C–H Functionalization of Amines *via* Alkene-Derived Nucleophiles through Cooperative Action of Chiral and Achiral Lewis Acid Catalysts: Applications in Enantioselective Synthesis

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1. Procedures, Materials and Instrumentation

1.1 General Experimental Procedures

All reactions were performed in standard, oven-dried glassware fitted with rubber septa under an inert atmosphere of nitrogen unless otherwise described. Stainless steel syringes or cannulas were used to transfer air- and moisture-sensitive liquids. Reported concentrations refer to solution volumes at room temperature. Evaporation and concentration *in vacuo* were performed using house vacuum (ca. 40 mm Hg). Column chromatography was performed with SiliaFlash® 60 (40–63 micron) silica gel from Silicycle. Thin layer chromatography (TLC) was used for reaction monitoring and product detection using pre-coated glass plates covered with 0.25 mm silica gel with fluorescent indicator; visualization by UV light (λ_{ex} = 254 nm) or $KMnO_4$ stain.

1.2 Materials

Reagents were purchased in reagent grade from commercial suppliers and used without further purification, unless otherwise described. H_2O, in synthetic procedures, refers to distilled water. Chiral ligands were prepared accordingly to the procedures previously reported in the literature.[1]

1.3 Instrumentation

Proton nuclear magnetic resonance (^1H NMR) spectra and proton-decoupled carbon nuclear magnetic resonance (^{13}C {^1H} NMR) spectra were recorded at 25°C (unless stated otherwise) on Inova 600 (600 MHz) or Varian Unity/Inova 500 (500 MHz) or Oxford AS400 (400 MHz) spectrometers at the Boston College nuclear magnetic resonance facility. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent. Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent. The solvent peak was referenced to 0 ppm for ^1H for tetramethylsilane and 77.0 ppm for ^{13}C for $CDCl_3$. Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sp = septet, m = multiplet), coupling constants in Hertz (Hz).

Optical rotations were measured using a 1 mL cell with a 5 cm path length on a Rudolph Research Analytical Autopol IV Polarimeter. Infrared spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer. Data are represented as follows: frequency of absorption (cm^{-1}). High-resolution mass spectrometry was performed on a JEOL AccuTOF-DART (positive mode) or Agilent 6220 TOF-ESI (positive mode) at the Mass Spectrometry Facility, Boston College. Chiral HPLC analyses were carried using Agilent 1200 series instruments with Daicel CHIRALPAK® columns or Daicel CHIRALCEL® columns (internal diameter 4.6 mm, column length 250 mm, particle size 5 µm).

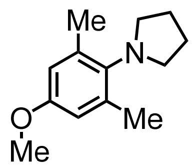
1.4 Abbreviations Used

Bn = benzyl, Boc = *tert*-butoxycarbonyl, DART = direct analysis in real time, DCM = dichloromethane, dr = diastereomeric ratio, er = enantiomeric ratio, ESI = electrospray ionization, Et_2O = diethyl ether, Et_3N = triethylamine, EtOAc = ethyl acetate, H_2O = water, HPLC = high pressure liquid chromatography, HR = high-resolution, LC = liquid chromatography, MS = mass spectrometry, NA = not applicable, PTLC = preparative thin layer chromatography, TBS = *tert*-butyldimethylsilyl, Tf = triflurommethanesulfonate, THF = tetrahydrofuran, TOF = time-of-flight.

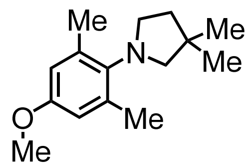
2. Experimental Section

2.1 Substrate Preparation

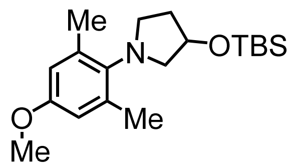
Table SI-1. List of Amine Substrates



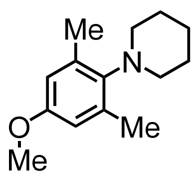
1a



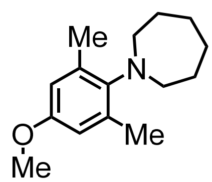
1l



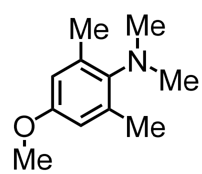
1m



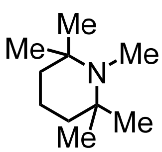
1n



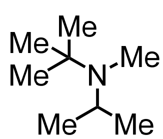
1o



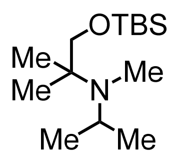
1p



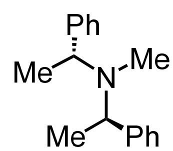
1q



1r



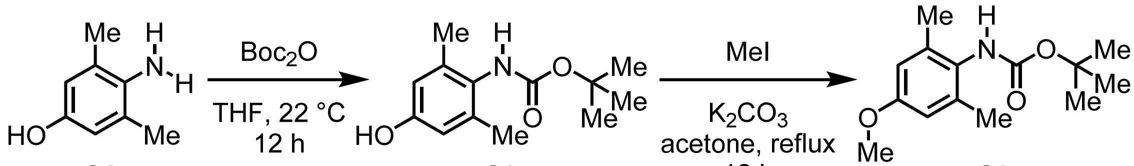
1s



1t

Amines **1q** and **1r** were obtained from commercial sources. Substrates **1a**,[2] **1l**,[2] **1m**,[2] **1n**,[2] **1o**,[2] 1p,[3] 1s[4-6] and **1t**[7,8] were prepared accordingly to the literature procedures. The spectroscopic data for the newly synthesized molecules **(1a**, **1l**, **1m**, **1n**, **1o**, **1p**, **1s**, and **1t)** are described as the following.

Preparation of Amine Substrates[9,10]

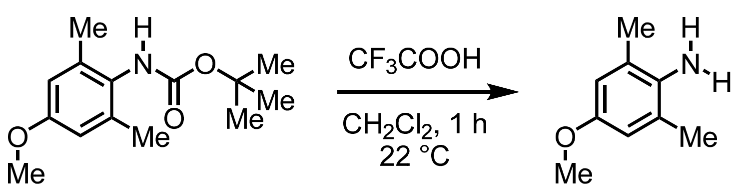


S1 **S2** **S3**

***tert*-Butyl (4-hydroxy-2,6-dimethylphenyl)carbamate (S2)**: *tert*-Butyl (4-hydroxy-2,6-dimethylphenyl)carbamate was prepared following a known procedure.[9] To a solution of 4-amino-3,5-dimethylphenol (**S1**, 10.0 g, 72.9 mmol) in THF (200 mL), was added di-*tert*-butyl dicarbonate (16.7 mL, 72.9 mmol) in a dropwise manner. The reaction mixture was allowed to stir at 22 °C for 12 hours. Upon completion, the reaction mixture was concentrated and used without further purification. The spectroscopic data of **S2** matched those reported by Nam.[10]

***tert*-Butyl (4-methoxy-2,6-dimethylphenyl)carbamate (S3)**: *tert*-Butyl (4-methoxy-2,6-dimethylphenyl)carbamate was prepared following a known procedure.[11] Carbamate **S2** (8.6 g, 36.4 mmol) was dissolved in acetone (50 mL). To the solution was added potassium carbonate (6.1 g, 54.6 mmol) and iodomethane (2.3 mL, 36.4 mmol), dropwise. The reaction mixture was heated to reflux and allowed to stir for 12 hours. Upon completion (monitored by TLC), the reaction was quenched with a saturated aqueous solution of KOH (50 mL), extracted with Et_2O (3 x 50 mL), dried ($MgSO_4$), and concentrated *in vacuo*. The crude reaction mixture was subjected to silica gel chromatography to afford a colorless solid (5.9 g, 65% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.60 (s, 2H), 3.76 (s, 3H), 2.24 (s, 6H), 1.49 (s, 9H).

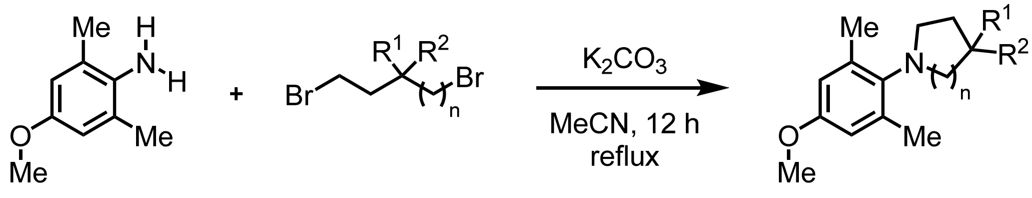
Procedure for the Removal of *N*-Boc Group[12]



S3 **S4**

To a solution of carbamate **S3** in DCM (0.3 M), CF_3COOH (5.0 equiv.) was added dropwise at 22 °C. Upon completion of the reaction (monitored by TLC), aqueous $NaHCO_3$ was added until the solution was alkaline, extracted with DCM, dried ($MgSO_4$), filtered, and concentrated. The crude reaction mixture was subjected to silica gel chromatography (hexanes/EtOAc = 19:1) to give the product as a yellow liquid. The spectroscopic data of **S4** matched those reported by Organ.[13]

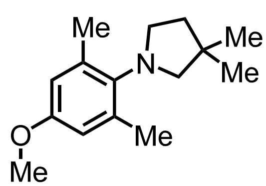
General Procedure for Cyclic Amine Substrates



S4 **1a**, **1l**, **1m**, **1n**, **1o**

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine (1a)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine was prepared following a known procedure.[2] A mixture of aniline **S4** (1.0 g, 6.6 mmol), K_2CO_3 (2.7 g, 19.8 mmol), and 1,4-dibromobutane (1.2 mL, 9.9 mmol) in acetonitrile (10 mL) was heated to reflux for 12 hours. Upon completion, the reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$, extracted with EtOAc (3 x 25 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude reaction mixture was subjected to silica gel chromatography (hexanes/EtOAc = 29:1) to give the product as a yellow liquid (1.1 g, 82%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.58 (s, 2H), 3.75 (s, 3H), 3.20 – 3.08 (m, 4H), 2.23 (s, 6H), 1.99 – 1.90 (m, 4H).

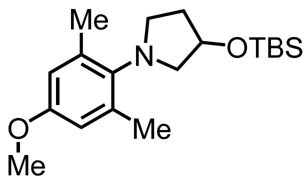


1l

1-(4-Methoxy-2,6-dimethylphenyl)-3,3-dimethylpyrrolidine (1l)

1-(4-Methoxy-2,6-dimethylphenyl)-3,3-dimethylpyrrolidine was synthesized using the **General Procedure for Cyclic Amine Substrates** on a 5.9 mmol scale, using 1,4-dibromo-2,2-dimethylbutane. The product was obtained as a colorless liquid (1.2 g, 88%). **^{1}H NMR**

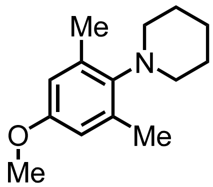
(600 MHz, $CDCl_3$) δ 6.57 (s, 2H), 3.75 (s, 3H), 3.25 (t, *J* = 6.9 Hz, 2H), 2.90 (s, 2H), 2.24 (s, 6H), 1.73 (t, *J* = 6.9 Hz, 2H), 1.18 (s, 6H).



1m

3-((*tert*-Butyldimethylsilyl)oxy)-1-(4-methoxy-2,6-dimethylphenyl)pyrrolidine (1m)

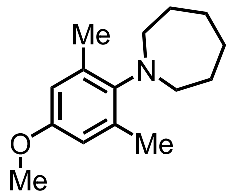
3-((*tert*-Butyldimethylsilyl)oxy)-1-(4-methoxy-2,6-dimethylphenyl)pyrrolidine was synthesized using the **General Procedure for Cyclic Amine Substrates** on a 16.5 mmol scale, using *tert*-butyl((1,4-dibromobutan-2-yl)oxy)dimethylsilane. The product was obtained as a colorless liquid (4.9 g, 89%). ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 6.57 (s, 2H), 4.48 (tt, *J* = 5.2, 3.5 Hz, 1H), 3.75 (s, 3H), 3.41 – 3.35 (m, 2H), 3.08 (td, *J* = 7.8, 4.1 Hz, 1H), 3.02 (dd, *J* = 8.9, 3.1 Hz, 1H), 2.25 (s, 6H), 2.12 – 2.04 (m, 1H), 1.92 – 1.85 (m, 1H), 0.90 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H).



1n

1-(4-Methoxy-2,6-dimethylphenyl)piperidine (1n)

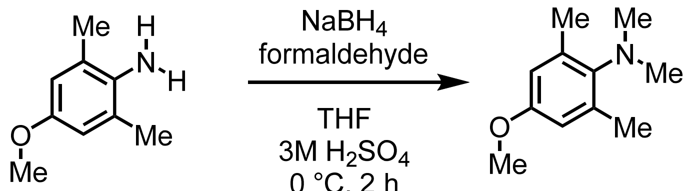
1-(4-Methoxy-2,6-dimethylphenyl)piperidine was prepared using the **General Procedure for Cyclic Amine Substrates** on 1.0 mmol scale, using 1,5-dibromopentane. The product was obtained as a white solid (165 mg, 75%). ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 6.52 (s, 2H), 3.74 (s, 3H), 2.98 (t, *J* = 5.1 Hz, 4H), 2.29 (s, 6H), 1.65 – 1.58 (m, 4H), 1.58 – 1.51 (m, 2H).



1o

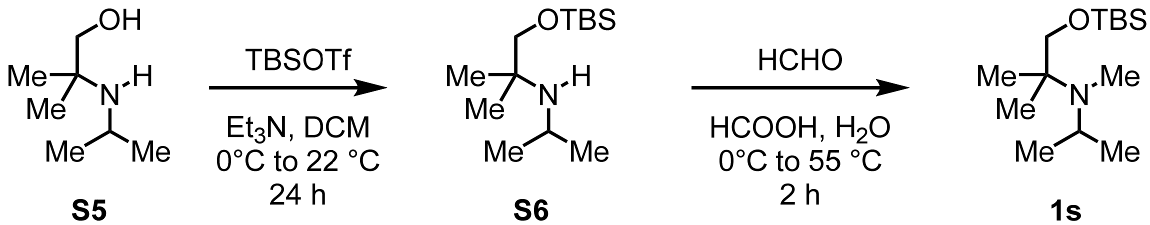
1-(4-Methoxy-2,6-dimethylphenyl)azepane (1o)

1-(4-Methoxy-2,6-dimethylphenyl)azepane was prepared using the **General Procedure for Cyclic Amine Substrates** on 4.7 mmol scale, using 1,6-dibromohexane. The product was obtained as a colorless oil (371 mg, 34%). ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 6.56 (s, 2H), 3.75 (s, 3H), 3.09 – 3.01 (m, 4H), 2.29 (s, 6H), 1.70 (s, 8H).



4-Methoxy-*N,N*,2,6-tetramethylaniline (1p)

4-Methoxy-*N,N*,2,6-tetramethylaniline was prepared following a known procedure.[3] To a solution of formaldehyde (37% aq. solution, 2.95 mL, 39.7 mmol) and sulfuric acid (3 M, 15.9 mmol) was added 4-methoxy-2,6-dimethylaniline **S4** (1.0 g, 6.6 mmol) in THF (50 mL) at 0 °C. Subsequently, $NaBH_4$ (1.75 g, 46.3 mmol) was added in portions to the reaction mixture while cooling. Upon completion of the reaction (monitored by TLC), the crude reaction mixture was made basic with aq. NaOH (1 M). The supernatant was decanted and the residue is treated with water (10 mL) and extracted with Et_2O (3 x 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude reaction mixture was subjected to silica gel chromatography (hexanes/EtOAc = 9:1) and amine **1p** was obtained as a colorless oil (1.1 g, 94%). ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 6.54 (s, 2H), 3.75 (s, 3H), 2.79 (s, 6H), 2.28 (s, 6H).

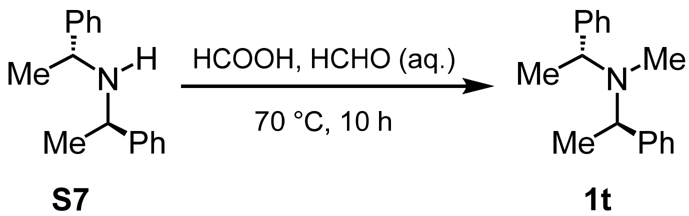


1-((*tert*-Butyldimethylsilyl)oxy)-*N*-isopropyl-2-methylpropan-2-amine (S6)

1-((*tert*-Butyldimethylsilyl)oxy)-*N*-isopropyl-2-methylpropan-2-amine was prepared following a known procedure.[4] To a solution of 2-(isopropylamino)-2-methylpropan-1-ol[5] (20 mmol), and triethylamine (26 mmol) in DCM (50 mL) at 0 °C was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (26 mmol) dropwise. The reaction mixture was allowed to stir at room temperature for 24 hours. Upon completion, the reaction was quenched with H_2O (20 mL), the organic phase was separated and the aqueous phase was extracted with DCM (3 × 50 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude reaction mixture was subjected to silica gel chromatography (hexanes/Et_3N = 20:1) to afford **S6** (4.68 g, 19.08 mmol, 95%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.32 (s, 2H), 2.87 (m, 1H), 1.04 (d, *J* = 6.3 Hz, 6H), 1.01 (s, 6H), 0.89 (s, 9H), 0.04 (s, 6H).

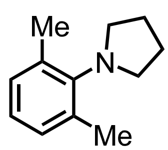
1-((*tert*-Butyldimethylsilyl)oxy)-*N*-isopropyl-*N*,2-dimethylpropan-2-amine (1s)

1-((*tert*-Butyldimethylsilyl)oxy)-*N*-isopropyl-*N*,2-dimethylpropan-2-amine was prepared following a known procedure.[6] A 37% aq. solution of formaldehyde (1.6 g, 22 mmol) was added to a mixture of 1-((*tert*-butyldimethylsilyl)oxy)-*N*-isopropyl-2-methylpropan-2-amine **S6** (4.43 g, 18.1 mmol) and 88% formic acid (1.8 g, 39 mmol) at 0 °C. The reaction mixture was kept at 55 °C for 2 hours. Upon completion (monitored by TLC), the reaction was quenched with 8.0 M KOH (10 mL), extracted with Et_2O (3 x 50 mL), dried ($MgSO_4$), and concentrated *in vacuo*. The crude reaction mixture was subjected to silica gel chromatography (hexanes/Et_3N = 50:1) to afford a colorless oil (3.2 g, 68% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.43 (s, 2H), 3.31 (hept, *J* = 6.6 Hz, 1H), 2.21 (s, 3H), 1.05 (s, 6H), 1.00 (d, *J* = 6.8 Hz, 6H), 0.89 (s, 9H), 0.03 (s, 6H).



(*R*)-*N*-Methyl-1-phenyl-*N*-((*R*)-1-phenylethyl)ethan-1-amine (1t)

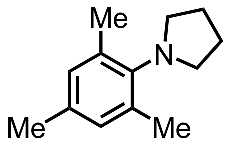
(*R*)-*N*-Methyl-1-phenyl-*N*-((*R*)-1-phenylethyl)ethan-1-amine was prepared following a known procedure.[7] A 37% aq. solution of formaldehyde (4.4 mmol) was added to a mixture of (*R*)-bis((*R*)-1-phenylethyl)amine **S7** (0.54 g, 2.2 mmol) and 88% formic acid (8.8 mmol) at 0 °C. The reaction mixture was kept at 70 °C for 10 hours. Upon completion (monitored by TLC), the reaction was basified with 1 M NaOH, extracted with EtOAc (3 x 40 mL), dried ($MgSO_4$), and concentrated *in vacuo*. The crude reaction mixture was subjected to silica gel chromatography (hexanes/Et_3N = 50:1) to afford a colorless oil (440 mg, 84% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 7H), 7.26 – 7.21 (m, 2H), 3.82 (q, J = 6.8 Hz, 2H), 2.00 (s, 3H), 1.33 (d, J = 6.8 Hz, 6H).[8]



1w

1-(2,6-dimethylphenyl)pyrrolidine (1w)

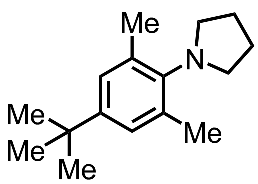
1-(2,6-dimethylphenyl)pyrrolidine was prepared using the **General Procedure for Cyclic Amine Substrates** on 41 mmol scale. The product was obtained as a colorless oil (6.2 g, 86%). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.06 – 7.00 (m, 2H), 6.97 (q, J = 7.9 Hz, 1H), 3.25 – 3.08 (m, 4H), 2.26 (d, J = 3.9 Hz, 6H), 2.05 – 1.92 (m, 4H).



1x

1-(2,6-dimethylphenyl)pyrrolidine (1x)

1-(2,6-dimethylphenyl)pyrrolidine was prepared using the **General Procedure for Cyclic Amine Substrates** on 37 mmol scale. The product was obtained as a colorless oil (6.5 g, 93%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.86 (d, J = 1.5 Hz, 2H), 3.25 – 3.11 (m, 4H), 2.26 (d, J = 1.5 Hz, 3H), 2.23 (d, J = 1.5 Hz, 6H), 1.97 (td, J = 6.3, 5.5, 2.9 Hz, 4H).

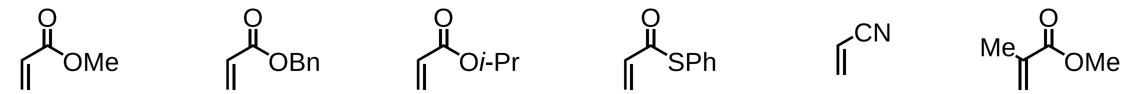


1y

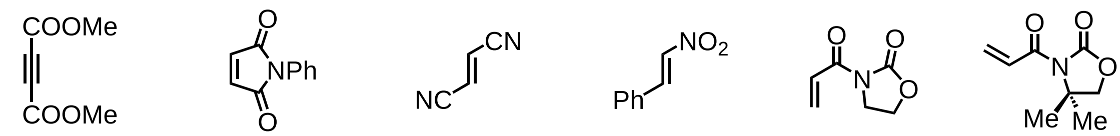
1-(4-(*tert*-Butyl)-2,6-dimethylphenyl)pyrrolidine (1y)

1-(4-(*tert*-Butyl)-2,6-dimethylphenyl)pyrrolidinewas prepared using the **General Procedure for Cyclic Amine Substrates** on 5.6 mmol scale. The product was obtained as a colorless oil (1.2 g, 92%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.03 (d, J = 0.9 Hz, 2H), 3.22 – 3.10 (m, 4H), 2.25 (d, J = 0.6 Hz, 6H), 2.02 – 1.90 (m, 4H), 1.29 (s, 9H).

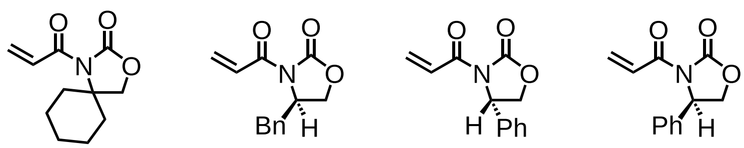
Table SI-2. *α,β*-Unsaturated Substrates



2a **2c** **2d** **2e** **2f** **2g**



2h **2i** **2j** **2k** **2q** **2r**



2s **2t** **2u-(*S*)** **2u-(*R*)**

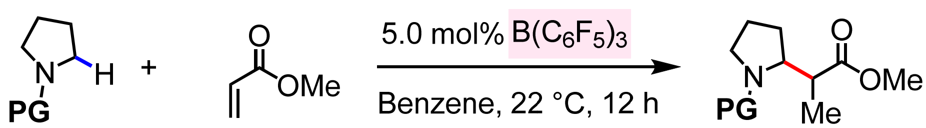
α,β-Unsaturated molecules **2a**, **2c**, **2f**, **2g**, **2h**, **2i**, **2j**, and **2k** were obtained from commercial sources. Substrates **2d**,[14] **2e**,[15] **2q**,[16] **2r**,[17] **2s**,[17] **2t**,[16] **2u-(*S*)**,[16] and **2u-(*R*)**[16] were prepared accordingly to the procedures previously reported in the literatures. Substrates **2q**, **2r**, **2s**, **2t**, **2u-(*S*)**, and **2u-(*R*)** were prepared fresh and stored in the freezer for up to 1 month.

2.2 Optimization Studies

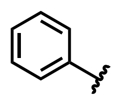
Experimental Procedure for the Optimization of the Amine Protecting Group (Table SI-3)

An oven-dried sealed tube equipped with a magnetic stir bar was used. Amine **1** (0.20 mmol), methyl acrylate **2a** (0.24 mmol), $B(C_6F_5)_3$ (0.01 mmol), and benzene (0.2 mL) were added to the reaction vessel under nitrogen atmosphere. The reaction mixture was stirred at 22 °C for 12 h. Upon completion, the reaction mixture was concentrated *in vacuo*. The product yield was determined by the ^{1}H NMR analysis of the unpurified product mixture using mesitylene as the internal standard.

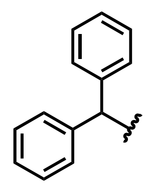
Table SI-3. Evaluation of Amine Protecting Group



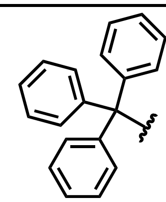
1 **2a** **3**



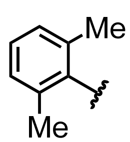
3-PG1
<10% yield



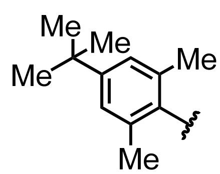
3-PG2
<10% yield



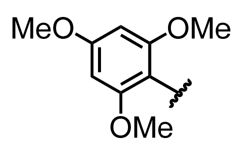
3-PG3
<10% yield



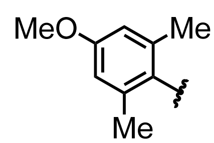
3-PG4
>95% yield



3-PG5
92% yield



3-PG6
<10% yield



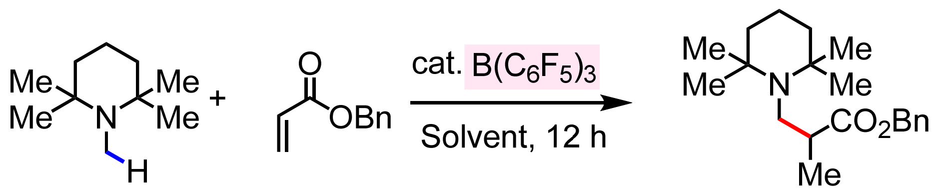
3-PG7
>95% yield

[a] Conditions: **1** (0.2 mmol), **2a** (0.24 mmol), $B(C_6F_5)_3$ (5.0 mol%), benzene (0.2 mL), under N_2, 22 °C, 12 h. [b] The yield was determined by ^{1}H NMR analysis of the unpurified product mixture using mesitylene as the internal standard.

Experimental Procedure for the Optimization of the 1,2,2,6,6-Pentamethylpiperidine Substrate (Table SI-4)

An oven-dried sealed tube equipped with a magnetic stir bar was used. Amine **1q** (0.20 mmol), benzyl acrylate **2c** (0.24 mmol), $B(C_6F_5)_3$, and solvent (0.4 mL) were added to the reaction vessel under nitrogen atmosphere. Then, the reaction mixture was stirred for 12 h. Upon completion, the reaction mixture was concentrated *in vacuo*. The product yield was determined by the ^{1}H NMR analysis of the unpurified product mixture using mesitylene as the internal standard.

Table SI-4. Evaluation of Substrate **1q**



1q **2c** **4a**

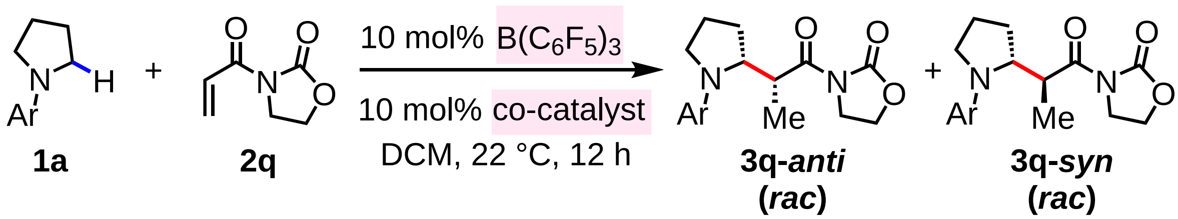
entry	Temp (°C)	$B(C_6F_5)_3$ (mol%)	Solvent	**4a** (%)
1	22	5	DCM	< 5
2	22	5	Benzene	< 5
3	22	10	Benzene	85
4	70	10	Benzene	99

[a] Conditions: **1q** (0.2 mmol), **2c** (0.24 mmol), $B(C_6F_5)_3$ (cat.), solvent (0.4 mL), under N_2, 12 h. [b] The yield was determined by ^{1}H NMR analysis of the unpurified product mixture using mesitylene as the internal standard.

Experimental Procedure for the Optimization of the Lewis Acid Co-Catalyst (Table SI-5)

An oven-dried sealed tube equipped with a magnetic stir bar was used. 1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.10 mmol), 3-acryloyloxazolidin-2-one **2q** (0.12 mmol), $B(C_6F_5)_3$ (0.01 mmol), Lewis acid co-catalyst (0.01 mmol) and DCM (0.3 mL) were added to the reaction vessel under nitrogen atmosphere. The reaction mixture was stirred at 22 °C for 12 h. Upon completion, the reaction mixture was filtered through silica gel and concentrated *in vacuo*. The product yield was determined by the ^{1}H NMR analysis of the unpurified product mixture using mesitylene as the internal standard.

Table SI-5. Evaluation of Co-Catalyst



entry	co-catalyst	yield (%)	***anti:syn***
1	None	35	3.2:1
2	CuOTf·Toluene	86	2.6:1
3	$Ni(OTf)_2$	31	4.2:1
4	$Mg(OTf)_2$	38	3.8:1

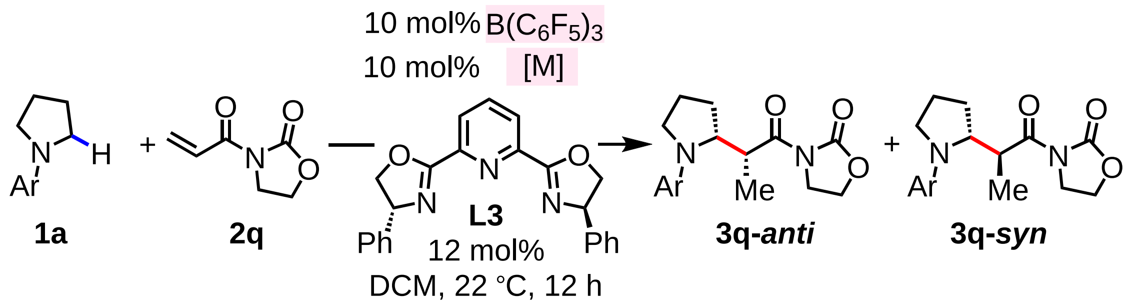
[a] Conditions: **1a** (0.1 mmol), **2q** (0.12 mmol), $B(C_6F_5)_3$ (10 mol%), cocatalyst (10 mol%), DCM (0.3 mL), under N_2, 22 °C, 12 h. [b] The yield was determined by ^{1}H NMR analysis of the unpurified product mixture using mesitylene as the internal standard.

Experimental Procedure for the Optimization of the Metal with L3 (Table SI-6)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To this tube were added Lewis acid co-catalyst (0.01 mmol), 2,6-bis((*R*)-4-phenyl-4,5-dihydrooxazol-2-yl)pyridine **L3** (0.012 mmol), and DCM (0.2 mL) under nitrogen atmosphere. The mixture was stirred for 20 min at 22 °C. Subsequently, 3-acryloyloxazolidin-2-one **2q** (0.12 mmol), 1-(4-methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.10 mmol), $B(C_6F_5)_3$ (0.01 mmol) and DCM (0.1 mL) were added to the reaction vessel, and the resulting mixture was stirred at 22 °C for 12 h. Upon completion, the reaction mixture was filtered through a plug of silica gel and concentrated *in vacuo*. The product yield and *anti:syn* ratio were determined by the ^{1}H NMR analysis of the unpurified product mixture using mesitylene as the internal standard.

The Mannich product was purified and isolated by preparative TLC (4:1 hexanes/EtOAc). The er value of each diastereomer was determined by HPLC analysis of the isolated product.

Table SI-6. Evaluation of Metal with **L3**



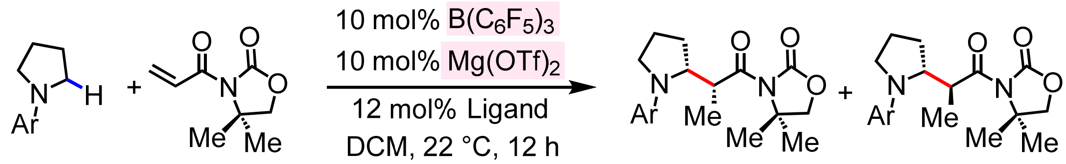
entry	[M]	yield (%)	***anti*:*syn***	enantiomeric ratio	
				3q-*anti*	**3q-*syn***
1	None(without **L3**)	35	4.8:1	NA	NA
2	None(with **L3**)	<5	NA	NA	NA
3	CuOTf·Toluene	71	3.2:1	50:50	50:50
4	$Zn(OTf)_2$	15	1:1	50:50	50:50
5	$Mg(ClO_4)_2$	40	3.4:1	50:50	50:50
6	$Sc(OTf)_3$	<5	NA	NA	NA
7	$Ni(BF_4)_2 \cdot H_2O$	<5	NA	NA	NA
8	$Fe(ClO_4)_3 \cdot H_2O$	<5	NA	NA	NA
9	$Mg(OTf)_2$	66	2.3:1	72:28	75:25

[a] Conditions: **1a** (0.1 mmol), **2q** (0.12 mmol), $B(C_6F_5)_3$ (10 mol%), [M] (10 mol%), **L3** (12 mol%), DCM (0.3 mL), under N_2, 22 °C, 12 h. [b] The yield and *anti:syn* ratio were determined by ^1H NMR analysis of the unpurified product mixture using mesitylene as the internal standard.

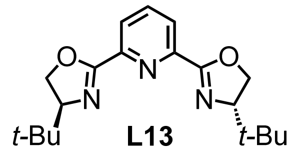
Experimental Procedure for the Optimization of PyBOX Ligand (Table SI-7)

An oven-dried sealed tube equipped with a magnetic stir bar was used. To this tube were added $Mg(OTf)_2$ (0.01 mmol), ligand (0.012 mmol), DCM (0.2 mL) under nitrogen atmosphere. The mixture was stirred for 20 min at 22 °C. Subsequently, 3-acryloyl-4,4-dimethyloxazolidin-2-one **2r** (0.12 mmol), 1-(4-methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.10 mmol), $B(C_6F_5)_3$ (0.01 mmol), and DCM (0.1 mL) were added to the reaction vessel, and the resulting mixture was stirred at 22 °C for 12 h. Upon completion, the reaction mixture was filtered through a pad of silica gel and concentrated *in vacuo*. The product yield and *anti:syn* ratio were determined by the ^{1}H NMR analysis of the unpurified product mixture using mesitylene as the internal standard. The Mannich product was purified and isolated by preparative TLC (4:1 hexanes/EtOAc). The er values of each diastereomer was determined by HPLC analysis of the isolated product.

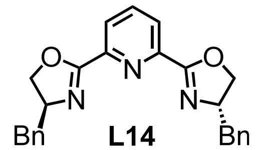
Table SI-7. Evaluation of Chiral Ligands



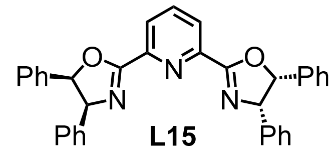
1a + **2r** → **3r-*anti*** + **3r-*syn***



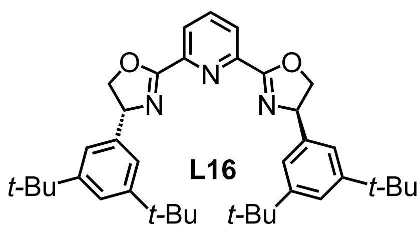
3r, <5% yield



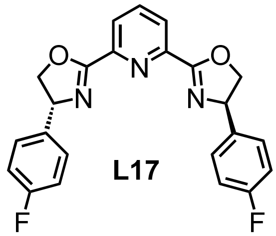
3r, 39% yield
anti*:*syn 4.5:1
anti, 34:66 er
syn, 28:72 er



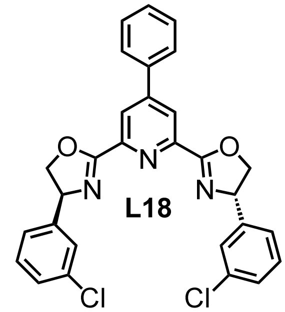
3r, <5% yield



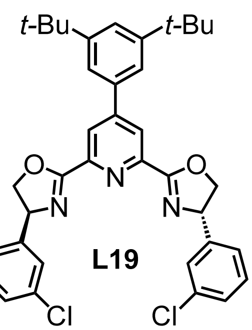
3r, <5% yield



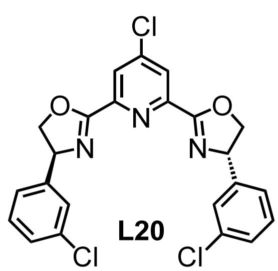
3r, 26% yield
anti*:*syn 3.3:1
anti, 93:7 er
syn, 94:6 er



3r,<5% yield



3r,<5% yield

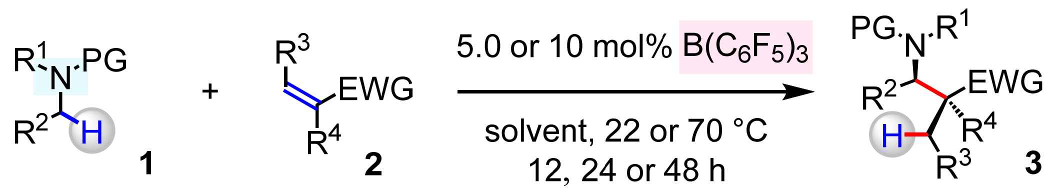


3r, 69% yield
anti*:*syn 4.3:1
anti, 4:96 er
syn, 3:97 er

[a] Conditions: **1a** (0.1 mmol), **2r** (0.12 mmol), $B(C_6F_5)_3$ (10 mol%), $Mg(OTf)_2$ (10 mol%), Ligand (12 mol%), DCM (0.3 mL), under N_2, 22 °C, 12 h. [b] The yield was determined by ^1H NMR analysis of the unpurified product mixture using mesitylene as the internal standard.

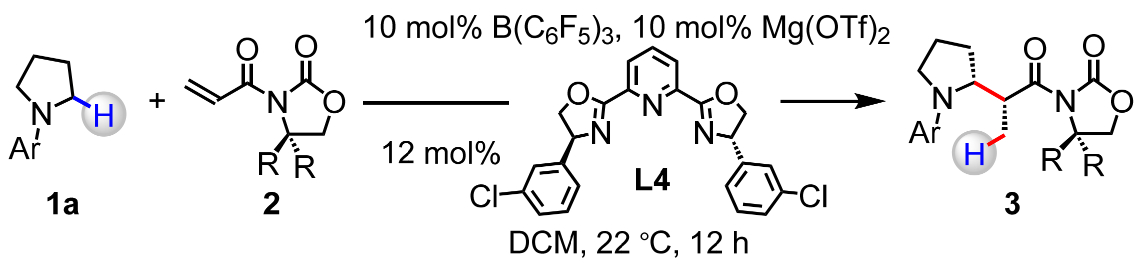
2.3 General Procedures for the Stereoselective Coupling of *N*-Alkylamines and *α,β*-Unsaturated Molecules

General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions



To a 15 mL oven-dried sealed tube was added amine **1** (0.2 mmol, 1 equiv.), *α,β*-unsaturated compound **2** (0.24 mmol, 1.2 equiv.), a catalytic amount of $B(C_6F_5)_3$ and solvent under nitrogen atmosphere. The reaction mixture was stirred at either 22 °C or 70 °C for 12 to 48 hours (see **SI-Section 3.2** for details). Upon completion, the reaction mixture was diluted with EtOAc, concentrated *in vacuo* and purified by silica gel column chromatography.

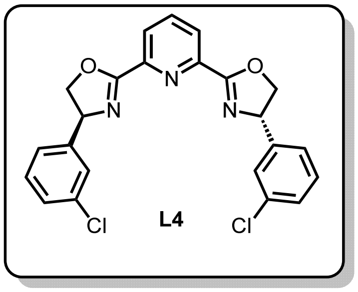
General Procedure for Stereoselective Mannich Reactions



An oven-dried sealed tube equipped with a magnetic stir bar was used. To this tube were added $Mg(OTf)_2$ (0.02 mmol), ligand **L4** (0.024 mmol), DCM (0.2 mL) under nitrogen atmosphere. The mixture was stirred for 20 min at 22 °C, then oxazolidinone substrate **2** (0.30 mmol), 1-(4-methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.20 mmol), $B(C_6F_5)_3$ (0.02 mmol), and DCM (0.1 mL) were added to the vessel. The reaction mixture was stirred at 22 °C for 12 h. Upon completion, the crude mixture was filtered through a pad of silica gel and concentrated *in vacuo*. The Mannich product was purified and isolated by silica gel column chromatography. The *anti*:*syn* ratio was determined by ^{1}H NMR analysis of the crude reaction mixture. The er values of each diastereomer was determined by HPLC analysis of the isolated product.

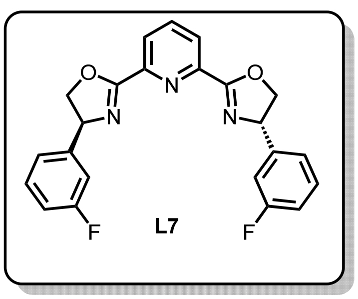
3. Analytical Data

3.1 Characterization of Chiral Ligands



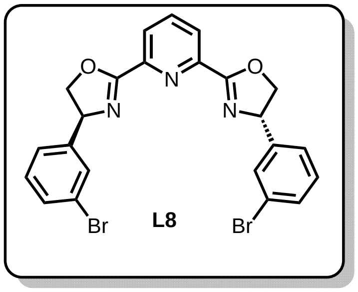
2,6-Bis((*S*)-4-(3-chlorophenyl)-4,5-dihydrooxazol-2-yl)pyridine (L4)

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.9 Hz, 2H), 7.95 (t, *J* = 7.8 Hz, 1H), 7.33 (s, 2H), 7.31 – 7.26 (m, 4H), 7.20 (dt, *J* = 7.0, 1.8 Hz, 2H), 5.45 (dd, *J* = 10.3, 8.5 Hz, 2H), 4.93 (dd, *J* = 10.4, 8.7 Hz, 2H), 4.39 (t, *J* = 8.6 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.46, 149.22, 146.34, 140.24, 137.38, 132.75, 130.64, 129.64, 129.13, 127.62, 77.92, 72.43; **IR** (neat) 3061, 2967, 2899, 1637, 1571, 1429, 1379, 1250, 1106, 1075, 969, 784, 735, 691 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{23}H_{18}N_3O_2Cl_2$ (MH^+): 438.0776; found: 438.0784.



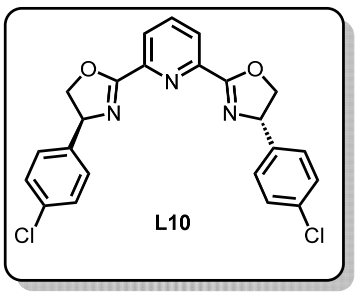
2,6-Bis((*S*)-4-(3-fluorophenyl)-4,5-dihydrooxazol-2-yl)pyridine (L7)

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (d, *J* = 7.8 Hz, 2H), 7.93 (t, *J* = 7.9 Hz, 1H), 7.31 (td, *J* = 7.9, 5.8 Hz, 2H), 7.09 (dt, *J* = 7.6, 1.2 Hz, 2H), 7.03 (dt, *J* = 9.7, 2.1 Hz, 2H), 6.98 (td, *J* = 8.4, 2.4 Hz, 2H), 5.45 (dd, *J* = 10.3, 8.6 Hz, 2H), 4.92 (dd, *J* = 10.4, 8.6 Hz, 2H), 4.38 (t, *J* = 8.6 Hz, 2H).; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.67, 162.97 (d, *J* = 248 Hz), 146.50, 144.15 (d, *J* = 6.9 Hz), 137.47, 130.27 (d, *J* = 8.1 Hz), 126.34, 122.29 (d, *J* = 2.8 Hz), 114.60 (d, *J* = 21.0 Hz), 113.67 (d, *J* = 22.0 Hz), 75.17, 69.68 (d, *J* = 1.8 Hz); **IR** (neat) 3066, 2969, 2901, 1637, 1588, 1448, 1379, 1246, 1140, 1106, 1075, 972, 879, 785, 742, 694 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{23}H_{18}N_3O_2F_2$ (MH^+): 406.1367; found: 406.1383.



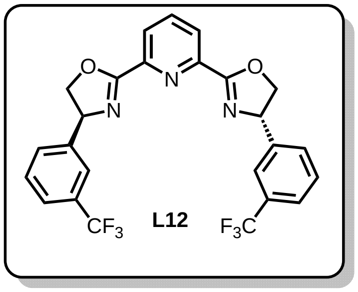
2,6-Bis((*S*)-4-(3-bromophenyl)-4,5-dihydrooxazol-2-yl)pyridine (L8)

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.9 Hz, 2H), 7.95 (t, *J* = 7.9 Hz, 1H), 7.48 (s, 2H), 7.43 (dt, *J* = 7.3, 1.9 Hz, 2H), 7.26 – 7.21 (m, 4H), 5.44 (t, *J* = 10.4, 2H), 4.92 (t, *J* = 10.4, 2H), 4.38 (t, *J* = 8.6 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.70, 146.46, 143.85, 137.49, 130.82, 130.28, 129.79, 126.40, 125.35, 122.83, 75.16, 69.64; **IR** (neat) 3359, 2967, 2898, 1636, 1568, 1473, 1378, 1252, 1106, 1072, 968, 782, 736, 691 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{23}H_{18}N_3O_2Br_2$ (MH^+): 525.9766; found: 525.9753.



2,6-Bis((*S*)-4-(4-chlorophenyl)-4,5-dihydrooxazol-2-yl)pyridine (L10)

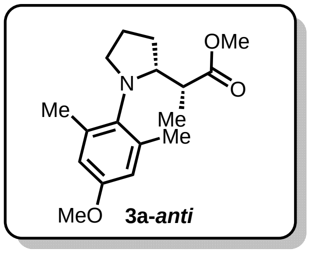
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (d, *J* = 7.8 Hz, 2H), 7.93 (t, *J* = 7.8 Hz, 1H), 7.35 – 7.32 (m, 4H), 7.28 – 7.24 (m, 4H), 5.44 (dd, *J* = 10.3, 8.6 Hz, 2H), 4.92 (dd, *J* = 10.3, 8.7 Hz, 2H), 4.37 (t, *J* = 8.6 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ163.61, 146.58, 140.14, 137.50, 133.57, 128.91, 128.12, 126.35, 75.30, 69.63; **IR** (neat) 2985, 2963, 2928, 2897, 1636, 1488, 1377, 1256, 1104, 1071, 1014, 918, 840 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{23}H_{18}N_3O_2Cl_2$ (MH^+): 438.0776; found: 438.0788.

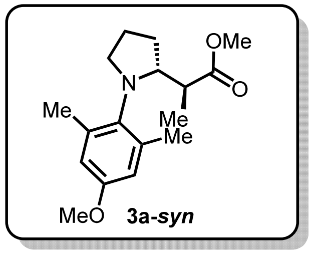


2,6-Bis((*S*)-4-(3-(trifluoromethyl)phenyl)-4,5-dihydrooxazol-2-yl)pyridine (L12)

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (d, *J* = 7.9 Hz, 2H), 7.97 (t, *J* = 7.8 Hz, 1H), 7.60 (s, 2H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.51 (dt, *J* = 15.2, 7.7 Hz, 4H), 5.55 (dd, *J* = 10.4, 8.7 Hz, 2H), 4.98 (dd, *J* = 10.4, 8.7 Hz, 2H), 4.41 (t, *J* = 8.7 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.89, 146.47, 142.58, 137.62, 131.11 (q, *J* = 32.4 Hz), 130.16, 129.29, 126.49, 124.64 (q, *J* = 3.7 Hz), 123.82 (q, *J* = 243 Hz), 123.61 (q, *J* = 3.9 Hz), 75.18, 69.84; **IR** (neat) 3068, 2970, 2903, 1639, 1326, 1162, 1120, 1073, 804, 702 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{25}H_{18}N_3O_2F_6$ (MH^+): 506.1303; found: 506.1317.

3.2 Characterization of the Mannich Products



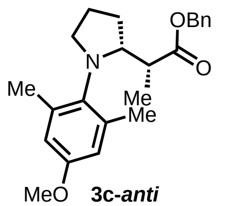


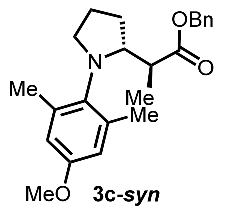
Methyl 2-(1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoate (3a)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.2 mmol, 1 equiv.) was reacted with methyl acrylate **2a** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (5.0 mol%) as the Lewis acid catalyst, benzene (0.2 mL) as the solvent and was carried out for 12 h at 22 °C. ^{1}H NMR analysis of the crude material revealed that **3a-*anti*** and **3a-*syn*** were obtained in the ratio of 2.3:1. After purification by column chromatography (hexanes: EtOAc = 20:1), **3a** was obtained as a mixture of diastereomers (56 mg, 97%). Further purification was carried out by PTLC using hexanes: DCM = 5:1 as the eluent to separate **3a-*anti*** and **3a-*syn***.

3a-*anti*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.56 (d, *J* = 3.0 Hz, 1H), 6.53 (d, *J* = 3.0 Hz, 1H), 3.88 (q, *J* = 6.4 Hz, 1H), 3.74 (s, 3H), 3.31 – 3.28 (m, 4H), 2.98 (q, *J* = 7.7 Hz, 1H), 2.36 (p, *J* = 6.8 Hz, 1H), 2.27 (s, 3H), 2.24 (s, 3H), 2.07 (dq, *J* = 12.4, 7.5 Hz, 1H), 1.96 – 1.87 (m, 2H), 1.77 (dq, *J* = 12.8, 6.1 Hz, 1H), 1.11 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ176.15, 156.58, 140.66, 138.50, 137.45, 114.41, 112.93, 62.75, 55.18, 52.70, 51.09, 45.22, 29.06, 24.99, 19.49, 19.23, 13.47; **IR** (neat) 2947, 1733, 1061, 1484, 1464, 1434, 1319, 1260, 1194, 1154, 1066 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{17}H_{26}NO_3$ (MH^+): 292.1913; found: 292.1921.

3a-*syn*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.57 (d, *J* = 3.1 Hz, 1H), 6.54 (d, *J* = 2.8 Hz, 1H), 3.88 – 3.81 (m, 1H), 3.74 (s, 3H), 3.44 (s, 3H), 3.27 (td, *J* = 8.1, 7.5, 2.8 Hz, 1H), 2.92 (td, *J* = 8.5, 6.6 Hz, 1H), 2.45 (ddd, *J* = 7.0, 5.6, 1.4 Hz, 1H), 2.29 (s, 3H), 2.23 (s, 3H), 2.15 – 2.08 (m, 1H), 1.97 – 1.84 (m, 3H), 1.01 (dd, *J* = 7.0, 1.4 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.94, 156.40, 140.30, 138.86, 137.24, 114.49, 113.03, 63.59, 55.17, 53.38, 51.08, 45.89, 29.82, 25.11, 19.43, 19.09, 13.81; **IR** (neat) 2948, 1733, 1602, 1483, 1463, 1318, 1257, 1193, 1154, 1068cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{17}H_{26}NO_3$ (MH^+): 292.1913; found: 292.1919.



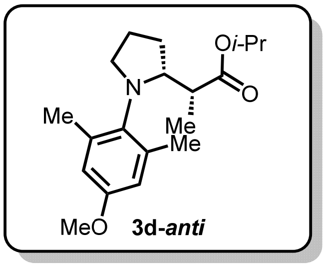


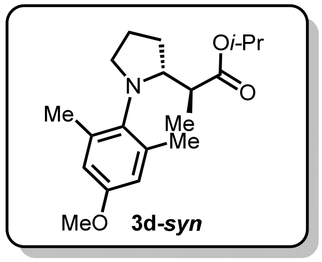
Benzyl 2-(1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoate (3c)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.1 mmol, 1.0 equiv.) was reacted with benzyl acrylate **2c** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (5.0 mol%) as the Lewis acid catalyst, benzene (0.2 mL) as the solvent and was carried out for 12 h at 22 °C. ^{1}H NMR analysis of the crude material revealed that **3c-*anti*** and **3c-*syn*** were obtained in the ratio of 2.5:1. After purification by column chromatography (hexanes: EtOAc = 30:1), **3c** was obtained as a mixture of diastereomers (67 mg, 91%). Further purification was carried out by PTLC using hexanes: DCM = 5:1 as the eluent to separate **3c-*anti*** and **3c-*syn***.

3c-*anti*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 3H), 7.24 – 7.19 (m, 2H), 6.54 (d, J = 3.1 Hz, 1H), 6.51 (d, J = 3.1 Hz, 1H), 4.77 – 4.62 (m, 2H), 3.95 – 3.91 (m, 1H), 3.72 (s, 3H), 3.30 (ddd, J = 8.4, 7.0, 4.8 Hz, 1H), 2.98 (dt, J = 8.4, 7.4 Hz, 1H), 2.42 (p, J = 6.8 Hz, 1H), 2.26 (s, 3H), 2.21 (s, 3H), 2.09 – 2.02 (m, 1H) 1.96 – 1.85 (m, 2H), 1.80 – 1.74 (m, 1H), 1.14 (d, J = 7.0 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ178.15, 159.21, 143.29, 141.19, 140.08, 138.85, 130.99, 130.52, 130.49, 117.13, 115.61, 68.38, 65.35, 57.80, 55.34, 47.94, 31.64, 27.66, 22.12, 21.95, 16.08; **IR** (neat) 2944, 2878, 2837, 1731, 1602, 1483, 1464, 1318, 1263, 1192, 1154, 1068, 697 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{23}H_{30}NO_3$ (MH^+): 368.2226; found: 368.2237.

3c-*syn*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H), 6.56 (d, J = 3.1 Hz, 1H), 6.51 (d, J = 3.1 Hz, 1H), 4.95 (d, J = 12.3 Hz, 1H), 4.71 (d, J = 12.3 Hz, 1H), 3.88 (ddd, J = 8.2, 5.5, 2.8 Hz, 1H), 3.73 (s, 3H), 3.33 – 3.20 (m, 1H), 2.91 (td, J = 8.6, 6.6 Hz, 1H), 2.50 (qd, J = 7.0, 5.5 Hz, 1H), 2.27 (s, 3H), 2.20 (s, 3H), 2.16 – 2.07 (m, 1H), 1.94 – 1.84 (m, 3H), 1.04 (d, J = 7.0 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.27, 156.40, 140.38, 138.96, 137.23, 136.12, 128.39, 128.18, 128.01, 114.53, 113.06, 65.89, 63.65, 55.15, 53.45, 46.14, 29.93, 25.18, 19.39, 19.20, 13.72; **IR** (neat) 2940, 1731, 1602, 1483, 1463, 1256, 1192, 1154, 1068, 698 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{23}H_{30}NO_3$ (MH^+): 368.2226; found: 368.2239.



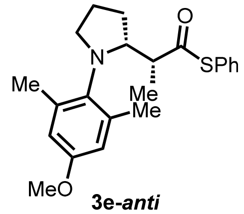


Isopropyl 2-(1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoate (3d)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.2 mmol, 1.0 equiv.) was reacted with isopropyl acrylate **2d** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (5.0 mol%) as the Lewis acid catalyst, benzene (0.2 mL) as the solvent and was carried out for 12 h at 22 °C. ^{1}H NMR analysis of the crude material revealed that **3d-*anti*** and **3d-*syn*** were obtained in the ratio of 2.1:1. After purification by column chromatography (hexanes: Et_2O = 32:1), **3d** was obtained as a mixture of diastereomers (50 mg, 78%). Further purification was carried out by PTLC using hexanes: Et_2O = 9:1 as the eluent to separate **3d-*anti*** and **3d-*syn***.

3d-*anti*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 – 6.55 (m, 1H), 6.54 (d, *J* = 2.8 Hz, 1H), 4.65 (hept, *J* = 6.2 Hz, 1H), 3.91 (dt, *J* = 7.7, 5.4 Hz, 1H), 3.74 (s, 3H), 3.29 (ddd, *J* = 8.4, 6.8, 4.6 Hz, 1H), 2.98 (q, *J* = 7.6 Hz, 1H), 2.35 – 2.29 (m, 1H), 2.27 (s, 3H), 2.25 (s, 3H), 2.07 – 1.99 (m, 1H), 1.96 – 1.88 (m, 2H), 1.83 – 1.77 (m, 1H), 1.11 (dd, *J* = 7.1, 0.6 Hz, 3H), 1.08 (d, *J* = 6.3 Hz, 3H), 1.05 (d, *J* = 6.2 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ175.17, 156.59, 140.52, 138.46, 137.62, 114.53, 112.98, 67.07, 62.41, 55.14, 52.63, 44.84, 28.37, 25.14, 21.61, 21.53, 19.47, 19.29, 12.81; **IR** (neat) 2973, 1731, 1602, 1481, 1464, 1371, 1317, 1260, 1153, 1105, 1067, 854, 698 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{19}H_{30}NO_3$ (MH^+): 320.2226; found: 320.2221.

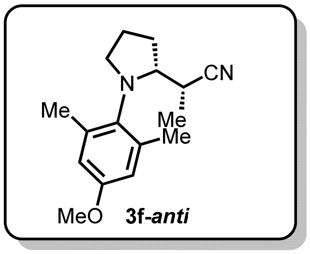
3d-*syn*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.57 (d, *J* = 3.0 Hz, 1H), 6.53 (d, *J* = 3.0 Hz, 1H), 4.82 (hept, *J* = 6.3 Hz, 1H), 3.78 (ddd, *J* = 8.6, 6.0, 2.9 Hz, 1H), 3.74 (s, 3H), 3.27 (td, *J* = 7.9, 2.6 Hz, 1H), 2.92 (td, *J* = 8.6, 6.5 Hz, 1H), 2.43 – 2.36 (m, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 2.17 – 2.09 (m, 1H), 1.98 – 1.91 (m, 1H), 1.91 – 1.85 (m, 2H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.08 (d, *J* = 6.3 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.07, 156.40, 140.34, 139.26, 137.18, 114.47, 113.03, 67.05, 63.81, 55.12, 53.47, 46.73, 30.06, 25.23, 21.75, 21.51, 19.32, 19.25, 14.19; **IR** (neat) 2974, 1723, 1603, 1464, 1317, 1255, 1153, 1107, 1068, 854 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{19}H_{30}NO_3$ (MH^+): 320.2226; found: 320.2216.

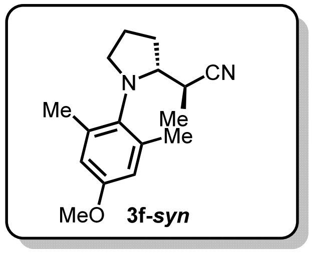


3e-*anti*

***S*-Phenyl 2-(1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanethioate (3e)**

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.2 mmol, 1.0 equiv.) was reacted with *S*-phenyl prop-2-enethioate **2e** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (5.0 mol%) as the Lewis acid catalyst, benzene (0.2 mL) as the solvent and was carried out for 12 h at 22 °C. ^{1}H NMR analysis of the crude material revealed that **3e-*anti*** and **3e-*syn*** were obtained in the ratio of 1.8:1. After purification by column chromatography (hexanes: Et_2O = 30:1), **3e** was obtained as a mixture of diastereomers (39 mg, 53%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 3H), 7.16 – 7.11 (m, 2H), 6.59 (s, 1H), 6.55 (s, 1H), 4.06 (dt, *J* = 7.3, 5.7 Hz, 1H), 3.76 (s, 3H), 3.33 (ddd, *J* = 8.4, 6.9, 4.9 Hz, 1H), 3.00 (q, *J* = 7.6 Hz, 1H), 2.70 – 2.62 (m, 1H), 2.32 (s, 3H), 2.25 (s, 3H), 2.11 – 1.98 (m, 1H), 1.97 – 1.88 (m, 2H), 1.86 – 1.80 (m, 1H), 1.22 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ200.02, 156.83, 140.56, 138.79, 137.16, 134.45, 129.05, 128.95, 128.82, 114.49, 113.19, 62.62, 55.14, 53.47, 52.52, 28.86, 25.02, 19.60, 19.46, 13.74; **HRMS** (DART) m/z Calcd for $C_{22}H_{27}NO_2S$ (MH^+): 370.1835; found: 370.1833.



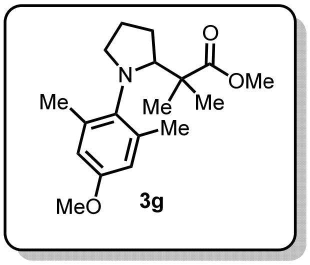


2-(1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanenitrile (3f)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.2 mmol, 1.0 equiv.) was reacted with acrylonitrile **2f** (0.5 mmol, 2.5 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (10 mol%) as the Lewis acid catalyst, benzene (0.4 mL) as the solvent and was carried out for 48 h at 70 °C. ^{1}H NMR analysis of the crude material revealed that **3f-*anti*** and **3f-*syn*** were obtained in the ratio of 1.3:1. After purification by column chromatography (hexanes: Et_2O = 10:1), **3f** was obtained as a mixture of diastereomers (25.9 mg, 50%). Further purification was carried out by PTLC using hexanes: Et_2O = 20:1 as the eluent to separate **3f-*anti*** and **3f-*syn***.

3f-*anti*: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.60 (d, *J* = 3.0 Hz, 1H), 6.56 (d, *J* = 3.0 Hz, 1H), 3.80 – 3.72 (m, 4H), 3.36 (td, *J* = 8.0, 2.5 Hz, 1H), 3.02 (td, *J* = 8.9, 6.6 Hz, 1H), 2.53 (qd, *J* = 7.2, 3.5 Hz, 1H), 2.34 (s, 3H), 2.28 – 2.23 (m, 1H), 2.22 (s, 3H), 2.14 – 2.09 (m, 1H), 2.01 – 1.90 (m, 2H), 1.18 (d, *J* = 7.3 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.90, 140.27, 137.84, 137.15, 122.67, 114.79, 113.33, 63.27, 55.18, 53.61, 32.33, 29.68, 25.28, 19.35, 19.21, 13.96; **IR** (neat) 2951, 2242, 2228, 1603, 1483, 1464, 1318, 1262, 1192, 1154, 1068, 837 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{16}H_{23}N_2O$ (MH^+): 259.1810; found: 259.1807.

3f-*syn*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.62 (d, *J* = 3.0 Hz, 1H), 6.56 (d, *J* = 3.0 Hz, 1H), 3.76 (s, 3H), 3.46 (dt, *J* = 8.0, 3.9 Hz, 1H), 3.35 (td, *J* = 7.8, 3.2 Hz, 1H), 3.10 – 3.02 (m, 1H), 2.56 (qd, *J* = 7.3, 3.7 Hz, 1H), 2.39 (s, 3H), 2.30 – 2.24 (m, 1H), 2.23 – 2.17 (m, 4H), 2.04 (td, *J* = 8.3, 3.9 Hz, 1H), 1.97 (dq, *J* = 11.2, 3.7 Hz, 1H), 1.15 (d, *J* = 7.3 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.06, 141.27, 137.95, 136.32, 122.75, 114.76, 113.22, 64.69, 55.20, 52.47, 31.66, 28.33, 24.69, 19.22, 19.14, 15.56; **IR** (neat) 2951, 2837, 2239, 1602, 1544, 1483, 1464, 1318, 1267, 1192, 1155, 1067, 858 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{16}H_{23}N_2O$ (MH^+): 259.1810; found: 259.1816.

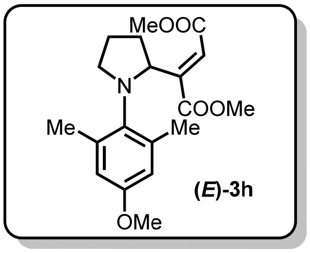


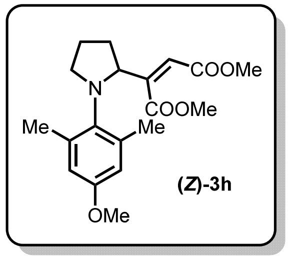
Methyl 2-(1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)-2-methylpropanoate (3g)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.2 mmol, 1.0 equiv.) was reacted with methyl methacrylate **2g** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (10 mol%) as the Lewis acid catalyst, benzene (0.4 mL) as the solvent and was carried out for 24 h at 70 °C.

After purification by column chromatography (hexanes: Et_2O = 40:1), **3g** was obtained as a colorless oil (59.1 mg, 97%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.54 (q, *J* = 3.1 Hz, 2H), 4.05 (dd, *J* = 9.4, 2.2 Hz, 1H), 3.73 (s, 3H), 3.29 (ddd, *J* = 9.1, 6.9, 2.5 Hz, 1H), 3.07 (s, 3H), 2.90 (td, *J* = 8.9, 6.8 Hz, 1H), 2.29 (s, 3H), 2.25 (s, 3H), 2.13 – 2.05 (m, 1H), 1.92 – 1.80 (m, 3H), 1.11 (s, 3H), 1.08 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 177.75, 156.09, 139.88, 139.75, 136.75, 114.62, 112.92, 66.82, 55.14, 54.48, 50.89, 47.67, 27.60, 25.61, 23.22, 19.66, 19.60, 19.38; **IR** (neat) 2947, 2836, 1731, 1602, 1466, 1315, 1253, 1191, 1128, 1069, 839 cm^{-1}; **HRMS** (DART) Calcd for $C_{18}H_{28}NO_3$ (MH^+): 306.2069; found: 306.2067.





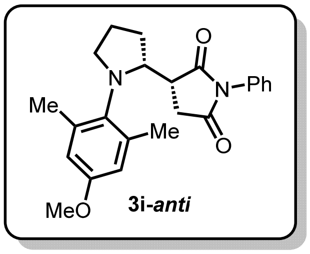
Dimethyl 2-(1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)fumarate (3h)

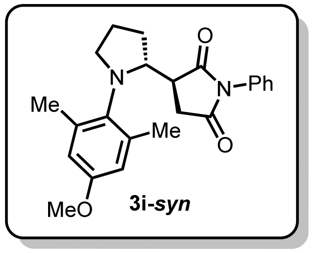
1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.2 mmol, 1.0 equiv.) was reacted with dimethyl but-2-ynedioate **2h** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (10 mol%) as the Lewis acid catalyst, benzene (0.4 mL) as the solvent and was carried out for 24 h at 70 °C. ^{1}H NMR analysis of the crude material revealed that *(E)*-**3h** and *(Z)*-**3h** were obtained in the ratio of 1:1.6. After purification by column chromatography (hexanes: Et_2O = 5:1), (*E*)-**3h** was obtained as yellow liquid (29.8 mg, 21%) and (*Z*)-**3h** was obtained as colorless liquid (42.5 mg, 31%). The relative configuration was assigned based on NOESY experiments (see SI Section 8 for NOE spectra).

(E)-**3h:** ^{1}**H NMR** (600 MHz, $CDCl_3$) δ 6.51 (s, 2H), 6.27 (s, 1H), 5.50 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.77 (s, 3H), 3.72 (s, 3H), 3.61 (s, 3H), 3.44 – 3.39 (m, 1H), 3.06 – 3.00 (m, 1H), 2.47 – 2.41 (m, 1H), 2.35 – 2.09 (m, 8H), 2.06 – 1.95 (m, 1H); ^{13}**C NMR** (126 MHz, $CDCl_3$) δ167.82, 165.81, 156.51, 152.38, 137.97, 124.82, 114.52, 113.01, 58.58, 55.10, 53.87, 51.91, 51.61, 31.95, 25.91, 19.11; **IR** (neat) 2951, 2848, 1729, 1603, 1434, 1256, 1206, 1154, 1114, 1069, 855 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{19}H_{26}NO_5$ (MH^+): 348.1811; found: 348.1822.

(Z)-**3h**: ^{1}**H NMR** (600 MHz, $CDCl_3$) δ 6.55 (s, 2H), 5.99 (d, *J* = 1.1 Hz, 1H), 4.35 – 4.28 (m, 1H), 3.77 (d, *J* = 1.7 Hz, 3H), 3.74 (d, *J* = 1.7 Hz, 3H), 3.67 (d, *J* = 1.8 Hz, 3H), 3.41 – 3.37 (m, 1H), 3.01 (dt, *J* = 10.2, 7.8 Hz, 1H), 2.32 – 2.28 (m, 7H), 2.16 – 2.09 (m, 1H), 2.04 – 1.95 (m, 1H); ^{13}**C NMR** (151 MHz, $CDCl_3$) δ1168.74, 165.68, 156.67, 153.77, 137.33, 119.00, 114.06, 113.51, 64.34, 55.14, 52.96, 52.16, 51.73, 31.92, 24.69, 19.61; **IR** (neat) 2950, 2838,

1724, 1602, 1434, 1316, 1255, 1193, 1153, 1067, 854 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{19}H_{26}NO_5$ (MH^+): 348.1811; found: 348.1810.





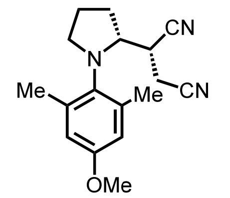
1-(4-Methoxy-2,6-dimethylphenyl)-1'-phenyl-[2,3'-bipyrrolidine]-2',5'-dione (3i)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.2 mmol, 1.0 equiv.) was reacted with 1-phenyl-1*H*-pyrrole-2,5-dione **2i** (0.24 mmol, 1.2 equiv.) following the **General Procedure for B(C_6F_5)$_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (5.0 mol%) as the Lewis acid catalyst, benzene (0.2 mL) as the solvent and was carried out for 12 h at 22 °C. ^{1}H NMR analysis of the crude material revealed that **3i-*anti*** and **3i-*syn*** were obtained in the ratio of 4.5:1. After purification by column chromatography (hexanes: EtOAc = 5:1), **3i** was obtained as a mixture of diastereomers (75 mg, 99%). Further purification was carried out by PTLC to separate **3i-*anti*** and **3i-*syn***.

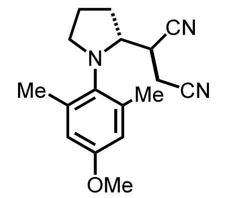
3i-*anti*: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.46 (t, J = 7.7 Hz, 2H), 7.41 – 7.35 (m, 1H), 7.27 – 7.22 (m, 2H), 6.62 – 6.56 (m, 2H), 4.31 (td, J = 6.8, 4.0 Hz, 1H), 3.76 (s, 3H), 3.38 – 3.30 (m, 1H), 3.16 – 3.07 (m, 1H), 2.98 – 2.93 (m, 1H), 2.89 (dd, J = 18.8, 4.0 Hz, 1H), 2.71 (dd, J = 18.8, 9.2 Hz, 1H), 2.32 (s, 3H), 2.26 (s, 3H), 2.14 – 1.98 (m, 3H), 1.64 (dt, J = 11.2, 6.6 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.83, 176.39, 157.02, 139.77, 138.32, 135.60, 131.86, 129.14, 128.55, 126.40, 114.92, 113.36, 60.83, 55.23, 51.83, 43.23, 30.71, 26.29, 24.59, 19.84, 18.86; **IR** (neat) 2946, 1711, 1599, 1498, 1384, 1181, 1154, 692 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{23}H_{27}N_2O_3$ (MH^+): 379.2022; found: 379.2039.

3i-*syn*: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 3H), 6.79 – 6.74 (m, 2H), 6.55 – 6.49 (m, 2H), 4.53 (td, J = 7.0, 2.9 Hz, 1H), 3.72 (s, 3H), 3.44 (dt, J = 8.8, 6.2 Hz, 1H), 3.12 (dd, J = 18.1, 4.8 Hz, 1H), 3.07 – 2.96 (m, 2H), 2.78 (dd, J = 18.1, 9.5 Hz, 1H), 2.35 – 2.27 (m, 4H), 2.25 (s, 3H), 2.04 – 1.95 (m, 2H), 1.89 – 1.80 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ

177.40, 176.25, 156.94, 139.01, 138.23, 136.96, 131.73, 128.69, 128.19, 126.28, 115.23, 113.44, 59.44, 55.14, 54.07, 45.55, 31.70, 29.86, 24.66, 20.26, 18.77; **IR** (neat) 2951, 1709, 1600, 1499, 1382, 1180, 1068, 694 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{23}H_{27}N_2O_3$ (MH^+): 379.2022; found: 379.2036.



3j-*anti*



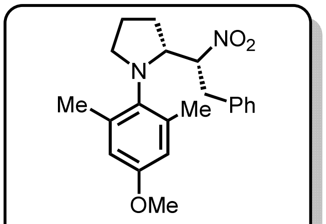
3j-*syn*

2-(1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)succinonitrile (3j)

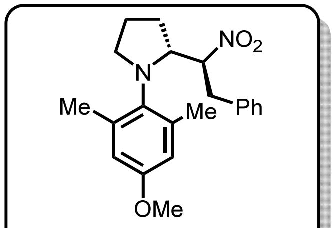
1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.2 mmol, 1.0 equiv.) was reacted with fumaronitrile **2j** (0.5 mmol, 2.5 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (10 mol%) as the Lewis acid catalyst, benzene (0.4 mL) as the solvent and was carried out for 48 h at 70 °C. ^{1}H NMR analysis of the crude material revealed that **3j-*anti*** and **3j-*syn*** were obtained in the ratio of 1.2:1. After purification by column chromatography (hexanes: EtOAc = 3:1), **3j-*anti*** was obtained as a red oil (28.3 mg, 50%) and **3j-*syn*** was obtained as a red oil (23.6 mg, 41%).

3j-*anti*: ^{1}H NMR (500 MHz, Acetone-*d*$_6$) δ 6.61 (s, 2H), 3.75 (s, 3H), 3.47 (tdd, *J* = 7.6, 5.6, 1.3 Hz, 1H), 3.42 – 3.38 (m, 1H), 3.34 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 3.29 (tdd, *J* = 8.3, 3.1, 1.2 Hz, 1H), 3.19 – 3.13 (m, 2H), 3.11 – 3.04 (m, 1H), 2.83 – 2.77 (m, 1H), 2.41 – 2.33 (m, 1H), 2.26 (s, 6H), 2.07 – 2.01 (m, 1H); **^{13}C NMR** (126 MHz, Acetone-*d*$_6$) δ 157.14, 139.18, 136.83, 118.91, 116.76, 113.54, 54.47, 53.73, 49.52, 40.88, 31.89, 29.96, 19.60, 18.07; **IR** (neat) 2958, 2917, 2839, 2190, 1601, 1485, 1468, 1321, 1275, 1193, 1154, 1066, 856 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{17}H_{22}N_3O$ (MH^+): 284.1763; found: 284.1762.

3j-*syn*: ^{1}H NMR (400 MHz, Acetone-*d*$_6$) δ 6.57 (s, 2H), 3.70 (s, 3H), 3.49 – 3.37 (m, 2H), 3.30 (dt, *J* = 8.8, 7.6 Hz, 1H), 3.25 – 3.19 (m, 2H), 3.14 – 2.99 (m, 2H), 2.80 – 2.73 (m, 1H), 2.31 – 2.24 (m, 1H), 2.23 (s, 6H), 2.00 – 1.89 (m, 1H); **^{13}C NMR** (126 MHz, Acetone-*d*$_6$) δ 157.16, 139.19, 136.80, 118.87, 116.77, 113.55, 54.47, 53.48, 49.54, 40.86, 31.87, 30.15, 19.41, 18.06; **IR** (neat) 2922, 2837, 2188, 1602, 1485, 1321, 1275, 1193, 1154, 1066, 856 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{17}H_{22}N_3O$ (MH^+): 284.1763; found: 284.1772.



3k-*anti*



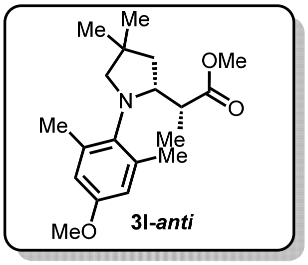
3k-*syn*

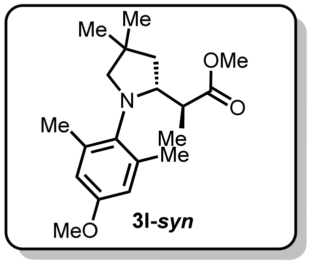
1-(4-Methoxy-2,6-dimethylphenyl)-2-(1-nitro-2-phenylethyl)pyrrolidine (3k)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (0.2 mmol, 1.0 equiv.) was reacted with (*E*)-(2-nitrovinyl)benzene **2k** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (10 mol%) as the Lewis acid catalyst, benzene (0.4 mL) as the solvent and was carried out for 24 h at 70 °C. ^{1}H NMR analysis of the crude material revealed that **3k-*anti*** and **3k-*syn*** were obtained in the ratio of 1.2:1. After purification by column chromatography (hexanes: Et_2O = 15:1), **3k** was obtained as a mixture of diastereomers (59.7 mg, 84%). Further purification was carried out by PTLC using hexanes: Et_2O = 4:1 as the eluent to separate **3k-*anti*** and **3k-*syn***.

3k-*anti*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.3 Hz, 2H), 7.24 – 7.18 (m, 3H), 6.51 (s, 2H), 4.78 (dd, *J* = 12.3, 5.1 Hz, 1H), 4.67 (dd, *J* = 12.2, 9.9 Hz, 1H), 3.71 (s, 3H), 3.44 (td, *J* = 10.2, 5.1 Hz, 1H), 3.36 – 3.29 (m, 1H), 3.28 – 3.23 (m, 1H), 2.83 (dd, *J* = 8.2, 2.6 Hz, 2H), 2.68 (p, *J* = 8.7 Hz, 1H), 2.24 – 2.17 (m, 7H), 1.87 (p, *J* = 9.3 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.75, 139.42, 139.23, 137.31, 128.81, 127.71, 127.47, 113.50, 80.12, 55.42, 55.21, 50.46, 49.04, 43.13, 31.42, 18.81; **IR** (neat) 2918, 2850, 1552, 1485, 1378, 1154, 1060, 701 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{21}H_{27}N_2O_3$ (MH^+): 355.2022; found: 355.2027.

3k-*syn*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, *J* = 7.5 Hz, 2H), 7.30 – 7.24 (m, 3H), 6.58 (s, 2H), 4.67 (t, *J* = 11.2 Hz, 1H), 4.58 (dd, *J* = 12.1, 5.0 Hz, 1H), 3.76 (s, 3H), 3.50 – 3.42 (m, 1H), 3.33 (t, *J* = 8.5 Hz, 1H), 3.20 – 3.09 (m, 3H), 2.68 – 2.58 (m, 1H), 2.24 (s, 6H), 1.74 (d, *J* = 8.1 Hz, 1H), 1.63 (t, *J* = 10.3 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.87, 139.55, 139.23, 137.28, 128.88, 127.74 – 127.71 (m), 127.68, 113.58, 80.09, 55.24, 54.86, 49.70, 48.87, 43.16, 31.80, 18.81; **IR** (neat) 2920, 2851, 1552, 1485, 1378, 1278, 1154, 1029, 858 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{21}H_{27}N_2O_3$ (MH^+): 355.2022; found: 355.2017.



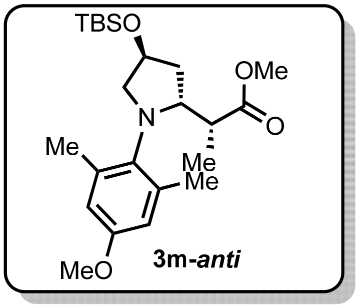


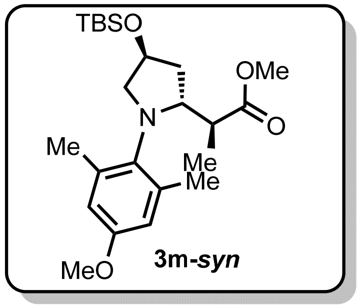
Methyl 2-(1-(4-methoxy-2,6-dimethylphenyl)-4,4-dimethylpyrrolidin-2-yl)propanoate (3l)

1-(4-Methoxy-2,6-dimethylphenyl)-3,3-dimethylpyrrolidine **1l** (0.2 mmol, 1.0 equiv.) was reacted with methyl acrylate **2a** (0.24 mmol, 1.2 equiv.) following the **General Procedure for B(C_6F_5)$_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (5.0 mol%) as the Lewis acid catalyst, benzene (0.2 mL) as the solvent and was carried out for 12 h at 22 °C. ^{1}H NMR analysis of the crude material revealed that **3l-*anti*** and **3l-*syn*** were obtained in the ratio of 3.0:1. After purification by column chromatography (hexanes: Et_2O = 65:1), **3l-*anti*** was obtained as a white solid (44.9 mg, 70%), **3l-*syn*** was obtained as a colorless oil (15.6 mg, 24%).

3l-*anti*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.55 (d, *J* = 3.0 Hz, 1H), 6.48 (d, *J* = 3.0 Hz, 1H), 4.05 (q, *J* = 7.9, 7.4 Hz, 1H), 3.73 (d, *J* = 1.0 Hz, 3H), 3.11 (s, 3H), 3.08 (d, *J* = 8.3 Hz, 1H), 2.82 (d, *J* = 8.3 Hz, 1H), 2.36 (p, *J* = 6.9 Hz, 1H), 2.29 (s, 3H), 2.29 (s, 3H), 1.81 (dd, *J* = 12.2, 6.8 Hz, 1H), 1.52 (dd, *J* = 12.2, 8.0 Hz, 1H), 1.20 (s, 3H), 1.15 (s, 3H), 1.02 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.13, 156.49, 140.51, 139.29, 135.67, 114.06, 112.99, 65.99, 61.88, 55.13, 50.99, 45.26, 44.71, 36.29, 29.42, 28.57, 19.67, 19.42, 14.69; **IR** (neat) 2950, 1734, 1602, 1482, 1465, 1269, 1193, 1154, 854 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{19}H_{30}NO_3$ (MH^+): 320.2226; found: 320.2241.

3l-*syn*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.57 (d, *J* = 3.0 Hz, 1H), 6.50 (d, *J* = 3.0 Hz, 1H), 3.90 (q, *J* = 7.1 Hz, 1H), 3.75 (s, 3H), 3.57 (s, 3H), 3.03 (d, *J* = 8.4 Hz, 1H), 2.82 (d, *J* = 8.4 Hz, 1H), 2.54 (p, *J* = 7.0 Hz, 1H), 2.28 (s, 3H), 2.27 (s, 3H), 1.88 (dd, *J* = 12.6, 7.7 Hz, 1H), 1.67 (dd, *J* = 12.6, 6.3 Hz, 1H), 1.22 (s, 3H), 1.12 (s, 3H), 0.87 (dd, *J* = 6.9, 0.8 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.99, 156.37, 139.80, 137.76, 137.31, 114.38, 113.25, 66.51, 63.09, 55.12, 51.18, 46.03, 44.69, 36.78, 29.18, 28.44, 19.80, 19.35, 15.36; **IR** (neat) 2951, 1735, 1603, 1483, 1465, 1256, 1192, 1155, 1069, 855 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{19}H_{30}NO_3$ (MH^+): 320.2226; found: 320.2240.



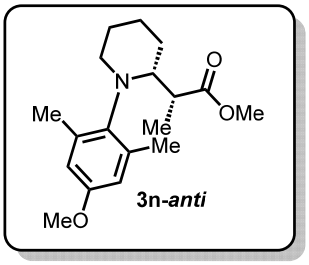


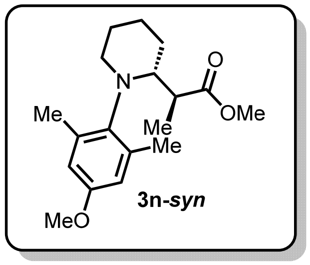
Methyl 2-(4-((*tert*-butyldimethylsilyl)oxy)-1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoate (3m)

3-((*tert*-Butyldimethylsilyl)oxy)-1-(4-methoxy-2,6-dimethylphenyl)pyrrolidine **1m** (0.2 mmol, 1.0 equiv.) was reacted with methyl acrylate **2a** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (5.0 mol%) as the Lewis acid catalyst, benzene (0.2 mL) as the solvent and was carried out for 12 h at 22 °C. ^{1}H NMR analysis of the crude material revealed that **3m-*anti***, **3m-*anti'*** and **3m-*syn***, **3m-*syn'*** were obtained in the ratio of 6.9:5.9:3.0:1. After purification by column chromatography (hexanes: Et_2O = 13:1), **3m** was obtained as a mixture of diastereomers (69 mg, 82%). Further purification was carried out by PTLC to separate **3m-*anti*** and **3m-*syn***. The relative configuration of the pyrrolidine substituents was assigned *anti* based on NOESY experiments (See SI Section 8 for NOE spectra).

3m-*anti*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.56 (d, *J* = 3.0 Hz, 1H), 6.53 (d, *J* = 3.1 Hz, 1H), 4.41 (t, *J* = 4.7 Hz, 1H), 4.09 – 4.04 (m, 1H), 3.74 (s, 3H), 3.55 (dd, *J* = 9.2, 5.2 Hz, 1H), 3.47 (s, 3H), 2.81 (dd, *J* = 9.2, 3.6 Hz, 1H), 2.42 (qd, *J* = 6.9, 5.1 Hz, 1H), 2.33 (s, 3H), 2.23 (s, 3H), 2.06 (ddd, *J* = 12.6, 7.0, 5.6 Hz, 1H), 1.98 (ddd, *J* = 12.1, 7.1, 4.3 Hz, 1H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.69, 156.49, 140.12, 137.95, 137.61, 114.40, 112.91, 70.94, 61.96, 61.80, 55.14, 51.11, 44.49, 39.07, 25.84, 19.25, 19.06, 18.08, 14.14, -4.75, -4.81.; **IR** (neat) 2951, 2929, 2856, 1735, 1603, 1464, 1318, 1253, 1154, 1068, 1024, 832, 774 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{23}H_{40}NO_4Si$ (MH^+): 422.2727; found: 422.2724.

3m-*syn*: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.54 (s, 1H), 6.52 (s, 1H), 4.38 (dp, *J* = 5.1, 2.6 Hz, 1H), 4.14 (q, *J* = 7.3 Hz, 1H), 3.73 (s, 3H), 3.60 (dd, *J* = 9.5, 4.9 Hz, 1H), 3.18 (s, 3H), 2.83 (d, *J* = 9.5 Hz, 1H), 2.34 (s, 3H), 2.32 – 2.27 (m, 1H), 2.25 (s, 3H), 1.97 (ddd, *J* = 12.6, 6.3, 2.8 Hz, 1H), 1.78 – 1.72 (m, 1H), 1.06 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.00, 156.64, 140.64, 139.64, 136.23, 114.17, 112.69, 70.84, 62.00, 60.91, 55.13, 51.04, 45.25, 39.67, 25.80, 19.23, 19.02, 18.04, 14.17, -4.77, -4.81; **IR** (neat) 2952, 2928, 2856, 1737, 1604, 1465, 1319, 1258, 1155, 1069, 1028, 853, 775 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{23}H_{40}NO_4Si$ (MH^+): 422.2727; found: 422.2741.



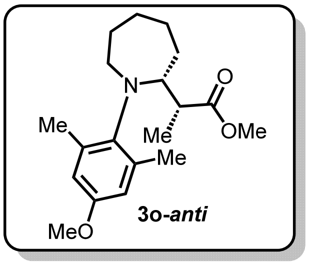


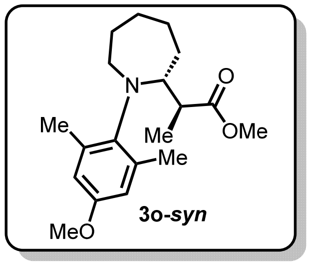
Methyl 2-(1-(4-methoxy-2,6-dimethylphenyl)piperidin-2-yl)propanoate (3n)

1-(4-Methoxy-2,6-dimethylphenyl)piperidine **1n** (0.2 mmol, 1.0 equiv.) was reacted with methyl acrylate **2a** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (5.0 mol%) as the Lewis acid catalyst, benzene (0.2 mL) as the solvent and was carried out for 12 h at 22 °C. ^{1}H NMR analysis of the crude material revealed that **3n-*anti*** and **3n-*syn*** were obtained in the ratio of 10:1.0. After purification by column chromatography (hexanes: Et_2O = 19:1), **3n** was obtained as a mixture of diastereomers (39 mg, 63%). Further purification was carried out by PTLC using DCM: hexanes = 3:2 as the eluent to separate **3n-*anti*** and **3n-*syn***.

3n-*anti*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.60 (d, *J* = 3.0 Hz, 1H), 6.43 (d, *J* = 3.0 Hz, 1H), 3.73 (s, 3H), 3.67 (dt, *J* = 9.7, 3.3 Hz, 1H), 3.60 (s, 3H), 3.10 – 3.04 (m, 1H), 2.84 – 2.79 (m, 1H), 2.44 (qd, *J* = 7.0, 3.6 Hz, 1H), 2.37 (s, 3H), 2.30 (s, 3H), 1.89 – 1.83 (m, 1H), 1.62 – 1.56 (m, 2H), 1.48 – 1.34 (m, 3H), 0.86 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.75, 156.37, 139.40, 139.16, 138.38, 114.25, 113.48, 59.55, 55.01, 52.36, 51.48, 41.05, 27.32, 26.71, 24.93, 20.00, 19.10, 9.73; **IR** (neat) 2922, 2851, 1736, 1602, 1481, 1464, 1211, 1169, 1151, 1111, 1069, 855 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{18}H_{28}NO_3$ (MH^+): 306.2069; found: 306.2078.

3n-*syn*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.60 (d, *J* = 3.0 Hz, 1H), 6.44 (d, *J* = 3.0 Hz, 1H), 3.75 (s, 3H), 3.49 (s, 3H), 3.23 (dt, *J* = 10.6, 2.9 Hz, 1H), 3.00 (td, *J* = 11.7, 3.1 Hz, 1H), 2.84 (dd, *J* = 11.9, 3.8 Hz, 1H), 2.53 (qd, *J* = 7.3, 3.3 Hz, 1H), 2.26 (s, 3H), 2.22 (s, 3H), 1.89 (dt, *J* = 12.8, 4.1 Hz, 1H), 1.84 – 1.79 (m, 1H), 1.66 – 1.50 (m, 3H), 1.33 (tdt, *J* = 12.8, 9.0, 3.9 Hz, 1H), 1.08 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ175.16, 156.35, 140.27, 140.09, 137.64, 113.81, 113.39, 62.81, 55.08, 52.67, 50.96, 40.51, 27.88, 26.72, 25.21, 20.01, 19.31, 15.72; **HRMS** (DART) m/z Calcd for $C_{18}H_{28}NO_3$ (MH^+): 306.2069; found: 306.207.



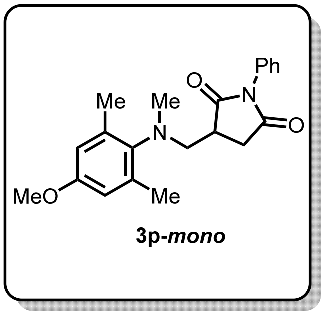


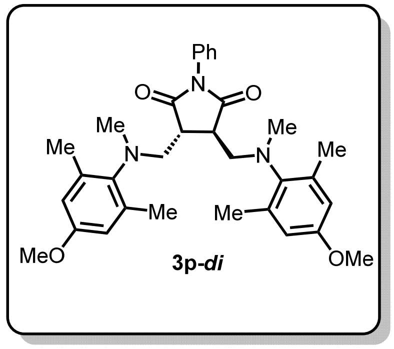
Methyl 2-(1-(4-methoxy-2,6-dimethylphenyl)azepan-2-yl)propanoate (3o)

1-(4-Methoxy-2,6-dimethylphenyl)azepane **1o** (0.2 mmol, 1.0 equiv.) was reacted with methyl acrylate **2a** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (5.0 mol%) as the Lewis acid catalyst, benzene (0.2 mL) as the solvent and was carried out for 12 h at 22 °C. ^{1}H NMR analysis of the crude material revealed that **3o-*anti*** and **3o-*syn*** were obtained in the ratio of 2.0:1.0. After purification by column chromatography (hexanes: Et_2O = 32:1), **3o** was obtained as a mixture of diastereomers (42 mg, 66%). Further purification was carried out by PTLC using DCM: hexanes = 3:2 as the eluent to seperate **3o-*anti*** and **3o-*syn***.

3o-*anti*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 – 6.55 (m, 2H), 3.79 (dt, *J* = 10.0, 4.3 Hz, 1H), 3.74 (s, 3H), 3.46 (s, 3H), 3.31 (ddd, *J* = 14.8, 9.9, 1.4 Hz, 1H), 3.15 – 3.07 (m, 1H), 2.45 (qd, *J* = 7.0, 4.1 Hz, 1H), 2.39 (s, 3H), 2.26 (s, 3H), 1.94 – 1.86 (m, 1H), 1.84 – 1.61 (m, 5H), 1.51 (dtt, *J* = 13.8, 9.2, 2.1 Hz, 1H), 1.44 – 1.33 (m, 1H), 1.13 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 176.17, 155.89, 141.39, 138.66, 137.90, 114.30, 113.83, 62.11, 55.16, 53.14, 51.31, 43.91, 32.32, 30.01, 29.34, 26.25, 20.43, 19.96, 12.12; **IR** (neat) 2923, 2849, 1731, 1602, 1481, 1433, 1309, 1253, 1196, 1162, 1069, 853 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{19}H_{30}NO_3$ (MH^+): 320.2226; found: 320.2231.

3o-*syn*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.57 (dd, *J* = 22.4, 3.1 Hz, 2H), 3.74 (s, 3H), 3.50 (s, 3H), 3.46 – 3.38 (m, 2H), 3.01 (dd, *J* = 15.1, 5.6 Hz, 1H), 2.50 (qd, *J* = 7.1, 3.2 Hz, 1H), 2.38 (s, 3H), 2.29 (s, 3H), 2.01 – 1.91 (m, 2H), 1.86 – 1.68 (m, 3H), 1.58 (dt, *J* = 13.9, 4.7 Hz, 1H), 1.48 – 1.40 (m, 1H), 1.33 (qt, *J* = 12.1, 3.9 Hz, 1H), 0.99 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.02, 155.64, 141.55, 138.84, 137.01, 114.15, 113.98, 64.74, 55.13, 52.06, 50.99, 44.29, 32.46, 30.80, 30.13, 26.62, 20.59, 19.78, 14.94; **IR** (neat) 2925, 2851, 1732, 1602, 1482, 1411, 1308, 1254, 1196, 1164, 1070, 853 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{19}H_{30}NO_3$ (MH^+): 320.2226; found: 320.2211.



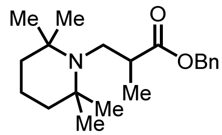


3-(((4-Methoxy-2,6-dimethylphenyl)(methyl)amino)methyl)-1-phenylpyrrolidine-2,5-dione (3p-*mono*)

4-Methoxy-*N,N*,2,6-tetramethylaniline **1p** (0.2 mmol, 1.0 equiv.) was reacted with 1-phenyl-1*H*-pyrrole-2,5-dione **2i** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (10 mol%) as the Lewis acid catalyst, benzene (0.2 mL) as the solvent and was carried out for 24 h at 70 °C. After purification by column chromatography (hexanes: EtOAc = 4:1), **3p-*mono*** was obtained as a white solid (44 mg, 62%), **3p-*di*** was obtained as a white solid (14 mg, 27%).

3p-*mono*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (t, *J* = 7.7 Hz, 2H), 7.40 – 7.36 (m, 1H), 7.26 – 7.23 (m, 2H), 6.56 (s, 2H), 3.75 (s, 3H), 3.69 (dd, *J* = 13.2, 4.1 Hz, 1H), 3.36 (dd, *J* = 13.2, 8.4 Hz, 1H), 3.09 (tt, *J* = 8.8, 4.5 Hz, 1H), 2.94 – 2.81 (m, 2H), 2.78 (s, 3H), 2.31 (s, 3H), 2.29 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.55, 178.67, 159.44, 144.29, 140.69, 140.49, 134.57, 131.80, 131.20, 129.04, 116.79, 116.71, 59.99, 57.88, 44.59, 43.98, 36.31, 22.11, 21.98; **IR** (neat) 2929, 2849, 1710, 1599, 1499, 1384, 1177, 1063, 756, 696 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{21}H_{25}N_2O_3$ (MH^+): 353.1865; found: 353.187.

