Squaramide-Catalyzed Enantioselective Michael Addition of Masked Acyl Cyanides to Substituted Enones

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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, geranyl bromide, sulfur trioxide pyridine complex, (R) camphorsulfonic acid, tetrabutylammonium fluoride in THF (1M), Hydrogen fluoride triethylamine complex, boron trifluoride etherate, and trimethylsilyl triflate were purchased from Aldrich. Phosphorus pentoxide and acetic acid were purchased from Fisher. All commercially obtained reagents were used as received. Ambient temperature refers to 22–26 °C. Lower temperatures were maintained using ice (0 °C), a Thermo NEXLAB Cryotrol (−40 to 23 °C), iPrOH/ 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 ^{13}C 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 (acetone at 2.05 ppm, DMSO at 2.50 ppm) unless otherwise stated. C^{13} NMR spectra were calibrated to residual solvent signals at ($CHCl_3$ at 77.23 ppm, acetone at 29.84 ppm, DMSO at 39.52 ppm) Data for ^{1}H 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. LRMS were recorded on Waters 3100 Mass Detector using electrospray ionization (ESI). High-resolution mass spectra were recorded at Old Dominion University, VA, on a Bruker 12 Tesla APEX Qe FTICR mass spectrometer or an Agilent 6224 Tof-MS (with a Mixed [MM] ionization mode). Optical rotations were measured on a Perkin Elmer 141 polarimeter using a 100 mm path-length cell.

Aryl-Alkyl Enones (**1o-r**)[1], and **1s**[2] were prepared according to literature procedure. Benzotriazole-derived enone **1m** was prepared as reported by Katrizky.[3] (*E*)-1-phenylbut-2-en-1-one (**1n**) was prepared as reported by Patrick.[4] All other aryl-aryl (**1b-i**) or styrenyl enones (**1j, 1k)** were prepared according to known literature procedure.[5] MAC reagent **2** and **4** were prepared according to Nemoto.[6] Amine **VIe** and squarate **VId** were prepared according to literature procedure.[7,8] Aldehyde **16** was prepared from known literature procedures.[9, 10]

Regarding reference 2 (a), Professor David A. Evans released an unpublished document that discusses the concept of dissonant/consonant reactivity. It can be accessed online through a Google search of the title of the document: "An Organizational Format for the Classification of Functional Groups". The first hit from the search provides the correct link to the pdf of the document:
http://isites.harvard.edu/fs/docs/icb.topic93502.files/Lectures_and_Handouts/30-Handouts/DAE_CD_Manuscript.pdf[11]

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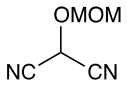
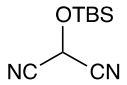
Procedure for the Synthesis of MAC Reagents.



2-(methoxymethoxy)malononitrile (2): In a 100-mL round bottom flask equipped with a magnetic stir bar, acetylmalononitrile (1.38 g, 12.77 mmol) was dissolved in 30 mL of water. 9 mL of a 32% of peracetic acid (in AcOH) solution was diluted in 21 mL of acetic acid (now 9.6%) and was added via pipette to the aqueous solution of acetylmalononitrile. The resulting clear solution was stirred at room temperature for 2 h. The stir bar was removed, and the flask was concentrated on a rotary evaporator (20 mm Hg, 30 °C) until most of the volatiles were removed. (~1–2 mL of residue remains) A stir bar was added to the residual clear oil and stirred under high vacuum (<1 mmHg) for 4 h to remove the remaining volatiles. (NOTE: Although we never witnessed any complications, a blast shield was used as a precautionary measure during the concentration of peracetic acid.) The resulting crude whitish residue (hydroxymalononitrile) was suspended in CH_2Cl_2 (75 mL). Dimethoxymethane (10.2 mL, 0.127 mol) was added in one portion. P_2O_5 (6.60 g, 23.2 mmol) was then added as a solid in one portion. (Note: The solid P_2O_5 may clump, preventing efficient stirring, but does not affect the progress of the reaction.) After 14 h, the solvent is decanted from the P_2O_5 into a separatory funnel and the P_2O_5 was washed with CH_2Cl_2 (2x10 mL). The combined organic layer was washed with sat. aq. $NaHCO_3$ (15 mL, 2x) and brine (15 mL, 1x), dried over Na_2SO_4, concentrated, and purified by column chromatography (SiO_2: 10% EtOAc/Hexanes) to afford 1.00 g of MOM-MAC **2** (62%) as a white crystalline solid.

^{1}H NMR (500 MHz; $CDCl_3$) δ 5.36 (s, 1H), 4.92 (s, 2H), 3.55 (s, 3H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 110.6, 96.2, 57.2, 51.9

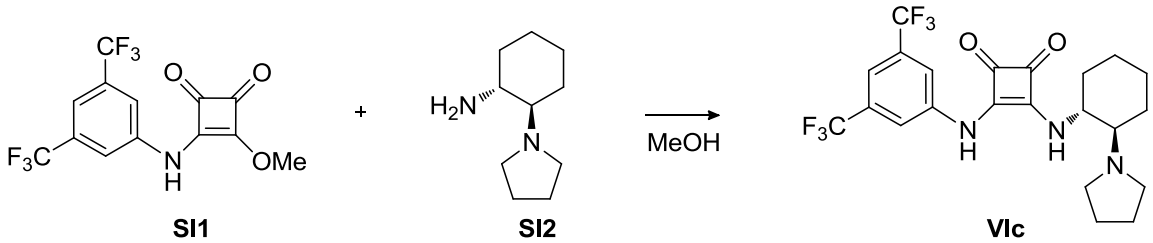


2-(*tert*-butyldimethylsilyloxy)malononitrile (4): In a 100-mL round bottom flask equipped with a magnetic stir bar, acetylmalononitrile (0.7 g, 6.47 mmol) was dissolved in 15 mL of water. 5 mL of a 32% of peracetic acid (in AcOH) solution was diluted in 10 mL of acetic acid (now 10.7%) and was added via pipette to the aqueous solution of acetylmalononitrile. The resulting clear solution was stirred at room temperature for 2 h. The stir bar was removed, and the flask was concentrated on a rotary evaporator (20 mm Hg, 30 °C) until most of the volatiles were removed. (~1–2 mL of residue remains) A stir bar was added to the residual clear oil and stirred under high vacuum (<1 mmHg) for 4 h to remove the remaining volatiles. (NOTE: Although we never witnessed any complications, a blast shield was used as a precautionary measure during the concentration of peracetic acid.) The resulting crude whitish residue (hydroxymalononitrile) was dissolved in 18 mL DMF. The solution was cooled to 0 °C and TBSCl (1.7 g, 9.7 mmol) was added as a solid in one portion. Imidazole (0.66 g, 9.7 mmol) was then added in portions, and the reaction was stirred for 30 min. The reaction was warmed to RT and stirred for an additional 30 min before diluting with 40 mL of Et_2O. The solution was transferred with a separatory funnel and washed with 30 mL H_2O, 20 mL aq. $NaHCO_3$, and 20 mL brine. The organic layer was dried over $MgSO_4$, concentrated and purified by column chromatography (SiO_2: 2-3% EtOAc/Hexanes) to afford 990 mg of TBS-MAC **4** (78%) as a clear oil.

^{1}H NMR (500 MHz; $CDCl_3$) δ 5.36 (s, 1H), 0.96 (s, 9H), 0.31 (s, 6H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 112.4, 50.92, 35.6, 25.2, -5.3

Synthesis of Catalyst VIc



3-((3,5-bis(trifluoromethyl)phenyl)amino)-4-(((1*R*,2*R*)-2-(pyrrolidin-1-yl)cyclohexyl)amino)cyclobut-3-ene-1,2-dione (**VIc**): In a 25-mL round bottom flask, amine **SI2**[6] (180 mg, 1.07 mmol) was dissolved in 4 mL of MeOH. Squarate **SI1**[7] (435, mg 1.23 mmol) was added as a solid in one portion resulting in a yellow solution. After 15 min, the product precipitated out. After 16 h, the reaction mixture was diluted with 3 mL of Et_2O and filtered through a Buchner funnel. The product was washed 2x with Et_2O (5 mL), dried, and collected as a white solid (410 mg, 80% yield).

Analytical data for **VIc**:
IR (film): 3186, 3139, 2946, 2860, 2791, 1796, 1662, 1578, 1558, 1490, 1459, 1382, 1276, 1182, 1165, 1125

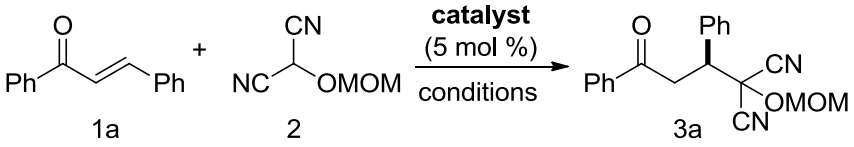
^{1}H NMR (500 MHz; DMSO) δ 10.20 (bs, 1H), 8.06 (s, 2H), 7.80 (bs, 1H), 7.66 (s, 8H), 3.96 (bs, 1H), 2.69 – 2.58 (m, 2H), 2.58 – 2.47 (m, 3H), 2.05 (m, 1H), 1.87 – 1.79 (m, 1H), 1.76 – 1.69 (m, 1H), 1.63 (m, 5H), 1.44 – 1.21 (m, 4H).

^{13}C NMR (125 MHz; DMSO) δ 184.45, 180.11, 169.56, 162.12, 141.25, 131.35 (dd, J=265, 135), 123.185 (dd, J = 2170, 1085), 117.96, 114.49, 62.39, 55.37, 47.64, 32.55, 23.36, 22.77.

LRMS (ES): Mass calcd for $C_{22}H_{23}F_6N_3O_2$ $[M+H]^+$, 476. Found $[M+H]^+$, 476

$[\alpha]^{23.6}_D$ = –44.8° (c = 1.0, MeOH)

Figure 1: Catalyst screening and reaction optimization



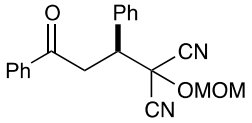
entry	catalyst	solvent	temp (°C)	time (h)	conversion (%)[c]	ee (%)[d]
1	I	CH_2Cl_2	23	15	62	8
2	II	CH_2Cl_2	23	15	23	–63
3	III	CH_2Cl_2	23	15	48	–81
4	IV	CH_2Cl_2	23	15	62	79
5	V	CH_2Cl_2	23	15	44	–57
6	VIa	CH_2Cl_2	23	23	91	84
7	VIb	CH_2Cl_2	23	15	95	80
8	VIc	CH_2Cl_2	23	23	99	90
9	VIc	CH_2Cl_2	–30	15	86	97
10	VIc	CH_2Cl_2	23	2	81	91
11	VIc[e]	CH_2Cl_2	23	2	65	90
12	VIc[f]	CH_2Cl_2	23	2	85	91
13	VIc	THF	23	3	17	71
14	VIc	MeOH	23	3	95	8
15	VIc	Toluene	23	3	20	81
16	VIc	DCE	23	3	75	91
17	VIc	MeCN	23	3	71	40
18	VIc	Hexanes	23	3	72	88

[a]Conditions: Reactions performed with **1a** (0.1 mmol), **2** (0.1 mmol), catalyst (5 mol %), solvent (1 mL). [c]Conversion determined by 500 MHz ^{1}H NMR spectroscropy. [d]Enantiomeric excess determined by Chiralcel IA. [e]Reaction run with 1 mol % catalyst. [f]Reaction run with 10 mol % catalyst.

General Procedure for the Michael Addition of MAC Reagents to Enones

To a 16 x 125 mm test tube equipped with a teflon-coated magnetic stir bar was added enone (0.36 mmol), MAC (0.3 mmol), and CH_2Cl_2 (0.6 mL, 0.5 M). The test tube was capped with a septum, purged with N_2, and set to the desired temperature. The reaction was allowed to stir for 15 min at the desired temperature before catalyst **VIc** (0.015 mmol) was added as a solid in one portion. The reaction was analyzed by ^{1}H NMR and TLC for conversion to product. Upon completion, the reaction was concentrated in vacuo to afford a sticky residue. Purification by flash column chromatography produced the desired product.

Michael Addition Reactions



(*S*)-2-(methoxymethoxy)-2-(3-oxo-1,3-diphenylpropyl)malononitrile (**3a**): Prepared according to modified general procedure using enone **1a** (750 mg, 3.6 mmol), MAC **2** (378 mg, 3.0 mmol), and catalyst **VIc** (71.3 mg, 0.15 mmol) in CH_2Cl_2 (6 mL) at –30 °C for 24 h. After concentration, the reaction mixture was treated with 10 mL of Et_2O, and filtered to isolate the catalyst (60 mg, 84% recovery), The filtrate is concentrated and purified by flash column chromatography (SiO_2, 10 - 15% EtOAc/Hexanes) to afford 983 mg (98%) of **3a** as a colorless oil.

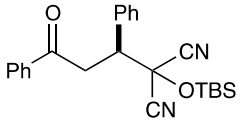
Analytical data for **3a**:
IR (film): 3064, 3035, 2940, 2832, 1688, 1597, 1581, 1498, 1449, 1419, 1367, 1348, 1277, 1220, 1164, 1110, 1066, 1027, 1003, 966, 923, 769, 751, 713, 690, 643

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.94 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.62 – 7.56 (m, 1H), 7.54 – 7.50 (m, 4H), 7.47 (t, *J* = 7.8 Hz, 3H), 7.41 – 7.33 (m, 4H), 5.06 (d, *J* = 7.2 Hz, 1H), 5.04 (d, *J* = 7.2 Hz, 1H), 4.27 (dd, *J* = 9.7, 3.5 Hz, 1H), 3.87 (dd, *J* = 17.4, 9.7 Hz, 1H), 3.69 (dd, *J* = 17.4, 3.6 Hz, 1H), 3.47 (s, 3H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 195.2, 136.4, 134.3, 133.8, 129.7 (x2), 129.3, 129.0 (x2), 128.9 (x2), 128.2 (x2), 112.7 (x2), 96.7, 70.1, 57.6, 49.5, 38.7

HRMS (MM) Mass calcd for $C_{20}H_{18}N_2O_3$ [M+Na]+, 357.1215. Found $[M+Na]^+$, 357.1207

$[\alpha]^{23.6}_D$ = –28.5° (c = 1.0, $CHCl_3$)
Enantiomeric excess (97% ee) was measured by HPLC (Chiralcel IA, 3% IPA/Hexanes, 1 mL/min, Rt_1 = 14.0, Rt_2 = 16.98



(*S*)-2-((*tert*-butyldimethylsilyl)oxy)-2-(3-oxo-1,3-diphenylpropyl)malononitrile (**5a**): Prepared according to general procedure using enone **1a** (750 mg, 3.6 mmol), MAC **4** (589.0 mg, 3.0 mmol), and catalyst **VIc** (71.3 mg, 0.15 mmol) in CH_2Cl_2 (6 mL) at –20 °C for 36 h. After concentration, the reaction mixture was treated with 10 mL of Et_2O, and filtered to isolate the catalyst (57 mg, 80% recovery), The filtrate is concentrated and purified by flash column chromatography (SiO_2, 3-4% EtOAc/Hexanes) to afford 1.16 g (96%) of **5a** as a colorless oil.

Analytical data for **5a**:
IR (film): 3065, 3036, 2956, 2932, 2887, 2860, 1691, 1597, 1581, 1498, 1472, 1464, 1449, 1364, 1266, 1219, 1131, 1004, 844, 788, 750, 690.

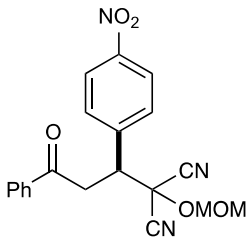
^{1}H NMR (500 MHz; $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.63 – 7.56 (m, 1H), 7.51 – 7.44 (m, 4H), 7.40 –

7.30 (m, 3H), 4.18 (dd, *J* = 9.7, 3.6 Hz, 1H), 3.84 (dd, *J* = 17.4, 9.8 Hz, 1H), 3.65 (dd, *J* = 17.4, 3.6 Hz, 1H), 0.90 (s, 9H), 0.30 (s, 3H), 0.29 (s, 3H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 195.2, 136.4, 134.4, 133.8, 129.7 (x2), 129.2, 128.9 (x2), 128.8 (x2), 128.2 (x2), 114.7 (x2), 68.0, 51.1, 38.4, 25.3 (x3), 18.2, -4.5, -4.6

HRMS (MM) Mass calcd for $C_{24}H_{28}N_2O_2Si$ $[M+Na]^+$, 427.1818. Found $[M+Na]^+$, 427.1809

$[\alpha]^{23.6}_D$ = –25.4° (c = 1.0, $CHCl_3$)
Enantiomeric excess (96% ee) was measured by HPLC (Chiralcel IA, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 7.2, Rt_2 = 9.1



(*S*)-2-(methoxymethoxy)-2-(1-(4-nitrophenyl)-3-oxo-3-phenylpropyl)malononitrile (**3b**): Prepared according to general procedure using enone **1b** (91 mg, 0.36 mmol), MAC **2** (38 mg, 0.3 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –30 °C for 20 h. Purified by flash column chromatography (SiO_2, 15 – 25 % EtOAc/Hexanes) to afford 112 mg (98%) of **1b** as a colorless oil.

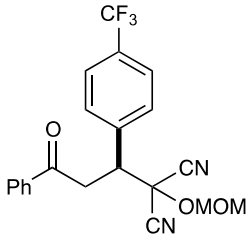
Analytical data for **1b**:
IR (film): 3083, 2942, 2850, 1688, 1653, 1599, 1524, 1449, 1350, 1277, 1221, 1164, 1110, 1077, 1032, 968, 924, 859, 753, 737, 720, 690

^{1}H NMR (500 MHz; $CDCl_3$) δ 8.22 (dd, *J* = 8.8, 1.2 Hz, 2H), 7.93 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.73 – 7.67 (m, 2H), 7.61 (tq, *J* = 7.4, 1.2 Hz, 1H), 7.52 – 7.44 (m, 2H), 5.08 (d, *J* = 7.2 Hz, 1H), 5.07 (d, *J* = 7.2 Hz, 1H), 4.36 (dd, *J* = 10.4, 3.2 Hz, 1H), 3.93 (dd, *J* = 17.8, 10.4 Hz, 1H), 3.76 (dd, *J* = 17.7, 3.2 Hz, 1H), 3.49 (s, 3H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 194.5, 148.4, 141.7, 135.8, 134.2, 130.8 (x2), 129.0 (x2), 128.2 (x2), 124.0 (x2), 112.3 (x2), 96.9, 69.1, 57.7, 49.3, 38.7

LRMS (ES): Mass calcd for $C_{20}H_{17}N_3O_5$ $[M+H]^+$, 380. Found $[M+H]^+$, 380

$[\alpha]^{23.6}_D$ = –70° (c = 1.0, $CHCl_3$)
Enantiomeric excess (97% ee) was measured by HPLC (Chiralcel IA, 15% EtOH/Hexanes, 1 mL/min, Rt_1 = 18.2, Rt_2 = 23.1



(*S*)-2-(methoxymethoxy)-2-(1-(4-trifluoromethylphenyl)-3-oxo-3-phenylpropyl)malononitrile (**3c**): Prepared according to general procedure using enone **1c** (99 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –30 °C for 24 h. Purified by flash column chromatography (SiO_2, 15% EtOAc/Hexanes) to afford 118 mg (98%) of **3c** as a colorless oil.

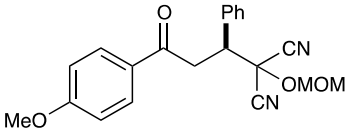
Analytical data for **3c**:
IR (film): 3063, 2963, 2942, 2850, 2834, 1689, 1621, 1597, 1450, 1425, 1328, 1301, 1278, 1222, 1166, 1119, 1069, 1033, 1018, 968, 924, 852, 764, 689

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.94 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.64 (s, 4H), 7.62 – 7.58 (m, 1H), 7.51 – 7.45 (m, 2H), 5.08 (d, *J* = 7.2 Hz, 1H), 5.06 (d, *J* = 7.2 Hz, 1H), 4.34 (dd, *J* = 10.1, 3.3 Hz, 1H), 3.92 (dd, *J* = 17.7, 10.1 Hz, 1H), 3.74 (dd, *J* = 17.7, 3.3 Hz, 1H), 3.48 (s, 3H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 194.7, 138.5, 138.5, 136.0, 134.0, 130.2 (x3), 129.0 (x3), 128.1 (x3), 125.9 (q, *J* = 7.3, 3.6 Hz, 1H), 112.5, 112.4, 96.9, 69.4, 57.6, 49.2, 38.6

LRMS (ES): Mass calcd for $C_{21}H_{17}F_3N_2O_3$ $[M+H]^+$, 403. Found $[M+H]^+$, 403

$[\alpha]^{23.6}_D$ = –49.4° (c = 1.0, $CHCl_3$)
Enantiomeric excess (97% ee) was measured by HPLC (Chiralcel OD-H, 4% IPA/Hexanes, 1 mL/min, Rt_1 = 13.7, Rt_2 = 17.4



(*S*)-2-(methoxymethoxy)-2-(3-(4-methoxyphenyl)-3-oxo-1-phenylpropyl)malononitrile (**3d**): Prepared according to general procedure using enone **1d** (86 mg, 0.36 mmol), MAC **2** (38 mg, 0.3 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at 0 °C for 28 h. Purified by flash column chromatography (SiO_2, 15-20% EtOAc/Hexanes) to afford 110 mg (99%) of **3d** as a colorless oil.

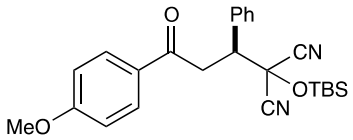
Analytical data for **3d**:
IR (film): 3064, 3035, 3009, 2962, 2939, 2841, 1678, 1601, 1575, 1512, 1456, 1421, 1367, 1348, 1311, 1292, 1263, 1227, 1170, 1111, 1065, 1028, 967, 925, 836, 704

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.92 (d, *J* = 9.0 Hz, 2H), 7.50 (dd, *J* = 8.0, 1.7 Hz, 2H), 7.39 – 7.31 (m, 3H), 6.93 (d, *J* = 8.9 Hz, 2H), 5.05 (d, *J* = 7.2 Hz, 1H), 5.03 (d, *J* = 7.2 Hz, 1H), 4.27 (dd, *J* = 9.7, 3.6 Hz, 1H), 3.85 (s, 4H), 3.83 (dd, J = 17.2, 9.8 Hz, 1H), 3.62 (dd, *J* = 17.2, 3.6 Hz, 1H), 3.46 (s, 3H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 193.6, 164.0, 134.5, 130.5 (x2), 129.6 (x2), 129.4, 129.1, 128.9 (x2), 114.0 (x2), 112.7 (x2), 96.6, 70.1, 57.5, 55.6, 49.6, 38.2

LRMS (ES): Mass calcd for $C_{21}H_{20}N_2O_4$ $[M+H]^+$, 365. Found $[M+H]^+$, 365

$[\alpha]^{23.6}_D$ = –51.9° (c = 1.0, $CHCl_3$)
Enantiomeric excess (92% ee) was measured by HPLC (Chiralcel IA, 10% EtOH/Hexanes, 1 mL/min, Rt_1 = 19.08, Rt_2 = 20.90



(*S*)-2-((*tert*-butyldimethylsilyl)oxy)-2-(3-(4-methoxyphenyl)-3-oxo-1-phenylpropyl)malononitrile (**5d**): Prepared according to general procedure using enone **1d** (84 mg, 0.36 mmol), MAC **4** (59 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at 0 °C for 72h. Purified by flash column chromatography (SiO_2, 5→ 10 % Et_2O/Hexanes) to afford 124 mg (96%) of **5d** as a colorless oil.

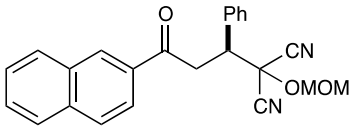
Analytical data for **5d**:
IR (film): 3065, 3036, 3009, 2956, 2933, 2899, 2860, 1681, 1601, 1576, 1512, 1471, 1464, 1456, 1421, 1364, 1263, 1225, 1171, 1131, 1030, 843, 787, 701, 681

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.93 (d, *J* = 8.9 Hz, 2H), 7.48 (dd, *J* = 8.0, 1.7 Hz, 2H), 7.38 – 7.30 (m, 3H), 6.93 (d, *J* = 8.9 Hz, 2H), 4.20 (dd, *J* = 9.7, 3.6 Hz, 1H), 3.84 (s, 3H), 3.81 (dd, *J* = 17.2, 9.7 Hz, 1H), 3.61 (dd, *J* = 17.2, 3.6 Hz, 1H), 0.91 (s, 9H), 0.31 (s, 3H), 0.30 (s, 3H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 193.5, 163.9, 134.6, 130.4 (x2), 129.6 (x2), 129.4, 129.0, 128.7 (x2), 114.7 (x2), 114.0 (x2), 68.0, 55.5, 51.1, 37.9, 25.3 (x3), 18.13, -4.6, -4.7

LRMS (ES): Mass calcd for $C_{25}H_{30}N_2O_3Si$ $[M+H]^+$, 435. Found $[M+H]^+$, 435

$[\alpha]^{23.6}_D$ = –42.7° (c = 1.0, $CHCl_3$)
Enantiomeric excess (90% ee) was measured by HPLC (Chiralcel OD-H, 4% IPA/Hexanes, 1 mL/min, Rt_1 = 7.3, Rt_2 = 8.6



(***S*)-2-(methoxymethoxy)-2-(3-(naphthalen-2-yl)-3-oxo-1-phenylpropyl)malononitrile** (**3e**): Prepared according to general procedure using enone **1e** (93 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (6 mL) at –30 °C for 24 h. Purified by flash column chromatography (SiO_2, 10 – 15% EtOAc/Hexanes) to afford 114 mg (99%) of **3e** as a colorless oil.

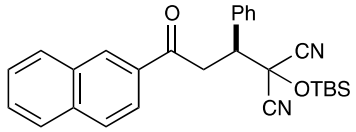
Analytical data for **3e**:
IR (film): 3062, 3035, 2962, 1684, 1628, 1470, 1456, 1437, 1371, 1292, 1279, 1216, 1184, 1164, 1125, 1110, 1065, 1029, 967, 929, 862, 824, 744, 703

^{1}H NMR (500 MHz; $CDCl_3$) δ 8.49 (s, 1H), 8.00 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.97 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.89 (d, *J* = 6.1 Hz, 1H), 7.88 – 7.86 (m, 1H), 7.64 – 7.58 (m, 2H), 7.56 (m, 2H), 7.41 – 7.33 (m, 3H), 5.09 (dd, *J* = 7.1, 0.7 Hz, 1H), 5.07 (dd, *J* = 7.2, 0.8 Hz, 1H), 4.34 (ddd, *J* = 9.7, 3.6, 1.5 Hz, 1H), 4.02 (ddd, *J* = 17.2, 9.7, 1.3 Hz, 1H), 3.82 (ddd, *J* = 17.3, 3.7, 1.3 Hz, 1H), 3.49 (s, 3H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 195.1, 135.9, 134.4, 133.7, 132.5, 130.0, 129.7 (x3), 129.3, 129.0 (x3), 128.8, 127.9, 127.2, 123.7, 112.8, 112.7, 96.7, 70.1, 57.6, 49.6, 38.7

LRMS (ES): Mass calcd for $C_{24}H_{20}N_2O_3$ $[M+H]^+$, 385. Found $[M+H]^+$, 385

$[\alpha]^{23.6}_D$ = –92.7° (c = 1.0, $CHCl_3$)
Enantiomeric excess (98% ee) was measured by HPLC (Chiralcel IA, 7% EtOH/Hexanes, 1 mL/min, Rt_1 = 15.5, Rt_2 = 18.7



(*S*)-2-((*tert*-butyldimethylsilyl)oxy)-2-(3-(naphthalen-2-yl)-3-oxo-1-phenylpropyl)malononitrile (**5e**): Prepared according to general procedure using enone **1e** (93 mg, 0.36 mmol), MAC **4** (59 mg, 0.3 mmol), and catalyst **VIc** (7.1 mg, 0.3 mmol) in CH_2Cl_2 (0.6 mL) at –20 °C for 36 h. Purified by flash column chromatography (SiO_2, 5→ 10 % Et_2O/Hexanes) to afford 130 mg (95%) of **5e** as a colorless oil.

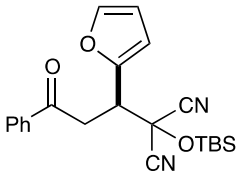
Analytical data for **5e**:
IR (film): 3062, 3036, 2955, 2932, 2886, 2860, 1685, 1628, 1597, 1498, 1471, 1364, 1267, 1215, 1185, 1126, 1005, 943, 898, 844, 787, 744, 701

^{1}H NMR (500 MHz; $CDCl_3$) δ 8.48 (s, 1H), 7.99 (ddd, *J* = 10.5, 8.4, 1.5 Hz, 2H), 7.92 – 7.86 (m, 2H), 7.63 (ddd, *J* = 8.1, 6.8, 1.4 Hz, 1H), 7.58 (ddd, *J* = 8.1, 6.9, 1.4 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.42 – 7.32 (m, 3H), 4.27 (dd, *J* = 9.7, 3.6 Hz, 1H), 4.00 (dd, *J* = 17.2, 9.7 Hz, 1H), 3.80 (dd, *J* = 17.2, 3.7 Hz, 1H), 0.92 (s, 9H), 0.33 (s, 3H), 0.33 (s, 3H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 195.1, 135.9, 134.5, 133.8, 132.5, 130.0, 129.8, 129.7 (x2), 129.1, 128.9, 128.8 (x2), 128.8, 127.9, 127.1, 123.7, 114.8, 114.7, 68.0, 51.3, 38.5, 25.4 (x3), 18.2, -4.5, -4.6

LRMS (ES): Mass calcd for $C_{28}H_{30}N_2O_2Si$ $[M+H]^+$, 455. Found $[M+H]^+$, 455

$[\alpha]^{23.6}_D$ = –85.7° (c = 1.0, $CHCl_3$)
Enantiomeric excess (97% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 9.2, Rt_2 = 10.8



(*S*)-2-((*tert*-butyldimethylsilyl)oxy)-2-(1-(furan-2-yl)-3-oxo-3-phenylpropyl)malononitrile (**5f**): Prepared according to general procedure using enone **1f** (71 mg, 0.36 mmol), MAC **4** (59 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at 0 °C for 24 h. Purified by flash column chromatography (SiO_2, 5% Et_2O/Hexanes) to afford 110 mg (93%) of **5f** as a colorless oil.

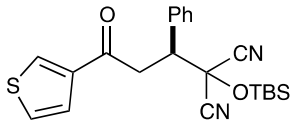
Analytical data for **5f**:
IR (film): 2955, 2932, 2887, 2860, 1692, 1598, 1472, 1449, 1363, 1267, 1218, 1137, 1015, 845, 788, 759, 743, 689

^{1}H NMR (500 MHz; $CDCl_3$) δ 8.02 – 7.93 (m, 2H), 7.65 – 7.56 (m, 1H), 7.49 (dd, *J* = 8.3, 7.2 Hz, 2H), 7.40 (dd, *J* = 1.8, 0.8 Hz, 1H), 6.49 (dd, *J* = 3.3, 0.6 Hz, 1H), 6.36 (dd, *J* = 3.3, 1.8 Hz, 1H), 4.36 (dd, *J* = 10.0, 3.3 Hz, 1H), 3.88 (dd, *J* = 17.3, 10.0 Hz, 1H), 3.53 (dd, *J* = 17.4, 3.3 Hz, 1H), 0.90 (s, 9H), 0.34 (s, 3H), 0.33 (s, 3H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 194.9, 147.9, 143.4, 136.2, 133.8, 128.9 (x2), 128.2 (x2), 114.4 (x2), 110.9 (x2), 66.8, 45.5, 36.8, 25.2 (x3), 18.1, -4.6 (x2).

LRMS (ES): Mass calcd for $C_{22}H_{26}N_2O_3Si$ $[M+Na]^+$, 417. Found $[M+H]^+$, 417

$[\alpha]^{23.6}_D$ = –10° (c = 1.0, $CHCl_3$)
Enantiomeric excess (90% ee) was measured by HPLC (Chiralcel AD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 6.38, Rt_2 = 6.80



(*S*)-2-((*tert*-butyldimethylsilyl)oxy)-2-(3-oxo-1-phenyl-3-(thiophen-3-yl)propyl)malononitrile (**5g**): Prepared according to general procedure using enone **1g** (77 mg, 0.36 mmol), MAC **4** (59 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –10 °C for 48 h. Purified by flash column chromatography (SiO_2, 5 – 10 % Et_2O/Hexanes) to afford 116 mg (94%) of **5g** as a colorless oil.

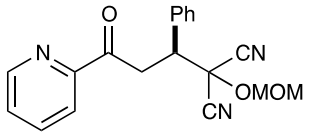
Analytical data for **5g**:
IR (film): 3109, 3066, 3035, 2955, 2932, 2886, 2860, 1682, 1512, 1498, 1472, 1464, 1456, 1412, 1266, 1231, 1174, 1131, 1093, 1077, 1052, 1005, 941, 844, 787, 760, 700

^{1}H NMR (500 MHz; $CDCl_3$) δ 8.10 (dd, *J* = 2.9, 1.3 Hz, 1H), 7.51 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.49 – 7.45 (m, 2H), 7.39 – 7.32 (m, 3H), 7.31 (dd, *J* = 5.1, 2.9 Hz, 1H), 4.16 (dd, *J* = 9.5, 3.9 Hz, 1H), 3.71 (dd, *J* = 17.2, 9.5 Hz, 1H), 3.58 (dd, *J* = 17.1, 3.9 Hz, 1H), 0.90 (s, 9H), 0.30 (s, 3H), 0.29 (s, 3H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 189.3, 141.6, 134.4, 132.5, 129.6 (x2), 129.1, 128.8 (x2), 126.9 (x2), 114.7, 114.6, 67.9, 51.0, 39.5, 25.3, 18.2, -4.6, -4.7

LRMS (ES): Mass calcd for $C_{22}H_{26}N_2O_2SSi$ $[M+H]^+$, 411. Found $[M+H]^+$, 411

$[\alpha]^{23.6}_D$ = –29.2° (c = 1.0, $CHCl_3$)
Enantiomeric excess (90% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 8.5, Rt_2 = 11.0



(*S*)-2-(methoxymethoxy)-2-(3-oxo-1-phenyl-3-(pyridin-2-yl)propyl)malononitrile (**3h**): Prepared according to general procedure using enone **1h** (75 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –30 °C for 30 h. Purified by flash column chromatography (SiO_2, 15% EtOAc/Hexanes) to afford 98 mg (98%) of **3h** as a colorless oil.

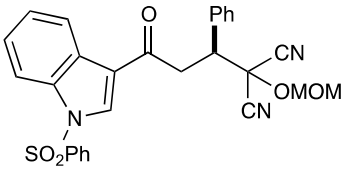
Analytical data for **3h**:
IR (film): 3060, 3035, 3008, 2962, 2940, 2849, 2832, 1702, 1584, 1570, 1456, 1438, 1366, 1347, 1300, 1282, 1221, 1164, 1110, 1067, 1030, 996, 962, 926, 765, 700

^{1}H NMR (500 MHz; $CDCl_3$) δ 8.74 – 8.68 (m, 1H), 7.93 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.79 (td, *J* = 7.7, 1.7 Hz, 1H), 7.52 (dd, *J* = 7.9, 1.7 Hz, 2H), 7.48 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 7.38 – 7.29 (m, 3H), 5.04 (d, *J* = 7.2 Hz, 1H), 5.02 (d, *J* = 7.2 Hz, 1H), 4.31 – 4.24 (m, 2H), 3.88 (dd, J = 14.4, 10.5 Hz, 1H), 3.46 (s, 3H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 197.3, 152.6, 149.2, 137.1, 134.4, 129.9 (x2), 129.1, 128.8 (x2), 127.7, 122.1, 112.9, 112.6, 96.6, 70.2, 57.5, 49.7, 37.9

LRMS (ES): Mass calcd for $C_{19}H_{17}N_3O_3$ $[M+H]^+$, 336. Found $[M+H]^+$, 336

$[\alpha]^{23.6}_D$ = –35.8° (c = 1.0, $CHCl_3$)
Enantiomeric excess (92% ee) was measured by HPLC (Chiralcel IA, 7% IPA/Hexanes, 1 mL/min, Rt_1 = 11.3, Rt_2 = 12.2



(*S*)-2-(methoxymethoxy)-2-(3-oxo-1-phenyl-3-(1-benzenesulfonyl-1*H*-indol-3-yl)propyl)malononitrile (**3i**): Prepared according to general procedure using enone **1i** (140 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at 0 °C for 36 h. Purified by flash column chromatography (SiO_2, 30% EtOAc/Hexanes) to afford 150 mg (97%) of **3i** as a thick amorphous solid.

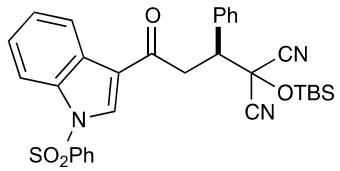
Analytical data for **3i**:
IR (film): 3130, 3063, 3035, 3008, 2962, 2939, 2905, 2849, 2832, 1669, 1605, 1584, 1539, 1497, 1479, 1448, 1385, 1338, 1292, 1267, 1167, 1139, 1109, 1087, 1026, 987, 922, 751, 732, 700, 684, 593, 571, 552

^{1}H NMR (500 MHz; $CDCl_3$) δ 8.34 – 8.29 (m, 1H), 8.23 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 8.6 Hz, 2H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.65 – 7.57 (m, 1H), 7.57 – 7.48 (m, 4H), 7.42 – 7.33 (m, 4H), 7.33 – 7.28 (m, 1H), 5.07 (d, J = 7.4 Hz, 2H), 5.06 (d, J = 7.8 Hz, 1H), 4.32 – 4.25 (m, 1H), 3.83 – 3.73 (m, 1H), 3.67 – 3.59 (m, 1H), 3.47 (s, 3H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 190.6, 137.5 134.9 (x3), 134.3, 131.9, 129.8 (x2), 129.7, 129.3, 129.0 (x2) , 127.4, 127.3 (x2), 126.2, 125.2, 123.2, 121.0, 113.2, 112.8, 112.6, 96.7, 70.0, 57.6, 49.5, 40.0.

LRMS (ES): Mass calcd for $C_{28}H_{23}N_3O_5S$ $[M–C_3H_4NO]^+$, 443. Found $[M+H]^+$, 443

$[\alpha]^{23.6}_D$ = –14.5° (c = 1.0, $CHCl_3$)
Enantiomeric excess (90% ee) was measured by HPLC (Chiralcel IA, 10% EtOH/Hexanes, 1.1 mL/min, Rt_1 = 16.4, Rt_2 = 21.3



(*S*)-2-(3-(1-benzenesulfonyl-indol-3-yl)-3-oxo-1-phenylpropyl)-2-((*tert*-butyldimethylsilyl)oxy)malononitrile (**5i**): Prepared according to general procedure using enone **1i** (140 mg, 0.36 mmol), MAC **4** (59 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at 0 °C for 72 h. Purified by flash column chromatography (SiO_2, 20% EtOAc/Hexanes) to afford 156 mg (90%) of **5i** as a colorless oil.

