Supporting information

Bis(imidazolidine)pyridine-$NiCl_2$ Catalyst for Nitro-Mannich Reaction of Isatin-derived *N*-Boc Ketimines: Asymmetric Synthesis of Chiral 3-Substituted 3-Amino-2-oxindoles

Takayoshi Arai,*,† Eri Matsumura,† Hyuma Masu‡

†Department of Chemistry, Graduate School of Science, Chiba University
1-33 Yayoi, Inage, Chiba 263-8522, Japan
‡Center for Analytical Instrumentation, Chiba University, Inage, Chiba 263-8522, Japan

Contents

1. General

Dry solvents were purchased from commercial suppliers and used without further purification. Analytical thin-layer chromatography (TLC) was performed on glass plates coated with 0.25 mm 230-400 mesh silica gel containing a fluorescent indicator (Merck, #1.05715.0009). Silica gel column chromatography was performed on Kanto silica gel 60 (spherical, 100-210 μm). ^{1}H NMR spectra were recorded on JEOL ECS-400 (400 MHz), ECA-500 (500 MHz) spectrometers. Chemical shifts of ^{1}H NMR spectra were reported relative to tetramethylsilane (δ 0). ^{13}C NMR spectra were recorded on JEOL ECS-400 (100 MHz), ECA-500 (125 MHz) spectrometers. Chemical shifts of ^{13}C NMR spectra were reported relative to $CDCl_3$ (δ 77.0), acetone-d_6 (δ 29.84) or DMSO-d_6 (δ 39.52). Splitting patterns were reported as s, singlet; d, doublet; t, triplet; q, quartet; dd, double doublet; m, multiplet; br, broad.

General experimental details for synthesis of PyBidine ligand have been described.[1)] Substrates were synthesized according to known procedure.[2, 3)]

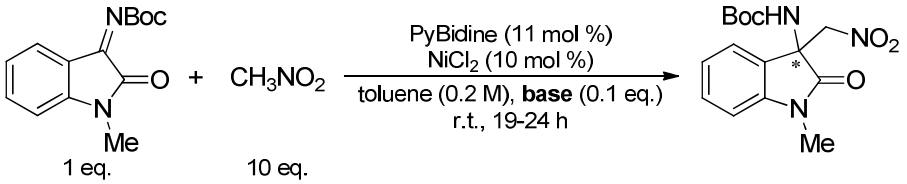
(1) Arai, T.; Mishiro, A.; Yokoyama, N.; Suzuki, K.; Sato, H. *J. Am. Chem. Soc.* **2010**, *132*, 5338.
(2) Hara, N.; Nakamura, S.; Sano, M.; Tamura, R.; Funahashi, Y.; Shibata, N. *Chem. Eur. J.* **2012**, *18*, 9276.
(3) Matestic, L.; Locke, J. M.; Vine, K. L.; Ranson, M.; Bremner, J. B.; Skropeta, D. *Tetrahedron* **2012**, *68*, 6810.

2. General procedure for enantioselective nitro-Mannich reaction

PyBidine (0.011 mmol) and $NiCl_2$ (0.01 mmol) were added to a two-necked round-bottomed flask containing a stir bar under Ar. Dichloromethane (2.00 mL) was added to the flask and the mixture was stirred for 6 hours. After removal of the solvent under reduced pressure, toluene (1.00 mL) was added as a reaction solvent. To the resulting solution, nitromethane (2.00 mmol), DIPEA (0.02 mmol) and *N*-Boc ketimine (0.20 mmol) were added at 30 ºC. After being stirred for appropriate time, the reaction mixture was quenched by water, extracted with ethyl acetate, dried with Na_2SO_4. After removal of the solvent under reduced pressure, the resulting crude mixture was purified by silica gel column chromatography to give the product. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC by using Daicel Chiralcel OD-H and Chiralpak AD-H columns.

3. Optimization of reaction condition

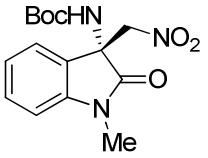
Table S1. Effect of base



entry	base	yield (%)	ee (%)
1	**DIPEA**	**99**	**95**
2	TEA	99	95
3	K_2CO_3	92	79
4	-	31	90

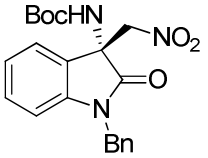
4. Analytical data for product of nitro-Mannich reaction

(*R*)-*tert*-butyl (1-methyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (2a)



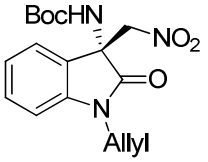
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32 (s, 9H), 3.28 (s, 3H), 4.60 (d, *J*= 12.2 Hz, 1H), 4.92 (d, *J*= 12.5 Hz, 1H), 5.96 (s, 1H), 6.90 (d, *J*= 7.0 Hz, 1H), 7.08-7.12 (m, 1H), 7.36-7.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.86, 28.04, 59.79, 77.81, 81.18, 108.88, 123.47, 124.28, 125.82, 130.40, 143.25, 153.65, 172.64; HRMS (ESI+) calcd for $C_{15}H_{18}O_5N_3$ $(M-H)^-$ 320.1252: found 320.1259; enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); minor enantiomer Rt= 10.1 min, major enantiomer Rt= 15.4 min; $[\alpha]_D^{18}$= -6.0 (*c*= 1.0, $CHCl_3$, 94% ee).

(*R*)-*tert*-butyl (1-benzyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (2b)



^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (s, 9H), 4.66 (d, *J*= 12.2 Hz, 1H), 4.88 (d, *J*= 15.4 Hz, 1H), 4.97-5.07 (m, 2H), 5.92 (s, 1H), 6.77 (d, *J*= 7.9 Hz, 1H), 7.04-7.08 (m, 1H), 7.23-7.38 (m, 6H), 7.45 (d, *J*= 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.09, 44.51, 59.87, 77.76, 81.26, 109.95, 123.45, 124.47, 125.80, 127.34, 127.85, 128.89, 130.29, 135.02, 142.43, 153.74, 172.87; HRMS (ESI+) calcd for $C_{21}H_{22}O_5N_3$ $(M-H)^-$ 396.1565: found 396.1572; enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (hexane:2-propanol= 70:30, 1.0 ml/min, 254 nm); minor enantiomer Rt= 9.3 min, major enantiomer Rt= 16.4 min; $[\alpha]_D^{20}$= -5.9 (*c*= 1.0, $CHCl_3$, 84% ee).

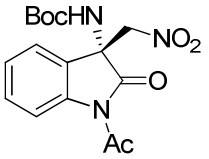
(*R*)-*tert*-butyl (1-allyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (2c)



^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (s, 9H), 4.28-4.33 (m, 1H), 4.47 (dd, *J*= 5.0, 16.3 Hz, 1H), 4.64 (d, *J*= 12.5 Hz, 1H), 5.00 (d, *J*= 12.5 Hz, 1H), 5.25-5.29 (m, 1H), 5.32-5.38 (m, 1H), 5.80-5.91 (m,

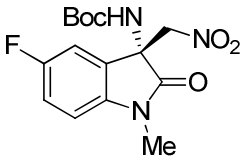
2H), 6.89 (d, *J*= 7.7 Hz, 1H), 7.06-7.11 (m, 1H), 7.32-7.36 (m, 1H), 7.47 (d, *J*= 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.09, 43.00, 59.75, 77.73, 81.22, 109.81, 118.28, 123.40, 124.58, 125.76, 130.29, 130.65, 142.54, 153.71, 172.54; HRMS (ESI+) calcd for $C_{17}H_{20}O_5N_3$ $(M-H)^-$ 346.1408: found 346.1421; enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); minor enantiomer Rt= 8.6 min, major enantiomer Rt= 10.9 min; $[\alpha]_D^{21}$= -4.8 (*c*= 1.0, $CHCl_3$, 84% ee).

(*R*)-*tert*-butyl (1-acetyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (2d)



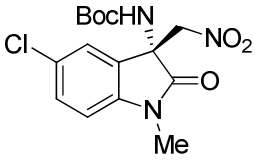
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (s, 9H), 2.71 (s, 3H), 4.68 (d, *J*= 12.5 Hz, 1H), 4.81 (d, *J*= 12.5 Hz, 1H), 6.18 (s, 1H), 7.22-7.26 (m, 1H), 7.33-7.35 (m, 1H), 7.41-7.46 (m, 1H), 8.28 (d, *J*= 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.60, 27.95, 60.19, 78.19, 81.98, 117.04, 122.98, 125.06, 125.87, 130.86, 139.88, 153.49, 170.40, 173.53; HRMS (ESI+) calcd for $C_{16}H_{18}O_6N_3$ $(M-H)^-$ 348.1201: found 348.1210; enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); major enantiomer Rt= 13.5 min, minor enantiomer Rt= 23.7 min; $[\alpha]_D^{22}$= -11.5 (*c*= 0.5, $CHCl_3$, 57% ee).

(*R*)-*tert*-butyl (5-fluoro-1-methyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (2e)



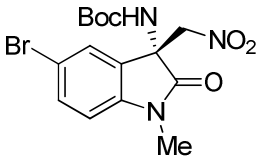
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (s, 9H), 3.27 (s, 3H), 4.62 (d, *J*= 12.5 Hz, 1H), 4.96 (d, *J*= 12.5 Hz, 1H), 5.90 (s, 1H), 6.84 (dd, *J*= 4.1, 8.6 Hz, 1H), 7.07-7.12 (m, 1H), 7.24-7.27 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.01, 28.05, 59.87, 77.43, 81.48, 109.53 (d, *J*= 7.6 Hz), 112.97 (d, *J*= 24.8 Hz), 116.75 (d, *J*= 22.9 Hz), 127.29 (d, *J*= 6.7 Hz), 139.31, 153.67, 159.41 (d, *J*= 242.2 Hz), 172.44; HRMS (ESI+) calcd for $C_{15}H_{17}O_5N_3F$ $(M-H)^-$ 338.1158: found 338.1169; enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (hexane:2-propanol= 80:20, 1.0 ml/min, 254 nm); major enantiomer Rt= 12.4 min, minor enantiomer Rt= 14.9 min; $[\alpha]_D^{19}$= -2.5 (*c*= 1.0, $CHCl_3$, 82% ee).

(*R*)-*tert*-butyl (5-chloro-1-methyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (2f)



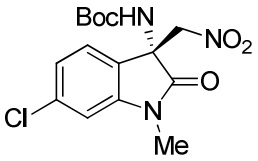
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (s, 9H), 3.27 (s, 3H), 4.60 (d, *J*= 12.7 Hz, 1H), 4.93 (d, *J*= 12.7 Hz, 1H), 5.87 (s, 1H), 6.83 (d, *J*= 8.2 Hz, 1H), 7.35-7.38 (m, 1H), 7.44 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.00, 28.06, 59.69, 77.42, 81.55, 109.88, 124.93, 127.41, 128.91, 130.37, 141.92, 153.63, 172.29; HRMS (ESI+) calcd for $C_{15}H_{17}O_5N_3Cl$ $(M-H)^-$ 354.0862: found 354.0873; enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); minor enantiomer Rt= 14.4 min, major enantiomer Rt= 20.4 min; $[\alpha]_D^{20}$= -19.4 (*c*= 1.0, $CHCl_3$, 88% ee).

(*R*)-*tert*-butyl (5-bromo-1-methyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (2g)



^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (s, 9H), 3.26 (s, 3H), 4.62 (d, *J*= 12.5 Hz, 1H), 4.92 (d, *J*= 12.7 Hz, 1H), 6.01 (s, 1H), 6.79 (d, *J*= 8.2 Hz, 1H), 7.49-7.52 (m, 1H), 7.56 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.92, 28.02, 59.59, 77.38, 81.50, 110.33, 116.01, 127.48, 127.76, 133.24, 142.41, 153.60, 172.18; HRMS (ESI+) calcd for $C_{15}H_{17}O_5N_3Br$ $(M-H)^-$ 398.0357: found 398.0367; enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); major enantiomer Rt= 25.5 min, minor enantiomer Rt= 29.5 min; $[\alpha]_D^{18}$= -27.8 (*c*= 1.0, $CHCl_3$, 80% ee).

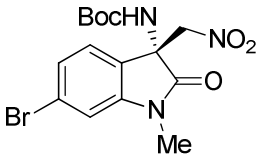
(*R*)-*tert*-butyl (6-chloro-1-methyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (2h)



^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (s, 9H), 3.27 (s, 3H), 4.57 (d, *J*= 12.2 Hz, 1H), 4.94 (d, *J*= 12.5 Hz, 1H), 5.87 (s, 1H), 6.91 (d, *J*= 1.6 Hz, 1H), 7.07 (dd, *J*= 1.8, 7.9 Hz, 1H), 7.36 (d, *J*= 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.00, 28.05, 59.41, 77.56, 81.46, 109.75, 123.32, 124.09, 125.43, 136.40, 144.55, 153.62, 172.66; HRMS (ESI+) calcd for $C_{15}H_{17}O_5N_3Cl$ $(M-H)^-$ 354.0862: found 354.0872; enantiomeric excess was determined by HPLC with a Chiralcel OD-H column

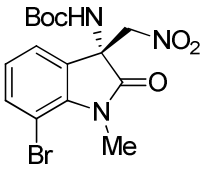
(hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); minor enantiomer Rt= 13.3 min, major enantiomer Rt= 20.7 min; $[\alpha]_D^{20}$= +5.7 (*c*= 1.0, $CHCl_3$, 86% ee).

(*R*)-*tert*-butyl (6-bromo-1-methyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (2i)



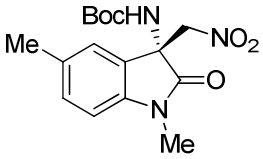
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (s, 9H), 3.26 (s, 3H), 4.57 (d, *J*= 12.5 Hz, 1H), 4.94 (d, *J*= 12.5 Hz, 1H), 5.92 (s, 1H), 7.06 (d, *J*= 1.6 Hz, 1H), 7.23 (dd, *J*= 1.6, 7.9 Hz, 1H), 7.30 (d, *J*= 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.00, 28.05, 59.47, 77.48, 81.48, 112.52, 124.27, 124.64, 125.70, 126.28, 144.62, 153.61, 172.54; HRMS (ESI+) calcd for $C_{15}H_{17}O_5N_3Br$ $(M-H)^-$ 398.0357: found 398.0374; enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); major enantiomer Rt= 16.3 min, minor enantiomer Rt= 18.4 min; $[\alpha]_D^{22}$= +9.3 (*c*= 1.0, $CHCl_3$, 81% ee).

(*R*)-*tert*-butyl (7-bromo-1-methyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (2j)



^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (s, 9H), 3.66 (s, 3H), 4.54 (d, *J*= 12.5 Hz, 1H), 4.87 (d, *J*= 12.5 Hz, 1H), 6.03 (s, 1H), 6.92-6.96 (m, 1H), 7.30 (d, *J*= 7.3 Hz, 1H), 7.49 (dd, *J*= 1.1, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.04, 30.61, 59.35, 77.84, 81.52, 103.25, 122.95, 124.55, 128.97, 136.07, 140.60, 153.49, 173.21; HRMS (ESI+) calcd for $C_{15}H_{17}O_5N_3Br$ $(M-H)^-$ 398.0357: found 398.0373; enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); minor enantiomer Rt= 22.5 min, major enantiomer Rt= 40.7 min; $[\alpha]_D^{20}$= +18.2 (*c*= 1.0, $CHCl_3$, 78% ee).

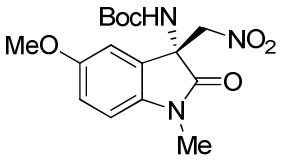
(*R*)-*tert*-butyl (1,5-dimethyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (2k)



^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (s, 9H), 2.33 (s, 3H), 3.26 (s, 3H), 4.58 (d, *J*= 12.5 Hz, 1H), 4.90 (d, *J*= 12.5 Hz, 1H), 5.91 (s, 1H), 6.79 (d, *J*= 7.9 Hz, 1H), 7.16-7.19 (m, 1H), 7.22 (s, 1H); ^{13}C

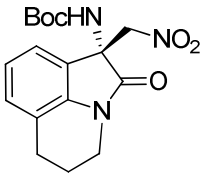
NMR (100 MHz, $CDCl_3$): δ 21.07, 26.87, 28.05, 59.89, 77.86, 81.10, 108.63, 124.93, 125.83, 130.64, 133.18, 140.82, 153.67, 172.54; HRMS (ESI+) calcd for $C_{16}H_{20}O_5N_3$ $(M-H)^-$ 334.1408: found 334.1420; enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); minor enantiomer Rt= 11.8 min, major enantiomer Rt= 14.7 min; $[\alpha]_D^{21}$= -20.4 (*c*= 1.0, $CHCl_3$, 95% ee).

(*R*)-*tert*-butyl (5-methoxy-1-methyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (2l)



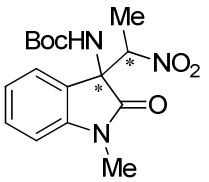
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (s, 9H), 3.26 (s, 3H), 3.78 (s, 3H), 4.59 (d, *J*= 12.5 Hz, 1H), 4.93 (d, *J*= 12.2 Hz, 1H), 5.89 (s, 1H), 6.81 (d, *J*= 8.4 Hz, 1H), 6.89-6.91 (m, 1H), 7.06 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.91, 28.05, 55.85, 60.09, 77.75, 81.17, 109.35, 111.51, 114.86, 127.03, 136.53, 153.68, 156.47, 172.32; HRMS (ESI+) calcd for $C_{16}H_{20}O_6N_3$ $(M-H)^-$ 350.1358: found 350.1368; enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); minor enantiomer Rt= 18.6 min, major enantiomer Rt= 21.0 min; $[\alpha]_D^{21}$= -22.6 (*c*= 1.0, $CHCl_3$, 92% ee).

(*R*)-*tert*-butyl
(1-(nitromethyl)-2-oxo-2,4,5,6-tetrahydro-1H-pyrrolo[3,2,1-ij]quinolin-1-yl)carbamate
(2m)



^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (s, 9H), 1.96-2.13 (m, 2H), 2.78-2.81 (m, 2H), 3.69-3.84 (m, 2H), 4.65 (d, *J*= 12.5 Hz, 1H), 4.99 (d, *J*= 12.2 Hz, 1H), 5.84 (s, 1H), 6.96-6.99 (m, 1H), 7.12 (dd, *J*= 0.7, 7.7 Hz, 1H), 7.24-7.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.81, 24.35, 28.10, 39.30, 60.89, 77.64, 81.02, 120.86, 122.58, 122.87, 124.42, 129.24, 139.10, 153.78, 171.44; HRMS (ESI+) calcd for $C_{17}H_{20}O_5N_3$ $(M-H)^-$ 346.1408: found 346.1422; enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane:2-propanol= 80:20, 1.0 ml/min, 254 nm); minor enantiomer Rt= 7.7 min, major enantiomer Rt= 13.4 min; $[\alpha]_D^{23}$= +13.0 (*c*= 1.0, $CHCl_3$, 94% ee).

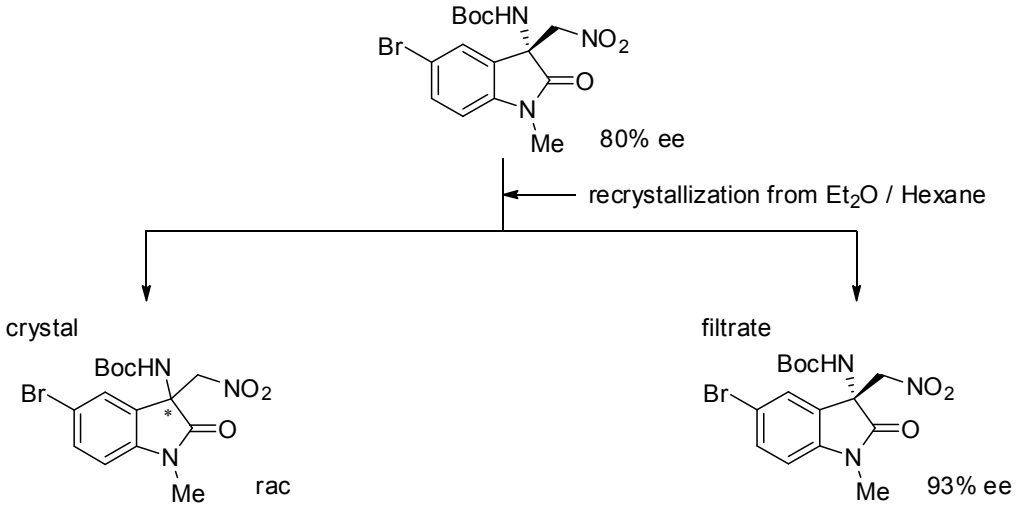
***tert*-butyl (1-methyl-3-(1-nitroethyl)-2-oxoindolin-3-yl)carbamate (2n)**



major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (s, 9H), 1.74 (d, *J*= 6.8 Hz, 3H), 3.26 (s, 3H), 4.66-4.68 (m, 1H), 6.11 (s, 1H), 6.88 (d, *J*= 7.9 Hz, 1H), 7.04-7.11 (m, 1H), 7.15-7.18 (m, 1H), 7.34-7.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 80/20 diastereomixture): δ 12.80, 13.02, 26.65, 26.75, 27.96, 29.62, 61.83, 62.74, 80.92, 84.66, 85.44, 108.41, 108.63, 122.96, 123.19, 123.36, 124.07, 126.92, 130.15, 130.25, 143.05, 144.00, 153.27, 153.78, 172.17, 173.11; HRMS (ESI+) calcd for $C_{16}H_{20}O_5N_3$ $(M-H)^-$ 334.1408: found 334.1420; enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); minor enantiomer Rt= 9.2 min, major enantiomer Rt= 22.8 min; $[\alpha]_D^{22}$= -40.2 (*c*= 1.0, $CHCl_3$, 80/20 diastereomixture, 90% ee).

minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (s, 9H), 1.74 (d, *J*= 6.8 Hz, 3H), 3.26 (s, 3H), 4.98-5.03 (m, 1H), 6.11 (s, 1H), 6.88 (d, *J*= 7.9 Hz, 1H), 7.04-7.11 (m, 1H), 7.15-7.18 (m, 1H), 7.34-7.40 (m, 1H); enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); minor enantiomer Rt= 7.7 min, major enantiomer Rt= 16.4 min.