3,4-Bis(((4-methoxy-2,6-dimethylphenyl)(methyl)amino)methyl)-1-phenylpyrrolidine-2,5-dione (3p-*di*): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48 – 7.44 (m, 2H), 7.40 – 7.36 (m, 1H), 7.22 (dt, *J* = 8.4, 1.2 Hz, 2H), 6.51 (d, *J* = 3.0 Hz, 2H), 6.48 (d, *J* = 3.0 Hz, 2H), 3.73 (s, 6H), 3.56 (dd, *J* = 13.5, 5.3 Hz, 2H), 3.40 (dd, *J* = 13.5, 3.5 Hz, 2H), 3.01 (t, *J* = 4.1 Hz, 2H), 2.64 (s, 6H), 2.24 (s, 6H), 2.21 (s, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.99, 159.25, 145.08, 140.33, 139.93, 134.80, 131.75, 131.08, 128.98, 116.98, 116.52, 59.49, 57.81, 48.28, 45.00, 22.20, 21.93; **IR** (neat) 2960, 2921, 1710, 1600, 1485, 1368, 1315, 1191, 1154, 1063 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{32}H_{40}N_3O_4$ (MH^+): 530.3019; found: 530.3021.

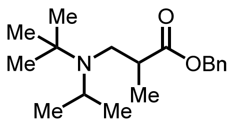


4a

Benzyl 2-methyl-3-(2,2,6,6-tetramethylpiperidin-1-yl)propanoate (4a)

1,2,2,6,6-Pentamethylpiperidine **1q** (0.2 mmol, 1.0 equiv.) was reacted with benzyl acrylate **2c** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (10 mol%) as the Lewis acid catalyst, benzene (0.4 mL) as the solvent and was carried out for 12 h at 70 °C. After purification by column chromatography (hexanes: EtOAc = 10:1), **4a** was obtained as a colorless oil (57.8 mg, 91%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H), 5.16 – 5.04 (m, 2H), 2.89 (dd, *J* = 15.4, 7.5 Hz, 1H), 2.64 (td, *J* = 7.5, 5.8 Hz, 1H), 2.48 (dd, *J* = 15.4, 5.6 Hz, 1H), 1.51 (s, 2H), 1.38 (dd, *J* = 6.7, 4.4 Hz, 4H), 1.13 (d, *J* = 7.1 Hz, 3H), 1.01 (s, 6H), 0.95 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ177.08, 136.33, 128.44, 128.00, 127.95, 65.78, 54.62, 48.86, 44.16, 41.29, 17.81, 16.08; **IR** (neat) 2965, 2927, 1733, 1456, 1379, 1364, 1256, 1164, 696 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{20}H_{32}NO_2$ (MH^+): 318.2433; found: 318.2443.

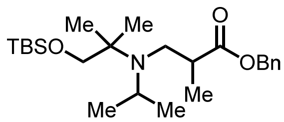


4b

Benzyl 3-(*tert*-butyl(isopropyl)amino)-2-methylpropanoate (4b)

N-Isopropyl-*N*,2-dimethylpropan-2-amine **1r** was reacted with benzyl acrylate **2c** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (10 mol%) as the Lewis acid catalyst, benzene (0.4 mL) as the solvent and was carried out for 12 h at 70 °C. After purification by column chromatography (hexanes: EtOAc = 5:1), **4b** was obtained as a colorless oil (49.4 mg, 85%).

^{1}H NMR (500 MHz, Acetone-d_6) δ 7.44 – 7.29 (m, 5H), 5.18 – 5.06 (m, 2H), 3.29 (hept, *J* = 6.8 Hz, 1H), 2.90 (dd, *J* = 14.3, 8.2 Hz, 1H), 2.65 (dp, *J* = 8.1, 6.8 Hz, 1H), 2.56 (dd, *J* = 14.3, 6.4 Hz, 1H), 1.09 (d, *J* = 6.9 Hz,3H), 1.08 (s, 9H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (126 MHz, Acetone-d_6) δ 175.66, 136.88, 128.31, 127.85, 127.77, 65.17, 55.37, 46.88, 46.39, 42.76, 27.98, 22.16, 14.76; **IR** (neat) 2970, 2875, 1732, 1455, 1380, 1360, 1246, 1210, 1155, 748, 734 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{18}H_{30}NO_2$ (MH^+): 292.2277; found: 292.2281.

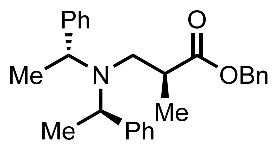


4c

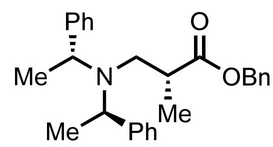
Benzyl 3-((1-((*tert*-butyldimethylsilyl)oxy)-2-methylpropan-2-yl)(isopropyl)amino)-2-methylpropanoate (4c)

1-((*tert*-Butyldimethylsilyl)oxy)-*N*-isopropyl-*N*,2-dimethylpropan-2-amine **1s** (0.2 mmol, 1.0 equiv.) was reacted with benzyl acrylate **2c** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (10 mol%) as the Lewis acid catalyst, benzene (0.2 mL) as the solvent and was carried out for 12 h at 22 °C.. After purification by column chromatography (hexanes: Et_3N = 49:1), **4c** was obtained as a colorless oil (76.6 mg, 91%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 5H), 5.14 – 5.05 (m, 2H), 3.39 – 3.33 (m, 2H), 3.25 (qd, *J* = 8.2, 7.5, 5.3 Hz, 1H), 3.04 – 2.97 (m, 1H), 2.70 – 2.59 (m, 2H), 1.09 (dt, *J* = 6.7, 1.6 Hz, 3H), 1.01 (d, *J* = 9.7 Hz, 9H), 0.95 (dt, *J* = 6.7, 1.5 Hz, 3H), 0.87 (t, *J* = 1.5 Hz, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ176.71, 136.41, 128.41, 127.99, 127.91, 69.57, 65.71, 59.29, 47.35, 46.42, 42.93, 25.85, 24.32, 24.28, 18.17, 15.22, -5.57; **IR** (neat) 2956, 2929, 2856, 1734, 1461, 1250, 1156, 1085, 834, 773, 667 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{24}H_{44}NO_3Si$ (MH^+): 422.309; found: 422.3102.



4d-(*R*,*S*)



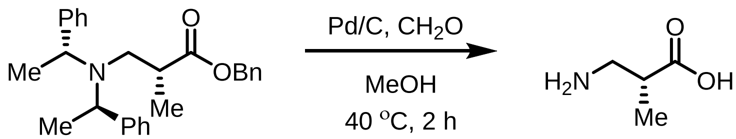
4d-(*R*,*R*)

Benzyl 3-(bis((*R*)-1-phenylethyl)amino)-2-methylpropanoate (4d)

(*R*)-*N*-Methyl-1-phenyl-*N*-((*R*)-1-phenylethyl)ethan-1-amine **1t** (0.2 mmol, 1 equiv.) was reacted with benzyl acrylate **2c** (0.24 mmol, 1.2 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (10 mol%) as the Lewis acid catalyst, DCM (0.4 mL) as the solvent and was carried out for 12 h at 70 °C. ^{1}H NMR analysis of the crude material revealed that **4d-(*R*,*S*)** and **4d-(*R*,*R*)** were obtained in the ratio of 1.5:1.0. After purification by column chromatography (hexanes: Et_2O = 30:1), **4d** was obtained as a colorless oil (72.5 mg, 91%). Further purification was carried out by PTLC using Et_2O: hexanes = 1:9 as the eluent to separate **4d-(*R*,*S*)** and **4d-(*R*,*R*)**.

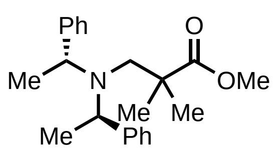
4d-(*R*,*S*): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 4H), 7.28 – 7.18 (m, 6H), 5.19 – 5.07 (m, 2H), 3.84 (q, *J* = 6.9 Hz, 2H), 3.10 (dd, *J* = 14.0, 8.3 Hz, 1H), 2.52 (q, *J* = 7.1 Hz, 1H), 2.36 (dd, *J* = 14.0, 6.2 Hz, 1H), 1.33 (d, *J* = 6.9 Hz, 6H), 0.90 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ176.41, 144.40, 136.23, 128.50, 128.14, 128.06, 127.98, 127.93, 126.61, 65.98, 58.44, 50.11, 41.61, 18.90, 15.17; **IR** (neat) 2971, 1731, 1492, 1452, 1174, 1144, 748, 695 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{27}H_{32}NO_2$ (MH^+): 402.2433; found: 402.2451.

4d-(*R*,*R*): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 12.7, 6.9 Hz, 2H), 7.28 – 7.23 (m, 6H), 7.19 (q, *J* = 4.9, 4.5 Hz, 2H), 4.97 (d, *J* = 12.5 Hz, 1H), 4.83 (d, *J* = 12.5 Hz,1H), 3.94 (q, *J* = 6.9 Hz, 2H), 2.80 (qd, *J* = 13.8, 7.2 Hz, 2H), 2.62 (h, *J* = 7.0 Hz, 1H), 1.37 (d, *J* = 6.8 Hz, 6H), 1.13 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.77, 144.39, 136.28, 128.43, 127.94, 127.92, 126.55, 65.83, 57.66, 49.72, 40.68, 18.04, 15.43; **IR** (neat) 2970, 1732, 1492, 1452, 1356, 1218, 1177, 751, 698 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{27}H_{32}NO_2$ (MH^+): 402.2433; found: 402.2442.



4d-(*R*,*R*)

The minor diastereomer was obtained from 3 reactions following the General Procedure using $B(C_6F_5)_3$ (10 mol%), DCM (0.6 mL) as the solvent and was carried out for 12 h at 70 °C on 0.6 mmol scale. The derivatization of the minor diastereomer was performed based on the literature previously reported.[18] The minor diastereomer (190 mg, 0.47 mmol) was dissolved in a solution of 4.4% formic acid in MeOH (9.4 mL), whereupon Pd-C (10 mol%, 162 mg) was added. The reaction mixture was then heated at 40 °C for 2 h. Upon cooling, the suspension was filtered through a pad of Celite and the mixture was concentrated to remove the solvent and volatile side products to obtain the product as a colorless oil (48 mg, >95% yield). $[\alpha]^{25}_{D}$ = –4.8° (c = 1.0, H_2O). Based on the observed optical rotation value, the absolute configuration of the minor diastereomer was assigned as **4d-(*R*,*R*)**.[18]



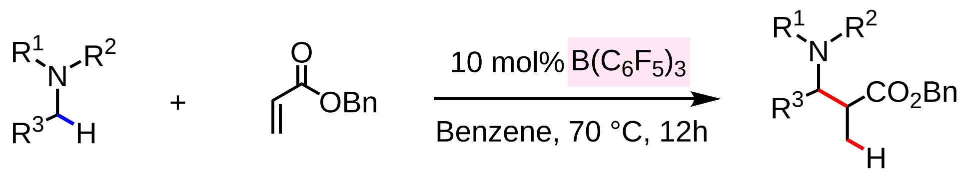
4e

Methyl 3-(bis((*R*)-1-phenylethyl)amino)-2,2-dimethylpropanoate (4e)

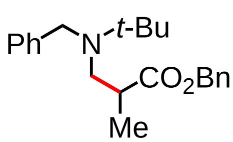
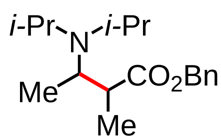
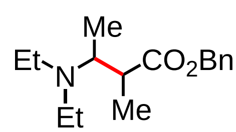
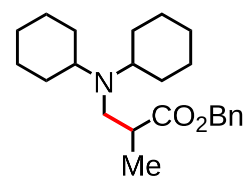
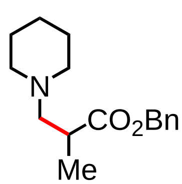
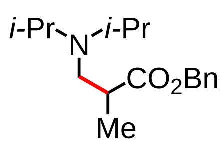
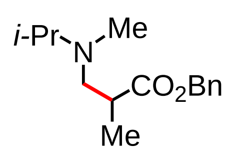
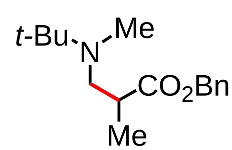
(*R*)-*N*-Methyl-1-phenyl-*N*-((*R*)-1-phenylethyl)ethan-1-amine **1t** (0.2 mmol, 1.0 equiv.) was reacted with methyl methacrylate **2g** (0.5 mmol, 2.5 equiv.) following the **General Procedure for $B(C_6F_5)_3$-Catalyzed Racemic Mannich Reactions** using $B(C_6F_5)_3$ (10 mol%) as the Lewis acid catalyst, DCM (0.4 mL) as the solvent and was carried out for 12 h at 70 °C. After purification by column chromatography (hexanes: Et_2O = 50:1), **4e** was obtained as a colorless oil (64.2 mg, 95%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.15 (m, 10H), 3.89 (q, *J* = 6.9 Hz, 2H), 3.57 (s, 3H), 3.17 (d, *J* = 14.0 Hz, 1H), 2.47 (d, *J* = 14.0 Hz, 1H), 1.43 (d, *J* = 6.9 Hz, 6H), 1.03 (s, 3H), 0.81 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ178.87, 144.42, 128.29, 127.70, 126.46, 55.57, 54.17, 51.58, 42.75, 26.08, 22.24, 14.80; **IR** (neat) 2970, 2932, 1732, 1493, 1452, 1178, 1148, 749, 698 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{22}H_{30}NO_2$ (MH^+): 340.2277; found: 340.2277.

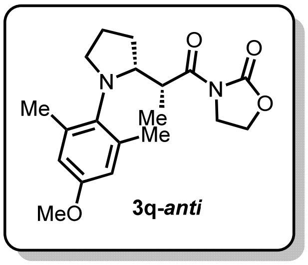
Table SI-8. Evaluation of Trialkylamine Substrates



1 **2c** **4**

			
4k, < 5% yield	**4l**, < 5% yield	**4m**, < 5% yield	**4n**, < 5% yield
			
4o, < 5% yield	**4p**, 11% yield	**4q**, < 5% yield	**4r**, < 5% yield

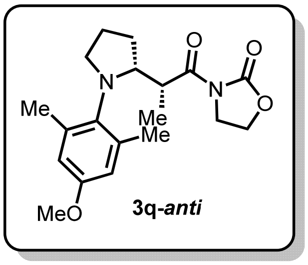
[a] Conditions: **1** (0.2 mmol), **2c** (0.24 mmol), benzene (0.4 mL), under N_2, 70 °C, 12 h. [b] The yield was determined by ^{1}H NMR analysis of the unpurified product mixture using mesitylene as the internal standard.



3-(2-(1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoyl)oxazolidin-2-one (3q)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** was reacted with 3-acryloyloxazolidin-2-one **2q** following the **General Procedure for Stereoselective Mannich Reactions**. The ^{1}H NMR analysis of the crude material revealed **3q** was obtained in >95% yield as a mixture of diastereomers; the ratio of **3q-*anti*** and **3q-*syn*** was determined to be 1.6:1. $[\alpha]^{25}_D = -18.2°$ (c = 1.0, EtOH). The absolute configuration of **3q-*anti*** was assigned in analogy (see SI Section 4).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.55 (d, *J* = 2.9 Hz, 1H), 6.49 (d, *J* = 3.0 Hz, 1H), 4.20 (td, *J* = 9.0, 4.8 Hz, 1H), 4.04 – 3.99 (m, 2H), 3.73 (s, 3H), 3.68 (dd, *J* = 8.0, 6.7 Hz, 1H), 3.60 (dt, *J* = 10.5, 9.1 Hz, 1H), 3.32 (q, *J* = 7.5 Hz, 1H), 3.13 (ddd, *J* = 10.4, 9.2, 4.8 Hz, 1H), 2.99 (td, *J* = 8.4, 4.6 Hz, 1H), 2.27 (s, 3H), 2.22 (s, 3H), 2.14 – 2.08 (m, 1H), 2.01 – 1.94 (m, 1H), 1.93 – 1.86 (m, 1H), 1.77 – 1.71 (m, 1H), 1.12 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ176.38, 156.66, 152.99, 141.13, 140.81, 136.78, 113.74, 112.42, 62.76, 61.67, 55.16, 51.74, 42.88, 42.58, 30.84, 24.38, 19.40, 19.14, 15.56; **IR** (neat) 2962, 2837, 1775, 1695, 1601, 1478, 1384, 1267, 1221, 1194, 1154, 1066 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{19}H_{27}N_2O_4$ (MH^+): 347.1971; found: 347.1964. **HPLC** (Chiralpak IA; 10%/ 90% isopropanol/ hexanes, 1.0 mL/min; **3q-*anti*:** tr = 6.8 min (major), 6.2 min (minor); 80:20 er; **3q-*syn***: 8.4 min (major), 7.6 min (minor) 68:32 er).

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Acq. Method     : column1 10% IPA 90% hexane 60min-1.0mL.M
Analysis Method : C:\Chem32\1\Data\JOE 2017-06-17 18-41-04\column1 10% IPA 90% hexane 60min-1
                  .0mL.M (Sequence Method)
Last changed    : 6/17/2017 6:41:05 PM by SYSTEM
Method Info     : Washing 60min-10% iPrOH 90% hexane-1.0mL
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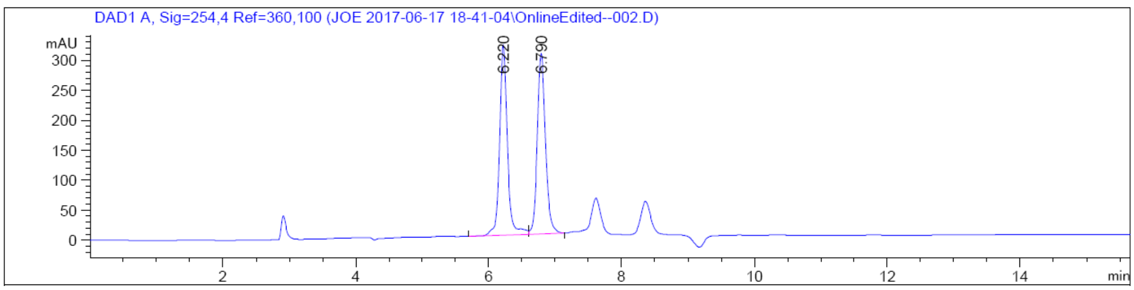
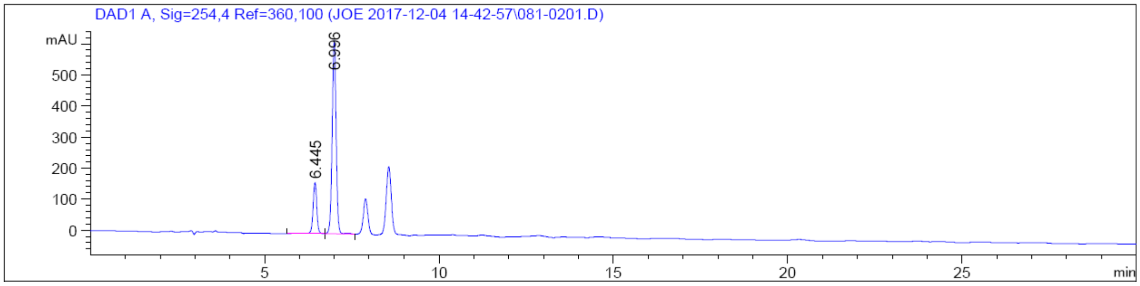


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.220	BV R	0.1227	2598.01807	317.40524	50.1526
2	6.790	VB	0.1303	2582.20337	300.33380	49.8474

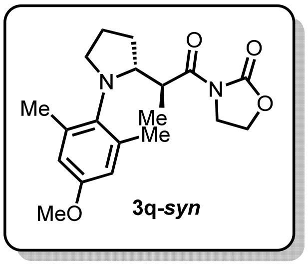
```
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                         Location :   81
Injection Date  : 12/4/2017 3:14:54 PM                  Inj :   1
                                                Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-12-04 14-42-57\column1 10% IPA 90% hexane 30min-1
                  .0mL.M (Sequence Method)
Last changed    : 12/4/2017 2:42:59 PM by SYSTEM
Method Info     : Washing 30min-10% iPrOH 90% hexane-1.0mL

Additional Info : Peak(s) manually integrated
```



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.445	VB R	0.1153	1247.11548	163.76060	19.9504
2	6.996	BV R	0.1234	5003.96973	619.55853	80.0496

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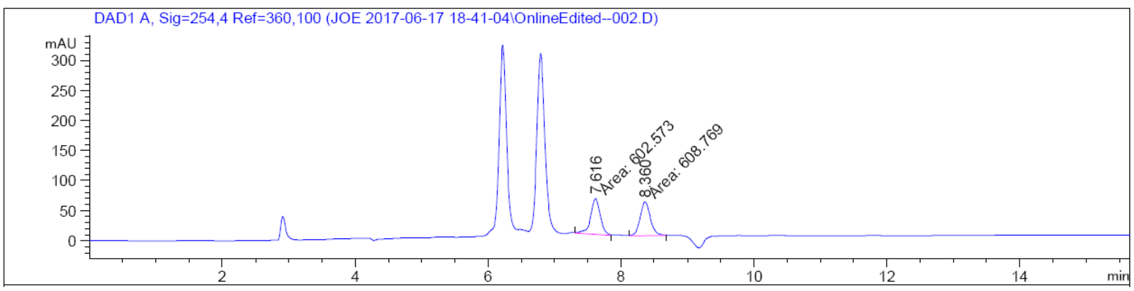
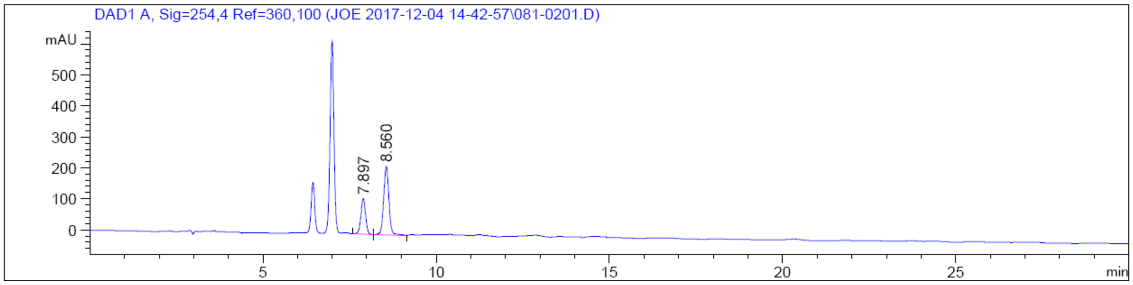
Acq. Operator   : SYSTEM                          Seq. Line :   2
                                                   Location :  11
Injection Date  : 6/17/2017 6:58:53 PM                  Inj :   1
Acq. Method     : column1 10% IPA 90% hexane 60min-1.0mL.M
Analysis Method : C:\Chem32\1\Data\JOE 2017-06-17 18-41-04\column1 10% IPA 90% hexane 60min-1
                  .0mL.M (Sequence Method)
Last changed    : 6/17/2017 6:41:05 PM by SYSTEM
Method Info     : Washing 60min-10% iPrOH 90% hexane-1.0mL
```



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

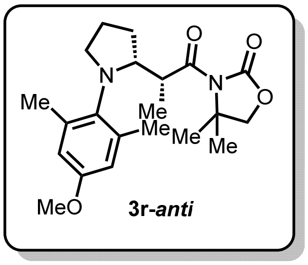
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.616	MM	0.1688	602.57312	59.48536	49.7443
2	8.360	MM	0.1794	608.76910	56.56682	50.2557

```
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                         Location :   81
Injection Date  : 12/4/2017 3:14:54 PM                  Inj :   1
                                                 Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-12-04 14-42-57\column1 10% IPA 90% hexane 30min-1
                  .0mL.M (Sequence Method)
Last changed    : 12/4/2017 2:42:59 PM by SYSTEM
Method Info     : Washing 30min-10% iPrOH 90% hexane-1.0mL
```



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

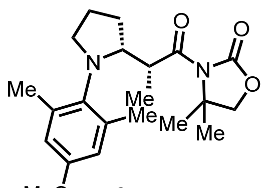
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.897	BB	0.1432	1078.82910	115.25144	31.6807
2	8.560	BB	0.1625	2326.48999	221.55330	68.3193



3-(2-(1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoyl)-4,4-dimethyloxazolidin-2-one (3r)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** was reacted with 3-acryloyl-4,4-dimethyloxazolidin-2-one **2r** following the **General Procedure for Stereoselective Mannich Reactions**. The ^{1}H NMR analysis of the crude material revealed **3r** was obtained in 88% yield as a mixture of diastereomers; the ratio of **3r-*anti*** and **3r-*syn*** was determined to be 4.3:1. $[\alpha]^{25}_{D}$ = –31.1° (c = 1.0, EtOH). The absolute configuration of **3r-*anti*** was assigned as described in SI Section 4.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.53 – 6.50 (m, 2H), 4.02 (q, *J* = 6.7 Hz, 1H), 3.84 (d, *J* = 8.3 Hz, 1H), 3.74 (d, *J* = 8.4 Hz, 1H), 3,73 – 3.71 (m, 4H), 3.30 (ddd, *J* = 8.4, 7.2, 5.6 Hz, 1H), 2.97 (td, *J* = 7.9, 6.1 Hz, 1H), 2.26 (s, 3H), 2.24 (s, 3H), 2.10 (dtd, *J* = 11.8, 7.0, 5.9 Hz, 1H), 2.01 – 1.88 (m, 2H), 1.87 – 1.80 (m, 1H), 1.37 (s, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 1.10 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.09, 156.68, 153.51, 140.56, 139.49, 137.55, 114.39, 112.82, 74.69, 61.81, 55.13, 53.97, 52.52, 44.23, 29.90, 25.05, 24.43, 24.13, 19.35, 14.97; **IR** (neat) 2963, 2836, 1773, 1698, 1602, 1481, 1376, 1303, 1176, 1154, 1071, 765 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{21}H_{31}N_2O_4$ (MH^+): 375.2284; found: 375.2292. **HPLC** (Chiralpak IC; 2.5%/ 97.5% isopropanol/ hexanes, 0.5 mL/min; **3r-*anti*:** tr = 25.1 min (major), 19.3 min (minor); 97:3 er; **3r-*syn***: 22.1 min (major), 20.9 min (minor) 98:2 er).



3r-*anti*

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                                                Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-08-07 23-36-08\column1 2.5% IPA 97.5% hex 40min-0
                  .5mL.M (Sequence Method)
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Method Info     : Washing 40min-2.5% iPrOH 97.5% hexane-0.5mL
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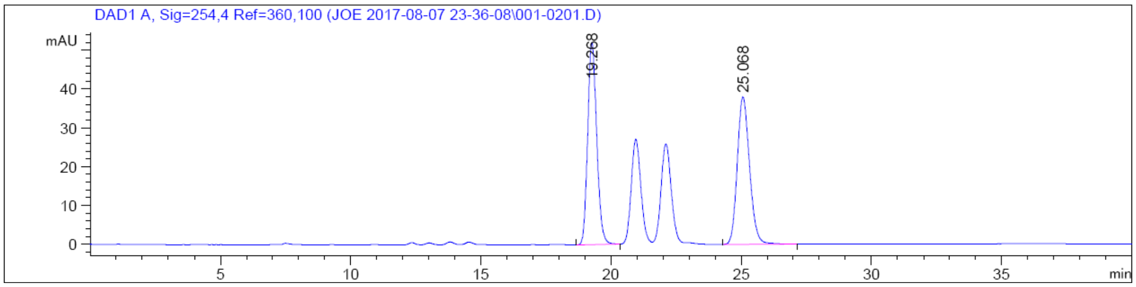

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.268	BB	0.3750	1255.30591	52.11531	50.1904
2	25.068	BB	0.5073	1245.78149	37.91677	49.8096

```
Acq. Operator   : SYSTEM                        Seq. Line :   4
Acq. Instrument : Wasa_LC1                       Location :   12
Injection Date  : 8/9/2017 10:38:27 PM                Inj :   1
                                               Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-08-09 21-23-42\column1 2.5% IPA 97.5% hex 40min-0
                  .5mL.M (Sequence Method)
Last changed    : 8/9/2017 9:23:43 PM by SYSTEM
Method Info     : Washing 40min-2.5% iPrOH 97.5% hexane-0.5mL
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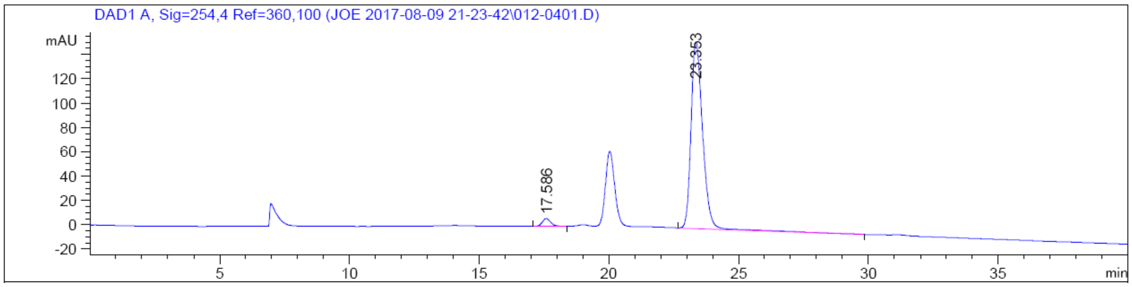
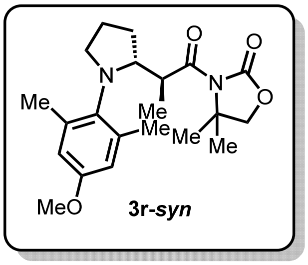


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.586	BB	0.3424	139.11646	6.28083	2.8199
2	23.353	BB	0.4809	4794.23730	153.27171	97.1801

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Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                         Location :   1
Injection Date  : 8/7/2017 11:53:09 PM                  Inj :   1
                                                Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-08-07 23-36-08\column1 2.5% IPA 97.5% hex 40min-0
                  .5mL.M (Sequence Method)
Last changed    : 8/7/2017 11:36:10 PM by SYSTEM
Method Info     : Washing 40min-2.5% iPrOH 97.5% hexane-0.5mL
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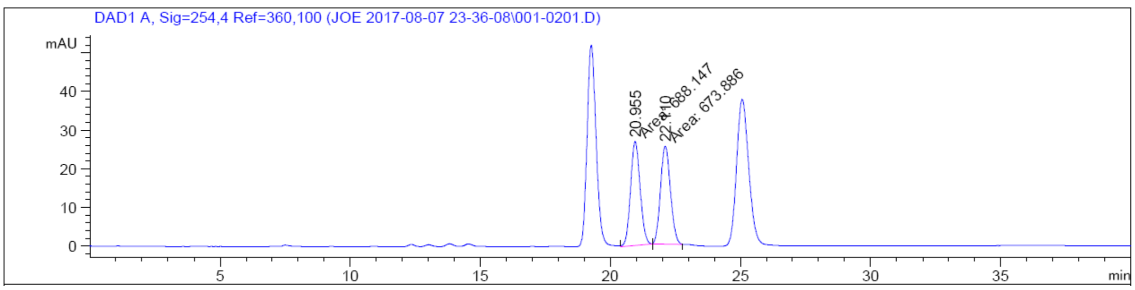

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.955	MM	0.4269	688.14746	26.86458	50.5235
2	22.110	MM	0.4435	673.88586	25.32295	49.4765

```
Acq. Operator   : SYSTEM                          Seq. Line :   4
Acq. Instrument : Wasa_LC1                         Location :   12
Injection Date  : 8/9/2017 10:38:27 PM                  Inj :   1
                                                Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-08-09 21-23-42\column1 2.5% IPA 97.5% hex 40min-0
                  .5mL.M (Sequence Method)
Last changed    : 8/9/2017 9:23:43 PM by SYSTEM
Method Info     : Washing 40min-2.5% iPrOH 97.5% hexane-0.5mL
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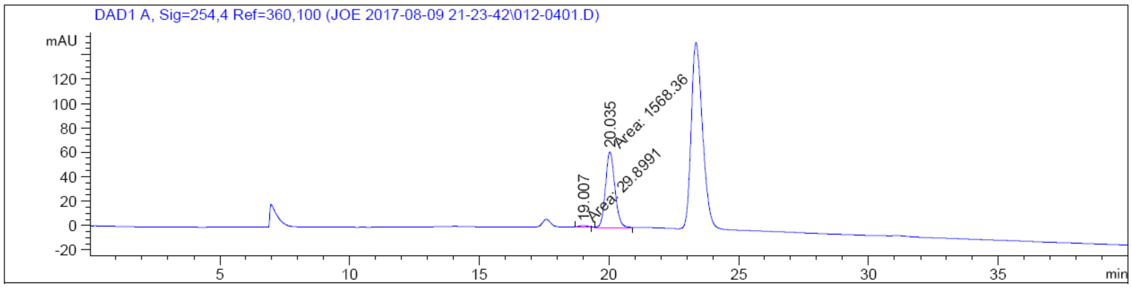
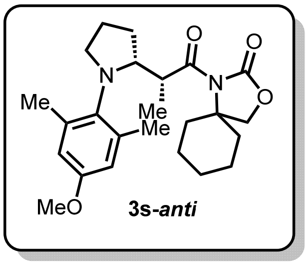


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

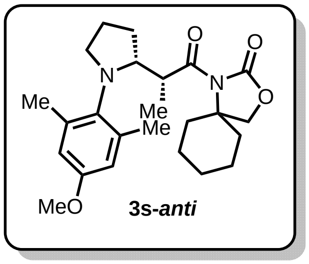
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.007	MM	0.3936	29.89911	1.26620	1.8707
2	20.035	MM	0.4209	1568.36365	62.10253	98.1293



1-(2-(1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoyl)-3-oxa-1-azaspiro[4.5]decan-2-one (3s)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** was reacted with 1-acryloyl-3-oxa-1-azaspiro[4.5]decan-2-one **2s** following the **General Procedure for Stereoselective Mannich Reactions**. The ^{1}H NMR analysis of the crude material revealed **3s** was obtained in 79% yield as a mixture of diastereomers; the ratio of **3s-*anti*** and **3s-*syn*** was determined to be 5.6:1. $[\alpha]^{25}_{D}$ = –47.5° (c = 1.0, EtOH). The absolute configuration of **3s-*anti*** was assigned in analogy (see SI Section 4).

^{1}H NMR (600 MHz, $CDCl_3$) δ6.52 (t, *J* = 2.8 Hz, 2H), 4.07 (d, *J* = 8.5 Hz, 1H), 3.99 (q, *J* = 6.6 Hz, 1H), 3.87 (dd, *J* = 8.5, 1.1 Hz, 1H), 3.75 (t, *J* = 6.8 Hz, 1H), 3.71 (s, 3H), 3.29 (td, *J* = 7.8, 5.5 Hz, 1H), 2.97 (td, *J* = 8.0, 6.5 Hz, 1H), 2.25 (s, 3H), 2.24 (s, 3H), 2.17 – 2.06 (m, 2H), 1.97 – 1.89 (m, 2H), 1.85 (ddd, *J* = 11.3, 7.4, 5.7 Hz, 1H), 1.76 – 1.69 (m, 1H), 1.66 – 1.62 (m, 1H), 1.57 – 1.53 (m, 1H), 1.49 – 1.45 (m, 1H), 1.18 – 1.08 (m, 7H), 1.07 – 1.01 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 177.55, 156.67, 154.03, 140.52, 139.28, 137.62, 114.27, 112.91, 71.29, 63.87, 61.87, 55.08, 52.57, 44.34, 31.89, 31.21, 29.65, 25.16, 24.02, 22.86, 22.81, 19.39, 19.21, 14.79; **IR** (neat) 2929, 2860, 1771, 1698, 1602, 1482, 1456, 1375, 1318, 1262, 1224, 1157, 1071 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{24}H_{35}N_2O_4$ (MH^+): 415.2597; found: 415.2594. **HPLC** (Chiralcel IA; 2.5%/ 97.5% isopropanol/ hexanes, 0.5 mL/min; **3s-*anti*:** tr = 12.6 min (major), 14.7 min (minor); 95:5 er; **3s-*syn***: 13.4 min (major), 16.9 min (minor) 98:2 er).

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Analysis Method : C:\Chem32\1\Data\JOE 2017-07-22 16-24-18\column1 2.5% IPA 97.5% hex 40min-0
                  .5mL.M (Sequence Method)
Last changed    : 7/22/2017 4:24:19 PM by SYSTEM
Method Info     : Washing 40min-2.5% iPrOH 97.5% hexane-0.5mL
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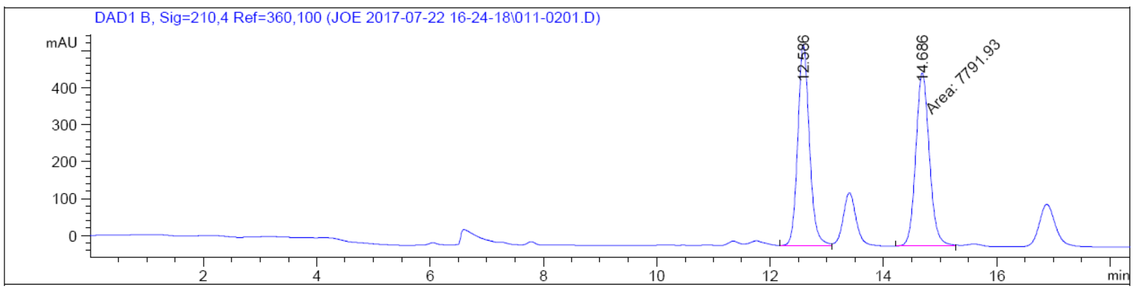

Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.586	BV	0.2193	7810.43555	544.58679	50.0593
2	14.686	MM	0.2769	7791.93359	469.04736	49.9407

```
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                         Location :   1
Injection Date  : 7/31/2017 3:20:09 PM                  Inj :   1
                                               Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-07-31 15-02-20\column1 2.5% IPA 97.5% hex 40min-0
                  .5mL.M (Sequence Method)
Last changed    : 7/31/2017 3:02:21 PM by SYSTEM
Method Info     : Washing 40min-2.5% iPrOH 97.5% hexane-0.5mL
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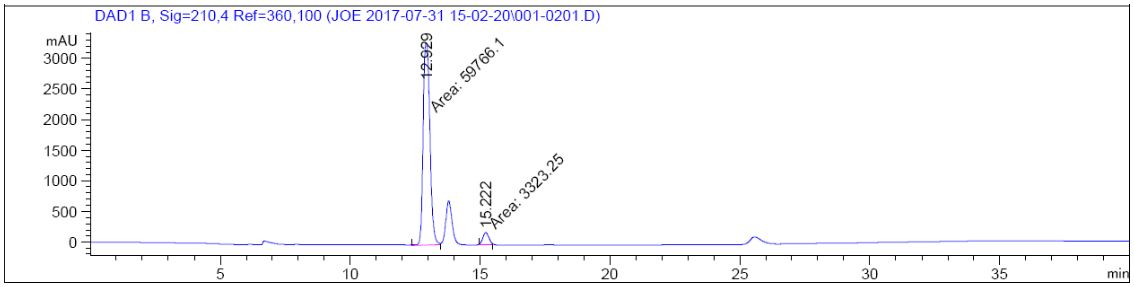
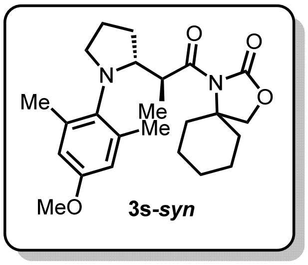


Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.929	MM	0.3012	5.97661e4	3306.89624	94.7325
2	15.222	MM	0.2748	3323.25269	201.53804	5.2675

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                                                   Location :  11
Injection Date  : 7/22/2017 4:42:06 PM                  Inj :   1
Acq. Method     : column1 2.5% IPA 97.5% hex 40min-0.5mL.M
Analysis Method : C:\Chem32\1\Data\JOE 2017-07-22 16-24-18\column1 2.5% IPA 97.5% hex 40min-0
                  .5mL.M (Sequence Method)
Last changed    : 7/22/2017 4:24:19 PM by SYSTEM
Method Info     : Washing 40min-2.5% iPrOH 97.5% hexane-0.5mL
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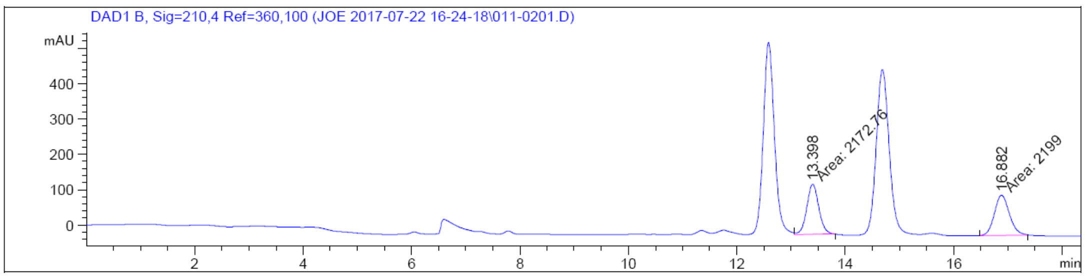

Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.398	MM	0.2555	2172.76001	141.74721	49.6999
2	16.882	MM	0.3208	2199.00220	114.25597	50.3001

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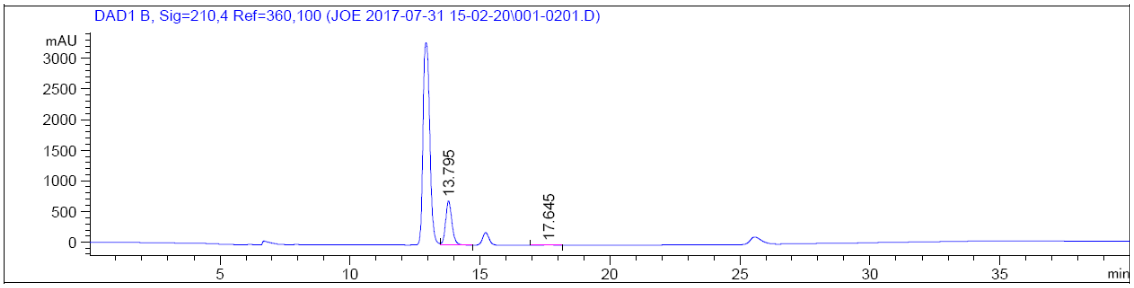
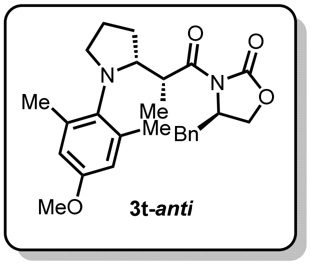
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                         Location :   1
Injection Date  : 7/31/2017 3:20:09 PM                  Inj :   1
                                                Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-07-31 15-02-20\column1 2.5% IPA 97.5% hex 40min-0
                  .5mL.M (Sequence Method)
Last changed    : 7/31/2017 3:02:21 PM by SYSTEM
Method Info     : Washing 40min-2.5% iPrOH 97.5% hexane-0.5mL
```



Signal 2: DAD1 B, Sig=210,4 Ref=360,100

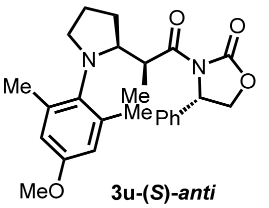
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.795	VB	0.2598	1.22359e4	721.54706	98.0554
2	17.645	BB	0.3192	242.66100	11.73826	1.9446



(4*R*)-4-Benzyl-3-(2-(1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoyl)oxazolidin-2-one (3t)

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** was reacted with (*R*)-3-acryloyl-4-benzyloxazolidin-2-one **2t** following the **General Procedure for Stereoselective Mannich Reactions**. The ^{1}H NMR analysis of the crude material revealed **3t** was obtained in 66% yield as a mixture of diastereomers; the ratio of diastereomers was determined to be 12:2:1:0. The absolute configuration of **3t-*anti*** was assigned in analogy (see SI Section 4).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 3H), 7.10 – 7.04 (m, 2H), 6.50 (s, 2H), 4.05 (td, *J* = 8.2, 5.9 Hz, 1H), 3.93 (dd, *J* = 8.3, 1.5 Hz, 1H), 3.85 – 3.75 (m, 2H), 3.68 (s, 3H), 3.66 – 3.59 (m,1H), 3.32 (q, *J* = 7.5 Hz, 1H), 3.03 – 2.97 (m, 2H), 2.62 (dd, *J* = 13.5, 8.7 Hz, 1H), 2.26 (s, 3H), 2.24 (s, 3H), 2.16 – 2.09 (m, 1H), 2.01 – 1.89 (m, 2H), 1.74 (dq, *J* = 11.0, 8.4 Hz, 1H), 1.17 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.69, 159.38, 155.53, 143.80, 143.76, 139.38, 138.03, 131.99, 131.41, 129.81, 116.32, 115.15, 68.53, 65.16, 57.76, 54.24, 45.64, 40.32, 33.56, 27.05, 22.09, 21.82, 18.53; **IR** (neat) 2959, 2923, 2852, 1776, 1692, 1601, 1481, 1383, 1210, 1154, 1067, 703 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{26}H_{33}N_2O_4$ (MH^+): 437.244; found: 437.2436.

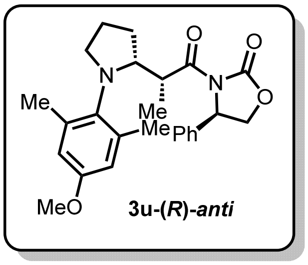


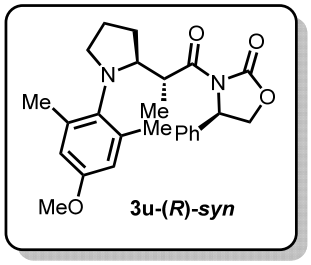
3u-(*S*)-*anti*

(4*S*)-3-(2-(1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoyl)-4-phenyloxazolidin-2-one (3u-(*S*))

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** was reacted with (*S*)-3-acryloyl-4-phenyloxazolidin-2-one **2u-(*S*)** following the **General Procedure for Stereoselective Mannich Reactions**. The ^{1}H NMR analysis of the crude material revealed **3u-(*S*)** was obtained in 61% yield as a mixture of diastereomers; the ratio of diaseteromers was determined to be 3.6:2.1:1:0. The absolute configuration of **3u(*S*)-*anti*** was assigned in analogy (see SI Section 4).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 3H), 7.21 – 7.17 (m, 2H), 6.53 (s, 2H), 5.31 (dd, *J* = 8.8, 3.8 Hz, 1H), 4.57 (t, *J* = 8.8 Hz, 1H), 4.18 (dd, *J* = 8.9, 3.9 Hz, 1H), 3.87 (dt, *J* = 7.1, 4.5 Hz, 1H), 3.75 (s, 3H), 3.70 – 3.65 (m, 1H), 3.23 (ddd, *J* = 8.5, 6.9, 3.4 Hz, 1H), 2.97 (q, *J* = 8.1 Hz, 1H), 2.24 (s, 3H), 2.19 (s, 3H), 1.85 – 1.79 (m, 2H), 1.76 – 1.72 (m, 2H), 1.19 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ175.62, 156.54, 152.95, 140.31, 139.24, 138.23, 137.51, 129.04, 128.52, 125.95, 114.60, 113.01, 69.58, 61.75, 57.73, 55.04, 52.75, 42.76, 27.18, 25.66, 19.30, 19.25, 11.35; **IR** (neat) 2955, 2835, 1777, 1699, 1602, 1480, 1457, 1382, 1316, 1262, 1194, 1153, 699 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{25}H_{31}N_2O_4$ (MH^+): 423.2284; found: 423.2267.



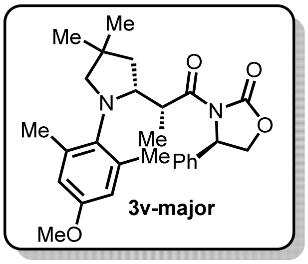


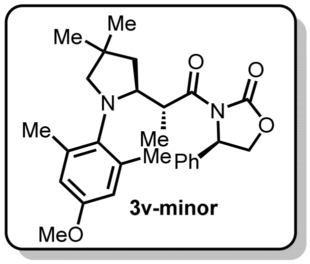
(*R*)-3-((*R*)-2-((*R*)-1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoyl)-4-phenyloxazolidin-2-one (3u-(*R*))

1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidine **1a** was reacted with (*R*)-3-acryloyl-4-phenyloxazolidin-2-one **2u-(*R*)** following the **General Procedure for Stereoselective Mannich Reactions**. The ^{1}H NMR analysis of the crude material revealed **3u-(*R*)** was obtained in >95% yield as a mixture of diastereomers; the ratio of **3u-(*R*)-*anti*** and **3u-(*R*)-*syn*** was determined to be 87:13. $[\alpha]^{25}_{D}$ = −160.8° (c = 1.0, EtOH). The absolute configurations of **3u-(*R*)-*anti*** and **3u-(*R*)-*syn*** were assigned as described in SI Section 4.

3u-(*R*)-*anti*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.4 Hz, 2H), 7.26 – 7.23 (m, 1H), 7.06 (d, *J* = 7.5 Hz,2H), 6.60 (d, *J* = 3.0 Hz, 1H), 6.54 (d, *J* = 3.0 Hz, 1H), 4.56 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.27 (t, *J* = 8.4 Hz, 1H), 4.03 – 3.94 (m, 2H), 3.77 (s, 3H), 3.71 (q, *J* = 7.3 Hz, 1H), 3.33 (q, *J* = 7.5 Hz, 1H), 3.01 (td, *J* = 8.4, 4.6 Hz, 1H), 2.31 (s, 3H), 2.21 (s, 3H), 2.13 – 2.04 (m, 1H), 2.10 – 2.05 (m, 1H), 1.92 – 1.86 (m, 1H), 1.74 – 1.68 (m, 1H), 1.07 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.18, 156.76, 153.16, 141.34, 141.23, 139.54, 136.71, 128.97, 128.20, 125.13, 113.83, 112.42, 69.76, 62.38, 57.37, 55.24, 51.45, 42.74, 30.73, 24.36, 19.38, 19.21, 15.57; **IR** (neat) 2962, 2836, 1776, 1698, 1600, 1479, 1456, 1380, 1193, 1153, 699 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{25}H_{31}N_2O_4$ (MH^+): 423.2284; found: 423.2282.

3u-(*R*)-*syn*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 2H), 7.28 – 7.24 (m, 1H), 7.16 – 7.12 (m, 2H), 6.59 (d, *J* = 3.1 Hz, 1H), 6.54 (d, *J* = 3.1 Hz, 1H), 4.70 (dd, *J* = 8.4, 2.9 Hz, 1H), 4.37 (t, *J* = 8.5 Hz, 1H), 4.13 – 4.03 (m, 2H), 3.81 – 3.70 (m, 4H), 3.35 – 3.26 (m, 1H), 2.95 – 2.85 (m, 1H), 2.31 (s, 3H), 2.28 – 2.19 (m, 4H), 2.03 – 1.94 (m, 1H), 1.91 – 1.85 (m, 1H), 1.84 – 1.80 (m, 1H), 1.00 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.96, 156.36, 153.47, 140.71, 139.45, 139.38, 136.97, 128.99, 128.37, 125.50, 114.38, 113.01, 69.99, 62.52, 57.85, 55.21, 53.64, 44.56, 30.93, 25.25, 19.37, 19.31, 12.56; **IR** (neat) 2957, 2835, 1774, 1701, 1602, 1479, 1457, 1380, 1317, 1193, 1042, 698 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{25}H_{31}N_2O_4$ (MH^+): 423.2284; found: 423.2291.





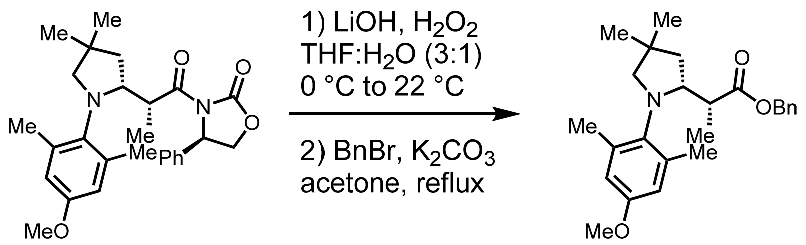
(4*R*)-3-(2-(1-(4-Methoxy-2,6-dimethylphenyl)-4,4-dimethylpyrrolidin-2-yl)propanoyl)-4-phenyloxazolidin-2-one (3v)

1-(4-Methoxy-2,6-dimethylphenyl)-3,3-dimethylpyrrolidine **1l** was reacted with (*R*)-3-acryloyl-4-phenyloxazolidin-2-one **2u-(*R*)** following the **General Procedure for Stereoselective Mannich Reactions**. ^{1}H NMR analysis of the crude material revealed that **3v-major** and **3v-minor** were obtained in the ratio of 58:17:0:0. After purification by column chromatography (hexanes: Et_2O = 17:3 then 15:5), **3v-major** (52 mg, 58%) and **3v-minor** (15 mg, 17%) were obtained as single diastereomers. The absolute configurations of **3v-major** and **3v-minor** were assigned in analogy, see SI Section 4.

3v-major: ^{1}H NMR (500 MHz, $CDCl_3$) δ7.34 – 7.20 (m, 3H), 7.08 – 7.02 (m, 2H), 6.60 (d, *J* = 3.0 Hz, 1H), 6.53 (d, *J* = 3.0 Hz, 1H), 4.45 (dd, *J* = 8.4, 2.2 Hz, 1H), 4.23 – 4.11 (m, 2H), 4.01 – 3.93 (m, 1H), 3.81 – 3.71 (m, 4H), 3.17 (d, *J* = 7.9 Hz, 1H), 2.80 (d, *J* = 7.9 Hz, 1H), 2.33 (s, 3H), 2.24 (s, 3H), 1.78 (dd, *J* = 11.6, 5.5 Hz, 1H), 1.56 (dd, *J* = 11.7, 9.7 Hz, 1H), 1.19 (s, 3H), 1.17 (s, 3H), 1.00 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ175.02, 156.78, 153.15, 142.50, 141.45, 139.61, 135.71, 128.95, 128.18, 125.13, 113.69, 112.45, 69.74, 65.06, 61.89, 57.39, 55.29, 46.19, 42.64, 36.69, 29.22, 28.41, 19.65, 19.32, 16.14; **IR** (neat) 2953, 2863, 2836, 1780, 1698, 1600, 1481, 1380, 1196, 1154, 702 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{27}H_{35}N_2O_4$ (MH^+): 451.2597; found: 451.2612; $[\alpha]^{25}_D$ = –152.7° (c = 1.0, EtOH).

3v-minor: ^{1}H NMR (500 MHz, $CDCl_3$) δ7.41 – 7.30 (m, 3H), 7.16 – 7.11 (m, 2H), 6.48 (d, *J* = 3.1 Hz, 1H), 6.40 (d, *J* = 3.0 Hz, 1H), 5.27 (dd, *J* = 8.8, 4.0 Hz, 1H), 4.57 (t, *J* = 8.8 Hz, 1H), 4.18 (ddd, *J* = 12.5, 8.8, 5.2 Hz, 2H), 3.81 (t, *J* = 6.6 Hz, 1H), 3.73 (s, 3H), 3.03 (d, *J* = 8.4 Hz, 1H), 2.76 (d, *J* = 8.4 Hz, 1H), 2.25 (s, 6H), 1.50 (dd, *J* = 12.3, 8.6 Hz, 1H), 1.24 –

1.18 (m, 1H), 1.12 (s, 3H), 1.05 (s, 3H), 1.01 (d, J = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ175.64, 156.34, 153.13, 139.35, 139.04, 139.01, 135.49, 129.03, 128.49, 126.08, 114.39, 113.25, 69.63, 65.92, 60.12, 57.85, 54.98, 42.68, 41.06, 36.01, 29.47, 28.77, 19.71, 19.35, 12.66; **IR** (neat) 2952, 2920, 2850, 1779, 1702, 1481, 1381, 1319, 1193, 1067, 700 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{27}H_{35}N_2O_4$ (MH^+): 451.2597; found: 451.2613.



3v-major **5v-major**, 91% yield >99:1 er

3v-major was transformed into the corresponding benzyl ester **5v-major** following previously reported literatures.[19,20]

(*R*)-2-((*R*)-1-(4-Methoxy-2,6-dimethylphenyl)-4,4-dimethylpyrrolidin-2-yl)propanoic acid

(*R*)-2-((*R*)-1-(4-Methoxy-2,6-dimethylphenyl)-4,4-dimethylpyrrolidin-2-yl)propanoic acid was prepared by following a known procedure.[19] To a solution of Mannich product **3v-major** (90 mg, 0.2 mmol) in THF:H_2O (3:1, 2.4 mL) at 0 °C was added H_2O_2 (30% v/v, 0.02 mL, 0.8 mmol) and 2 M LiOH (0.14 mL, 0.28 mmol), dropwise. The mixture was stirred at 22 °C for 5 h, whereupon the reaction was quenched with $NaHSO_3$. The crude mixture was then concentrated *in vacuo*, then diluted with EtOAc (2 mL), H_2O (2 mL), and 1 M NaOH (2 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 x 5 mL). Subsequently, the aqueous layer was acidified with 6 M HCl (2 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), filtered. and concentrated *in vacuo* to afford (*R*)-2-((*R*)-1-(4-Methoxy-2,6-dimethylphenyl)-4,4-dimethylpyrrolidin-2-yl)propanoic acid as a yellow solid (60 mg, 98%) which was used without further purification.

Benzyl (*R*)-2-((*R*)-1-(4-methoxy-2,6-dimethylphenyl)-4,4-dimethylpyrrolidin-2-yl)propanoate (5v-major)

Benzyl (*R*)-2-((*R*)-1-(4-methoxy-2,6-dimethylphenyl)-4,4-dimethylpyrrolidin-2-yl)propanoate was prepared by following a known procedure.[20] Benzyl bromide (0.12 mL, 1.0 mmol) was added dropwise to a mixture of (*R*)-2-((*R*)-1-(4-Methoxy-2,6-dimethylphenyl)-4,4-dimethylpyrrolidin-2-yl)propanoic acid (61 mg, 0.2 mmol) and K_2CO_3 (28 mg, 0.2 mmol) in acetone (1.0 mL). The reaction mixture was heated at reflux for 12 h. The reaction mixture was filtered through a pad of celite and the solvent was evaporated by rotary evaporation. The crude product was purified by silica gel column chromatography (19:1 Hexanes: Et_2O) to afford **5v-major** as a colorless oil (74 mg, 93% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ7.31 (qd, *J* = 7.7, 4.0 Hz, 3H), 7.20 (d, *J* = 7.2 Hz, 2H), 6.51 (d, *J* = 3.0 Hz, 1H), 6.47 (d, *J* = 3.1 Hz, 1H), 4.61 – 4.38 (m, 2H), 4.10 (q, *J* = 7.6 Hz, 1H), 3.70 (s, 3H), 3.12 – 3.02 (m, 1H), 2.87 – 2.77 (m, 1H), 2.48 – 2.38 (m, 1H), 2.29 (s, 3H), 2.27 (s, 3H), 1.82 – 1.75 (m, 1H), 1.52 (dd, *J* = 12.2, 8.1 Hz, 1H), 1.21 – 1.18 (m, 3H), 1.14 (d, *J* = 1.3 Hz, 3H), 1.05 (dd, *J* = 7.0, 1.4 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ175.54, 156.49, 140.47, 139.41, 136.16, 135.67, 128.28, 127.80, 127.75, 114.24, 113.04, 65.96, 65.69, 61.86, 55.10, 45.25, 44.63, 36.32, 29.44, 28.59, 19.73, 19.52, 14.66; **HPLC** (Chiralpak AD-H; 1%/ 99% isopropanol/ hexanes, 0.5 mL/min; **5v-major:** tr = 11.4 min (minor), 12.1 min (major); >99:1 er.

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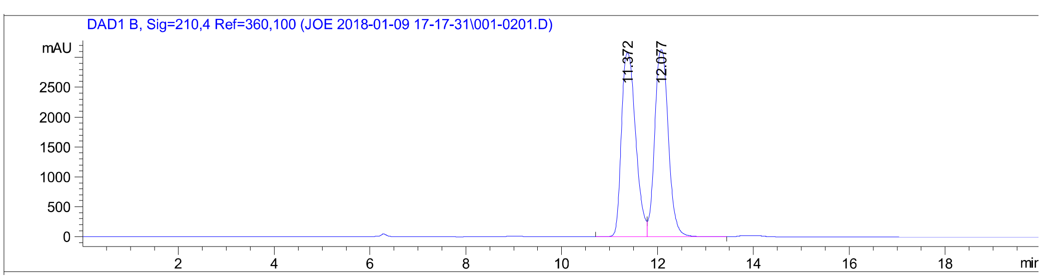

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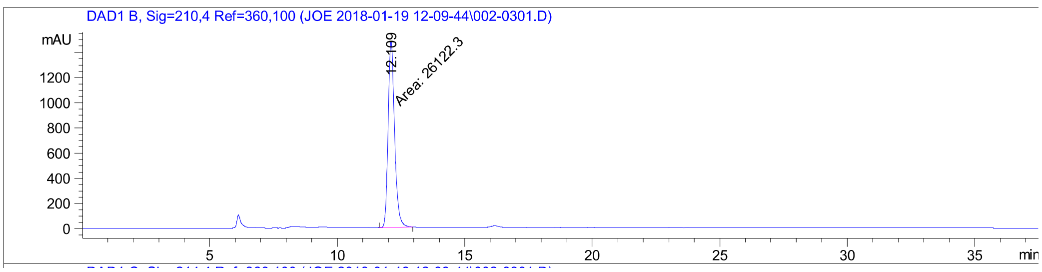

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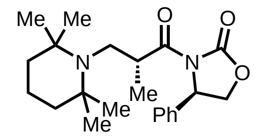
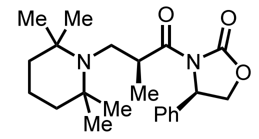


4f-major



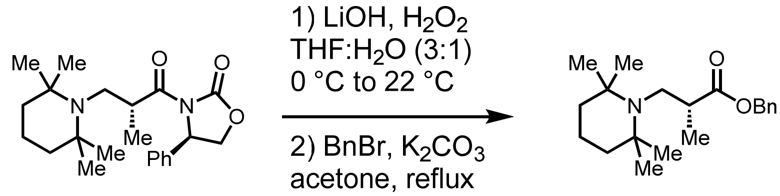
4f-minor

(4*R*)-3-(2-Methyl-3-(2,2,6,6-tetramethylpiperidin-1-yl)propanoyl)-4-phenyloxazolidin-2-one (4f)

1,2,2,6,6-Pentamethylpiperidine **1q** was reacted with (*R*)-3-acryloyl-4-phenyloxazolidin-2-one **2u-(*R*)** following the **General Procedure for Stereoselective Mannich Reactions** at 50 °C. ^{1}H NMR analysis of the crude material revealed that **4f-major** and **4f-minor** were obtained in the ratio of 2.0:1. After purification by PTLC (hexanes: EtOAc: Et_3N = 16:4:1), **4f-major** (35 mg, 47%) and **4f-minor** (28 mg, 24%) were obtained as single diastereomers.

4f-major: ^{1}H NMR (500 MHz, $CDCl_3$) δ7.37 (t, *J* = 7.0 Hz, 2H), 7.33 (d, *J* = 6.8 Hz, 1H), 7.29 – 7.25 (m, 2H), 5.44 – 5.36 (m, 1H), 4.69 – 4.60 (m, 1H), 4.23 (ddd, *J* = 8.9, 3.4, 1.6 Hz, 1H), 4.03 (p, *J* = 6.8 Hz, 1H), 2.95 (dd, *J* = 15.5, 6.5 Hz, 1H), 2.49 (dd, *J* = 15.5, 5.8 Hz, 1H), 1.51 (d, *J* = 5.9 Hz, 2H), 1.39 (dd, *J* = 8.5, 4.6 Hz,4H), 1.10 (d, *J* = 7.1 Hz,3H), 1.03 (s, 6H), 0.97 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ177.60, 153.26, 139.37, 129.12, 128.51, 125.60, 69.57, 57.82, 54.61, 47.77, 41.38, 41.26, 17.81, 16.41; **IR** (neat) 2963, 2926, 1780, 1699, 1381, 1320, 1242, 1197, 1042, 761 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{22}H_{33}N_2O_3$ (MH^+): 373.2491; found: 373.2504; $[\alpha]^{25}_D$ = –107.9° (c = 0.3, EtOH).

4f-minor: ^{1}H NMR (500 MHz, $CDCl_3$) δ7.40 – 7.30 (m, 5H), 5.45 (dd, *J* = 8.9, 4.0 Hz, 1H), 4.67 (dd, *J* = 9.6, 8.2 Hz, 1H), 4.31 – 4.24 (m, 1H), 3.97 (q, *J* = 6.8 Hz, 1H), 2.90 (dd, *J* = 15.4, 6.3 Hz, 1H), 2.37 (dd, *J* = 15.4, 6.3 Hz, 1H), 1.47 (s, 2H), 1.32 (t, *J* = 6.0 Hz, 4H), 1.16 (dd, *J* = 7.1, 1.3 Hz, 3H), 0.96 (s, 6H), 0.78 (s, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ177.67, 153.35, 139.33, 129.03, 128.59, 126.34, 69.52, 57.88, 54.57, 47.48, 41.59, 41.35, 17.82, 16.43; **IR** (neat) 2964, 2925, 2872, 1777, 1700, 1457, 1380, 1319, 1196, 1044, 949, 699 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{22}H_{33}N_2O_3$ (MH^+): 373.2491; found: 373.2474.



4f-major

4a, 83% yield
>99:1 er

4f-major was transformed into the corresponding benzyl ester **4a** following previously reported literatures.[19,20] **HPLC** (Chiralcel OD-H; 2.5%/ 97.5% isopropanol/ hexanes, 0.3 mL/min; **4a:** tr = 12.6 min (major), 13.3 min (minor); >99:1 er.

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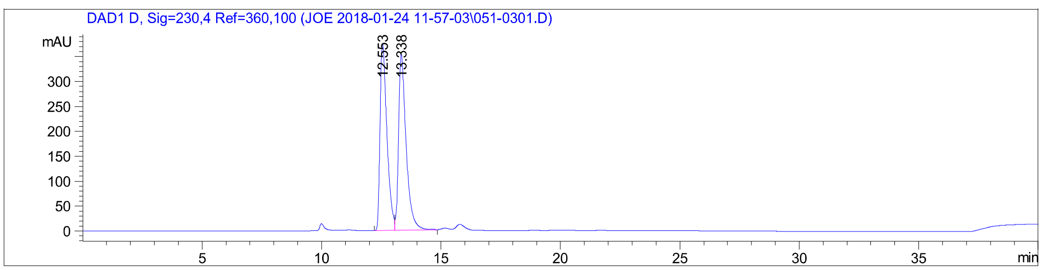
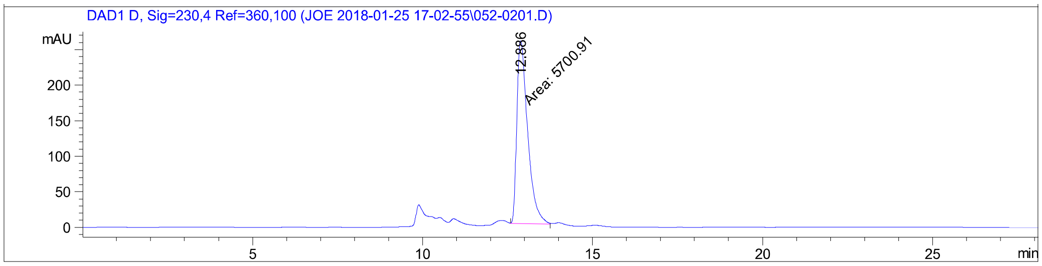
                                               Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2018-01-24 11-57-03\column1 2.5%IPA 97.5% hexane 40min
                  -0.3mL.M (Sequence Method)
Last changed    : 1/24/2018 11:57:04 AM by SYSTEM
Method Info     : Column1 40min-2.5% iPrOH 97.5% hexane-0.3mL
```



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

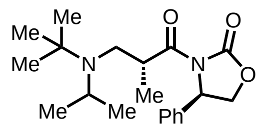
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.553	BV	0.2982	7523.91992	374.85226	49.2105
2	13.338	VB	0.3294	7765.33203	351.95917	50.7895

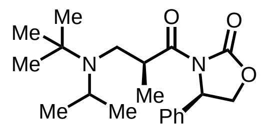
```
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                          Location :   52
Injection Date  : 1/25/2018 5:34:58 PM                   Inj :   1
                                                Inj Volume : 8.000 µl
Method          : C:\Chem32\1\Data\JOE 2018-01-25 17-02-55\column1 2.5% IPA 97.5% hex 30min-0
                  .3mL.M (Sequence Method)
Last changed    : 1/25/2018 5:02:57 PM by SYSTEM
Method Info     : Washing 40min-2.5% iPrOH 97.5% hexane-0.5mL
```



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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.886	MM	0.3695	5700.90869	257.16043	100.0000



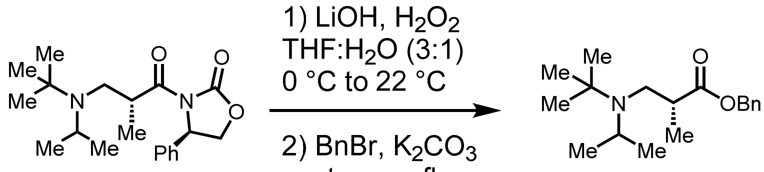


(4*R*)-3-(3-(*tert*-Butyl(isopropyl)amino)-2-methylpropanoyl)-4-phenyloxazolidin-2-one (4g)

N-Isopropyl-*N*,2-dimethylpropan-2-amine **1r** was reacted with (*R*)-3-acryloyl-4-phenyloxazolidin-2-one **2u-(*R*)** following the **General Procedure for Stereoselective Mannich Reactions**. ^{1}H NMR analysis of the crude material revealed that **4g-major** and **4g-minor** were obtained in the ratio of 1.8:1. After purification by PTLC (hexanes: EtOAc: Et_3N = 16:4:1), **4g-major** (35 mg, 50%) and **4g-minor** (14 mg, 20%) were obtained as single diastereomers.

4g-major: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 8.1, 6.5 Hz, 2H), 7.33 (d, *J* = 7.3 Hz, 1H), 7.28 (dd, *J* = 7.0, 1.8 Hz, 2H), 5.42 (dd, *J* = 8.5, 3.3 Hz, 1H), 4.65 (t, *J* = 8.7 Hz, 1H), 4.23 (dd, *J* = 8.8, 3.3 Hz, 1H), 4.02 (q, *J* = 6.9 Hz, 1H), 3.23 (p, *J* = 6.7 Hz, 1H), 2.92 (dd, *J* = 14.6, 7.4 Hz, 1H), 2.51 (dd, *J* = 14.6, 6.5 Hz, 1H), 1.07 (d, *J* = 5.5 Hz, 12H), 0.99 (d, *J* = 6.7 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ177.22, 153.39, 139.43, 129.14, 128.50, 125.58, 69.66, 57.75, 55.75, 46.54, 46.26, 40.01, 28.46, 23.14, 22.32, 15.54; **IR** (neat) 2965, 2924, 2854, 1761, 1701, 1384, 1197, 1078, 699 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{20}H_{31}N_2O_3$ (MH^+): 347.2335; found: 347.232; $[\alpha]^{25}_D$ = –80.2° (c = 0.5, EtOH).

4g-minor: ^{1}H NMR (500 MHz, $CDCl_3$) δ7.40 – 7.30 (m, 5H), 5.46 (dd, *J* = 8.9, 4.3 Hz, 1H), 4.72 – 4.63 (m, 1H), 4.30 – 4.20 (m, 1H), 4.01 (q, *J* = 7.0 Hz, 1H), 3.20 – 3.11 (m, 1H), 3.00 – 2.87 (m, 1H), 2.39 (dd, *J* = 14.3, 6.3 Hz, 1H), 1.11 (dd, *J* = 6.9, 1.4 Hz, 3H), 1.00 – 0.97 (m, 3H), 0.95 (s, 9H), 0.83 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ177.24, 153.51, 139.27, 128.97, 128.49, 126.28, 69.54, 57.83, 55.66, 46.57, 46.47, 40.03, 28.36, 23.48, 21.94, 15.52; **IR** (neat) 2969, 2928, 2873, 1776, 1703, 1457, 1383, 1320, 1198, 1043, 698 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{20}H_{31}N_2O_3$ (MH^+): 347.2335; found: 347.235.

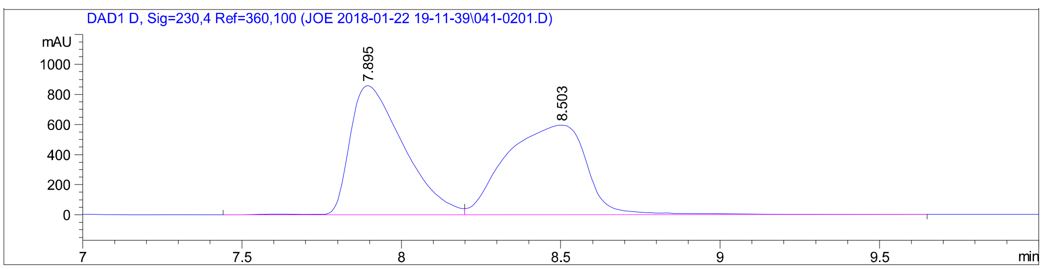


4g-major

4b, 80% yield
>99:1 er

4g-major was transformed into the corresponding benzyl ester **4b** following previously reported literatures.[19,20] **HPLC** (Chiralcel OD-H; 0.5%/ 99.5% isopropanol/ hexanes, 1.0 mL/min; **4b:** tr = 7.9 min (major), 8.5 min (minor); >99:1 er.

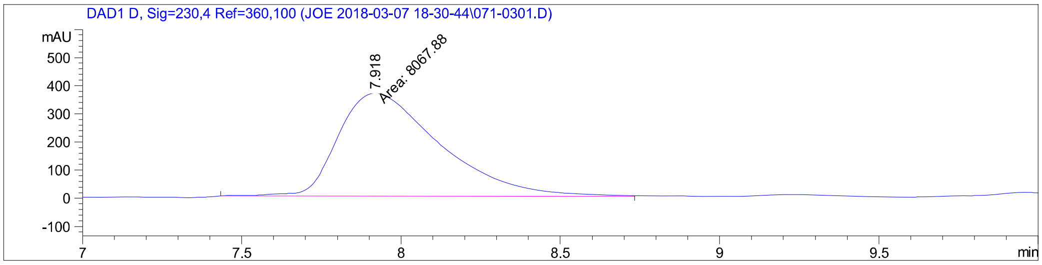
```
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                         Location :   41
Injection Date  : 1/22/2018 8:13:40 PM                  Inj :   1
                                                Inj Volume : 4.000 µl
Acq. Method     : C:\Chem32\1\Data\JOE 2018-01-22 19-11-39\column1 1% IPA 99% hex 60min-0.5mL
                  .M
```



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

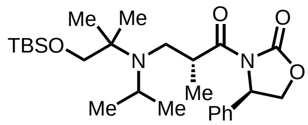
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.895	VV R	0.1798	1.00079e4	856.65320	48.9703
2	8.503	VB	0.2983	1.04288e4	595.46783	51.0297

```
Acq. Operator   : SYSTEM                          Seq. Line :   3
Acq. Instrument : Wasa_LC1                         Location :   71
Injection Date  : 3/7/2018 8:14:34 PM                   Inj :   1
                                                 Inj Volume : 8.000 µl
Acq. Method     : C:\Chem32\1\Data\JOE 2018-03-07 18-30-44\column1 1% IPA 99% hex 40min-0.5mL
                  .M
```



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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.918	MM	0.3683	8067.87891	365.05762	100.0000

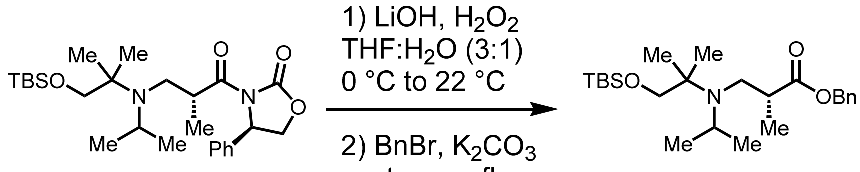


4h

(4*R*)-3-(3-((1-((*tert*-Butyldimethylsilyl)oxy)-2-methylpropan-2-yl)(isopropyl)amino)-2-methylpropanoyl)-4-phenyloxazolidin-2-one (4h)

1-((*tert*-Butyldimethylsilyl)oxy)-*N*-ethyl-*N*-isopropyl-2-methylpropan-2-amine **1s** was reacted with (*R*)-3-acryloyl-4-phenyloxazolidin-2-one **2u-(*R*)** following the **General Procedure for Stereoselective Mannich Reactions**. ^{1}H NMR analysis of the crude material revealed that **4h-major** and **4h-minor** were obtained in the ratio of 7.4:1. After purification by silica gel column chromatography (hexanes: Et_3N = 50:1 then 19:1), **4h-major** (71 mg, 70%) and **4h-minor** (9 mg, 10%) were obtained as single diastereomers.

4h-major*:* ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 8.2, 6.7 Hz, 2H), 7.33 (d, *J* = 7.1 Hz, 1H), 7.29 – 7.27 (m, 2H), 5.42 (dd, *J* = 8.5, 3.2 Hz, 1H), 4.64 (t, *J* = 8.7 Hz, 1H), 4.23 (dd, *J* = 8.8, 3.3 Hz, 1H), 3.99 (h, *J* = 7.0 Hz, 1H), 3.43 – 3.34 (m, 2H), 3.27 (p, *J* = 6.7 Hz, 1H), 3.03 (dd, *J* = 14.8, 7.3 Hz, 1H), 2.68 (dd, *J* = 14.8, 6.6 Hz, 1H), 1.06 (d, *J* = 7.2 Hz, 9H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.02 (d, *J* = 1.3 Hz, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ179.81, 156.03, 142.11, 131.81, 131.17, 128.25, 72.31, 72.21, 62.06, 60.42, 49.16, 49.04, 42.75, 28.52, 26.84, 26.81, 20.84, 18.14, -2.91; **IR** (neat) 2956, 2925, 2854, 1781, 1702, 1459, 1381, 1195, 1086, 1044, 836, 774 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{26}H_{45}N_2O_4Si$ (MH^+): 477.3147; found: 477.3171; $[\alpha]^{25}_{D}$ = −60.9° (c = 0.8, EtOH).

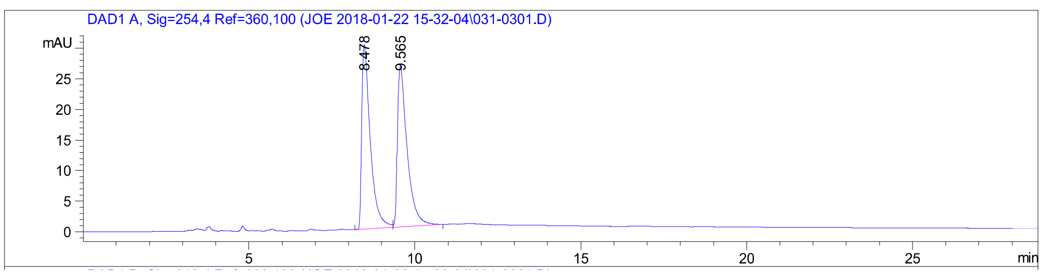


4h-major

4c, 87% yield
>99:1 er

4h-major was transformed into the corresponding benzyl ester **4c** following previously reported literatures.[19,20] **HPLC** (Chiralcel OD-H; 0.5%/ 99.5% isopropanol/ hexanes, 1.0 mL/min; **4c:** tr = 8.5 min (minor), 9.6 min (major); >99:1 er.

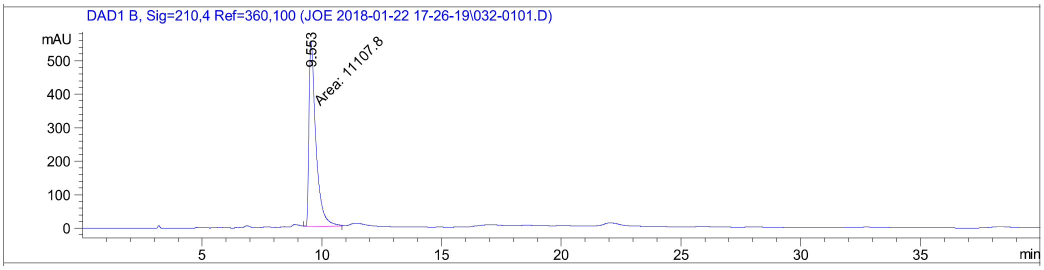
```
Acq. Operator   : SYSTEM                          Seq. Line :   3
Acq. Instrument : Wasa_LC1                         Location :   31
Injection Date  : 1/22/2018 4:55:37 PM                  Inj :   1
                                                Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2018-01-22 15-32-04\column1 0.5% IPA 99.5% hex 40min-1
                  .0mL.M (Sequence Method)
Last changed    : 1/22/2018 3:32:06 PM by SYSTEM
Method Info     : Column1 40min-0.5% iPrOH 99.5% hexane-1.0mL
```



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

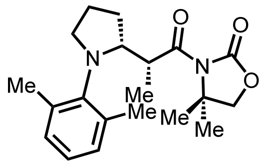
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.478	BV	0.2633	540.04773	30.10438	50.2350
2	9.565	VB	0.3001	534.99445	26.21741	49.7650

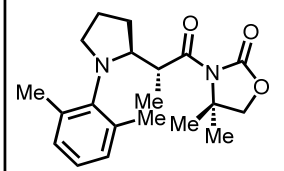
```
Acq. Operator   : SYSTEM                          Seq. Line :   1
Acq. Instrument : Wasa_LC1                         Location :   32
Injection Date  : 1/22/2018 5:27:21 PM                  Inj :   1
                                                 Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2018-01-22 17-26-19\column1 0.5% IPA 99.5% hex 40min-1
                  .0mL.M (Sequence Method)
Last changed    : 1/22/2018 5:26:21 PM by SYSTEM
Method Info     : Column1 40min-0.5% iPrOH 99.5% hexane-1.0mL
```



Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.553	MM	0.3346	1.11078e4	553.30640	100.0000





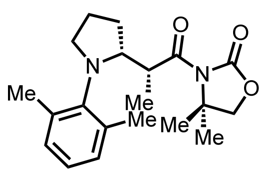
3-(2-(1-(2,6-dimethylphenyl)pyrrolidin-2-yl)propanoyl)-4,4-dimethyloxazolidin-2-one (3w)

1-(2,6-dimethylphenyl)pyrrolidine **1w** was reacted with 3-acryloyl-4,4-dimethyloxazolidin-2-one **2r** following the **General Procedure for Stereoselective Mannich Reactions**. The ^{1}H NMR analysis of the crude material revealed that **3w-*anti*** and **3w-*syn*** were obtained in the ratio of 3.8:1. After purification by column chromatography (hexanes: Et_2O = 19:1 then 9:1), **3w-*anti*** (39 mg, 56%) and **3w-*syn*** (10 mg, 15%) were obtained as single diastereomers. The absolute configurations of **3w-*anti*** and **3w-*syn*** were assigned in analogy, see SI Section 4.

3w-*anti*: ^{1}**H NMR** (600 MHz, $CDCl_3$) δ 6.98 – 6.89 (m, 3H), 4.09 (q, *J* = 6.7 Hz, 1H), 3.83 (d, *J* = 8.2 Hz, 1H), 3.78 – 3.70 (m, 2H), 3.34 (ddd, *J* = 8.2, 7.0, 5.4 Hz, 1H), 2.96 (td, *J* = 7.9, 6.2 Hz, 1H), 2.27 (d, *J* = 1.9 Hz, 6H), 2.13 (dq, *J* = 12.0, 6.7 Hz, 1H), 2.02 – 1.82 (m, 3H), 1.35 (s, 3H), 1.12 (d, *J* = 6.9 Hz, 3H), 1.04 (s, 3H); ^{13}**C NMR** (151 MHz, $CDCl_3$) δ 177.04, 153.56, 144.81, 139.12, 137.98, 129.43, 127.90, 125.16, 74.71, 61.71, 60.25, 52.50, 44.52, 29.84, 25.27, 24.43, 24.08, 19.28, 18.98, 14.99; **IR** (neat) 2965, 2874, 1774, 1699, 1466, 1374, 1304, 1219, 1176, 1085, 1035, 766 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{20}H_{28}N_2O_3$ (MH^+): 345.2172; found: 345.2181; $[\alpha]^{25}_D$ = –36.2° (c = 0.8, EtOH); **HPLC** (Chiralcel IC; 5.0%/ 95.0% *n*-butanol/ hexanes, 0.2 mL/min; tr = 27.3 min (minor), 30.4 min (major); 89:11 er.

3w-*syn*: ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 6.98 (t, *J* = 8.1 Hz, 2H), 6.92 (t, *J* = 7.4 Hz, 1H), 4.04 (ddd, *J* = 8.9, 6.5, 2.7 Hz, 1H), 3.90 (d, *J* = 8.3 Hz, 1H), 3.82 (d, *J* = 8.3 Hz, 1H), 3.75 (q, *J* = 6.7 Hz, 1H), 3.36 (td, *J* = 7.9, 2.8 Hz, 1H), 2.89 (td, *J* = 8.9, 6.7 Hz, 1H), 2.35 (s, 3H), 2.27 (s, 1H), 2.25 (s, 3H), 2.09 – 1.96 (m, 1H), 1.95 – 1.84 (m, 1H), 1.75 (ddt, *J* = 12.9, 6.7, 2.9 Hz, 1H), 1.45 (s, 3H), 1.17 (s, 3H), 1.00 (d, *J* = 6.7 Hz, 3H); ^{13}**C NMR** (151 MHz, $CDCl_3$) δ

177.12, 153.92, 146.85, 138.99, 135.49, 129.56, 128.34, 124.83, 74.93, 63.31, 60.53, 53.70, 46.52, 31.66, 25.46, 24.62, 23.87, 19.31, 19.12, 13.65; **IR** (neat) 2965, 2874, 1774, 1699, 1466, 1374, 1304, 1219, 1176, 1085, 1035, 766 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{20}H_{28}N_2O_3$ (MH^+): 345.2172; found: 345.2181; **HPLC** (Chiralcel IC; 5.0%/ 95.0% *n*-butanol/ hexanes, 0.5 mL/min; tr = 10.5 min (minor), 11.7 min (major); 93:7 er.



3w-*anti*

```
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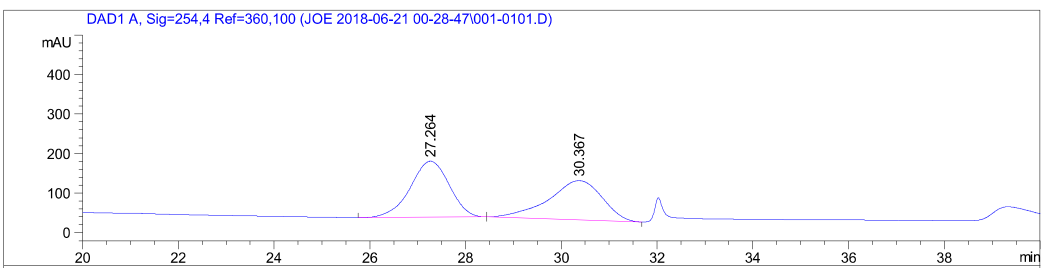
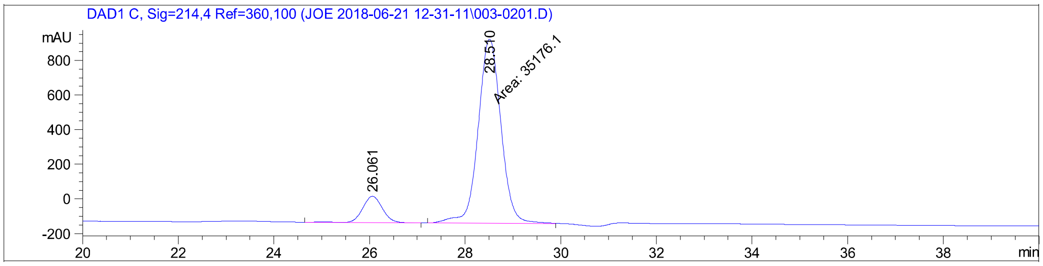
Injection Date  : 6/21/2018 12:30:35 AM                 Inj :   1
                                                 Inj Volume : 6.000 µl
Acq. Method     : C:\Chem32\1\Data\JOE 2018-06-21 00-28-47\column2 5.0%BuOH 95% hex 60min-0.
                  2mL.M
```



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

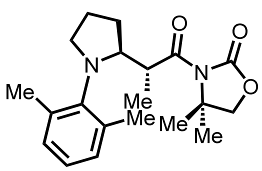
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.264	BB	0.8812	8043.24463	141.49239	51.0721
2	30.367	BB	1.1558	7705.54541	99.46435	48.9279

```
Acq. Operator   : SYSTEM                        Seq. Line :   2
Acq. Instrument : Wasa_LC1                       Location :   3
Injection Date  : 6/21/2018 1:04:03 PM                Inj :   1
                                               Inj Volume : 6.000 µl
Acq. Method     : C:\Chem32\1\Data\JOE 2018-06-21 12-31-11\column2 5.0%BuOH 95% hex 60min-0.
                  2mL.M
```



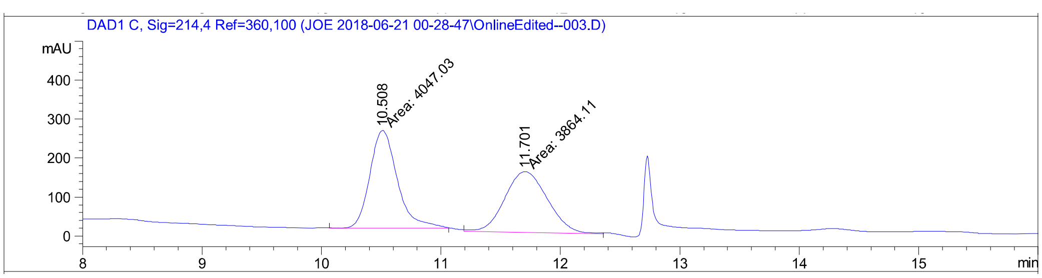
Signal 3: DAD1 C, Sig=214,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.061	VB R	0.4427	4418.16357	152.59972	11.1586
2	28.510	MM	0.5518	3.51761e4	1062.52637	88.8414



3w-*syn*

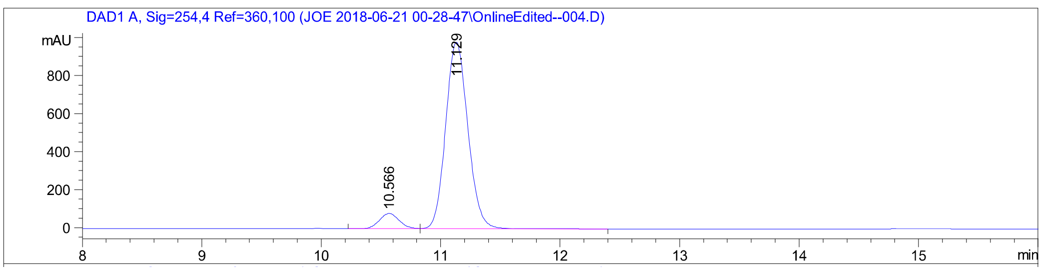
```
Acq. Operator   : SYSTEM                        Seq. Line :   3
Acq. Instrument : Wasa_LC1                       Location :   2
Injection Date  : 6/21/2018 2:32:30 AM                Inj :   1
                                               Inj Volume : 6.000 µl
Acq. Method     : C:\Chem32\1\Data\JOE 2018-06-21 00-28-47\column2 5.0%BuOH 95% hex 20min-0.
                  5mL.M
```



Signal 3: DAD1 C, Sig=214,4 Ref=360,100

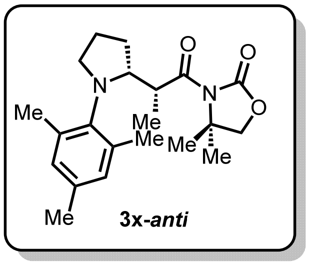
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.508	MM	0.2688	4047.02881	250.90140	51.1561
2	11.701	MM	0.4140	3864.10767	155.56763	48.8439

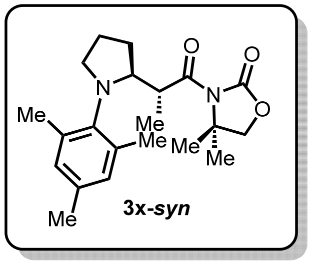
Acq. Operator : SYSTEM Seq. Line : 4
Acq. Instrument : Wasa_LC1 Location : 4
Injection Date : 6/21/2018 2:53:28 AM Inj : 1
Inj Volume : 6.000 µl
Acq. Method : C:\Chem32\1\Data\JOE 2018-06-21 00-28-47\column2 5.0%BuOH 95% hex 20min-0.5mL.M



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.566	BV	0.1815	936.54675	80.62458	6.8448
2	11.129	VB	0.2014	1.27461e4	982.07147	93.1552





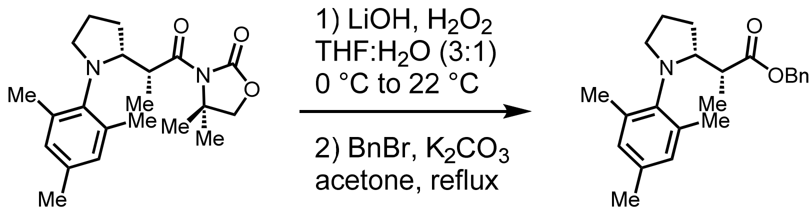
3-(2-(1-mesitylpyrrolidin-2-yl)propanoyl)-4,4-dimethyloxazolidin-2-one (3x)

1-mesitylpyrrolidine **1x** was reacted with 3-acryloyl-4,4-dimethyloxazolidin-2-one **2r** following the **General Procedure for Stereoselective Mannich Reactions**. The ^{1}H NMR analysis of the crude material revealed that **3x-*anti*** and **3x-*syn*** were obtained in the ratio of 3.5:1. After purification by column chromatography (hexanes: Et_2O = 19:1 then 9:1), **3x-*anti*** (39 mg, 54%) and **3x-*syn*** (11 mg, 15%) were obtained as single diastereomers. The absolute configurations of **3x-*anti*** and **3x-*syn*** were assigned in analogy, see SI Section 4.

3x-*anti*: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.77 (d, *J* = 9.0 Hz, 2H), 4.04 (q, *J* = 6.7 Hz, 1H), 3.83 (d, *J* = 8.2 Hz, 1H), 3.78 – 3.63 (m, 2H), 3.31 (td, *J* = 7.8, 5.6 Hz, 1H), 2.95 (td, *J* = 7.9, 6.2 Hz, 1H), 2.23 (d, *J* = 6.3 Hz, 6H), 2.19 (s, 3H), 2.14 – 2.06 (m, 1H), 1.99 – 1.88 (m, 2H), 1.88 – 1.78 (m, 1H), 1.36 (s, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 1.06 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 177.11, 153.53, 141.99, 139.02, 137.81, 134.53, 130.16, 128.62, 74.71, 61.73, 60.24, 52.53, 44.37, 29.81, 25.19, 24.46, 23.91, 20.70, 19.10, 18.84, 14.84; **IR** (neat) 2965, 1775, 1700, 1477, 1375, 1304, 1176, 1084, 765 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{21}H_{30}N_2O_3$ (MH^+): 359.2329; found: 359.2311; $[\alpha]^{25}_{D}$ = −10.6° (c = 0.3, EtOH).

