Electronic Supplementary Information

Enantioselective Direct Michael Addition of Cyanohydrin Ether Derivatives to Enones Catalyzed by Chiral Bis(guanidino)iminophosphorane Organosuperbase

Saikat Das,[1] Azusa Kondoh,[2,*] Masahiro Terada[1,*]

Graduate School of Science, Tohoku University

[1] Department of Chemistry, Graduate School of Science, Tohoku University,

Sendai 980-8578, Japan

[2] Research and Analytical Center for Giant Molecules, Graduate School of Science

Tohoku University, Sendai 980-8578, Japan

Contents

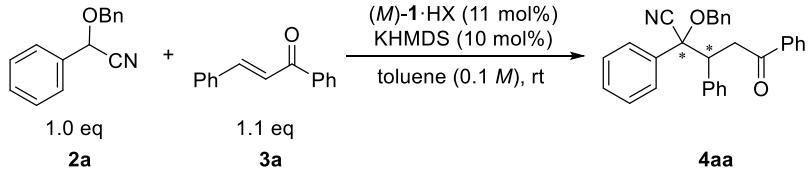
1. General information

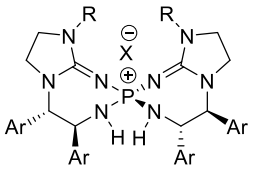
Unless otherwise noted, the reactions were carried out with dried glassware under argon or nitrogen atmosphere. Analytical thin layer chromatography (TLC) was performed on Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm). Flash column chromatography was performed on silica gel 60N (spherical, neutral, 40-50 m; Kanto Chemical Co., Inc.). ^{1}H NMR spectra were recorded on a JEOL JNM-ECA600 (600 MHz) spectrometer. Chemical shifts are reported in ppm from the solvent resonance or tetramethylsilane (TMS) as the internal standard ($CDCl_3$: 7.27 ppm, TMS: 0.00 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad) and coupling constants (Hz). ^{13}C NMR spectra were recorded on a JEOL JNM-ECA600 (150 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from the solvent resonance as the internal standard ($CDCl_3$: 77.0 ppm). ^{19}F NMR spectra were recorded on a JEOL JNM-ECA600 (565 MHz) spectrometer. Chemical shifts are reported in ppm from the $C_6F_5CF_3$ (-67.2 ppm) resonance as the external standard. Optically rotations were measured on a Jasco P-1020 digital polarimeter with a sodium lamp and reported as follows; $[\alpha]^{T}_{D}$ (c = g/100 mL, solvent). HPLC analysis was performed on a JASCO LC-2000 Plus system with UV and CD detectors. Infrared spectra were recorded on a JASCO FT/IR-4100 spectrometer. High resolution mass spectra analysis was performed on a Bruker Daltonics solariX 9.4T FT-ICR-MS spectrometer at the Research and Analytical Center for Giant Molecules, Graduate School of Science, Tohoku University.

Materials: Unless otherwise noted, materials were purchased from Wako Pure Chemical Industries, Ltd., Tokyo Chemical Industry Co., LTD., Aldrich Inc., and other commercial suppliers and were used without purification. Dichloromethane, diethyl ether, tetrahydrofuran and toluene were supplied from Kanto Chemical Co., Inc. as “Dehydrated solvent system”. Other solvents were purchased from commercial suppliers as dehydrated solvents, and used under argon atmosphere.

2. Additional Experimental Results

Table S1. Investigation of catalysts[a]



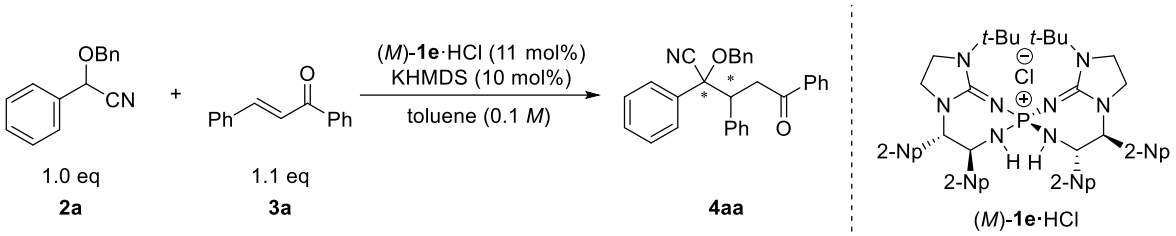


(*M*)-**1a**·HBr: R = Me, Ar = Ph, X = Br
(*M*)-**1b**·HCl: R = *t*-Bu, Ar = Ph, X = Cl
(*M*)-**1c**·HCl: R = Bn, Ar = Ph, X = Cl
(*M*)-**1d**·HCl: R = Bzh, Ar = Ph, X = Cl
(*M*)-**1e**·HCl: R = *t*-Bu, Ar = 2-Np, X = Cl
(*M*)-**1f**·HCl: R = Ad, Ar = Ph, X = Cl
(*M*)-**1g**·HCl: R = *t*-Bu, Ar = 1-Np, X = Cl

Entry	Cat.	Solvent	T(°C)	Time (h)	Yield (%)[b]	Dr[c]	ee (%)[d]
1	(*M*)-**1a**·HBr	toluene	rt	6 h	93	60:40	25/6
2	(*M*)-**1b**·HCl	toluene	rt	6 h	69	70:30	38/8
3	(*M*)-**1c**·HCl	toluene	rt	6 h	83	64:36	11/8
4	(*M*)-**1d**·HCl	toluene	rt	6 h	95	66:34	6/6
5	(*M*)-**1e**·HCl	toluene	rt	6 h	91	78:22	55/32
6	(*M*)-**1f**·HCl	toluene	rt	6 h	72	67:33	32/14
7	(*M*)-**1g**·HCl	toluene	rt	6 h	61	79:21	56/26

[a]Unless otherwise noted, all reactions were carried out using (*M*)-**1**·HX (5.5 μmol) with KHMDS (5.0 μmol), **2a** (0.050 mmol), and **3a** (0.055 mmol) in toluene (0.5 mL) at the indicated temperature. [b]Yields were determined by crude NMR spectroscopy using CH_2Br_2 as the internal standard [c]Diastereomeric ratio was determined by crude NMR spectroscopy. [d]Enantiomeric excess of **4aa** was determined by chiral-stationary-phase HPLC analysis.

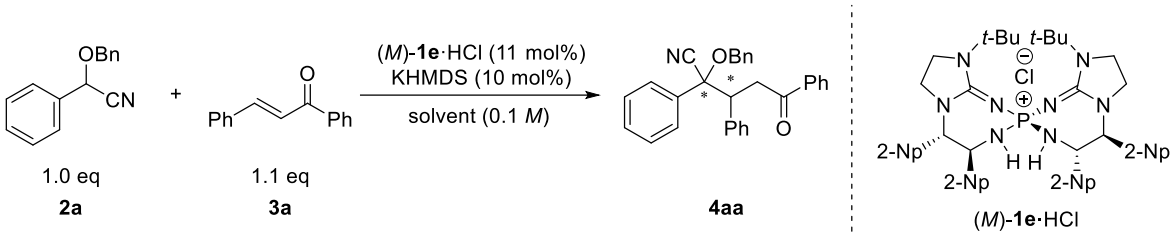
Table S2: Investigation of temperature effect[a]



Entry	Cat.	Solvent	T(°C)	Time (h)	Yield (%)[b]	Dr[c]	ee (%)[d]
1	(*M*)-**1e**·HCl	toluene	rt	6 h	91	78:22	55/32
2	(*M*)-**1e**·HCl	toluene	–20°C	24h	75	84:16	70/32
3	(*M*)-**1e**·HCl	toluene	–40°C	24 h	65	87:13	68/--
4	(*M*)-**1e**·HCl	toluene	–60°C	24 h	5	85:15	--/--

[a]Unless otherwise noted, all reactions were carried out using (*M*)-**1e**·HCl (5.5 μmol) with KHMDS (5.0 μmol), **2a** (0.050 mmol), and **3a** (0.055 mmol) in toluene (0.5 mL) at the indicated temperature. [b]Yields were determined by crude NMR spectroscopy using CH_2Br_2 as the internal standard [c]Diastereomeric ratio was determined by crude NMR spectroscopy. [d]Enantiomeric excess of **4aa** was determined by chiral-stationary-phase HPLC analysis.

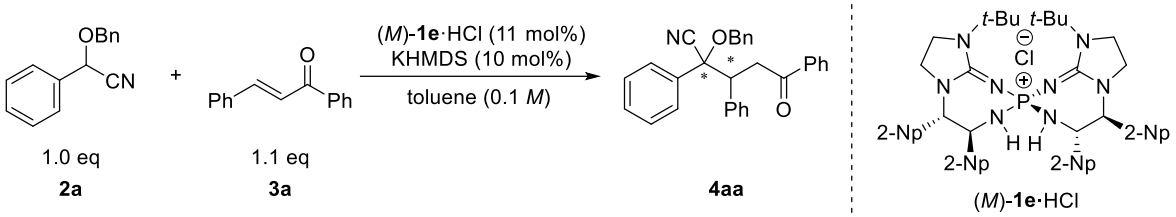
Table S3: Screening of solvents[a]



Entry	Cat.	Solvent	T(°C)	Time (h)	Yield (%)[b]	Dr[c]	ee (%)[d]
1	(*M*)-**1e**·HCl	toluene	–20°C	24h	75	84:16	70/32
2	(*M*)-**1e**·HCl	THF	–20°C	24h	87	23:77	2/10
3	(*M*)-**1e**·HCl	Et_2O	–20°C	24h	78	78:22	62/8
4	(*M*)-**1e**·HCl	EtOAc	–20°C	24h	No reaction	–:--	--/--
5	(*M*)-**1e**·HCl	CH_3CN	–20°C	24h	73	22:78	4/6
6	(*M*)-**1e**·HCl	trifluorotoluene	–20°C	24h	24	63:37	--/--
7	(*M*)-**1e**·HCl	chlorobenene	–20°C	24h	13	69:31	--/--

[a]Unless otherwise noted, all reactions were carried out using (*M*)-**1e**·HCl (5.5 μmol) with KHMDS (5.0 μmol), **2a** (0.050 mmol), and **3a** (0.055 mmol) in toluene (0.5 mL) at the indicated temperature. [b]Yields were determined by crude NMR spectroscopy using CH_2Br_2 as the internal standard [c]Diastereomeric ratio was determined by crude NMR spectroscopy. [d]Enantiomeric excess of **4aa** was determined by chiral-stationary-phase HPLC analysis.

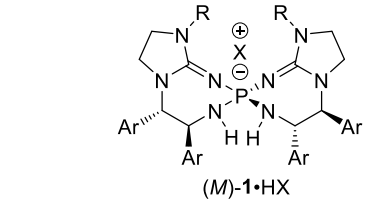
Table S4: Control experiments to check racemization over time[a]



Entry	Cat.	Solvent	T(°C)	Time (h)	Yield (%)[b]	Dr[c]	ee (%)[d]
1	(*M*)-**1e**·HCl	toluene	–20°C	24 h	75	84:16	70/32
2	(*M*)-**1e**·HCl	toluene	–20°C	4 h	43	84:16	70/--

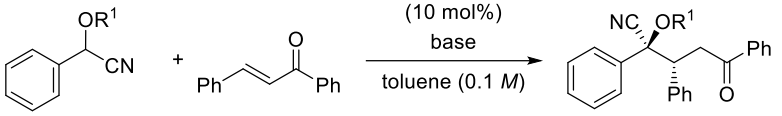
[a]Unless otherwise noted, all reactions were carried out using (*M*)-**1e**·HCl (5.5 μmol) with KHMDS (5.0 μmol), **2a** (0.050 mmol), and **3a** (0.055 mmol) in toluene (0.5 mL) at the indicated temperature. [b]Yields were determined by crude NMR spectroscopy using CH_2Br_2 as the internal standard [c]Diastereomeric ratio was determined by crude NMR spectroscopy. [d]Enantiomeric excess of **4aa** was determined by chiral-stationary-phase HPLC analysis.

Table S5: Optimization of reaction conditions[a]



(*M*)-**1**•HX

1a: R = Me, Ar = Ph, X = Br
1b: R = *t*-Bu, Ar = Ph, X = Cl
1c: R = Bn, Ar = Ph, X = Cl
1d: R = Bzh, Ar = Ph, X = Cl
1e: R = *t*-Bu, Ar = 2-naphthyl, X = Cl



2 (1.0 eq.) **3a** (1.1 eq.) **4**

a: R^1 = Bn
b: R^1 = naphthalen-2-ylmethyl (Nap)

aa: R^1 = Bn
ba: R^1 = Nap

Entry	1 (mol%)	Base (mol%)	R^1	T(°C)	Time (h)	Yield (%)[b]	Dr[c]	Ee (%)[d]
1	(*M*)-**1a**·HBr (11)	KHMDS (10)	Bn	rt	6 h	93	60:40	25/6
2	(*M*)-**1b**·HCl (11)	KHMDS (10)	Bn	rt	6 h	69	70:30	38/8
3	(*M*)-**1c**·HCl (11)	KHMDS (10)	Bn	rt	6 h	83	64:36	11/8
4	(*M*)-**1d**·HCl (11)	KHMDS (10)	Bn	rt	6 h	95	66:34	6/6
5	(*M*)-**1e**·HCl (11)	KHMDS (10)	Bn	rt	6 h	91	78:22	55/32
6	(*M*)-**1e**·HCl (11)	KHMDS (10)	Bn	–20°C	24 h	75	84:16	69/26
7	(*M*)-**1e**·HCl (11)	KHMDS (10)	Nap	–20°C	24 h	76	84:16	79
8	(*M*)-**1e**·HCl (11)	KHMDS (10)	Nap	–40°C	24 h	89	87:13	84
9	(*M*)-**1e**·HCl (11)	KHMDS (10)	Nap	–60°C	48 h	53	89:11	83
10	(*M*)-**1e**·HCl (10)	KHMDS (15)	Nap	–60°C	24 h	88	90:10	90
11	(*M*)-**1e**·HCl (10)	KHMDS (20)	Nap	–60°C	24 h	95	90:10	92/43
12	(*M*)-**1e**·HCl (10)	KHMDS (30)	Nap	–60°C	24 h	85	90:10	90
13	(*M*)-**1e**·HCl (10)	KHMDS (20)	Nap	–78°C	24 h	66	90:10	90
14	(*M*)-**1e**·HCl (10)	NaHMDS (20)	Nap	–60°C	24 h	96	87:13	90
15	(*M*)-**1e**·HCl (10)	tBuOK (20)	Nap	–60°C	24 h	84	90:10	90
16	(*M*)-**1e**·HCl (10)	LiHMDS (20)	Nap	–60°C	24 h	trace	--	--
17[e]	(*M*)-**1e**·HCl (10)	KHMDS (20)	Nap	–60°C	24 h	91	90:10	91
18[f]	(*M*)-**1e**·HCl (10)	KHMDS (20)	Nap	–60°C	24 h	84	90:10	91

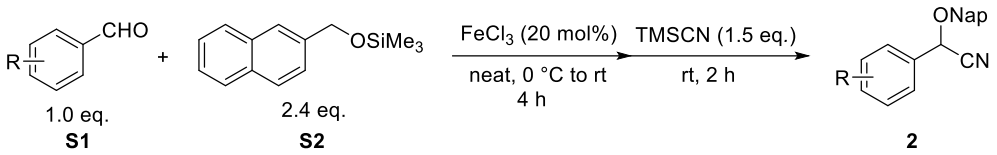
[a]Unless otherwise noted, all reactions were carried out using (*M*)-**1**·HX (5.0-5.5 μmol) with KHMDS (5.0-15.0 μmol), **2a** (0.050 mmol), and **3a** (0.055 mmol) in toluene (0.5 mL) at the indicated temperature. [b]Yields were determined by crude NMR spectroscopy using CH_2Br_2 as the internal standard [c]Diastereomeric ratio was determined by crude NMR spectroscopy. [d]Enantiomeric excess of **4aa** was determined by chiral-stationary-phase HPLC analysis. [e]1.1 equiv of **2b** and 1.0 equiv of **3a** were used. [f]1.0 equiv of **2b** and 1.5 equiv of **3a** were used.

3. Experimental Procedure and Analytical Data

Cyanohydrin benzyl ether **2a** was prepared according to the procedure in the literature.[S1]

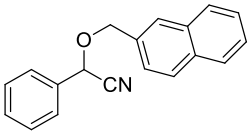
Synthesis and characterization of 2-(naphthalen-2-ylmethoxy)-2-arylacetonitrile (S3):

Method A:



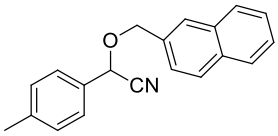
To a magnetically stirred suspension of anhydrous iron (III) chloride (0.13 mmol, 20 mol%) and (naphthalen-2-ylmethoxy)trimethylsilane (**S2**,15.8 mmol, 2.4 equiv) at 0 °C was added aldehyde **S1** (6.6 mmol, 1.0 equiv). The reaction mixture was warmed to room temperature and stirred for 4 h under argon atmosphere. Trimethylsilyl cyanide (9.9 mmol, 1.5 equiv) was then added, and the resulting mixture was stirred at room temperature for 2 h. The mixture was diluted with CH_2Cl_2 (15 mL), and quenched with a phosphate buffer (pH = 7). The product was extracted with CH_2Cl_2 (10 mL × 3), and the combined organic layer was dried over Na_2SO_4. Evaporation of the solvent and purification of the residue on silica gel column furnished 2-(naphthalen-2-ylmethoxy)-2-arylacetonitrile **2**.

2-(naphthalen-2-ylmethoxy)-2-phenylacetonitrile (2b):



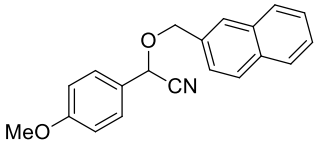
Purified by silica gel flash column chromatography (Hexane/EtOAc = 24/1); White solid (64% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, J = 8.4 Hz, 1H), 7.88-7.86 (m, 3H), 7.54-7.51 (m, 5H), 7.46-7.43 (m, 3H), 5.29 (s, 1H), 5.02 (d, J = 12.6 Hz, 1H), 4.87 (d, J = 12.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 133.4, 133.3, 133.2, 133.1, 129.8, 129.0, 128.7, 128.0, 127.8, 127.7, 127.4, 126.4 (2C), 125.8, 117.2, 71.8, 69.3; IR (ATR): 3063, 3051, 2918, 2872, 2238, 1508, 1453, 1220, 1174, 1062, 1005, 822, 733 cm^{-1}; HRMS (ESI) Calcd for $C_{19}H_{15}NO$ $[M+Na]^+$ 296.1046, Found 296.1046; mp. 79.0-81.0 °C.

2-(naphthalen-2-ylmethoxy)-2-(*p*-tolyl)acetonitrile (2c):



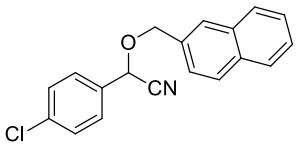
Purified by silica gel flash column chromatography (Hexane/EtOAc = 24/1); White solid (65% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89-7.85 (m, 4H), 7.53-7.50 (m, 3H), 7.40 (d, J = 7.2 Hz, 2H), 7.25 (d, J = 7.2 Hz, 2H), 5.26 (s, 1H), 4.98 (d, J = 12.0 Hz, 1H), 4.85 (d, J = 11.4 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.8, 133.21, 133.19, 133.1, 130.4, 129.6, 128.6, 127.9, 127.7, 127.5, 127.4, 126.3 (2C), 125.7, 117.3, 71.5, 69.2, 21.2; IR (ATR): 3052, 3033, 2919, 2867, 2236, 1510, 1220, 1174, 1066, 1009, 863, 811**,** 772 cm^{-1}; HRMS (ESI) Calcd for $C_{20}H_{17}NO$ $[M+Na]^+$ 310.1202, Found 310.1202; mp. 74.0-76.0 °C.

2-(4-methoxyphenyl)-2-(naphthalen-2-ylmethoxy)acetonitrile (2d):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 6/1); White solid (70% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90-7.86 (m, 4H), 7.54-7.51 (m, 3H), 7.44 (d, J = 7.8 Hz, 2H), 6.96 (d, J = 8.4 Hz, 2H), 5.24 (s, 1H), 4.98 (d, J = 12.0 Hz, 1H), 4.84 (d, J = 12.0 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.7, 133.2 (2C), 133.1, 129.0, 128.6, 127.9, 127.7, 127.5, 126.4, 126.3, 125.8, 125.5, 117.4, 114.3, 71.4, 68.9, 55.3; IR (ATR): 3054, 3010, 2957, 2911, 2838, 2234, 1542, 1463, 1220, 1175, 1061, 1031, 816, 772 cm^{-1}; HRMS (ESI) Calcd for $C_{20}H_{17}NO_2$ $[M+Na]^+$ 326.1151, Found 326.1151; mp. 70.0-72.0 °C.

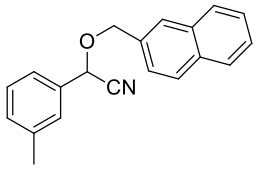
2-(4-chlorophenyl)-2-(naphthalen-2-ylmethoxy)acetonitrile (2e):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 24/1); White solid (30% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91-7.86 (m, 4H), 7.54 (m, 2H), 7.50 (dd, J = 8.4, 1.8 Hz, 1H), 7.45-7.41 (m, 4H), 5.24 (s, 1H), 5.03 (d, J = 12.0 Hz, 1H), 4.86 (d, J = 12.0 Hz, 1H); ^{13}C

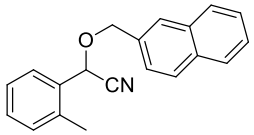
NMR (150 MHz, $CDCl_3$) δ 135.9, 133.3, 133.1, 132.7, 131.9, 129.3, 128.8, 128.7, 128.0, 127.8, 127.7, 126.5 (2C), 125.7, 116.8, 71.9, 68.5; IR (ATR): 3054, 2920, 2870, 2236, 1492, 1403, 1220, 1065, 1014, 817, 772 cm^{-1}; HRMS (ESI) Calcd for $C_{19}H_{14}ClNO$ $[M+Na]^+$ 330.0656, Found 330.0656; mp. 85.0-87.0 °C.

2-(naphthalen-2-ylmethoxy)-2-(*m*-tolyl)acetonitrile (2h):



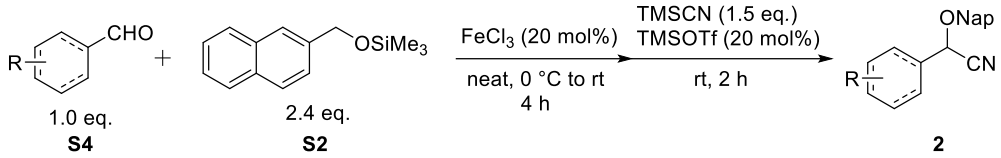
Purified by silica gel flash column chromatography (Hexane/EtOAc = 24/1); White solid (74% yield); ^1H NMR (600 MHz, $CDCl_3$) δ 7.90-7.87 (m, 4H), 7.55-7.51 (m, 3H), 7.35-7.29 (m, 3H), 7.25 (d, J = 6.6 Hz, 1H), 5.26 (s, 1H), 5.01 (d, J = 12.0 Hz, 1H), 4.87 (d, J = 11.4 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.8, 133.2, 133.13, 133.07, 133.0, 130.4, 128.7, 128.5, 127.9, 127.8, 127.6, 127.4, 126.2, 125.6, 124.4, 117.2, 71.6, 69.3, 21.2; IR (ATR): 3055, 3025, 2920, 2868, 2236, 1509, 1458, 1273, 1220, 1157, 1063, 818, 772 cm^{-1}; HRMS (ESI) Calcd for $C_{20}H_{17}NO$ $[M+Na]^+$ 310.1202, Found 310.1202; mp. 49.0-51.0 °C.

2-(naphthalen-2-ylmethoxy)-2-(o-tolyl)acetonitrile (2j):



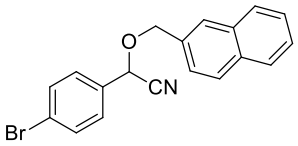
Purified by silica gel flash column chromatography (Hexane/EtOAc = 24/1); White solid (68% yield); ^1H NMR (600 MHz, $CDCl_3$) δ 7.89-7.87 (m, 4H), 7.62 (t, J = 6.6 Hz, 1H), 7.54-7.49 (m, 3H), 7.36-7.33 (m, 1H), 7.31-7.28 (m, 1H), 7.24 (dd, J = 7.8, 3.0 Hz, 1H), 5.40 (d, J = 4.2 Hz, 1H), 5.00 (dd, J = 12.0, 2.4 Hz, 1H), 4.87 (dd, J = 12.0, 2.4 Hz, 1H), 2.34 (d, J = 4.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.5, 133.2, 133.1, 133.0, 131.3, 131.1, 129.9, 128.5, 128.1, 127.9, 127.7, 127.6, 126.4, 126.3 (2C), 125.8, 117.0, 71.7, 67.7, 18.7; IR (ATR): 3055, 3025, 2924, 2869, 2235, 1273, 1176, 1124, 1063, 856, 817, 749 cm^{-1}; HRMS (ESI) Calcd for $C_{20}H_{17}NO$ $[M+Na]^+$ 310.1202, Found 310.1202; mp. 53.0-55.0 °C.

Method B:



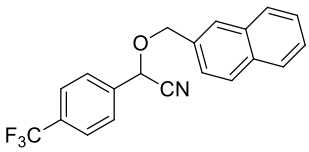
To a magnetically stirred suspension of anhydrous iron (III) chloride (0.13 mmol, 20 mol%) and (naphthalen-2-ylmethoxy)trimethylsilane (**S2**, 15.8 mmol, 2.4 equiv) at 0 °C was added aldehyde **S4** (6.6 mmol, 1.0 equiv). The reaction mixture was warmed to room temperature and stirred for 4 h under argon atmosphere. Trimethylsilyl cyanide (9.9 mmol, 1.5 equiv) followed by trimethylsilyl trifluoromethanesulfonate (1.3 mmol, 20 mol%) was then added, and the resulting mixture was stirred at room temperature for 2 h. The mixture was diluted with CH_2Cl_2 (15 mL), and quenched with a phosphate buffer (pH = 7). The product was extracted with CH_2Cl_2 (10 mL × 3), and the combined organic layer was dried over Na_2SO_4. Evaporation of the solvent and purification of the residue on silica gel column furnished 2-(naphthalen-2-ylmethoxy)-2-arylacetonitrile **2**.

2-(4-bromophenyl)-2-(naphthalen-2-ylmethoxy)acetonitrile (2f):



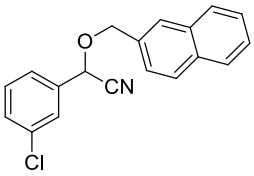
Purified by silica gel flash column chromatography (Hexane/EtOAc = 24/1); White solid (79% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90-7.85 (m, 4H), 7.58 (d, J = 8.4 Hz, 2H), 7.55-7.52 (m, 2H), 7.50 (dd, J = 8.4, 1.8 Hz, 1H), 7.38 (d, J = 9.0 Hz, 2H), 5.23 (s, 1H), 5.02 (d, J = 12.0 Hz, 1H), 4.86 (d, J = 12.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 133.3, 133.1, 132.7, 132.4, 132.2, 128.9, 128.8, 128.0, 127.8 (2C), 126.5 (2C), 125.7, 124.1, 116.8, 71.9, 68.5; IR (ATR): 3054, 3026, 2937, 2917, 2872, 2241, 1487, 1400, 1220, 1069, 1007, 819, 799, 772 cm^{-1}; HRMS (FD+) Calcd for $C_{19}H_{14}BrNO$ $[M]^+$ 351.0259, Found 351.0257; mp. 80.0-82.0 °C.

2-(naphthalen-2-ylmethoxy)-2-(4-(trifluoromethyl)phenyl)acetonitrile (2g):



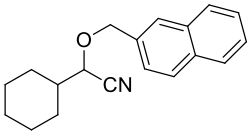
Purified by silica gel flash column chromatography (Hexane/EtOAc = 24/1); White solid (75% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, J = 7.8 Hz, 1H), 7.89-7.87 (m, 3H), 7.71 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 8.4 Hz, 2H), 7.55-7.53 (m, 2H), 7.51 (dd, J = 8.4, 1.8 Hz, 1H), 5.32 (s, 1H), 5.08 (d, J = 11.4 Hz, 1H), 4.90 (d, J = 11.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.2, 133.4, 133.1, 132.5, 132.0 (q, J = 30.0 Hz), 128.9, 128.0, 127.9, 127.8, 127.7, 126.61, 126.59, 126.1 (q, J = 4.4 Hz), 125.7, 123.6 (q, J = 271.5 Hz), 116.6, 72.2, 68.4; ^{19}F NMR (565 MHz, $CDCl_3$) δ –62.8; IR (ATR): 3062, 2870, 2243, 1414, 1326, 1220, 1169, 1122, 1067, 1018, 817, 772 cm^{-1}; HRMS (ESI) Calcd for $C_{20}H_{14}F_3NO$ $[M+Na]^+$ 364.0920, Found 364.0920; mp. 88.0-90.0 °C.

2-(3-chlorophenyl)-2-(naphthalen-2-ylmethoxy)acetonitrile (2i):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 24/1); White solid (71% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91-7.86 (m, 4H), 7.55-7.53 (m, 2H), 7.51-7.49 (dd J = 8.4, 2.4 Hz, 1H), 7.45-7.41 (m, 4H), 5.25 (s, 1H), 5.03 (d, J = 12.0 Hz, 1H), 4.86 (d, J = 12.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.9, 133.3, 133.1, 132.7, 131.9, 129.3 (2C), 128.8, 128.7 (2C), 128.0, 127.7 (2C), 126.5 (2C), 125.7, 116.8, 71.9, 68.5; IR (ATR): 3052, 3025, 2939, 2920, 2871, 2236, 1492, 1402, 1173, 1009, 989, 820, 772 cm^{-1}; HRMS (FD+) Calcd for $C_{19}H_{14}ClNO$ $[M]^+$ 307.0764, Found 307.0763; mp. 85.0-87.0 °C.

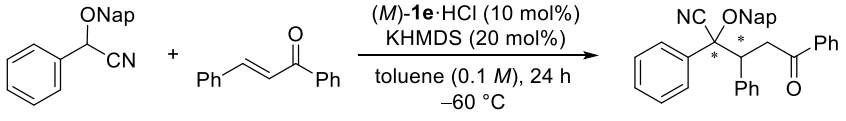
2-cyclohexyl-2-(naphthalen-2-ylmethoxy)acetonitrile (2k):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 24/1); White solid (78% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88-7.86 (m, 3H), 7.82 (s, 1H), 7.54-7.51 (m, 2H), 7.47 (dd, J = 8.4, 1.2 Hz, 1H), 5.03 (d, J = 12.6 Hz, 1H), 4.69 (d, J = 12.6 Hz, 1H), 3.97 (d, J = 6.0 Hz, 1H), 1.93-1.89 (m, 2H), 1.85-1.77 (m, 3H), 1.71-1.68 (m, 1H), 1.32-1.09 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 133.4, 133.2, 133.1, 128.5, 127.9, 127.7, 127.4, 126.3, 126.3, 125.8, 117.7, 72.6, 72.3, 41.0, 28.5, 28.2, 25.9, 25.48, 25.46; IR (ATR): 3056, 2927, 2854, 2234, 1509, 1450, 1331, 1220, 1088, 1070, 855, 817, 749 cm^{-1}; HRMS (ESI) Calcd for $C_{19}H_{21}NO$ $[M+Na]^+$ 302.1515, Found 302.1515; mp. 79.0-81.0 °C.

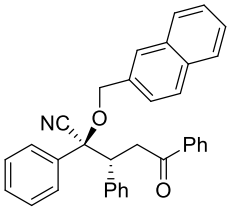
5. Catalytic enantioselective Michael addition of cyanohydrin ether derivatives to enones

5.1 Typical procedure



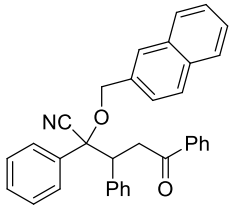
To a dried test tube was added (*M*)-**1e**·HCl (4.7 mg, 5.0 μmol), and then anhydrous toluene (0.5 mL) was added under argon atmosphere. A solution of KHMDS in toluene (0.5 *M*, 20 μL, 10.0 μmol) was added to the suspension at room temperature, and the resulting mixture was stirred for 5 min. Next, the mixture was cooled to –60 °C, cyanohydrin ether **2b** (13.7 mg, 0.050 mmol) was added in one portion, and the mixture was stirred for 1 min. Then chalcone (**3a**, 11.5 mg, 0.055 mmol) was added to the solution. After that, the reaction mixture was stirred at –60 °C for 24 h. The reaction was quenched with saturated aq. NH_4Cl (1.0 mL), and the product was extracted with EtOAc (2.0 mL × 3). The combined organic phase was dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash chromatography (Hexane/EtOAc = 19/1) to afford **4ba** (20.2 mg, 84% yield) as a white solid with 92% ee.

(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,3,5-triphenylpentanenitrile (4ba):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (20.2 mg, 84% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 11.8 (minor), 14.0 (major) min; 92% ee; Optical rotation $[\alpha]_D^{22}$ = +103.9 (*c* 1.3, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.2 Hz, 2H), 7.84-7.82 (m, 1H), 7.79-7.77 (m, 2H), 7.69 (s, 1H), 7.50-7.47 (m, 3H), 7.39-7.33 (m, 8H), 7.14-7.10 (m, 3H), 7.07 (dd, *J* = 6.8, 1.8 Hz, 2H), 4.76 (d, *J* = 10.2 Hz, 1H), 4.48 (d, *J* = 10.8 Hz, 1H), 4.19 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.13 (dd, *J* = 17.4, 4.8 Hz, 1H), 3.75 (dd, *J* = 17.4, 8.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.2, 136.9, 136.9, 135.6, 133.8, 133.1, 133.0 (2C), 129.3, 129.2, 128.6, 128.4, 128.1, 128.0, 128.0, 127.9, 127.6, 127.5, 126.6, 126.5, 126.1, 126.1, 125.6, 117.7, 85.7, 69.3, 52.7, 39.6; IR (ATR): 3059, 3031, 2953, 2924, 2870**,** 2854, 2233, 1685, 1591, 1449, 1218, 1065, 1050, 818, 772, 699 cm^{-1}; HRMS (FD+) Calcd for $C_{34}H_{27}NO_2$ $[M]^+$ 481.2042, Found 481.2040; mp. 91.0-93.0 °C.

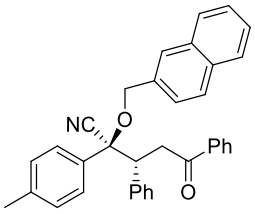
2-(naphthalen-2-ylmethoxy)-5-oxo-2,3,5-triphenylpentanenitrile: (minor)



minor

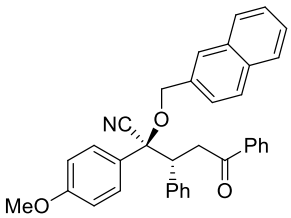
Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); colorless oil (2.2 mg, 9% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 11.4 (minor), 12.3 (major) min; 43% ee; Optical rotation $[\alpha]_D^{22}$ = –7.5 (*c* 0.8, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83-7.76 (m, 5H), 7.60 (s, 1H), 7.51-7.46 (m, 5H), 7.39-7.37 (m, 5H), 7.29-7.27 (m, 2H), 7.27-7.24 (m, 4H), 4.75 (d, *J* = 12.0 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.15 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.87 (dd, *J* = 17.4, 11.4 Hz, 1H), 3.38 (dd, *J* = 17.4, 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.5, 137.1, 136.6, 135.4, 134.3, 133.2 (2C), 132.9, 130.0, 129.5, 128.7, 128.5, 128.04, 127.97, 127.9 (2C), 127.68, 127.65, 126.7, 126.2, 126.00, 125.97, 125.1, 118.1, 84.8, 69.0, 52.0, 39.4; IR (ATR): 3060, 3031, 2926, 2872**,** 2233, 1685, 1598, 1448, 1270, 1219, 1079, 817, 749, 699 cm^{-1}; HRMS (FD+) Calcd for $C_{34}H_{27}NO_2$ $[M]^+$ 481.2042, Found 481.2041.

(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-3,5-diphenyl-2-(*p*-tolyl)pentanenitrile (4ca):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (15.2 mg, 61% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 10.4 (minor), 13.5 (major) min; 88% ee; Optical rotation $[\alpha]_D^{22}$ = +119.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 8.4, 1.8 Hz, 2H), 7.83-7.81 (m, 1H), 7.78-7.76 (m, 2H), 7.67 (s, 1H), 7.49-7.46 (m, 3H), 7.35 (dd, *J* = 8.4, 7.2 Hz, 2H), 7.32 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.14-7.12 (m, 5H), 7.09-7.07 (m, 2H), 4.72 (d, *J* = 10.2 Hz, 1H), 4.45 (d, *J* = 10.2 Hz, 1H), 4.17 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.10 (dd, *J* = 16.8, 4.8 Hz, 1H), 3.71 (dd, *J* = 16.8, 8.4 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.3, 139.2, 137.1, 136.9, 133.9, 133.1, 133.0, 132.9, 132.5, 129.3 (2C), 128.4, 128.09, 128.05, 128.0, 127.9, 127.6, 127.4, 126.6, 126.5, 126.1, 126.0, 125.6, 117.9, 85.5, 69.1, 52.6, 39.7, 21.1; IR (ATR): 3059, 3030, 2923, 2867**,** 2234, 1686, 1598, 1448, 1219, 1082, 814, 689 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{29}NO_2$ $[M]^+$ 495.2198, Found 495.2196; mp. 139.0-141.0 °C.

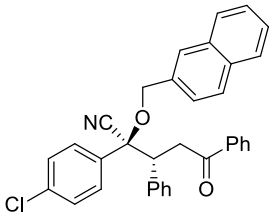
(2*S*,3*R*)-2-(4-methoxyphenyl)-2-(naphthalen-2-ylmethoxy)-5-oxo-3,5-diphenylpentanenitrile (4da):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 13/1); White solid (14.9 mg, 58% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 21.5 (minor), 27.3 (major) min; 73% ee; Optical rotation $[\alpha]_D^{22}$ = +106.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.81-7.79 (m, 1H), 7.76-7.74 (m, 2H), 7.64 (s, 1H), 7.47-7.44 (m, 3H), 7.33 (dd, *J* = 7.8, 7.2 Hz, 2H), 7.30 (dd, *J* = 8.4, 1.8 Hz, 1H),

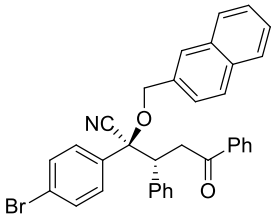
7.26 (d, *J* = 9.0 Hz, 2H), 7.12-7.11 (m, 3H), 7.07-7.06 (m, 2H), 6.81 (d, *J* = 9.0 Hz, 2H), 4.70 (d, *J* = 11.4 Hz, 1H), 4.43 (d, *J* = 11.4 Hz, 1H), 4.14 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.09 (dd, *J* = 17.4, 4.8 Hz, 1H), 3.79 (s, 3H), 3.69 (dd, *J* = 17.4, 8.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.4, 160.2, 137.1, 136.9, 133.9, 133.1, 132.9 (2C), 129.2, 128.4, 128.10, 128.06, 128.0, 127.94, 127.92, 127.7, 127.4 (2C), 126.6, 126.1, 126.0, 125.6, 117.9, 113.9, 85.3, 69.1, 55.3, 52.7, 39.7; IR (ATR): 3059, 3030, 2961, 2930, 2860**,** 2839, 2234, 1686, 1510, 1448, 1255, 1219, 1082, 1032, 815, 689 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{29}NO_3$ $[M]^+$ 511.2147, Found 511.2145; mp. 135.0-137.0 °C.

(2*S*,3*R*)-2-(4-chlorophenyl)-2-(naphthalen-2-ylmethoxy)-5-oxo-3,5-diphenylpentanenitrile (4ea):



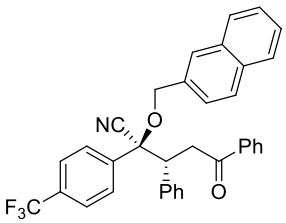
Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (22.2 mg, 86% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 11.6 (minor), 15.1 (major) min; 87% ee; Optical rotation $[\alpha]_D^{22}$ = +109.9 (*c* 1.8, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.4, 1.8 Hz, 2H), 7.83-7.82 (m, 1H), 7.78-7.76 (m, 2H), 7.65 (s, 1H), 7.51-7.47 (m, 3H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.31-7.28 (m, 5H), 7.16-7.13 (m, 3H), 7.08-7.05 (m, 2H), 4.75 (d, *J* = 10.8 Hz, 1H), 4.42 (d, *J* = 10.8 Hz, 1H), 4.14 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.10 (dd, *J* = 16.2, 4.8 Hz, 1H), 3.72 (dd, *J* = 16.8, 7.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.0, 136.8, 136.6, 135.3, 134.3, 133.5, 133.12, 133.06, 133.0, 129.2, 128.9, 128.5, 128.2 (2C), 128.1, 128.0, 127.9, 127.72, 127.67, 126.7, 126.22, 126.18, 125.5, 117.4, 85.2, 69.5, 52.7, 39.7; IR (ATR): 3059, 3031, 2925, 2855**,** 2234, 1685, 1597, 1490, 1449, 1267, 1092, 1067, 817, 749, 701 cm^{-1}; HRMS (FD+) Calcd for $C_{34}H_{26}ClNO_2$ $[M]^+$ 515.1652, Found 515.1650; mp. 93.0-95.0 °C.

(2*S*,3*R*)-2-(4-bromophenyl)-2-(naphthalen-2-ylmethoxy)-5-oxo-3,5-diphenylpentanenitrile (4fa):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (21.4 mg, 77% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 14.0 (minor), 17.7 (major) min; 83% ee; Optical rotation $[\alpha]_D^{22}$ = +131.8 (*c* 0.7, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.2 Hz, 2H), 7.83-7.82 (m, 1H), 7.78-7.76 (m, 2H), 7.65 (s, 1H), 7.50-7.47 (m, 3H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.36 (dd, *J* = 8.4, 7.8 Hz, 2H), 7.30 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 2H), 7.16-7.14 (m, 3H), 7.08-7.06 (m, 2H), 4.75 (d, *J* = 10.8 Hz, 1H), 4.42 (d, *J* = 10.8 Hz, 1H), 4.14 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.10 (dd, *J* = 16.2, 4.8 Hz, 1H), 3.72 (dd, *J* = 16.2, 7.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.0, 136.8, 136.6, 134.9, 133.4, 133.10, 133.06, 133.0, 131.8, 129.2, 128.5, 128.24, 128.23 (2C), 128.1, 127.9, 127.74, 127.66, 126.7, 126.21, 126.18, 125.5, 123.5, 117.3, 85.2, 69.5, 52.6, 39.7; IR (ATR): 3059, 3031, 2925, 2871**,** 2233, 1685, 1597, 1486, 1448, 1267, 1219, 1074, 1009, 817, 749 cm^{-1}; HRMS (FD+) Calcd for $C_{34}H_{26}BrNO_2$ $[M]^+$ 559.1147, Found 559.1146; mp. 112.0-114.0 °C.

