Supporting Information

Direct Conversion of Primary Alcohols to 1,2-Amino Alcohols: Enantioselective Iridium-Catalyzed Carbonyl Reductive Coupling of Phthalimido-Allene *via* Hydrogen Auto-Transfer

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General Information

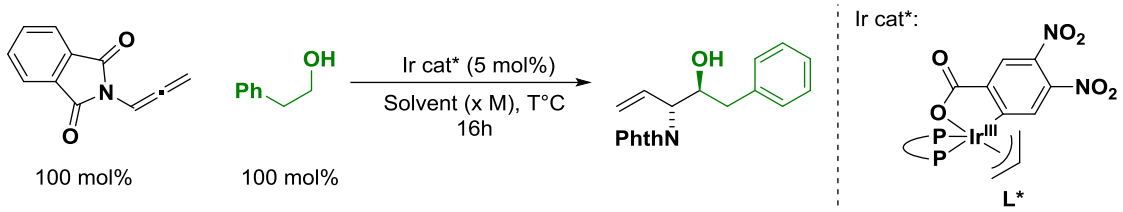
All reactions were run under an atmosphere of argon, unless otherwise indicated. Resealable pressure tubes (13x100 mm) were purchased from Fischer Scientific (catalog number 14–959–35C) and were flame dried followed by cooling in a desiccator or under a stream of argon prior to use. All commercial reagents and anhydrous solvents were used as received from vendors (Strem Chemicals, Fischer Scientific, Sigma Aldrich and Combi Blocks) without further purification. Preparative column chromatography employing Silicycle silica gel (40-63 μm) was performed according to the method of Still.[1] Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Dynamic Absorbents F254). Visualization was accomplished with UV light followed by dipping in CAM, *p*-Anisaldehyde (PAA), or $KMnO_4$ stain solution followed by heating. Specific optical rotations were recorded on an Atago AP-300 automatic polarimeter at the sodium line (589.3 nm) in $CHCl_3$. Solution concentrations are given in the units of 10^{-2} g mL^{-1}. Racemic reactions were conducted using racemic catalyst prepared in utilizing racemic BINAP ligand.

Spectroscopy, Spectrometry, and Data Collection

Infrared spectra were recorded on a Perkin-Elmer 1600 spectrometer. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion (M+H, M+Na), or a suitable fragment ion. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with a Varian INOVA (500 MHz) spectrometer equipped with a Bruker AVANCE III cryoprobe. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from tetramethylsilane or ppm relative to the center of the singlet at 7.26 ppm for deuteriochloroform. Data reported as multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Integration and coupling constants were reported in Hertz (Hz). Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a Varian INOVA (125 MHz) spectrometer and were routinely run with broadband decoupling. Chemical shifts are reported in delta (δ) units, ppm relative to the center of the triplet at 77.16 ppm for deuteriochloroform. Fluorine-19 nuclear magnetic resonance (^{19}F NMR) spectra were recorded with a Varian INOVA (470 MHz) spectrometer. Deuterium nuclear magnetic resonance (^{2}H NMR) spectra were recorded in $CHCl_3$ solution with a Varian Gemini 500 (77 MHz) spectrometer (relaxation delay 2.00s).

Experimental Details and Spectral Data

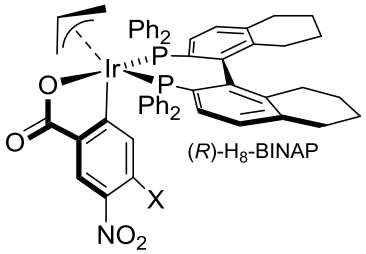
Selected Optimization Experiments



Entry	L*	Solvent (M)	Temp (°C)	Yield (%)	ee (%)	dr
1	(*R*)-DTBM-SEGPHOS	THF (0.2 M)	100	<10	N/D	N/D
2	(*R*)-Cl,MeO-BIPHEP	THF (0.2 M)	100	42	87	>20:1
3	(*R*)-Tol-BINAP	THF (0.2 M)	100	31	85	>20:1
4	(*R*)-H8-BINAP	THF (0.2 M)	100	69	96	>20:1
5	(*R*)-H8-BINAP	Dioxane (0.2 M)	100	68	94	>20:1
6	(*R*)-H8-BINAP	PhMe (0.2 M)	100	59	92	>20:1
7	(*R*)-H8-BINAP	THF (0.5 M)	100	60	94	>20:1
8	(*R*)-H8-BINAP	THF (0.1 M)	100	37	97	>20:1
9	(*R*)-H8-BINAP	THF (0.2 M)	90	65	96	>20:1
10	(*R*)-H8-BINAP	THF (0.2 M)	80	40	96	>20:1
11[a]	(*R*)-H8-BINAP	THF (0.2 M)	100	71	96	>20:1

[a]150 mol% of phthalimido-allene 1 and 48 h reaction time

Synthesis of Ir-V and Ir-VI



(*R*)-Ir-V: X = CN
(*R*)-Ir-VI: X = NO_2

To a dried pressure tube with a magnetic stir bar under an argon atmosphere charged with Cs_2CO_3 (586 mg, 1.80 mmol, 225 mol%), the corresponding benzoic acid (1.60 mmol, 200 mol%), (*R*)-H_8-BINAP (505mg, 0.80 mmol, 100 mol%), and $[Ir(cod)Cl]_2$ (268 mg, 0.40 mmol, 50 mol%) was added THF (8 mL, 0.1 M) followed by allyl acetate (0.22 mL, 2.0 mmol, 250 mol%). The resulting mixture was stirred at ambient temperature for 30 min, at which point the reaction vessel was transferred to an oil bath at 80 °C. After stirring for 120 min, the reaction mixture was allowed to cool to ambient temperature. The mixture was filtered through a celite plug with the aid of THF. The filtrate was concentrated *in vacuo* and the residue subjected to column chromatography (SiO_2, 20:1 DCM:THF). The gum-like product was dissolved in a minimum volume of THF and precipitated upon rapid addition of hexanes. The product was filtered and washed with hexanes, followed by removal of trace amount of solvent *in vacuo*.

(R)-Ir-V: 4-cyano-3-nitrobenzoic acid (307 mg) was used. The title complex was obtained as light yellow powder in 85% yield (716 mg).

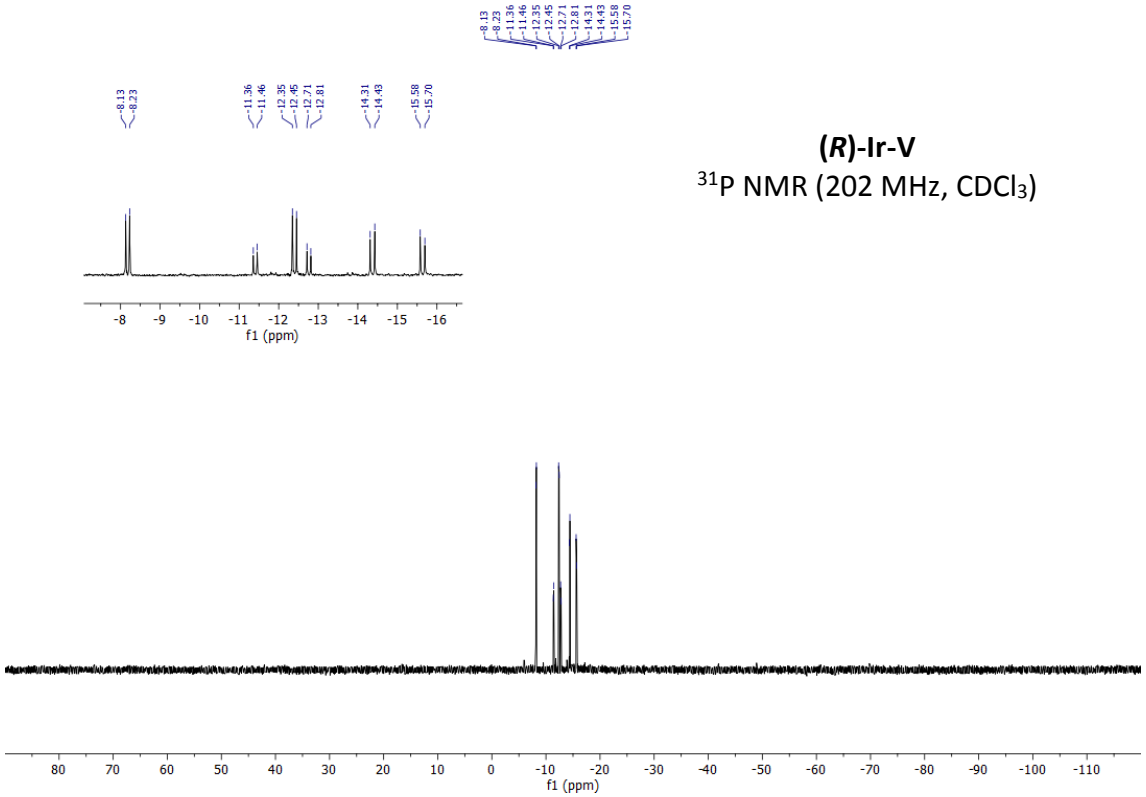
(*R*)-Ir-VI: 3,4-dinitrobenzoic acid (340 mg) was used. The title complex was obtained as light yellow powder in 86% yield (736 mg).

(*R*)-Ir-V:

^{31}P NMR (202 MHz, $CDCl_3$): δ −8.18 (d, *J* = 20.0 Hz), −11.41 (d, *J* = 19.9 Hz), −12.40 (d, *J* = 21.0 Hz), −12.76 (d, *J* = 19.7 Hz), −14.37 (d, *J* = 23.7 Hz), −15.64 (d, *J* = 23.7 Hz).

HRMS (H+, *m/z*) for $C_{55}H_{47}IrN_2O_4P_2$: calcd. = 1053.2690; found = 1053.2675.

MP: [175-182] °C (decomposition)



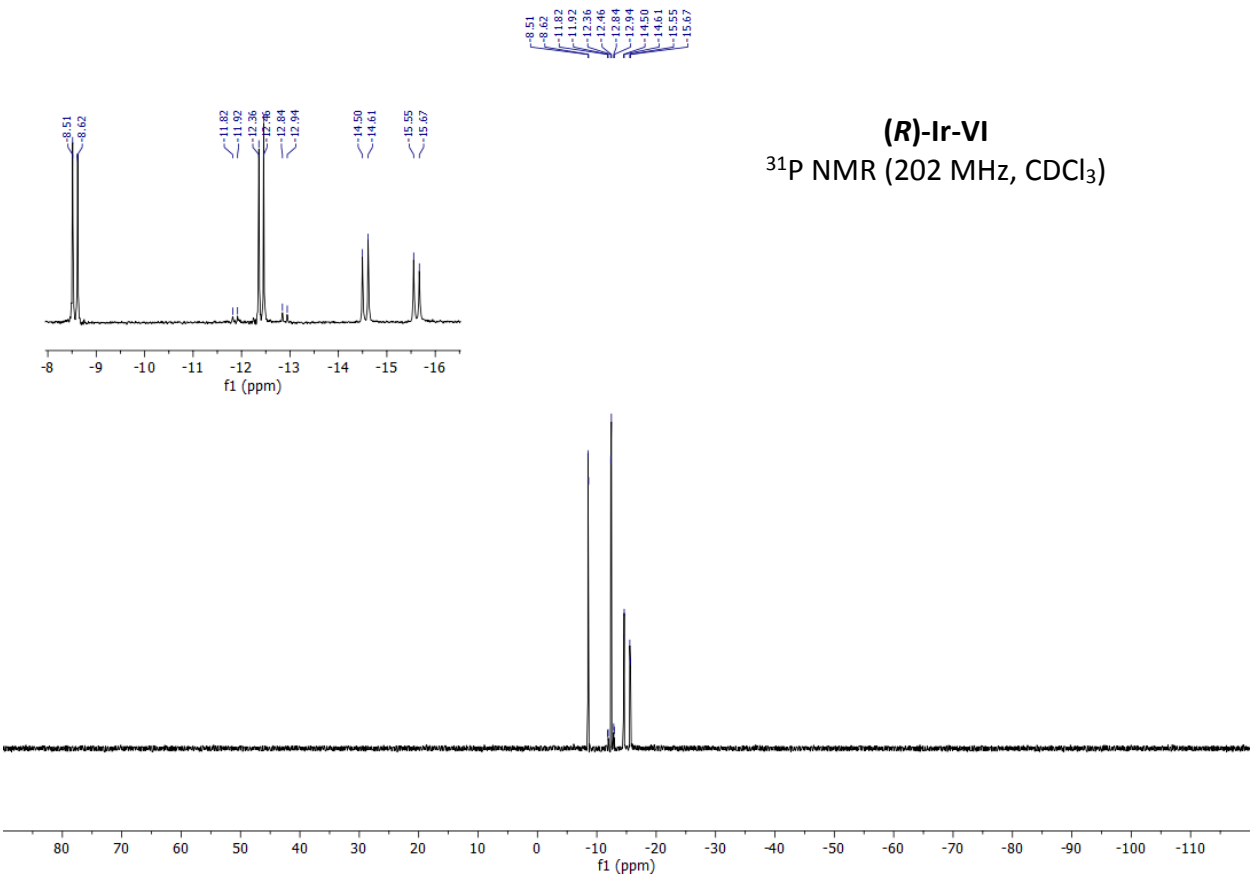
(*R*)-Ir-V
^{31}P NMR (202 MHz, $CDCl_3$)

(*R*)-Ir-VI:

^{31}P NMR (202 MHz, $CDCl_3$): δ -8.56 (d, *J* = 20.7 Hz), -11.87 (d, *J* = 20.1 Hz), -12.41 (d, *J* = 20.0 Hz), -12.89 (d, *J* = 19.9 Hz), -14.56 (d, *J* = 23.7 Hz), -15.61 (d, *J* = 23.7 Hz).

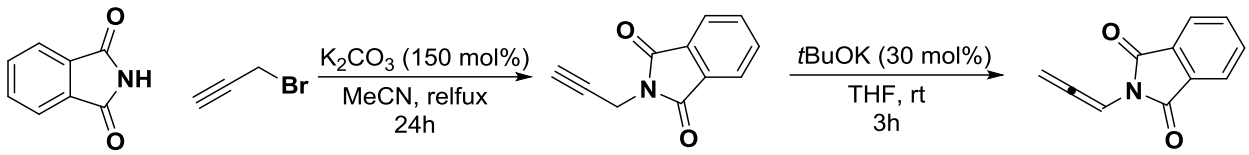
HRMS (H+, *m/z*) for $C_{54}H_{47}IrN_2O_6P_2$: calcd. = 1073.2588; found = 1073.2579.

MP: [226-232] °C (decomposition)



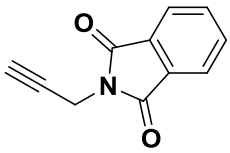
(*R*)-Ir-VI
^{31}P NMR (202 MHz, $CDCl_3$)

Synthesis of Phthalimido-Allene 1



(100 mol%) (150 mol%) **S1** 95% yield **1** 24% yield

Synthesis of N-Propargylphthalimide (S1)



S1

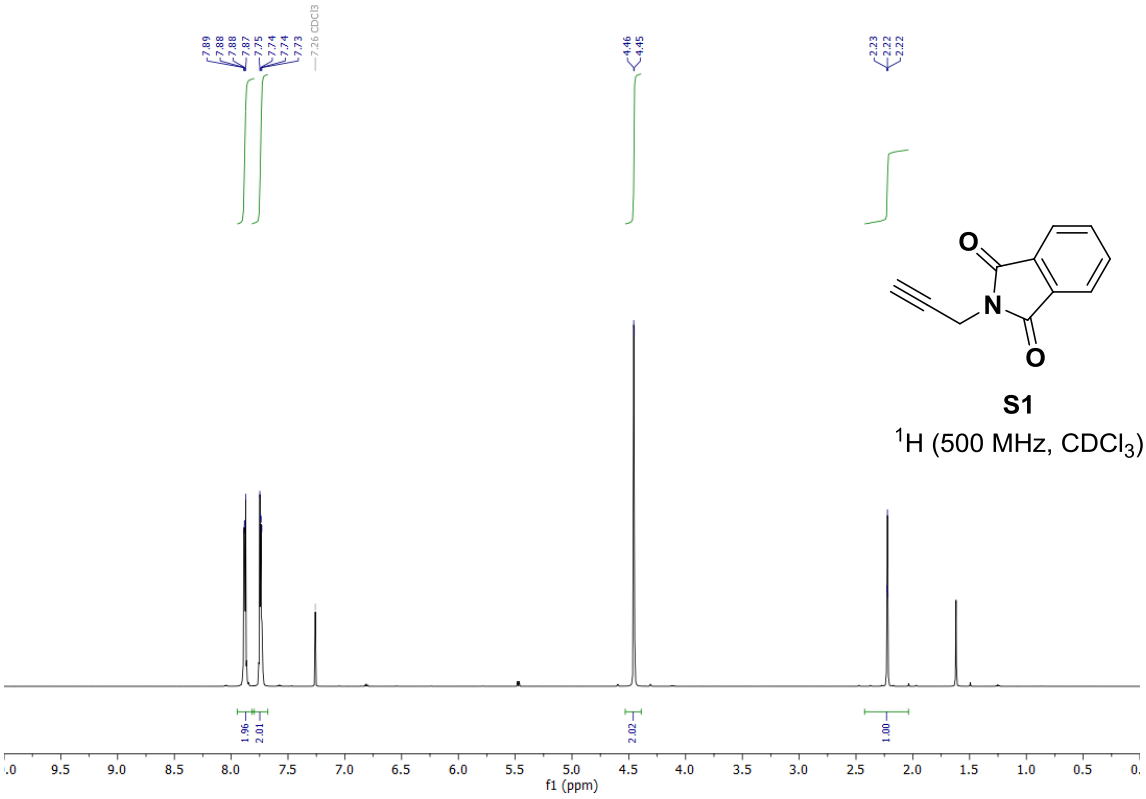
S1 can also be purchased and used from Combi-Blocks.

To a round-bottomed flask equipped with a magnetic stir bar under an argon atmosphere charged with phthalimide (15.2 g, 103 mmol, 100 mol%) and K_2CO_3 (21.4 g, 155 mmol, 150 mol%) in CH_3CN (250 mL) was added propargyl bromide (80% wt in PhMe, 23.0 g, 155 mmol, 150 mol%). The reaction mixture was allowed to stir for 24 hours at reflux. The hot reaction mixture was then filtered through a pad of Celite and washed with CH_3CN (3 x 15 mL). The mixture was then concentrated under reduced pressure. The residue was then solubilized in DCM, resulting in a suspension of starting material which was then filtered off through a pad of Celite. The resulting residue was concentrated under reduced pressure, dissolved in a minimum volume of DCM, and precipitated upon rapid addition of pentane. The product was filtered and washed with pentane, followed by removal of trace amount of solvent in vacuo, to provide a white solid (18.1 g, 97.8 mmol) in 95% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.88 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.0 Hz, 2H), 4.45 (d, *J* = 2.5 Hz, 1H), 2.22 (t, *J* = 2.5 Hz, 1H).

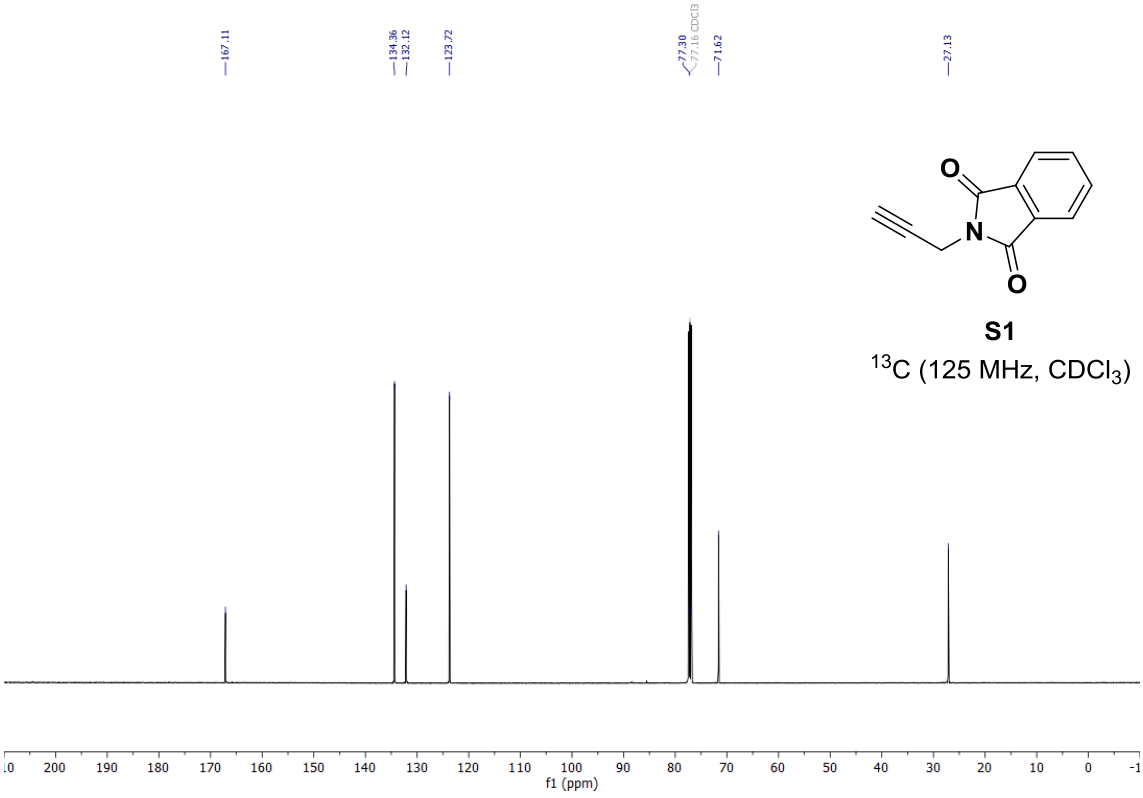
^{13}C NMR (125 MHz, $CDCl_3$) δ: 167.1, 134.4, 132.1, 123.7, 77.3, 71.6, 27.1.

The spectral data recorded for the compound was in complete agreement with the literature.[2]



S1

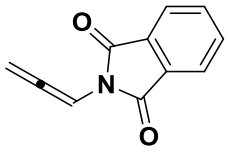
^{1}H (500 MHz, $CDCl_3$)



S1

^{13}C (125 MHz, $CDCl_3$)

Synthesis of Phthalimido-Allene (1)



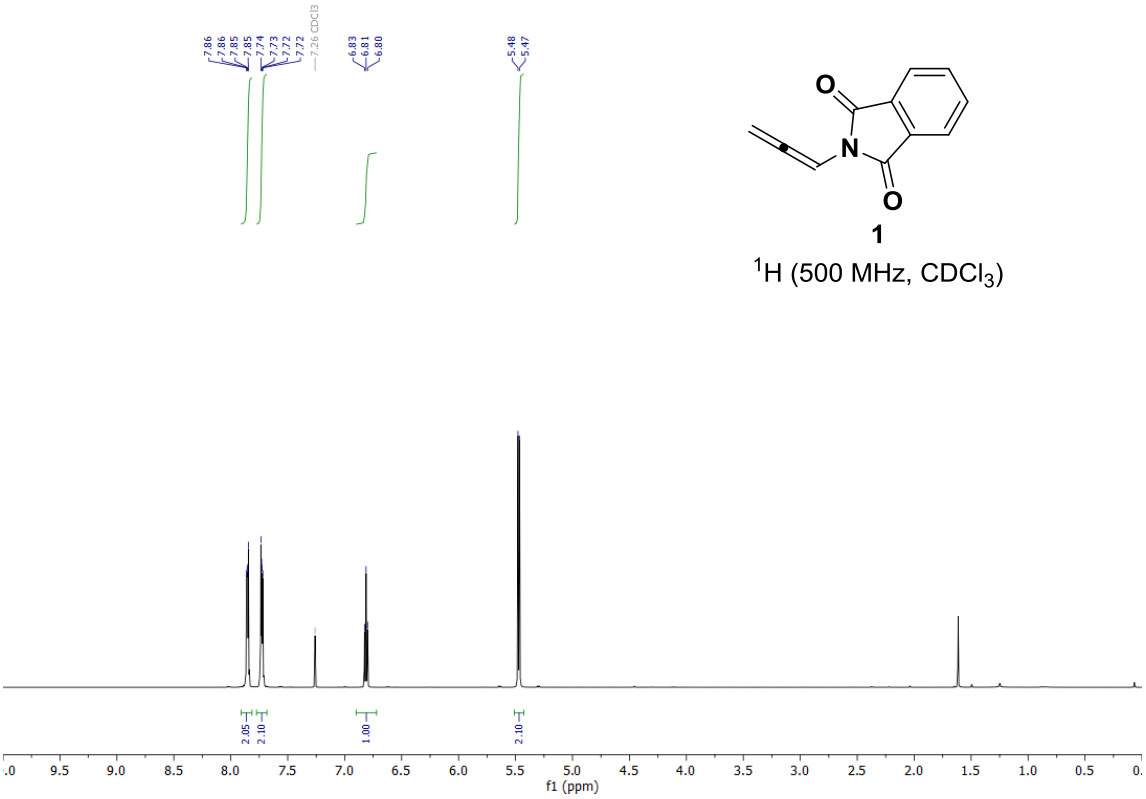
1

To a round-bottomed flask equipped with a magnetic stir bar under an argon atmosphere charged with N-propargylphthalimide **S1** (9.26 g, 50.0 mmol, 100 mol%) in dried THF (50 mL) was added potassium *tert*-butoxide (1.68 g, 15 mmol, 30 mol%). The reaction mixture was allowed to stir at ambient temperature for 3 hours. The reaction mixture was then filtered through a pad of Celite, washed with THF, and the solvent removed in vacuo. The residue was purified by flash column chromatography (SiO_2, 0-10% EtOAc in hexanes) to give the phthalimido-allene (2.21 g, 11.9 mmol) as a pale green crystalline solid in 24% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.85 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.81 (t, *J* = 6.7 Hz, 1H), 5.47 (d, *J* = 6.6 Hz, 1H).

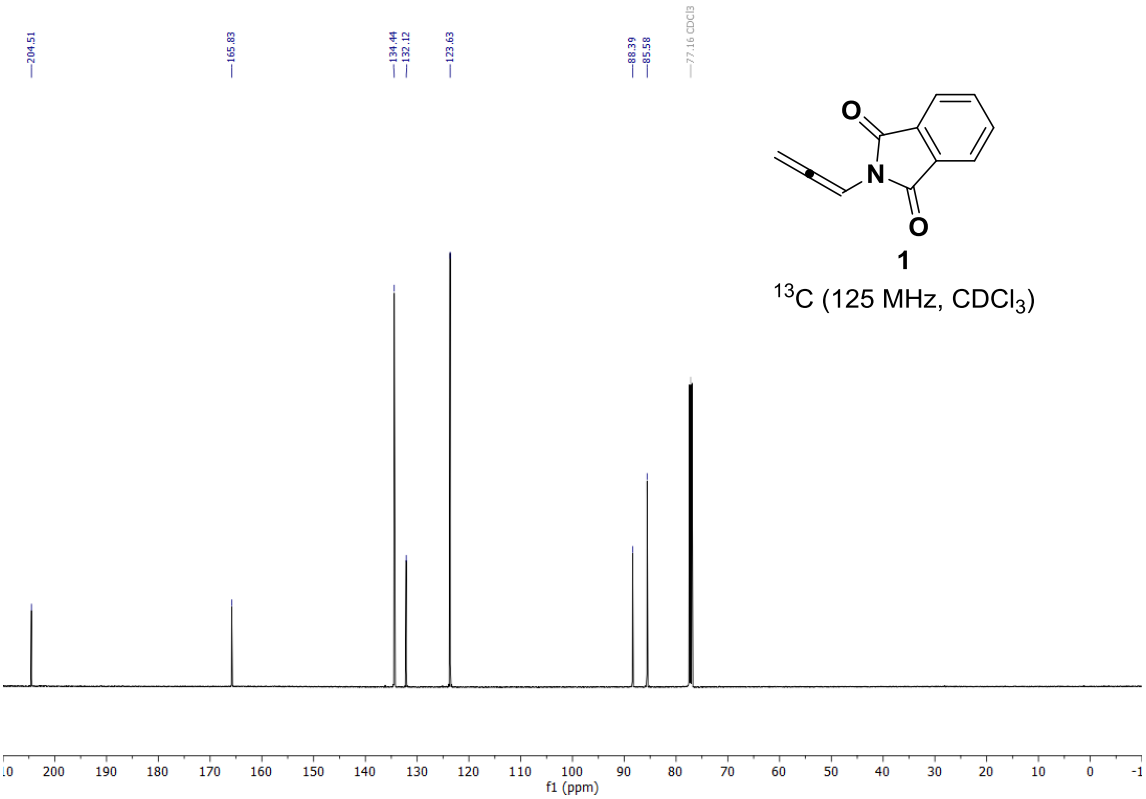
^{13}C NMR (125 MHz, $CDCl_3$) δ: 204.5, 165.8, 134.4, 133.1, 123.6, 88.4, 85.6.

The spectral data recorded for the compound was in complete agreement with the literature.[3]



1

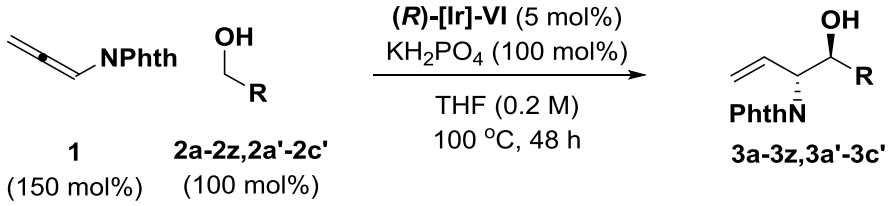
^{1}H (500 MHz, $CDCl_3$)



1

^{13}C (125 MHz, $CDCl_3$)

Procedures and Spectral Data for the Coupling Products of Phthalimido-Allene 1 and Alcohols 3a-3z, 3a'-3c'

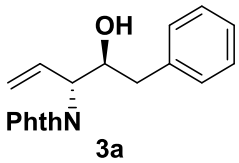


1 (150 mol%) **2a-2z,2a'-2c'** (100 mol%) **3a-3z,3a'-3c'**

General Procedure

To a dried pressure tube with a magnetic stir bar under an argon atmosphere charged with Ir-**VI** (10.7 mg, 0.01 mmol) (5 mol%), phthalimido-allene (55 mg, 0.3 mmol) (150 mol%), alcohol (0.2 mmol) (100 mol%), and KH_2PO_4 (27.2 mg, 0.2 mmol) (100 mol%) was added THF (1.0 mL) (0.2 M). The tube was sealed with a PTFE lined cap and the reaction mixture was allowed to stir for 48 hours at 100 °C. After reaching ambient temperature, the solvent was removed in vacuo and the residue was subjected to flash column chromatography (SiO_2) under the noted conditions to furnish the products **3a-3z, 3a'-3c'**.

2-((3*R*,4*S*)-4-hydroxy-5-phenylpent-1-en-3-yl)isoindoline-1,3-dione (3a)



3a

Alcohol **2a** (24.0 µL, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), the title compound **3a** (48.8 mg, 0.16 mmol, >20:1 dr) was obtained as a light yellow solid in 80% yield.

TLC (SiO_2) R_f = 0.35 (20:80 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.28 – 7.15 (m, 5H), 6.34 (ddd, *J* = 17.1, 10.3, 7.9 Hz, 1H), 5.36 (d, *J* = 10.7 Hz, 1H), 5.32 (d, *J* = 17.1 Hz, 1H), 4.78 – 4.76 (m, 1H), 4.41 (ddd, *J* = 7.7, 5.8, 4.7 Hz, 1H), 3.45 (brs, 1H), 2.90 – 2.81 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.6, 137.9, 134.4, 131.8, 131.4, 129.4, 128.7, 126.7, 123.7, 120.4, 73.0, 58.7, 40.9.

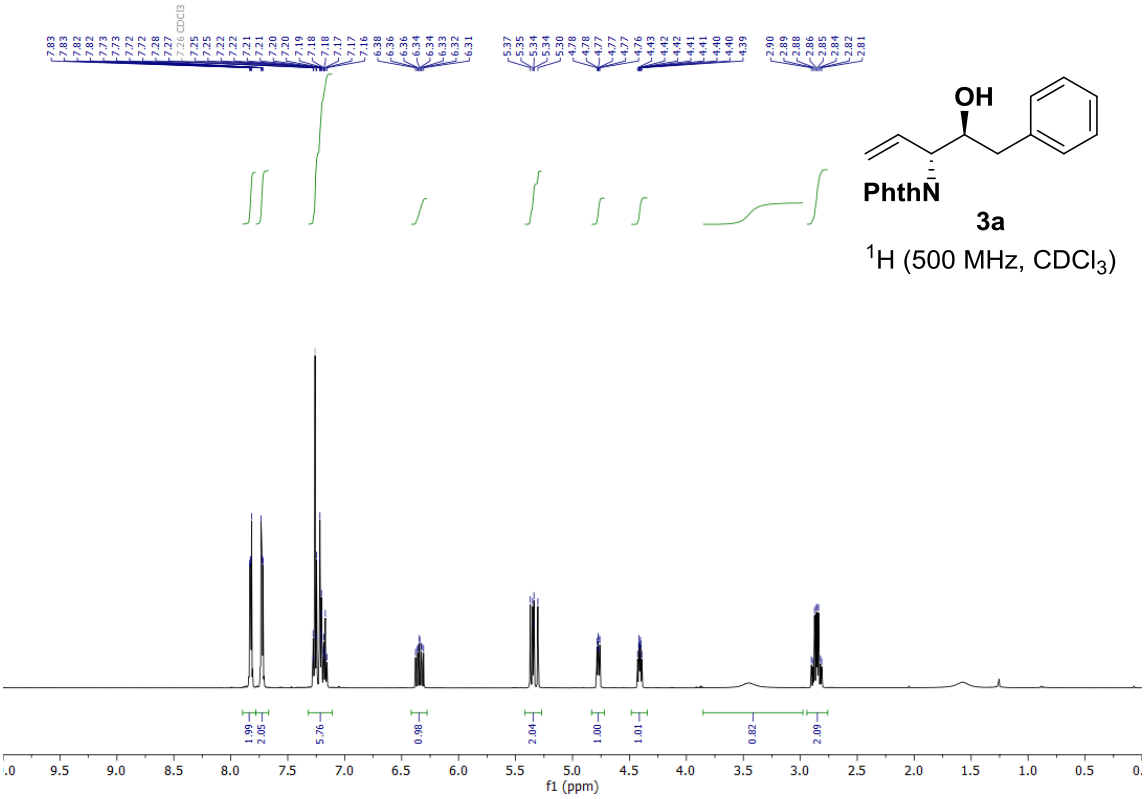
HRMS (Na+, *m/z*) for $C_{19}H_{17}NO_3$: calcd. = 330.1101; found = 330.1104.

FTIR (neat): 3549, 1698, 1383, 1334, 1055, 721, 703.

HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 96%.

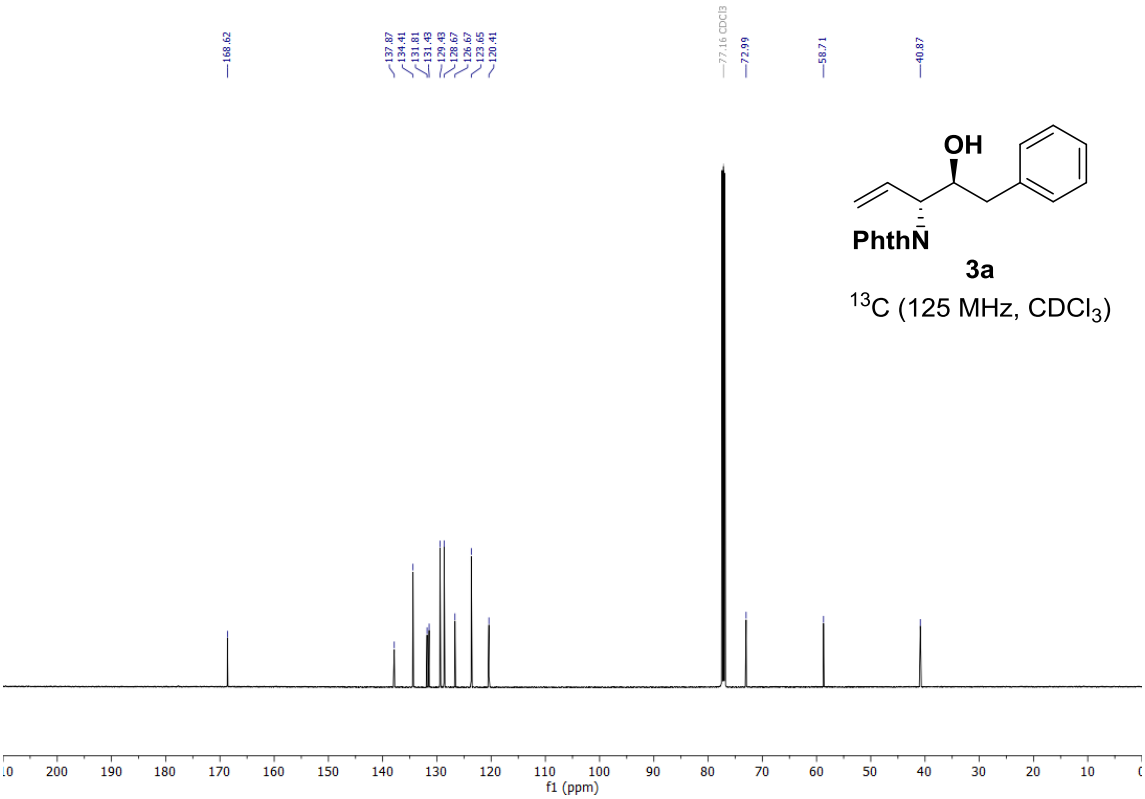
$[\alpha]_D^{34}$ = +56.6° (c = 1.31, $CHCl_3$).

MP [121 – 126] °C



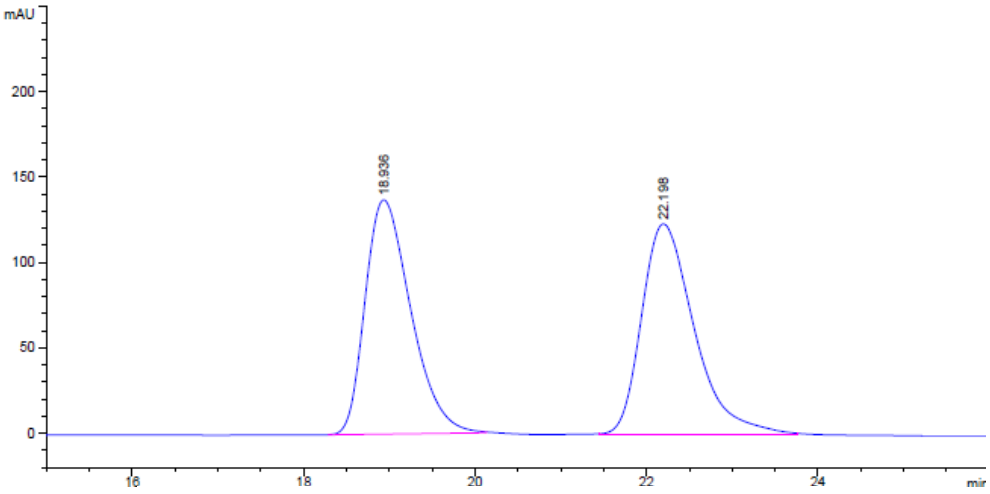
3a

^{1}H (500 MHz, $CDCl_3$)



3a

^{13}C (125 MHz, $CDCl_3$)



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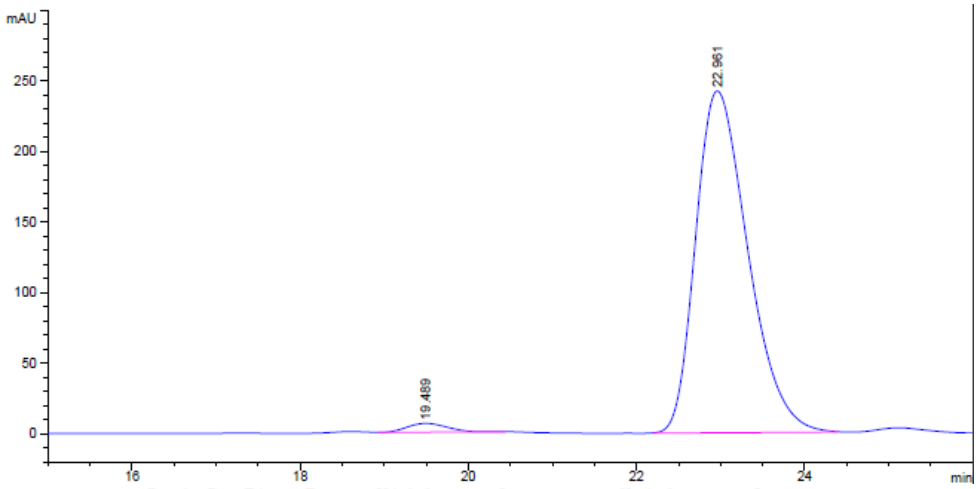

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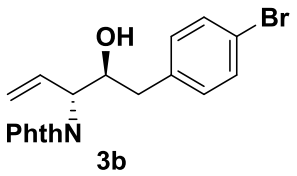
2	22.961	BB	0.6719	1.04640e4	242.27353	98.0543

2-((3*R*,4*S*)-5-(4-bromophenyl)-4-hydroxypent-1-en-3-yl)isoindoline-1,3-dione (3b)



3b

Alcohol **2b** (40.2 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), the title compound **3b** (49.9 mg, 0.13 mmol, >20:1 dr) was obtained as a pale yellow oil in 65% yield.

TLC (SiO_2) R_f = 0.33 (20:80 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.36 (d, *J* = 8.3 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.32 (ddd, *J* = 17.1, 10.3, 7.9 Hz, 1H), 5.36 (d, *J* = 10.7 Hz, 1H), 5.33 (d, *J* = 17.0 Hz, 1H), 4.75 – 4.72 (m, 1H), 4.39 – 4.35 (m, 1H), 3.47 (brs, 1H), 2.86 – 2.75 (m, 2H).

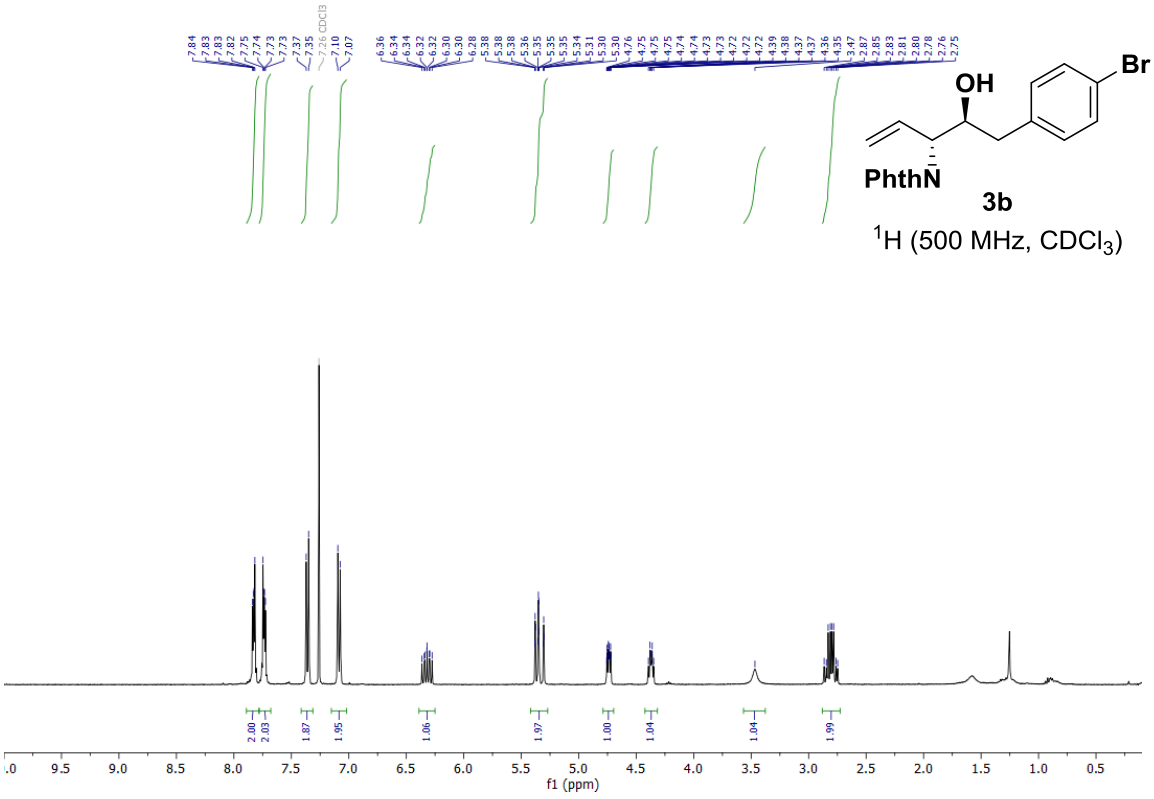
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.6, 137.0, 134.5, 131.7, 131.7, 131.3, 131.4, 123.7, 120.7, 120.6, 72.6, 58.9, 40.3.

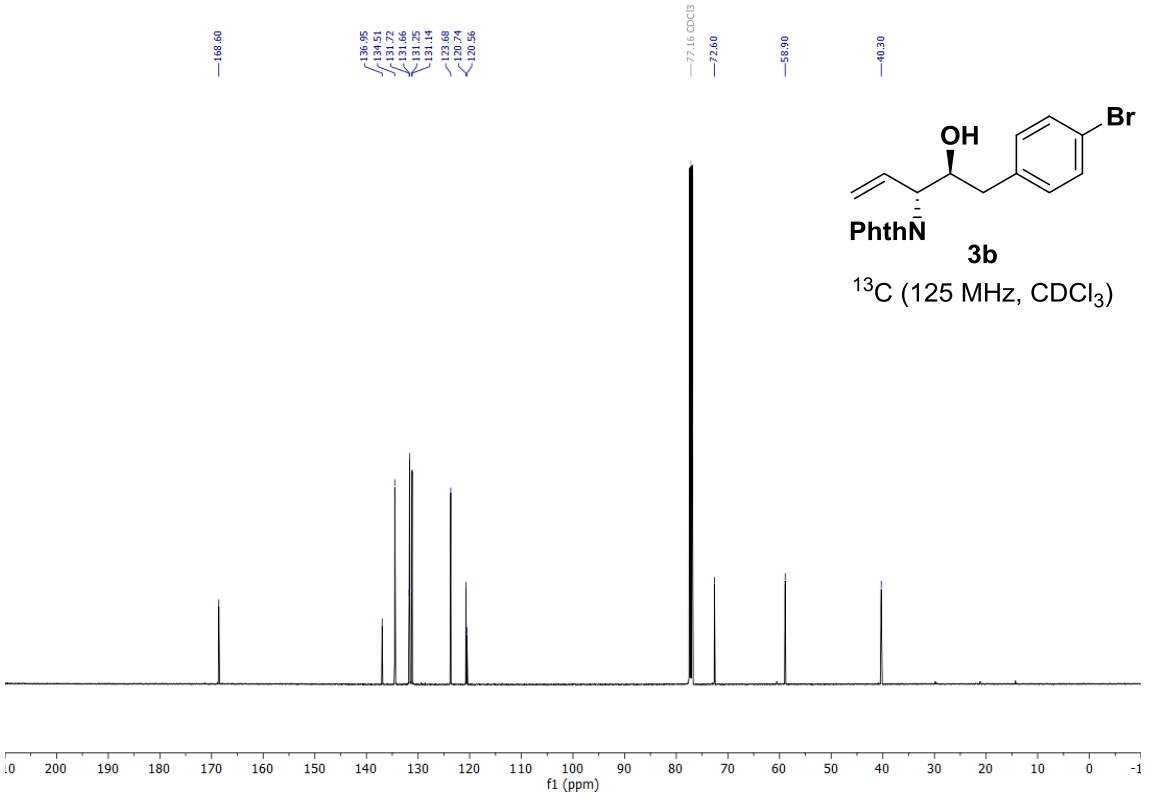
HRMS (H+, *m/z*) for $C_{19}H_{16}BrNO_3$: calcd. = 386.0386; found = 386.0380.

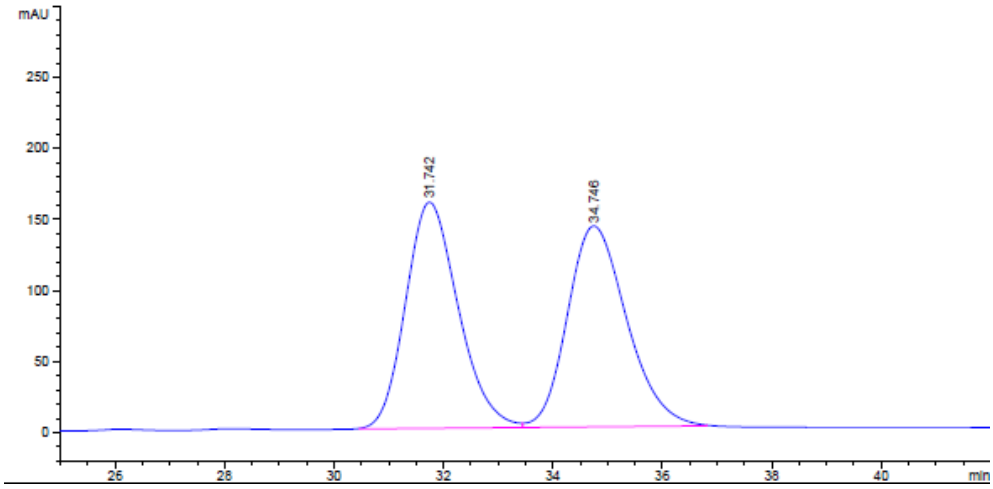
FTIR (neat): 3454, 2919, 2359, 1700, 1380, 1070, 717.

HPLC: (Chiralcel column AS-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 97%.

$[\alpha]_D^{34}$ = +47.9° (c = 0.93, $CHCl_3$).


Br
OH
PhthN
3b
1H (500 MHz, CDCl3)
f1 (ppm)


Br
OH
PhthN
3b
13C (125 MHz, CDCl3)
f1 (ppm)



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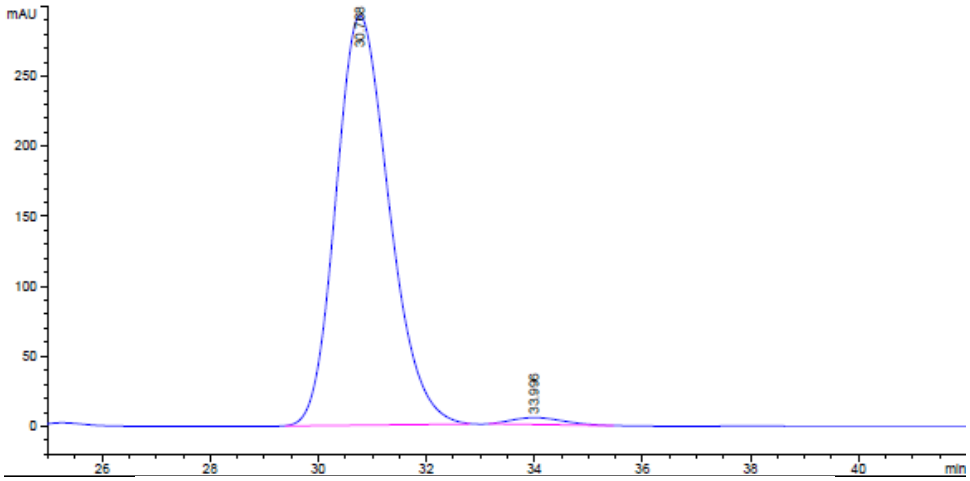

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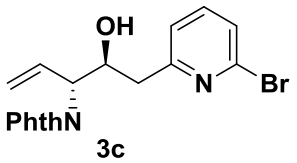
2	33.996	BB	0.7972	329.15945	4.96634	1.6155

2-((3*R*,4*S*,*E*)-4-hydroxy-6-phenylhexa-1,5-dien-3-yl)isoindoline-1,3-dione (3c)



3c

Alcohol **1c** (40.4 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), the title compound **3c** (47.1 mg, 0.12 mmol, >20:1 dr) was obtained as a light yellow oil in 61% yield.

TLC (SiO_2) R_f = 0.31 (40:60 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 1H), 7.12 (d, *J* = 7.5 Hz, 1H), 6.39 (ddd, *J* = 17.7, 10.3, 7.7 Hz, 1H), 5.35 – 5.30 (m, 2H), 4.79 (dd, *J* = 7.9, 5.3 Hz, 1H), 4.64 (dt, *J* = 8.1, 4.8 Hz, 1H), 3.01 – 2.93 (m, 2H).

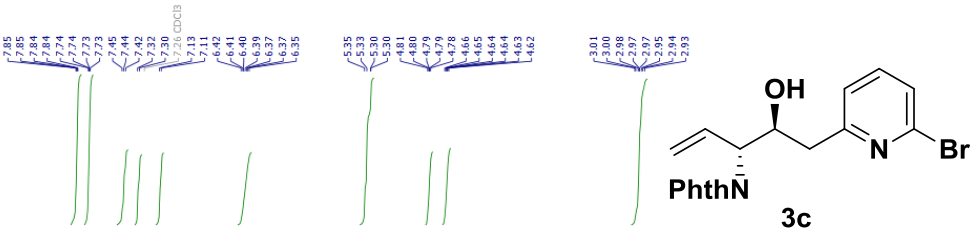
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.5, 160.3, 141.4, 138.9, 134.4, 131.8, 131.7, 126.2, 123.7, 123.1, 120.2, 71.3, 58.8, 41.4.

HRMS (H+, *m/z*) for $C_{18}H_{15}BrN_2O_3$: calcd. = 387.0339; found = 387.0334.

FTIR (neat): 3446, 1704, 1380, 1064, 751, 718.

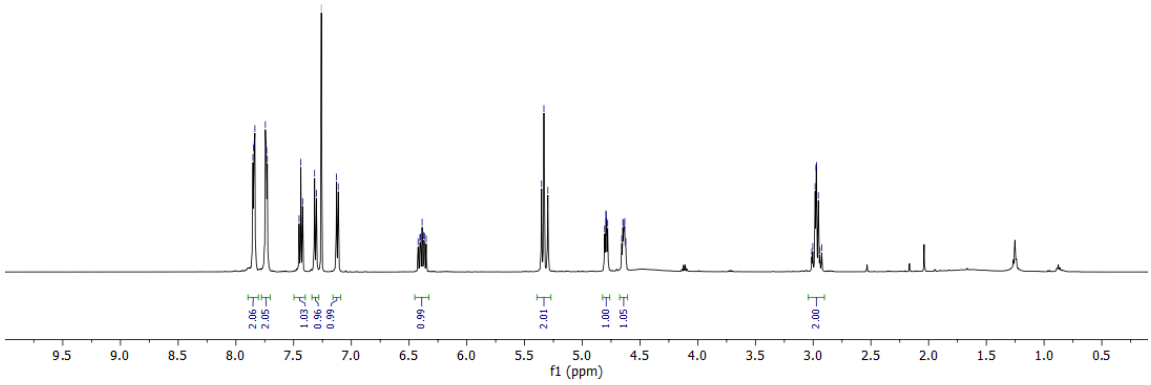
HPLC: (Chiralcel column AD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 96%.

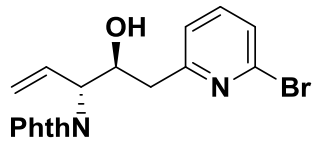
$[\alpha]_D^{24}$ = +47.5° (c = 0.80, $CHCl_3$).



3c

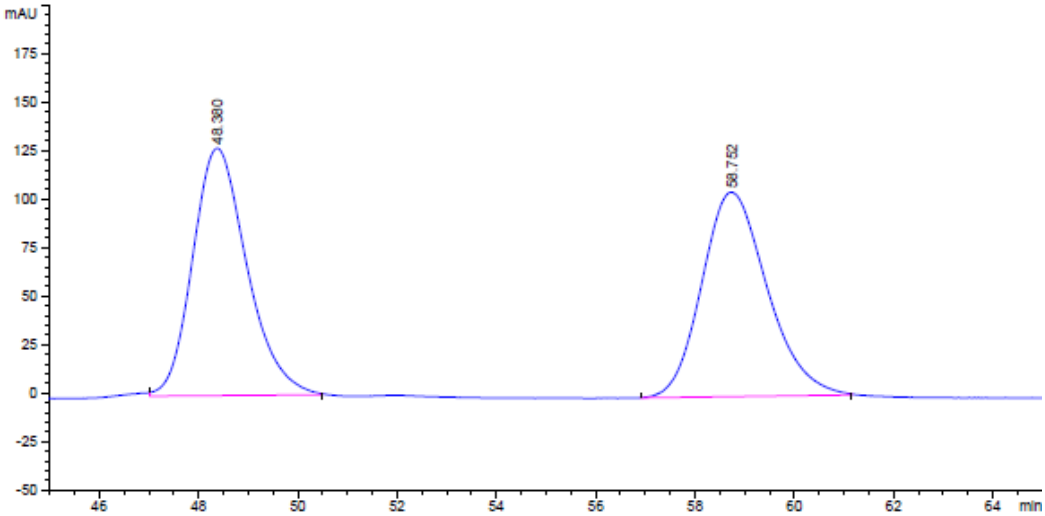
^{1}H (500 MHz, $CDCl_3$)



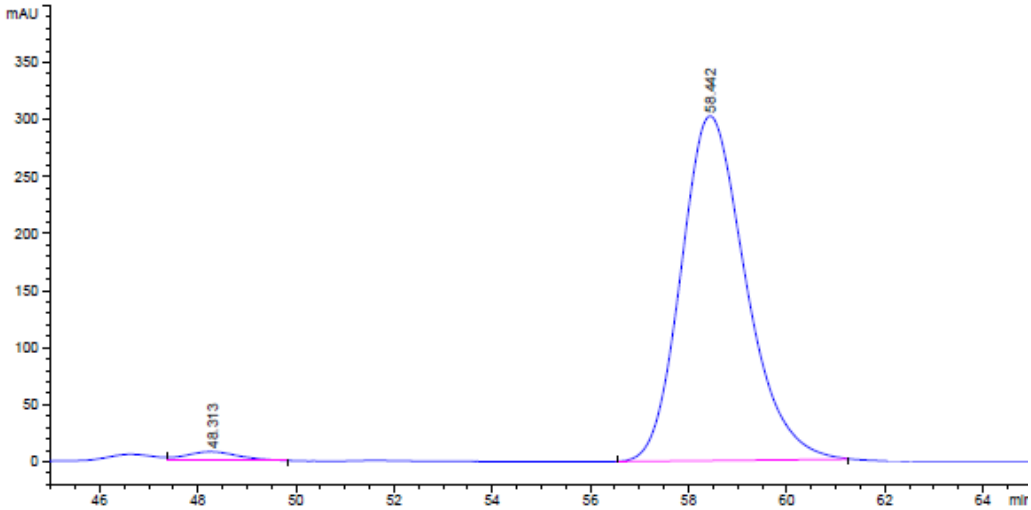


3c

^{13}C (125 MHz, $CDCl_3$)

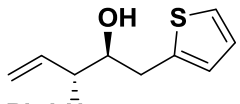


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	48.380	BB	1.0714	9698.82227	127.51176	50.1195
2	58.752	BB	1.0808	9652.58301	105.36746	49.8805



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	48.313	VB	0.8977	592.82471	7.80895	2.0989
2	58.442	BB	1.1362	2.76517e4	302.00626	97.9011

2-((3*R*,4*S*)-4-hydroxy-5-(thiophen-2-yl)pent-1-en-3-yl)isoindoline-1,3-dione (3d)



3d

Alcohol **2d** (25.6 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), the title compound **3d** (42.0 mg, 0.13 mmol, >20:1 dr) was obtained as a white solid in 67% yield.

