Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Chiral Organic Base Catalyst with Halogen Bonding Donor Functionality: Asymmetric Mannich Reaction of Malononitrile with *N*-Boc Aldimines and Ketimines

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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). IR spectra were recorded on JASCO FT/IR-4100 using ATR. ^{1}H-NMR spectra were recorded on JEOL ECS-400 (400 MHz), ECA-500 (500 MHz), ECX-400 (400 MHz) spectrometers. Chemical shifts of ^{1}H-NMR spectra were reported relative to tetramethyl silane (δ 0). ^{13}C-NMR spectra were recorded on JEOL ECS-400 (100 MHz), ECA-500 (125 MHz), ECX-400 (100 MHz) spectrometers. Chemical shifts of ^{13}C-NMR spectra were reported relative to $CDCl_3$ (δ 77.0). ^{19}F-NMR spectra were recorded on JEOL ECS-400 (376 MHz) spectrometer. Chemical shifts of ^{19}F-NMR spectra were reported relative to trifluorotoluene (δ −63.72). Splitting patterns were reported as s, singlet; d, doublet; t, triplet; m, multiplet; br, broad.

N-Boc aldimines were synthesized according to known procedure,[1] Isatin-derived *N*-Boc ketimines were synthesized according to known procedure.[2,3]

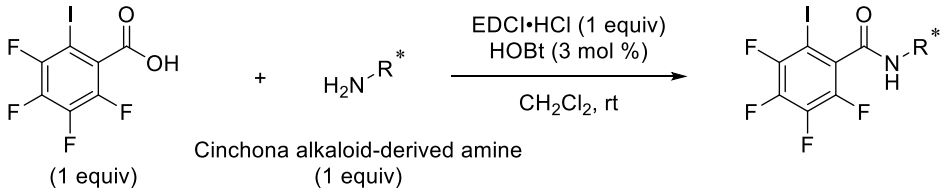
[1] Wenzel, A.-G.; Jacobsen, E.-N. *J. Am. Chem. Soc.* **2002**, *124*, 12964.

[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.

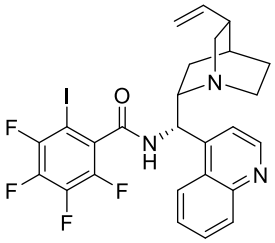
2. Synthesis of chiral halogen-bonding donor/organic base catalyst

A. 2a, 2b, 3a, and 3b



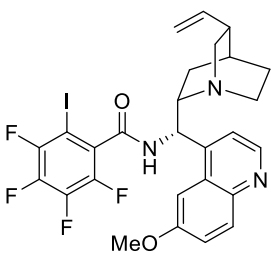
2,3,4,5-Tetrafluoro-6-iodobenzoic acid (0.5 mmol, 1.0 equiv, 0.1 M), cinchona alkaloid-derived amine (0.5 mmol, 1.0 equiv, 0.1 M), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide Hydrochloride (EDCI·HCl) (0.5 mmol, 1.0 equiv, 0.1 M), and 1-hydroxybenzotriazole (HOBt) (0.015 mmol, 0.03 equiv, 0.003 M) were added to a one-necked round flask containing a stir bar under Ar. CH_2Cl_2 (5 mL) was added to the flask, and the mixture was stirred at room temperature. After being stirred for appropriate time by TLC monitoring, additional CH_2Cl_2 was added. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated under reduced pressure. After purification by silica gel column chromatography (hexane/ethyl acetate/Et_3N = 1/1/0.03), product was obtained.

2,3,4,5-tetrafluoro-6-iodo-N-((*S*)-quinolin-4-yl((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)benzamide (2a)



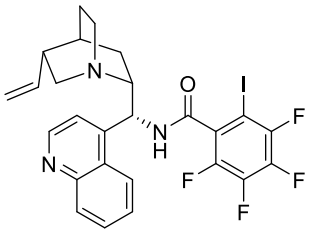
Cinchonidine-derived amine was used; reaction time: 14 h; white solids (85% yield); ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C): δ 8.93 (d, *J* = 4.4 Hz, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.74 (t, *J* = 8.4 Hz, 1H), 7.62 (t, *J* = 8.4 Hz, 1H), 7.61 (br, 1H), 7.55 (d, *J* = 4.4 Hz, 1H), 5.67 (ddd, *J* = 17.6, 10.0, 7.2 Hz, 1H), 5.45 (br, 1H), 4.98-4.90 (m, 2H), 3.28-3.22 (m, 3H), 2.78-2.72 (m, 2H), 2.33 (br, 1H), 1.73-1.43 (m, 4H), 1.11-1.06 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): –114.7 (m, 1F), –139.5 (m, 1F), –151.9 (m, 1F), –153.3 (m, 1F); {^{19}F}^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1, 150.0, 148.8, 147.8, 144.5, 140.9, 140.6, 140.3, 130.6, 129.2, 126.7, 123.4, 114.8, 74.9, 55.9, 40.9, 39.4, 27.8, 27.3, 25.9; IR (neat) 3299, 2945, 1657, 1497, 1457, 1024, 758 cm^{-1}; HRMS (ESI+) calcd for $C_{26}H_{23}F_4IN_3O$ $[M + H]^+$ 596.0816: found 596.0807; $[\alpha]_D^{24}$ = +46.2 (*c* = 1.0, $CHCl_3$).

2,3,4,5-tetrafluoro-6-iodo-N-((*S*)-(6-methoxyquinolin-4-yl)((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)benzamide (2b)



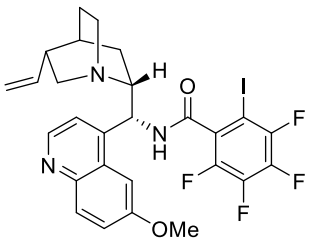
Quinine-derived amine was used; reaction time: 24 h; white solids (57% yield); ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C): δ 8.74 (d, *J* = 4.8 Hz, 1H), 8.05 (d, *J* = 9.2 Hz, 1H), 7.66 (br, 1H), 7.54 (br, 1H), 7.46 (d, *J* = 4.8 Hz, 1H), 7.40 (dd, *J* = 9.6, 2.8 Hz, 1H), 5.69 (ddd, *J* = 18.0, 10.0, 10.0 Hz, 1H), 5.52 (br, 1H), 4.98-4.92 (m, 2H), 3.98 (s, 3H), 3.26-3.06 (m, 3H), 2.79-2.65 (m, 2H), 2.32 (br, 1H), 1.72-1.65 (m, 3H), 1.49-1.44 (m, 1H), 1.09-1.05 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): –114.6 (m, 1F), –139.3 (m, 1F), –151.8 (m, 1F), –153.3 (m, 1F); {^{19}F}^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 158.0, 147.7, 147.4, 144.6, 144.4, 141.0, 140.4, 140.2, 131.7, 128.4, 126.6, 121.7, 118.9, 114.8, 101.7, 75.0, 60.8, 55.8, 51.3, 41.0, 39.4, 27.9, 27.3, 25.8; IR (neat) 3279, 2933, 1668, 1455, 1240, 736 cm^{-1}; HRMS (ESI+) calcd for $C_{27}H_{25}F_4IN_3O_2$ $[M + H]^+$ 626.0922: found 626.0906; $[\alpha]_D^{24}$ = +57.5 (*c* = 1.0, $CHCl_3$).

2,3,4,5-tetrafluoro-6-iodo-N-((*R*)-quinolin-4-yl((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)benzamide (3a)



Cinchonine-derived amine was used; reaction time: 12 h; white solids (68% yield); ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C): δ 8.90 (d, *J* = 4.8 Hz, 1H), 8.36 (d, *J* = 8.8 Hz, 1H), 8.15 (d, *J* = 8.8 Hz, 1H), 7.76-7.58 (m, 3H), 7.52 (d, *J* = 4.8 Hz, 1H), 5.96 (ddd, *J* = 17.6, 10.8, 6.8 Hz, 1H), 5.43 (br, 1H), 5.22-5.12 (m, 2H), 3.03-2.86 (m, 5H), 2.36-2.30 (m, 1H), 1.82-1.41 (m, 4H), 1.06-0.99 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): –114.7 (m, 1F), –139.5 (m, 1F), –152.0 (m, 1F), –153.3 (m, 1F); {^{19}F}^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1, 149.9, 148.8, 147.9, 144.5, 140.6, 140.4, 140.1, 130.6, 129.2, 126.8, 126.6, 123.4, 115.1, 74.9, 49.2, 47.2, 39.2, 27.4, 26.9, 25.5; IR (neat) 3297, 2939, 1655, 1497, 1456, 1024, 758 cm^{-1}; HRMS (ESI+) calcd for $C_{26}H_{23}F_4IN_3O$ $[M + H]^+$ 596.0816: found 596.0815; $[\alpha]_D^{24}$ = +46.6 (*c* = 1.0, $CHCl_3$).

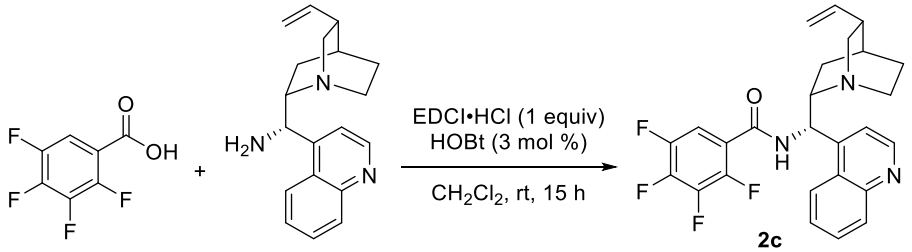
2,3,4,5-tetrafluoro-6-iodo-N-((*R*)-(6-methoxyquinolin-4-yl)((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)benzamide (3b)



Quinidine-derived amine was used; reaction time: 8 h; white solids (75% yield); ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C): δ 8.75 (d, *J* = 4.6 Hz, 1H), 8.04 (d, *J* = 9.4 Hz, 1H), 7.58 (br, 1H), 7.52 (br, 1H), 7.47 (d, *J* = 4.6 Hz, 1H), 7.39 (dd, *J* = 9.4, 2.5 Hz, 1H), 5.97 (ddd, *J* = 17.4, 11.0, 6.2 Hz, 1H), 5.20-5.10 (m, 2H), 3.98 (s, 3H), 3.10-2.87 (m, 5H), 2.37-2.31 (m, 1H), 1.61-1.44 (m, 4H), 1.11-1.05 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): –114.6 (m, 1F), –139.4 (m, 1F), –151.9 (m, 1F), –153.3 (m, 1F); {^{19}F}^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 157.9, 147.5, 147.2, 145.0, 144.4, 144.2, 140.5, 140.3, 140.0, 131.4, 128.3, 126.7, 122.2, 122.0, 118.6, 114.7, 101.0, 75.0, 60.8, 55.5, 50.6, 49.0, 46.8, 38.9, 39.4, 27.1, 26.5, 25.3; IR (neat) 3160, 2934, 1670, 1472, 1241, 748 cm^{-1}; HRMS (ESI+) calcd for $C_{27}H_{25}F_4IN_3O_2$ [M

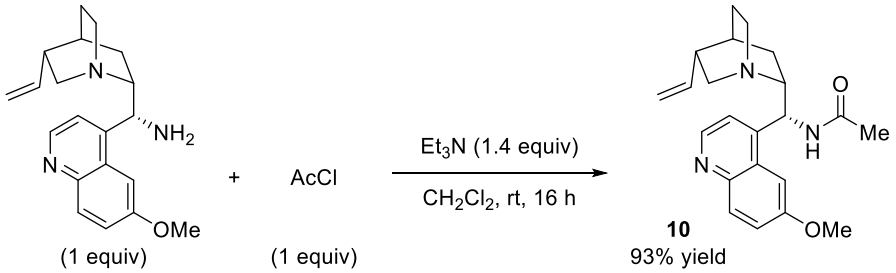
+ H]$^+$ 626.0922: found 626.0922; $[\alpha]_D^{20}$ = +44.2 (*c* = 1.0, $CHCl_3$).

B. 2,3,4,5-tetrafluoro-N-((*S*)-quinolin-4-yl((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)benzamide (2c)



2,3,4,5-Tetrafluorobenzoic acid (0.5 mmol, 1.0 equiv, 0.1 M), cinchonidine-derived amine (0.5 mmol, 1.0 equiv, 0.1 M), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide Hydrochloride (EDCI·HCl) (0.5 mmol, 1.0 equiv, 0.1 M), and 1-hydroxybenzotriazole (HOBt) (0.015 mmol, 0.03 equiv, 0.003 M) were added to a one-necked round flask containing a stir bar under Ar. CH_2Cl_2 (5 mL) was added to the flask, and the mixture was stirred at room temperature. After 15 h, additional CH_2Cl_2 was added. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated under reduced pressure. After purification by silica gel column chromatography (hexane/ethyl acetate/Et_3N = 1/1/0.03), product **2c** was obtained. Pale yellow oil (94% yield); ^{1}H NMR (500MHz, $CDCl_3$, 50 °C) δ 8.89 (d, *J* = 4.3 Hz, 1H), 8.38 (d, *J* = 8.6 Hz, 1H), 8.16-8.14 (m, 2H), 7.72 (t, *J* = 7.2 Hz, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.56-7.51 (m, 1H), 7.44 (d, *J* = 4.6 Hz, 1H), 5.74-5.67 (m, 1H), 5.41 (br, 1H), 4.99-4.93 (m, 2H), 3.30 (dd, *J* = 10.3, 13.8 Hz, 1H), 3.18 (br, 1H), 3.08 (br, 1H), 2.80-2.77 (m, 2H), 2.32 (br, 1H), 1.70-1.65 (m, 3H), 1.44-1.42 (m, 1H), 1.04-1.00 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): –137.9 (m, 1F), –139.7 (m, 1F), –150.2 (m, 1F), –155.1 (m, 1F); {^{19}F}^{13}C NMR (100 MHz, $CDCl_3$): δ 170.97, 160.22, 149.95, 148.48, 146.91, 146.14, 142.35, 141.06, 140.46, 130.52, 129.08, 126.72, 122.84, 117.42, 117.38, 114.52, 112.52, 60.22, 55.78, 40.70, 39.43, 27.70, 27.15, 25.78, 20.87, 14.03; IR (neat) 3334, 3077, 2944, 2868, 1670, 1478, 1360, 1244, 1037, 909, 729 cm^{-1}; HRMS (ESI+) calcd for $C_{26}H_{24}F_4N_3O$ [M + H]$^+$ 470.1850: found 470.1841; $[\alpha]_D^{21}$= –92.9 (*c* = 1.0, $CHCl_3$).

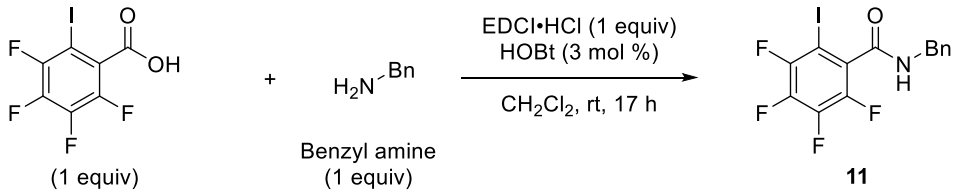
C. *N*-((*R*)-(6-methoxyquinolin-4-yl)((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)acetamide (10)



Quinidine-derived amine (1.0 mmol, 1.0 equiv, 0.1 M) and triethylamine (1.4 mmol, 1.4 equiv, 0.14 M) were dissolved in CH_2Cl_2 (10 mL). The solution was cooled to 0 °C, and acetyl chloride (1.0 mmol, 1.0 equiv, 0.1 M) was added slowly over 10 min. The reaction mixture was stirred at room temperature for 16 h, and CH_2Cl_2 was added. The organic layer was washed with sat. $NaHCO_3$ aq, dried over Na_2SO_4, and concentrated under reduced pressure. After purification by silica gel column chromatography ($CHCl_3$/MeOH = 20/1 to 10/1), product **10** was obtained. White solids (93% yield); ^{1}H NMR (400, Hz, $CDCl_3$, 50 °C): δ 8.71 (d, *J* = 4.8 Hz, 1H), 8.01 (d, *J* = 9.2 Hz, 1H),

7.61 (d, J = 2.8 Hz, 1H), 7.39-7.33 (m, 2H), 6.99 (br s, 1H), 5.95-5.87 (m, 1H), 5.36 (br s, 1H), 5.18-5.12 (m, 2H), 3.98 (s, 3H), 3.08-2.92 (m, 5H), 2.67 (br s, 1H), 2.36-2.30 (m, 1H), 1.97 (s, 3H), 1.68 (br, 1H), 1.64-1.49 (m, 2H), 1.33-1.25 (m, 1H), 1.06-0.99 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 157.5, 147.0, 145.4, 144.3, 140.0, 131.1, 121.8, 118.7, 114.5, 101.2, 77.2, 59.2, 56.2, 48.9, 46.5, 38.6, 26.9, 26.2, 25.3, 22.7; IR (neat) 3006, 2941, 1653, 1620, 1224, 1083, 908, 664 cm^{-1}; HRMS (ESI+) calcd for $C_{22}H_{28}O_2N_3$ $[M + H]^+$ 366.2176: found 366.2169; $[\alpha]_D^{20}$ =+188.5 (c = 1.0, $CHCl_3$).

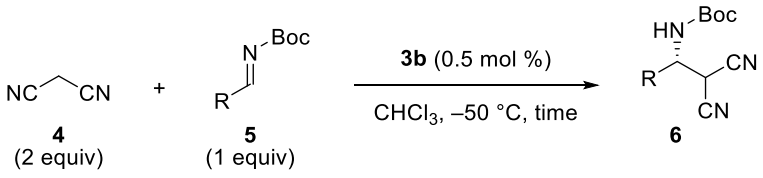
D. *N*-benzyl-2,3,4,5-tetrafluoro-6-iodobenzamide (11)



2,3,4,5-Tetrafluoro-6-iodobenzoic acid (0.5 mmol, 1.0 equiv, 0.1 M), benzyl amine (0.5 mmol, 1.0 equiv, 0.1 M), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide Hydrochloride (EDCI·HCl) (0.5 mmol, 1.0 equiv, 0.1 M), and 1-hydroxybenzotriazole (HOBt) (0.015 mmol, 0.03 equiv, 0.003 M) were added to a one-necked round flask containing a stir bar under Ar. CH_2Cl_2 (5 mL) was added to the flask, and the mixture was stirred at room temperature. After 17 h, additional CH_2Cl_2 was added. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was recrystallized from hexane/CH_2Cl_2 to give product **11**. White solids (52% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.31 (m, 5 H), 6.10 (br, 1H), 4.66 (d, J = 5.6 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$): –114.1 (m, 1F), –138.6 (m, 1F), –151.4 (m, 1F), –153.1 (m, 1F); {^{19}F}^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 147.6, 144.1, 140.4, 140.1, 136.6, 128.7, 127.8, 126.6, 74.9, 44.2; IR (neat) 3224, 3060, 1643, 1499, 1453, 744 cm^{-1}; HRMS (ESI+) calcd for $C_{14}H_7F_4INO$ $[M - H]^-$ 407.9508: found 407.9522.

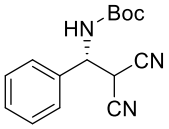
3. General procedure for asymmetric Mannich reaction of malononitrile with *N*-Boc aldimines

Catalyst **3b** (0.6 mg, 0.001 mmol, 0.005 eq) and malononitrile **4** (26.4 mg, 0.4 mmol, 2 eq) were added to a one-necked round flask containing a stir bar under Ar. $CHCl_3$ (2.0 ml) was added to the flask, and the mixture was stirred at –50 °C. To the resulting suspension, *N*-Boc imine **5** (0.2 mmol, 1.0 eq) was added. After being stirred for appropriate time, solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 4/1) to afford product. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC using Daicel Chiralcel AD-H, AD-3, OD-H, Chiralpak IA, and IC-3 column.



4. Analytical data for products of enantioselective Mannich reaction of malononitrile with *N*-Boc aldimines

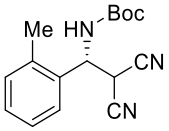
***tert*-butyl (*R*)-(2,2-dicyano-1-phenylethyl)carbamate (6a)**



Reaction time: 32 h; colorless oil (50.4 mg, 93% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (s, 5H), 5.28 (d, J = 5.5 Hz, 1H), 5.08 (t, J = 5.2 Hz, 1H), 4.82 (d, J = 4.30 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.8, 133.6, 130.2, 129.5, 127.0, 111.1, 110.8, 81.8, 55.6, 29.6, 28.3; IR (neat) 3385, 2979, 2900, 1684, 1508, 1291, 1252, 1165, 757 cm^{-1}; HRMS (ESI+) calcd for $C_{15}H_{17}N_3NaO_2$ $[M + Na]^+$ 294.1213: found 294.1208; $[\alpha]_D^{24}$ = +26.8 (c = 0.5, $CHCl_3$, 98% ee).

Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexane:2-propanol = 90:10, 0.5 mL/min, 254 nm); minor enantiomer t_R = 34.8 min, major enantiomer t_R = 20.7 min, 98% ee.

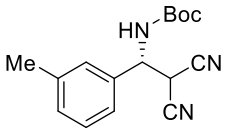
***tert*-butyl (*R*)-(2,2-dicyano-1-(o-tolyl)ethyl)carbamate (6b)**



Reaction time: 48 h; white solids (51.8 mg, 91% yield); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (br, 1H), 7.35-7.33 (m, 2H), 7.29-7.28 (m, 1H), 5.46 (t, J = 6.0 Hz, 1H), 5.14 (d, J = 5.5 Hz, 1H), 4.75 (d, J = 4.9 Hz, 1H), 2.46 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.8, 136.3, 132.7, 131.6, 129.8, 127.2, 125.1, 111.3, 110.8, 81.7, 50.6, 28.6, 28.1, 19.6; IR (neat) 3348, 2900, 1684, 1508, 1366, 1331, 1250, 1163, 794, 607 cm^{-1}; HRMS (ESI+) calcd for $C_{16}H_{19}N_3NaO_2$ $[M + Na]^+$ 308.1369: found 308.1365; $[\alpha]_D^{24}$ = +69.5 (c = 0.5, $CHCl_3$, 98% ee).

Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexane:2-propanol = 90:10, 0.3 mL/min, 254 nm); minor enantiomer t_R = 33.1 min, major enantiomer t_R = 34.8 min, 98% ee.

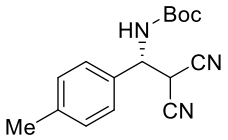
***tert*-butyl (*R*)-(2,2-dicyano-1-(m-tolyl)ethyl)carbamate (6c)**



Reaction time: 32 h; colorless oil (49.3 mg, 86% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.21 (m, 4H), 5.32 (br, 1H), 5.06 (t, J = 6.9 Hz, 1H), 4.78 (d, J = 6.0 Hz, 1H), 2.24 (s, 3H) 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.8, 139.4, 133.6, 130.9, 129.3, 127.6, 124.0, 111.1, 110.8, 81.7, 55.5, 29.6, 28.1, 21.4; IR (neat) 3346, 2979, 2927, 1703, 1509, 1368, 1250, 1159, 772 cm^{-1}; HRMS (ESI+) calcd for $C_{16}H_{19}N_3NaO_2$ $[M + Na]^+$ 308.1369: found 308.1362; $[\alpha]_D^{25}$ = +27.0 (c = 1.0, $CHCl_3$, 98% ee).

Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexane:2-propanol = 90:10, 0.5 mL/min, 254 nm); minor enantiomer t_R = 30.7 min, major enantiomer t_R = 17.9 min, 98% ee.

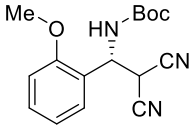
***tert*-butyl (*R*)-(2,2-dicyano-1-(p-tolyl)ethyl)carbamate (6d)**



Reaction time: 48 h; white solids (51.1 mg, 90% yield); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 8.6 Hz, 2H), 5.28 (br, 1H), 5.05 (t, J = 5.4 Hz, 1H), 4.79 (d, J = 4.3 Hz, 1H), 2.39 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.9, 140.3, 130.7, 130.1, 126.9, 111.1, 110.9, 81.7, 55.4, 29.7, 28.1, 21.9; IR (neat) 3347, 2980, 1703, 1508, 1368, 1249, 1161 cm^{-1}; HRMS (ESI+) calcd for $C_{16}H_{19}N_3NaO_2$ $[M + Na]^+$ 308.1369: found 308.1362; $[\alpha]_D^{25}$ = +33.1 (c = 0.5, $CHCl_3$, 97% ee).

Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexane:2-propanol = 90:10, 0.3 mL/min, 254 nm); minor enantiomer t_R = 49.2 min, major enantiomer t_R = 33.9 min, 97% ee.

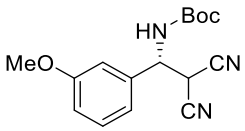
***tert*-butyl (*R*)-(2,2-dicyano-1-(2-methoxyphenyl)ethyl)carbamate (6e)**



Reaction time: 24 h; white solids (48.0 mg, 80% yield); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42-7.38 (m, 1H), 7.33 (d, J = 7.2 Hz, 1H), 7.04-7.01 (m, 1H), 6.97 (d, J = 8.3 Hz, 1H), 5.83 (d, J = 9.2 Hz, 1H), 5.55 (dd, J = 9.2, 7.2 Hz, 1H), 4.52 (d, J = 7.2 Hz, 1H), 3.91 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.4, 154.6, 131.1, 129.2, 122.2, 121.4, 111.33, 111.26, 111.18, 81.1, 55.5, 52.7, 28.9, 28.1; IR (neat) 3384, 2944, 1697, 1512, 1244, 1171 cm^{-1}; HRMS (ESI+) calcd for $C_{16}H_{19}N_3NaO_3$ $[M + Na]^+$ 324.1319: found 324.1315; $[\alpha]_D^{25}$ = +38.0 (c = 0.5, $CHCl_3$, 96% ee).

Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexane:2-propanol = 90:10, 1.0 mL/min, 254 nm); minor enantiomer t_R = 14.0 min, major enantiomer t_R = 16.7 min, 96% ee.

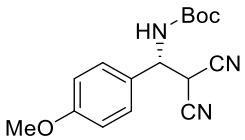
***tert*-butyl (*R*)-(2,2-dicyano-1-(3-methoxyphenyl)ethyl)carbamate (6f)**



Reaction time: 48 h; colorless oil (53.1 mg, 88% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (t, J = 8.0 Hz, 1H), 7.05-6.96 (m, 3H), 5.60 (br, 1H), 5.10 (t, J = 6.0 Hz, 1H), 4.76 (d, J = 4.1 Hz, 1H), 3.82 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.0, 154.8, 135.3, 130.5, 119.0, 115.4, 112.7, 111.2, 110.9, 81.6, 55.4, 55.3, 29.6, 28.1; IR (neat) 3347, 2979, 1703, 1512, 1251, 1161, 1219 cm^{-1}; HRMS (ESI+) calcd for $C_{16}H_{19}N_3NaO_3$ $[M + Na]^+$ 324.1319: found 324.1315; $[\alpha]_D^{25}$ = +32.3 (c = 0.5, $CHCl_3$, 97% ee).

Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (hexane:2-propanol = 90:10, 1.0 mL/min, 254 nm); minor enantiomer t_R = 27.7 min, major enantiomer t_R = 16.6 min, 97% ee.

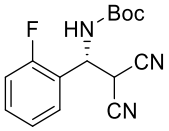
***tert*-butyl (*R*)-(2,2-dicyano-1-(4-methoxyphenyl)ethyl)carbamate (6g)**



Reaction time: 48 h; white solids (52.6 mg, 87% yield); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (d, J = 8.6 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 5.31 (br, 1H), 5.03 (t, J = 5.5 Hz, 1H), 4.80 (d, J = 3.4 Hz, 1H), 3.83 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.7, 154.9, 128.3, 125.7, 114.7, 111.2, 110.9, 81.7, 55.3, 55.2, 29.7, 28.1; IR (neat) 3385, 2978, 2910, 1692, 1614, 1506, 1456, 1162, 1112 cm^{-1}; HRMS (ESI+) calcd for $C_{16}H_{19}N_3NaO_3$ $[M + Na]^+$ 324.1319: found 324.1312; $[\alpha]_D^{25}$ = +33.2 (c = 0.5, $CHCl_3$, 89% ee).

Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexane:2-propanol = 90:10, 0.5 mL/min, 254 nm); minor enantiomer t_R = 27.4 min, major enantiomer t_R = 13.9 min, 89% ee.

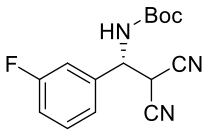
***tert*-butyl (*R*)-(2,2-dicyano-1-(2-fluorophenyl)ethyl)carbamate (6h)**



Reaction was performed in $CHCl_3$ (2.7 mL) at –20 °C for 24 h. White solids (49.3 mg, 85% yield); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51-7.43 (m, 2H), 7.29-7.26 (m, 1H), 7.21-7.17 (m, 1H), 5.57 (t, J = 6.3 Hz, 1H), 5.47 (d, J = 6.3 Hz, 1H), 4.57 (d, J = 5.7 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.0 (d, $^1J_{CF}$ = 246.8 Hz), 154.5, 131.9 (d, $^3J_{CF}$ = 8.3 Hz), 128.5, 125.3 (d, $^4J_{CF}$ = 3.6 Hz), 121.5 (d, $^3J_{CF}$ = 13.1 Hz), 116.5 (d, $^2J_{CF}$ = 21.5 Hz), 110.8, 110.5, 81.9, 50.4, 29.4, 28.1; IR (neat) 3386, 2926, 1685, 1507, 1492, 1168, 1085, 773 cm^{-1}; HRMS (ESI+) calcd for $C_{15}H_{16}FN_3NaO_2$ $[M + Na]^+$ 312.1119: found 312.1114; $[\alpha]_D^{25}$ = +22.9 (c = 0.5, $CHCl_3$, 93% ee).

Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane:2-propanol = 70:30, 0.3 mL/min, 254 nm); minor enantiomer t_R = 18.0 min, major enantiomer t_R = 20.6 min, 93% ee.

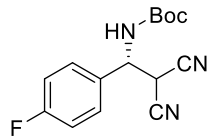
***tert*-butyl (*R*)-(2,2-dicyano-1-(3-fluorophenyl)ethyl)carbamate (6i)**



Reaction was performed in $CHCl_3$ (2.7 mL) at –20 °C for 24 h. Colorless oil (43.6 mg, 75% yield); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49-7.45 (m, 1H), 7.29-7.17 (m, 3H), 5.27 (br, 1H), 5.11 (t, J = 5.4 Hz, 1H), 5.80 (d, J = 3.8 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.9 (d, $^1J_{CF}$ = 248.0 Hz), 154.7, 135.9, 131.3 (d, $^3J_{CF}$ = 8.4 Hz), 122.8, 117.4 (d, $^2J_{CF}$ = 21.5 Hz), 114.4 (d, $^2J_{CF}$ = 22.7 Hz), 110.8, 110.5, 82.1, 55.1, 29.5, 28.1; IR (neat) 3339, 2981, 2932, 1703, 1514, 1250, 1220, 1158 cm^{-1}; HRMS (ESI+) calcd for $C_{15}H_{16}FN_3NaO_2$ $[M + Na]^+$ 312.1119: found 312.1116; $[\alpha]_D^{26}$ = +22.4 (c = 0.5, $CHCl_3$, 96% ee).

Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane:2-propanol = 90:10, 0.5 mL/min, 254 nm); minor enantiomer t_R = 49.2 min, major enantiomer t_R = 25.2 min, 96% ee.

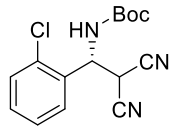
***tert*-butyl (*R*)-(2,2-dicyano-1-(4-fluorophenyl)ethyl)carbamate (6j)**



Reaction time: 36 h; colorless oil (46.4 mg, 80% yield); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50-7.48 (m, 2H), 7.19-7.16 (m, 2H), 5.22 (br, 1H), 5.08 (t, *J* = 5.5 Hz, 1H), 4.83 (d, *J* = 3.2 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6 (d, $^1J_{CF}$ = 249.2 Hz), 154.8, 129.6, 129.1 (d, $^3J_{CF}$ = 8.3 Hz), 116.7 (d, $^2J_{CF}$ = 22.7 Hz), 111.9, 110.7, 82.0, 55.1, 29.6, 28.1; IR (neat) 3348, 2982, 2930, 1704, 1509, 1220, 1159 cm^{-1}; HRMS (ESI+) calcd for $C_{15}H_{16}FN_3NaO_2$ [M + Na]$^+$ 312.1119: found 312.1117; $[\alpha]_D^{25}$ = +21.2 (*c* = 0.5, $CHCl_3$, 98% ee).

Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexane:2-propanol = 90:10, 0.5 mL/min, 254 nm); minor enantiomer t_R = 40.5 min, major enantiomer t_R = 20.4 min, 98% ee.

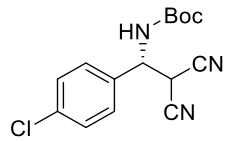
***tert*-butyl (*R*)-(1-(2-chlorophenyl)-2,2-dicyanoethyl)carbamate (6k)**



Reaction time: 26 h; white solids (47.6 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57-7.55 (m, 1H), 7.50-7.39 (m, 3H), 5.80 (dd, *J* = 7.8, 5.9 Hz, 1H), 5.45 (d, *J* = 6.9 Hz, 1H), 4.66 (d, *J* = 5.0 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4, 133.0, 132.1, 131.1, 130.6, 128.0, 127.8, 110.9, 110.4, 81.9, 51.8, 28.7, 28.1; IR (neat) 3335, 2979, 1708, 1514, 1369, 1249, 1162, 771 cm^{-1}; HRMS (ESI+) calcd for $C_{15}H_{16}ClN_3NaO_2$ [M + Na]$^+$ 328.0823: found 328.0821; $[\alpha]_D^{26}$ = +22.7 (*c* = 0.5, $CHCl_3$, 94% ee).

Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (hexane:2-propanol = 80:20, 0.5 mL/min, 254 nm) ; minor enantiomer tr = 12.6 min, major enantiomer tr = 18.8 min, 94% ee.

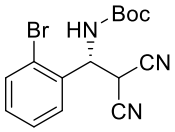
***tert*-butyl (*R*)-(1-(4-chlorophenyl)-2,2-dicyanoethyl)carbamate (6l)**



Reaction was performed in $CHCl_3$ (2.7 mL) at –20 °C for 48 h. White solids (47.5 mg, 78% yield); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48-7.42 (m, 4H), 5.22 (d, *J* = 4.3 Hz, 1H), 5.07 (t, *J* = 5.5 Hz, 1H), 4.82 (d, *J* = 3.7 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.7, 136.4, 132.1, 129.8, 128.4, 110.9, 110.6, 82.1, 55.2, 29.5, 28.1; IR (neat) 3375, 1693, 1515, 1493, 1246, 1167, 783, 594 cm^{-1}; HRMS (ESI+) calcd for $C_{15}H_{16}ClN_3NaO_2$ [M + Na]$^+$ 328.0823: found 328.0822; $[\alpha]_D^{26}$ = +29.1 (*c* = 0.5, $CHCl_3$, 96% ee).

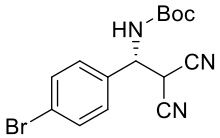
Enantiomeric excess was determined by HPLC with a Chiralpak IC-3 column (hexane:2-propanol = 95:5, 0.5 mL/min, 254 nm); minor enantiomer t_R = 27.0 min, major enantiomer t_R = 21.8 min, 96% ee.

***tert*-butyl (*R*)-(1-(2-bromophenyl)-2,2-dicyanoethyl)carbamate (6m)**



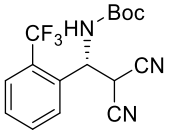
Reaction time: 48 h; colorless oil (64.0 mg, 91% yield); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 7.4 Hz, 1H), 7.46 (t, J = 7.4 Hz, 1H), 7.33-7.30 (m, 1H), 5.79 (dd, J = 8.0, 5.2 Hz, 1H), 5.44 (d, J = 6.9 Hz, 1H), 4.68 (d, J = 4.6 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.4, 133.9, 133.8, 131.3, 128.5, 127.8, 123.3, 110.9, 110.3, 81.9, 53.9, 28.7, 28.1; IR (neat) 3350, 2900, 1684, 1505, 1249, 1151, 754 cm^{-1}; HRMS (ESI+) calcd for $C_{15}H_{16}BrN_3NaO_2$ $[M + Na]^+$ 372.0318: found 372.0314; $[\alpha]_D^{26}$ = +15.7 (c = 0.5, $CHCl_3$, 93% ee).
Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexane:2-propanol = 80:20, 0.3 mL/min, 254 nm); minor enantiomer t_R = 20.7 min, major enantiomer t_R = 27.1 min, 93% ee.

***tert*-butyl (*R*)-(1-(4-bromophenyl)-2,2-dicyanoethyl)carbamate (6n)**



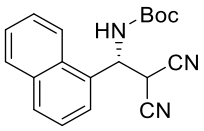
Reaction was performed in $CHCl_3$ (2.7 mL) at –20 °C for 24 h. White solids (53.0 mg, 76% yield);Colorless oil (53.1 mg, 88% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 5.23 (br, 1H), 5.08 (t, J = 5.5 Hz, 1H), 4.79 (d, J = 3.4 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.7, 132.7, 132.6, 128.7, 124.5, 110.8, 110.6, 82.1, 55.2, 29.5, 28.1; IR (neat) 3367, 2915, 1687, 1508, 1246, 1155 cm^{-1}; HRMS (ESI+) calcd for $C_{15}H_{15}BrN_3O_2$ $[M - H]^-$ 348.0353: found 348.0360; $[\alpha]_D^{26}$ = +29.2 (c = 0.5, $CHCl_3$, 95% ee).
Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (hexane:2-propanol = 70:30, 0.3 mL/min, 254 nm) ; minor enantiomer tr = 28.4 min, major enantiomer tr = 18.1 min, 95% ee.

***tert*-butyl (*R*)-(2,2-dicyano-1-(2-(trifluoromethyl)phenyl)ethyl)carbamate (6o)**



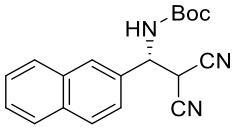
Reaction was performed in $CHCl_3$ (2.7 mL) at –20 °C for 24 h. Colorless oil (55.2 mg, 81% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94-7.44 (m, 4H), 5.66 (br, 1H), 5.32 (br, 1H), 4.73 (br, 1H), 1.47 (s, 9H); $\{^{19}F\}^{13}$C NMR (100 MHz, $CDCl_3$): δ 154.3, 133.3, 133.2, 130.1, 128.6, 127.4, 127.0, 123.6, 110.7, 110.4, 82.0, 50.2, 29.2, 28.0; IR (neat) 3346, 2982, 2934, 1704, 1456, 1367, 1312, 1120, 770 cm^{-1}; HRMS (ESI+) calcd for $C_{16}H_{15}F_3N_3O_2$ $[M - H]^-$ 338.1122: found 338.1118; $[\alpha]_D^{17}$ = +19.1 (c = 1.0, $CHCl_3$, 88% ee).
Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexane:2-propanol = 95:5, 1.5 mL/min, 254 nm); minor enantiomer t_R = 14.9 min, major enantiomer t_R = 45.2 min, 88% ee.

***tert*-butyl (*R*)-(2,2-dicyano-1-(naphthalen-1-yl)ethyl)carbamate (6p)**



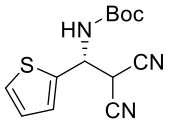
Reaction time: 48 h; white solids (64.0 mg, 99% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97-7.94 (m, 3H), 7.75 (d, *J* = 5.5 Hz, 1H), 7.64-7.53 (m, 3H), 6.14 (dd, *J* = 5.5, 4.1 Hz, 1H), 5.39 (d, *J* = 5.5 Hz, 1H), 4.79 (d, 4.1, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.8, 134.0, 130.6, 130.2, 130.0, 129.4, 127.6, 126.6, 125.1, 123.9, 121.8, 111.4, 110.8, 81.8, 50.3, 28.8, 28.1; IR (neat) 3350, 2994, 2898, 1682, 1507, 1330, 1251, 1162, 775 cm^{-1}; HRMS (ESI+) calcd for $C_{19}H_{19}N_3NaO_2$ $[M + Na]^+$ 344.1369: found 344.1361; $[\alpha]_D^{25}$ = +57.2 (*c* = 0.5, $CHCl_3$, 98% ee).
Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexane:2-propanol = 90:10, 1.0 mL/min, 254 nm); minor enantiomer t_R = 41.6 min, major enantiomer t_R = 12.8 min, 98% ee.

***tert*-butyl (*R*)-(2,2-dicyano-1-(naphthalen-2-yl)ethyl)carbamate (6q)**



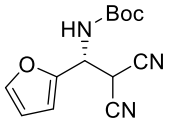
Reaction time: 40 h; white solids (52.0 mg, 81% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94-7.86 (m, 4H), 7.57-7.53 (m, 3H), 5.46 (br, 1H), 5.30-5.28 (m, 1H), 4.86 (d, *J* = 3.2 Hz, 1H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.9, 133.7, 132.9, 131.0, 129.6, 128.3, 127.8, 127.3, 127.1, 126.9, 123.7, 111.1, 110.8, 81.8, 55.7, 29.7, 28.1; IR (neat) 3343, 2904, 1687, 1509, 1323, 1244, 1159, 856, 748, 616 cm^{-1}; HRMS (ESI+) calcd for $C_{19}H_{19}N_3NaO_2$ $[M + Na]^+$ 344.1369: found 344.1363; $[\alpha]_D^{25}$ = +63.9 (*c* = 0.5, $CHCl_3$, 98% ee).
Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexane:2-propanol = 90:10, 0.5 mL/min, 254 nm); minor enantiomer t_R = 54.7 min, major enantiomer t_R = 26.6 min, 98% ee.

***tert*-butyl (*R*)-(2,2-dicyano-1-(thiophen-2-yl)ethyl)carbamate (6r)**



Reaction time: 72 h; white solids (44.5 mg, 80% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (dd, *J* = 5.3, 1.2 Hz, 1H), 7.32 (d, *J* = 3.4 Hz, 1H), 7.09 (dd, *J* = 5.0, 3.6 Hz, 1H), 5.40 (t, *J* = 6.0 Hz, 1H), 5.27 (d, *J* = 6.2 Hz, 1H), 4.79 (d, *J* = 3.7 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4, 135.5, 127.6, 127.4, 127.0, 110.9, 110.6, 82.1, 51.8, 30.2, 28.1; IR (neat) 3331, 1692, 1510, 1247, 1159, 619 cm^{-1}; HRMS (ESI+) calcd for $C_{13}H_{15}N_3NaO_2S$ $[M + Na]^+$ 300.0777: found 300.0776; $[\alpha]_D^{26}$ = +22.6 (*c* = 0.5, $CHCl_3$, 73% ee).
Enantiomeric excess was determined by HPLC with a Chiralcel AD-3 column (hexane:2-propanol = 80:20, 0.5 mL/min, 254 nm) ; minor enantiomer tr = 21.6 min, major enantiomer tr = 16.1 min, 73% ee.

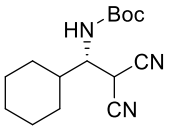
***tert*-butyl (*R*)-(2,2-dicyano-1-(furan-2-yl)ethyl)carbamate (6s)**



Reaction was performed in $CHCl_3$ (2.7 mL) at –20 °C for 24 h. White solids (36.1 mg, 69% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 1.8 Hz, 1H), 6.57 (d, *J* = 3.2 Hz, 1H), 6.45 (dd, *J* = 3.4, 2.0 Hz, 1H), 5.44 (d, *J* = 7.8 Hz, 1H), 5.33 (dd, *J* = 7.8, 5.2 Hz, 1H), 4.58 (d, *J* = 5.0 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4, 146.3, 144.0, 111.0, 110.6, 110.5, 110.0, 82.0, 49.9, 28.6, 28.1; IR (neat) 3336, 2909, 1687, 1500, 1249, 1156, 1016, 751 cm^{-1}; HRMS (ESI+) calcd for $C_{13}H_{15}N_3NaO_3$ $[M + Na]^+$ 284.1006: found 284.1005; $[\alpha]_D^{26}$ = +2.1 (*c* = 0.5, $CHCl_3$, 81% ee).

Enantiomeric excess was determined by HPLC with a Chiralpak IC-3 column (hexane:2-propanol = 70:30, 0.5 mL/min, 220 nm) ; minor enantiomer tr = 25.7 min, major enantiomer tr = 22.4 min, 81% ee.

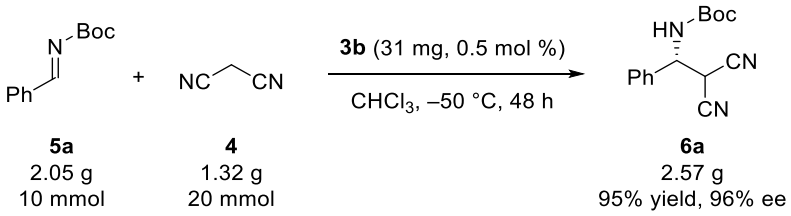
***tert*-butyl (*S*)-(2,2-dicyano-1-cyclohexylethyl)carbamate (6t)**



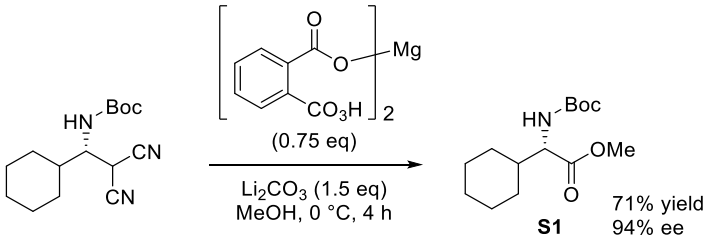
Reaction was performed with 1 mol % of **1d** for 96 h. White solids (40.6 mg, 73% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.79 (d, *J*= 9.6 Hz, 1H), 4.17 (d, *J*= 4.4 Hz, 1H), 4.05-3.99 (m, 1H), 1.84-1.63 (m, 6H), 1.47 (s, 9H), 1.37-1.02 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0, 111.4, 111.3, 81.2, 55.8, 39.9, 30.0, 28.4, 28.2, 27.0, 25.60, 25.57, 25.5; IR (neat) 3355, 2931, 2856, 1705, 1516, 1368, 1256, 1170 cm^{-1}; HRMS (ESI+) calcd for $C_{15}H_{23}N_3NaO_2$ $[M + Na]^+$ 300.1682: found 300.1677; $[\alpha]_D^{26}$ = –64.5 (*c* = 0.5, $CHCl_3$).

5. Gram-scale synthesis of 6a

Catalyst **3b** (31 mg, 0.05 mmol, 0.005 eq) and malononitrile **4** (1.32 g, 20 mmol, 2 eq) were added to a one-necked round flask containing a stir bar under Ar. $CHCl_3$ (100 ml) was added to the flask, and the mixture was stirred at –50 °C. To the resulting suspension, *N*-Boc imine **5a** (2.16 g, 10 mmol, 1.0 eq) was added. After being stirred for 48 h, solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 4/1 to 0/1) to afford colorless oil **6a** (2.57 g, 95% yield, 96% ee). 30 mg of catalyst **3b** were recovered after silica gel column chromatography (97% recovery).



6. Transformation of *tert*-butyl (*S*)-(2,2-dicyano-1-cyclohexylethyl)carbamate (6t)



Magnesium monoperoxyphthalate hexahydrate (39.0 mg, 0.062 mmol, 0.75 eq) was added to a stirred solution of *tert*-butyl (*S*)-(2,2-dicyano-1-cyclohexylethyl)carbamate (**6s**) (23.0 mg, 0.083 mmol, 1.0 eq) and Li_2CO_3 (9.2 mg, 0.124 mmol, 1.5 eq) in methanol (0.83 ml) at 0 °C. After stirring for 4 h, the reaction mixture was quenched by water and extracted with CH_2Cl_2 three times. The combined organic layers were dried over Na_2SO_4. After removal of Na_2SO_4 by filtration, solvent was removed under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 10/1) to give the product **S1** as white solids (16.0 mg, 71% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.02 (d, J = 9.2 Hz, 1H), 4.20 (dd, J = 9.2, 5.2 Hz, 1H), 3.73 (s, 3H), 1.77-1.56 (m, 6H), 1.44 (s, 9H), 1.30-1.03 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.9, 155.6, 79.7, 58.2, 52.0, 41.0, 29.4, 28.3, 28.1, 25.9; IR (neat) 3378, 2929, 1744, 1681, 1509, 1152 cm^{-1}; HRMS (ESI+) calcd for $C_{14}H_{25}NNaO_4$ $[M + Na]^+$ 294.1676: found 294.1674; $[\alpha]_D^{26}$ = +22.1 (c = 0.5, $CHCl_3$).

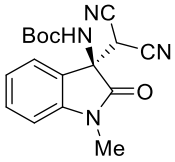
Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (hexane:2-propanol = 99:1, 1.0 mL/min, 220 nm) ; major enantiomer tr = 26.5 min, minor enantiomer tr = 18.9 min, 94% ee.

7. General procedure for asymmetric Mannich reaction of malononitrile with *N*-Boc ketimines

Catalyst **3b** (1.3 mg, 0.002 mmol, 0.02 eq) and malononitrile (7.3 mg, 0.11 mmol, 1.1 eq) were added to a one-necked round flask containing a stir bar under Ar. $CHCl_3$ (1.0 ml) was added to the flask, and the mixture was stirred at –50 °C. To the resulting suspension, *N*-Boc imine **7** (0.1 mmol, 1.0 eq) was added. After being stirred for appropriate time, solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 2/1) to afford product. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC using Daicel Chiralcel AD-H, and Chiralpak IC-3 column.