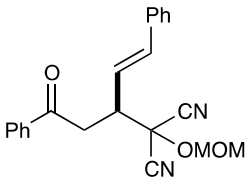
Analytical data for **5i**:
IR (film): 3129, 3063, 3035, 2955, 2932, 2886, 2860, 1670, 1539, 1479, 1472, 1448, 1386, 1338, 1291, 1265, 1189, 1169, 1138, 1109, 1088, 1003, 989, 844, 788, 769, 751, 730, 700, 684, 593, 583, 571, 551

^{1}H NMR (500 MHz; $CDCl_3$) δ 8.31 (s, 1H), 8.22 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.94 – 7.88 (m, 3H), 7.57 – 7.52 (m, 1H), 7.52 – 7.48 (m, 2H), 7.47 – 7.41 (m, 2H), 7.36 – 7.24 (m, 5H), 4.22 (dd, *J* = 9.2, 4.0 Hz, 1H), 3.74 (dd, *J* = 16.7, 9.2 Hz, 1H), 3.63 (dd, *J* = 16.7, 4.0 Hz, 1H), 0.87 (s, 9H), 0.29 (s, 3H), 0.27 (s, 3H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 190.6, 137.4, 134.8, 134.7, 134.4, 131.8, 129.7 (x2), 129.6 (x2), 129.1, 128.8 (x2), 127.3, 127.1 (x2), 126.1, 125.0, 123.1, 121.0, 114.7, 114.6, 113.1, 67.9, 51.0, 39.7, 25.2 (x3), 18.1, -4.6, -4.7

LRMS (ES): Mass calcd for $C_{32}H_{33}N_3O_4SSi$ $[M+H]^+$, 584. Found $[M+H]^+$, 584

$[\alpha]^{23.6}_D$ = –12.8° (c = 1.0, $CHCl_3$)
Enantiomeric excess (89% ee) was measured by HPLC (Chiralcel OD-H, 4% IPA/Hexanes, 1 mL/min, Rt_1 = 9.9, Rt_2 = 11.3



(*S*,*E*)-2-(methoxymethoxy)-2-(5-oxo-1,5-diphenylpent-1-en-3-yl)malononitrile (**3j**): Prepared according to general procedure using enone **1j** (84 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –10 °C for 28 h. Purified by flash column chromatography (SiO_2, 15% EtOAc/Hexanes) to afford 107 mg (98%) of **3j** as a colorless oil.

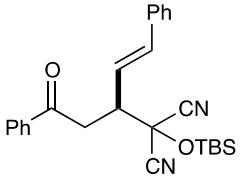
Analytical data for **3j**:
IR (film): 3060, 3028, 2962, 2940, 2832, 1688, 1597, 1580, 1449, 1362, 1282, 1219, 1164, 1106, 1030, 970, 931, 753, 690

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.99 – 7.92 (m, 2H), 7.61 – 7.55 (m, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.39 – 7.33 (m, 2H), 7.32 – 7.27 (m, 2H), 7.24 (t, *J* = 7.4 Hz, 1H), 6.83 (d, *J* = 15.7 Hz, 1H), 6.06 (dddd, *J* = 15.7, 9.0, 2.7, 1.3 Hz, 1H), 5.06 (s, 2H), 3.94 – 3.86 (m, 1H), 3.51 (s, 3H), 3.49 – 3.44 (m, 2H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 195.3, 138.3, 136.4, 135.7, 133.7, 128.9 (x2), 128.7 (x2), 128.6, 128.2 (x2), 126.9 (x2), 121.5, 112.7, 112.5, 96.6, 69.4, 57.5, 47.6, 38.2

LRMS (ES): Mass calcd for $C_{22}H_{20}N_2O_3$ $[M+H]^+$, 361. Found $[M+H]^+$, 361

$[\alpha]^{23.6}_D$ = +14.3° (c = 1.0, $CHCl_3$)
Enantiomeric excess (95% ee) was measured by HPLC (Chiralcel IA, 10% EtOH/Hexanes, 1 mL/min, Rt_1 = 8.4, Rt_2 = 10.4



(*S*,*E*)-2-((*tert*-butyldimethylsilyl)oxy)-2-(5-oxo-1,5-diphenylpent-1-en-3-yl)malononitrile (**5j**): Prepared according to general procedure using enone **1j** (84 mg, 0.36 mmol), MAC **4**(59 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at 0 °C for 48 h. Purified by flash column chromatography (SiO_2, % 5 Et_2O/Hexanes) to afford 124 mg (96%) of **5j** as a colorless oil.

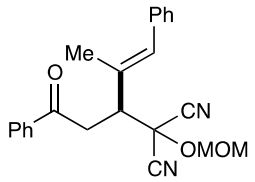
Analytical data for **5j**:
IR (film): 3028, 2931, 2860, 1690, 1598, 1559, 1496, 1472, 1449, 1363, 1261, 1218, 1135, 1003, 968, 843, 787, 750, 689

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.95 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.60 – 7.55 (m, 1H), 7.47 (dd, *J* = 8.4, 7.2 Hz, 2H), 7.36 – 7.33 (m, 2H), 7.31 – 7.26 (m, 2H), 7.26 – 7.22 (m, 1H), 6.80 (d, *J* = 15.7 Hz, 1H), 6.02 (dd, *J* = 15.7, 9.1 Hz, 1H), 3.80 (tdd, *J* = 9.0, 3.5, 0.8 Hz, 1H), 3.47 (dd, *J* = 16.9, 3.5 Hz, 1H), 3.40 (dd, *J* = 16.9, 9.1 Hz, 1H), 0.92 (s, 9H), 0.39 (s, 3H), 0.37 (s, 3H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 195.3, 138.4, 136.5, 135.8, 133.7, 128.9 (x2), 128.7 (x2), 128.5, 128.2 (x2), 126.9 (x2), 121.8, 114.7, 114.5, 67.4, 49.4, 38.0, 25.3 (x2), 18.2, -4.50 (x2)

LRMS (ES): Mass calcd for $C_{26}H_{30}N_2O_2Si$ $[M+H]^+$, 431. Found $[M+H]^+$, 431

$[\alpha]^{23.6}_D$ = +3.4° (c = 1.0, $CHCl_3$)
Enantiomeric excess (94% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 9.4, Rt_2 = 15.0



(*S*,*E*)-2-(methoxymethoxy)-2-(2-methyl-5-oxo-1,5-diphenylpent-1-en-3-yl)malononitrile (**3k**):
Prepared according to general procedure using enone **1k** (89 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at 23 °C for 24 h. Purified by flash column chromatography (SiO_2, 15% EtOAc/Hexanes) to afford 110 mg (97%) of **3k** as a colorless oil.

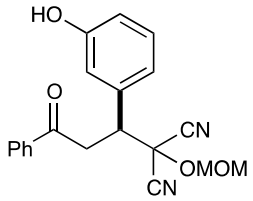
Analytical data for **3k**:
IR (film): 3101, 3082, 3058, 3025, 2960, 2939, 2920, 2851, 2831, 1686, 1598, 1449, 1356, 1280, 1218, 1164, 1020, 924, 757, 690

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.98 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.63 – 7.56 (m, 1H), 7.49 (dd, *J* = 8.4, 7.1 Hz, 2H), 7.34 – 7.27 (m, 2H), 7.24 – 7.16 (m, 3H), 6.75 (d, *J* = 1.6 Hz, 1H), 5.10 (d, *J* = 7.2 Hz, 1H), 5.07 (d, *J* = 7.2 Hz, 1H), 3.78 – 3.69 (m, 2H), 3.53 (s, 3H), 3.48 (dd, *J* = 14.9, 1.3 Hz, 1H), 2.09 (d, *J* = 1.5 Hz, 3H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 195.7, 136.6, 136.4, 133.7, 132.6, 132.4, 129.0 (x2), 128.9 (x2), 128.2 (x2), 128.1 (x2), 127.1, 112.9, 112.8, 96.5, 69.4, 57.6, 51.8, 37.9, 18.6

LRMS (ES): Mass calcd for $C_{23}H_{22}N_2O_3$ $[M+Na]^+$, 397. Found $[M+H]^+$, 397

$[\alpha]^{23.6}_D$ = –25.4° (c = 1.0, $CHCl_3$)
Enantiomeric excess (88% ee) was measured by HPLC (Chiralcel OD-H, 7% IPA/Hexanes, 1 mL/min, Rt_1 = 8.3, Rt_2 = 9.7



(*S*)-2-(1-(3-hydroxyphenyl)-3-oxo-3-phenylpropyl)-2-(methoxymethoxy)malononitrile (**3l**): Prepared according to general procedure using enone **1l** (81 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at 23 °C for 24 h. Purified by flash column chromatography (SiO_2, 25% EtOAc/Hexanes) to afford 99 mg (96%) of **3l** as a thick colorless oil.

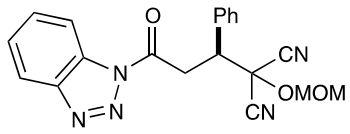
Analytical data for **3l**:
IR (film): 3439, 3060, 2963, 2941, 2849, 2832, 1685, 1592, 1493, 1457, 1450, 1356, 1310, 1281, 1220, 1163, 1110, 1069, 1027, 1001, 974, 924, 899, 766, 738, 692

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.98 – 7.89 (m, 2H), 7.62 – 7.54 (m, 1H), 7.45 (td, *J* = 8.0, 7.5, 1.6 Hz, 2H), 7.24 – 7.15 (m, 1H), 7.05 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.01 (t, *J* = 2.1 Hz, 1H), 6.82 – 6.74 (m, 1H), 6.22 (s, 1H), 5.05 (d, J = 7.3 Hz, 1H), 5.02 (d, *J* = 7.2 Hz, 1H), 4.21 (dd, *J* = 9.5, 3.7 Hz, 1H), 3.84 (dd, *J* = 17.5, 9.5 Hz, 1H), 3.67 (dd, *J* = 17.4, 3.7 Hz, 1H), 3.46 (s, 3H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 196.1, 156.1, 136.1, 135.8, 133.9, 130.1, 128.9 (x2), 128.2 (x2), 121.5, 116.8, 116.4, 112.7, 112.5, 96.6, 70.0, 57.5, 49.3, 38.7

LRMS (ES): Mass calcd for $C_{20}H_{18}N_2O_4$ $[2M+Na]^+$, 723. Found $[M+H]^+$, 723

$[\alpha]^{23.6}_D$ = –27.2° (c = 1.0, $CHCl_3$)
Enantiomeric excess (92% ee) was measured by HPLC (Chiralcel IA, 10% EtOH/Hexanes, 1 mL/min, Rt_1 = 16.6, Rt_2 = 19.9



(*S*)-2-(3-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)-3-oxo-1-phenylpropyl)-2-(methoxymethoxy)malononitrile (**3m**): Prepared according to general procedure with the addition of 50 mg of powdered 3 Å activated molecular sieves. Enone **1m** (90 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –10 °C for 72 h. Purified by flash column chromatography (SiO_2, 15% EtOAc/Hexanes) to afford 110 mg (96%) of **3m** as a colorless solid.

Analytical data for **3m**:
IR (film): 3064, 3035, 3008, 2962, 2941, 2905, 2849, 2832, 1740, 1606, 1597, 1497, 1485, 1452, 1397, 1359, 1325, 309, 1232, 1217, 1166, 1111, 1066, 1031, 1004, 963, 927, 829, 783, 771, 752, 738, 705, 659, 619

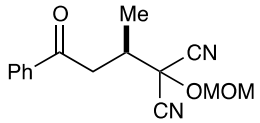
^{1}H NMR (500 MHz; $CDCl_3$) δ 8.14 (dt, *J* = 8.3, 1.0 Hz, 1H), 8.10 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.64 – 7.56

(m, 3H), 7.49 (ddd, *J* = 8.2, 7.1, 1.1 Hz, 1H), 7.42 – 7.34 (m, 3H), 5.07 (d, J = 7.2 Hz, 1H), 5.06 (d, J = 7.1 Hz, 1H), 4.41 (dd, *J* = 17.0, 9.9 Hz, 1H), 4.32 (dd, *J* = 9.9, 3.9 Hz, 1H), 4.14 (dd, *J* = 17.0, 3.9 Hz, 1H), 3.49 (s, 3H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 168.6, 146.3, 133.2, 130.9, 130.8, 129.7 (x3), 129.1 (x2), 126.6, 120.4, 114.3, 112.5, 112.0, 96.8, 69.8, 57.6, 49.9, 36.0

LRMS (ES): Mass calcd for $C_{20}H_{17}N_5O_3$ $[M+H]^+$, 376. Found $[M+H]^+$, 376

$[\alpha]^{23.6}_D$ = +8.2° (c = 1.0, $CHCl_3$)
Enantiomeric excess (89% ee) was measured by HPLC (Chiralcel AD-H, 6% IPA/Hexanes, 1 mL/min, Rt_1 = 20.2, Rt_2 = 21.5



(*R*)-2-(methoxymethoxy)-2-(4-oxo-4-phenylbutan-2-yl)malononitrile (**3n**): Prepared according to general procedure using enone **1n** (68 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –30 °C for 20 h. Purified by flash column chromatography (SiO_2, 10% EtOAc/Hexanes) to afford 77 mg (96%) of **3n** as a colorless oil.

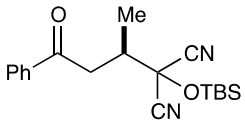
Analytical data for **3n**:
IR (film): 3062, 2973, 2941, 2906, 2849, 2832, 1688, 1598, 1582, 1449, 1365, 1289, 1215, 1166, 1109, 1045, 1001, 967, 940, 755, 690

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.97 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.65 – 7.57 (m, 1H), 7.50 (dd, *J* = 8.3, 7.2 Hz, 2H), 5.06 (s, 2H), 3.53 (s, 3H), 3.40 (dd, *J* = 16.3, 1.6 Hz, 1H), 3.18 – 3.05 (m, 2H), 1.34 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 196.1, 136.5, 133.8, 128.9 (x2), 128.2 (x2), 112.9, 112.6, 96.6, 70.2, 57.6, 39.7, 39.3, 15.2.

HRMS (MM) Mass calcd for $C_{15}H_{16}N_2O_3$ $[M+H]^+$, 295.1161. Found $[M+H]^+$, 295.1051

$[\alpha]^{23.6}_D$ = +20° (c 0.5, $CHCl_3$)
Enantiomeric excess (96% ee) was measured by HPLC (Chiralcel AS-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 10.1, Rt_2 = 10.96



(*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-(4-oxo-4-phenylbutan-2-yl)malononitrile (**5n**): Prepared according to general procedure using enone **1n** (67 mg, 0.36 mmol), MAC **4** (59 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –20 °C for 36 h. Purified by flash column chromatography (SiO_2, 5% Et_2O/Hexanes) to afford 100 mg (98%) of **5n** as a colorless oil.

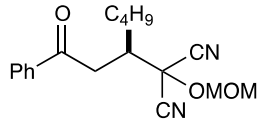
Analytical data for **5n**:
IR (film): 3088, 3063, 3030, 2956, 2933, 2898, 2887, 2861, 1690, 1598, 1582, 1472, 1464, 1449, 1391, 1364, 1286, 1265, 1213, 1182, 1153, 1132, 1107, 1044, 1026, 1002, 961, 877, 843, 813, 787, 754, 686

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.97 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.64 – 7.58 (m, 1H), 7.50 (dd, *J* = 8.3, 7.2 Hz, 2H), 3.42 – 3.32 (m, 1H), 3.08 – 2.97 (m, 2H), 1.29 (s, 3H), 1.28 (s, 1H), 0.93 (s, 9H), 0.40 (s, 3H), 0.38 (s, 3H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 196.2, 136.6, 133.8, 128.9 (x2), 128.2 (x2), 114.8, 114.6, 68.1, 41.0, 39.5, 25.3 (x3), 18.2, 14.9, -4.5 (x2)

LRMS (ES): Mass calcd for $C_{19}H_{26}N_2O_2Si$ $[M–CN]^+$, 316. Found $[M+H]^+$, 316

$[\alpha]^{23.6}_D$ = +23.6° (c = 1.0, $CHCl_3$)
Enantiomeric excess (94% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 4.5, Rt_2 = 5.4



(*R*)-2-(methoxymethoxy)-2-(1-oxo-1-phenylheptan-3-yl)malononitrile (**3o**): Prepared according to general procedure using enone **1o** (68 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –30 °C for 28 h. Purified by flash column chromatography (SiO_2, 15% EtOAc/Hexanes) to afford 91 mg (96%) of **3o** as a colorless oil.

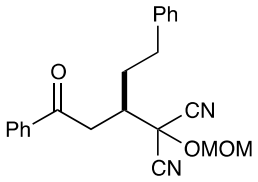
Analytical data for **3o**:
IR (film): 3062, 2959, 2936, 2872, 2832, 1690, 1653, 1598, 1581, 1466, 1449, 1419, 1363, 1319, 1280, 1220, 1165, 1108, 1067, 1031, 1002, 976, 932, 757, 690

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.98 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.63 – 7.58 (m, 1H), 7.50 (dd, *J* = 8.4, 7.1 Hz, 2H), 5.00-4.97 (m, 2H), 3.47 (s, 3H), 3.34 (dd, *J* = 17.5, 4.6 Hz, 1H), 3.21 (dddd, *J* = 9.7, 6.3, 4.6, 3.6 Hz, 1H), 3.08 (dd, *J* = 17.4, 6.2 Hz, 1H), 1.94 – 1.85 (m, 1H), 1.60 – 1.50 (m, 1H), 1.44 – 1.28 (m, 3H), 0.89 (t, *J* = 7.1 Hz, 3H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 196.3, 136.5, 133.7, 128.9 (x2), 128.2 (x2), 113.2, 112.8, 96.4 (t, *J* = 2.0 Hz), 70.2, 57.5 (q, *J* = 1.7 Hz), 43.2, 38.6, 30.6, 29.2, 22.7, 13.9

LRMS (ES): Mass calcd for $C_{18}H_{22}N_2O_3$ $[M+Na]^+$, 337. Found $[M+Na]^+$, 337

$[\alpha]^{23.6}_D$ = –19.1° (c = 1.0, $CHCl_3$)
Enantiomeric excess (97% ee) was measured by HPLC (Chiralcel AS-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 7.97, Rt_2 = 8.4



(*R*)-2-(methoxymethoxy)-2-(1-oxo-1,5-diphenylpentan-3-yl)malononitrile (**3p**): Prepared according to general procedure using enone **1p** (85 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –30 °C for 24 h. Purified by flash column chromatography (SiO_2, 15% EtOAc/Hexanes) to afford 107 mg (98%) of **3p** as a colorless oil.

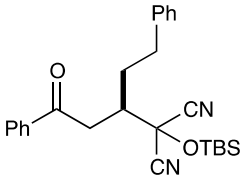
Analytical data for **3p**:
IR (film): 3086, 3062, 3028, 3004, 2938, 2865, 2832, 1689, 1598, 1582, 1497, 1449, 1418, 1362, 1281, 1218, 1164, 1105, 1091, 1076, 1033, 1002, 924, 755, 700, 691

^{1}H NMR (500 MHz; $CDCl_3$) δ 8.04 – 7.97 (m, 2H), 7.66 – 7.60 (m, 1H), 7.52 (t, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.24 – 7.17 (m, 3H), 5.02 (t, J = 7.4 Hz, 1 H), 5.01 (t, J = 7.4 Hz, 1H), 3.49 (s, 3H), 3.43 (dd, *J* = 17.4, 4.4 Hz, 1H), 3.34-3.29 (m, 1H), 3.20 (dd, *J* = 17.4, 6.5 Hz, 1H), 2.77 (t, *J* = 8.2 Hz, 2H), 2.30 – 2.18 (m, 1H), 1.96 – 1.84 (m, 1H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 196.0, 140.5, 136.3, 133.7, 128.9 (x2), 128.6 (x2), 128.4 (x2), 128.2 (x2), 126.4, 113.0, 112.7, 96.4 (t, *J* = 1.6 Hz), 70.0, 57.5 (q, *J* = 1.5 Hz), 43.0, 38.7, 33.5, 32.8

LRMS (ES): Mass calcd for $C_{22}H_{22}N_2O_3$ $[M+H]^+$, 363. Found $[M+H]^+$, 363

$[\alpha]^{23.6}_D$ = –8.2° (c 0.33, $CHCl_3$)
Enantiomeric excess (96% ee) was measured by HPLC (Chiralcel IA, 3% IPA/Hexanes, 1 mL/min, Rt_1 = 11.6, Rt_2 = 12.3



(*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-(1-oxo-1,5-diphenylpentan-3-yl)malononitrile (**5p**): Prepared according to general procedure using enone **1p** (85 mg, 0.36 mmol), MAC **4** (59 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –20 °C for 36 h. Purified by flash column chromatography (SiO_2, 5% Et_2O/Hexanes) to afford 120 mg (92%) of **5p** as a colorless oil.

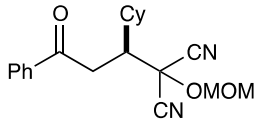
Analytical data for **5p**:
IR (film): 3087, 3063, 3028, 2954, 2932, 2898, 2887, 2861, 1690, 1598, 1582, 1497, 1472, 1464, 1449, 1363, 1265, 1217, 1134, 1003, 844, 787, 753, 698, 690

^{1}H NMR (500 MHz; $CDCl_3$) δ 8.02 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.67 – 7.60 (m, 1H), 7.53 (t, *J* = 7.8 Hz, 2H), 7.33 – 7.26 (m, 2H), 7.25 – 7.16 (m, 3H), 3.44 (dd, *J* = 17.5, 4.1 Hz, 1H), 3.25 (ddt, *J* = 8.8, 7.6, 3.8 Hz, 1H), 3.15 (dd, *J* = 17.5, 6.7 Hz, 1H), 2.77 (t, *J* = 8.2 Hz, 3H), 2.26 – 2.15 (m, 1H), 1.91 – 1.79 (m, 1H), 0.91 (s, 9H), 0.42 (s, 3H), 0.35 (s, 3H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 195.9, 140.6, 136.3, 133.7, 128.9 (x2), 128.6 (x2), 128.4 (x2), 128.2 (x2), 126.4, 115.0, 114.7, 67.9, 44.4, 38.6, 33.6, 32.7, 25.3 (x3), 18.1, -4.52 (x2)

LRMS (ES): Mass calcd for $C_{26}H_{32}N_2O_2Si$ $[M–CN]^+$, 406. Found $[M–CN]^+$, 406

$[\alpha]^{23.6}_D$ = –7.2° (c = 1.0, $CHCl_3$)
Enantiomeric excess (94% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 9.4, Rt_2 = 10.3



(*S*)-2-(1-cyclohexyl-3-oxo-3-phenylpropyl)-2-(methoxymethoxy)malononitrile (**3q**): Prepared according to general procedure using enone **1q** (77 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at 23 °C for 24 h. Purified by flash column chromatography (SiO_2, 15% EtOAc/Hexanes) to afford 96 mg (94%) of **3q** as a colorless oil.

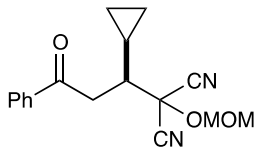
Analytical data for **3q**:
IR (film): 3061, 2930, 2854, 1690, 1598, 1581, 1449, 1380, 1276, 1221, 1181, 1106, 1076, 1017, 984, 929, 758, 690

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.99 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.64 – 7.58 (m, 1H), 7.50 (dd, *J* = 8.4, 7.0 Hz, 2H), 4.99 (d, *J* = 7.2 Hz, 1H), 4.96 (d, *J* = 7.2 Hz, 1H), 3.46 (s, 3H), 3.29 – 3.21 (m, 2H), 3.20-3.17 (m, 1H), 1.99-1.92 (m, 2H), 1.81 – 1.72 (m, 3H), 1.70 – 1.62 (m, 1H), 1.38 – 1.22 (m, 2H), 1.22 – 1.01 (m, 3H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 196.5, 136.4, 133.6, 128.9 (x2), 128.2 (x2), 113.2, 113.2, 96.2 69.4, 57.5 (m), 47.7, 39.0, 35.2, 32.6, 28.7, 26.6, 26.3, 26.0

LRMS (ES): Mass calcd for $C_{20}H_{24}N_2O_3$ $[M+Na]^+$, 363. Found $[M+Na]^+$, 363

$[\alpha]^{23.6}_D$ = –14.8° (c = 1.0, $CHCl_3$)
Enantiomeric excess (89% ee) was measured by HPLC (Chiralcel AD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 15.3, Rt_2 = 16.3



(*S*)-2-(1-cyclopropyl-3-oxo-3-phenylpropyl)-2-(methoxymethoxy)malononitrile (**3r**): Prepared according to general procedure using enone **1r** (62 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –30 °C for 24 h. Purified by flash column chromatography (SiO_2, 15% EtOAc/Hexanes) to afford 88 mg (98%) of **3r** as a colorless oil.

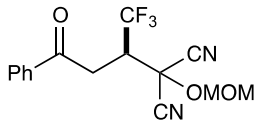
Analytical data for **3r**:
IR (film): 3087, 3067, 3009, 2962, 2940, 2849, 2832, 1688, 1597, 1581, 1449, 1361, 1276, 1216, 1165, 1109, 1096, 1028, 1002, 988, 964, 939, 923, 752, 690

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.97 (dd, *J* = 8.0, 1.4 Hz, 2H), 7.63 – 7.57 (m, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 5.01 (dd, *J* = 7.2, 0.8 Hz, 1H), 4.98 (dd, *J* = 7.2, 0.8 Hz, 1H), 3.46 (d, *J* = 0.9 Hz, 3H), 3.41 (dd, *J* = 16.8, 4.6 Hz, 1H), 3.23 (dd, *J* = 16.7, 6.9 Hz, 1H), 2.55 (ddd, *J* = 9.9, 6.9, 4.6 Hz, 1H), 1.00 (dtt, *J* = 10.1, 8.0, 4.9 Hz, 1H), 0.87 – 0.79 (m, 1H), 0.79 – 0.71 (m, 1H), 0.58 – 0.48 (m, 1H), 0.36 (dddd, *J* = 9.5, 5.9, 4.8, 1.0 Hz, 1H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 196.5, 136.7, 133.6, 128.9 (x2), 128.2 (x2), 113.2, 112.8, 96.3 (t, *J* = 1.4 Hz), 69.8, 57.5-57.4 (m), 48.0, 39.3, 12.6, 6.7, 3.2

LRMS (ES): Mass calcd for $C_{17}H_{18}N_2O_3$ $[M+H]^+$, 299. Found $[M+H]^+$, 299

$[\alpha]^{23.6}_D$ = +48.6° (c = 1.0, $CHCl_3$)
Enantiomeric excess (97% ee) was measured by HPLC (Chiralcel AS-H, 3% IPA/Hexanes, 1 mL/min, Rt_1 = 9.3, Rt_2 = 10.9



(*R*)-2-(methoxymethoxy)-2-(1,1,1-trifluoro-4-oxo-4-phenylbutan-2-yl)malononitrile (**3s**): Prepared according to general procedure using enone **1s** (72 mg, 0.36 mmol), MAC **2** (38 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –30 °C for 24 h. Purified by flash column chromatography (SiO_2, 15% EtOAc/Hexanes) to afford 97 mg (99%) of **3s** as a colorless oil.

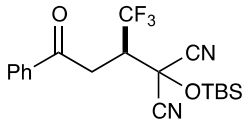
Analytical data for **3s**:
IR (film): 3064, 2947, 2851, 2835, 1694, 1598, 1582, 1450, 1380, 1359, 1380, 1276, 1185, 1168, 1139, 1107, 1092, 1043, 1023, 968, 924, 758, 741, 689

^{1}H NMR (500 MHz; $CDCl_3$) δ 8.00 (dt, *J* = 8.5, 1.4 Hz, 2H), 7.69 – 7.62 (m, 1H), 7.57 – 7.50 (m, 2H), 5.10 (d, *J* = 7.3 Hz, 1H), 5.08 (d, *J* = 7.2 Hz, 1H), 4.28 (qdd, *J* = 8.0, 6.1, 4.4 Hz, 1H), 3.56 (dd, *J* = 18.3, 6.1 Hz, 1H), 3.52 (s, 3H), 3.42 (ddd, *J* = 18.3, 4.4, 1.2 Hz, 1H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 192.6, 135.3, 134.4, 129.1 (x2), 128.4 (x2), 125.2, 123.0, 111.3, 111.1, 96.8, 64.6, 57.8, 57.8, 46.8 (q, *J* = 28.1 Hz), 34.1 (q, *J* = 1.4 Hz)

LRMS (ES): Mass calcd for $C_{15}H_{13}F_3N_2O_3$ $[M+H]^+$, 327. Found $[M+H]^+$, 327

$[\alpha]^{23.6}_D$ = +0.4° (c = 1.0, $CHCl_3$)
Enantiomeric excess (94% ee) was measured by HPLC (Chiralcel AD-H, 4% IPA/Hexanes, 1 mL/min, Rt_1 = 7.9, Rt_2 = 8.6



(*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-(1,1,1-trifluoro-4-oxo-4-phenylbutan-2-yl)malononitrile (**5s**): Prepared according to general procedure using enone **1s** (72 mg, 0.36 mmol), MAC **4** (59 mg, 0.30 mmol), and catalyst **VIc** (7.1 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) at –20 °C for 36 h. Purified by flash column chromatography (SiO_2, 5% Et_2O/Hexanes) to afford 110 mg (93%) of **5s** as a colorless oil.

Analytical data for **5s**:
IR (film): 2955, 2935, 2889, 2863, 1695, 1598, 1582, 1473, 1466, 1450, 1381, 1363, 1357, 1266, 1230, 1217, 1184, 1144, 1121, 1095, 1075, 1023, 1003, 958, 923

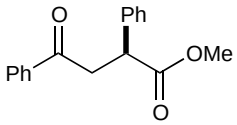
^{1}H NMR (500 MHz; $CDCl_3$) δ 8.00 (dt, *J* = 8.5, 1.6 Hz, 2H), 7.68 – 7.63 (m, 1H), 7.53 (tt, *J* = 7.4, 1.4 Hz, 2H), 4.19 (qdd, *J* = 8.1, 5.9, 4.3 Hz, 1H), 3.52 (dd, *J* = 18.5, 5.9 Hz, 1H), 3.36 (ddd, *J* = 18.5, 4.3, 1.2 Hz, 1H), 0.90 (s, 9H), 0.41 (s, 3H), 0.37 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 192.6, 135.4, 134.4, 129.1 (x2), 128.4 (x2), 125.4, 123.2, 113.4 (x2), 48.0 (q, *J* = 27.6 H), 34.0 (d, *J* = 1.9 Hz), 25.1 (x3), 18.2, -4.6 (x2)

LRMS (ES): Mass calcd for $C_{19}H_{23}F_3N_2O_2Si$ $[M–C_{18}H_{15}N_2Si]^+$, 228. Found $[M+H]^+$, 228

$[\alpha]^{23.6}_D$ = +2.8° (c 0.5, $CHCl_3$)
Enantiomeric excess (85% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 4.32 , Rt_2 = 4.87

Functionalization of 5a (TBS MAC adducts)



(*S*)-methyl 4-oxo-2,4-diphenylbutanoate (**7**): Adduct **5a** (66 mg, 0.163 mmol) was dissolved in 1.1 mL of THF. The reaction mixture was stirred at –30° C for 10 min before a 0.6 M solution of 3HF:Et_3N (37.2 mg, 0.22 mmol, in 0.37 mL THF) was added dropwise at –30 °C. The clear reaction mixture was stirred for 2 h at –30 °C and then diluted with 1 mL of MeOH. The reaction mixture was then cooled to –40 °C, and methanolic Et_3N (49.5 mg, 0.49 mmol, in 0.5 mL MeOH) was added dropwise. The reaction is stirred for an additional 45 min before allowing to warm to 0 °C. The reaction was then quenched with 2 ml 1 M HCl, extracted with Et_2O (5 mL, 2x), dried over $MgSO_4$, concentrated, and purified by flash column chromatography (SiO_2, 15% EtOAc/Hexanes) to afford 41 mg of **7** (93% yield) as a colorless oil.

Analytical data for **7**:
IR (film): 3087, 3063, 2954, 2932, 2899, 2887, 2861, 1690, 1598, 1582, 1497, 1472, 1464, 1449, 1415, 1363, 1265, 1217, 1134, 1003, 844, 787, 753, 698, 690

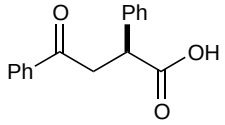
^{1}H NMR (500 MHz; $CDCl_3$) δ 7.98 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.60 – 7.54 (m, 1H), 7.48 – 7.43 (m, 1H),

7.39 – 7.33 (m, 2H), 7.33 – 7.27 (m, 1H), 4.31 (dd, *J* = 10.4, 4.0 Hz, 1H), 3.96 (dd, *J* = 18.1, 10.4 Hz, 1H), 3.70 (s, 2H), 3.28 (dd, *J* = 18.1, 4.0 Hz, 1H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 197.7, 173.9, 138.5, 136.5, 133.4, 129.0 (x2), 128.7 (x2), 128.2 (x2), 127.9 (x2), 127.7, 52.4, 46.5, 42.9

LRMS (ES): Mass calcd for $C_{17}H_{16}O_3$ $[M+Na]^+$, 291. Found $[M+H]^+$, 291

$[\alpha]^{23.6}_D$ = +110.1 (c = 1.0, $CHCl_3$)
Enantiomeric excess (96% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 15.1, Rt_2 = 15.9



(*S*)-4-oxo-2,4-diphenylbutanoic acid (**8**): In a one-dram vial equipped with a Teflon-coated magnetic stir bar, addcut **5a** (53 mg, 0.131 mmol) was dissolved in 5.24 ml of a 1:1:2 (H_2O (1.31 mL), THF (1.31 mL), AcOH (2.62 mL). In a separate vial, TBAF (0.16 mmol, 0.16 mL, 1M THF) was dissolved in a mixture of 0.5 mL THF and 0.64 mL H_2O. The resulting solution of TBAF (now 0.1 M in 1:1 THF:H_2O) was added dropwise to the solution of TBS-MAC Enone. The reaction was allowed to stir for 24 h and diluted with 4 mL of H_2O. The reaction mixture was extracted with Et_2O (5 mL, 2x), dried over $MgSO_4$, and purified by flash column chromatography (SiO_2: 25% EtOAc/Hexanes, 1% AcOH) to afford 31 mg of acid **8** (94 % yield) as a while solid.

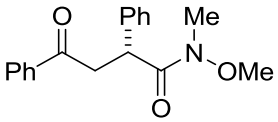
Analytical data for **8**:
IR (film): 2919, 1699, 1678, 1597, 1294, 1237, 1203, 757, 687

^{1}H NMR (500 MHz; $CDCl_3$) δ ^{1}H NMR (500 MHz , $CDCl_3$) □ = 7.96 (dd, *J* = 1.1, 8.4 Hz, 2 H), 7.61 - 7.48 (m, 1 H), 7.48 - 7.40 (m, 2 H), 7.40 - 7.26 (m, 5 H), 4.31 (dd, *J* = 4.3, 10.1 Hz, 1 H), 3.89 (dd, *J* = 10.1, 18.0 Hz, 1 H), 3.29 (dd, *J* = 4.3, 18.0 Hz, 1 H)

^{13}C NMR (125 MHz; $CDCl_3$) δ ^{13}C NMR (125 MHz ,$CDCl_3$) □ = 197.5, 179.2, 137.9, 136.5, 133.6, 129.2, 128.8, 128.3, 128.2, 128.0, 46.5, 42.5

HRMS (MM) Mass calcd for $C_{16}H_{14}O_3$ $[M–H_2O]^+$, 236.0837. Found $[M–H_2O]^+$, 236.0815

$[\alpha]^{23.6}_D$ = +126° (c = 1.0, $CHCl_3$)
Enantiomeric excess (92% ee) was measured by HPLC (Chiralcel AD-H, 15% EtOH/Hexanes, 1.2 mL/min, Rt_1 = 15.9, Rt_2 = 18.2



(*R*)-*N*-methoxy-*N*-methyl-4-oxo-2,4-diphenylbutanamide (**10**): Adduct **5a** (50 mg, 0.124 mmol) (note: opposite enantiomer used here) was dissolved in 0.93 mL of THF. The reaction mixture was stirred at –30° C for 10 min before a 0.6 M solution of 3HF:Et_3N (27 mg, 0.174 mmol, in 0.29 mL THF) was added dropwise at –30 °C. The clear reaction mixture was stirred for 2 h at –30 °C. The reaction mixture was then cooled to –40 °C. In a separate test tube, *N*,*O*-dimethylhydroxylamine hydrochloride (24 mg, 0.25 mmol,) is suspended in 1.5 mL CH_2Cl_2 and treated with Et_3N (31 mg, 0.31 mmol) and stirred atambient temperature. Additional CH_2Cl_2 (0.4 mL) was added until fully dissolved. (It is important that the hydroxylamine is fully in solution, to avoid racemization). The glycine solution was then added dropwise to the –40 °C reaction mixture. Additional Et_3N (31 mg, 0.31 mmol) was then added and the reaction was stirred for an additional 60 min before warming to 0 °C. The reaction was then quenched with 2 ml sat. NH_4Cl, extracted with EtOAc (5 mL, 2x), dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 25% EtOAc/Hexanes) to afford 36 mg of **10** (98% yield) as a white solid.

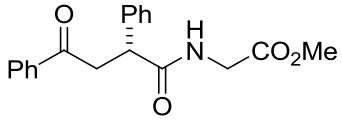
Analytical data for **10**:
IR (film): 3061, 3029, 2970, 2938, 2908, 1684, 1656, 1598, 1581, 1495, 1449, 1419, 1387, 1359, 1336, 1248, 1205, 1179, 1009, 984, 756, 746, 700, 691

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.98 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.56 – 7.51 (m, 1H), 7.43 (dd, *J* = 8.4, 7.1 Hz, 2H), 7.41 – 7.37 (m, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.24 (m, 1H), 4.80 – 4.68 (m, 1H), 4.09 (dd, *J* = 18.0, 10.7 Hz, 1H), 3.67 (s, 3H), 3.19 (s, 3H), 3.14 (dd, *J* = 18.0, 3.5 Hz, 1H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 198.5, 173.5, 139.4, 136.7, 133.2, 128.9 (x2), 128.6 (x2), 128.2 (x2), 128.1 (x2), 127.3, 61.2, 43.4, 43.2, 32.4

LRMS (ES): Mass calcd for $C_{18}H_{19}NO_3$ $[M+Na]^+$, 298. Found $[M+Na]^+$, 320

$[\alpha]^{23.6}_D$ = –151.4° (c = 1.0, $CHCl_3$)
Enantiomeric excess (95% ee) was measured by HPLC (Chiralcel OD-H, 10% IPA/Hexanes, 1 mL/min, Rt_1 = 10.9, Rt_2 = 15.7



(*R*)-methyl 2-(4-oxo-2,4-diphenylbutanamido)acetate (**11**): Adduct **5a** (84 mg, 0.21 mmol) enone adduct (note: opposite enantiomer used) was dissolved in 1.56 mL of THF. The reaction mixture was stirred at –30° C for 10 min before a 0.6 M solution of 3HF:Et_3N (47 mg, 0.29 mmol, in 0.48 mL THF) was added dropwise at –30 °C. The clear reaction mixture was stirred for 2 h at –30 °C. The reaction mixture was then cooled to –40 °C. In a separate test tube, glycine hydrochloride (52 mg, 0.41 mmol,) is suspended in 2 mL CH_2Cl_2 and treated with Et_3N (53 mg, 0.52 mmol) and stirred at ambient temperature. Additional CH_2Cl_2 (0.4 mL) was added until glycine was fully dissolved. (It is important that glycine is fully in solution, to avoid racemization) The glycine solution was then added dropwise to the –40 °C reaction mixture. Additional Et_3N (53 mg, 0.52 mmol) was then added and the reaction was stirred for an additional 45 min before warming to 0 °C. The reaction was then quenched with 2 ml 1 M HCl, extracted with EtOAc (5 mL, 2x), dried over Na_2SO_4, concentrated, and purified by flash column chromatography (SiO_2, 25% EtOAc/Hexanes) to afford 63 mg of **11** (93% yield) as a white solid.