3x-*syn*: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.79 (d, *J* = 14.1 Hz, 2H), 4.02 – 3.93 (m, 1H), 3.90 (dd, *J* = 8.3, 1.2 Hz, 1H), 3.82 (d, *J* = 8.3 Hz, 1H), 3.74 (p, *J* = 6.7 Hz, 1H), 3.32 (td, *J* = 9.6, 5.0 Hz, 1H), 2.87 (q, *J* = 8.3 Hz, 1H), 2.30 (s, 3H), 2.27 – 2.21 (m, 1H), 2.20 (s, 6H), 2.06 – 1.94 (m, 1H), 1.88 (d, *J* = 9.8 Hz, 1H), 1.73 (dd, *J* = 14.3, 6.7 Hz, 1H), 1.45 (s, 3H), 1.18 (s, 3H), 0.99 (dd, *J* = 6.8, 1.2 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 177.21, 153.92, 144.21, 138.73, 135.22, 134.22, 130.20, 129.05, 74.92, 63.38, 60.53, 53.84, 46.51, 31.64, 25.42, 24.64, 23.80, 20.66, 19.17, 18.98, 13.74; **IR** (neat) 2965, 1775, 1700, 1477, 1375, 1304, 1176, 1084, 765 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{21}H_{30}N_2O_3$ (MH^+): 359.2329; found:

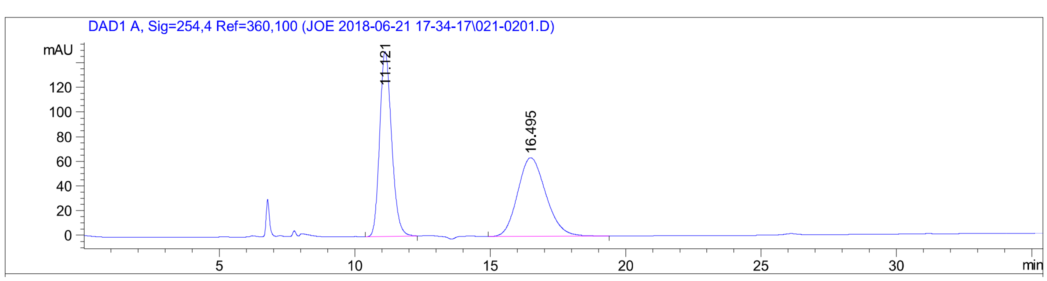
359.2311; **HPLC** (Chiralpak AS-H then OD-H; 2.5%/ 97.5% isopropanol/ hexanes, 0.5 mL/min; tr = 19.7 min (major), 19.9 min (minor); 93:7 er.



3x-*anti* **5x-*anti***, 90% yield
89:11 er

3x-*anti* was transformed into the corresponding benzyl ester **5x-*anti*** following previously reported literatures.[19,20] **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35 – 7.25 (m, 3H), 7.22 – 7.17 (m, 2H), 6.79 (d, *J* = 20.5 Hz, 2H), 4.69 (d, *J* = 12.4 Hz, 1H), 4.62 (d, *J* = 12.5 Hz, 1H), 3.96 (dt, *J* = 7.5, 5.6 Hz, 1H), 3.37 – 3.26 (m, 1H), 2.97 (q, *J* = 7.7 Hz, 1H), 2.42 (p, *J* = 6.8 Hz, 1H), 2.24 (s, 3H), 2.20 (d, *J* = 8.8 Hz, 6H), 2.05 (dq, *J* = 12.2, 7.6 Hz, 1H), 1.96 – 1.86 (m, 2H), 1.82 – 1.73 (m, 1H), 1.15 – 1.11 (m, 3H); **IR** (neat) 2921, 2852, 1718, 1480, 1455, 1373, 1262, 1183, 1150, 1110, 851, 750, 696 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{23}H_{30}NO_2$ (MH^+): 352.2271; found: 352.2254; $[\alpha]^{25}_D$ = –30.1° (c = 0.4, EtOH); **HPLC** (Chiralpak OJ-H; 1.0%/ 99.0% isopropanol/ hexanes, 0.5 mL/min; tr = 11.1 min (minor), 16.5 min (major); 89:11 er.

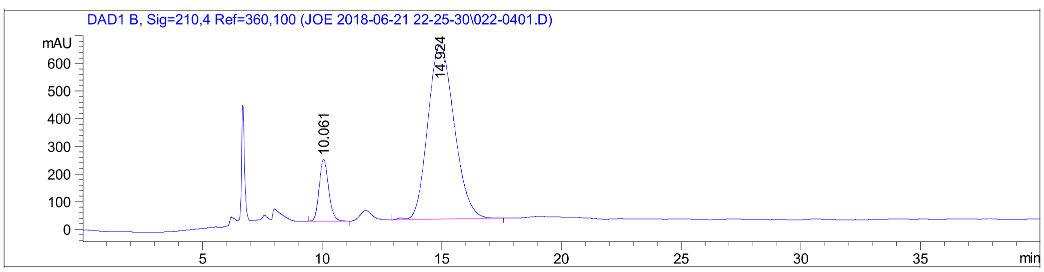
```
Acq. Operator   : SYSTEM                         Seq. Line :   2
Acq. Instrument : Wasa_LC1                        Location :   21
Injection Date  : 6/21/2018 6:16:21 PM                 Inj :   1
                                                Inj Volume : 8.000 µl
Method          : C:\Chem32\1\Data\JOE 2018-06-21 17-34-17\column1 1% IPA 99% hex 40min-0.5mL
                  .M (Sequence Method)
```



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

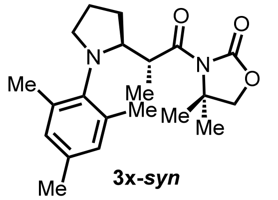
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.121	BB	0.4735	4593.83643	149.91234	49.8195
2	16.495	BB	1.1162	4627.12061	63.79744	50.1805

Acq. Operator : SYSTEM Seq. Line : 4
Acq. Instrument : Wasa_LC1 Location : 22
Injection Date : 6/22/2018 12:30:17 AM Inj : 1
Inj Volume : 8.000 µl
Method : C:\Chem32\1\Data\JOE 2018-06-21 22-25-30\column1 1% IPA 99% hex 40min-0.5mL .M (Sequence Method)



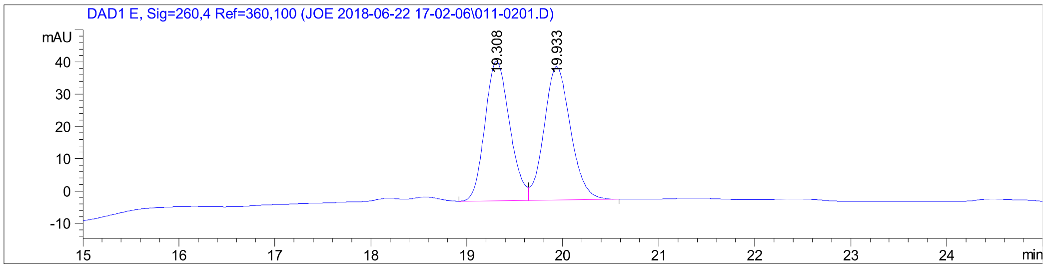
Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.061	BB	0.4193	6072.40137	223.25262	11.2162
2	14.924	VB R	1.1847	4.80673e4	629.66699	88.7838



3x-*syn*

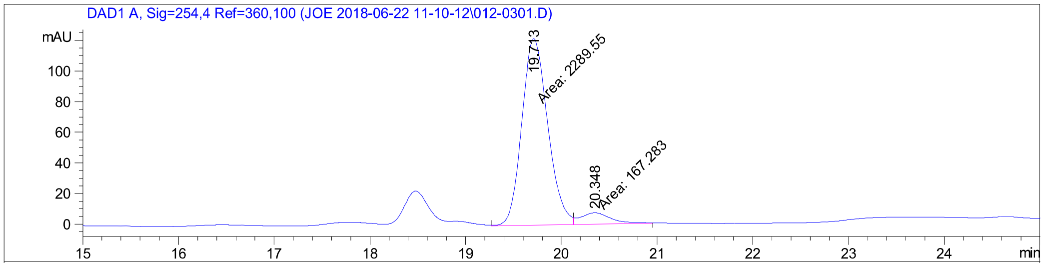
```
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                         Location :   11
Injection Date  : 6/22/2018 6:04:59 PM                  Inj :   1
                                                 Inj Volume : 4.000 µl
Acq. Method     : C:\Chem32\1\Data\JOE 2018-06-22 17-02-06\column1 2.5% IPA 97.5% hex 40min-0
                  .5mL.M
```



Signal 5: DAD1 E, Sig=260,4 Ref=360,100

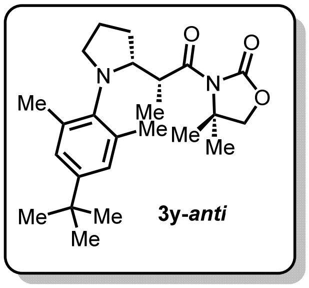
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.308	BV	0.2767	774.05029	43.28084	49.4364
2	19.933	VB	0.2932	791.69958	41.37559	50.5636

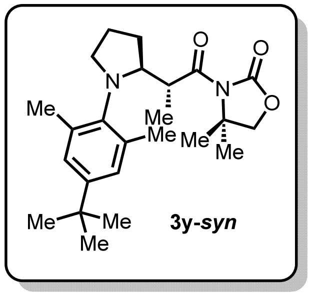
```
Acq. Operator   : SYSTEM                         Seq. Line :   3
Acq. Instrument : Wasa_LC1                        Location :   12
Injection Date  : 6/22/2018 12:33:57 PM                Inj :   1
                                               Inj Volume : 4.000 µl
Acq. Method     : C:\Chem32\1\Data\JOE 2018-06-22 11-10-12\column1 2.5% IPA 97.5% hex 40min-0
                  .5mL.M
```



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.713	MM	0.3134	2289.55151	121.74718	93.1911
2	20.348	MM	0.3734	167.28326	7.46763	6.8089





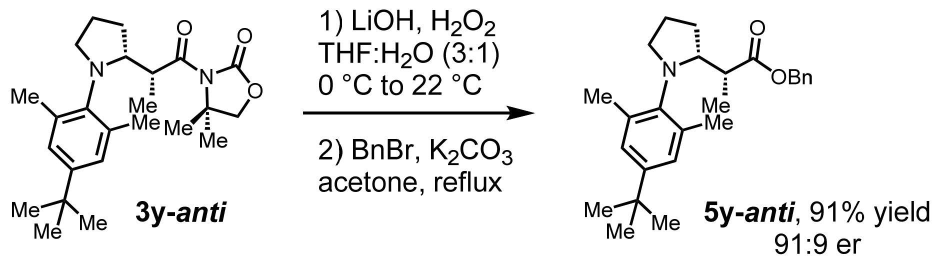
3-(2-(1-(4-(*tert*-Butyl)-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoyl)-4,4-dimethyloxazolidin-2-one (3y)

1-(4-(*tert*-Butyl)-2,6-dimethylphenyl)pyrrolidine **1y** was reacted with 3-acryloyl-4,4-dimethyloxazolidin-2-one **2r** following the **General Procedure for Stereoselective Mannich Reactions**. The ^{1}H NMR analysis of the crude material revealed that **3y-*anti*** and **3y-*syn*** were obtained in the ratio of 4.4:1. After purification by column chromatography (hexanes: Et_2O = 19:1 then 9:1), **3y-*anti*** (46 mg, 57%) and **3y-*syn*** (10 mg, 13%) were obtained as single diastereomers. The absolute configurations of **3y-*anti*** and **3y-*syn*** were assigned in analogy, see SI Section 4.

3y-*anti*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 – 6.91 (m, 2H), 4.10 (q, *J* = 6.8 Hz, 1H), 3.83 (dd, *J* = 8.2, 1.0 Hz, 1H), 3.77 – 3.67 (m, 2H), 3.38 – 3.26 (m, 1H), 2.99 – 2.89 (m, 1H), 2.26 (d, *J* = 3.0 Hz, 6H), 2.17 – 2.08 (m, 1H), 1.90 (dddd, *J* = 27.8, 23.7, 12.1, 6.6 Hz, 3H), 1.34 (s, 3H), 1.25 (d, *J* = 1.0 Hz, 9H), 1.12 (dd, *J* = 7.0, 1.0 Hz, 3H), 0.98 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.07, 153.57, 147.42, 142.12, 138.16, 137.05, 126.32, 124.94, 74.70, 61.68, 60.22, 52.76, 44.74, 34.01, 31.46, 30.16, 25.20, 24.40, 24.18, 19.55, 19.23, 15.34; **IR** (neat) 2963, 2871, 1774, 1700, 1483, 1459, 1373, 1305, 1221, 1176, 1084, 766 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{24}H_{36}N_2O_3$ (MH^+): 401.2799; found: 401.2789; $[\alpha]^{25}_{D}$ = –40.6° (c = 1.0, EtOH).

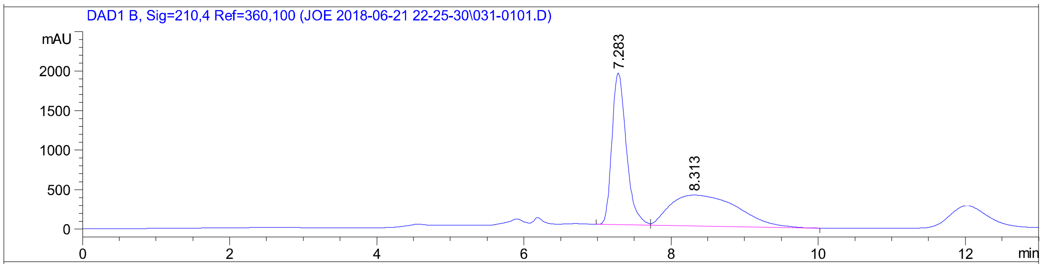
3y-*syn*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 – 6.87 (m, 2H), 4.06 (ddd, *J* = 8.4, 5.4, 2.4 Hz, 1H), 3.87 (d, *J* = 8.3 Hz, 1H), 3.73 (dd, *J* = 12.8, 7.4 Hz, 2H), 3.41 – 3.28 (m, 1H), 2.89 (ddd, *J* = 9.5, 8.5, 6.5 Hz, 1H), 2.34 (s, 3H), 2.32 – 2.25 (m, 1H), 2.22 (s, 3H), 2.09 – 1.94 (m, 1H), 1.94 – 1.84 (m, 1H), 1.78 (ddt, *J* = 12.6, 7.2, 2.7 Hz, 1H), 1.42 (s, 3H), 1.25 (s, 9H), 1.06 (d, *J*

= 6.7 Hz, 3H), 1.00 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.79, 153.95, 147.42, 143.99, 138.31, 134.51, 126.44, 125.34, 74.92, 63.20, 60.51, 54.05, 46.42, 33.98, 31.61, 31.41, 25.52, 24.58, 24.45, 23.65, 19.54, 12.71; **IR** (neat) 2963, 2871, 1774, 1700, 1483, 1459, 1373, 1305, 1221, 1176, 1084, 766 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{24}H_{36}N_2O_3$ (MH^+): 401.2799; found: 401.2789; **HPLC** (Chiralpak IA then OJ-H; 1.0%/ 99.0% isopropanol/ hexanes, 0.1 mL/min; tr = 103.3 min (major), 108.1 min (minor); 98:2 er.



3y-*anti* was transformed into the corresponding benzyl ester **5y-*anti*** following previously reported literatures.[19,20] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 3H), 7.21 – 7.18 (m, 2H), 7.00 (d, *J* = 2.4 Hz, 1H), 6.96 (d, *J* = 2.4 Hz, 1H), 4.65 (d, *J* = 12.5 Hz, 1H), 4.54 (d, *J* = 12.5 Hz, 1H), 3.98 (td, *J* = 6.9, 5.3 Hz, 1H), 3.39 – 3.29 (m, 1H), 3.00 (q, *J* = 7.7 Hz, 1H), 2.43 (p, *J* = 6.9 Hz, 1H), 2.29 (s, 3H), 2.24 (s, 3H), 2.07 (dq, *J* = 12.1, 7.6 Hz, 1H), 1.98 – 1.85 (m, 2H), 1.84 – 1.73 (m, 1H), 1.25 (s, 9H), 1.13 (d, *J* = 7.0 Hz, 3H); **IR** (neat) 2959, 2924, 2869, 2359, 2158, 1720, 1553, 1482, 1455, 1361, 1222, 1151, 1109, 732, 696 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{26}H_{36}NO_2$ (MH^+): 394.2741; found: 394.2733; $[\alpha]^{25}_D$ = –38.9° (c = 0.5, EtOH); **HPLC** (Chiralpak OJ-H; 1.0%/ 99.0% isopropanol/ hexanes, 0.5 mL/min; tr = 7.3 min (minor), 8.3 min (major); 91:9 er.

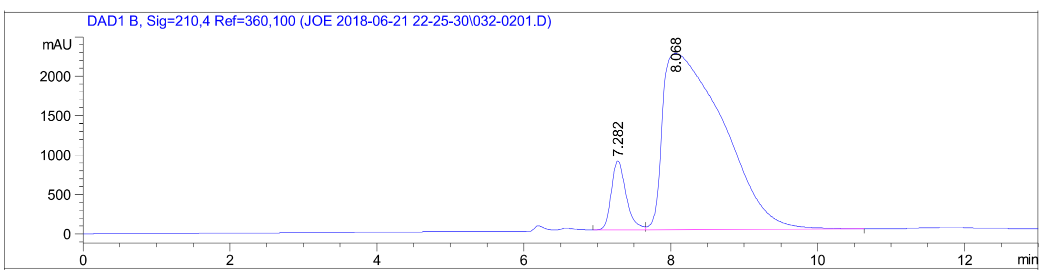
Acq. Operator : SYSTEM Seq. Line : 1
Acq. Instrument : Wasa_LC1 Location : 31
Injection Date : 6/21/2018 10:27:23 PM Inj : 1
Inj Volume : 8.000 µl
Acq. Method : C:\Chem32\1\Data\JOE 2018-06-21 22-25-30\column1 1% IPA 99% hex 40min-0.5mL .M



Signal 2: DAD1 B, Sig=210,4 Ref=360,100

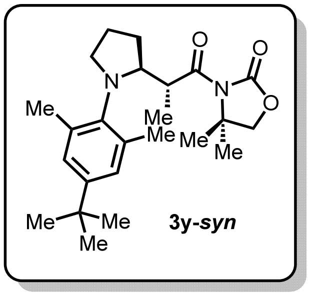
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.283	BV	0.2095	2.62151e4	1917.36487	50.9982
2	8.313	VB	1.0825	2.51889e4	390.51810	49.0018

Acq. Operator : SYSTEM Seq. Line : 2
Acq. Instrument : Wasa_LC1 Location : 32
Injection Date : 6/21/2018 11:08:21 PM Inj : 1
Inj Volume : 8.000 µl
Acq. Method : C:\Chem32\1\Data\JOE 2018-06-21 22-25-30\column1 1% IPA 99% hex 40min-0.5mL .M



Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.282	BV	0.2137	1.23096e4	877.13251	8.7194
2	8.068	VB	0.8255	1.28865e5	2238.84619	91.2806



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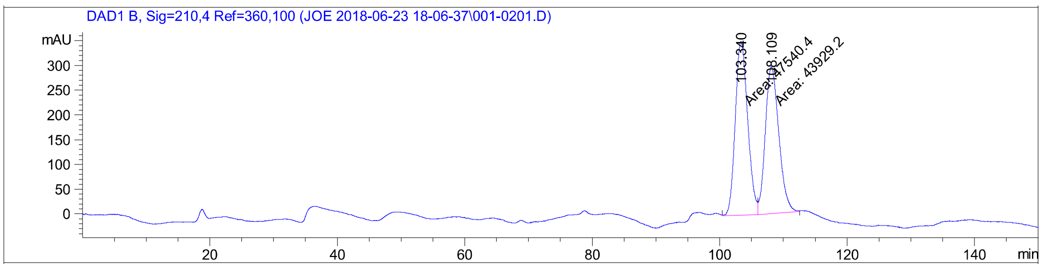
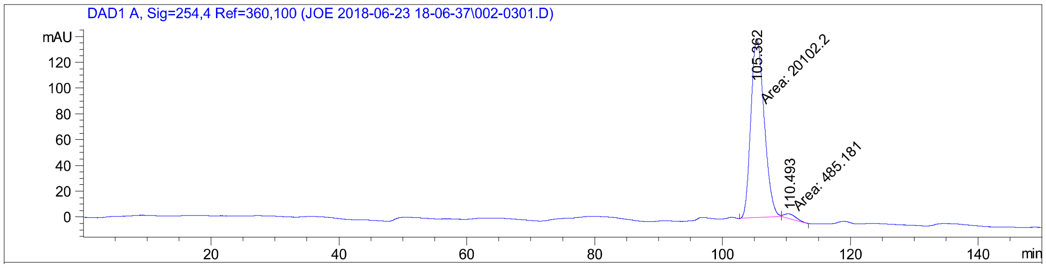
Acq. Operator   : SYSTEM                          Seq. Line :    2
Acq. Instrument : Wasa_LC1                         Location :    1
Injection Date  : 6/23/2018 7:08:43 PM                  Inj :    1
                                                 Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2018-06-23 18-06-37\column1 1% IPA 99% hex 150min-0.
                  1mL.M (Sequence Method)
Last changed    : 6/23/2018 6:06:40 PM by SYSTEM
Method Info     : column1 1% IPA 99% hex-150min-0.1mL
```



Signal 2: DAD1 B, Sig=210,4 Ref=360,100

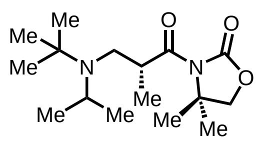
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	103.340	MM	2.2579	4.75404e4	350.91858	51.9740
2	108.109	MM	2.4702	4.39292e4	296.39090	48.0260

```
Acq. Operator   : SYSTEM                          Seq. Line :   3
Acq. Instrument : Wasa_LC1                         Location :   2
Injection Date  : 6/23/2018 9:39:38 PM                  Inj :   1
                                                Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2018-06-23 18-06-37\column1 1% IPA 99% hex 150min-0.
                  1mL.M (Sequence Method)
Last changed    : 6/23/2018 6:06:40 PM by SYSTEM
Method Info     : column1 1% IPA 99% hex-150min-0.1mL
```



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	105.362	MM	2.4176	2.01022e4	138.58492	97.6433
2	110.493	MM	2.1680	485.18082	3.72993	2.3567

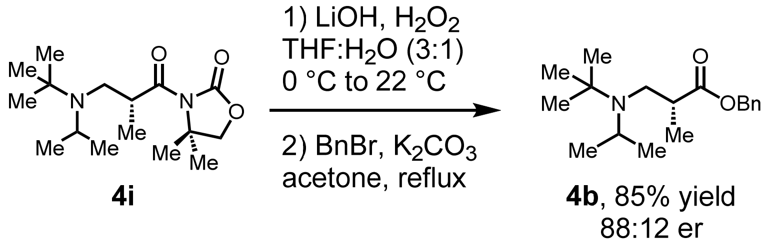


4i

3-(3-(*tert*-Butyl(isopropyl)amino)-2-methylpropanoyl)-4,4-dimethyloxazolidin-2-one (4i)

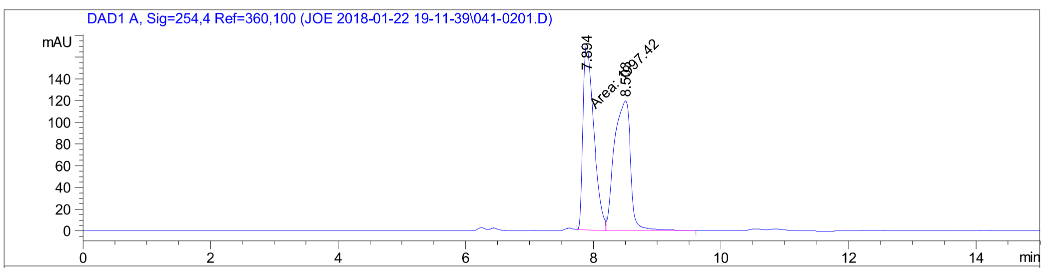
N-Isopropyl-*N*,2-dimethylpropan-2-amine **1r** was reacted with 3-acryloyl-4,4-dimethyloxazolidin-2-one **2r** following the **General Procedure for Stereoselective Mannich Reactions**. After purification by silica gel column chromatography (hexanes: Et_3N = 98.5 : 1.5), **4i** (30.8 mg, 52%) was obtained as a colorless oil.

4i: ^{1}**H NMR** (600 MHz, $CDCl_3$) δ 4.01 – 3.93 (m, 2H), 3.83 (h, *J* = 6.9 Hz, 1H), 3.24 (hept, *J* = 6.8 Hz, 1H), 3.02 (dd, *J* = 14.2, 7.9 Hz, 1H), 2.49 (dd, *J* = 14.2, 6.3 Hz, 1H), 1.58 (s, 3H), 1.56 (s, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.06 (s, 9H), 1.01 (dd, *J* = 9.1, 6.8 Hz, 6H); ^{13}**C NMR** (151 MHz, $CDCl_3$) δ 178.92, 153.92, 75.03, 60.62, 55.73, 46.50, 46.47, 41.02, 28.49, 24.85, 24.81, 23.48, 22.12, 15.70; **IR** (neat) 2969, 2874, 1774, 1703, 1460, 1366, 1305, 1223, 1177, 1082, 939, 765 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{16}H_{30}N_2O_3$ (MH^+): 299.2329; found: 299.2338; $[\alpha]^{25}_{D}$ = –20.7° (c = 1.0, EtOH).



4i was transformed into the corresponding benzyl ester **4b** following previously reported literatures.[19,20] **HPLC** (Chiralcel OD-H; 0.5%/ 99.5% isopropanol/ hexanes, 1.0 mL/min; **4b:** tr = 7.9 min (major), 8.5 min (minor); 88:12 er.

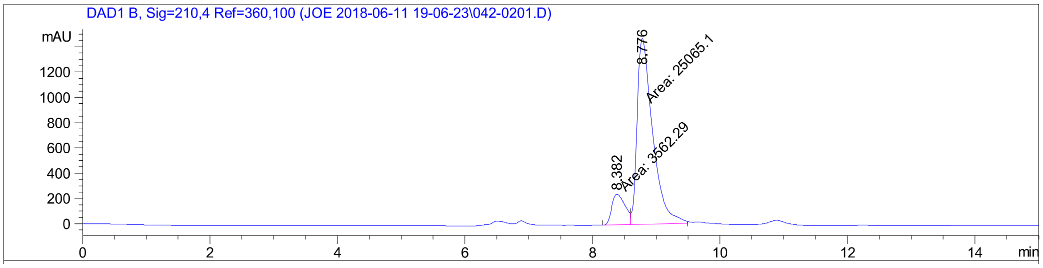
```
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                         Location :   41
Injection Date  : 1/22/2018 8:13:40 PM                  Inj :   1
                                                 Inj Volume : 4.000 µl
Acq. Method     : C:\Chem32\1\Data\JOE 2018-01-22 19-11-39\column1 1% IPA 99% hex 60min-0.5mL
                  .M
```



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

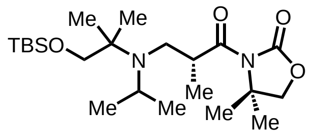
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.894	MM	0.1943	1997.41541	171.33118	48.6461
2	8.503	VB	0.3002	2108.59668	119.28552	51.3539

```
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                         Location :   42
Injection Date  : 6/11/2018 7:49:16 PM                  Inj :   1
                                                 Inj Volume : 4.000 µl
Acq. Method     : C:\Chem32\1\Data\JOE 2018-06-11 19-06-23\column1 1% IPA 99% hex 30min-0.5mL
                  .M
```



Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.382	MF	0.2447	3562.28613	242.67213	12.4436
2	8.776	FM	0.2838	2.50651e4	1471.84851	87.5564

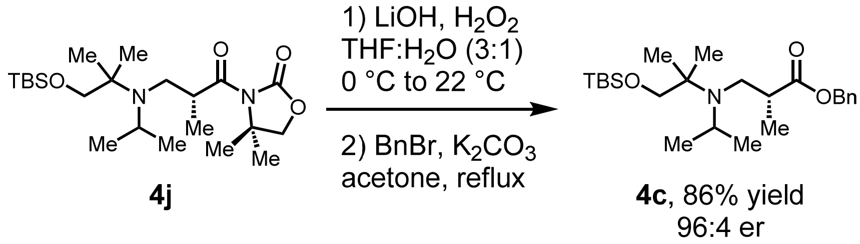


4j

3-(3-((1-((*tert*-Butyldimethylsilyl)oxy)-2-methylpropan-2-yl)(isopropyl)amino)-2-methylpropanoyl)-4,4-dimethyloxazolidin-2-one (4j)

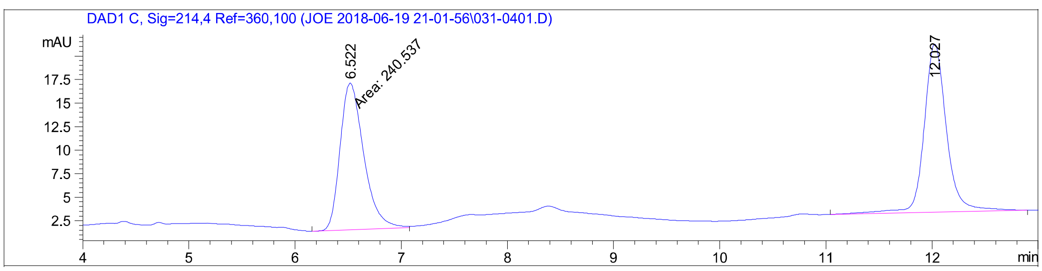
1-((*tert*-Butyldimethylsilyl)oxy)-*N*-ethyl-*N*-isopropyl-2-methylpropan-2-amine **1s** was reacted with 3-acryloyl-4,4-dimethyloxazolidin-2-one **2r** following the **General Procedure for Stereoselective Mannich Reactions**. After purification by silica gel column chromatography (hexanes: Et_3N = 98.5 : 1.5), **4j** (40 mg, 46%) was obtained as a colorless oil.

4j: ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 4.03 – 3.91 (m, 2H), 3.81 (h, *J* = 6.9 Hz, 1H), 3.37 (s, 2H), 3.26 (h, *J* = 6.7 Hz, 1H), 3.13 (dd, *J* = 14.4, 7.8 Hz, 1H), 2.64 (dd, *J* = 14.4, 6.6 Hz, 1H), 1.56 (d, *J* = 7.3 Hz, 6H), 1.09 (d, *J* = 6.8 Hz, 3H), 1.07 – 0.99 (m, 12H), 0.88 (s, 9H), 0.01 (s, 6H); ^{13}**C NMR** (151 MHz, $CDCl_3$) δ 178.83, 153.87, 75.00, 69.38, 60.57, 59.40, 46.88, 46.31, 41.06, 25.84, 24.80, 24.34, 24.24, 23.52, 22.22, 18.15, 15.51, -5.60; **IR** (neat) 2958, 2930, 2888, 2857, 1780, 1705, 1467, 1387, 1362, 1304, 1252, 1087, 837, 774 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{22}H_{44}N_2O_4Si$ (MH^+): 429.3143; found: 429.3133; $[\alpha]^{25}_D$ = –7.3° (c = 1.0, EtOH).



4j was transformed into the corresponding benzyl ester **4c** following previously reported literatures.[19,20] **HPLC** (Chiralcel OD-H; 0.5%/ 99.5% *n*-butanol/ hexanes, 1.0 mL/min; **4c:** tr = 6.5 min (minor), 12.0 min (major); 96:4 er.

```
Acq. Operator   : SYSTEM                          Seq. Line :   4
Acq. Instrument : Wasa_LC1                          Location :   31
Injection Date  : 6/19/2018 11:06:37 PM                  Inj :   1
                                                  Inj Volume : 4.000 µl
Acq. Method     : C:\Chem32\1\Data\JOE 2018-06-19 21-01-56\column1 0.5% nBuOH 99.5% hex 40min
                  -1.0mL.M
Last changed    : 6/19/2018 9:01:59 PM by SYSTEM
Analysis Method : C:\Chem32\1\Data\JOE 2018-06-19 21-01-56\column1 0.5% nBuOH 99.5% hex 40min
                  -1.0mL.M (Sequence Method)
```



Signal 3: DAD1 C, Sig=214,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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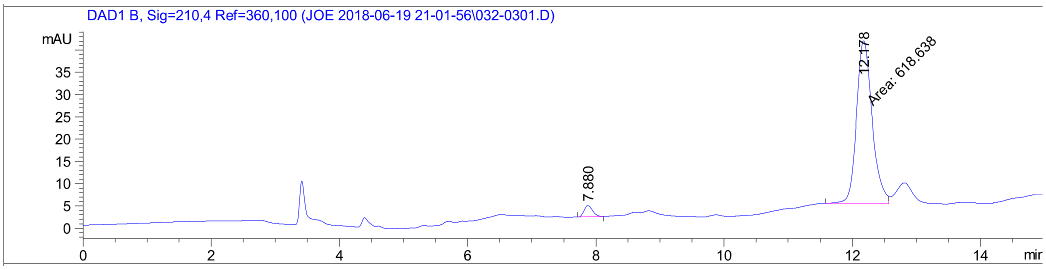
2	12.027	BB	0.2228	261.75095	17.87901	52.1118

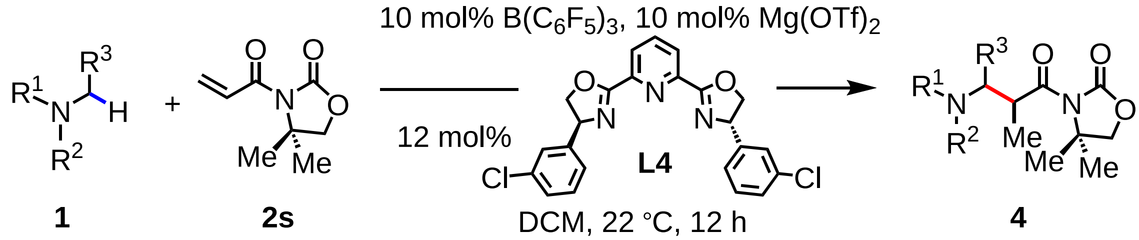
```
Acq. Operator   : SYSTEM                          Seq. Line :    3
Acq. Instrument : Wasa_LC1                         Location :   32
Injection Date  : 6/19/2018 10:25:42 PM                 Inj :    1
                                                 Inj Volume : 4.000 µl
Acq. Method     : C:\Chem32\1\Data\JOE 2018-06-19 21-01-56\column1 0.5% nBuOH 99.5% hex 40min
                  -1.0mL.M
Last changed    : 6/19/2018 9:01:59 PM by SYSTEM
Analysis Method : C:\Chem32\1\Data\JOE 2018-06-19 21-01-56\column1 0.5% nBuOH 99.5% hex 40min
                  -1.0mL.M (Sequence Method)
```

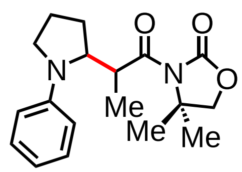
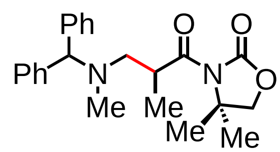
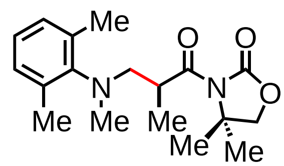
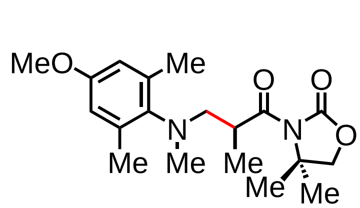
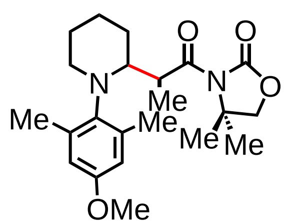
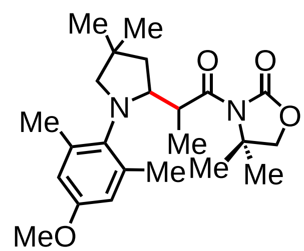


Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.880	BB	0.1410	22.67528	2.51915	3.5358
2	12.178	MF	0.2820	618.63849	36.55745	96.4642

Table SI-9. Evaluation of Amine Substrates for the Stereoselective Mannich Reactions.



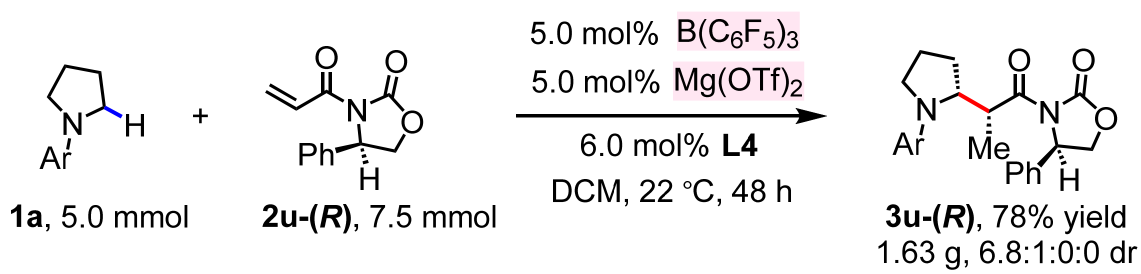
		
4s, < 3% yield	**4t**, < 3% yield	**4u**, < 3% yield
		
4v, < 3% yield	**4w**, < 3% yield	**4x**, 39% yield

[a] Conditions: **1** (0.2 mmol), **2s** (0.3 mmol), $B(C_6F_5)_3$ (10 mol%), $Mg(OTf)_2$ (10 mol%), **L4** (12 mol%), DCM (0.3 mL), under N_2, 22 °C, 12 h. [b] The yield and was determined by ^1H NMR analysis of the unpurified product mixture using mesitylene as the internal standard.

4. Procedure for Large Scale Reaction, Determination of Absolute Configuration, Derivatizations of the Mannich Products and Control Experiments

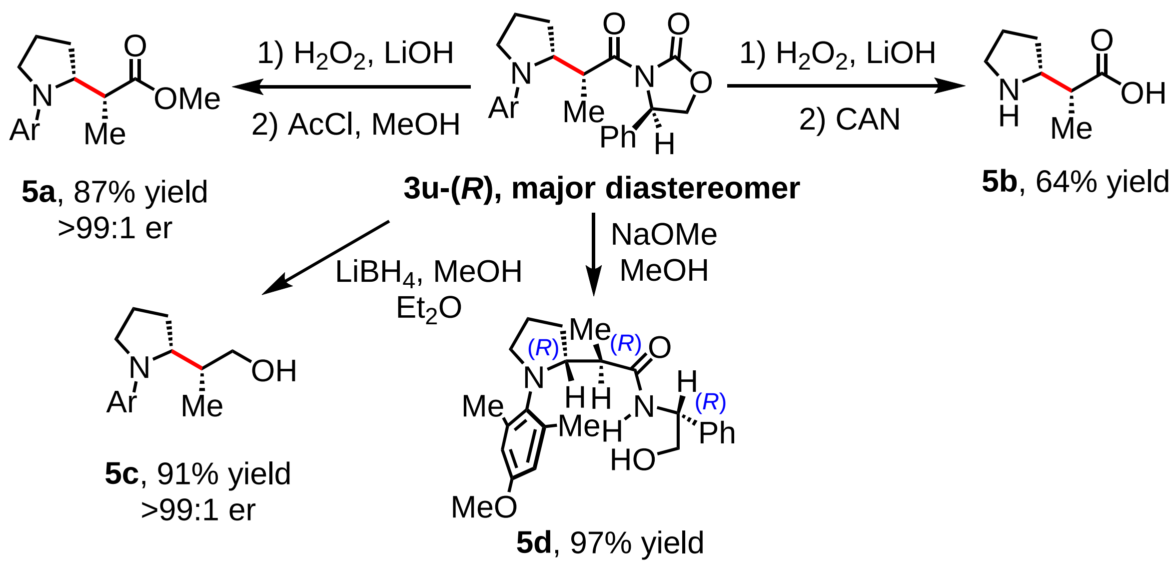
4.1 Procedure for the Large Scale Reaction

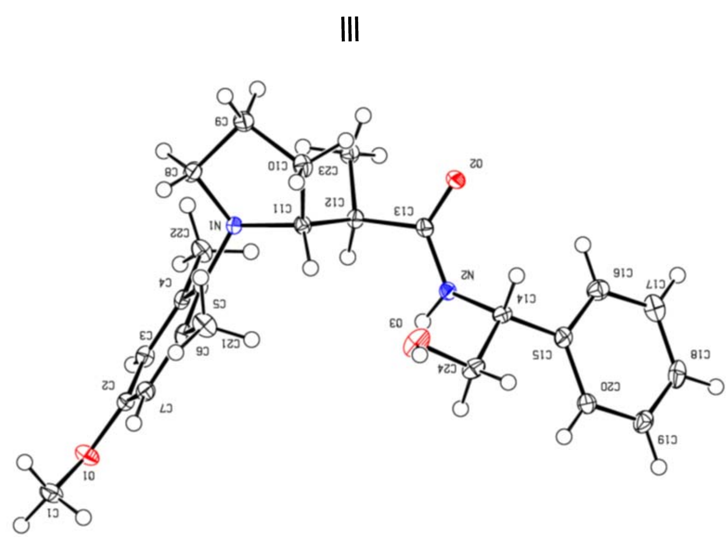
We carried out the following studies in order to determine the absolute configuration of enantioenriched products **3q, 3r**, **3s**, **3t**, **3u-(S)**, **3u-(*R*),** and **3v** and the relative configuration of products **3a** to **3p** and **4a** to **4h**. We first obtained product **3u-(*R*)** in 1.63 g by the following procedure.



To a 35 mL oven-dried sealed tube was added $Mg(OTf)_2$ (0.25 mmol), ligand **L4** (0.30 mmol), DCM (10 mL) under nitrogen atmosphere. The mixture was stirred for 30 min at 22 °C, then (*R*)-3-acryloyl-4-phenyloxazolidin-2-one **2u-(*R*)** (1.3 g, 6.0 mmol), 1-(4-methoxy-2,6-dimethylphenyl)pyrrolidine **1a** (1.02 g, 5.0 mmol), $B(C_6F_5)_3$ (0.25 mmol), and DCM (5.0 mL) were added to the vessel. The reaction mixture was stirred at 22 °C for 48 h. Upon completion, the solvent was removed *in vacuo*. The *anti*:*syn* ratio was determined to be 6.8:1:0:0 by ^{1}H NMR analysis of the crude reaction mixture. Purification by silica gel column chromatography using 4:1 hexanes:Et_2O gave the product as a colorless solid as a mixture of diastereomers (1.63 g, 78% yield). Further purification was carried out by silica gel column chromatography using 4:1 hexanes:Et_2O to obtain the major diastereomer in 1.47 g as a colorless oil.

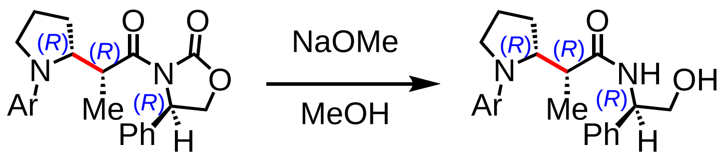
We then subjected **3u-(*R*)** to the following derivatization studies which yielded **5a**, **5b**, **5c**, and **5d**.





4.2 Determination of the Absolute Configuration

The absolute configuration of **3u-(*R*)-major** was determined by X-ray crystallographic analysis of **5d-major**.



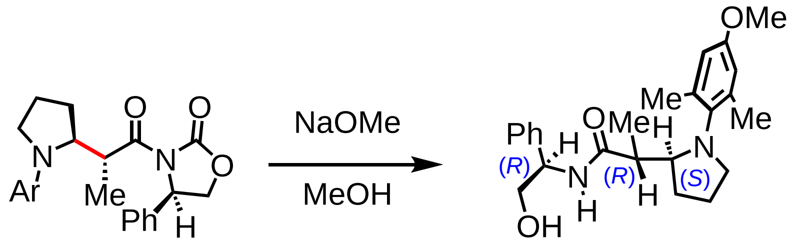
3u-(*R*)-major **5d-major**, 97% yield

(*R*)-*N*-((*R*)-2-Hydroxy-1-phenylethyl)-2-((*R*)-1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanamide (5d-major)

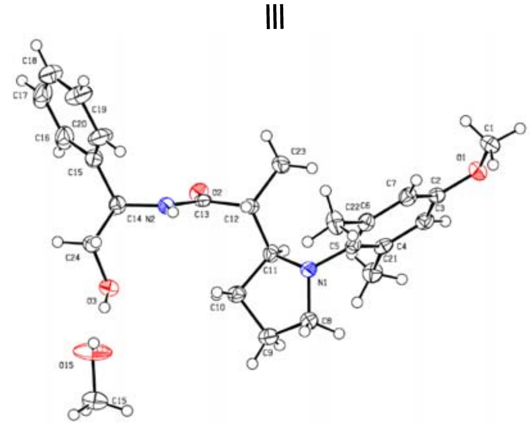
(*R*)-*N*-((*R*)-2-Hydroxy-1-phenylethyl)-2-((*R*)-1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanamide (**5d-major**) was synthesized following a known procedure.[21] A solution of **3u-(*R*)-major** (590 mg, 1.4 mmol) in MeOH (3.5 mL) was chilled to 0 °C, whereupon NaOMe (827 mg, 15.3 mmol) was added portionwise. The reaction was allowed to stir for 1 h, whereupon the reaction was quenched with aq. NH_4Cl (3 mL). The aqueous layer was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (3:1 hexanes:EtOAc) to afford **5d-major** as a crystalline solid (393 mg, 97% yield). The solid material was recrystallized in 19:1 hexanes:isopropanol to obtain a single crystal, which was subjected to the X-ray crystallographic analysis. The X-ray crystallographic analysis revealed that the absolute configuration of **5d-major** is (*R,R,R*); see SI Section 8 for X-ray crystallographic data.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.5 Hz, 2H), 7.29 – 7.25 (m, 1H), 7.20 – 7.17 (m, 2H), 6.59 (d, *J* = 3.0 Hz, 1H), 6.56 (d, *J* = 3.1 Hz, 1H), 5.89 (d, *J* = 6.3 Hz, 1H), 4.74 (td, *J* = 6.0, 3.6 Hz, 1H), 3.92 (dt, *J* = 7.1, 5.4 Hz, 1H), 3.75 (s, 3H), 3.63 (tdd, *J* = 10.7, 8.9, 7.2, 3.6 Hz, 2H), 3.26 (dt, *J* = 8.4, 5.9 Hz, 1H), 2.98 (q, *J* = 7.6 Hz, 1H), 2.89 (d, *J* = 6.1 Hz, 1H), 2.29 (s, 3H), 2.25 (s, 3H), 2.17 (qd, *J* = 6.9, 5.1 Hz, 1H), 2.07 (dq, *J* = 11.7, 7.5, 7.1 Hz, 1H), 1.93 – 1.83 (m, 3H), 1.13 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.92, 159.42, 142.80, 141.78, 141.64, 140.38, 131.52, 130.50, 129.26, 117.31, 115.72, 69.52, 65.50, 59.15, 57.85, 55.28, 49.10, 31.64, 27.75, 22.27, 22.18, 16.66; **IR** (neat) 3383, 3305, 2952, 1644, 1602, 1601, 1512, 1492, 1466, 1261, 1154,1068, 700 cm^{-1}; **HRMS** (DART) m/z Calcd for $C_{26}H_{33}N_2O_4$ (MH^+): 274.1596; found: 274.1588.

The absolute configuration of **3u-(*R*)-minor** was determined by X-ray crystallographic analysis of **5d-minor**.



3u-(*R*)-minor **5d-minor**, 97% yield



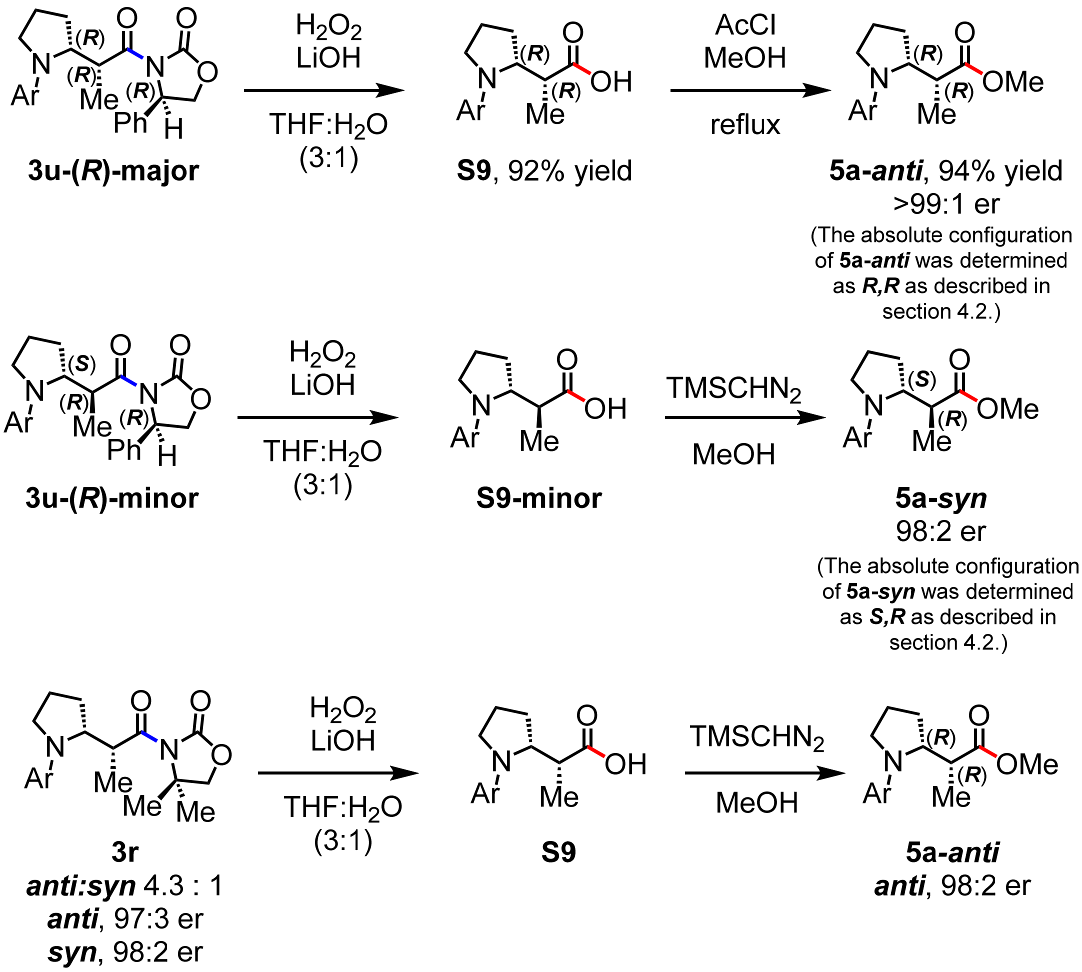
(*R*)-*N*-((*R*)-2-Hydroxy-1-phenylethyl)-2-((*S*)-1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanamide (5d-minor)

(*R*)-*N*-((*R*)-2-Hydroxy-1-phenylethyl)-2-((*S*)-1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanamide (**5d-minor**) was synthesized following a known procedure[21], and the Mannich product **5d-minor** was obtained as a colorless oil. Upon addition of isopropanol, **5d-minor** precipitated to a white solid. **5d-minor** was recrystallized using the vapor-vapor diffusion method, using MeOH to dissolve the product in an inner vial, and pentane as the precipitant placed in the outer vial in order for slow diffusion to occur into the inner vial. The solution was cooled to 0 °C, whereupon a crystal was obtained for X-ray crystallography. The X-ray crystallographic analysis revealed that the absolute configuration of **5d-minor** is (*R,R,S*), see SI Section 8 for X-ray crystallographic data.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.24 (m, 5H), 6.94 (d, *J* = 6.2 Hz, 1H), 6.58 – 6.50 (m, 2H), 4.99 (td, *J* = 6.5, 3.7 Hz, 1H), 3.97 – 3.88 (m, 1H), 3.88 – 3.81 (m, 1H), 3.74 (s, 3H), 3.72 – 3.67 (m, 1H), 3.33 (dq, *J* = 9.7, 3.3 Hz, 2H), 3.04 – 2.94 (m, 1H), 2.37 – 2.31 (m, 1H), 2.25 (s, 3H), 2.20 (dd, *J* = 12.3, 8.3 Hz, 1H), 2.16 (s, 3H), 2.10 – 2.02 (m, 1H), 1.97 (ddq, *J* = 20.5, 12.3, 4.4 Hz, 1H), 0.97 (dd, *J* = 7.0, 1.1 Hz, 3H).

4.3 Procedures for the Derivatization of Enantioenriched Mannich Products

Compounds **3u-(*R*)-*anti***, **3u-(*R*)-*syn***, and **3r** could be converted into the corresponding methyl esters (**5a-*anti*** or **5a-*syn***).



(*R*)-2-((*R*)-1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoic acid (S9)

(*R*)-2-((*R*)-1-(4-Methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoic acid was prepared by following a known procedure.[19] To a solution of Mannich product **3u-(*R*)-major** (169 mg, 0.4 mmol) in THF:H_2O (3:1, 4.8 mL) at 0 °C was added H_2O_2 (30% v/v, 0.16 mL, 1.6 mmol) and 2 M LiOH (0.28 mL, 0.56 mmol), dropwise. The mixture was stirred at 22 °C for 5 h, whereupon the reaction was quenched with $NaHSO_3$. The crude mixture was then concentrated *in vacuo*, then diluted with EtOAc (10 mL), H_2O (10 mL), and 1 M NaOH (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 x

15 mL). Subsequently, the aqueous layer was acidified with 6 M HCl (3 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), filtered. and concentrated *in vacuo* to afford **S9** as a colorless solid (102 mg, 92%) which was used without further purification. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.66 – 6.40 (m, 1H), 3.92 (dt, *J* = 9.0, 4.9 Hz, 1H), 3.71 (s, 3H), 3.34 (td, *J* = 7.9, 3.9 Hz, 1H), 3.02 (q, *J* = 8.1 Hz, 1H), 2.39 (m, 1H), 2.29 (s, 3H), 2.25 (s, 3H), 2.16 – 2.06 (m, 1H), 2.02 – 1.89 (m, 1H), 1.87 – 1.78 (m, 1H), 1.12 (d, *J* = 7.1 Hz, 3H).

Methyl (*R*)-2-((*R*)-1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoate (5a-*anti*)

Methyl (*R*)-2-((*R*)-1-(4-methoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propanoate was prepared by following a known procedure.[22] Acetyl chloride (0.14 mL, 2.0 mmol) was added dropwise to a solution of propanoic acid **S9** (111 mg, 0.4 mmol) in MeOH (1.8 mL). The reaction mixture was heated at reflux for 12 h. The reaction mixture was concentrated *in vacuo*, then saturated K_2CO_3 (6 mL) was added at 0 °C. The aqueous layer was extracted with DCM (3 x 10 mL) and the combined organic layers were washed with brine (15 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (50:1 Hexanes: Et_2O) to afford **5a** as a colorless oil (110 mg, 94% yield). **HPLC** (Chiralpak IC then Chiralcel OJ-H; 1%/ 99% isopropanol/ hexanes, 0.5 mL/min; **5a-*anti*:** tr = 33.1 min (major), 42.1 min (minor); >99:1 er.

```
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                         Location :   41
Injection Date  : 12/7/2017 9:33:45 PM                  Inj :   1
                                                Inj Volume : 8.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-12-07 19-50-57\column2 1% IPA 99% hexane 50min-0.
                  5mL.M (Sequence Method)
Last changed    : 12/7/2017 7:50:58 PM by SYSTEM
Method Info     : Column2 50min-1% iPrOH 99% hexane-0.5mL
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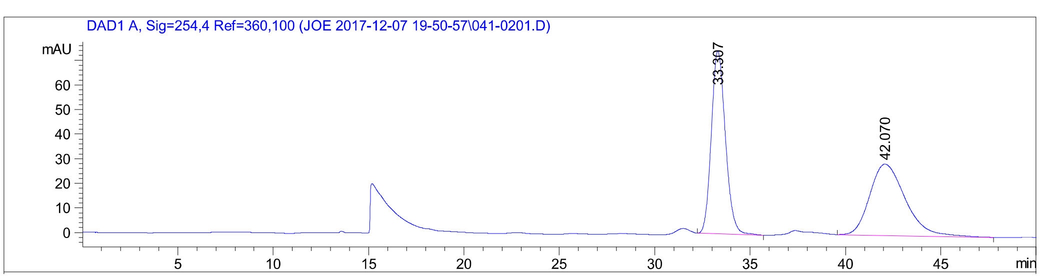
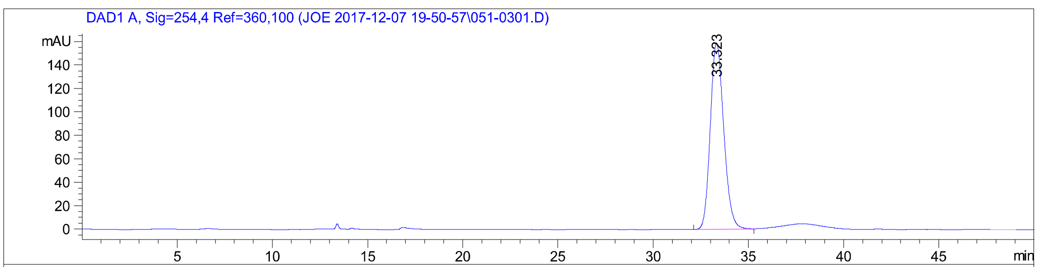


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.307	BB	0.7908	3803.36499	74.34589	50.3094
2	42.070	BB	1.9461	3756.58228	28.98495	49.6906

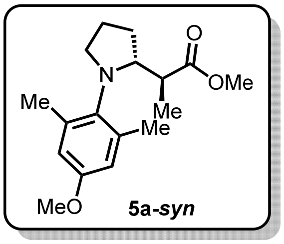
Acq. Operator : SYSTEM Seq. Line : 3
Acq. Instrument : Wasa_LC1 Location : 51
Injection Date : 12/7/2017 10:24:43 PM Inj : 1
Inj Volume : 8.000 µl
Method : C:\Chem32\1\Data\JOE 2017-12-07 19-50-57\column2 1% IPA 99% hexane 50min-0.5mL.M (Sequence Method)
Last changed : 12/7/2017 7:50:58 PM by SYSTEM
Method Info : Column2 50min-1% iPrOH 99% hexane-0.5mL



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

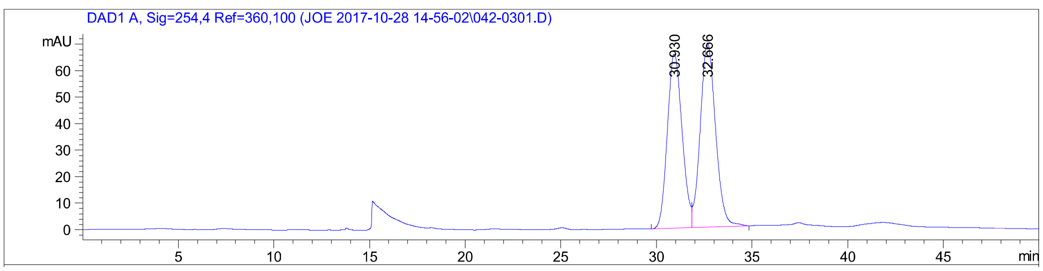
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.323	BB	0.7542	7793.69141	158.89992	100.0000

3u-(*R*)-minor and **3r** were subjected to analogous conditions to afford **5a-*syn*** and **5a-*anti***.[23] **3r** was carried through as a mixture of diastereomers.



5a-*syn* from **3u-(*R*)-minor: HPLC** (Chiralpak IC then Chiralcel OJ-H; 1%/ 99% isopropanol/ hexanes, 0.5 mL/min; tr = 30.9 min (major), 32.6 min (minor); 98:2 er.

```
Acq. Operator   : SYSTEM                        Seq. Line :   3
Acq. Instrument : Wasa_LC1                       Location :   42
Injection Date  : 10/28/2017 4:40:15 PM               Inj :   1
                                               Inj Volume : 8.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-10-28 14-56-02\column2 1% IPA 99% hexane 50min-0.
                  5mL.M (Sequence Method)
Last changed    : 10/28/2017 2:56:04 PM by SYSTEM
Method Info     : Column2 50min-1% iPrOH 99% hexane-0.5mL
```



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.930	BV	0.8350	3518.35767	65.67362	47.7326
2	32.666	VB	0.8595	3852.61475	69.41617	52.2674

Acq. Operator : SYSTEM   Seq. Line : 2
Acq. Instrument : Wasa_LC1   Location : 21
Injection Date : 10/30/2017 9:45:42 PM   Inj : 1
Inj Volume : 8.000 µl
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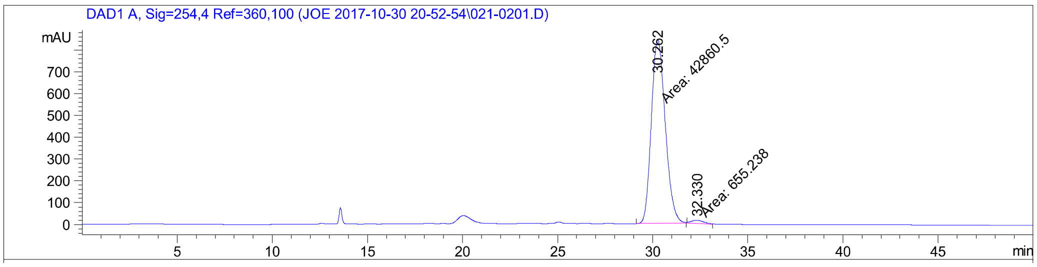
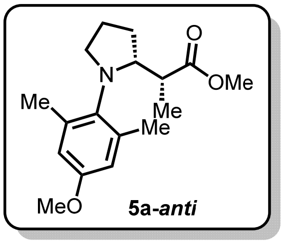
Last changed : 10/30/2017 8:52:56 PM by SYSTEM
Method Info : Column2 50min-1% iPrOH 99% hexane-0.5mL



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.262	MM	0.8462	4.28605e4	844.14630	98.4942
2	32.330	MM	0.7432	655.23840	14.69504	1.5058

Product **5a**, derived from **3r**, was isolated as a mixture of diastereomers. The following is the HPLC trace for the mixture of **5a-*anti*** and **5a-*syn*.**



5a-*anti* (from 3r): HPLC (Chiralpak IC then Chiralcel OJ-H; 1%/ 99% isopropanol/ hexanes, 0.5 mL/min; **5a-*anti*:** tr = 33.3 min (major), 42.0 min (minor); 98:2 er.

```
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                         Location :   11
Injection Date  : 10/11/2017 4:19:51 PM                 Inj :   1
                                                Inj Volume : 2.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-10-11 15-27-57\column2 1% IPA 99% hexane 50min-0.
                  5mL.M (Sequence Method)
Last changed    : 10/11/2017 3:27:59 PM by SYSTEM
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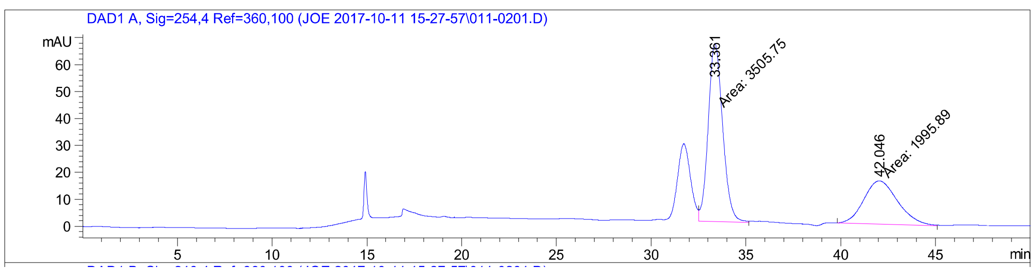
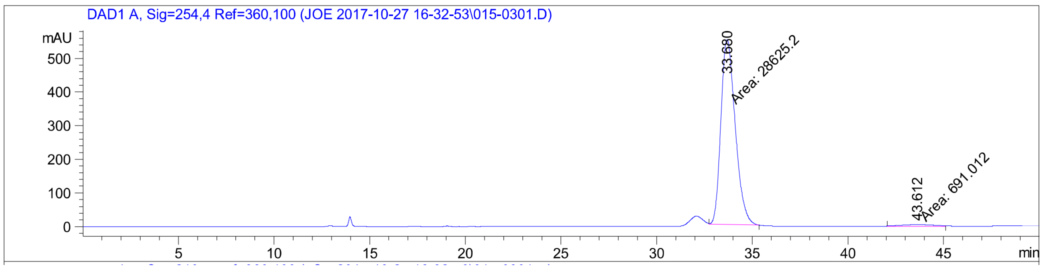


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

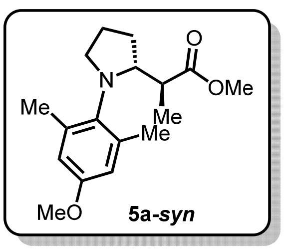
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.361	FM	0.8837	3505.75146	66.12045	63.7219
2	42.046	MM	2.0717	1995.89001	16.05654	36.2781

```
Acq. Operator   : SYSTEM                          Seq. Line :   3
Acq. Instrument : Wasa_LC1                         Location :   15
Injection Date  : 10/27/2017 6:16:42 PM                 Inj :   1
                                                 Inj Volume : 8.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-10-27 16-32-53\column2 1% IPA 99% hexane 50min-0.
                  5mL.M (Sequence Method)
Last changed    : 10/27/2017 4:32:55 PM by SYSTEM
Method Info     : Column2 50min-1% iPrOH 99% hexane-0.5mL
```



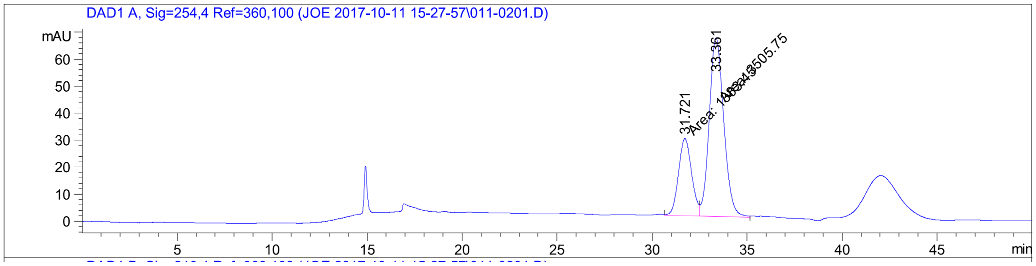
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.680	MM	0.8687	2.86252e4	549.18225	97.6429
2	43.612	MM	2.0869	691.01215	5.51856	2.3571



5a-*syn* (from 3r): HPLC (Chiralpak IC then Chiralcel OJ-H; 1%/ 99% isopropanol/ hexanes, 0.5 mL/min; tr = 33.4 min (major), 31.7 min (minor); >99:1 er.

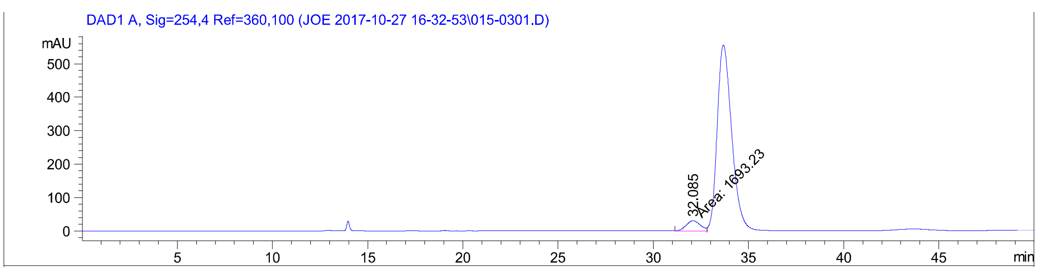
```
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : Wasa_LC1                         Location :   11
Injection Date  : 10/11/2017 4:19:51 PM                 Inj :   1
                                                 Inj Volume : 2.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-10-11 15-27-57\column2 1% IPA 99% hexane 50min-0.
                  5mL.M (Sequence Method)
Last changed    : 10/11/2017 3:27:59 PM by SYSTEM
Method Info     : Column2 50min-1% iPrOH 99% hexane-0.5mL
```



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.721	MF	0.8048	1383.45337	28.65113	28.2961
2	33.361	FM	0.8837	3505.75146	66.12045	71.7039

```
Acq. Operator   : SYSTEM                          Seq. Line :    3
Acq. Instrument : Wasa_LC1                         Location :   15
Injection Date  : 10/27/2017 6:16:42 PM                 Inj :    1
                                                Inj Volume : 8.000 µl
Method          : C:\Chem32\1\Data\JOE 2017-10-27 16-32-53\column2 1% IPA 99% hexane 50min-0.
                  5mL.M (Sequence Method)
Last changed    : 10/27/2017 4:32:55 PM by SYSTEM
Method Info     : Column2 50min-1% iPrOH 99% hexane-0.5mL
```

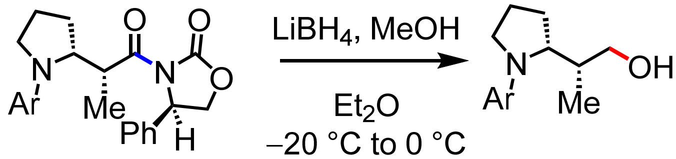


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.085	MM	0.8934	1693.23450	31.58757	100.0000

By comparing the HPLC traces of **5a-*anti*** and **5a-*syn*** prepared as above, we determined that the absolute configuration of **3r-*anti*** is (*R*,*R*).

Procedure for the Removal of the Chiral Auxiliary to obtain Amino Alcohol 5c



(*R*)-2-((*R*)-1-(4-Mmethoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propan-1-ol (5c)

(*R*)-2-((*R*)-1-(4-Mmethoxy-2,6-dimethylphenyl)pyrrolidin-2-yl)propan-1-ol (5c) was prepared using a known procedure.[24] A solution of $LiBH_4$ in THF (2 M, 0.15 mL, 0.3 mmol) was added to a solution of imide **3u-(*R*)-*anti*** (85 mg, 0.2 mmol) in Et_2O (2.0 mL) under N_2 atmosphere at –20 °C. Subsequently, MeOH (0.3 mmol) was added dropwise at –20 °C. The reaction mixture was then allowed to stir at 0 °C for 1 h. Upon completion of the reaction (monitored by TLC), aq. $NaHCO_3$ (2 mL) was added slowly and was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (3:1 Hexanes: Et_2O) to afford **5c** as a colorless solid (48 mg, 91% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.58 (s, 1H), 6.53 (s, 1H), 3.74 (s, 3H), 3.70 – 3.59 (m, 1H), 3.49 – 3.33 (m, 2H), 3.27 (ddd, J = 11.7, 5.7, 3.6 Hz, 1H), 2.98 (q, J = 7.8 Hz, 1H), 2.30 (s, 3H), 2.24 (s, 3H), 2.01 – 1.84 (m, 3H), 1.82 – 1.67 (m, 1H), 1.57 (dt, J = 6.5, 3.3 Hz, 1H), 1.30 (s, 1H), 0.90 (dd, J = 6.9, 1.1 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.37, 140.26, 138.58, 137.74, 114.65, 113.16, 66.70, 62.12, 55.11, 52.43, 40.16, 27.26, 25.47, 19.63, 19.33, 12.24; **HPLC** (Chiralpak AD-H; 2.5%/ 98.5% isopropanol/ hexanes, 0.5 mL/min; **5c:** tr = 29.6 min (minor), 33.4 min (major); >99:1 er.