8. Analytical data for products of enantioselective Mannich reaction of malononitrile with *N*-Boc ketimines

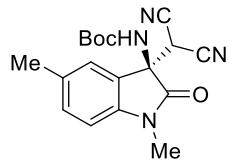
tert-butyl (*R*)-(3-(dicyanomethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (8a)



Reaction time: 20 h; pale pink solids (29.6 mg, 91% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.21 (t, *J* = 7.8 Hz, 1H), 6.96 (d, *J* = 7.8 Hz, 1H), 5.75 (br, 1H), 5.43 (br, 1H), 3.31 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 154.5, 143.4, 131.7, 125.5, 124.6, 124.3, 109.7, 109.3, 109.1, 82.3, 60.7, 29.3, 28.0, 26.9; IR (neat) 3284, 2900, 1703, 1613, 1518, 1496, 1470, 1130 cm^{-1}; HRMS (ESI+) calcd for $C_{17}H_{18}N_4NaO_3$ $[M + Na]^+$ 349.1271: found 349.1269; $[\alpha]_D^{25}$ = –23.0 (*c* = 0.01, $CHCl_3$, 82% ee).

Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (hexane:2-propanol = 90:10, 1.0 mL/min, 254 nm); minor enantiomer t_R = 56.0 min, major enantiomer t_R = 39.2 min, 82% ee.

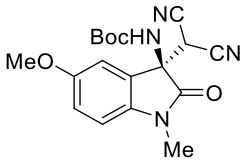
tert-butyl (*R*)-(3-(dicyanomethyl)-1,5-dimethyl-2-oxoindolin-3-yl)carbamate (8b)



Reaction time: 20 h; pale pink solids (32.1 mg, 94% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (s, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 5.63 (br, 1H), 5.44 (br, 1H), 3.29 (s, 3H), 2.39 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 154.5, 141.0, 134.2, 132.0, 126.2, 124.5, 109.8, 109.2, 109.0, 82.3, 60.8, 29.3, 28.0, 26.9, 21.2; IR (neat) 3288, 2904, 2382, 2349, 1704, 1620, 1502, 1367, 1252, 1164 cm^{-1}; HRMS (ESI+) calcd for $C_{18}H_{20}N_4NaO_3$ $[M + Na]^+$ 363.1428: found 363.1425; $[\alpha]_D^{25}$ = –70.7(*c* = 0.01, $CHCl_3$, 82% ee).

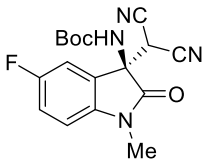
Enantiomeric excess was determined by HPLC with a Chiralpak IC-3 column (hexane:2-propanol = 90:10, 0.3 mL/min, 254 nm); minor enantiomer t_R = 42.8 min, major enantiomer t_R = 39.0 min, 82% ee.

tert-butyl (*R*)-(3-(dicyanomethyl)-5-methoxy-1-methyl-2-oxoindolin-3-yl)carbamate (8c)



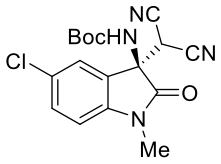
Reaction time: 30 h; pale purple solids (34.8 mg, 97% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J = 2.3 Hz, 1H), 7.98 (dd, J = 8.7, 2.7 Hz, 1H), 6.87 (d, J = 8.7 Hz, 1H), 5.63 (br, 1H), 5.43 (br, 1H), 3.83 (s, 3H), 3.29 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 156.9, 154.6, 136.6, 125.6, 116.1, 112.7, 109.9, 109.7, 109.1, 82.4, 60.9, 55.8, 29.2, 28.0, 26.9; IR (neat) 3284, 2901, 2360, 2341, 1704, 1604, 1497, 1366, 1286, 1038 cm^{-1}; HRMS (ESI+) calcd for $C_{18}H_{20}N_4NaO_4$ $[M + Na]^+$ 379.1377: found 379.1374; $[\alpha]_D^{26}$ = –60.0 (c = 0.001, $CHCl_3$, 85% ee).
Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (hexane:2-propanol = 90:10, 1.0 mL/min, 254 nm); minor enantiomer t_R = 62.2 min, major enantiomer t_R = 45.3 min, 85% ee.

***tert*-butyl (*R*)-(3-(dicyanomethyl)-5-fluoro-1-methyl-2-oxoindolin-3-yl)carbamate (8d)**



Reaction time: 16 h; pale pink solids (33.0 mg, 96% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (dd, J = 7.8, 2.5 Hz, 1H), 7.22-7.17 (m, 1H), 6.91 (dd, J = 8.9, 4.1 Hz, 1H), 5.65 (br, 1H), 5.40 (br, 1H), 3.31 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 159.7 (d, $^{1}J_{CF}$ = 246.2 Hz), 154.5, 139.4, 125.9 (d, $^{3}J_{CF}$ = 8.6 Hz), 118.2 (d, $^{2}J_{CF}$ = 24.0 Hz), 114.4 (d, $^{2}J_{CF}$ = 26.8 Hz), 110.1 (d, $^{3}J_{CF}$ = 8.6 Hz), 109.4, 108.8, 82.7, 60.8, 29.1, 28.0, 27.0; IR (neat) 3279, 2923, 2359, 1736, 1687, 1520, 1488, 1372, 1286, 1162 cm^{-1}; HRMS (ESI+) calcd for $C_{17}H_{17}FN_4NaO_3$ $[M + Na]^+$ 367.1177: found 367.1175; $[\alpha]_D^{25}$ = –56.4 (c = 0.02, $CHCl_3$, 80% ee).
Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (hexane:2-propanol = 90:10, 1.0 mL/min, 254 nm); minor enantiomer t_R = 29.6 min, major enantiomer t_R = 22.5 min, 80% ee.

***tert*-butyl (*R*)-(5-chloro-3-(dicyanomethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (8e)**



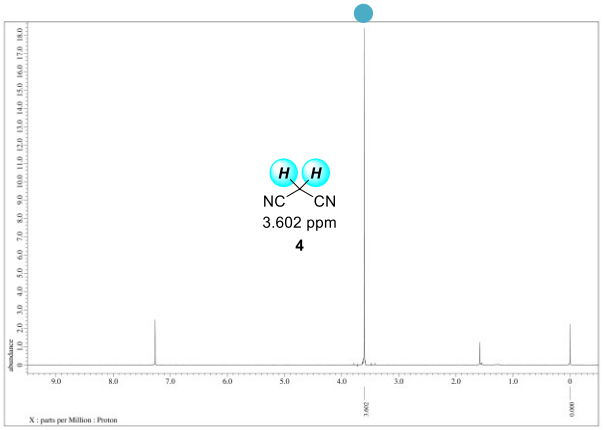
Reaction time: 16 h; pale pink solids (29.2 mg, 81% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 2.1 Hz, 1H), 7.46 (dd, J = 8.4, 2.0 Hz, 1H), 6.90 (d, J = 8.5 Hz, 1H), 5.70 (br, 1H), 5.37 (br, 1H), 3.31 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 154.4, 142.0, 131.7, 129.8, 126.3, 126.0, 110.3, 109.4, 108.7, 82.8, 60.7, 29.2, 28.0, 27.0; IR (neat) 3304, 2898, 2361, 2340, 1729, 1685, 1611, 1519, 1368, 1283, 1157, 1103 cm^{-1}; HRMS (ESI+) calcd for $C_{17}H_{17}ClN_4NaO_3$ $[M + Na]^+$ 383.0881: found 383.0878; $[\alpha]_D^{25}$ = –32.4 (c = 0.01, $CHCl_3$, 80% ee).
Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (hexane:2-propanol = 90:10, 1.0 mL/min, 254 nm); minor enantiomer t_R = 27.4 min, major enantiomer t_R = 21.1 min, 80% ee.

9. NMR study

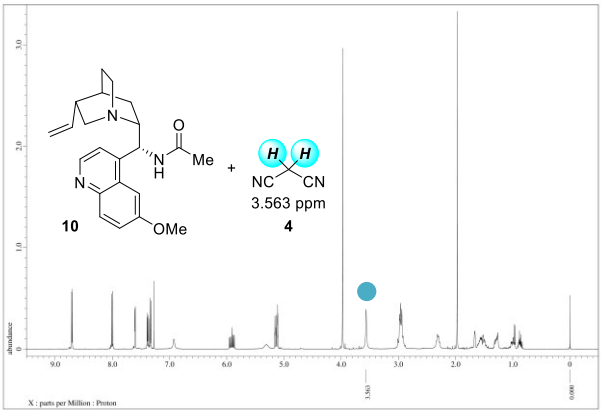
(1) ^{1}H-NMR analysis on interaction between **10** and malononitrile **4** (1:1 ratio).

Chart-a is a ^{1}H-NMR spectrum of malononitrile **4** (0.1 M) in $CDCl_3$. Chemical shift of methylene protons is 3.602 ppm. Chart-b is a ^{1}H-NMR spectrum of **10** (0.1 M) and malononitrile **4** (0.1 M) in $CDCl_3$. Chemical shift of methylene protons is 3.563 ppm. *The acidic methylene protons of malononitrile **4** broadened and shifted up-field by 0.039 ppm.*

(chart-a)



(chart-b)



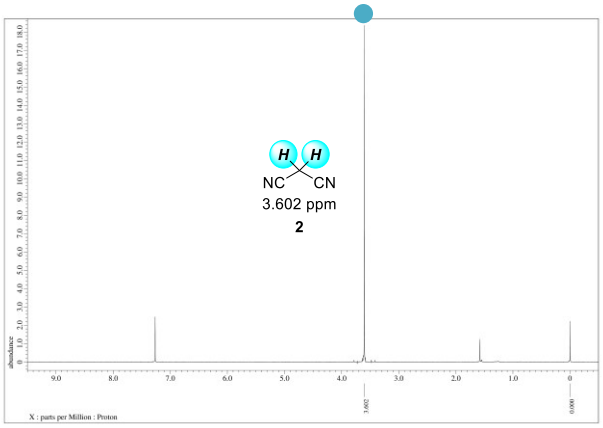
(2) ^{1}H-NMR analysis on interaction between **10** and *N*-Boc imine **5a** (1:1 ratio).

Mixing of **10** (0.1 M) and *N*-Boc imine **5a** (0.1 M) in $CDCl_3$ did not produce any obvious changes in the ^{1}H-NMR spectrum.

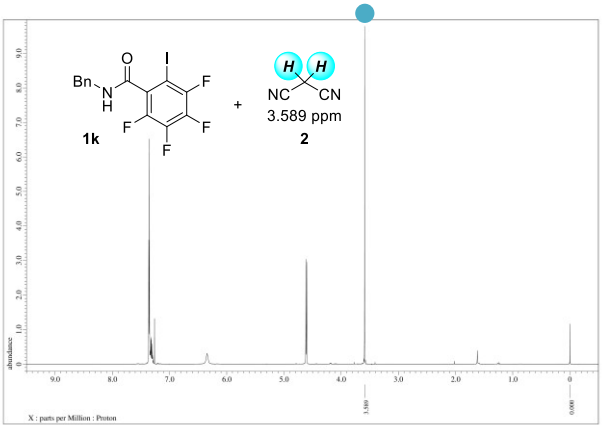
(3) ^{1}H-NMR analysis on interaction between **11** and malononitrile **4** (1:1 ratio).

Chart-a is a ^{1}H-NMR spectrum of malononitrile **4** (0.1 M) in $CDCl_3$. Chemical shift of methylene protons is 3.602 ppm. Chart-c is a ^{1}H-NMR spectrum of **11** (0.1 M) and malononitrile **4** (0.1 M) in $CDCl_3$. Chemical shift of methylene protons is 3.589 ppm. *The methylene protons of malononitrile **4** slightly shifted up-field by 0.013 ppm.*

(chart-a)



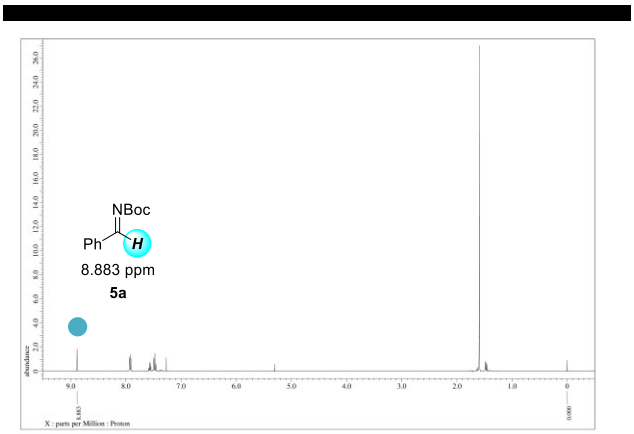
(chart-c)



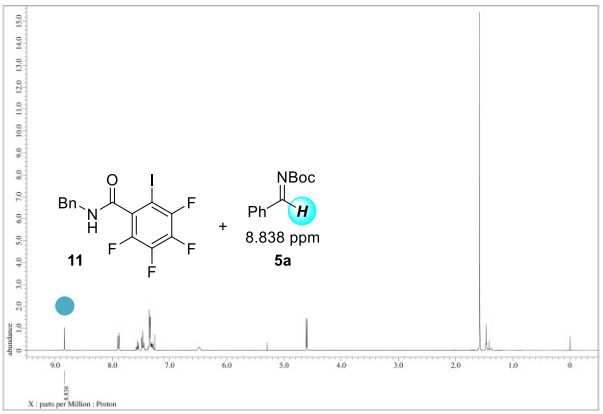
(4) ^{1}H-NMR analysis on interaction between **11** and *N*-Boc imine **5a** (1:1 ratio).

Chart-d is a ^{1}H-NMR spectrum of *N*-Boc imine **5a** (0.1 M) in $CDCl_3$. Chemical shift of iminoproton is 8.883 ppm. Chart-e is a ^{1}H-NMR spectrum of **11** (0.1 M) and *N*-Boc imine **5a** (0.1 M) in $CDCl_3$. Chemical shift of iminoproton is 8.838 ppm. *Iminoproton of N-Boc imine **5a** shifted up-field by 0.045 ppm*.

(chart-d)



(chart-e)



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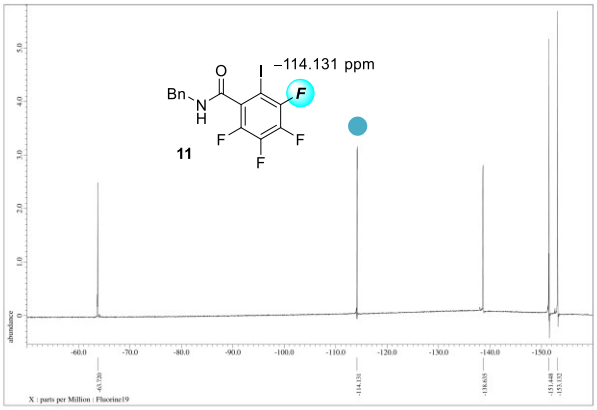
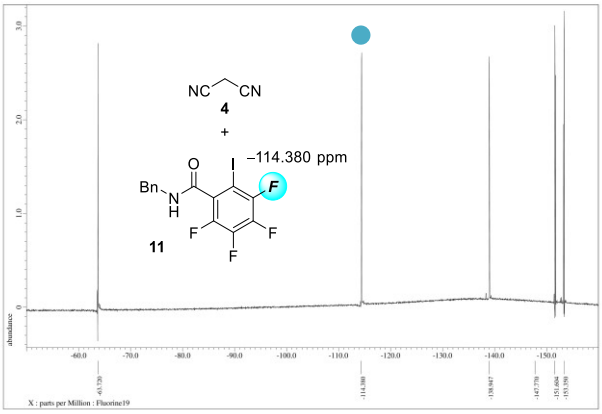
(5) ^{19}F-NMR analysis on interaction between **11** and malononitrile **4** (1:10 ratio).

Chemical shifts of ^{19}F-NMR spectra were reported relative to trifluorotoluene (δ −63.72). Chart-f is a ^{19}F -NMR spectrum of **11** (0.1 M) in $CDCl_3$. Chemical shift of fluorine atom *ortho* to the iodo group (these appear at roughly –115 ppm) is –114.131 ppm. Chart-g is a ^{19}F-NMR spectrum of **11** (0.1 M) and malononitrile **4** (1.0 M) in $CDCl_3$. Chemical shift of the fluorine atom is –114.380 ppm. *The fluorine atom ortho to the iodo group of **11** shifted up-field by 0.249 ppm.*

(chart-f)



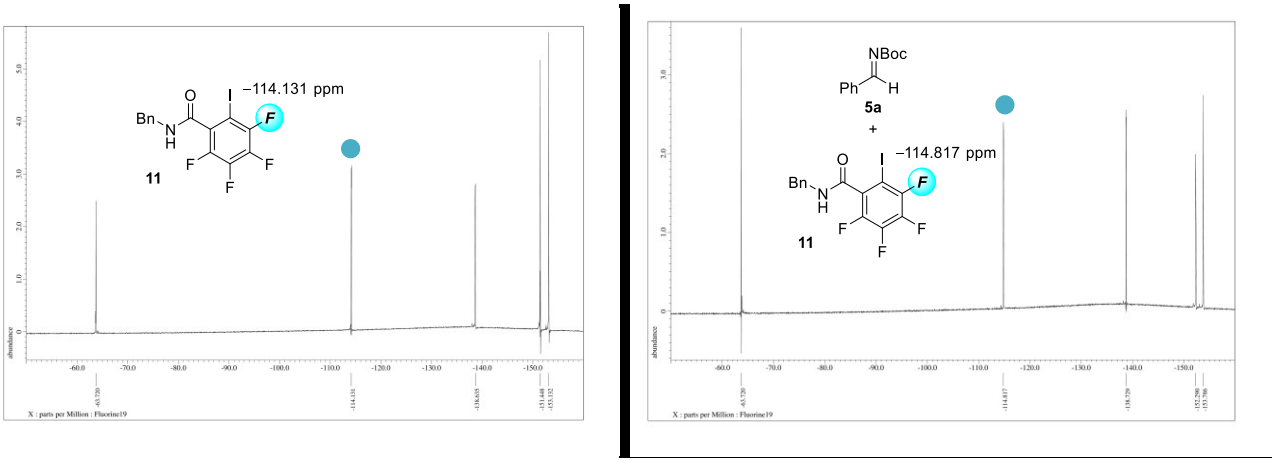
(chart-g)



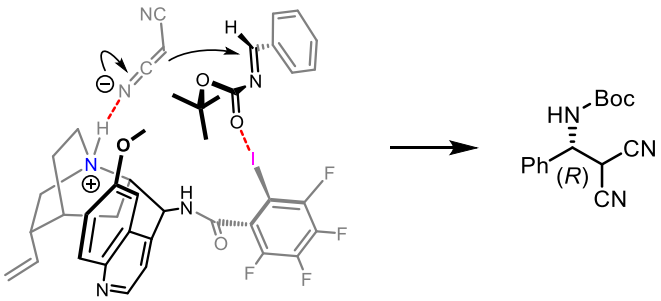
(6) ^{19}F-NMR analysis on interaction between **11** and *N*-Boc imine **5a** (1:10 ratio).

Chemical shifts of ^{19}F-NMR spectra were reported relative to trifluorotoluene (δ −63.72). Chart-f is a ^{19}F -NMR spectrum of **11** (0.1 M) in $CDCl_3$. Chemical shift of fluorine atom *ortho* to the iodo group (these appear at roughly –115 ppm) is –114.131 ppm. Chart-h is a ^{19}F-NMR spectrum of **11** (0.1 M) and *N*-Boc imine **5a** (1.0 M) in $CDCl_3$. Chemical shift of the fluorine atom is –114.817 ppm. *The fluorine atom ortho to the iodo group of **11** shifted up-field by 0.686 ppm.*

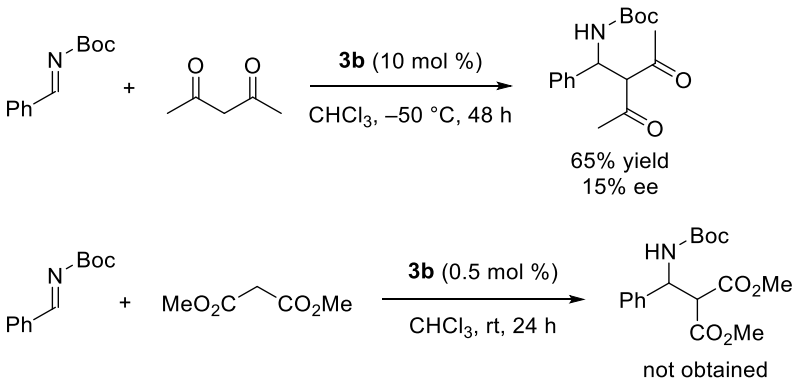
(chart-f) (chart-h)



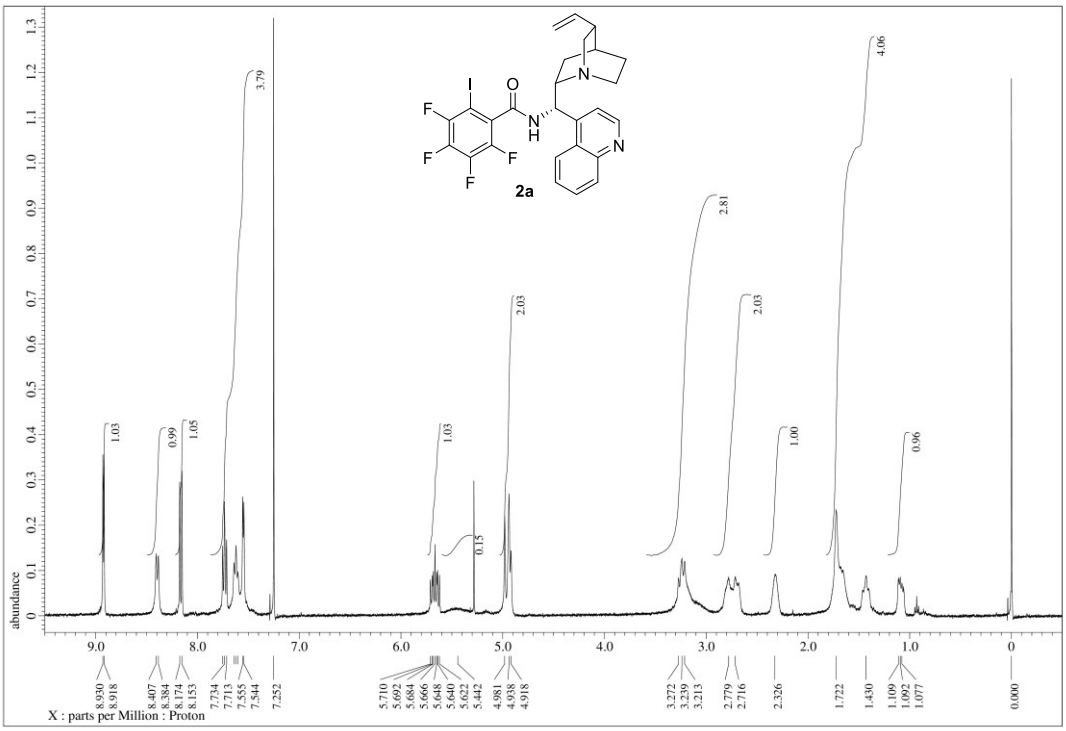
10. Plausible transition state model

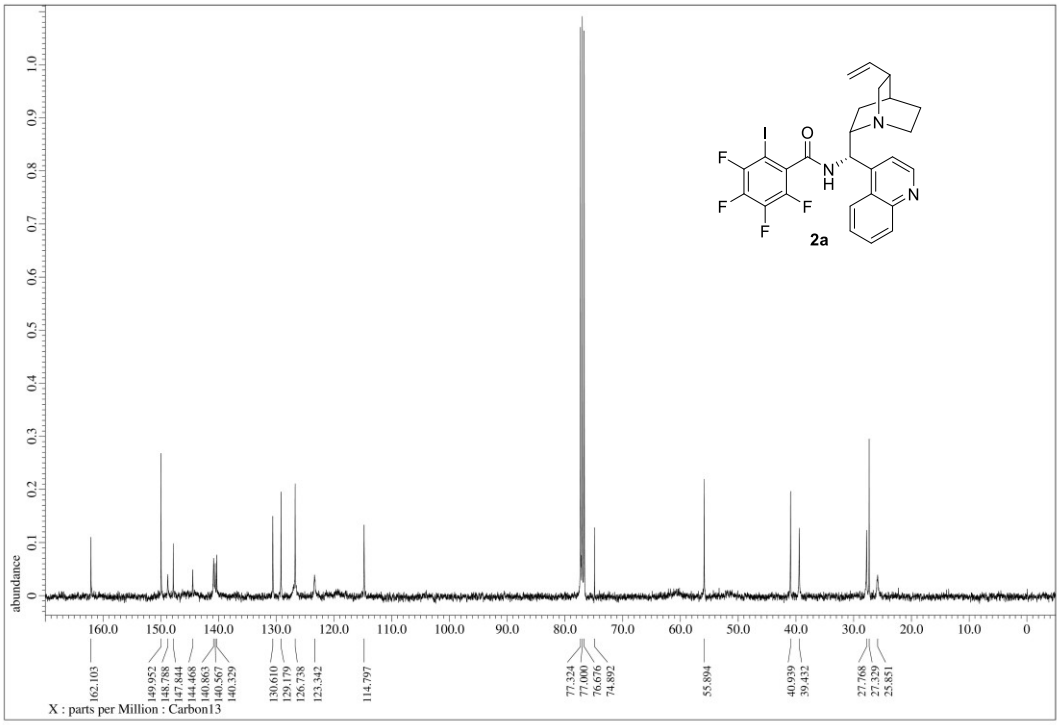


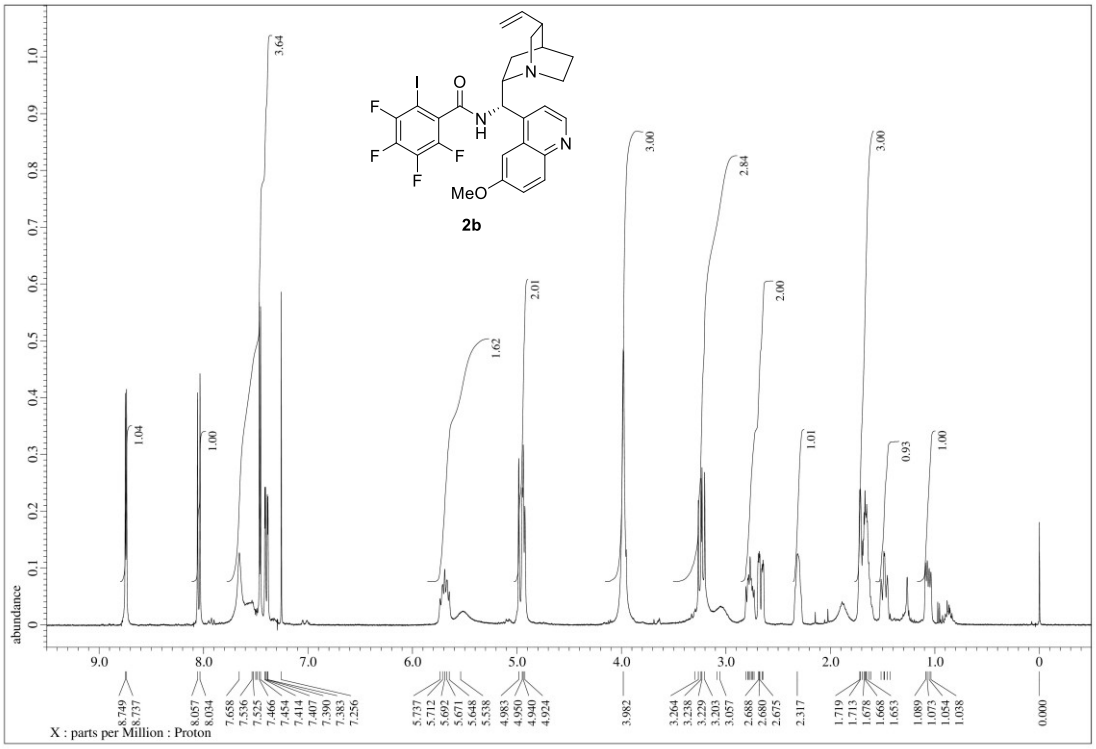
11. Asymmetric Mannich reaction of other nucleophiles with *N*-Boc aldimine

