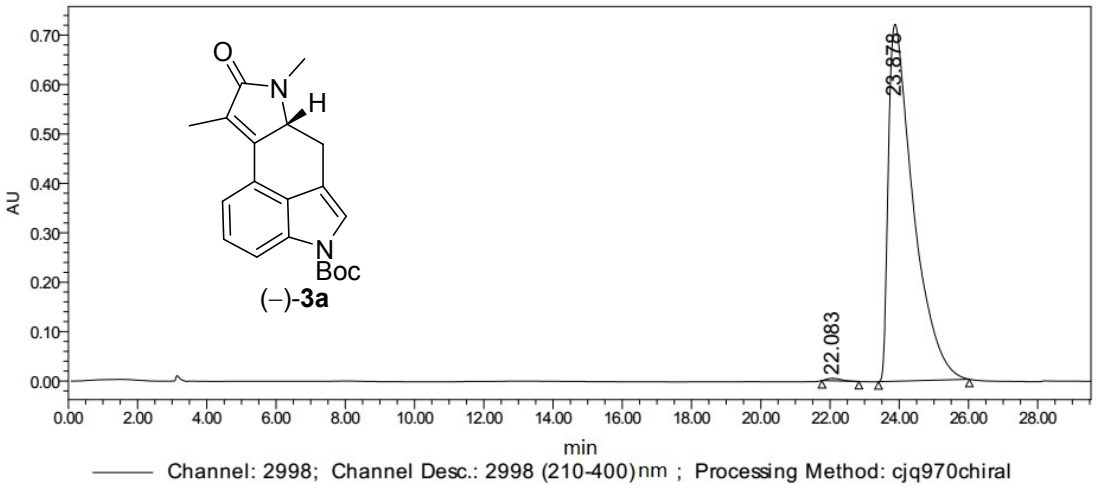
	Channel	Retention time (min)	Area (μv.s)	% Area	Height (μv)
1	2998 (210-400)	10.009	520064	1.75	34387
2	2998 (210-400)	10.746	29266191	98.25	1610825

Compound (±)-**14a** was prepared as the similar procedure of (–)-**14a**.

HPLC spectra of (±)-**3a** and (–)-**3a**



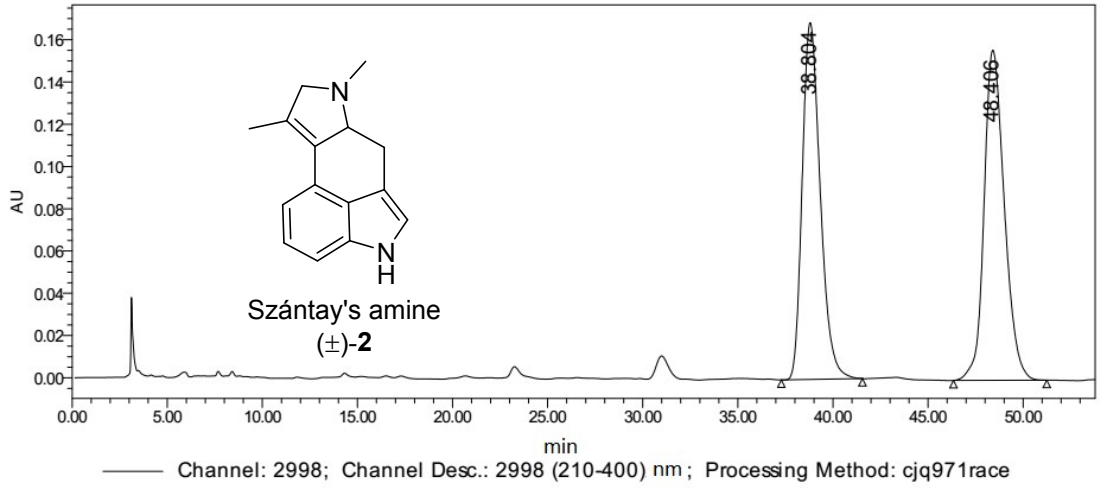
	Channel	Retention time (min)	Area (μv.s)	% Area	Height (μv)
1	2998 (210-400) nm	22.350	9076186	49.93	233673
2	2998 (210-400) nm	24.795	9102058	50.07	195288



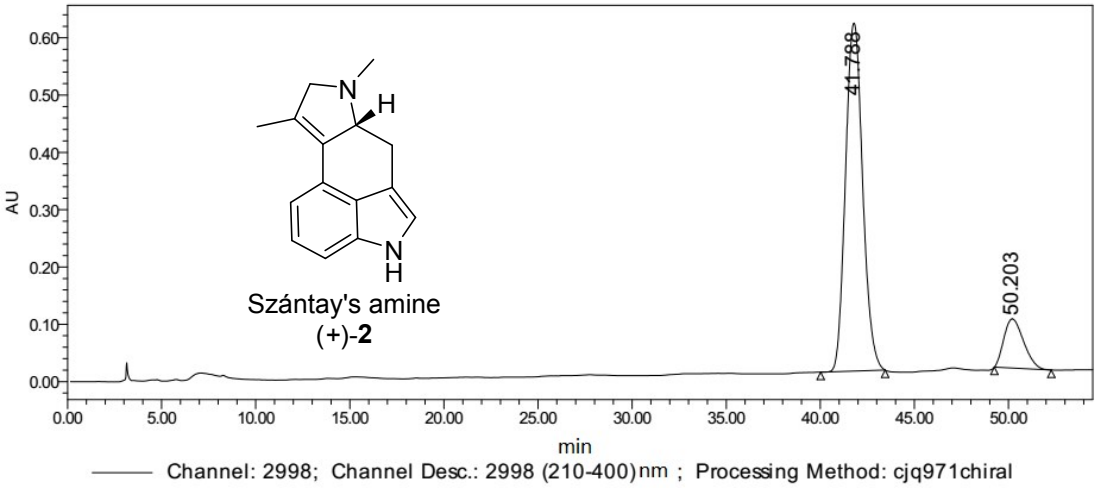
	Channel	Retention time (min)	Area (μv.s)	% Area	Height (μv)
1	2998 (210-400)	22.083	144614	0.40	5068
2	2998 (210-400)	23.878	36139714	99.60	722234

Compound (±)-**3a** was prepared as the similar procedure of (–)-**3a**.