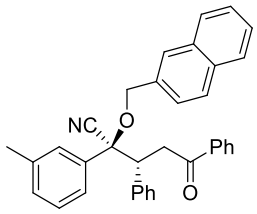
(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-3,5-diphenyl-2-(4-(trifluoromethyl)phenyl) pentanenitrile (4ga):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); pale yellow sticky oil (15.0 mg, 54% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 9.7 (minor), 13.4 (major) min; 73% ee; Optical rotation $[\alpha]_D^{22}$ = +91.0 (*c* 0.4, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.4, 1.8 Hz, 2H), 7.84-7.82 (m, 1H), 7.79-7.77 (m, 2H), 7.67 (s, 1H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.51-7.47 (m, 5H), 7.37 (dd, *J* = 8.4, 7.8 Hz, 2H), 7.31 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.17-7.11 (m, 3H), 7.04 (dd, *J* = 7.8, 1.8 Hz, 2H), 4.79 (d, *J* = 11.4 Hz, 1H), 4.43 (d, *J* = 11.4 Hz, 1H), 4.16 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.11 (dd, *J* = 16.8, 4.8

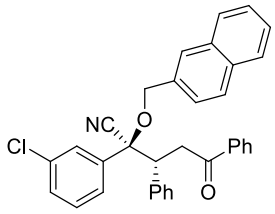
Hz, 1H), 3.75 (dd, *J* = 16.8, 8.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.9, 139.8, 136.8, 136.3, 133.2, 133.13, 133.10, 133.05, 131.6 (q, *J* = 33.0 Hz), 129.1, 128.5, 128.3 (2C), 128.1, 127.94, 127.86, 127.7, 127.1, 126.8, 126.27, 126.25, 125.6 (q, *J* = 2.9 Hz), 125.5, 123.6 (q, *J* = 270.0 Hz), 117.2, 85.3, 69.7, 52.7, 39.7; ^{19}F NMR (565 MHz, $CDCl_3$) δ –62.6; IR (ATR): 3060, 3031, 2927, 2871**,** 2234, 1686, 1597, 1449, 1412, 1324, 1219, 1168, 1125, 1068, 817, 770 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{26}F_3NO_2$ $[M]^+$ 549.1916, Found 549.1915.

(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-3,5-diphenyl-2-(m-tolyl)pentanenitrile (4ha):



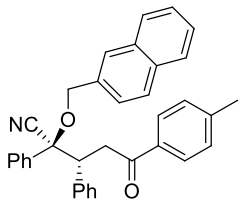
Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (17.5 mg, 70% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 8.3 (minor), 9.8 (major) min; 88% ee; Optical rotation $[\alpha]_D^{22}$ = +106.2 (*c* 1.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.83-7.82 (m, 1H), 7.78-7.77 (m, 2H), 7.67 (s, 1H), 7.50-7.46 (m, 3H), 7.36 (dd, *J* = 8.4, 7.8 Hz, 2H), 7.33 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.22-7.20 (m, 1H), 7.18-7.16 (m, 1H), 7.16-7.11 (m, 5H), 7.08-7.06 (m, 2H), 4.74 (d, *J* = 10.8 Hz, 1H), 4.49 (d, *J* = 10.8 Hz, 1H), 4.17 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.11 (dd, *J* = 17.4, 4.8 Hz, 1H), 3.71 (dd, *J* = 17.4, 8.4 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.3, 138.4, 137.0, 136.9, 135.4, 133.9, 133.1, 133.0, 132.9, 130.0, 129.2, 128.4 (2C), 128.1, 128.06, 128.0, 127.9, 127.6, 127.5, 127.2, 126.7, 126.11, 126.05, 125.6, 123.7, 117.9, 85.7, 69.3, 52.6, 39.6, 21.4; IR (ATR): 3059, 3030, 2921, 2864**,** 2233, 1686, 1597, 1490, 1449, 1267, 1092, 1067, 817, 749, 701 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{29}NO_2$ $[M]^+$ 495.2198, Found 495.2197; mp. 78.0-80.0 °C.

(2*S*,3*R*)-2-(3-chlorophenyl)-2-(naphthalen-2-ylmethoxy)-5-oxo-3,5-diphenylpentanenitrile (4ia):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (20.0 mg, 76% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 14.1 (minor), 16.6 (major) min; 85% ee; Optical rotation $[\alpha]_D^{22}$ = +107.9 (*c* 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.8 Hz, 2H), 7.83-7.81 (m, 1H), 7.78-7.76 (m, 2H), 7.65 (s, 1H), 7.50-7.47 (m, 3H), 7.36 (dd, *J* = 8.4, 7.8 Hz, 2H), 7.31-7.28 (m, 5H), 7.16-7.13 (m, 3H), 7.07-7.06 (m, 2H), 4.75 (d, *J* = 10.2 Hz, 1H), 4.42 (d, *J* = 10.2 Hz, 1H), 4.14 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.10 (dd, *J* = 16.8, 4.8 Hz, 1H), 3.72 (dd, *J* = 16.8, 7.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.1, 136.8, 136.6, 135.3, 134.3, 133.4, 133.11, 133.07, 133.0, 129.2, 128.9, 128.5, 128.2 (2C), 128.1, 128.0 (2C), 127.9, 127.73, 127.67 (2C), 126.7, 126.22, 126.18, 125.5, 117.4, 85.2, 69.5, 52.7, 39.7; IR (ATR): 3059, 3030, 2921, 2864**,** 2233, 1686, 1597, 1449, 1270, 1217, 1083, 1002, 819, 747, 710 cm^{-1}; HRMS (FD+) Calcd for $C_{34}H_{26}ClNO_2$ $[M]^+$ 515.1652, Found 515.1651; mp. 97.0-99.0 °C.

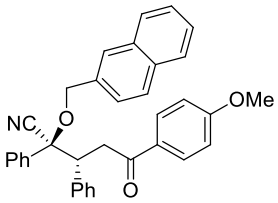
(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,3-diphenyl-5-(*p*-tolyl)pentanenitrile (4bb):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (18.0 mg, 72% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 12.3 (minor), 18.4 (major) min; 92% ee; Optical rotation $[\alpha]_D^{22}$ = +99.2 (*c* 1.4, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83-7.80 (m, 3H), 7.77 (d, *J* = 7.8 Hz, 2H), 7.67 (s, 1H), 7.50-7.48 (m, 2H), 7.37-3.35 (m, 2H), 7.35-7.31 (m, 4H), 7.14-7.09 (m, 5H), 7.05 (dd, *J* = 7.8, 1.8 Hz, 2H), 4.74 (d, *J* = 11.4 Hz, 1H), 4.47 (d, *J* = 10.8 Hz, 1H), 4.18 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.09 (dd, *J* = 16.8, 4.8 Hz, 1H), 3.70 (dd, *J* = 16.8, 8.4 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.9, 143.8, 137.0, 135.6, 134.4, 133.8, 133.1, 133.0, 129.3, 129.2, 129.1, 128.6, 128.2, 128.1,

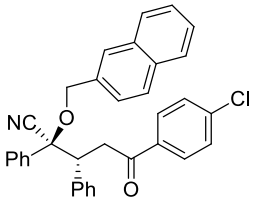
128.0, 127.9, 127.6, 127.5, 126.61, 126.57, 126.1, 126.0, 125.6, 117.8, 85.7, 69.3, 52.8, 39.5, 21.6; IR (ATR): 3060, 3031, 2922, 2866**,** 2233, 1683, 1605, 1449, 1270, 1223, 1180, 1081, 1004, 816, 753, 699 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{29}NO_2$ $[M]^+$ 495.2198, Found 495.2197; mp. 88.0-90.0 °C.

(2*S*,3*R*)-5-(4-methoxyphenyl)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,3-diphenylpentanenitrile (4bc):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 10/1); White solid (12.8 mg, 50% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 19.1 (minor), 31.9 (major) min; 89% ee; Optical rotation $[\alpha]_D^{22}$ = +90.4 (*c* 0.9, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 9.0 Hz, 2H), 7.83-7.82 (m, 1H), 7.79-7.76 (m, 2H), 7.68 (s, 1H), 7.50-7.47 (m, 2H), 7.37-7.35 (m, 2H), 7.34-7.32 (m, 4H), 7.13-7.09 (m, 3H), 7.05 (dd, *J* = 7.8, 1.8 Hz, 2H), 6.81 (d, *J* = 9.0 Hz, 2H), 4.74 (d, *J* = 10.8 Hz, 1H), 4.46 (d, *J* = 10.8 Hz, 1H), 4.17 (dd, *J* = 17.4, 5.4 Hz, 1H), 4.07 (dd, *J* = 8.4, 5.4 Hz, 1H), 3.80 (s, 3H), 3.66 (dd, *J* = 17.4, 8.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.8, 163.3, 137.1, 135.6, 133.8, 133.1, 133.0, 130.4, 130.0, 129.25, 129.21, 128.6, 128.1, 128.0, 127.9, 127.6, 127.4, 126.61, 126.56, 126.1, 126.0, 125.6, 117.8, 113.6, 85.8, 69.3, 55.4, 52.9, 39.2; IR (ATR): 3060, 3019, 2933, 2840**,** 2234, 1676, 1600, 1510, 1259, 1220, 1169, 1030, 1004, 699 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{29}NO_3$ $[M]^+$ 511.2147, Found 511.2145; mp. 98.0-100.0 °C.

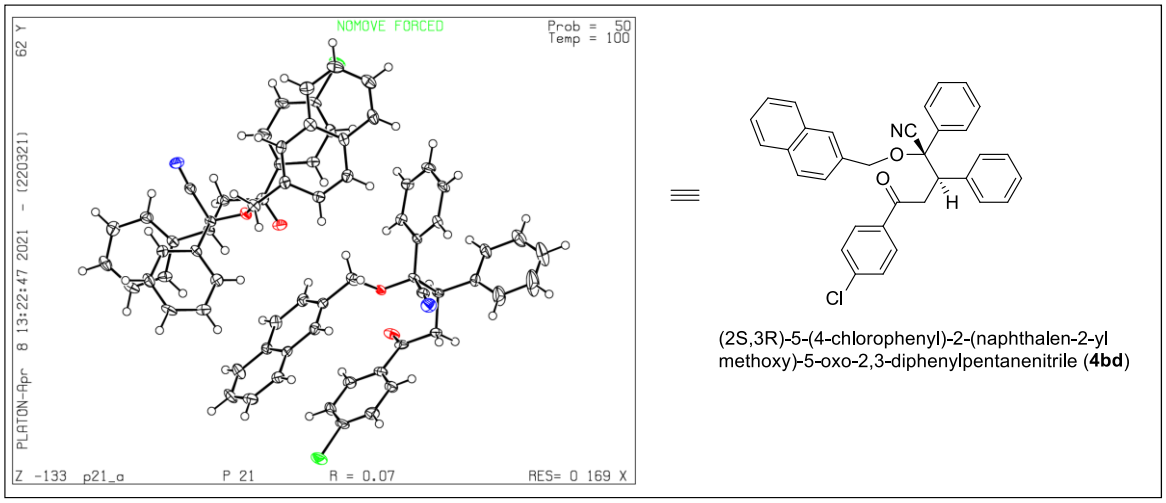
(2*S*,3*R*)-5-(4-chlorophenyl)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,3-diphenylpentanenitrile (4bd):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (20.2 mg, 78% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm,

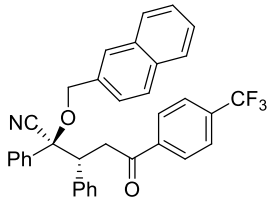
25 °C) 10.9 (minor), 14.2 (major) min; 92% ee; Optical rotation $[\alpha]_D^{22}$ = +60.3 (*c* 0.8, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.85-7.83 (m, 1H), 7.80-7.76 (m, 4H), 7.64 (s, 1H), 7.52-7.49 (m, 2H), 7.37-7.32 (m, 5H), 7.31 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.16-7.11 (m, 3H), 7.04 (d, *J* = 7.8 Hz, 2H), 4.69 (d, *J* = 10.2 Hz, 1H), 4.45 (d, *J* = 10.2 Hz, 1H), 4.16 (dd, *J* = 7.8, 5.4 Hz, 1H), 4.10 (dd, *J* = 17.4, 5.4 Hz, 1H), 3.58 (dd, *J* = 17.4, 7.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.1, 139.4, 136.8, 135.4, 135.2, 133.6, 133.1, 133.0, 129.42, 129.36, 129.2, 128.7, 128.6, 128.13, 128.08, 127.9, 127.7, 127.6, 126.8, 126.6, 126.23, 126.18, 125.7, 117.6, 85.8, 69.4, 52.9, 39.6; IR (ATR): 3060, 3031, 2917, 2871**,** 2233, 1686, 1589, 1399, 1269, 1091, 1004, 751, 698 cm^{-1}; HRMS (FD+) Calcd for $C_{34}H_{26}ClNO_2$ $[M]^+$ 515.1652, Found 515.1650; mp. 100.0-102.0 °C.

ORTEP diagram of 4bd CCDC No. 2076236 Recrystallized from $CHCl_3$/MeOH (1:1).



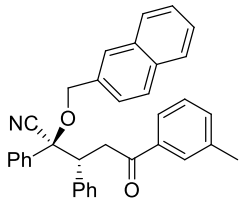
(2S,3R)-5-(4-chlorophenyl)-2-(naphthalen-2-yl methoxy)-5-oxo-2,3-diphenylpentanenitrile (**4bd**)

(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,3-diphenyl-5-(4-(trifluoromethyl)phenyl) pentanenitrile (4be):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (13.8 mg, 50% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 9.5 (minor), 13.0 (major) min; 80% ee; Optical rotation $[\alpha]_D^{22}$ = +54.4 (*c* 0.7, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.8 Hz, 2H), 7.83-7.81 (m, 1H), 7.76-7.73 (m, 2H), 7.63 (s, 1H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.51-7.49 (m, 2H), 7.39-7.34 (m, 5H), 7.29 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.18-7.12 (m, 3H), 7.04 (d, *J* = 7.8 Hz, 2H), 4.67 (d, *J* = 10.8 Hz, 1H), 4.45 (d, *J* = 10.8 Hz, 1H), 4.20-4.15 (m, 2H), 3.61-3.55 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.4, 139.6, 136.6, 135.3, 134.1 (q, *J* = 33.0 Hz), 133.5, 133.1, 133.0, 129.4, 129.2, 128.7, 128.3, 128.1 (2C), 127.8, 127.72, 127.65, 126.9, 126.6, 126.3, 126.2, 125.7, 125.4 (q, *J* = 4.2 Hz), 123.5 (q, *J* = 271.5 Hz), 117.6, 85.8, 69.4, 52.9, 40.0; ^{19}F NMR (565 MHz, $CDCl_3$) δ –63.0; IR (ATR): 3061, 3033, 2926, 2875**,** 2233, 1693, 1451, 1409, 1324, 1219, 1170, 1129, 1066, 772, 701 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{29}F_3NO_2$ $[M]^+$ 549.1916, Found 549.1915; mp. 99.0-101.0 °C.

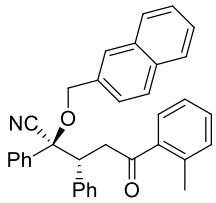
(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,3-diphenyl-5-(*m*-tolyl)pentanenitrile (4bf):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (17.5 mg, 70% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 9.7 (minor), 11.4 (major) min; 89% ee; Optical rotation $[\alpha]_D^{22}$ = +104.6 (*c* 1.2, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.83-7.82 (m, 1H), 7.79-7.76 (m, 2H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.68 (s, 2H), 7.50-7.47 (m, 2H), 7.38-7.35 (m, 2H), 7.35-7.31 (m, 4H), 7.29-7.25 (m, 2H), 7.13-7.10 (m, 3H), 7.06-7.05 (m, 2H), 4.75 (d, *J* = 11.4 Hz, 1H), 4.47 (d, *J* = 11.4 Hz, 1H), 4.18 (dd, *J* = 8.4,

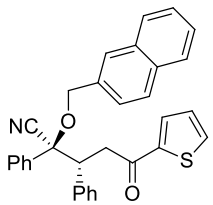
4.8 Hz, 1H), 4.11 (dd, *J* = 17.4, 4.8 Hz, 1H), 3.71 (dd, *J* = 17.4, 8.4 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.4, 138.3, 137.0, 136.9, 135.6, 133.81, 133.75, 133.1, 133.0, 129.3, 129.2, 128.6 (2C), 128.3, 128.1, 128.0, 127.9, 127.7, 127.5, 126.60, 126.57, 126.13, 126.06, 125.6, 125.3, 117.8, 85.7, 69.2, 52.7, 39.7, 21.2; IR (ATR): 3060, 3031, 2921, 2864**,** 2233, 1684, 1602, 1449, 1344, 1272, 1219, 1081, 814, 771, 751, 700 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{29}NO_2$ $[M]^+$ 495.2198, Found 495.2196; mp. 127.0-129.0 °C.

(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,3-diphenyl-5-(*o*-tolyl)pentanenitrile (4bg):



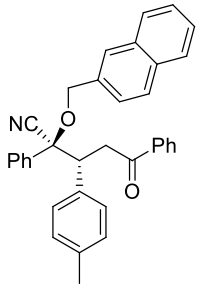
Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (12.4 mg, 50% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 220 nm, 25 °C) 7.3 (minor), 9.3 (major) min; 41% ee; Optical rotation $[\alpha]_D^{22}$ = +23.2 (*c* 0.4, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85-7.83 (m, 1H), 7.82-7.80 (m, 2H), 7.74 (s, 1H), 7.62 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.52-7.49 (m, 2H), 7.40-7.36 (m, 3H), 7.35-7.32 (m, 3H), 7.30 (ddd, *J* = 7.8, 7.2, 1.2 Hz, 1H), 7.20 (dd, *J* = 7.8, 7.2 Hz, 1H), 7.16-7.10 (m, 3H), 7.07 (d, *J* = 7.8 Hz, 1H), 7.02 (d, *J* = 7.2 Hz, 2H), 4.77 (d, *J* = 11.4 Hz, 1H), 4.48 (d, *J* = 11.4 Hz, 1H), 4.10 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.01 (dd, *J* = 16.8, 4.8 Hz, 1H), 3.70 (dd, *J* = 16.8, 9.0 Hz, 1H), 2.09 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 201.4, 138.1, 138.0, 136.8, 135.6, 133.9, 133.2, 133.0, 131.7, 131.1, 129.34, 129.29, 128.6, 128.21, 128.18, 128.0, 127.9, 127.7, 127.5, 126.9, 126.6, 126.2, 126.1, 125.8, 125.5, 117.7, 85.6, 69.4, 52.8, 42.7, 20.7; IR (ATR): 3060, 3029, 2926, 2865**,** 2233, 1687, 1602, 1450, 1216, 1081, 856, 815, 748, 699 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{29}NO_2$ $[M]^+$ 495.2198, Found 495.2197; mp. 100.0-102.0 °C.

(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,3-diphenyl-5-(thiophen-2-yl)pentanenitrile (4bh):



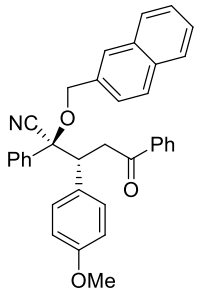
Purified by silica gel flash column chromatography (Hexane/EtOAc = 12/1); White solid (15.8 mg, 65% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 13.1 (minor), 14.8 (major) min; 79% ee; Optical rotation $[\alpha]_D^{22}$ = +102.5 (*c* 0.7, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.81-7.79 (m, 2H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.67 (s, 1H), 7.51-7.47 (m, 3H), 7.37-7.35 (m, 2H), 7.34-7.31 (m, 4H), 7.16-7.11 (m, 3H), 7.06-7.03 (m, 3H), 4.73 (d, *J* = 10.8 Hz, 1H), 4.46 (d, *J* = 11.4 Hz, 1H), 4.16 (dd, *J* = 7.8, 6.0 Hz, 1H), 4.06 (dd, *J* = 16.2, 6.0 Hz, 1H), 3.60 (dd, *J* = 16.2, 7.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.1, 144.3, 136.7, 135.5, 133.7 (2C), 133.1, 132.9, 131.9, 129.3, 129.2, 128.6, 128.11, 128.05, 128.0, 127.9, 127.63, 127.58, 126.6, 126.5, 126.1, 126.0, 125.5, 117.6, 85.8, 69.3, 52.8, 40.5; IR (ATR): 3060, 3031, 2956, 2926, 2860**,** 2232, 1662, 1518, 1415, 1220, 1080, 771, 700 cm^{-1}; HRMS (FD+) Calcd for $C_{32}H_{25}NO_2S$ $[M]^+$ 487.1606, Found 487.1604; mp. 156.0-158.0 °C.

(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,5-diphenyl-3-(*p*-tolyl)pentanenitrile (4bi):



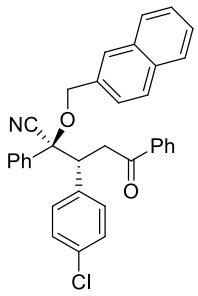
Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (20.7 mg, 84% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 9.9 (minor), 15.0 (major) min; 87% ee; Optical rotation $[\alpha]_D^{22}$ = +116.0 (*c* 1.5, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* 7.2 Hz, 2H), 7.83-7.81 (m, 1H), 7.79-7.76 (m, 2H), 7.67 (s, 1H), 7.50-7.46 (m, 3H), 7.39-7.32 (m, 8H), 6.94 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 4.74 (d, *J* = 11.4 Hz, 1H), 4.46 (d, *J* = 11.4 Hz, 1H), 4.15 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.10 (dd, *J* = 17.2, 4.8 Hz, 1H), 3.70 (dd, *J* = 17.2, 8.4 Hz, 1H), 2.23 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.4, 137.1, 136.9, 135.7, 133.84, 133.82, 133.1, 133.0, 132.9, 129.2, 129.0, 128.7, 128.6, 128.4, 128.11, 128.07, 127.9, 127.6, 126.6 (2C), 126.13, 126.05, 125.6, 117.8, 85.8, 69.3, 52.3, 39.6, 21.0; IR (ATR): 3059, 3024, 2968, 2917, 2866**,** 2232, 1686, 1598, 1492, 1448, 1360, 1272, 1213, 1082, 1002, 815, 731 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{29}NO_2$ $[M]^+$ 495.2198, Found 495.2198; mp. 92.0-94.0 °C.

(2*S*,3*R*)-3-(4-methoxyphenyl)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,5-diphenylpentanenitrile (4bj):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 12/1); White solid (23.1 mg, 90% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 12.1 (minor), 20.3 (major) min; 91% ee; Optical rotation $[\alpha]_D^{22}$ = +115.4 (*c* 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.2 Hz, 2H), 7.83-7.81 (m, 1H), 7.79-7.77 (m, 2H), 7.68 (s, 1H), 7.49-7.46 (m, 3H), 7.38-7.32 (m, 8H), 6.96 (d, *J* = 9.0 Hz, 2H), 6.65 (d, *J* = 9.0 Hz, 2H), 4.74 (d, *J* = 11.4 Hz, 1H), 4.46 (d, *J* = 11.4 Hz, 1H), 4.12 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.08 (dd, *J* = 16.8, 4.8 Hz, 1H), 3.72 (s, 3H), 3.69 (dd, *J* = 16.8, 8.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.4, 158.8, 136.9, 135.7, 133.8, 133.1, 133.0, 132.9, 130.2, 129.2, 128.9, 128.6, 128.4, 128.12, 128.06, 127.9, 127.7, 126.64, 126.60, 126.14, 126.06, 125.6, 117.8, 113.4, 85.8, 69.3, 55.1, 51.9, 39.7; IR (ATR): 3059, 3024, 2932, 2836**,** 2232, 1685, 1513, 1448, 1361, 1250, 1180, 1080, 1034, 816, 752, 701 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{29}NO_3$ $[M]^+$ 511.2147, Found 511.2146; mp. 83.0-85.0 °C.

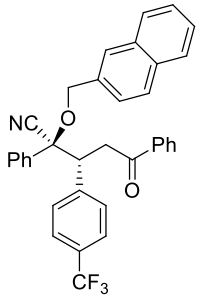
(2*S*,3*R*)-3-(4-chlorophenyl)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,5-diphenylpentanenitrile (4bk):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (19.3 mg, 75% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm,

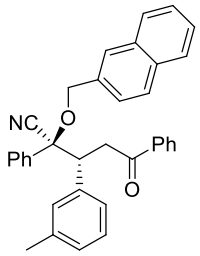
25 °C) 9.8 (minor), 15.3 (major) min; 86% ee; Optical rotation $[\alpha]_D^{22}$ = +109.5 (*c* 1.3, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.2 Hz, 2H), 7.84-7.82 (m, 1H), 7.79-7.78 (m, 2H), 7.69 (s, 1H), 7.51-7.49 (m, 3H), 7.39-7.36 (m, 7H), 7.34 (dd, *J* = 9.0, 1.8 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 4.75 (d, *J* = 10.8 Hz, 1H), 4.47 (d, *J* = 10.8 Hz, 1H), 4.14 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.08 (dd, *J* = 17.4, 4.8 Hz, 1H), 3.71 (dd, *J* = 17.4, 9.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.0, 136.7, 135.5, 135.3, 133.6, 133.4, 133.2, 133.1, 133.0, 130.5, 129.5, 128.8, 128.5, 128.3, 128.2, 128.0, 127.9, 127.7, 126.8, 126.5, 126.21, 126.16, 125.6, 117.6, 85.3, 69.4, 52.1, 39.5; IR (ATR): 3059, 3029, 2924, 2874**,** 2233, 1685, 1598, 1493, 1448, 1264, 1206, 1068, 1052, 954, 752, 700 cm^{-1}; HRMS (FD+) Calcd for $C_{34}H_{26}ClNO_2$ $[M]^+$ 515.1652, Found 515.1650; mp. 91.0-93.0 °C.

(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,5-diphenyl-3-(4-(trifluoromethyl)phenyl) pentanenitrile (4bl):



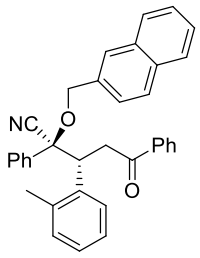
Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (16.4 mg, 59% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 8.6 (minor), 13.3 (major) min; 76% ee; Optical rotation $[\alpha]_D^{22}$ = +100.6 (*c* 0.9, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.2 Hz, 2H), 7.84-7.82 (m, 1H), 7.81-7.78 (m, 2H), 7.70 (s, 1H), 7.52-7.48 (m, 3H), 7.40-7.35 (m, 10H), 7.19 (d, *J* = 7.2 Hz, 2H), 4.77 (d, *J* = 10.8 Hz, 1H), 4.49 (d, *J* = 10.8 Hz, 1H), 4.23 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.12 (dd, *J* = 17.4, 4.8 Hz, 1H), 3.78 (dd, *J* = 17.4, 9.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.8, 141.1, 136.6, 135.1, 133.5, 133.3, 133.1, 133.0, 129.70 (q, *J* = 31.5 Hz), 129.65, 129.6, 128.9, 128.6, 128.3, 128.0, 127.9, 127.7, 126.8, 126.5, 126.24, 126.20, 125.6, 125.0 (q, *J* = 2.9 Hz), 123.9 (q, *J* = 270.0 Hz), 117.5, 85.1, 69.5, 52.5, 39.4; ^{19}F NMR (565 MHz, $CDCl_3$) δ –62.5; IR (ATR): 3059, 3028, 2958, 2929, 2861**,** 2233, 1724, 1687, 1449, 1324, 1166, 1117, 1065, 816, 753, 701 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{26}F_3NO_2$ $[M]^+$ 549.1916, Found 549.1914; mp. 113.0-115.0 °C.

(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,5-diphenyl-3-(*m*-tolyl)pentanenitrile (4bm):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (21.6 mg, 87% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 8.7 (minor), 10.7 (major) min; 90% ee; Optical rotation $[\alpha]_D^{22}$ = +107.9 (*c* 1.4, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.83-7.82 (m, 1H), 7.78-7.76 (m, 2H), 7.68 (s, 1H), 7.49-7.47 (m, 3H), 7.37-7.32 (m, 8H), 7.01 (dd, *J* = 7.8, 7.2 Hz, 1H), 6.94 (d, *J* = 7.2 Hz, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 6.81 (s, 1H), 4.75 (d, *J* = 11.4 Hz, 1H), 4.47 (d, *J* = 11.4 Hz, 1H), 4.14-4.08 (m, 2H), 3.71 (dd, *J* = 16.8, 7.8 Hz, 1H), 2.17 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.3, 137.5, 136.9, 136.8, 135.7, 133.8, 133.1, 133.0, 132.9, 130.1, 129.2, 128.5 (2C), 128.4, 128.2, 128.11, 128.07, 127.9, 127.8, 127.6, 126.64, 126.62, 126.12, 126.05, 125.6, 117.7, 85.7, 69.3, 52.6, 39.5, 21.3; IR (ATR): 3058, 3026, 2920, 2866**,** 2233, 1686, 1598, 1448, 1360, 1270, 1217, 1082, 1002, 752, 699 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{29}NO_2$ $[M]^+$ 495.2198, Found 495.2197; mp. 58.0-60.0 °C.

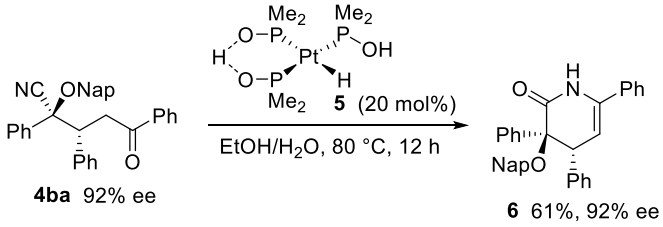
(2*S*,3*R*)-2-(naphthalen-2-ylmethoxy)-5-oxo-2,5-diphenyl-3-(*o*-tolyl)pentanenitrile (4bn):



Purified by silica gel flash column chromatography (Hexane/EtOAc = 19/1); White solid (16.8 mg, 68% yield); HPLC analysis DAICEL Chiralcel IA-3 (Hexane/IPA = 92/8, 0.8 mL/min, 254 nm, 25 °C) 7.2 (minor), 8.4 (major) min; 68% ee; Optical rotation $[\alpha]_D^{22}$ = +84.7 (*c* 0.9, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.2 Hz, 2H), 7.86-7.84 (m, 1H), 7.83-7.81 (m, 2H), 7.76 (s, 1H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.52-7.47 (m, 3H), 7.41 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.38-7.28 (m,

7H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.07 (t, *J* = 7.8 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 4.85 (d, *J* = 10.8 Hz, 1H), 4.58 (d, *J* = 10.8 Hz, 1H), 4.44 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.06 (dd, *J* = 17.4, 4.8 Hz, 1H), 3.76 (dd, *J* = 17.4, 9.0 Hz, 1H), 1.88 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.5, 138.2, 136.9, 135.8, 135.2, 133.9, 133.2, 133.00, 132.96, 130.3, 129.2, 128.5, 128.4, 128.2, 128.0, 127.9, 127.7, 127.3, 127.2, 126.64, 126.59, 126.2, 126.1, 125.8, 125.6, 118.2, 85.2, 69.2, 46.7, 41.0, 19.4; IR (ATR): 3058, 3026, 2920, 2863**,** 2233, 1686, 1598, 1513, 1448, 1360, 1270, 1219, 1083, 1002, 815, 752, 700, 688 cm^{-1}; HRMS (FD+) Calcd for $C_{35}H_{29}NO_2$ $[M]^+$ 495.2198, Found 495.2196; mp. 117.0-119.0 °C.

Transformation of product

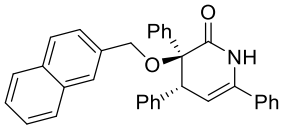


4ba 92% ee

6 61%, 92% ee

To a dried test tube were added **4ba** (24.1 mg, 0.050 mmol, 92% ee), Pt catalyst **5** (4.3 mg, 0.010 mmol), EtOH (0.40 mL) and H_2O (0.10 mL) under argon atmosphere. The reaction mixture was stirred at 80 °C for 12 h. After cooled to room temperature, the mixture was diluted with EtOAc (2.0 mL) and H_2O (2.0 mL), and the product was extracted with EtOAc (2.0 mL × 3). The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash chromatography (Hexane/EtOAc = 3/1) to afford **6** (14.7 mg, 61% yield) as a white solid with 92% ee.

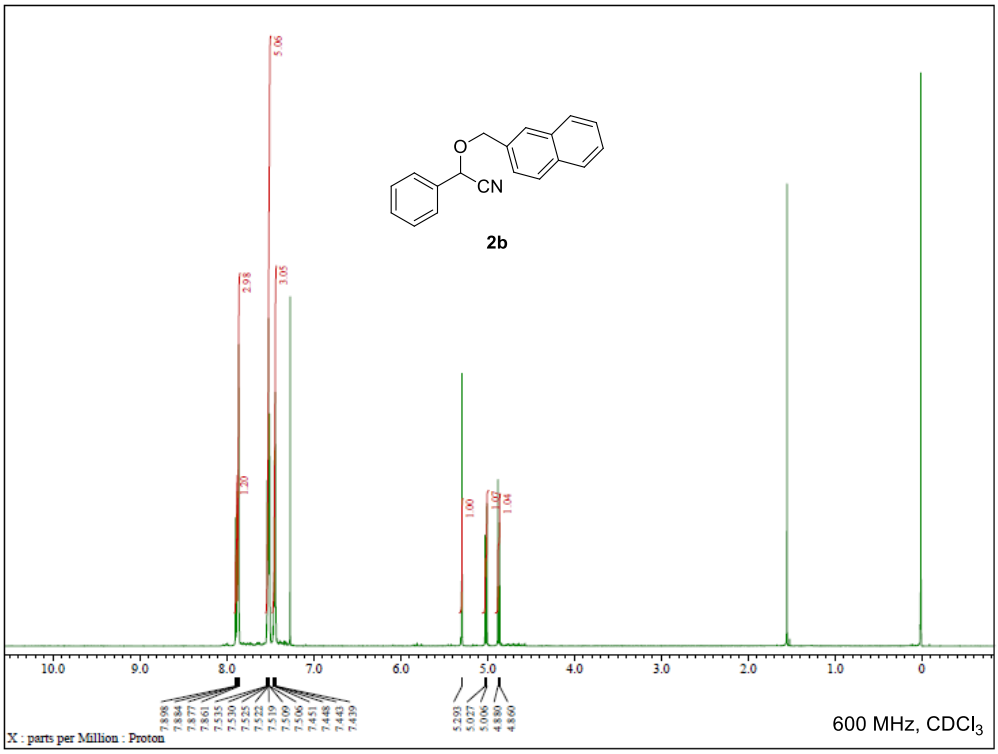
(3*S*,4*R*)-3-(naphthalen-2-ylmethoxy)-3,4,6-triphenyl-3,4-dihydropyridin-2(1*H*)-one (6):

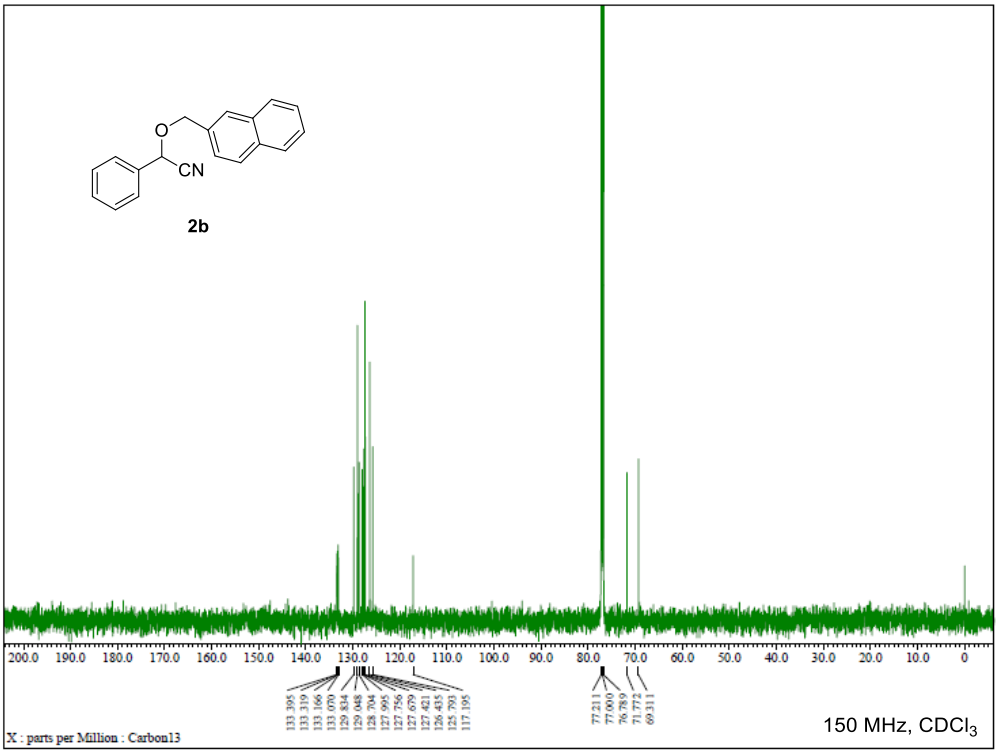


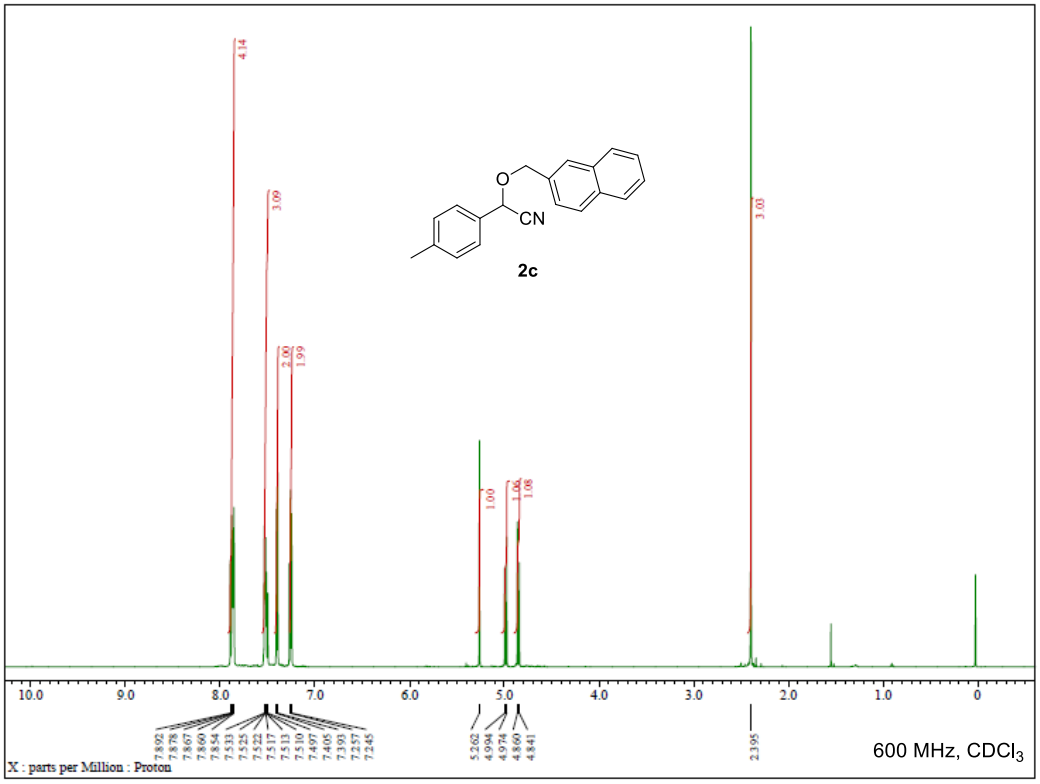
Purified by silica gel flash column chromatography (Hexane/EtOAc = 3/1); White solid (14.7 mg, 61% yield); HPLC analysis DAICEL Chiralcel AD-3 (Hexane/IPA = 90/10, 0.9 mL/min, 254 nm, 30 °C) 17.6 (minor), 19.2 (major) min; 92% ee; Optical rotation $[\alpha]_D^{22}$ = +414.6 (*c* 0.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.82-7.79 (m, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.73-7.66

(m, 2H), 7.50-7.37 (m, 8H), 7.19 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.17-7.11 (m, 5H), 7.06 (dd, *J* = 7.8, 7.2 Hz, 2H), 6.80 (d, *J* = 7.2 Hz, 2H), 5.77 (dd, *J* = 5.4, 1.8 Hz, 1H), 4.86 (d, *J* = 12.6 Hz, 1H), 4.78 (d, *J* = 12.6 Hz, 1H), 4.13 (d, *J* = 5.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.0, 136.6, 136.0, 135.7, 135.0, 134.5, 133.3, 132.8, 129.4, 129.00, 128.99, 128.2, 127.98, 127.96, 127.92, 127.61, 127.56, 127.3, 127.2, 125.9, 125.71, 125.68, 125.5, 125.0, 107.3, 83.8, 67.9, 54.2; IR (ATR): 3220, 3060, 3029, 2934, 1681, 1496, 1453, 1376, 1257, 1057, 786, 758 cm^{-1}; HRMS (FD+) Calcd for $C_{34}H_{27}NO_2$ $[M]^+$ 481.2042, Found 481.2041; mp. 96.0-98.0 °C.