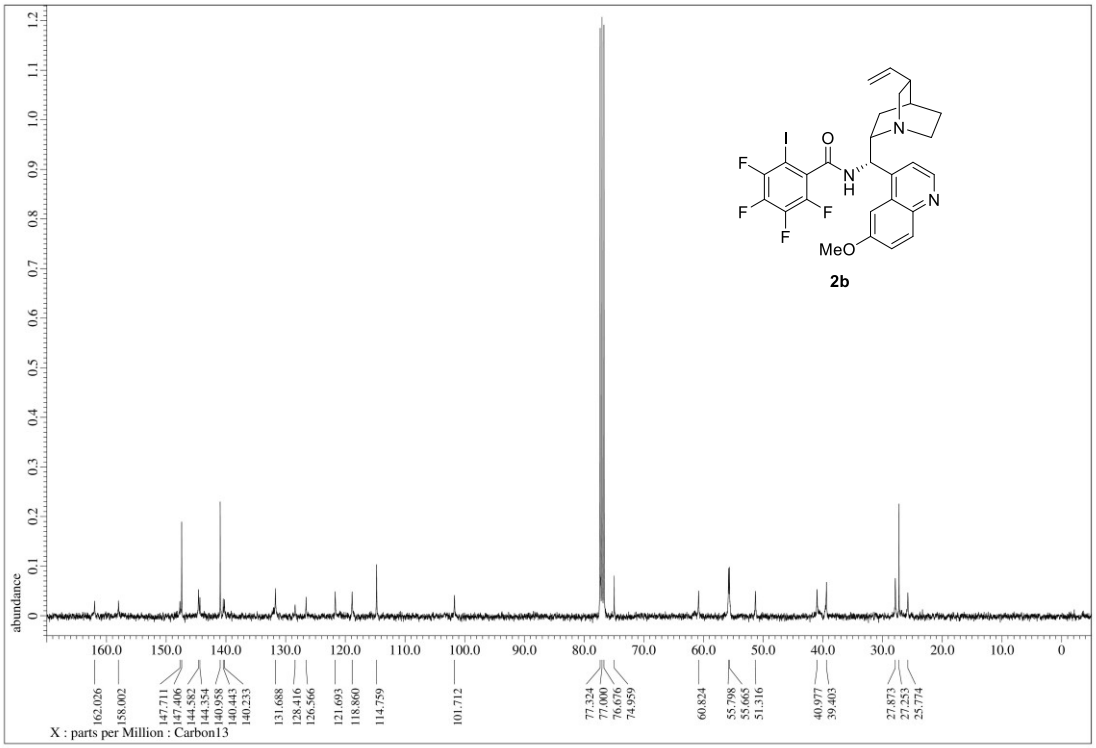


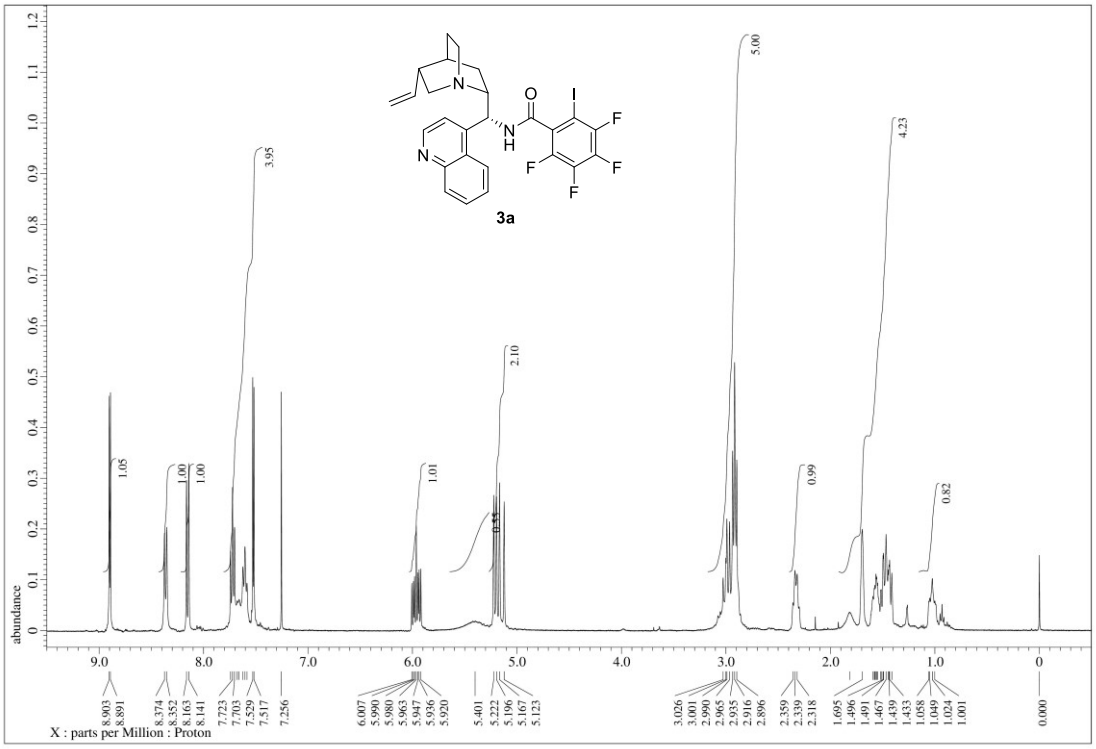
12. ^{1}H-NMR and ^{13}C-NMR spectra

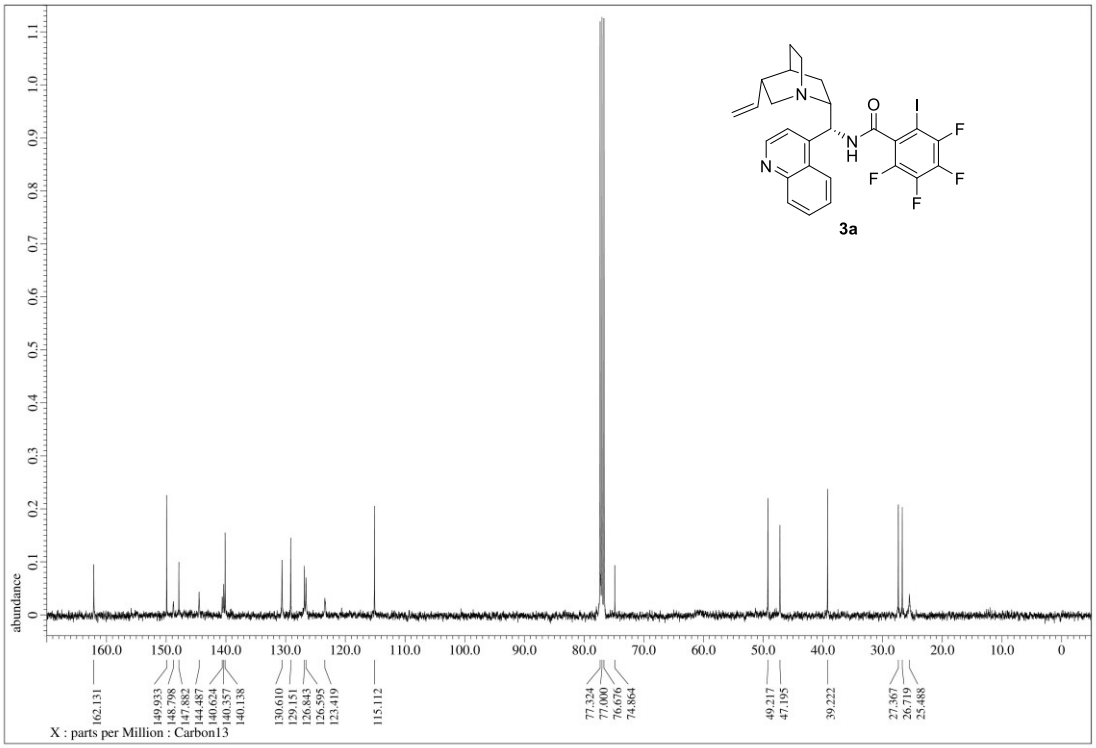


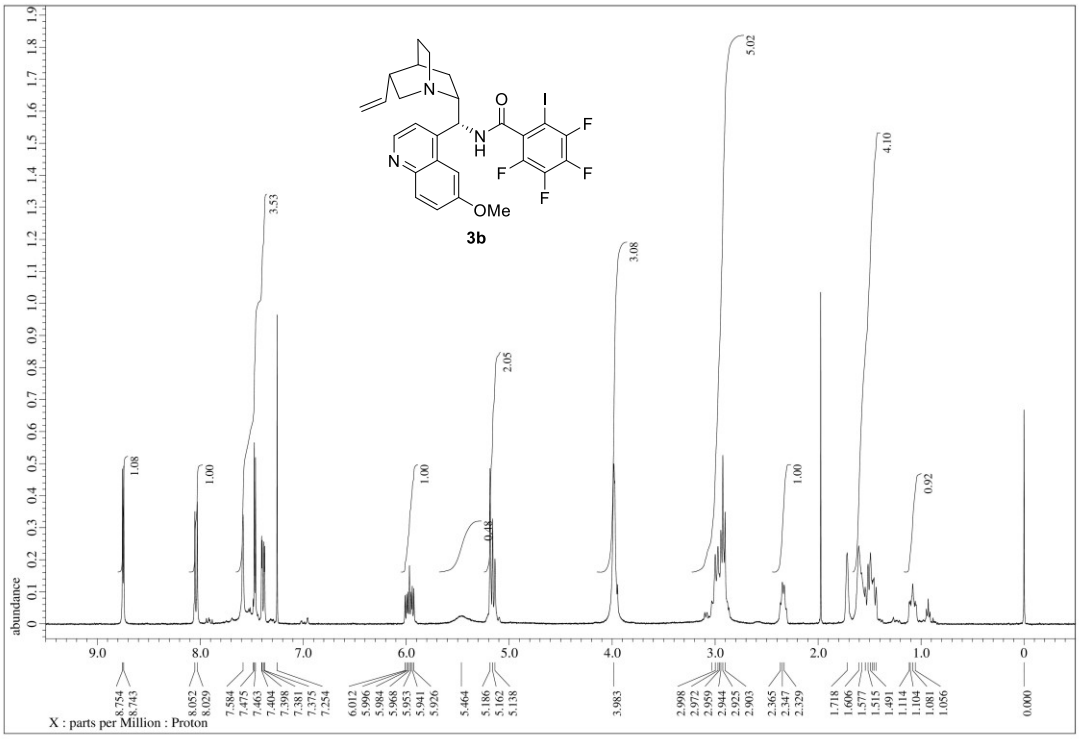


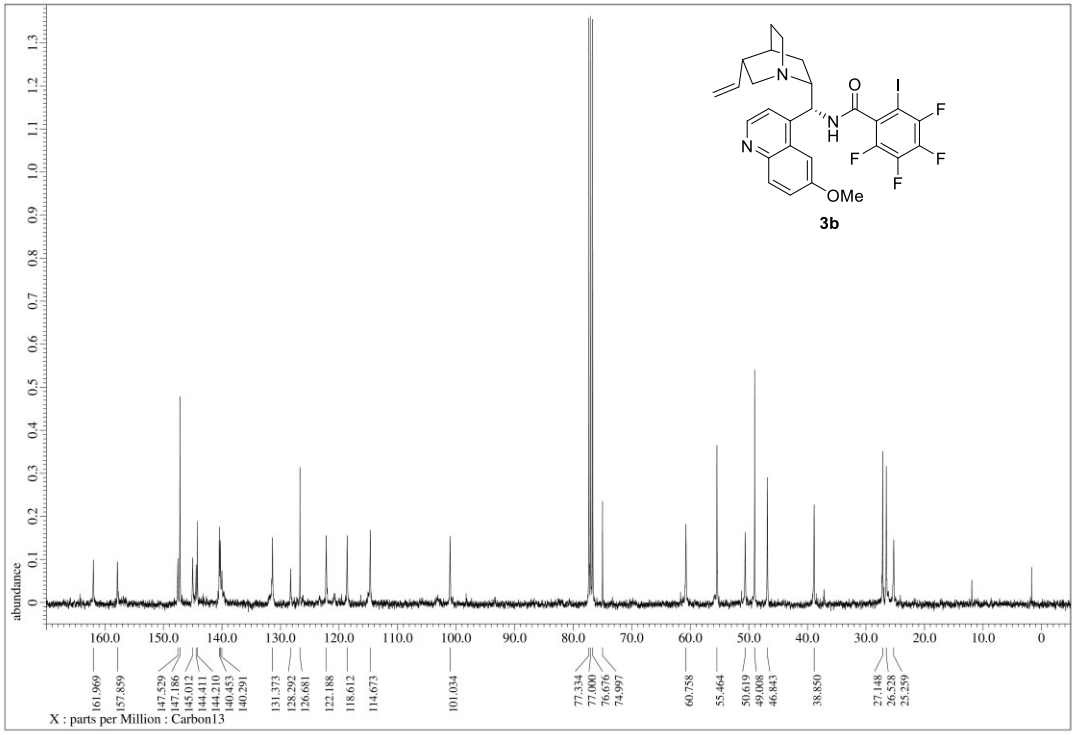

2b
abundance
X : parts per Million : Proton

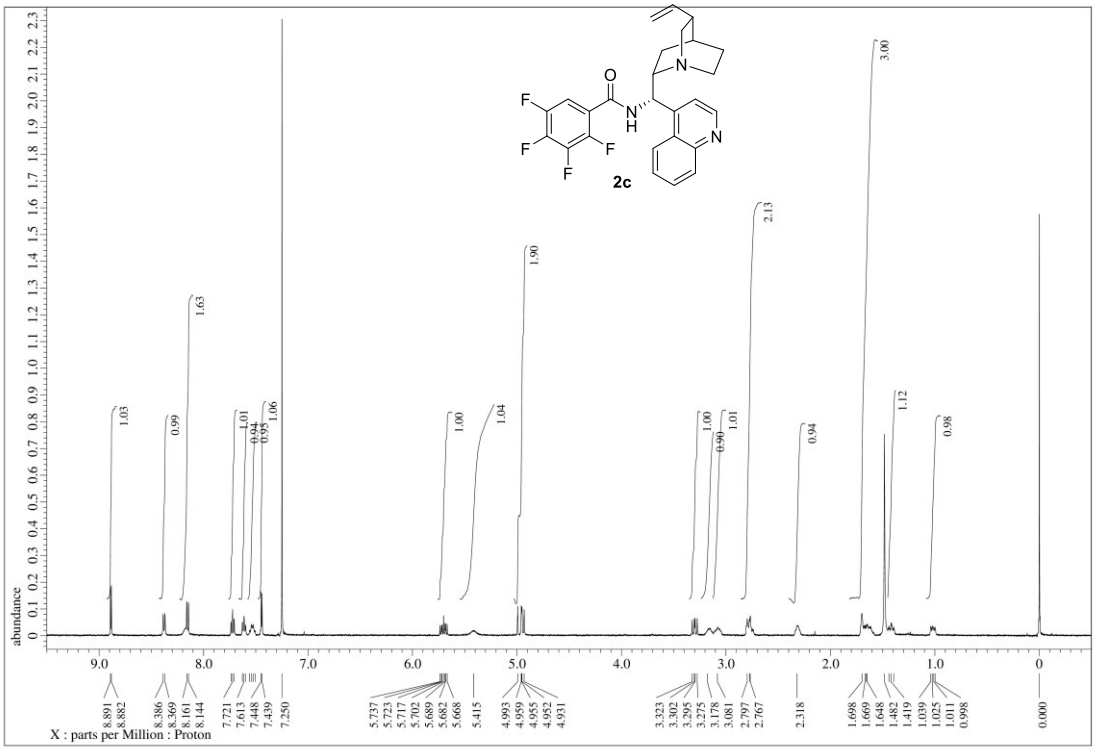

2b
abundance
X : parts per Million : Carbon13

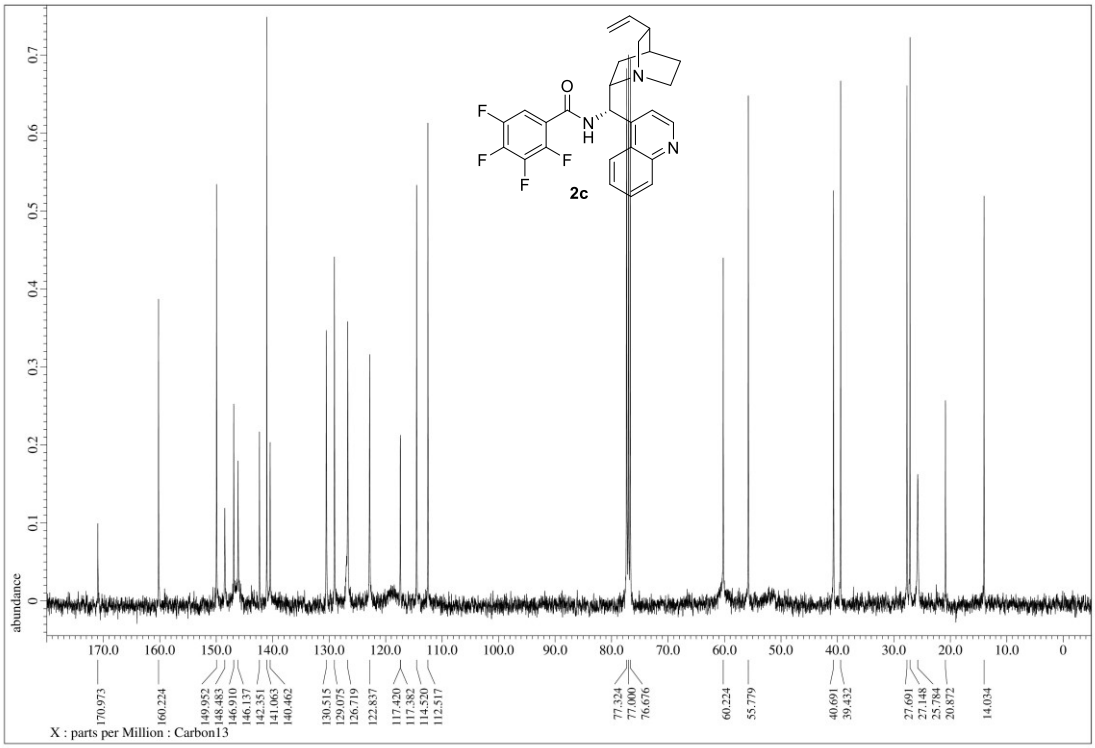

3a
abundance
X : parts per Million : Proton

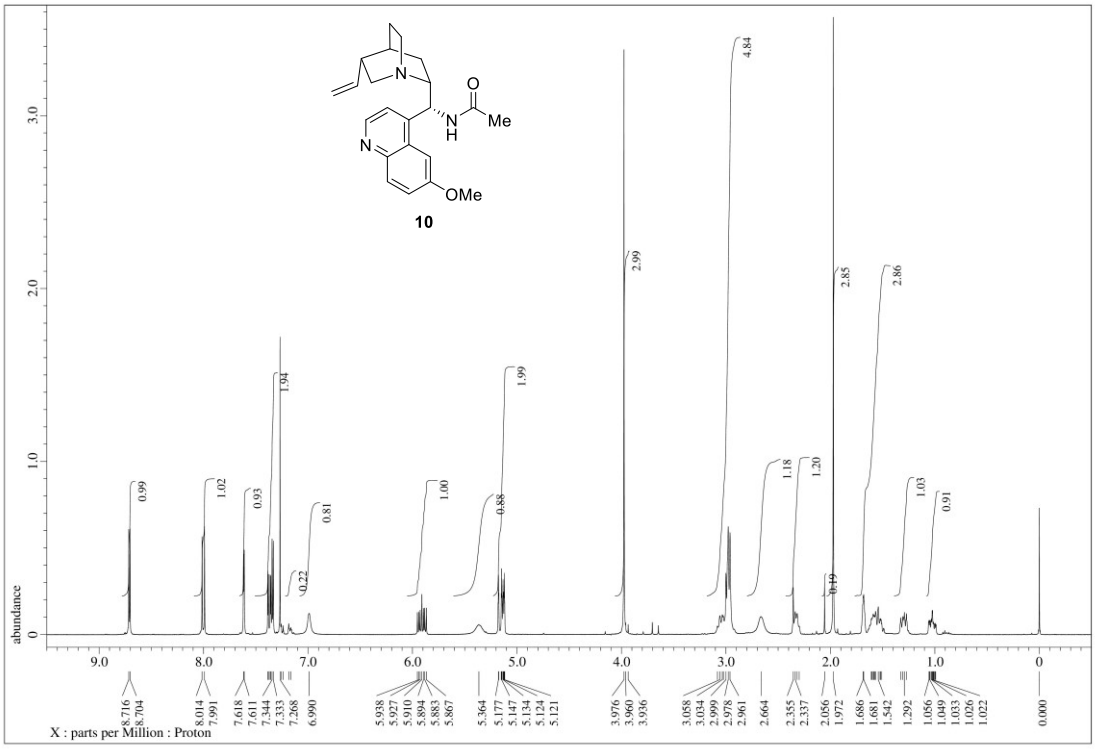

3a
abundance
X : parts per Million : Carbon13

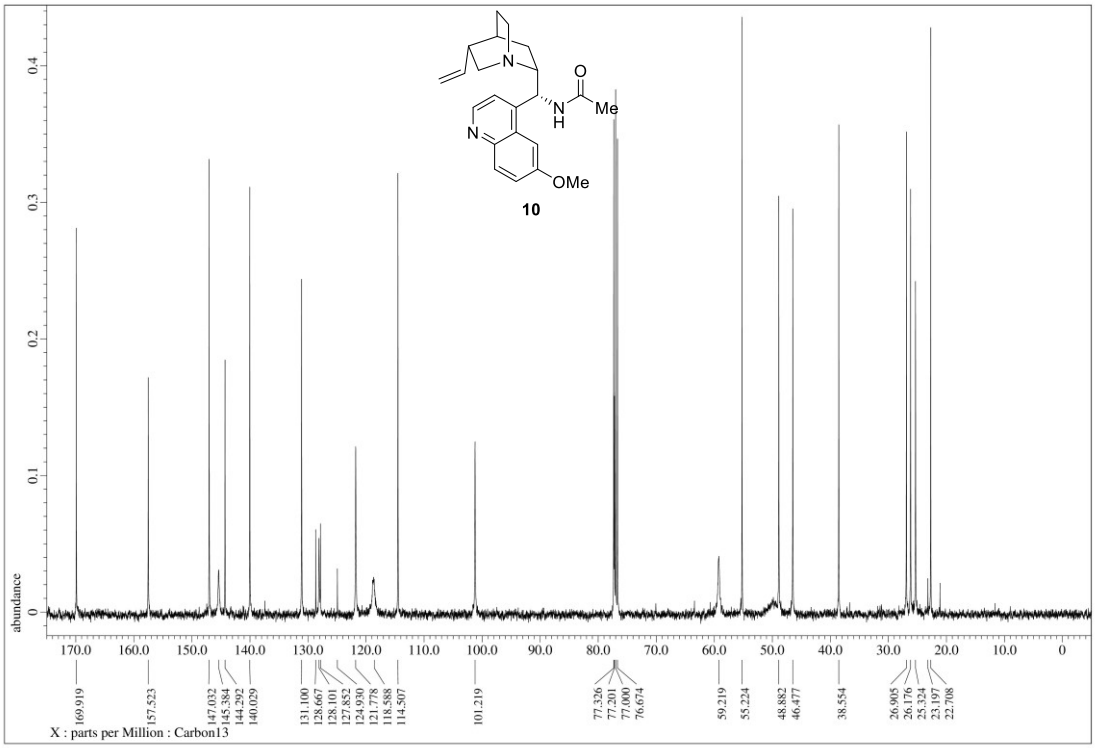

3b
abundance
X : parts per Million : Proton

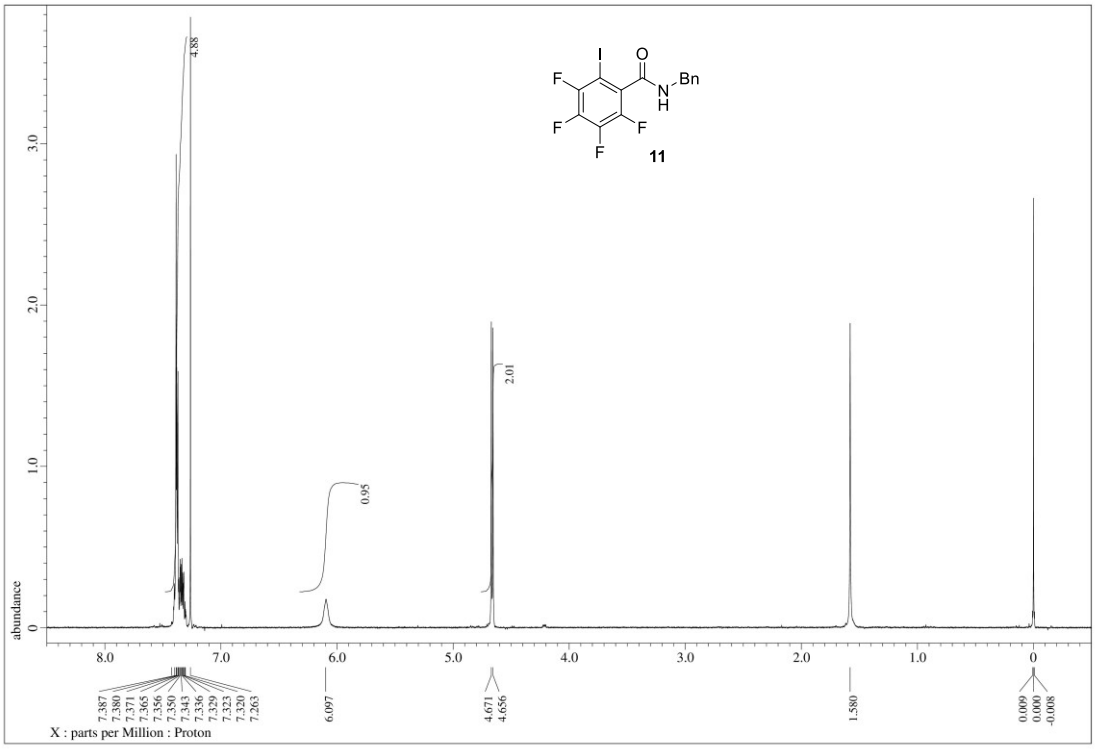

3b
abundance
X : parts per Million : Carbon13

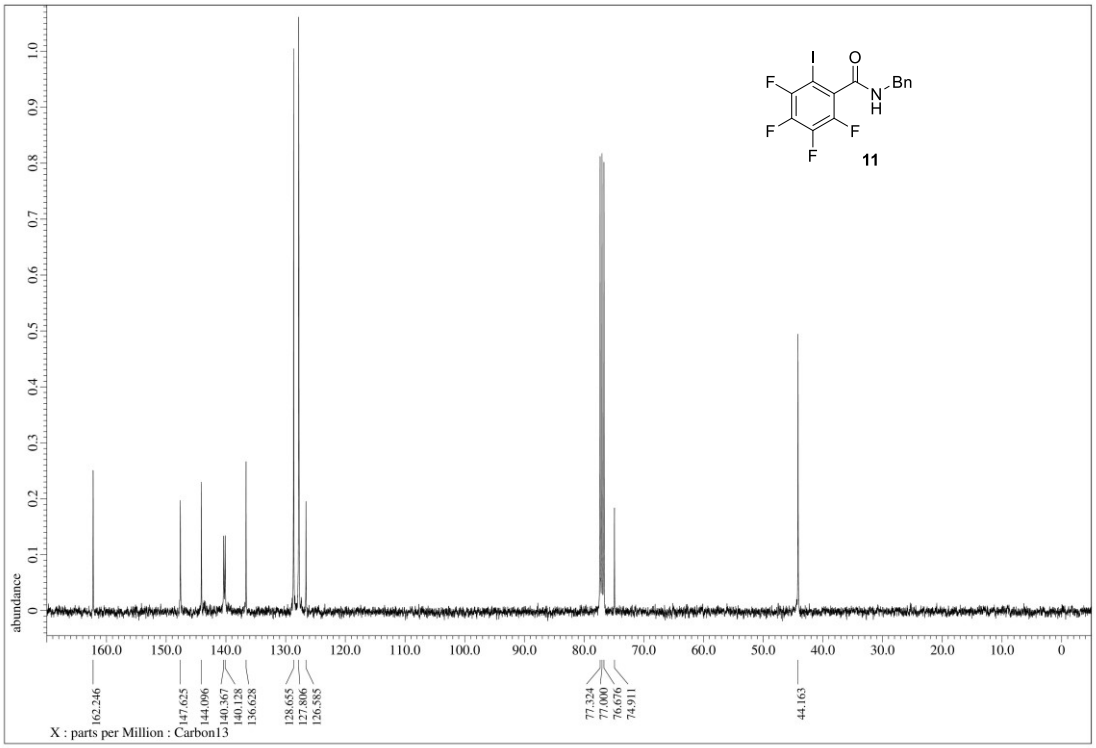

2c
abundance
X : parts per Million : Proton

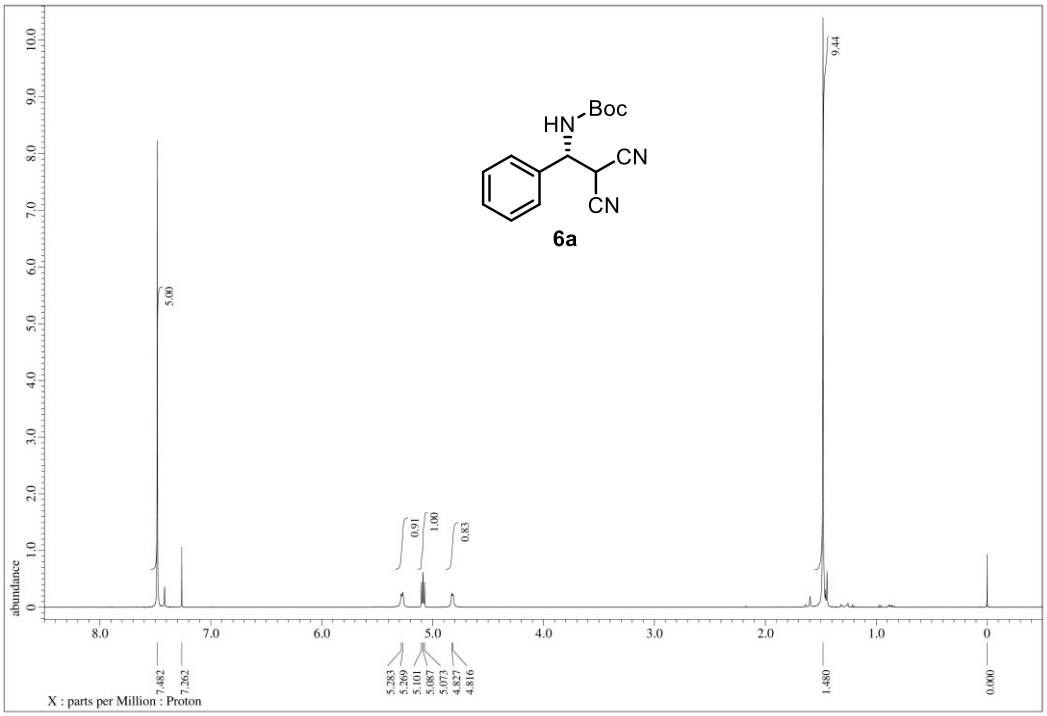

2c
abundance
X : parts per Million : Carbon13

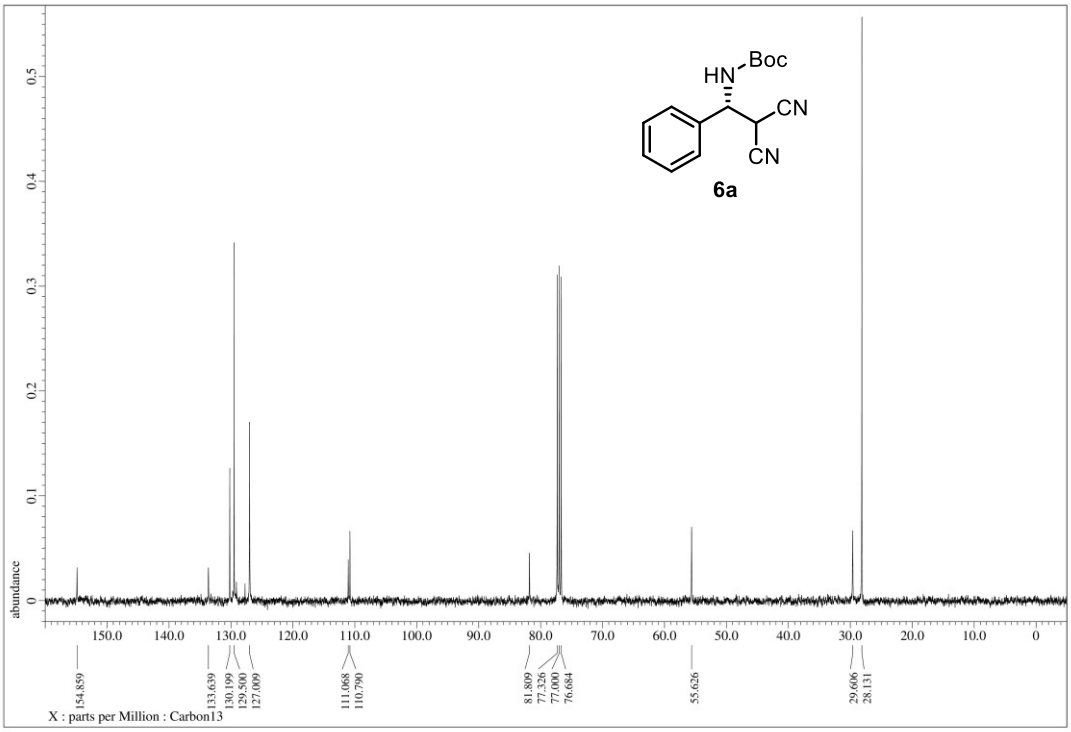

10
abundance
X : parts per Million : Proton

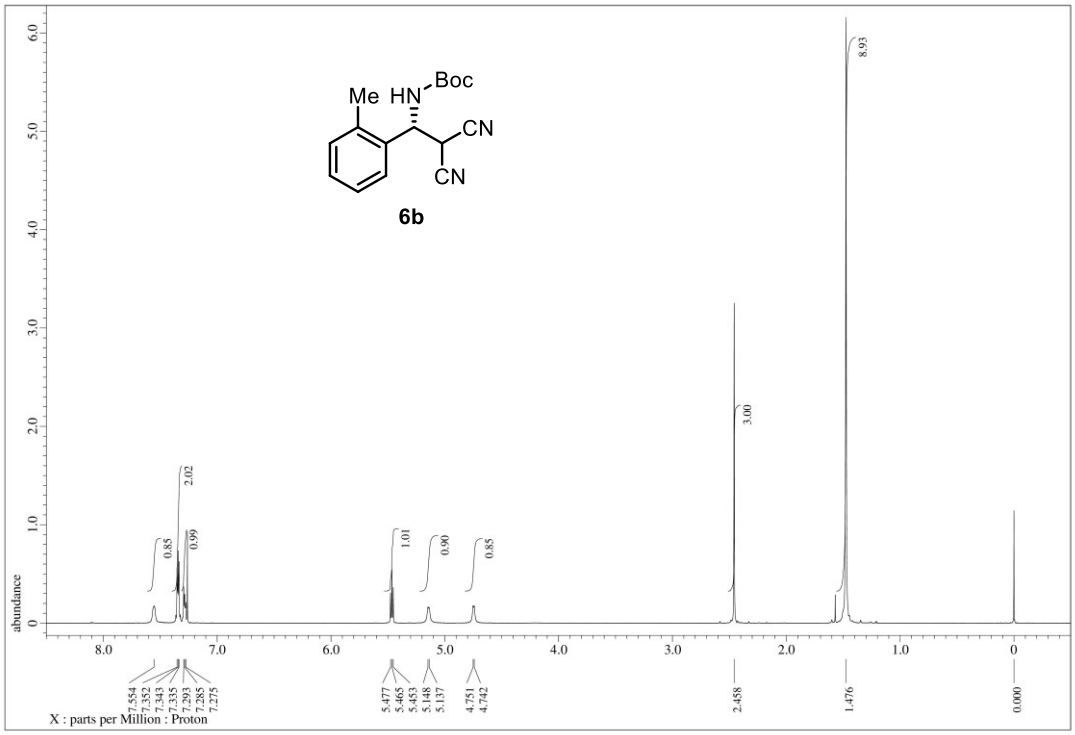

10
abundance
X : parts per Million : Carbon13

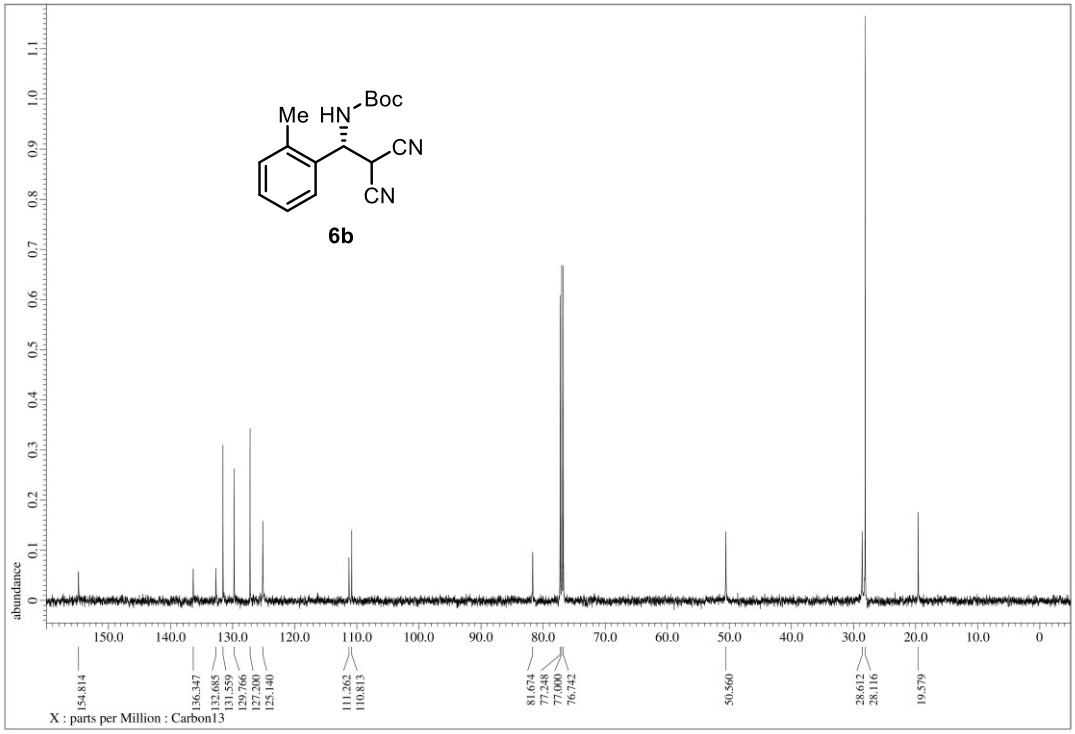

4.88
2.01
0.95
11
abundance
X : parts per Million : Proton
7.387
7.380
7.371
7.365
7.356
7.350
7.343
7.336
7.329
7.323
7.320
7.263
6.097
4.671
4.656
1.580
0.009
0.000
-0.008

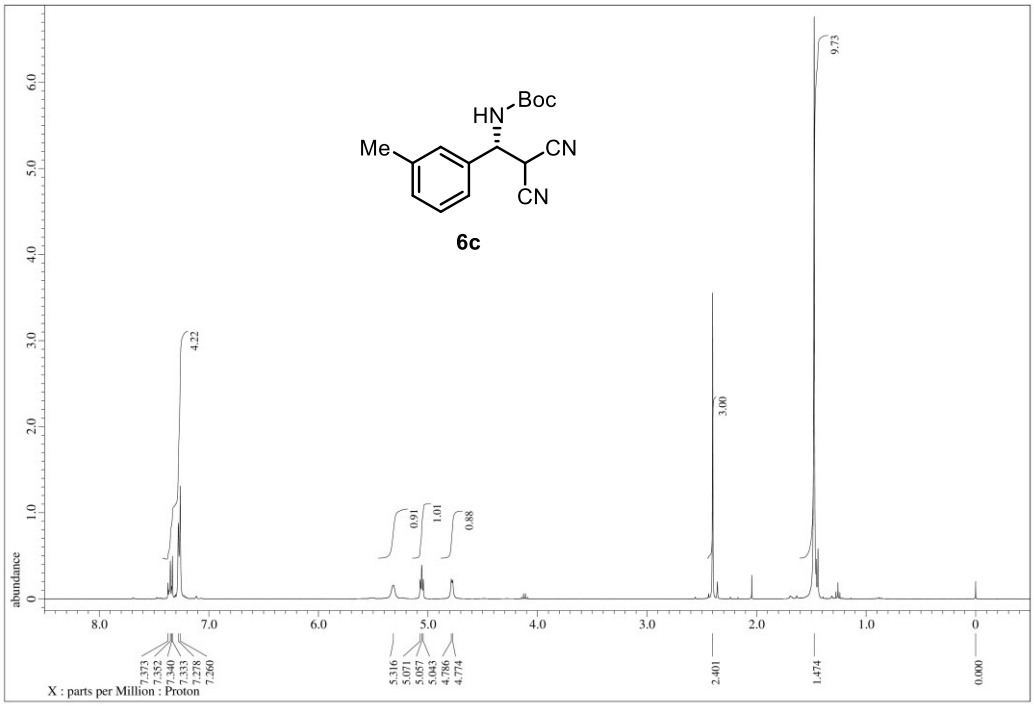

11
abundance
X : parts per Million : Carbon13
162.246
147.625
144.096
140.367
140.128
136.628
128.655
127.806
126.585
77.324
77.000
76.676
74.911
44.163

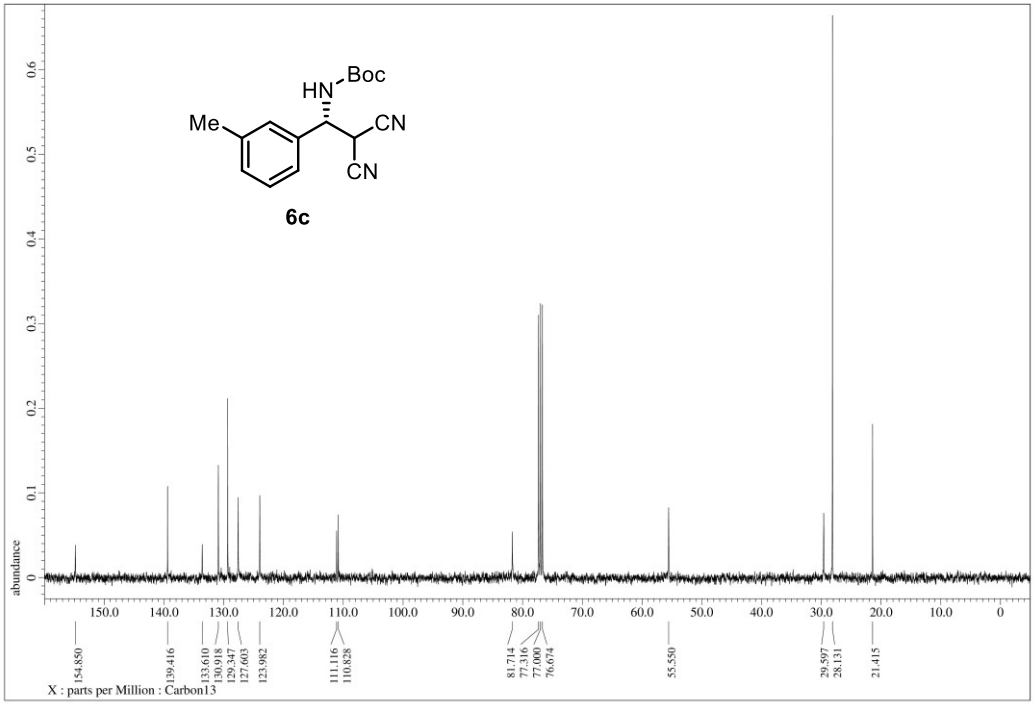

HN
Boc
CN
CN
6a
9.44
5.00
0.91
1.00
0.83
abundance
X : parts per Million : Proton
7.482
7.262
5.283
5.269
5.101
5.087
5.073
4.827
4.816
1.480
0.000

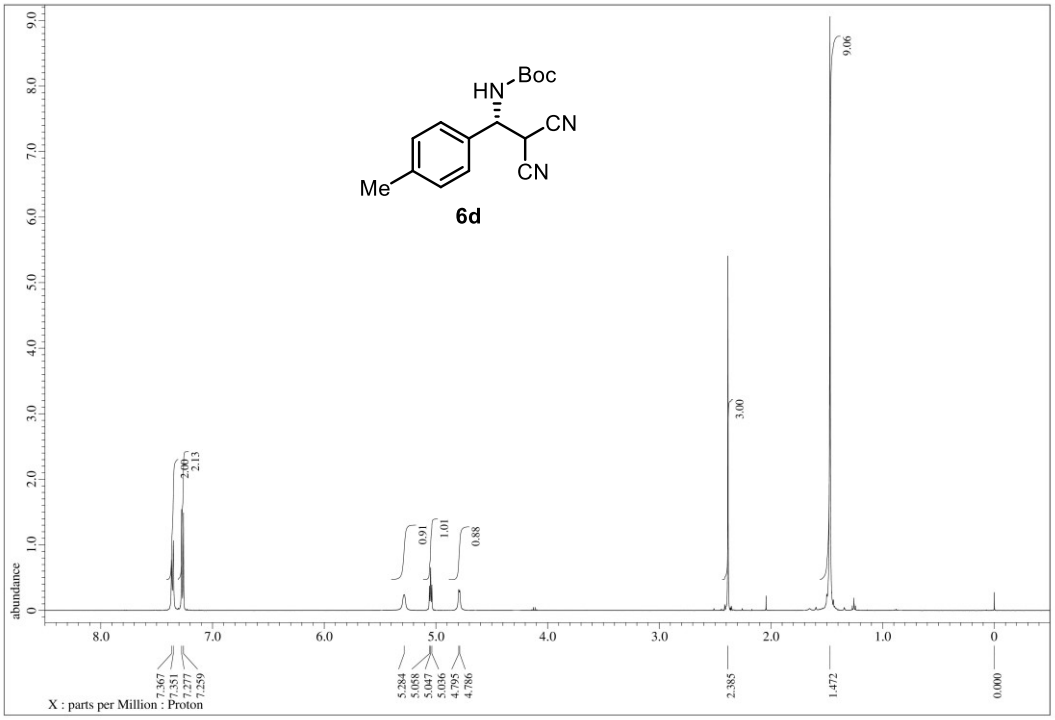

HN
Boc
CN
CN
6a
abundance
X : parts per Million : Carbon13
154.859
133.639
130.199
129.500
127.009
111.068
110.790
81.809
77.326
77.000
76.684
55.626
29.606
28.131

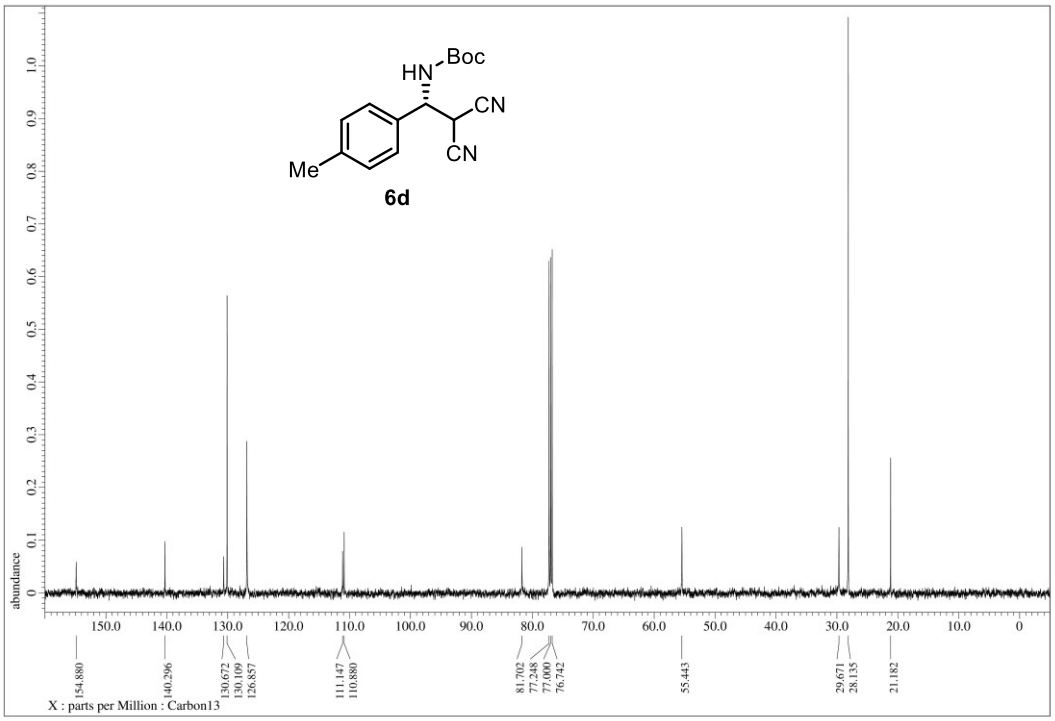

Me HN Boc
CN
CN
6b
abundance
X : parts per Million : Proton

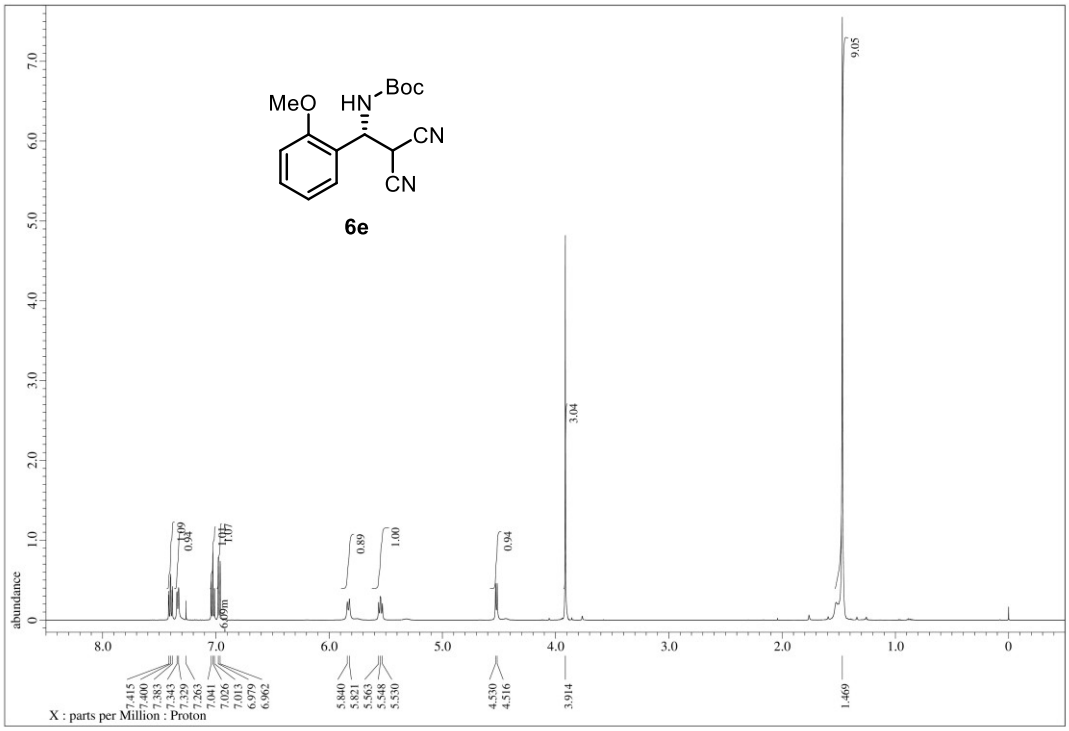

Me HN Boc
CN
CN
6b
abundance
X : parts per Million : Carbon13

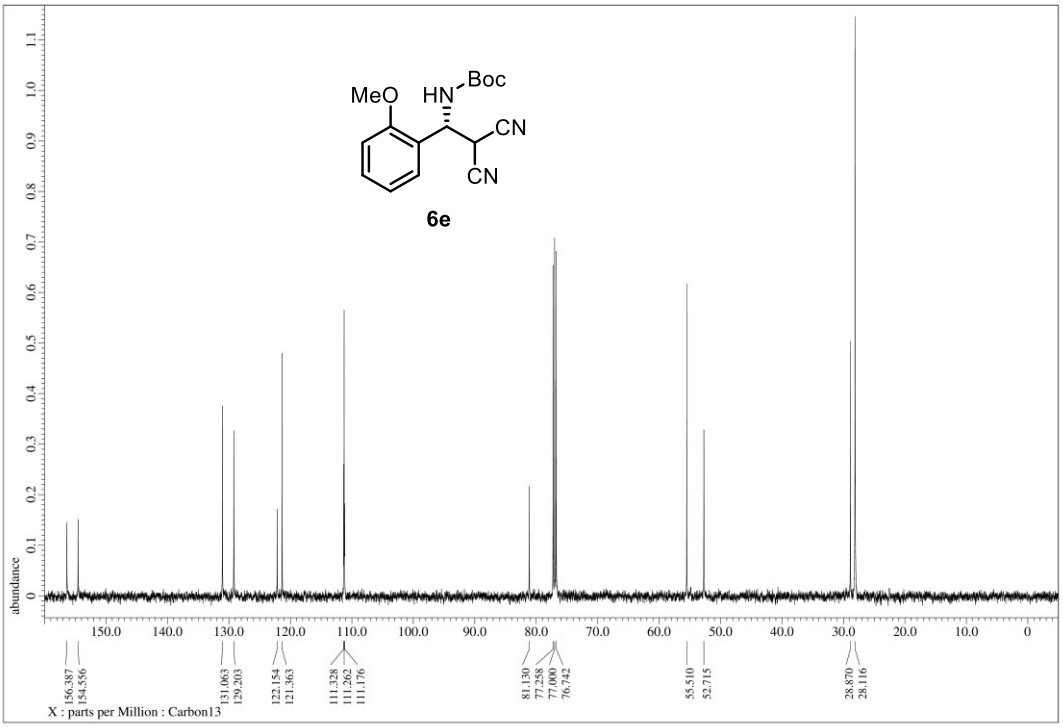

HN
Boc
Me
CN
CN
6c
9.73
4.22
3.00
0.91
1.01
0.88
abundance
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.373
7.352
7.340
7.333
7.278
7.260
5.316
5.071
5.057
5.043
4.786
4.774
2.401
1.474
0.000
X : parts per Million : Proton

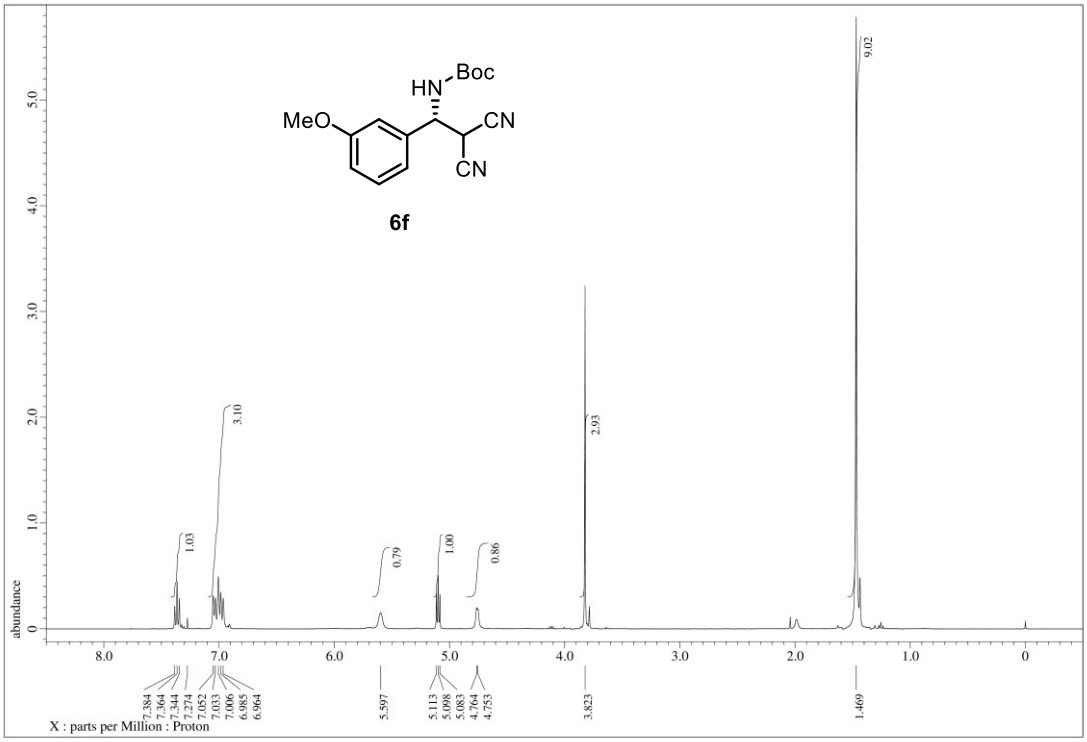

HN
Boc
Me
CN
CN
6c
abundance
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
154.850
139.416
133.610
130.918
129.547
127.603
123.982
111.116
110.828
81.714
77.316
77.000
76.674
55.550
29.597
28.131
21.415
X : parts per Million : Carbon13

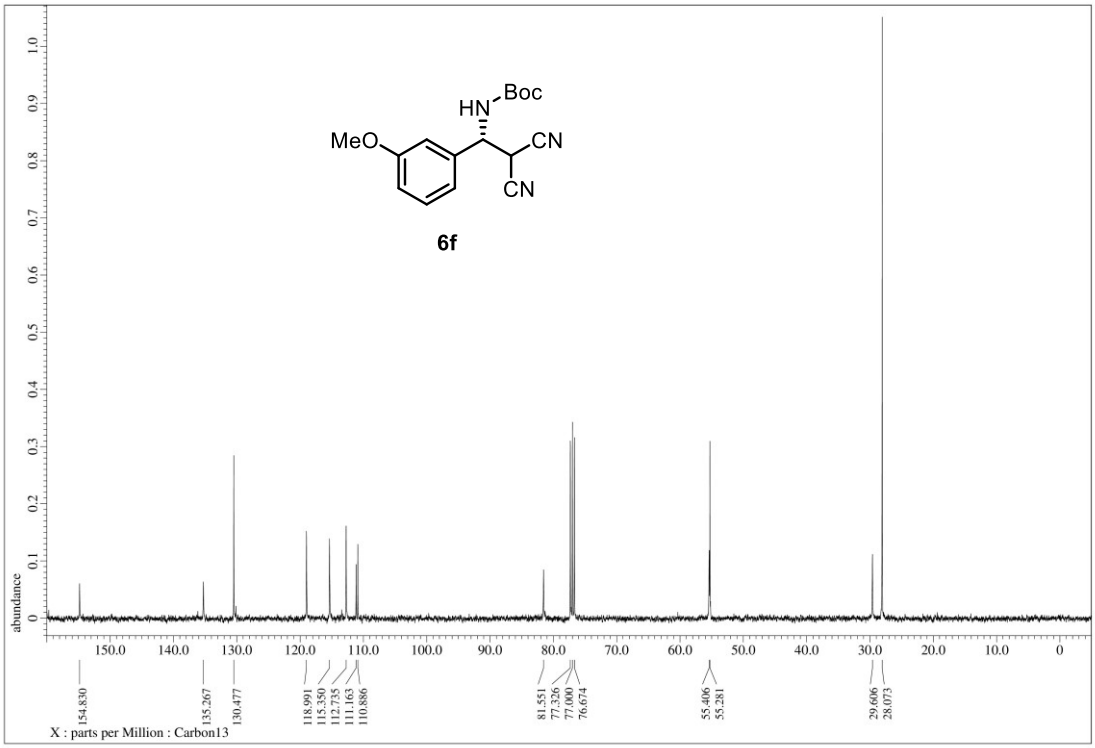

HN
Boc
CN
CN
Me
6d
9.06
3.00
2.13
2.00
0.91
1.01
0.88
abundance
X : parts per Million : Proton
7.367
7.351
7.277
7.259
5.284
5.058
5.047
5.036
4.795
4.786
2.385
1.472
0.000

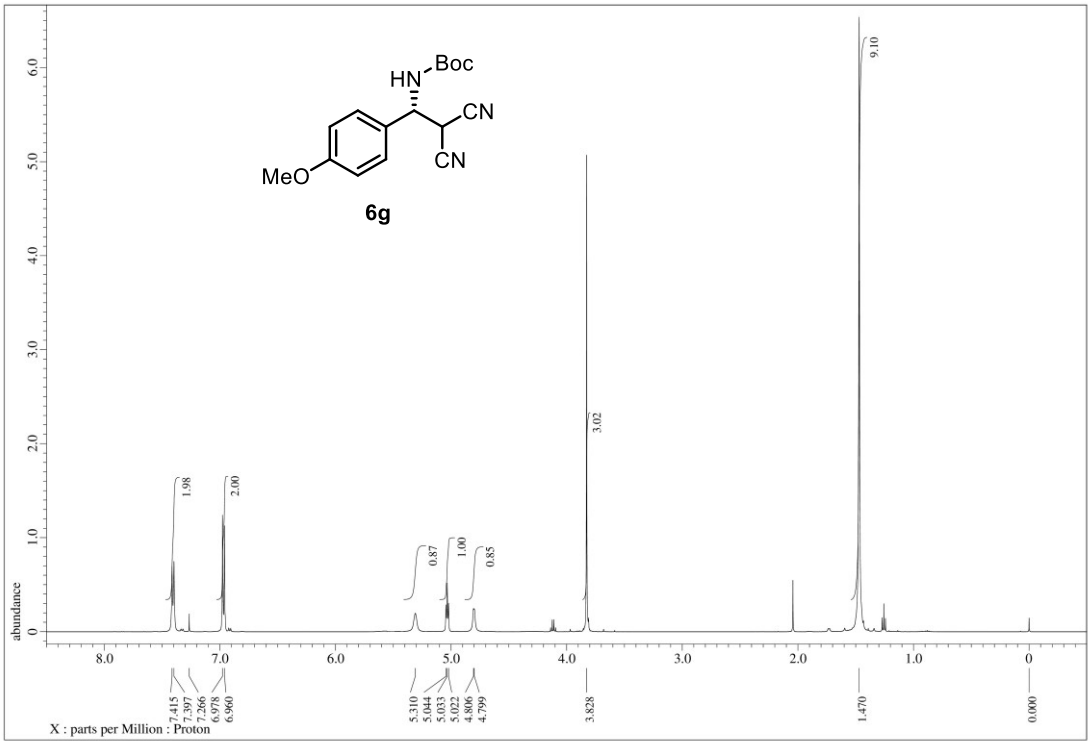

HN
Boc
CN
CN
Me
6d
abundance
X : parts per Million : Carbon13
154.880
140.296
130.672
130.109
126.857
111.147
110.880
81.702
77.248
77.000
76.742
55.443
29.671
28.135
21.182

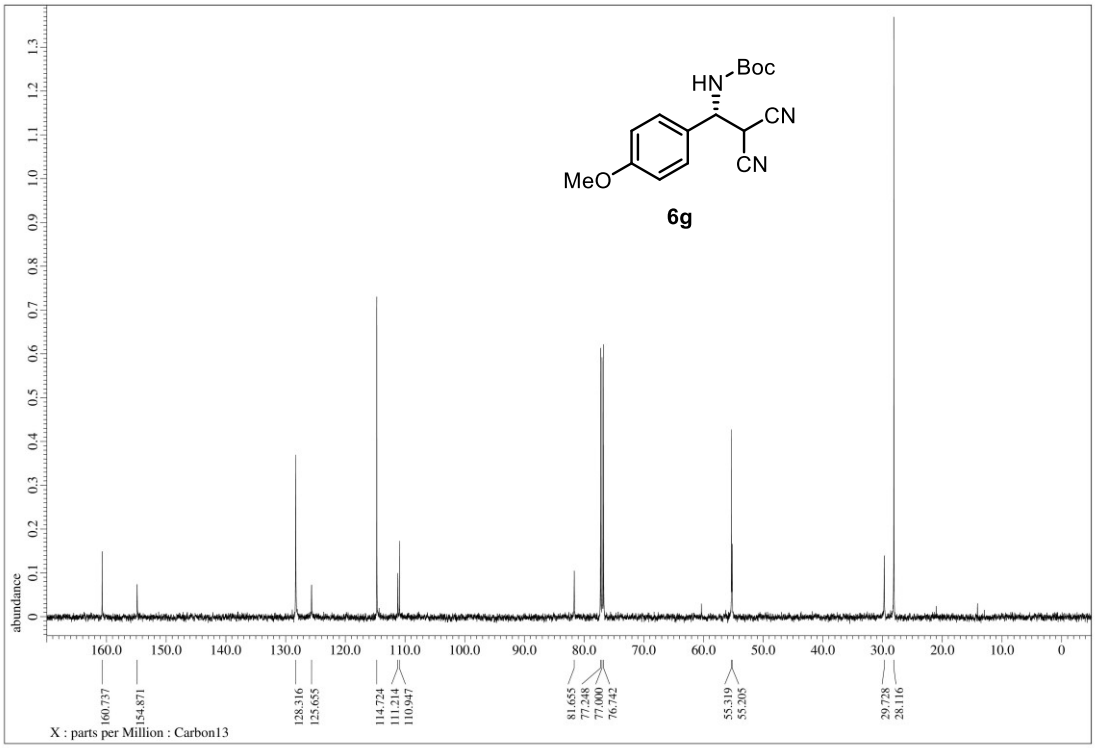

MeO
HN
Boc
CN
CN
6e
abundance
X : parts per Million : Proton

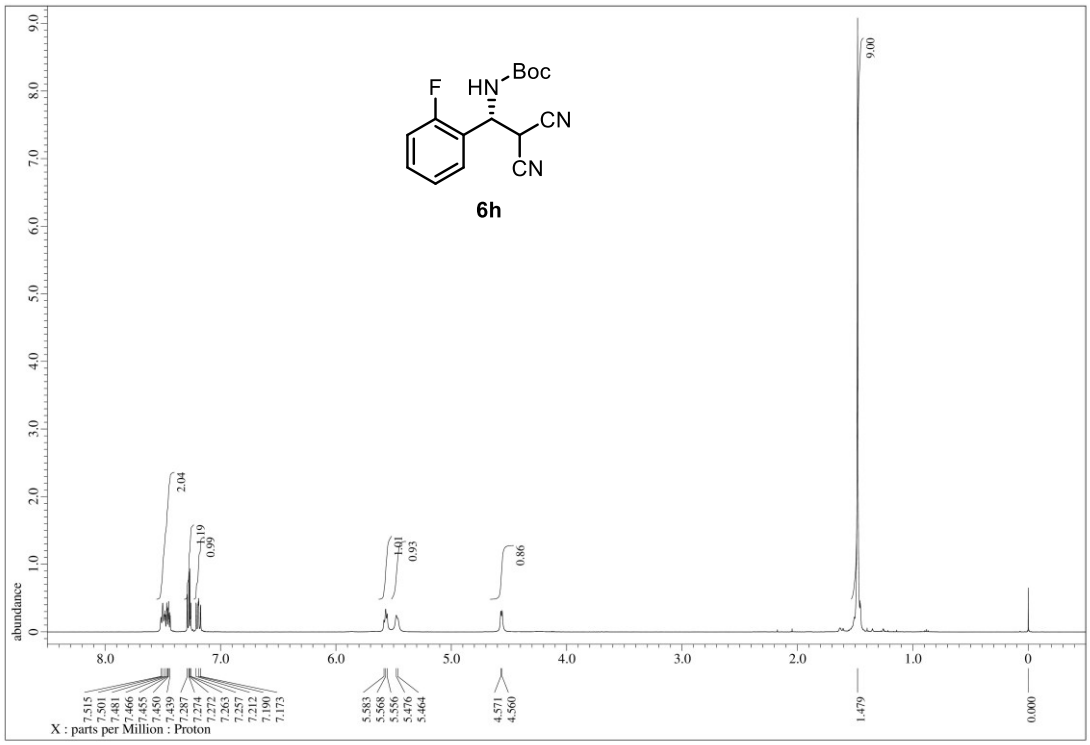

MeO
HN
Boc
CN
CN
6e
abundance
X : parts per Million : Carbon13

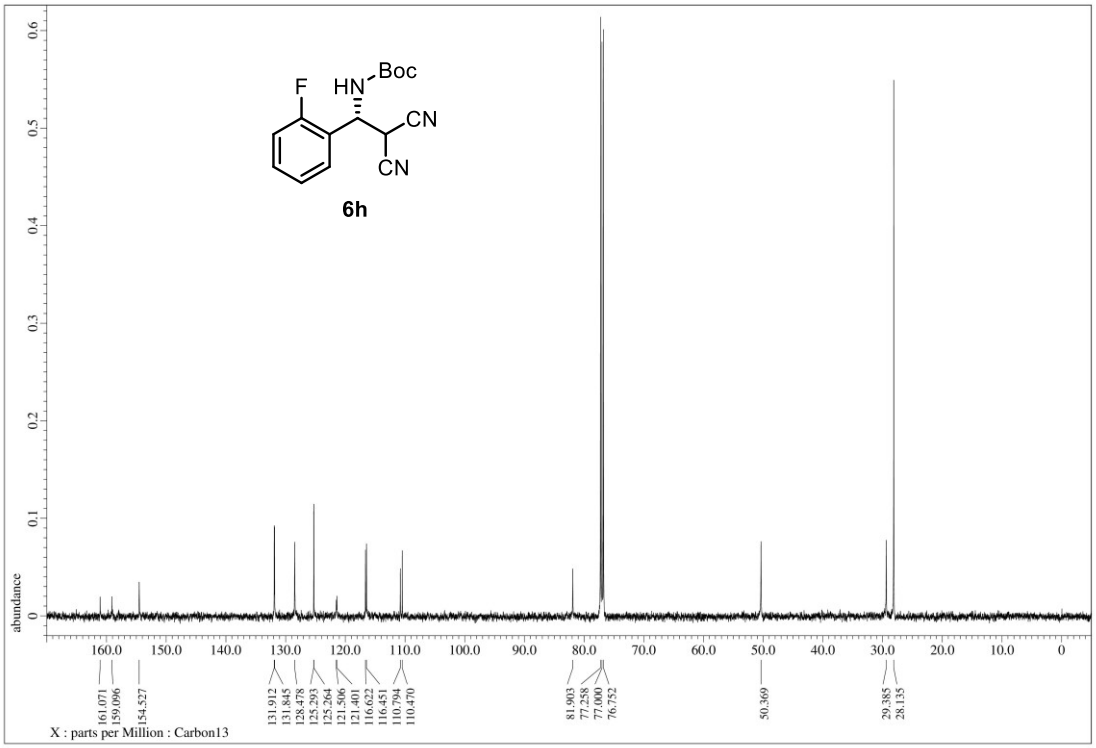

HN
Boc
MeO
CN
CN
6f
abundance
9.02
3.10
2.93
1.03
0.79
1.00
0.86
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.384
7.364
7.344
7.274
7.052
7.033
7.006
6.985
6.964
5.597
5.113
5.098
5.083
4.764
4.753
3.823
1.469
X : parts per Million : Proton