```
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Injection Date  : 1/9/2018 8:29:07 PM                 Inj :   1
                                              Inj Volume : 4.000 µl
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                  .5mL.M (Sequence Method)
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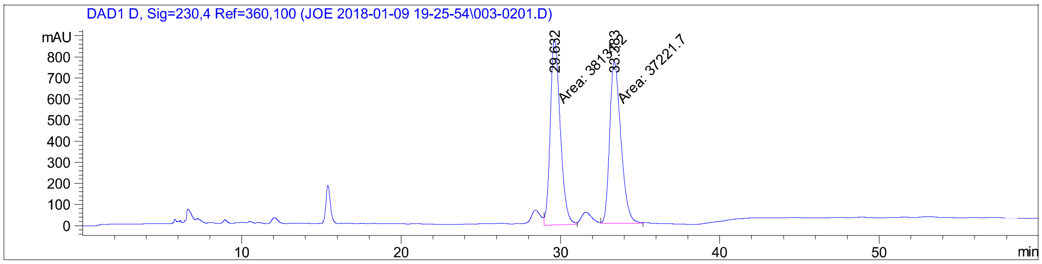
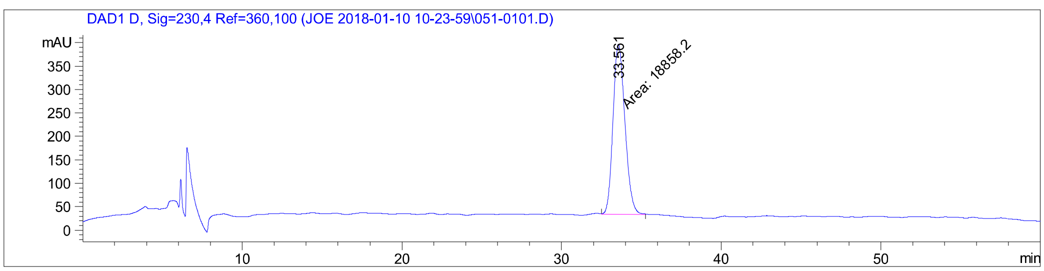
Method Info     : Washing 40min-2.5% iPrOH 97.5% hexane-0.5mL
```



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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.632	MM	0.7208	3.81312e4	881.72113	50.6034
2	33.383	MM	0.8097	3.72217e4	766.20929	49.3966

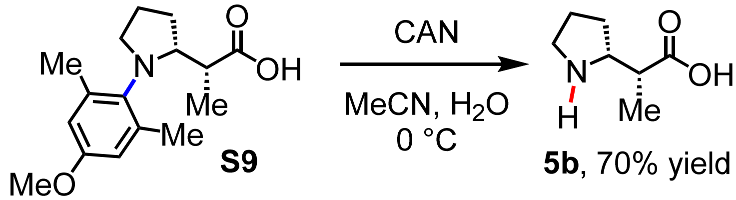
```
Acq. Operator   : SYSTEM                          Seq. Line :   1
Acq. Instrument : Wasa_LC1                         Location :   51
Injection Date  : 1/10/2018 10:26:15 AM                 Inj :   1
                                                 Inj Volume : 4.000 µl
Method          : C:\Chem32\1\Data\JOE 2018-01-10 10-23-59\column1 2.5% IPA 97.5% hex 60min-0
                  .5mL.M (Sequence Method)
Last changed    : 1/10/2018 10:24:01 AM by SYSTEM
Method Info     : Washing 40min-2.5% iPrOH 97.5% hexane-0.5mL
```



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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.561	MM	0.8663	1.88582e4	362.82062	100.0000

Procedure for the Removal of the *para*-Methoxyphenyl Group



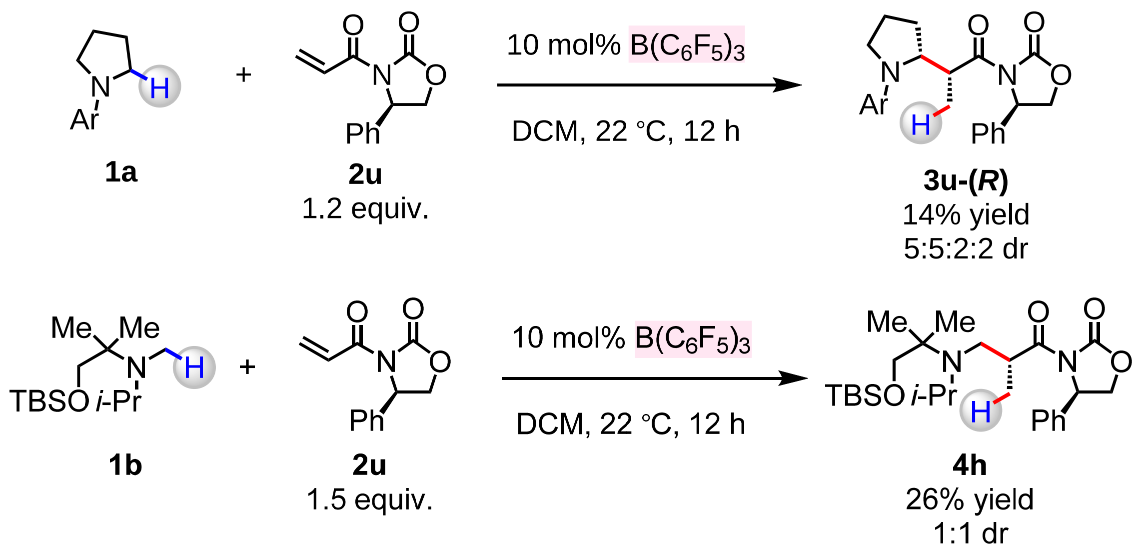
(*R*)-2-((*R*)-Pyrrolidin-2-yl)propanoic acid (5b)

(*R*)-2-((*R*)-Pyrrolidin-2-yl)propanoic acid (**5b**) was prepared using a known procedure.[25] A solution of ceric ammonium nitrate (CAN, 548 mg, 1.0 mmol) in H_2O (3.3 mL, 0.3 M to CAN) was added to a solution of propanoic acid **S9** (55.5 mg, 0.2 mmol) in MeCN (2 mL) at 0 °C under N_2 atmosphere. The mixture was stirred at 0 °C for 1 h, whereupon the reaction was diluted with EtOAc (2 mL) then concentrated *in vacuo* to remove volatile side products and solvent (H_2O was evaporated by azeotropic distillation with toluene). The solid residue was then filtered over a pad of Celite using EtOAc as the eluent. The filtrate was concentrated to afford **5b** as a solid (19.9 mg, 70% yield). **^{1}H NMR** (500 MHz, D_2O) δ 3.75 (q, J = 9.1 Hz, 1H), 3.36 (dt, J = 19.6, 11.4 Hz, 2H), 2.90 (ddt, J = 13.5, 8.5, 4.1 Hz, 1H), 2.33 (td, J = 7.6, 7.1, 3.8 Hz, 1H), 2.17 – 2.07 (m, 1H), 2.01 (dt, J = 14.0, 8.4 Hz, 1H), 1.84 – 1.70 (m, 1H), 1.35 (dd, J = 7.2, 2.0 Hz, 3H).

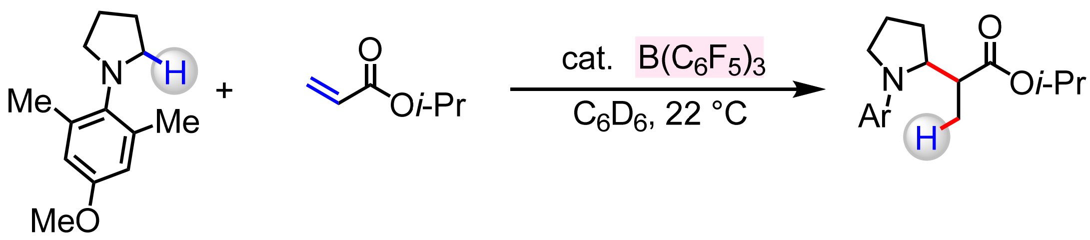
4.5 Effect of $Mg(OTf)_2$/L4 Co-Catalyst in the Diastereoselective C–C Bond Forming Reactions

Experimental Procedure

An oven-dried sealed tube equipped with a magnetic stir bar was used. Amine **1** (0.20 mmol), (*R*)-3-acryloyl-4-phenyloxazolidin-2-one **2u-(*R*)** (0.24 mmol), $B(C_6F_5)_3$ (0.02 mmol), and DCM (0.3 mL) were added under nitrogen atmosphere. The reaction mixture was stirred at 22 °C for 12 h. Upon completion, the reaction mixture was concentrated *in vacuo*. The product yield was determined by the ^{1}H NMR analysis of the crude product using mesitylene as the internal standard.


10 mol% B(C6F5)3
DCM, 22 °C, 12 h
1a
2u
1.2 equiv.
3u-(R)
14% yield
5:5:2:2 dr
1b
2u
1.5 equiv.
4h
26% yield
1:1 dr

5. Kinetics Experiment Data for $B(C_6F_5)_3$-Catalyzed C–C Bond Forming Reactions



1, 0.30 mmol **2d,** 0.36 mmol **3d**

General Procedure for time course reaction monitoring by *in situ* ¹H NMR

In a nitrogen-filled glove box, 1-(4-methoxy-2,6-dimethylphenyl)pyrrolidine (400 mg, 1.95 mmol), isopropyl acrylate (269 mg, 2.3 mmol), mesitylene (235 mg, 1.95 mmol), was weighed in a 20 mL dram vial, which was dissolved in C_6D_6 (1.63 mL, Stock Solution A). In another 20 mL dram vial, $B(C_6F_5)_3$ (0.125 mmol) was weighed and dissolved in C_6D_6 (1.5 mL, Stock Solution B). Using stock solutions A and B and neat C_6D_6 (in total of 0.6 mL), reaction mixtures with 0.3 mmol of 1-(4-methoxy-2,6-dimethylphenyl)pyrrolidine and the following amount of $B(C_6F_5)_3$ were prepared (2.50, 3.75, 5.00, 6.25, 7.50, and 8.75 mol%) and placed in a J-Young tube. After the J-Young tube was tightly capped with the Teflon plug, ^{1}H NMR spectra were acquired using a pre-acquisition delay in array mode, with a spectrum taken every 30 seconds for the length of the experiment. The data were processed using MestReNova and peak integrations were normalized using mesitylene as the internal standard.

A study was conducted following the procedure for time course reaction monitoring by ^{1}H NMR (using internal standard) while varying [$B(C_6F_5)_3$] in order to find the order of the catalyst in the reaction.[26,27]

Figure 1.

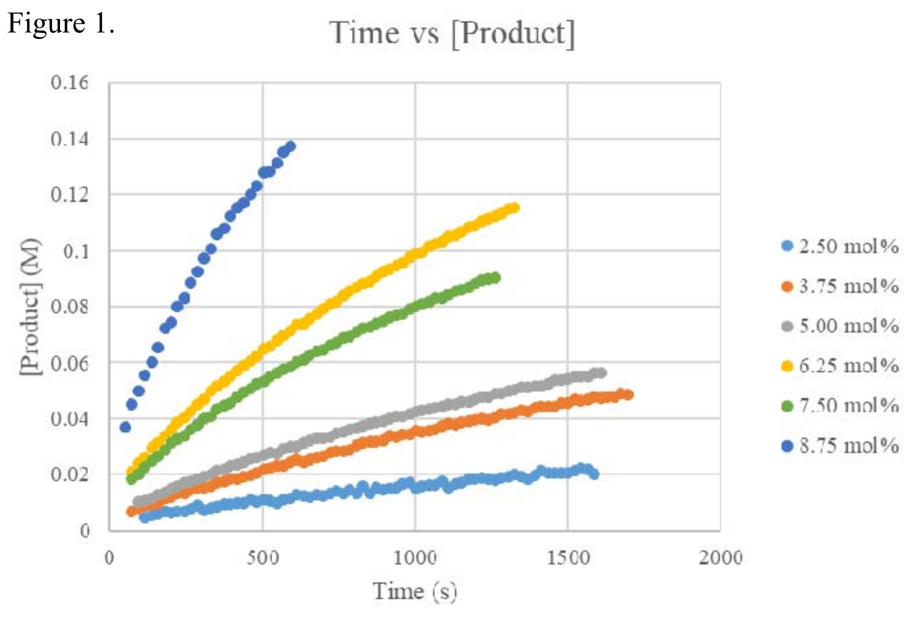


Figure 2.

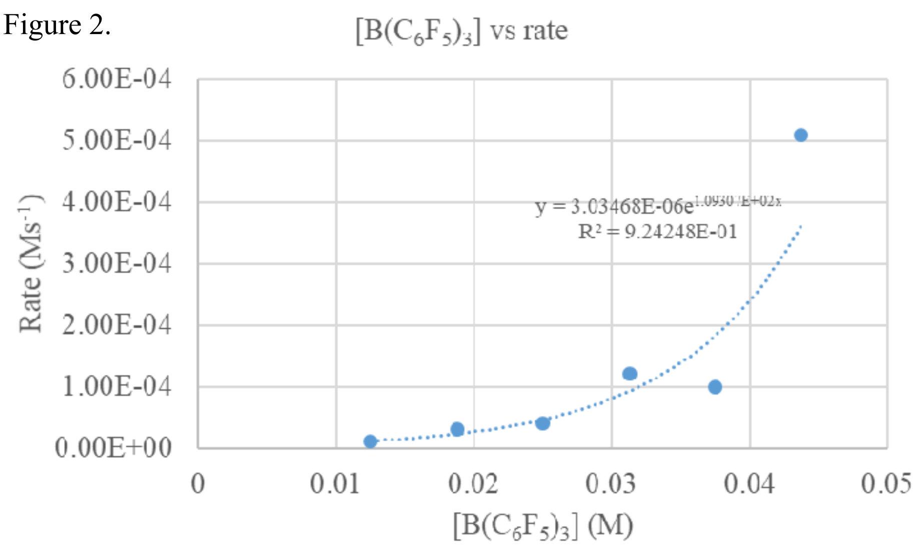


Figure 3.

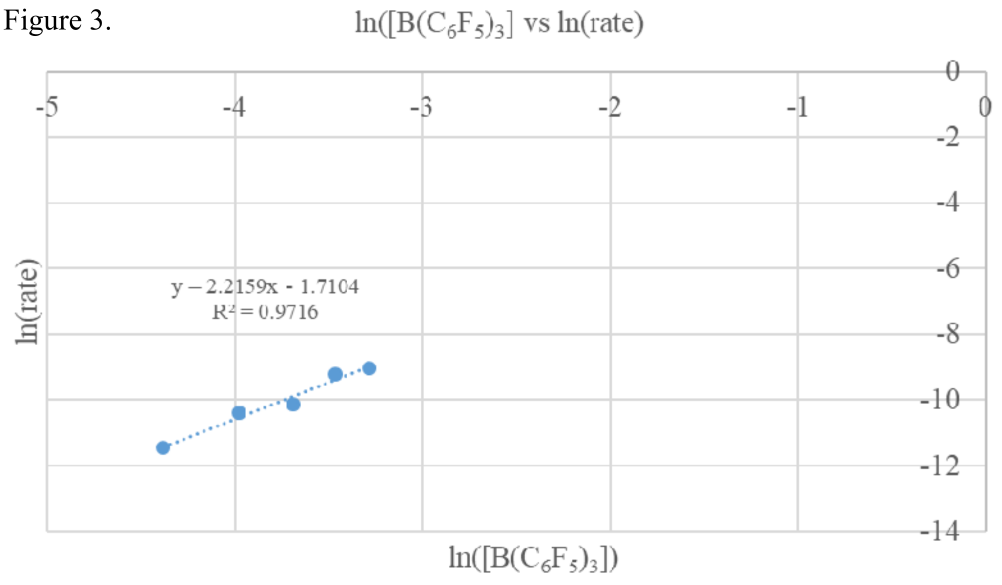


Figure 4.

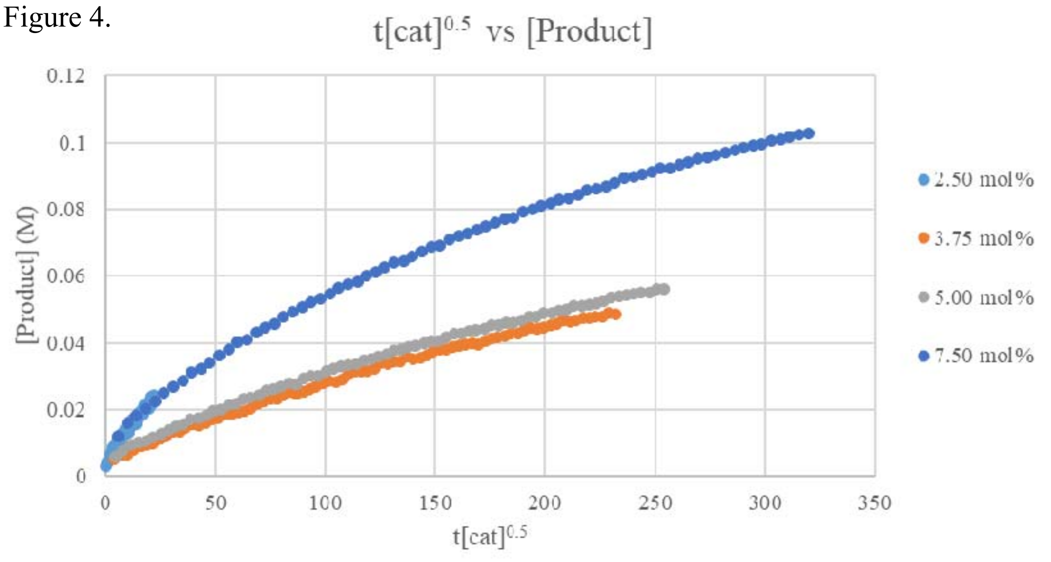


Figure 5.

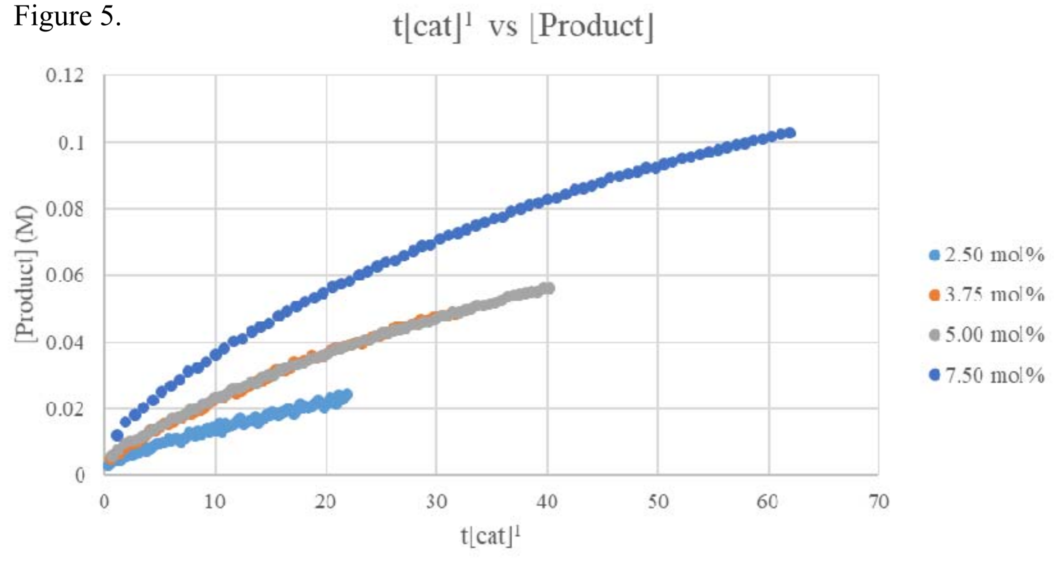
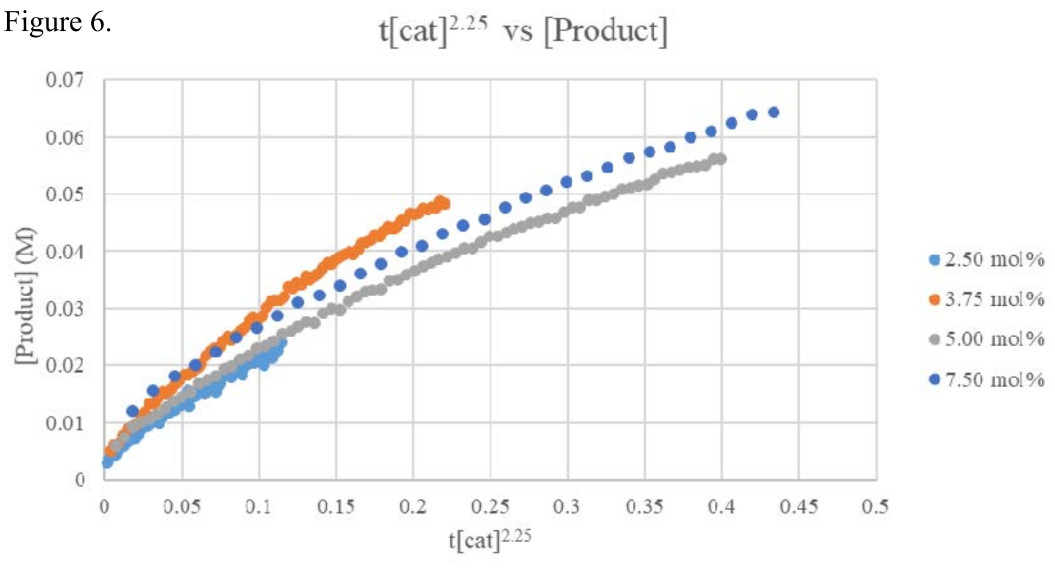


Figure 6.



6. Density Functional Theory (DFT) Calculations

DFT computations[28] were performed with the Gaussian 09 suite of programs.[29] Geometries were optimized with the M06L[30] functional and the def2-SVP basis set[31] in conjunction with the corresponding Coulomb fitting basis set to speed up calculations (denoted DF; density fitting).[32] An ultrafine integration grid was applied. The effect of a polar reaction medium (dichloromethane, DCM) was approximated by means of an integral equation formalism variant of the polarizable continuum model (IEFPCM).[33] Stationary points were probed through vibrational analysis and Gibbs free energy corrections were performed under standard conditions (298.15 K, 1.0 atm). Additionally, we probed the performance of various density functionals through single-point energy calculations at the geometries optimized with the level described above by means of the SMD[34] solvation model with DCM as solvent and the larger def2-TZVPP basis set.[31] Since the correct density functional is not known we tested several state of the art approaches that have been developed over the past decade, all of which are have been designed to account for dispersion:[28,35] M06L,[30] M06,[30] MN15,[28i] ωB97XD[36] and PBE0-D3BJ.[28b,37] Additionally, results with the corresponding parent functionals ωB97X and PBE0[28b] are included. In the manuscript we only report the M06L/def2-TZVPP$_{DCM(SMD)}$//M06L/DF-def2-SVP$_{DCM(IEFPCM)}$ energies and the comparison of other density functionals is provided in Figures S4-S12. Images of computed geometries are shown in Figures S1−S3 and a file for convenient viewing of computed geometries with the program Mercury 3.3 is appended as separate "coordinates.xyz" file in SI Section 9.[38]

6.1 Challenges and Simplifications

(a) All transition state calculations have been carried out in absence of the triflate counterions, rendering the overall charge of the transition state structures +2 (Figure S1). Furthermore, the solvent has been approximated by a contiuum and it is assumed that the M06L/DF-def2-SVP$_{DCM(IEFPCM)}$ optimized structures are an appropriate reflection of the geometry in solution. Nonetheless, the exact solution geometry is likely unknown.

(b) Initial scans of the potential energy surface have revealed a very flat region for C–C distances between 2.2 and 2.6 Å and attempts to locate a transition state were unsuccessful in most instances. We hence decided to perform a number of constrained optimizations in 0.03–0.10 Å intervals (Figures S4–S8), including the assessment of thermal corrections to the free energy (G_{corr}; see Figure S4c). The largest energy values from Figures S4–S8 have been used in the comparsion of various density functionals (Figures S9–S12).

(c) The stereochemical model under investigation resembles molecular balance experiments designed to assess the contribution of dispersion interactions in solution.[39,40] The challenge here lies in the accurate comparison of two kinds of molecular assemblies: that is, in some structures dispersion is a dominant contributor to the interaction energy (for example, **IX'** and **X'**; Figure S1), whereas dispersion interactions are much less pronounced in alternative geometries (for example, **XI** and **XII**; Figure S1).

(d) Accurate electronic energies are likely not sufficient in assessing the relative energies of **IX–XII**. Equally important are thermal/entropic contributions ($G_{corr} = \Delta G - \Delta E$; see Figure S4c). The large G_{corr}-values for **IX'** and **X'** (22–23 kcal/mol) are expected and are likely the result from significantly reduced vibrational freedom due to the close alignment between the aryl ring of the substrate and the ligand. It is, however, much less clear why the G_{corr}-values for structures **IX**, **X**, **XI** and **XII** fluctuate between 17–20 kcal/mol. We assume an error bar of 1–2 kcal/mol, particularly since G_{corr}-values for the immediate sphere of solvent molecules, which has not been explicitly modeled, are unknown.

(e) To assess the error due to basis set incompleteness associated with the def2-TZVPP basis set we performed additional single point calculations with M06L/DF-def2-$QZVPP_{DCM(SMD)}$. The energies relative to the separate iminium ion and Z-enolate complex increased by less than 0.3 kcal/mol, suggesting that the def2-TZVPP basis set is of sufficient quality.

6.2 The Stereochemical Model

An extended stereochemical model (than the one provided in the manuscript) for reaction of **L3**–Mg-enolate complex with the *in situ* generated iminium ion is shown in Figure S1 and the computed electronic (ΔE) and free energies (ΔE) at the M06L/DF-def2-$TZVPP_{DCM(SMD)}$//M06L/DF-def2-$SVP_{DCM(IEFPCM)}$ level of theory are provided in Figure S2. In addition to the four modes shown in the manuscript (**IX–XII**), we considered two additional modes that lead to the minor diastereomer (i.e., **IX'** and **X'**), wherein the iminium ion is approaching the enolate nucleophile with its aryl ring pointing up. It appears that accurate determination of free energy values is challenging and will strongly depend on the attenuation of dispersion interactions in solution[39,40]. For instance, we find that functionals accounting for dispersion (e.g., M06–L) clearly favor pathway **IX'** over **XI** electronically (ΔE values), particularly with the small def2-SVP basis set applied during geometry optimization (−8.8 vs −5.0 kcal/mol; grey curve in Figure S2). While correcting for basis set incompleteness reduces the energy difference to 2.0 kcal/mol (−3.3 vs −1.3 kcal/mol; red curve in Figure S2), it is only after addition of thermal corrections ($\Delta G = \Delta E + G_{corr}$) when **XI** becomes the most favorable mode of addition (19.1 vs 18.1 kcal/mol; blue curve in Figure S2).

6.3 Steric Influence of the *para*-Substituent on the Substrate on Diastereoselectivity

Based on these large fluctuations in the relative energy between pathways **IX'** and **XI** we decided to test experimentally the influence of substituent R on diastereoselectivity (Figure S3a). We hypothesized that increasing the size of R would lead to destabilization of mode **IX'** and result in an increase in d.r. We indeed observed a minor effect when R is altered from H to *tert*-butyl (3.8:1.0 vs 4.4:1.0 d.r.), although this change is likely too small to render **IX'** the major pathway for generation of the minor diastereomer. In addition to these experimental trends we investigated the effect of a more sizable *tert*-butyl group on the relative energy between **IX'** and **XI** computationally (labeled as $\mathbf{IX'}_{t\text{-Bu}}$ and $\mathbf{XI}_{t\text{-Bu}}$; Figure S3b). While the electronic energy (ΔE) of **IX'** is 2.0 kcal/mol lower than for **XI** (R = OMe), $\mathbf{IX'}_{t\text{-Bu}}$ is destabilized by 0.8 kcal/mol relative to $\mathbf{XI}_{t\text{-Bu}}$. A side view of the corresponding transition state structures for **IX'** and **IX'$_{t\text{-Bu}}$** illustrates the significantly increased steric demand in the latter structure. This is reflected in the longer distance between C^2 on the substrate and C^1 on the ligand in **IX'$_{t\text{-Bu}}$** (3.65 Å; Figure S2), as opposed to **IX'** (3.15 Å).

On the basis of these results we propose that the minor diastereomer is generated through a combination of pathways **IX'** and **IX**, with **IX** likely being favored, otherwise a much more pronounced effect on diastereoselectivity would be expected.

6.4 Comparison of Results with Various Density Functionals

A comparison of electronic energies (ΔE) with a range of density functionals is provided in Figures S9−S10, the corresponding free energy values are shown in Figures S11−S12. Various state of the art methods (M06L, M06, MN15, ωB97XD and PBE0-D3BJ) yield similar electronic energies relative to the separate iminium ion and Z-enolate complex (Figure S9−S10), while ΔE-values are significantly larger with density functionals that do not properly account for dispersion (ωB97X and PBE0). It is worth mentioning that the electronic energy of **IX'** is predicted to be lower than that of **XI** by approximately 3 kcal/mol with functionals M06L, M06, MN15, ωB97XD and PBE0-D3BJ (Figure S10), whereas **IX'** is destabilized relative to **XI** by approximately 3 kcal/mol with ωB97X and PBE0 (Figure S9). These data indicate that dispersion terms (D) contribute about 6 kcal/mol to the stabilization of **IX'** relative to **XI**. After addition of thermal contributions (G_{corr}; cf. Figure S4c) the energy values for **IX'** and **XI** are of similar magnitude with functionals M06L, M06, MN15, ωB97XD and PBE0-D3BJ (Figure S12). Based on these results and considering the expected error bar associated with density functionals (>1−2 kcal/mol),[28] we chose to report the single point energies with M06-L, which is also the method used during geometry optimization.

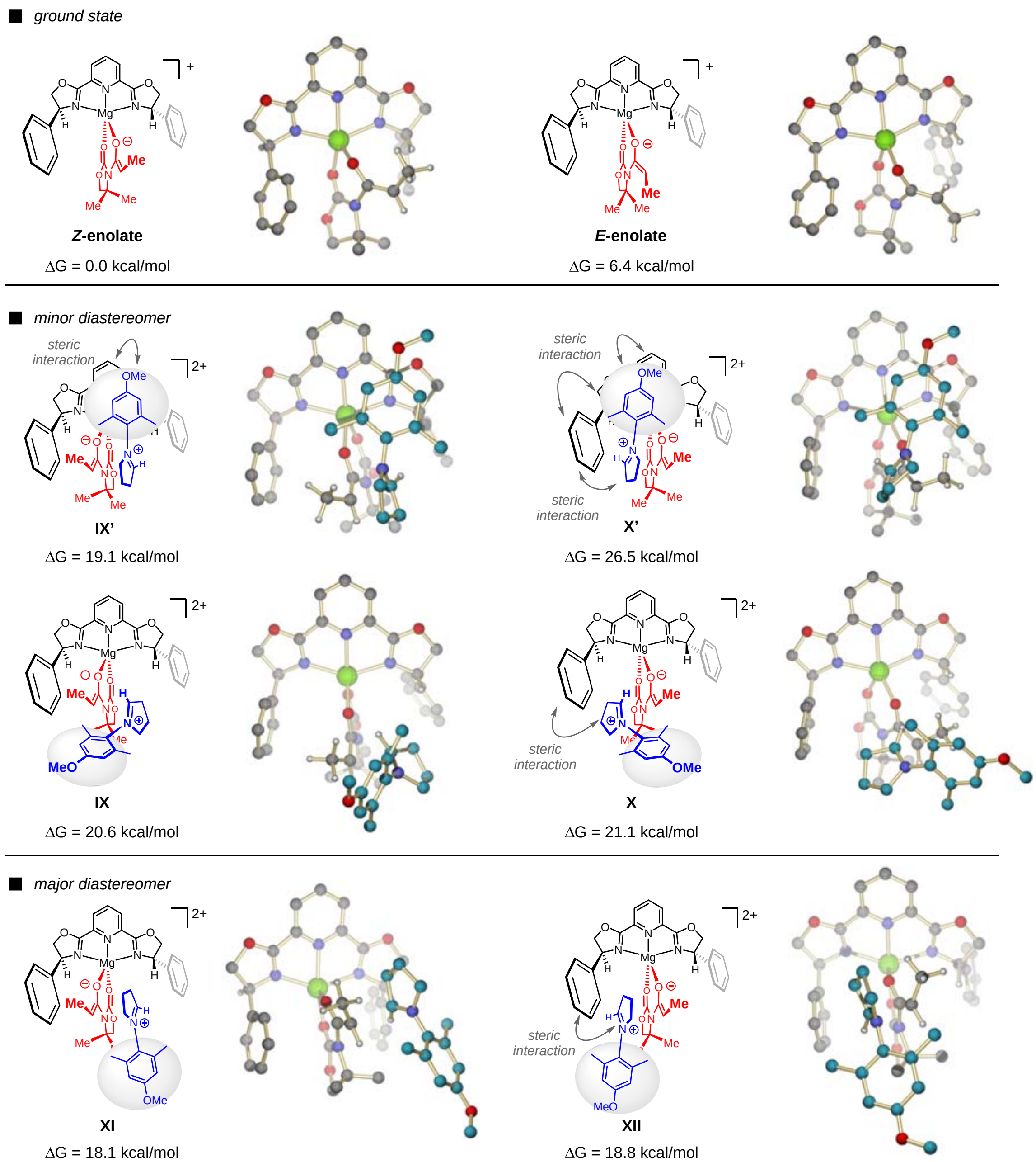


Figure S1. Geometries of computed structures [M06L/DF-def2-SVP$_{DCM(IEFPCM)}$] including free energy values obtained at the M06L/DF-def2-TZVPP$_{DCM(SMD)}$//M06L/DF-def2-SVP$_{DCM(IEFPCM)}$ level of theory; the C–C distance between the electrophilic carbon on the iminium and the nucleophilic carbon on the enolate has been constrained to 2.3 Å.

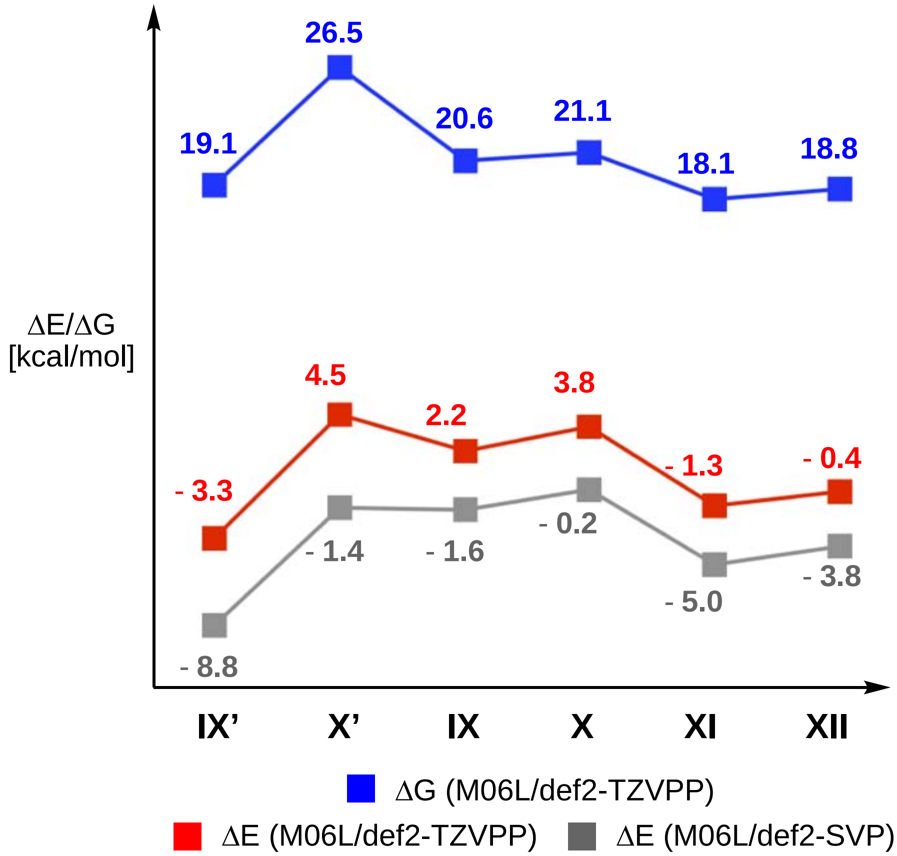
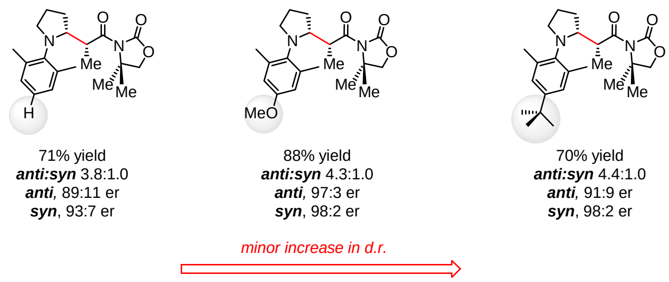


Figure S2. Comparison of electronic and free energies for transition states **IX'**–**XII** obtained at the M06L/DF-def2-TZVPP$_{DCM(SMD)}$//M06L/DF-def2-SVP$_{DCM(IEFPCM)}$ level of theory.

a Experimentally observed influcence of the size of the *para* substituent on the substrate on diastereoselectivity



b Computationally investigated influcence of a *tert*-butyl group in *para* position of the substrate on diastereoselectivity

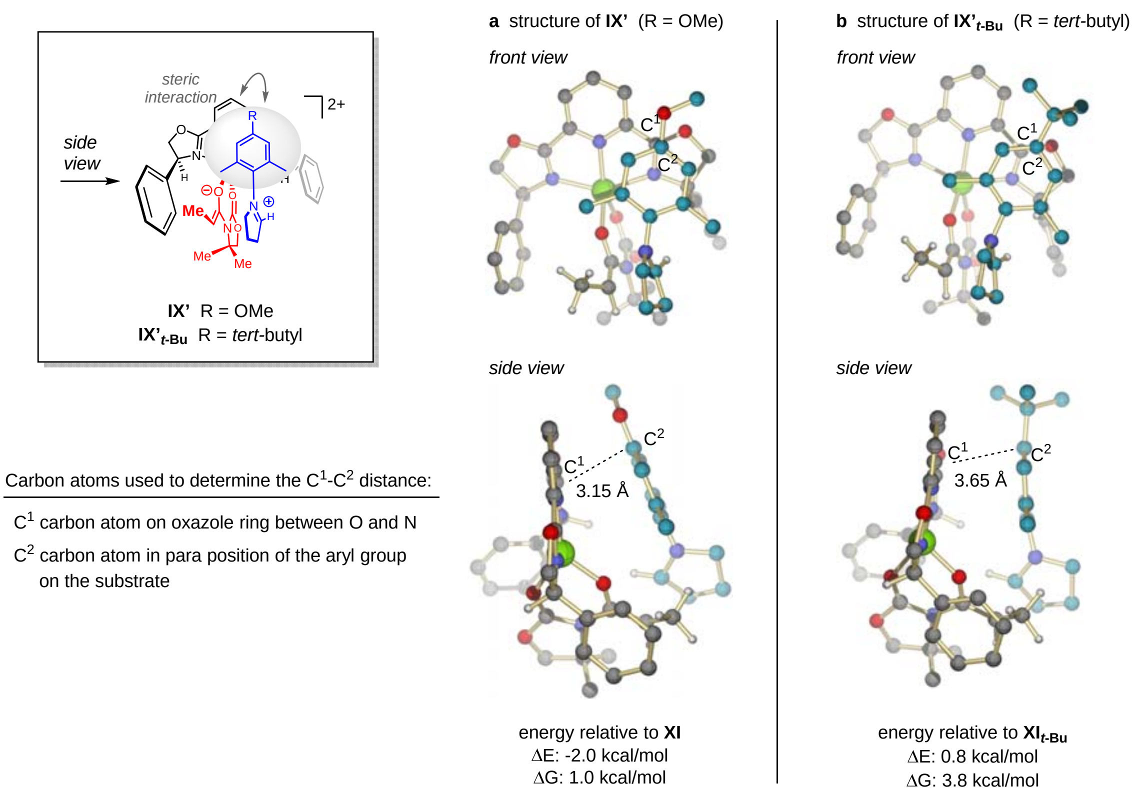


Figure S3. Influence of the para-substituent on the substrate on the relative energy between **IX'** and **XI**; electronic and free energies have been assessed at the M06L/DF-def2-TZVPP$_{DCM(SMD)}$//M06L/DF-def2-SVP$_{DCM(IEFPCM)}$ level of theory; the C–C distance between the electrophilic carbon on the iminium and the nucleophilic carbon on the enolate has been constrained to 2.3 Å.

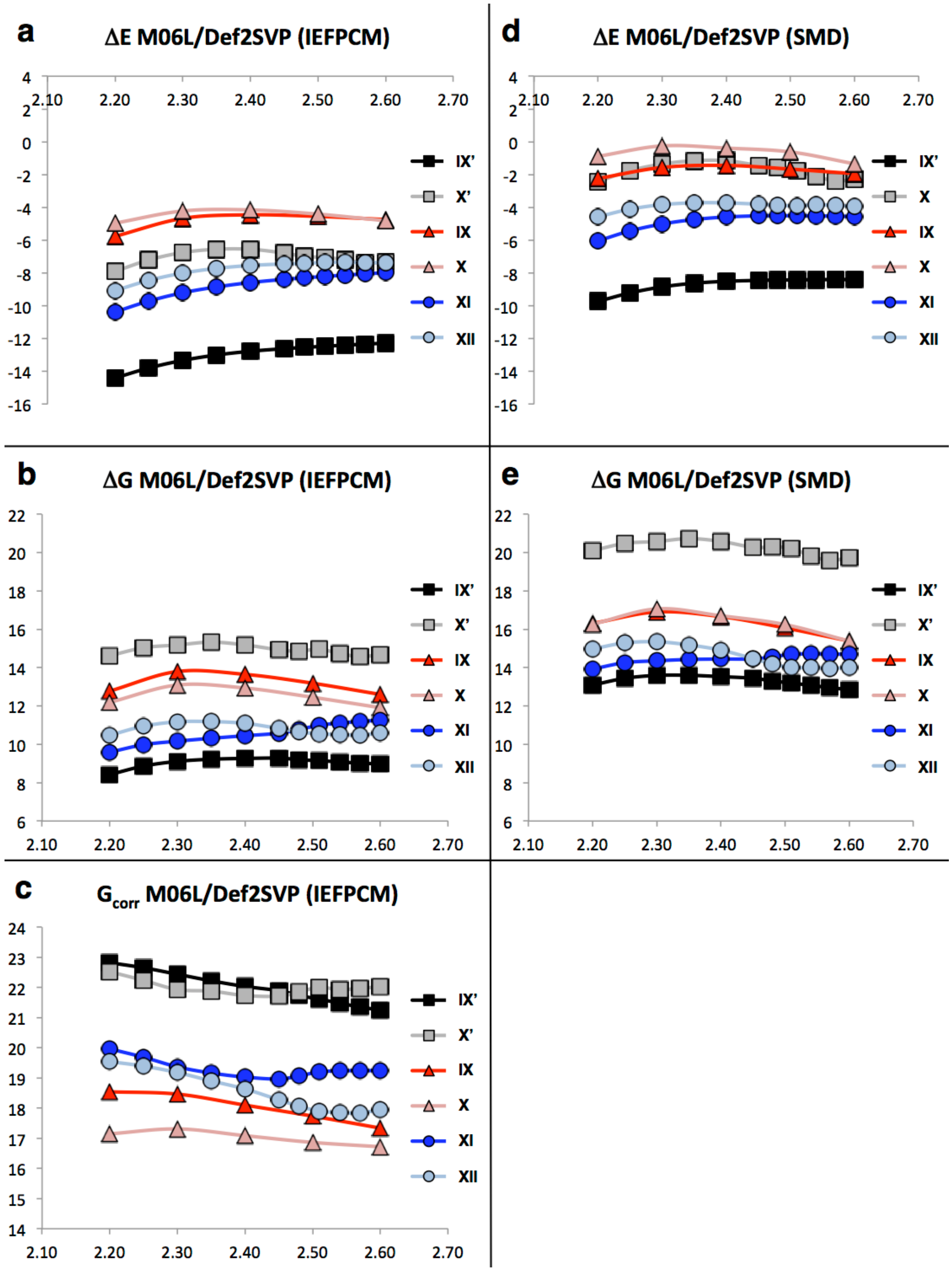


Figure S4. **(a)** Electronic energies (ΔE), **(b)** free energies (ΔG) and **(c)** thermal corrections to the free energy (G_{corr}) at the level of optimization [M06L/DF-def2-$SVP_{DCM(IEFPCM)}$] as a function of the C–C distance [Å] and **(d,e)** single point energies with the SMD solvation model [M06L/DF-def2-$SVP_{DCM(SMD)}$]; ΔG = ΔE + G_{corr}.

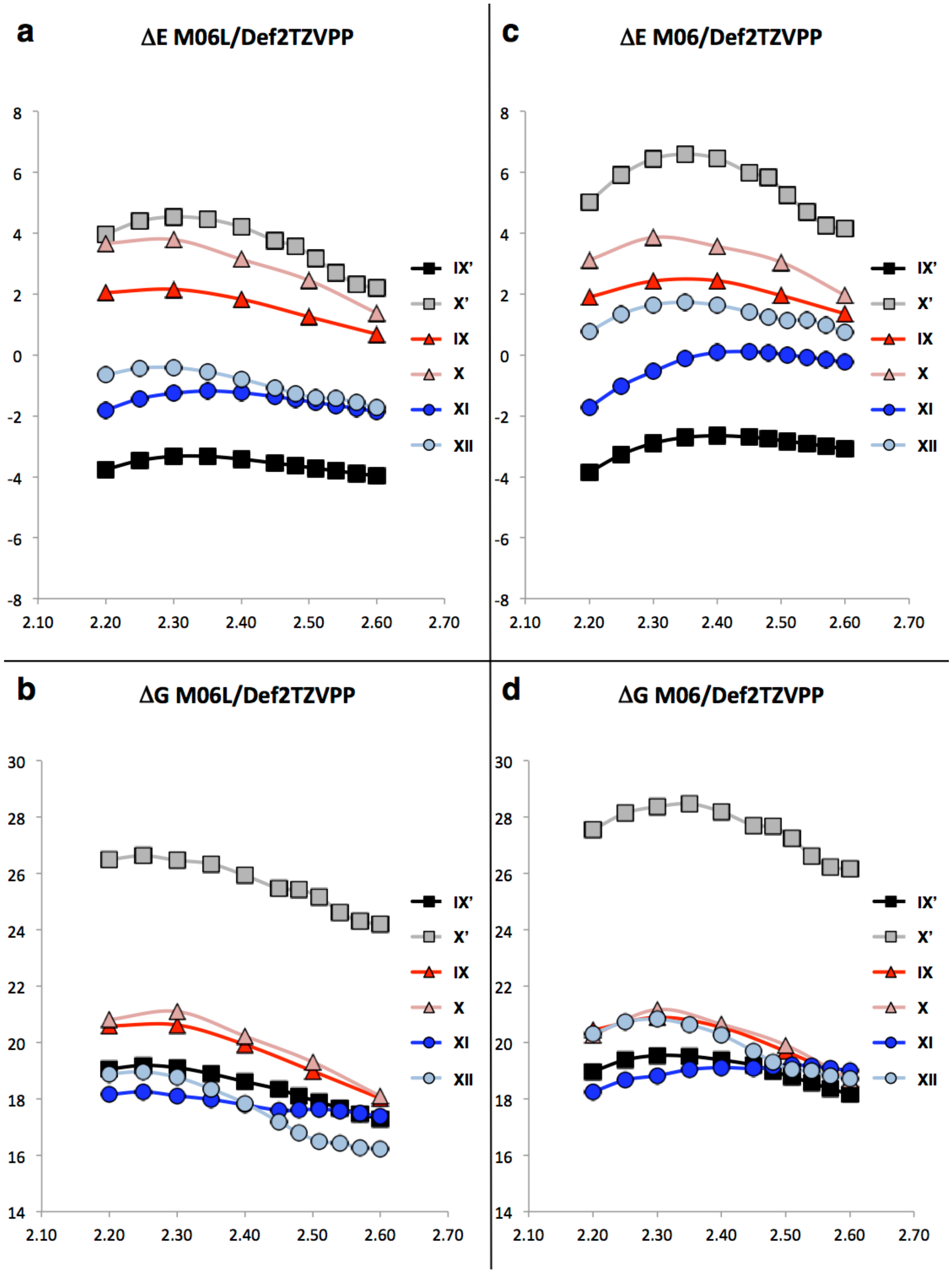


Figure S5. **(a,b)** Single point electronic energies (ΔE) and free energies (ΔG) at the M06L/DF-def2-TZVPP$_{DCM(SMD)}$ level as a function of the C–C distance [Å]; **(c,d)** single point electronic energies (ΔE) and free energies (ΔG) at the M06/def2-TZVPP$_{DCM(SMD)}$ level as a function of the C–C distance [Å]; ΔG = ΔE + G_{corr}.

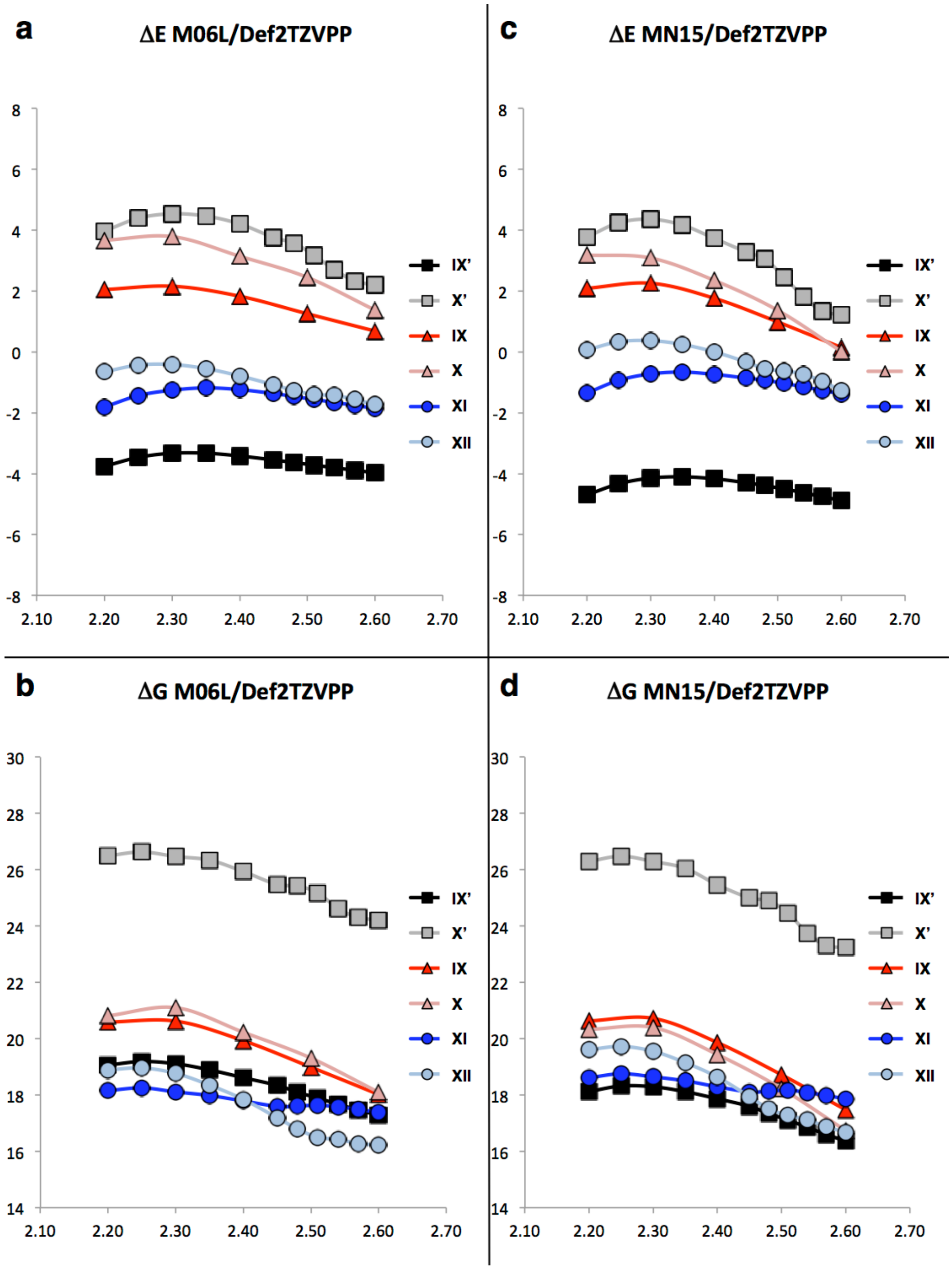


Figure S6. **(a,b)** Single point electronic energies (ΔE) and free energies (ΔG) at the M06L/DF-def2-TZVPP$_{DCM(SMD)}$ level as a function of the C–C distance [Å]; **(c,d)** single point electronic energies (ΔE) and free energies (ΔG) at the MN15/def2-TZVPP$_{DCM(SMD)}$ level as a function of the C–C distance [Å]; ΔG = ΔE + G_{corr}.

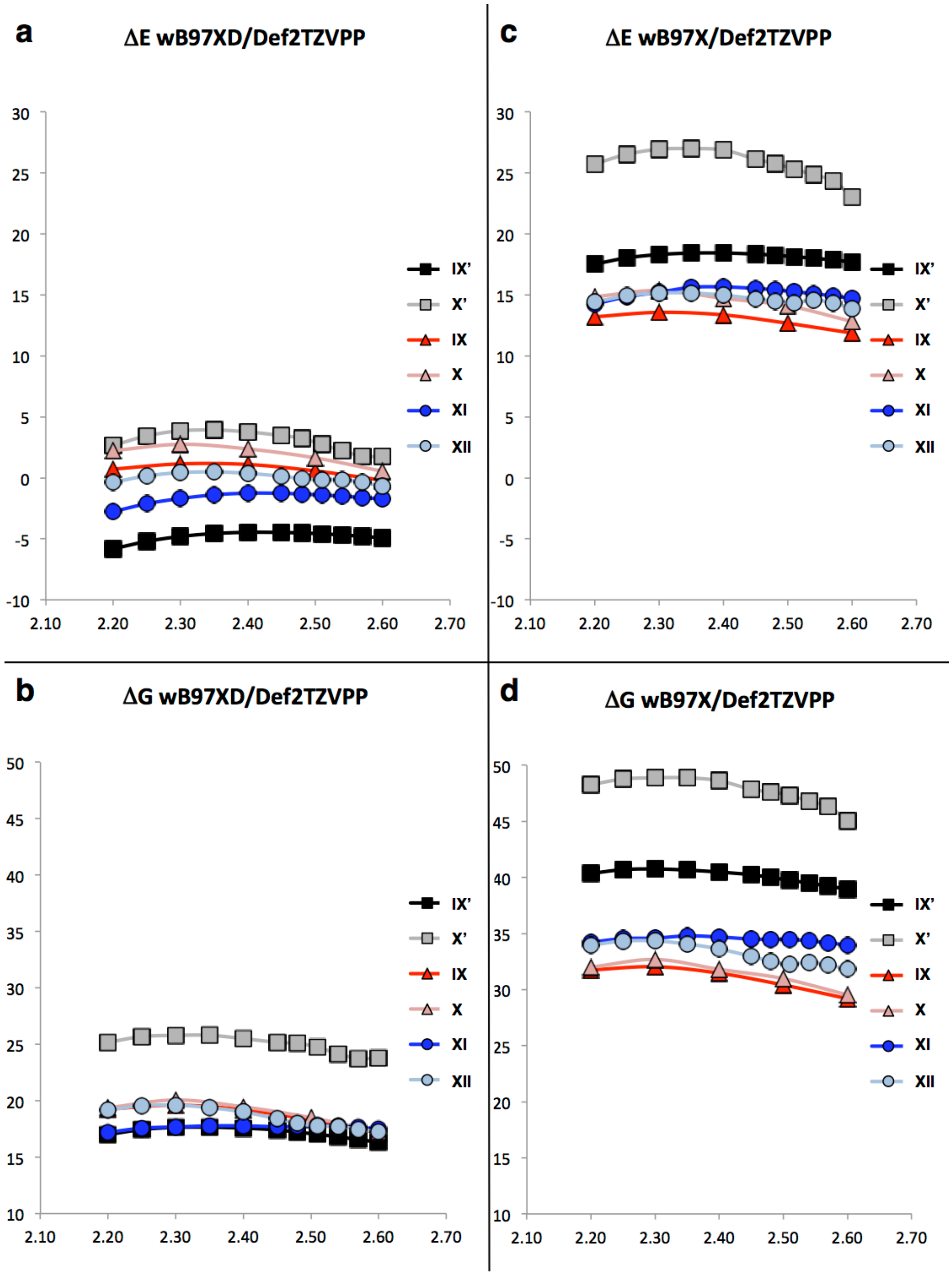


Figure S7. **(a,b)** Single point electronic energies (ΔE) and free energies (ΔG) at the ωB97XD/DF-def2-TZVPP$_{DCM(SMD)}$ level as a function of the C–C distance [Å]; **(c,d)** single point electronic energies (ΔE) and free energies (ΔG) at the ωB97X/def2-TZVPP$_{DCM(SMD)}$ level as a function of the C–C distance [Å]; $\Delta G = \Delta E + G_{corr}$.

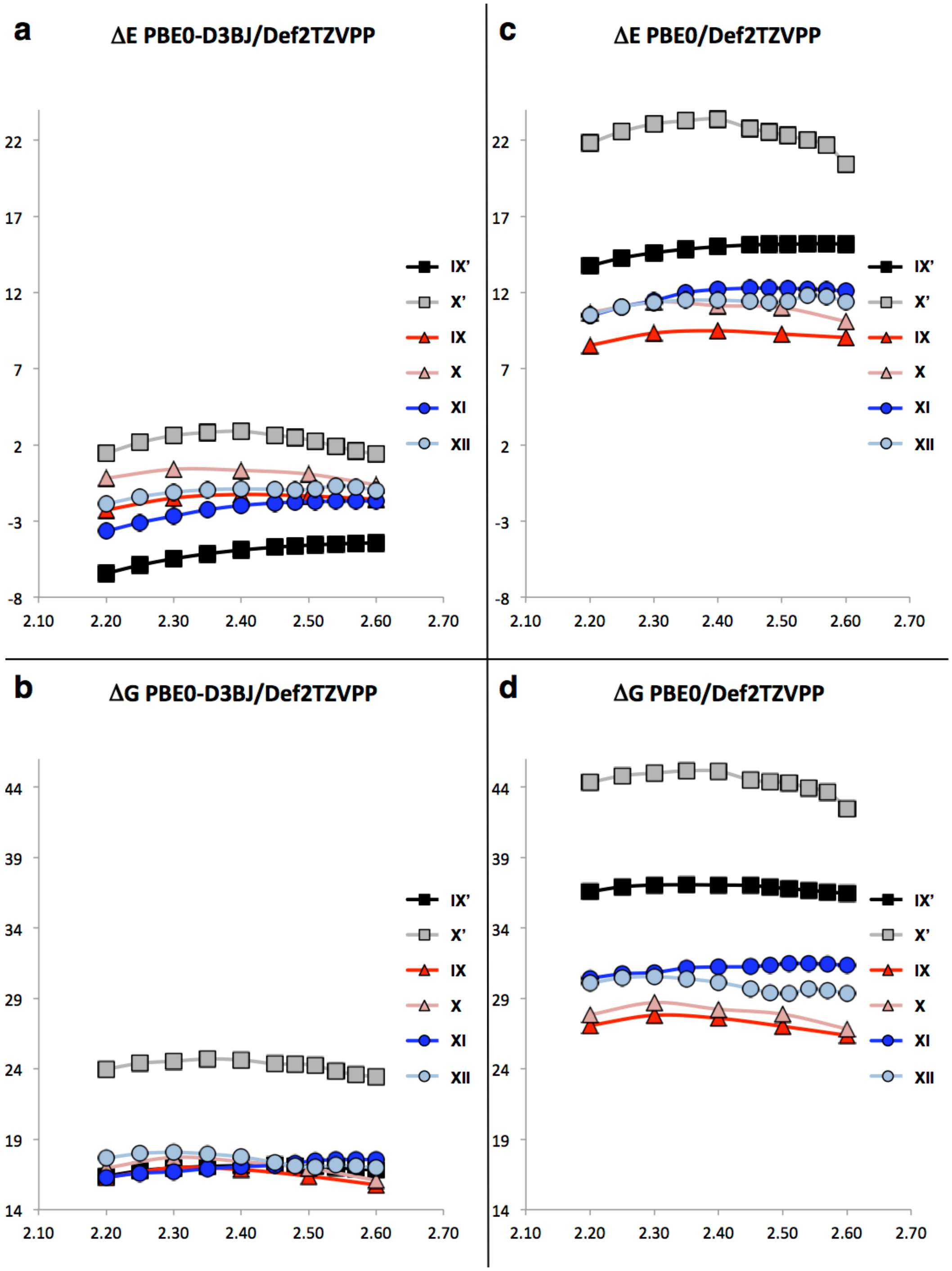


Figure S8. **(a,b)** Single point electronic energies (ΔE) and free energies (ΔG) at the PBE0-D3BJ/DF-def2-TZVPP$_{DCM(SMD)}$ level as a function of the C–C distance [Å]; **(c,d)** single point electronic energies (ΔE) and free energies (ΔG) at the PBE0/def2-TZVPP$_{DCM(SMD)}$ level as a function of the C–C distance [Å]; ΔG = ΔE + G_{corr}.

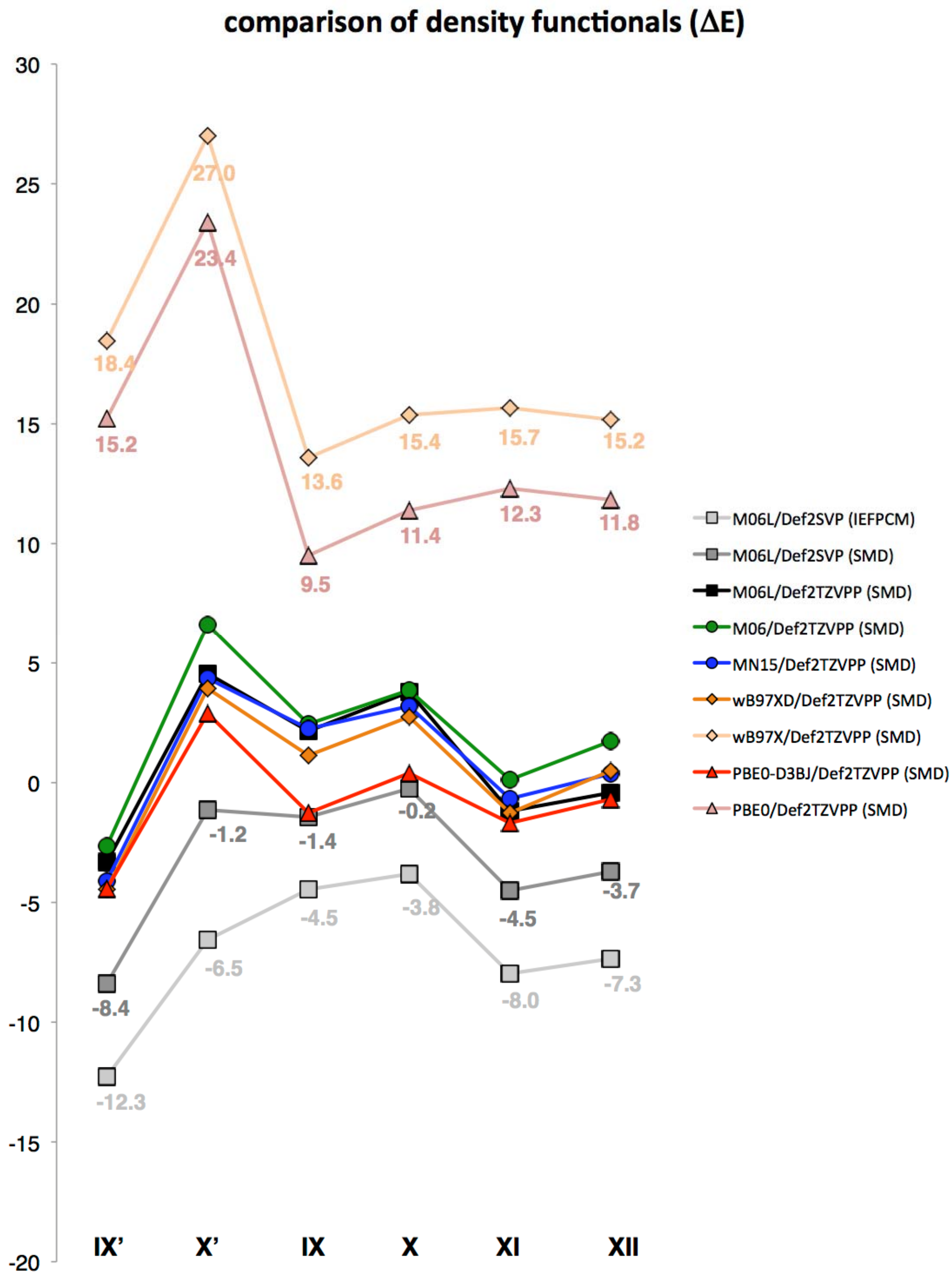


Figure S9. Comparison of electronic energies (ΔE in kcal/mol) for **IX'–XII** obtained with several density functionals; the maximum values from the corresponding graphs in Figures S4–S8 have been used.

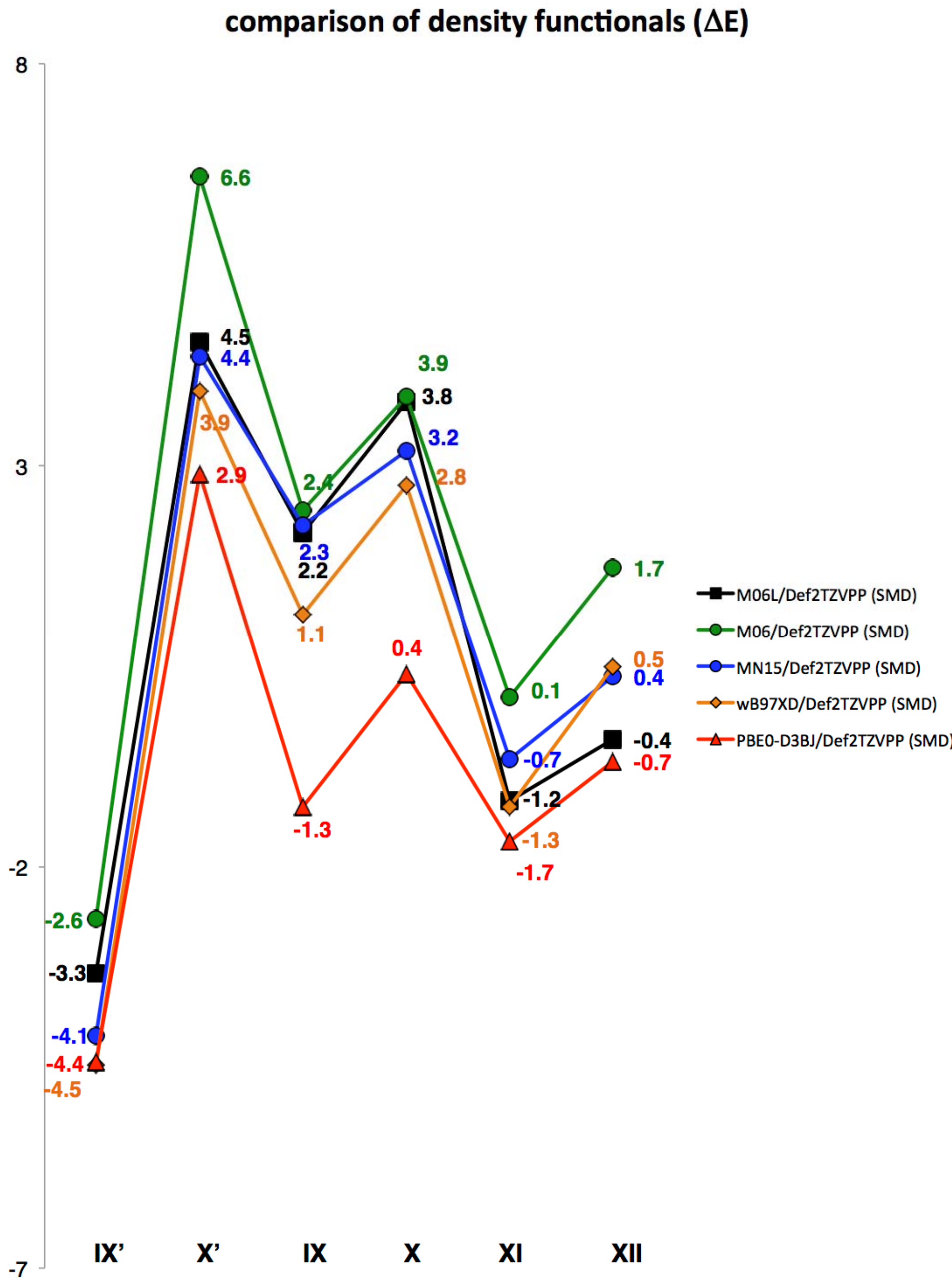