Analytical data for **11**:
IR (film): 3327, 3061, 3029, 3004, 2952, 1752, 1683, 1598, 1539, 1449, 1437, 1368, 1207, 1181, 992, 755, 699

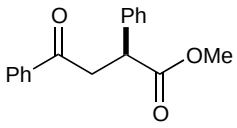
^{1}H NMR (500 MHz; $CDCl_3$) δ 7.95 (d, *J* = 7.8 Hz, 2H), 7.60 – 7.48 (m, 1H), 7.48 – 7.37 (m, 4H), 7.37 – 7.30 (m, 2H), 7.26 (t, *J* = 6.8 Hz, 2H), 6.42 (s, 1H), 4.28 (dd, *J* = 9.0, 4.7 Hz, 1H), 4.06 (ddd, *J* = 18.0, 9.0, 1.5 Hz, 1H), 3.97 (dd, *J* = 5.4, 2.6 Hz, 2H), 3.66 (d, *J* = 3.0 Hz, 3H), 3.29 – 3.16 (m, 1H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 198.1, 173.0, 170.2, 139.3, 136.6, 133.2, 128.98 (x2), 128.6 (x2), 128.2 (x2), 128.1 (x2), 127.6, 52.2, 47.5, 42.6, 41.6

LRMS (ES): Mass calcd for $C_{19}H_{19}NO_4$ $[M+Na]^+$, 348. Found $[M+H]^+$, 348

$[\alpha]^{23.6}_D$ = –79.0° (c =0.5, $CHCl_3$)
Enantiomeric excess (95% ee) was measured by HPLC (Chiralcel IA, 20% EtOH/Hexanes, 1 mL/min, Rt_1 = 21.98, Rt_2 = 32.9

Functionalization of 3a (from MOM MAC)



(*S*)-methyl 4-oxo-2,4-diphenylbutanoate (**7**): To a 1-dram vial was added adduct **3a** (53 mg, 0.159 mmol), 1:1 AcOH/DME (318 mL, 0.5 M), and (*R*)-CSA (18 mg, 0.0795 mmol). The vial was capped and the reaction was heated to 60 °C. After 2 h the reaction was completed as determined by ^{1}H NMR. The reaction mixture was cooled to ambient temperature, diluted with anhydrous MeOH (318 uL), and cooled to –40 °C. 1:1 MeOH/Et_3N (904 μL, 20.4 equiv. of Et_3N) was added dropwise over 10 min. After 1 h, the reaction was warmed to 0 °C. After 30 min at 0 °C, the reaction was slowly quenched with sat. aq. NH_4Cl. The mixture was extracted three times with CH_2Cl_2 and the combined organics were dried over anh. Na_2SO_4 and concentrated. Purified by flash column chromatography (SiO_2, 20→30% EtOAc/Hexanes) to afford 40 mg (93%) of 7 as a colorless oil.

Analytical data for **7**:
IR (film): 3086, 3062, 3004, 2951, 2919, 2849, 1735, 1685, 1597, 1582, 1496, 1449, 1436, 1398, 1363, 1349, 1336, 1295, 1257, 1229, 1204, 1166, 1091, 1076, 1023, 1002, 965, 850, 756, 698, 692

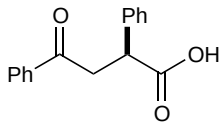
^{1}H NMR (500 MHz; $CDCl_3$) δ 8.00 – 7.96 (m, 2H), 7.57 (ddt, *J* = 8.6, 6.9, 1.3 Hz, 1H), 7.46 (ddt, *J* = 7.9, 6.5, 1.2 Hz, 2H), 7.38 – 7.33 (m, 4H), 7.32 – 7.27 (m, 1H), 4.31 (dd, *J* = 10.3, 4.0 Hz, 1H), 3.96 (dd, *J* = 18.0, 10.4 Hz, 1H), 3.70 (s, 3H), 3.28 (dd, *J* = 18.0, 4.0 Hz, 1H).

^{13}C NMR (125 MHz; $CDCl_3$) δ 197.7, 174.0, 138.5, 136.5, 133.44, 129.0 (x2), 128.7 (x2), 128.2 (x2), 127.9 (x2), 127.7, 52.5, 46.47, 42.9

LRMS (ES): Mass calcd for $C_{17}H_{16}O_3$ $[M+Na]^+$, 291. Found $[M+H]^+$, 291

$[\alpha]^{23.6}_D$ = +103.1° (c =1.0, $CHCl_3$)

Enantiomeric excess (96% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 24.7, Rt_2 = 26.7

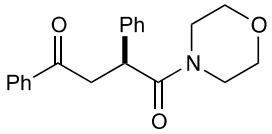


(*S*)-4-oxo-2,4-diphenylbutanoic acid (**8**): To an oven-dried 2-dram vial was added MAC adduct **3a** (117 mg, 0.350 mmol), (*R*)-CSA (407 mg) and 1:1 AcOH/H_2O (1.75 mL). The vial was sealed with a cap and heated to 60 °C. After 15 h the reaction was completed as judged by ^{1}H NMR. The reaction mixture was cooled to ambient temperature, at which point white solid started to crash out. The mixture was extracted three times with CH_2Cl_2 and dried over anh. Na_2SO_4. Puried by flash column chromatrography (SiO_2, 50% EtOAc/Hexanes) to afford an off-white solid (84 mg, 94%).

Analytical data for **8** is the same as the acid derived from TBS MAC **adduct** (**5a**).

[α]$^{23.6}_{D}$ = +131° (c = 1.0, $CHCl_3$)

Enantiomeric excess (94% ee) was measured by HPLC (Chiralcel AD-H, 15% EtOH/Hexanes, 1.2 mL/min, Rt_1 = 16.5, Rt_2 =18.0



(*S*)-1-morpholino-2,4-diphenylbutane-1,4-dione (**9**): To a 1-dram vial was added adduct **3a** (56 mg, 0.167 mmol), (*R*)-CSA (78 mg, 0.334 mmol), AcOH (19 uL, 0.334 mmol), and DME (334 uL). The vial was capped and the reaction was heated to 70 °C. After 2 h the conversion to cyanohydrin was completed as determined by ^{1}H NMR. The reaction mixture was cooled to ambient temperature, diluted with DME (1 mL), and cooled to –45 °C. 1:1 Morpholine/DME (74 uL, 2.5 equiv. of morpholine) was added dropwise over 1 min, then 1:1 Et_3N/DME (350 uL, 7.5 equiv. of Et_3N) was added dropwise over 7 min. After 10 min, the reaction was warmed to 0 °C. After 30 min at 0 °C, the reaction was slowly quenched with sat. aq. NH_4Cl. The mixture was extracted three times with CH_2Cl_2, and the combined organics were dried over anh. Na_2SO_4 and concentrated. Purified by flash column chromatography (SiO_2, 30% EtOAc/Hexanes) to afford 47 mg (94%) of **9** as an off-white residue which, over the course of two weeks, crystallized into an off-white solid.

Analytical data for **9**:
IR (film): 3060, 3027, 2962, 2919, 2855, 1684, 1645, 1457, 1449, 1436, 1360, 1269, 1234, 1205, 1179, 1114, 1030, 756, 702, 691

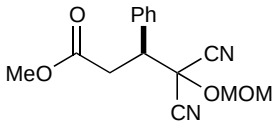
^{1}H NMR (500 MHz; $CDCl_3$) δ 7.98 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.54 (ddt, *J* = 7.9, 6.9, 1.3 Hz, 1H), 7.46 – 7.41 (m, 2H), 7.38 – 7.26 (m, 5H), 4.53 (dd, *J* = 9.9, 3.6 Hz, 1H), 4.14 (dd, *J* = 17.8, 9.9 Hz, 1H), 3.76 – 3.49 (m, 6H), 3.44 – 3.38 (m, 1H), 3.19 – 3.13 (m 1H), 3.07 (dd, *J* = 17.8, 3.7 Hz, 1H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 198.6, 170.9, 139.4, 136.7, 133.3, 129.3 (x2), 128.6 (x2), 128.3 (x2), 127.8 (x2), 127.5, 66.9, 66.4, 46.3, 44.3, 44.2, 42.8

LRMS (ES): Mass calcd for $C_{20}H_{21}NO_3$ $[M+Na]^+$, 346. Found $[M+H]^+$, 346

$[\alpha]^{23.6}_D$ = +124.9° (c = 1.0, $CHCl_3$)
Enantiomeric excess (94% ee) was measured by HPLC (Chiralcel OD-H, 10% IPA/Hexanes, 1 mL/min, Rt_1 = 16.4, Rt_2 = 18.7

Determination of absolute configuration



(*S*)-methyl 4,4-dicyano-4-(methoxymethoxy)-3-phenylbutanoate (**12**): To a 16 x 125 mm test tube was added CH_2Cl_2 (1.2 mL), enone **1m** (180 mg, 0.722 mmol), MAC **2** (76 mg, 0.60 mmol) and 120 mg of activated powdered 3 Å molecular sieves. The test tube was sealed with a rubber septum, purged with N_2, and was placed in a –10 °C bath for 10 min before catalyst **VIc** (14.2 mg, 0.03 mmol) was added as a solid. The reaction was resealed and stirred at –10 °C for 72 h and then diluted with 0.6 mL of MeOH. The reaction was then treated with methanolic Et_3N (60.7 mg, 0.6 mmol in 0.4 mL of MeOH). The reaction was warmed up to 0 °C and stirred for an additional 30 min. The reaction was quenched with 5 mL aq HCl (1M), and extracted with CH_2Cl_2 (5 mL, 2x), dried over Na_2SO_4, concentrated and purified by flash column chromatography (SiO_2: 10% EtOAc/Hexanes) to afford 160 mg of **12** (93%) as a clear oil.

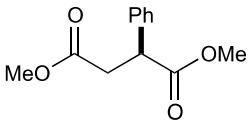
Analytical data for **12**:
IR (film): 3066, 3035, 3006, 2955, 2905, 2849, 2833, 1741, 1498, 1456, 1438, 1373, 1348, 1295, 1267, 1218, 1165, 1111, 1072, 1030, 971, 928, 896, 794, 774, 743, 702

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.47 – 7.42 (m, 2H), 7.41-7.35 (m, 3H), 5.04 (d, J = 7.2 Hz, 1H), 5.02 (d, J = 7.3 Hz, 1H), 3.95 (dd, *J* = 9.9, 4.8 Hz, 1H), 3.58 (s, 3H), 3.46 (s, 3H), 3.16 (dd, *J* = 16.2, 4.8 Hz, 1H), 3.07 (dd, *J* = 16.2, 9.9 Hz, 1H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 170.2, 133.5, 129.5 (x2), 129.4, 128.9 (x2), 112.5, 112.1, 96.6, 69.7, 57.4, 52.2, 50.3, 34.7

HRMS (MM) Mass calcd for $C_{15}H_{16}N_2O_4$ $[M]^-$ 288.111, Found $[M+Na]^-$288.1122

$[\alpha]^{23.6}_D$ = +25.5° (c = 1.0, $CHCl_3$)
Enantiomeric excess (88% ee) was measured by HPLC (Chiralcel AD-H, 7% IPA/Hexanes, 1 mL/min, Rt_1 = 7.0, Rt_2 = 7.8



(*S*)-dimethyl 2-phenylsuccinate (**13**): To a 1-dram vial was added **12** (60 mg, 0.208 mmol), 1:1 AcOH/MeOH (0.42 mL, 0.5 M), and (*R*)-CSA (24 mg, 0.104 mmol). The vial was capped and the reaction was heated to 60 °C. After 3 h, the reaction was completed as determined by ^{1}H NMR. The reaction mixture was cooled to ambient temperature, diluted with MeOH (1 mL), and cooled to –40 °C. A 1:1 MeOH/Et_3N (404 mg, 4.0 mmol, 19.3 equiv.of Et_3N, in 0.56 mL MeOH) was added dropwise over 10 minutes. After 1 h, the reaction was warmed to 0 °C. After 30 min at 0 °C, the reaction was slowly quenched with 5 mL HCl (1M). The mixture was extracted three times with Et_2O and the combined organics were dried over anh. $MgSO_4$, concentrated, and purified by flash column chromatography (SiO_2, 7% EtOAc/Hexanes) to afford 37 mg (80%) of **13** as a colorless oil.

Analytical data for **13**:

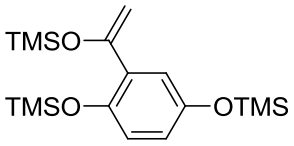
IR (film): 3088, 3064, 3031, 3004, 2953, 2848, 1734, 1700, 1684, 1653, 1559, 1497, 1456, 1437, 1338, 1296, 1252, 1231, 1197, 1161, 1094, 1073, 1006, 967, 858, 844, 778, 733, 698, 668

^{1}H NMR (500 MHz; $CDCl_3$) δ 7.36 – 7.30 (m, 2H), 7.30 – 7.25 (m, 3H), 4.09 (dd, *J* = 10.1, 5.2 Hz, 1H), 3.67 (s, 3H), 3.67 (s, 3H), 3.21 (dd, *J* = 17.0, 10.1 Hz, 1H), 2.67 (dd, *J* = 17.0, 5.2 Hz, 1H)

^{13}C NMR (125 MHz; $CDCl_3$) δ 173.5, 172.1, 137.8, 129.0 (x2), 127.8 (x3), 52.5, 52.0, 47.2, 37.7

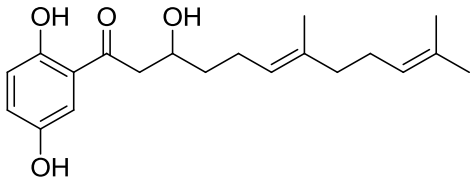
$[\alpha]^{23.6}_D$ = +102 °C (c = 0.5, MeOH) (lit. $[\alpha]^{20}_D$ = +124 (*c* 0.5, MeOH))[12]
Enantiomeric excess (87% ee) was measured by HPLC (Chiralcel IA, 1% IPA/Hexanes, 1 mL/min, Rt_1 = 15.7, Rt_2 = 19.4

Total Synthesis of Fornicin C



(2-(1-(trimethylsilyloxy)vinyl)-1,4-phenylene)bis(oxy)bis(trimethylsilane) (**15**): In a 50-mL round bottom flask equipped with a stir bar was added 2,5-dihydroxyacetophenone (365 mg, 2.4 mmol) and 20 mL of CH_2Cl_2. The reaction mixture was sealed with a rubber septum, purged with N_2, and placed in a –30° bath for 10 min. Et_3N (1.67 mL, 12 mmol) was added dropwise, turning the suspension to a yellow solution. TMSOTf (1.74 mL, 9.6 mmol) was then added dropwise via syringe. During the addition, the yellow reaction becomes clear. The reaction was allowed to warm up to –10 °C and stirred for an additional 30 min. The reaction was quenched with 4 mL of sat. aq. $NaHCO_3$, and stirred for an additional 5 min. The reaction mixture was transferred to a separatory funnel and washed with additional sat. aq. $NaHCO_3$ (2x, 10 mL), and brine (10 mL, 1x). The resulting organic phase was dried over Na_2SO_4, concentrated, and dried for 30 min in vacuum to afford silyl enol ether **15** (876 mg, 99%) which was used directly in the next step.

[12] Bettoni, G.; Cellucci, C.; Tortorella, V. *J. Heterocycl. Chem.* **1976**, 1053.



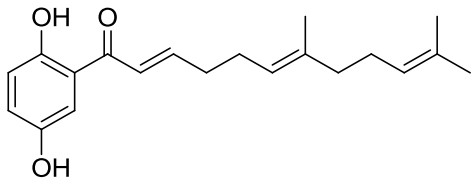
(E)-1-(2,5-dihydroxyphenyl)-3-hydroxy-7,11-dimethyldodeca-6,10-dien-1-one (**17**): In a 50-mL round bottom flask, **15** (876 mg, 2.4 mmol) was dissolved in 20 mL of CH_2Cl_2. Aldehyde **16**[8,9] (360 mg, 2 mmol), was added and the reaction was placed in a –78 °C bath. After stirring for 20 min, BF_3OEt_2 (0.37 mL, 3 mmol) was added dropwise over 5 min resulting in a bright yellow solution. The reaction was stirred for 1 h and then quenched slowly with Et_3N (0.56 mL, 4 mmol). Then sat. aq. $NaHCO_3$ (4 mL) was added and the reaction was allowed to warm to ambient temperature. The reaction mixture was transferred to a separatory funnel, and was diluted with 10 mL $NaHCO_3$ and 10 mL brine. The reaction mixture was extracted with CH_2Cl_2 (10 mL, 2x), concentrated on a rotary evaporator, redissolved in 10 ml of 4:1:1 THF:H_2O:AcOH and stirred for 20 min. The reaction was then diluted with 20 mL of CH_2Cl_2 and quenched slowly with 15 mL sat. aq. $NaHCO_3$. The mixture was extracted with CH_2Cl_2 (10 mL, 2x), dried over Na_2SO_4, concentrated and purified by column chromatography (SiO_2, 20% EtOAc/Hexanes) to afford 606 mg (90%) of **17** as a dark yellow oil.

Analytical data for **17**:
IR (film): 3357, 2924, 1644, 1621, 1485, 1445, 1376, 1267, 1174, 1062, 999, 826, 792, 739, 684

^{1}H NMR (500 MHz; $CDCl_3$) δ 1.48 - 1.72 (m, 11 H) 1.93 - 2.02 (m, 2 H) 2.02 - 2.10 (m, 2 H) 2.10 - 2.22 (m, 2 H) 2.98 - 3.11 (m, 2 H) 3.50 (br. s., 1 H) 4.22 - 4.32 (m, 1 H) 5.03 - 5.17 (m, 2 H) 6.62 (br. s., 1 H) 6.82 (d, *J*=8.85 Hz, 1 H) 7.00 (dd, *J*=8.85, 3.05 Hz, 1 H) 7.10 (d, *J*=3.05 Hz, 1 H) 11.67 (s, 1 H)

^{13}C NMR (125 MHz; $CDCl_3$) δ = 205.8, 156.5, 148.1, 136.5, 131.7, 125.8, 124.4, 123.4, 119.5, 119.3, 115.0, 67.9, 44.9, 39.9, 36.6, 26.8, 25.9, 24.2, 17.9, 16.2

HRMS (MM) Mass calcd for $C_{20}H_{28}O_4$ [M] , 332.1988. Found $[M]^-$, 332.1936



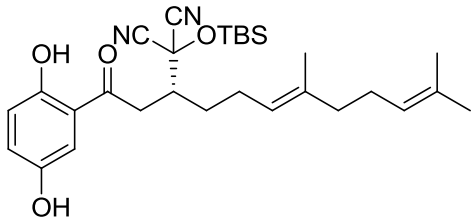
(2*E*,6*E*)-1-(2,5-dihydroxyphenyl)-7,11-dimethyldodeca-2,6,10-trien-1-one (**18**): **17** (70 mg, 0.23 mmol) was dissolved in 2 mL DMF. Sulfur trioxide pyridine complex (47 mg, 0.32 mmol) was dissolved in 1 mL of DMF, and added dropwise over 1.5 h via syringe pump. After an additional 1.5 h, ^{1}H NMR showed complete consumption of starting material to the sulfonated products. The reaction is placed in a 40 °C oil bath, and allowed to stir for 24 h. The light yellow solution turns dark yellow as the enone forms. The reaction is then diluted with 4 mL of H_2O, 3 mL of 1M HCl, extracted with Et_2O (5 ml, 3x), dried over $MgSO_4$, concentrated and purified by flash column chromatography (SiO_2, 10% EtOAc/Hexanes) to afford 47 mg (71%) of **18** as a dark yellow oil.

Analytical data for **18**:
IR (film): 3395, 2966, 2922, 2855, 1650, 1591, 1468, 1436, 1385, 1353, 1272, 1185, 831, 786

^{1}H NMR (500 MHz, $CDCl_3$) δ = 12.42 - 12.31 (m, 1 H), 7.31 - 7.23 (m, 1 H), 7.23 - 7.1 (m, 1 H), 7.04 (d, *J* = 7.0 Hz, 1 H), 6.93 (d, *J* = 15.3 Hz, 1 H), 6.89 (d, *J* = 8.5 Hz, 1 H), 5.74 - 5.53 (m, 1 H), 5.14 (t, *J* = 6.9 Hz, 1 H), 5.08 (t, *J* = 6.7 Hz, 1 H), 2.36 (q, *J* = 6.8 Hz, 2 H), 2.21 (q, *J* = 7.0 Hz, 2 H), 2.11 - 2.03 (m, 2 H), 2.03 - 1.95 (m, 2 H), 1.67 (s, 3 H), 1.64 - 1.56 (m, 6 H)

^{13}C NMR (125 MHz, $CDCl_3$) δ = 194.1, 157.6, 151.2, 147.9, 136.9, 131.7, 125.1, 124.3, 124.1, 122.7, 119.5, 119.4, 115.1, 39.8, 33.4, 26.8, 26.7, 25.8, 17.9, 16.3

HRMS (MM) Mass calcd for $C_{20}H_{26}NO_3$ [M^-], 314.1882. Found [M^-], 314.1867



(*E*)-2-(tert-butyldimethylsilyloxy)-2-(1-(2,5-dihydroxyphenyl)-7,11-dimethyl-1-oxododeca-6,10-dien-3-yl)malononitrile (**19**): Enone **18** (103 mg, 0.327 mmol) and MAC **4** (54 mg, 0.27 mmol) was dissolved in CH_2Cl_2 (0.6 mL). The reaction mixture was degassed 3x using freeze-pump-thaw method. The reaction was then sealed under N_2 and placed in a 0 °C bath. Catalyst **VIc** (6.4 mg, 0.014 mmol) was added as a solid to the reaction mixture. The reaction was stirred at 0 °C for 24 h. The reaction was then warmed to 10 °C for another 24 h. Finally, the reaction was warmed to ambient temperature and stirred for an additional 24h. The reaction was then quenched with 1 mL aq. HCl, and extracted with CH_2Cl_2, dried over Na_2SO_4, concentrated and purified by flash column chromatography (SiO_2, 10% EtOAc/Hexanes) to afford 145 mg (87%) of **19** as an orange oil.

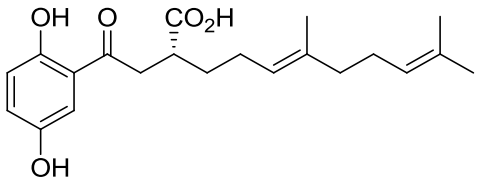
Analytical data for **19**:
IR (film): 3421, 2931, 2860, 1647, 1484. 1441, 1295, 1261, 1180, 1133, 842, 787

^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.71 (d, *J* = 1.5 Hz, 1 H), 7.21 (d, *J* = 2.7 Hz, 1 H), 7.06 (dd, *J* = 3.1, 8.9 Hz, 1 H), 6.90 (d, *J* = 9.2 Hz, 1 H), 5.30 (br. s., 1 H), 5.13 - 5.01 (m, 2 H), 3.30 (dd, *J* = 4.9, 17.7 Hz, 1 H), 3.17 - 3.07 (m, 1 H), 3.00 (dd, *J* = 5.8, 17.4 Hz, 1 H), 2.17 - 2.01 (m, 4 H), 2.00 - 1.92 (m, 2 H), 1.92 - 1.83 (m, 1 H), 1.73 - 1.64 (m, 3 H), 1.59 (s, 3 H), 1.54 (s, 4 H), 0.93 - 0.80 (m, 9 H), 0.38 (s, 3 H), 0.29 (s, 3 H)

^{13}C NMR (125 MHz, $CDCl_3$) δ = 201.6, 156.9, 148.0, 137.5, 131.7, 125.7, 124.3, 124.3, 122.3, 119.8, 118.8, 115.1, 114.8, 114.4, 68.1, 44.2, 39.8, 38.0, 30.7, 26.7, 25.9, 25.6, 25.3, 18.2, 17.9, 16.3, -4.4, -4.5

HRMS (MM) Mass calcd for $C_{29}H_{42}N_2O_4Si$ $[M+Na]^+$, 533.2812 Found $[M+Na]^+$, 533.281

$[\alpha]^{23.6}_D$ = –18° (c = 0.5, $CHCl_3$)
Enantiomeric excess (92% ee) was measured by HPLC (Chiralcel AD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 15.5, Rt_2 = 21.8



Fornicin C (**20**): MAC adduct **19** (47 mg, 0.092 mmol) was dissolved in 0.37 mL of 1:1:2 H_2O (0.92 mL):THF(0.92 mL):AcOH(1.84 mL). TBAF (0.11 mL, 1M THF), was dissolved in 0.4 mL THF, and 0.5 mL H_2O. The solution of TBAF (now 0.1 M in 1:1 THF:H_2O) was added dropwise to the solution of TBS adduct **19**. The reaction was allowed to stir for 24 h. The reaction mixture was diluted with 4 mL of H_2O, extracted with Et_2O (5 mL, 2x), dried over anh. $MgSO_4$, and purified by flash column chromatography (SiO_2: 20% EtOAc/Hexanes, 1% AcOH) to afford 30 mg of fornicin C (**20**) (91 % yield) as a light yellow solid.

Analytical data for **20**:
IR (film): 3357, 2966, 2923, 1708, 1626, 1486, 1442, 1375, 1273, 1178, 792

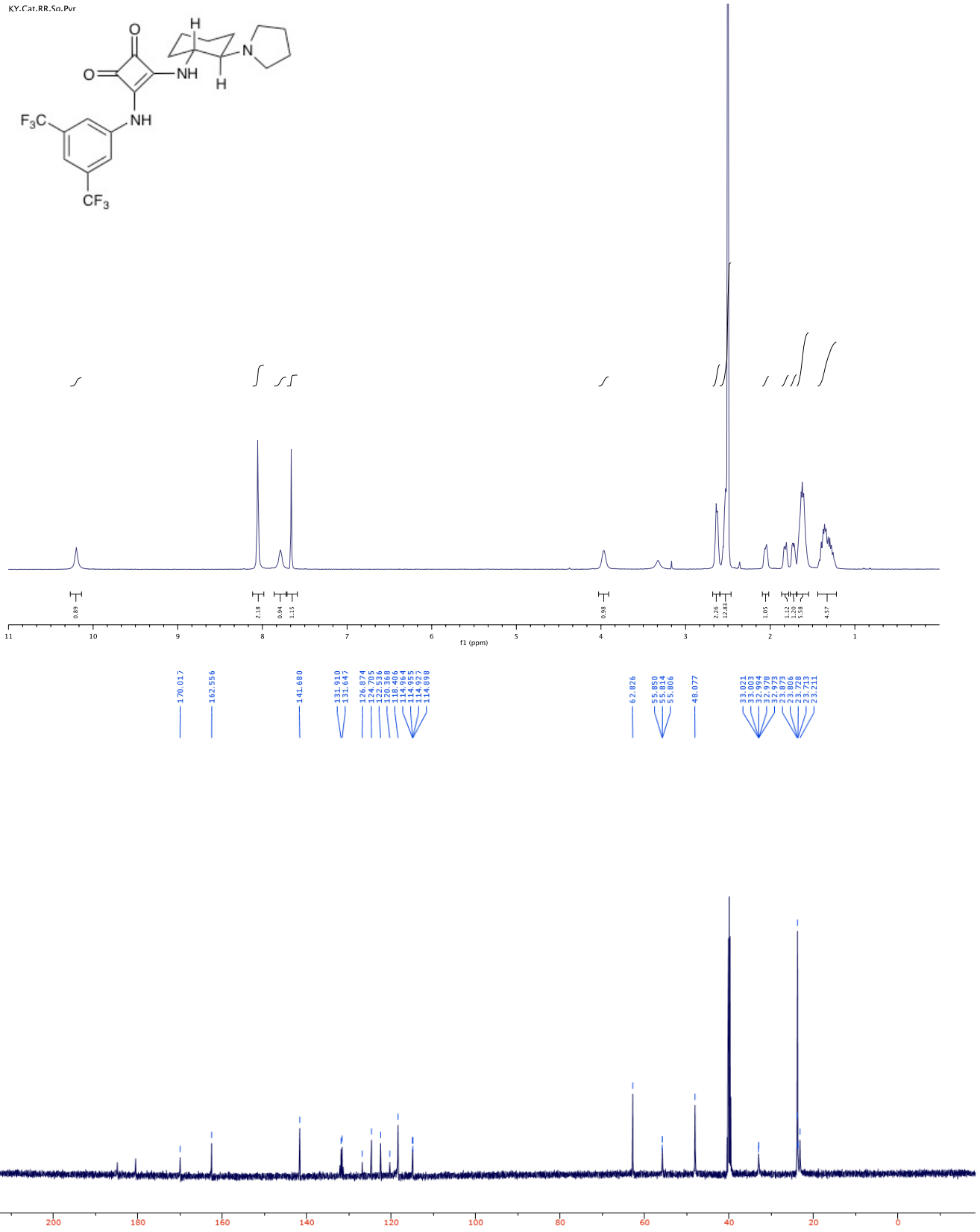
^{1}H NMR (500 MHz, d6-Acetone) δ = 11.59 (br. s., 1 H), 7.48 - 7.34 (m, 1 H), 7.09 (dd, *J* = 3.1, 8.9 Hz, 1 H), 6.81 (d, *J* = 8.9 Hz, 1 H), 5.22 - 5.14 (m, 1 H), 5.14 - 5.06 (m, 1 H), 3.52 (dd, *J* = 9.5, 18.0 Hz, 1 H), 3.20 (dd, *J* = 4.3, 18.0 Hz, 1 H), 3.08 - 2.99 (m, 1 H), 2.21 - 2.12 (m, 2 H), 2.12 - 2.06 (m, 2 H), 2.02 - 1.95 (m, 2 H), 1.80 (tdd, *J* = 6.8, 8.8, 13.5 Hz, 1 H), 1.72 - 1.66 (m, 1 H), 1.65 - 1.61 (m, 6 H), 1.59 (s, 3 H)

^{13}C NMR ^{13}C NMR (125 MHz, d6-Acetone) δ = 205.7, 176.5, 156.5, 150.2, 136.5, 131.7, 125.7, 125.1, 124.4, 120.0, 119.5, 115.5, 40.5, 40.4, 40.1, 32.7, 27.3, 26.2, 25.8, 17.7, 16.1

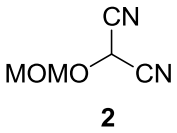
HRMS (MM): Mass calcd for $C_{21}H_{28}O_5$ $[M+Cl]^-$, 395.1625. Found $[M+Cl]^-$, 395.1622

$[\alpha]^{23.6}_D$ = +18° (c = 0.5, MeOH)
Enantiomeric excess (92% ee) was measured by HPLC (Chiralcel AD-H, 10% IPA/Hexanes, 1 mL/min, Rt_1 = 15.8, Rt_2 = 23.9

Selected NMR Spectra Catalyst **VIc**



MAC Reagents



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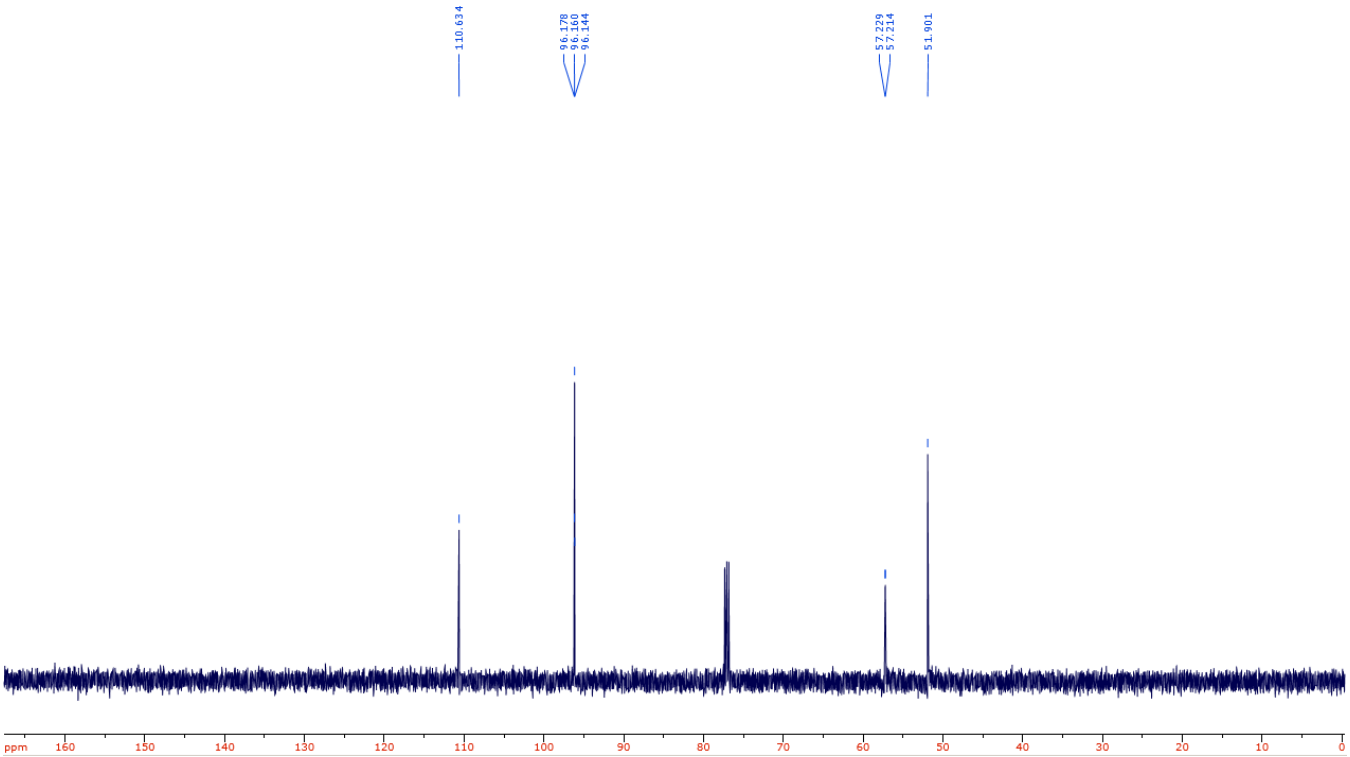

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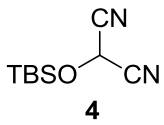
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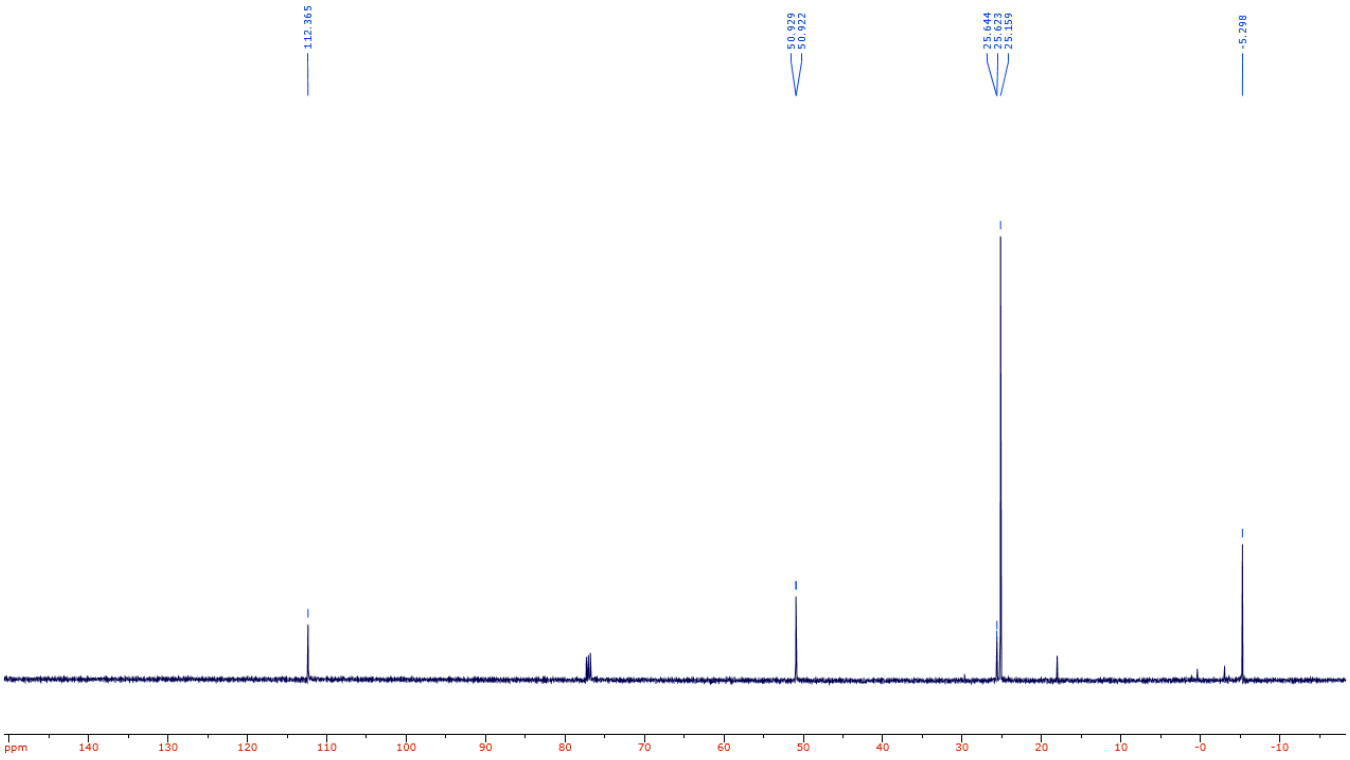
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Michael Addition Adducts

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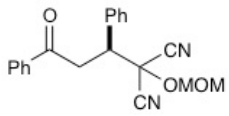