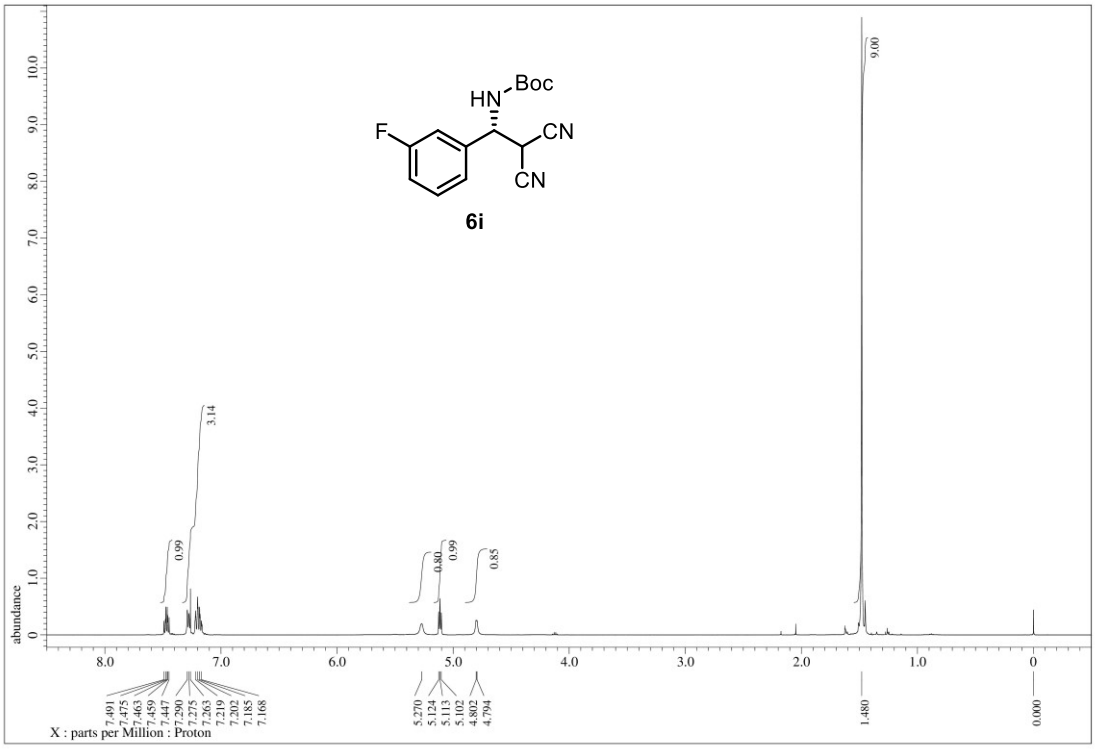

HN
Boc
MeO
CN
CN
6f
abundance
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
154.830
135.267
130.477
118.991
115.350
112.735
111.163
110.886
81.551
77.326
77.000
76.674
55.406
55.281
29.606
28.073
X : parts per Million : Carbon13

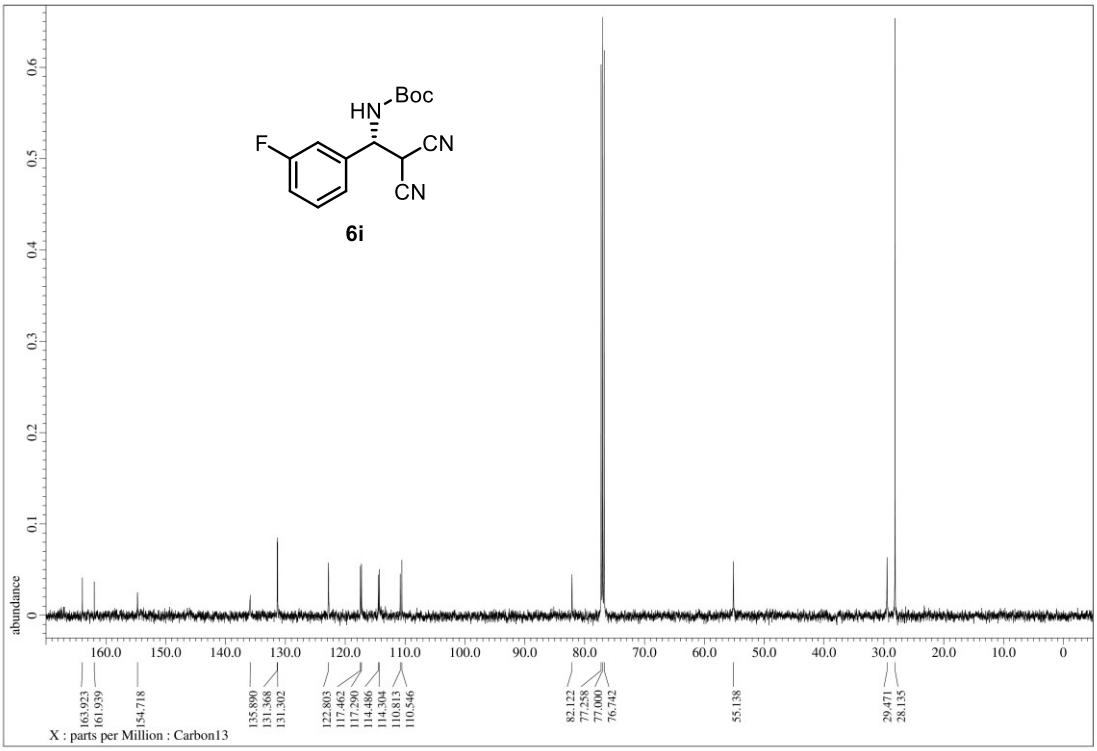

HN
Boc
CN
CN
MeO
6g
abundance
9.10
3.02
1.98
2.00
0.87
1.00
0.85
7.415
7.397
7.266
6.978
6.960
5.310
5.044
5.033
5.022
4.806
4.799
3.828
1.470
0.000
X : parts per Million : Proton

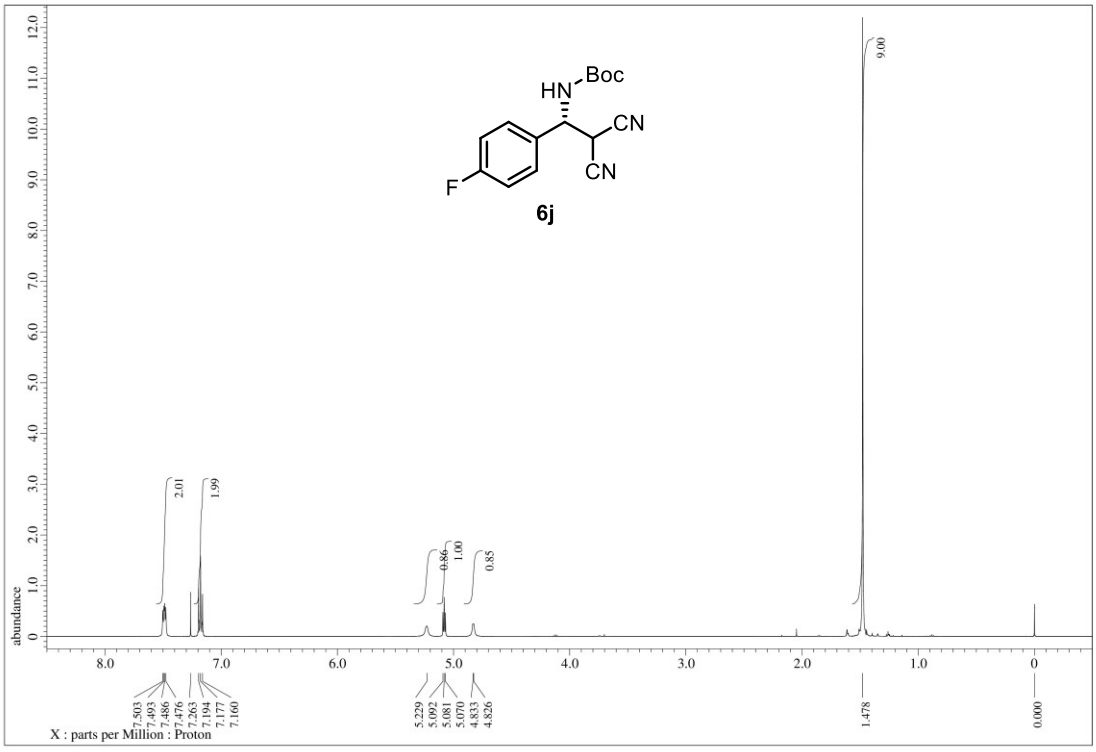

HN
Boc
CN
CN
MeO
6g
abundance
160.737
154.871
128.316
125.655
114.724
111.214
110.947
81.655
77.248
77.000
76.742
55.319
55.205
29.728
28.116
X : parts per Million : Carbon13

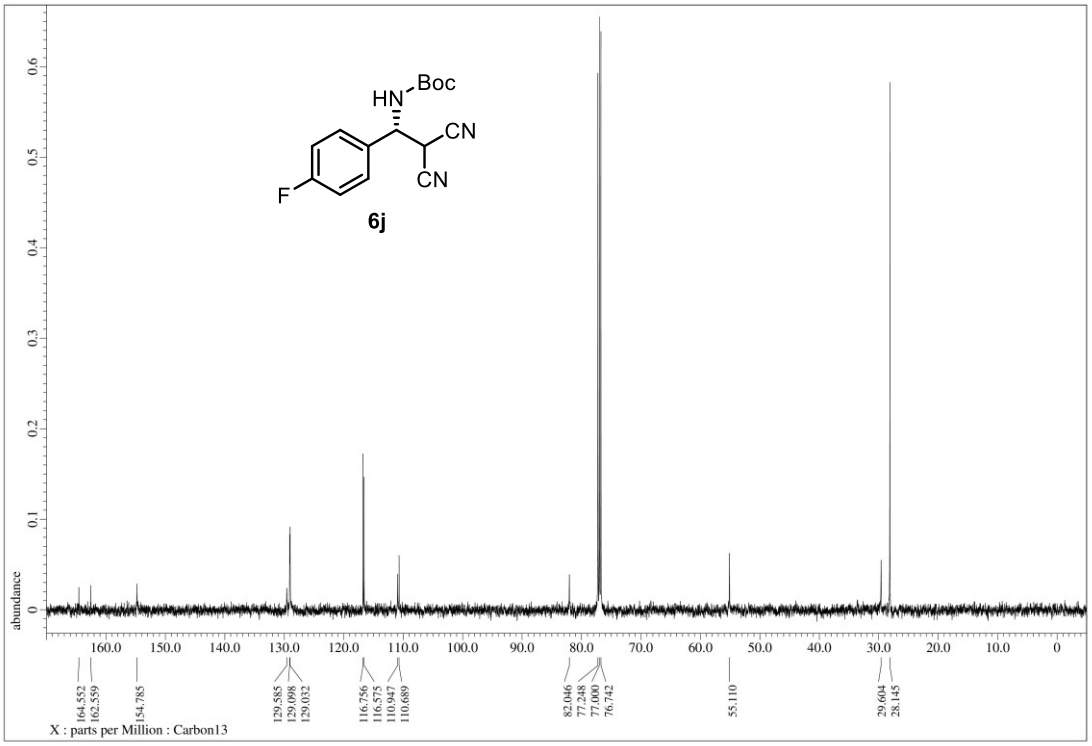

F
HN
Boc
CN
CN
6h
abundance
X : parts per Million : Proton

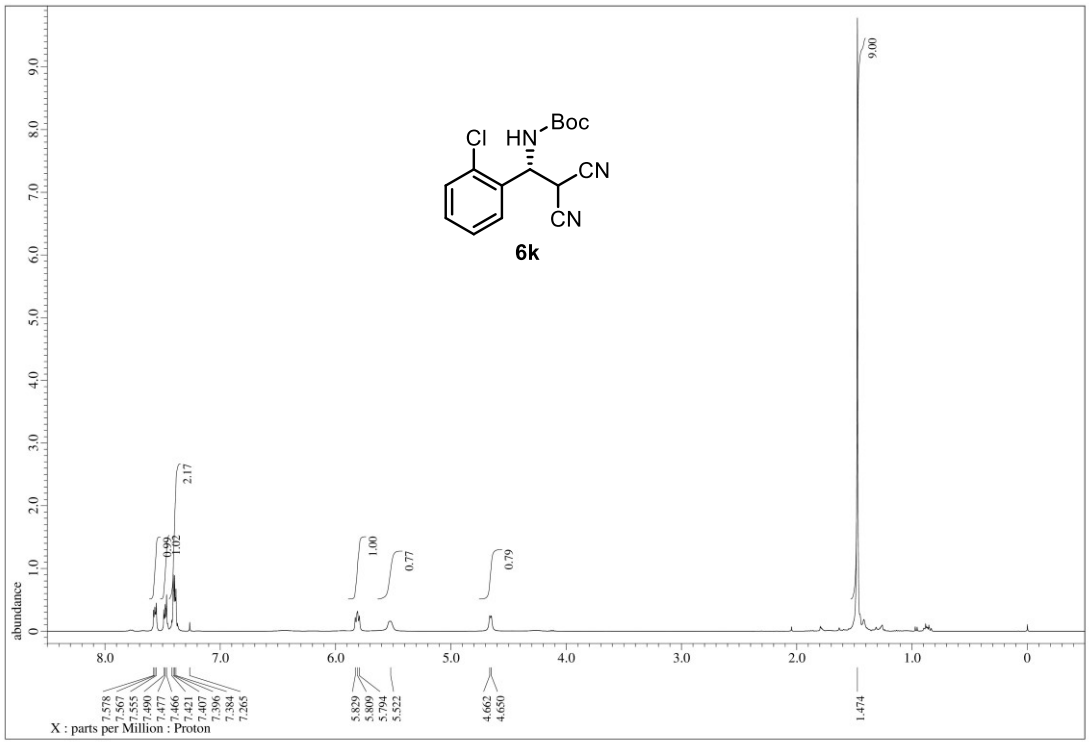

F
HN
Boc
CN
CN
6h
abundance
X : parts per Million : Carbon13

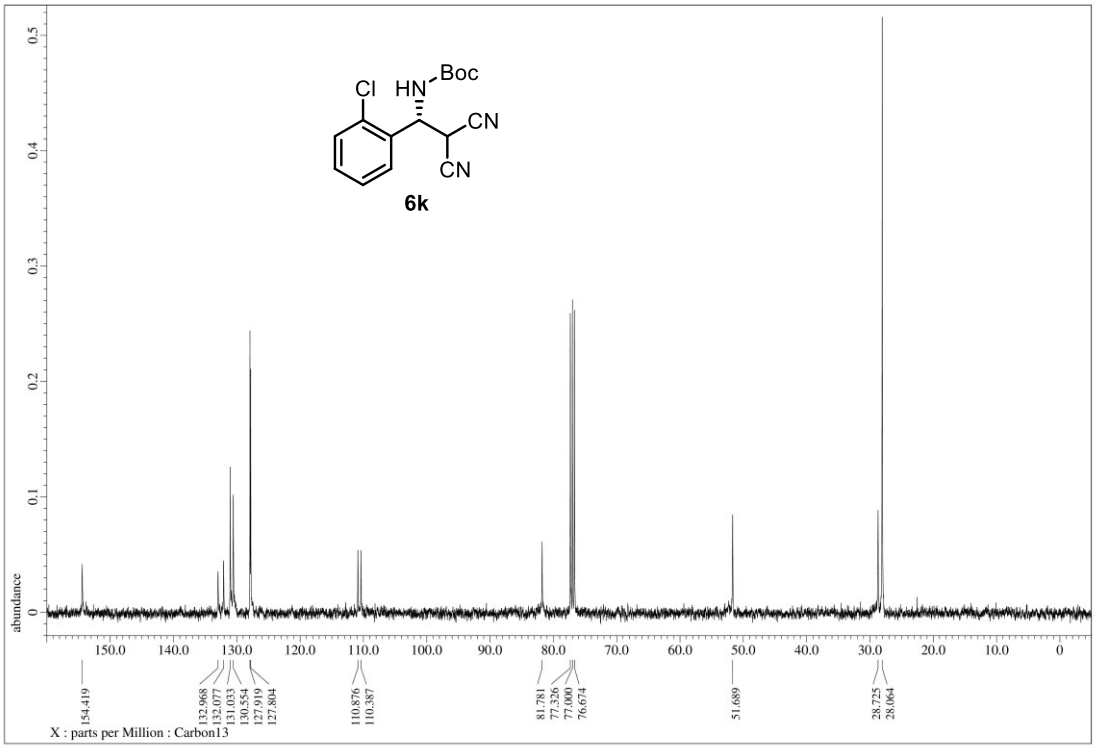

HN
Boc
F
CN
CN
6i
abundance
X : parts per Million : Proton

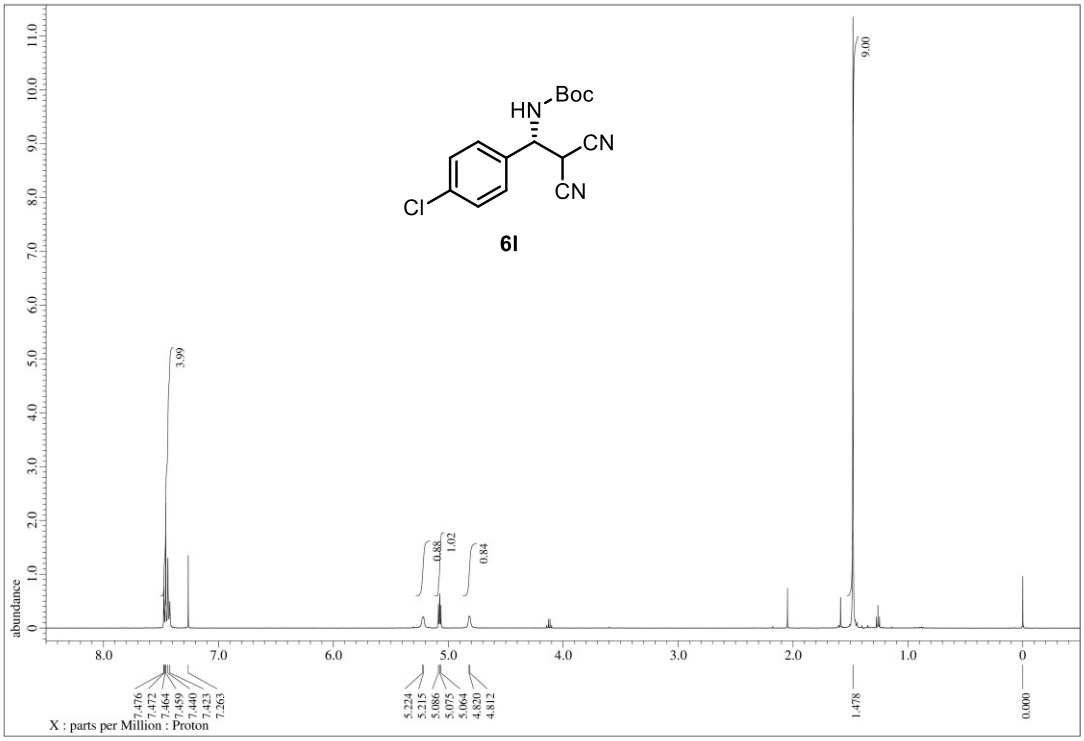

HN
Boc
F
CN
CN
6i
abundance
X : parts per Million : Carbon13

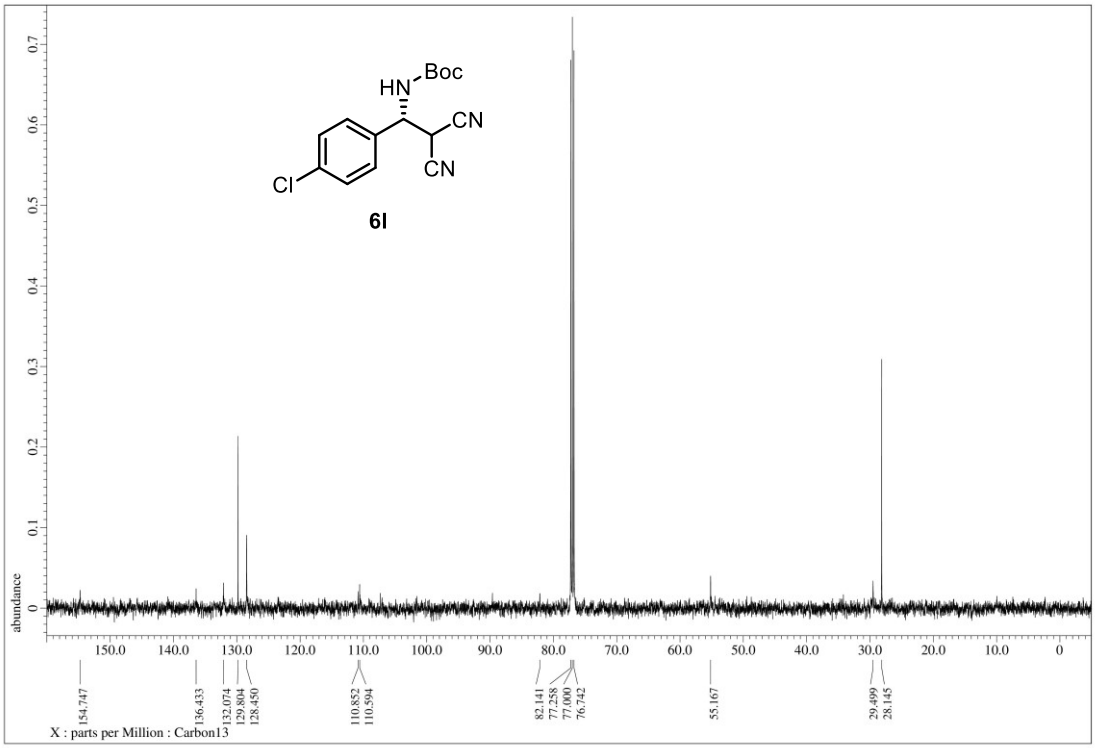

HN
Boc
CN
CN
F
6j
abundance
X : parts per Million : Proton

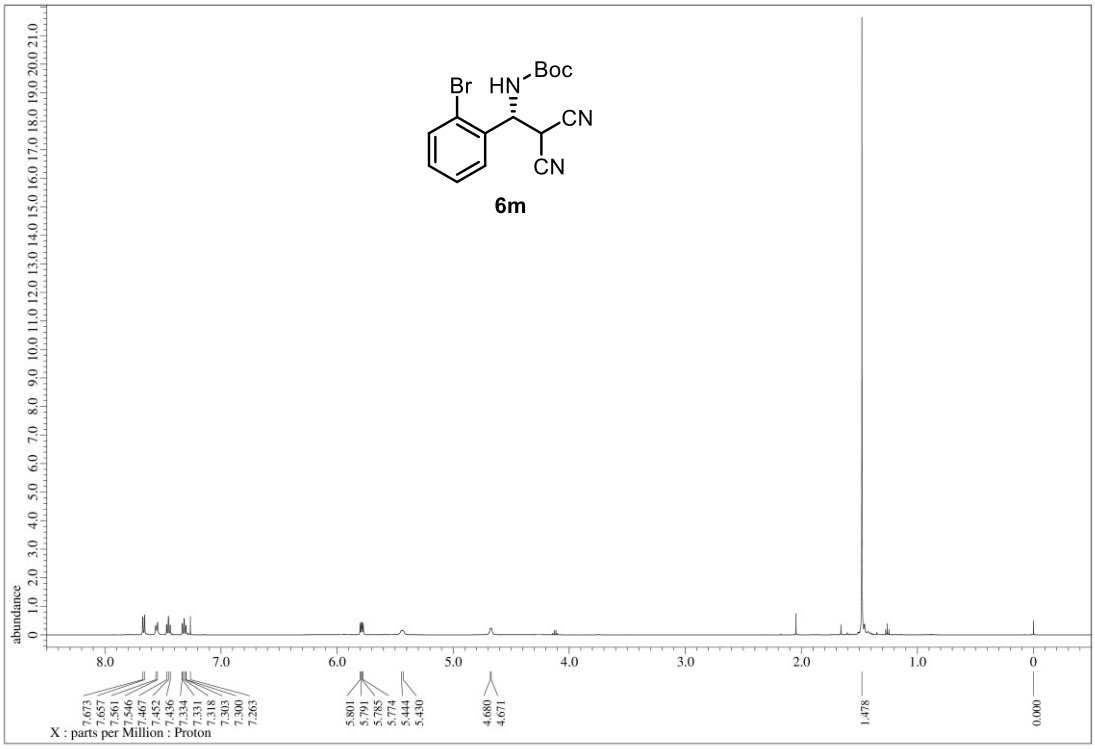

HN
Boc
CN
CN
F
6j
abundance
X : parts per Million : Carbon13

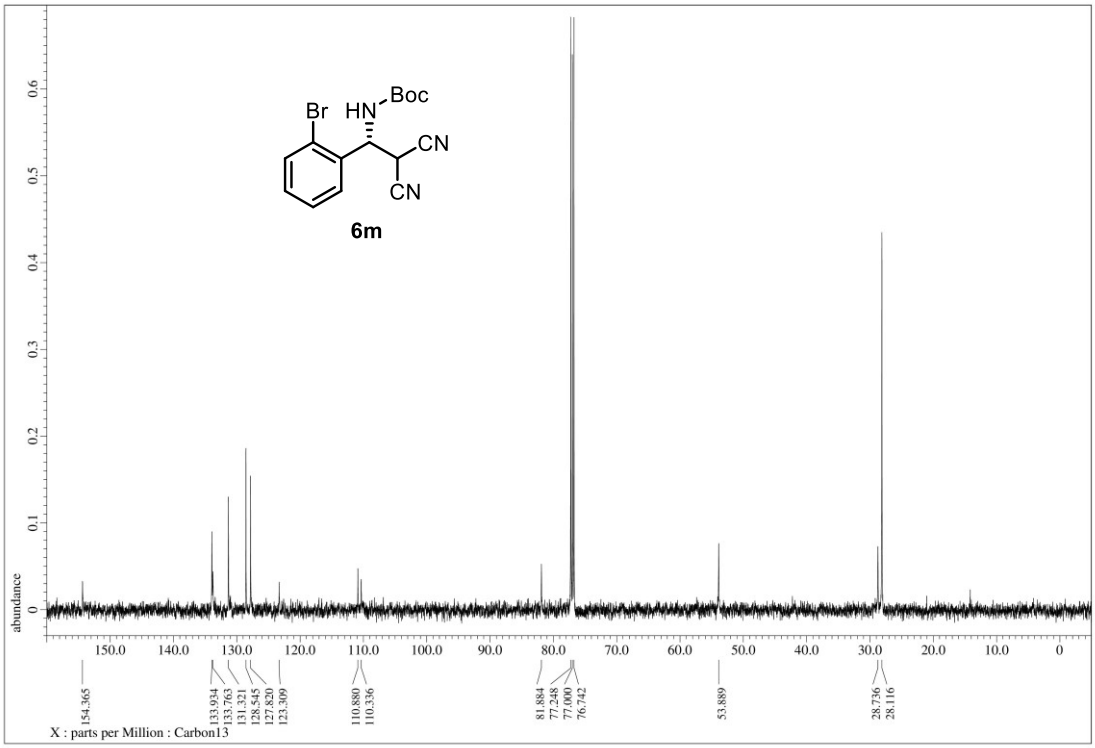

Cl
HN
Boc
CN
CN
6k
abundance
X : parts per Million : Proton

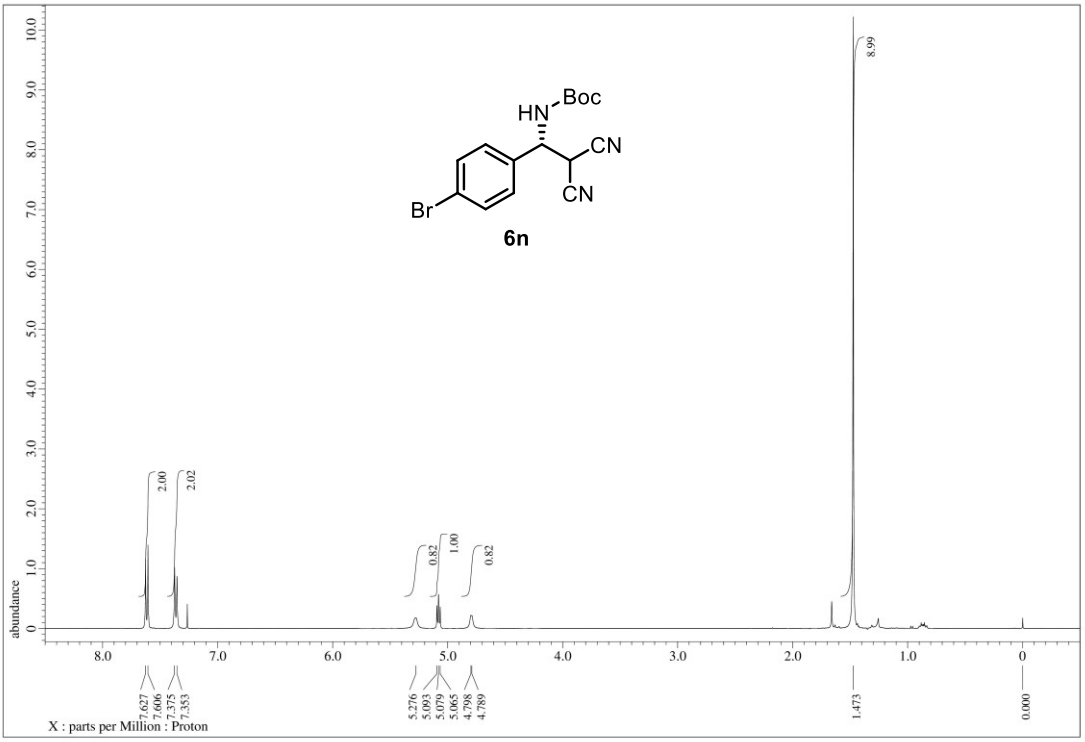

Cl
HN
Boc
CN
CN
6k
abundance
X : parts per Million : Carbon13

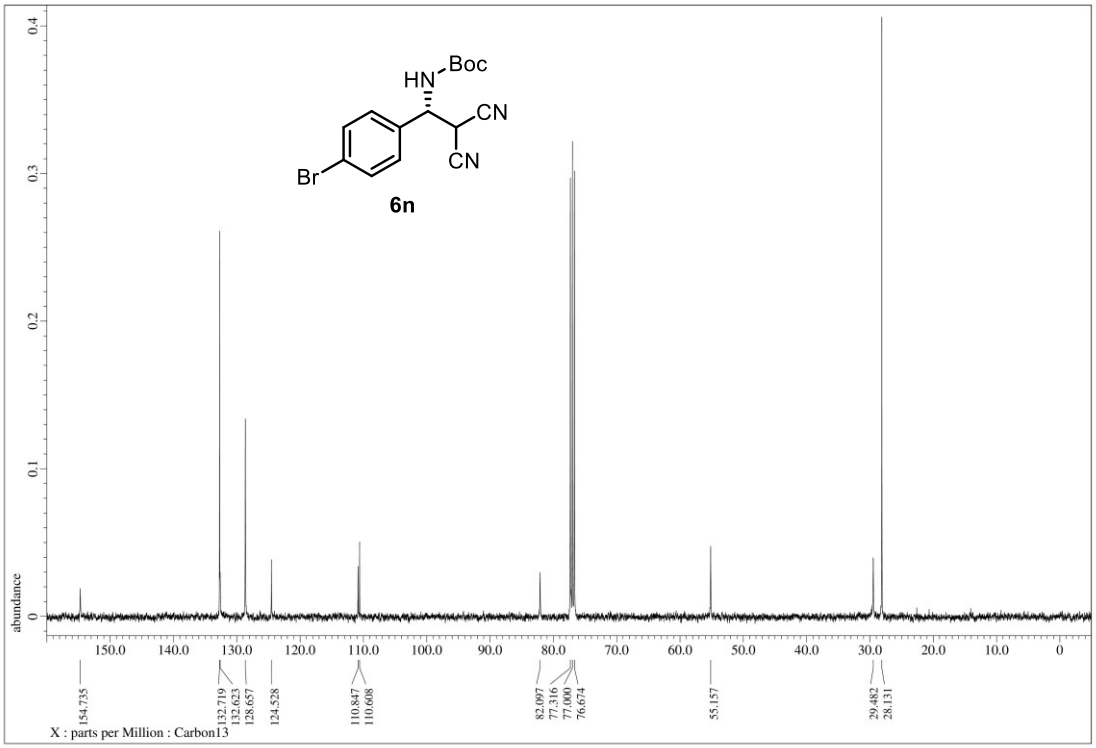

HN
Boc
CN
CN
Cl
6l
abundance
X : parts per Million : Proton
9.00
3.99
0.88
1.02
0.84
7.476
7.472
7.464
7.459
7.440
7.423
7.263
5.224
5.215
5.086
5.075
5.064
4.820
4.812
1.478
0.000

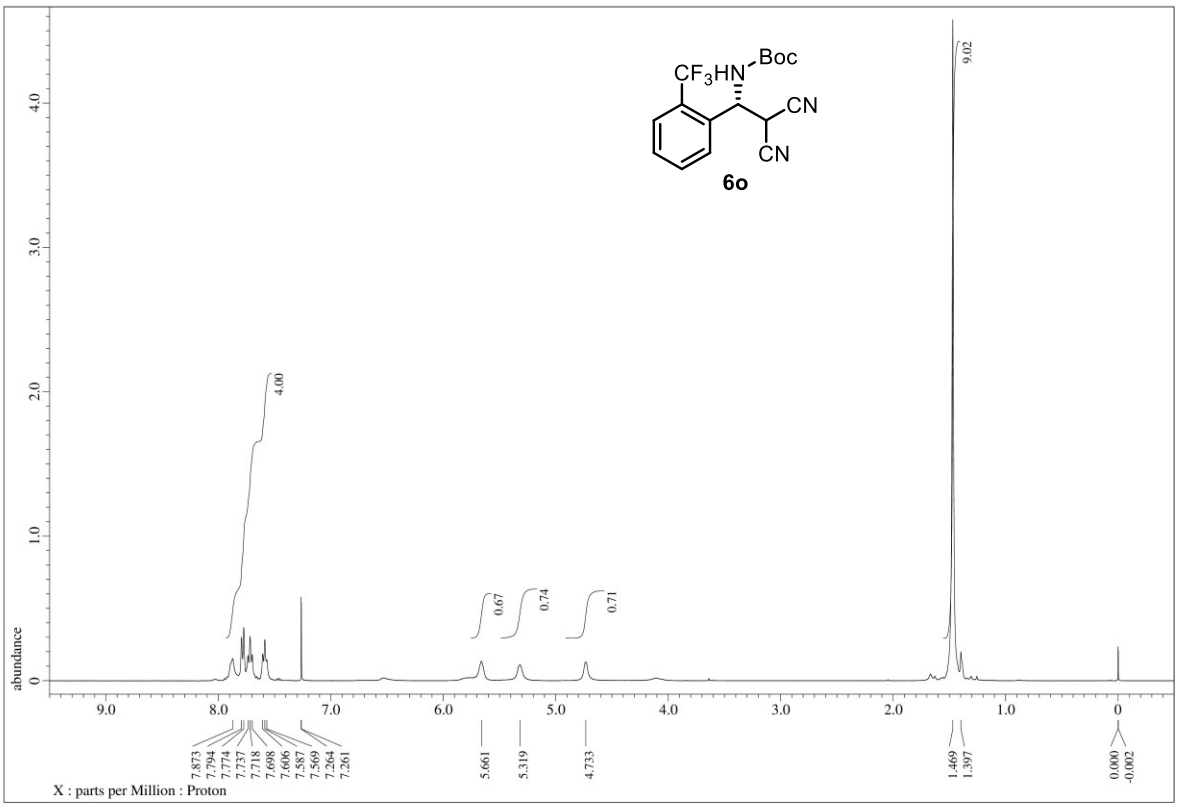

HN
Boc
CN
CN
Cl
6l
abundance
X : parts per Million : Carbon13
154.747
136.433
132.074
129.804
128.450
110.852
110.594
82.141
77.258
77.000
76.742
55.167
29.499
28.145

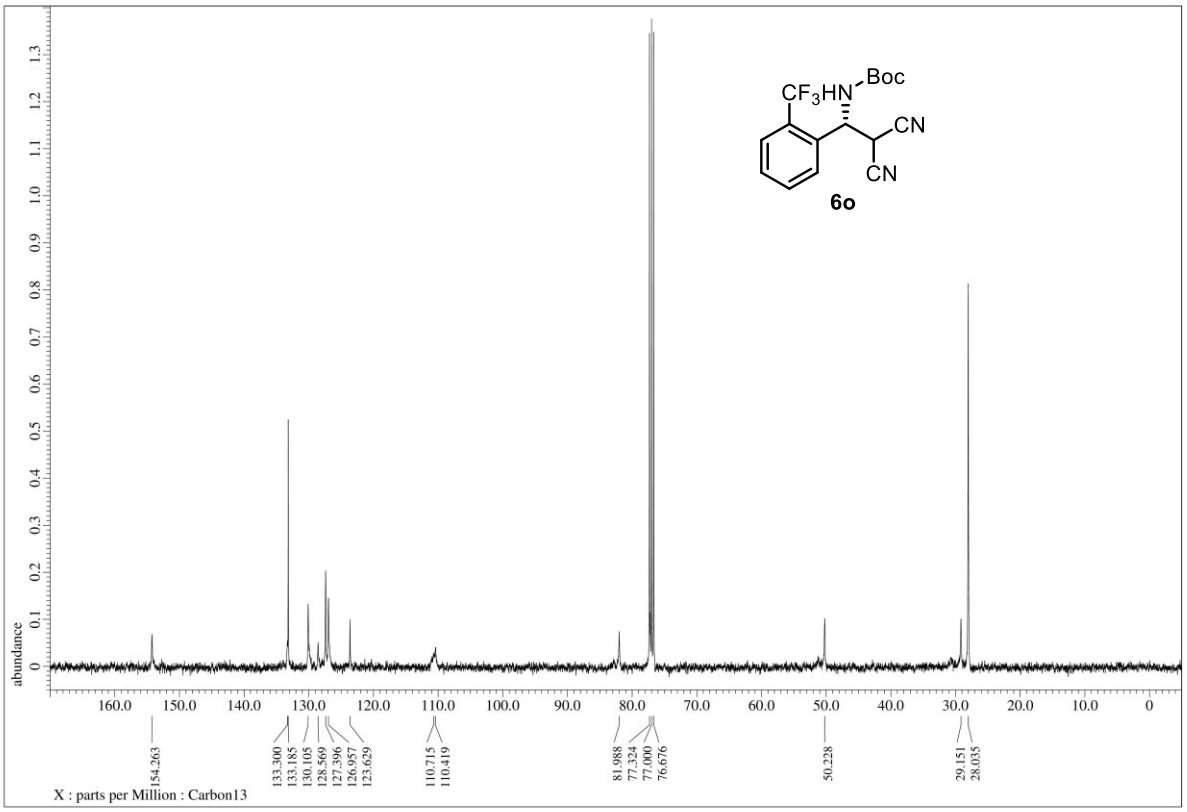

Br
HN
Boc
CN
CN
6m
abundance
X : parts per Million : Proton
7.673
7.657
7.561
7.546
7.467
7.452
7.436
7.334
7.331
7.318
7.303
7.300
7.263
5.801
5.791
5.785
5.774
5.444
5.430
4.680
4.671
1.478
0.000

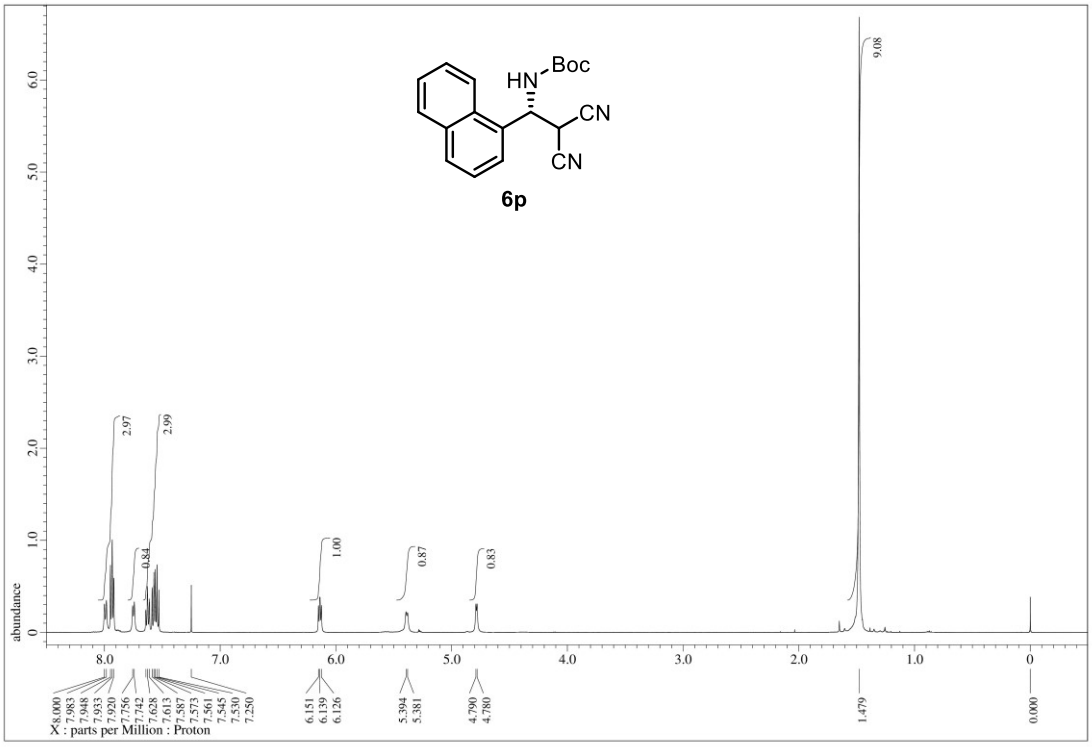

Br
HN
Boc
CN
CN
6m
abundance
X : parts per Million : Carbon13
154.365
133.934
133.763
131.321
128.545
127.820
123.309
110.880
110.336
81.884
77.248
77.000
76.742
53.889
28.736
28.116

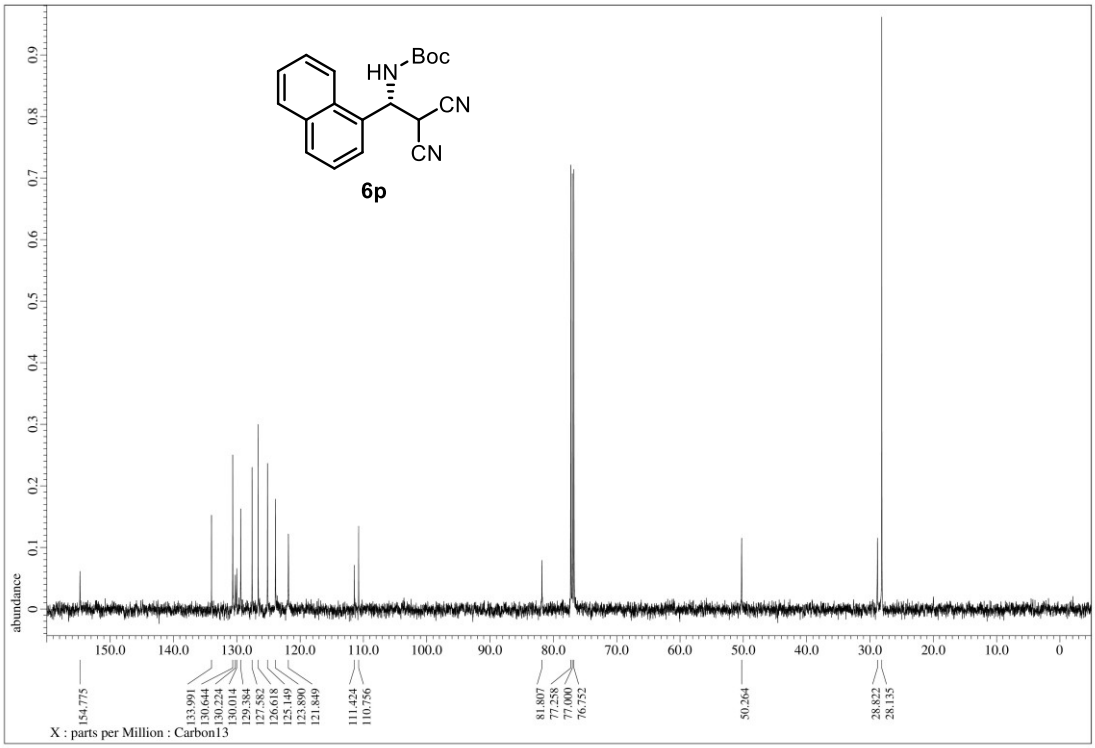

HN
Boc
CN
CN
Br
6n
abundance
X : parts per Million : Proton

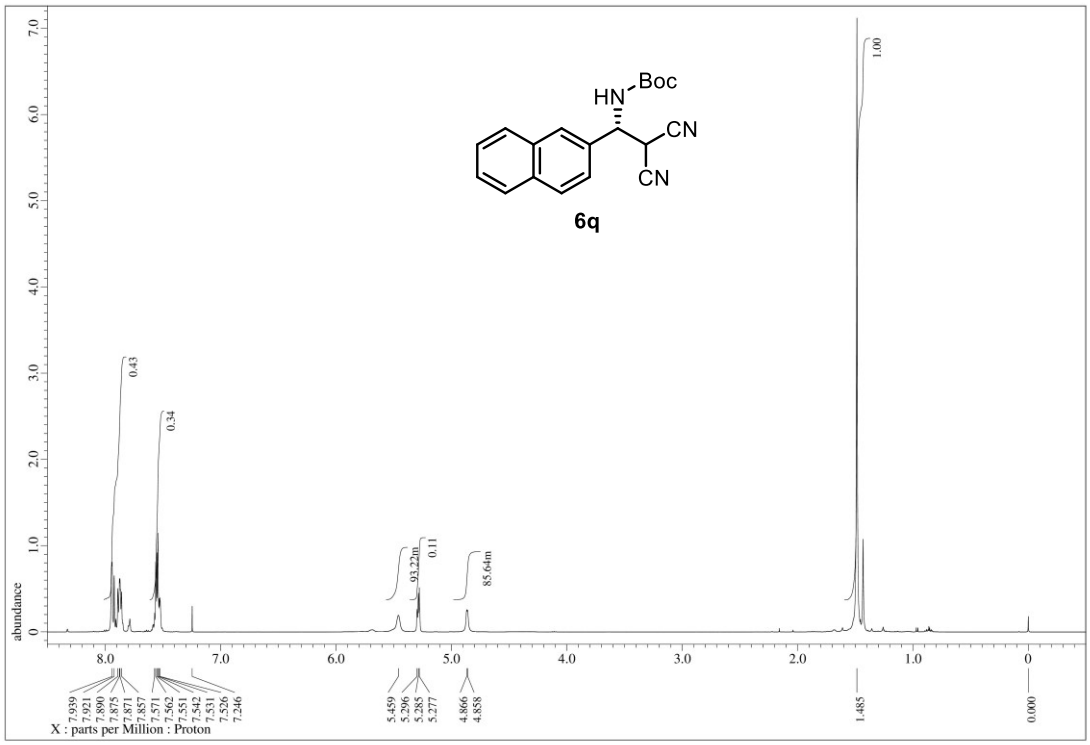

HN
Boc
CN
CN
Br
6n
abundance
X : parts per Million : Carbon13

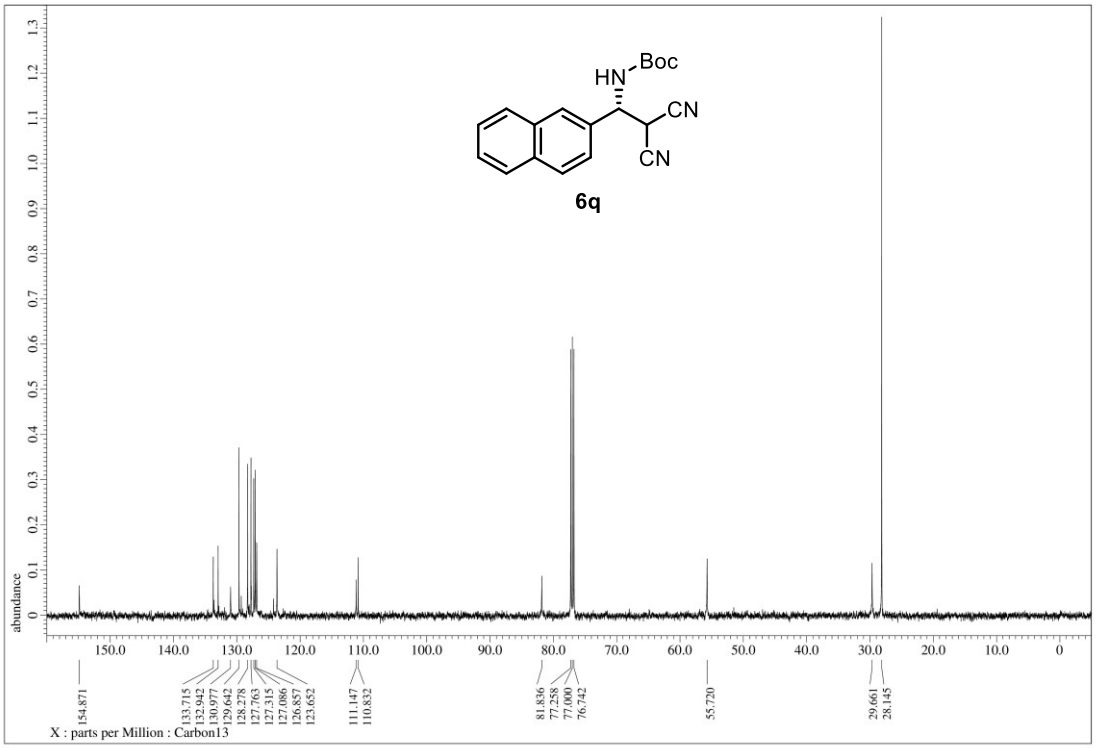

CF3HN
Boc
CN
CN
6o
9.02
4.00
0.67
0.74
0.71
abundance
7.873
7.794
7.774
7.737
7.718
7.698
7.606
7.587
7.569
7.264
7.261
5.661
5.319
4.733
1.469
1.397
0.000
-0.002
X : parts per Million : Proton