5. X-ray crystallographic analysis of rac-2g



Scheme S1. Recrystallization of nitro-Mannich product 2g

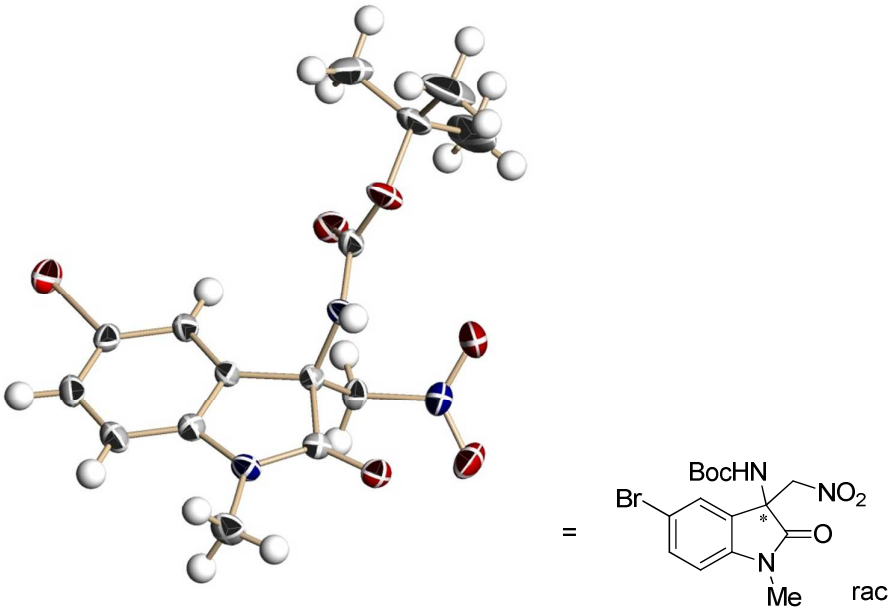
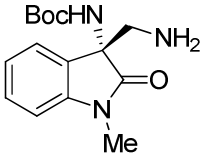


Figure S1. X-ray structure of *rac*. nitro-Mannich product 2g

6. Reduction of nitro group

Tert-butyl (1-methyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (**2a**, 0.19 mmol) and $NiCl_2 \cdot 6H_2O$ (0.19 mmol) were added to a two-necked round-bottomed flask containing a stir bar under Ar. Methanol (1.90 mL) was added to the flask and the mixture was stirred at 0 ºC. Sodium borohydride (2.28 mmol) was added and stirred for 40 min at 0 ºC. The reaction mixture was quenched by saturated NH_4Cl aq., extracted with dichloromethane, dried with Na_2SO_4. The resulting solution was concentrated under reduced pressure to afford adduct. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC by using Daicel Chiralpak AS-H column.

(*R*)-*tert*-butyl (3-(aminomethyl)-1-methyl-2-oxoindolin-3-yl)carbamate

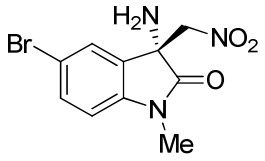


^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (s, 9H), 2.95 (s, 2H), 3.24 (s, 3H), 5.96 (s, 1H), 6.85 (d, *J*= 7.7 Hz, 1H), 7.05-7.09 (m, 1H), 7.26-7.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.23, 27.87, 48.21, 62.35, 79.99, 108.01, 122.26, 122.51, 128.70, 130.12, 143.17, 154.47, 176.48; HRMS (ESI+) calcd for $C_{15}H_{22}O_3N_3$ $(M+H)^+$ 292.1656: found 292.1651; enantiomeric excess was determined by HPLC with a Chiralpak AS-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm); major enantiomer Rt= 13.9 min, minor enantiomer Rt= 19.6 min; $[\alpha]_D^{21}$= -28.2 (*c*= 1.0, $CHCl_3$, 97% ee).

7. Deprotection of Boc group

Tert-butyl (5-bromo-1-methyl-3-(nitromethyl)-2-oxoindolin-3-yl)carbamate (**2g**, 0.17 mmol) was added to a round-bottomed flask containing a stir bar under air. Dichloromethane (3.40 mL) was added to the flask and the mixture was stirred at 0 ºC. TFA (1.70 mL) was added and stirred for 30 min at 0 ºC. The reaction mixture was concentrated under reduced pressure and azeotroped with toluene. The resulting crude mixture was purified by silica gel column chromatography to give the product. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC by using Daicel Chiralcel OD-H column.

(*R*)-3-amino-5-bromo-1-methyl-3-(nitromethyl)indolin-2-one

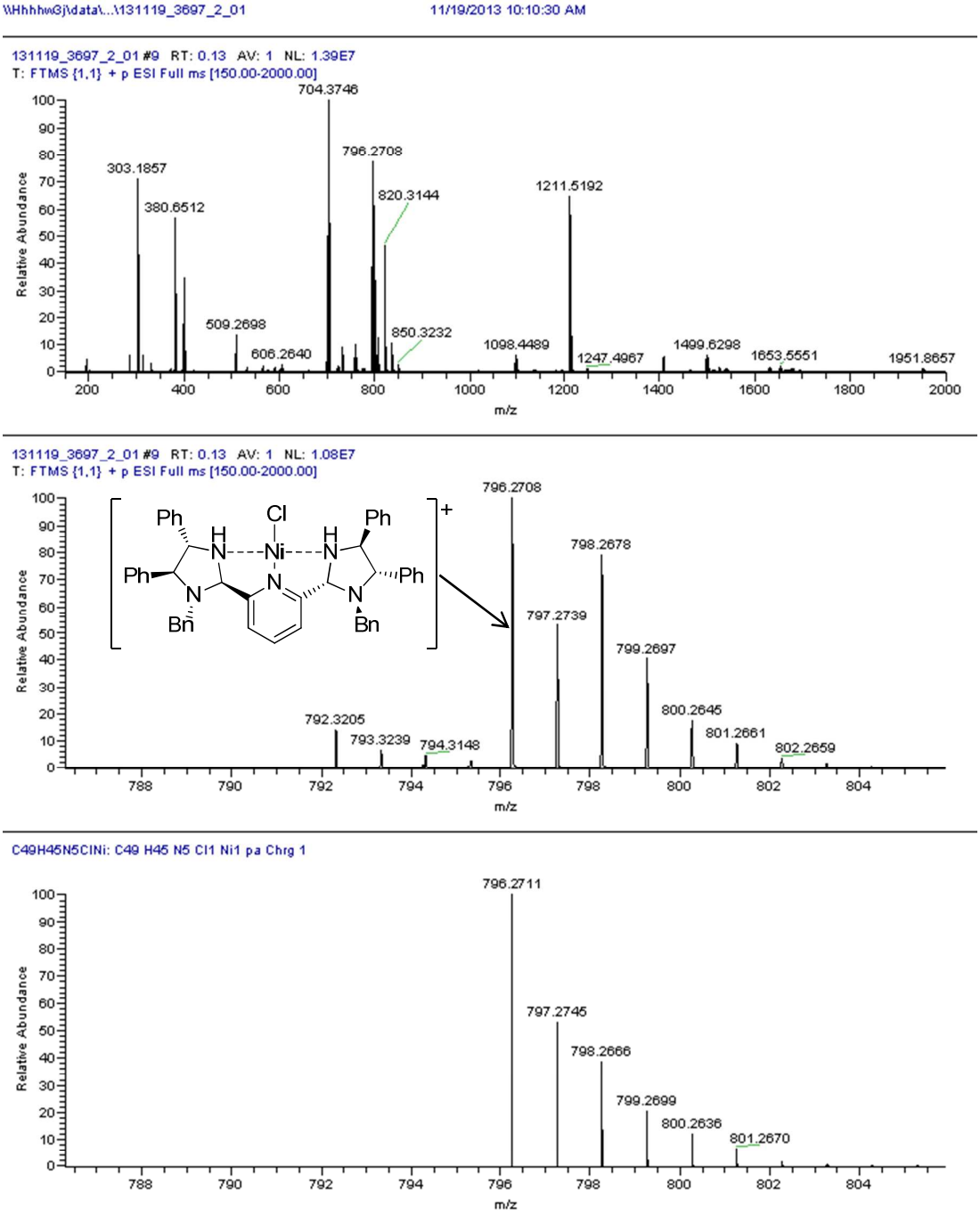


^{1}H NMR (400 MHz, $CDCl_3$): δ 3.25 (s, 3H), 4.78-4.78 (m, 2H), 6.78-6.80 (m, 1H), 7.50-7.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.69, 58.93, 79.11, 110.45, 115.92, 127.24, 129.29, 133.37, 142.82, 176.09; HRMS (ESI+) calcd for $C_{10}H_{11}O_3N_3Br$ $(M+H)^+$ 299.9978: found 299.9978; enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane:2-propanol= 70:30, 1.0 ml/min, 254 nm); minor enantiomer Rt= 19.6 min, major enantiomer Rt= 29.7 min; $[\alpha]_D^{19}$= -60.4 (*c*= 1.0, $CHCl_3$, 81% ee).

8. ESI-MS spectra

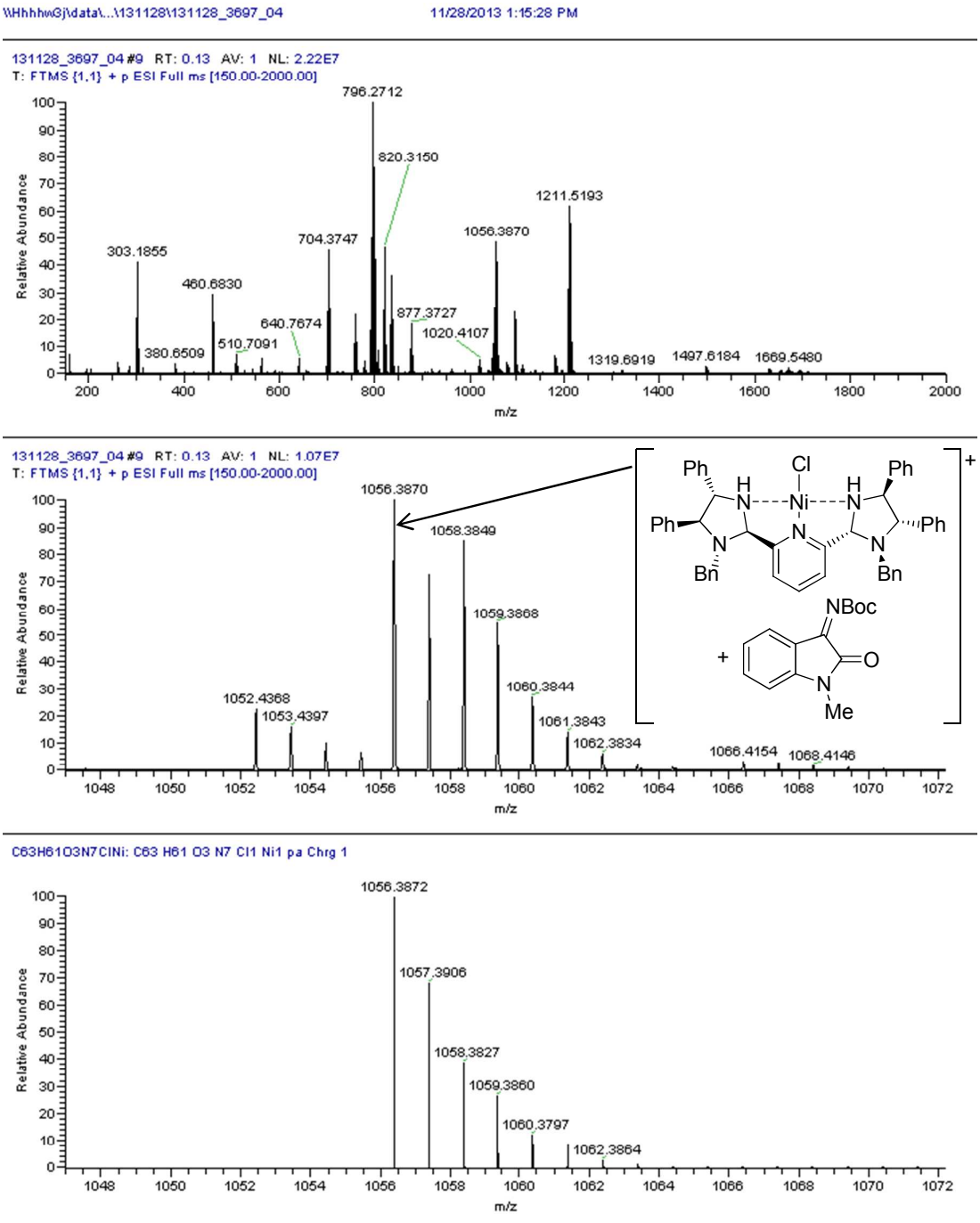
ESI-MS of PyBidine-$NiCl_2$ complex

HRMS (ESI+) calcd for $[PyBidine\text{-}NiCl]^+$ ($C_{49}H_{45}N_5ClNi$) 796.2711: found 796.2708.

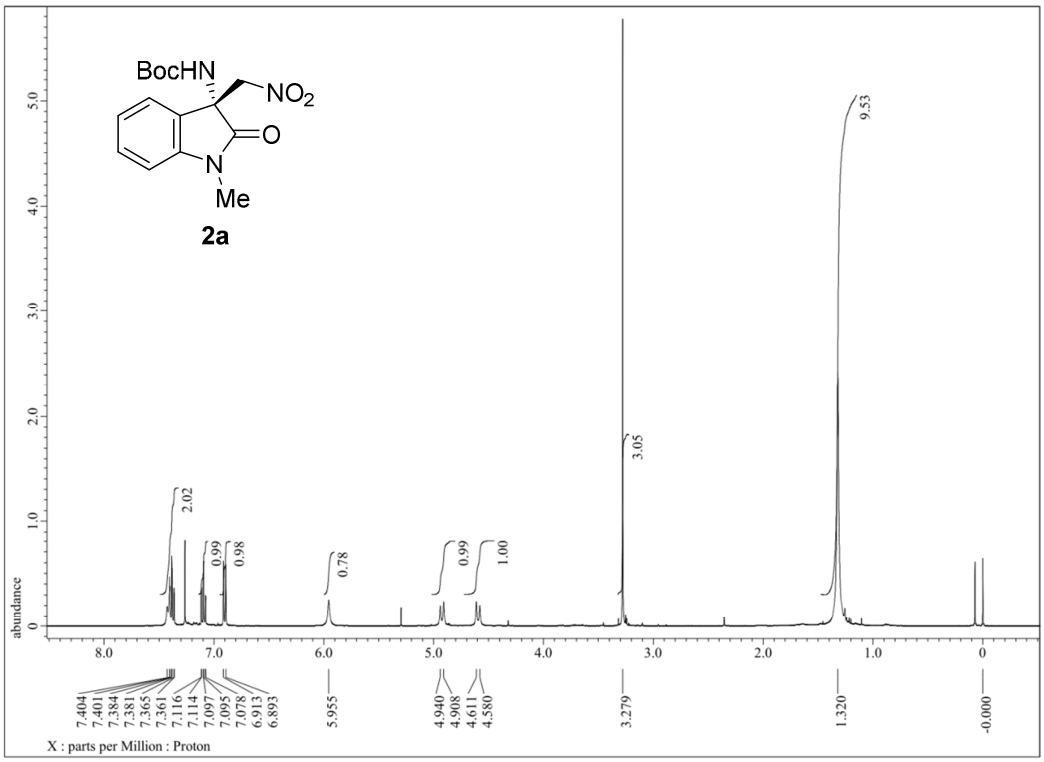


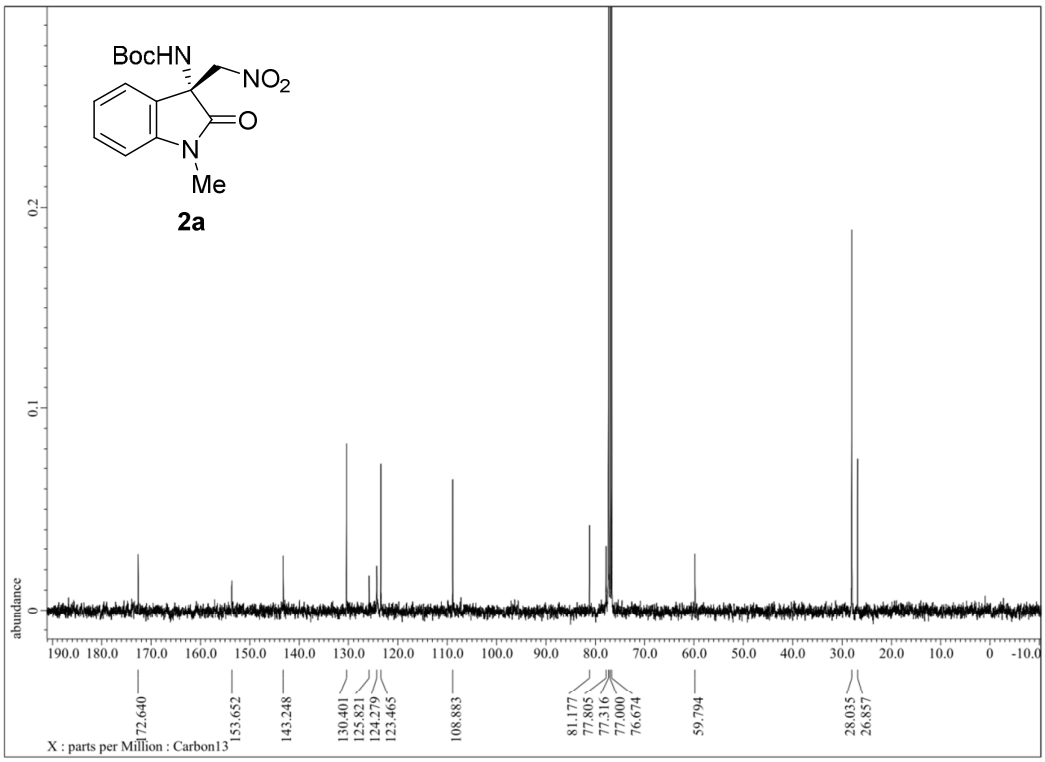
ESI-MS of PyBidine-$NiCl_2$ complex with isatin-derived *N*-Boc ketimine

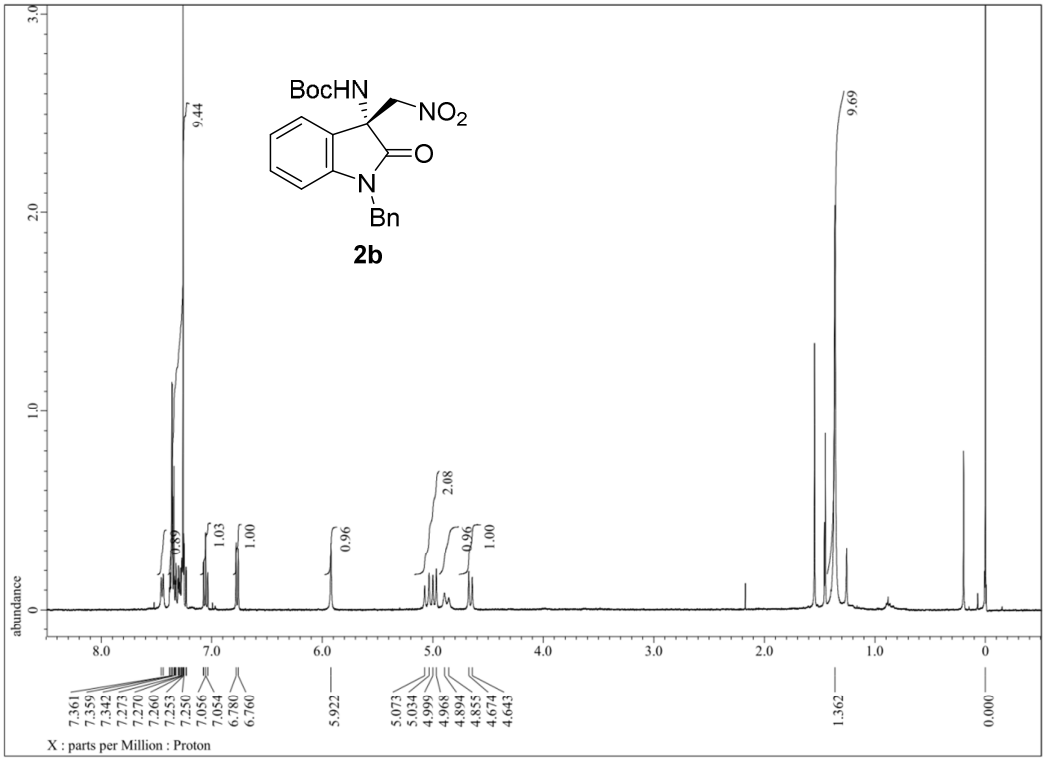
HRMS (ESI+) calcd for [PyBidine-NiCl + ketimine]$^+$ ($C_{63}H_{61}O_3N_7ClNi$) 1056.3872: found 1056.3870.