TLC (SiO_2) R_f = 0.28 (20:80 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.15 (d, *J* = 5.1 Hz, 1H), 6.94 – 6.91 (m, 1H), 6.86 (d, *J* = 3.1 Hz, 1H), 6.37 – 6.27 (m, 1H), 5.34 (dd, *J* = 19.6, 13.7 Hz, 2H), 4.80 (dd, *J* = 7.8, 4.3 Hz, 1H), 4.43 – 4.32 (m, 1H), 3.76 (s, 1H), 3.08 (d, *J* = 6.6 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 139.8, 134.5, 131.8, 131.0, 127.0, 126.3, 124.5, 123.7, 120.6, 77.2, 73.1, 58.4, 34.9.

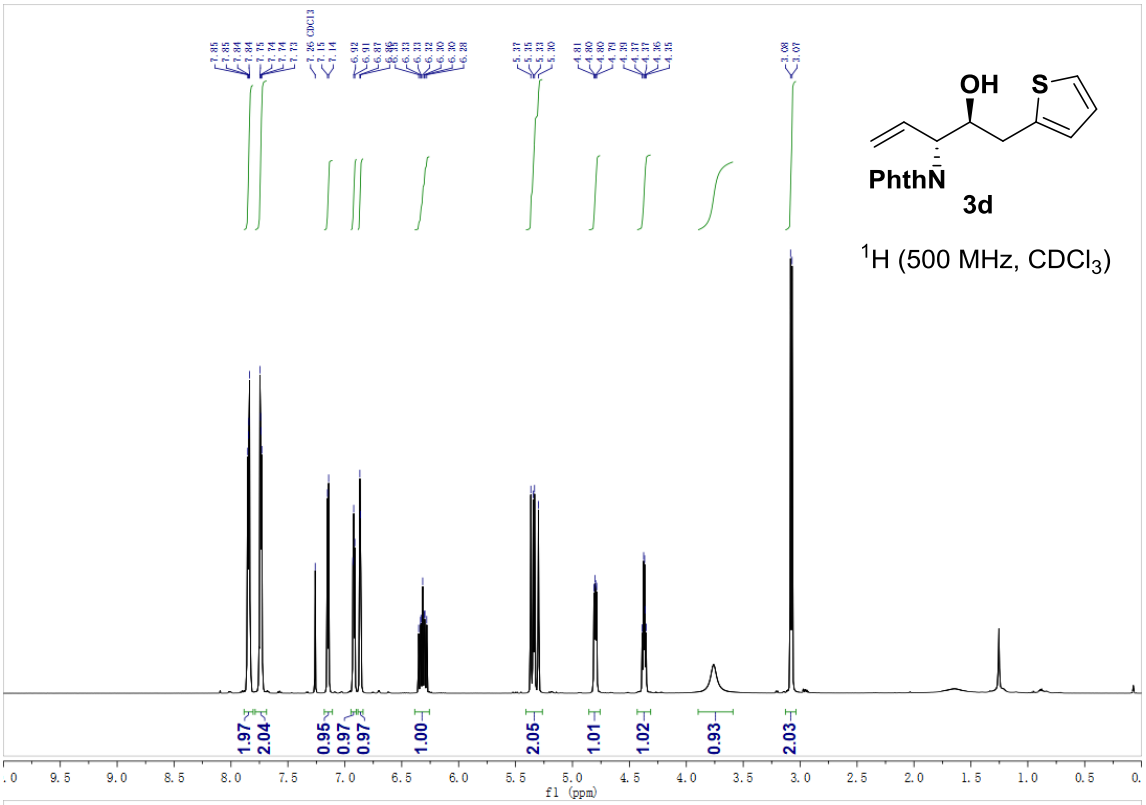
HRMS (Na+, *m/z*) for $C_{17}H_{15}NO_3S$: calcd. = 336.0665; found = 336.0667.

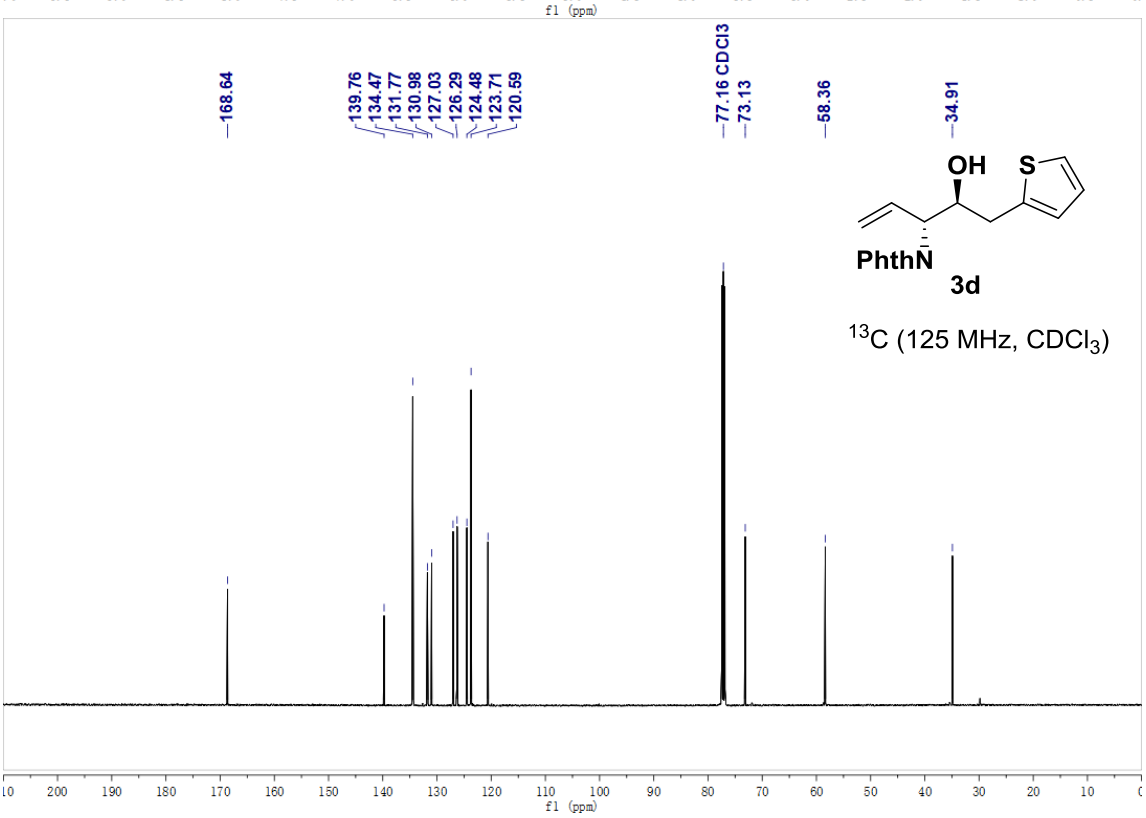
FTIR (neat): 3451, 2360, 2341, 1703, 1381, 1261, 1063, 749.

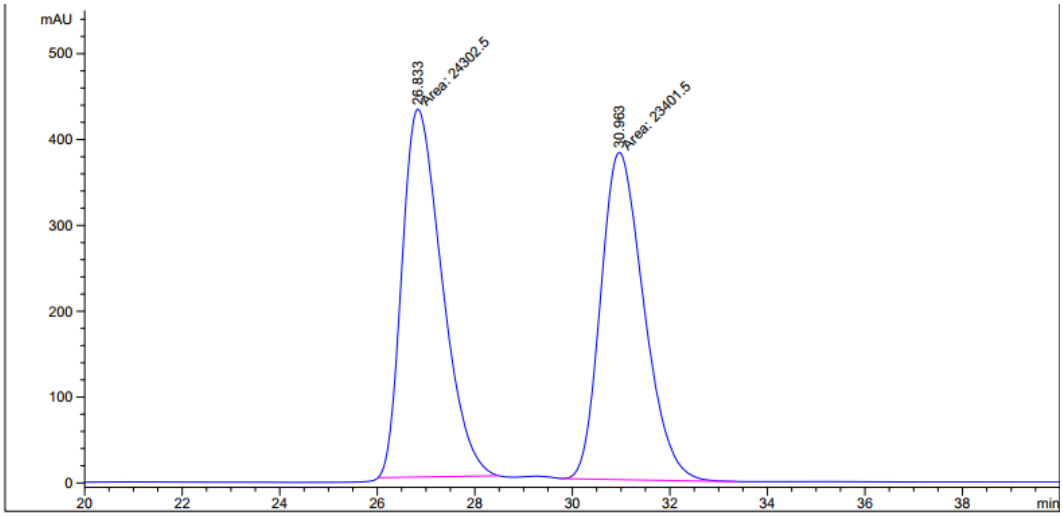
HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 92%.

$[\alpha]_D^{34}$ = +72.3° (c = 0.4, $CHCl_3$).

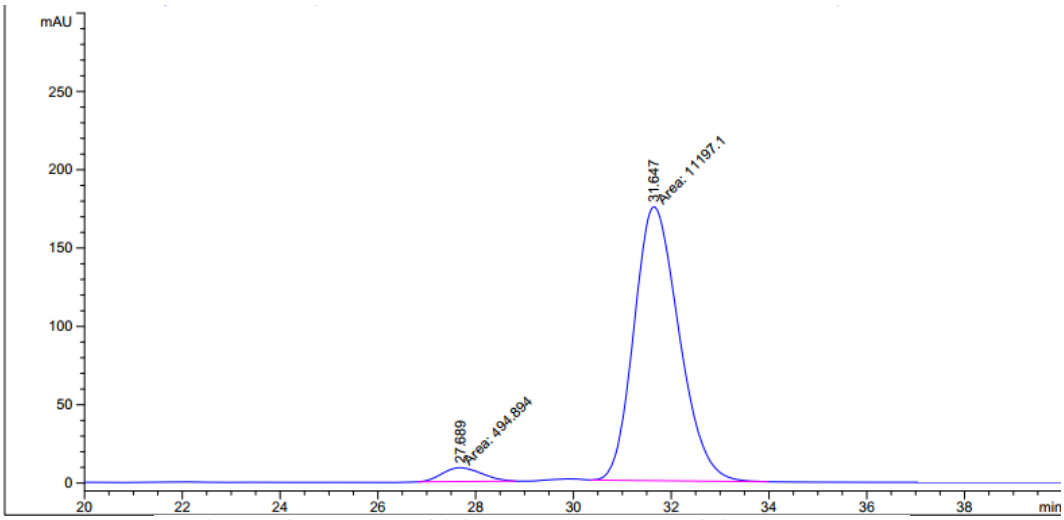
MP: [80 – 84] °C


OH
S
PhthN
3d
^{1}H (500 MHz, $CDCl_3$)
1.97
2.04
0.95
0.97
0.97
1.00
2.05
1.01
1.02
0.93
2.03
f1 (ppm)


168.64
139.76
134.47
131.77
130.98
127.03
126.29
124.48
123.71
120.59
77.16 CDCl3
73.13
58.36
34.91
OH
S
PhthN
3d
^{13}C (125 MHz, $CDCl_3$)
f1 (ppm)

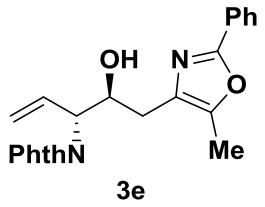


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.833	MM	0.9451	2.43025e4	428.55585	50.9444
2	30.963	MM	1.0235	2.34015e4	381.08691	49.0556



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.689	MM	0.9312	494.89352	8.85730	4.2327
2	31.647	MM	1.0678	1.11971e4	174.77449	95.7673

2-((3*R*,4*S*)-4-hydroxy-5-(5-methyl-2-phenyloxazol-4-yl)pent-1-en-3-yl)isoindoline-1,3-dione (3e)



3e

Alcohol **2e** (40.6 mg, 0.2 mmol) was subjected to standard reaction conditions with 7.5 mol% catalyst (100 °C, 48 h). Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), the title compound **3e** (54.9 mg, 0.14 mmol, >20:1 dr) was obtained as a white solid in 71% yield.

TLC (SiO_2) R_f = 0.4 (40:60 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93-7.91 (m, 2H), 7.82-7.81 (m, 2H), 7.70-7.69 (m, 2H), 7.42-7.39 (m, 3H), 6.41 (ddd, *J* = 17.1, 10.3, 7.6 Hz, 1H), 5.32 (ddt, *J* = 7.4, 3.0, 1.2 Hz, 2H), 4.79 (ddt, *J* = 7.5, 6.2, 1.1 Hz, 1H), 4.61 (td, *J* = 6.7, 4.9 Hz, 1H), 2.70 (ddd, *J* = 4.8, 15.0, 37.7 Hz, 2H), 2.23 (s, 3H), 1.64 (bs, 1H).

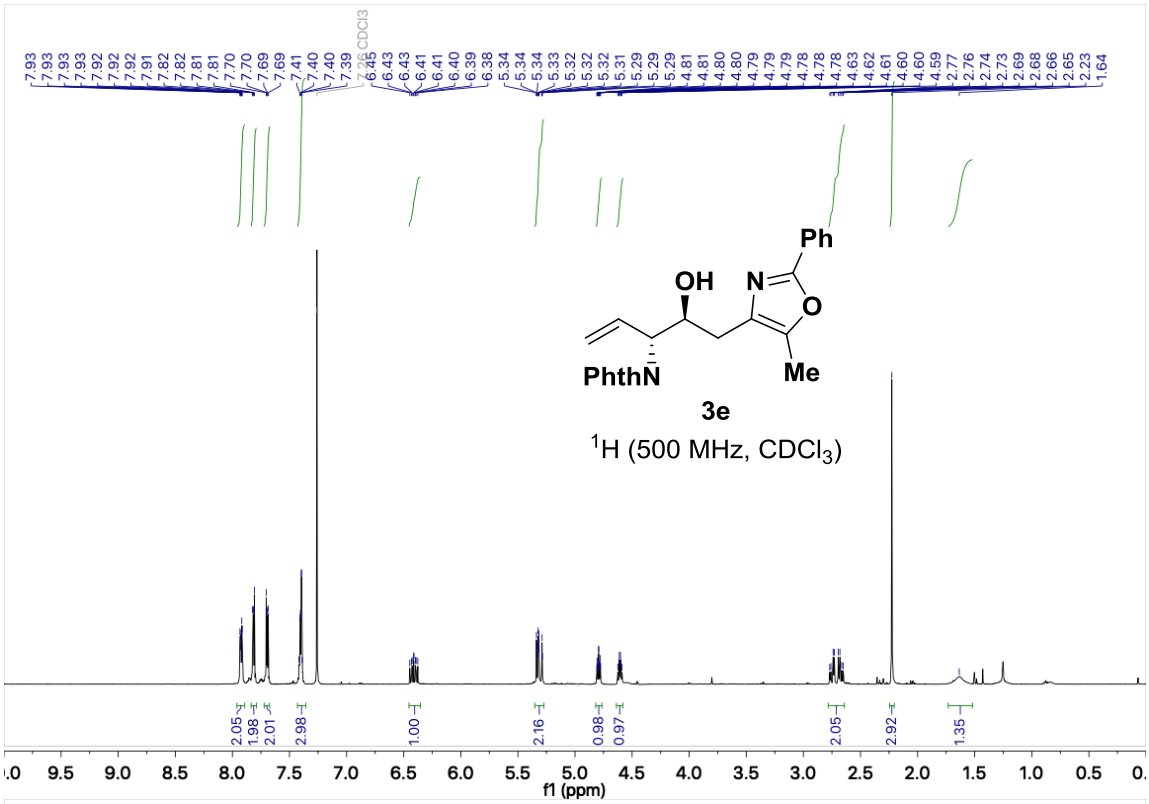
^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 159.6, 145.0, 134.3, 132.5, 132.3, 131.8, 130.2, 128.8, 127.4, 126.2, 123.5, 119.7, 70.9, 58.3, 29.8, 10.3.

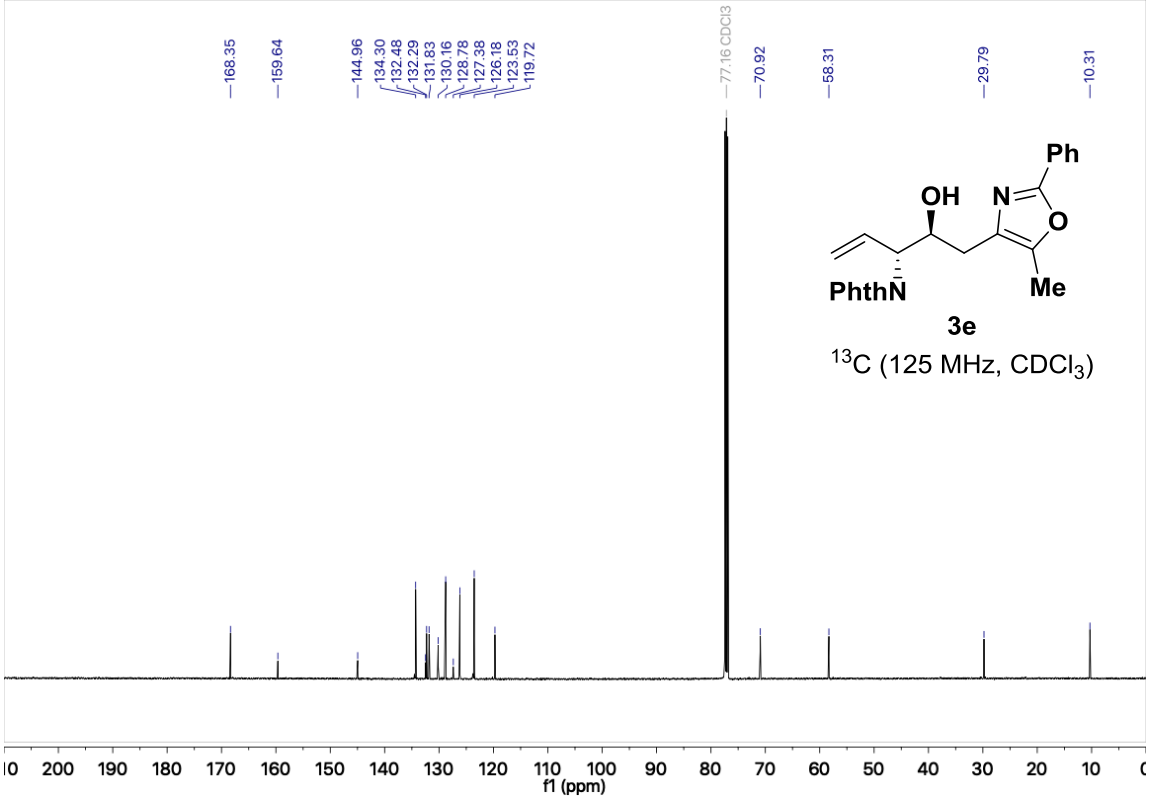
HRMS (H+, *m/z*) for $C_{23}H_{21}N_2O_4$: calcd. = 389.1496; found = 389.1499.

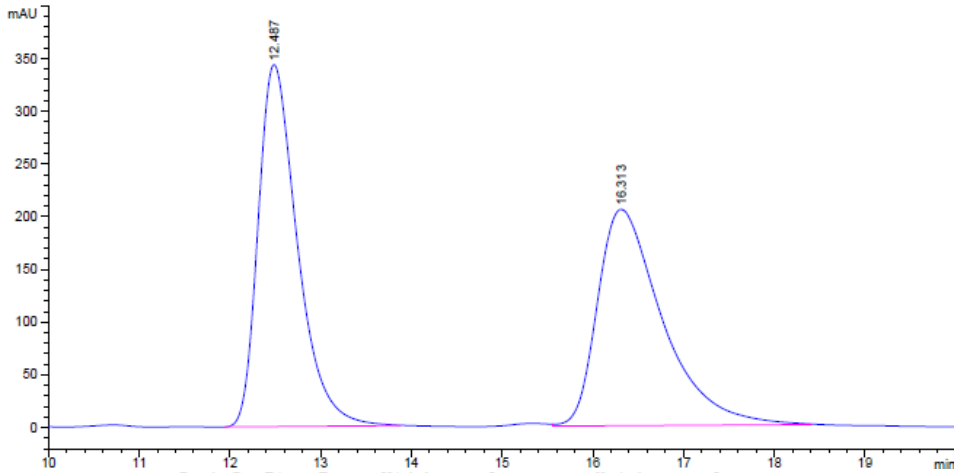
FTIR (neat): 2923, 2853, 1710, 1382, 1334, 1066, 718, 692.

HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 90:10, 1.0 mL/min, 230 nm) ee = 96%.

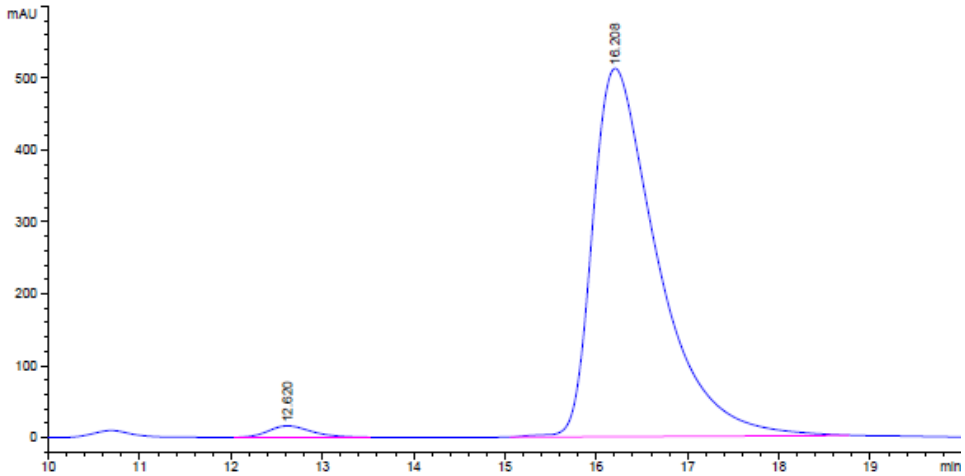
$[\alpha]_D^{34}$ = +23.8° (c = 1.3, $CHCl_3$).


Ph
OH
N
O
PhthN
Me
3e
^{1}H (500 MHz, $CDCl_3$)
f1 (ppm)


Ph
OH
N
O
PhthN
Me
3e
^{13}C (125 MHz, $CDCl_3$)
f1 (ppm)

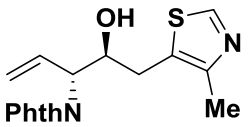


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.487	BB	0.4589	1.03227e4	343.20798	50.2761
2	16.313	VB	0.7523	1.02094e4	205.26210	49.7239



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.620	BB	0.5049	534.04919	16.10544	2.0688
2	16.208	BB	0.7320	2.52809e4	512.01331	97.9312

2-((3*R*,4*S*)-4-hydroxy-5-(4-methylthiazol-5-yl)pent-1-en-3-yl)isoindoline-1,3-dione (3f)



3f

Alcohol **2f** (28.6 mg, 0.2 mmol) was subjected to standard reaction conditions with longer reaction time (100 °C, 72 h). Upon flash column chromatography (SiO_2, 50:50 EtOAc:hexanes), the title compound **3f** (47.0 mg, 0.144 mmol, >20:1 dr) was obtained as a white solid in 72% yield.

TLC (SiO_2) R_f = 0.29 (60:40 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.4, 3.0 Hz, 2H), 6.37 – 6.24 (m, 1H), 5.41 – 5.23 (m, 2H), 4.75 (dd, *J* = 7.9, 4.4 Hz, 1H), 4.31 (dt, *J* = 7.9, 5.0 Hz, 1H), 4.09 (d, *J* = 6.8 Hz, 1H), 3.03 – 2.92 (m, 2H), 2.34 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 150.4, 150.0, 134.6, 131.7, 130.9, 127.0, 123.7, 120.8, 72.6, 58.7, 31.4, 15.2.

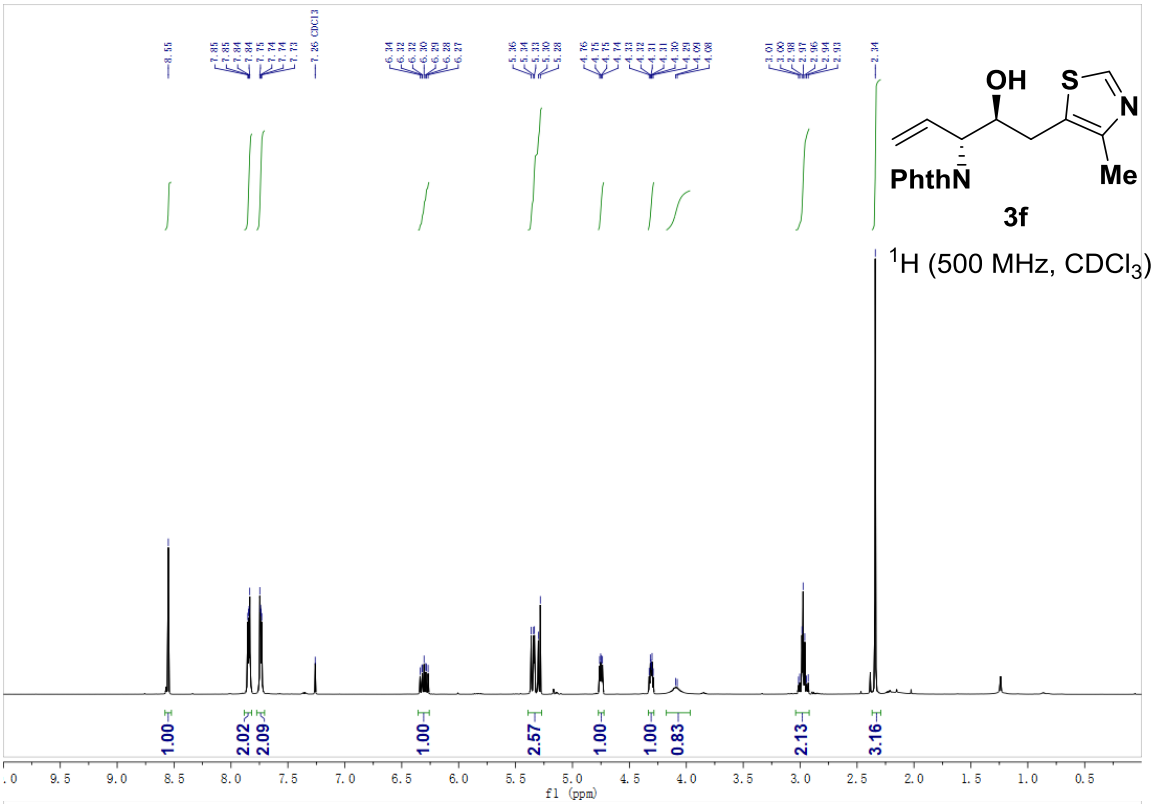
HRMS (H+, *m/z*) for $C_{17}H_{17}N_2O_3S$: calcd. = 329.0954; found = 329.0957.

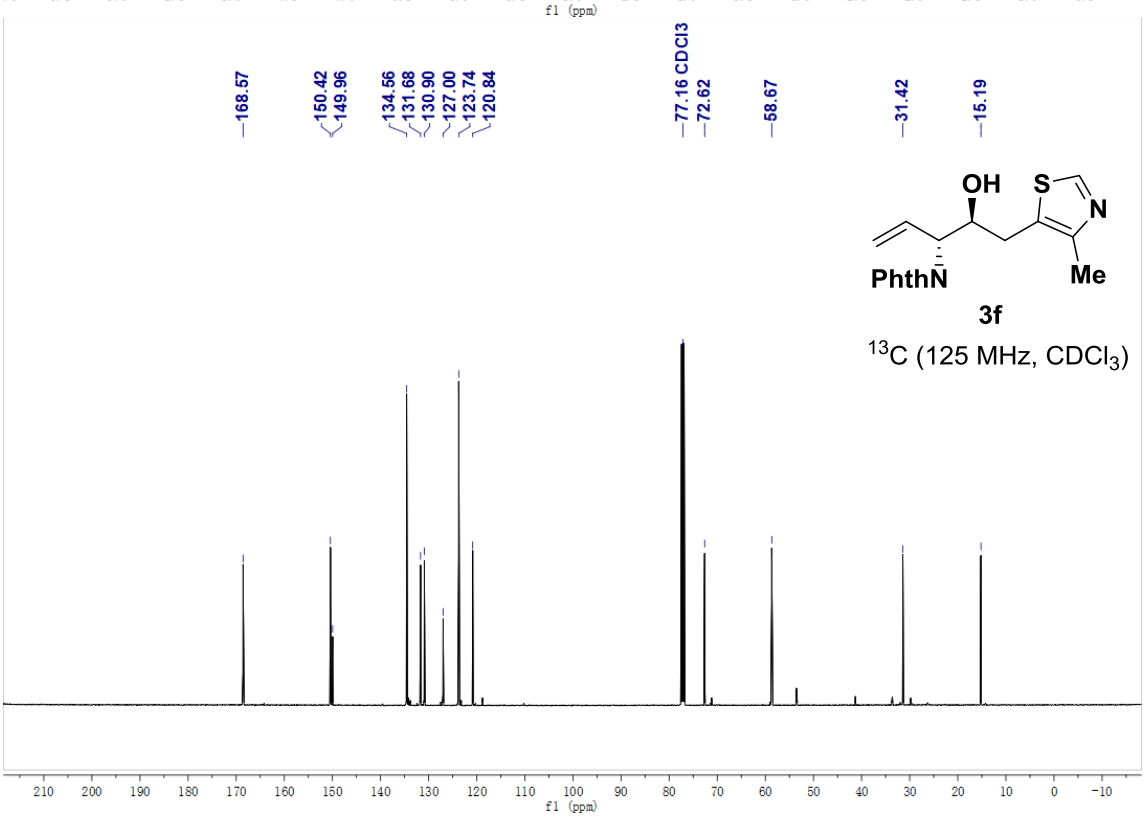
FTIR (neat): 3724, 3004, 2360, 2341, 1706, 1275, 260, 750, 669.

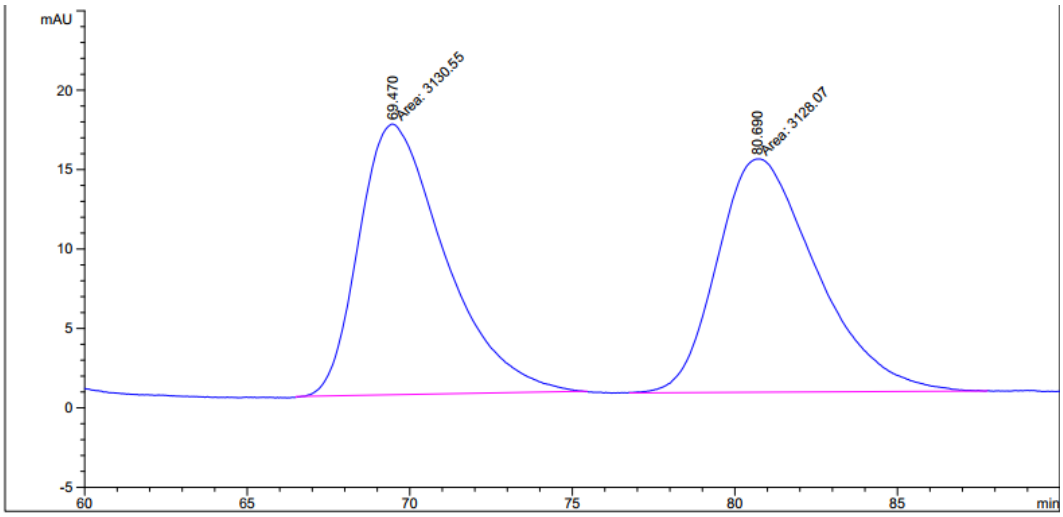
HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 94%.

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{34}}$ = +15.7° (c = 0.87, $CHCl_3$).

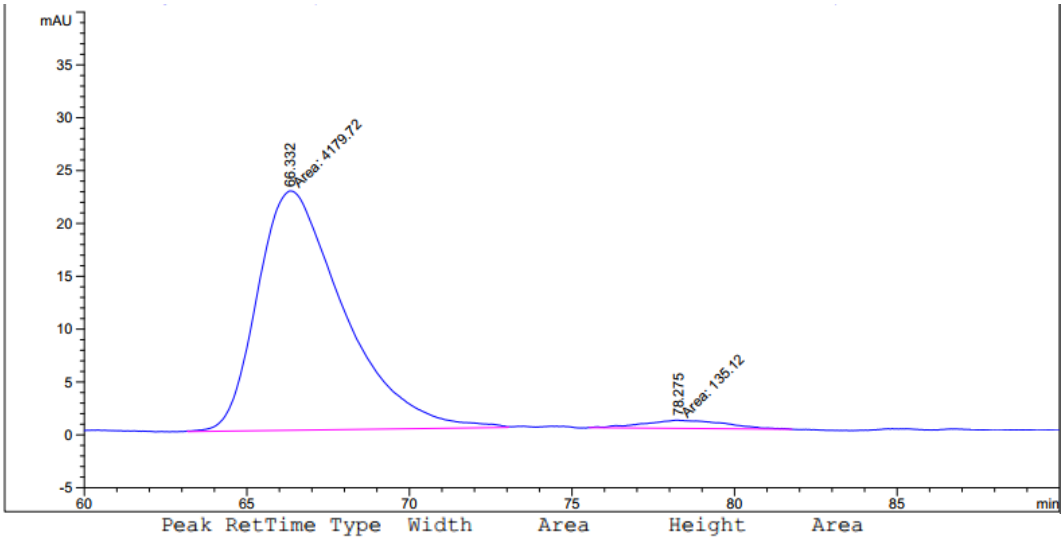
MP: [118-120] °C


OH
S
N
PhthN
Me
3f
1H (500 MHz, CDCl3)
1.00
2.02
2.09
1.00
2.57
1.00
1.00
0.83
2.13
3.16
f1 (ppm)


168.57
150.42
149.96
134.56
131.68
130.90
127.00
123.74
120.84
77.16 CDCl3
72.62
58.67
31.42
15.19
OH
S
N
PhthN
Me
3f
13C (125 MHz, CDCl3)
f1 (ppm)

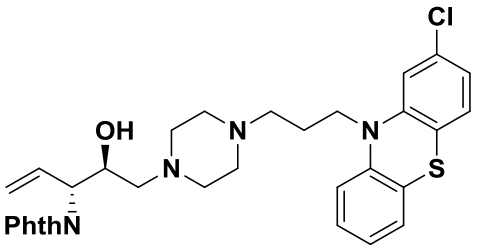


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	69.470	MM	3.0613	3130.54517	17.04343	50.0198
2	80.690	MM	3.5493	3128.07153	14.68869	49.9802



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	66.332	MM	3.0769	4179.72021	22.64035	96.8685
2	78.275	MM	2.9204	135.11977	7.71122e-1	3.1315

2-((3*R*,4*S*)-5-(4-(3-(2-chloro-10H-phenothiazin-10-yl)propyl)piperazin-1-yl)-4-hydroxypent-1-en-3-yl)isoindoline-1,3-dione (3g)



3g

Alcohol **2g** (80.8 mg, 0.2 mmol) was subjected to standard reaction conditions with 7.5 mol% catalyst (100 °C, 48 h). Upon flash column chromatography (SiO_2, 100% EtOAc), the title compound **3g** (68.3 mg, 0.116 mmol, >20:1 dr) was obtained as a pale yellow solid in 58% yield.

TLC (SiO_2) R_f = 0.3 (100% EtOAc)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.84 (dd, *J* = 5.1, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.2, 3.0 Hz, 2H), 7.12 (dd, *J* = 16.8, 8.0 Hz, 2H), 7.00 (d, *J* = 8.1 Hz, 1H), 6.91 (t, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 2H), 6.81 (s, 1H), 6.42 – 6.30 (m, 1H), 5.35 – 5.24 (m, 2H), 4.74 (t, *J* = 7.3 Hz, 1H), 4.30 (dd, *J* = 13.4, 7.0 Hz, 1H), 3.86 (t, *J* = 6.7 Hz, 2H), 2.51 (s, 2H), 2.48 – 2.27 (m, 10H), 2.00 – 1.79 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.4, 146.6, 144.6, 134.3, 133.3, 132.5, 131.9, 128.0, 127.6, 127.5, 124.9, 123.6, 123.0, 122.4, 119.6, 115.9, 77.2, 66.4, 61.2, 57.9, 55.4, 53.2, 45.4, 24.1.

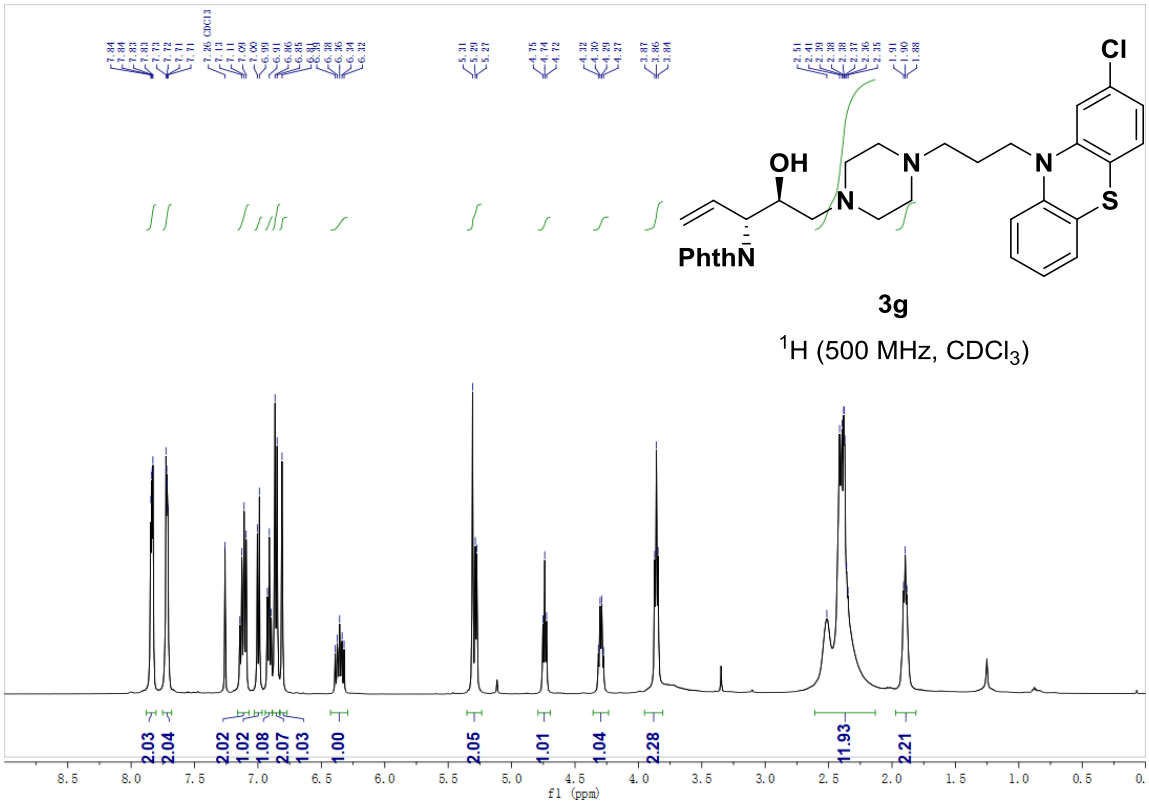
HRMS (H+, *m/z*) for $C_{32}H_{33}ClN_4O_3S$: calcd. = 589.2035; found = 589.2038.

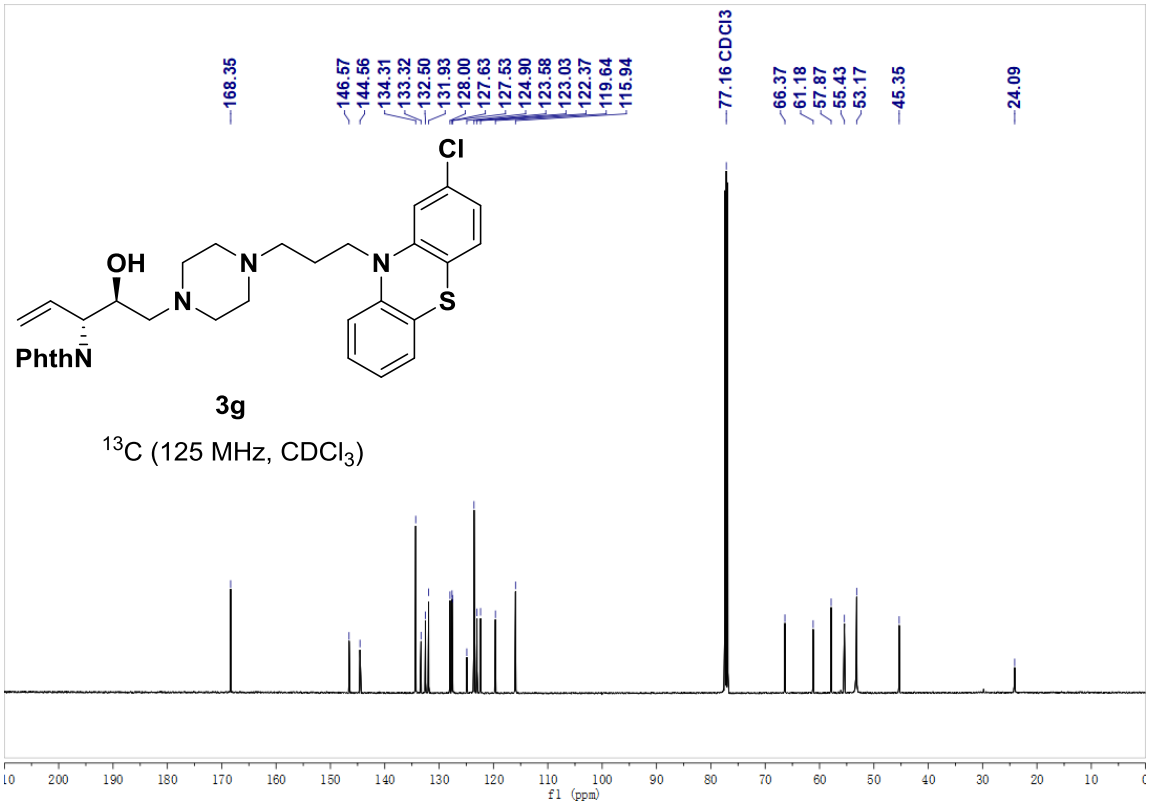
FTIR (neat): 3452, 2940, 2815, 1769, 1708, 1566, 1458, 1382, 1127, 749.

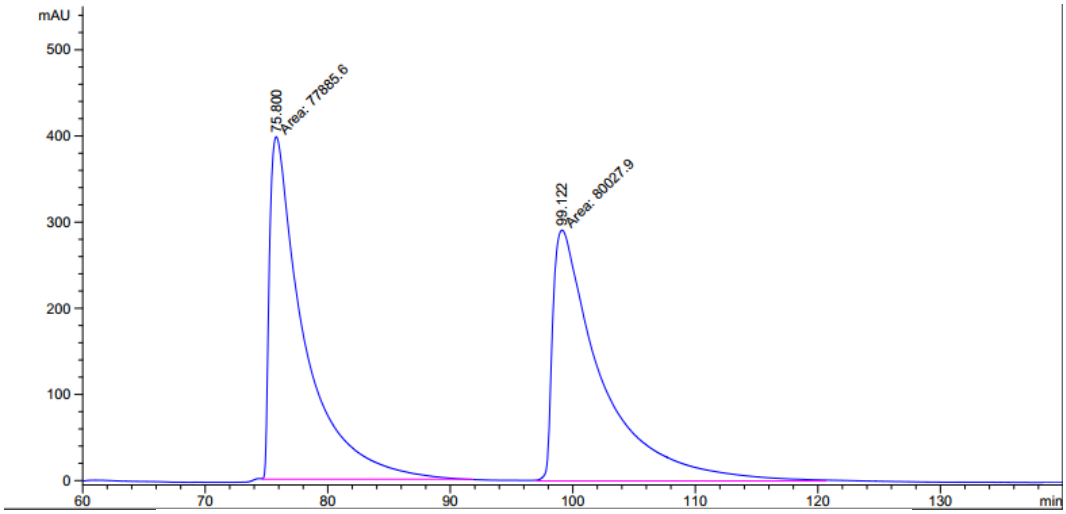
HPLC: (Chiralcel column AD-H, Hexane:2-PrOH = 90:10, 1.0 mL/min, 230 nm) ee = 98%.

$[\alpha]_D^{24}$ = +34.0° (c = 0.80, $CHCl_3$).

MP: [63-66] °C


Cl
OH
N
N
N
S
PhthN
3g
1H (500 MHz, CDCl3)
2.03
2.04
2.02
1.02
1.08
2.07
1.03
1.00
2.05
1.01
1.04
2.28
11.93
2.21
f1 (ppm)


168.35
146.57
144.56
134.31
133.32
132.50
131.93
128.00
127.63
127.53
124.90
123.58
123.03
122.37
119.64
115.94
77.16 CDCl3
66.37
61.18
57.87
55.43
53.17
45.35
24.09
Cl
OH
N
N
N
S
PhthN
3g
13C (125 MHz, CDCl3)
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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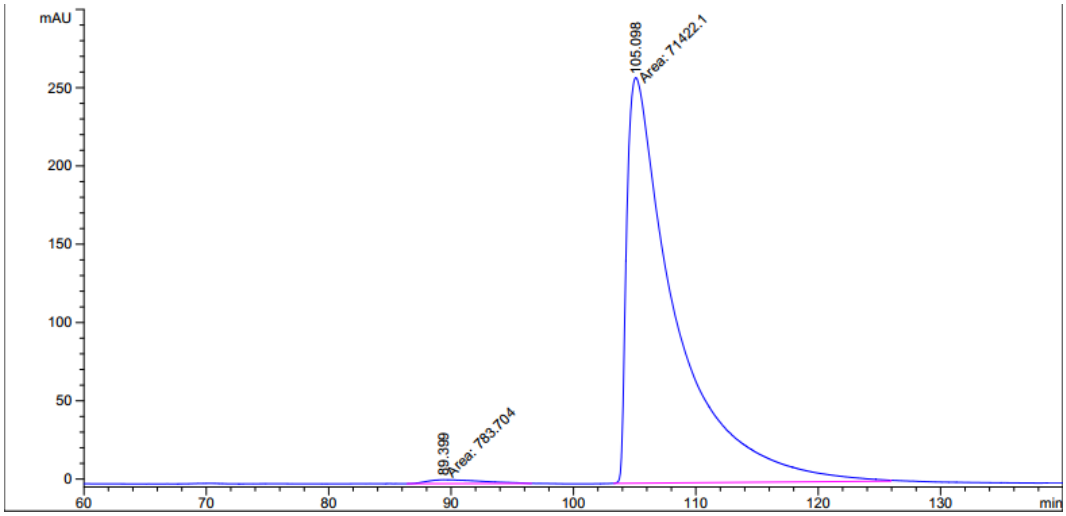
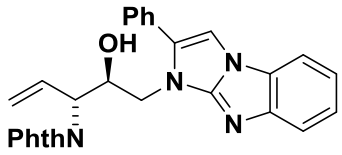
2	99.122	MM	4.5815	8.00279e4	291.12387	50.6783



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	89.399	MM	5.2784	783.70435	2.47459	1.0854
2	105.098	MM	4.5953	7.14221e4	259.04156	98.9146

2-((3*R*,4*S*)-4-hydroxy-5-(2-phenyl-1*H*-benzo[*d*]imidazo[1,2-*a*]imidazol-1-yl)pent-1-en-3-yl)isoindoline-1,3-dione (3h)



3h

Alcohol **2h** (55.4 mg, 0.2 mmol) was subjected to standard reaction conditions with 7.5 mol% catalyst (100 °C, 48 h). Upon flash column chromatography (SiO_2, 30:70 EtOAc:Toluene), the title compound **3h** (52.7 mg, 0.114 mmol, >20:1 dr) was obtained as a pale yellow solid in 57% yield.

TLC (SiO_2) R_f = 0.38 (30:70 EtOAc:Toluene)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.75 – 7.70 (m, 4H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 7.7 Hz, 1H), 7.24 – 7.22 (m, 3H), 7.18 – 7.11 (m, 4H), 6.31 (ddd, *J* = 17.4, 10.3, 7.2 Hz, 1H), 5.23 (d, *J* = 10.3 Hz, 1H), 5.16 (d, *J* = 17.2 Hz, 1H), 4.84 – 4.81 (m, 1H), 4.72 (t, *J* = 7.7 Hz, 1H), 4.23 – 4.12 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 167.9, 134.2, 133.9, 133.2, 131.7, 129.4, 129.1, 128.8, 127.8, 127.3, 123.5, 123.4, 119.5, 119.2, 118.2, 110.3, 103.5, 70.9, 55.9, 48.6.

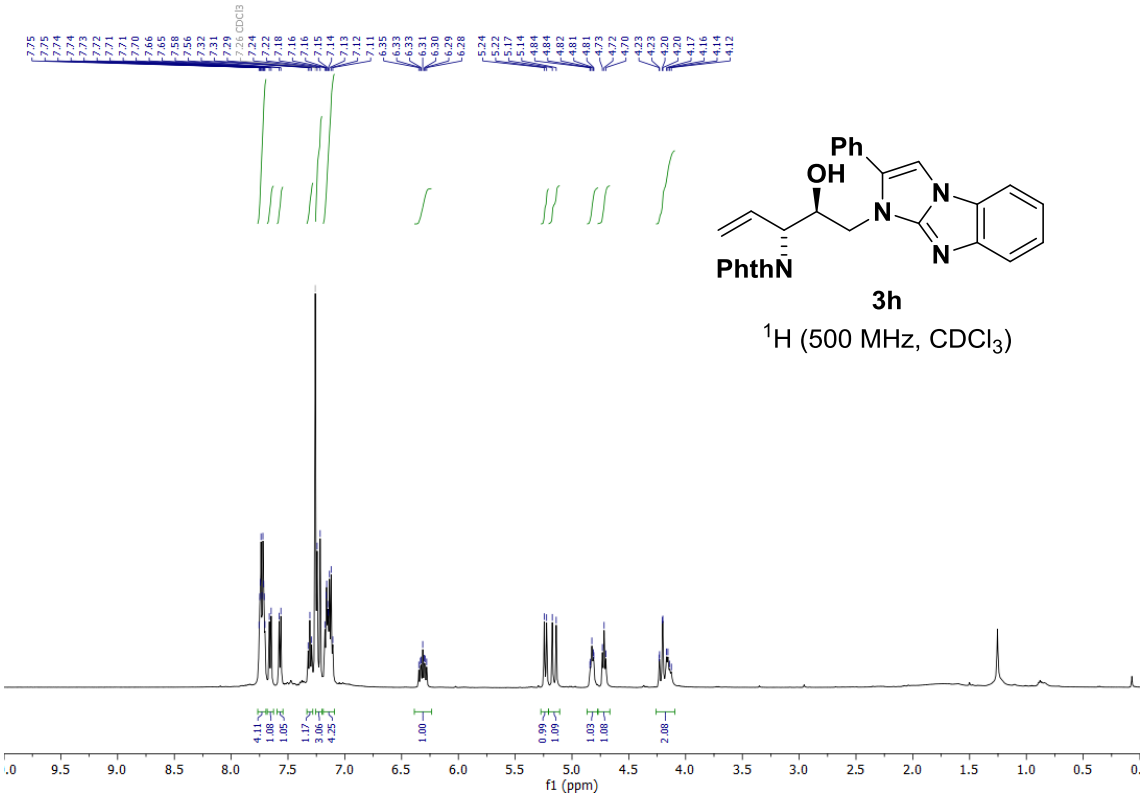
HRMS (Na+, *m/z*) for $C_{28}H_{22}N_4O_3$: calcd. = 485.1584; found = 485.1592.

FTIR (neat): 2922, 1708, 1635, 1558, 1380, 1239, 1066, 740, 718.

HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 90:10, 1.0 mL/min, 230 nm) ee = 98%.

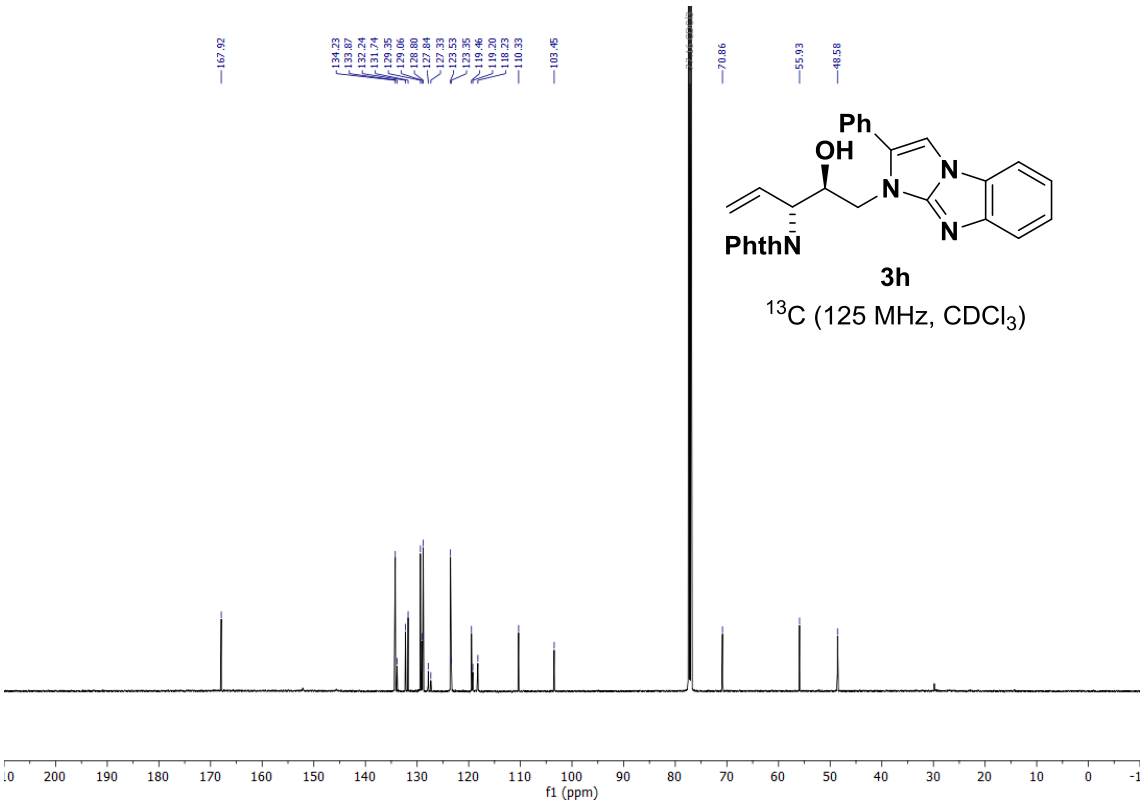
$[\alpha]_D^{34}$ = +3.4° (c = 1.18, $CHCl_3$).

MP [63 – 65] °C



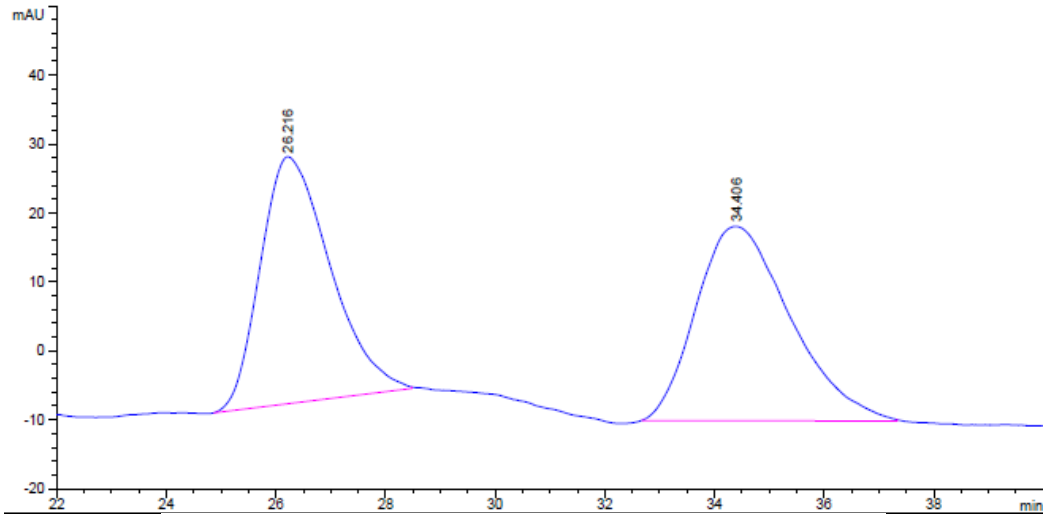
3h

^{1}H (500 MHz, $CDCl_3$)

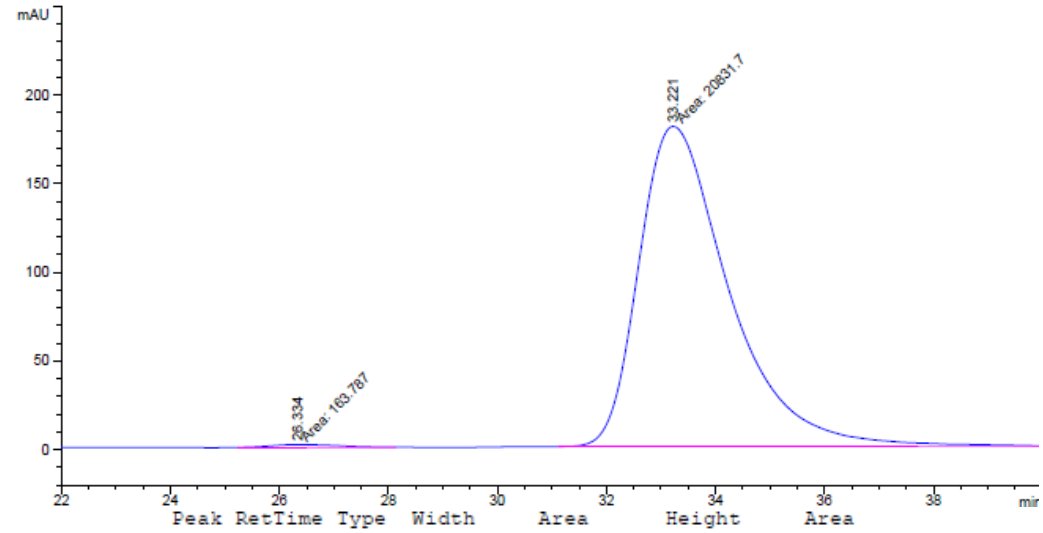


3h

^{13}C (125 MHz, $CDCl_3$)

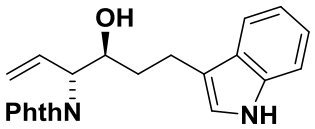


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.216	BB	1.1818	3170.46460	35.84736	48.4240
2	34.406	BB	1.4265	3376.83398	28.21054	51.5760



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.334	MM	1.5118	163.78746	1.80560	0.7801
2	33.221	MM	1.9236	2.08317e4	180.48880	99.2199

2-((3*R*,4*S*,*E*)-7-(benzyloxy)-4-hydroxyhepta-1,5-dien-3-yl)isoindoline-1,3-dione (3i)



3i

Alcohol **1i** (35.0 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h) with 7.5 mol% Ir-**VI**. Upon flash column chromatography (SiO_2, 30:80 EtOAc:hexanes), the title compound **3i** (53.9 mg, 0.15 mmol, >20:1 dr) was obtained as a yellow solid in 75% yield.

