Synthesis of α-Amino Acid Derivatives and Peptides via Enantioselective Addition of Masked Acyl Cyanides to Imines

Kin S. Yang and Viresh H. Rawal*

Searle Chemistry Laboratory, Department of Chemistry, The University of Chicago
5735 South Ellis Avenue, Chicago, IL 60637

Table of Contents

General Information

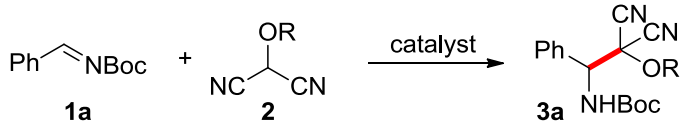
Unless stated otherwise, reactions were performed in oven-dried glassware under a nitrogen atmosphere. Solvents were purified over activated alumina using an Innovative Technology solvent purification system. Acetylmalononitrile, peracetic acid, tetrabutylammonium fluoride solution (THF, 1.0 M), Tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF), pyrrolidine, benzyl amine, glycine methyl ester HCl, valine methyl ester HCl, phenylalanine ethyl ester HCl, and trifluoroacetic acid were purchased from Aldrich and used as received. Ambient temperature refers to 22–26 °C. Lower temperatures were maintained using ice (0 °C), a Thermo NEXLAB Cryotrol (−45 to 23 °C), Acetone/CO_2(s) (−78 °C) baths. Thin-layer chromatography (TLC) was performed using Whatman silica gel 60 Å F254 plates (250 μm) with F-254 fluorescent indicator and visualized by UV fluorescence quenching, ceric ammonium molybdate or potassium permanganate staining. SiliCycle SiliaFlash P60 silica gel (particle size 40–63 μm) was used for flash chromatography. Chiral HPLC was performed on a Agilent HPLC with a Chiralcel® or ChiralPak® OD-H, IA, AS-H or AD-H column (250 mm x 10 mm, 5 μm particle size, 1.0 mL/min flow rate) equipped with a guard, employing a mixture of isopropanol and hexanes. Melting points were measured on a Thomas Hoover Uni-Melt capillary melting point apparatus and are uncorrected. ^{1}H and 13C NMR spectra were recorded on Bruker DRX-500 and DMX-500 (at 500 MHz and 125 MHz, respectively) and are reported relative to Me_4Si (δ 0.0) or residual solvent signals unless otherwise stated. C^{13} NMR spectra were calibrated to residual solvent signals ($CHCl_3$ at 77.23 ppm) Data for 1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Infrared spectra were recorded on a Nicolet 6700 FT-IR spectrometer and are reported in frequency of absorption (cm^{-1}) using NaBr salt plates using a thin film. High-resolution mass spectra were recorded on an Agilent 6224 Tof-MS (with positive Electrospray ionization mode[+ESi]). Optical rotations were measured on a Perkin Elmer 141 polarimeter using a 100 mm path-length cell.

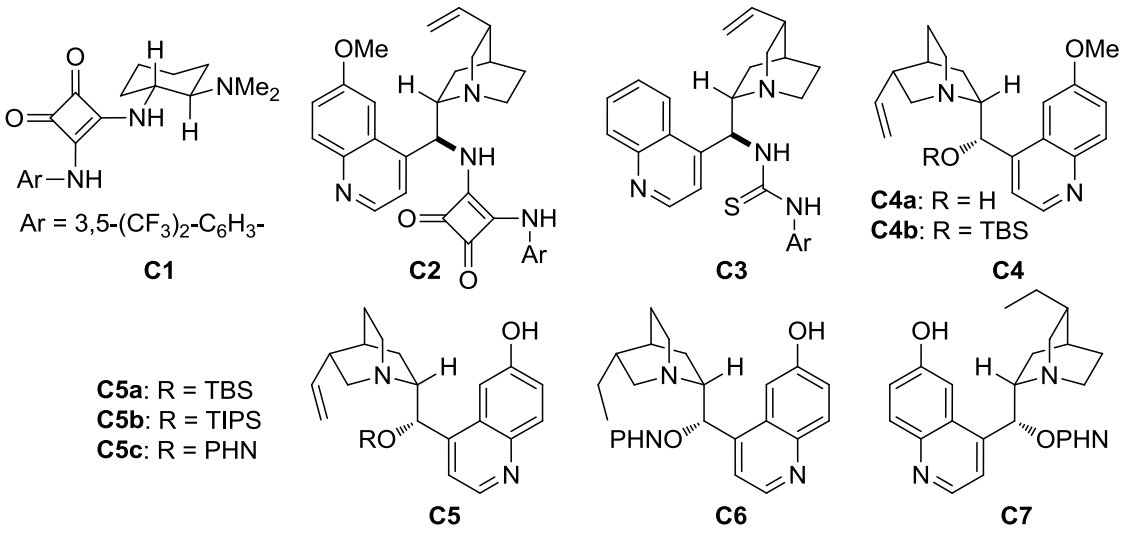
Imines (**1o-r**)[1], and **1s**[2] were prepared according to literature procedure. MAC reagent **2** was prepared as described previously.[3] Catalyst **III** prepared according to reported procedure.[4]

(1) Best, D.; Kujawa, S.; Lam, H.W. *J. Am. Chem. Soc.* **2012,** *134*, 18193.
(2) Kanazawa, A.M.; Denis, J.; Greene, A.E. *J. Org. Chem.* **1994,** *59*, 1238.
(3) (a) Nemoto, H.; Li, X. M.; Ma, R. J.; Suzuki, I.; Shibuya, M. *Tetrahedron Lett.* **2003,** *44*, 73.; (b) Yang, K. S.; Nibbs, A. E.; Turkmen, Y. E.; Rawal, V. H. *J. Am. Chem. Soc.* **2013**, *135*, 16050.
(4) Wang, Y.; Li, H. M.; Wang, Y. Q.; Liu, Y.; Foxman, B. M.; Deng, L. *J. Am. Chem. Soc.* **2007**, *129*, 6364.

General Procedure for the optimization of MAC addition to Imines.

To a 1 dram (4 mL) vial equipped with a magnetic stir bar was added imine **1** (10.3 mg, 0.05 mmol). A solution of MAC reagent **2** (0.05 mmol) in solvent was added and the solution was stirred. Catalyst was added as a solid and the vial was sealed. The reaction was monitored by crude analysis of ^{1}H NMR aliquots. The reaction mixture was filtered through a plug of silica, and analyzed by chiral HPLC for determination of enantioselectivity.





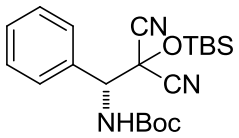
entry[a]	catalyst	R	solvent (M)	temp (°C)	time (h)	conv.[b] (%)	e.r.[c]
1	**C1**	MOM	$CHCl_3$ (0.08)	23	3	>95	26.5:73.5
2	**C2**	MOM	$CHCl_3$ (0.08)	23	3	>95	85.5:14.5
3	**C3**	MOM	$CHCl_3$ (0.08)	23	3	>95	67.5:32.5
4	**C4a**	TBS	toluene (0.3)	23	1.5	>95	41.5:58.5
5	**C4b**	TBS	toluene (0.3)	23	1.5	80	47:53
6	**C5a**	TBS	toluene (0.3)	23	1.5	>95	86.5:13.5
7	**C5a**	TBS	$CHCl_3$ (0.3)	23	1.5	>95	90:10
8	**C5a**	TBS	$CHCl_3$ (0.3)	–40	17	>95	94:6
9	**C5b**	TBS	$CHCl_3$ (0.1)	–40	17	70	94.5:5.5
10	**C5b**	MOM	$CHCl_3$ (0.1)	–40	17	77	84:16
11	**C5c**	TBS	$CHCl_3$ (0.3)	–40	23	69	95.5:4.5
12	**C6**	TBS	$CHCl_3$ (0.2)	–40	20	92	97:3
13	**C6**	TBS	$CHCl_3$ (0.05)	23	1	50	95:5
14	**C6**	TBS	toluene (0.05)	23	1	55	96:4
15	**C6**	TBS	toluene (0.1)	–20	21	81	95:5
16	**C6**	TBS	toluene (0.3)	23	1	>95	95:5
17[d]	**C6**	TBS	toluene (0.07)	23	1	53	96:4
18[d]	**C7**	TBS	toluene (0.07)	23	1	40	6.5:93.5

[a]Conditions: 1a (0.05 mmol), 2 (0.05 mmol), catalyst (5 mol %). [b]% conversion determined by 1H NMR. [c]e.r. determined by chiral stationary phase HPLC. [d] Catalyst (2.5 mol%).

General Procedure for the addition of MAC Reagents to Imines

To a 2 dram (8 mL) vial equipped with a magnetic stir bar was added imine **1** (0.33 mmol). A solution of TBS MAC reagent **2** (58.9 mg, 0.3 mmol) in 4.5 mL of toluene was added and the solution was stirred at 23 °C. Catalyst **III** (3.66 mg, 0.0075 mmol, 2.5 mol %) was added as a solid and the vial was sealed. The reaction was monitored by ^{1}H NMR, and upon completion, was concentrated to afford a sticky residue. Purification by flash column chromatography produced the desired product **3**.

Imine Addition Reactions



(*R*)-*tert*-butyl (2-((*tert*-butyldimethylsilyl)oxy)-2,2-dicyano-1-phenylethyl)carbamate

(**3a**): Prepared according to general procedure using imine **1a** (67.7 mg, 0.33 mmol), MAC **2** (58.9 mg, 0.3 mmol), and catalyst **III** (3.66 mg, 0.0075 mmol) in toluene (4.5 mL) at 23 °C for 16 h. Purified by flash column chromatography (SiO_2, 10% Et_2O/Hexanes) to afford 115 mg (96%) of **3a** as an amorphous solid.

Preparative Scale: Modified general procedure using imine **1a** (564 mg, 2.75 mmol), MAC **2** (491 mg, 2.5 mmol), and catalyst **III** (12.2 mg, 0.025 mmol, 1 mol%) in toluene (37.5 mL) at 23 °C for 36 h. Purified by flash column chromatography (SiO_2, 10% Et_2O/Hexanes) to afford 0.984 g (98%) of **3a** as an amorphous solid.

IR (film): 3371, 2958, 2933, 2861, 2243, 1707, 1521, 1367, 1259, 1153, 843, 787, 703

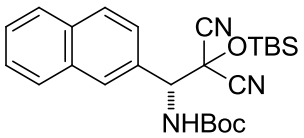
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (s, 5H), 5.49 (s, 1H), 5.39 (s, 1H), 1.46 (s, 9H), 0.85 (s, 9H), 0.27 (s, 3H), 0.21 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.53, 133.16, 129.83, 128.81, 128.63, 114.35, 114.20, 81.52, 68.21, 61.60, 28.37, 25.31, 18.20, -4.54, -4.68.

HRMS (+ ESi) Mass calcd. for $C_{21}H_{31}N_3O_3Si$ $[M+H]^+$: 402.2207, Found $[M+H]^+$: 402.2194.

$[\alpha]^{23.6}_D$ = + 7.0° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 96:4, Rt_1 = 5.1 min, Rt_2 = 6.4 min, Chiralcel OD-H, 1% IPA/Hexanes, 1 mL/min.



(*R*)-*tert*-butyl (2-((*tert*-butyldimethylsilyl)oxy)-2,2-dicyano-1-(naphthalen-2-yl)ethyl)carbamate

(**3b**): Prepared according to general procedure using imine **1b** (84.3 mg, 0.33 mmol), MAC **2** (58.9 mg, 0.3 mmol), and catalyst **III** (3.66 mg, 0.0075 mmol) in toluene (4.5 mL) at 23 °C for 16 h. Purified by flash column chromatography (SiO_2, 5% EtOAc/Hexanes) to afford 126 mg (93%) of **3b** as an amorphous solid.

IR (film): 3367, 2931, 2850, 2243, 1706, 1506, 1368, 1150, 843, 786

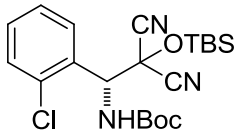
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 – 7.79 (m, 4H), 7.56 – 7.43 (m, 3H), 5.62 (s, 1H), 5.57 (s, 1H), 1.47 (s, 9H), 0.85 (s, 9H), 0.26 (s, 3H), 0.19 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.60, 133.79, 132.96, 130.60, 128.65, 128.60, 128.39, 127.88, 127.20, 126.93, 125.44, 114.38, 114.27, 81.60, 68.23, 61.87, 28.39, 25.32, 18.21, -4.52, -4.63.

HRMS (+ ESi) Mass calcd. for $C_{25}H_{34}N_3O_3Si$ $[M+H]^+$: 452.2364, Found $[M+H]^+$: 452.2354.

$[\alpha]^{23.6}_D$ = –16.0° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 95.5:4.5, Rt_1 = 5.7 min, Rt_2 = 11.9 min, Chiralcel OD-H, 1% IPA/Hexanes, 1 mL/min



(*R*)-*tert*-butyl (2-((*tert*-butyldimethylsilyl)oxy)-1-(2-chlorophenyl)-2,2-dicyanoethyl)carbamate

(**3c**): Prepared according to modified general procedure using imine **1c** (79.0 mg, 0.33 mmol), MAC **2** (58.9 mg, 0.3 mmol), and catalyst **III** (7.33 mg, 0.015 mmol, 5 mol %) in toluene (4.5 mL) at 23 °C for 72 h. Purified by flash column chromatography (SiO_2, 10% Et_2O/Hexanes) to afford 124 mg (95%) of **3c** as a viscous oil.

IR (film): 3282, 2932, 2861, 2243, 1708, 1473, 1376, 1259, 1156, 843, 787, 754

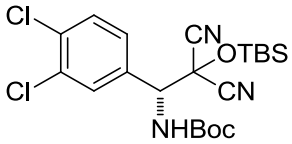
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 – 7.40 (m, 2H), 7.37 – 7.30 (m, 2H), 6.15 (s, 1H), 5.46 (s, 1H), 1.46 (s, 9H), 0.84 (s, 9H), 0.29 (s, 3H), 0.29 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.30, 135.34, 132.10, 130.79, 130.35, 128.37, 127.35, 114.12 (x2), 81.69, 67.63, 56.93, 28.34, 25.29, 18.20, -4.45, -4.62.

HRMS (+ ESi) Mass calcd. for $C_{21}H_{31}ClN_3O_3Si$ $[M+H]^+$: 436.1818, Found $[M+H]^+$: 436.1801.

$[\alpha]^{23.6}_D$ = – 4.0° (c = 0.5 , $CHCl_3$)

Enantiomeric ratio: 92.5:7.5, Rt_1 = 8.7 min, Rt_2 = 11.7 min, Chiralcel AD-H, 2% IPA/Hexanes, 1 mL/min



(*R*)-*tert*-butyl (2-((*tert*-butyldimethylsilyl)oxy)-2,2-dicyano-1-(3,4-dichlorophenyl)ethyl)carbamate

(**3d**): Prepared according to general procedure using imine **1d** (90.5 mg, 0.33 mmol), MAC **2** (58.9 mg, 0.3 mmol), and catalyst **III** (3.66 mg, 0.0075 mmol) in toluene (4.5 mL) at 23 °C for 14 h. Purified by flash column chromatography (SiO_2, 33% Dichloromethane/Hexanes to 66% Dichloromethane/Hexanes) to afford 137 mg (97%) of **3d** as an amorphous solid.

IR (film): 3362, 2957, 2932, 2861, 2244, 1707, 1473, 1368, 1259, 1146, 842, 787

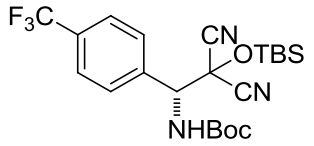
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.3 Hz, 2H), 7.28 – 7.24 (m, 1H), 5.40 (s, 1H), 5.36 (s, 1H) 1.47 (s, 9H), 0.88 (s, 9H), 0.30 (s, 3H), 0.26 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.29, 134.31, 133.53, 133.18, 130.90, 130.81, 127.77, 113.94, 113.82, 82.14, 67.66, 60.75, 28.38, 25.35, 18.26, -4.50, -4.57.

HRMS (+ ESi) Mass calcd. for $C_{21}H_{30}Cl_2N_3O_3Si$ $[M+H]^+$: 470.1428, Found $[M+H]^+$: 470.1403

$[\alpha]^{23.6}_D$ = – 1.7° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 94:6, Rt_1 = 5.0 min, Rt_2 = 7.0 min, Chiralcel OD-H, 1% IPA/Hexanes, 1 mL/min



(*R*)-*tert*-butyl (2-((*tert*-butyldimethylsilyl)oxy)-2,2-dicyano-1-(4-(trifluoromethyl)phenyl)ethyl)carbamate

(**3e**): Prepared according to general procedure using imine **1e** (90.3 mg, 0.33 mmol), MAC **2** (58.9 mg, 0.3 mmol), and catalyst **III** (3.66 mg, 0.0075 mmol) in toluene (4.5 mL) at 23 °C for 14 h. Purified by flash column chromatography (SiO_2, 10% Et_2O/Hexanes) to afford 138 mg (98%) of **3e** as an amorphous solid.

IR (film): 3363, 2934, 2863, 2244, 1708, 1513, 1368, 1327, 1260, 1168, 1134, 1070, 840, 787

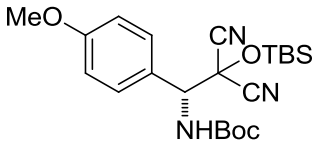
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 5.57 (s, 1H), 5.49 (s, 1H), 1.47 (s, 9H), 0.85 (s, *J* = 48.3 Hz, 9H), 0.29 (s, 3H), 0.23 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.41, 137.23, 132.04 (q, *J* = 33.2 Hz), 129.25, 125.73, 123.87 (q, *J* = 272.4 Hz), 114.05, 113.92, 81.94, 67.84, 61.24, 28.33, 25.27, 18.20, -4.55, -4.67.

HRMS (+ ESi) Mass calcd. for $C_{22}H_{31}F_3N_3O_3Si$ $[M+H]^+$: 470.2081, Found $[M+H]^+$: 470.2058.

$[\alpha]^{23.6}_D$ = + 5.3° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 94:6, Rt_1 = 4.5, Rt_2 = 5.5, Chiralcel OD-H, 1% IPA/Hexanes, 1 mL/min



(*R*)-*tert*-butyl (2-((*tert*-butyldimethylsilyl)oxy)-2,2-dicyano-1-(4-methoxyphenyl)ethyl)carbamate

(**3f**): Prepared according to general procedure using imine **1f** (77.6 mg, 0.33 mmol), MAC **2** (58.9 mg, 0.3 mmol), and catalyst **III** (3.66 mg, 0.0075 mmol) in toluene (4.5 mL) at 23 °C for 24 h. Purified by flash column chromatography (SiO_2, 10% Et_2O/Hexanes) to afford 124 mg (96%) of **3f** as an amorphous solid.

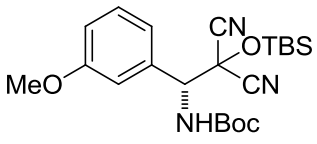
IR (film): 3371, 2933, 2861, 2243, 1707, 1512, 1367, 1256, 1154, 1032, 835, 787

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 2H), 6.96 – 6.87 (m, 2H), 5.49 (s, 1H), 5.33 (s, 1H), 3.81 (s,3H), 1.45 (s, 9H), 0.87 (s, 9H), 0.28 (s, 3H), 0.23 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.70, 154.48, 129.82, 125.29, 114.41, 114.30, 114.17, 81.36, 68.33, 61.26, 55.47, 28.36, 25.33, 18.19, -4.54, -4.64.
HRMS (+ ESi) Mass calcd. for $C_{22}H_{34}N_3O_4Si$ $[M+Na]^+$: 454.2133, Found $[M+Na]^+$: 454.2120.

$[\alpha]^{23.6}_D$ = – 4.2° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 95:5, Rt_1 = 5.8, Rt_2 = 7.8, Chiralcel OD-H, 1% IPA/Hexanes, 1 mL/min



(*R*)-*tert*-butyl (2-((*tert*-butyldimethylsilyl)oxy)-2,2-dicyano-1-(3-methoxyphenyl)ethyl)carbamate

(**3g**): Prepared according to general procedure using imine **1g** (77.6 mg, 0.33 mmol), MAC **2** (58.9 mg, 0.3

mmol), and catalyst **III** (3.66 mg, 0.0075 mmol) in toluene (4.5 mL) at 23 °C for 14 h. Purified by flash column chromatography (SiO_2, 75% Dichloromethane/Hexanes, then 10% EtOAc/Hexanes) to afford 125 mg (97%) of **3g** as an amorphous solid.

IR (film): 3365, 2933, 2861, 2243, 1707, 1603, 1494, 1367, 1258, 1153, 1044. 844, 786

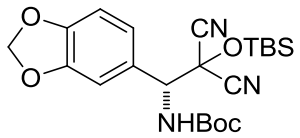
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 8.4, 7.7 Hz, 1H), 6.99 (d, *J* = 7.7 Hz, 1H), 6.96 – 6.91 (m, 2H), 5.49 (d, *J* = 7.9 Hz, 1H), 5.34 (d, *J* = 7.8 Hz, 1H), 3.81 (s, 3H), 1.46 (s, 9H), 0.86 (s, 9H), 0.28 (s, 3H), 0.23 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.86, 154.52, 134.69, 129.89, 120.69, 115.33, 114.55, 114.38, 114.27, 81.53, 68.16, 61.71, 55.51, 28.38, 25.32, 18.20, -4.52, -4.65.

HRMS (+ ESi) Mass calcd. for $C_{22}H_{34}N_3O_4Si$ $[M+Na]^+$: 454.2133, Found $[M+Na]^+$: 454.2123.

$[\alpha]^{23.6}_D$ = + 1.4° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 97:3, Rt_1 = 5.6, Rt_2 = 7.0, Chiralcel OD-H, 1% IPA/Hexanes, 1 mL/min



(*R*)-*tert*-butyl (1-(benzo[*d*][1,3]dioxol-5-yl)-2-((*tert*-butyldimethylsilyl)oxy)-2,2-dicyanoethyl)carbamate

(**3h**): Prepared according to general procedure using imine **1h** (82.3 mg, 0.33 mmol), MAC **2** (58.9 mg, 0.3 mmol), and catalyst **III** (3.66 mg, 0.0075 mmol) in toluene (4.5 mL) at 23 °C for 16 h. Purified by flash column chromatography (SiO_2, 10% Et_2O, 30% $CHCl_3$, 60% Hexanes) to afford 128 mg (96%) of **3h** as an amorphous solid.

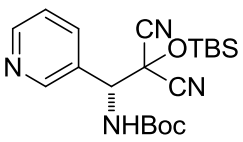
IR (film): 3376, 2957, 2932, 2861, 2243, 1706, 1505, 1490, 1368, 1242, 1155, 1041, 844, 787

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 – 6.85 (m, 2H), 6.81 (d, *J* = 8.4 Hz, 1H), 5.98 (s, 2H), 5.44 (s, 1H), 5.29 (s, 1H), 1.46 (s, 9H), 0.88 (s, 9H), 0.30 (s, 3H), 0.26 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.42, 148.79, 148.07, 126.96, 122.64, 114.30, 114.19, 108.73, 108.44, 101.66, 81.45, 68.18, 61.53, 28.34, 25.33, 18.20, -4.52, -4.62.
HRMS (+ ESi) Mass calcd. for $C_{22}H_{31}N_3O_5Si$ $[M+Na]^+$: 468.1925, Found $[M+Na]^+$: 468.1918.

$[\alpha]^{23.6}_D$ = – 2.8° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 96:4, Rt_1 = 6.7, Rt_2 = 9.3, Chiralcel OD-H, 1% IPA/Hexanes, 1 mL/min



(*R*)-*tert*-butyl (2-((*tert*-butyldimethylsilyl)oxy)-2,2-dicyano-1-(pyridin-3-yl)ethyl)carbamate

(**3i**): Prepared according to general procedure using imine **1i** (68.1 mg, 0.33 mmol), MAC **2** (58.9 mg, 0.3 mmol), and catalyst **III** (3.66 mg, 0.0075 mmol) in toluene (4.5 mL) at 23 °C for 14 h. Purified by flash column chromatography (SiO_2, 30% EtOAc/Hexanes) to afford 118 mg (98%) of **3i** as an amorphous solid.

IR (film): 3310, 2957, 2933, 2861, 2243, 1721, 1522, 1368, 1257, 1154, 1048, 843,787

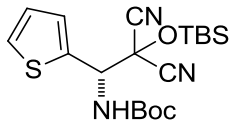
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (s, 2H), 7.79 (d, *J* = 6.4 Hz, 1H), 7.37 (dd, *J* = 7.8, 4.9 Hz, 1H), 5.85 (s, 1H), 5.49 (s, 1H), 1.47 (s, 9H), 0.85 (s, 9H), 0.29 (s, 3H), 0.23 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.47, 150.94, 150.14, 135.81, 129.30, 123.54, 114.02, 113.85, 81.95, 67.81, 59.79, 28.31, 25.27, 18.17, -4.53, -4.66.

HRMS (+ ESi) Mass calcd. for $C_{20}H_{31}N_4O_3Si$ $[M+H]^+$: 403.2160, Found $[M+H]^+$: 403.2151.

$[\alpha]^{23.6}_D$ = + 3.1° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 93:7, Rt_1 = 6.3, Rt_2 = 8.0, Chiralcel AD-H, 8% IPA/Hexanes, 1 mL/min



(*S*)-*tert*-butyl (2-((*tert*-butyldimethylsilyl)oxy)-2,2-dicyano-1-(thiophen-2-yl)ethyl)carbamate

(**3j**): Prepared according to general procedure using imine **1j** (69.7 mg, 0.33 mmol), MAC **2** (58.9 mg, 0.3 mmol), and catalyst **III** (3.66 mg, 0.0075 mmol) in toluene (4.5 mL) at 23 °C for 12 h. Purified by flash column chromatography (SiO_2, 10% Et_2O/Hexanes) to afford 121 mg (99%) of **3j** as an amorphous solid.

IR (film): 3357, 2933, 2861, 2243, 1710, 1506, 1368, 1258, 1156, 842, 787

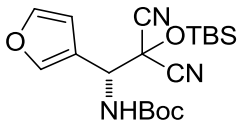
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 5.1, 0.9 Hz, 1H), 7.22 (d, *J* = 3.5 Hz, 1H), 7.04 (dd, *J* = 5.0, 3.7 Hz, 1H), 5.68 (d, *J* = 8.9 Hz, 1H), 5.42 (s, 1H), 1.47 (s, 9H), 0.92 (s, 9H), 0.33 (s, 3H), 0.30 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.28, 135.24, 128.17, 127.11, 127.05, 114.05, 113.98, 81.63, 68.13, 58.08, 28.30, 25.32, 18.19, -4.53, -4.64.

HRMS (+ ESi) Mass calcd. for $C_{19}H_{29}N_3O_3SSi$ $[M+Na]^+$: 430.1591, Found $[M+Na]^+$: 430.158.

$[\alpha]^{23.6}_D$ = + 0.5° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 97.5:2.5, Rt_1 = 5.0, Rt_2 = 5.7, Chiralcel AD-H, 8% IPA/Hexanes, 1 mL/min



(*R*)-*tert*-butyl (2-((*tert*-butyldimethylsilyl)oxy)-2,2-dicyano-1-(furan-3-yl)ethyl)carbamate

(**3k**): Prepared according to general procedure using imine **1k** (64.4 mg, 0.33 mmol), MAC **2** (58.9 mg, 0.3 mmol), and catalyst **III** (3.66 mg, 0.0075 mmol) in toluene (4.5 mL) at 23 °C for 36 h. Purified by flash column chromatography (SiO_2, 10% Et_2O/Hexanes) to afford 113 mg (96%) of **3k** as an amorphous solid.

IR (film): 3364, 2933, 2861, 2244, 1708, 1506, 1358, 1259, 1156, 1023, 844, 787

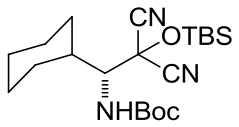
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.45 (t, *J* = 1.5 Hz, 1H), 6.52 (d, *J* = 0.7 Hz, 1H), 5.38 (s, 1H), 5.26 (s, 1H), 1.47 (s, 9H), 0.90 (s, 9H), 0.33 (s, 3H), 0.31 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.47, 143.97, 141.89, 118.82, 114.36, 114.31, 109.39, 81.60, 68.14, 55.22, 28.38, 25.33, 18.21, -4.49, -4.58.

HRMS (+ ESi) Mass calcd. for $C_{19}H_{29}N_3O_4Si$ $[M+Na]^+$: 414.1820, Found $[M+Na]^+$: 414.1809

[α]$^{23.6}_{D}$ = 7.3° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 93.5:6.5, Rt_1 = 5.0, Rt_2 = 5.7, Chiralcel OD-H, 1% IPA/Hexanes, 1 mL/min



(*R*)-*tert*-butyl (2-((*tert*-butyldimethylsilyl)oxy)-2,2-dicyano-1-cyclohexylethyl)carbamate

(**3l**): Prepared according to modified general procedure using imine **1l** (69.7 mg, 0.33 mmol), MAC **2** (58.9 mg, 0.3 mmol), and catalyst **III** (7.33 mg, 0.015 mmol) in toluene (3 mL) at 23 °C for 72 h. Purified by flash column chromatography (SiO_2, 10% Et_2O/Hexanes) to afford 110 mg (90%) of **3l** as a clear viscous oil.