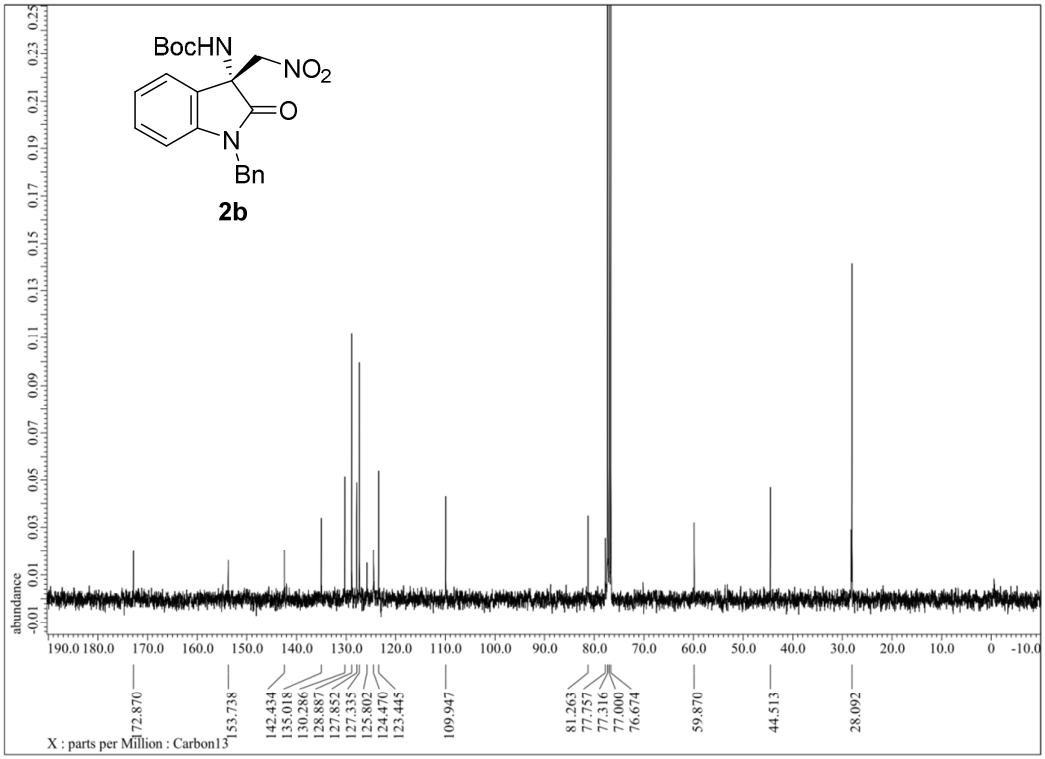


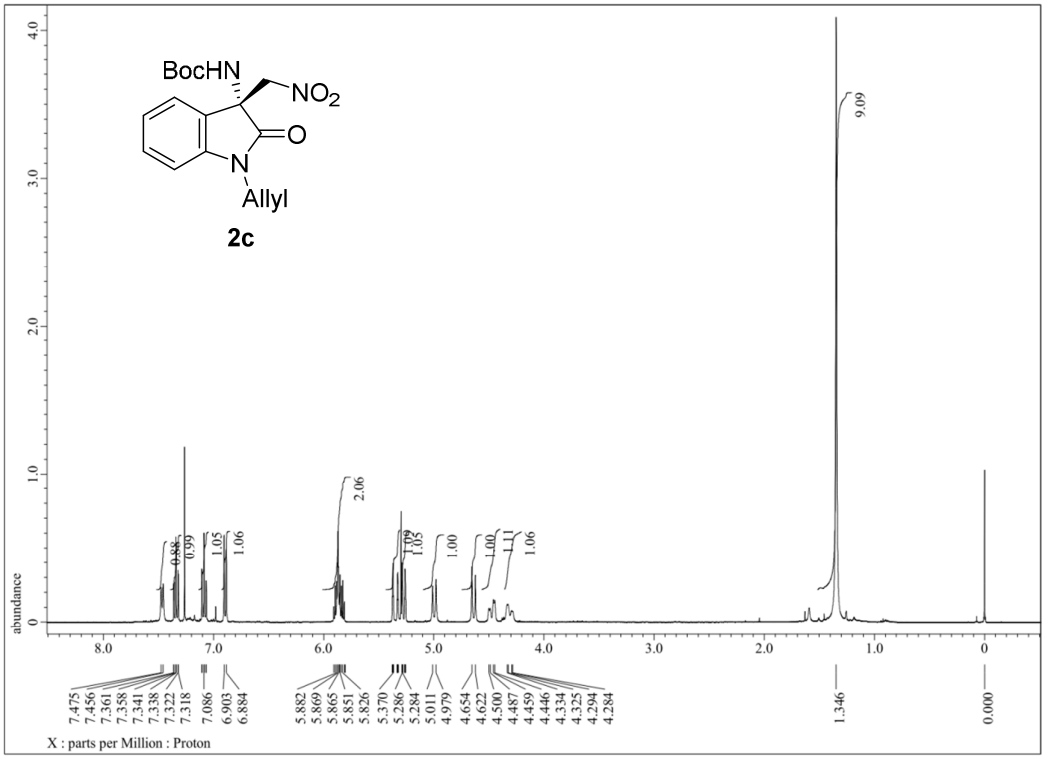
9. ^{1}H NMR and ^{13}C NMR spectra

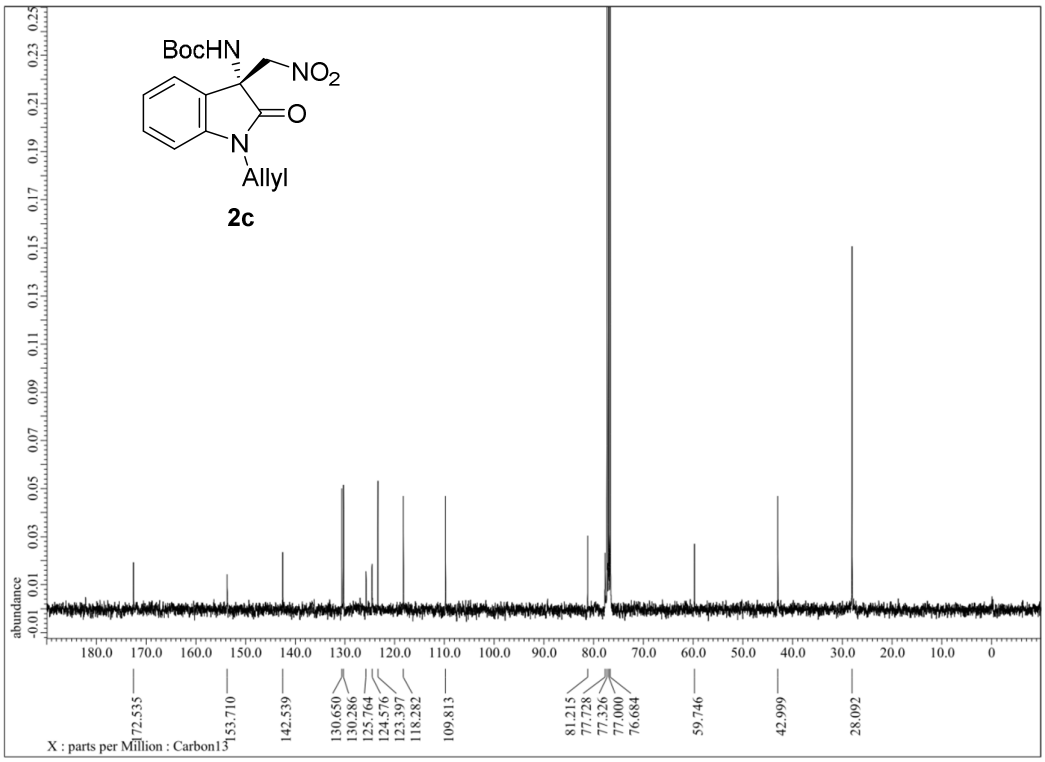


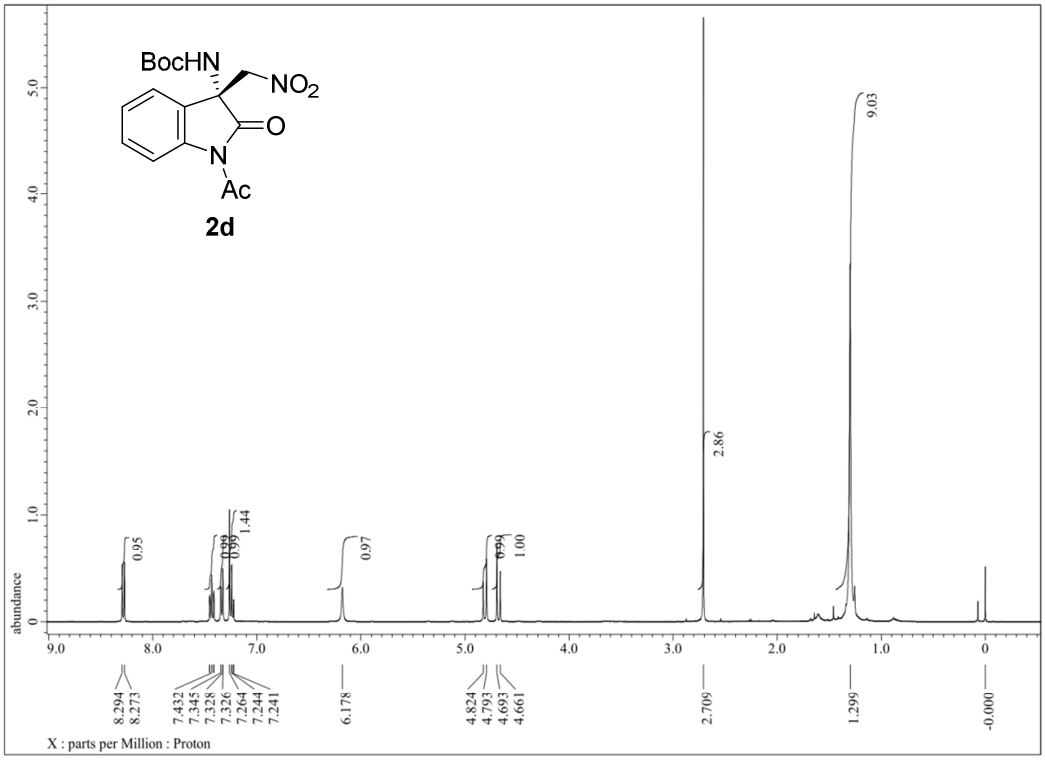


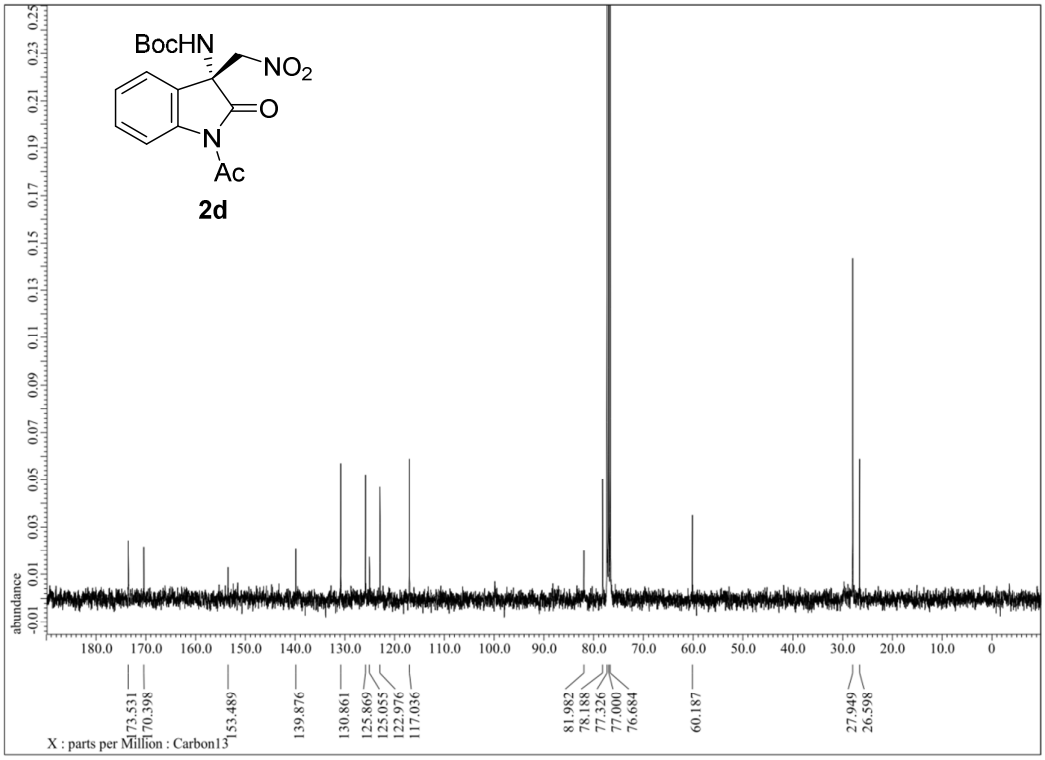

BocHN
NO2
O
N
Bn
2b
9.44
9.69
2.08
1.03
1.00
0.96
0.96
1.00
0.89
abundance
X : parts per Million : Proton