TLC (SiO_2) R_f = 0.28 (30:80 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.95 (s, 1H), 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.17 – 7.12 (m, 1H), 7.06 (dd, *J* = 11.0, 3.9 Hz, 1H), 7.00 (s, 1H), 6.30 (ddd, *J* = 17.9, 10.3, 7.7 Hz, 1H), 5.34 – 5.23 (m, 2H), 4.75 (dd, *J* = 7.7, 3.8 Hz, 1H), 4.17 – 4.12 (m, 1H), 3.01 (td, *J* = 8.8, 4.3 Hz, 1H), 2.95 – 2.86 (m, 1H), 2.06 – 1.90 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.8, 136.5, 134.4, 131. 8, 131.3, 127.5, 123.7, 122.0, 121.6, 120.1, 119.3, 119.1, 115.9, 111.2, 77.2, 71.8, 59.6, 34.7, 21.4.

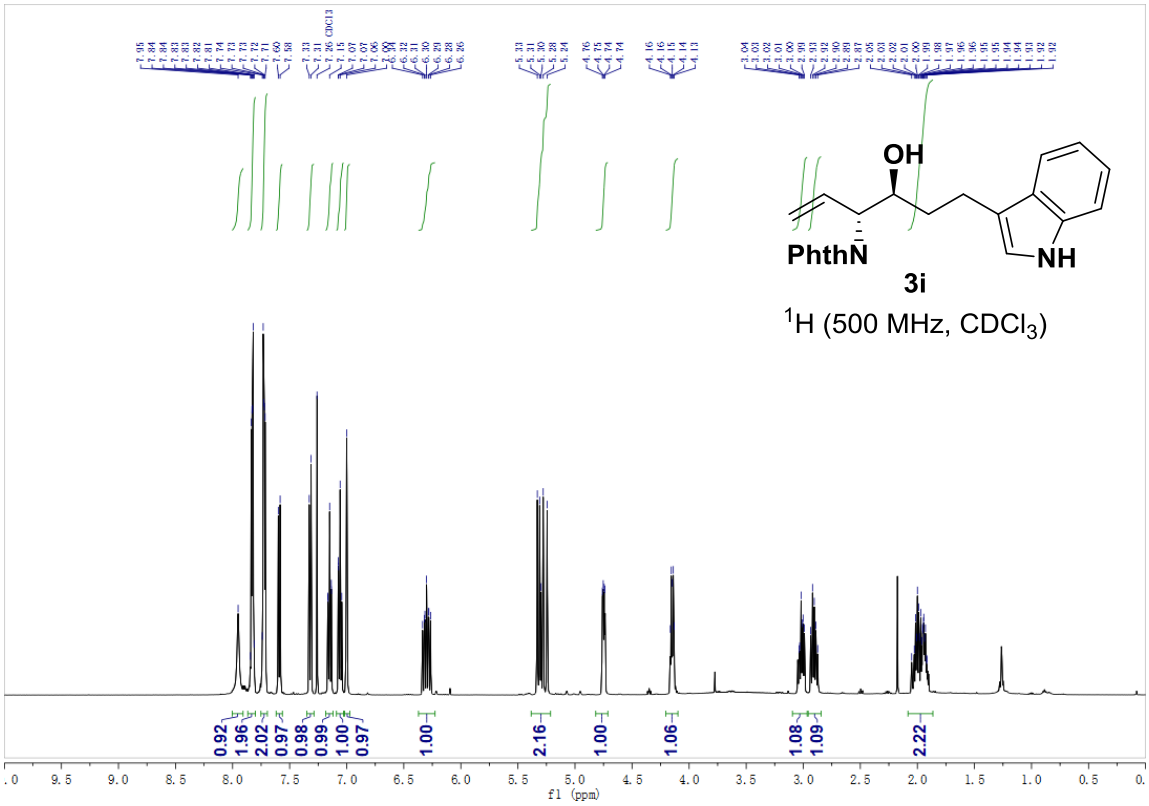
HRMS (Na+, *m/z*) for $C_{22}H_{20}N_2O_3$: calcd. = 383.1366; found = 383.1376.

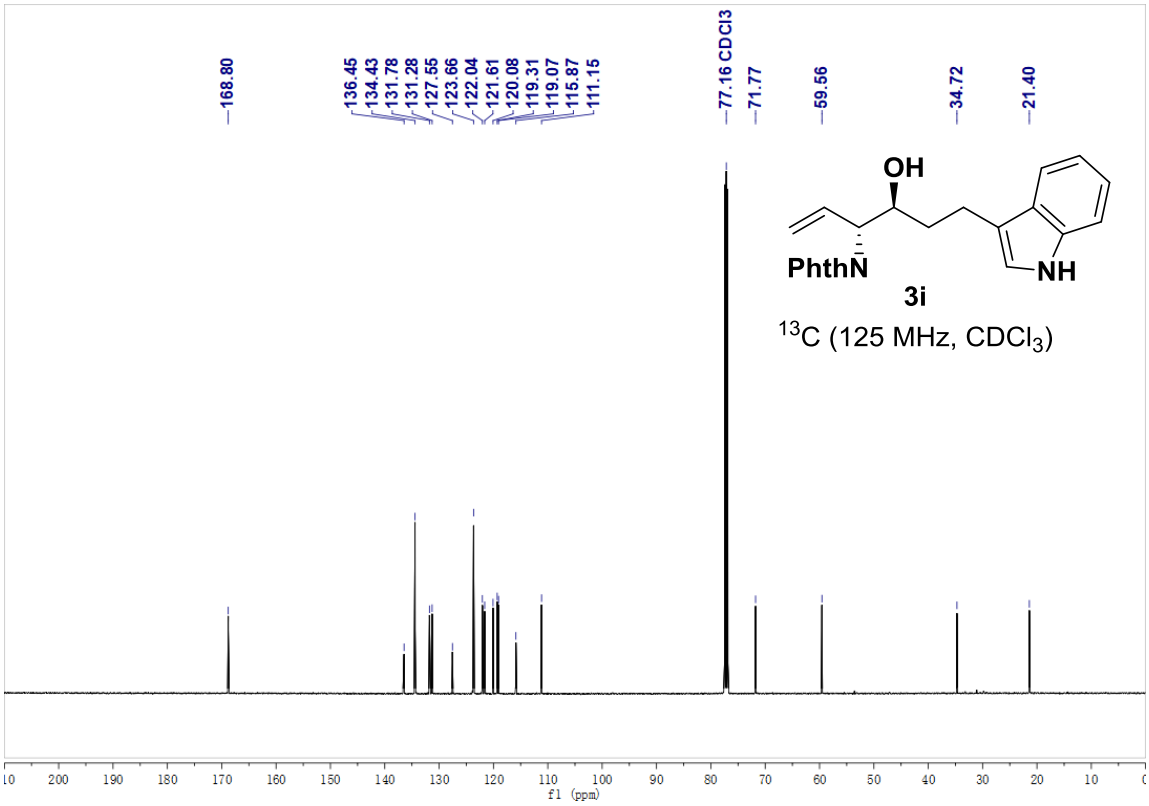
FTIR (neat): 3335, 1708, 1639, 1274, 1263, 764, 734, 703.

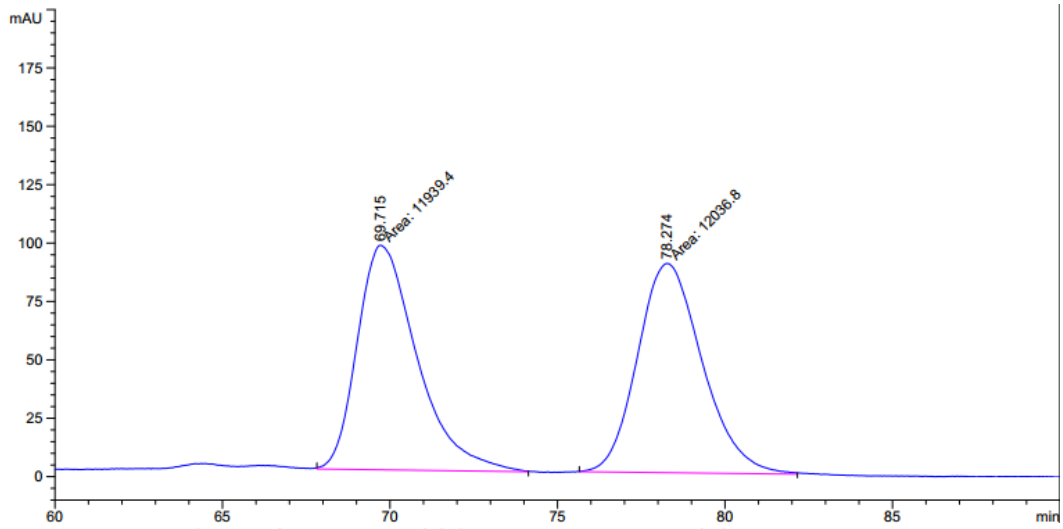
HPLC: (Chiralcel column ADH, Hexane:2-PrOH = 90:10, 1.0 mL/min, 230 nm) ee = 96%.

$[\alpha]_D^{24}$ = 68.0° (c = 0.37, $CHCl_3$).

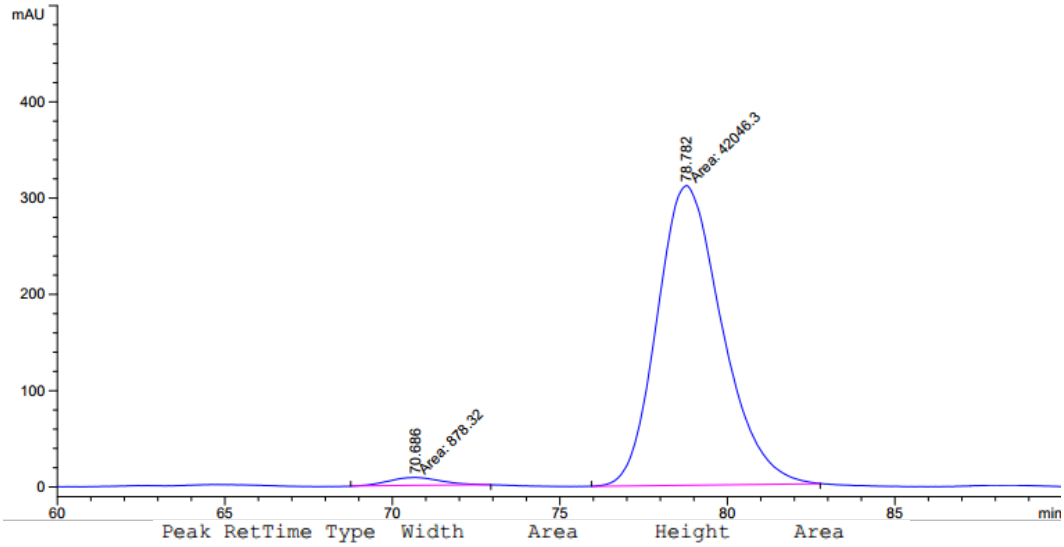
MP : 80-85 °C


OH
PhthN
NH
3i
^{1}H (500 MHz, $CDCl_3$)
f1 (ppm)


168.80
136.45
134.43
131.78
131.28
127.55
123.66
122.04
121.61
120.08
119.31
119.07
115.87
111.15
77.16 CDCl3
71.77
59.56
34.72
21.40
OH
PhthN
NH
3i
^{13}C (125 MHz, $CDCl_3$)
f1 (ppm)

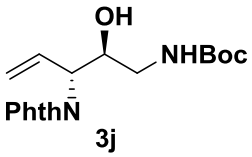


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	69.715	MM	2.0699	1.19394e4	96.13758	49.7969
2	78.274	MM	2.2381	1.20368e4	89.63525	50.2031



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	70.686	MM	1.7774	878.31970	8.23615	2.0462
2	78.782	MM	2.2519	4.20462e4	311.18958	97.9538

***tert*-butyl ((2*S*,3*R*)-3-(1,3-dioxoisoindolin-2-yl)-2-hydroxypent-4-en-1-yl)carbamate (3j)**



3j

Alcohol **2j** (32.2 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 30:70 EtOAc:hexanes), the title compound **3j** (45.1 mg, 0.13 mmol, >20:1 dr) was obtained as a pale yellow oil in 66% yield.

TLC (SiO_2) R_f = 0.32 (30:70 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.85 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.27 (ddd, *J* = 17.1, 10.3, 7.9 Hz, 1H), 5.33 (d, *J* = 10.7 Hz, 1H), 5.31 (d, *J* = 17.1 Hz, 1H), 4.97 (brs, 1H), 4.76 – 4.74 (m, 1H), 4.25 (brs, 1H), 3.86 (brs, 1H), 3.46 – 3.40 (m, 1H), 3.15 – 3.10 (m, 1H), 1.43 (brs, 9H).

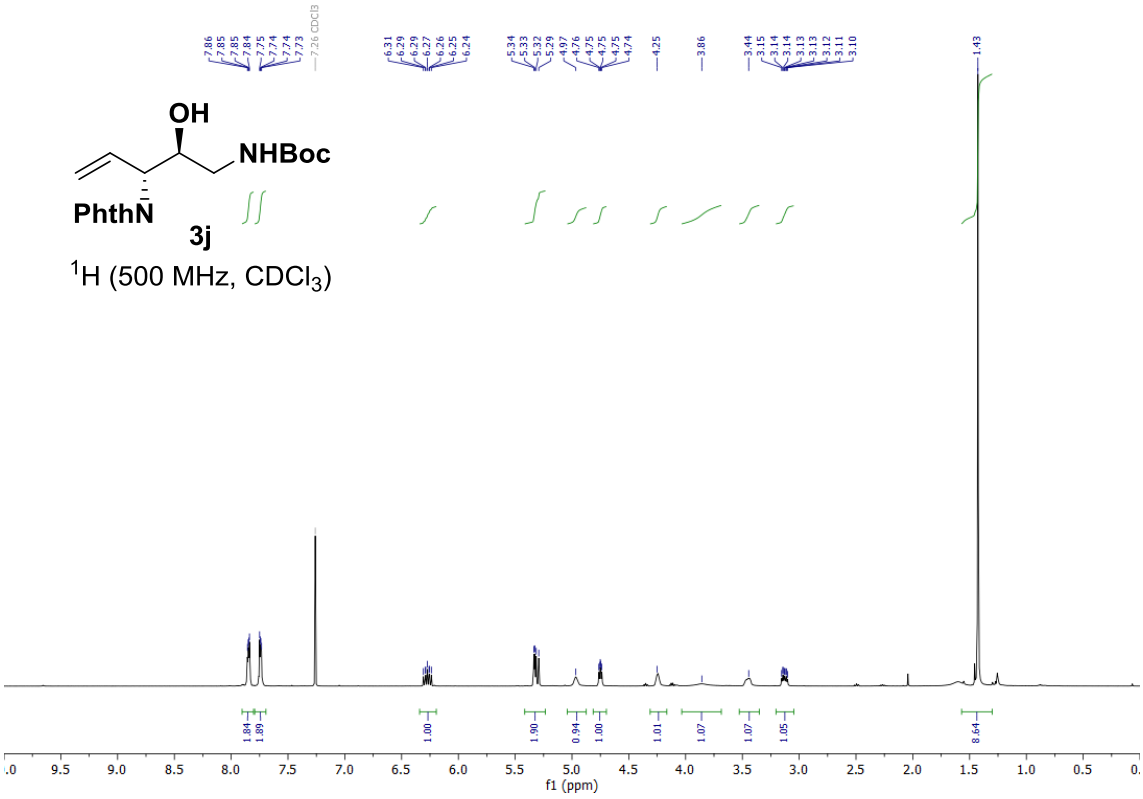
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.5 (2C), 156.7, 134.5 (2C), 131.8 (2C), 131.4, 123.7 (2C), 120.4, 79.9, 71.3, 56.8, 43.6, 28.5 (3C).

HRMS (Na+, *m/z*) for $C_{18}H_{22}N_2O_5$: calcd. = 369.1421; found = 369.1427.

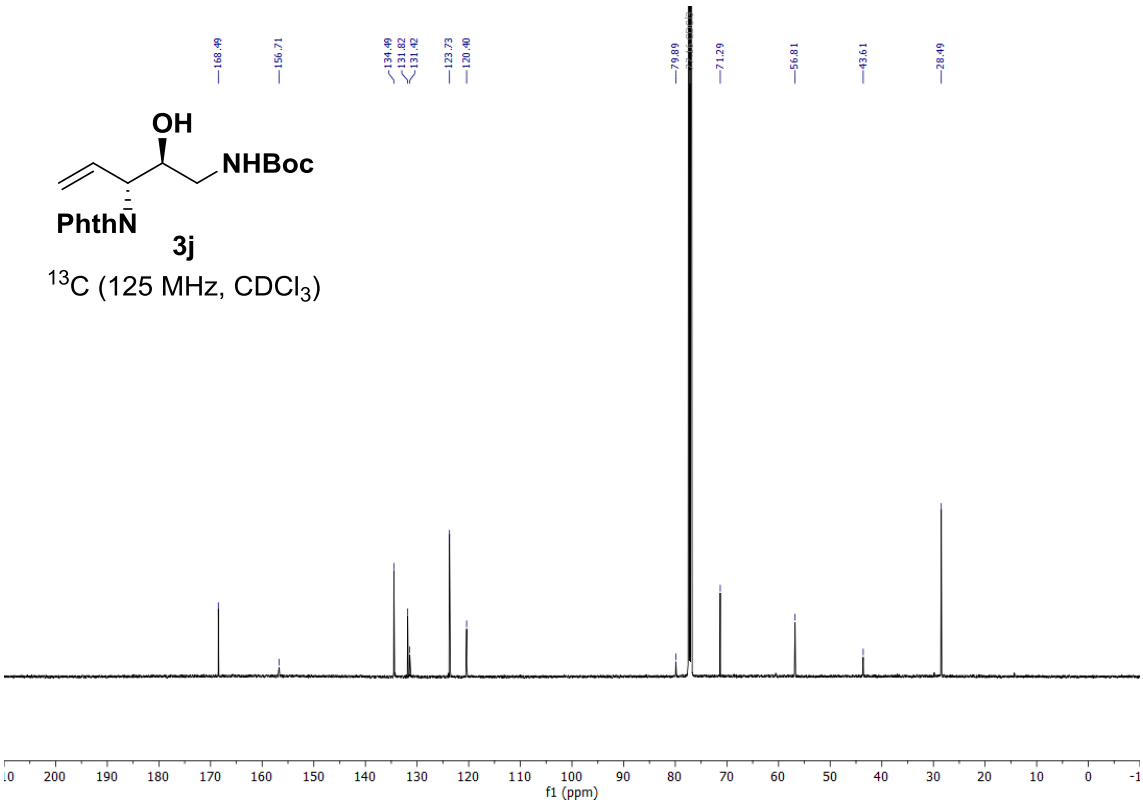
FTIR (neat): 3372, 2978, 1704, 1513, 1381, 1165, 1060

HPLC: (Chiralcel column AD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 97%.

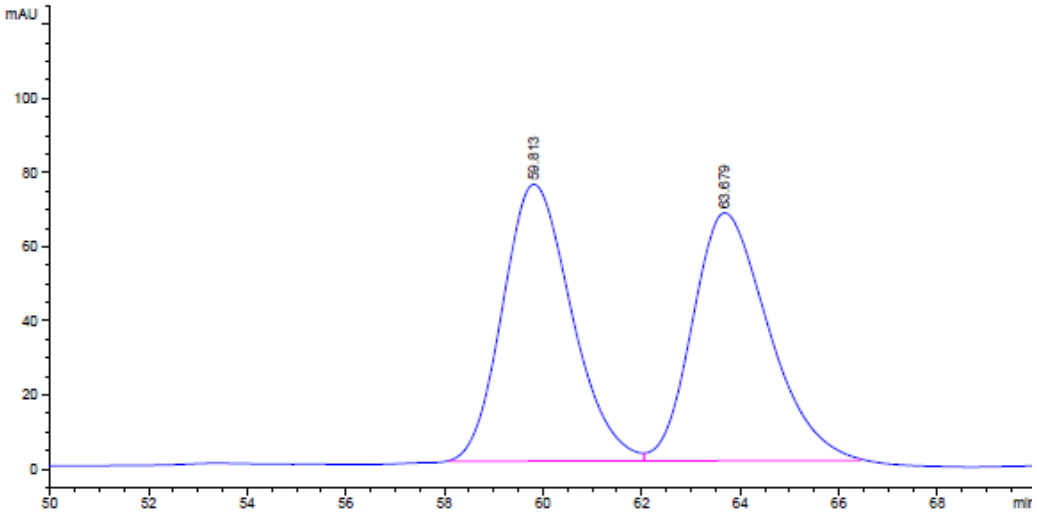
$[\alpha]_D^{34}$ = +30.6° (c = 0.98, $CHCl_3$).



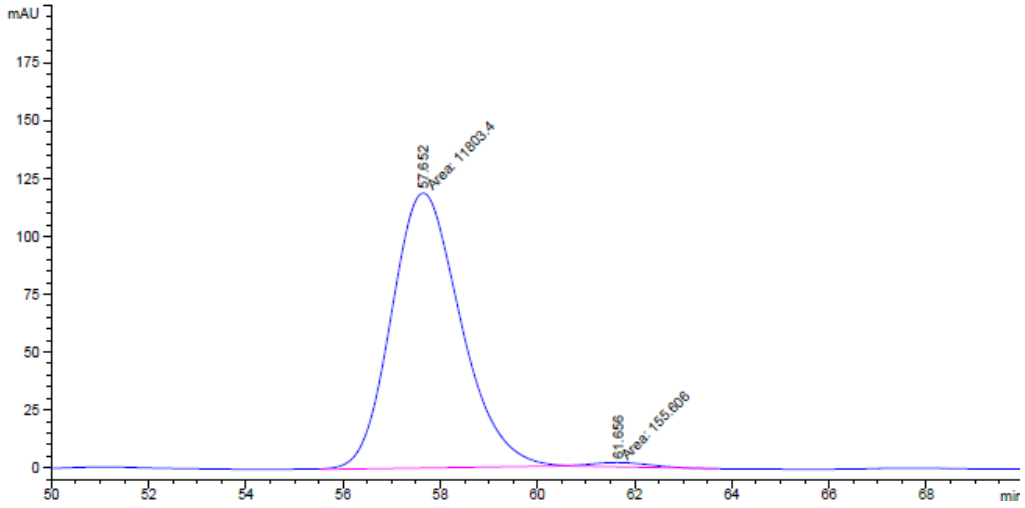
^{1}H (500 MHz, $CDCl_3$)



^{13}C (125 MHz, $CDCl_3$)

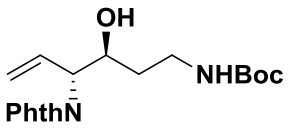


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	59.813	BV	1.4024	7249.68799	74.69029	50.3267
2	63.679	VB	1.4085	7155.55469	66.86340	49.6733



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	57.652	MM	1.6554	1.18034e4	118.84019	98.6988
2	61.656	MM	1.3738	155.60645	1.88773	1.3012

***tert*-butyl ((3*S*,4*R*)-4-(1,3-dioxoisoindolin-2-yl)-3-hydroxyhex-5-en-1-yl)carbamate (3k)**



3k

Alcohol **2k** (35.0 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 40:60 EtOAc:hexanes), the title compound **3k** (43.2 mg, 0.12 mmol, >20:1 dr) was obtained as a pale yellow oil in 60% yield.

TLC (SiO_2) R_f = 0.29 (50:50 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.84 (d, *J* = 3.2 Hz, 2H), 7.77 – 7.69 (m, 2H), 6.35 – 6.22 (m, 1H), 5.28 (dd, *J* = 19.2, 13.9 Hz, 2H), 4.97 (s, 1H), 4.70 – 4.63 (m, 1H), 4.22 – 4.16 (m, 2H), 3.42 (s, 1H), 3.17 (dd, *J* = 13.0, 5.1 Hz, 1H), 1.73 – 1.56 (m, 2H), 1.41 (s, 9H).

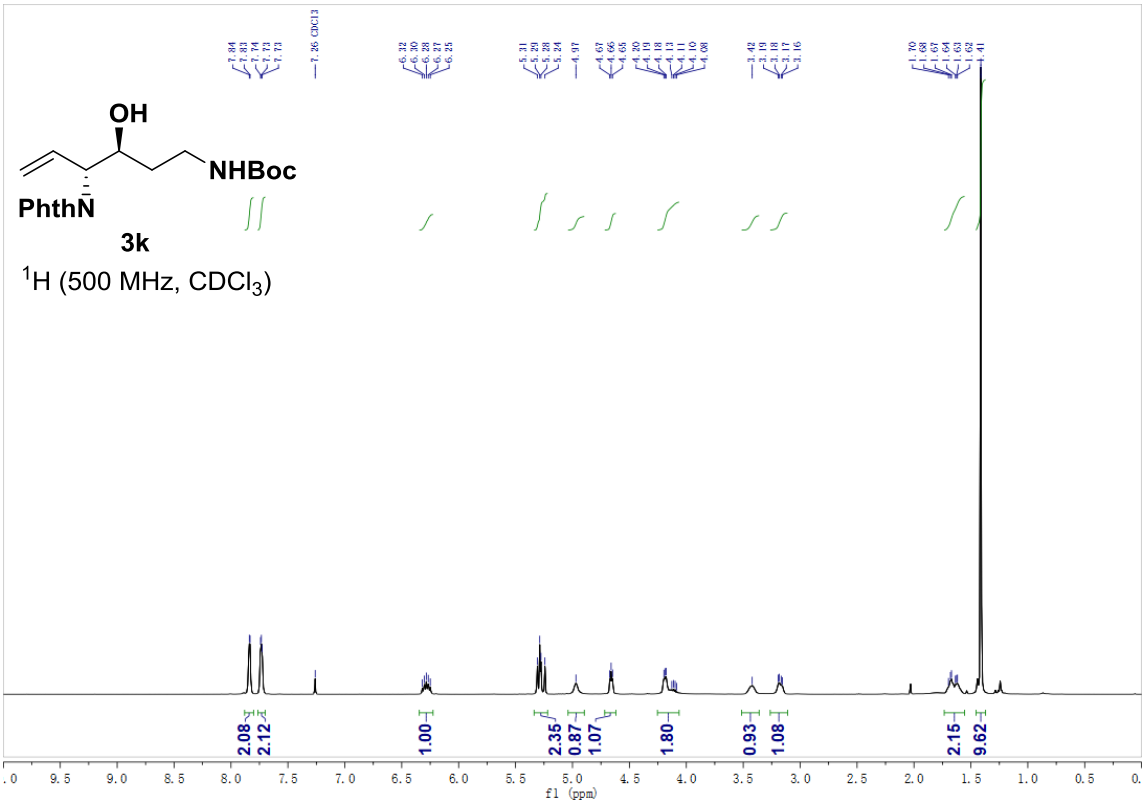
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.6, 156.7, 134.4, 131.8, 123.7, 120.0, 79.5, 70.0, 59.4, 37.6, 34.4, 28.5.

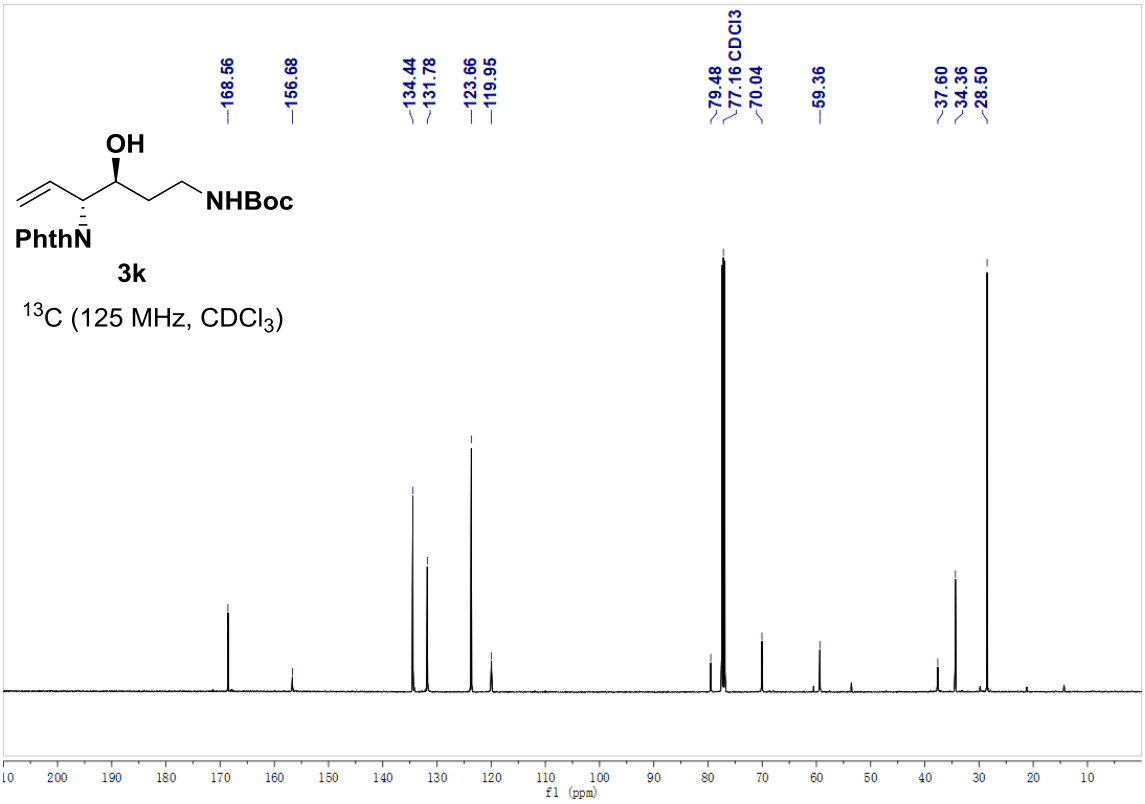
HRMS (H+, *m/z*) for $C_{19}H_{24}N_2O_5$: calcd. = 361.1758; found = 361.1756.

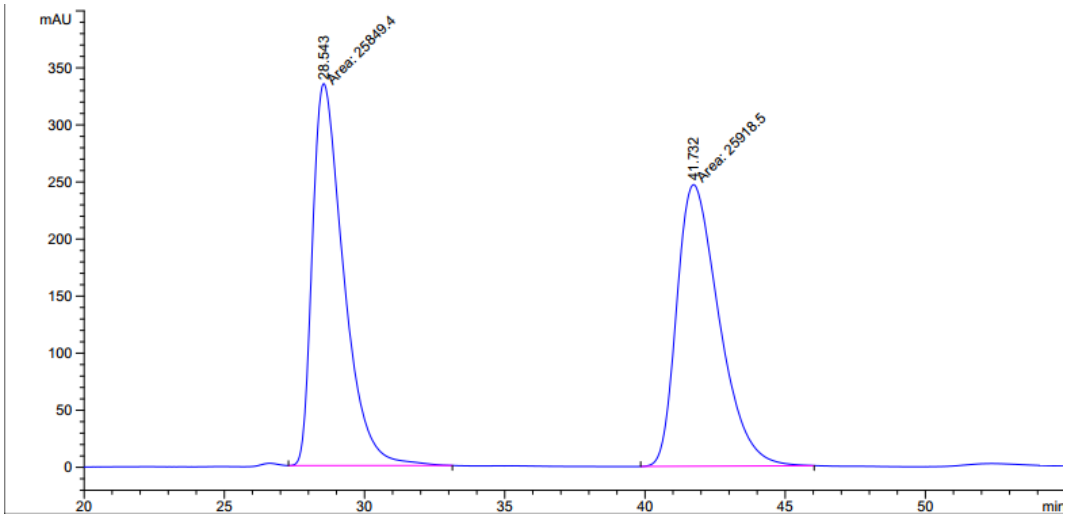
FTIR (neat): 3363, 2360, 2340, 1635, 1274, 1263, 763, 748.

HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 94%.

$[\alpha]_D^{34}$ = +44.9° (c = 0.67, $CHCl_3$).


OH
NHBoc
PhthN
3k
1H (500 MHz, CDCl3)
7.84
7.83
7.74
7.73
7.73
7.26 CDCl3
6.32
6.30
6.28
6.27
6.25
5.31
5.29
5.28
5.24
4.97
4.67
4.66
4.65
4.20
4.19
4.18
4.13
4.11
4.10
4.08
3.48
3.19
3.18
3.17
3.16
1.70
1.68
1.67
1.64
1.63
1.62
1.41
2.08
2.12
1.00
2.35
0.87
1.07
1.80
0.93
1.08
2.15
9.62
f1 (ppm)


OH
NHBoc
PhthN
3k
13C (125 MHz, CDCl3)
168.56
156.68
134.44
131.78
123.66
119.95
79.48
77.16 CDCl3
70.04
59.36
37.60
34.36
28.50
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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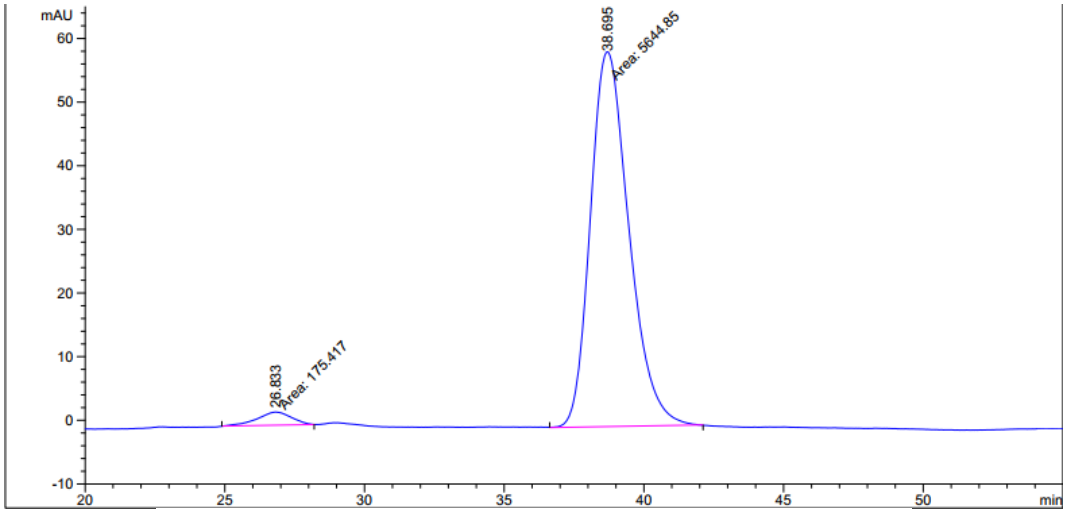
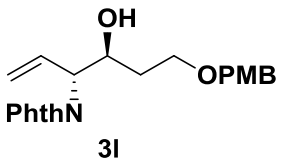
2	41.732	MM	1.7510	2.59185e4	246.69958	50.0667



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.833	MM	1.4119	175.41704	2.07075	3.0139
2	38.695	MM	1.5974	5644.85156	58.89788	96.9861

2-((3*R*,4*S*)-4-hydroxy-6-((4-methoxybenzyl)oxy)hex-1-en-3-yl)isoindoline-1,3-dione (3l)



3l

Alcohol Oxidation level: Alcohol **2l** (39.2 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 30:70 EtOAc:hexanes), the title compound **3l** (54.2 mg, 0.142 mmol, >20:1 dr) was obtained as a colorless oil in 71% yield.

Aldehyde Oxidation level: dehydro-**2l** (38.8 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h) with 7.5% catalyst of Ir-**VI** and 300 mol% 2-PrOH (36.0 mg). Upon flash column chromatography (SiO_2, 30:70 EtOAc:hexanes), the title compound **3l** (47.3 mg, 0.124 mmol, >20:1 dr) was obtained as a colorless oil in 62% yield.

TLC (SiO_2) R_f = 0.28 (30:70 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.38 – 6.28 (m, 1H), 5.32 – 5.23 (m, 2H), 4.72 (dd, *J* = 7.0, 6.2 Hz, 1H), 4.46 – 4.39 (m, 2H), 4.35 (dd, *J* = 12.1, 5.8 Hz, 1H), 3.92 (s, 1H), 3.78 (s, 3H), 3.71 – 3.65 (m, 1H), 3.64 – 3.58 (m, 1H), 1.85 – 1.77 (m, 2H).

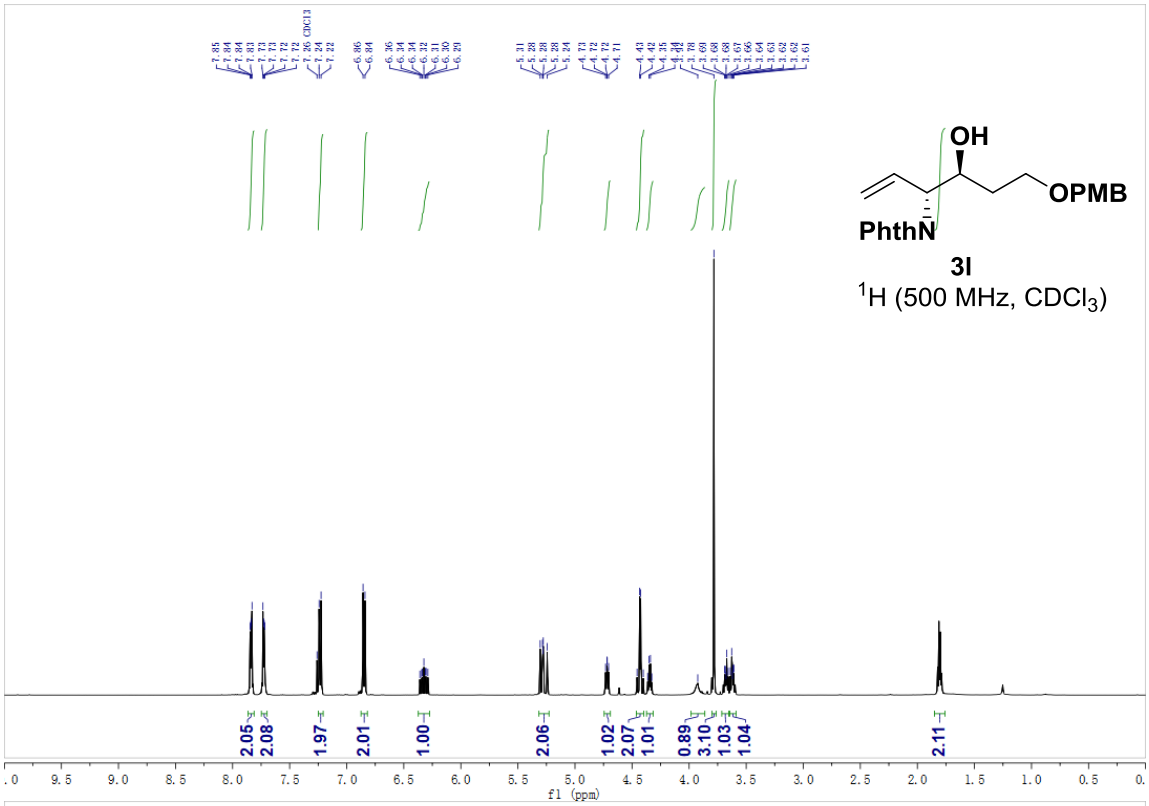
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.5, 159.3, 134.4, 131.9, 130.2, 129.5, 123.6, 123.6, 119.8, 113.9, 77.2, 73.1, 70.6, 67.8, 59.2, 55.4, 33.8.

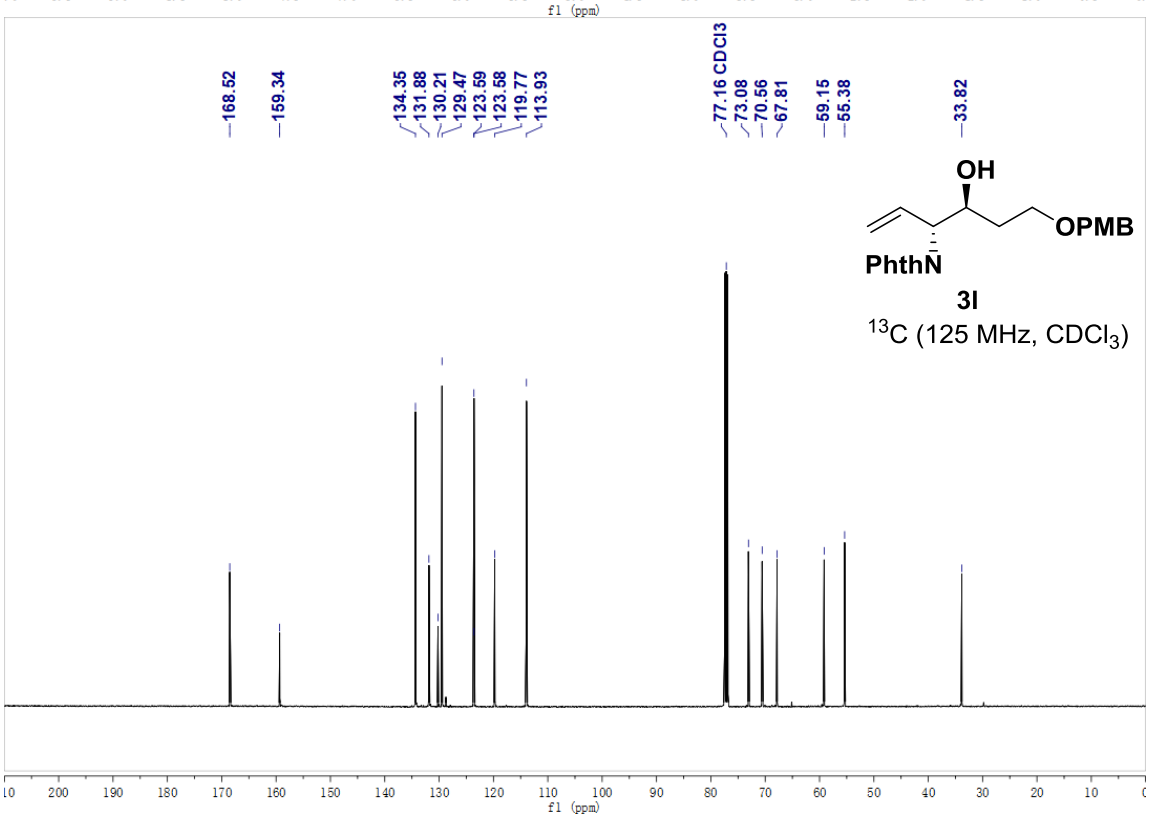
HRMS (Na+, *m/z*) for $C_{22}H_{23}NO_5$: calcd. = 404.1468; found = 404.1476.

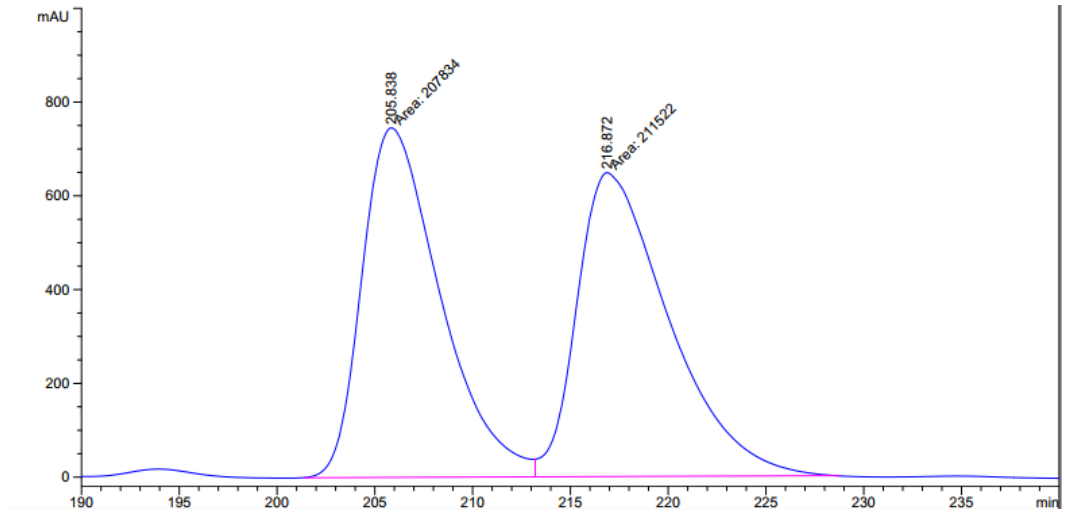
FTIR (neat): 3404, 1770, 1709, 1513, 1382, 1265, 1085, 733, 703.

HPLC: (Chiralcel column AD-H, Hexane:2-PrOH = 96:4, 1.0 mL/min, 230 nm) ee = 96%.

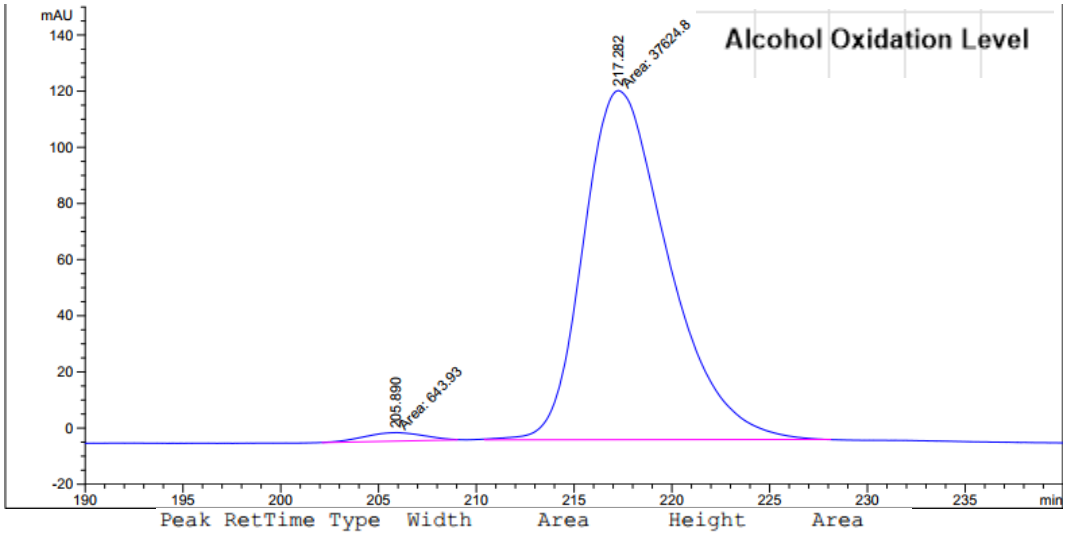
$[\alpha]_D^{34}$ = +32.5° (c = 0.83, $CHCl_3$).


OH
OPMB
PhthN
3l
1H (500 MHz, CDCl3)
2.05
2.08
1.97
2.01
1.00
2.06
1.02
2.07
1.01
0.89
3.10
1.03
1.04
2.11
f1 (ppm)

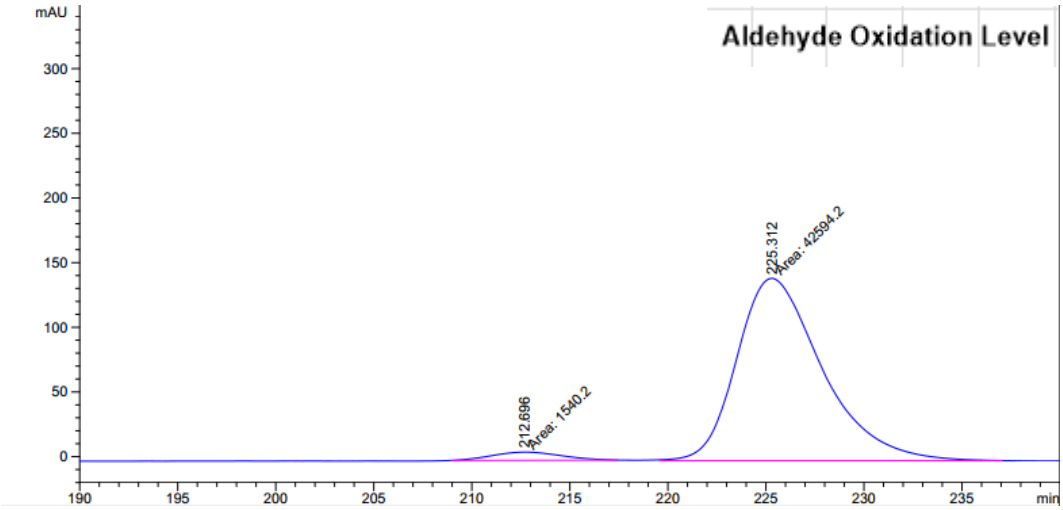

168.52
159.34
134.35
131.88
130.21
129.47
123.59
123.58
119.77
113.93
77.16 CDCl3
73.08
70.56
67.81
59.15
55.38
33.82
OH
OPMB
PhthN
3l
13C (125 MHz, CDCl3)
f1 (ppm)



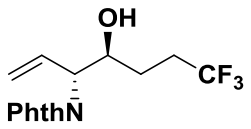
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	205.838	MF	4.6470	2.07834e5	745.40668	49.5603
2	216.872	FM	5.4390	2.11522e5	648.16034	50.4397



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	205.890	MM	3.5313	643.92981	3.03916	1.6827
2	217.282	MM	5.0435	3.76248e4	124.33395	98.3173


Aldehyde Oxidation Level
mAU
300
250
200
150
100
50
0
212.696
Area: 1540.2
225.312
Area: 42594.2
190
195
200
205
210
215
220
225
230
235
min

2-((3*R*,4*S*)-7,7,7-trifluoro-4-hydroxyhept-1-en-3-yl)isoindoline-1,3-dione (3m)



3m

Alcohol **2m** (25.6 mg, 0.2 mmol) was subjected to standard reaction conditions with 7.5% mol of (R)-**Ir-VI** (100 °C, 48 h). Upon flash column chromatography (SiO_2, 15:85 EtOAc:hexanes), the title compound **3m** (47.0 mg, 0.15 mmol, >20:1 dr) was obtained as a white solid in 75% yield.

TLC (SiO_2) R_f = 0.28 (15:85 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.4, 3.0 Hz, 2H), 6.32 – 6.18 (m, 1H), 5.46 – 5.26 (m, 2H), 4.67 (dd, *J* = 8.0, 3.8 Hz, 1H), 4.21 – 4.00 (m, 1H), 3.80 (s, 1H), 2.57 – 2.33 (m, 1H), 2.27 – 2.10 (m, 1H), 1.83 – 1.72 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.7, 134.6, 131.7, 130.6, 123.8, 121.1, 77.2, 70.8, 59.6, 30.34 (q, *J* = 29.0 Hz), 26.8, 26.8.

^{19}F NMR (470 MHz, $CDCl_3$) δ: -66.4 (t, *J* = 10.9 Hz).

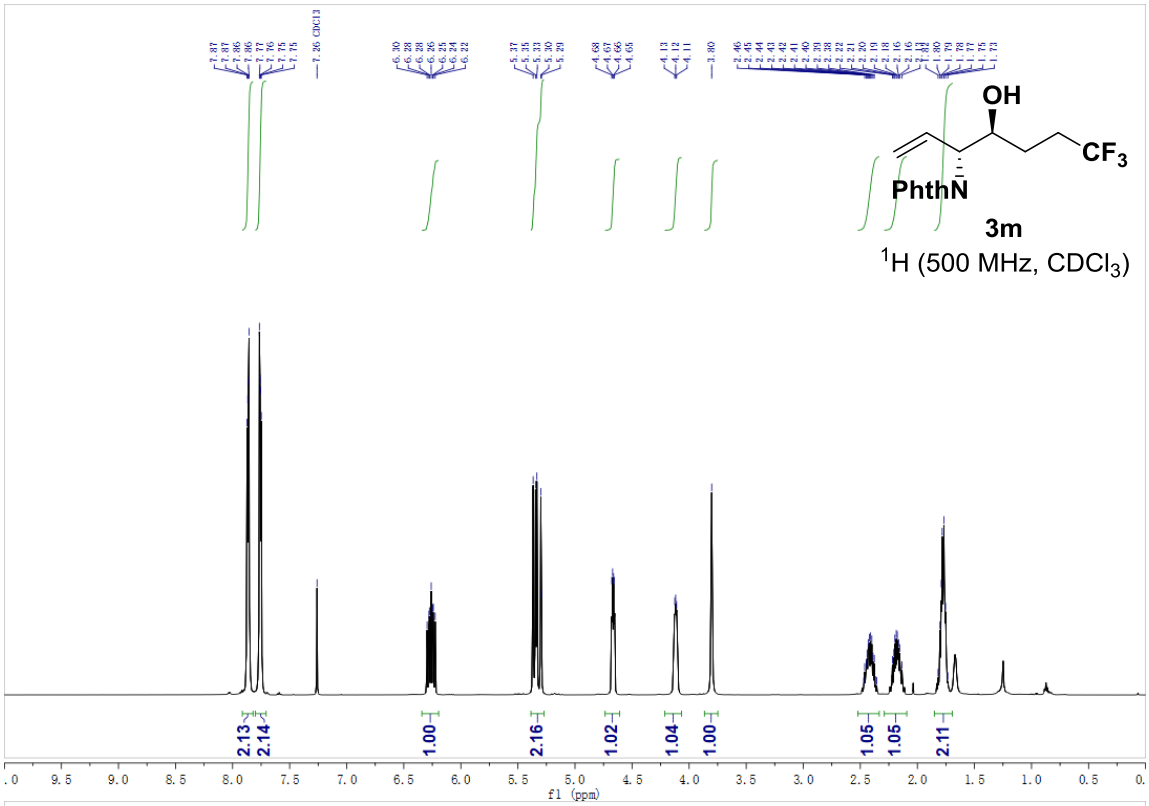
HRMS (H+, *m/z*) for $C_{15}H_{14}F_3NO_3$: calcd. = 314.0999; found =314.1001.

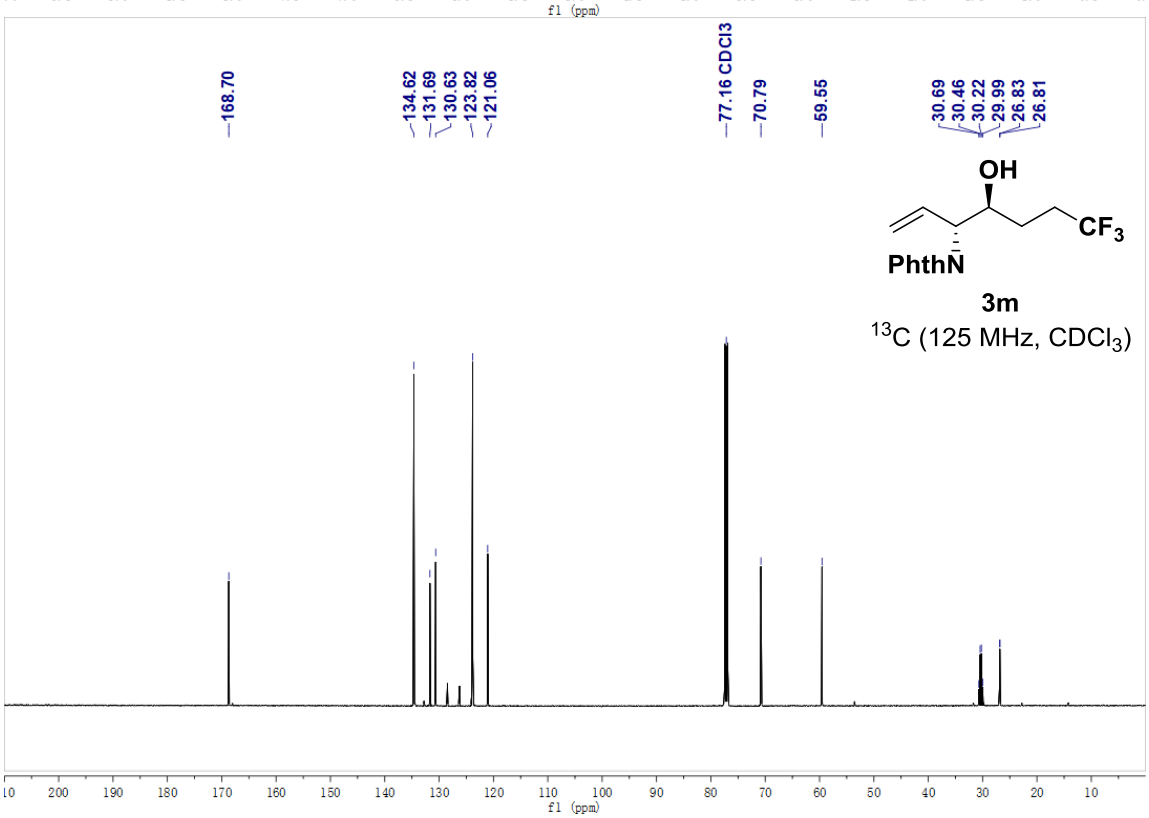
FTIR (neat): 3346, 2360, 2341, 1704, 1382, 1275, 1137, 749.

