Supporting Information for:

Modular access to vicinally functionalized allylic morpholinonates, thiomorpholinonates and piperidinonates by substrate-controlled annulation of 1,3-azadienes with hexacyclic anhydrides

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Contents:

2. Experimental Section

All experiments involving air and moisture sensitive reagents such as palladium precatalysts and organolithium reagents were carried out under an inert atmosphere of nitrogen and using freshly distilled solvents. Column chromatography was performed on silica gel (230-400 mesh). Thin-layer chromatography (TLC) was performed using Silicycle SiliaplateTM glass backed plates (250 μm thickness, 60 Å porosity, F-254 indicator) and visualized using UV (254 nm) or CAM, *p*-anisaldehyde, or $KMnO_4$ stain. Unless otherwise indicated, ^1H, ^{13}C, and DEPT-135 NMR, COSY 45, HMQC, and NOESY spectra were acquired using DMSO-d_6, CD_3OD or $CDCl_3$ as solvent at room temperature. Chemical shifts are quoted in parts per million (ppm). HRMS-EI^+ data were obtained using either electronspray ionization (ESI) or electron impact (EI) techniques. High-resolution ESI was obtained on an LTQ-FT (ion trap; analyzed using Excalibur). High resolution EI was obtained on an Autospec (magnetic sector; analyzed using MassLynx).

General Procedure A: Synthesis of 1,3-azadienes

To a round-bottom flask equipped with a stir bar was added the enal (10 mmol), amine (1 to 1.5 equiv), benzene (50 mL), and anhydrous $MgSO_4$ (2 g). The cloudy suspension was allowed to stir at room temperature. After complete consumption of the amine (based on TLC monitoring), the mixture was filtered through and concentrated under reduced pressure to obtain the crude enamine, which was used in the next step without further purification.

Note: The azadienes need to be stored in the refrigerator when not used immediately.

General Procedure B: Reaction of 1,3-azadienes with hexacyclic anhydrides[1]

A 5 mL screw-cap vial was flame-dried, evacuated and flushed with nitrogen. A solution of the 1,3-azadiene (1.0 mL, 0.10 M in freshly distilled toluene) was added to the vial at room temperature followed by the cyclic anhydride (1 to 1.1 equiv). The contents were placed in a pre-heated oil bath thermostatted at the desired temperature (e.g., 90 ^oC for diglycolic anhydride). After complete consumption of the enal (as judged by TLC and NMR), the mixture/suspension was cooled to room temperature and washed several times with petroleum ether, then concentrated under reduced pressure to afford the crude cycloadducts.

General Procedure C: Methyl esterification of cycloadducts

To a stirring suspension of the acid (1 mmol), dissolved in DMF (5 mL), and K_2CO_3 (6 equiv) was added methyl iodide (3 equiv) under nitrogen atmosphere. The reaction mixture was stirred for 12 to 18 h (TLC monitoring). After complete conversion, it was diluted with water and extracted with EtOAc (2×20 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to give the desired ester.

General Procedure D: Organolithium addition

To the crude lactamoyl ester (1.0 mmol) dissolved in freshly distilled THF (5 mL), was slowly added butyllithium (2.0 mL, 2.0 M solution in hexanes, 4 equiv) under nitrogen at –78 °C. After complete consumption of the ester (as indicated by TLC and GC-MS), the mixture quenched by slow addition of *sat.* aq NH_4Cl. The mixture was diluted with Et_2O. The layers were separated and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over Na_2SO_4 for 30 min, filtered, and concentrated under reduced pressure to give the desired product. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with Hexane/EtOAc (1:2).

General Procedure E: Catalytic hydrogenation

To a round-bottomed flask equipped with a magnetic stir bar was added EtOAc and 10% Pd/C at room temperature. A solution of the alkene in EtOAc was added. The flask was degassed and placed under an inert atmosphere of nitrogen. After complete addition of the alkene, the nitrogen line was cut off. A balloon of H_2 was attached and the reaction mixture was stirred at r.t. After complete consumption of the allylic lactam (based on GC-MS or TLC monitoring), the mixture was filtered through Celite and concentrated under reduced pressure.

General Procedure F: Epoxidation

To a 10 mL vial, in a 0 °C bath, equipped with a magnetic stir bar under a N_2 atmosphere, was added the allylic lactam (0.50 mmol) and CH_2Cl_2 (5 mL). *m*-CPBA (1.0 mmol, 2 equiv) was then added in one portion. After being stirred for 16 h, during which time the bath was allowed to expire, the reaction mixture was quenched by the sequential addition of *sat.* $Na_2S_2O_{3(aq)}$ solution (5 mL) along with 10% NaOH solution (5 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The

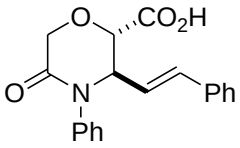
organic layers were combined, washed with 10% NaOH (2 × 5 mL) and then with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo* to afford the crude epoxide.

General Procedure G: Pd-catalyzed etherification

To an oven dried vial equipped with a stir bar was added the crude alcohol, prepared using General Procedure D (1.0 mmol) in hexafluorobenzene (5 mL). $Pd(OAc)_2$ (12 mg, 5 mol %), Li_2CO_3 (1.5 mmol, 1.5 equiv), and $PhI(OAc)_2$ (1.5 mmol, 1.5 equiv) were then added. The contents were then stirred at 100 °C for the indicated length of time prior to cooling to room temperature. The mixture was filtered through a pad of Celite and washed with EtOAc. The filtrate was concentrated under reduced pressure to give the crude product, which was directly subjected to flash column chromatography.

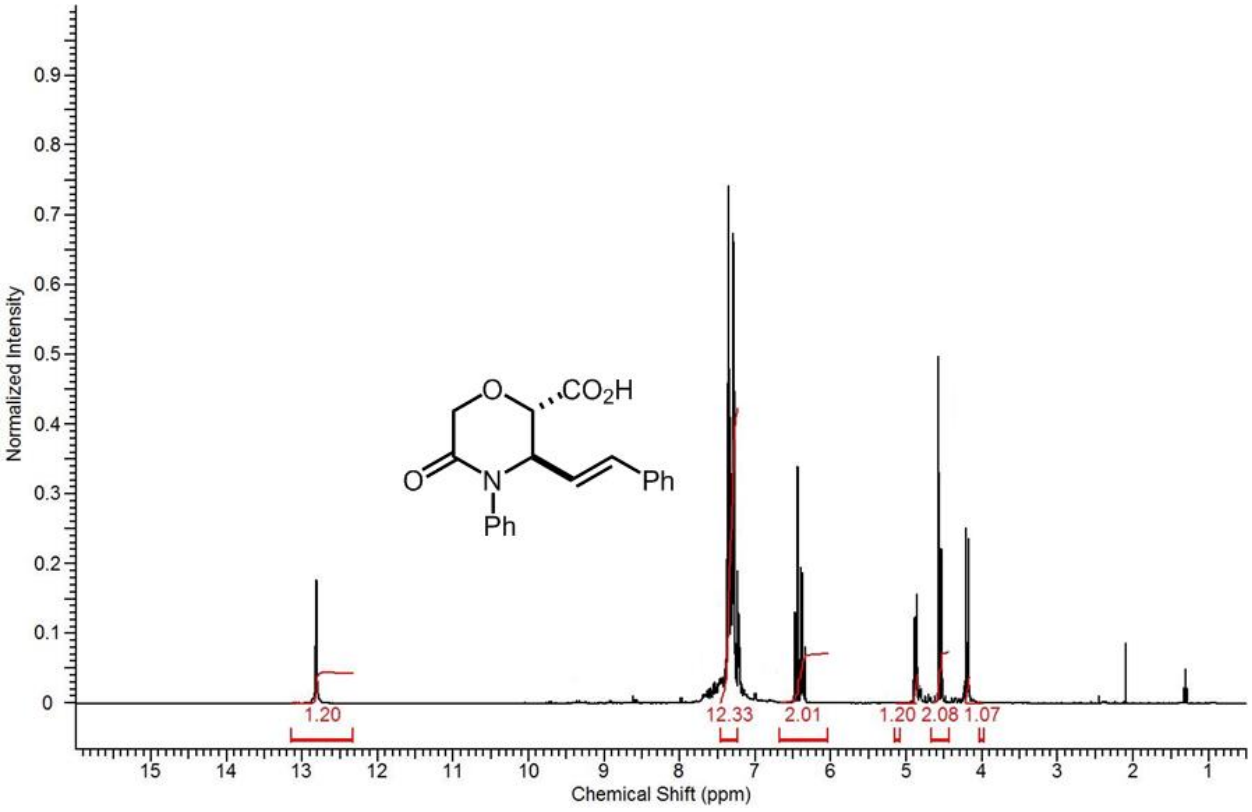
General Procedure H: Vilsmeier-Haack reaction[2,3]

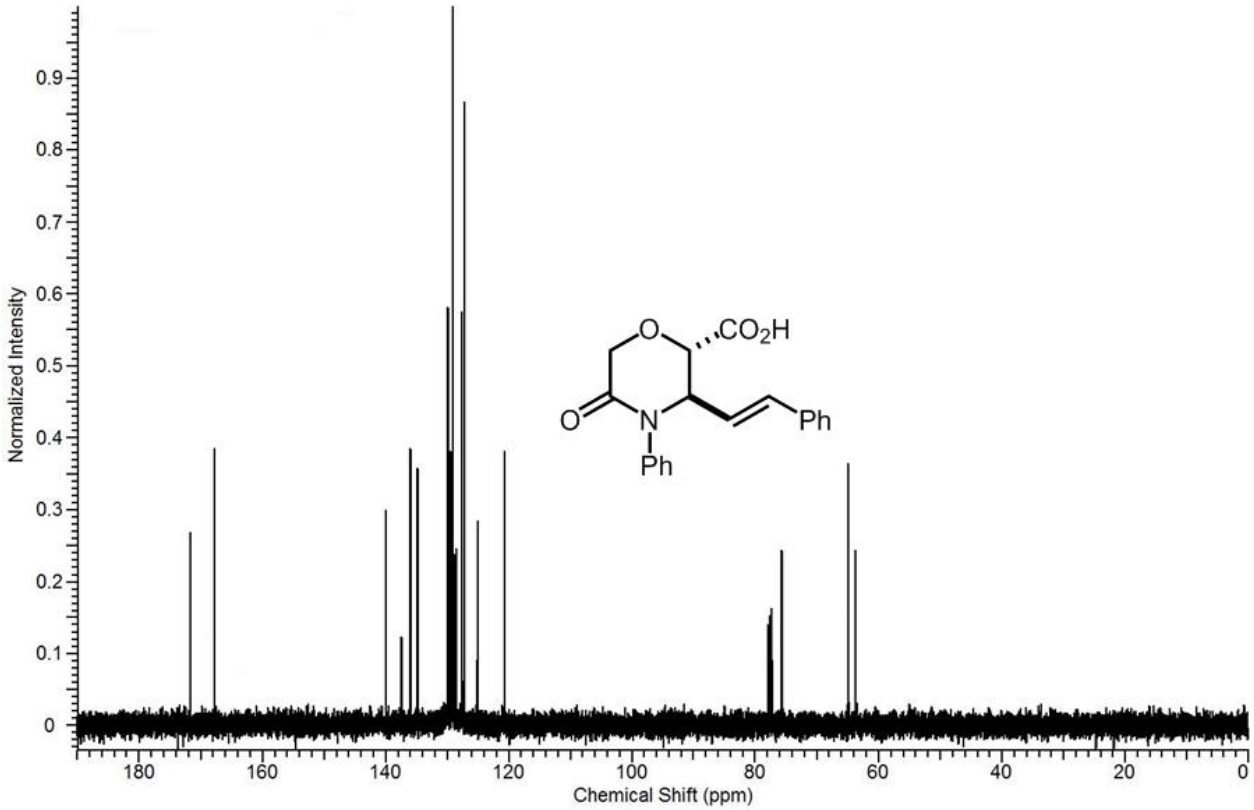
To a solution of DMF (6 mmol, 6 equiv) in CH_2Cl_2 (5 mL) at 0 ^oC was added dropwise, phosphorus oxychloride (3 mmol, 3 equiv). The resulting pale yellow mixture was refluxed for 40 min. A solution of the lactam (1 mmol, 1 equiv) in CH_2Cl_2 (5 mL) was added slowly under reflux. After complete addition of the lactam, the mixture was cooled to room temperature and stirred for the indicated time period (TLC and LC-MS monitoring was used to follow the extent of the reaction). Upon completion, the mixture was poured into a large flask containing crushed ice. After stirring at rt for 60 min, the layers were separated. Powdered K_2CO_3 was added slowly to the mixture and the flask was swirled after each addition (***Caution***: it bubbles vigorously). The addition/swirling was continued until persistent cloudiness was observed. The neutralized/slightly basic mixture was extracted three times with CH_2Cl_2 and washed with brine. The combined organic layers were dried over Na_2SO_4 for 30 min. The mixture was filtered and concentrated under reduced pressure to give the desired product as an oil.



5a1

Prepared from imine **4a** (207 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv), using General Procedure B. T = 90 ^{o}C, time = 18 h. An analytical sample was obtained after a series of washes with petroleum ether. 1H NMR (400 MHz, CDCl3) δ 12.86 (1H, s), 7.56 to 7.12 (5H, m), 6.49 to 6.34 (2H, m), 4.90 (1H, d), 4.58 (2H, dd), 4.20 (1H, d). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7, 167.6, 140.0, 138.3, 137.4, 136.0, 136.0, 134.8, 134.3, 132.7, 131.9, 130.5, 129.8, 129.8, 129.6, 129.6, 129.4, 129.2, 129.1, 129.0, 128.8, 128.8, 128.4, 127.6, 127.3, 127.2, 125.8, 125.3, 125.1, 121.0, 75.7, 72.1, 69.8, 68.4, 65.3, 64.9, 63.8. **HRMS-EI**$^{+}$ (*m/z*): calc'd for $C_{19}H_{17}NO_4$ 323.1158; found 323.1163.

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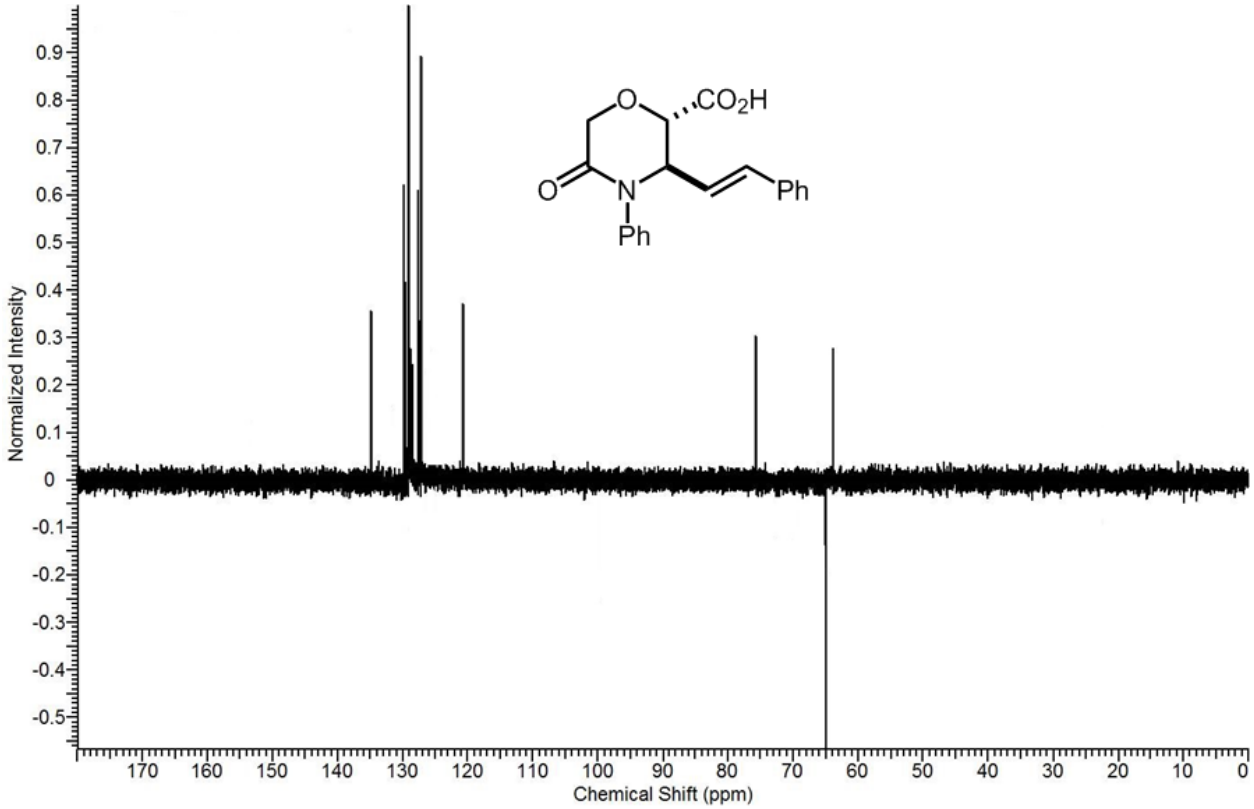
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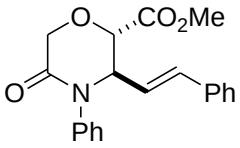
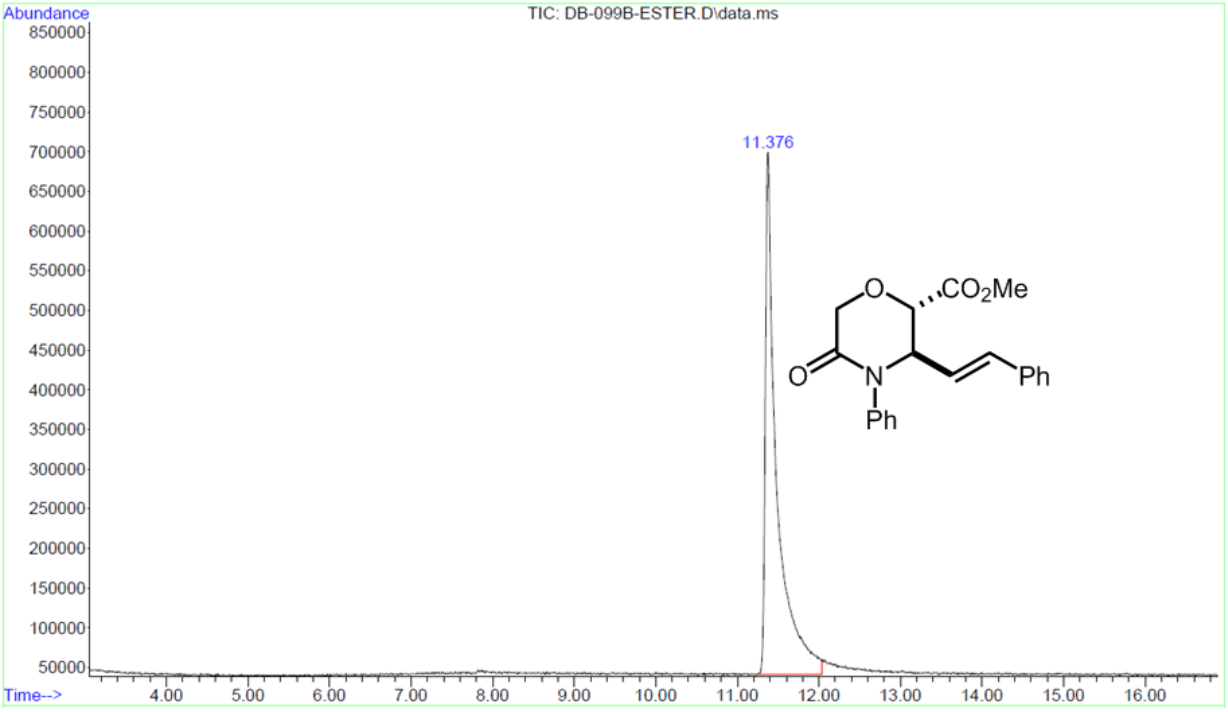
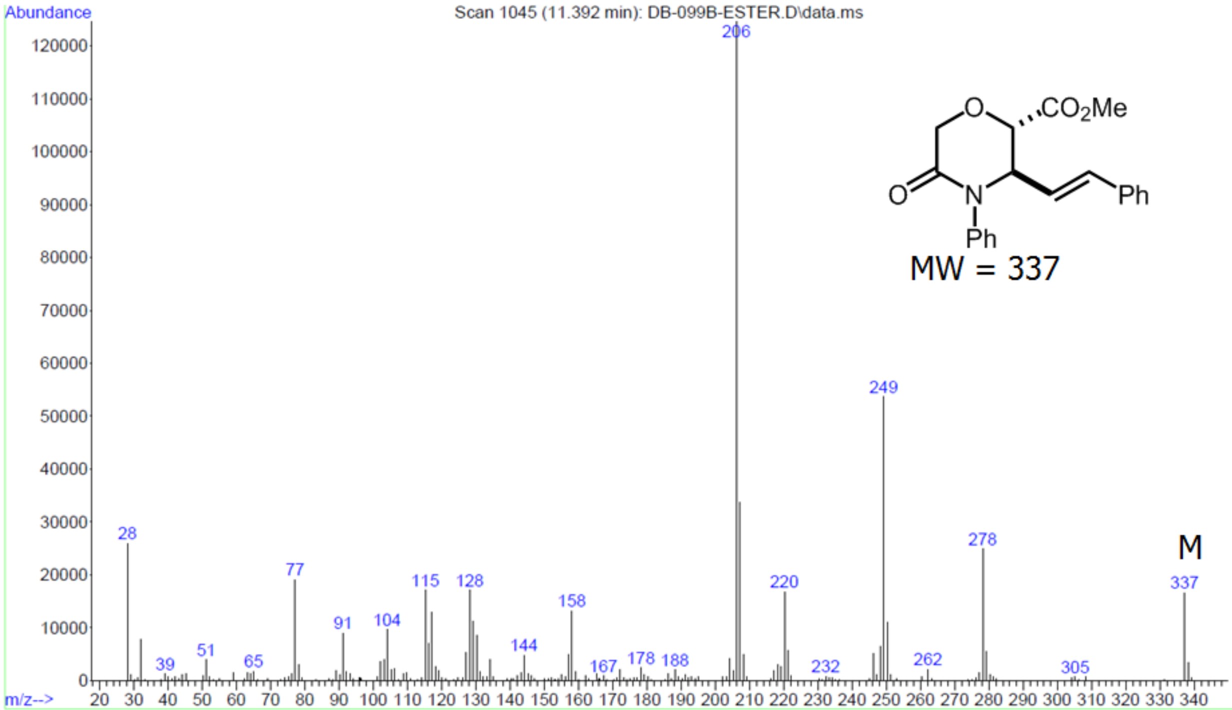


5a2

Prepared from crude **5a1** using General Procedure C. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100) then 100% MeOH. Yield = 280 mg, 83% over 2 steps, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 to 7.19 (10H, m), 6.48 (1H, d), 6.35 (1H, dd), 4.85 (1H, d), 4.75 (1H, dd), 4.53 (1H, d), 4.27 (1H, d), 3.77 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.66, 165.73, 139.87, 135.55, 134.57, 129.49, 129.45, 129.26, 129.08, 128.78, 128.56, 128.35, 127.83, 127.01, 126.78, 124.74, 119.84, 75.79, 65.51, 63.26, 52.07. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{20}H_{19}NO_4$ 337.1314; found 337.1317.

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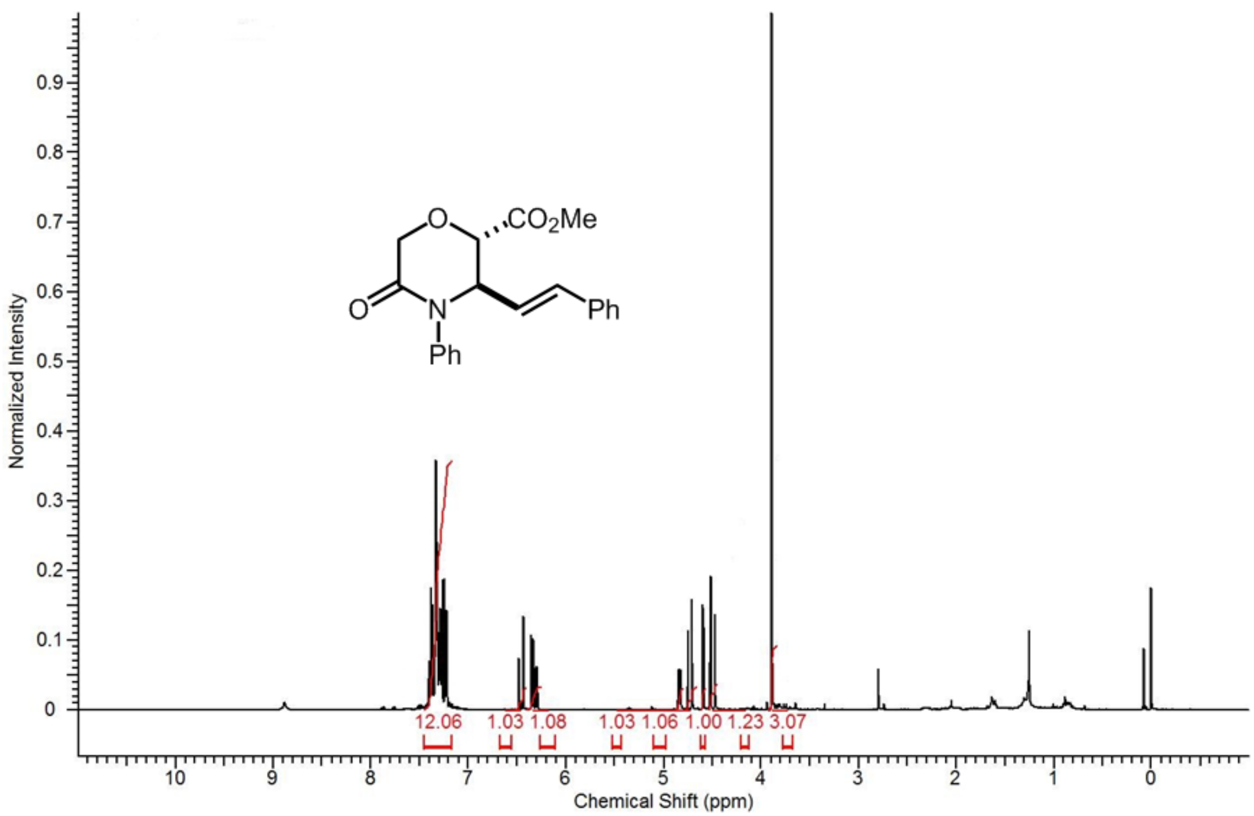
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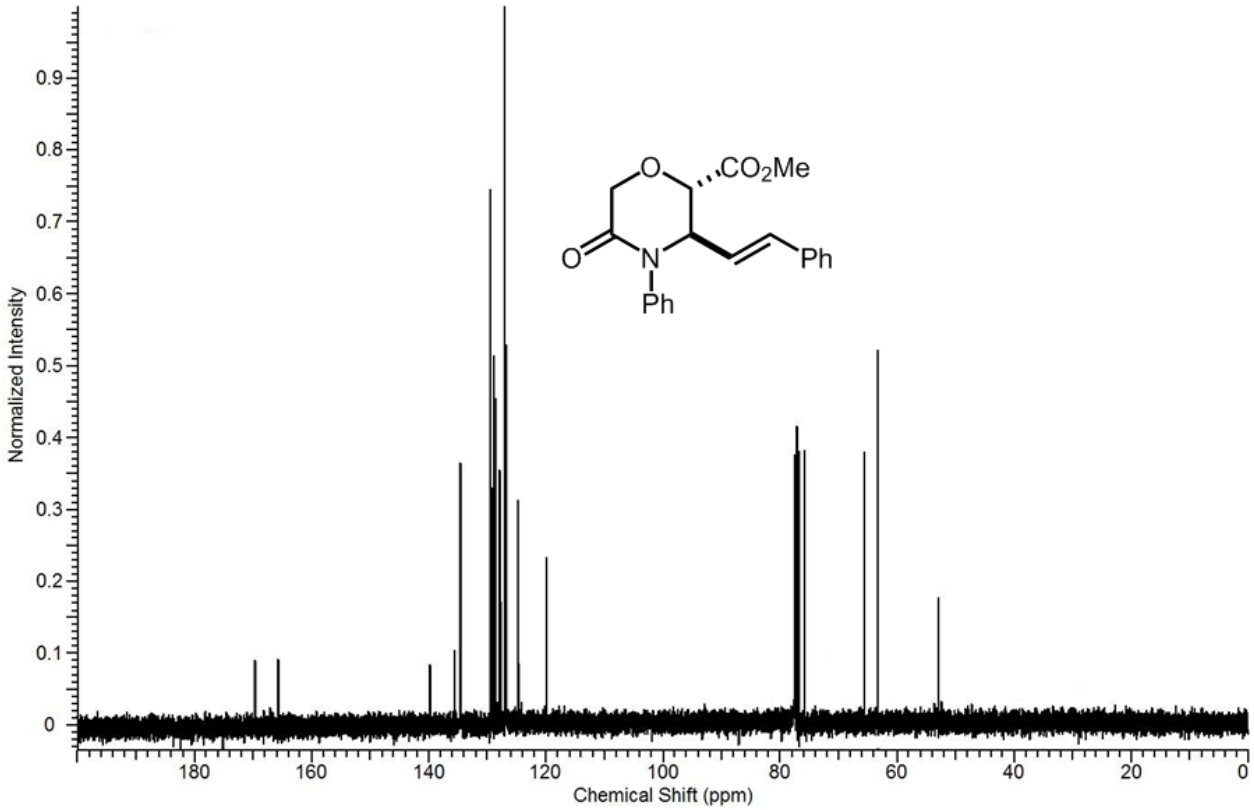
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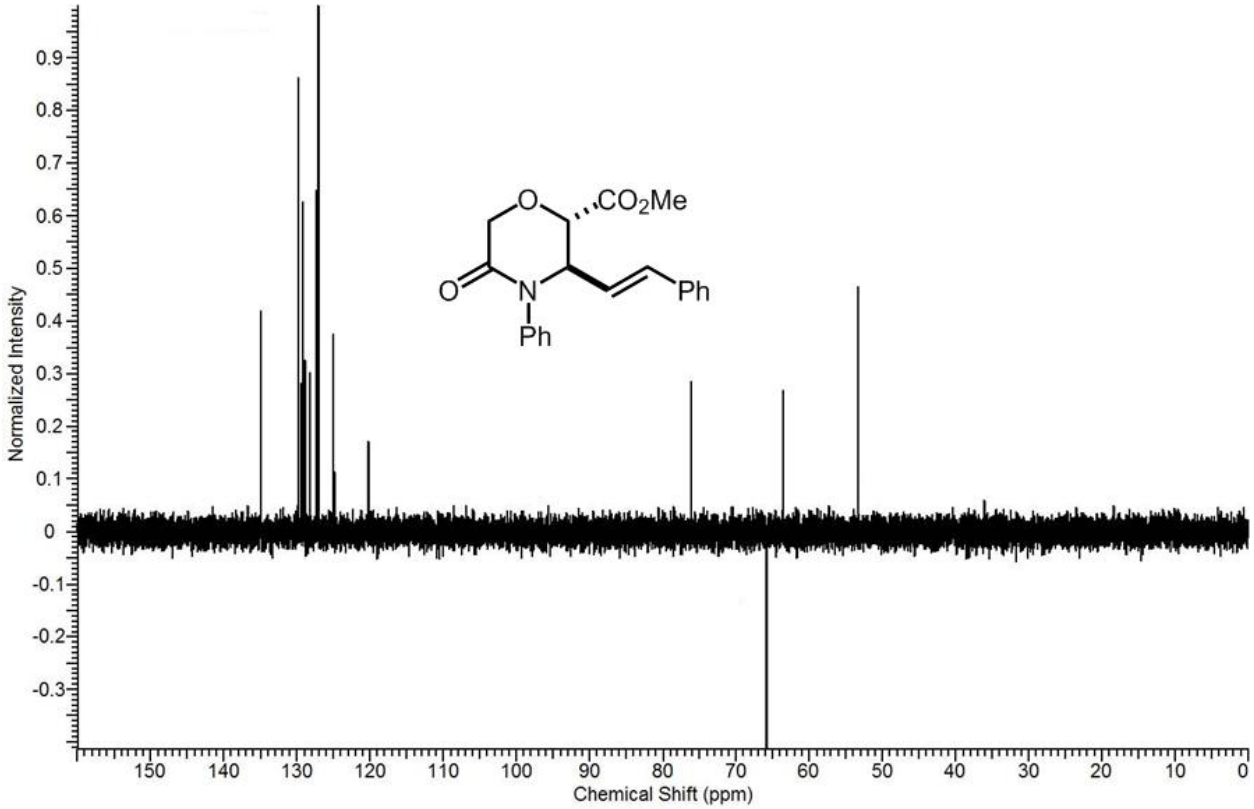
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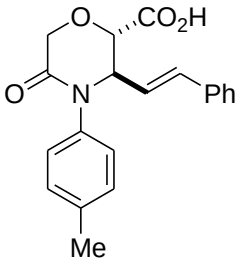
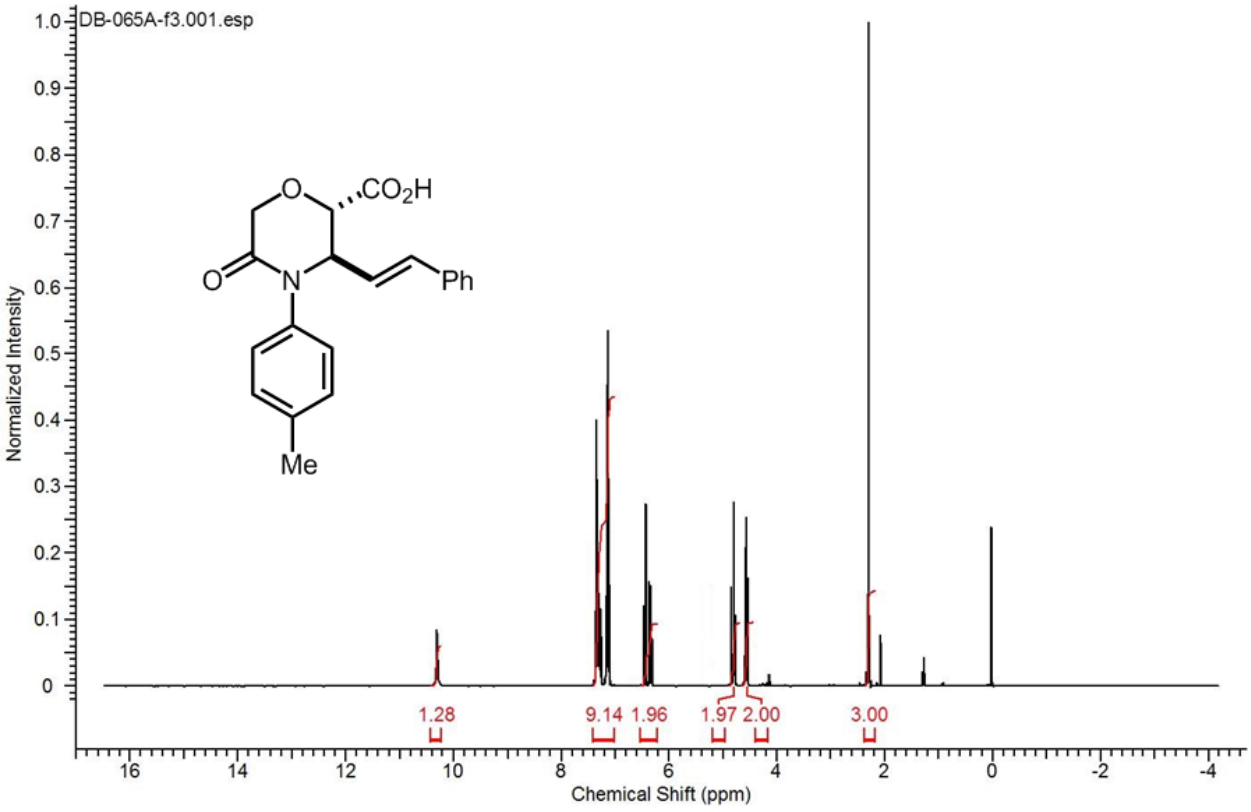
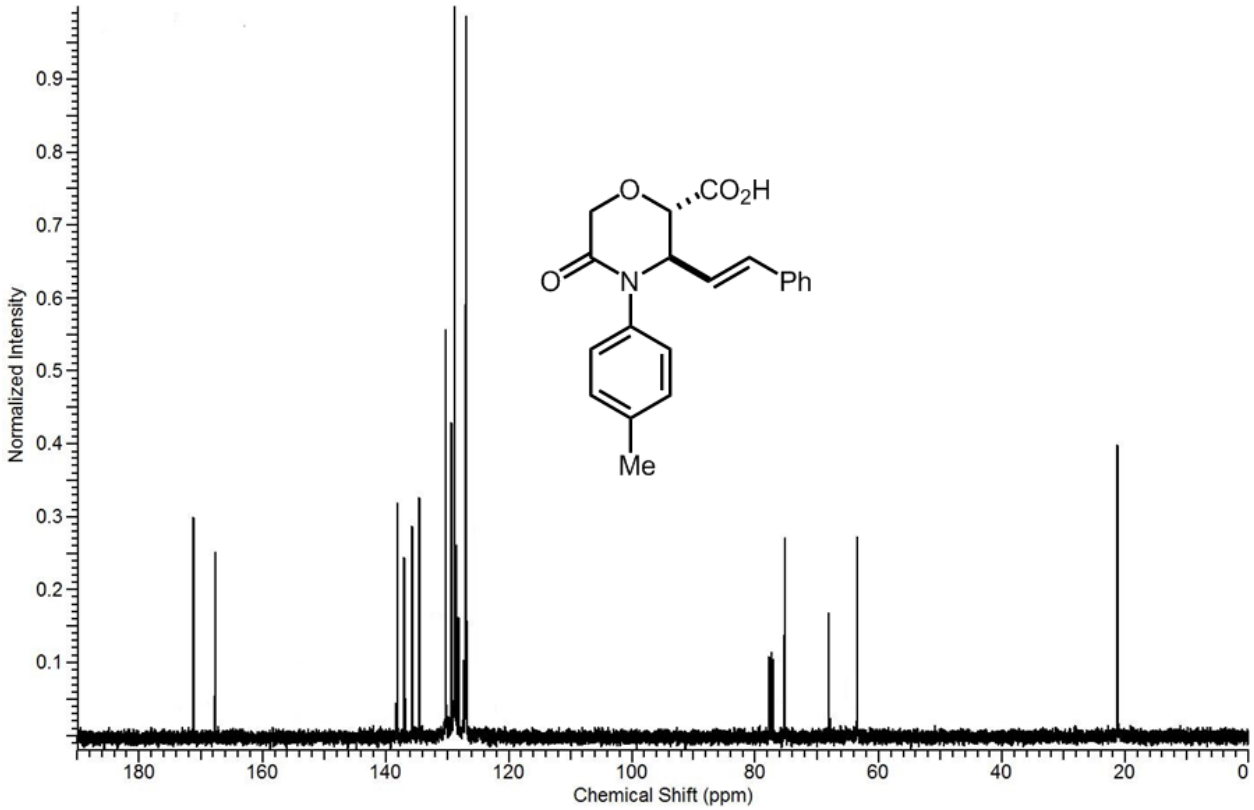


5b1

Prepared from imine **4c** (221 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv), using General Procedure B. T = 90 ^{o}C, time = 18 h. An analytical sample was obtained after a series of washes with cold petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.30 (1H, s, broad), 7.40 to 7.11 (9H, m), 6.47 to 6.32 (2H, m), 4.85 (2H, m), 4.57 (2H, m), 2.30 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 167.7, 137.7, 137.3, 135.6, 134.5, 130.5, 129.1, 128.9, 127.2, 127.2, 124.8, 75.5, 65.4, 63.8, 21.5. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{20}H_{19}NO_4$ 337.1314; found 337.1318.

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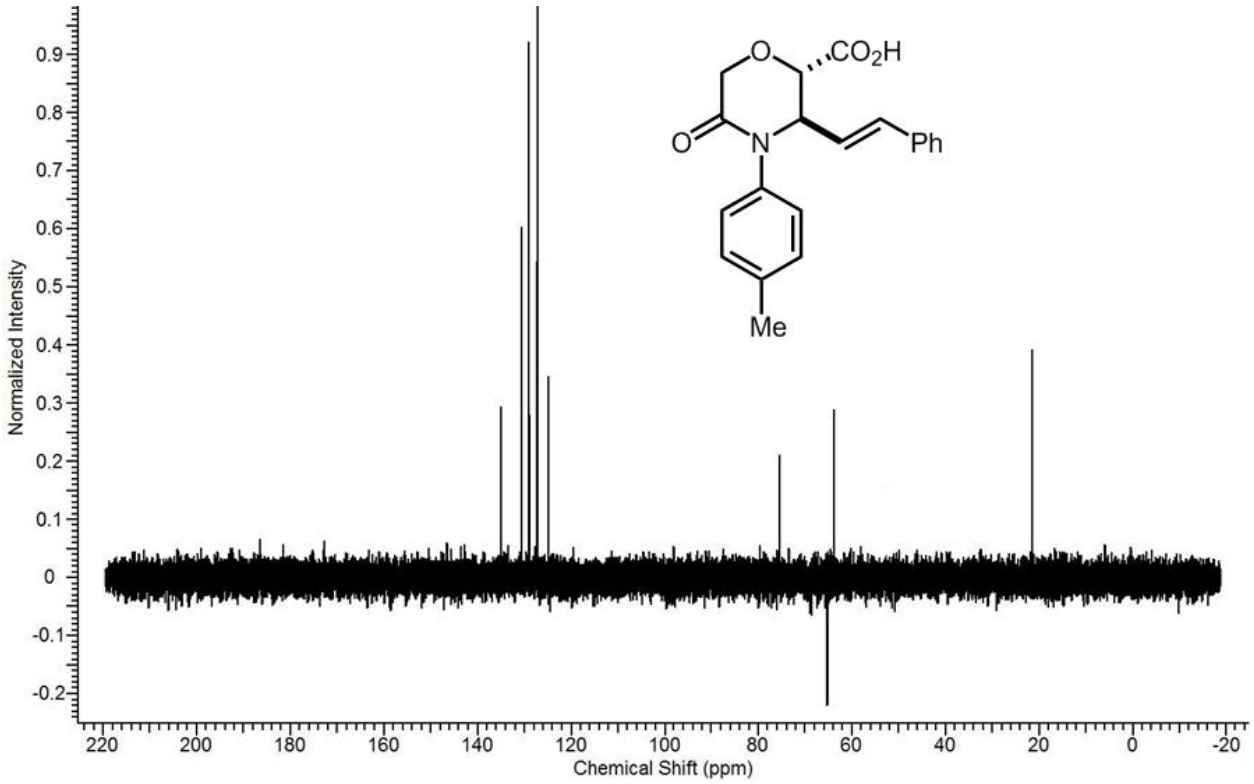
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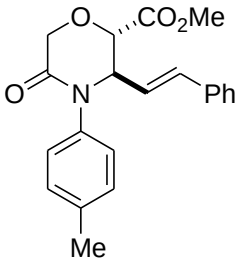
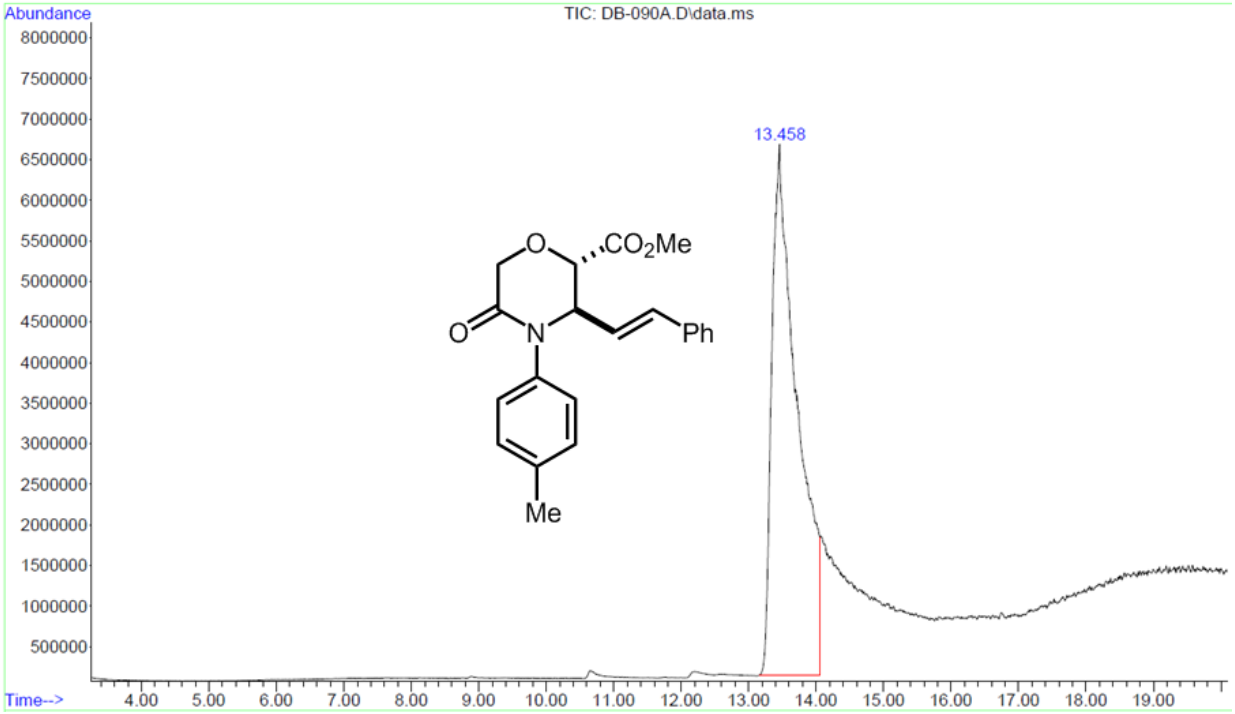
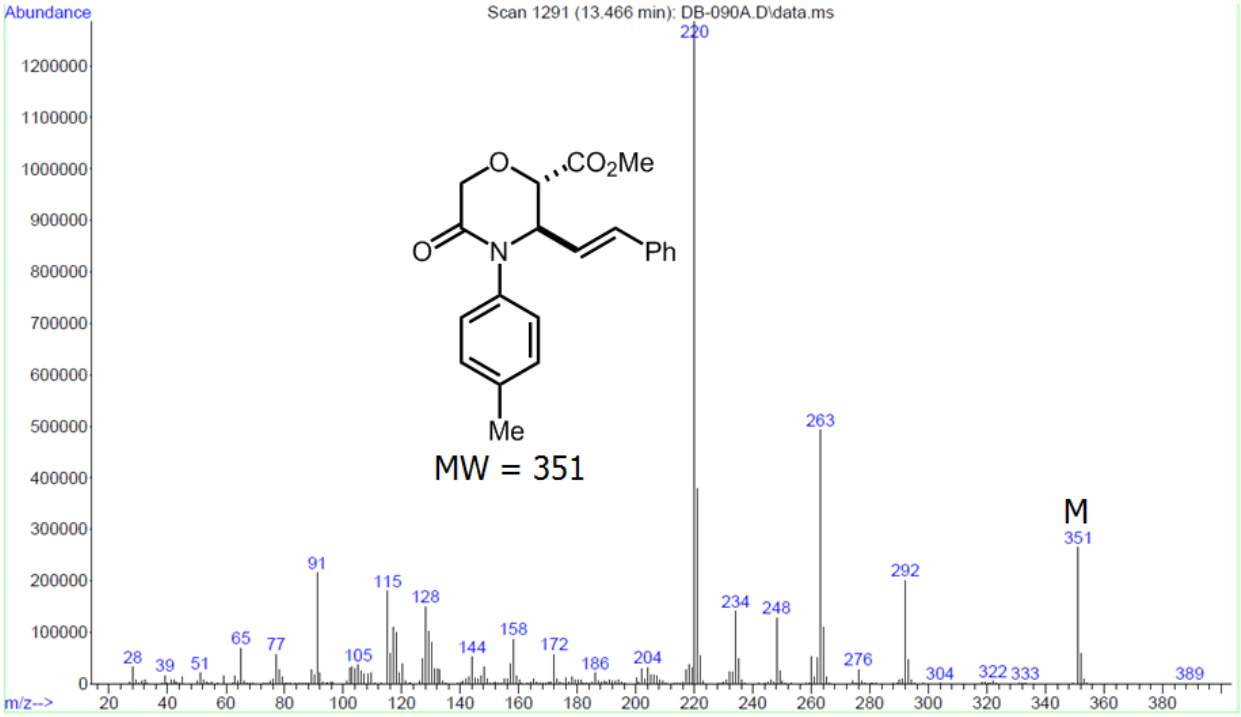


5b2

Prepared from crude **5b1** using General Procedure C. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100) then 100% MeOH. Yield = 313 mg, 89% over 2 steps, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 to 7.11 (9H, m), 6.45 (1H, d), 6.32 (1H, dd), 4.82 to 4.47 (4H, dd), 3.88 (3H, s), 2.38 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 165.8, 137.7, 137.2, 135.6, 134.4, 130.1, 128.8, 128.5, 126.8, 126.8, 124.8, 75.8, 65.5, 63.3, 53.0, 21.2. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{21}H_{21}NO_4$ 351.1417; found 351.1421.

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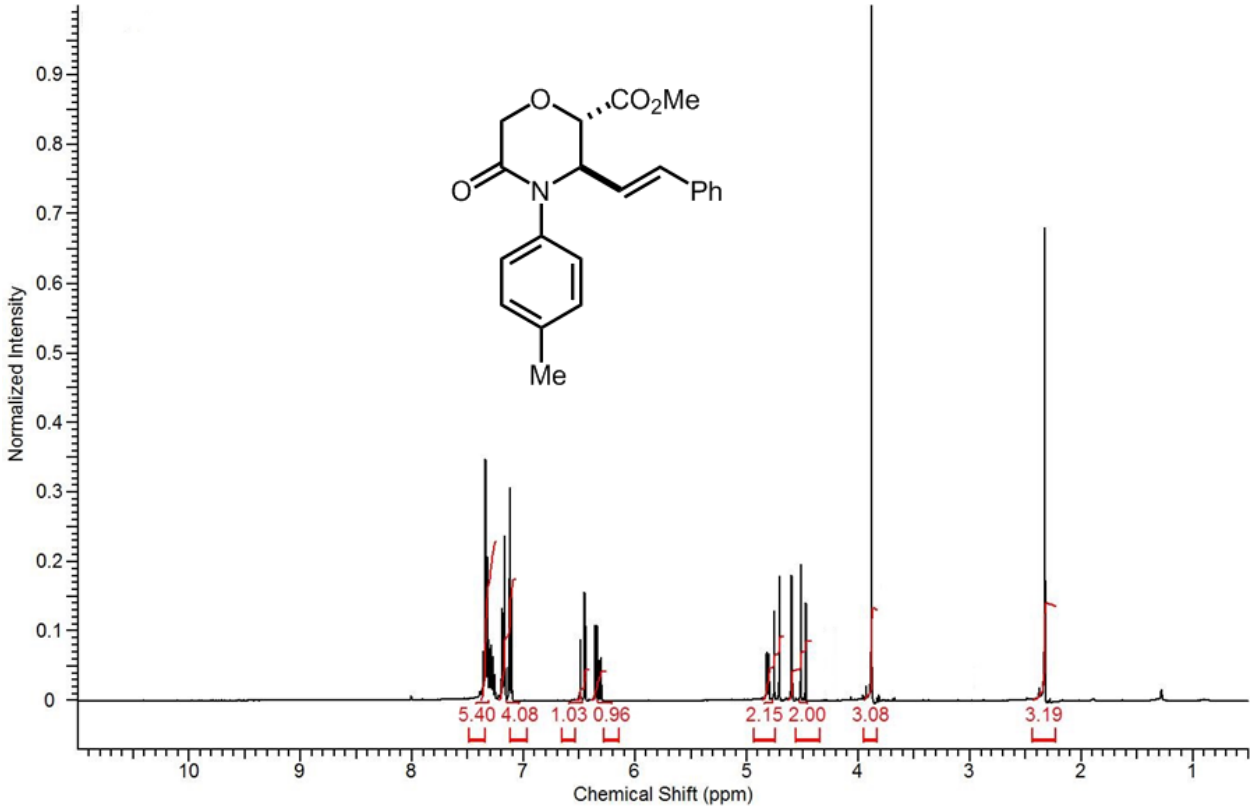
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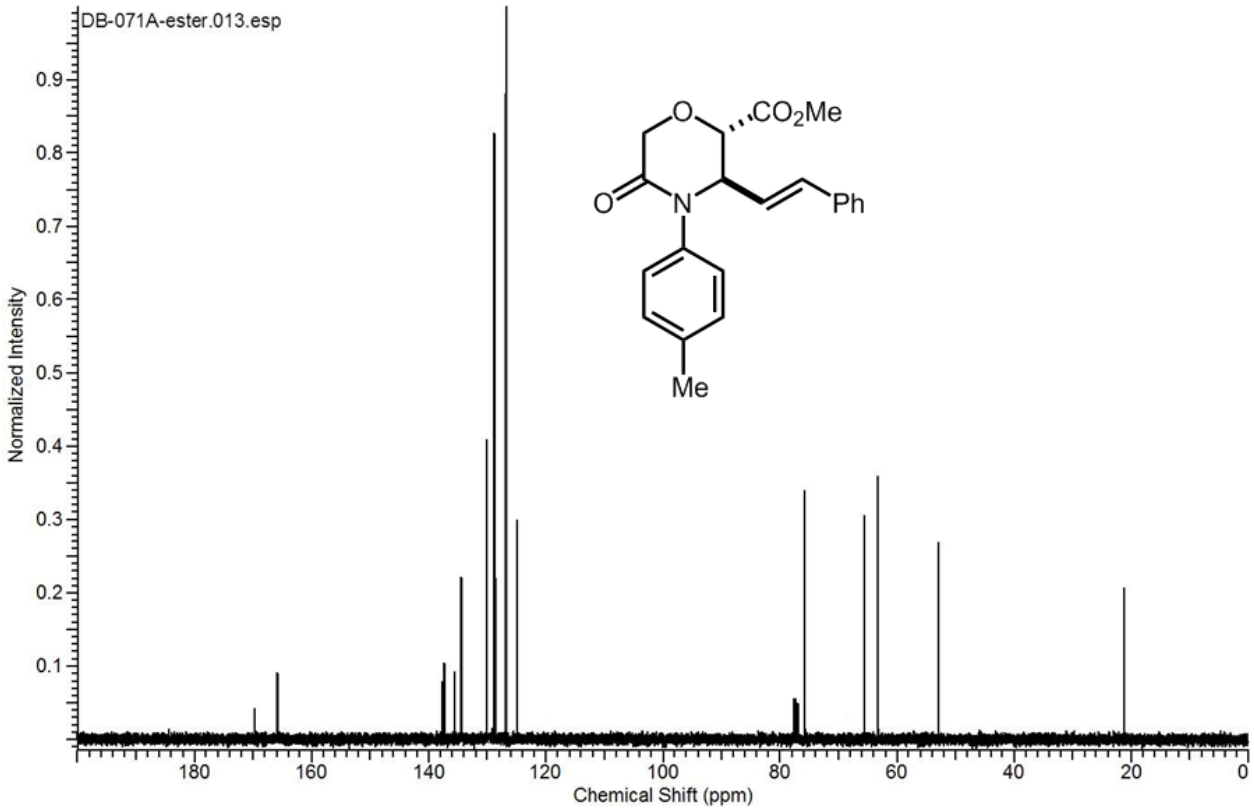
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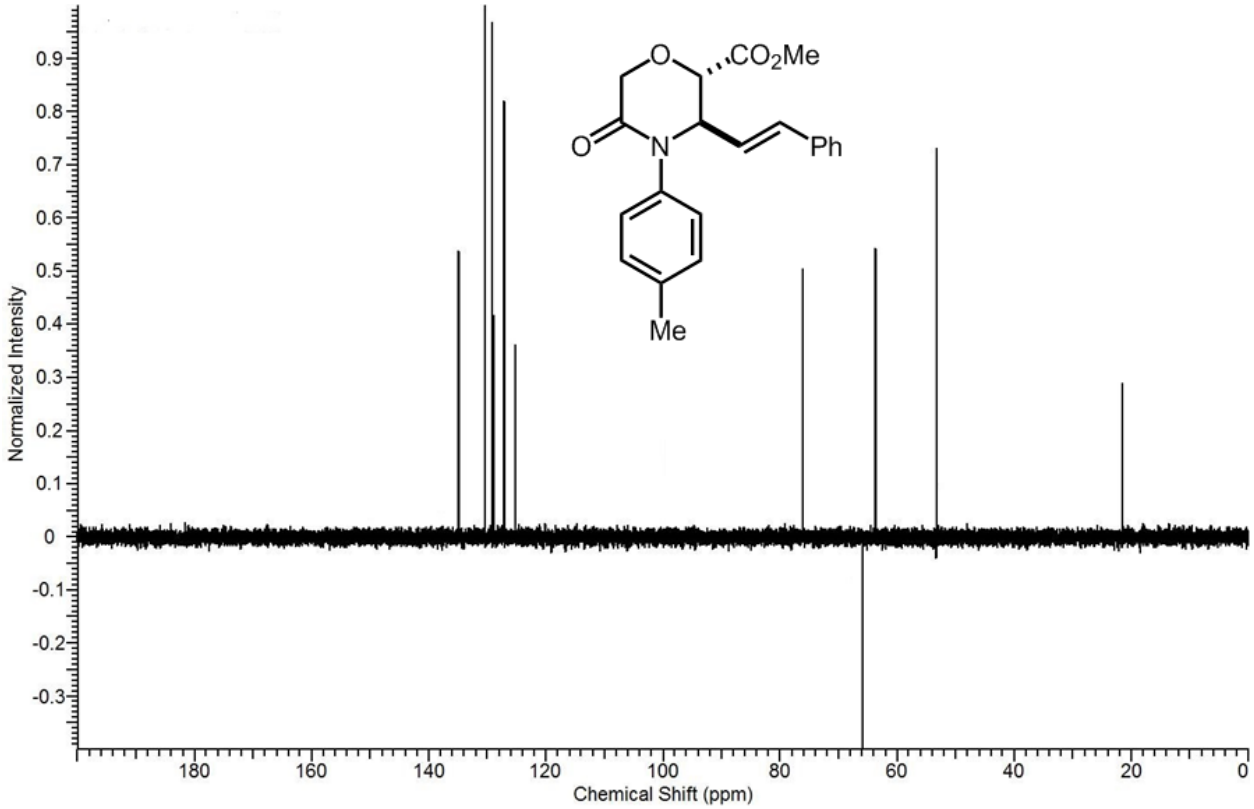
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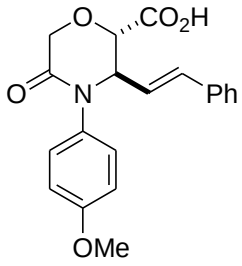
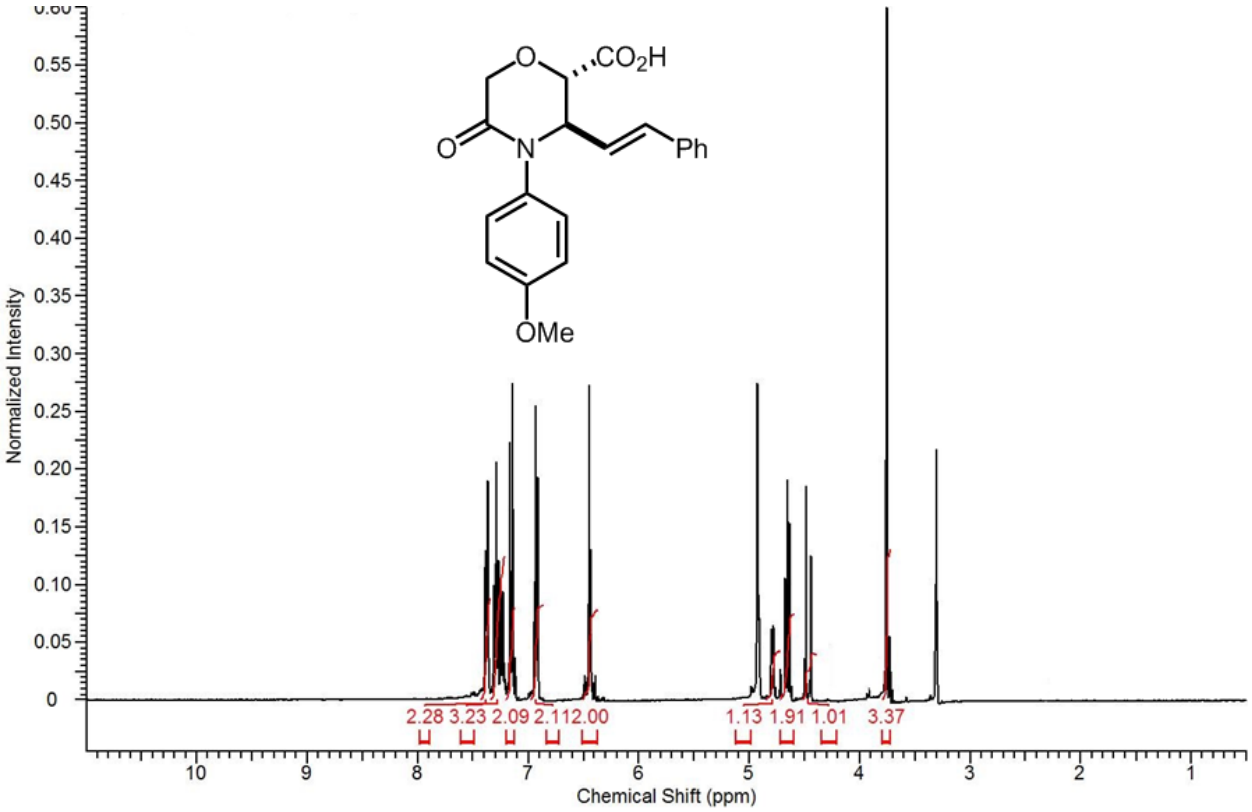
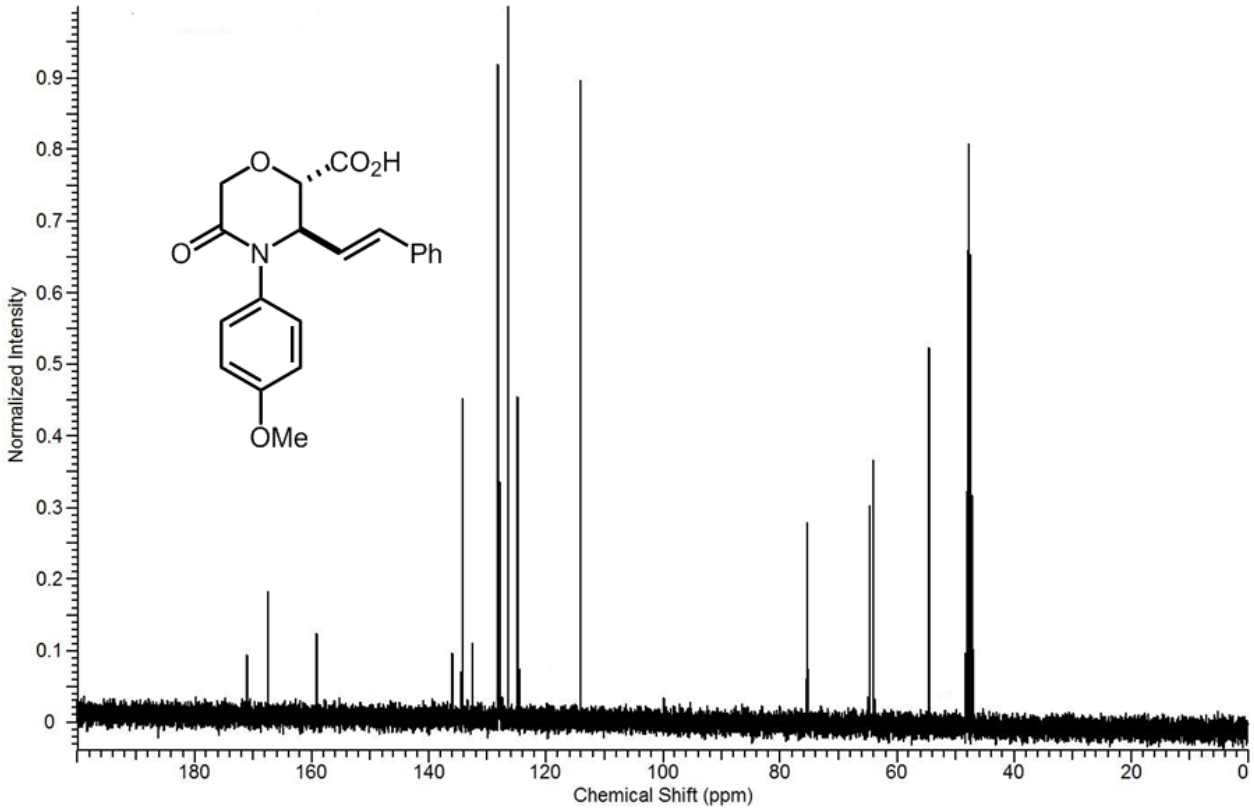


5c1

Prepared from imine **4b** (237 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv), using General Procedure B. T = 90 ^{o}C, time = 18 h. An analytical sample was obtained after a series of washes with cold petroleum ether. Yield = 300 mg, 84%. ^{1}H NMR (400 MHz, MeOH) δ 7.39 to 7.12 (5H, m), 6.92 (2H, d), 6.48 (2H, d), 4.79 (1H, d), 4.65 to 4.61 (2H, dd), 4.44 (1H, d), 3.77 (3H, s). ^{13}C NMR (101 MHz, MeOH) δ 170.9, 167.4, 159.1, 135.9, 134.4, 134.1, 132.5, 128.3, 128.1, 128.1, 127.9, 127.9, 126.4, 124.8, 114.1, 75.4, 64.6, 63.8, 54.5. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{20}H_{19}NO_5$ 353.1263; found 353.1267.

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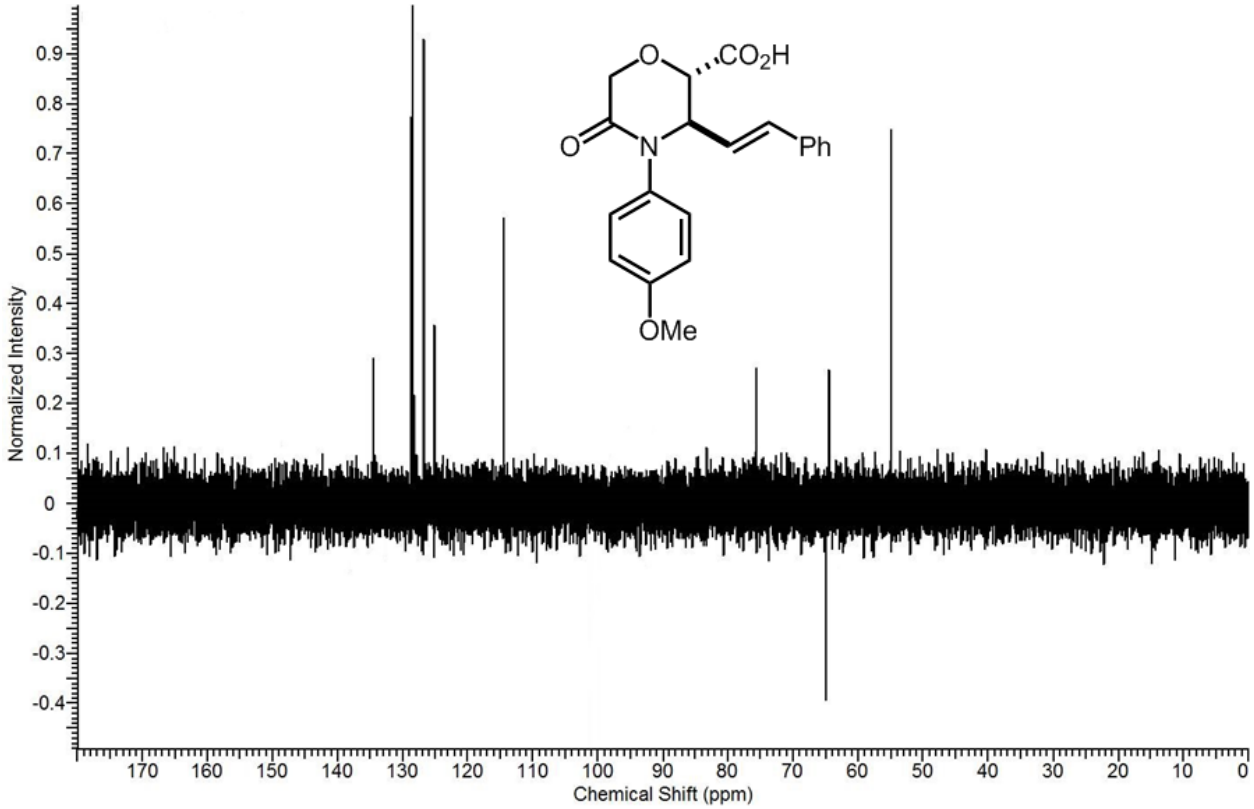
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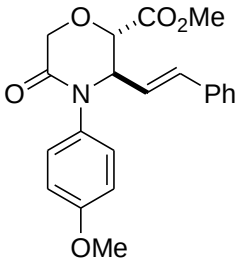
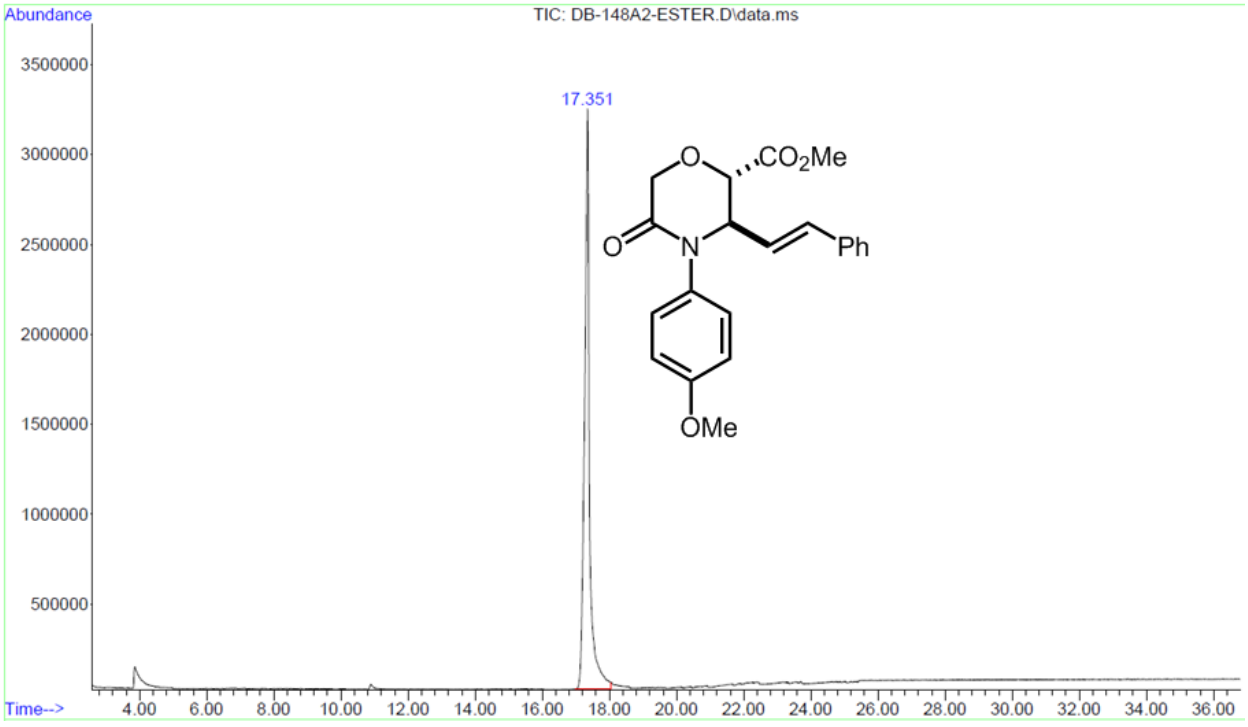
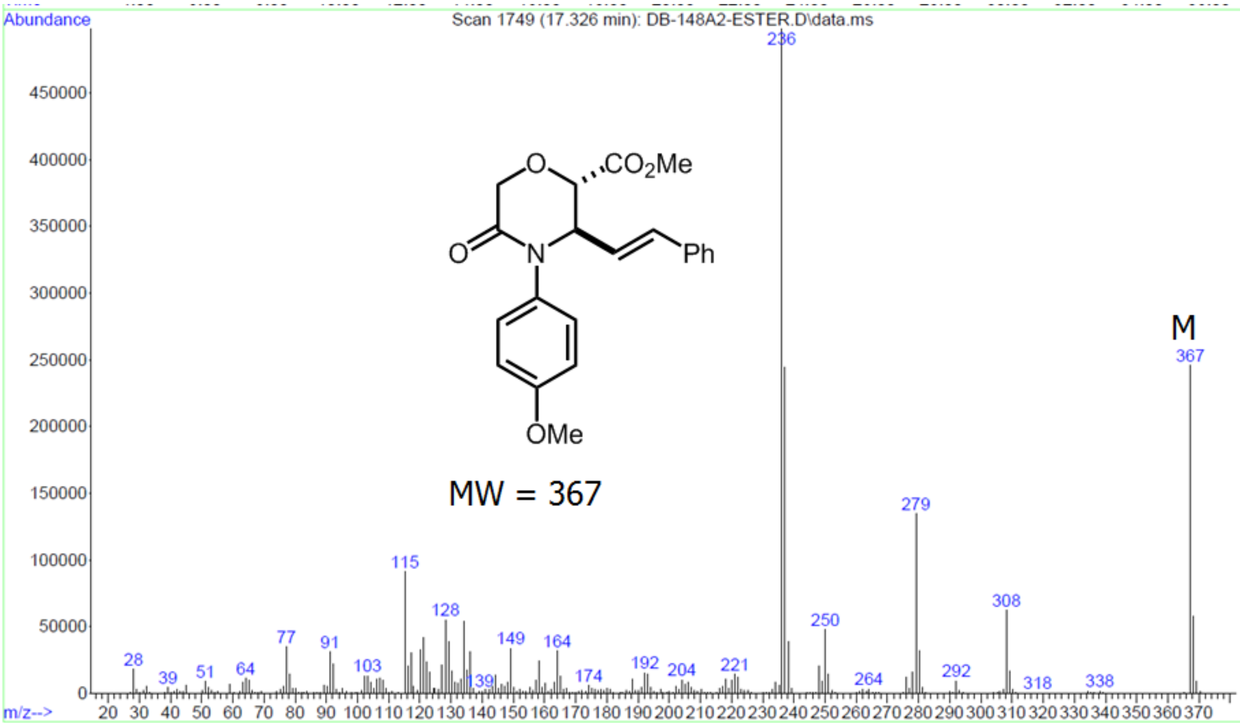


5c2

Prepared from crude **5c1** using General Procedure C. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100) then 100% MeOH. Yield = 338 mg, 92% over 2 steps, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 to 7.25 (5H, m), 7.13 (2H, d), 6.88 (2H, d), 6.42 to 6.28 (2H, m), 4.77 to 4.44 (3H, m), 3.87 to 3.75 (7H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 165.9, 158.8, 136.3, 135.5, 134.6, 132.5, 129.3, 128.8, 128.7, 128.7, 128.5, 128.3, 126.8, 126.7, 124.7, 114.1, 75.7, 65.5, 63.5, 55.5, 52.7. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{21}H_{21}NO_5$ 367.1420; found 367.1416.