4. ^{1}H NMR and ^{13}C NMR Spectra



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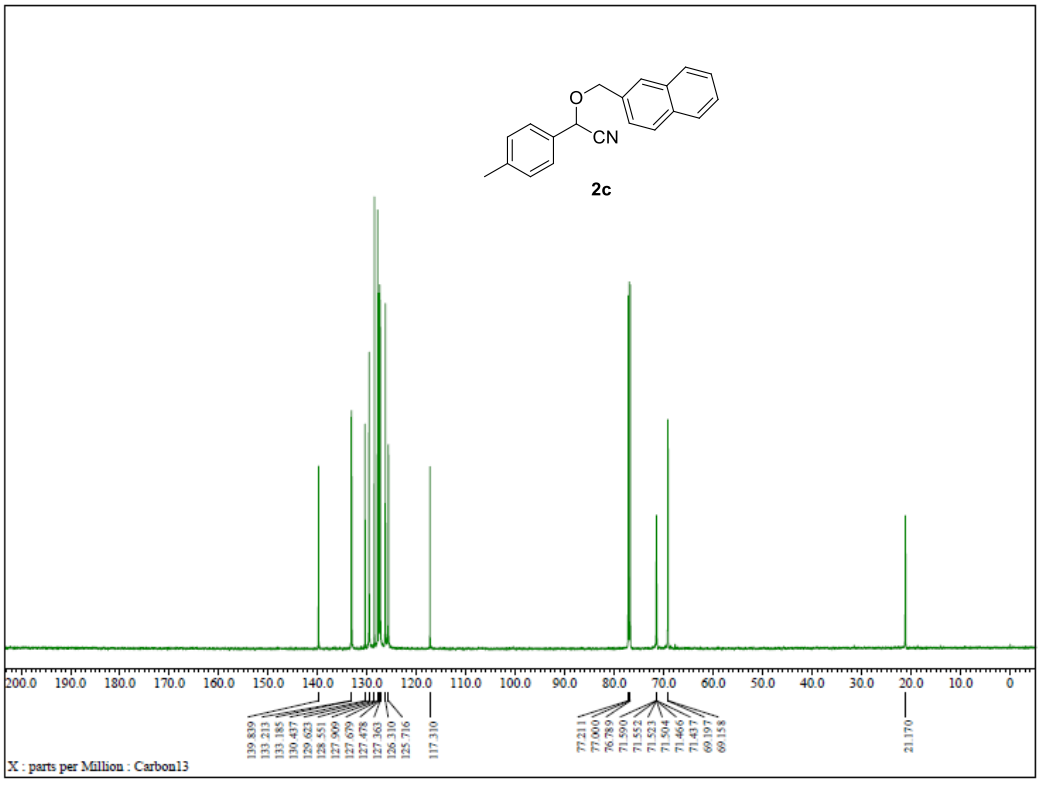
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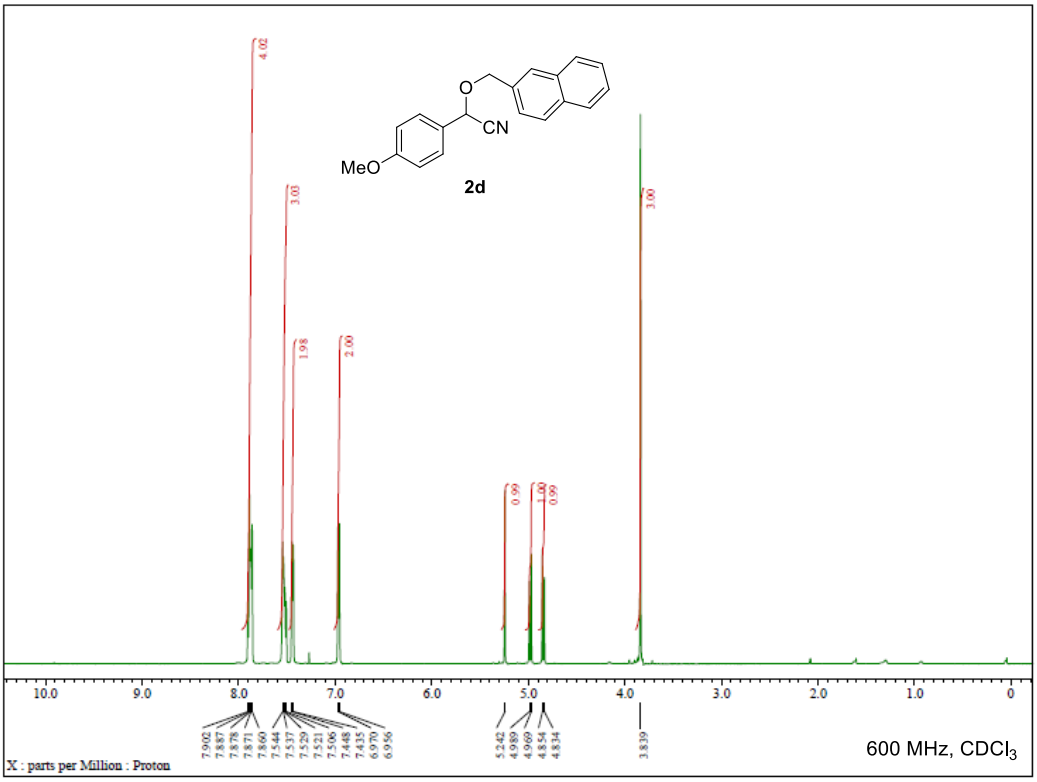
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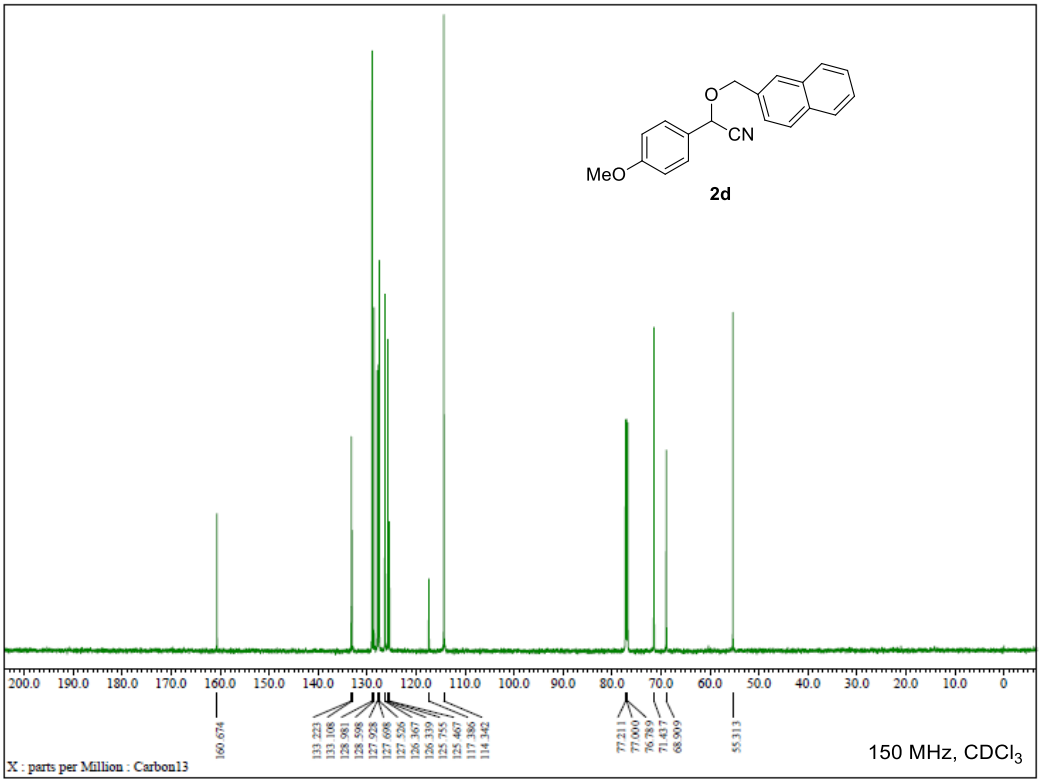
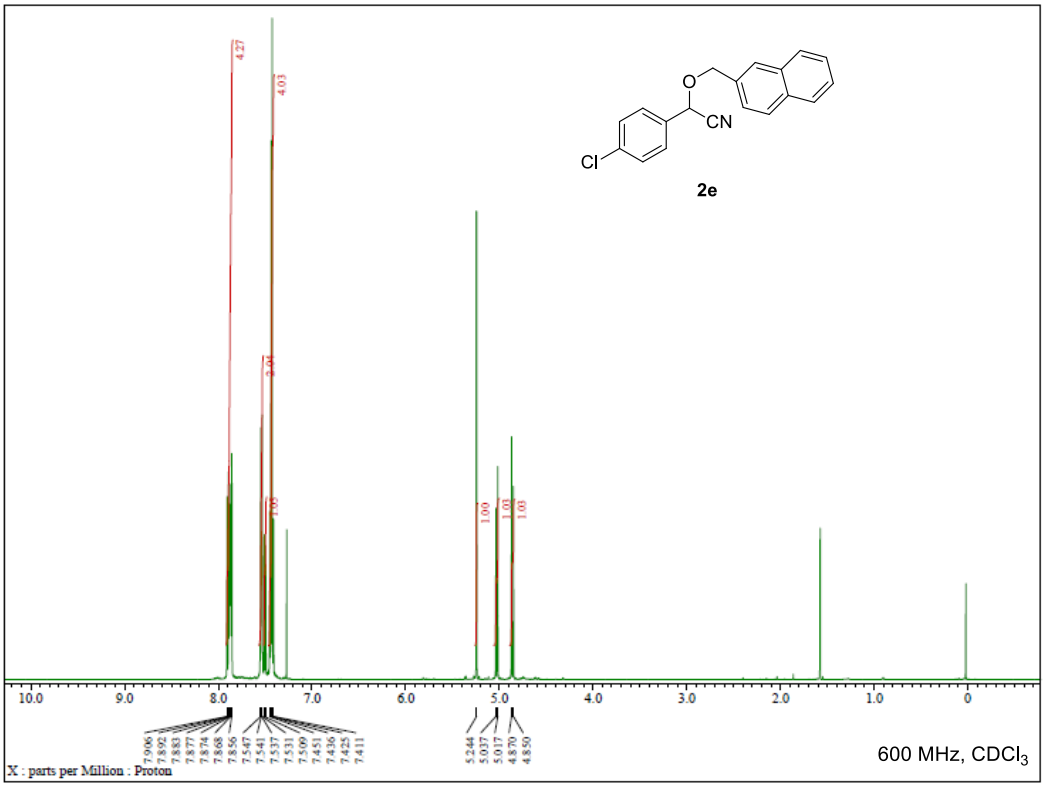
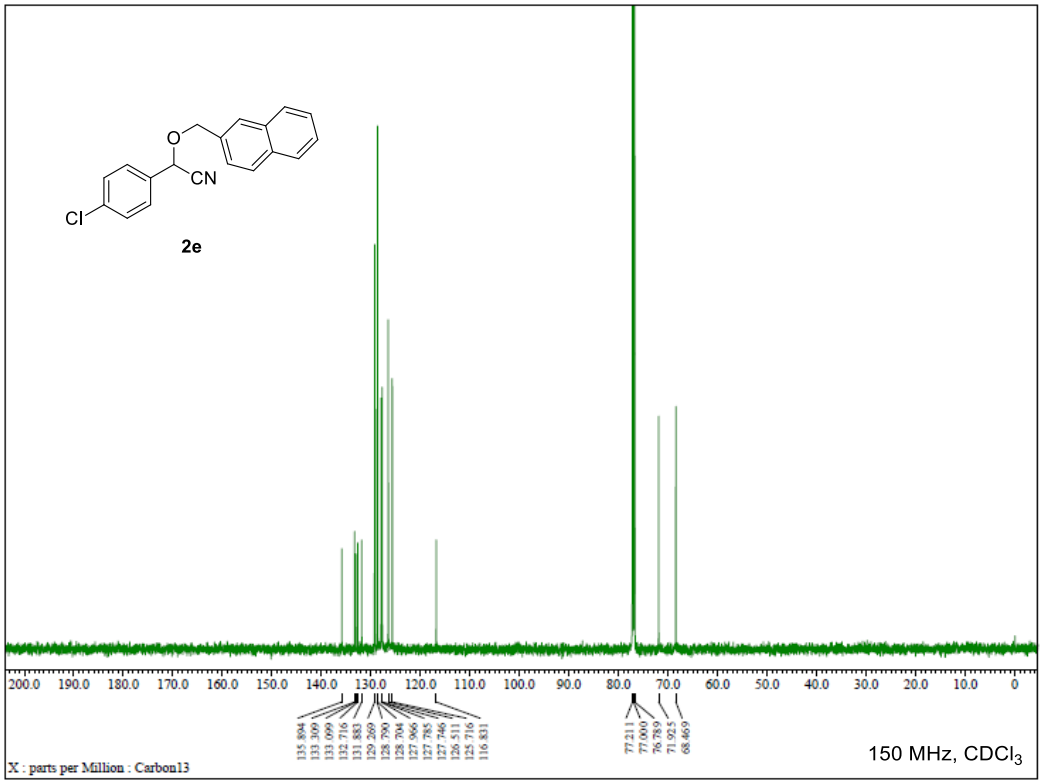
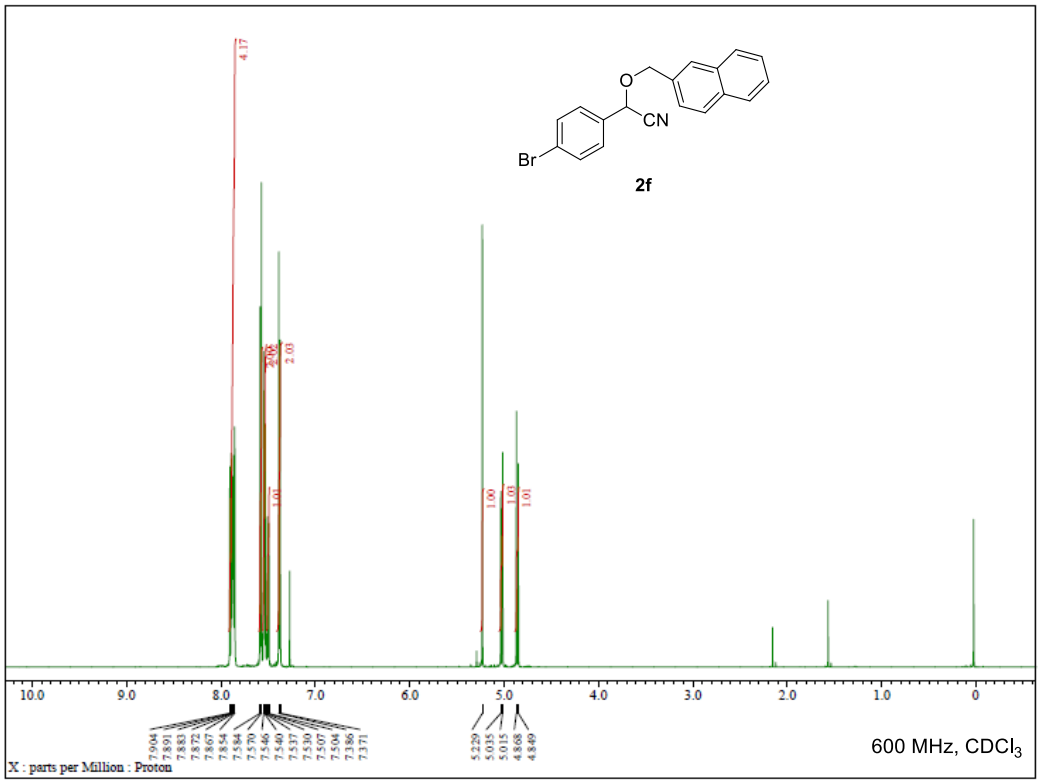
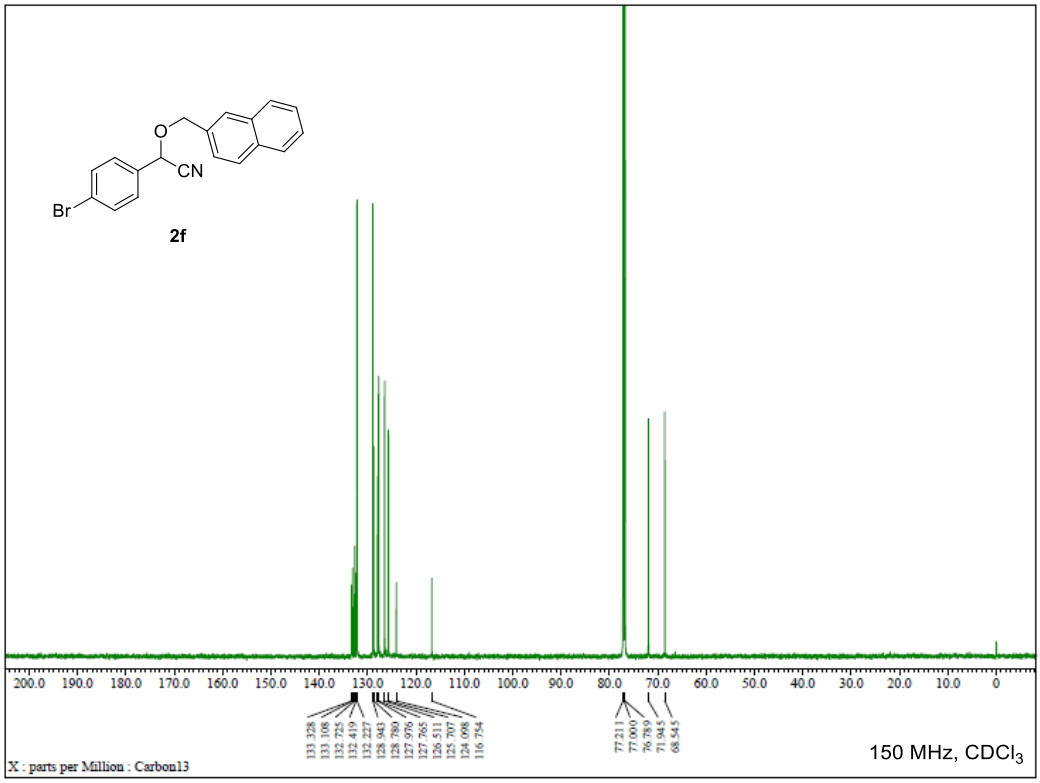
600 MHz, CDCl3

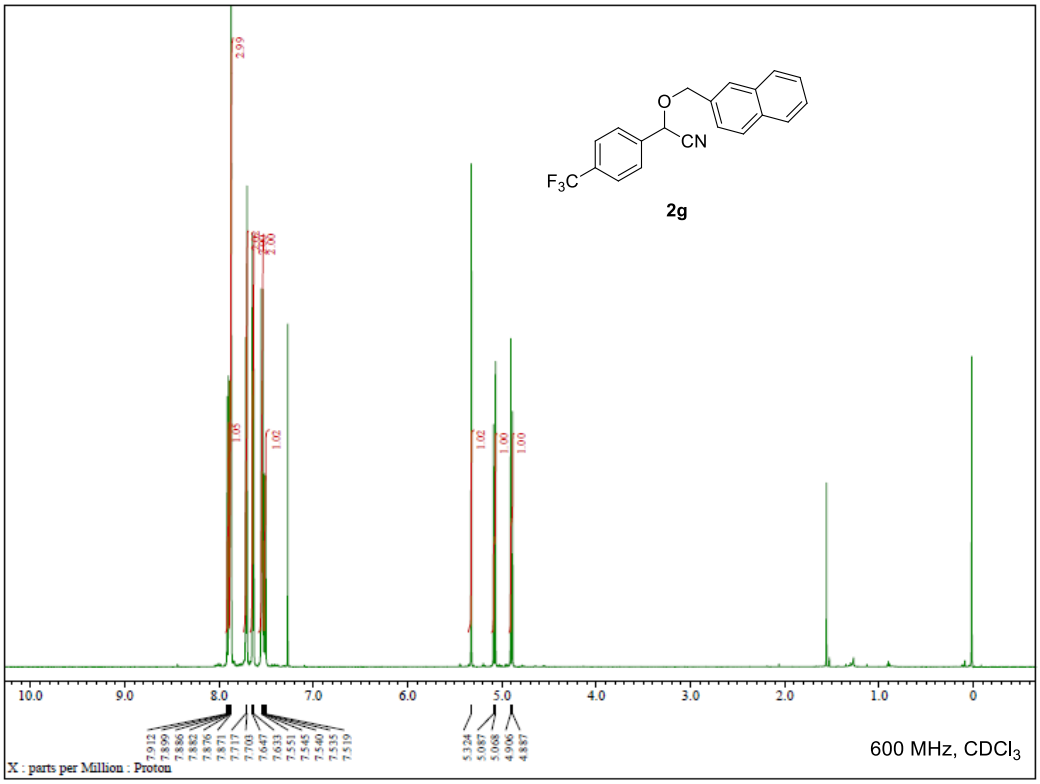

MeO
O
CN
2d
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
160.674
133.223
133.108
128.981
128.598
127.928
127.698
127.526
126.367
126.339
125.755
125.467
117.386
114.342
77.211
77.000
76.789
71.437
68.909
55.313
X : parts per Million : Carbon13
150 MHz, CDCl3

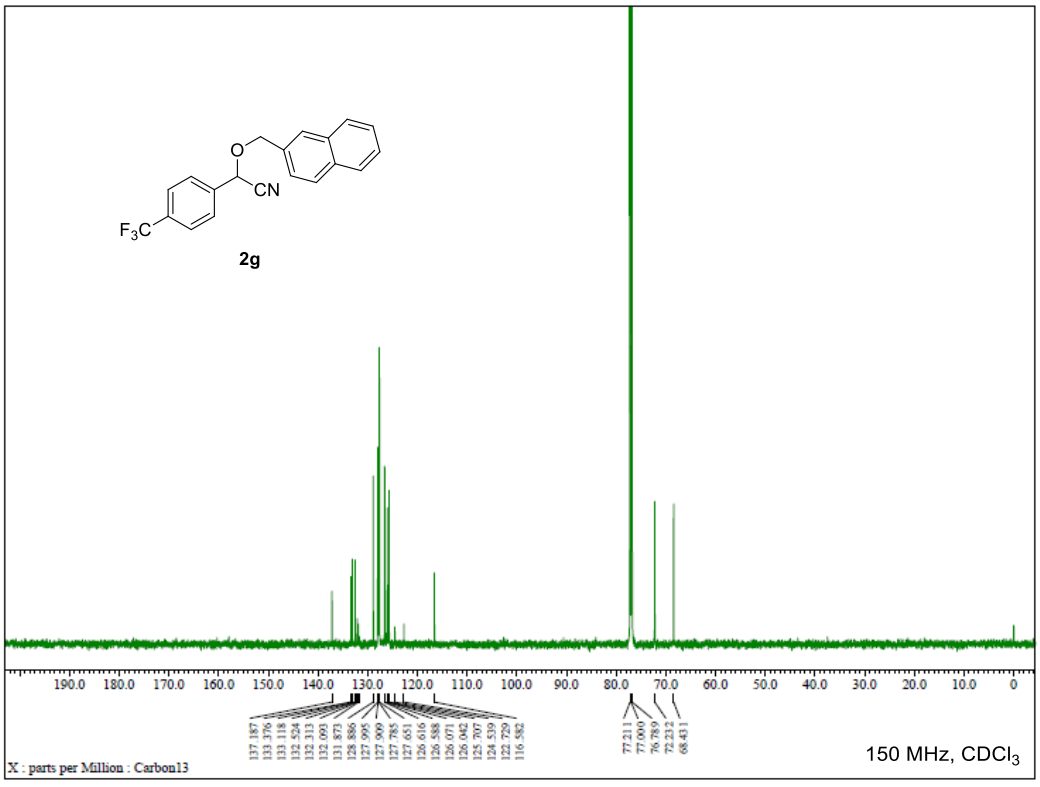

4.27
4.03
2.04
2.00
1.00
1.01
1.08
O
CN
Cl
2e
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.906
7.892
7.883
7.877
7.874
7.868
7.856
7.547
7.541
7.537
7.531
7.509
7.451
7.436
7.425
7.411
5.244
5.037
5.017
4.870
4.850
X : parts per Million : Proton
600 MHz, CDCl3

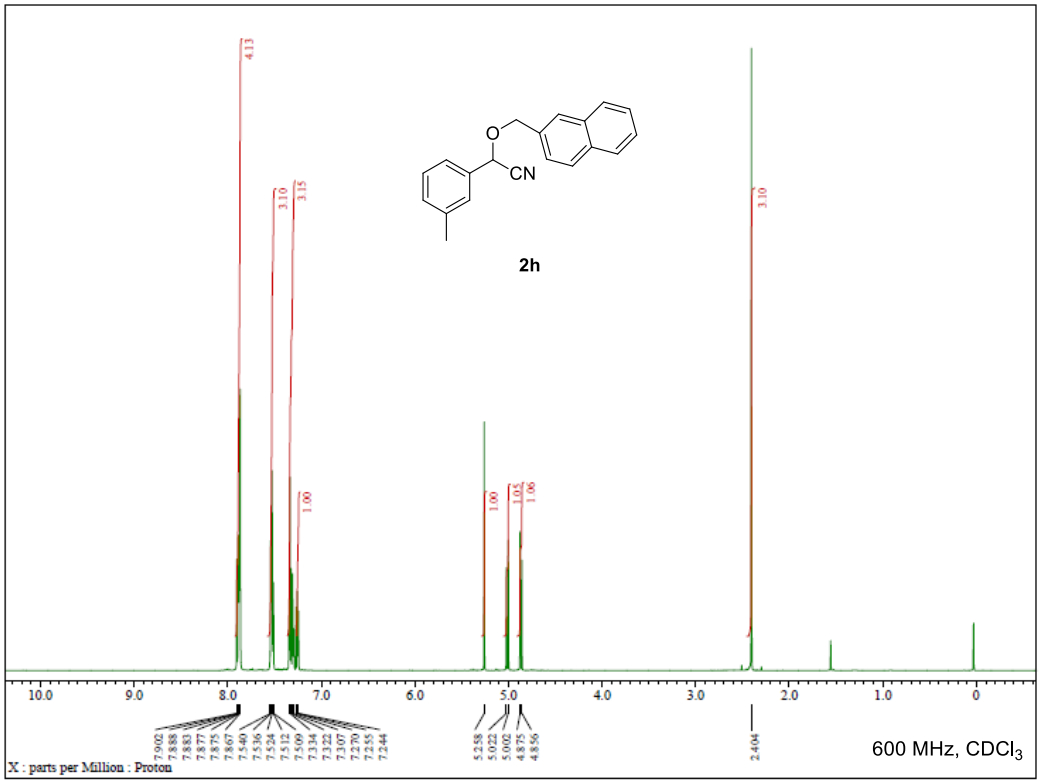

O
CN
Cl
2e
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
135.894
133.309
133.099
132.716
131.883
129.269
128.790
128.704
127.966
127.785
127.746
126.511
125.716
116.831
77.211
77.000
76.789
71.925
68.469
X : parts per Million : Carbon13
150 MHz, CDCl3

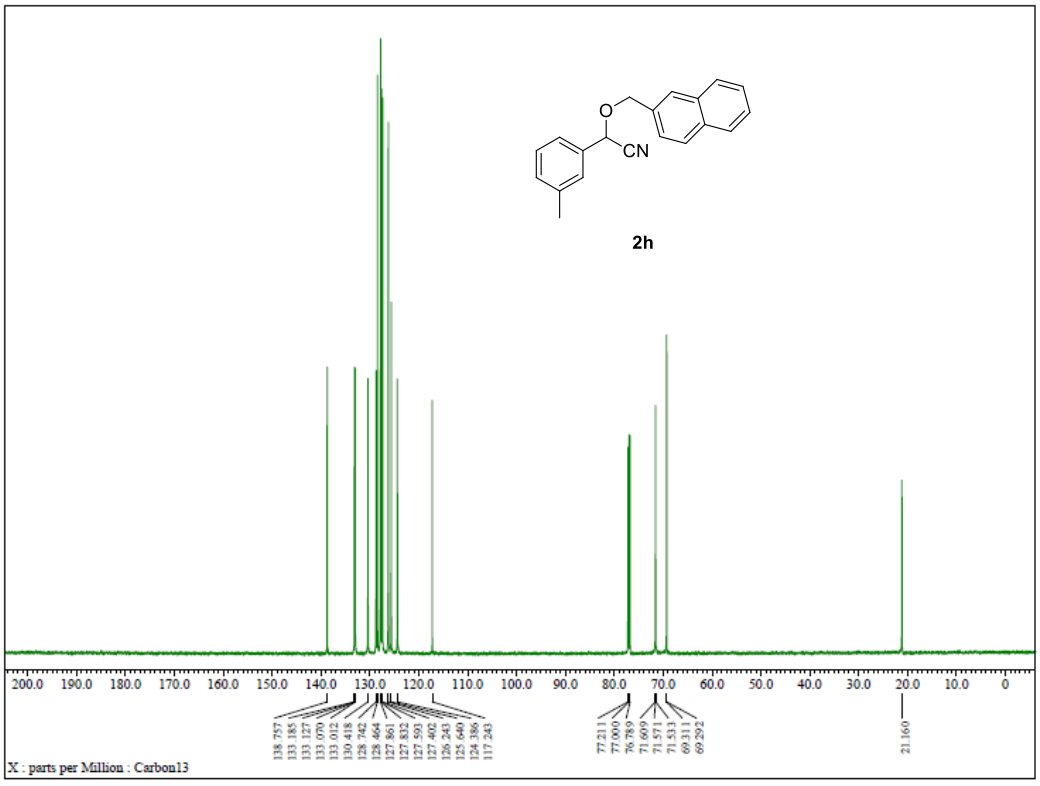

Br
O
CN
2f
600 MHz, CDCl3
X : parts per Million : Proton

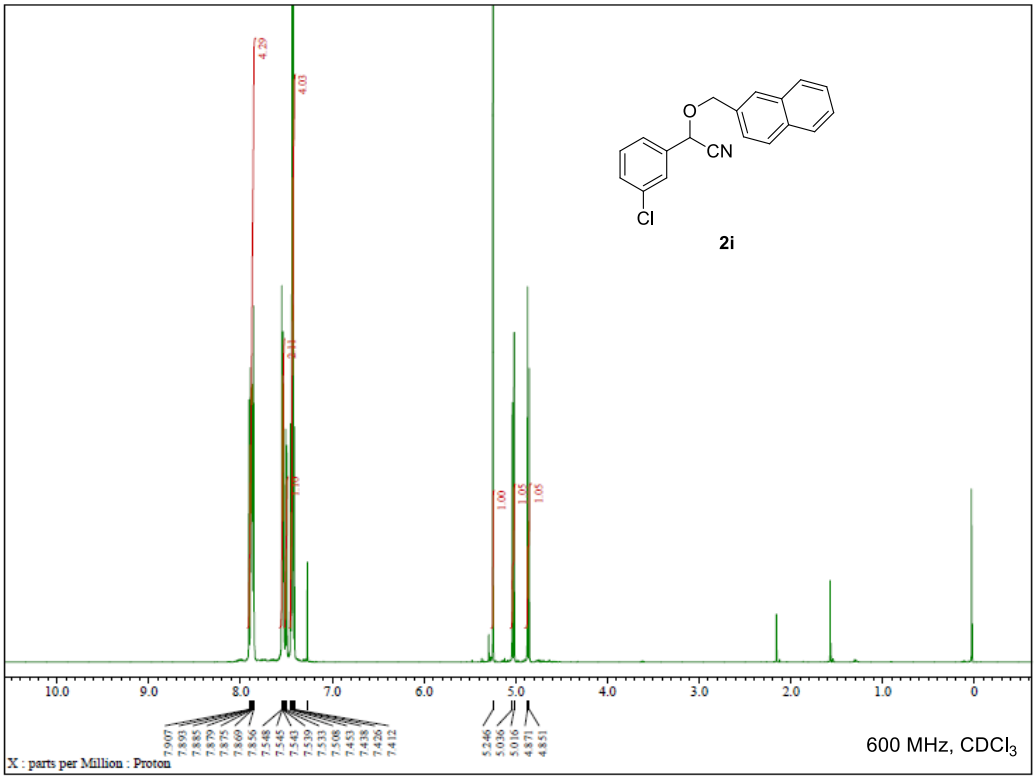

Br
O
CN
2f
150 MHz, CDCl3
X : parts per Million : Carbon13

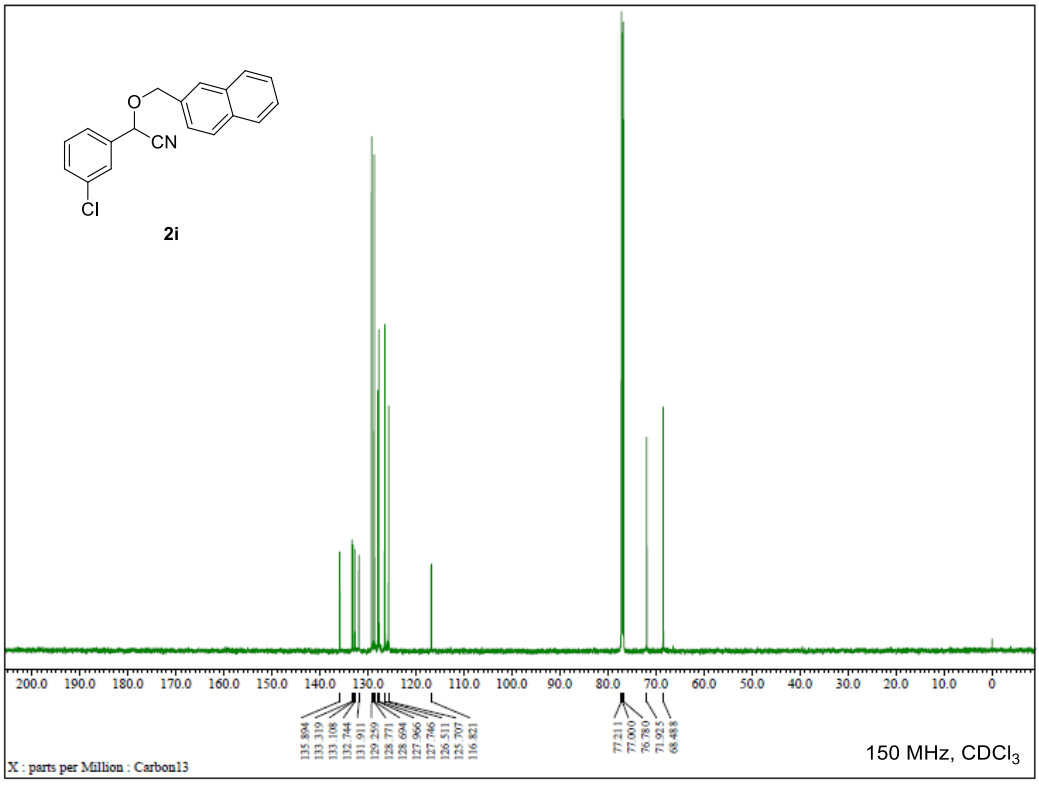

2g
600 MHz, CDCl3
X : parts per Million : Proton

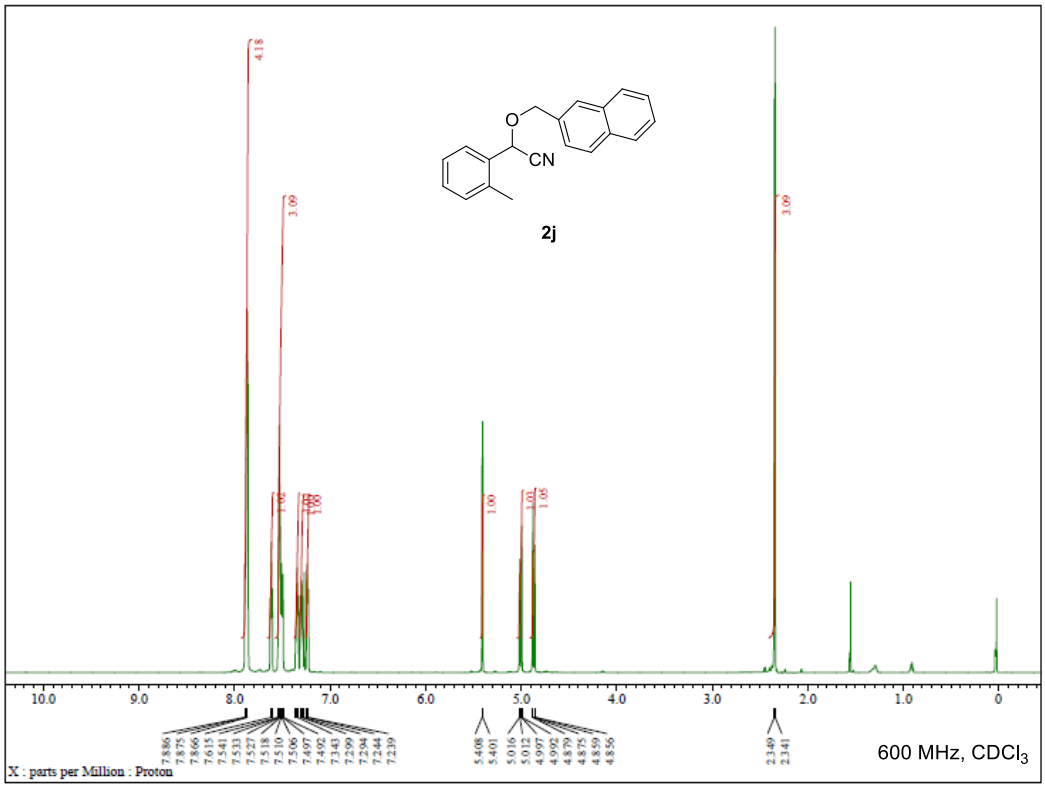

2g
150 MHz, CDCl3
X : parts per Million : Carbon13

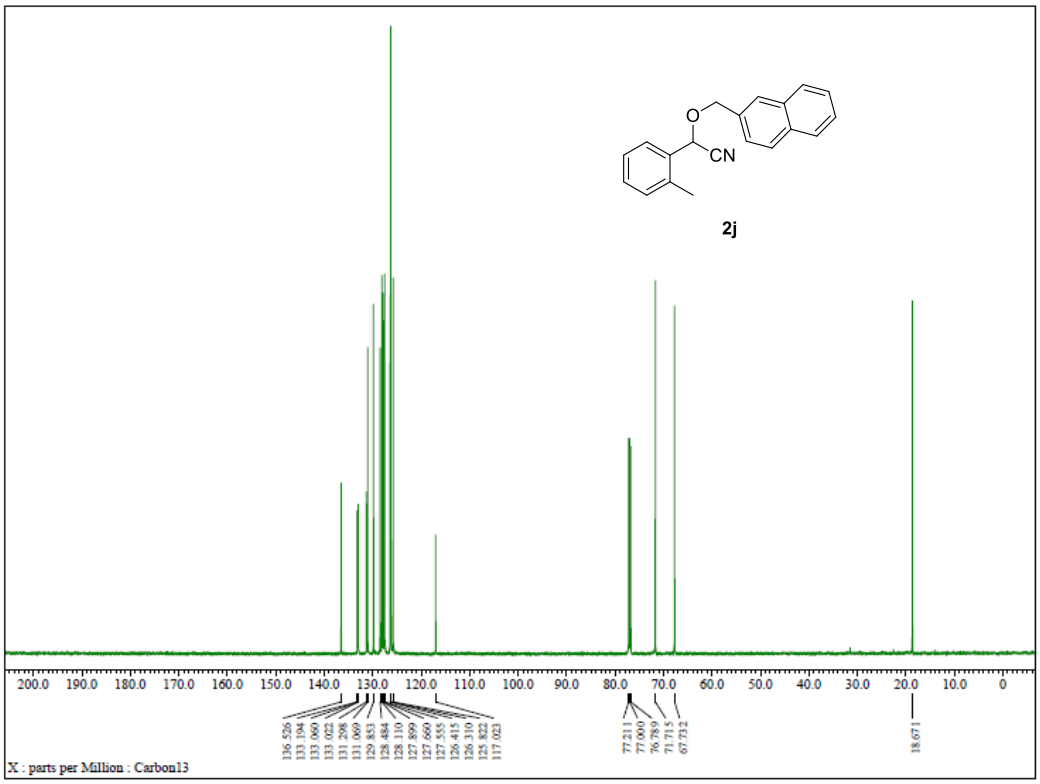

O
CN
2h
X : parts per Million : Proton
600 MHz, CDCl3


O
CN
2h
X : parts per Million : Carbon13
150 MHz, CDCl3

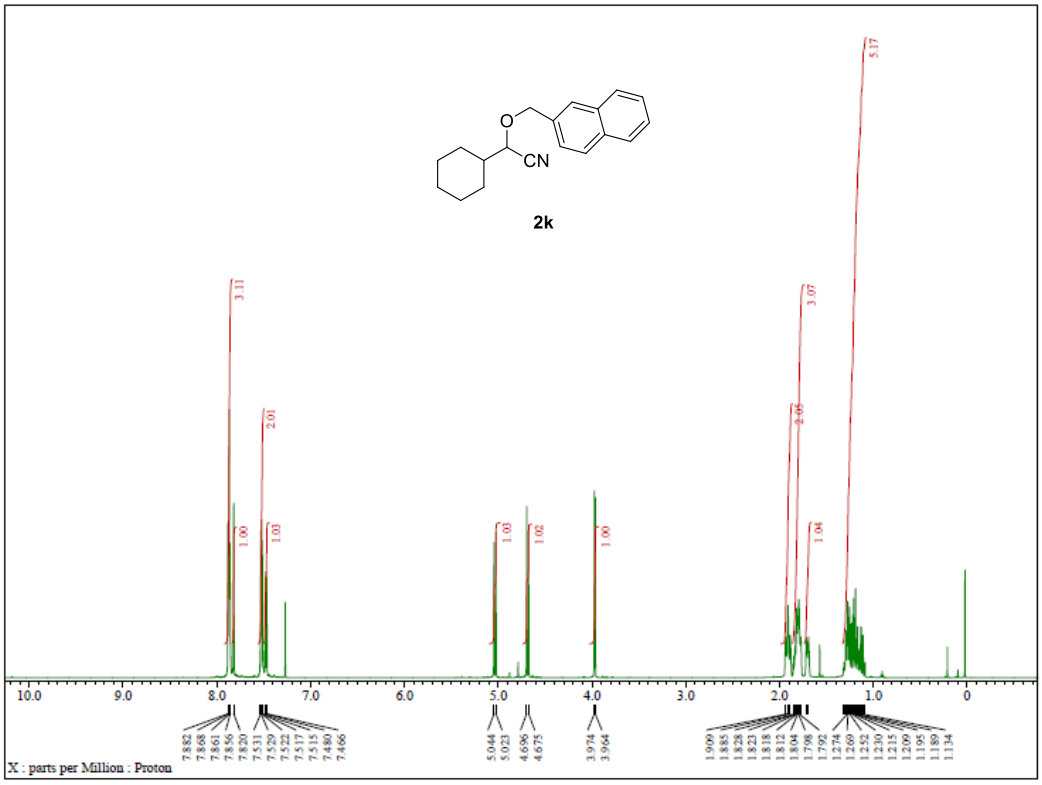

O
CN
Cl
2i
4.29
4.03
2.11
4.00
1.00
1.05
1.05
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.907
7.893
7.885
7.879
7.875
7.869
7.856
7.548
7.545
7.543
7.539
7.533
7.508
7.453
7.438
7.426
7.412
5.246
5.036
5.016
4.871
4.851
X : parts per Million : Proton
600 MHz, CDCl3


O
CN
Cl
2i
200.0
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
135.894
133.319
133.108
132.744
131.911
129.259
128.771
128.694
127.966
127.746
126.511
125.707
116.821
77.211
77.000
76.789
71.925
68.488
X : parts per Million : Carbon13
150 MHz, CDCl3