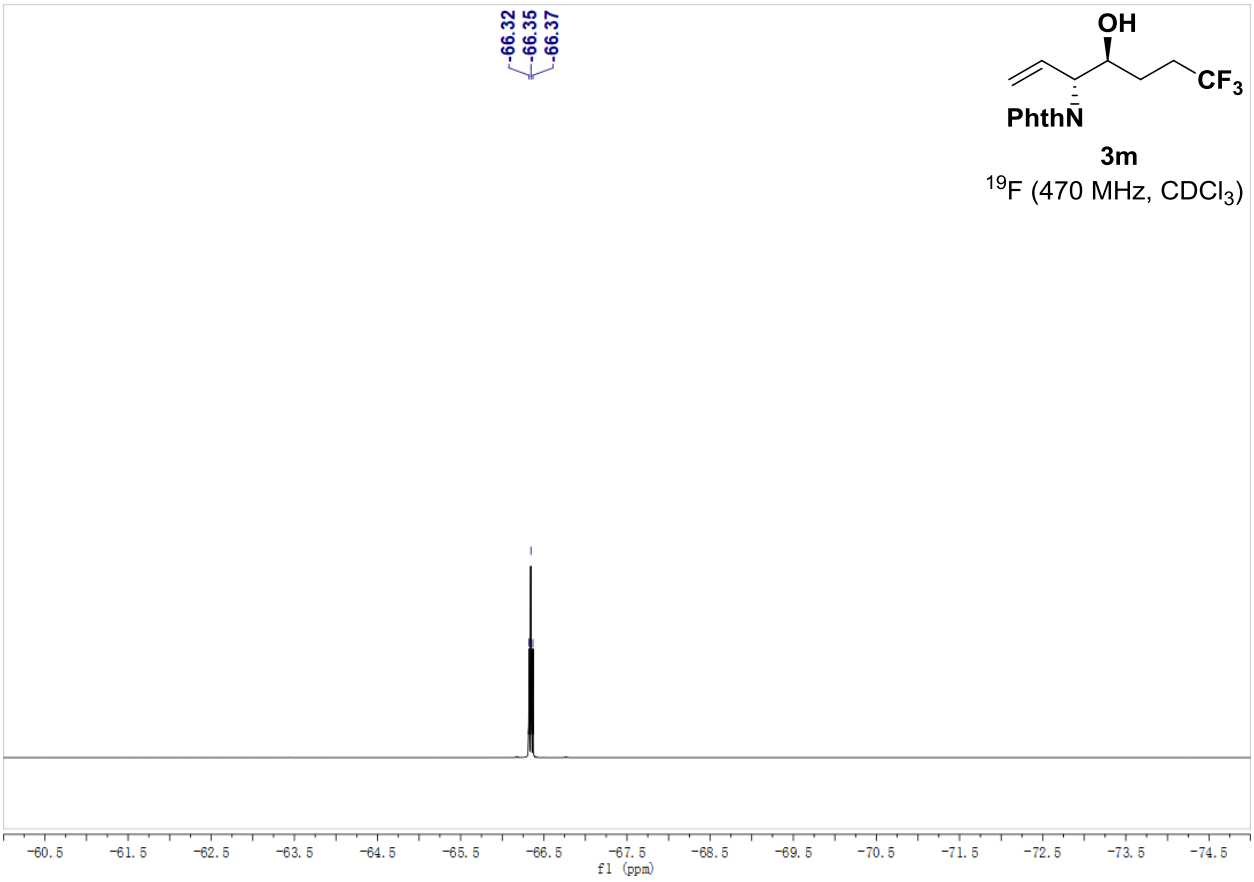
HPLC: (Chiralcel column AD-H, Hexane:2-PrOH = 97:3, 1.0 mL/min, 230 nm) ee = 94%.

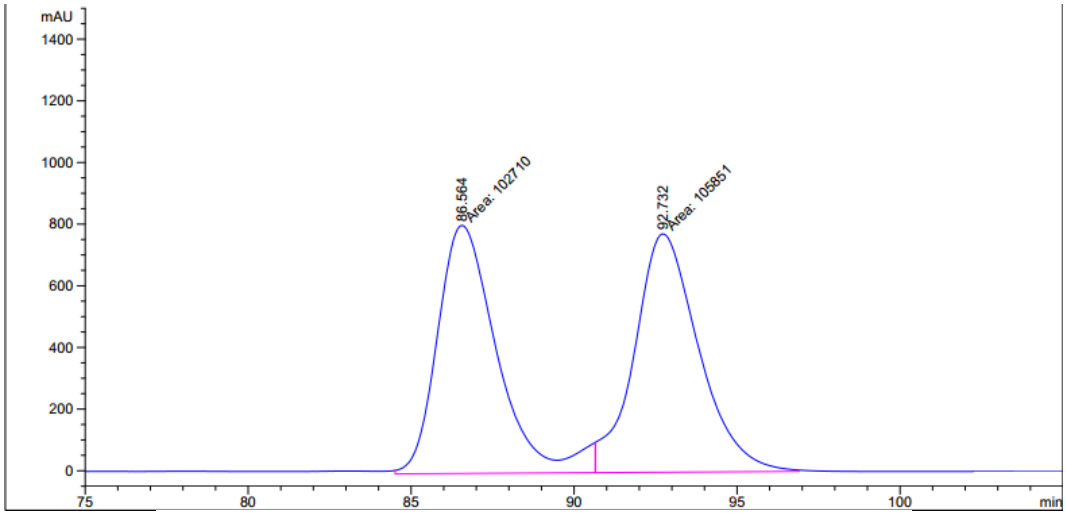
$[\alpha]_D^{24}$ = +40.5° (c = 0.74, $CHCl_3$).

MP [60 – 64] °C

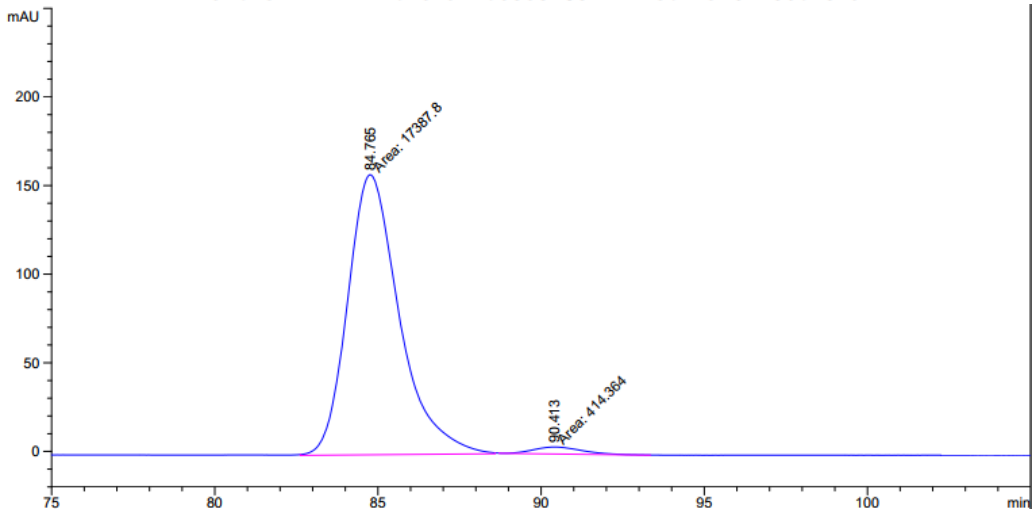

OH
CF3
PhthN
3m
1H (500 MHz, CDCl3)
2.13
2.14
1.00
2.16
1.02
1.04
1.00
1.05
1.05
2.11
f1 (ppm)


168.70
134.62
131.69
130.63
123.82
121.06
77.16 CDCl3
70.79
59.55
30.69
30.46
30.22
29.99
26.83
26.81
OH
CF3
PhthN
3m
13C (125 MHz, CDCl3)
f1 (ppm)


-66.32
-66.35
-66.37
OH
CF3
PhthN
3m
19F (470 MHz, CDCl3)
-60.5
-61.5
-62.5
-63.5
-64.5
-65.5
-66.5
-67.5
-68.5
-69.5
-70.5
-71.5
-72.5
-73.5
-74.5
f1 (ppm)

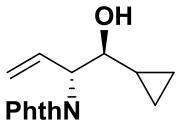


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	86.564	MF	2.1271	1.02710e5	804.78033	49.2471
2	92.732	FM	2.2819	1.05851e5	773.11945	50.7529



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	84.765	MM	1.8340	1.73878e4	158.01463	97.6724
2	90.413	MM	1.7555	414.36432	3.93394	2.3276

2-((1*S*,2*R*)-1-cyclopropyl-1-hydroxybut-3-en-2-yl)isoindoline-1,3-dione (3n)



3n

Alcohol **2n** (14.4 mg, 0.2 mmol) was subjected to standard reaction conditions using 5 mol% of (R)-**Ir-V** as catalyst (100 °C, 48 h). Upon flash column chromatography (SiO_2, 40:60 EtOAc:hexanes), the title compound **3n** (29.8 mg, 0.16 mmol, >20:1 dr) was obtained as a pale yellow solid in 58% yield.

TLC (SiO_2) R_f = 0.28 (20:80 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.85 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.4, 3.1 Hz, 2H), 6.38 (ddd, *J* = 17.6, 9.9, 7.9 Hz, 1H), 5.32 (dd, *J* = 13.7, 2.3 Hz, 2H), 4.93 – 4.79 (m, 1H), 3.40 (dd, *J* = 8.7, 5.8 Hz, 1H), 3.09 (s, 1H), 1.09 – 0.91 (m, 1H), 0.61 – 0.48 (m, 1H), 0.44 – 0.31 (m, 2H), 0.23 – 0.11 (m, 1H).
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.7, 134.4, 132.1, 131.8, 123.6, 120.0, 77.2, 76.3, 59.7, 15.3, 2.6, 2.4.

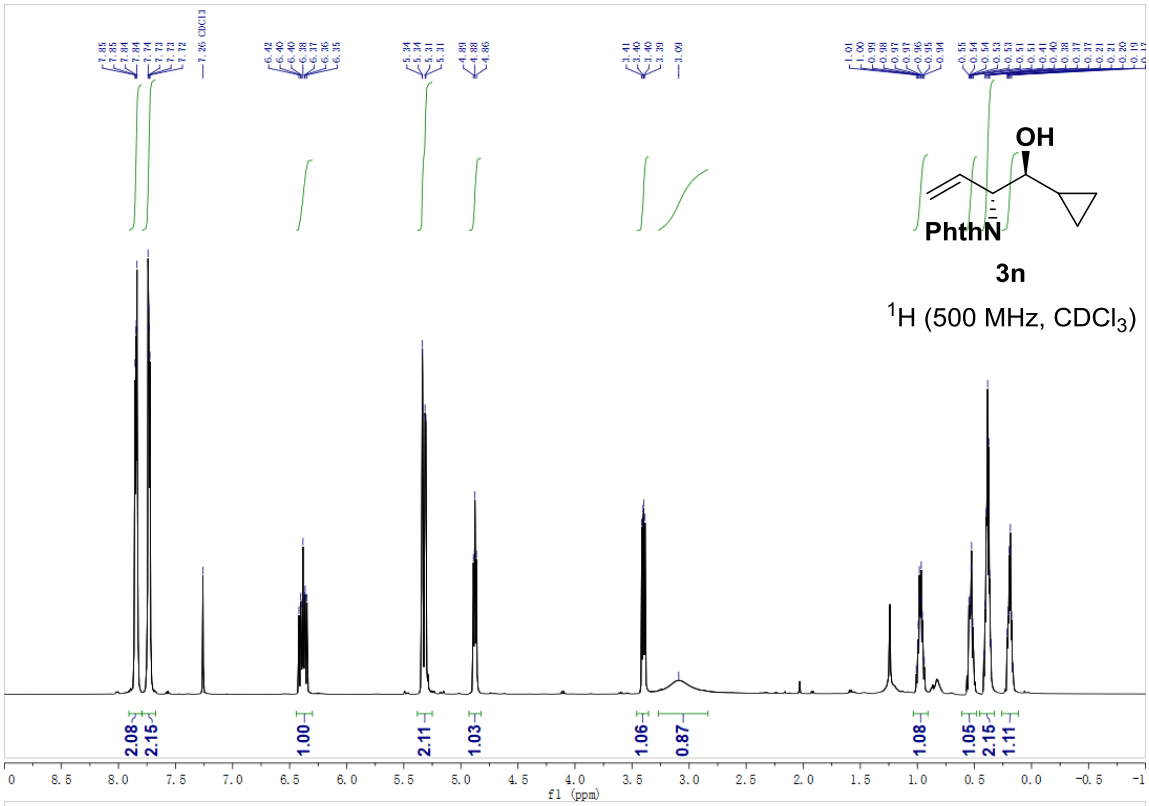
HRMS (Na+, *m/z*) for $C_{15}H_{15}NO_3$: calcd. = 280.0944; found = 280.0946.

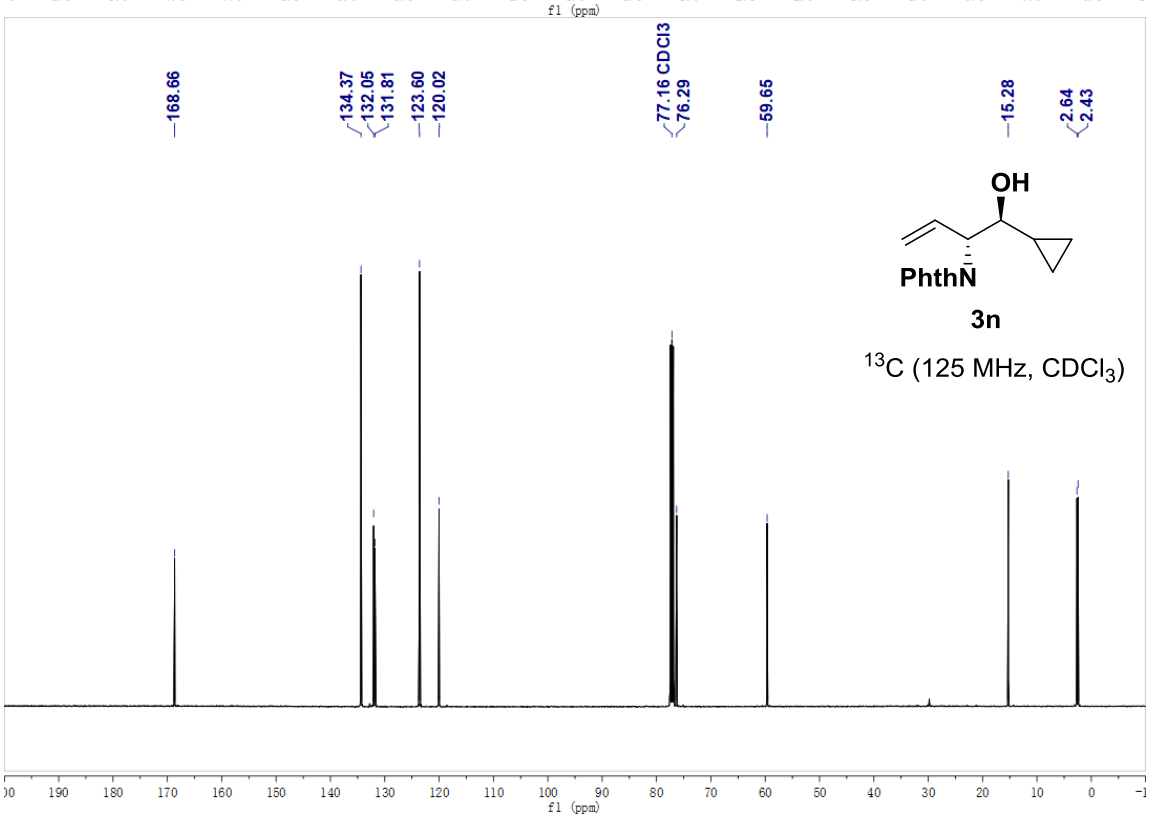
FTIR (neat): 3363, 2359, 2340, 1711, 1264, 1085, 733, 703.

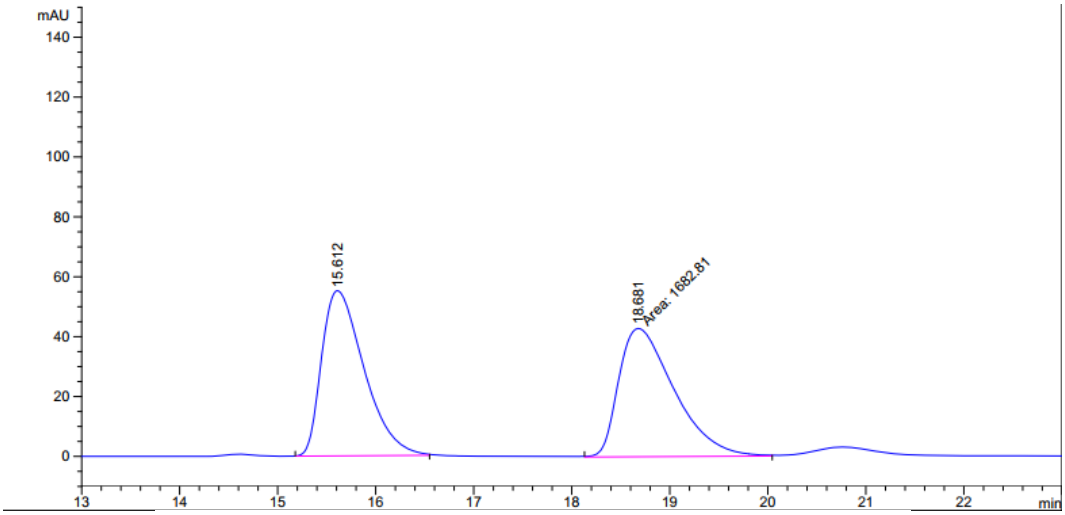
HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 96%.

$[\alpha]_D^{24}$ = +20.4° (c = 1.10, $CHCl_3$).

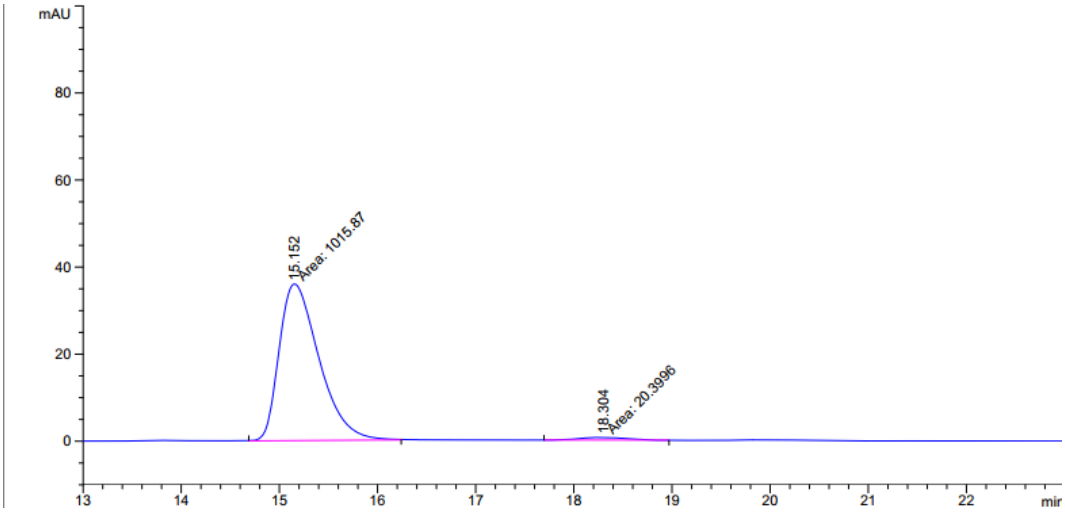
MP [55 – 60] °C


OH
PhthN
3n
^{1}H (500 MHz, $CDCl_3$)
2.08
2.15
1.00
2.11
1.03
1.06
0.87
1.08
1.05
2.15
1.11
f1 (ppm)


168.66
134.37
132.05
131.81
123.60
120.02
77.16 CDCl3
76.29
59.65
15.28
2.64
2.43
OH
PhthN
3n
^{13}C (125 MHz, $CDCl_3$)
f1 (ppm)

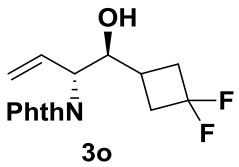


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.612	BB	0.4650	1659.61731	55.16368	49.6531
2	18.681	MM	0.6546	1682.80798	42.84468	50.3469



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.152	MM	0.4708	1015.86859	35.96019	98.0314
2	18.304	MM	0.5429	20.39956	6.26202e-1	1.9686

2-((1*S*,2*R*)-1-cyclopropyl-1-hydroxybut-3-en-2-yl)isoindoline-1,3-dione (3o)



3o

Alcohol **2o** (24.4 mg, 0.2 mmol) was subjected to standard reaction conditions with longer reaction time (100 °C, 72 h). Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), the title compound **3o** (37.5 mg, 0.122 mmol, >20:1 dr) was obtained as a white solid in 61% yield.

TLC (SiO_2) R_f = 0.26 (20:80 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.76 (dd, *J* = 5.4, 3.0 Hz, 2H), 6.26 (ddd, *J* = 17.2, 10.2, 8.2 Hz, 1H), 5.32 (dd, *J* = 20.1, 13.7 Hz, 2H), 4.63 (dd, *J* = 8.1, 4.1 Hz, 1H), 4.06 (d, *J* = 4.2 Hz, 1H), 3.73 (d, *J* = 2.1 Hz, 1H), 2.72 – 2.38 (m, 4H), 2.30 (dd, *J* = 8.0, 3.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.8, 134.6, 134.5, 131. 7, 130.8, 123.8, 123.7, 121.0, 77.2, 73.9, 57.7, 37.3 (m), 36.8 (m), 26.4.

^{19}F NMR (470 MHz, $CDCl_3$) δ: -82.3 (tt, *J* = 12.0, 5.9 Hz), -82.7 (ddt, *J* = 17.6, 11.9, 5.8 Hz), -96.6 (m), -97.0 (m).

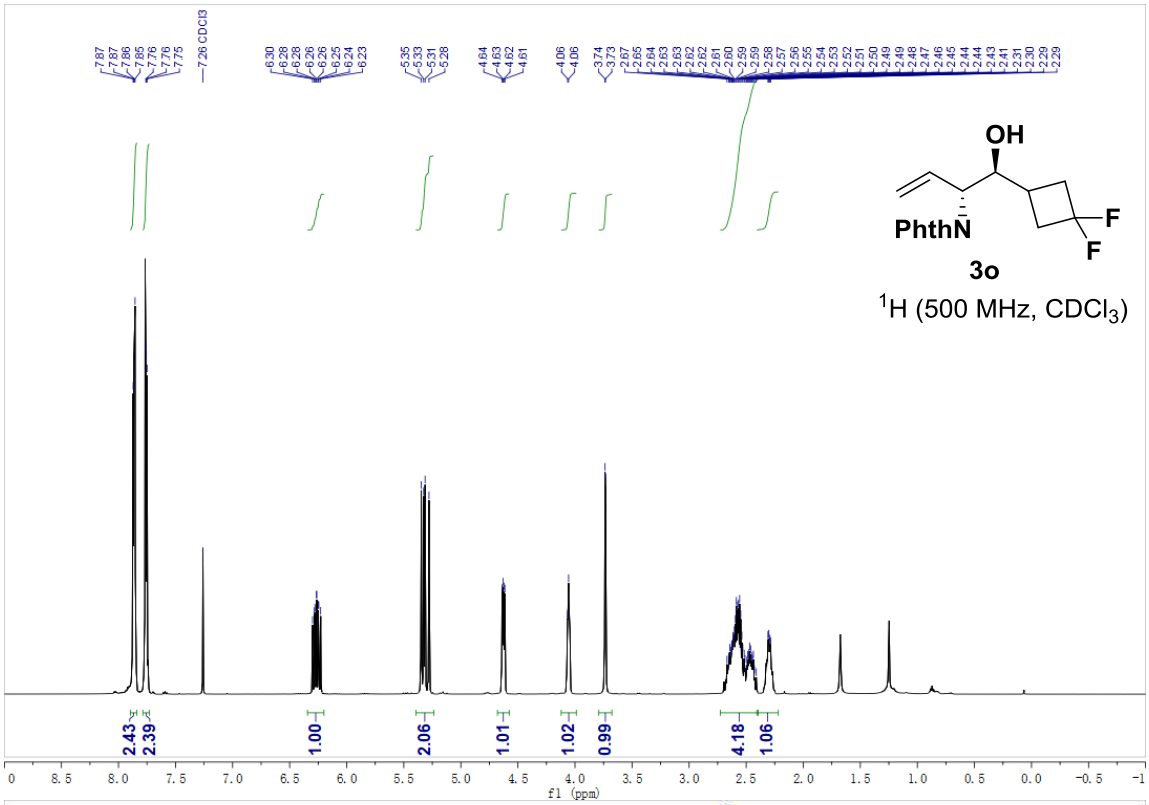
HRMS (Na+, *m/z*) for $C_{16}H_{15}F_2NO_3$: calcd. = 330.0912; found = 330.0916.

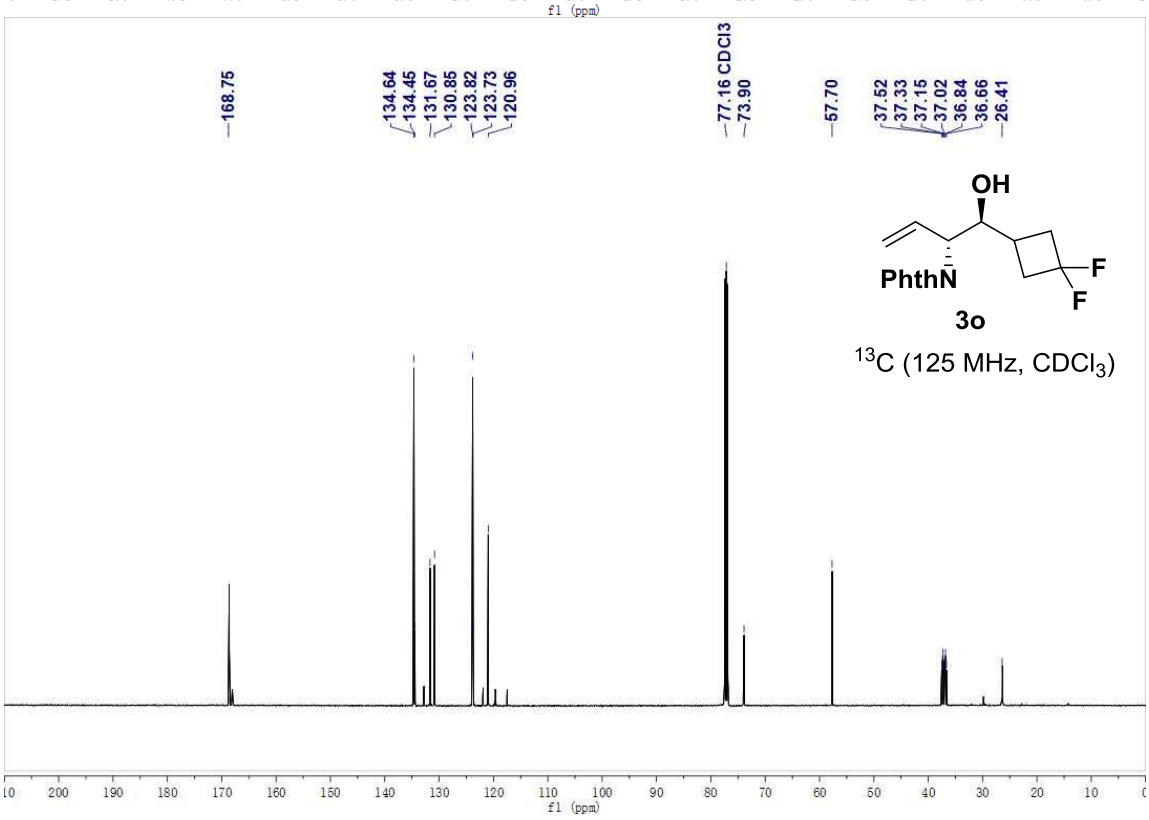
FTIR (neat): 3469, 2631, 2340, 1705, 1382, 1296, 1265, 1070, 763.

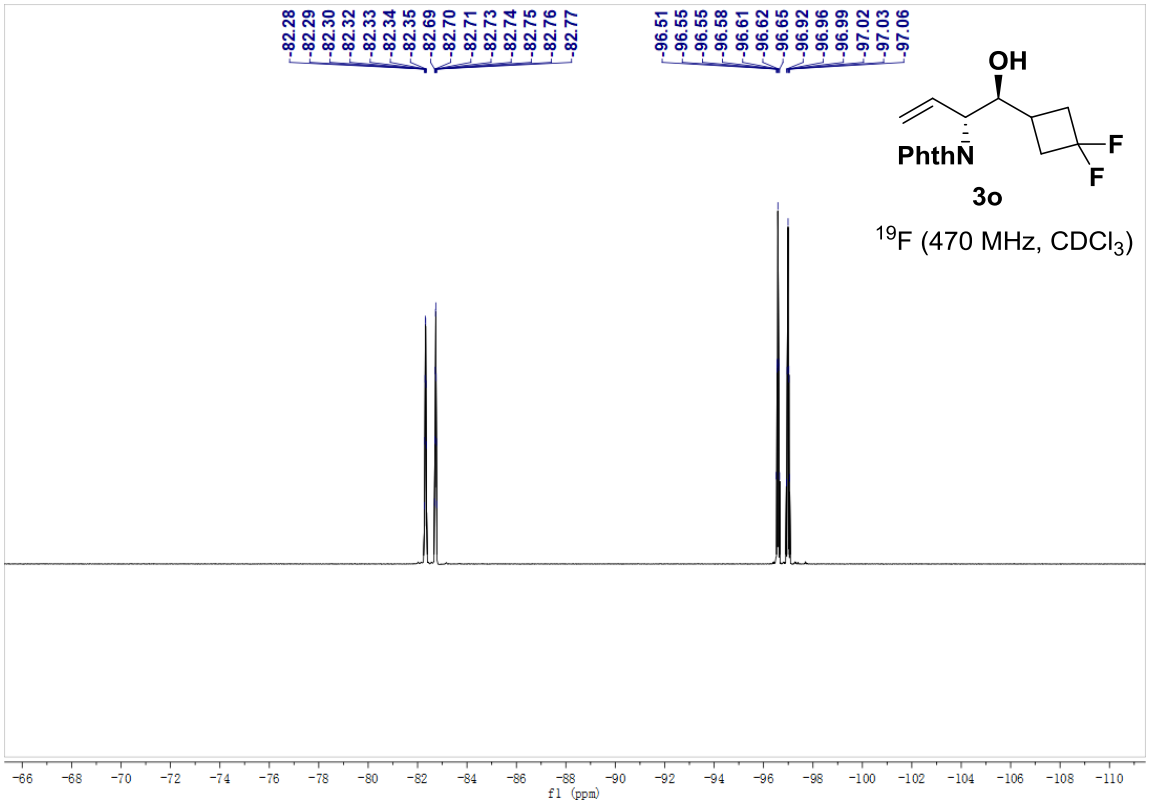
HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 94%.

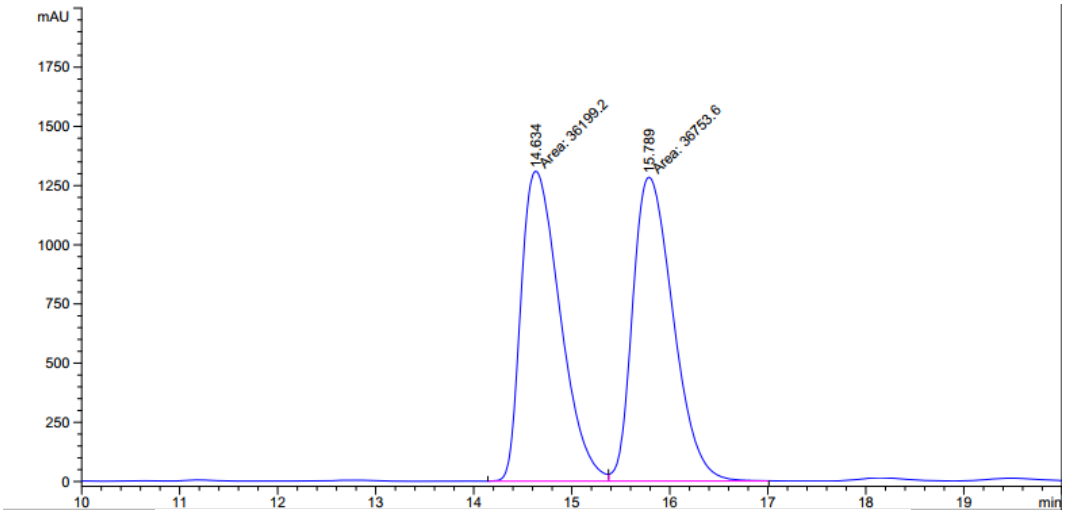
$[\alpha]_D^{34}$ = +14.0° (c = 0.87, $CHCl_3$).

MP [78 – 80] °C

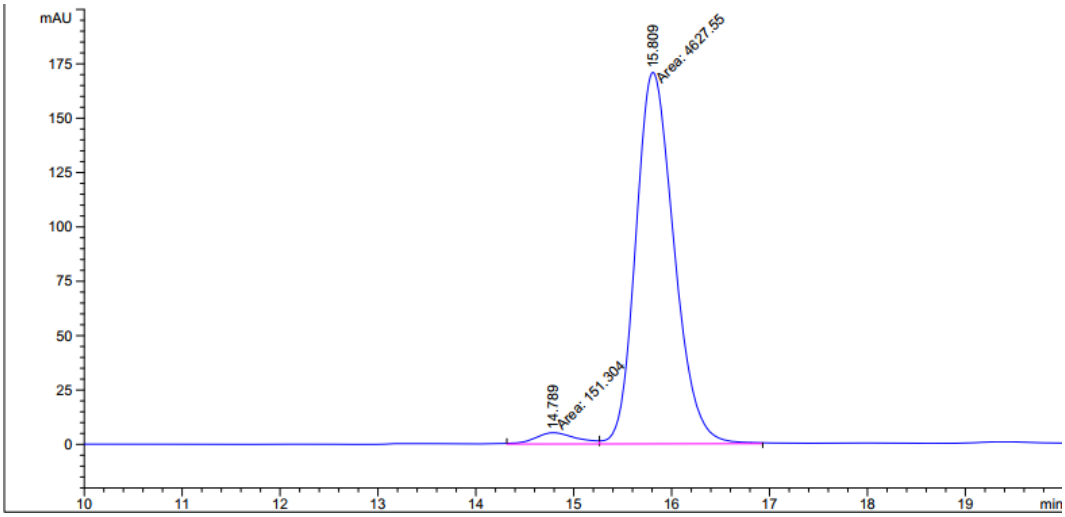

OH
PhthN
F
F
3o
^{1}H (500 MHz, $CDCl_3$)
2.43
2.39
1.00
2.06
1.01
1.02
0.99
4.18
1.06
f1 (ppm)


OH
PhthN
F
F
3o
^{13}C (125 MHz, $CDCl_3$)
168.75
134.64
134.45
131.67
130.85
123.82
123.73
120.96
77.16 CDCl3
73.90
57.70
37.52
37.33
37.15
37.02
36.84
36.66
26.41
f1 (ppm)


-82.28
-82.29
-82.30
-82.32
-82.33
-82.34
-82.35
-82.69
-82.70
-82.71
-82.73
-82.74
-82.75
-82.76
-82.77
-96.51
-96.55
-96.55
-96.58
-96.61
-96.62
-96.65
-96.92
-96.96
-96.99
-97.02
-97.03
-97.06
OH
PhthN
F
F
3o
19F (470 MHz, CDCl3)
-66
-68
-70
-72
-74
-76
-78
-80
-82
-84
-86
-88
-90
-92
-94
-96
-98
-100
-102
-104
-106
-108
-110
f1 (ppm)

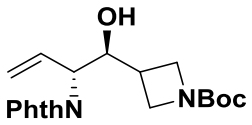


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.634	MF	0.4608	3.61992e4	1309.30823	49.6201
2	15.789	FM	0.4772	3.67536e4	1283.57446	50.3799



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.789	MF	0.4843	151.30403	5.20708	3.1661
2	15.809	FM	0.4515	4627.54736	170.80737	96.8339

***tert*-butyl 3-((1*S*,2*R*)-2-(1,3-dioxoisoindolin-2-yl)-1-hydroxybut-3-en-1-yl)azetidine-1-carboxylate (3p)**



3p

Alcohol **2p** (37.4 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 30:70 EtOAc:hexanes), the title compound **3p** (49.9 mg, 0.134 mmol, >20:1 dr) was obtained as a light yellow solid in 67% yield.

TLC (SiO_2) R_f = 0.20 (30:70 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.85 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.75 (dd, *J* = 5.4, 3.0 Hz, 2H), 6.30 – 6.21 (m, 1H), 5.29 (dd, *J* = 26.8, 13.7 Hz, 2H), 4.59 (dd, *J* = 8.1, 3.8 Hz, 1H), 4.18 (dd, *J* = 7.6, 3.8 Hz, 1H), 3.97 – 3.91 (m, 3H), 3.75 (dd, *J* = 8.5, 5.9 Hz, 1H), 2.74 – 2.64 (m, 1H), 1.40 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.6, 156.4, 134.5, 131.6, 130.7, 123.7, 120.8, 79.5, 77.2, 73.7, 57.4, 51.1, 31.8, 28.5.

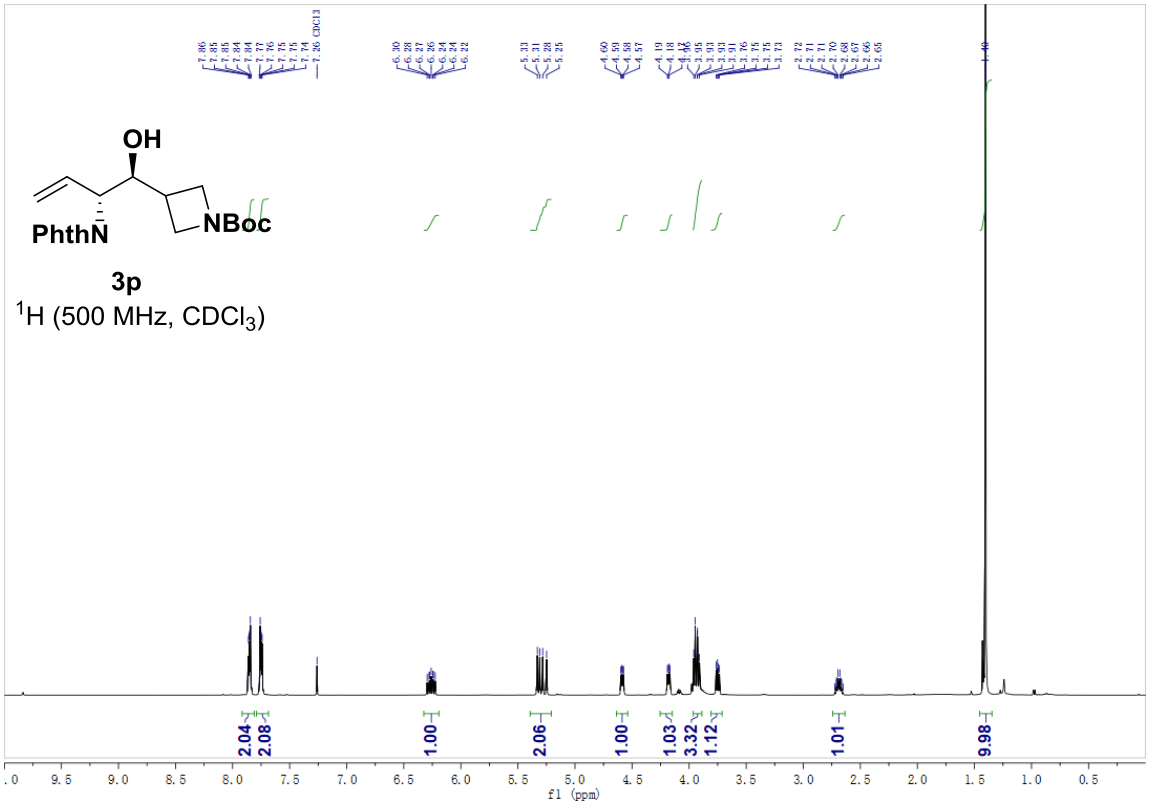
HRMS (K+, *m/z*) for $C_{20}H_{24}N_2O_5$: calcd. = 411.1317; found = 411.1323.

FTIR (neat): 3362, 2360, 2341, 1706, 1275, 1260, 764, 750.

HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 97%.

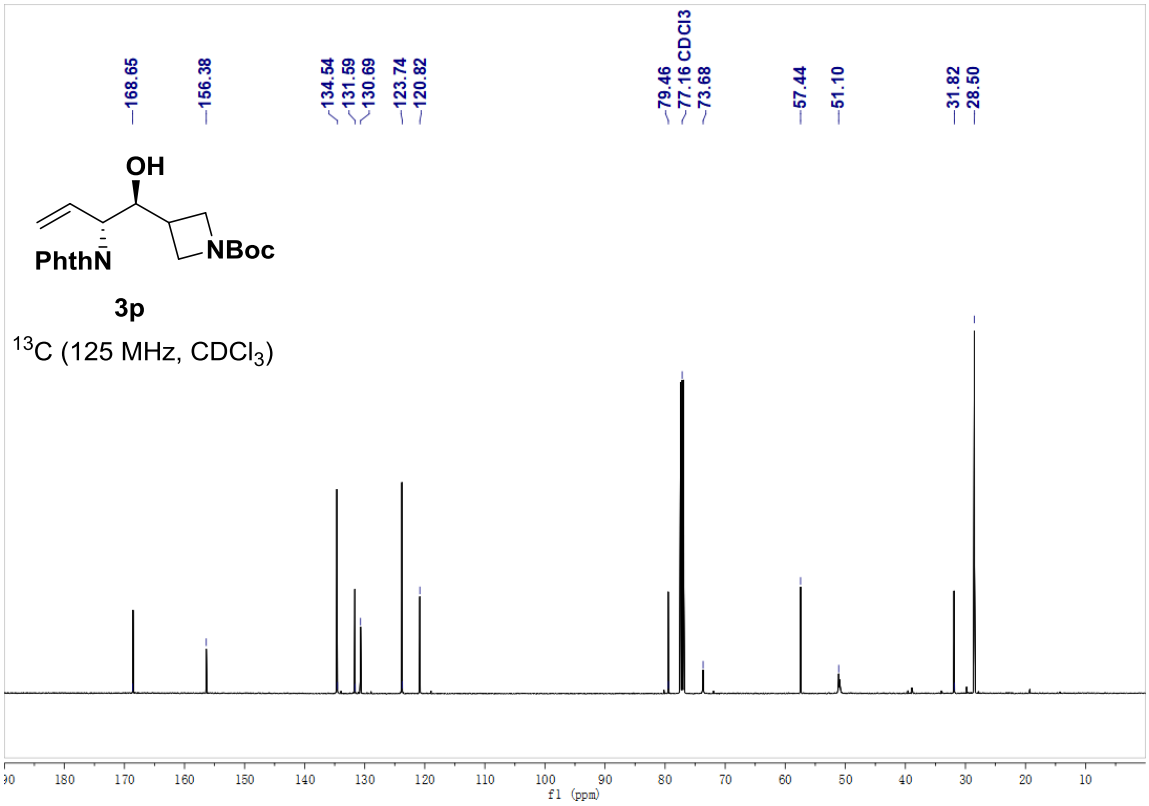
$[\alpha]_D^{34}$ = +27.7° (c = 0.64, $CHCl_3$).

MP [90 – 93] °C



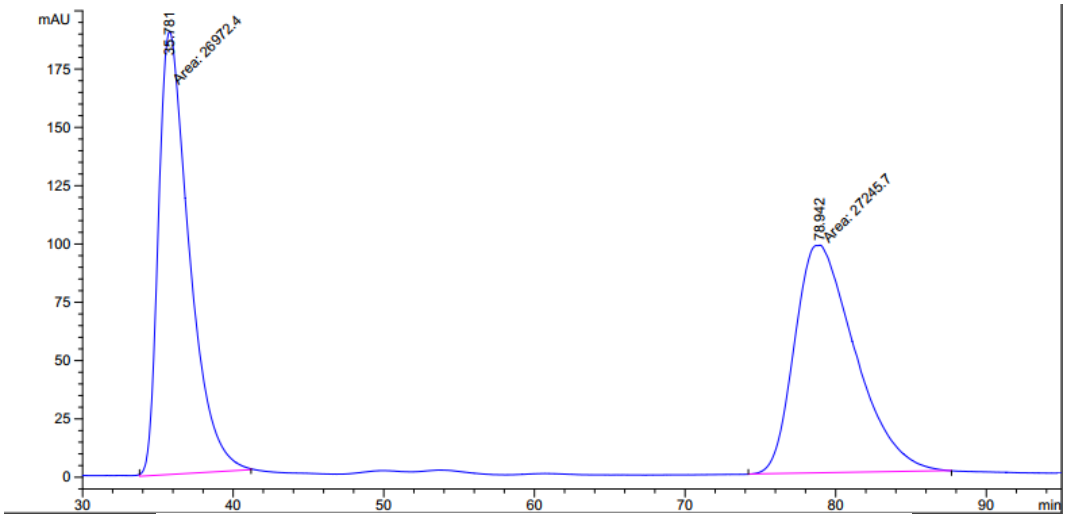
3p

^{1}H (500 MHz, $CDCl_3$)

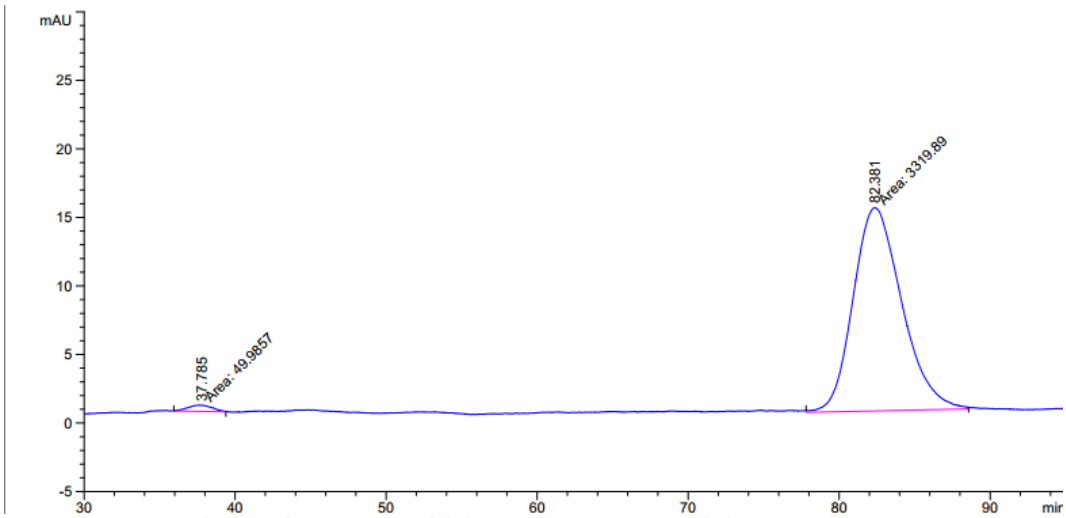


3p

^{13}C (125 MHz, $CDCl_3$)

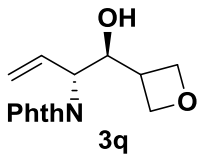


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.781	MM	2.3684	2.69724e4	189.80540	49.7479
2	78.942	MM	4.6552	2.72457e4	97.54673	50.2521



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.785	MM	1.8635	49.98568	4.47063e-1	1.4833
2	82.381	MM	3.7299	3319.89307	14.83440	98.5167

2-((1*S*,2*R*)-1-hydroxy-1-(oxetan-3-yl)but-3-en-2-yl)isoindoline-1,3-dione (3q)



3q

Alcohol **2q** (17.6 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 30:70 EtOAc:hexanes), the title compound **3q** (43.0 mg, 0.16 mmol, >20:1 dr) was obtained as a pale yellow oil in 79% yield.

TLC (SiO_2) R_f = 0.28 (30:70 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.24 (ddd, *J* = 17.1, 10.3, 7.9 Hz, 1H), 5.32 (d, *J* = 10.7 Hz, 1H), 5.26 (d, *J* = 17.1 Hz, 1H), 4.75 (d, *J* = 7.1 Hz, 2H), 4.71 (dd, *J* = 8.1, 6.1 Hz, 1H), 4.56 – 4.53 (m, 2H), 4.36 (dd, *J* = 8.0, 3.5 Hz, 1H), 3.92 (brs, 1H), 3.23 – 3.15 (m, 1H).

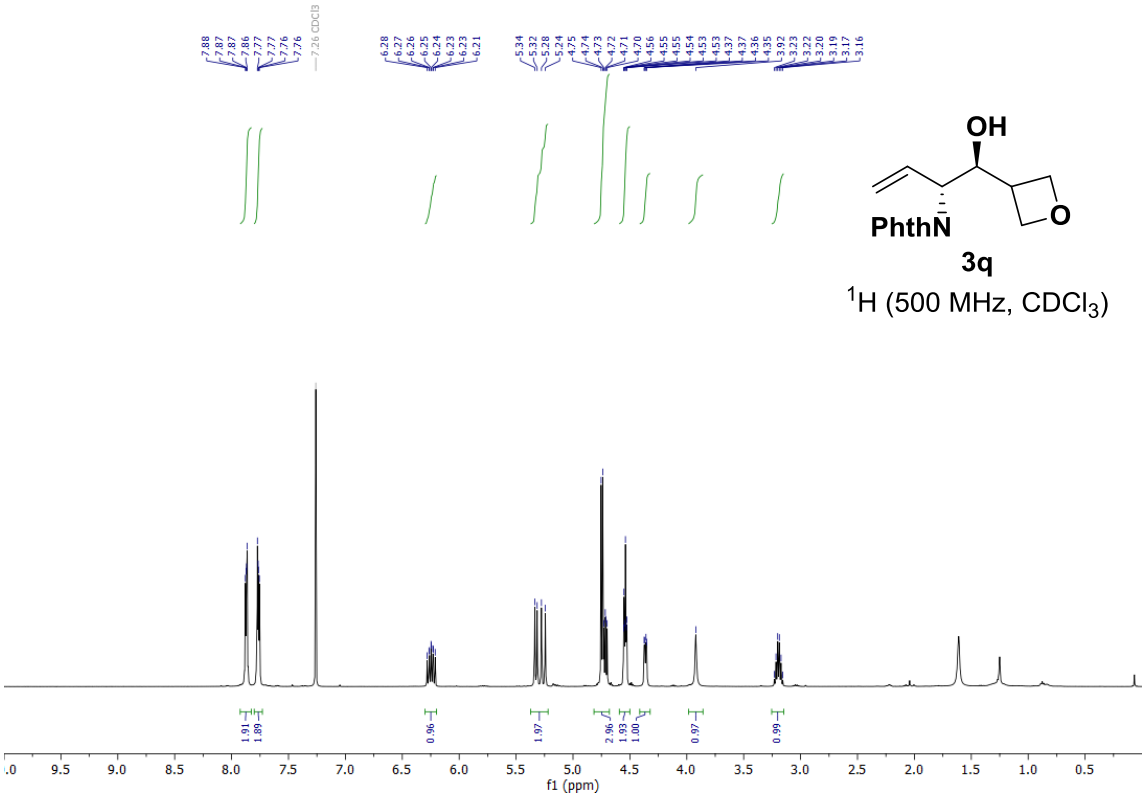
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.7, 134.7, 131.7, 130.5, 123.9, 120.9, 74.1, 73.9, 73.4, 57.5, 38.2.

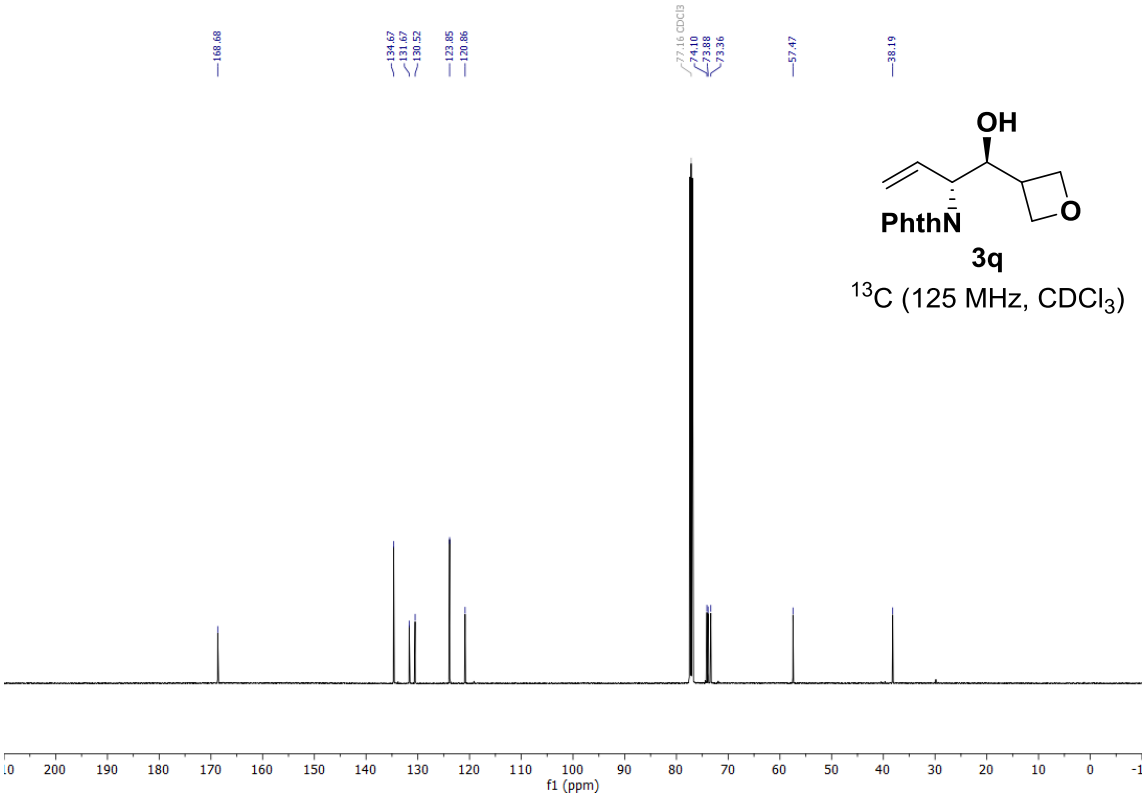
HRMS (Na+, *m/z*) for $C_{15}H_{15}NO_4$: calcd. = 296.0893; found = 296.0901.

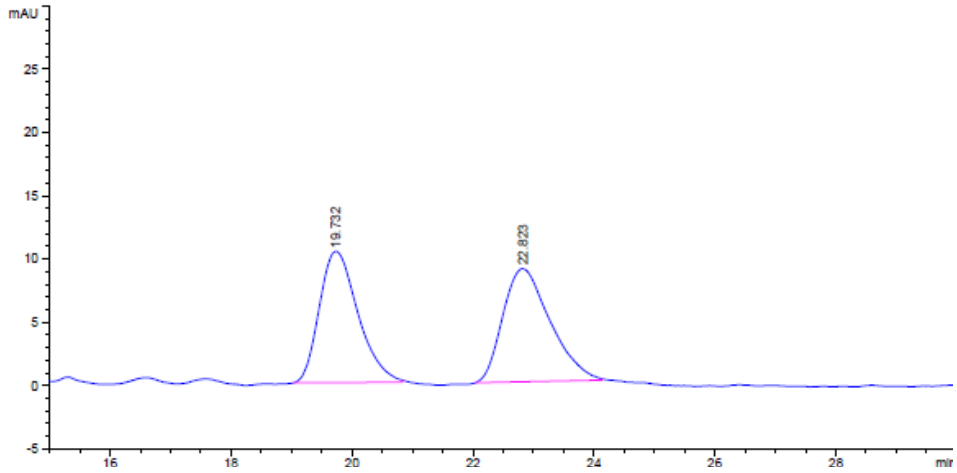
FTIR (neat): 3408, 2959, 2880, 1703, 1380, 973, 718.

HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 90:10, 1.0 mL/min, 230 nm) ee = 96%.

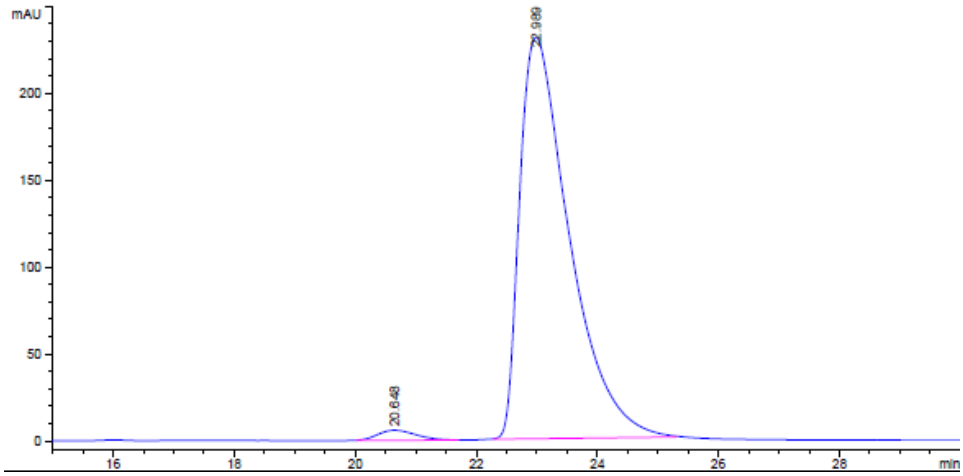
$[\alpha]_D^{34}$ = +38.7° (c = 0.92, $CHCl_3$).


OH
PhthN
O
3q
^{1}H (500 MHz, $CDCl_3$)
f1 (ppm)


OH
PhthN
O
3q
^{13}C (125 MHz, $CDCl_3$)
f1 (ppm)

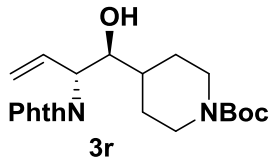


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.732	BB	0.6014	460.60611	10.38528	48.6908
2	22.823	BB	0.7026	485.37595	8.95144	51.3092



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.648	BB	0.5823	251.40669	5.76996	1.8696
2	22.989	BB	0.8464	1.31956e4	231.01495	98.1304

***tert*-butyl 4-((1*S*,2*R*)-2-(1,3-dioxoisoindolin-2-yl)-1-hydroxybut-3-en-1-yl)piperidine-1-carboxylate (3r)**



3r

Alcohol **2r** (40.3 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 25:75 EtOAc:hexanes), the title compound **3r** (56.0 mg, 0.14 mmol, >20:1 dr) was obtained as white solid in 70% yield.

TLC (SiO_2) R_f = 0.30 (30:70 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.75 (dd, *J* = 5.4, 3.0 Hz, 2H), 6.33 – 6.23 (m, 1H), 5.34 – 5.23 (m, 2H), 4.89 (dd, *J* = 7.6, 4.2 Hz, 1H), 4.18 – 4.08 (m, 2H), 3.85 (dd, *J* = 6.0, 4.4 Hz, 1H), 3.58 (s, 1H), 2.71 – 2.56 (m, 2H), 1.90 (d, *J* = 13.2 Hz, 1H), 1.67 (d, *J* = 12.7 Hz, 1H), 1.61 – 1.52 (m, 1H), 1.44 (s, 9H), 1.41 – 1.28 (m, 2H)..

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.7, 154.9, 134.6, 131.8, 131.5, 123.8, 120.2, 79.5, 77.2, 75.5, 56.4, 39.0, 29.0, 28.6, 26.9.