HPLC spectra of Szántay's amine (±)-**2** and (+)-**2**

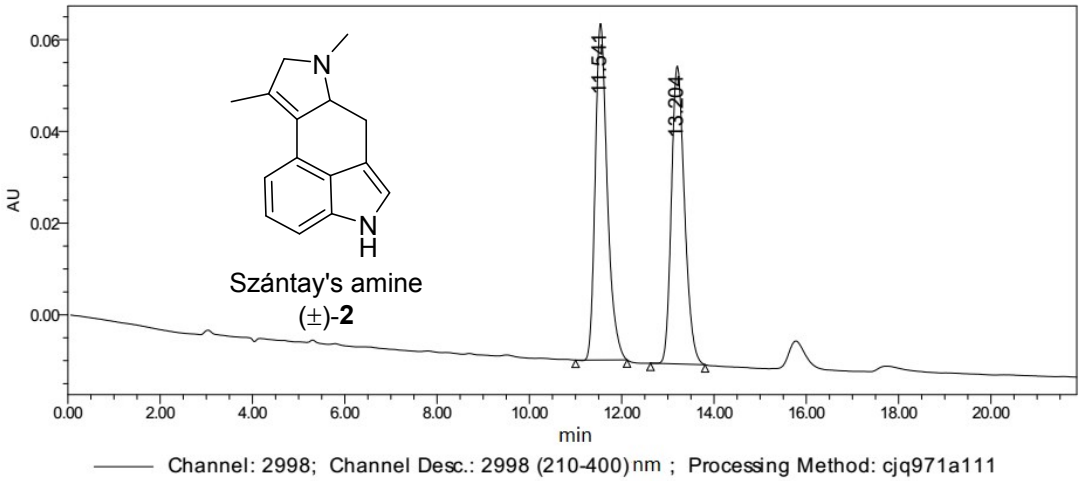


	Channel	Retention time (min)	Area (μv.s)	% Area	Height (μv)
1	2998 (210-400) nm	38.804	11096163	48.95	168779
2	2998 (210-400) nm	48.406	11574312	51.05	156205

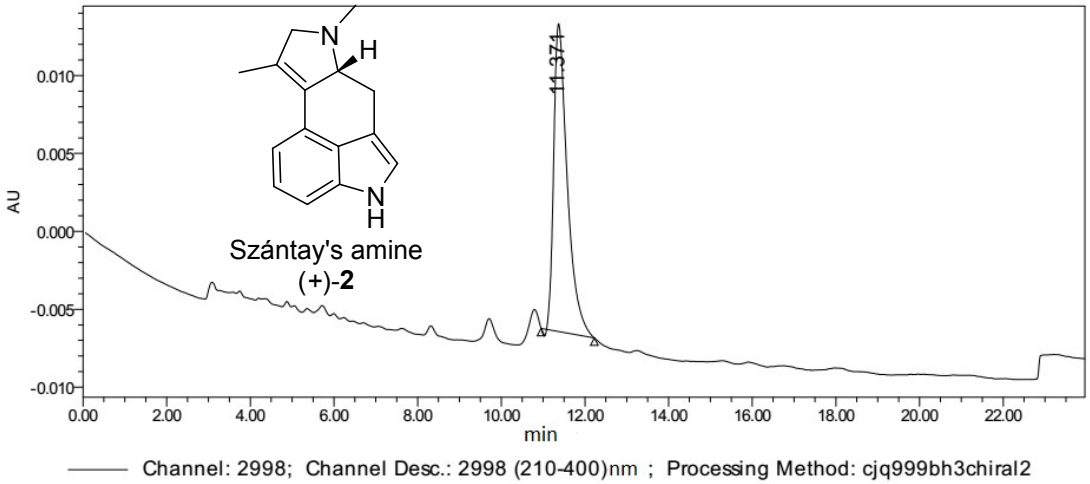


	Channel	Retention time (min)	Area (μv.s)	%Area	Height (μv)
1	2998 (210-400) nm	41.788	38511573	86.06	607030
2	2998 (210-400) nm	50.203	6237336	13.94	85687

Szántay's amine (±)-**2** was prepared as the similar procedure of Szántay's amine (+)-**2**. Reduction reaction of (–)-**3a** was heated under reflux overnight. The enantiomeric excess of Szántay's amine (+)-**2** was determined using a chiral HPLC (AD-H column, *n*-hexane/*i*-PrOH = 97:3, 1 mL/min) to be 72% after purification by flash column chromatography.



	Channel	Retention time (min)	Area (μv.s)	% Area	Height (μv)
1	2998 (210-400)nm	11.541	1333603	50.93	73364
2	2998 (210-400)nm	13.204	1285070	49.07	64929



	Channel	Retention time (min)	Area (μv.s)	% Area	Height (μv)
1	2998 (210-400)	11.371	447146	100.00	19747

The reduction reaction time of (–)-**3a** was shortened to 2 hours. The enantiomeric excess Szántay's amine (+)-**2** was determined using a chiral HPLC (AD-H column, *n*-hexane/*i*-PrOH = 92:8, 1 mL/min) to be more than 99% after purification by flash column chromatography.