Figure S10. Comparison of electronic energies (ΔE in kcal/mol) for **IX'**–**XII** obtained with several density functionals; expansion of the energy range between –7 and 8 kcal/mol in Figure S9.

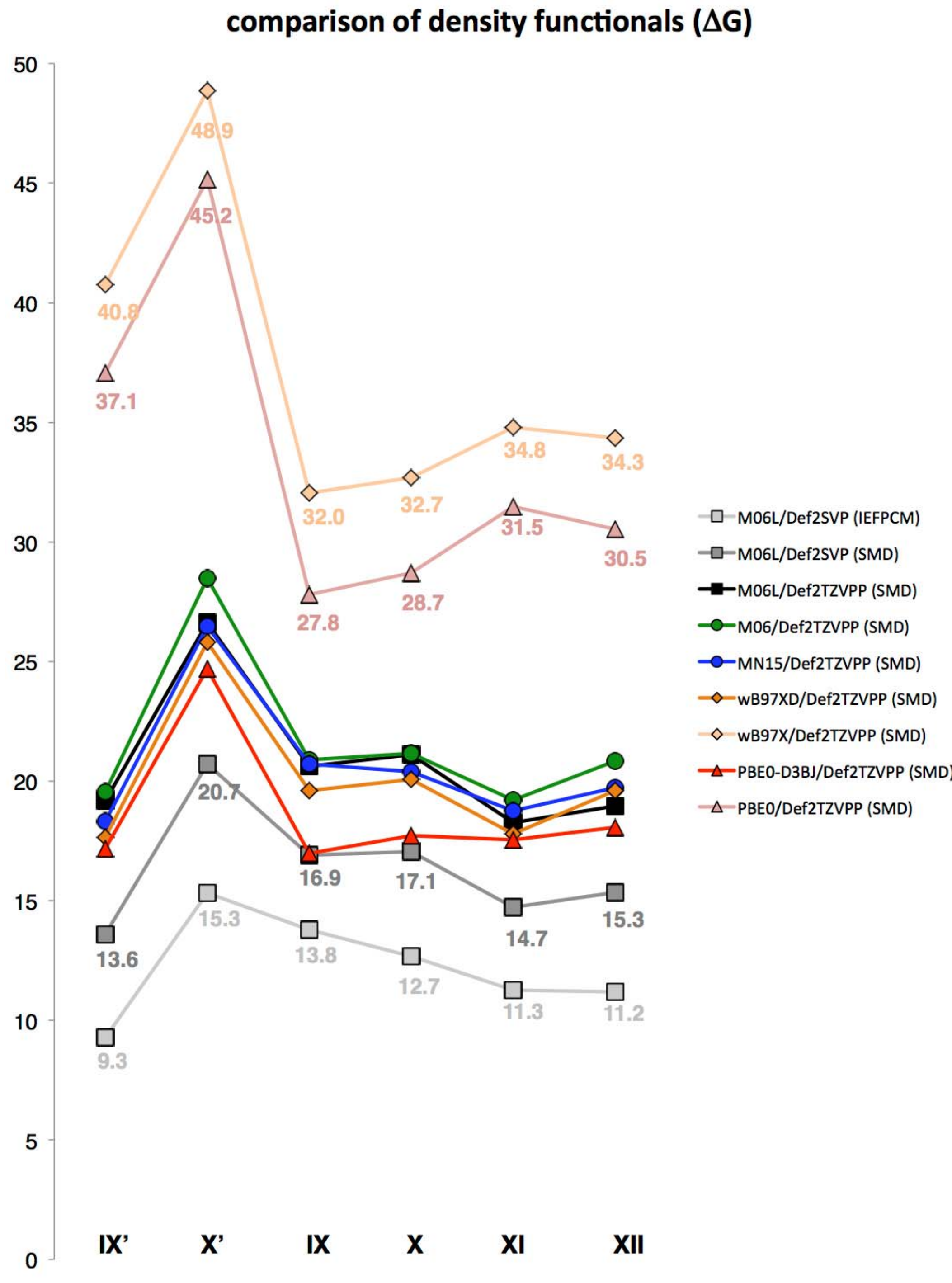


Figure S11. Comparison of free energies (ΔG in kcal/mol) for **IX’–XII** obtained with several density functionals; the maximum values from the corresponding graphs in Figures S4–S8 have been used.

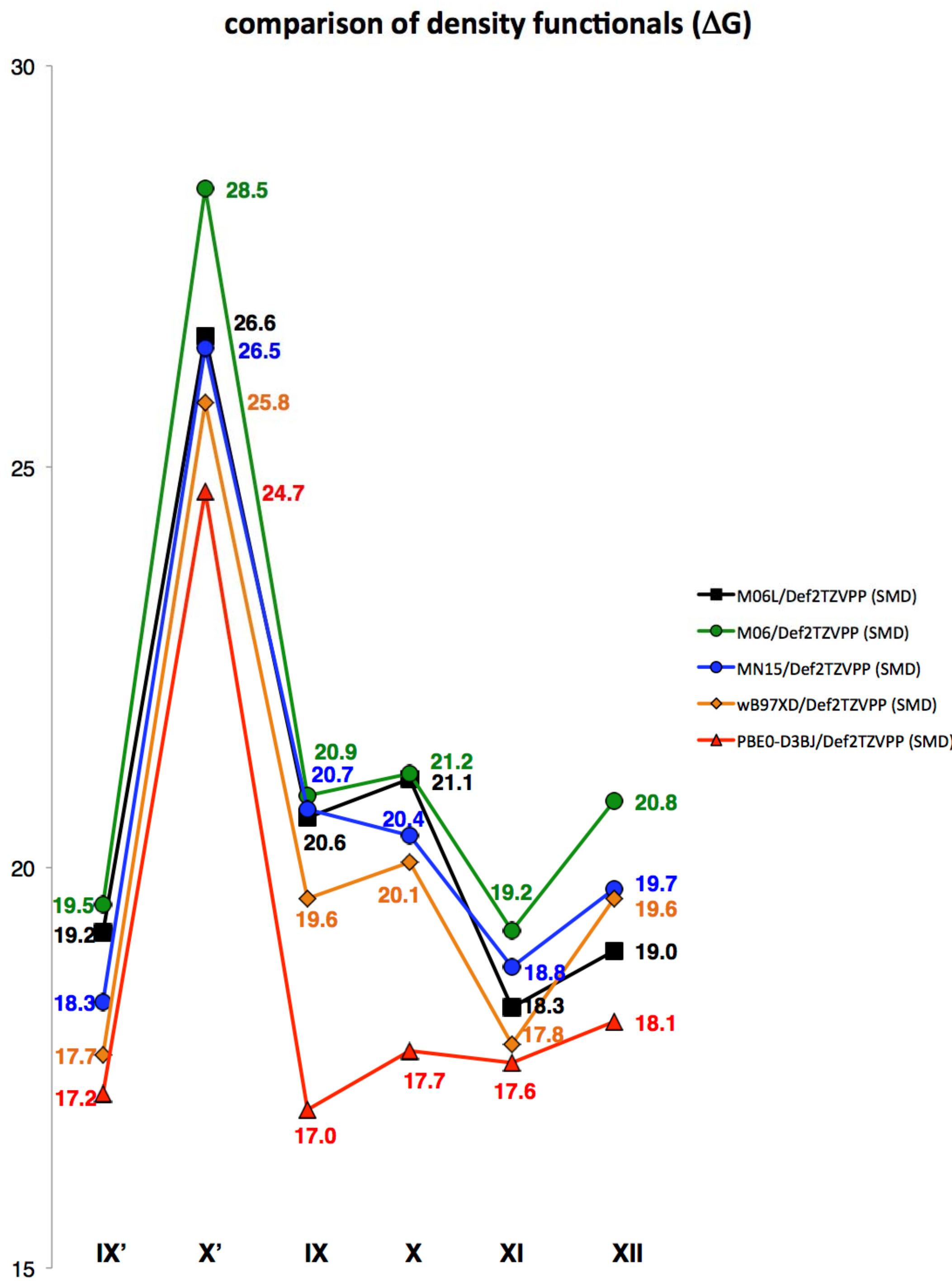


Figure S12. Comparison of free energies (ΔG in kcal/mol) for **IX'–XII** obtained with several density functionals; expansion of the energy range between 15 and 30 kcal/mol in Figure S11.

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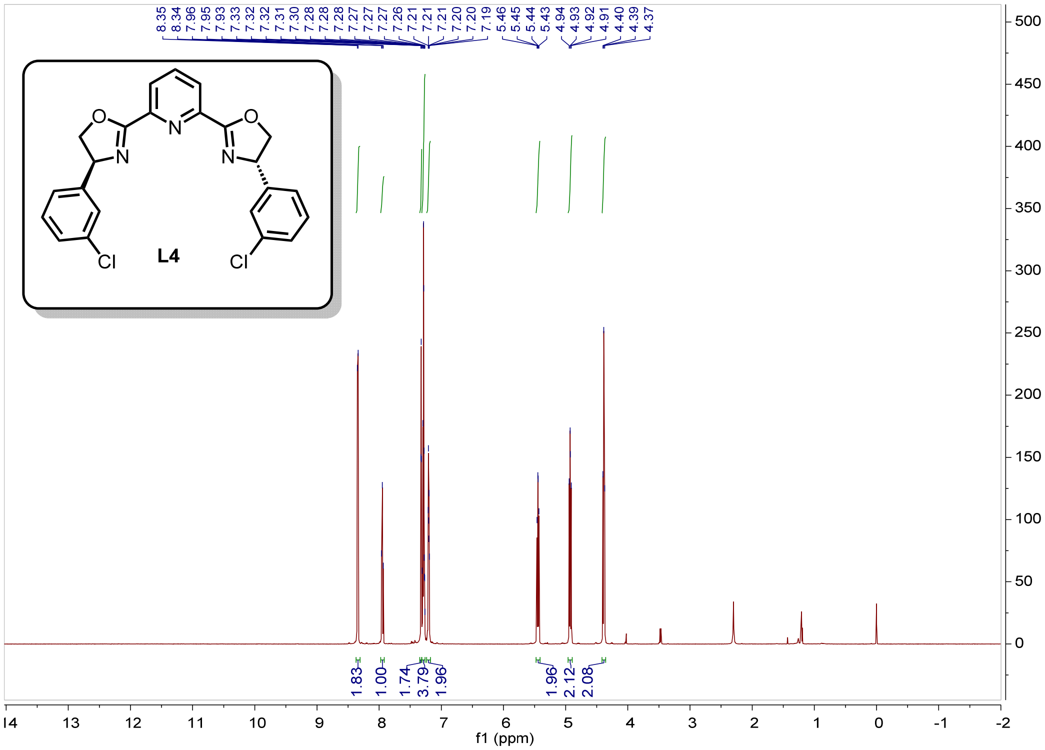
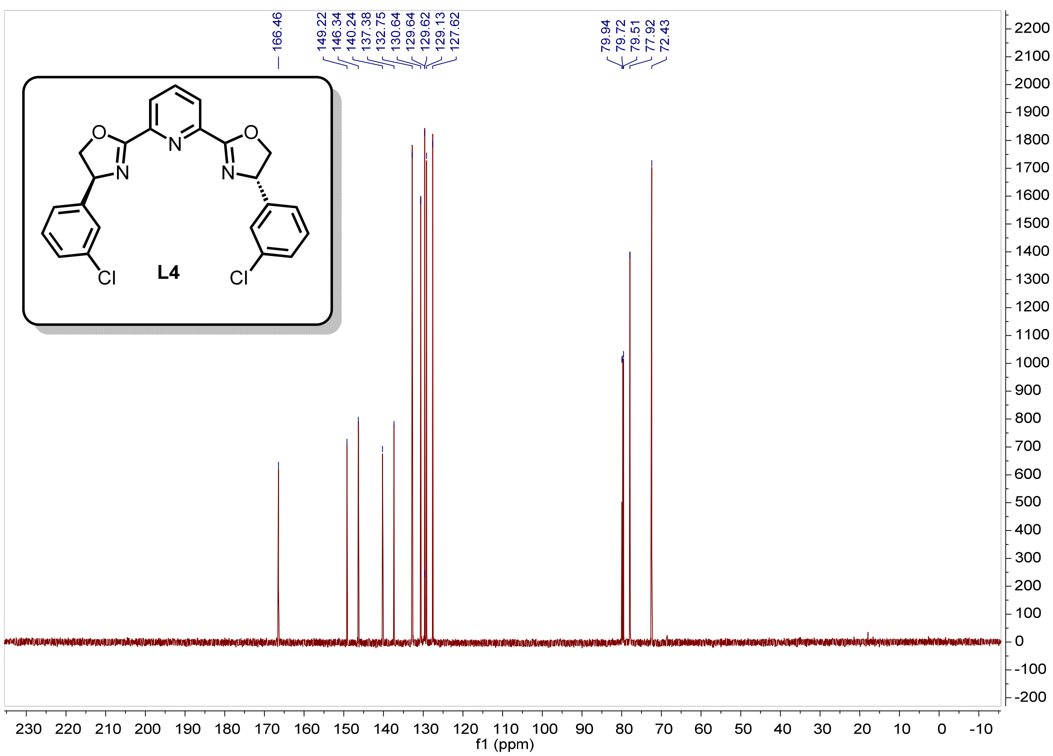
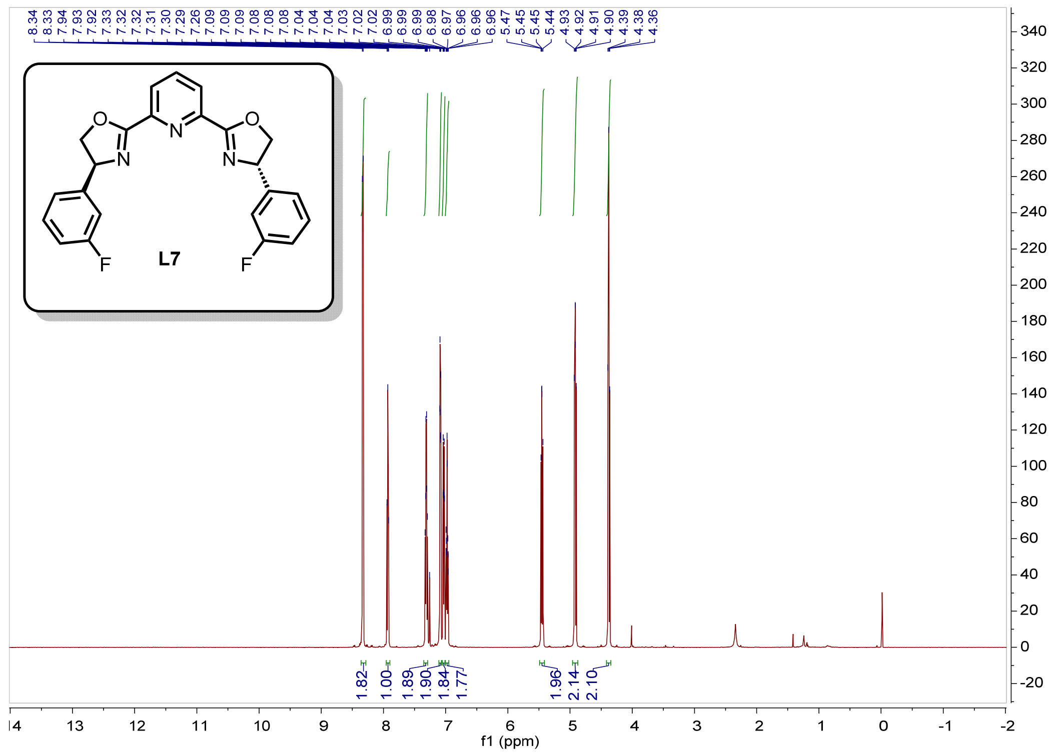
8. NMR Spectra for New Compounds



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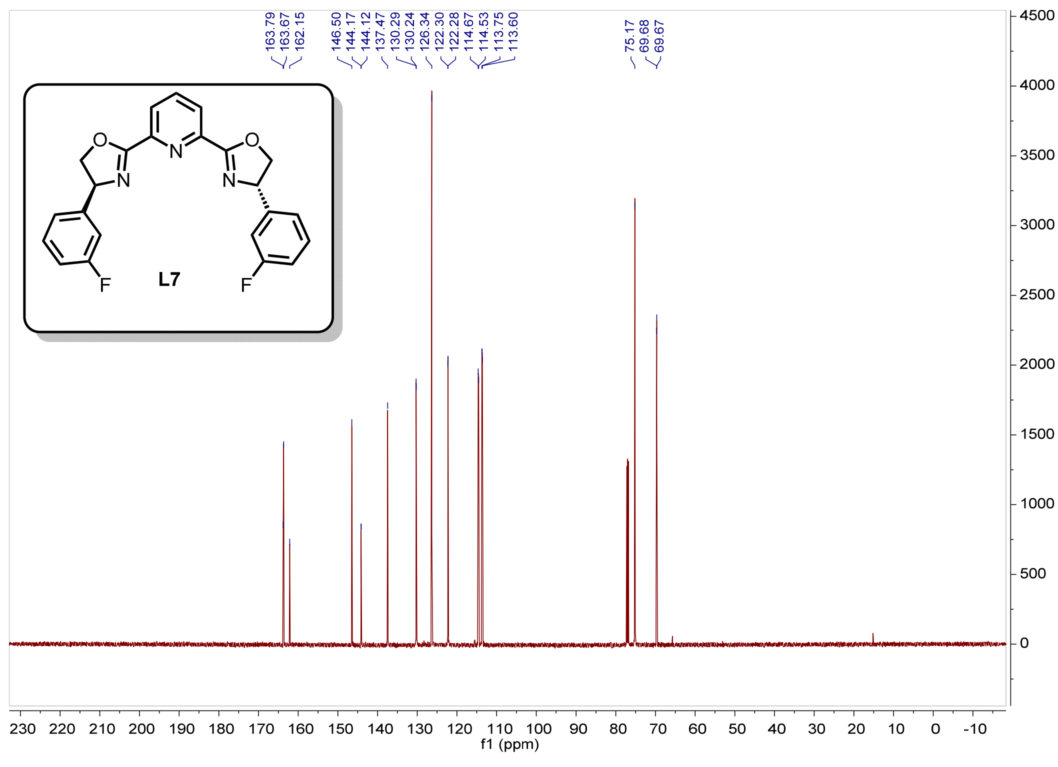
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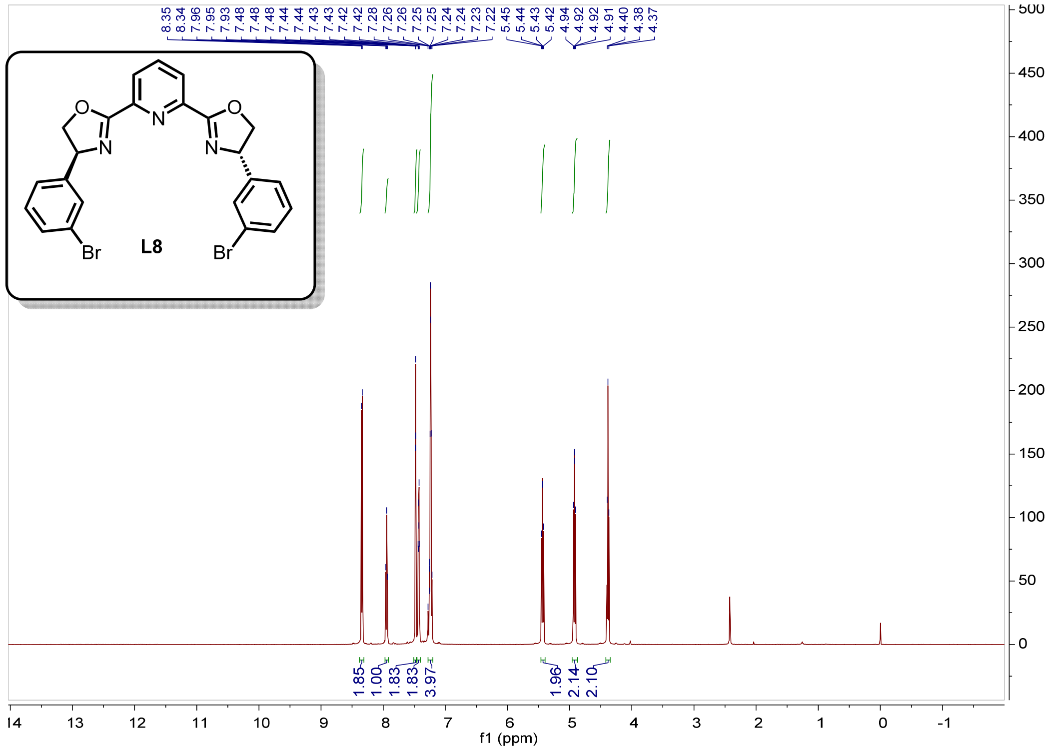
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7.42
7.28
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7.26
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7.24
7.24
7.23
7.23
7.22
5.45
5.44
5.43
5.42
4.94
4.92
4.92
4.91
4.40
4.38
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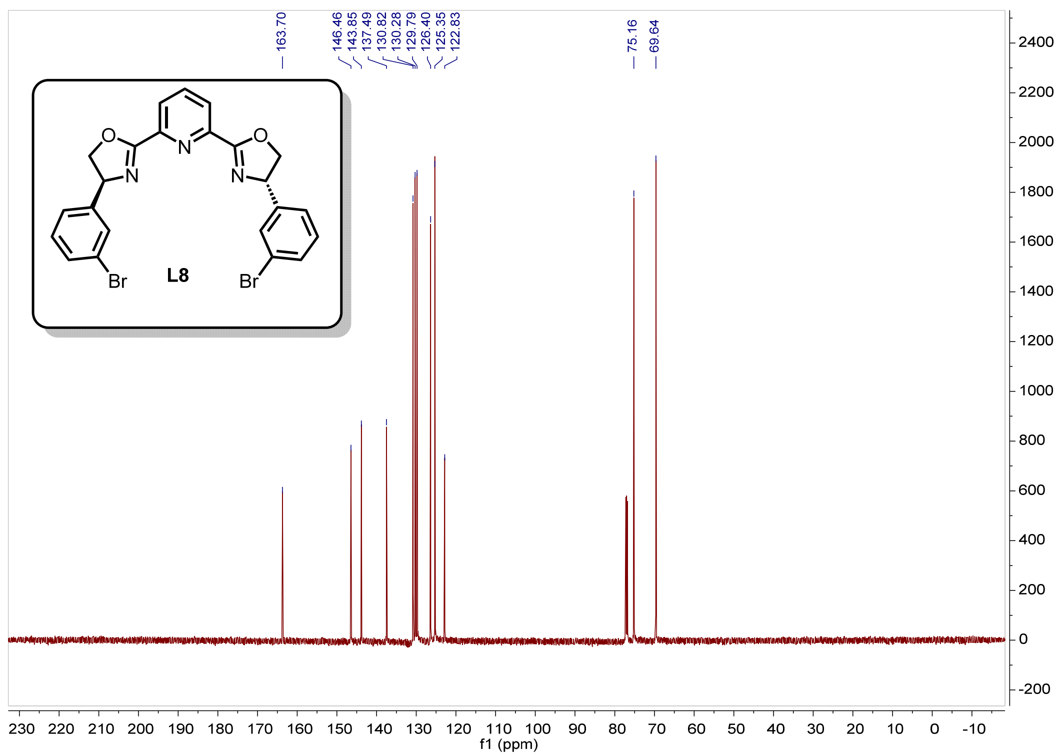
f1 (ppm)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Br
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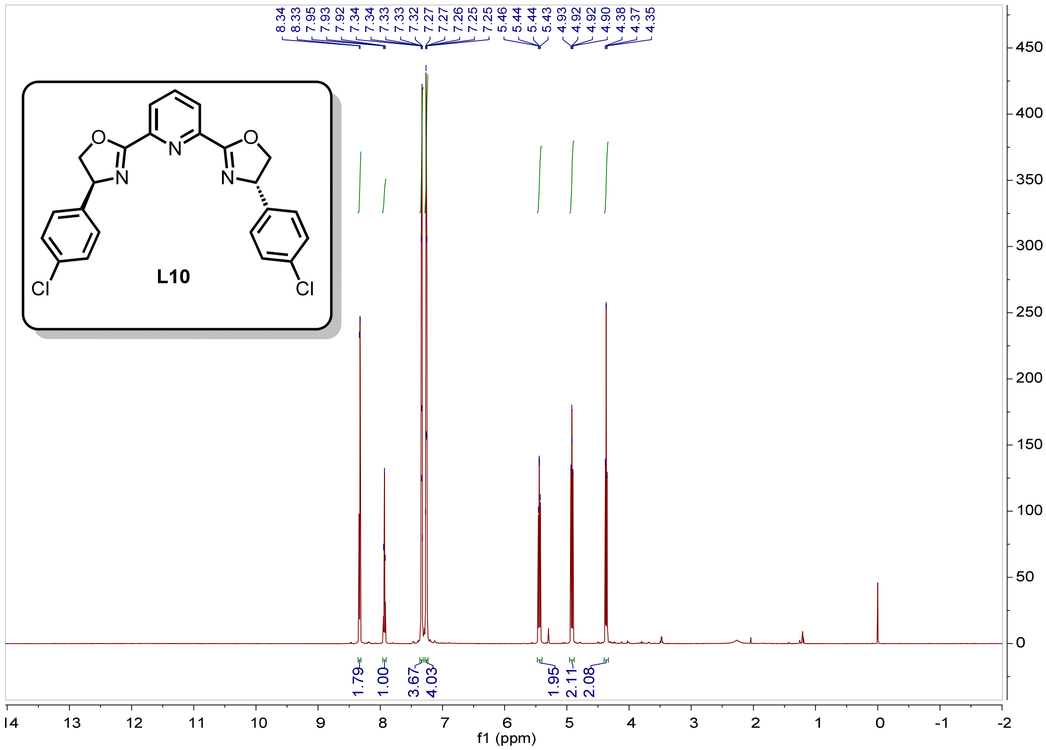

8.34
8.33
7.95
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7.34
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7.33
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7.32
7.27
7.27
7.26
7.25
7.25
5.46
5.44
5.44
5.43
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4.92
4.92
4.90
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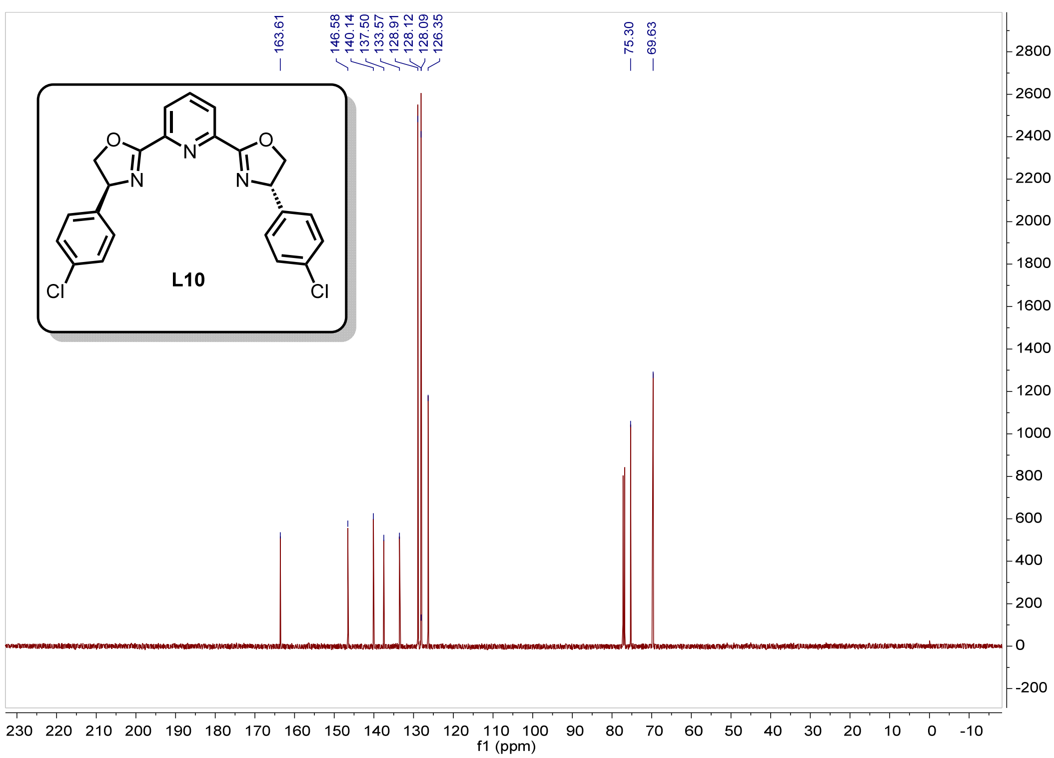

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L10
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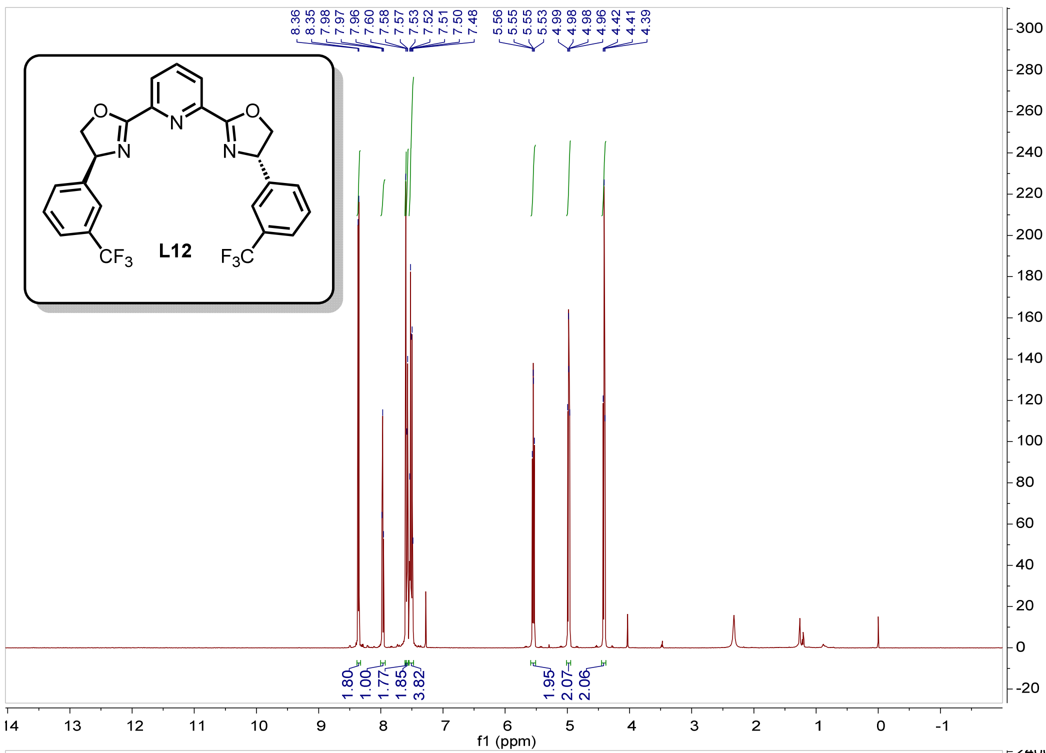

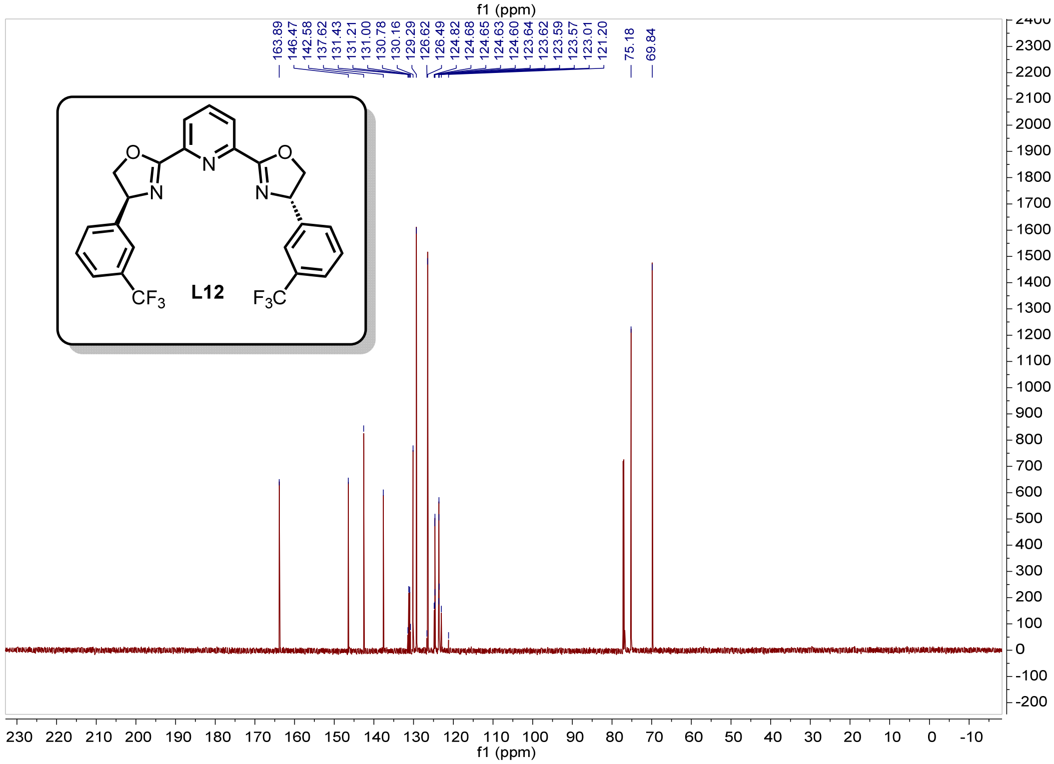

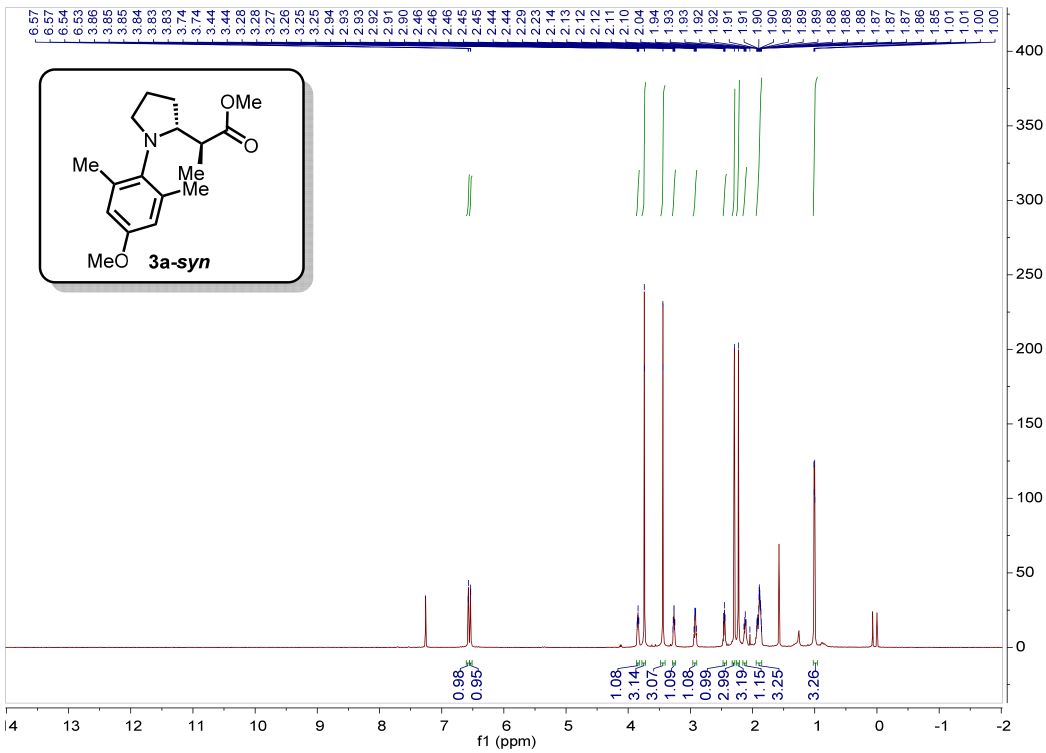
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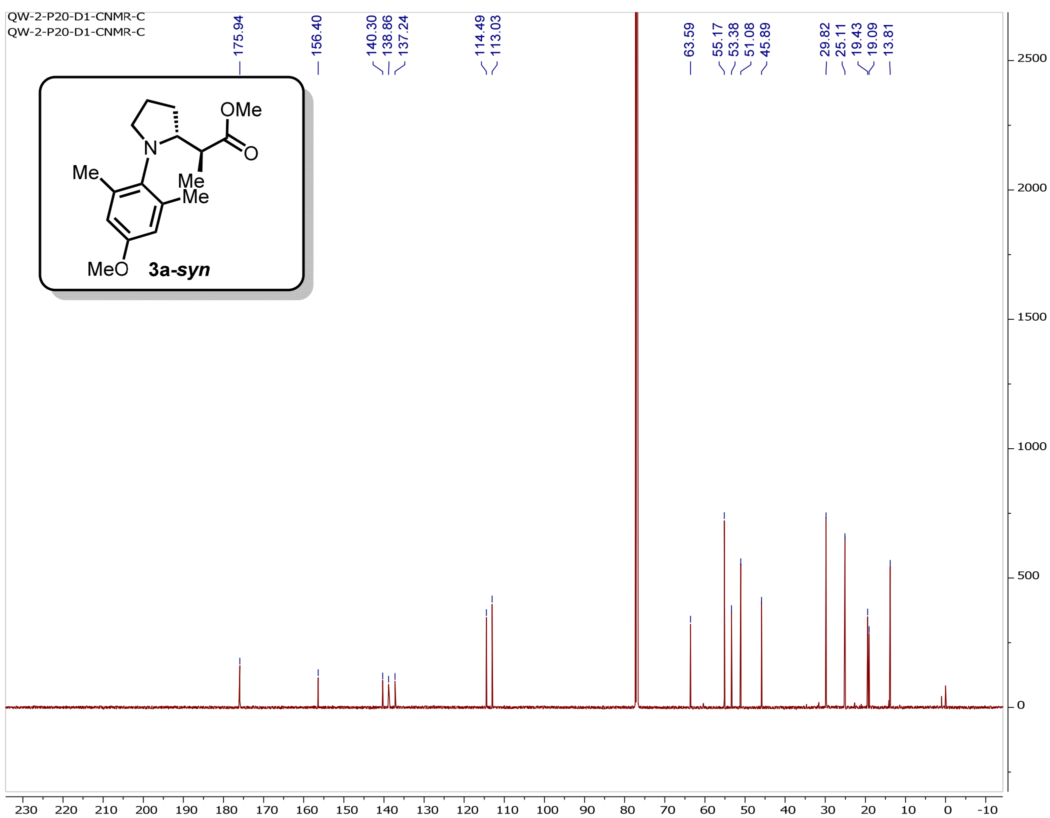
3a-syn
f1 (ppm)


QW-2-P20-D1-CNMR-C
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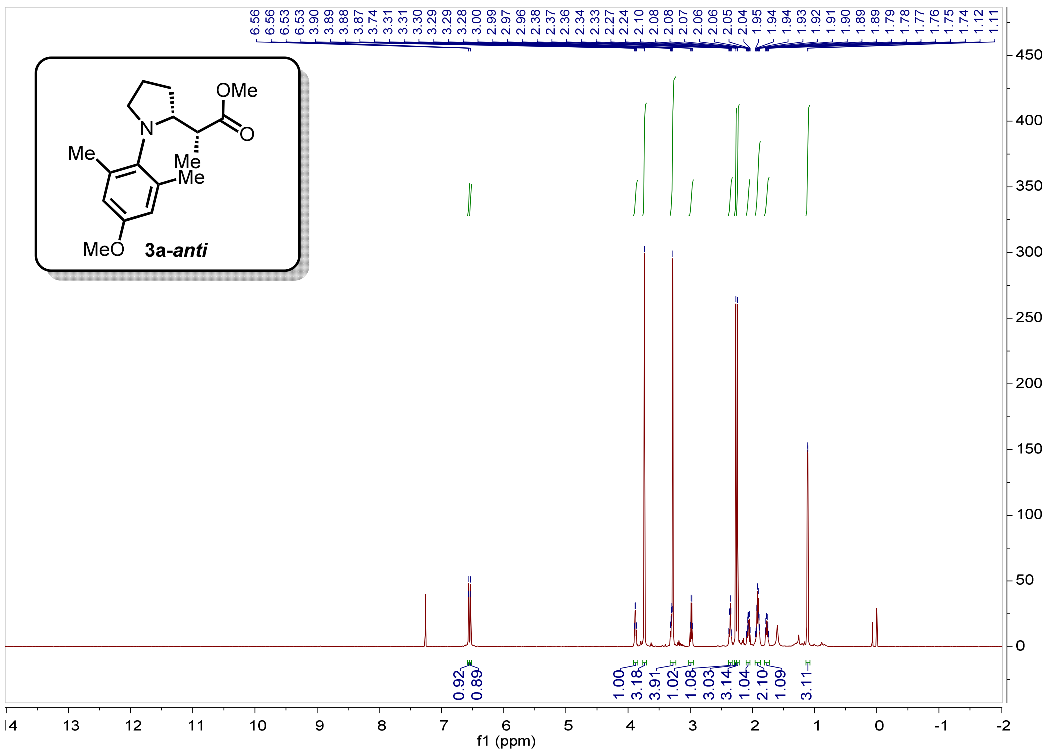
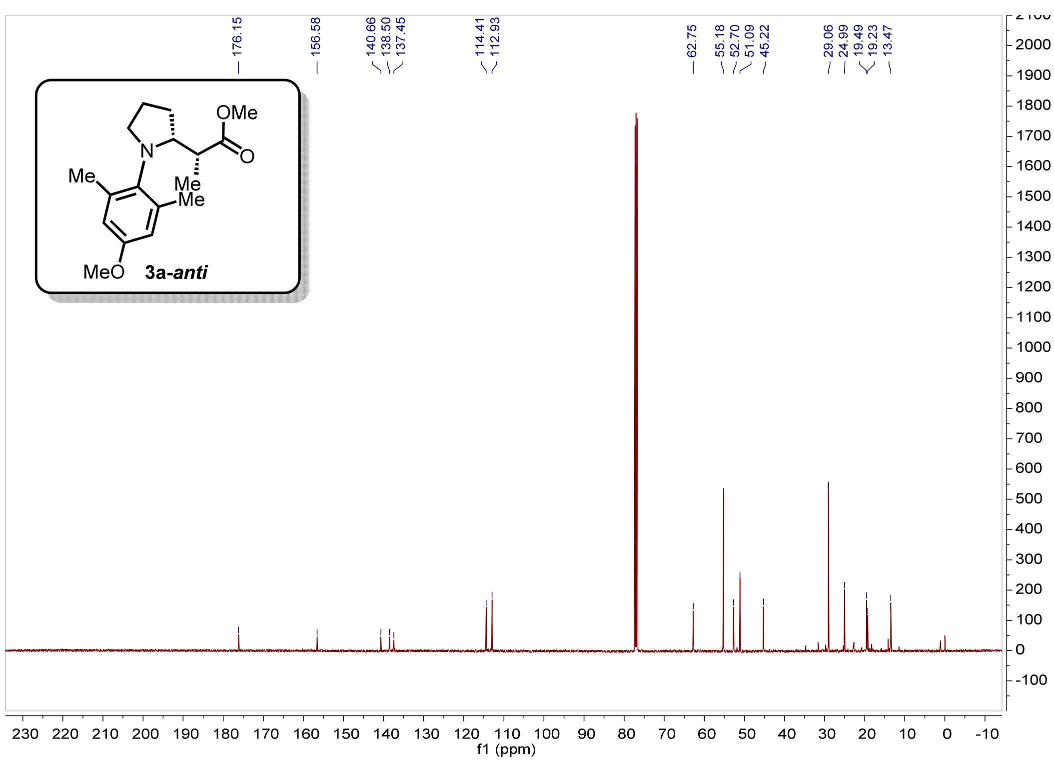
140.30
138.86
137.24
114.49
113.03
63.59
55.17
53.38
51.08
45.89
29.82
25.11
19.43
19.09
13.81
OMe
N
Me
Me
Me
MeO
3a-syn
f1 (ppm)



OMe
N
O
Me
Me
Me
MeO
3a-anti
f1 (ppm)



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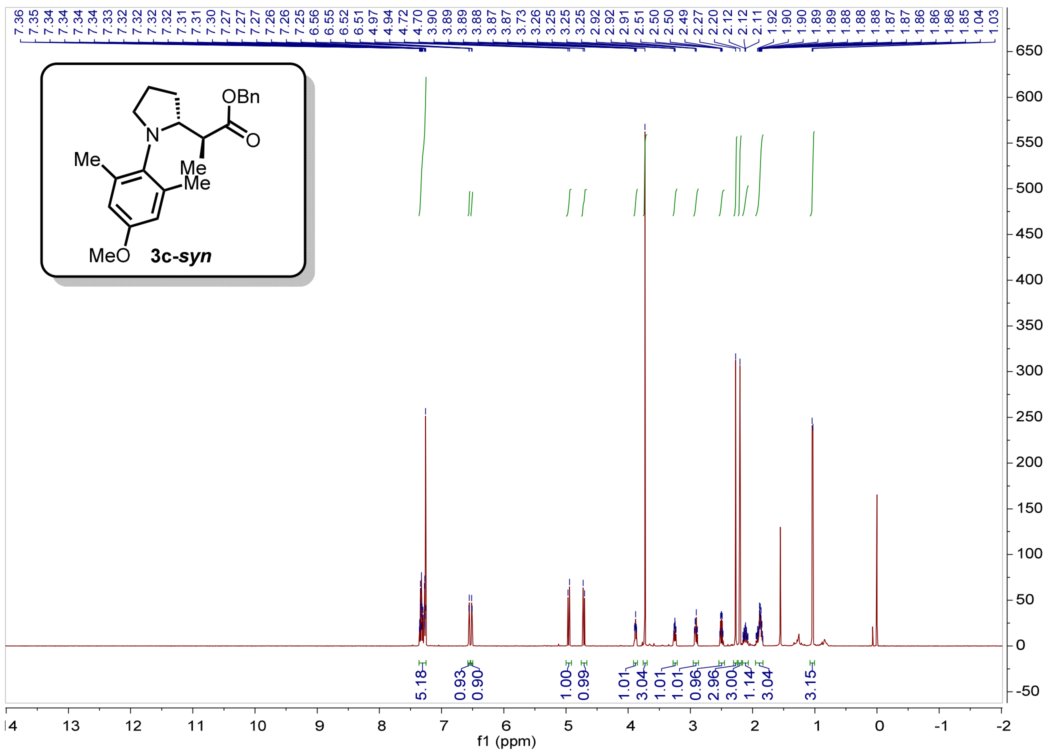
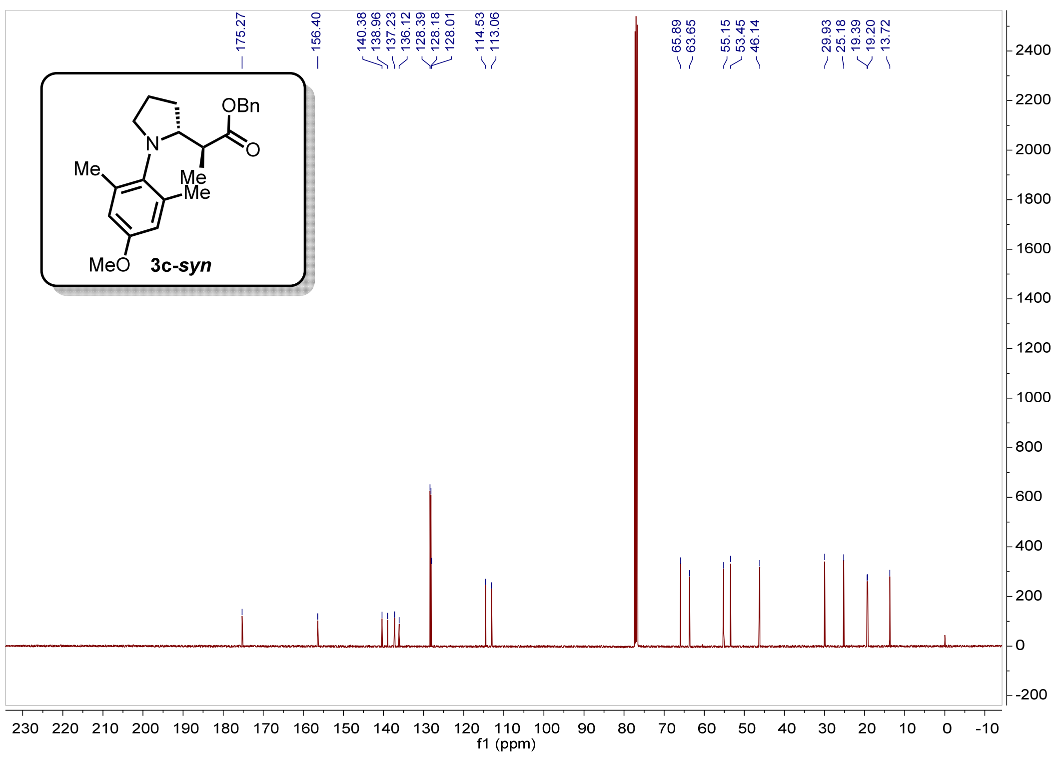
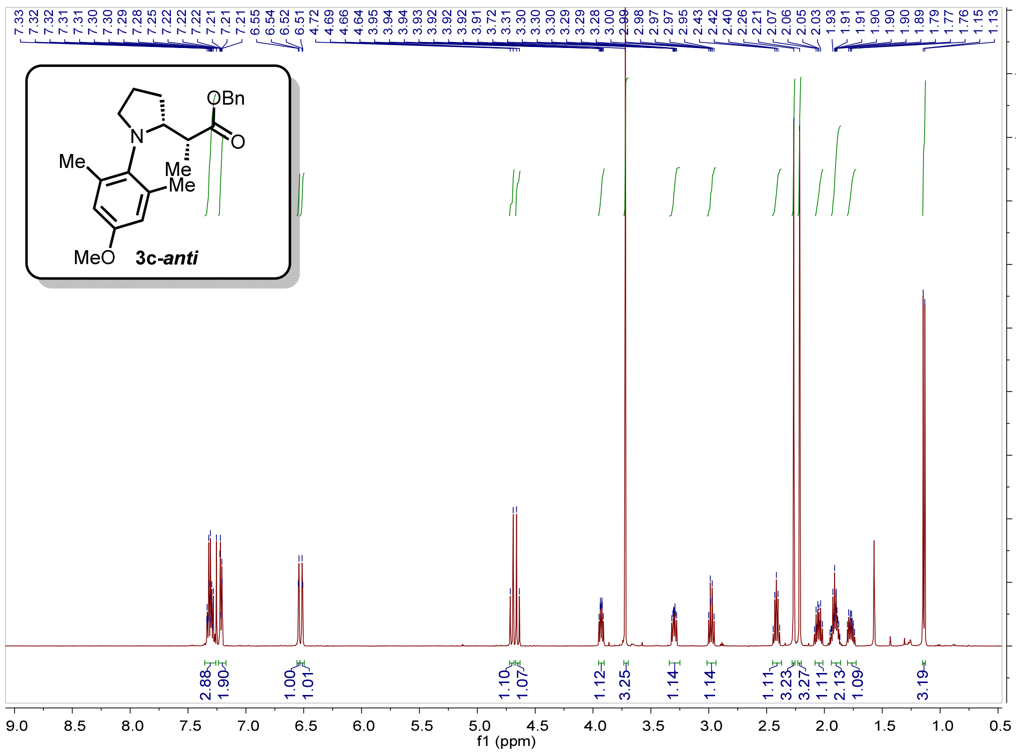
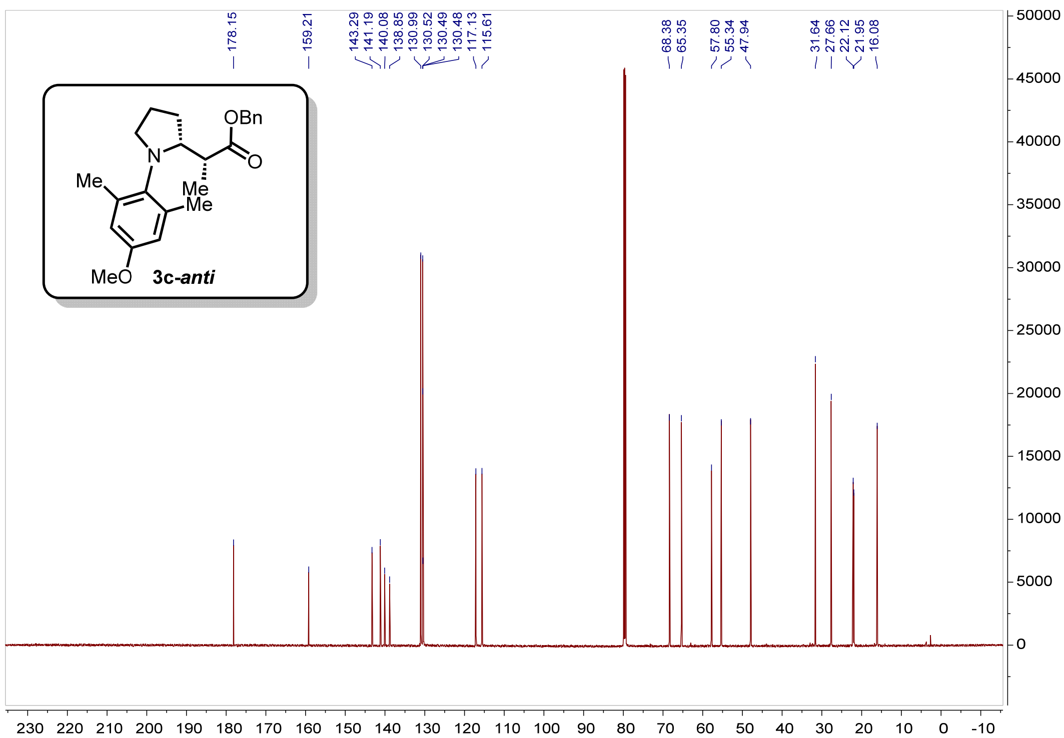
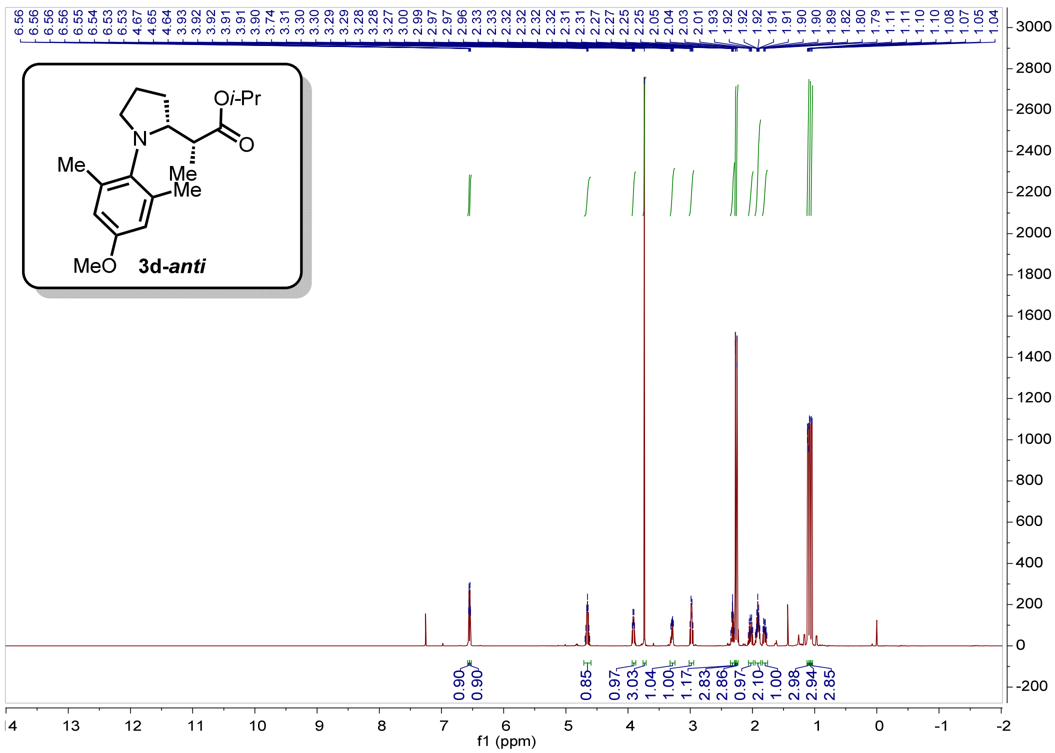
156.58
140.66
138.50
137.45
114.41
112.93
62.75
55.18
52.70
51.09
45.22
29.06
24.99
19.49
19.23
13.47
OMe
N
O
Me
Me
Me
MeO
3a-anti
f1 (ppm)

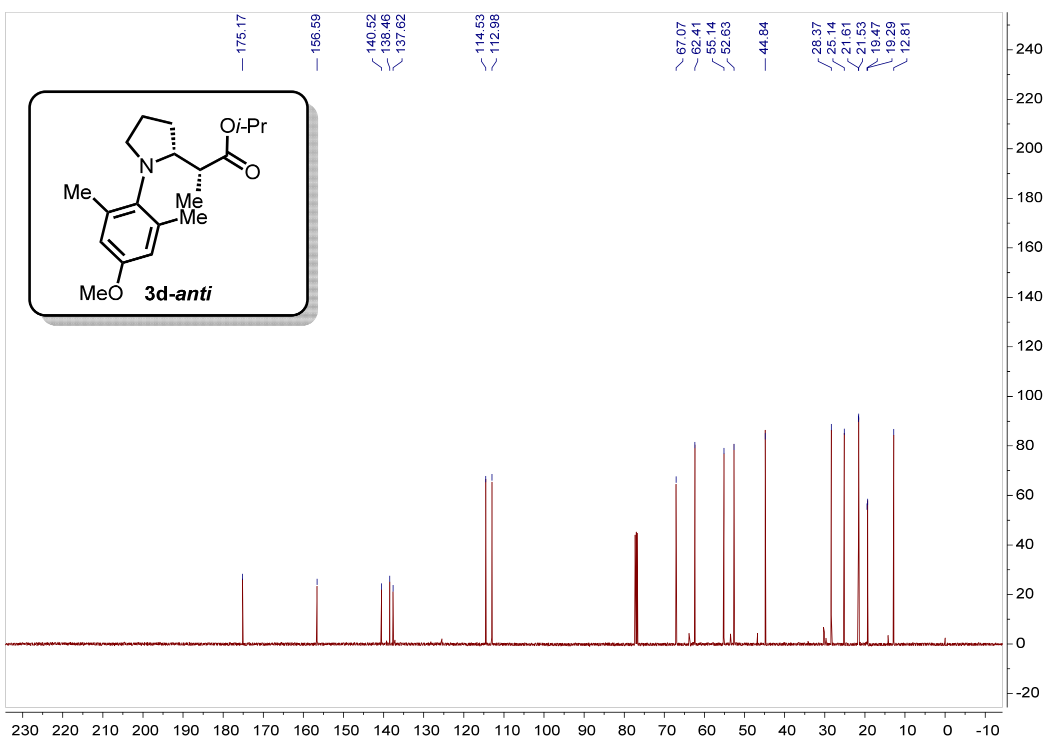


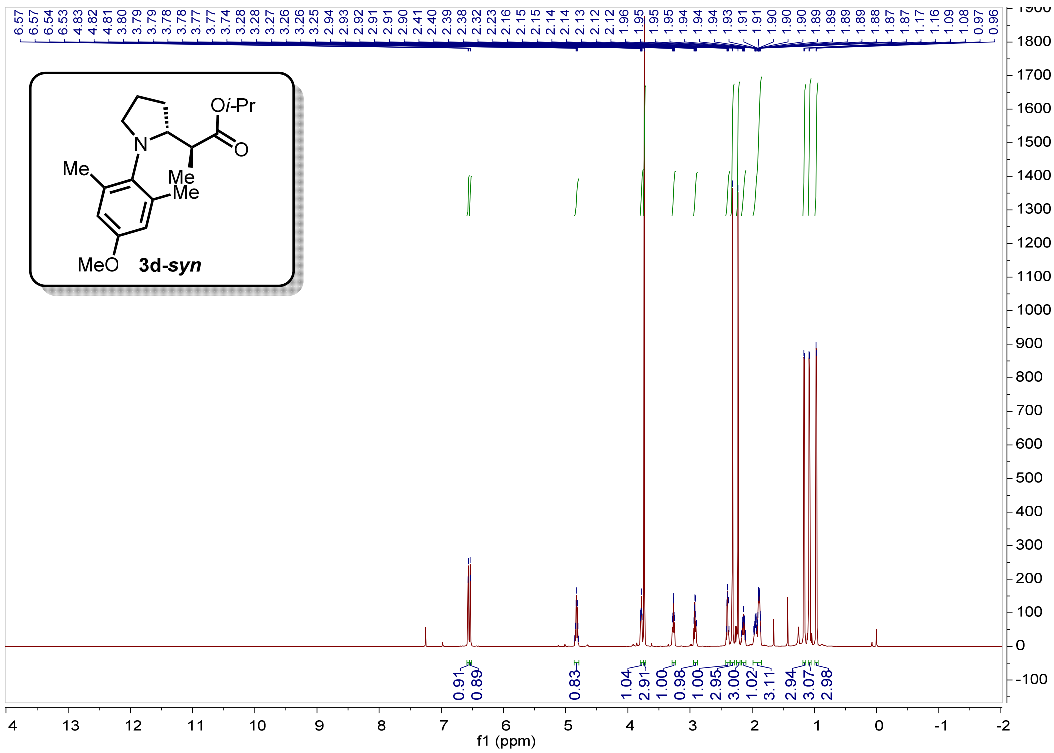




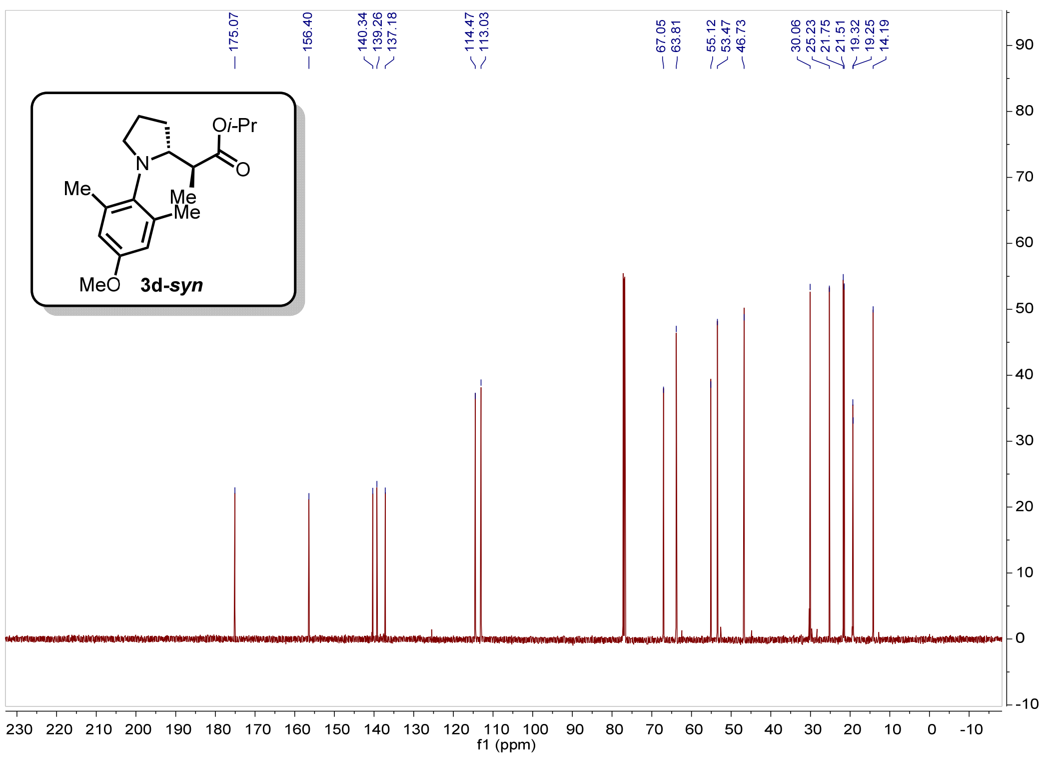




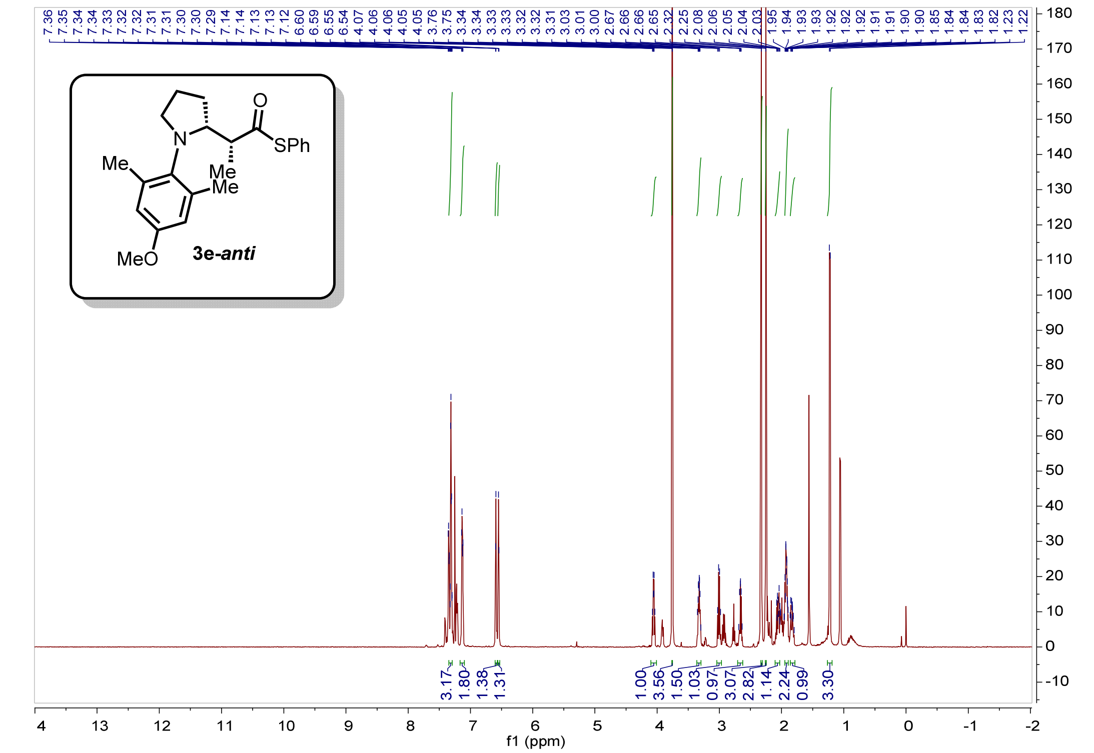


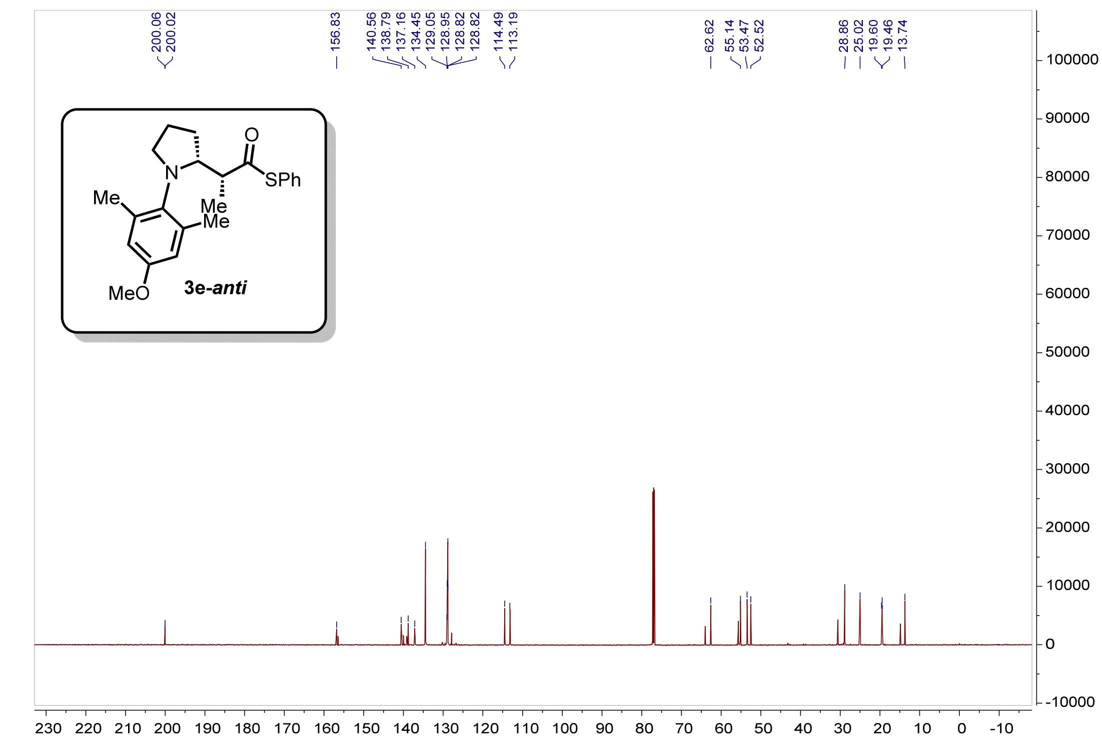


Oi-Pr
N
O
Me
Me
Me
MeO
3d-syn
f1 (ppm)



Oi-Pr
N
O
Me
Me
Me
MeO
3d-syn
f1 (ppm)


3e-anti
Me
Me
Me
MeO
SPh
O
N
f1 (ppm)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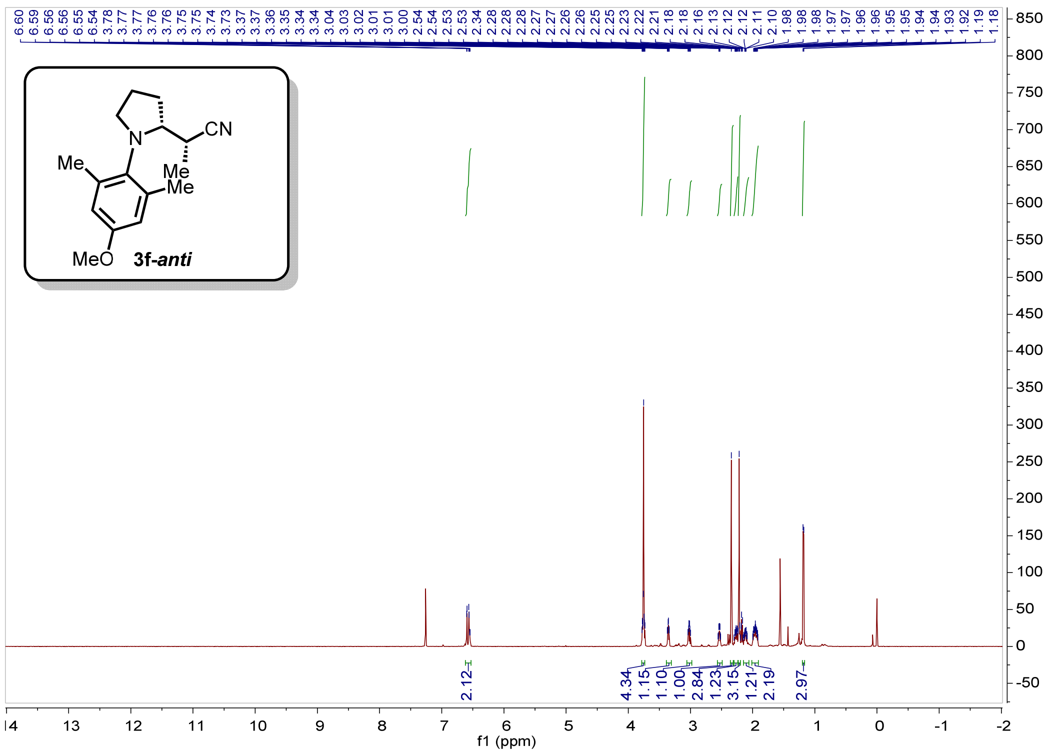
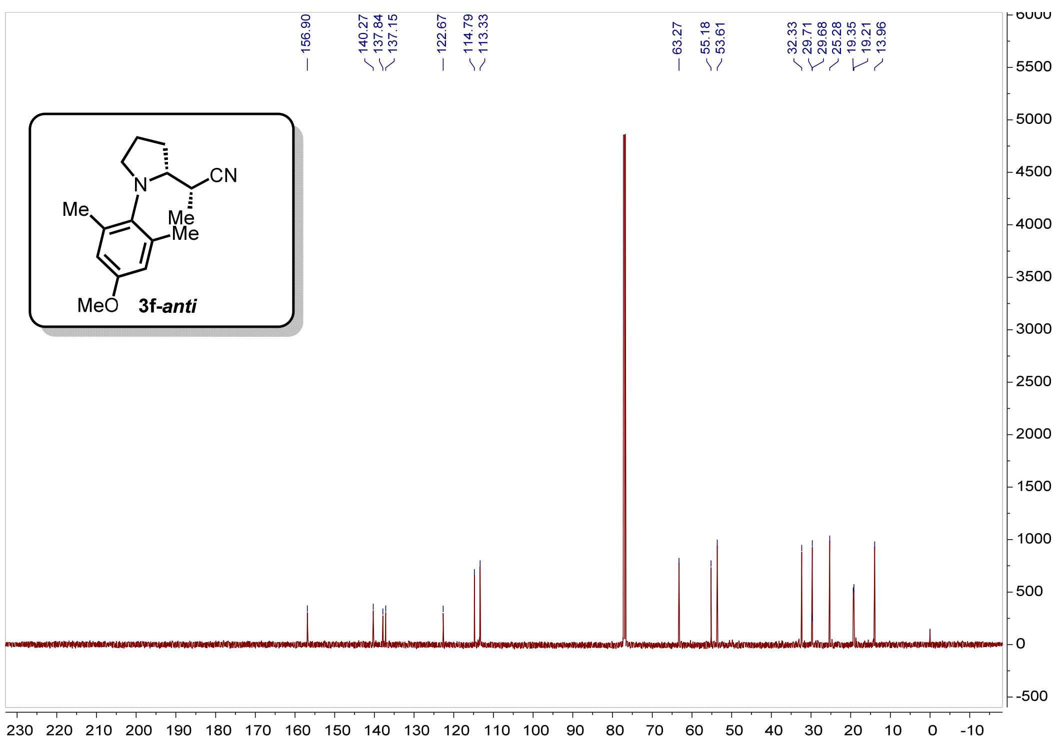
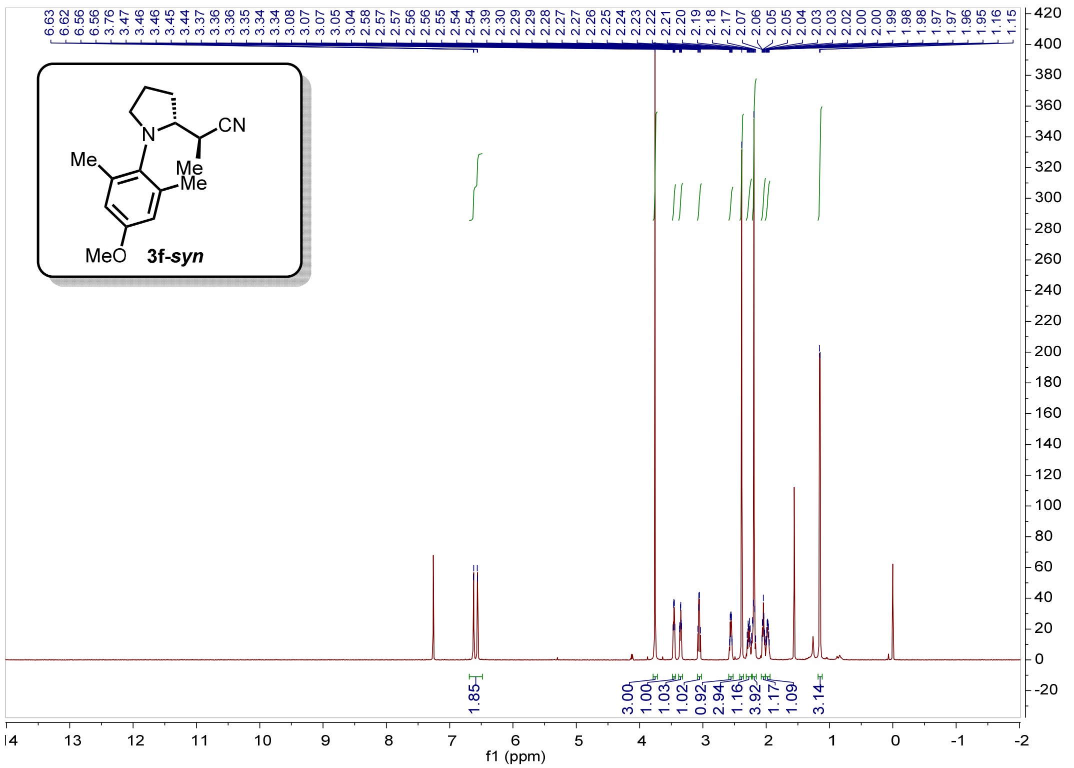
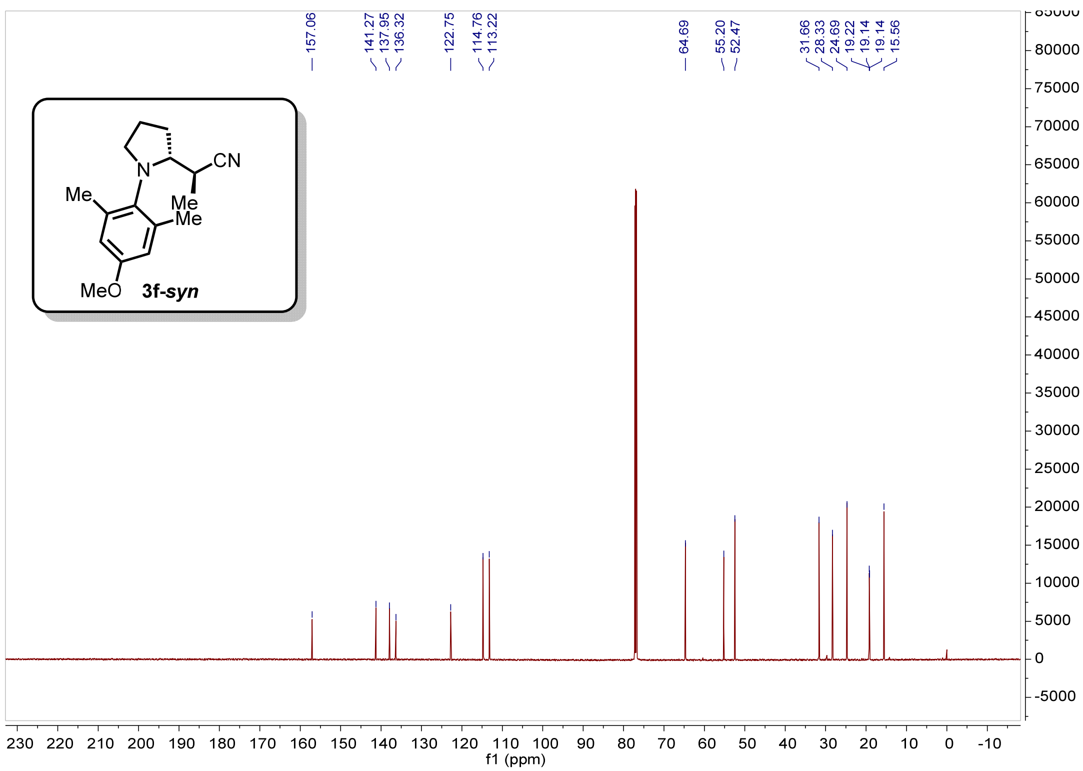
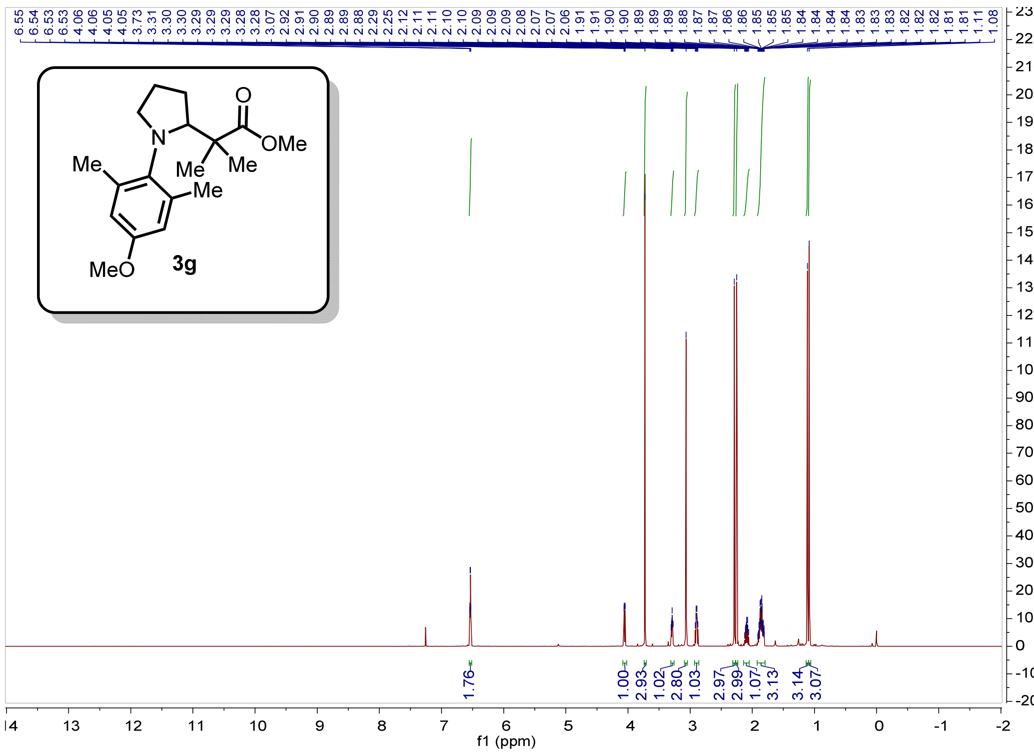
200.02
156.83
140.56
138.79
137.16
134.45
129.05
128.95
128.82
128.82
114.49
113.19
62.62
55.14
53.47
52.52
28.86
25.02
19.60
19.46
13.74
3e-anti
Me
Me
Me
MeO
SPh
O
N
f1 (ppm)


3f-anti
f1 (ppm)


3f-anti
f1 (ppm)







6.55
6.54
6.53
6.53
4.06
4.06
4.05
4.05
3.73
3.31
3.30
3.30
3.29
3.29
3.29
3.28
3.28
3.07
2.92
2.91
2.90
2.89
2.89
2.88
2.29
2.25
2.12
2.11
2.11
2.10
2.10
2.09
2.09
2.09
2.08
2.07
2.07
2.06
1.91
1.91
1.90
1.90
1.89
1.89
1.89
1.88
1.87
1.87
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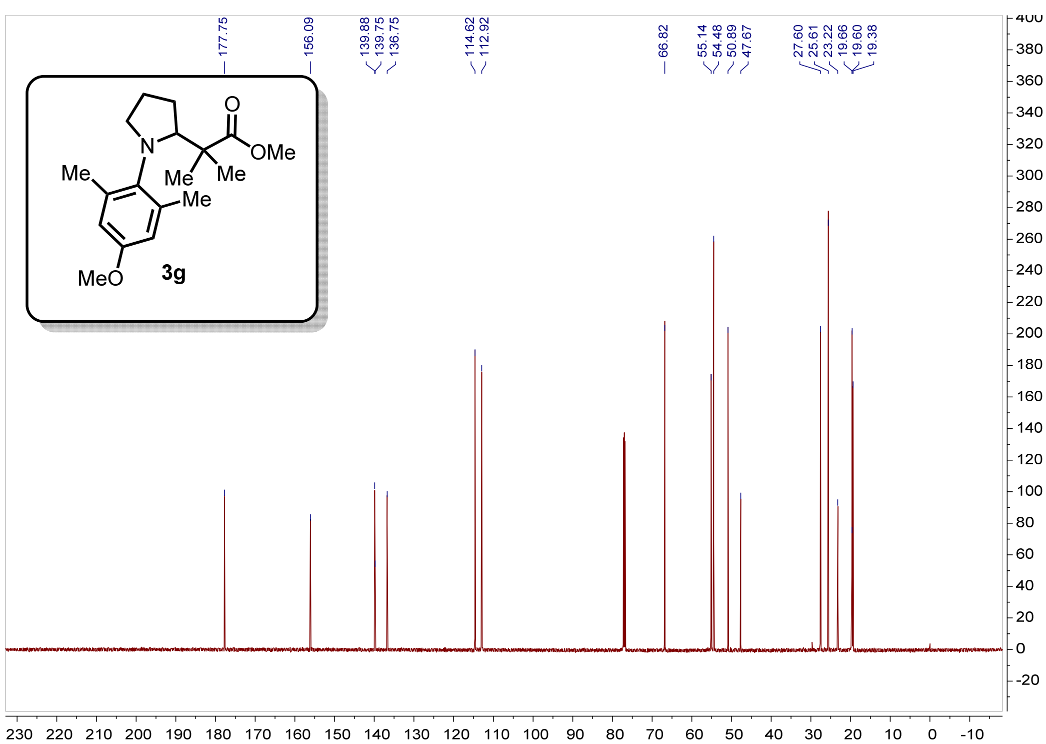
1.84
1.84
1.83
1.83
1.82
1.82
1.82
1.81
1.81
1.11
1.08
O
N
OMe
Me
Me
Me
Me
MeO
3g
1.76
1.00
2.93
1.02
2.80
1.03
2.97
2.99
1.07
3.13
3.14
3.07
f1 (ppm)



177.75
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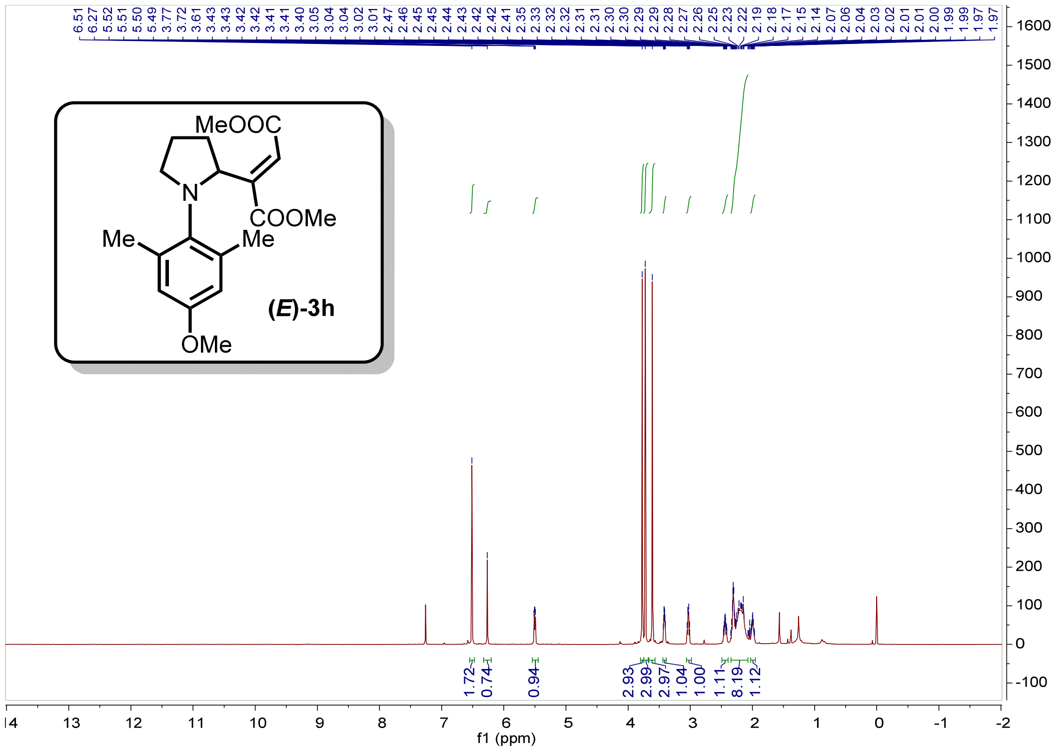
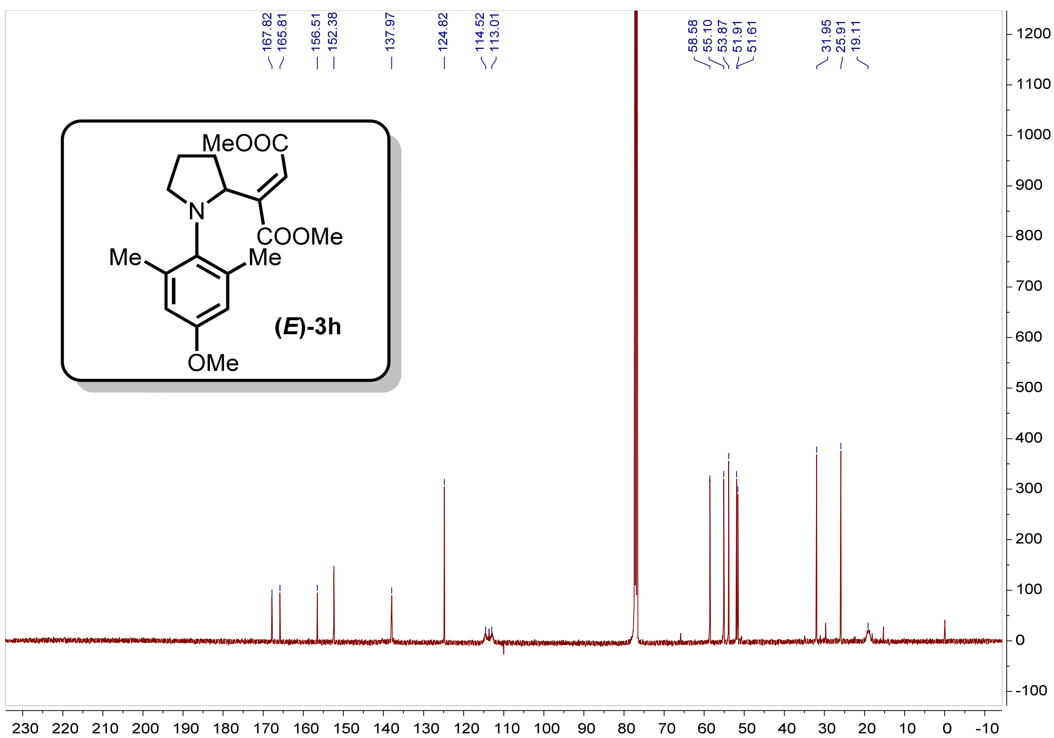
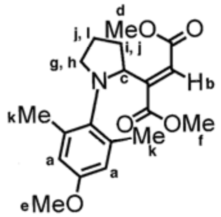
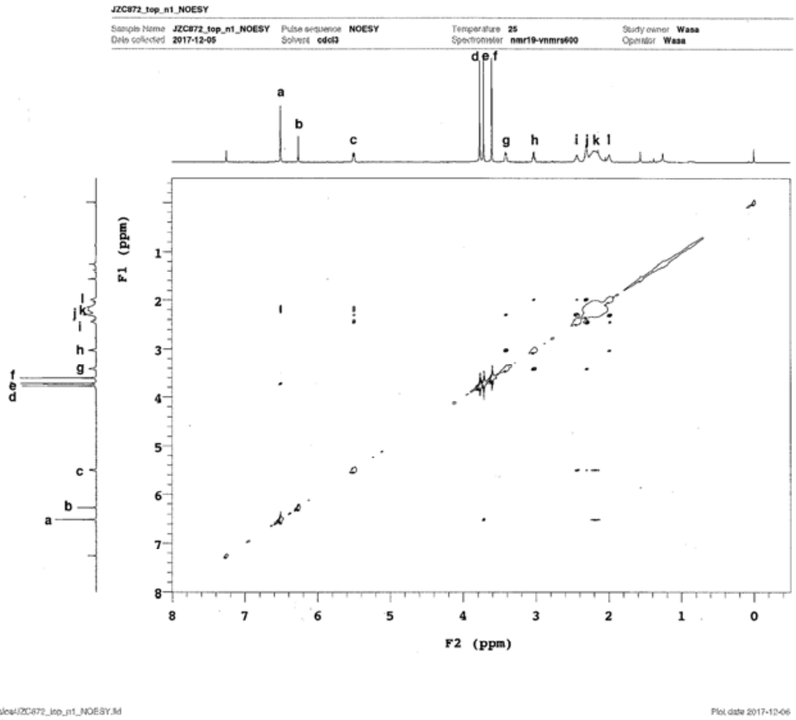
139.88
139.75
136.75
114.62
112.92
66.82
55.14
54.48
50.89
47.67
27.60
25.61
23.22
19.66
19.60
19.38
O
N
OMe
Me
Me
Me
Me
MeO
3g
f1 (ppm)

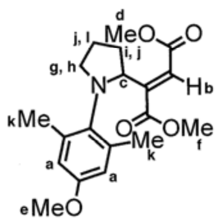




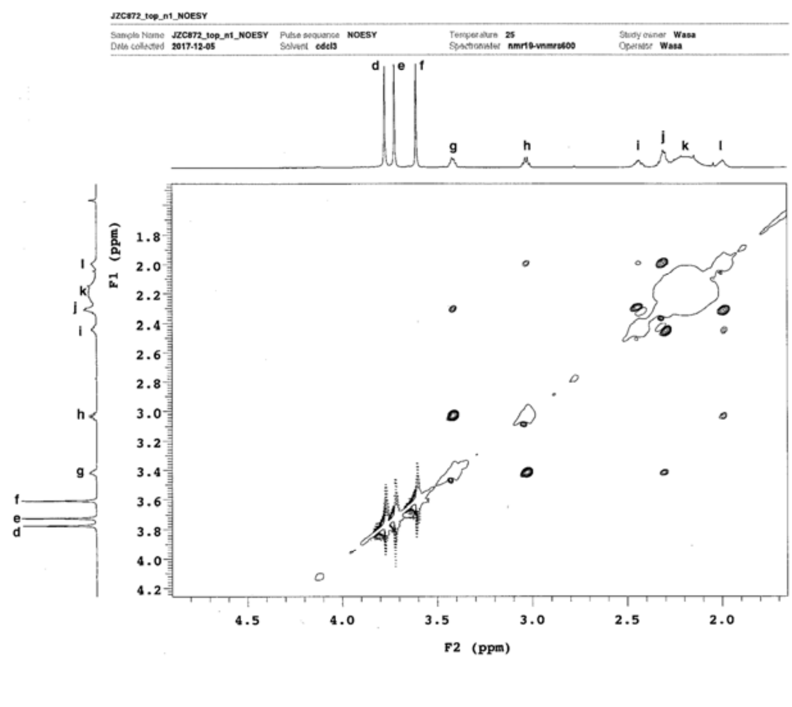


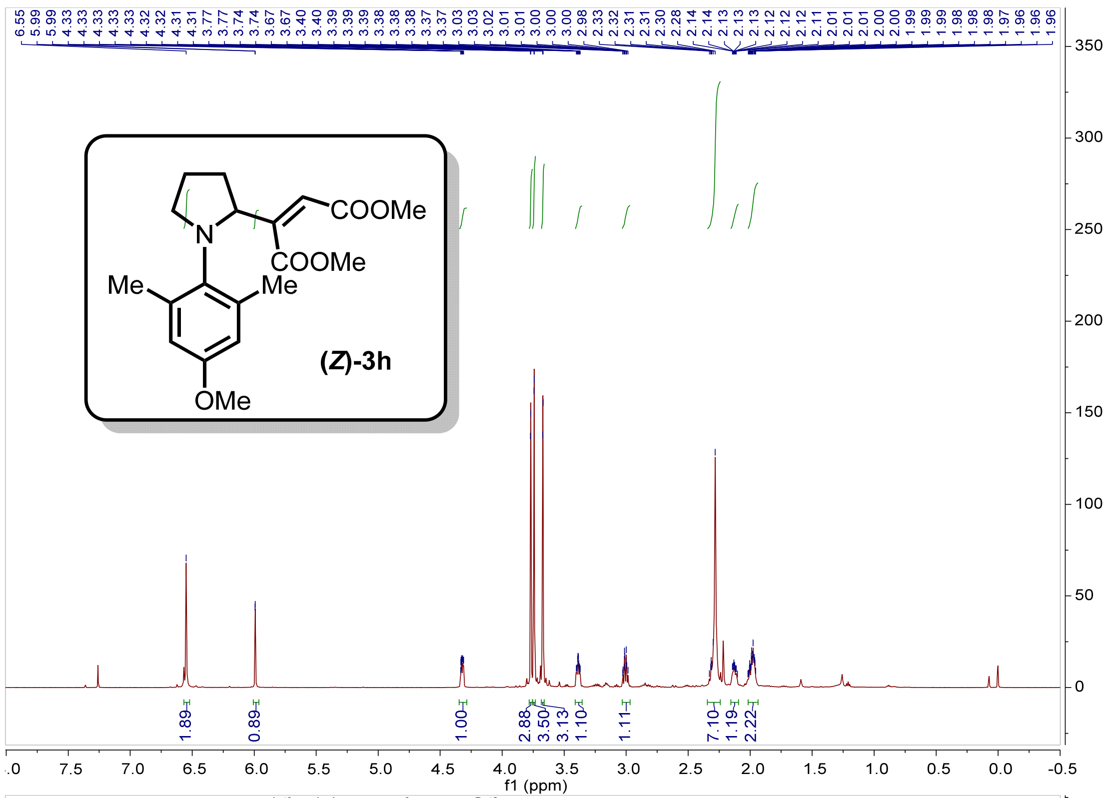
(*E*)-3h

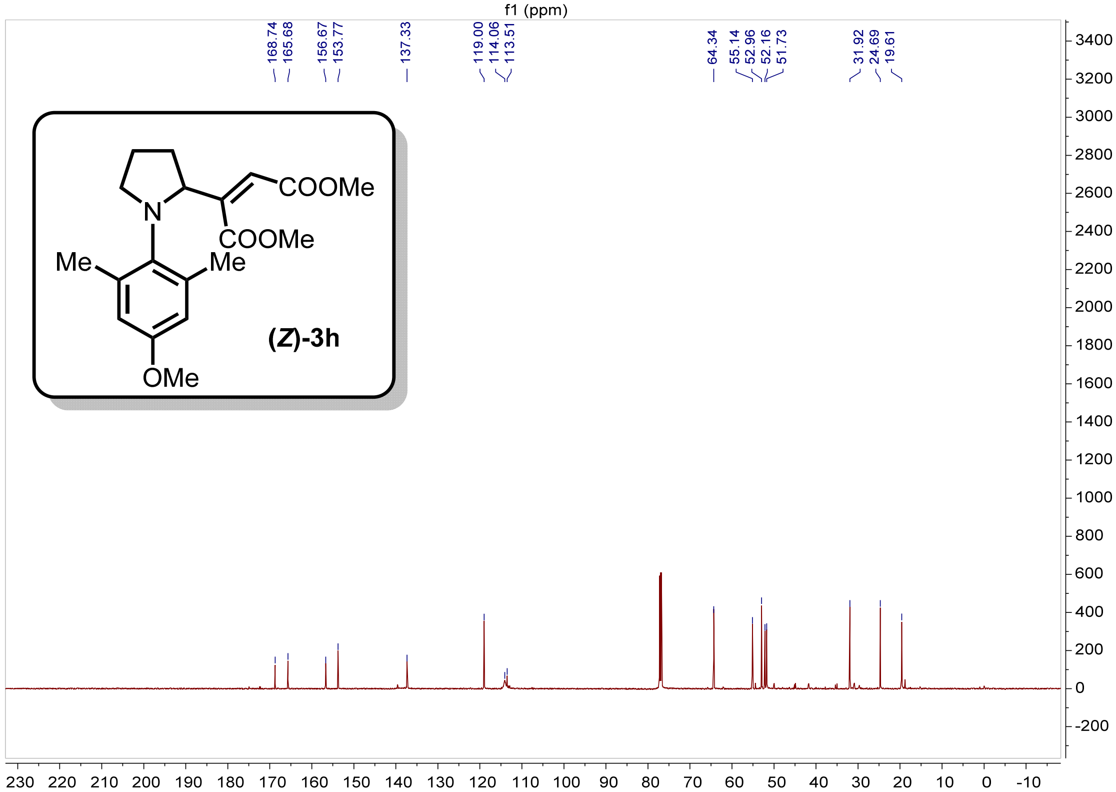

JZC872_top_n1_NOESY
Sample Name JZC872_top_n1_NOESY
Date collected 2017-12-05
Pulse sequence NOESY
Solvent cdcl3
Temperature 25
Spectrometer nmr19-vnmrs600
Study owner Wasa
Operator Wasa
F1 (ppm)
F2 (ppm)
Plot date 2017-12-06

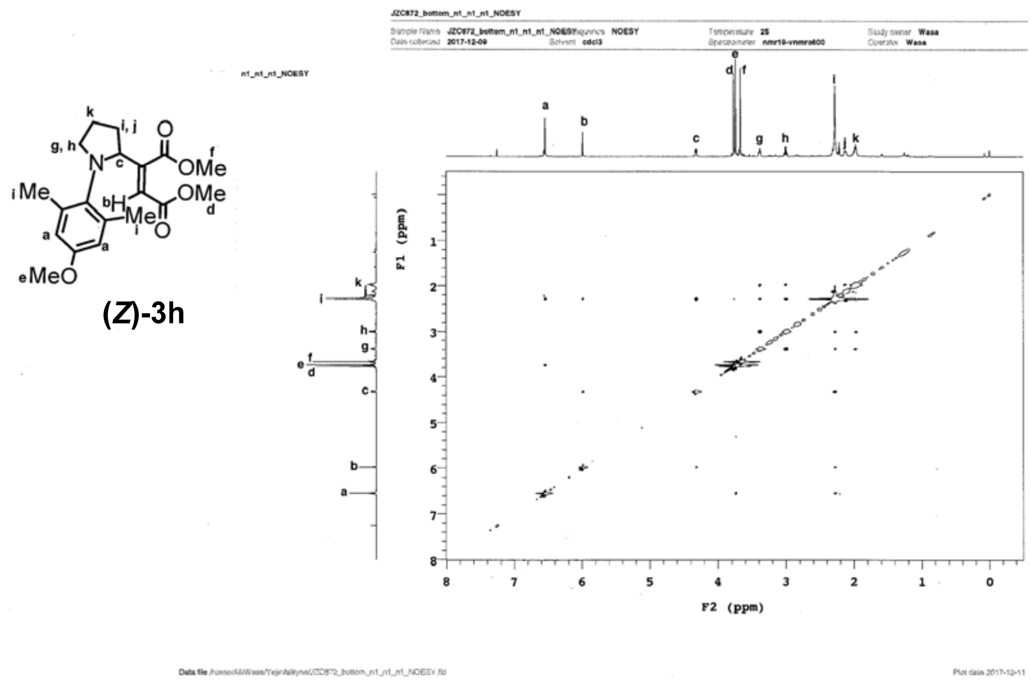


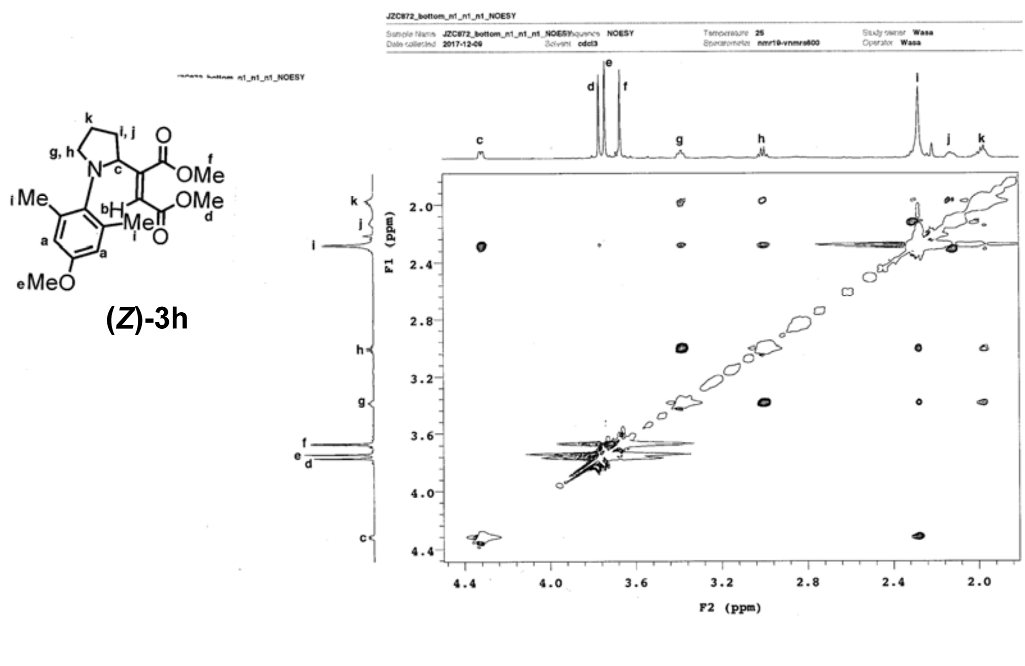
(*E*)-3h

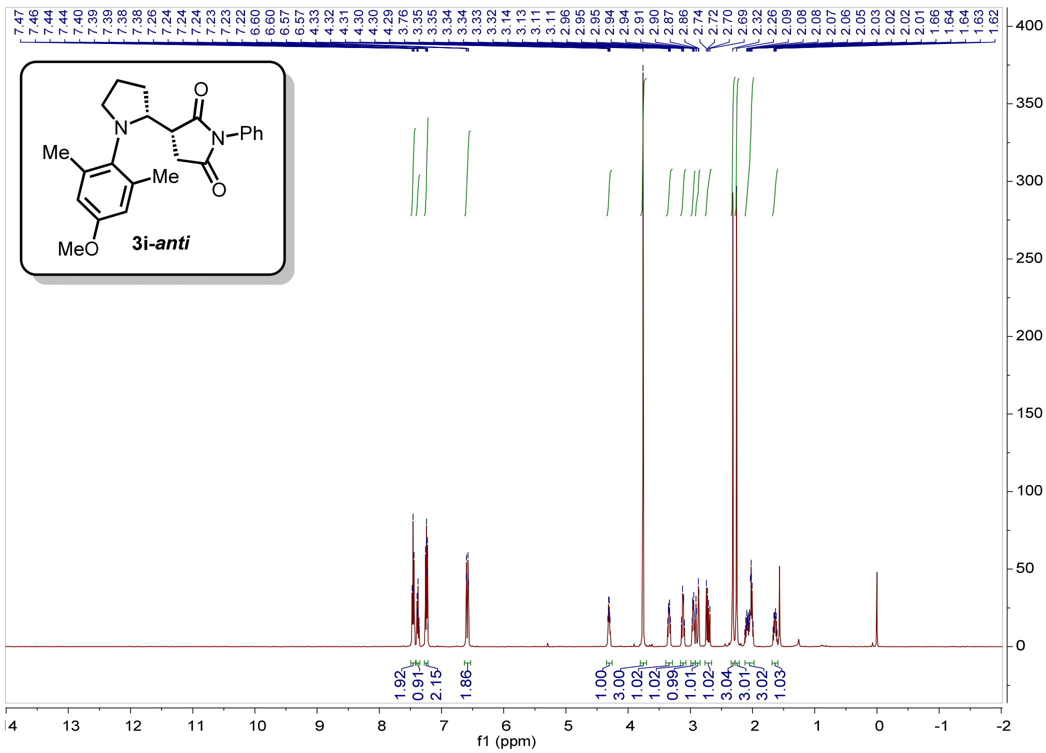

JZC872_top_n1_NOESY
Sample Name JZC872_top_n1_NOESY
Date collected 2017-12-05
Pulse sequence NOESY
Solvent cdcl3
Temperature 25
Spectrometer nmr19-vnmrs600
Study owner Wasa
Operator Wasa
F1 (ppm)
F2 (ppm)
Plot date 2017-12-06

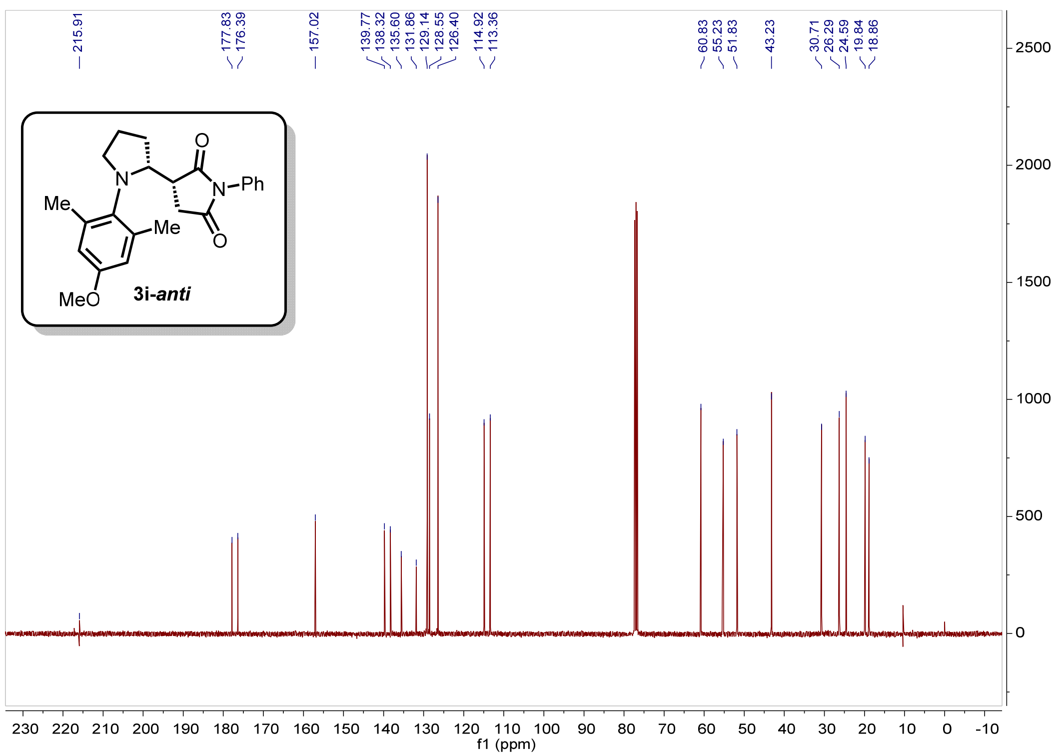

COOMe
N
COOMe
Me
Me
OMe
(Z)-3h
f1 (ppm)

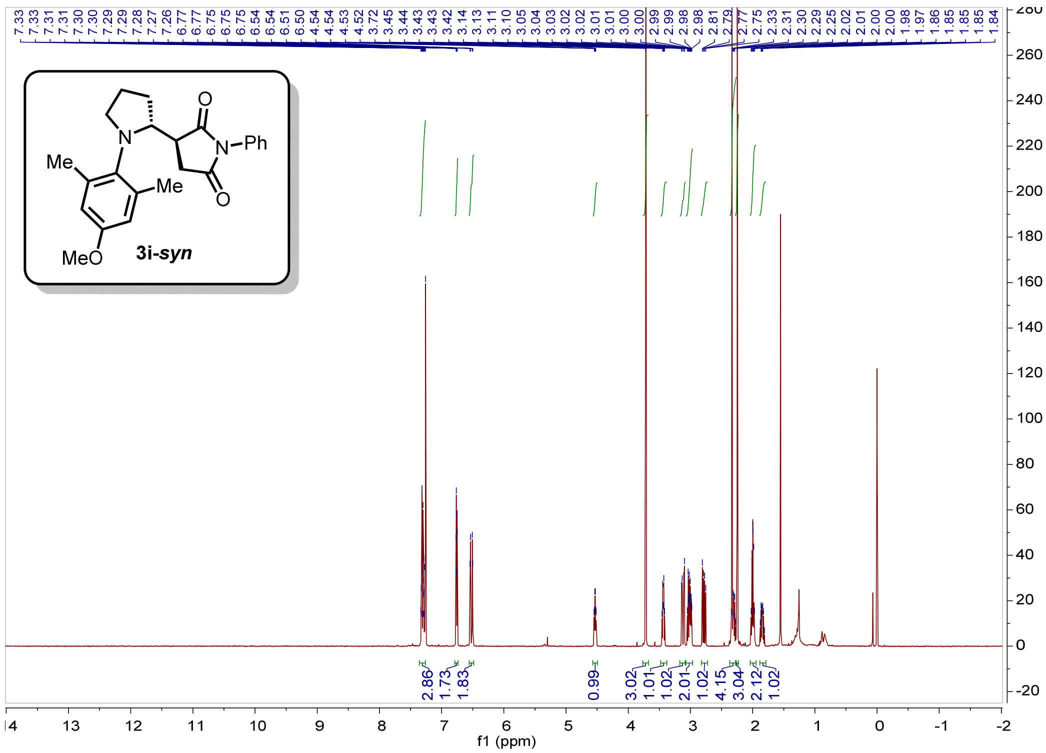

168.74
165.68
156.67
153.77
137.33
119.00
114.06
113.51
64.34
55.14
52.96
52.16
51.73
31.92
24.69
19.61
COOMe
N
COOMe
Me
Me
OMe
(Z)-3h
f1 (ppm)

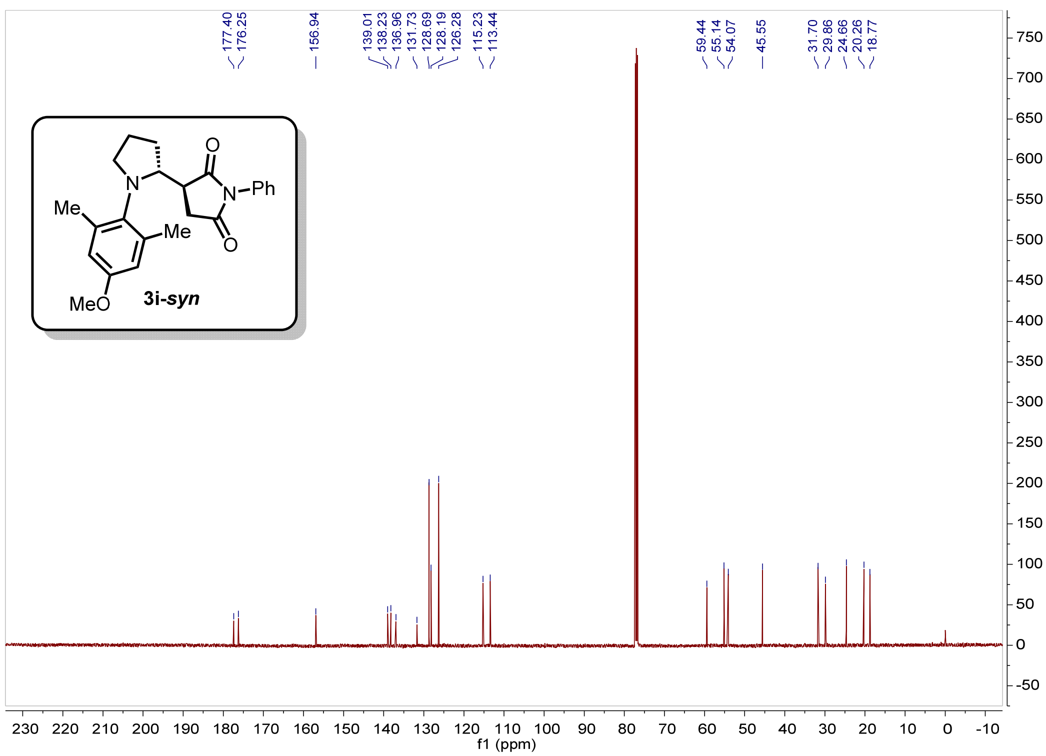









7.33 7.33 7.31 7.31 7.30 7.30 7.29 7.29 7.28 7.27 7.26 6.77 6.75 6.75 6.54 6.54 6.51 6.50 4.54 4.54 4.53 4.52 3.72 3.45 3.44 3.43 3.43 3.42 3.14 3.13 3.11 3.10 3.05 3.04 3.03 3.02 3.02 3.01 3.01 3.00 3.00 2.99 2.99 2.98 2.98 2.81 2.79 2.77 2.75 2.33 2.31 2.30 2.29 2.25 2.02 2.01 2.00 2.00 1.98 1.97 1.86 1.85 1.85 1.84
Me
Me
MeO
N
O
N–Ph
O
3i-syn
2.86
1.73
1.83
0.99
3.02
1.01
1.02
2.01
1.02
4.15
3.04
2.12
1.02
f1 (ppm)


177.40 176.25
156.94
139.01 138.23 136.96 131.73 128.69 128.19 126.28 115.23 113.44
59.44 55.14 54.07
45.55
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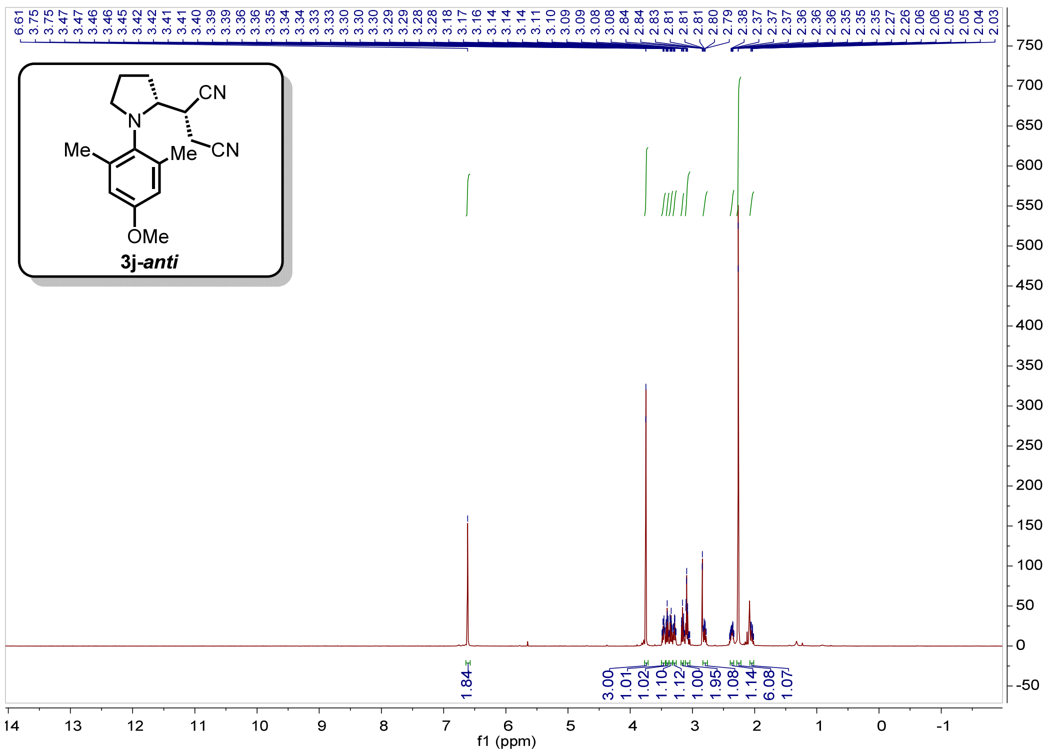
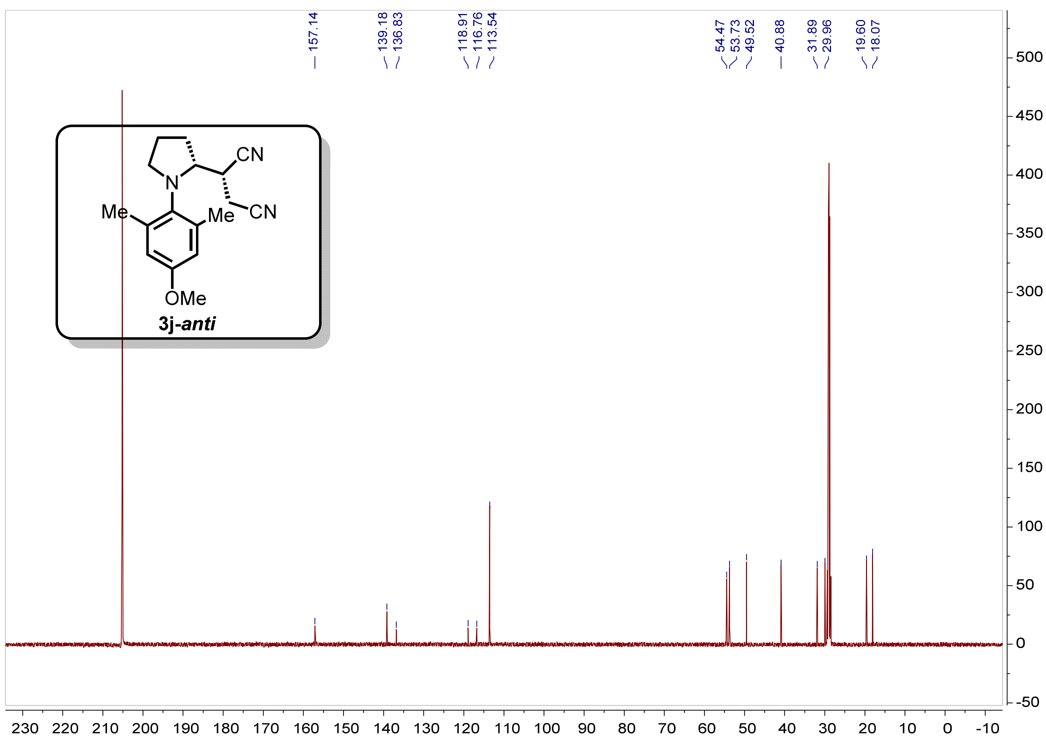
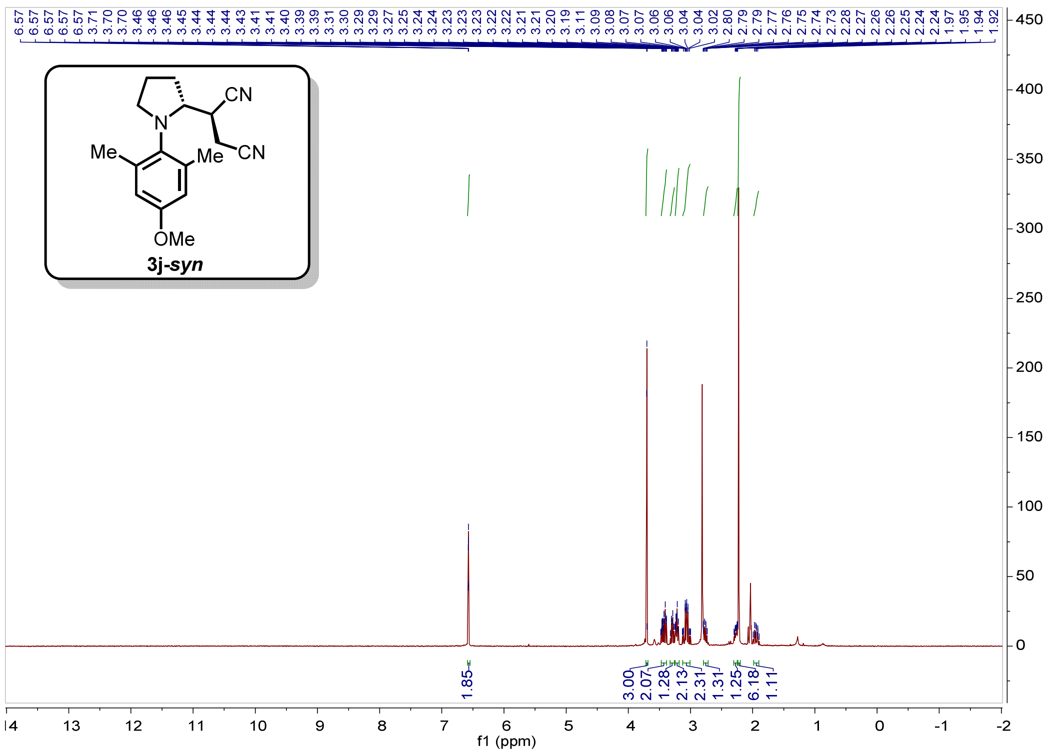
Me
MeO
N
O
N–Ph
O
3i-syn
f1 (ppm)



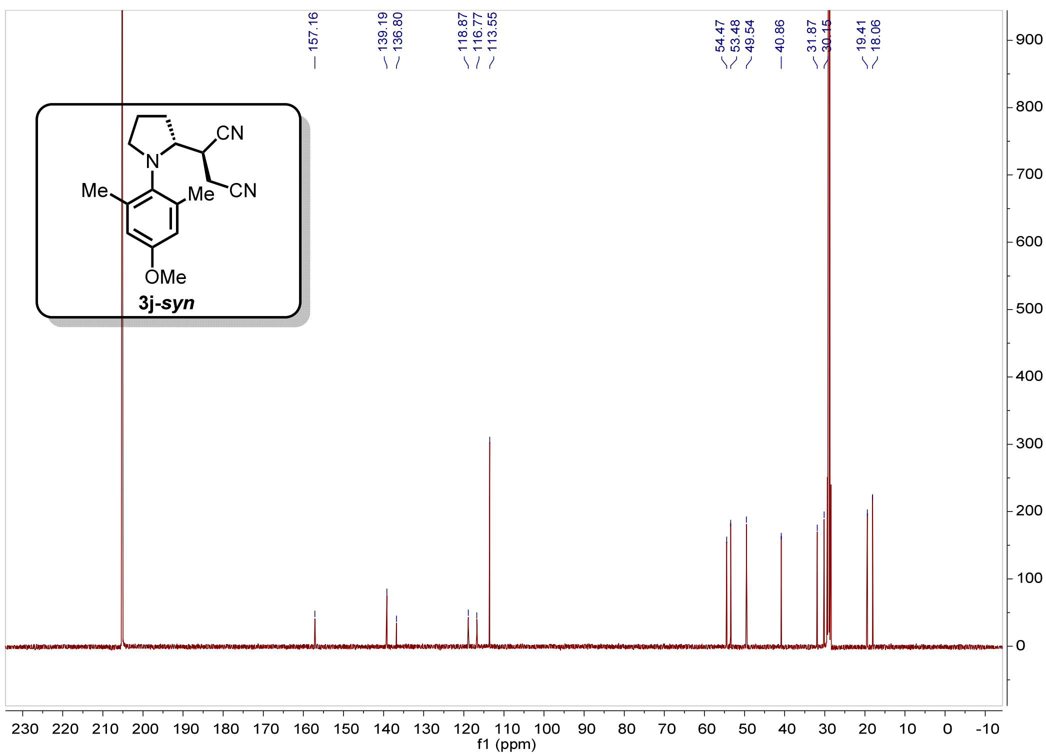
CN
N
CN
Me
Me
OMe
3j-*anti*
f1 (ppm)



157.14
139.18
136.83
118.91
116.76
113.54
54.47
53.73
49.52
40.88
31.89
29.96
19.60
18.07
CN
N
CN
Me
Me
OMe
3j-*anti*
f1 (ppm)



CN
N
Me
Me
CN
OMe
3j-*syn*



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113.55
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53.48
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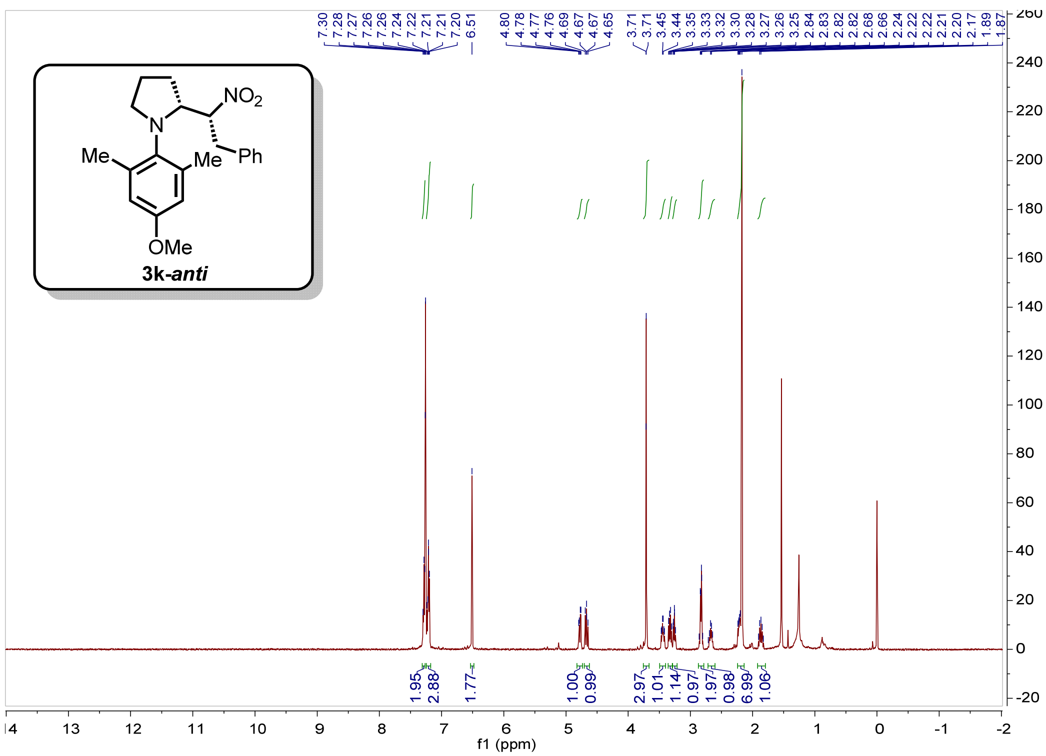
30.15
19.41
18.06
CN
N
Me
Me
CN
OMe
3j-*syn*
f1 (ppm)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7.27
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7.26
7.24
7.22
7.21
7.21
7.20
6.51
4.80
4.78
4.77
4.76
4.69
4.67
4.67
4.65
3.71
3.71
3.45
3.44
3.35
3.33
3.32
3.30
3.28
3.27
3.26
3.25
2.84
2.83
2.82
2.82
2.68
2.66
2.24
2.22
2.22
2.21
2.20
2.17
1.89
1.87
NO2
N
Me
Me
Ph
OMe
3k-anti
1.95
2.88
1.77
1.00
0.99
2.97
1.01
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0.97
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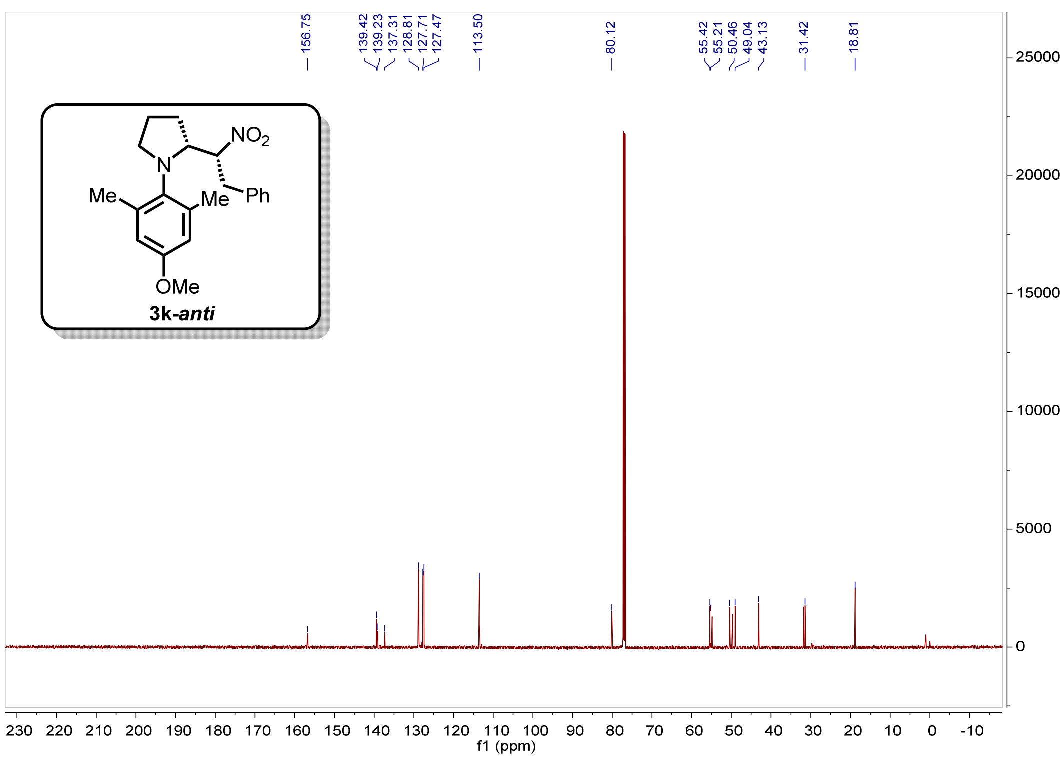
0.98
6.99
1.06
f1 (ppm)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127.71
127.47
113.50
80.12
55.42
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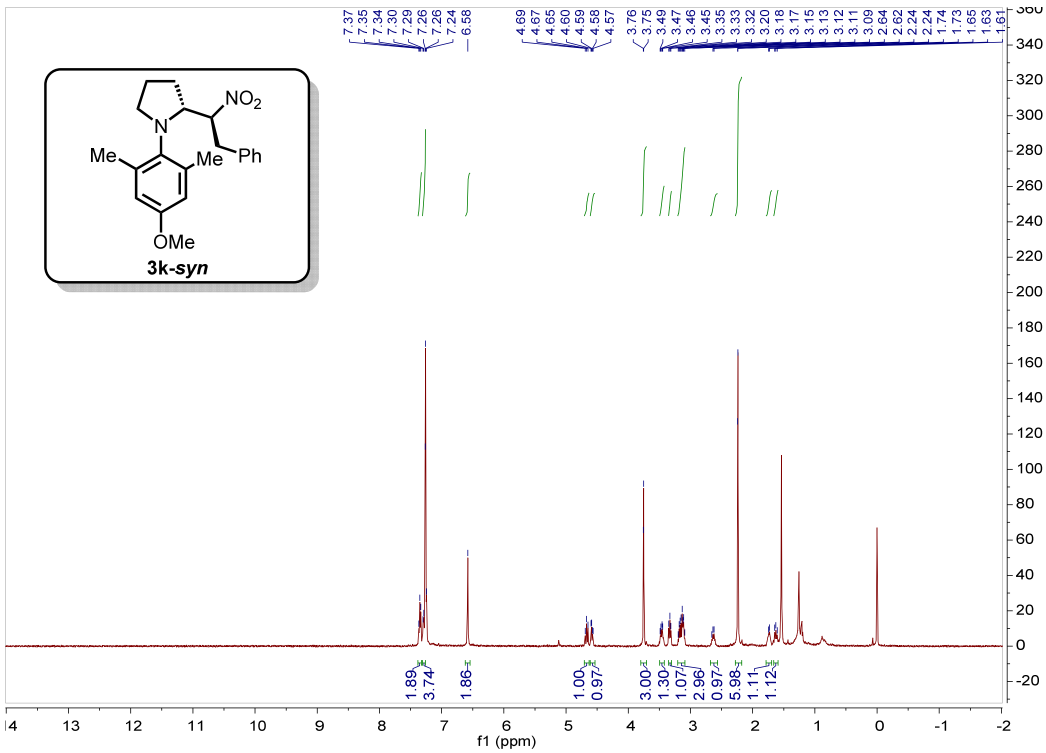
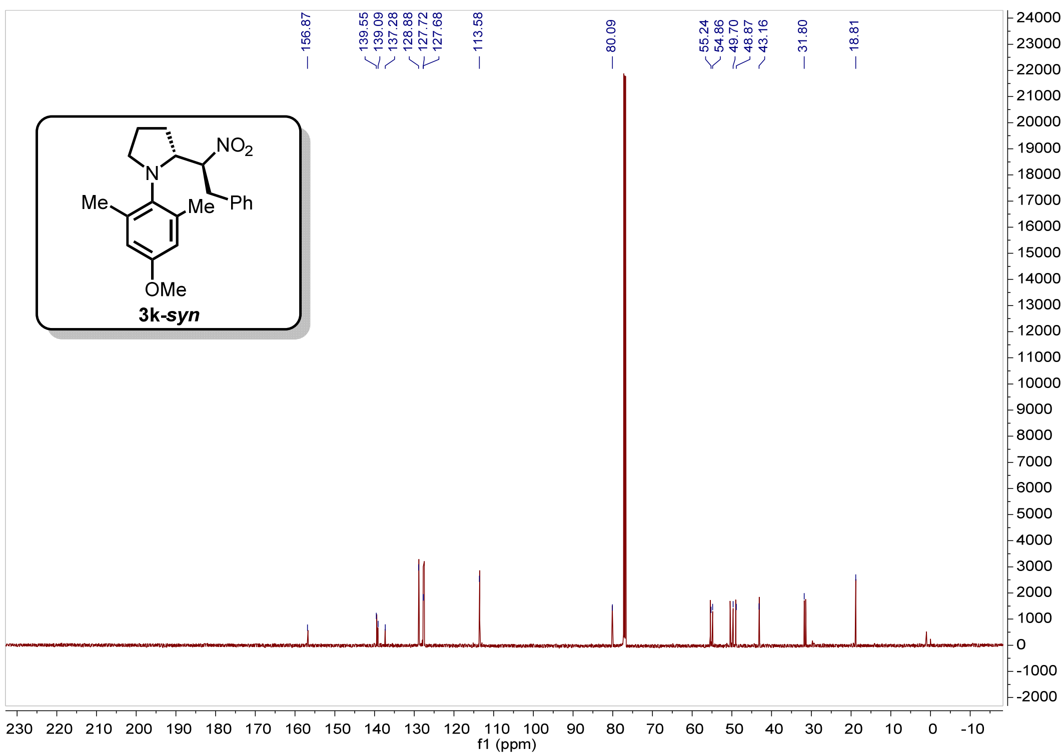
43.13
31.42
18.81
NO2
N
Me
Me
Ph
OMe
3k-anti
f1 (ppm)


NO2
N
Me
Me
Ph
OMe
3k-syn
f1 (ppm)


NO2
N
Me
Me
Ph
OMe
3k-syn
156.87
139.55
139.09
137.28
128.88
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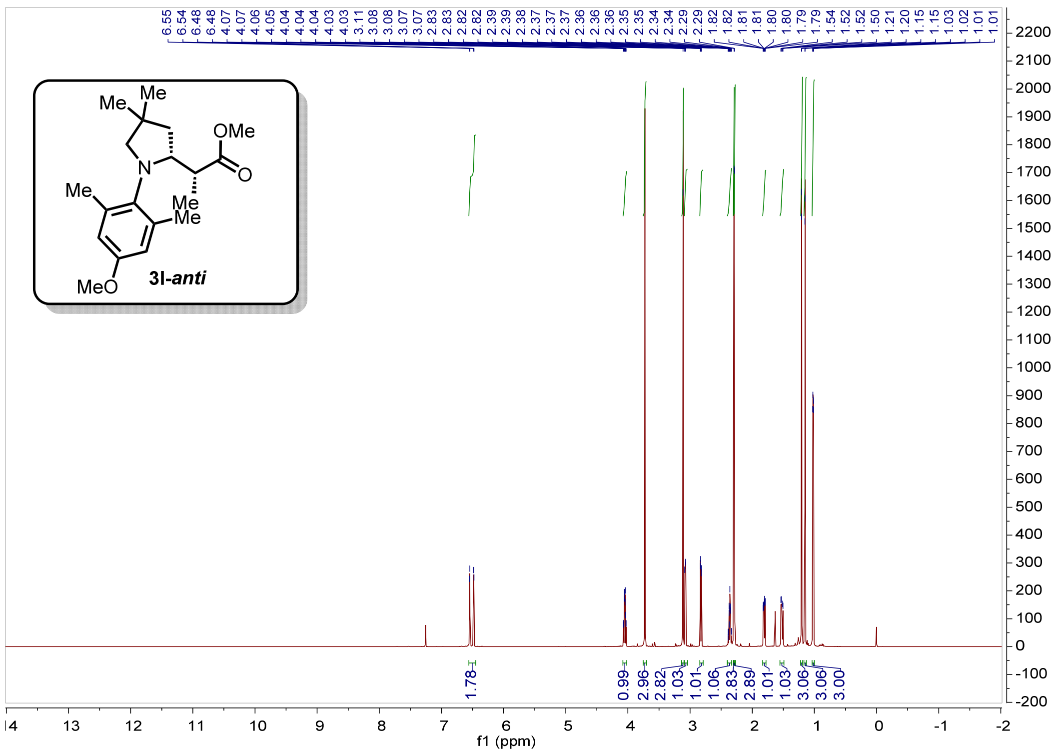
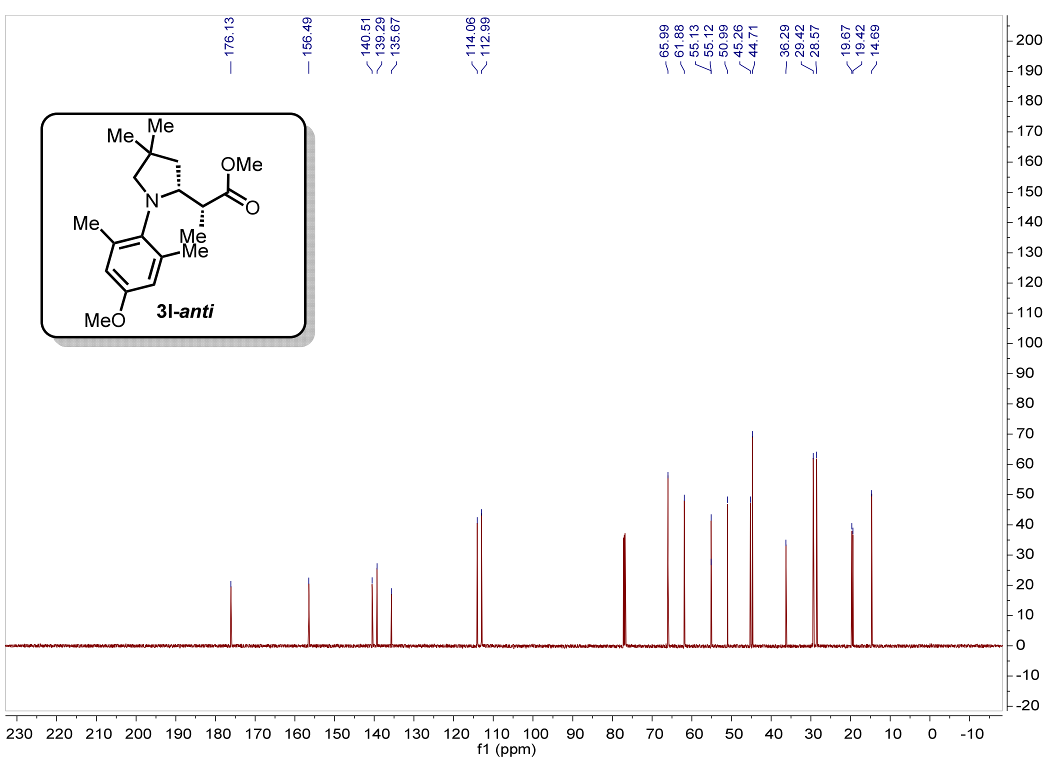
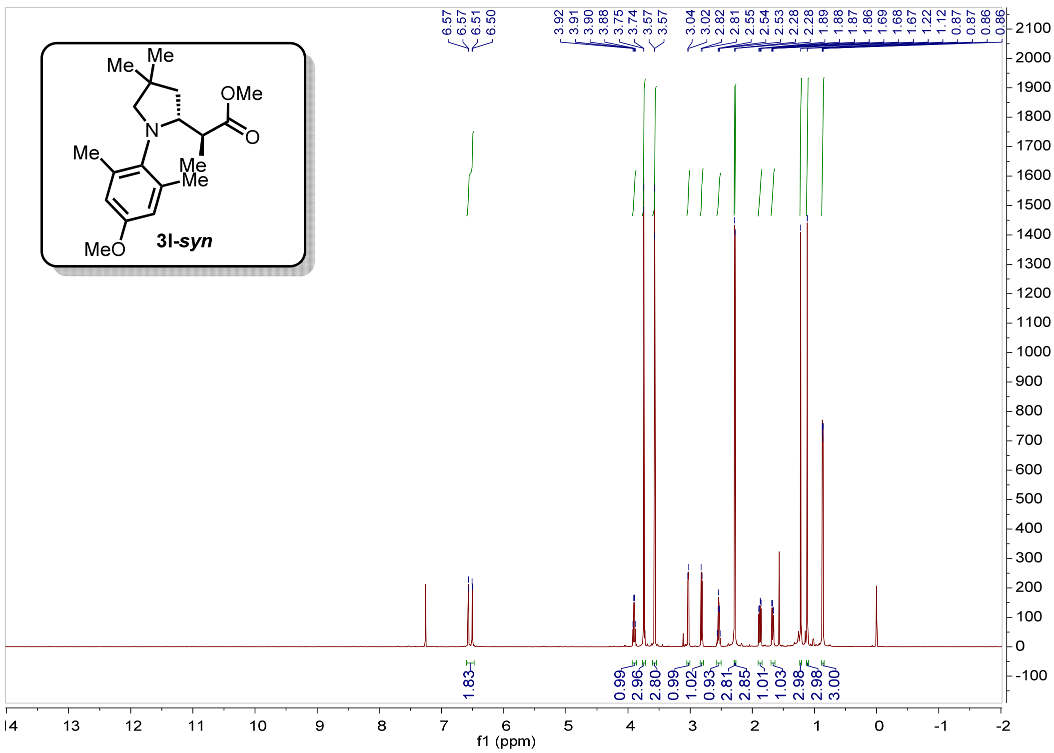
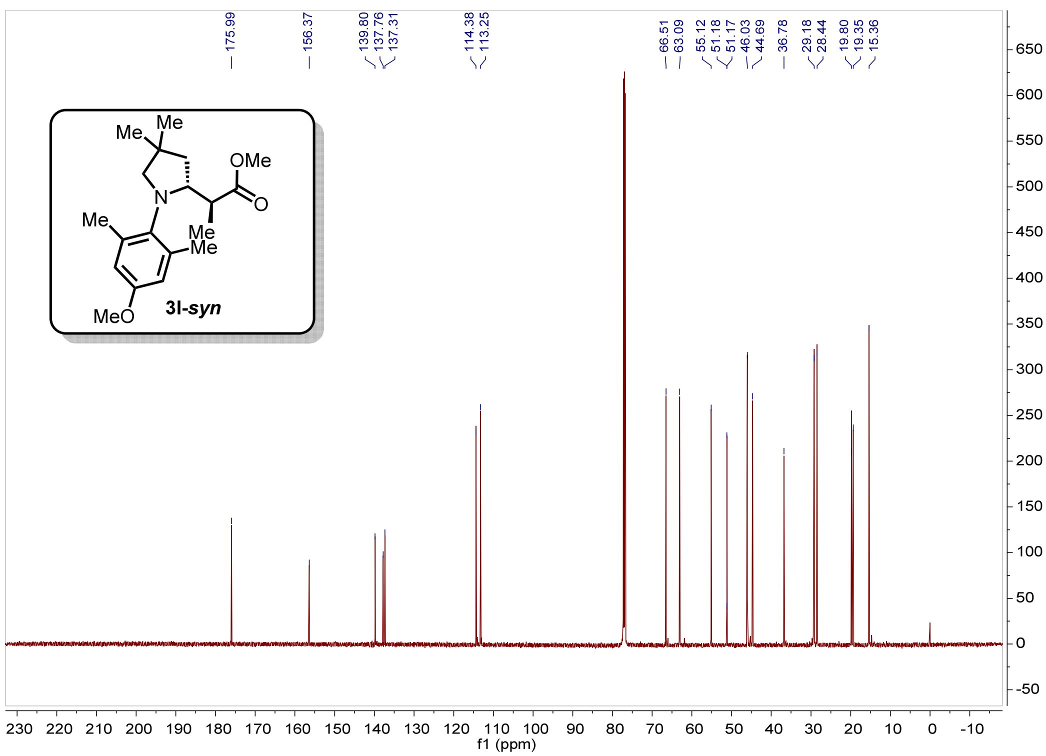
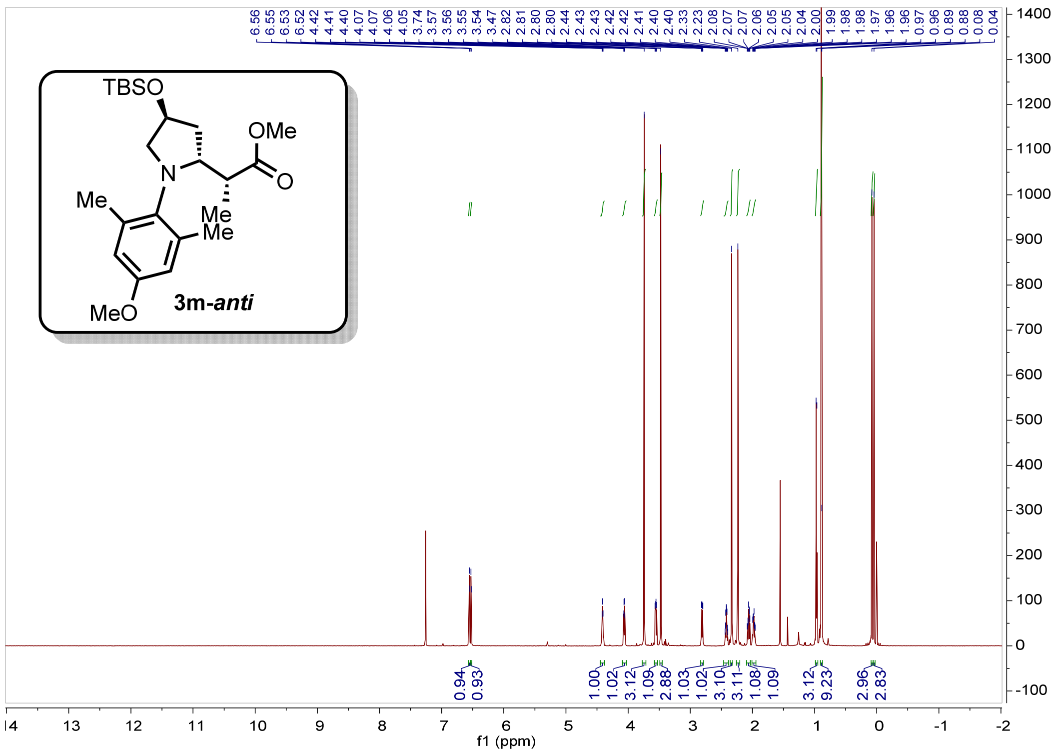
80.09
55.24
54.86
49.70
48.87
43.16
31.80
18.81
f1 (ppm)

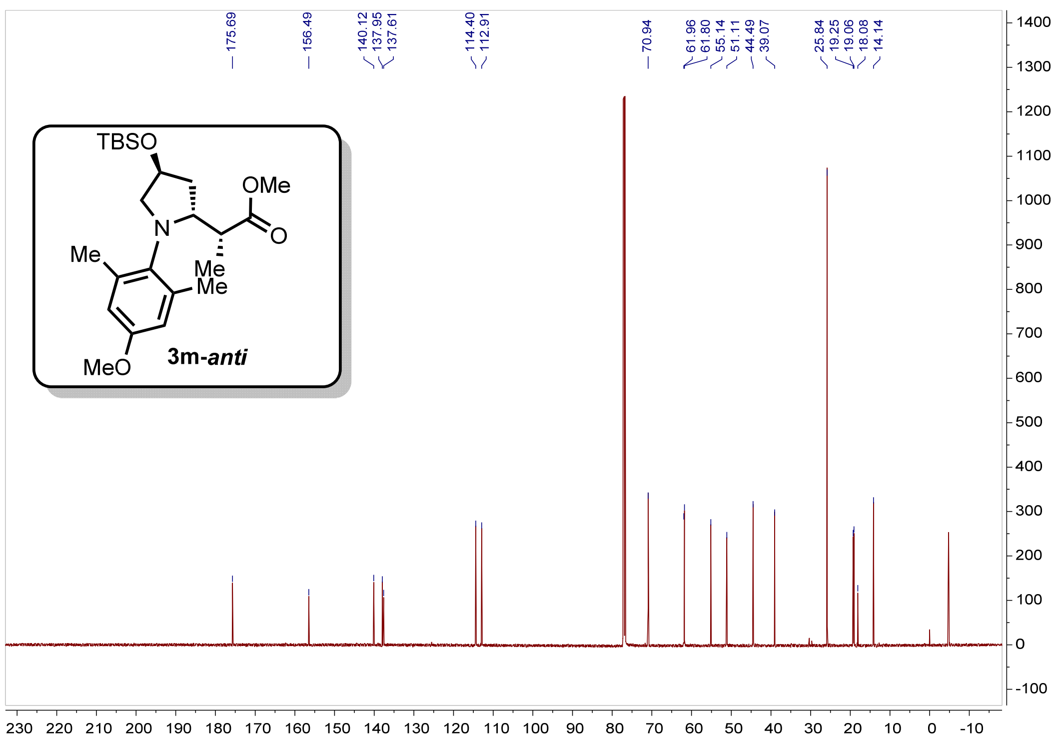









TBSO
OMe
N
O
Me
Me
Me
MeO
3m-anti
f1 (ppm)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70.94
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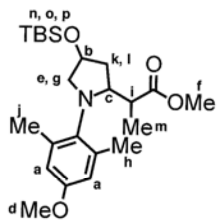
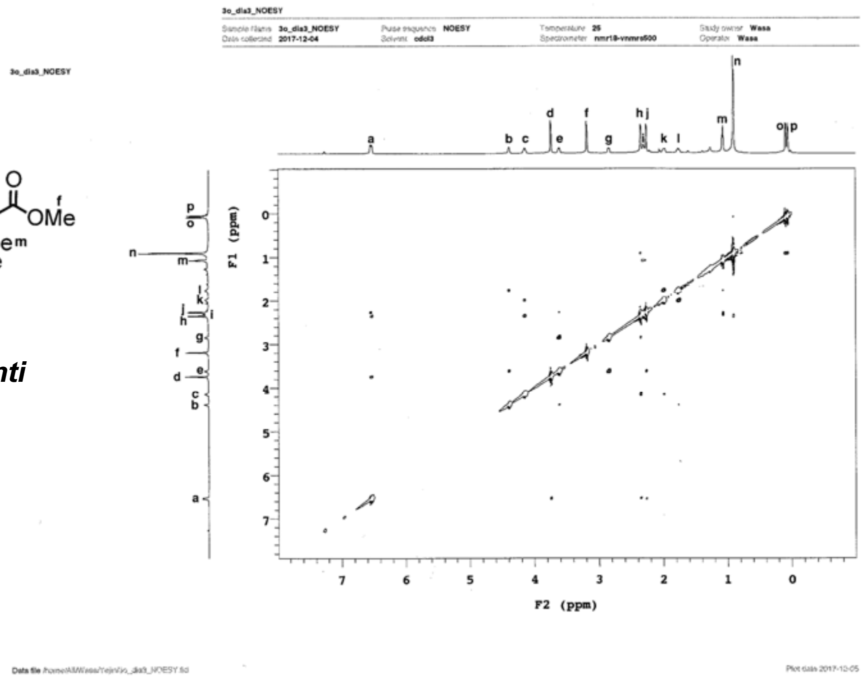
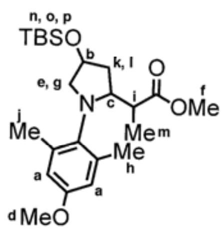
55.14
51.11
44.49
39.07
25.84
19.25
19.06
18.08
14.14
TBSO
OMe
N
O
Me
Me
Me
MeO
3m-anti
f1 (ppm)

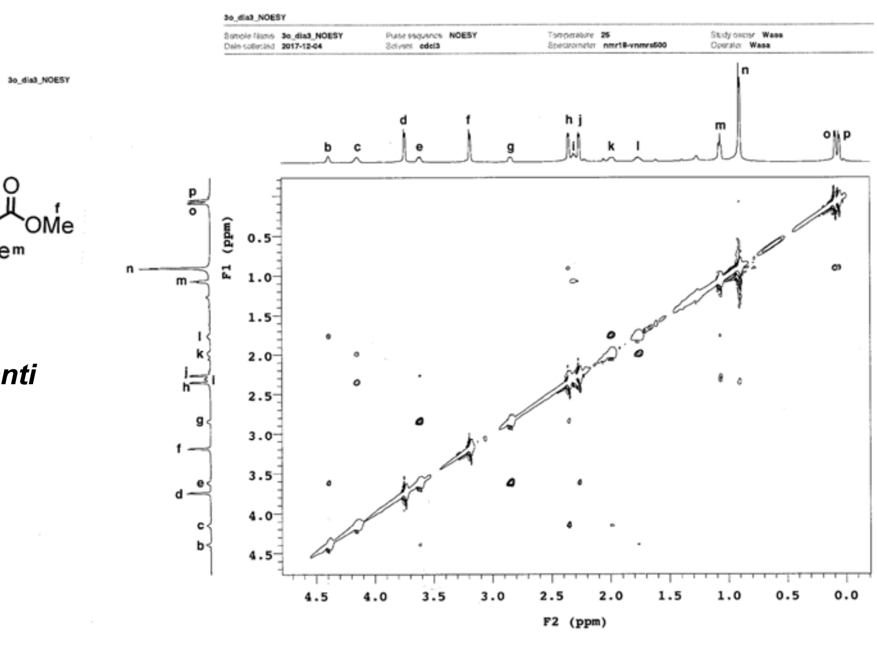


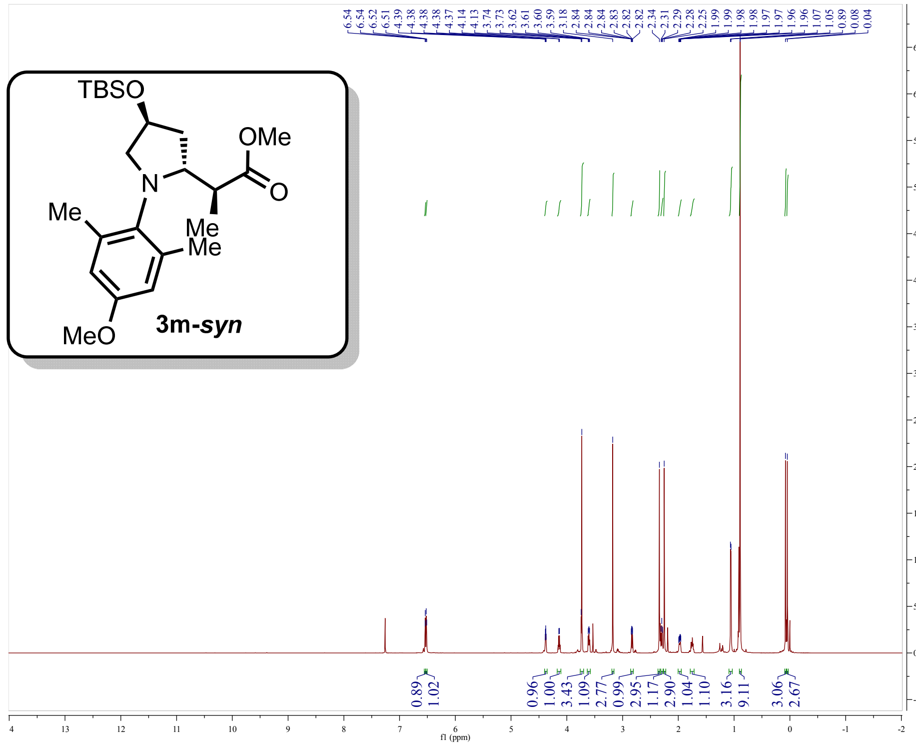
3m-*anti*

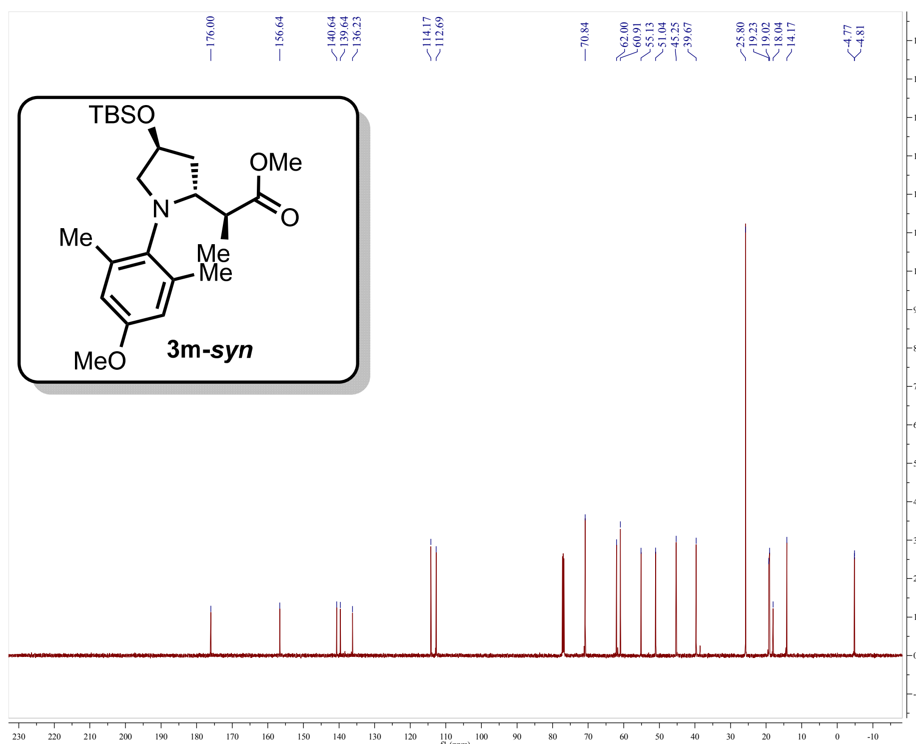


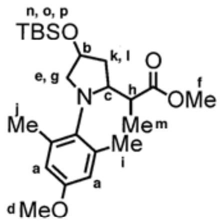


3m-*anti*

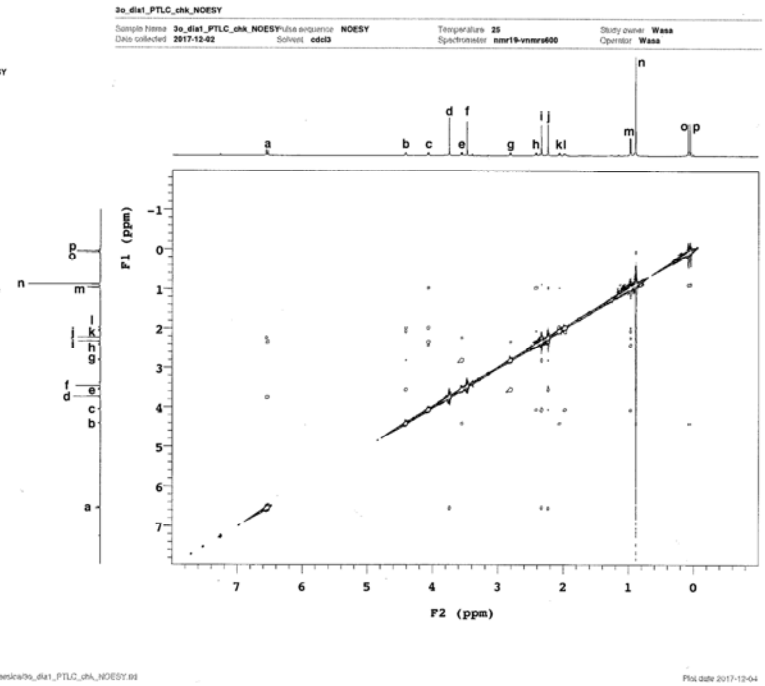


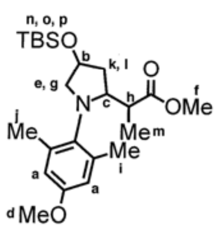

TBSO
OMe
N
O
Me
Me
Me
MeO
3m-syn
f1 (ppm)


TBSO
OMe
N
O
Me
Me
Me
MeO
3m-syn
f1 (ppm)


n, o, p
TBSO
b
k, l
e, g
N
c
h
OMe
f
Me
j
Me
m
Me
i
a
a
d MeO

3m-*syn*


3o_dia1_PTLC_chk_NOESY
Pulse sequence NOESY
Date collected 2017-12-02
Solvent cdcl3
Temperature 25
Spectrometer nmr19-vnmrs600
Study owner Wasa
Operator Wasa
F1 (ppm)
F2 (ppm)
Plot date 2017-12-04


n, o, p
TBSO
b
k, l
e, g
N
c
h
OMe
f
Me
j
Me
m
Me
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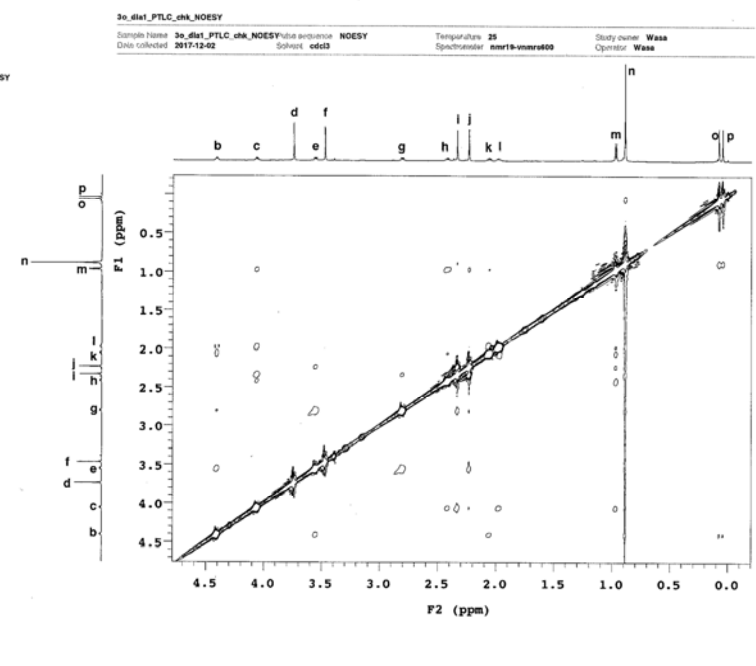
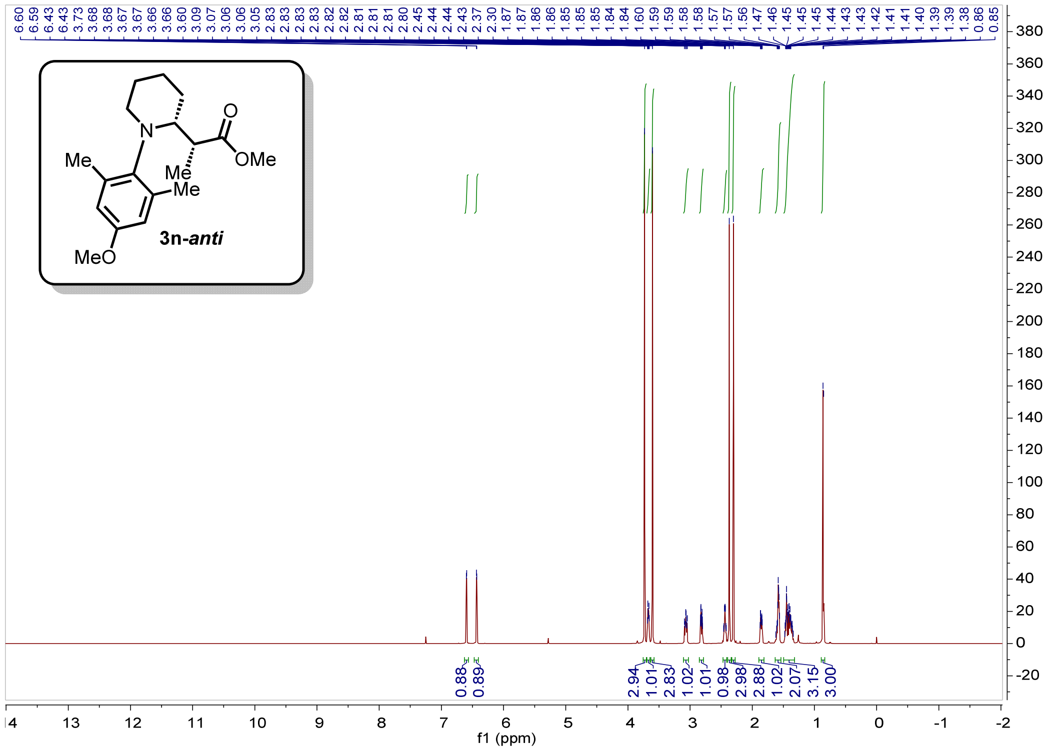
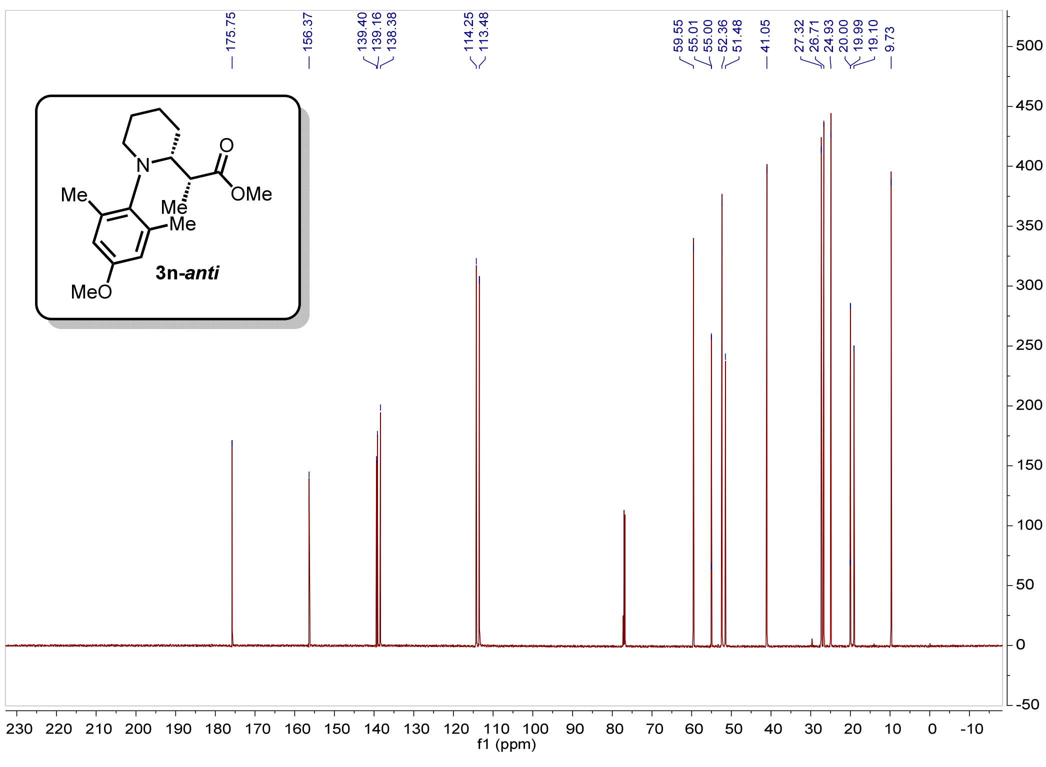
a
d MeO

3m-*syn*


3o_dia1_PTLC_chk_NOESY
Pulse sequence NOESY
Date collected 2017-12-02
Solvent cdcl3
Temperature 25
Spectrometer nmr19-vnmrs600
Study owner Wasa
Operator Wasa
F1 (ppm)
F2 (ppm)
Plot date 2017-12-04


3n-anti
f1 (ppm)


3n-anti
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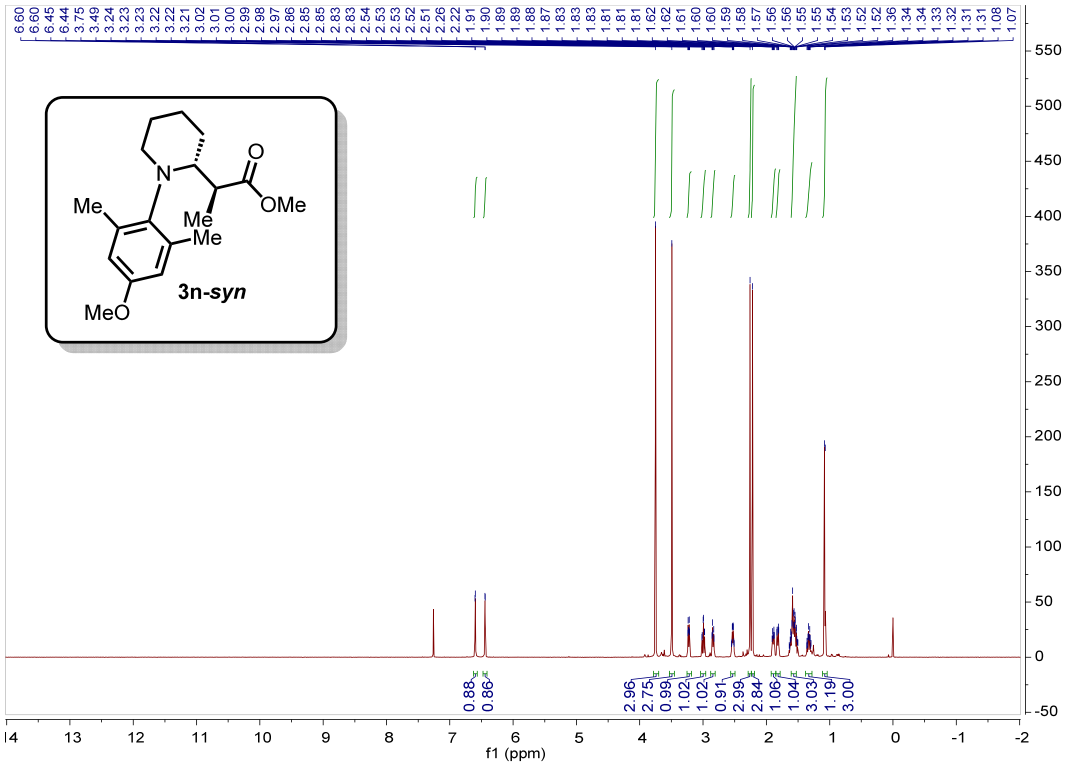
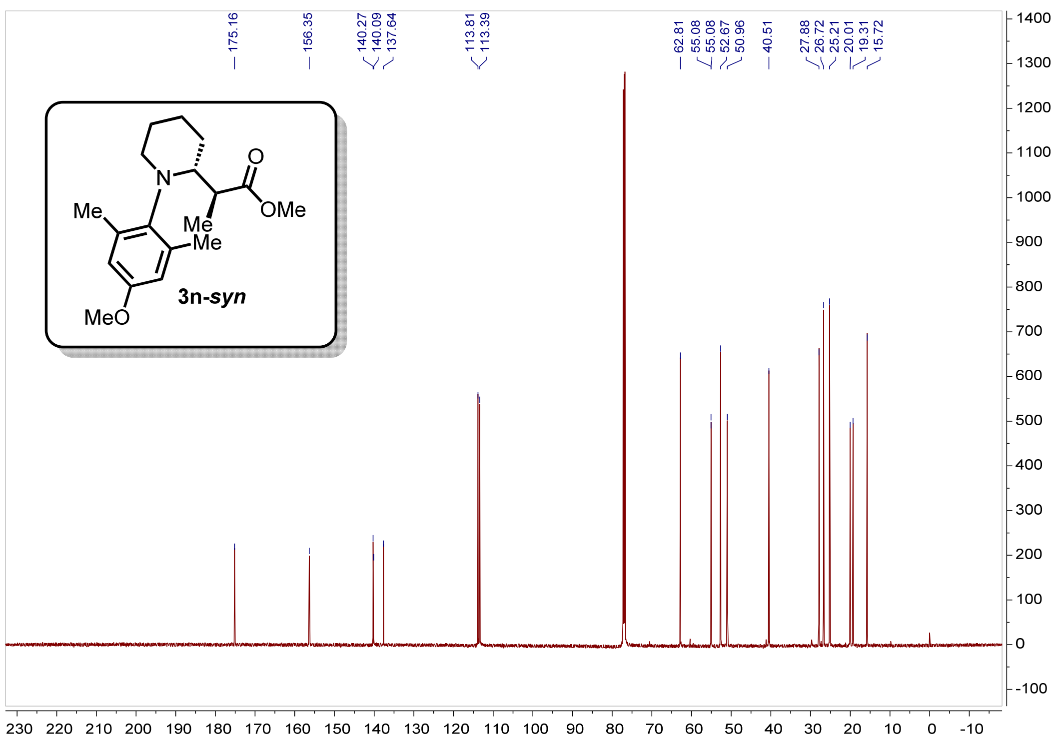
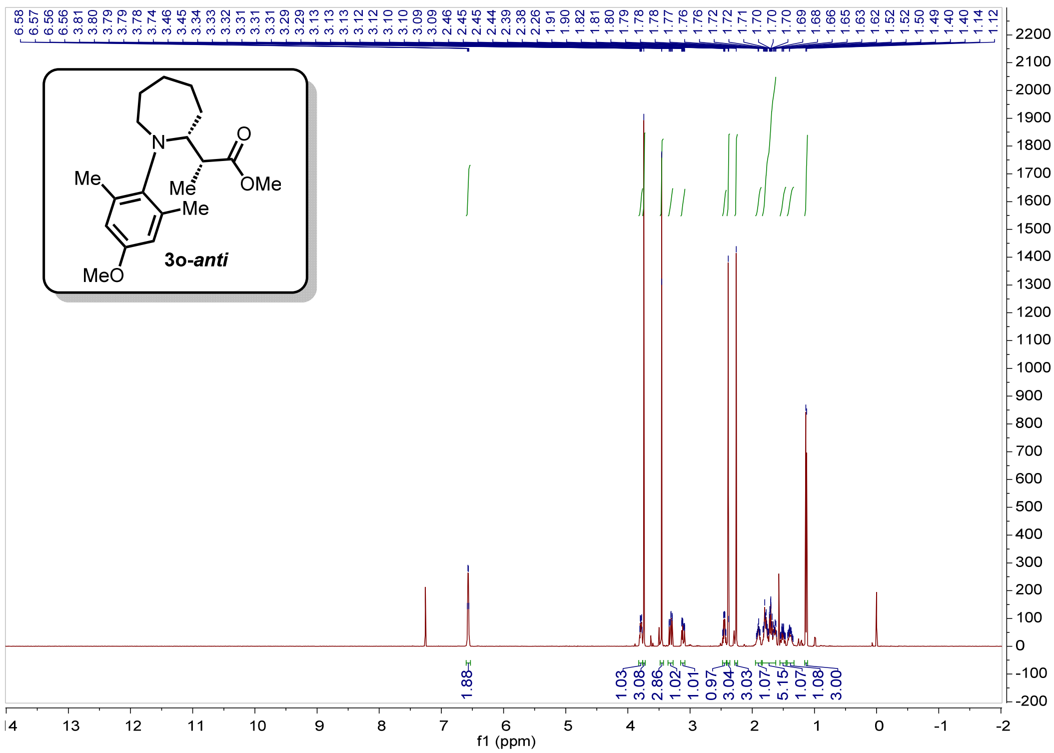
156.37
139.40
139.16
138.38
114.25
113.48
59.55
55.01
55.00
52.36
51.48
41.05
27.32
26.71
24.93
20.00
19.99
19.10
9.73
f1 (ppm)



6.60 6.60 6.45 6.44 3.75 3.49 3.24 3.23 3.23 3.22 3.22 3.21 3.02 3.01 3.00 2.99 2.98 2.97 2.86 2.85 2.83 2.83 2.54 2.53 2.53 2.52 2.51 2.26 2.22 1.91 1.90 1.89 1.88 1.87 1.83 1.83 1.81 1.81 1.81 1.62 1.62 1.61 1.60 1.60 1.59 1.58 1.57 1.56 1.56 1.55 1.55 1.54 1.53 1.52 1.52 1.36 1.34 1.34 1.33 1.32 1.31 1.08 1.07
Me
N
O
OMe
Me
Me
MeO
3n-*syn*
0.88 0.86 2.96 2.75 0.99 1.02 1.02 0.91 2.99 2.84 1.06 1.04 3.03 1.19 3.00
f1 (ppm)



175.16 156.35 140.27 140.09 137.64 113.81 113.39 62.81 55.08 55.08 52.67 50.96 40.51 27.88 26.72 25.21 20.01 19.31 15.72
Me
N
O
OMe
Me
Me
MeO
3n-*syn*
f1 (ppm)



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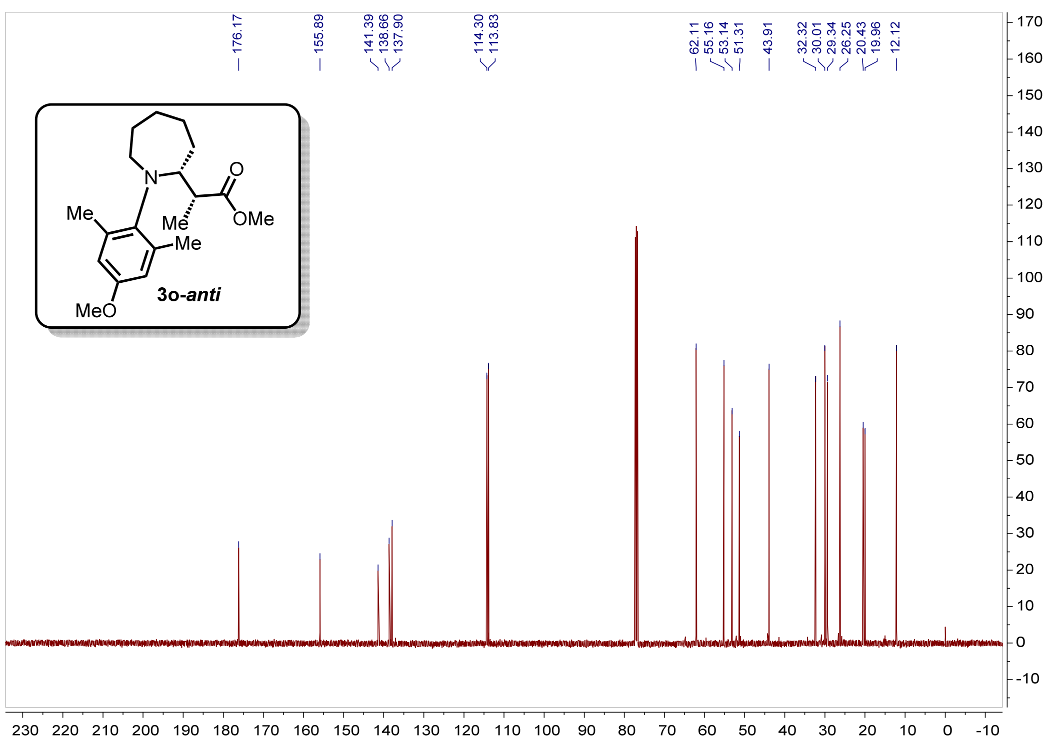
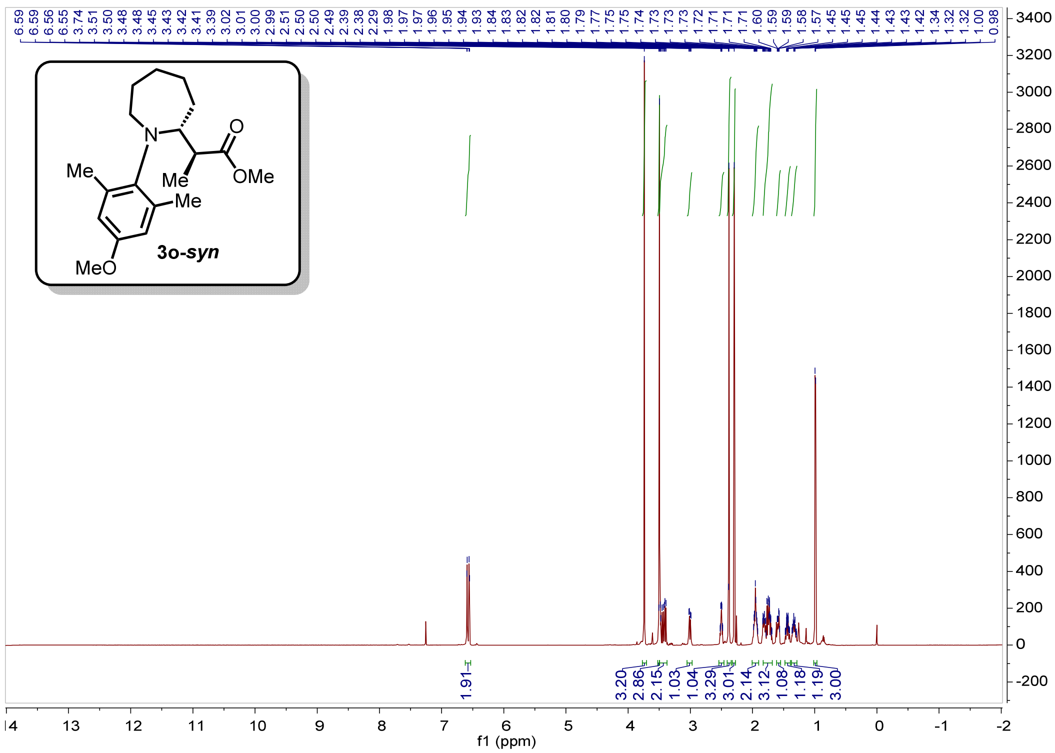
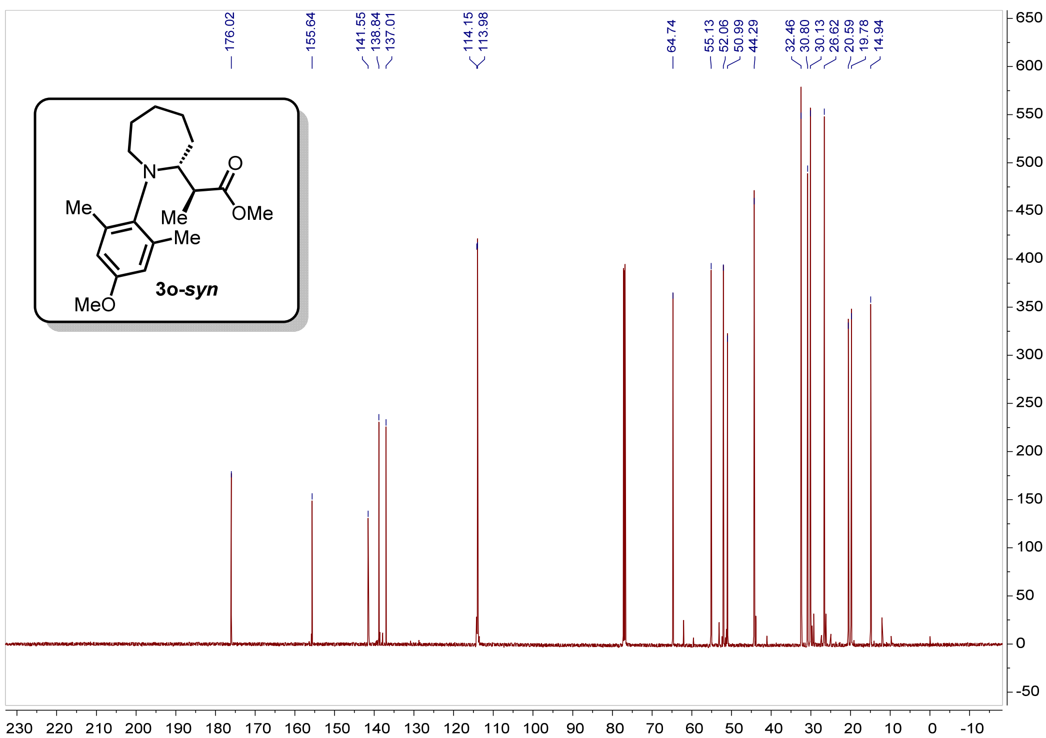
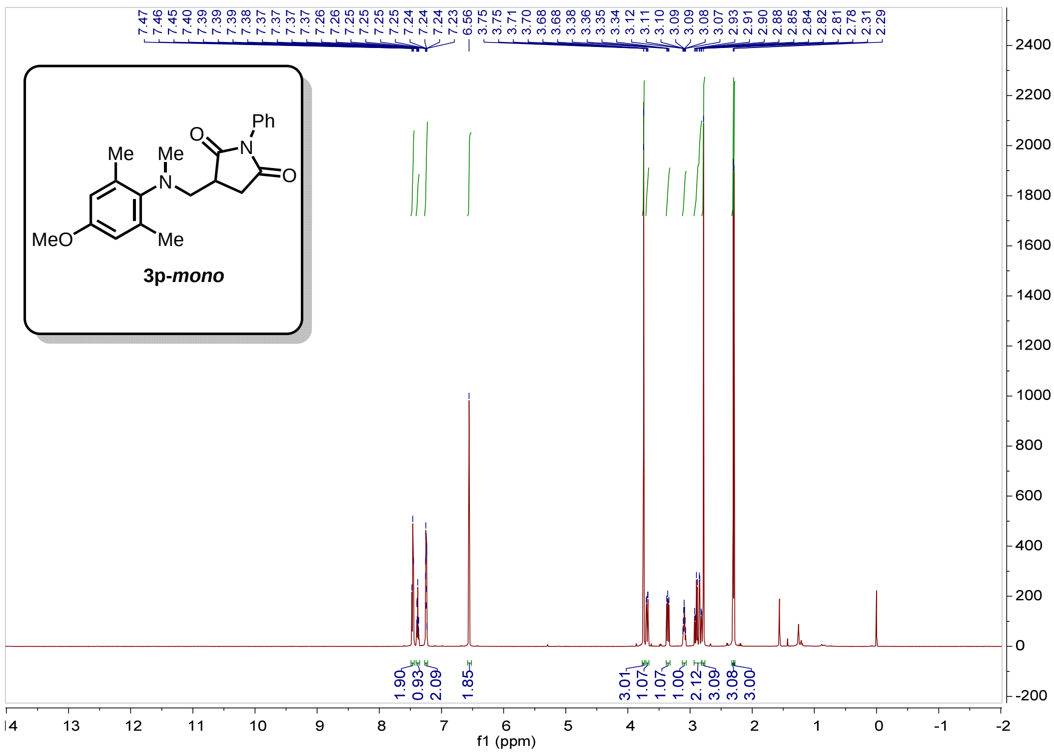
6.57
6.56
6.56
3.81
3.80
3.79
3.79
3.78
3.74
3.46
3.45
3.34
3.33
3.32
3.31
3.31
3.31
3.29
3.13
3.13
3.13
3.12
3.10
3.10
3.09
3.09
2.46
2.45
2.45
2.44
2.39
2.38
2.26
1.91
1.90
1.82
1.81
1.80
1.79
1.78
1.78
1.77
1.76
1.76
1.72
1.72
1.71
1.70
1.70
1.70
1.69
1.68
1.66
1.65
1.63
1.62
1.52
1.50
1.49
1.40
1.14
1.12
Me
Me
OMe
N
O
Me
MeO
3o-anti
1.88
1.03
3.08
2.86
1.02
1.01
0.97
3.04
3.03
1.07
5.15
1.07
1.08
3.00
f1 (ppm)



176.17
155.89
141.39
138.66
137.90
114.30
113.83
62.11
55.16
53.14
51.31
43.91
32.32
30.01
29.34
26.25
20.43
19.96
12.12
Me
Me
OMe
N
O
Me
MeO
3o-anti
f1 (ppm)


3o-syn
f1 (ppm)


3o-syn
f1 (ppm)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7.39
7.39
7.38
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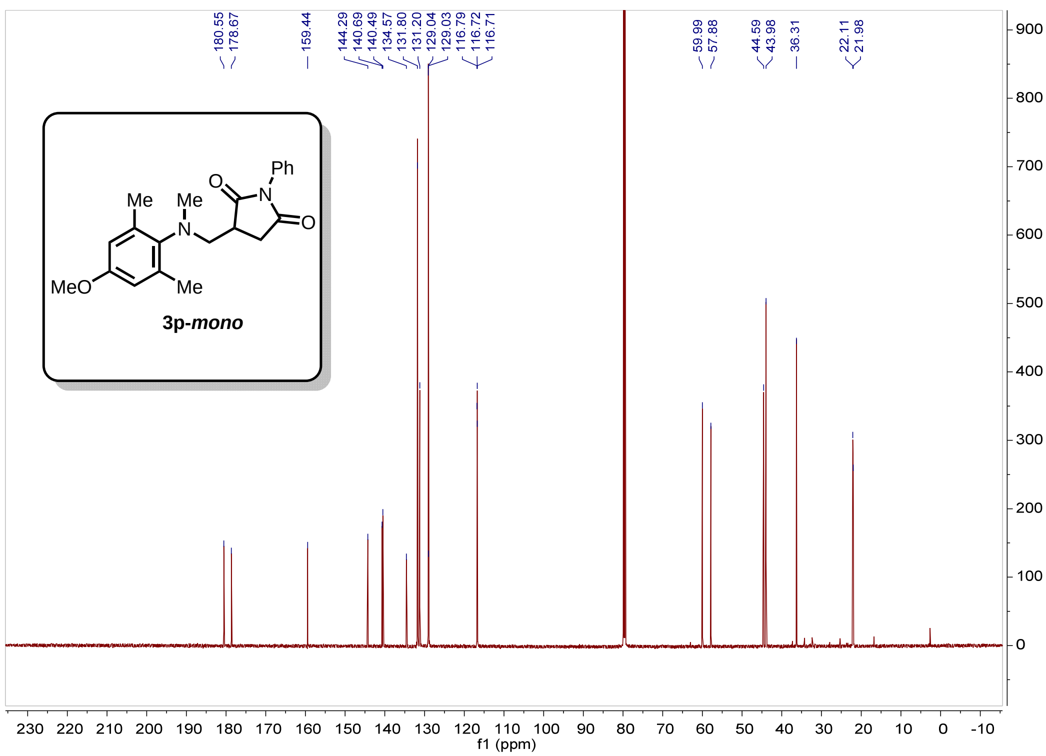
7.26
7.25
7.25
7.25
7.25
7.24
7.24
7.24
7.23
6.56
3.75
3.75
3.71
3.70
3.68
3.68
3.38
3.36
3.35
3.34
3.12
3.11
3.10
3.09
3.09
3.08
3.07
2.93
2.91
2.90
2.88
2.85
2.84
2.82
2.81
2.78
2.31
2.29
Ph
O
N
O
Me
Me
N
MeO
Me
3p-*mono*
1.90
0.93
2.09
1.85
3.01
1.07
1.07
1.00
2.12
3.09
3.08
3.00
f1 (ppm)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159.44
144.29
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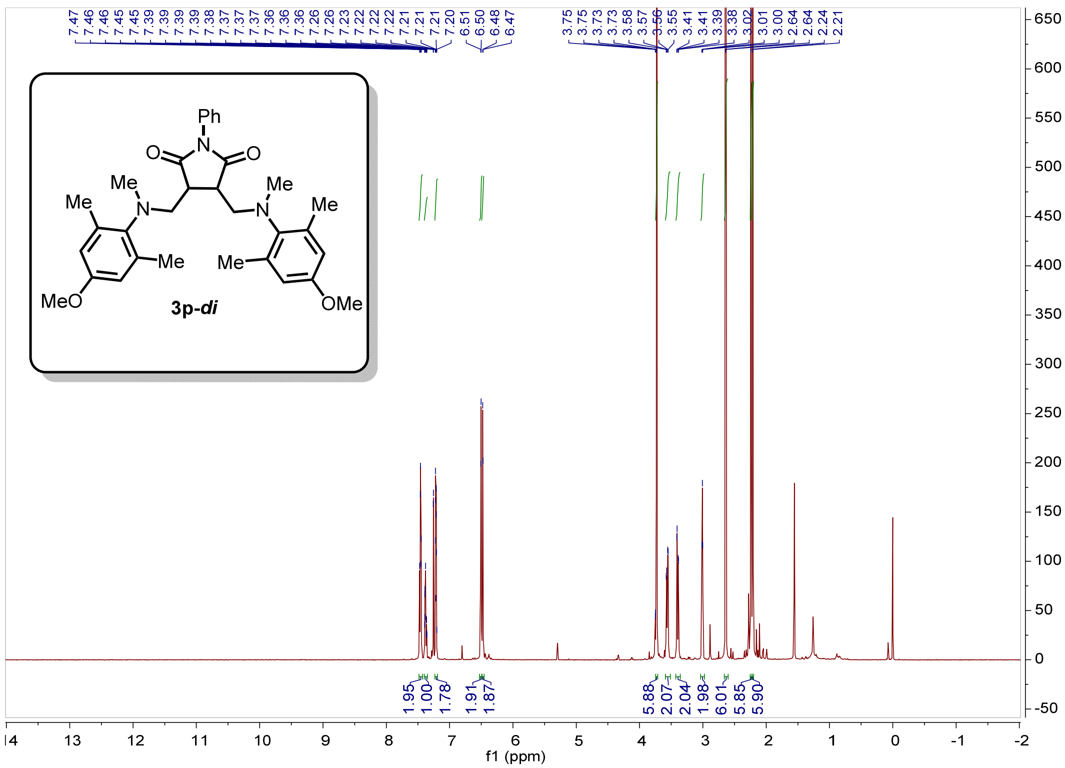
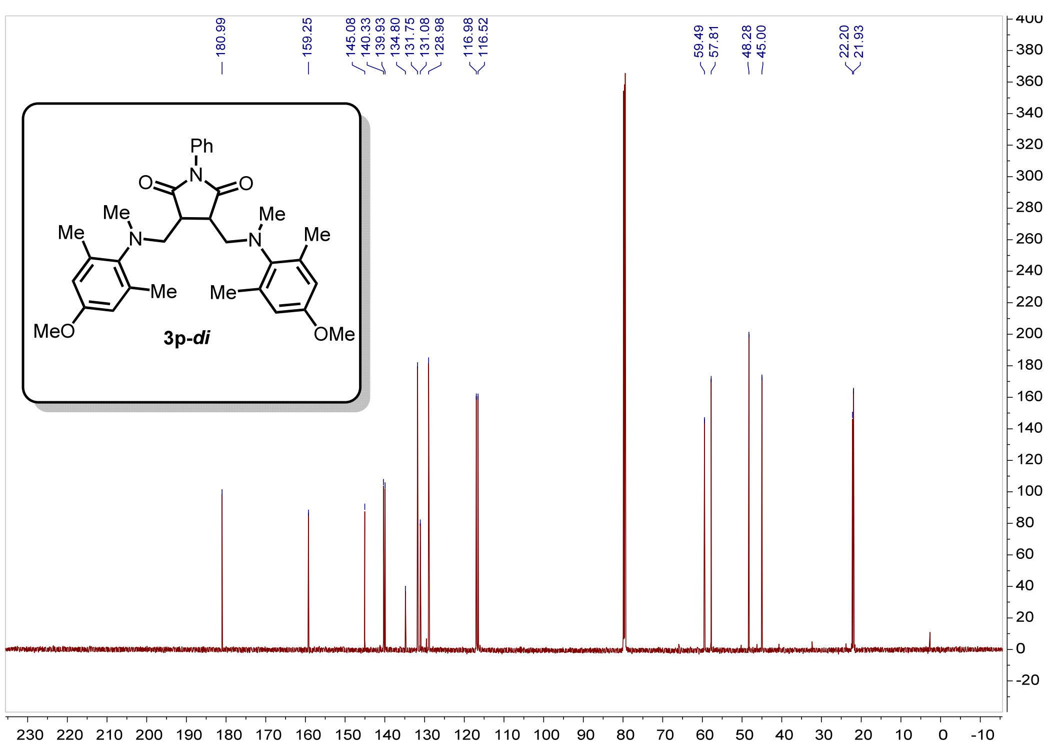
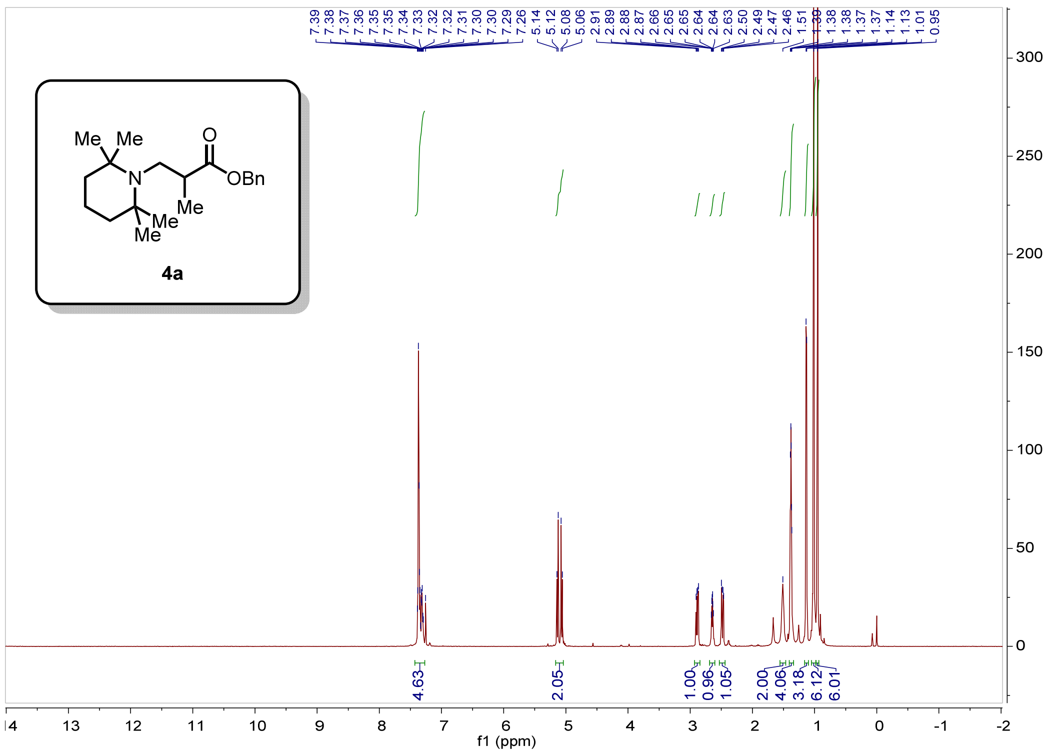
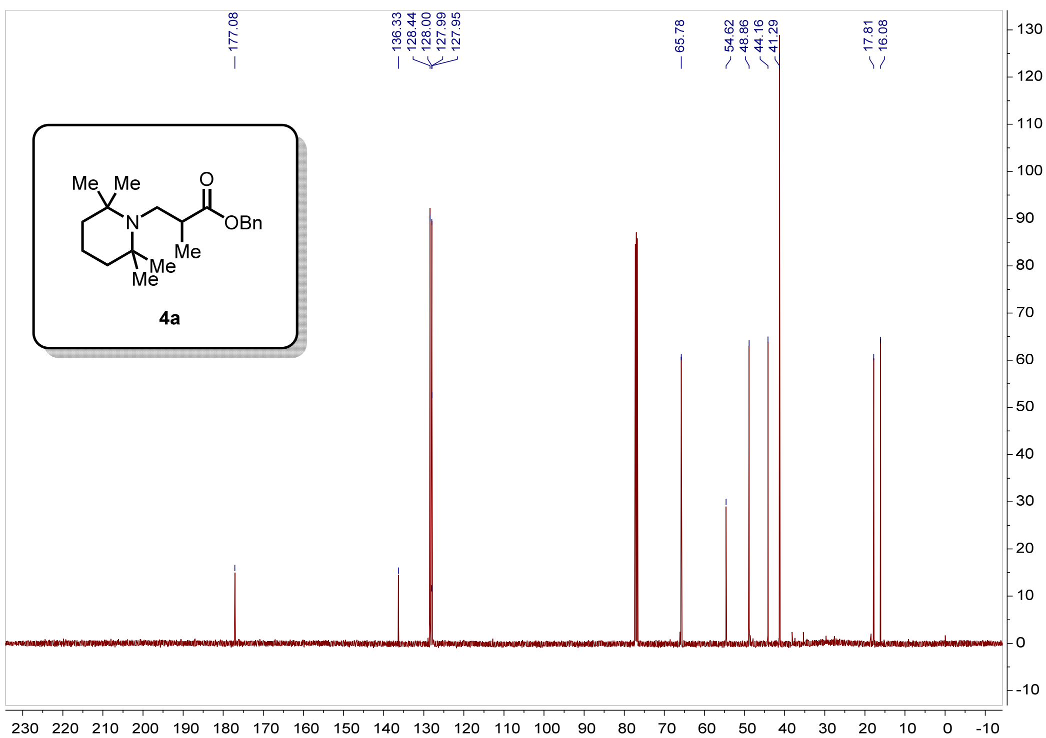
140.49
134.57
131.80
131.20
129.04
129.03
116.79
116.72
116.71
59.99
57.88
44.59
43.98
36.31
22.11
21.98
Ph
O
N
O
Me
Me
N
MeO
Me
3p-*mono*
f1 (ppm)







4a
f1 (ppm)



177.08
136.33
128.44
128.00
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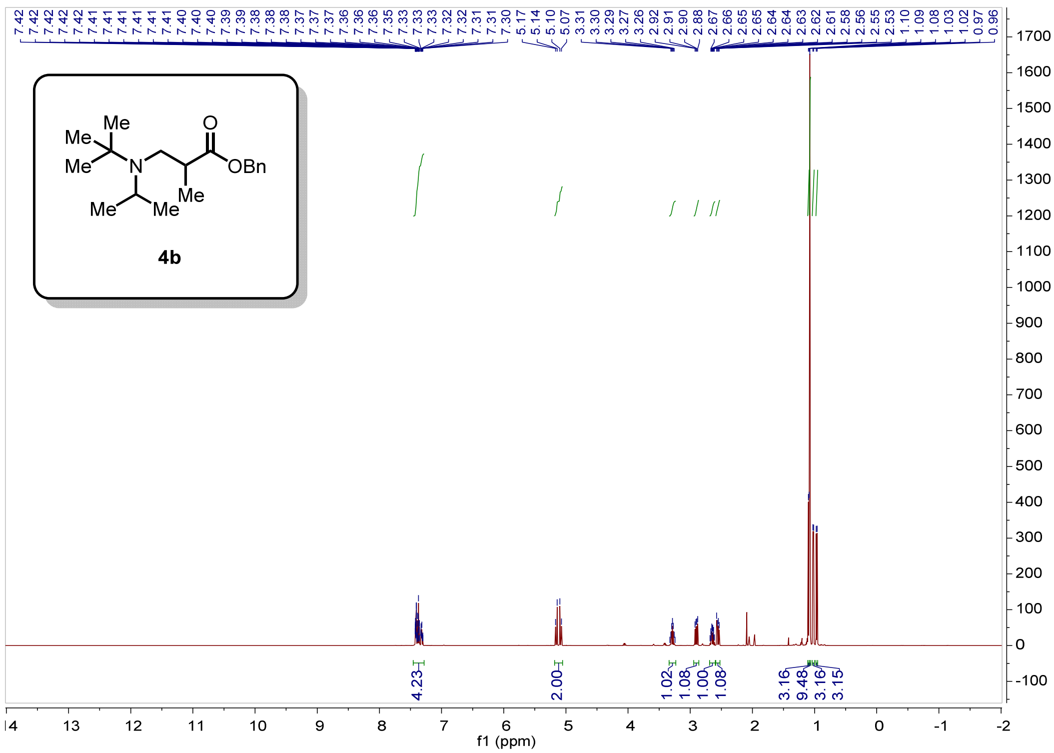
127.95
65.78
54.62
48.86
44.16
41.29
17.81
16.08
4a
f1 (ppm)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7.35
7.33
7.33
7.33
7.32
7.32
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7.30
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5.14
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5.07
3.31
3.30
3.29
3.27
3.26
2.92
2.91
2.90
2.88
2.67
2.66
2.65
2.64
2.64
2.63
2.62
2.61
2.58
2.56
2.55
2.53
1.10
1.09
1.08
1.03
1.02
0.97
0.96
Me
Me
Me
N
O
OBn
Me
Me
Me
4b
4.23
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1.02
1.08
1.00
1.08
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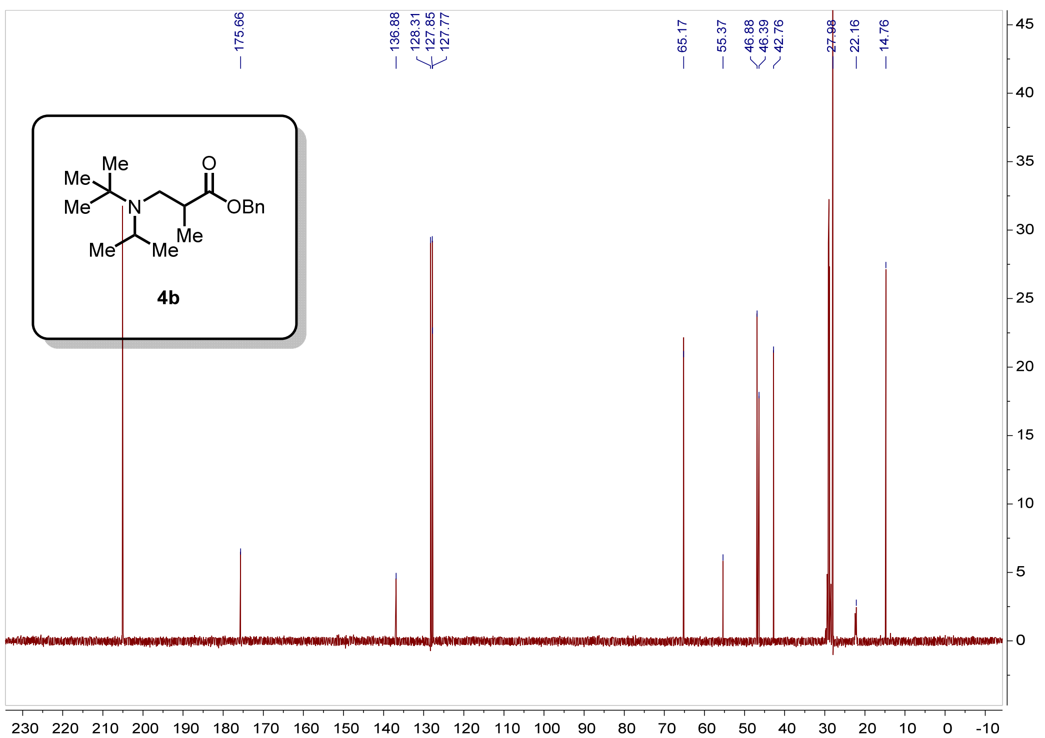
9.48
3.16
3.15
f1 (ppm)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65.17
55.37
46.88
46.39
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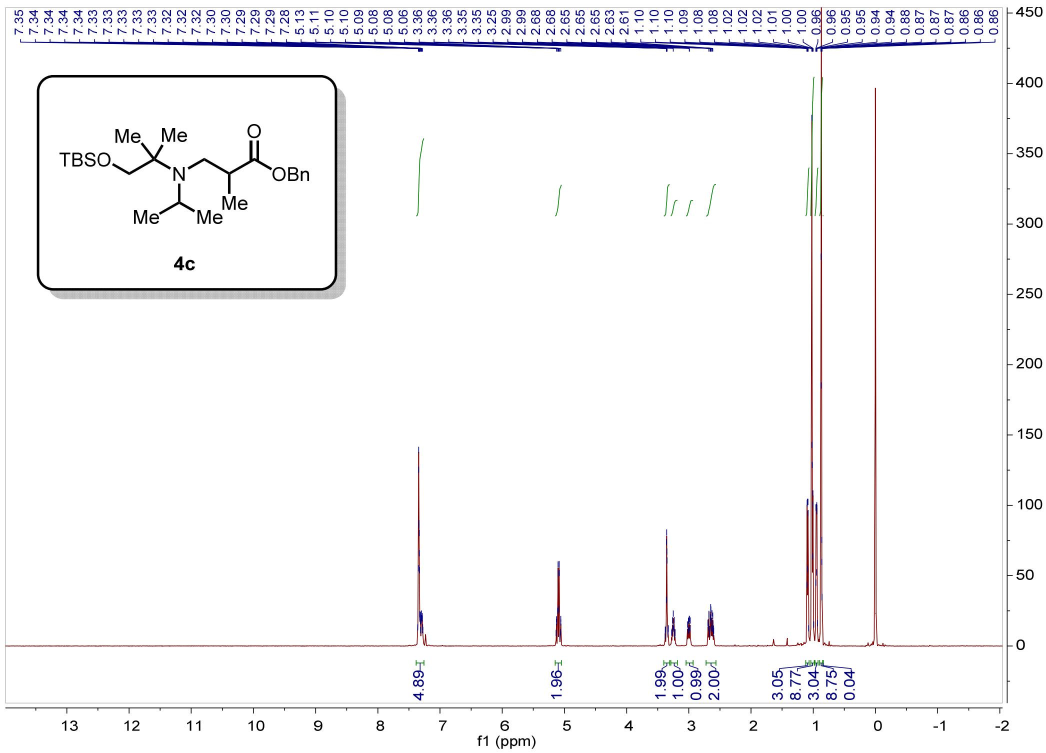
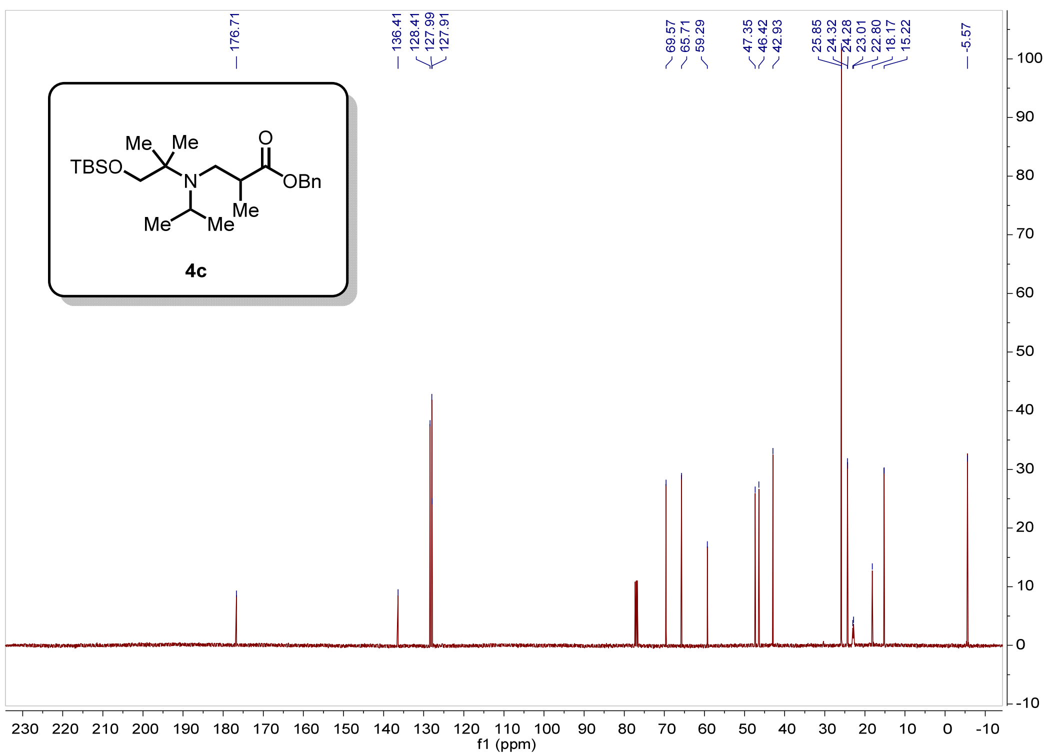
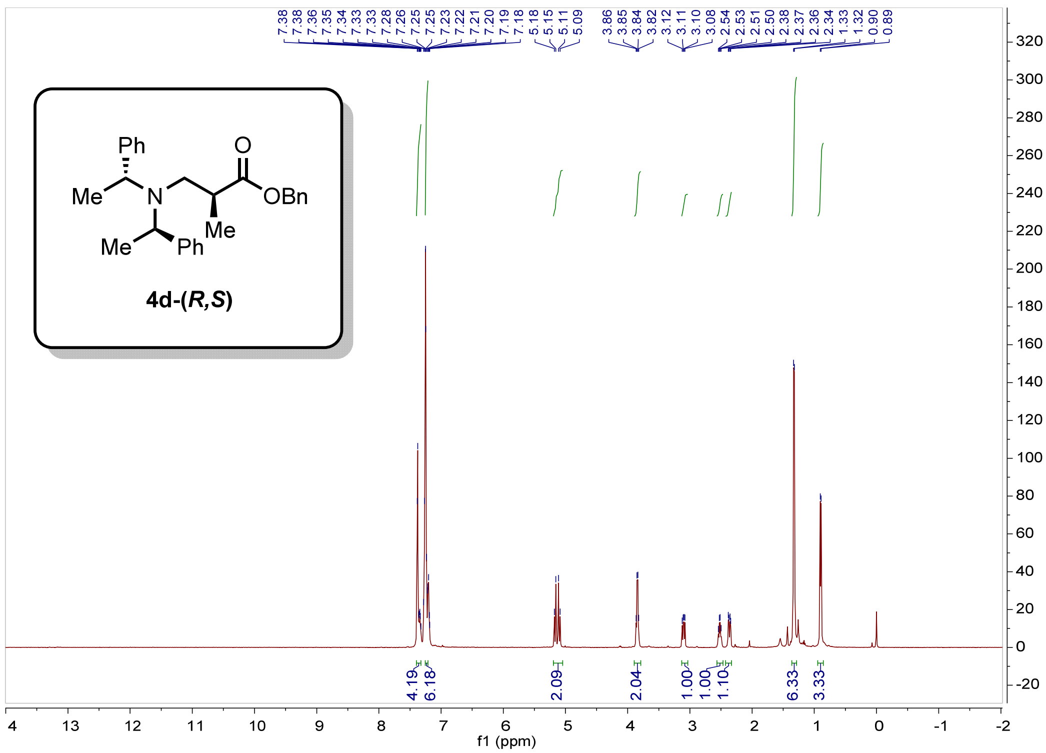
22.16
14.76
Me
Me
Me
N
O
OBn
Me
Me
Me
4b
f1 (ppm)







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7.22
7.21
7.20
7.19
7.18
5.18
5.15
5.11
5.09
3.86
3.85
3.84
3.82
3.12
3.11
3.10
3.08
2.54
2.53
2.51
2.50
2.38
2.37
2.36
2.34
1.33
1.32
0.90
0.89
4.19
6.18
2.09
2.04
1.00
1.00
1.10
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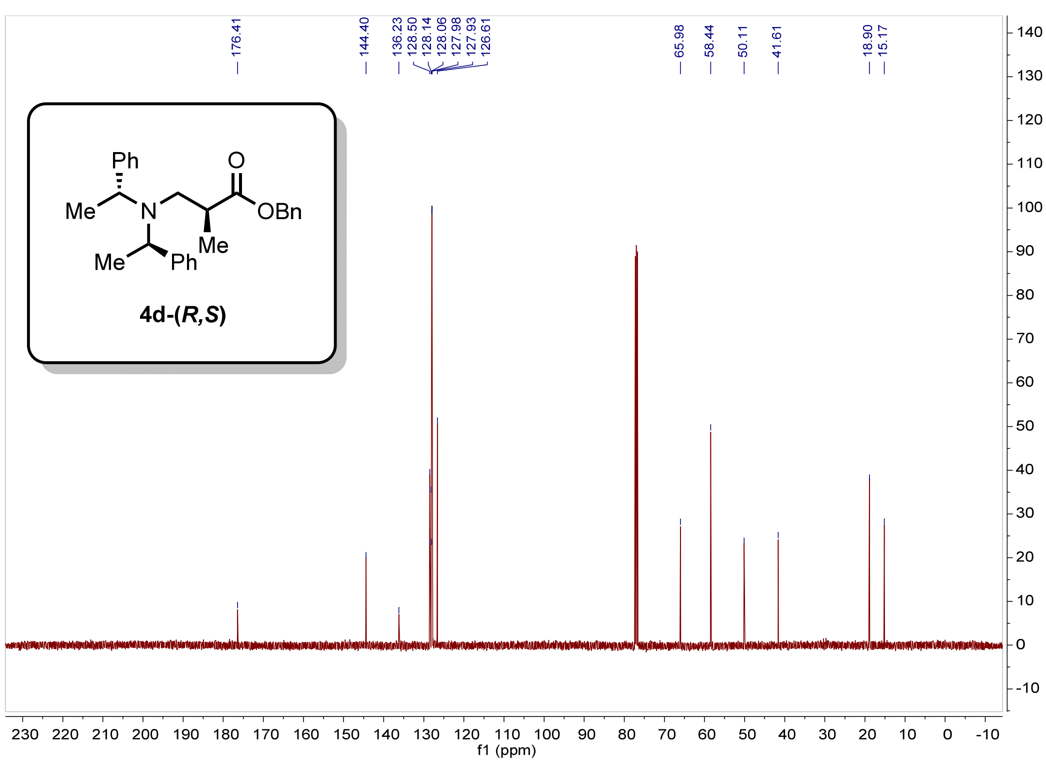
3.33
f1 (ppm)
Ph
O
Me
N
OBn
Me
Me
Ph
4d-(R,S)



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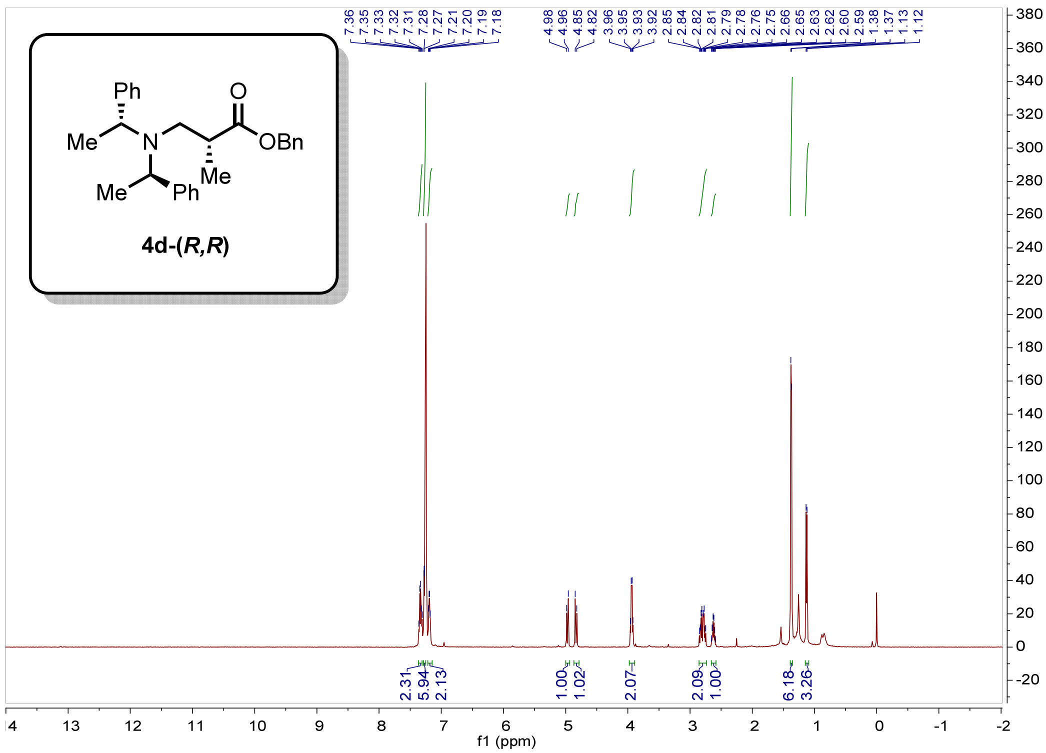
128.14
128.06
127.98
127.93
126.61
65.98
58.44
50.11
41.61
18.90
15.17
f1 (ppm)
Ph
O
Me
N
OBn
Me
Me
Ph
4d-(R,S)



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4.82
3.96
3.95
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3.92
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2.82
2.81
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2.78
2.76
2.75
2.66
2.65
2.63
2.62
2.60
2.59
1.38
1.37
1.13
1.12
Ph
O
Me
N
OBn
Me
Ph
Me
4d-(*R*,*R*)
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2.13
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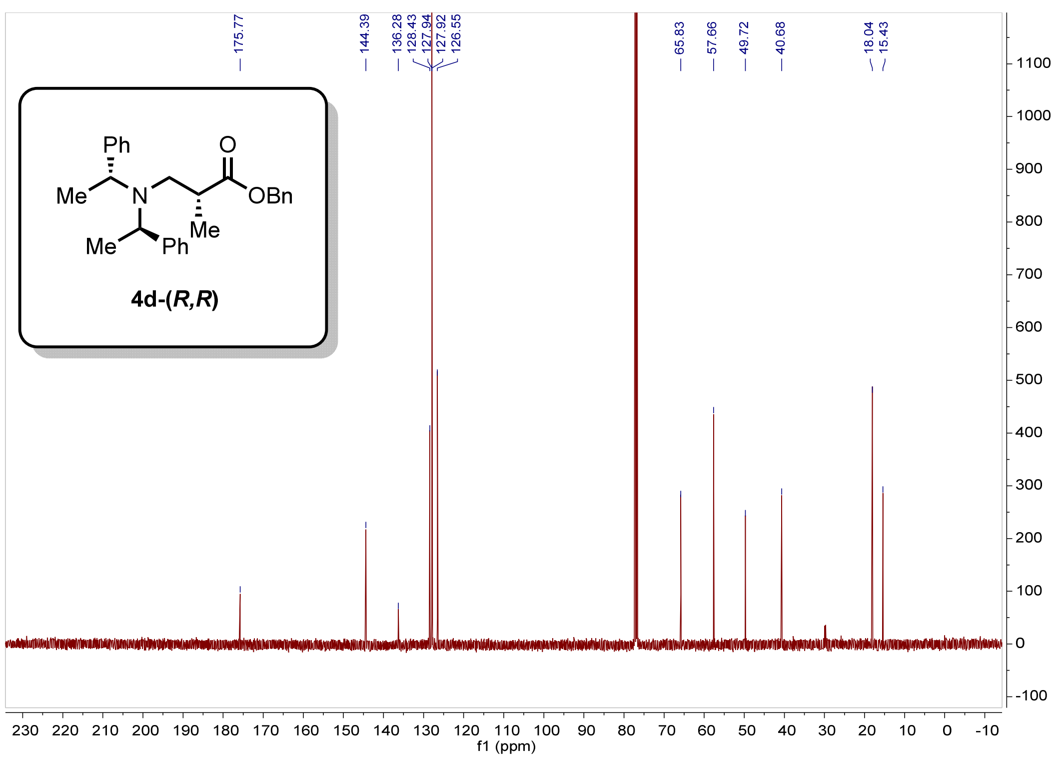
1.02
2.07
2.09
1.00
6.18
3.26
f1 (ppm)



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127.92
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65.83
57.66
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40.68
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15.43
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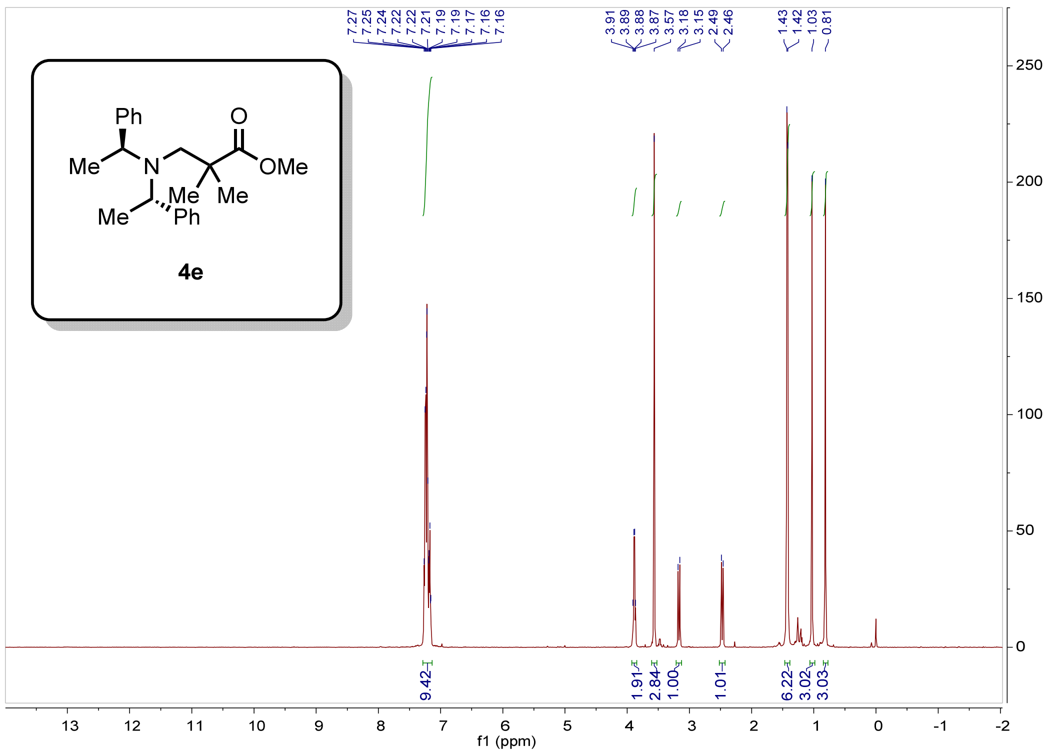
N
OBn
Me
Ph
Me
4d-(*R*,*R*)
f1 (ppm)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7.16
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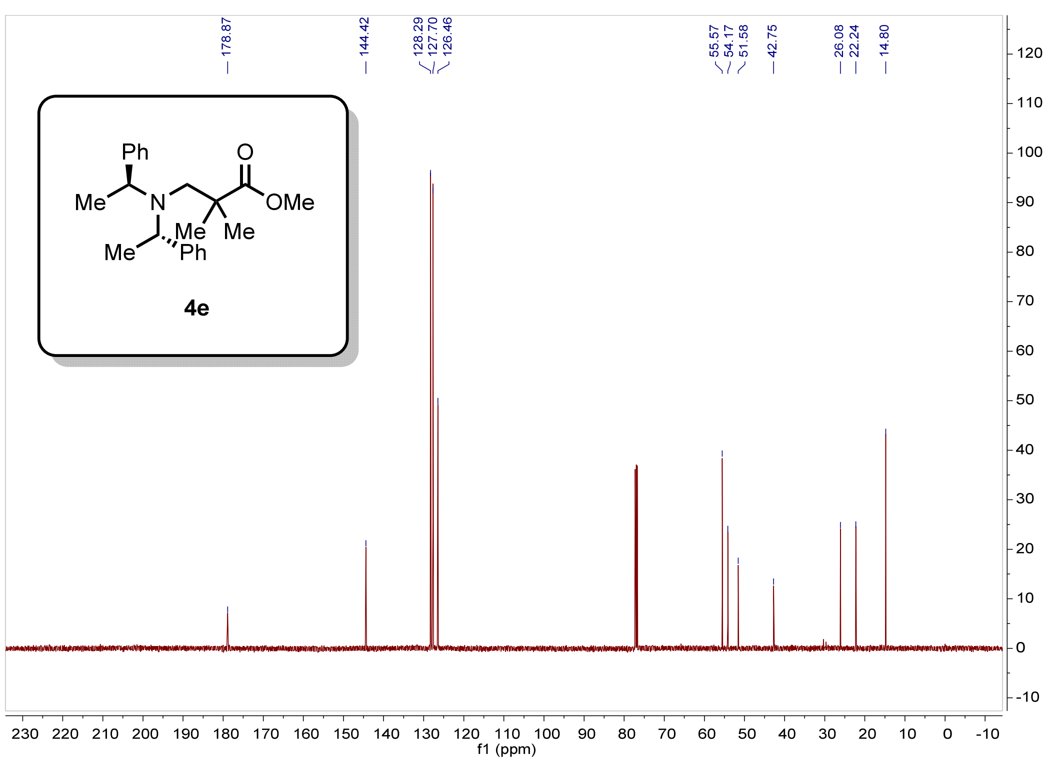
3.89
3.88
3.87
3.57
3.18
3.15
2.49
2.46
1.43
1.42
1.03
0.81
Ph
O
Me
N
OMe
Me
Me
Me
Ph
4e
9.42
1.91
2.84
1.00
1.01
6.22
3.02
3.03
f1 (ppm)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51.58
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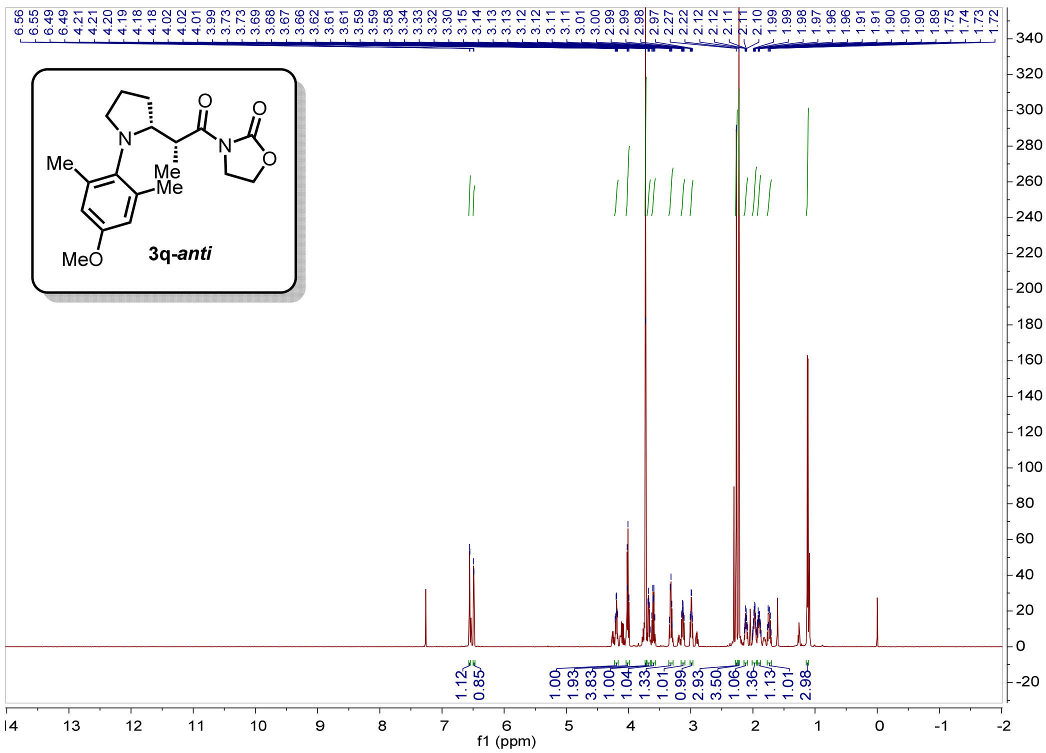
22.24
14.80
Ph
O
Me
N
OMe
Me
Me
Me
Ph
4e
f1 (ppm)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3.73
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3.62
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3.33
3.32
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2.97
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2.12
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2.10
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1.99
1.98
1.97
1.96
1.96
1.91
1.91
1.90
1.90
1.89
1.75
1.74
1.73
1.72
Me
Me
Me
MeO
N
O
O
N
O
3q-anti
1.12
0.85
1.00
1.93
3.83
1.00
1.04
1.33
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0.99
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3.50
1.06
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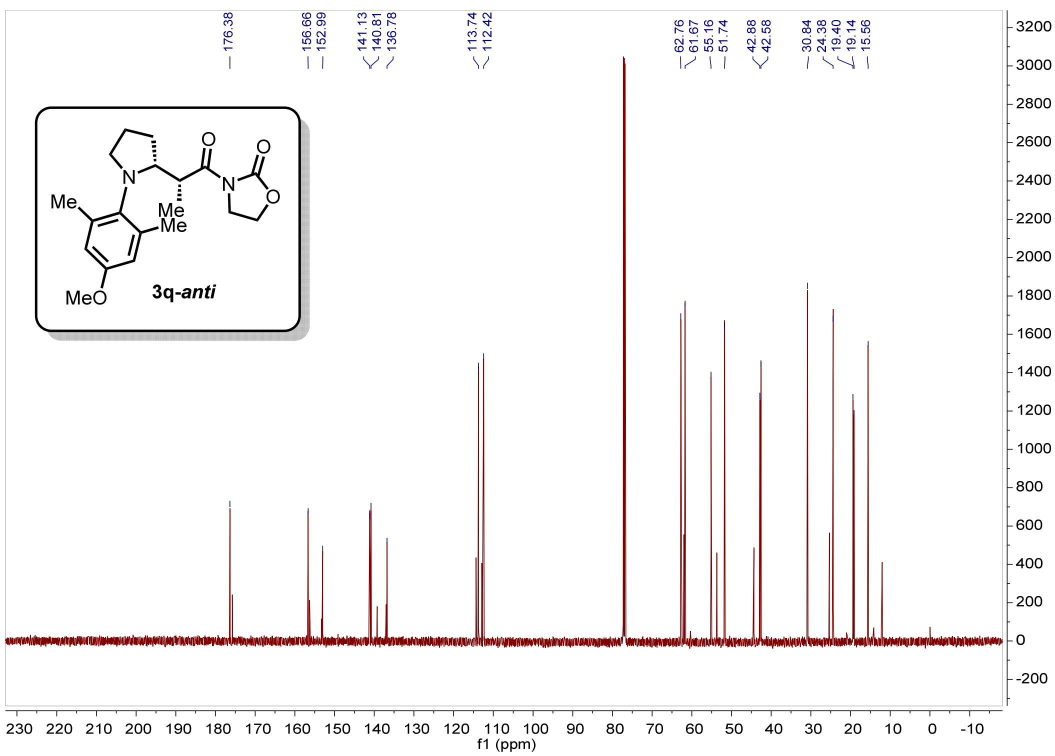
1.13
1.01
2.98
f1 (ppm)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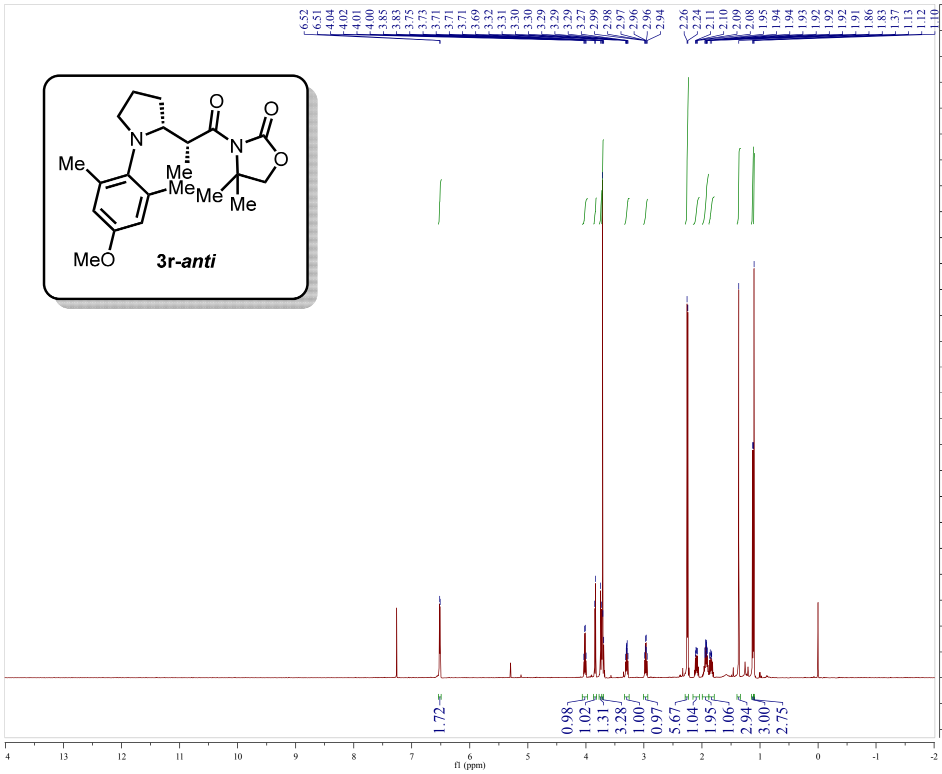
42.88
42.58
30.84
24.38
19.40
19.14
15.56
Me
Me
Me
MeO
N
O
O
N
O
3q-anti
f1 (ppm)


Me
N
O
N
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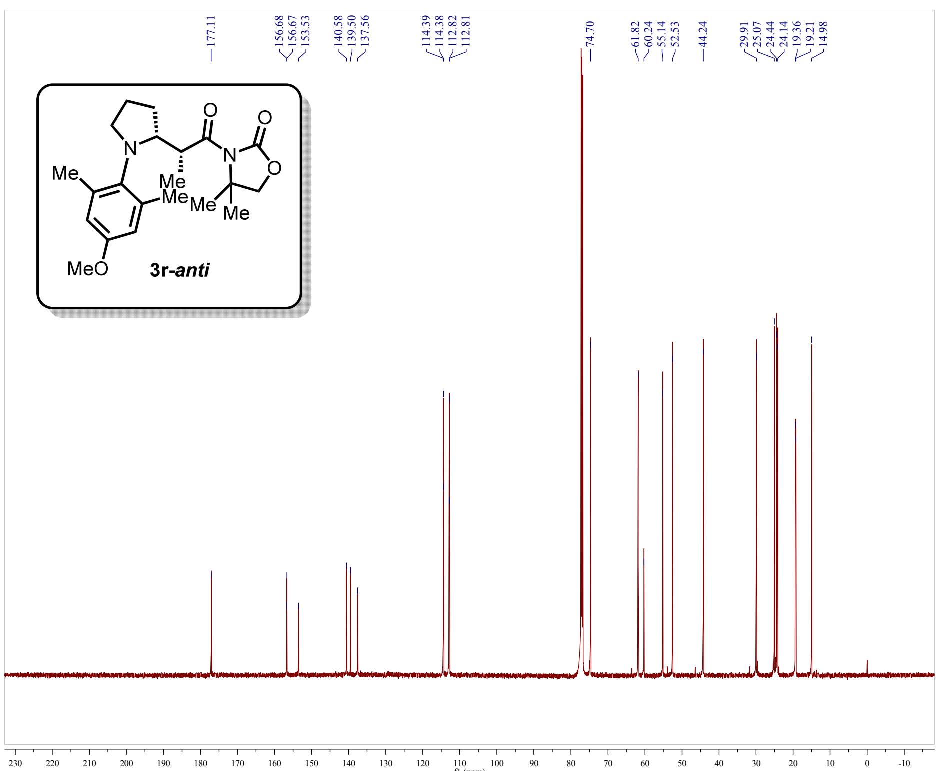
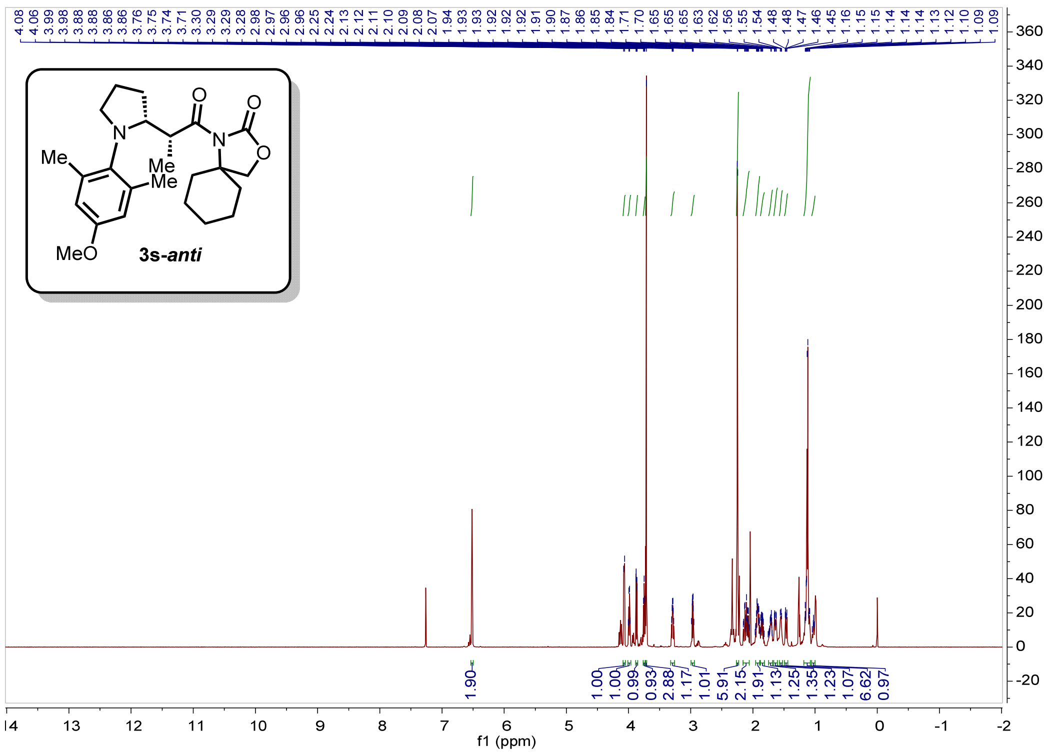
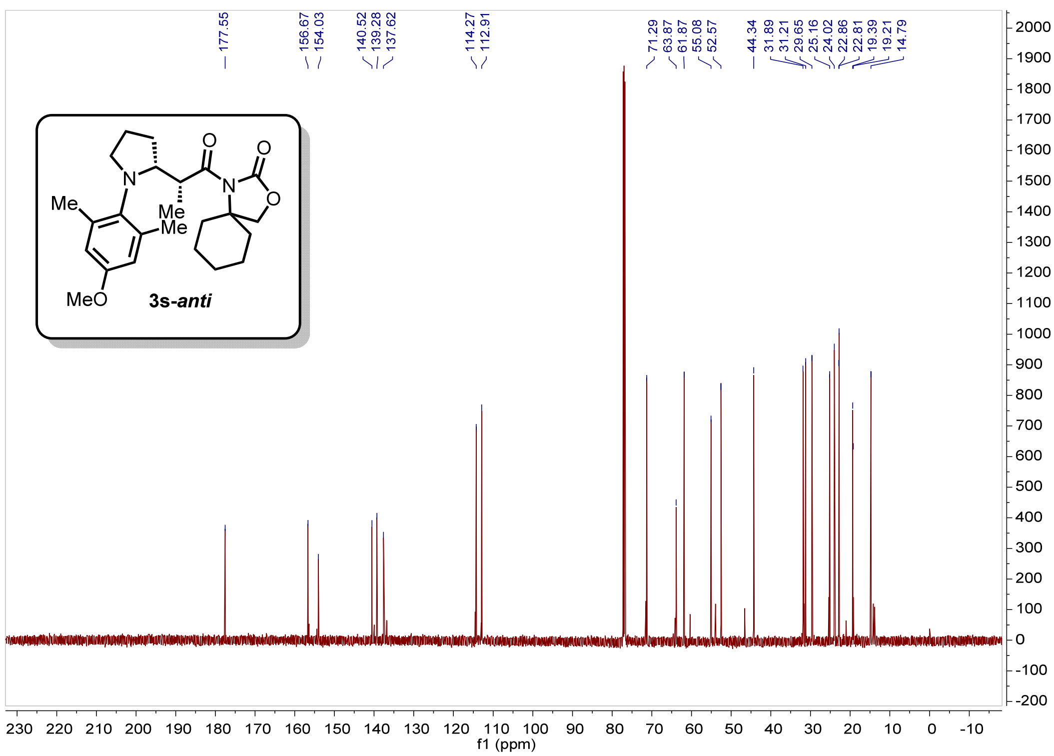
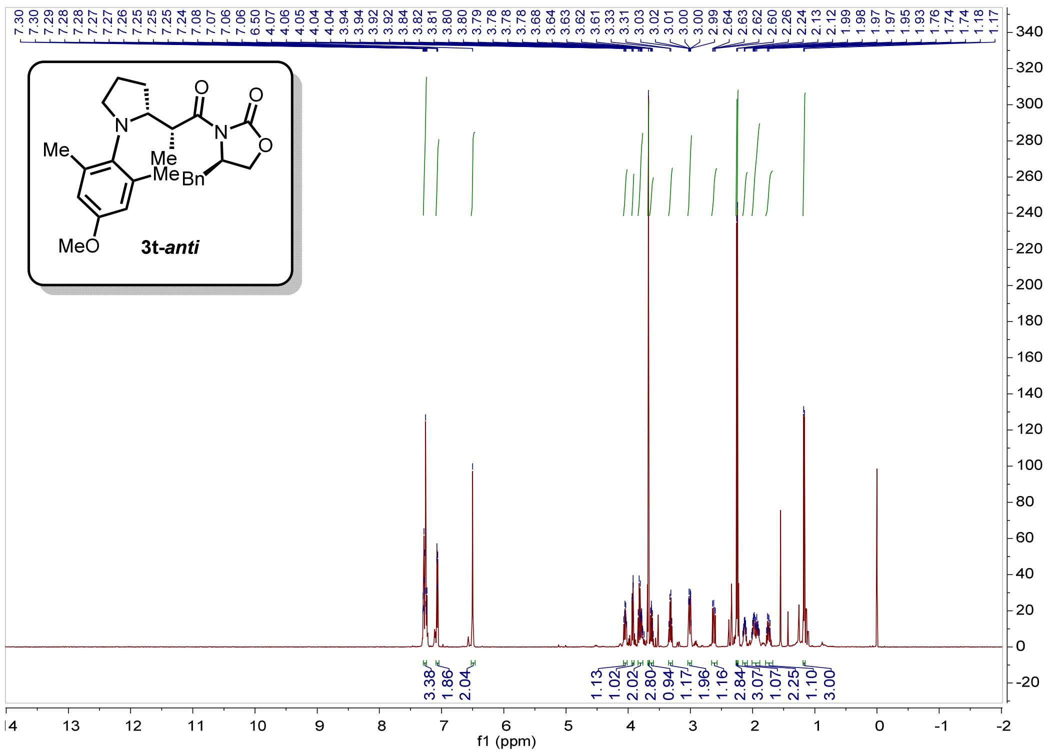
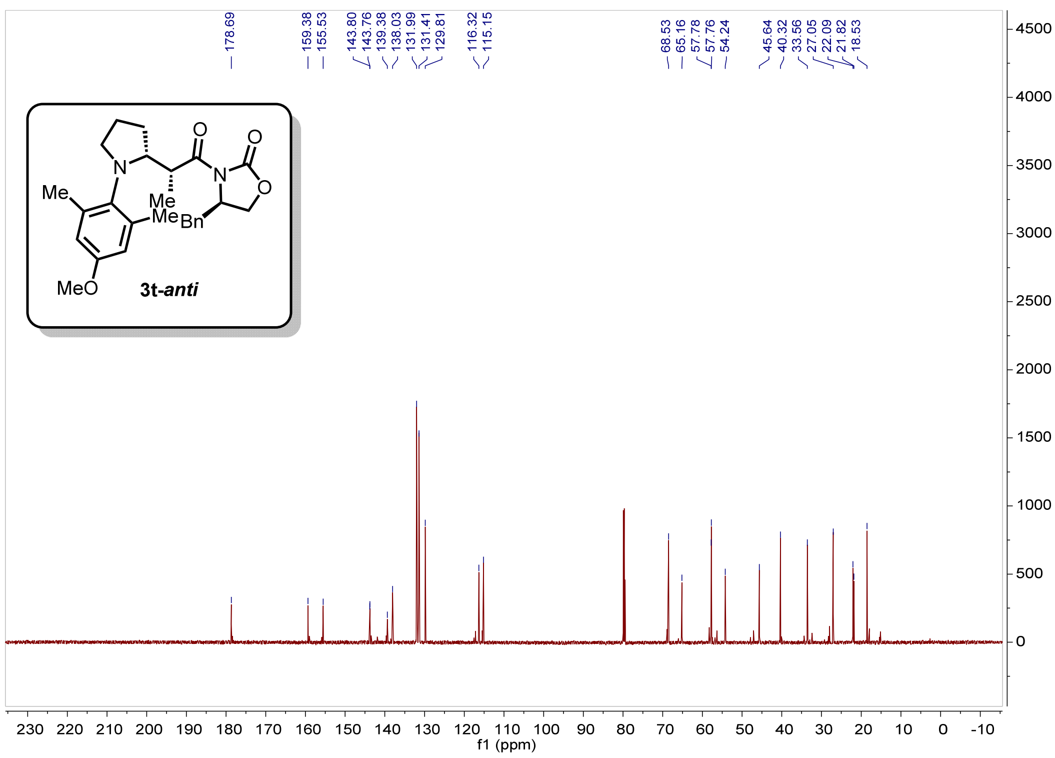
O
Me
Me
Me
Me
MeO
3r-anti
fl (ppm)

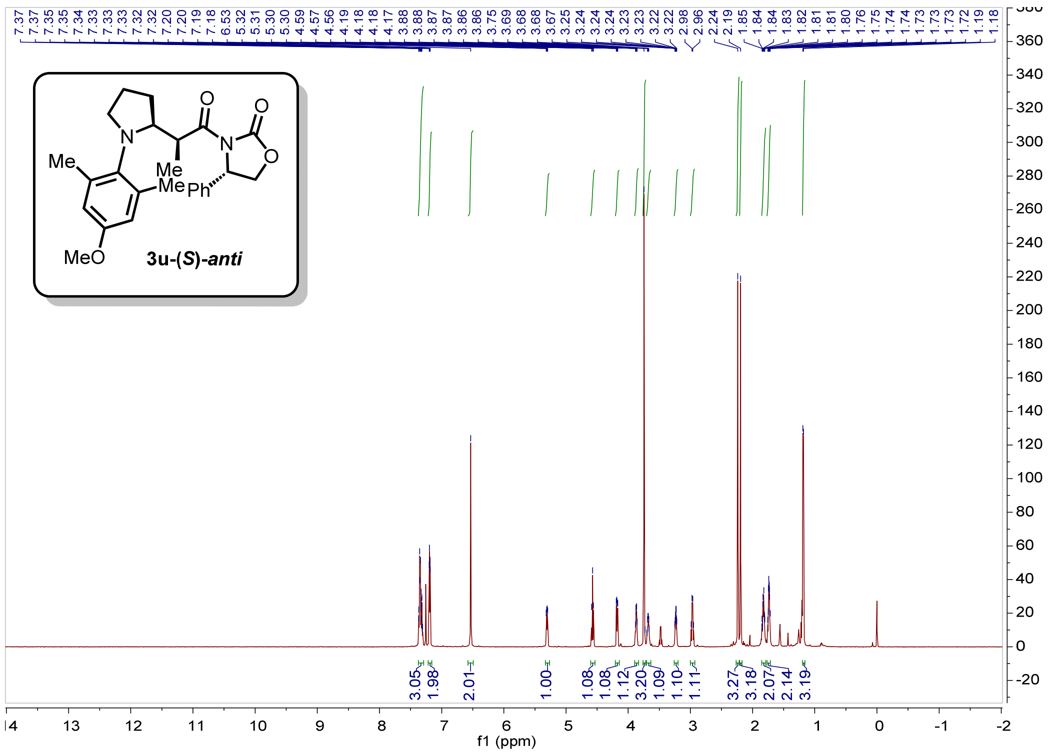

Me
N
O
N
O
O
Me
Me
Me
Me
MeO
3r-anti
fl (ppm)







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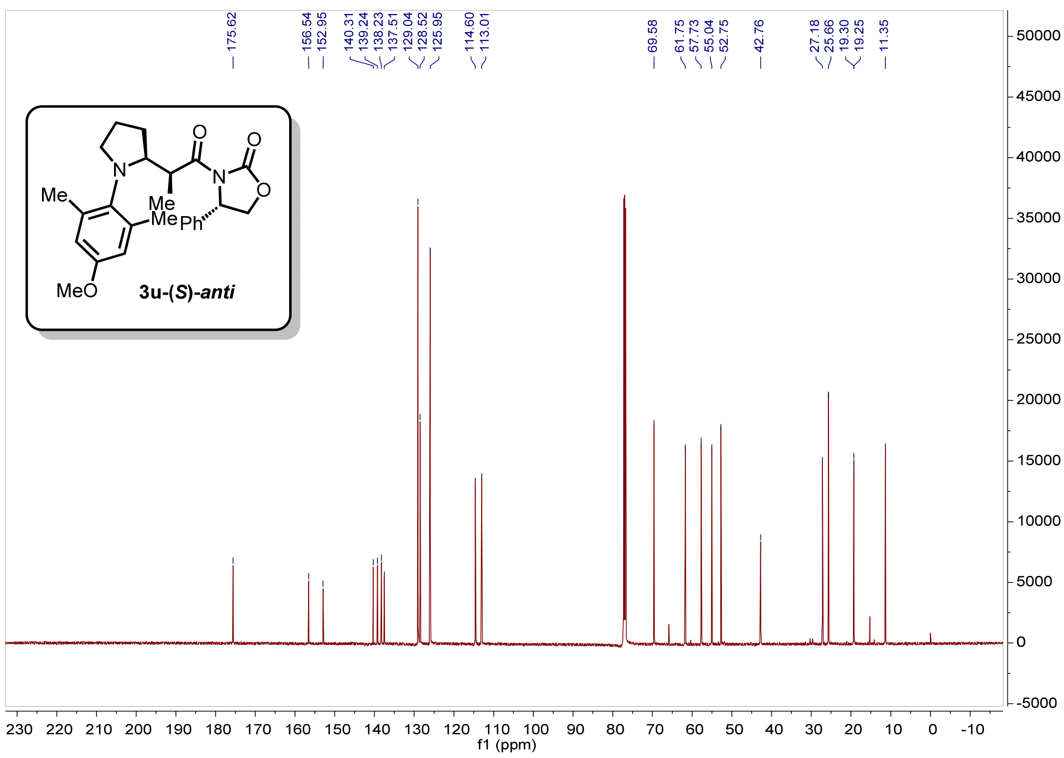
f1 (ppm)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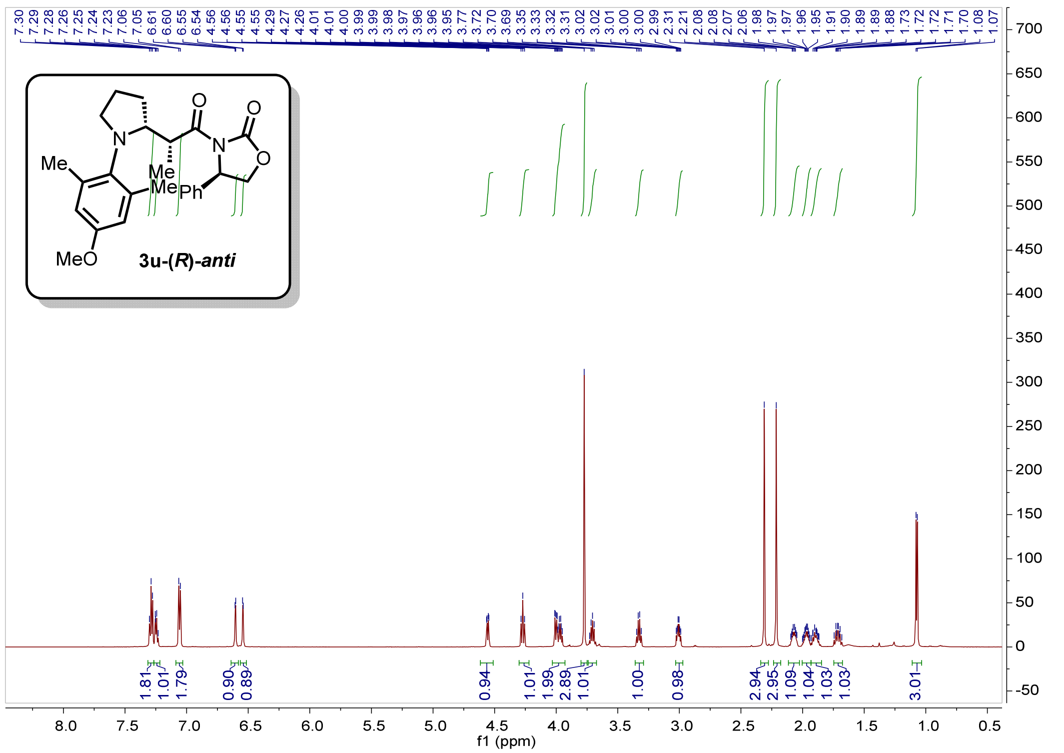
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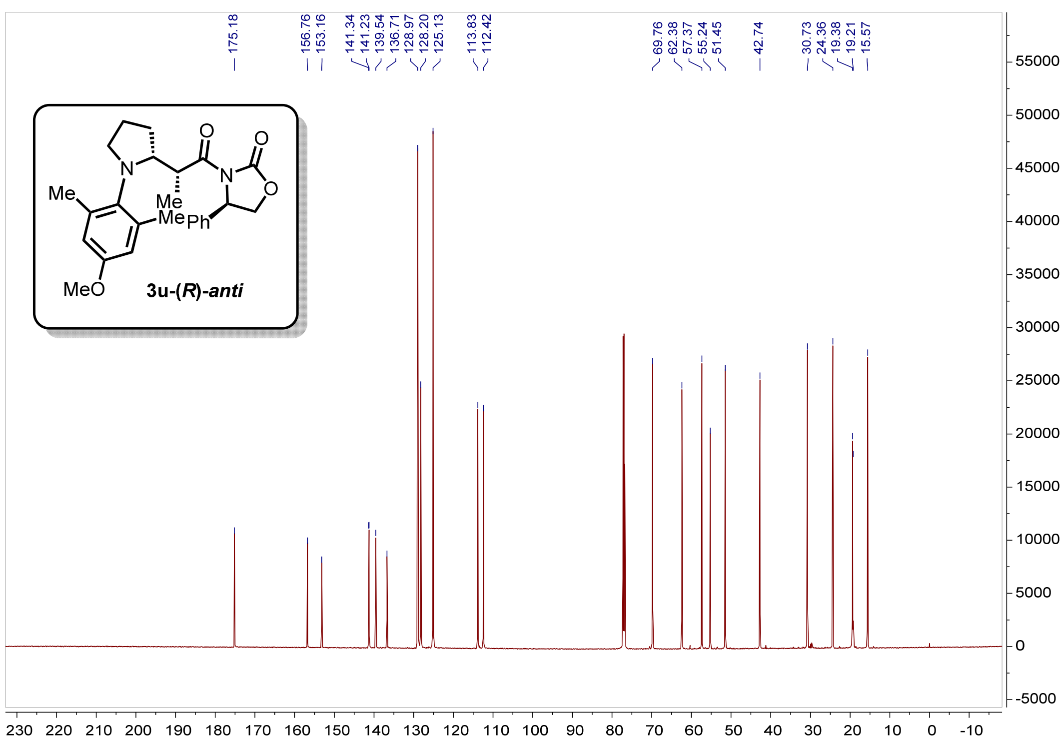
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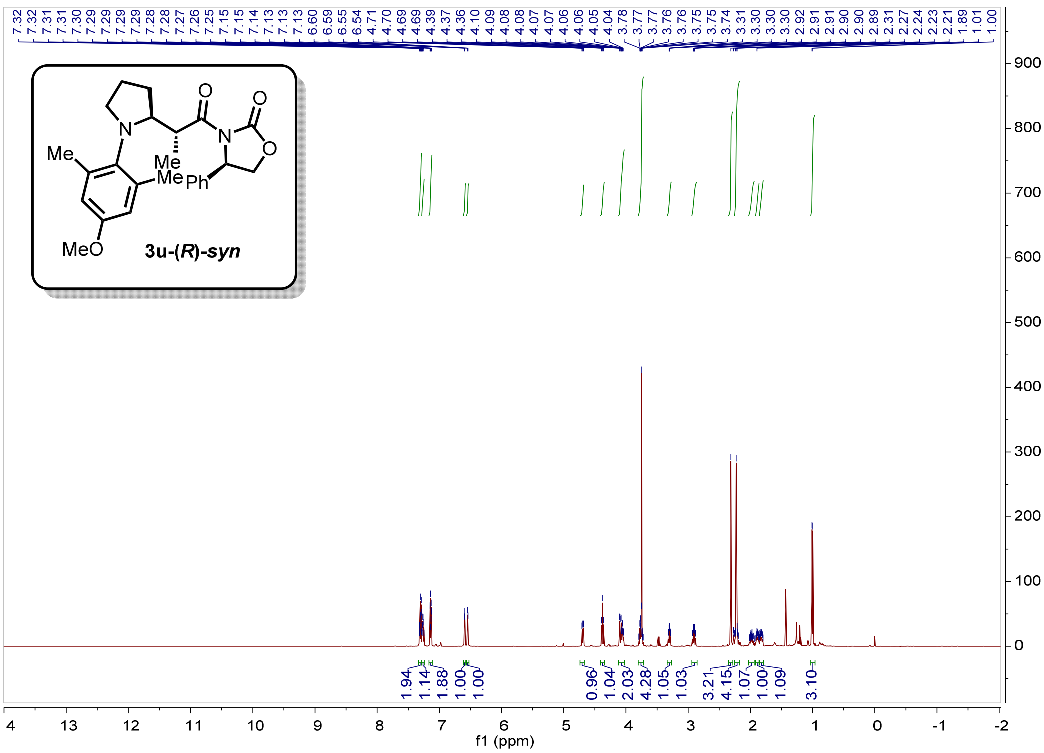
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Me
Me
Me
Ph
MeO
3u-(R)-syn
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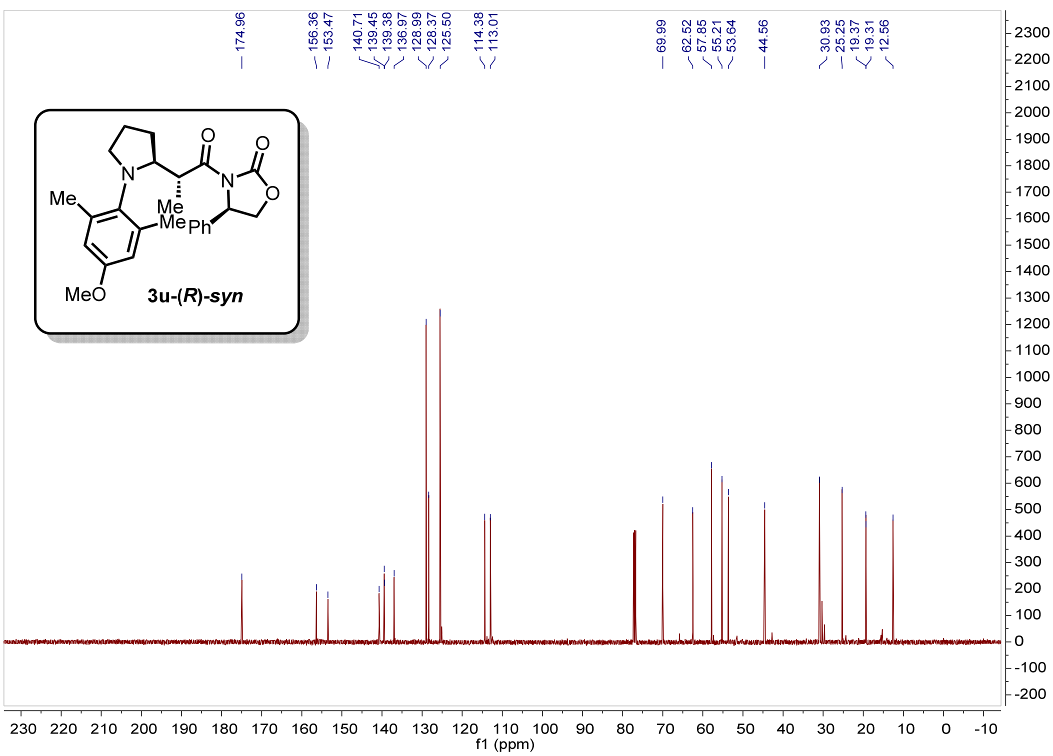
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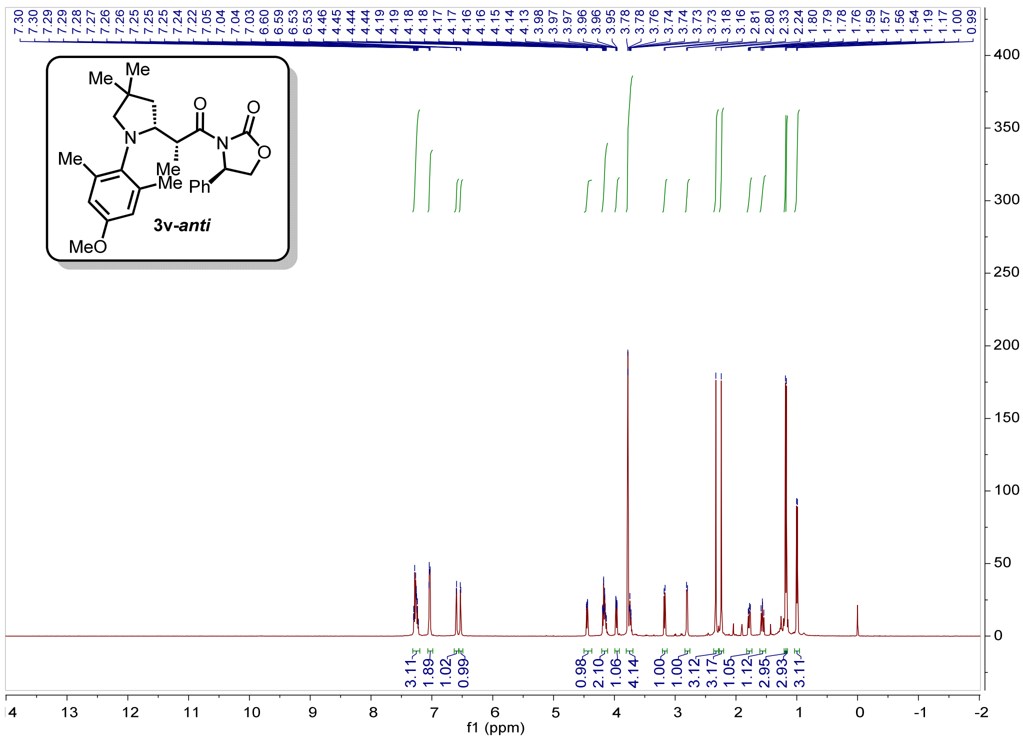
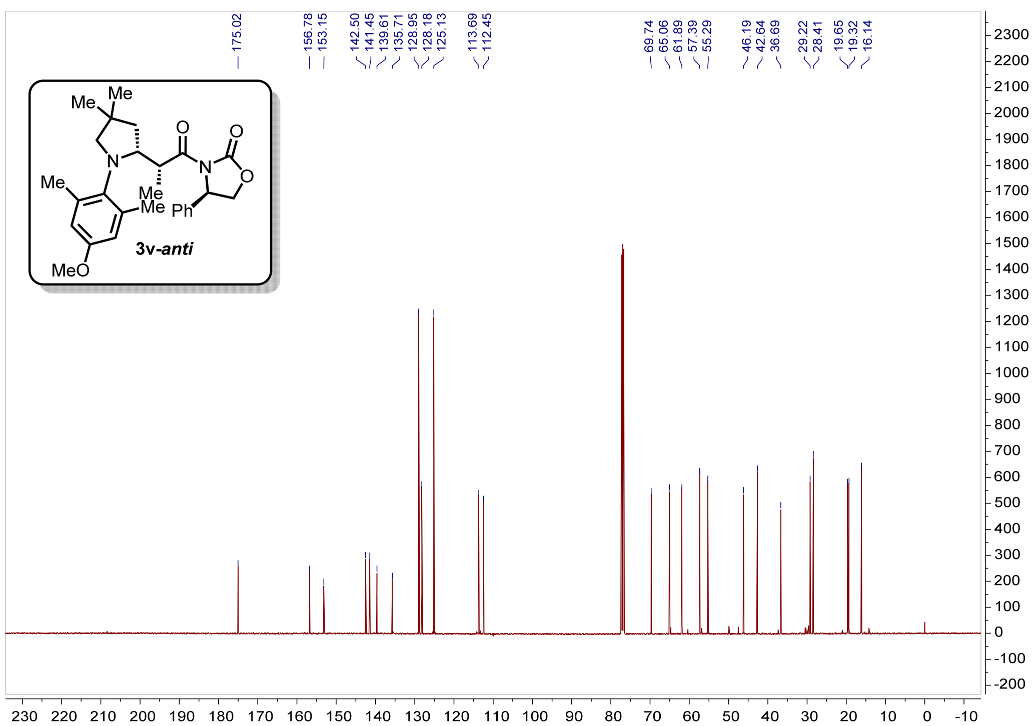