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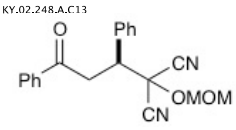
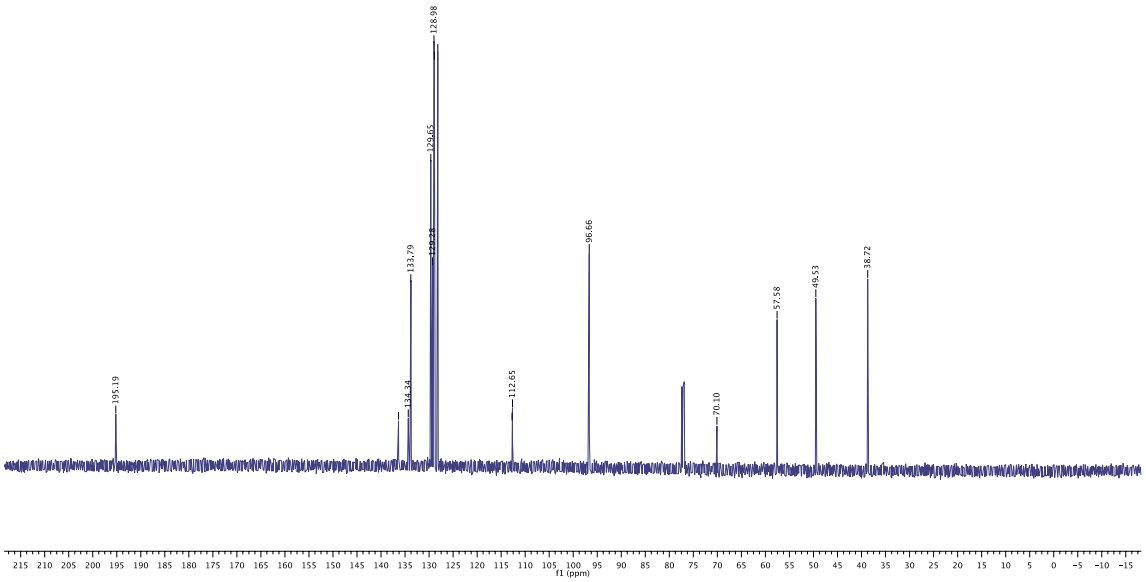
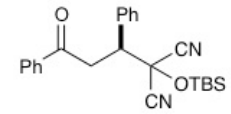
KY.02.248.A.C13



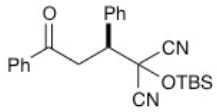


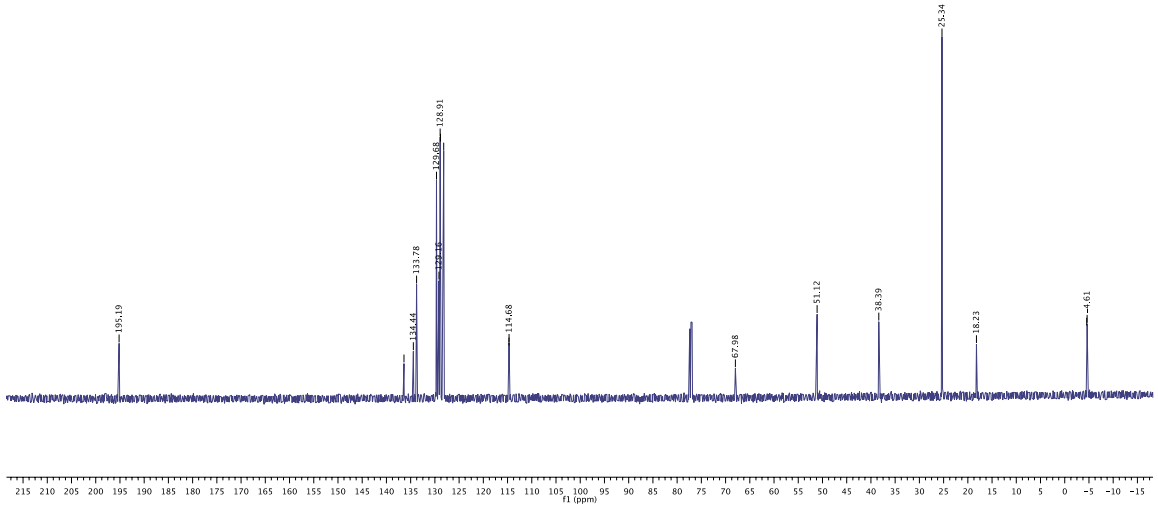
KY.02.256.TBS.1H



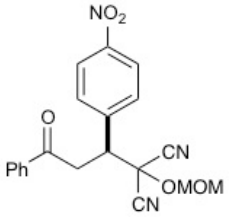
5a

KY.02.256.TBS.13C



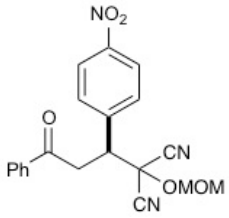


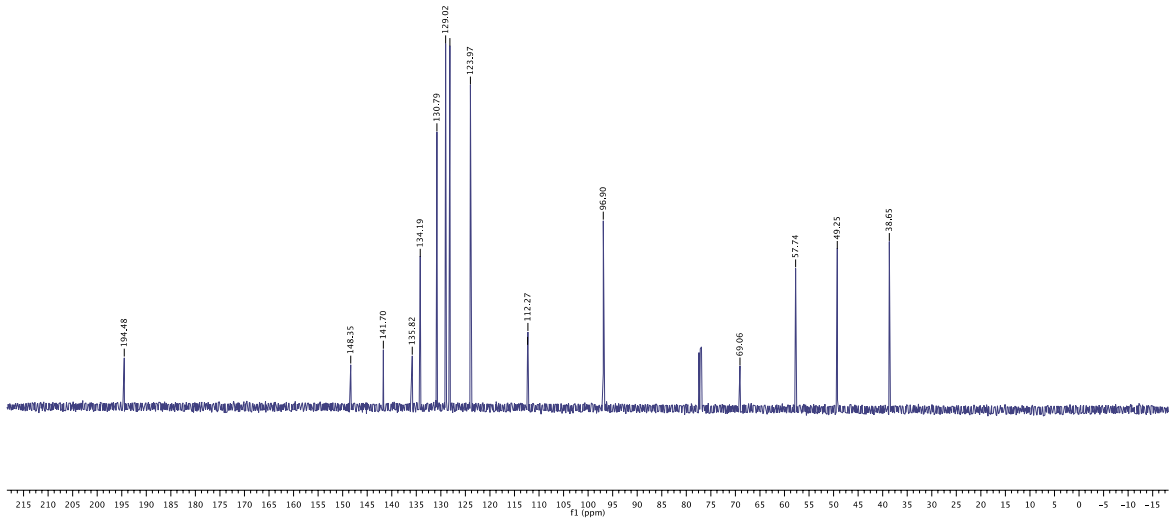
KY.02.249.A.1H

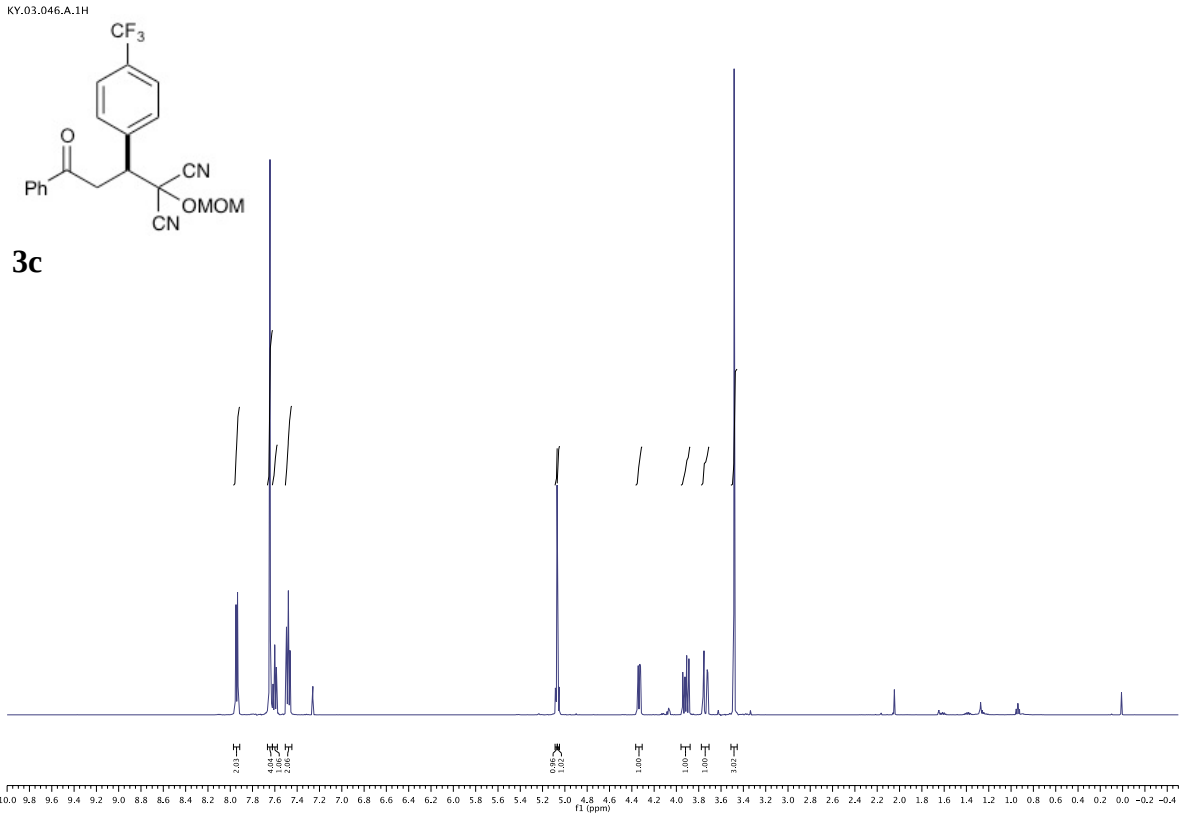


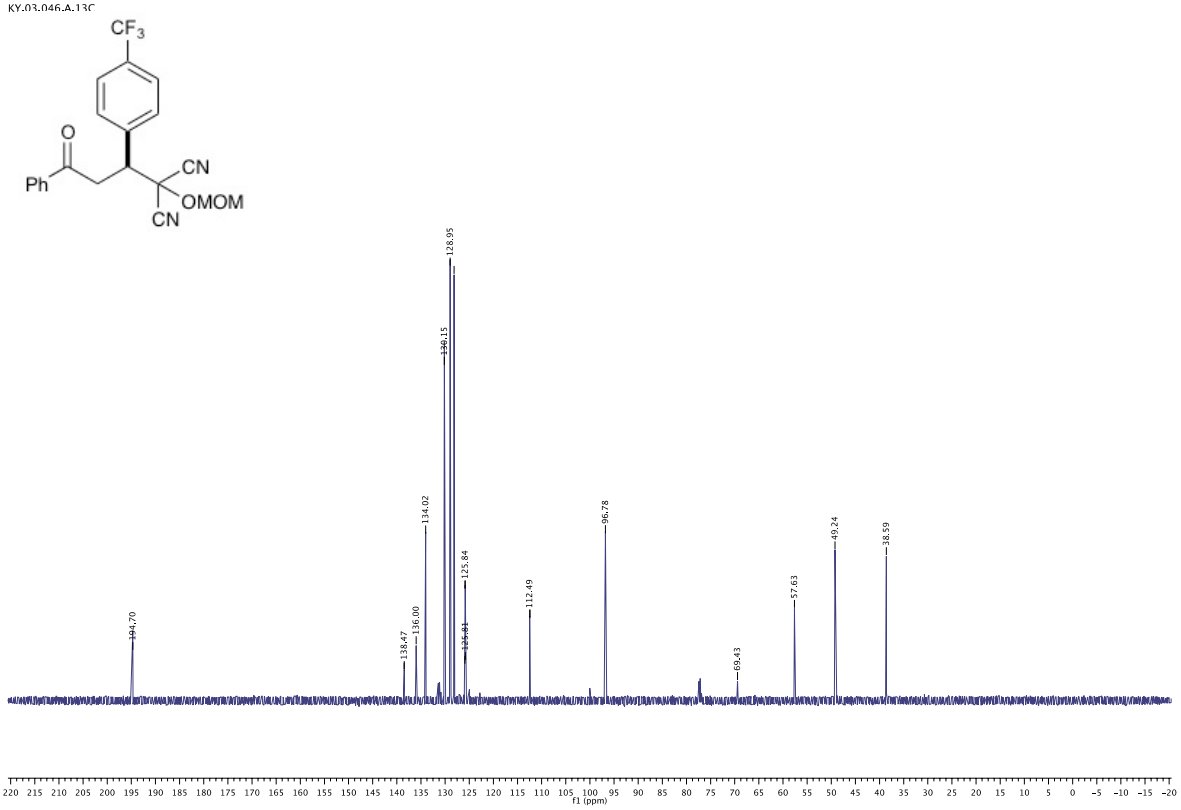
3b

KY.02.249.A.13C

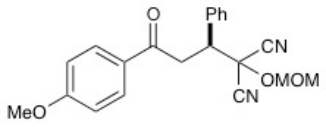





KY.03.046.A.1H
CF3
O
Ph
CN
OMOM
CN
3c
f1 (ppm)

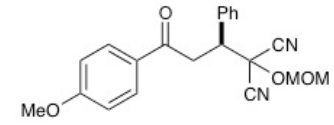

KY.03.046.A.13C
CF3
O
Ph
CN
OMOM
CN
194.70
138.47
136.00
134.02
130.15
128.95
125.84
125.81
112.49
96.78
69.43
57.63
49.24
38.59
f1 (ppm)

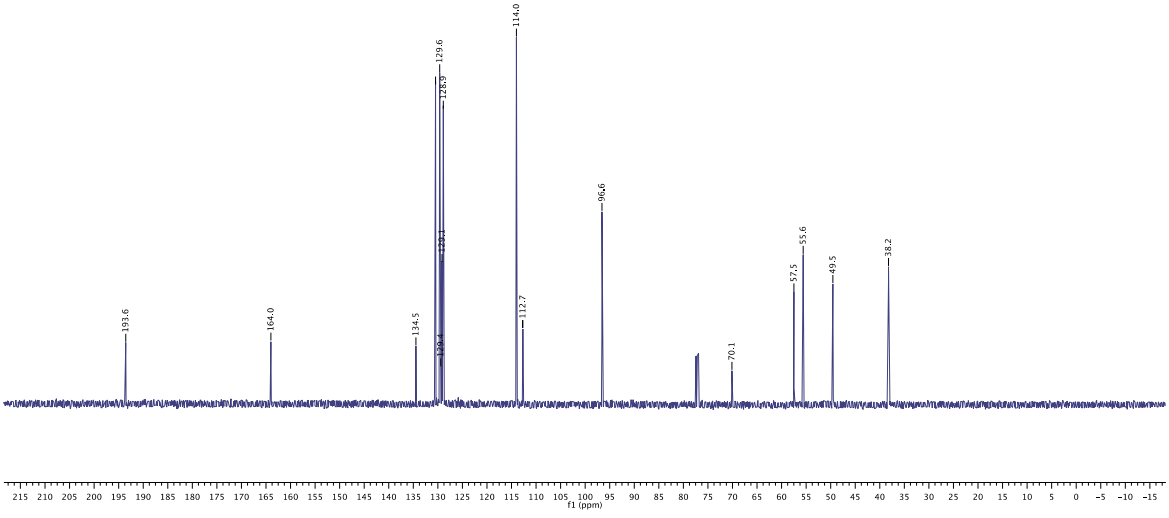
KY.03.050.A.1H

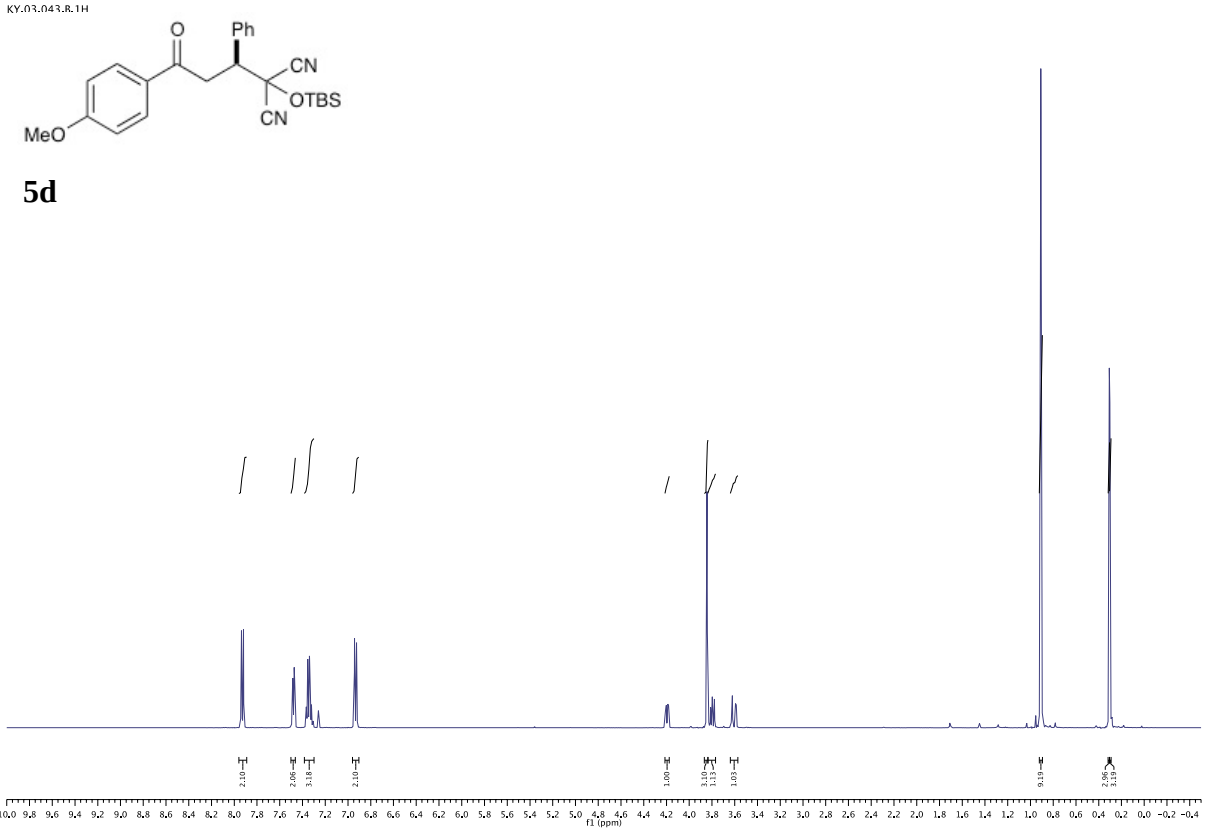


3d

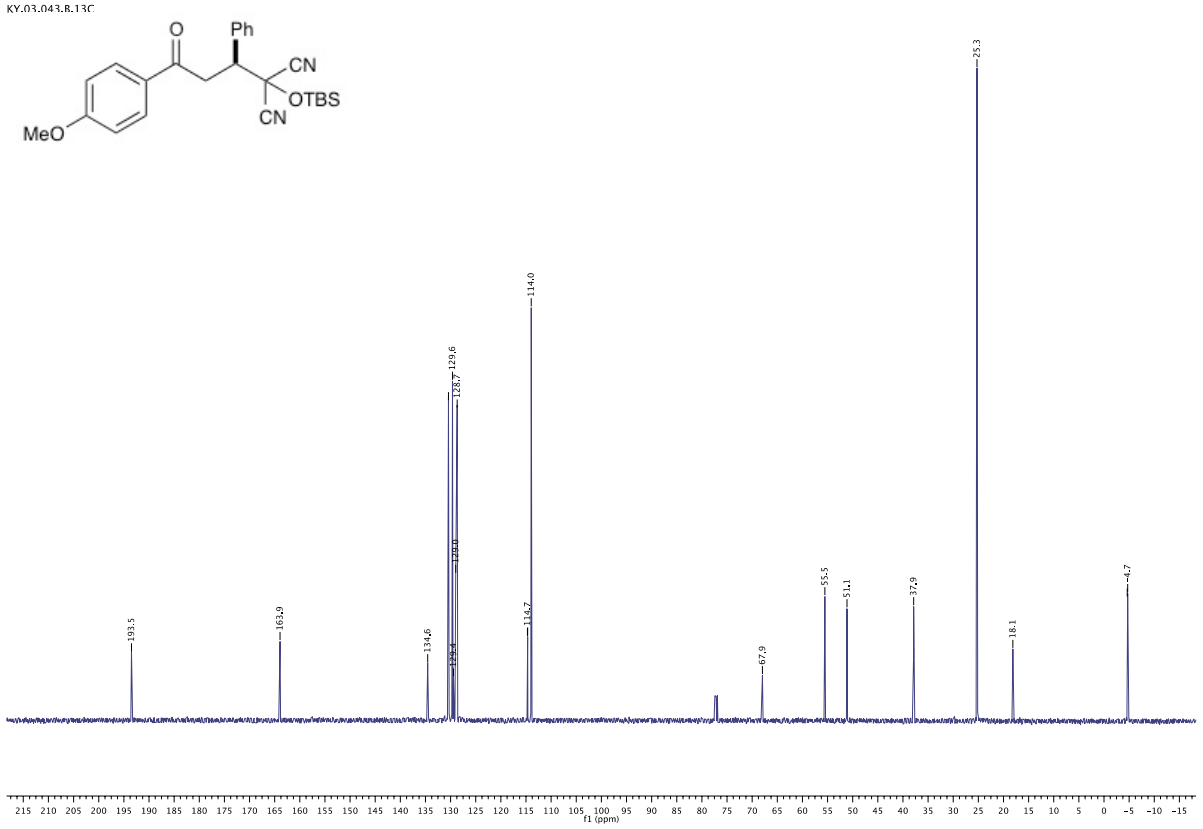
KY.03.050.A.13C



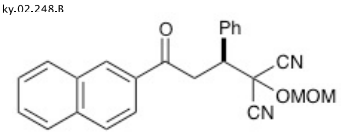



KY-03-043-R-1H
O
Ph
CN
OTBS
CN
MeO
f1 (ppm)

5d

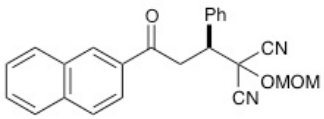

KY-03-043-R-13C
O
Ph
CN
OTBS
CN
MeO
193.5
163.9
134.6
129.6
128.7
114.0
114.7
67.9
55.5
51.1
37.9
25.3
18.1
-4.7
f1 (ppm)

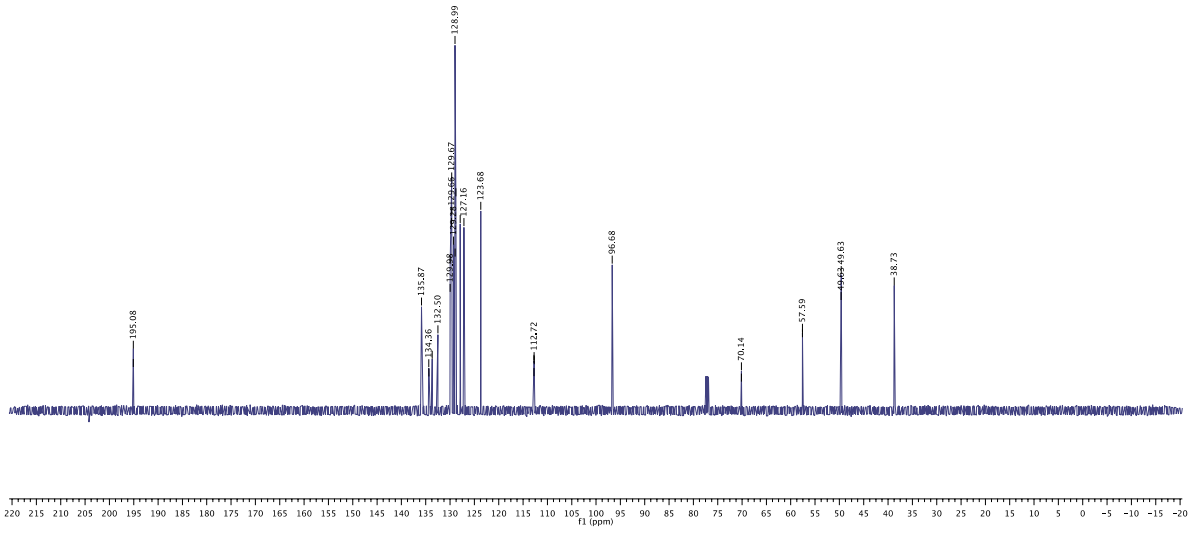
ky.02.248.B



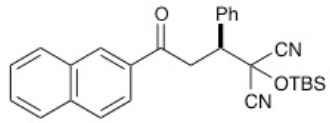
3e

ky.02.248.B.13C



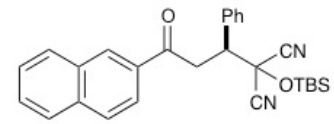


KY-03-038-R-1HC

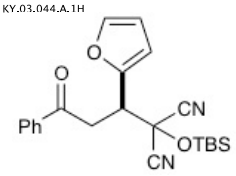


5e

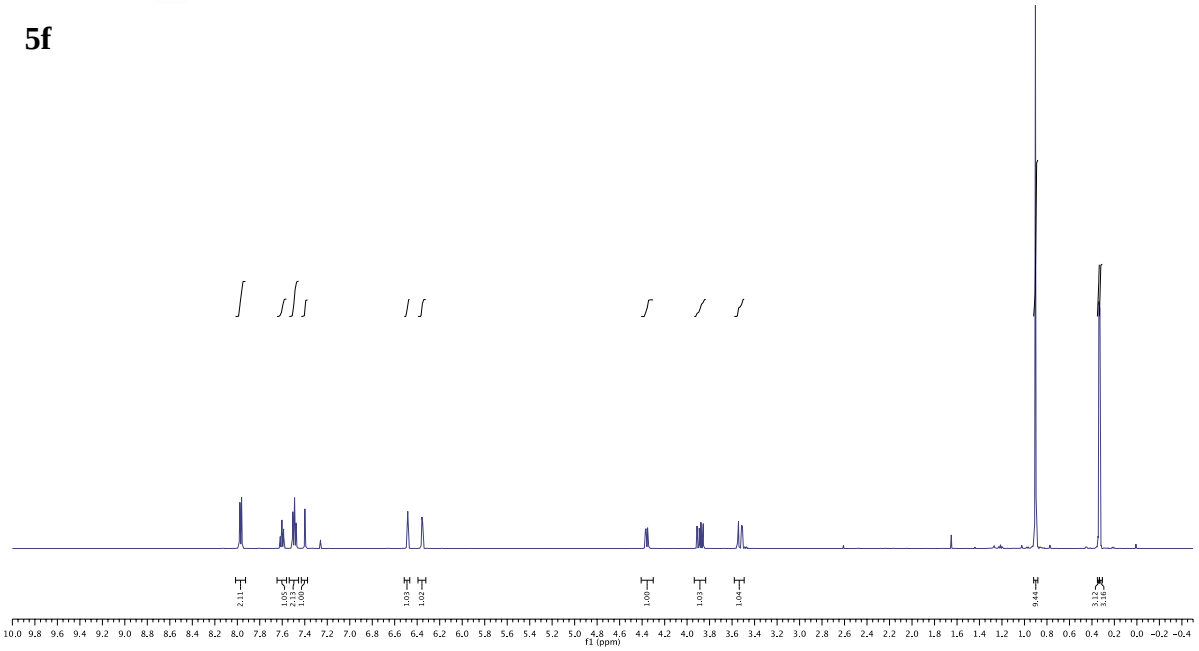
KY-03-038-R-13C



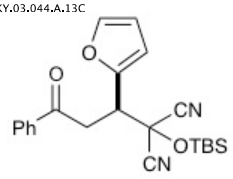
KY.03.044.A.1H



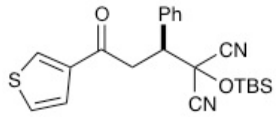
5f



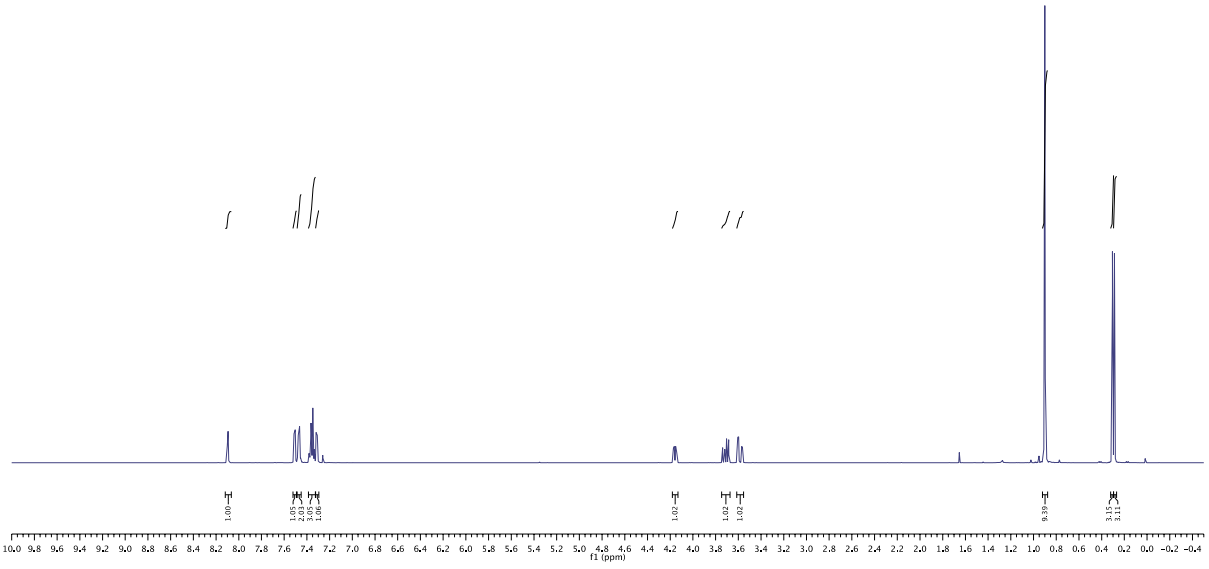
KY.03.044.A.13C



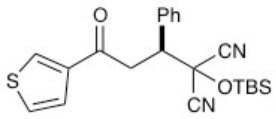
KY.03.042.C.1H

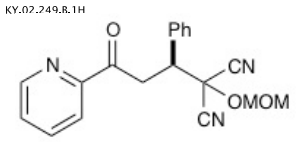


5g



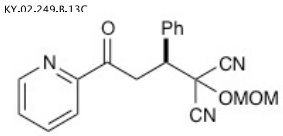
KY.03.042.C.13C

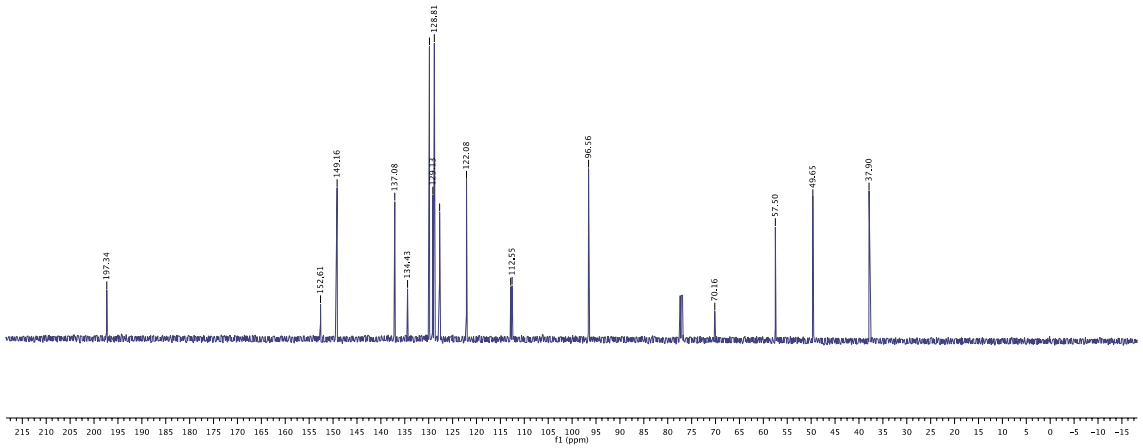



KY.02.249.R.1H
O
Ph
N
CN
OMOM
CN

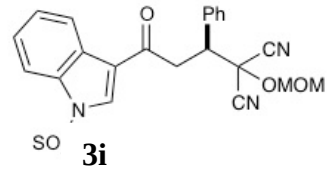
3h

0.97
0.97
1.01
2.08
1.00
3.09
0.98
1.01
2.05
1.00
2.82
f1 (ppm)


KY.02.249.R.13C
O
Ph
N
CN
OMOM
CN

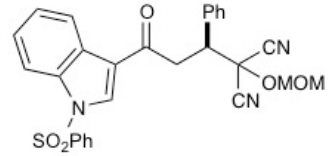

197.34
152.61
149.16
137.08
136.43
128.81
129.13
122.08
112.55
96.56
70.16
57.50
49.65
37.90
f1 (ppm)

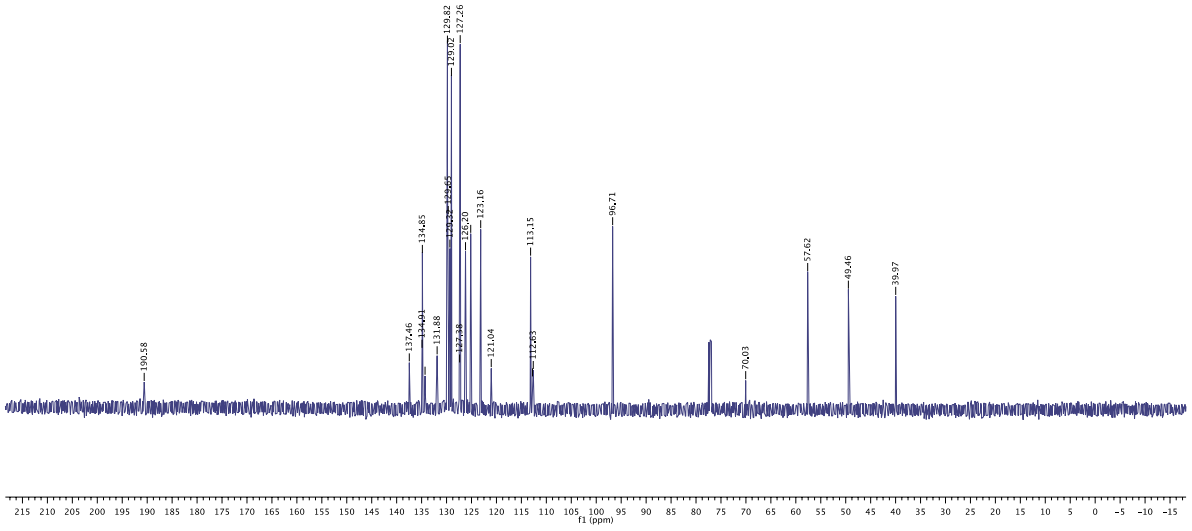
KY.03.050.B.1H



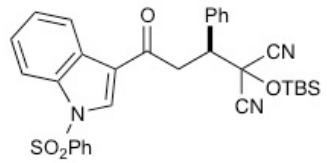
3i

KY.03.050.B.13C



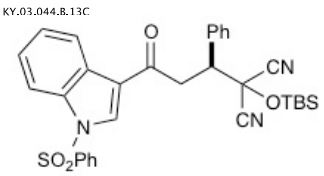


KY.03.044.B.1H

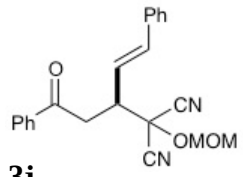


5i

KY.03.044.B.13C

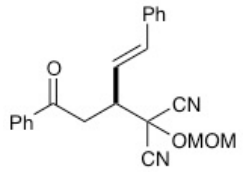


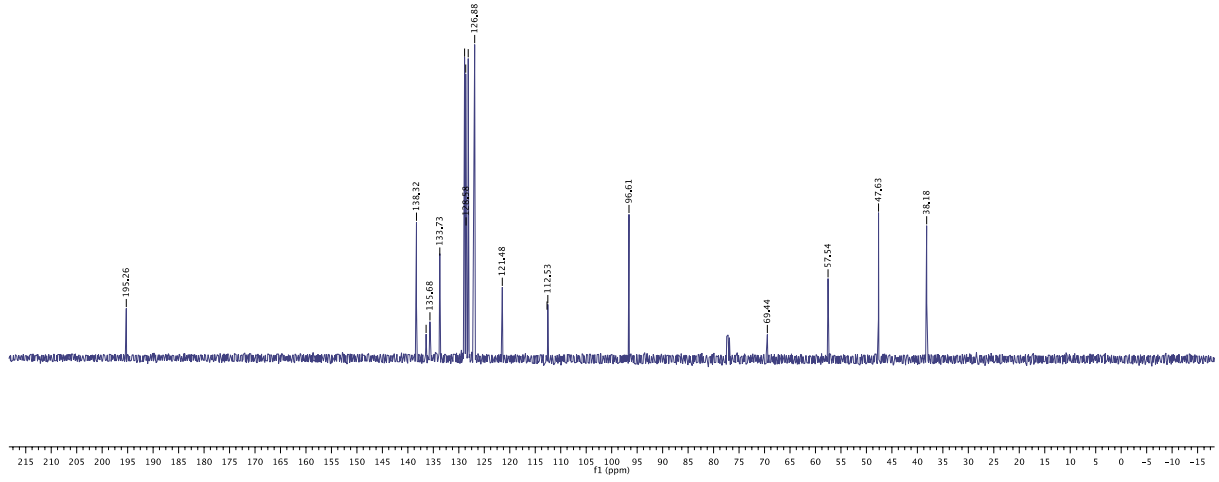
KY.03.051.A.1H

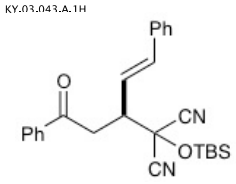


3j

KY.03.051.A.13C

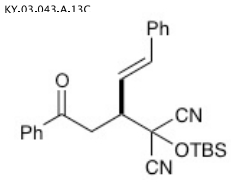





Ph
O
Ph
CN
OTBS
CN

5j

f1 (ppm)