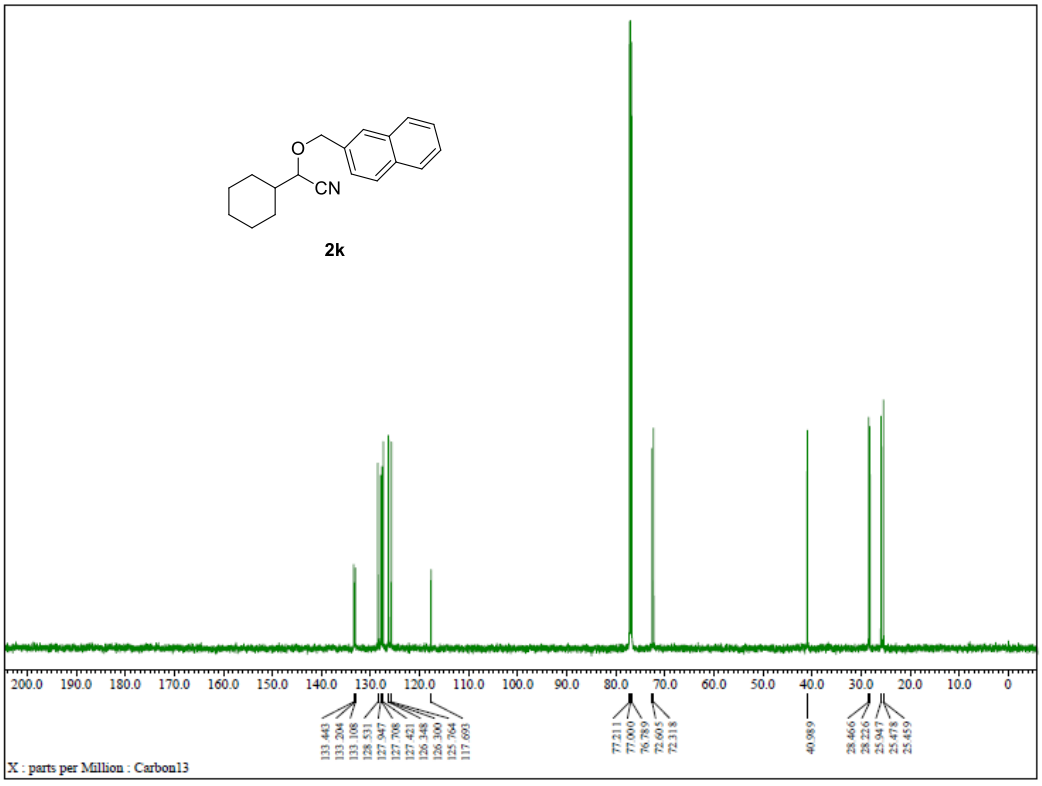




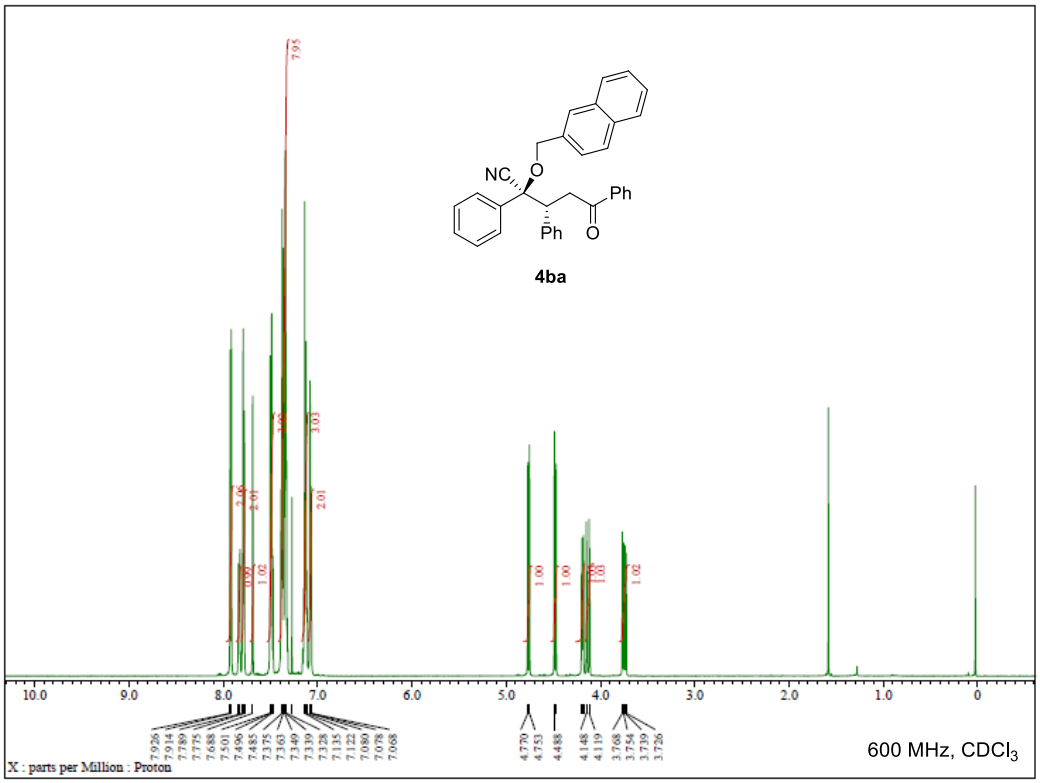
150 MHz, $CDCl_3$

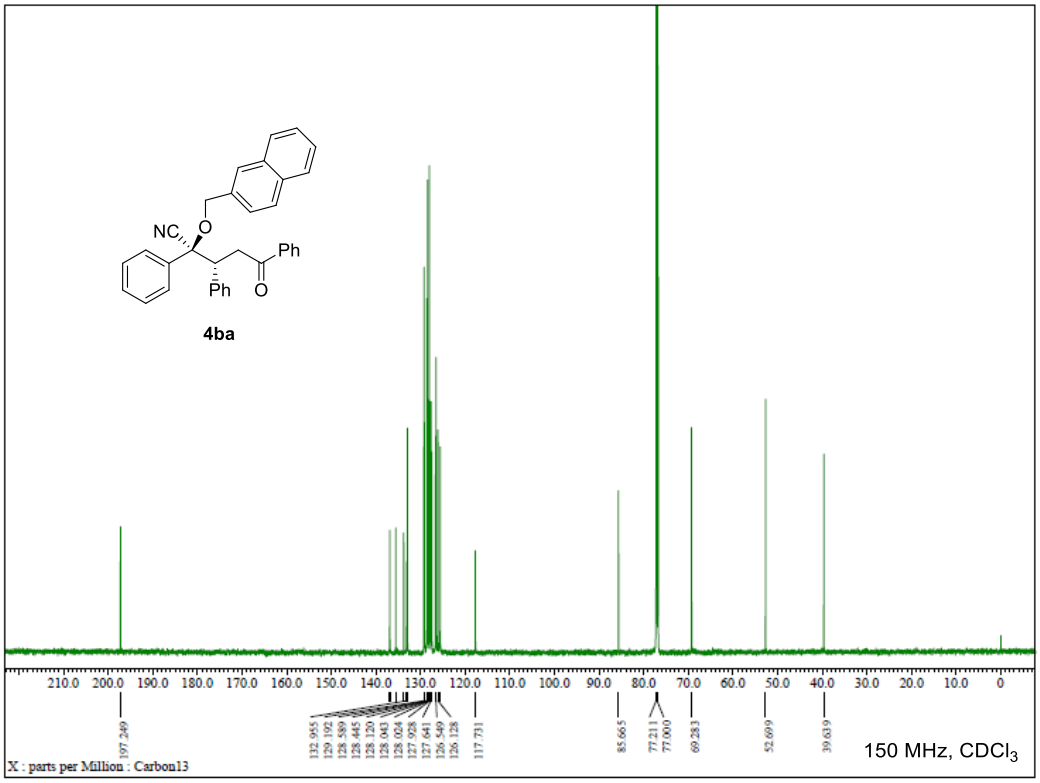


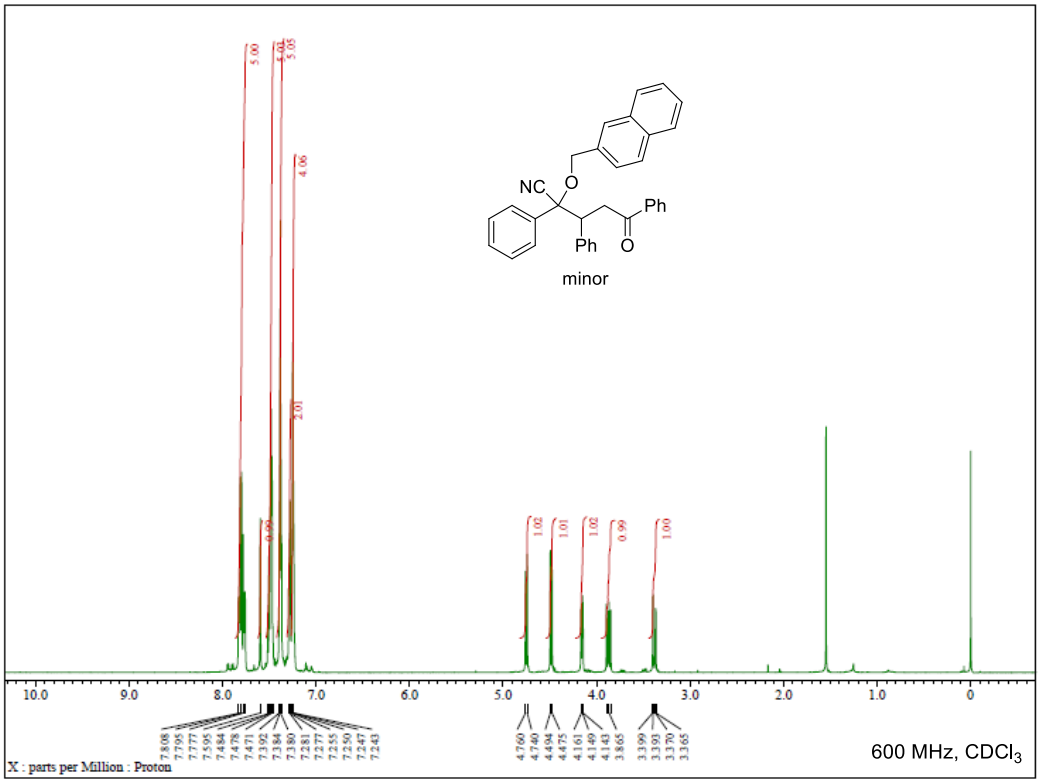
600 MHz, $CDCl_3$

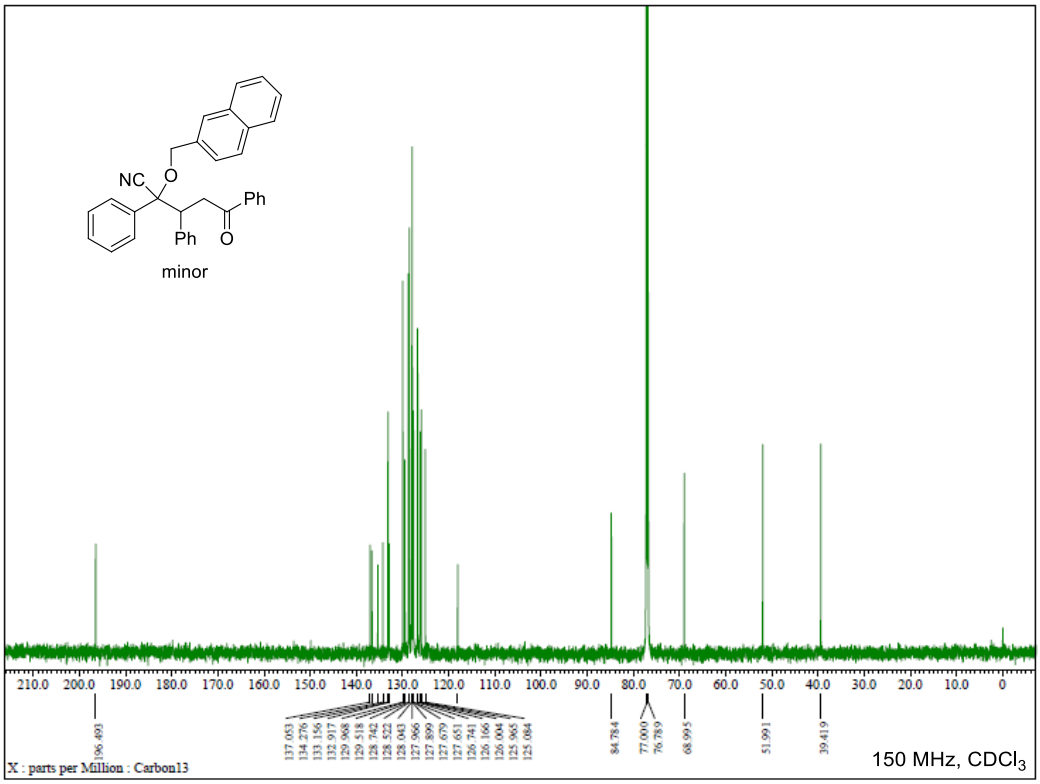


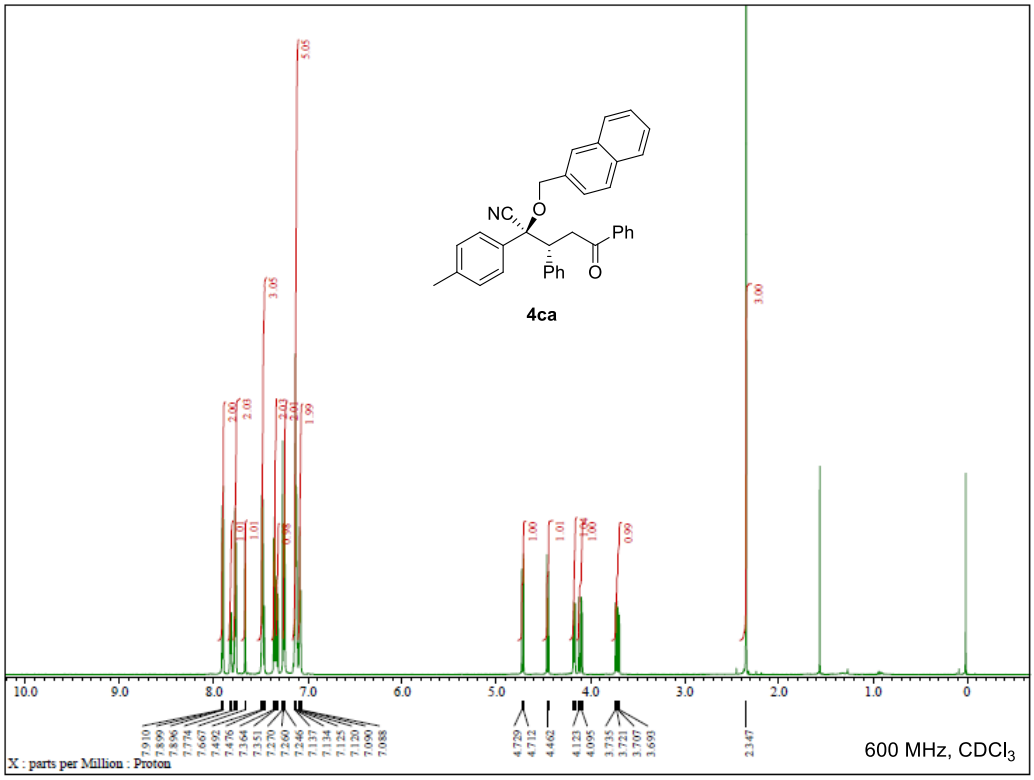
150 MHz, $CDCl_3$

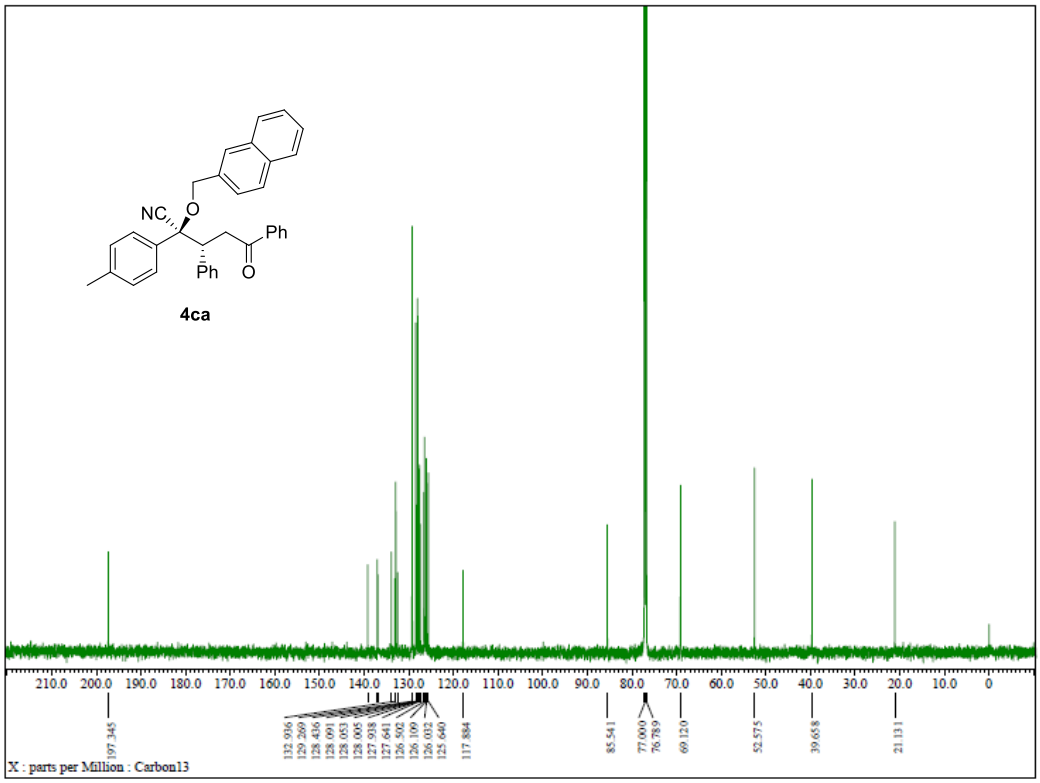

NC
O
Ph
Ph
O
4ba
600 MHz, CDCl3
X : parts per Million : Proton


NC
O
Ph
Ph
O
4ba
150 MHz, CDCl3
X : parts per Million : Carbon13

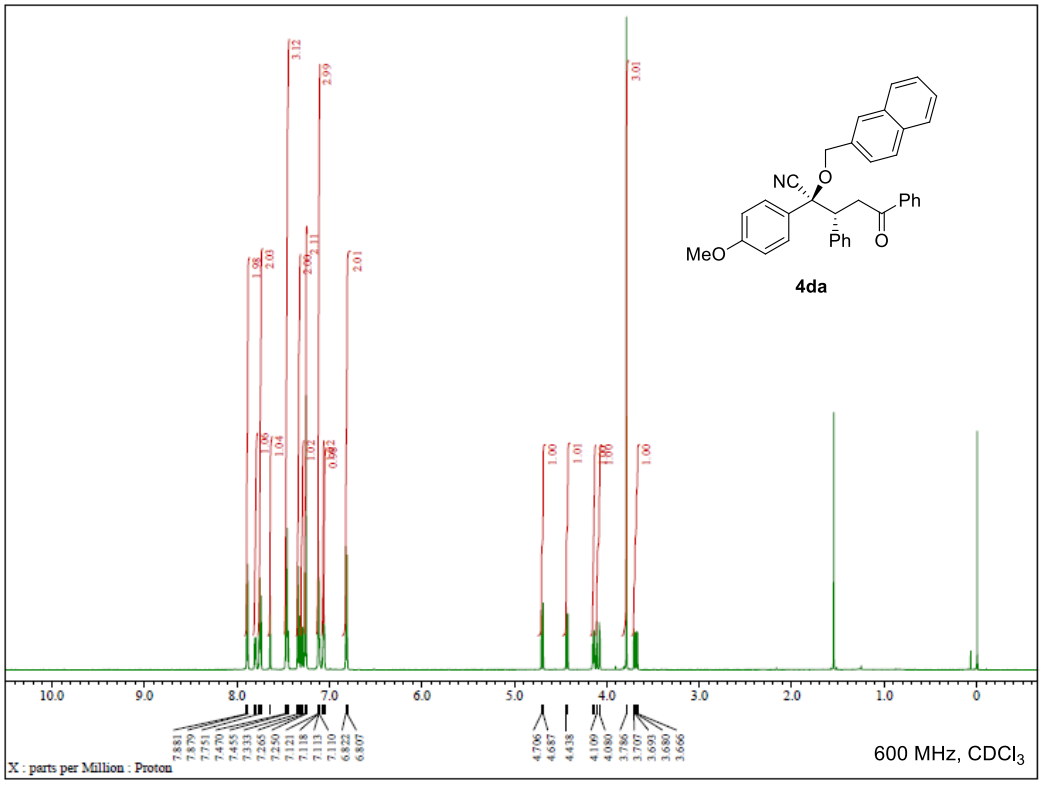

NC
O
Ph
Ph
O
minor
600 MHz, CDCl3
X : parts per Million : Proton

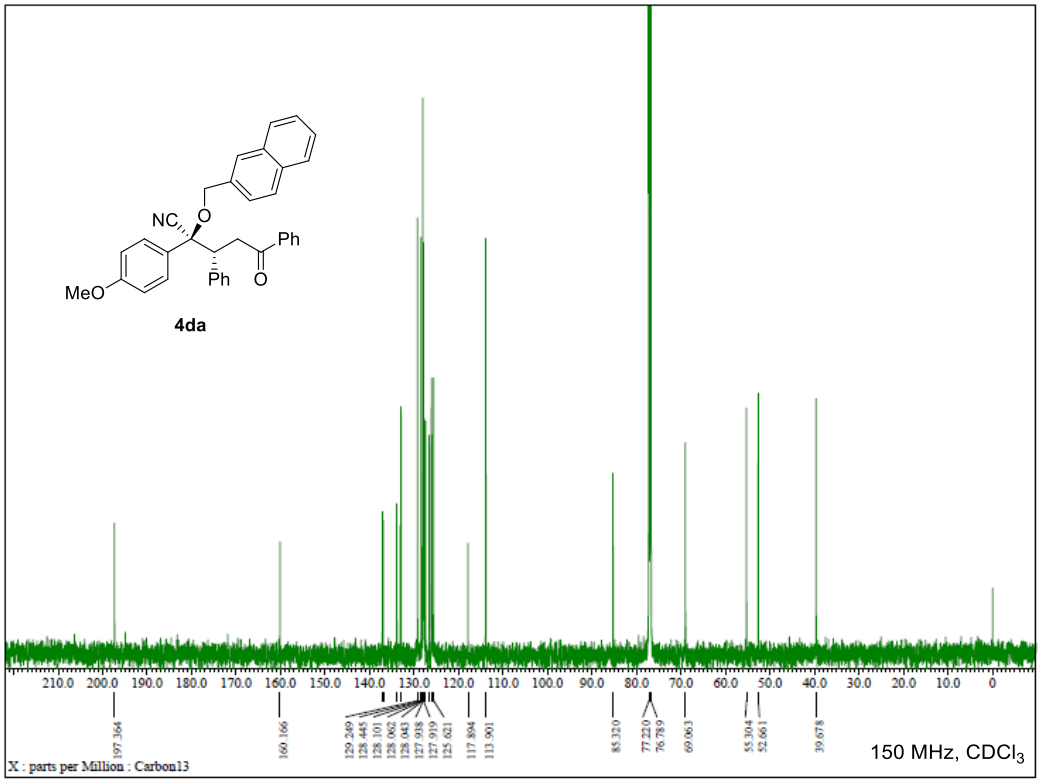

NC
O
Ph
Ph
O
minor
150 MHz, CDCl3
X : parts per Million : Carbon13

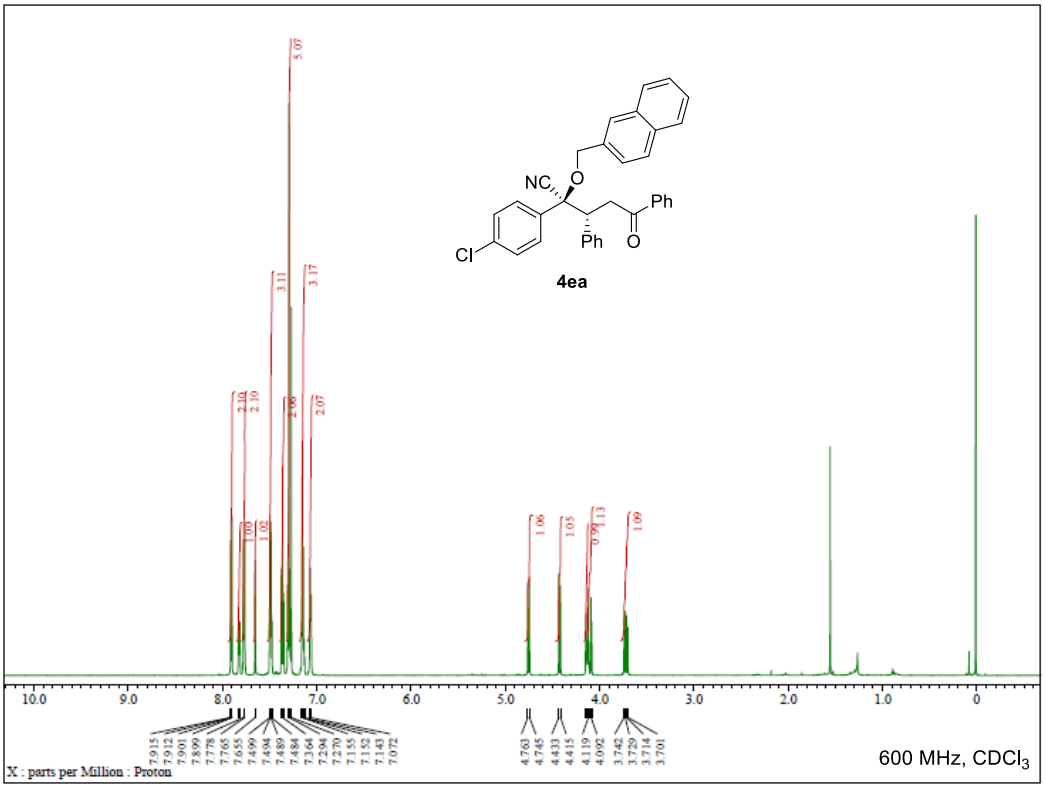


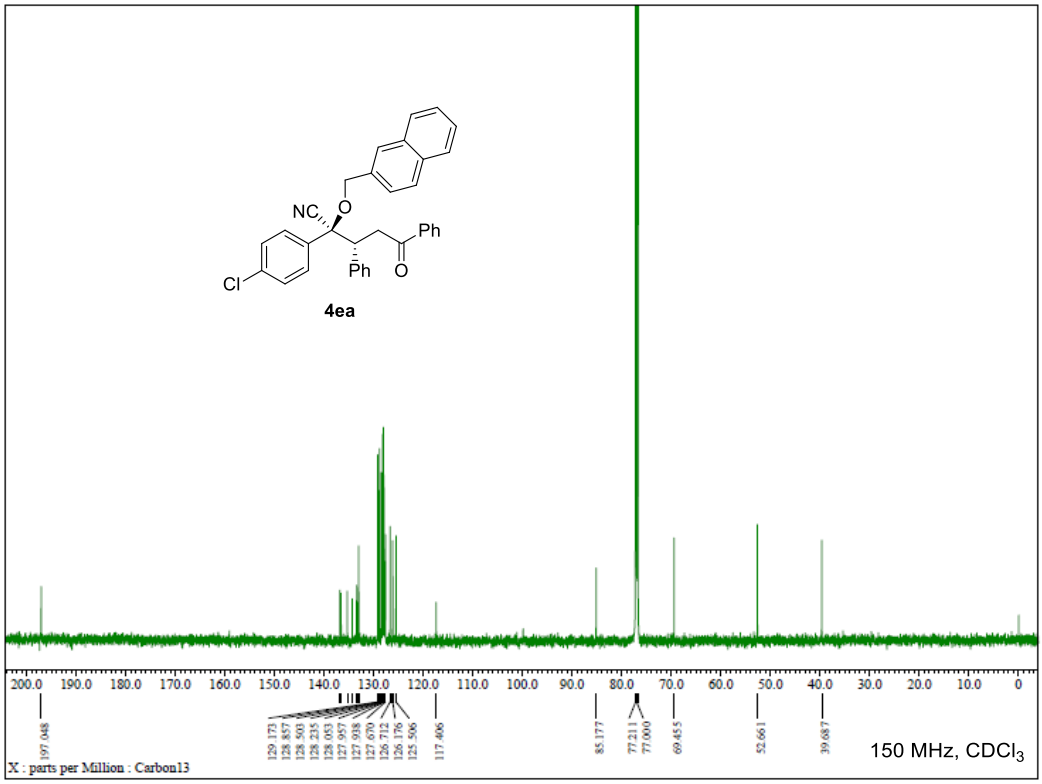


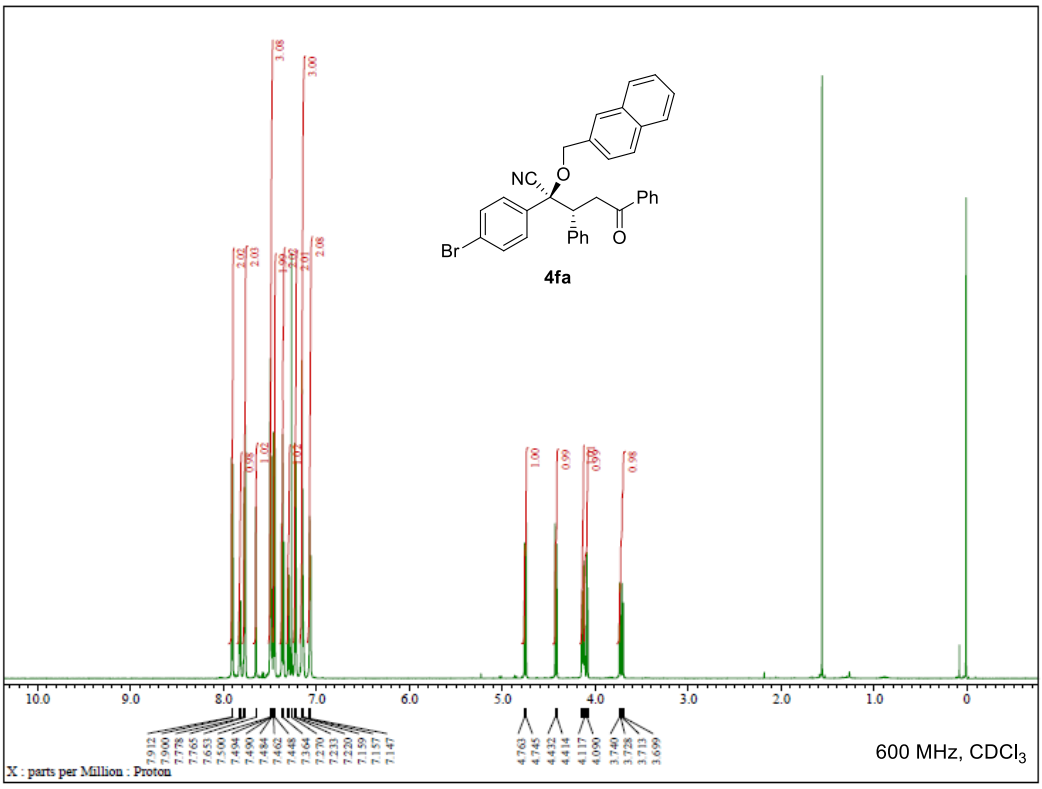
150 MHz, $CDCl_3$

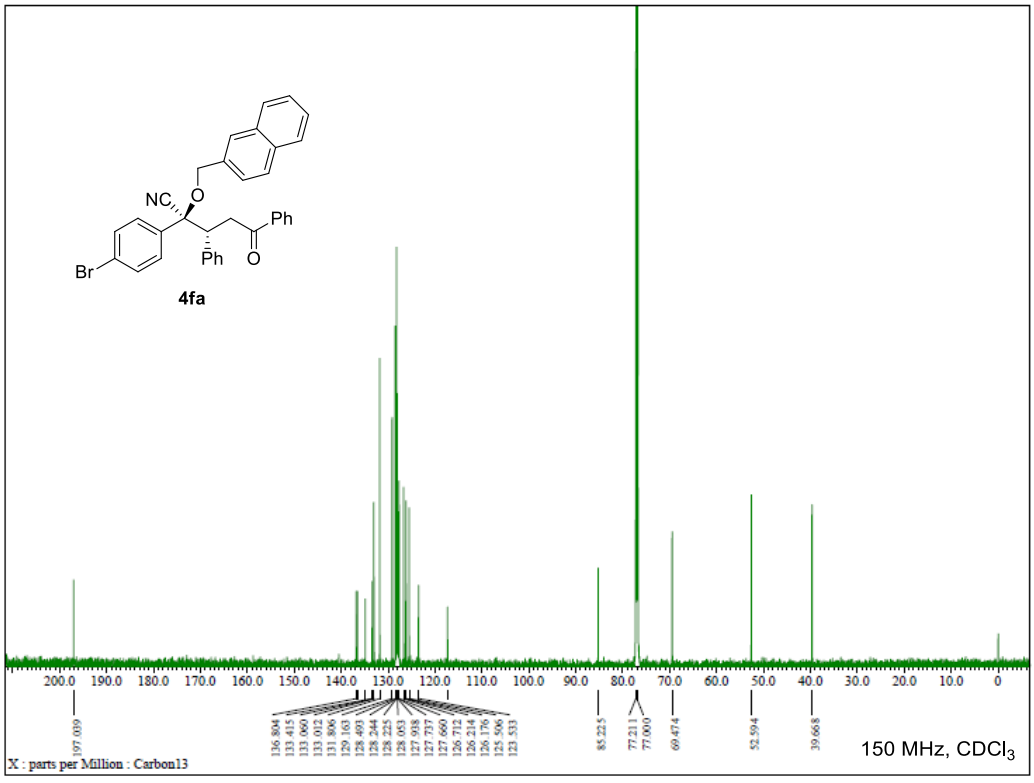

NC
O
Ph
Ph
O
MeO
4da
X : parts per Million : Proton
600 MHz, CDCl3

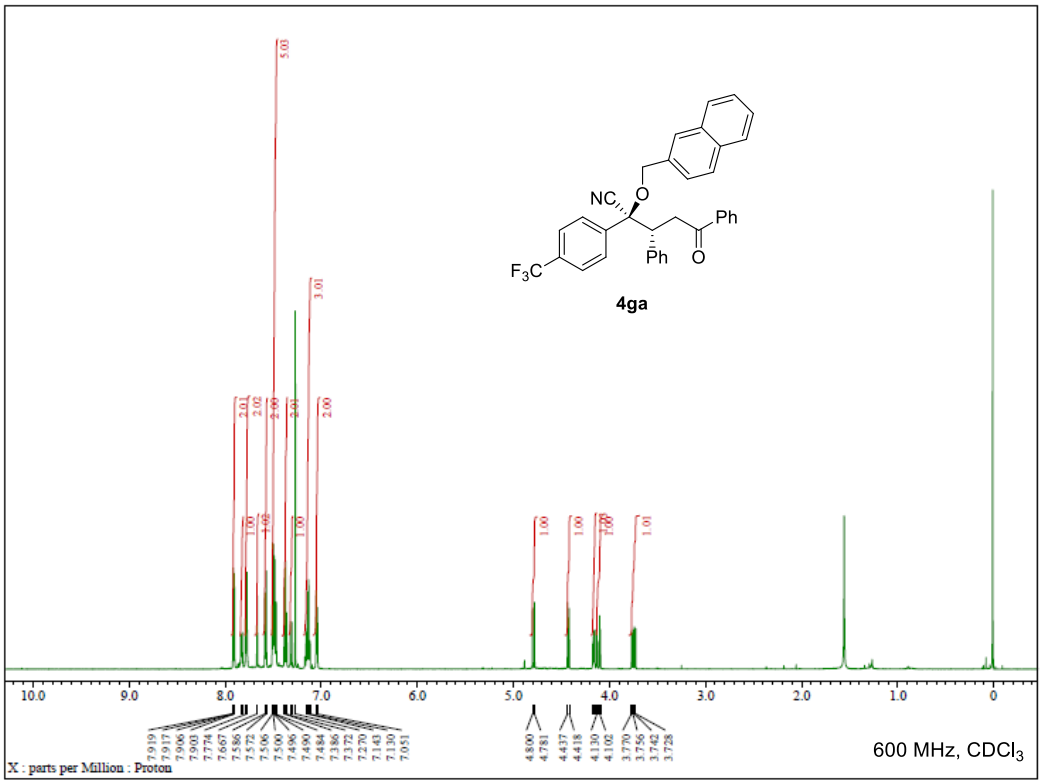

NC
O
Ph
Ph
O
MeO
4da
X : parts per Million : Carbon13
150 MHz, CDCl3

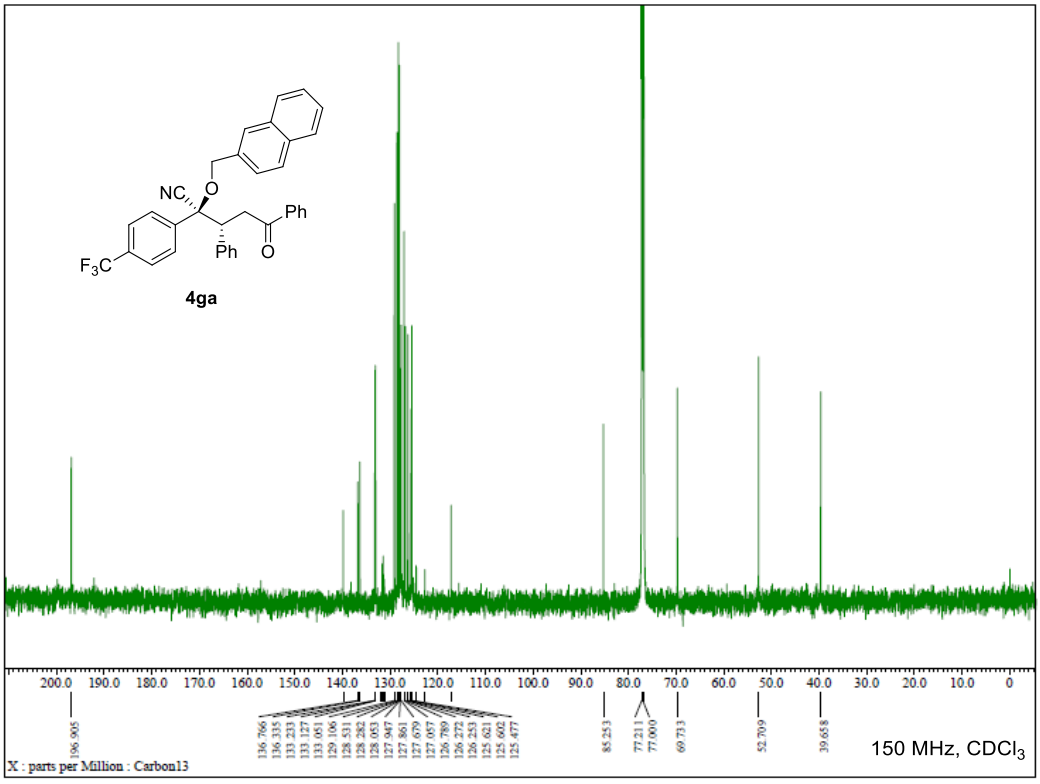

NC
O
Ph
Ph
O
Cl
4ea
X : parts per Million : Proton
600 MHz, CDCl3

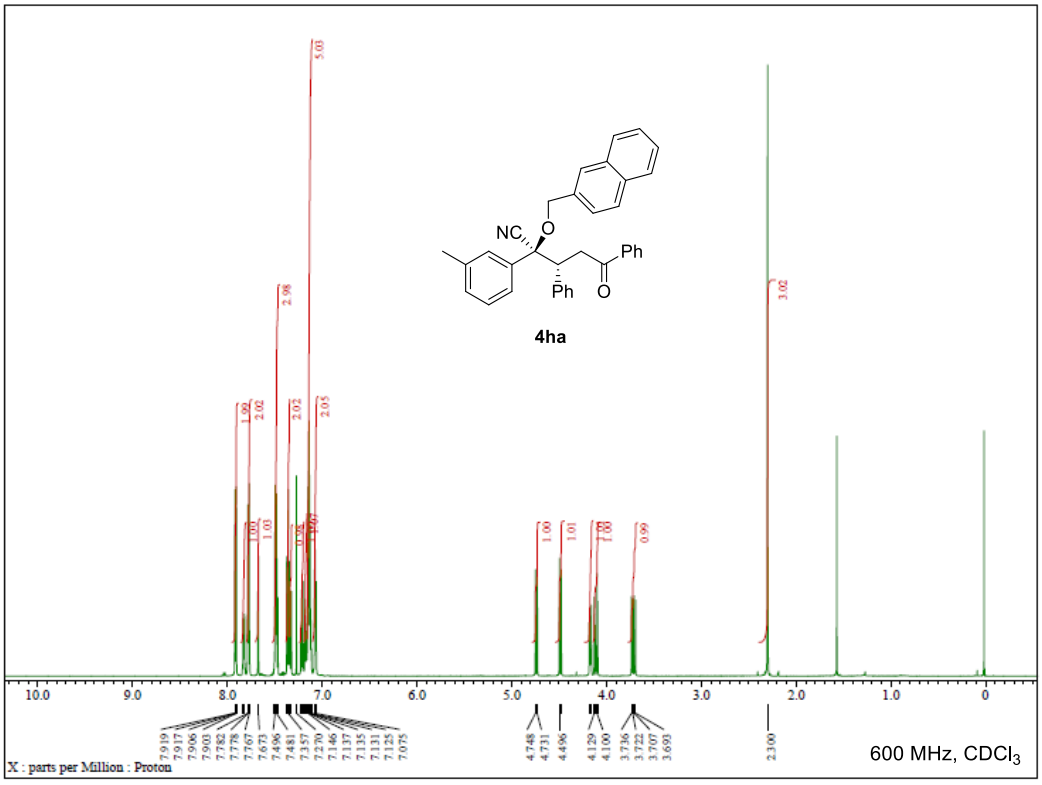

NC
O
Ph
Ph
O
Cl
4ea
X : parts per Million : Carbon13
150 MHz, CDCl3

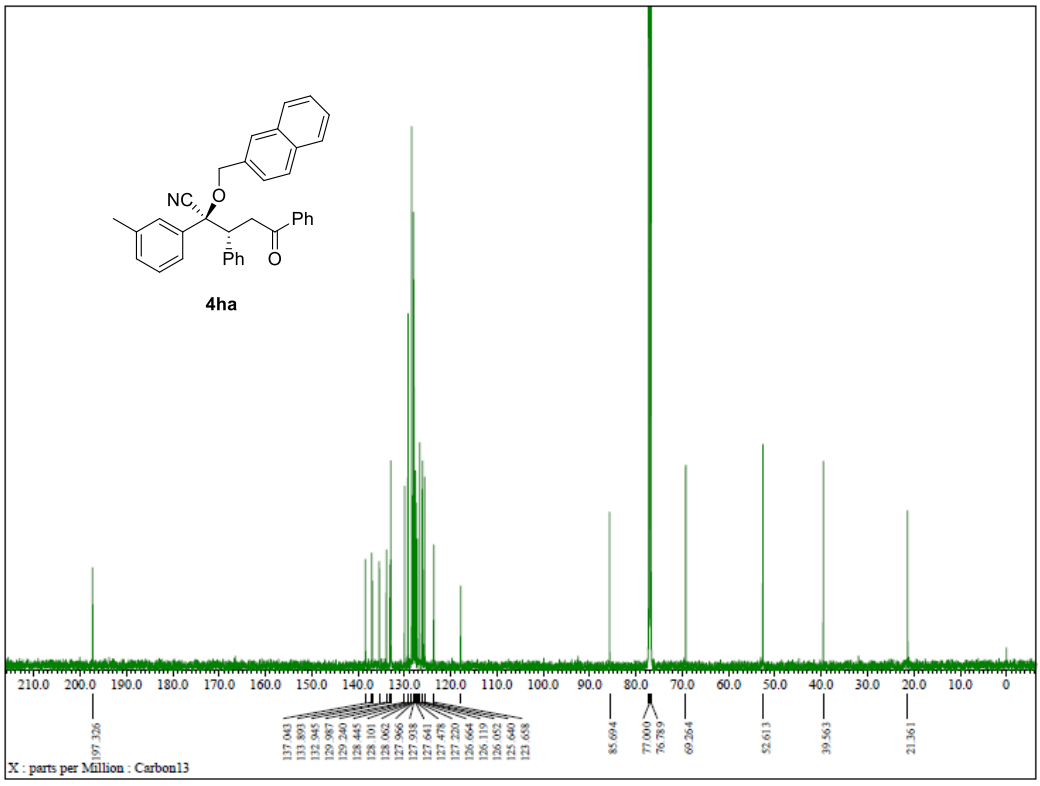

NC
O
Ph
Ph
O
Br
4fa
600 MHz, CDCl3
X : parts per Million : Proton


NC
O
Ph
Ph
O
Br
4fa
150 MHz, CDCl3
X : parts per Million : Carbon13

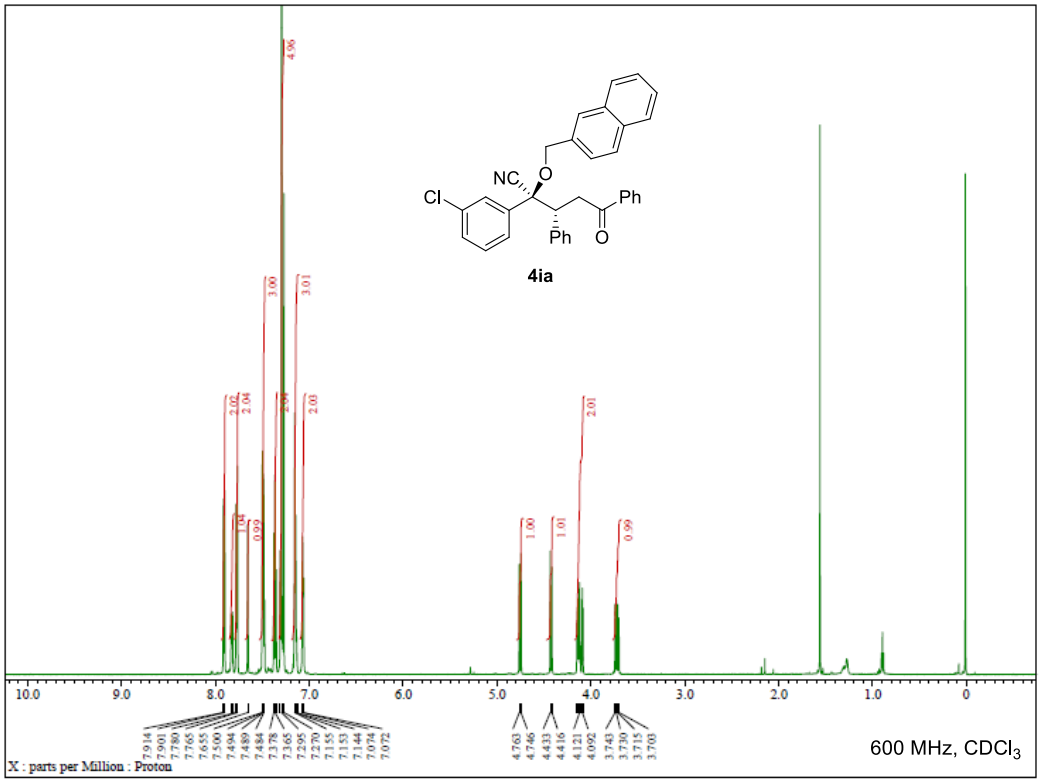