IR (film): 3363, 2931, 2858, 2242, 1709, 1506, 1367, 1259, 1153, 1007, 843, 786

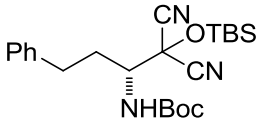
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.85 (d, *J* = 10.9 Hz, 1H), 4.17 (dd, *J* = 10.9, 3.9 Hz, 1H), 1.97 – 1.62 (m, 6H), 1.47 (s, 9H), 1.35 – 1.00 (m, 5H), 0.94 (s, 9H), 0.38 (s, 3H), 0.37 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.19, 114.80, 114.70, 80.87, 66.96, 61.92, 38.70, 31.41, 28.36, 27.49, 26.19, 25.89, 25.88, 25.33, 18.20, -4.47, -4.57.

HRMS (+ ESi) Mass calcd. for $C_{21}H_{37}N_3O_3Si$ $[M+H]^+$: 430.2491, Found $[M+H]^+$: 430.2496

[α]$^{23.6}_{D}$ = 29.6° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 92:8 (derived from benzyl amide (**8**),)



(*R*)-*tert*-butyl (1-((*tert*-butyldimethylsilyl)oxy)-1,1-dicyano-4-phenylbutan-2-yl)carbamate

(**3m**): To a 1 dram (4 mL) vial equipped with a magnetic stir bar was added imine **1m** (84.0 mg 0.33 mmol). A solution of MAC **2** (58.9 mg, 0.3 mmol) in 0.6 mL of $CHCl_3$ was added. The sealed vial was submerged in a –40 °C bath and stirred for 10 minutes before catalyst **III** (7.33 mg, 0.015 mmol, 5 mol %) was added as a solid. The vial was re-sealed, stirred for 30 h, warmed to 23 °C, concentrated, and purified by flash column chromatography (SiO_2, 5% to 10% EtOAc/Hexanes) to afford 116 mg (90%) of **3m** as a clear viscous oil.

IR (film): 3374, 2932, 2861, 2243, 1709, 1497, 1367, 1259, 1141, 1048, 843, 787

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.4 Hz, 2H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.17 (d, *J* = 7.2 Hz, 2H), 4.72 (d, *J* = 10.4 Hz, 1H), 4.27 (td, *J* = 11.4, 2.1 Hz, 1H), 2.81 (dd, *J* = 8.6, 5.3 Hz, 1H), 2.67 (dd, *J* = 14.0, 8.0 Hz, 1H), 2.26 – 2.11 (m, 1H), 1.87 – 1.71 (m, 1H), 1.48 (s, 9H), 0.90 (s, 9H), 0.35 (s, 3H), 0.33 (s,3).

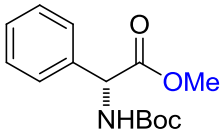
^{13}C NMR (126 MHz, $CDCl_3$) δ 154.96, 140.12, 128.85, 128.58, 126.66, 114.35, 114.28, 81.15, 67.94, 58.01, 31.90, 31.33, 28.42, 25.37, 18.22, -4.47, -4.51.

HRMS (+ ESi) Mass calcd. for $C_{23}H_{35}N_3O_3Si$ $[M+Na]^+$: 452.2340, Found $[M+Na]^+$: 452.2331

[α]$^{23.6}_{D}$ = + 39.4° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 92:8, Rt_1 = 12.2, Rt_2 = 15.9, Chiralcel AD-H, 1% IPA/Hexanes, 1 mL/min

Experimental protocols for the unmasking 3a



(*R*)-methyl 2-((*tert*-butoxycarbonyl)amino)-2-phenylacetate

(**4a**): To a 2 dram (8 mL) vial was added adduct **3a** (68 mg, 0.17 mmol), 1.10 mL MeOH, and 0.57 mL THF. The vial was sealed with a Septa-cap, and cooled to –45 °C for 15 minutes before TBAF (1.0 M in THF) (0.19 mL, 0.19 mmol) was added dropwise over 5 minutes. The reaction was allowed to stir for 2 hours at –45 °C before being quenched with aq. NH_4Cl (3 mL), and H_2O (3 mL). The reaction was warmed to ambient temperature, and extracted with EtOAc (10 mL, 3x) The combined organic solvents were dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 10% to 15% EtOAc/Hexanes) to afford 42 mg (93%) of **4a** as a white solid.

IR (film): 3374, 2977, 1746, 1715, 1497, 1436, 1165, 1053

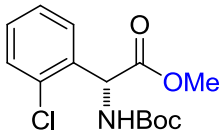
1H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.29 (m, 5H), 5.56 (d, *J* = 5.6 Hz, 1H), 5.32 (d, *J* = 7.4 Hz, 1H), 3.71 (s, 3H), 1.43 (s, 9H).

13C NMR (126 MHz, $CDCl_3$) δ 171.85, 155.02, 137.14, 129.09, 128.63, 127.34, 80.35, 57.82, 52.85, 28.50.

HRMS (+ ESi) Mass calcd. for $C_{14}H_{19}NO_4$ $[M+H]^+$: 266.1387, Found $[M+H]^+$: 266.1350

$[\alpha]^{23.6}_D$ = – 119.4° (c = 1.0 , $CHCl_3$) Lit: **$[\alpha]^{20}_D$**: – 130 (c = 1.0 , $CHCl_3$)[5]

Enantiomeric ratio: 96:4, Rt_1 = 5.9, Rt_2 = 6.8, Chiralcel OD-H, 4% IPA/Hexanes, 1 mL/min.



(*R*)-methyl 2-((*tert*-butoxycarbonyl)amino)-2-(2-chlorophenyl)acetate

(**4c**): To a 2 dram (8 mL) vial was added adduct **3c** (84 mg, 0.193 mmol), 1.33 mL MeOH, and 0.67 mL THF. The vial was sealed with a Septa-cap, and cooled to –45 °C for 15 minutes before TBAF (1.0 M in THF) (0.21 mL, 0.21 mmol) was added dropwise over 5 minutes. The reaction was allowed to stir for 2 hours at –45 °C before being quenched with aq. NH_4Cl (3 mL). The reaction was warmed to ambient temperature, diluted with EtOAc (10 mL), H_2O (5 mL), and brine (2 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (10 mL, 2x). The combined organic solvents were dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 10% EtOAc/Hexanes) to afford 55 mg (95%) of **4c** as a white solid.

IR (film): 3373, 2977, 1748, 1715, 1494, 1162, 1054, 755

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.31 (m, 2H), 7.27 – 7.20 (m, 2H), 5.72 (br m, 2H), 3.71 (s, 3H), 1.42 (s, 9H).

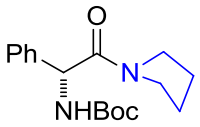
(5) Yuste, F.; Ortiz, B.; Carrasco, A.; Peralta, M.; Quintero, L.; Sanchez-Obregon, R.; Walls, F.; Ruano, J. L. G. *Tetrahedron: Asymmetry.* **2000**, *11*, 3079.

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.15, 154.94, 135.37, 133.70, 130.17, 129.88, 129.67, 127.33, 80.27, 55.70, 52.91, 28.36.

HRMS (+ ESi) Mass calcd. for $C_{14}H_{18}ClNO_4$ $[M+Na]^+$: 322.0817, Found $[M+Na]^+$: 322.0813

$[\alpha]^{23.6}_D$ = – 100.5° (c = 1.0 , $CHCl_3$) Lit **$[\alpha]^{25}_D$**: 119.3 (c = 1.0 , $CHCl_3$) [6]

Enantiomeric ratio: 92.5:7.5, Rt_1 = 7.7, Rt_2 = 9.2, Chiralcel OD-H, 3% IPA/Hexanes, 1 mL/min



(*R*)-*tert*-butyl (2-oxo-1-phenyl-2-(pyrrolidin-1-yl)ethyl)carbamate

(**5**): To a 1 dram (4 mL) vial was added adduct **3a** (71 mg, 0.177 mmol), pyrrolidine (37.8 mg, 0.531 mmol), and 0.54 mL Dichloromethane. The vial was sealed with a Septa-cap, and cooled to –78 °C in a CO_2/Acetone bath for 15 minutes before TASF (58.5 mg, 0.21 mmol) in DCM (0.12 mL) (1.8 M) was added dropwise over 5 minutes. The reaction was allowed to stir for 1.5 hours at –78 °C before being quenched with aq. HCl (1.0M, 3 mL). The reaction was warmed to ambient temperature, diluted with EtOAc (10 mL), H_2O (5 mL), and brine (2 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (10 mL, 2x). The combined organic solvents were dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 50% EtOAc/Hexanes) to afford 52 mg (96%) of **5** as a white solid.

IR (film): 3411, 3324, 2974, 2877, 1711, 1645, 1435, 1166, 1053, 700

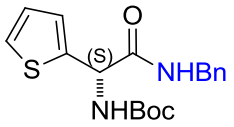
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.28 (m, 5H), 6.05 (d, *J* = 7.4 Hz, 1H), 5.37 (d, *J* = 7.7 Hz, 1H), 3.62 – 3.50 (m, 2H), 3.46 – 3.34 (m, 1H), 3.14 – 3.00 (m, 1H), 1.96 – 1.63 (m, 4H), 1.41 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.59, 155.23, 138.04, 129.06, 128.26, 128.10, 79.75, 56.73, 46.38, 46.28, 28.54, 26.07, 24.14.

HRMS (+ ESi) Mass calcd. for $C_{17}H_{24}N_2O_3$ $[M+Na]^+$: 327.1679, Found $[M+Na]^+$: 327.1674.

$[\alpha]^{23.6}_D$ = = – 129.8° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 96:4, Rt_1 = 8.0, Rt_2 = 9.4, Chiralcel OD-H, 6% IPA/Hexanes, 1 mL/min



(*S*)-*tert*-butyl (2-(benzylamino)-2-oxo-1-(thiophen-2-yl)ethyl)carbamate

(**6**): To a 1 dram (4 mL) vial was added adduct **3j** (82 mg, 0.20 mmol), benzylamine (64.3 mg, 0.60 mmol) and 0.60 mL Dichloromethane. The vial was sealed with a Septa-cap, and cooled to –78 °C in a CO_2/Acetone bath for 15 minutes before TASF (66.1 mg, 0.24 mmol) in DCM (0.13 mL) (1.8 M) was added dropwise over 5 minutes. The reaction was allowed to stir for 2 hours at –78 °C before being quenched with aq. HCl (1.0M, 3 mL). The reaction was warmed to ambient temperature, diluted with EtOAc (10 mL), H_2O (5 mL), and brine (2 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (10 mL, 2x). The combined organic solvents were dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 30% EtOAc/Hexanes) to afford 65 mg (93%) of **6** as a white solid.

(6) Ferraboschi, P.; De Mieri, M.; Galimberti, F. *Tetrahedron: Asymmetry.* **2010**, *21*, 2136.

IR (film): 3308, 2977, 2929, 1693, 1660, 1496, 1367, 1247, 1164, 1064, 697.

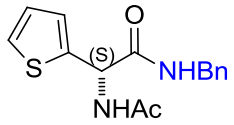
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.19 (m, 4H), 7.15 (d, *J* = 6.8 Hz, 2H), 7.01 (d, *J* = 3.4 Hz, 1H), 6.90 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.86 (s, 1H), 5.87 (s, 1H), 5.59 (s, 1H), 4.40 (ddd, *J* = 36.4, 15.0, 5.8 Hz, 2H), 1.37 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.65, 155.30, 141.02, 137.86, 128.76, 127.69, 127.59, 127.03, 126.22, 125.83, 80.49, 54.24, 43.80, 28.40.

HRMS (+ ESi) Mass calcd. for $C_{18}H_{22}N_2O_3S$ $[M+H]^+$: 347.1424, Found $[M+H]^+$: 347.1414

$[\alpha]^{23.6}_D$ = = – 63.8° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 97.5:2.5, Rt_1 = 10.0, Rt_2 = 15.0, Chiralcel OD-H, 5% IPA/Hexanes, 1 mL/min



(*S*)-2-acetamido-*N*-benzyl-2-(thiophen-2-yl)acetamide

(**7**): To a 1 dram (4 mL) vial was added **6** (35 mg, 0.1 mmol), and 0.50 mL Dichloromethane. The vial was sealed with a Septa-cap, and cooled to 0 °C in an ice bath for 15 minutes before Trifluoroacetic acid (0.5 mL) was added dropwise. The reaction was allowed to stir for 1 hour at 0 °C, before being concentrated in vacuo with stirring at 0 °C. The ice bath was removed and the dry residue was re-dissolved in pyridine (0.5 mL). Acetic Anhydride (102 mg, 1 mmol) was added and the reaction was stirred with 2 h at ambient temperature. The reaction was diluted with 15 mL EtOAc, and washed with aq. $NaHCO_3$ (5 mL), aq HCl (1.0M, 5 mL), and Brine (5 mL). The organic layer was dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 50% to 100% EtOAc/Hexanes) to afford 27.7 mg (96%) of **7** as a white solid.

IR (film): 3283, 3065, 1638, 1539, 1376, 1229, 696.

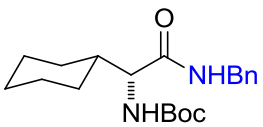
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (t, *J* = 5.1 Hz, 1H), 7.30 – 7.23 (m, 3H), 7.22 – 7.16 (m, 3H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 3.4 Hz, 1H), 6.90 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.02 (d, *J* = 7.7 Hz, 1H), 4.39 (ddd, *J* = 20.5, 14.5, 5.5 Hz, 2H), 1.88 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.02, 169.53, 140.76, 137.71, 128.84, 127.89, 127.71, 127.07, 126.52, 125.86, 52.65, 44.04, 23.11.

HRMS (+ ESi) Mass calcd. for $C_{15}H_{16}N_2O_2S$ $[M+H]^+$: 289.1005, Found $[M+H]^+$: 289.0997

$[\alpha]^{23.6}_D$ = = – 90.0° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 97.5:2.5, Rt_1 = 6.4, Rt_2 = 13.5, Chiralcel AD-H, 25% IPA/Hexanes, 1 mL/min



(*R*)-*tert*-butyl (2-(benzylamino)-1-cyclohexyl-2-oxoethyl)carbamate

(**8**): To a 2 dram (8 mL) vial was added adduct **3a** (110 mg, 0.27 mmol), benzylamine (86.8 mg, 0.81 mmol) and 0.82 mL Dichloromethane. The vial was sealed with a Septa-cap, and cooled to –78 °C in a CO_2/Acetone bath for 15 minutes before TASF (89 mg, 0.32 mmol) in DCM (0.18 mL) (1.8 M) was added dropwise over 5

minutes. The reaction was allowed to stir for 1.5 hours at –78 °C before being quenched with aq. HCl (1.0M, 5 mL). The reaction was warmed to ambient temperature, diluted with EtOAc (10 mL), H_2O (5 mL), and brine (2 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (10 mL, 2x). The combined organic solvents were dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 20% EtOAc/Hexanes) to afford 90 mg (92%) of **8** as a clear viscous oil.

IR (film): 3296, 2927, 2852, 1684, 1653, 1522, 1455, 1294, 1245, 1173, 697.

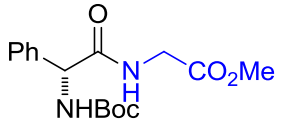
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 2H), 7.26 – 7.20 (m, 3H), 6.76 (s, 1H), 5.25 (d, *J* = 8.6 Hz, 1H), 4.40 (ddd, *J* = 36.7, 14.9, 5.6 Hz, 2H), 3.97 (t, *J* = 7.4 Hz, 1H), 1.88 – 1.56 (m, 6H), 1.39 (s, *J* = 10.0 Hz, 9H), 1.29 – 0.67 (m, 5H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.86, 156.11, 138.31, 128.77, 127.81, 127.54, 79.92, 59.85, 43.54, 40.51, 29.95, 28.66, 28.48, 26.31, 26.11.

HRMS (+ ESi) Mass calcd. for $C_{20}H_{30}N_2O_3$ $[M+Na]^+$: 369.2149, Found $[M+Na]^+$: 369.2143

$[\alpha]^{23.6}_D$ = = – 0.3° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 92:8, Rt_1 = 6.1, Rt_2 = 8.1, Chiralcel AD-H, 10% IPA/Hexanes, 1 mL/min



(*R*)-methyl 2-(2-((*tert*-butoxycarbonyl)amino)-2-phenylacetamido)acetate

(**9**): To a 1 dram (4 mL) vial was added adduct **3a** (70 mg, 0.174 mmol), 0.52 mL Dichloromethane, glycine methyl ester hydrochloride (43.8 mg, 0.348 mmol), diisopropyl ethyl amine (45.1 mg, 0.348 mmol, and stirred at ambient temperature until dissolution. The vial was sealed with a Septa-cap, and cooled to –78 °C in a CO_2/Acetone bath for 15 minutes before TASF (58 mg, 0.21 mmol) in DCM (0.12 mL) (1.8 M) was added dropwise over 5 minutes. The reaction was allowed to stir for 2 hours at –78 °C before being quenched with aq. HCl (1.0M, 3 mL). The reaction was warmed to ambient temperature, diluted with EtOAc (10 mL), H_2O (5 mL), and brine (2 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (10 mL, 2x). The combined organic solvents were dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 35% EtOAc/Hexanes) to afford 52.0 mg (93%) of **9** as a white solid.

IR (film): 3320, 2977, 1751, 1667, 1497, 1367, 1167, 698.

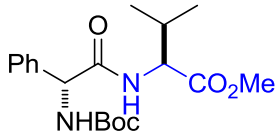
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 5H), 6.66 (s, 1H), 5.82 (s, 1H), 5.26 (s, 1H), 3.99 (ddd, *J* = 22.3, 18.2, 4.8 Hz, 2H), 3.70 (s, 3H), 1.41 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.70, 170.08, 155.30, 138.20, 129.12, 128.54, 127.47, 80.29, 58.59, 52.48, 41.53, 28.45.

HRMS (+ ESi) Mass calcd. for $C_{16}H_{22}N_2O_5$ $[M+Na]^+$: 345.1421, Found $[M+Na]^+$: 345.1415.

$[\alpha]^{23.6}_D$ = = – 81.4° (c = 1.0 , $CHCl_3$)

Enantiomeric ratio: 96:4, Rt_1 = 17.6, Rt_2 = 24.0, Chiralcel AD-H, 10% IPA/Hexanes, 1 mL/min



(*S*)-methyl 2-((*R*)-2-((*tert*-butoxycarbonyl)amino)-2-phenylacetamido)-3-methylbutanoate

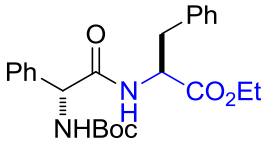
(**10**): To a 2 dram (8 mL) vial was added adduct **3a** (82 mg, 0.204 mmol), valine methyl ester [7] (80.4 mg, 0.612 mmol), and Dichloromethane (0.62 mL). The vial was sealed with a Septa-cap, and cooled to −45 °C in cryogenic bath for 15 minutes before TASF (67.4 mg, 0.245 mmol) in DCM (0.135 mL) (1.8 M) was added dropwise over 5 minutes. The reaction was allowed to stir for 6 hours at −45 °C before being quenched slowly by the dropwise addition of a 1.0 M solution of Trifluoroacetic acid in DCM (2 mL, 2 mmol) over 5 minutes. Aq. HCl (1.0M, 3 mL) was added and the reaction was warmed to ambient temperature, diluted with EtOAc (20 mL), and washed aq. HCl (1.0 M, 10 mL, 2x), sat. $NaHCO_3$ (10 mL), and brine (5 mL). [8] The organic layer was separated and dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 20-25% EtOAc/Hexanes) to afford 53.6 mg (72%) of **10** as a white solid.

IR (film): 3318, 2967, 1742, 1716, 1662, 1450, 1366, 1054, 698.

^{1}H NMR (major diastereomer) (500 MHz, $CDCl_3$) δ 7.44 – 7.28 (m, 5H), 6.32 (d, *J* = 8.7 Hz, 1H), 5.77 (s, 1H), 5.19 (s, 1H), 4.54 (dd, *J* = 9.0, 4.9 Hz, 1H), 3.74 (s, 3H), 2.11 – 2.03 (m, 1H), 1.41 (s, 9H), 0.74 (d, *J* = 6.9 Hz, 3H), 0.69 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (major diastereomer) (126 MHz, $CDCl_3$) δ 172.31, 170.11, 155.17, 138.68, 129.22, 128.60, 127.38, 80.31, 59.08, 57.25, 52.43, 31.52, 28.47, 18.92, 17.47.

HRMS (+ ESi) Mass calcd. for $C_{19}H_{28}N_2O_5$ $[M+Na]^+$: 387.1890, Found $[M+Na]^+$: 387.1883



(*S*)-ethyl 2-((*R*)-2-((*tert*-butoxycarbonyl)amino)-2-phenylacetamido)-3-phenylpropanoate

(**11**): To a 2 dram (8 mL) vial was added adduct **3a** (73 mg, 0.182 mmol), Phenylalanine ethyl ester[7] (105.4 mg, 0.545 mmol), and Dichloromethane (0.55 mL). The vial was sealed with a Septa-cap, and cooled to −45 °C in cryogenic bath for 15 minutes before TASF (60 mg, 0.218 mmol) in DCM (0.12 mL) (1.8 M) was added dropwise over 5 minutes. The reaction was allowed to stir for 5 hours at −45 °C before being quenched slowly by the dropwise addition of a 1.0 M solution of Trifluoroacetic acid in DCM (2 mL, 2 mmol) over 5 minutes. Aq. HCl (1.0M, 3 mL) was added and the reaction was warmed to ambient temperature, diluted with EtOAc (20 mL), and washed aq. HCl (1.0 M, 10 mL, 2x), sat. $NaHCO_3$ (10 mL), and brine (5 mL).[8] The organic layer was separated and dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 20-25% EtOAc/Hexanes) to afford 54.2 mg (70%) of **11** as a white solid.

IR (film): 3320, 2978, 2931, 1734, 1717, 1662, 1497, 1367, 1168, 699.

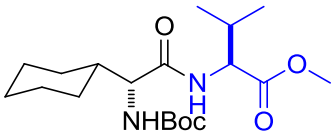
^{1}H NMR (major diastereomer) (500 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.06 (t, *J* =

[7] Free base obtained by washing the amino ester hydrochloride salt with sat. aq. K_2CO_3, extraction with DCM, and concentration. The concentrated free base was stable for weeks in the fridge.
[8] It is essential to wash away excess free amine with aq. HCl prior to washing with aq. $NaHCO_3$ (to remove TFA) since the amine will react with the unreacted acyl cyanide at elevated temperatures and lead to noticeable epimerization.

7.5 Hz, 2H), 6.66 (d, *J* = 6.2 Hz, 2H), 6.15 (s, 1H), 5.82 (s, 1H), 5.08 (s, 1H), 4.87 (dt, *J* = 8.0, 5.4 Hz, 1H), 4.22 – 4.11 (m, 2H), 3.03 – 2.88 (m, 2H), 1.41 (s, 9H), 1.25 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (major diastereomer) (126 MHz, $CDCl_3$) δ 171.09, 169.55, 155.18, 138.62, 135.37, 129.37, 129.32, 128.62, 128.58, 127.48, 127.13, 80.21, 61.85, 58.87, 53.27, 37.86, 28.49, 14.30.

HRMS (+ ESi) Mass calcd. for $C_{24}H_{30}N_2O_5$ $[M+Na]^+$: 449.2047, Found $[M+Na]^+$: 449.2043



(*S*)-methyl 2-((*R*)-2-((*tert*-butoxycarbonyl)amino)-2-cyclohexylacetamido)-3-methylbutanoate

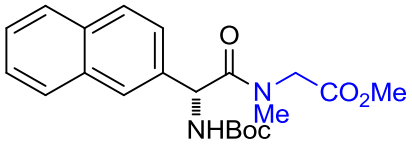
(**12**): To a 1 dram (4 mL) vial was added adduct **3a** (32 mg, 0.079 mmol), valine methyl ester[7] (20.6 mg, 0.157 mmol), and Dichloromethane (0.24 mL). The vial was sealed with a Septa-cap, and cooled to −78 °C in cryogenic bath for 15 minutes before TASF (26 mg, 0.094 mmol) in DCM (0.052 mL) (1.8 M) was added dropwise over 5 minutes. The reaction was allowed to stir for 3 hours at −78 °C, and another 5 hours at −45 °C before being quenched with aq. HCl (1.0M, 2 mL). The reaction was warmed to ambient temperature, diluted with EtOAc (10 mL), H_2O (3mL), and brine (2 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (10 mL, 2x). The combined organic solvents were dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 20% EtOAc/Hexanes) to afford 27 mg (93%) of **12** as an amorphous solid.

IR (film): 3314, 2926, 2852, 1746, 1682, 1650, 1530, 1450, 1366, 1256, 1177, 1018

^{1}H NMR (major diastereomer) (500 MHz, $CDCl_3$) δ 6.51 (d, *J* = 8.7 Hz, 1H), 5.05 (s, 1H), 4.55 (dd, *J* = 8.7, 4.8 Hz, 1H), 3.99 (s, 1H), 3.74 (s, 3H), 2.25 – 2.13 (m, 1H), 1.90 – 1.79 (m, 1H), 1.79 – 1.62 (m, 5H), 1.44 (d, *J* = 3.4 Hz, 9H), 1.34 – 1.18 (m, 3H), 1.18 – 1.06 (m, 2H), 1.01 (ddd, *J* = 25.0, 12.5, 3.5 Hz, 1H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (major diastereomer) (126 MHz, $CDCl_3$) δ 172.40, 171.62, 80.14, 59.86, 57.20, 52.33, 40.48, 31.37, 30.05, 28.50, 28.17, 26.29, 26.23, 26.18, 19.16, 17.94.

HRMS (+ ESi) Mass calcd. for $C_{19}H_{34}N_2O_5Si$ $[M+Na]^+$: 393.2360, Found $[M+Na]^+$: 393.2354.



(*R*)-methyl 2-(2-((*tert*-butoxycarbonyl)amino)-*N*-methyl-2-(naphthalen-2-yl)acetamido)acetate

(**13**): To a 1 dram (4 mL) vial was added adduct **3b** (49 mg, 0.1085 mmol), sarcosine methyl ester[7] (33.6 mg, 0.325 mmol), and dichloromethane (0.33 mL). The vial was sealed with a Septa-cap, and cooled to −78 °C in cryogenic bath for 15 minutes before TASF (36 mg, 0.13 mmol) in dichloromethane (0.072 mL) (1.8 M) was added dropwise over 5 minutes. The reaction was allowed to stir for 2 hours at −78 °C, and another 5 hours at −45 °C before being quenched by the dropwise addition of a 1.0 M solution of Trifluoroacetic acid in DCM (1 mL, 2 mmol) over 5 minutes. Aq. HCl (1.0M, 2 mL) was added and the reaction was warmed to ambient temperature, diluted with EtOAc (15 mL), and washed aq. HCl (1.0 M, 5 mL, 2x), sat. $NaHCO_3$ (10 mL), and brine (5 mL).[8] The organic layer was separated and dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 25-30% EtOAc/Hexanes) to afford 34 mg (81%) of **13** as an amorphous solid.

IR (film): - 3419, 3328, 2977, 2849, 1751, 1707, 1653, 1486, 1405, 1366, 1165, 751

^{1}H NMR - (major rotamer) (500 MHz, CDCl3) δ 7.93 – 7.77 (m, 4H), 7.58 – 7.40 (m, 3H), 6.03 (d, J = 7.8 Hz, 1H), 5.80 (d, J = 7.9 Hz, 1H), 4.16 (dd, J = 145.6, 17.2 Hz, 2H), 3.73 (s, 3H), 2.95 (s, 3H), 1.41 (s, 9H).