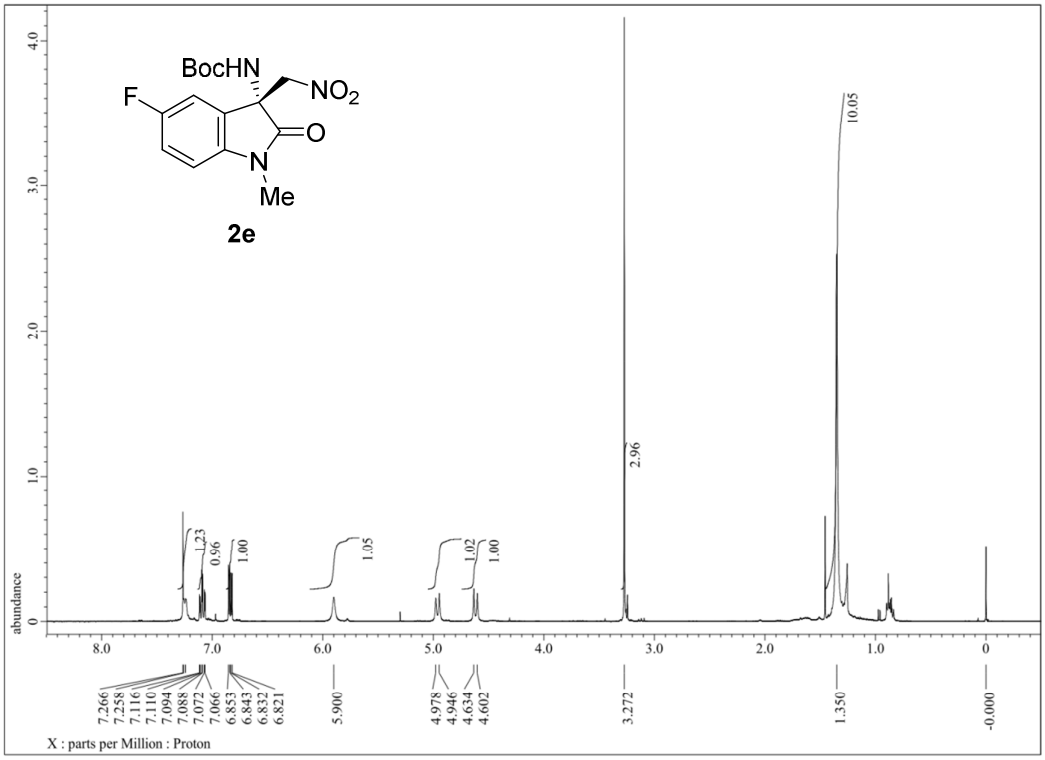

BocHN
NO2
O
N
Bn
2b
abundance
X : parts per Million : Carbon13

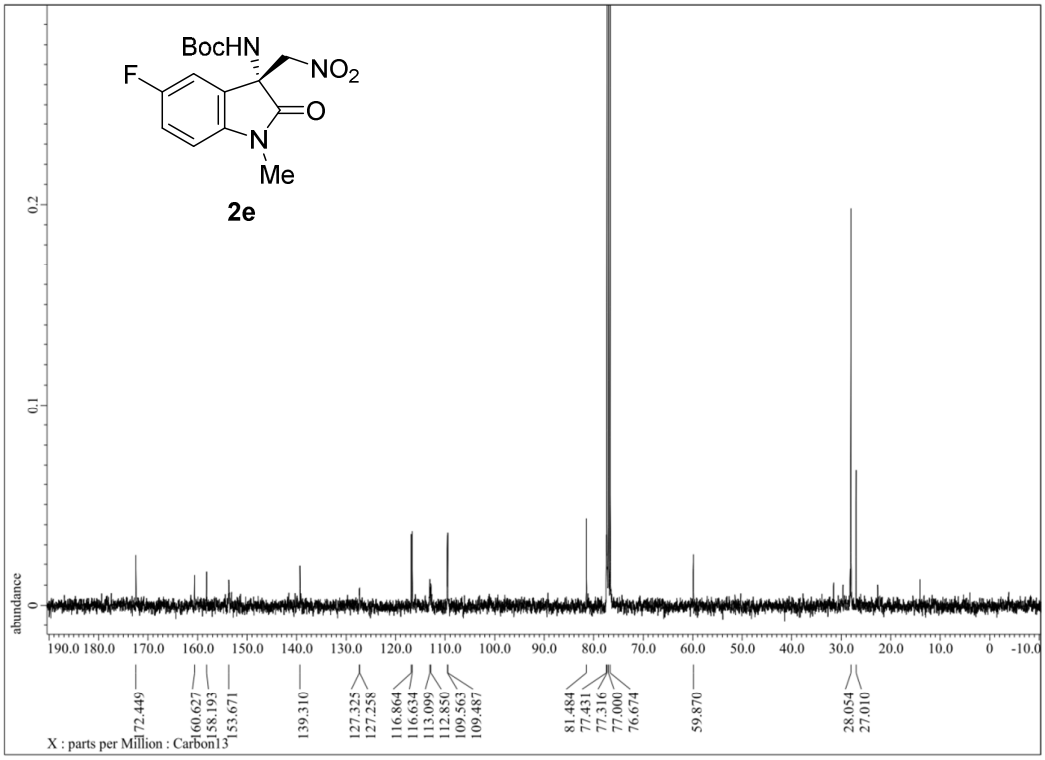

BocHN
NO2
O
N
Allyl
2c
abundance
X : parts per Million : Proton

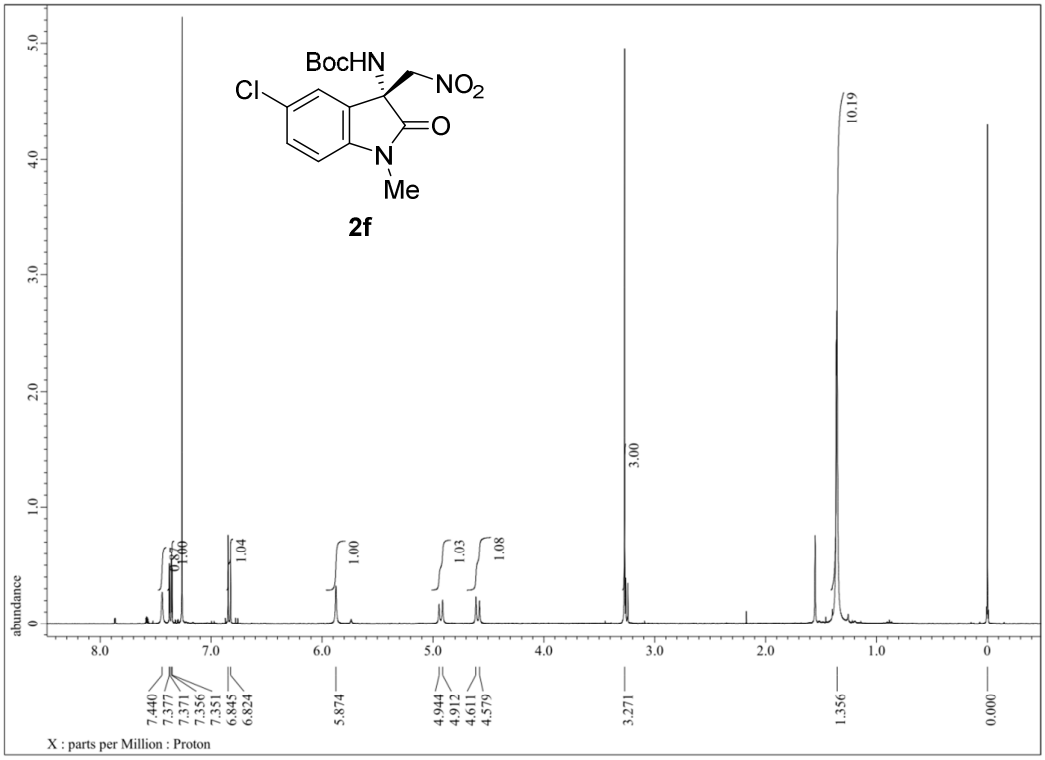

BocHN
NO2
O
N
Allyl
2c
abundance
X : parts per Million : Carbon13

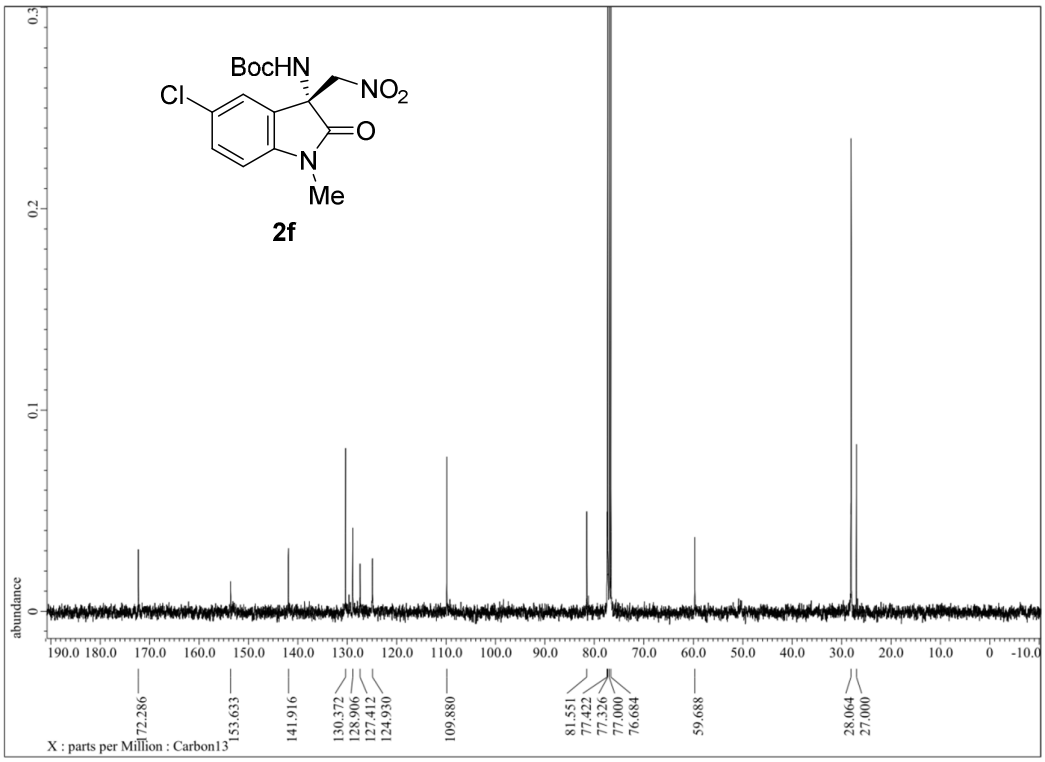

BocHN
NO2
O
N
Ac
2d
abundance
X : parts per Million : Proton

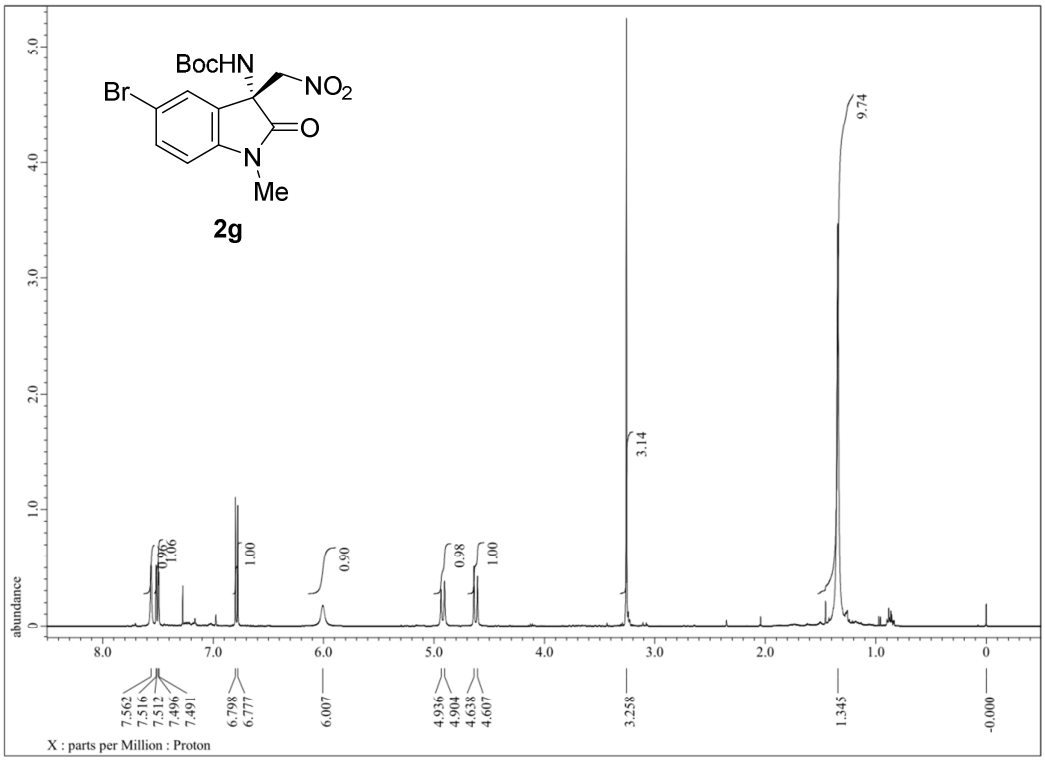

BocHN
NO2
O
N
Ac
2d
abundance
X : parts per Million : Carbon13

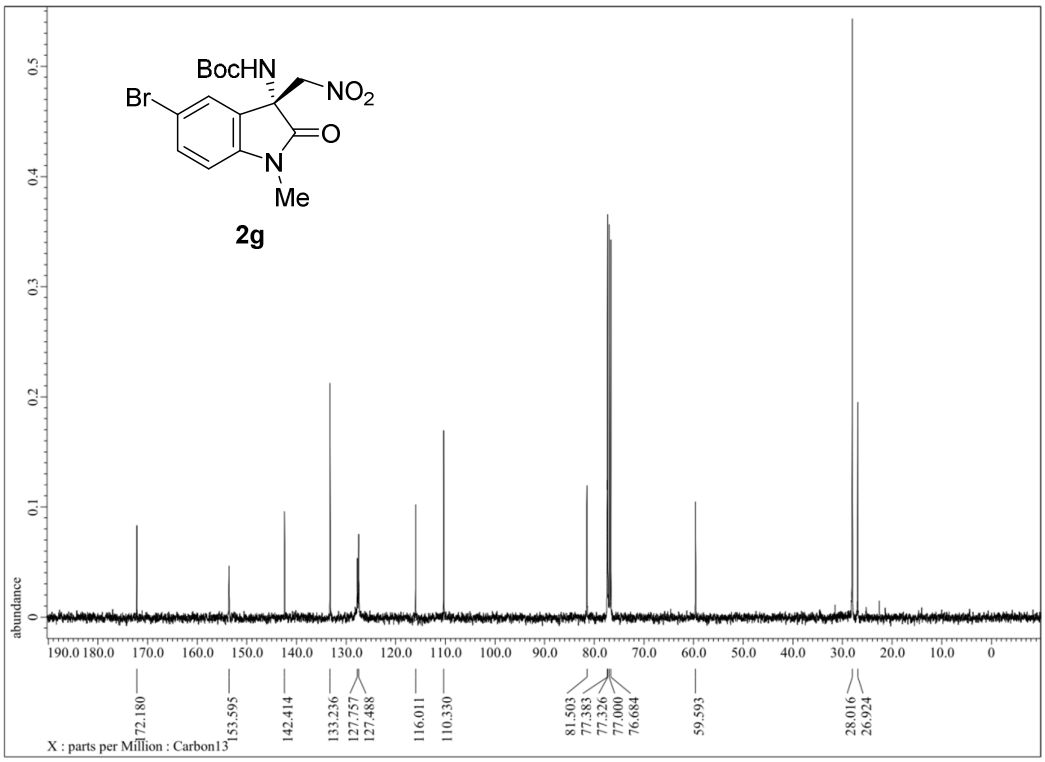

BocHN
NO2
F
O
N
Me
2e
abundance
X : parts per Million : Proton

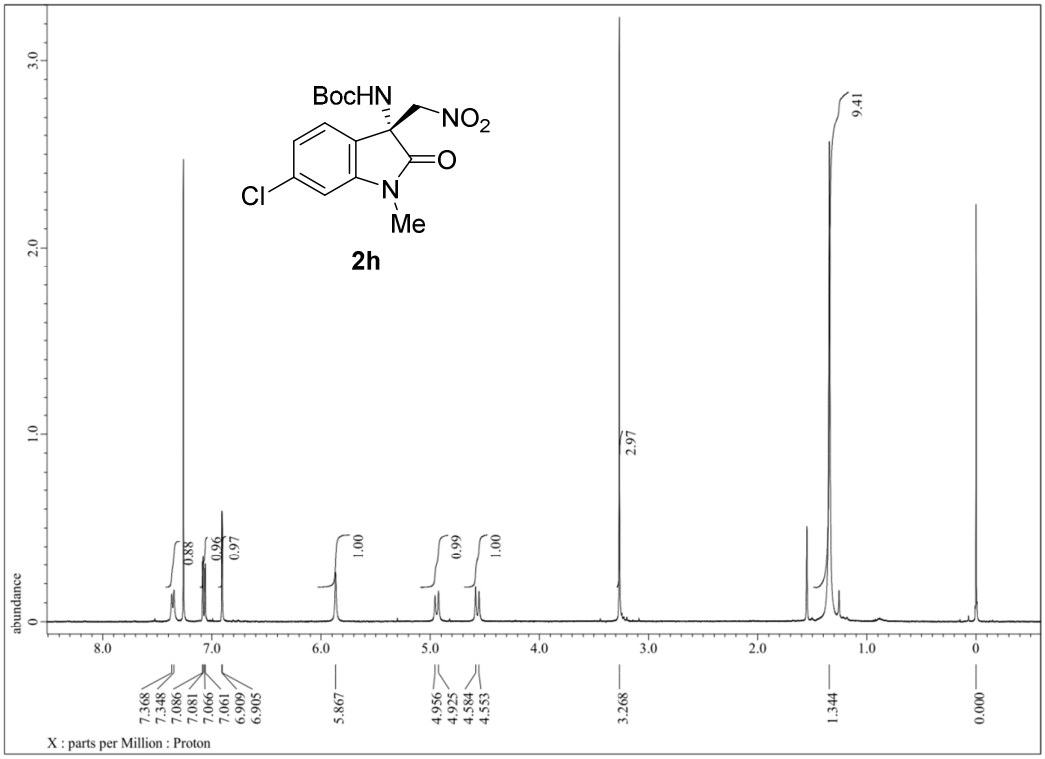

BocHN
NO2
F
O
N
Me
2e
abundance
X : parts per Million : Carbon13

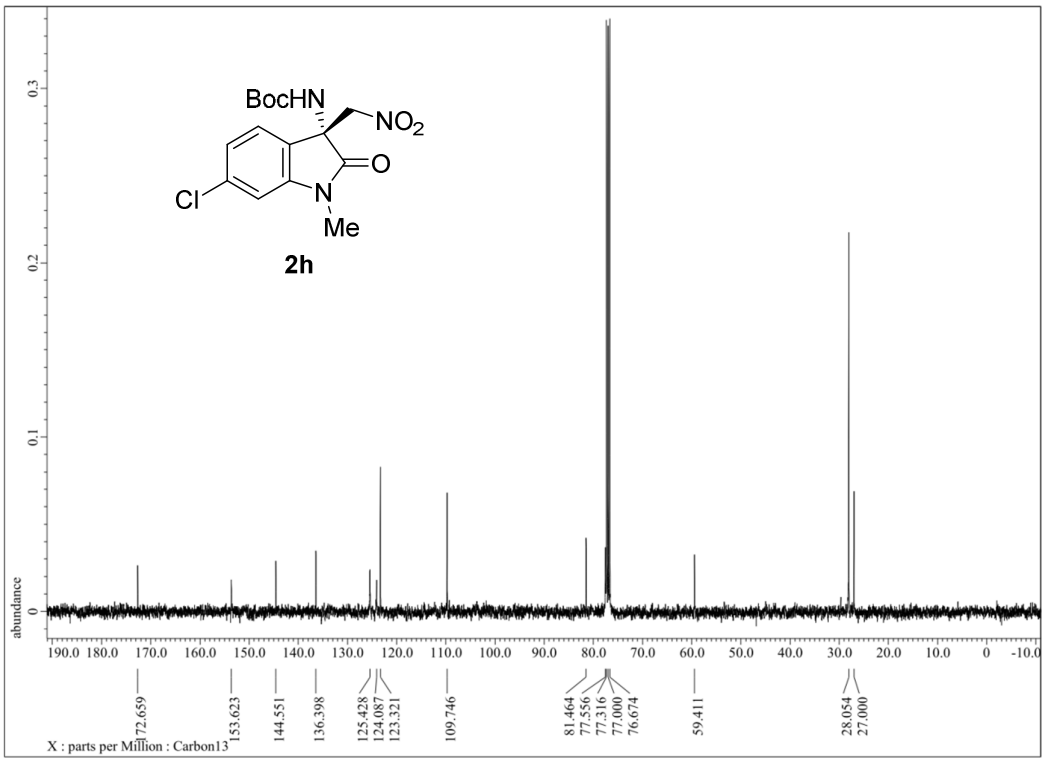

BocHN
NO2
Cl
O
N
Me
2f
abundance
X : parts per Million : Proton

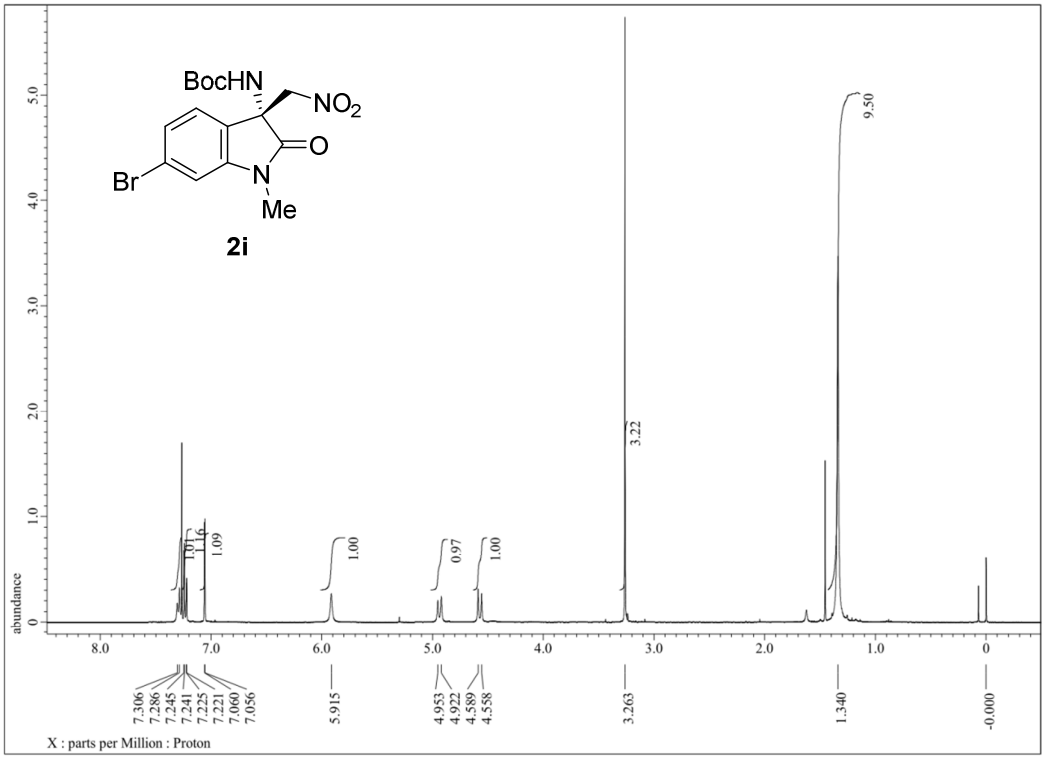

BocHN
NO2
Cl
O
N
Me
2f
abundance
X : parts per Million : Carbon13

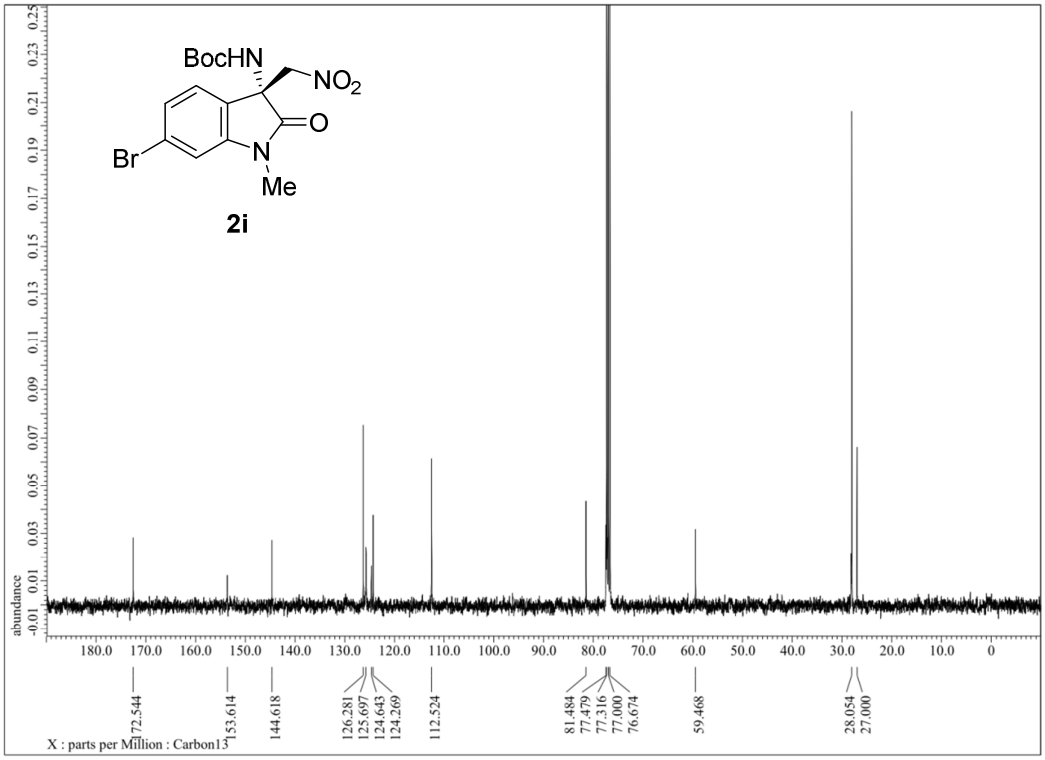

BocHN
Br
NO2
O
N
Me
2g
abundance
X : parts per Million : Proton

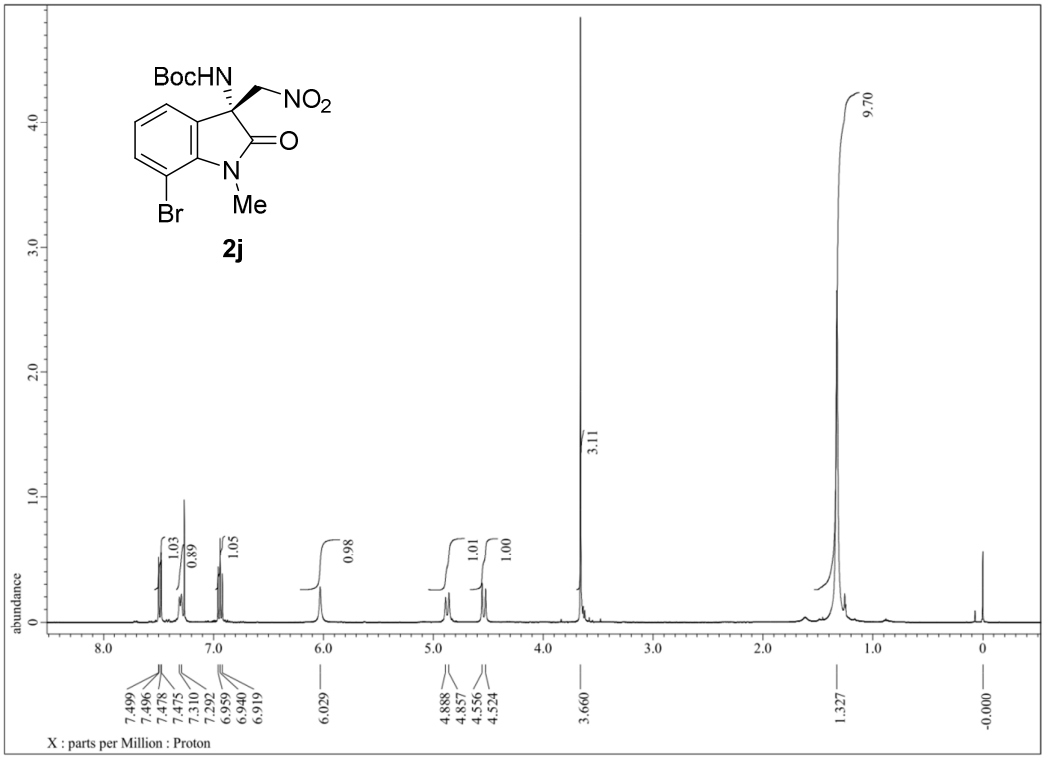

BocHN
Br
NO2
O
N
Me
2g
abundance
X : parts per Million : Carbon13

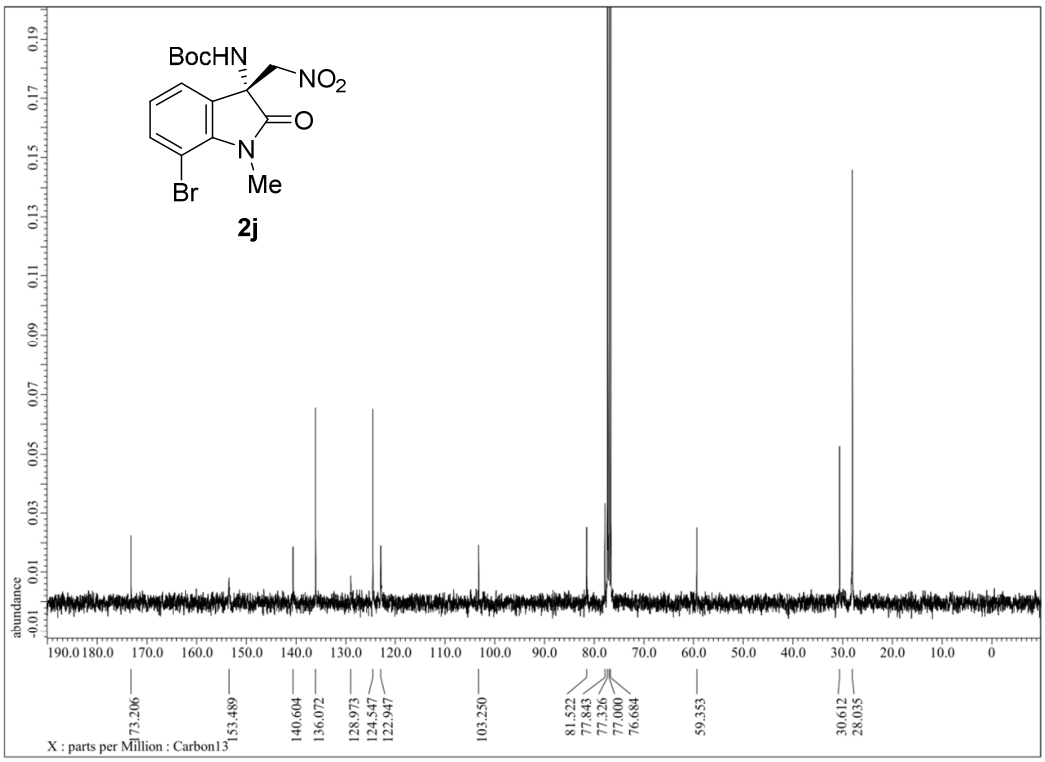

BocHN
NO2
O
Cl
N
Me
2h
abundance
X : parts per Million : Proton

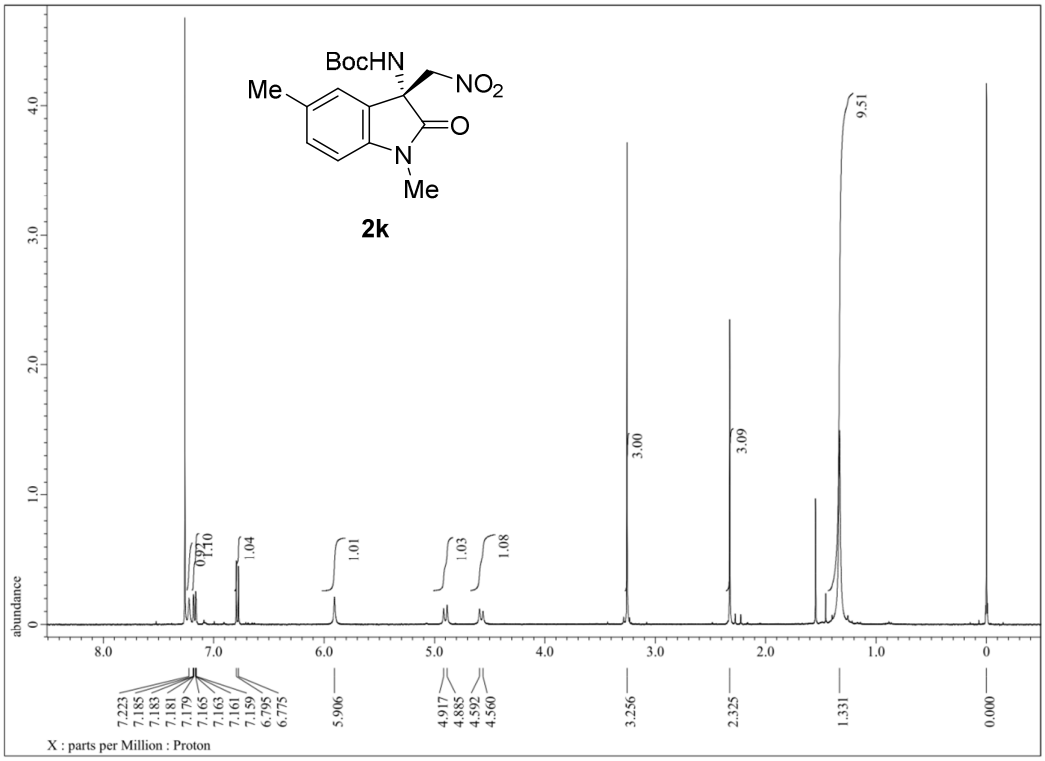

BocHN
NO2
O
Cl
N
Me
2h
abundance
X : parts per Million : Carbon13

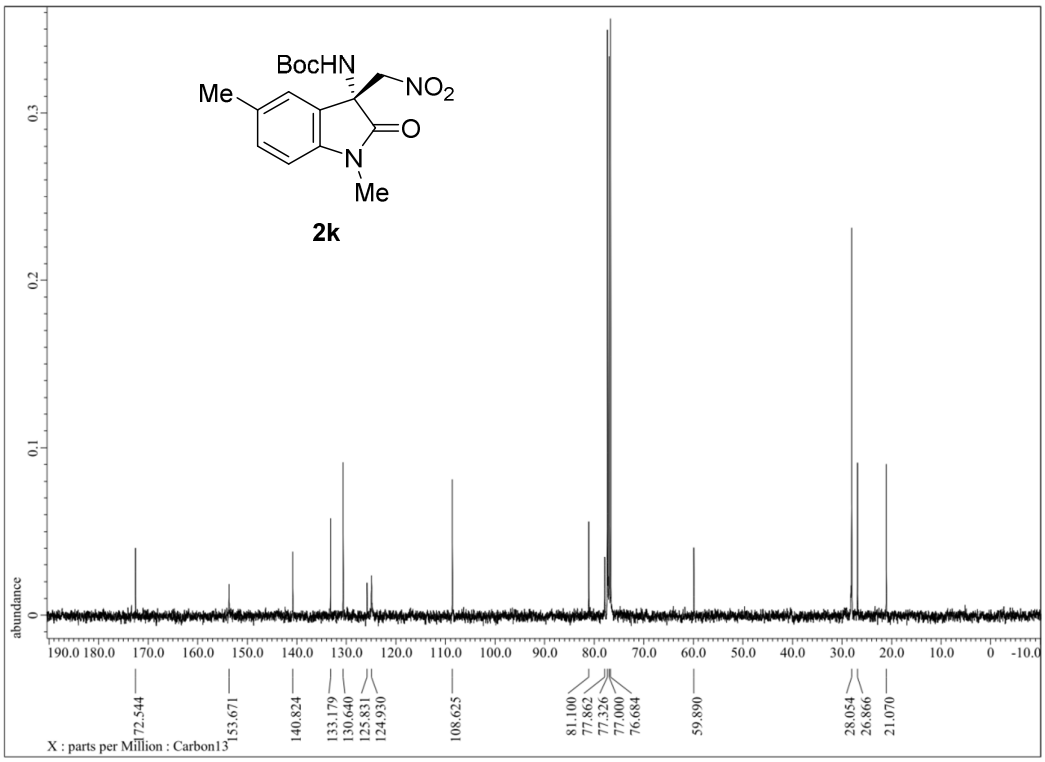

BocHN
NO2
O
Br
N
Me
2i
abundance
1.01
1.16
1.09
1.00
0.97
1.00
3.22
9.50
7.306
7.286
7.245
7.241
7.225
7.221
7.060
7.056
5.915
4.953
4.922
4.589
4.558
3.263
1.340
-0.000
X : parts per Million : Proton