NC
O
Ph
Ph
O
F3C
4ga
600 MHz, CDCl3
X : parts per Million : Proton

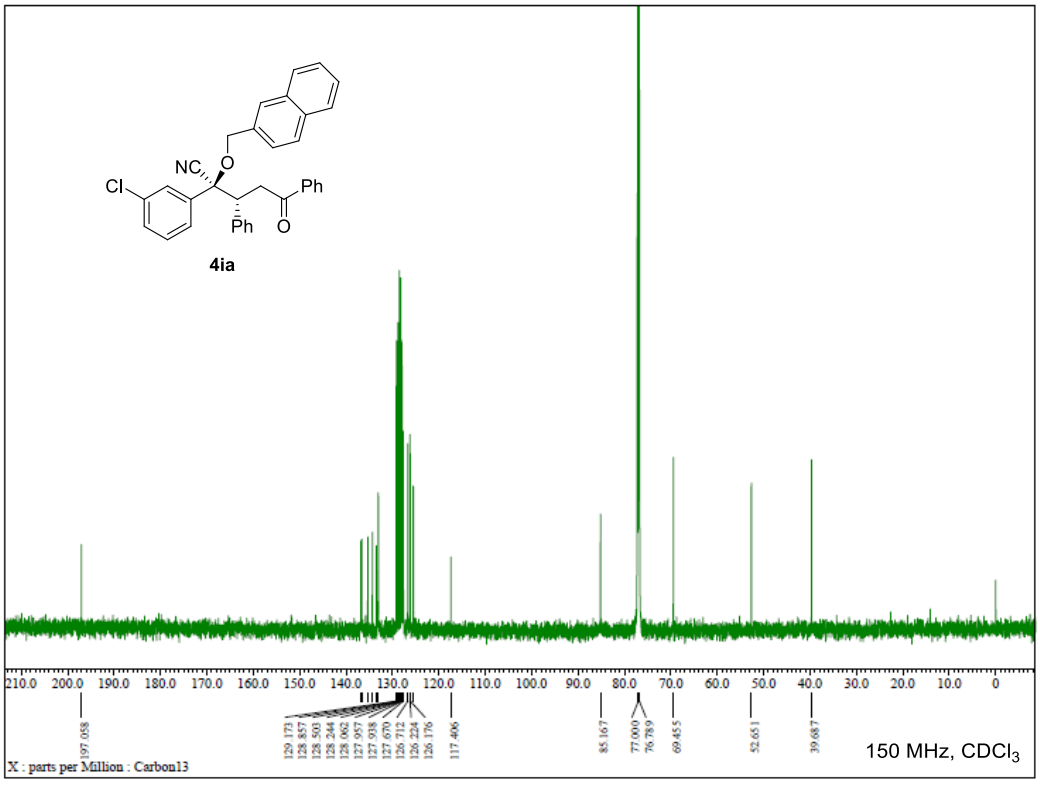

NC
O
Ph
Ph
O
F3C
4ga
150 MHz, CDCl3
X : parts per Million : Carbon13

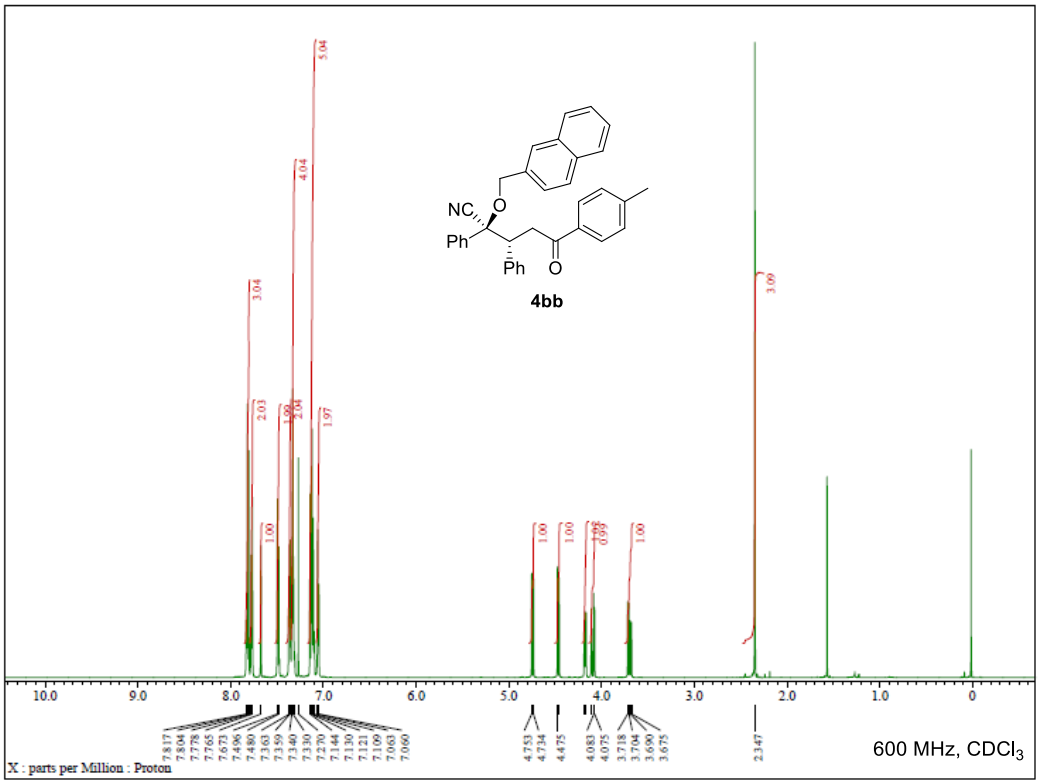


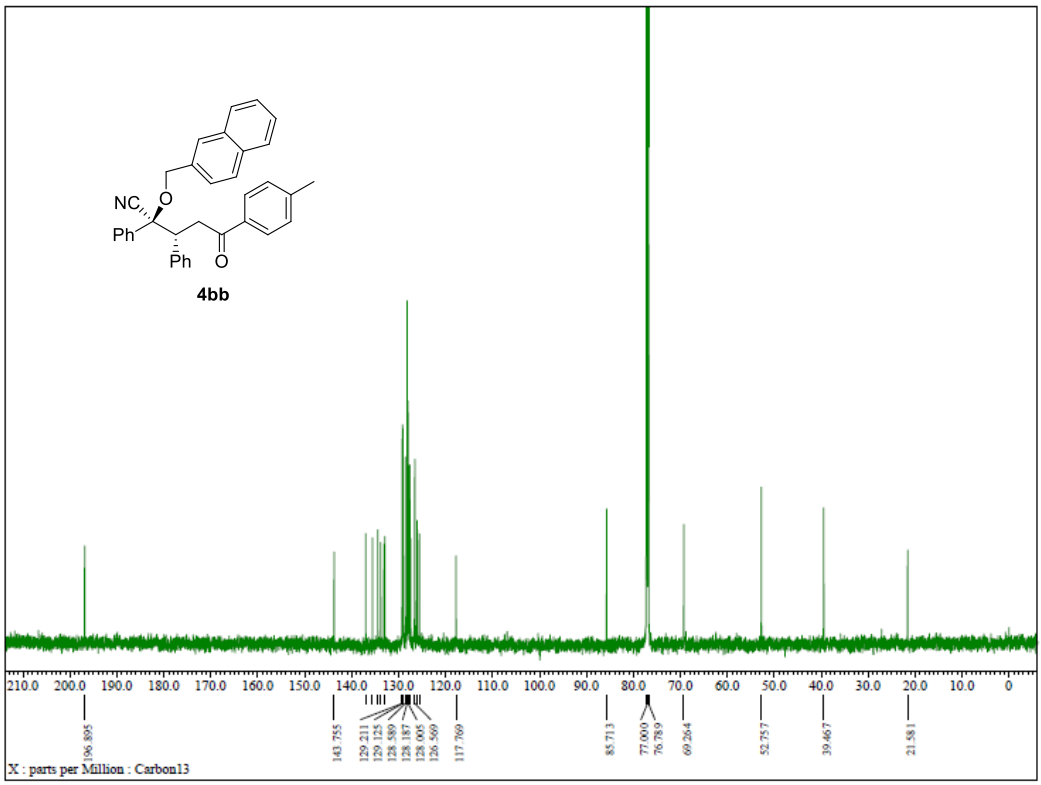


150 MHz, $CDCl_3$

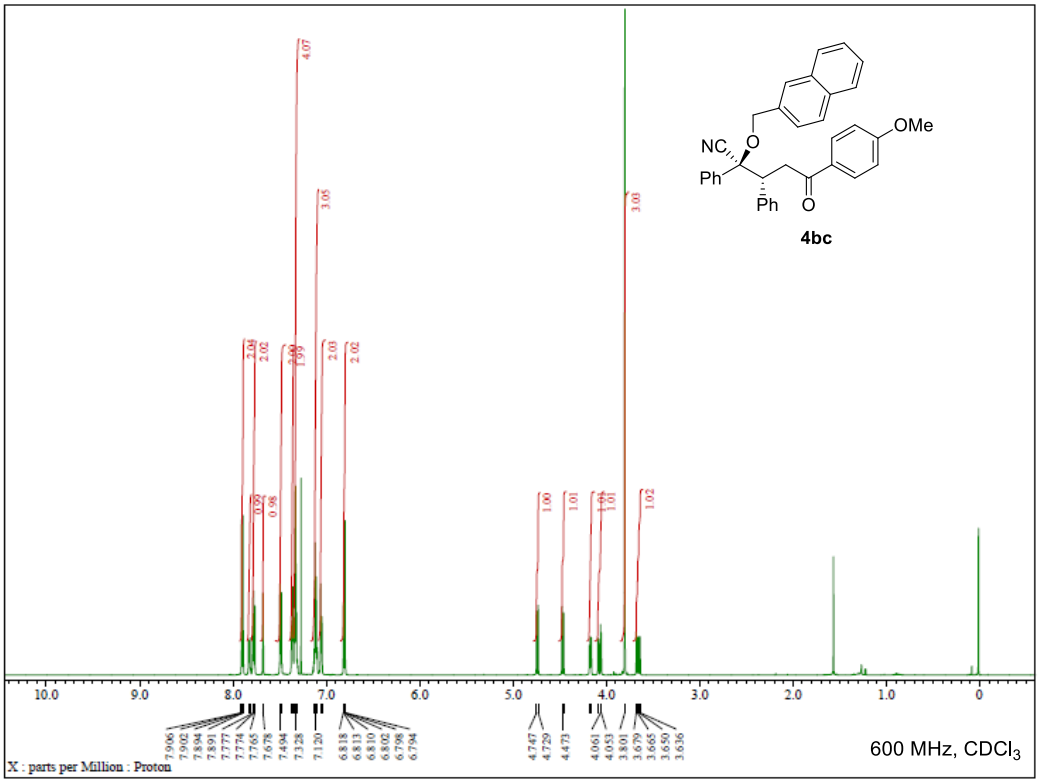

NC
O
Cl
Ph
Ph
O
4ia
600 MHz, CDCl3
X : parts per Million : Proton

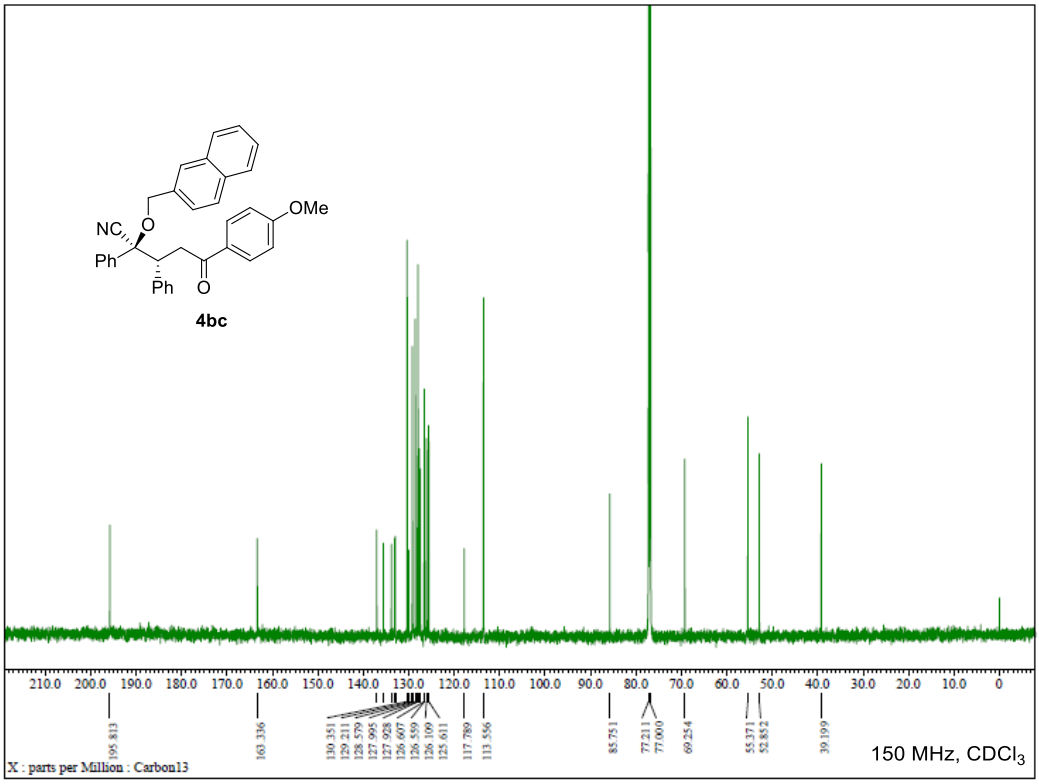

NC
O
Cl
Ph
Ph
O
4ia
150 MHz, CDCl3
X : parts per Million : Carbon13

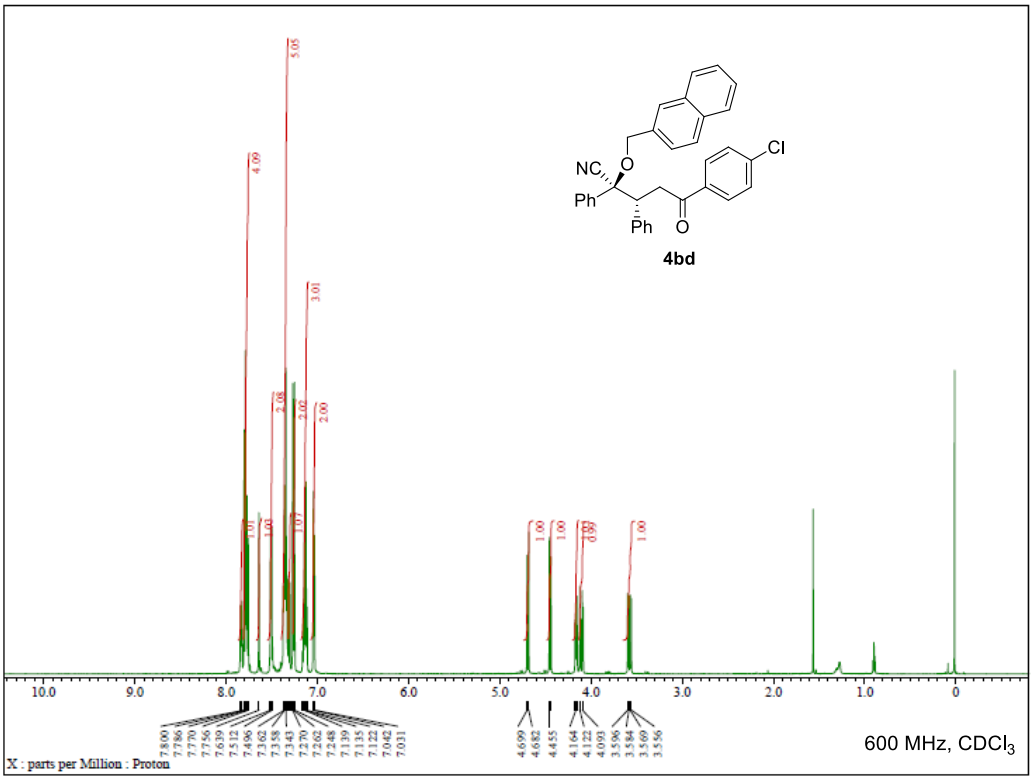


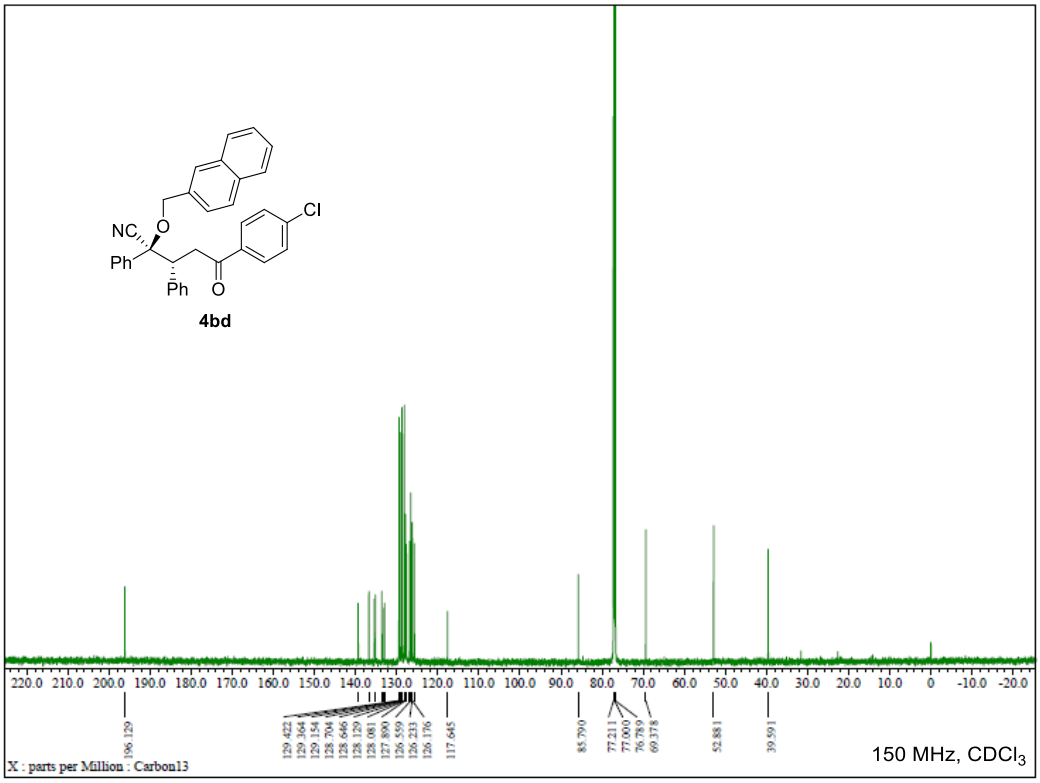


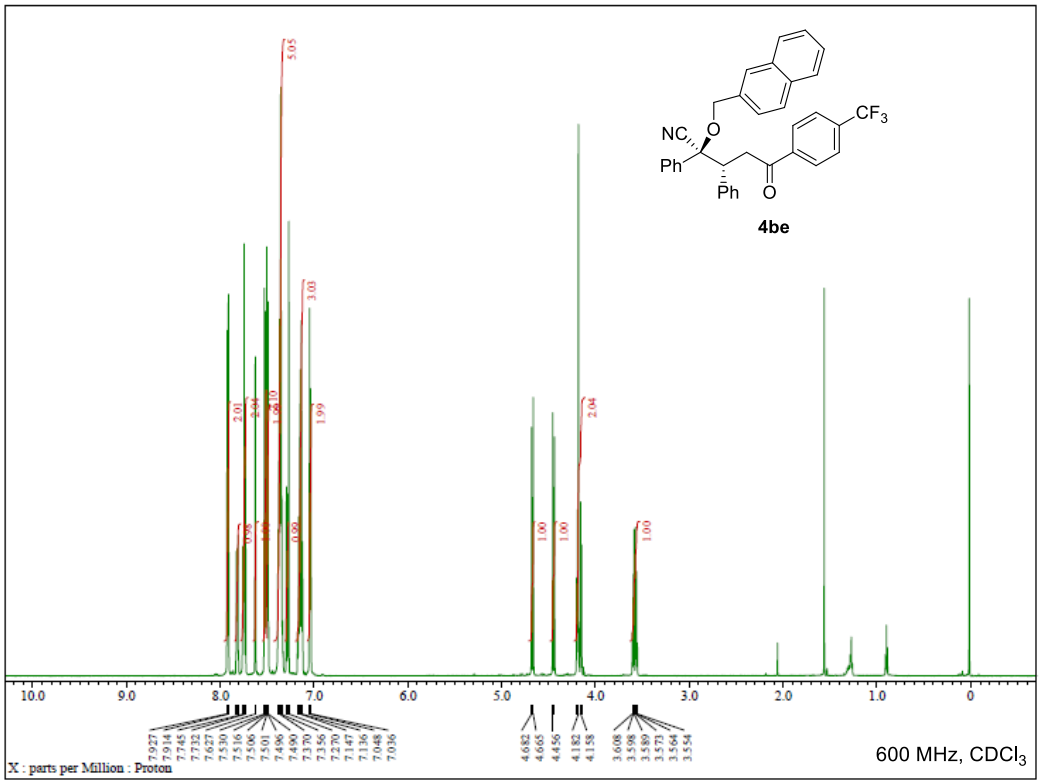
150 MHz, $CDCl_3$

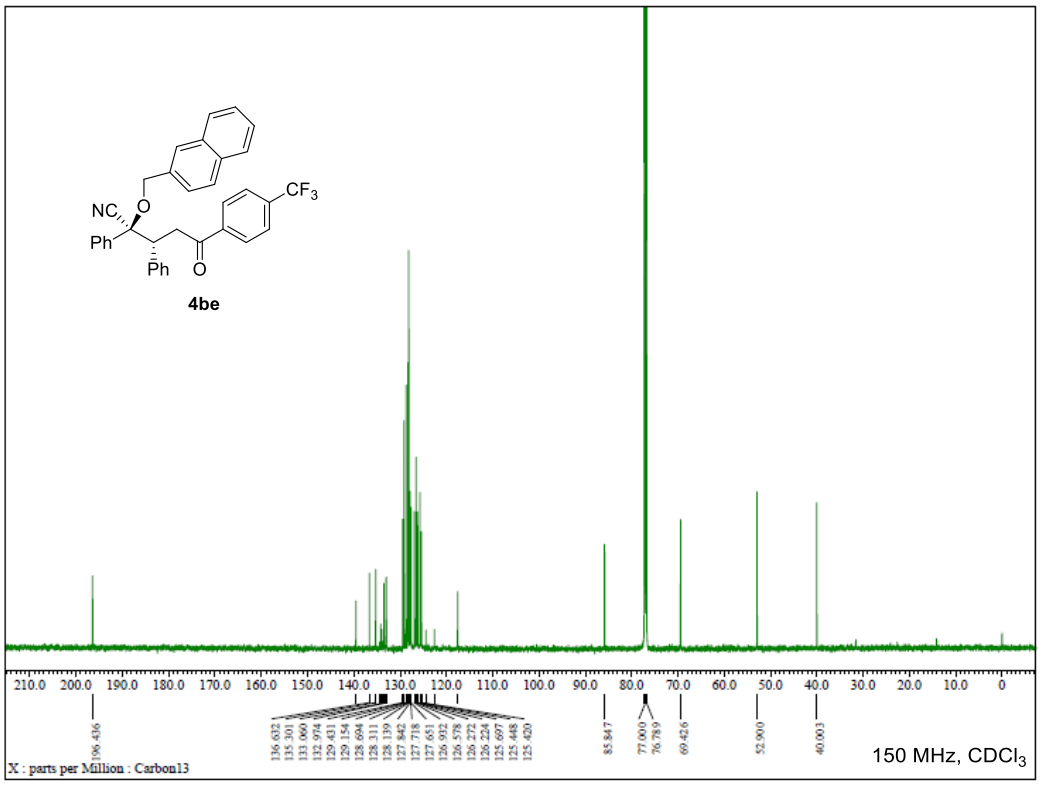

4bc
600 MHz, CDCl3
X : parts per Million : Proton

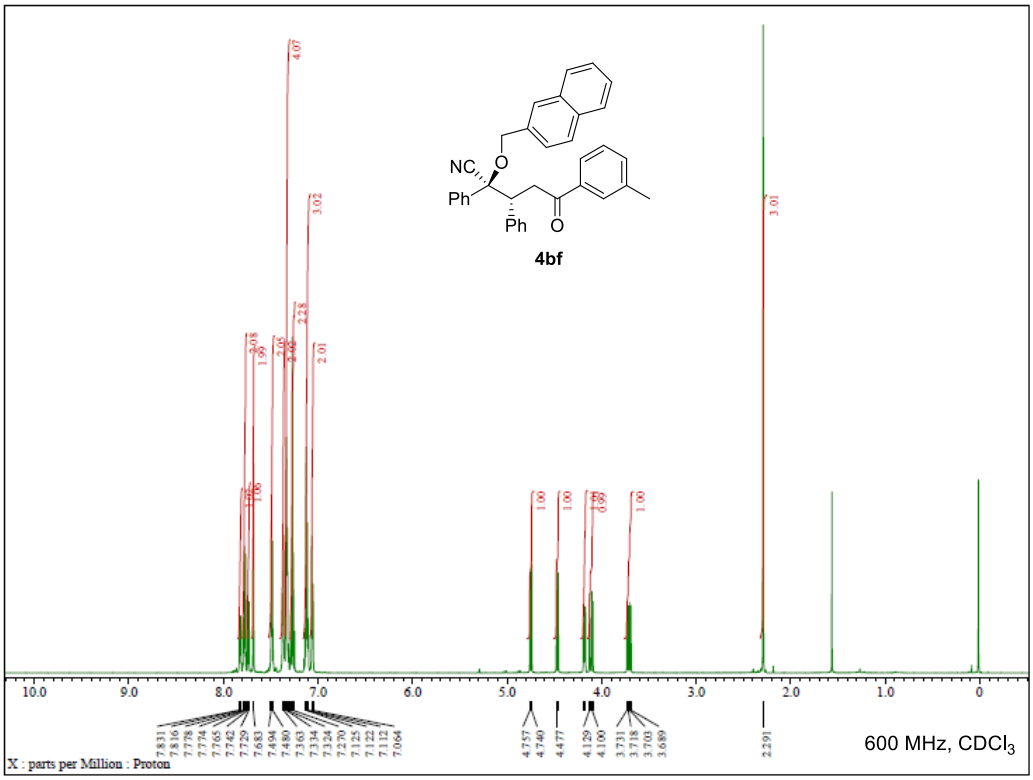

4bc
150 MHz, CDCl3
X : parts per Million : Carbon13

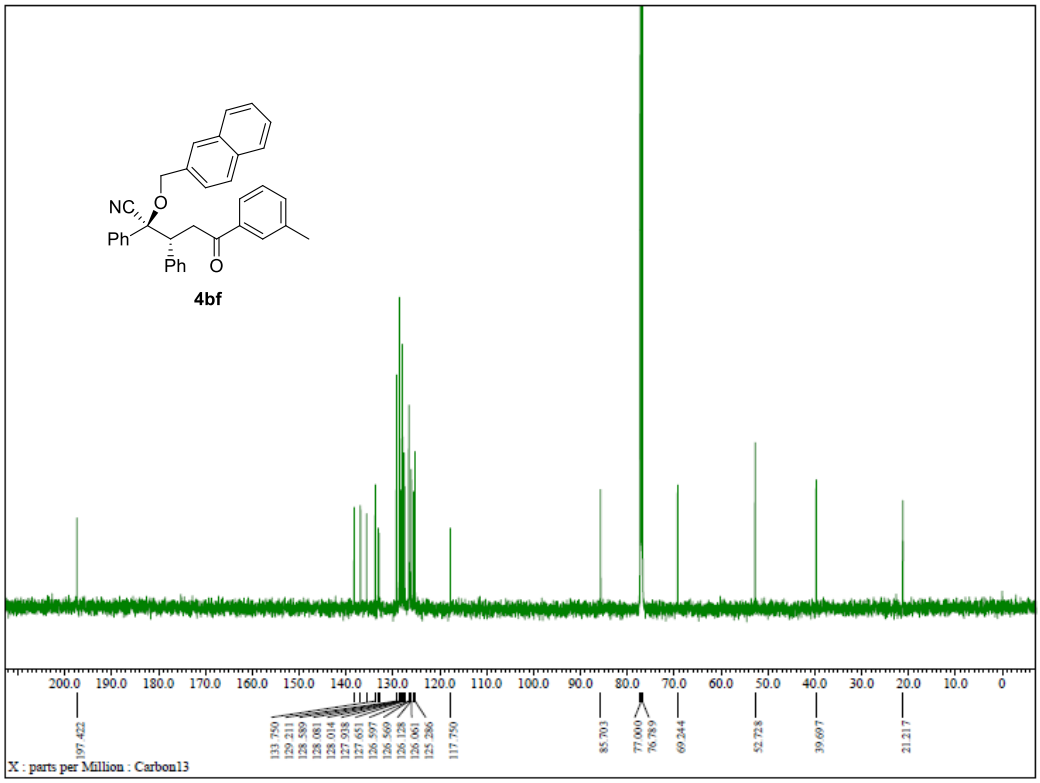

NC
O
Ph
Ph
O
Cl
4bd
600 MHz, CDCl3
X : parts per Million : Proton


NC
O
Ph
Ph
O
Cl
4bd
150 MHz, CDCl3
X : parts per Million : Carbon13

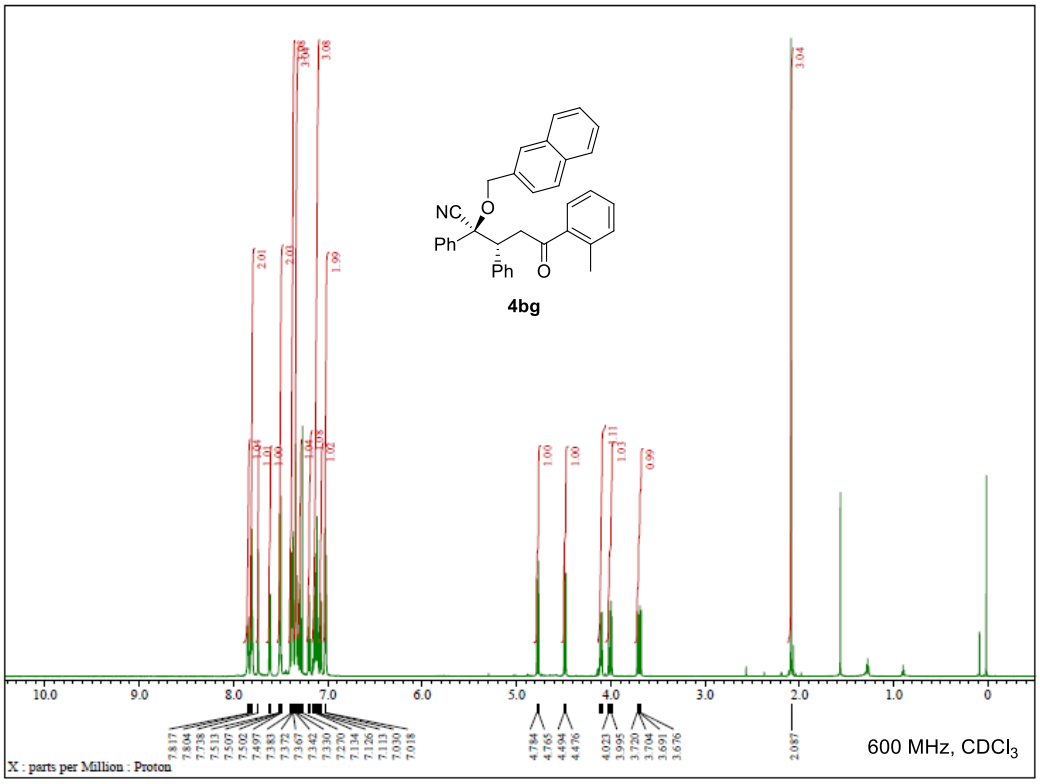

NC
O
Ph
Ph
O
CF3
4be
X : parts per Million : Proton
600 MHz, CDCl3

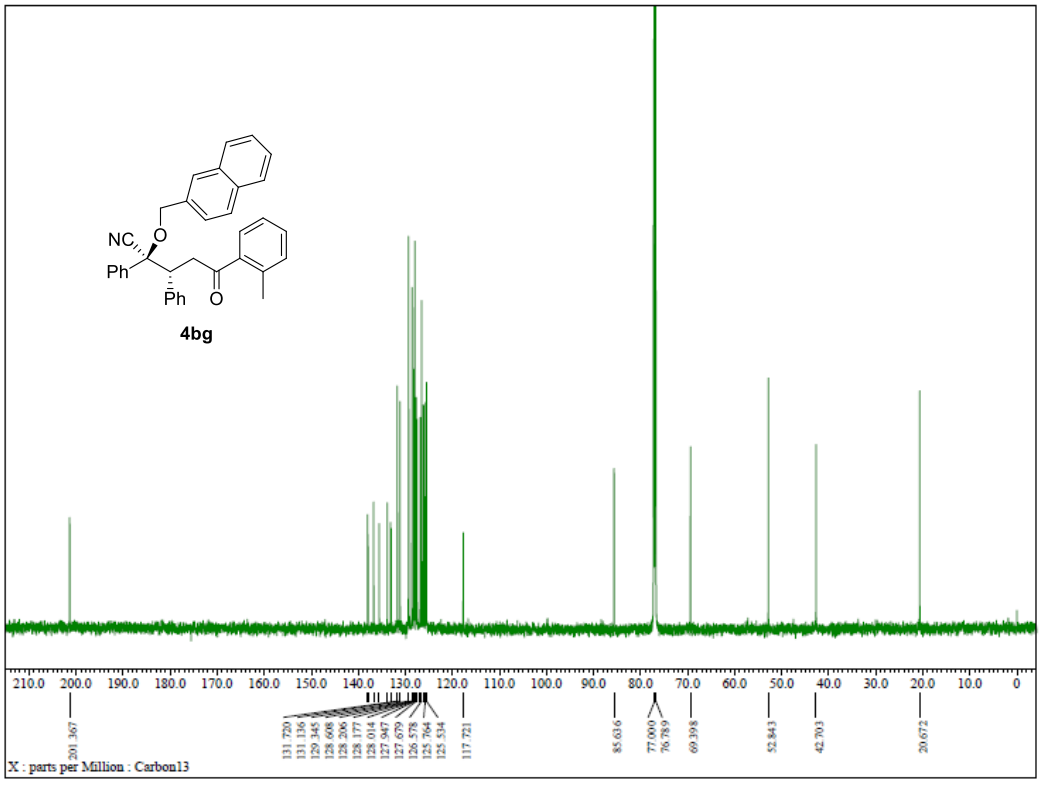

NC
O
Ph
Ph
O
CF3
4be
X : parts per Million : Carbon13
150 MHz, CDCl3



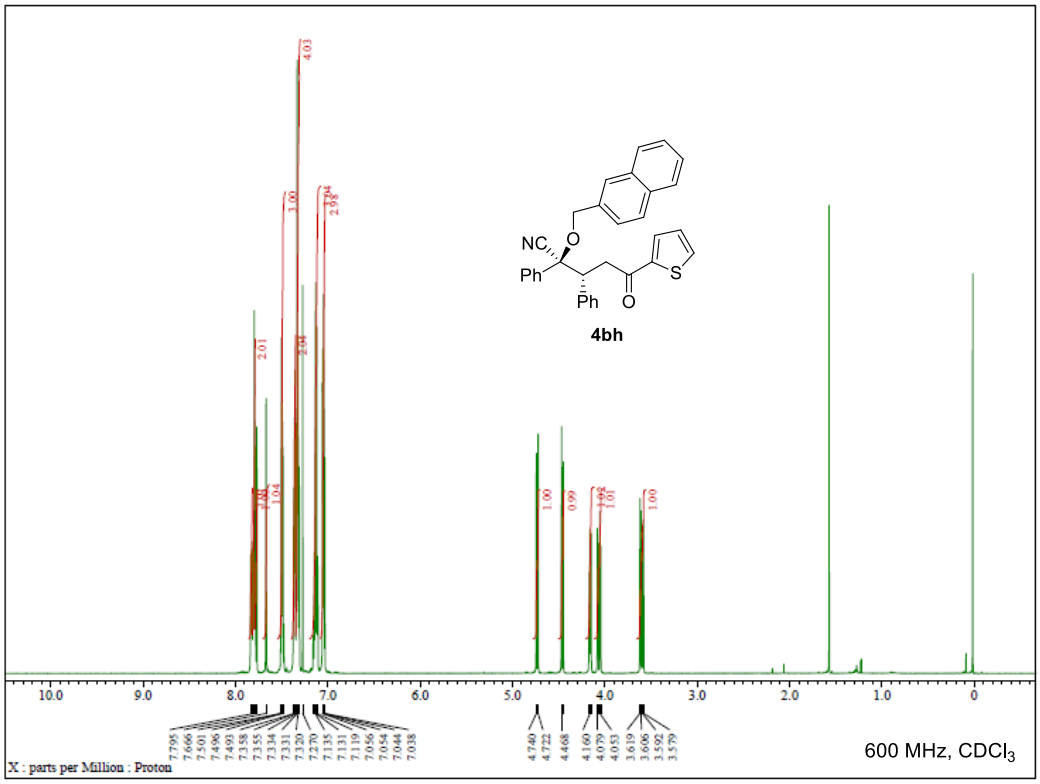


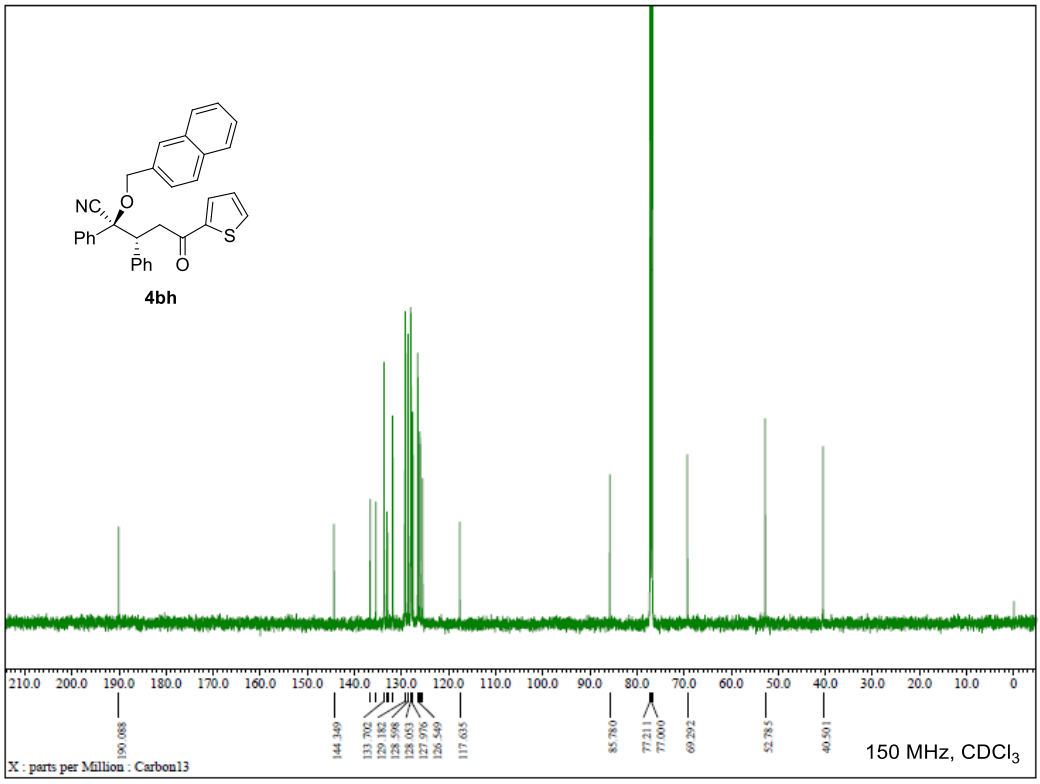
150 MHz, $CDCl_3$

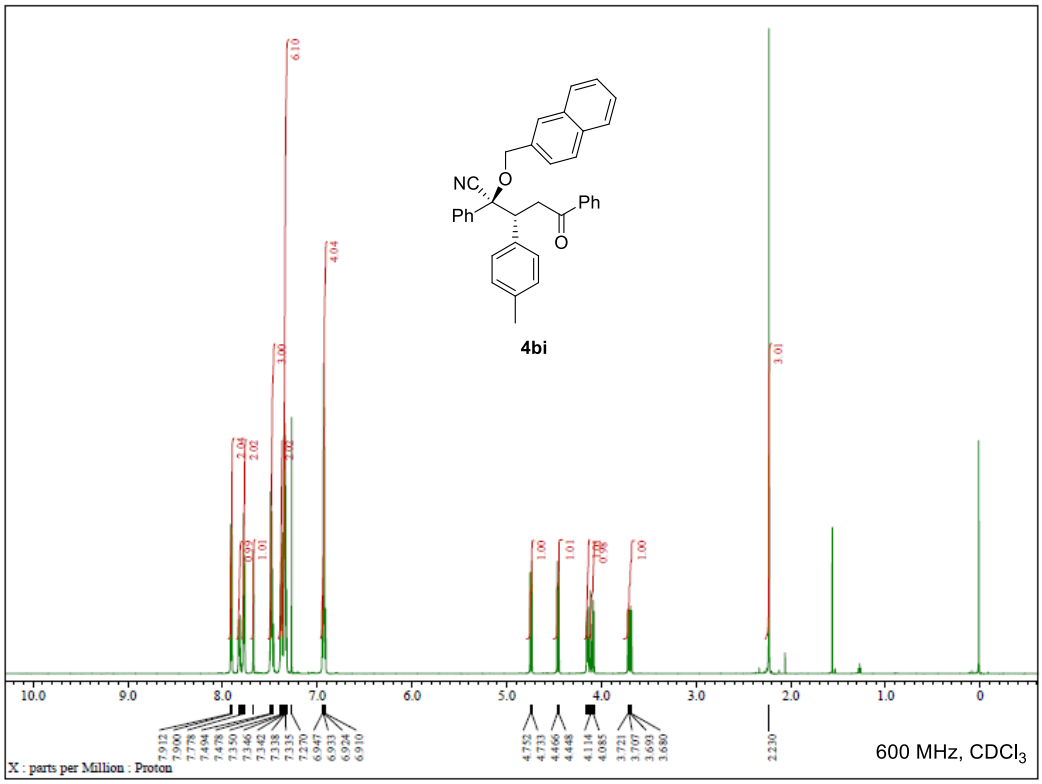


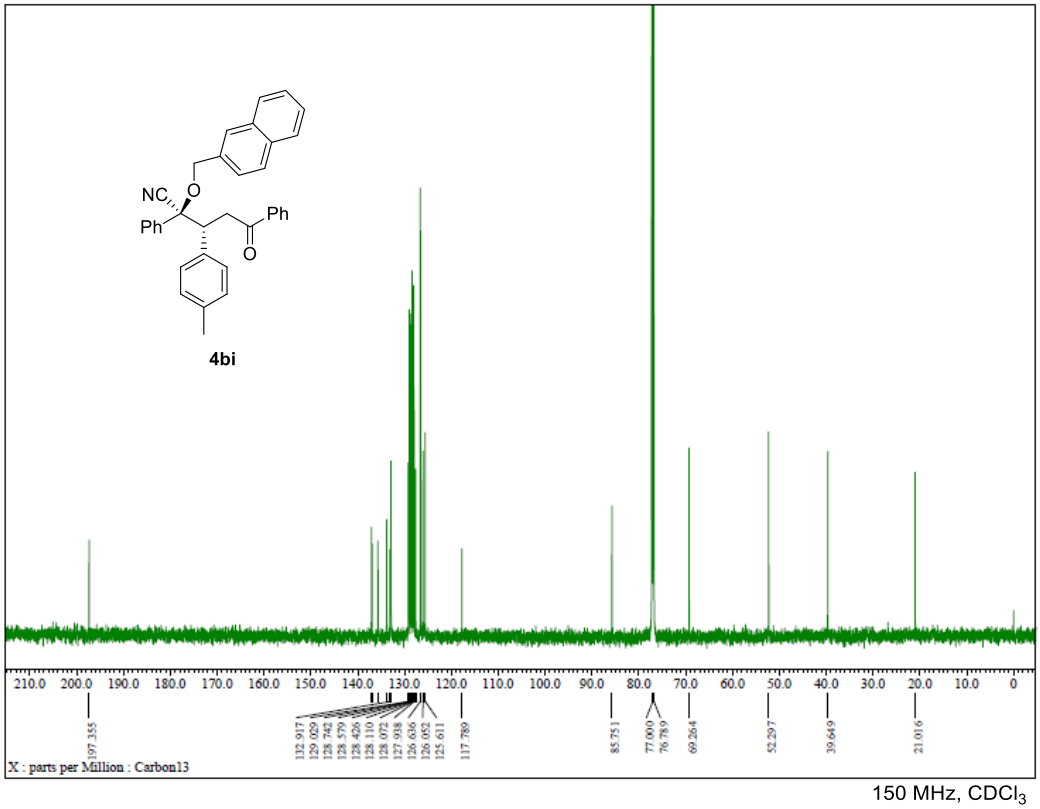


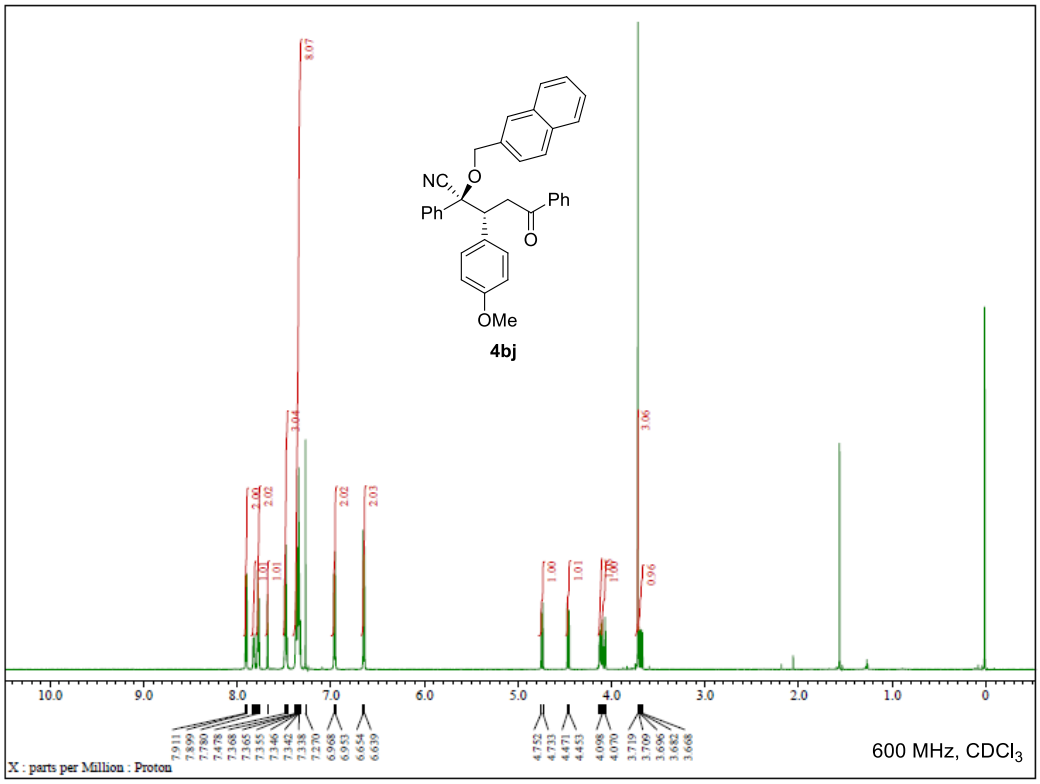
150 MHz, $CDCl_3$