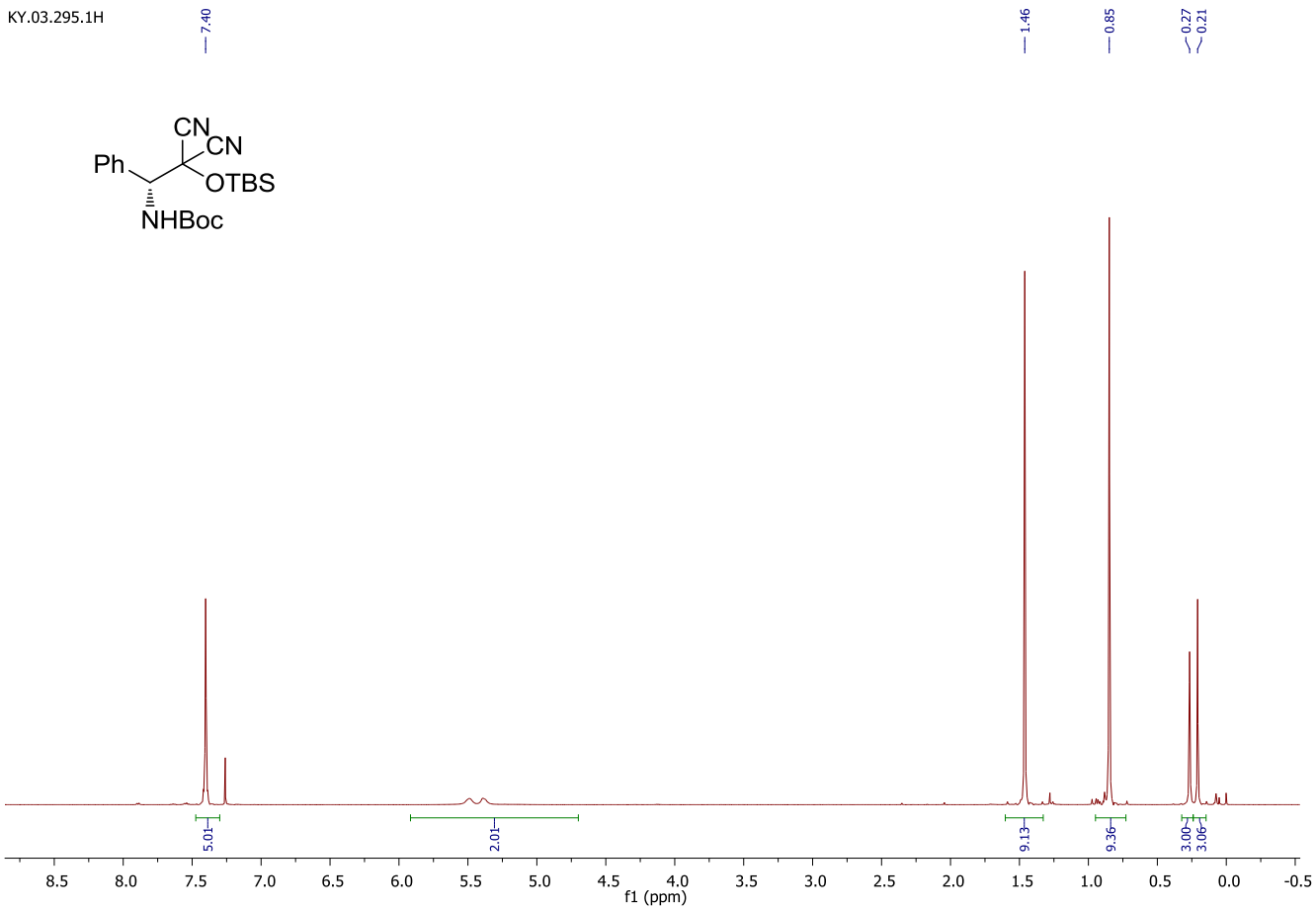
^{13}C NMR – (major rotamer) (126 MHz, CDCl3) δ 171.07, 169.35, 155.30, 134.89, 133.56, 133.29, 129.10, 128.40, 127.86, 127.40, 126.59, 126.54, 125.73, 80.02, 55.62, 52.38, 50.16, 36.57, 28.56

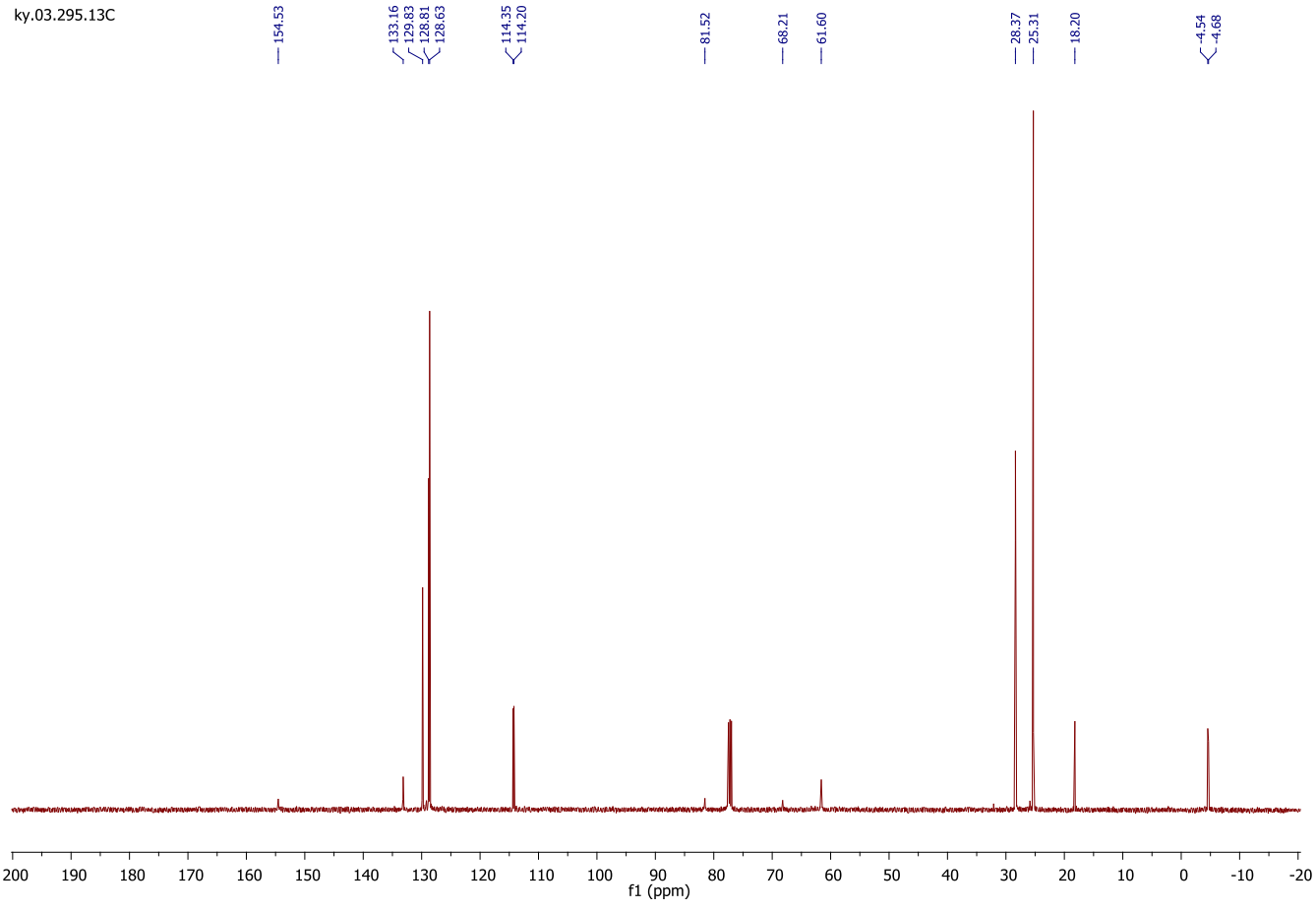
HRMS (+ ESi) Mass calcd. for $C_{21}H_{27}N_2O_5$ $[M+H]^+$: 387.1914, Found $[M+Na]^+$: 387.1898.

$[\alpha]^{23.6}_D$ = = – 147.6° (c = 1.0 , $CHCl_3$)

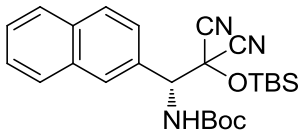
Enantiomeric ratio: 95.5:4.5, Rt_1 = 10.7, Rt_2 = 13.5, Chiralcel OD-H, 10% IPA/Hexanes, 1 mL/min