Ph
O
Ph
CN
OTBS
CN

195.34
138.35
135.81
133.74
130.30
129.52
126.85
121.79
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67.38
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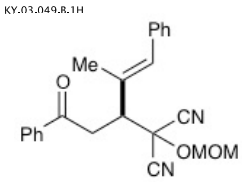
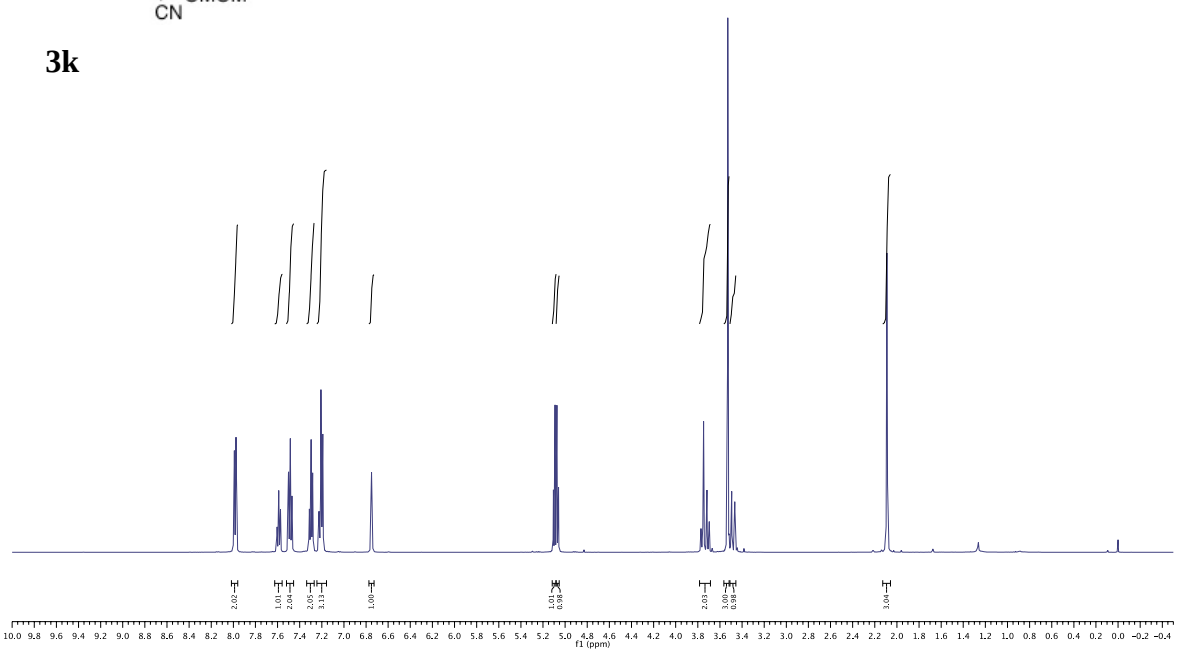
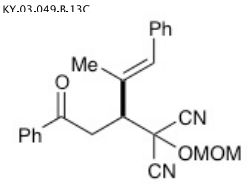
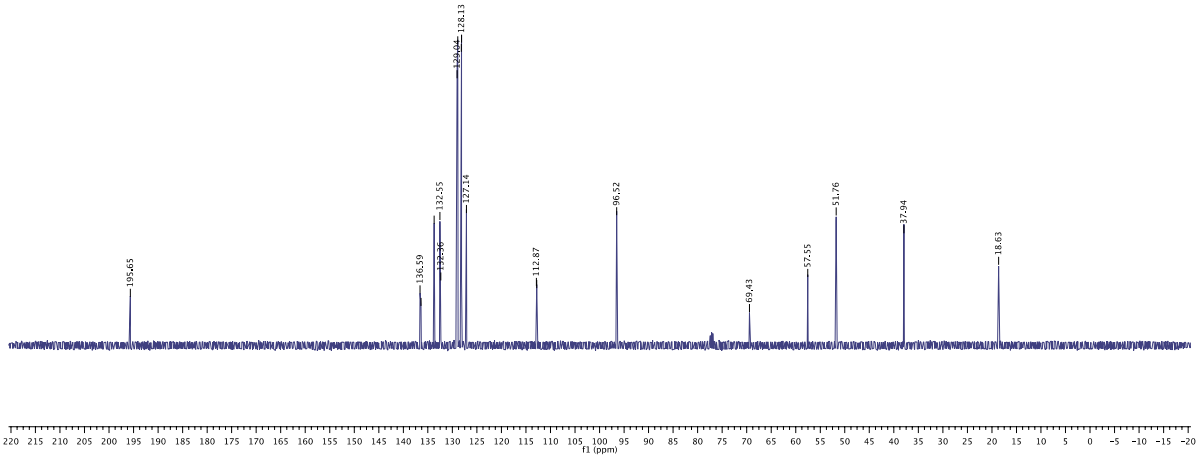
37.97
25.30
18.21
-4.50
f1 (ppm)

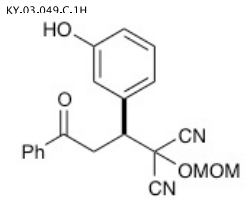

Ph
Me
O
Ph
CN
OMOM
CN

3k



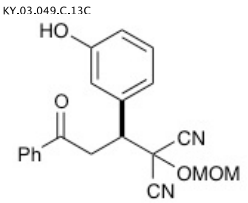

Ph
Me
O
Ph
CN
OMOM
CN

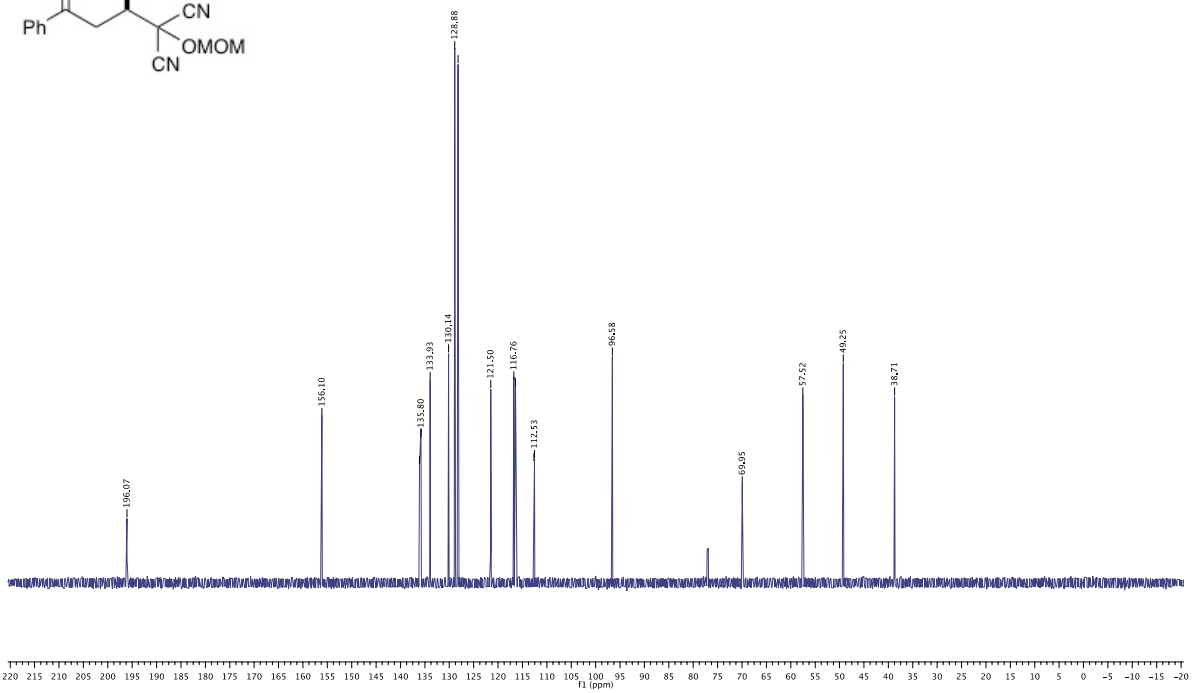

195.65
136.59
132.55
128.13
127.14
112.87
96.52
69.43
57.55
51.76
37.94
18.63


KY.03.049.C.1H
HO
O
Ph
CN
OMOM
CN

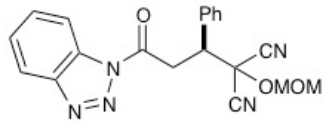
3l

f1 (ppm)


KY.03.049.C.13C
HO
O
Ph
CN
OMOM
CN

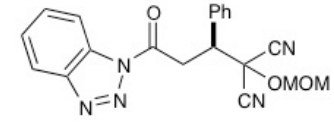

196.07
156.10
135.80
133.93
130.14
128.88
121.50
116.76
112.53
96.58
69.05
57.52
49.25
38.71
f1 (ppm)

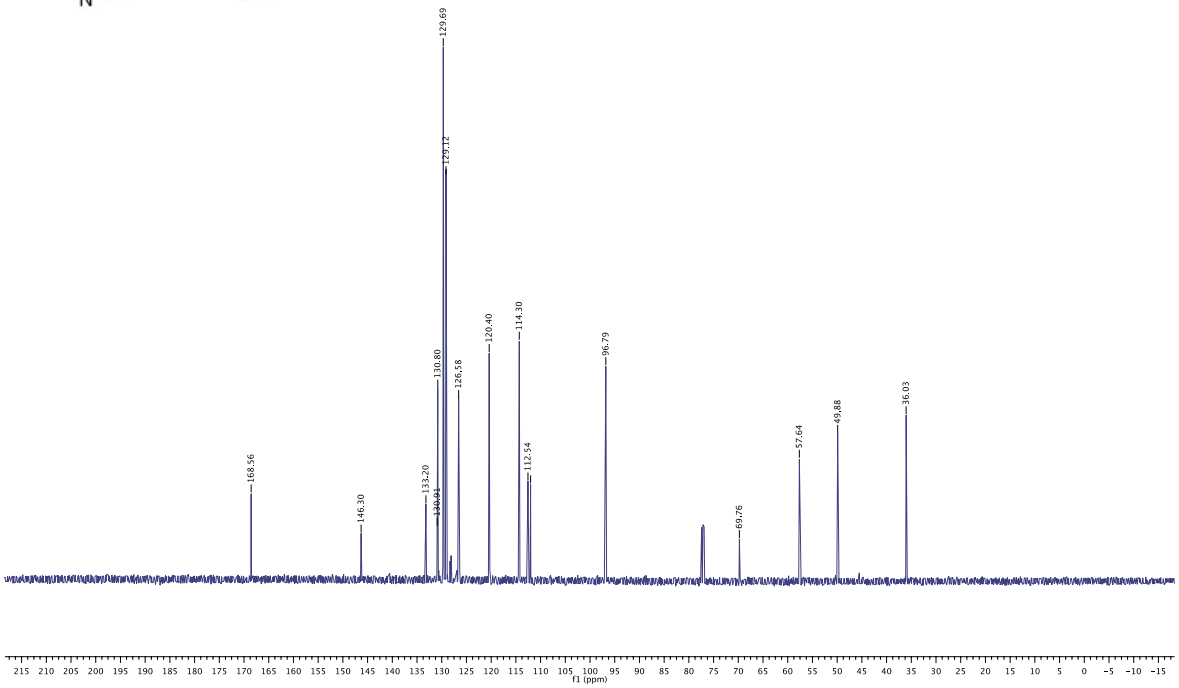
KY.03.047.C.1H



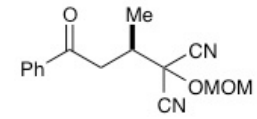
3m

KY.03.047.C.13C



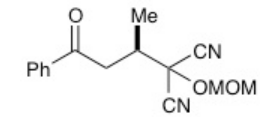


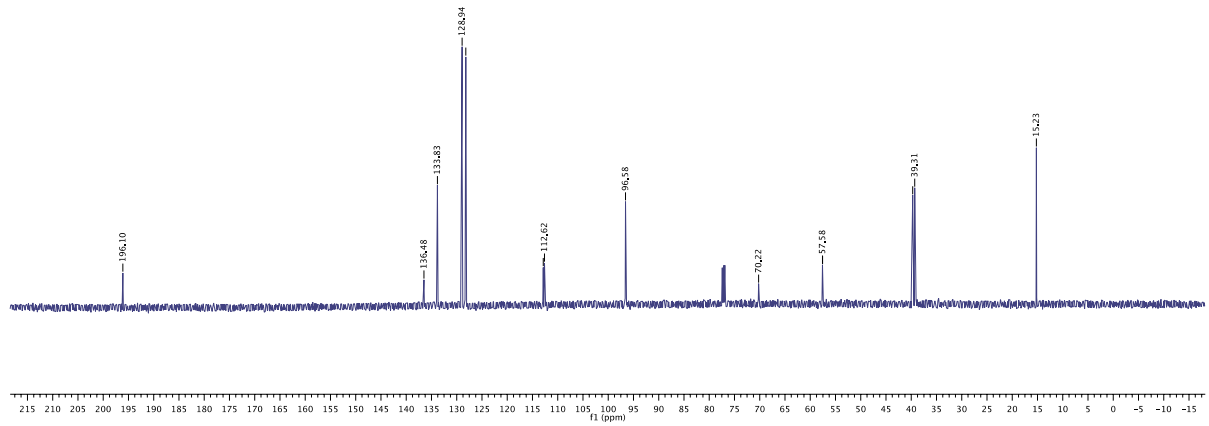
KY.02.269.Me.1H



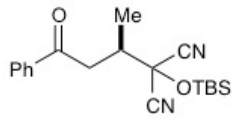
3n

KY.02.269.Me.13C





KY.03.038.A.1H



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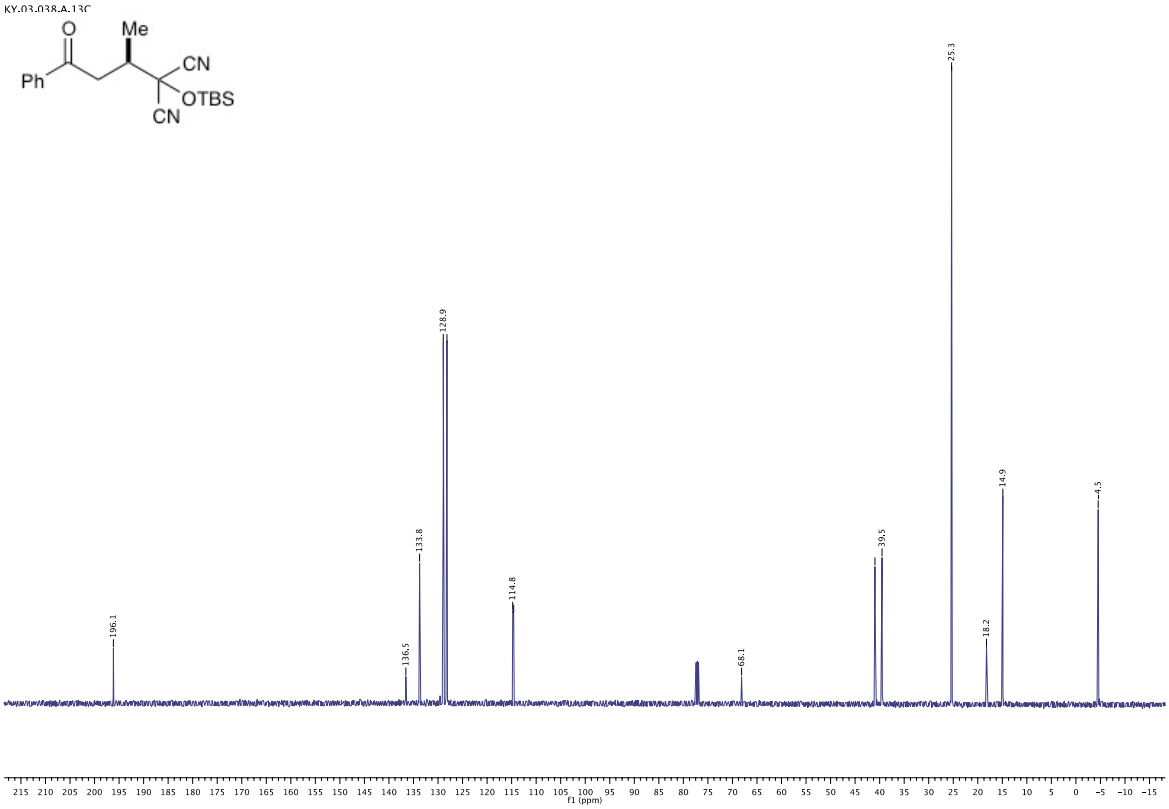
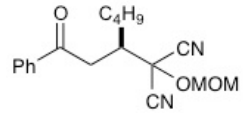
KY.03.038.A.13C

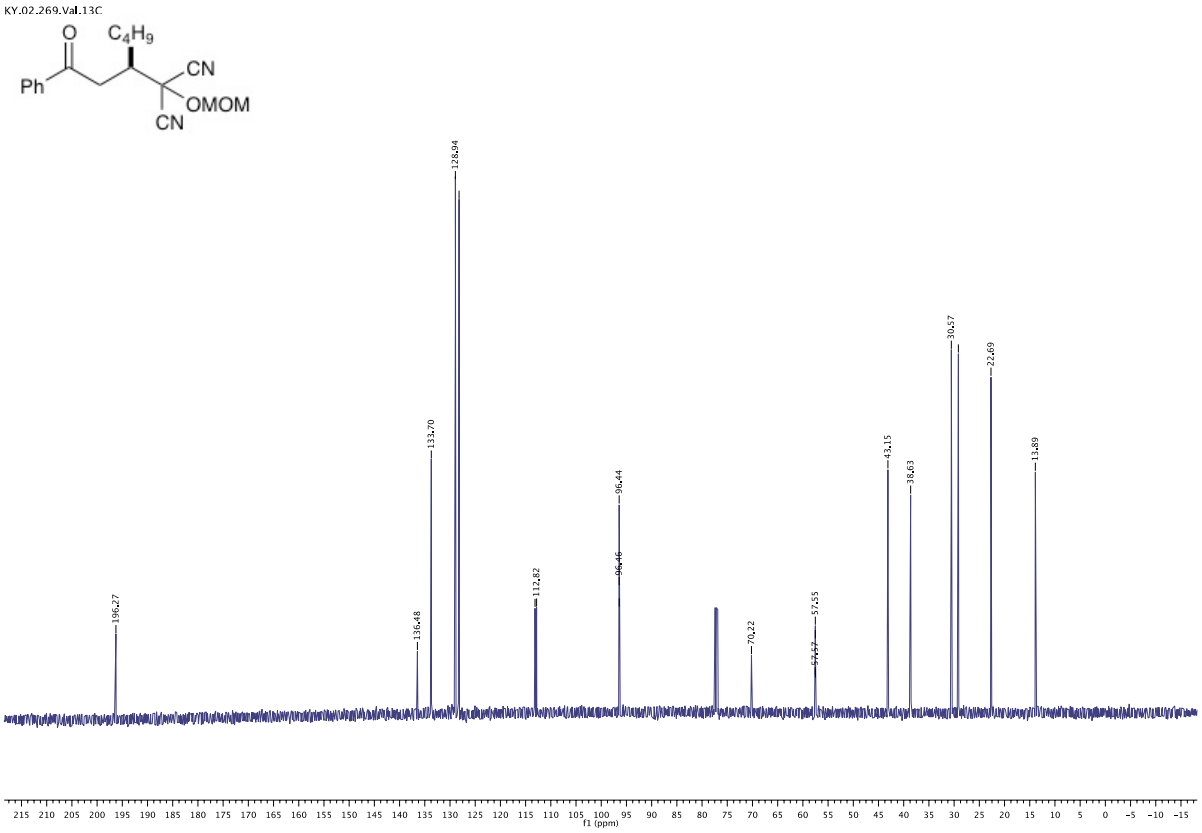


KY.02.269.Val.1H

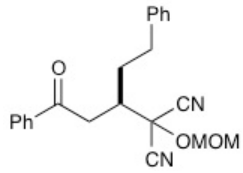


3o

KY.02.269.Val.13C

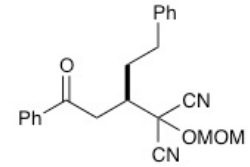


KY.02.261.B.1H

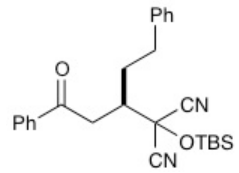


3p

KY.02.261.B.13C

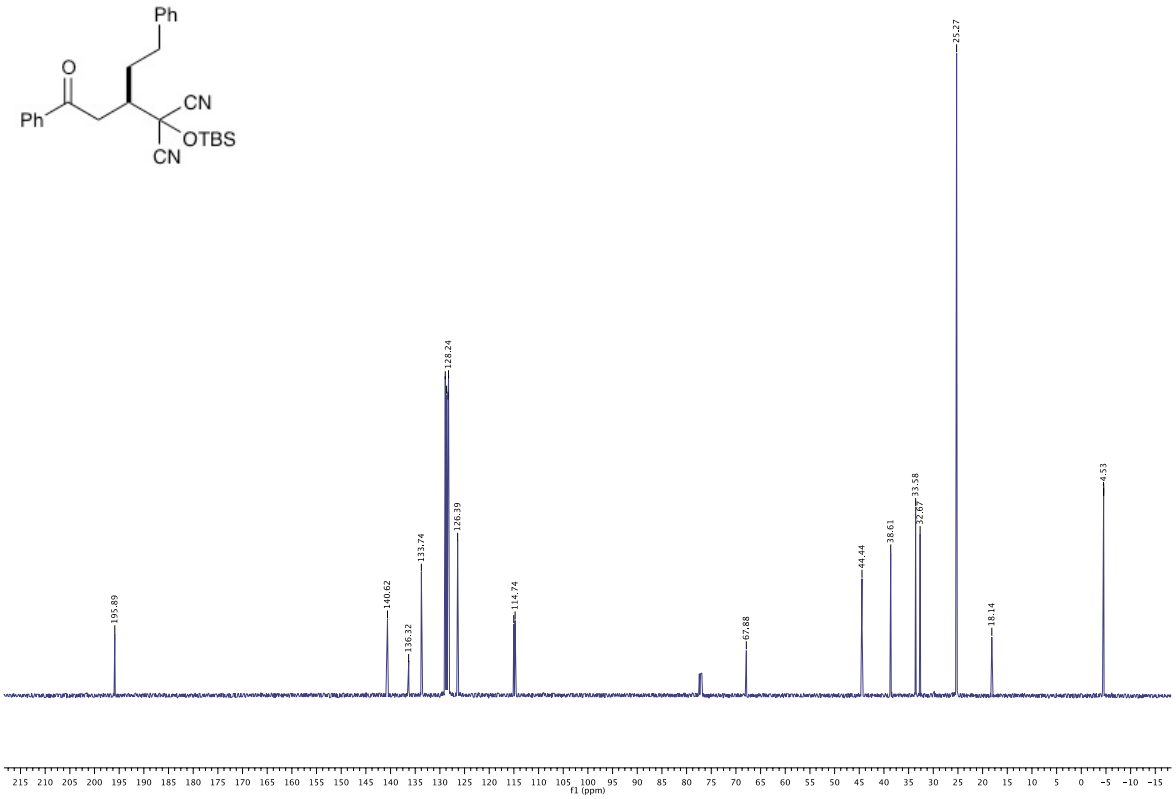


KY.03.034.A.1H

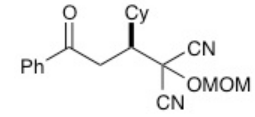


5p

KY.03.034.A.13C



KY.03.049.A.1H



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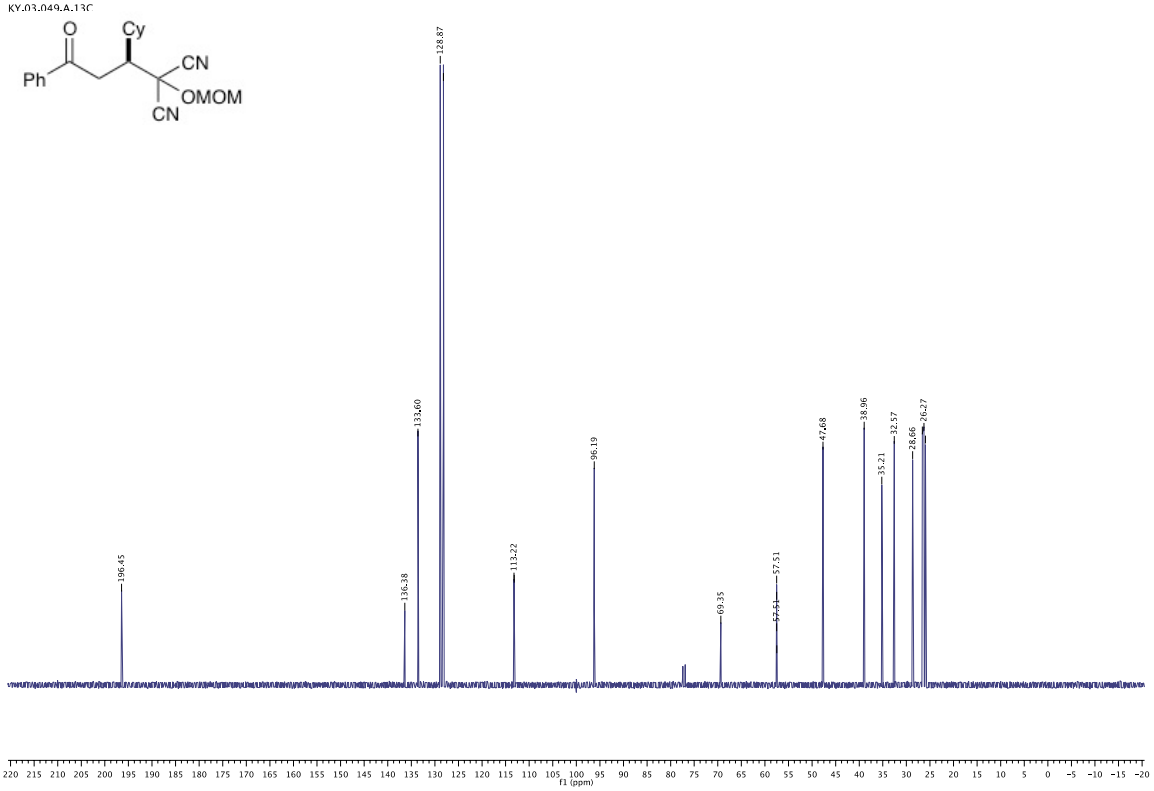
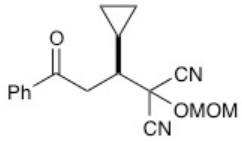
KY.03.049.A.13C

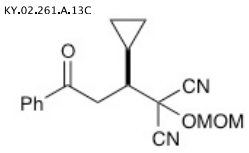


KY.02.261.A.1H

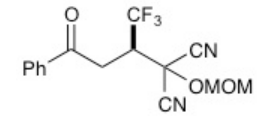


3r

KY.02.261.A.13C

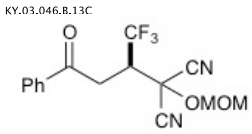


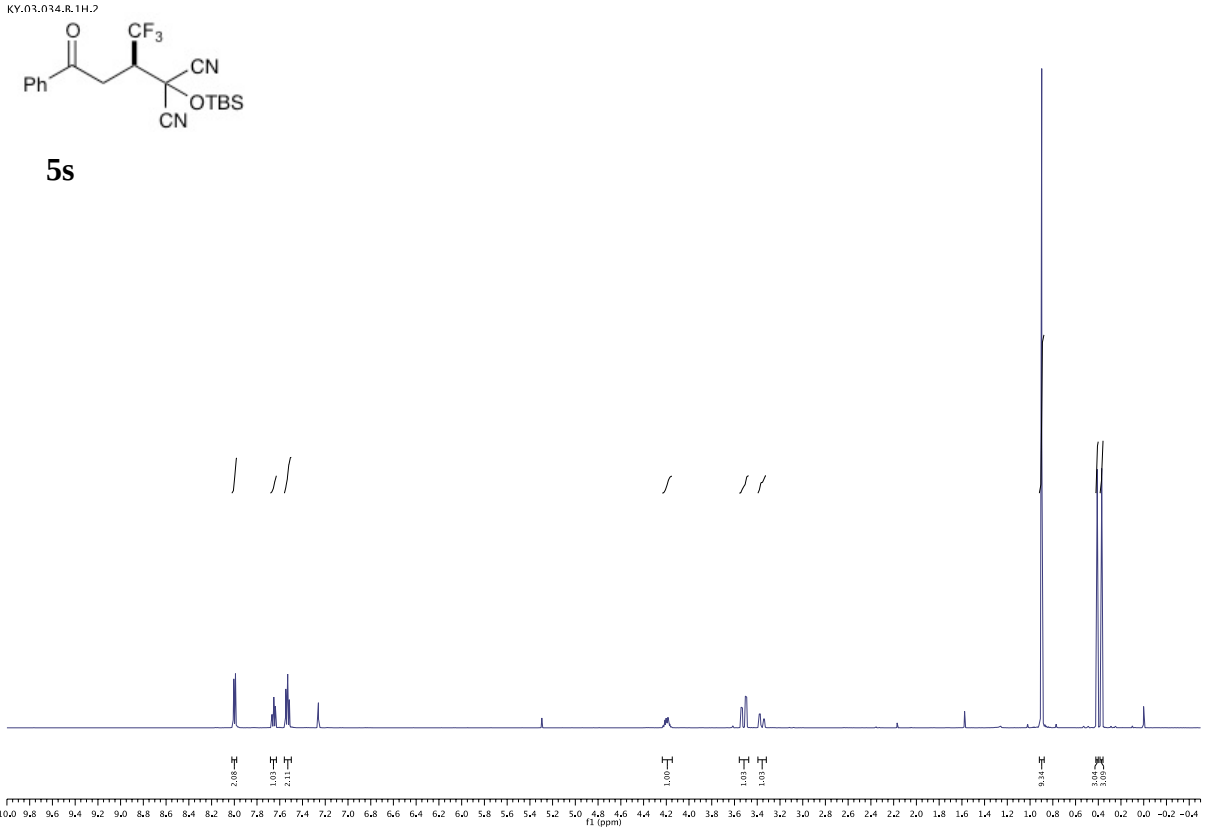
KY.03.046.B.1H



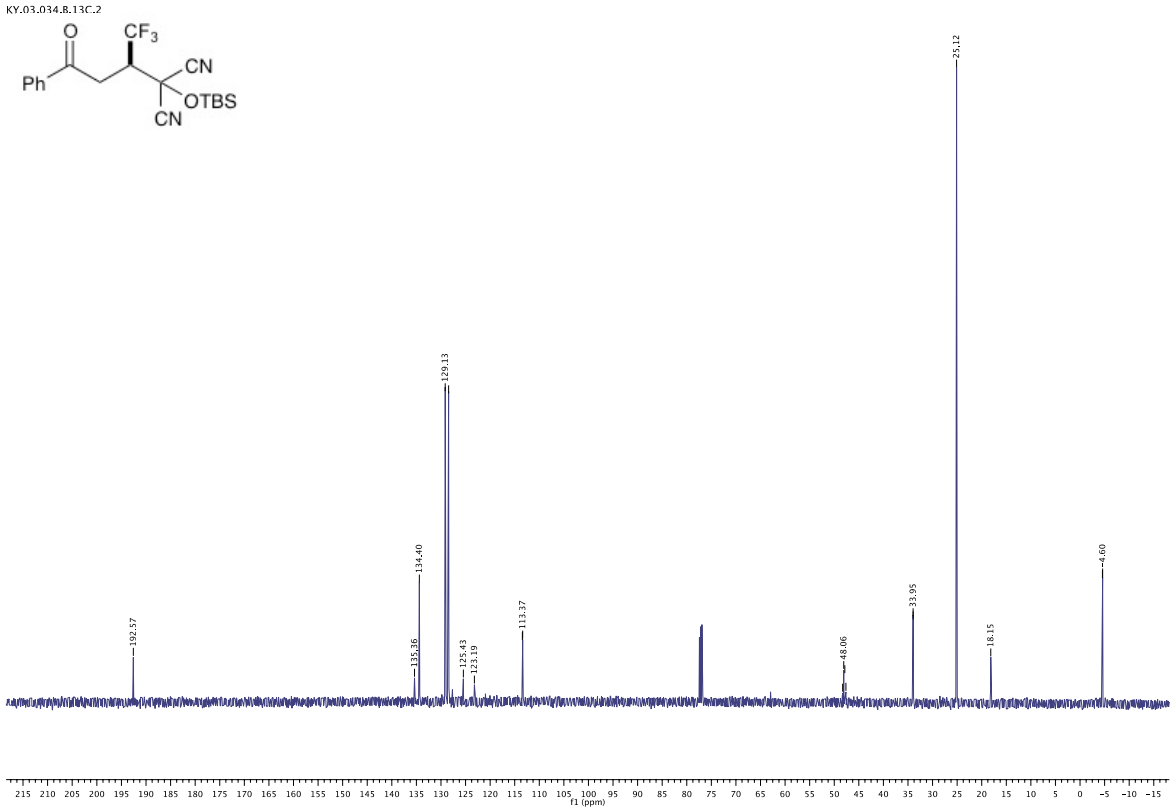
3s

KY.03.046.B.13C



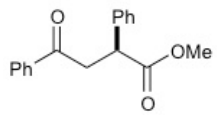

KY.03.034.B.1H.2
O
CF3
Ph
CN
OTBS
CN
2.08
1.03
2.11
1.00
1.03
1.03
9.34
3.04
3.09
F1 (ppm)

5s


KY.03.034.B.13C.2
O
CF3
Ph
CN
OTBS
CN
192.57
135.36
134.40
129.13
125.43
123.19
113.37
48.06
33.95
25.12
18.15
4.60
F1 (ppm)

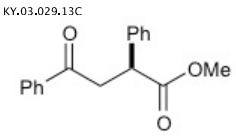
Functionalization of 5a (from TBS MAC)

KY.03.029.1H

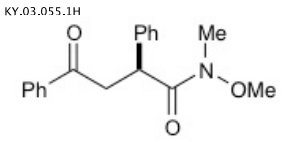


7

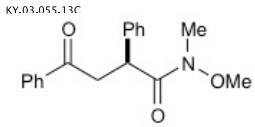
KY.03.029.13C

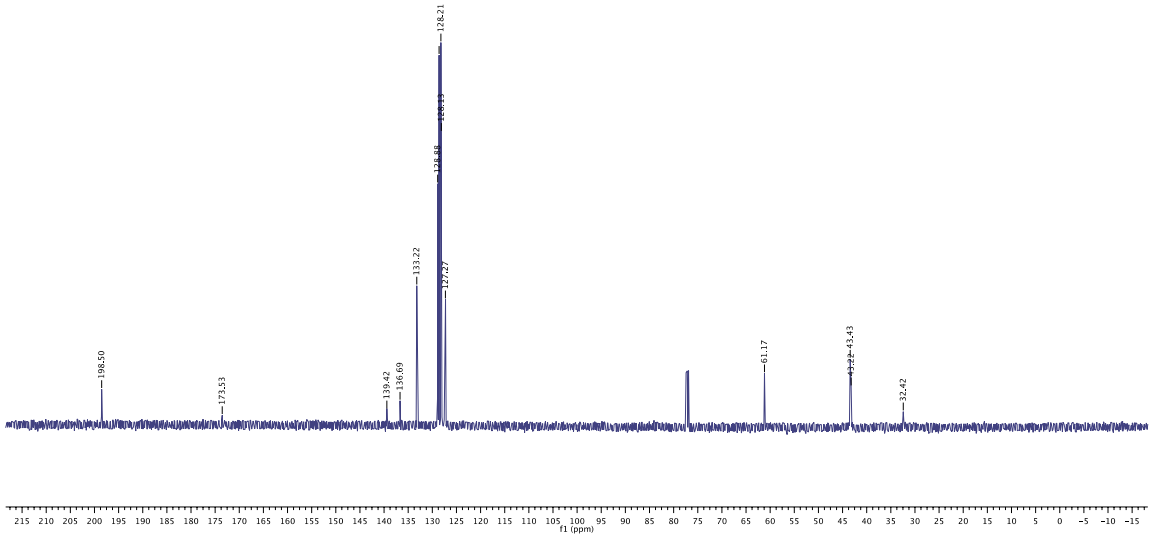


KY.03.055.1H

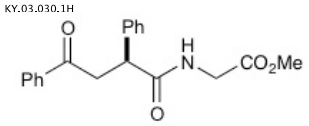


10



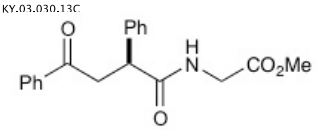


KY.03.030.1H



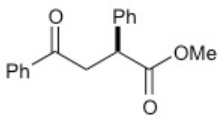
11

KY.03.030.13C



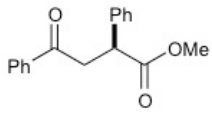
Functionalization of 3a (from MOM MAC)

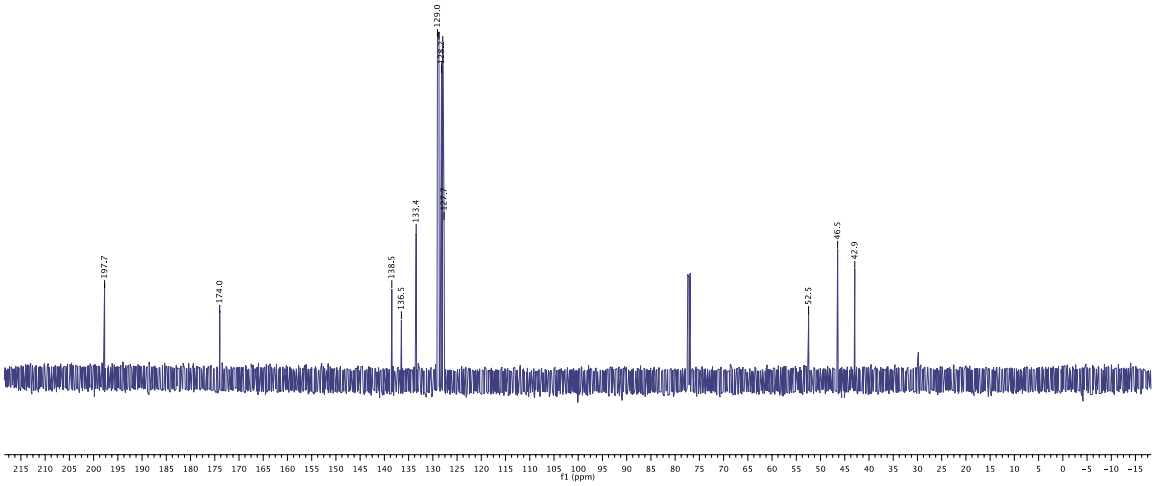
aen1-208 1H

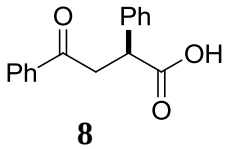


7

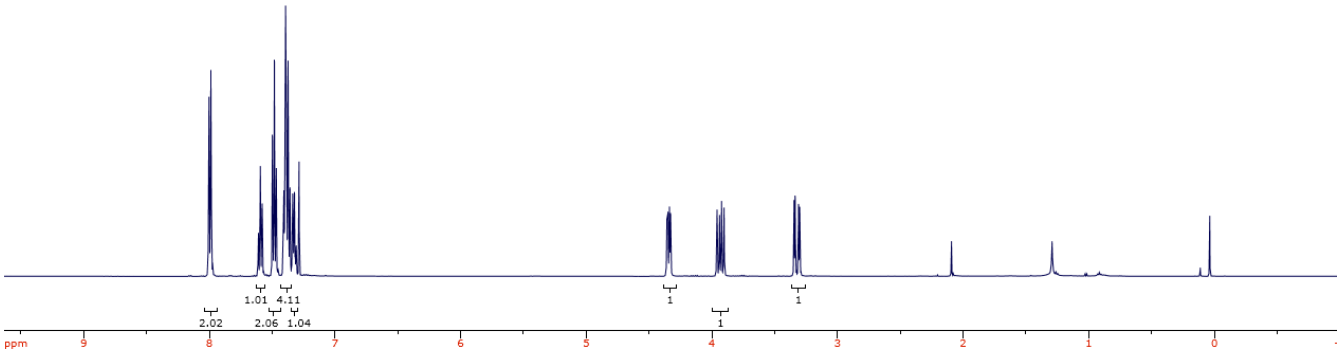
aen1-208 13C



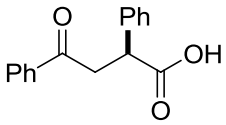


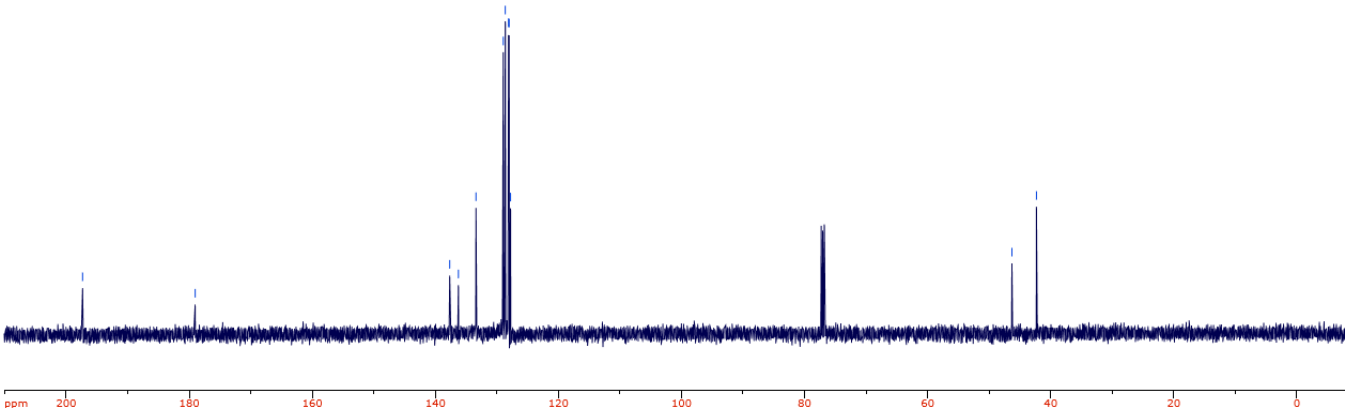

O
Ph
Ph
OH
O

8

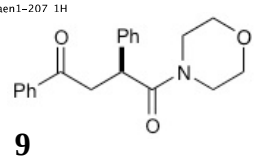

2.02
1.01
2.06
4.11
1.04
1
1
1
ppm
9
8
7
6
5
4
3
2
1
0


197.347
179.054
137.675
136.266
133.406
128.977
128.645
128.125
128.020
127.797
46.309
42.317