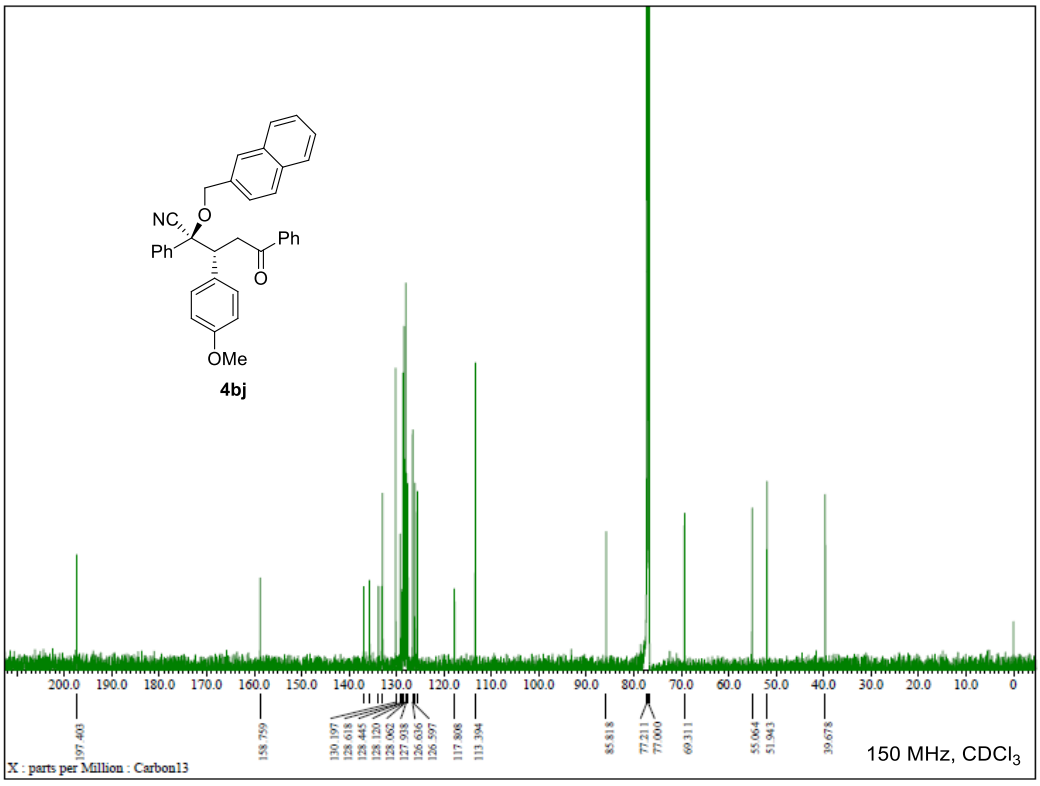

NC
O
Ph
Ph
O
S
4bh
X : parts per Million : Proton
600 MHz, CDCl3

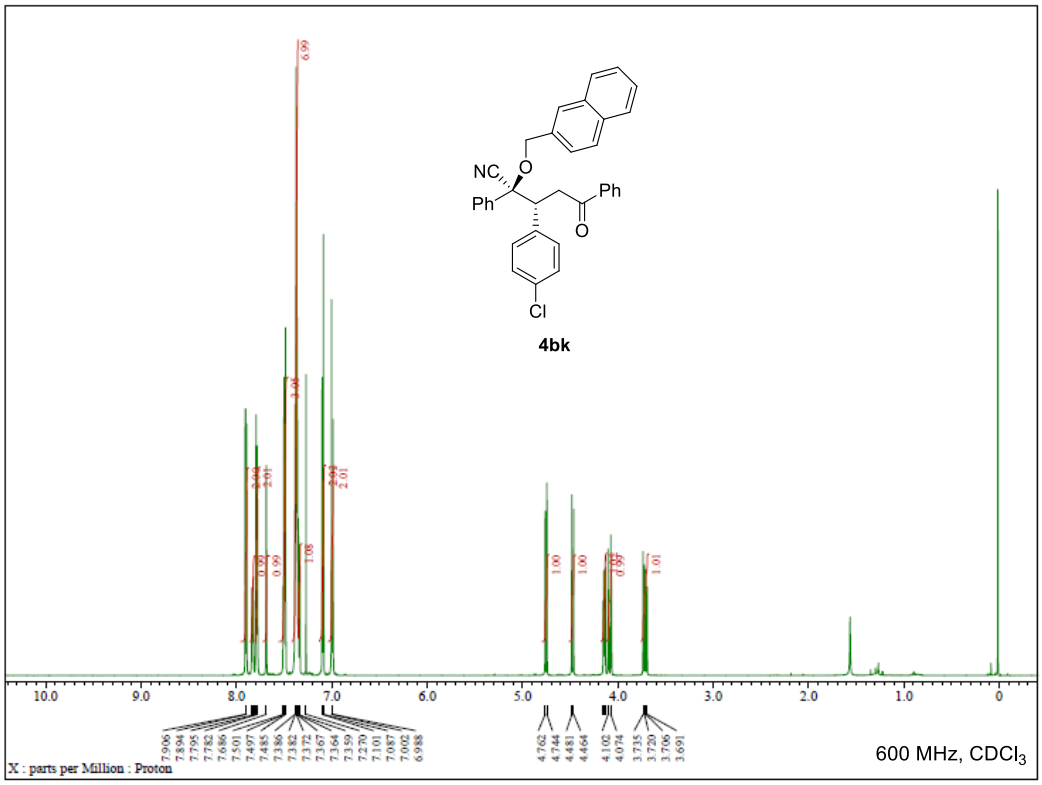

NC
O
Ph
Ph
O
S
4bh
X : parts per Million : Carbon13
150 MHz, CDCl3

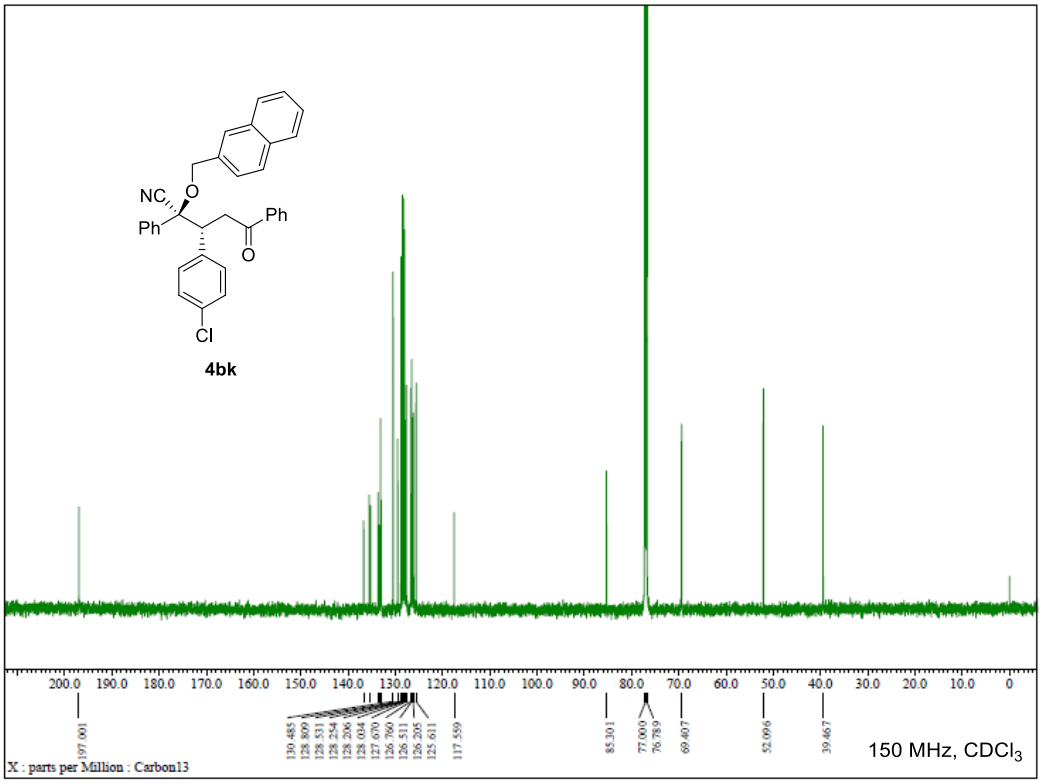

NC
O
Ph
Ph
O
4bi
X : parts per Million : Proton
600 MHz, CDCl3

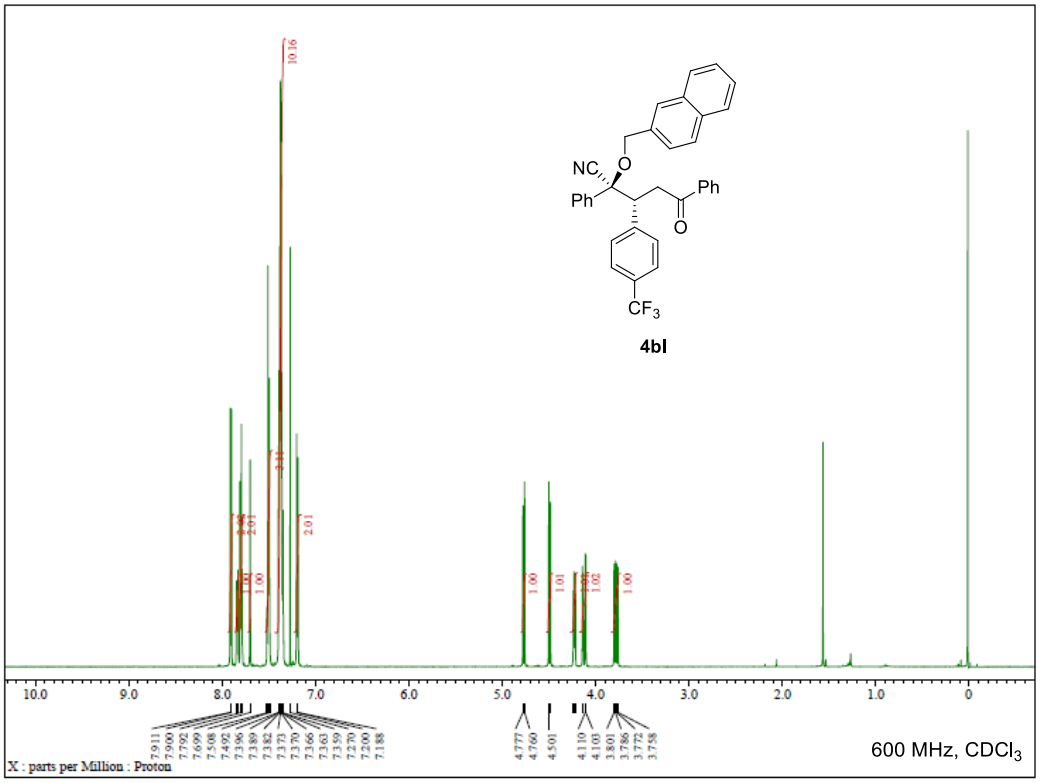

NC
O
Ph
Ph
O
4bi
X : parts per Million : Carbon13
150 MHz, CDCl3

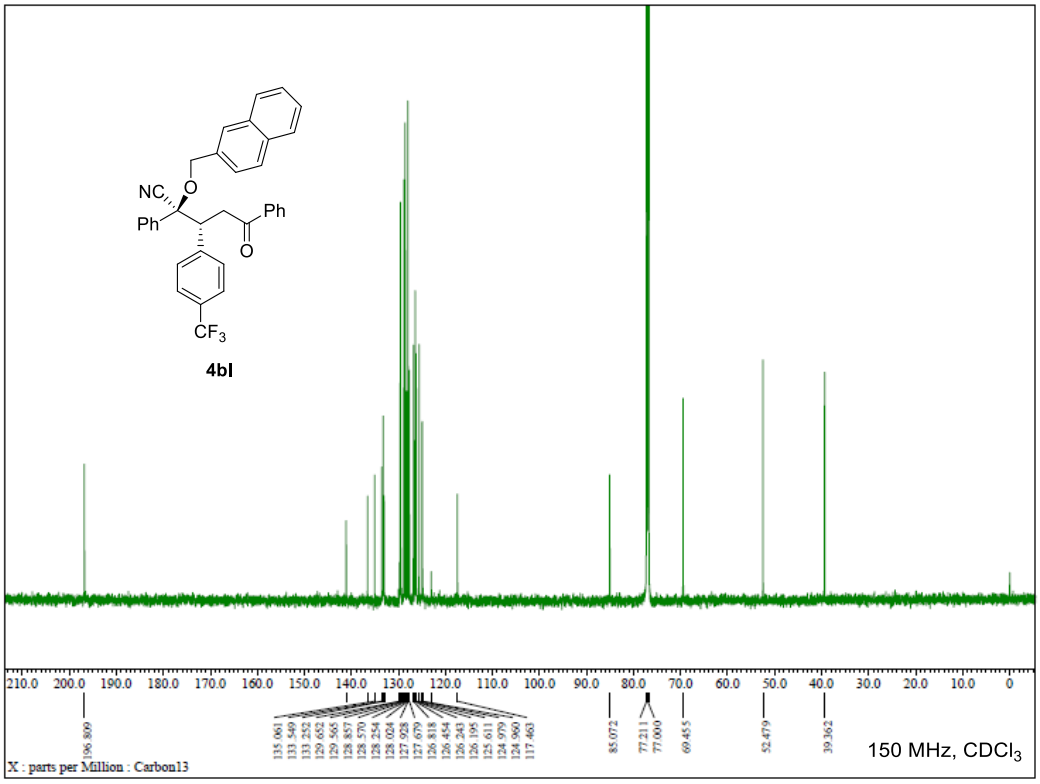

NC
O
Ph
Ph
O
OMe
4bj
600 MHz, CDCl3
X : parts per Million : Proton

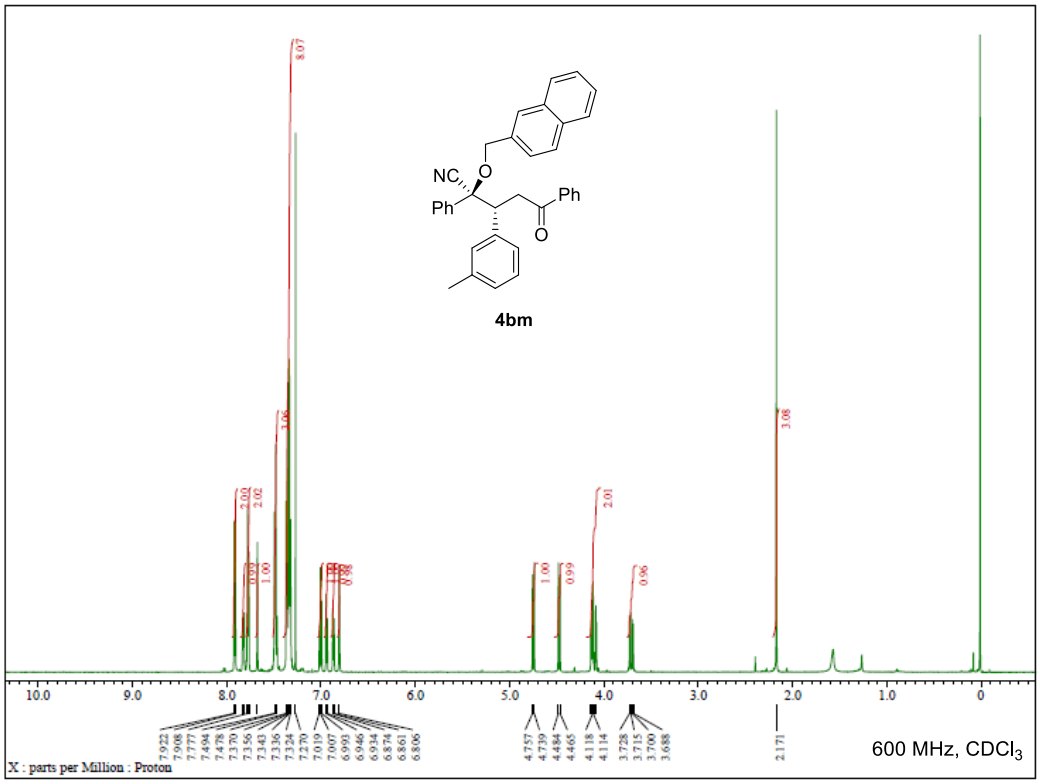

NC
O
Ph
Ph
O
OMe
4bj
150 MHz, CDCl3
X : parts per Million : Carbon13

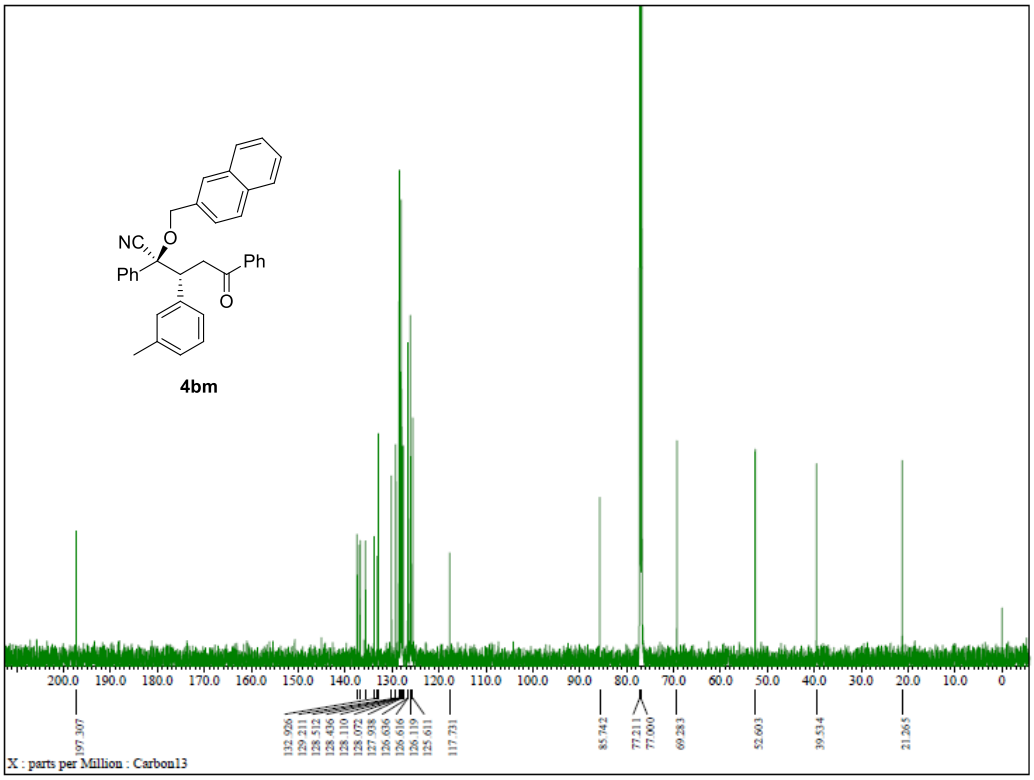

NC
O
Ph
Ph
O
Cl
4bk
X : parts per Million : Proton
600 MHz, CDCl3

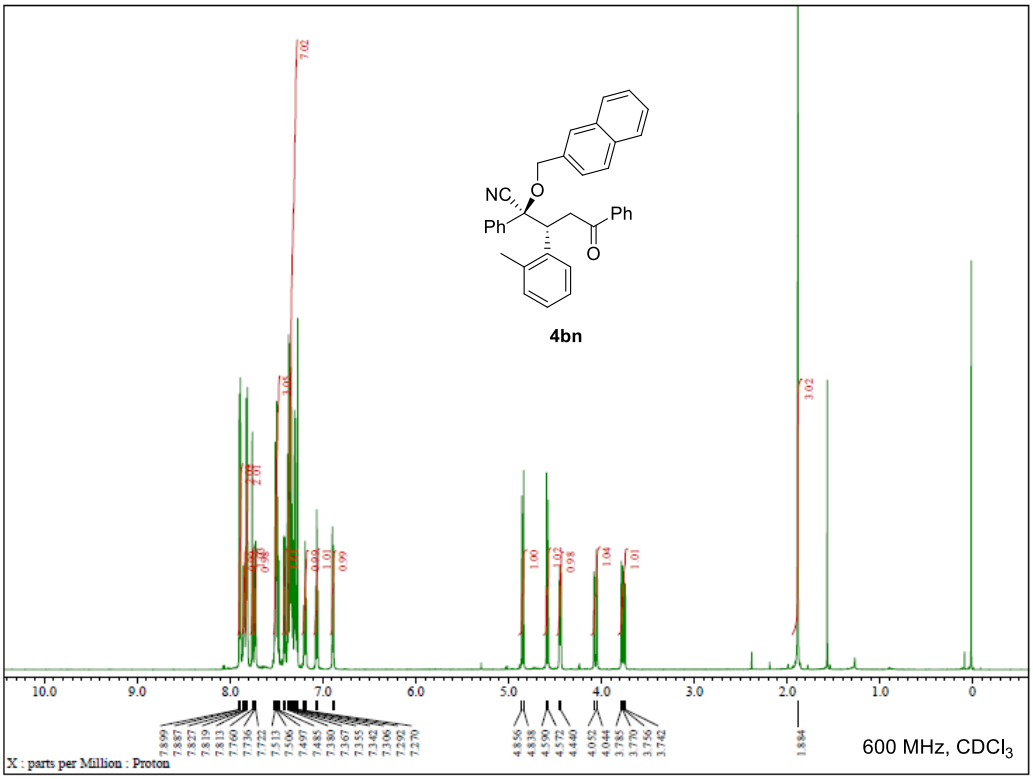

NC
O
Ph
Ph
O
Cl
4bk
X : parts per Million : Carbon13
150 MHz, CDCl3

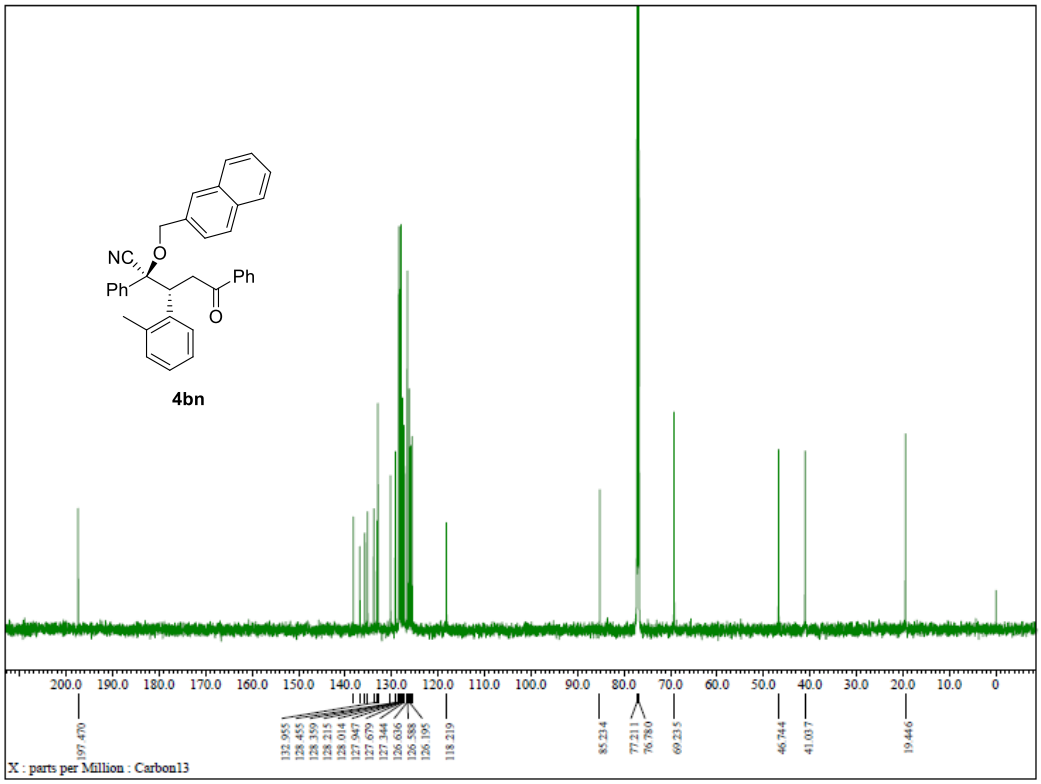

NC
O
Ph
Ph
O
CF3
4bl
600 MHz, CDCl3
X : parts per Million : Proton


NC
O
Ph
Ph
O
CF3
4bl
150 MHz, CDCl3
X : parts per Million : Carbon13

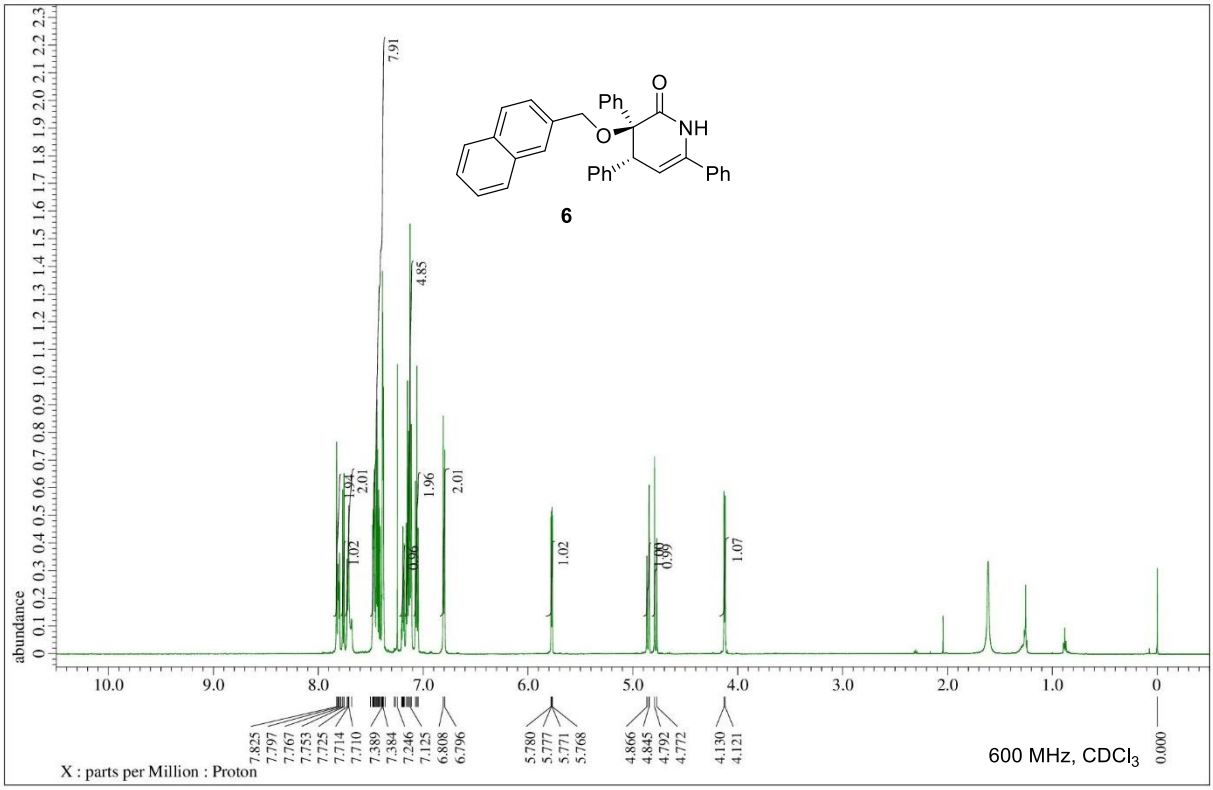

NC
O
Ph
Ph
O
4bm
600 MHz, CDCl3
X : parts per Million : Proton

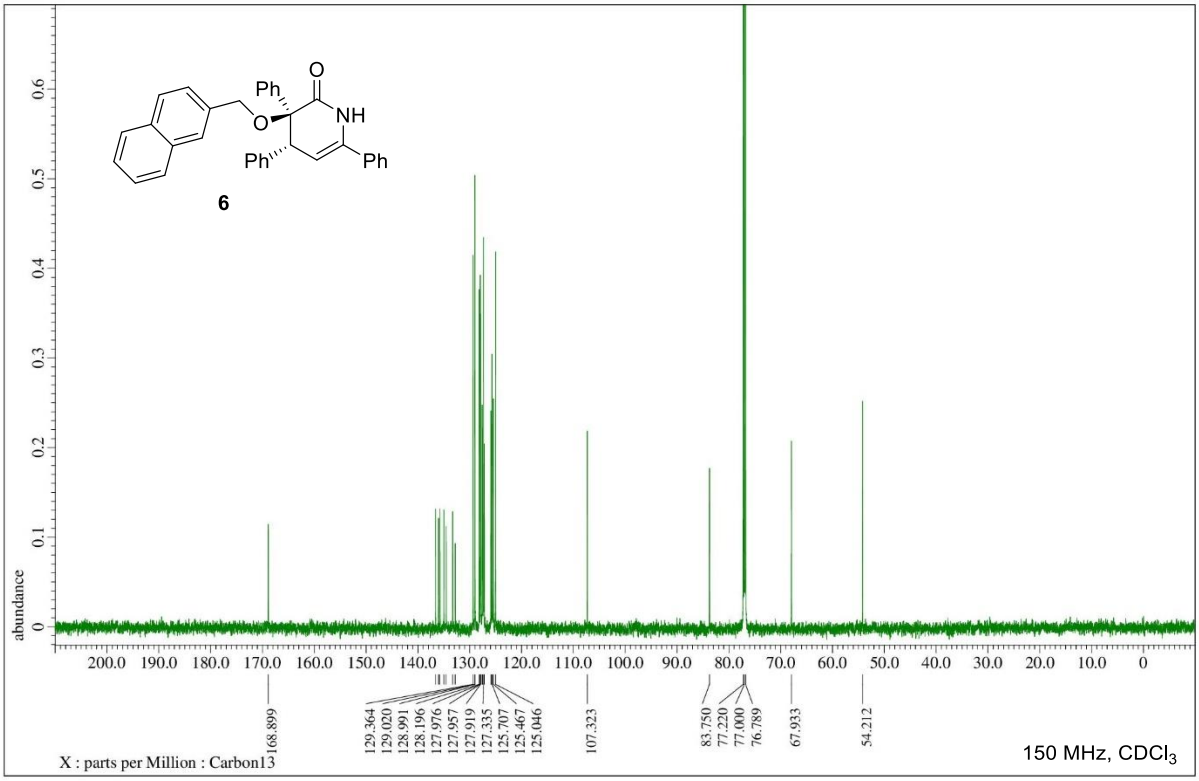

NC
O
Ph
Ph
O
4bm
150 MHz, CDCl3
X : parts per Million : Carbon13



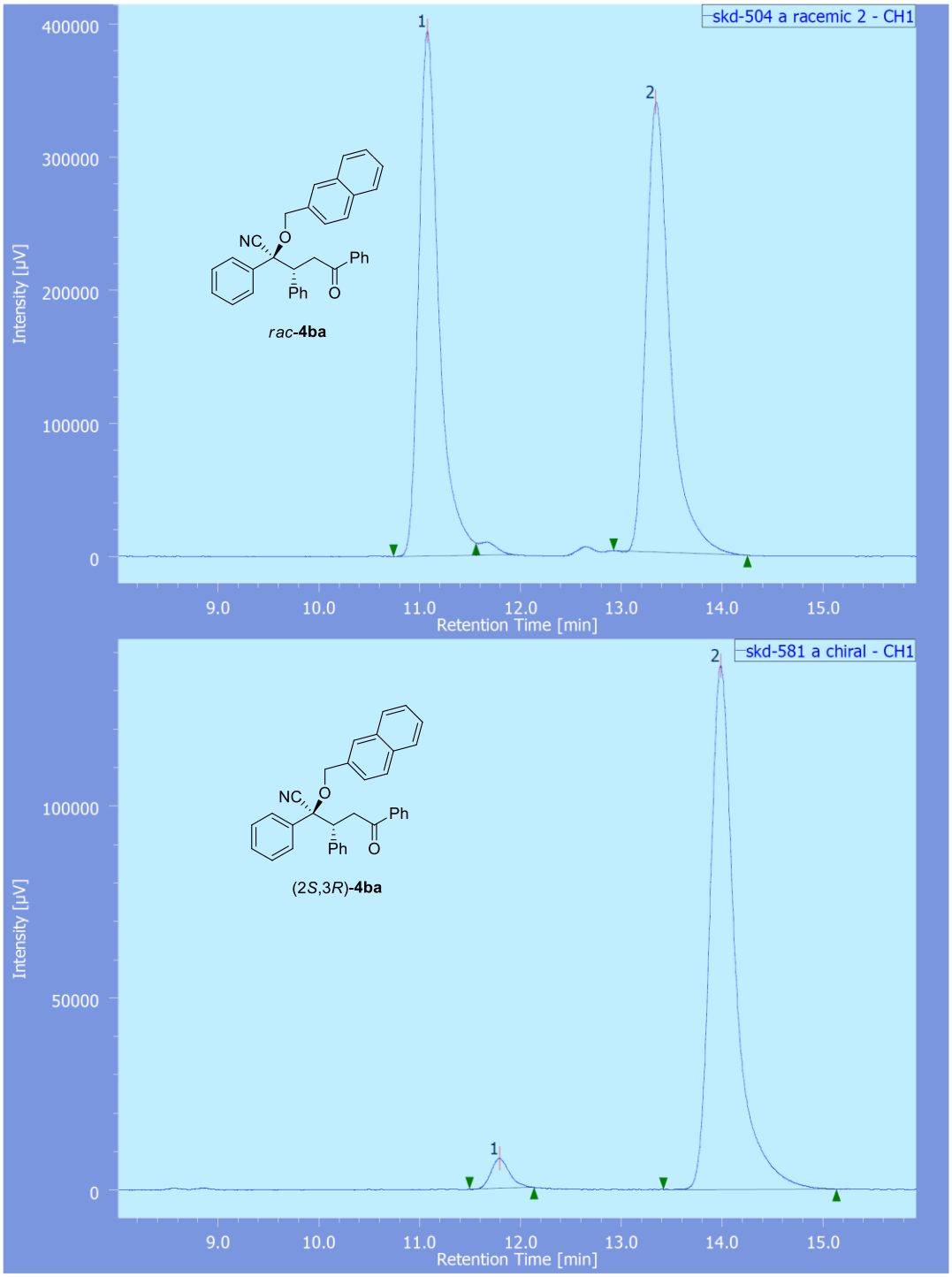


150 MHz, $CDCl_3$

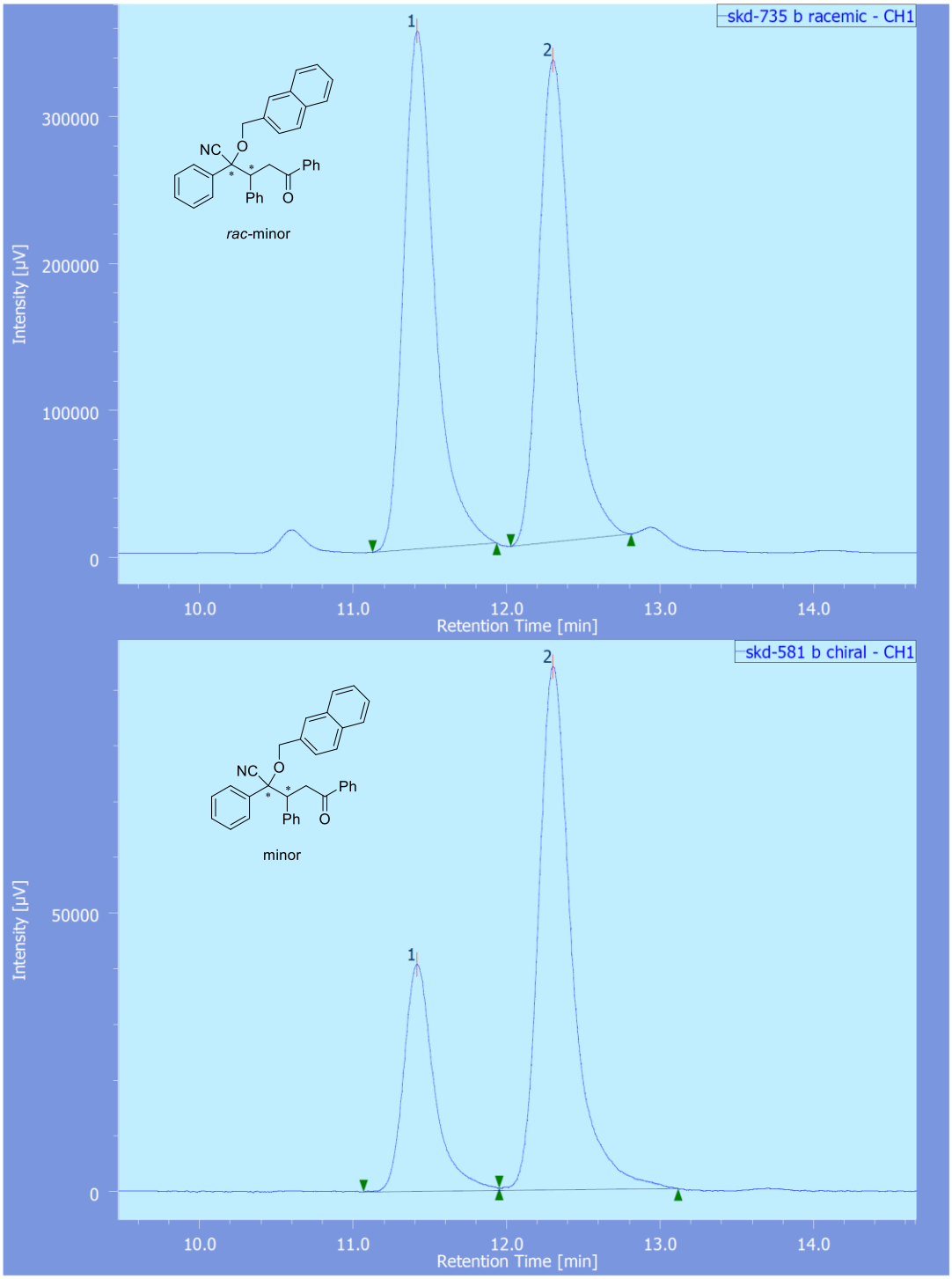

Ph
O
NH
Ph
O
Ph
6
7.91
4.85
2.01
1.96
2.01
1.02
1.02
1.07
abundance
X : parts per Million : Proton
600 MHz, CDCl3