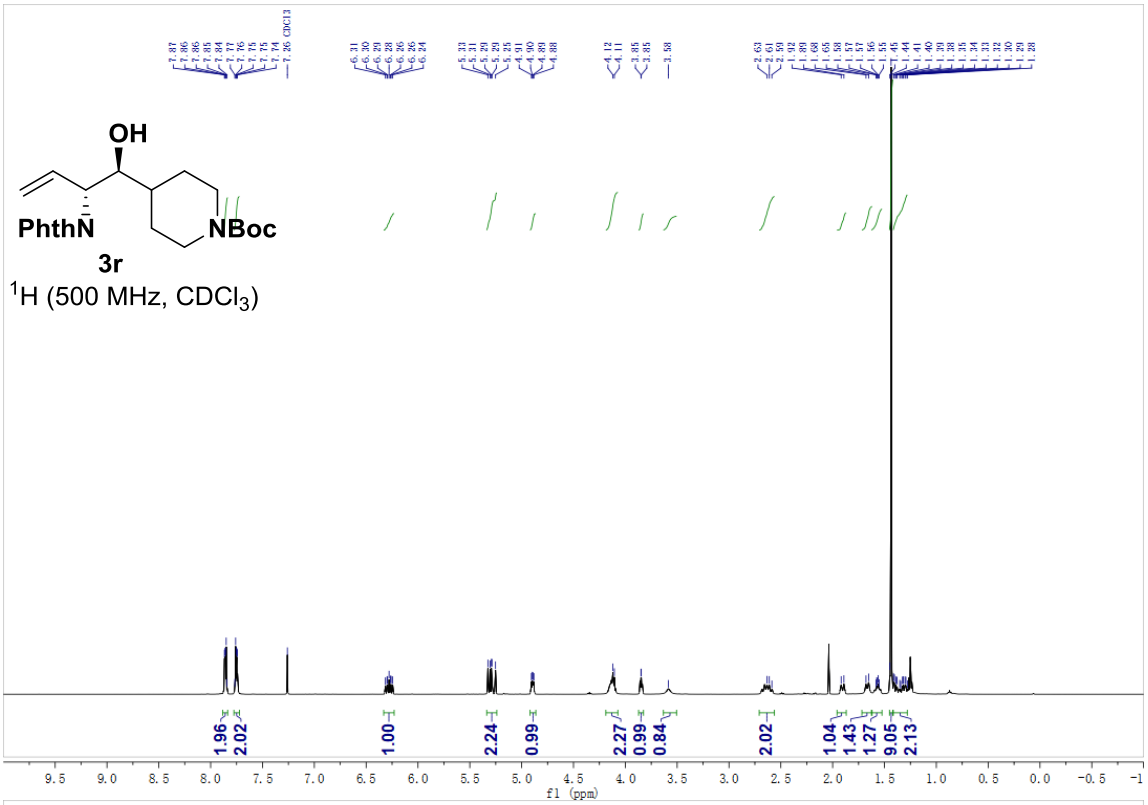
HRMS (K+, *m/z*) for $C_{22}H_{28}N_2O_5$: calcd. = 439.1630; found = 439.1629.

FTIR (neat): 3725, 2989, 2360, 2341, 1707, 1275, 1260, 764, 749, 668.

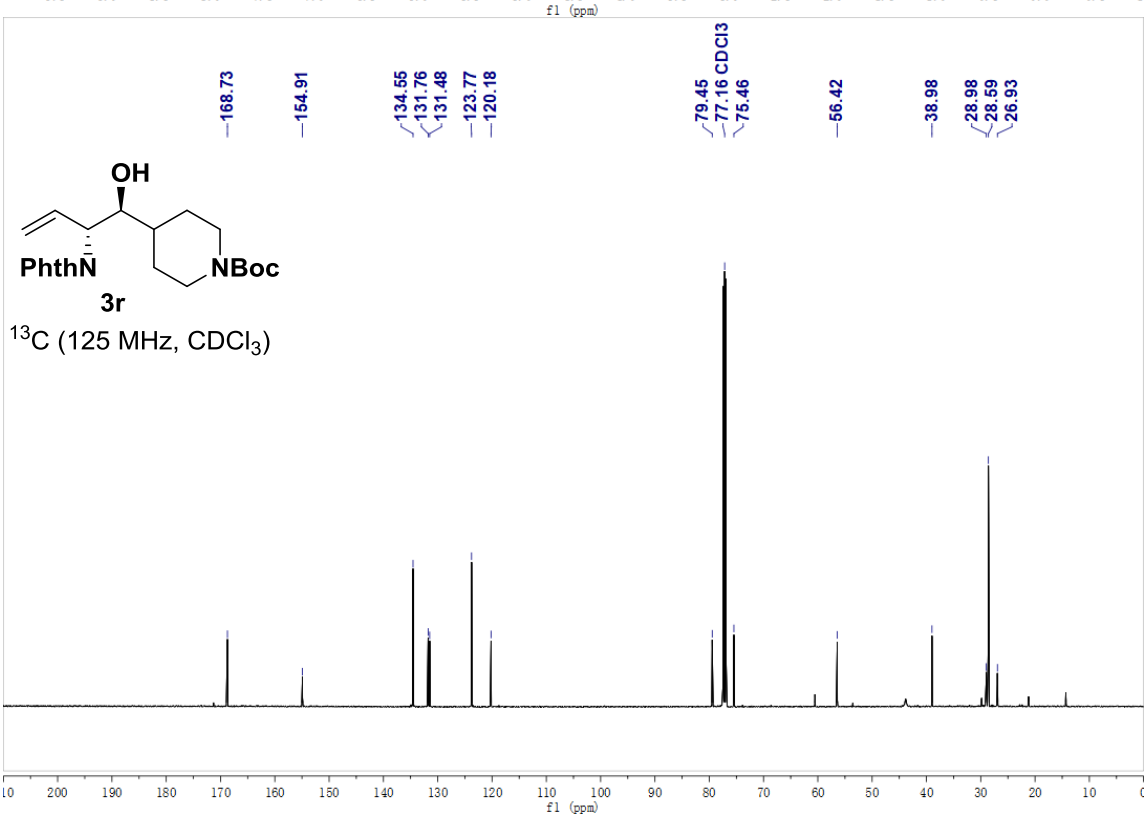
HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 93:7, 1.0 mL/min, 230 nm) ee = 93%.

$[\alpha]_D^{34}$ = +12.6° (c = 0.85, $CHCl_3$).

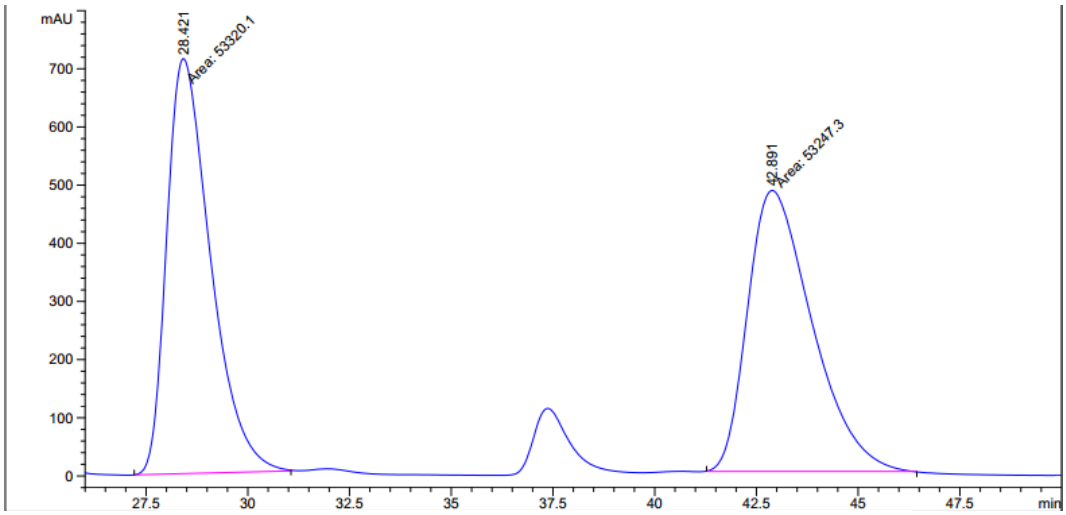
MP [102 – 106] °C



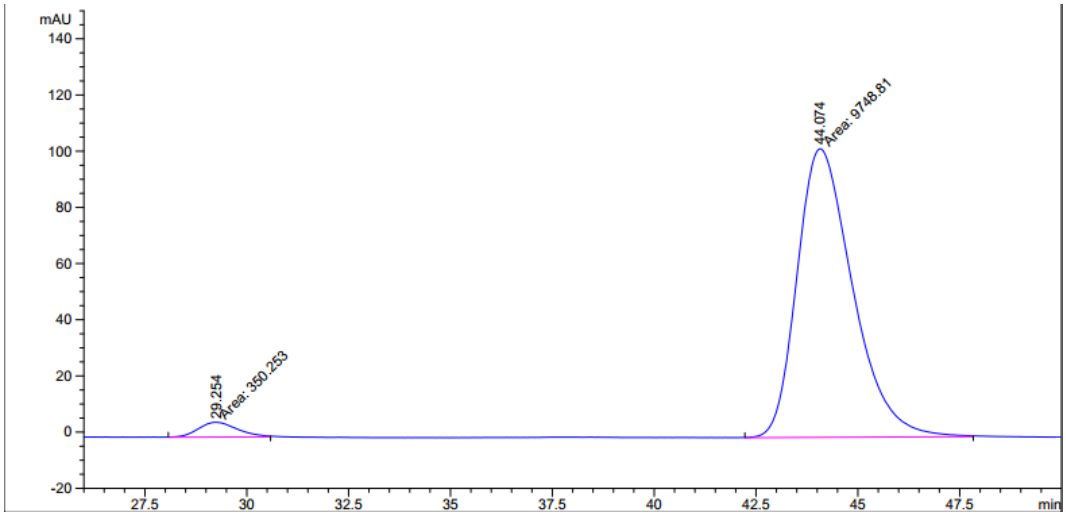
^{1}H (500 MHz, $CDCl_3$)



^{13}C (125 MHz, $CDCl_3$)

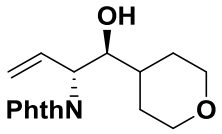


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.421	MM	1.2455	5.33201e4	713.50885	50.0341
2	42.891	MM	1.8368	5.32473e4	483.16492	49.9659



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.254	MM	1.1063	350.25256	5.27671	3.4682
2	44.074	MM	1.5813	9748.81250	102.74837	96.5318

2-((1*S*,2*R*)-1-hydroxy-1-(tetrahydro-2H-pyran-4-yl)but-3-en-2-yl)isoindoline-1,3-dione (3s)



3s

Alcohol **2s** (23.2 mg, 0.2 mmol) was subjected to standard reaction conditions with 7.5 mol% catalyst (100 °C, 48 h). Upon flash column chromatography (SiO_2, 30:70 EtOAc:hexanes), the title compound **3s** (47.6 mg, 0.158 mmol, >20:1 dr) was obtained as colorless oil in 79% yield.

TLC (SiO_2) R_f = 0.24 (30:70 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.75 (dd, *J* = 5.3, 3.0 Hz, 2H), 6.28 (ddd, *J* = 17.6, 10.2, 7.7 Hz, 1H), 5.29 (dd, *J* = 26.4, 13.7 Hz, 2H), 4.90 (dd, *J* = 7.4, 3.8 Hz, 1H), 3.99 (d, *J* = 11.8 Hz, 2H), 3.82 (dd, *J* = 6.3, 4.0 Hz, 1H), 3.71 (s, 1H), 3.40 – 3.28 (m, 2H), 1.85 (d, *J* = 13.3 Hz, 1H), 1.72 – 1.43 (m, 4H).

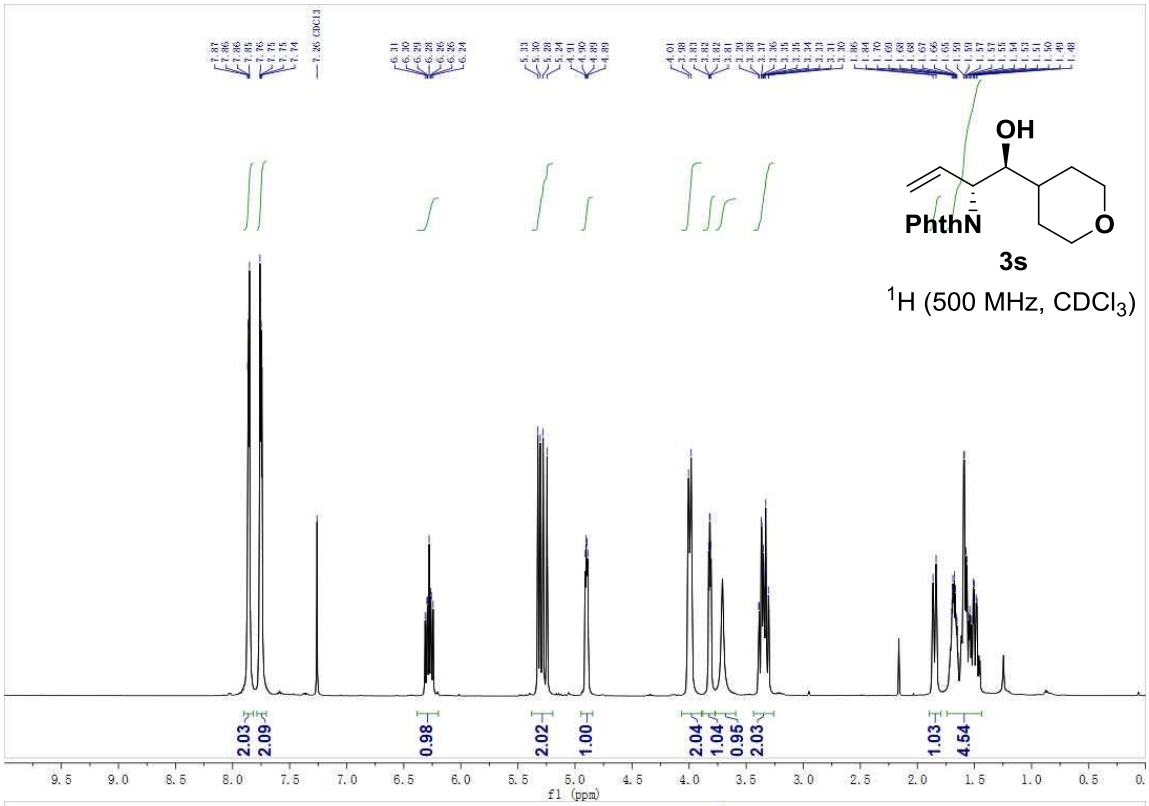
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.7, 134.6, 131.8, 131.5, 123.8, 120.1, 77.2, 75. 8, 68.1, 67.7, 56.2, 37.9, 29.7, 28.0.

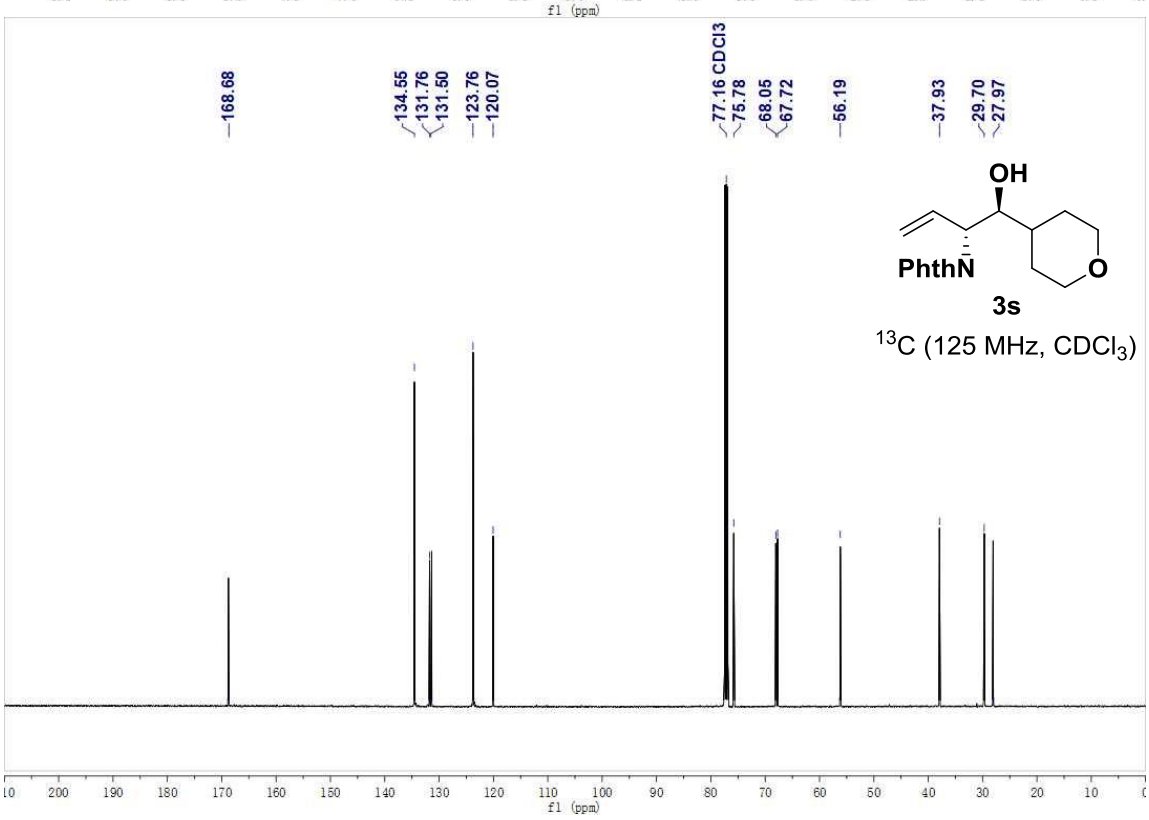
HRMS (H+, *m/z*) for $C_{17}H_{19}NO_4$: calcd. = 302.1387; found = 302.1392.

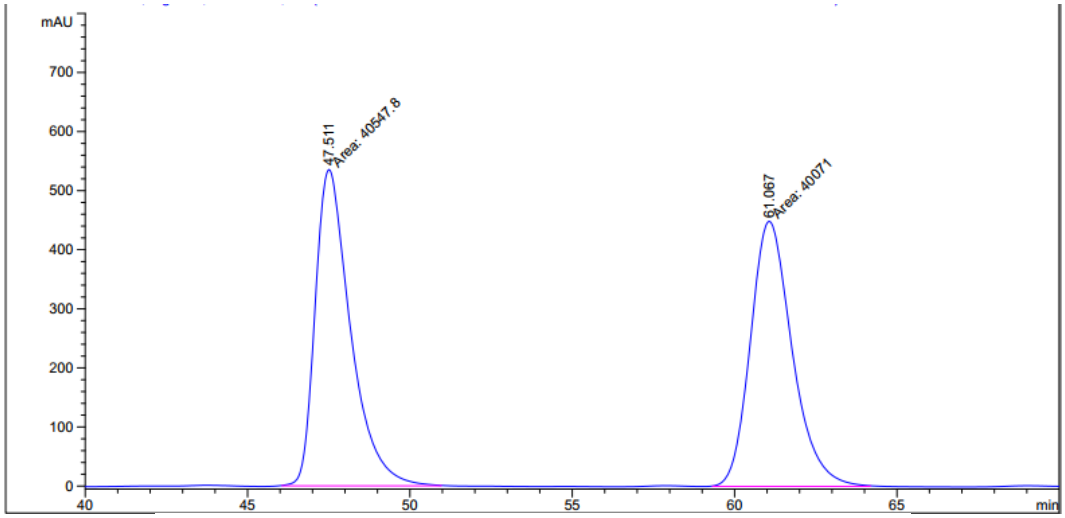
FTIR (neat): 2987, 2360, 2341, 1705, 1383, 1266, 1079, 731.

HPLC: (Chiralcel column AD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 94%.

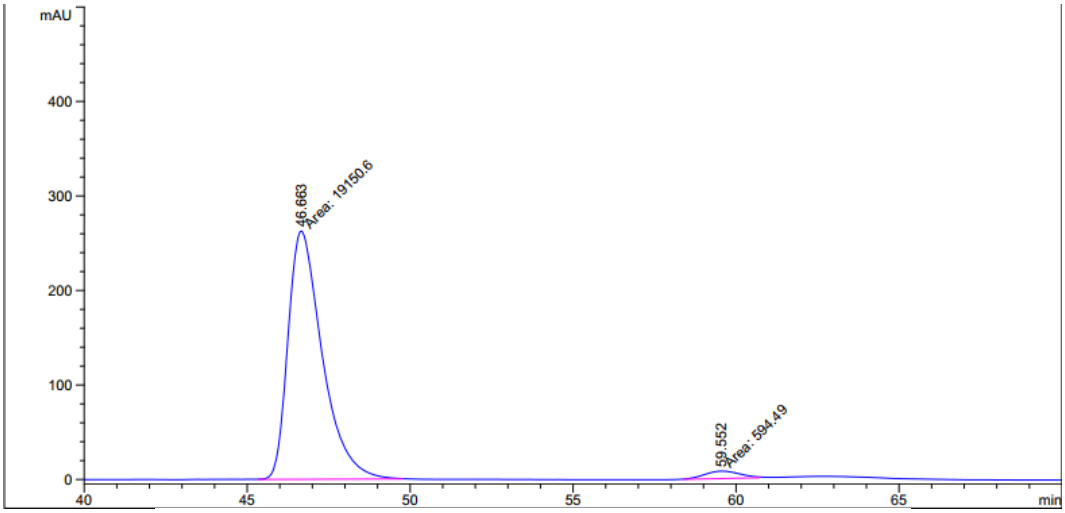
$[\alpha]_D^{24}$ = +42.7° (c = 0.70, $CHCl_3$).


OH
PhthN
O
3s
^{1}H (500 MHz, $CDCl_3$)
2.03
2.09
0.98
2.02
1.00
2.04
1.04
0.95
2.03
1.03
4.54
f1 (ppm)


168.68
134.55
131.76
131.50
123.76
120.07
77.16 CDCl3
75.78
68.05
67.72
56.19
37.93
29.70
27.97
OH
PhthN
O
3s
^{13}C (125 MHz, $CDCl_3$)
f1 (ppm)

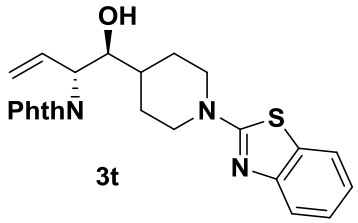


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	47.511	MM	1.2626	4.05478e4	535.22595	50.2957
2	61.067	MM	1.4888	4.00710e4	448.58865	49.7043



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	46.663	MM	1.2153	1.91506e4	262.63974	96.9892
2	59.552	MM	1.2566	594.48975	7.88482	3.0108

2-((1*S*,2*R*)-1-(1-(benzo[*d*]thiazol-2-yl)piperidin-4-yl)-1-hydroxybut-3-en-2-yl)isoindoline-1,3-dione (3t)



Alcohol **2t** (49.7 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 30:70 EtOAc:hexanes), the title compound **3t** (58.0 mg, 0.134 mmol, >20:1 dr) was obtained as a light yellow solid in 67% yield.

TLC (SiO_2) R_f = 0.30 (30:70 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.87 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.56 (dd, *J* = 17.4, 7.9 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.30 (ddd, *J* = 17.8, 10.3, 7.8 Hz, 1H), 5.33 (dd, *J* = 19.2, 13.7 Hz, 2H), 4.92 (dd, *J* = 7.6, 4.2 Hz, 1H), 4.24 (d, *J* = 12.4 Hz, 1H), 4.14 (dd, *J* = 9.7, 7.3 Hz, 1H), 3.90 (t, *J* = 6.1 Hz, 1H), 3.63 (d, *J* = 2.4 Hz, 1H), 3.15 – 3.03 (m, 2H), 2.09 (d, *J* = 13.2 Hz, 1H), 1.84 (d, *J* = 12.5 Hz, 1H), 1.74 – 1.51 (m, 4H), 1.26 (t, *J* = 7.1 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.7, 134.6, 131.7, 131.3, 126.1, 123.9, 121.4, 120.8, 120.5, 119.0, 77.2, 75.2, 56.5, 49.1, 48.6, 38.8, 28.5, 26.5.

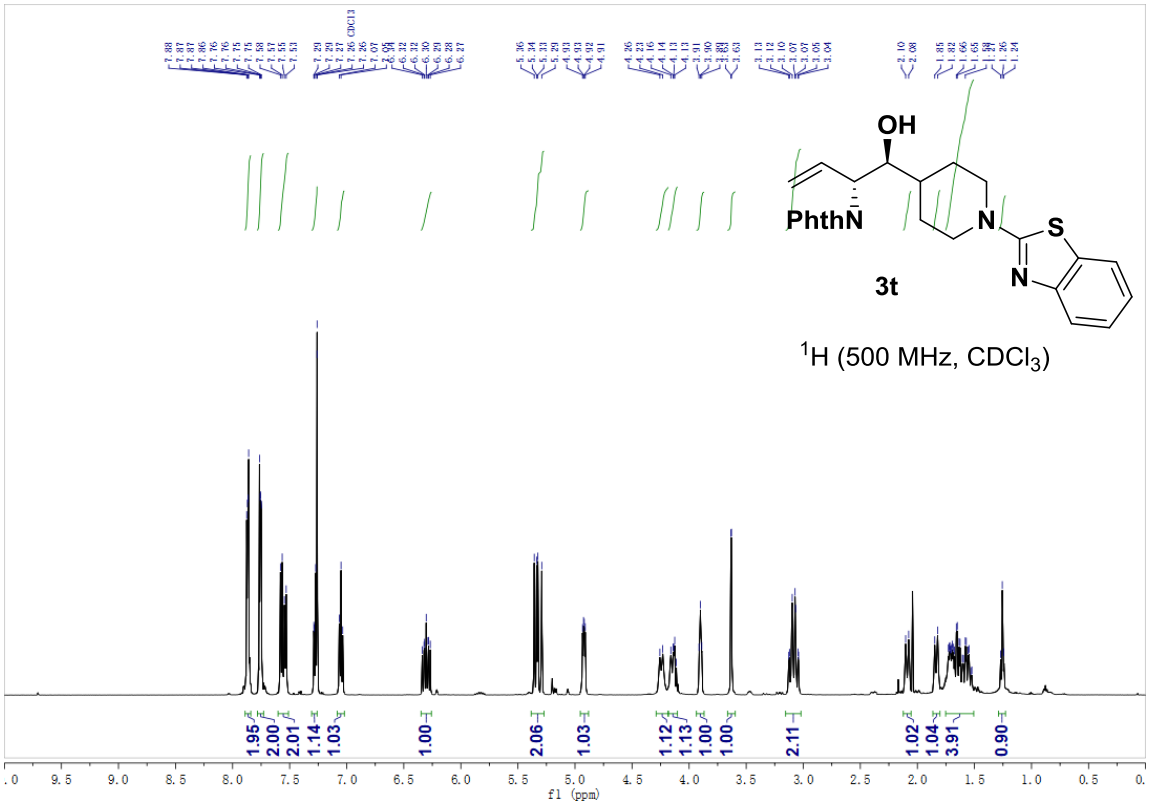
HRMS (H+, *m/z*) for $C_{24}H_{23}N_3O_3S$: calcd. = 434.1533; found = 434.1534.

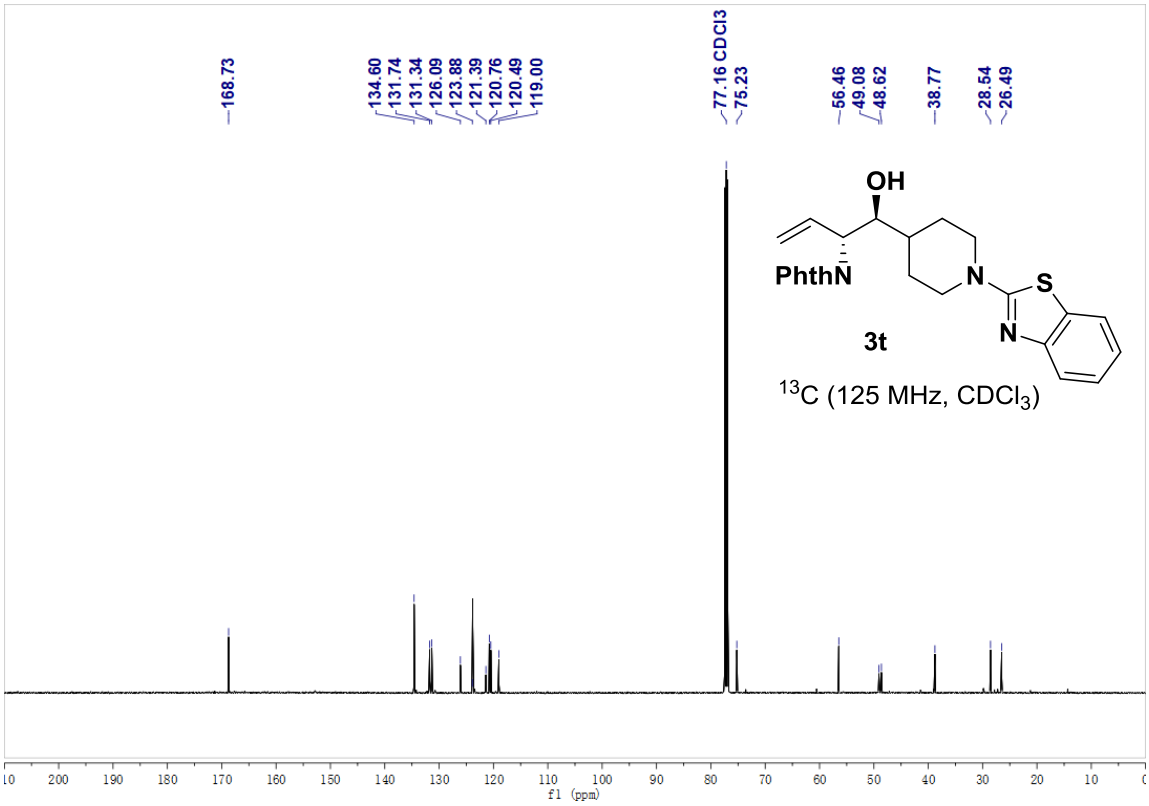
FTIR (neat): 2923, 2360, 2341, 1705, 1356, 1275, 763, 750.

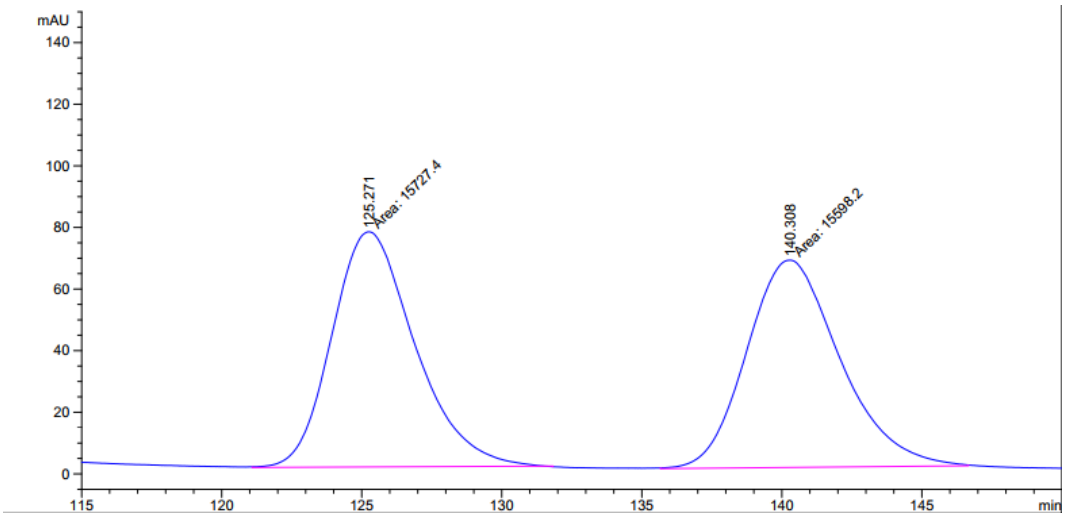
HPLC: (Chiralcel column AD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 94%.

$[\alpha]_D^{34}$ = +52.0° (c = 0.72, $CHCl_3$).

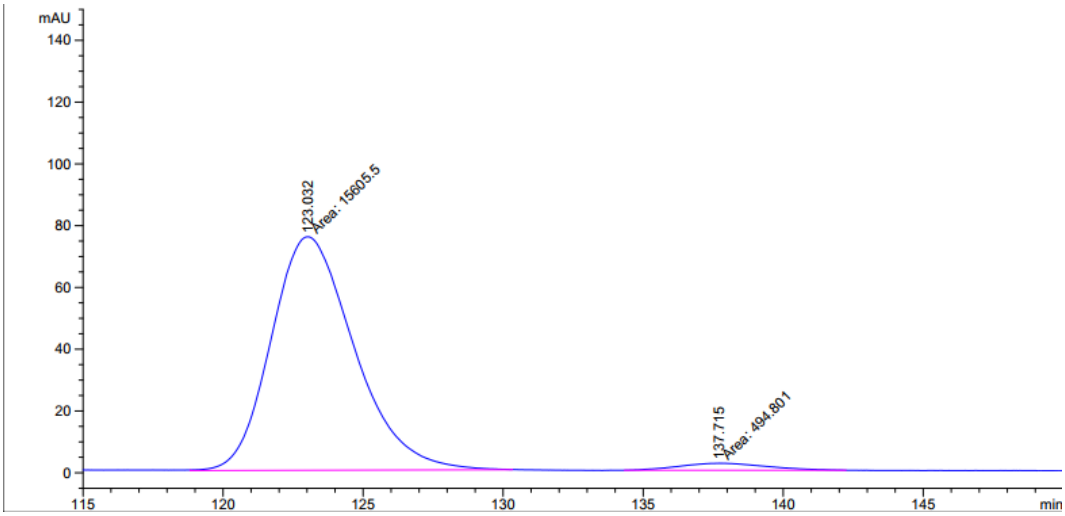
MP [80 – 84] °C


OH
PhthN
N
S
N
3t
^{1}H (500 MHz, $CDCl_3$)
f1 (ppm)


168.73
134.60
131.74
131.34
126.09
123.88
121.39
120.76
120.49
119.00
77.16 CDCl3
75.23
56.46
49.08
48.62
38.77
28.54
26.49
OH
PhthN
N
S
N
3t
^{13}C (125 MHz, $CDCl_3$)
f1 (ppm)

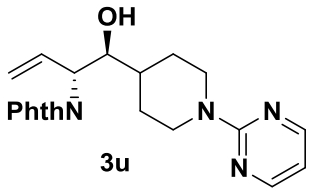


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	125.271	MM	3.4347	1.57274e4	76.31709	50.2062
2	140.308	MM	3.8646	1.55982e4	67.26893	49.7938



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	123.032	MM	3.4409	1.56055e4	75.58755	96.9268
2	137.715	MM	3.6153	494.80118	2.28103	3.0732

2-((1*S*,2*R*)-1-hydroxy-1-(1-(pyrimidin-2-yl)piperidin-4-yl)but-3-en-2-yl)isoindoline-1,3-dione (3u)



3u

Alcohol **2u** (38.6 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h) using 7.5 mol% of (R)-Ir-**VI**. Upon flash column chromatography (SiO_2, 30:70 EtOAc:hexanes), the title compound **3u** (54.5 mg, 0.144 mmol, >20:1 dr) was obtained as a pale yellow oil in 72% yield.

TLC (SiO_2) R_f = 0.2 (30:70 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.28 (d, *J* = 4.7 Hz, 2H), 7.86 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.75 (dd, *J* = 5.4, 3.0 Hz, 2H), 6.43 (t, *J* = 4.7 Hz, 1H), 6.36 – 6.24 (m, 1H), 5.31 (dd, *J* = 20.9, 13.7 Hz, 2H), 4.94 (dd, *J* = 7.5, 4.1 Hz, 1H), 4.80 (d, *J* = 12.0 Hz, 2H), 3.90 – 3.83 (m, 1H), 3.62 (d, *J* = 2.4 Hz, 1H), 2.82 (dtd, *J* = 15.5, 13.1, 2.5 Hz, 2H), 2.03 (d, *J* = 13.1 Hz, 1H), 1.79 (d, *J* = 12.8 Hz, 1H), 1.72 (tt, *J* = 6.8, 4.2 Hz, 1H), 1.44 (dddd, *J* = 29.0, 25.0, 12.6, 4.3 Hz, 2H)..

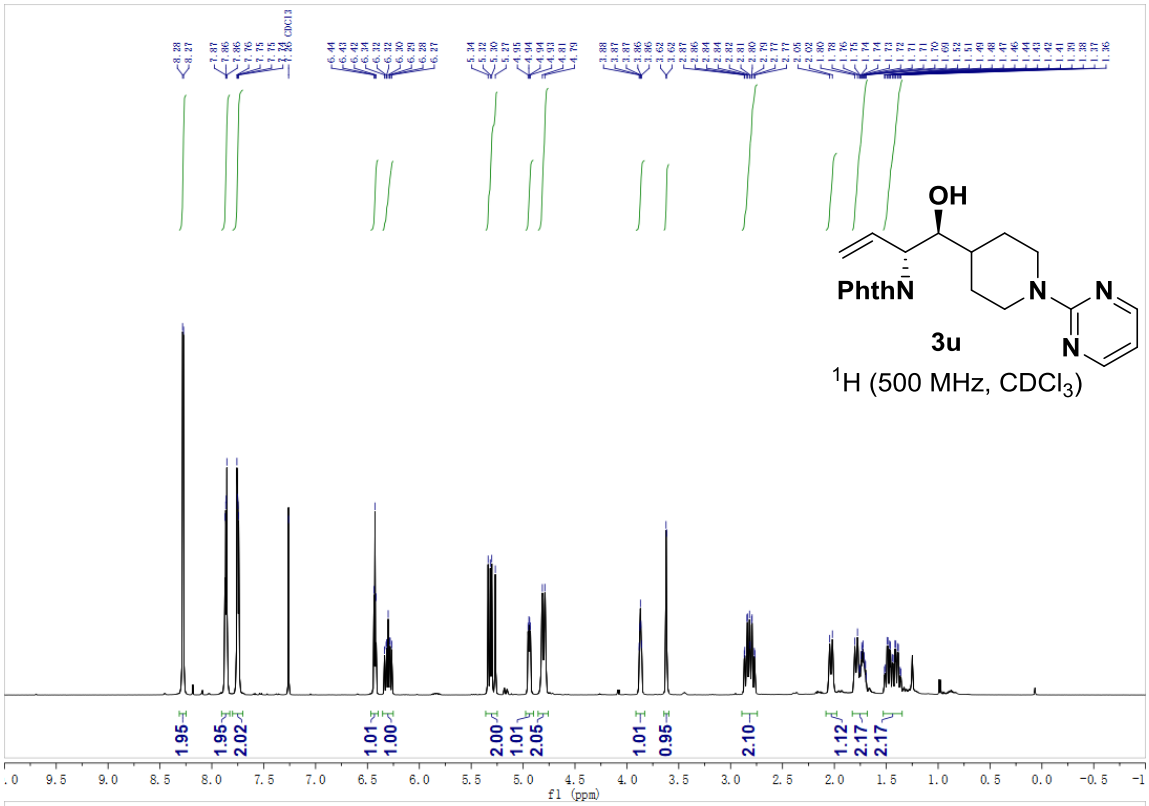
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.8, 157.8, 134.5, 131.8, 131.5, 123.8, 120.1, 77.2, 75.6, 56.5, 44.0, 43.9, 39.3, 28.9, 26.9.

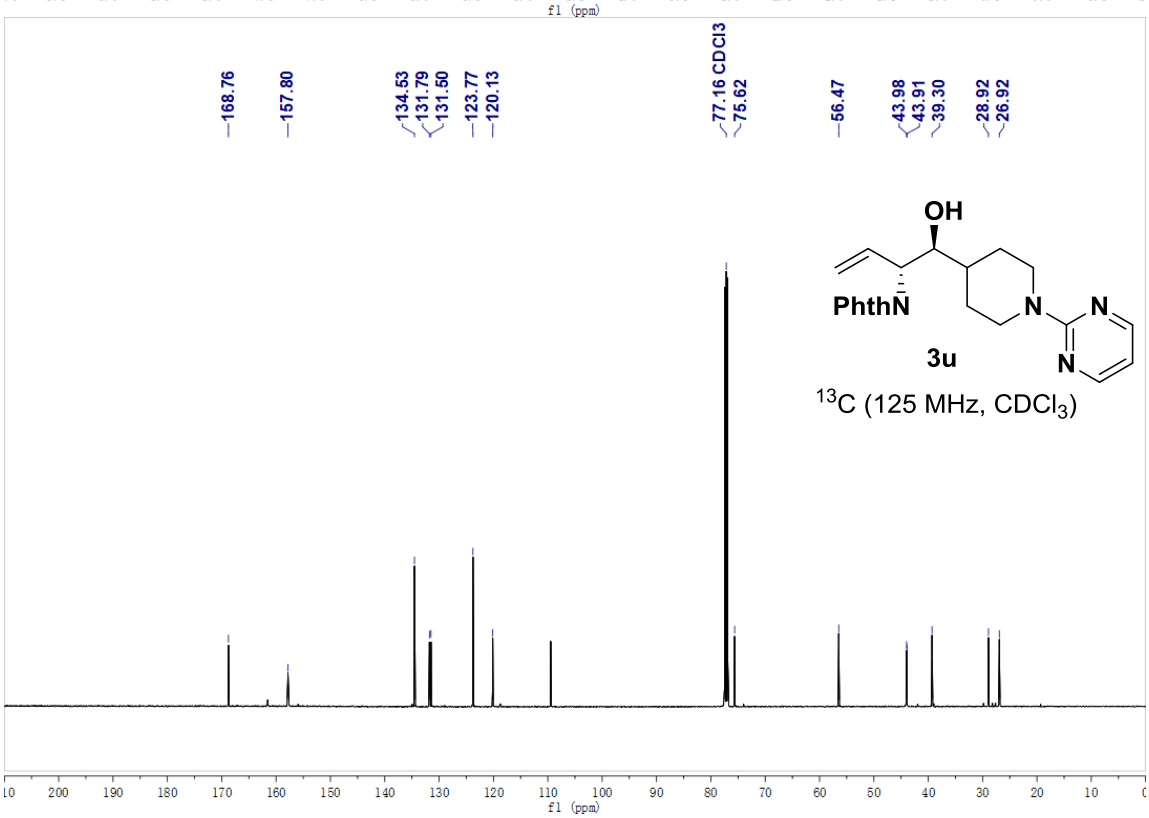
HRMS (Na+, *m/z*) for $C_{21}H_{22}N_4O_3$: calcd. = 401.1584; found = 401.1594.

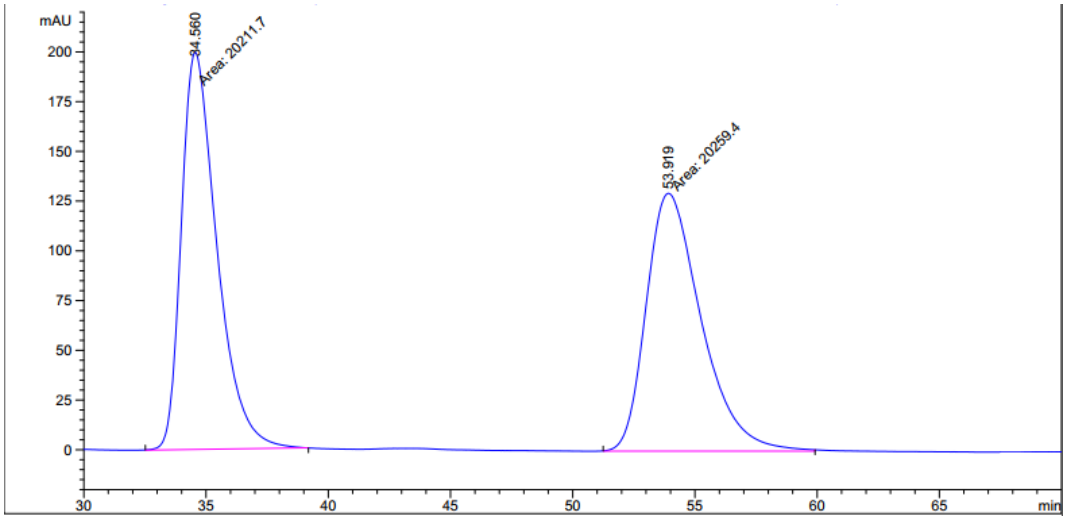
FTIR (neat): 3356, 1707, 1587, 1264, 1073, 976, 733, 703.

HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 95%.

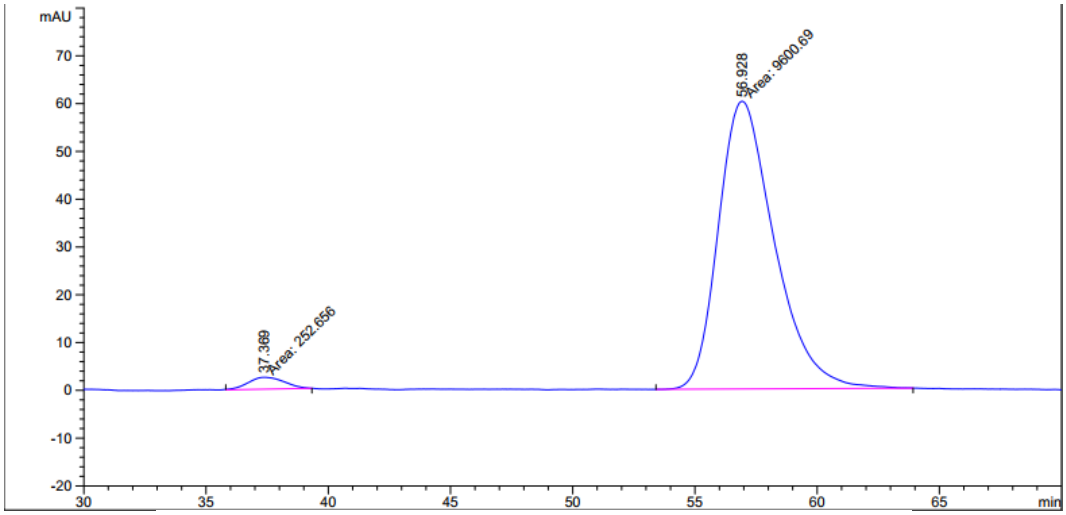
$[\alpha]_D^{34}$ = +35.5° (c = 0.77, $CHCl_3$).


OH
PhthN
N
N
N
3u
^{1}H (500 MHz, $CDCl_3$)
1.95
1.95
2.02
1.01
1.00
2.00
1.01
2.05
1.01
0.95
2.10
1.12
2.17
2.17
f1 (ppm)


168.76
157.80
134.53
131.79
131.50
123.77
120.13
77.16 CDCl3
75.62
56.47
43.98
43.91
39.30
28.92
26.92
OH
PhthN
N
N
N
3u
^{13}C (125 MHz, $CDCl_3$)
f1 (ppm)

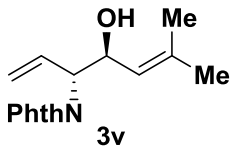


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.560	MM	1.6868	2.02117e4	199.70801	49.9411
2	53.919	MM	2.6059	2.02594e4	129.57588	50.0589



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.369	MM	1.7079	252.65567	2.46558	2.5642
2	56.928	MM	2.6581	9600.69336	60.19681	97.4358

2-((3*R*,4*S*)-4-hydroxy-6-methylhepta-1,5-dien-3-yl)isoindoline-1,3-dione (3v)



3v

Alcohol **2v** (17.2 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), the title compound **3v** (38.0 mg, 0.14 mmol, >20:1 dr) was obtained as a light yellow solid in 70% yield.

TLC (SiO_2) R_f = 0.2 (20:80 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.38 (ddd, *J* = 17.2, 10.4, 7.8 Hz, 1H), 5.32 (ddd, *J* = 15.1, 10.6, 3.6 Hz, 2H), 5.22 – 5.13 (m, 1H), 4.91 (dd, *J* = 8.9, 6.8 Hz, 1H), 4.67 (dd, *J* = 7.7, 6.8 Hz, 1H), 1.61 (dd, *J* = 11.3, 0.9 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.5, 138.5, 134.3, 132.1, 131.8, 124.0, 123.6, 120.4, 77.2, 68.8, 59.4, 25.9, 18.5.

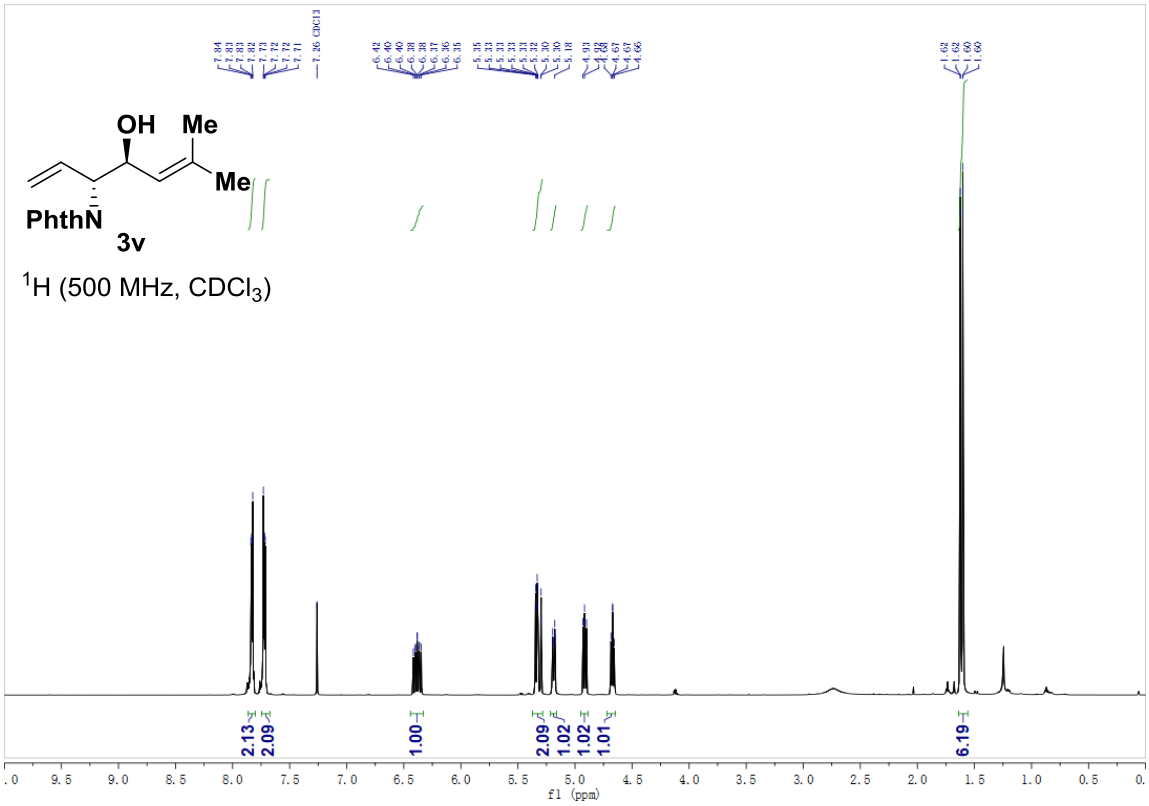
HRMS (Na+, *m/z*) for $C_{16}H_{17}NO_3$: calcd. = 294.1101; found = 294.1108.

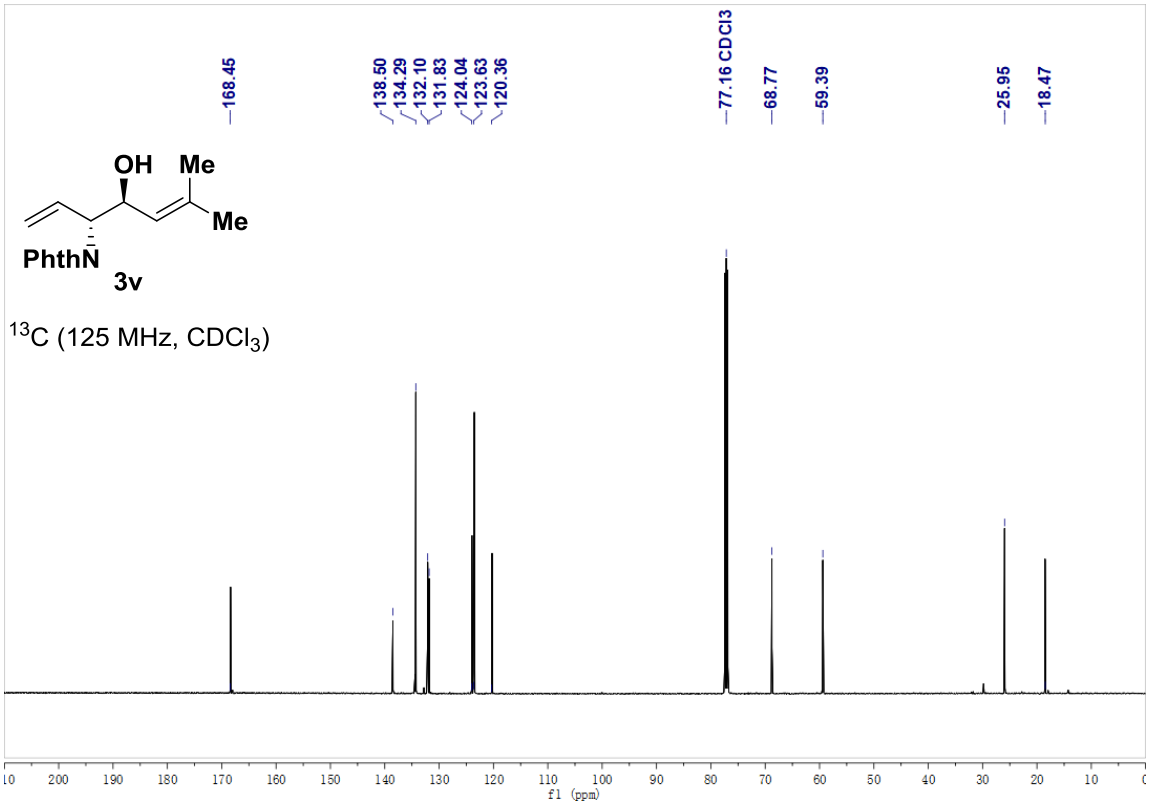
FTIR (neat): 2988, 2358, 2340, 1769, 1703, 764, 733.

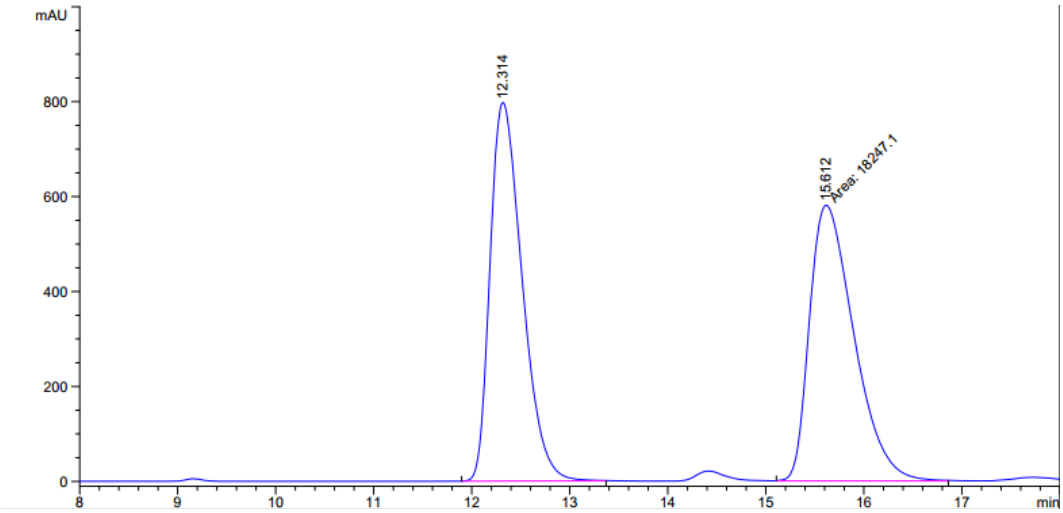
HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 86%.

$[\alpha]_D^{34}$ = +46.3° (c = 0.62 $CHCl_3$).

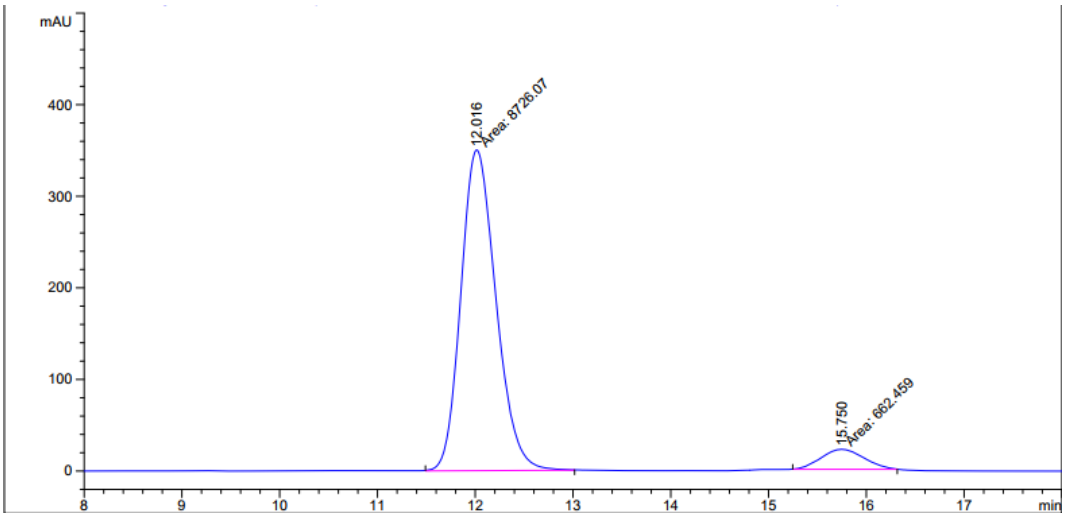
MP [78-82] °C


OH
Me
Me
PhthN
3v
1H (500 MHz, CDCl3)
2.13
2.09
1.00
2.09
1.02
1.02
1.01
6.19
f1 (ppm)


168.45
138.50
134.29
132.10
131.83
124.04
123.63
120.36
77.16 CDCl3
68.77
59.39
25.95
18.47
OH
Me
Me
PhthN
3v
13C (125 MHz, CDCl3)
f1 (ppm)

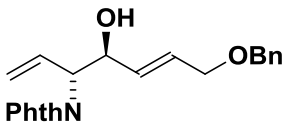


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.314	BB	0.3551	1.81240e4	797.47308	49.8308
2	15.612	MM	0.5239	1.82471e4	580.51849	50.1692



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.016	MM	0.4152	8726.07422	350.31497	92.9440
2	15.750	MM	0.5071	662.45856	21.77350	7.0560

2-((3*R*,4*S*,*E*)-7-(benzyloxy)-4-hydroxyhepta-1,5-dien-3-yl)isoindoline-1,3-dione (3w)



3w

Alcohol **1w** (35.6 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), the title compound **3w** (50 mg, 0.138 mmol, >20:1 dr) was obtained as a light yellow oil in 69% yield.

TLC (SiO_2) R_f = 0.30 (30:80 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.87 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.36 – 7.29 (m, 3H), 7.27 – 7.24 (m, 2H), 6.36 (ddd, *J* = 17.5, 10.3, 7.3 Hz, 1H), 5.95 (dd, *J* = 13.3, 7.7 Hz, 1H), 5.81 (dd, *J* = 15.5, 6.6 Hz, 1H), 5.41 – 5.31 (m, 2H), 4.79 (dt, *J* = 23.1, 6.2 Hz, 2H), 4.40 (s, 2H), 4.00 (qd, *J* = 13.0, 5.6 Hz, 2H), 3.28 (s, 1H).