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

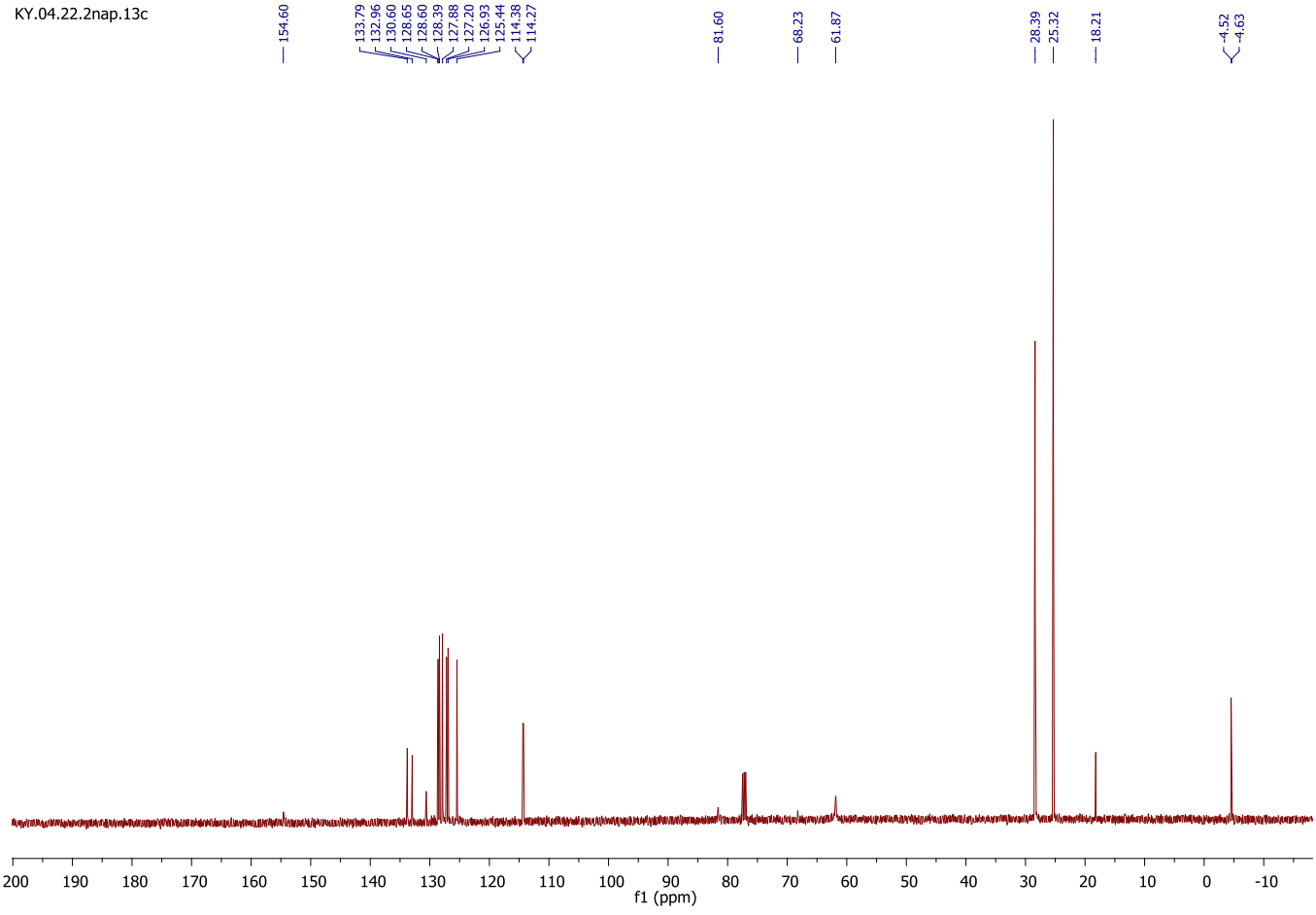




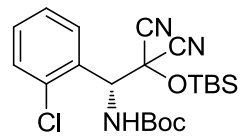
KY.04.22.2nap.1H



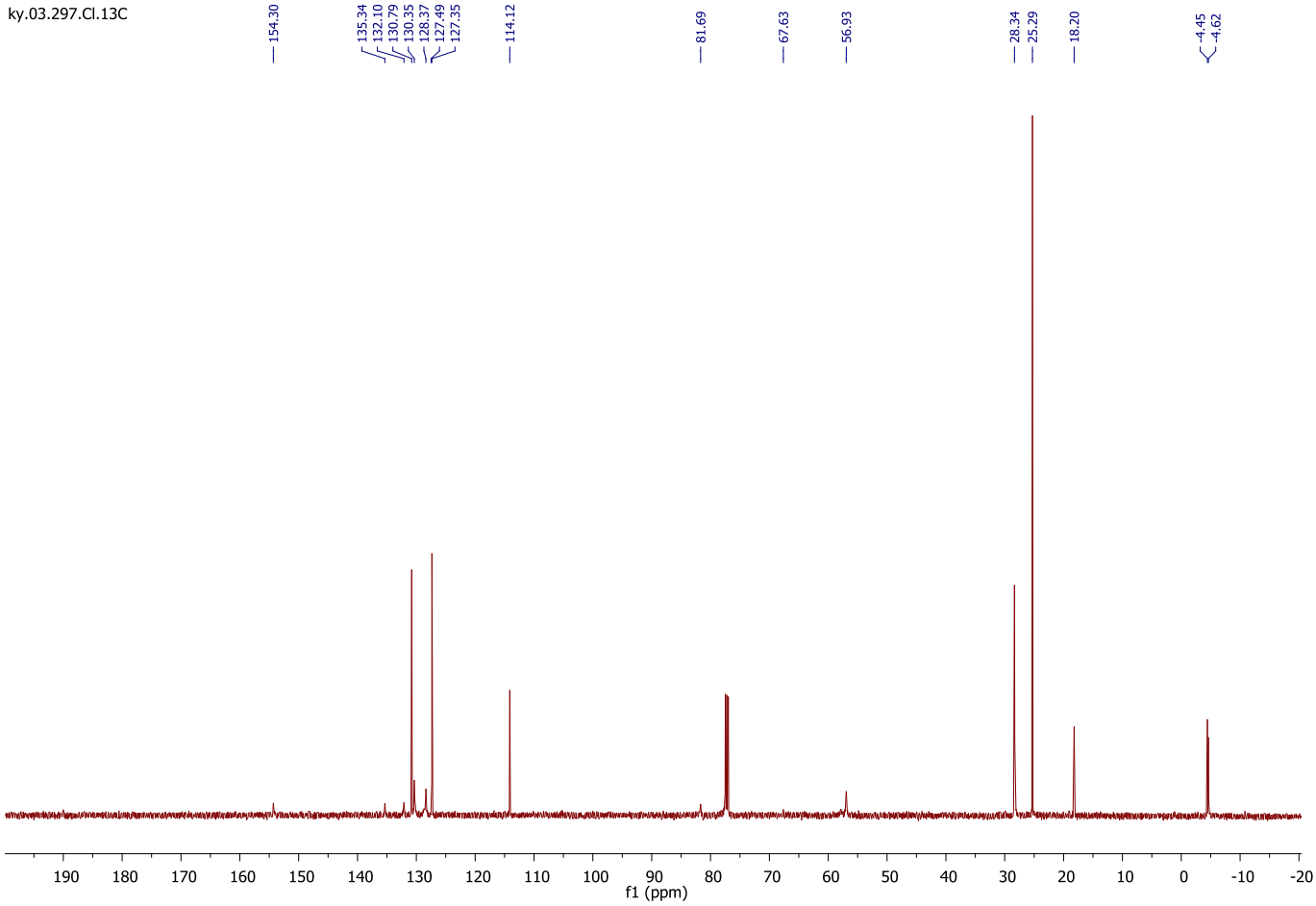
KY.04.22.2nap.13c



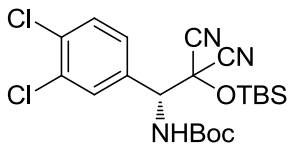
KY.03.297.Cl.1H



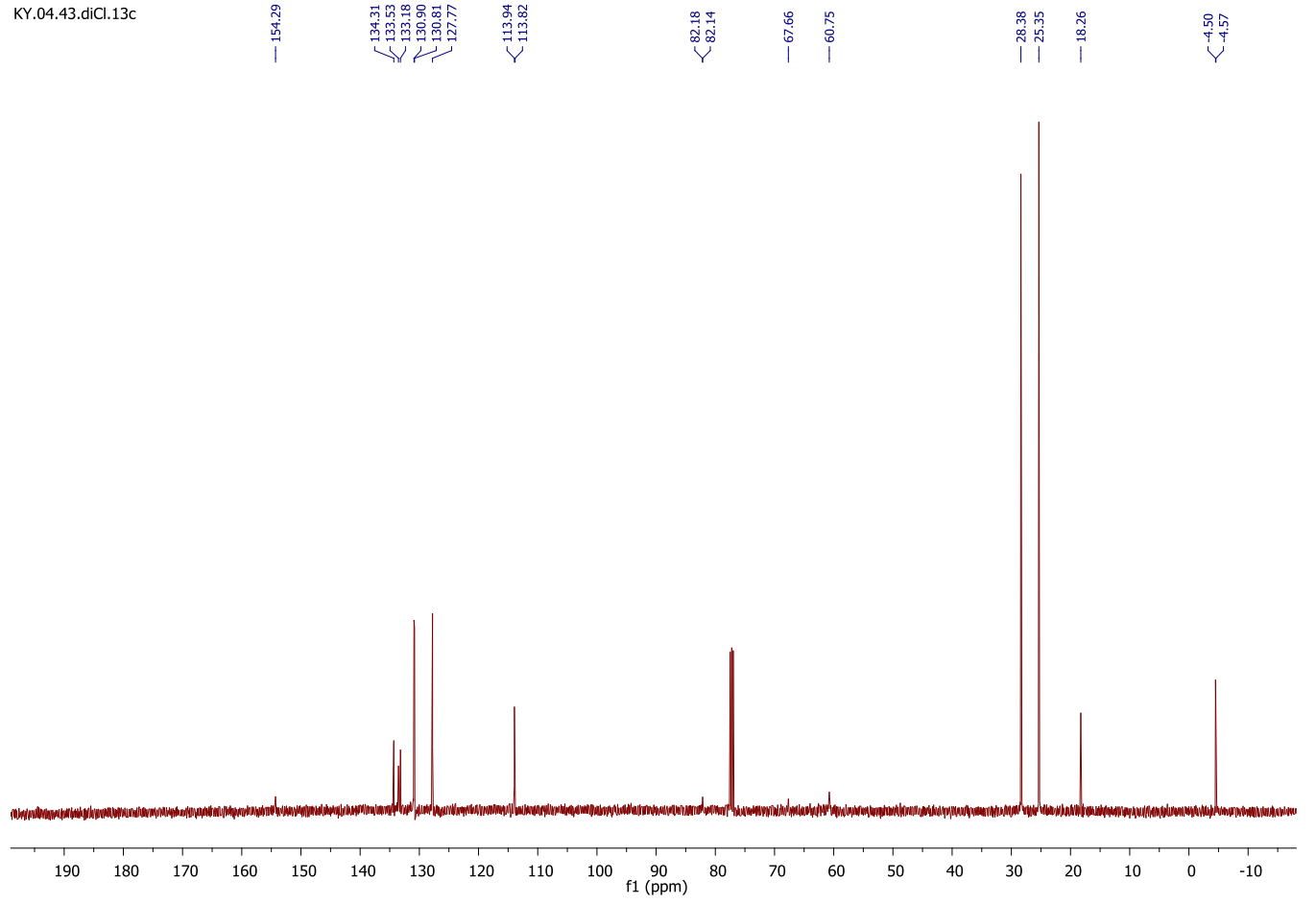
ky.03.297.Cl.13C



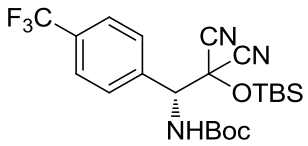
KY.04.43.dicl.1H



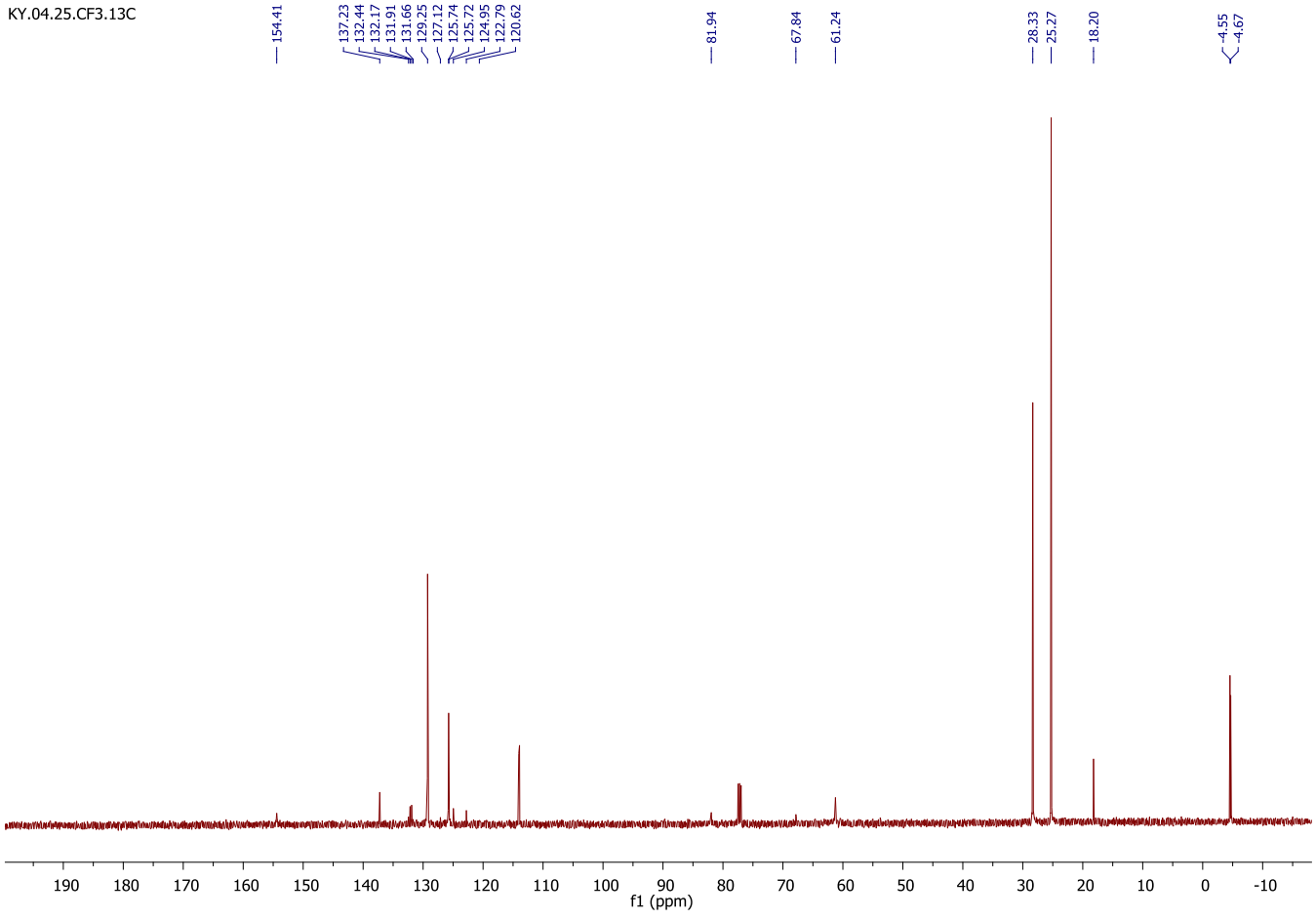
KY.04.43.diCl.13c

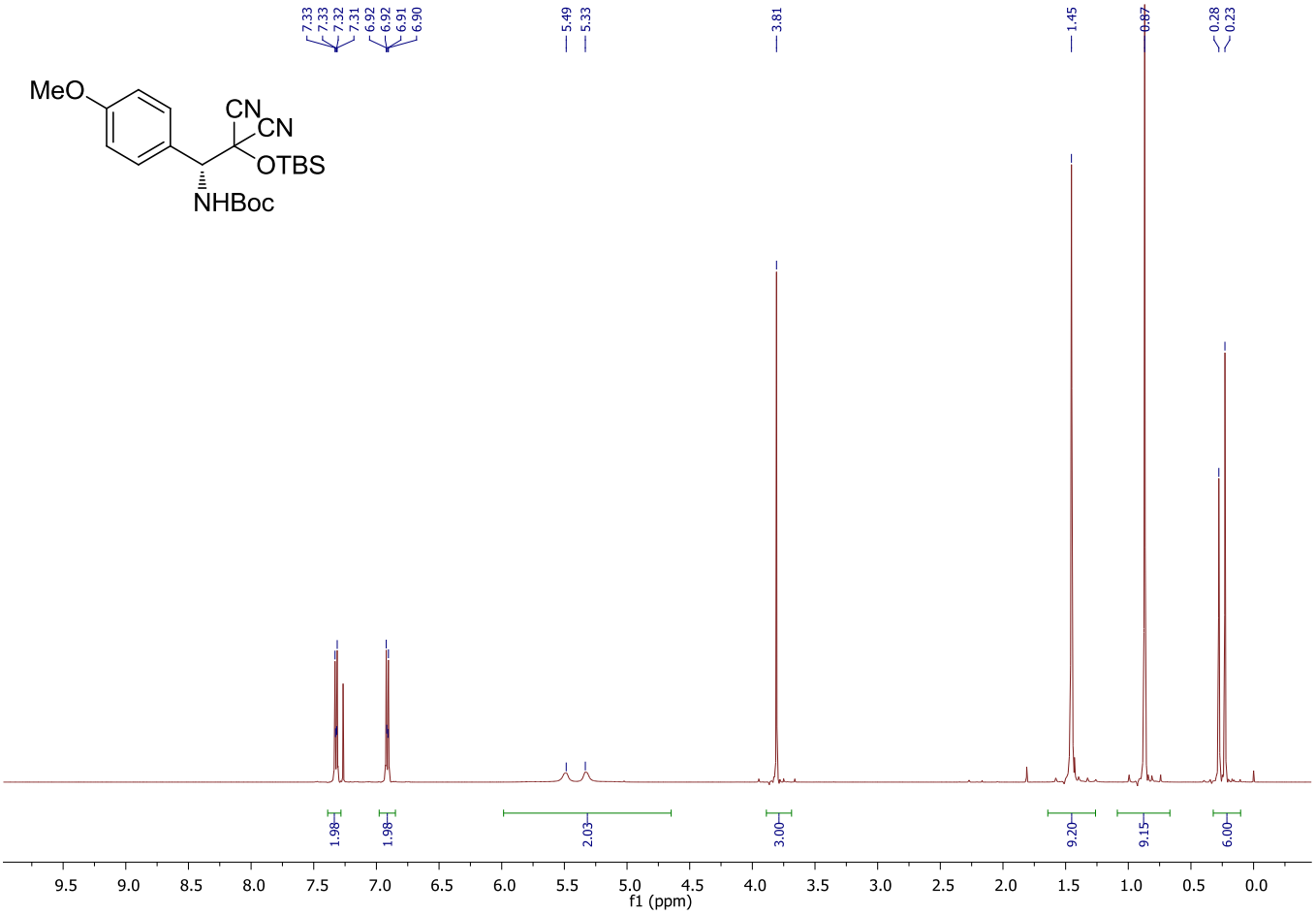


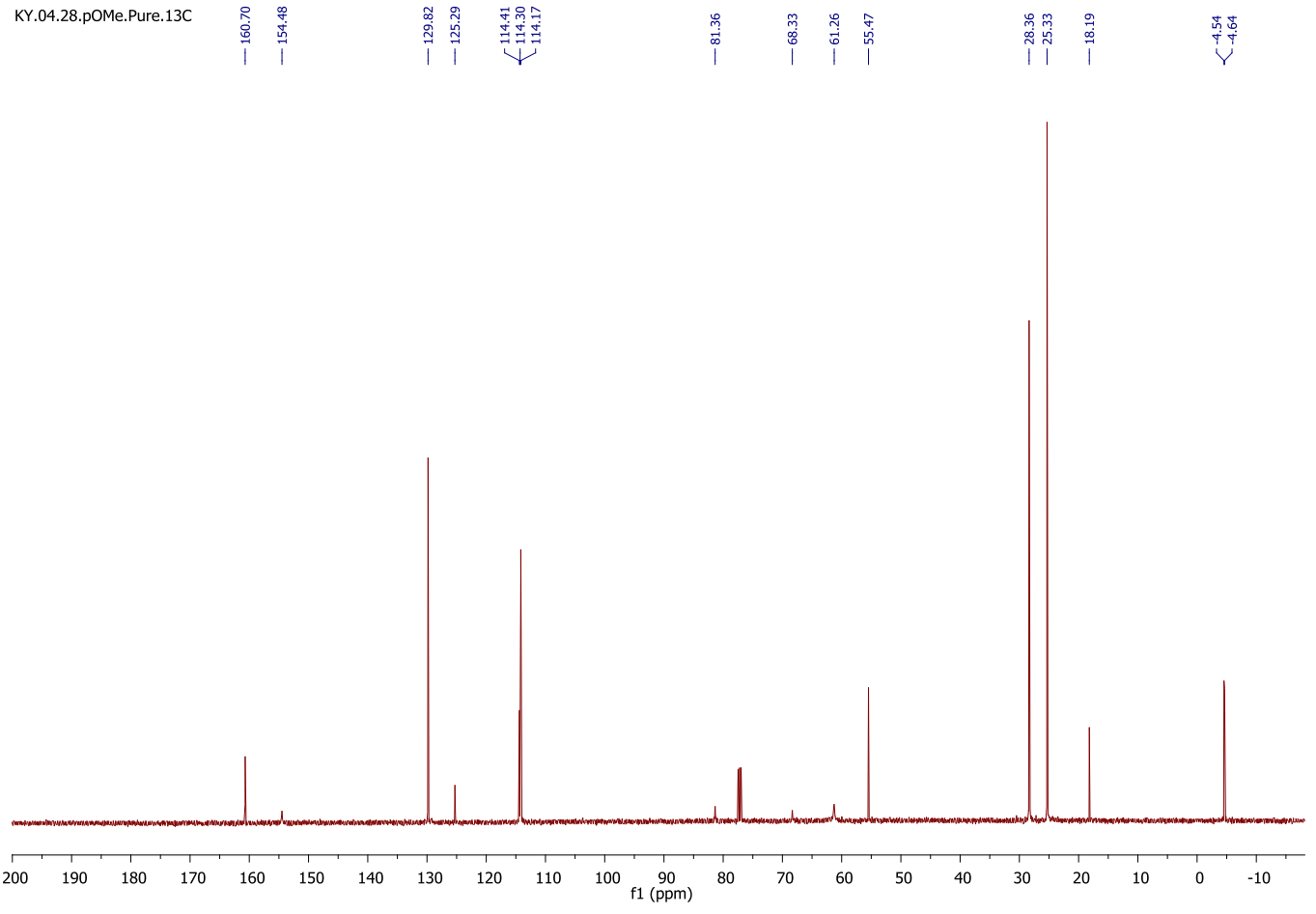
KY.04.25.CF3.1H



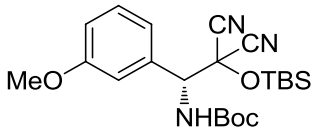
KY.04.25.CF3.13C



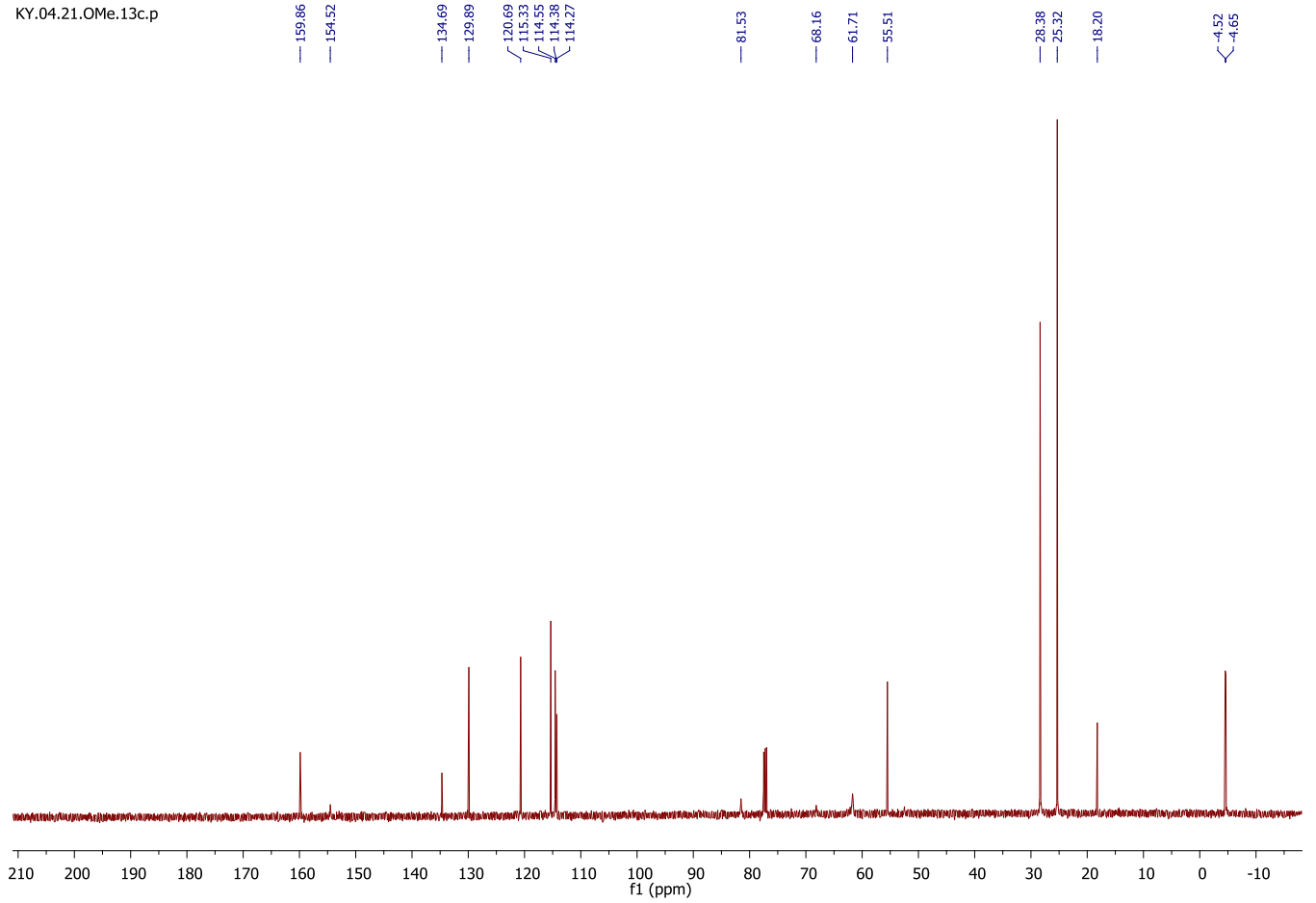

MeO
CN
CN
OTBS
NHBoc
7.33
7.33
7.32
7.31
6.92
6.92
6.91
6.90
5.49
5.33
3.81
1.45
0.87
0.28
0.23
1.98
1.98
2.03
3.00
9.20
9.15
6.00
f1 (ppm)


KY.04.28.pOMe.Pure.13C
160.70
154.48
129.82
125.29
114.41
114.30
114.17
81.36
68.33
61.26
55.47
28.36
25.33
18.19
-4.54
-4.64
f1 (ppm)