O
Ph
Ph
OH
O

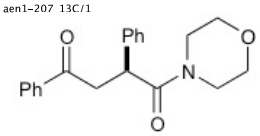

ppm
200
180
160
140
120
100
80
60
40
20
0

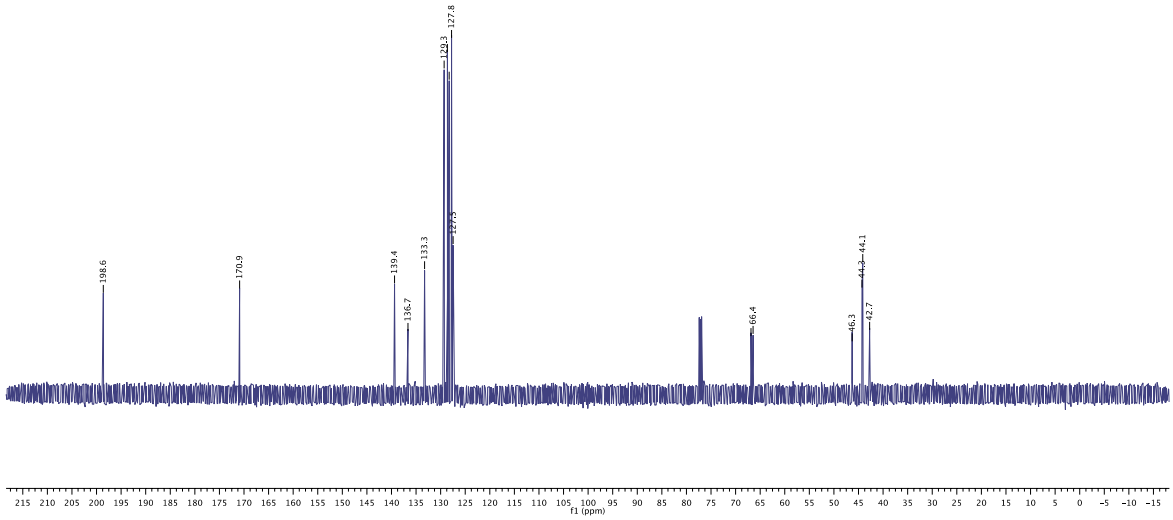
aen1-207 1H



9

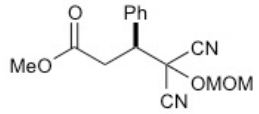
aen1-207 13C/1



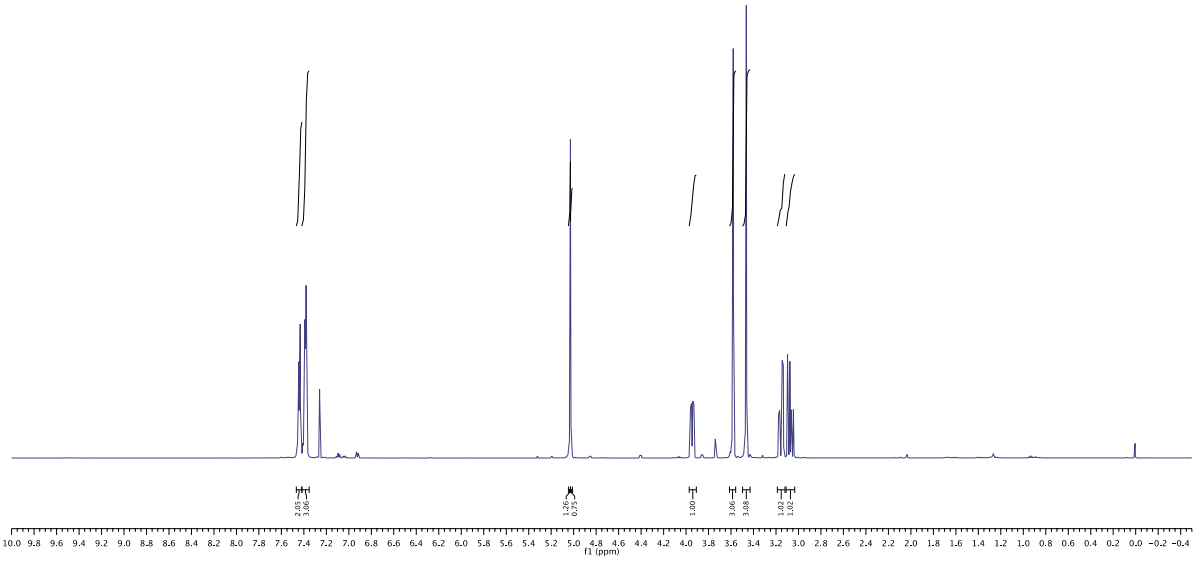


Synthesis of Succinic Diester from **3a**

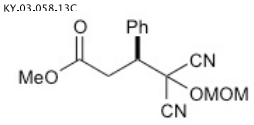
KY.03.058.1H



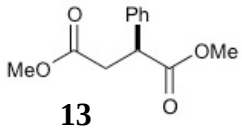
12



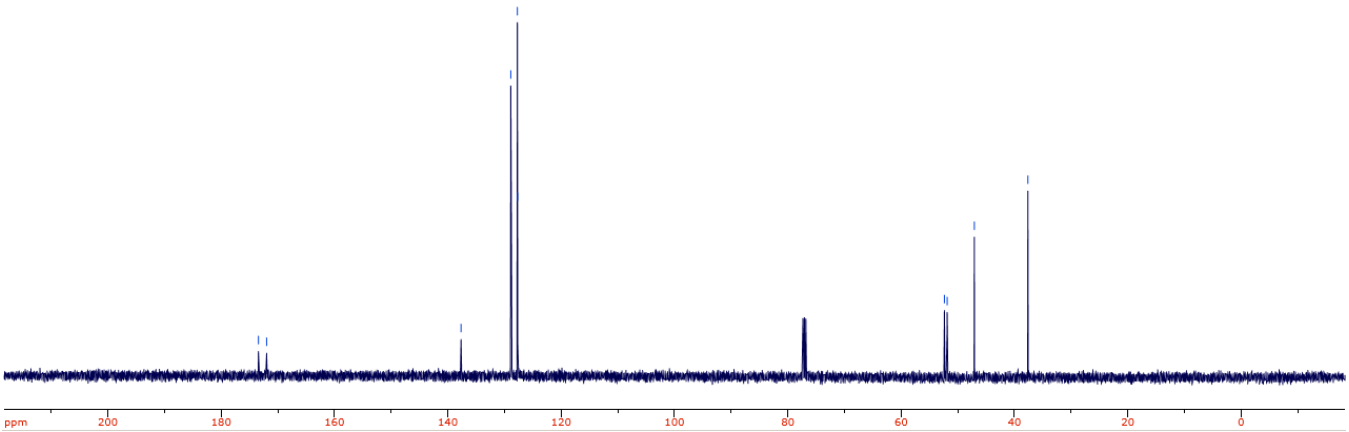
KY.03.058.13C



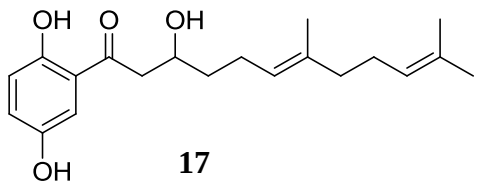
KY.03.063.oure.1H



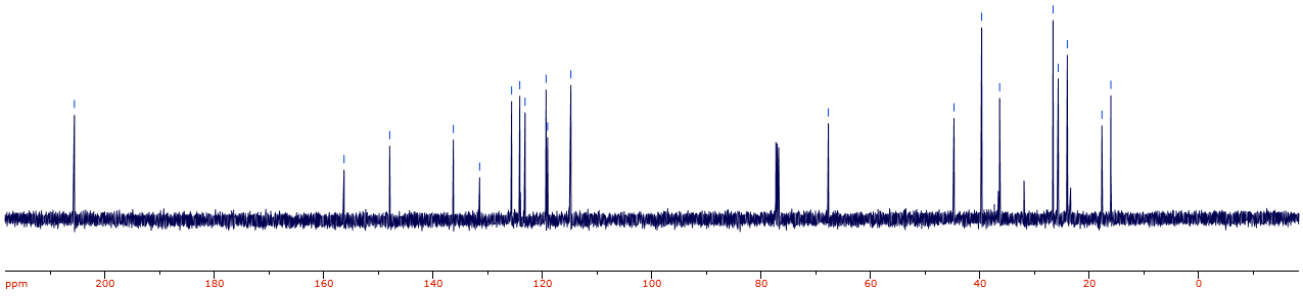
13

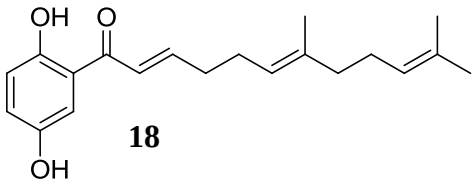


Total Synthesis of Fornicin C



17

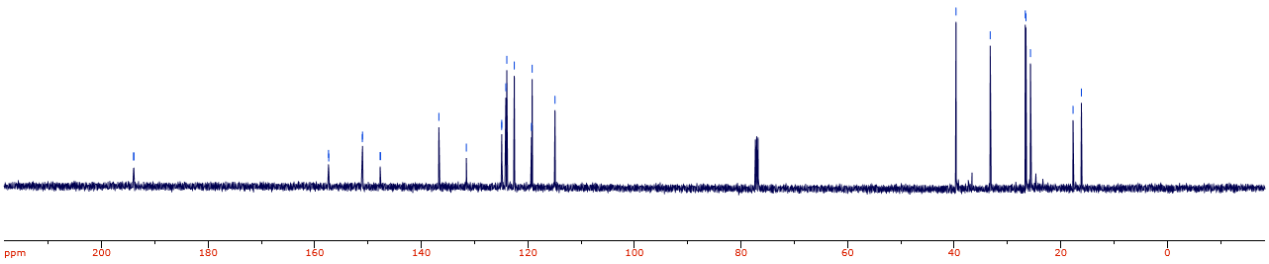


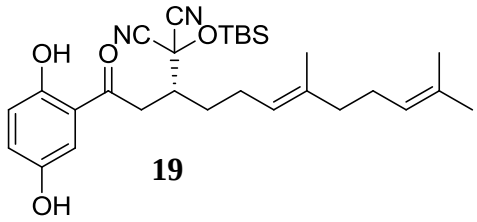

OH
O
OH

18

1.12
1.04
0.855
2.08
4.43
6.42
1
1.07
2.08
1.97
2.19
3.23
ppm 12.5
12.0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
-0.0

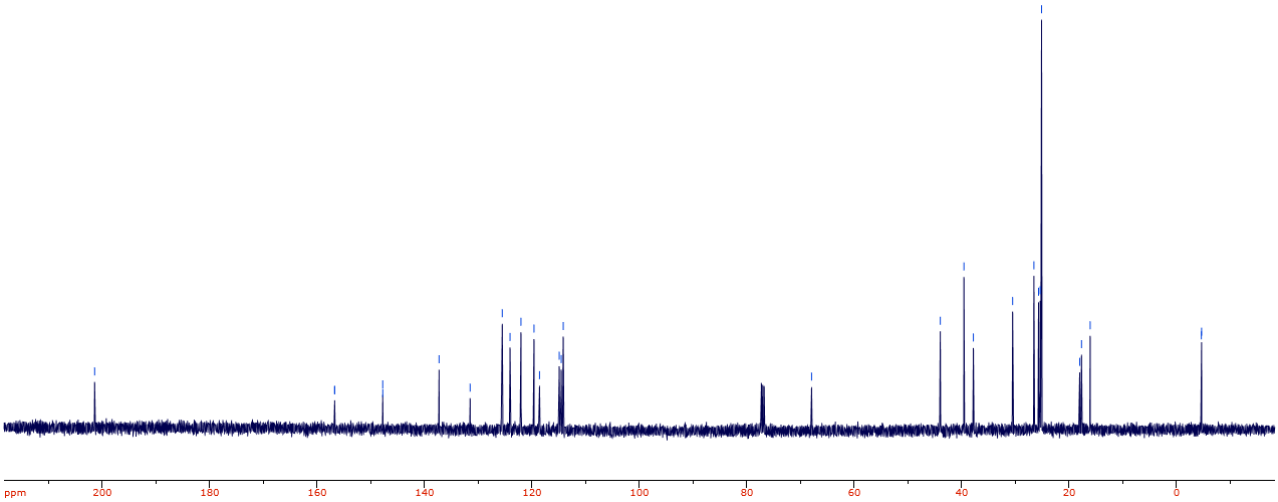

193.983
193.952
157.414
157.363
151.061
151.028
147.778
147.663
136.709
131.549
124.923
124.903
124.438
124.355
122.555
119.324
118.700
114.914
39.663
33.240
26.665
26.529
25.684
17.699
16.137

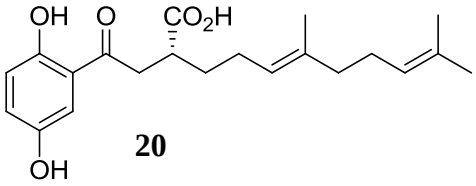

ppm
200
180
160
140
120
100
80
60
40
20
0


CN
NC
OTBS
OH
O
OH

19

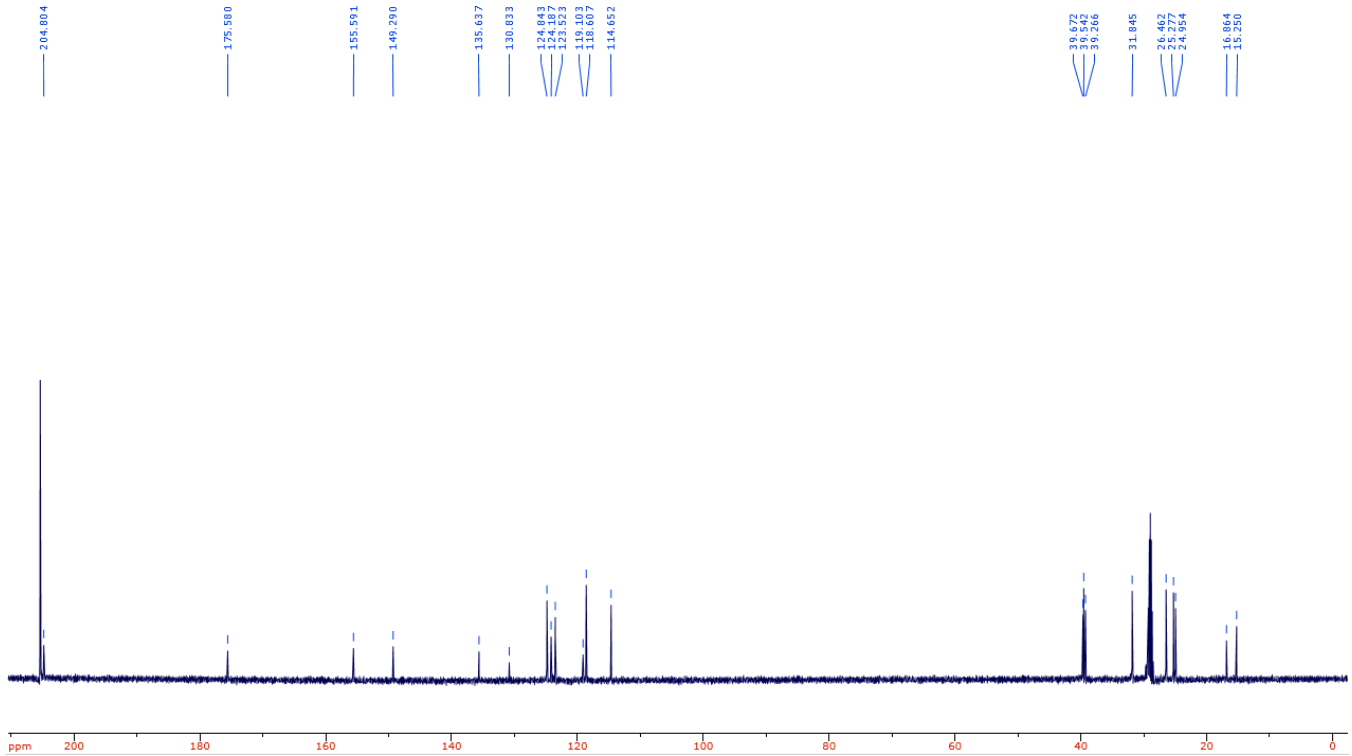

201.438
156.752
156.744
147.805
147.790
137.309
131.526
125.541
124.098
123.083
116.604
118.600
114.941
114.555
114.194
67.947
43.987
39.586
37.836
30.521
26.557
25.697
25.394
25.136
18.030
17.689
16.084
-4.605
-4.650



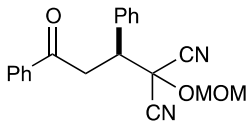

OH
O
CO2H
OH

20

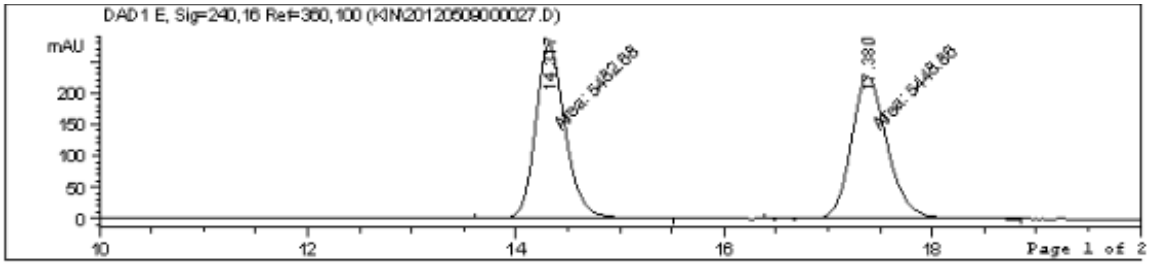
0.832
1
1.01
0.986
0.999
0.964
0.993
1.02
1.03
1.98
2.08
2.3
1.06
1.15
9.09
ppm
11.5
11.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0


204.804
175.580
155.591
149.290
135.637
130.833
124.843
124.187
123.523
119.103
118.607
114.652
39.672
39.542
39.266
31.845
26.462
25.577
24.954
16.864
15.250
ppm
200
180
160
140
120
100
80
60
40
20
0

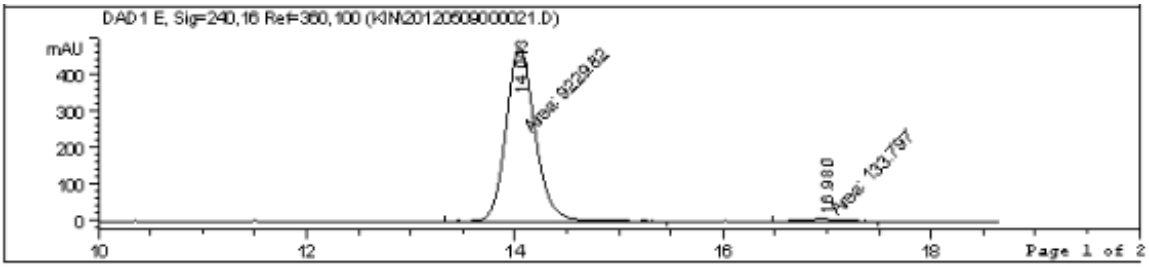
HPLC Traces for Michael Addition Adducts



3a

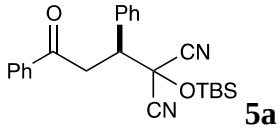


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.317	MM	0.3281	5482.67822	278.51114	50.1547
2	17.380	MM	0.4023	5448.85645	225.74504	49.8453

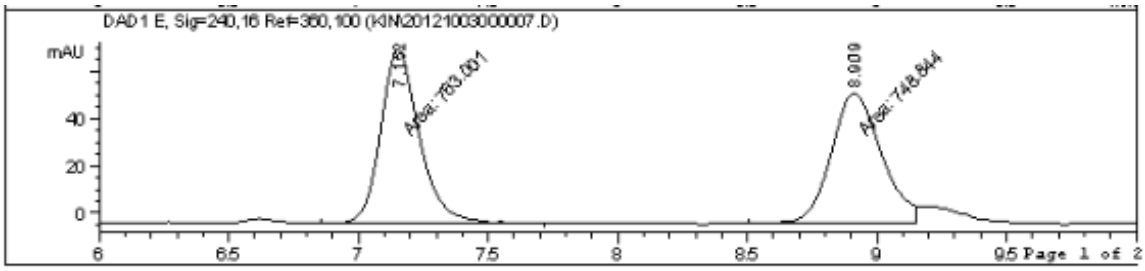


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.043	MM	0.3208	9229.82324	479.56891	98.5711
2	16.980	MM	0.3681	133.79689	6.05863	1.4289

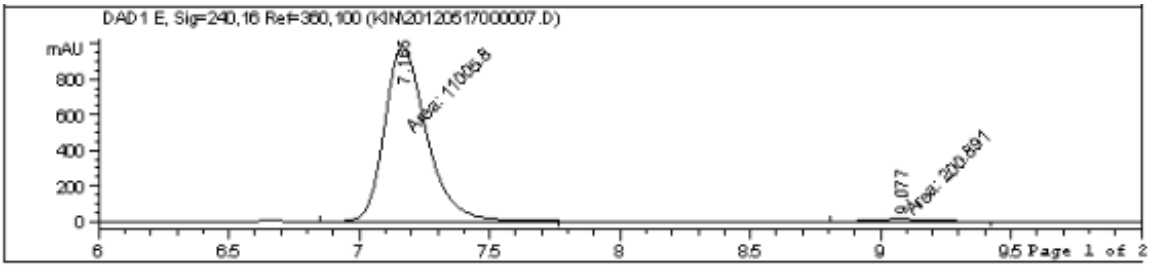
Enantiomeric excess (97% ee) was measured by HPLC (Chiralcel IA, 3% IPA/Hexanes, 1 mL/min, Rt_1 = 14.0, Rt_2 = 16.98



5a

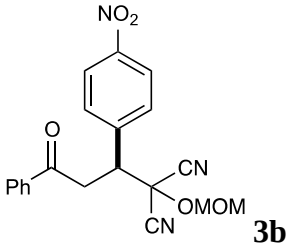


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.152	MM	0.1726	753.00140	73.56905	50.4682
2	8.909	MF	0.2264	748.84395	55.12918	49.5318

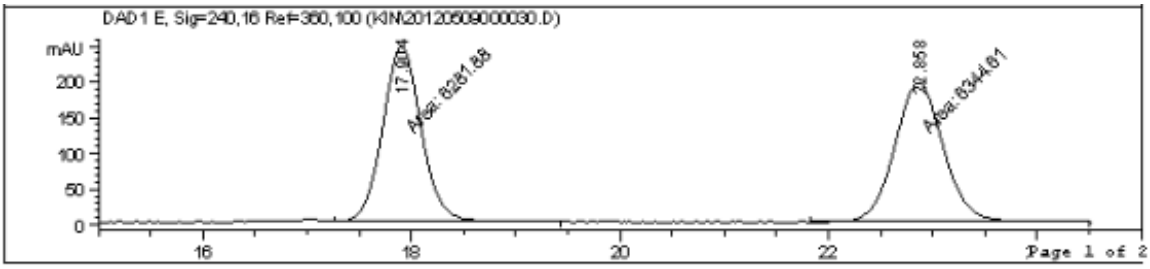


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.165	MM	0.1864	1.10058e4	984.06708	98.2074
2	9.077	MM	0.2434	200.89079	13.75446	1.7926

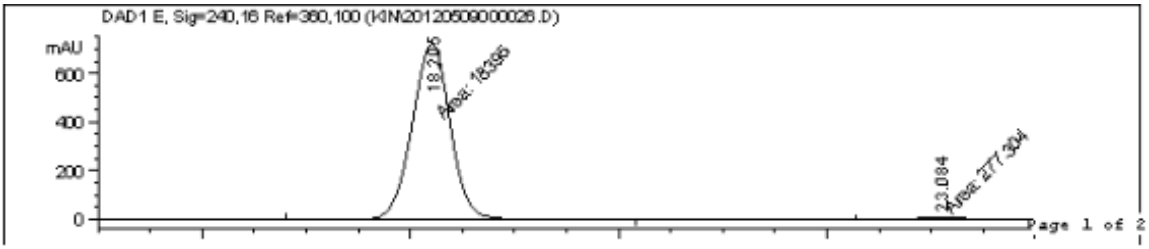
Enantiomeric excess (96% ee) was measured by HPLC (Chiralcel IA, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 7.2, Rt_2 = 9.1



3b

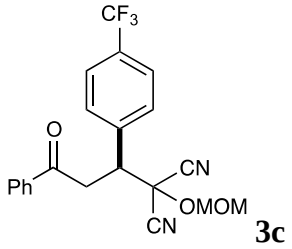


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.904	MM	0.4286	6281.87500	244.25079	49.7516
2	22.858	MM	0.5447	6344.61279	194.13542	50.2484

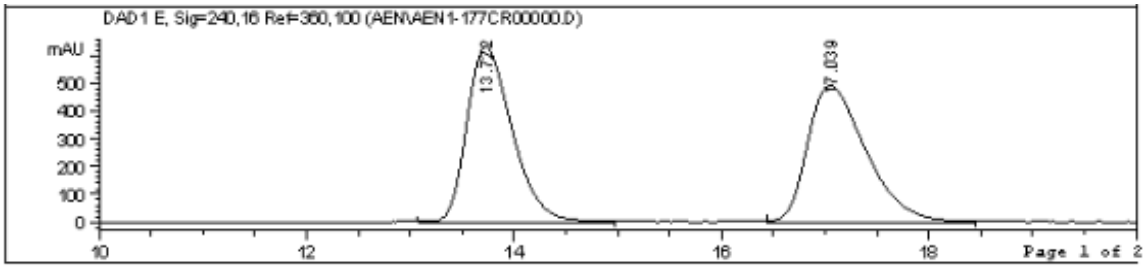


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.205	MM	0.4251	1.83950e4	721.26532	98.5149
2	23.084	MM	0.5141	277.30447	8.98993	1.4851

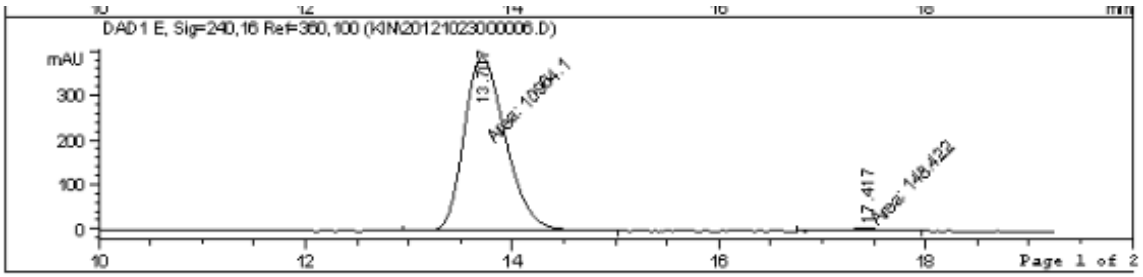
Enantiomeric excess (97% ee) was measured by HPLC (Chiralcel IA, 15% EtOH/Hexanes, 1 mL/min, Rt_1 = 18.2, Rt_2 = 23.1



3c

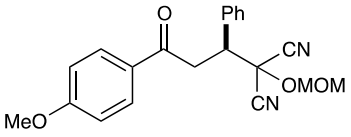


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.722	VB	0.4441	1.92072e4	632.74469	49.9400
2	17.039	VB	0.5617	1.92534e4	492.89282	50.0600

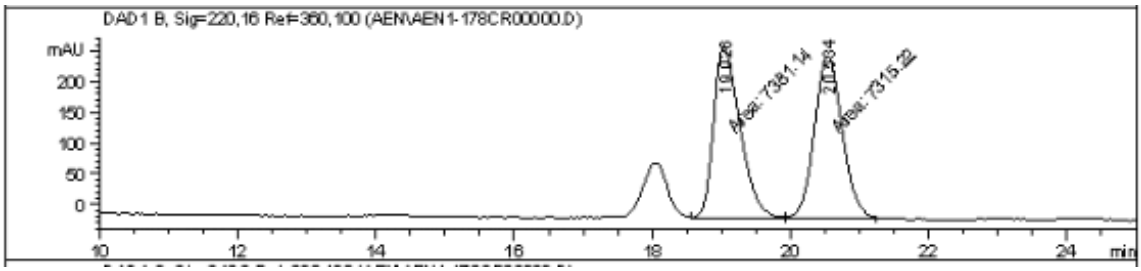


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.707	MM	0.4669	1.09641e4	391.36951	98.6644
2	17.417	MM	0.5142	148.42195	4.81089	1.3356

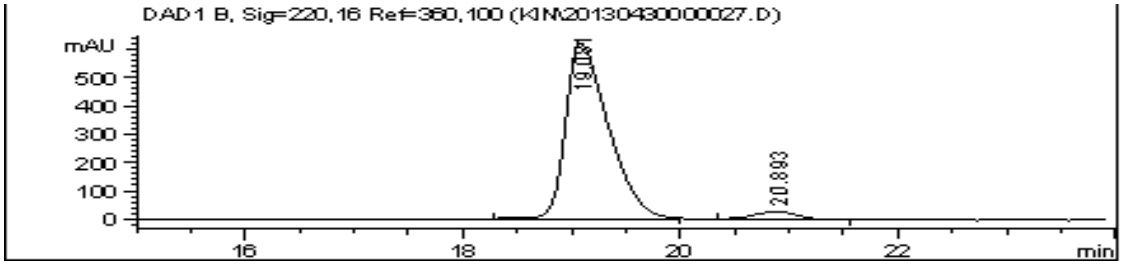
Enantiomeric excess (97% ee) was measured by HPLC (Chiralcel OD-H, 4% IPA/Hexanes, 1 mL/min, Rt_1 = 13.7, Rt_2 = 17.4



3d

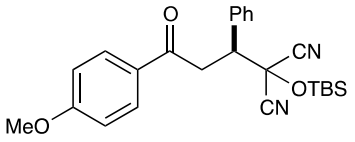


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.026	MM	0.4426	7381.13672	277.95538	50.2242
2	20.534	MM	0.4637	7315.22363	262.95016	49.7758

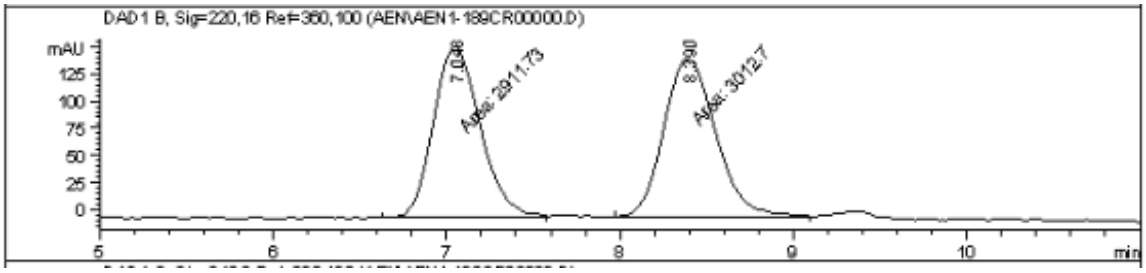


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.081	BB	0.4006	1.71669e4	620.92609	95.6594
2	20.893	BB	0.3456	778.95526	27.74458	4.3406

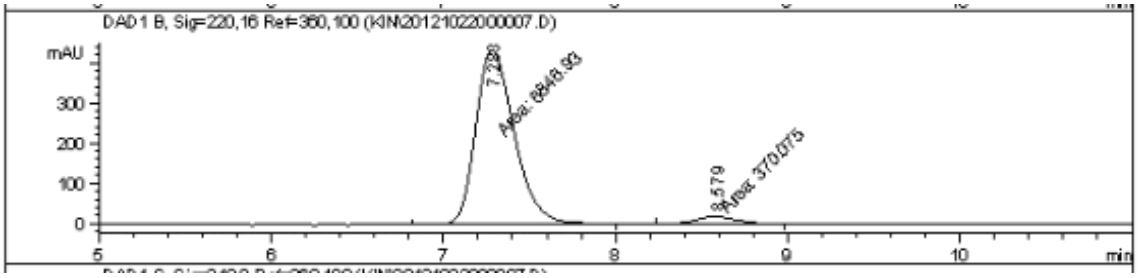
Enantiomeric excess (92% ee) was measured by HPLC (Chiralcel IA, 10% EtOH/Hexanes, 1 mL/min, Rt_1 = 14.98, Rt_2 = 16.8



5d

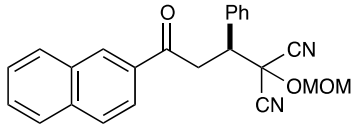


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.048	MM	0.3094	2911.72607	156.85152	49.1478
2	8.390	MM	0.3465	3012.70361	144.89948	50.8522

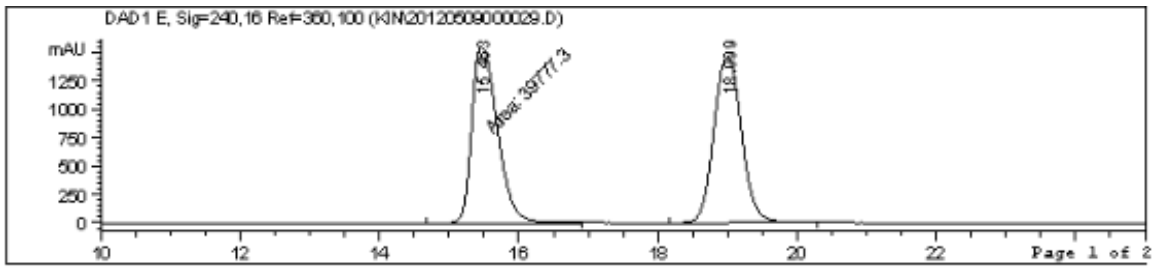


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.283	MM	0.2623	6846.92969	435.01834	94.8722
2	8.579	MM	0.3039	370.07526	20.29711	5.1278

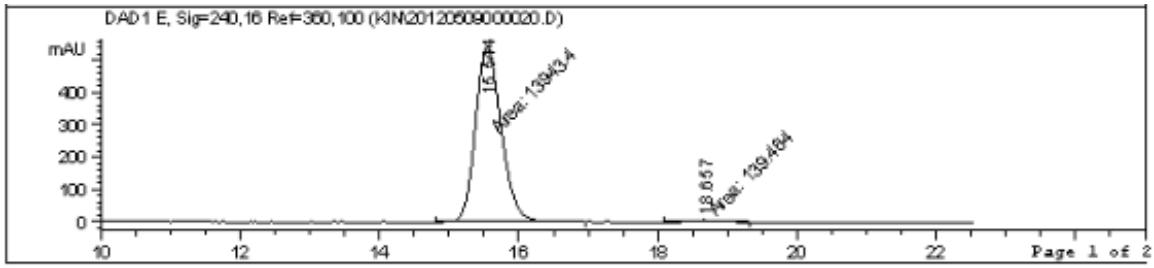
Enantiomeric excess (90% ee) was measured by HPLC (Chiralcel OD-H, 4% IPA/Hexanes, 1 mL/min, Rt_1 = 7.3, Rt_2 = 8.6



1e

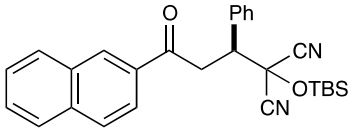


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.463	MM	0.4271	3.97773e4	1552.37195	49.5619
2	18.999	BB	0.3591	4.04805e4	1470.85608	50.4381

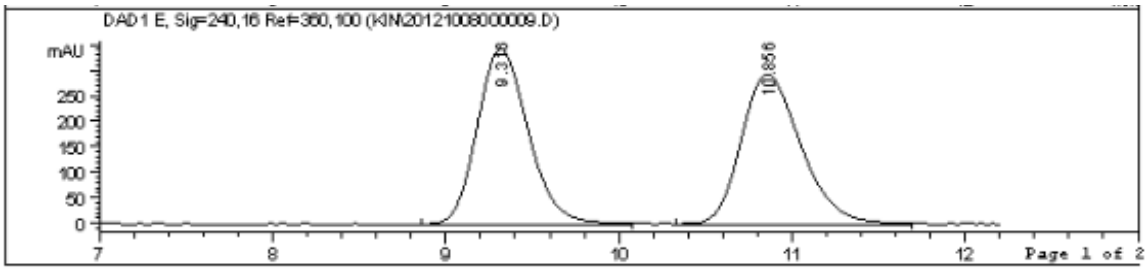


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.544	MM	0.4285	1.39434e4	542.32574	99.0097
2	18.657	MM	0.3911	139.46436	5.94375	0.9903