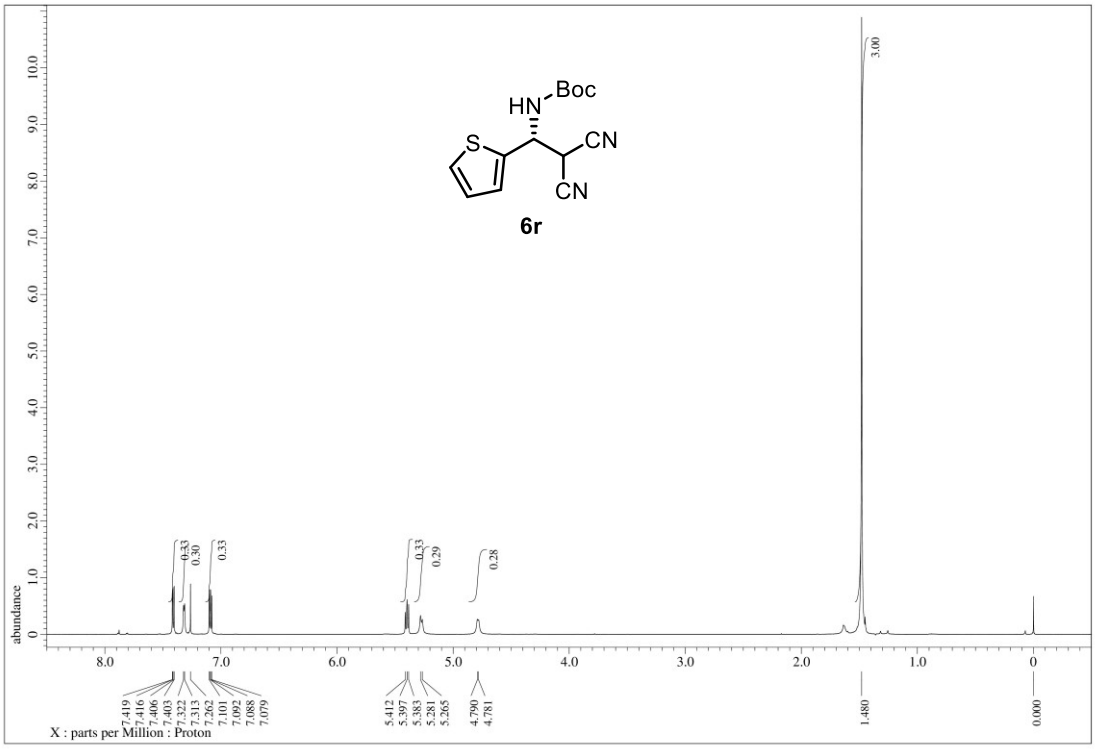

CF3HN
Boc
CN
CN
6o
abundance
154.263
133.300
133.185
130.105
128.569
127.396
126.957
123.629
110.715
110.419
81.988
77.324
77.000
76.676
50.228
29.151
28.035
X : parts per Million : Carbon13

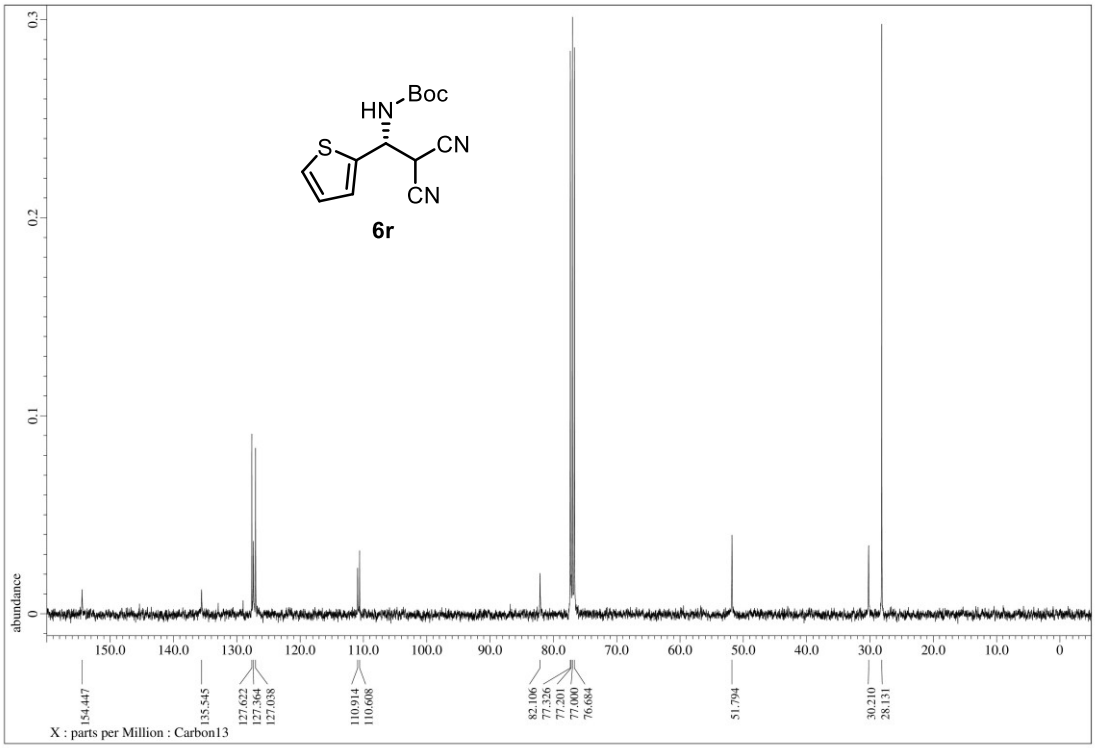

HN
Boc
CN
CN
6p
abundance
X : parts per Million : Proton

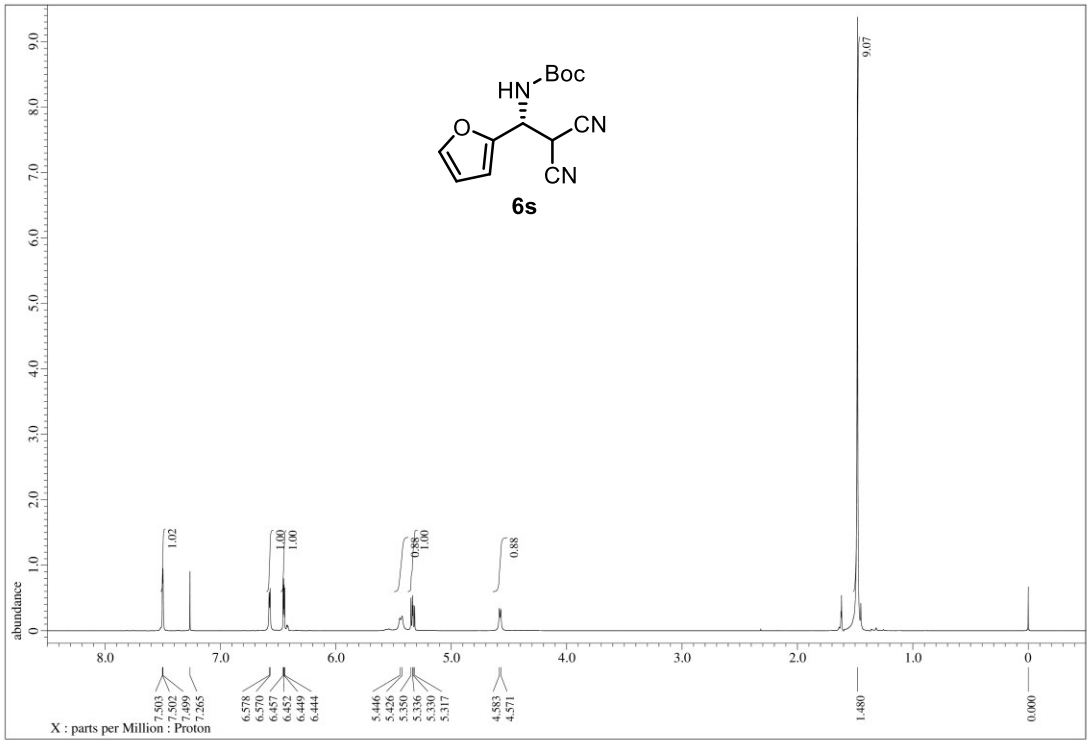

HN
Boc
CN
CN
6p
abundance
X : parts per Million : Carbon13

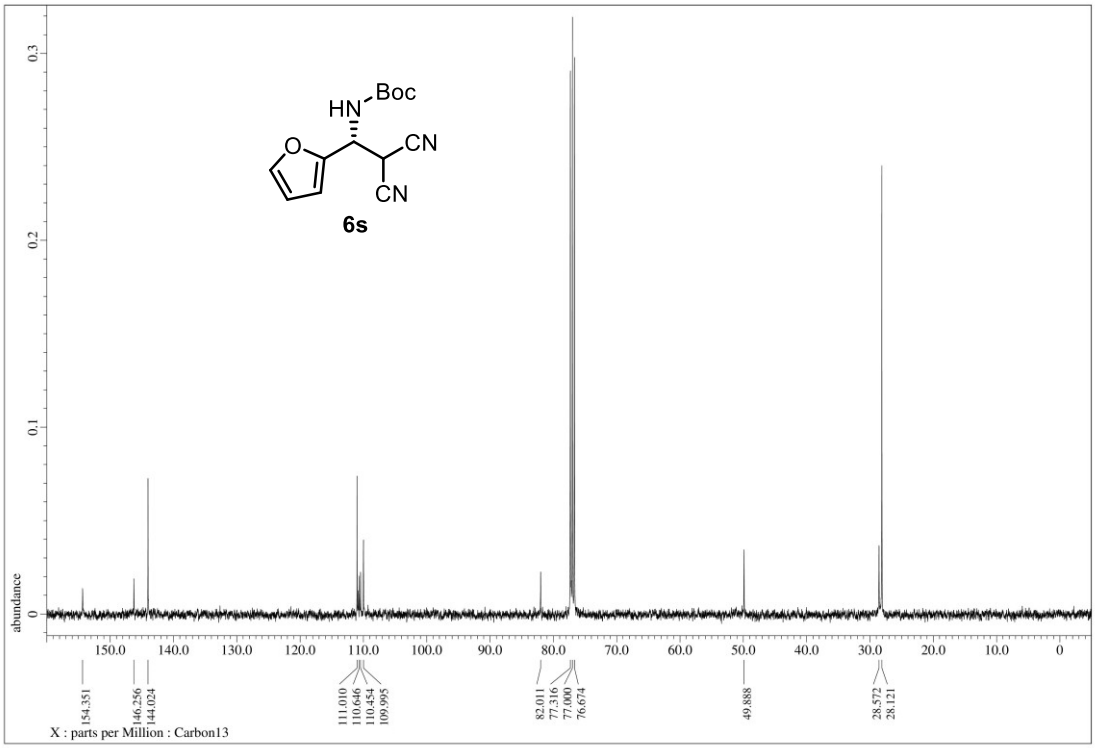

HN
Boc
CN
CN
6q
abundance
X : parts per Million : Proton

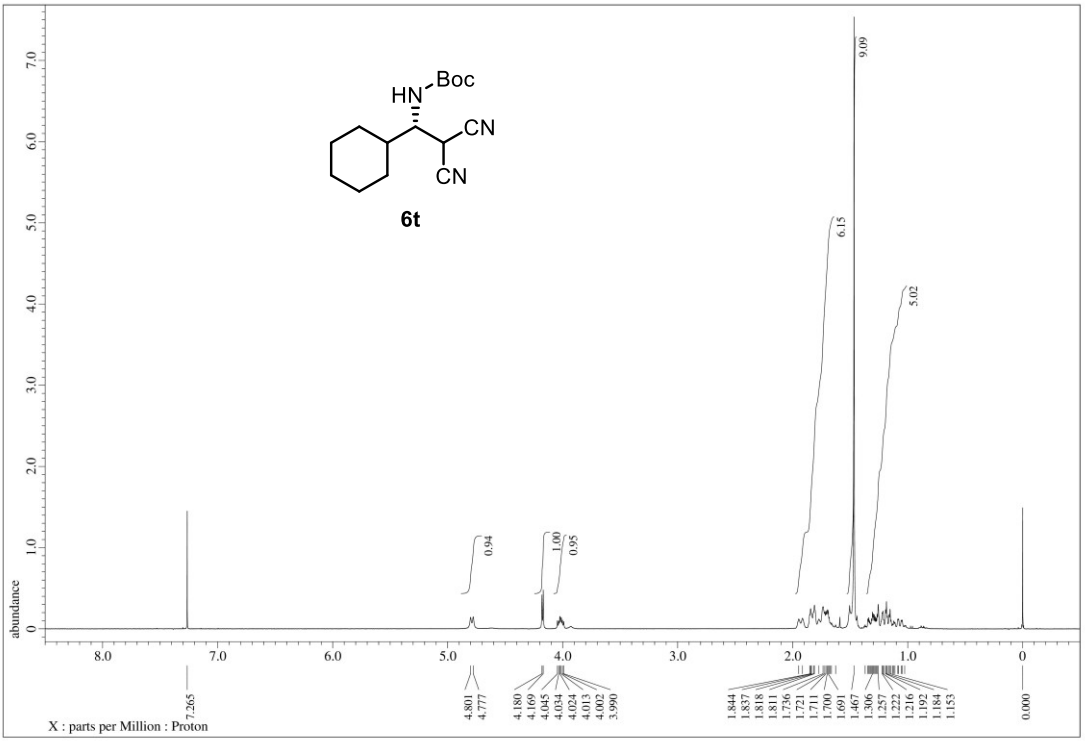

HN
Boc
CN
CN
6q
abundance
X : parts per Million : Carbon13

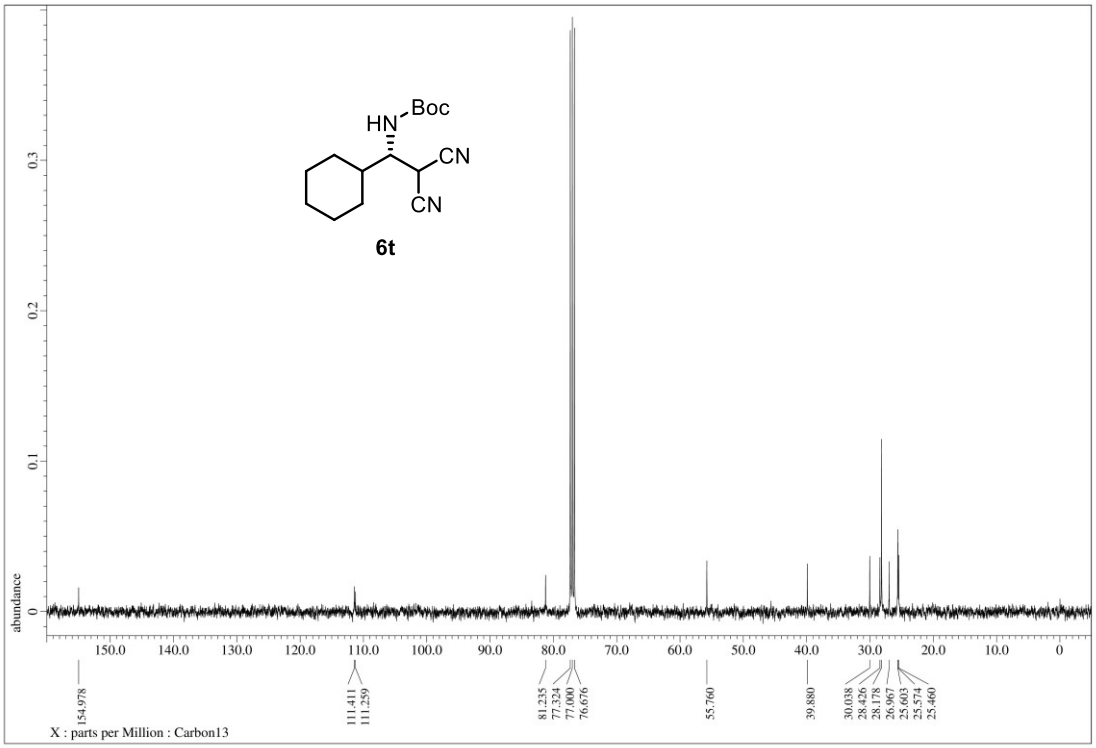

HN
Boc
S
CN
CN
6r
abundance
X : parts per Million : Proton

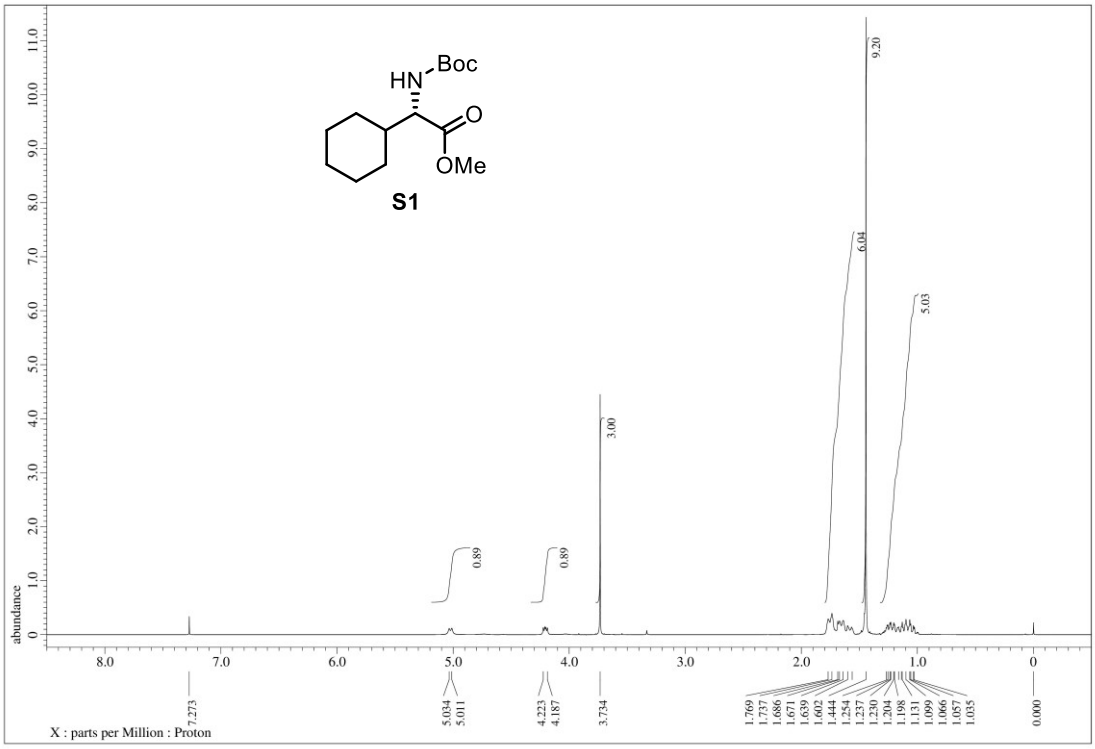

HN
Boc
S
CN
CN
6r
abundance
X : parts per Million : Carbon13

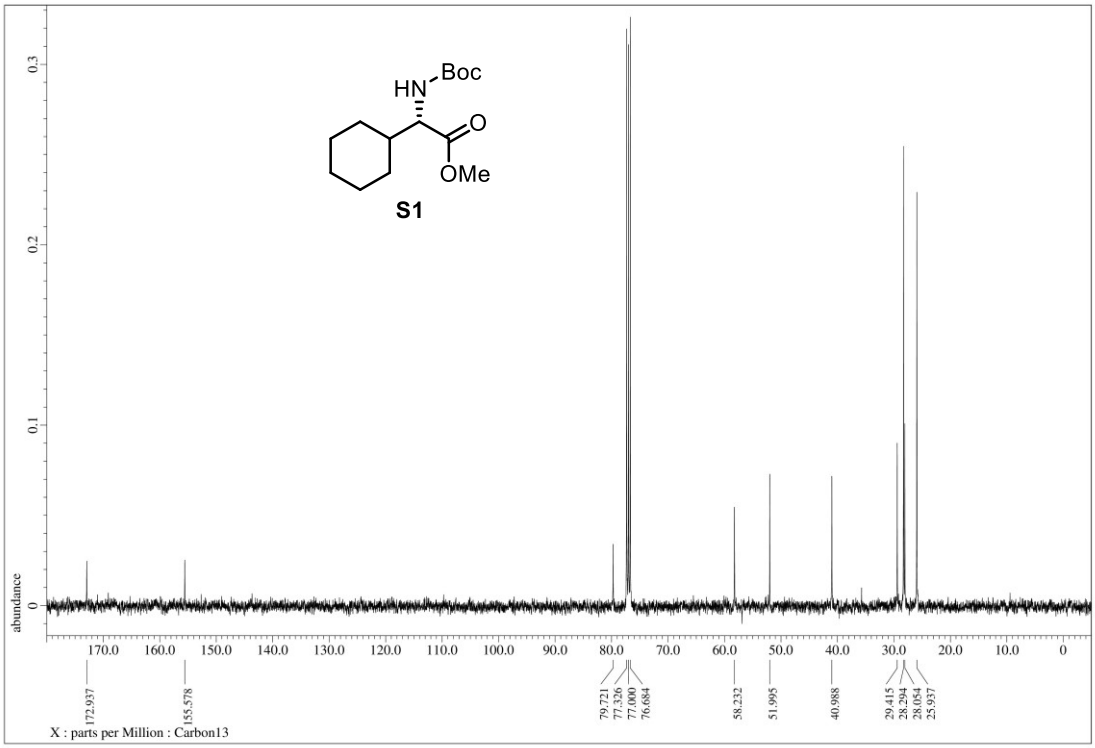

HN
Boc
O
CN
CN
6s
abundance
X : parts per Million : Proton

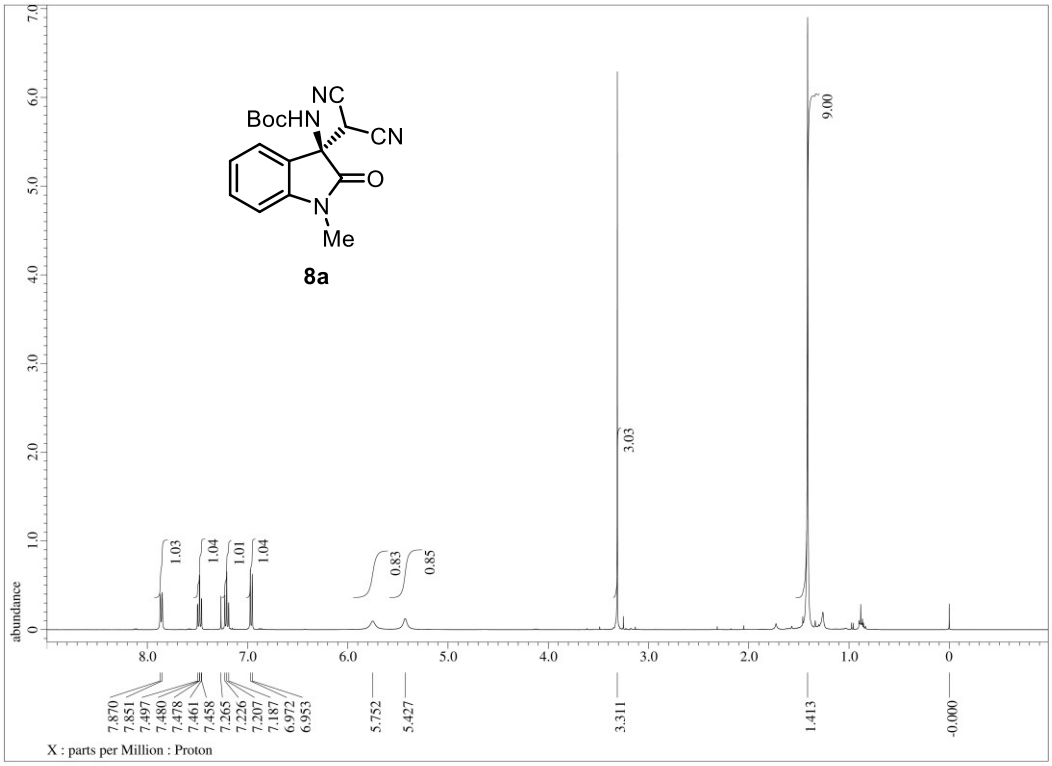

HN
Boc
O
CN
CN
6s
abundance
X : parts per Million : Carbon13

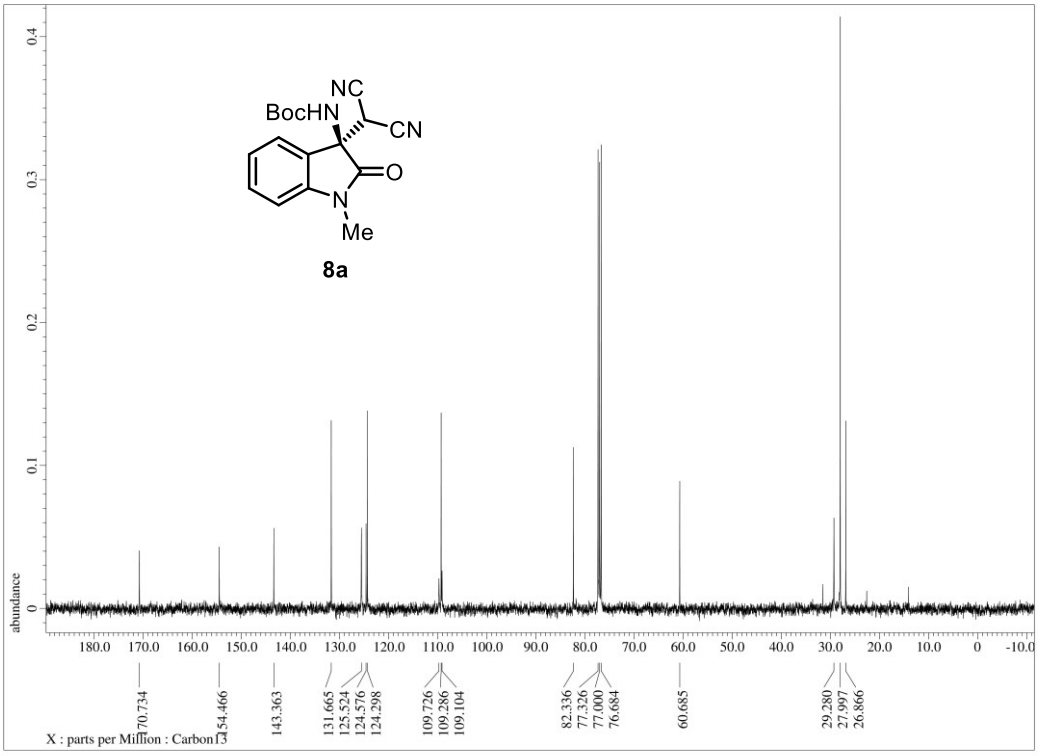

HN
Boc
CN
CN
6t
abundance
X : parts per Million : Proton
9.09
6.15
5.02
0.94
1.00
0.95
7.265
4.801
4.777
4.180
4.169
4.045
4.034
4.024
4.013
4.002
3.990
1.844
1.837
1.818
1.811
1.736
1.721
1.711
1.700
1.691
1.467
1.306
1.257
1.222
1.216
1.192
1.184
1.153
0.000

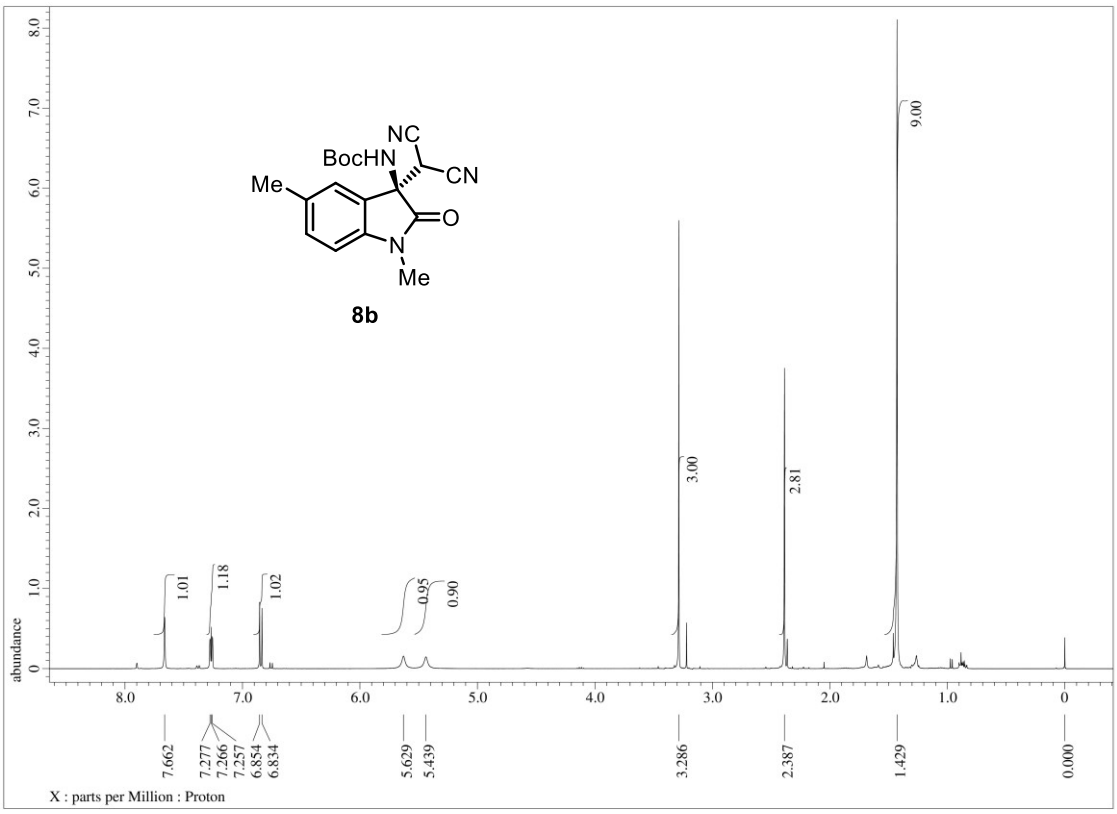

HN
Boc
CN
CN
6t
abundance
X : parts per Million : Carbon13
154.978
111.411
111.259
81.235
77.324
77.000
76.676
55.760
39.880
30.038
28.426
28.178
26.967
25.603
25.574
25.460

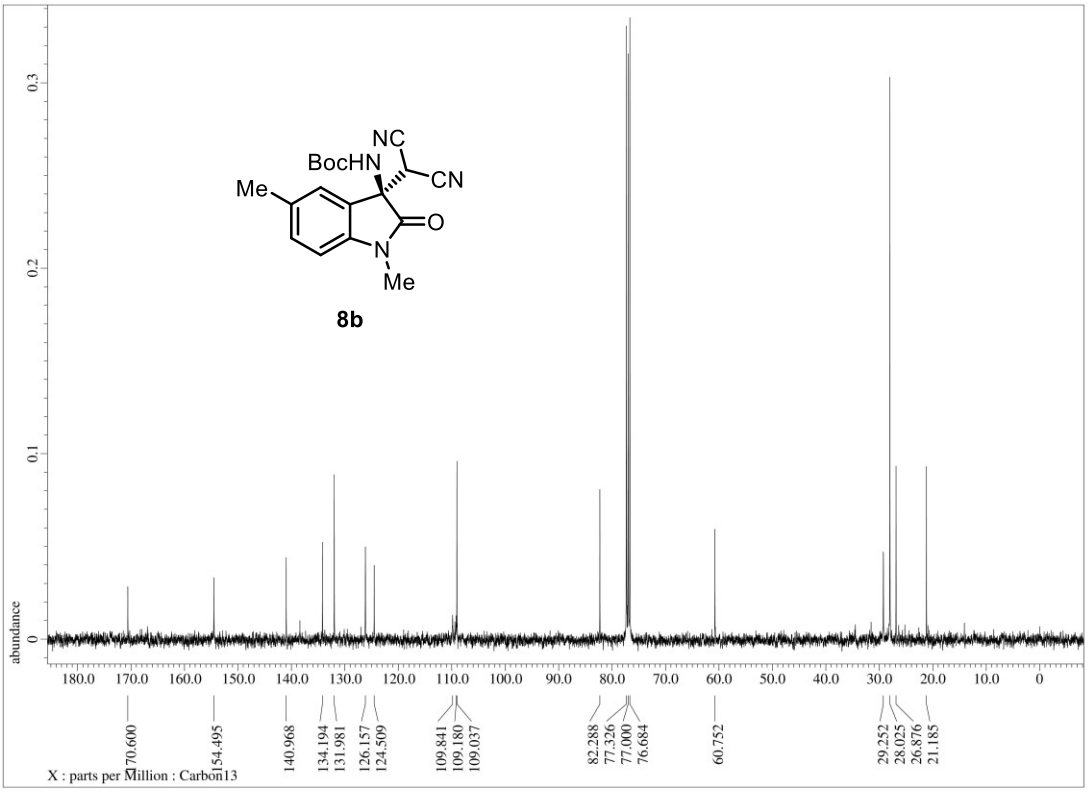

HN
Boc
O
OMe
S1
abundance
9.20
6.04
5.03
3.00
0.89
0.89
X : parts per Million : Proton

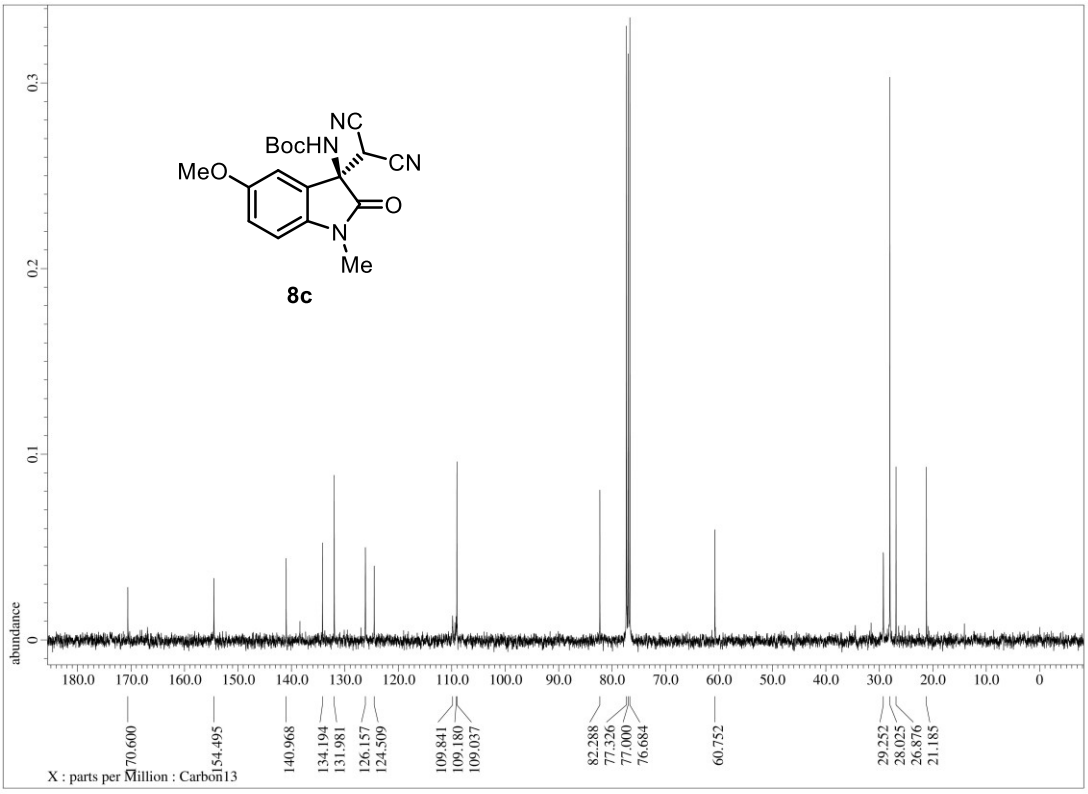

HN
Boc
O
OMe
S1
abundance
X : parts per Million : Carbon13

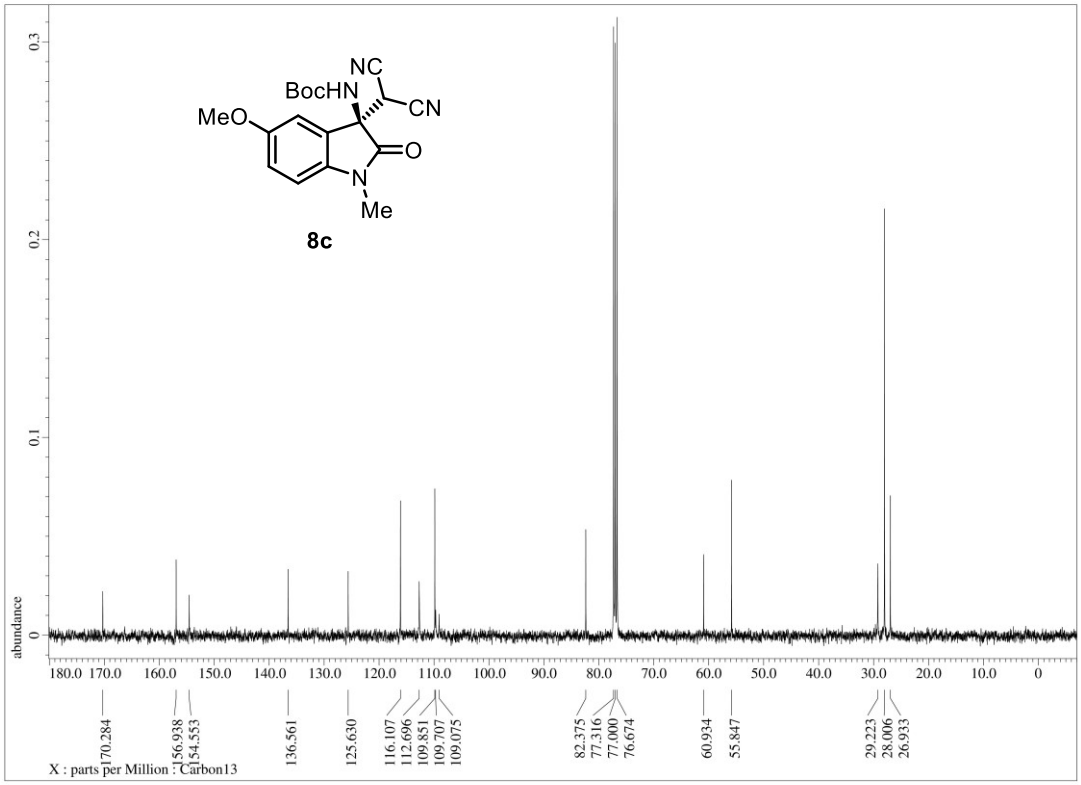

NC
BocHN
CN
O
N
Me
8a
abundance
X : parts per Million : Proton
1.03
1.04
1.01
1.04
0.83
0.85
3.03
9.00
7.870
7.851
7.497
7.480
7.478
7.461
7.458
7.265
7.226
7.207
7.187
6.972
6.953
5.752
5.427
3.311
1.413
-0.000

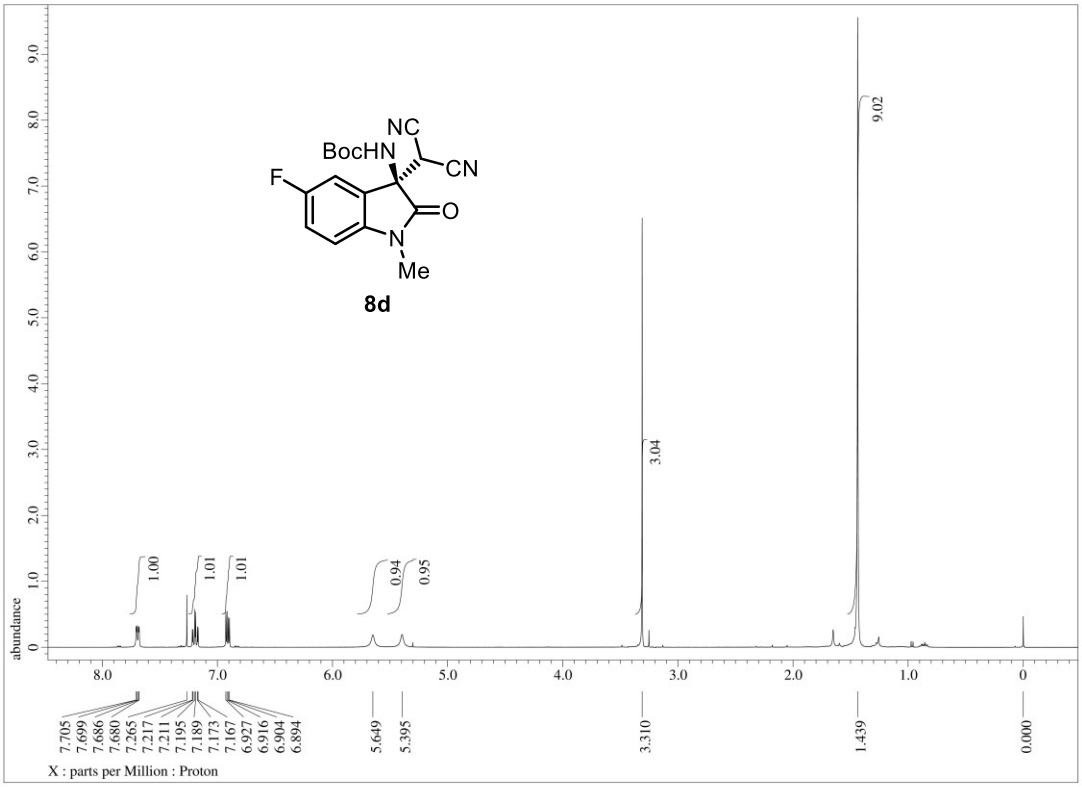

NC
BocHN
CN
O
N
Me
8a
abundance
X : parts per Million : Carbon 13
170.734
154.466
143.363
131.665
125.524
124.576
124.298
109.726
109.286
109.104
82.336
77.326
77.000
76.684
60.685
29.280
27.997
26.866

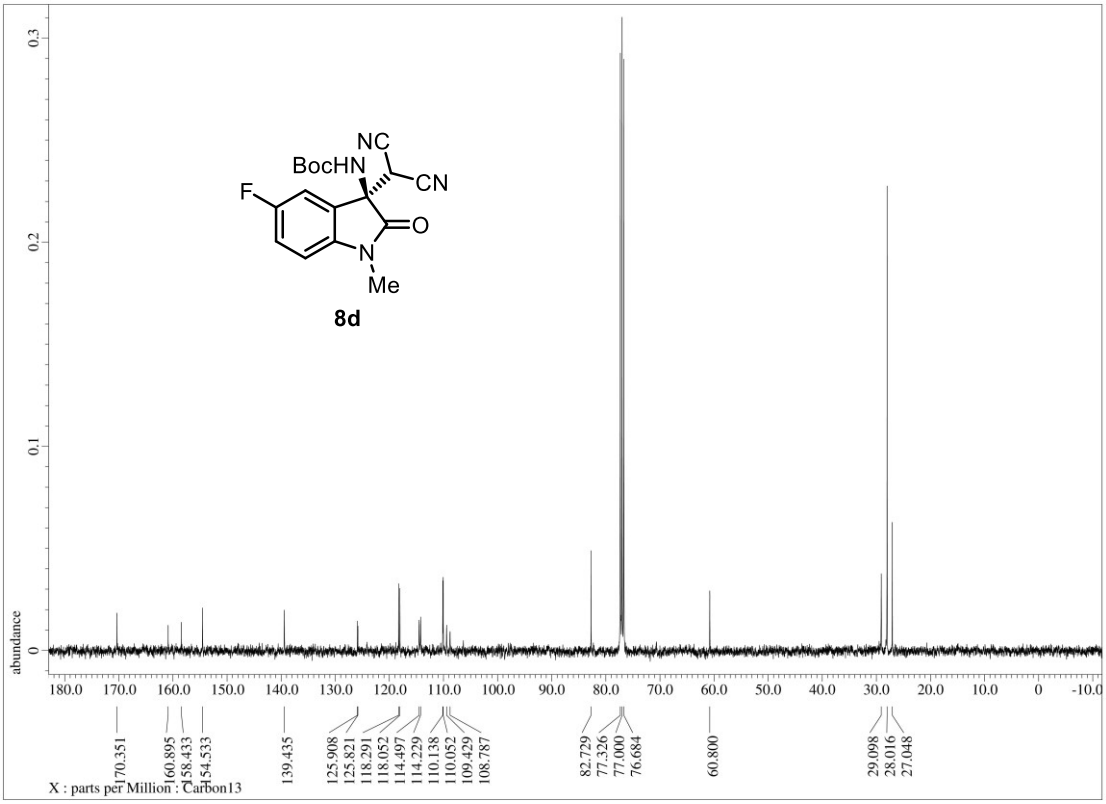

NC
BocHN
CN
Me
O
N
Me
8b
abundance
1.01
1.18
1.02
0.95
0.90
3.00
2.81
9.00
7.662
7.277
7.266
7.257
6.854
6.834
5.629
5.439
3.286
2.387
1.429
0.000
X : parts per Million : Proton

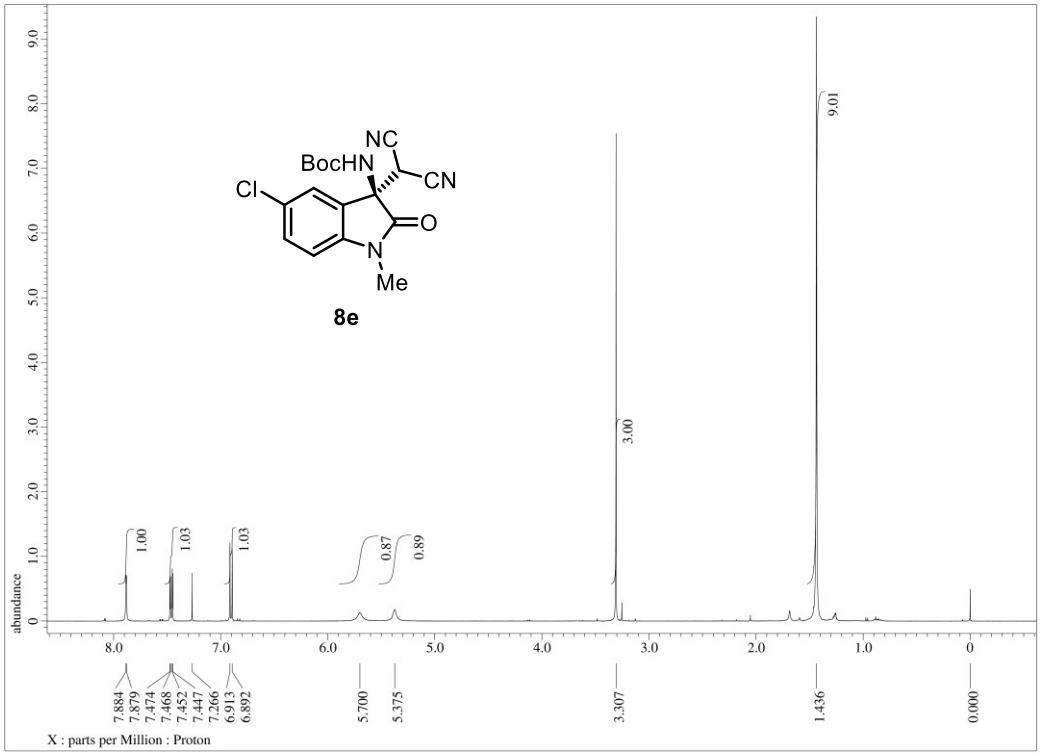

NC
BocHN
CN
Me
O
N
Me
8b
abundance
170.600
154.495
140.968
134.194
131.981
126.157
124.509
109.841
109.180
109.037
82.288
77.326
77.000
76.684
60.752
29.252
28.025
26.876
21.185
X : parts per Million : Carbon13