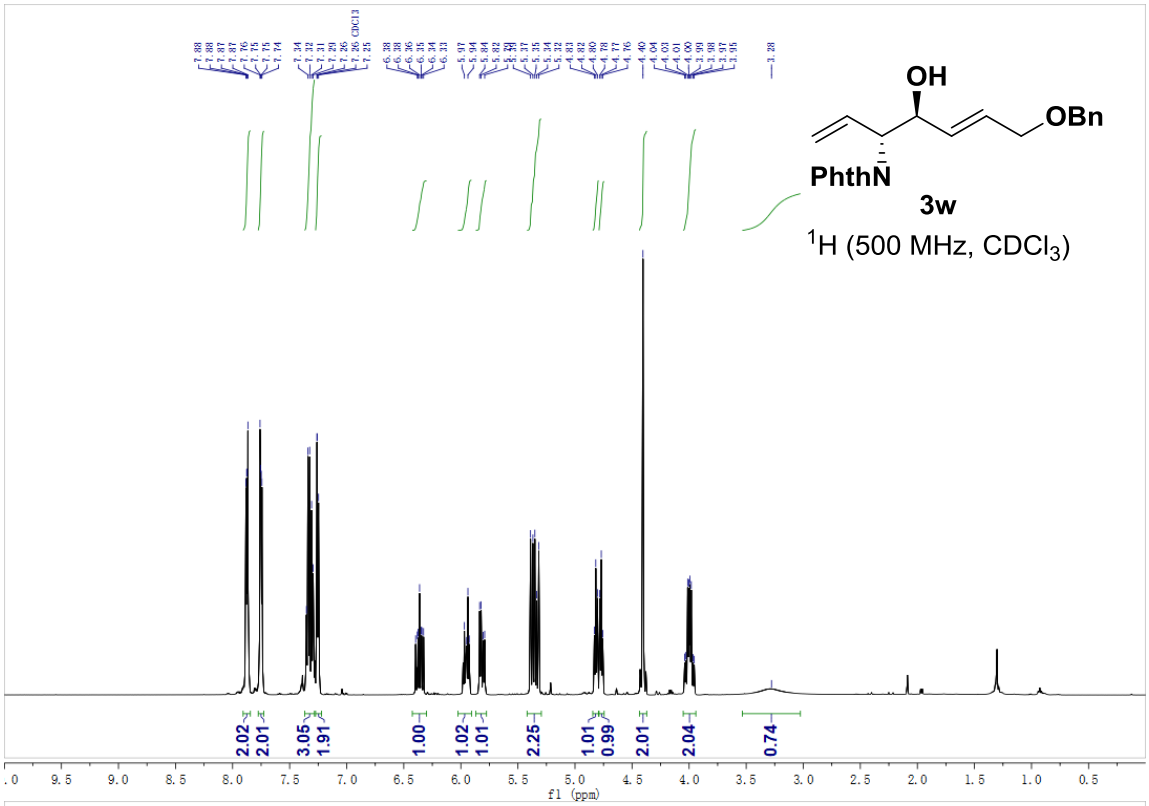
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.4, 138.2, 134.4, 131.7, 131.5, 131.4, 130.5, 128.4, 127.7, 127.7, 123.6, 120.1, 77.2, 72.3, 71.9, 69.8, 59.0.

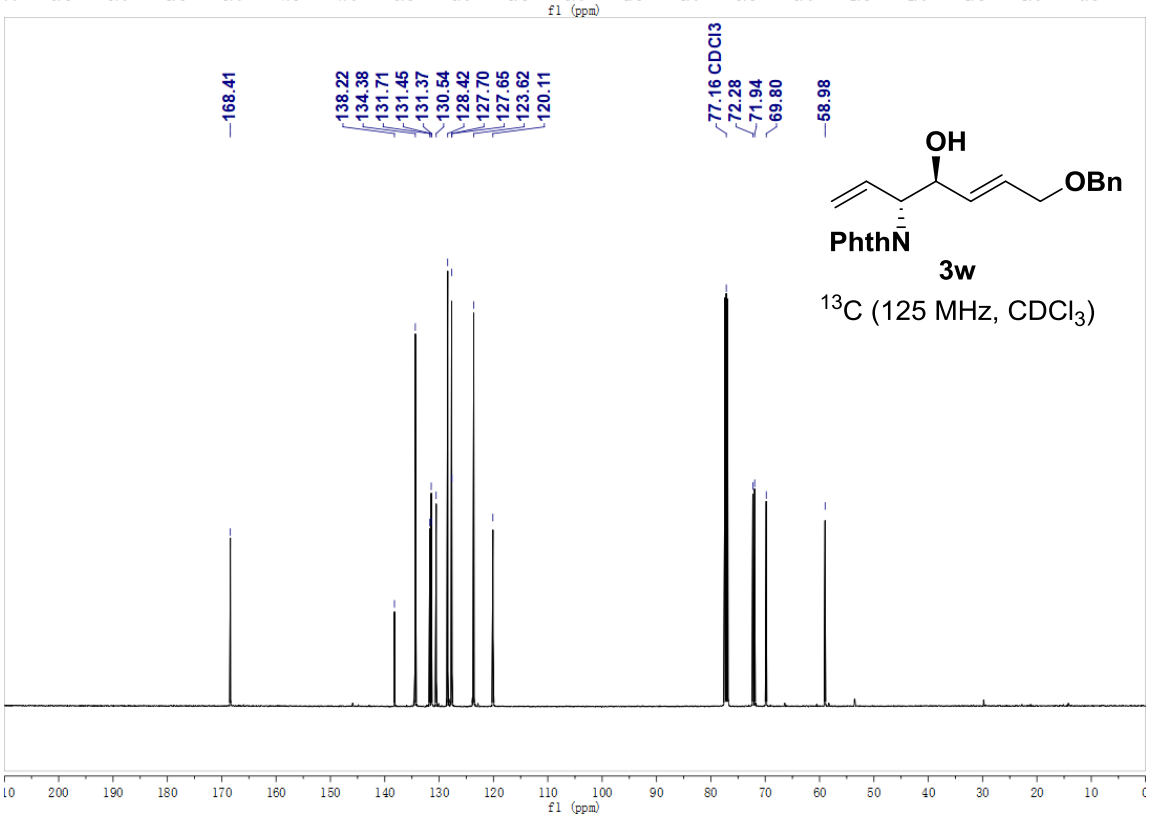
HRMS (Na+, *m/z*) for $C_{22}H_{21}NO_4$: calcd. = 386.1363; found = 386.1361.

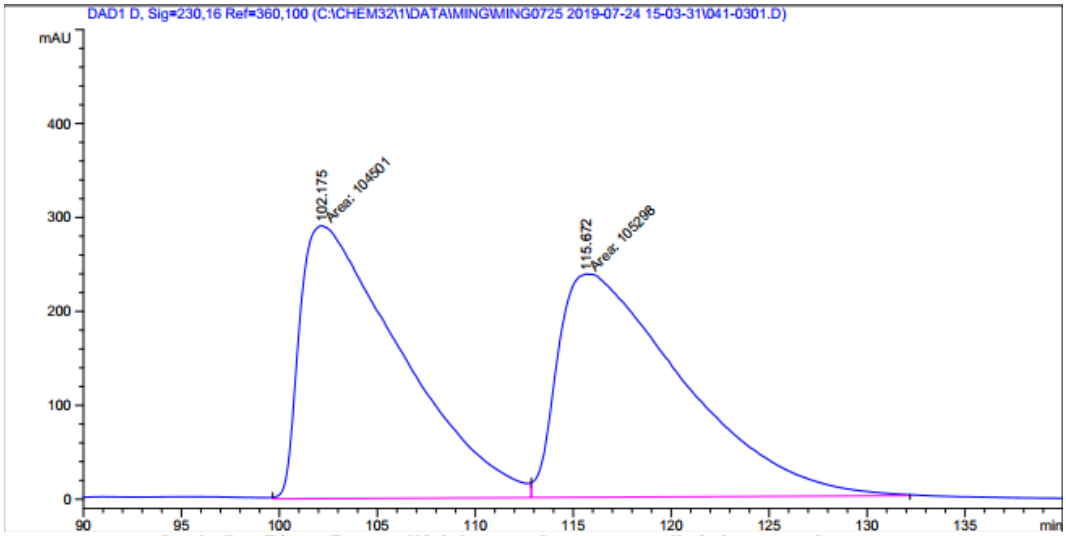
FTIR (neat): 2988, 2358, 2340, 1769, 1703, 1383, 1264, 764.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 86%.

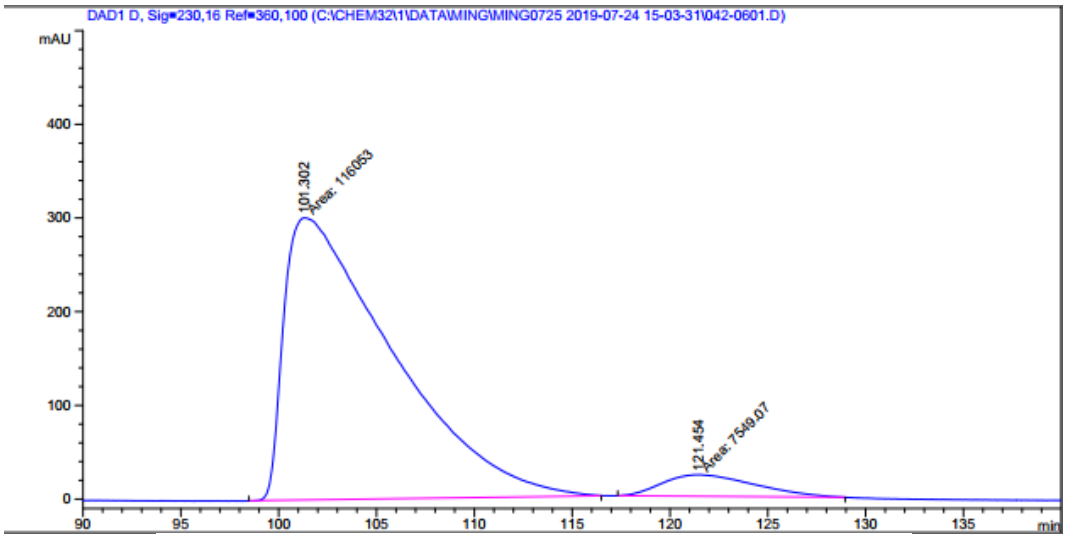
$[\alpha]_D^{24}$ = 75.2° (c = 0.37, $CHCl_3$).


OH
OBn
PhthN
3w
^{1}H (500 MHz, $CDCl_3$)
2.02
2.01
3.05
1.91
1.00
1.02
1.01
2.25
1.01
0.99
2.01
2.04
0.74
f1 (ppm)


168.41
138.22
134.38
131.71
131.45
131.37
130.54
128.42
127.70
127.65
123.62
120.11
77.16 CDCl3
72.28
71.94
69.80
58.98
OH
OBn
PhthN
3w
^{13}C (125 MHz, $CDCl_3$)
f1 (ppm)

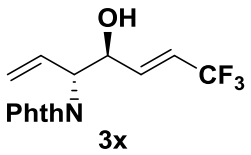


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	102.175	MF	5.9982	1.04501e5	290.36563	49.8101
2	115.672	FM	7.3818	1.05298e5	237.74234	50.1899



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	101.302	MM	6.4237	1.16053e5	301.10715	93.8924
2	121.454	MM	5.4559	7549.06543	23.06065	6.1076

2-((3*R*,4*S*,*E*)-7,7,7-trifluoro-4-hydroxyhepta-1,5-dien-3-yl)isoindoline-1,3-dione (3x)



3x

Alcohol **2x** (25.2 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h) using 7.5 mol% of (R)-Ir-**VI**. Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), the title compound **3x** (38.1 mg, 0.12 mmol, >20:1 dr) was obtained as a light yellow solid in 61% yield.

TLC (SiO_2) R_f = 0.40 (20:80 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.78 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.41 (ddq, *J* = 15.6, 4.3, 2.2 Hz, 1H), 6.17 (ddd, *J* = 17.0, 10.4, 6.7 Hz, 1H), 6.11 – 6.04 (m, 1H), 5.35 (d, *J* = 10.7 Hz, 1H), 5.23 (d, *J* = 17.0 Hz, 1H), 4.86 – 4.84 (m, 1H), 4.78 – 4.76 (m, 1H), 4.15 (brs, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.7, 138.0 (q, *J* = 6.3 Hz), 134.8, 131.6, 129.6, 124.0, 123.0 (q, *J* = 270 Hz), 120.9 (q, *J* = 121 Hz), 120.6, 71.2, 58.3.

^{19}F NMR (470 MHz, $CDCl_3$) δ: -64.4 (dt, J = 6.8, 2.6 Hz).

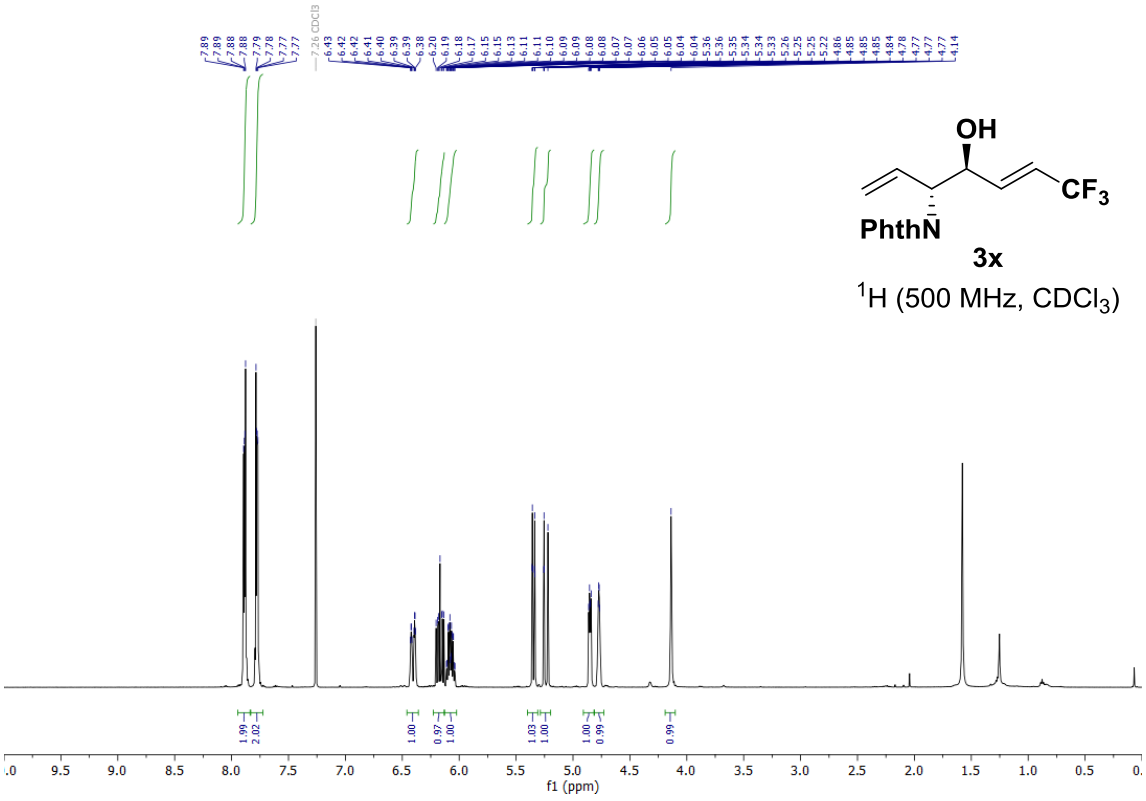
HRMS (Na+, *m/z*) for $C_{15}H_{12}F_3NO_3$: calcd. = 334.0665; found = 334.0661.

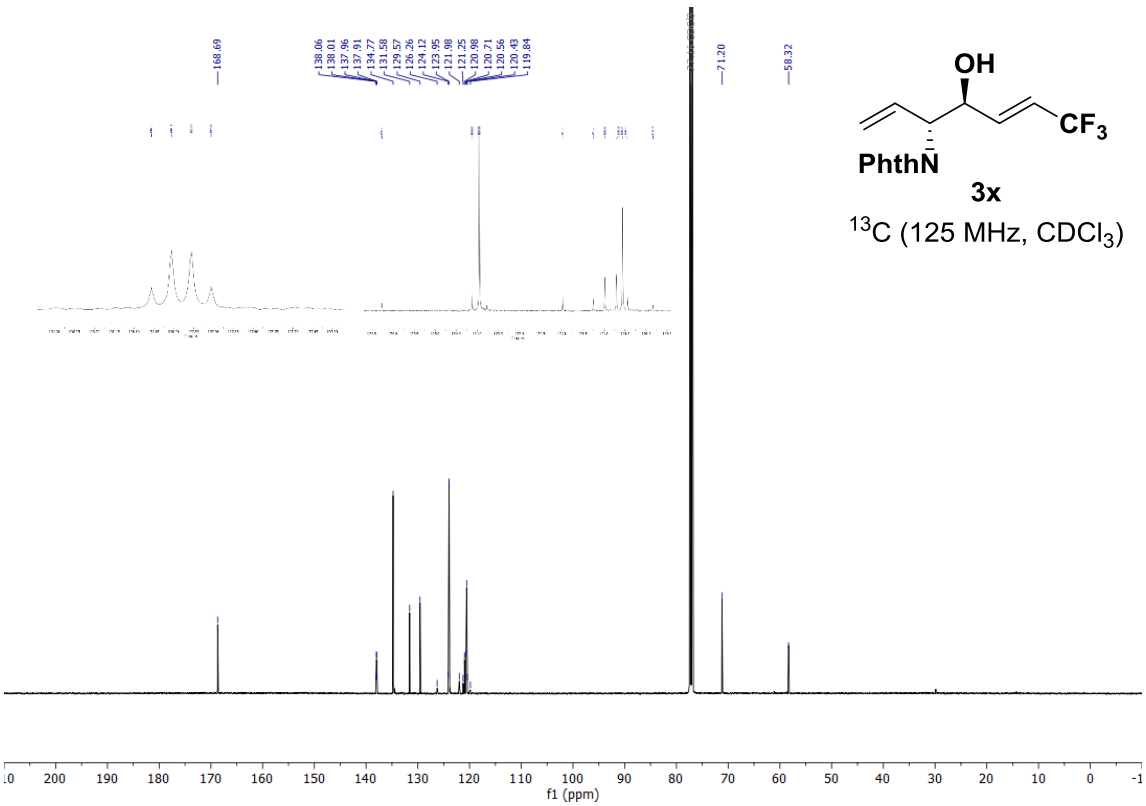
FTIR (neat): 3456, 3333, 2359, 1687, 1330, 1077, 712.

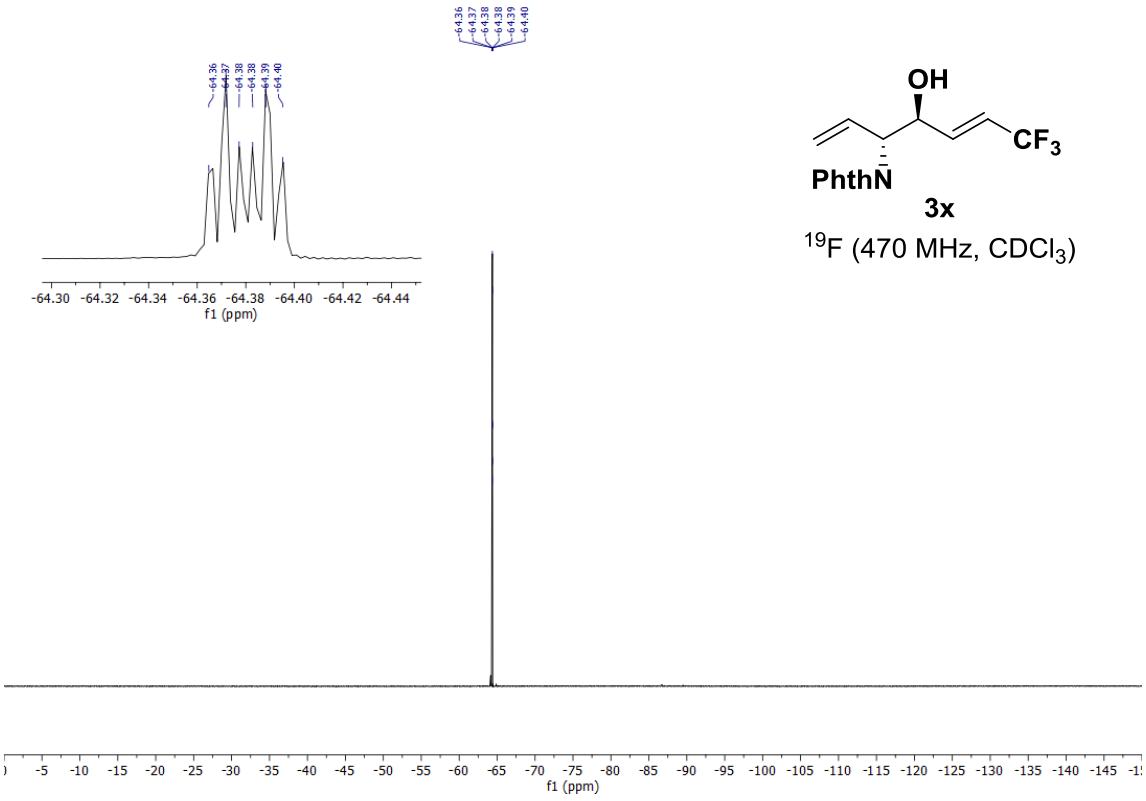
HPLC: (Chiralcel column AS-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 90%.

$[\alpha]_D^{34}$ = +38.6° (c = 1.18, $CHCl_3$).

MP [109 – 112] °C

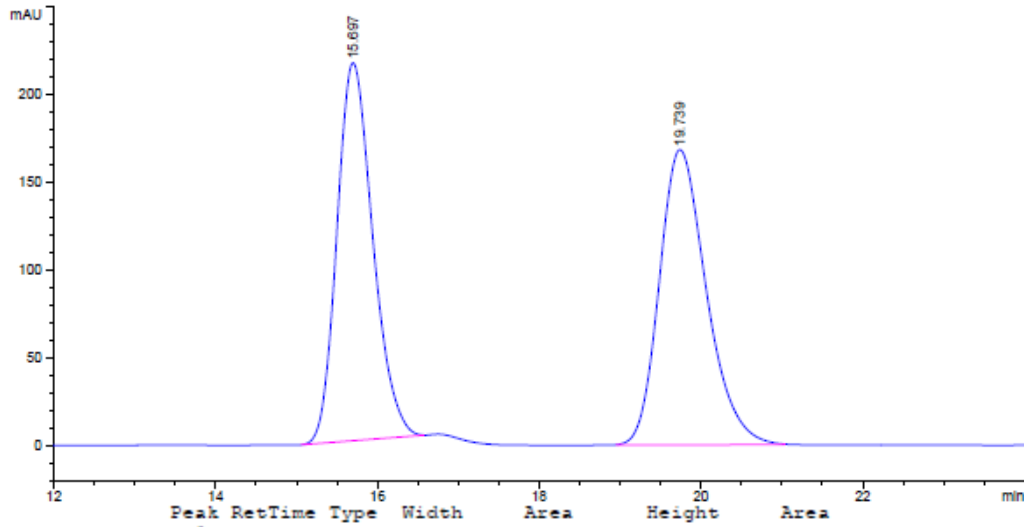

OH
CF3
PhthN
3x
1H (500 MHz, CDCl3)
f1 (ppm)


OH
CF3
PhthN
3x
13C (125 MHz, CDCl3)
f1 (ppm)

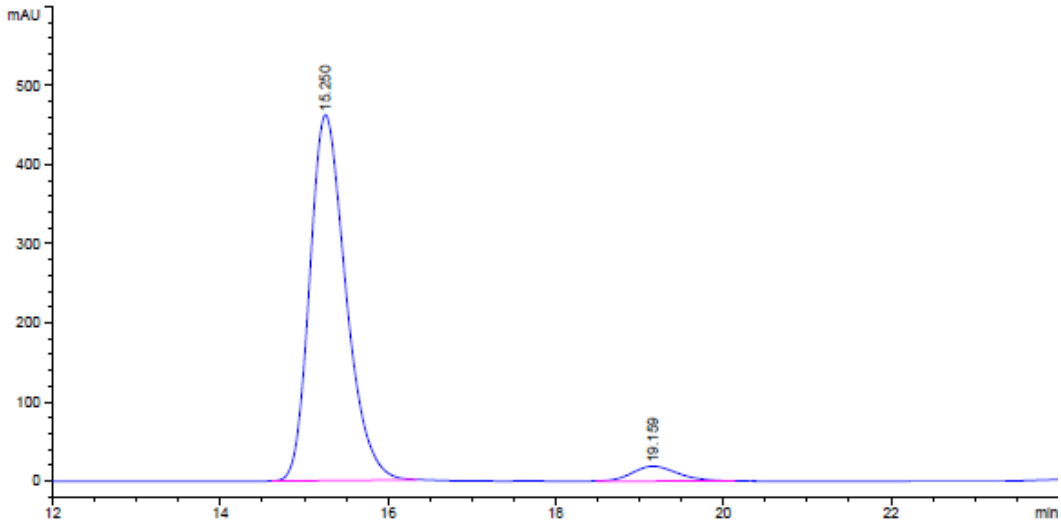


3x

^{19}F (470 MHz, $CDCl_3$)

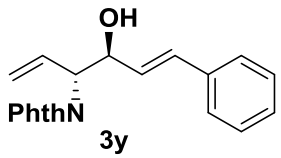


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.697	BB	0.4751	6620.58594	215.07155	49.3982
2	19.739	BB	0.6169	6781.90039	168.01593	50.6018



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.250	BB	0.4587	1.38192e4	462.34772	95.0950
2	19.159	BB	0.5691	712.79950	18.85224	4.9050

2-((3*R*,4*S*,*E*)-4-hydroxy-6-phenylhexa-1,5-dien-3-yl)isoindoline-1,3-dione (3y)



3y

Alcohol **1y** (27 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), the title compound **3y** (45 mg, 0.14 mmol, >20:1 dr) was obtained as a light yellow oil in 71% yield.

TLC (SiO_2) R_f = 0.35 (20:80 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.32 – 7.29 (m, 5H), 6.69 (d, *J* = 15.8 Hz, 1H), 6.36 (ddd, *J* = 17.0, 10.4, 6.7 Hz, 1H), 6.20 (dd, *J* = 15.9, 6.2 Hz, 1H), 5.35 (d, *J* = 10.7 Hz, 1H), 5.31 (d, *J* = 17.0 Hz, 1H), 4.89 – 4.84 (m, 2H), 3.34 (s, 1H).

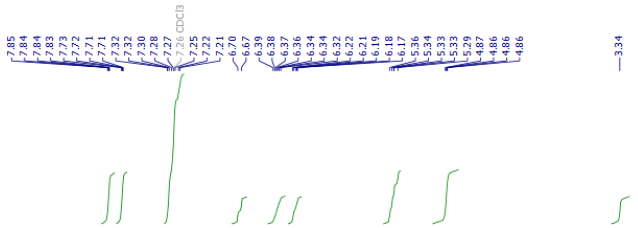
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.6, 136.5, 134.5, 133.2, 131.8, 131.3, 128.7, 128.1, 128.0, 126.8, 123.7, 120.2, 73.1, 59.2.

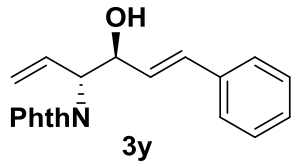
HRMS (Na+, *m/z*) for $C_{20}H_{17}NO_3$: calcd. = 342.1101; found = 342.1106.

FTIR (neat): 3456, 3333, 2359, 1687, 1330, 1077, 712.

HPLC: (Chiralcel column OD-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 230 nm) ee = 86%.

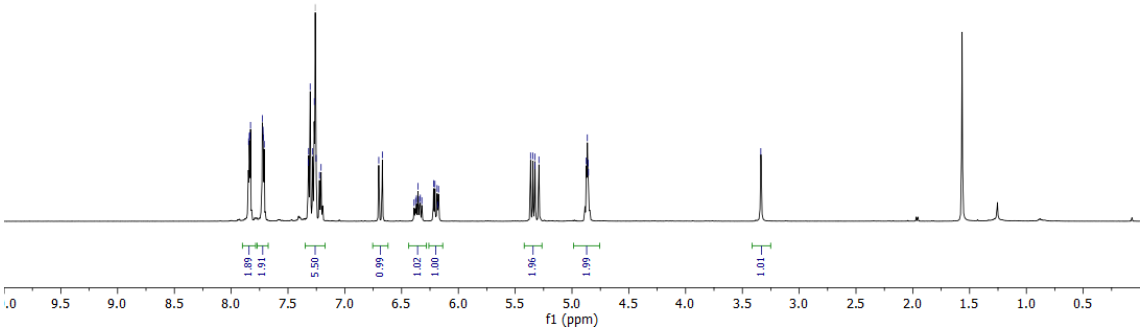
$[\alpha]_D^{24}$ = –7.9° (c = 0.95, $CHCl_3$).

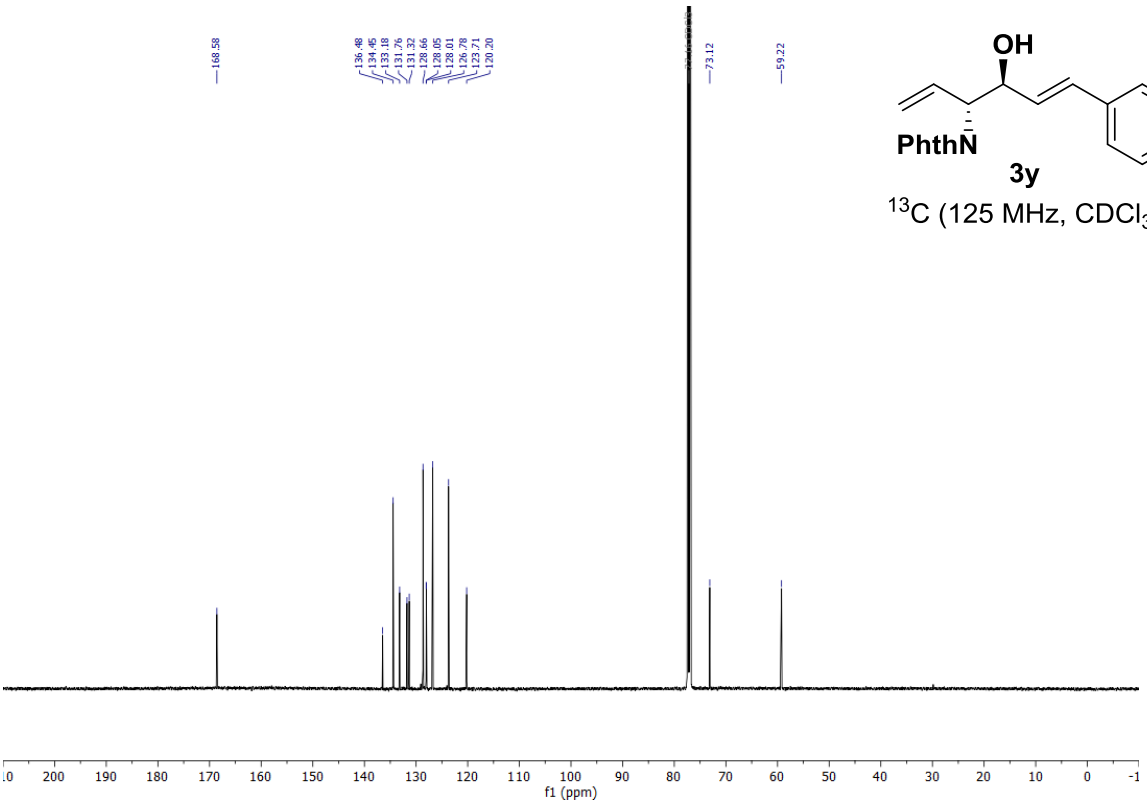




3y

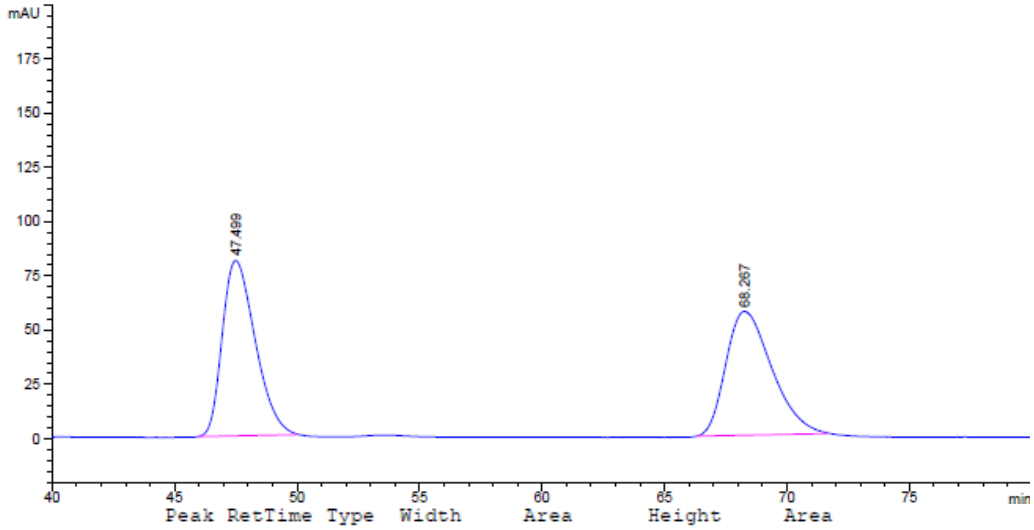
^{1}H (500 MHz, $CDCl_3$)



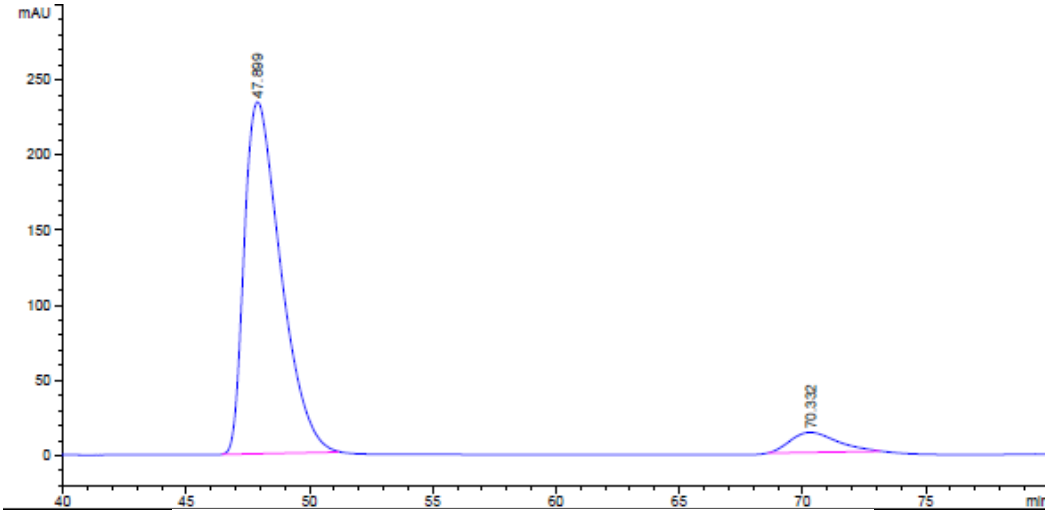


3y

^{13}C (125 MHz, $CDCl_3$)

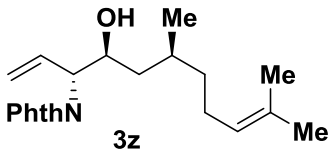


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	47.499	BB	1.3809	7560.30127	80.85515	50.3932
2	68.267	BB	1.6973	7442.33301	57.07264	49.6068



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	47.899	BB	1.5241	2.40848e4	234.12973	93.1743
2	70.332	BB	1.5583	1764.38269	13.32936	6.8257

2-((3*R*,4*S*,6*S*)-4-hydroxy-6,10-dimethylundeca-1,9-dien-3-yl)isoindoline-1,3-dione (3z)



3z

Alcohol **1z** (31.2 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 10:90 EtOAc:hexanes), the title compound **3z** (41.7 mg, 0.12 mmol, 10:1 dr) was obtained as a pale yellow oil in 62% yield.

TLC (SiO_2) R_f = 0.47 (20:80 EtOAc:hexanes)

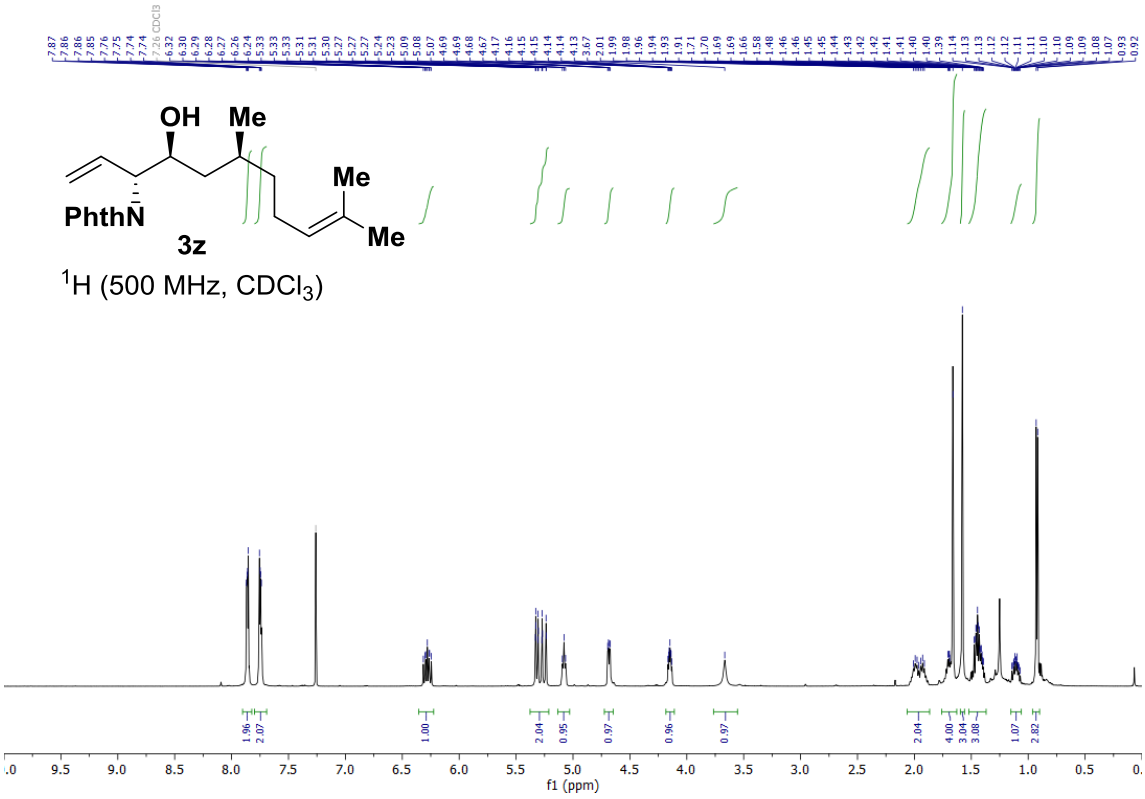
^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.28 (ddd, *J* = 17.6, 10.4, 7.8 Hz, 1H), 5.32 (d, *J* = 10.7 Hz, 1H), 5.26 (d, *J* = 17.3 Hz, 1H), 5.08 (t, *J* = 7.0 Hz, 1H), 4.68 (dd, *J* = 7.8, 3.4 Hz, 1H), 4.15 (ddd, *J* = 8.6, 5.2, 3.5 Hz, 1H), 3.67 (brs, 1H), 2.04 – 1.88 (m, 1H), 1.73 – 1.66 (m, 1H), 1.66 (s, 3H), 1.58 (s, 3H), 1.50 – 1.39 (m, 3H), 1.15 – 1.07 (m, 1H), 0.92 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.9, 134.5, 131.8, 131.4, 131.1, 124.9, 123.7, 120.1, 70.6, 59.6, 41.6, 36.4, 29.3, 25.9, 25.5, 20.4, 17.8.

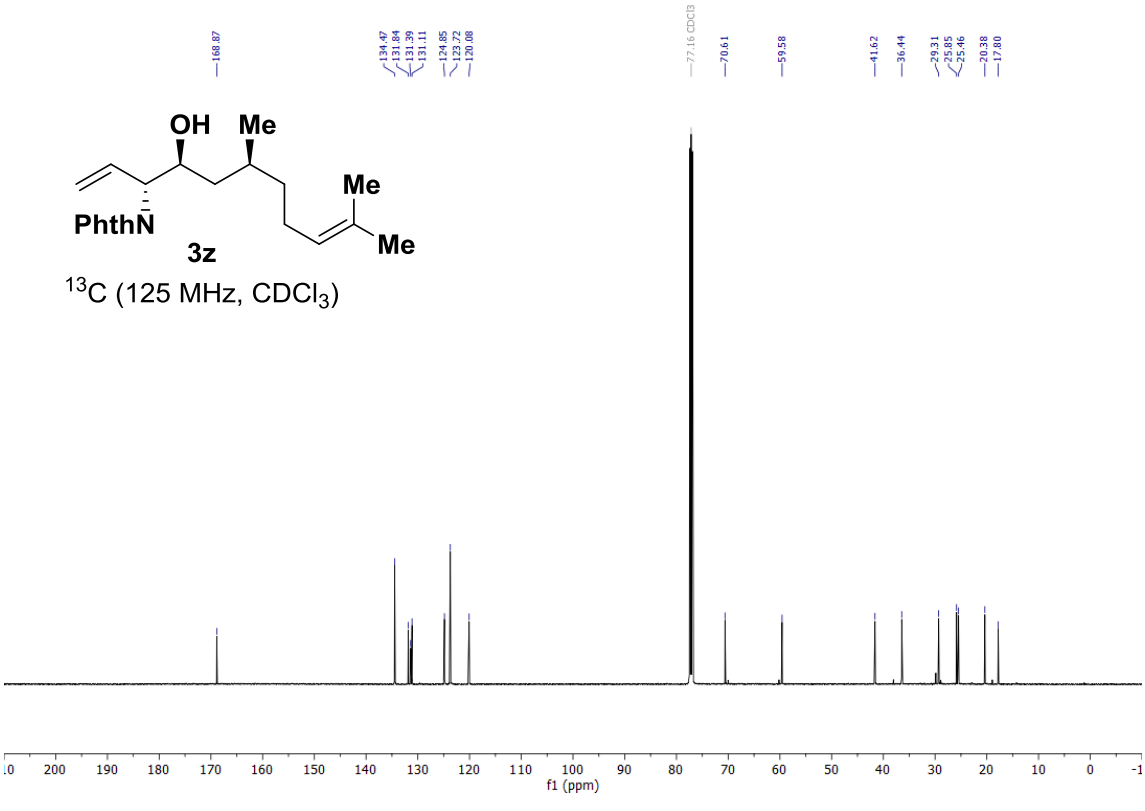
HRMS (Na+, *m/z*) for $C_{21}H_{27}NO_3$: calcd. = 364.1883; found = 364.1882.

FTIR (neat): 3466, 2921, 1704, 1380, 1065, 719.

$[\alpha]_D^{34}$ = +39.5° (c = 1.37, $CHCl_3$).

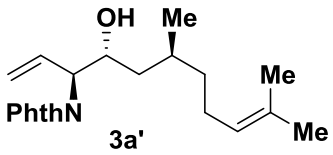


^{1}H (500 MHz, $CDCl_3$)



^{13}C (125 MHz, $CDCl_3$)

2-((3*S*,4*R*,6*S*)-4-hydroxy-6,10-dimethylundeca-1,9-dien-3-yl)isoindoline-1,3-dione (3a')



3a'

Alcohol **2a'** (31.2 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h) using 5 mol% of (*S*)-Ir-**IV**. Upon flash column chromatography (SiO_2, 10:90 EtOAc:hexanes), the title compound **3a'** (43.1 mg, 0.13 mmol, 13:1 dr) was obtained as a pale yellow oil in 64% yield.

TLC (SiO_2) R_f = 0.47 (20:80 EtOAc:hexanes)

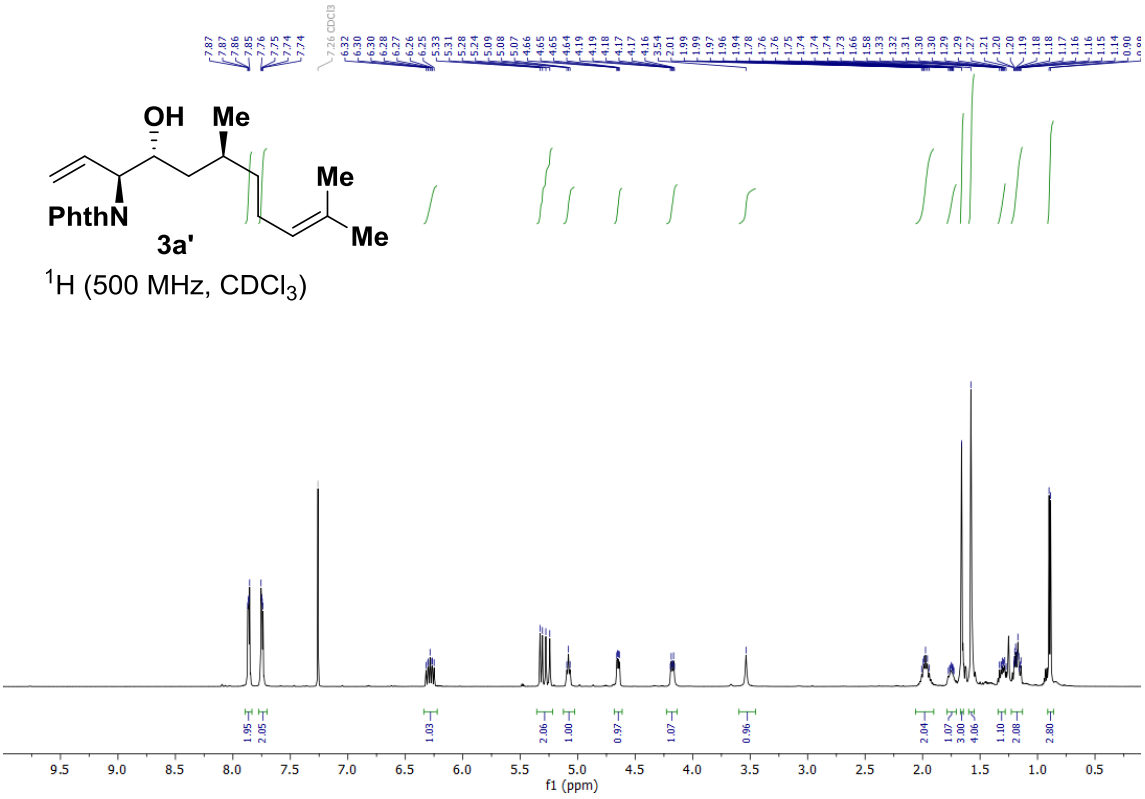
^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.28 (ddd, *J* = 17.6, 10.4, 7.8 Hz, 1H), 5.32 (d, *J* = 10.7 Hz, 1H), 5.27 (d, *J* = 17.3 Hz, 1H), 5.08 (t, *J* = 7.1 Hz, 1H), 4.65 (dd, *J* = 7.8, 3.9 Hz, 1H), 4.18 (ddd, *J* = 10.3, 3.7 Hz, 1H), 3.54 (brs, 1H), 2.03 – 1.93 (m, 2H), 1.77 – 1.72 (m, 1H), 1.66 (s, 3H), 1.58 (brs, 4H), 1.34 – 1.28 (m, 1H), 1.21 – 1.14 (m, 2H), 0.90 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.8, 134.5, 131.9, 131.4, 131.4, 124.9, 123.7, 120.1, 70.0, 60.2, 41.7, 38.0, 27.9, 25.9, 25.6, 18.9, 17.8.

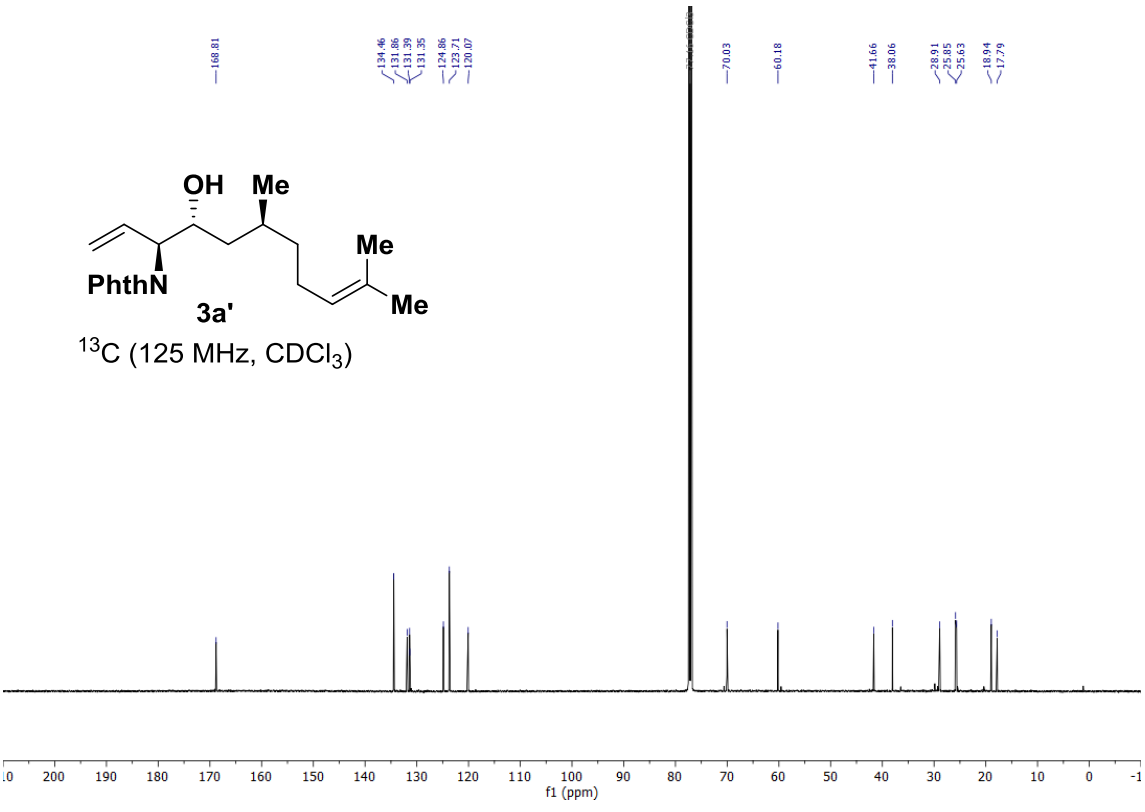
HRMS (Na+, *m/z*) for $C_{21}H_{27}NO_3$: calcd. = 364.1883; found = 364.1883.

FTIR (neat): 3454, 2923, 1703, 1381, 1066, 719.

$[\alpha]_D^{34}$ = −18.2° (c = 1.44, $CHCl_3$).

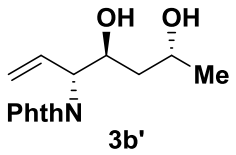


^{1}H (500 MHz, $CDCl_3$)



^{13}C (125 MHz, $CDCl_3$)

2-((3*R*,4*S*,6*R*)-4,6-dihydroxyhept-1-en-3-yl)isoindoline-1,3-dione (3b')



3b'

Alcohol **2b'** (18.0 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h) using 7.5 mol% of (*R*)-**Ir-VI**. Upon flash column chromatography (SiO_2, 50:50 EtOAc:hexanes), the title compound **3b'** (39.6 mg, 0.14 mmol, 20:1 dr) was obtained as a white solid in 72% yield.

TLC (SiO_2) R_f = 0.38 (50:50 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.30 (ddd, *J* = 17.6, 10.4, 7.7 Hz, 1H), 5.33 (d, *J* = 10.7 Hz, 1H), 5.29 (d, *J* = 17.3 Hz, 1H), 4.71 (dd, *J* = 7.8, 4.4 Hz, 1H), 4.44 (dt, *J* = 9.8, 3.4 Hz, 1H), 4.20 – 4.13 (m, 1H), 1.77 (ddd, *J* = 14.3, 9.6, 2.9 Hz, 1H), 1.77 (ddd, *J* = 14.3, 8.4, 3.1 Hz, 1H), 1.23 (d, *J* = 6.3 Hz, 3H).

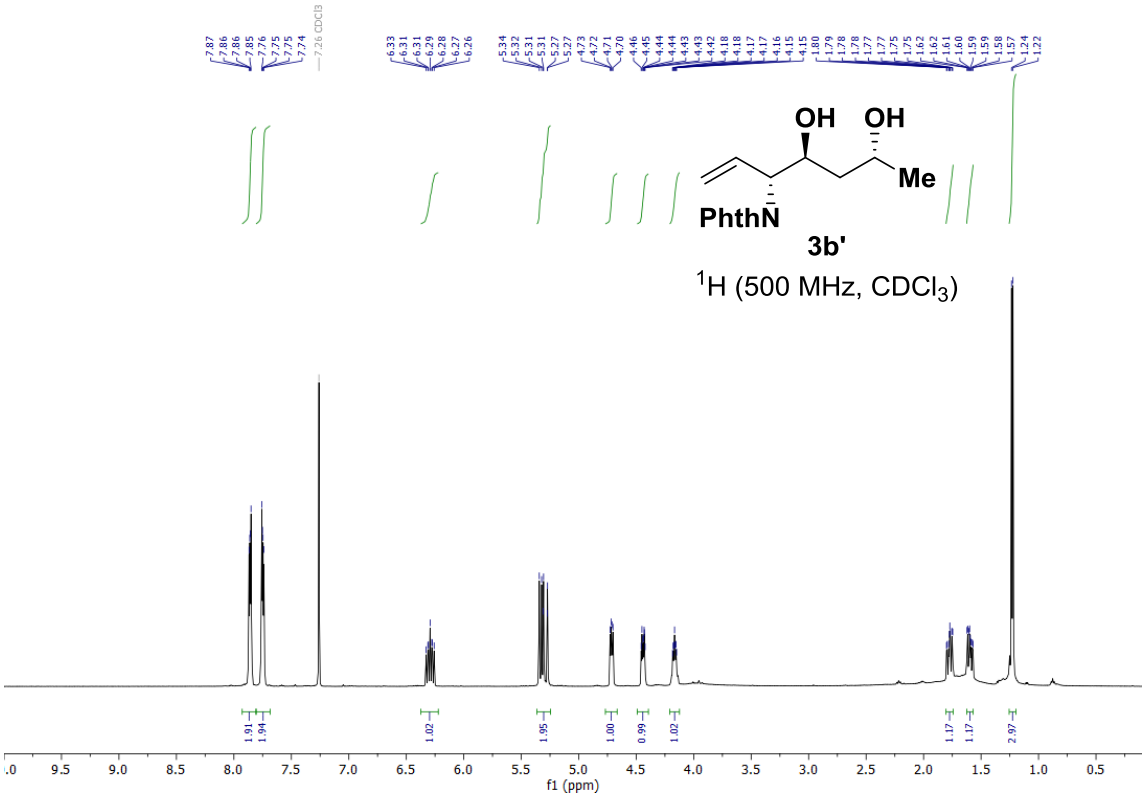
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.7, 134.5, 131.8, 131.3, 123.8, 120.3, 69.6, 65.2, 59.5, 41.7, 23.7.

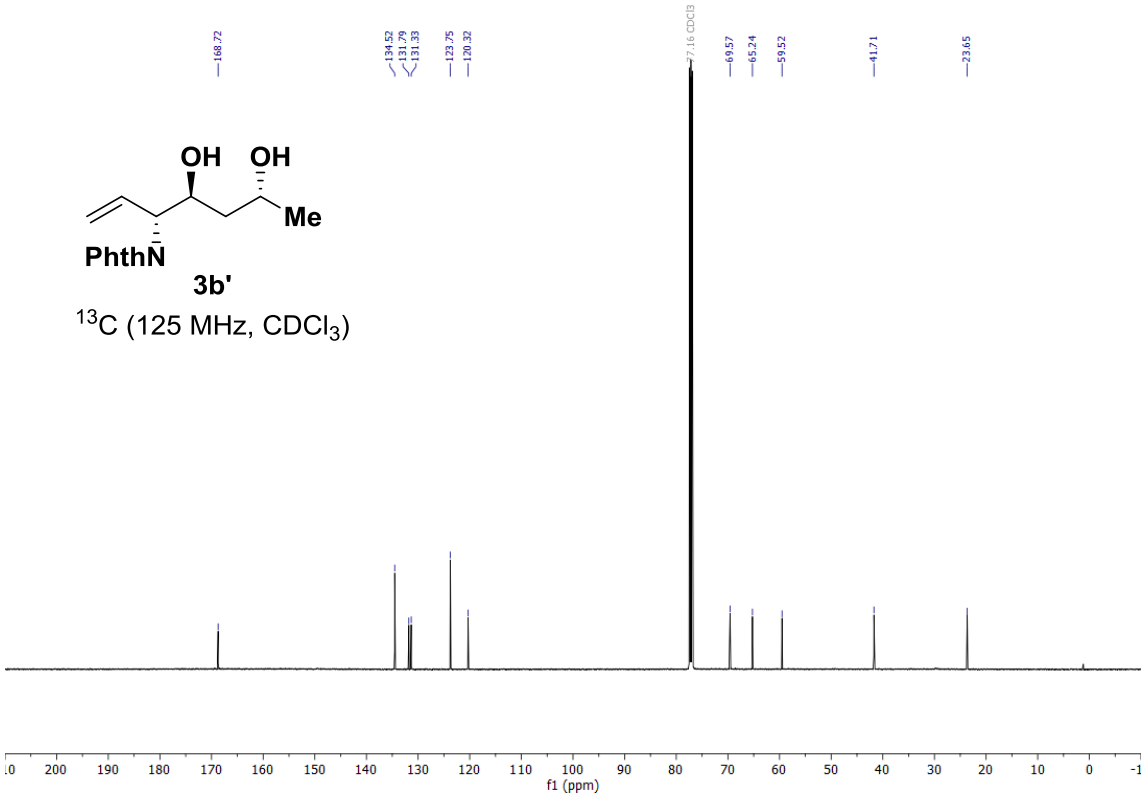
HRMS (Na+, *m/z*) for $C_{15}H_{17}NO_4$: calcd. = 298.1050; found = 298.1054.

FTIR (neat): 3457, 3378, 2963, 2359, 1693, 1386, 988, 890, 711.

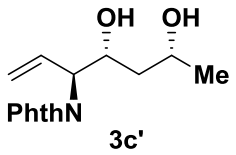
$[\alpha]_D^{34}$ = +56.9° (c = 1.30, $CHCl_3$).

MP [123 – 127] °C


OH
OH
Me
PhthN
3b'
1H (500 MHz, CDCl3)
f1 (ppm)


OH
OH
Me
PhthN
3b'
13C (125 MHz, CDCl3)
f1 (ppm)

2-((3*S*,4*R*,6*R*)-4,6-dihydroxyhept-1-en-3-yl)isoindoline-1,3-dione (3c')



3c'

Alcohol **2c'** (18 mg, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h) using 7.5 mol% of (*S*)-Ir-**IV**. Upon flash column chromatography (SiO_2, 50:50 EtOAc:hexanes), the title compound **3c'** (36.3 mg, 0.13 mmol, 20:1 dr) was obtained as a white solid in 66% yield.