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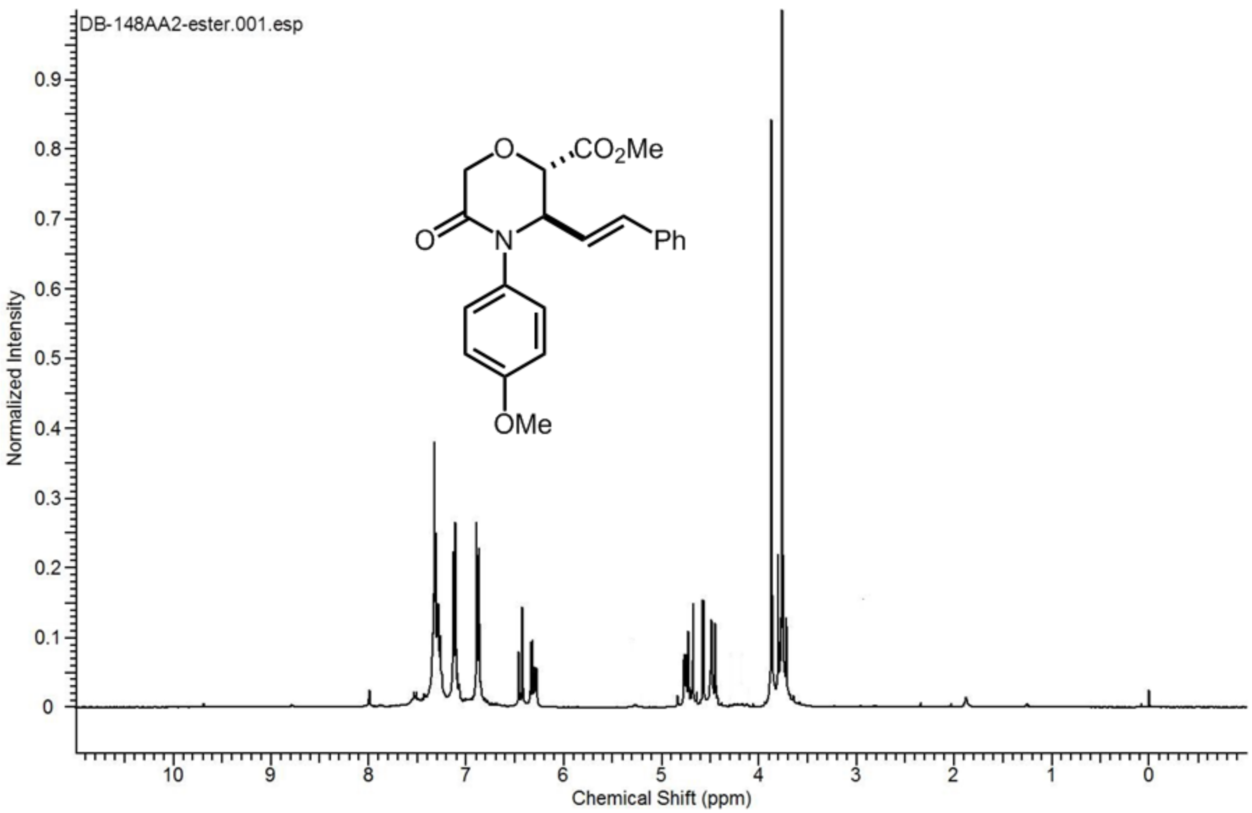
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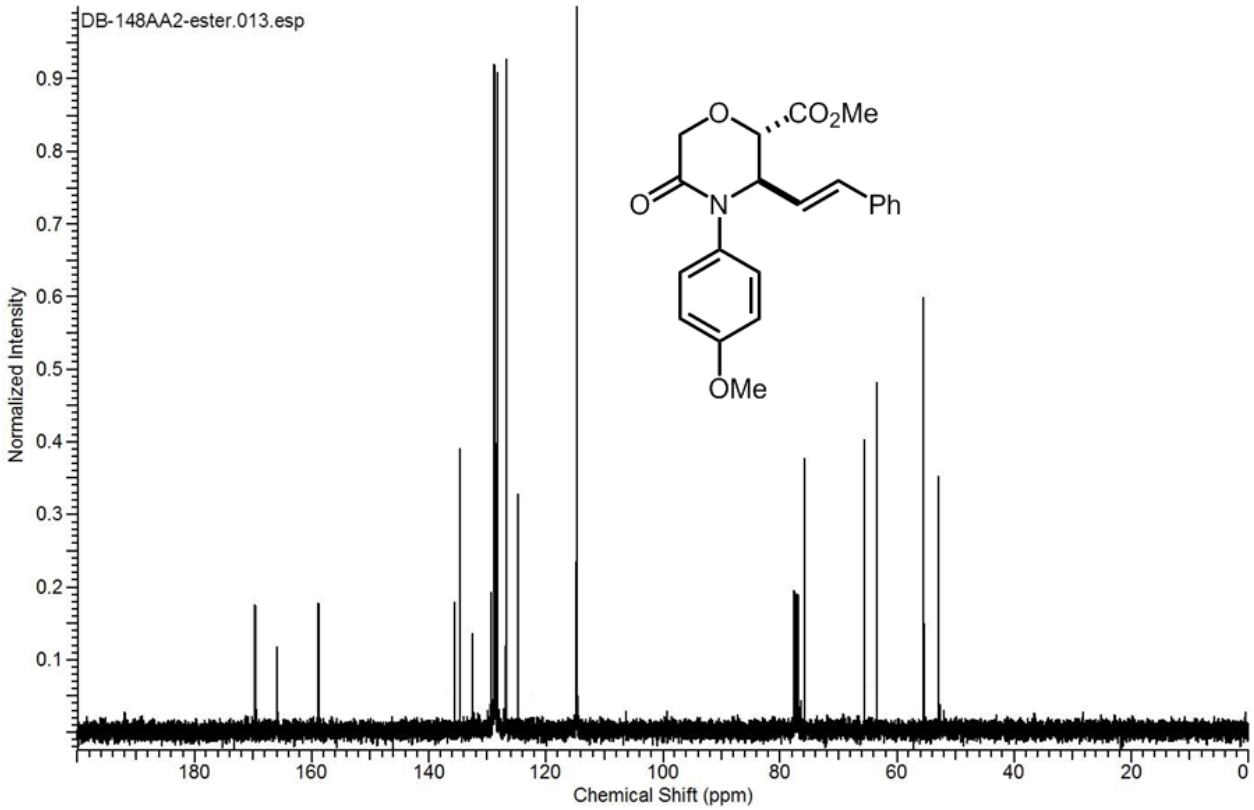
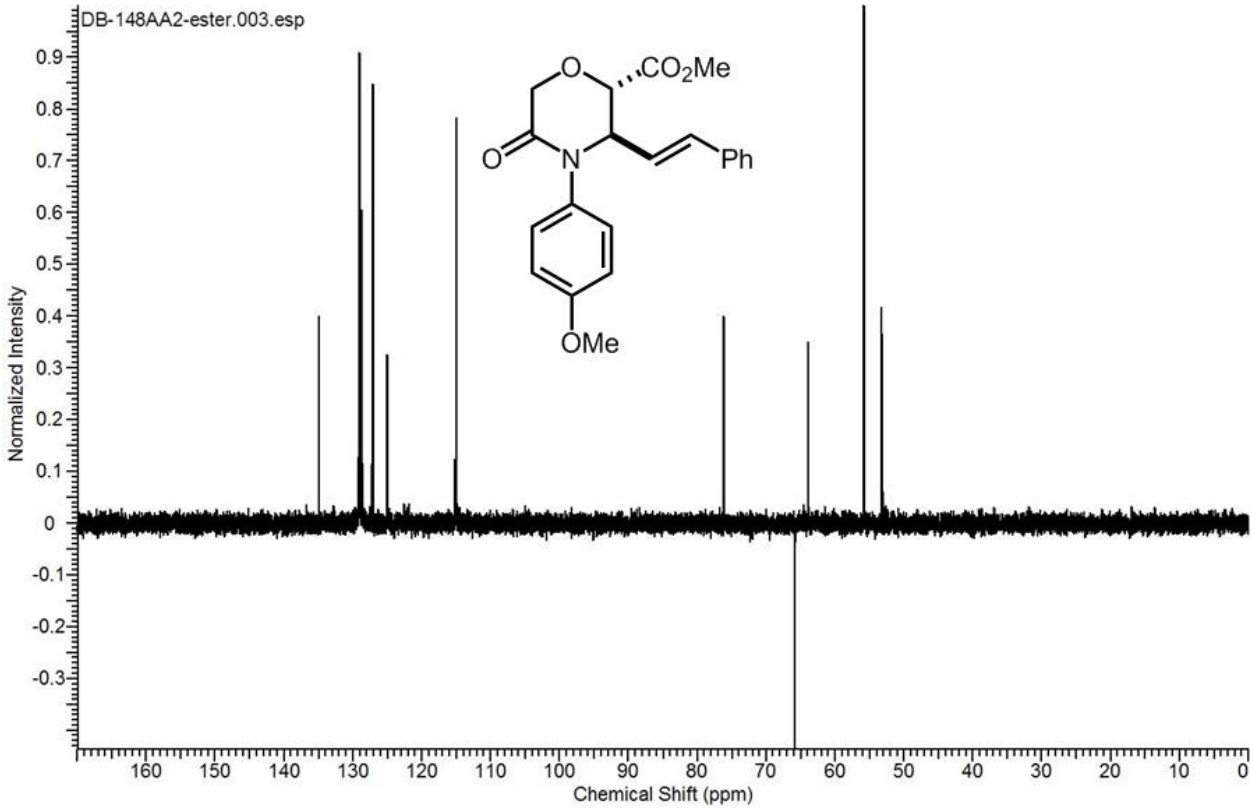
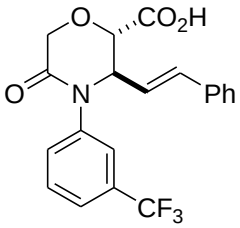
Ph
OMe

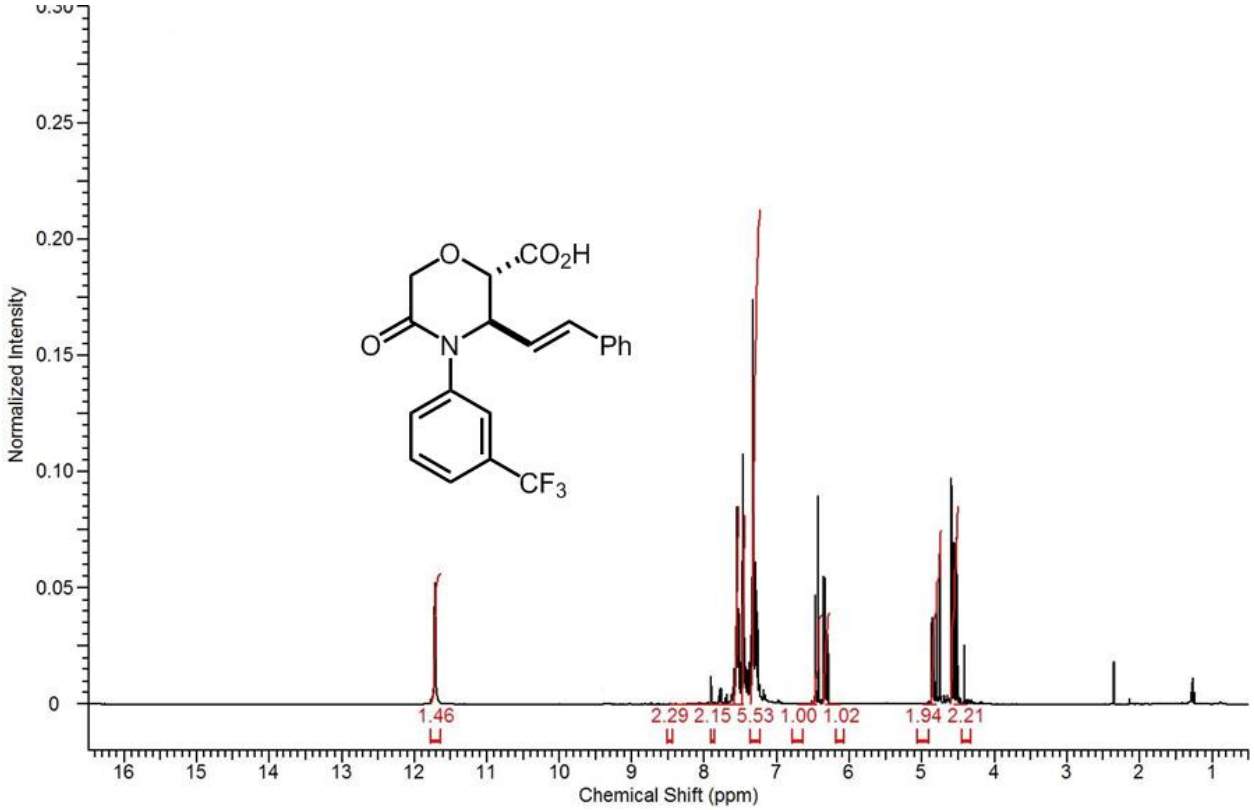

DB-148AA2-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
OMe

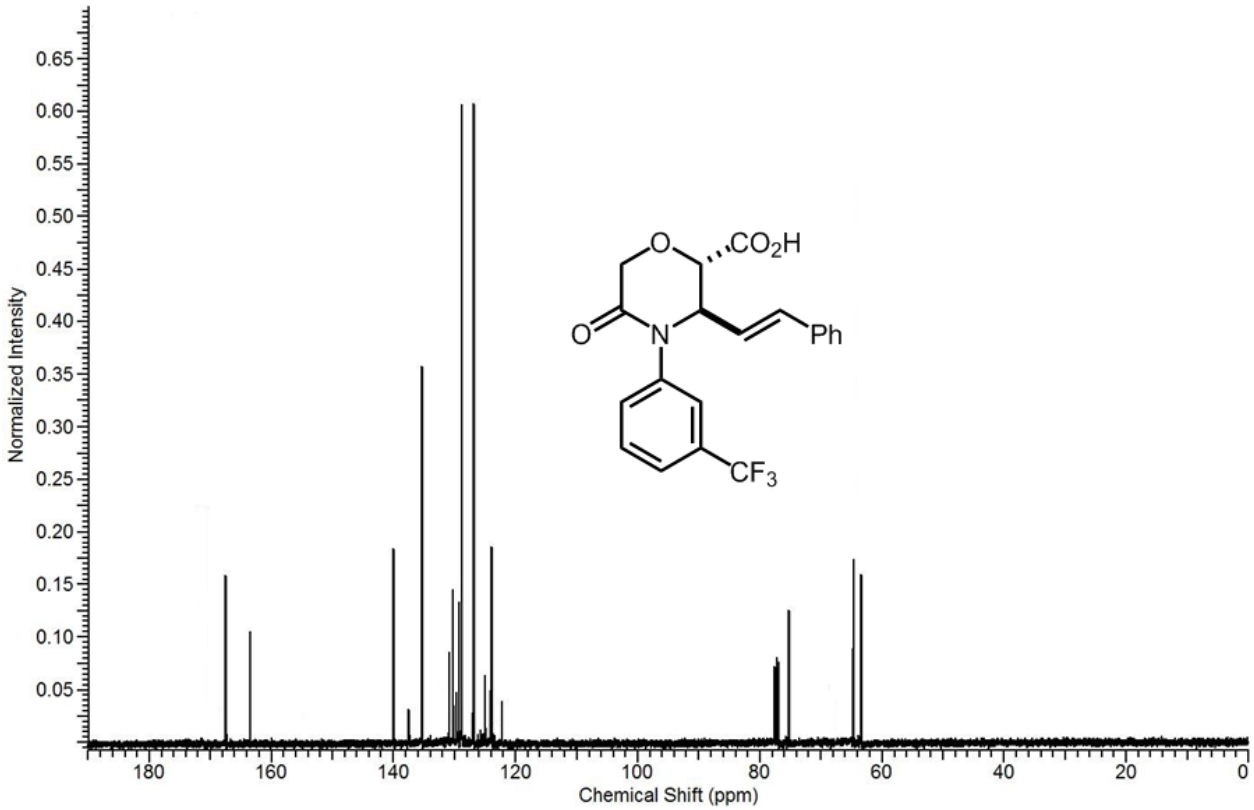

DB-148AA2-ester.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
OMe

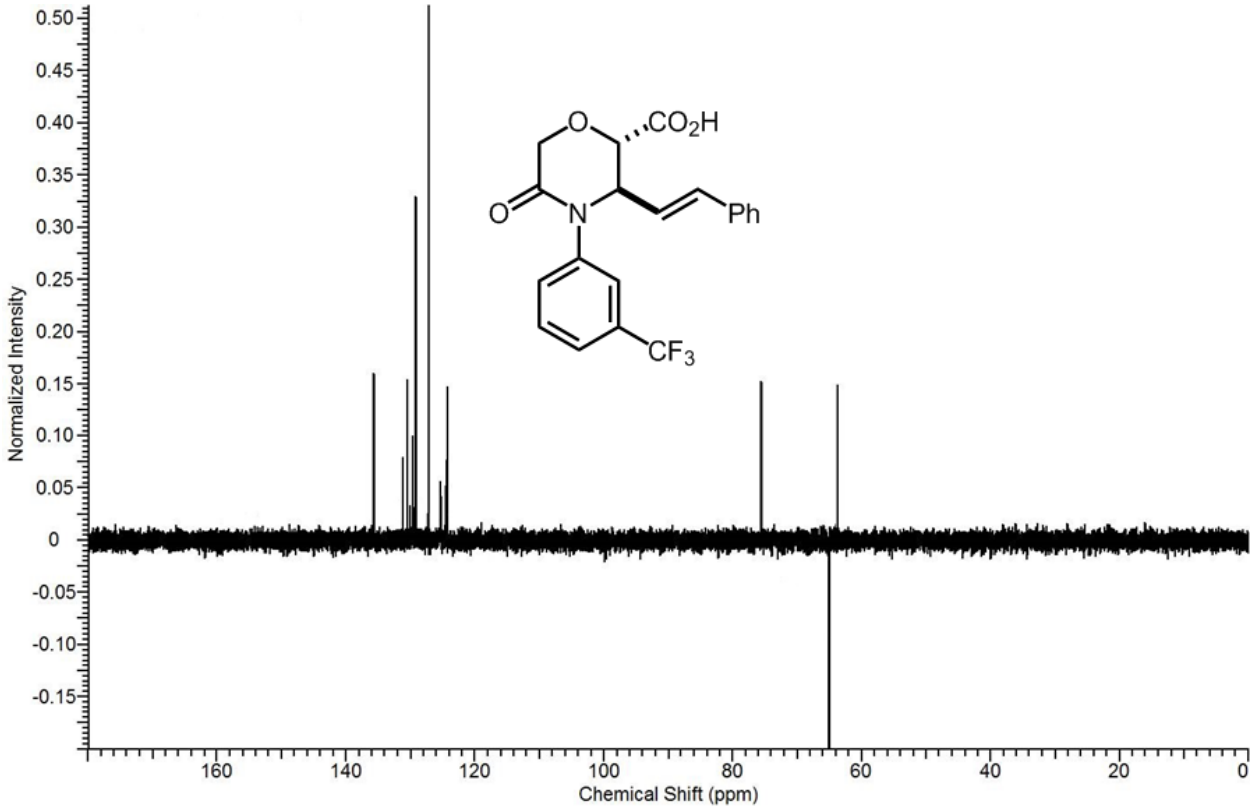


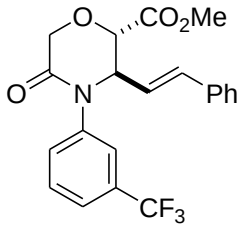
5d1

Prepared from imine **4e** (275 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv), using General Procedure B. T = 100 ^{o}C, time = 18 h. An analytical sample was obtained after a series of washes with cold petroleum ether^{1}H NMR (400 MHz, $CDCl_3$) δ 11.77 (1H, s), 7.69 to 7.24 (4H, m), 6.43 to 6.30 (2H, m), 4.86 to 4.74 (2H, dd), 4.60 to 4.48 (2H, dd). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.97, 163.48, 139.95, 139.84, 137.52, 137.33, 135.28, 133.90, 132.28, 132.10, 131.95, 131.67, 131.62, 131.30, 131.11, 130.81, 130.18, 130.10, 129.69, 129.46, 129.28, 129.23, 129.13, 129.09, 128.82, 128.77, 128.56, 128.32, 128.23, 127.66, 126.94, 126.84, 126.15, 125.72, 124.97, 124.94, 124.19, 124.15, 124.11, 123.94, 123.42, 122.24, 75.73, 65.02, 63.83. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{20}H_{16}F_3NO_4$ 391.1031; found 391.1022.



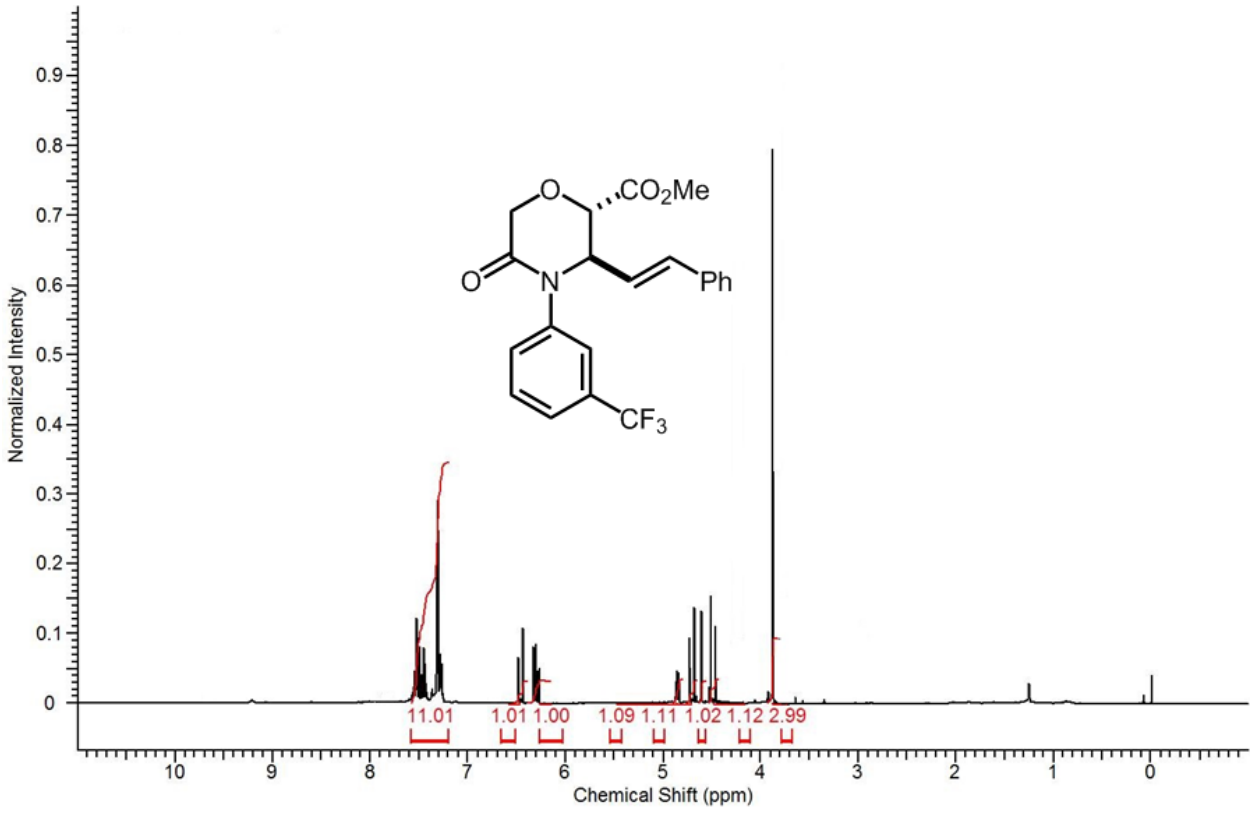

Normalized Intensity
Chemical Shift (ppm)
O
CO2H
O
N
Ph
CF3

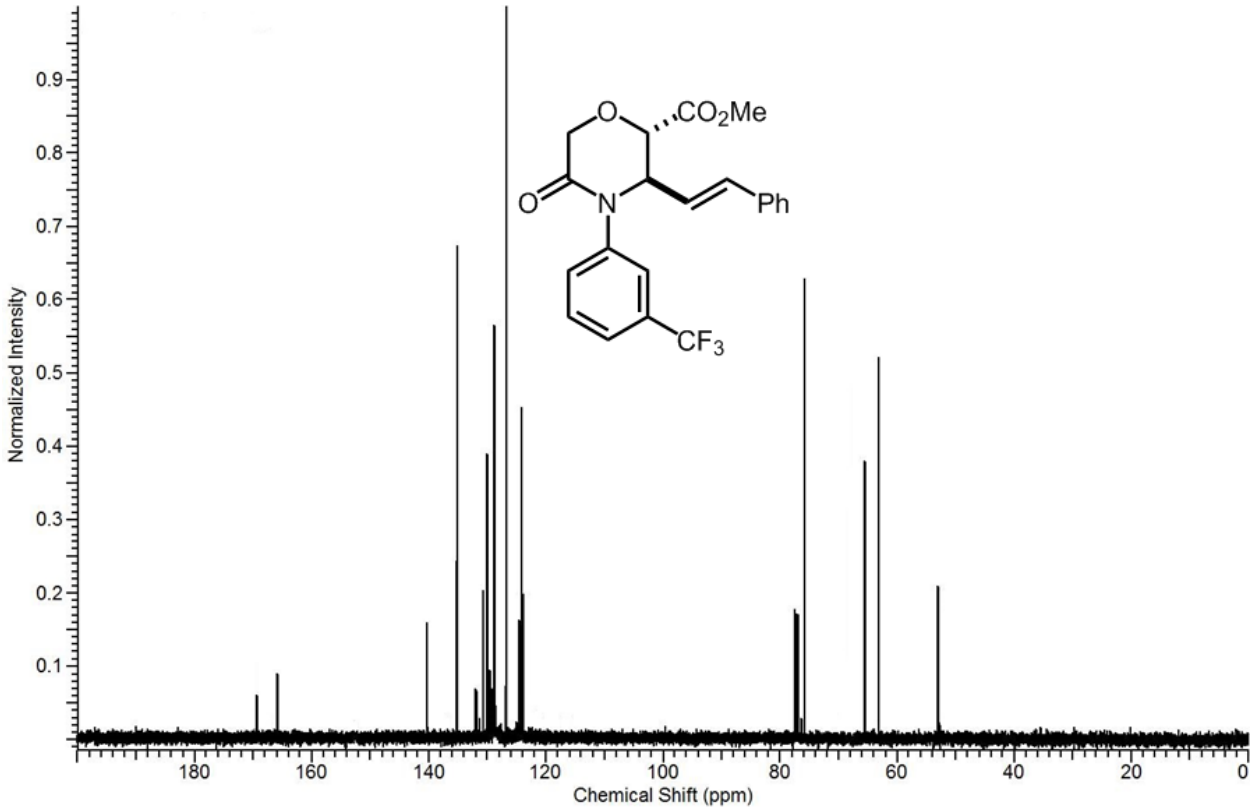

Normalized Intensity
Chemical Shift (ppm)
O
CO2H
O
N
Ph
CF3

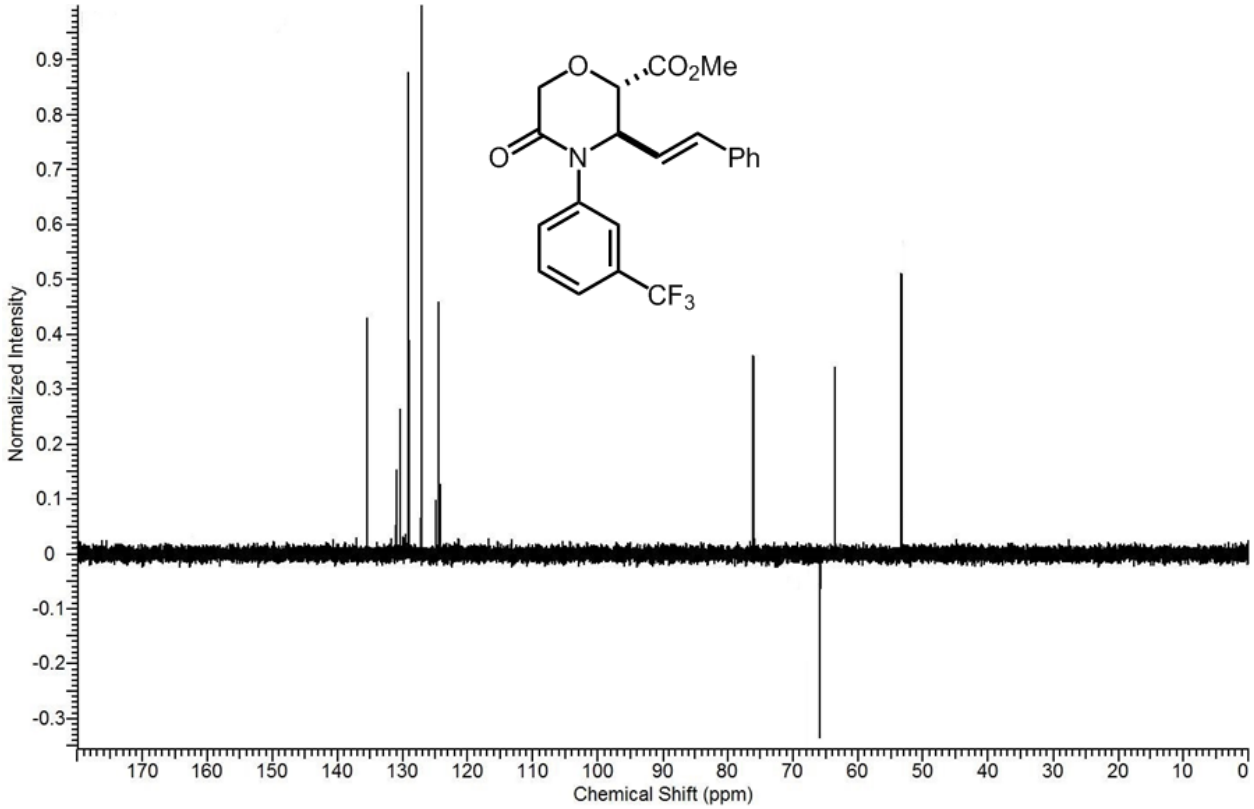


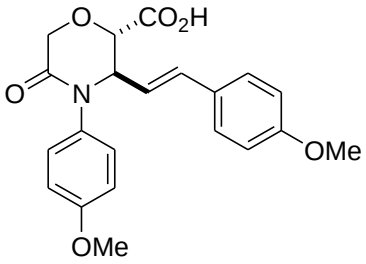
5d2

Prepared from crude **5d1** using General Procedure C. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100) then 100% MeOH. Yield = 304 mg, 75% over 2 steps, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 to 7.25 (4H, m), 6.44 (1H, d), 6.28 (1H, dd), 4.85 (1H, d), 4.72 (1H, d), 4.56 (1H, d), 4.30 (1H, d), 3.77 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.15, 165.81, 140.32, 136.82, 132.02, 131.69, 131.35, 130.64, 130.06, 129.98, 129.58, 129.35, 129.17, 128.80, 128.75, 128.72, 128.63, 128.56, 127.99, 126.83, 126.77, 124.94, 124.62, 124.59, 124.55, 124.51, 124.18, 123.91, 123.87, 123.83, 123.79, 122.85, 122.23, 75.76, 65.52, 63.93, 53.03. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{21}H_{18}F_3NO_4$ 405.1188; found 405.1194.



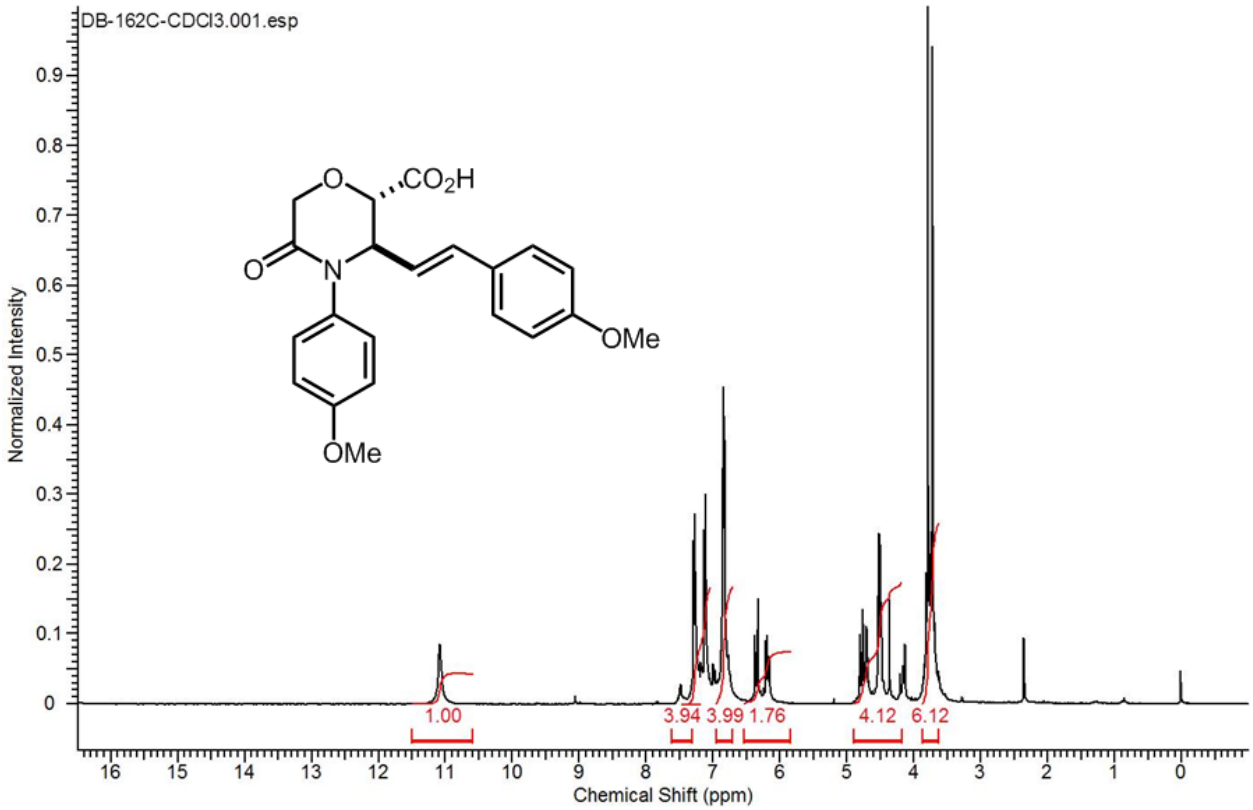

Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
CF3

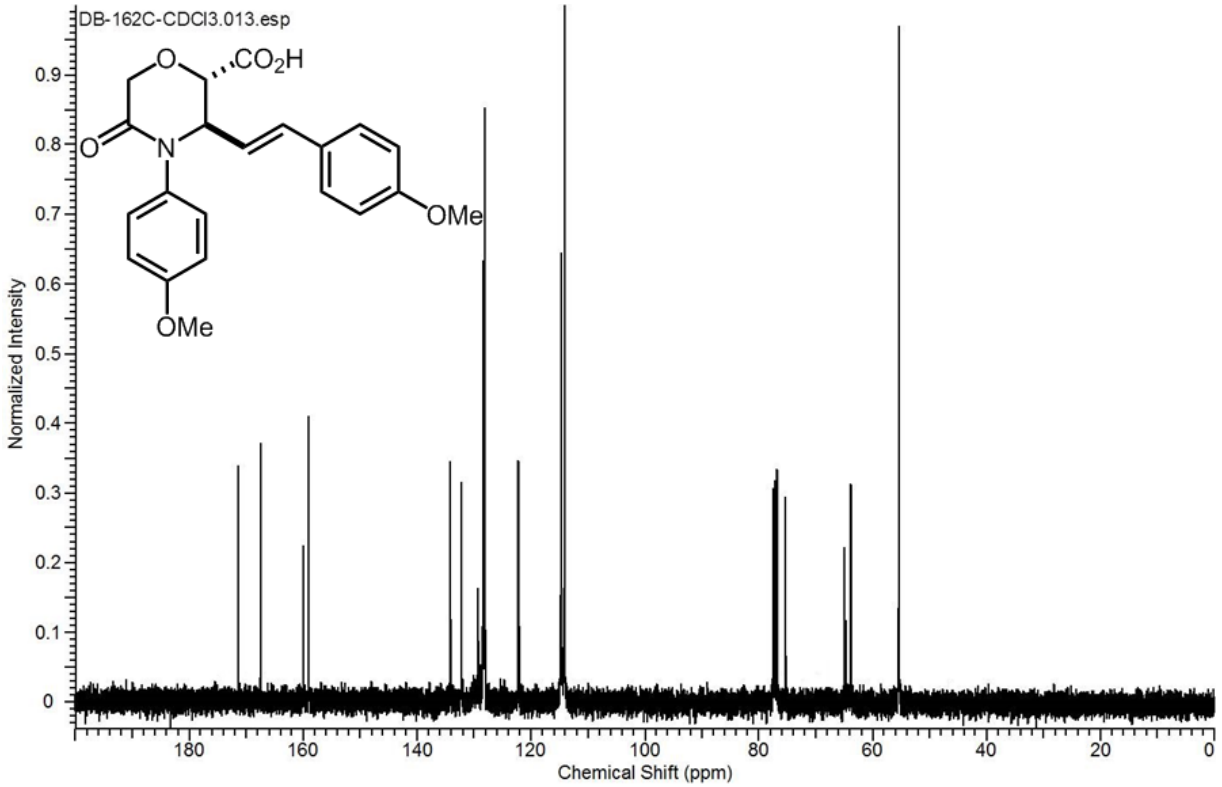

Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
CF3

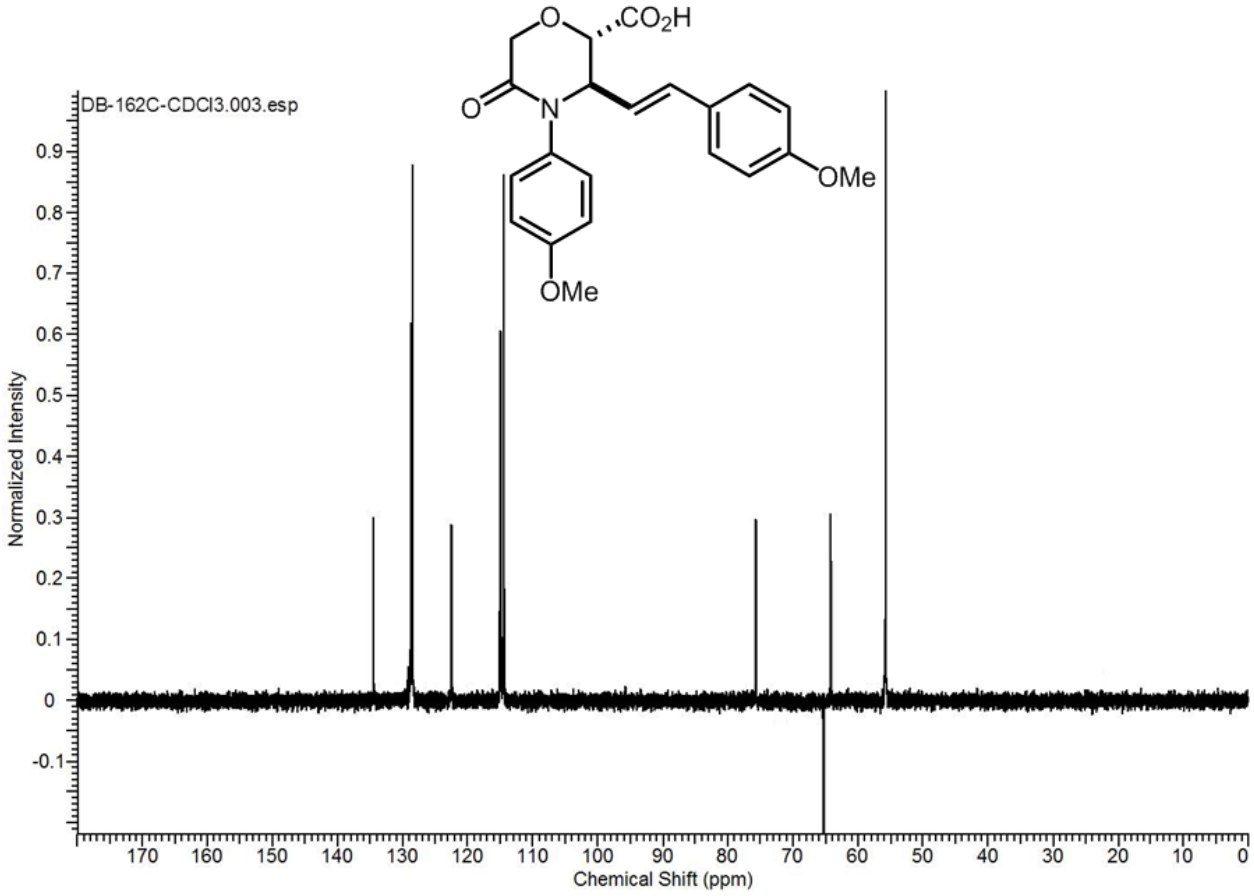


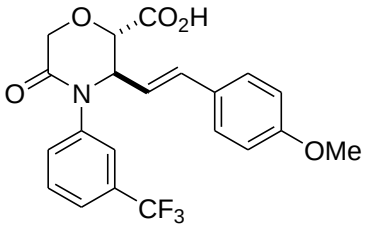
5e1

Prepared from imine **4f** (267 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv), using General Procedure B. T = 90 ^{o}C, time = 18 h. Yield = 314 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.08 (1H, s, br), 7.51 to 6.77 (8H, m), 6.37 to 6.13 (2H, m), 4.81 to 4.20 (4H, m), 3.76 to 3.67 (6H, overlapping singlets). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 167.5, 159.8, 158.9, 136.2, 134.1, 132.2, 130.0, 129.3, 129.1, 128.7, 128.4, 128.3, 128.3, 128.1, 125.4, 122.2, 122.1, 114.2, 114.1, 75.9, 68.1, 64.4, 63.8, 55.4, 55.3. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{21}H_{21}NO_6$ 383.1369; found 383.1376.



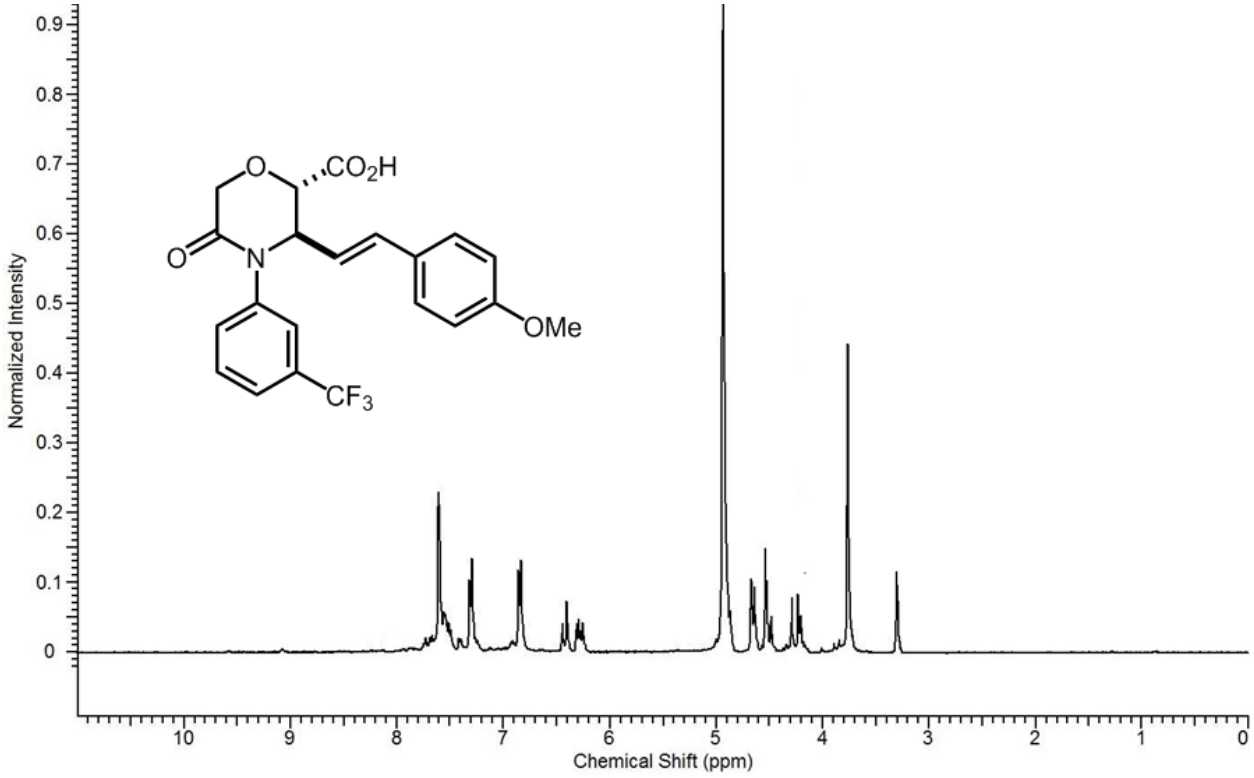

DB-162C-CDCl3.013.esp
CO2H
O
N
OMe
OMe
Normalized Intensity
Chemical Shift (ppm)

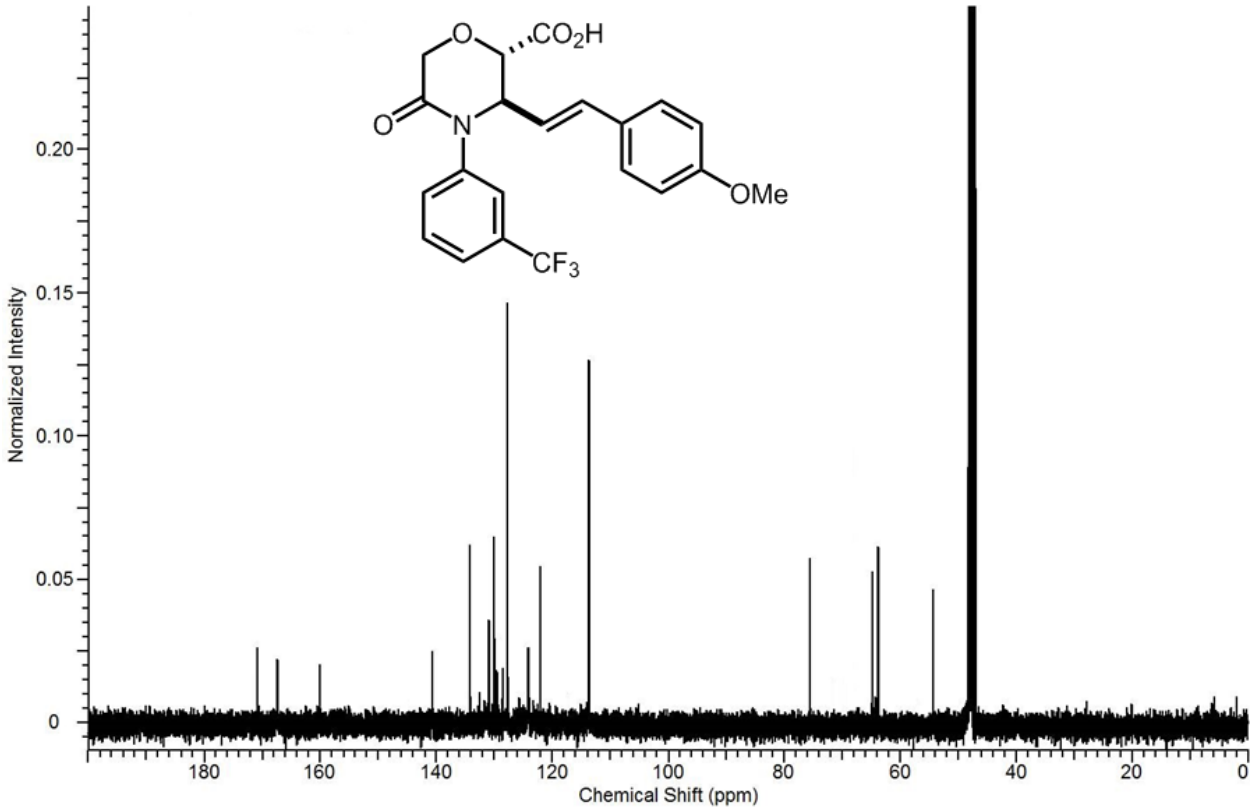

DB-162C-CDCl3.003.esp
CO2H
O
N
OMe
OMe
Normalized Intensity
Chemical Shift (ppm)

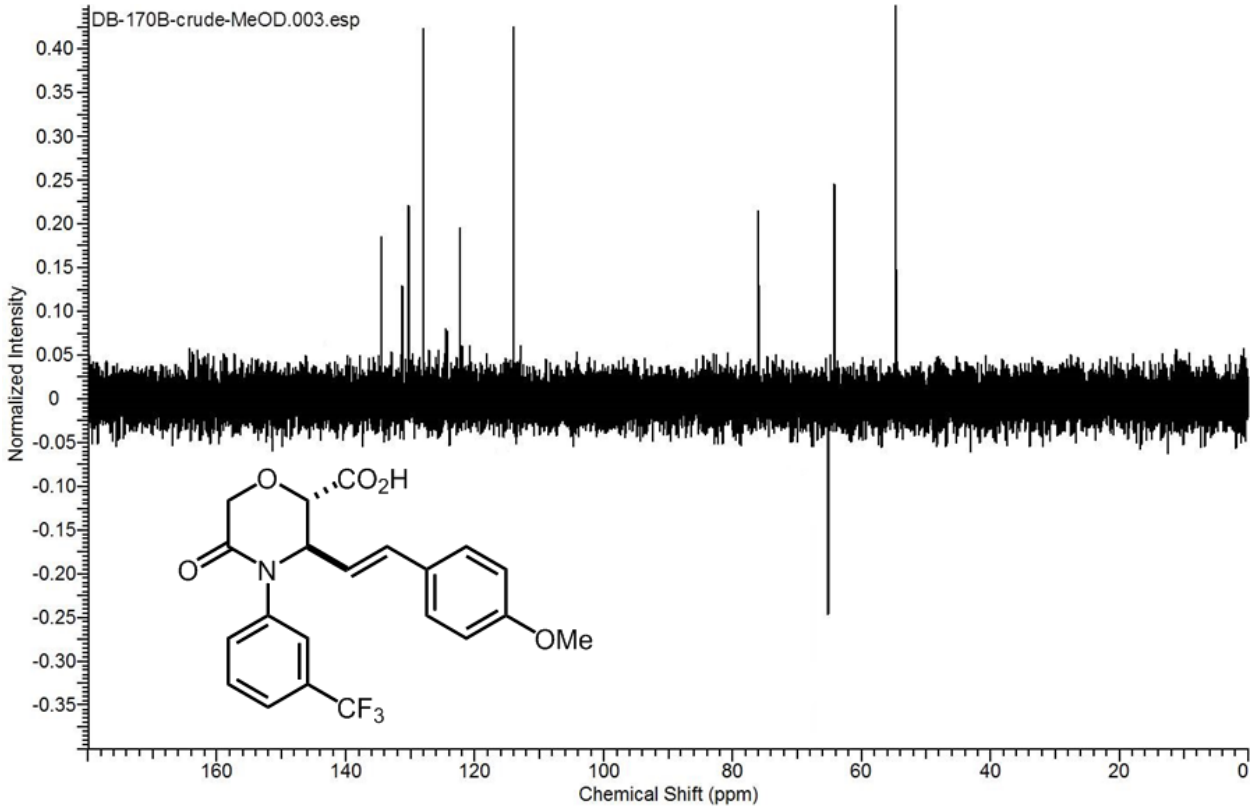


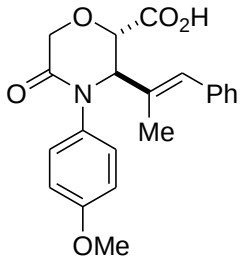
5f1

Prepared from imine **4h** (305 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedure B. T = 100 ^{o}C, time = 22 h. Yield = 295 mg, 70%. ^{1}H NMR (400 MHz, MeOH) δ 7.61 to 7.49 (4H, m) 7.32 (2H, d), 6.83 (2H, d), 6.44 to 6.29 (2H, m), 4.87 to 4.23 (4H, m), 3.76 (3H, s). ^{13}C NMR (101 MHz, MeOH) δ 170.8, 167.3, 160.0, 140.6, 134.1, 132.5, 131.0, 130.8, 129.9, 129.6, 129.4, 128.4, 127.7, 124.2, 124.1, 124.0, 123.2, 122.1, 113.7, 75.6, 64.8, 63.8, 54.3. **HRMS-EI**$^{+}$ (*m/z*): calc'd for $C_{21}H_{18}F_3NO_5$ 421.1137; found 421.1143.



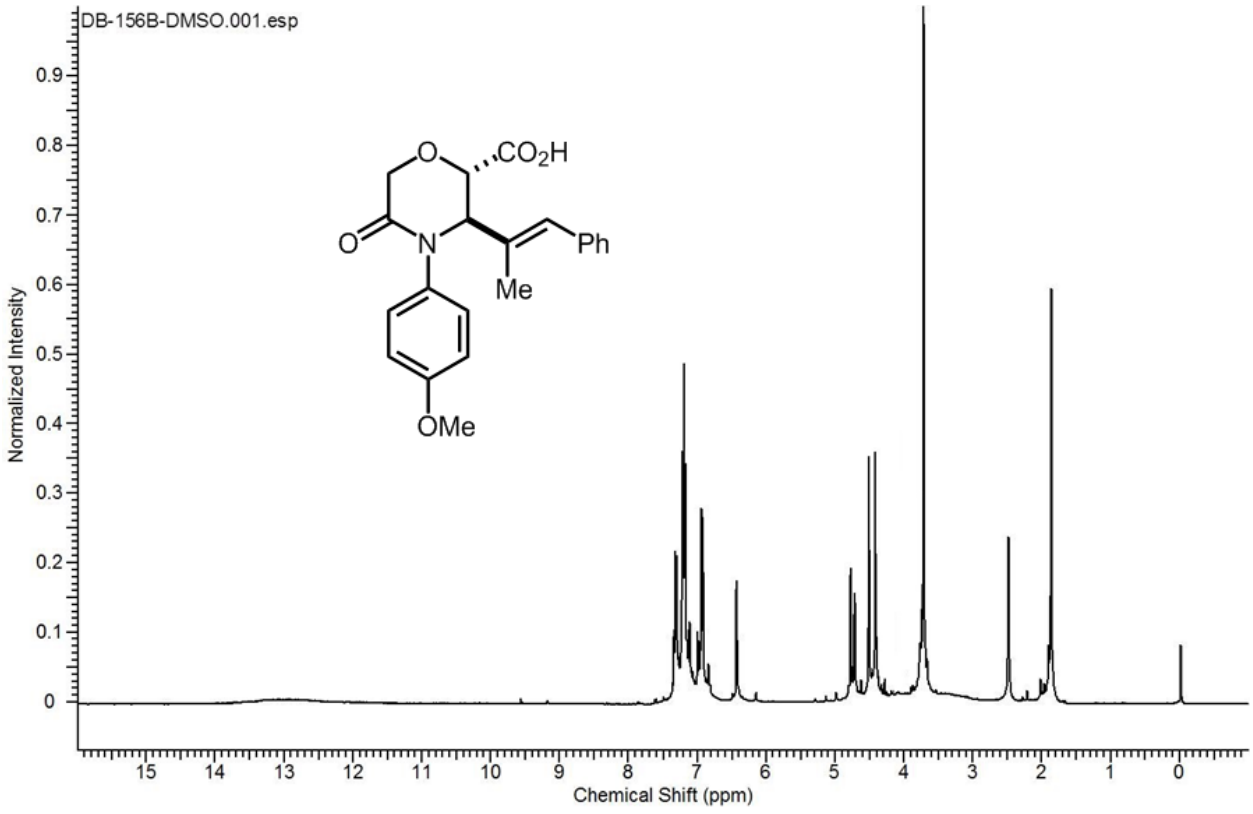

CO2H
O
N
OMe
CF3
Normalized Intensity
0.20
0.15
0.10
0.05
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

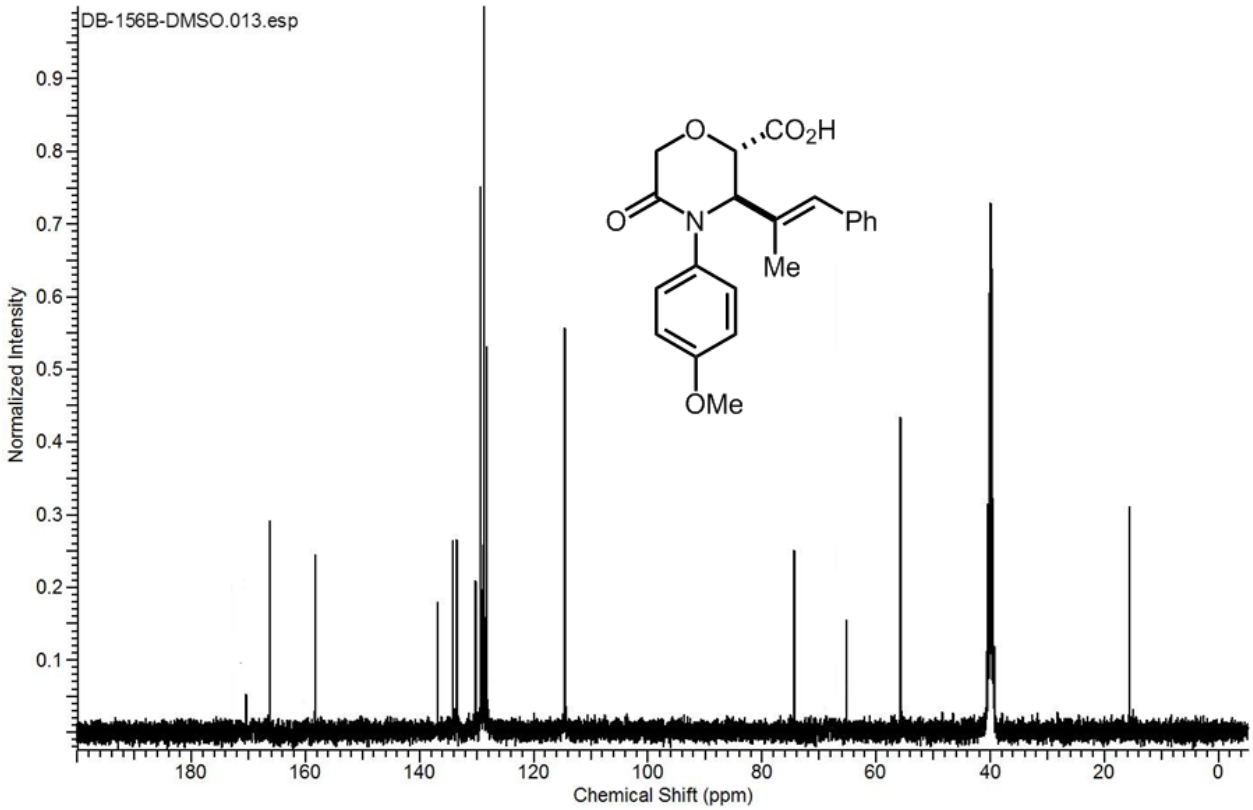

DB-170B-crude-MeOD.003.esp
CO2H
O
N
OMe
CF3
Normalized Intensity
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
-0.10
-0.15
-0.20
-0.25
-0.30
-0.35
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

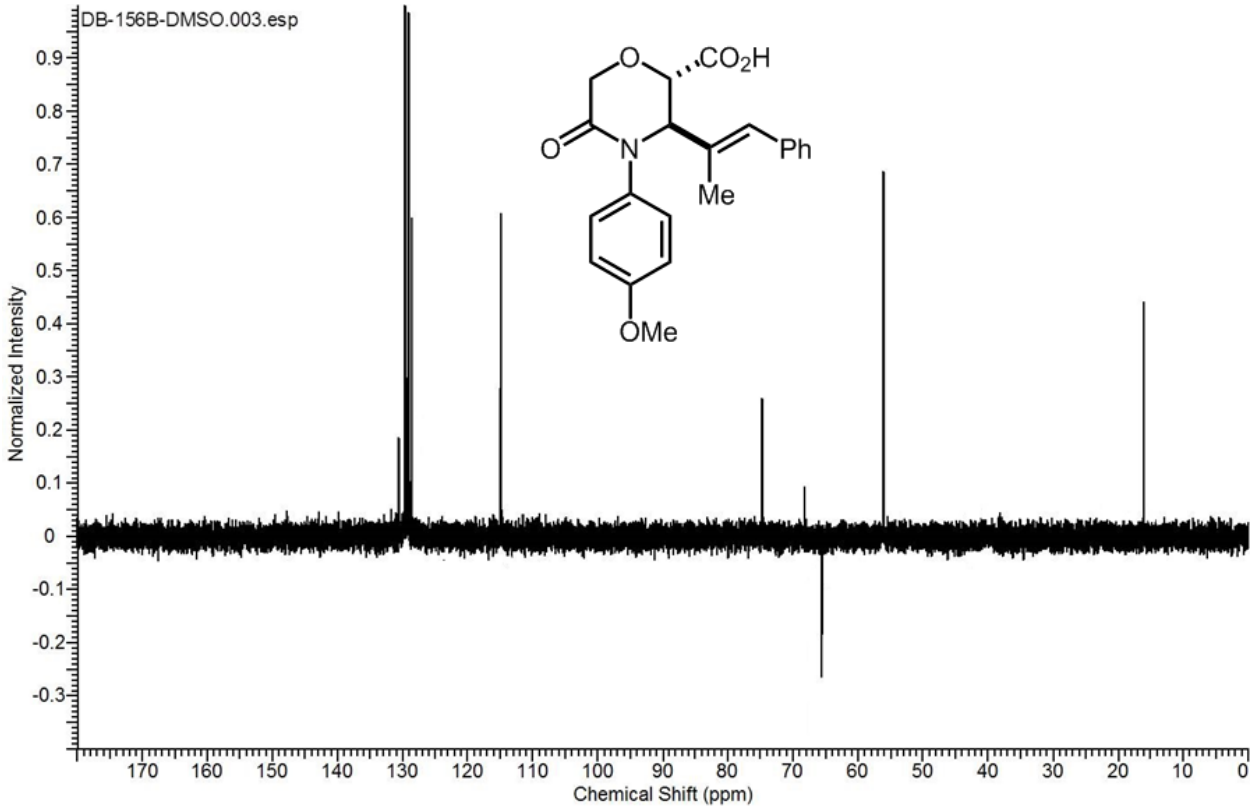


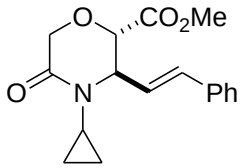
5g1

Prepared from imine **4i** (251 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedure B. T = 90 ^{o}C, time = 22 h. Yield = 290 mg, 79%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.10 (1H, s, br), 7.36 to 6.83 (9H, m), 6.49 (1H, s), 4.77 to 4.12 (4H, dd), 3.72 (3H, s), 1.86 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 166.3, 159.5, 136.9, 133.8, 131.4, 130.2, 129.3, 129.2, 128.2, 127.9, 126.1, 114.5, 74.3, 65.3, 55.8, 15.7. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{21}H_{21}NO_6$ 383.1369; found 383.1376.



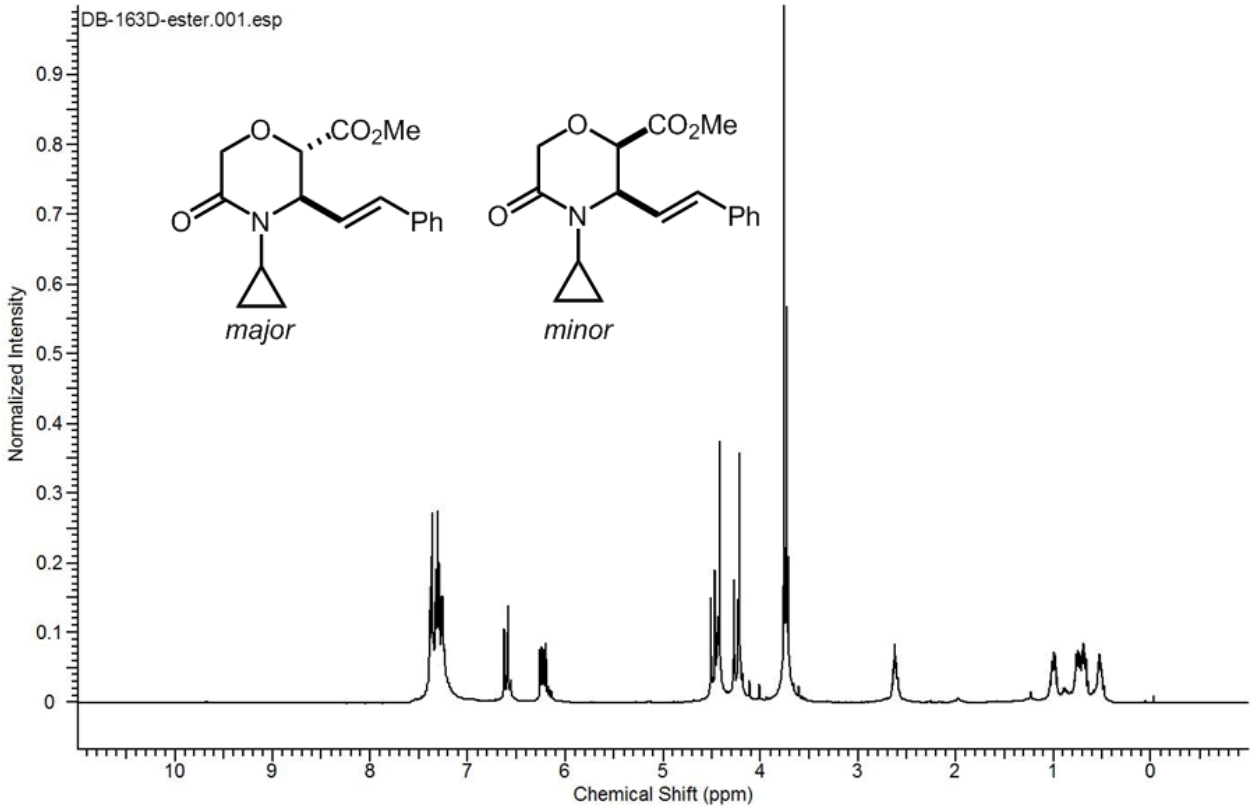

DB-156B-DMSO.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
Ph
Me
OMe

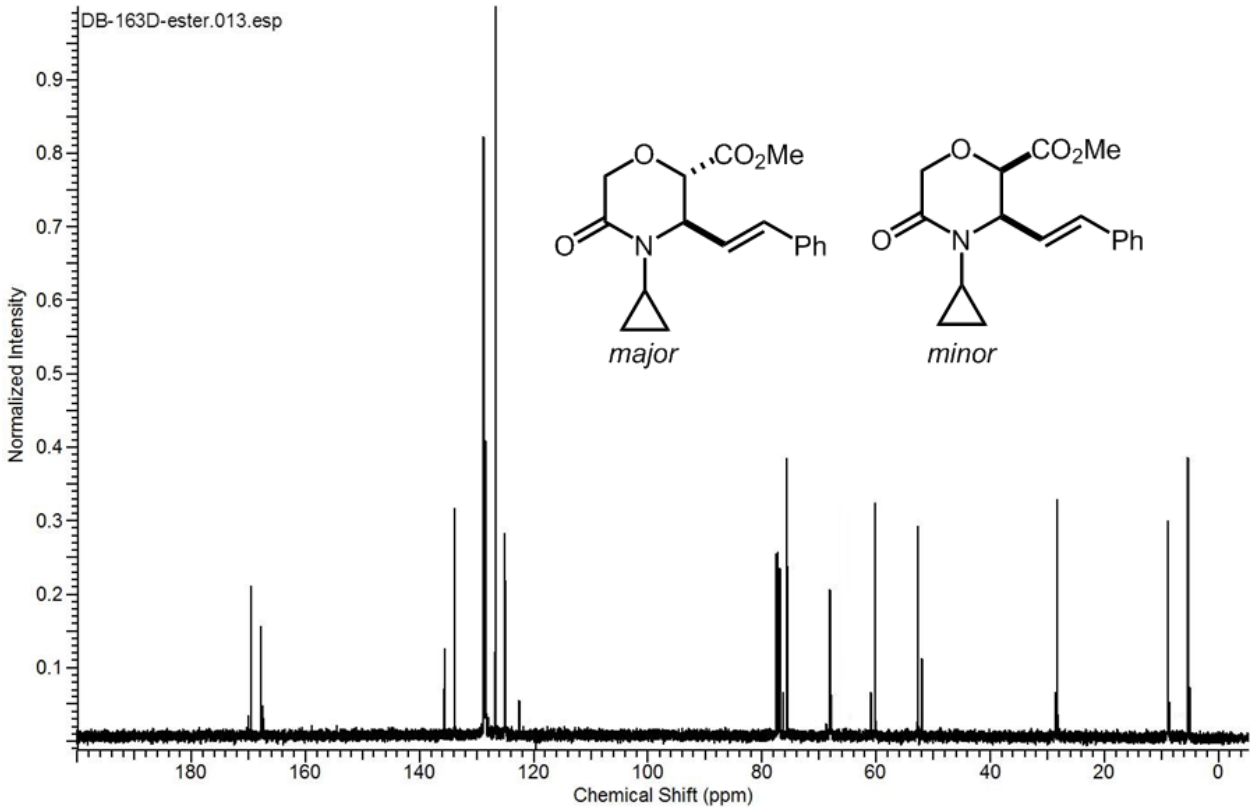

DB-156B-DMSO.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
Ph
Me
OMe

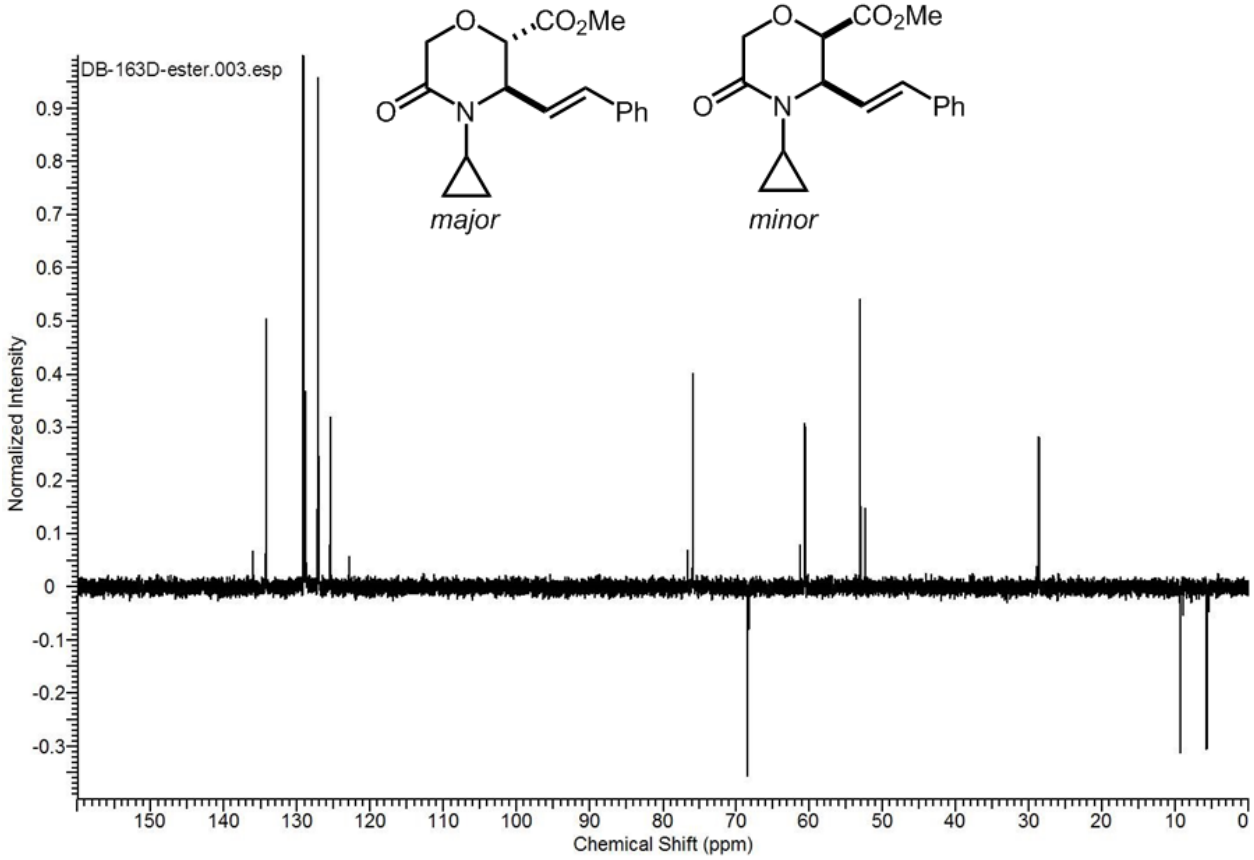


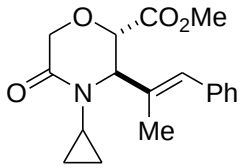
5h2

Prepared from imine **4k** (171 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedures B and C. T = 90 ^{o}C, time = 12 h. Yield = 217 mg, 72%, 80:20 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 to 7.25 (10H, m), 6.69 to 6.56 (2H, dd), 6.26 to 6.14 (2H, dd), 4.51 to 4.00 (8H, dd), 3.80 to 3.71 (6H, m), 2.65 to 2.60 (2H, m), 0.99 to 0.48 (8H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 169.5, 167.8, 167.3, 135.6, 135.6, 133.9, 128.7, 128.7, 128.5, 128.4, 126.8, 126.7, 125.1, 122.5, 76.3, 75.5, 68.7, 68.1, 60.9, 60.2, 52.7, 52.0, 28.6, 28.3, 8.5, 7.4, 6.3, 5.0. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{17}H_{19}NO_4$ 301.1314; found 301.1310.



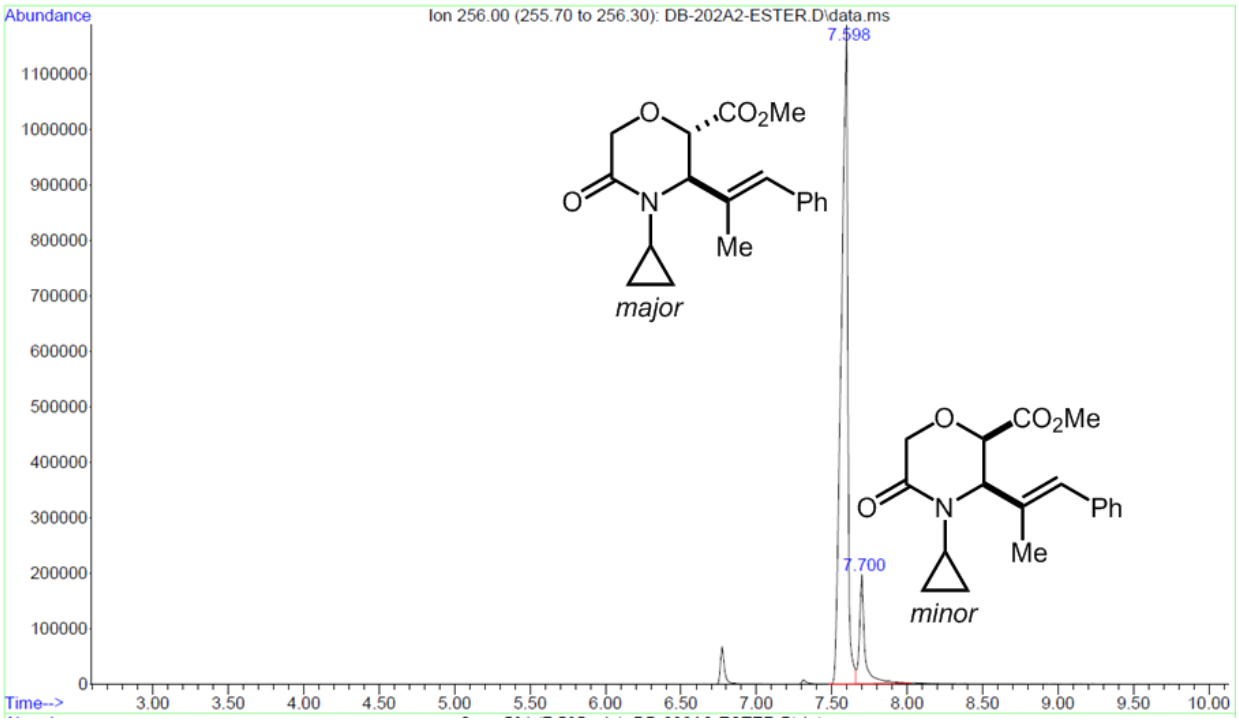

DB-163D-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
major
minor

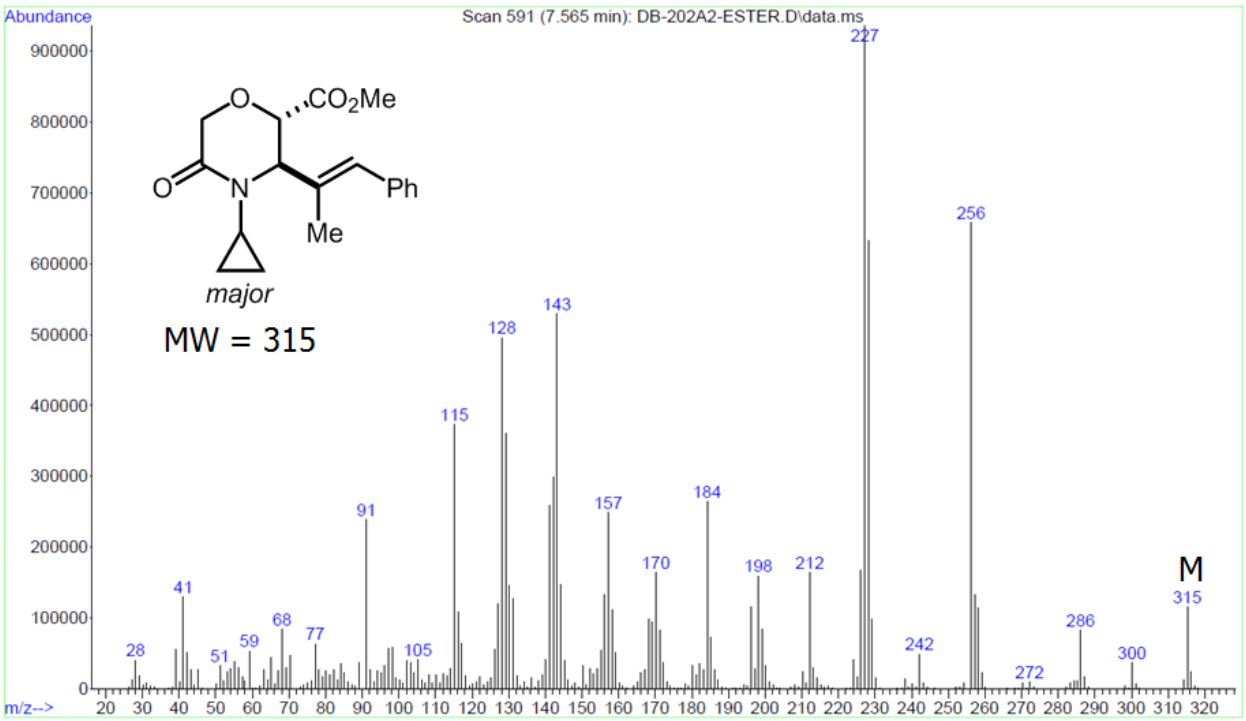

DB-163D-ester.003.esp
Normalized Intensity
Chemical Shift (ppm)
major
minor

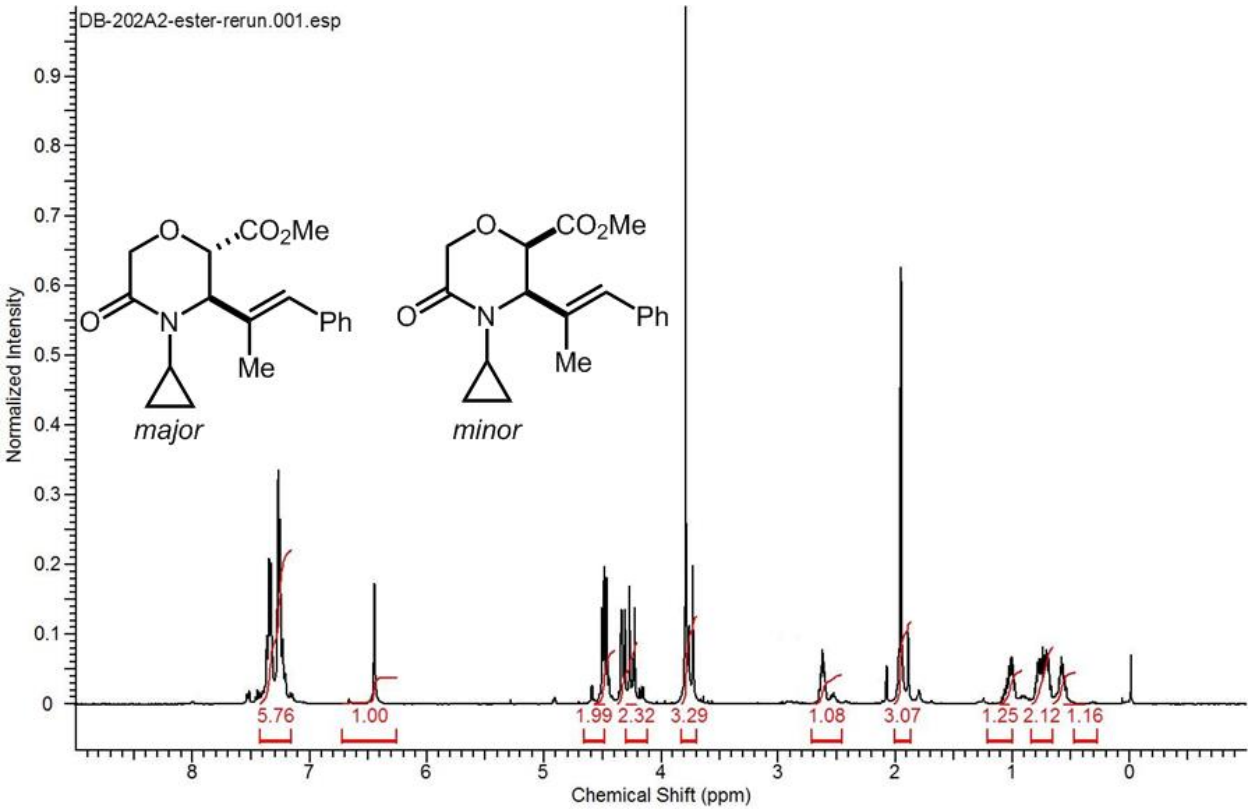


5i2

Prepared from imine **4l** (185 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedures B and C. T = 90 ^{o}C, time = 12 h. Yield = 221 mg, 70%, 87:13 dr. ^{1}H NMR (400 MHz, $CDCl_3$) 7.54 to 7.14 (5H, m), 6.65 (1H, s), 4.60 to 4.15 (4H, m), 3.79 (3H, s), 2.65 to 2.49 (1H, m), 1.89 (3H, s), 1.07 to 0.54 (4H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 168.3, 136.6, 133.4, 131.6, 130.1, 129.3, 129.0, 128.4, 127.3, 127.2, 126.8, 119.6, 76.8, 74.8, 68.2, 67.6, 65.7, 65.6, 65.1, 52.8, 52.6, 28.6, 28.4, 15.2, 14.4, 8.5, 8.3, 5.7, 5.0. **HRMS-EI**$^{+}$ (*m/z*): calc'd for $C_{18}H_{21}NO_4$ 315.1471; found 315.1476.