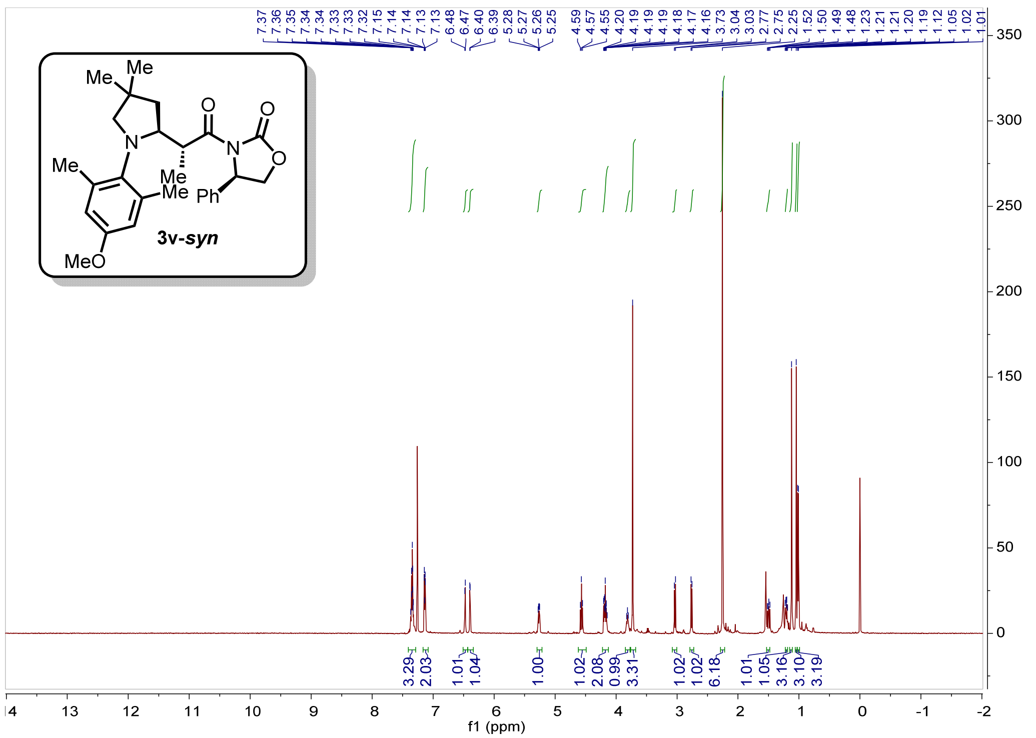
Me
Ph
MeO
3u-(R)-syn
f1 (ppm)



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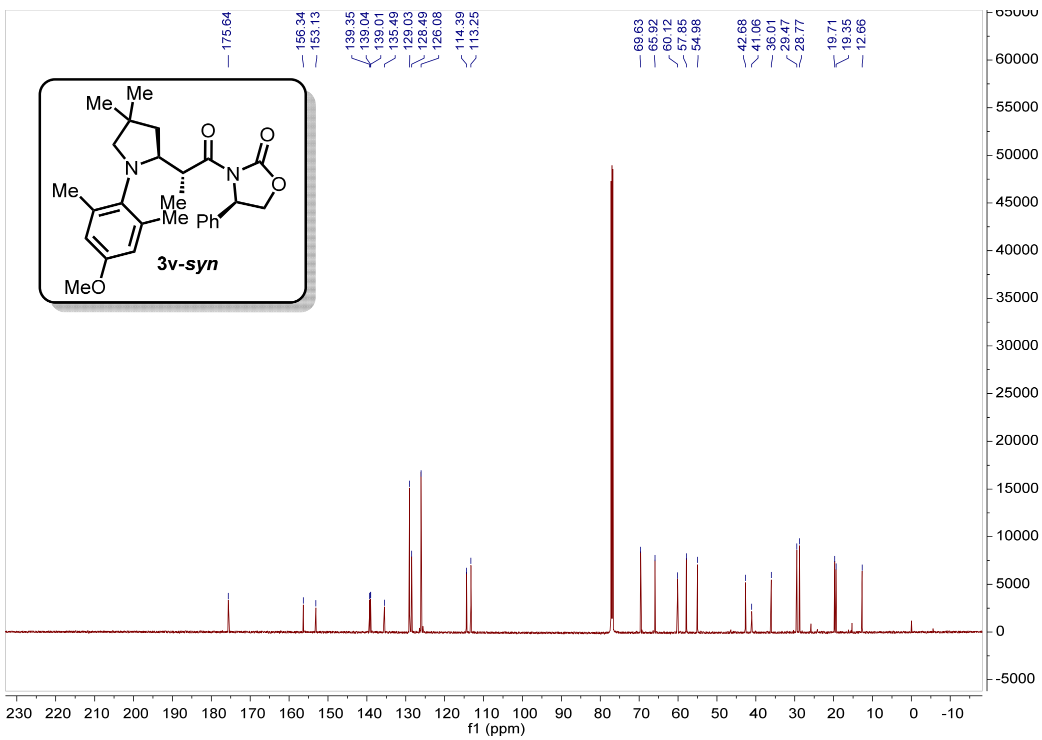
f1 (ppm)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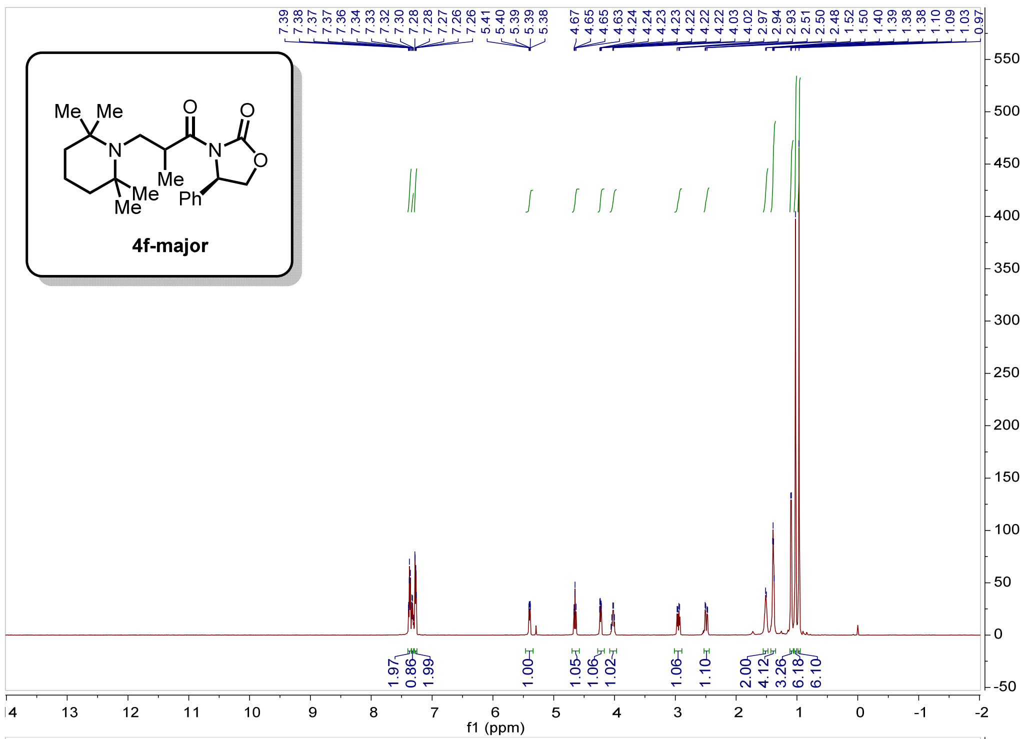

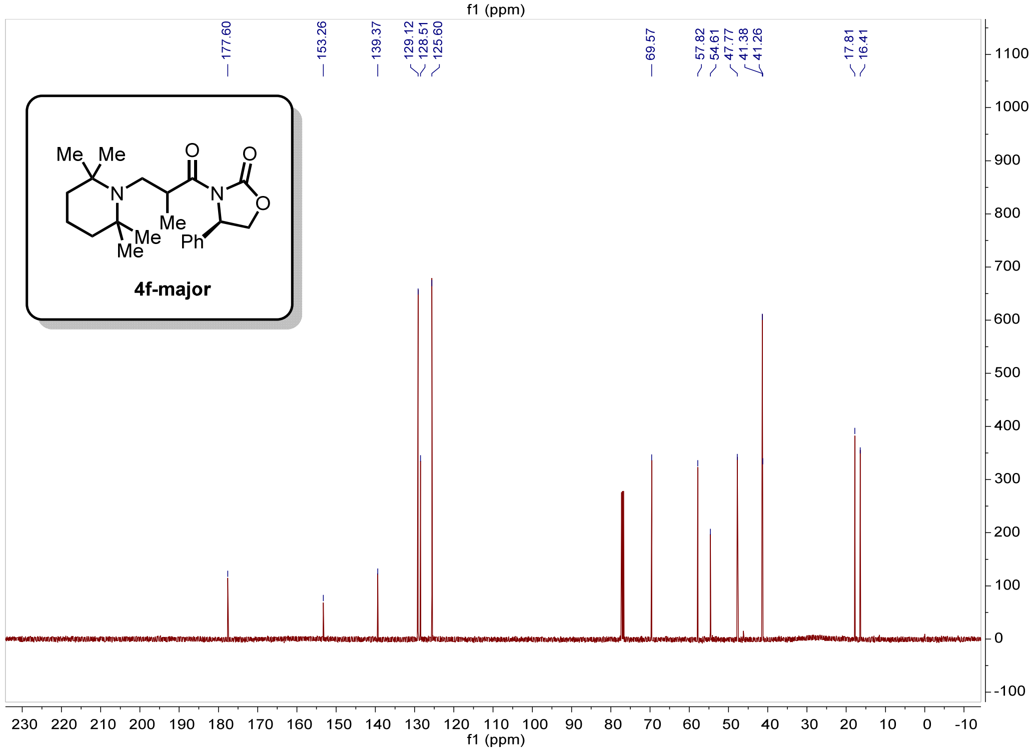

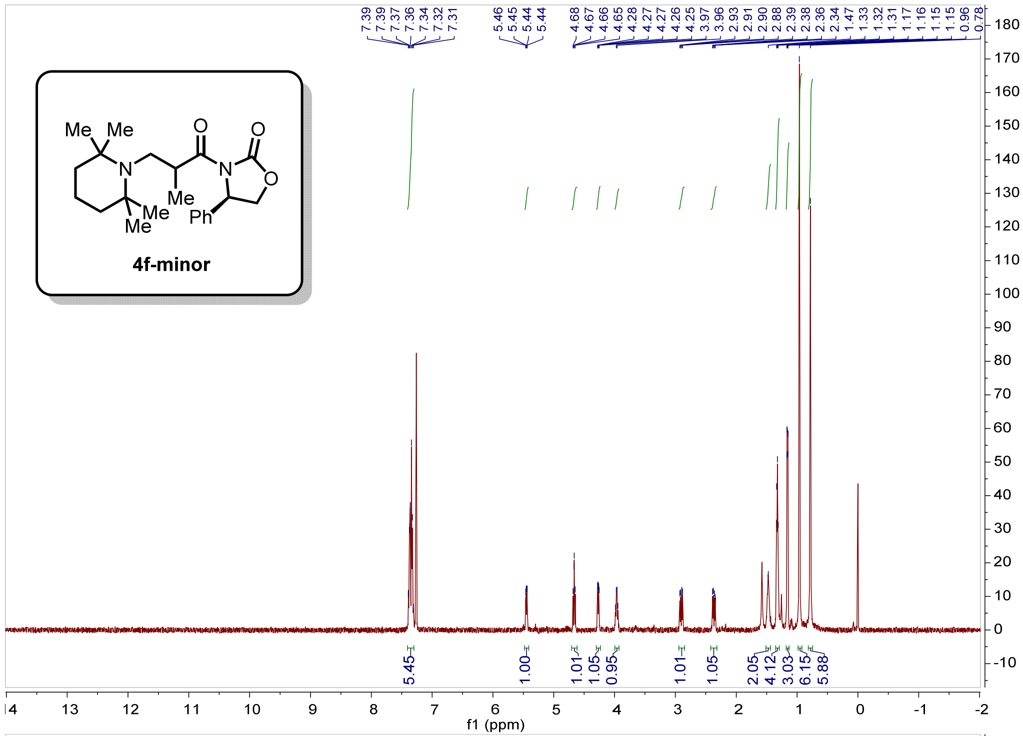

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4.67
4.66
4.65
4.28
4.27
4.27
4.26
4.25
3.97
3.96
2.93
2.91
2.90
2.88
2.39
2.38
2.36
2.34
1.47
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1.32
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Me
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Me
Me
Ph
4f-minor
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2.05
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3.03
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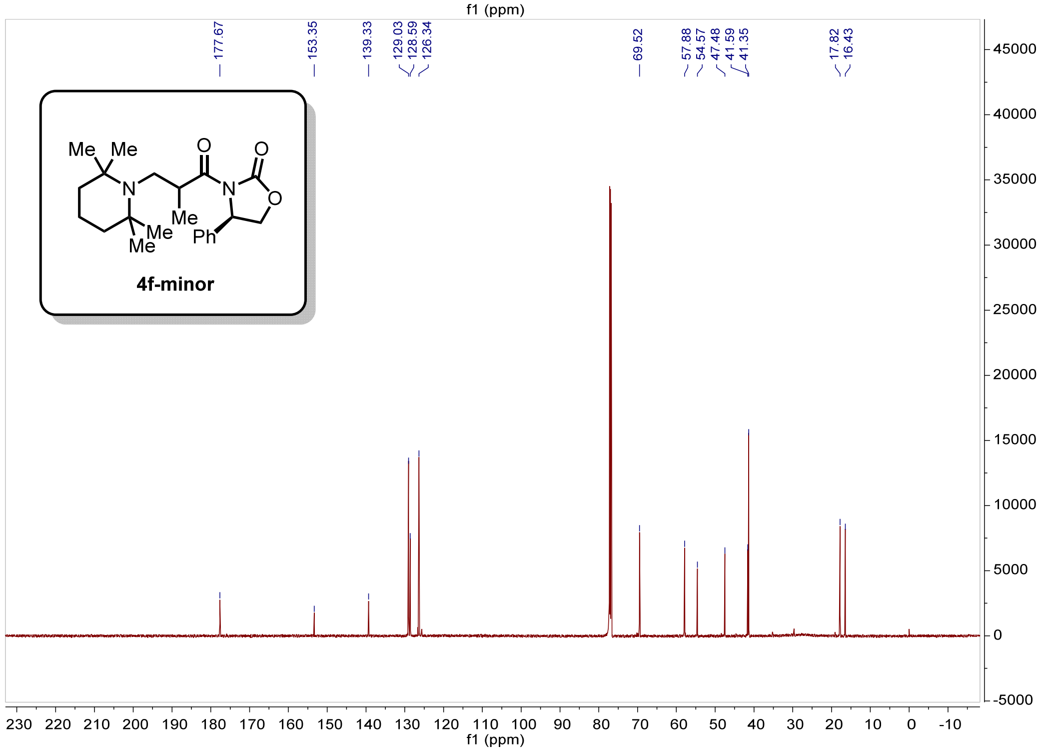
f1 (ppm)



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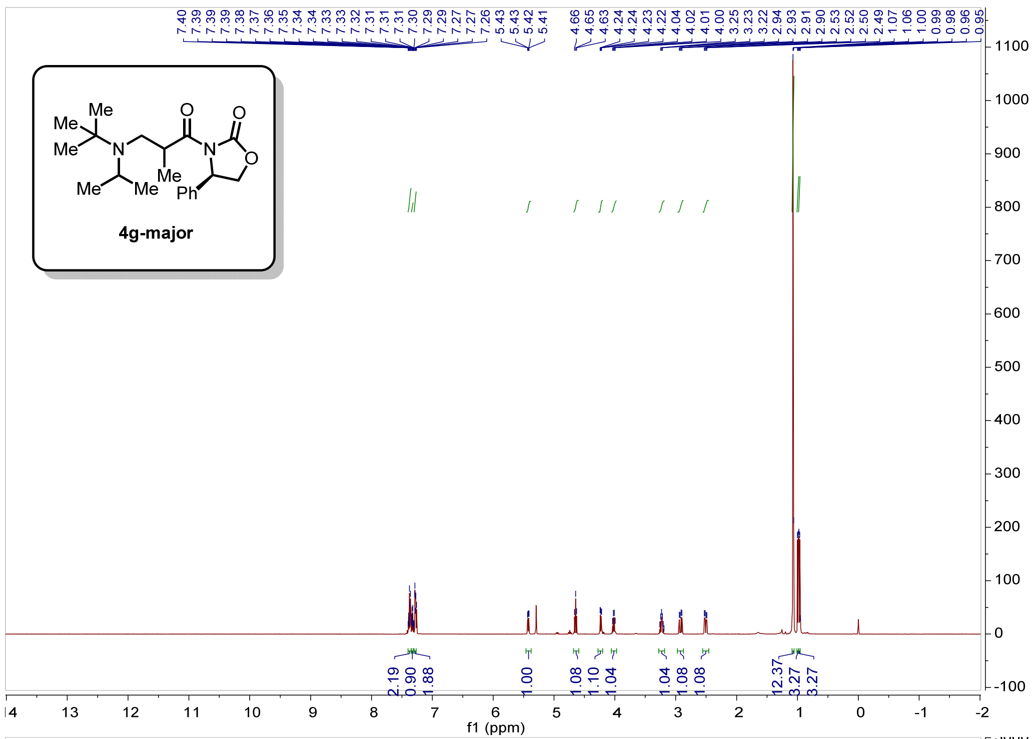
Me
Me
Me
Ph
4f-minor
f1 (ppm)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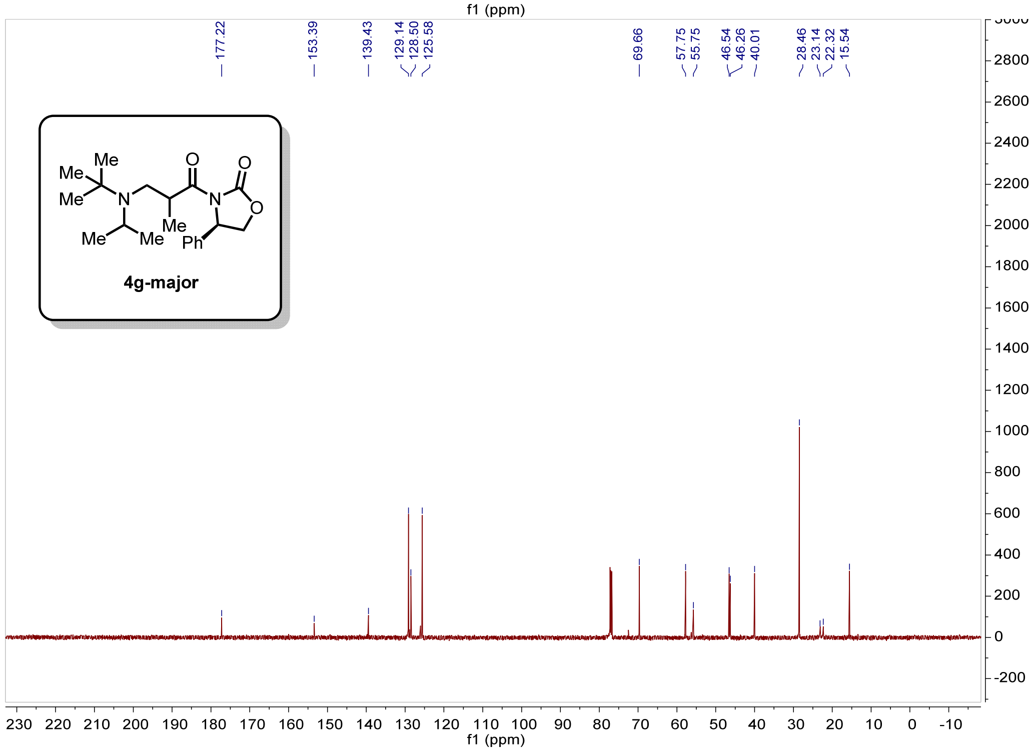
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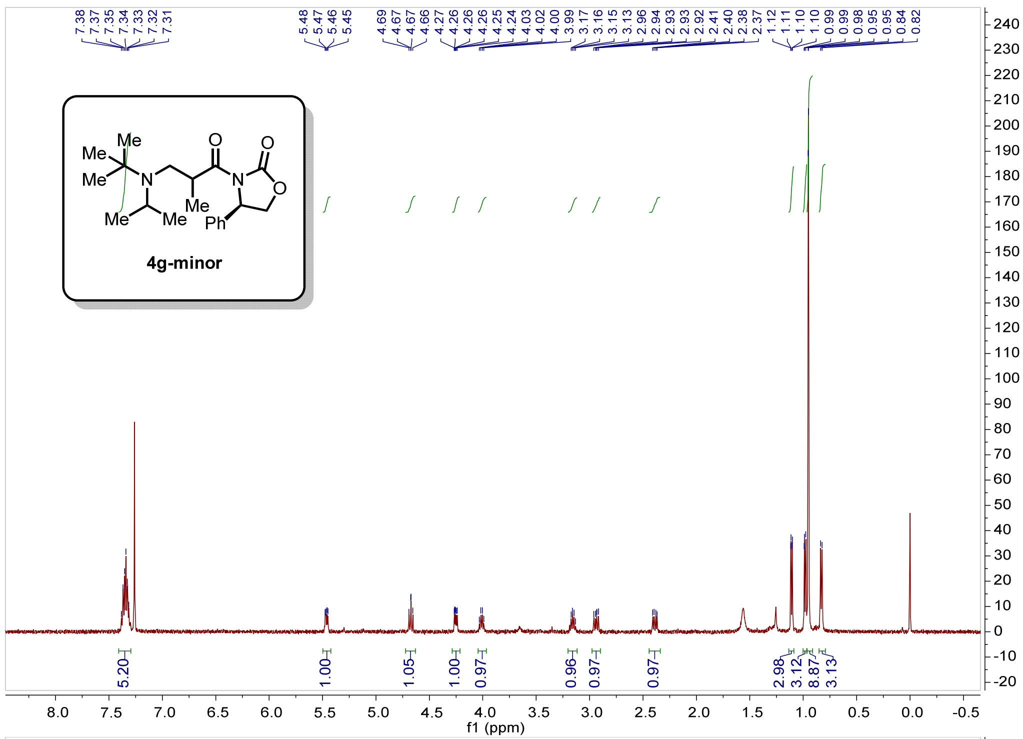

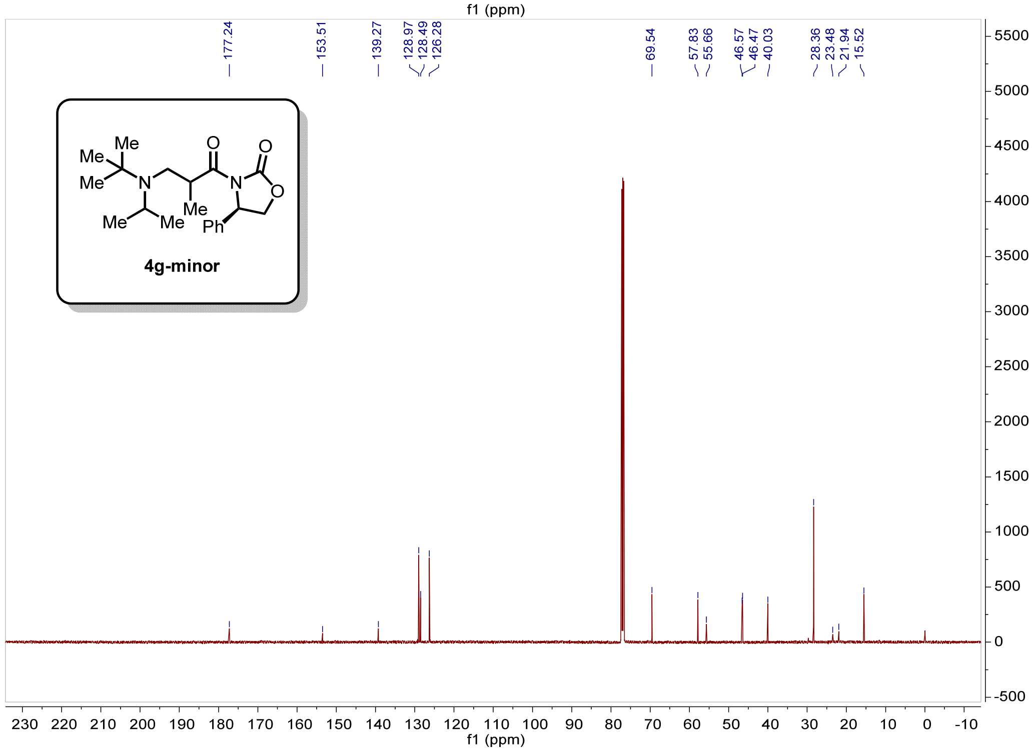

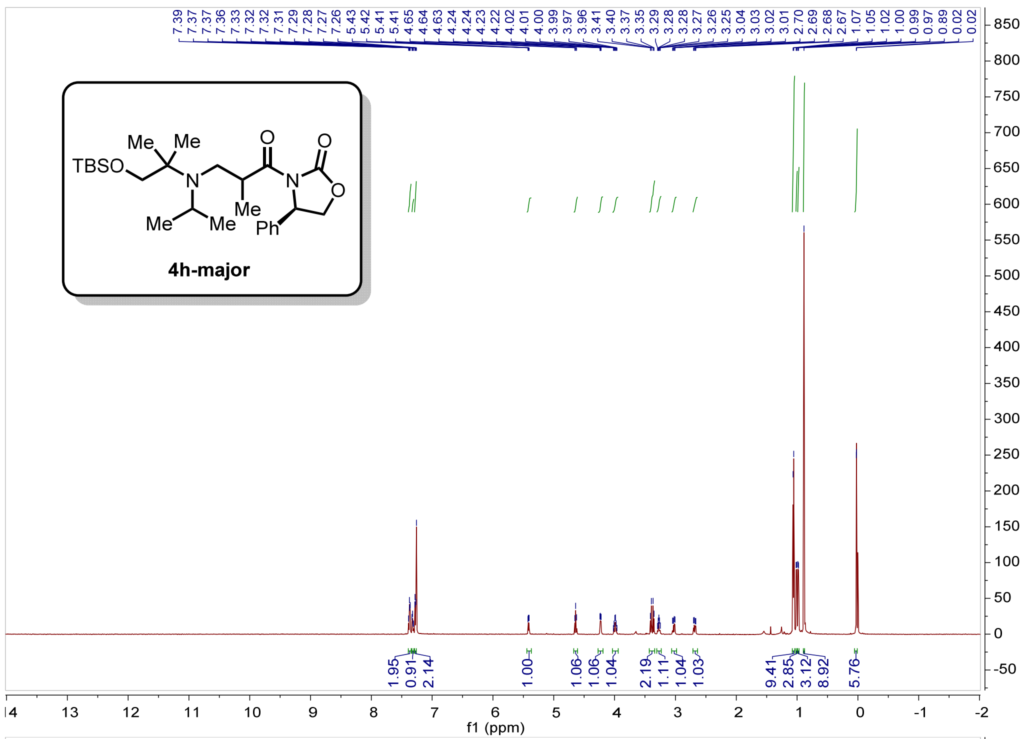

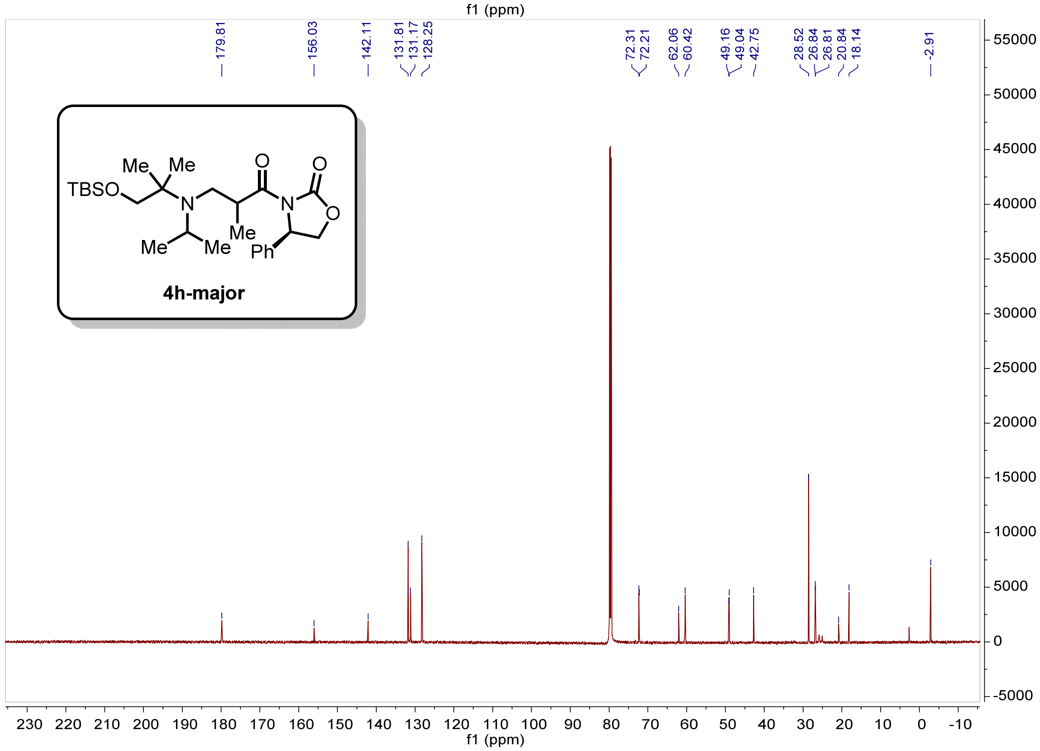

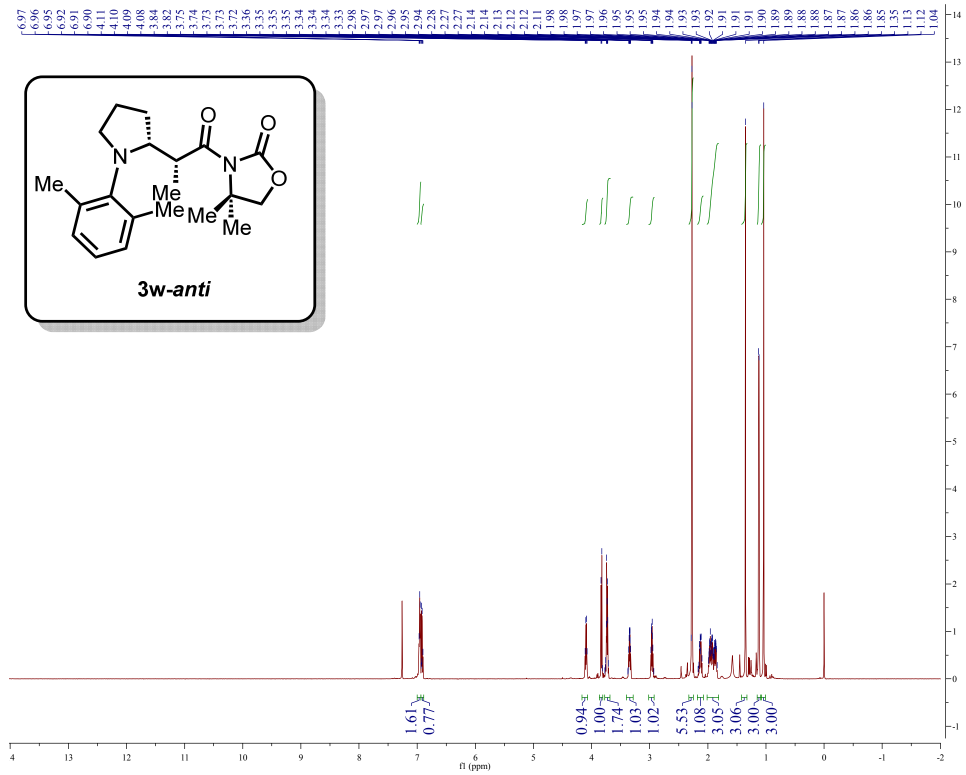
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Me
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O
O
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3w-anti
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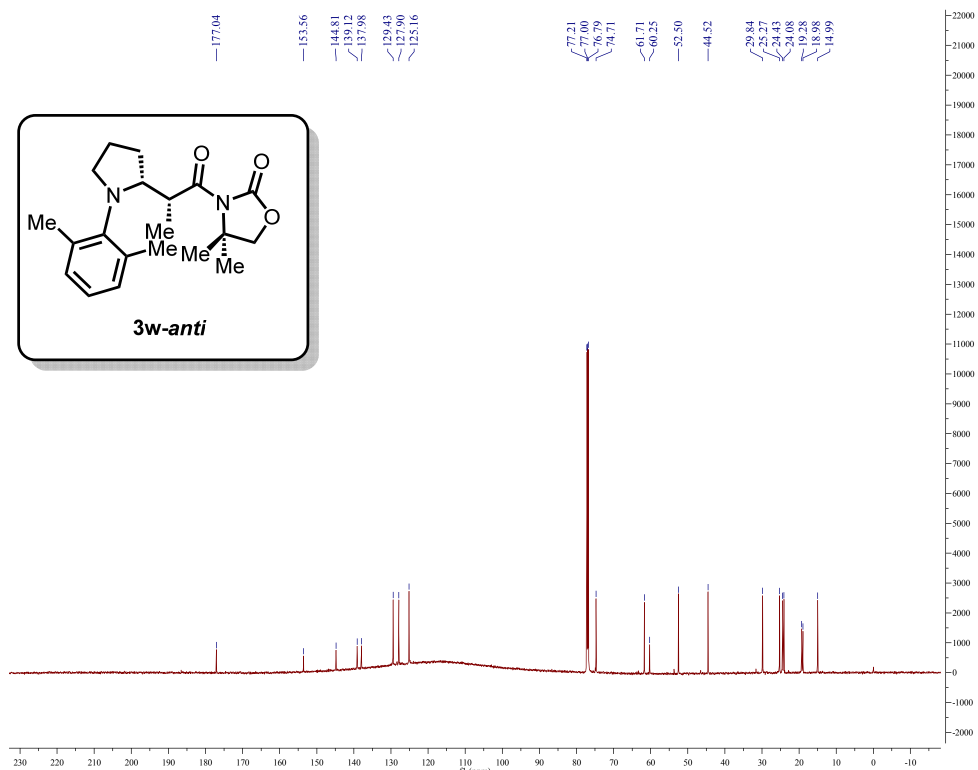
f1 (ppm)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61.71 60.25
52.50
44.52
29.84 25.27 24.43 24.08 19.28 18.98 14.99
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N
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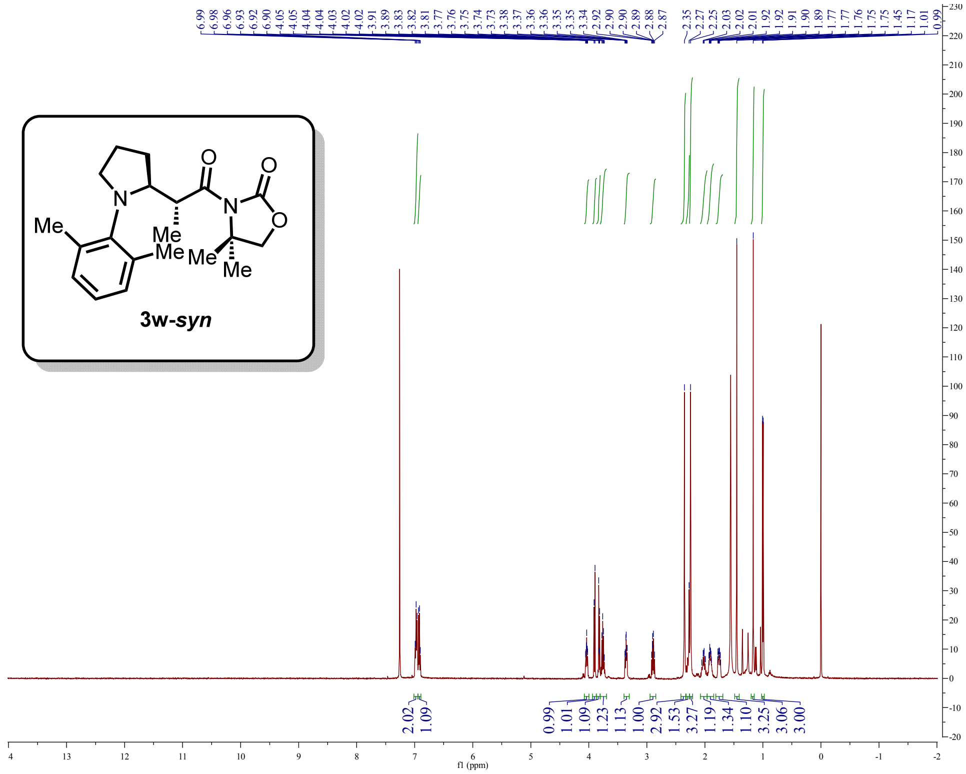
f1 (ppm)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Me
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O
N
O
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1.01
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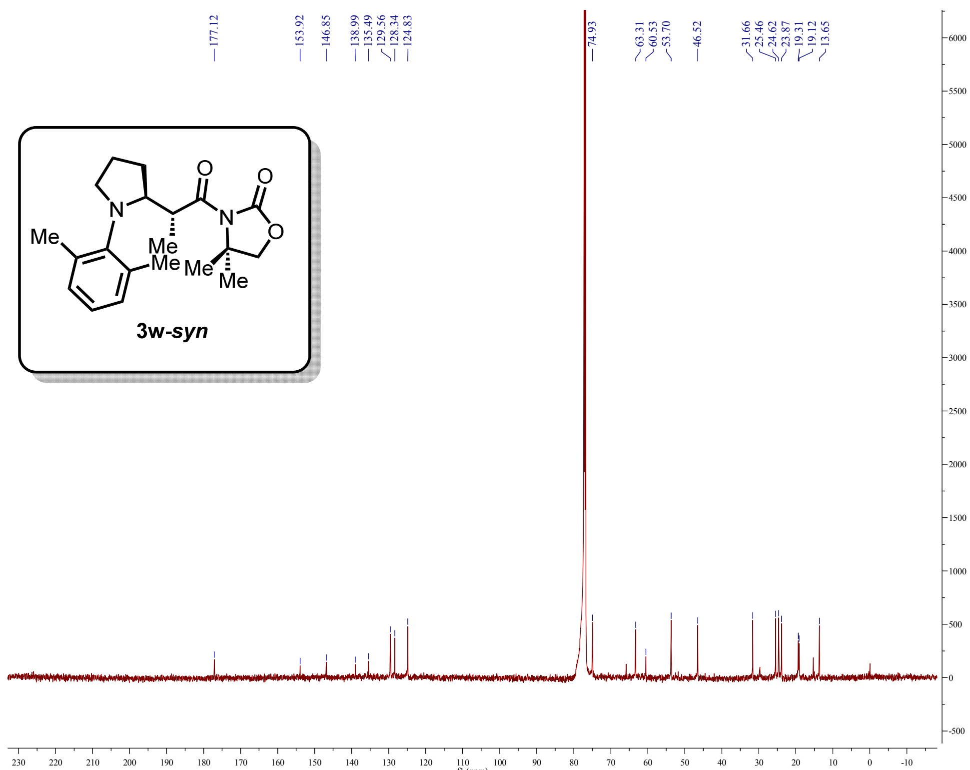
3.00
f1 (ppm)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24.62
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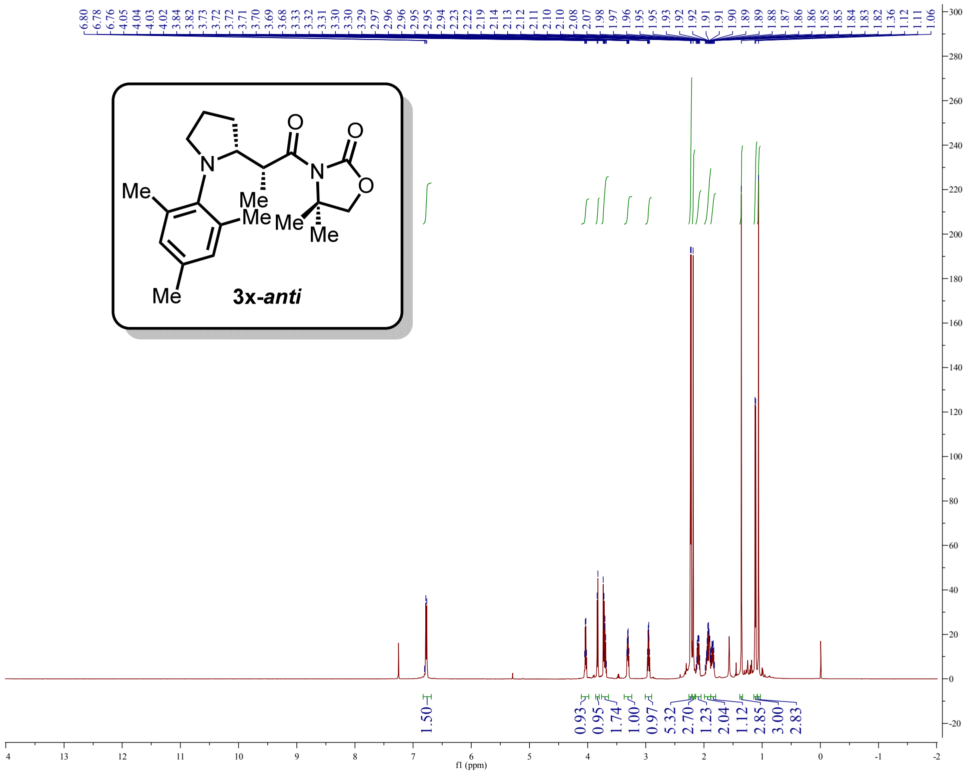
f1 (ppm)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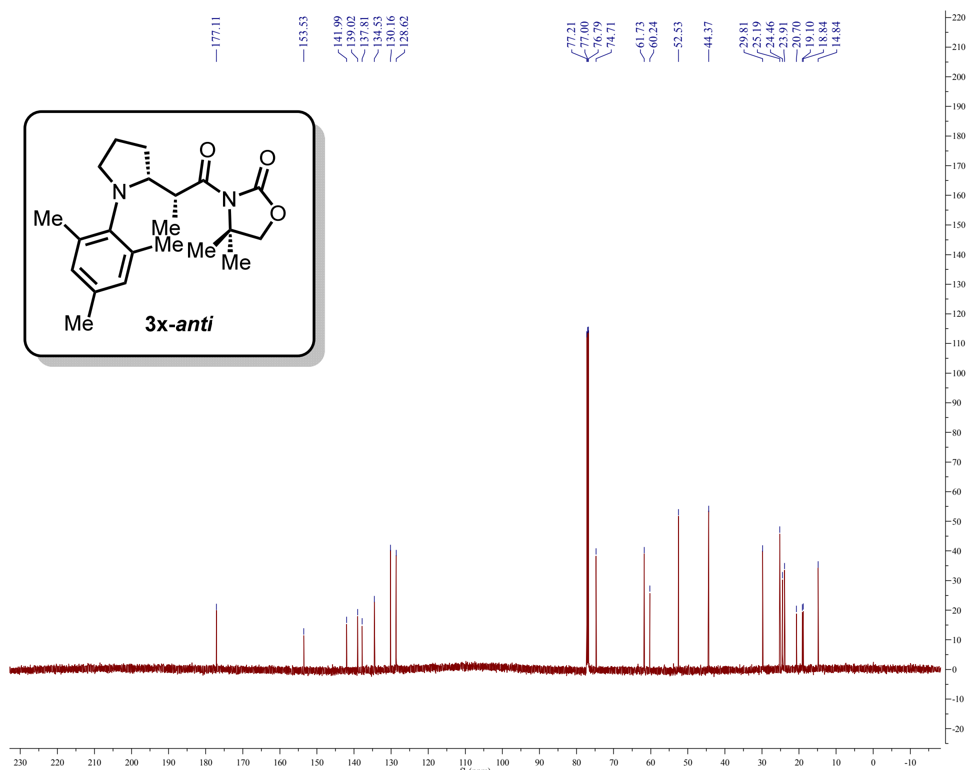
f1 (ppm)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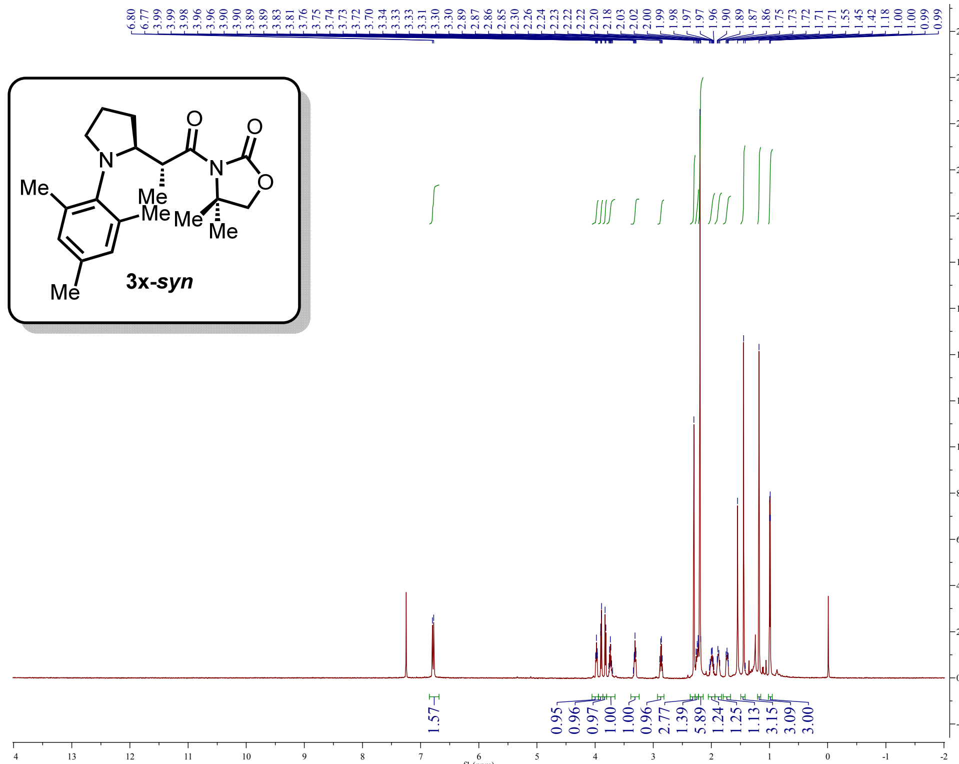
f1 (ppm)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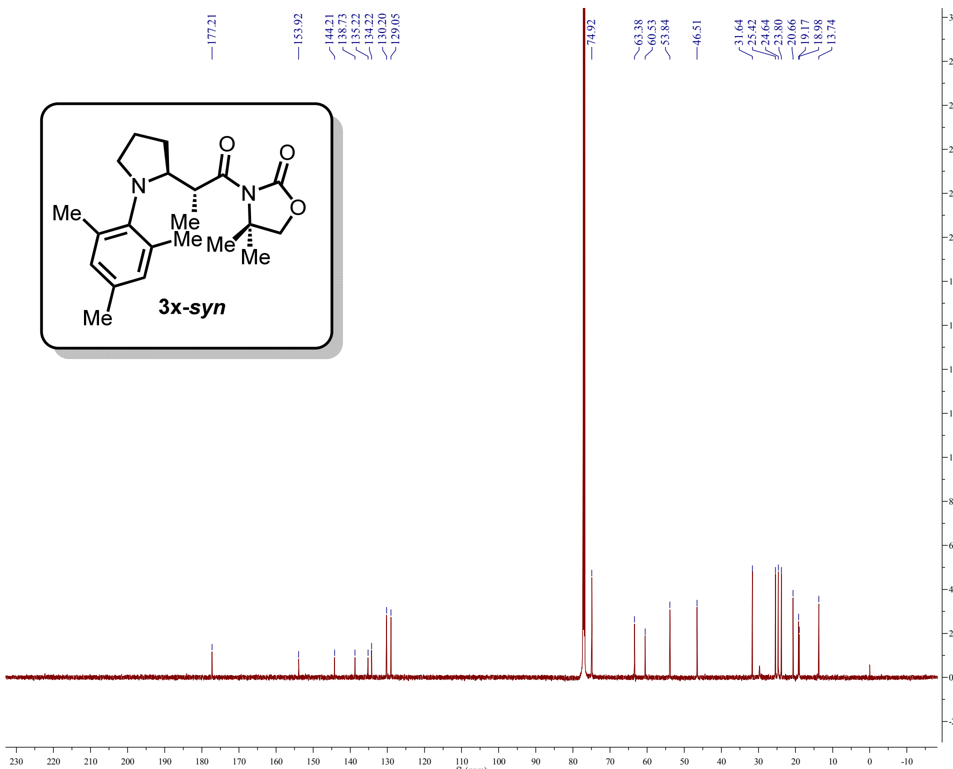
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24.64
23.80
20.66
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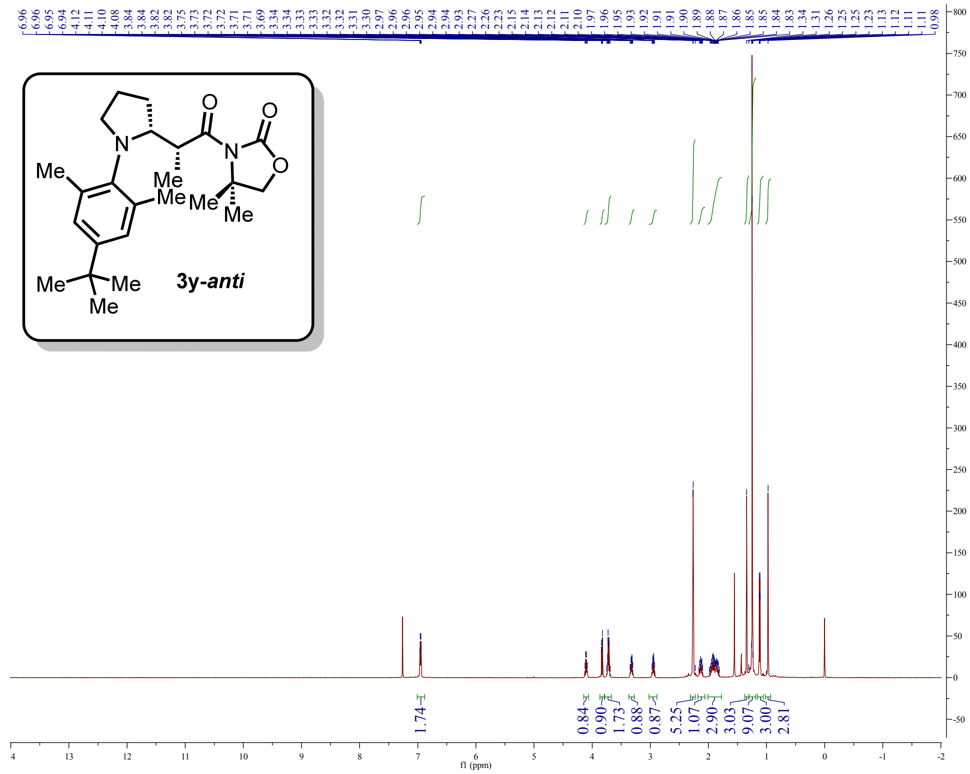
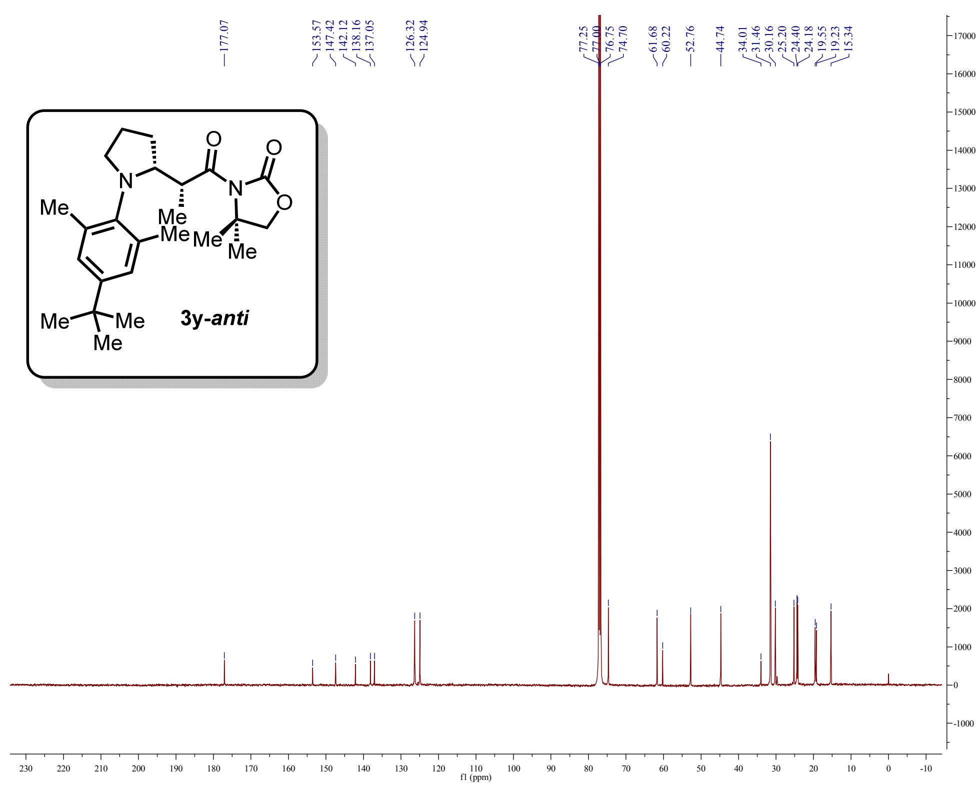
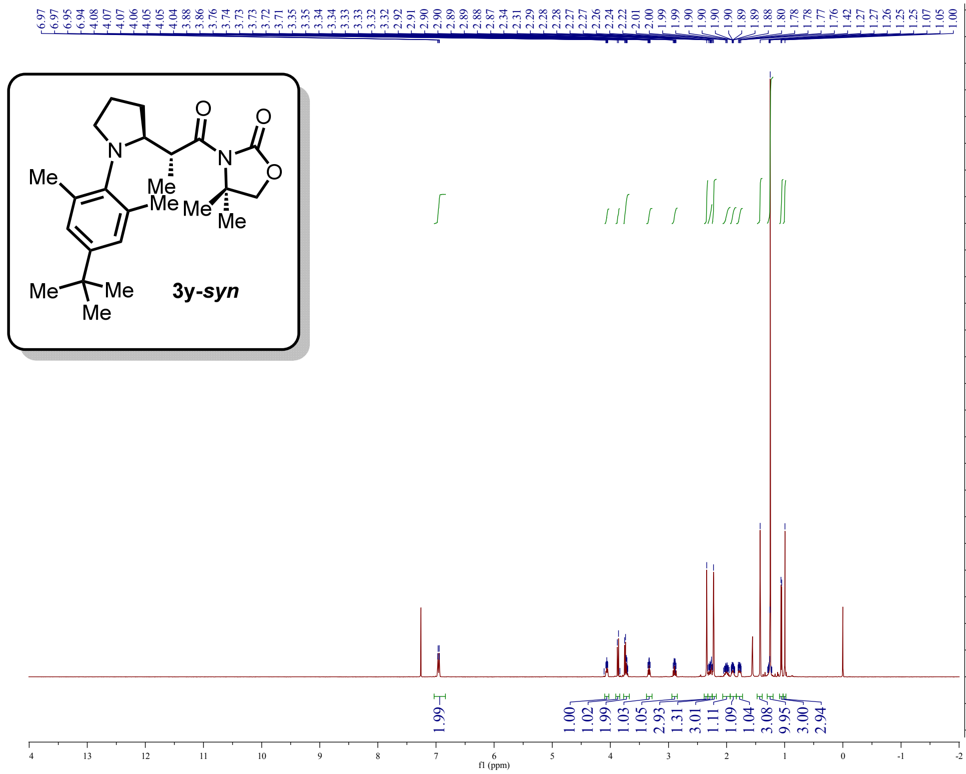
f1 (ppm)



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1.99
1.00 1.02 1.99 1.03 1.05 2.93 1.31 3.01 1.11 1.09 1.04 3.08 9.95 3.00 2.94
f1 (ppm)
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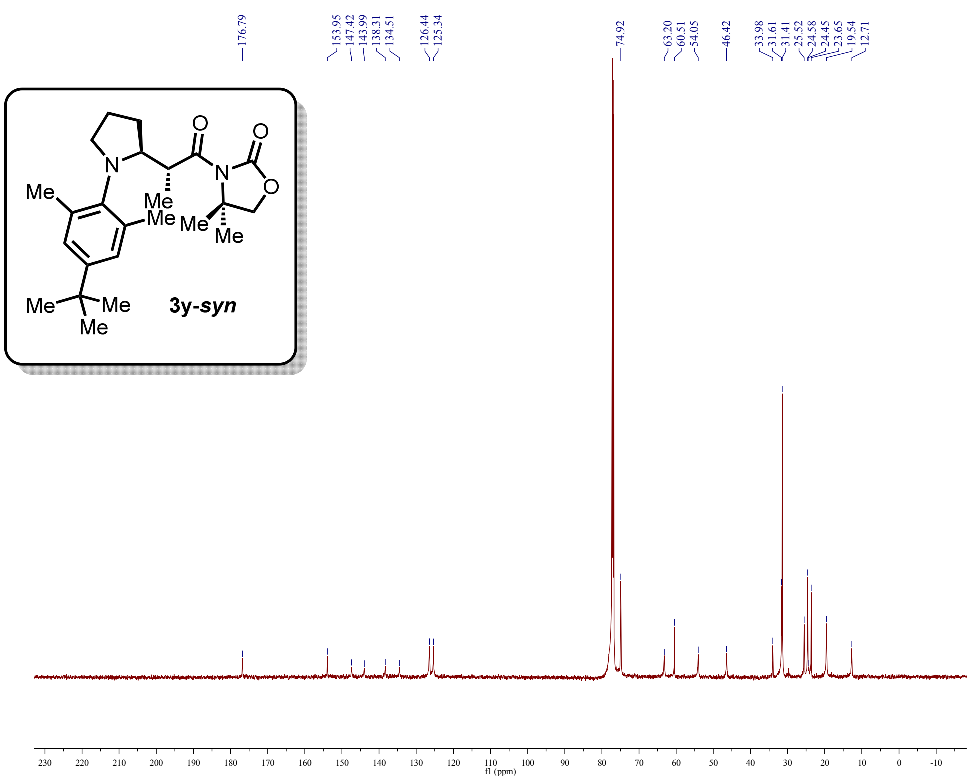
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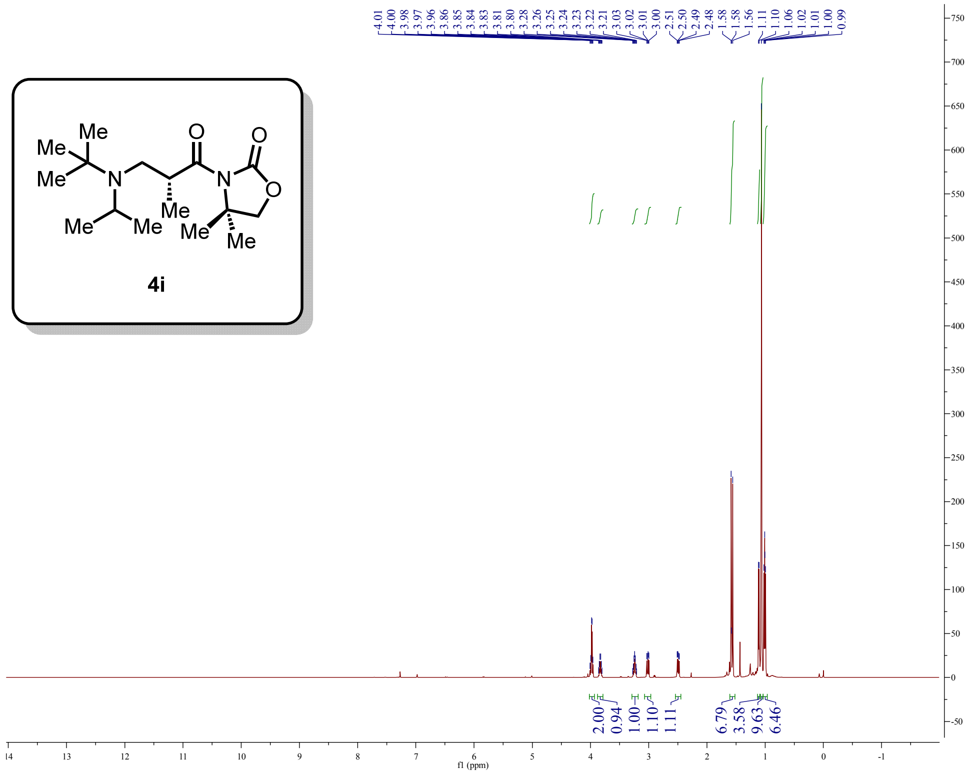
f1 (ppm)
3y-*syn*



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6.46
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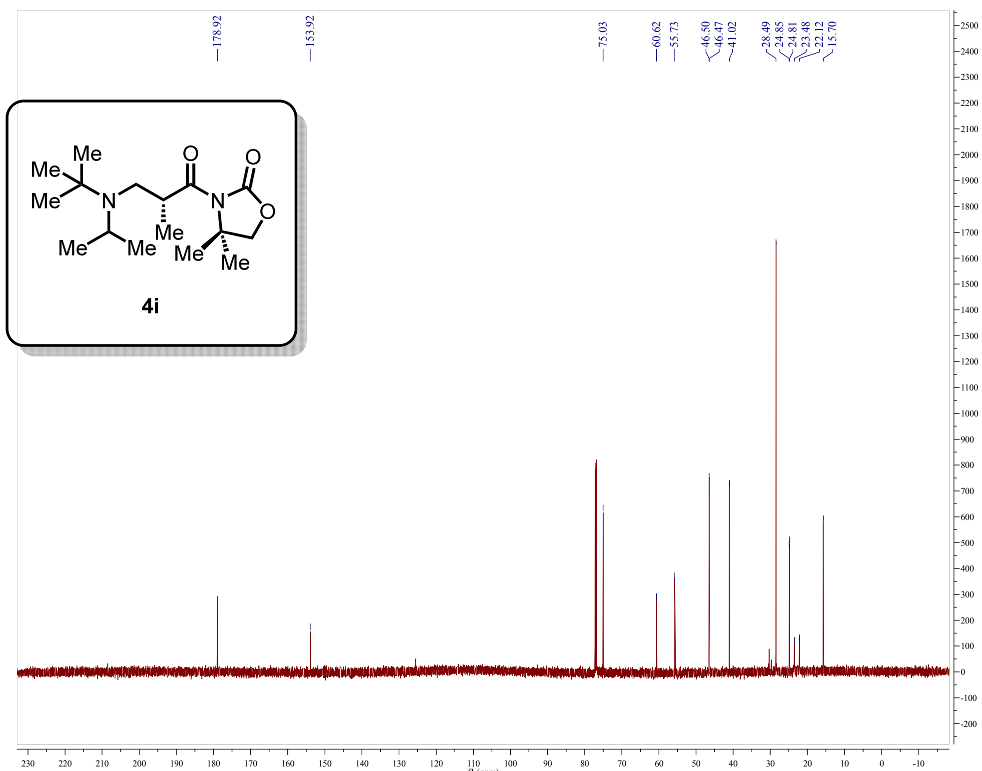

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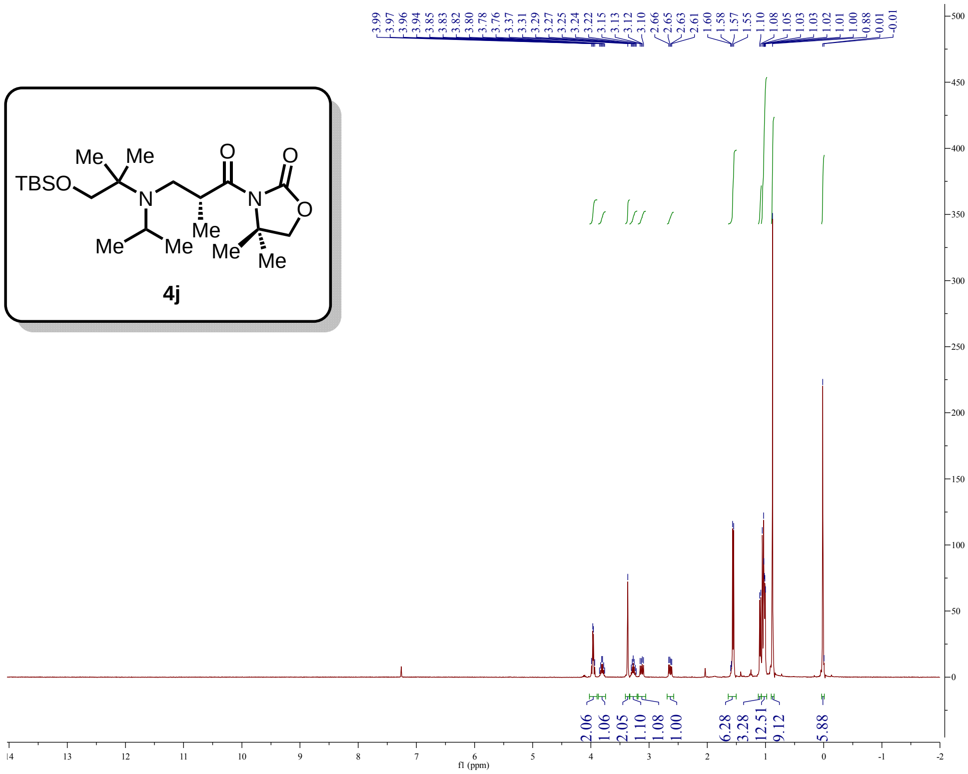
f1 (ppm)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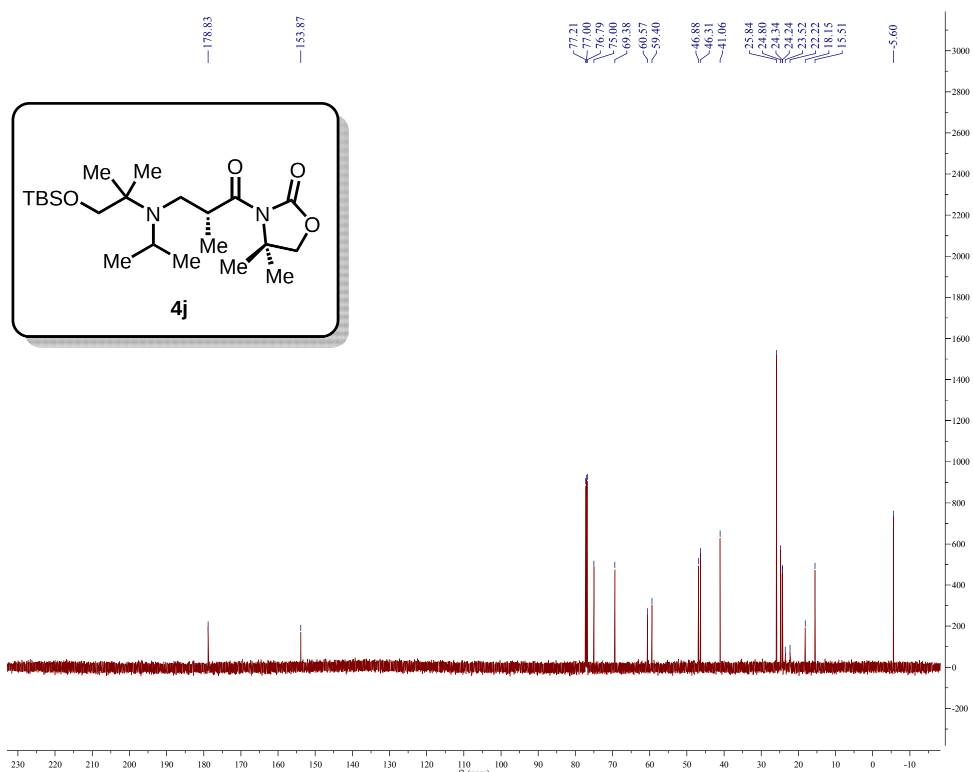
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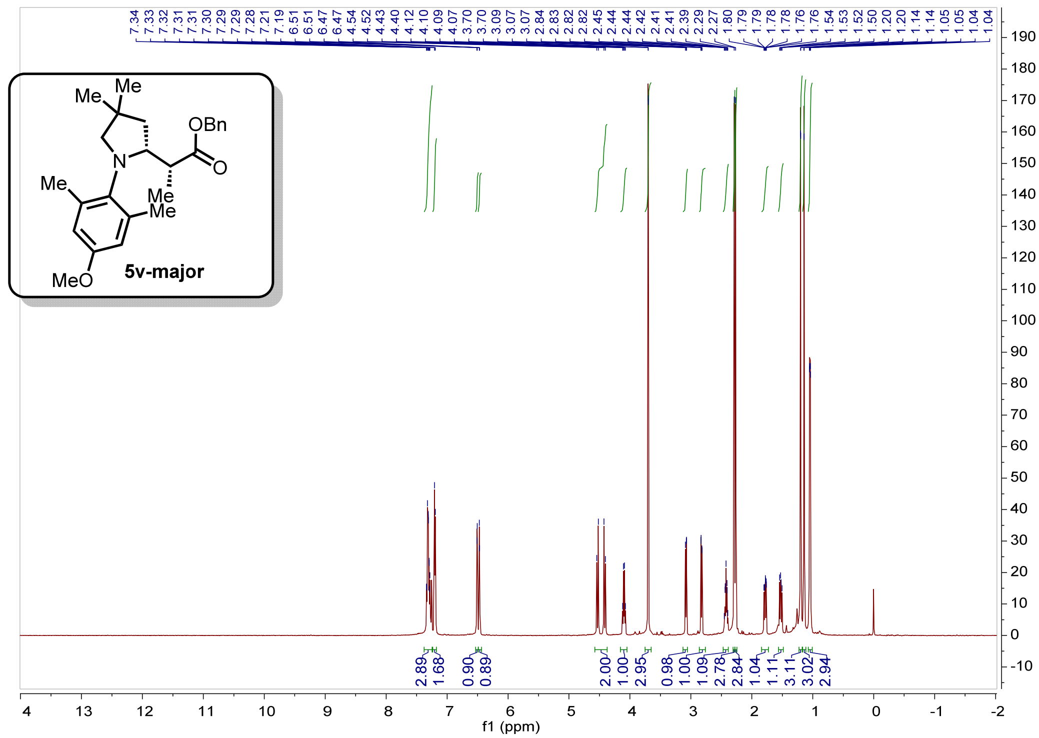
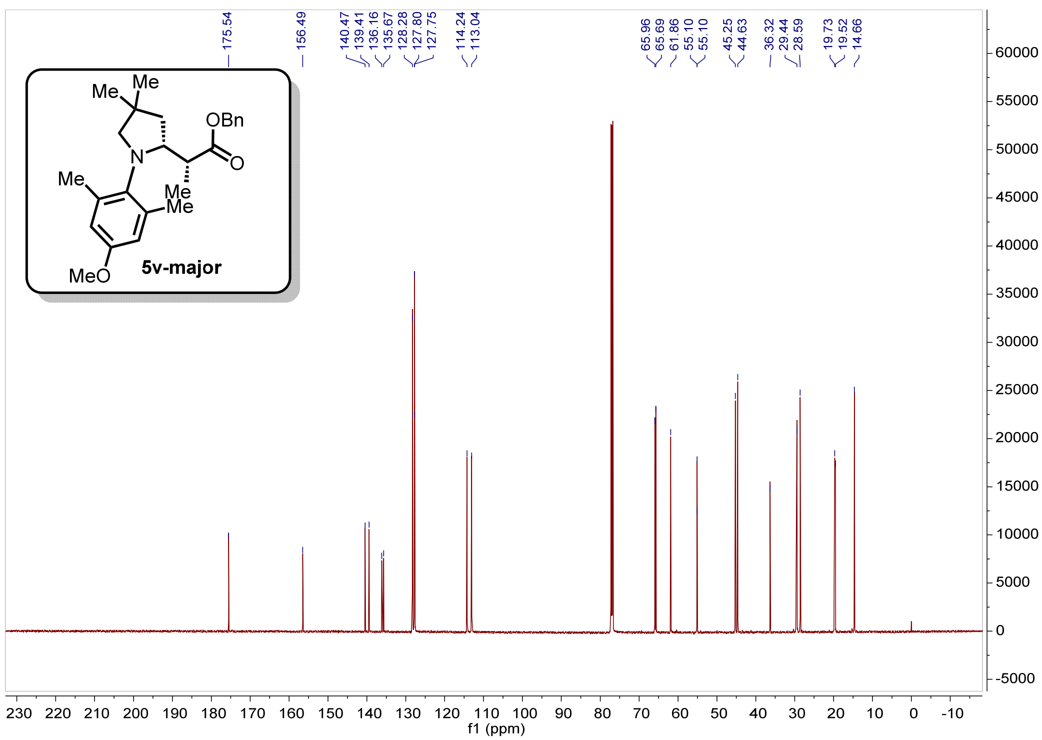
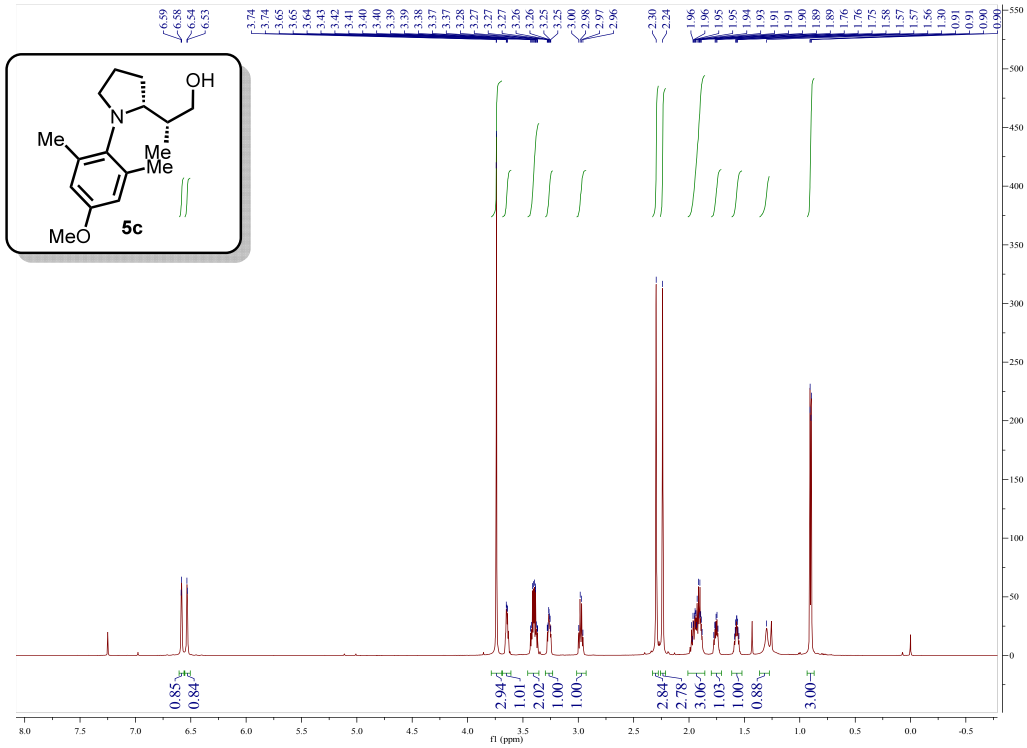
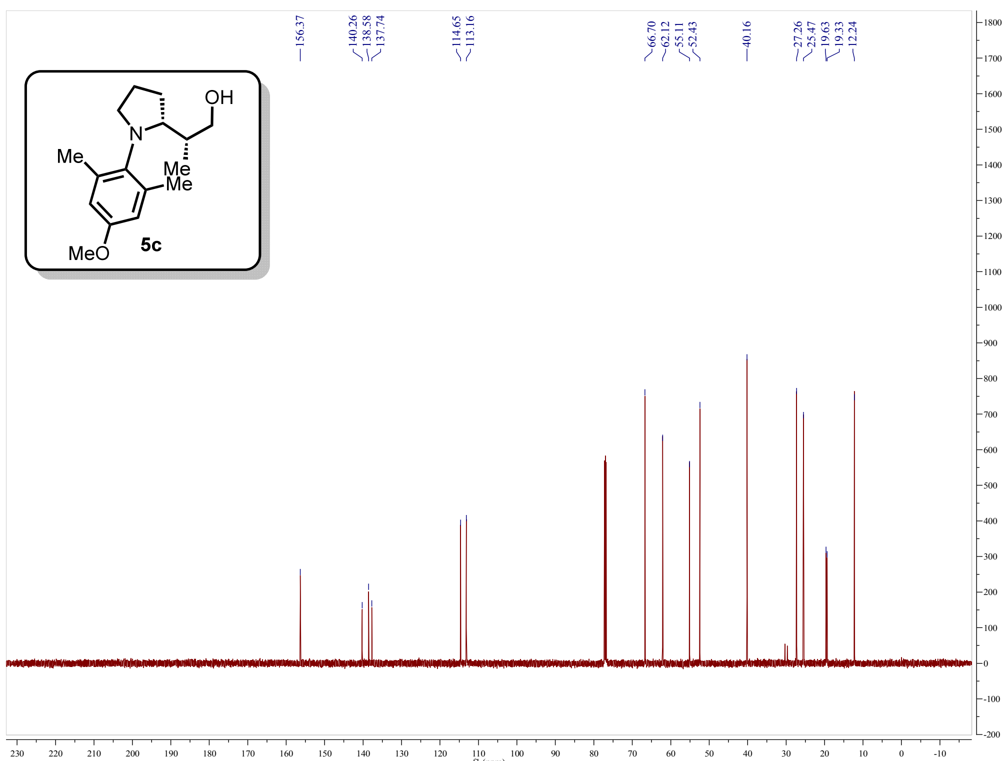
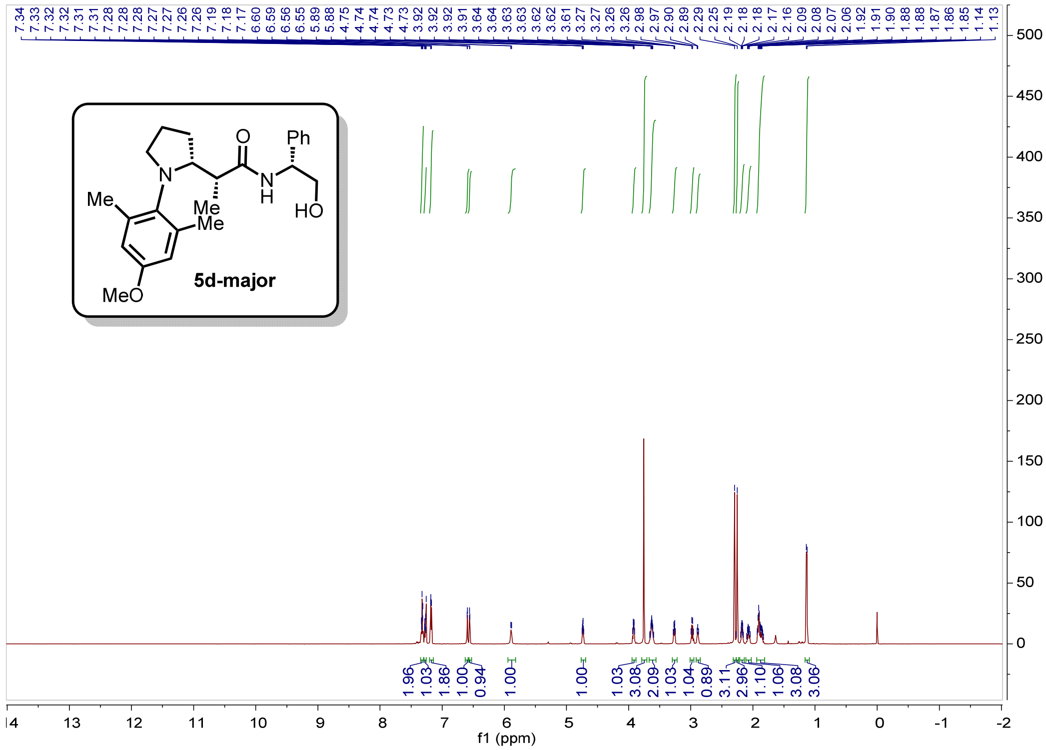
-5.60
f1 (ppm)

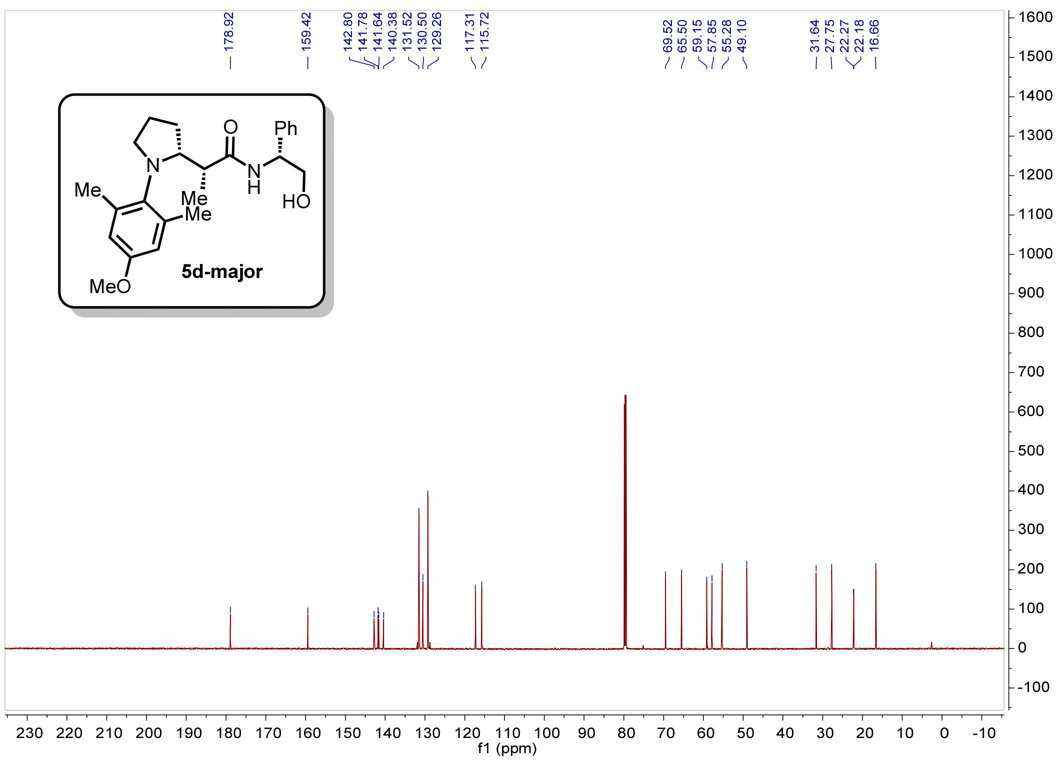









7.34 7.33 7.32 7.31 7.31 7.28 7.28 7.28 7.27 7.27 7.26 7.26 7.19 7.18 7.17 6.60 6.59 6.56 6.55 5.89 5.88 4.75 4.74 4.74 4.73 4.73 3.92 3.92 3.92 3.91 3.64 3.64 3.63 3.63 3.62 3.62 3.61 3.27 3.27 3.26 2.98 2.97 2.90 2.89 2.29 2.25 2.19 2.18 2.18 2.17 2.16 2.09 2.08 2.07 2.06 1.92 1.91 1.90 1.88 1.88 1.87 1.86 1.85 1.14 1.13
Me
Me
Me
O
Ph
N
N
H
HO
MeO
5d-major
1.96 1.03 1.86 1.00 0.94 1.00 1.00 1.03 3.08 2.09 1.03 1.04 0.89 3.11 2.96 1.10 1.06 3.08 3.06
f1 (ppm)


178.92
159.42
142.80 141.78 141.64 140.38 131.52 130.50 129.26
117.31 115.72
69.52 65.50 59.15 57.85 55.28 49.10
31.64 27.75 22.27 22.18 16.66
Me
Me
Me
O
Ph
N
N
H
HO
MeO
5d-major
f1 (ppm)

9. X-Ray Crystallography Data of 5d-major and 5d-minor

X-Ray Crystallography Data of 5d-major

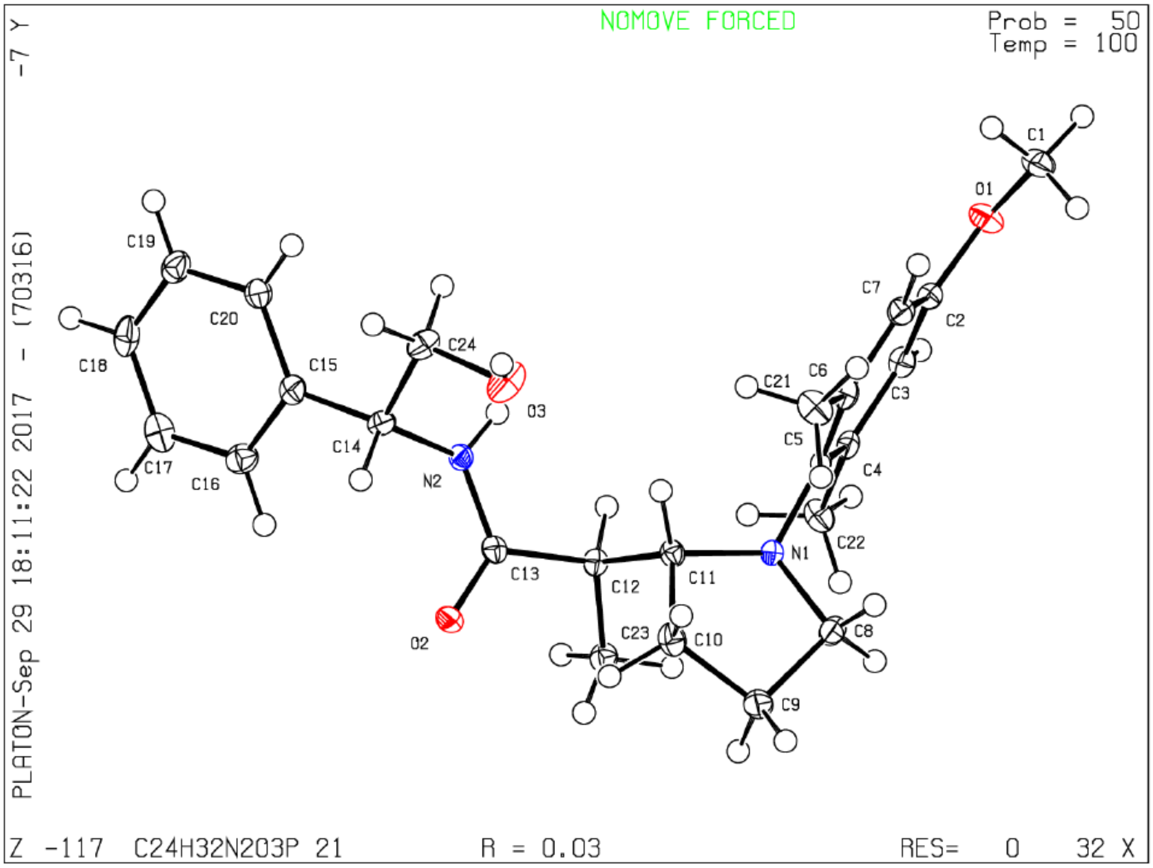


Table SI-10. Crystal data and structure refinement for $C_{24}H_{32}N_2O_3$.

Identification code	$C_{24}H_{32}N_2O_3$	
Empirical formula	C24 H32 N2 O3	
Formula weight	396.51	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 9.6090(4) Å	a= 90°.
	b = 8.9512(4) Å	b= 101.0730(10)°.
	c = 12.4737(5) Å	g = 90°.
Volume	1052.92(8) $Å^3$	
Z	2	

Density (calculated)	1.251 Mg/m^3
Absorption coefficient	0.653 mm^{-1}
F(000)	428
Crystal size	0.560 x 0.460 x 0.280 mm^3
Theta range for data collection	3.611 to 66.644°.
Index ranges	-11<=h<=11, -10<=k<=10, -14<=l<=14
Reflections collected	19999
Independent reflections	3701 [R(int) = 0.0307]
Completeness to theta = 66.644°	99.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7528 and 0.6460
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3701 / 3 / 274
Goodness-of-fit on F^2	1.062
Final R indices [I>2sigma(I)]	R1 = 0.0265, wR2 = 0.0684
R indices (all data)	R1 = 0.0265, wR2 = 0.0684
Absolute structure parameter	0.00(4)
Extinction coefficient	n/a
Largest diff. peak and hole	0.202 and -0.152 e.$Å^{-3}$

Table SI-11. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for $C_{24}H_{32}N_2O_3$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	3778(1)	479(1)	3668(1)	19(1)
O(2)	3233(1)	7976(1)	8767(1)	18(1)
O(3)	5761(1)	4564(2)	9403(1)	24(1)
N(1)	1480(1)	4266(2)	6437(1)	13(1)
N(2)	5086(1)	7038(2)	8098(1)	12(1)
C(1)	4082(2)	-1055(2)	3948(2)	21(1)
C(2)	3296(2)	1369(2)	4423(1)	15(1)
C(3)	2672(2)	2705(2)	4018(1)	15(1)
C(4)	2108(2)	3670(2)	4694(1)	14(1)
C(5)	2169(2)	3294(2)	5797(1)	12(1)
C(6)	2841(2)	1965(2)	6215(1)	14(1)
C(7)	3406(2)	1008(2)	5518(2)	15(1)
C(8)	88(2)	3780(2)	6616(1)	17(1)
C(9)	-193(2)	4773(2)	7542(2)	18(1)
C(10)	1290(2)	5034(2)	8226(1)	17(1)
C(11)	2283(2)	5042(2)	7394(1)	13(1)
C(12)	2722(2)	6636(2)	7062(1)	13(1)
C(13)	3703(2)	7297(2)	8049(1)	12(1)
C(14)	6166(2)	7167(2)	9095(1)	14(1)
C(15)	7229(2)	8400(2)	9002(1)	14(1)
C(16)	6755(2)	9878(2)	8888(2)	19(1)
C(17)	7683(2)	11043(2)	8816(2)	22(1)
C(18)	9111(2)	10750(2)	8856(2)	21(1)
C(19)	9598(2)	9294(2)	8968(1)	20(1)
C(20)	8666(2)	8124(2)	9044(1)	16(1)
C(21)	3003(2)	1548(2)	7406(2)	20(1)
C(22)	1424(2)	5109(2)	4235(1)	18(1)
C(23)	1464(2)	7650(2)	6638(1)	16(1)
C(24)	6834(2)	5629(2)	9354(2)	18(1)

Table SI-12. Bond lengths [Å] and angles [°] for $C_{24}H_{32}N_2O_3$.

O(1)-C(2)	1.380(2)
O(1)-C(1)	1.434(2)
O(2)-C(13)	1.236(2)
O(3)-C(24)	1.415(2)
O(3)-H(3O)	0.85(2)
N(1)-C(5)	1.427(2)
N(1)-C(8)	1.464(2)
N(1)-C(11)	1.466(2)
N(2)-C(13)	1.339(2)
N(2)-C(14)	1.464(2)
N(2)-H(2N)	0.854(18)
C(1)-H(1A)	0.9800
C(1)-H(1B)	0.9800
C(1)-H(1C)	0.9800
C(2)-C(7)	1.388(3)
C(2)-C(3)	1.390(2)
C(3)-C(4)	1.388(2)
C(3)-H(3A)	0.9500
C(4)-C(5)	1.407(2)
C(4)-C(22)	1.508(2)
C(5)-C(6)	1.405(2)
C(6)-C(7)	1.402(3)
C(6)-C(21)	1.510(2)
C(7)-H(7)	0.9500
C(8)-C(9)	1.523(2)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(10)	1.532(2)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(10)-C(11)	1.539(2)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900

C(11)-C(12)	1.566(2)
C(11)-H(11)	1.0000
C(12)-C(13)	1.520(2)
C(12)-C(23)	1.523(2)
C(12)-H(12)	1.0000
C(14)-C(15)	1.524(2)
C(14)-C(24)	1.527(2)
C(14)-H(14)	1.0000
C(15)-C(20)	1.394(2)
C(15)-C(16)	1.397(3)
C(16)-C(17)	1.386(3)
C(16)-H(16)	0.9500
C(17)-C(18)	1.389(3)
C(17)-H(17)	0.9500
C(18)-C(19)	1.383(3)
C(18)-H(18)	0.9500
C(19)-C(20)	1.393(3)
C(19)-H(19)	0.9500
C(20)-H(20)	0.9500
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(24)-H(24A)	0.9900
C(24)-H(24B)	0.9900
C(2)-O(1)-C(1)	117.77(14)
C(24)-O(3)-H(3O)	107.4(18)
C(5)-N(1)-C(8)	116.10(14)
C(5)-N(1)-C(11)	121.06(13)

C(8)-N(1)-C(11)	111.76(13)
C(13)-N(2)-C(14)	124.06(14)
C(13)-N(2)-H(2N)	117.4(14)
C(14)-N(2)-H(2N)	116.3(14)
O(1)-C(1)-H(1A)	109.5
O(1)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5
O(1)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5
H(1B)-C(1)-H(1C)	109.5
O(1)-C(2)-C(7)	124.44(16)
O(1)-C(2)-C(3)	115.22(15)
C(7)-C(2)-C(3)	120.33(15)
C(4)-C(3)-C(2)	120.41(15)
C(4)-C(3)-H(3A)	119.8
C(2)-C(3)-H(3A)	119.8
C(3)-C(4)-C(5)	119.86(16)
C(3)-C(4)-C(22)	119.57(15)
C(5)-C(4)-C(22)	120.57(15)
C(6)-C(5)-C(4)	119.67(15)
C(6)-C(5)-N(1)	122.55(15)
C(4)-C(5)-N(1)	117.71(15)
C(7)-C(6)-C(5)	119.52(16)
C(7)-C(6)-C(21)	118.62(16)
C(5)-C(6)-C(21)	121.84(16)
C(2)-C(7)-C(6)	120.14(16)
C(2)-C(7)-H(7)	119.9
C(6)-C(7)-H(7)	119.9
N(1)-C(8)-C(9)	103.99(14)
N(1)-C(8)-H(8A)	111.0
C(9)-C(8)-H(8A)	111.0
N(1)-C(8)-H(8B)	111.0
C(9)-C(8)-H(8B)	111.0
H(8A)-C(8)-H(8B)	109.0
C(8)-C(9)-C(10)	103.33(14)

C(8)-C(9)-H(9A)	111.1
C(10)-C(9)-H(9A)	111.1
C(8)-C(9)-H(9B)	111.1
C(10)-C(9)-H(9B)	111.1
H(9A)-C(9)-H(9B)	109.1
C(9)-C(10)-C(11)	104.84(14)
C(9)-C(10)-H(10A)	110.8
C(11)-C(10)-H(10A)	110.8
C(9)-C(10)-H(10B)	110.8
C(11)-C(10)-H(10B)	110.8
H(10A)-C(10)-H(10B)	108.9
N(1)-C(11)-C(10)	104.45(13)
N(1)-C(11)-C(12)	110.05(13)
C(10)-C(11)-C(12)	114.55(14)
N(1)-C(11)-H(11)	109.2
C(10)-C(11)-H(11)	109.2
C(12)-C(11)-H(11)	109.2
C(13)-C(12)-C(23)	112.13(14)
C(13)-C(12)-C(11)	107.31(14)
C(23)-C(12)-C(11)	113.50(14)
C(13)-C(12)-H(12)	107.9
C(23)-C(12)-H(12)	107.9
C(11)-C(12)-H(12)	107.9
O(2)-C(13)-N(2)	123.33(15)
O(2)-C(13)-C(12)	121.49(15)
N(2)-C(13)-C(12)	115.13(14)
N(2)-C(14)-C(15)	111.66(14)
N(2)-C(14)-C(24)	108.00(14)
C(15)-C(14)-C(24)	114.08(13)
N(2)-C(14)-H(14)	107.6
C(15)-C(14)-H(14)	107.6
C(24)-C(14)-H(14)	107.6
C(20)-C(15)-C(16)	118.26(17)
C(20)-C(15)-C(14)	122.85(16)
C(16)-C(15)-C(14)	118.87(15)

C(17)-C(16)-C(15)	121.15(17)
C(17)-C(16)-H(16)	119.4
C(15)-C(16)-H(16)	119.4
C(16)-C(17)-C(18)	119.96(18)
C(16)-C(17)-H(17)	120.0
C(18)-C(17)-H(17)	120.0
C(19)-C(18)-C(17)	119.60(17)
C(19)-C(18)-H(18)	120.2
C(17)-C(18)-H(18)	120.2
C(18)-C(19)-C(20)	120.45(17)
C(18)-C(19)-H(19)	119.8
C(20)-C(19)-H(19)	119.8
C(19)-C(20)-C(15)	120.58(17)
C(19)-C(20)-H(20)	119.7
C(15)-C(20)-H(20)	119.7
C(6)-C(21)-H(21A)	109.5
C(6)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(6)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(4)-C(22)-H(22A)	109.5
C(4)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(4)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(12)-C(23)-H(23A)	109.5
C(12)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(12)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
O(3)-C(24)-C(14)	109.66(14)
O(3)-C(24)-H(24A)	109.7

C(14)-C(24)-H(24A)	109.7
O(3)-C(24)-H(24B)	109.7
C(14)-C(24)-H(24B)	109.7
H(24A)-C(24)-H(24B)	108.2

Symmetry transformations used to generate equivalent atoms:

Table SI-13. Anisotropic displacement parameters ($Å^2$x 10^3) for $C_{24}H_{32}N_2O_3$. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	24(1)	17(1)	18(1)	-1(1)	9(1)	4(1)
O(2)	15(1)	19(1)	19(1)	-7(1)	1(1)	3(1)
O(3)	20(1)	25(1)	26(1)	14(1)	-1(1)	-4(1)
N(1)	11(1)	14(1)	13(1)	-3(1)	1(1)	-1(1)
N(2)	13(1)	14(1)	10(1)	-2(1)	2(1)	-1(1)
C(1)	21(1)	16(1)	26(1)	-2(1)	7(1)	4(1)
C(2)	12(1)	16(1)	17(1)	-3(1)	4(1)	-2(1)
C(3)	16(1)	17(1)	11(1)	1(1)	2(1)	-2(1)
C(4)	12(1)	14(1)	14(1)	-1(1)	-1(1)	-3(1)
C(5)	11(1)	12(1)	13(1)	-2(1)	2(1)	-4(1)
C(6)	13(1)	13(1)	16(1)	1(1)	2(1)	-4(1)
C(7)	14(1)	11(1)	20(1)	2(1)	2(1)	0(1)
C(8)	13(1)	21(1)	18(1)	-3(1)	3(1)	-3(1)
C(9)	18(1)	18(1)	19(1)	-3(1)	8(1)	-2(1)
C(10)	22(1)	17(1)	13(1)	-1(1)	4(1)	-3(1)
C(11)	14(1)	12(1)	12(1)	0(1)	1(1)	0(1)
C(12)	13(1)	13(1)	12(1)	0(1)	1(1)	-1(1)
C(13)	15(1)	8(1)	13(1)	2(1)	2(1)	0(1)
C(14)	12(1)	19(1)	10(1)	0(1)	2(1)	1(1)
C(15)	16(1)	20(1)	7(1)	-2(1)	1(1)	-1(1)
C(16)	17(1)	21(1)	17(1)	1(1)	2(1)	2(1)
C(17)	30(1)	18(1)	18(1)	-1(1)	2(1)	-2(1)
C(18)	25(1)	25(1)	14(1)	-3(1)	3(1)	-11(1)
C(19)	16(1)	29(1)	15(1)	-6(1)	3(1)	-5(1)
C(20)	16(1)	21(1)	11(1)	-4(1)	1(1)	0(1)
C(21)	28(1)	17(1)	16(1)	4(1)	5(1)	2(1)
C(22)	24(1)	15(1)	13(1)	0(1)	1(1)	2(1)
C(23)	16(1)	15(1)	16(1)	1(1)	0(1)	0(1)
C(24)	14(1)	20(1)	19(1)	5(1)	2(1)	0(1)

Table SI-14. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for $C_{24}H_{32}N_2O_3$.

	x	y	z	U(eq)
H(3O)	6050(30)	4010(30)	9961(19)	34(7)
H(2N)	5320(20)	6540(20)	7575(16)	12(5)
H(1A)	4909	-1113	4545	31
H(1B)	4284	-1591	3310	31
H(1C)	3263	-1512	4182	31
H(3A)	2630	2960	3273	18
H(7)	3866	110	5797	18
H(8A)	105	2713	6827	21
H(8B)	-647	3927	5950	21
H(9A)	-814	4266	7976	21
H(9B)	-639	5727	7258	21
H(10A)	1551	4224	8767	20
H(10B)	1334	6001	8617	20
H(11)	3156	4455	7694	15
H(12)	3277	6515	6467	16
H(14)	5672	7442	9704	16
H(16)	5779	10088	8859	22
H(17)	7342	12041	8738	27
H(18)	9750	11546	8806	26
H(19)	10574	9090	8995	24
H(20)	9013	7128	9124	20
H(21A)	3183	473	7492	30
H(21B)	2130	1798	7664	30
H(21C)	3800	2101	7834	30
H(22A)	467	5178	4397	26
H(22B)	1366	5128	3442	26
H(22C)	1993	5957	4568	26
H(23A)	980	7902	7238	24
H(23B)	802	7132	6061	24

H(23C)	1800	8567	6342	24
H(24A)	7368	5341	8782	22
H(24B)	7506	5662	10063	22

Table SI-15. Torsion angles [°] for $C_{24}H_{32}N_2O_3$.

C(1)-O(1)-C(2)-C(7)	16.3(2)
C(1)-O(1)-C(2)-C(3)	-163.85(15)
O(1)-C(2)-C(3)-C(4)	178.00(15)
C(7)-C(2)-C(3)-C(4)	-2.2(2)
C(2)-C(3)-C(4)-C(5)	0.0(2)
C(2)-C(3)-C(4)-C(22)	-179.48(15)
C(3)-C(4)-C(5)-C(6)	2.0(2)
C(22)-C(4)-C(5)-C(6)	-178.54(15)
C(3)-C(4)-C(5)-N(1)	-175.27(14)
C(22)-C(4)-C(5)-N(1)	4.2(2)
C(8)-N(1)-C(5)-C(6)	-76.47(19)
C(11)-N(1)-C(5)-C(6)	64.5(2)
C(8)-N(1)-C(5)-C(4)	100.69(18)
C(11)-N(1)-C(5)-C(4)	-118.33(17)
C(4)-C(5)-C(6)-C(7)	-1.8(2)
N(1)-C(5)-C(6)-C(7)	175.31(15)
C(4)-C(5)-C(6)-C(21)	176.78(16)
N(1)-C(5)-C(6)-C(21)	-6.1(2)
O(1)-C(2)-C(7)-C(6)	-177.86(15)
C(3)-C(2)-C(7)-C(6)	2.3(2)
C(5)-C(6)-C(7)-C(2)	-0.3(2)
C(21)-C(6)-C(7)-C(2)	-178.97(16)
C(5)-N(1)-C(8)-C(9)	165.36(14)
C(11)-N(1)-C(8)-C(9)	20.86(19)
N(1)-C(8)-C(9)-C(10)	-32.52(18)
C(8)-C(9)-C(10)-C(11)	32.71(18)
C(5)-N(1)-C(11)-C(10)	-142.80(15)
C(8)-N(1)-C(11)-C(10)	-0.30(18)
C(5)-N(1)-C(11)-C(12)	93.78(17)
C(8)-N(1)-C(11)-C(12)	-123.72(15)
C(9)-C(10)-C(11)-N(1)	-20.34(17)
C(9)-C(10)-C(11)-C(12)	100.12(17)
N(1)-C(11)-C(12)-C(13)	-172.91(13)

C(10)-C(11)-C(12)-C(13)	69.79(18)
N(1)-C(11)-C(12)-C(23)	62.63(17)
C(10)-C(11)-C(12)-C(23)	-54.7(2)
C(14)-N(2)-C(13)-O(2)	16.3(3)
C(14)-N(2)-C(13)-C(12)	-161.18(15)
C(23)-C(12)-C(13)-O(2)	39.1(2)
C(11)-C(12)-C(13)-O(2)	-86.24(18)
C(23)-C(12)-C(13)-N(2)	-143.46(15)
C(11)-C(12)-C(13)-N(2)	91.25(16)
C(13)-N(2)-C(14)-C(15)	-116.08(17)
C(13)-N(2)-C(14)-C(24)	117.72(17)
N(2)-C(14)-C(15)-C(20)	-116.86(17)
C(24)-C(14)-C(15)-C(20)	5.9(2)
N(2)-C(14)-C(15)-C(16)	64.2(2)
C(24)-C(14)-C(15)-C(16)	-172.99(16)
C(20)-C(15)-C(16)-C(17)	0.1(3)
C(14)-C(15)-C(16)-C(17)	179.08(15)
C(15)-C(16)-C(17)-C(18)	0.0(3)
C(16)-C(17)-C(18)-C(19)	0.0(3)
C(17)-C(18)-C(19)-C(20)	-0.1(3)
C(18)-C(19)-C(20)-C(15)	0.3(3)
C(16)-C(15)-C(20)-C(19)	-0.2(2)
C(14)-C(15)-C(20)-C(19)	-179.18(15)
N(2)-C(14)-C(24)-O(3)	-54.14(18)
C(15)-C(14)-C(24)-O(3)	-178.91(13)

Symmetry transformations used to generate equivalent atoms:

Table SI-16. Hydrogen bonds for $C_{24}H_{32}N_2O_3$ [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(3)-H(3O)...O(2)#1	0.85(2)	1.85(2)	2.7054(18)	175(3)
N(2)-H(2N)...O(1)#2	0.854(18)	2.139(19)	2.9855(19)	170.7(19)

Symmetry transformations used to generate equivalent atoms:
#1 -x+1,y-1/2,-z+2 #2 -x+1,y+1/2,-z+1

X-Ray Crystallography Data of 5d-minor

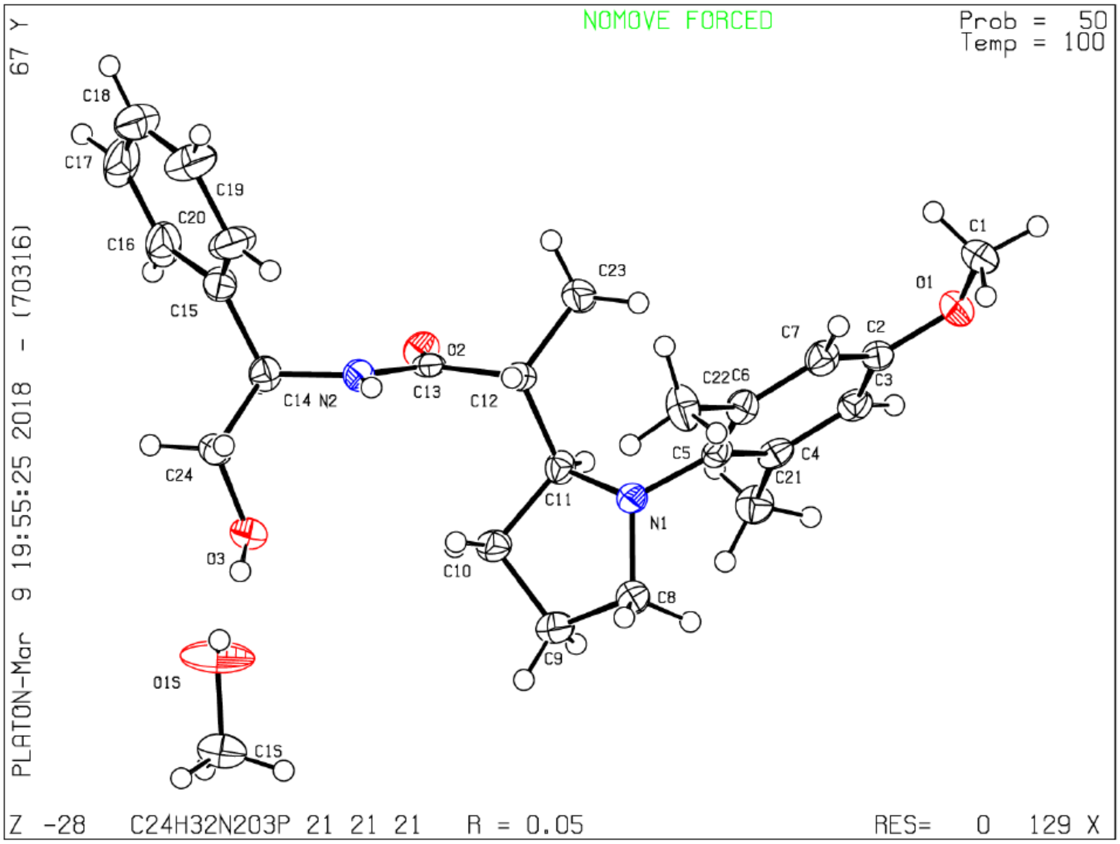


Table SI-17. Crystal data and structure refinement for $C_{24}H_{32}N_2O_3(CH_3OH)$.

Identification code	$C_{24}H_{32}N_2O_3(CH_3OH)$	
Empirical formula	C25 H36 N2 O4	
Formula weight	428.56	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.8167(3) Å	α= 90°.
	b = 15.1723(5) Å	β= 90°.
	c = 20.1325(7) Å	γ = 90°.
Volume	2387.66(15) $Å^3$	
Z	4	
Density (calculated)	1.192 Mg/m^3	
Absorption coefficient	0.642 mm^{-1}	

F(000)	928
Crystal size	0.420 x 0.120 x 0.080 mm^3
Theta range for data collection	3.648 to 66.655°.
Index ranges	-9<=h<=9, -18<=k<=18, -23<=l<=23
Reflections collected	16235
Independent reflections	4210 [R(int) = 0.0707]
Completeness to theta = 66.655°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7533 and 0.5967
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4210 / 3 / 291
Goodness-of-fit on F^2	1.026
Final R indices [I>2sigma(I)]	R1 = 0.0461, wR2 = 0.1154
R indices (all data)	R1 = 0.0574, wR2 = 0.1232
Absolute structure parameter	0.4(2)
Extinction coefficient	n/a
Largest diff. peak and hole	0.329 and -0.277 e.Å^{-3}

Table SI-18. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103) for $C_{24}H_{32}N_2O_3(CH_3OH)$. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1)	6880(3)	8180(2)	6883(1)	30(1)
O(2)	447(3)	3858(2)	6329(1)	27(1)
O(3)	844(3)	2292(2)	4622(1)	29(1)
N(1)	4030(3)	5621(2)	5210(1)	23(1)
N(2)	2348(3)	2929(2)	5834(1)	23(1)
C(1)	8564(5)	8055(2)	7136(2)	34(1)
C(2)	6263(4)	7545(2)	6459(2)	24(1)
C(3)	4600(5)	7669(2)	6227(2)	26(1)
C(4)	3840(4)	7059(2)	5808(2)	24(1)
C(5)	4759(4)	6301(2)	5619(2)	22(1)
C(6)	6457(4)	6202(2)	5827(2)	26(1)
C(7)	7195(4)	6821(2)	6252(2)	27(1)
C(8)	3785(5)	5818(2)	4498(2)	29(1)
C(9)	2138(5)	5349(2)	4310(2)	34(1)
C(10)	1970(5)	4630(2)	4834(2)	28(1)
C(11)	2608(4)	5086(2)	5465(2)	24(1)
C(12)	3190(4)	4437(2)	6013(2)	22(1)
C(13)	1866(4)	3714(2)	6078(2)	22(1)
C(14)	1262(4)	2154(2)	5799(2)	25(1)