TLC (SiO_2) R_f = 0.38 (50:50 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.27 (ddd, *J* = 17.6, 10.4, 7.7 Hz, 1H), 5.34 (d, *J* = 10.7 Hz, 1H), 5.28 (d, *J* = 17.3 Hz, 1H), 4.67 (dd, *J* = 7.8, 3.8 Hz, 1H), 4.35 (dt, *J* = 10.9, 3.1 Hz, 1H), 4.10 – 4.03 (m, 1H), 1.72 (ddd, *J* = 14.2, 10.8, 9.4 Hz, 1H), 1.77 (dt, *J* = 14.2, 2.5 Hz, 1H), 1.19 (d, *J* = 6.3 Hz, 3H).

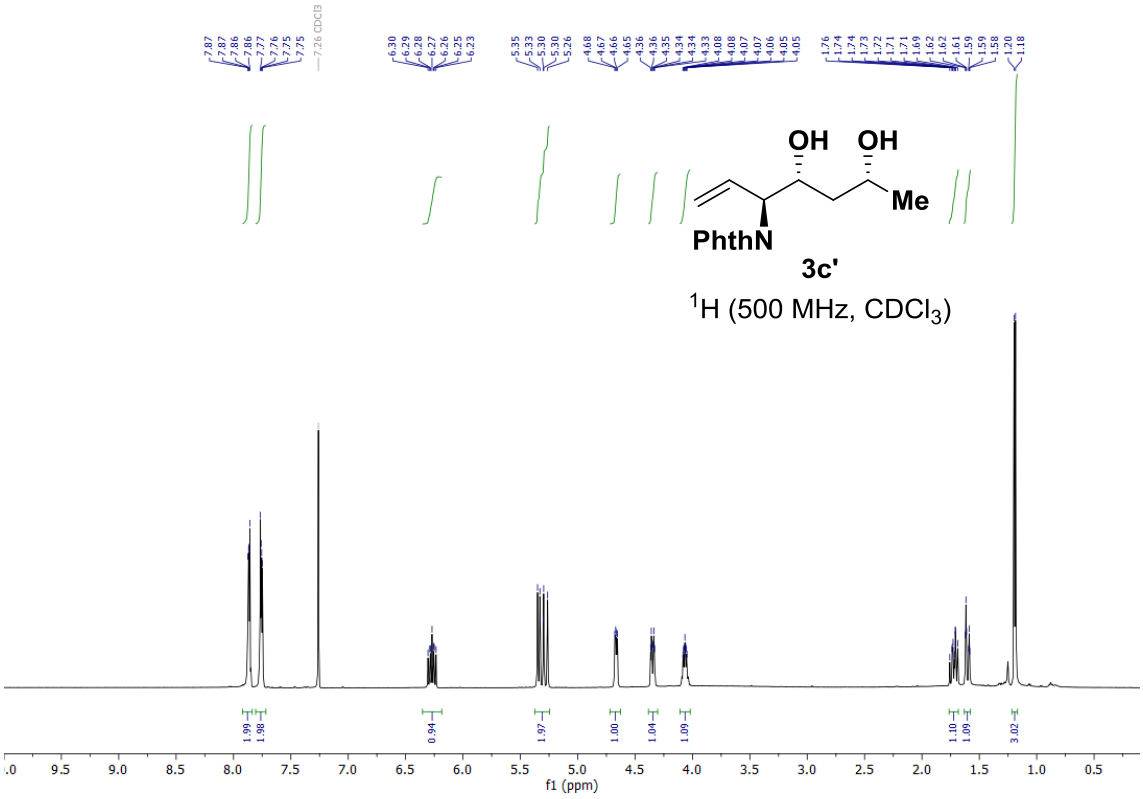
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.8, 134.6, 131.8, 130.9, 123.8, 120.4, 73.4, 68.2, 59.8, 42.0, 23.8.

HRMS (Na+, *m/z*) for $C_{15}H_{17}NO_4$: calcd. = 298.1050; found = 298.1053.

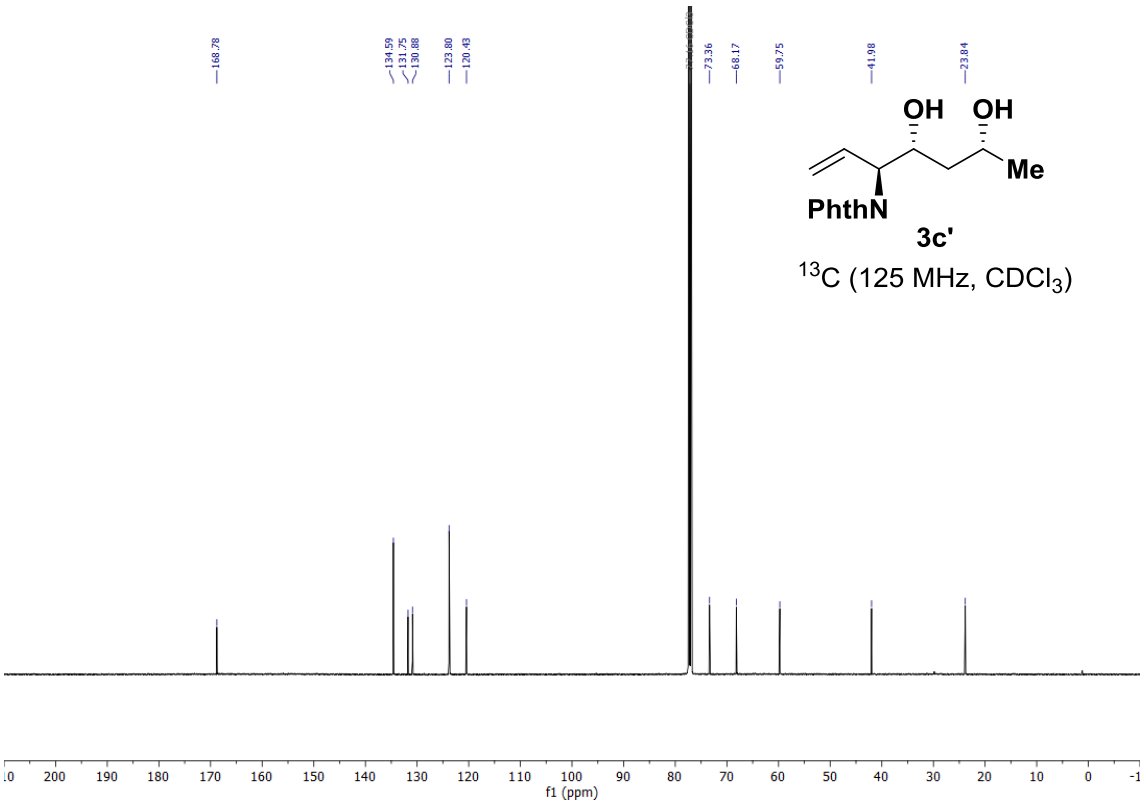
FTIR (neat): 3197, 2966, 2360, 1699, 1381, 1323, 1073, 713.

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{34}}$ = –76.1° (c = 0.90, $CHCl_3$).

MP [108 – 111] °C



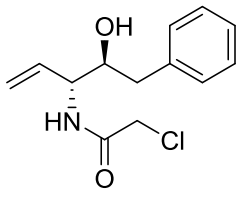
^{1}H (500 MHz, $CDCl_3$)



^{13}C (125 MHz, $CDCl_3$)

Procedures and Spectral Data for the Elaboration of Morpholine 5a

2-chloro-*N*-((3*R*,4*S*)-4-hydroxy-5-phenylpent-1-en-3-yl)acetamide (4a)



4a

To a round bottom flask charged with coupling product **3a** (92.2 mg, 0.3 mmol, 100 mol%) was added a solution of $N_2H_4 \bullet H_2O$ in DCM and MeOH (4:6:2, 12 mL) and the reaction mixture was stirred at room temperature for 6 hours. The reaction mixture was diluted with water (5 mL) and the mixture was transferred to a separatory funnel. The aqueous layer was extracted with DCM (6 x 10 mL). The combined organic extracts were washed with a saturated solution of sodium bicarbonate followed by brine. The solution was dried ($MgSO_4$), filtered, and the solvent was removed *in vacuo*. The residue was then dissolved in DCM (2 mL, 0.15 M) and triethylamine added (81 µL, 0.6 mmol, 200 mol%). The reaction was stirred at -10 °C for 5 minutes and chloroacetyl chloride added dropwise (24 µL, 0.6 mmol, 200 mol%). The reaction mixture was stirred at -10 °C for 30 minutes and then quenched by addition of a saturated solution of ammonium chloride. The mixture was then diluted with EtOAc and the mixture transferred to a separatory funnel. The phases were separated and the organic layer was washed with saturated solutions of ammonium chloride and sodium bicarbonate followed by brine. The solution was dried ($MgSO_4$), filtered, and the solvent was removed *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, 60:40 EtOAC:hexanes) to yield the title compound **4a** (62.4 mg, 0.25 mmol, >20:1 dr) as a white solid in 82% yield.

TLC (SiO_2) R_f = 0.28 (60:40 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.34 – 7.31 (m, 2H), 7.26 – 7.20 (m, 3H), 7.10 (d, *J* = 7.7 Hz, 1H), 5.97 (ddd, *J* = 17.3, 10.5, 7.0 Hz, 1H), 5.38 – 5.33 (m, 2H), 4.56 – 4.52 (m, 2H), 4.06 (brs, 2H), 3.99 (dt, *J* = 9.4, 3.7 Hz, 1H), 2.82 (dd, *J* = 13.8, 4.2 Hz, 1H), 2.71 (dt, *J* = 13.8, 9.4 Hz, 1H), 1.19 (d, *J* = 6.3 Hz, 3H).

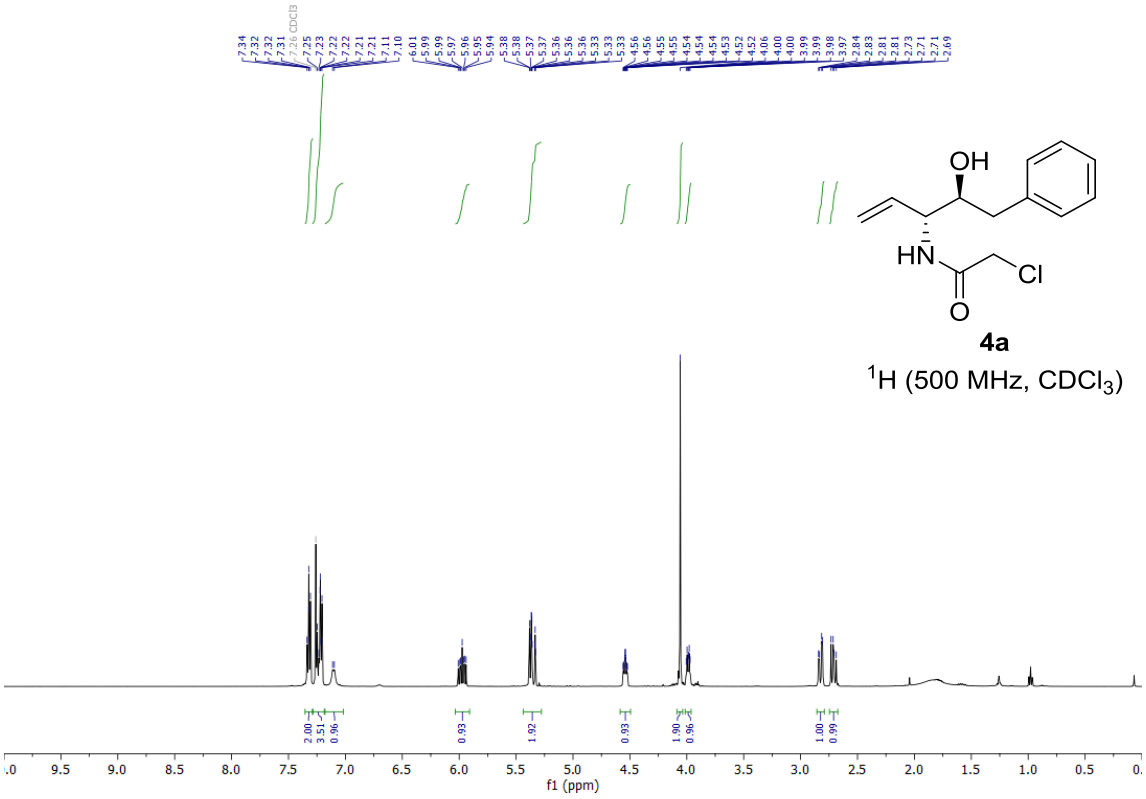
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.6, 137.5, 132.3, 129.4, 129.0, 127.0, 119.3, 74.4, 56.3, 42.8, 40.7.

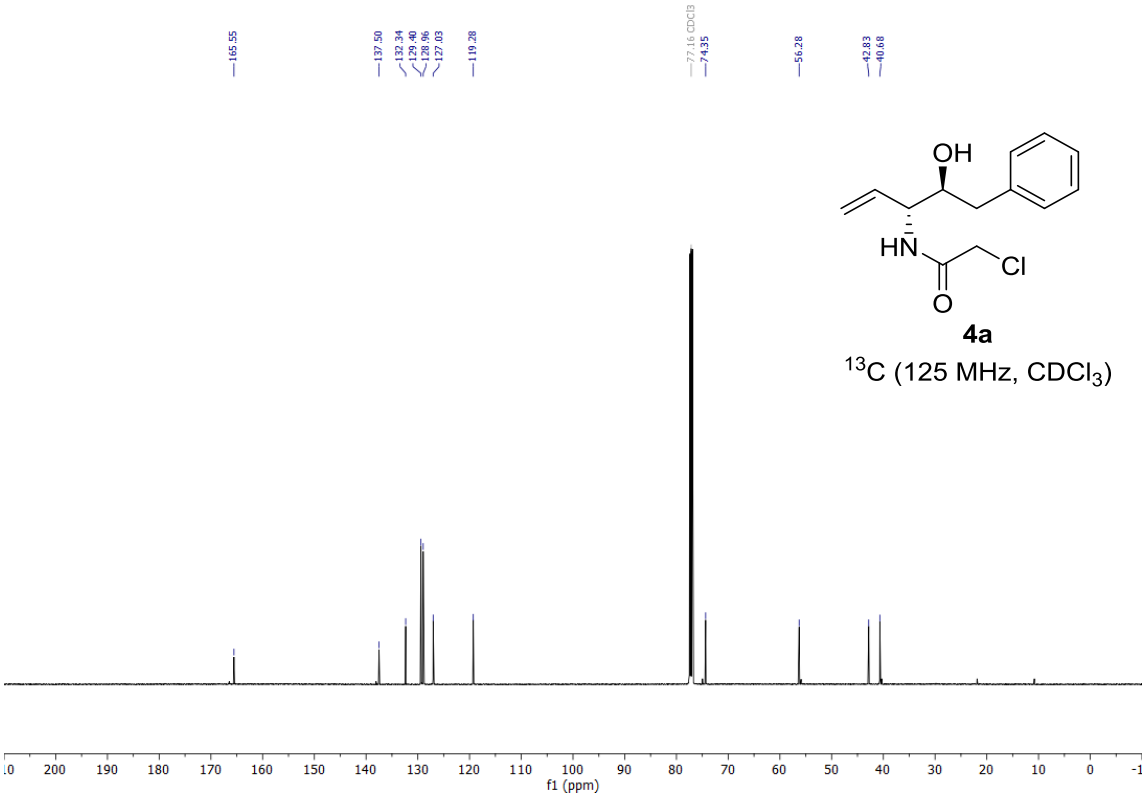
HRMS (Na+, *m/z*) for $C_{13}H_{16}ClNO_2$: calcd. = 276.0762; found = 276.0767.

FTIR (neat): 3289, 2918, 1640, 1533, 1267, 1053, 936, 752, 699.

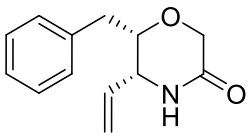
$[\alpha]_D^{34}$ = +37.1° (c = 0.93, $CHCl_3$).

MP [81 – 85] °C


OH
HN
Cl
O
4a
1H (500 MHz, CDCl3)
f1 (ppm)


OH
HN
Cl
O
4a
13C (125 MHz, CDCl3)
f1 (ppm)

(5*R*,6*S*)-6-benzyl-5-vinylmorpholin-3-one (S1a)



S1a

To a flame dried round bottomed flask charged with **4a** (52.7 mg, 0.21 mmol, 100 mol%) in THF (0.084 M) was added DMF (0.5 mL). The reaction mixture was stirred at 0 °C for 5 minutes before addition of NaH (60% w/w, 21 mg, 0.52 mmol, 250 mol%). The mixture was then stirred at 0 °C for 40 minutes. Saturated solution of ammonium chloride and EtOAC were then added and the reaction mixture transferred to a separatory funnel. The phases were separated and the organic phase washed with saturated solutions of ammonium chloride and sodium bicarbonate followed by brine. The solution was dried ($MgSO_4$), filtered, and the solvent was removed *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, 70:30 EtOAC:hexanes) to yield the title compound **S1a** (33.6 mg, 0.15 mmol, >20:1 dr) as a pale-yellow oil in 74% yield.

TLC (SiO_2) R_f = 0.42 (80:20 EtOAc:hexanes)

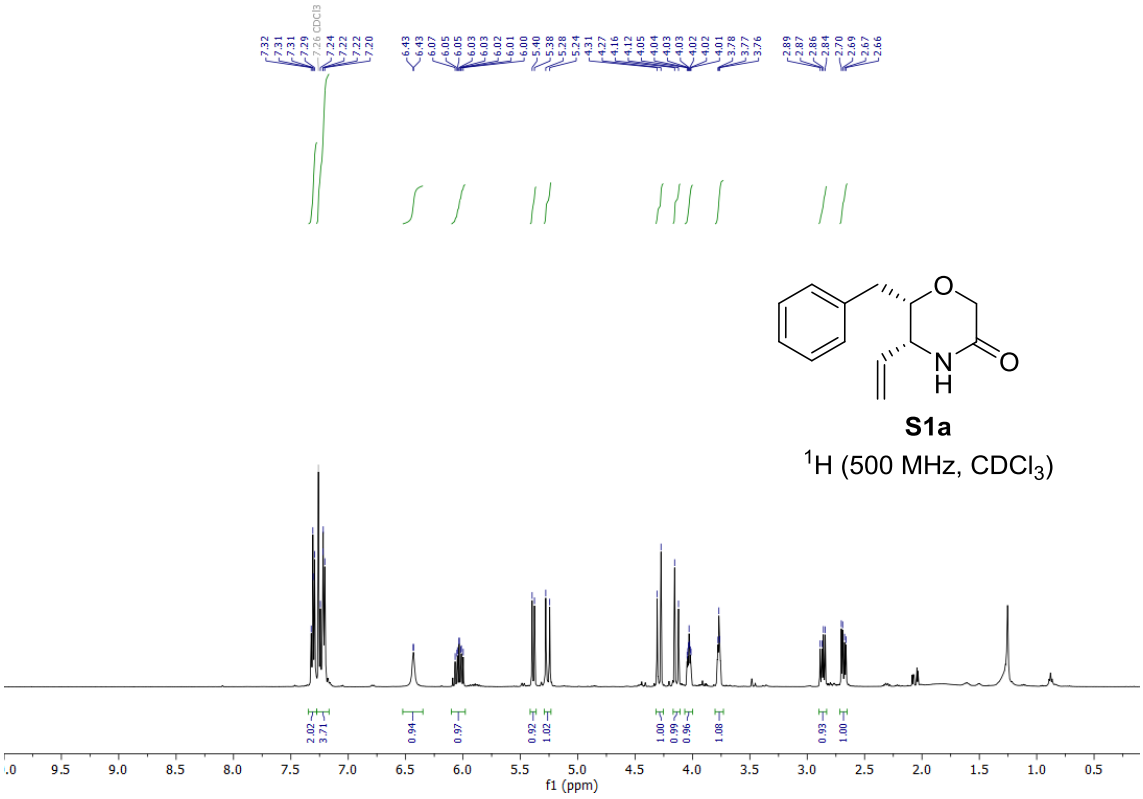
^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.32 – 7.29 (m, 2H), 7.26 – 7.20 (m, 3H), 6.42 (brs, 1H), 5.97 (ddd, *J* = 17.4, 10.1, 7.9 Hz, 1H), 5.39 (d, *J* = 10.2 Hz, 1H), 5.26 (d, *J* = 17.1 Hz, 1H), 4.29 (d, *J* = 16.9 Hz, 1H), 4.14 (d, *J* = 16.9 Hz, 1H), 4.05 – 4.01 (m, 1H), 3.78 – 3.75 (m, 1H), 2.87 (dd, *J* = 14.3, 8.0 Hz, 1H), 2.68 (dd, *J* = 14.3, 5.9 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.8, 137.3, 134.1, 129.3, 128.7, 126.9, 119.8, 68.2, 57.8, 37.8.

HRMS (H+, *m/z*) for $C_{13}H_{15}NO_2$: calcd. = 218.1176; found = 218.1175.

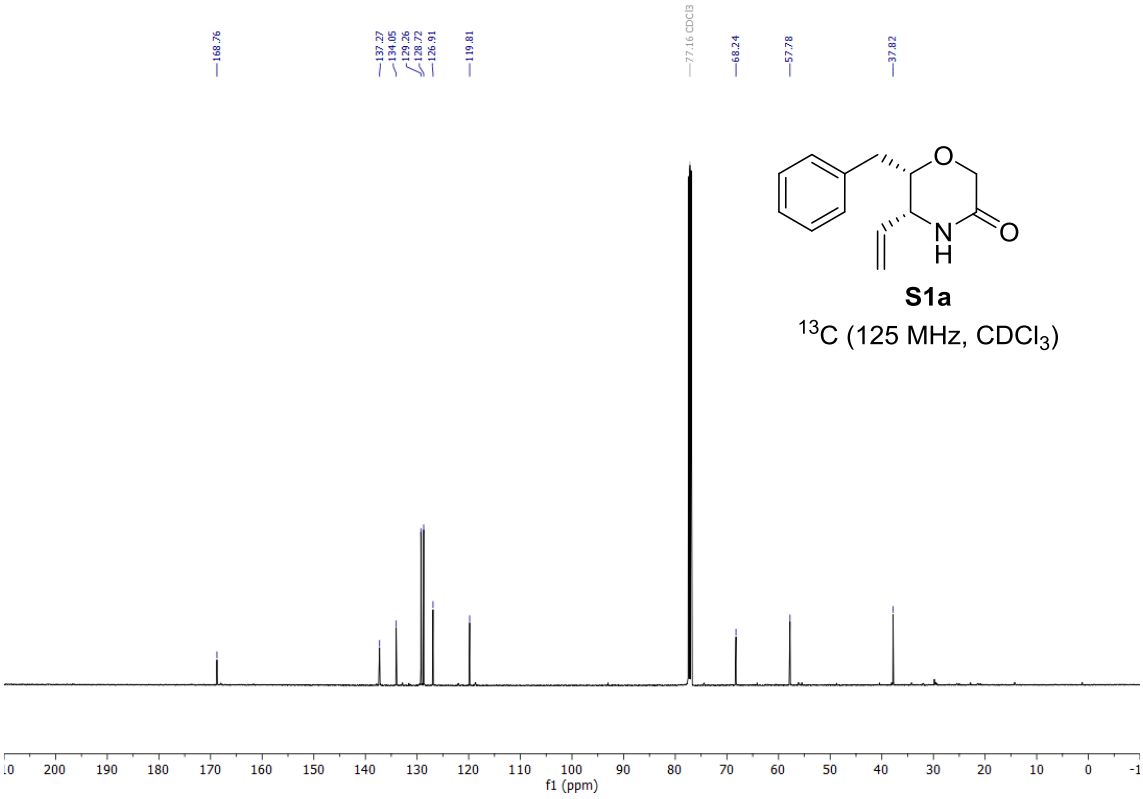
FTIR (neat): 3217, 3028, 2923, 1668, 1420, 1112, 740, 699.

$[\alpha]_D^{34}$ = +64.8° (c = 1.18, $CHCl_3$).



S1a

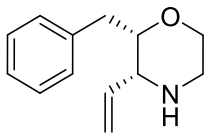
^{1}H (500 MHz, $CDCl_3$)



S1a

^{13}C (125 MHz, $CDCl_3$)

(2*S*,3*R*)-2-benzyl-3-vinylmorpholine (5a)



5a

To a flame dried round bottomed flask charged with $LiAlH_4$ (20 mg, 0.30 mmol, 300 mol%) in THF (0.05 M) was added **S1a** (21.7 mg, 0.1 mmol, 100 mol%) in THF (0.05 M) at 0 °C. The reaction mixture was stirred reflux for 6 hours. Water (30 µL), NaOH (10% aq. Solution, 30 µL), and MgSO4 added to the reaction mixture. The resulting mixture was filtered over a celite plug, washed with MeOH, and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, 95:5 DCM:MeOH) to yield the title compound **5a** (14.6 mg, 0.07 mmol, >20:1 dr) as a pale-yellow oil in 72% yield.

TLC (SiO_2) R_f = 0.22 (95:5 DCM:MeOH)

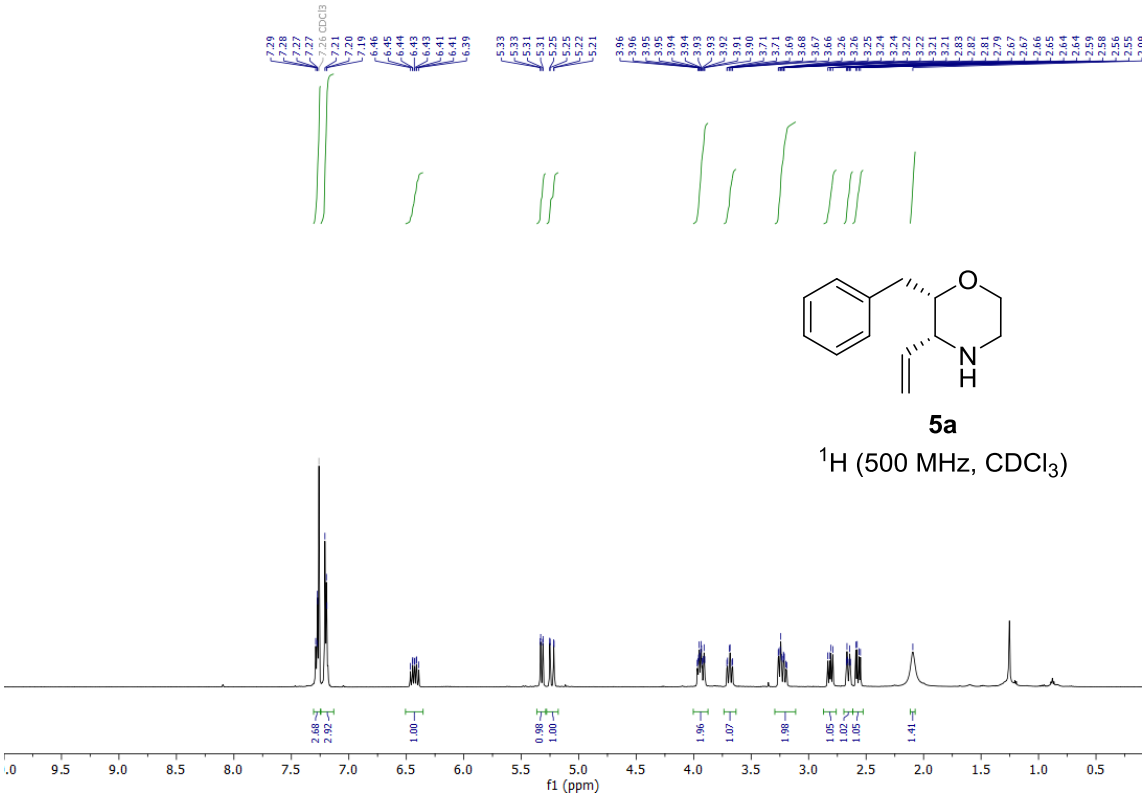
^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.29 – 7.26 (m, 2H), 7.21 – 7.19 (m, 3H), 6.43 (dt, *J* = 17.1, 9.6 Hz, 1H), 5.33 (d, *J* = 9.7 Hz, 1H), 5.24 (d, *J* = 17.3 Hz, 1H), 3.96 (ddd, *J* = 8.4, 6.0, 2.6 Hz, 1H), 3.93 (dt, *J* = 11.5, 3.0 Hz, 1H), 3.69 (td, *J* = 11.1, 2.8 Hz, 1H), 3.25 (dd, *J* = 8.8, 2.7 Hz, 1H), 3.21 (td, *J* = 11.4, 3.6 Hz, 1H), 2.81 (dd, *J* = 14.3, 8.0 Hz, 1H), 2.66 (dt, *J* = 12.2, 2.8 Hz, 1H), 2.57 (dd, *J* = 14.2, 6.0 Hz, 1H), 2.09 (brs, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 138.2, 134.2, 129.4, 128.5, 126.4, 119.6, 79.1, 67.1, 58.7, 40.6, 38.3.

HRMS (H+, *m/z*) for $C_{13}H_{17}NO$: calcd. = 204.1383; found = 204.1387.

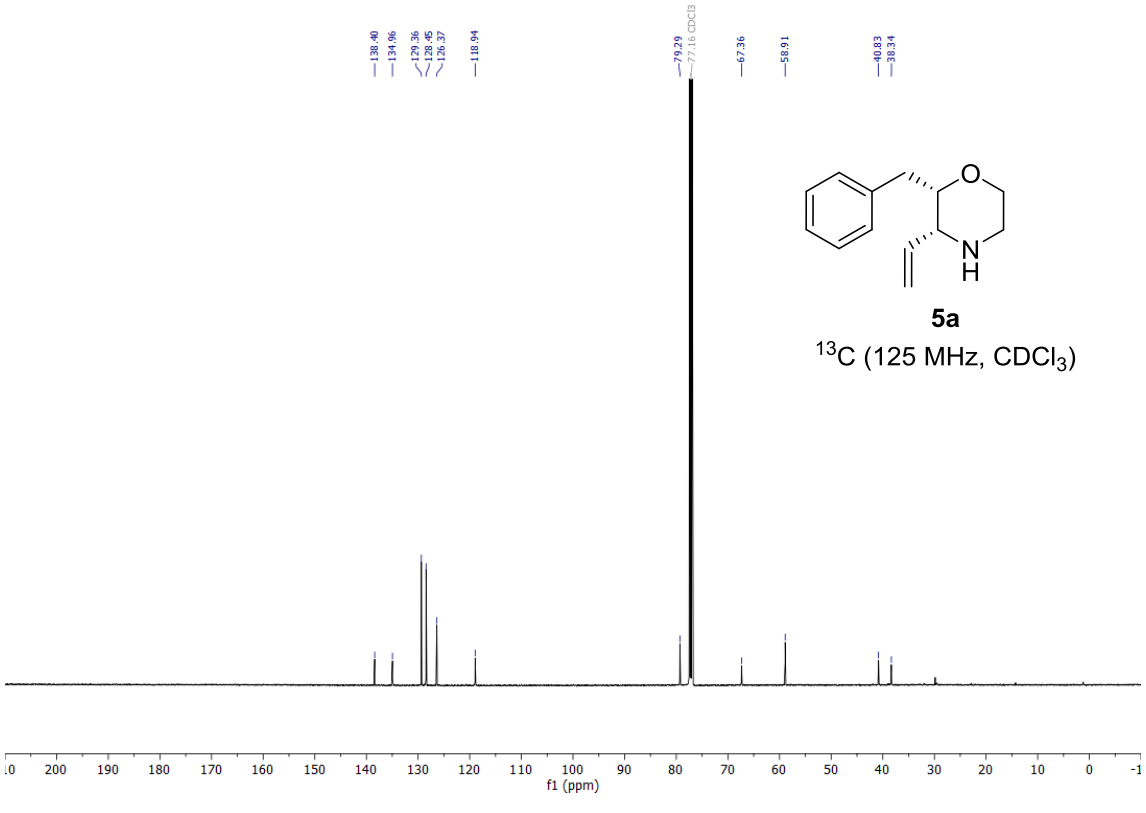
FTIR (neat): 2921, 2854, 1454, 1085, 923, 698.

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{34}}$ = –8.2° (c = 0.79, $CHCl_3$).



5a

^{1}H (500 MHz, $CDCl_3$)

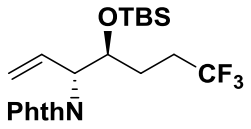


5a

^{13}C (125 MHz, $CDCl_3$)

Procedures and Spectral Data for the Elaboration of Amino-Acid 6m

2-((3*R*,4*S*)-4-((tert-butyldimethylsilyl)oxy)-7,7,7-trifluorohept-1-en-3-yl)isoindoline-1,3-dione (S2m)



S2m

To a solution of alcohol **3m** (50.0 mg, 0.117 mmol, 100 mol%) in dried DMF (220 µL) was added Et_3N (82 µL, 0.585 mmol, 500 mol%), TBSCl (44.0 mg, 0.293 mmol, 250 mol%) and 4-(dimethylamino)pyridine (2.9 mg, 0.0232 mmol, 20 mol%). The reaction was heated to 45 °C for 48 h. The contents were diluted with CH_2Cl_2 (2 mL) and washed with H_2O (2 mL). The aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL), and the combined organic phases were washed with brine (2 mL), dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was subjected to flash chromatography on silica (EtOAc:hexanes 10:90) to furnish the title compound **S2m** (43.5 mg, 0.102 mmol) in 87% yield as a clear oil.

TLC (SiO_2) R_f = 0.26 (10:90 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.85 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.4, 3.0 Hz, 2H), 6.25 (ddd, *J* = 17.2, 10.1, 7.2 Hz, 1H), 5.25 – 5.22 (m, 2H), 4.62 – 4.55 (m, 2H), 2.35 – 2.24 (m, 1H), 2.21 – 2.10 (m, 1H), 1.80 – 1.73 (m, 1H), 1.61 – 1.54 (m, 1H), 0.90 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H).

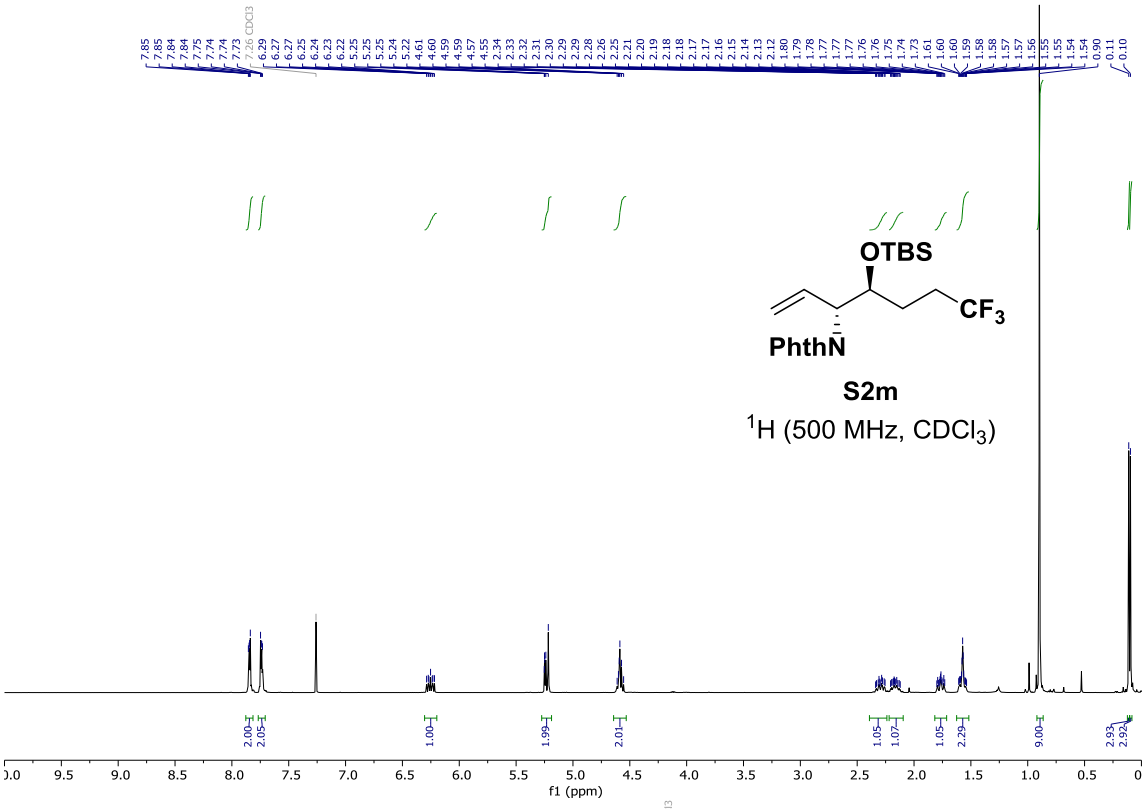
^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.0, 134.4, 133.4, 131.8, 127.6 (q, *J* = 275.8 Hz), 123.6, 120.0, 68.9, 57.1, 27.6 (q, *J* = 29.0 Hz), 25.9, 18.1, – 4.2, – 4.2.

^{19}F NMR (470 MHz, $CDCl_3$) δ: -66.5 (t, *J* = 10.8 Hz).

HRMS (Na+, *m/z*) for $C_{21}H_{28}F_3NO_3Si$: calcd. = 450.1683; found =450.1686.

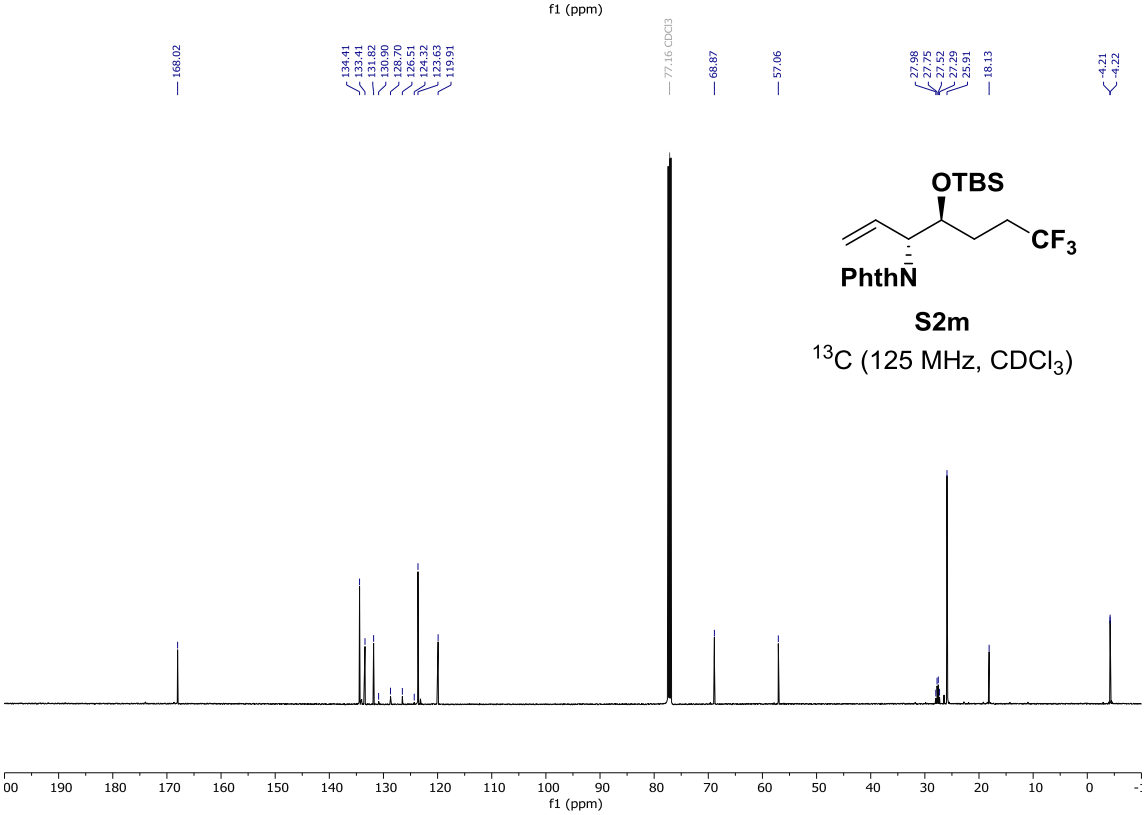
FTIR (neat): 2956, 2931, 2858, 1716, 1379, 1254, 1060, 834, 717.

$[\alpha]_D^{24}$ = +52.2° (c = 1.13, $CHCl_3$).



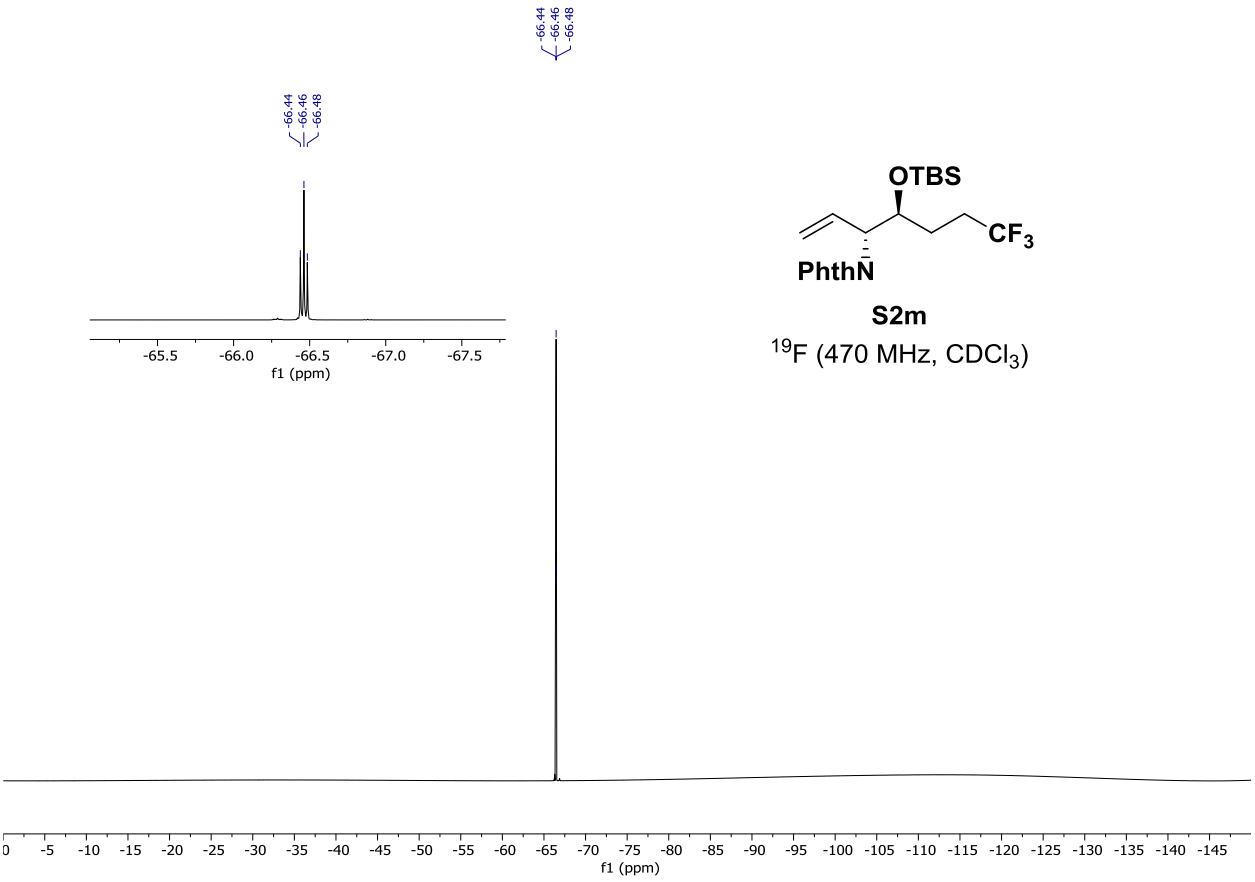
S2m

^{1}H (500 MHz, $CDCl_3$)

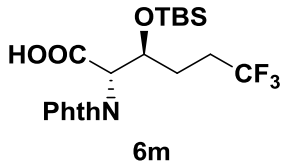


S2m

^{13}C (125 MHz, $CDCl_3$)


-66.44
-66.46
-66.48
-66.44
-66.46
-66.48
-65.5
-66.0
-66.5
-67.0
-67.5
f1 (ppm)
OTBS
CF3
PhthN
S2m
19F (470 MHz, CDCl3)
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
f1 (ppm)

(2*S*,3*S*)-3-((tert-butyldimethylsilyl)oxy)-2-(1,3-dioxoisoindolin-2-yl)-6,6,6-trifluorohexanoic acid (6m)



6m

To a stirred solution of **S2a** (100.0 mg, 0.230 mmol, 100 mol%), in 0.650 mL CCl_4, 0.650 mL CH_3CN, and 1.0 mL H_2O was added $NaIO_4$ (201.2 mg, 0.940 mmol, 400 mol%). After all the $NaIO_4$ had dissolved, $RuCl_3.H_2O$ (4.8 mg, 0.023 mmol, 10 mol%) was added, and the reaction mixture was stirred vigorously for 24 h at 25 °C. The contents were diluted with DCM (5 mL) and washed with H_2O (5 mL). The aqueous layer was extracted with DCM (3 x 5 mL), and the combined organic phases were washed with brine (5 mL), dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was subjected to flash chromatography on silica (Hexanes/MeOH 90:10) to furnish the title compound **6a** (59.2 mg, 0.136 mmol) in 59% yield as a white solid.

TLC (SiO_2) R_f = 0.22 (10:90 MeOH:DCM)

^{1}H NMR (500 MHz, MeOD) δ: 7.89 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.83 (dd, *J* = 5.4, 3.0 Hz, 2H), 4.73 – 4.70 (m, 1H), 2.28 – 2.13 (m, 2H), 2.10 – 2.03 (m, 1H), 1.62 – 1.54 (m, 1H), 0.85 (s, 9H), 0.23 (s, 3H), 0.14 (s, 3H).

^{13}C NMR (125 MHz, MeOD) δ: 170.2, 168.0, 134.4, 131.6, 127.3 (q, *J* = 275.8 Hz), 122.9, 78.1, 70.0, 30.0 (q, *J* = 29.0 Hz), 26.4, 24.9, 17.4, – 5.7, – 6.0.

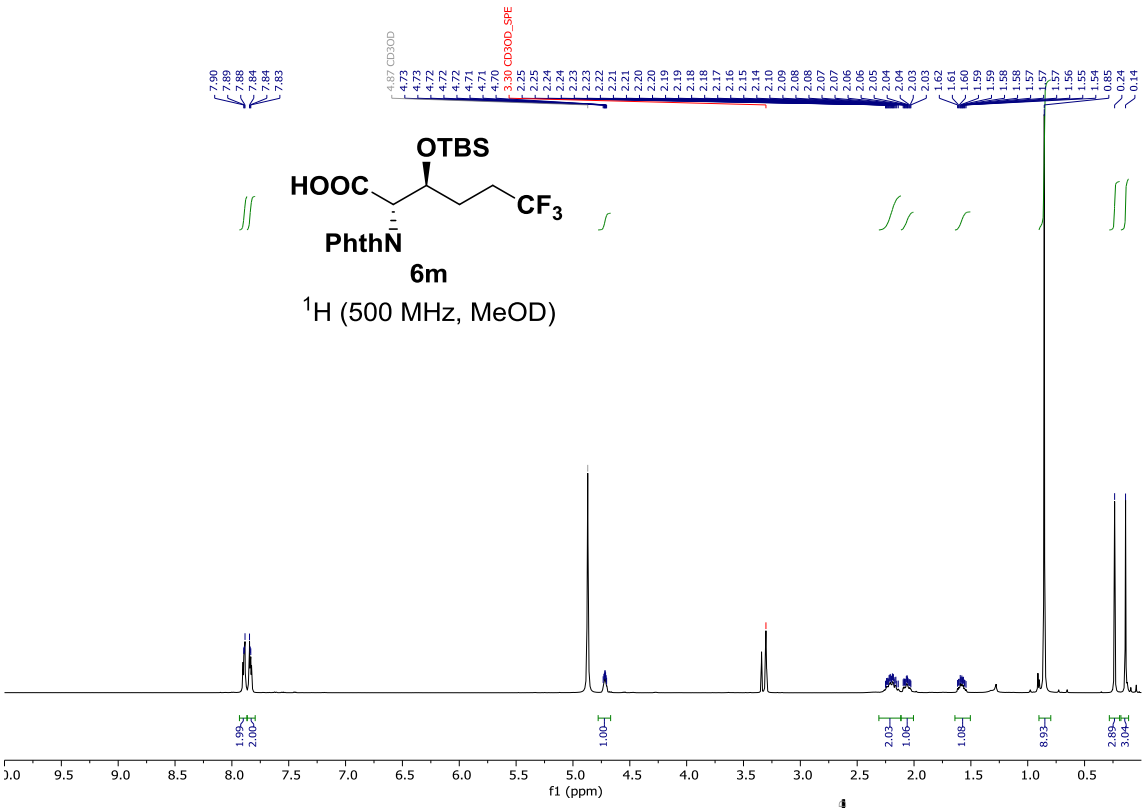
^{19}F NMR (470 MHz, MeOD) δ: -68.0 (t, *J* = 10.8 Hz).

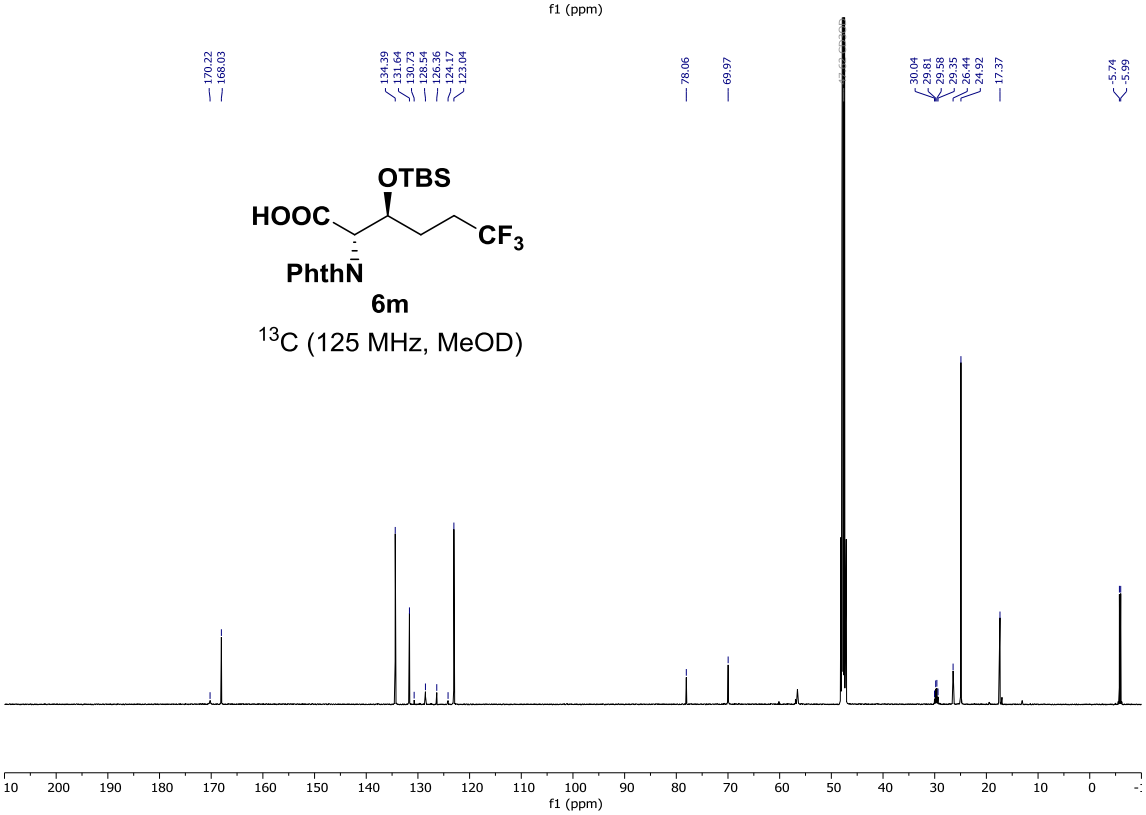
HRMS (Na+, *m/z*) for $C_{20}H_{26}F_3NO_5Si$: calcd. = 468.1425; found =468.1425.

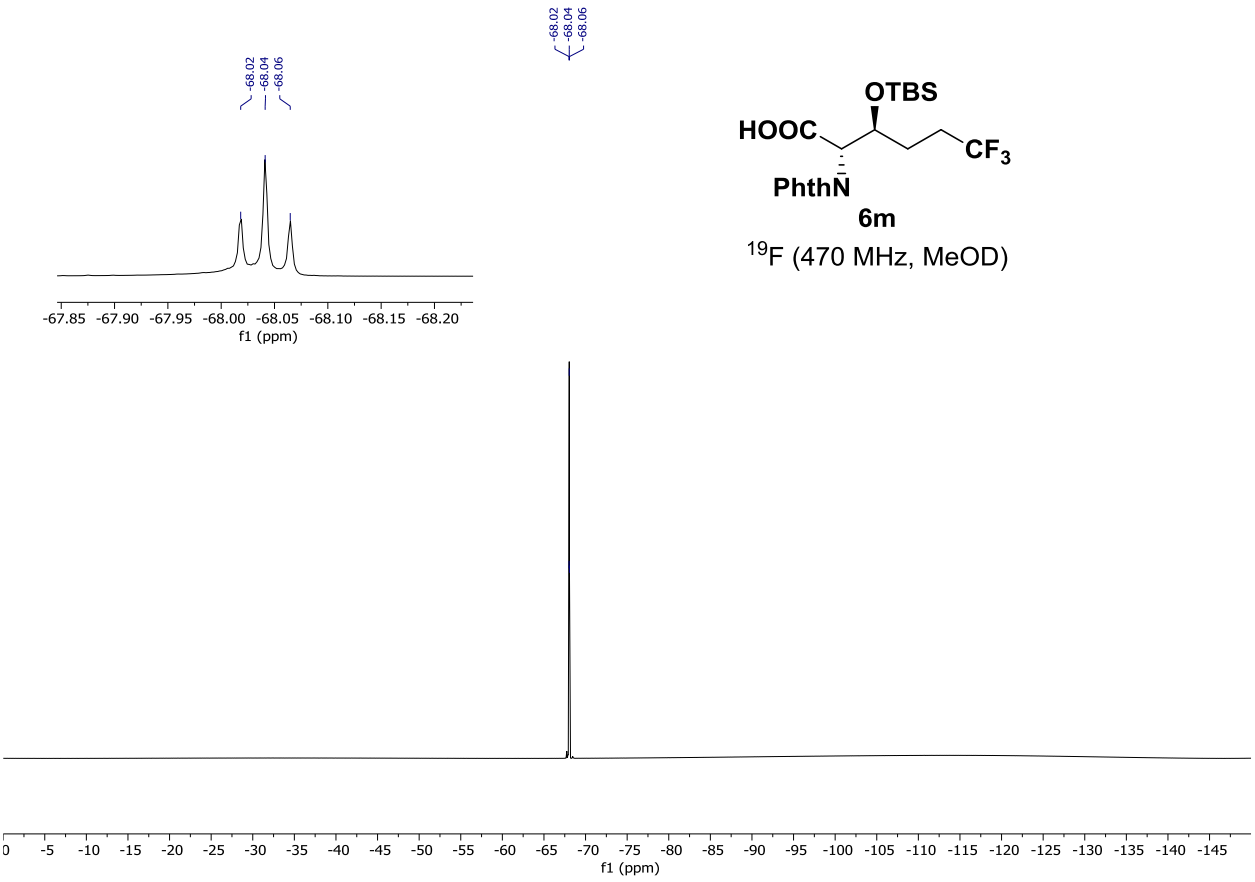
FTIR (neat): 2935, 2360, 1720, 1385, 1253, 1066, 835, 777, 721.

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{24}}$ = –31.1° (c = 1.83, $CHCl_3$).