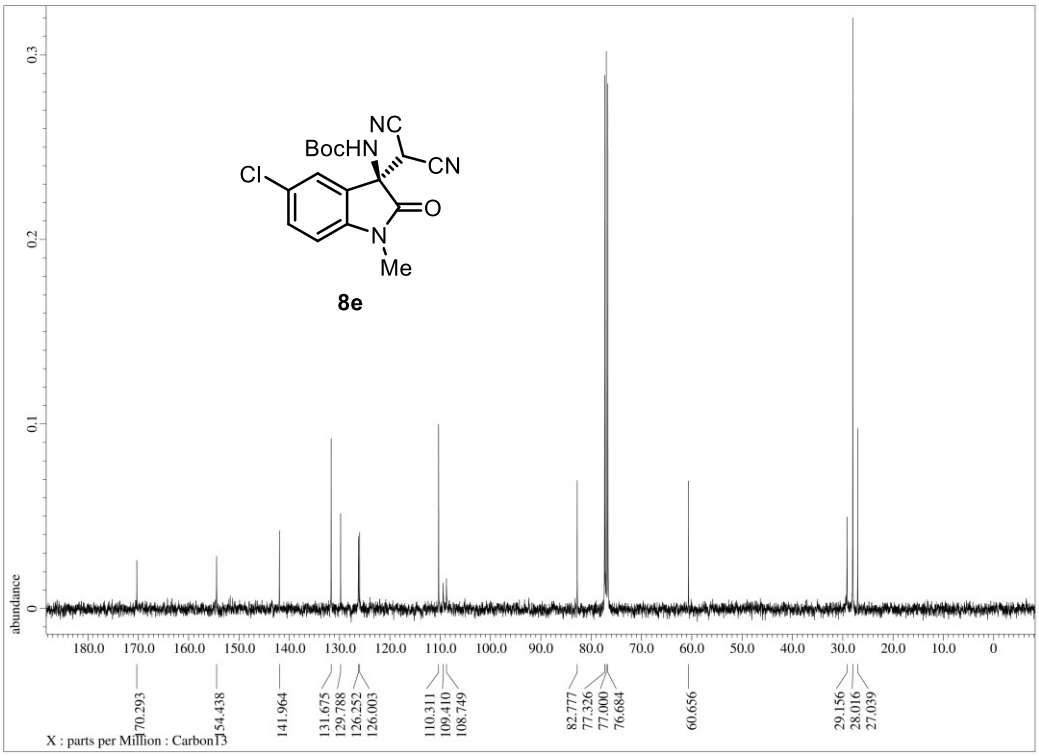

NC
BocHN
CN
MeO
O
N
Me
8c
abundance
X : parts per Million : Carbon13
170.600
154.495
140.968
134.194
131.981
126.157
124.509
109.841
109.180
109.037
82.288
77.326
77.000
76.684
60.752
29.252
28.025
26.876
21.185


NC
BocHN
CN
MeO
O
N
Me
8c
abundance
X : parts per Million : Carbon13
170.284
156.938
154.553
136.561
125.630
116.107
112.696
109.851
109.707
109.075
82.375
77.316
77.000
76.674
60.934
55.847
29.223
28.006
26.933


NC
BocHN
CN
F
O
N
Me
8d
abundance
X : parts per Million : Proton
7.705
7.699
7.686
7.680
7.265
7.217
7.211
7.195
7.189
7.173
7.167
6.927
6.916
6.904
6.894
5.649
5.395
3.310
1.439
0.000
1.00
1.01
1.01
0.94
0.95
3.04
9.02

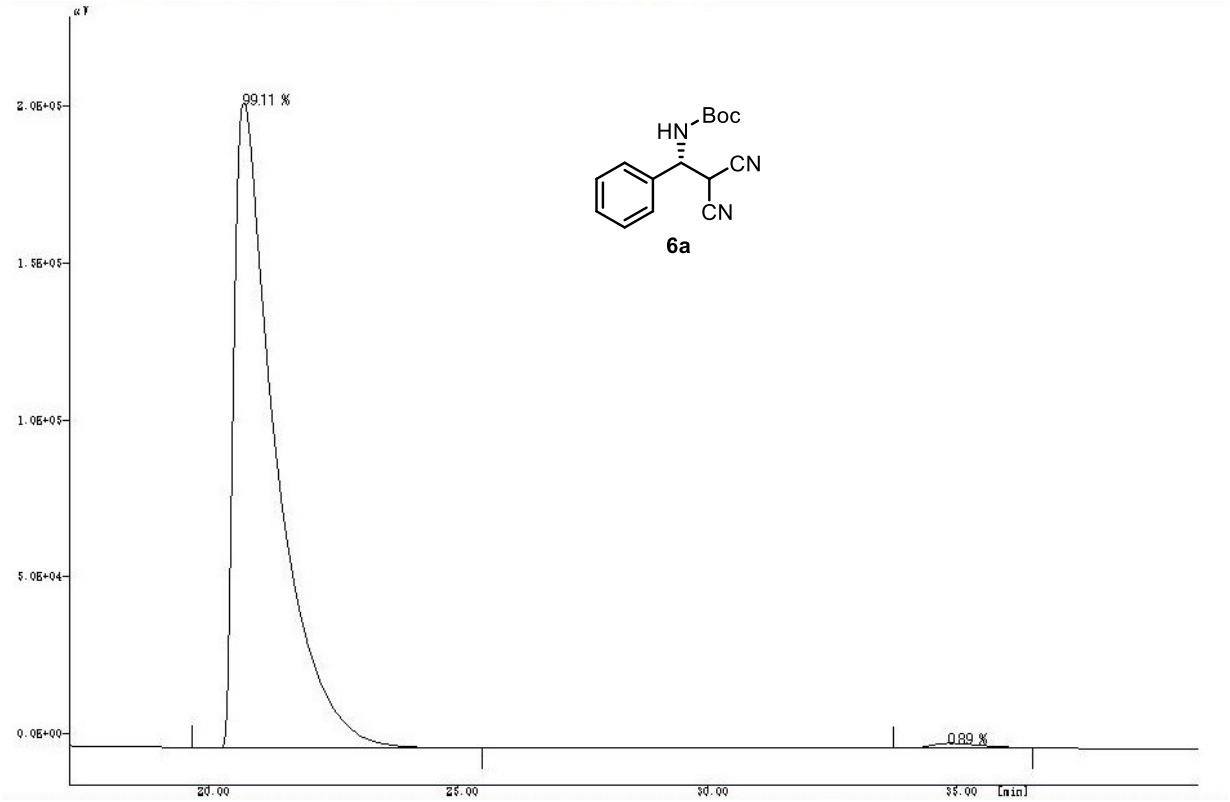

NC
BocHN
CN
F
O
N
Me
8d
abundance
X : parts per Million : Carbon13
170.351
160.895
158.433
154.533
139.435
125.908
125.821
118.291
118.052
114.497
114.229
110.138
110.052
109.429
108.787
82.729
77.326
77.000
76.684
60.800
29.098
28.016
27.048

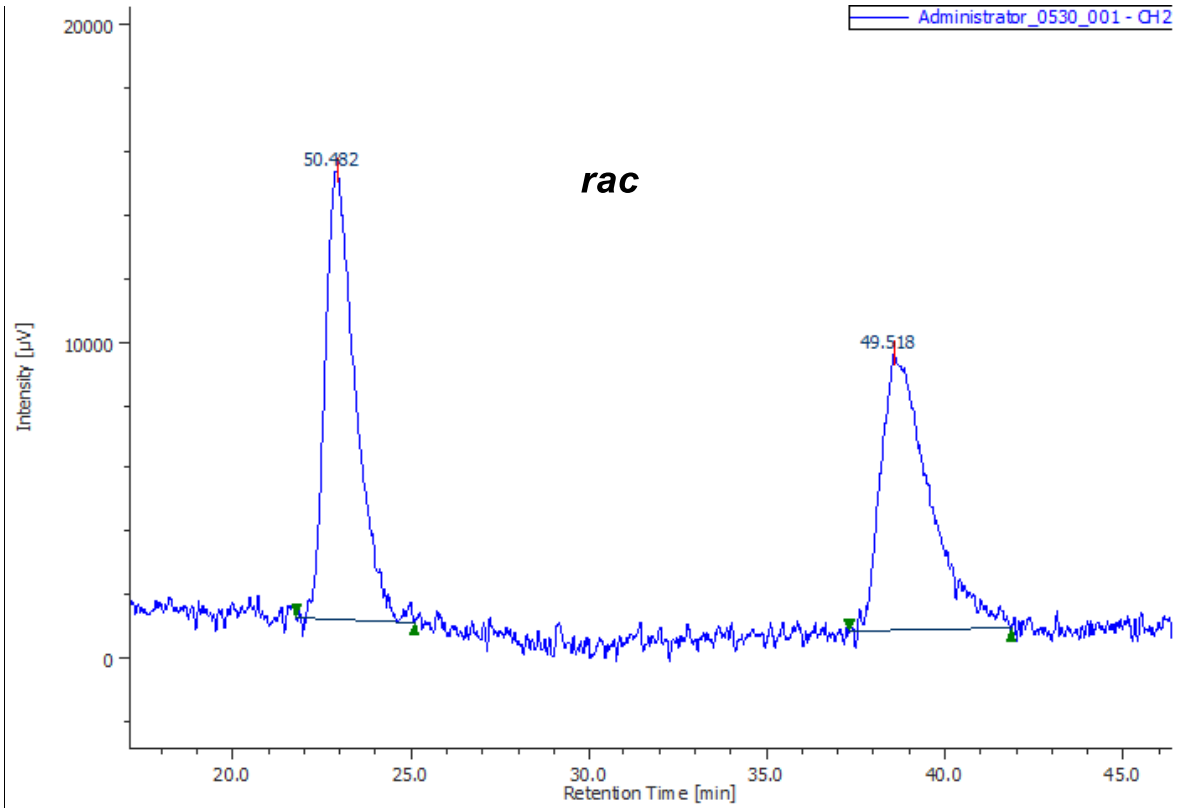

NC
BocHN
CN
Cl
O
N
Me
8e
9.01
3.00
1.00
1.03
1.03
0.87
0.89
abundance
7.884
7.879
7.474
7.468
7.452
7.447
7.266
6.913
6.892
5.700
5.375
3.307
1.436
0.000
X : parts per Million : Proton


NC
BocHN
CN
Cl
O
N
Me
8e
abundance
170.293
154.438
141.964
131.675
129.788
126.252
126.003
110.311
109.410
108.749
82.777
77.326
77.000
76.684
60.656
29.156
28.016
27.039
X : parts per Million : Carbon13

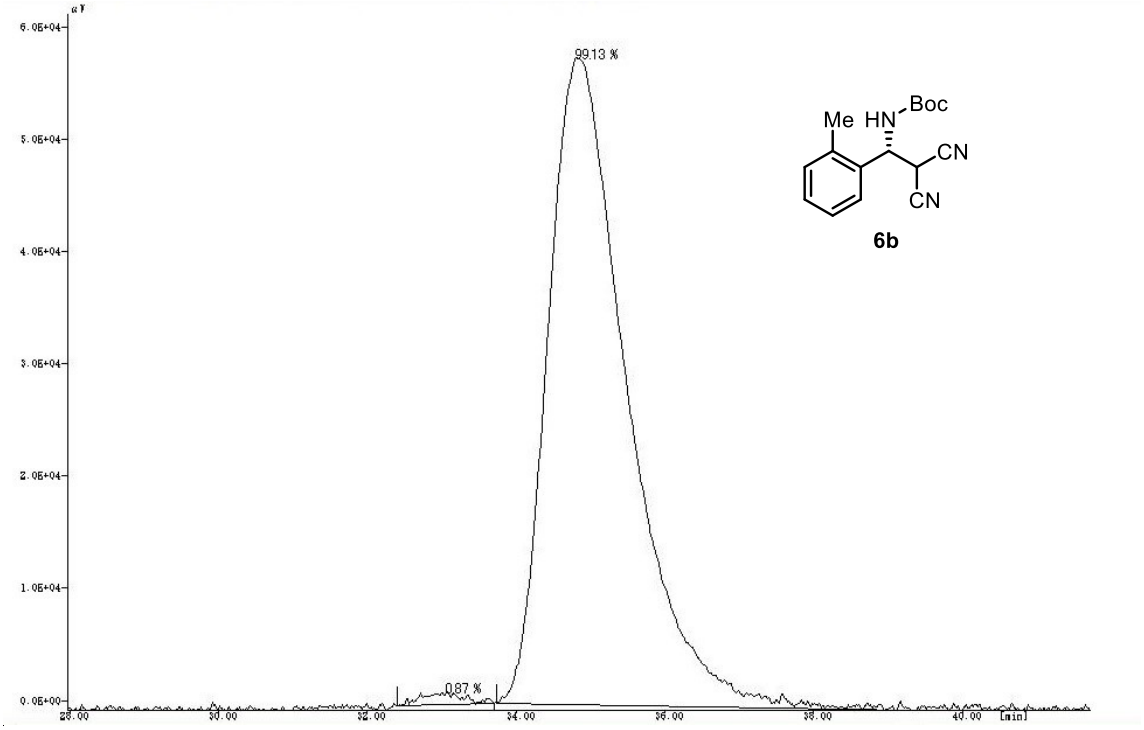
13. HPLC spectra

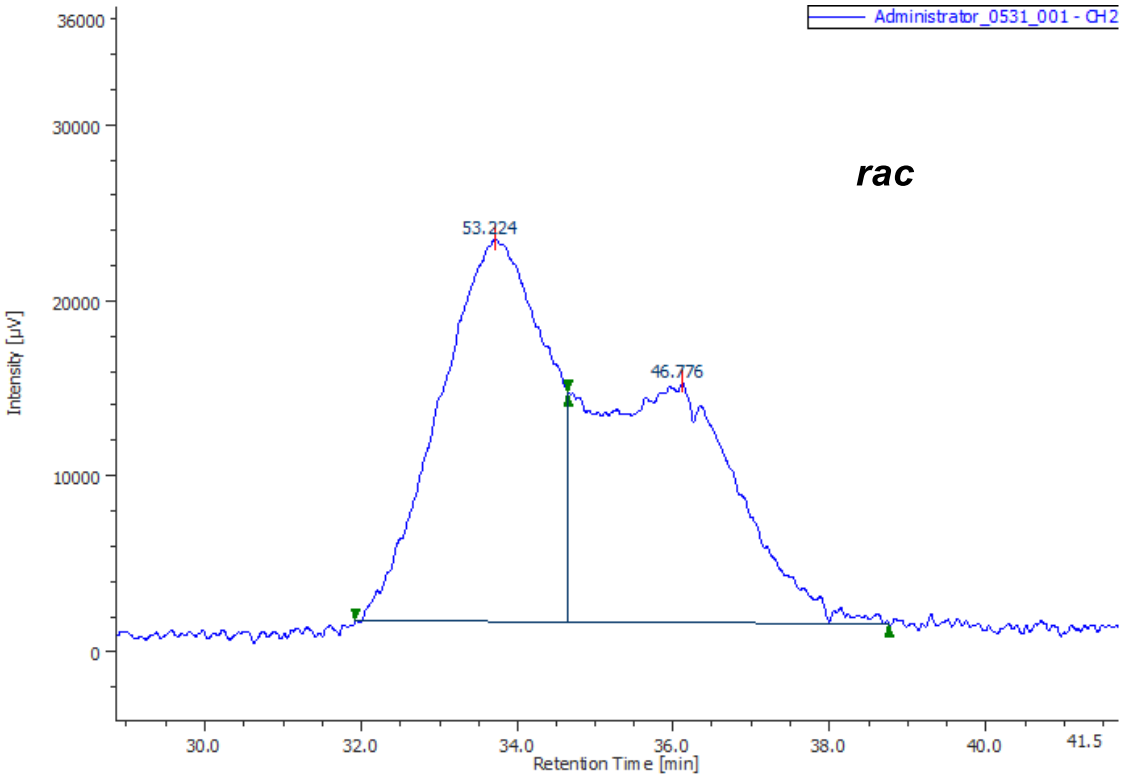
HPLC



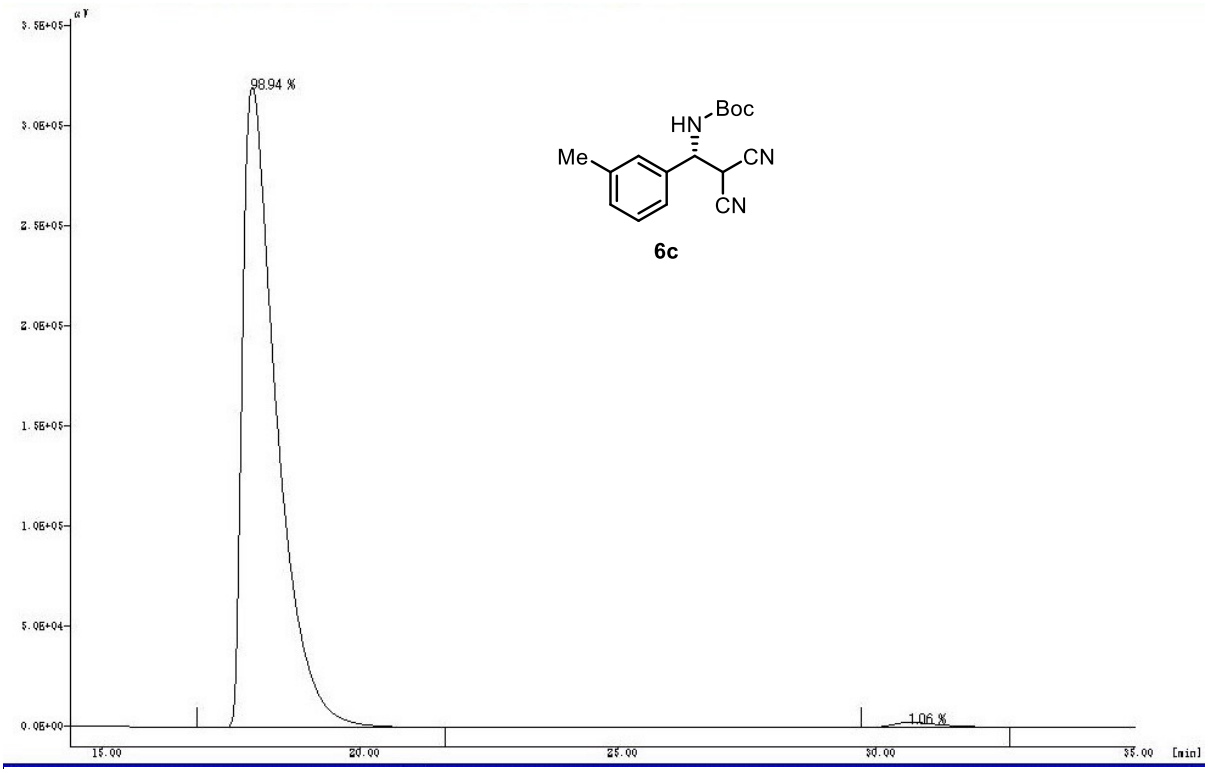


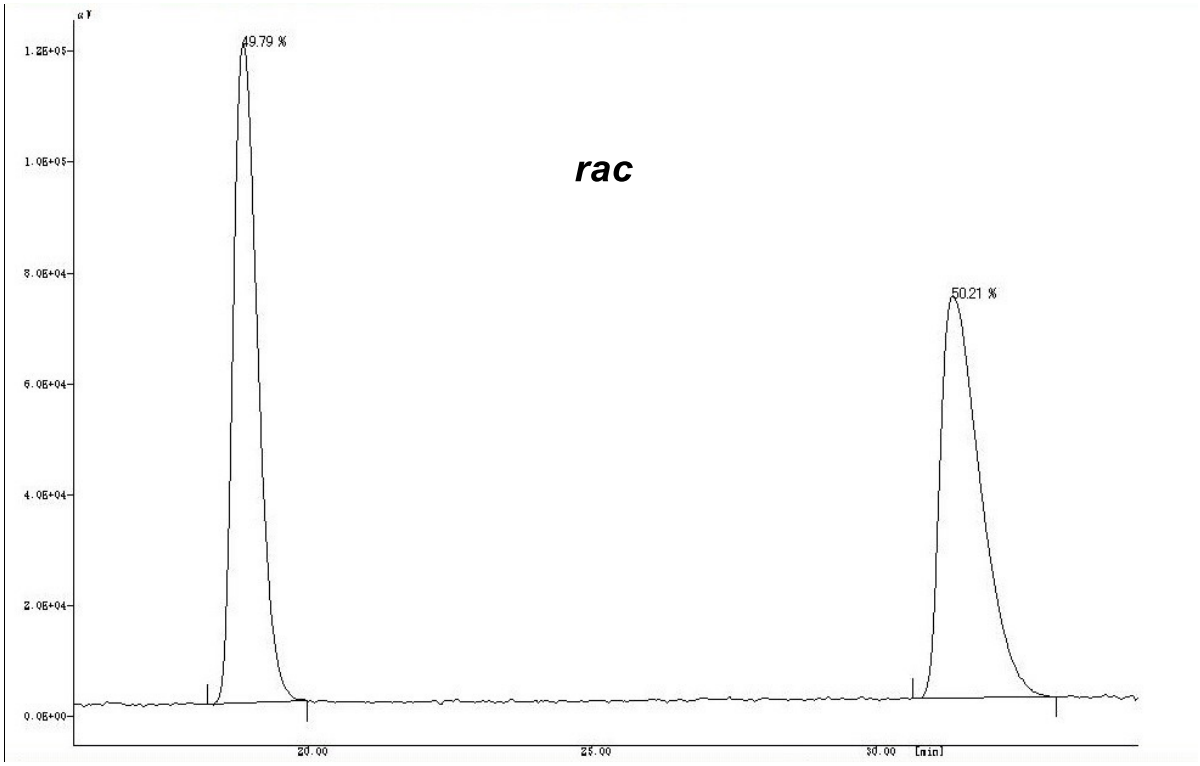
Chiralpak IA column (hexane:2-propanol = 90:10, 0.5 mL/min, 254 nm)



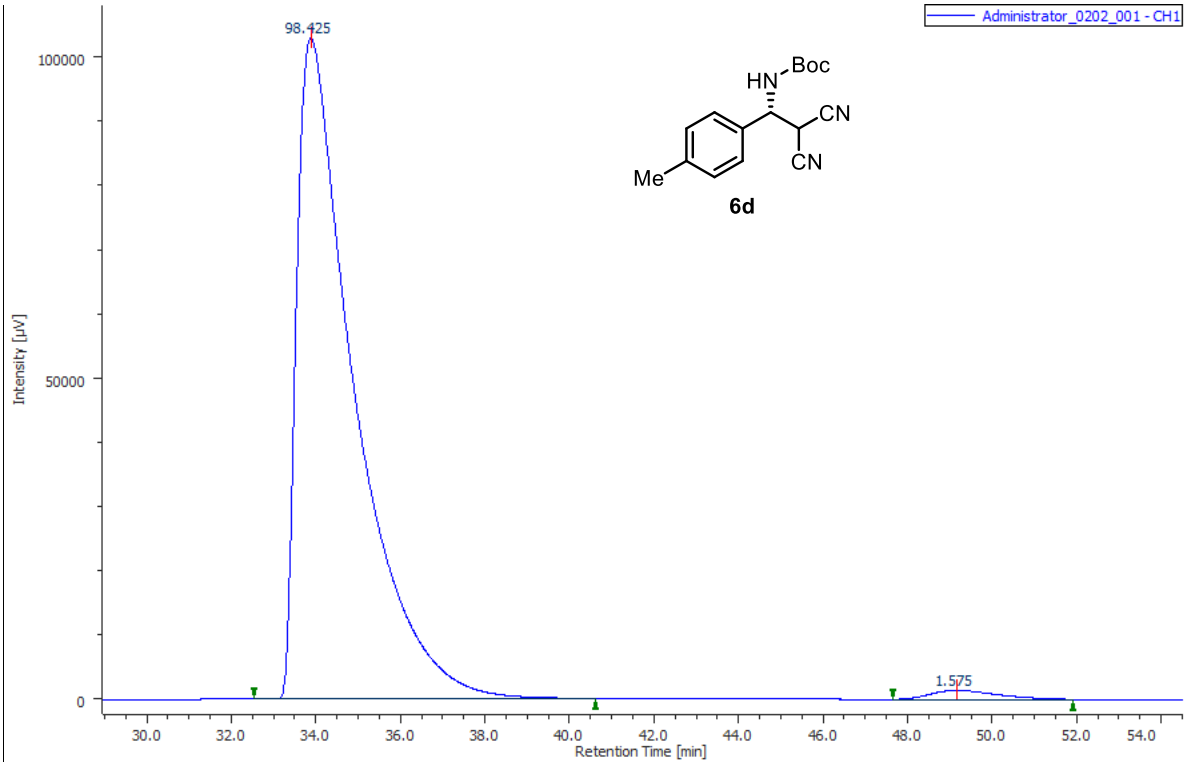


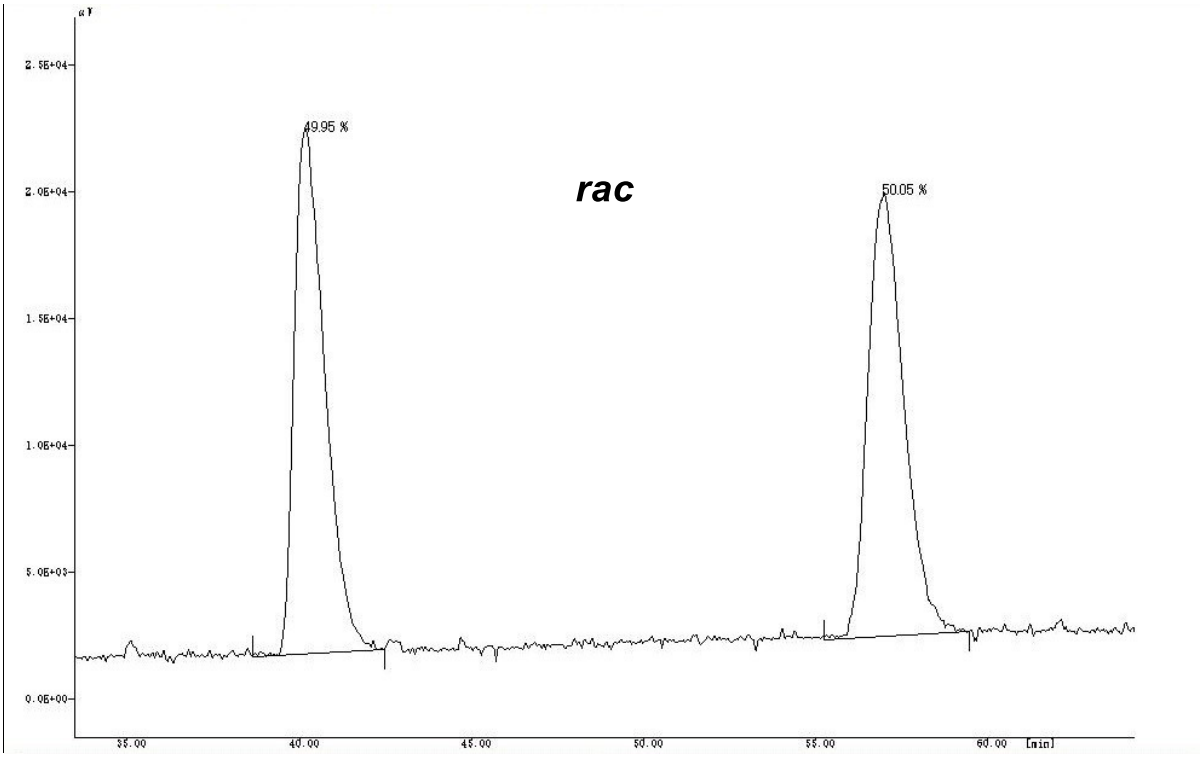
Chiralpak IA column (hexane:2-propanol = 90:10, 0.3 mL/min, 254 nm)



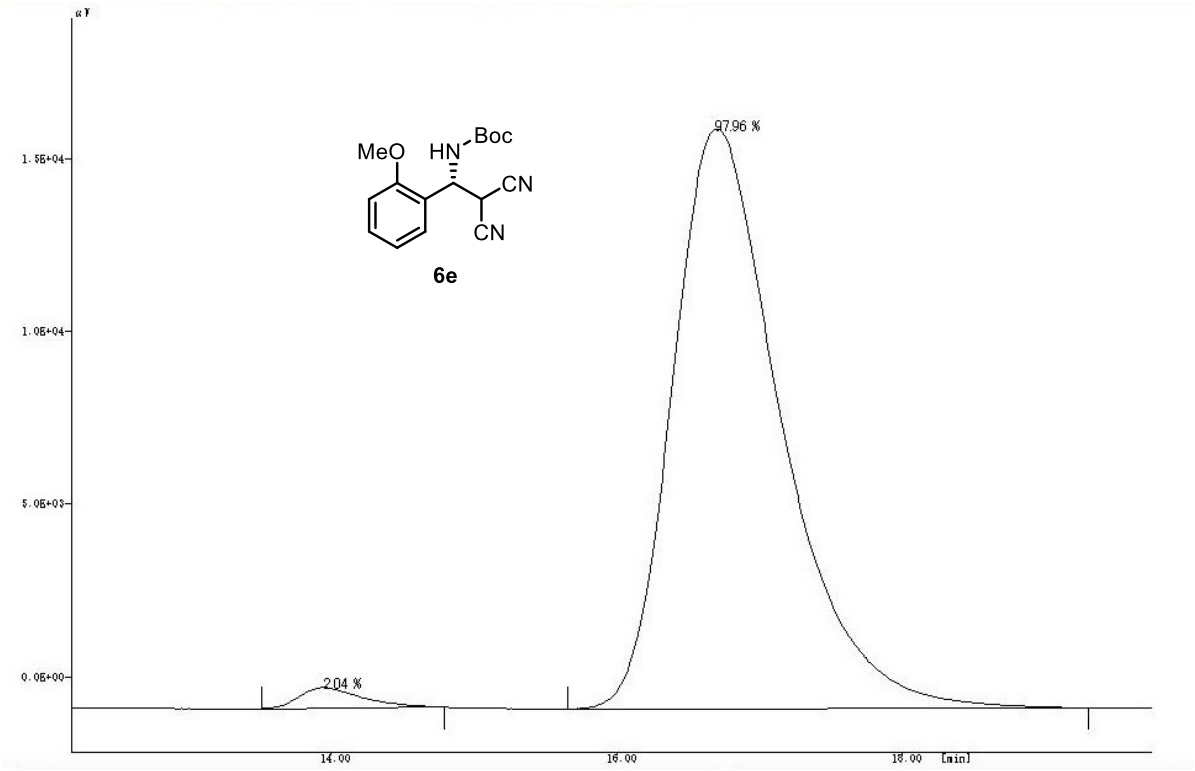


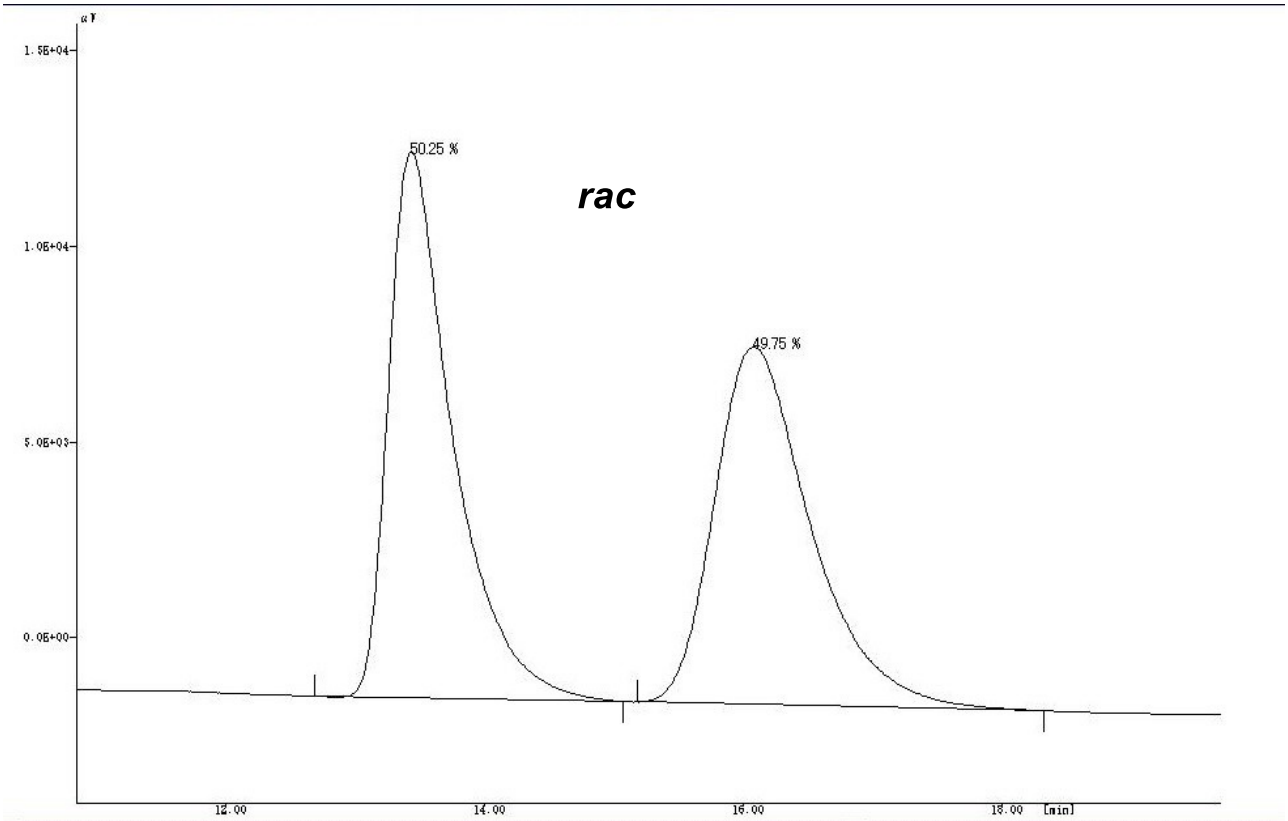
Chiralpak IA column (hexane:2-propanol = 90:10, 0.5 mL/min, 254 nm)



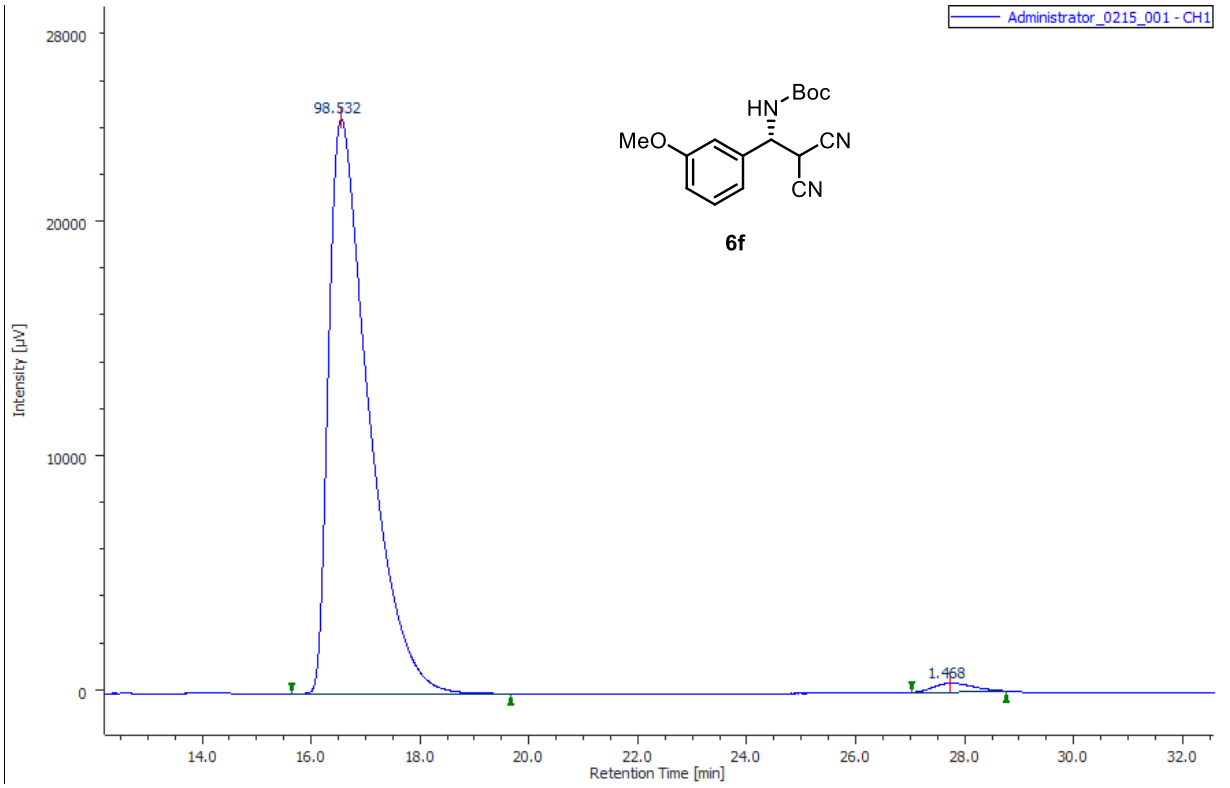


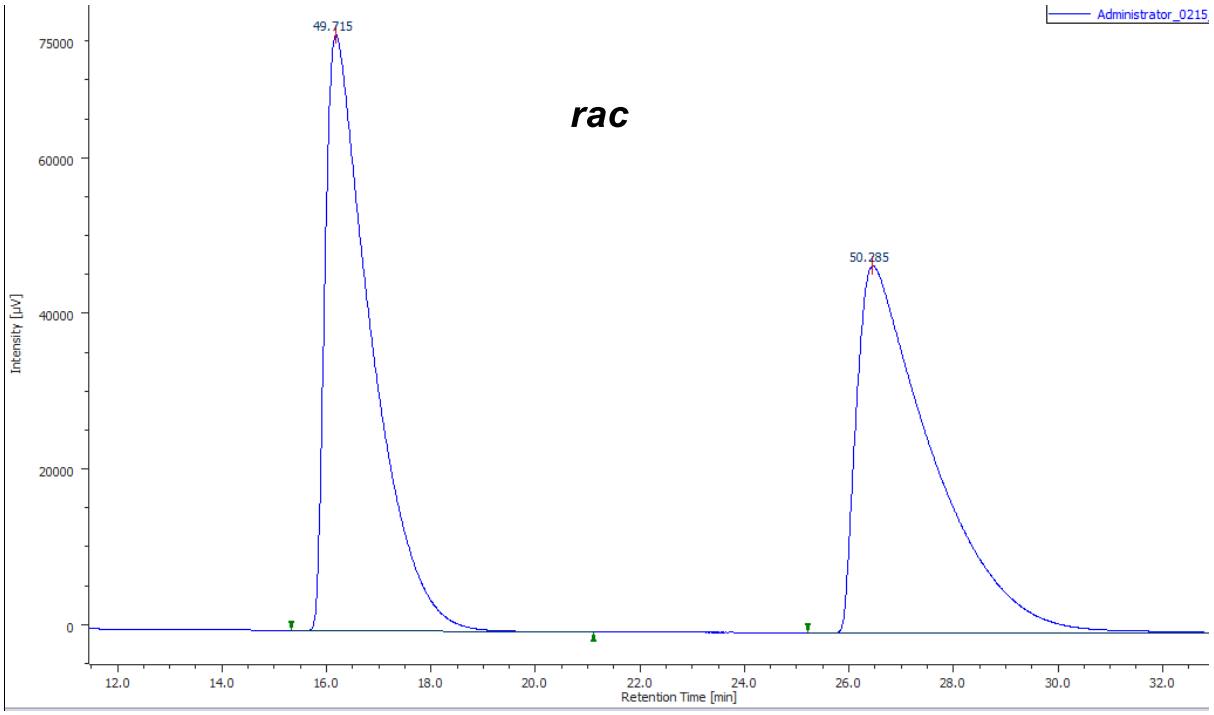
Chiralpak IA column (hexane:2-propanol = 90:10, 0.3 mL/min, 254 nm)



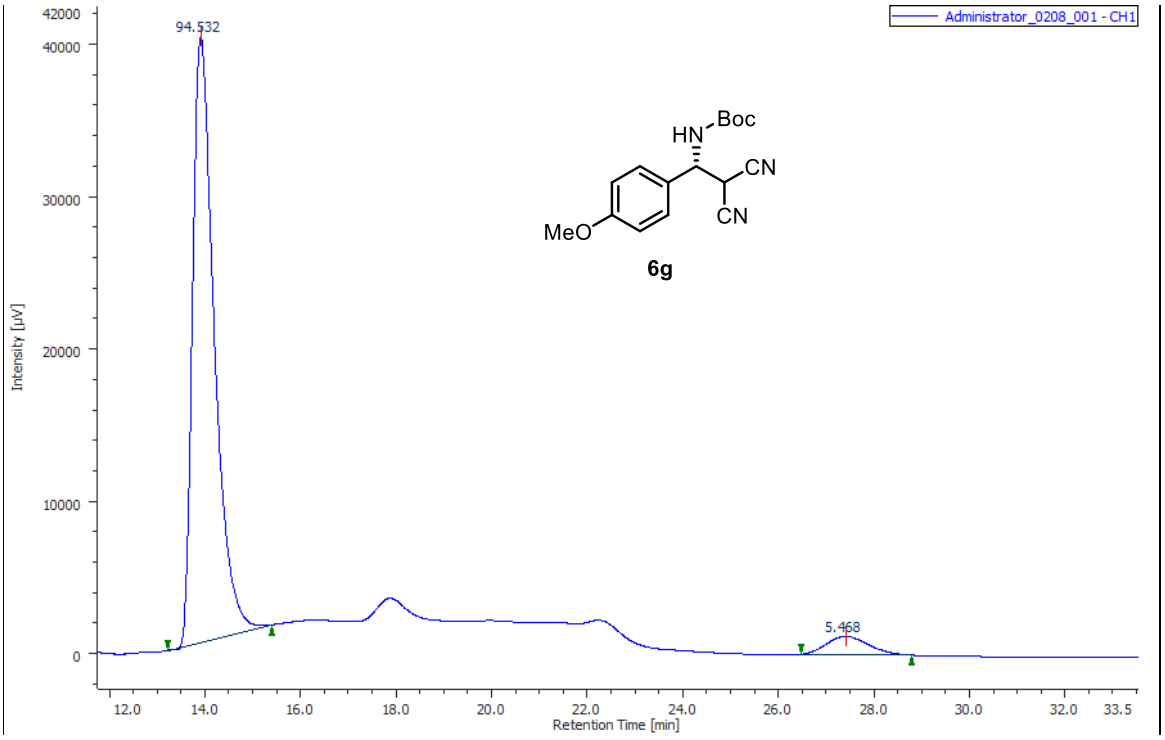


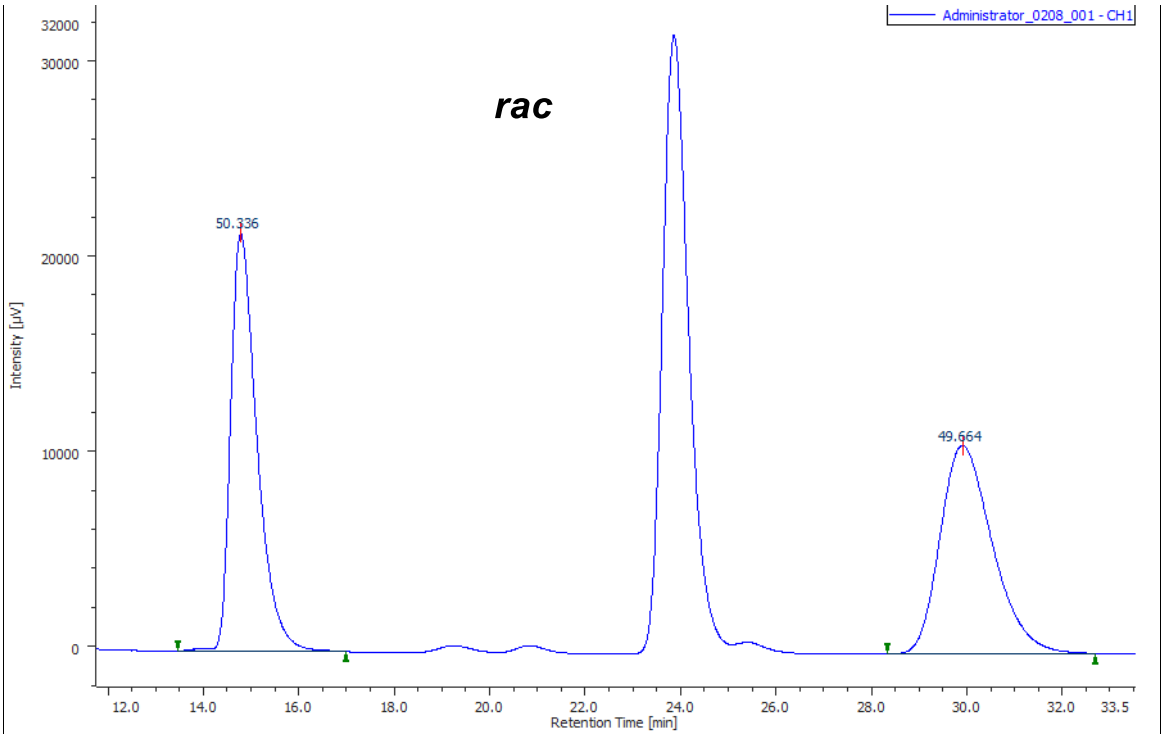
Chiralcel AD-H column (hexane:2-propanol = 70:30, 0.5 mL/min, 254 nm)