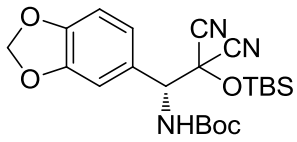
KY.04.21.OMe.1H.p



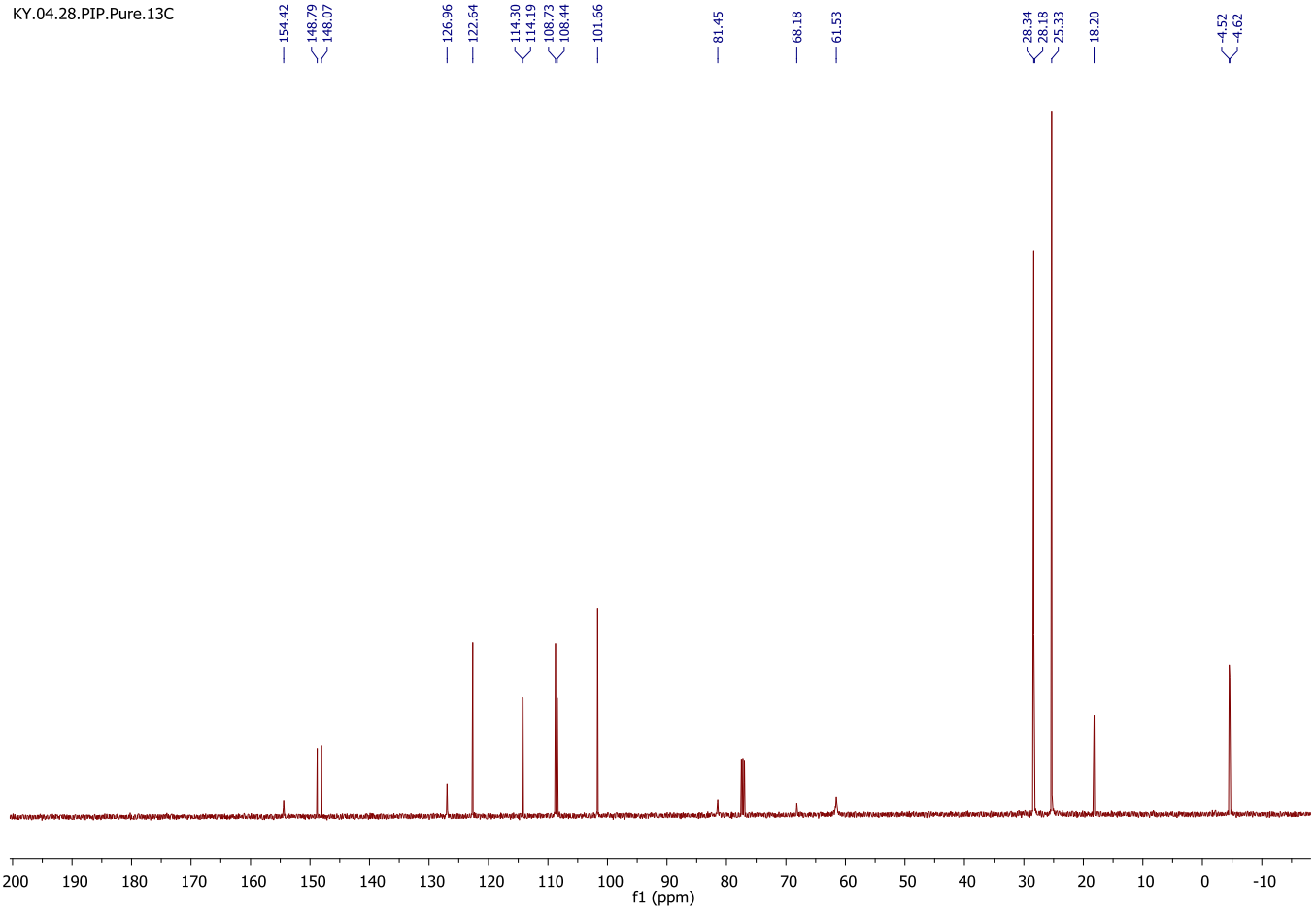
KY.04.21.OMe.13c.p



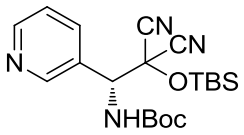
KY.04.28.PIP.Pure.1H



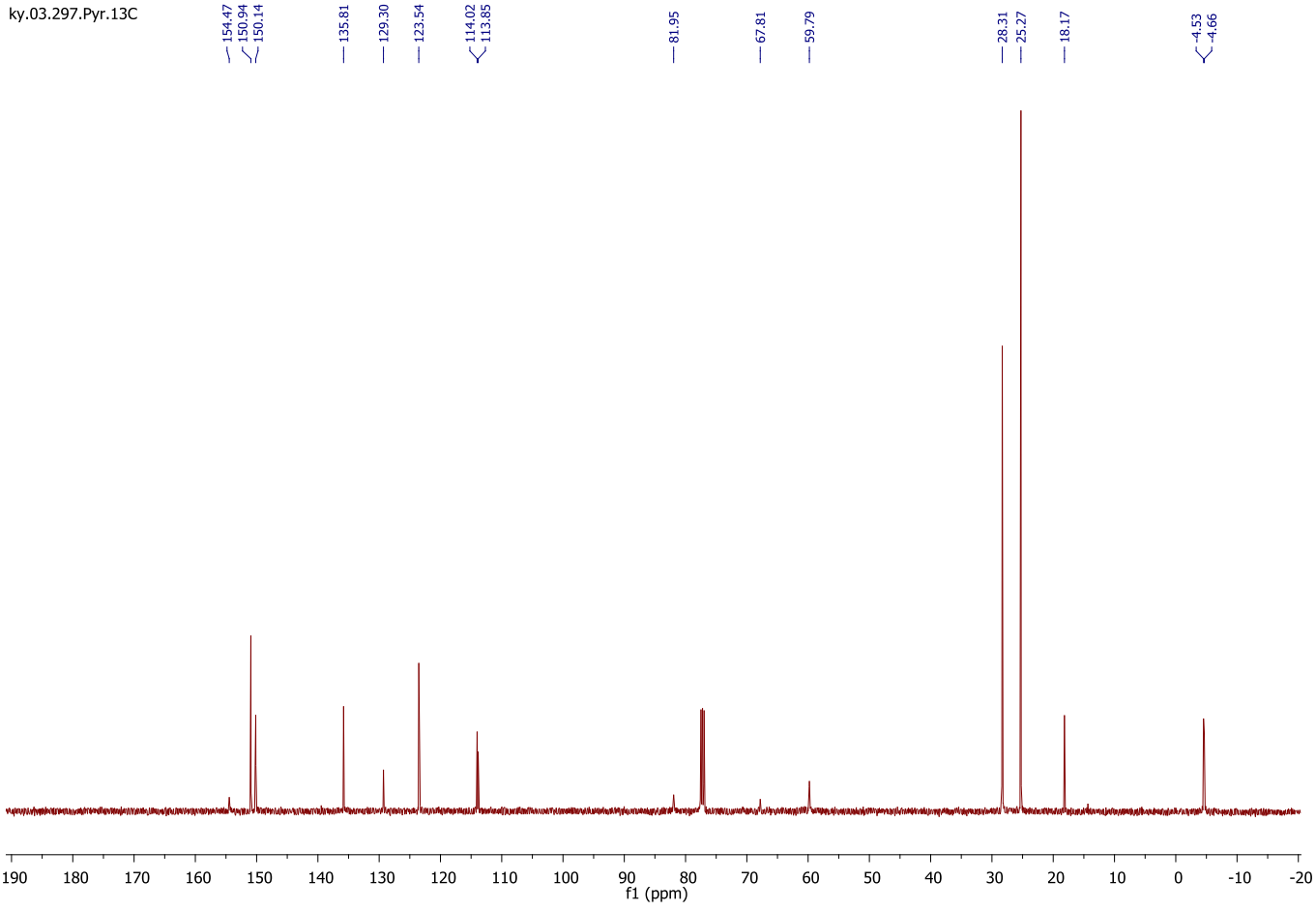
KY.04.28.PIP.Pure.13C



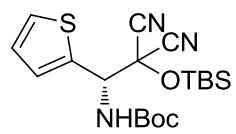
ky.03.297.Pyr.1H



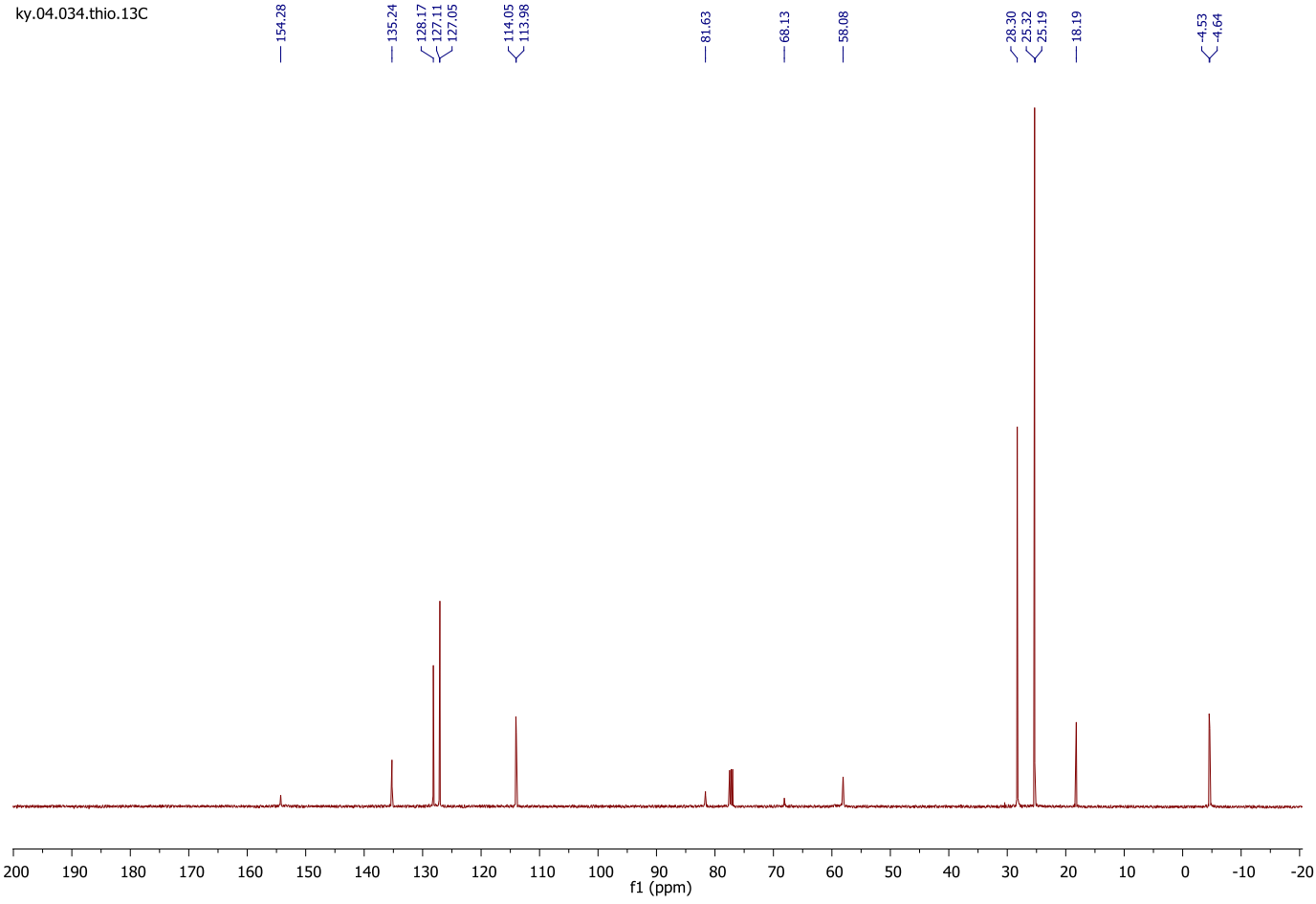
ky.03.297.Pyr.13C



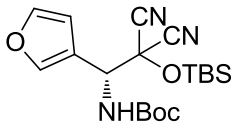
ky.04.034.thio.1H



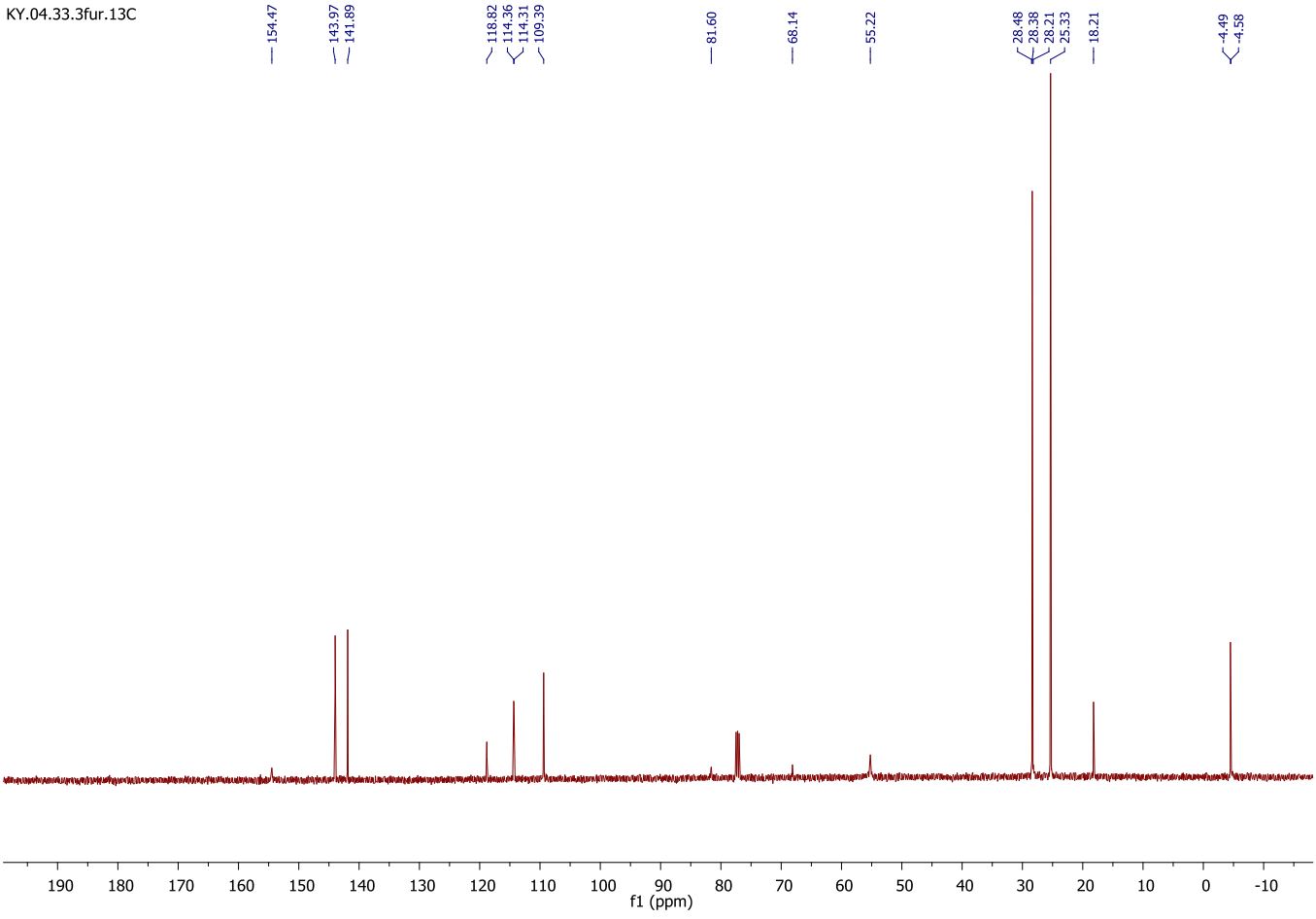
ky.04.034.thio.13C



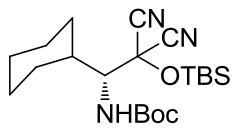
KY.04.33.3fur.1H



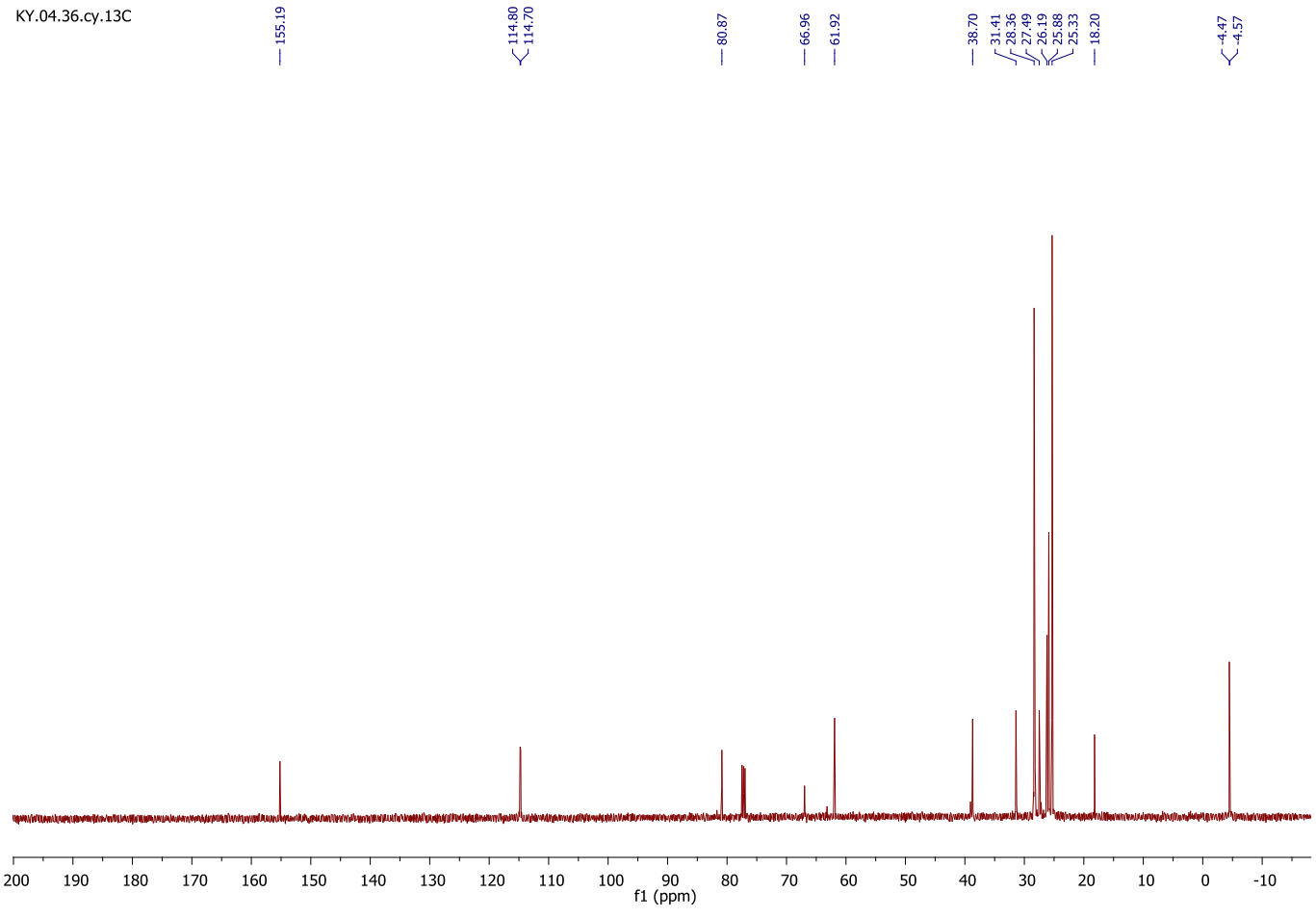
KY.04.33.3fur.13C



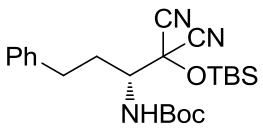
KY.04.36.cy.1H



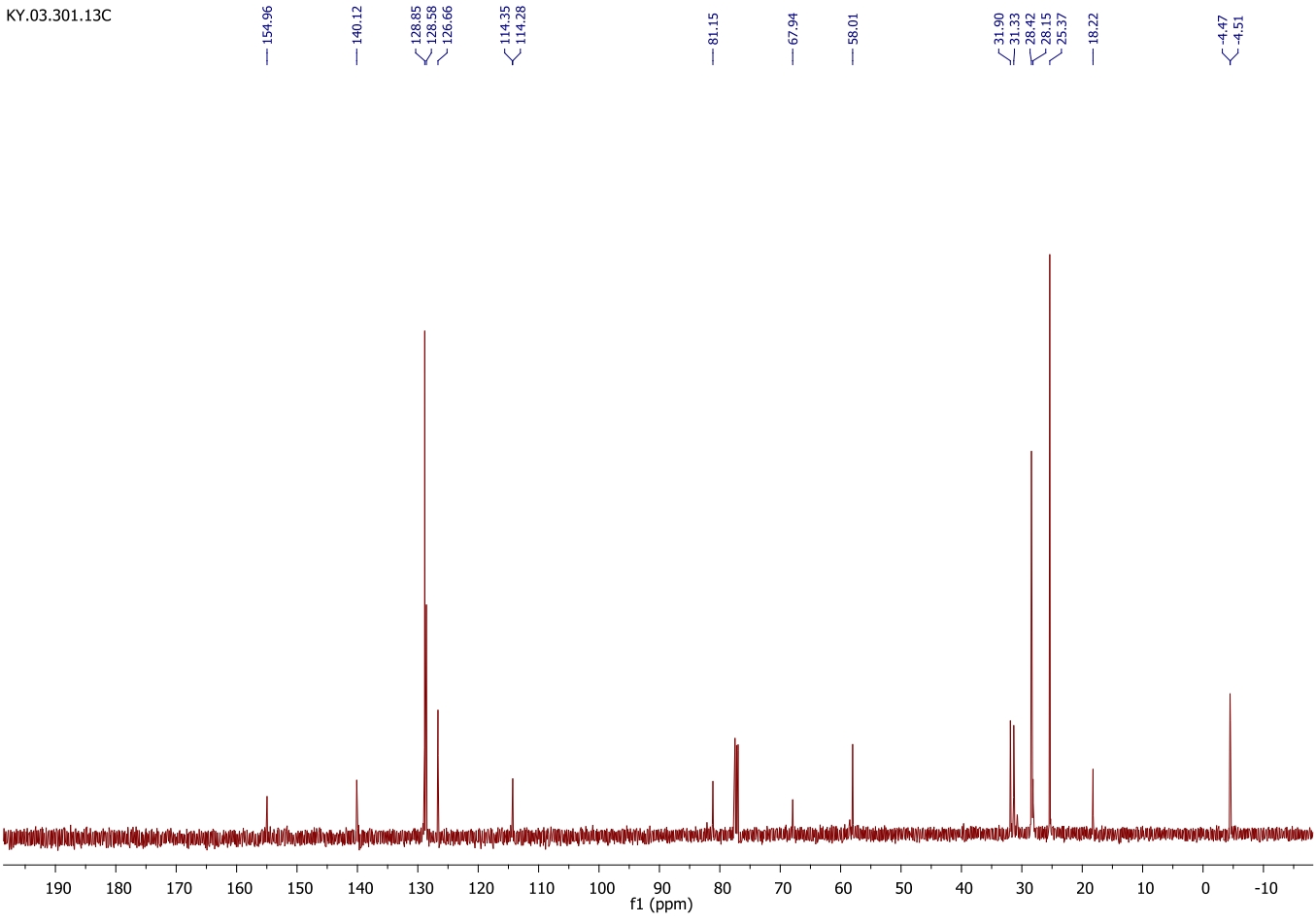
KY.04.36.cy.13C



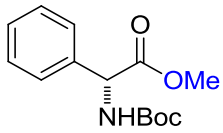
KY.03.301.1H



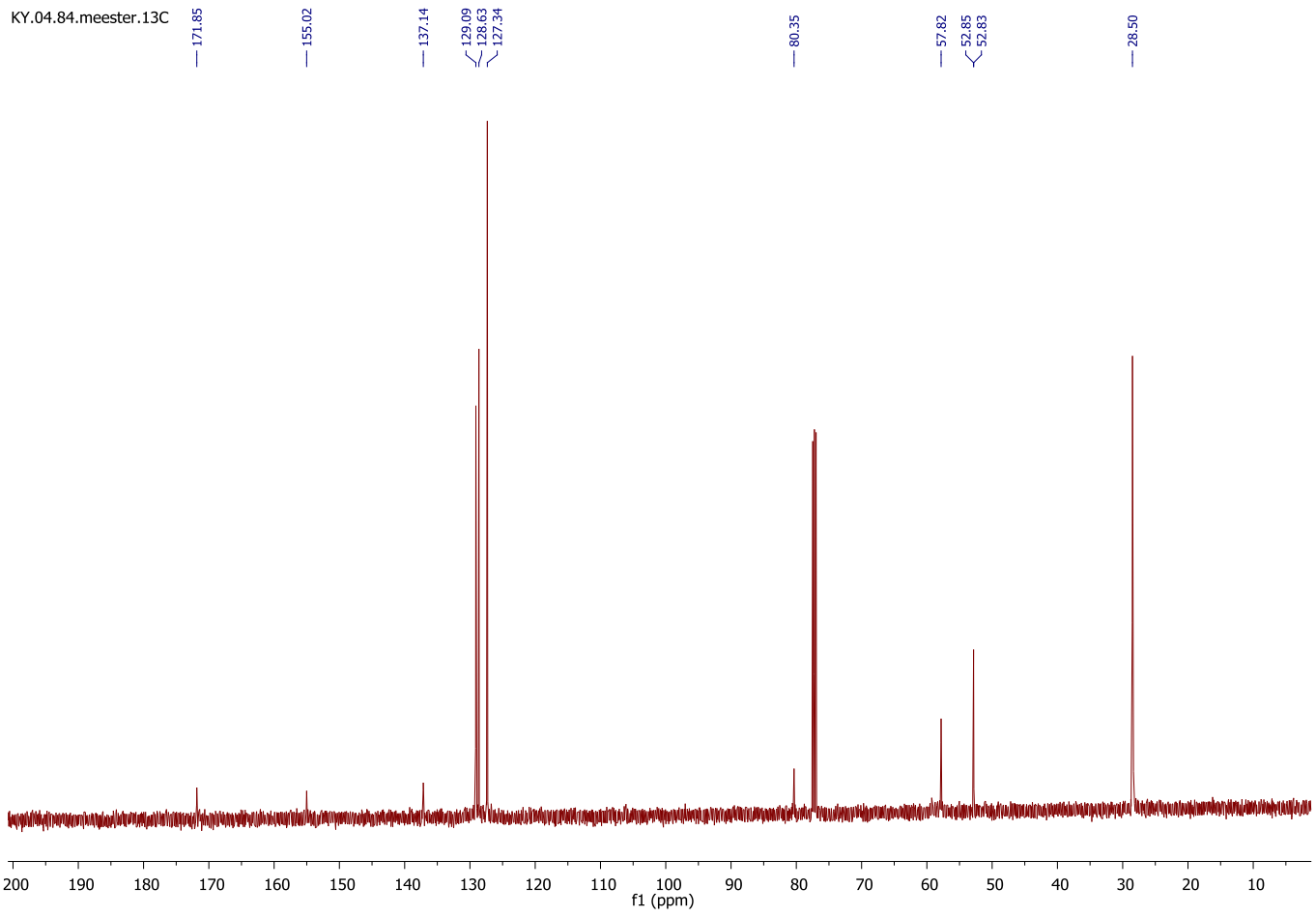
KY.03.301.13C



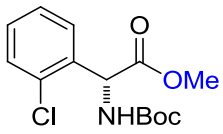
KY.04.84.MeEst.1H



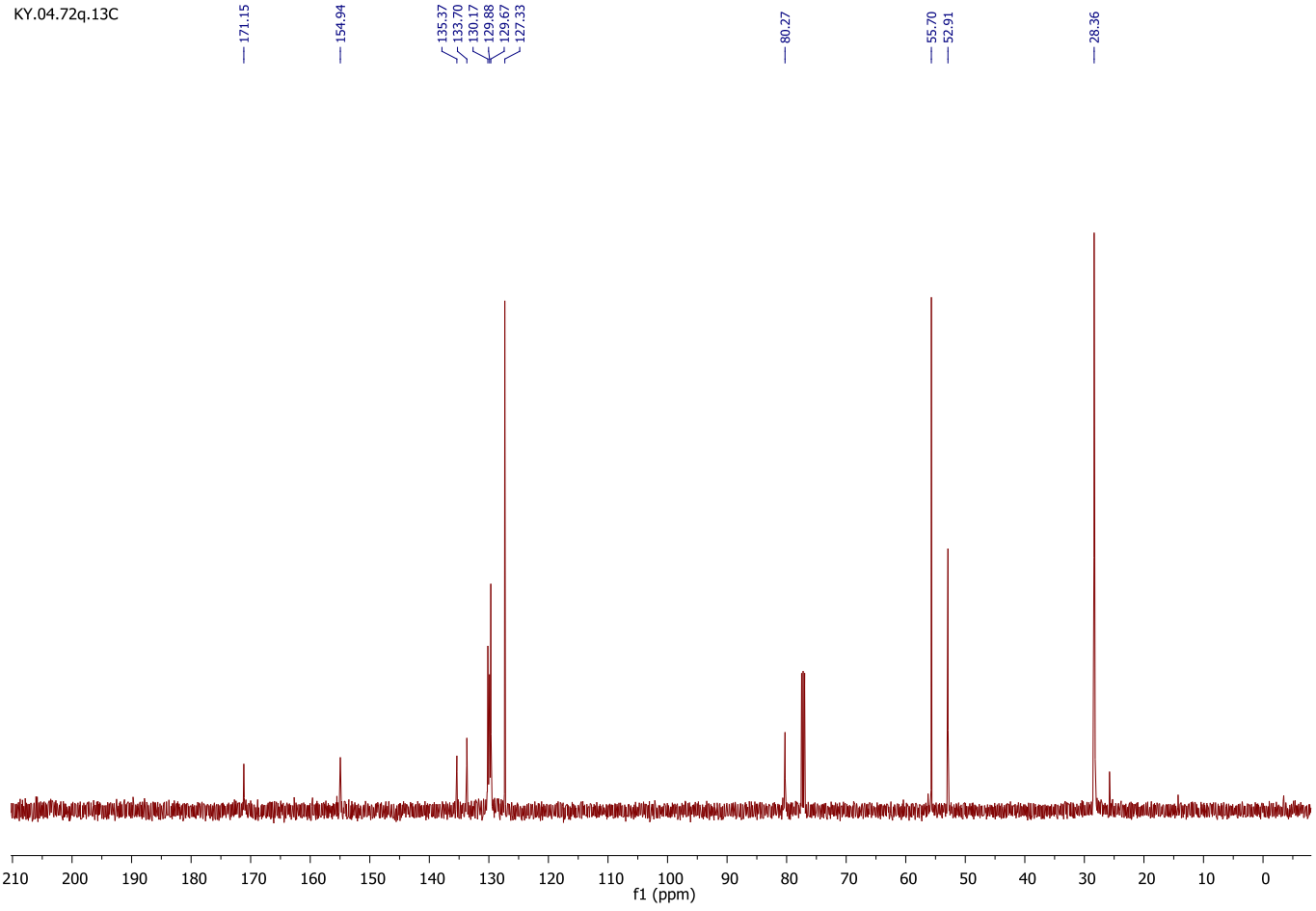
KY.04.84.meester.13C



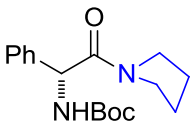
KY.04.72q.1H



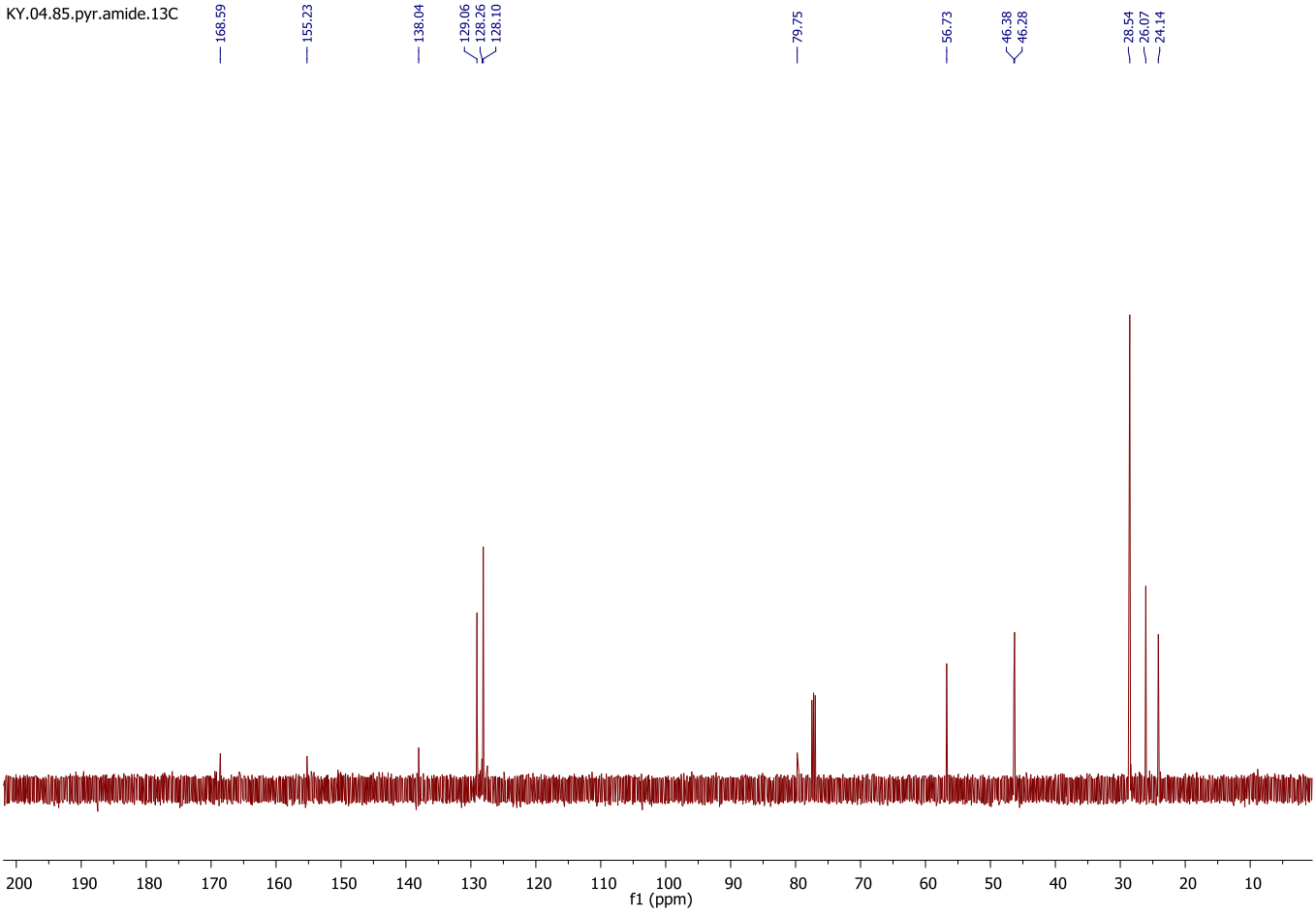
KY.04.72q.13C



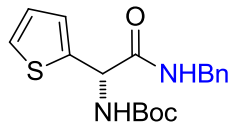
KY.04.85.pyr.amide.1H



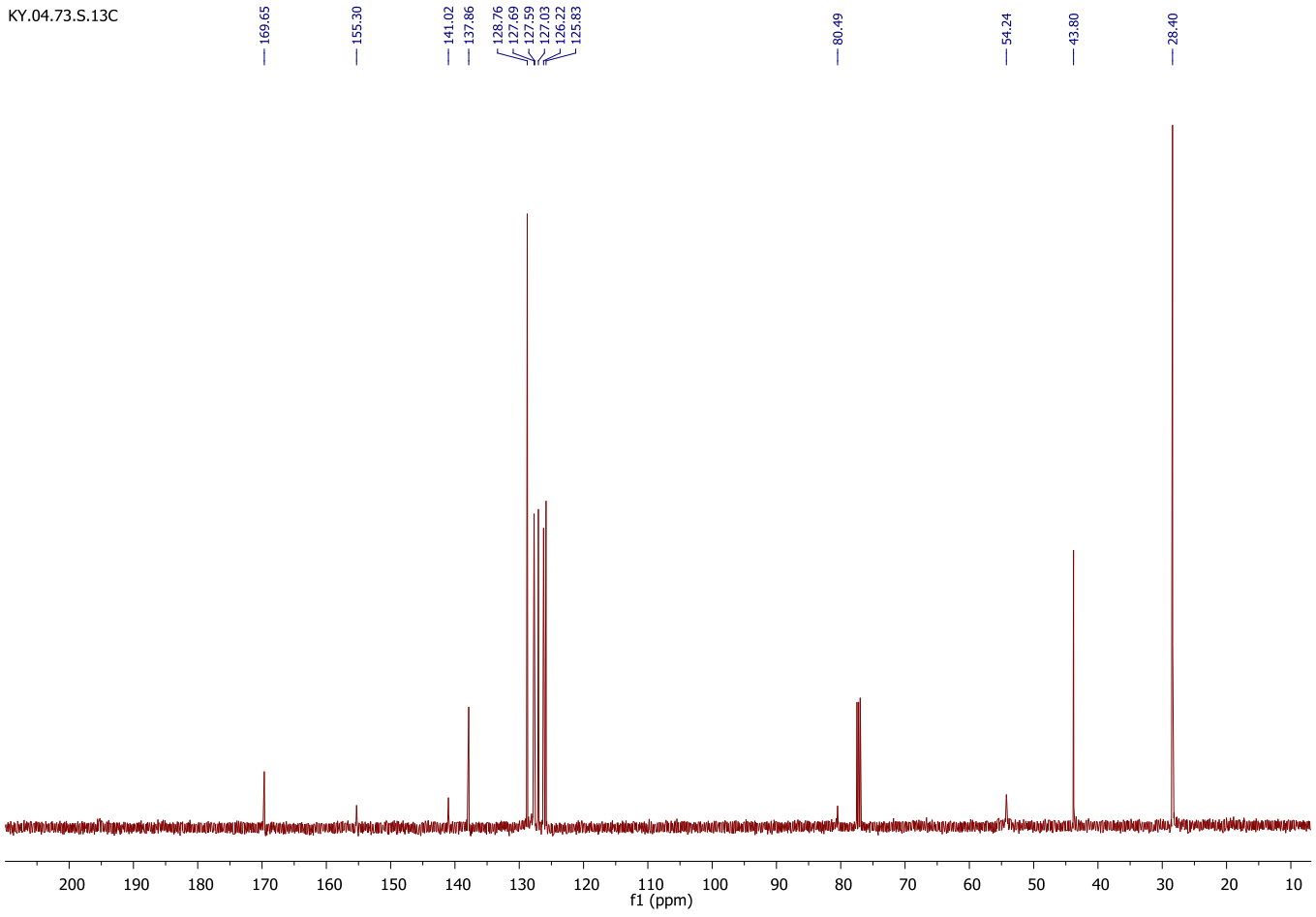
KY.04.85.pyr.amide.13C



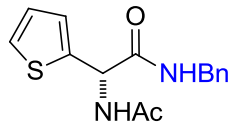
KY.04.73.S.1H

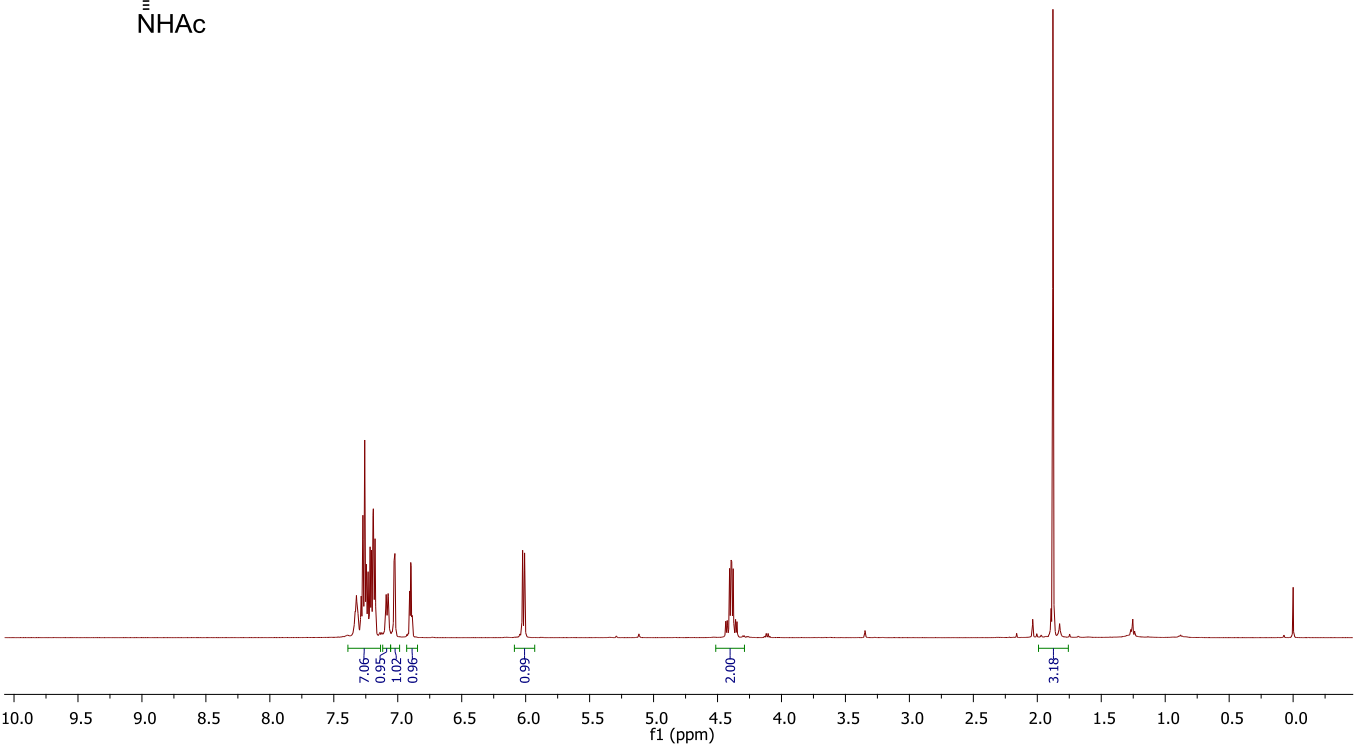


KY.04.73.S.13C

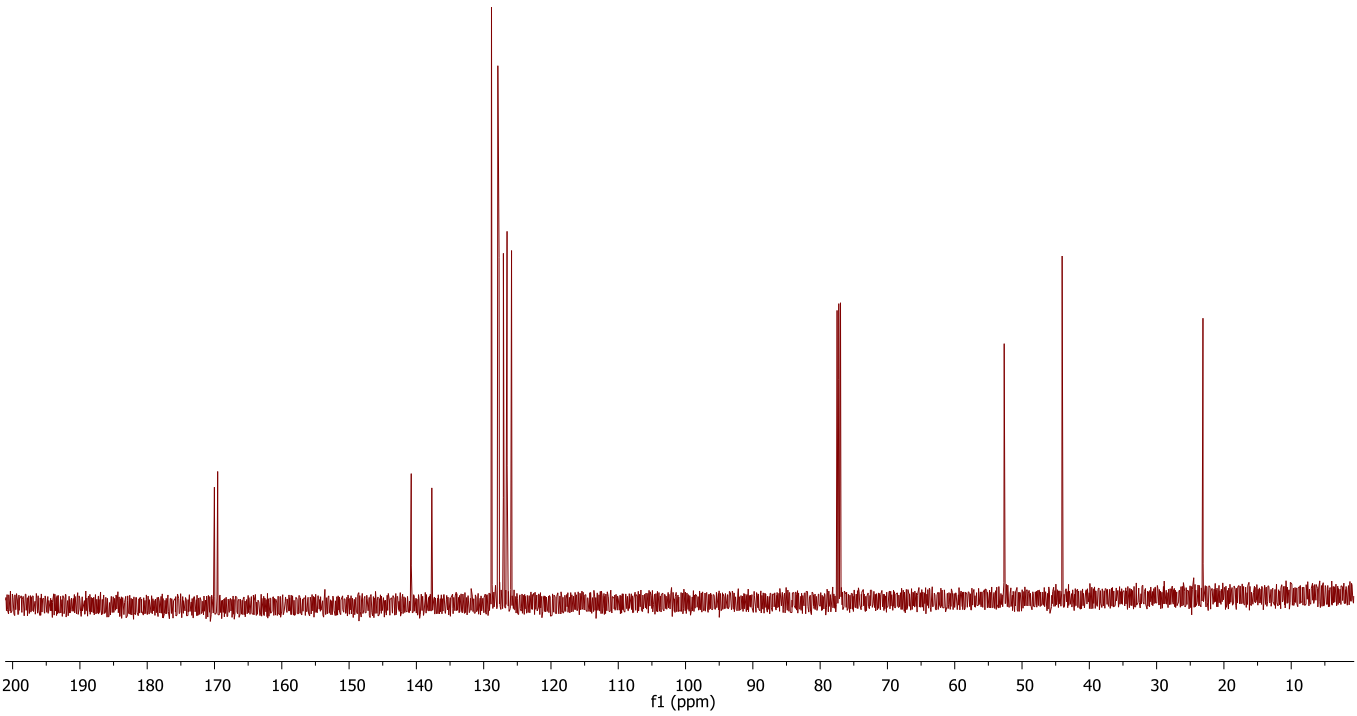


KY.04.88.1H

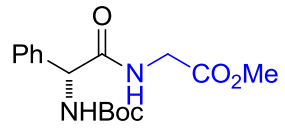




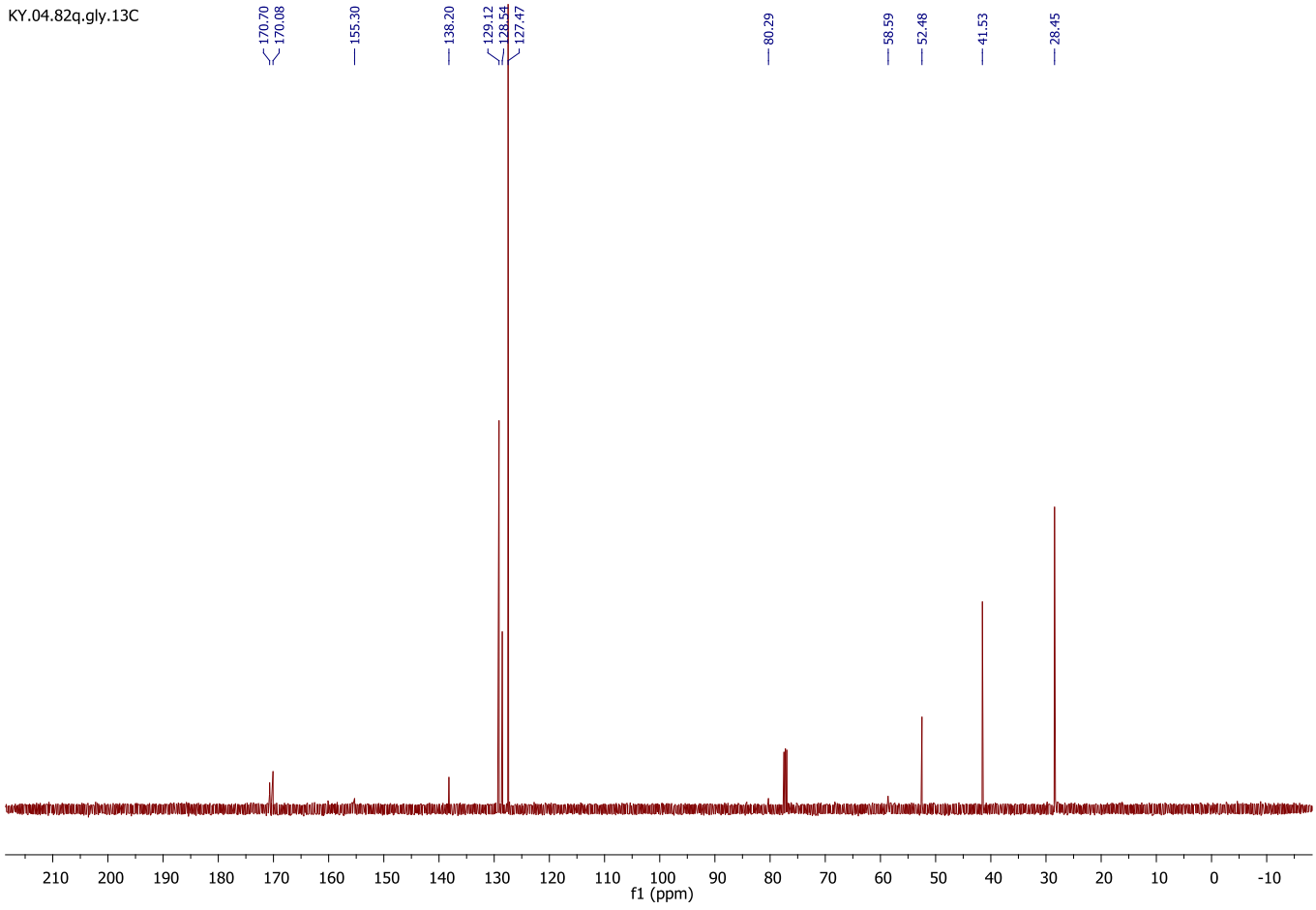
KY.04.88.13C



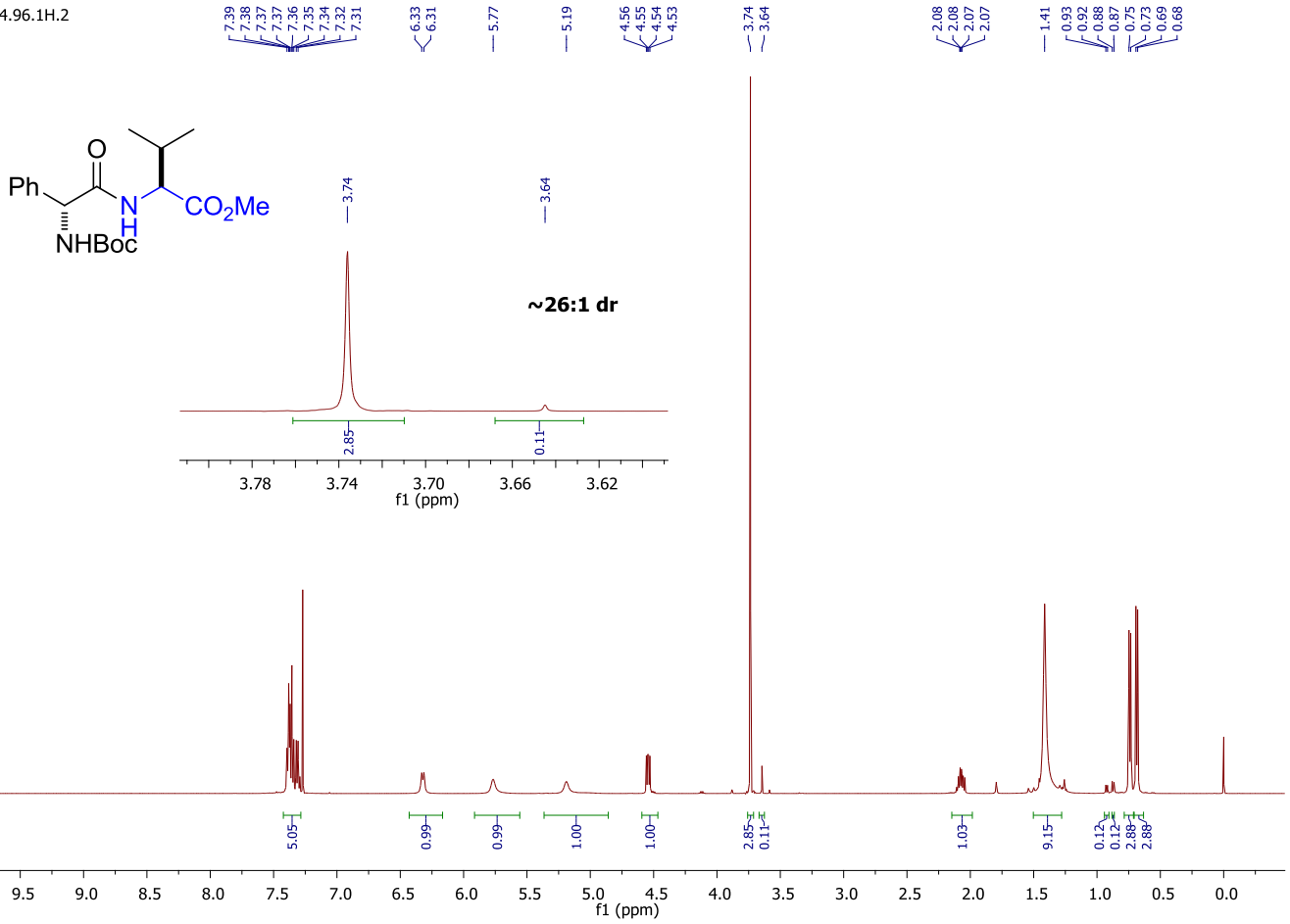