Abundance
Scan 591 (7.565 min): DB-202A2-ESTER.D\data.ms
CO2Me
O
N
Ph
Me
major
MW = 315
M
m/z-->


DB-202A2-ester-rerun.001.esp
Normalized Intensity
major
minor
5.76
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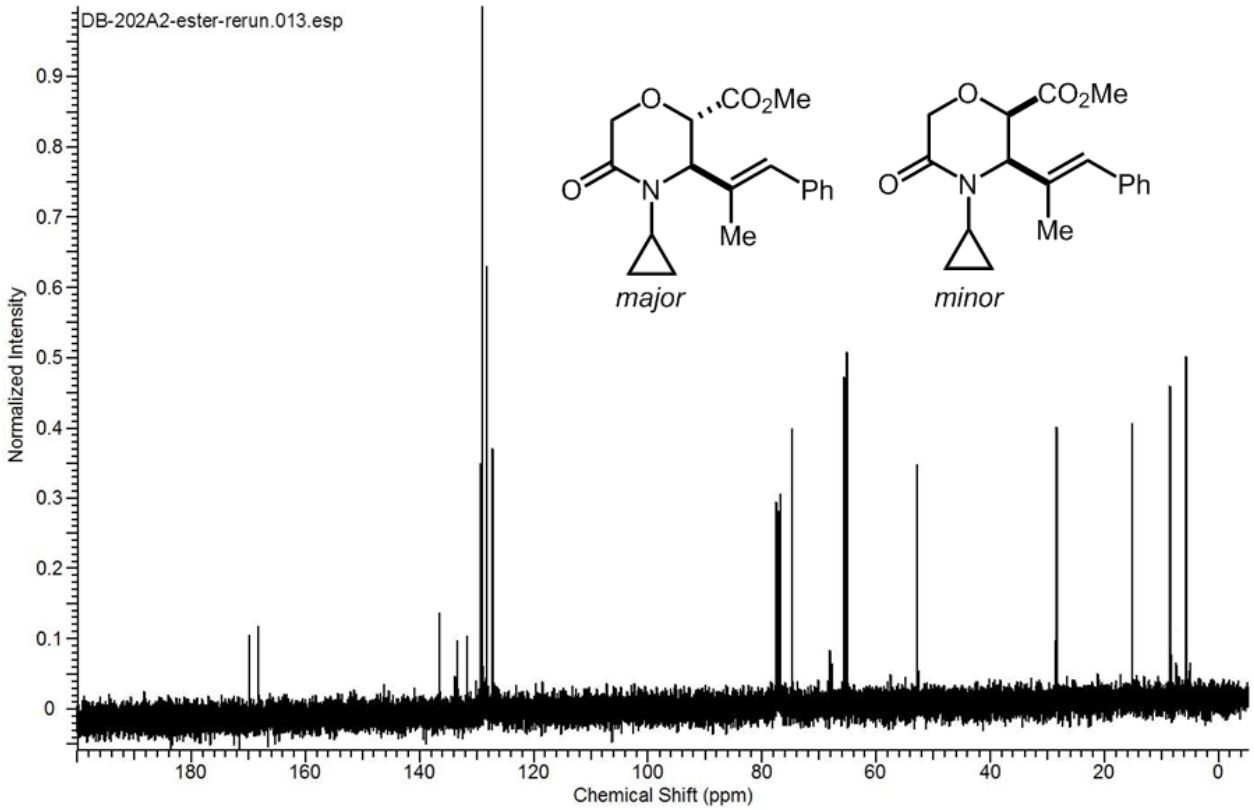
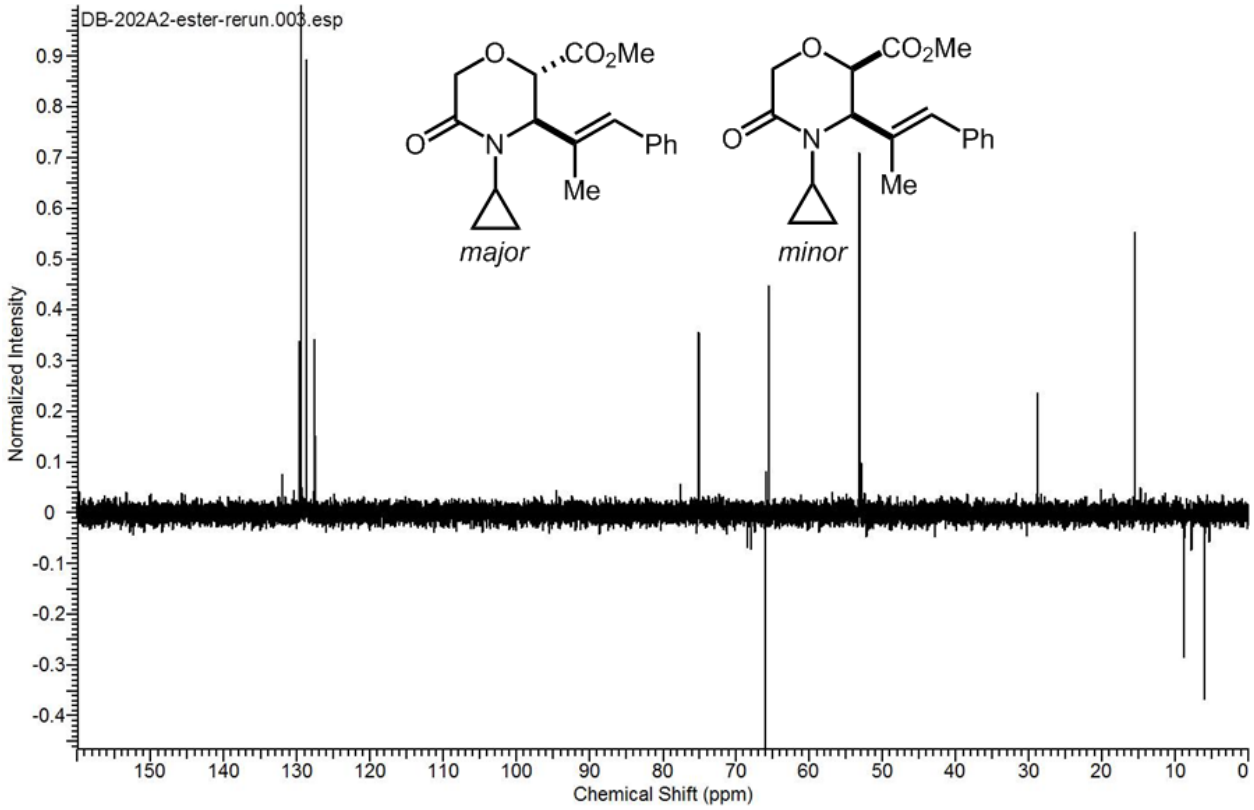
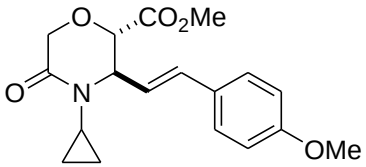
1.99
2.32
3.29
1.08
3.07
1.25
2.12
1.16
Chemical Shift (ppm)

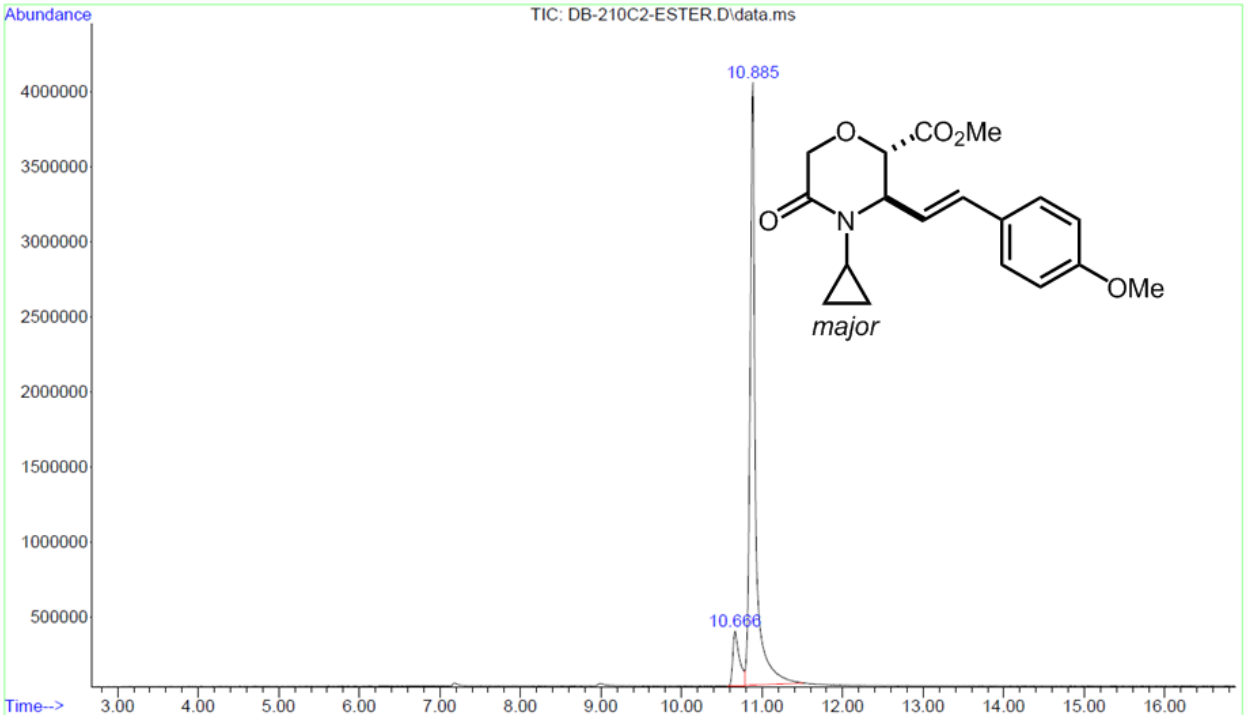

DB-202A2-ester-rerun.013.esp
Normalized Intensity
Chemical Shift (ppm)
major
minor

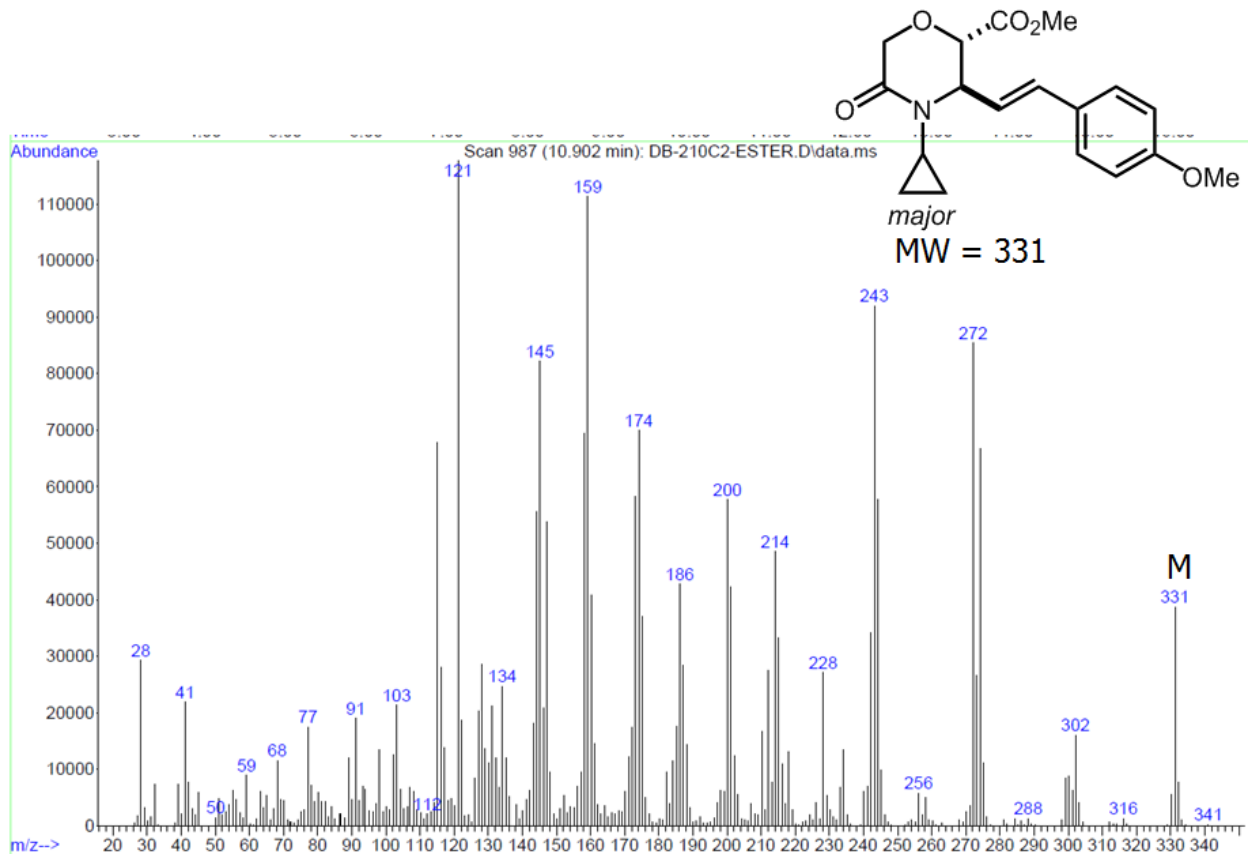

DB-202A2-ester-rerun.003.esp
Normalized Intensity
Chemical Shift (ppm)
major
minor



5j2

Prepared from imine **4t** (201 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedures B and C. T = 90 ^{o}C, time = 16 h. Yield = 268 mg, 81%, 85:15 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 to 7.22 (4H, major & minor), 6.89 to 6.72 (4H, mixture), 6.56 to 6.47 (2H, mixture), 6.18 to 5.96 (2H, mixture), 4.47 to 4.09 (8H, mixture), 3.80 to 3.71 (6H, mixture), 2.60 to 2.47 (2H, mixture), 0.99 to 0.48 (8H, mixture). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.43, 169.61, 167.83, 167.38, 159.89, 159.83, 135.05, 133.33, 130.39, 129.71, 128.92, 128.85, 128.31, 128.09, 127.99, 126.78, 126.47, 122.70, 120.09, 114.5, 114.4, 76.3, 75.6, 68.67, 68.05, 65.35, 61.02, 55.34, 55.29, 52.64, 52.62, 29.70, 28.55, 8.56, 7.37, 6.33, 5.34. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{18}H_{21}NO_5$ 331.1420; found 331.1425.

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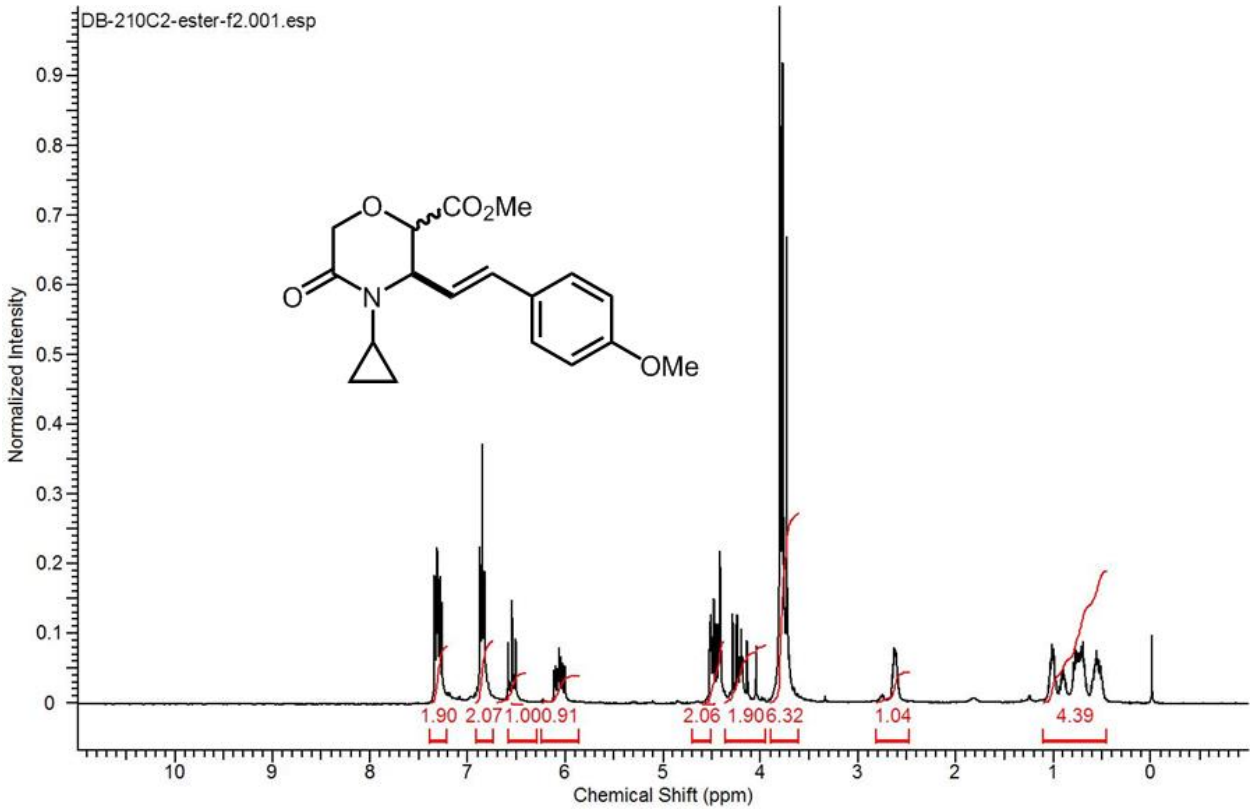
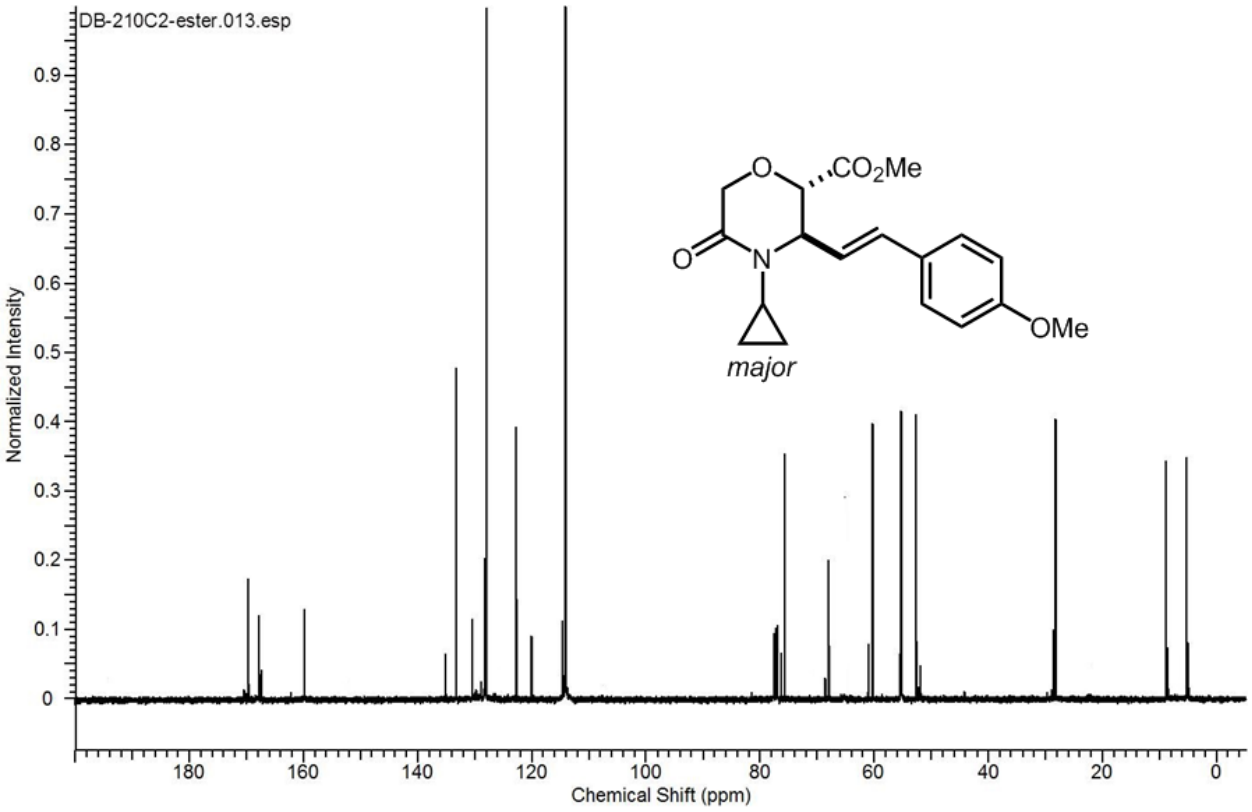
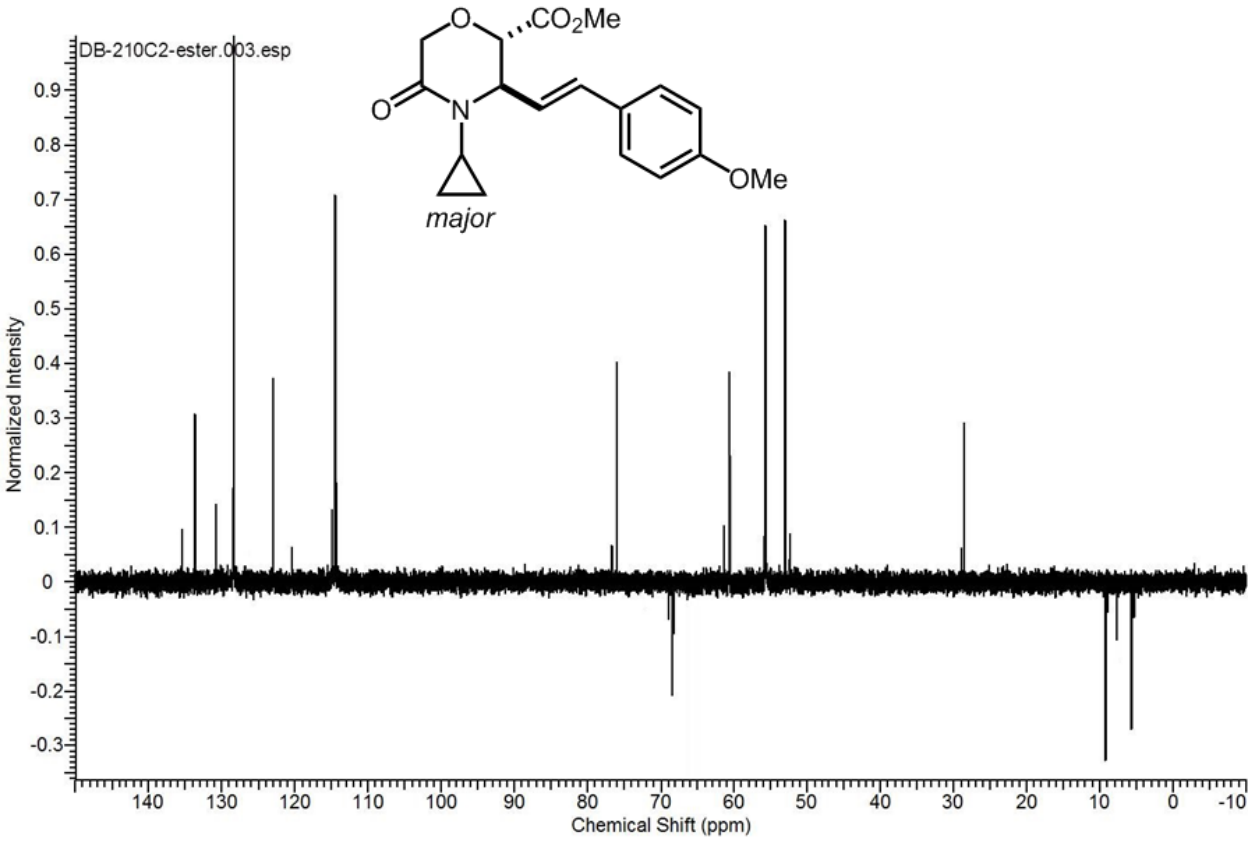
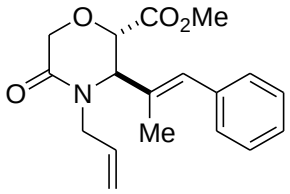
Abundance
Scan 987 (10.902 min): DB-210C2-ESTER.D\data.ms
M
m/z-->


DB-210C2-ester-f2.001.esp
Normalized Intensity
1.90 2.07 1.00 0.91 2.06 1.90 6.32 1.04 4.39
Chemical Shift (ppm)

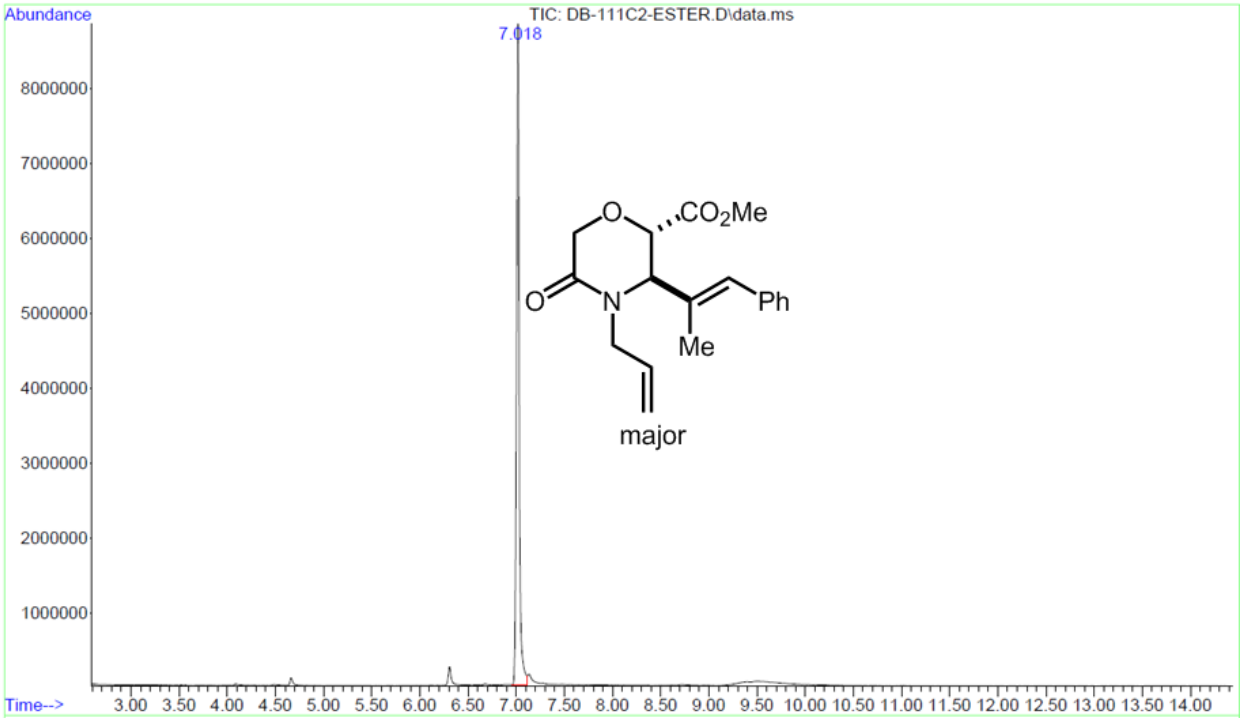

DB-210C2-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
major

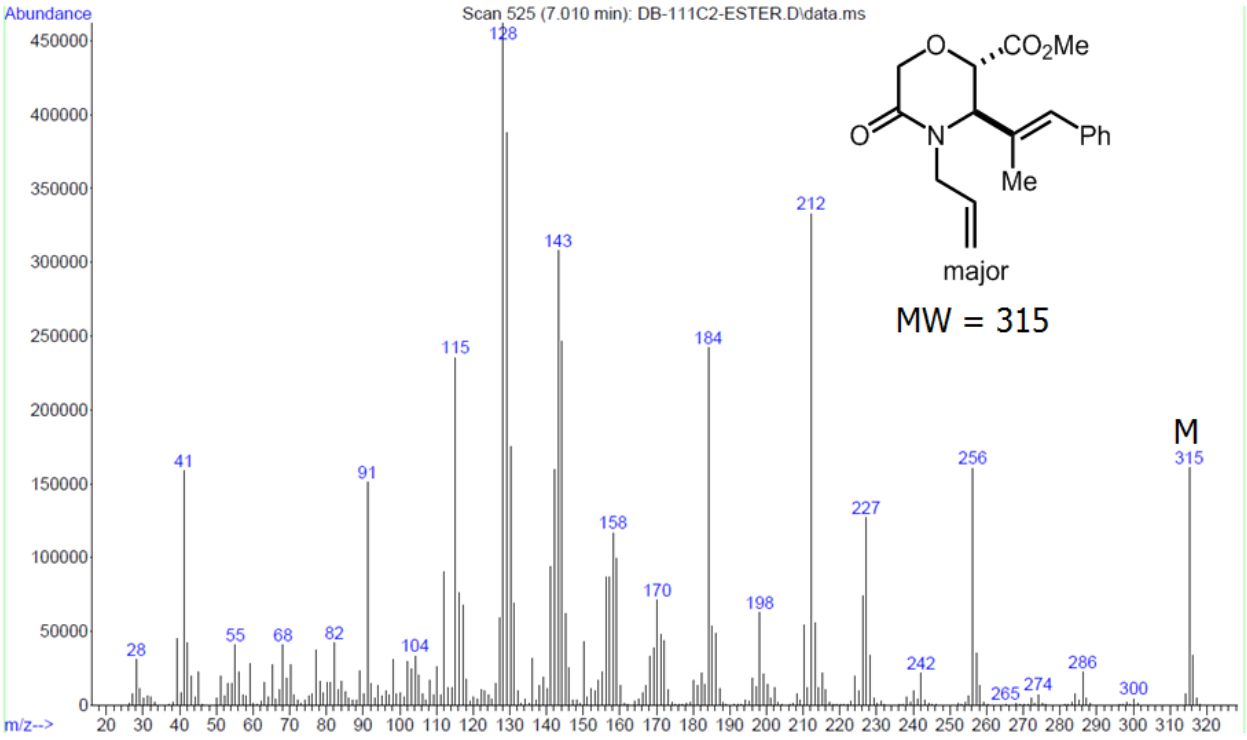

DB-210C2-ester.003.esp
Normalized Intensity
Chemical Shift (ppm)
major

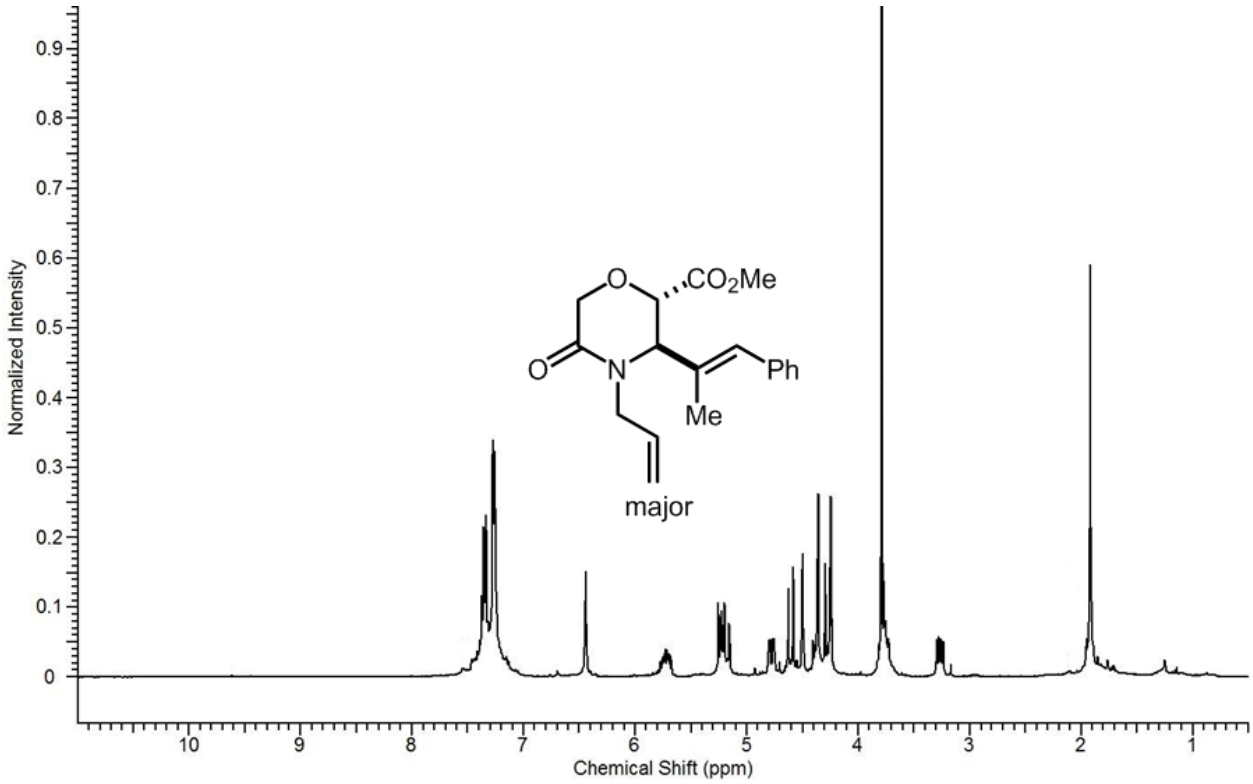


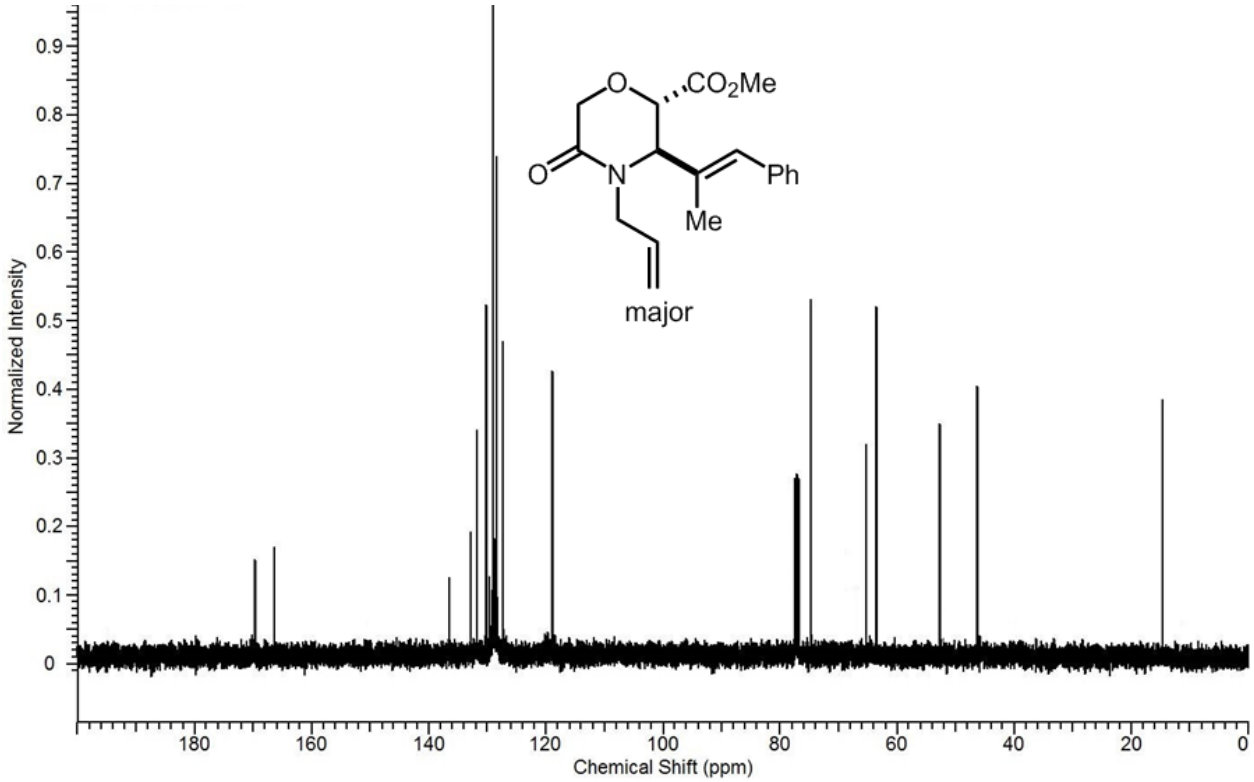
5k2

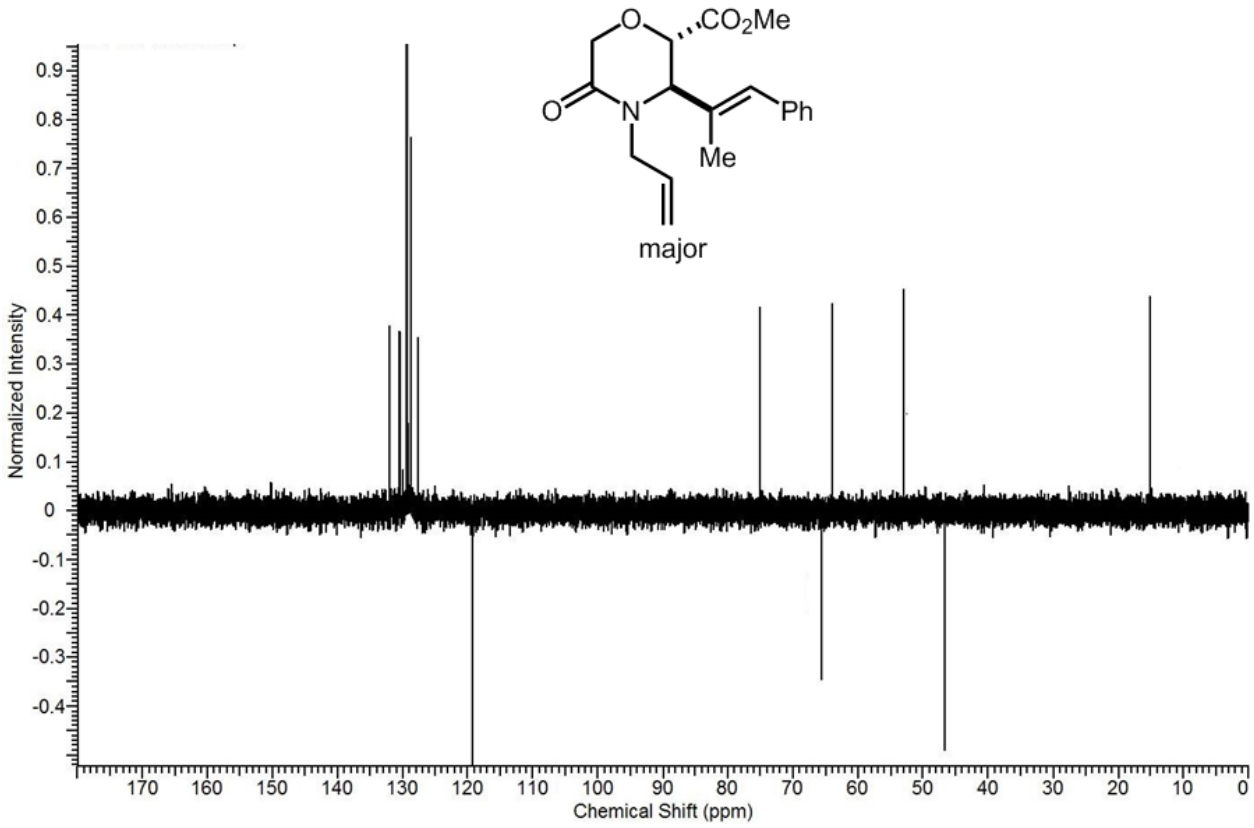
Prepared from imine **4v** (185 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedures B and C. T = 90 ^{o}C, time = 16 h. Yield = 277 mg, 88%, 92:8 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 to 6.97 (5H,m), 6.48 (1H, s), 5.81 to 5.67 (1H, m), 5.30 to 5.12 (2H, m), 4.79, to 4.21 (5H, m), 3.79 (3H, s), 3.30 to 3.22 (1H, dd), 1.84 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 169.7, 168.7, 166.4, 137.5, 136.4, 133.9, 132.9, 132.5, 132.3, 132.0, 131.8, 130.2, 129.8, 129.1, 129.0, 128.4, 128.2, 128.2, 128.2, 127.4, 127.3, 126.8, 126.6, 119.2, 118.9, 118.4, 116.6, 77.5, 77.4, 77.2, 76.8, 74.8, 71.3, 69.4, 68.6, 68.1, 67.8, 67.4, 65.3, 63.6, 52.7, 52.2, 52.0, 50.5, 46.4, 46.3, 41.3, 40.7, 17.2, 14.7, 14.2. **HRMS-EI+** (*m/z*): calc'd for $C_{18}H_{21}NO_4$ 315.1471; found 315.1475.

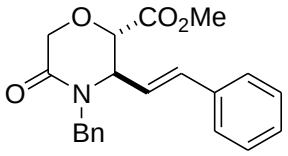



Abundance
Scan 525 (7.010 min): DB-111C2-ESTER.D\data.ms
m/z-->
major
MW = 315
M
315
128
212
143
115
184
41
91
158
227
256
170
198
242
286
265
274
300
28
55
68
82
104


Normalized Intensity
Chemical Shift (ppm)
major

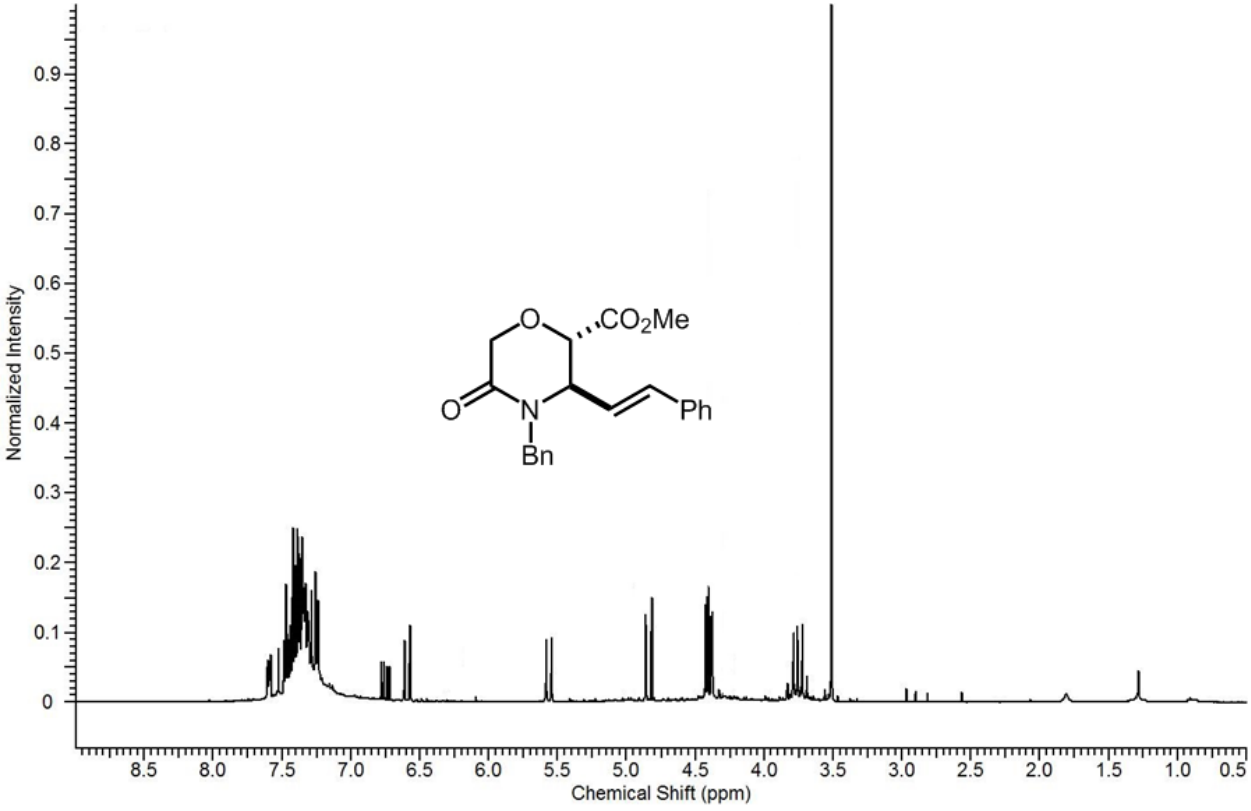

CO2Me
O
N
O
Ph
Me
major
Normalized Intensity
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

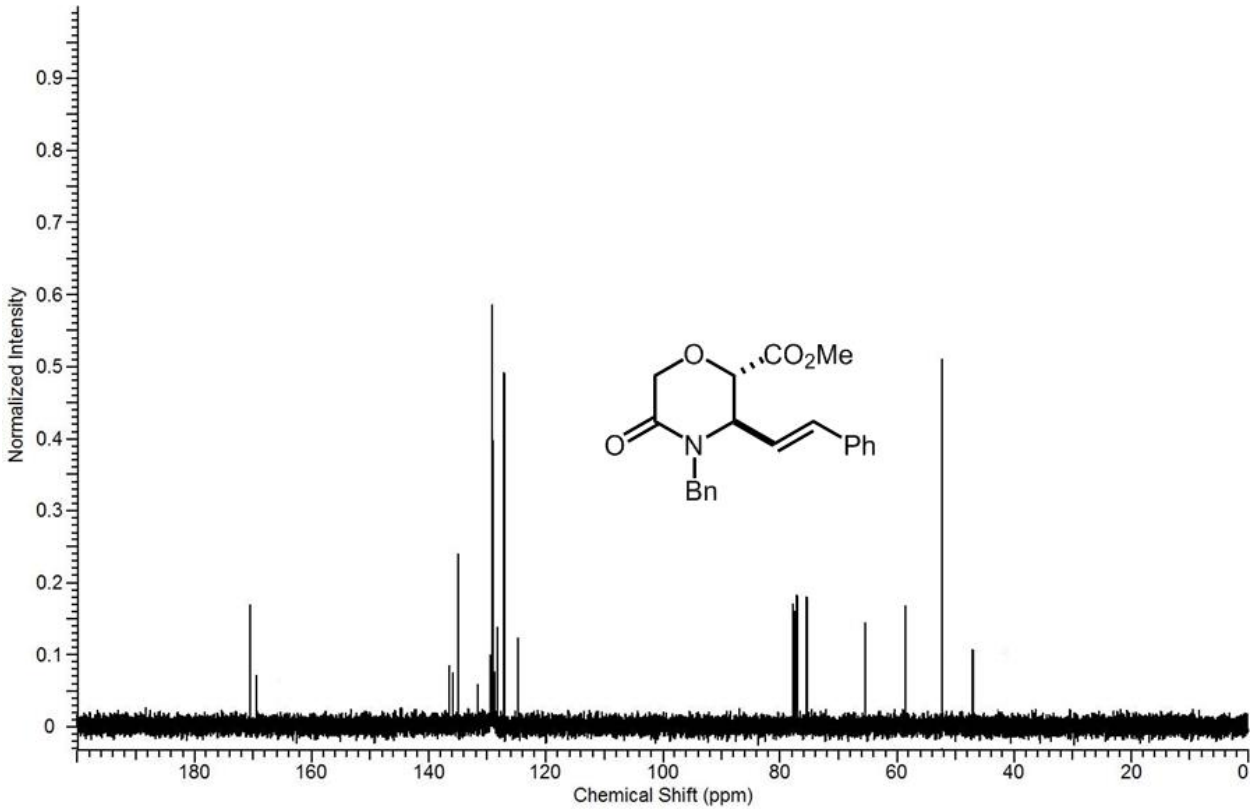

CO2Me
O
N
O
Ph
Me
major
Normalized Intensity
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

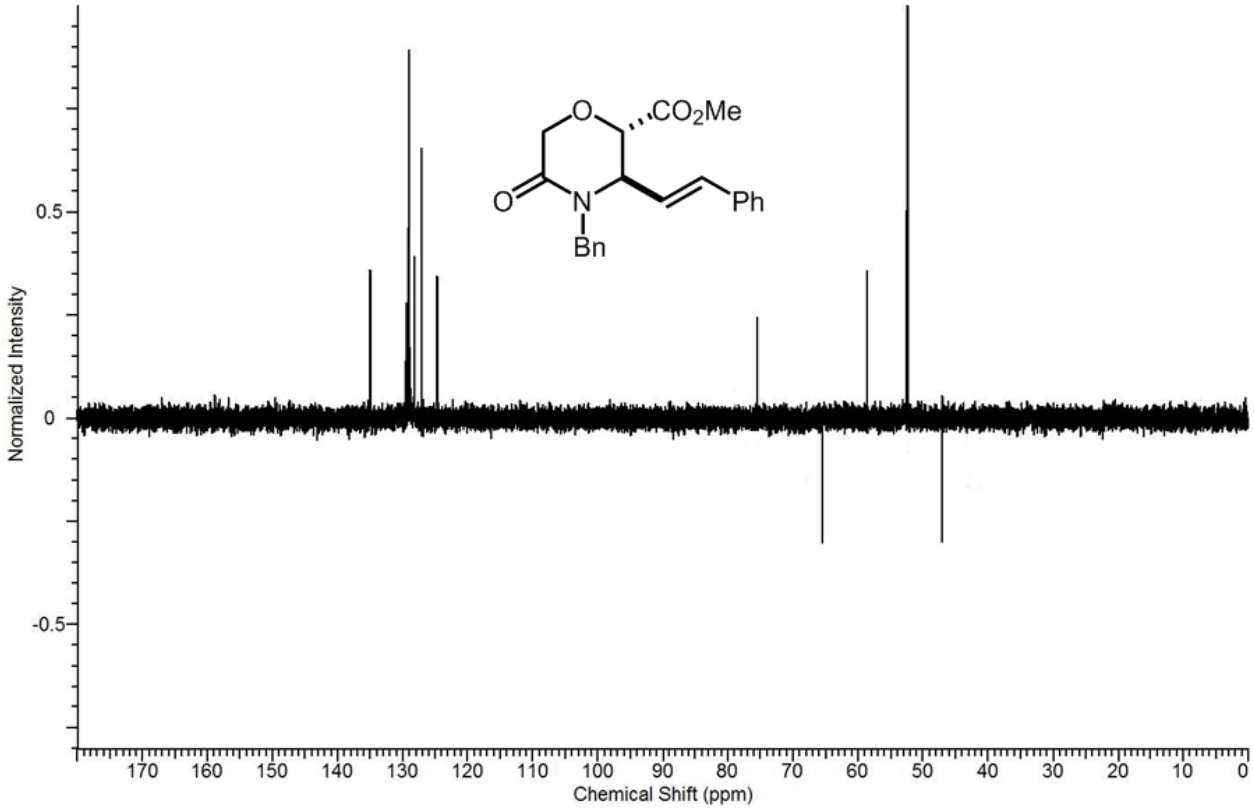


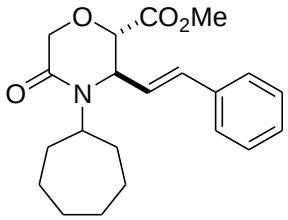
5l2

Prepared from imine **4u** (221 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedures B and C. T = 90 ^{o}C, time = 16 h. Yield = 277 mg, 79%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 to 6.76 (10 H, m), 6.74 to 6.70 (1H, dd), 6.59 to 6.51 (1H, dd), 5.56 (1H, d), 4.84 (1H, d), 4.42 to 4.35 (2H, m), 3.77 to 3.66 (2H, m), 3.49 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.47, 166.39, 137.01, 136.39, 135.76, 134.93, 131.68, 129.51, 129.37, 129.35, 129.17, 129.03, 128.98, 128.90, 128.75, 128.21, 127.22, 127.14, 124.77, 75.45, 65.44, 58.58, 52.62, 47.07. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{21}H_{21}NO_4$ 351.1471; found 351.1476.



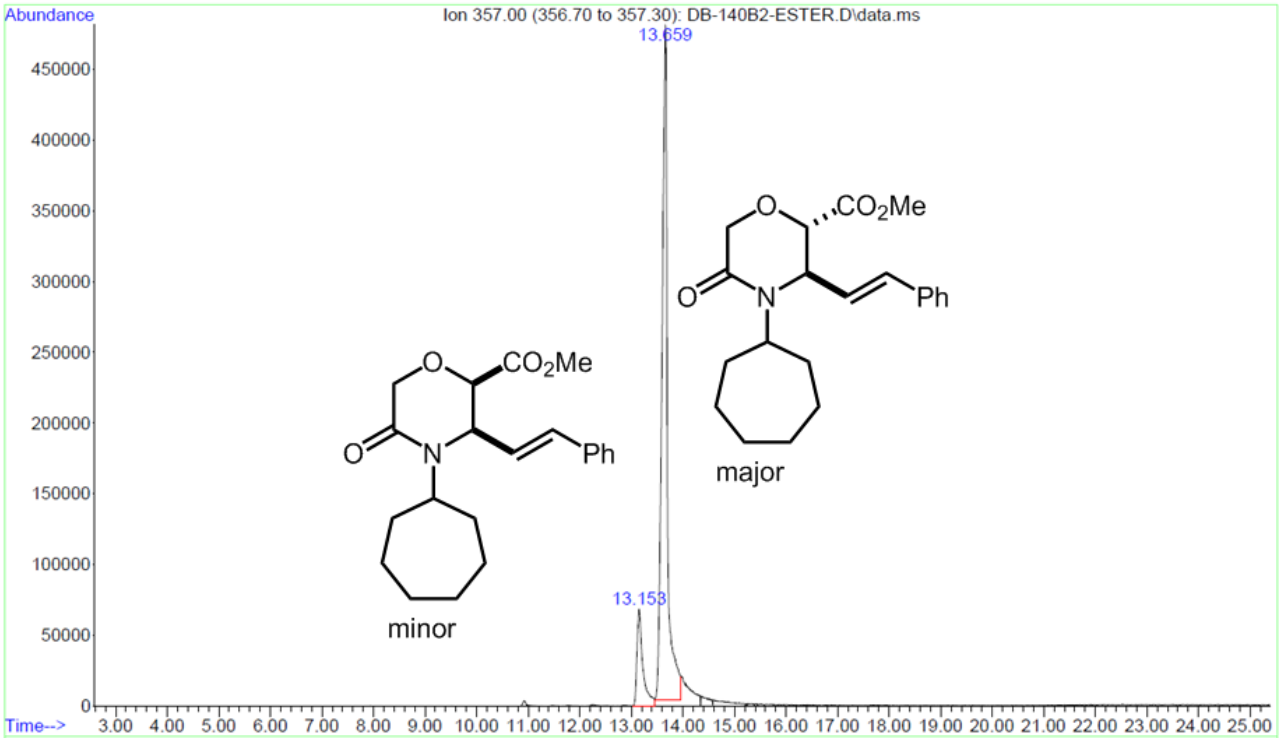

Normalized Intensity
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
O
CO2Me
O
N
Ph
Bn
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

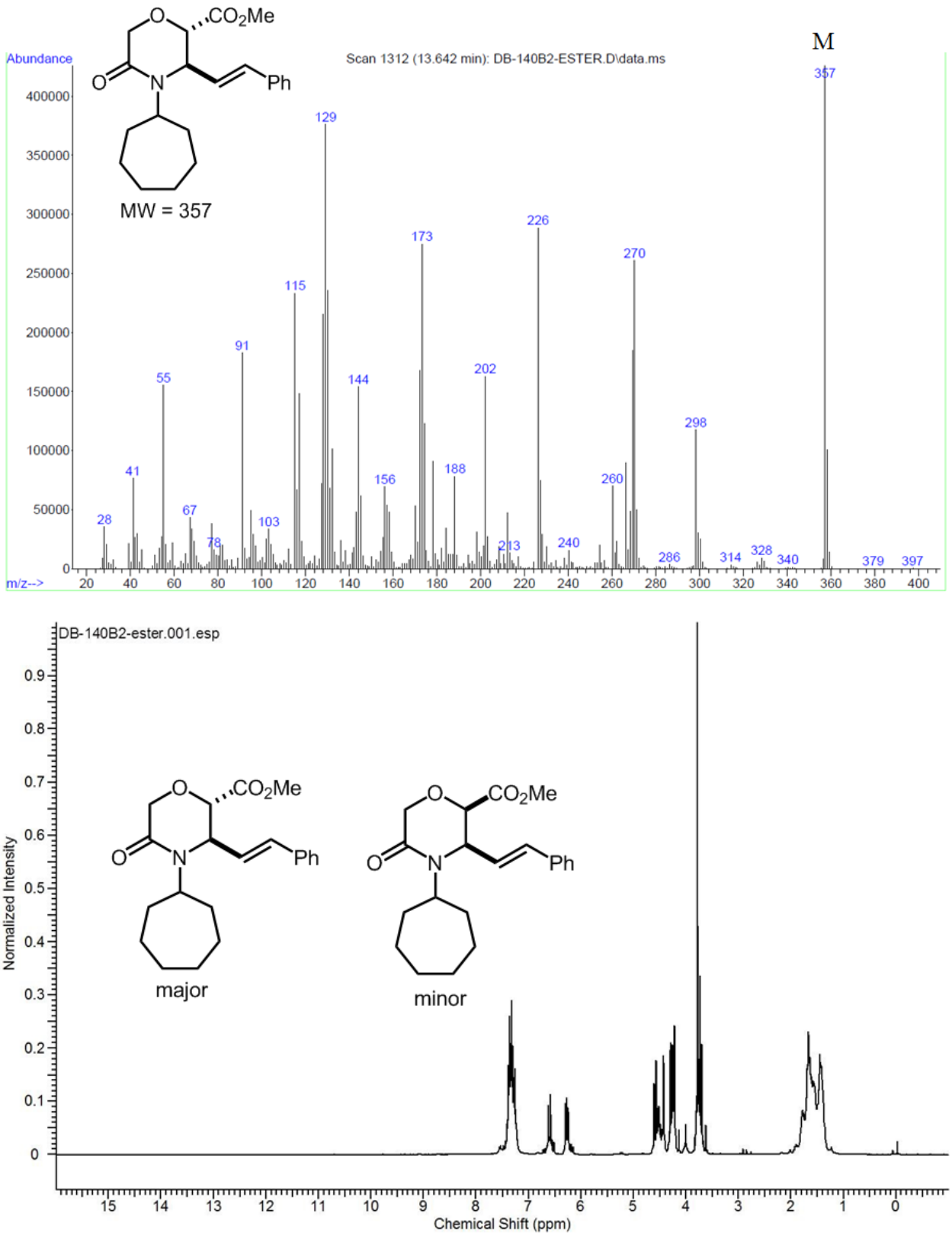

Normalized Intensity
0.5
0
-0.5
O
CO2Me
O
N
Ph
Bn
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

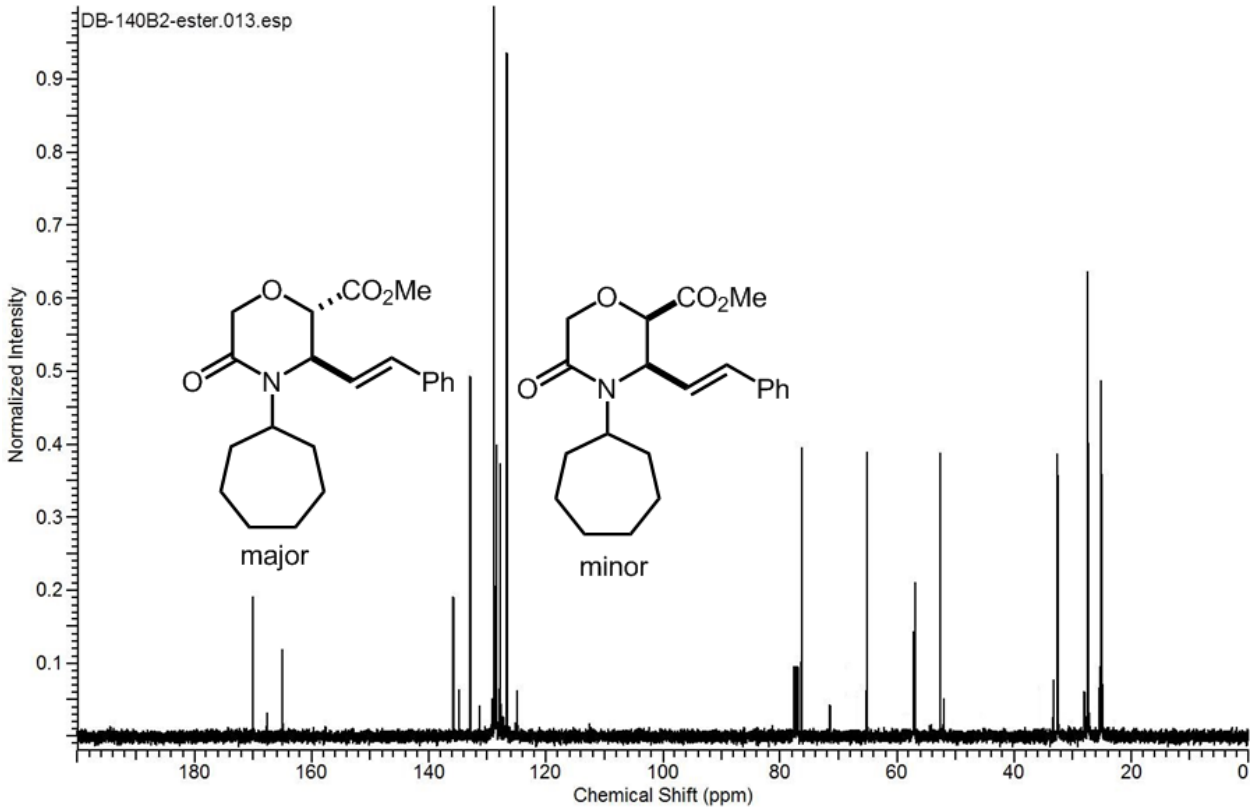


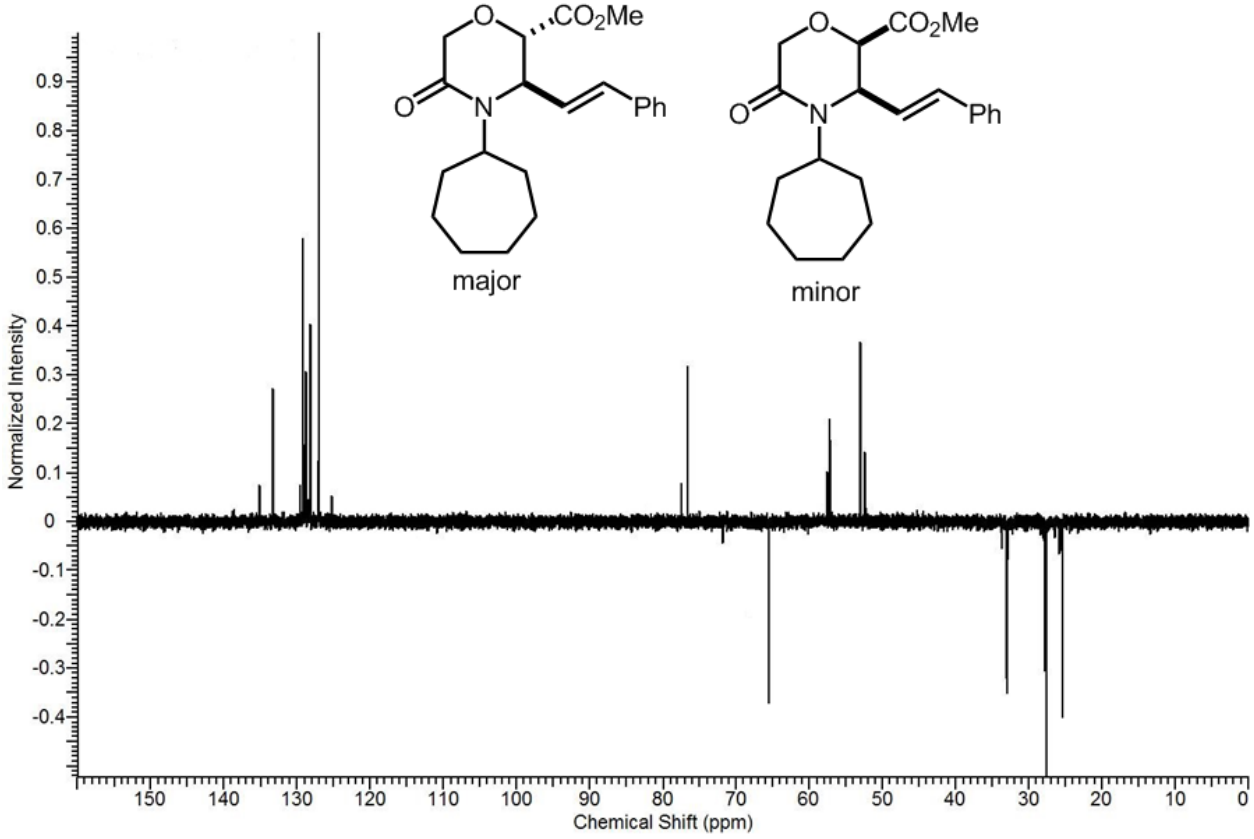
5m2

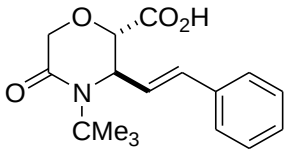
Prepared from imine **4m** (227 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedures B and C. T = 90 ^{o}C, time = 16 h. Yield =282 mg, 79%, 81:19 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 to 7.21 (5H, m), 6.73 to 6.51 (1H, dd), 6.33 to 6.14 (1H, dd), 4.64 to 3.60 (8H, m), 1.93 to 1.36 (12H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.77, 170.00, 167.60, 165.07, 164.74, 152.88, 135.73, 134.77, 132.95, 131.34, 129.16, 128.80, 128.75, 128.71, 128.55, 128.49, 128.41, 128.02, 127.81, 127.29, 126.78, 126.70, 125.10, 124.86, 108.25, 81.25, 77.55, 77.23, 77.11, 76.91, 76.29, 71.47, 68.71, 68.11, 68.05, 67.80, 65.14, 59.05, 58.40, 57.24, 56.87, 54.08, 52.69, 52.65, 52.03, 49.94, 44.95, 35.04, 33.41, 33.28, 32.73, 32.63, 32.57, 31.89, 28.06, 27.71, 27.46, 27.29, 27.27, 26.13, 25.48, 25.34, 25.11, 25.02, 24.07. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{21}H_{27}NO_4$ 357.1940; found 357.1944.




Abundance
Scan 1312 (13.642 min): DB-140B2-ESTER.D\data.ms
M
357
MW = 357
129
226
173
270
115
91
144
202
55
298
188
156
260
41
67
103
28
78
213
240
286
314
328
340
379
397
m/z-->
DB-140B2-ester.001.esp
Normalized Intensity
major
minor
Chemical Shift (ppm)

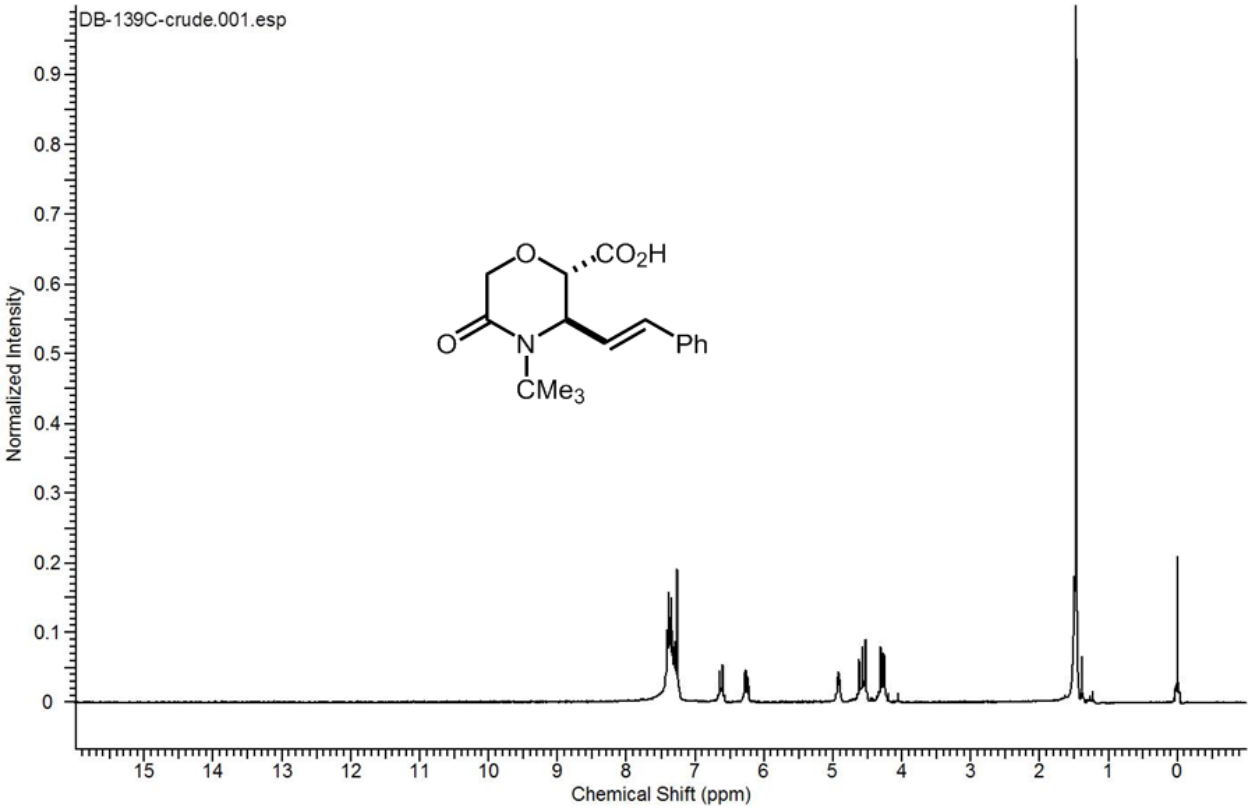

DB-140B2-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
major
minor

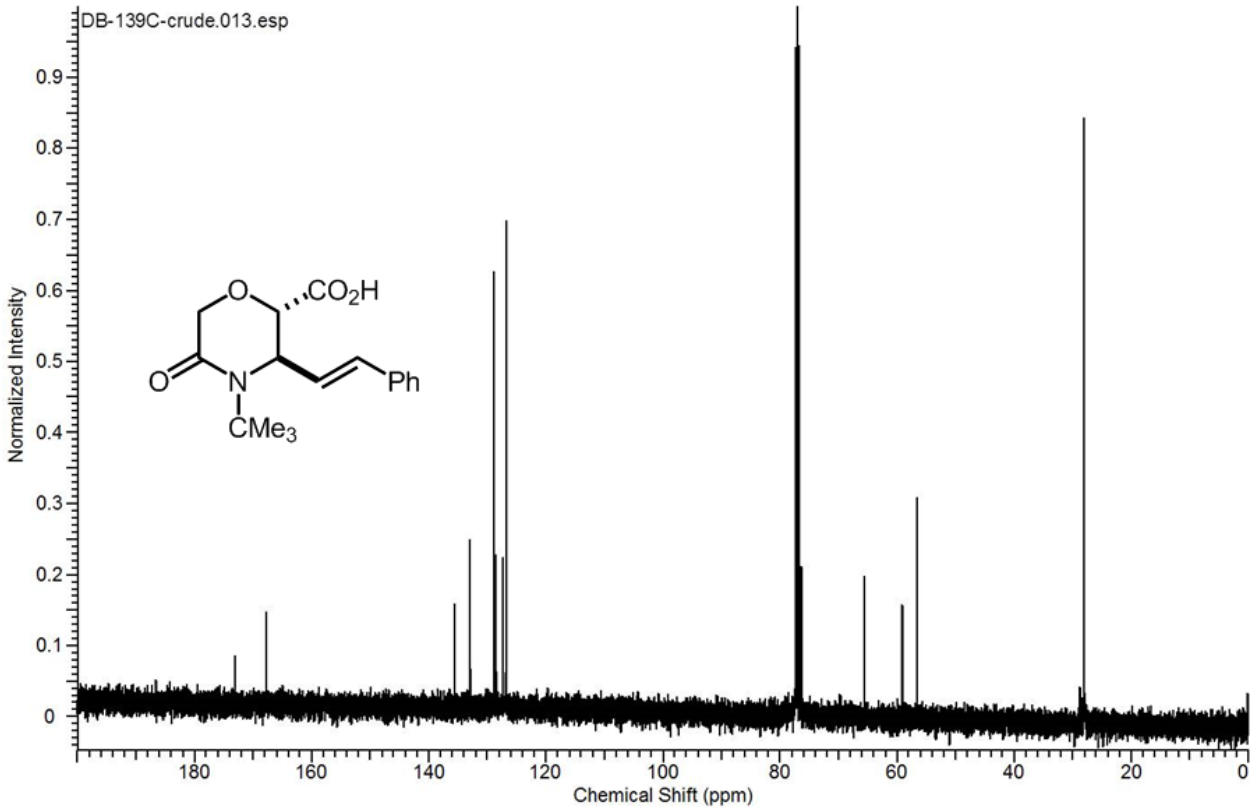

Normalized Intensity
Chemical Shift (ppm)
major
minor

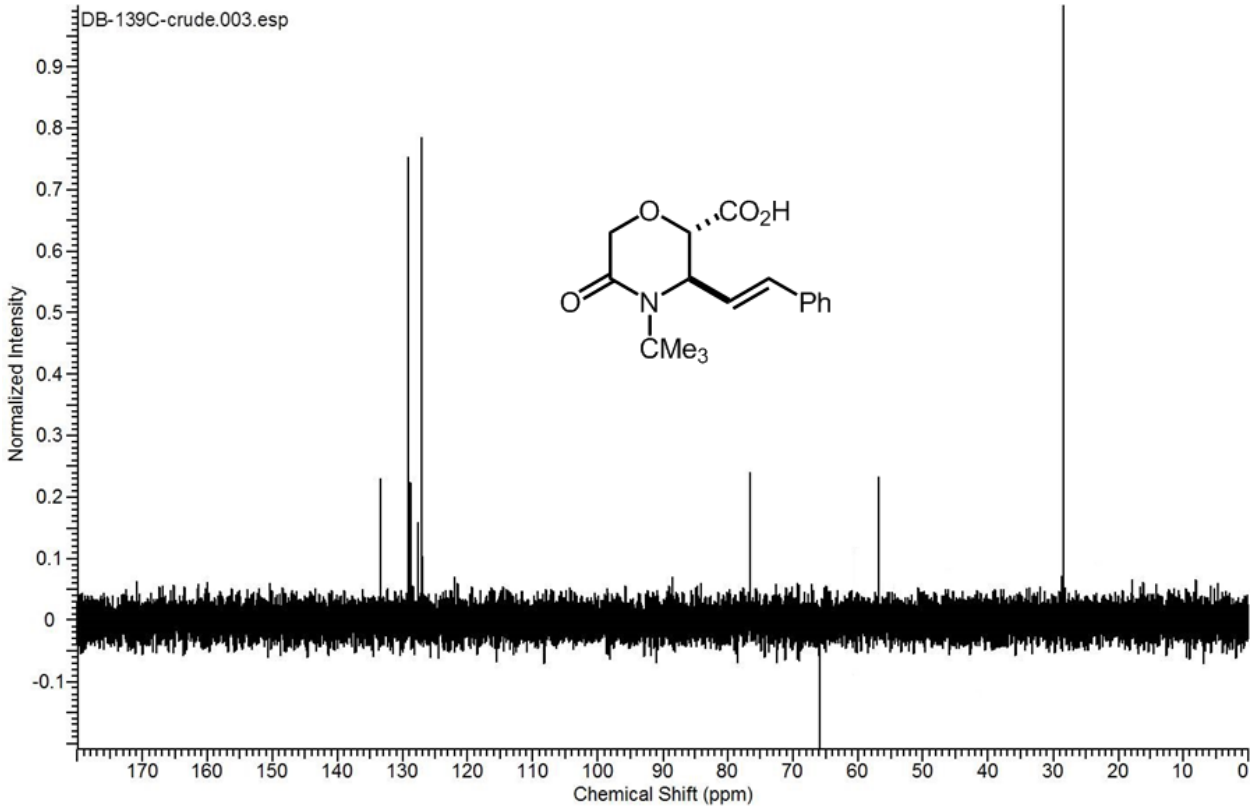


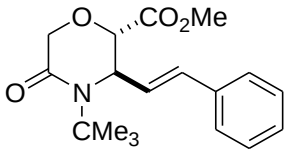
5n1

Prepared from imine **4n** (187 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedure B. T = 90 ^{o}C, time = 12 h. An analytical sample was obtained after a series of washes with cold petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 to 7.22 (5H, m), 6.63 (1H, d), 6.30 (1H, dd), 4.95 (1H, d), 4.71 to 4.53 (2H, dd) , 4.21 (1H, d), 1.40 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 167.8, 135.6, 133.0, 128.8, 128.8, 128.5, 127.4, 126.8, 126.7, 76.3, 65.6, 61.2, 59.1, 28.4. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{17}H_{21}NO_4$ 303.1471; found 303.1467.



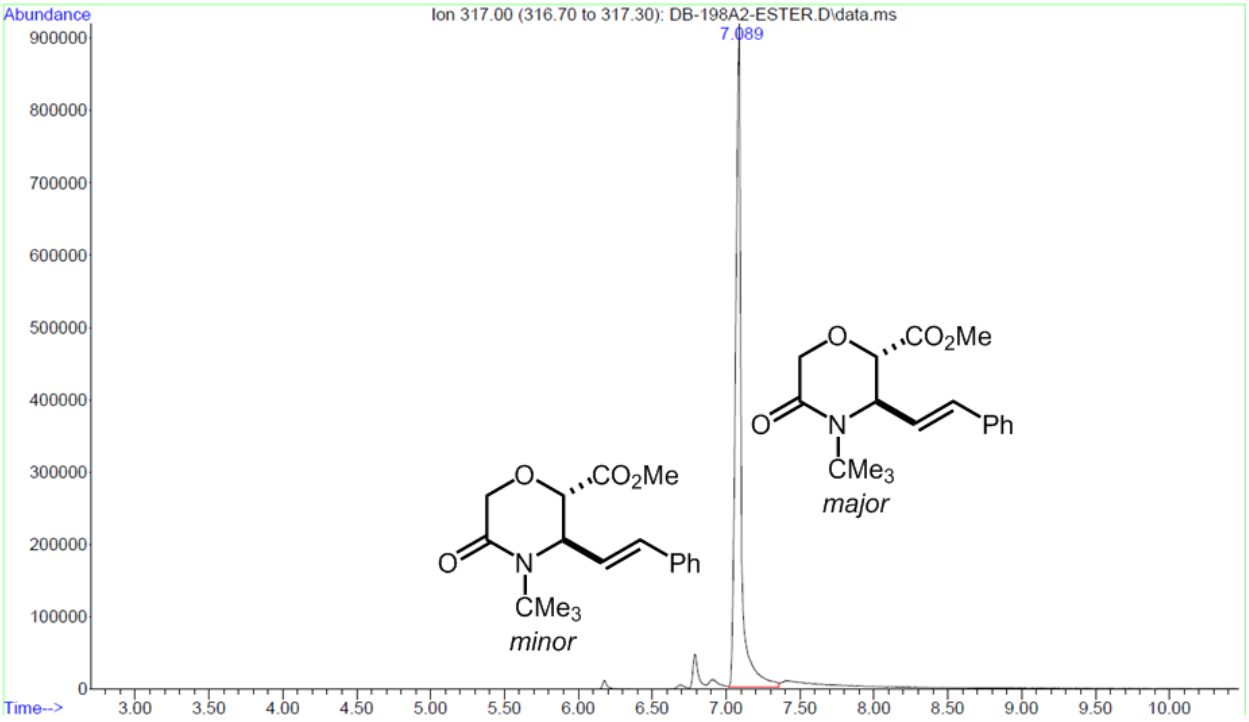

DB-139C-crude.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
Ph
CMe3

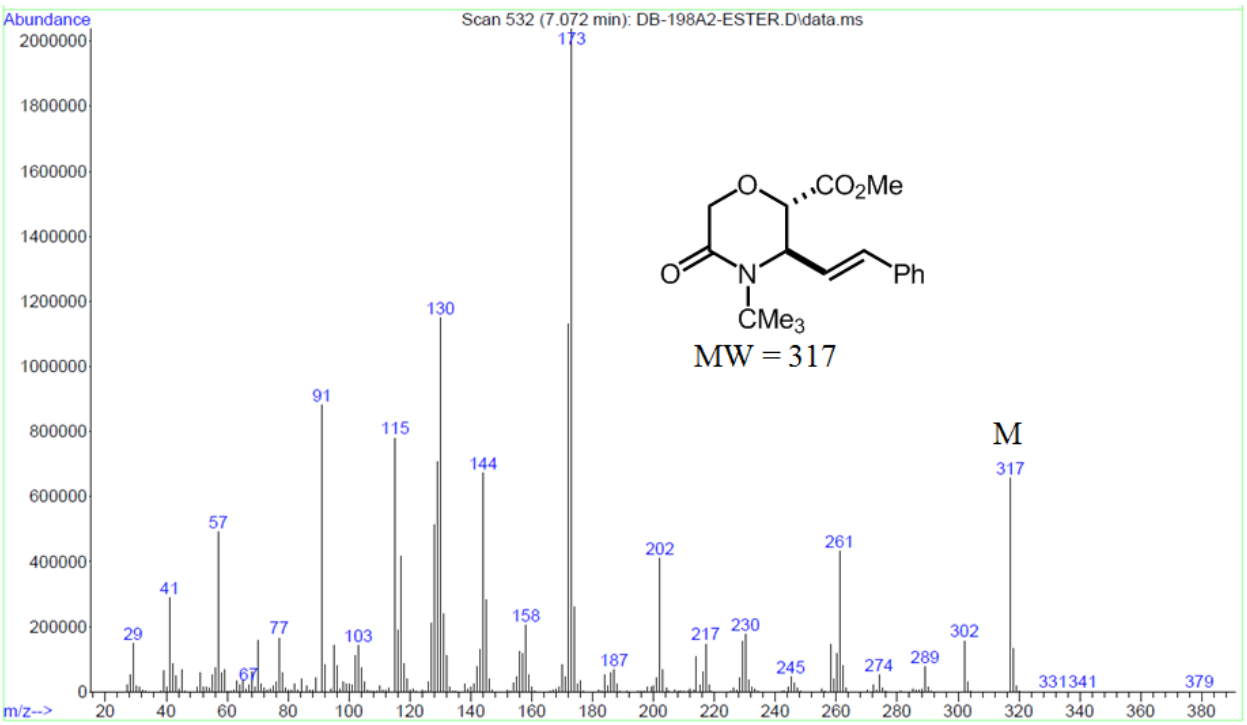

DB-139C-crude.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
Ph
CMe3

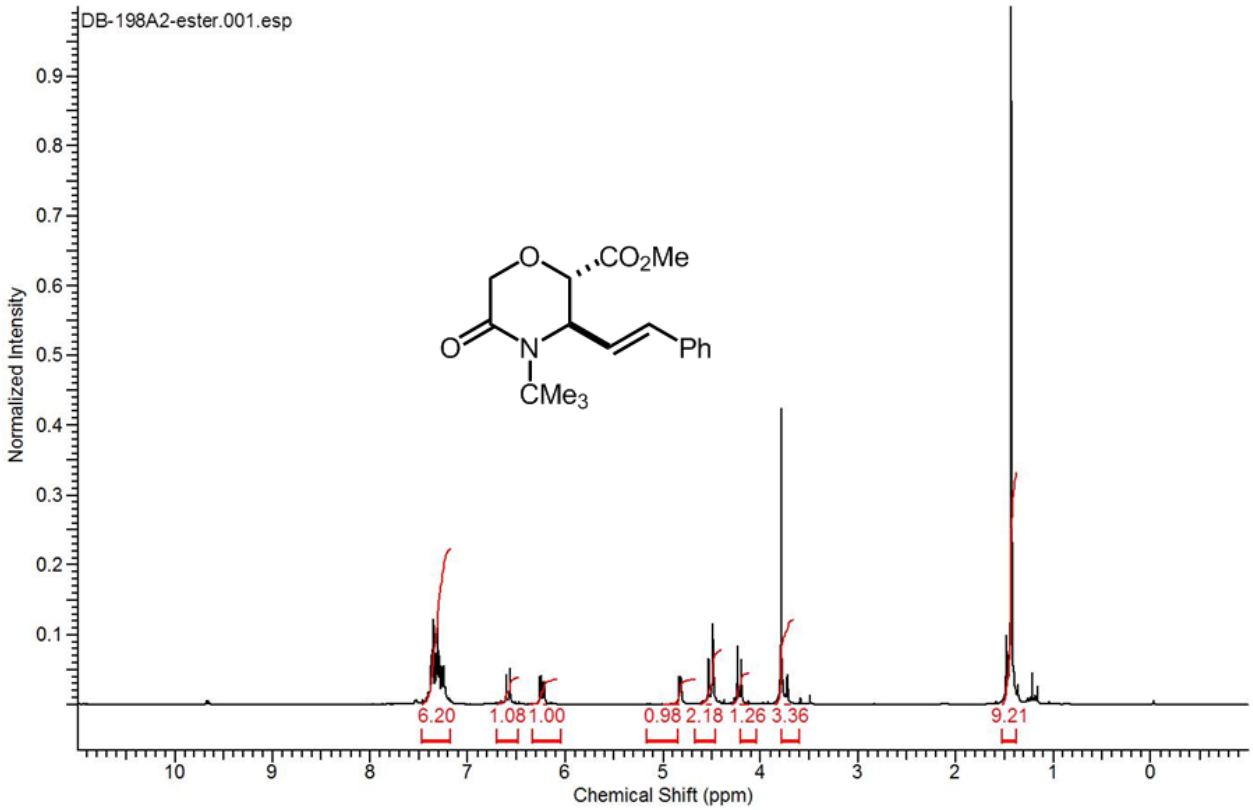


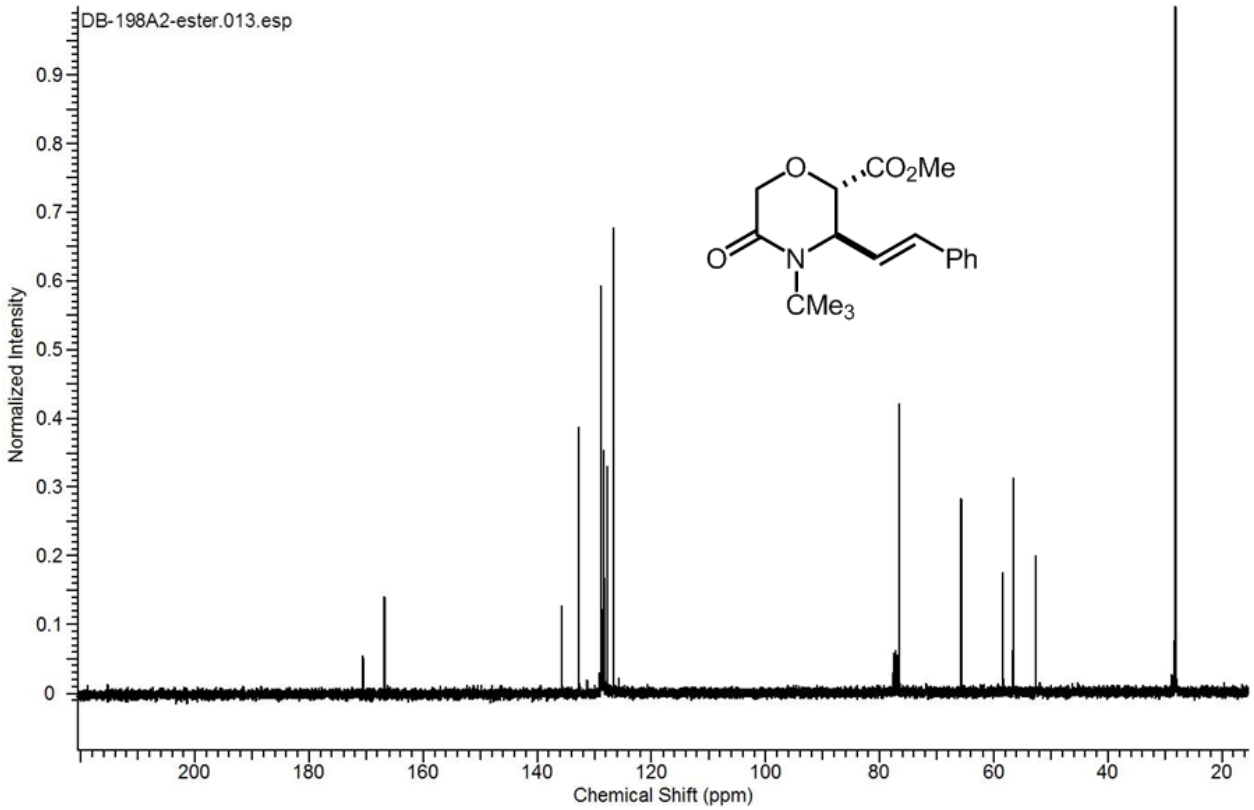
5n2

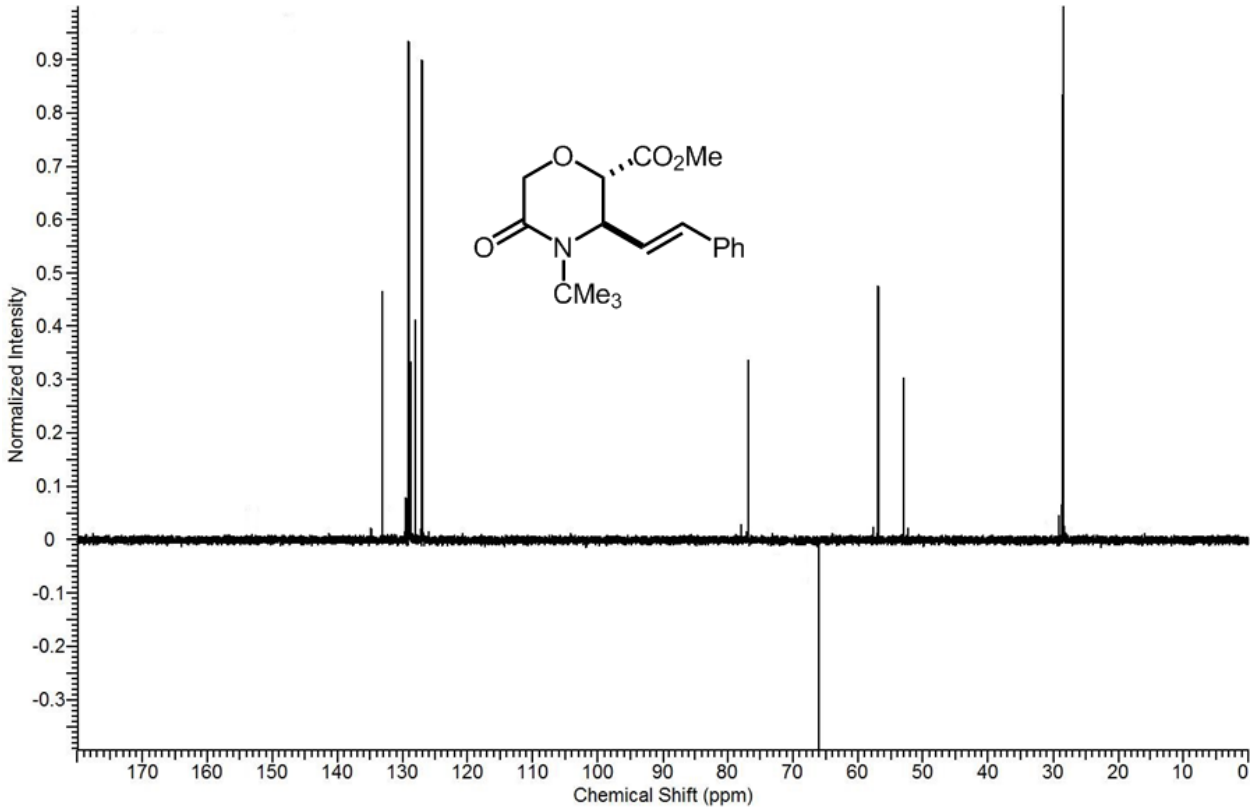
Prepared from crude **5n1** using General Procedure C. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100) then 100% MeOH. Yield = 260 mg, 82% over 2 steps, 96:4 dr. ^{1}H NMR (400 MHz, CDCl3) δ 7.55 to 7.16 (5H, m), 6.66, (1H, d), 6.26 to 6.09 (1H, dd), 4.83 (1H, d), 4.58 to 4.32 (2H, dd), 4.25 (1H, d), 3.74 (3H, s), 1.43 (9H, s). ^{13}C NMR (101 MHz, CDCl3) δ 170.4, 167.8, 135.7, 135.7, 134.5, 134.0, 132.7, 131.3, 129.1, 128.9, 128.8, 128.7, 128.7, 128.6, 128.6, 128.5, 128.4, 128.3, 128.2, 127.7, 127.2, 127.1, 126.7, 126.6, 125.7, 80.2, 78.4, 77.6, 77.6, 77.3, 77.0, 76.6, 71.8, 71.7, 70.4, 68.6, 68.1, 68.0, 65.7, 59.2, 58.4, 57.3, 56.6, 52.6, 52.0, 51.8, 51.0, 45.8, 45.3, 36.5, 29.9, 28.8, 28.4, 28.1, 27.9. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{18}H_{23}NO_4$ 317.1627; found 317.1629.