MP [62 – 65] °C

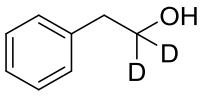

OTBS
HOOC
CF3
PhthN
6m
1H (500 MHz, MeOD)
f1 (ppm)


OTBS
HOOC
CF3
PhthN
6m
13C (125 MHz, MeOD)
f1 (ppm)


-68.02
-68.04
-68.06
OTBS
HOOC
CF3
PhthN
6m
19F (470 MHz, MeOD)
-67.85 -67.90 -67.95 -68.00 -68.05 -68.10 -68.15 -68.20
f1 (ppm)
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145
f1 (ppm)

Isotopic Labeling Studies

2-phenylethan-1,1-d_2-1-ol (deuterio-2a)



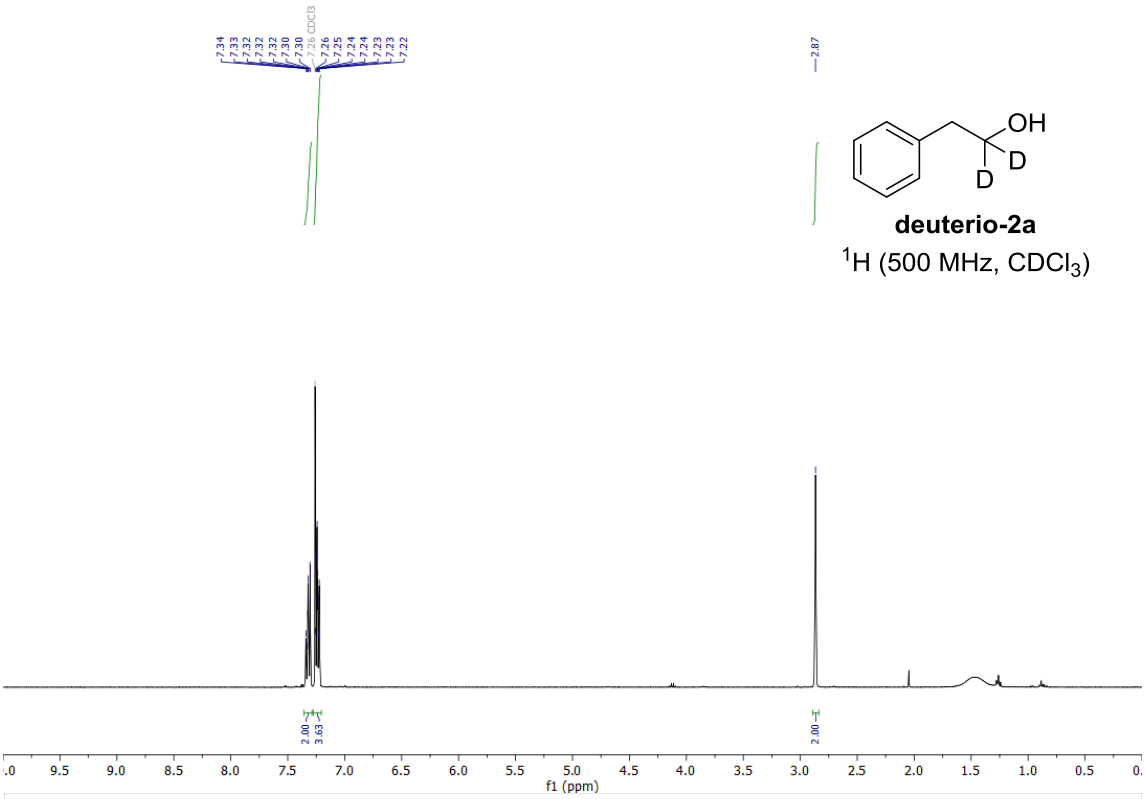
deuterio-2a

The title compound was synthesized over one step from 2-phenylacetic acid following literature procedures.[4]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.34 – 7.30 (m, 2H), 7.26 – 7.22 (m, 3H), 2.86 (brs, 2H)

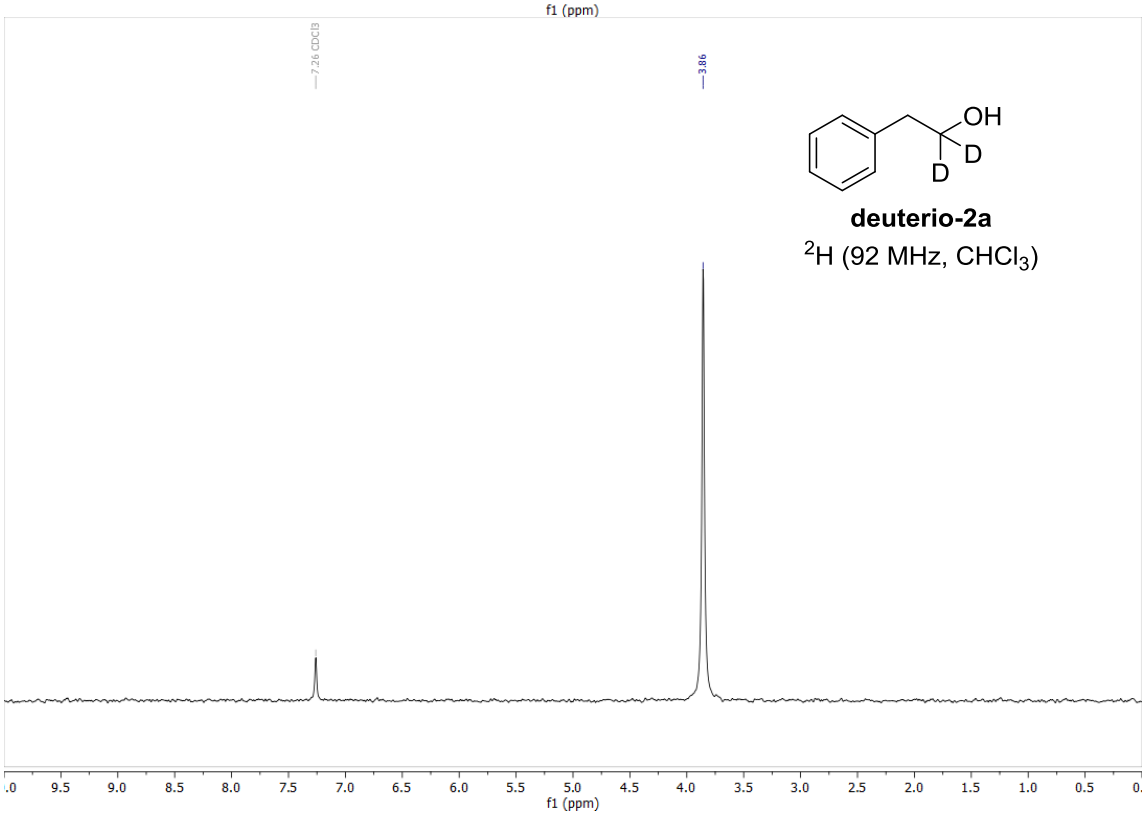
^{2}H NMR (92 MHz, $CHCl_3$) δ: 3.86 (brs, 2D)

HRMS (H+, *m/z*) for $C_8H_8D_2O$: calcd. = 124.0857; found = 124.0861.



deuterio-2a

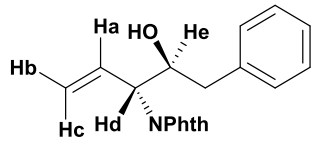
^{1}H (500 MHz, $CDCl_3$)



deuterio-2a

^{2}H (92 MHz, $CHCl_3$)

2-((3*R*,4*S*)-4-hydroxy-5-phenylpent-1-en-3-yl)isoindoline-1,3-dione-d (deuterio-3a)



deuterio-3a

Ha (60% ^{2}H), Hb,Hc (25% ^{2}H)

Hd (<1%), He (>99% ^{2}H)

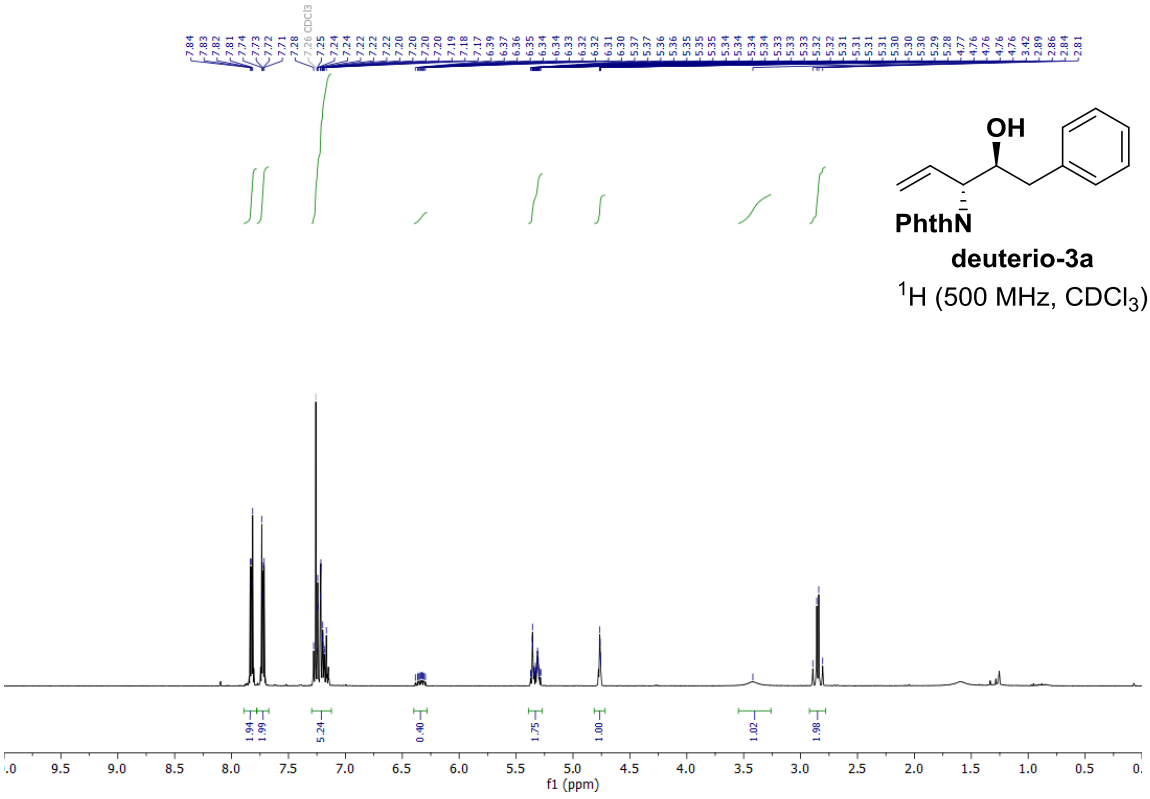
Alcohol **deuterio-2a** (24.0 µL, 0.2 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), the title compound **deuterio-3a** (41.8 mg, 0.14 mmol, >20:1 dr) was obtained as a light yellow solid in 68% yield.

TLC (SiO_2) R_f = 0.35 (20:80 EtOAc:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.28 – 7.15 (m, 5H), 6.39 – 6.30 (m, 0.4H), 5.37 – 5.28 (m, 1.75H), 4.78 – 4.76 (m, 1H), 3.42 (brs, 1H), 2.89 – 2.81 (m, 2H).

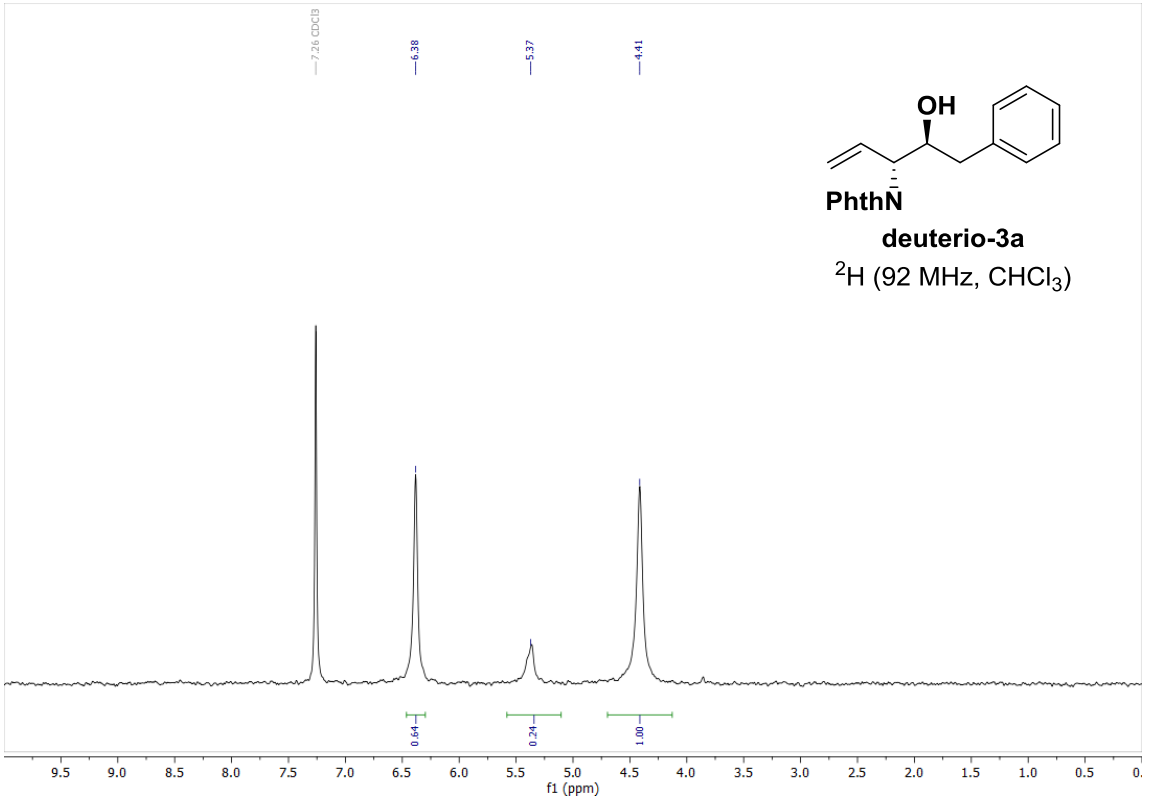
^{2}H NMR (92 MHz, $CHCl_3$) δ: 6.38 (brs, 0.6D), 5.37 (brs, 0.25D), 4.41 (brs, 1D).

HRMS (H+, *m/z*) for $C_{19}H_{15}D_2NO_3$: calcd. = 310.1407; found = 310.1416.



deuterio-3a

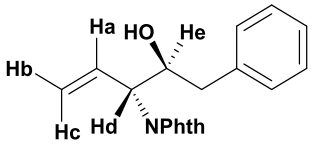
^{1}H (500 MHz, $CDCl_3$)



deuterio-3a

^{2}H (92 MHz, $CHCl_3$)

Competition experiment:



deuterio-3a and 3a

Ha (5% ^{2}H), Hb,Hc (<1% ^{2}H)

Hd (<1%), He (30% ^{2}H)

A mix of Alcohol **2a** (120 µL, 1.0 mmol) and Alcohol **deuterio-2a** (120.0 µL, 1.0 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), title compounds **deuterio-3a** and **3a** (31.9 mg, 0.10 mmol, >20:1 dr) was obtained as a light yellow solid in 52% yield.

TLC (SiO_2) R_f = 0.35 (20:80 EtOAc:hexanes)

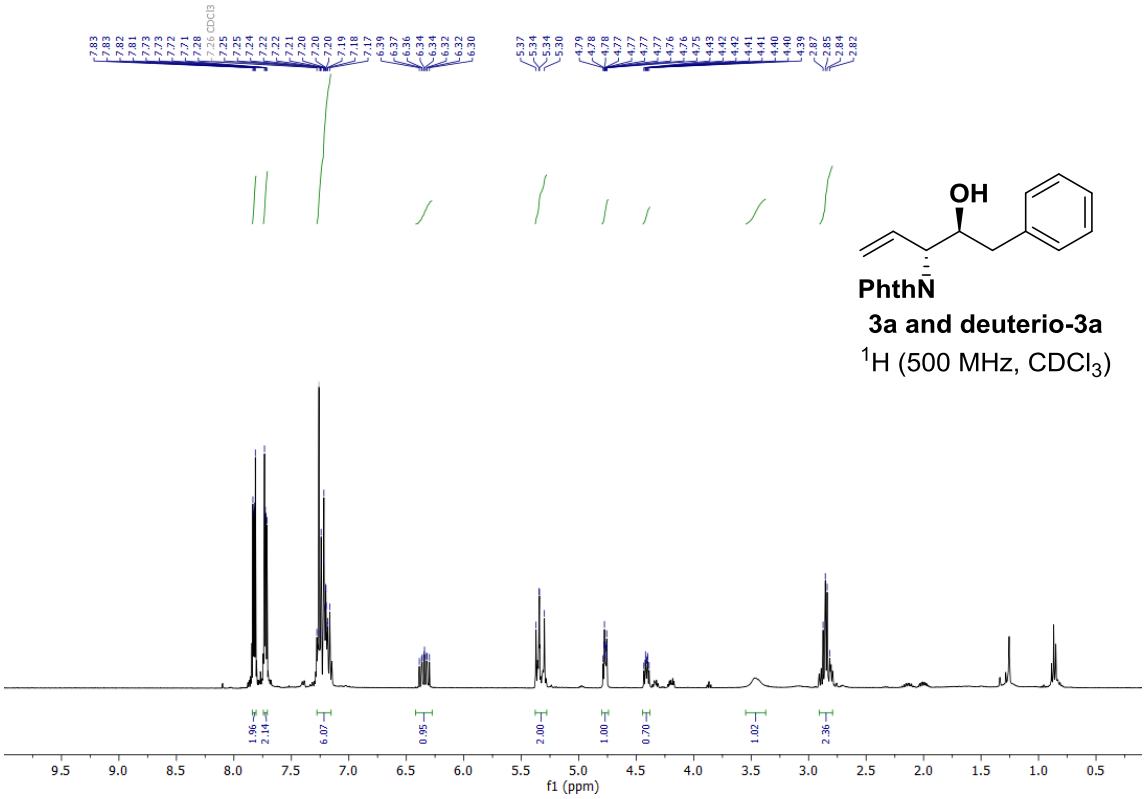
^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.28 – 7.15 (m, 5H), 6.39 – 6.30 (m, 0.85H), 5.37 – 5.28 (m, 1.95H), 4.78 – 4.76 (m, 1H), 4.41 (ddd, *J* = 7.8, 5.9, 4.7 Hz, 0.7H), 3.42 (brs, 1H), 2.89 – 2.81 (m, 2H).

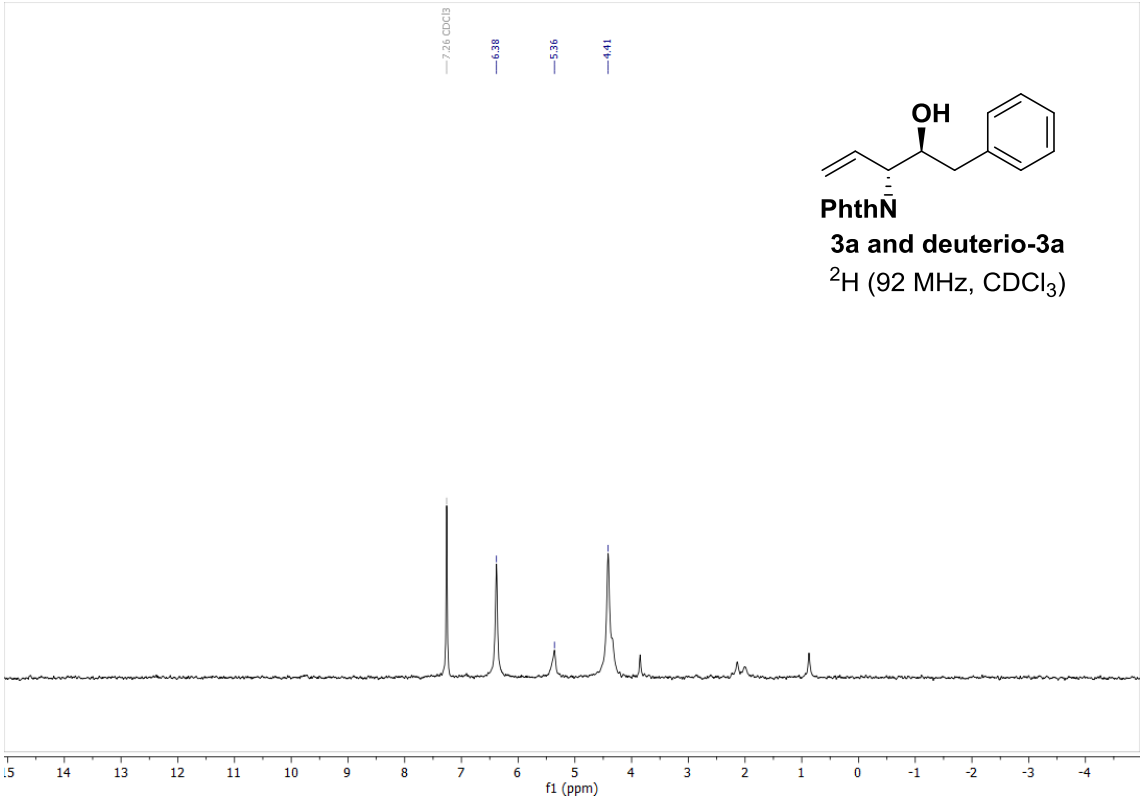
^{2}H NMR (92 MHz, $CHCl_3$) δ: 6.38 (brs, 1D), 5.37 (brs, 1D), 4.41 (brs, 1D).

HRMS (Na+, *m/z*) for $C_{19}H_{17}NO_3$: calcd. = 330.1101; found = 330.1105.

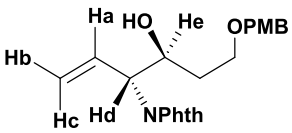
HRMS (Na+, *m/z*) for $C_{19}H_{16}DNO_3$: calcd. = 331.1163; found = 331.1164.

HRMS (Na+, *m/z*) for $C_{19}H_{15}D_2NO_3$: calcd. = 332.1226; found = 332.1226.


OH
PhthN
3a and deuterio-3a
1H (500 MHz, CDCl3)
f1 (ppm)

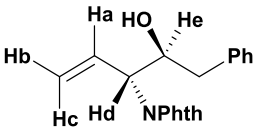

OH
PhthN
3a and deuterio-3a
2H (92 MHz, CDCl3)
f1 (ppm)

Intermolecular competition experiment:



deuterio-3l

Ha (64% ^{2}H), Hb,Hc (19% ^{2}H)
Hd (<1%), He (<1% ^{2}H)



deuterio-3a

Ha (61% ^{2}H), Hb,Hc (19% ^{2}H)
Hd (<1%), He (>99% ^{2}H)

A mix of **dehydro-2l** (19 mg, 0.1 mmol) and Alcohol **deuterio-2a** (12 µL, 0.1 mmol) was subjected to standard reaction conditions (100 °C, 48 h). Upon flash column chromatography (SiO_2, 20:80 EtOAc:hexanes), title compounds **deuterio-3a** (13.0 mg, 0.042 mmol, 21% yield) and **deuterio-3l** (21.3 mg, 0.056 mmol, 28% yield) were obtained as a light yellow solid and pale yellow oil respectively.

TLC (SiO_2) $R_{f\text{-}\mathbf{deutreio\text{-}3a}}$ = 0.35 (20:80 EtOAc:hexanes)

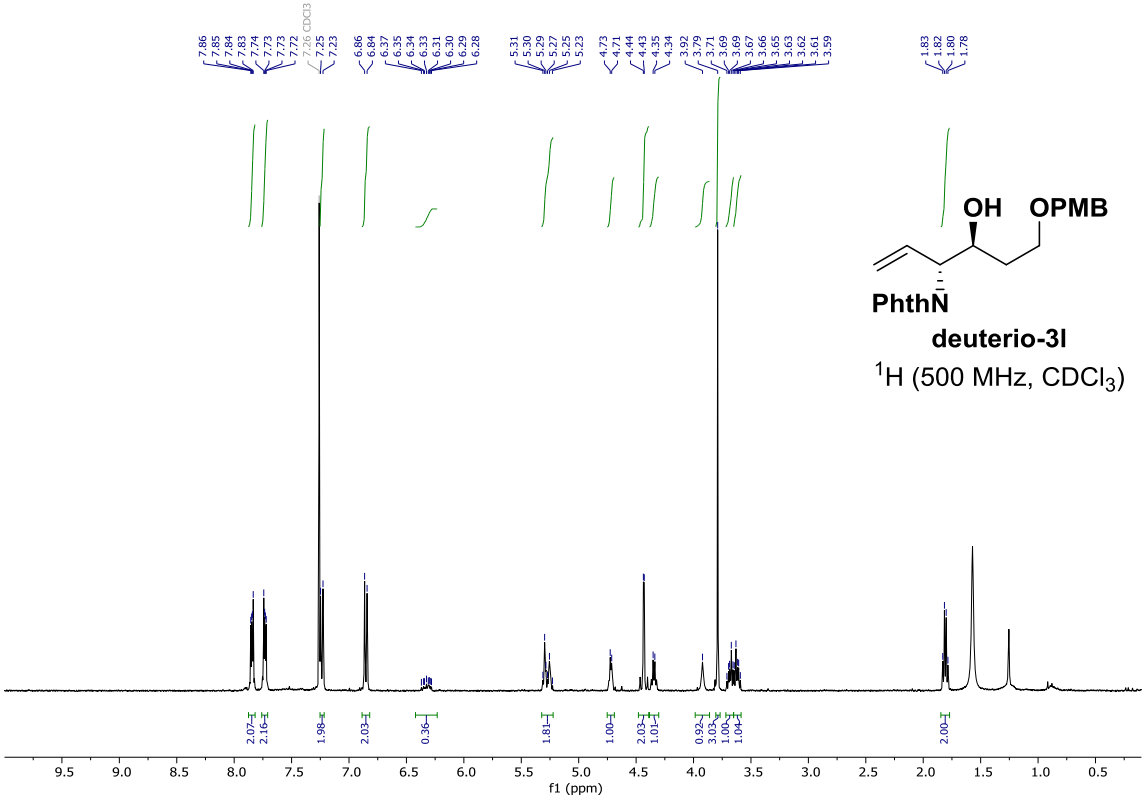
TLC (SiO_2) $R_{f\text{-}\mathbf{deuterio\text{-}3l}}$ = 0.28 (30:70 EtOAc:hexanes)

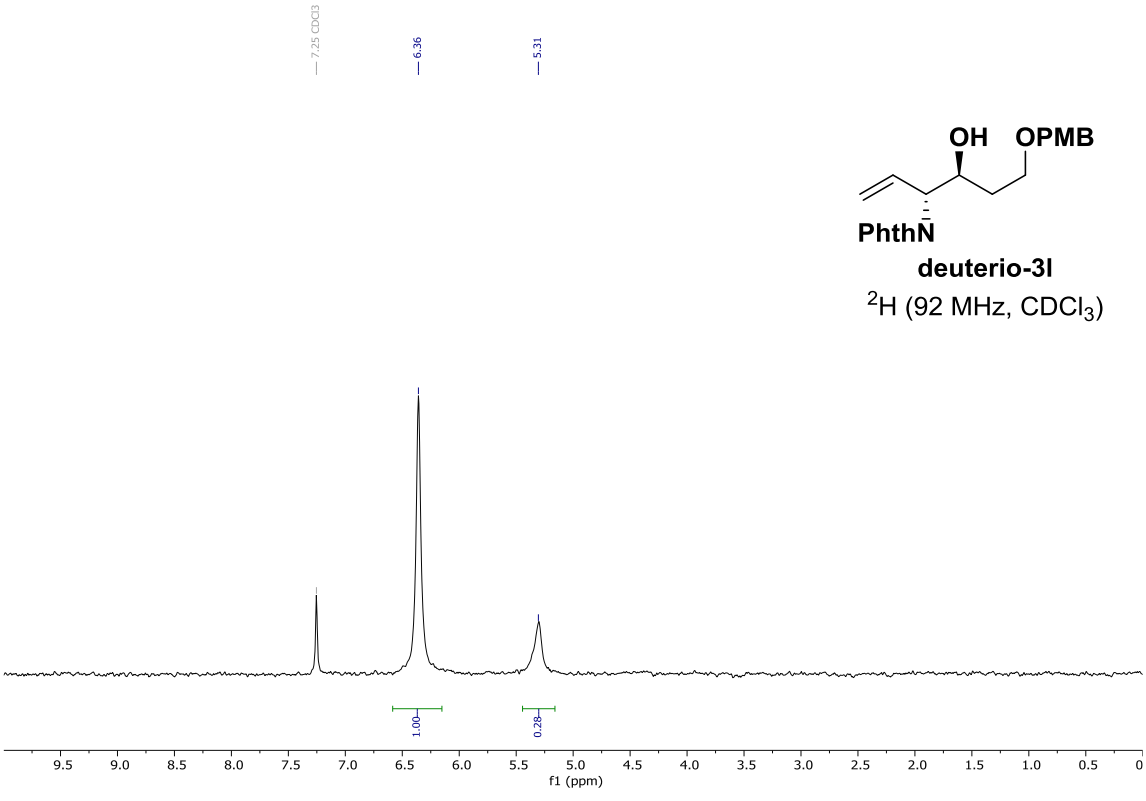
Deuterio-3l:

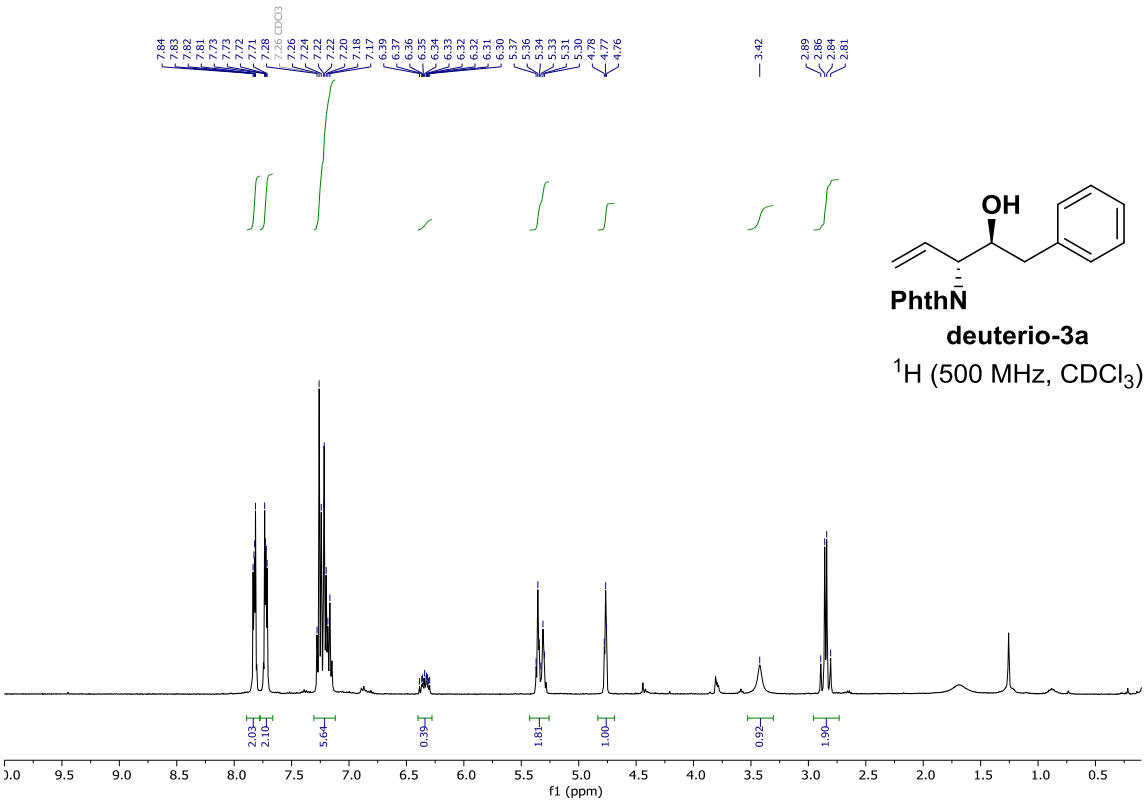
^{1}H NMR (500 MHz, CDCl3) δ: 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.38 – 6.28 (m, 0.4H), 5.32 – 5.23 (m, 1.90H), 4.74 – 4.69 (m, 1H), 4.46 – 4.39 (m, 2H), 4.35 (dd, *J* = 12.1, 5.8 Hz, 1H), 3.92 (s, 1H), 3.78 (s, 3H), 3.71 – 3.65 (m, 1H), 3.64 – 3.58 (m, 1H), 1.85 – 1.77 (m, 2H).

^{2}H NMR (92 MHz, $CHCl_3$) δ: 6.36 (brs, 1D), 5.31 (brs, 1D)

HRMS (Na+, *m/z*) for $C_{22}H_{22}DNO_5$: calcd. = 405.1531; found = 405.1530.


OH
OPMB
PhthN
deuterio-3l
1H (500 MHz, CDCl3)
f1 (ppm)

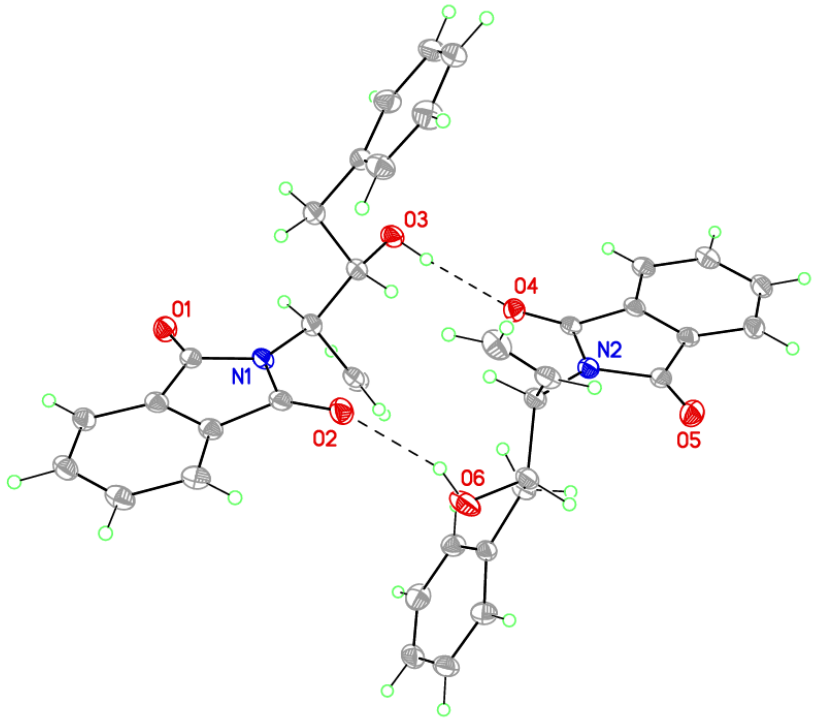

OH
OPMB
PhthN
deuterio-3l
2H (92 MHz, CDCl3)
f1 (ppm)


OH
PhthN
deuterio-3a
1H (500 MHz, CDCl3)
f1 (ppm)

Single Crystal Diffraction Data for Coupling Product 3a

Empirical formula	C19 H17 N O3	
Formula weight	307.33	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal system	triclinic	
Space group	P 1	
Unit cell dimensions	a = 7.6636(2) Å	α= 86.249(2)°.
	b = 9.5929(2) Å	β= 76.166(2)°.
	c = 10.8499(2) Å	γ = 79.110(2)°.
Volume	760.39(3) $Å^3$	
Z	2	
Density (calculated)	1.342 Mg/m^3	
Absorption coefficient	0.738 mm^{-1}	
F(000)	324	
Crystal size	0.34 x 0.12 x 0.065 mm^3	
Theta range for data collection	4.197 to 75.699°.	
Index ranges	-9<=h<=9, -11<=k<=12, -13<=l<=13	
Reflections collected	26510	
Independent reflections	5735 [R(int) = 0.0395]	
Completeness to theta = 67.684°	99.7 %	
Absorption correction	Gaussian and multi-scan	
Max. and min. transmission	1.00 and 0.534	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5735 / 3 / 433	
Goodness-of-fit on F^2	1.048	
Final R indices [I>2sigma(I)]	R1 = 0.0357, wR2 = 0.0952	
R indices (all data)	R1 = 0.0367, wR2 = 0.0961	
Absolute structure parameter	0.04(10)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.175 and -0.218 $e.Å^{-3}$	

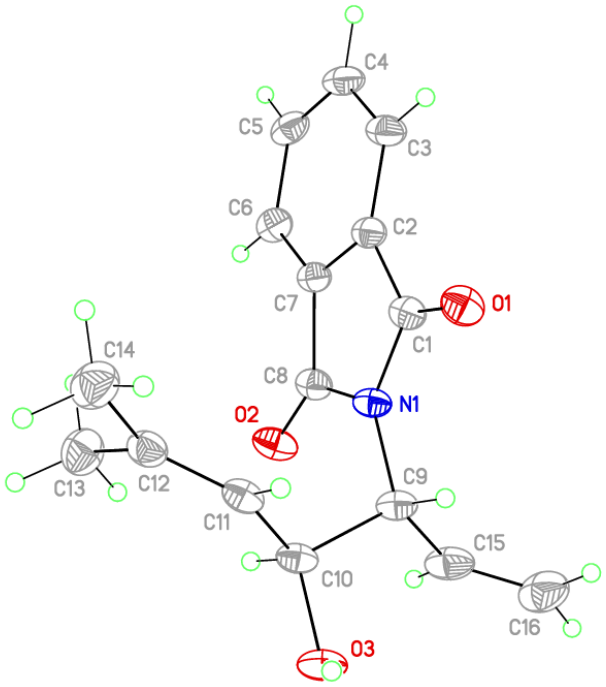
Figure 1. View of H-bound dimer formed in **3a** showing the heteroatom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. Dashed lines are indicative of an H-bonding interaction.



Single Crystal Diffraction Data for Coupling Product 3v

Empirical formula	C16 H17 N O3	
Formula weight	271.30	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	P 21	
Unit cell dimensions	a = 8.3815(2) Å	α= 90°.
	b = 22.4250(2) Å	β= 117.675(2)°.
	c = 8.6781(2) Å	γ = 90°.
Volume	1444.49(5) $Å^3$	
Z	4	
Density (calculated)	1.248 Mg/m^3	
Absorption coefficient	0.702 mm^{-1}	
F(000)	576	
Crystal size	0.31 x 0.18 x 0.11 mm^3	
Theta range for data collection	3.943 to 76.170°.	
Index ranges	-10<=h<=10, -28<=k<=28, -10<=l<=10	
Reflections collected	33708	
Independent reflections	5984 [R(int) = 0.0393]	
Completeness to theta = 67.684°	100.0 %	
Absorption correction	Gaussian and multi-scan	
Max. and min. transmission	1.00 and 0.713	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5984 / 1 / 389	
Goodness-of-fit on F^2	1.020	
Final R indices [I>2sigma(I)]	R1 = 0.0372, wR2 = 0.1006	
R indices (all data)	R1 = 0.0378, wR2 = 0.1026	
Absolute structure parameter	-0.09(6)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.385 and -0.211 $e.Å^{-3}$	

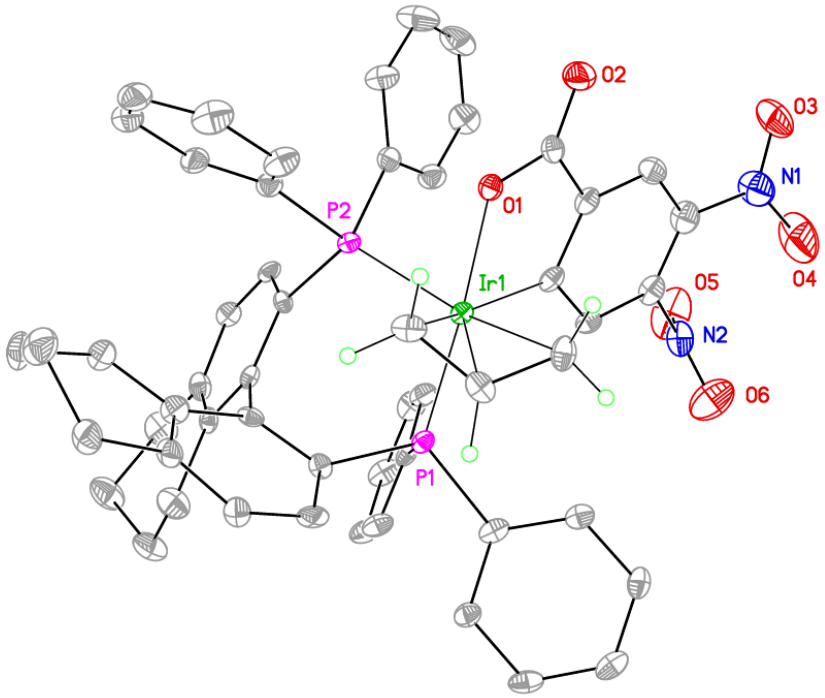
Figure 2. View of **3v** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



Single Crystal Diffraction Data for Ir-VI

Empirical formula	C58 H55 Ir N2 O7 P2	
Formula weight	1146.18	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 14.339(2) Å	α= 90°.
	b = 17.764(2) Å	β= 90°.
	c = 18.920(3) Å	γ = 90°.
Volume	4819.4(11) $Å^3$	
Z	4	
Density (calculated)	1.580 Mg/m^3	
Absorption coefficient	2.896 mm^{-1}	
F(000)	2320	
Crystal size	0.220 x 0.110 x 0.100 mm^3	
Theta range for data collection	2.293 to 28.413°.	
Index ranges	-19<=h<=19, -23<=k<=23, -25<=l<=25	
Reflections collected	67534	
Independent reflections	12021 [R(int) = 0.0906]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Numerical	
Max. and min. transmission	1.00 and 0.759	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	12021 / 420 / 631	
Goodness-of-fit on F^2	1.024	
Final R indices [I>2sigma(I)]	R1 = 0.0377, wR2 = 0.0773	
R indices (all data)	R1 = 0.0489, wR2 = 0.0806	
Absolute structure parameter	-0.007(4)	
Extinction coefficient	n/a	
Largest diff. peak and hole	1.197 and -0.918 $e.Å^{-3}$	

Figure 3. View of the Ir complex showing the heteroatom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms have been omitted for clarity.



Kinetic Studies

Standard Conditions: To a dried 5 mL volumetric flask under an argon atmosphere charged with with (R)-Ir-**VI** (53.7mg, 0.05 mmol, 5 mol%), phthalimido-allene (277.8 mg, 1.5 mmol, 150 mol%), KH_2PO_4 (136.1 mg, 1 mmol, 100 mol%), and 1,3,5-trimethoxybenzene (internal standard, 168.2 mg , 1 mmol, 100 mol%) was added 2-phenylethanol (120 μL, 1 mmol, 100 mol%). The flask was then filled to the mark with dioxane and sonicated until full dissolution. The reaction mixture was then transfer *via* syringe to a condenser-tube sealed with a rubber septa under an argon atmosphere. The reaction mixture was then heated to 100 °C.

Reaction progress was monitored by sampling followed by NMR analysis. The reaction was sampled by removable of approximately 100 μL of the reaction mixture *via* syringe and dilution with $CDCl_3$.

Table S1. Further reaction conditions for the kinetic experiments.

Experiment	[Ir] (M)	[1] (M)	[2a] (M)	[excess] [1]-[2a] (M)	Note
Standard	0.01	0.3	0.2	0.1	-
Different excess 1	0.01	0.6	0.2	0.4	-
Different excess 2	0.01	0.3	0.4	-0.1	-
Same excess	0.01	0.2	0.1	0.1	-
Same excess product addition	0.01	0.2	0.1	0.1	**3a** 0.08M
Increased catalyst	0.02	0.3	0.2	0.1	-
Added Aldehyde	0.01	0.3	0.2	0.1	*dehydro*-**2a** 0.01M

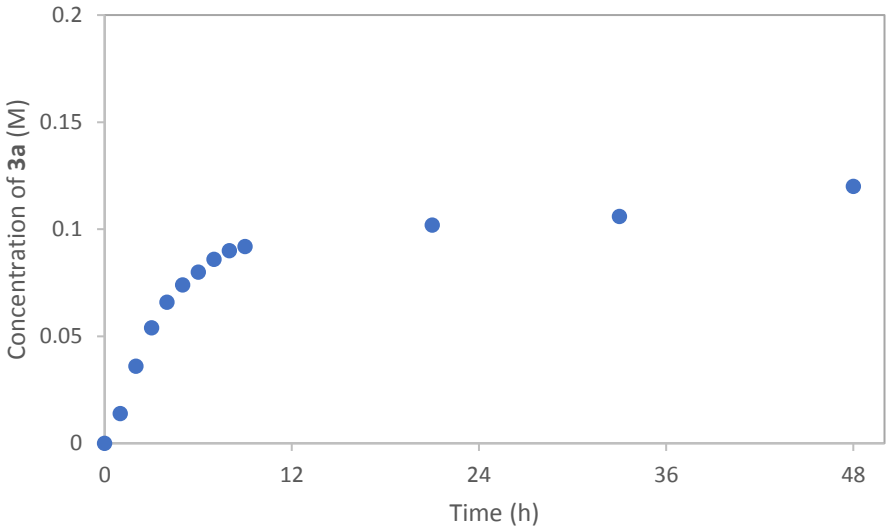


Figure 4. Product formation under standard conditions.

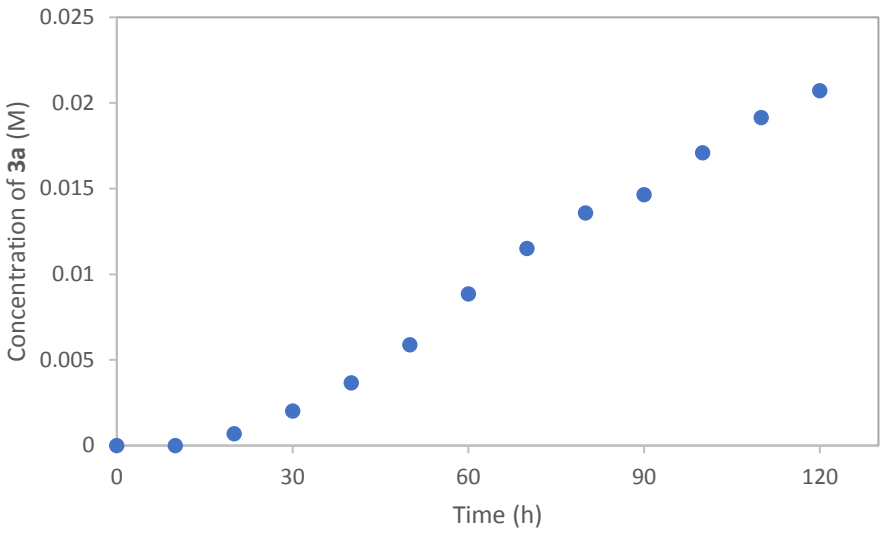


Figure 5. Product formation under standard conditions. Reaction monitored for first 2 hours to determine initial rate.

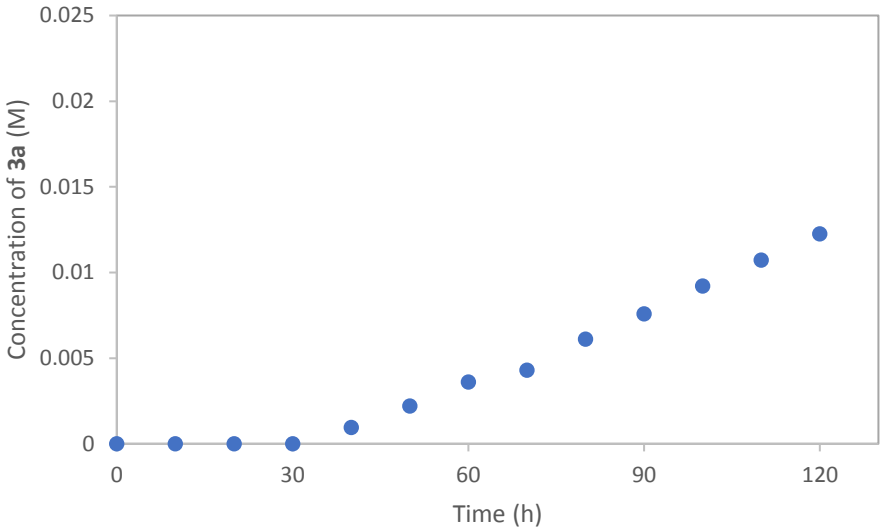


Figure 6. Product formation under standard conditions utilizing **deuterio-2a**. Reaction monitored for first 2 hours to determine initial rate.

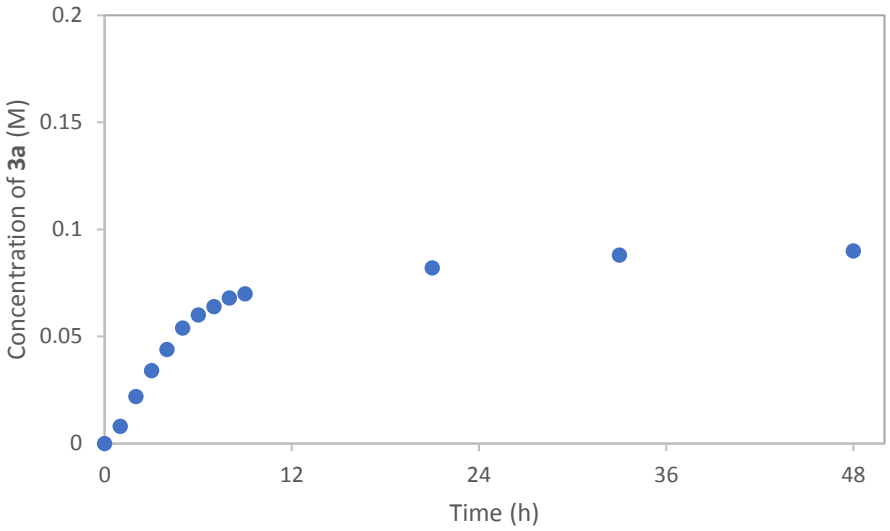


Figure 7. Product formation under different excess 1 conditions.

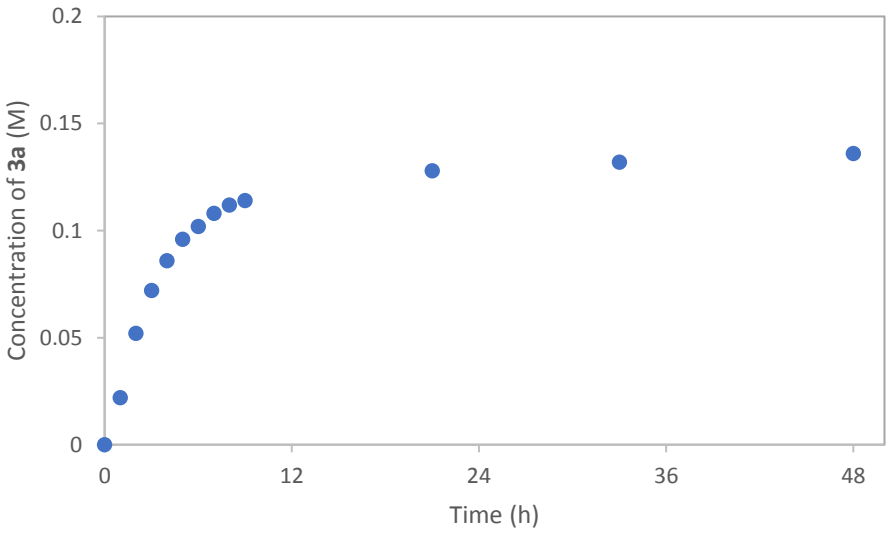


Figure 8. Product formation under different excess 2 conditions.

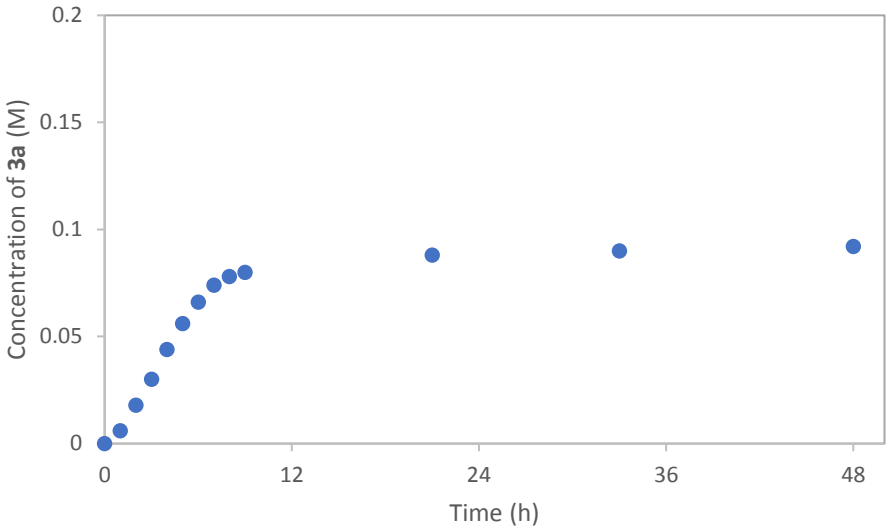


Figure 9. Product formation under same excess conditions.

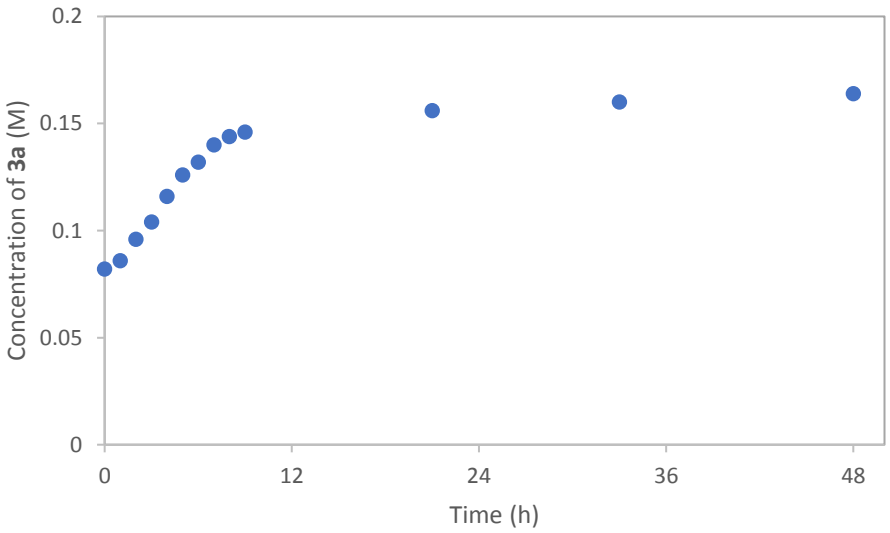


Figure 10. Product formation under same excess conditions with product addition.

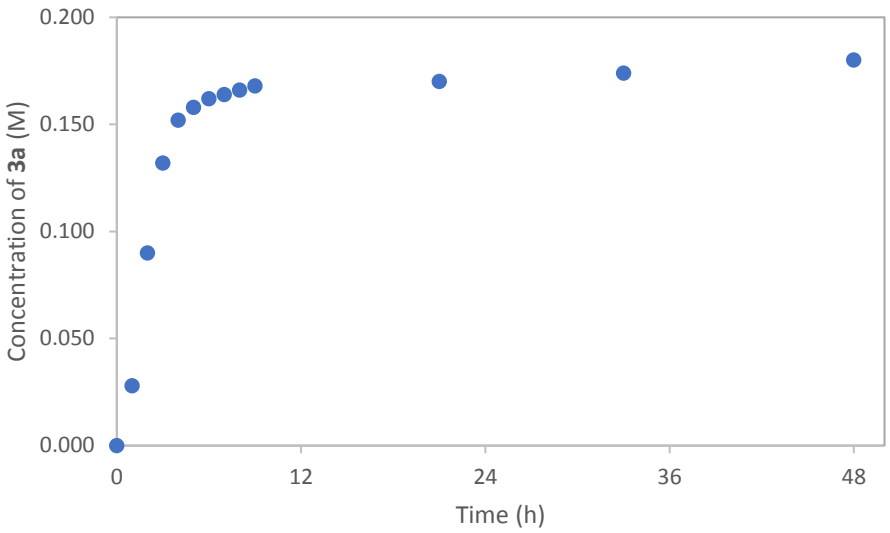


Figure 11. Product formation under increased catalyst conditions.

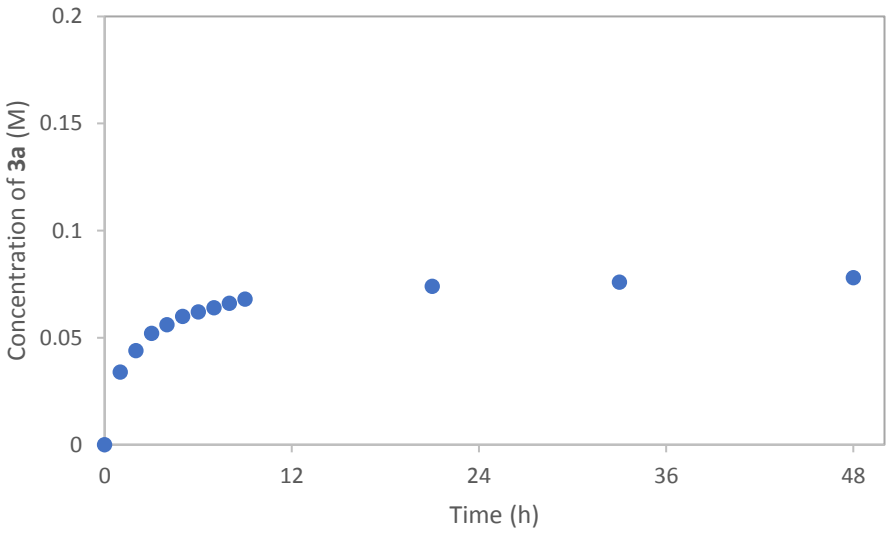


Figure 12. Product formation under standard conditions with 10 mol% aldehyde *dehydro*-**2a** added.

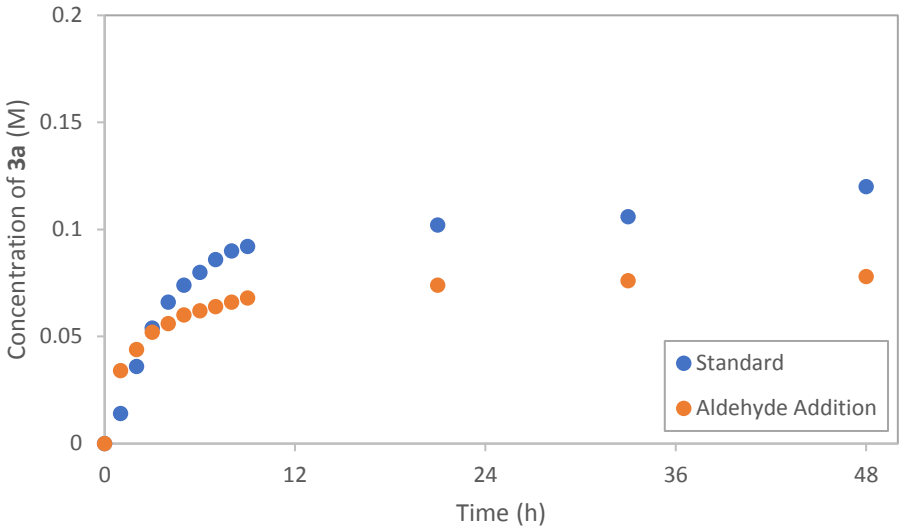


Figure 13. Product formation under standard conditions with 10 mol% aldehyde *dehydro*-**2a** added comparison to standard conditions – negative order.

In order to determine if any catalyst deactivation occurred during the reaction the same excess protocol was utilized. The collected product concentration data for both the standard and same excess data sets were converted to alcohol concentration data ($[\mathbf{2a}]_t = [\mathbf{2a}]_0 - [\mathbf{3a}]_t$). Since the starting concentration of the same excess experiments is different than that of the standard experiment, the same excess time data was adjusted accordingly. This method is representative of starting the reaction from two different starting points. At the point where the standard data set reaches the starting point of the same excess data set they then represent a reaction with the same conditions, with the exception of the first containing product already present and a catalyst that has completed more turnovers.[5] The failure of these two curves to overlap indicates that significant catalyst deactivation occurs. Additionally, in the case of the same excess conditions with product addition, a slight shift towards the standard conditions indicates that the product is contributing to the deactivation pathway. This is only a moderate contribution.

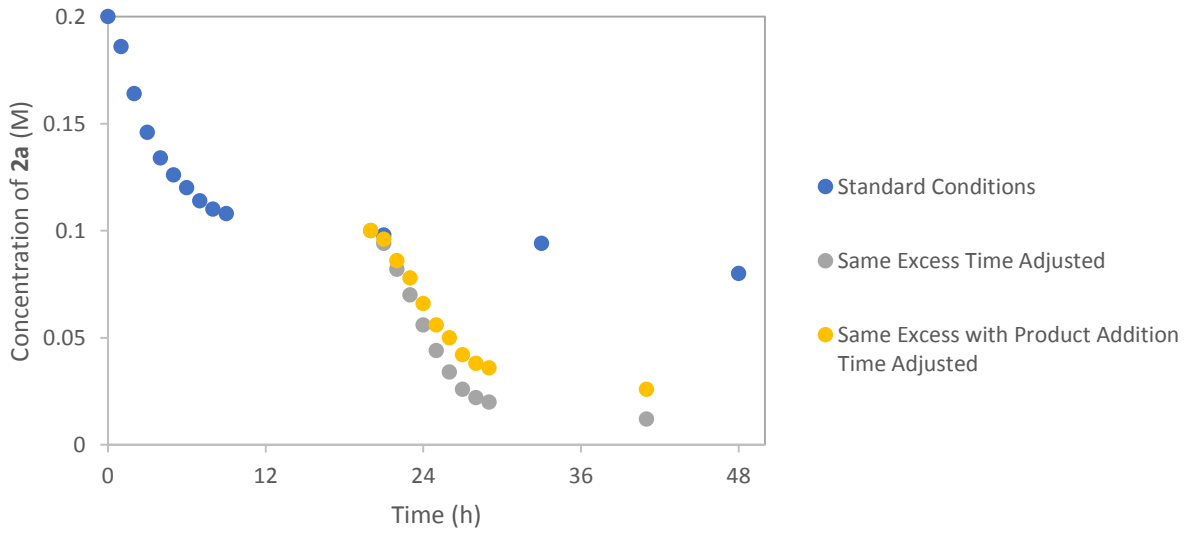


Figure 14. Evaluation of catalyst performance utilizing same excess protocol.

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(5) For a review on reaction progress kinetic analysis, see: Blackmond, D. G. *Angew. Chem. Int. Ed.* **2005**, *44*, 4302.