KY.04.82q.gly.1H



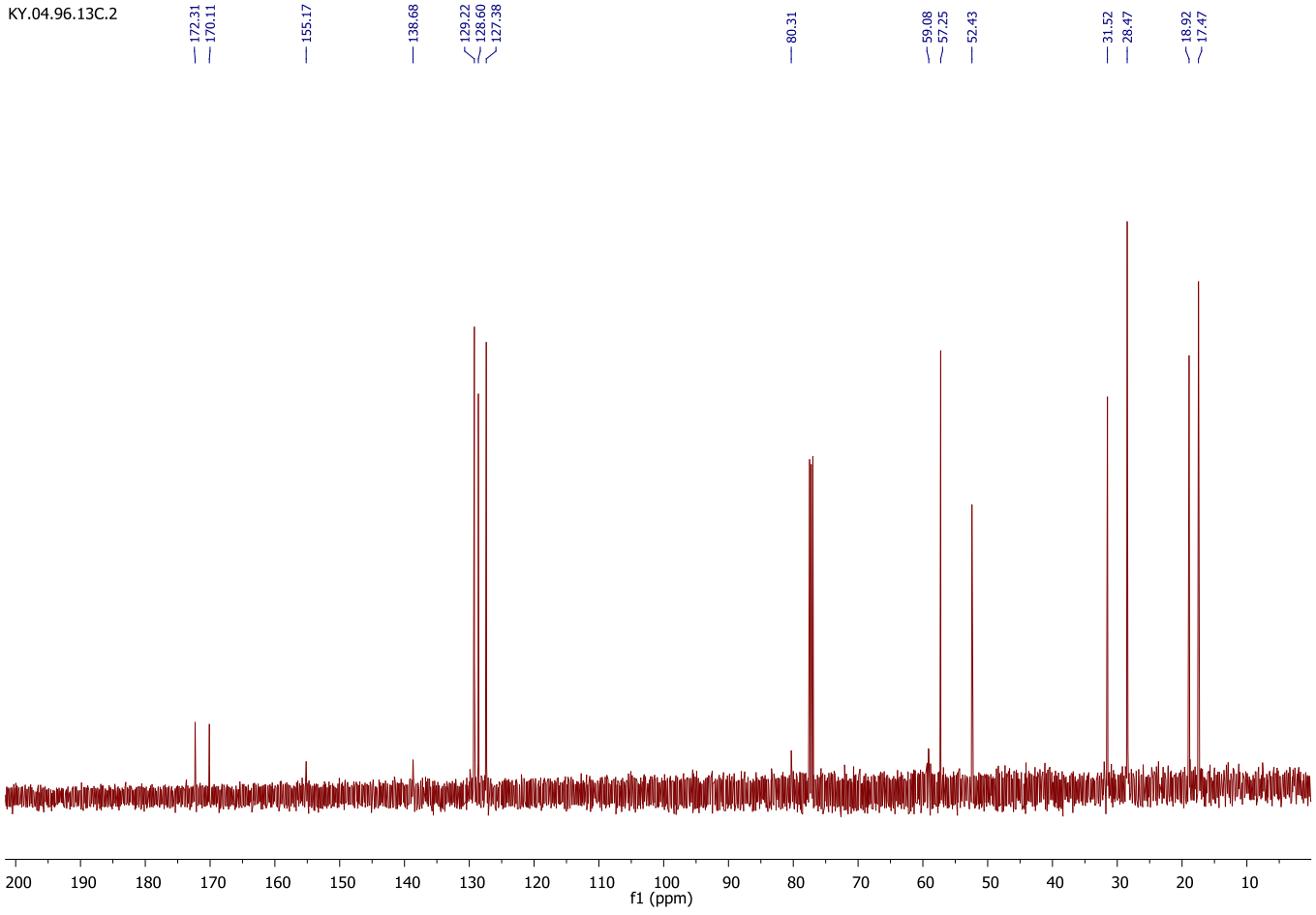
KY.04.82q.gly.13C



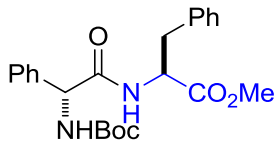
KY.04.96.1H.2



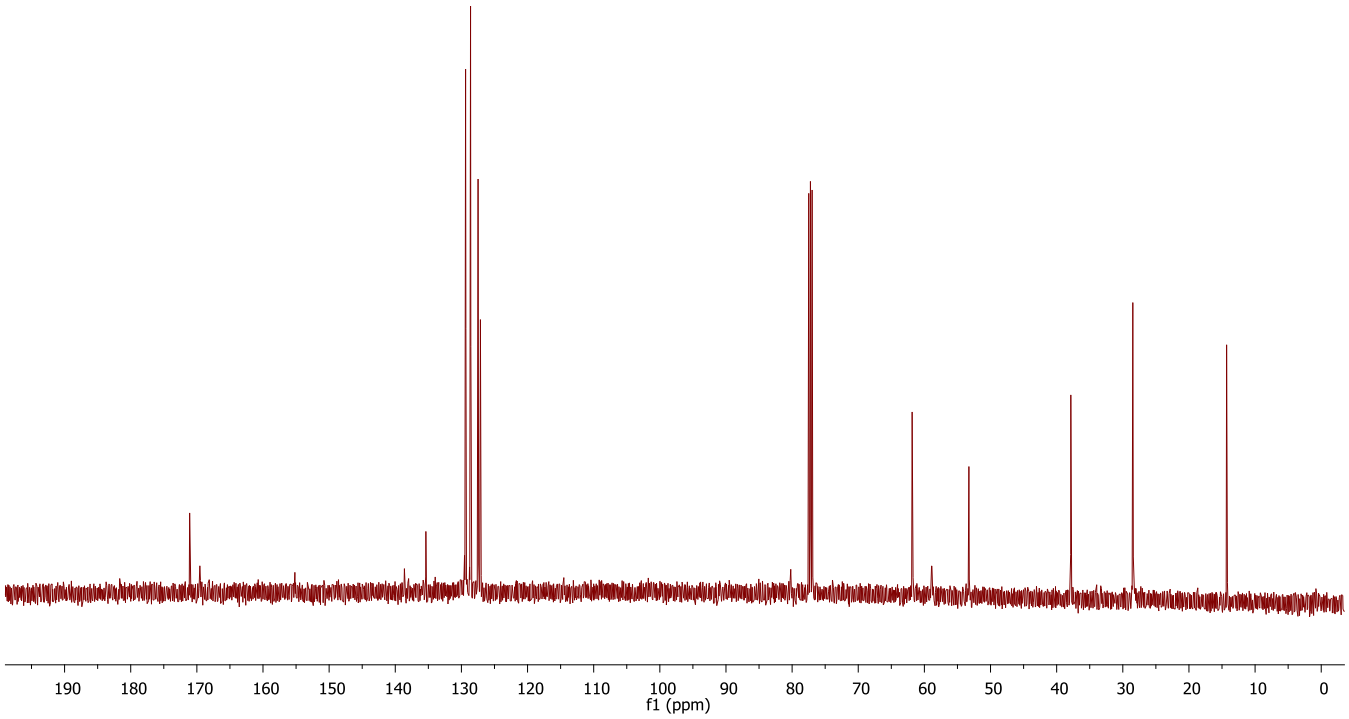
KY.04.96.13C.2



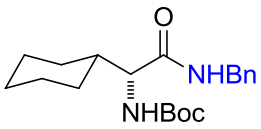
KY.04.99.phen.col



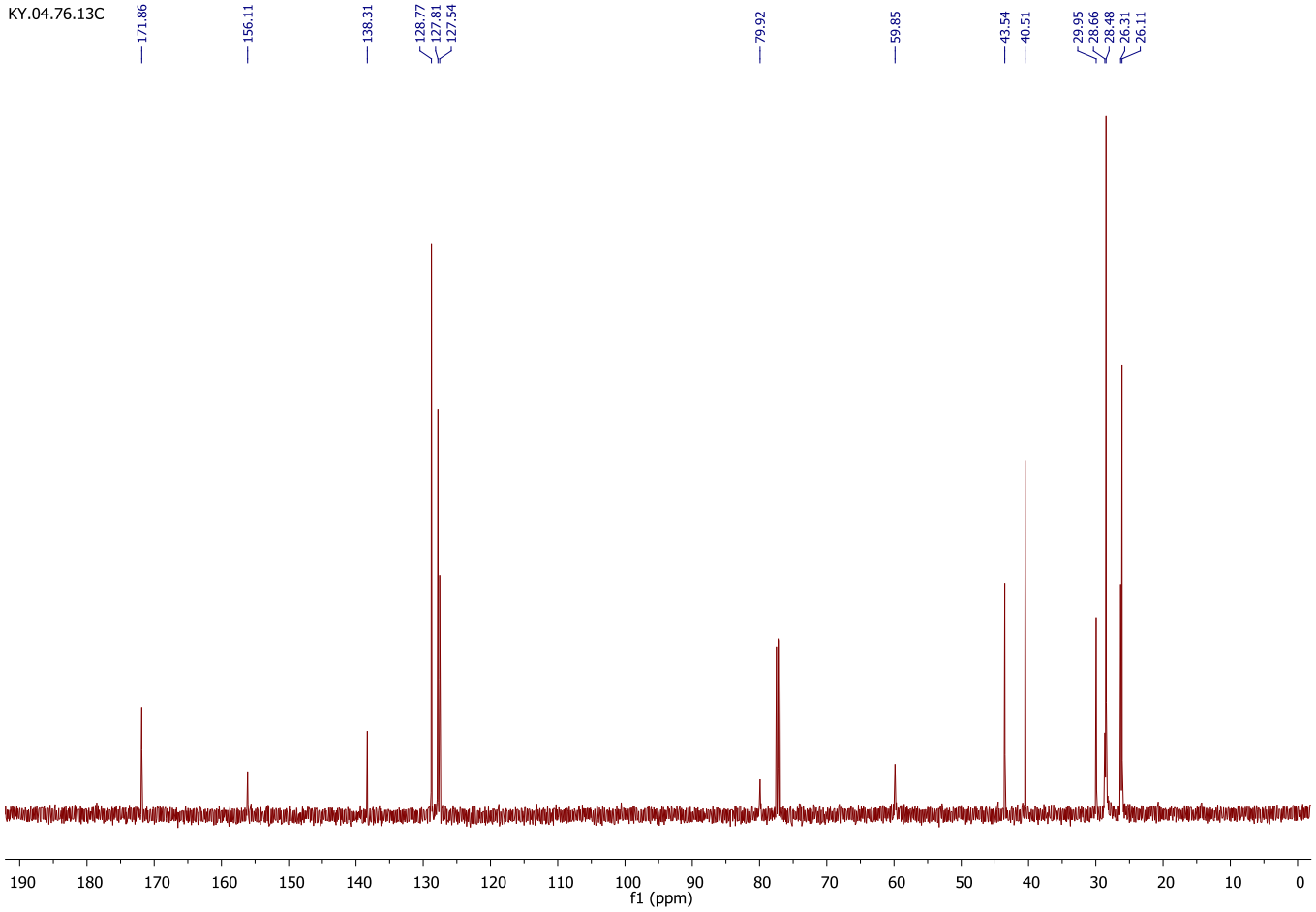
KY.04.99.phen.13C



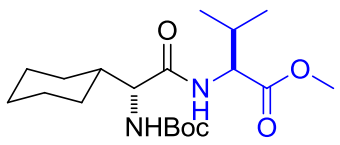
KY.04.76.1H



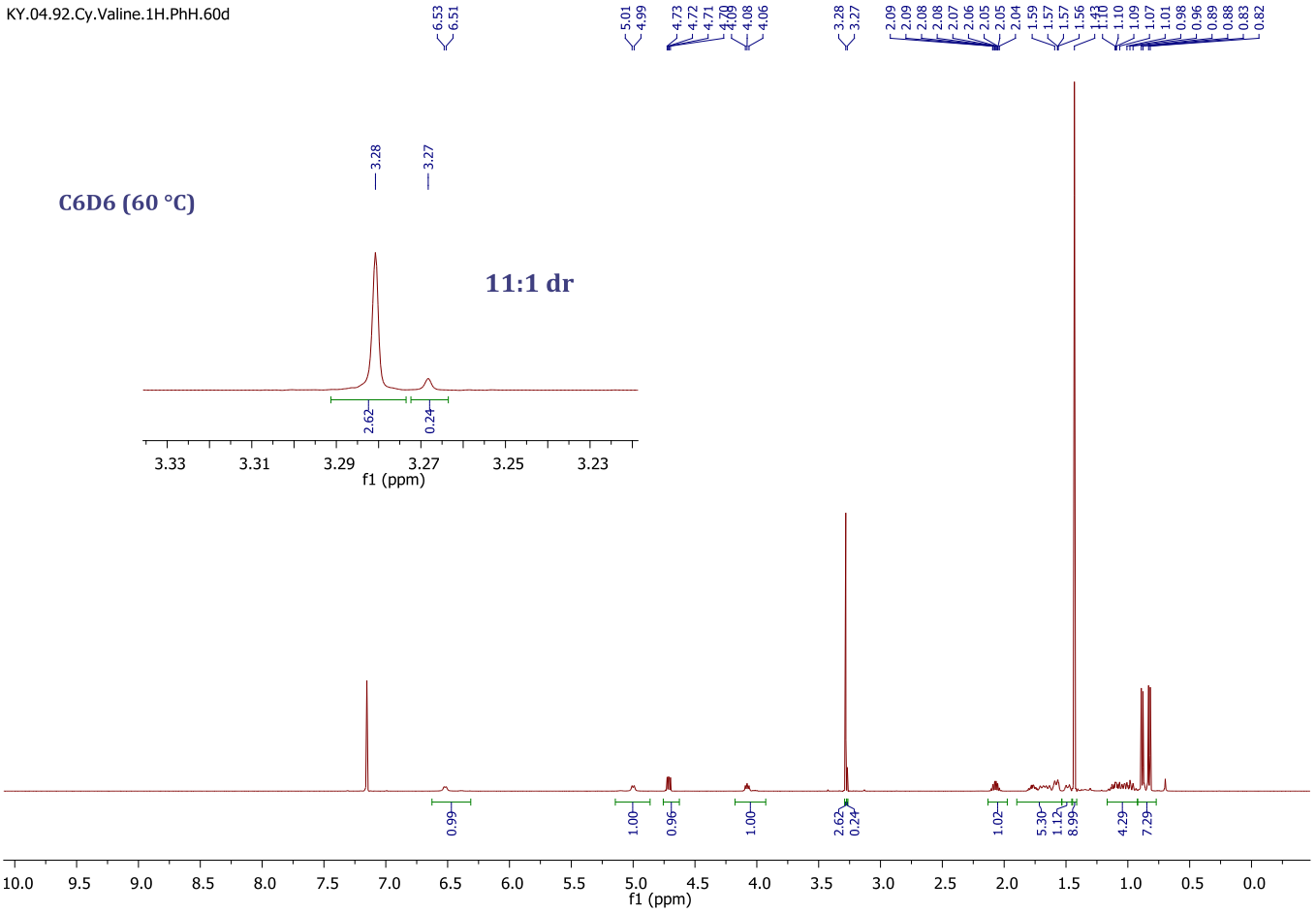
KY.04.76.13C



KY.04.92.Cy.Valine.1H

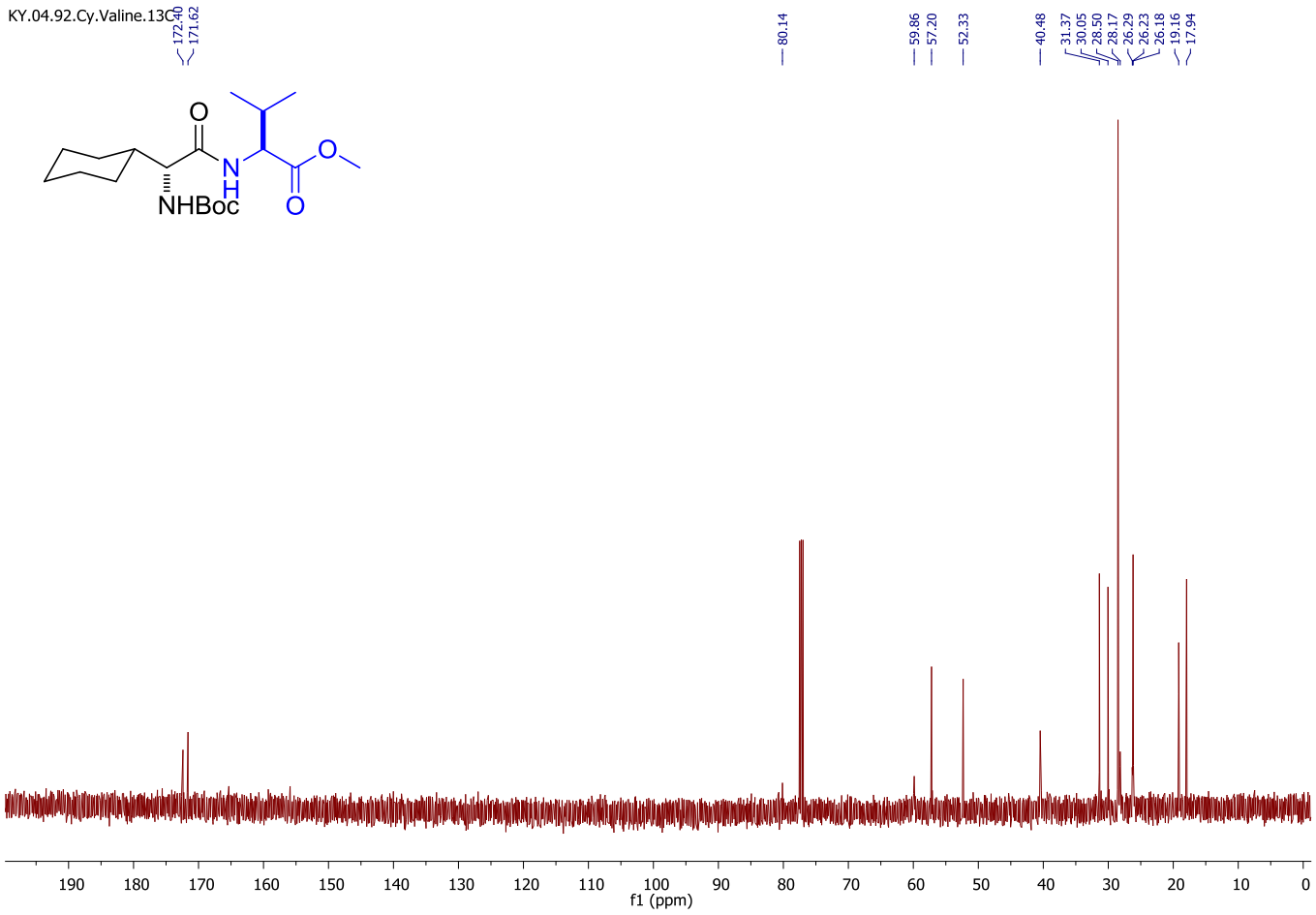


KY.04.92.Cy.Valine.1H.PhH.60d

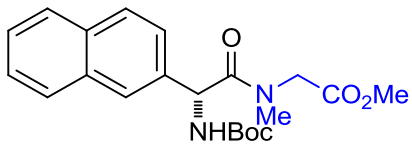


C6D6 (60 °C)

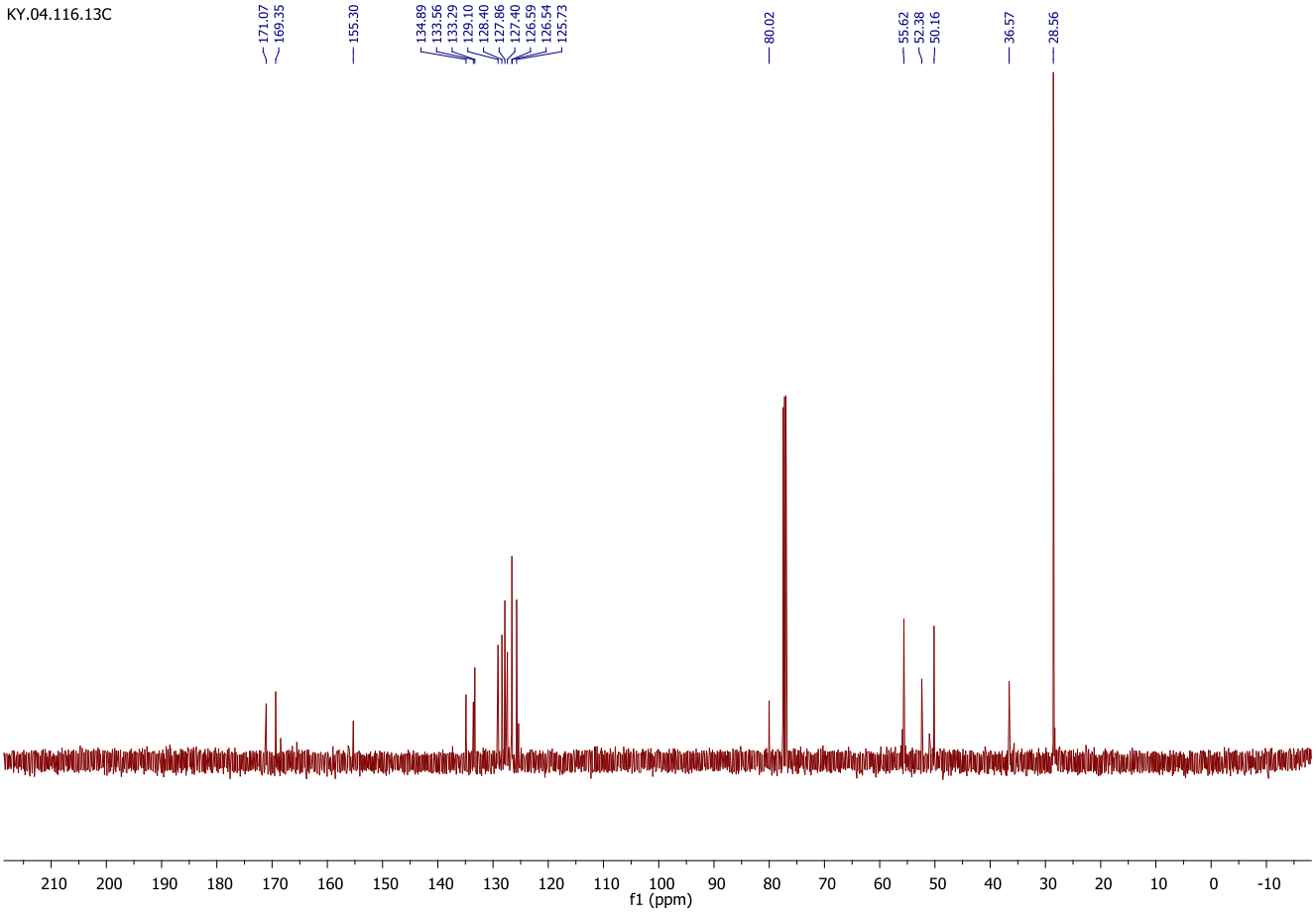
11:1 dr


KY.04.92.Cy.Valine.13C
172.40
171.62
80.14
59.86
57.20
52.33
40.48
31.37
30.05
28.50
28.17
26.29
26.23
26.18
19.16
17.94
O
N
H
O
O
NHBoc
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

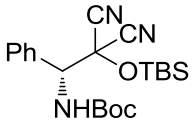
KY.04.116.1H

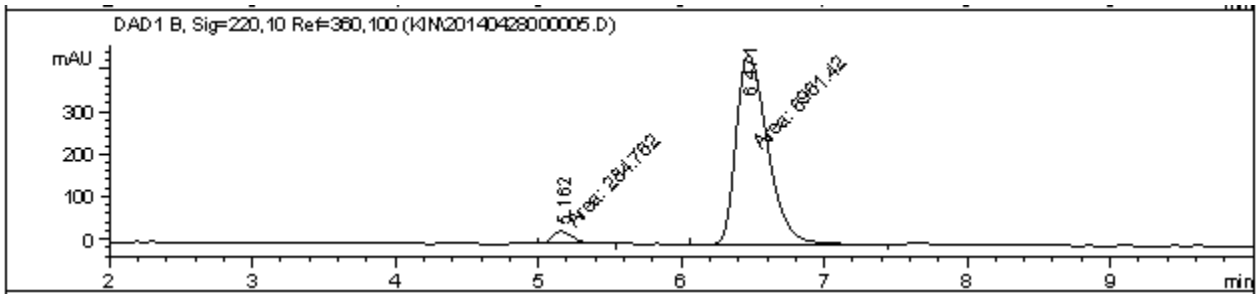


KY.04.116.13C



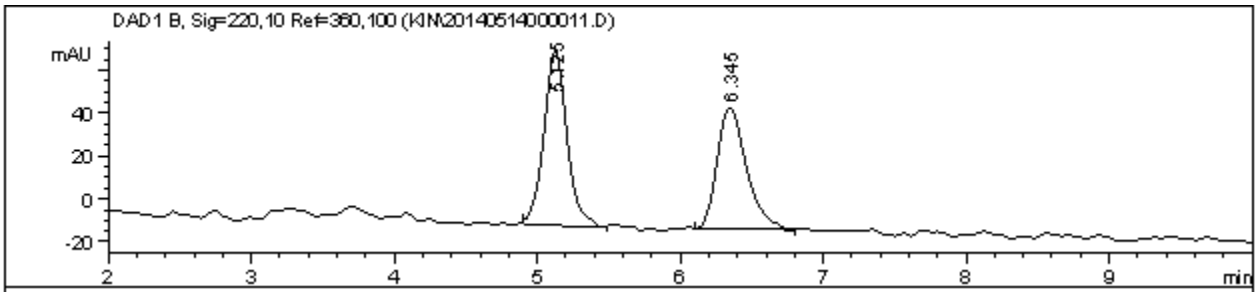
HPLC Traces of Racemic and Enantioenriched Compounds





Signal 2: DAD1 B, Sig=220,10 Ref=360,100

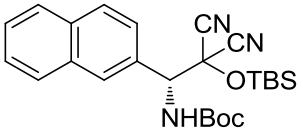
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.162	MM	0.1631	284.76154	29.10411	3.9298
2	6.471	MM	0.2587	6961.41895	448.50278	96.0702
Totals :				7246.18048	477.60689	

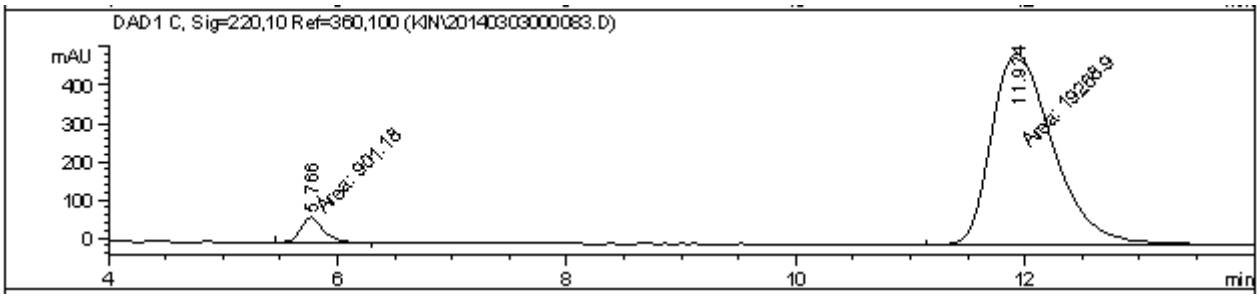


Signal 2: DAD1 B, Sig=220,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.125	BB	0.1708	917.36328	81.82123	53.0653
2	6.345	BB	0.2189	811.37970	56.72670	46.9347
Totals :				1728.74298	138.54792	