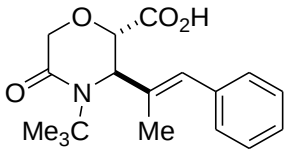



Abundance
Scan 532 (7.072 min): DB-198A2-ESTER.D\data.ms
m/z-->
MW = 317
M
317
173
130
91
115
144
57
41
29
77
67
103
158
187
202
217
230
245
261
274
289
302
331341
379


DB-198A2-ester.001.esp
Normalized Intensity
Chemical Shift (ppm)
6.20
1.08
1.00
0.98
2.18
1.26
3.36
9.21

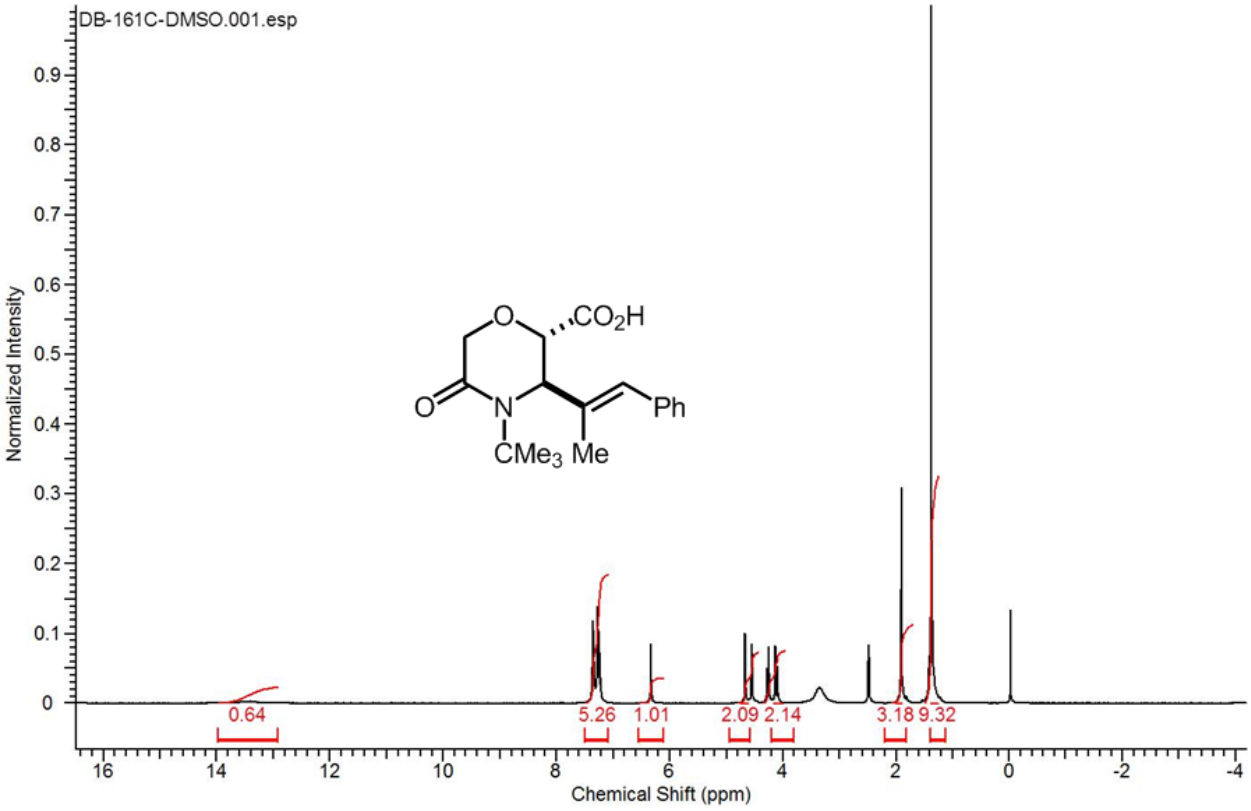

DB-198A2-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
CMe3

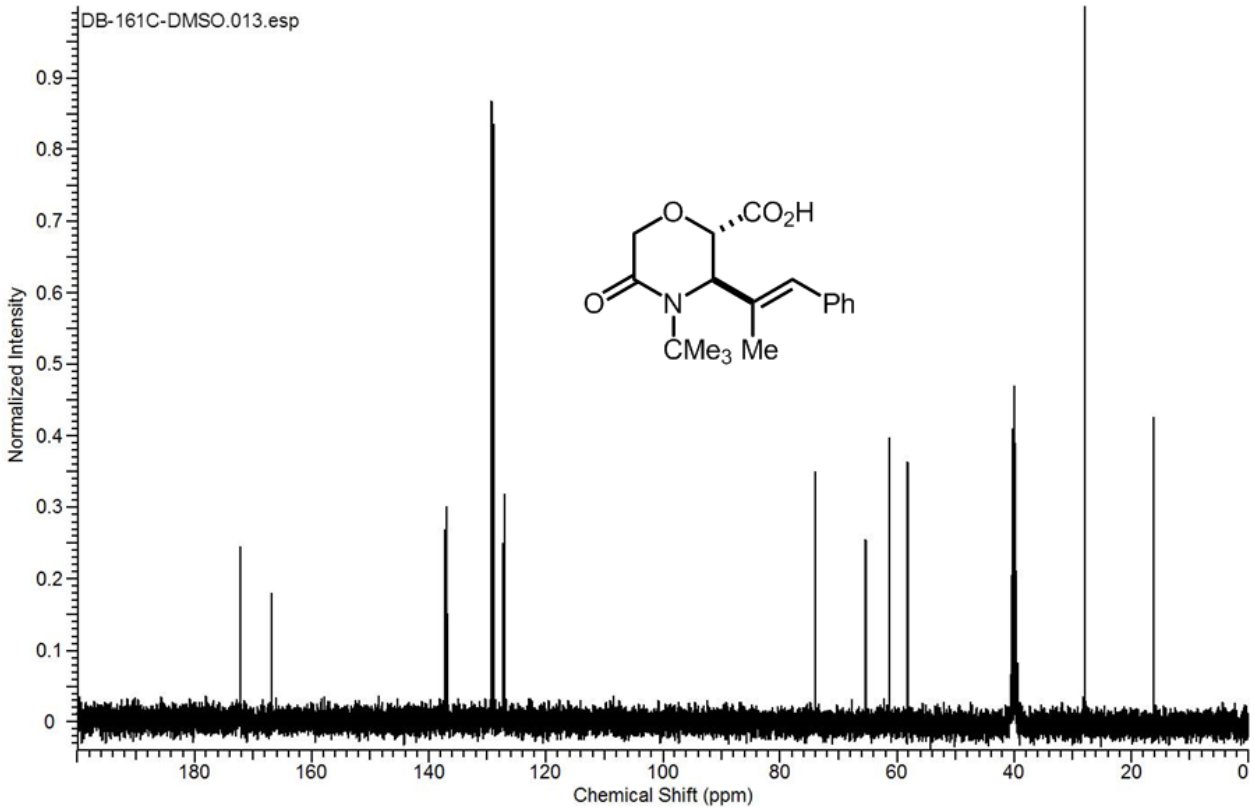

Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
CMe3

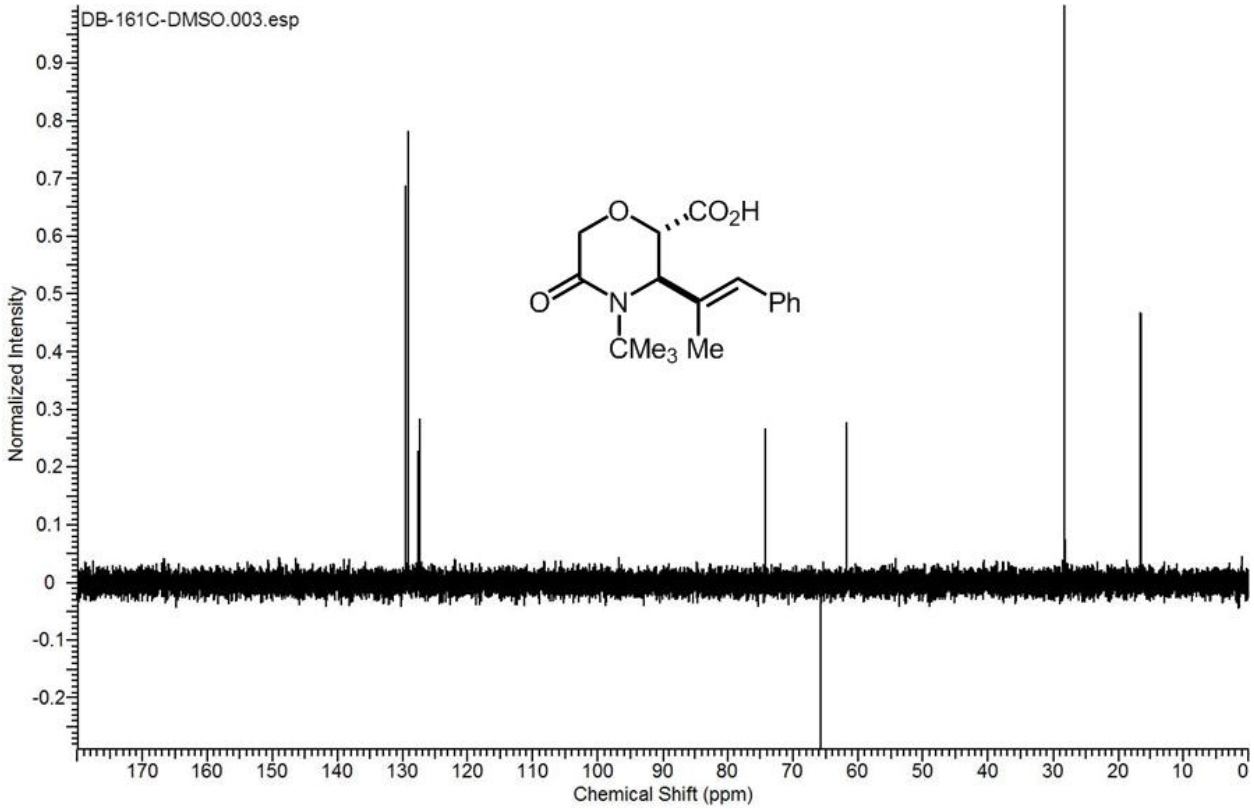


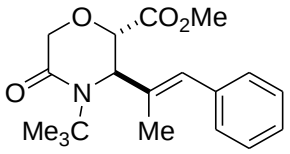
5o1

Prepared from imine **4o** (201 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedure B. T = 90 ^{o}C, time = 18 h. An analytical sample was obtained after a series of washes with cold petroleum ether. ^{1}H NMR (400 MHz, DMSO) δ 13.45 (1H, s, br), 7.37 to 7.22 (5H, m), 6.37 (1H, s), 4.67 to 4.54 (2H, dd), 4.28 to 4.09 (2H, dd), 1.91 (3H, s), 1.37 (9H, s). ^{13}C NMR (101 MHz, DMSO) δ 172.2, 166.8, 137.2, 136.9, 129.2, 128.8, 127.3, 127.0, 74.0, 65.4, 61.4, 58.2, 40.6, 40.4, 40.2, 40.0, 39.8, 39.6, 39.4, 27.9, 16.2. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{18}H_{23}NO_4$ 317.1627; found 317.1627.



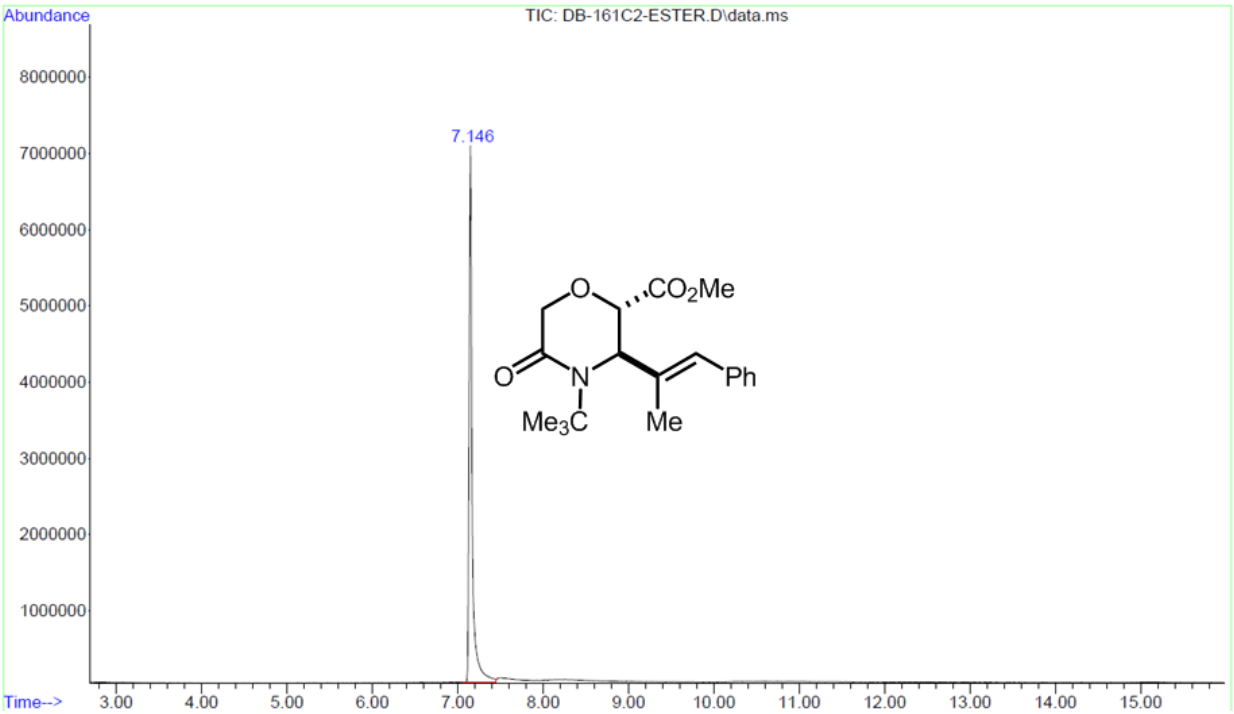

DB-161C-DMSO.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
Ph
CMe3 Me

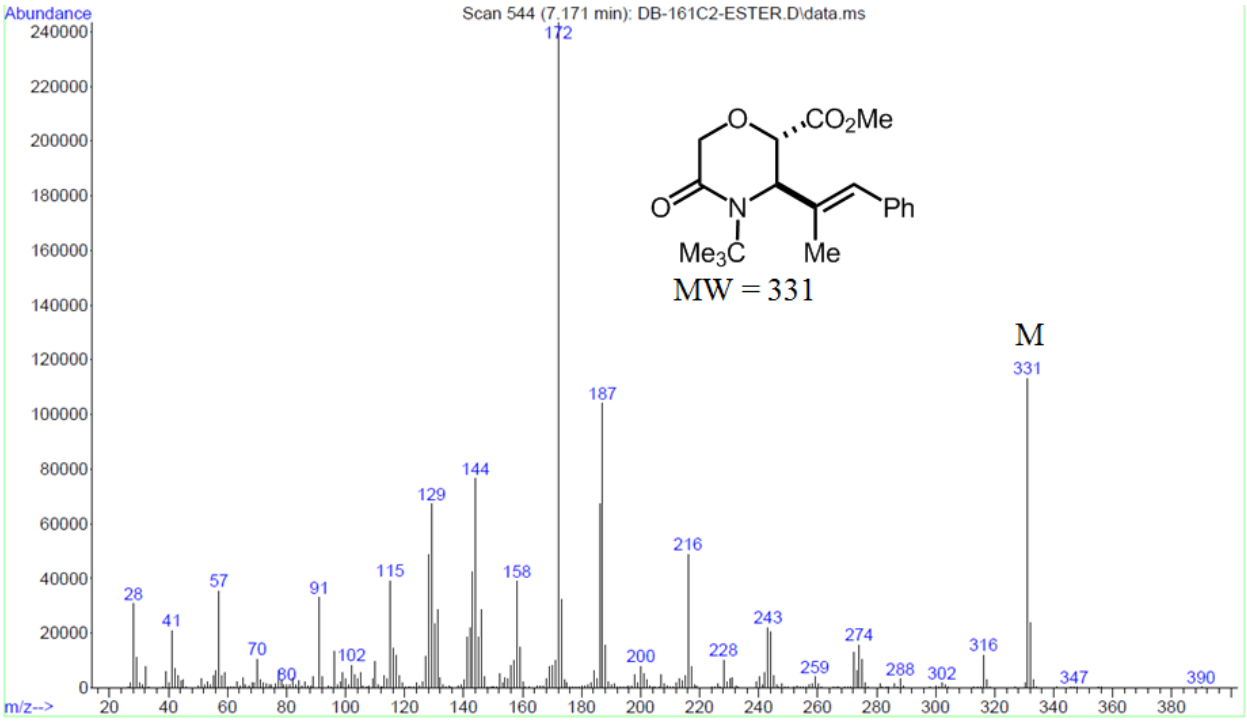

DB-161C-DMSO.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
Ph
CMe3 Me

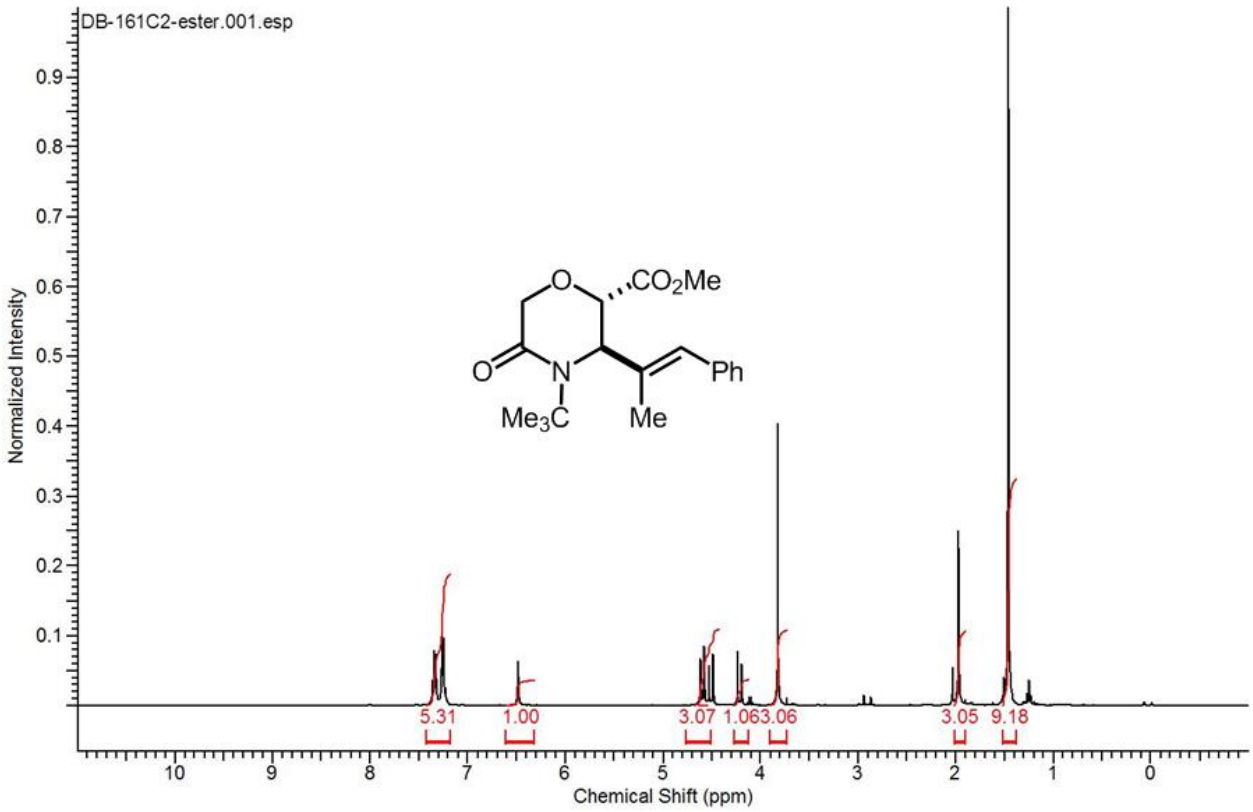


5o2

Prepared from crude **5o1** using General Procedure C. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100) then 100% MeOH. Yield = 252 mg, 76% over 2 steps, >99:1 dr. 1H NMR (400 MHz, CDCl3) δ 7.36 to 7.20 (5H, m), 6.48 (1H, s), 4.62 to 4.53 (3H, m), 4.23 (1H, d), 3.73 (3H, s), 1.97 (3H, s), 1.46 (9H, s). ^{13}C NMR (101 MHz, CDCl3) δ 170.9, 167.0, 136.8, 135.3, 129.0, 128.3, 127.1, 77.5, 77.1, 76.8, 74.8, 65.8, 61.6, 60.4, 58.8, 52.8, 28.2, 28.0, 16.0, 14.3. 28.2. **HRMS-EI**$^{+}$ (*m/z*): calc'd for $C_{19}H_{25}NO_4$ 331.1784; found 331.1788.




Abundance
Scan 544 (7.171 min): DB-161C2-ESTER.D\data.ms
m/z-->
MW = 331
M
331
172
187
144
129
216
115
158
91
57
28
41
70
80
102
200
228
243
259
274
288
302
316
347
390
CO2Me
Ph
Me3C
Me


DB-161C2-ester.001.esp
Normalized Intensity
Chemical Shift (ppm)
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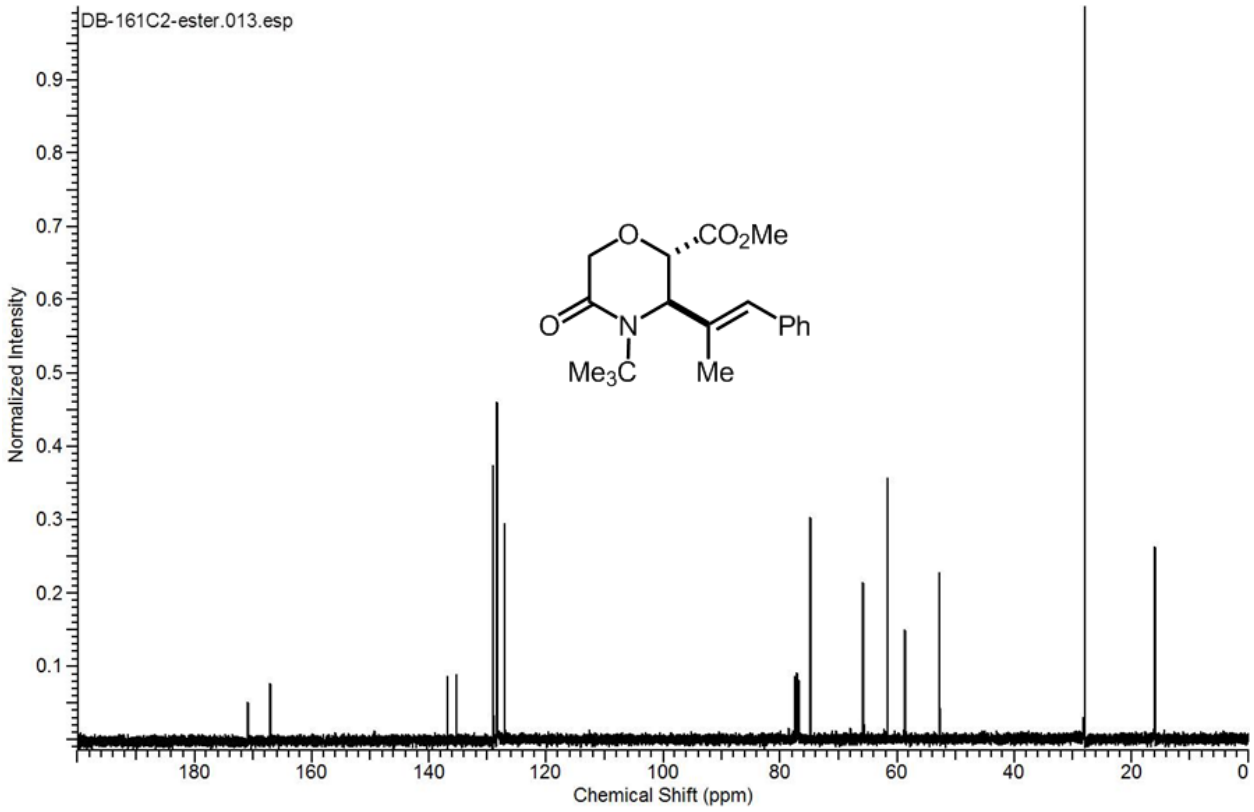
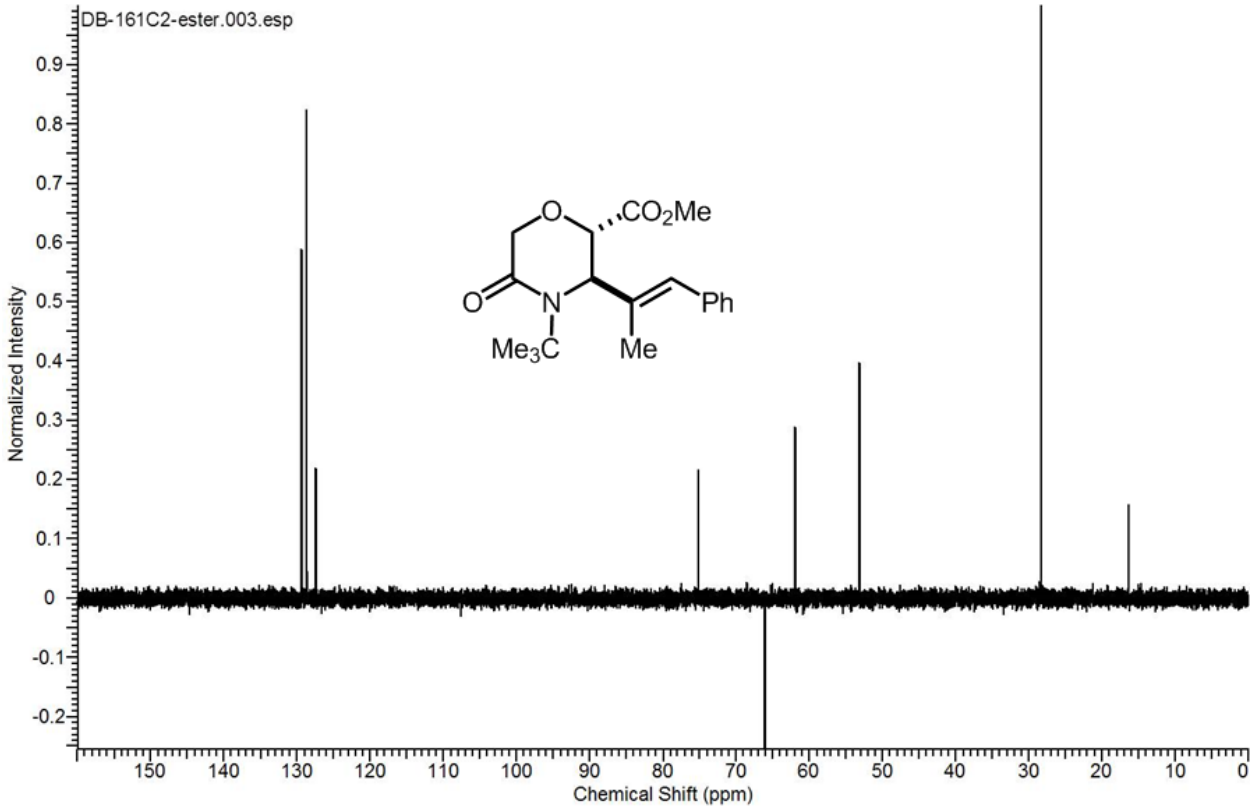
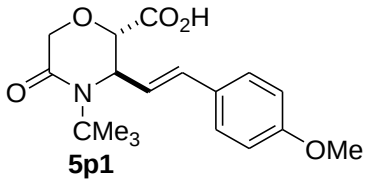
1.00
3.07
1.06
3.06
3.05
9.18
CO2Me
Ph
Me3C
Me

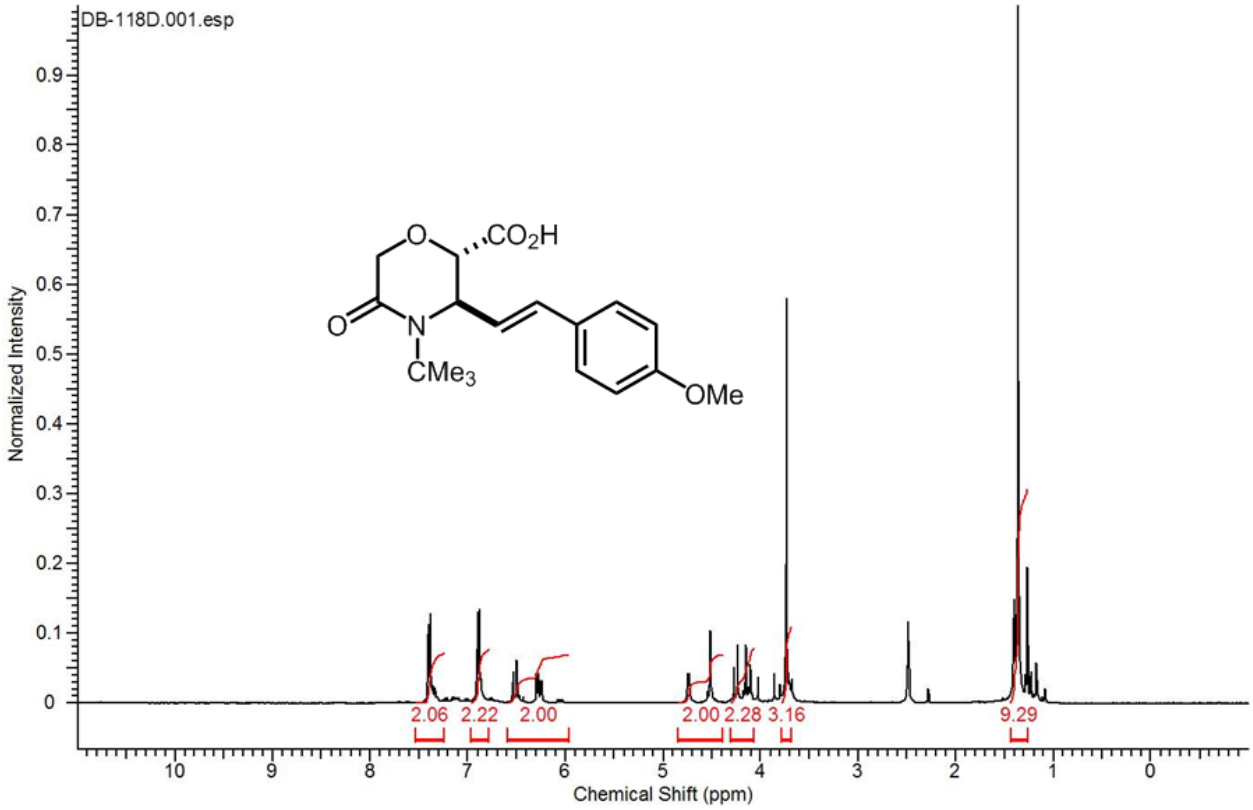

DB-161C2-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
Me3C
Me

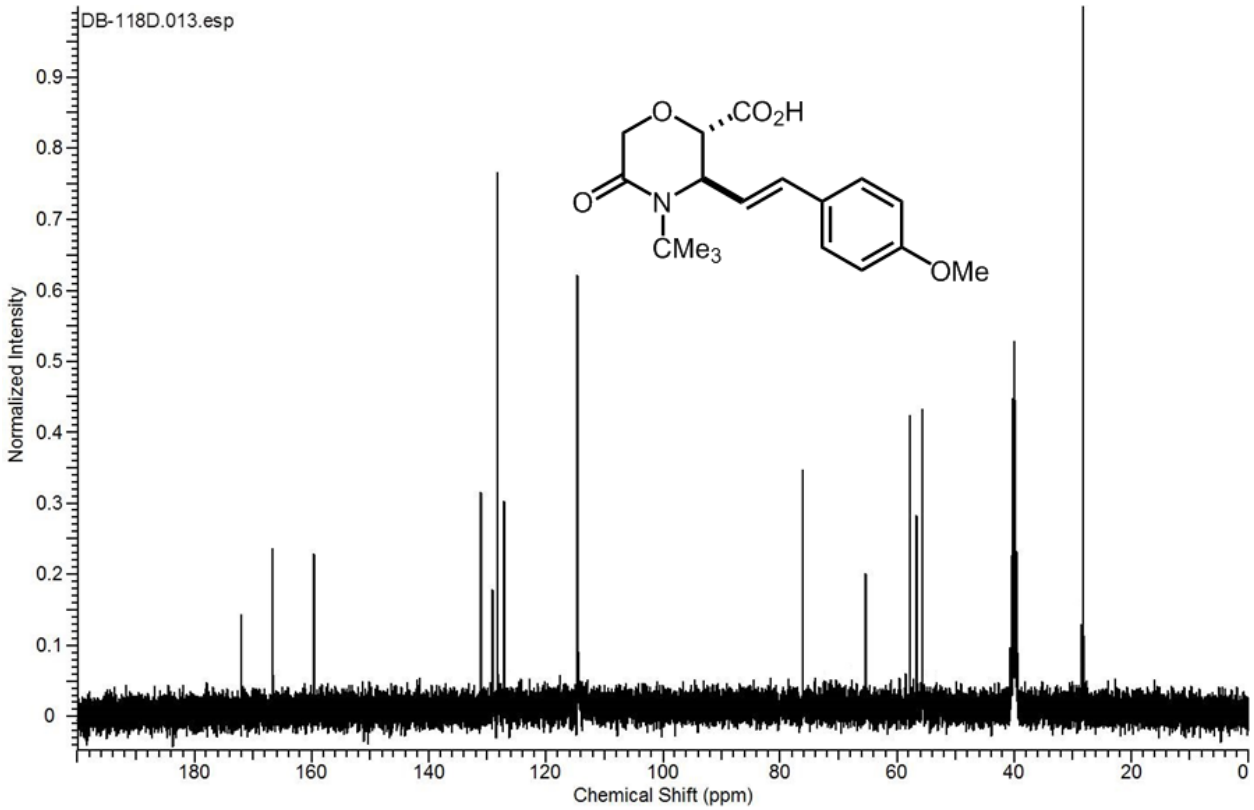

DB-161C2-ester.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
Me3C
Me

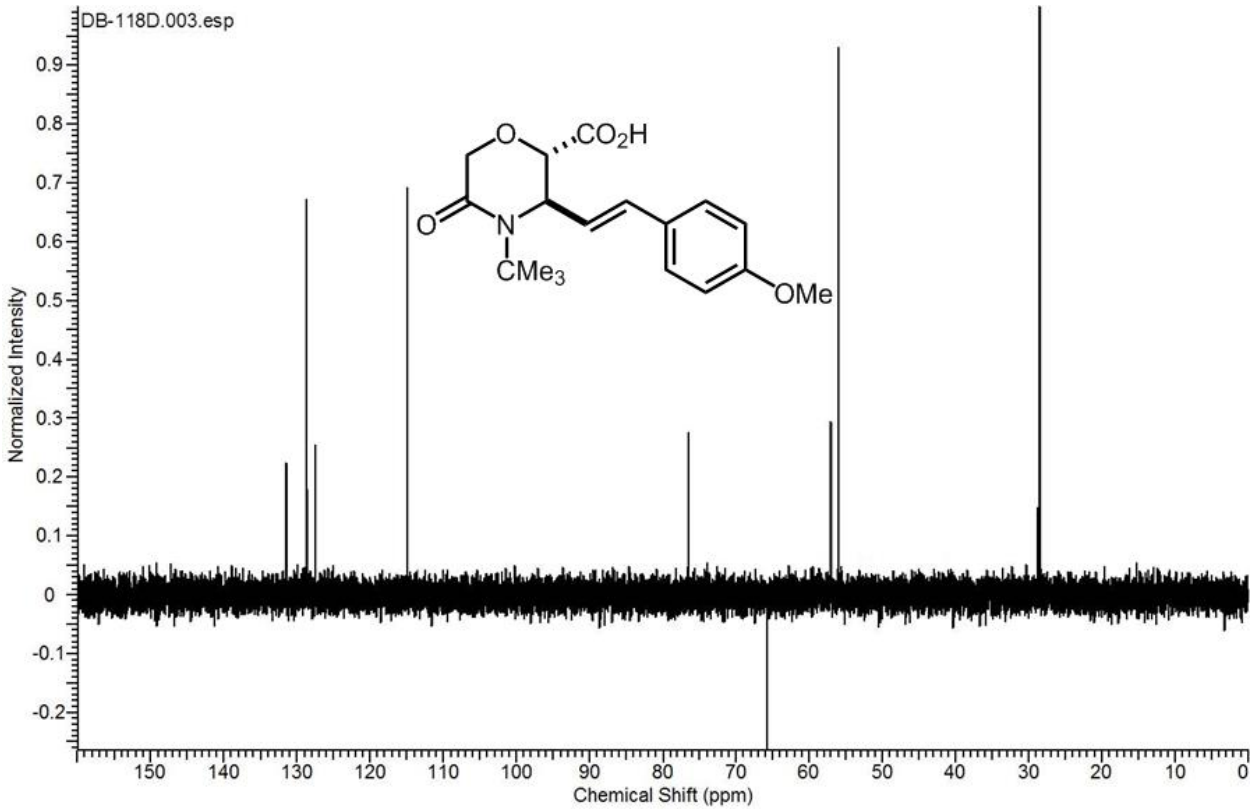


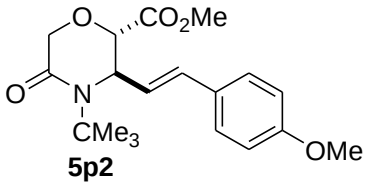
5p1

Prepared from imine **4r** (217 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedure B. T = 90 ^{o}C, time = 18 h. An analytical sample was obtained after a series of washes with cold petroleum ether. 1H NMR (400 MHz, DMSO) δ 13.38 (1H, s, br), 7.41 (2H, d), 6.90 (2H, d), 6.50 (1H, d), 6.30 (1H, dd), 4.74 (1H, d), 4.55 (1H, d), 4.29 to 4.09 (2H, dd), 3.80 (3H, s), 1.36 (9H, s). 13C NMR (101 MHz, DMSO) δ 172.0, 166.7, 159.6, 133.0, 131.2, 129.1, 128.3, 127.2, 114.6, 76.2, 68.8, 65.4, 58.5, 57.7, 56.7, 55.7, 40.7, 40.4, 40.2, 40.0, 39.8, 39.6, 39.4, 30.0, 29.0, 28.4, 28.2. **HRMS-EI+** (*m/z*): calc'd for $C_{18}H_{23}NO_5$ 333.1576; found 333.1580.



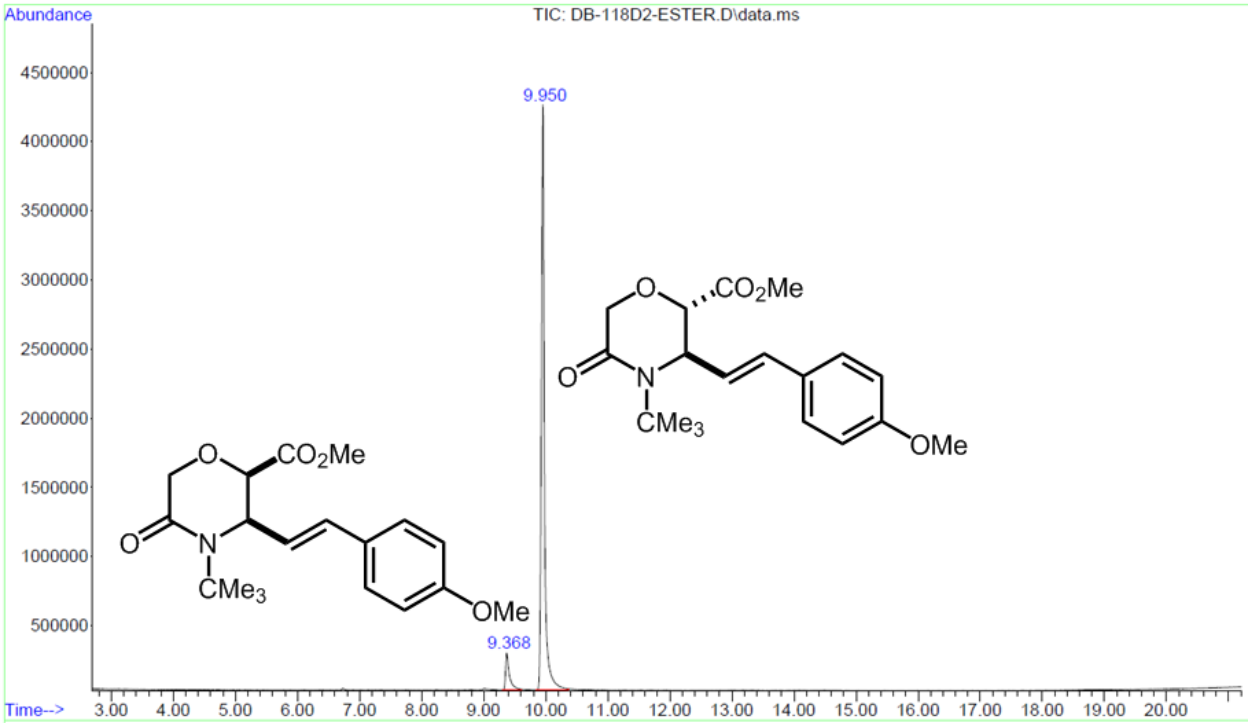

DB-118D.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
CMe3
OMe

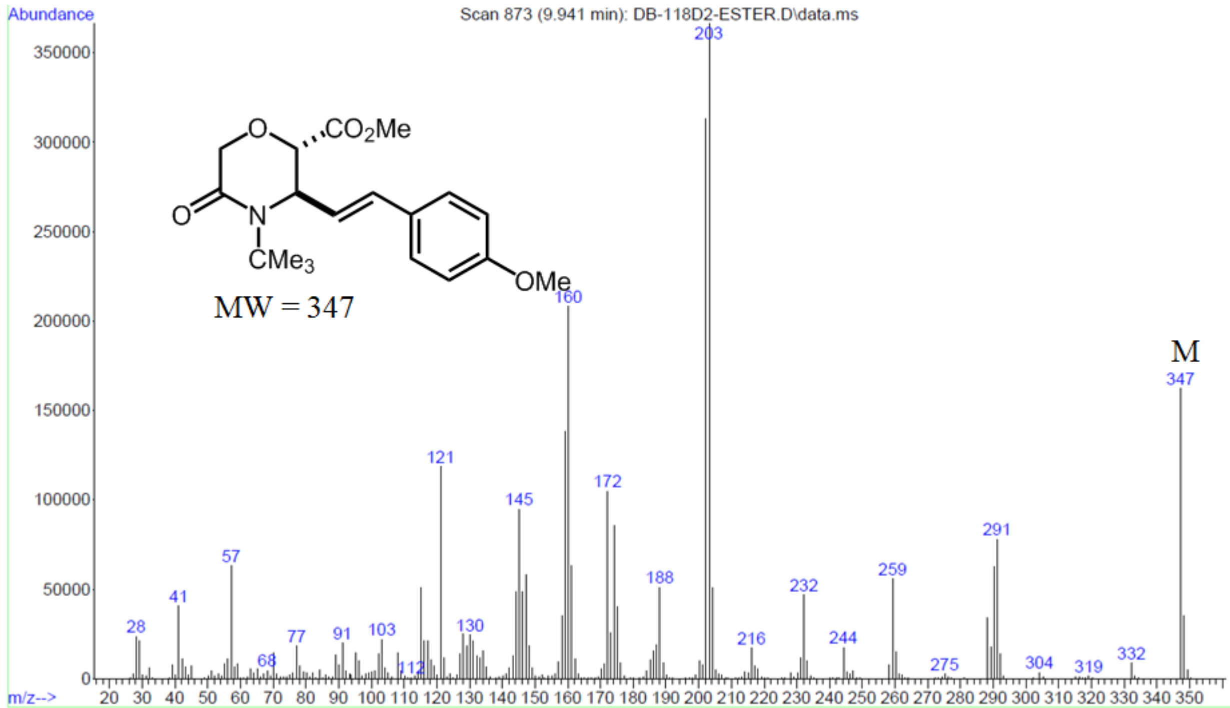

DB-118D.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
CMe3
OMe



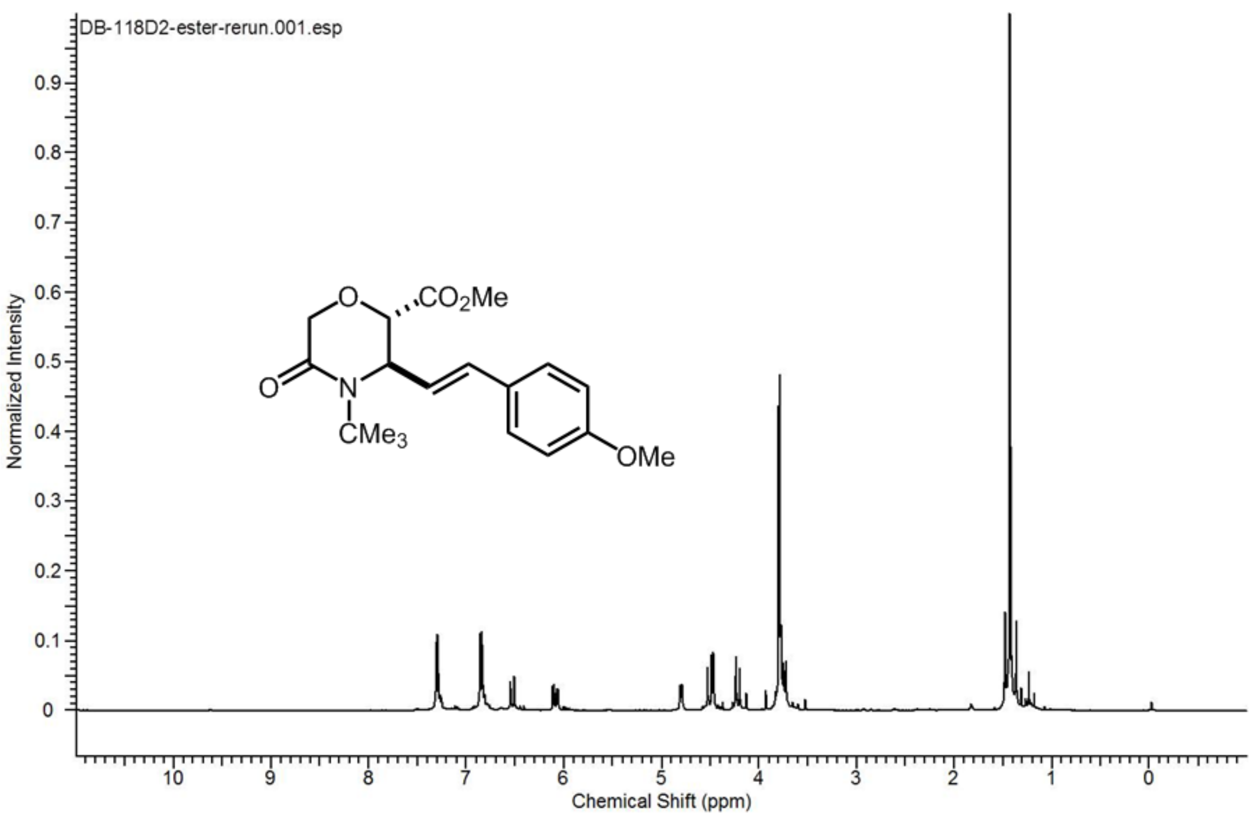
5p2

Prepared from crude **5p1** using General Procedure C. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100) then 100% MeOH. Yield = 274 mg, 79% over 2 steps, 93:7 dr. 1H NMR (400 MHz, CDCl3) δ 7.48 (2H, d), 6.88 (2H, d), 6.52 (1H, d), 6.09 (1H, dd), 4.78 (1H, d), 4.55 to 4.34 (2H, dd), 4.19 to 4.15 (1H, dd), 3.79 to 3.71 (6H, overlapping singlets),1.33 (9H, s). 13C NMR (101 MHz, CDCl3) δ 170.5, 166.7, 62.5, 159.8, 152.3, 133.9, 132.1, 130.4, 129.9, 128.4, 128.0, 127.9, 125.4, 123.3, 114.6, 114.2, 114.1, 113.5, 78.6, 77.0, 76.7, 71.8, 68.6, 68.1, 68.0, 65.7, 59.2, 58.3, 57.4, 56.6, 55.3, 52.6, 51.8, 28.8, 28.4. **HRMS-EI**$^+$ (*m/z*): calc'd for $C_{19}H_{25}NO_5$ 347.1733; found 347.1729.

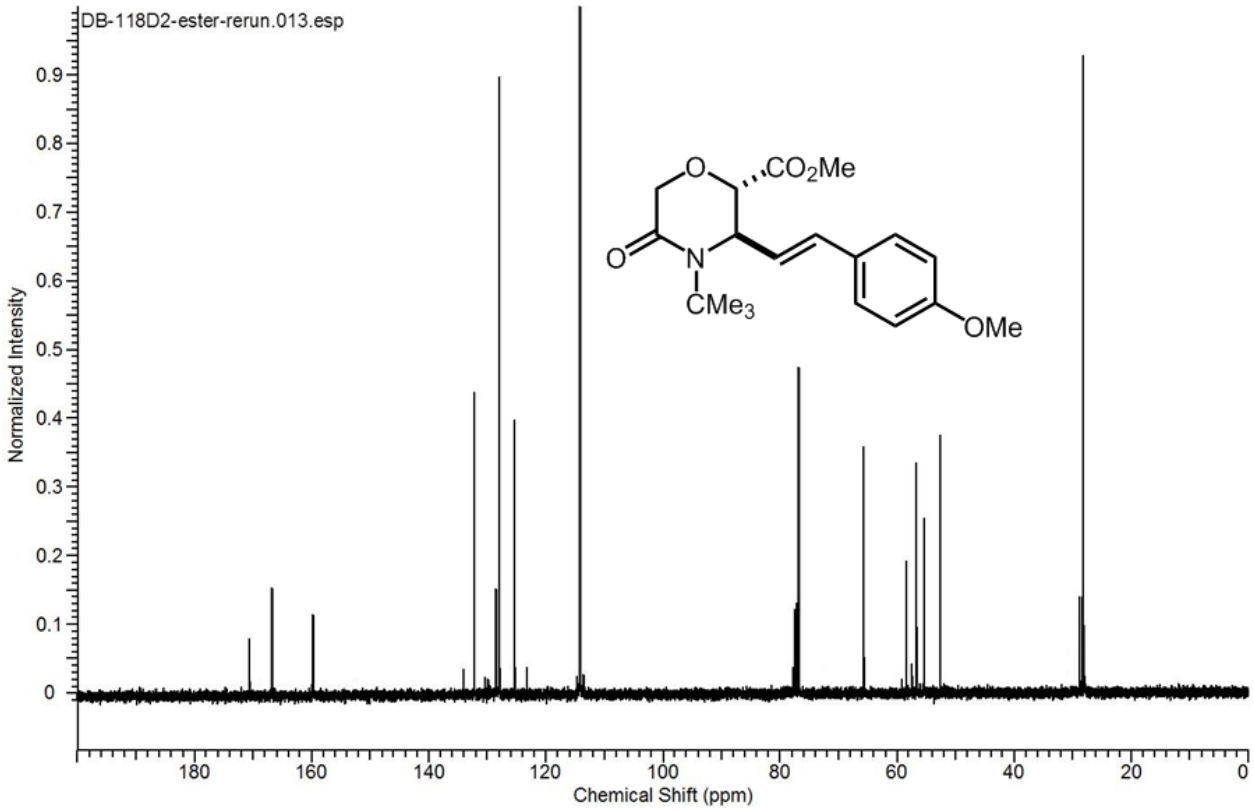


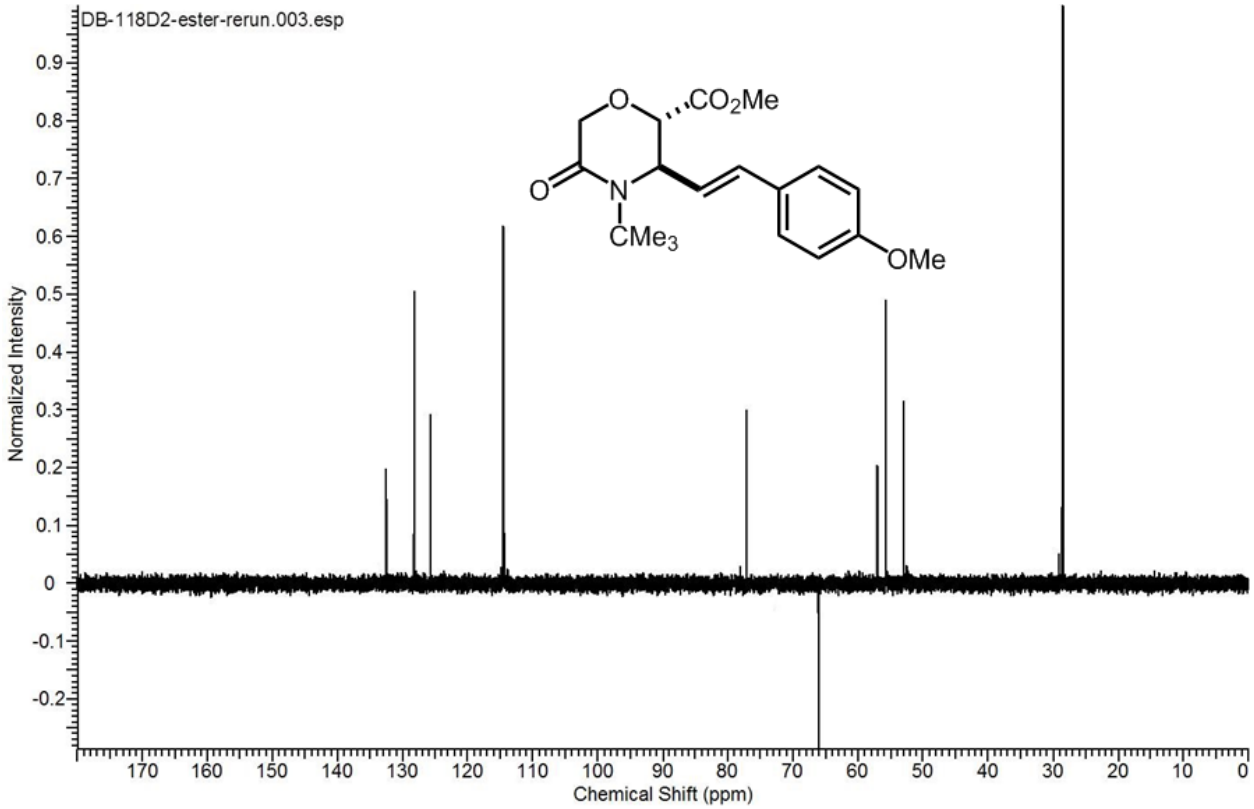


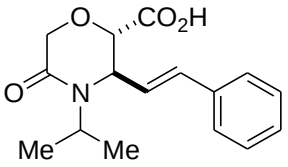
Abundance
Scan 873 (9.941 min): DB-118D2-ESTER.D\data.ms
CO2Me
O
N
CMe3
OMe
MW = 347
M
347
203
160
121
145
172
188
291
259
232
244
216
57
41
28
77
91
103
130
68
112
275
304
319
332
m/z-->



DB-118D2-ester-rerun.001.esp
Normalized Intensity
CO2Me
O
N
CMe3
OMe
Chemical Shift (ppm)

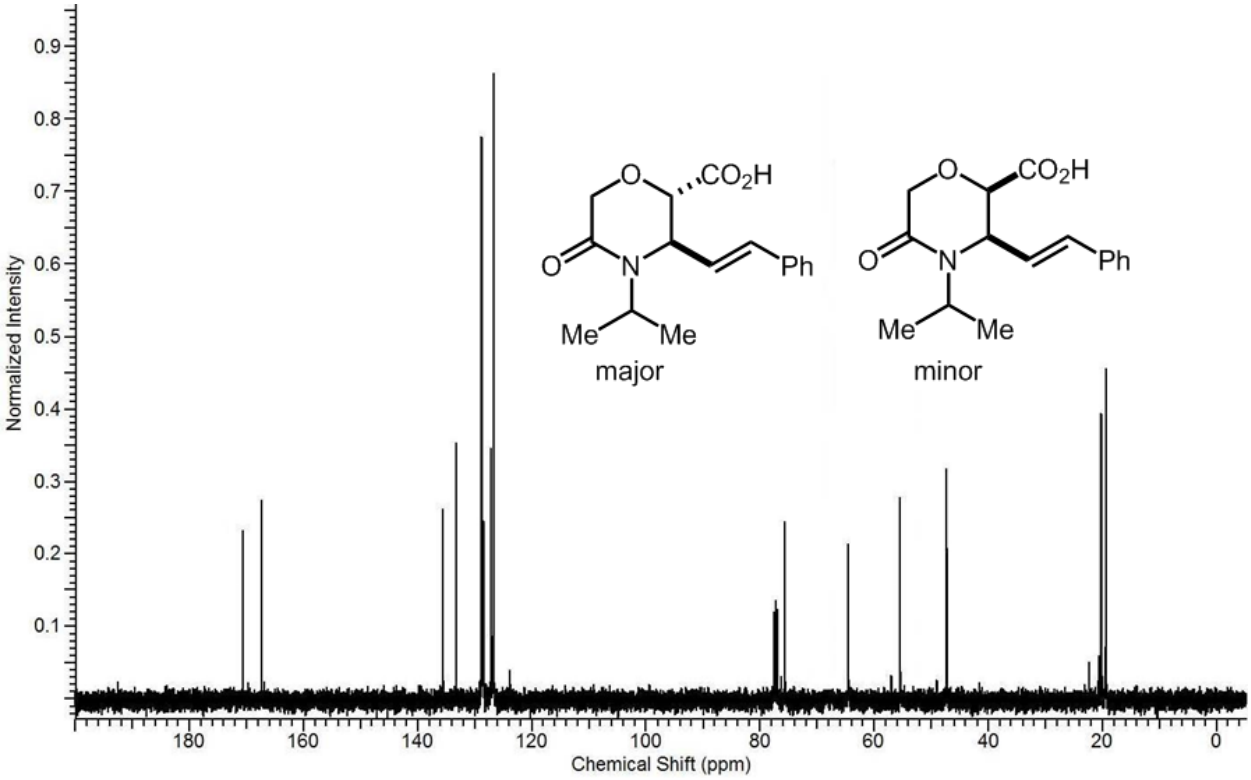

DB-118D2-ester-rerun.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
CMe3
OMe

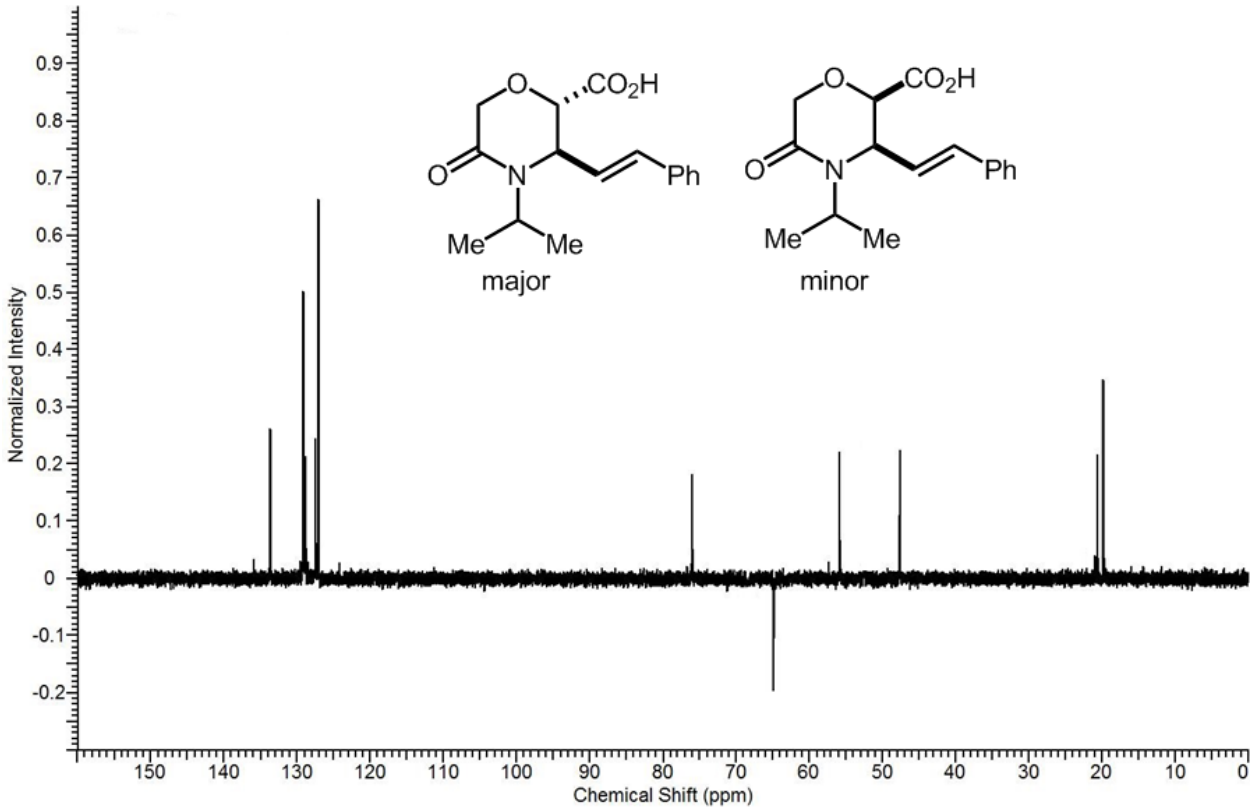

DB-118D2-ester-rerun.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
CMe3
OMe

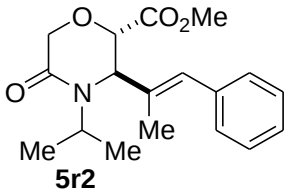


5q1

Prepared from imine **4p** (305 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedure B. T = 90 ^{o}C, time = 16 h. Yield = 295 mg, 82%, 83:17 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.31 (1H, s, br), 7.40 to 7.11 (5H, m), 6.62 (1H, d),6.27 to 6.20 (1H, dd), 4.67 to 4.46 (3H, m), 4.39 to 4.21 (1H, m),4.10 (1H, d), 1.27 to 1.18 (6H, dd). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 172.2, 170.7, 167.4, 167.0, 135.6, 135.6, 133.3, 129.2, 128.8, 128.7, 128.5, 128.1, 127.2, 126.9, 126.7, 123.8, 77.6, 77.3, 77.0, 76.4, 75.6, 70.8, 68.8, 68.2, 68.1, 68.1, 67.3, 64.5, 57.0, 55.5, 52.2, 49.0, 47.3, 45.3, 22.4, 20.6, 20.2, 19.6, 19.5. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{16}H_{19}NO_4$ 289.1314; found 289.1318.

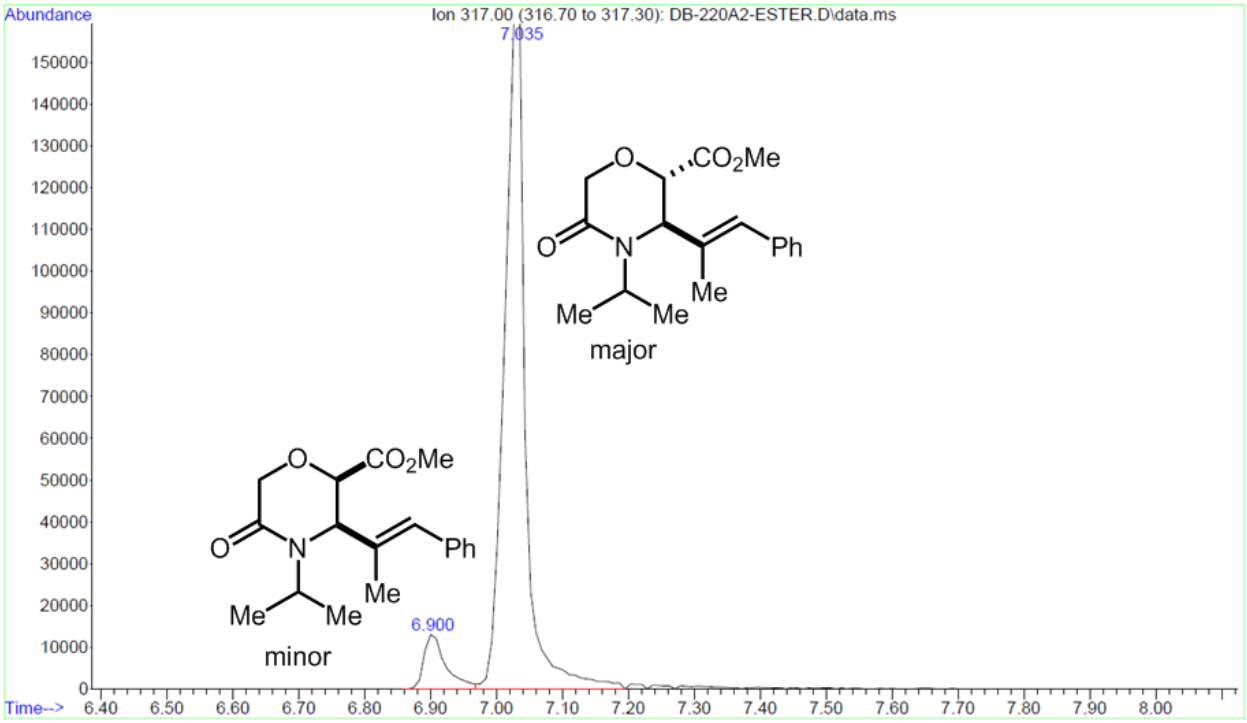


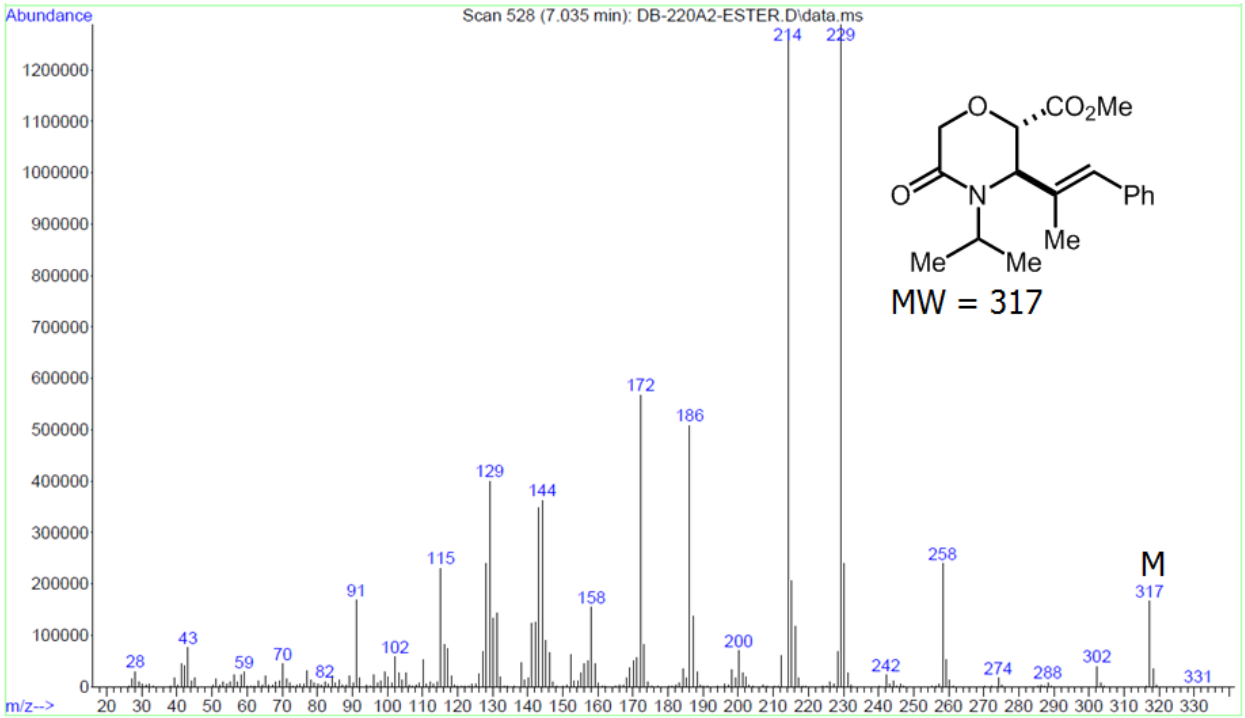


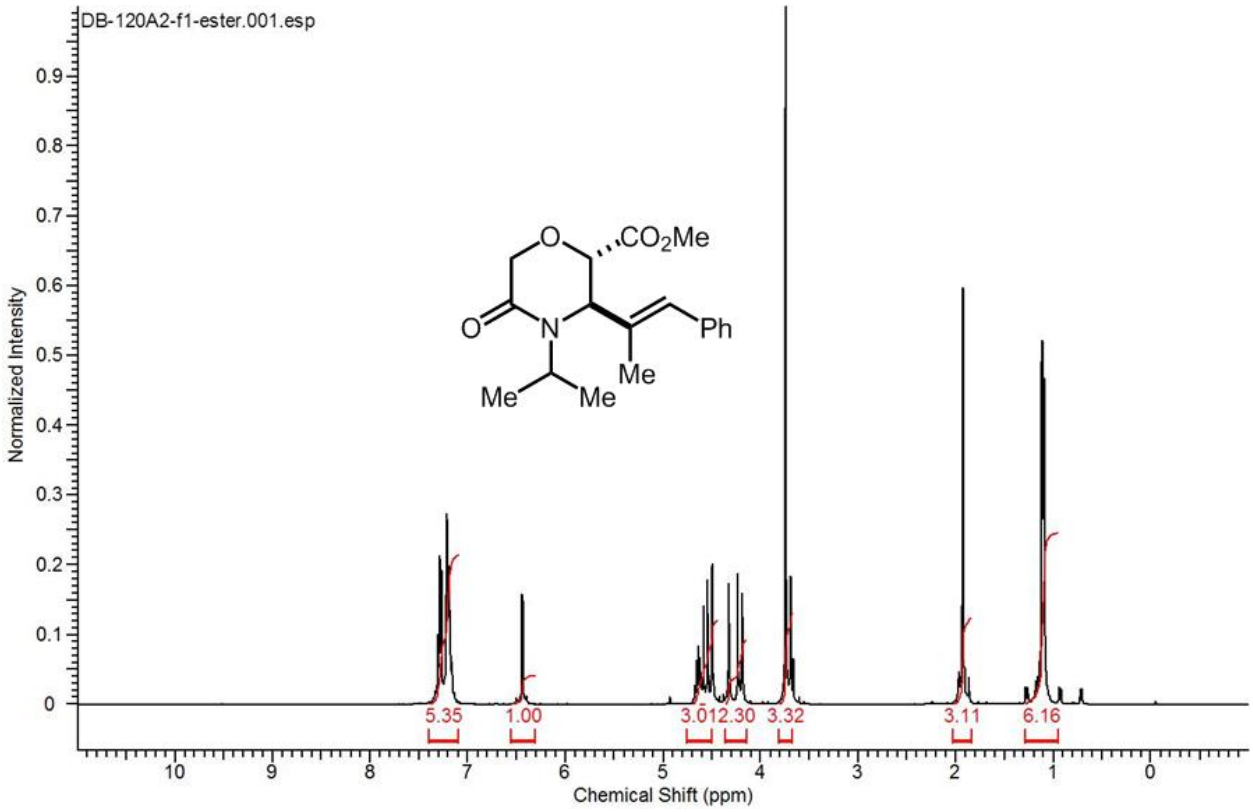


5r2

Prepared from imine **4q** (187 mg, 1.0 mmol) and diglycolic anhydride (128 mg, 1.1 equiv) using General Procedures B and C. T = 90 ^{o}C, time = 12 h. Yield =289 mg, 91%, 92:8 dr. 1H NMR (400 MHz, $CDCl_3$) δ 7.36 to 7.20 (5H, m), 6.48 (1H, s), 4.62 to 4.53 (3H, m), 4.23 (1H, d), 3.73 (3H, s), 1.97 (3H, s), 1.46 (6H, dd). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 166.1, 136.7, 135.6, 131.2, 129.7, 128.9, 128.7, 128.5, 128.3, 127.3, 127.2, 127.1, 77.7, 77.6, 77.3, 77.0, 76.7, 74.8, 68.0, 67.3, 64.9, 64.6, 61.8, 60.1, 52.6, 52.4, 51.9, 51.9, 48.0, 46.4, 46.0, 20.2, 30.0, 19.6, 19.3, 19.0, 18.9, 15.5, 14.6. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{18}H_{23}NO_4$ 317.1627; found 317.1622.