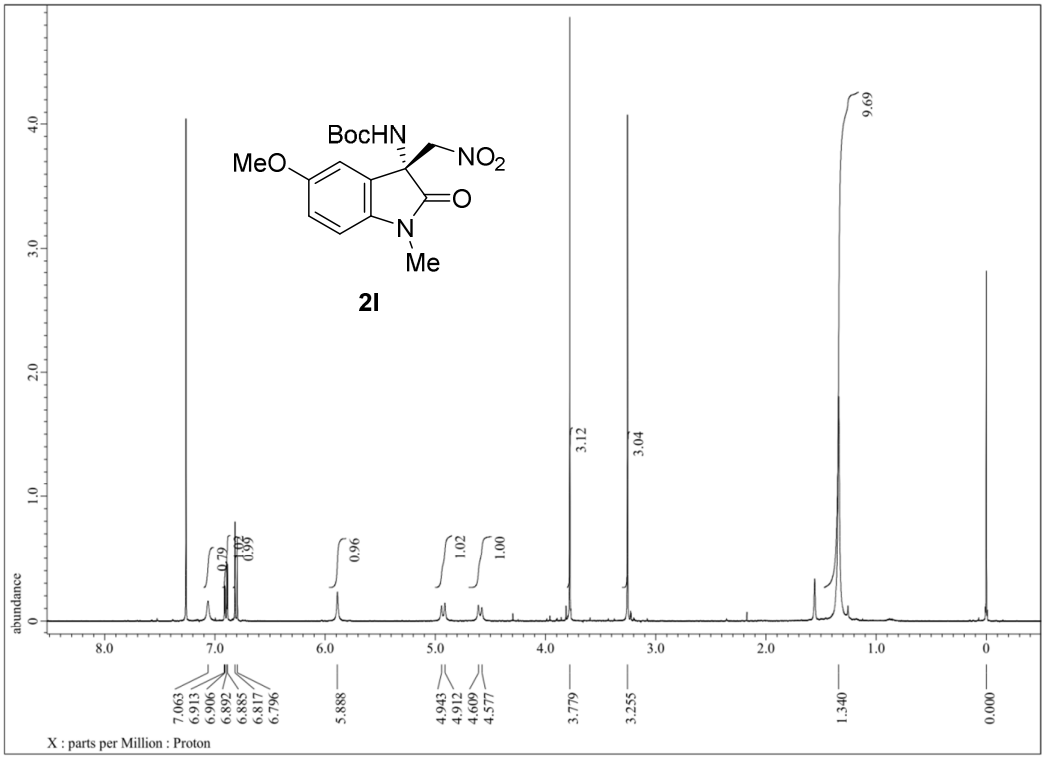

BocHN
NO2
O
Br
N
Me
2i
abundance
172.544
153.614
144.618
126.281
125.697
124.643
124.269
112.524
81.484
77.479
77.316
77.000
76.674
59.468
28.054
27.000
X : parts per Million : Carbon13

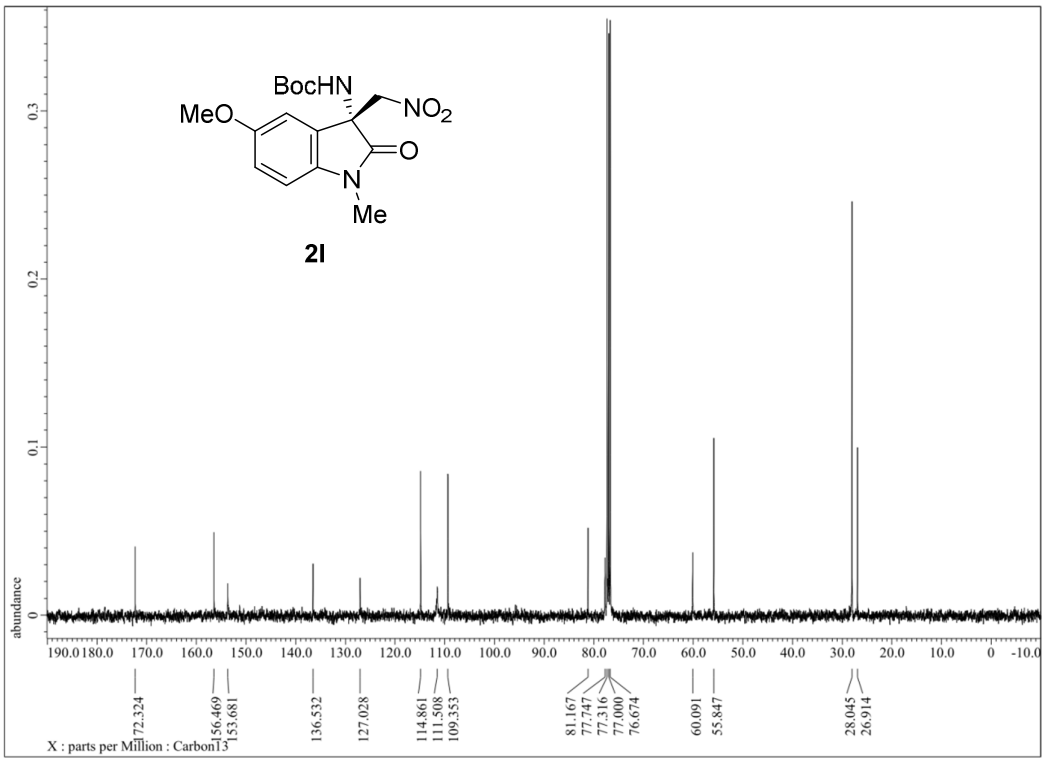

BocHN
NO2
O
N
Me
Br
2j
abundance
9.70
3.11
1.03
0.89
1.05
0.98
1.01
1.00
7.499
7.496
7.478
7.475
7.310
7.292
6.959
6.940
6.919
6.029
4.888
4.857
4.556
4.524
3.660
1.327
-0.000
X : parts per Million : Proton

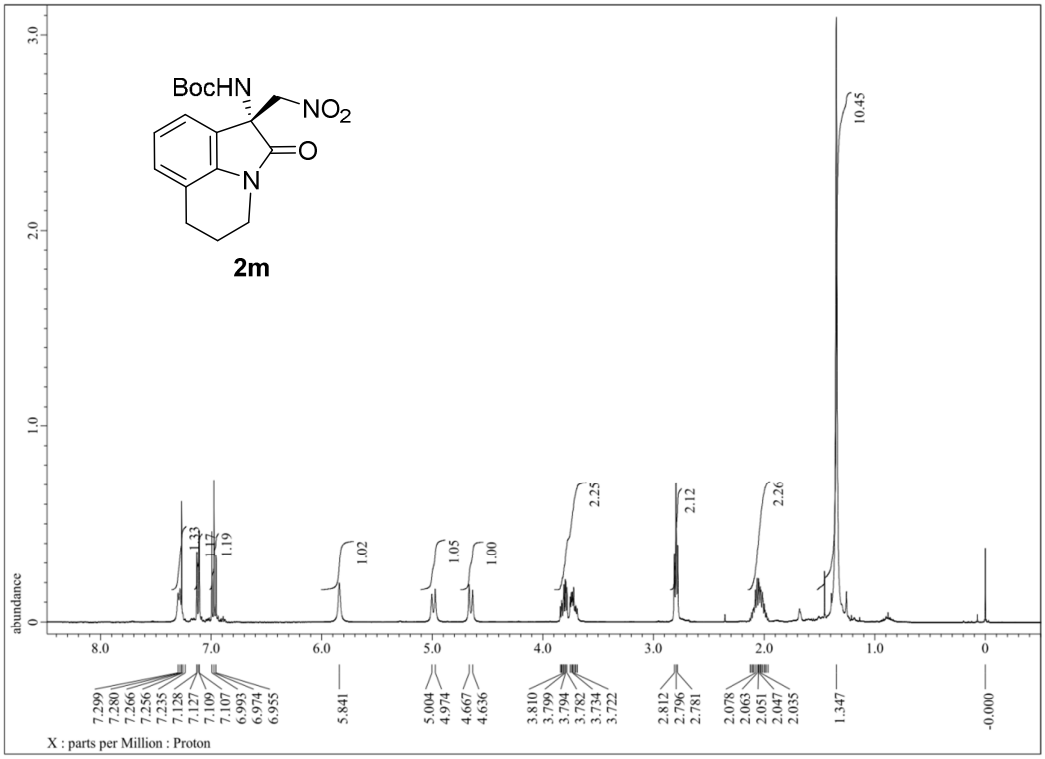

BocHN
NO2
O
N
Me
Br
2j
abundance
173.206
153.489
140.604
136.072
128.973
124.547
122.947
103.250
81.522
77.843
77.326
77.000
76.684
59.353
30.612
28.035
X : parts per Million : Carbon13

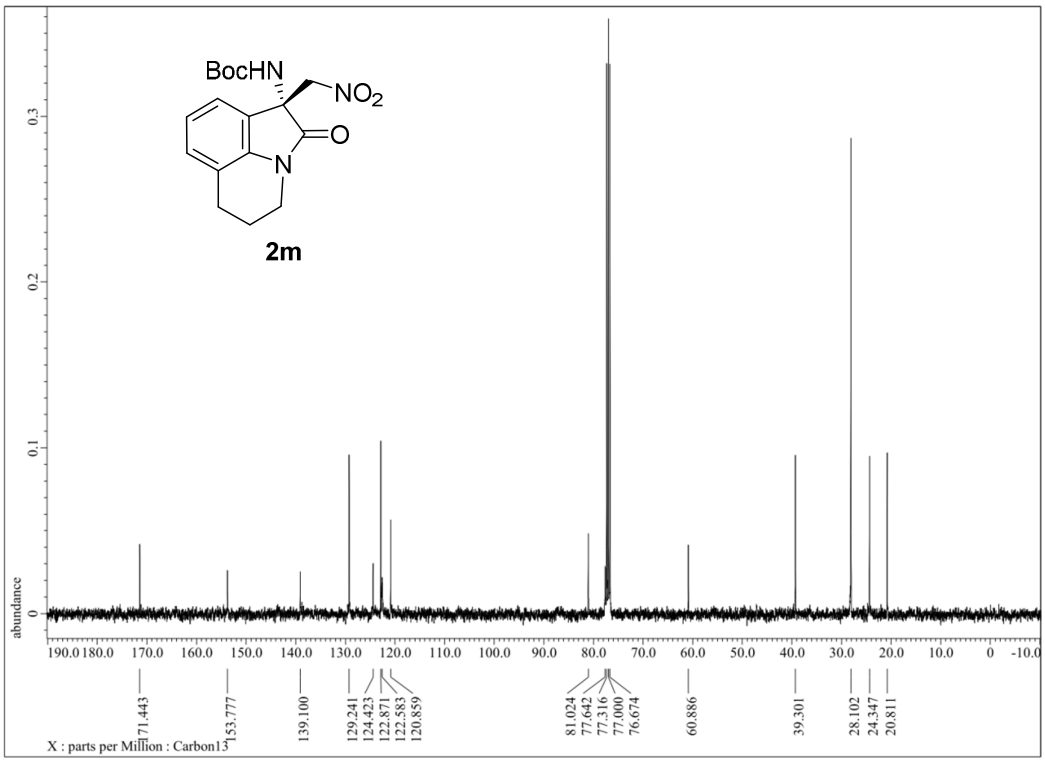

BocHN
NO2
Me
O
N
Me
2k
abundance
X : parts per Million : Proton

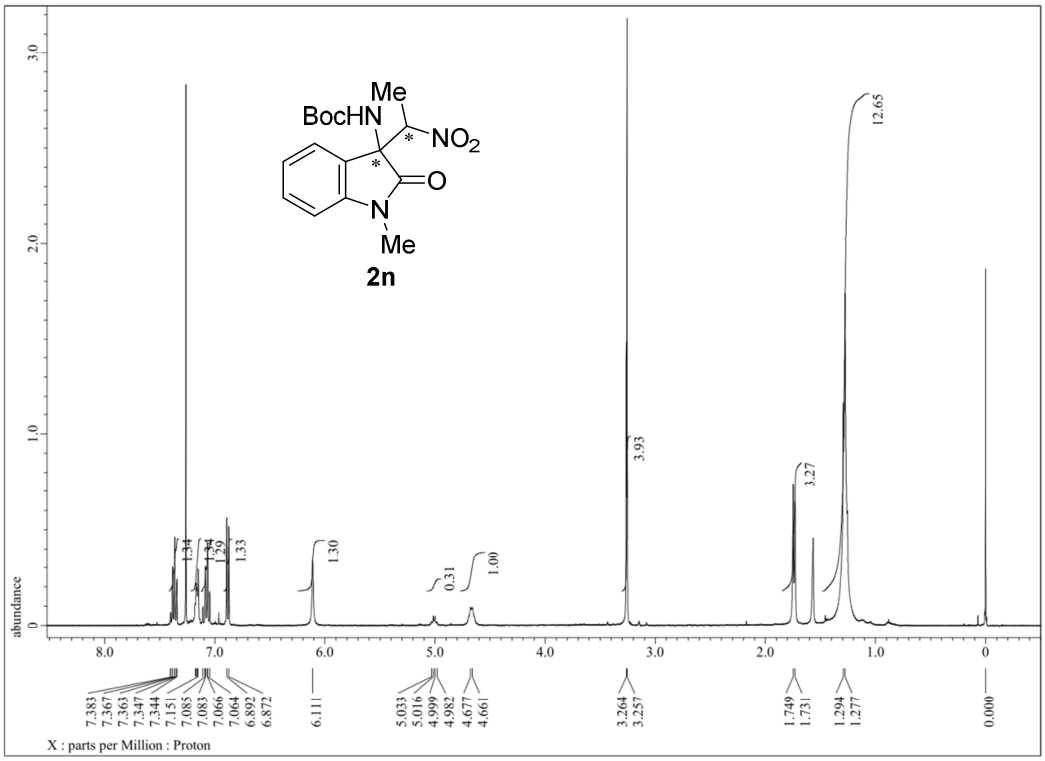

BocHN
NO2
Me
O
N
Me
2k
abundance
X : parts per Million : Carbon13

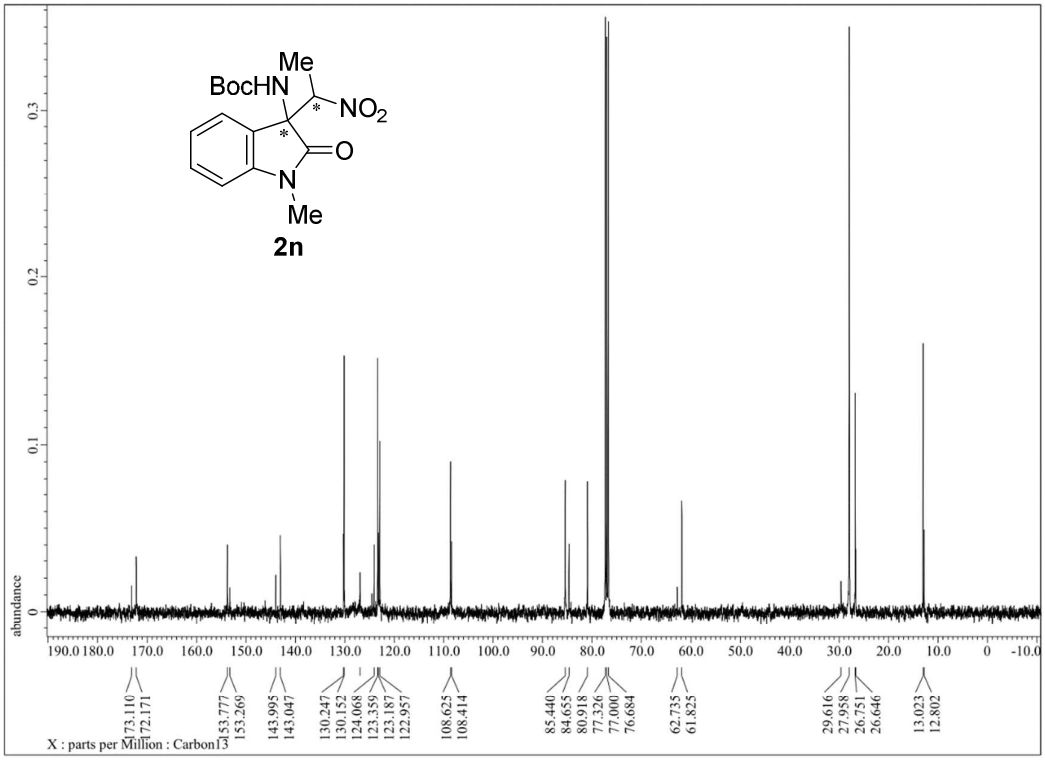

BocHN
NO2
MeO
O
N
Me
2l
abundance
9.69
3.12
3.04
0.79
1.02
0.99
0.96
1.02
1.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.063
6.913
6.906
6.892
6.885
6.817
6.796
5.888
4.943
4.912
4.669
4.577
3.779
3.255
1.340
0.000
X : parts per Million : Proton


BocHN
NO2
MeO
O
N
Me
2l
abundance
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0
172.324
156.469
153.681
136.532
127.028
114.861
111.508
109.353
81.167
77.747
77.316
77.000
76.674
60.091
55.847
28.045
26.914
X : parts per Million : Carbon13

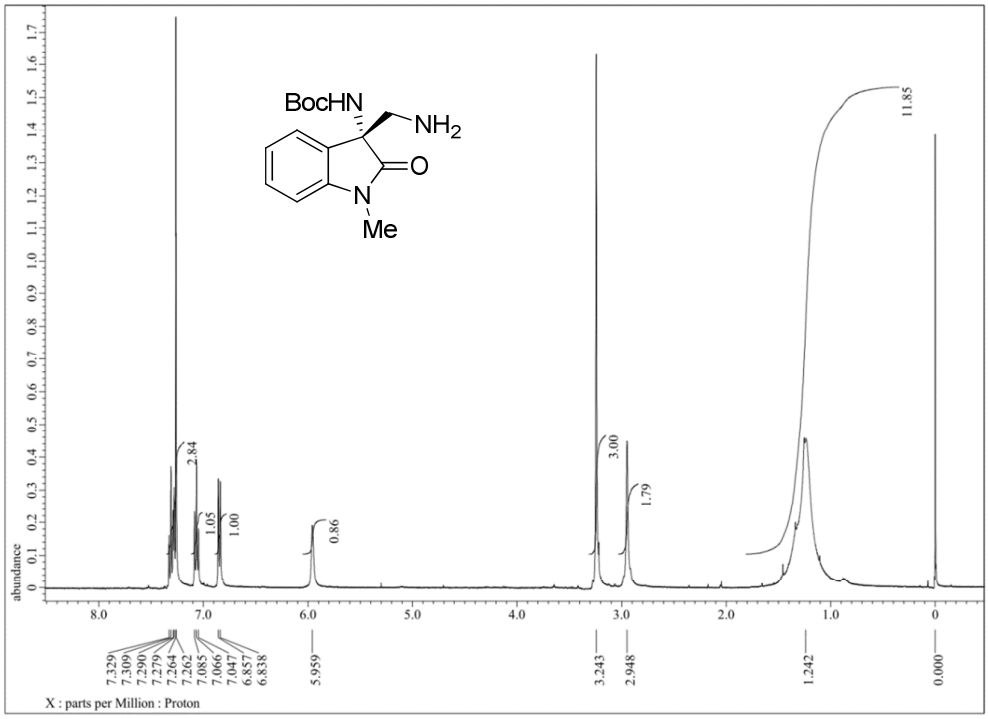

BocHN
NO2
O
N
2m
abundance
X : parts per Million : Proton

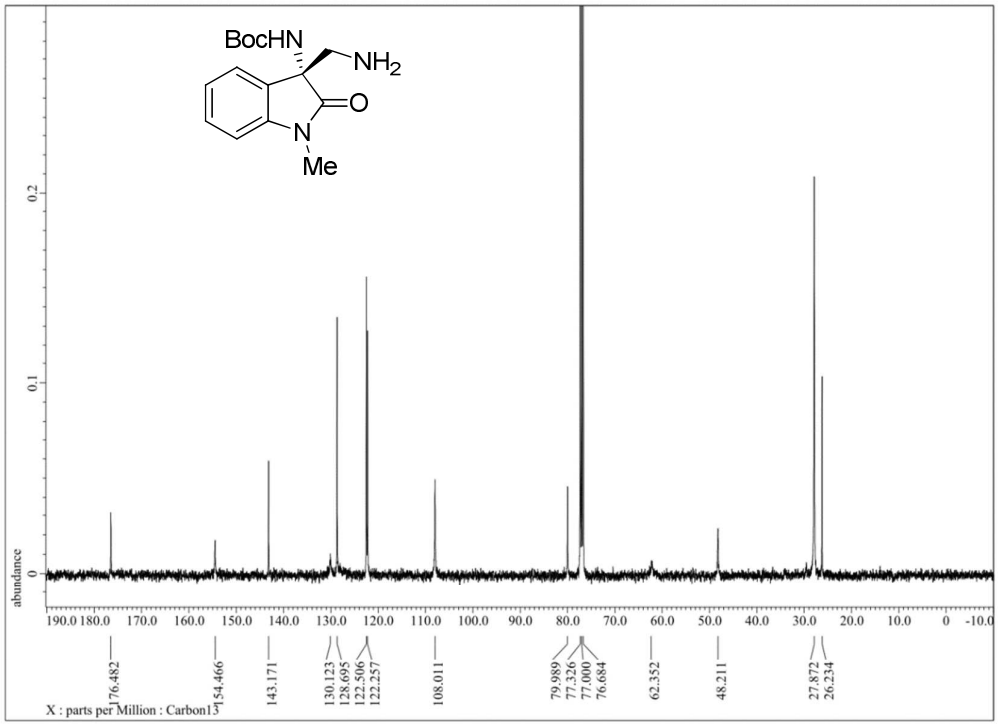

BocHN
NO2
O
N
2m
abundance
X : parts per Million : Carbon13


Me
BocHN
NO2
O
N
Me
2n
12.65
3.93
3.27
1.34
1.34
1.29
1.34
1.33
1.30
0.31
1.00
abundance
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.383
7.367
7.363
7.347
7.344
7.151
7.085
7.083
7.066
7.064
6.892
6.872
6.111
5.033
5.016
4.999
4.982
4.677
4.661
3.264
3.257
1.749
1.731
1.294
1.277
0.000
X : parts per Million : Proton