C(15)	1653(5)	1492(2)	6348(2)	32(1)
C(16)	348(6)	1077(3)	6685(2)	43(1)
C(17)	744(8)	456(3)	7186(2)	56(1)
C(18)	2407(8)	270(3)	7337(2)	55(1)
C(19)	3694(8)	661(3)	6996(2)	58(1)
C(20)	3326(6)	1271(3)	6503(2)	43(1)
C(21)	2027(4)	7231(2)	5579(2)	31(1)
C(22)	7494(5)	5420(2)	5612(2)	35(1)
C(23)	3432(5)	4884(2)	6690(2)	32(1)
C(24)	1480(4)	1717(2)	5124(2)	26(1)

C(1S)	1972(5)	2149(3)	2839(2)	41(1)
O(1S)	2391(4)	1889(3)	3488(1)	59(1)

Table SI-19. Bond lengths [Å] and angles [°] for $C_{24}H_{32}N_2O_3(CH_3OH)$.

O(1)-C(2)	1.376(4)
O(1)-C(1)	1.424(4)
O(2)-C(13)	1.238(4)
O(3)-C(24)	1.422(4)
O(3)-H(3O)	0.84(2)
N(1)-C(5)	1.438(4)
N(1)-C(11)	1.469(4)
N(1)-C(8)	1.476(4)
N(2)-C(13)	1.343(4)
N(2)-C(14)	1.452(4)
N(2)-H(2N)	0.88(2)
C(1)-H(1A)	0.9800
C(1)-H(1B)	0.9800
C(1)-H(1C)	0.9800
C(2)-C(7)	1.383(5)
C(2)-C(3)	1.394(5)
C(3)-C(4)	1.385(5)
C(3)-H(3)	0.9500
C(4)-C(5)	1.408(5)
C(4)-C(21)	1.513(5)
C(5)-C(6)	1.399(5)
C(6)-C(7)	1.395(5)
C(6)-C(22)	1.501(5)
C(7)-H(7)	0.9500
C(8)-C(9)	1.519(5)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(10)	1.523(5)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(10)-C(11)	1.531(5)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900

C(11)-C(12)	1.547(4)
C(11)-H(11)	1.0000
C(12)-C(13)	1.514(5)
C(12)-C(23)	1.535(5)
C(12)-H(12)	1.0000
C(14)-C(24)	1.522(4)
C(14)-C(15)	1.524(5)
C(14)-H(14)	1.0000
C(15)-C(16)	1.378(5)
C(15)-C(20)	1.386(6)
C(16)-C(17)	1.414(7)
C(16)-H(16)	0.9500
C(17)-C(18)	1.365(8)
C(17)-H(17)	0.9500
C(18)-C(19)	1.355(8)
C(18)-H(18)	0.9500
C(19)-C(20)	1.386(6)
C(19)-H(19)	0.9500
C(20)-H(20)	0.9500
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(24)-H(24A)	0.9900
C(24)-H(24B)	0.9900
C(1S)-O(1S)	1.403(5)
C(1S)-H(1S1)	0.9800
C(1S)-H(1S2)	0.9800
C(1S)-H(1S3)	0.9800
O(1S)-H(1SO)	0.85(3)

C(2)-O(1)-C(1)	116.9(3)
C(24)-O(3)-H(3O)	106(3)
C(5)-N(1)-C(11)	119.7(2)
C(5)-N(1)-C(8)	117.6(2)
C(11)-N(1)-C(8)	110.7(3)
C(13)-N(2)-C(14)	124.9(3)
C(13)-N(2)-H(2N)	116(3)
C(14)-N(2)-H(2N)	119(3)
O(1)-C(1)-H(1A)	109.5
O(1)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5
O(1)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5
H(1B)-C(1)-H(1C)	109.5
O(1)-C(2)-C(7)	124.0(3)
O(1)-C(2)-C(3)	116.2(3)
C(7)-C(2)-C(3)	119.8(3)
C(4)-C(3)-C(2)	120.9(3)
C(4)-C(3)-H(3)	119.5
C(2)-C(3)-H(3)	119.5
C(3)-C(4)-C(5)	119.4(3)
C(3)-C(4)-C(21)	118.1(3)
C(5)-C(4)-C(21)	122.5(3)
C(6)-C(5)-C(4)	119.4(3)
C(6)-C(5)-N(1)	118.0(3)
C(4)-C(5)-N(1)	122.6(3)
C(7)-C(6)-C(5)	120.2(3)
C(7)-C(6)-C(22)	119.0(3)
C(5)-C(6)-C(22)	120.7(3)
C(2)-C(7)-C(6)	120.1(3)
C(2)-C(7)-H(7)	120.0
C(6)-C(7)-H(7)	120.0
N(1)-C(8)-C(9)	104.9(3)
N(1)-C(8)-H(8A)	110.8

C(9)-C(8)-H(8A)	110.8
N(1)-C(8)-H(8B)	110.8
C(9)-C(8)-H(8B)	110.8
H(8A)-C(8)-H(8B)	108.8
C(8)-C(9)-C(10)	103.7(3)
C(8)-C(9)-H(9A)	111.0
C(10)-C(9)-H(9A)	111.0
C(8)-C(9)-H(9B)	111.0
C(10)-C(9)-H(9B)	111.0
H(9A)-C(9)-H(9B)	109.0
C(9)-C(10)-C(11)	102.9(3)
C(9)-C(10)-H(10A)	111.2
C(11)-C(10)-H(10A)	111.2
C(9)-C(10)-H(10B)	111.2
C(11)-C(10)-H(10B)	111.2
H(10A)-C(10)-H(10B)	109.1
N(1)-C(11)-C(10)	101.9(3)
N(1)-C(11)-C(12)	112.3(3)
C(10)-C(11)-C(12)	113.6(3)
N(1)-C(11)-H(11)	109.6
C(10)-C(11)-H(11)	109.6
C(12)-C(11)-H(11)	109.6
C(13)-C(12)-C(23)	109.1(3)
C(13)-C(12)-C(11)	108.8(3)
C(23)-C(12)-C(11)	112.9(3)
C(13)-C(12)-H(12)	108.7
C(23)-C(12)-H(12)	108.7
C(11)-C(12)-H(12)	108.7
O(2)-C(13)-N(2)	123.9(3)
O(2)-C(13)-C(12)	121.3(3)
N(2)-C(13)-C(12)	114.8(3)
N(2)-C(14)-C(24)	109.3(3)
N(2)-C(14)-C(15)	112.4(3)
C(24)-C(14)-C(15)	109.8(3)
N(2)-C(14)-H(14)	108.4

C(24)-C(14)-H(14)	108.4
C(15)-C(14)-H(14)	108.4
C(16)-C(15)-C(20)	118.5(4)
C(16)-C(15)-C(14)	120.7(4)
C(20)-C(15)-C(14)	120.8(3)
C(15)-C(16)-C(17)	119.6(5)
C(15)-C(16)-H(16)	120.2
C(17)-C(16)-H(16)	120.2
C(18)-C(17)-C(16)	120.3(4)
C(18)-C(17)-H(17)	119.8
C(16)-C(17)-H(17)	119.8
C(19)-C(18)-C(17)	120.2(4)
C(19)-C(18)-H(18)	119.9
C(17)-C(18)-H(18)	119.9
C(18)-C(19)-C(20)	120.0(5)
C(18)-C(19)-H(19)	120.0
C(20)-C(19)-H(19)	120.0
C(15)-C(20)-C(19)	121.3(4)
C(15)-C(20)-H(20)	119.4
C(19)-C(20)-H(20)	119.4
C(4)-C(21)-H(21A)	109.5
C(4)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(4)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(6)-C(22)-H(22A)	109.5
C(6)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(6)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(12)-C(23)-H(23A)	109.5
C(12)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5

C(12)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
O(3)-C(24)-C(14)	109.1(3)
O(3)-C(24)-H(24A)	109.9
C(14)-C(24)-H(24A)	109.9
O(3)-C(24)-H(24B)	109.9
C(14)-C(24)-H(24B)	109.9
H(24A)-C(24)-H(24B)	108.3
O(1S)-C(1S)-H(1S1)	109.5
O(1S)-C(1S)-H(1S2)	109.5
H(1S1)-C(1S)-H(1S2)	109.5
O(1S)-C(1S)-H(1S3)	109.5
H(1S1)-C(1S)-H(1S3)	109.5
H(1S2)-C(1S)-H(1S3)	109.5
C(1S)-O(1S)-H(1SO)	111(4)

Symmetry transformations used to generate equivalent atoms:

Table SI-20. Anisotropic displacement parameters (Å2x 103) for $C_{24}H_{32}N_2O_3(CH_3OH)$. The anisotropic displacement factor exponent takes the form: -2p2[h2 a*2U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13
O(1)	36(1)	30(1)	26(1)	-6(1)	-2(1)
O(2)	24(1)	29(1)	28(1)	2(1)	6(1)
O(3)	30(1)	33(1)	24(1)	0(1)	-5(1)
N(1)	25(1)	25(1)	21(1)	2(1)	0(1)
N(2)	22(1)	25(1)	22(1)	0(1)	2(1)
C(1)	39(2)	37(2)	25(2)	-3(2)	-6(2)
C(2)	30(2)	25(2)	18(2)	1(1)	4(1)
C(3)	31(2)	25(2)	22(2)	2(1)	7(1)
C(4)	24(2)	26(2)	22(2)	6(1)	5(1)
C(5)	23(2)	22(1)	20(2)	4(1)	4(1)
C(6)	26(2)	23(1)	28(2)	1(1)	2(1)
C(7)	23(2)	29(2)	31(2)	4(1)	-1(1)
C(8)	33(2)	29(2)	24(2)	1(1)	2(2)
C(9)	39(2)	35(2)	27(2)	7(2)	-6(2)
C(10)	27(2)	29(2)	27(2)	5(1)	-6(1)
C(11)	21(2)	22(1)	28(2)	2(1)	-2(1)
C(12)	21(2)	27(2)	18(2)	1(1)	0(1)
C(13)	26(2)	26(2)	14(1)	4(1)	-2(1)
C(14)	24(2)	26(2)	26(2)	-2(1)	4(1)
C(15)	45(2)	28(2)	24(2)	-2(1)	6(2)
C(16)	56(3)	36(2)	37(2)	-6(2)	17(2)
C(17)	87(4)	38(2)	42(2)	-4(2)	32(3)
C(18)	91(4)	43(2)	31(2)	8(2)	-2(2)
C(19)	74(3)	58(3)	41(2)	21(2)	-9(2)
C(20)	48(2)	50(2)	32(2)	17(2)	-5(2)
C(21)	27(2)	30(2)	37(2)	2(2)	-2(2)
C(22)	27(2)	29(2)	50(2)	-9(2)	-6(2)
C(23)	41(2)	34(2)	23(2)	0(1)	1(2)
C(24)	27(2)	28(2)	22(2)	-2(1)	-2(1)

C(1S)	41(2)	54(2)	28(2)	2(2)	-6(2)
O(1S)	36(2)	116(3)	26(1)	11(2)	0(1)

Table SI-21. Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 10 3) for $C_{24}H_{32}N_2O_3(CH_3OH)$.

	x	y	z	U(eq)
H(3O)	1380(50)	2170(30)	4271(15)	34
H(2N)	3380(30)	2900(30)	5658(18)	28
H(1A)	8861	8546	7430	50
H(1B)	8614	7501	7385	50
H(1C)	9378	8033	6766	50
H(3)	3979	8178	6357	31
H(7)	8341	6745	6399	33
H(8A)	4758	5593	4233	35
H(8B)	3680	6461	4425	35
H(9A)	2220	5092	3859	40
H(9B)	1152	5758	4325	40
H(10A)	2687	4113	4722	33
H(10B)	766	4438	4882	33
H(11)	1693	5481	5643	28
H(12)	4301	4166	5876	27
H(14)	44	2346	5845	30
H(16)	-810	1207	6582	52
H(17)	-153	166	7418	67
H(18)	2664	-136	7682	66
H(19)	4850	519	7095	69
H(20)	4237	1542	6267	52
H(21A)	1227	6907	5864	47
H(21B)	1896	7035	5119	47
H(21C)	1783	7863	5608	47
H(22A)	6806	5048	5317	53
H(22B)	8517	5622	5375	53
H(22C)	7837	5078	6003	53
H(23A)	4289	5353	6651	49
H(23B)	2343	5137	6837	49

H(23C)	3821	4447	7016	49
H(24A)	2706	1591	5042	31
H(24B)	846	1153	5113	31
H(1S1)	728	2210	2800	62
H(1S2)	2376	1702	2524	62
H(1S3)	2519	2715	2740	62
H(1SO)	3420(40)	1710(40)	3510(30)	71

Table SI-22. Torsion angles [°] for $C_{24}H_{32}N_2O_3(CH_3OH)$.

C(1)-O(1)-C(2)-C(7)	-2.2(4)
C(1)-O(1)-C(2)-C(3)	178.8(3)
O(1)-C(2)-C(3)-C(4)	-178.6(3)
C(7)-C(2)-C(3)-C(4)	2.3(5)
C(2)-C(3)-C(4)-C(5)	0.5(5)
C(2)-C(3)-C(4)-C(21)	179.5(3)
C(3)-C(4)-C(5)-C(6)	-3.7(5)
C(21)-C(4)-C(5)-C(6)	177.4(3)
C(3)-C(4)-C(5)-N(1)	177.3(3)
C(21)-C(4)-C(5)-N(1)	-1.7(5)
C(11)-N(1)-C(5)-C(6)	114.7(3)
C(8)-N(1)-C(5)-C(6)	-106.1(3)
C(11)-N(1)-C(5)-C(4)	-66.2(4)
C(8)-N(1)-C(5)-C(4)	73.0(4)
C(4)-C(5)-C(6)-C(7)	4.1(5)
N(1)-C(5)-C(6)-C(7)	-176.8(3)
C(4)-C(5)-C(6)-C(22)	-177.5(3)
N(1)-C(5)-C(6)-C(22)	1.6(5)
O(1)-C(2)-C(7)-C(6)	179.1(3)
C(3)-C(2)-C(7)-C(6)	-1.9(5)
C(5)-C(6)-C(7)-C(2)	-1.3(5)
C(22)-C(6)-C(7)-C(2)	-179.7(3)
C(5)-N(1)-C(8)-C(9)	-144.3(3)
C(11)-N(1)-C(8)-C(9)	-1.7(3)
N(1)-C(8)-C(9)-C(10)	-22.6(4)
C(8)-C(9)-C(10)-C(11)	37.8(4)
C(5)-N(1)-C(11)-C(10)	166.7(3)
C(8)-N(1)-C(11)-C(10)	25.0(3)
C(5)-N(1)-C(11)-C(12)	-71.3(3)
C(8)-N(1)-C(11)-C(12)	146.9(3)
C(9)-C(10)-C(11)-N(1)	-38.2(3)
C(9)-C(10)-C(11)-C(12)	-159.2(3)
N(1)-C(11)-C(12)-C(13)	-160.5(3)

C(10)-C(11)-C(12)-C(13) -45.6(4)
N(1)-C(11)-C(12)-C(23) 78.2(3)
C(10)-C(11)-C(12)-C(23)-166.8(3)
C(14)-N(2)-C(13)-O(2) 3.2(5)
C(14)-N(2)-C(13)-C(12) -175.6(3)
C(23)-C(12)-C(13)-O(2) 51.7(4)
C(11)-C(12)-C(13)-O(2) -71.9(4)
C(23)-C(12)-C(13)-N(2) -129.4(3)
C(11)-C(12)-C(13)-N(2) 107.0(3)
C(13)-N(2)-C(14)-C(24) 135.8(3)
C(13)-N(2)-C(14)-C(15) -102.0(4)
N(2)-C(14)-C(15)-C(16) 137.3(3)
C(24)-C(14)-C(15)-C(16)-100.8(4)
N(2)-C(14)-C(15)-C(20) -45.0(5)
C(24)-C(14)-C(15)-C(20) 76.9(4)
C(20)-C(15)-C(16)-C(17) 1.3(5)
C(14)-C(15)-C(16)-C(17)179.1(3)
C(15)-C(16)-C(17)-C(18) 0.3(6)
C(16)-C(17)-C(18)-C(19) -1.8(7)
C(17)-C(18)-C(19)-C(20) 1.6(8)
C(16)-C(15)-C(20)-C(19) -1.5(6)
C(14)-C(15)-C(20)-C(19)-179.2(4)
C(18)-C(19)-C(20)-C(15) 0.0(7)
N(2)-C(14)-C(24)-O(3) -65.8(3)
C(15)-C(14)-C(24)-O(3) 170.5(3)

Symmetry transformations used to generate equivalent atoms:

Table SI-23. Hydrogen bonds for $C_{24}H_{32}N_2O_3(CH_3OH)$ [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(3)-H(3O)...O(1S)	0.84(2)	1.81(2)	2.656(4)	176(4)
N(2)-H(2N)...O(3)#1	0.88(2)	2.03(2)	2.903(4)	170(4)
O(1S)-H(1SO)...O(2)#1	0.85(3)	1.84(3)	2.669(4)	168(6)

Symmetry transformations used to generate equivalent atoms:
#1 x+1/2,-y+1/2,-z+1

10. Coordinates after optimization with M06-L/DF-def2-SVP$_{DCM(IEFPCM)}$

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iminium / electronic energy: -635.485731273 a.u. / lowest freq: 54.97 cm-1

H	-4.280944	1.246655	0.144279
C	-3.936282	0.286217	0.551150
H	-4.644887	-0.009994	1.331258
C	-3.817817	-0.741253	-0.576945
C	-2.39465	-0.676214	-0.937741
C	-2.518176	0.421206	1.079821
N	-1.687524	-0.037129	-0.064347
H	-4.033748	-1.776626	-0.254397
H	-4.471043	-0.567655	-1.442443
H	-2.220158	1.434407	1.371343
H	-2.285955	-0.247939	1.923645
H	-1.918058	-1.115709	-1.817480
C	-0.116865	-2.456168	0.150192
C	0.508419	-1.099676	0.049178
H	2.50226	-1.875579	0.176402
C	1.899822	-0.972303	0.075781
C	-0.25796	0.074055	-0.061805
C	2.50452	0.287028	-0.015302
C	0.322465	1.357096	-0.146140
O	3.832047	0.486809	-0.002259
C	1.709365	1.437142	-0.129458
C	-0.501033	2.600405	-0.271456
H	2.205077	2.405919	-0.214159
H	-1.443575	2.436229	-0.810627
H	-0.756687	3.018090	0.714470
H	0.052465	3.382988	-0.803177
H	0.574579	-3.170649	0.610551
H	-1.03719	-2.456995	0.750503
H	-0.375695	-2.865215	-0.838029
C	4.684045	-0.635915	0.104437

H	5.708394	-0.252915	0.093834
H	4.515737	-1.182990	1.044393
H	4.550604	-1.326319	-0.742135

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Z_enolate / electronic energy: -1993.66785348 a.u. / lowest freq: -21.17 cm-1

C	2.465444	2.799716	0.429421
H	4.100355	4.049430	1.105293
C	3.069137	4.016079	0.753885
N	1.205699	2.738916	0.000517
C	2.30642	5.176581	0.613810
C	0.473495	3.842852	-0.134966
H	2.743964	6.145398	0.858359
C	0.985546	5.105100	0.165763
H	0.370091	5.997618	0.053741
O	-1.788514	4.479719	-0.747922
C	-3.025451	3.804817	-1.108844
C	-0.883238	3.527329	-0.614800
N	-1.212853	2.316945	-0.903987
C	-2.600509	2.343122	-1.376798
H	-3.715091	3.907611	-0.259053
H	-3.4494	4.317880	-1.978140
H	-4.344773	0.609018	-2.550152
C	-4.307249	0.486124	-1.464145
H	-5.772983	-1.096701	-1.444425
C	-5.107509	-0.472789	-0.843284
C	-3.451635	1.293380	-0.708155
C	-5.050755	-0.639071	0.540482
C	-3.396546	1.117093	0.679739
H	-5.672993	-1.394068	1.027909
C	-4.189548	0.154812	1.300178
H	-2.714436	1.725667	1.279743
H	-4.132378	0.021436	2.383275
H	-2.588725	2.140411	-2.461320

H	5.333278	-0.278219	0.222744
H	4.382203	-2.188735	-3.773866
H	3.282762	-4.401987	-3.462429
C	3.886016	-2.425528	-2.830029
C	3.267971	-3.665285	-2.656228
H	4.351806	-0.515408	-1.947113
C	3.870997	-1.487618	-1.800018
O	4.256727	1.279920	1.062850
C	4.527951	-0.145635	0.959965
C	2.631005	-3.959584	-1.451265
H	2.148237	-4.929701	-1.310925
C	3.059154	1.456385	0.526042
C	3.238702	-1.777975	-0.584835
C	2.613812	-3.018016	-0.421861
H	4.881525	-0.492753	1.936403
N	2.398443	0.422606	0.140647
C	3.182953	-0.757032	0.521433
H	2.103064	-3.234962	0.522640
H	2.659966	-1.216146	1.380400
Mg	0.284551	0.784349	-0.395727
C	0.957721	-1.146926	3.666367
C	0.249752	-1.897714	2.592832
C	-0.327284	-1.278108	1.526456
O	-0.324849	-0.009333	1.280021
H	-3.601927	-2.893763	-0.316092
C	-2.62023	-3.352507	-0.515758
H	-2.766754	-4.338781	-0.970736
O	-1.920686	-2.520560	-1.450322
C	-1.101551	-1.720043	-0.762366
C	-1.732148	-3.382844	0.733566
N	-1.033606	-2.079268	0.535013
O	-0.505965	-0.804381	-1.345061
C	-2.570376	-3.422222	1.995330

C	-0.752807	-4.548939	0.646362
H	-3.200146	-2.526624	2.079284
H	-3.229382	-4.301141	1.964803
H	-1.957074	-3.498435	2.900374
H	-0.211642	-4.533671	-0.310051
H	-0.014667	-4.540974	1.457190
H	-1.300673	-5.499351	0.706088
H	0.408215	-1.132330	4.624473
H	1.943851	-1.582705	3.898423
H	1.120434	-0.099664	3.374699
H	0.175759	-2.981181	2.685641

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E_enolate / electronic energy: -1993.65747922 a.u. / lowest freq: 20.48 cm-1

C	-3.312798	2.056740	-0.529501
H	-5.284118	2.867472	-0.910040
C	-4.246638	3.085904	-0.657174
N	-2.040896	2.300879	-0.218219
C	-3.804034	4.392712	-0.444523
C	-1.618476	3.542999	0.006600
H	-4.503607	5.224328	-0.538149
C	-2.473782	4.640222	-0.100353
H	-2.108872	5.650237	0.085436
O	0.371298	4.699983	0.760889
C	1.757112	4.367927	1.044332
C	-0.203219	3.562285	0.412566
N	0.478888	2.472663	0.489009
C	1.771649	2.824154	1.082952
H	2.369278	4.781920	0.230057
H	2.037632	4.849976	1.986455
H	4.17131	2.278005	2.198175
C	4.151464	2.034149	1.131933
H	6.217607	1.418643	1.086080
C	5.300469	1.550971	0.507729

C	2.96852	2.212885	0.404141
C	5.27495	1.230297	-0.850375
C	2.948033	1.886575	-0.955508
H	6.172898	0.847118	-1.340715
C	4.095579	1.394762	-1.577453
H	2.026088	2.008724	-1.528171
H	4.066727	1.138915	-2.639339
H	1.75249	2.470592	2.129984
H	-5.275157	-1.644300	-0.055809
H	-2.950414	-2.705760	3.805470
H	-1.618612	-4.760189	3.349164
C	-2.693387	-2.974206	2.778380
C	-1.946701	-4.126322	2.522340
H	-3.678355	-1.252297	1.934975
C	-3.106425	-2.161953	1.725037
O	-4.769111	0.156054	-0.941228
C	-4.666425	-1.294768	-0.901452
C	-1.625696	-4.466482	1.208761
H	-1.045725	-5.369239	1.000706
C	-3.558503	0.612164	-0.672843
C	-2.777581	-2.491027	0.404369
C	-2.041502	-3.651416	0.155653
H	-5.090762	-1.687444	-1.831497
N	-2.598751	-0.230437	-0.519698
C	-3.156293	-1.571626	-0.729239
H	-1.785335	-3.909436	-0.874649
H	-2.71861	-1.972080	-1.659998
Mg	-0.614129	0.631407	-0.099188
C	0.482175	-3.920167	-2.325515
C	0.329502	-2.440023	-2.355999
C	0.704748	-1.513723	-1.435743
O	0.430927	-0.244177	-1.490555
H	4.02575	-0.907668	0.588706

C	3.463201	-1.789868	0.935932
H	4.107436	-2.400149	1.578441
O	2.352287	-1.325407	1.717626
C	1.298784	-1.231021	0.902677
C	2.83318	-2.572255	-0.223203
N	1.498272	-1.886543	-0.259656
O	0.299743	-0.587785	1.246019
C	3.597915	-2.380812	-1.515294
C	2.716751	-4.040830	0.168912
H	3.640389	-1.319844	-1.796411
H	4.628088	-2.743769	-1.393674
H	3.142099	-2.940237	-2.341611
H	2.099013	-4.163301	1.070005
H	2.29559	-4.659894	-0.628083
H	3.717622	-4.435127	0.393115
H	-0.341334	-4.401573	-2.874424
H	1.407028	-4.301351	-2.798052
H	0.454831	-4.326934	-1.304641
H	-0.180595	-2.006970	-3.222121

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ts_IX’ / electronic energy: -2629.17482358 a.u. / lowest freq: -268.09 cm-1

H	3.012617	5.144450	-1.340197
H	-1.358056	5.710499	-2.612245
H	-1.52763	5.927383	-0.852536
O	0.263329	5.102259	-1.485753
C	-1.175437	5.246202	-1.636614
C	3.049742	4.055704	-1.307709
C	4.262707	3.363916	-1.298858
C	0.494273	3.810149	-1.369921
C	1.874986	3.303264	-1.289400
H	-1.653593	4.779959	1.053285
C	-1.725811	3.807319	-1.524035
H	-2.207411	3.506476	-2.468264

C	-2.52564	4.147442	0.859700
N	-0.505956	2.996970	-1.374010
C	-2.70632	3.563542	-0.400239
N	1.898109	1.972273	-1.243999
C	-3.459911	3.945873	1.873781
C	3.052091	1.307622	-1.238182
C	-3.817319	2.740387	-0.612022
H	-3.96427	2.276607	-1.592615
C	-4.57828	3.143145	1.645184
C	-4.748389	2.529028	0.405009
Mg	0.018787	0.885577	-1.196936
H	-5.313129	2.989539	2.438585
C	2.831109	-0.146948	-1.204365
H	-5.619386	1.895673	0.221577
O	-1.140874	0.338903	0.292869
N	1.640077	-0.635861	-1.148558
O	-1.258747	-0.225754	-2.300052
C	-2.035203	-0.524510	0.497325
H	1.509036	-1.550173	-3.756942
C	-2.06492	-1.057690	-1.894593
C	3.297463	-2.312507	-1.270890
C	1.77656	-2.095850	-1.091726
H	3.560216	-2.764802	-2.237154
H	-5.016893	-0.719873	-1.260371
N	-2.441061	-1.339714	-0.600248
C	0.931303	-2.427381	-3.449135
H	-4.977841	-0.962879	0.500315
O	-2.726691	-1.808041	-2.758692
C	0.932074	-2.823802	-2.106043
C	-4.917993	-1.475124	-0.467560
H	0.197768	-2.816344	-5.437787
C	0.197215	-3.138715	-4.394428
C	-3.627111	-2.267887	-0.624597

C	-3.489326	-2.792727	-2.058681
H	-5.777283	-2.154582	-0.541844
H	-4.453562	-2.911489	-2.565224
C	0.189459	-3.946385	-1.727480
H	-3.872791	-3.213611	1.348958
H	0.189507	-4.268430	-0.681226
C	-3.528118	-3.442900	0.335235
C	-0.533887	-4.264838	-4.011033
H	-2.937381	-3.742562	-2.108254
H	-2.504764	-3.839993	0.383067
C	-0.533535	-4.670154	-2.677239
H	-1.103575	-4.826574	-4.754436
H	-4.176342	-4.250299	-0.032515
H	-1.099026	-5.553721	-2.371177
H	-3.314356	4.419021	2.847387
H	5.201897	3.917874	-1.320427
C	4.28048	1.968319	-1.275561
H	5.214302	1.407453	-1.283647
O	3.859561	-0.974952	-1.247189
H	3.765744	-2.893040	-0.466656
H	1.461235	-2.417684	-0.084578
C	-2.564608	0.413380	2.741690
C	-2.575212	-0.728879	1.778699
H	-1.670257	0.438019	3.382330
H	-2.578611	1.381283	2.221298
H	-3.438888	0.377783	3.404986
H	-3.382096	-1.449844	1.883141
H	-2.256492	-1.315356	4.874574