Ph
O
NH
Ph
O
Ph
6
abundance
X : parts per Million : Carbon13
150 MHz, CDCl3

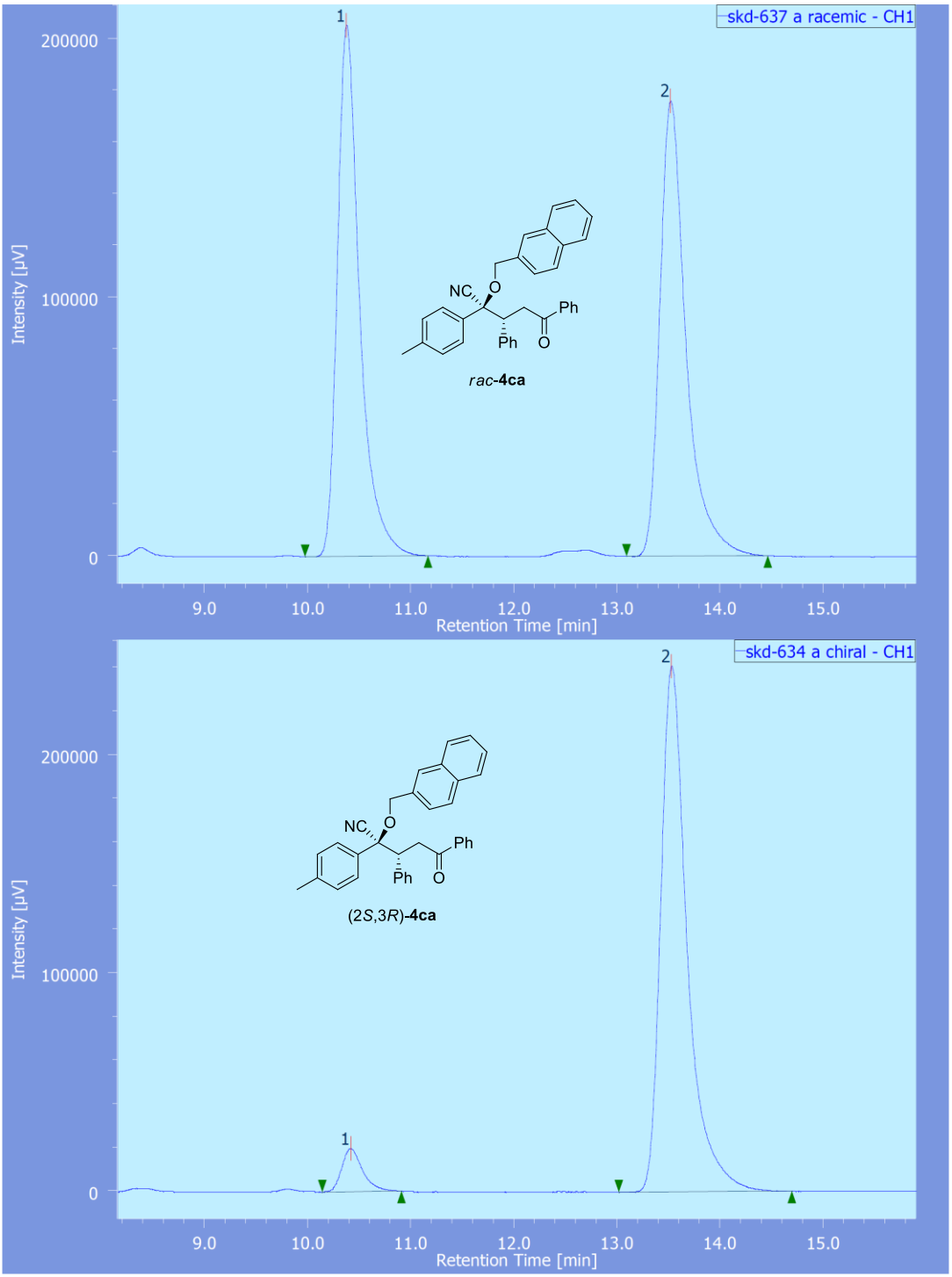
5. HPLC Chart



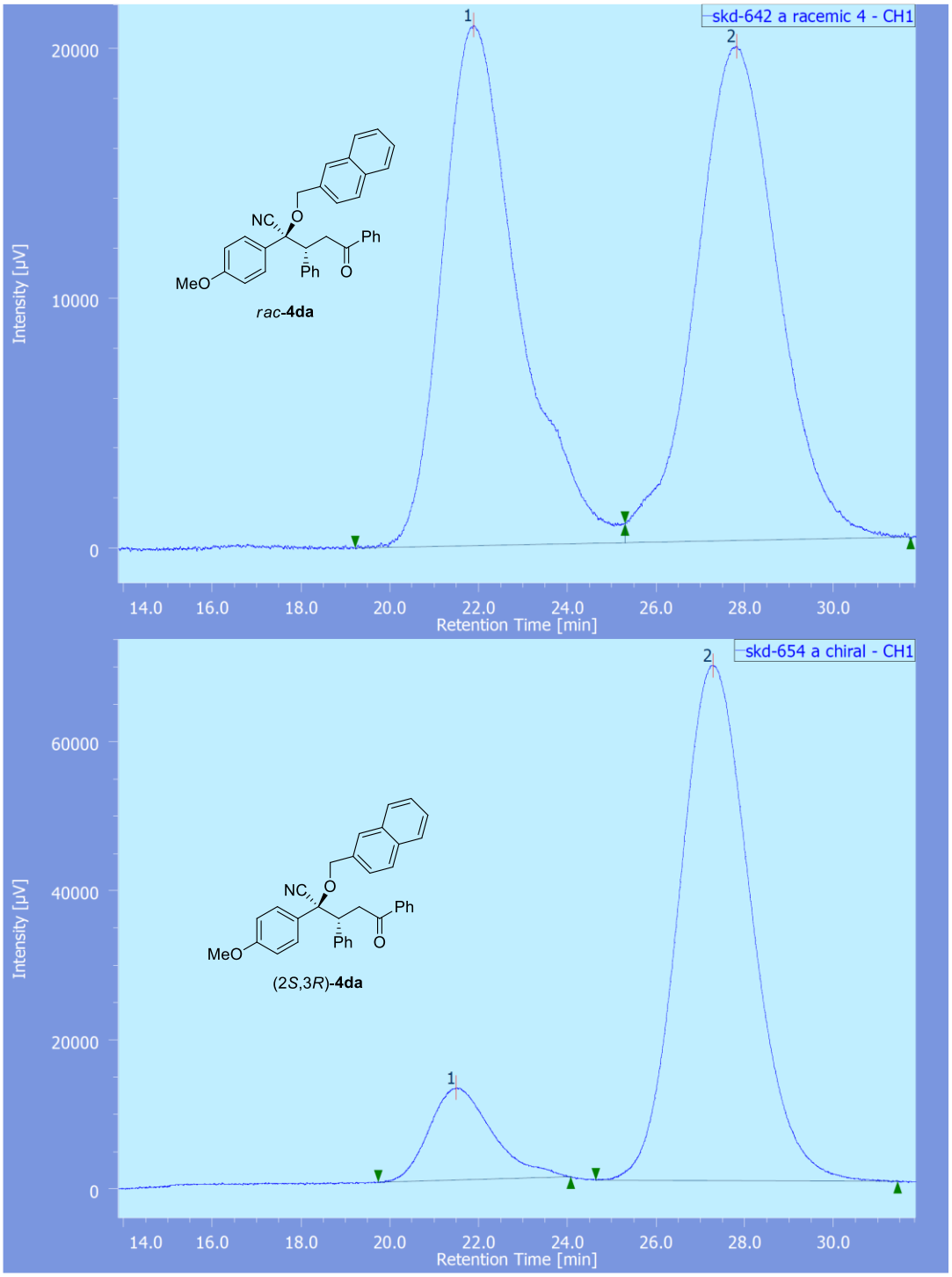
	Peak 1	Peak 2
Retention time (min)	11.8	14.0
Area (%)	4.1	95.9



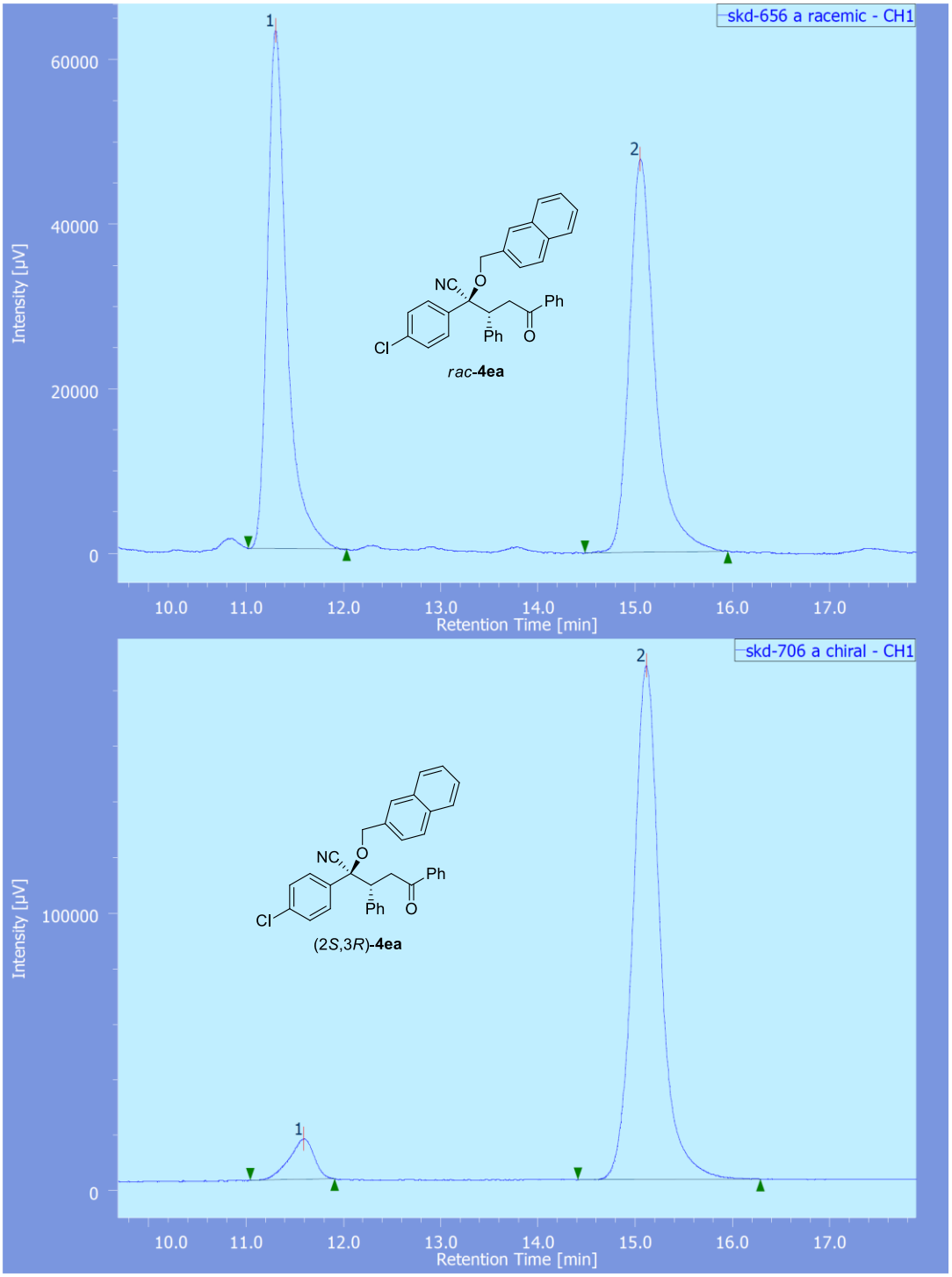
	Peak 1	Peak 2
Retention time (min)	11.4	12.3
Area (%)	28.4	71.6



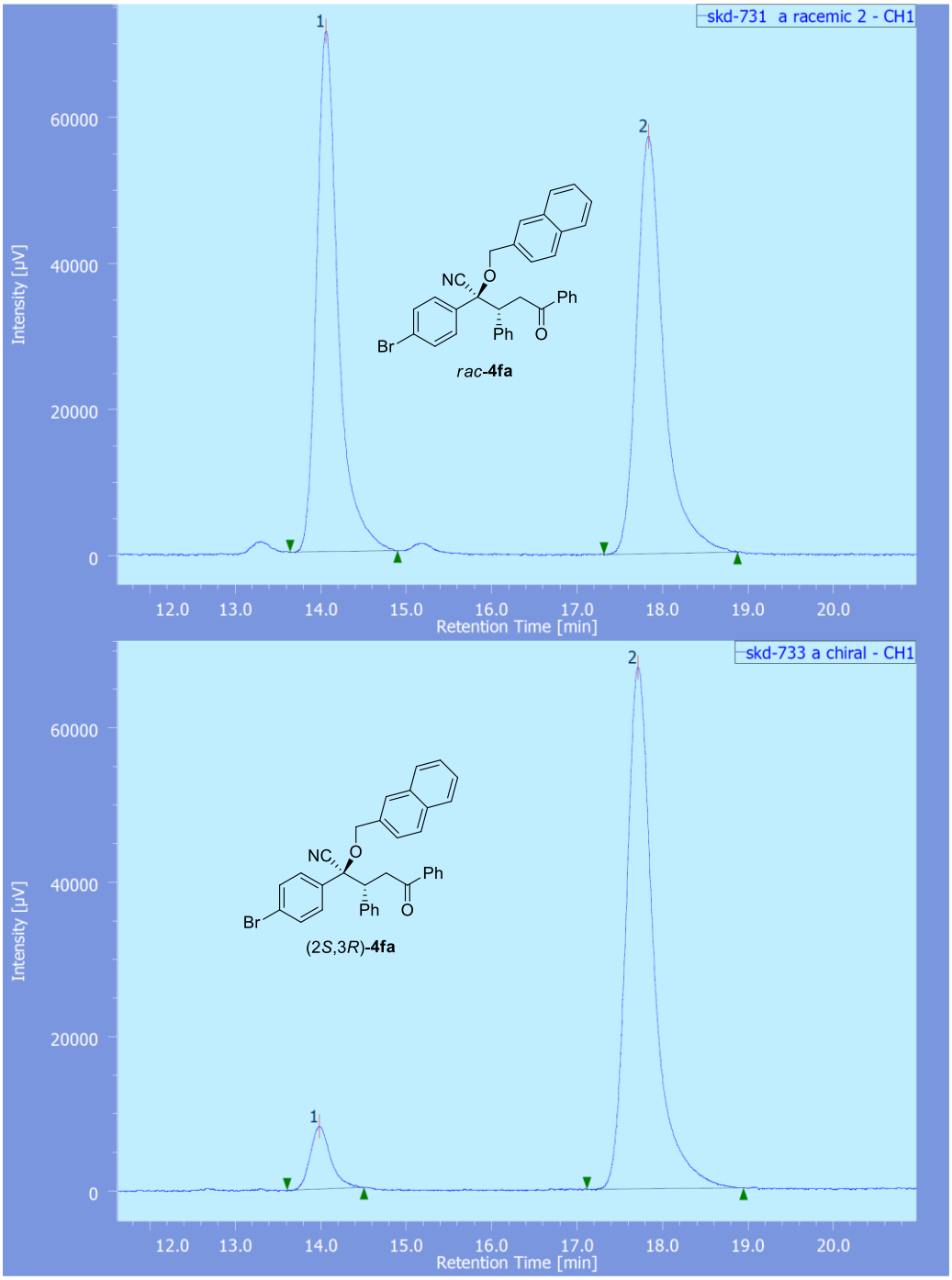
	Peak 1	Peak 2
Retention time (min)	10.4	13.5
Area (%)	6.1	93.9



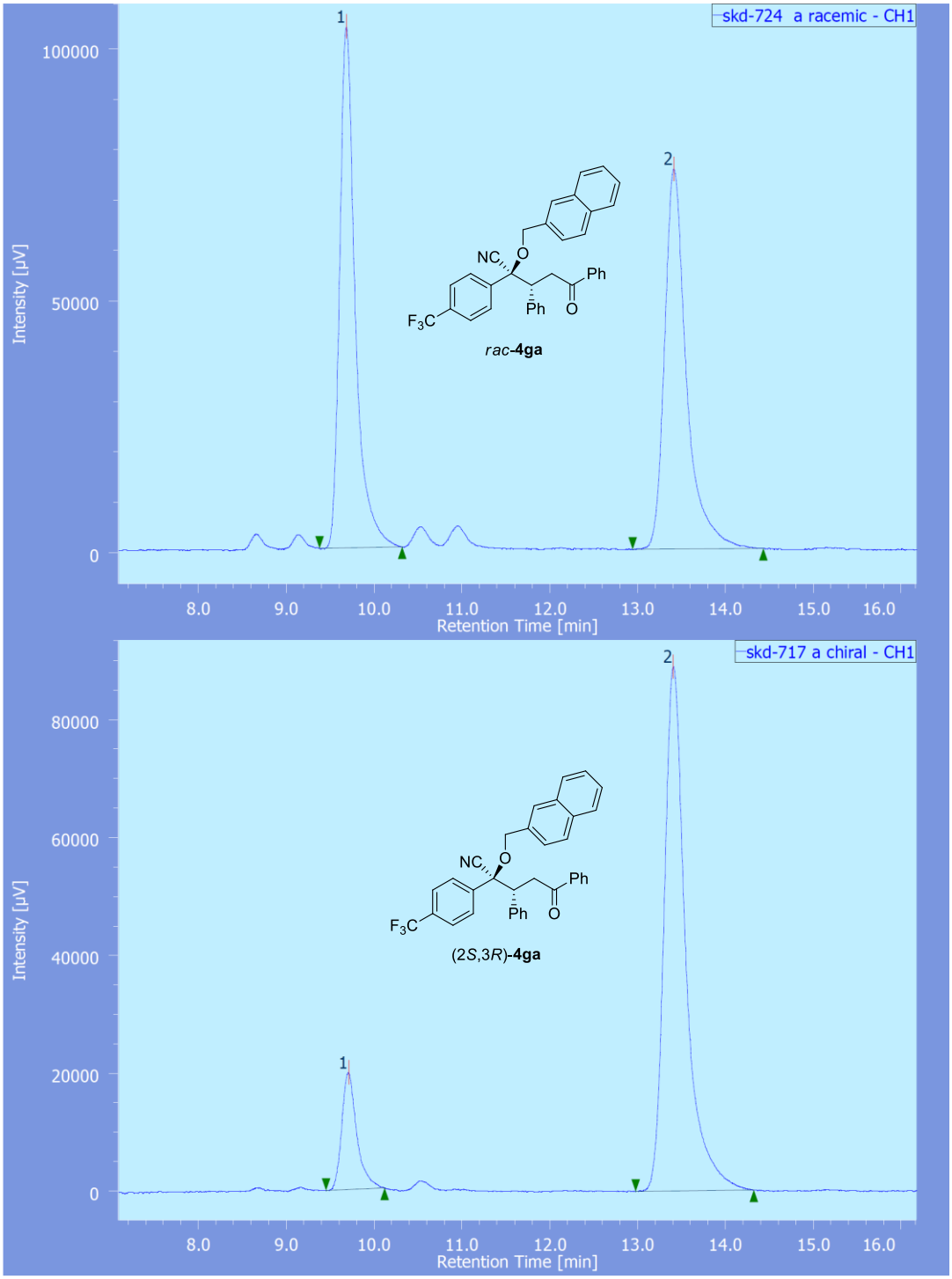
	Peak 1	Peak 2
Retention time (min)	21.5	27.3
Area (%)	13.5	86.5



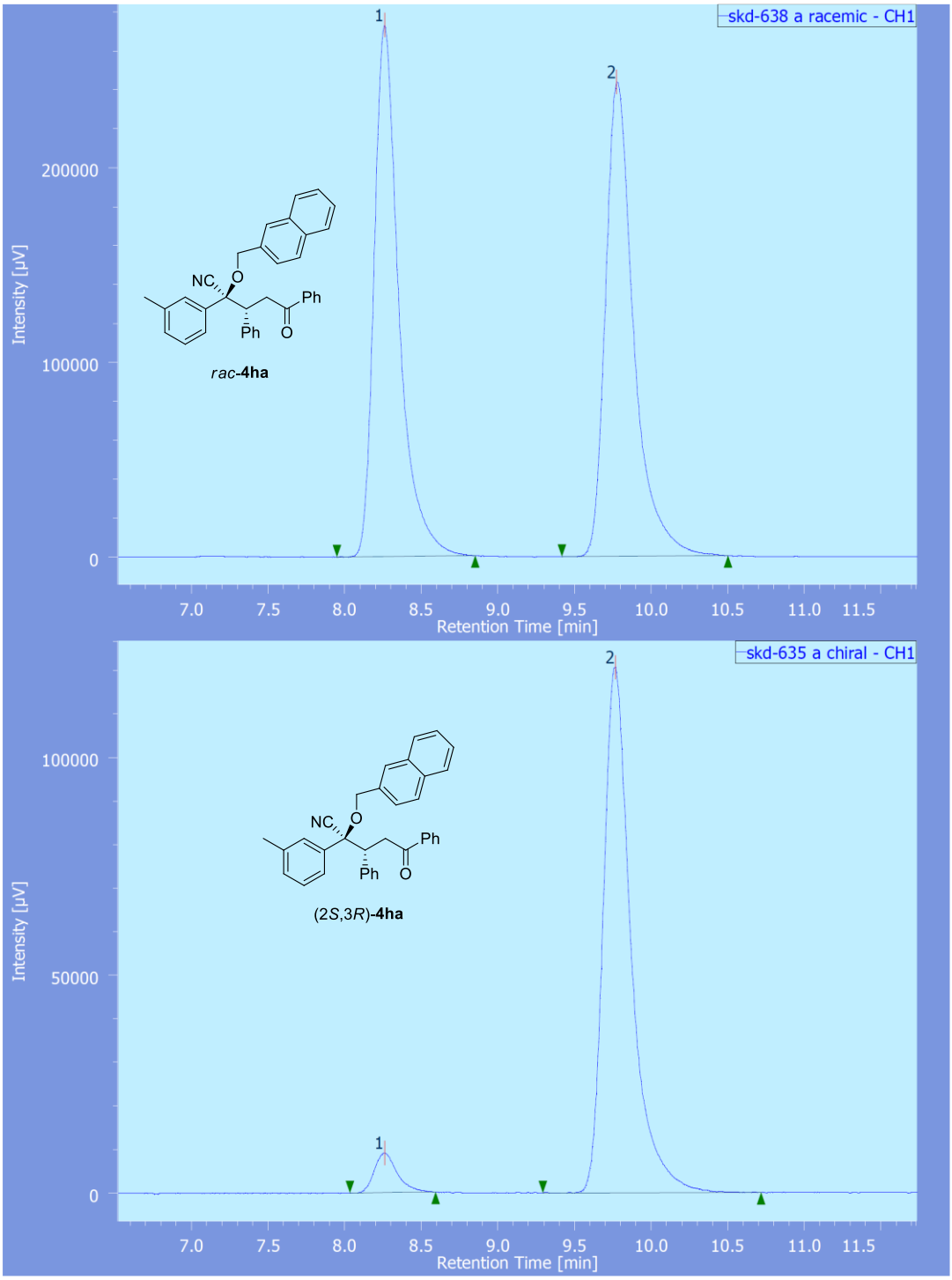
	Peak 1	Peak 2
Retention time (min)	11.6	15.1
Area (%)	6.8	93.2



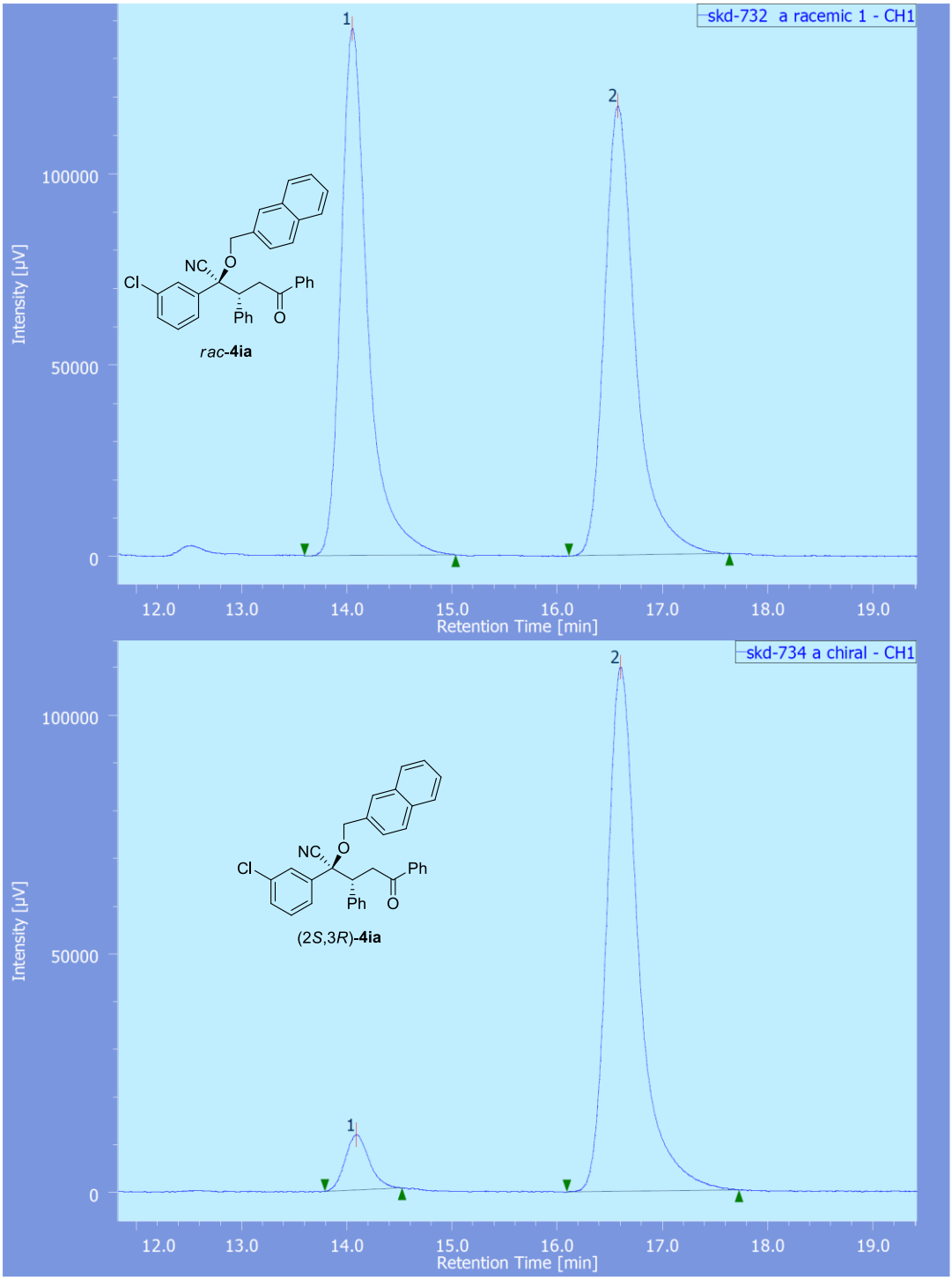
	Peak 1	Peak 2
Retention time (min)	14.0	17.7
Area (%)	8.2	91.7



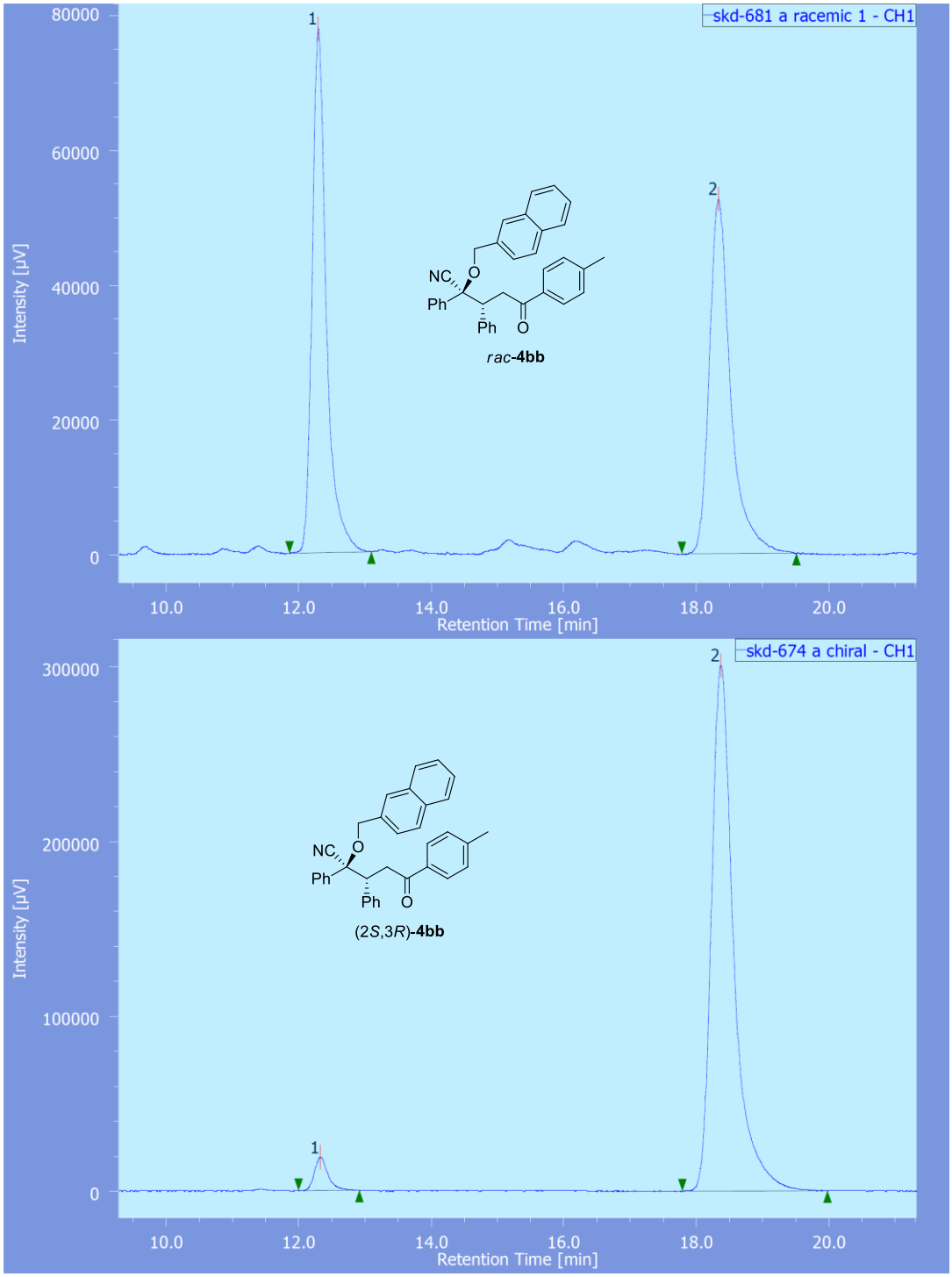
	Peak 1	Peak 2
Retention time (min)	9.7	13.4
Area (%)	13.5	86.5



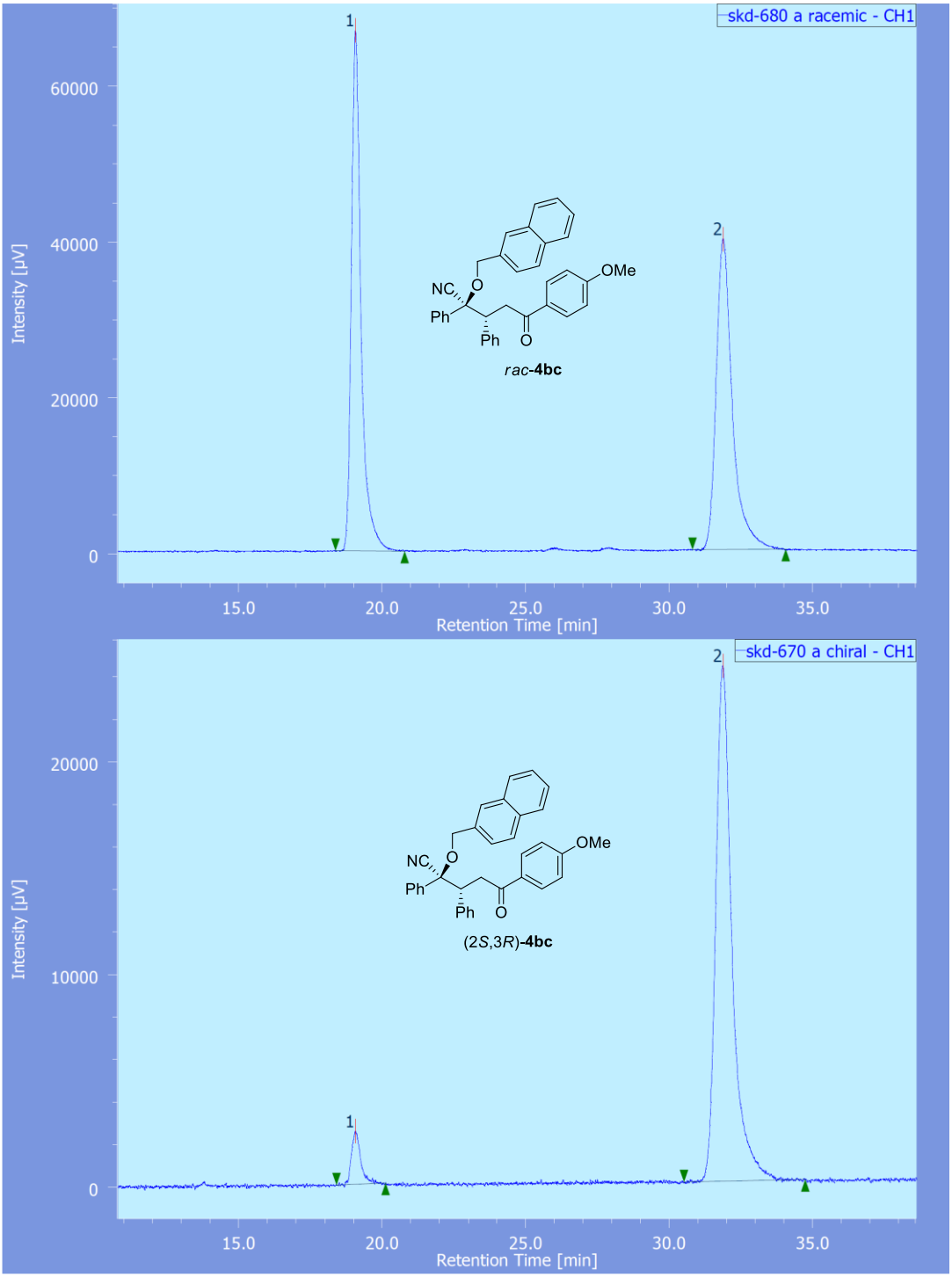
	Peak 1	Peak 2
Retention time (min)	8.3	9.8
Area (%)	5.9	94.1



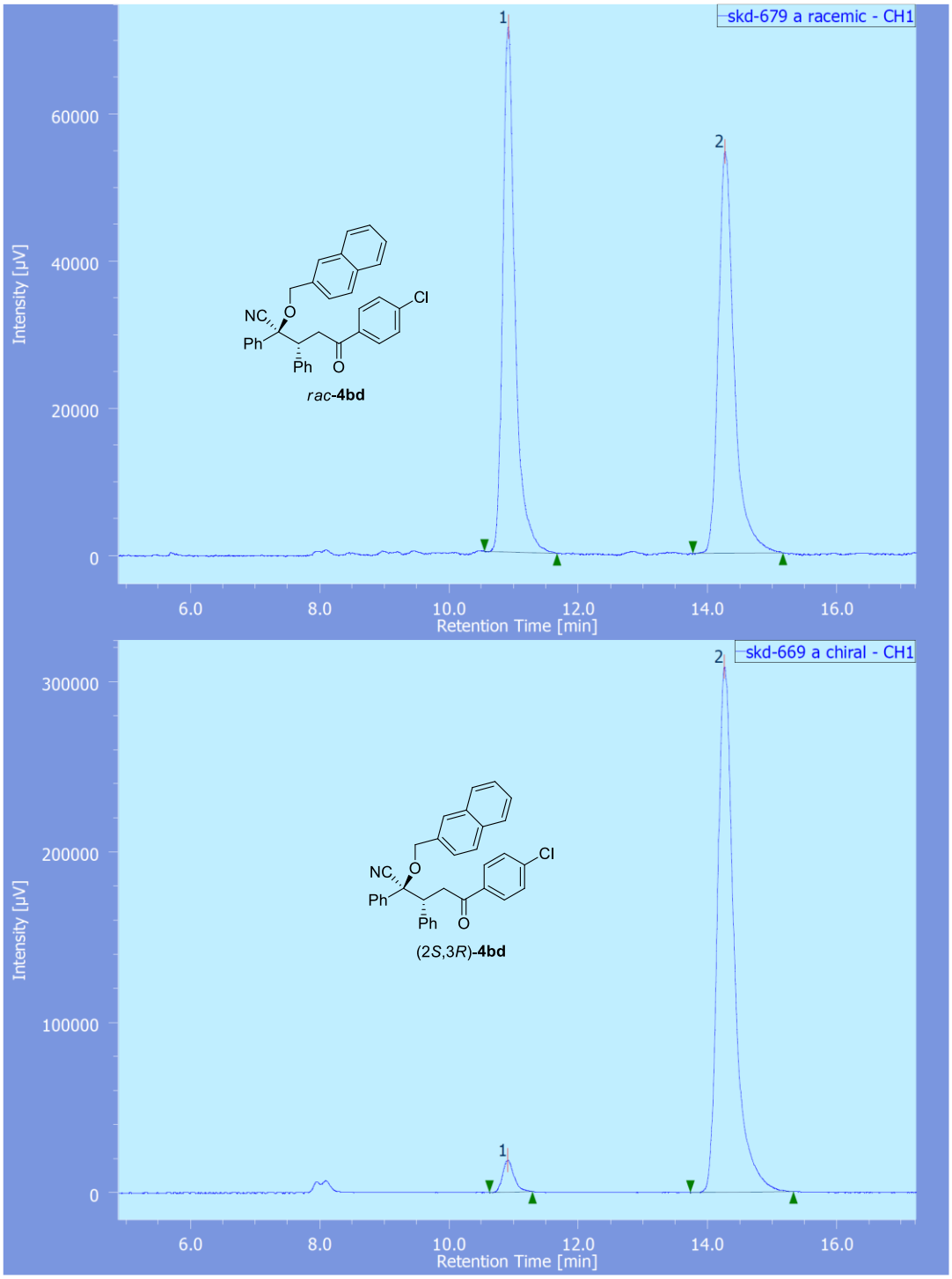
	Peak 1	Peak 2
Retention time (min)	14.1	16.6
Area (%)	7.5	92.5