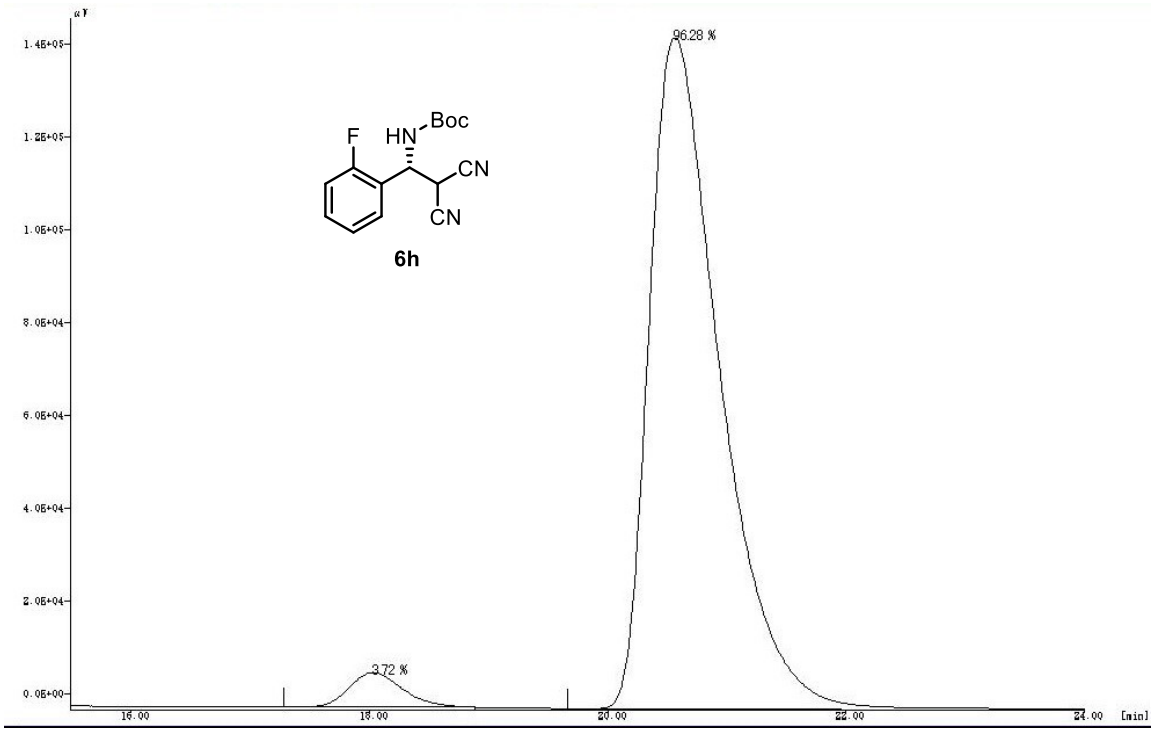


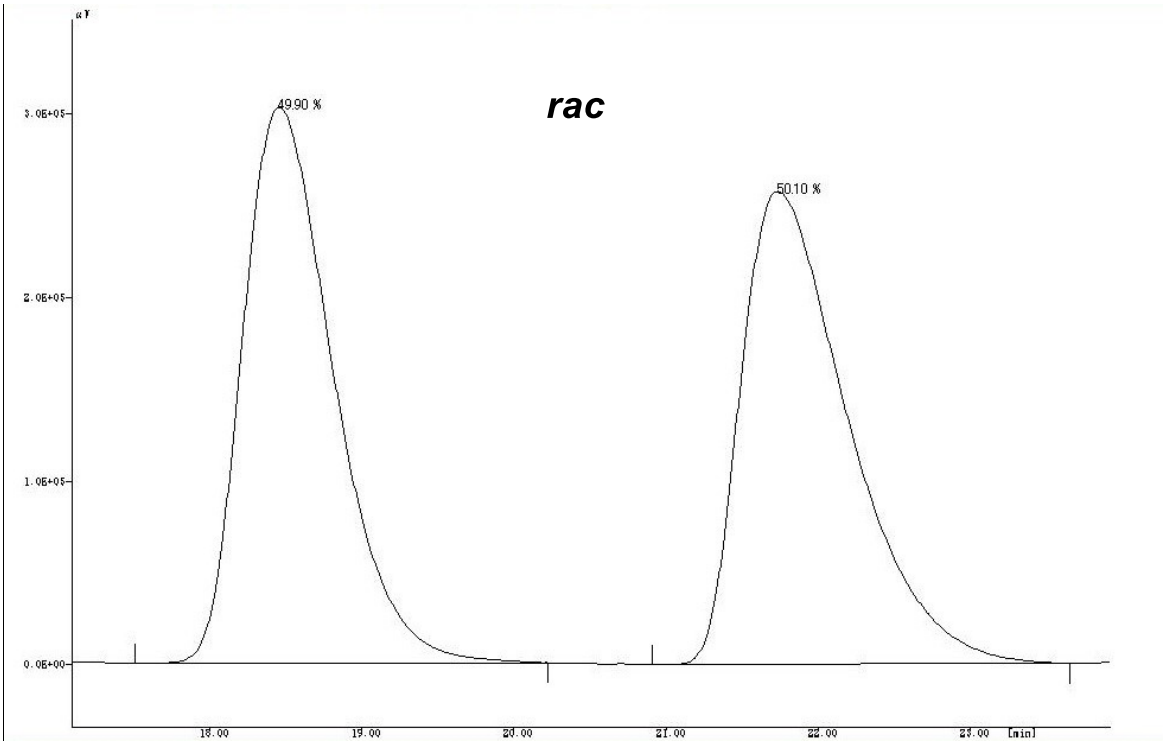
Chiralcel AD-H column (hexane:2-propanol = 85:15, 1.0 mL/min, 230 nm)



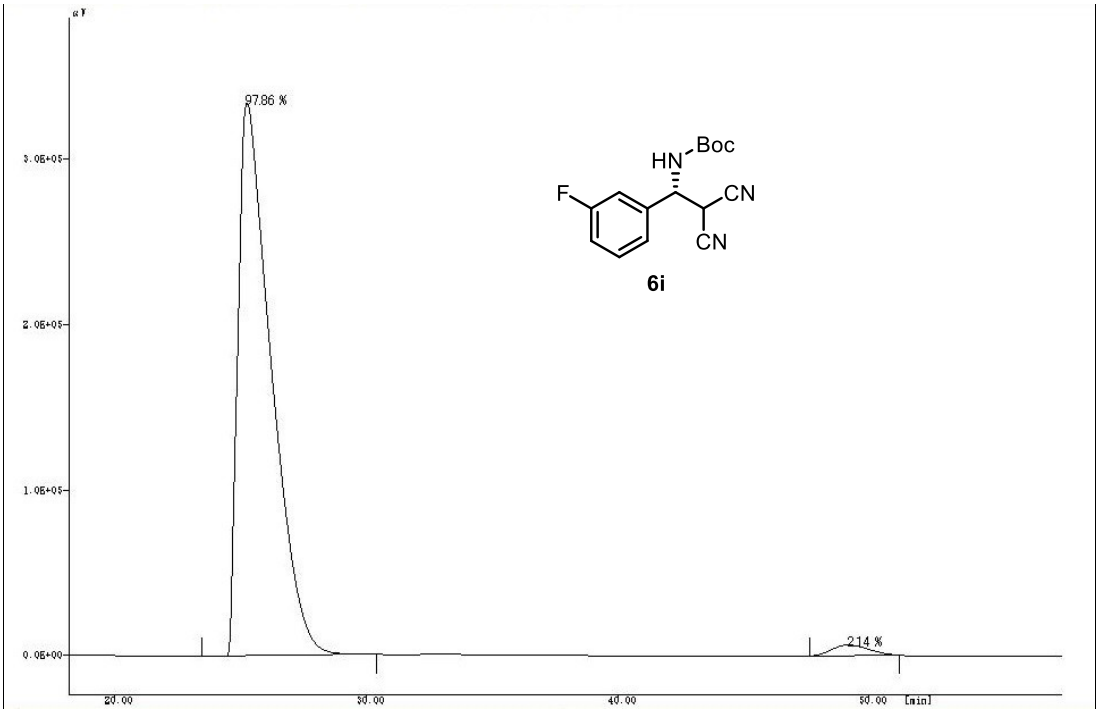


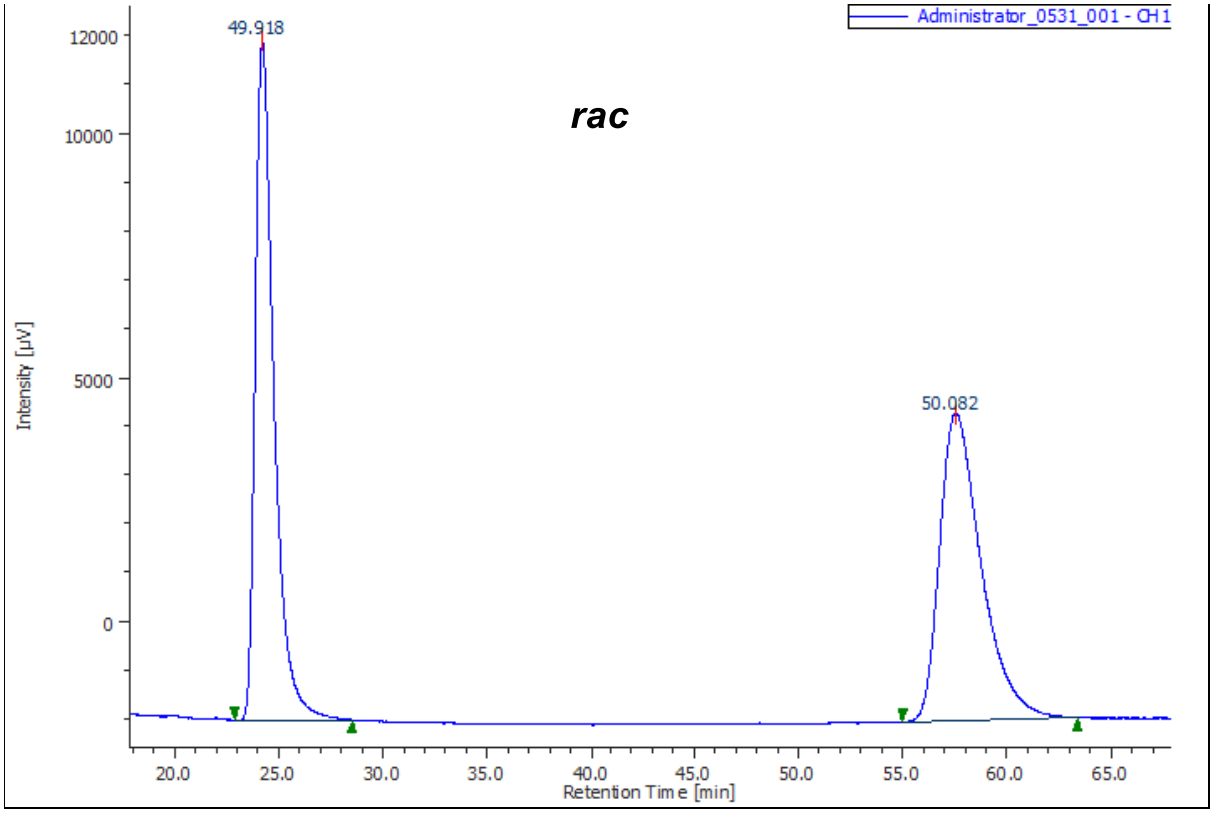
Chiralcel AD-H column (hexane:2-propanol = 85:15, 1.0 mL/min, 230 nm)



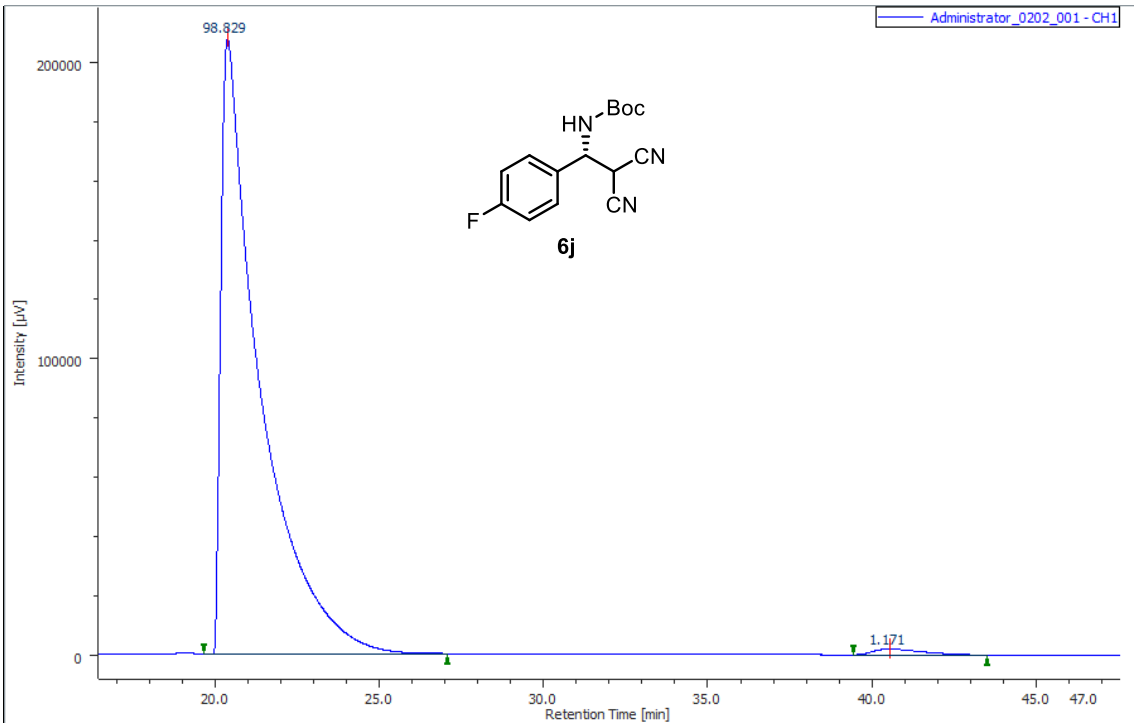


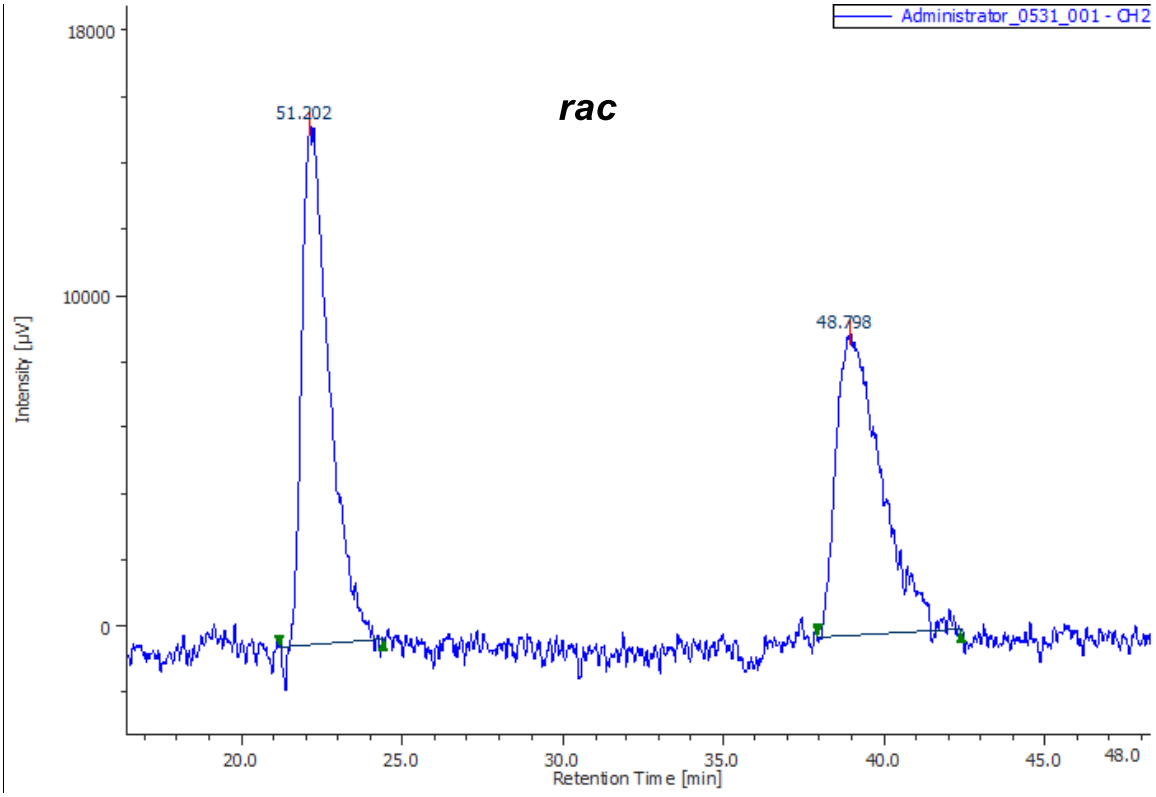
Chiralcel AD-H column (hexane:2-propanol = 85:15, 1.0 mL/min, 230 nm)



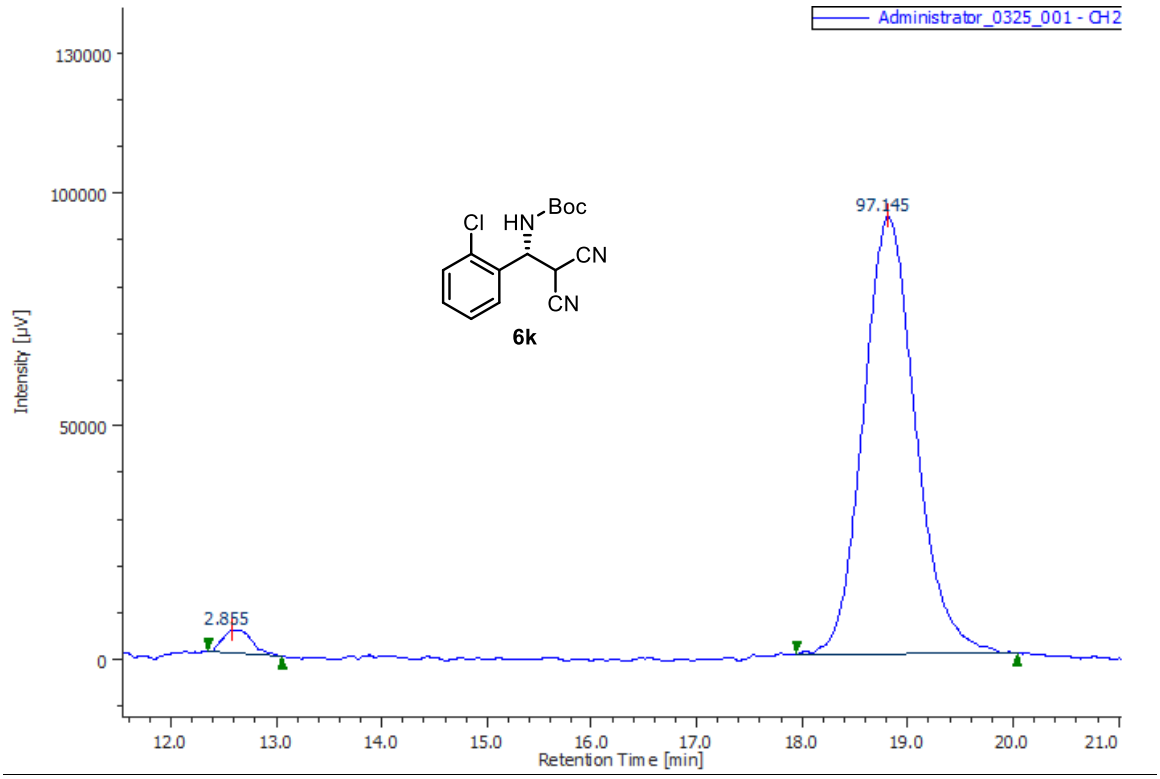


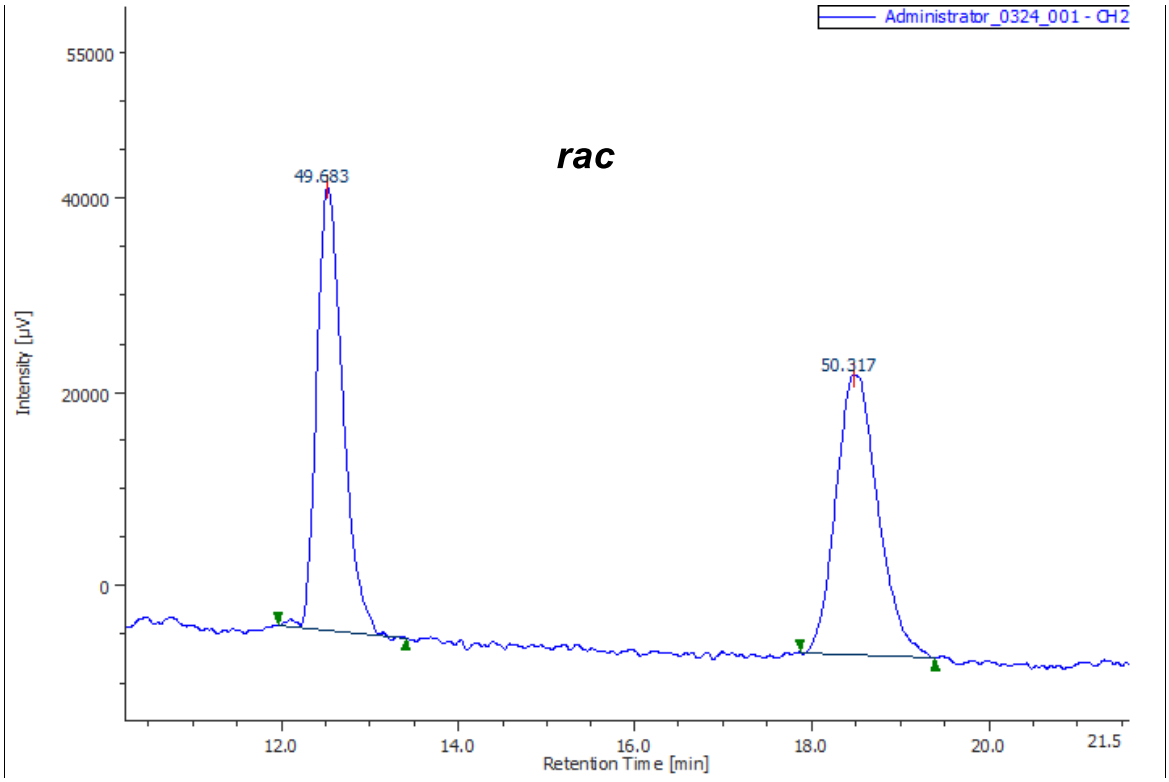
Chiralcel AD-H column (hexane:2-propanol = 85:15, 1.0 mL/min, 230 nm)



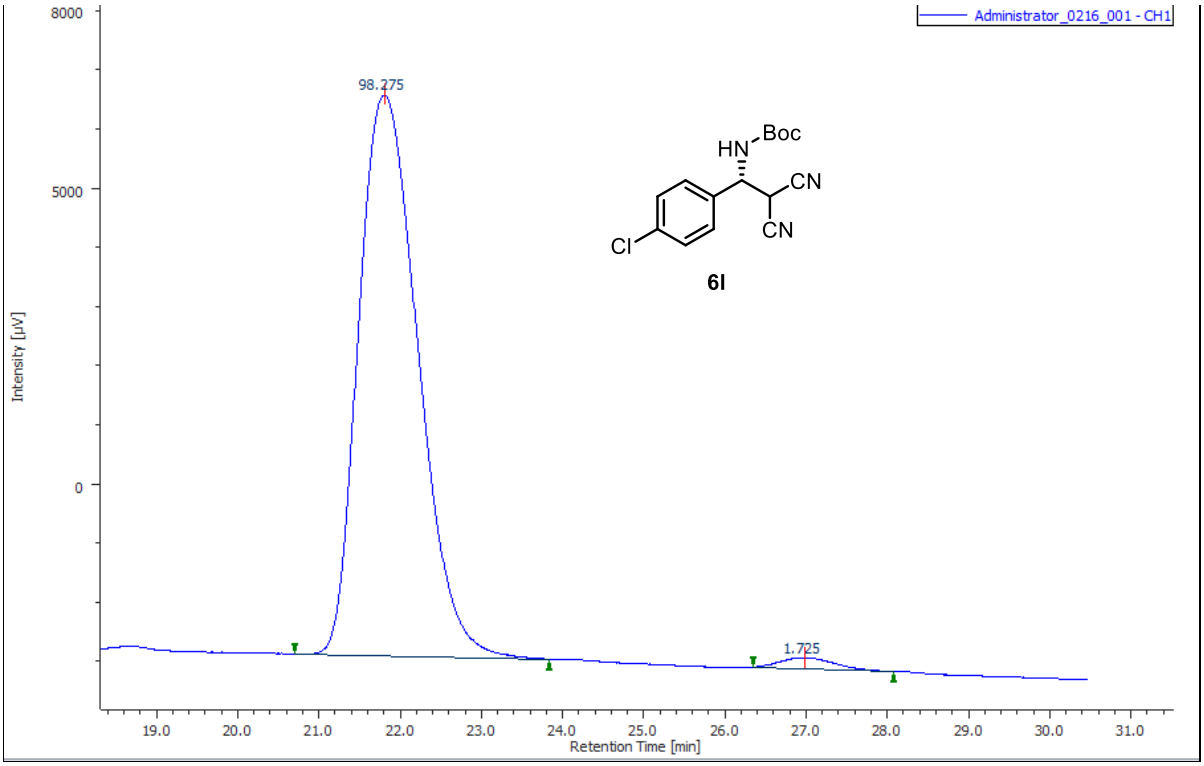


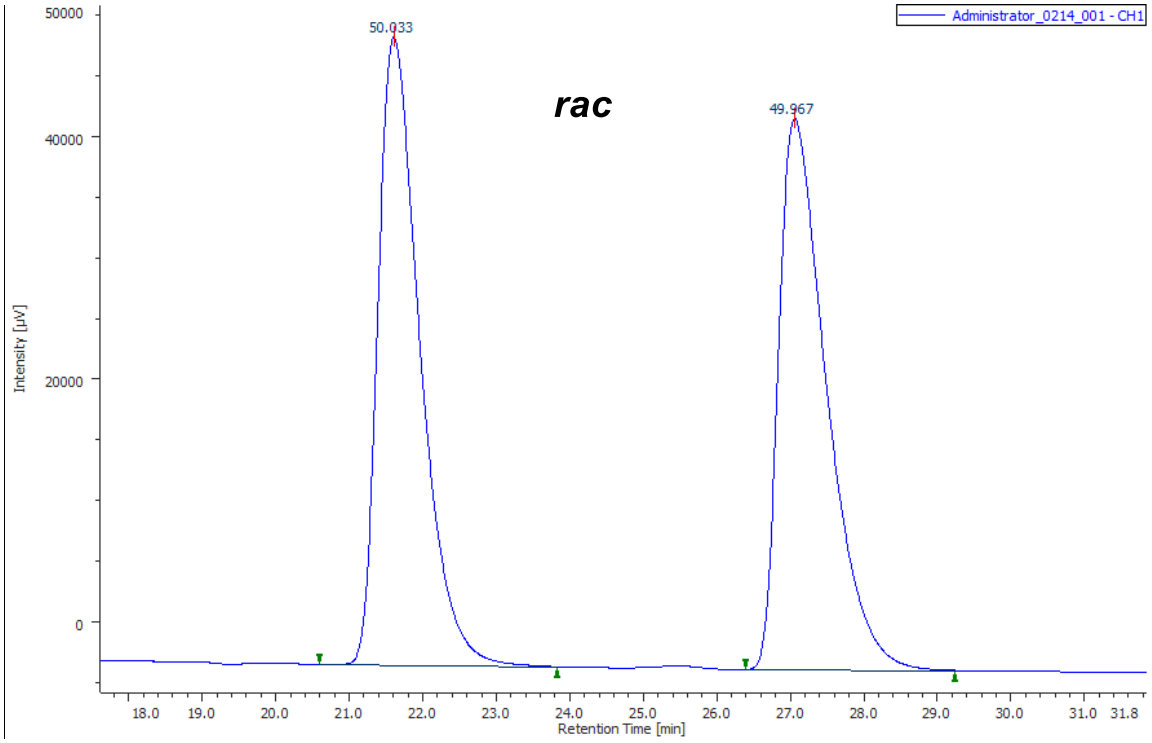
Chiralcel AD-H column (hexane:2-propanol = 85:15, 1.0 mL/min, 230 nm)



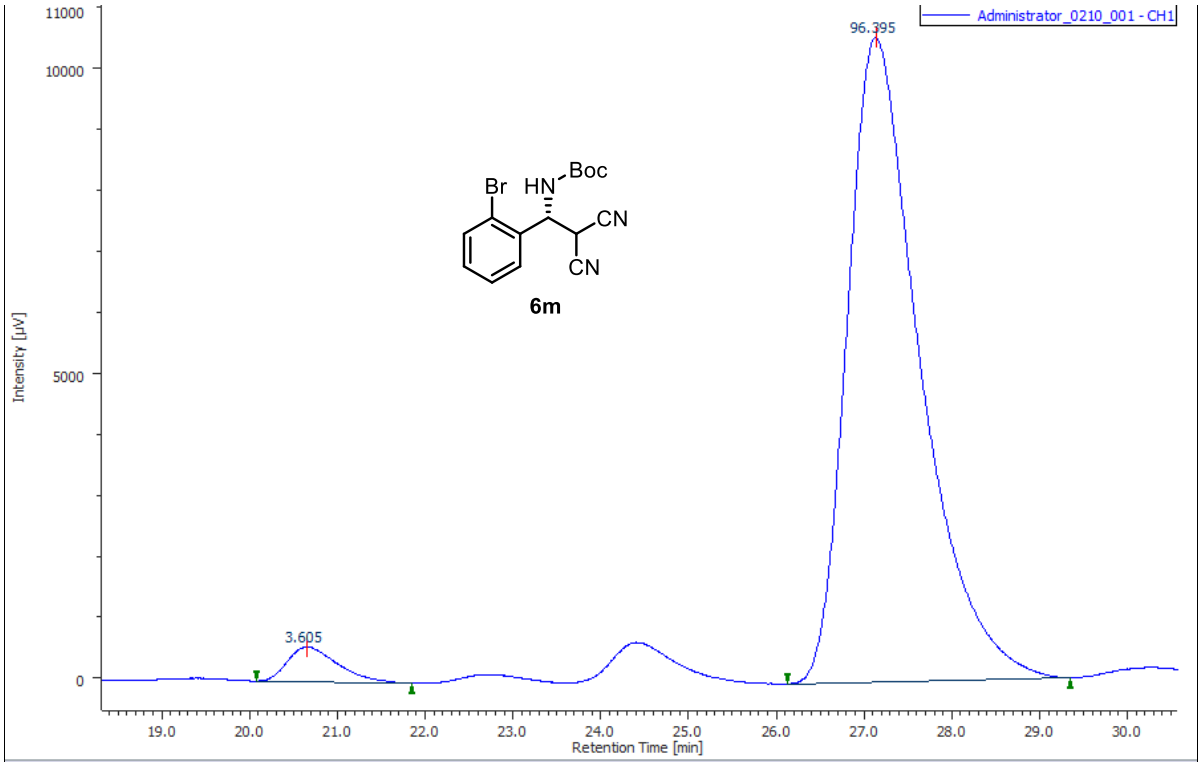


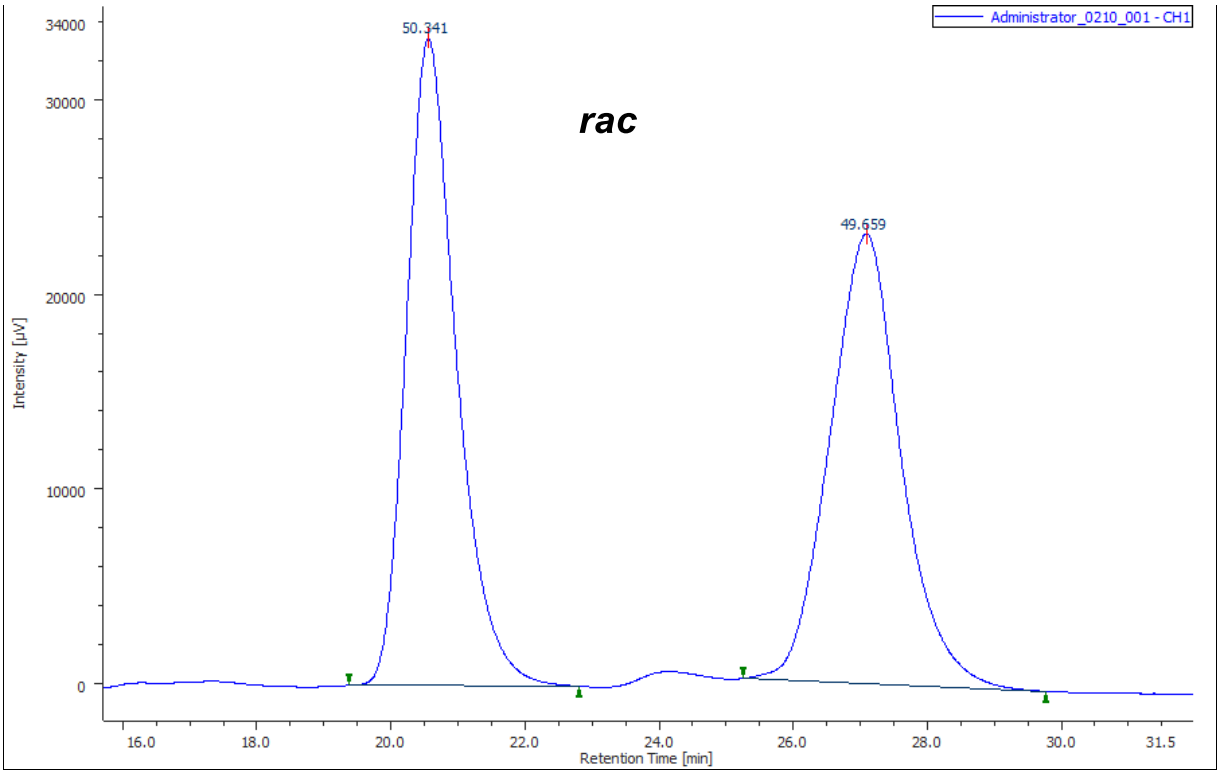
Chiralcel AD-H column (hexane:2-propanol = 85:15, 1.0 mL/min, 230 nm)



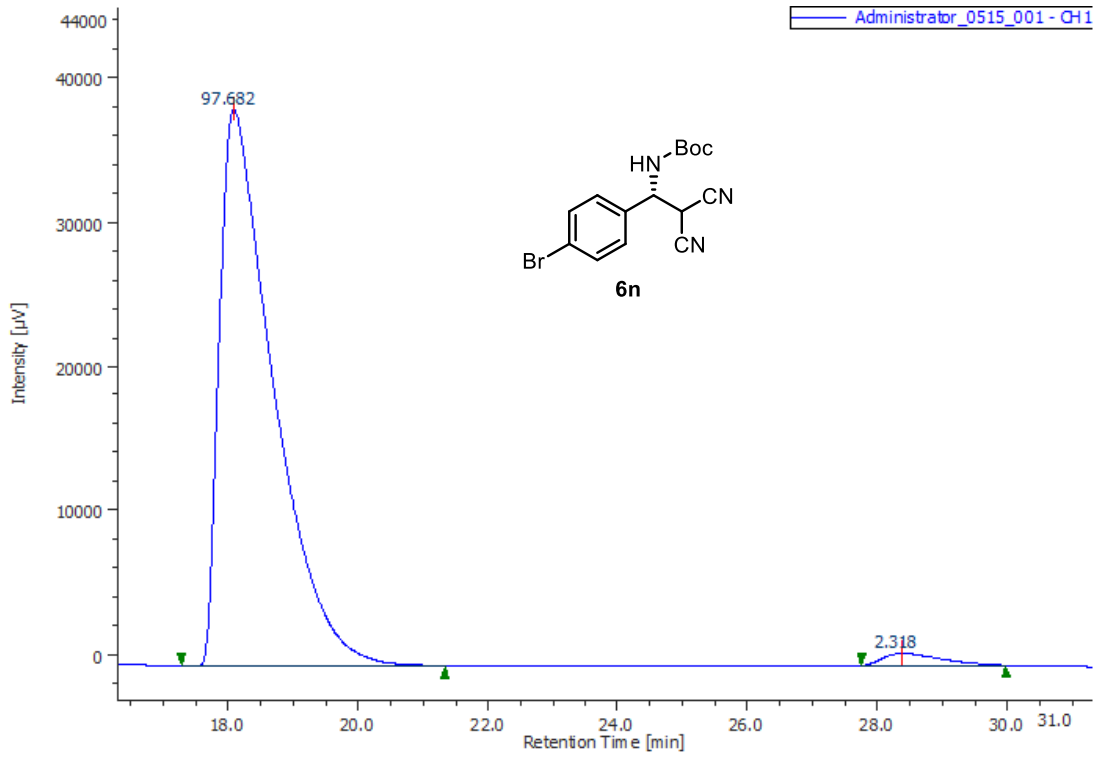


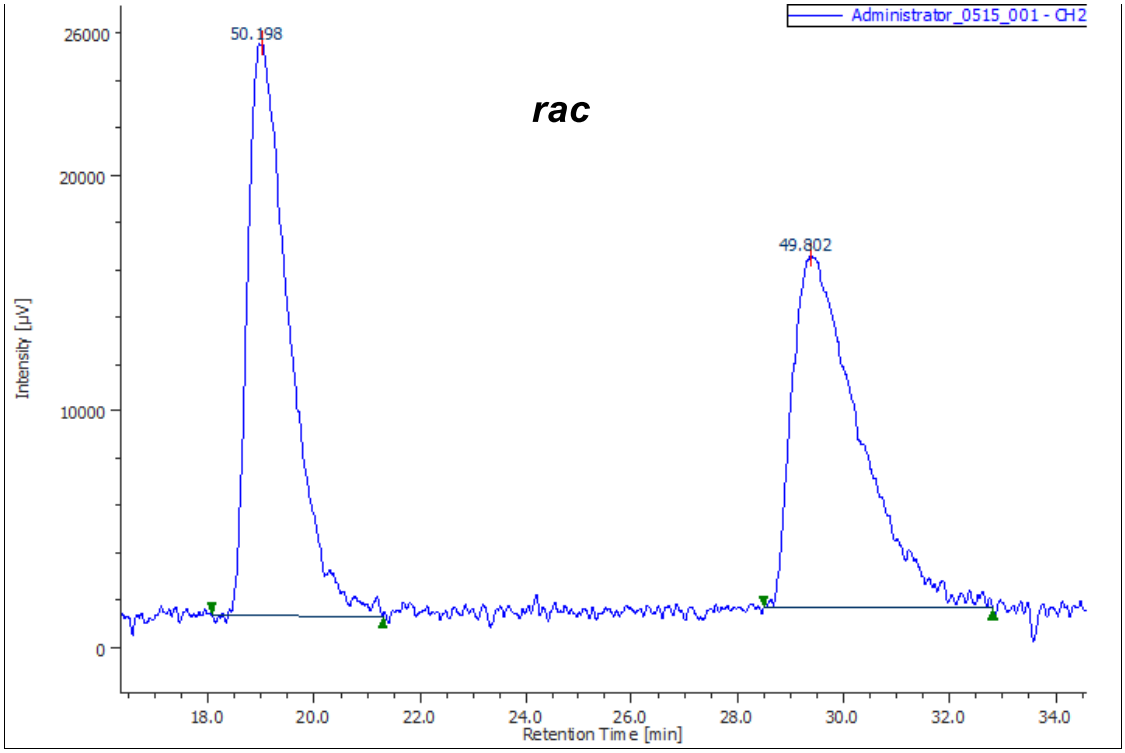
Chiralcel AD-H column (hexane:2-propanol = 85:15, 1.0 mL/min, 230 nm)



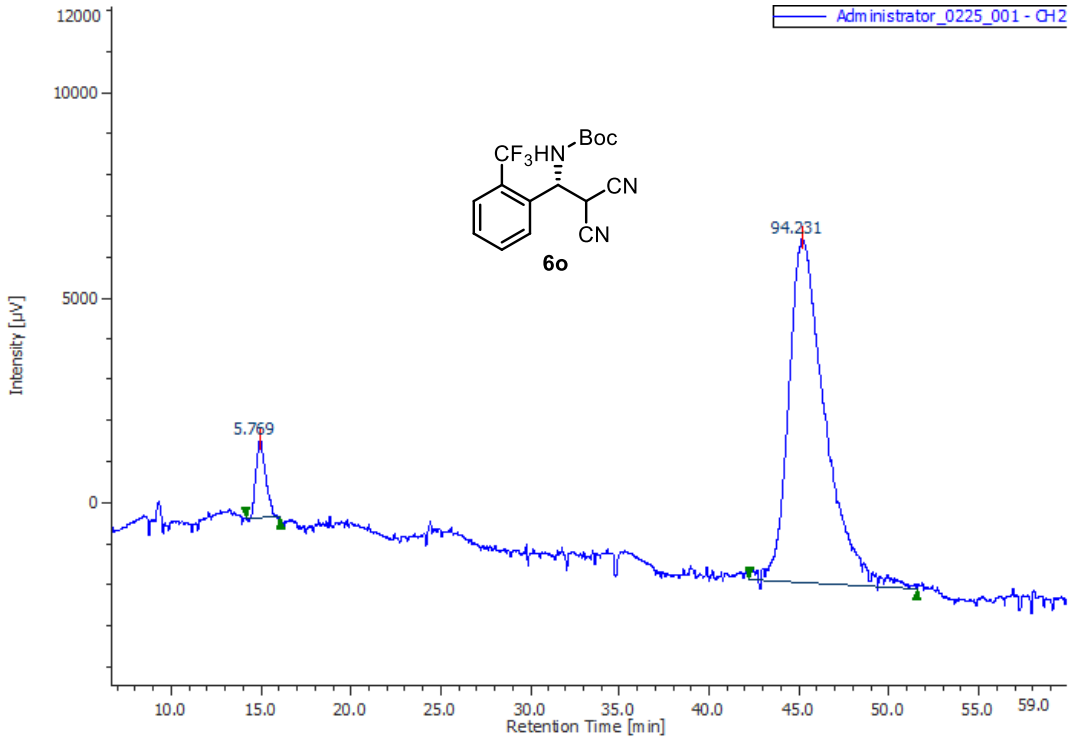


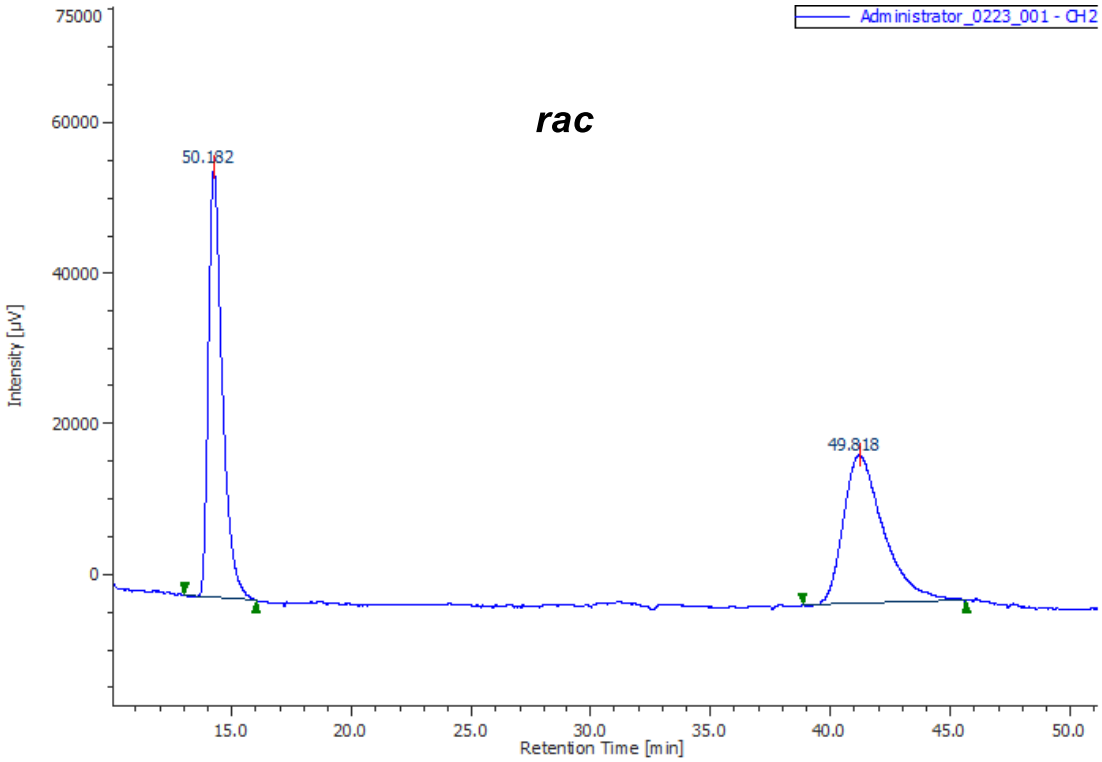
Chiralcel AD-H column (hexane:2-propanol = 85:15, 1.0 mL/min, 230 nm)



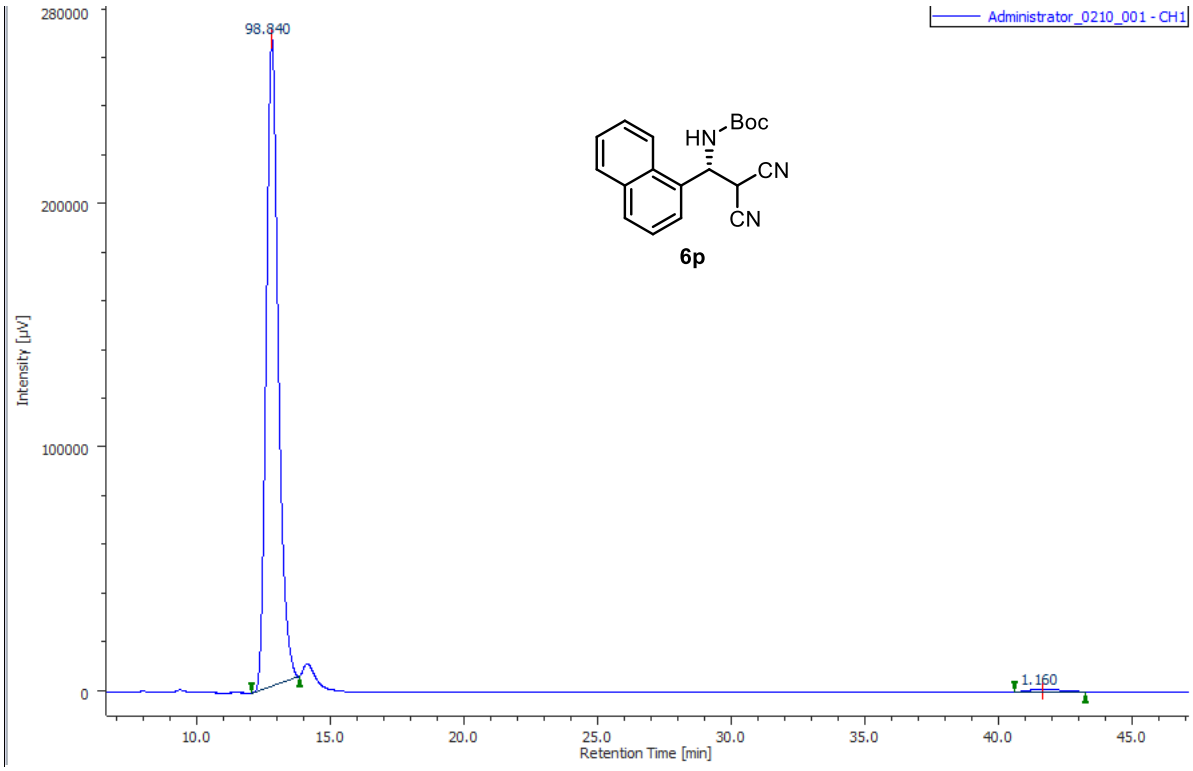


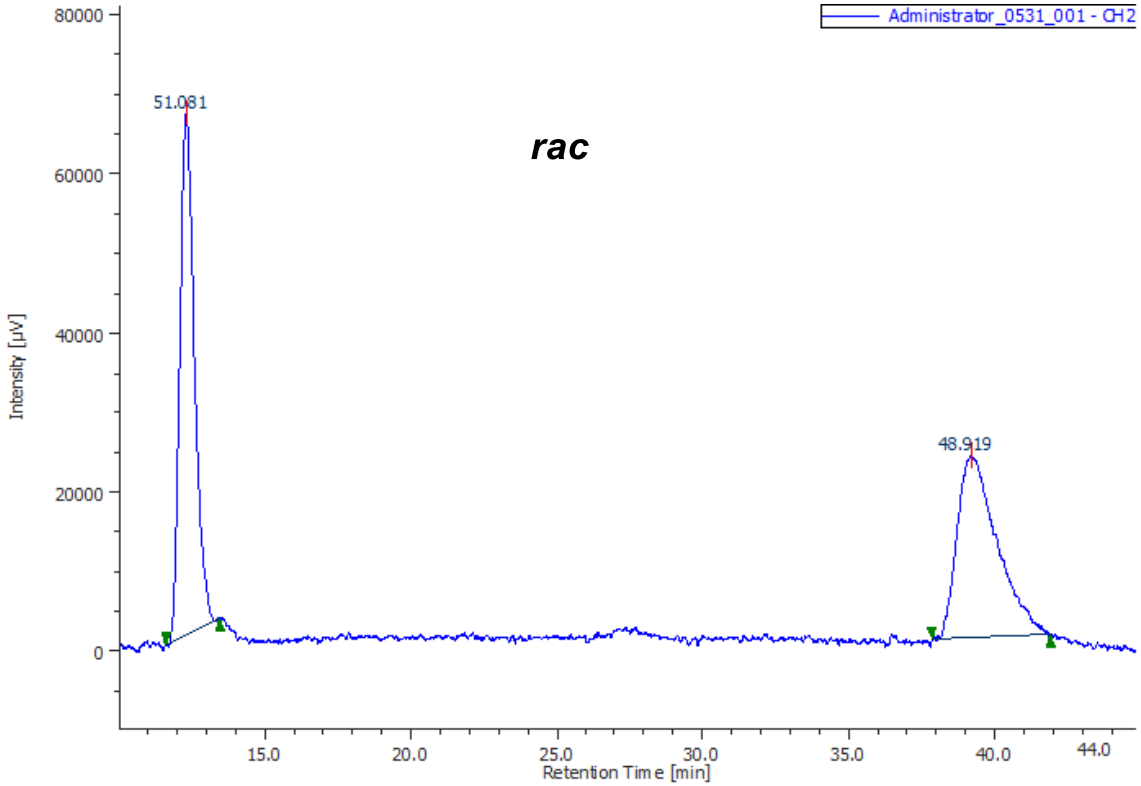
Chiralcel AD-H column (hexane:2-propanol = 85:15, 1.0 mL/min, 230 nm)