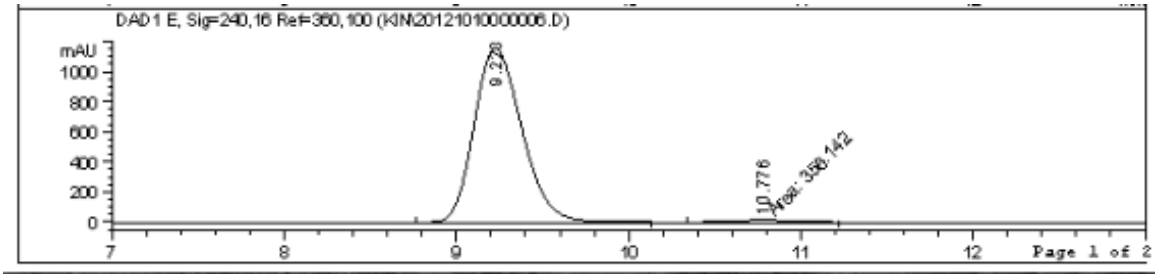
Enantiomeric excess (98% ee) was measured by HPLC (Chiralcel IA, 7% EtOH/Hexanes, 1 mL/min, Rt_1 = 15.5, Rt_2 = 18.7



5e

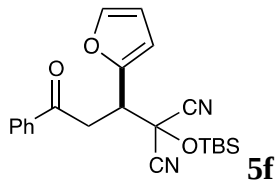


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.316	VB	0.3152	7054.97998	344.11081	50.0210
2	10.856	VB	0.3692	7049.06543	294.57782	49.9790

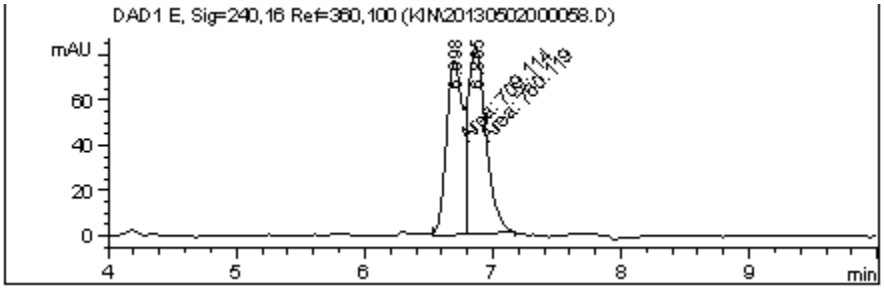


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.223	VB	0.3041	2.23920e4	1155.47144	98.4344
2	10.776	MM	0.3970	356.14169	14.95208	1.5656

Enantiomeric excess (97% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 9.2, Rt_2 = 10.8

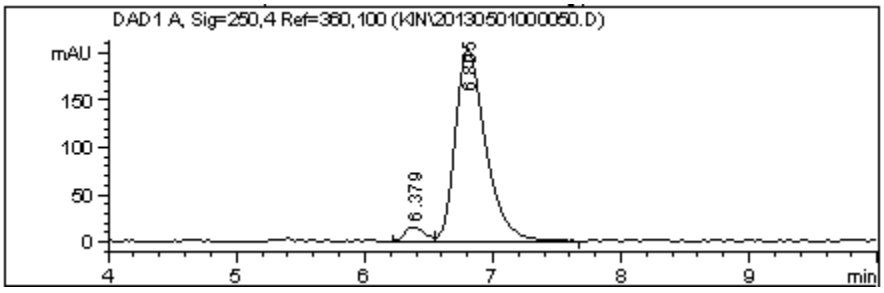


5f



Signal 5: DAD1 E, Sig=240,16 Ref=360,100

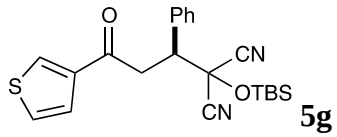
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.698	MM	0.1537	709.11414	76.91112	48.2642
2	6.865	MM	0.1532	760.11920	82.68867	51.7358



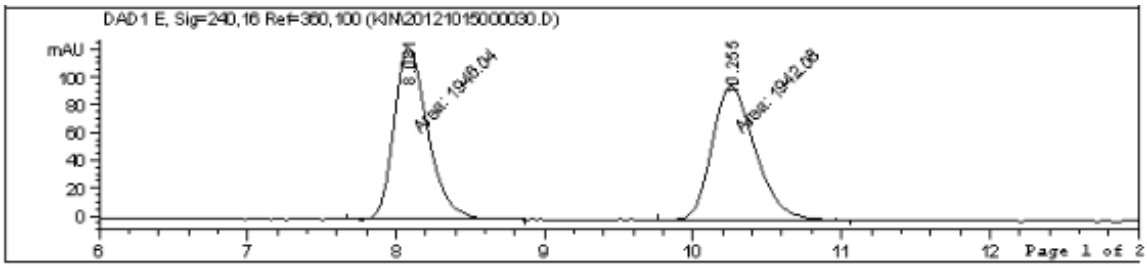
Signal 1: DAD1 A, Sig=250,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.379	BV	0.1665	181.03435	16.18402	5.0361
2	6.805	VB	0.2518	3413.67529	203.35841	94.9639

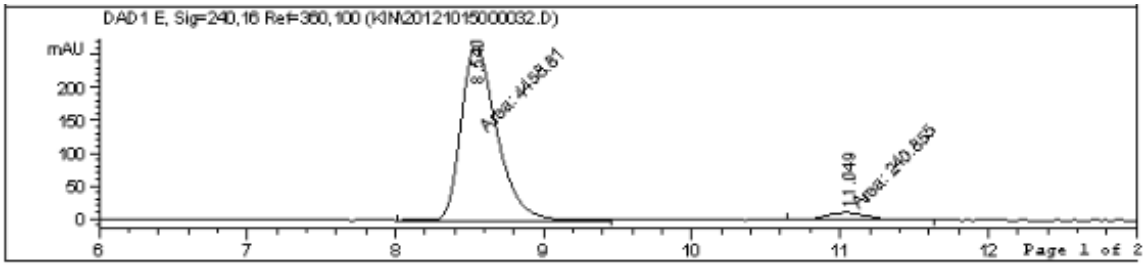
Enantiomeric excess (90% ee) was measured by HPLC (Chiralcel AD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 6.3, Rt_2 = 6.8



5g

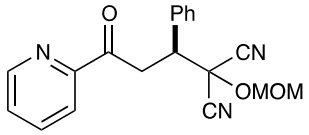


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.081	MM	0.2625	1946.03650	123.53961	50.0508
2	10.255	MM	0.3366	1942.08252	96.14926	49.9492

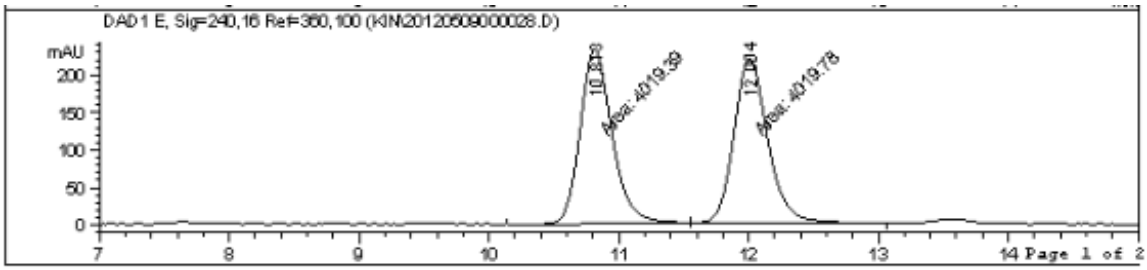


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.540	MM	0.2807	4458.81201	264.72549	94.8751
2	11.049	MM	0.3544	240.85480	11.32610	5.1249

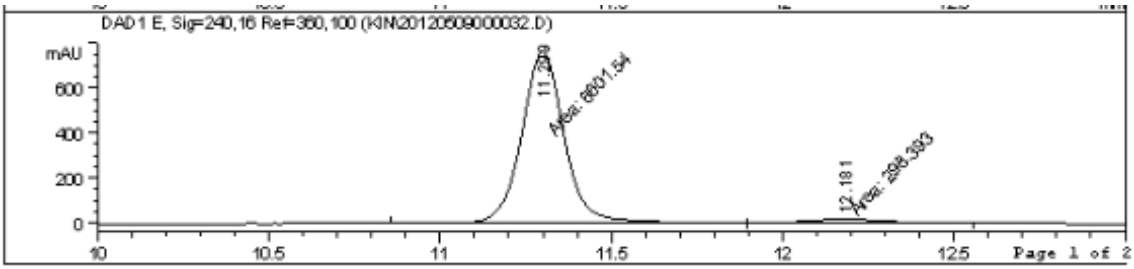
Enantiomeric excess (90% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 8.5, Rt_2 = 11.0



3h

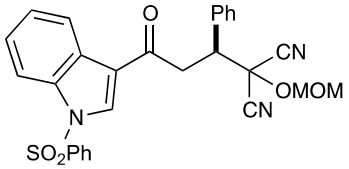


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.813	MF	0.2882	4019.38867	232.45528	49.9975
2	12.004	FM	0.3054	4019.78345	219.36412	50.0025

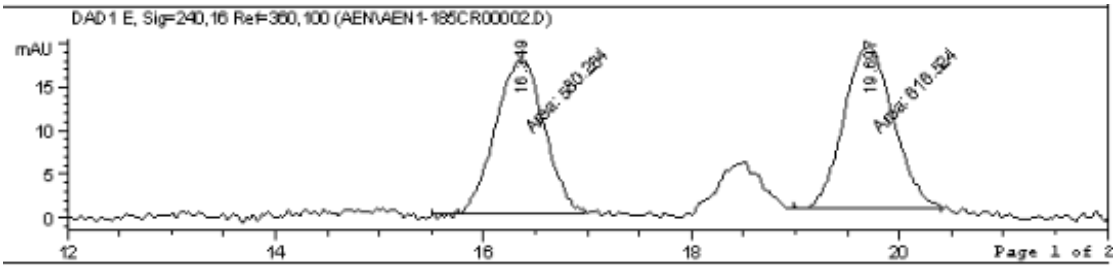


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.299	MM	0.1440	6601.53662	764.20398	95.6754
2	12.181	MM	0.2684	298.39310	18.53077	4.3246

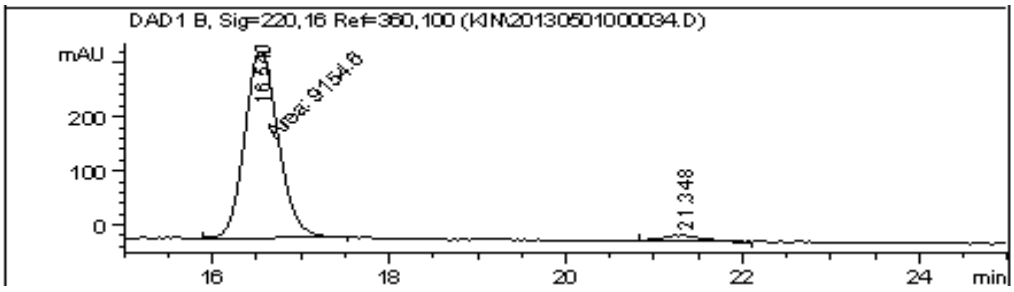
Enantiomeric excess (91% ee) was measured by HPLC (Chiralcel IA, 7% IPA/Hexanes, 1 mL/min, Rt_1 = 11.3, Rt_2 = 12.2



3i



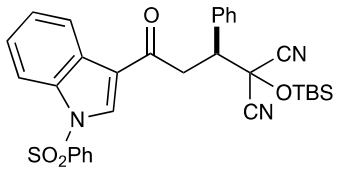
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.349	MM	0.5485	580.26434	17.63239	48.4851
2	19.697	MM	0.5551	616.52435	18.51226	51.5149



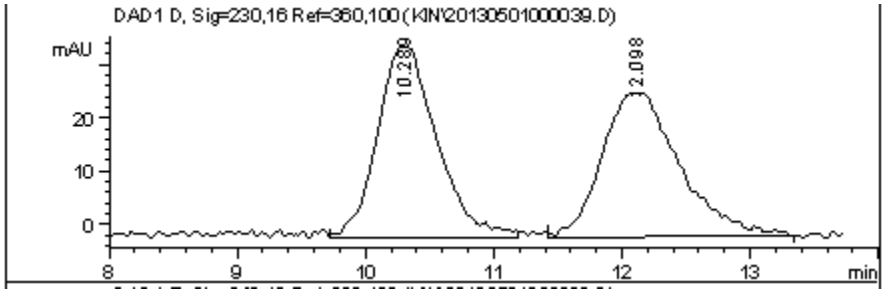
Signal 2: DAD1 B, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.540	MM	0.4421	9154.60254	345.11322	96.0906
2	21.348	BV	0.4030	372.44806	11.17029	3.9094
Totals :				9527.05060	356.28351	

Enantiomeric excess (92% ee) was measured by HPLC (Chiralcel IA, 10% EtOH/Hexanes, 1.1 mL/min, Rt_1 = 14.3, Rt_2 = 16.9

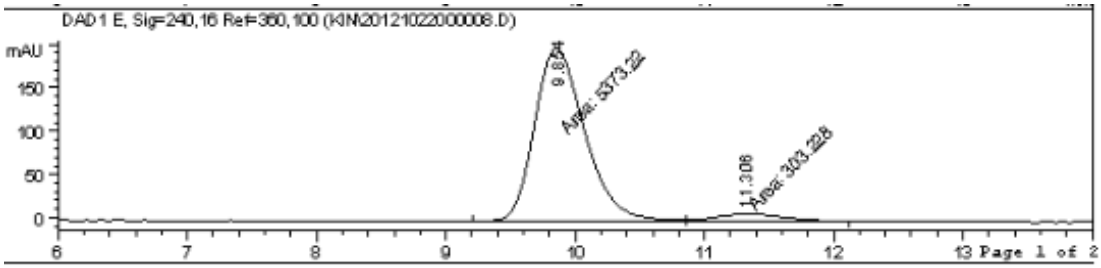


5i



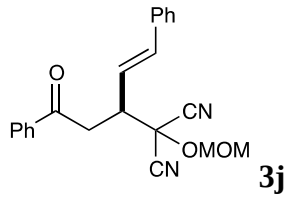
Signal 4: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.289	VB	0.4361	1150.34753	35.87642	50.1939
2	12.098	BB	0.4995	1141.46167	27.20297	49.8061



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.854	MF	0.4498	5373.22119	199.11612	94.6581
2	11.306	FM	0.5831	303.22842	8.66740	5.3419

Enantiomeric excess (89% ee) was measured by HPLC (Chiralcel OD-H, 4% IPA/Hexanes, 1 mL/min, Rt_1 = 9.9, Rt_2 = 11.3



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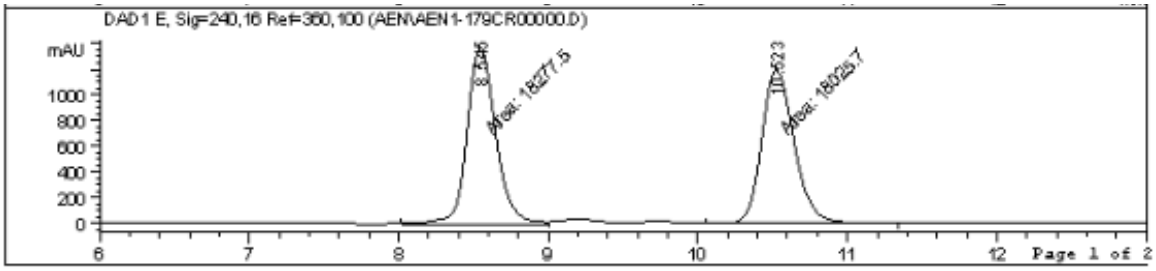
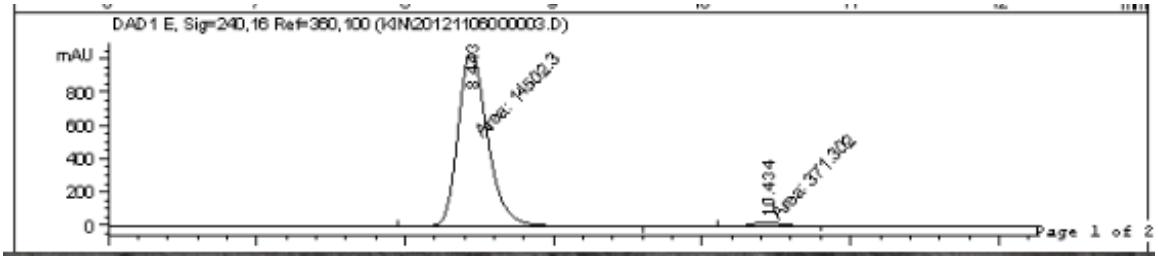
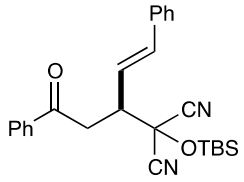


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.545	MM	0.2223	1.82775e4	1370.19897	50.3468
2	10.523	MM	0.2525	1.80257e4	1189.94397	49.6532

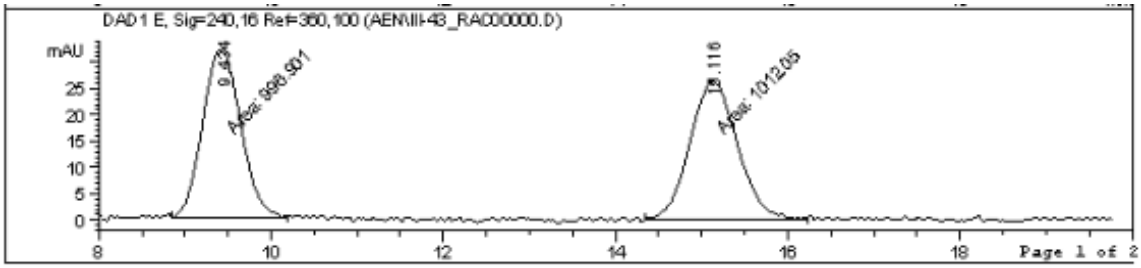


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.443	MM	0.2307	1.45023e4	1047.89502	97.5036
2	10.434	MM	0.2429	371.30151	25.47729	2.4964

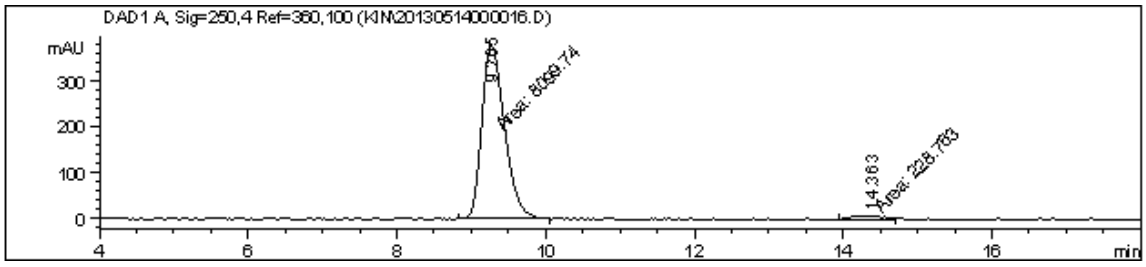
Enantiomeric excess (95% ee) was measured by HPLC (Chiralcel IA, 10% EtOH/Hexanes, 1 mL/min, Rt_1 = 8.4, Rt_2 = 10.4



5j

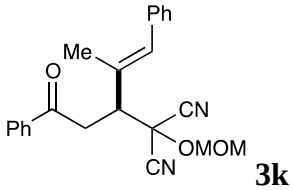


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.434	MM	0.5150	996.90125	32.26347	49.6229
2	15.116	MM	0.6321	1012.05139	26.68362	50.3771



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.265	MM	0.3552	8099.74268	380.03586	97.2533
2	14.363	MM	0.4513	228.76299	8.44903	2.7467

Enantiomeric excess (94% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 11.3, Rt_2 = 17.8



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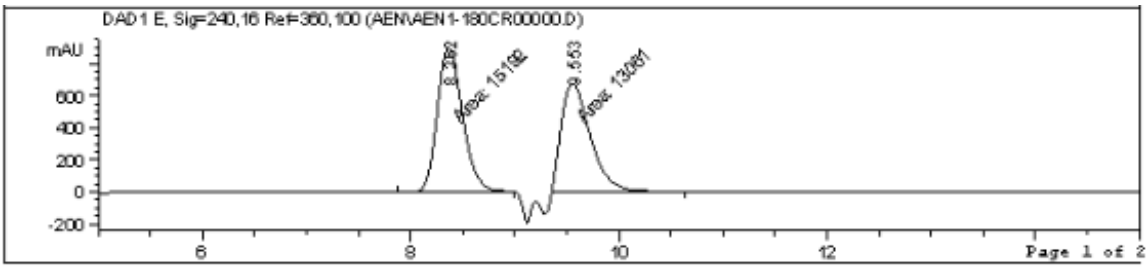
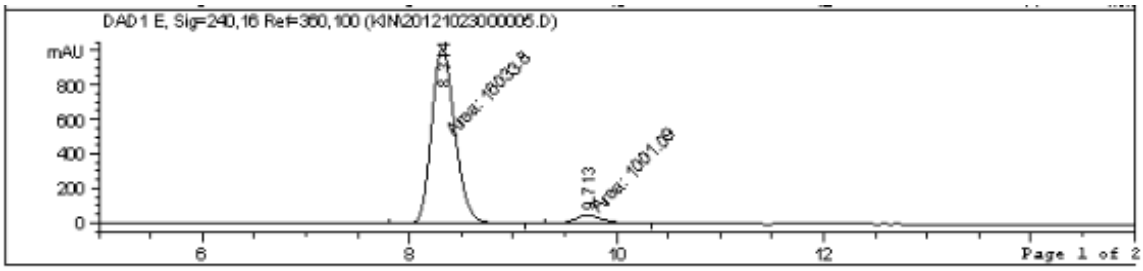
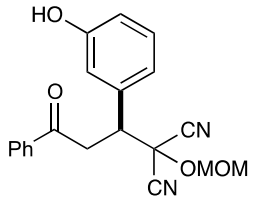


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.362	MM	0.2813	1.51920e4	900.14709	53.7713
2	9.553	MM	0.3231	1.30610e4	673.68451	46.2287



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.314	MM	0.2645	1.60338e4	1010.21722	94.1233
2	9.713	MM	0.3571	1001.08557	46.72836	5.8767

Enantiomeric excess (88% ee) was measured by HPLC (Chiralcel OD-H, 7% IPA/Hexanes, 1 mL/min, Rt_1 = 8.3, Rt_2 = 9.7



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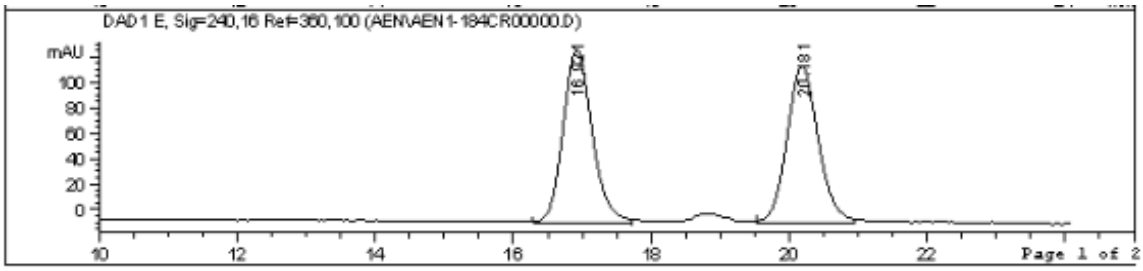
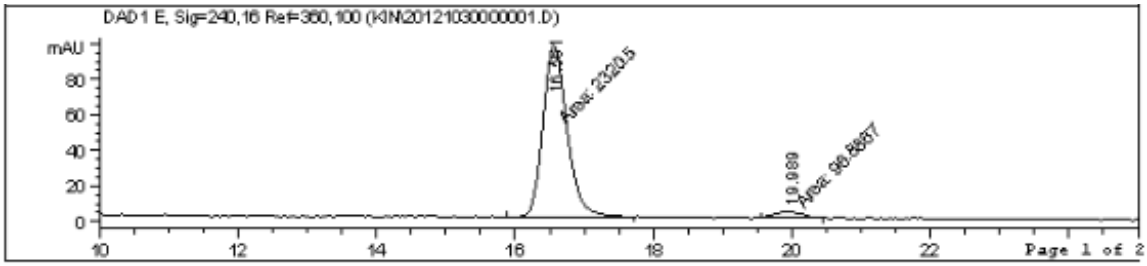
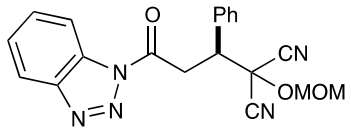


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.921	VV	0.4337	3978.15308	135.84450	50.2720
2	20.181	VV	0.4770	3935.11255	123.09692	49.7280



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.561	MM	0.4022	2320.50342	96.15486	95.9921
2	19.989	MM	0.4486	96.88666	3.59979	4.0079

Enantiomeric excess (92% ee) was measured by HPLC (Chiralcel IA, 10% EtOH/Hexanes, 1 mL/min, Rt_1 = 16.6, Rt_2 = 19.99



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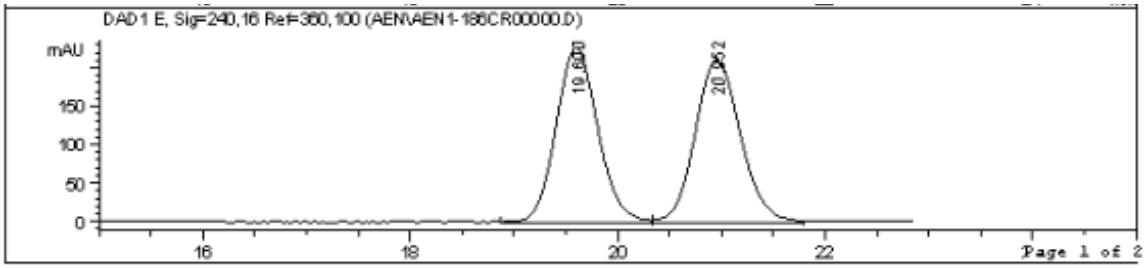
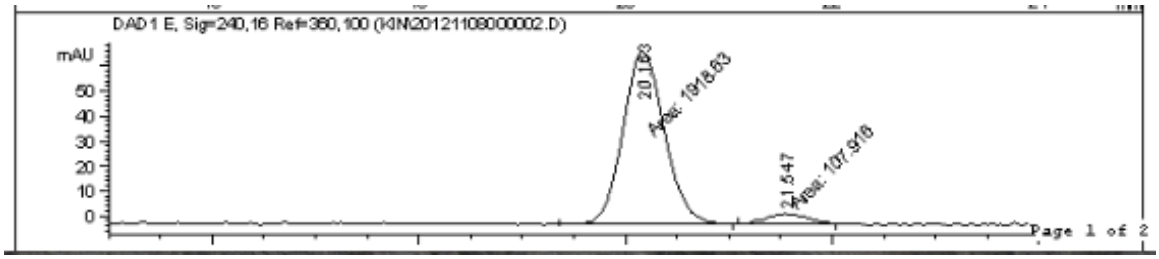
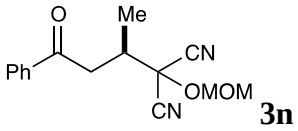


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.600	VV	0.4301	6359.70557	227.51653	49.7847
2	20.952	VB	0.4577	6414.71094	211.61069	50.2153



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.163	MM	0.4628	1918.63464	69.09690	94.6749
2	21.547	MM	0.4468	107.91570	4.02525	5.3251

Enantiomeric excess (89% ee) was measured by HPLC (Chiralcel AD-H, 6% IPA/Hexanes, 1 mL/min, Rt_1 = 20.2, Rt_2 = 21.5



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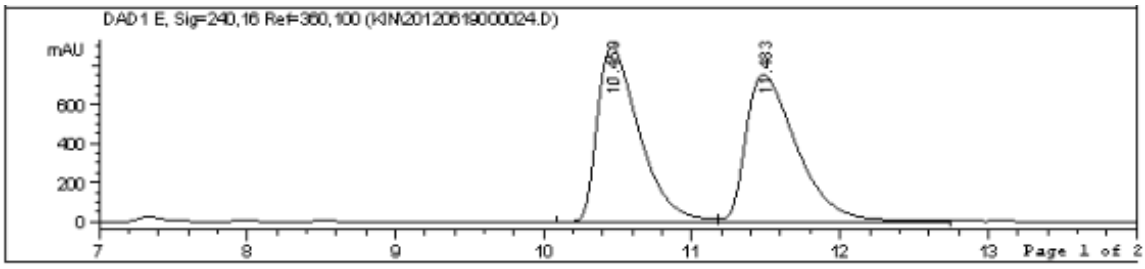
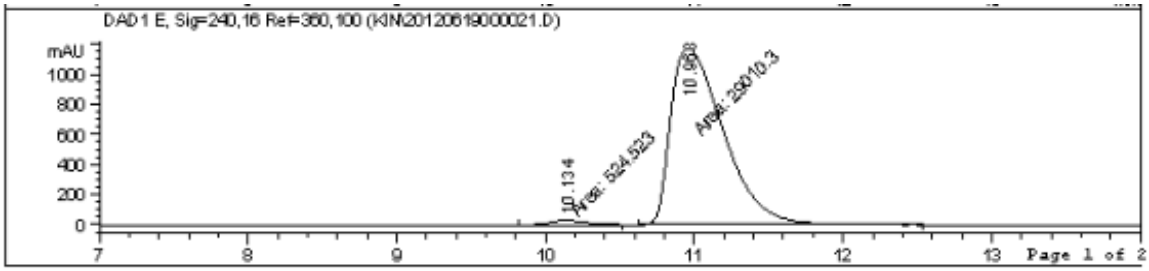
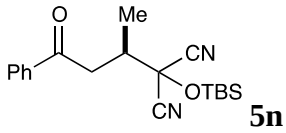


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.459	VV	0.2961	1.76878e4	896.71484	49.3896
2	11.483	VB	0.3544	1.81250e4	759.56500	50.6104



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.134	MM	0.2839	524.52325	30.79716	1.7759
2	10.963	MM	0.4137	2.90103e4	1168.82202	98.2241

Enantiomeric excess (96% ee) was measured by HPLC (Chiralcel AS-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 10.1, Rt_2 = 10.96



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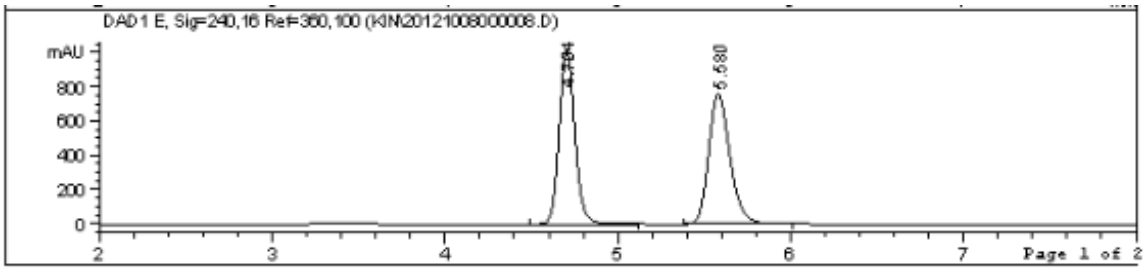
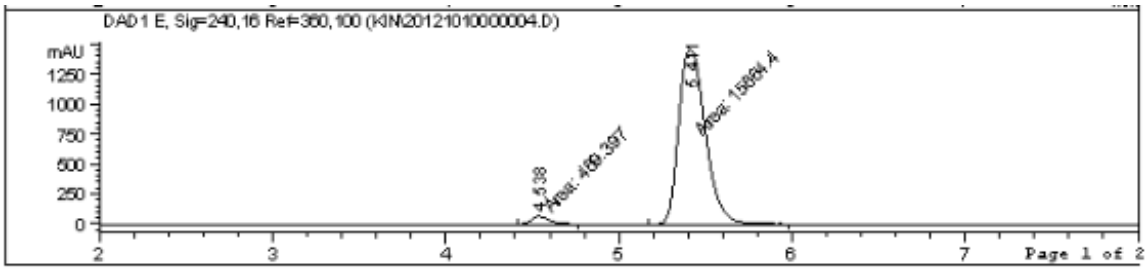
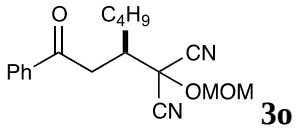


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.704	VB	0.0974	6422.09961	1021.12805	49.5889
2	5.580	VB	0.1322	6528.58447	760.42505	50.4111



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.538	MM	0.1201	469.39716	65.11942	2.9094
2	5.411	MM	0.1792	1.56644e4	1456.79980	97.0906

Enantiomeric excess (94% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 4.5, Rt_2 = 5.4



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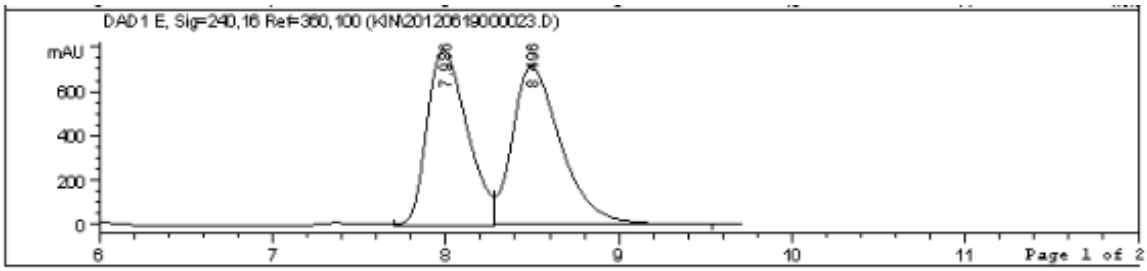
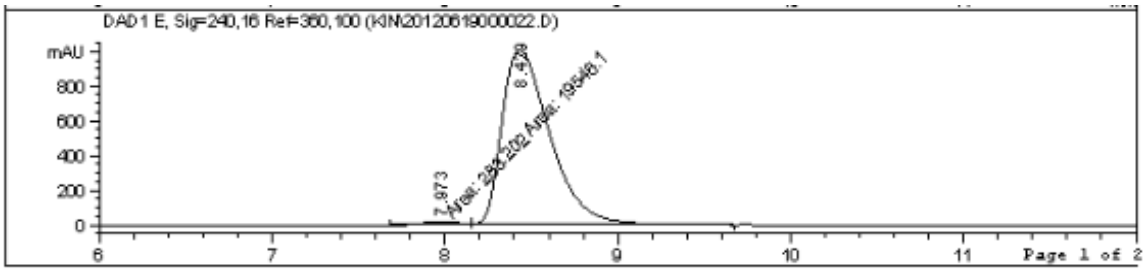
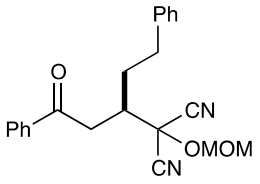


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.986	VV	0.2478	1.26928e4	788.70563	47.5205
2	8.496	VB	0.2991	1.40173e4	713.87817	52.4795



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.973	MF	0.2269	283.20175	20.80401	1.4282
2	8.429	FM	0.3227	1.95461e4	1009.36932	98.5718

Enantiomeric excess (97% ee) was measured by HPLC (Chiralcel AS-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 7.97, Rt_2 = 8.4



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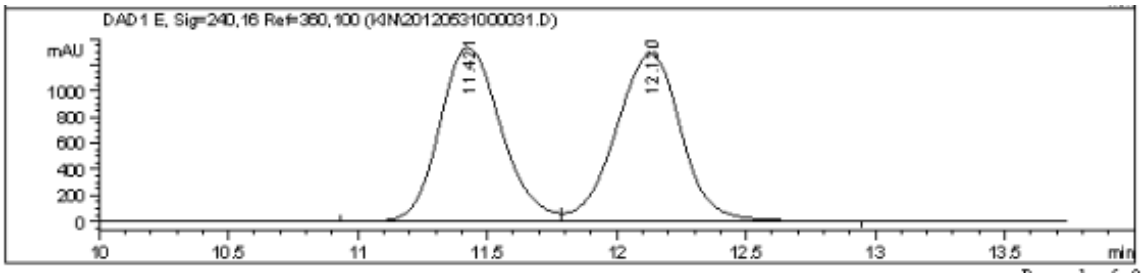
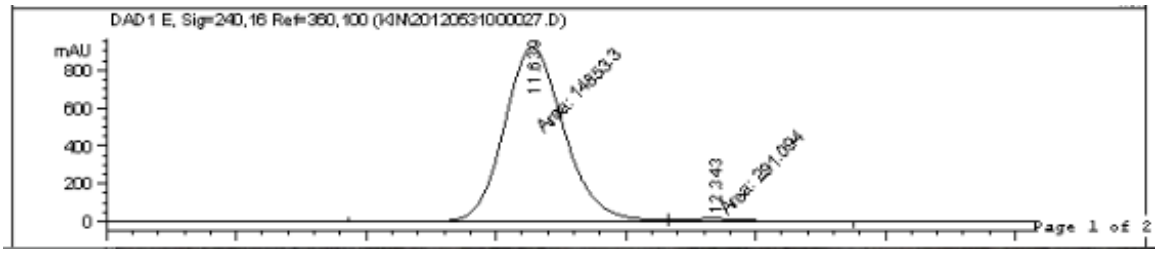
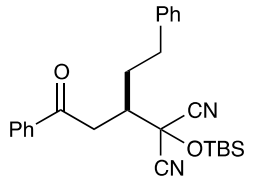


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.421	BV	0.2567	2.20497e4	1334.65540	49.3850
2	12.130	VB	0.2759	2.25989e4	1280.59119	50.6150



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.639	MF	0.2681	1.48533e4	923.33643	98.0779
2	12.343	FM	0.2961	291.09439	16.38369	1.9221

Enantiomeric excess (96% ee) was measured by HPLC (Chiralcel IA, 3% IPA/Hexanes, 1 mL/min, Rt_1 = 11.6, Rt_2 = 12.3



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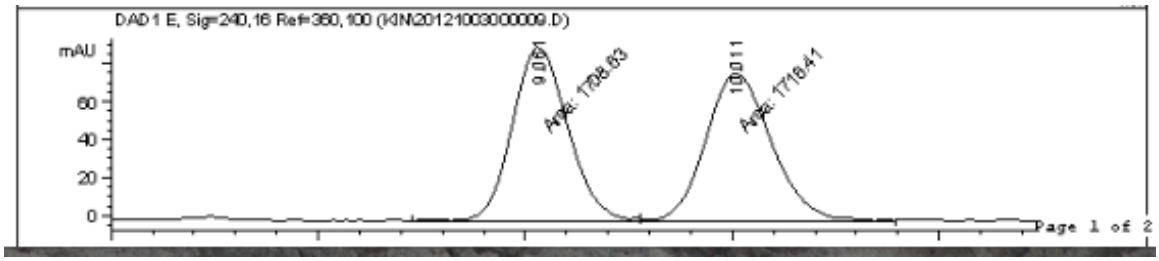
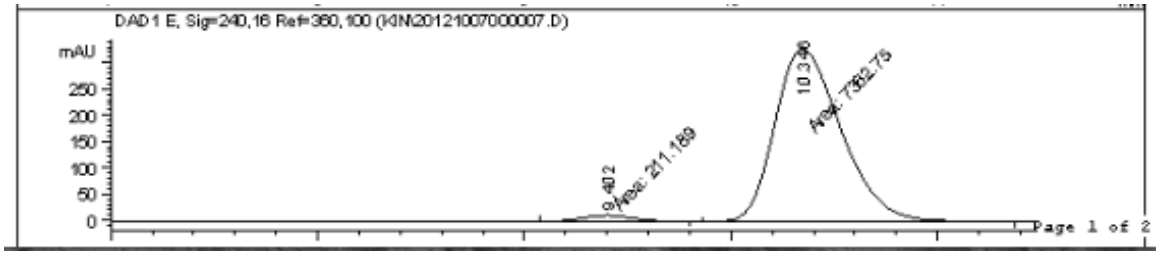
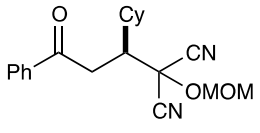