Abundance
Ion 317.00 (316.70 to 317.30): DB-220A2-ESTER.D\data.ms
7.035
6.900
major
minor
Time-->


Abundance
Scan 528 (7.035 min): DB-220A2-ESTER.D\data.ms
MW = 317
M
317
m/z-->


DB-120A2-f1-ester.001.esp
Normalized Intensity
Chemical Shift (ppm)
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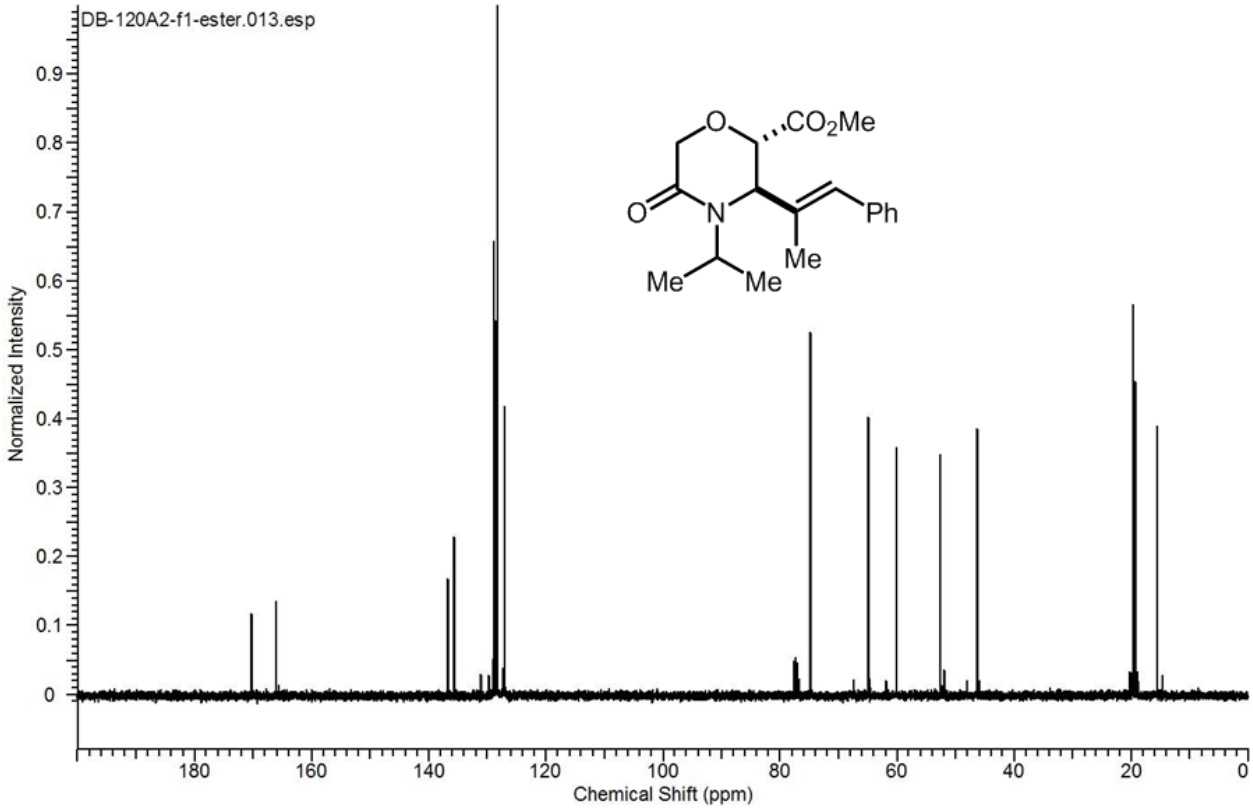
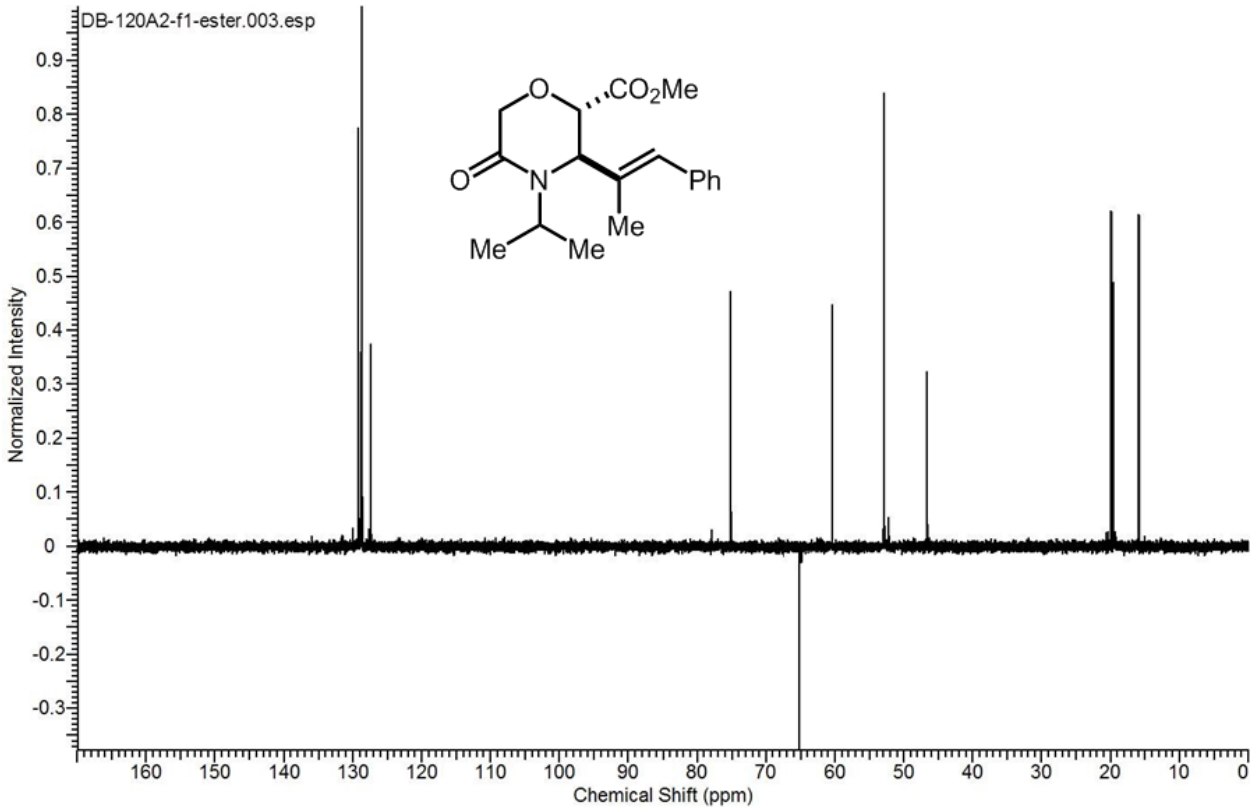
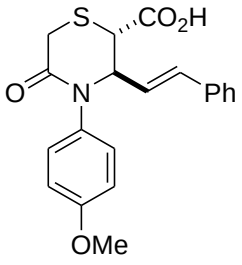
3.01
2.30
3.32
3.11
6.16
CO2Me
Ph
Me
Me
Me
O
N


DB-120A2-f1-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
Me
Me
Me
O
N

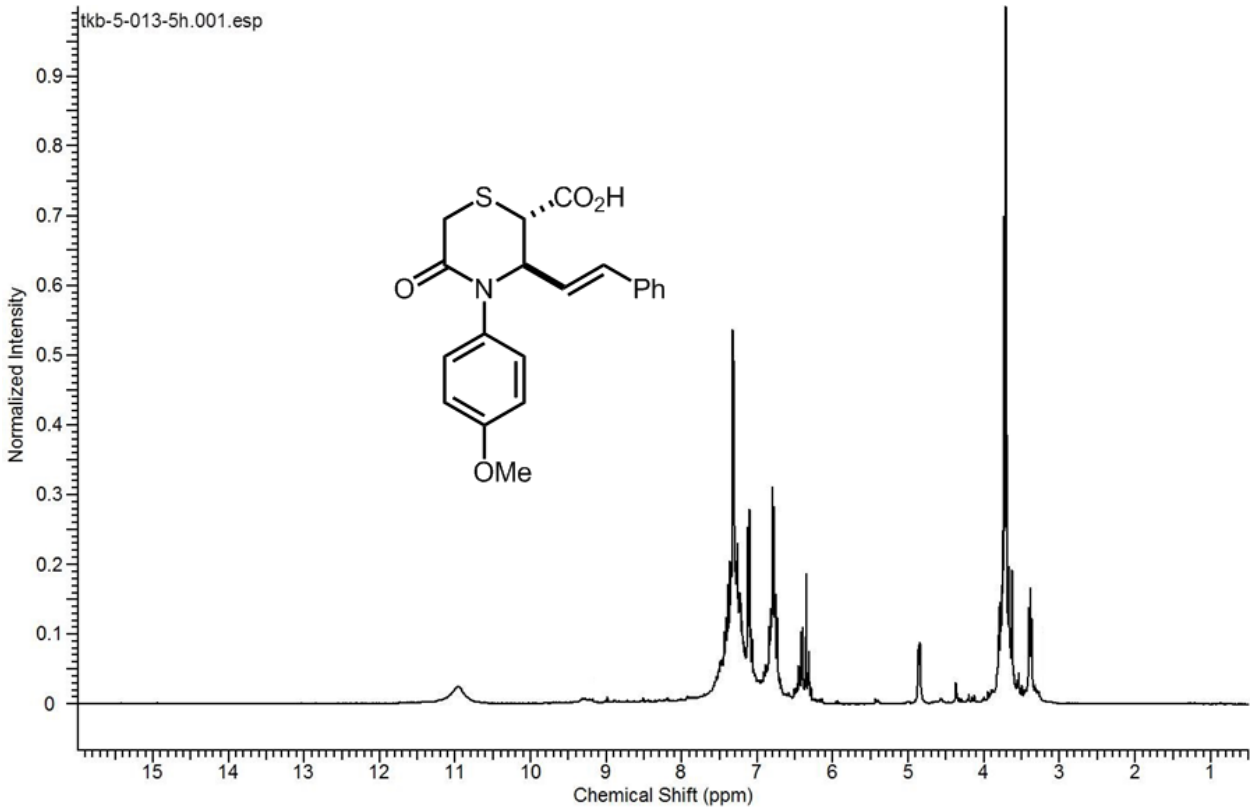


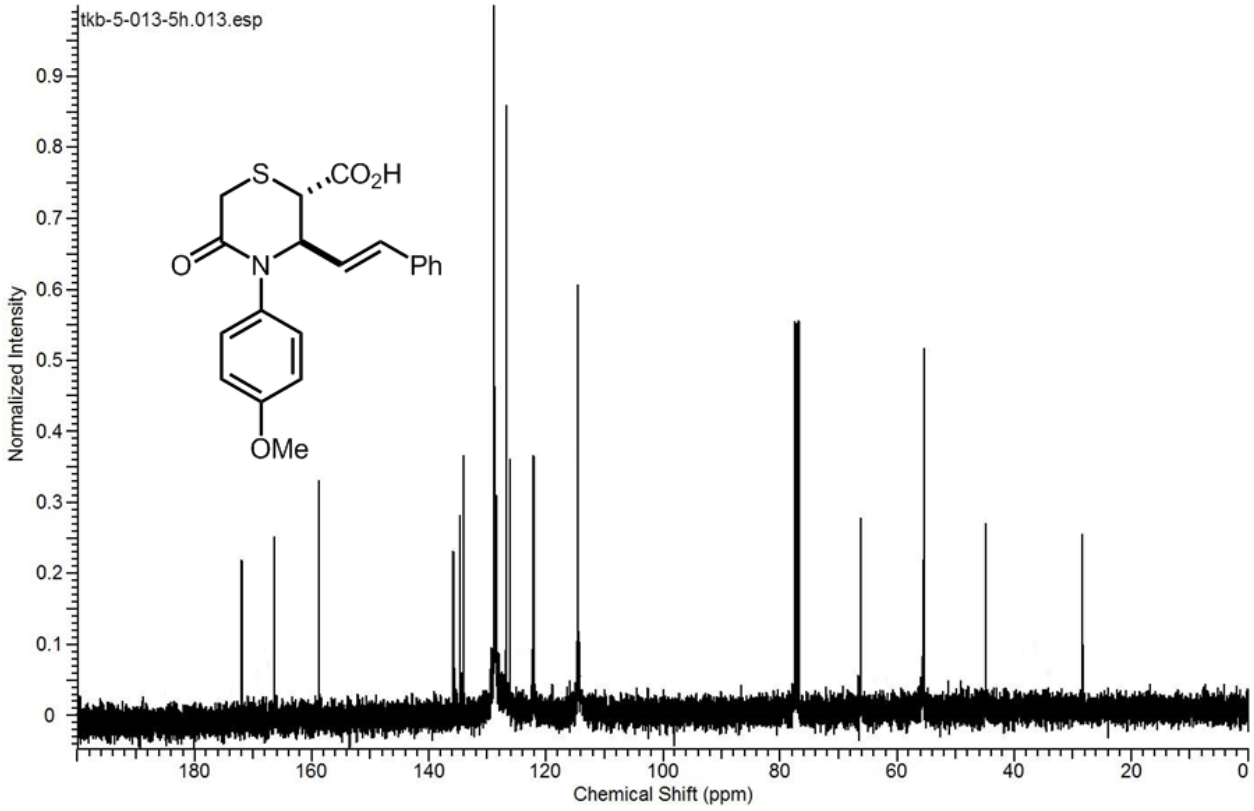


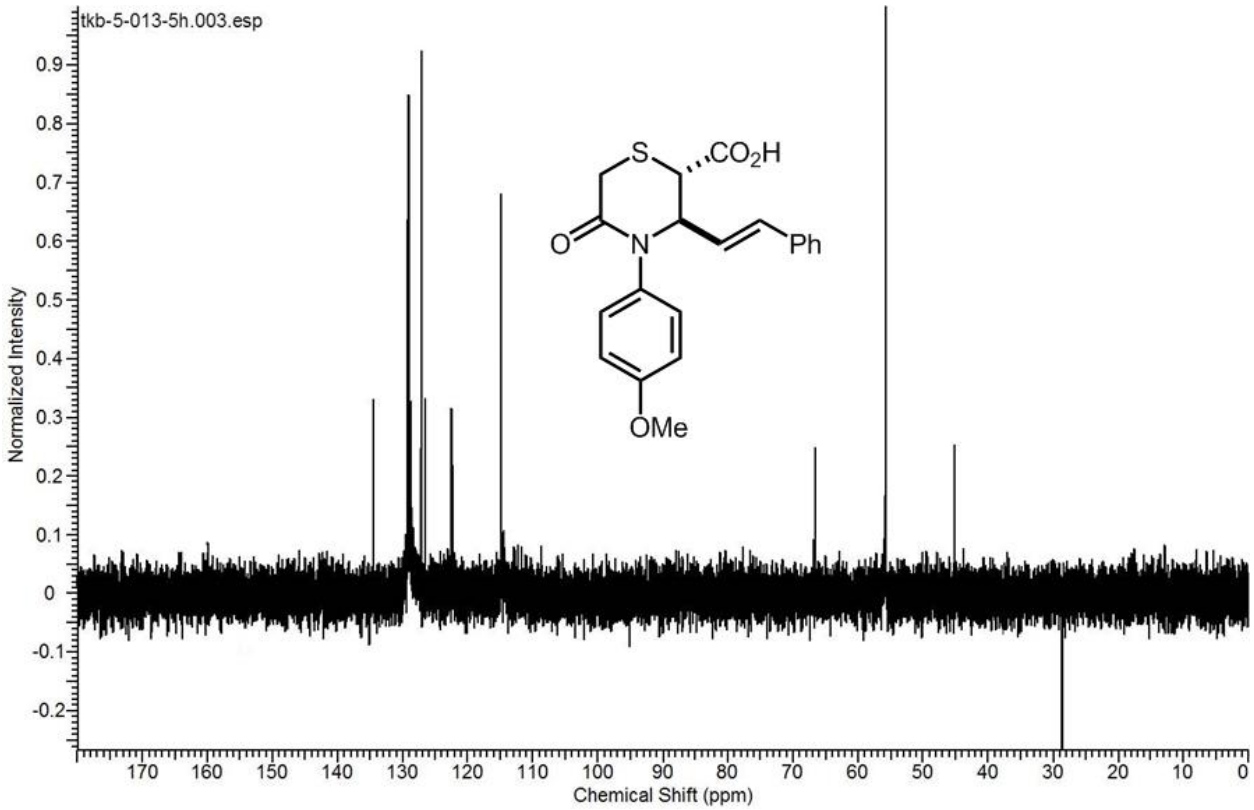
6c1

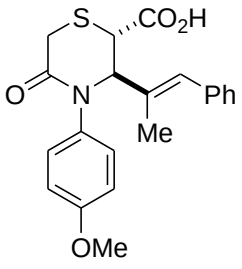
Prepared from imine **4b** (237 mg, 1.0 mmol) and thiodiglycolic anhydride (132 mg, 1.0 equiv), using General Procedure B. T = 60 ^{o}C, time = 12 h. An analytical sample was obtained after a series of washes with cold petroleum ether. Yield = 258 mg, 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.96 (1H, br. S), 7.52 to 7.09 (7H, m), 6.91 to 6.79 (2H, d), 6.58 to 6.32 (2H, m), 4.85 to 4.83 (1H, dd), 3.80 to 3.32 (6H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.19, 168.27, 158.78, 135.84, 134.61, 134.11, 130.75, 129.26, 128.06, 126.88, 122.31, 118.93, 66.58, 55.96, 44.84, 28.34.

HRMS-EI+ (*m/z*): calc'd for $C_{20}H_{19}NO_4S$ 369.1035; found 369.1039.


tkb-5-013-5h.001.esp
Normalized Intensity
Chemical Shift (ppm)
S
CO2H
O
N
Ph
OMe

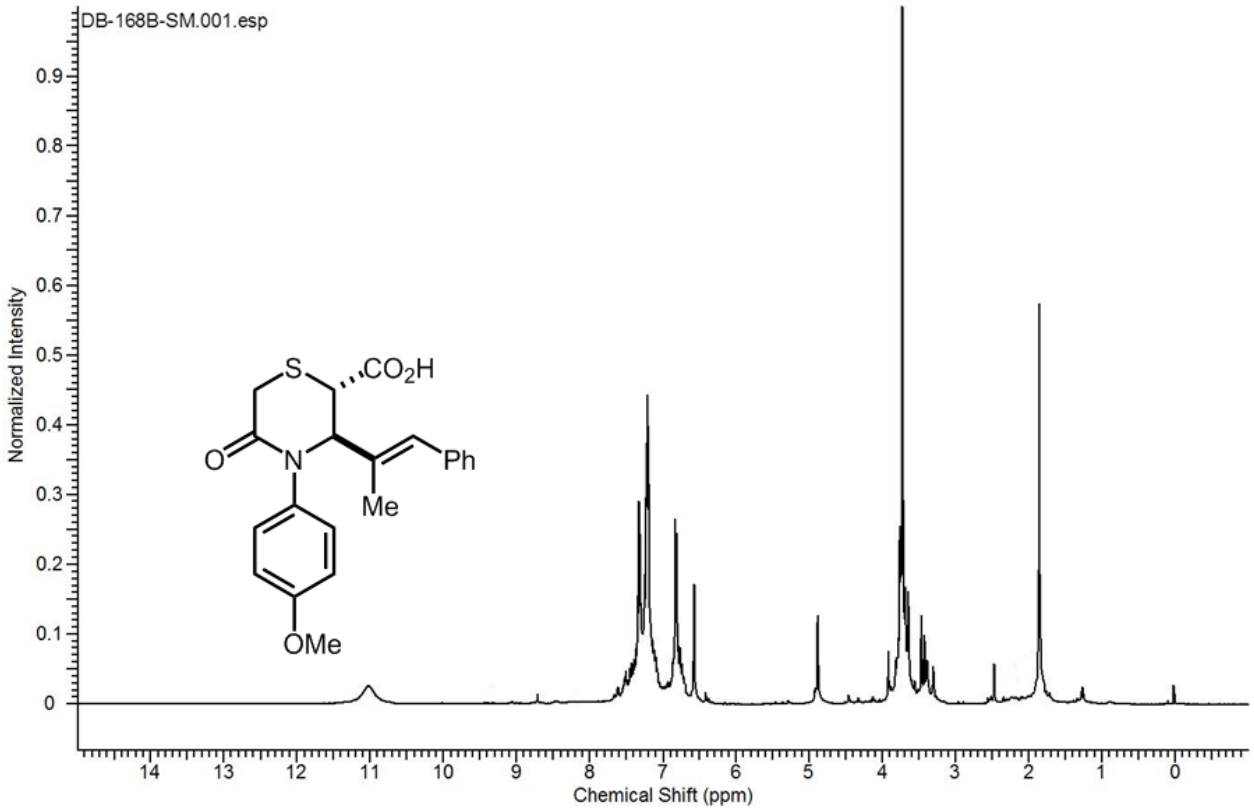

tkb-5-013-5h.013.esp
Normalized Intensity
Chemical Shift (ppm)
S
CO2H
O
N
Ph
OMe

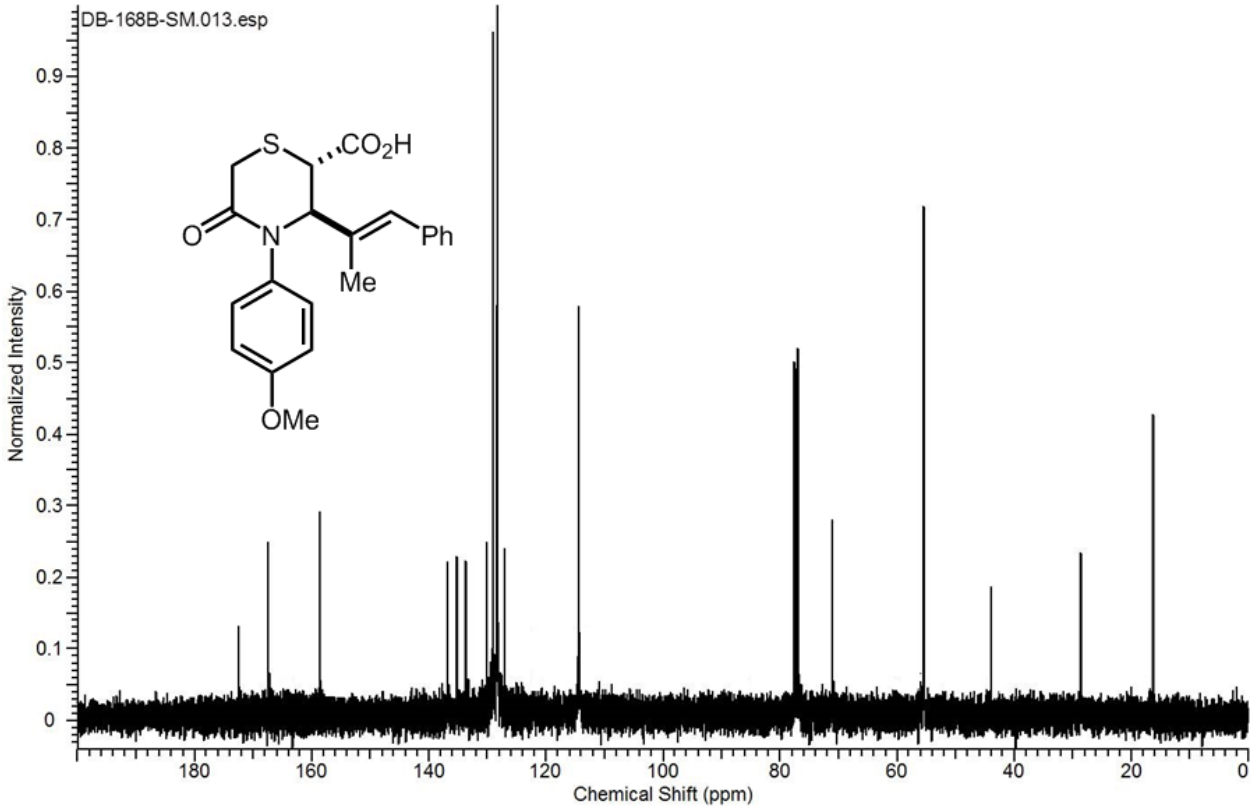


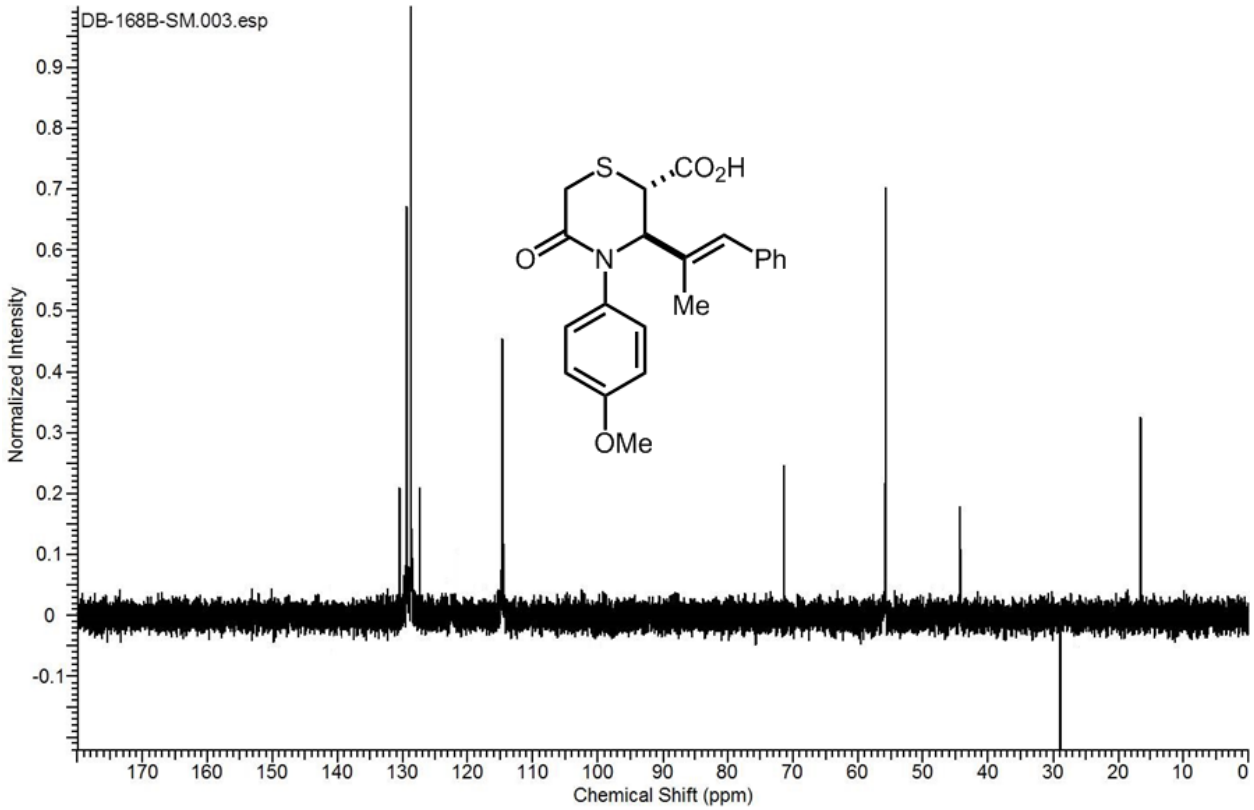


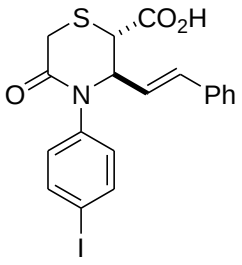
6d1

Prepared from imine **4i** (251 mg, 1.0 mmol) and thiodiglycolic anhydride (132 mg, 1.0 equiv) using General Procedure B. T = 60 ^{o}C, time = 12 h. Yield = 280 mg, 73%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.02 (1H, s br), 7.55 to 7.08 (5H, m), 6.95 to 6.81 (2H, d), 6.41 (1H, s), 4.89 (1H, d), 3.85 to 3.30 (6H, m), 1.86 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.48, 167.36, 158.59, 136.78, 135.18, 133.62, 130.15, 129.38, 129.02, 128.75, 127.09, 118.12, 71.05, 55.45, 43.98, 28.66, 18.23. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{21}H_{21}NO_4S$ 383.1191; found 383.1187.


DB-168B-SM.001.esp
Normalized Intensity
Chemical Shift (ppm)
S
CO2H
O
N
Ph
Me
OMe

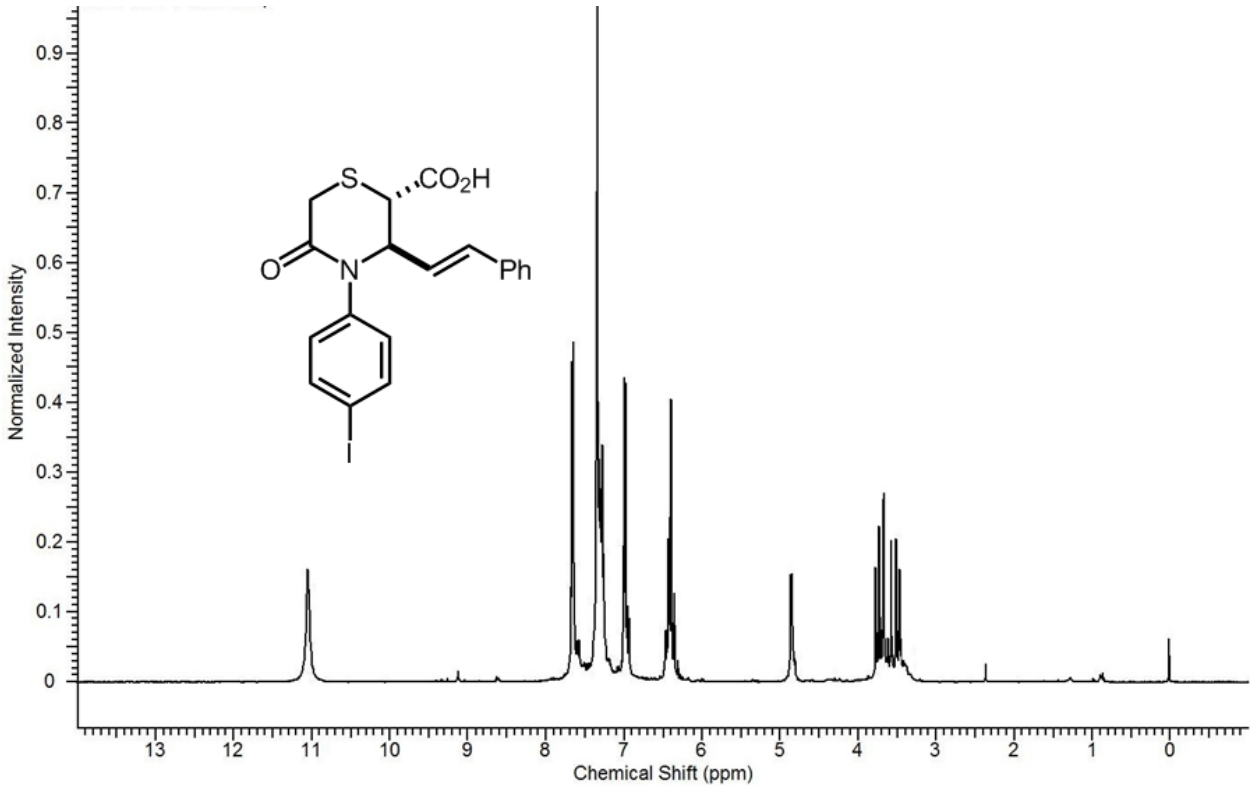

DB-168B-SM.013.esp
Normalized Intensity
Chemical Shift (ppm)
S
CO2H
O
N
Ph
Me
OMe

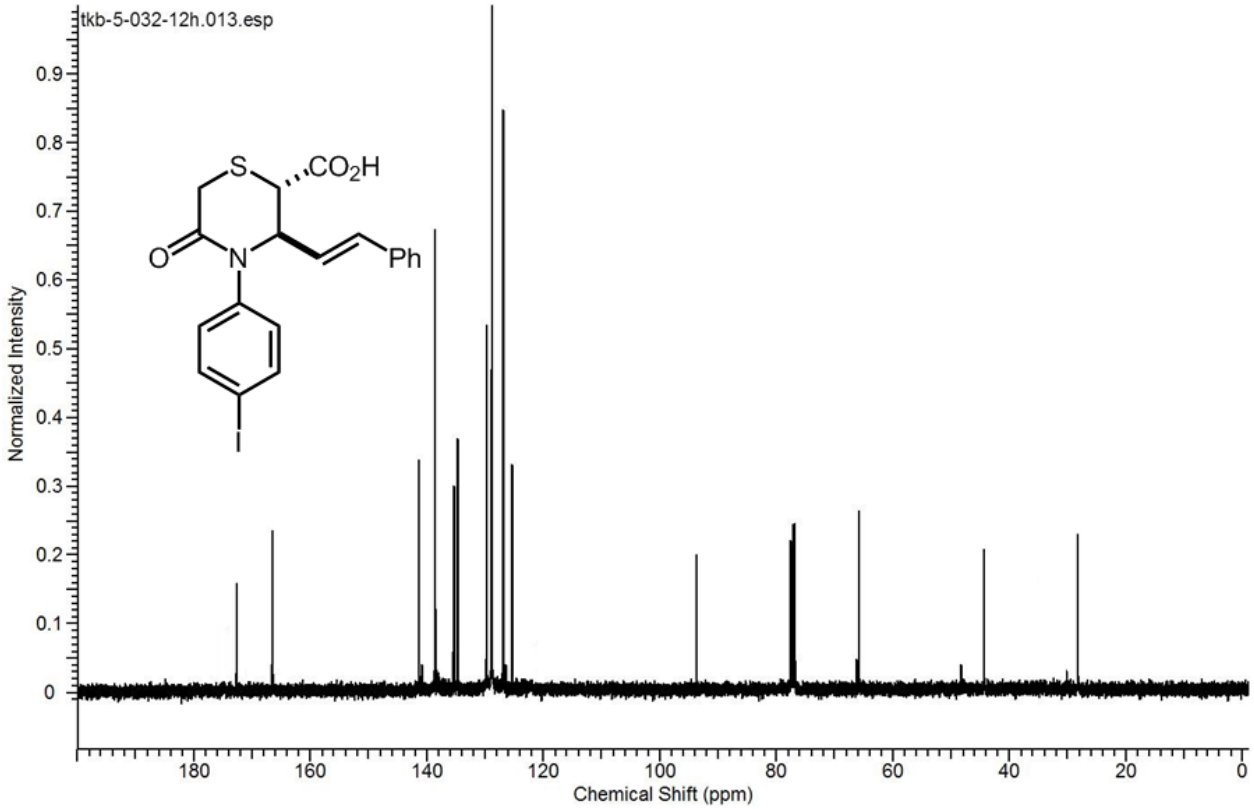


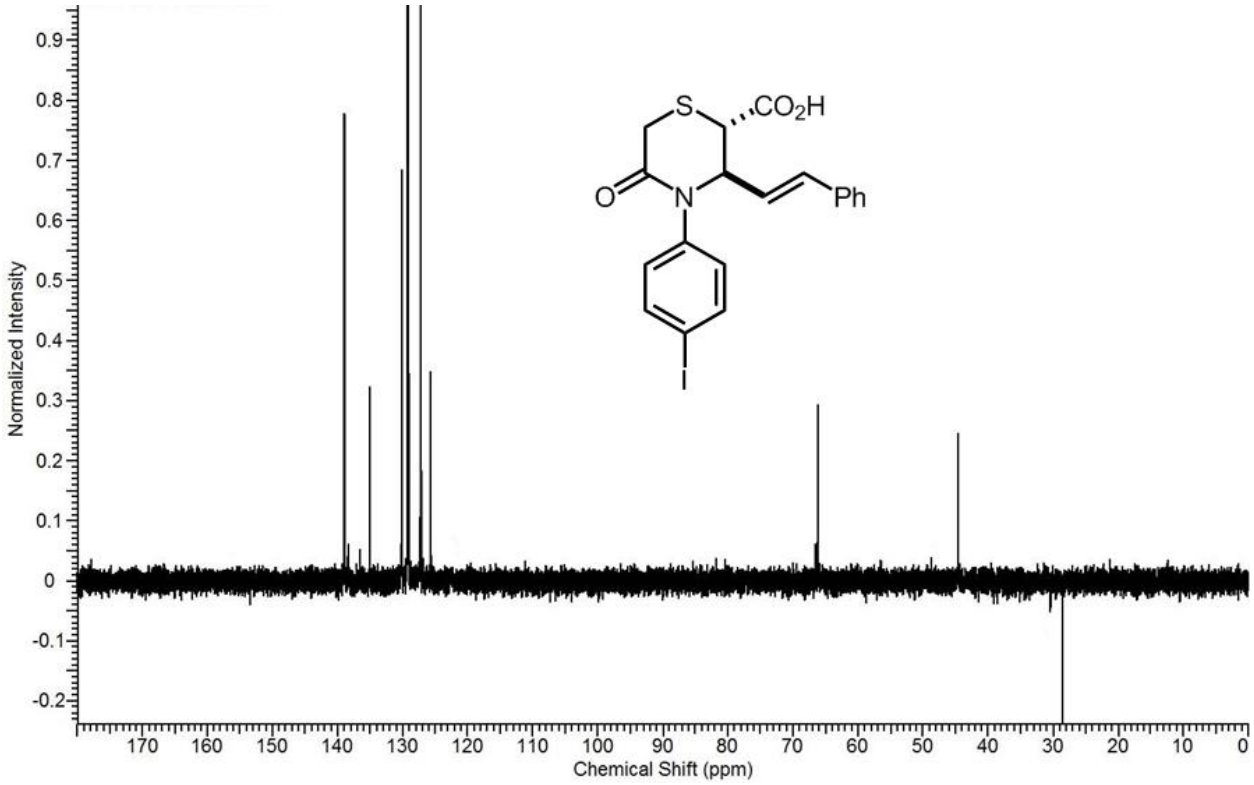


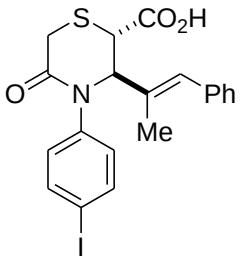
6e1

Prepared from thiodiglycolic anhydride (132 mg, 1.0 equiv) using General Procedure B. T = 60 ^{o}C, time = 16 h. Yield = 363 mg, 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.05 (1H, s br), 7.66 to 7.57 (2H, d), 7.38 to 7.19 (5H, m), 6.95 (2H, d), 6.46 to 6.39 (2H, m), 4.86 to 4.81 (1H, dd), 3.73 to 3.36 (3H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.84, 168.17, 141.39, 138.6, 137.99, 136.24, 134.74, 129.78, 128.78, 126.90, 125.35, 93.71, 66.28, 44.34, 28.27. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{19}H_{16}INO_3S$ 464.9896; found 465.0007.


Normalized Intensity
Chemical Shift (ppm)
S
CO2H
O
N
Ph
I

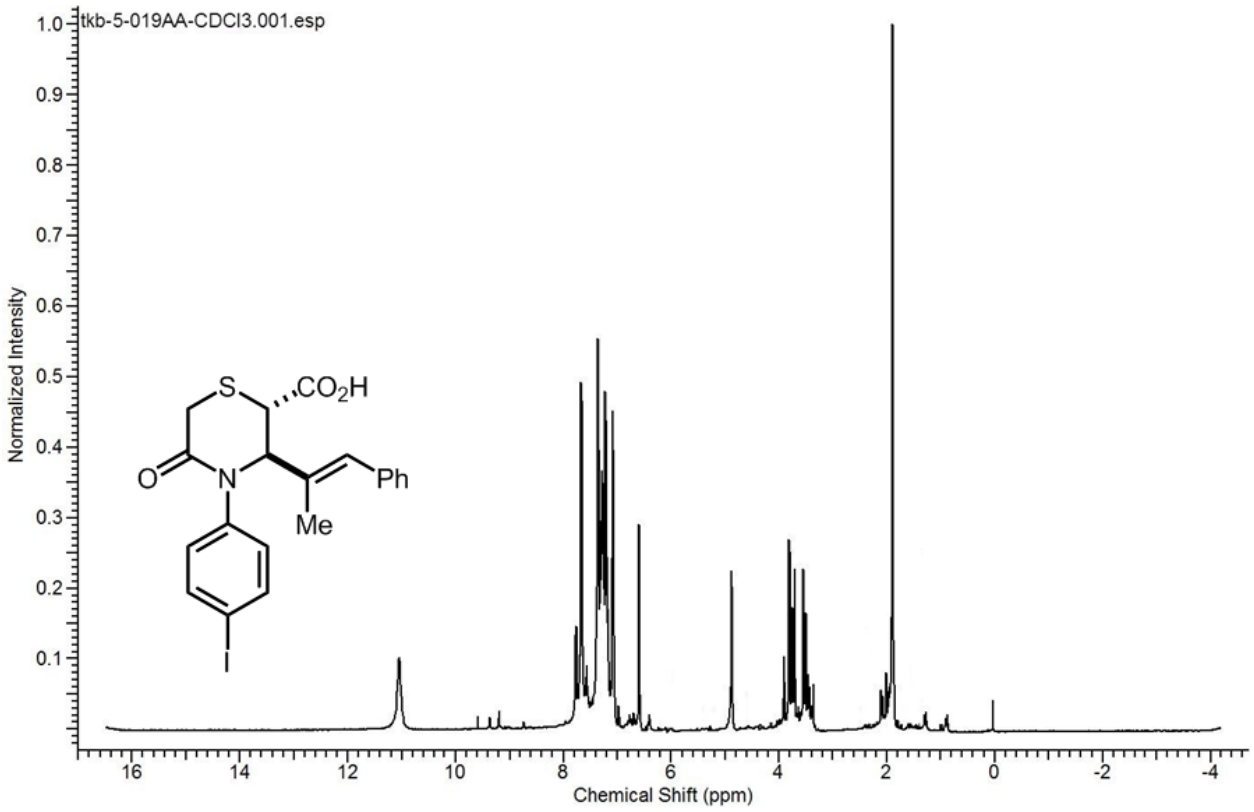

tkb-5-032-12h.013.esp
Normalized Intensity
Chemical Shift (ppm)
S
CO2H
O
N
Ph
I





6f1

Prepared from thiodiglycolic anhydride (132 mg, 1.0 equiv) using General Procedure B. T = 60 ^{o}C, time = 22 h. Yield = 407 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.04 (1H, s br), 7.81 to 7.03 (9H, m), 6.59 (1H, s), 4.88 (1H, d), 3.83 to 3.36 (3H, m), 1.87 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.93, 167.29, 141.96, 139.91, 138.46, 132.90, 130.73, 129.19, 128.45, 128.03, 127.41, 93.28, 70.43, 43.23, 28.53, 18.53. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{20}H_{18}INO_3S$ 479.0052; found 479.0061.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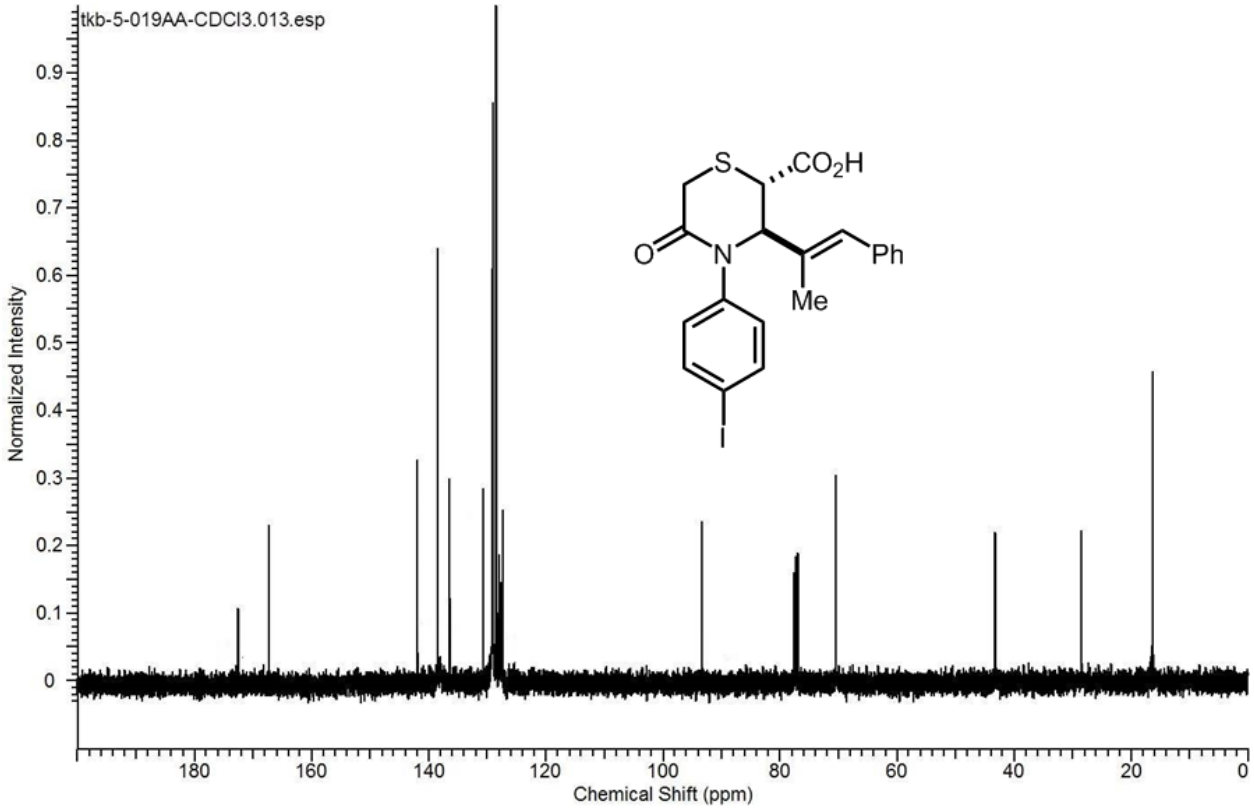
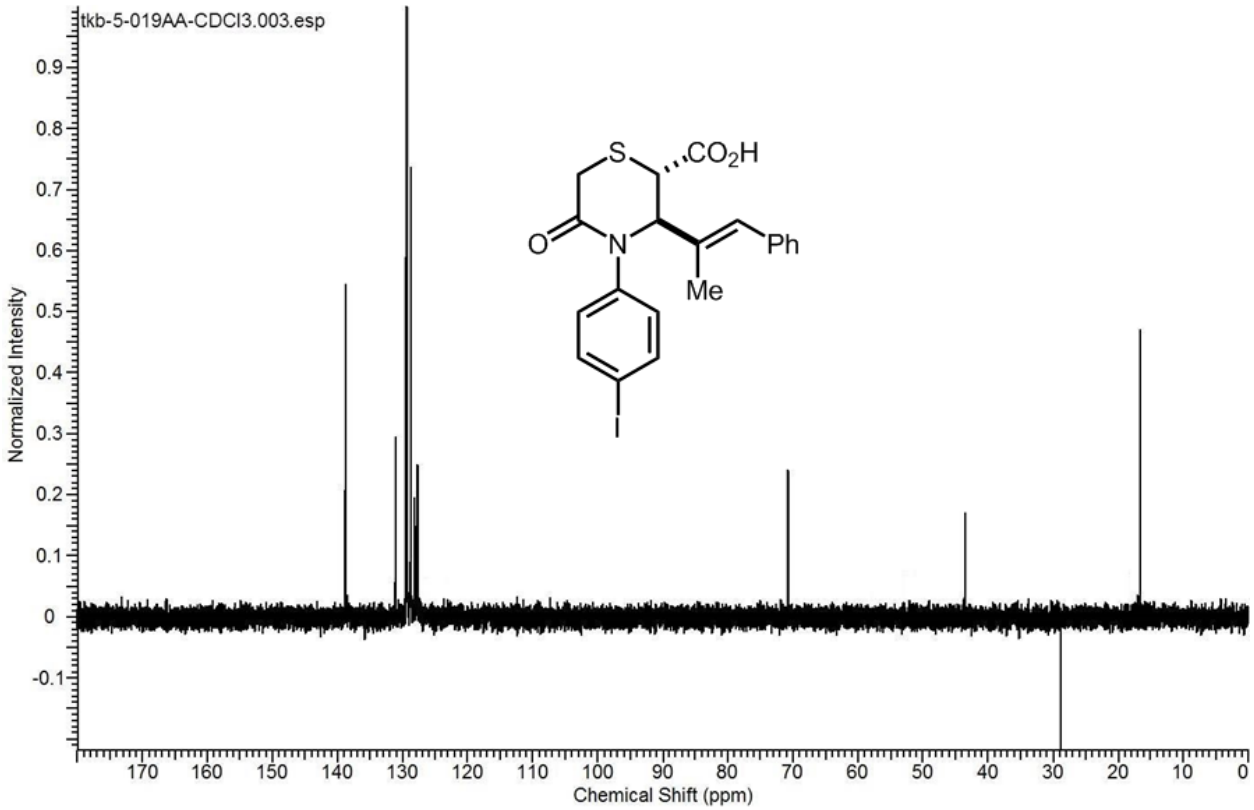
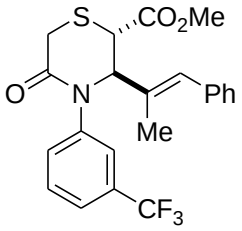
Normalized Intensity
Chemical Shift (ppm)
S
CO2H
O
N
Ph
Me
I

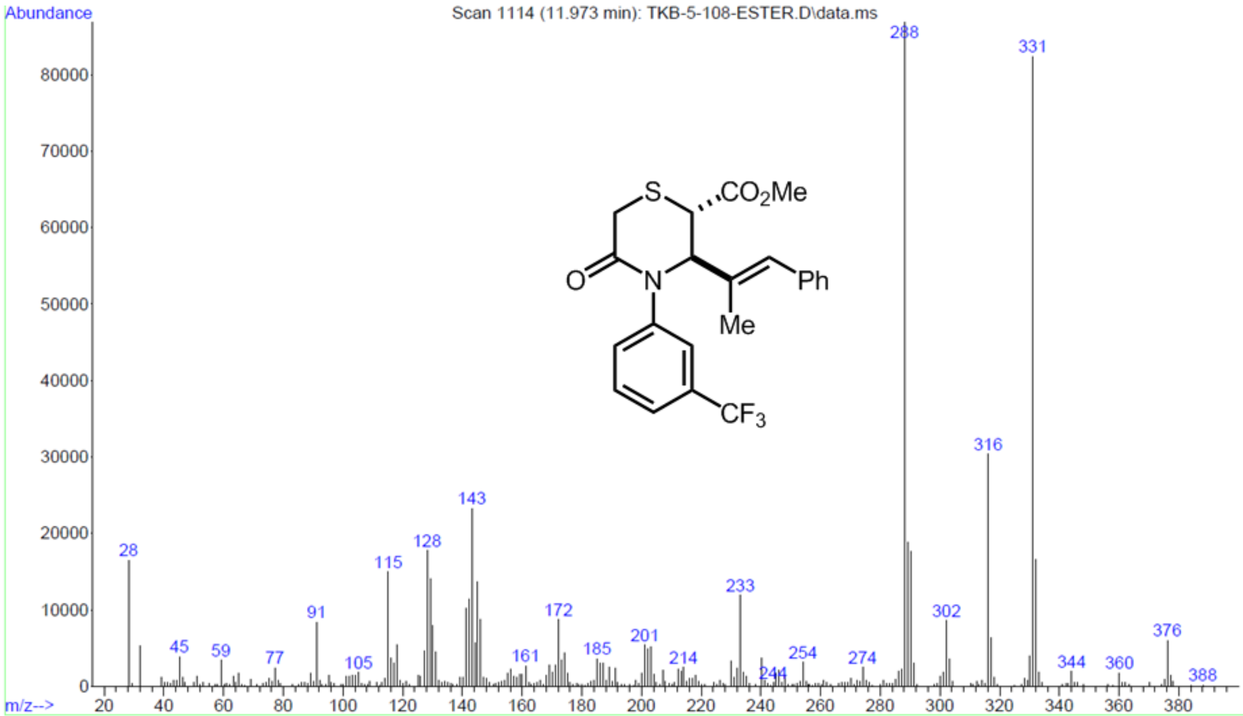

tkb-5-019AA-CDCl3.013.esp
Normalized Intensity
Chemical Shift (ppm)
S
CO2H
O
N
Ph
Me
I

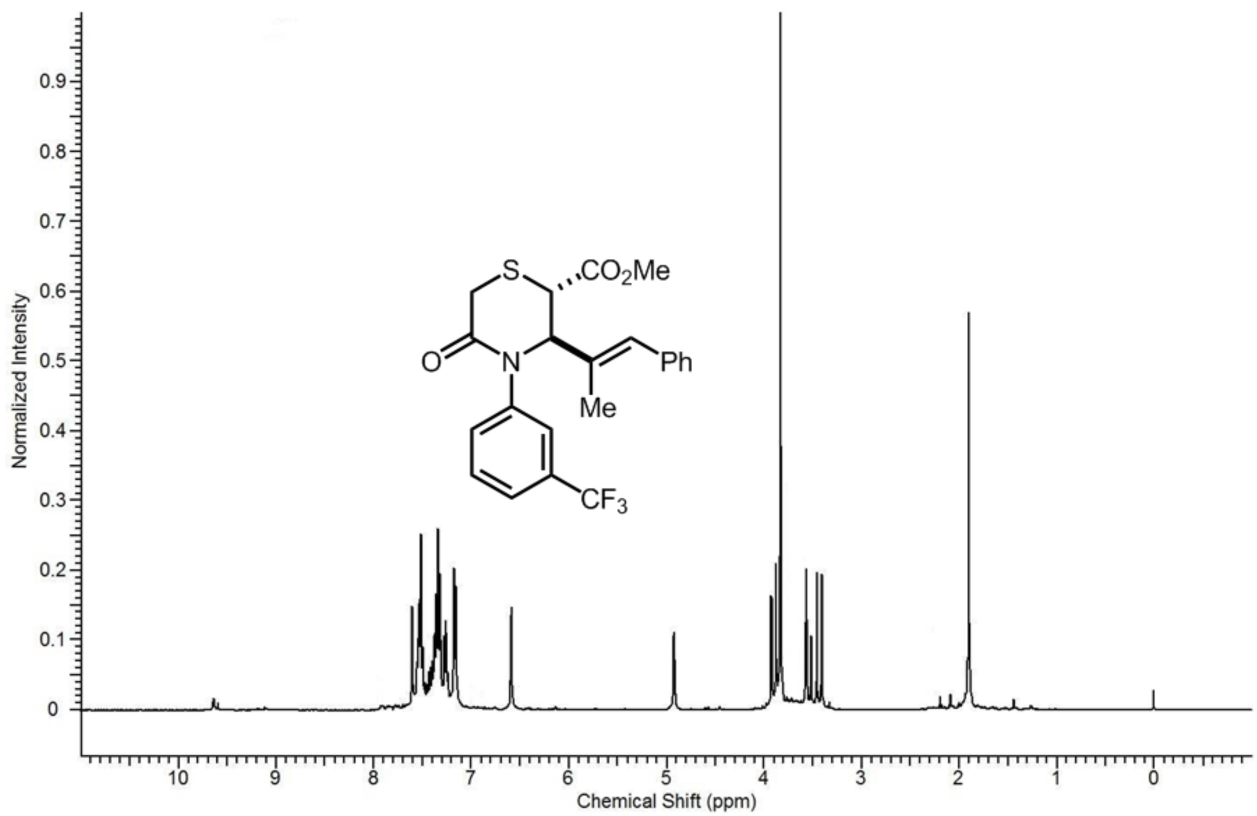


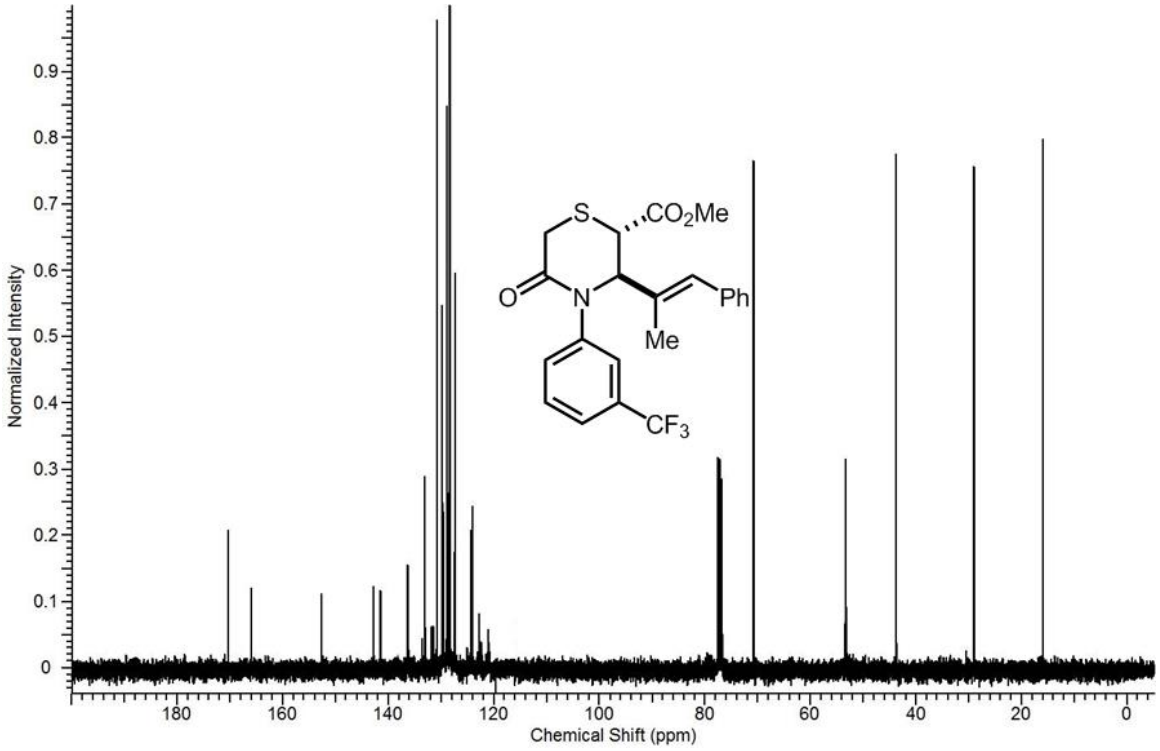


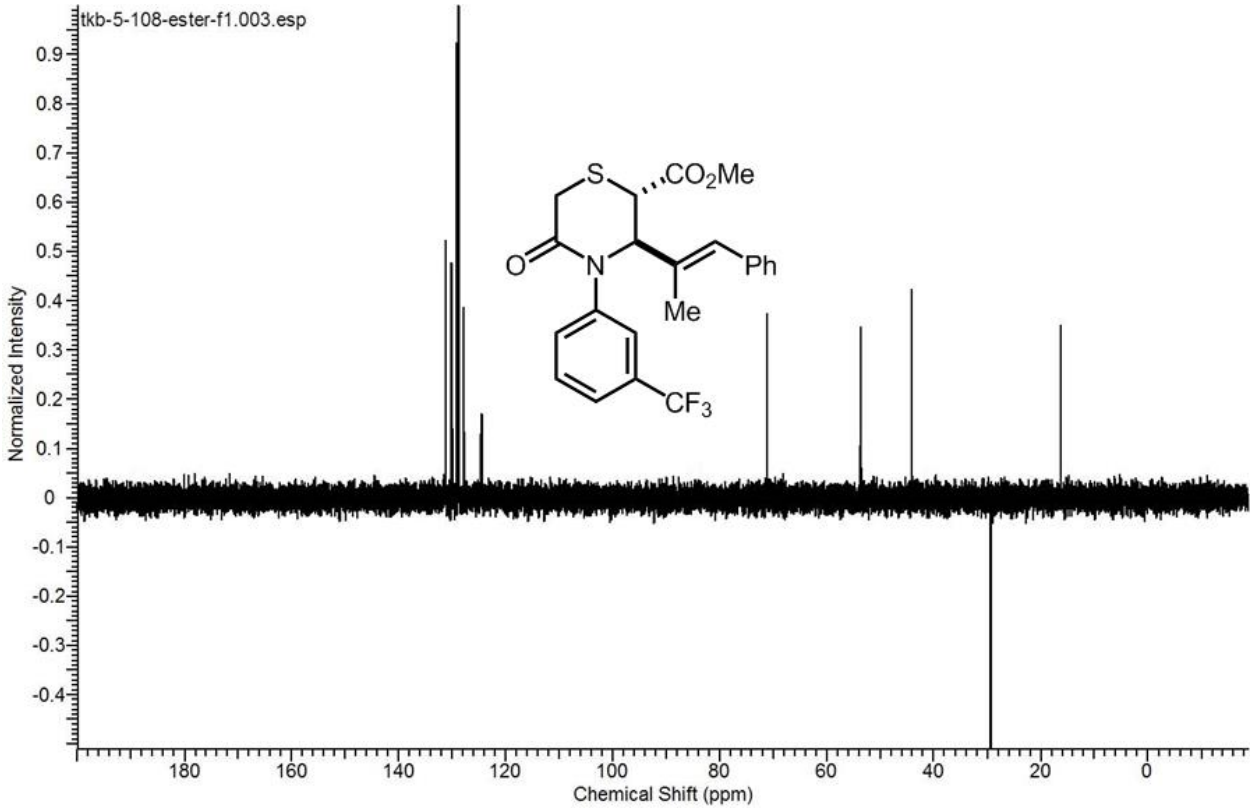
6g2

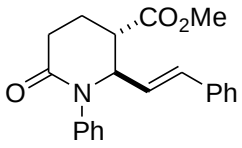
Prepared from thiodiglycolic anhydride (132 mg, 1.0 equiv) using General Procedures B & C. T = 60 ^{o}C, time = 22 h. Yield = 387 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 to 7.18 (9H, m), 6.62 (1H, s), 4.93 (1H, d), 3.93 to 3.87 (4H, m), 3.57 to 3.39 (2H, m), 1.96 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.37, 165.93, 152.71, 142.86, 141.45, 136.25, 133.03, 131.15, 130.83, 129.73, 129.70, 129.54, 128.52, 128.32, 127.40, 124.35, 124.31, 124.06, 122.78, 70.83, 53.38, 43.75, 29.05, 18.18. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{23}H_{20}F_3NO_3S$ 435.1116; found 435.1121.


Abundance
Scan 1114 (11.973 min): TKB-5-108-ESTER.D\data.ms
m/z-->
288
331
316
143
128
115
28
233
172
302
376
91
201
185
161
254
274
214
45
59
77
105
244
344
360
388
CO2Me
S
N
O
Ph
Me
CF3


Normalized Intensity
Chemical Shift (ppm)
CO2Me
S
N
O
Ph
Me
CF3

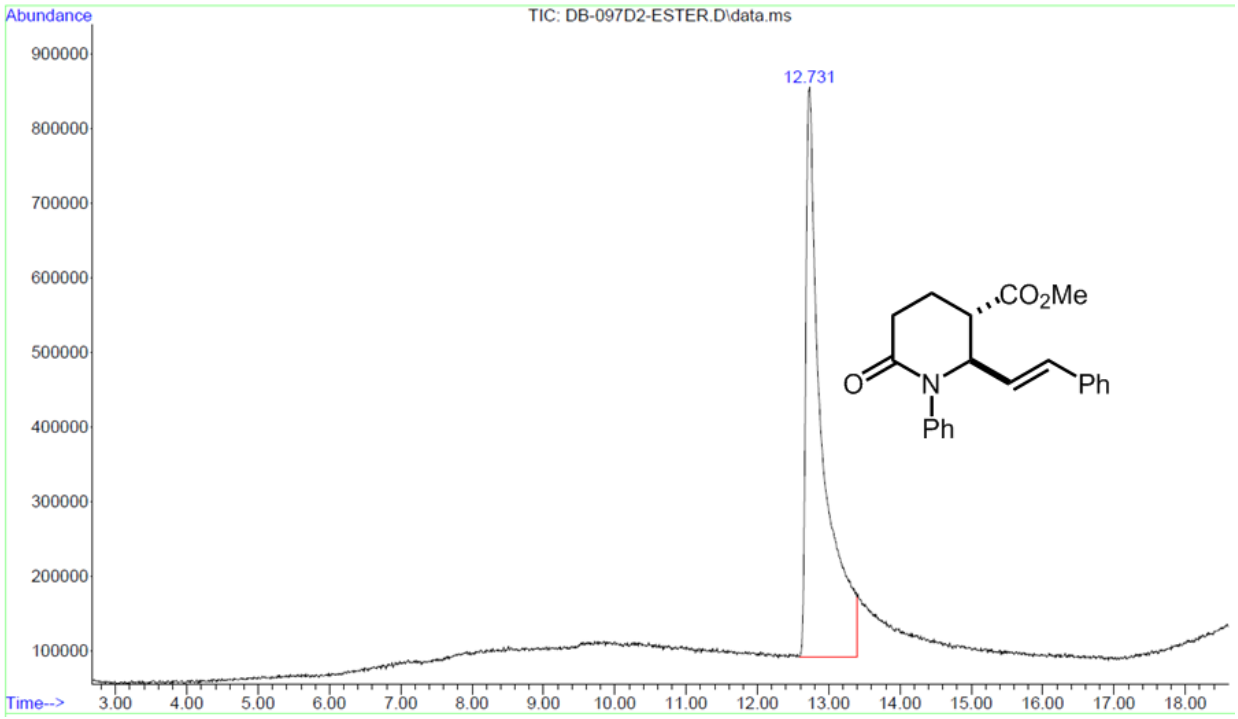

Normalized Intensity
Chemical Shift (ppm)
S
CO2Me
O
N
Ph
Me
CF3

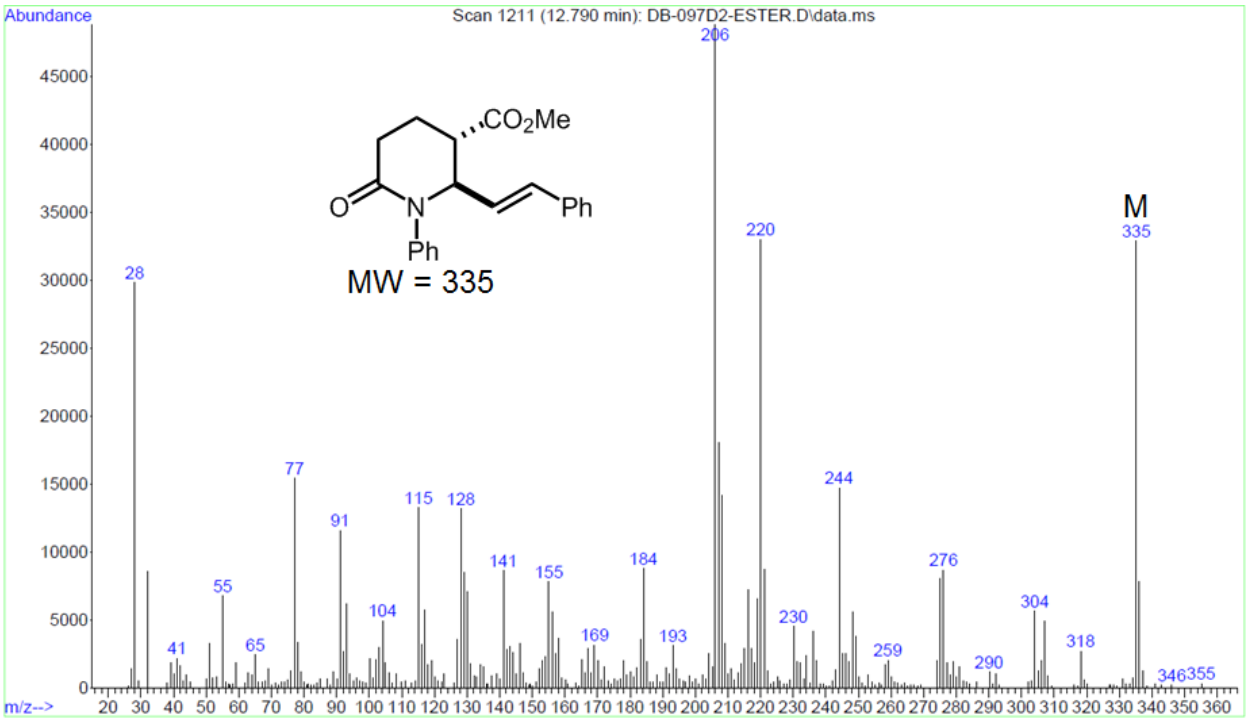

tkb-5-108-ester-f1.003.esp
Normalized Intensity
Chemical Shift (ppm)
S
CO2Me
O
N
Ph
Me
CF3



7a2

Prepared from imine **4a** and glutaric anhydride (114 mg, 1 equiv) using General Procedures B and C. Temp = 105 ^{o}C, time = 18 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100) then 100% MeOH. Yield = 268 mg, 80% over 2 steps, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 to 7.05 (10H, m), 6.39 (1H, d), 6.15 to 6.09 (1H, dd), 4.92 to 4.89 (1H, d), 3.79 (3H, s), 2.97 to 2.93 (1H, m), 2.73 to 2.61 (2H, m), 2.42 to 2.25 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 169.3, 141.9, 135.8, 134.8, 133.3, 129.1, 128.8, 128.2, 127.7, 127.3, 126.5, 124.4, 63.8, 52.5, 44.5, 29.9, 20.4. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{21}H_{21}NO_3$ 335.1521; found 335.1525.




Abundance
Scan 1211 (12.790 min): DB-097D2-ESTER.D\data.ms
206
220
M
335
28
77
91
115
128
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141
155
169
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193
230
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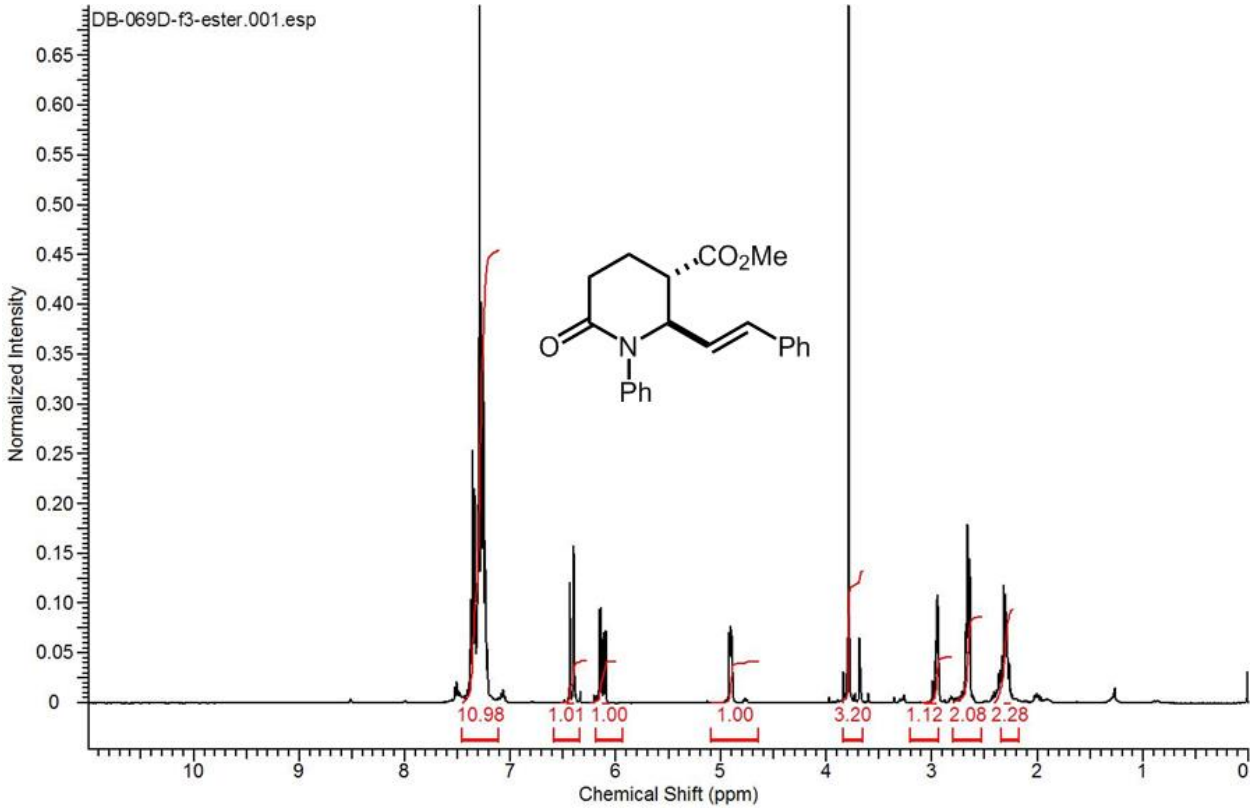
65
CO2Me
O
N
Ph
Ph
MW = 335
m/z-->


DB-069D-f3-ester.001.esp
Normalized Intensity
CO2Me
O
N
Ph
Ph
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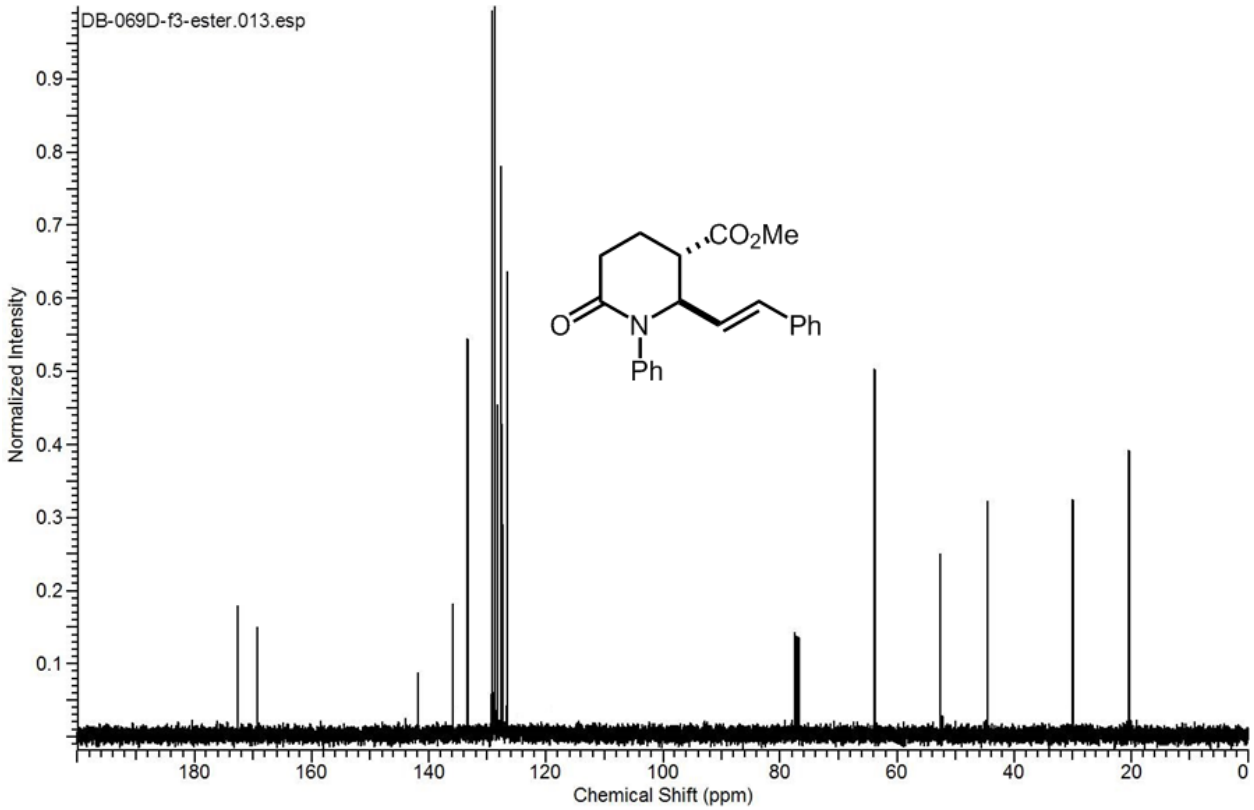
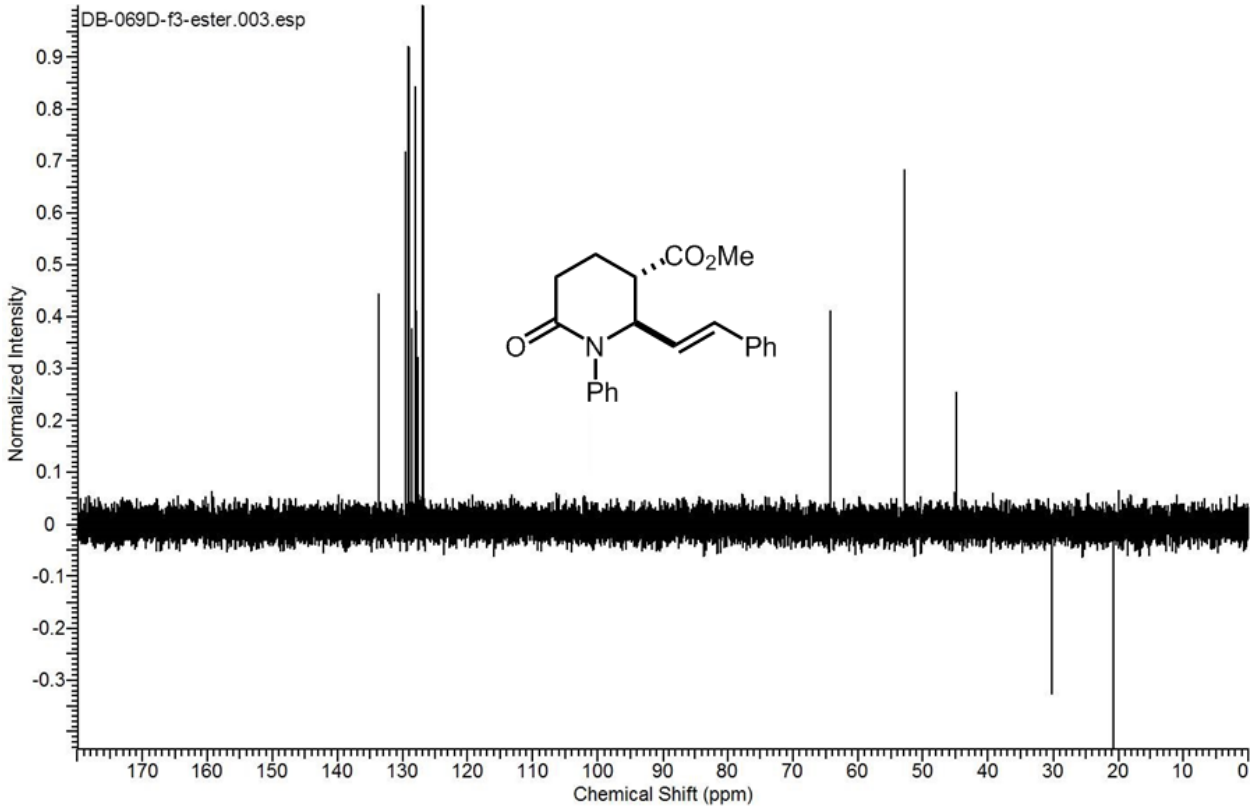
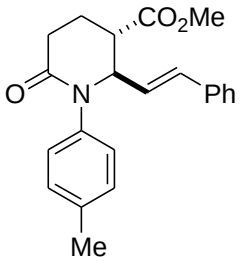
1.01
1.00
1.00
3.20
1.12
2.08
2.28
Chemical Shift (ppm)

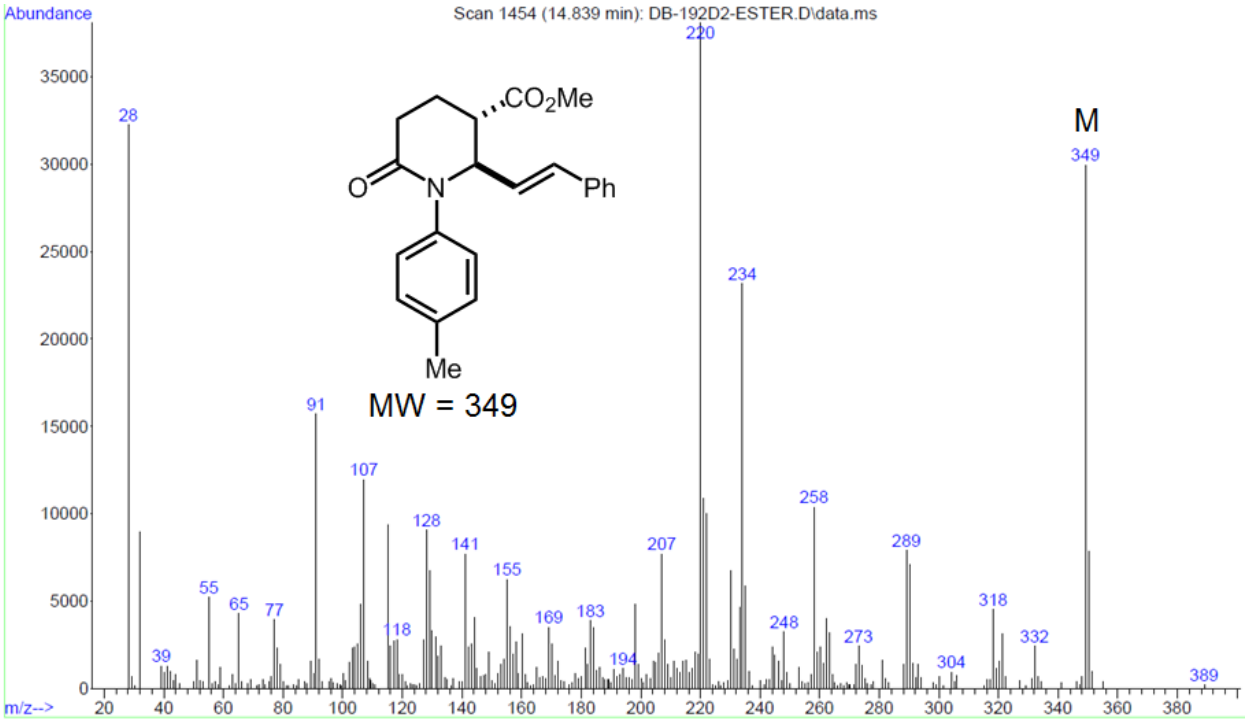

DB-069D-f3-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
O
N
Ph
Ph

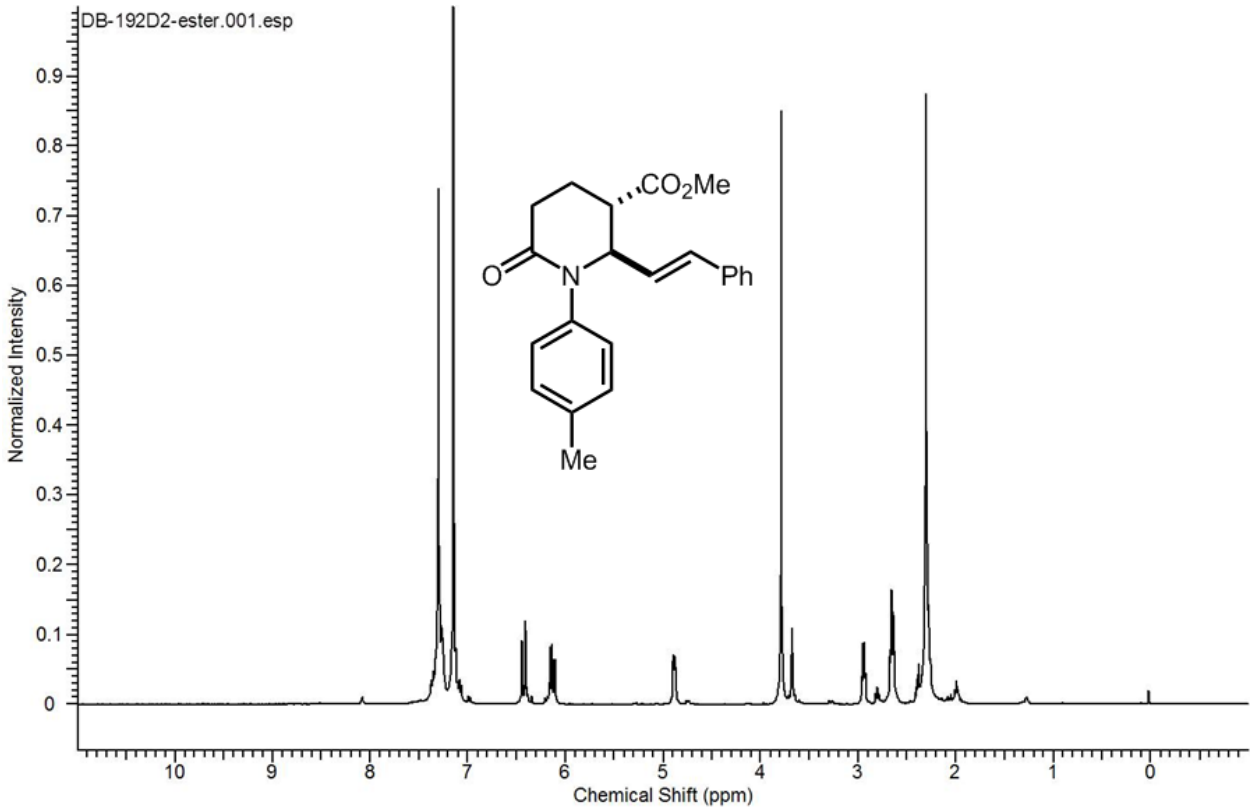

DB-069D-f3-ester.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
O
N
Ph
Ph

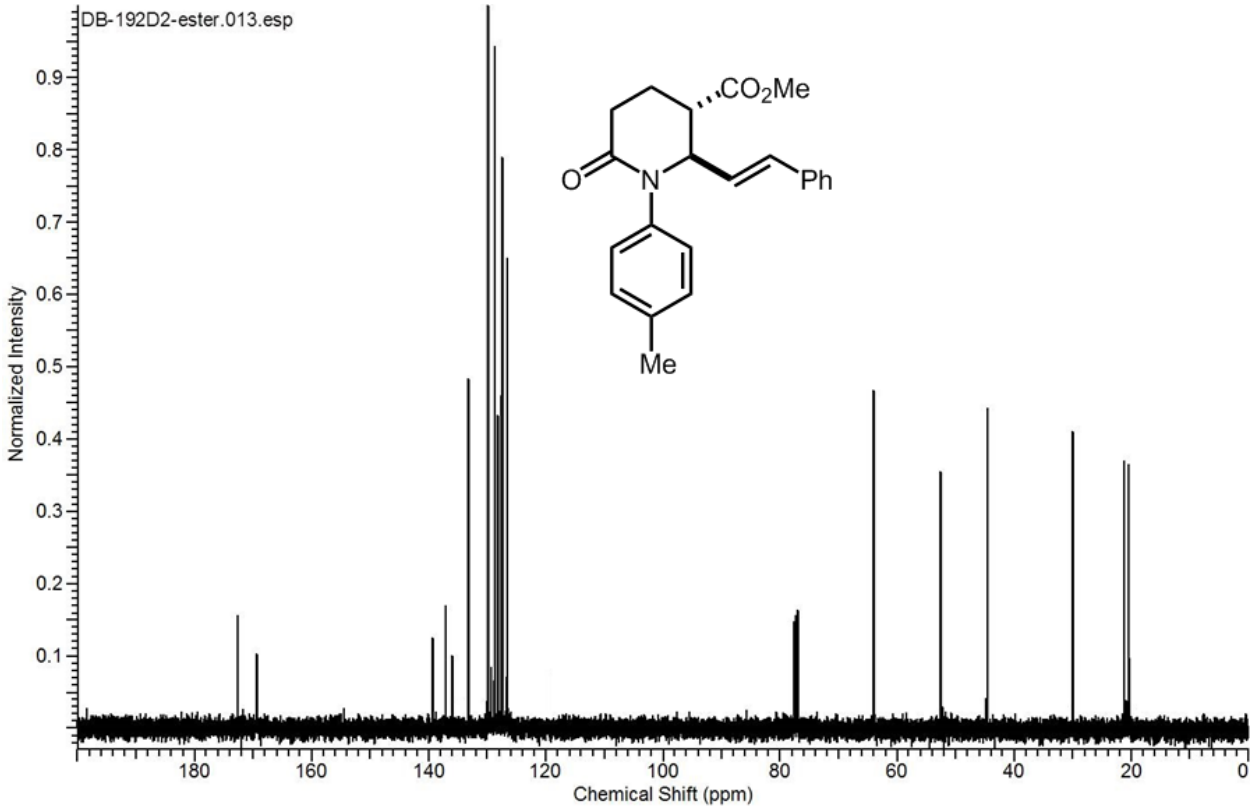


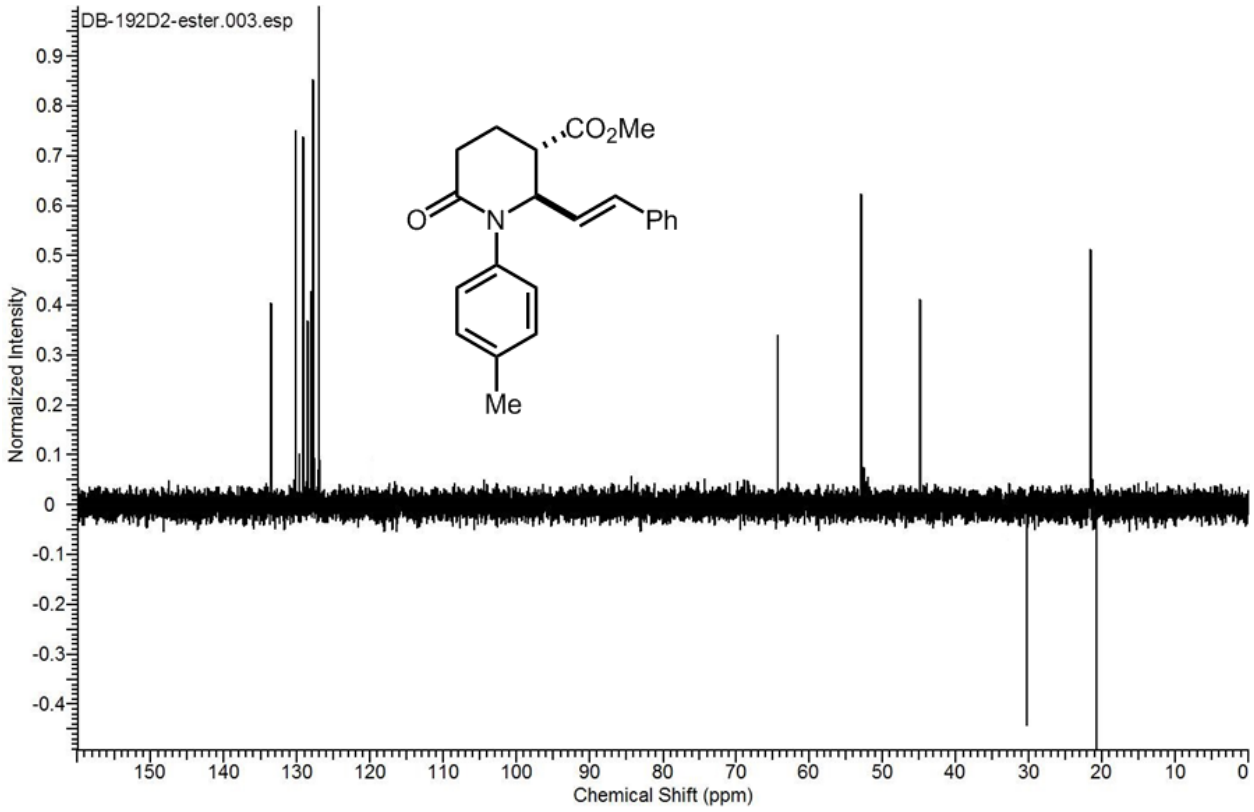
7b2

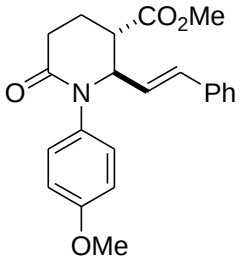
Prepared from imine **4c** (221 mg, 1.0 mmol) and glutaric anhydride (114 mg, 1.0 equiv), using General Procedures B and C. T = 105 ^{o}C, time = 18 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100) then 100% MeOH. Yield = 304 mg, 87% over 2 steps, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 to 7.00 (9H, m), 6.41 to 6.34 (1H, d), 6.18 to 6.10 (1H, dd), 4.90 to 4.87 (1H, dd), 3.77 (3H, s), 2.96 to 2.93 (1H, m), 2.70 to 2.61 (2H, m), 2.41 to 2.28 (5H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 169.4, 139.3, 137.0, 135.9, 134.8, 133.2, 130.0, 129.8, 129.3, 128.7, 128.3, 128.2, 128.1, 127.7, 127.47, 127.3, 126.7, 126.6, 124.5, 63.9, 52.5, 44.5, 29.9, 21.1, 20.8. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{22}H_{23}NO_3$ 349.1678; found 349.1672.