C	-1.401567	-2.000933	4.796254
H	-1.394024	-2.608387	5.708594
C	-1.508215	-2.837718	3.524048
C	-0.80048	-1.993483	2.514298
C	-0.106269	-1.226480	4.610636

N	0.075343	-1.190294	3.142445
H	-0.939308	-3.781174	3.619931
H	-2.53082	-3.122438	3.253243
H	-0.121916	-0.210723	5.031225
H	0.765521	-1.740355	5.052044
H	-0.538149	-2.347543	1.514111
C	2.056593	-3.191382	2.645251
C	2.327157	-1.738383	2.399025
H	4.366247	-2.108245	1.829878
C	3.5998	-1.344326	1.969166
C	1.335527	-0.757682	2.604338
C	3.891231	0.006700	1.761021
C	1.624644	0.613386	2.428612
O	5.0858	0.470381	1.340935
C	2.899177	0.968103	1.989352
C	0.624811	1.690269	2.698453
H	3.152178	2.021383	1.842885
H	0.232304	1.642166	3.724756
H	1.075551	2.682455	2.569736
H	-0.240413	1.613240	2.025500
H	2.985898	-3.772604	2.642963
H	1.562002	-3.365801	3.611114
H	1.401736	-3.638304	1.880017
C	6.1401	-0.452851	1.153613
H	7.012897	0.129307	0.842402
H	6.380253	-0.985088	2.086359
H	5.901596	-1.186898	0.368447

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ts_X’ / electronic energy: -2629.16434168 a.u. / lowest freq: -334.36 cm-1

C	3.434359	1.225466	-1.323674
H	5.594297	1.338844	-1.364001
C	4.65842	1.894172	-1.303235
N	2.275243	1.878243	-1.246726

C	4.636574	3.284675	-1.191081
C	2.250028	3.205875	-1.138380
H	5.57312	3.842988	-1.167229
C	3.420106	3.964837	-1.104424
H	3.376504	5.049805	-1.010191
O	0.634924	5.008722	-1.098767
C	-0.806786	5.159119	-0.997180
C	0.869733	3.710984	-1.069205
N	-0.130354	2.898757	-1.028102
C	-1.350417	3.721348	-1.120650
H	-1.023159	5.630253	-0.028198
H	-1.132473	5.831537	-1.797171
H	-3.805308	2.652942	-1.588040
C	-3.610003	2.775627	-0.517947
H	-5.531237	1.992167	0.087588
C	-4.573708	2.401332	0.419601
C	-2.395894	3.334974	-0.104390
C	-4.326239	2.565555	1.782217
C	-2.169754	3.522878	1.264555
H	-5.079022	2.268316	2.515895
C	-3.121513	3.130142	2.203424
H	-1.234694	3.977348	1.604944
H	-2.924884	3.273161	3.268755
H	-1.772523	3.552705	-2.125906
H	3.793982	-2.715448	-2.617551
H	-0.677961	-2.645364	-4.956673
H	-1.464883	-4.885075	-4.198812
C	-0.289193	-3.079473	-4.032536
C	-0.727702	-4.334810	-3.609856
H	0.995149	-1.394950	-3.617299
C	0.64972	-2.376112	-3.278916
O	4.234115	-1.076242	-1.427506
C	3.629338	-2.393714	-1.578797

C	-0.221808	-4.882978	-2.431015
H	-0.559719	-5.865557	-2.093749
C	3.219545	-0.228532	-1.385423
C	1.150236	-2.911980	-2.087126
C	0.709653	-4.173744	-1.674363
H	4.14213	-3.083490	-0.899855
N	2.025029	-0.702992	-1.357587
C	2.143619	-2.155298	-1.246326
H	1.092944	-4.599482	-0.742255
H	1.95315	-2.405490	-0.183896
Mg	0.360208	0.740604	-1.231396
C	-0.965441	-3.209999	1.264986
C	-1.977174	-2.176809	0.910809
C	-1.688817	-1.209387	-0.070874
O	-0.561585	-0.653985	-0.154870
H	-5.20592	0.439613	-1.698787
C	-4.636183	-0.382930	-2.156928
H	-5.263909	-0.870667	-2.910593
O	-3.494247	0.179036	-2.808073
C	-2.430412	0.046827	-2.026595
C	-4.079802	-1.357930	-1.112941
N	-2.714864	-0.747383	-0.940708
O	-1.374729	0.589674	-2.334515
C	-4.959416	-1.305105	0.128669
C	-3.952914	-2.760770	-1.690993
H	-4.773968	-0.396240	0.717504
H	-6.012204	-1.288603	-0.186429
H	-4.84992	-2.178231	0.780646
H	-3.431359	-2.748071	-2.658189
H	-3.405016	-3.432060	-1.017314
H	-4.952025	-3.187476	-1.850258
H	-1.073919	-3.539275	2.309237
H	-1.084038	-4.115392	0.646406

H	0.058457	-2.840259	1.119972
H	-3.010278	-2.512090	0.984797
H	-1.879284	-0.139193	5.435576
C	-2.016049	-1.122960	4.962153
H	-2.580307	-1.749949	5.662744
C	-2.695589	-0.966363	3.603387
C	-1.544908	-0.753693	2.665200
C	-0.665226	-1.712847	4.601331
N	-0.396307	-1.108867	3.276417
H	-3.249104	-1.879820	3.334698
H	-3.419595	-0.141586	3.551959
H	0.145557	-1.444647	5.291254
H	-0.700966	-2.812021	4.538693
H	-1.505268	0.049748	1.933265
C	1.744584	-3.158442	3.392946
C	1.938525	-1.780613	2.840087
H	3.983155	-2.227191	2.362790
C	3.212827	-1.454363	2.352386
C	0.924836	-0.797716	2.826726
C	3.499996	-0.171250	1.886662
C	1.231071	0.527422	2.427253
O	4.697008	0.214386	1.390706
C	2.507087	0.811752	1.949963
C	0.264243	1.658807	2.555991
H	2.768348	1.836217	1.672709
H	-0.417046	1.733091	1.694943
H	-0.374211	1.571437	3.447163
H	0.797358	2.616452	2.617477
H	1.779315	-3.156140	4.493019
H	0.787612	-3.608180	3.109620
H	2.543466	-3.829750	3.056177
C	5.773308	-0.698686	1.450399
H	6.642019	-0.188213	1.022803

H	5.999189	-0.983795	2.489292
H	5.573684	-1.608906	0.865031

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ts_IX / electronic energy: -2629.16102555 a.u. / lowest freq: -270.98 cm-1

H	4.596338	-4.722589	-2.281451
H	4.433831	-4.581214	2.318413
H	2.845729	-5.305109	1.954665
O	3.825532	-4.443927	0.346972
C	3.499016	-4.443860	1.763982
C	4.23251	-3.722777	-2.517525
C	4.392236	-3.166157	-3.787981
C	3.383433	-3.298860	-0.131976
C	3.596885	-2.948598	-1.546590
H	0.704165	-4.648905	1.255787
C	2.821608	-3.075971	2.007999
H	3.454372	-2.440070	2.648671
C	0.474138	-4.015080	2.118291
N	2.805651	-2.470631	0.668189
C	1.443924	-3.138159	2.621164
N	3.14404	-1.724773	-1.813393
C	-0.78043	-4.099264	2.716808
C	3.314758	-1.179882	-3.016373
C	1.122999	-2.322606	3.710159
H	1.875565	-1.632805	4.104037
C	-1.084329	-3.298365	3.819472
C	-0.134966	-2.402304	4.308761
Mg	2.144998	-0.588735	-0.233675
H	-2.065477	-3.370908	4.293932
C	2.808947	0.202304	-3.054622
H	-0.368889	-1.772261	5.170042
O	0.300196	-0.250976	0.394094
N	2.249345	0.731789	-2.020742
O	2.639702	0.662975	1.263643

C	-0.271624	0.502418	1.234501
H	4.09302	2.142714	-0.819370
C	1.904075	1.409722	1.902166
C	2.50183	2.267947	-3.791280
C	1.855112	2.093337	-2.398478
H	3.387461	2.918469	-3.777863
H	0.643639	0.929020	4.573250
N	0.53044	1.484881	1.900076
C	3.451355	3.014045	-0.664581
H	-1.066919	0.846803	4.094795
O	2.432389	2.270088	2.758250
C	2.256332	3.134107	-1.383012
C	-0.225479	1.528415	4.267944
H	4.748095	3.869701	0.828585
C	3.82061	3.985555	0.263779
C	0.098962	2.371524	3.041809
C	1.408941	3.137979	3.246603
H	-0.490682	2.184903	5.107124
H	1.614253	3.366544	4.297996
C	1.449157	4.258210	-1.170378
H	-1.99504	2.939037	2.650823
H	0.522316	4.375332	-1.739028
C	-0.989204	3.370539	2.699454
C	3.004627	5.096647	0.477733
H	1.446521	4.067857	2.657876
H	-0.767918	3.890328	1.757662
C	1.819323	5.233984	-0.245558
H	3.293594	5.857147	1.206732
H	-1.016856	4.132907	3.490300
H	1.178492	6.105076	-0.090204
H	-1.52522	-4.794140	2.322708
H	4.884252	-3.740396	-4.573861
C	3.941442	-1.871667	-4.053170

H	4.07575	-1.408515	-5.030554
O	2.950242	0.931309	-4.144454
H	1.814327	2.613208	-4.570061
H	0.755029	2.107309	-2.492084
C	-2.334774	-0.889924	1.251468
C	-1.6561	0.430990	1.451761
H	-3.425875	-0.796413	1.307031
H	-2.088409	-1.352853	0.283605
H	-2.037024	-1.616325	2.024646
H	-2.094291	1.083770	2.205311
H	-2.678207	3.812520	0.630169
C	-2.677361	3.604283	-0.448598
H	-2.573425	4.565653	-0.965477
C	-1.577294	2.607193	-0.798714
C	-2.237627	1.287086	-0.602241
C	-3.946861	2.865545	-0.827585
N	-3.560048	1.448307	-0.715791
H	-1.316808	2.682751	-1.871088
H	-0.639242	2.727207	-0.239485
H	-4.809587	3.093355	-0.188055
H	-4.25781	3.049553	-1.870781
H	-1.78271	0.345479	-0.918555
C	-3.415273	-0.186501	-3.108479
C	-4.474991	-0.377168	-2.068139
H	-5.41107	-1.979728	-3.147561
C	-5.446275	-1.370077	-2.243669
C	-4.524219	0.414202	-0.907599
C	-6.449411	-1.563573	-1.288419
C	-5.531625	0.236284	0.064665
O	-7.419669	-2.494266	-1.387521
C	-6.48093	-0.758783	-0.141476
C	-5.576742	1.067864	1.309198
H	-7.265429	-0.935783	0.597240

H	-6.227324	1.948100	1.188046
H	-5.985728	0.495963	2.151585
H	-4.584376	1.439239	1.601557
H	-3.740701	-0.577853	-4.079676
H	-3.147236	0.870415	-3.247348
H	-2.486792	-0.720714	-2.850428
C	-7.43661	-3.326421	-2.526452
H	-8.290299	-4.000844	-2.410842
H	-7.564551	-2.745626	-3.453216
H	-6.516538	-3.926209	-2.606706

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ts_X / electronic energy: -2629.16030608 a.u. / lowest freq: -275.30 cm-1

C	-3.364947	-2.783626	-2.062207
H	-4.068522	-4.512164	-3.159769
C	-4.119922	-3.429888	-3.041333
N	-3.417693	-1.463102	-1.894112
C	-4.944019	-2.643239	-3.848501
C	-4.219183	-0.711625	-2.646081
H	-5.548507	-3.111711	-4.626045
C	-5.010584	-1.262293	-3.654755
H	-5.660739	-0.629873	-4.259086
O	-5.048237	1.563674	-2.714741
C	-4.758183	2.830307	-2.062360
C	-4.19157	0.695334	-2.211981
N	-3.396629	1.079637	-1.273704
C	-3.791428	2.454066	-0.923482
H	-4.312742	3.496249	-2.815165
H	-5.705955	3.261219	-1.725014
H	-3.003462	3.606080	1.397538
C	-2.377096	3.917996	0.555763
H	-1.17886	5.264268	1.746680
C	-1.355922	4.849089	0.751580
C	-2.636328	3.401426	-0.719256

C	-0.584442	5.275665	-0.328685
C	-1.837452	3.815494	-1.792952
H	0.201401	6.020001	-0.181005
C	-0.823455	4.751748	-1.600159
H	-2.017798	3.415869	-2.795584
H	-0.217126	5.077182	-2.448853
H	-4.338081	2.383408	0.033184
H	-2.086175	-5.473937	0.845902
H	-3.081257	-2.192467	4.506972
H	-1.113222	-2.818438	5.902343
C	-2.188448	-2.614011	4.039105
C	-1.087404	-2.965011	4.820246
H	-3.02967	-2.541175	2.054230
C	-2.156933	-2.805431	2.657852
O	-2.266171	-4.712273	-1.070117
C	-1.445931	-4.976094	0.103702
C	0.049237	-3.499569	4.212783
H	0.916148	-3.775055	4.817392
C	-2.461758	-3.407226	-1.080538
C	-1.018702	-3.335042	2.039623
C	0.084585	-3.677780	2.830807
H	-0.639652	-5.655288	-0.190406
N	-1.84778	-2.683296	-0.211194
C	-0.974601	-3.574995	0.552021
H	0.979336	-4.094763	2.358984
H	0.059859	-3.395620	0.206275
Mg	-2.191379	-0.508522	-0.311282
C	2.323875	-1.261135	0.675198
C	1.748723	-0.006730	1.260914
C	0.368045	0.213731	1.150382
O	-0.286824	-0.195813	0.148775
H	-1.060243	3.320220	3.600450
C	-1.03451	2.264948	3.910999

H	-1.158597	2.210825	4.997892
O	-2.134017	1.592799	3.293108
C	-1.708507	0.949918	2.214582
C	0.218564	1.538056	3.410010
N	-0.337831	0.986094	2.124662
O	-2.522958	0.405313	1.475194
C	1.326087	2.557411	3.224821
C	0.591571	0.404001	4.355792
H	1.047957	3.307510	2.472046
H	1.471942	3.087414	4.176235
H	2.294735	2.121073	2.957380
H	-0.272156	-0.247438	4.550399
H	1.401414	-0.221548	3.962362
H	0.924949	0.819450	5.315878
H	3.418284	-1.218250	0.612265
H	2.079454	-2.141629	1.293744
H	1.941067	-1.471394	-0.334965
H	2.261691	0.377269	2.141347
H	2.554037	4.604752	-0.331730
C	2.681013	3.573212	0.017784
H	2.728783	3.608302	1.114964
C	1.562811	2.642274	-0.442698
C	2.237087	1.319293	-0.553794
C	3.938114	2.923151	-0.532907
N	3.551578	1.511772	-0.697294
H	0.662987	2.645788	0.188937
H	1.21655	2.911579	-1.457456
H	4.226156	3.312327	-1.524808
H	4.816799	3.019977	0.118631
H	1.763082	0.466574	-1.043234
C	5.678349	0.701058	1.077721
C	5.541799	0.150607	-0.307852
H	7.268503	-1.108408	-0.101124

C	6.463118	-0.796832	-0.767751
C	4.491532	0.539967	-1.155906
C	6.342666	-1.342545	-2.049852
C	4.359923	0.008460	-2.457476
O	7.184918	-2.260769	-2.564548
C	5.291755	-0.933816	-2.881966
C	3.253218	0.430251	-3.372737
H	5.225386	-1.362813	-3.884005
H	2.317599	-0.112388	-3.164043
H	3.025205	1.501922	-3.287790
H	3.507494	0.224590	-4.419096
H	6.337648	1.583021	1.102022
H	4.713632	1.008793	1.504019
H	6.126206	-0.037528	1.754365
C	8.264495	-2.698958	-1.768901
H	8.821158	-3.426714	-2.366871
H	8.935978	-1.868384	-1.501249
H	7.917228	-3.187308	-0.844956

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ts_XI / electronic energy: -2629.16825040 a.u. / lowest freq: -275.91 cm-1

C	-3.038962	-2.690639	-1.295570
H	-3.211177	-4.437890	-2.562970
C	-3.594733	-3.444762	-2.329470
N	-3.493622	-1.476558	-0.990053
C	-4.649986	-2.879273	-3.048357
C	-4.502124	-0.934761	-1.669583
H	-5.109632	-3.436112	-3.865718
C	-5.119009	-1.604279	-2.727326
H	-5.939536	-1.141835	-3.275716
O	-5.728222	1.158717	-1.762747
C	-5.725506	2.433087	-1.059765
C	-4.836744	0.402600	-1.151658
N	-4.252614	0.861900	-0.100480

C	-4.797896	2.201880	0.152995
H	-5.354147	3.193812	-1.760205
H	-6.760233	2.671296	-0.792816
H	-4.237091	3.669526	2.375468
C	-3.53013	3.864292	1.564277
H	-2.373913	5.279409	2.712025
C	-2.482759	4.766109	1.754102
C	-3.687481	3.205392	0.341414
C	-1.583808	5.015739	0.718411
C	-2.772262	3.452144	-0.689764
H	-0.769576	5.730719	0.861982
C	-1.728003	4.354291	-0.503756
H	-2.866683	2.922377	-1.643231
H	-1.022252	4.544631	-1.316703
H	-5.385931	2.155195	1.084301
H	-0.575326	-5.089016	1.136989
H	-2.124116	-3.930920	5.246129
H	-0.414983	-2.587108	6.459268
C	-1.342163	-3.409848	4.689683
C	-0.384039	-2.655862	5.369881
H	-2.065094	-4.086904	2.776000
C	-1.305022	-3.499036	3.299723
O	-1.289306	-4.225269	-0.604122
C	-0.277558	-4.294381	0.438649
C	0.611675	-1.991341	4.655194
H	1.363142	-1.398123	5.180608
C	-1.905207	-3.067999	-0.435644
C	-0.307825	-2.835685	2.575094
C	0.646545	-2.083618	3.264628
H	0.673674	-4.573356	-0.029241
N	-1.469175	-2.261368	0.468965
C	-0.284074	-2.887235	1.069748
H	1.420467	-1.556203	2.698438

H	0.594042	-2.308039	0.727103
Mg	-2.492617	-0.294180	0.566492
C	0.358375	1.489334	-2.875101
C	0.863733	1.355895	-1.478211
C	-0.045086	1.187163	-0.423079
O	-1.188452	0.678075	-0.587004
H	0.632747	3.669631	2.760608
C	1.107725	2.676875	2.749020
H	1.907181	2.651806	3.497302
O	0.116071	1.710136	3.109002
C	-0.384079	1.169369	2.008909
C	1.581489	2.276631	1.348171
N	0.35481	1.515978	0.906380
O	-1.376877	0.449923	2.078353
C	1.895641	3.532601	0.549651
C	2.777914	1.340388	1.423465
H	0.984106	4.038329	0.208370
H	2.438908	4.228949	1.203653
H	2.546858	3.350227	-0.312870
H	2.584028	0.483246	2.084494
H	3.062258	0.963398	0.432410
H	3.648193	1.879045	1.823156
H	1.135263	1.256234	-3.617461
H	-0.507214	0.840196	-3.067201
H	0.031582	2.520566	-3.091858
H	1.811476	1.843044	-1.255727
H	1.017601	-2.621703	-4.047030
C	1.230203	-1.659189	-3.567587
H	0.782038	-0.886608	-4.204574
C	0.664116	-1.577838	-2.146127
C	1.688611	-0.789826	-1.404321
C	2.727887	-1.422633	-3.405072
N	2.848061	-0.817791	-2.070745

H	-0.345065	-1.144848	-2.078372
H	0.608856	-2.581484	-1.685793
H	3.317384	-2.355085	-3.411568
H	3.158337	-0.766937	-4.176007
H	1.735328	-0.733894	-0.312811
C	4.318405	1.502154	-3.023292
C	4.812295	0.640823	-1.904763
H	6.562291	1.846189	-1.600625
C	6.017905	0.960765	-1.269483
C	4.102743	-0.492676	-1.473346
C	6.511806	0.162404	-0.232921
C	4.594634	-1.320298	-0.438073
O	7.660843	0.405095	0.426870
C	5.796643	-0.974207	0.170066
C	3.850995	-2.537882	0.018644
H	6.210775	-1.592550	0.969213
H	3.302143	-3.031023	-0.795545
H	4.534177	-3.275522	0.456159
H	3.114365	-2.300059	0.803804
H	4.6407	2.543441	-2.898865
H	4.717264	1.165320	-3.993144
H	3.224853	1.493434	-3.110058
C	8.427477	1.528117	0.048286
H	9.311849	1.536421	0.692136
H	8.750909	1.464017	-1.002128
H	7.871741	2.467674	0.192977

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ts_XII / electronic energy: -2629.16634263 a.u. / lowest freq: -291.86 cm-1

C	3.544859	-0.818209	-2.390199
H	3.943194	-0.966856	-4.515512
C	3.790717	-1.505516	-3.580265
N	3.355777	-1.461660	-1.242128
C	3.828093	-2.900310	-3.525531

C	3.371887	-2.790576	-1.184792
H	4.020408	-3.472852	-4.433800
C	3.610785	-3.568618	-2.318286
H	3.622127	-4.656763	-2.257368
O	2.961916	-4.552824	0.433632
C	2.655687	-4.662595	1.851365
C	3.075958	-3.263730	0.179121
N	2.882214	-2.425130	1.139112
C	2.505129	-3.203964	2.329712
H	1.747662	-5.269638	1.951666
H	3.488148	-5.193149	2.327686
H	1.885027	-1.570227	4.406084
C	0.993045	-1.897533	3.864430
H	-0.356006	-0.753353	5.099101
C	-0.264895	-1.435302	4.250336
C	1.128827	-2.776451	2.785314
C	-1.402716	-1.854972	3.561029
C	-0.016281	-3.181885	2.090141
H	-2.391553	-1.509624	3.874296
C	-1.275387	-2.730823	2.480923
H	0.072597	-3.860422	1.235200
H	-2.165091	-3.079590	1.950329
H	3.224493	-2.983338	3.133087
H	4.189694	3.369865	-2.950163
H	7.265457	3.764815	0.343521
H	6.334259	5.269772	2.096739
C	6.184768	3.888134	0.441854
C	5.662536	4.731045	1.425001
H	5.744578	2.541791	-1.182690
C	5.327864	3.203182	-0.416155
O	3.484495	1.448035	-3.251728
C	3.282034	2.790480	-2.734791
C	4.282235	4.883250	1.546036

H	3.868082	5.541690	2.312525
C	3.408812	0.637551	-2.212014
C	3.939623	3.352419	-0.302825
C	3.425509	4.194665	0.686454
H	2.440891	3.234505	-3.278779
N	3.1701	1.140623	-1.050555
C	3.018838	2.590725	-1.224295
H	2.342839	4.315100	0.782225
H	1.975364	2.849650	-0.969393
Mg	2.705549	-0.343061	0.516041
C	-0.573821	0.252536	-2.531824
C	-1.055261	0.541018	-1.146548
C	-0.150347	0.367757	-0.088763
O	0.827919	-0.423092	-0.167909
H	-1.608349	1.405386	3.654467
C	-1.087116	2.144722	3.027543
H	-1.278897	3.149531	3.418712
O	0.318292	1.886302	3.108411
C	0.690752	1.171810	2.057282
C	-1.43513	1.996935	1.543720
N	-0.342364	1.034360	1.162038
O	1.849512	0.772248	1.971245
C	-2.847138	1.460392	1.414088
C	-1.244915	3.318862	0.810482
H	-2.950362	0.468994	1.876357
H	-3.523996	2.136030	1.955535
H	-3.212304	1.419710	0.381502
H	-0.250714	3.740711	1.008565
H	-1.35831	3.212039	-0.274943
H	-1.992231	4.045270	1.155359
H	-1.402766	0.065266	-3.229712
H	-0.007365	1.103080	-2.951608
H	0.098942	-0.616691	-2.560407

H	-1.818544	1.313913	-1.049796
H	-1.487724	-2.213815	-3.350080
C	-2.142393	-2.680142	-2.602960
H	-2.186506	-3.747605	-2.848822
C	-1.614233	-2.428086	-1.187321
C	-2.412778	-1.264666	-0.714513
C	-3.52525	-2.036960	-2.623356
N	-3.51433	-1.132982	-1.462306
H	-1.836332	-3.278169	-0.517273
H	-0.528147	-2.264329	-1.116729
H	-3.744908	-1.488327	-3.550607
H	-4.342911	-2.763465	-2.478963
H	-2.46617	-0.973722	0.335218
C	-4.343168	1.144666	-3.068308
C	-5.053481	0.744993	-1.814590
H	-6.447408	2.370198	-1.959384
C	-6.149329	1.497667	-1.376369
C	-4.654729	-0.373123	-1.061512
C	-6.843116	1.140229	-0.216125
C	-5.360069	-0.761924	0.100349
O	-7.902759	1.815140	0.270770
C	-6.444197	0.008628	0.507783
C	-4.972232	-1.969936	0.895347
H	-7.014705	-0.267656	1.396978
H	-4.566389	-2.775816	0.268579
H	-4.209178	-1.735966	1.655077
H	-5.833001	-2.372895	1.442025
H	-3.270822	0.915787	-3.031233
H	-4.750968	0.619298	-3.946304
H	-4.454704	2.217431	-3.266932
C	-8.35599	2.950533	-0.434332
H	-9.21665	3.340395	0.117129
H	-7.582376	3.732376	-0.487397

H	-8.673648	2.694184	-1.456894