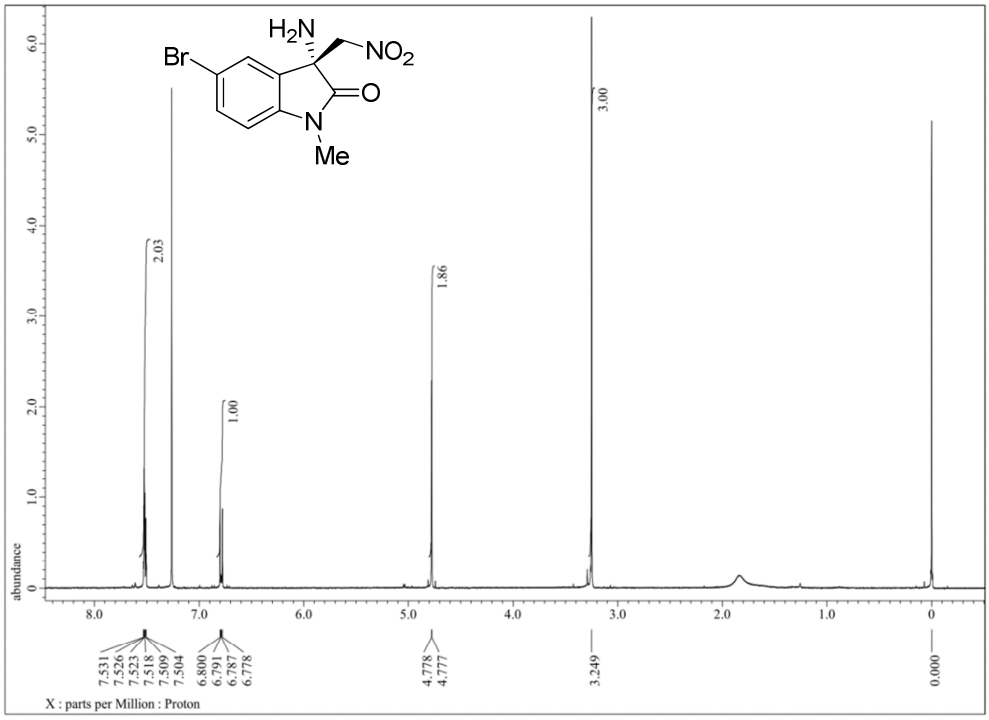

Me
BocHN
NO2
O
N
Me
2n
abundance
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0
173.110
172.171
153.777
153.269
143.995
143.047
130.247
130.152
124.068
123.359
123.187
122.957
108.625
108.414
85.440
84.655
80.918
77.326
77.000
76.684
62.735
61.825
29.616
27.958
26.751
26.646
13.023
12.802
X : parts per Million : Carbon13

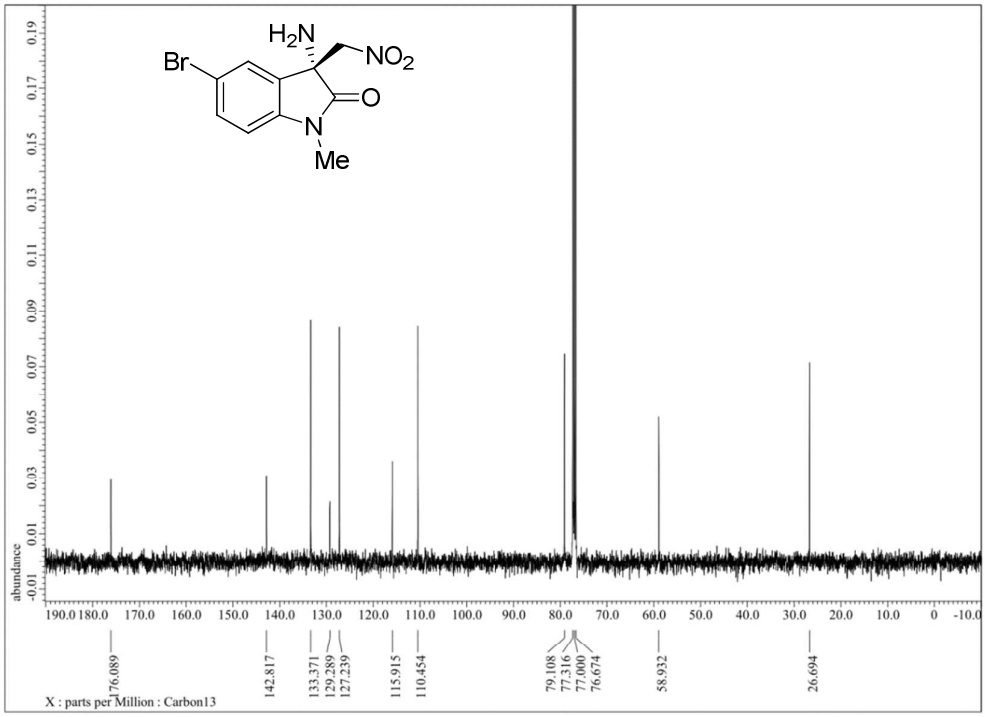
Product obtained by reduction of **2a** (Scheme 3)



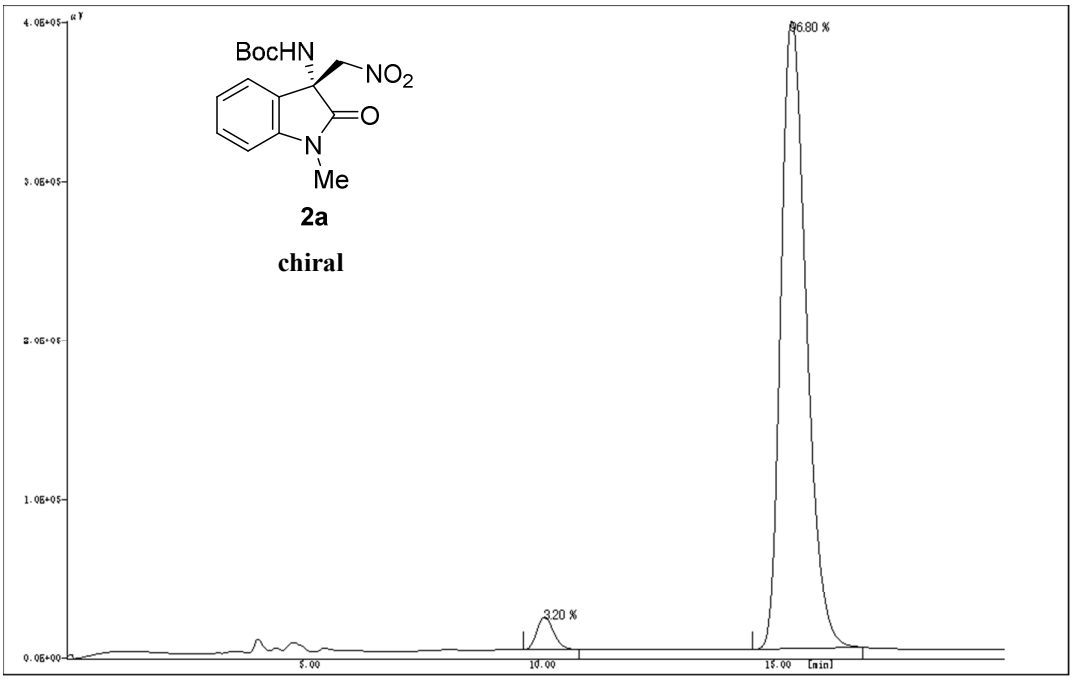


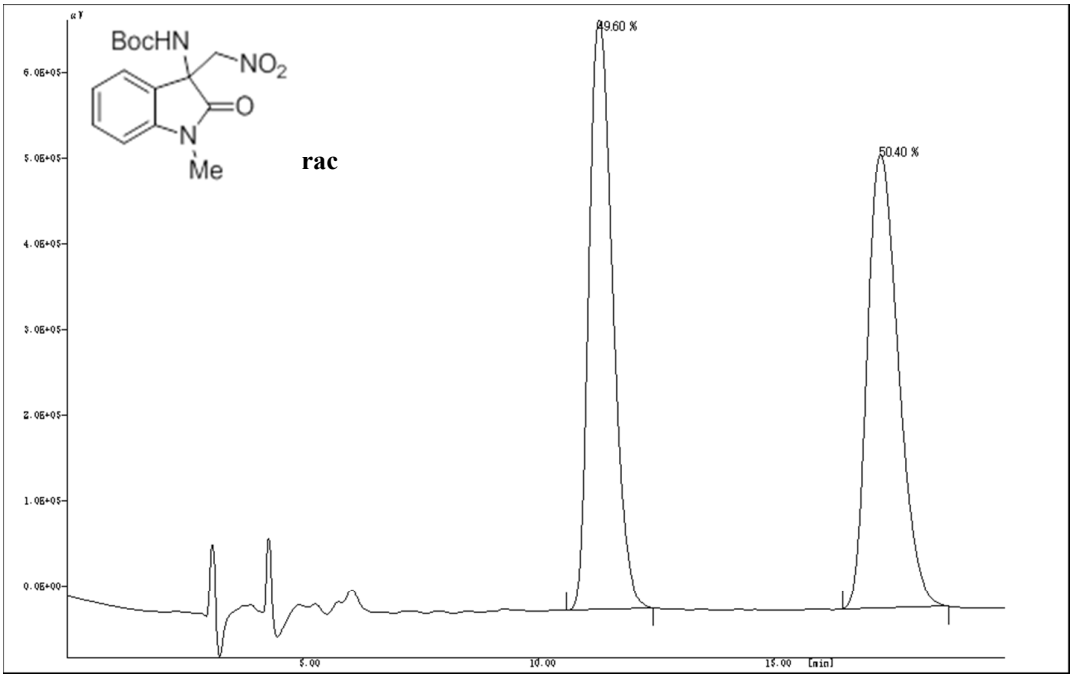
Product obtained by deprotection of Boc group from **2g** (Scheme 3)



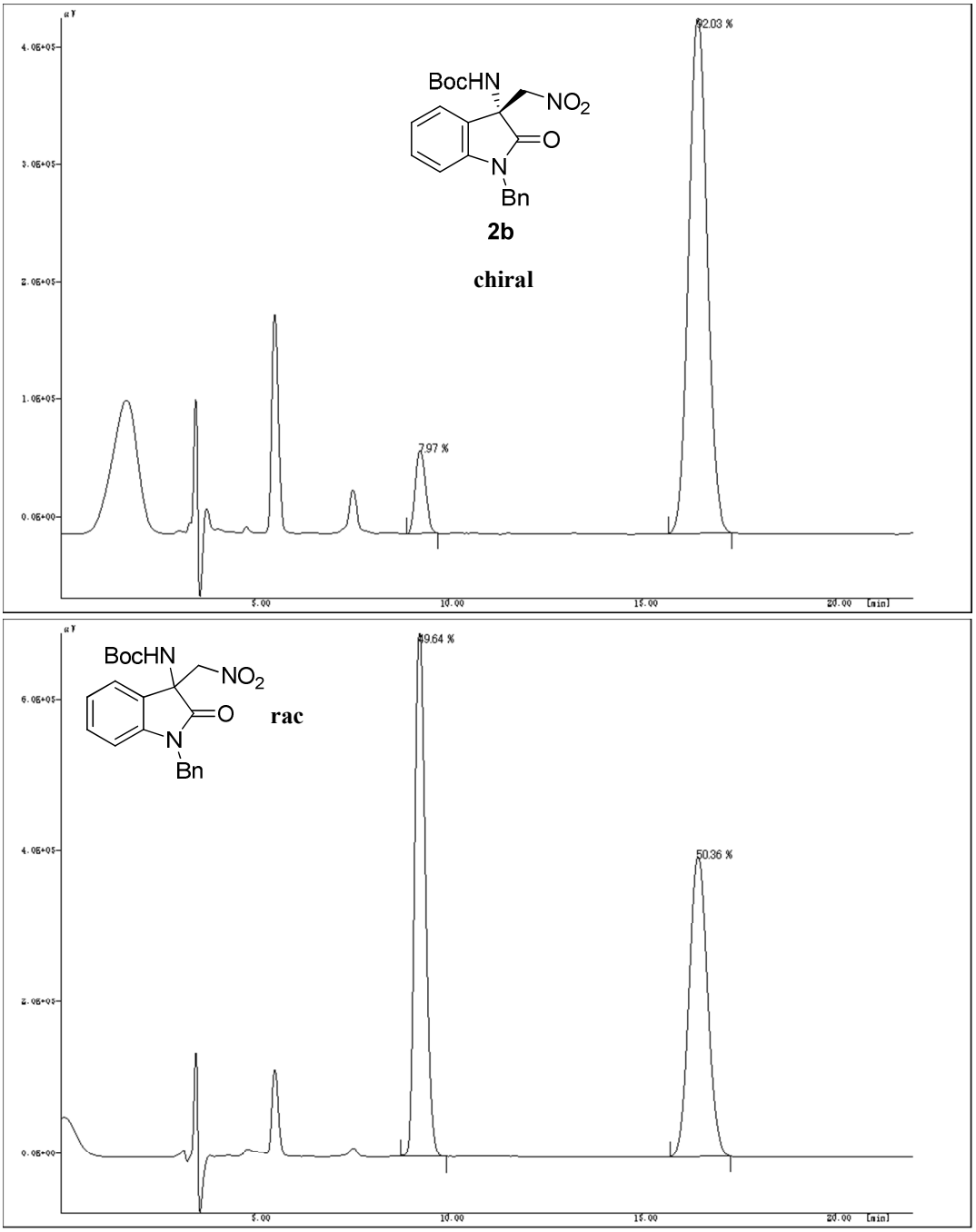


10. HPLC spectra

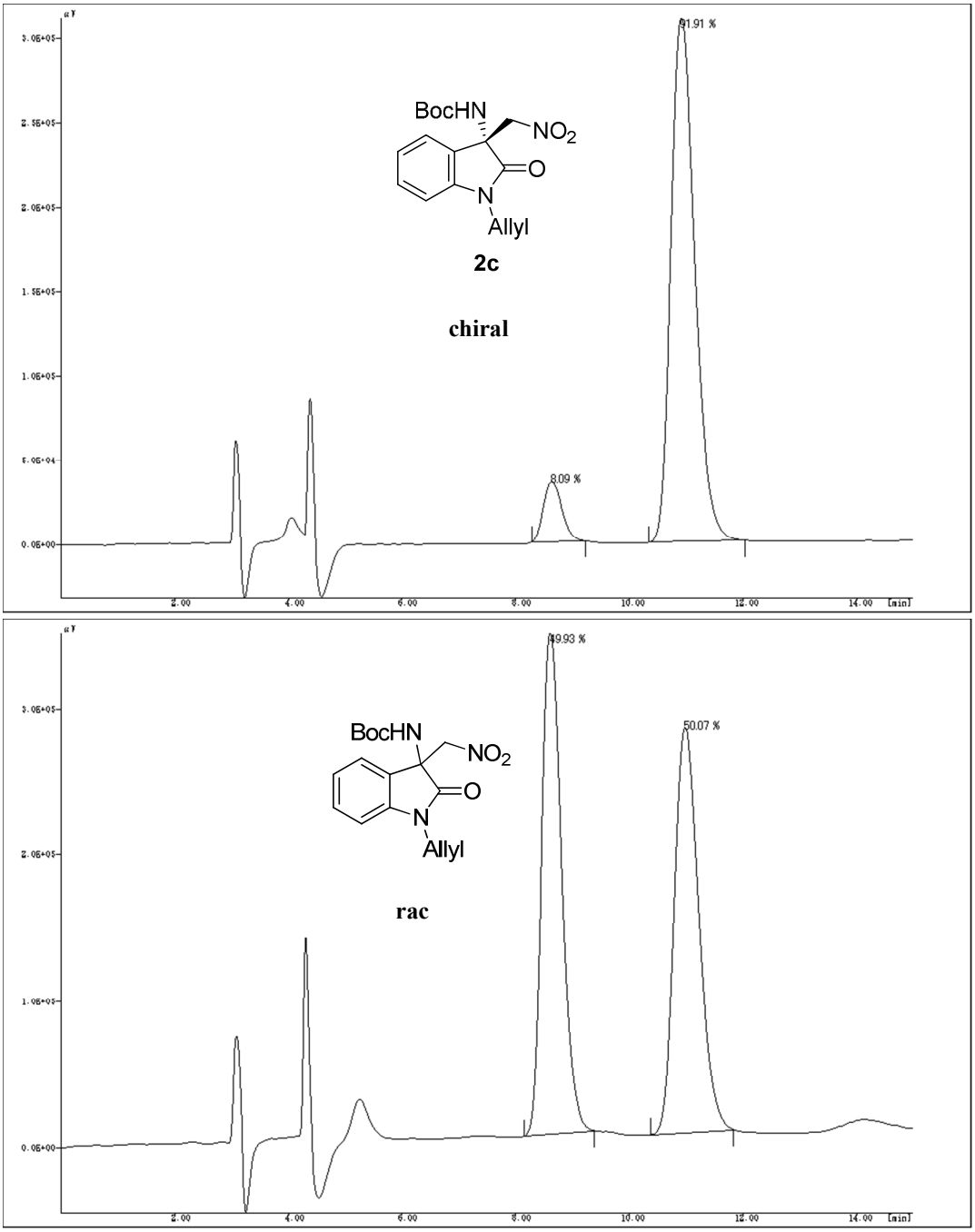




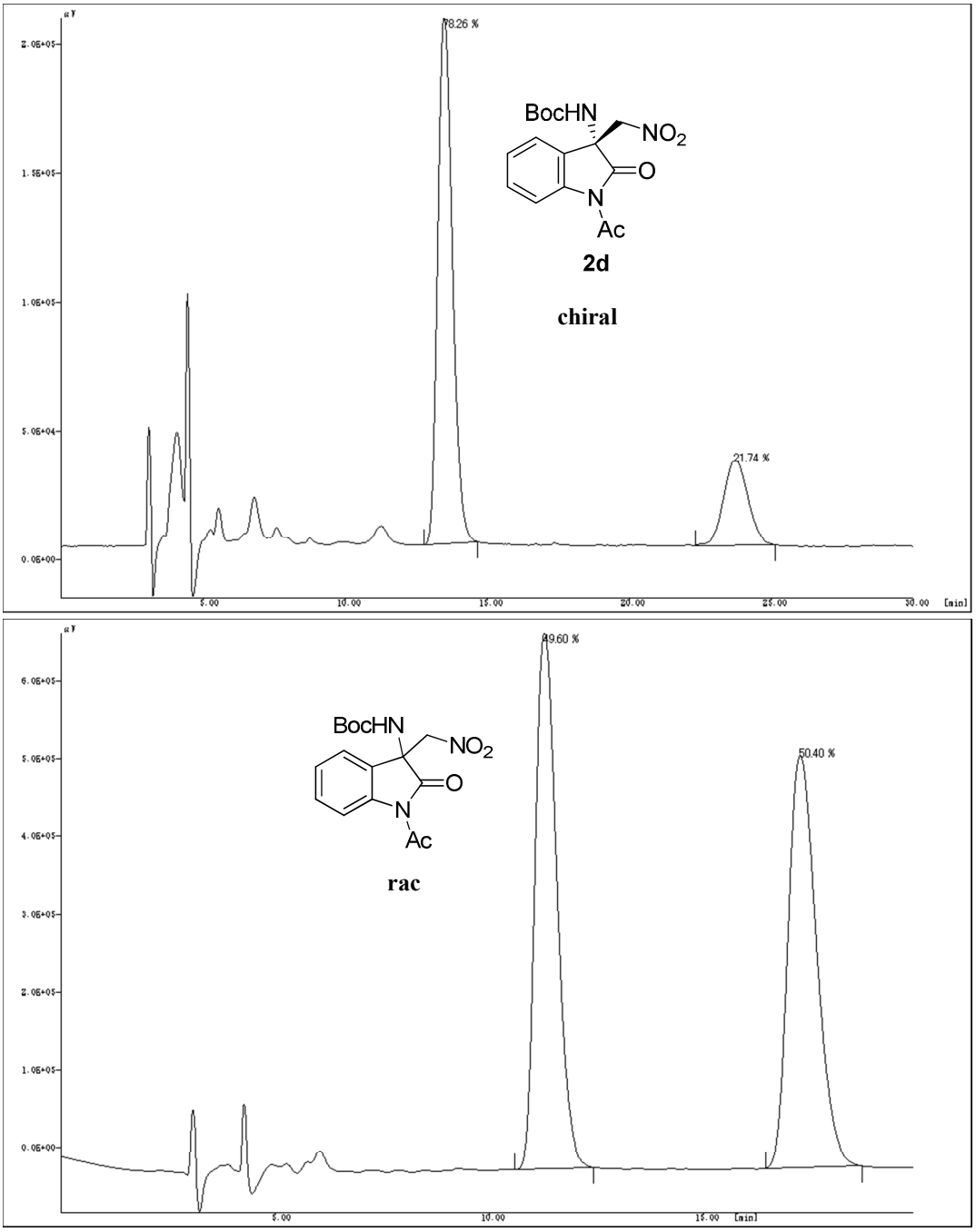
Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm)