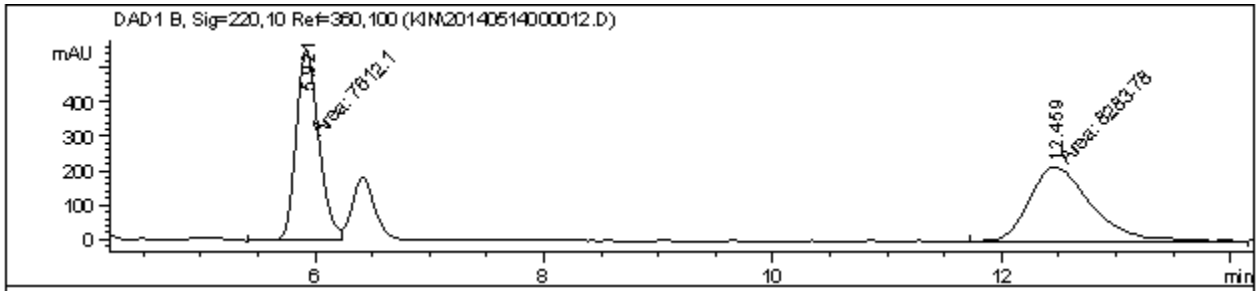
Enantiomeric ratio: 96:4
Rt_1 = 5.1 min, Rt_2 = 6.4 min
Chiracel OD-H, 1% IPA/Hexanes, 1 mL/min





Signal 3: DAD1 C, Sig=220,10 Ref=360,100

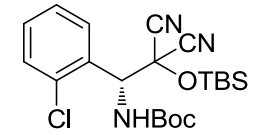
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.766	MM	0.2297	901.17969	65.39148	4.4679
2	11.924	MM	0.6373	1.92689e4	503.90161	95.5321
Totals :				2.01701e4	569.29309	

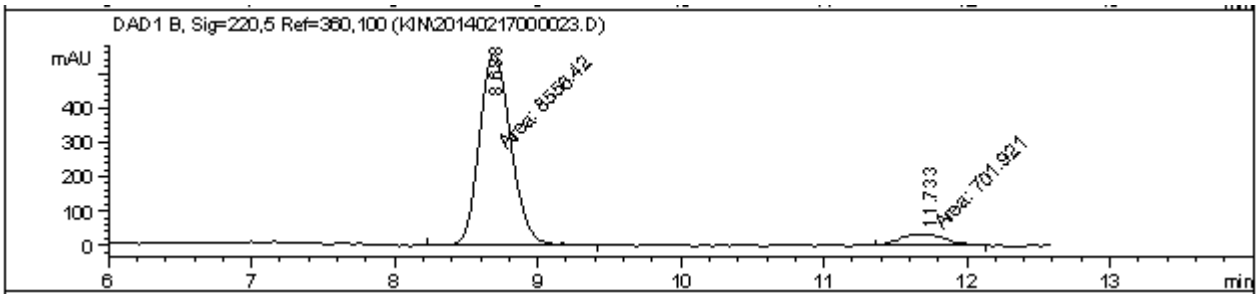


Signal 2: DAD1 B, Sig=220,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.921	MM	0.2292	7612.09521	553.58398	47.8872
2	12.459	MM	0.6338	8283.77930	217.82986	52.1128
Totals :				1.58959e4	771.41385	

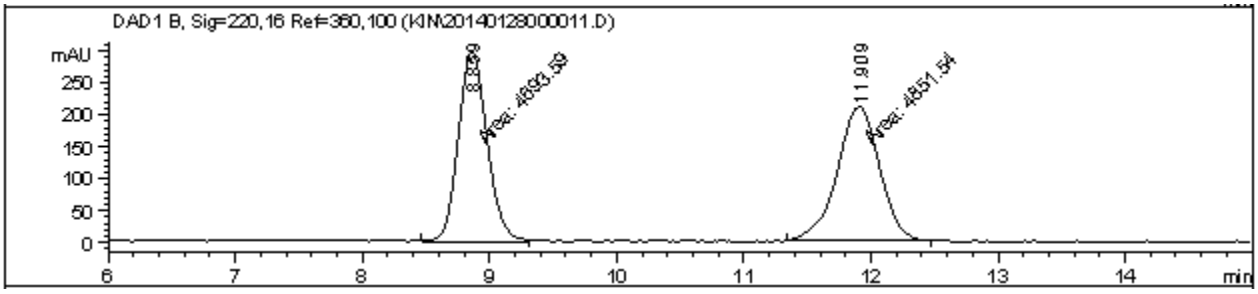
Enantiomeric ratio: 95.5:4.5,
Rt_1 = 5.7 min, Rt_2 = 11.9 min
Chiracel OD-H, 1% IPA/Hexanes, 1 mL/min





Signal 2: DAD1 B, Sig=220,5 Ref=360,100

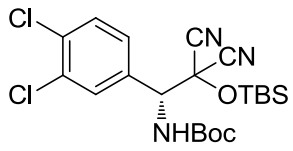
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.688	MM	0.2573	8556.41797	554.25000	92.4185
2	11.733	MM	0.3486	701.92084	33.56302	7.5815
Totals :				9258.33881	587.81302	

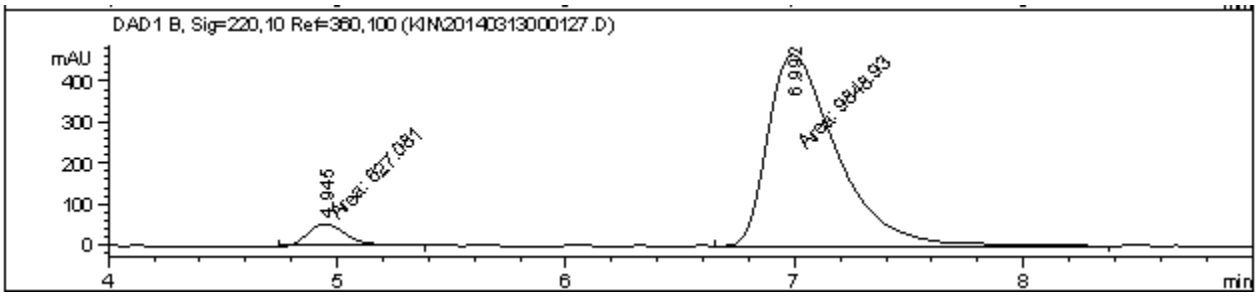


Signal 2: DAD1 B, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.859	MM	0.2625	4693.59229	298.00638	49.1726
2	11.909	MM	0.3865	4851.54395	209.18297	50.8274
Totals :				9545.13623	507.18935	

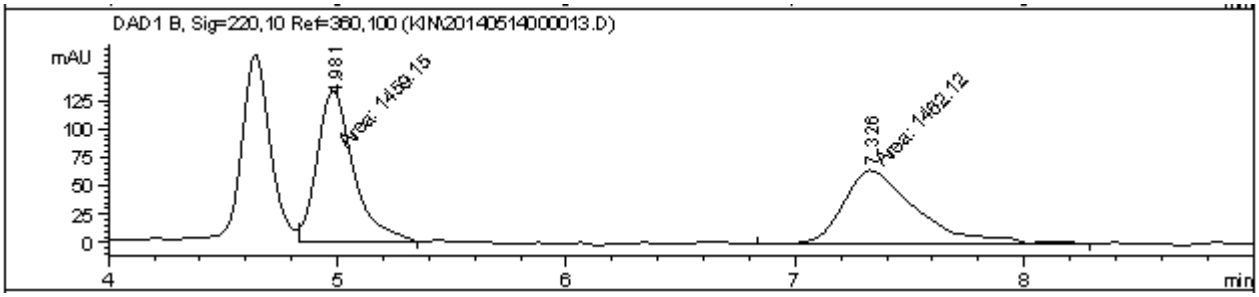
Enantiomeric ratio: 92.5:7.5
Rt_1 = 8.7 min, Rt_2 = 11.7 min
Chiracel AD-H, 2% IPA/Hexanes, 1 mL/min





Signal 3: DAD1 C, Sig=225,10 Ref=360,100

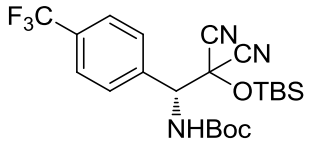
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.947	MM	0.1961	629.87152	53.53183	6.0194
2	6.992	MM	0.3446	9834.17578	475.57086	93.9806
Totals :				1.04640e4	529.10269	

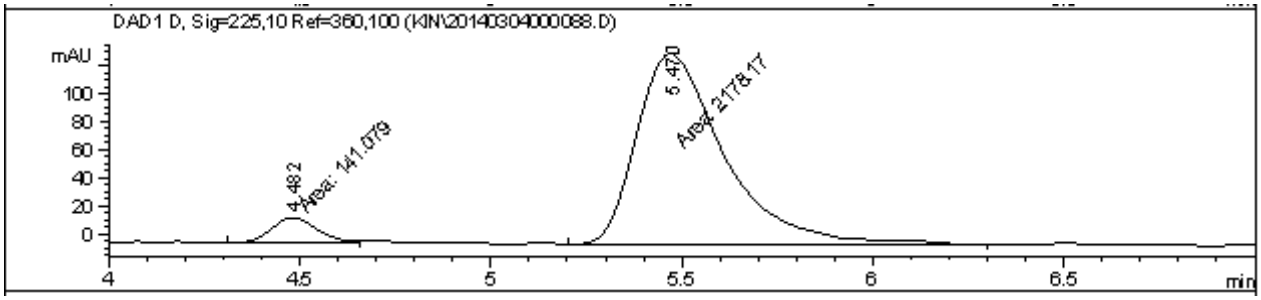


Signal 2: DAD1 B, Sig=220,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.981	MM	0.1824	1459.14526	133.31259	49.9491
2	7.326	MM	0.3740	1462.11633	65.15425	50.0509
Totals :				2921.26160	198.46684	

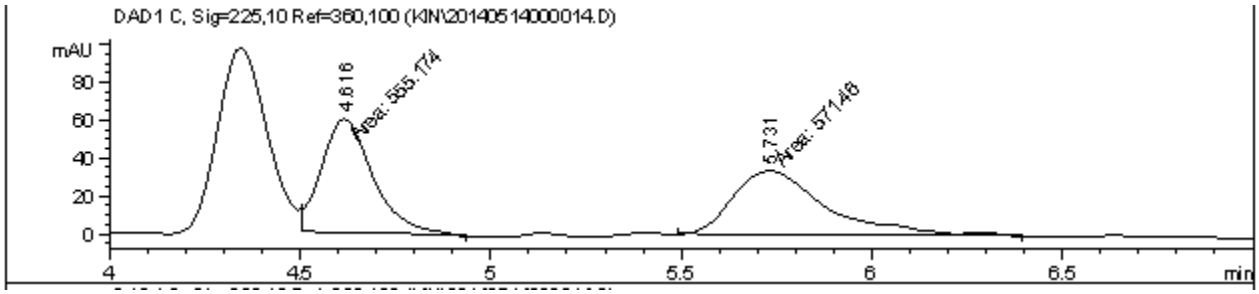
Enantiomeric ratio: 94:6
Rt_1 = 5.0 min, Rt_2 = 7.0 min
Chiracel OD-H, 1% IPA/Hexanes, 1 mL/min





Signal 4: DAD1 D, Sig=225,10 Ref=360,100

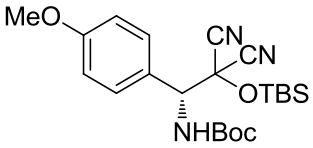
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.482	MM	0.1336	141.07899	17.59560	6.0830
2	5.470	MM	0.2662	2178.17212	136.39267	93.9170
Totals :				2319.25111	153.98827	

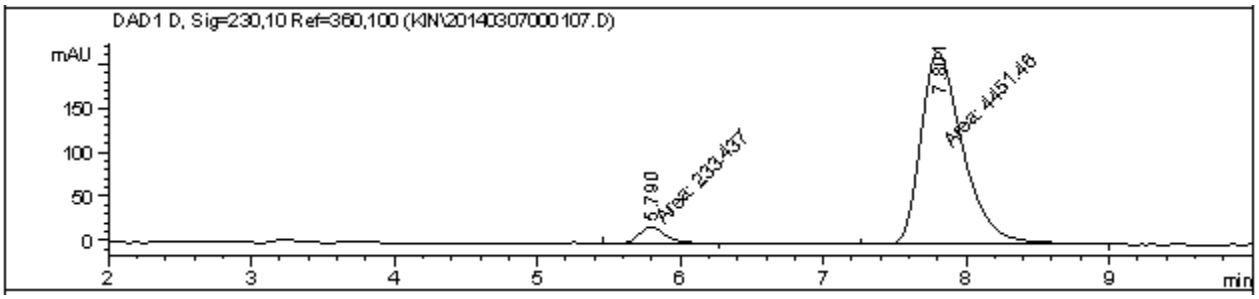


Signal 3: DAD1 C, Sig=225,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.616	MM	0.1534	555.17401	60.33183	49.2772
2	5.731	MM	0.2835	571.46014	33.59464	50.7228
Totals :				1126.63416	93.92646	

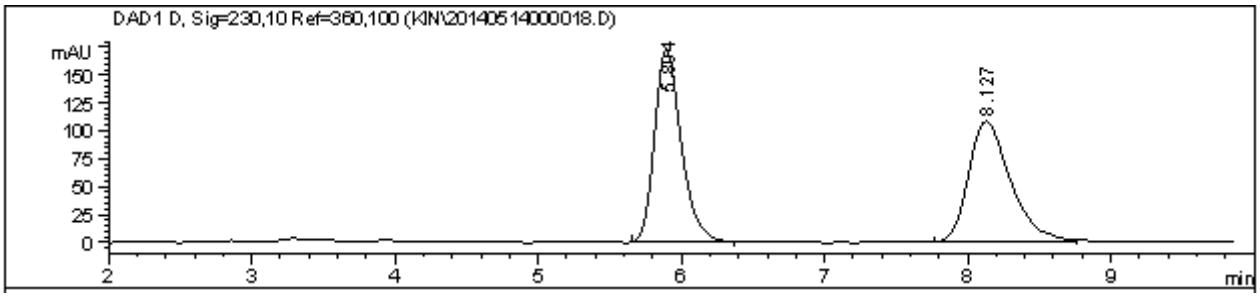
Enantiomeric ratio: 94:6
Rt_1 = 4.5, Rt_2 = 5.5
Chiracel OD-H, 1% IPA/Hexanes, 1 mL/min





Signal 4: DAD1 D, Sig=230,10 Ref=360,100

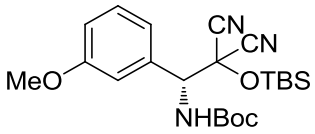
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.790	MM	0.2133	233.43719	18.24405	4.9828
2	7.801	MM	0.3407	4451.45947	217.73611	95.0172
Totals :				4684.89667	235.98016	

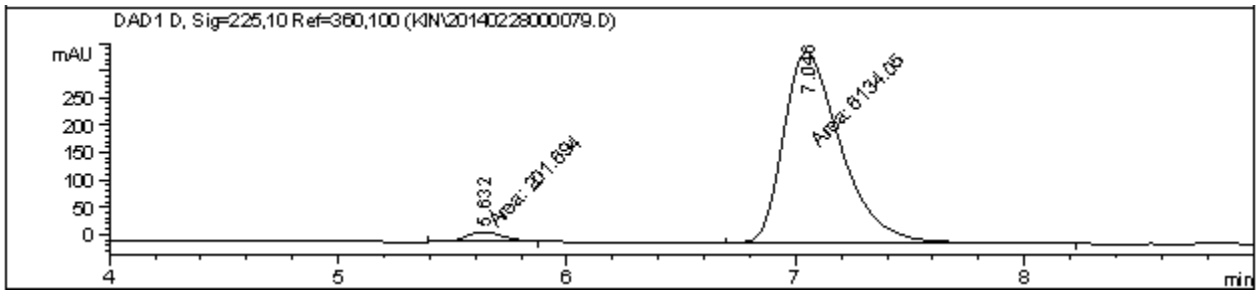


Signal 4: DAD1 D, Sig=230,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.894	BB	0.1991	2227.16089	171.96913	50.0732
2	8.127	BB	0.3114	2220.64575	108.21827	49.9268
Totals :				4447.80664	280.18740	

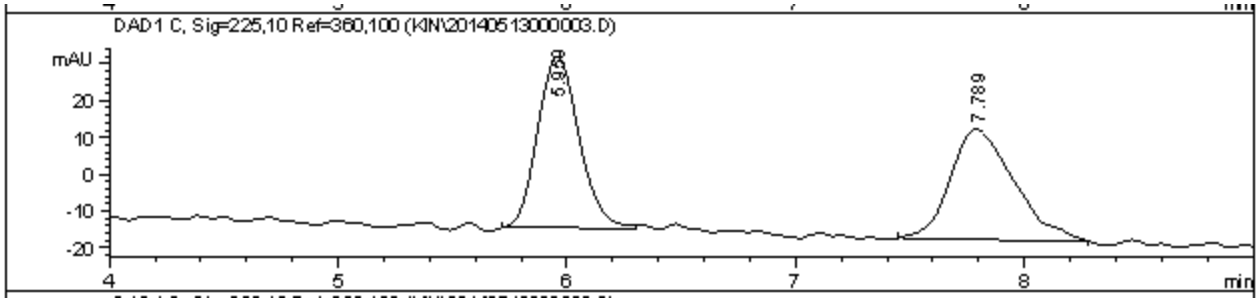
Enantiomeric ratio: 95:5
Rt_1 = 5.8, Rt_2 = 7.8
Chiracel OD-H, 1% IPA/Hexanes, 1 mL/min





Signal 4: DAD1 D, Sig=225,10 Ref=360,100

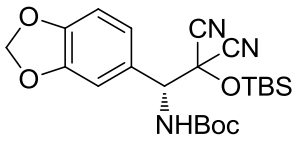
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.632	MM	0.1894	201.69406	17.74987	3.1834
2	7.046	MM	0.2917	6134.05225	350.48969	96.8166
Totals :				6335.74631	368.23956	

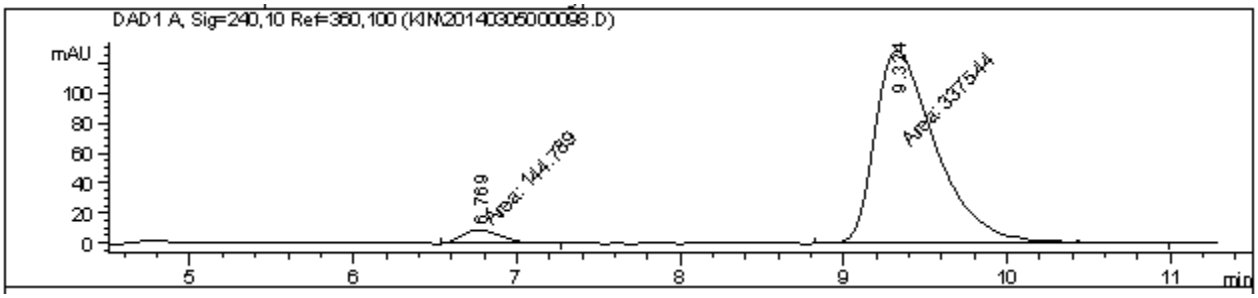


Signal 3: DAD1 C, Sig=225,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.959	BB	0.1948	586.71973	46.61628	50.1872
2	7.789	BB	0.2851	582.34247	30.18557	49.8128
Totals :				1169.06219	76.80185	

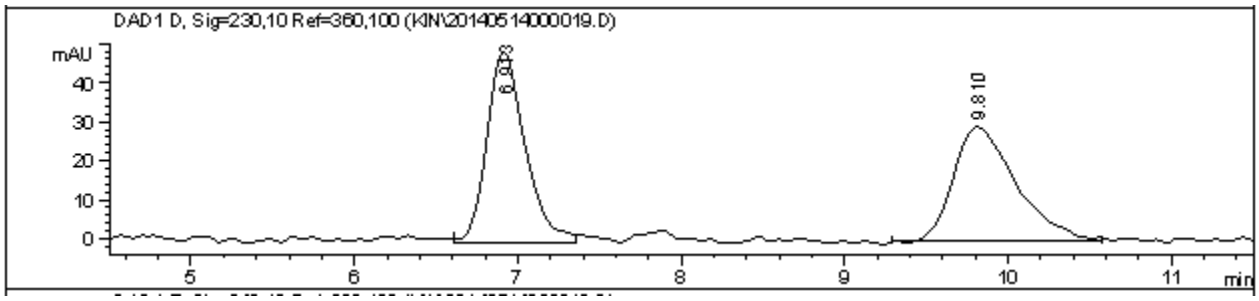
Enantiomeric ratio: 97:3
Rt_1 = 5.6, Rt_2 = 7.0
Chiracel OD-H, 1% IPA/Hexanes, 1 mL/min





Signal 1: DAD1 A, Sig=240,10 Ref=360,100

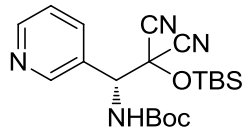
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.769	MM	0.2672	144.78928	9.03069	4.1131
2	9.324	MM	0.4378	3375.43799	128.48534	95.8869
Totals :				3520.22726	137.51602	

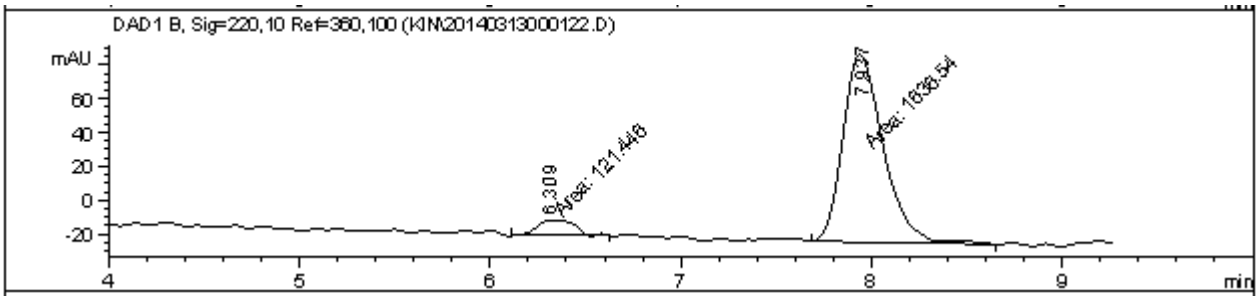


Signal 4: DAD1 D, Sig=230,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.913	BB	0.2498	793.47815	48.76608	50.2971
2	9.810	BB	0.3831	784.10358	29.40558	49.7029
Totals :				1577.58173	78.17166	

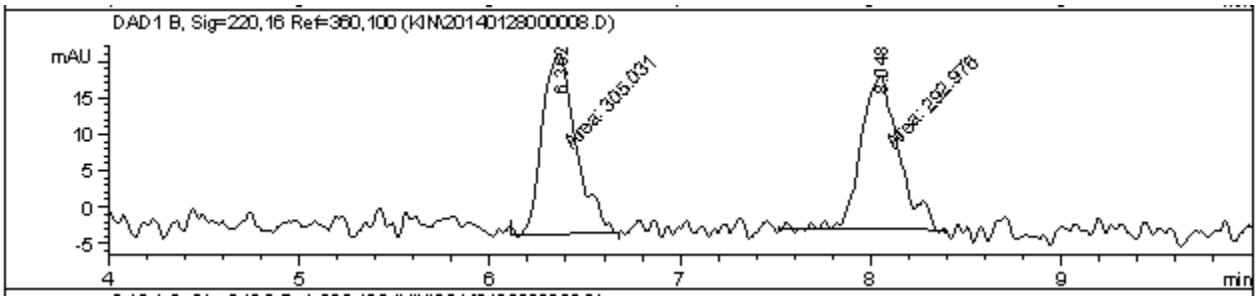
Enantiomeric ratio: 96:4
Rt_1 = 6.7, Rt_2 = 9.3
Chiracel OD-H, 1% IPA/Hexanes, 1 mL/min





Signal 2: DAD1 B, Sig=220,10 Ref=360,100

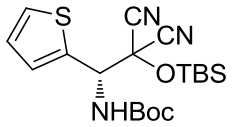
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.309	MM	0.2269	121.44621	8.92063	6.9083
2	7.937	MM	0.2452	1636.53870	111.22278	93.0917
Totals :				1757.98490	120.14341	

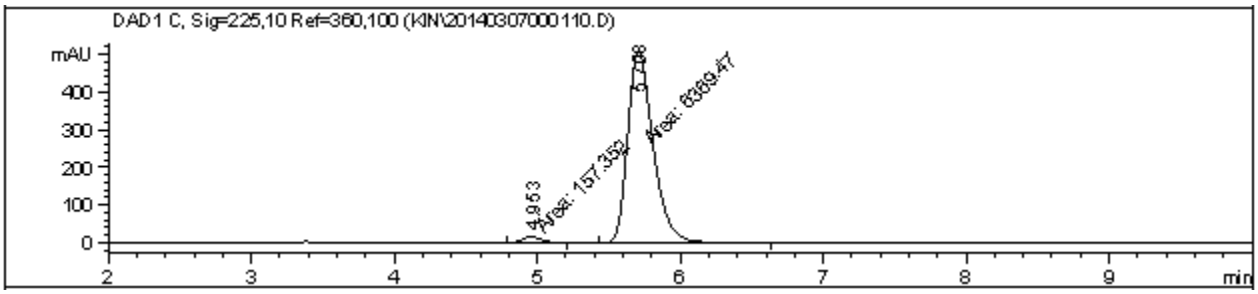


Signal 2: DAD1 B, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.362	MM	0.2057	305.03070	24.71835	51.0079
2	8.048	MM	0.2298	292.97632	21.25029	48.9921
Totals :				598.00702	45.96865	

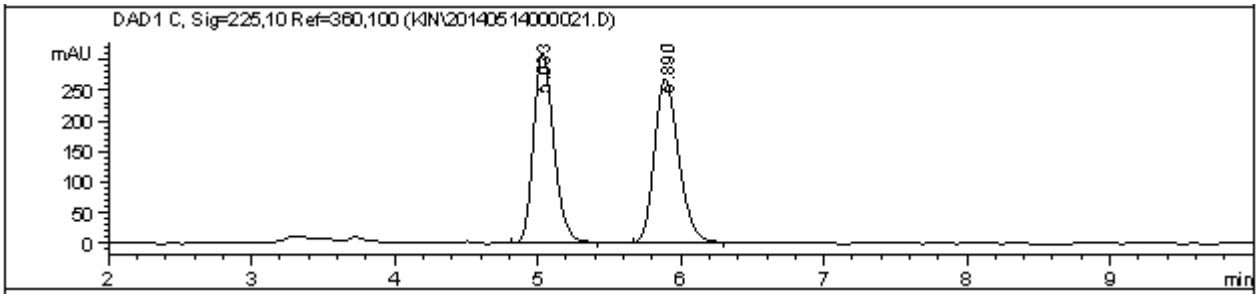
Enantiomeric ratio: 93:7
Rt_1 = 6.3, Rt_2 = 8.0
Chiracel AD-H, 8% IPA/Hexanes, 1 mL/min





Signal 3: DAD1 C, Sig=225,10 Ref=360,100

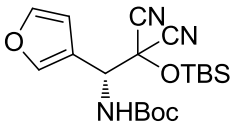
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.953	MM	0.1535	157.35161	17.08101	2.4108
2	5.708	MM	0.2075	6369.47266	511.51535	97.5892
Totals :				6526.82426	528.59636	

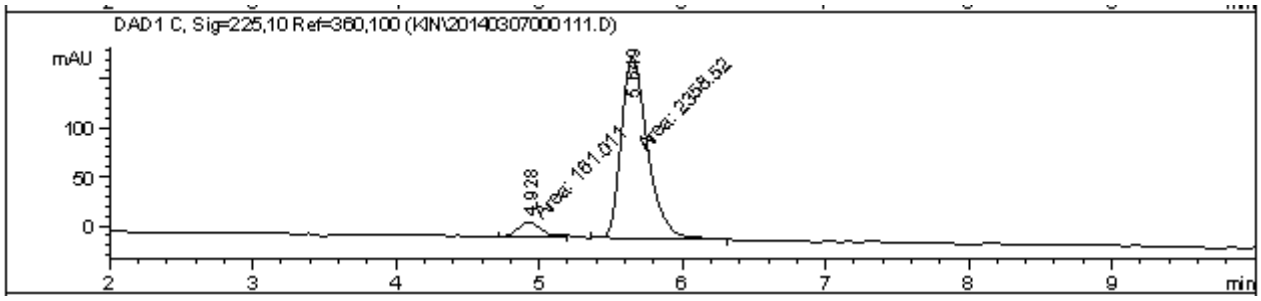


Signal 3: DAD1 C, Sig=225,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.033	BB	0.1506	3091.17236	314.55560	49.3359
2	5.890	BB	0.1816	3174.39160	269.19434	50.6641
Totals :				6265.56396	583.74994	

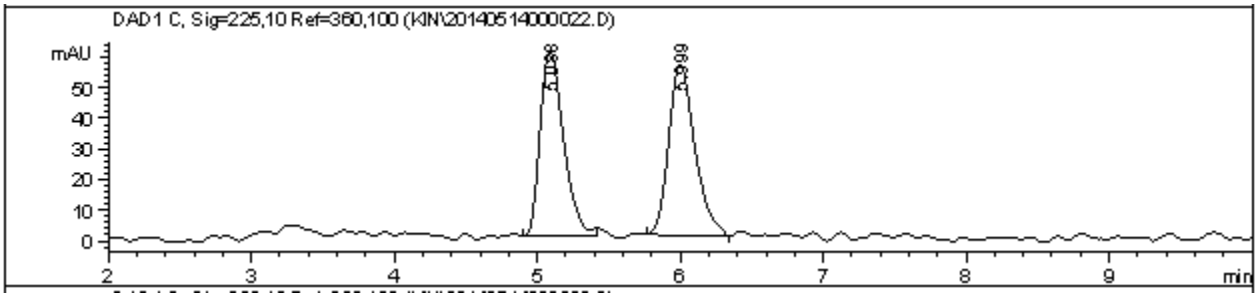
Enantiomeric ratio: 97.5:2.5
Rt_1 = 5.0, Rt_2 = 5.7
Chiracel AD-H, 8% IPA/Hexanes, 1 mL/min