DB-192D2-ester.001.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
N
O
Me

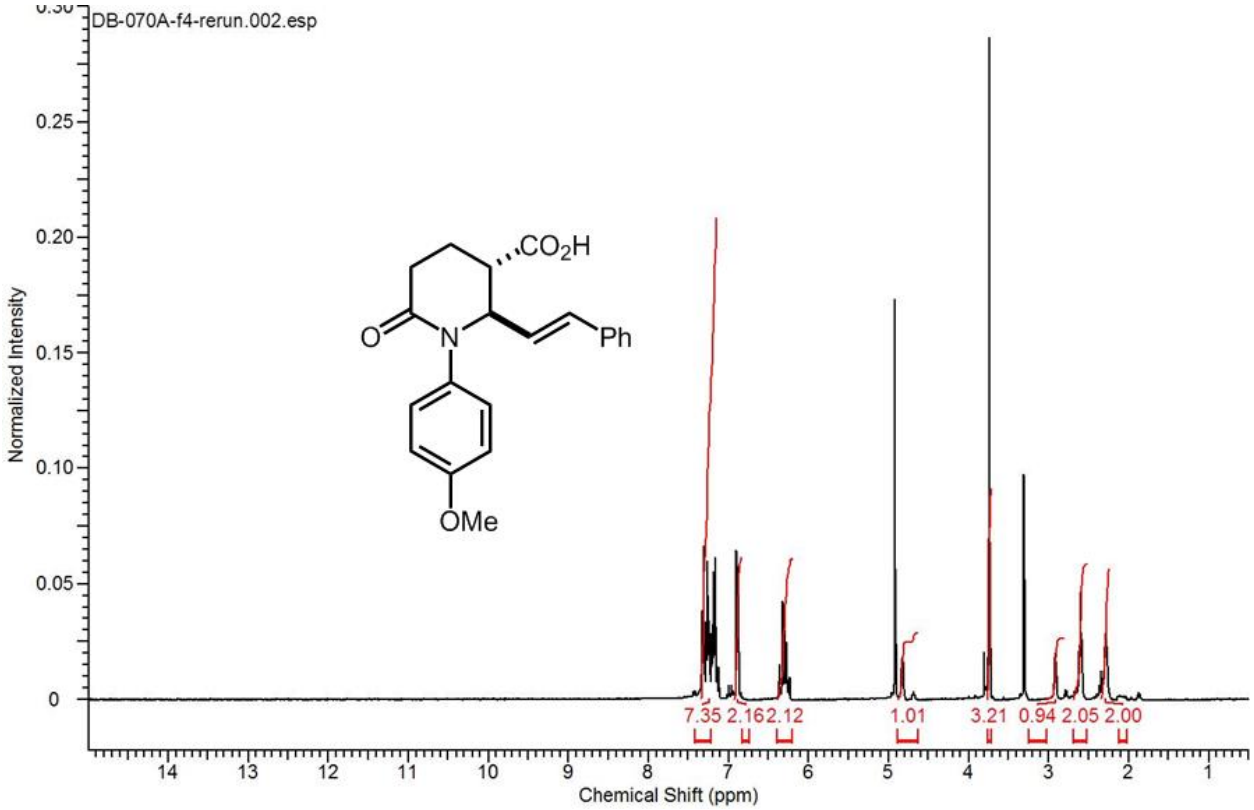

DB-192D2-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
N
O
Me





7c2

Prepared from imine **4b** (237 mg, 1.0 mmol) and glutaric anhydride (114 mg, 1.0 equiv), using General Procedures B and C. T = 105 ^{o}C, time = 18 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100) then 100% MeOH. Yield = 307 mg, 84% over 2 steps, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 to 7.15 (7H, m), 6.87 (2H, d), 6.38 to 6.31 (1H, d), 6.13 to 6.09 (1H, dd), 4.69 to 4.67 (1H, dd), 3.77 to 3.72 (6H, ss), 2.89 to 2.72 (1H, t), 2.65 to 2.56 (2H, m), 2.39 to 2.23 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 169.5, 158.4, 135.9, 134.9, 134.7, 133.2, 129.3, 128.8, 128.7, 128.7, 128.3, 128.2, 127.6, 126.7, 126.6, 124.5, 114.4, 64.1, 55.4, 52.4, 44.4, 29.9, 20.2. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{22}H_{23}NO_4$ 365.1627; found 365.1633.


DB-070A-f4-rerun.002.esp
Normalized Intensity
Chemical Shift (ppm)
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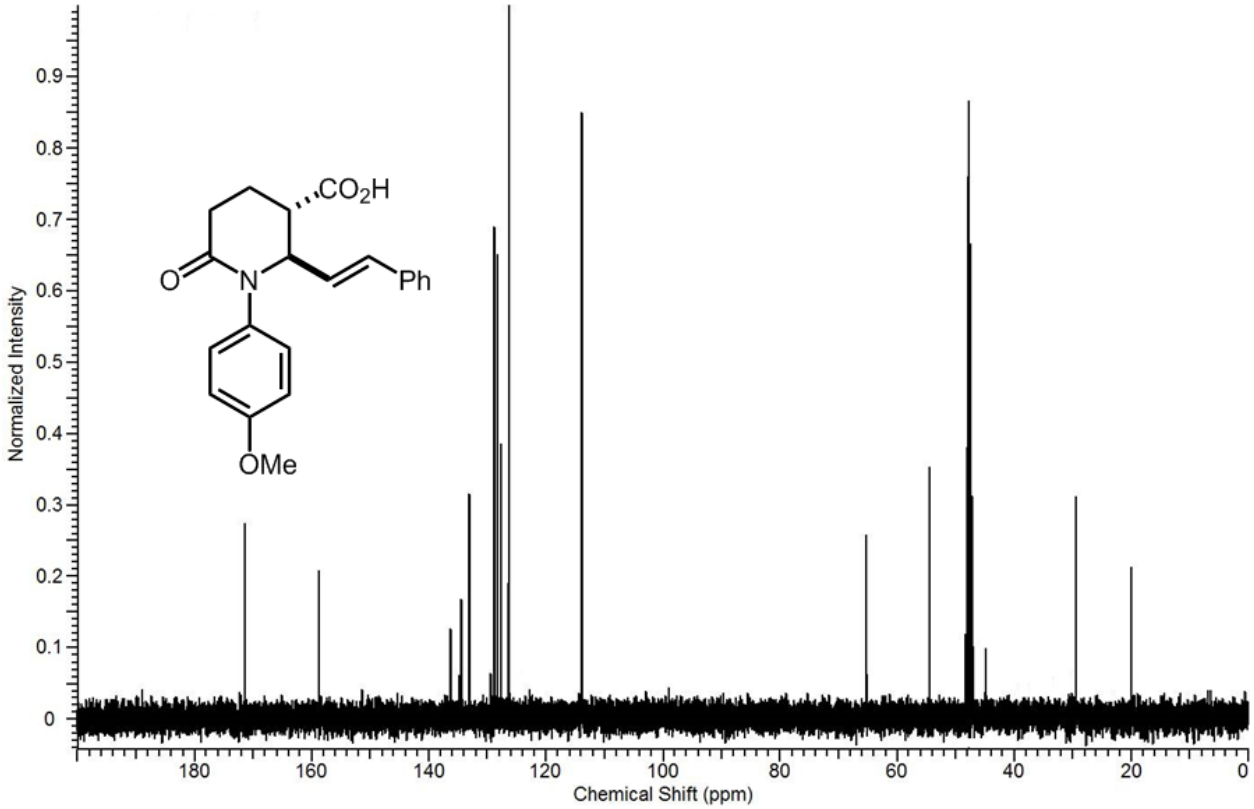
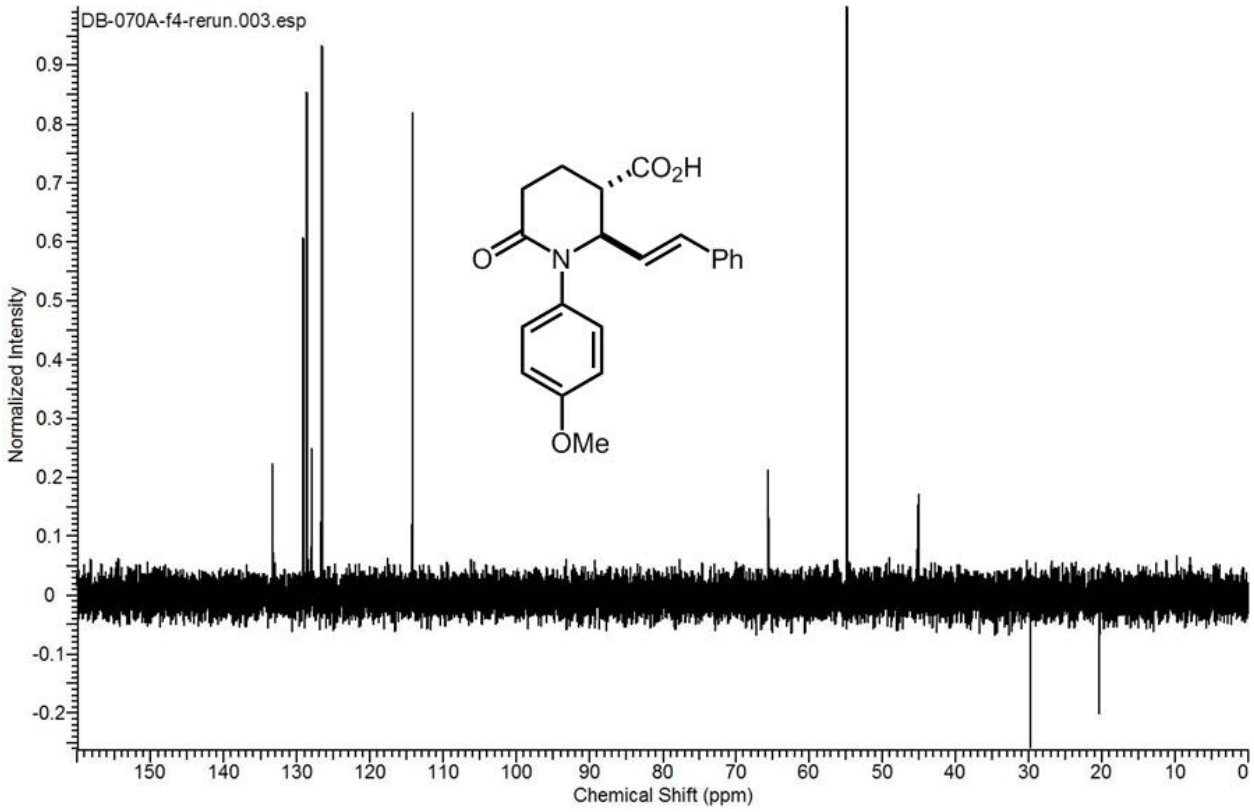
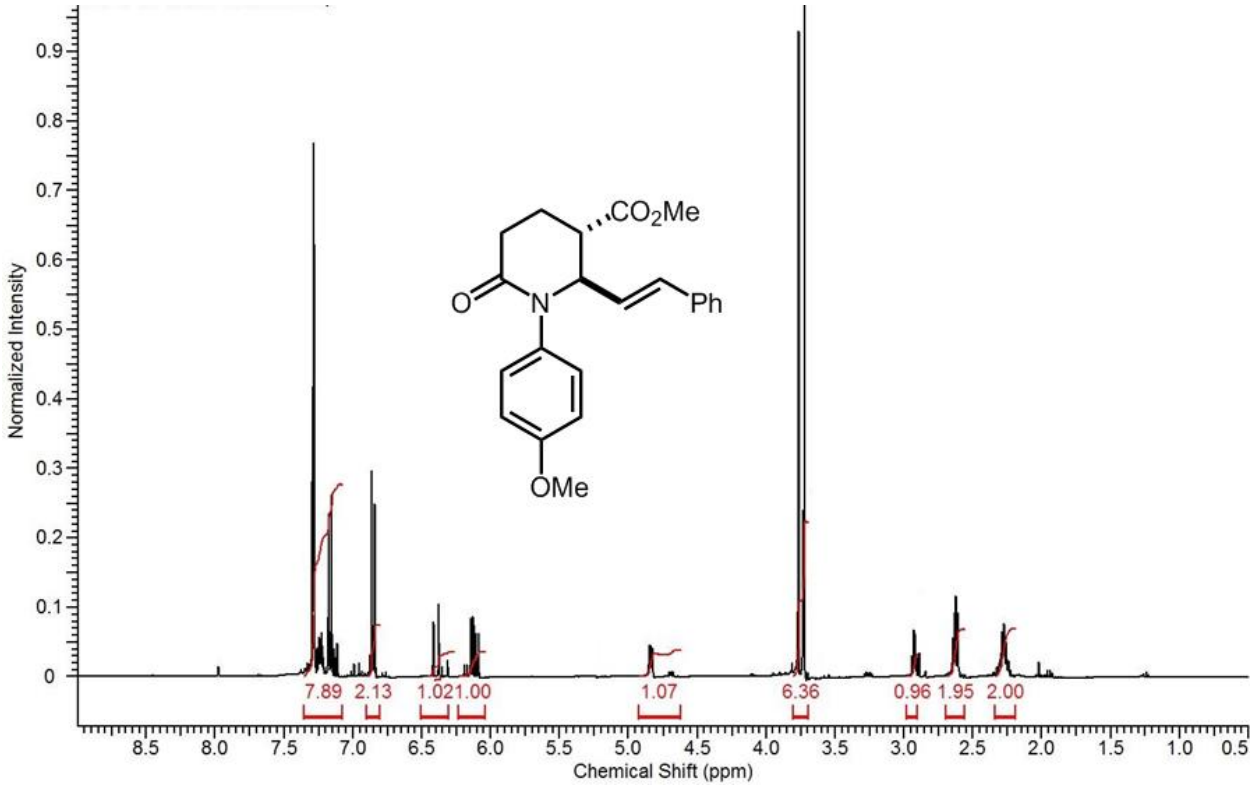
CO2H
Ph
OMe


Normalized Intensity
Chemical Shift (ppm)
CO2H
Ph
OMe


DB-070A-f4-rerun.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
Ph
OMe


Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
OMe
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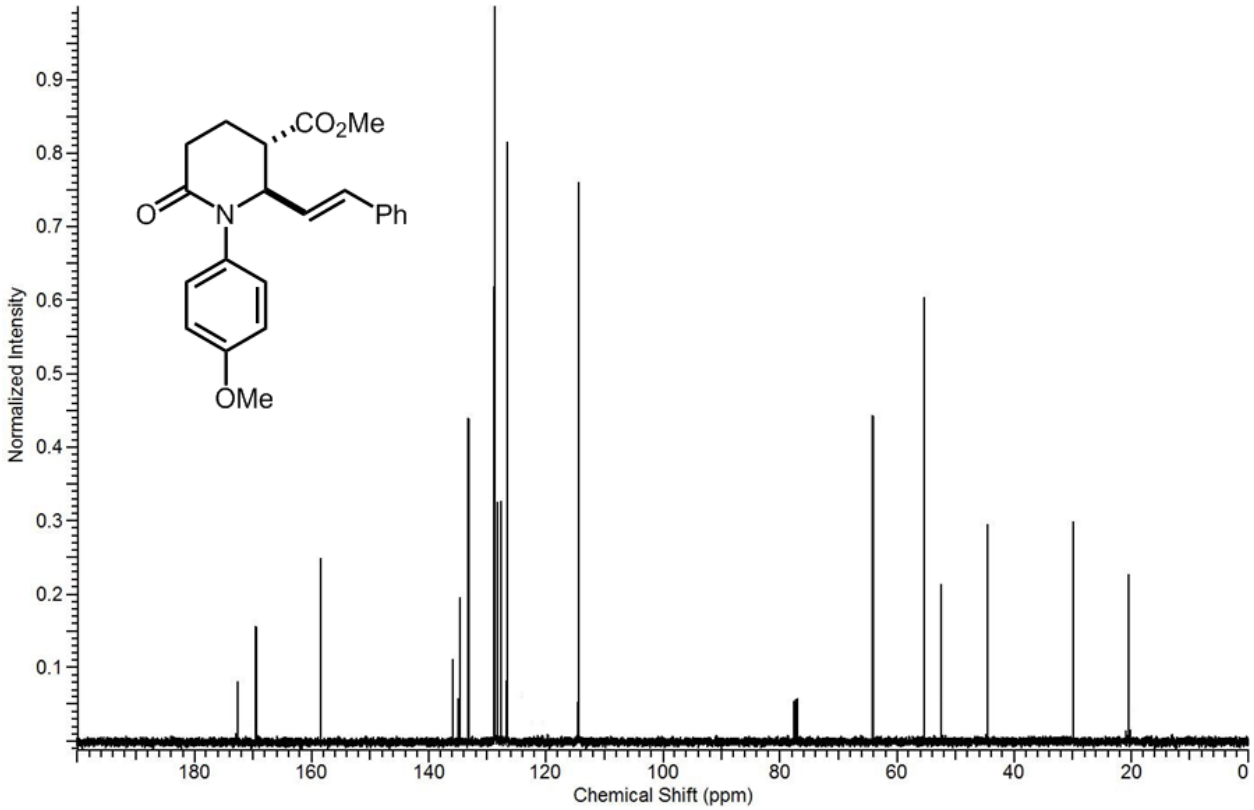
2.13
1.02
1.00
1.07
6.36
0.96
1.95
2.00


CO2Me
O
N
Ph
OMe
Normalized Intensity
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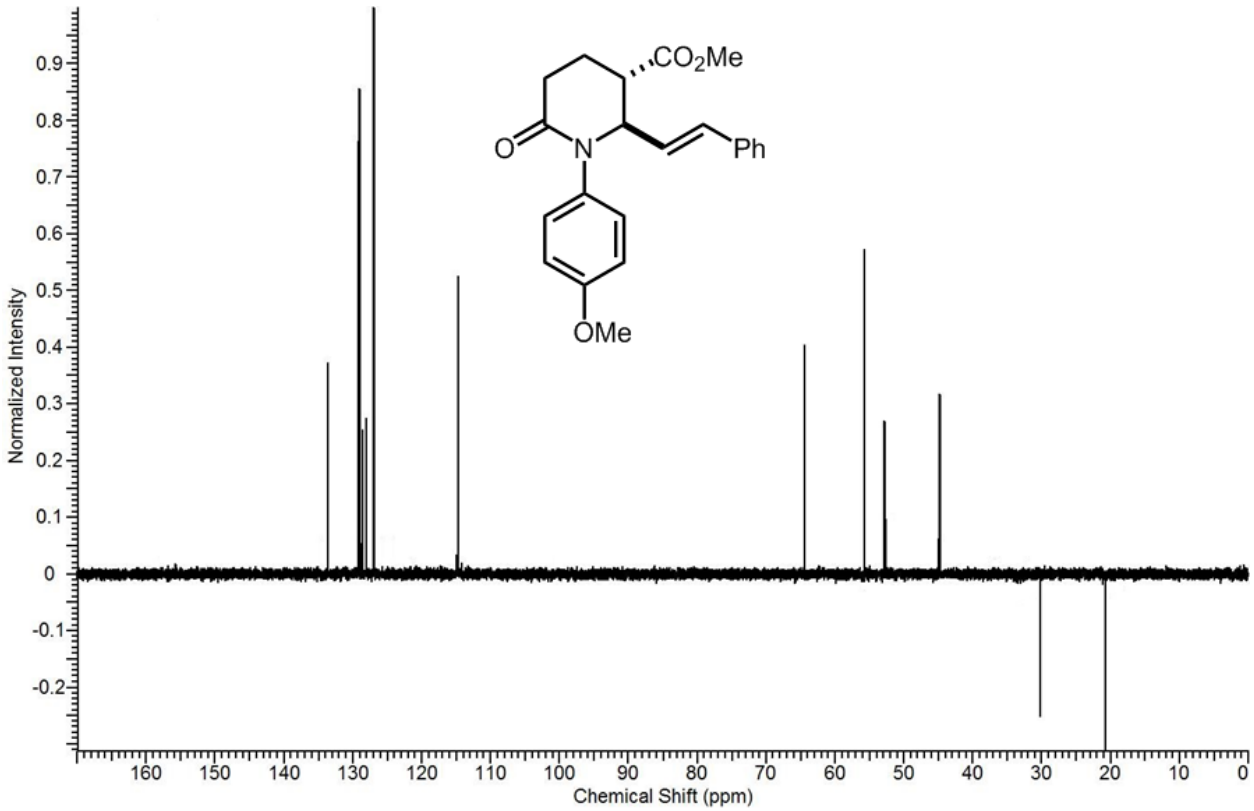
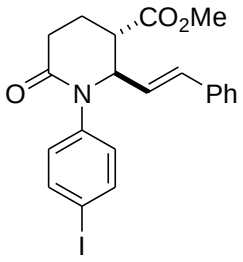
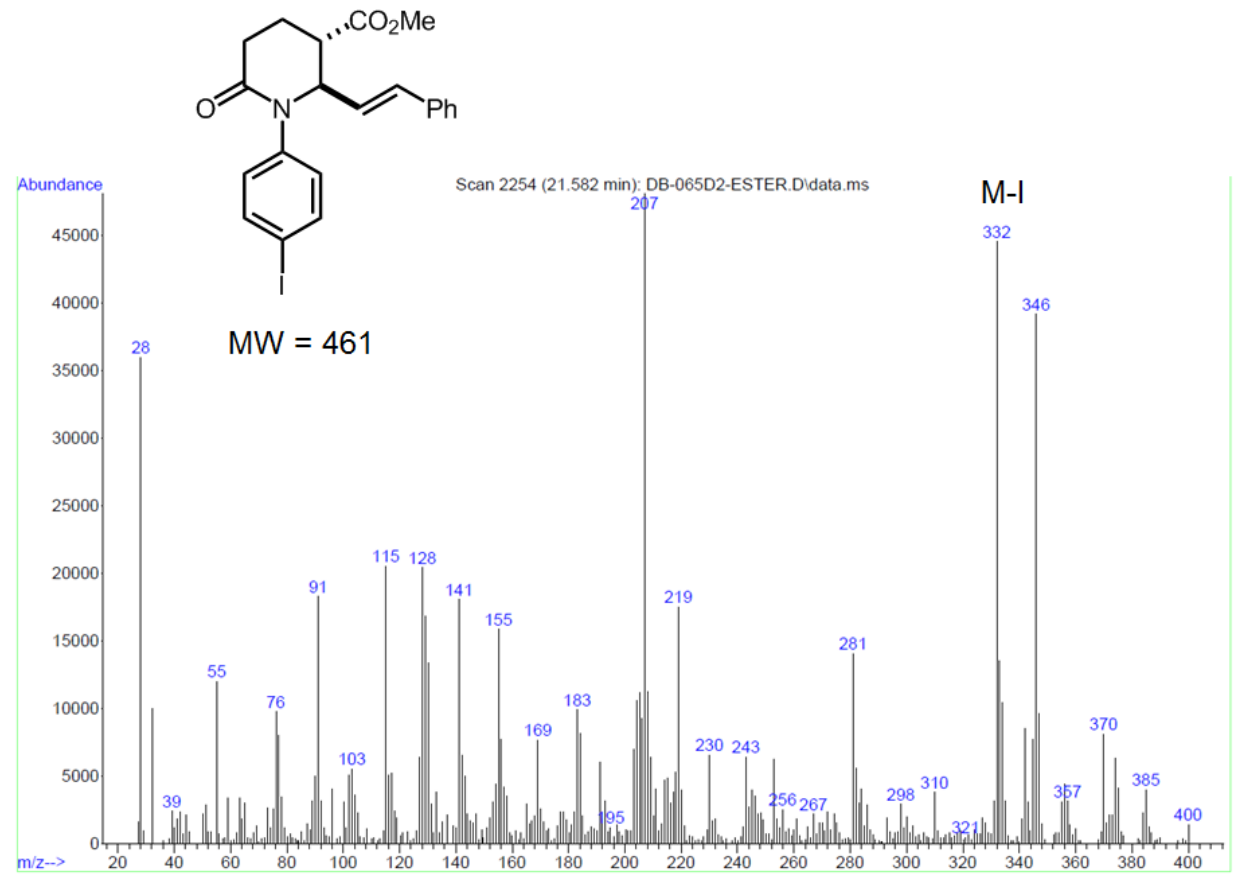
0.7
0.6
0.5
0.4
0.3
0.2
0.1
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

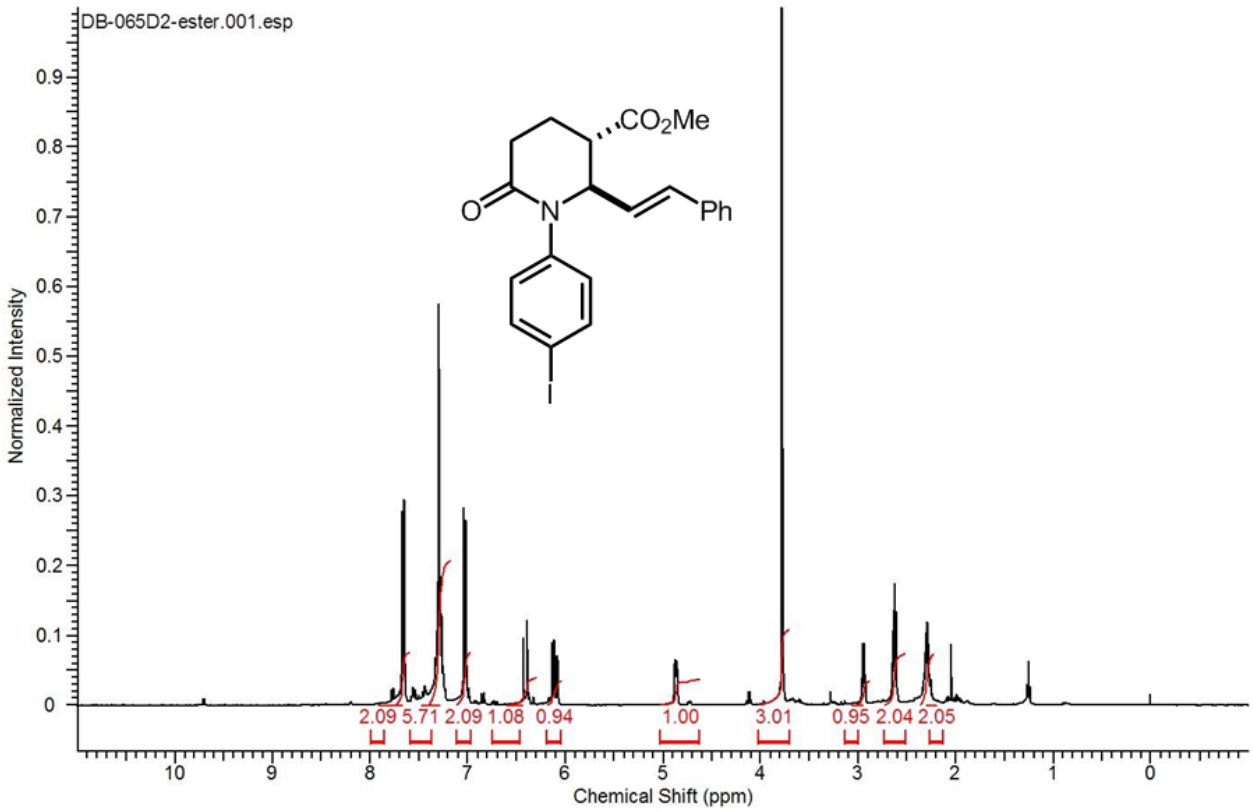

CO2Me
O
N
Ph
OMe
Normalized Intensity
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

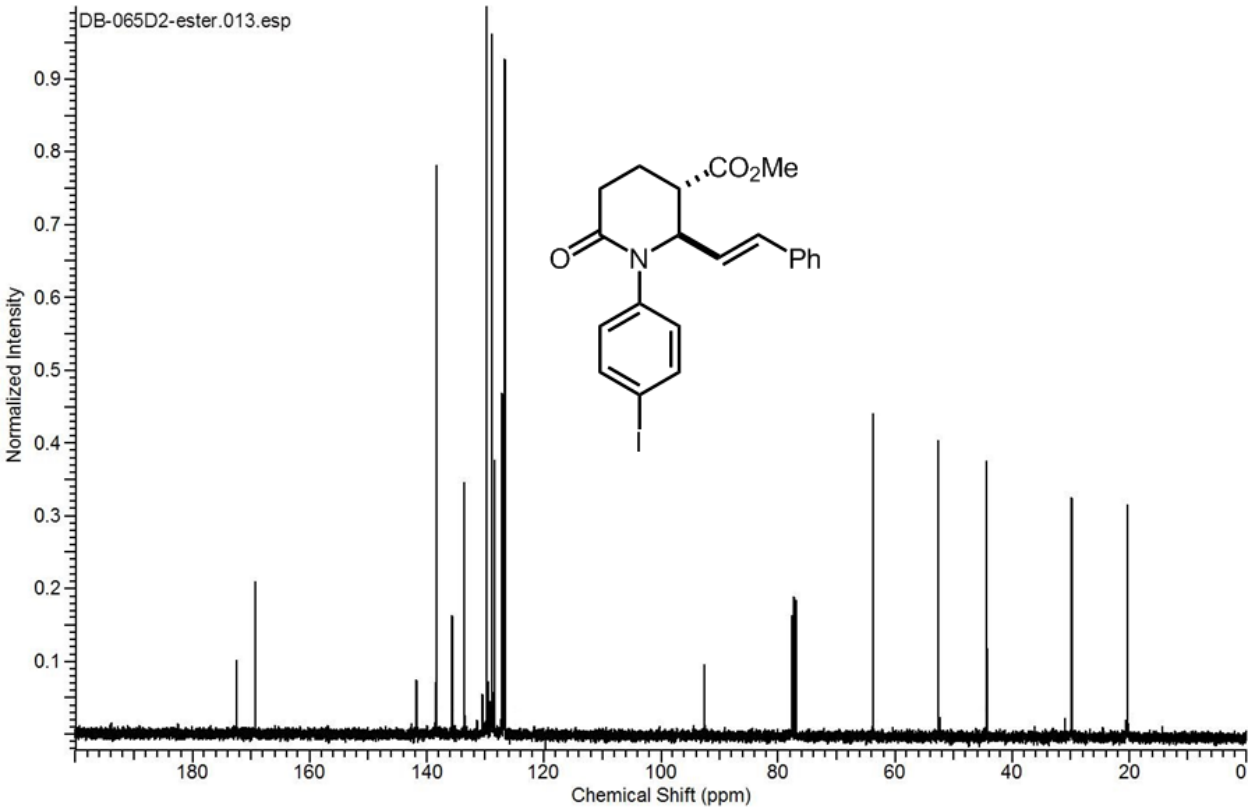


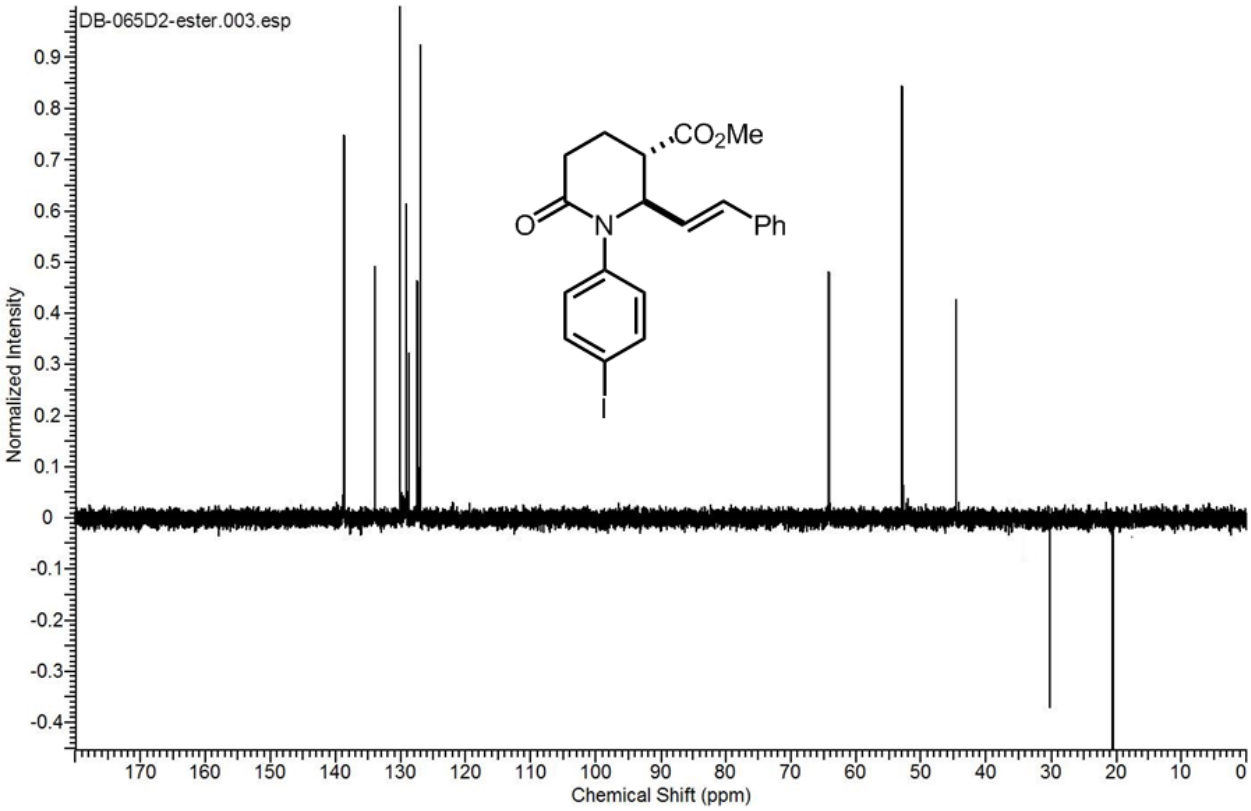
7d2

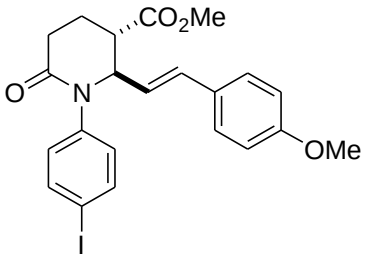
Prepared from imine **4d** (333 mg, 1.0 mmol) and glutaric anhydride (114 mg, 1.0 equiv), using General Procedures B and C. T = 105 ^{o}C, time = 22 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 346 mg, 75% over 2 steps, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (2H, d), 7.46 to 7.23 (5H, m), 7.04 (2H, d), 6.37 to 6.33 (1H, d), 6.16 to 6.08 (1H, dd), 4.88 to 4.85 (1H, dd), 3.78 (3H, s), 2.95 to 2.93 (1H, m), 2.69 to 2.61 (2H, m), 2.37 to 2.24 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 169.2, 141.7, 138.5, 138.3, 138.3, 137.7, 135.6, 135.1, 133.5, 131.3, 130.4, 129.7, 129.4, 129.2, 128.8, 128.5, 128.5, 128.4, 127.1, 126.7, 126.6, 124.1, 123.9, 92.5, 63.7, 52.3, 44.7, 29.8, 20.6. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{21}H_{20}INO_3$ 461.0488; found 461.0492.


CO2Me
O
N
Ph
I
MW = 461
Abundance
Scan 2254 (21.582 min): DB-065D2-ESTER.D\data.ms
M-I
m/z-->


DB-065D2-ester.001.esp
CO2Me
O
N
Ph
I
Normalized Intensity
2.09 5.71 2.09 1.08 0.94 1.00 3.01 0.95 2.04 2.05
Chemical Shift (ppm)

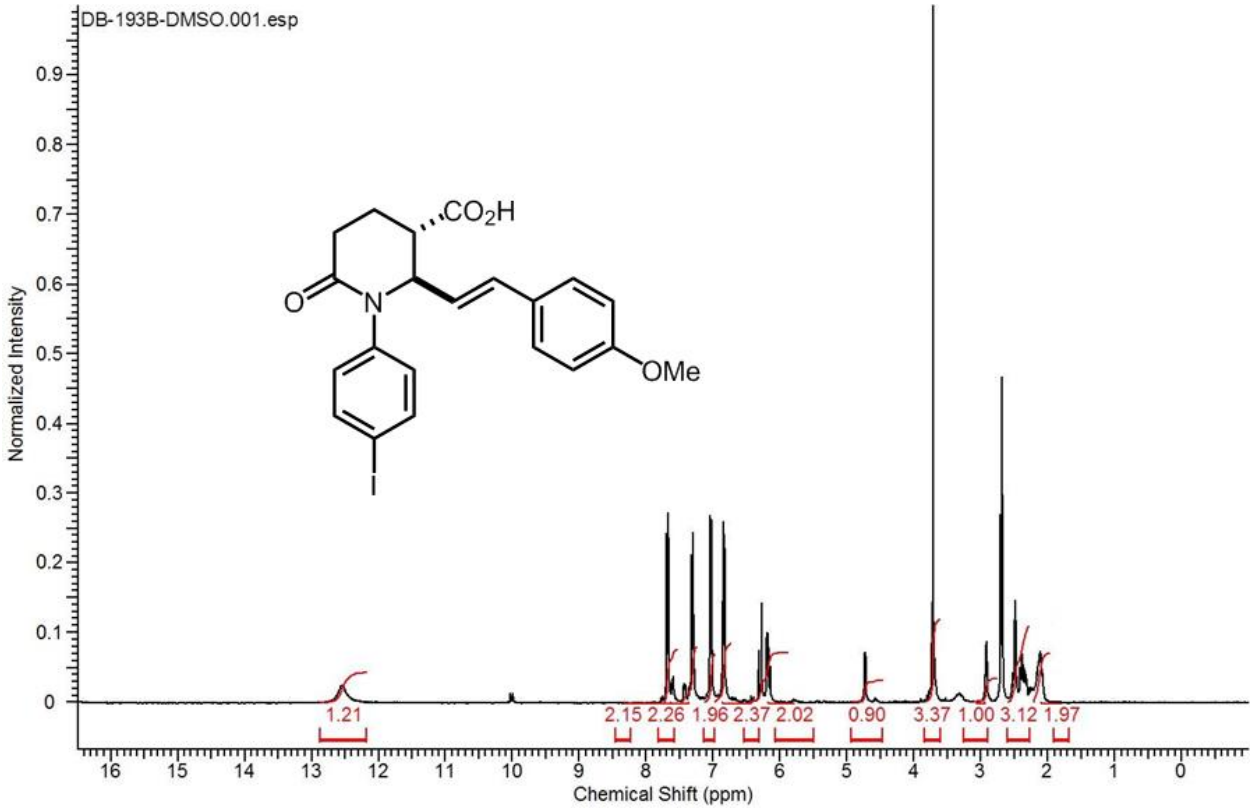

DB-065D2-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
O
N
I

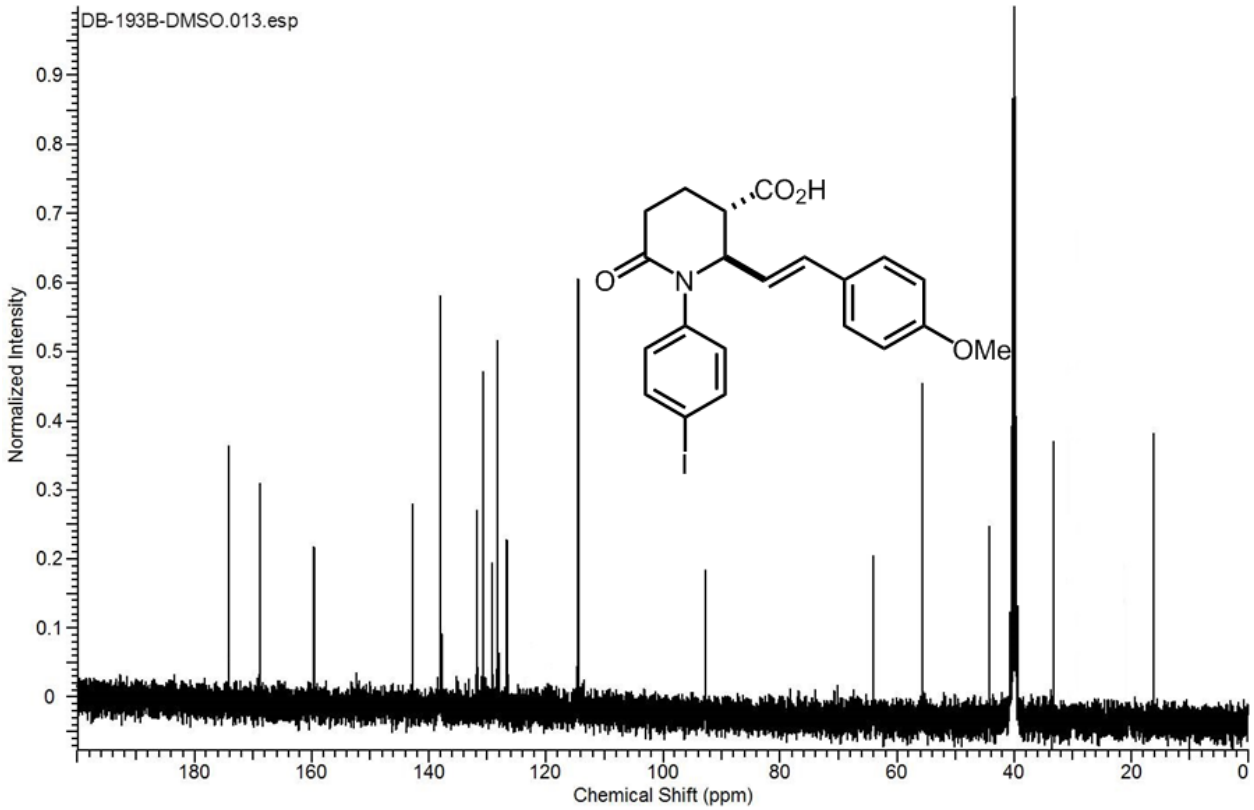

DB-065D2-ester.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
O
N
I

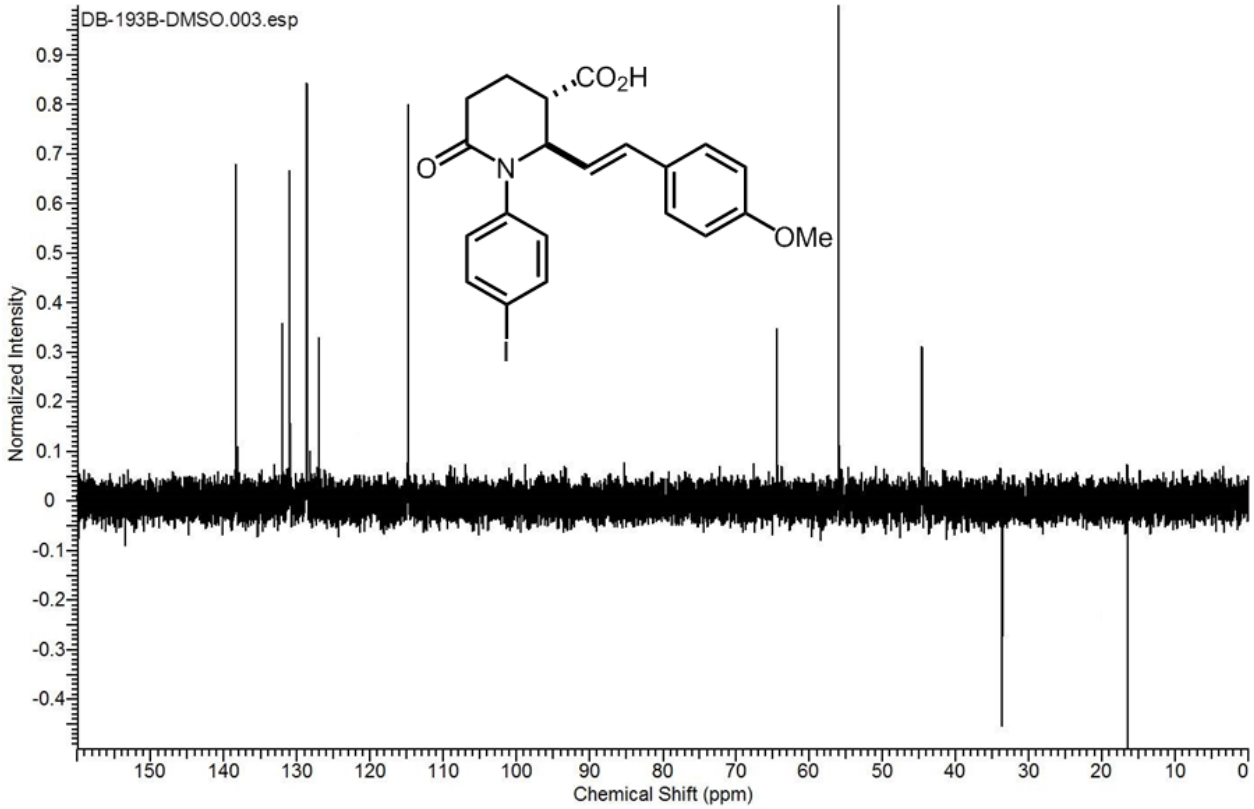


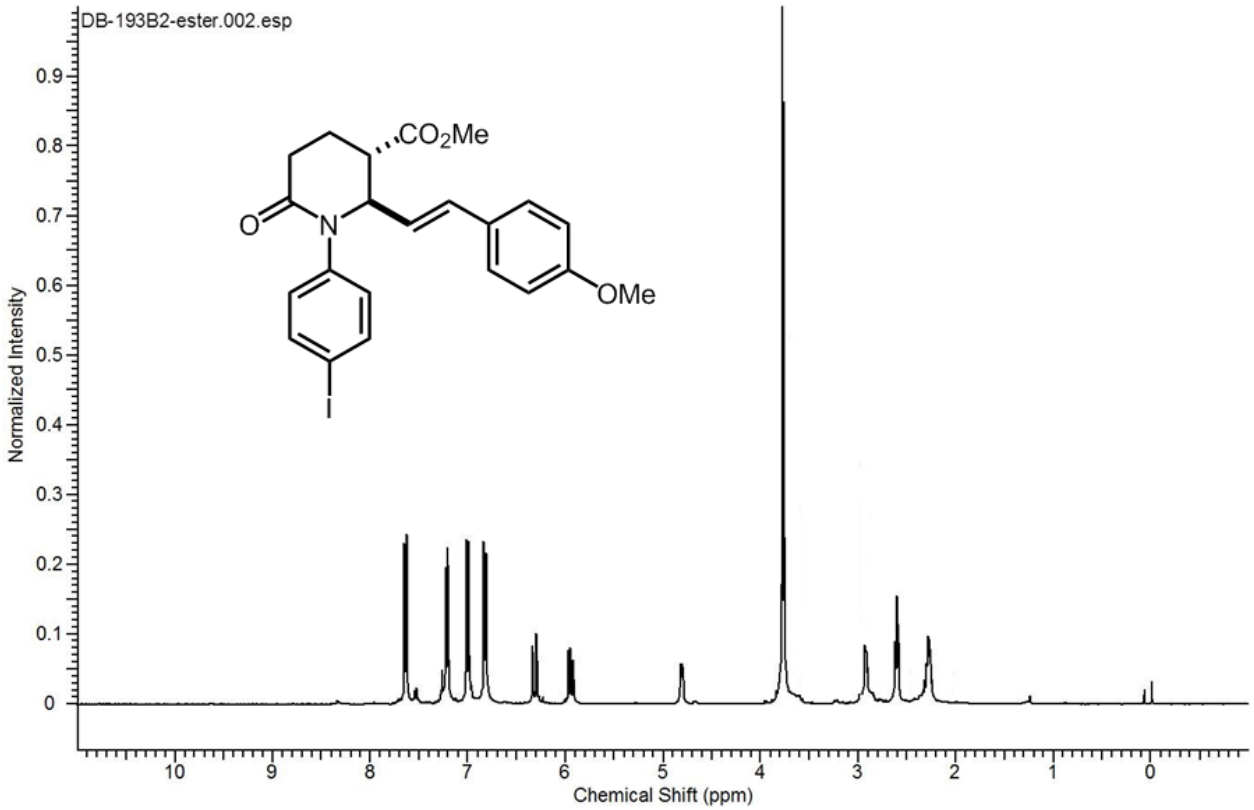
7e2

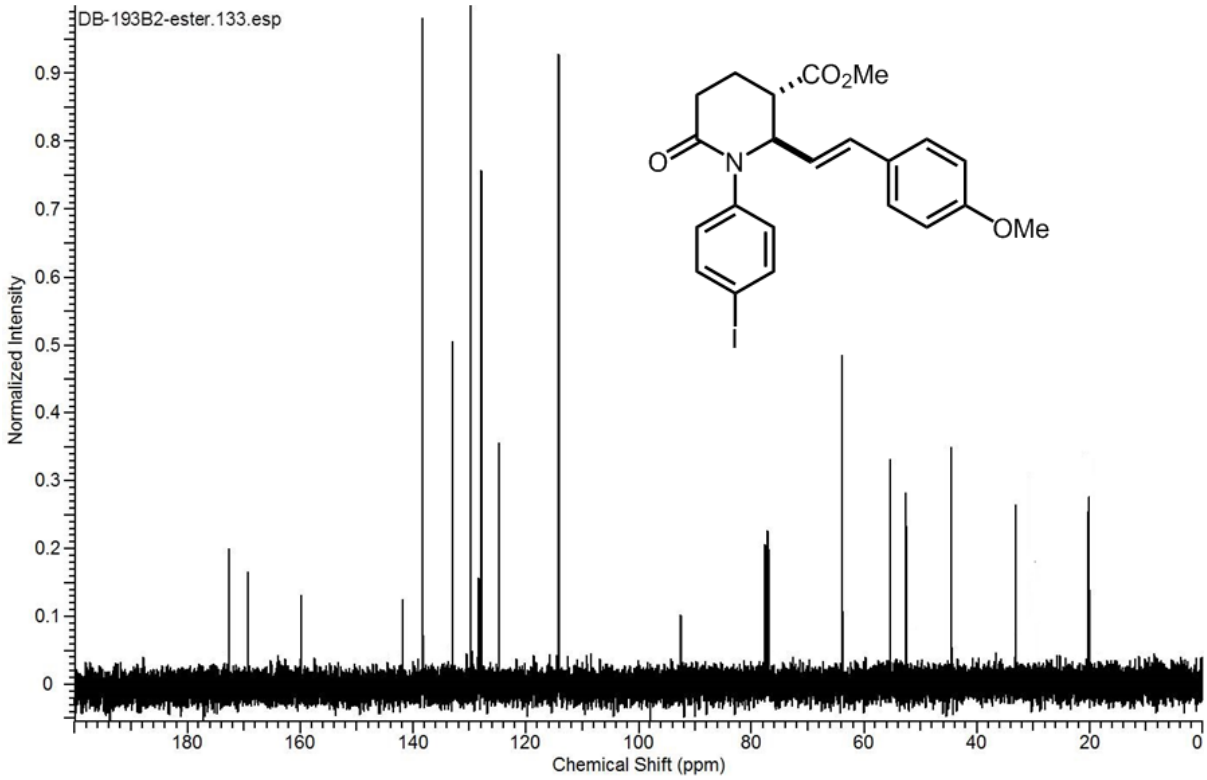
Prepared from imine **4g** (363 mg, 1.0 mmol) and glutaric anhydride (114 mg, 1.0 equiv), using General Procedures B and C. T = 105 ^{o}C, time = 22 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 339 mg, 69% over 2 steps, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (2H, d), 7.28 to 7.16 (3H, m), 7.04 to 6.98 (2H, m), 6.81 (2H, d), 6.27 (1H, d), 5.95 to 5.91 (1H, dd), 4.82 to 4.79 (1H, dd), 3.78 to 3.74 (6H, s,s), 2.93 to 2.90 (1H, m), 2.61 to 2.57 (2H, m), 2.38 to 2.24 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 169.2, 159.8, 141.7, 138.2, 137.7, 133.0, 129.7, 129.4, 128.3,, 127.8, 127.4, 124.7, 114.16, 92.5, 63.9, 55.41, 52.5, 44.4, 32.3, 20.1. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{22}H_{22}INO_4$ 491.0594; found 491.0590.

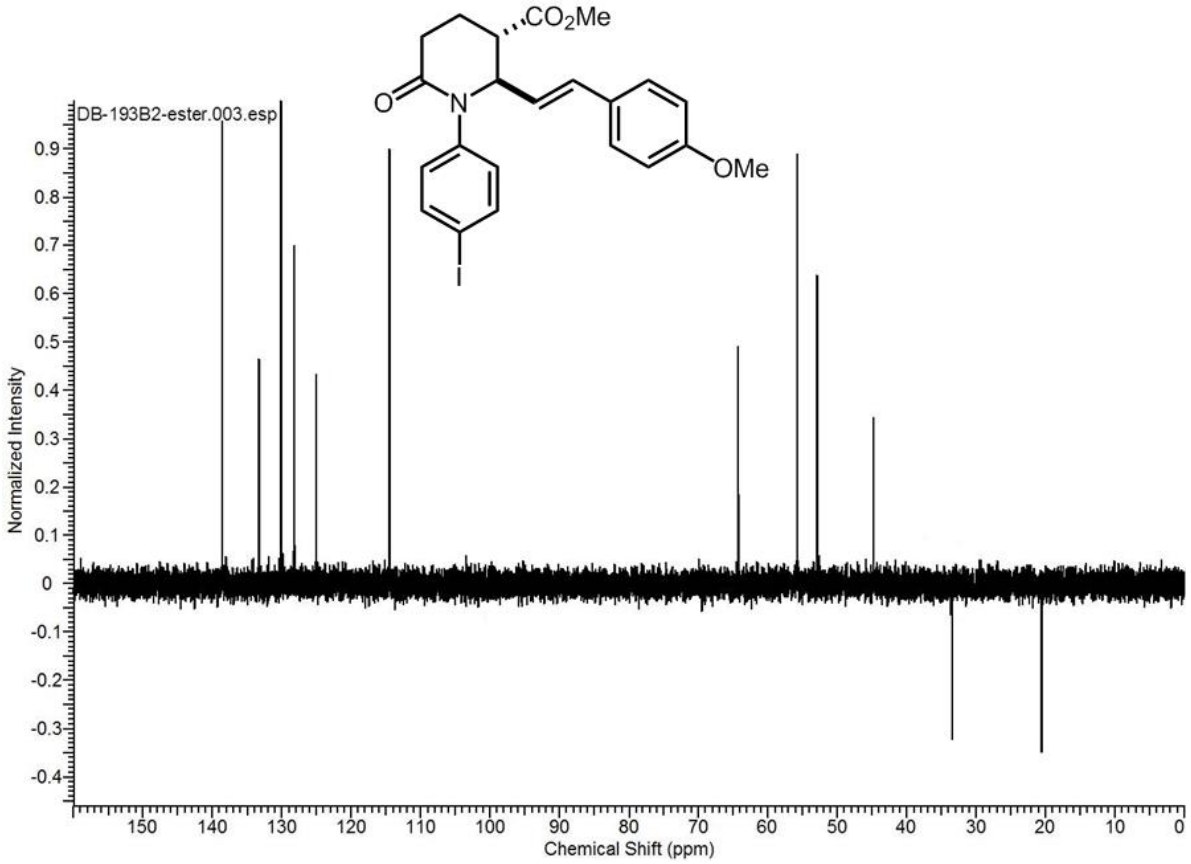


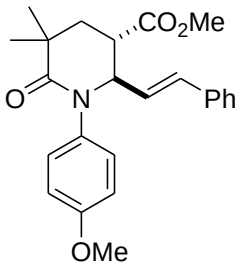

DB-193B-DMSO.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
O
N
OMe
I


DB-193B-DMSO.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
O
N
OMe
I


DB-193B2-ester.002.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
O
N
OMe
I

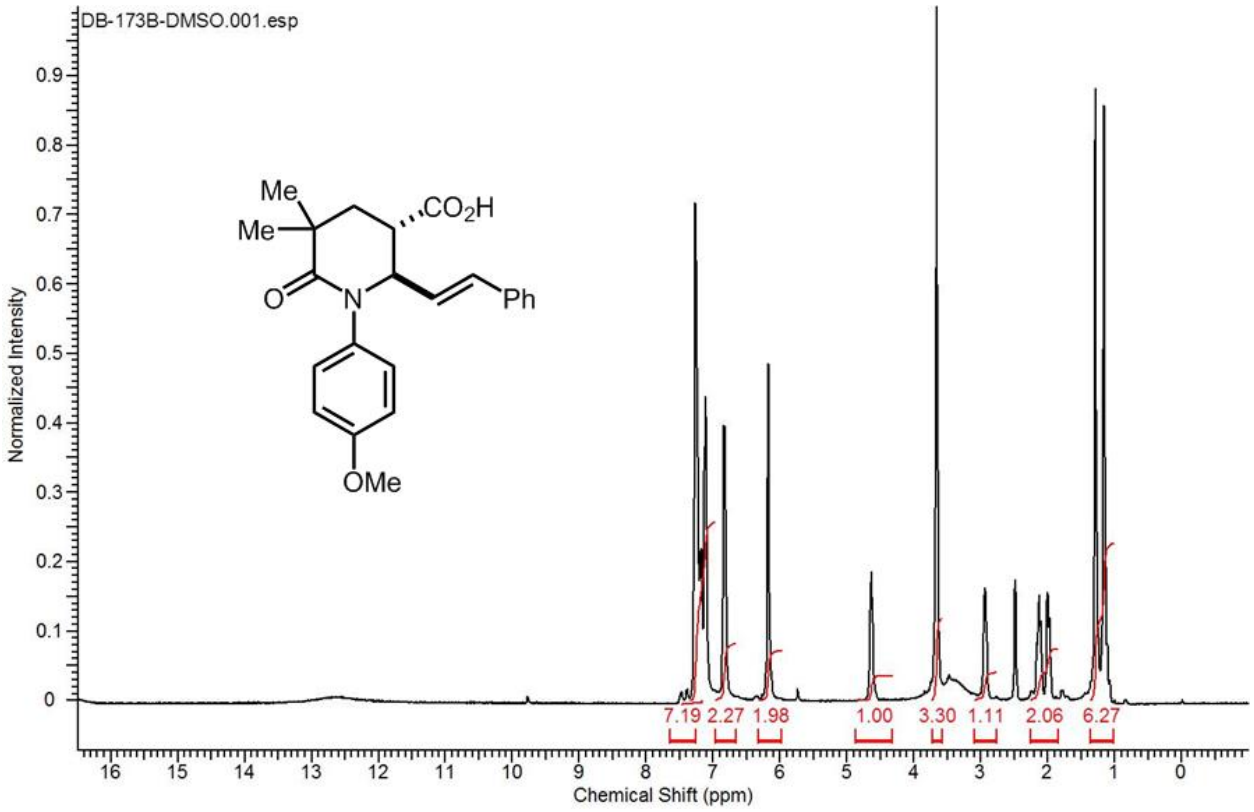

DB-193B2-ester.133.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
O
N
OMe
I

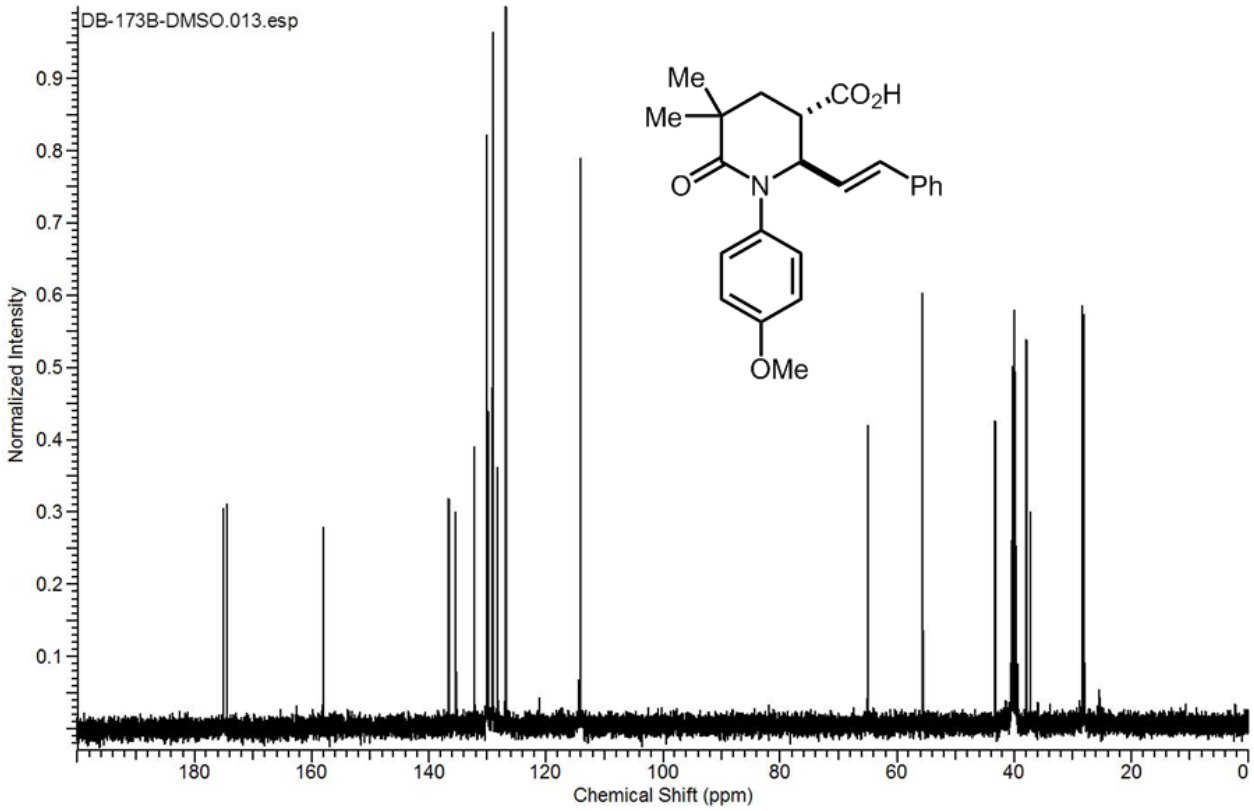


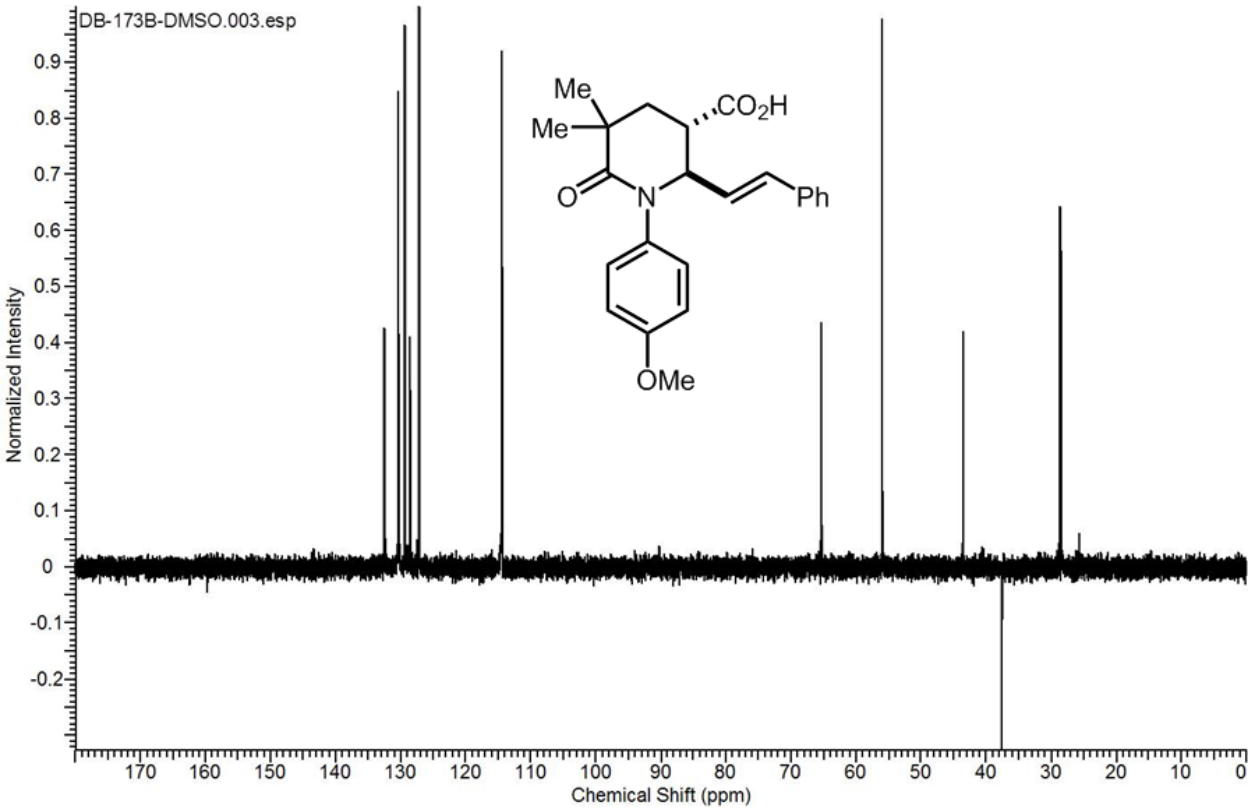


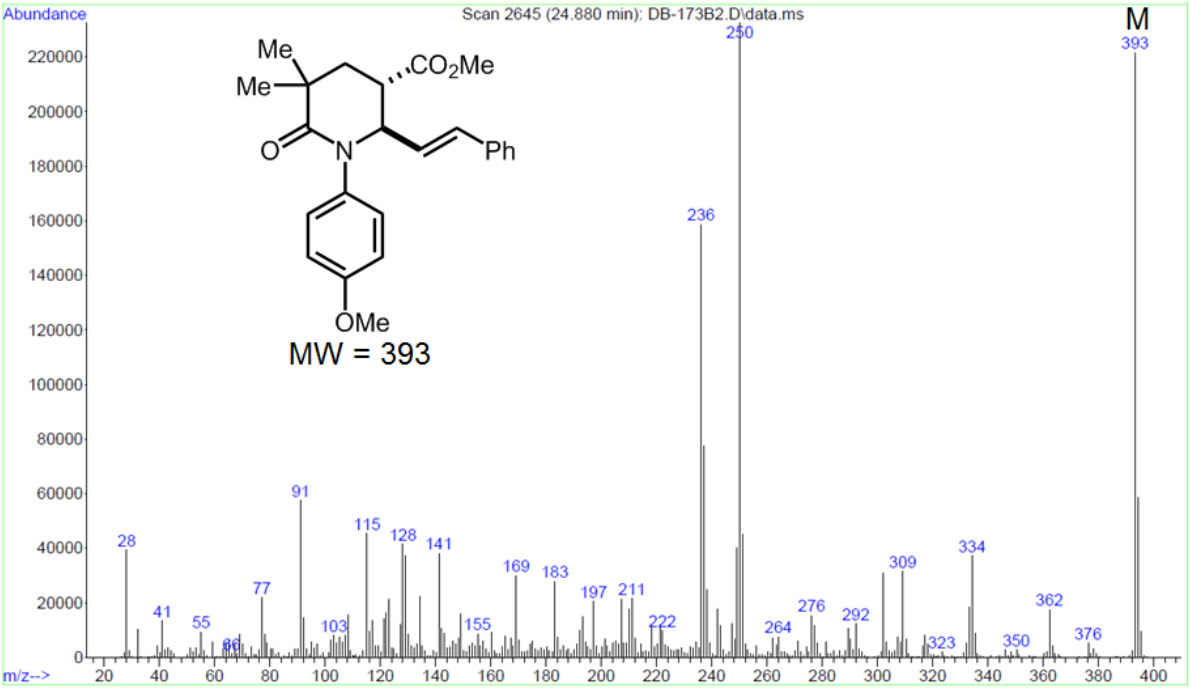
7f2

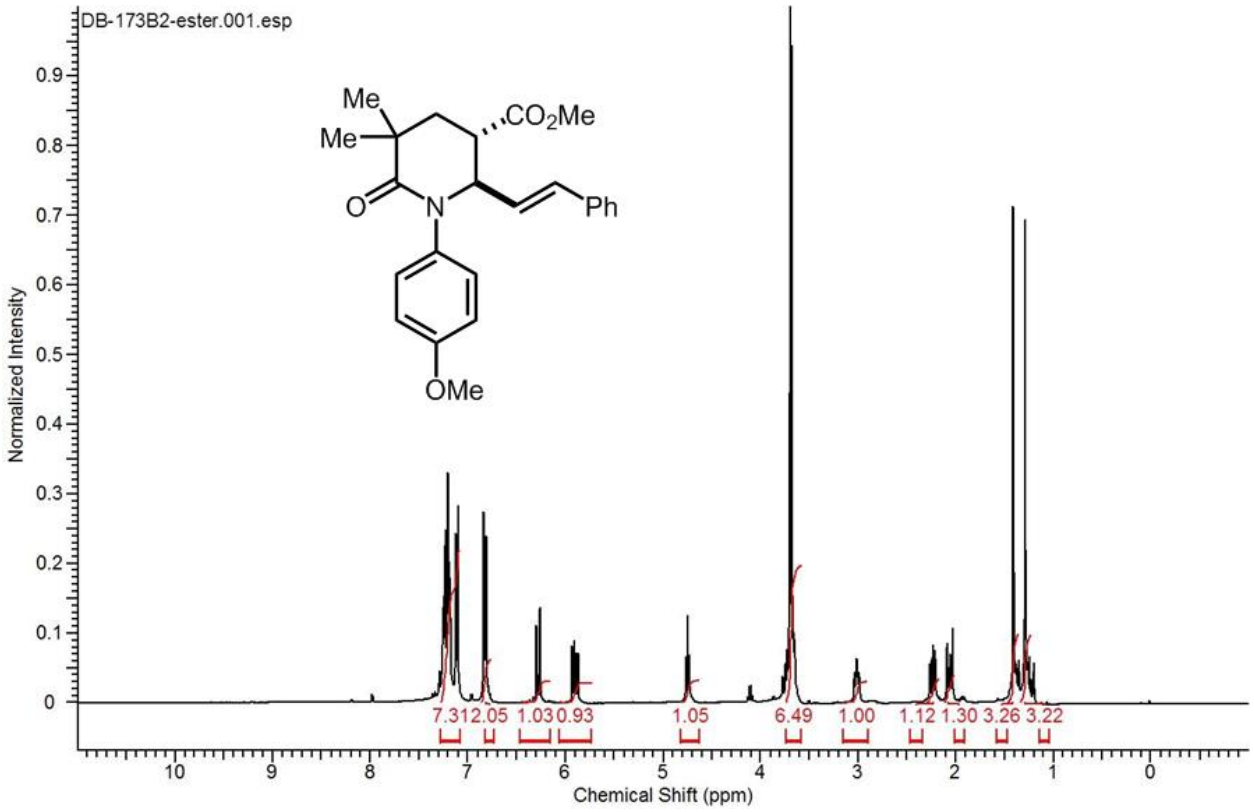
Prepared from imine **4b** (337 mg, 1.0 mmol) and 2,2-dimethyl glutaric anhydride (142 mg, 1.0 equiv), using General Procedures B and C. T = 110 ^{o}C, time = 26 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 339 mg, 77% over 2 steps, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 to 7.12 (7H, m), 6.84 to 6.81 (2H, d), 6.29 to 6.26 (1H, d), 5.91 to 5.87 (1H, dd), 4.75 to 4.70 (1H, t), 3.78 to 3.70 (6H, s,s), 3.03 to 2.98 (1H, m), 2.27 to 2.19 (1H, dd), 2.09 to 2.03 (1H, dd), 1.41 to 1.35 (6H, ss). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.6, 173.2, 158.2, 136.0, 134.9, 134.3, 133.3, 129.3, 129.2, 128.7, 128.6, 128.2, 128.2, 128.1, 128.0, 126.6, 114.5, 64.7, 55.3, 52.1, 43.4, 38.4, 38.0, 28.4, 27.8. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{24}H_{27}NO_4$ 393.1940; found 393.1944.