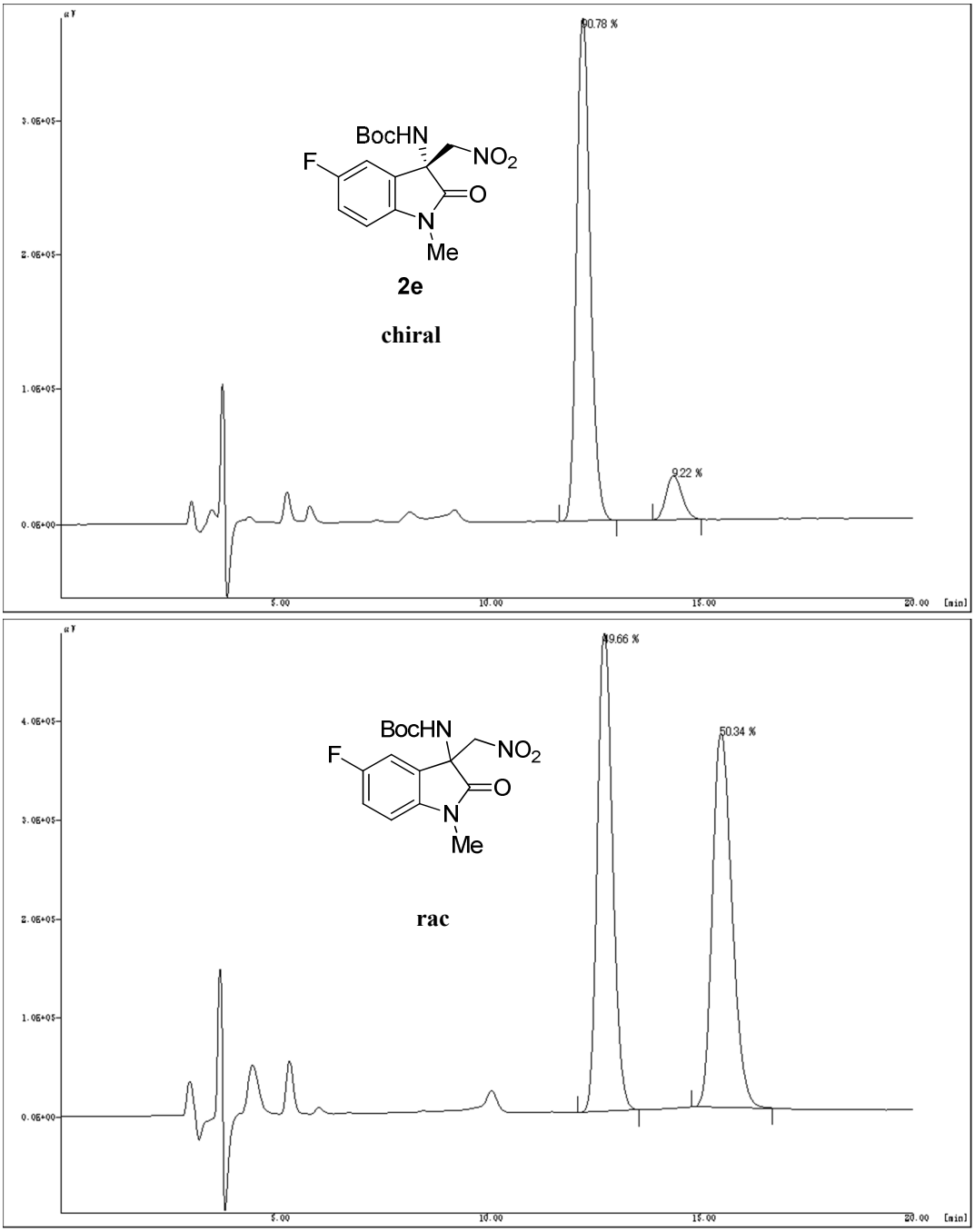
Chiralpak AD-H column (hexane:2-propanol= 70:30, 1.0 ml/min, 254 nm)



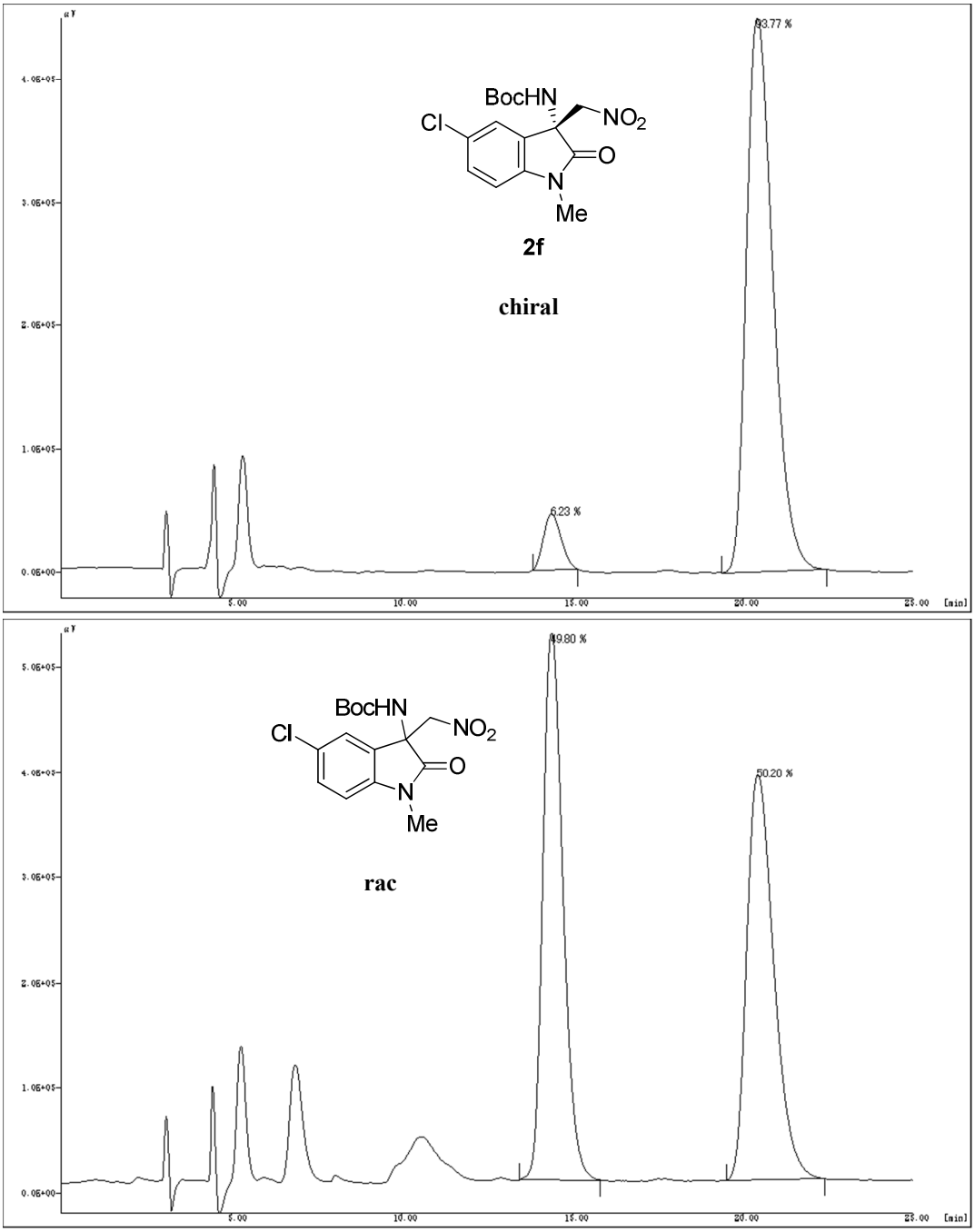
Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm)



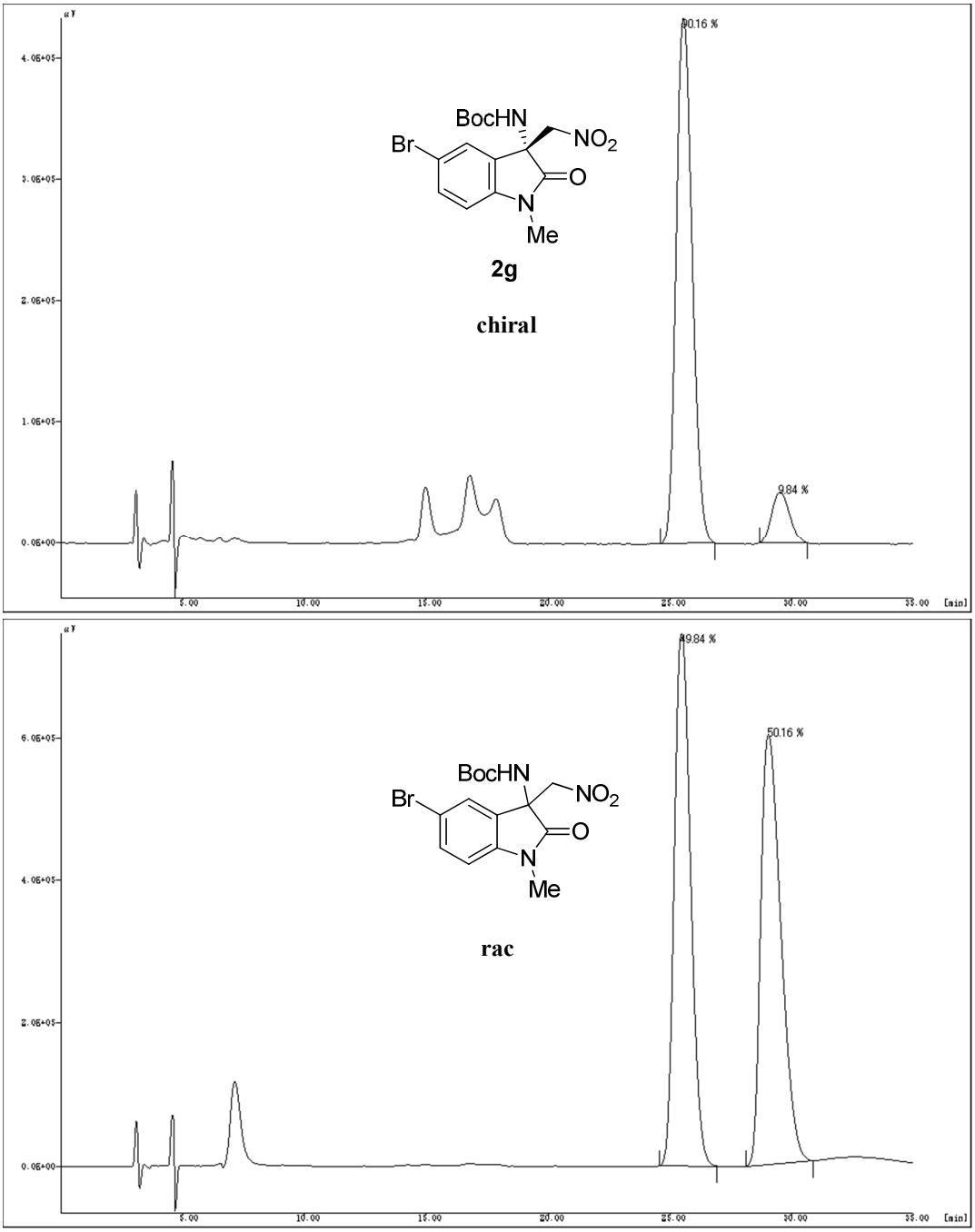
Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm)



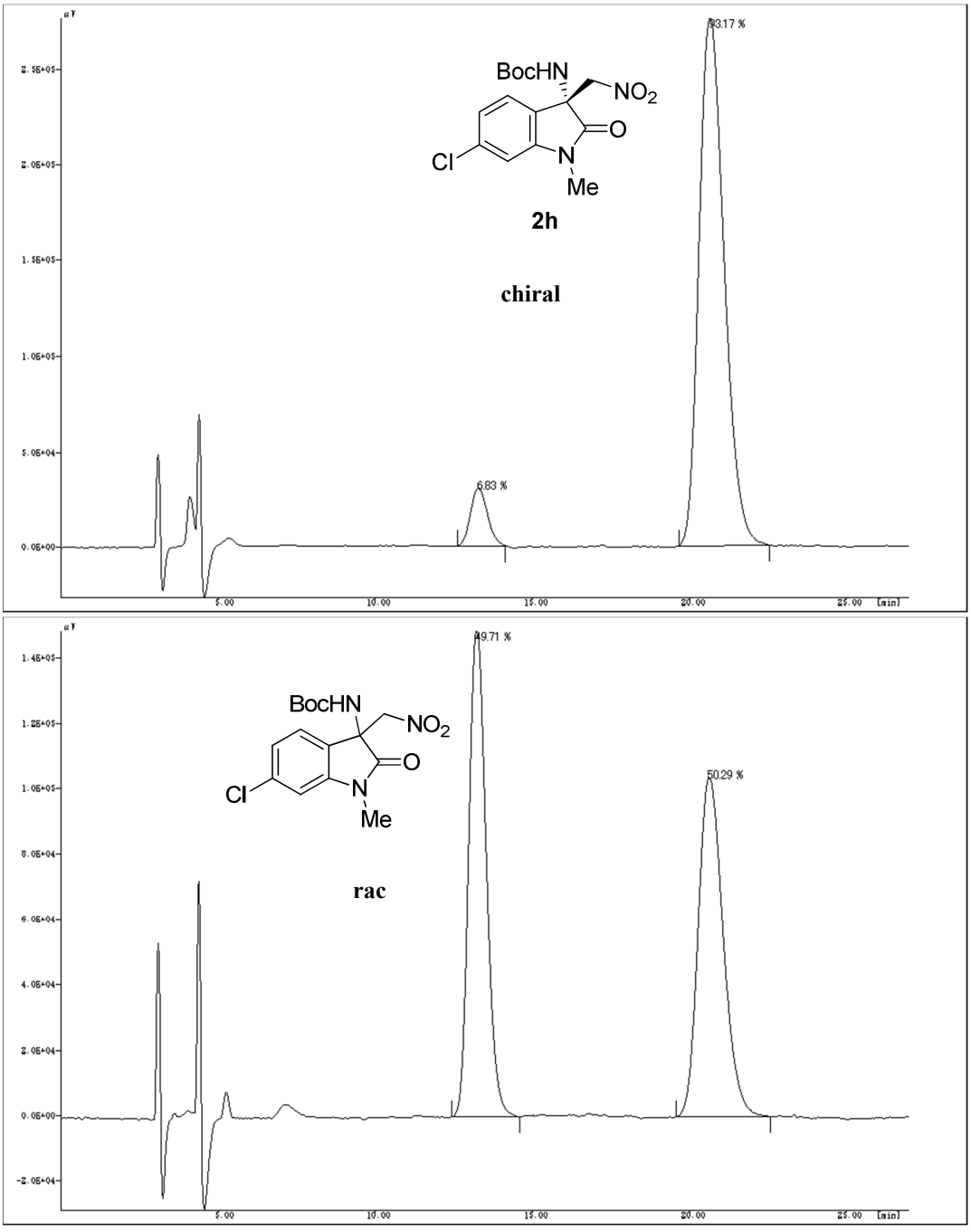
Chiralpak AD-H column (hexane:2-propanol= 80:20, 1.0 ml/min, 254 nm)



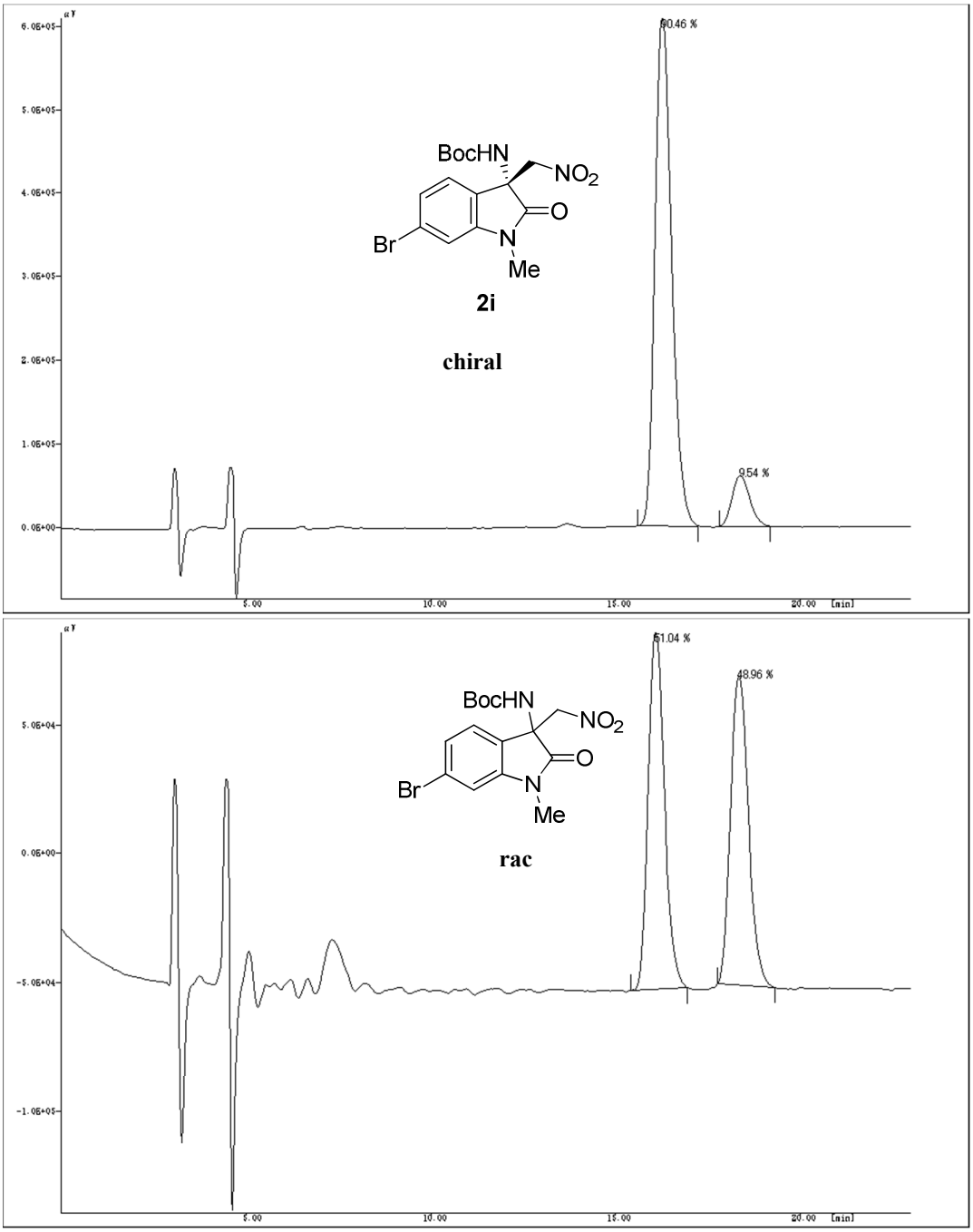
Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm)



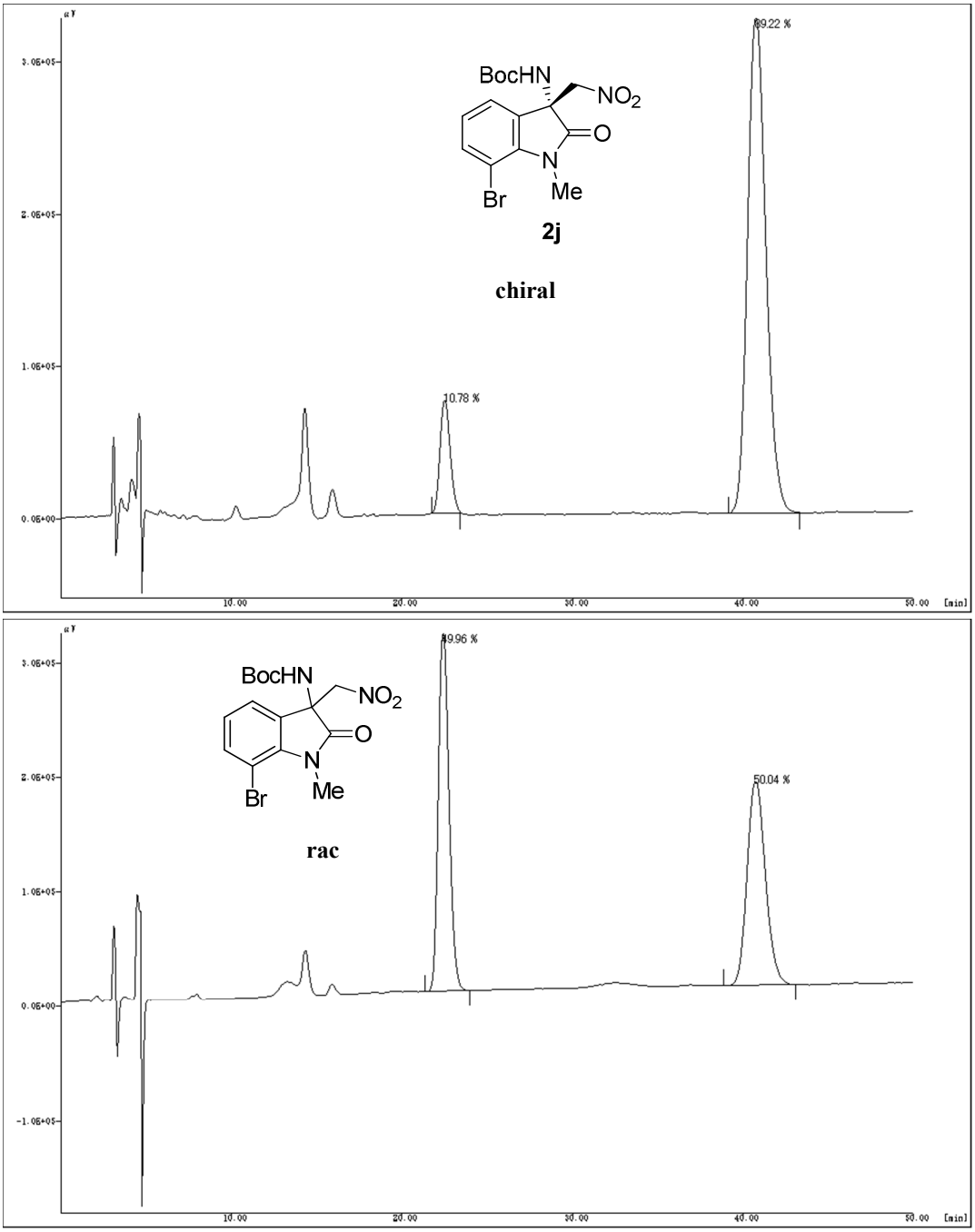
Chiralpak AD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm)