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.061	MF	0.3117	1708.62500	91.36168	49.8863
2	10.011	FM	0.3698	1716.41345	77.36601	50.1137



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.402	MM	0.2901	211.18944	12.13422	2.7884
2	10.346	MM	0.3719	7362.75146	329.99356	97.2116

Enantiomeric excess (94% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 9.4, Rt_2 = 10.3



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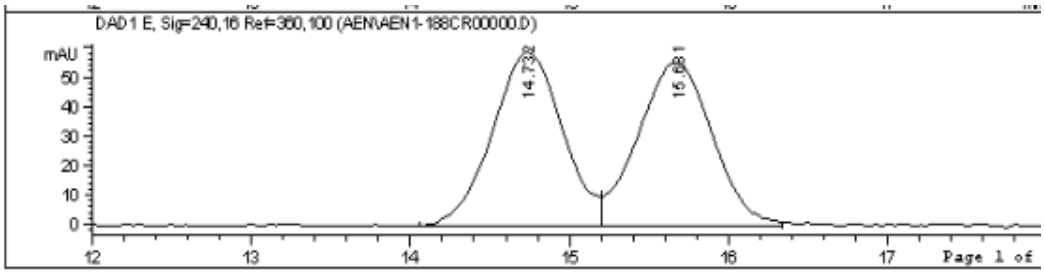
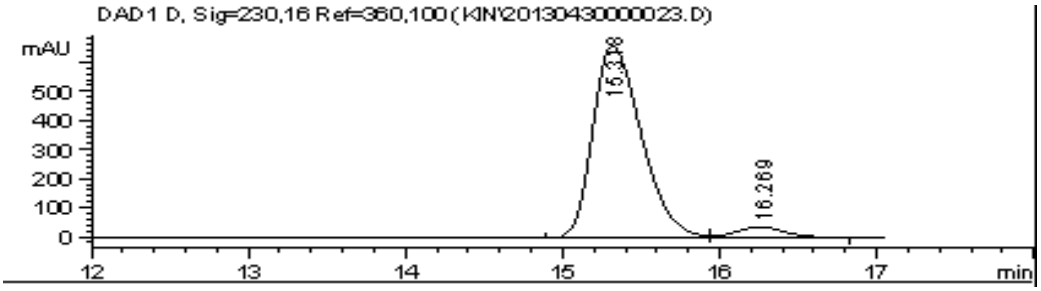


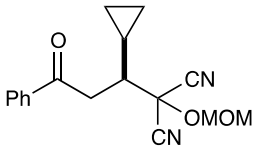
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.732	VV	0.3809	1826.23413	59.36001	50.0797
2	15.681	VV	0.4029	1820.42090	55.75108	49.9203



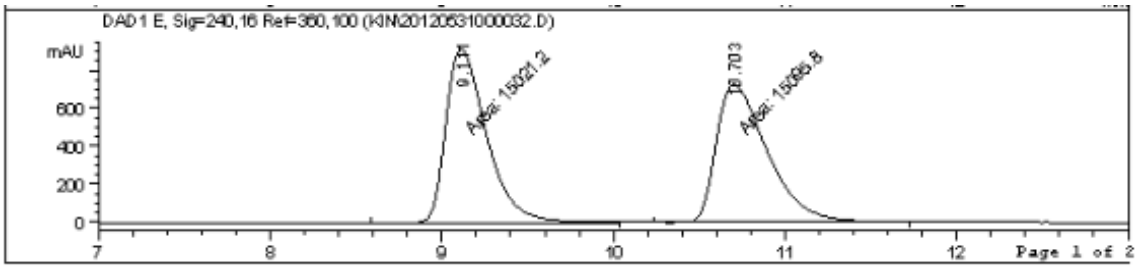
Signal 4: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.318	BV	0.3318	1.41904e4	662.64569	94.4147
2	16.269	VB	0.2929	839.45850	38.42511	5.5853

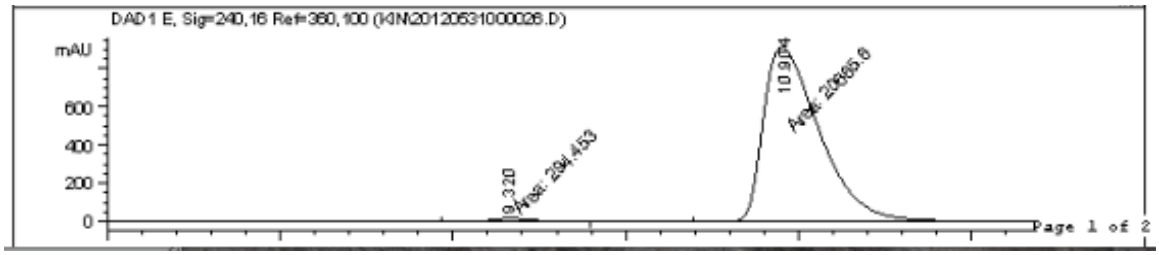
Enantiomeric excess (89% ee) was measured by HPLC (Chiralcel AD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 15.3, Rt_2 = 16.3



3r

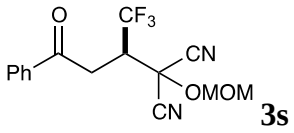


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.111	MM	0.2739	1.50212e4	914.01422	49.8762
2	10.703	MM	0.3449	1.50958e4	729.41174	50.1238

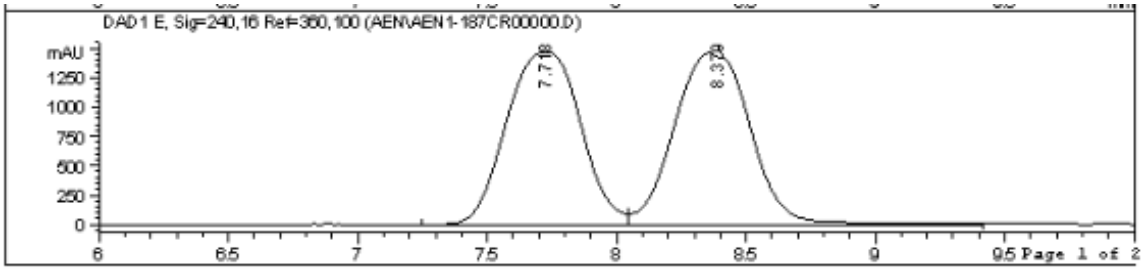


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.320	MM	0.2701	294.45319	18.16604	1.4048
2	10.904	MM	0.3764	2.06656e4	914.96112	98.5952

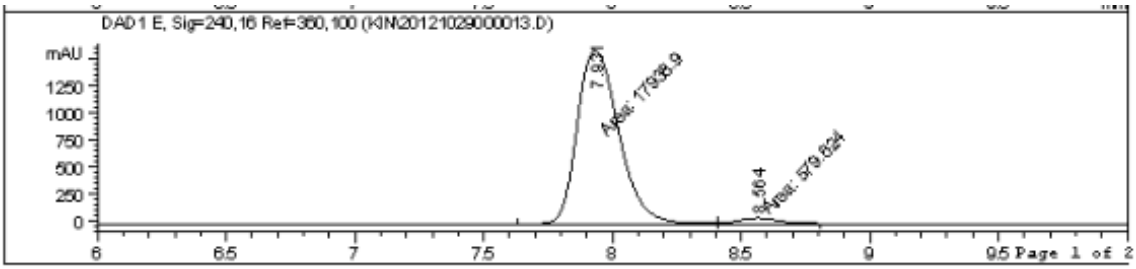
Enantiomeric excess (97% ee) was measured by HPLC (Chiralcel AS-H, 3% IPA/Hexanes, 1 mL/min, Rt_1 = 9.3, Rt_2 = 10.9



3s

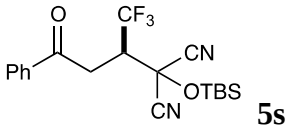


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.718	VV	0.2796	2.91989e4	1471.13245	49.2287
2	8.379	VB	0.2491	3.01139e4	1481.52087	50.7713

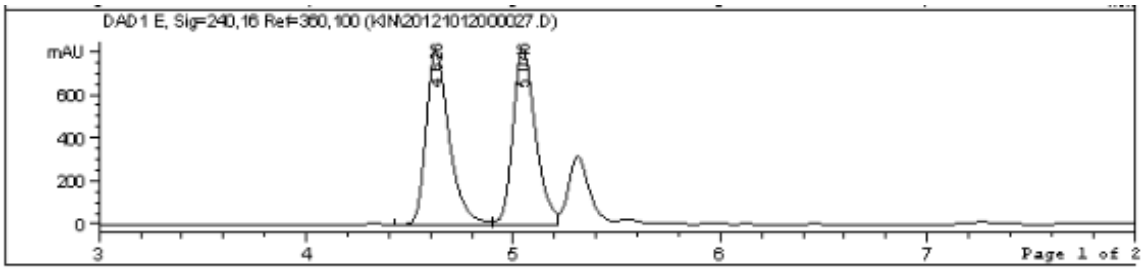


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.931	MM	0.1879	1.79389e4	1591.44592	96.8700
2	8.564	MM	0.1829	579.62408	52.82064	3.1300

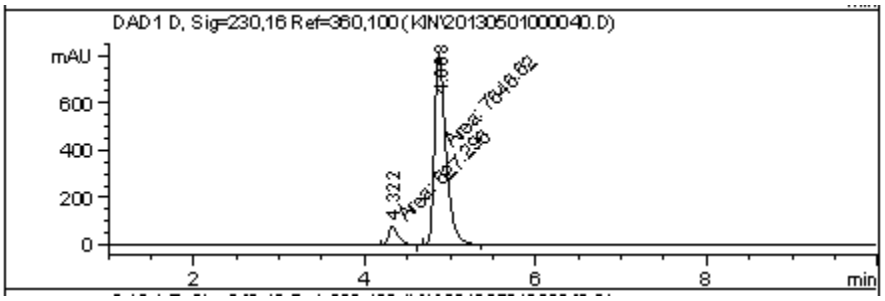
Enantiomeric excess (94% ee) was measured by HPLC (Chiralcel AD-H, 4% IPA/Hexanes, 1 mL/min, Rt_1 = 7.9, Rt_2 = 8.6



5s



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.626	VV	0.1181	6241.74219	808.13513	50.2806
2	5.046	VV	0.1168	6172.08496	811.05298	49.7194

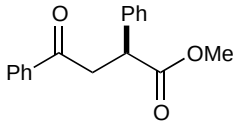


Signal 4: DAD1 D, Sig=230,16 Ref=360,100

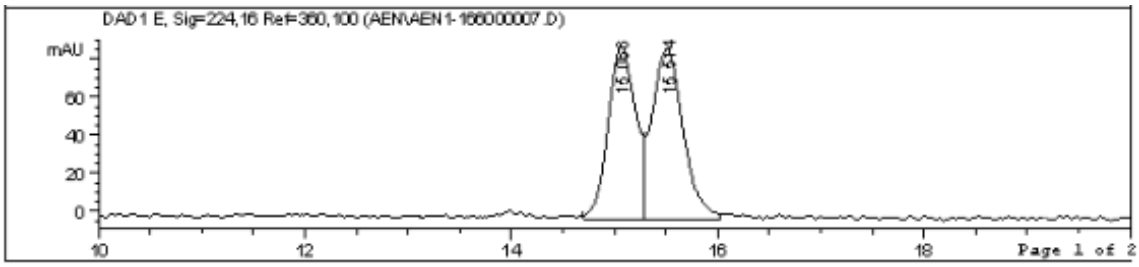
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.322	MM	0.1271	627.29620	82.27028	7.5816
2	4.868	MM	0.1563	7646.61719	815.23694	92.4184

Enantiomeric excess (85% ee) was measured by HPLC (Chiralcel OD-H, 1% IPA/Hexanes, 1 mL/min, Rt_1 = 4.3, Rt_2 = 4.9

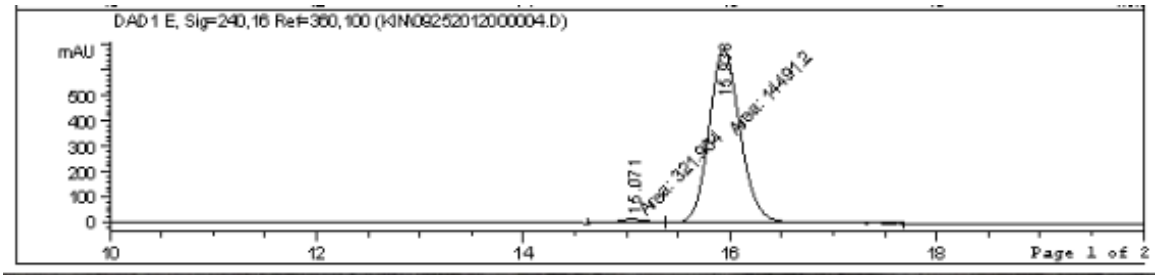
Functionalization of 5a (from TBS MAC)



7 (from 5a)

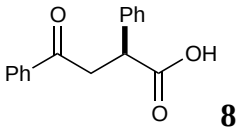


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.066	VV	0.2682	1713.73315	90.78651	47.7871
2	15.514	VV	0.2840	1872.44946	90.27586	52.2129

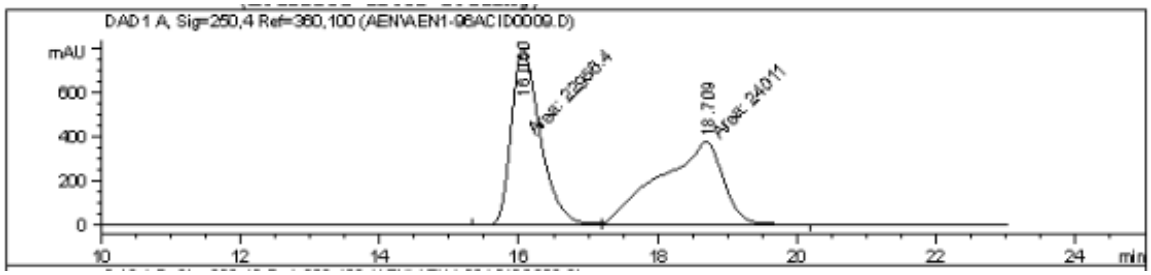


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.071	MF	0.3328	321.96436	16.12371	2.1735
2	15.938	FM	0.3518	1.44912e4	686.59778	97.8265

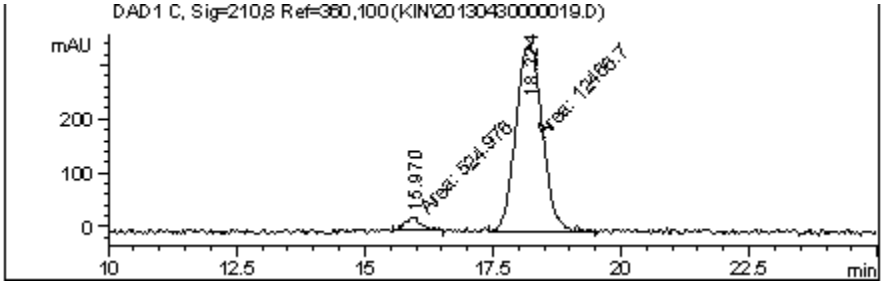
Enantiomeric excess (96% ee) was measured by HPLC (Chiralcel IA, 3% IPA/Hexanes, 1 mL/min, Rt_1 = 15.1, Rt_2 = 15.9



8 (from 5a)



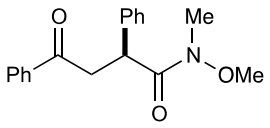
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.060	MF	0.4817	2.29564e4	794.25977	48.8772
2	18.709	FM	1.0701	2.40110e4	373.97354	51.1228



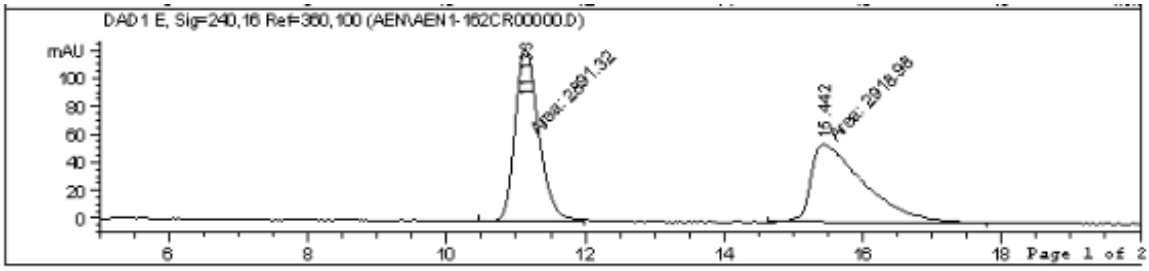
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.970	MM	0.3514	524.97559	24.89707	4.0409
2	18.224	MM	0.5973	1.24667e4	347.87949	95.9591

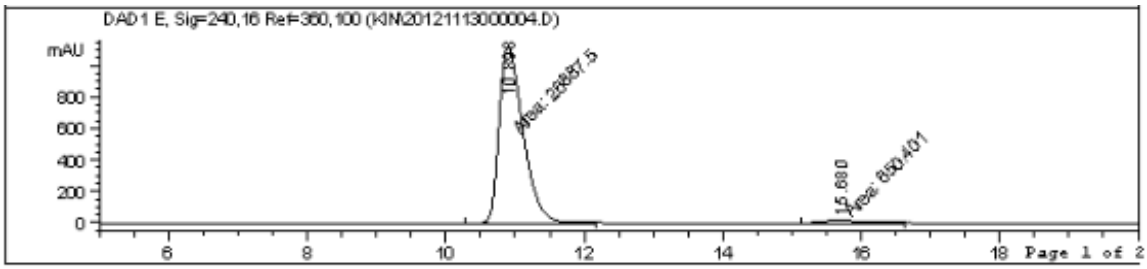
Enantiomeric excess (92% ee) was measured by HPLC (Chiralcel AD-H, 15% EtOH/Hexanes, 1.2 mL/min, Rt_1 = 16.0, Rt_2 = 18.2



10

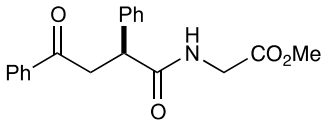


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.133	MM	0.3929	2891.32397	122.64952	49.7620
2	15.442	MM	0.8765	2918.97583	55.50390	50.2380

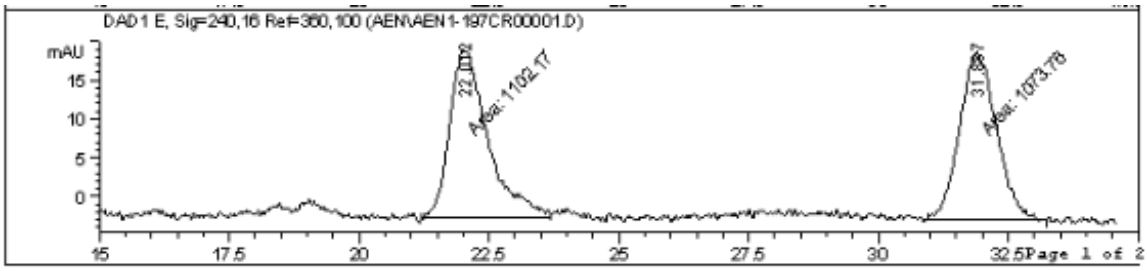


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.898	MM	0.4026	2.68875e4	1113.13074	97.6382
2	15.680	MM	0.7047	650.40149	15.38233	2.3618

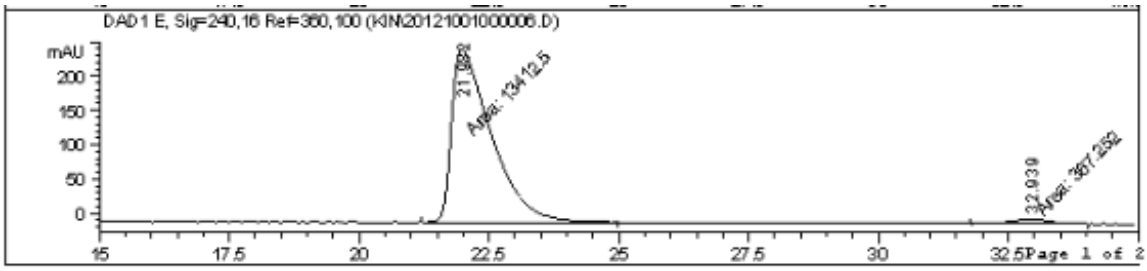
Enantiomeric excess (95% ee) was measured by HPLC (Chiralcel OD-H, 10% IPA/Hexanes, 1 mL/min, Rt_1 = 10.9, Rt_2 = 15.7



11



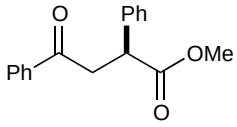
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.012	MM	0.8481	1102.16992	21.65931	50.6529
2	31.887	MM	0.8245	1073.75647	21.70561	49.3471



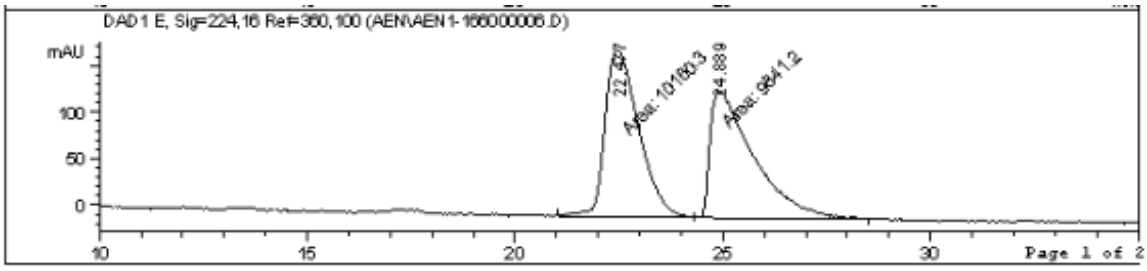
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.982	MM	0.8890	1.34125e4	251.44635	97.3348
2	32.939	MM	0.7937	367.25244	7.71217	2.6652

Enantiomeric excess (95% ee) was measured by HPLC (Chiralcel IA, 20% EtOH/Hexanes, 1 mL/min, Rt_1 = 21.98, Rt_2 = 32.9

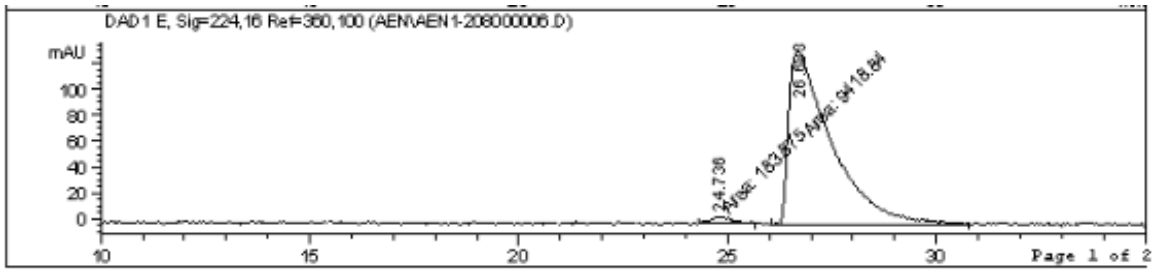
Functionalization of 3a (from MOM MAC)



7 (from 3a)

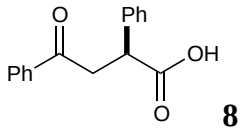


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.477	MM	0.9418	1.01603e4	179.80519	50.7976
2	24.889	MM	1.2112	9841.20410	135.42393	49.2024

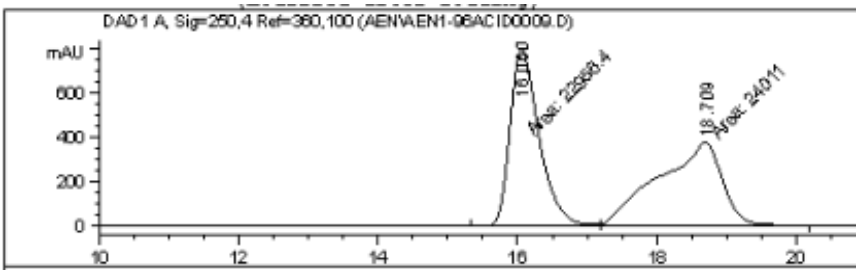


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.736	MM	0.6287	183.87469	4.87474	1.9148
2	26.683	MM	1.1708	9418.83789	134.08101	98.0852

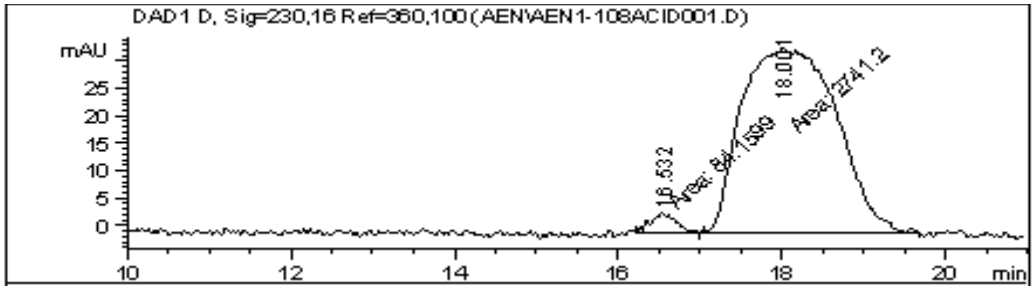
Enantiomeric excess (96% ee) was measured by HPLC (Chiralcel OD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 24.7, Rt_2 = 26.7



8 (from 3a)



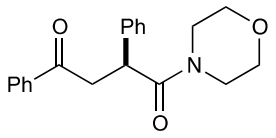
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.060	MF	0.4817	2.29564e4	794.25977	48.8772
2	18.709	FM	1.0701	2.40110e4	373.97354	51.1228



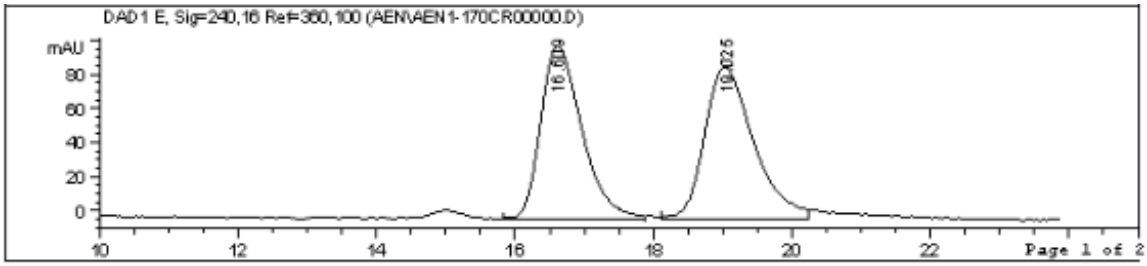
Signal 4: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.532	MM	0.3754	84.15991	3.73598	2.9787
2	18.001	MM	1.3431	2741.19849	34.01572	97.0213
Totals :				2825.35840	37.75170	

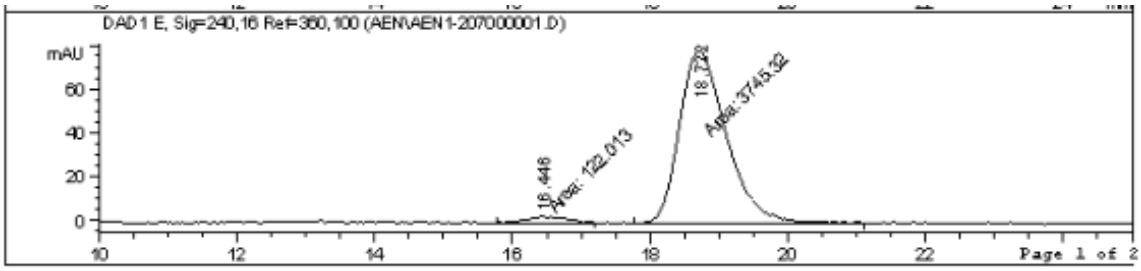
Enantiomeric excess (94% ee) was measured by HPLC (Chiralcel AD-H, 15% EtOH/Hexanes, 1.2 mL/min, Rt_1 = 16.5, Rt_2 =18.0



9



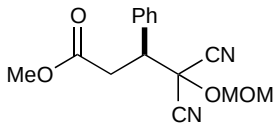
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.609	VV	0.5032	4234.32275	102.23381	48.6180
2	19.025	VV	0.6030	4475.04443	89.86695	51.3820



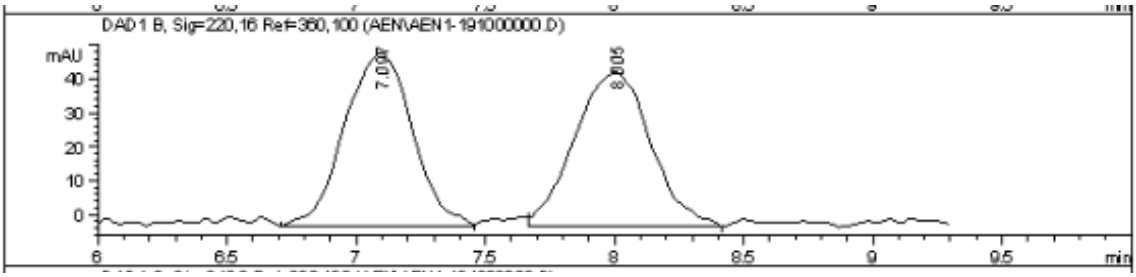
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.446	MM	0.6867	122.01315	2.96147	3.1550
2	18.722	MM	0.7946	3745.31860	78.56207	96.8450

Enantiomeric excess (94% ee) was measured by HPLC (Chiralcel OD-H, 10% IPA/Hexanes, 1 mL/min, Rt_1 = 16.4, Rt_2 = 18.7

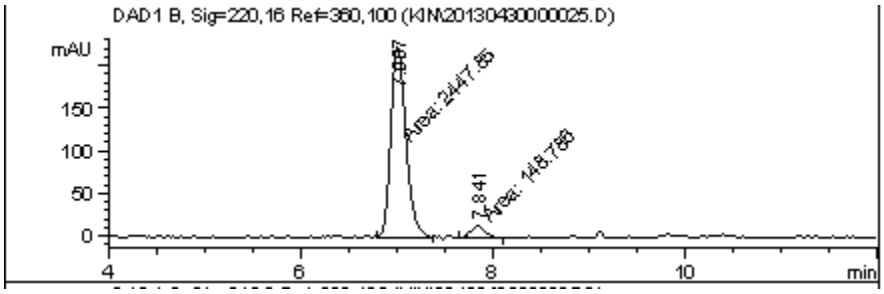
Synthesis of Succinic Diester 13



12



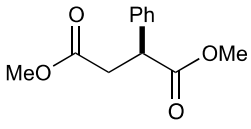
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.097	VV	0.2257	936.98352	51.16410	49.9831
2	8.005	VV	0.2545	937.61743	45.87346	50.0169



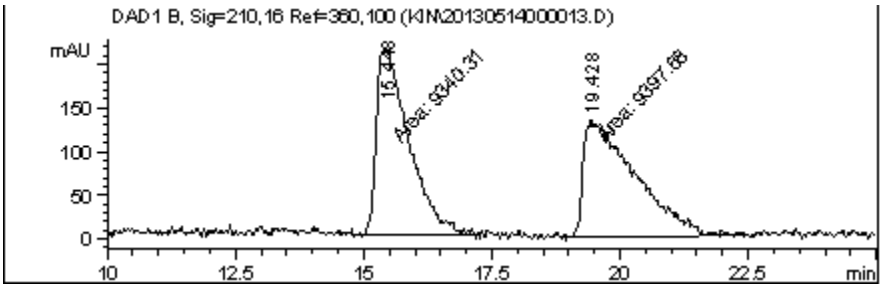
Signal 2: DAD1 B, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.007	MM	0.1824	2447.84839	223.69003	94.2700
2	7.841	MM	0.1773	148.78606	13.98635	5.7300

Enantiomeric excess (88% ee) was measured by HPLC (Chiralcel AD-H, 7% IPA/Hexanes, 1 mL/min, Rt_1 = 7.0, Rt_2 = 7.9

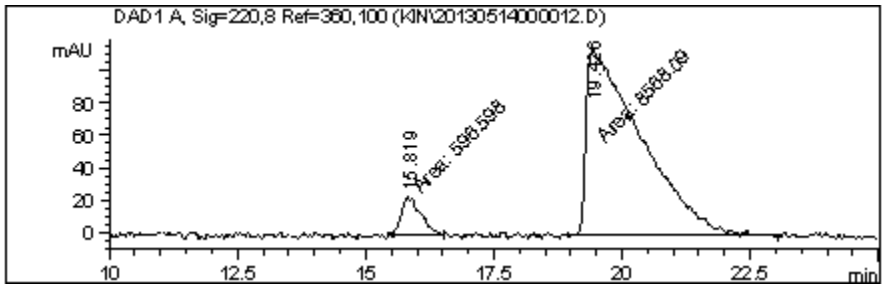


13



Signal 2: DAD1 B, Sig=210,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.448	MM	0.7289	9340.30664	213.57330	49.8469
2	19.428	MM	1.1704	9397.67676	133.82965	50.1531

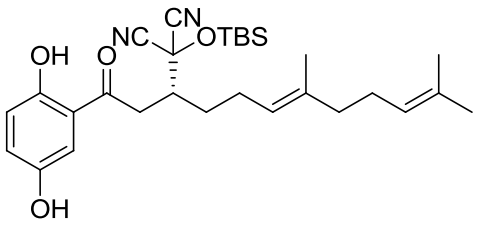


Signal 1: DAD1 A, Sig=220,8 Ref=360,100

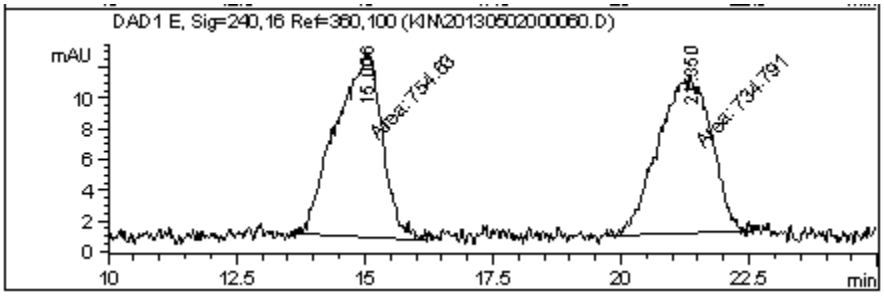
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.819	MM	0.4263	596.59814	23.32297	6.5097
2	19.426	MM	1.2345	8568.09473	115.67506	93.4903
Totals :				9164.69287	138.99802	

Enantiomeric excess (87% ee) was measured by HPLC (Chiralcel IA, 1% IPA/Hexanes, 1 mL/min, Rt_1 = 15.7, Rt_2 = 19.4

Total Synthesis of Fornicin C

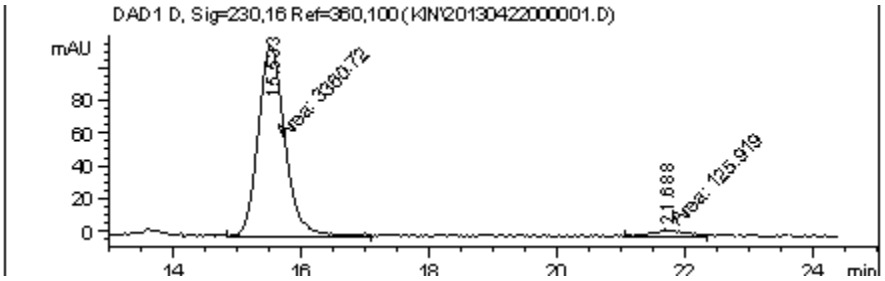


19



Signal 5: DAD1 E, Sig=240,16 Ref=360,100

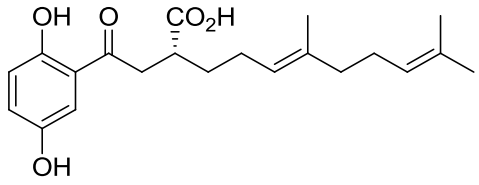
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.006	MM	1.0478	754.63000	12.00335	50.6660
2	21.350	MM	1.1817	734.79138	10.36392	49.3340



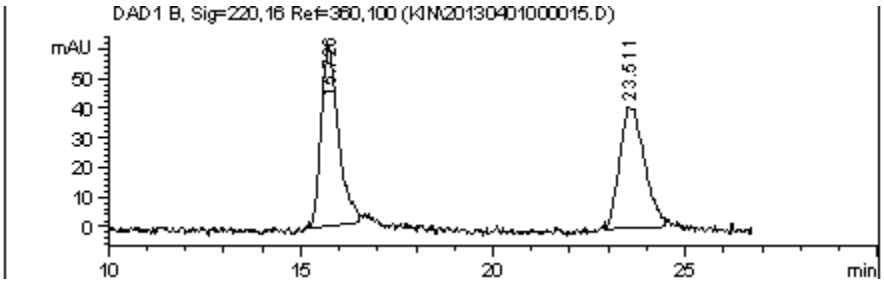
Signal 4: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.533	MM	0.4797	3360.71973	116.75571	96.3885
2	21.688	MM	0.5348	125.91933	3.92410	3.6115

Enantiomeric excess (92% ee) was measured by HPLC (Chiralcel AD-H, 2% IPA/Hexanes, 1 mL/min, Rt_1 = 15.5, Rt_2 = 21.7

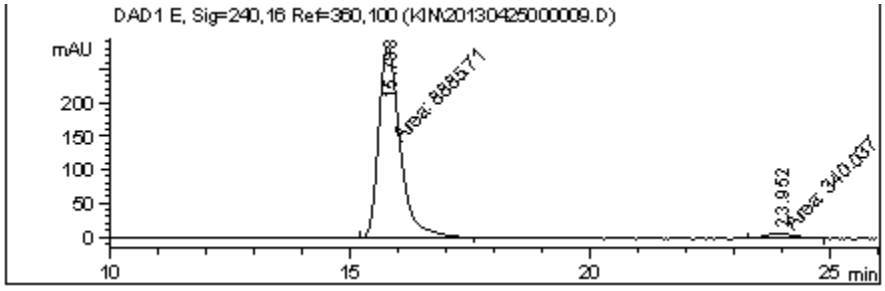


20



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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.726	BB	0.3924	1914.93445	61.31244	51.0808
2	23.511	BB	0.5446	1833.89917	41.10149	48.9192



Signal 5: DAD1 E, Sig=240,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.788	MM	0.5203	8885.71094	284.61926	96.3143
2	23.952	MM	0.7529	340.03668	7.52726	3.6857

Enantiomeric excess (92% ee) was measured by HPLC (Chiralcel AD-H, 10% IPA/Hexanes, 1 mL/min, Rt_1 = 15.8, Rt_2 = 24.0