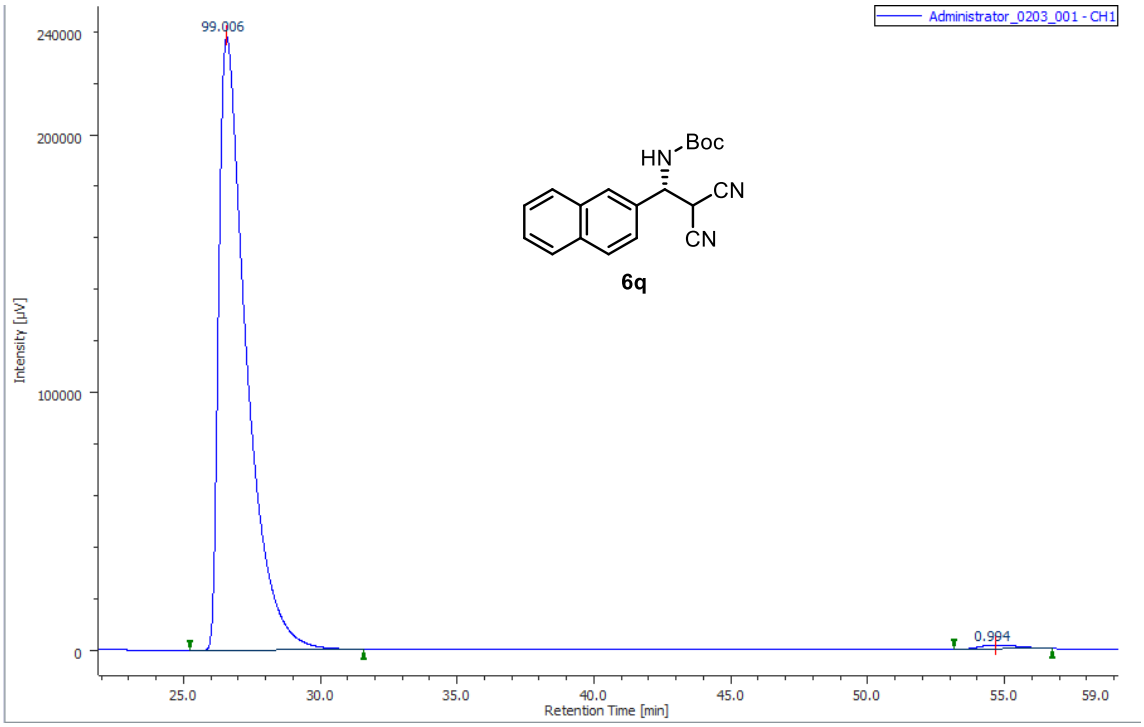


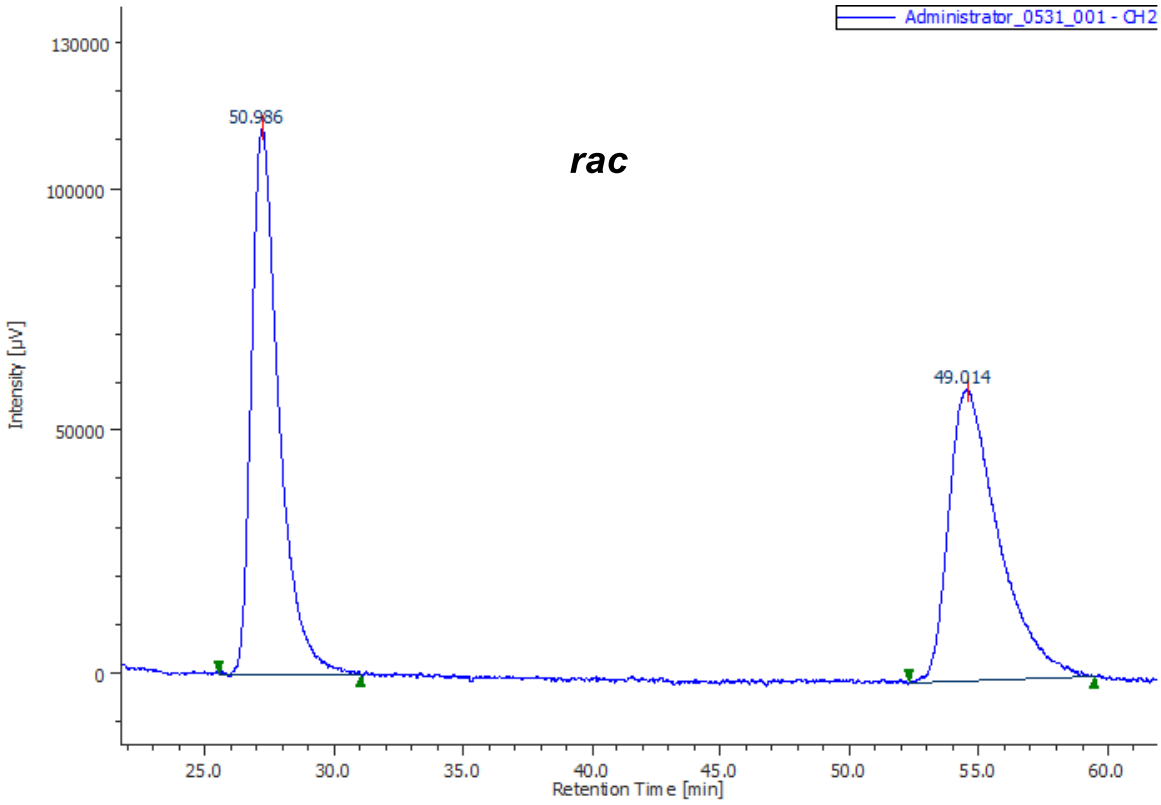
Chiralpak IA column (hexane:2-propanol = 95:5, 1.5 mL/min, 254 nm)



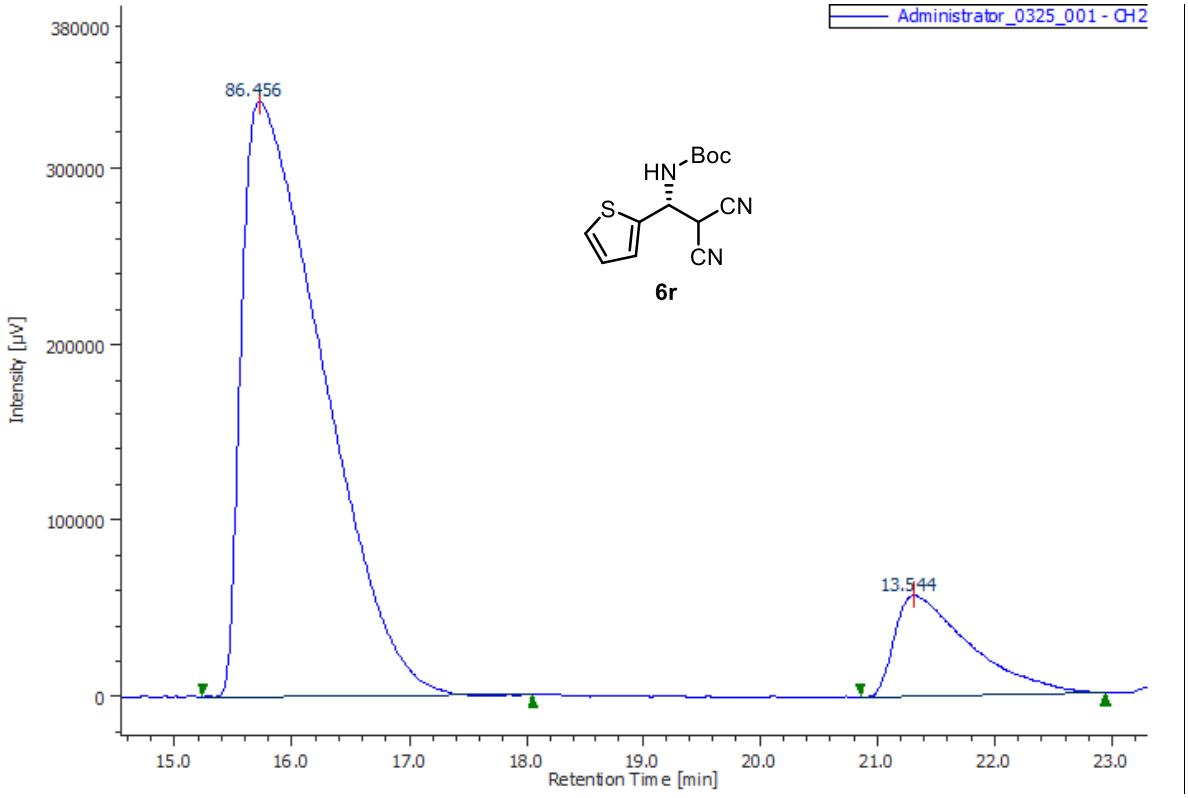


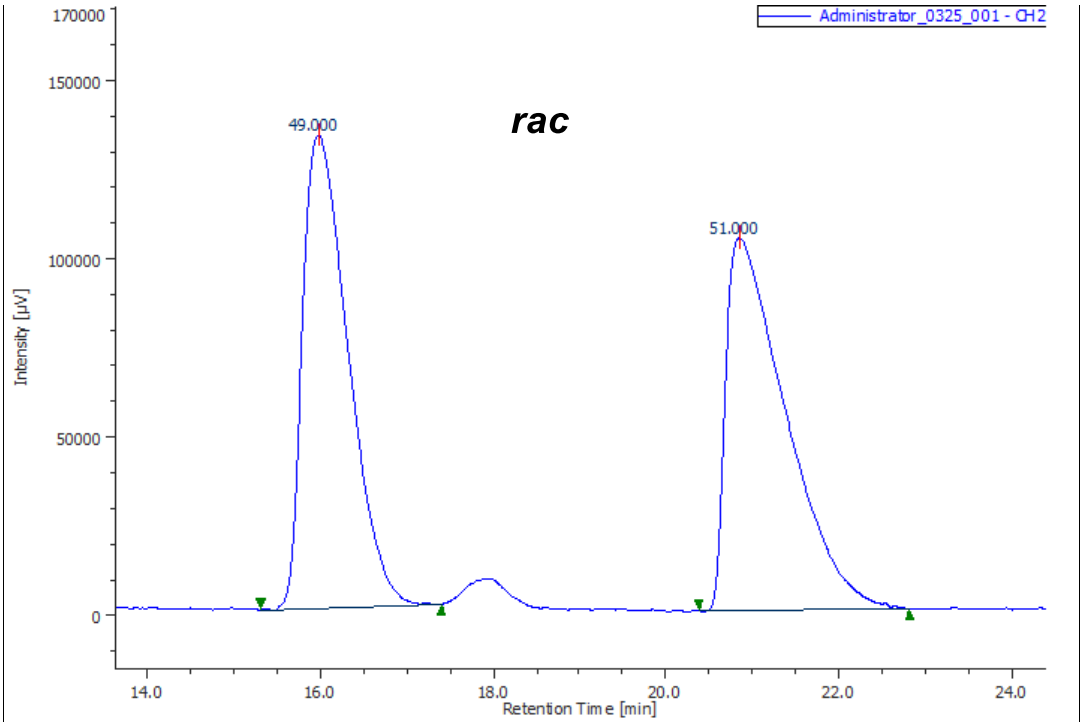
Chiralpak IA column (hexane:2-propanol = 90:10, 0.3 mL/min, 254 nm)



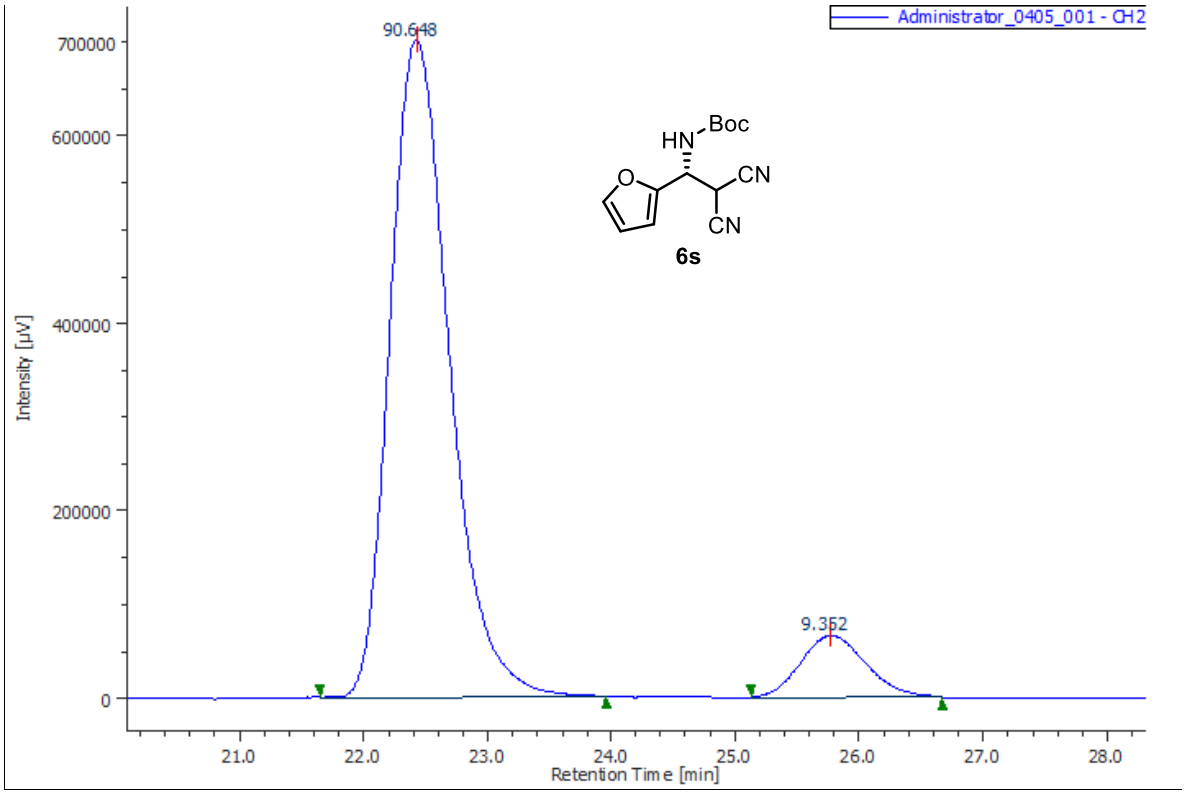


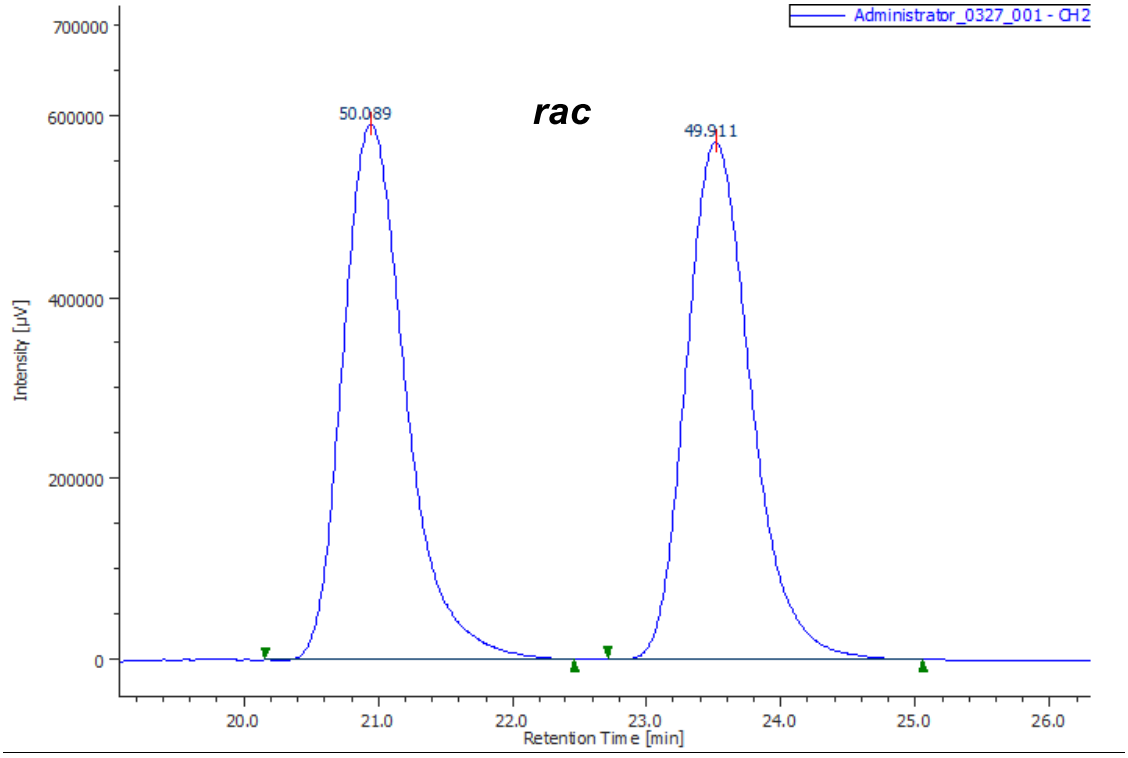
Chiralpak IA column (hexane:2-propanol = 90:10, 1.0 mL/min, 254 nm)



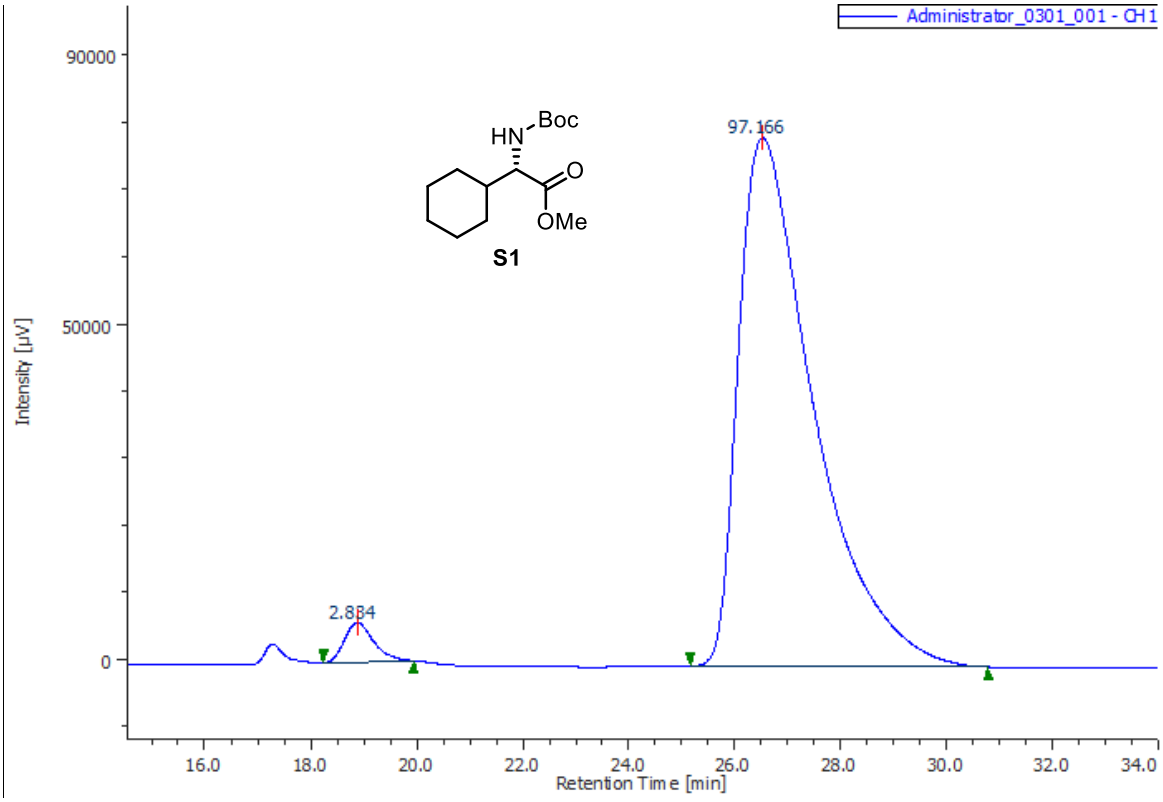


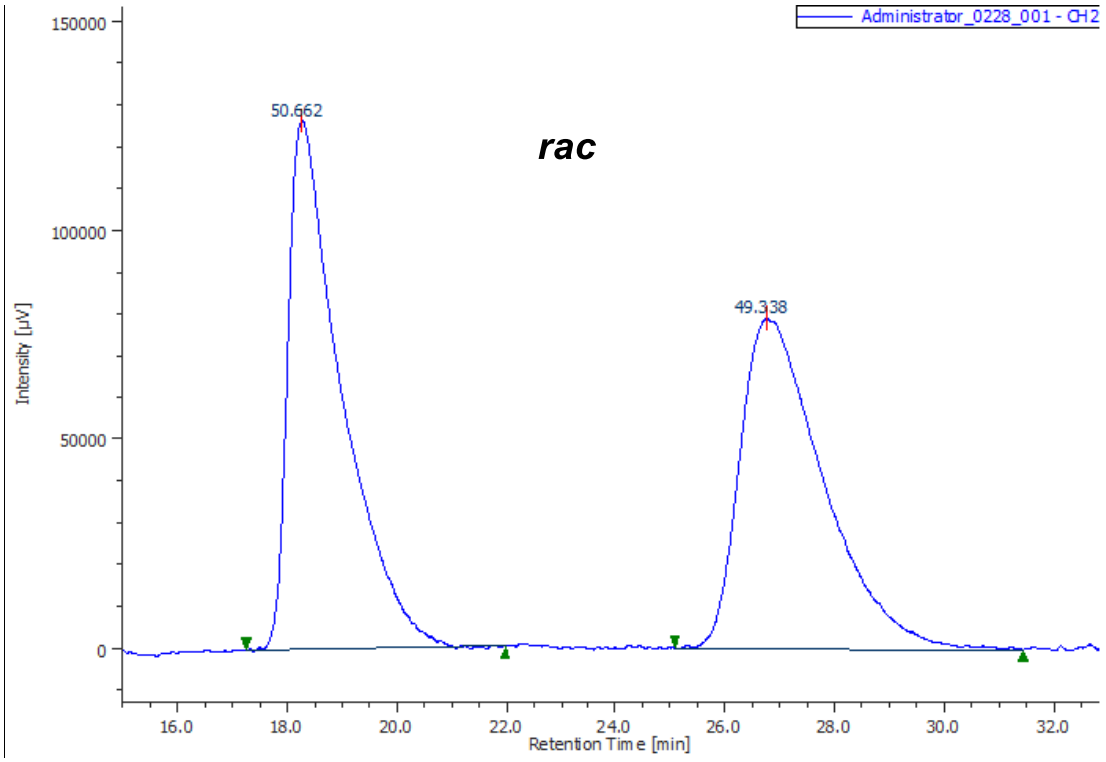
Chiralcel AD-H column (hexane:2-propanol = 85:15, 1.0 mL/min, 230 nm)



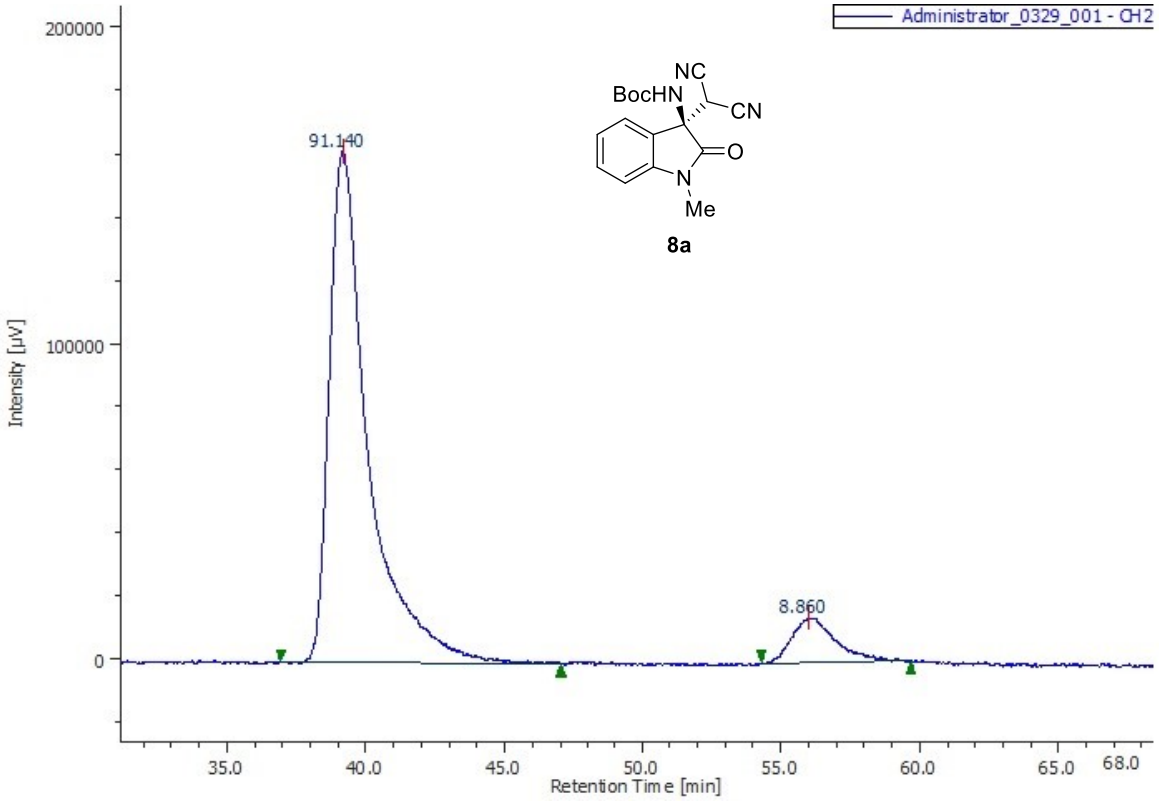


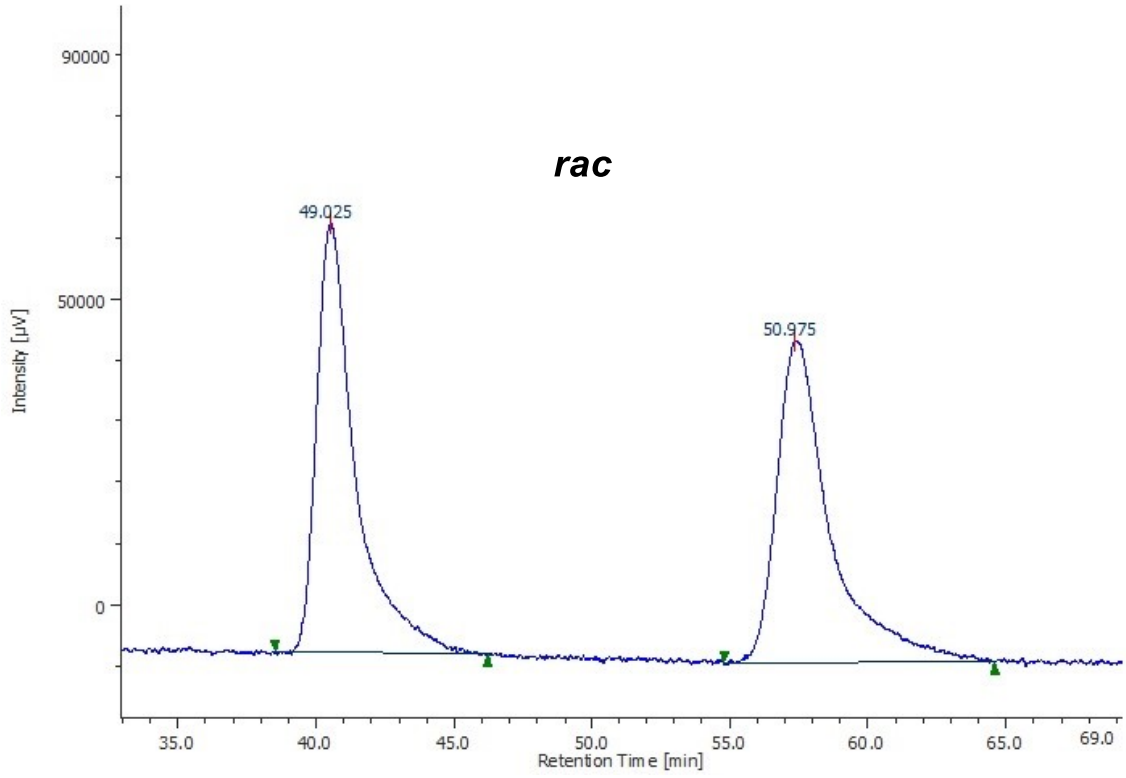
Chiralcel AD-H column (hexane:2-propanol = 85:15, 1.0 mL/min, 230 nm)



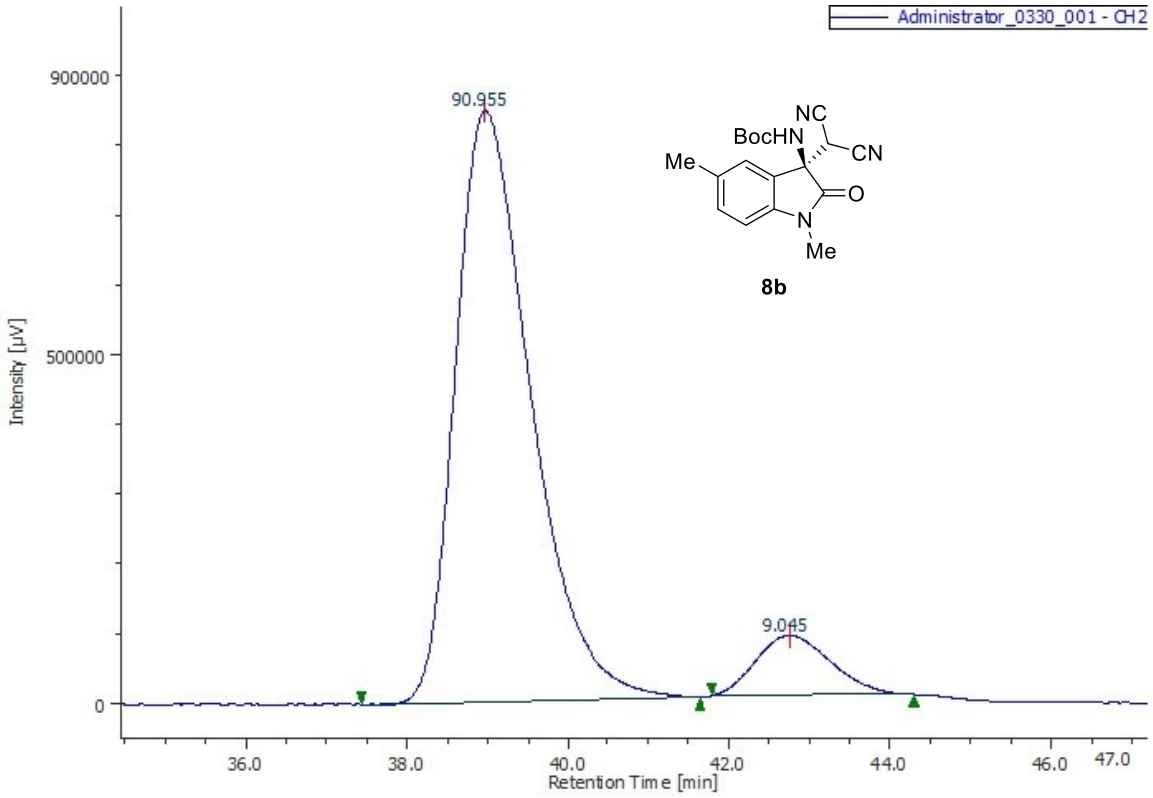


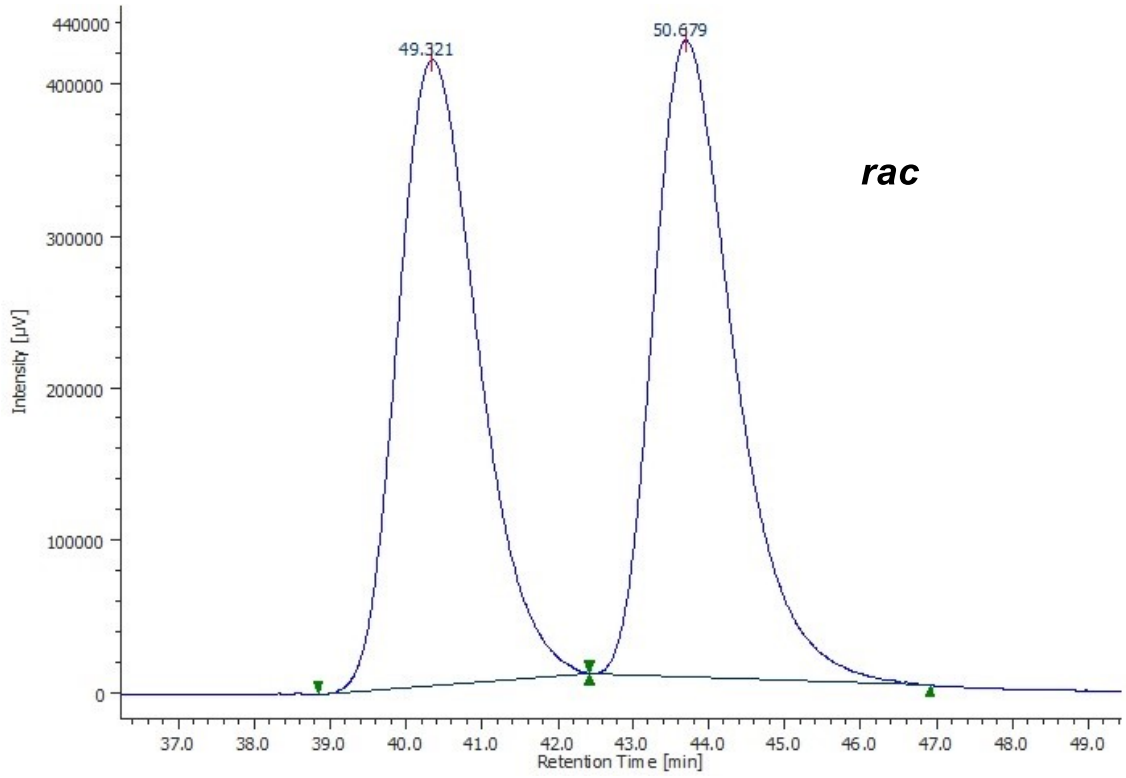
Chiralcel AD-H column (hexane:2-propanol = 85:15, 1.0 mL/min, 230 nm)



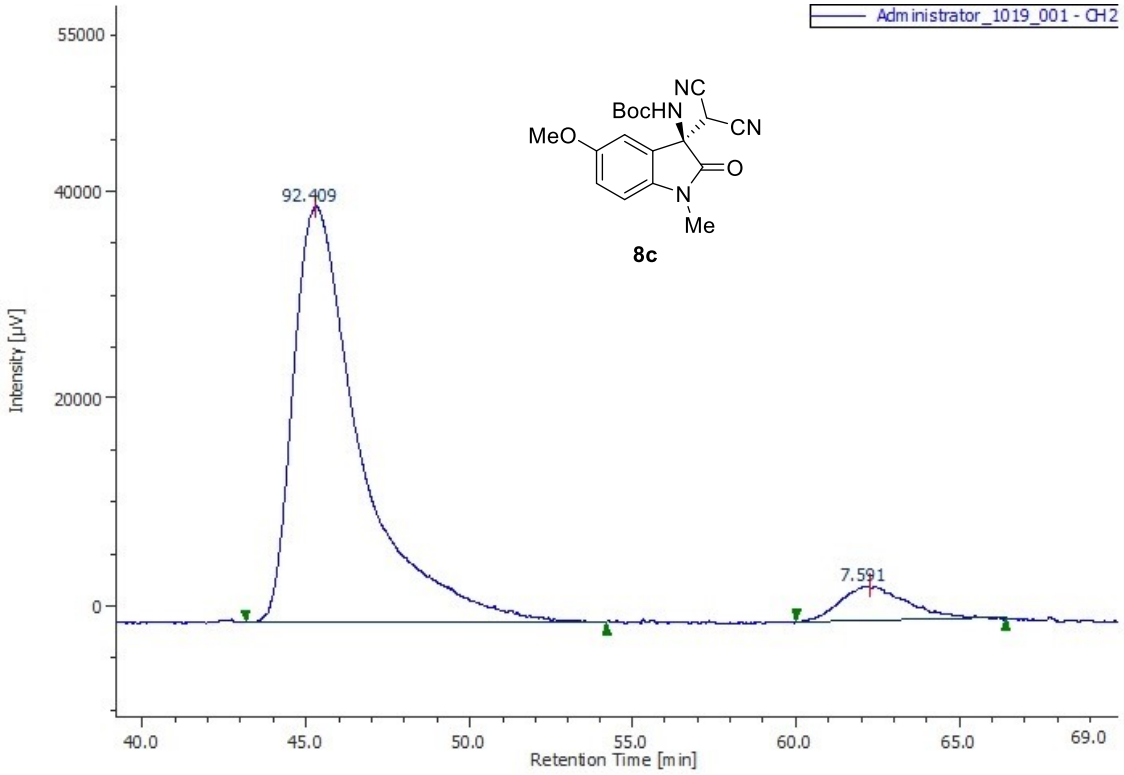


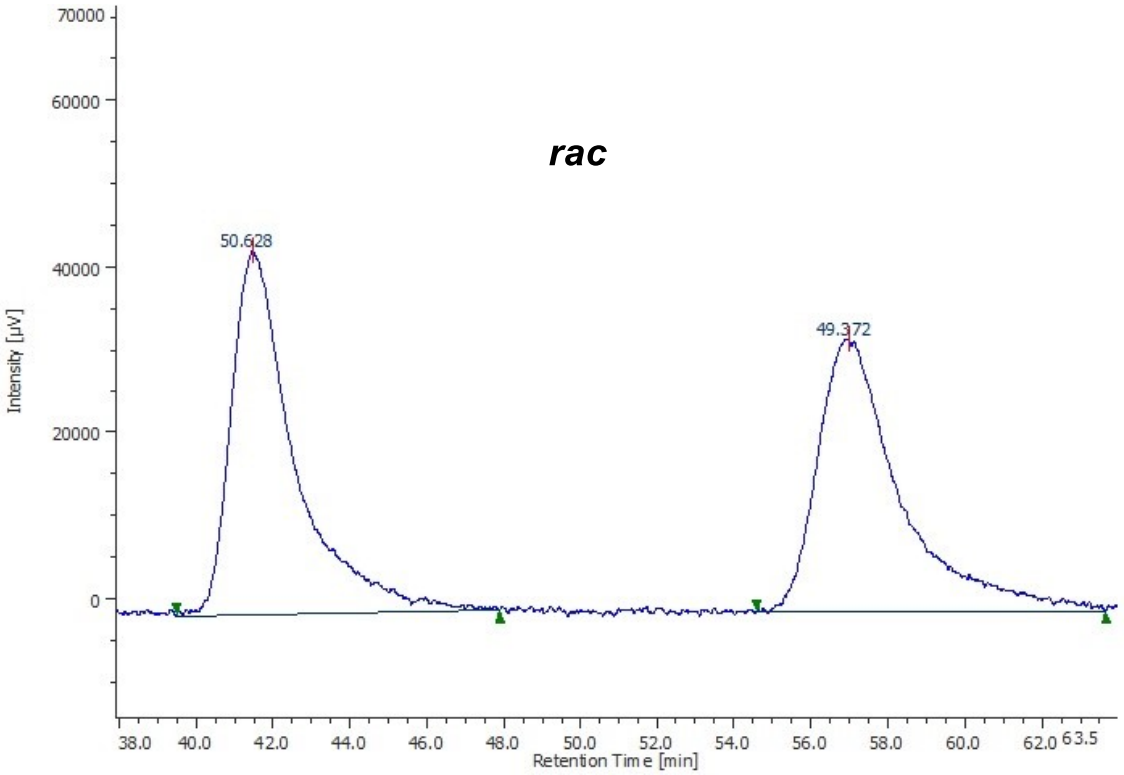
Chiralcel AD-H column (hexane:2-propanol = 90:10, 1.0 mL/min, 254 nm)



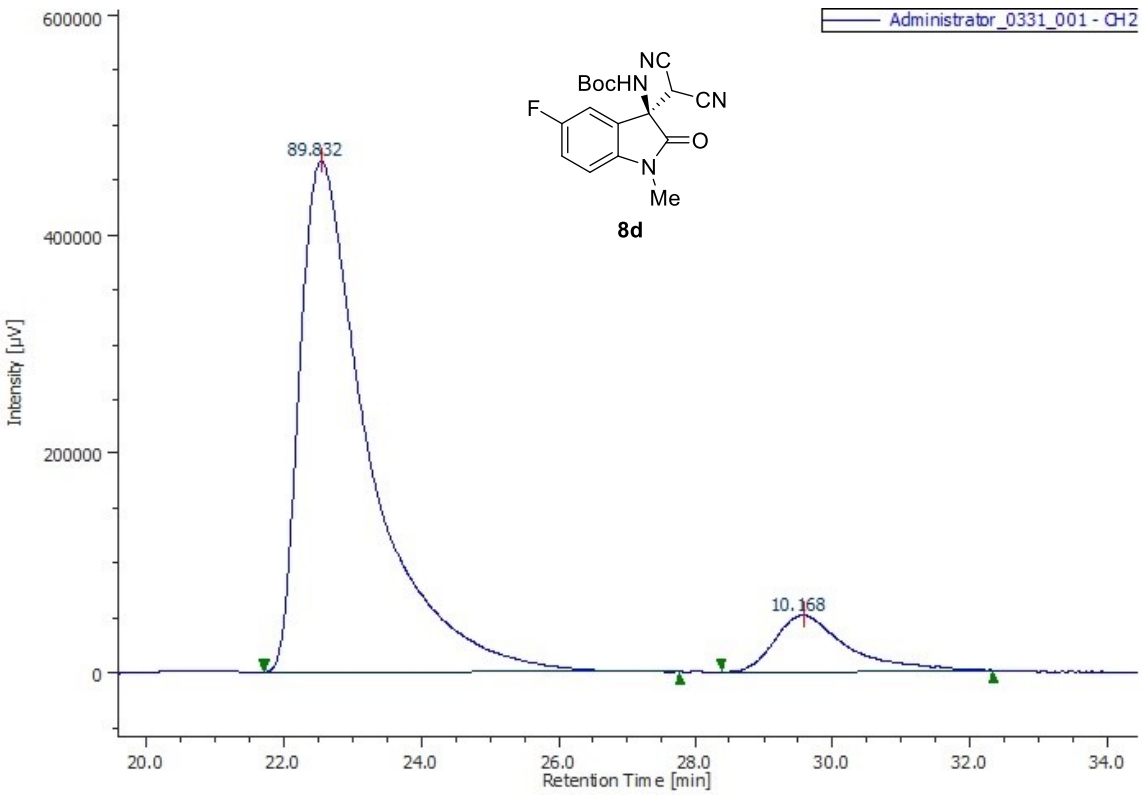


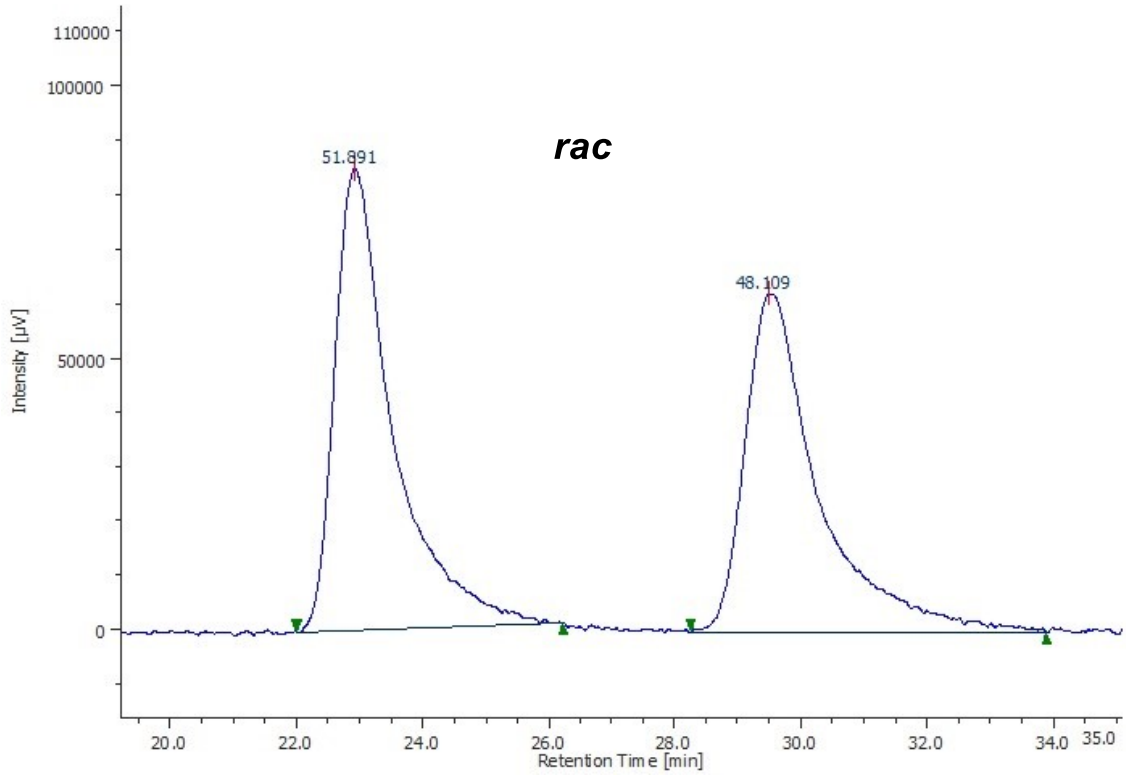
Chiralpak IC-3 column (hexane:2-propanol = 90:10, 0.3 mL/min, 254 nm)



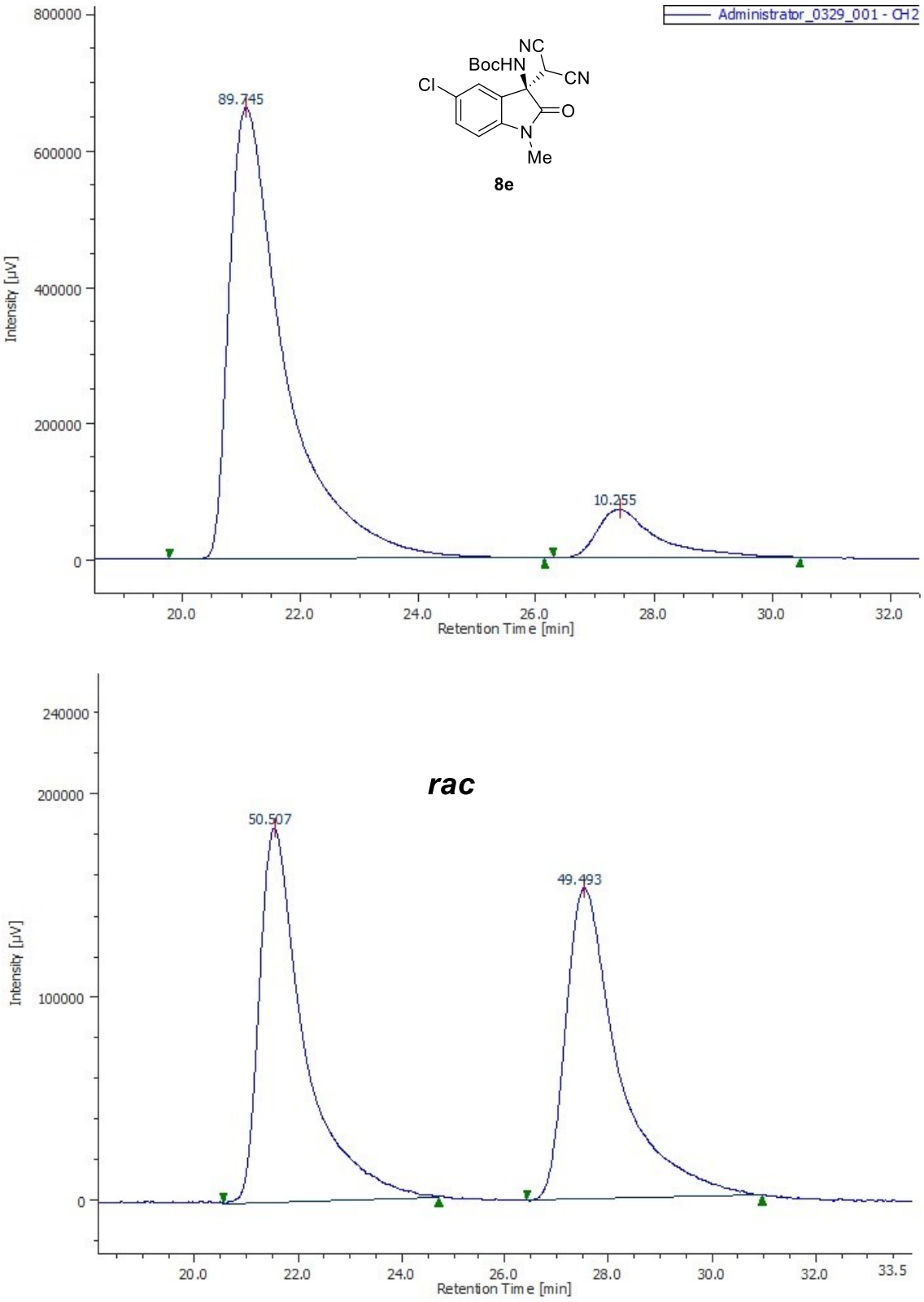


Chiralcel AD-H column (hexane:2-propanol = 90:10, 1.0 mL/min, 254 nm)





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



Chiralcel AD-H column (hexane:2-propanol = 90:10, 1.0 mL/min, 254 nm