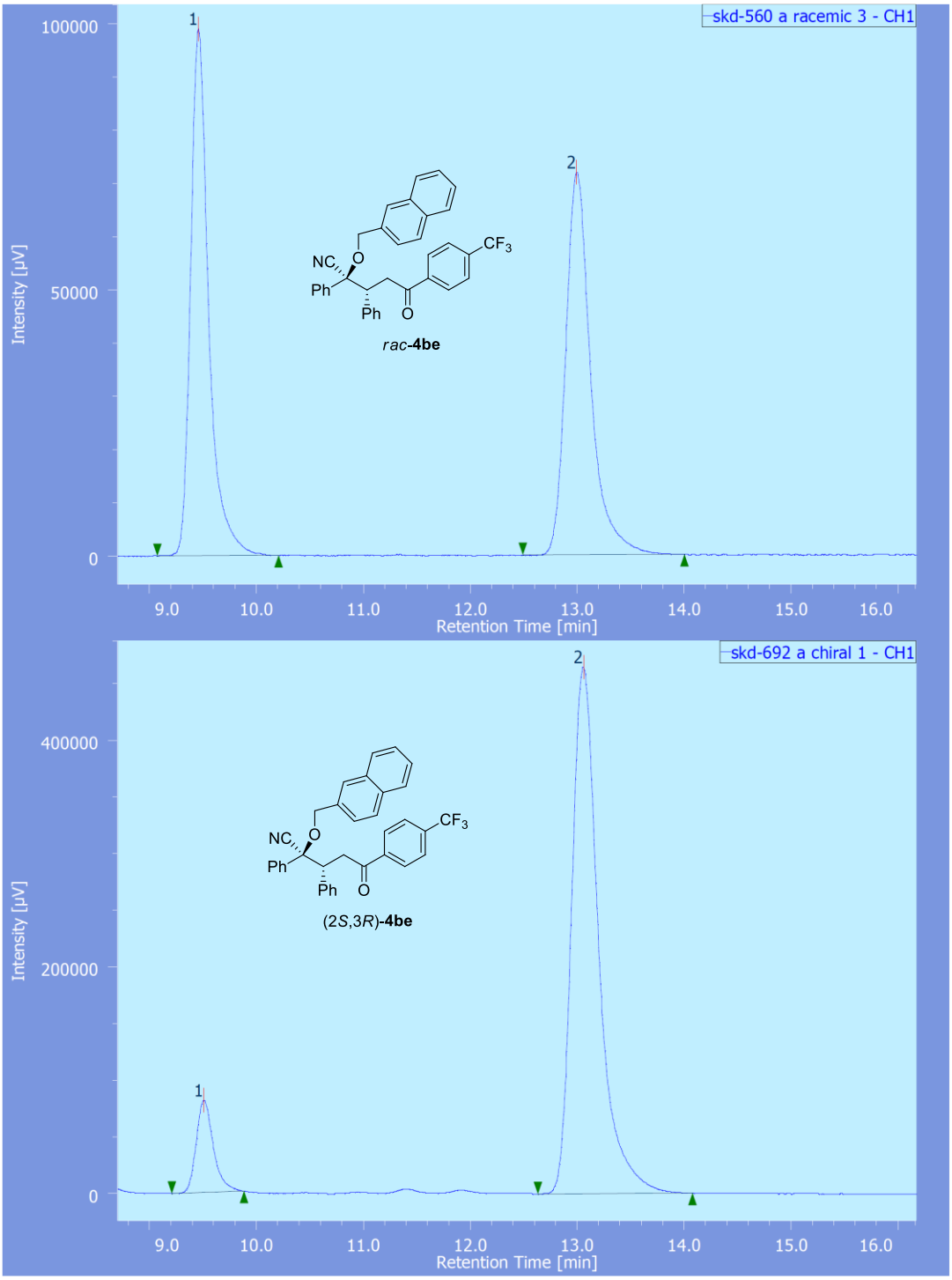
	Peak 1	Peak 2
Retention time (min)	12.3	18.4
Area (%)	3.8	96.2



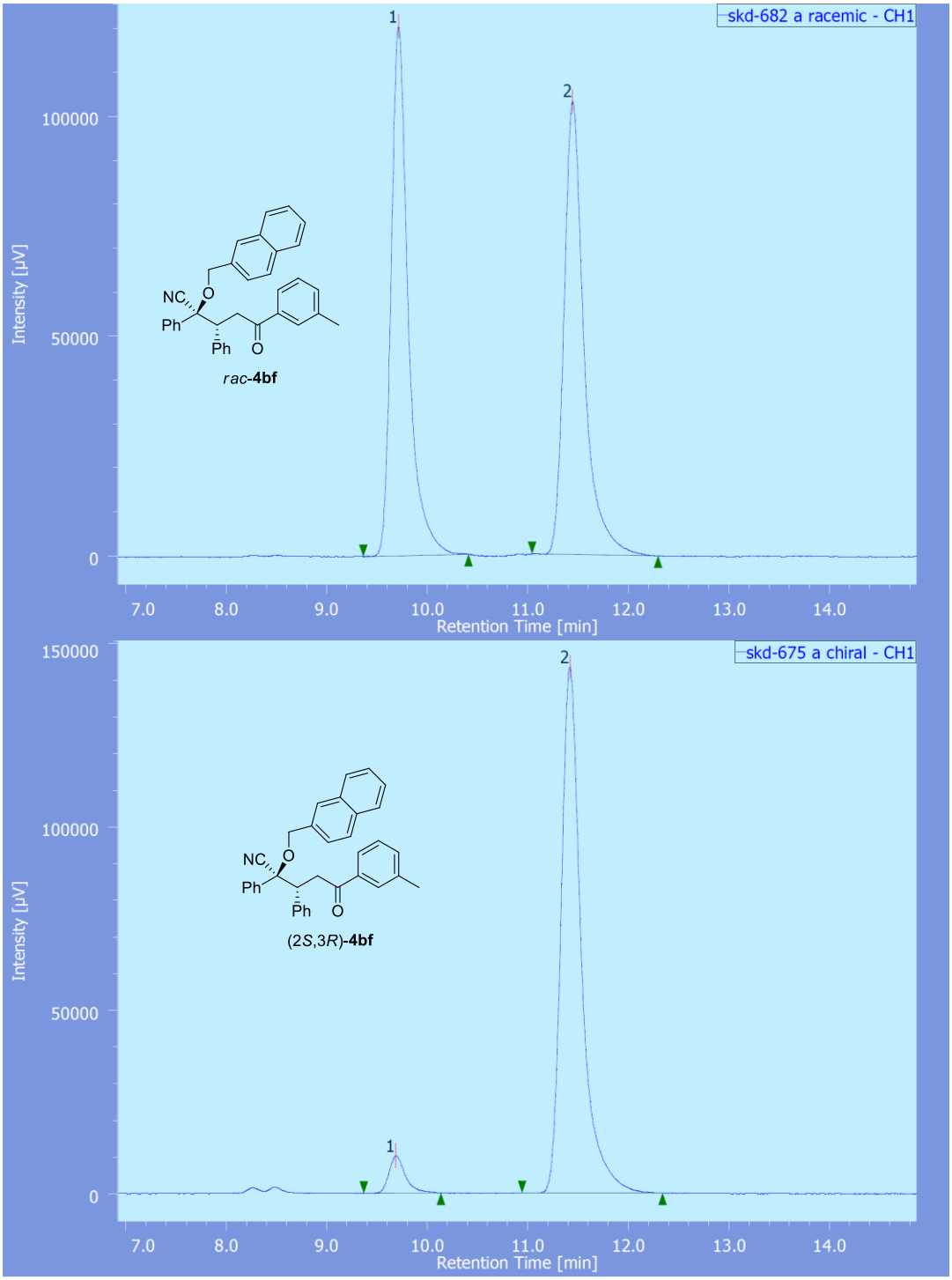
	Peak 1	Peak 2
Retention time (min)	19.1	31.9
Area (%)	5.5	94.5



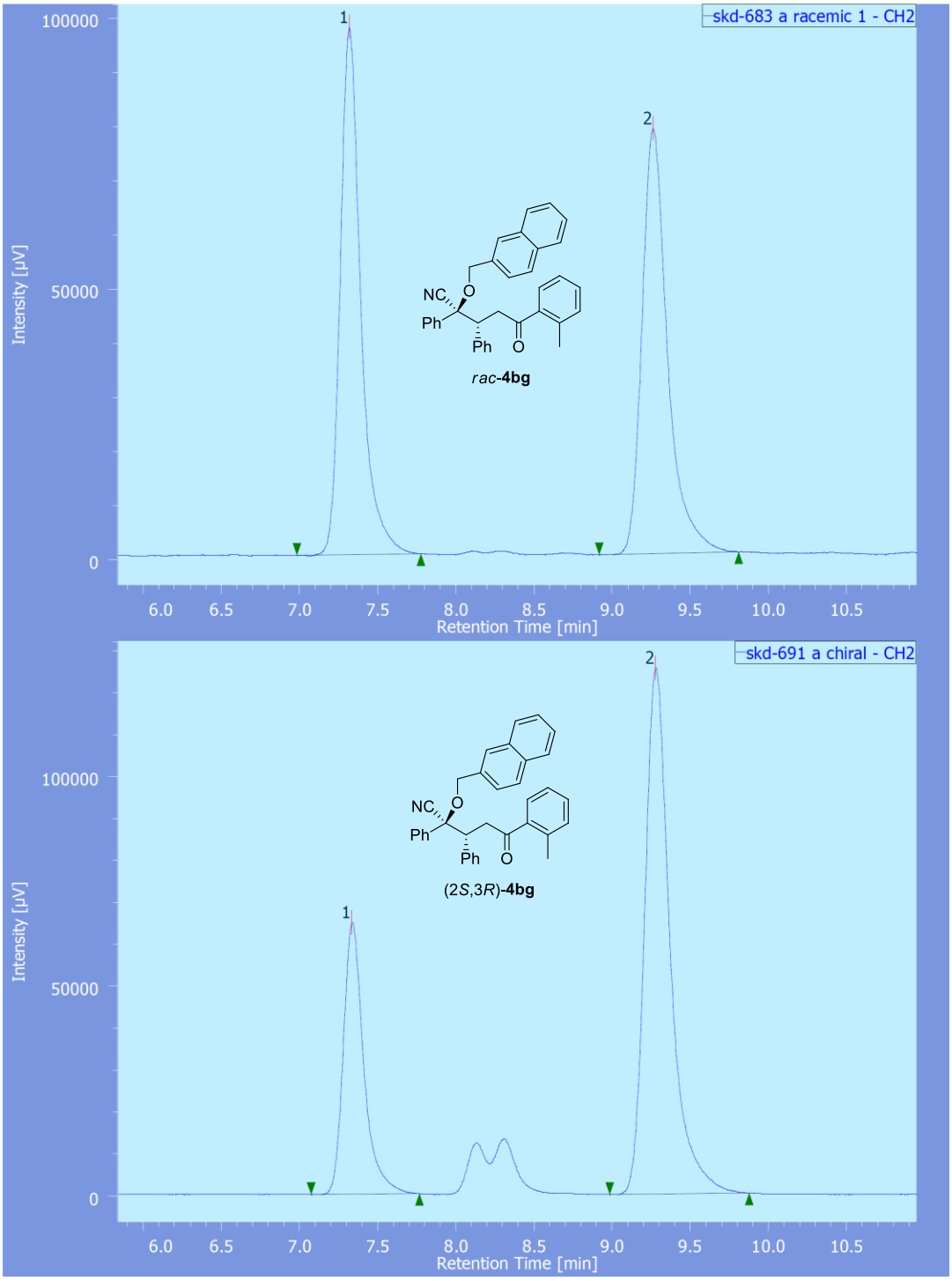
	Peak 1	Peak 2
Retention time (min)	10.9	14.2
Area (%)	4.0	96.0



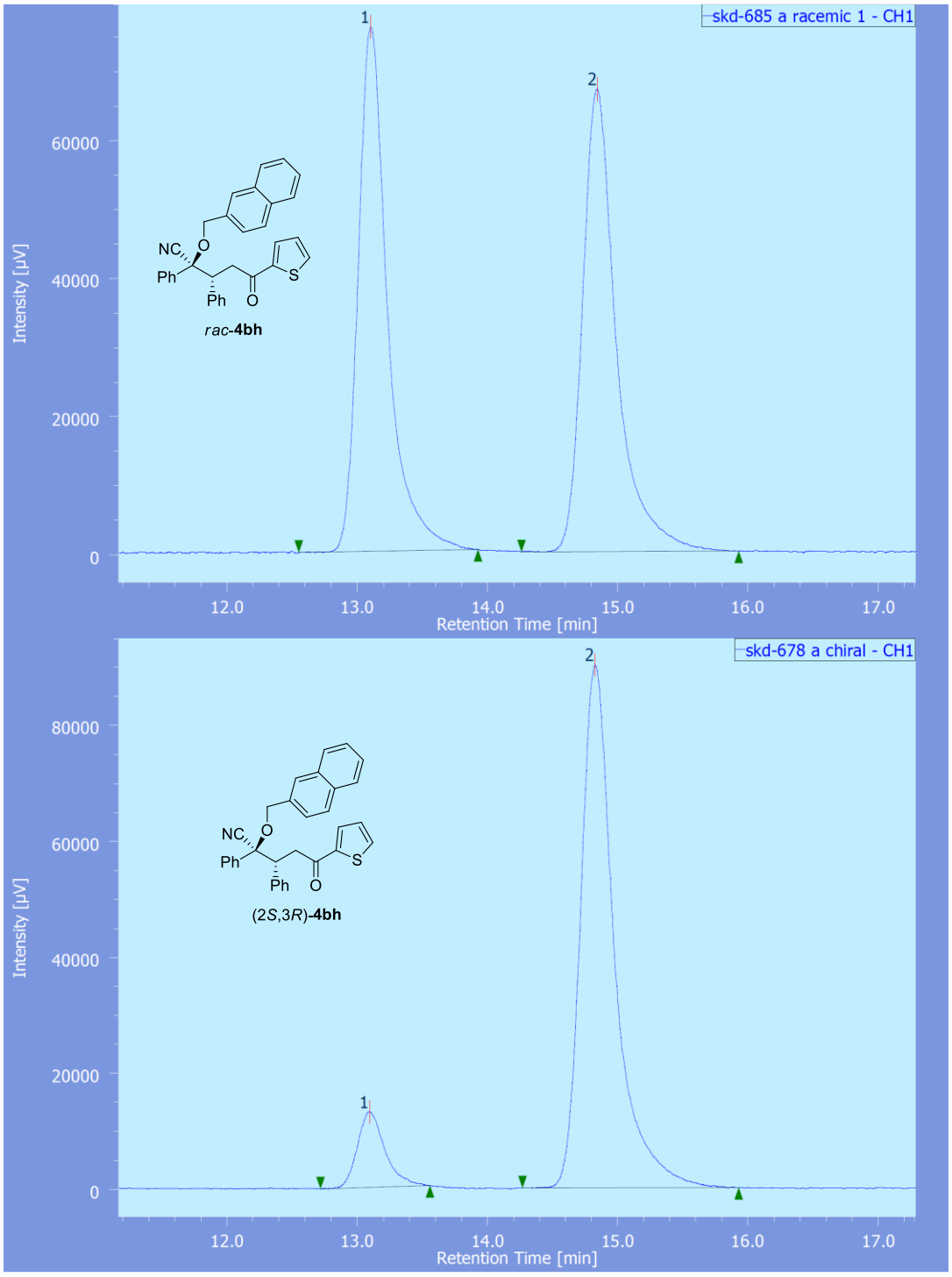
	Peak 1	Peak 2
Retention time (min)	9.5	13.1
Area (%)	10.0	90.0



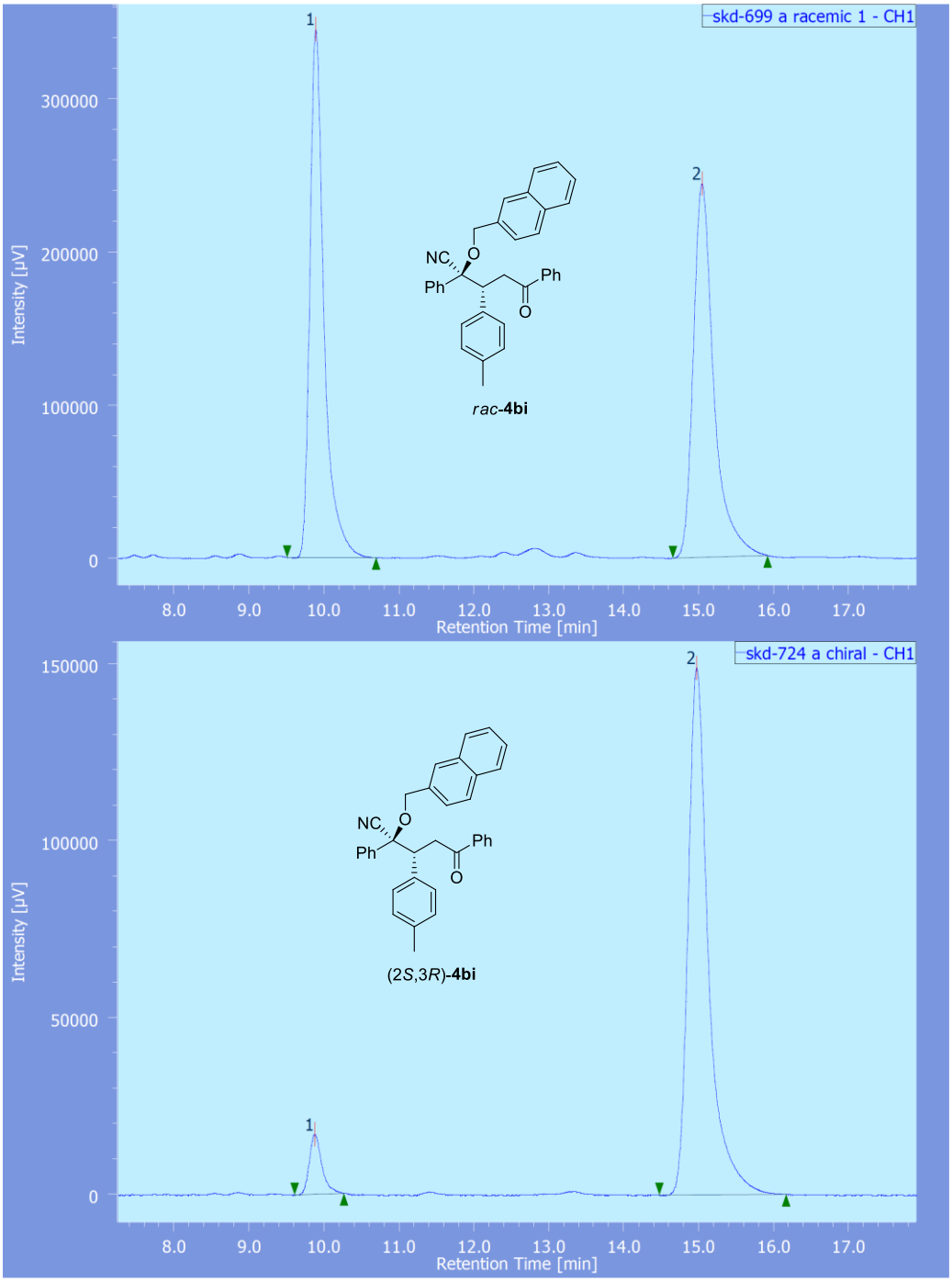
	Peak 1	Peak 2
Retention time (min)	9.7	11.4
Area (%)	5.5	94.5



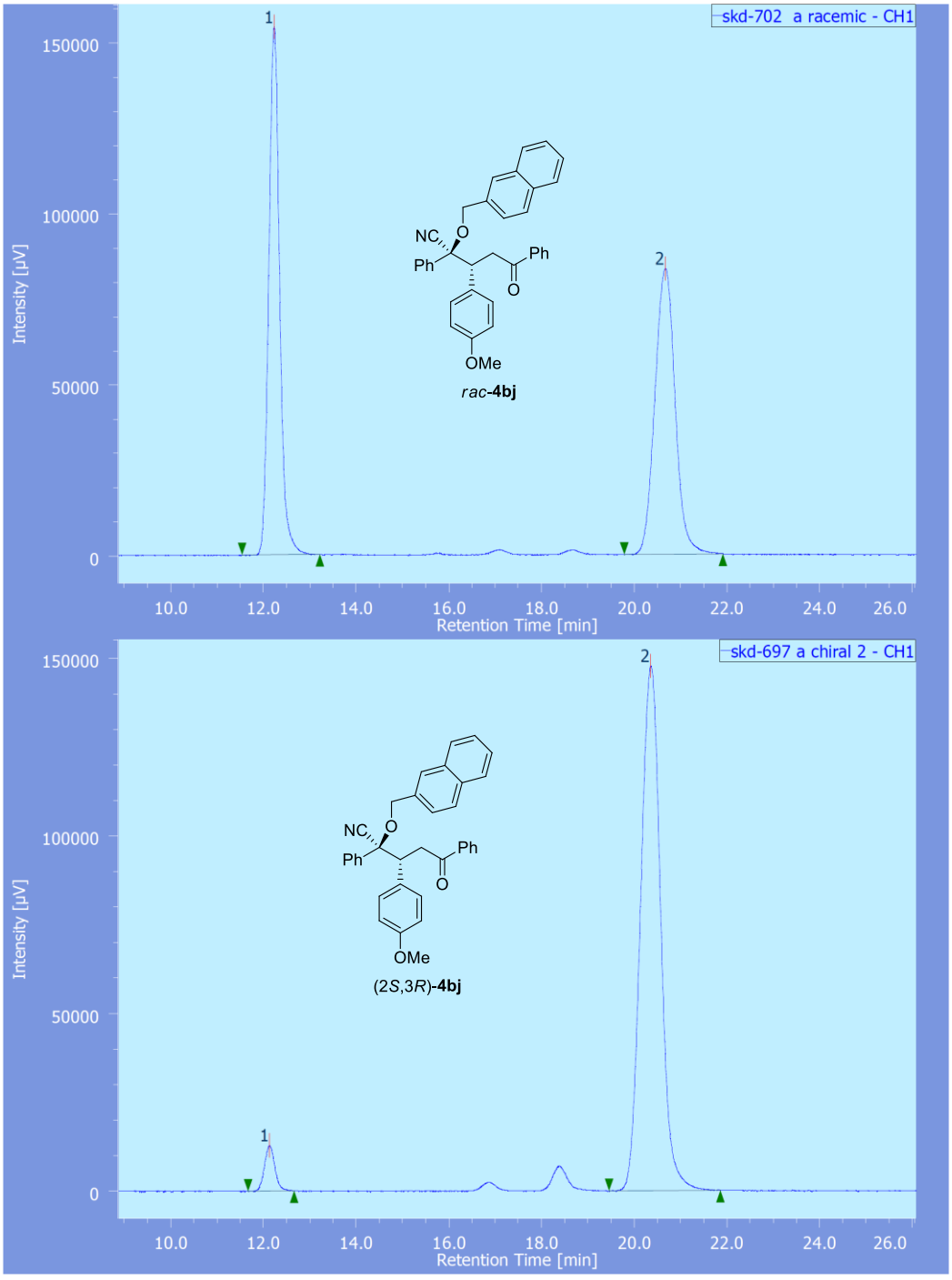
	Peak 1	Peak 2
Retention time (min)	7.3	9.3
Area (%)	29.4	70.6



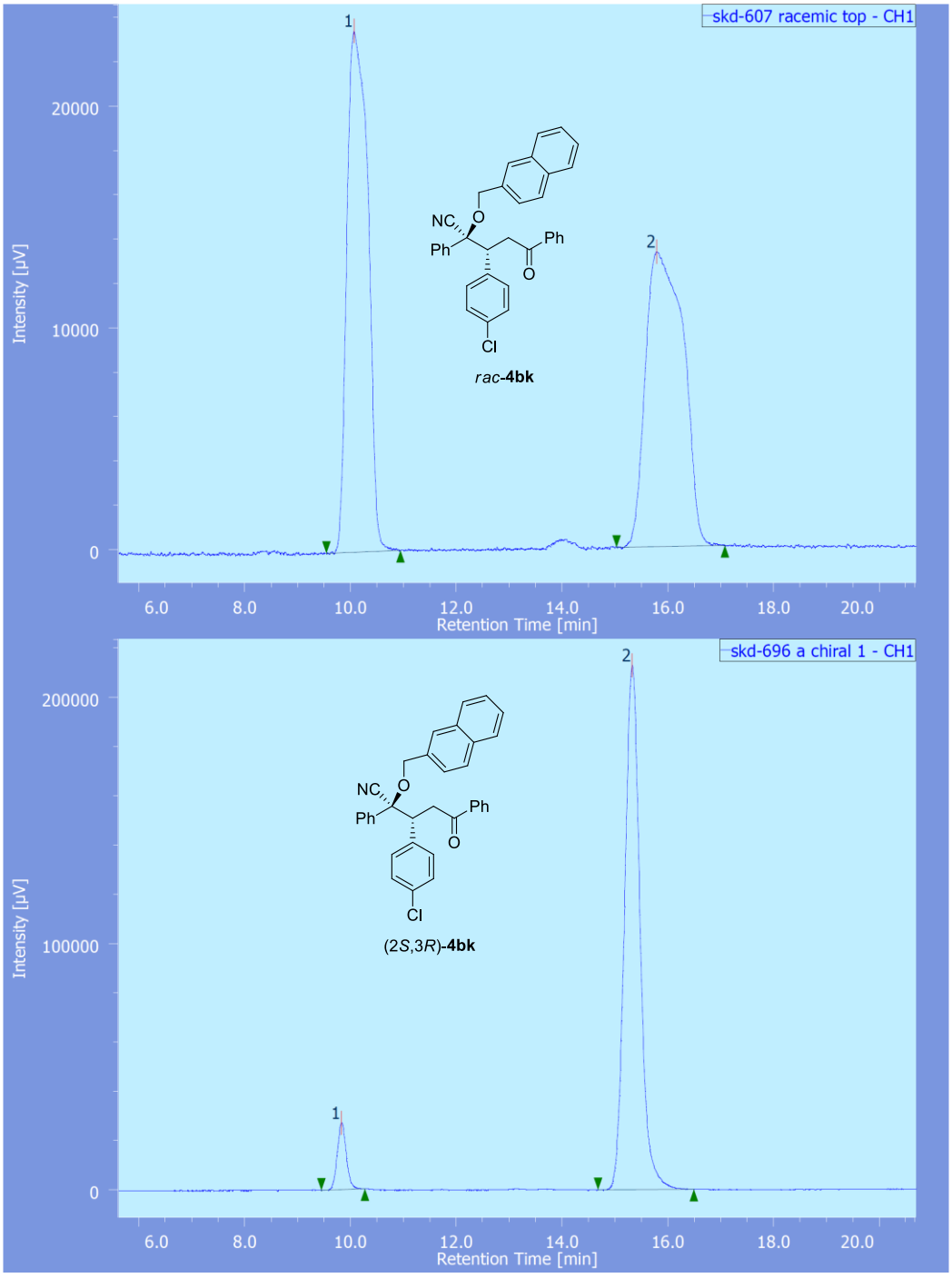
	Peak 1	Peak 2
Retention time (min)	13.1	14.8
Area (%)	10.5	89.4



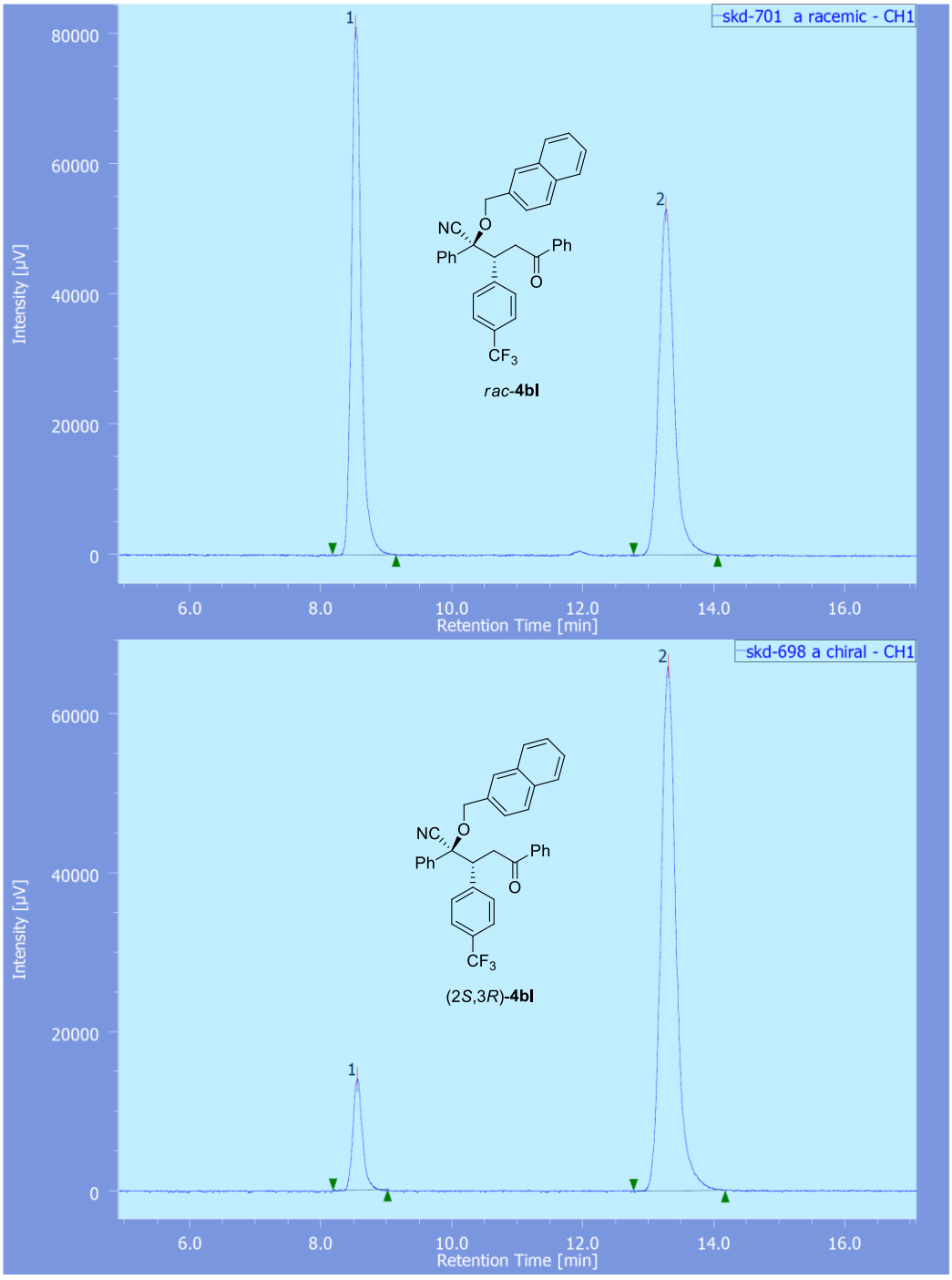
	Peak 1	Peak 2
Retention time (min)	9.9	15.0
Area (%)	6.6	93.4



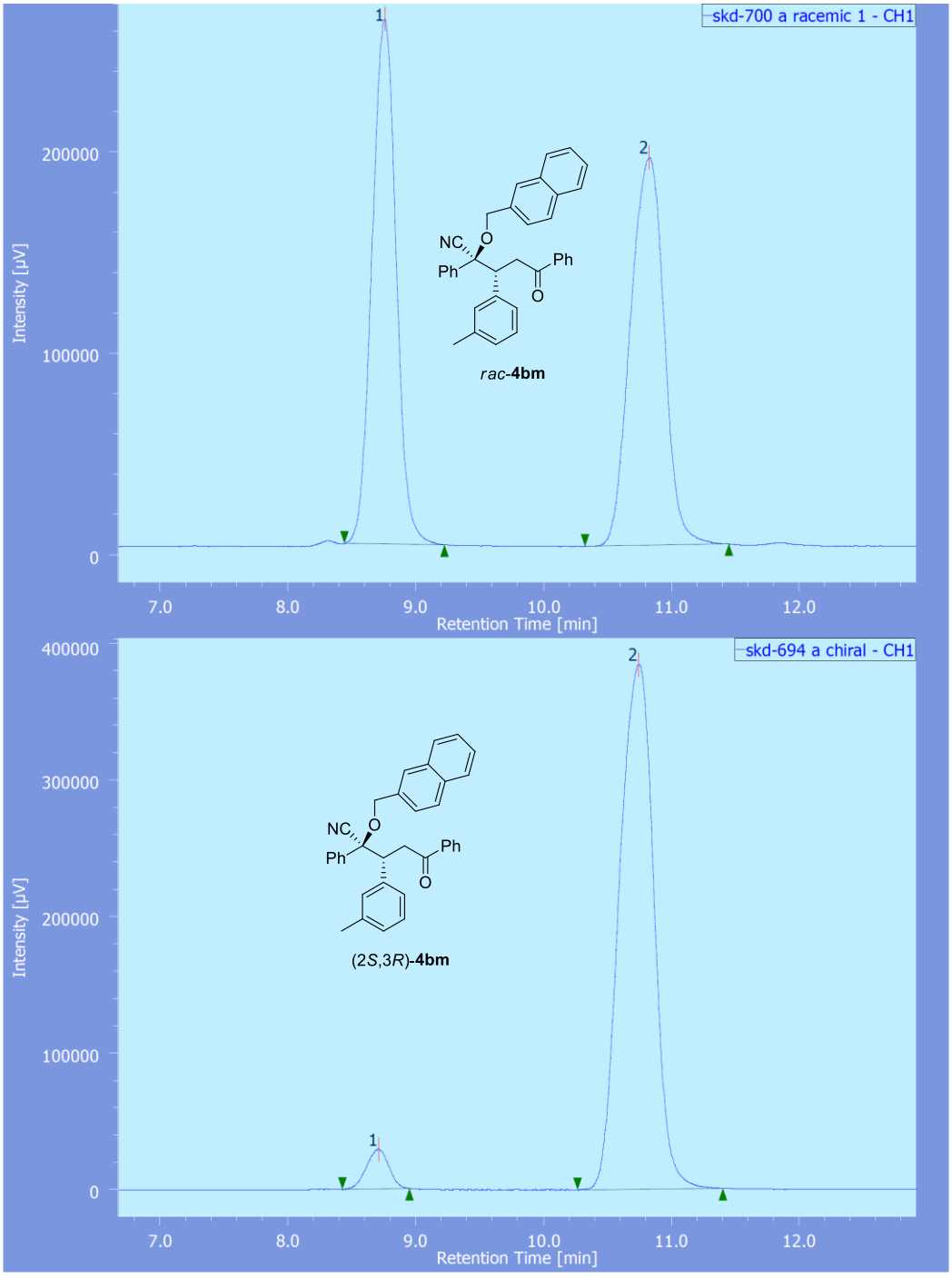
	Peak 1	Peak 2
Retention time (min)	12.1	20.3
Area (%)	4.4	95.6



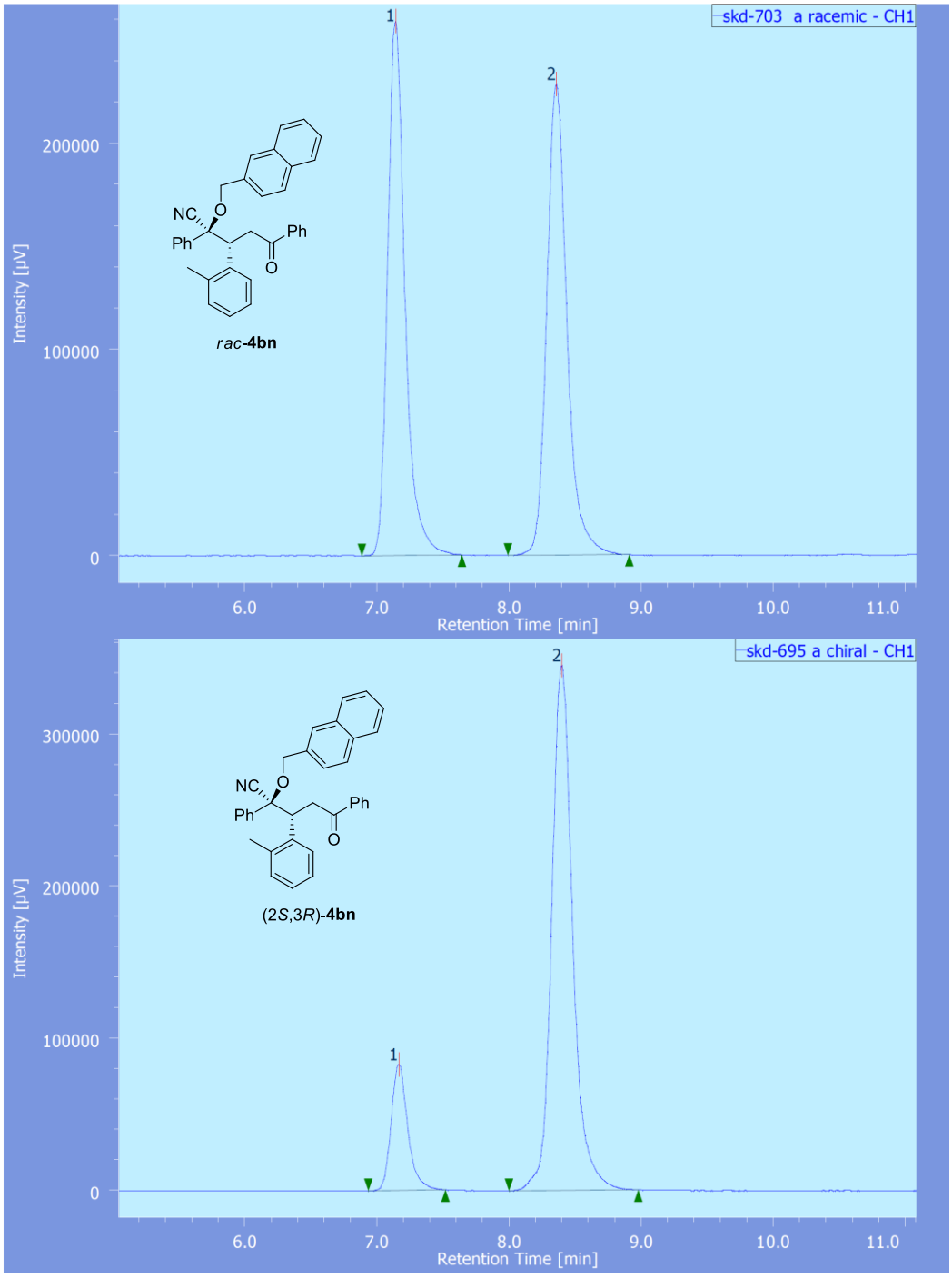
	Peak 1	Peak 2
Retention time (min)	16.4	27.8
Area (%)	6.9	93.1



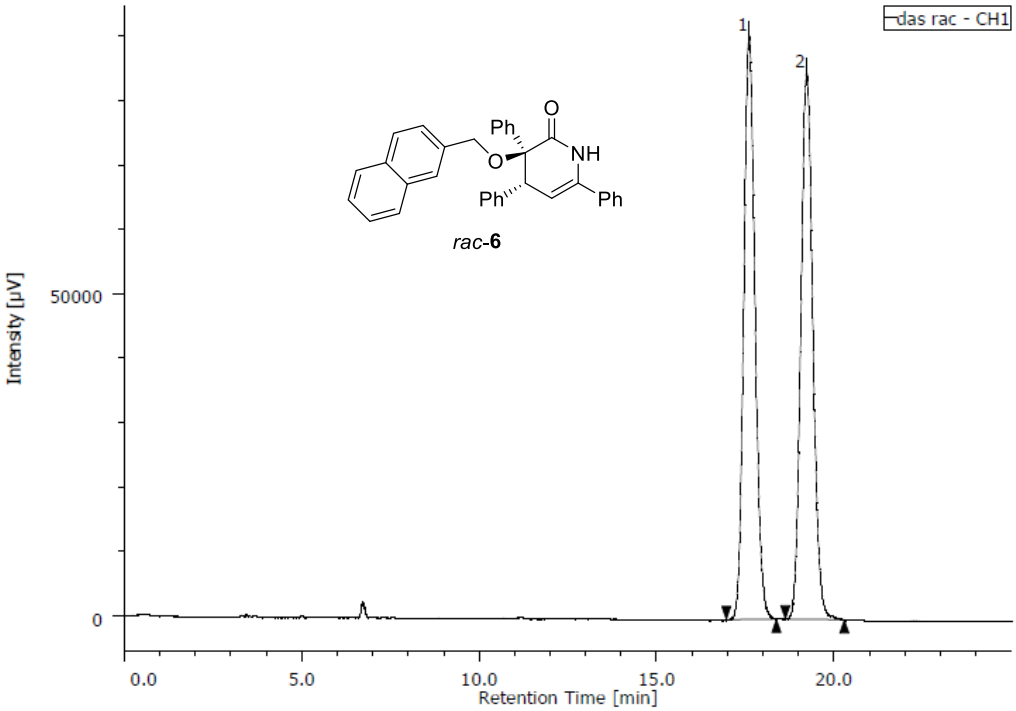
	Peak 1	Peak 2
Retention time (min)	8.6	13.3
Area (%)	11.6	88.4

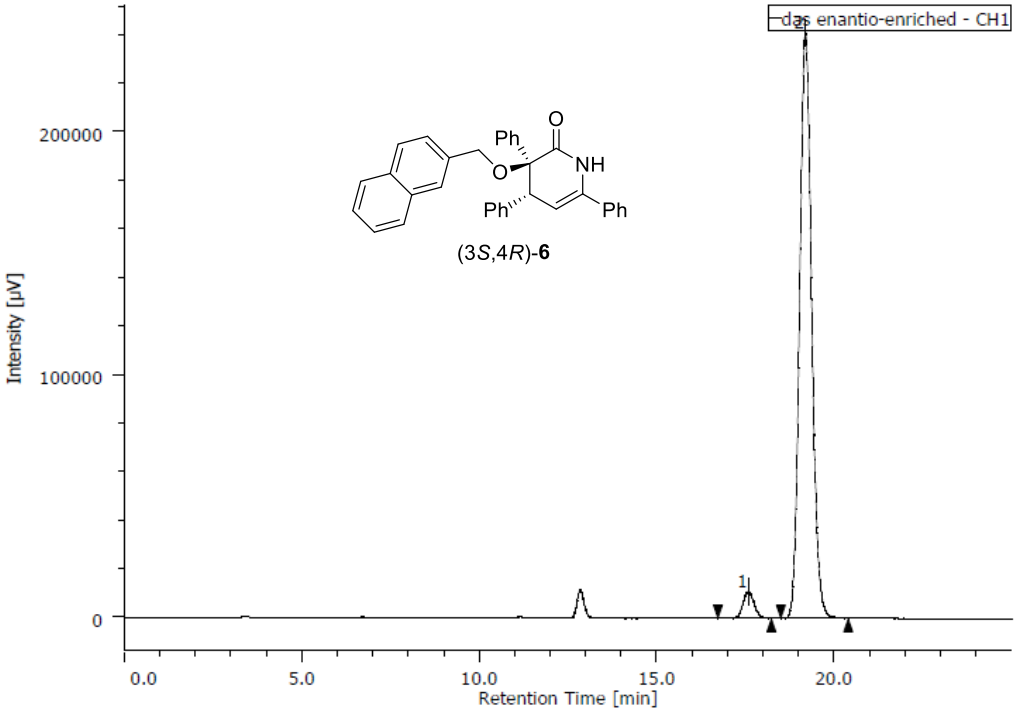


	Peak 1	Peak 2
Retention time (min)	8.7	10.7
Area (%)	4.7	95.2



	Peak 1	Peak 2
Retention time (min)	7.2	8.4
Area (%)	16.0	84.0





	Peak 1	Peak 2
Retention time (min)	17.6	19.2
Area (%)	4.1	95.9

6. References:

S1 K. Iwanami and T. Oriyama, *Chem. Lett.* 2004, **33**, 1324−1325.