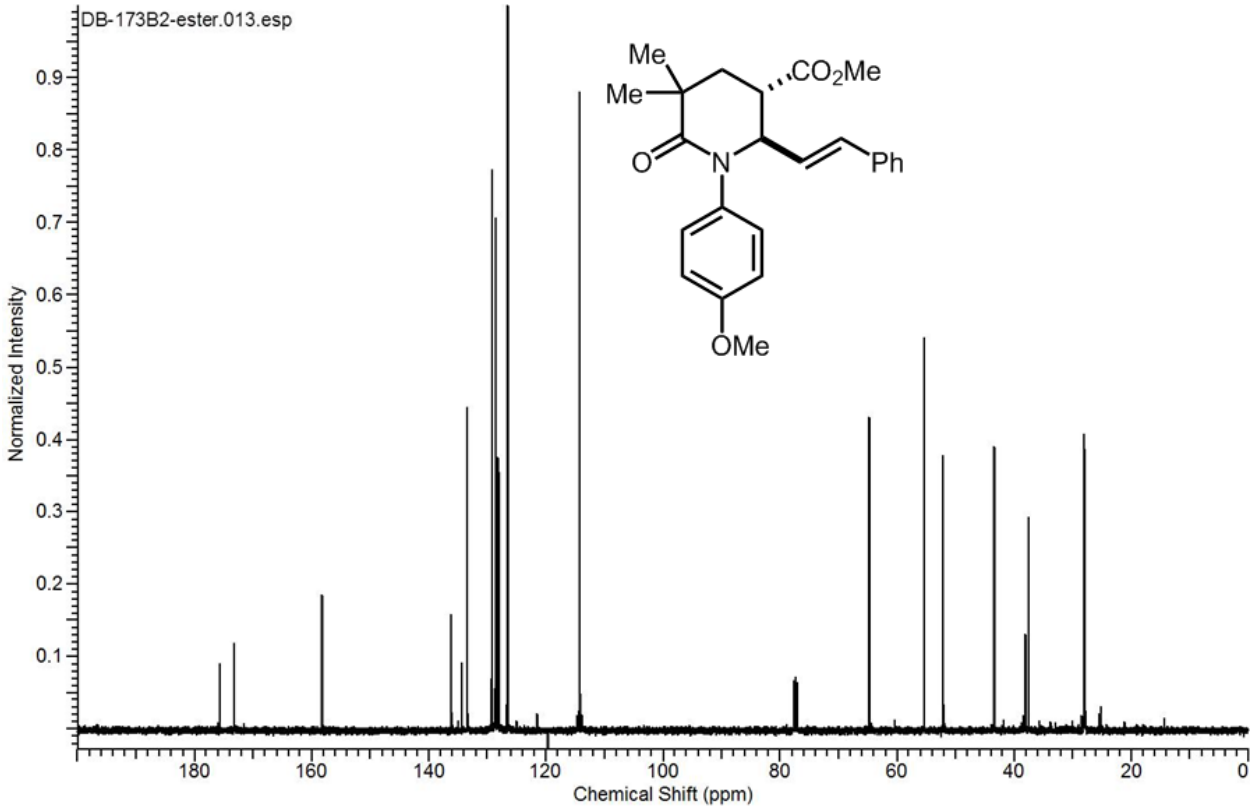

DB-173B-DMSO.001.esp
Normalized Intensity
Chemical Shift (ppm)
7.19 2.27 1.98 1.00 3.30 1.11 2.06 6.27
Me
Me
CO2H
O
N
Ph
OMe

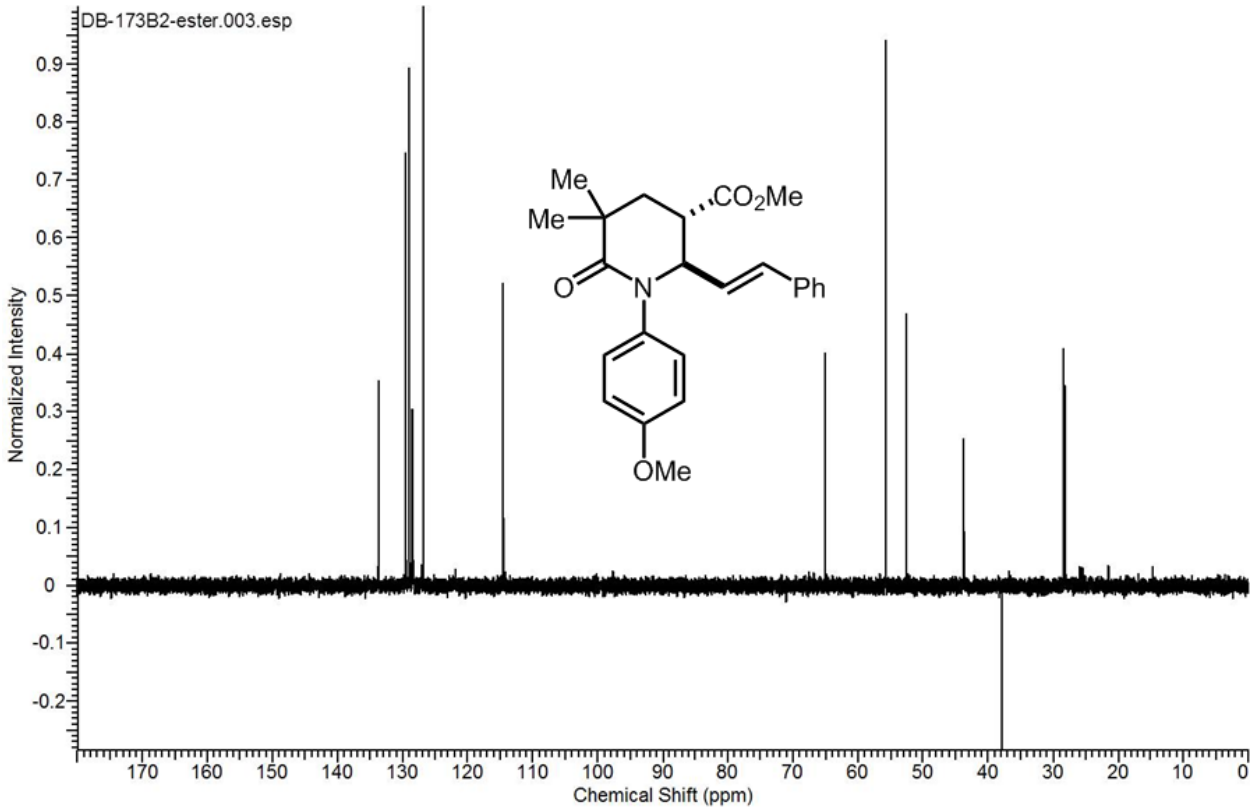

DB-173B-DMSO.013.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2H
O
N
Ph
OMe

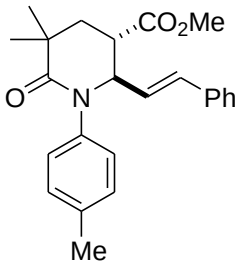

DB-173B-DMSO.003.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2H
O
N
Ph
OMe


Abundance
Scan 2645 (24.880 min): DB-173B2.D\data.ms
M
393
250
236
Me
Me
CO2Me
O
N
Ph
OMe
MW = 393
m/z-->


DB-173B2-ester.001.esp
Me
Me
CO2Me
O
N
Ph
OMe
Normalized Intensity
7.31 2.05 1.03 0.93 1.05 6.49 1.00 1.12 1.30 3.26 3.22
Chemical Shift (ppm)

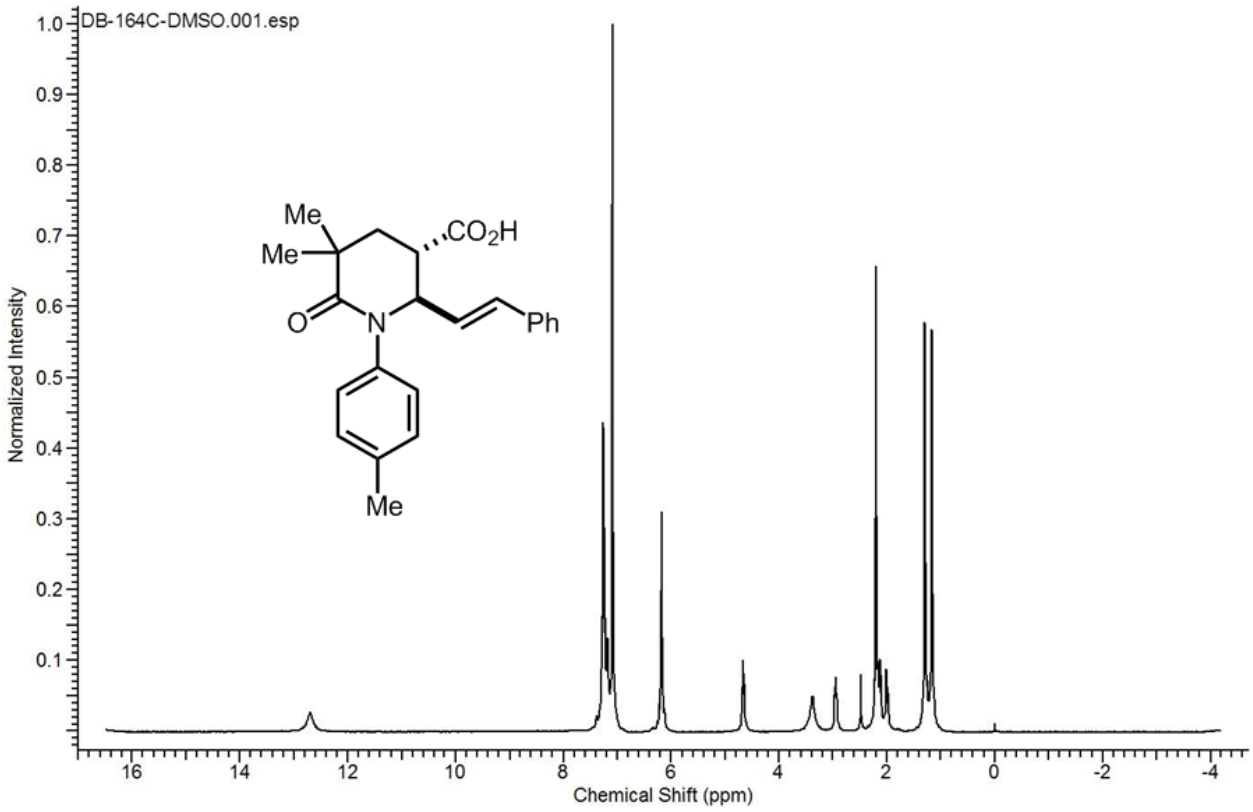

DB-173B2-ester.013.esp
Me
Me
CO2Me
O
N
Ph
OMe
Normalized Intensity
Chemical Shift (ppm)

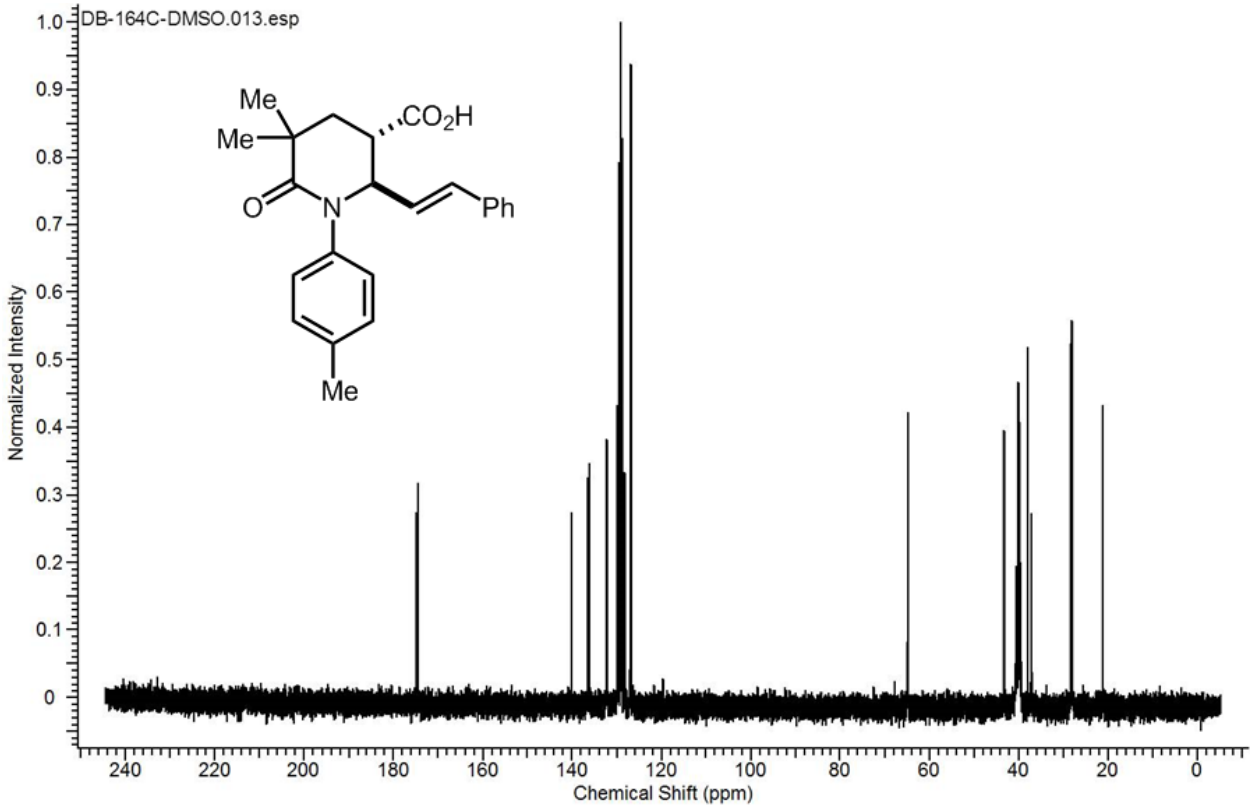


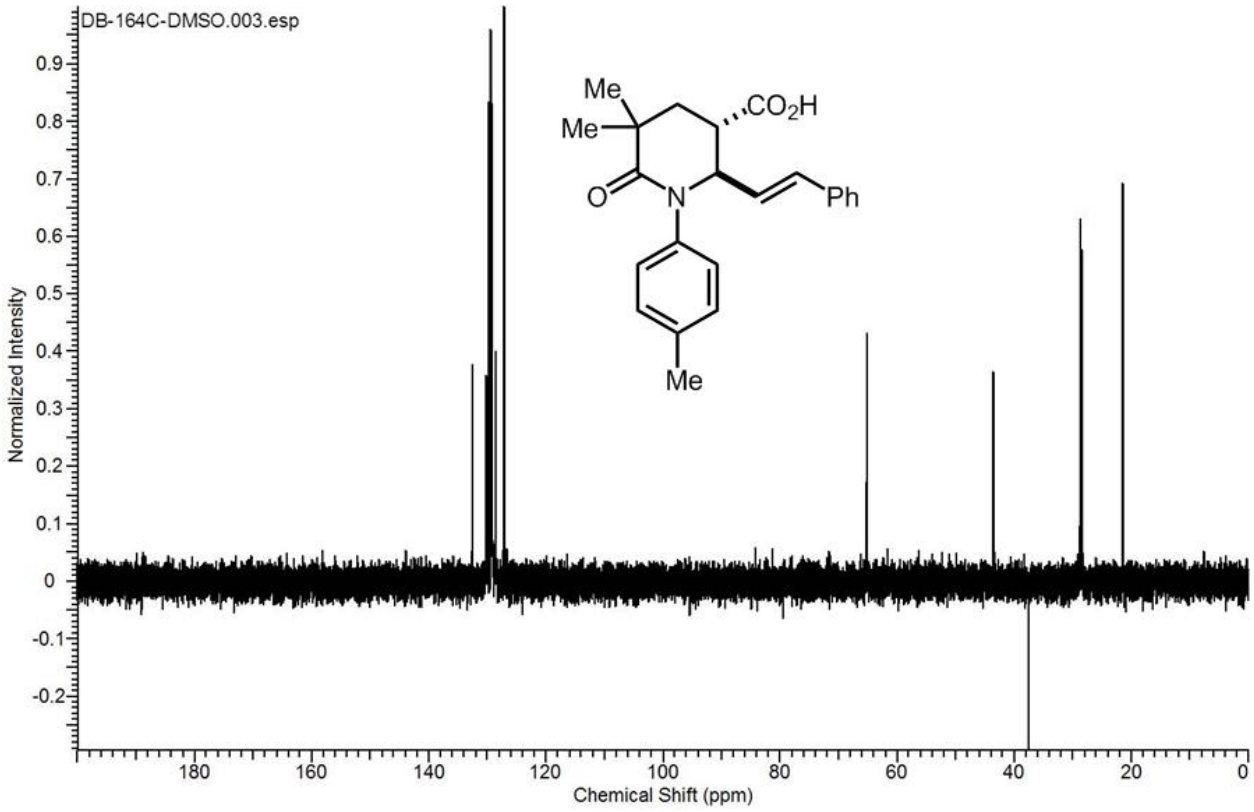


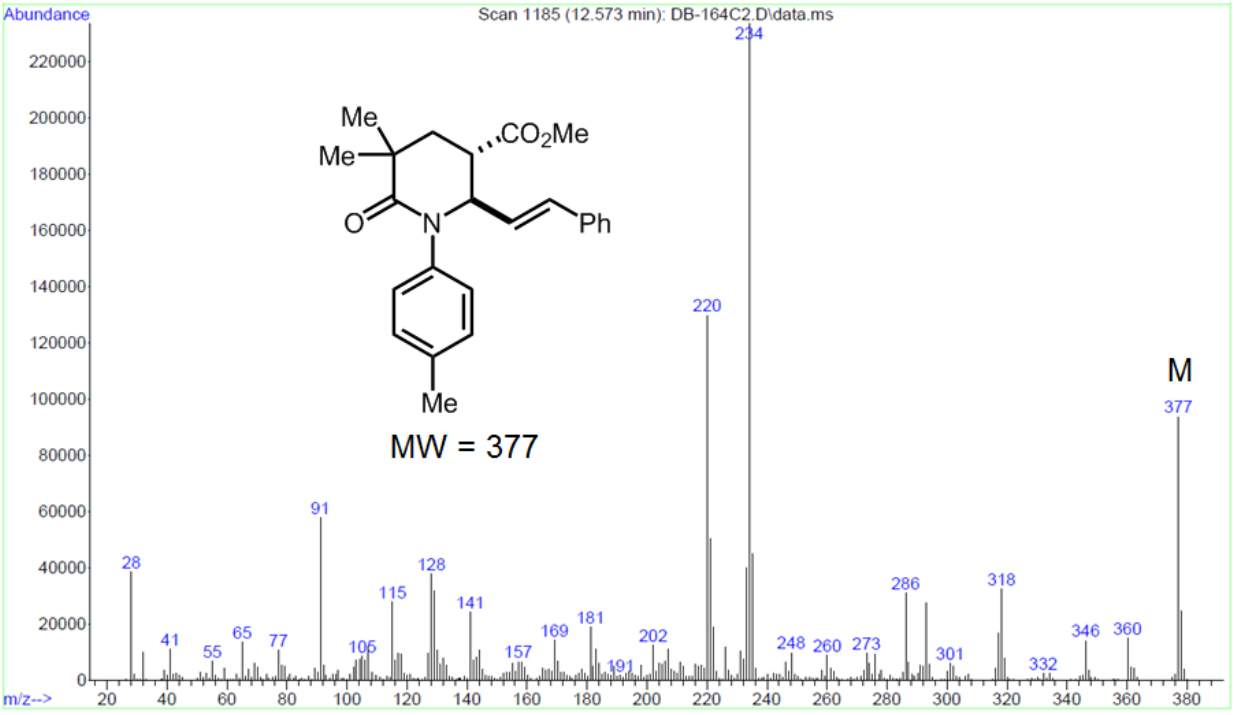
7g2

Prepared from imine **4c** (221 mg, 1.0 mmol) and 2,2-dimethyl glutaric anhydride (142 mg, 1.0 equiv), using General Procedures B and C. T = 110 ^{o}C, time = 26 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 317 mg, 84% over 2 steps, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ7.37 to 7.05 (9H, m), 6.29 to 6.25 (1H, d), 5.87 to 5.85 (1H, dd), 4.78 to 4.74 (1H, t), 3.77 (3H, s), 3.03 to 2.91 (1H, m), 2.36 to 2.26 (4H, m), 2.09 to 1.98 (1H, dd), 1.38 to 1.26 (6H, s,s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.5, 173.2, 138.8, 136.7, 136.1, 133.3, 129.6, 129.4, 129.1, 128.5, 128.2, 127.9, 127.9, 127.2, 126.6, 126.5, 64.5, 51.9, 43.5, 38.0, 37.5, 29.3, 27.8, 20.9. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{24}H_{27}NO_3$ 377.1991; found 377.1995.


DB-164C-DMSO.001.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2H
O
N
Ph
Me


DB-164C-DMSO.013.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2H
O
N
Ph
Me


DB-164C-DMSO.003.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2H
O
N
Ph
Me


Abundance
Scan 1185 (12.573 min): DB-164C2.D\data.ms
m/z-->
Me
Me
CO2Me
O
N
Ph
Me
MW = 377
M
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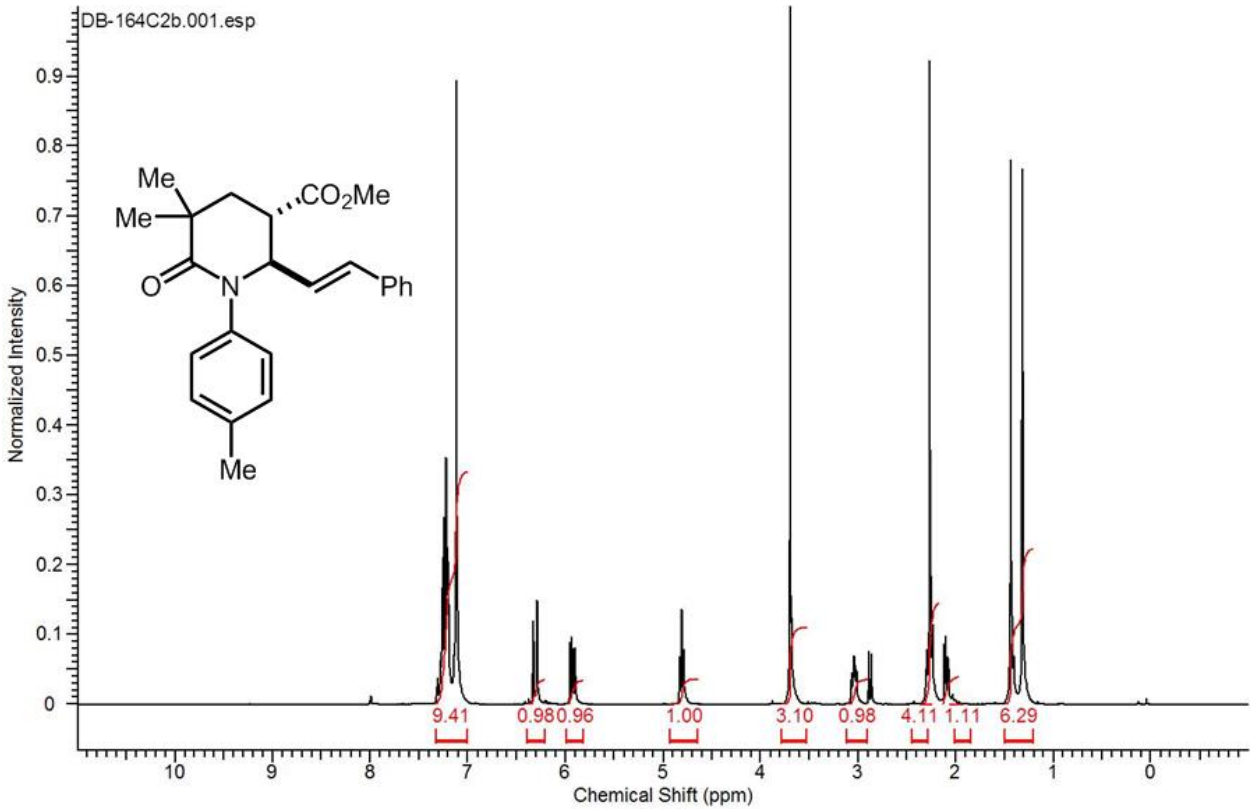
202
248
260
273
286
301
318
332
346
360


DB-164C2b.001.esp
Normalized Intensity
Chemical Shift (ppm)
9.41
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0.96
1.00
3.10
0.98
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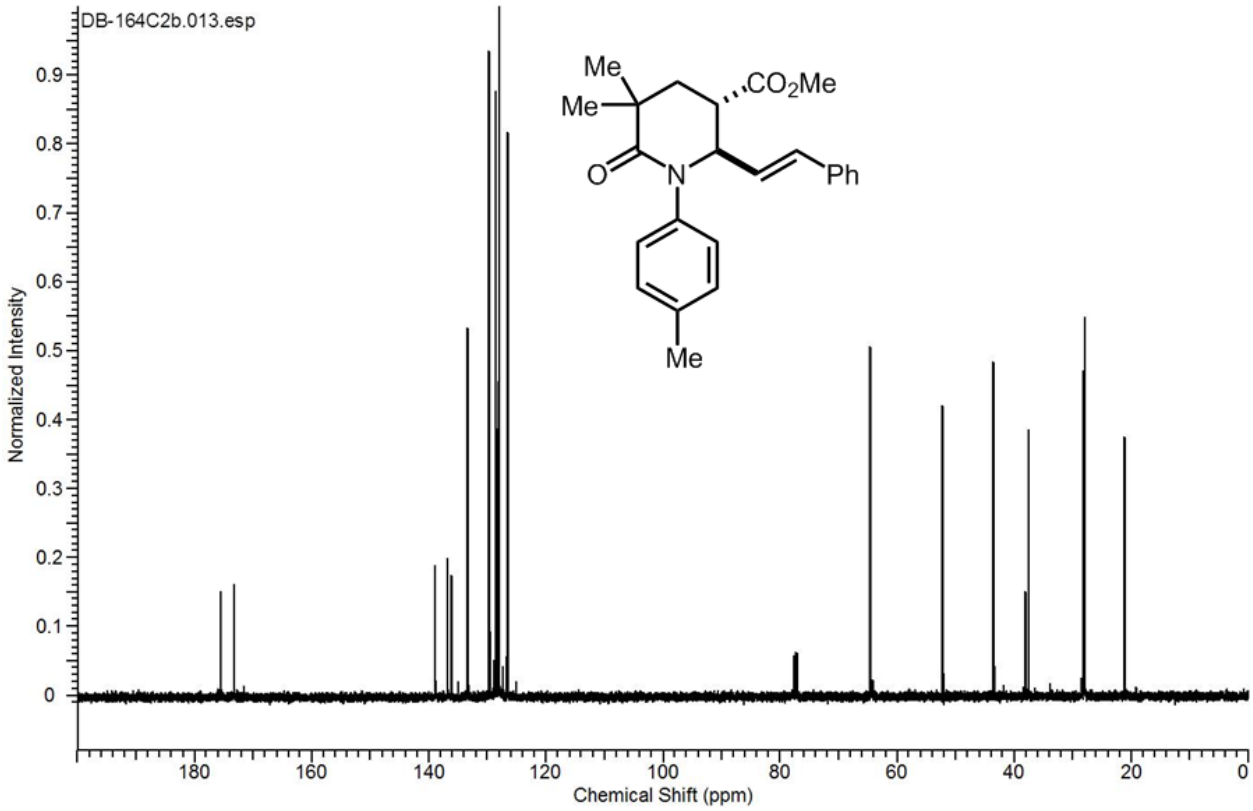
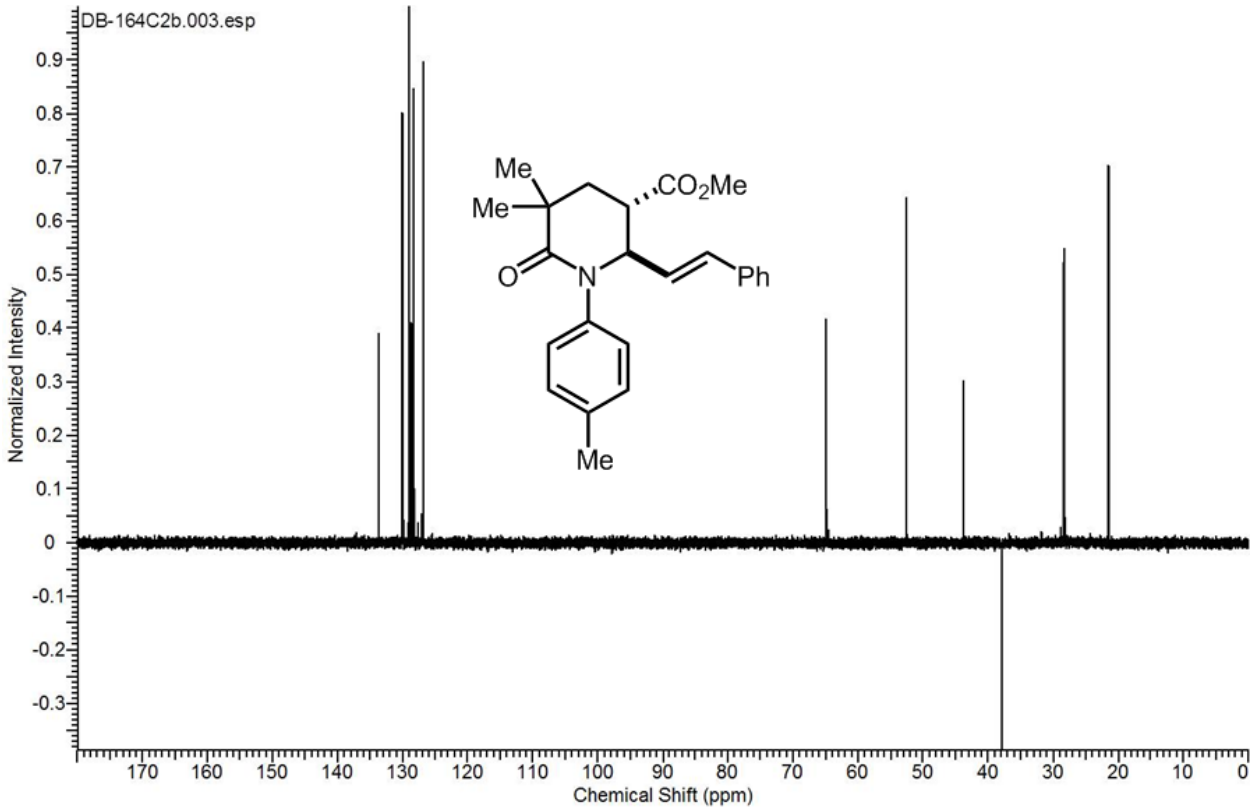
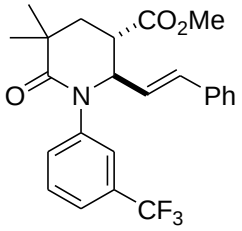
6.29
Me
Me
CO2Me
O
N
Ph
Me

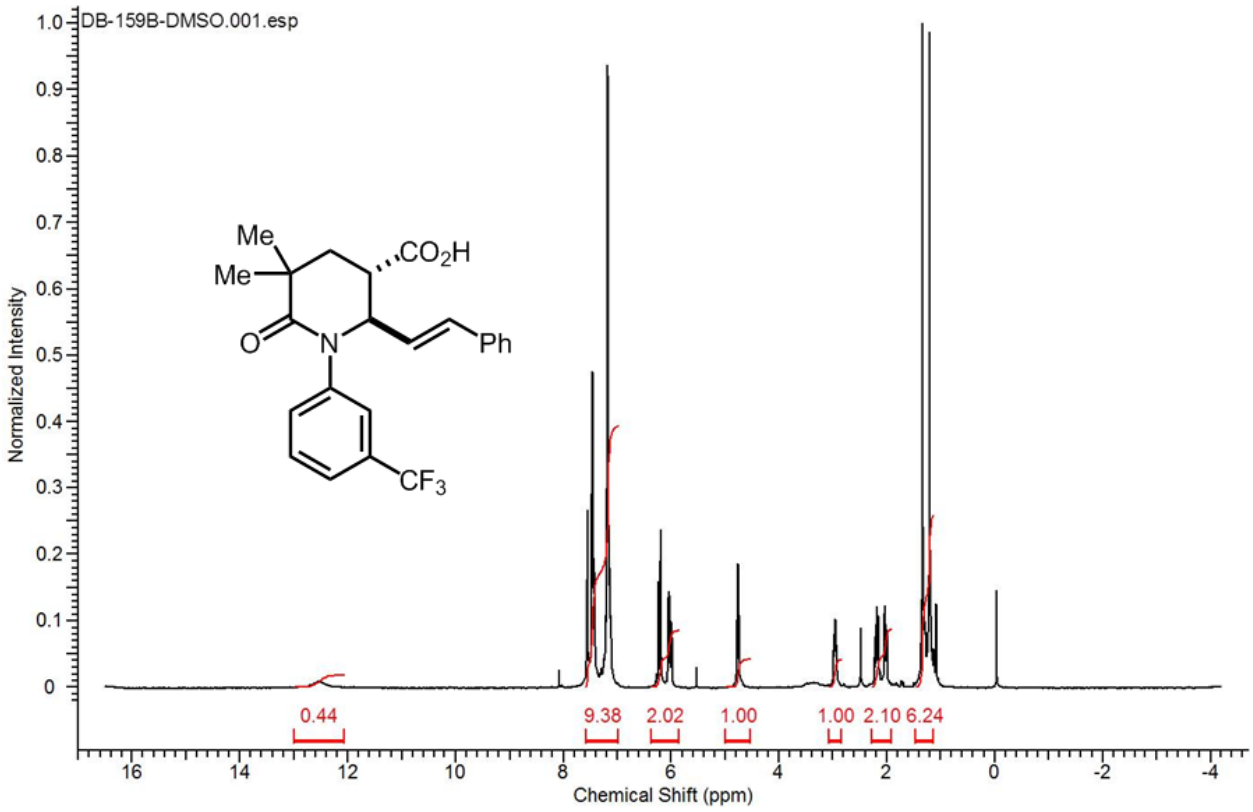

DB-164C2b.013.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2Me
O
N
Ph
Me





7h2

Prepared from imine **4e** (275 mg, 1.0 mmol) and 2,2-dimethyl glutaric anhydride (142 mg, 1.0 equiv), using General Procedures B and C. T = 110 ^{o}C, time = 36 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 302 mg, 70% over 2 steps, 96:4 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 to 7.16 (9H, m), 6.33 (1H, d), 5.85 to 5.82 (1H, dd), 4.85 to 4.81 (1H, t), 3.70 (3H, s), 3.07 to 2.91 (1H, m), 2.27 to 2.22 (1H, dd), 2.09 to 2.01 (1H, dd), 1.46 (3H, s) 1.43 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.6, 172.9, 142.0, 135.7, 134.3, 132.0, 131.4, 131.1, 129.4, 128.7, 128.6, 128.2, 127.4, 126.6, 126.4, 125.3, 125.2, 125.2, 125.2, 124.4, 64.6, 52.2, 43.3, 38.2, 37.4, 27.9. 27.3. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{24}H_{24}F_3NO_3$ 431.1708; found 431.1700.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Normalized Intensity
Chemical Shift (ppm)
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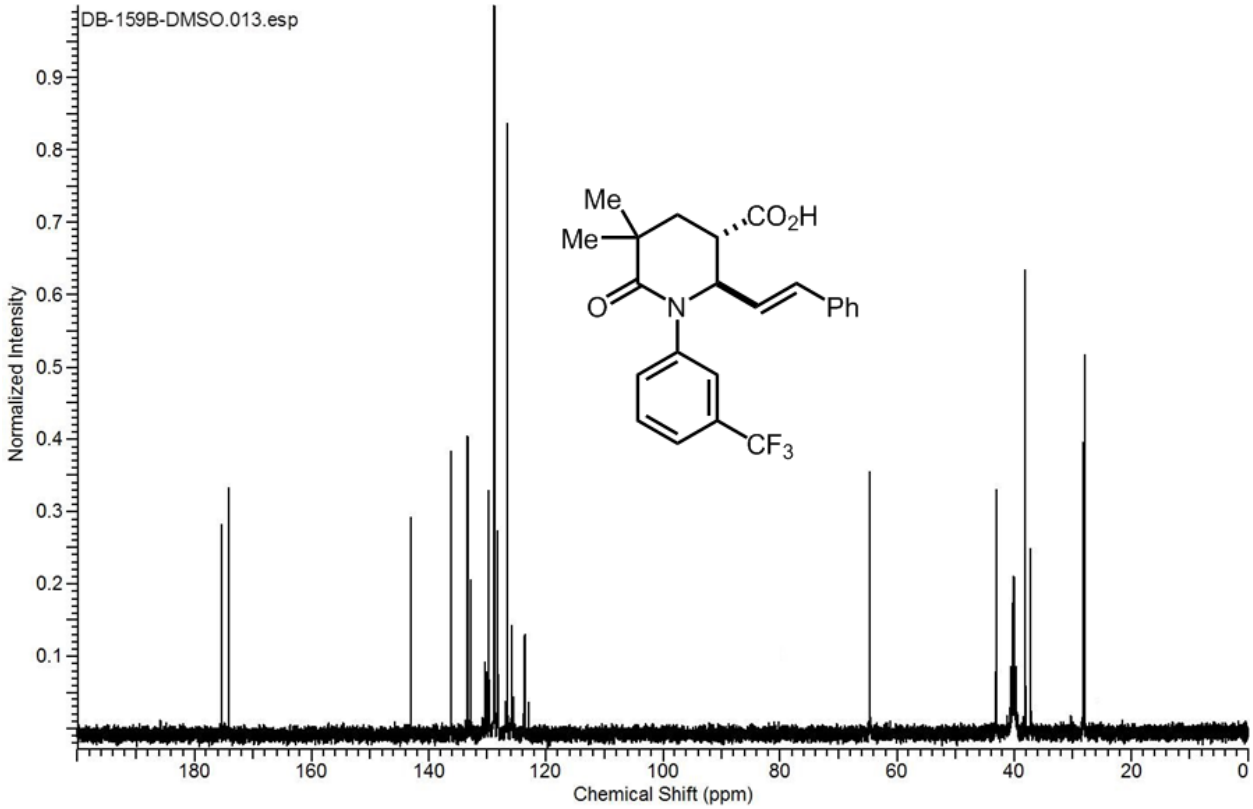
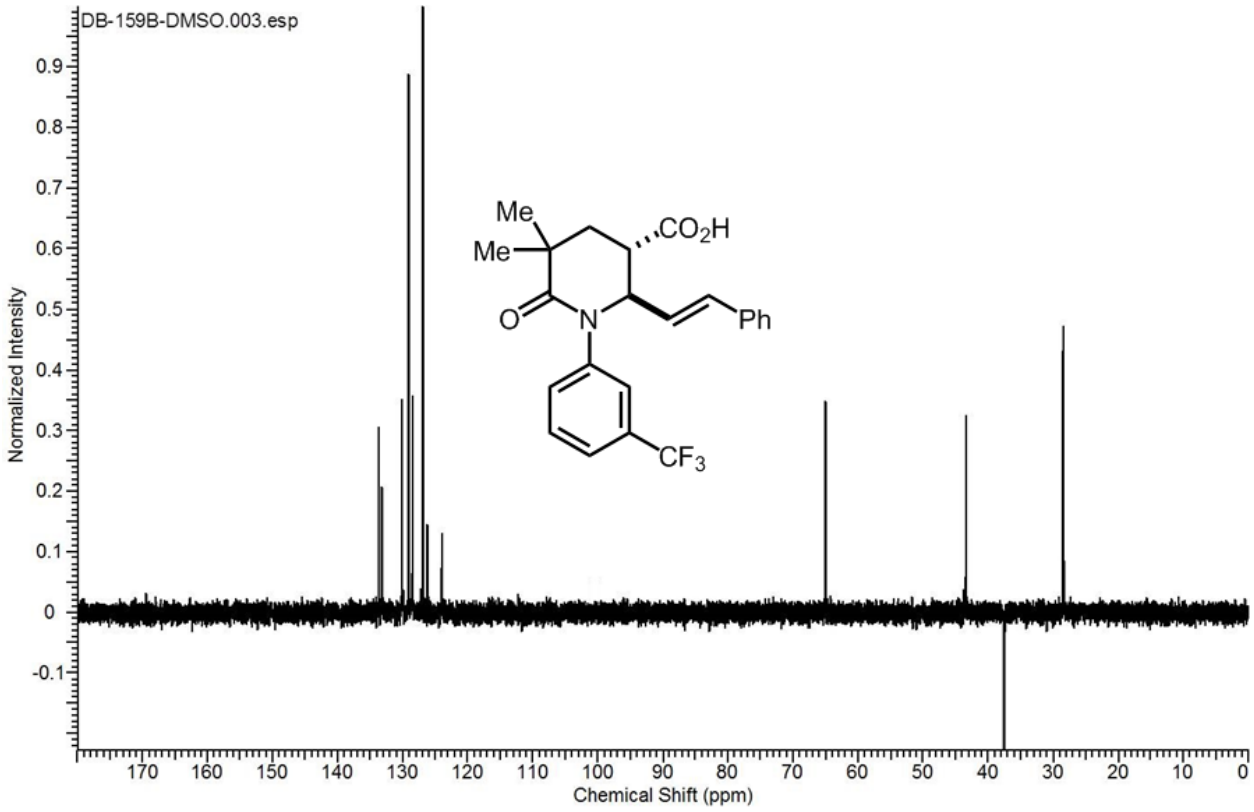
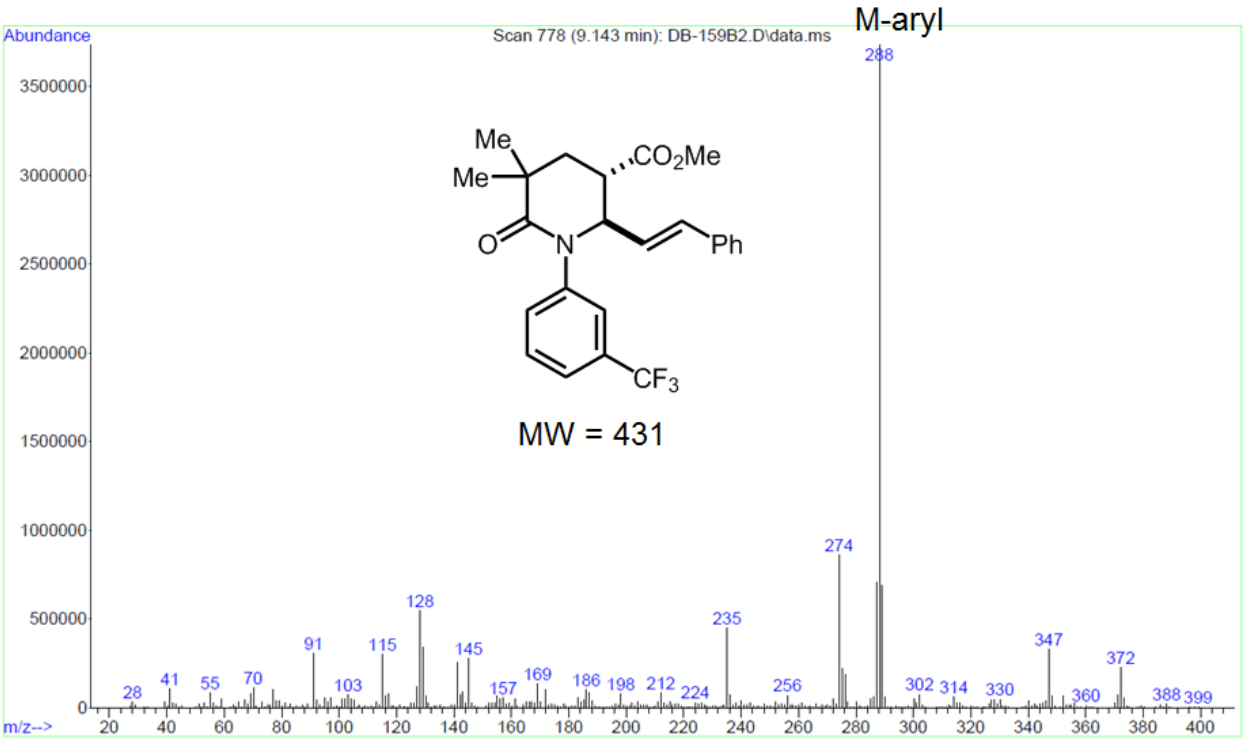
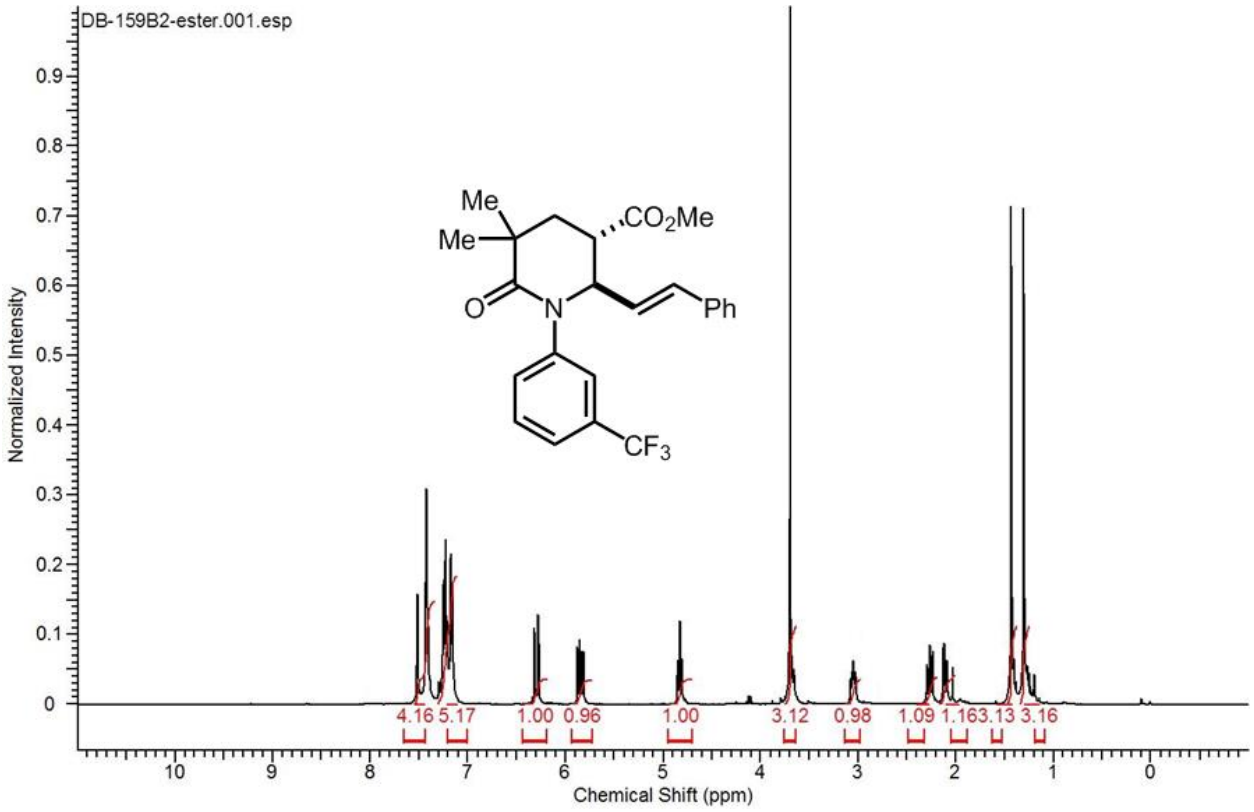
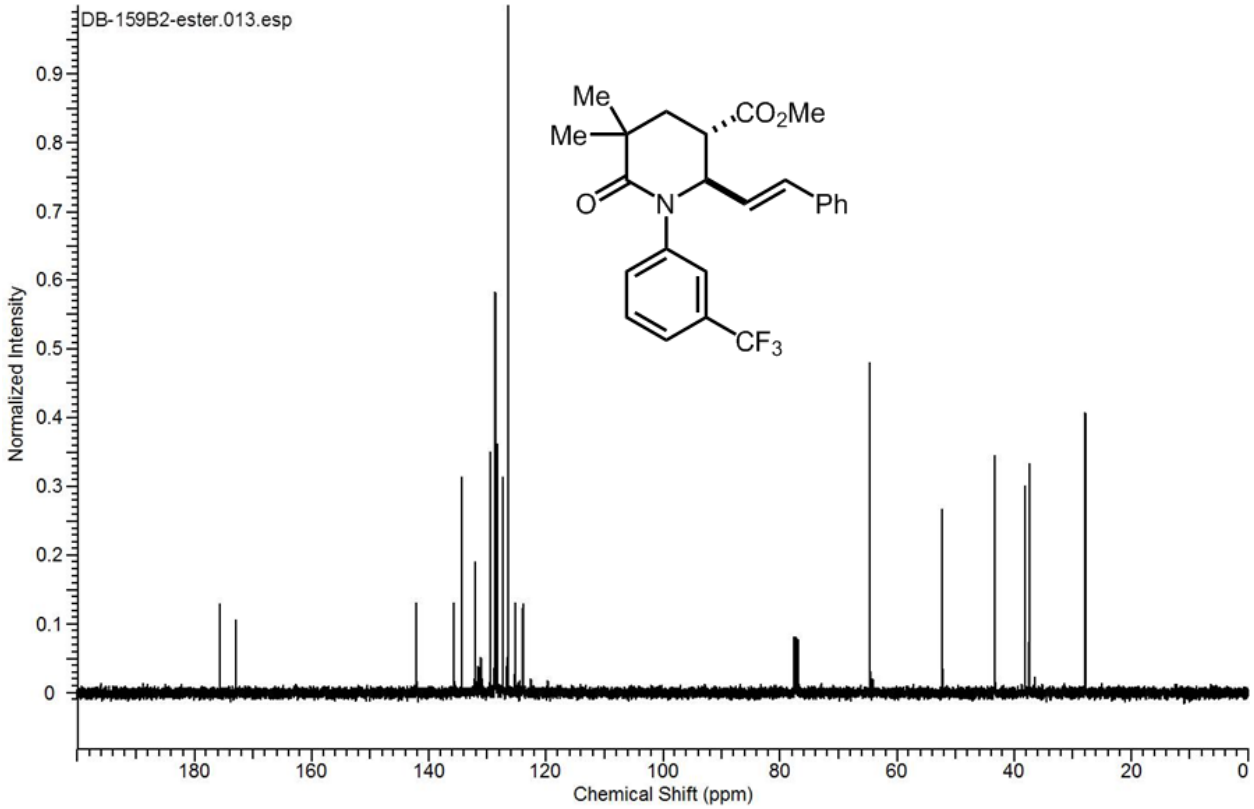
2.02
1.00
1.00
2.10
6.24
Me
Me
CO2H
O
N
Ph
CF3

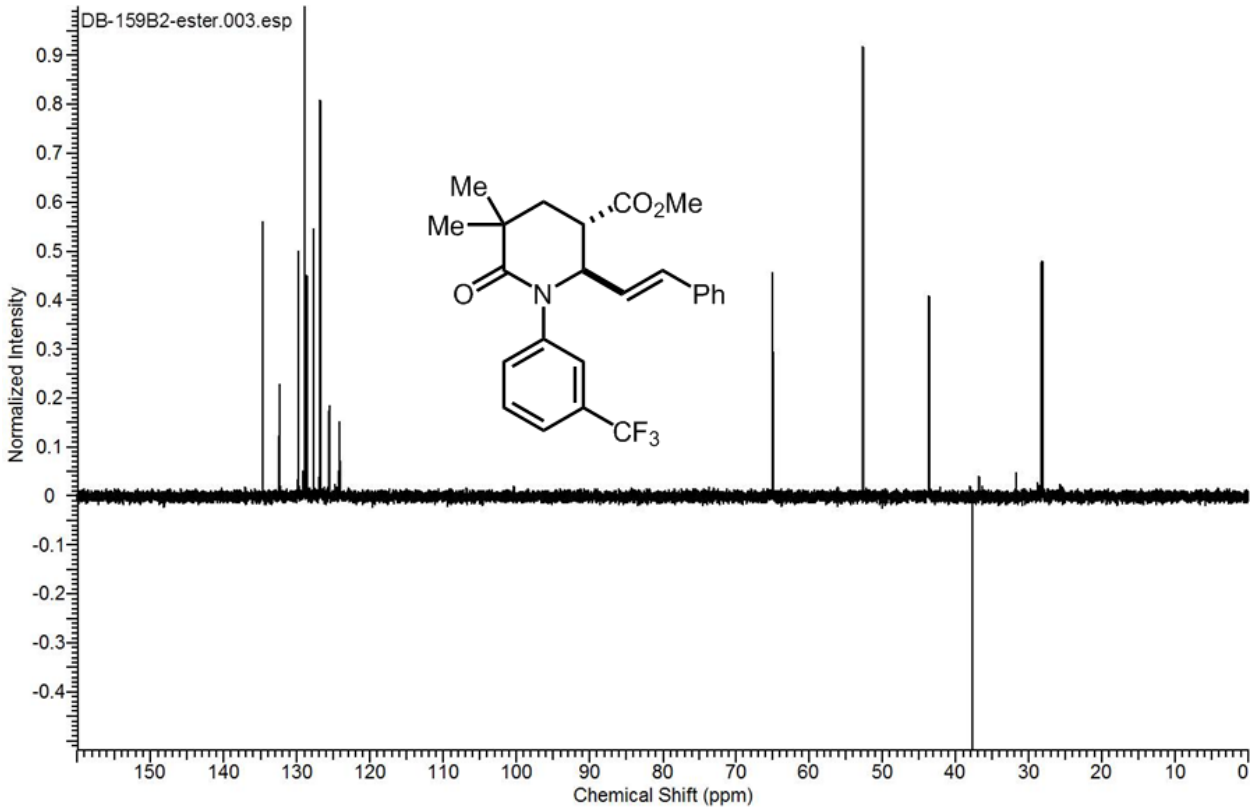

DB-159B-DMSO.013.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2H
O
N
Ph
CF3

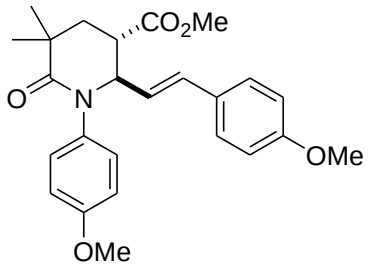

DB-159B-DMSO.003.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2H
O
N
Ph
CF3


M-aryl
Abundance
Scan 778 (9.143 min): DB-159B2.D\data.ms
m/z-->
Me
Me
CO2Me
O
N
Ph
CF3
MW = 431


DB-159B2-ester.001.esp
Normalized Intensity
Chemical Shift (ppm)
4.16 5.17 1.00 0.96 1.00 3.12 0.98 1.09 1.16 3.13 3.16
Me
Me
CO2Me
O
N
Ph
CF3

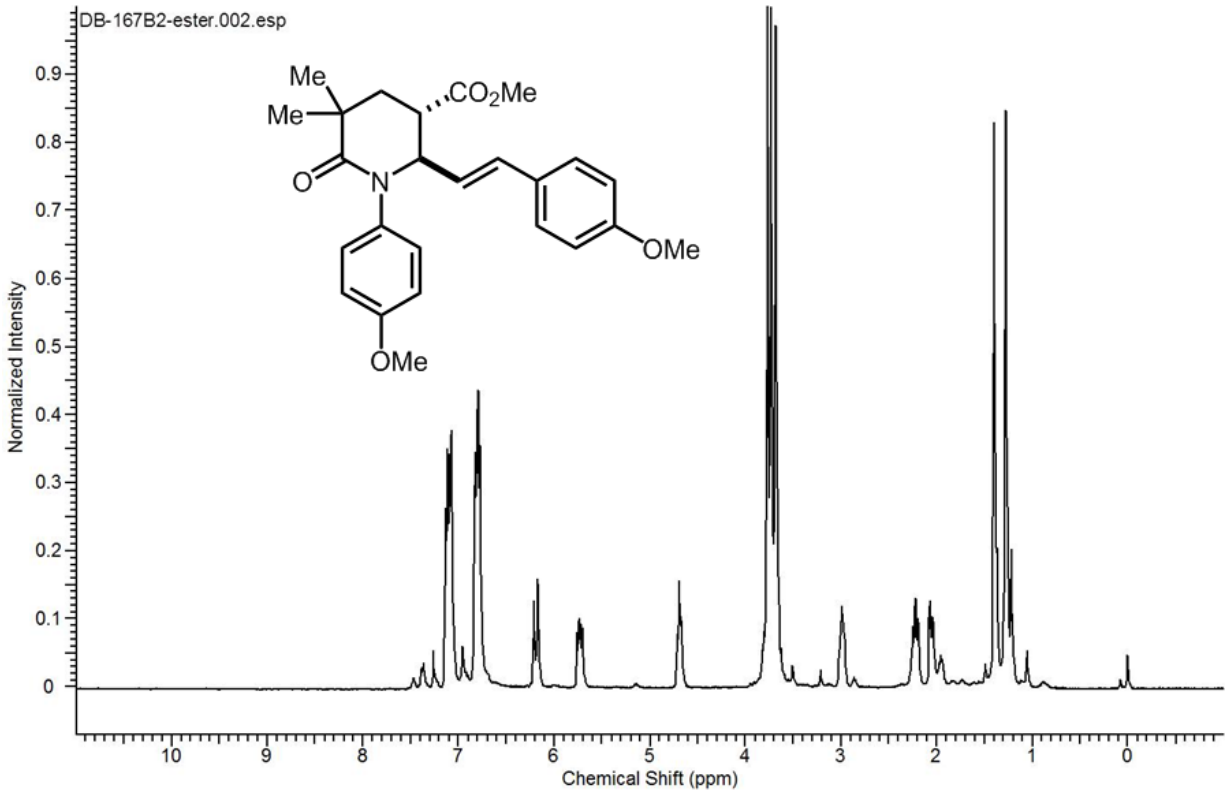

DB-159B2-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2Me
O
N
Ph
CF3

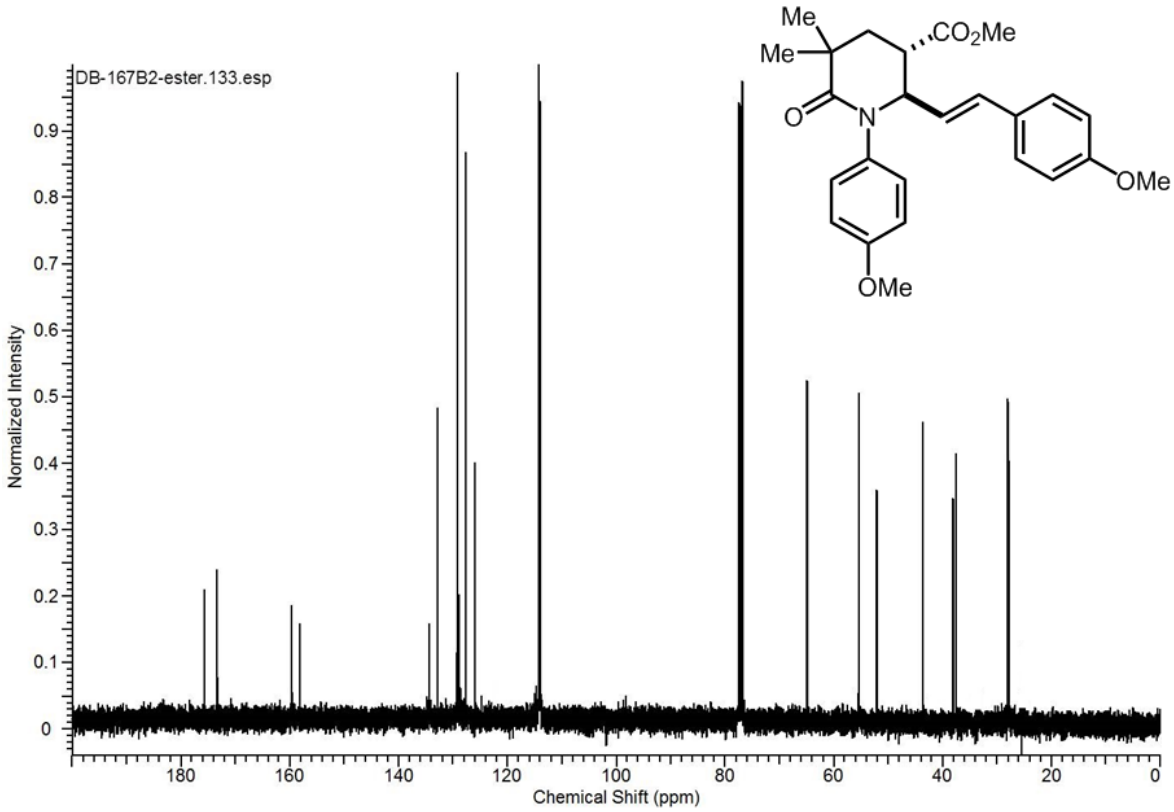


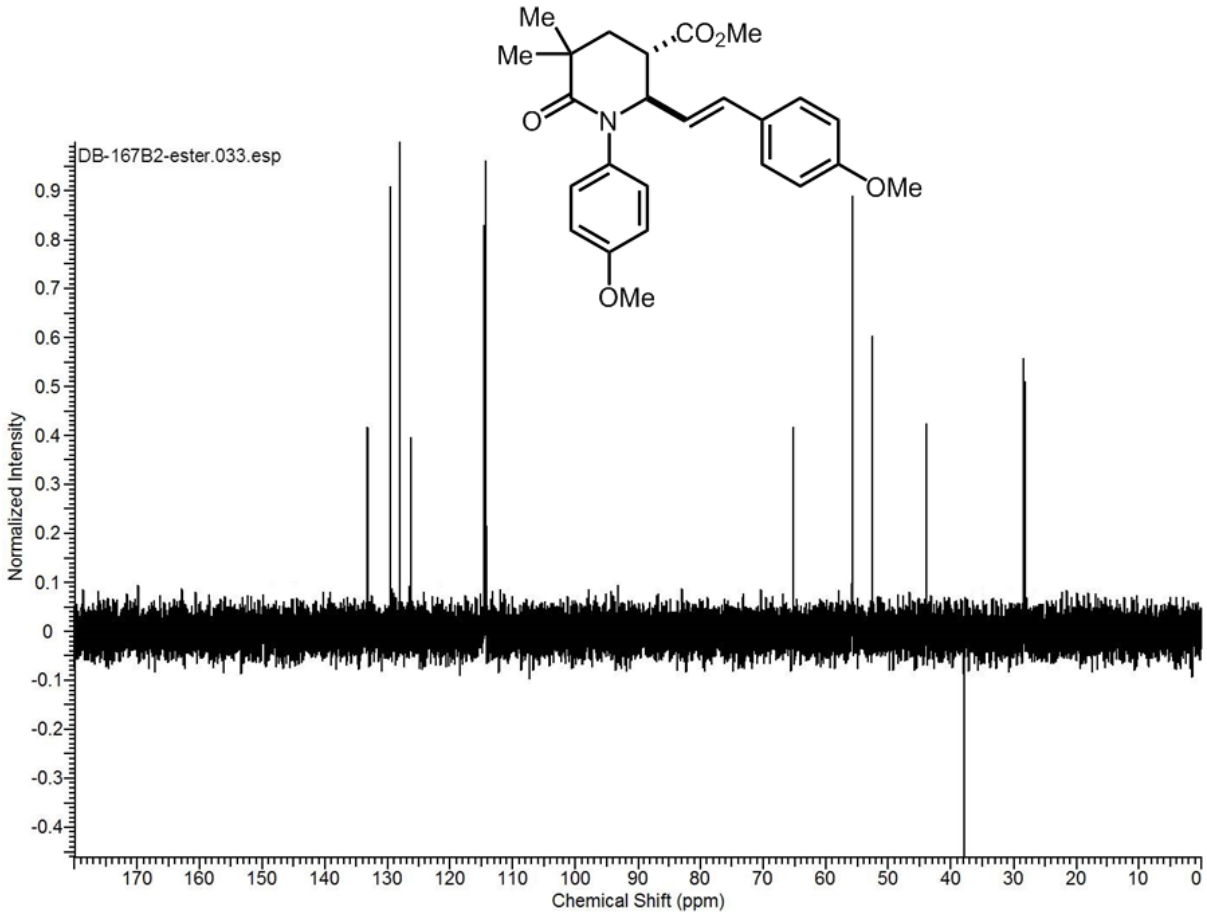


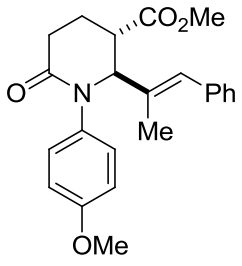
7i2

Prepared from imine **4f** (267 mg, 1.0 mmol) and 2,2-dimethyl glutaric anhydride (142 mg, 1.0 equiv), using General Procedures B and C. T = 105 ^{o}C, time = 22 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 351 mg, 83% over 2 steps, 96:4 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 to 7.07 (4H, m), 6.83 to 6.77 (4H, m), 6.21 to 6.17 (1H, d), 5.76 to 5.70 (1H, dd), 4.71 to 4.67 (1H, t), 3.82 to 3.68 (9H, m), 3.01 to 2.96 (1H, m), 2.25 to 2.19 (1H, dd), 2.08 to 1.92 (1H, dd), 1.40 to 1.37 (6H, s,s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.6, 173.3, 159.5, 158.1, 134.3, 132.8, 129.3, 129.0, 128.8, 128.6, 127.9, 127.7, 125.9, 114.6, 114.2, 114.0, 113.9, 64.8, 55.5, 55.3, 52.1, 43.6, 38.0, 37.5, 28.4, 28.0. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{25}H_{29}NO_5$ 423.2046; found 423.2051.


DB-167B2-ester.002.esp
Me
Me
CO2Me
O
N
OMe
OMe
Normalized Intensity
Chemical Shift (ppm)

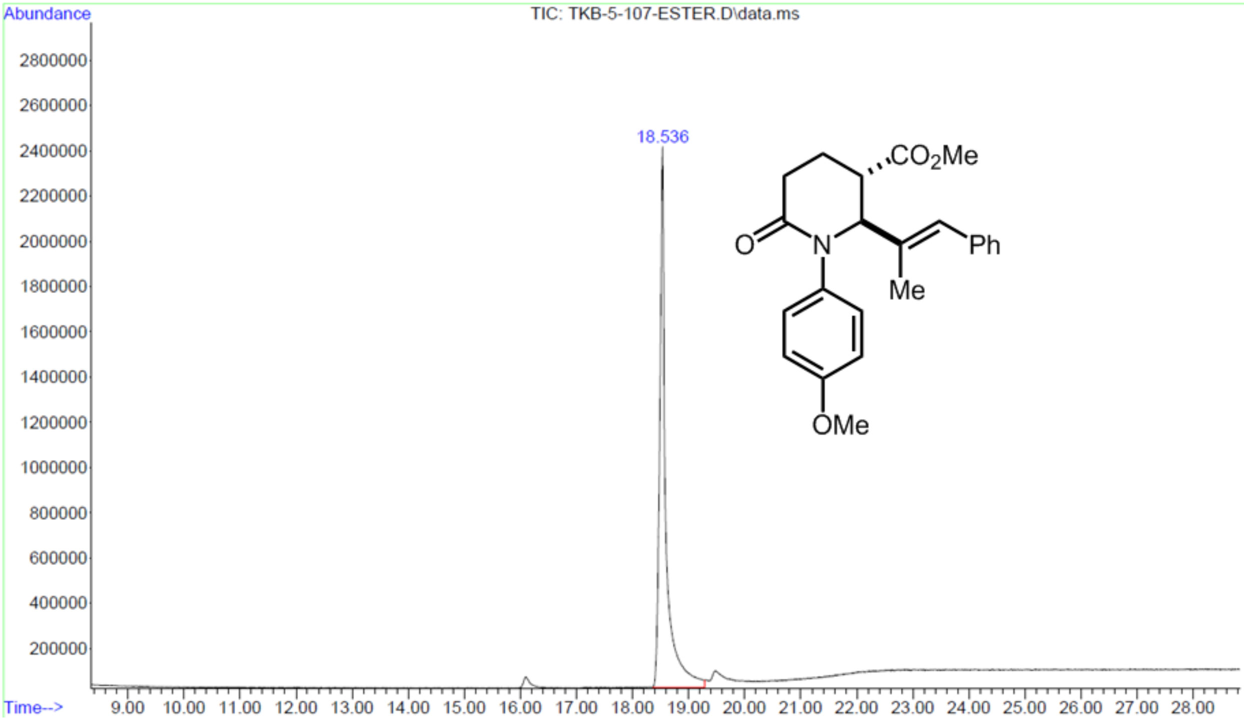

DB-167B2-ester.133.esp
Me
Me
CO2Me
O
N
OMe
OMe
Normalized Intensity
Chemical Shift (ppm)





7j2

Prepared from imine **4i** (251 mg, 1.0 mmol) and glutaric anhydride (114 mg, 1.0 equiv), using General Procedures B and C. T = 105 ^{o}C, time = 18 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 300 mg, 79% over 2 steps, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 to 7.12 (7H, m), 6.88 (2H, d), 6.43 (1H, s), 4.75 (1H, d), 3.77 to 3.66 (6H, s,s), 2.87 to 2.85 (1H, m), 2.71 to 2.58 (2H, m), 2.26 to 2.20 (2H, m), 1.80 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 170.0, 158.2, 136.8, 134.5, 129.7, 128.8, 128.4, 128.2, 126.9, 114.2, 69.6, 55.4, 52.4, 42.9, 30.4, 21.1, 15.3. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{23}H_{25}NO_4$ 379.1784; found 379.1789.


Abundance
TIC: TKB-5-107-ESTER.D\data.ms
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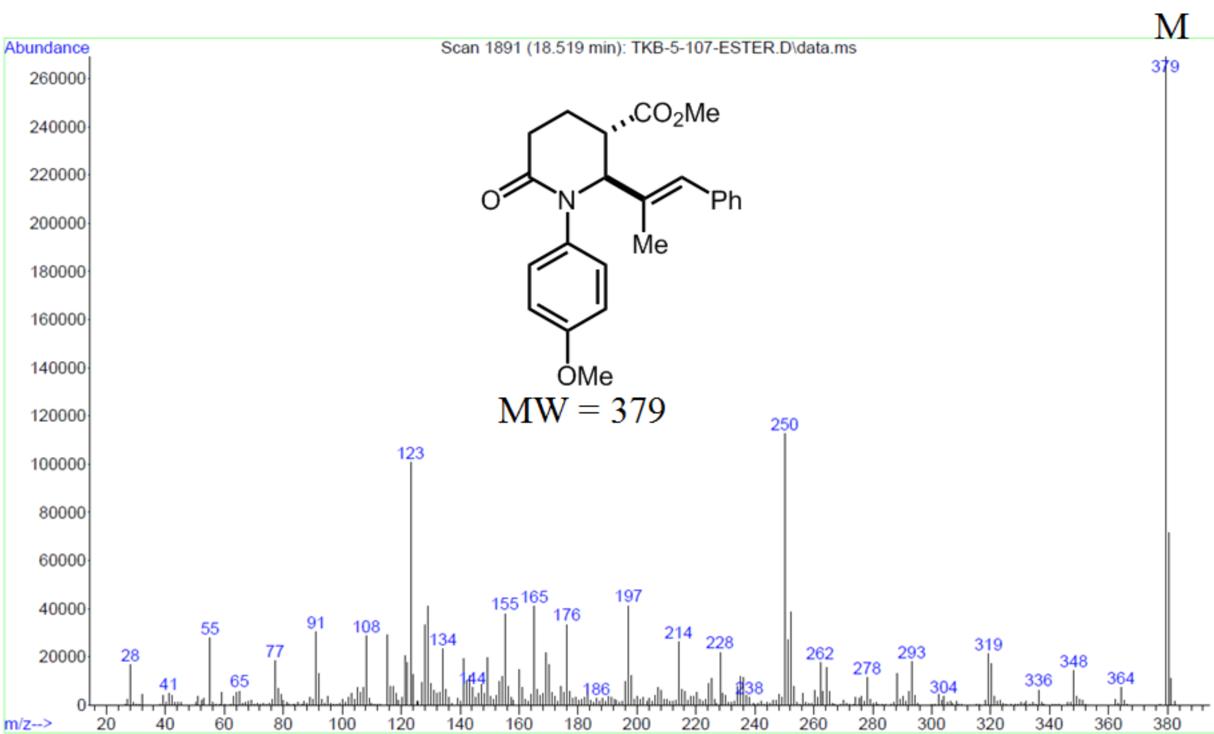
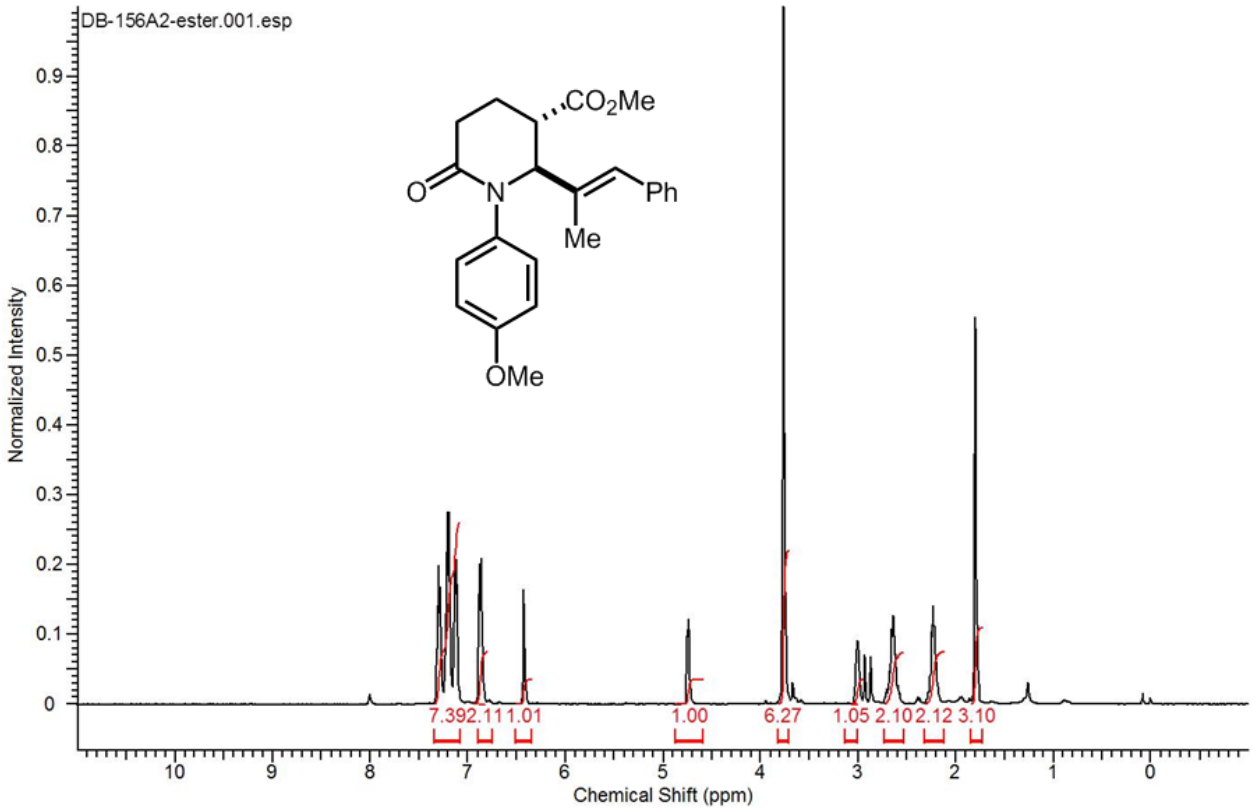
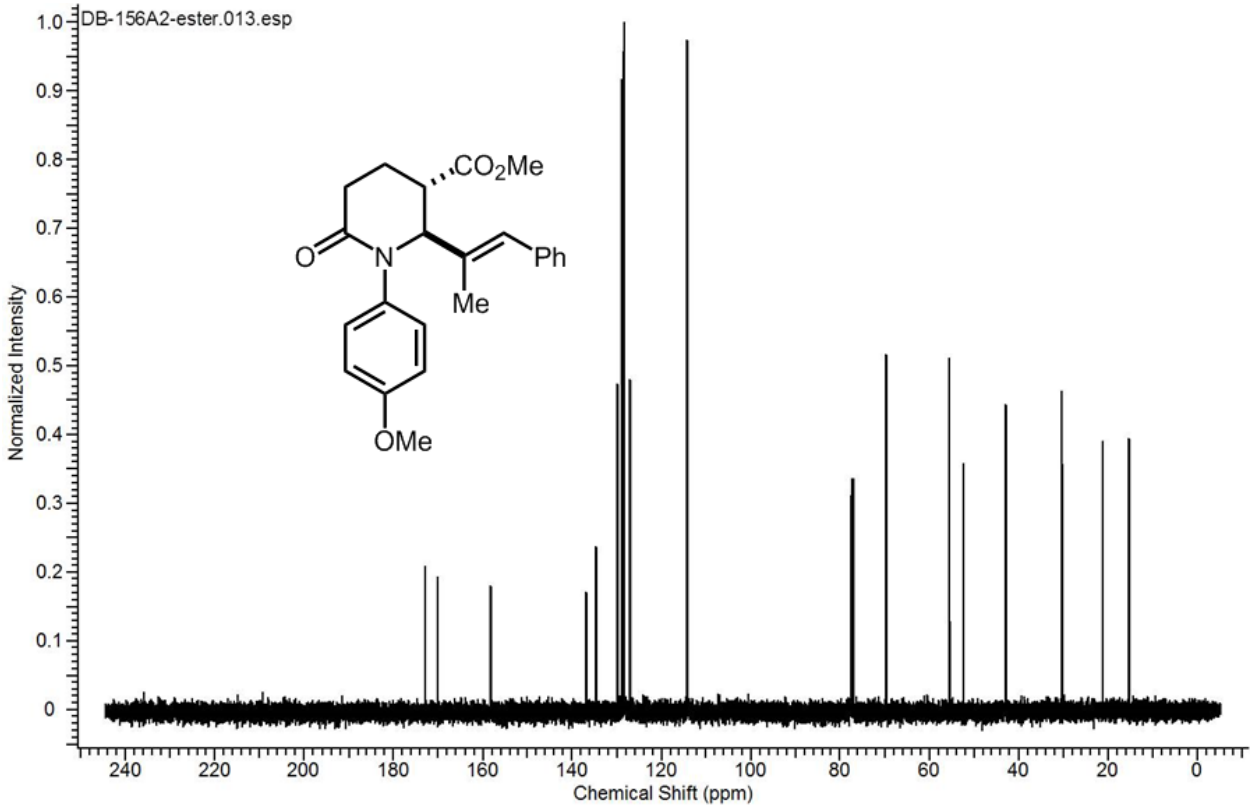
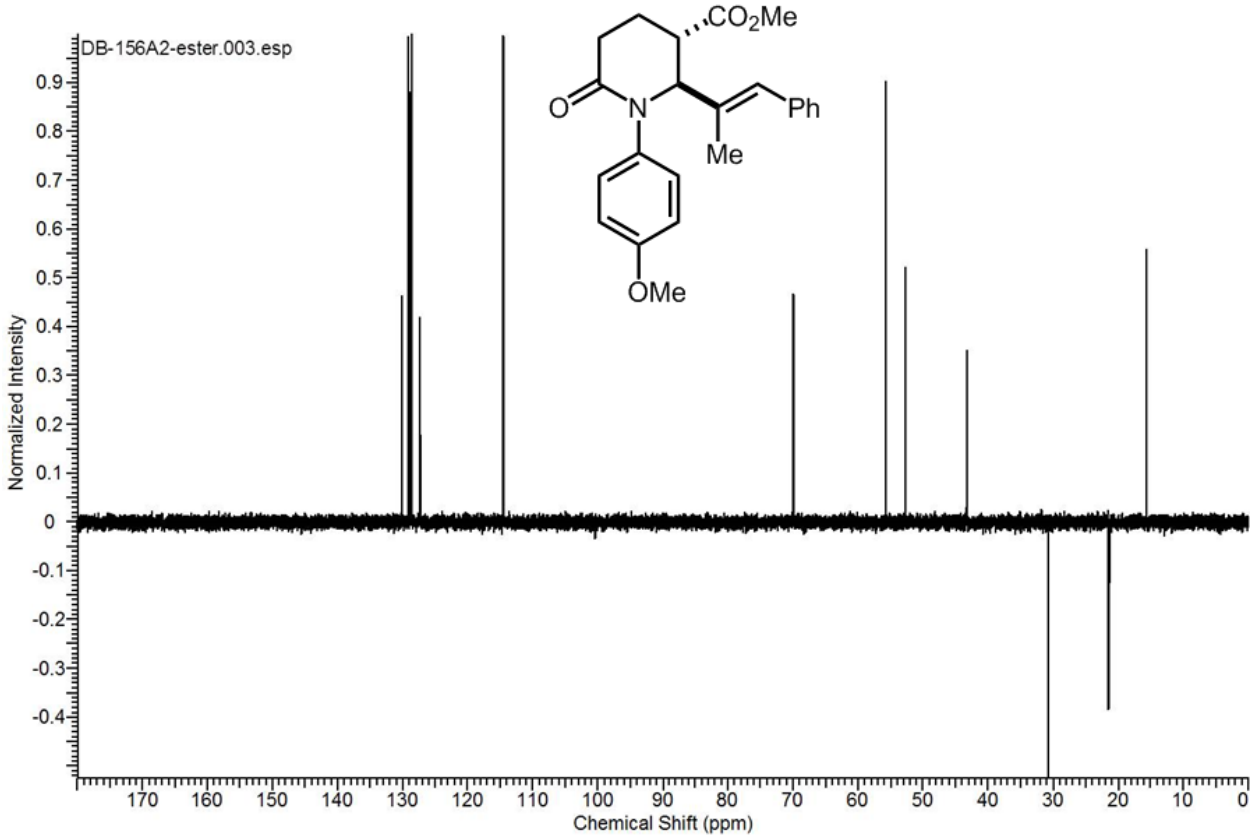
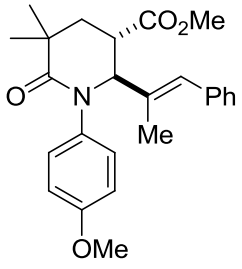
2600000
2400000
2200000
2000000
1800000
1600000
1400000
1200000
1000000
800000
600000
400000
200000
18.536
CO2Me
O
N
Ph
Me
OMe
Time-->
9.00 10.00 11.00 12.00 13.00 14.00 15.00 16.00 17.00 18.00 19.00 20.00 21.00 22.00 23.00 24.00 25.00 26.00 27.00 28.00


M
Abundance
Scan 1891 (18.519 min): TKB-5-107-ESTER.D\data.ms
379
CO2Me
O
N
Ph
Me
OMe
MW = 379
250
123
155 165
176
197
214
228
91
108
134
55
77
28
41
65
144
186
238
262
278
293
304
319
336
348
364
m/z-->
20 40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340 360 380


DB-156A2-ester.001.esp
Normalized Intensity
Chemical Shift (ppm)
7.39 2.11 1.01 1.00 6.27 1.05 2.10 2.12 3.10
CO2Me
Ph
Me
OMe

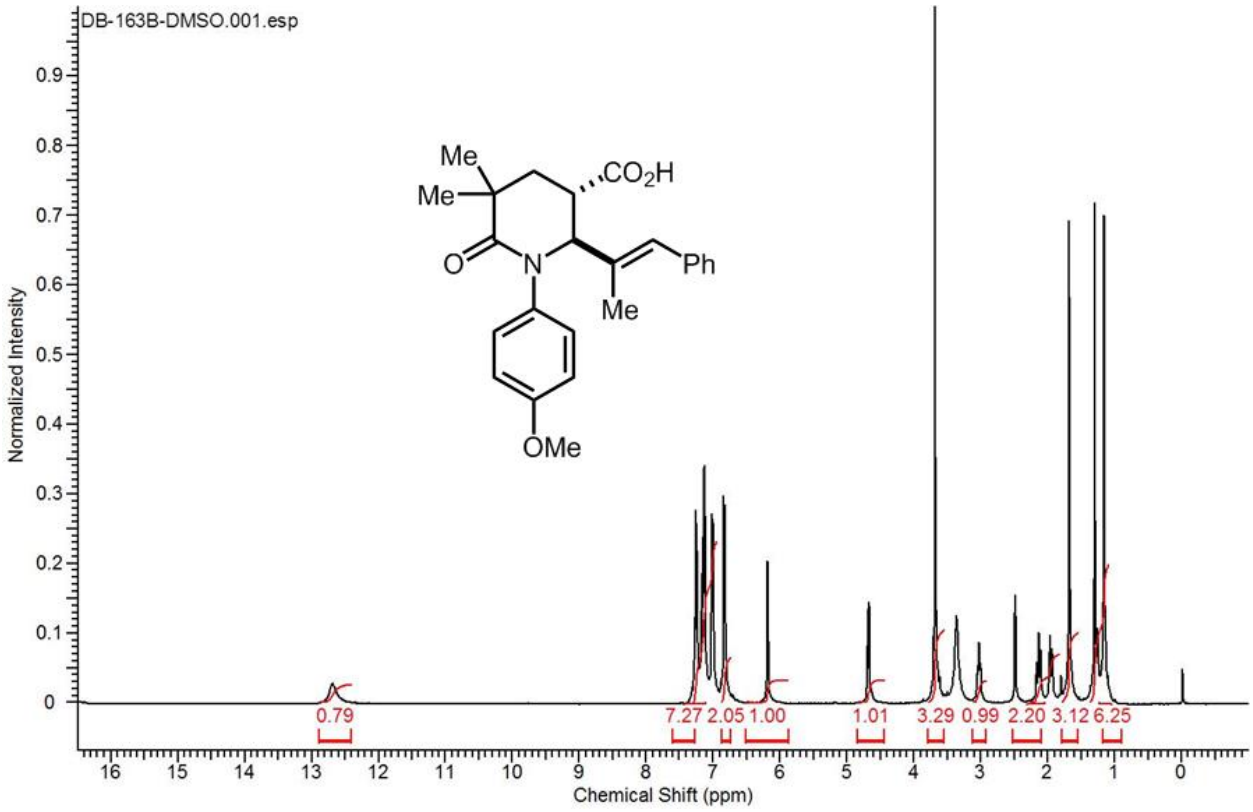

DB-156A2-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
Me
OMe

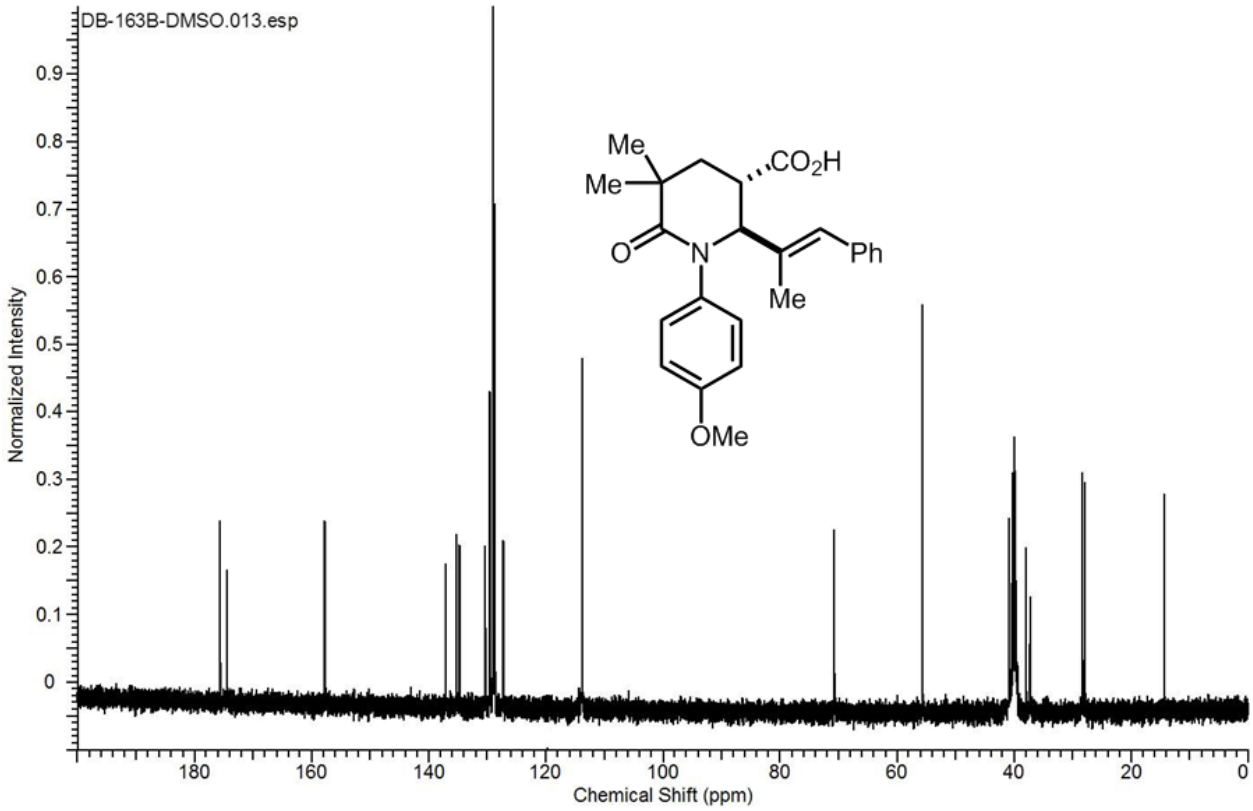


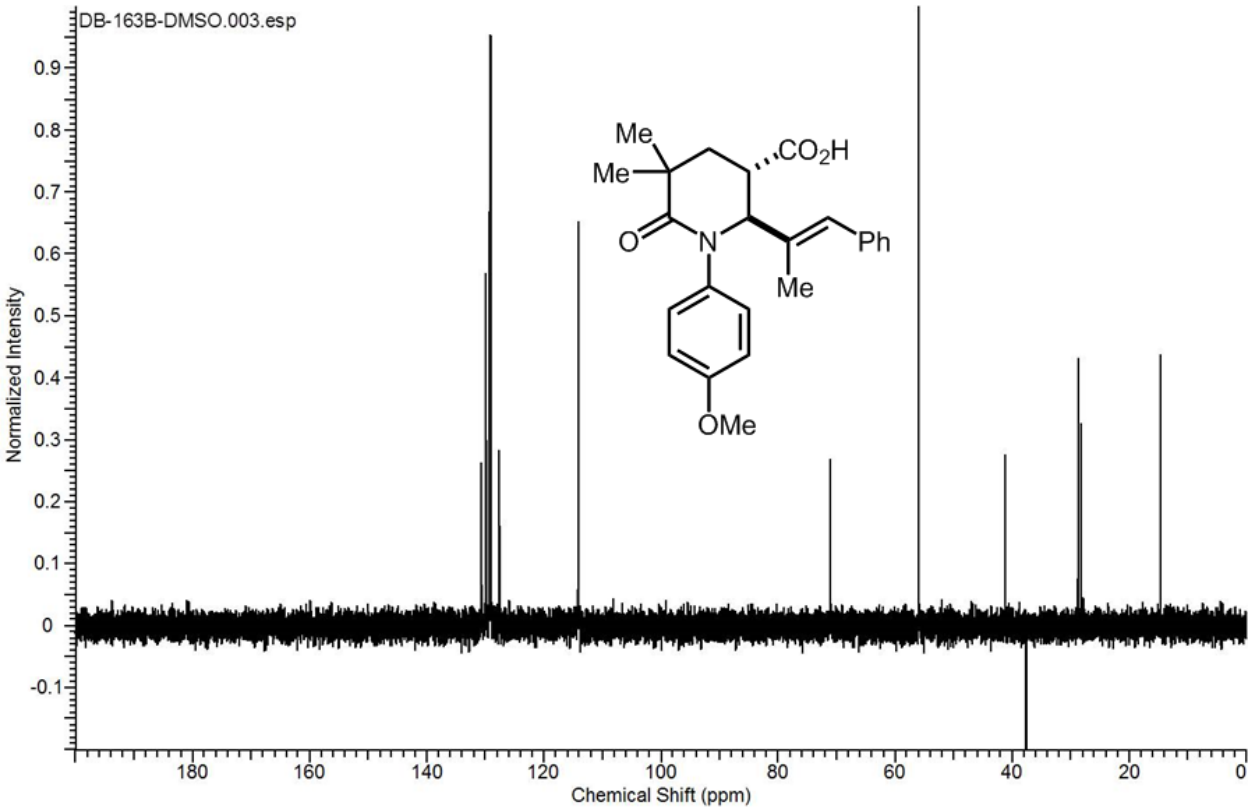


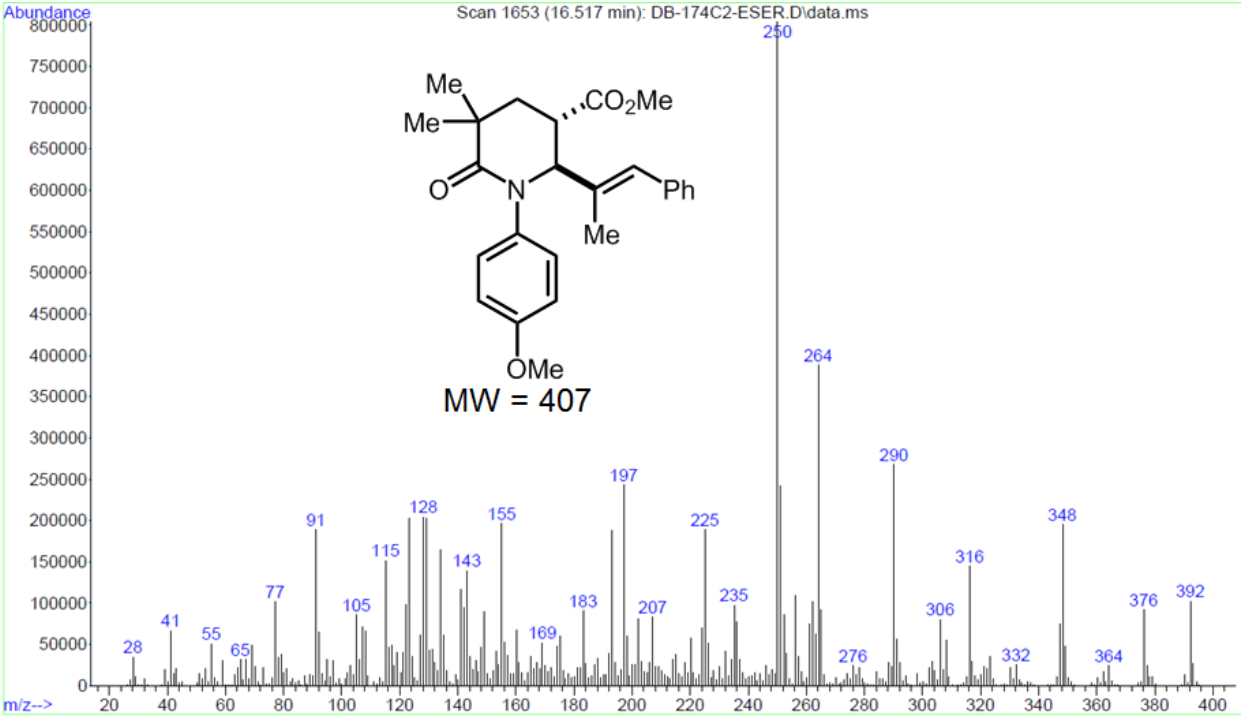
7k2

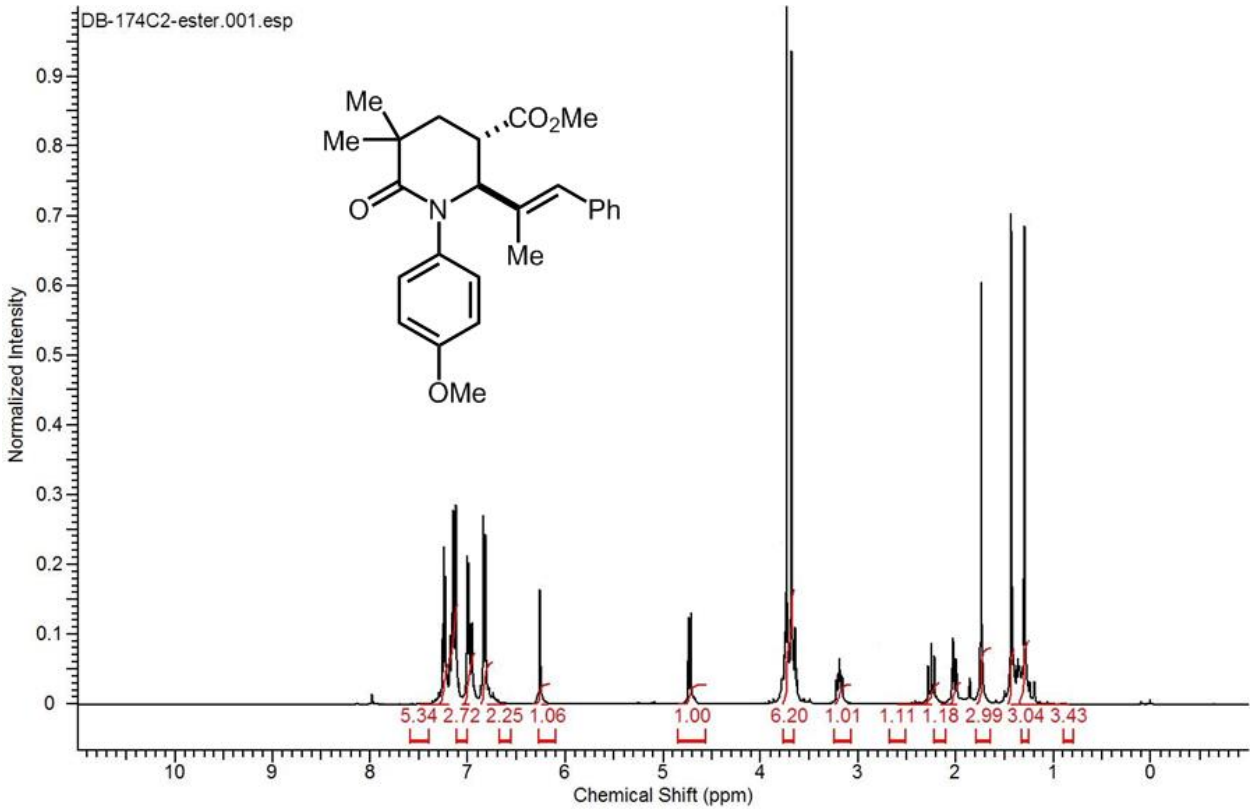
Prepared from imine **4i** (251 mg, 1.0 mmol) and 2,2-dimethyl glutaric anhydride (142 mg, 1.0 equiv), using General Procedures B and C. Temp = 110 ^{o}C, time = 36 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 300 mg, 79% over 2 steps, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 to 7.09 (5H, m), 7.01 to 6.96 (2H, d), 6.78 to 6.74 (2H, d), 6.26 (1H, s), 4.68 (1H, d), 3.78 to 3.73 (6H, s,s), 3.22 to 3.16 (1H, m), 2.31 to 2.19 (1H, dd), 2.03 to 1.97 (1H, dd), 1.74 (3H, s), 1.43 (3H, s), 1.41 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.1, 173.3, 159.3, 136.8, 134.2, 133.8, 132.9, 131.3, 131.2, 129.3, 129.0, 128.9, 128.8, 128.7, 128.4, 128.2, 128.1, 127.9, 127.1, 126.8, 114.5, 70.8, 55.4, 52.2, 41.78, 38.7, 38.1, 28.6, 28.2, 27.0, 13.7. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{25}H_{29}NO_4$ 407.2097; found 407.2093.