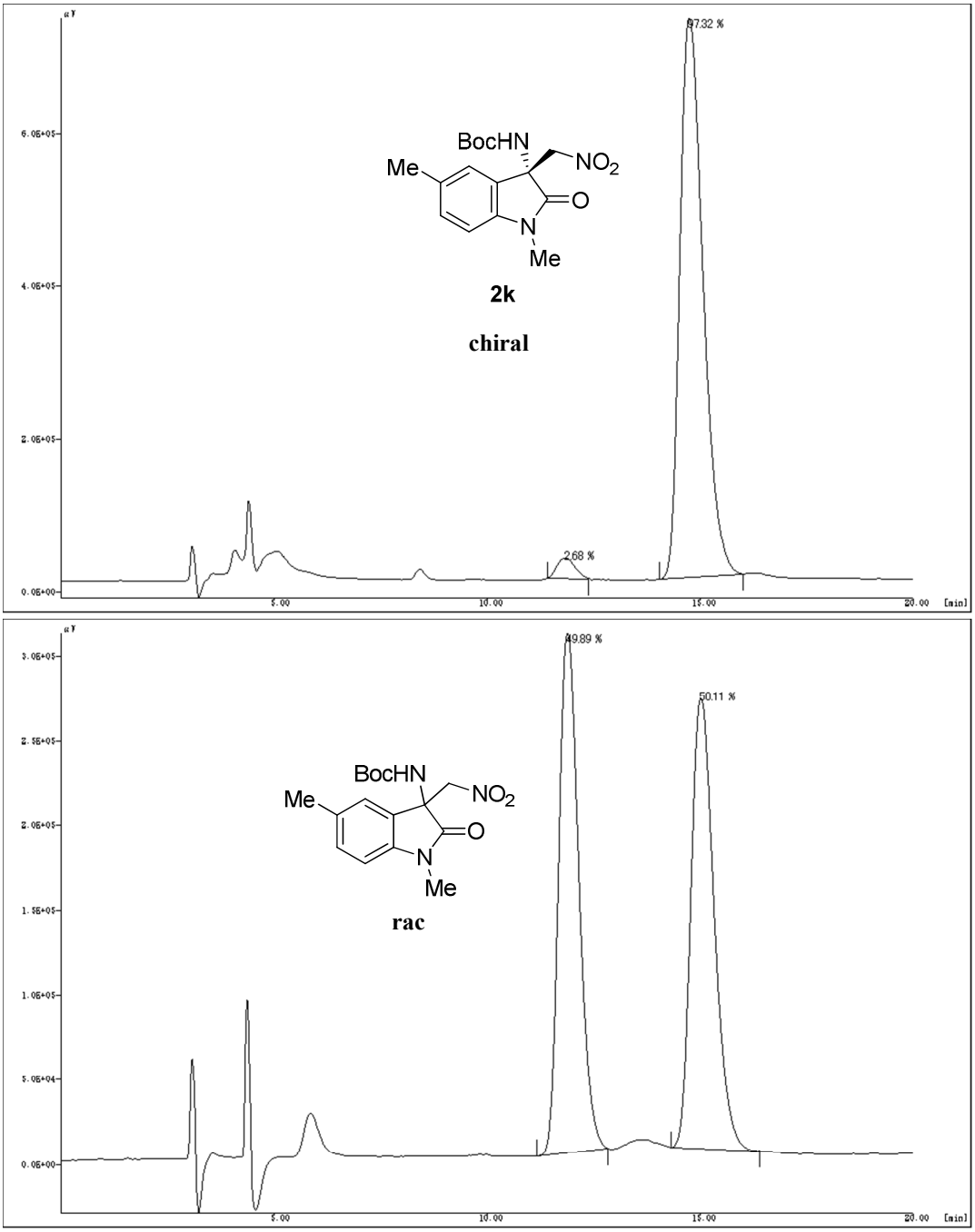
Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm)



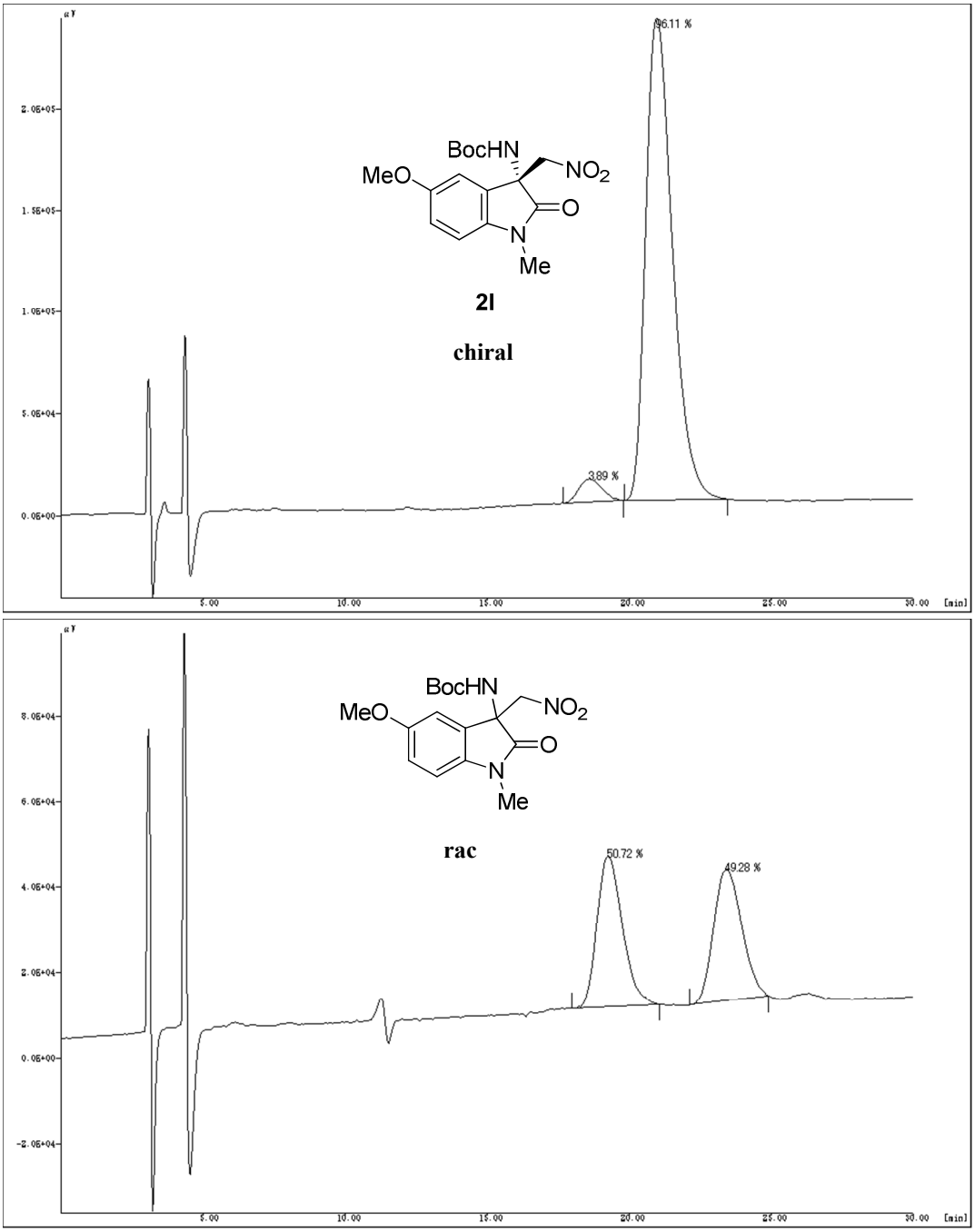
Chiralpak AD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm)



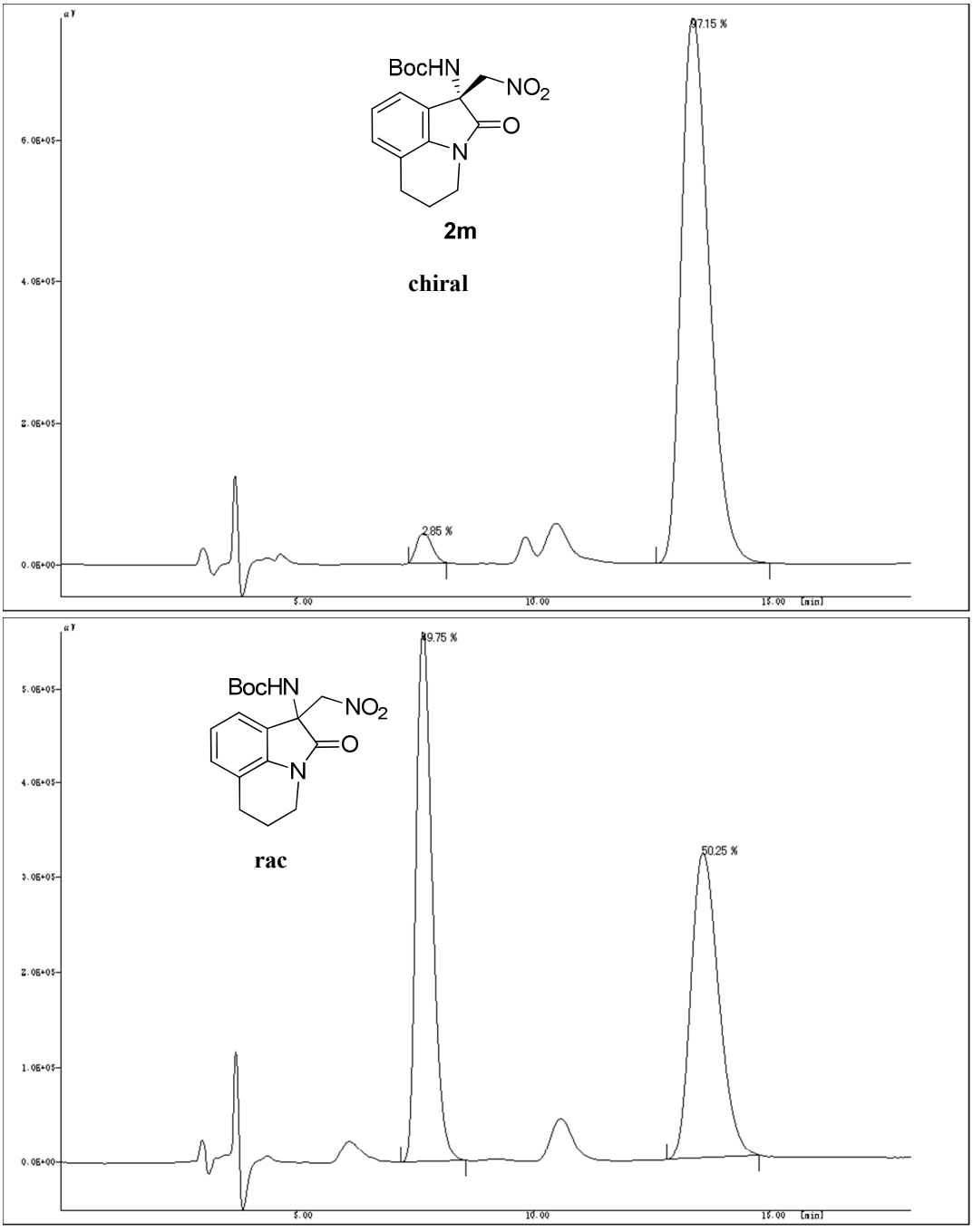
Chiralpak AD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm)



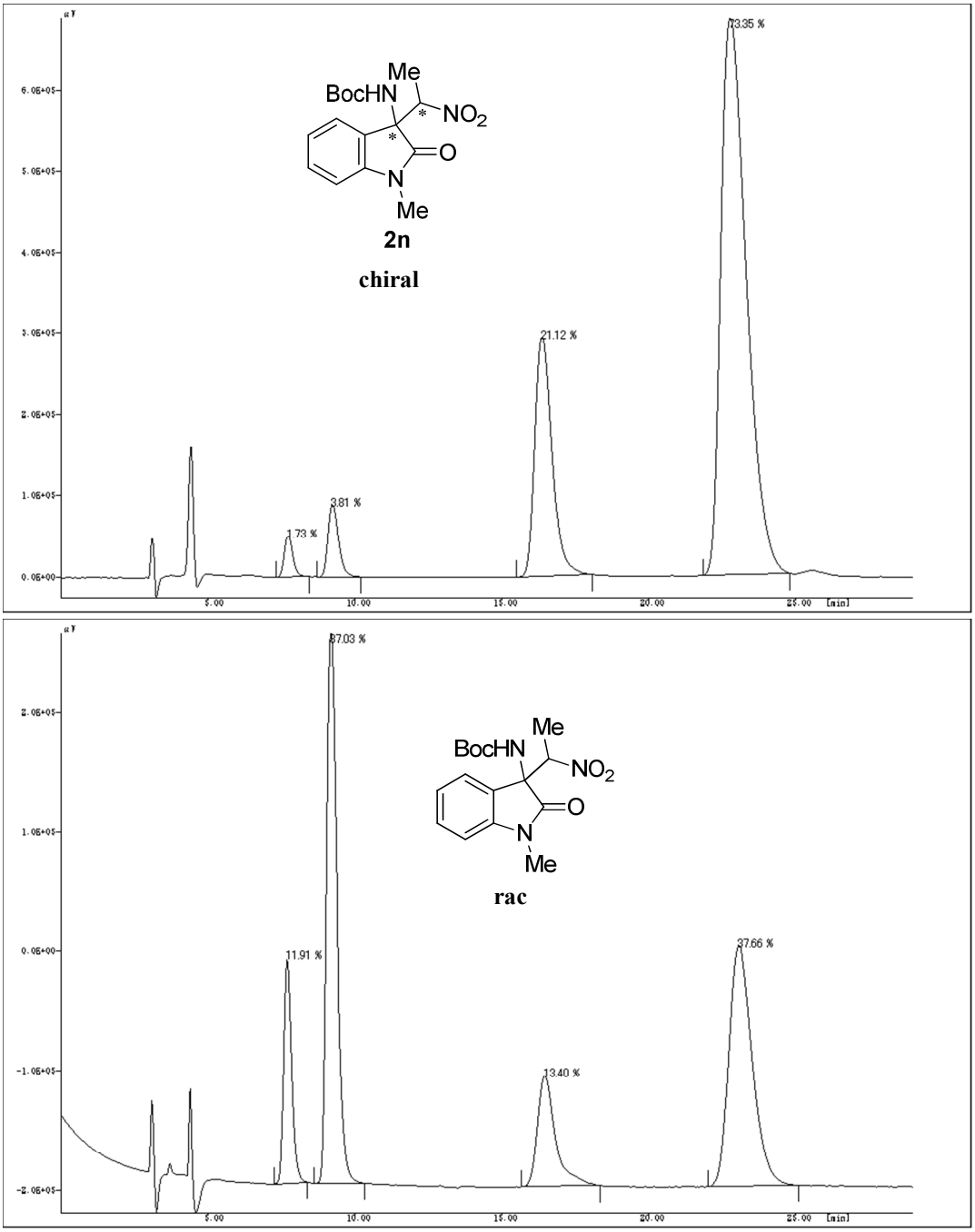
Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm)



Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm)

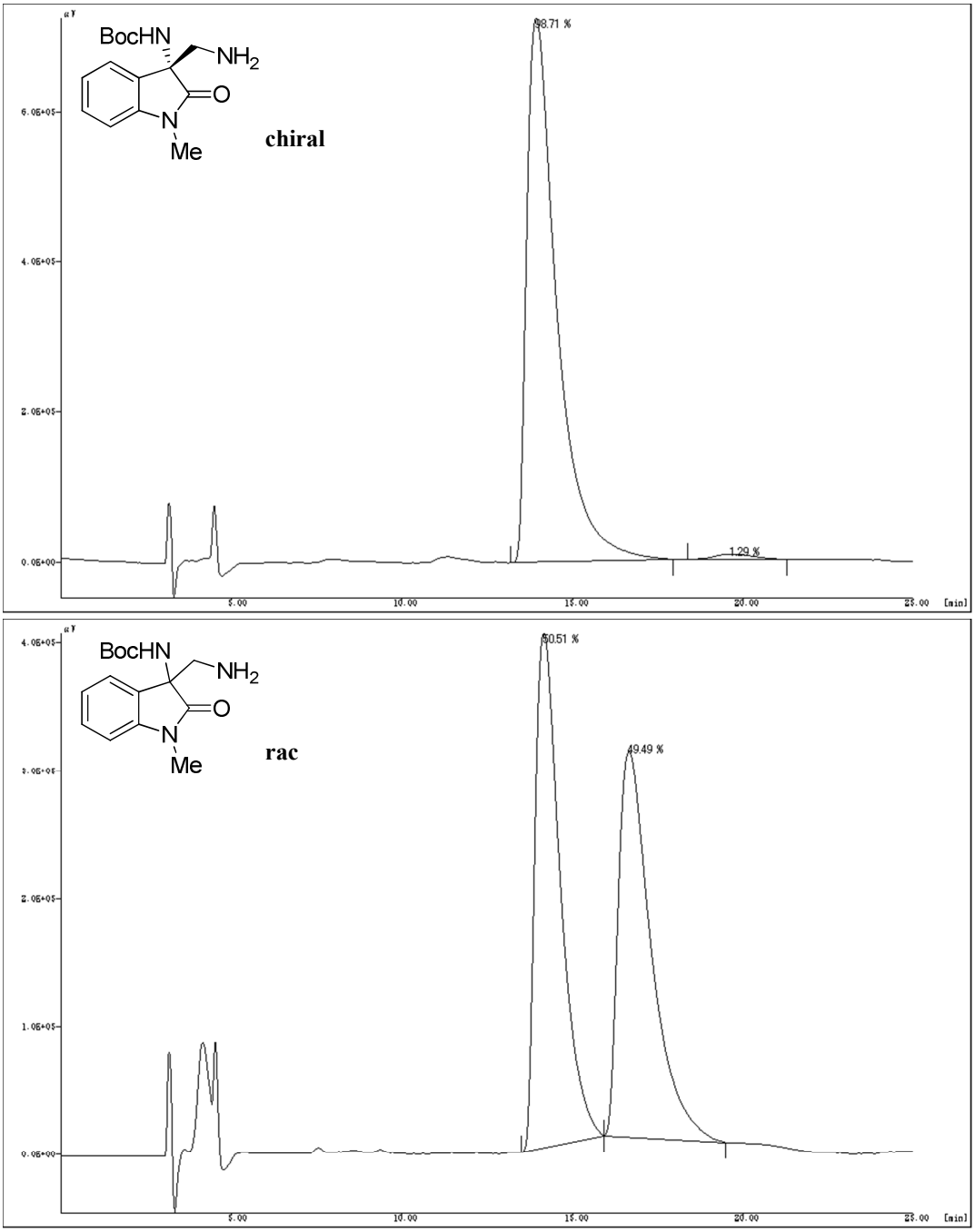


Chiralcel OD-H column (hexane:2-propanol= 80:20, 1.0 ml/min, 254 nm)



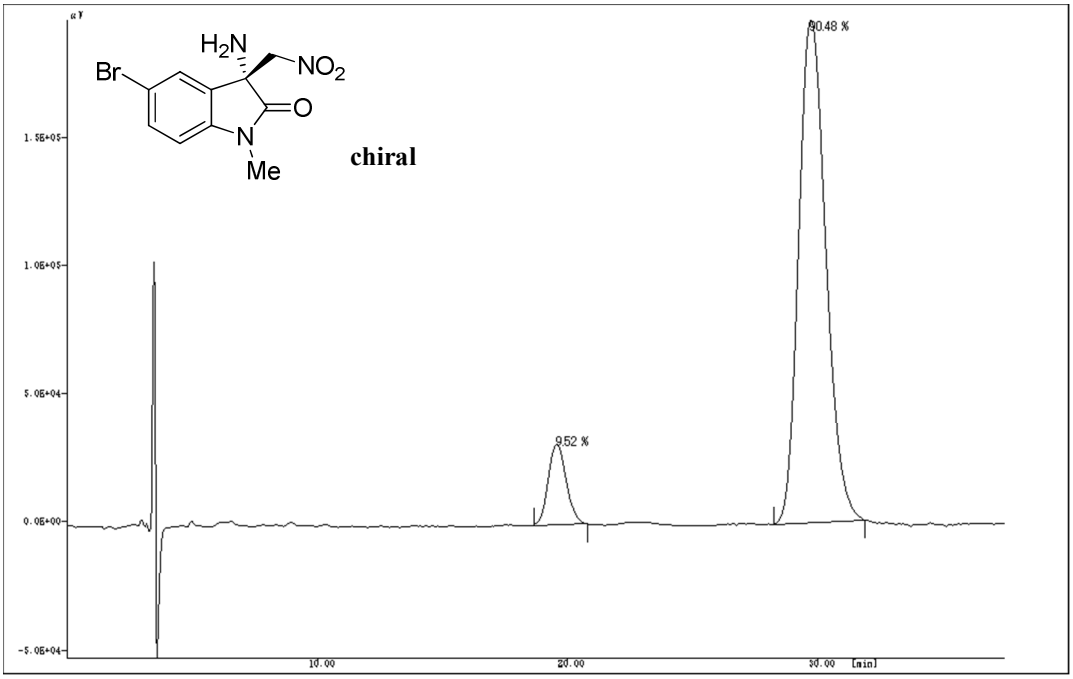
Chiralcel OD-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm)

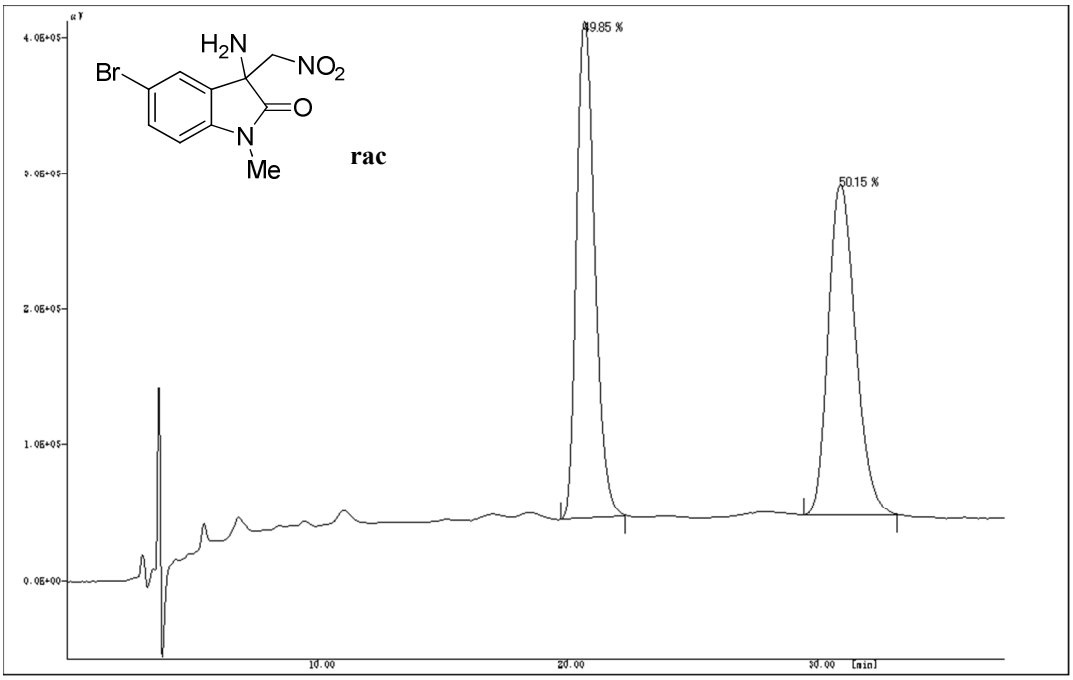
Product obtained by reduction of **2a** (Scheme 3)



Chiralpak AS-H column (hexane:2-propanol= 90:10, 1.0 ml/min, 254 nm)

Product obtained by deprotection of Boc group from **2g** (Scheme 3)





Chiralcel OD-H column (hexane:2-propanol= 70:30, 1.0 ml/min, 254 nm)