Signal 3: DAD1 C, Sig=225,10 Ref=360,100

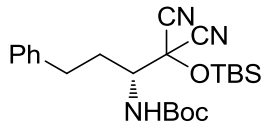
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.928	MM	0.1913	161.01129	14.02466	6.3905
2	5.649	MM	0.2114	2358.51953	185.94507	93.6095
Totals :				2519.53082	199.96972	

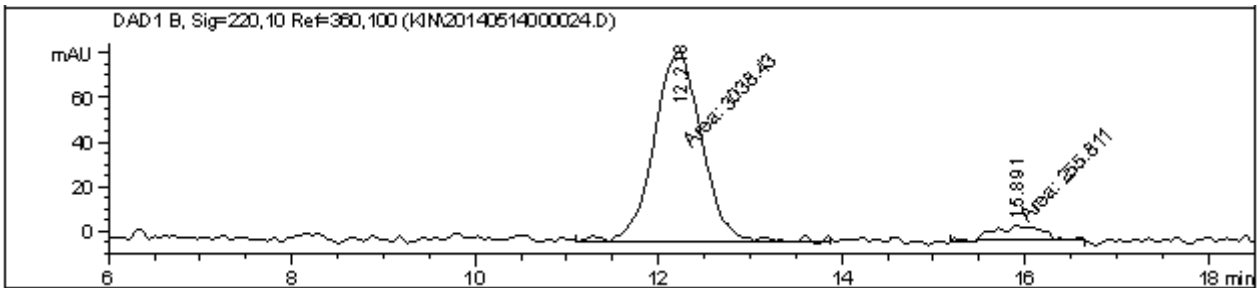


Signal 3: DAD1 C, Sig=225,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.088	BB	0.1730	694.02582	60.85961	49.3408
2	5.999	BV	0.1932	712.57019	55.72057	50.6592
Totals :				1406.59601	116.58018	

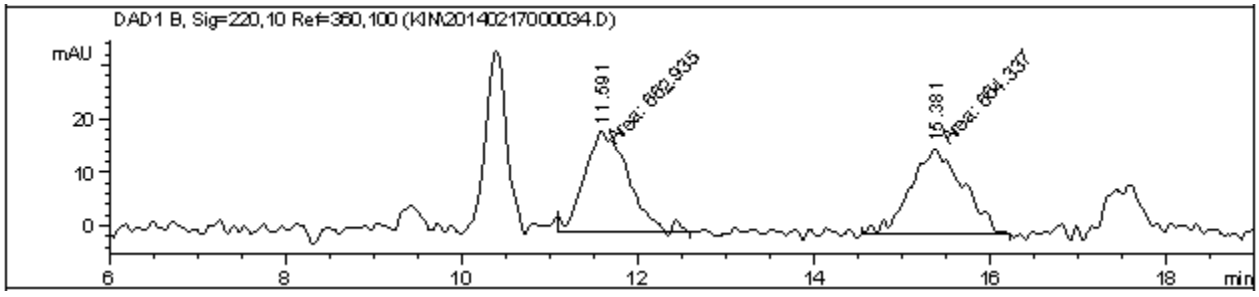
Enantiomeric ratio: 93.5:6.5
Rt_1 = 5.0, Rt_2 = 5.7
Chiracel OD-H, 1% IPA/Hexanes, 1 mL/min





Signal 2: DAD1 B, Sig=220,10 Ref=360,100

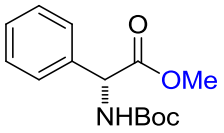
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.218	MM	0.5991	3038.42822	84.52692	92.2346
2	15.891	MM	0.6072	255.81119	7.02142	7.7654
Totals :				3294.23941	91.54834	

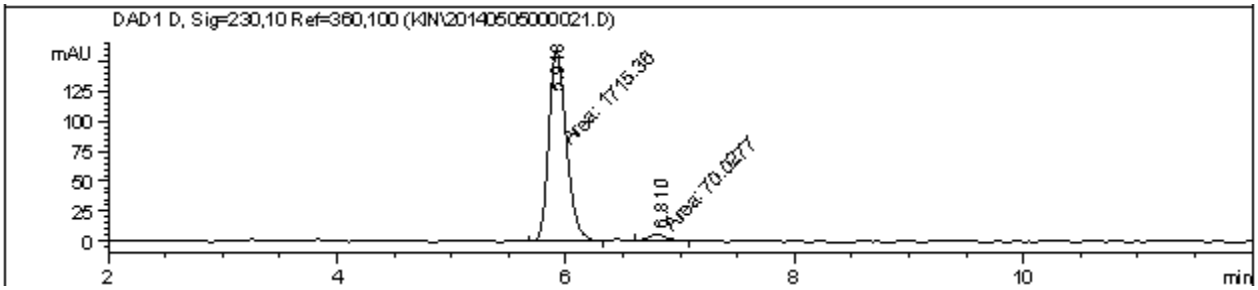


Signal 2: DAD1 B, Sig=220,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.591	MM	0.5781	662.93451	19.11344	49.9472
2	15.381	MM	0.6895	664.33679	16.05953	50.0528
Totals :				1327.27130	35.17297	

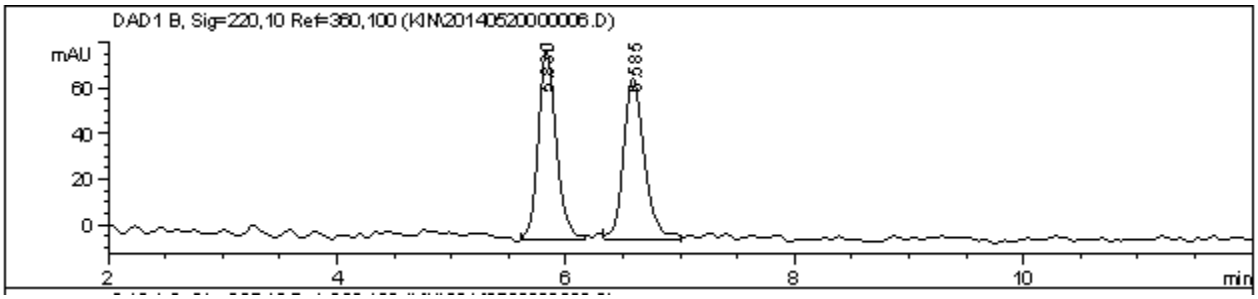
Enantiomeric ratio: 92:8,
Rt_1 = 12.2, Rt_2 = 15.9
Chiracel AD-H, 1% IPA/Hexanes, 1 mL/min





Signal 4: DAD1 D, Sig=230,10 Ref=360,100

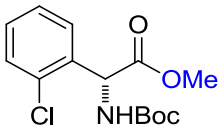
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.918	MM	0.1782	1715.36487	160.45755	96.0777
2	6.810	MM	0.1977	70.02773	5.90485	3.9223
Totals :				1785.39260	166.36240	

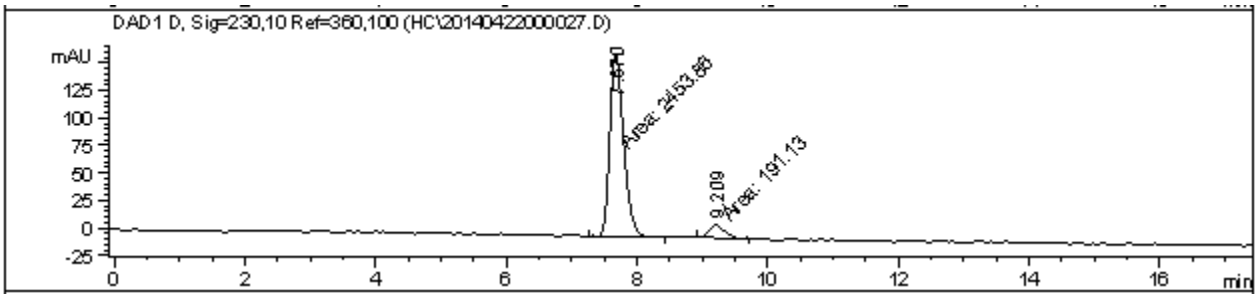


Signal 2: DAD1 B, Sig=220,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.830	BB	0.1677	909.79297	83.08879	50.0507
2	6.585	BB	0.1975	907.94800	70.83281	49.9493
Totals :				1817.74097	153.92160	

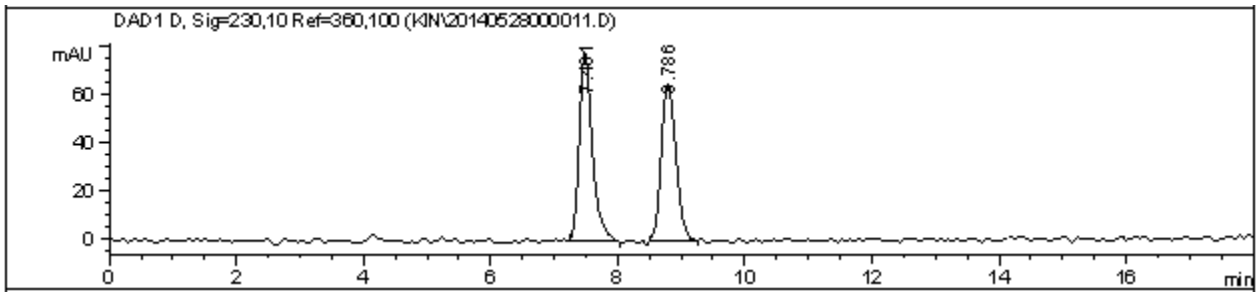
Enantiomeric ratio: 96:4
Rt_1 = 5.9, Rt_2 = 6.8
Chiracel OD-H, 4% IPA/Hexanes, 1 mL/min





Signal 4: DAD1 D, Sig=230,10 Ref=360,100

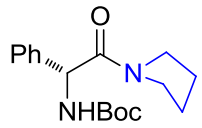
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.670	MM	0.2459	2453.85718	166.30014	92.7739
2	9.209	MM	0.2748	191.13040	11.59078	7.2261
Totals :				2644.98758	177.89092	

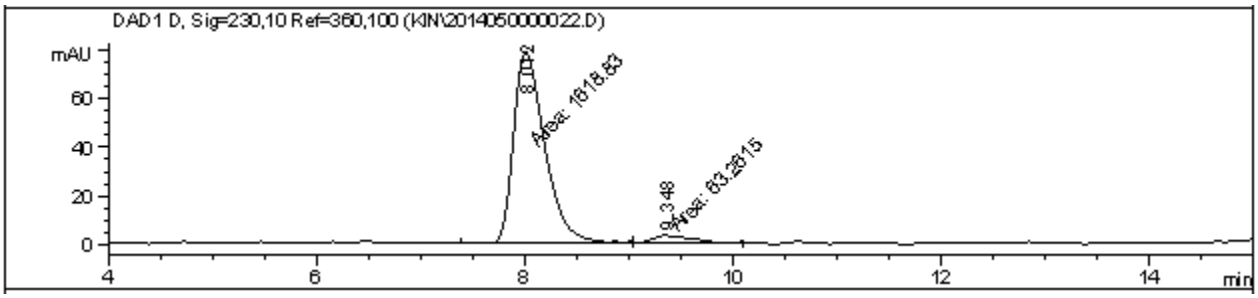


Signal 4: DAD1 D, Sig=230,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.481	BB	0.2148	1126.63782	78.78534	51.4616
2	8.786	BB	0.2620	1062.64001	65.23598	48.5384
Totals :				2189.27783	144.02132	

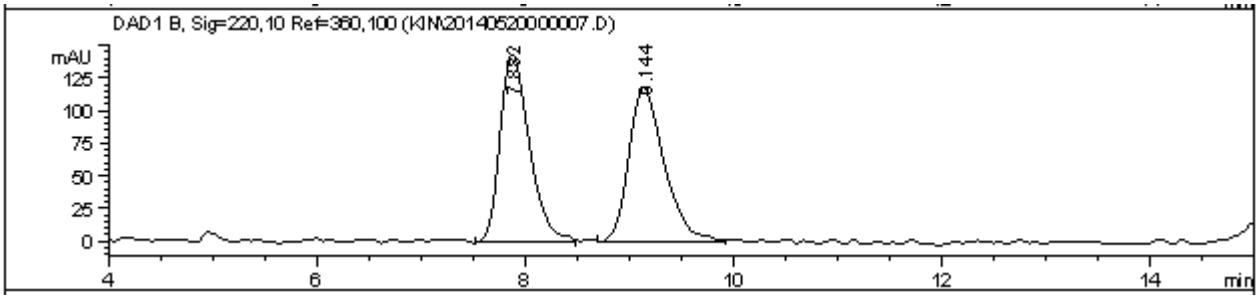
Enantiomeric ratio: 92.5:7.5
Rt_1 = 7.7, Rt_2 = 9.2
Chiracel OD-H, 3% IPA/Hexanes, 1 mL/min





Signal 2: DAD1 B, Sig=220,10 Ref=360,100

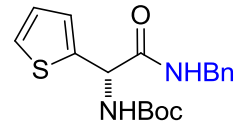
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.012	MM	0.3476	5512.33447	264.30740	96.0273
2	9.405	MM	0.3896	228.04552	9.75634	3.9727
Totals :				5740.37999	274.06374	

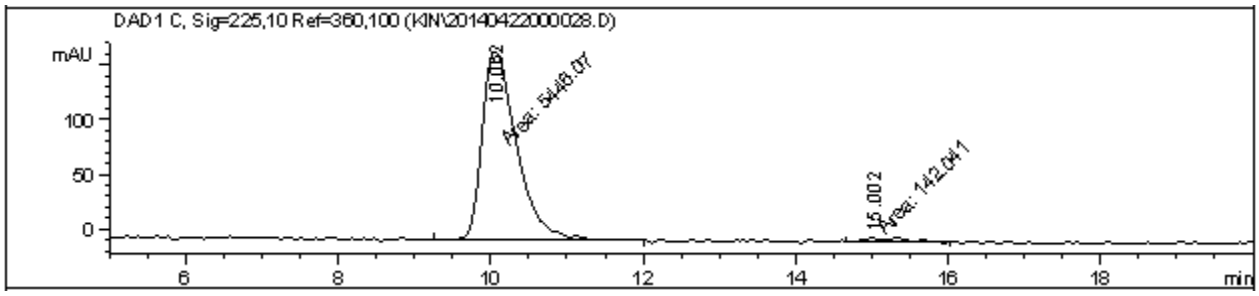


Signal 2: DAD1 B, Sig=220,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.882	BB	0.3053	2846.78418	144.86963	50.3484
2	9.144	BB	0.3642	2807.38599	118.58601	49.6516
Totals :				5654.17017	263.45564	

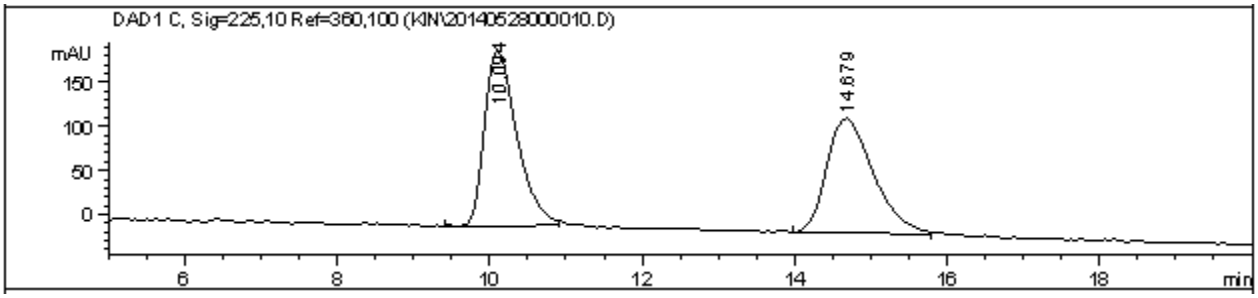
Enantiomeric ratio: 96:4
Rt_1 = 8.0, Rt_2 = 9.4
Chiracel OD-H, 6% IPA/Hexanes, 1 mL/min





Signal 3: DAD1 C, Sig=225,10 Ref=360,100

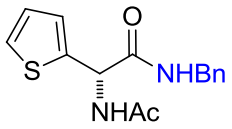
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.062	MM	0.5273	5446.06641	172.13522	97.4582
2	15.002	MM	0.5967	142.04095	3.96758	2.5418
Totals :				5588.10736	176.10280	

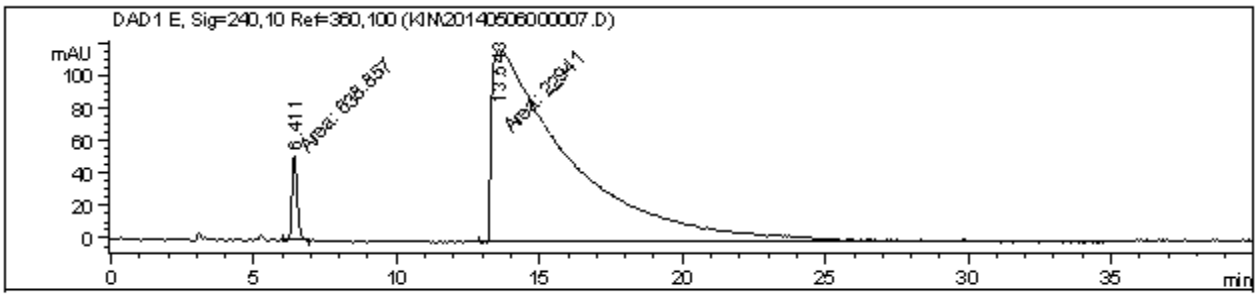


Signal 3: DAD1 C, Sig=225,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.094	BB	0.4471	5882.38477	197.73755	51.5364
2	14.679	BB	0.5860	5531.64795	129.58434	48.4636
Totals :				1.14140e4	327.32188	

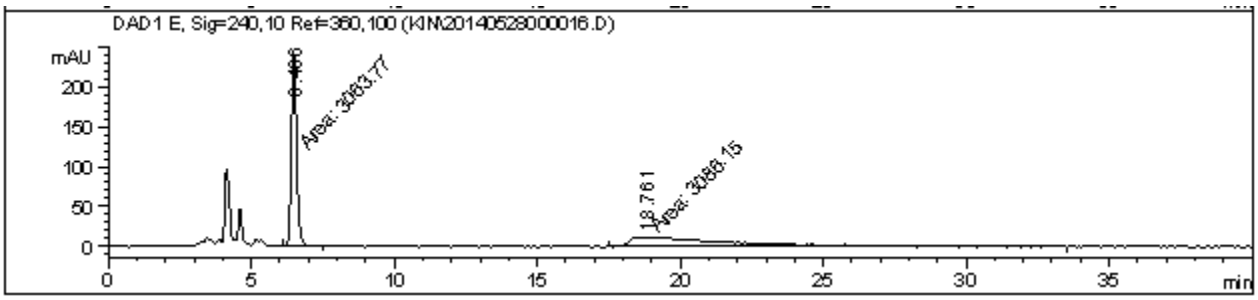
Enantiomeric ratio: 97.5:2.5
Rt_1 = 10.0, Rt_2 = 15.0
Chiracel OD-H, 5% IPA/Hexanes, 1 mL/min





Signal 5: DAD1 E, Sig=240,10 Ref=360,100

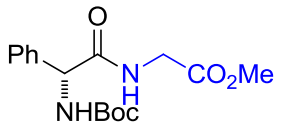
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.411	MM	0.2057	638.85657	51.75616	2.7093
2	13.543	MM	3.2340	2.29410e4	118.22781	97.2907

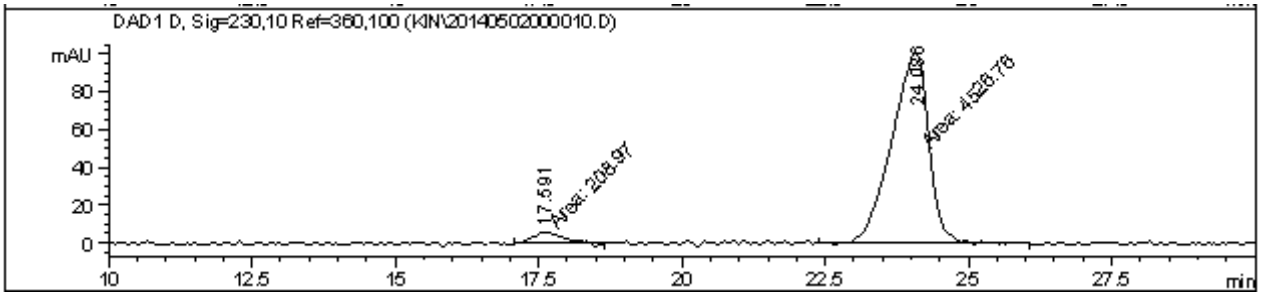


Signal 5: DAD1 E, Sig=240,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.486	MM	0.2129	3063.77368	239.85925	49.8181
2	18.761	MM	4.1374	3086.14917	12.43204	50.1819
Totals :				6149.92285	252.29129	

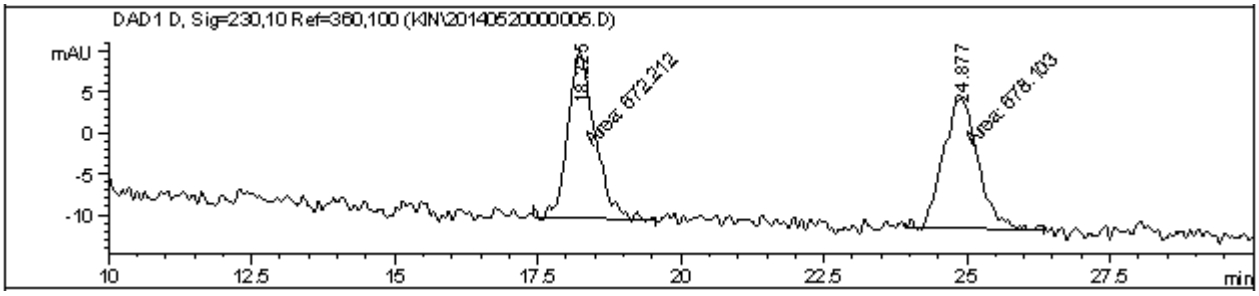
Enantiomeric ratio: 97.5:2.5
Rt_1 = 6.4, Rt_2 = 13.5
Chiracel AD-H, 25% IPA/Hexanes, 1 mL/min





Signal 2: DAD1 B, Sig=220,10 Ref=360,100

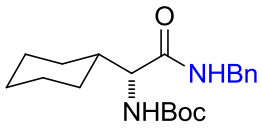
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.602	MM	0.5122	499.01599	16.23784	4.0211
2	24.079	MM	0.7649	1.19110e4	259.52893	95.9789
Totals :				1.24100e4	275.76677	

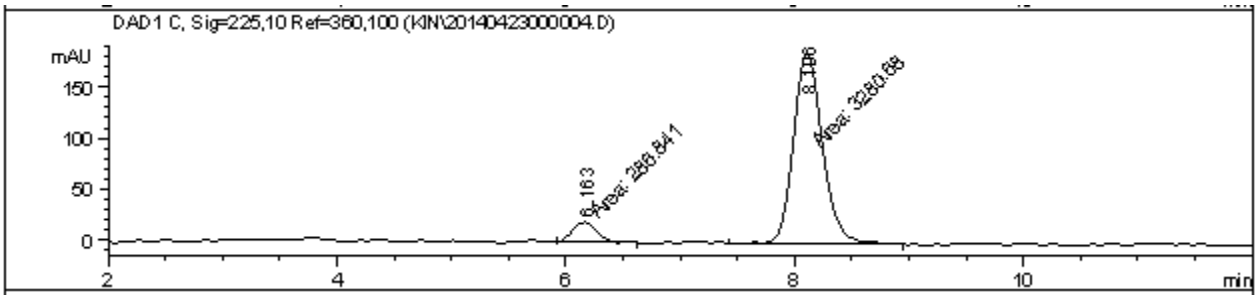


Signal 4: DAD1 D, Sig=230,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.225	MM	0.5480	672.21161	20.44411	49.7819
2	24.877	MM	0.7104	678.10254	15.90893	50.2181
Totals :				1350.31415	36.35304	

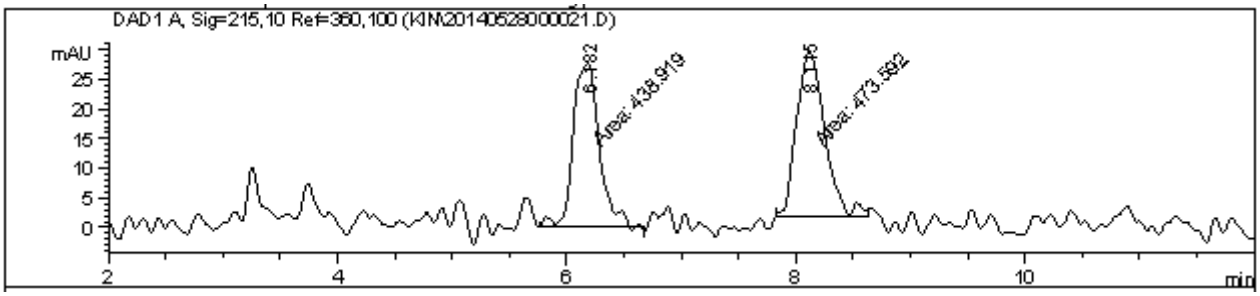
Enantiomeric ratio: 96:4
Rt_1 = 17.6, Rt_2 = 24.0
Chiracel AD-H, 10% IPA/Hexanes, 1 mL/min





Signal 3: DAD1 C, Sig=225,10 Ref=360,100

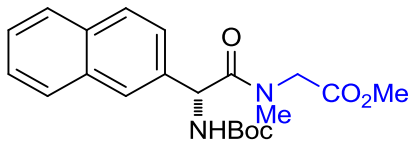
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.163	MM	0.2452	286.84122	19.49683	8.0404
2	8.106	MM	0.2941	3280.67505	185.92407	91.9596
Totals :				3567.51627	205.42090	

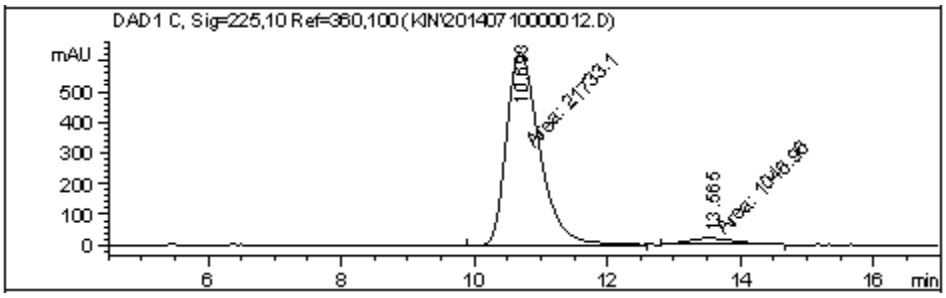


Signal 1: DAD1 A, Sig=215,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.182	MM	0.2653	438.91867	27.57840	48.1001
2	8.115	MM	0.2827	473.59158	27.91964	51.8999
Totals :				912.51025	55.49803	

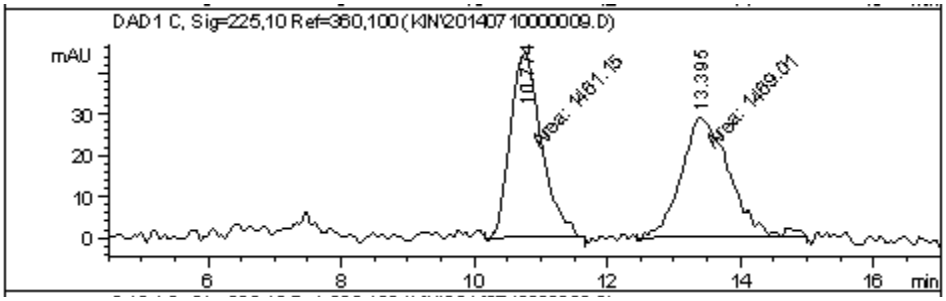
Enantiomeric ratio: 92:8
Rt_1 = 6.1, Rt_2 = 8.1
Chiracel AD-H, 10% IPA/Hexanes, 1 mL/min





Signal 3: DAD1 C, Sig=225,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.693	MM	0.5740	2.17331e4	631.06171	95.4041
2	13.565	MM	0.7872	1046.95850	22.16533	4.5959
Totals :				2.27800e4	653.22704	



Signal 3: DAD1 C, Sig=225,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.774	MM	0.5428	1461.14636	44.86652	49.8657
2	13.395	MM	0.8402	1469.01428	29.13858	50.1343
Totals :				2930.16064	74.00510	

Enantiomeric ratio: 95.5:4.5
Rt_1 = 10.7, Rt_2 = 13.5
Chiracel OD-H, 10% IPA/Hexanes, 1 mL/min