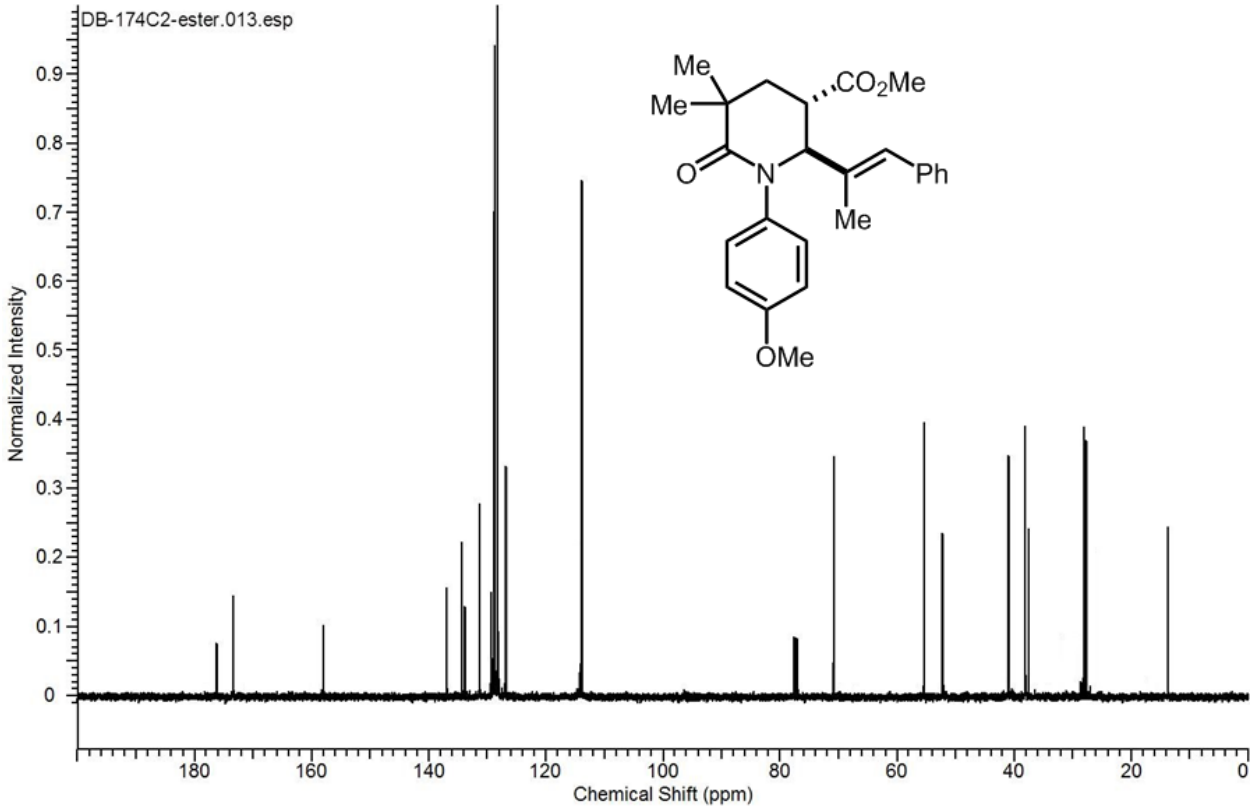

DB-163B-DMSO.001.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2H
O
N
Ph
Me
OMe
0.79
7.27
2.05
1.00
1.01
3.29
0.99
2.20
3.12
6.25

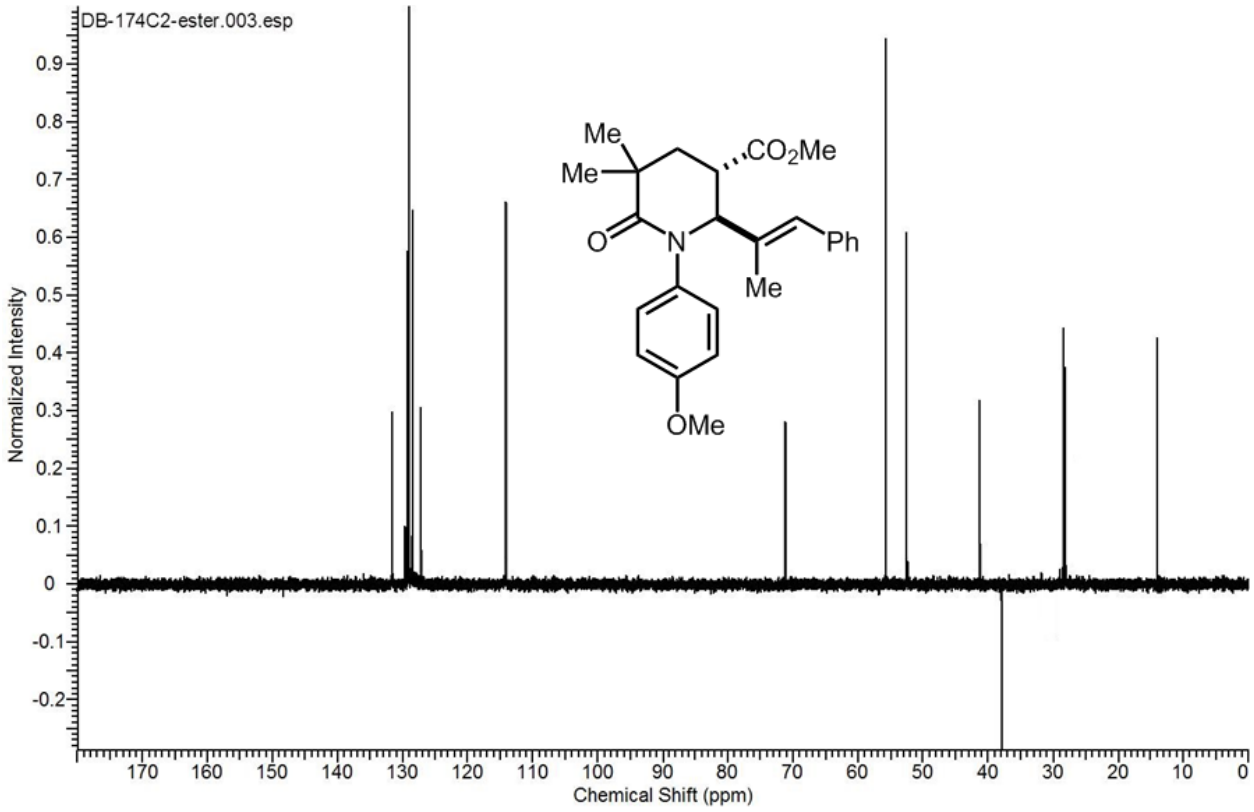

DB-163B-DMSO.013.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2H
O
N
Ph
Me
OMe

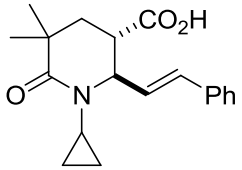

DB-163B-DMSO.003.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2H
O
N
Ph
Me
OMe


Abundance
Scan 1653 (16.517 min): DB-174C2-ESER.D\data.ms
m/z-->
Me
Me
CO2Me
O
N
Ph
Me
OMe
MW = 407


DB-174C2-ester.001.esp
Me
Me
CO2Me
O
N
Ph
Me
OMe
Normalized Intensity
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
5.34 2.72 2.25 1.06
1.00
6.20 1.01 1.11 1.18 2.99 3.04 3.43
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

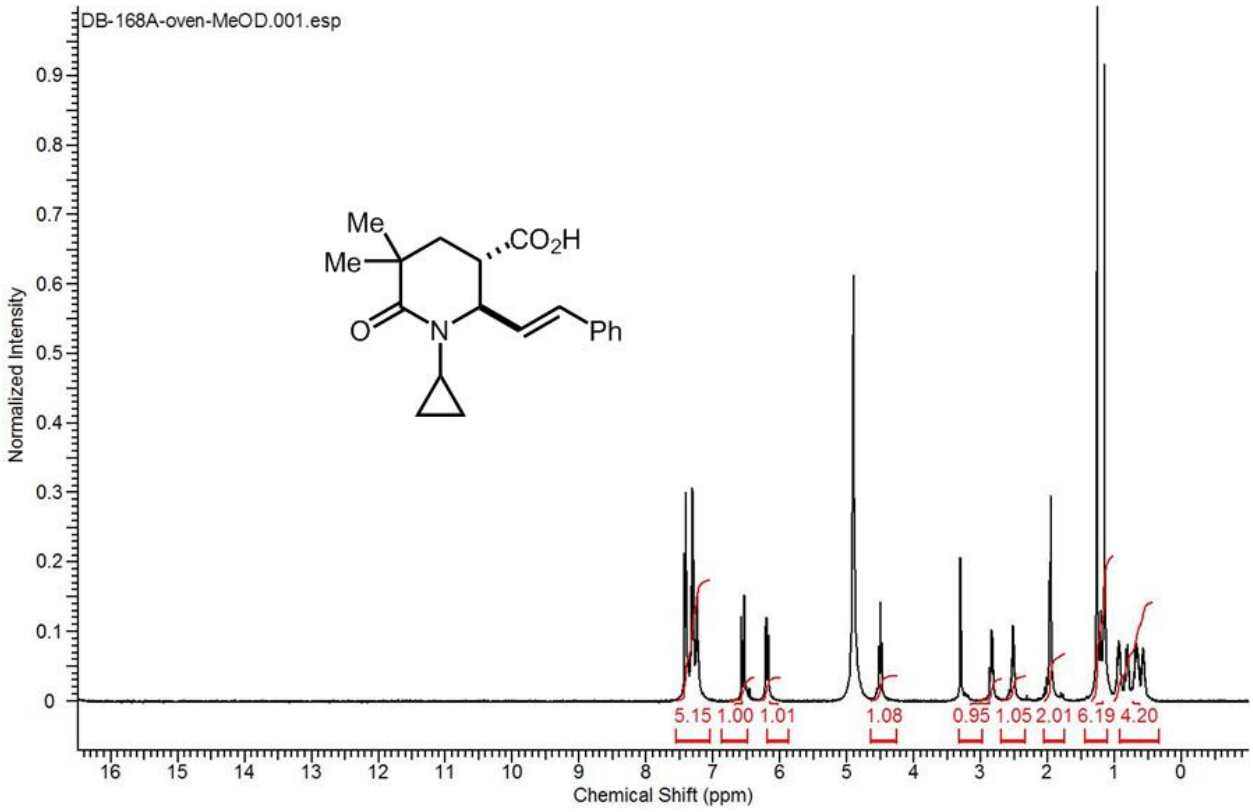

DB-174C2-ester.013.esp
Me
Me
CO2Me
O
N
Ph
Me
OMe
Normalized Intensity
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

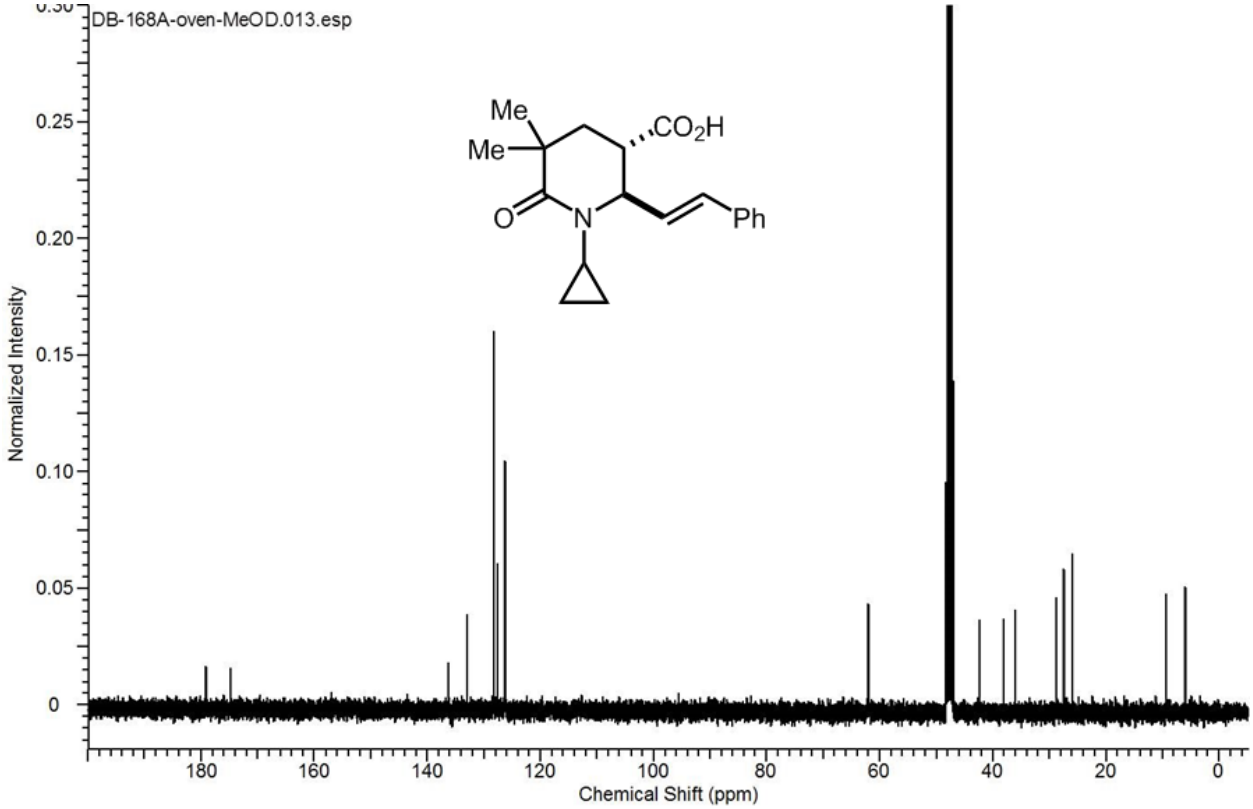


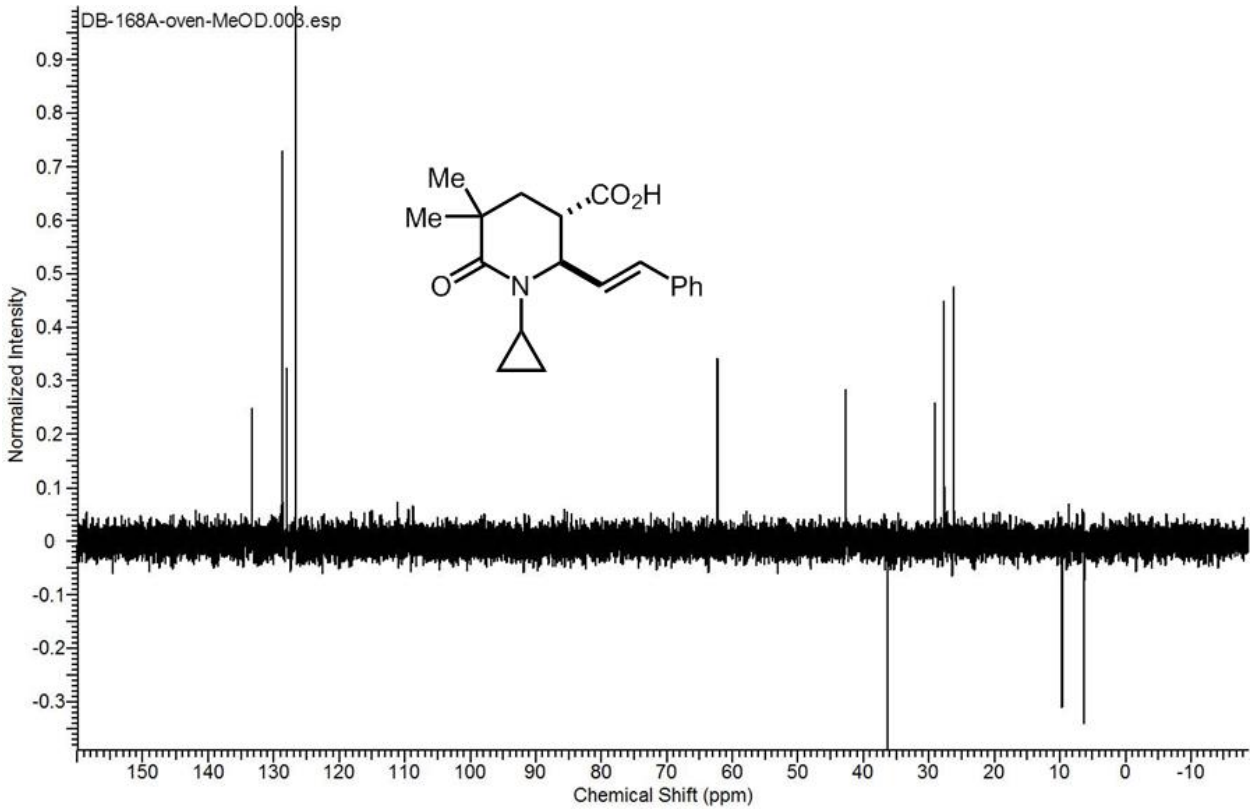


7i1

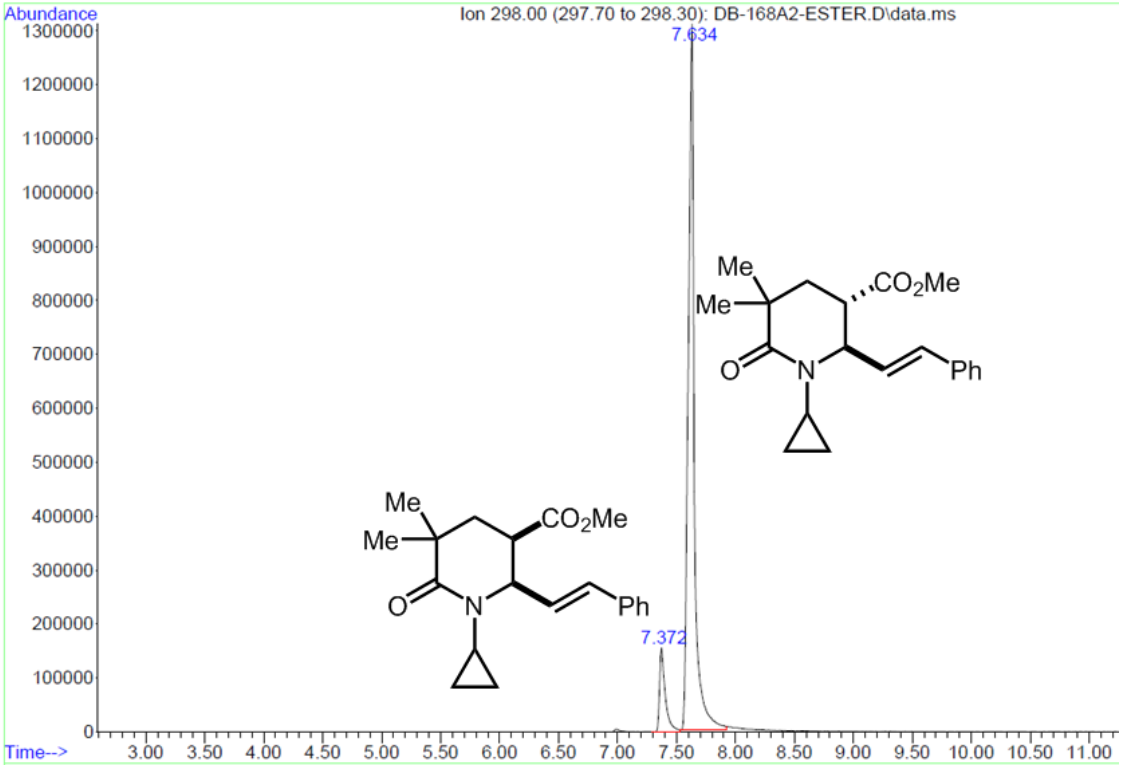
Prepared from imine **4k** (171 mg, 1.0 mmol) and 2,2-dimethyl glutaric anhydride (142 mg, 1.0 equiv), using General Procedures B and C. Temp = 100 ^{o}C, time = 18 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 235 mg, 75%, 98:2 dr. ^{1}H NMR (400 MHz, MeOH) δ 11.12 (1H, br. s), 7.42 to 7.22 (5H, m), 6.53 to 6.50 (1H, d), 6.22 to 6.16 (1H, dd), 4.50 to 4.48 (1H, t), 2.86 to 2.81 (1H, t), 2.57 to 2.48 (1H, t), 1.80 to 1.77 (2H, m), 1.26 to 0.53 (10H, m). ^{13}C NMR (101 MHz, MeOH) δ 179.1, 174.7, 136.2, 132.9, 128.3, 127.6, 126.2, 61.9, 48.2, 48.0, 48.0, 47.8, 47.8, 47.65, 47.5, 47.4, 47.3, 47.2, 47.1, 47.0, 42.3, 38.0, 36.0, 28.7, 27.3, 25.9, 9.34, 5.9. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{19}H_{23}NO_3$ 313.1678; found 313.1683.

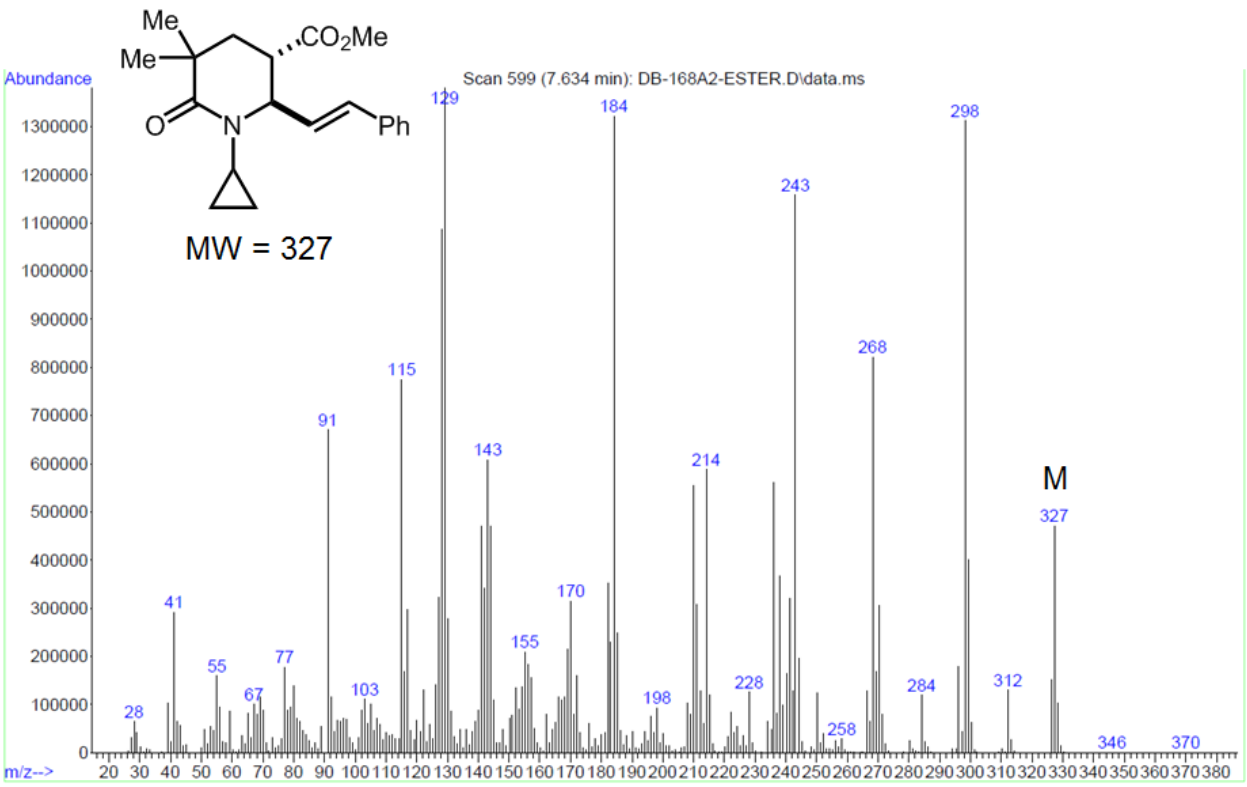

DB-168A-oven-MeOD.001.esp
Normalized Intensity
Chemical Shift (ppm)
5.15 1.00 1.01 1.08 0.95 1.05 2.01 6.19 4.20
Me
Me
CO2H
O
N
Ph

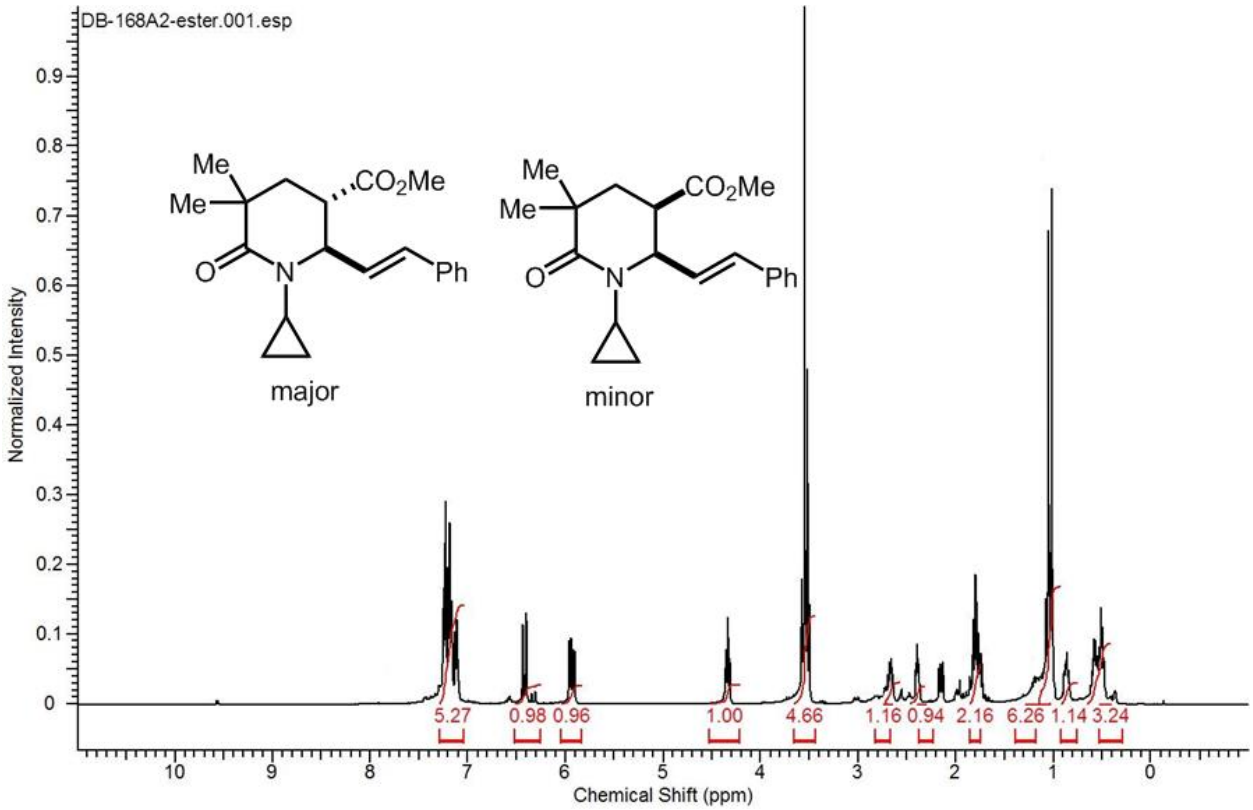

DB-168A-oven-MeOD.013.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2H
O
N
Ph

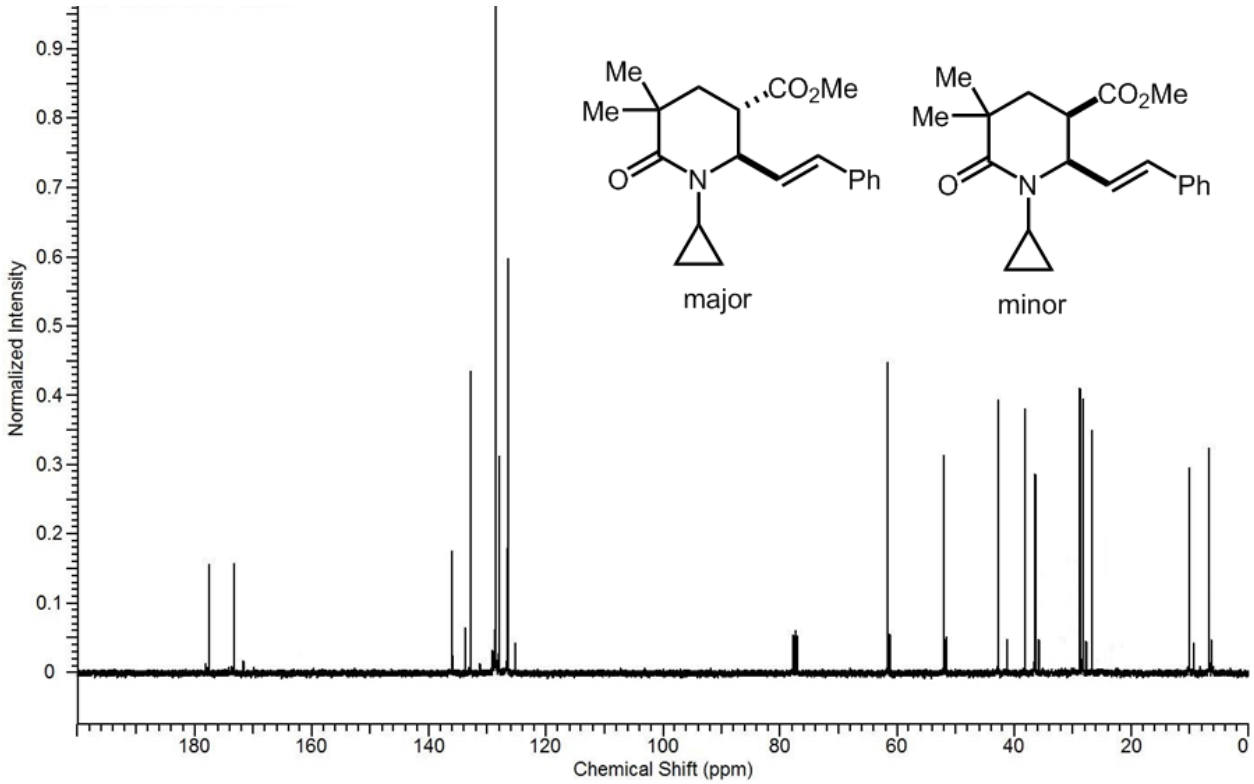


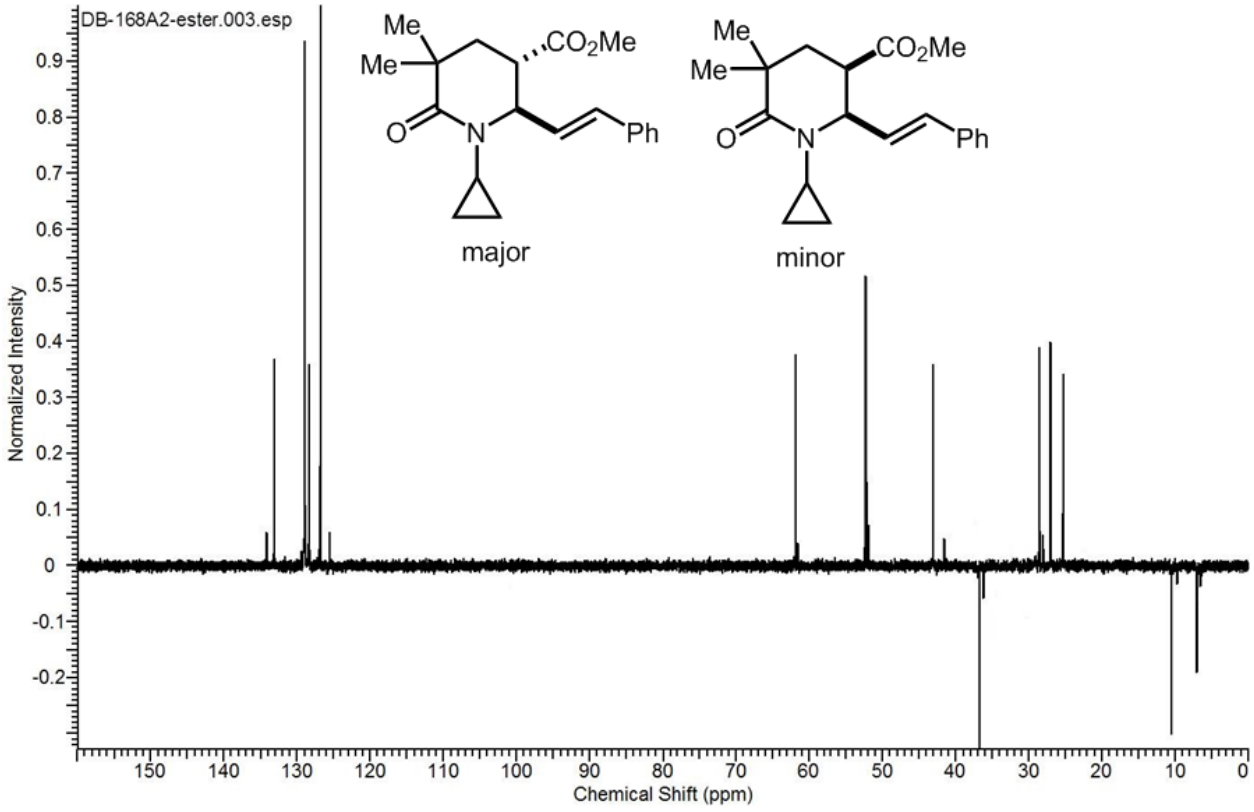
Methylation of the ester led to some minimal epimerization

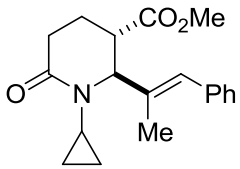



Me
Me
CO2Me
O
N
Ph
MW = 327
Abundance
Scan 599 (7.634 min): DB-168A2-ESTER.D\data.ms
M
m/z-->


DB-168A2-ester.001.esp
major
minor
Normalized Intensity
5.27
0.98
0.96
1.00
4.66
1.16
0.94
2.16
6.26
1.14
3.24
Chemical Shift (ppm)

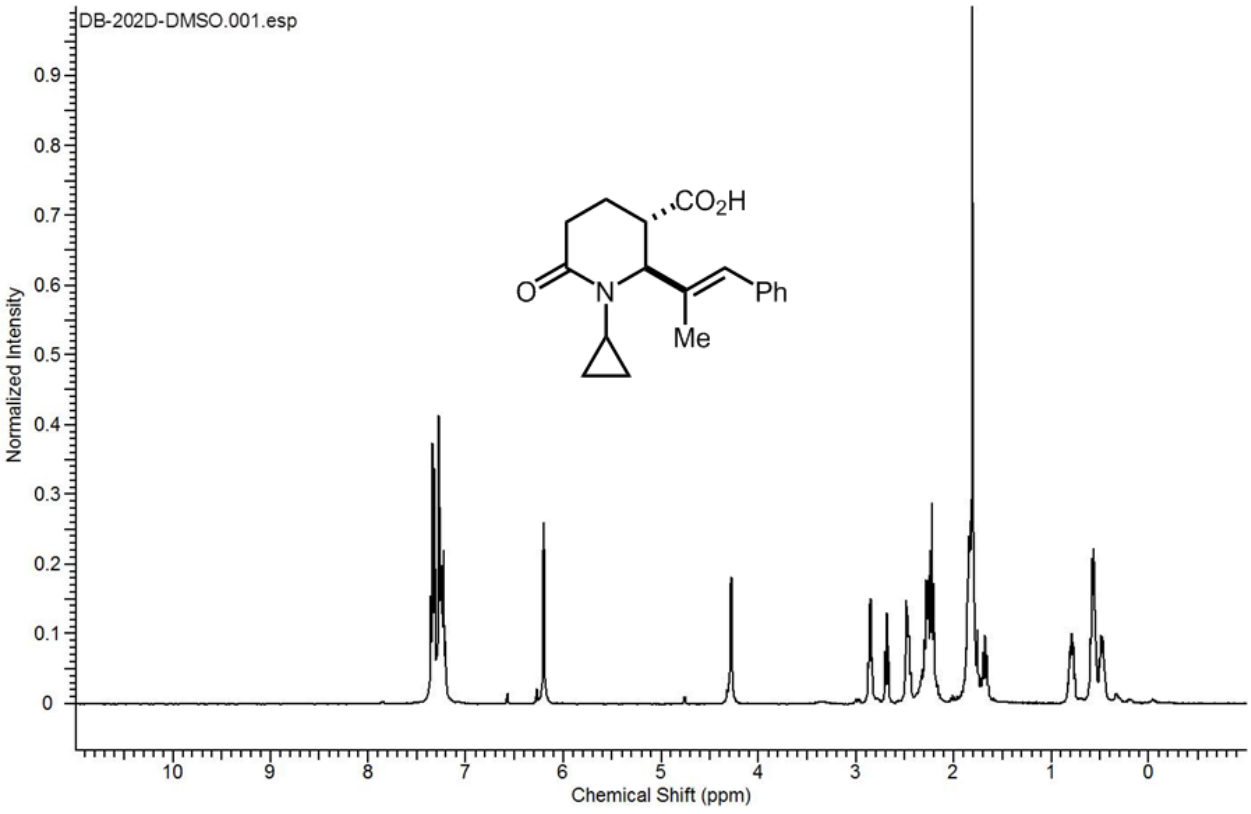

Me
Me
CO2Me
O
N
Ph
major
minor
Normalized Intensity
Chemical Shift (ppm)

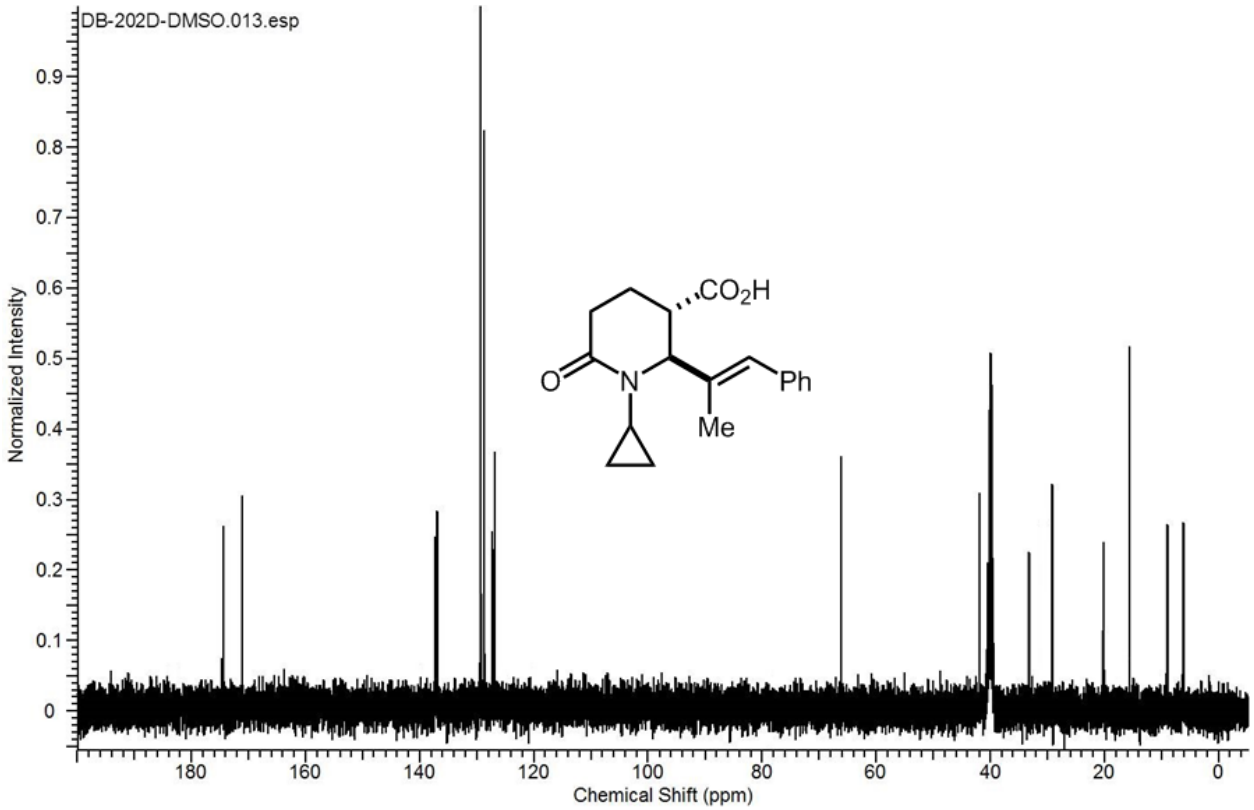

DB-168A2-ester.003.esp
major
minor
Normalized Intensity
Chemical Shift (ppm)

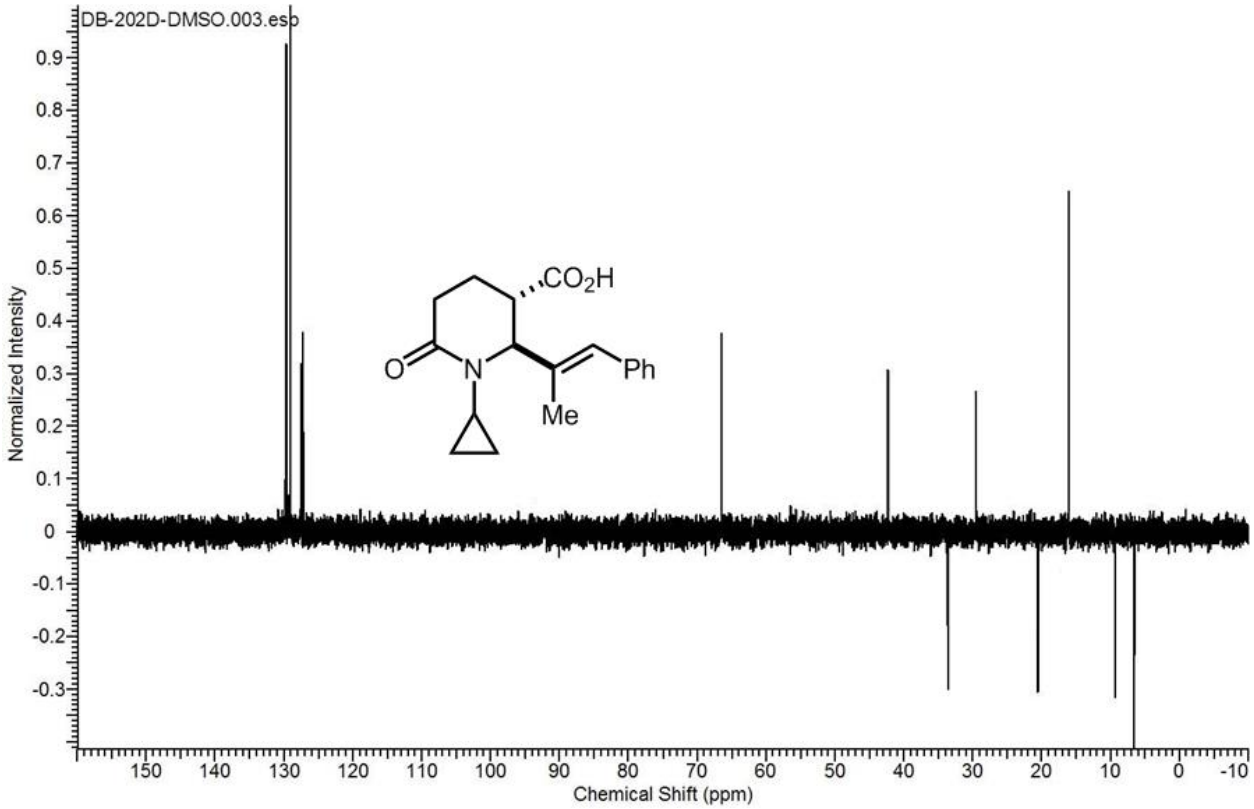


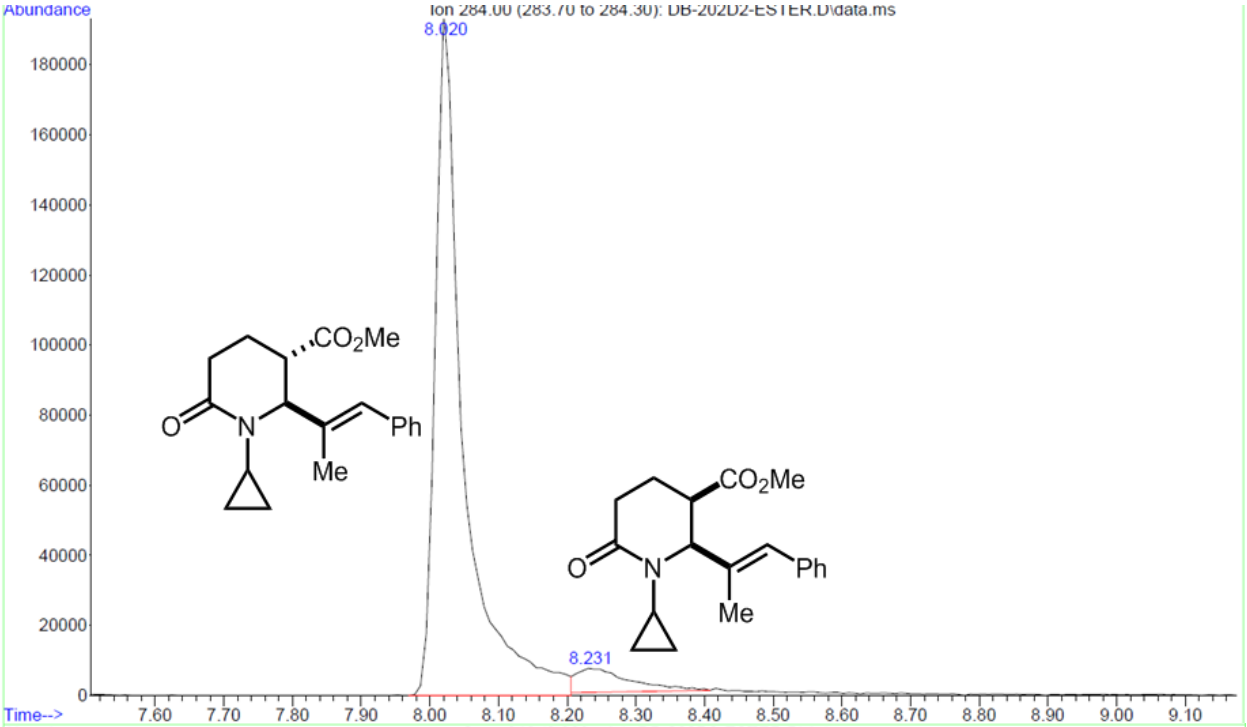
7m2

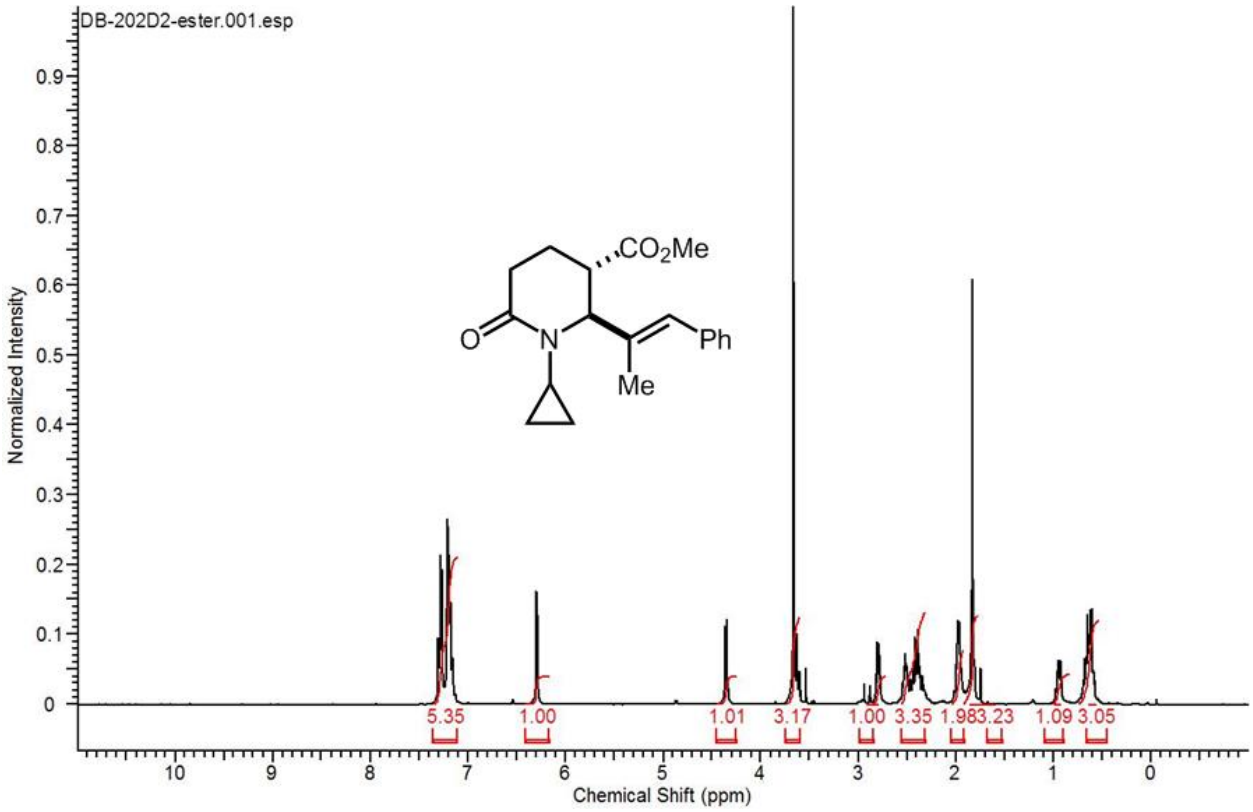
Prepared from imine **4l** (185 mg, 1.0 mmol) and glutaric anhydride (114 mg, 1.0 equiv), using General Procedures B and C. Temp = 100 ^{o}C, time = 18 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 226 mg, 72% over 2 steps, 98:2 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 to 7.13 (5H, m), 6.30 (1H, s), 4.36 to 4.33 (1H, d), 3.69 (3H, s), 2.88 to 2.80 (1H, dd), 2.54 to 2.30 (3H, m), 1.89 to 1.75 (5H, m), 0.96 to 0.91 (1H, m), 0.70 to 0.51 (3H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 171.7, 136.8, 135.2, 129.1, 128.9, 128.4, 128.2, 128.2, 128.2, 128.1, 127.0, 126.9, 66.2, 51.9, 42.3, 30.4, 28.0, 20.1, 16.4, 8.8, 5.6. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{19}H_{23}NO_3$ 313.1678; found 313.1683.




DB-202D-DMSO.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
O
N
Ph
Me


DB-202D-DMSO.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
O
N
Ph
Me


Abundance
Ion 284.00 (283.70 to 284.30): DB-202D2-ESTER.D\data.ms
8.020
8.231
CO2Me
Ph
Me
Time-->
Abundance
Scan 646 (8.028 min): DB-202D2-ESTER.D\data.ms
MW = 313
M
313
m/z-->


DB-202D2-ester.001.esp
Normalized Intensity
Chemical Shift (ppm)
5.35
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1.01
3.17
1.00
3.35
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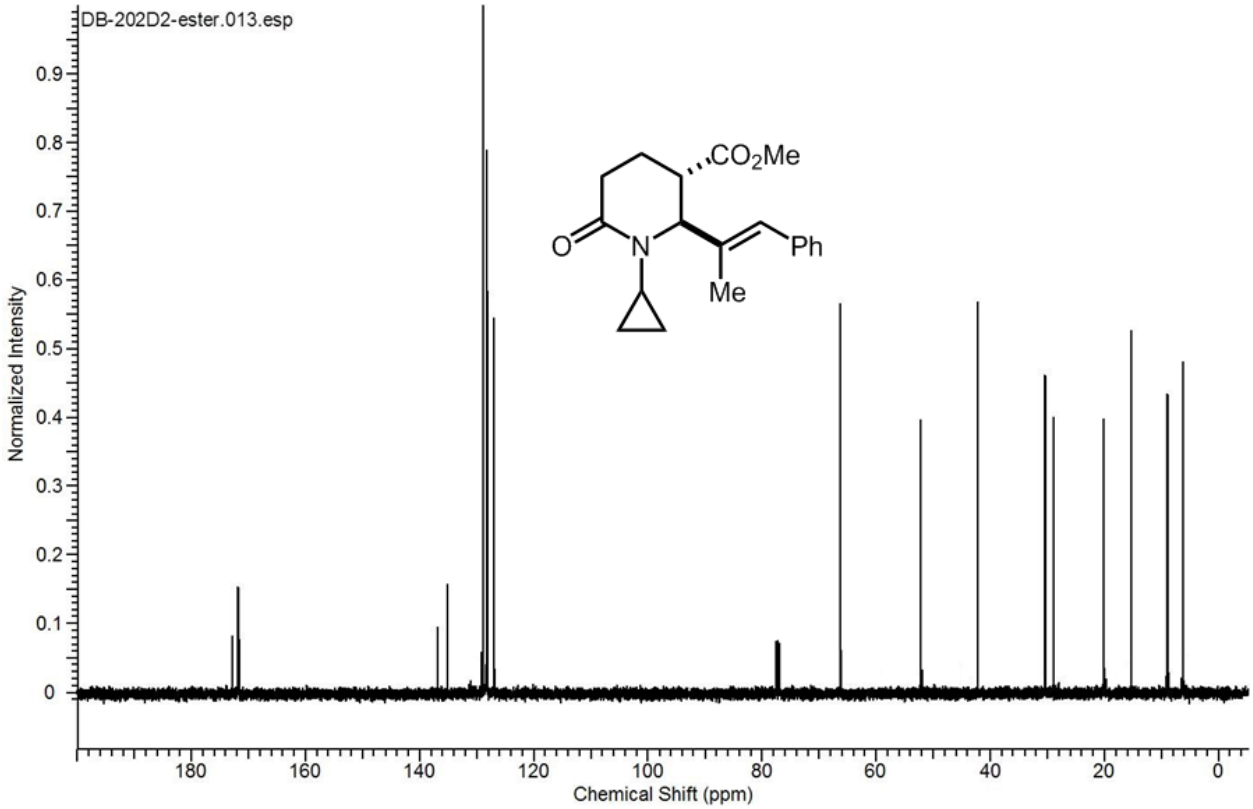
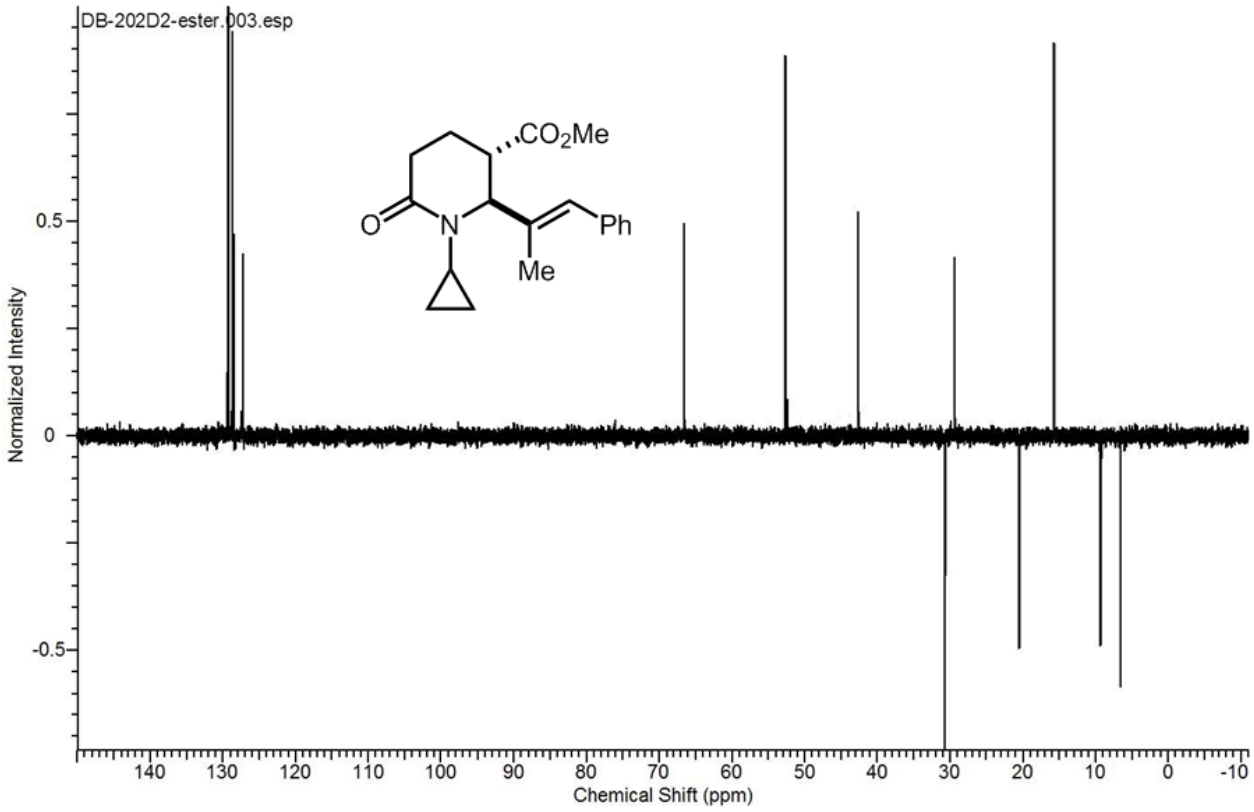
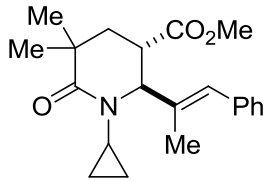
1.09
3.05
CO2Me
O
N
Ph
Me

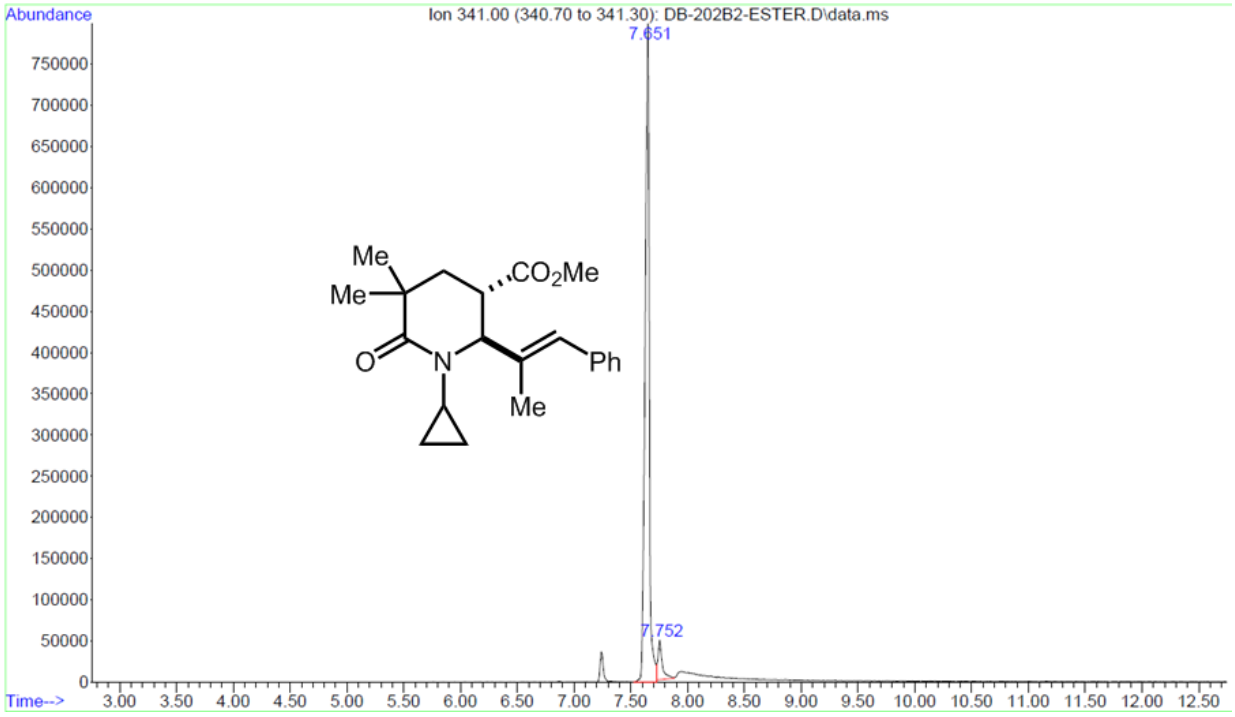

DB-202D2-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
O
N
Ph
Me

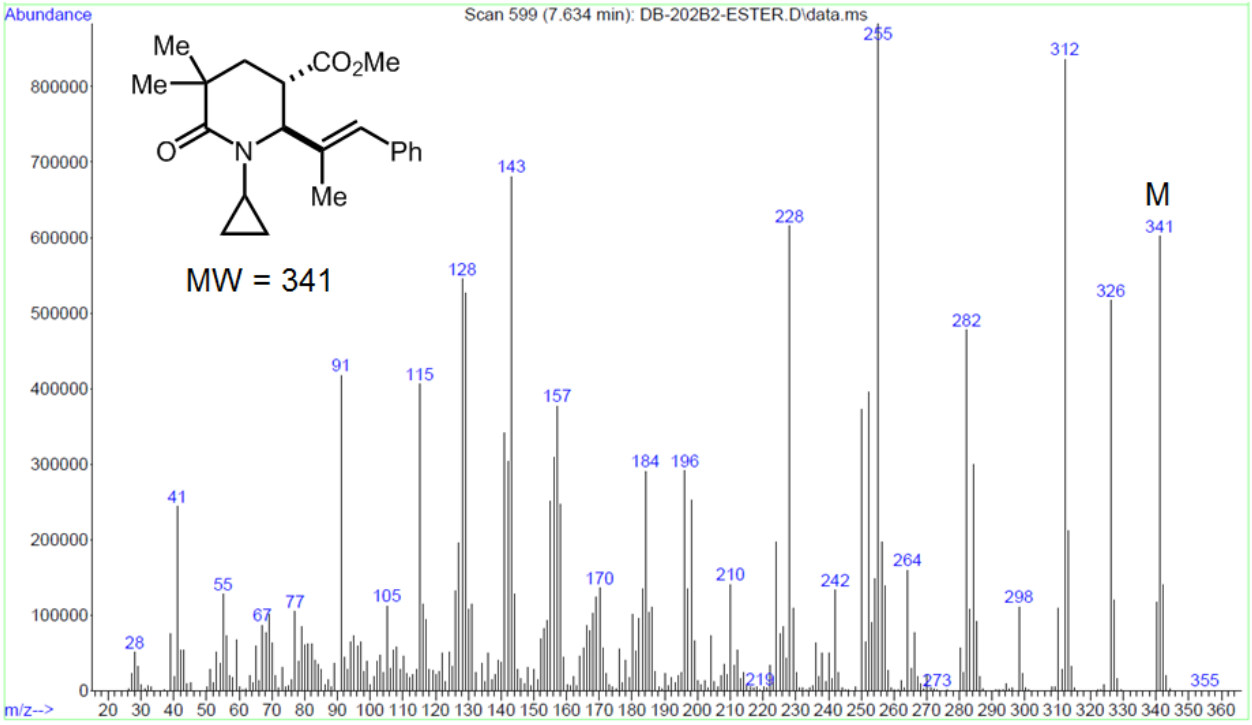


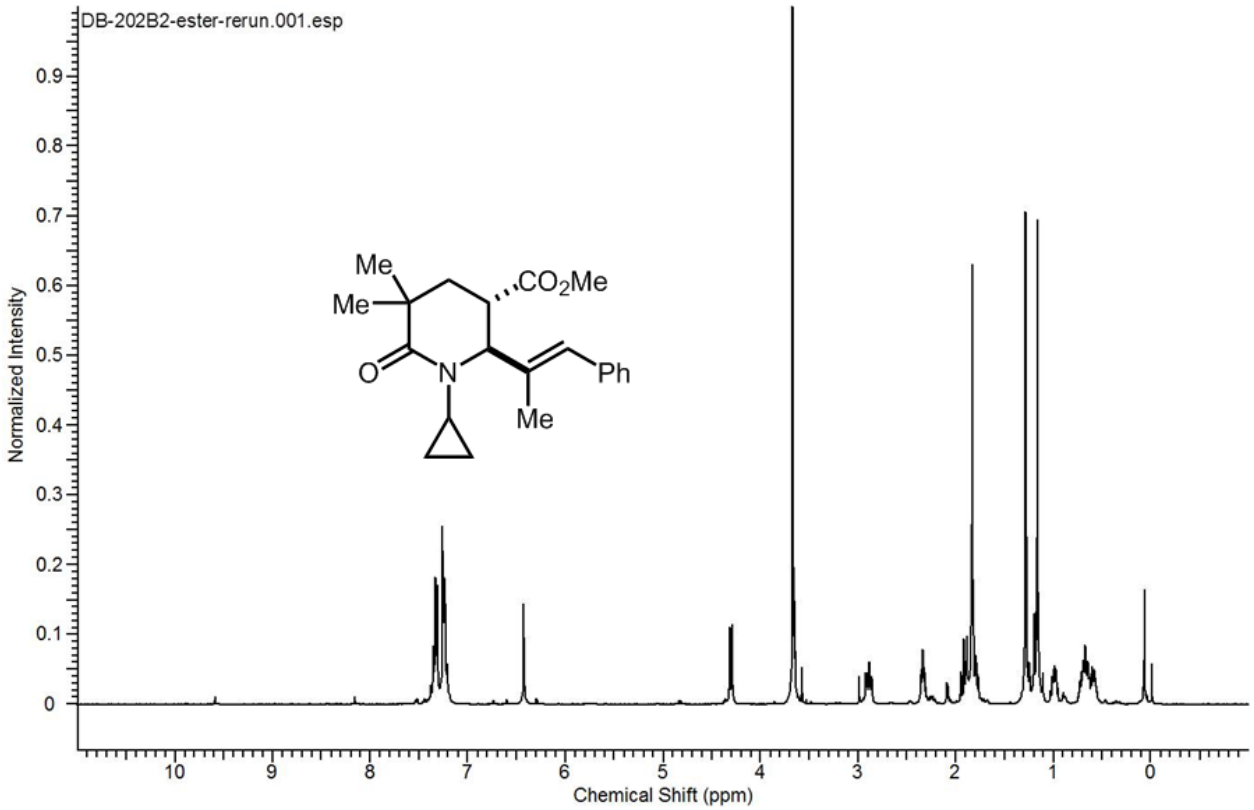


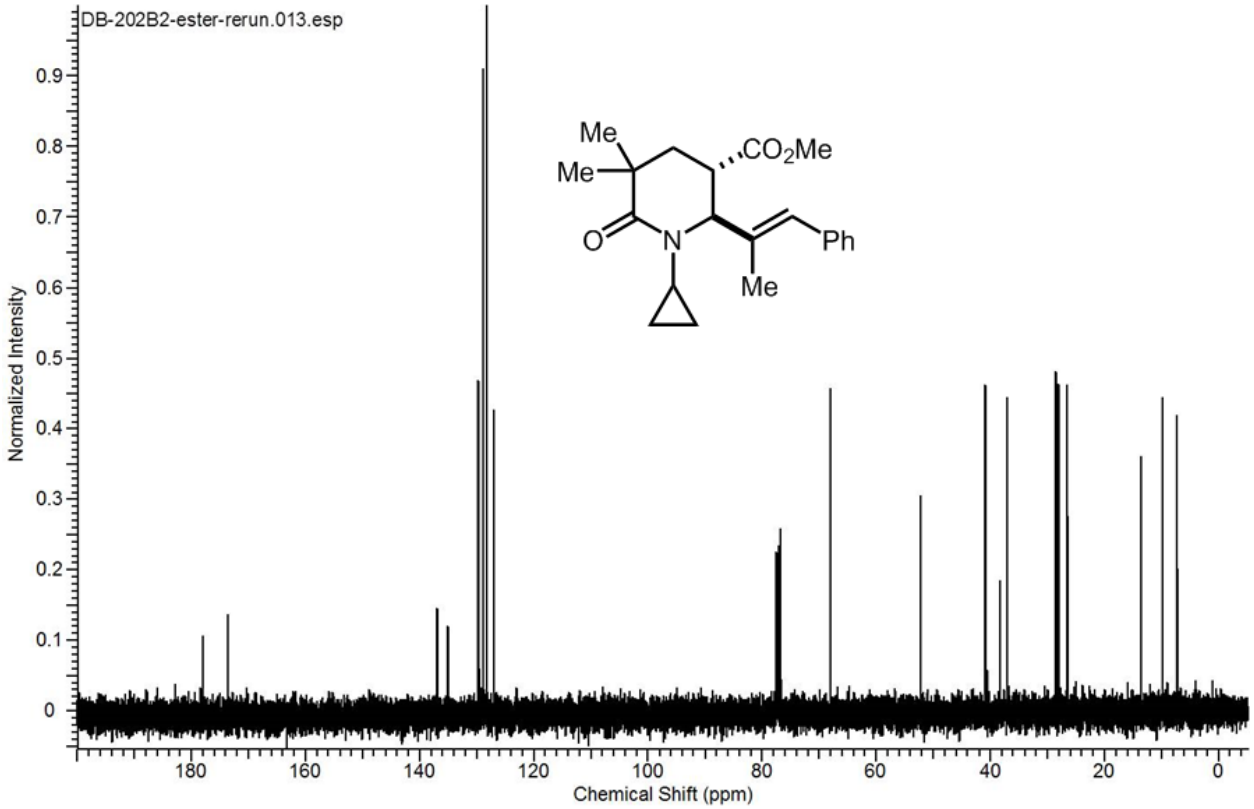
7n2

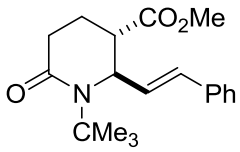
Prepared from imine **4l** (185 mg, 1.0 mmol) and 2,2-dimethyl glutaric anhydride (142 mg, 1.0 equiv), using General Procedures B and C. Temp = 100 ^{o}C, time = 18 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 239 mg, 70% over 2 steps, 98:2 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 to 7.21 (5H, m), 6.43 (1H, s), 4.37 (1H, d), 3.65 (3H, s),2.89 to 2.86 (1H, m), 2.36 to 2.31 (1H, t), 1.89 to 1.77 (5H, m), 1.32 to 1.25 (6H, s,s), 0.91 to 0.87 (1H, m), 0.70 to 0.55 (3H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.0, 173.6, 137.0, 135.0, 129.7, 128.9, 128.4, 128.3, 128.2, 126.9, 68.0, 52.1, 40.8, 38.3, 37.0, 28.5, 28.1, 26.4, 13.6, 9.8, 7.2. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{21}H_{27}NO_3$ 341.1991; found 341.1995.


Abundance
Ion 341.00 (340.70 to 341.30): DB-202B2-ESTER.D\data.ms
7.651
7.752
Me
Me
CO2Me
O
N
Ph
Me
Time-->


Abundance
Scan 599 (7.634 min): DB-202B2-ESTER.D\data.ms
Me
Me
CO2Me
O
N
Ph
Me
MW = 341
M
341
255
312
143
228
128
326
282
91
115
157
184
196
41
55
67
77
105
170
210
242
264
298
28
219
273
355
m/z-->

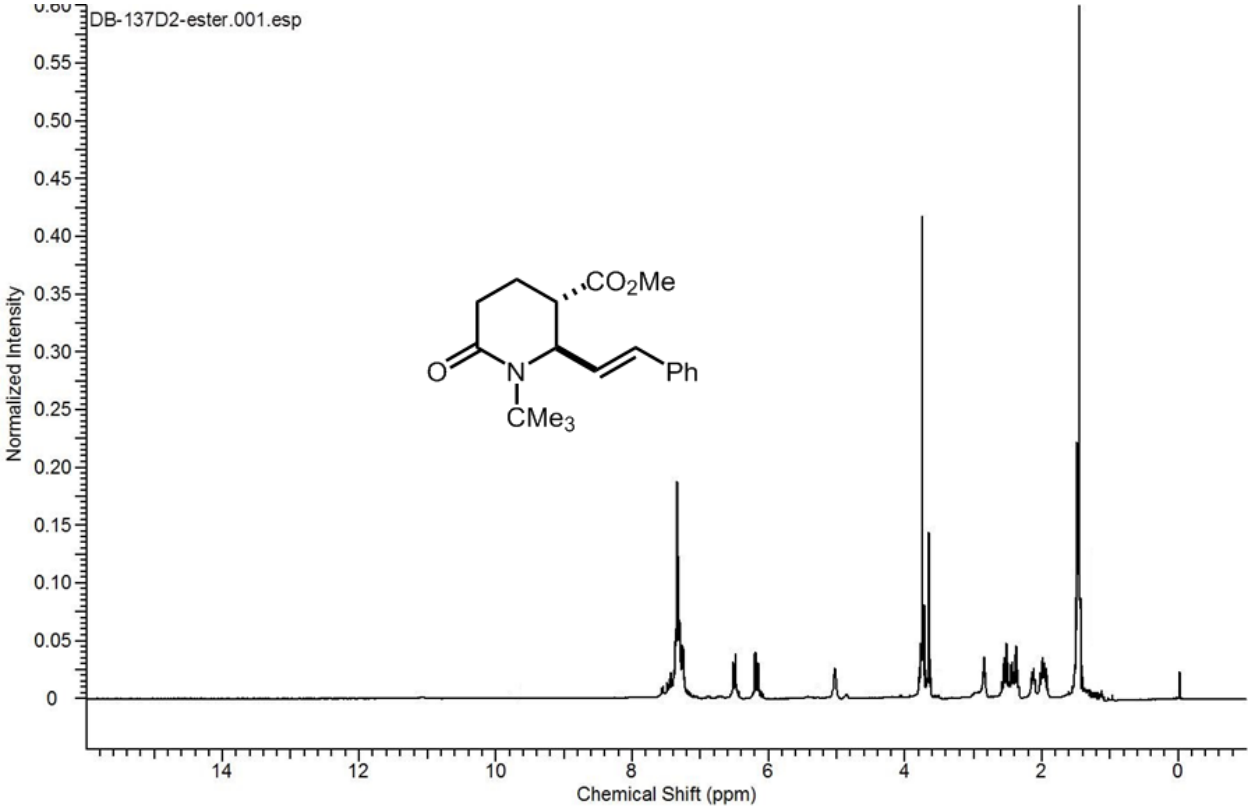

DB-202B2-ester-rerun.001.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2Me
O
N
Ph
Me

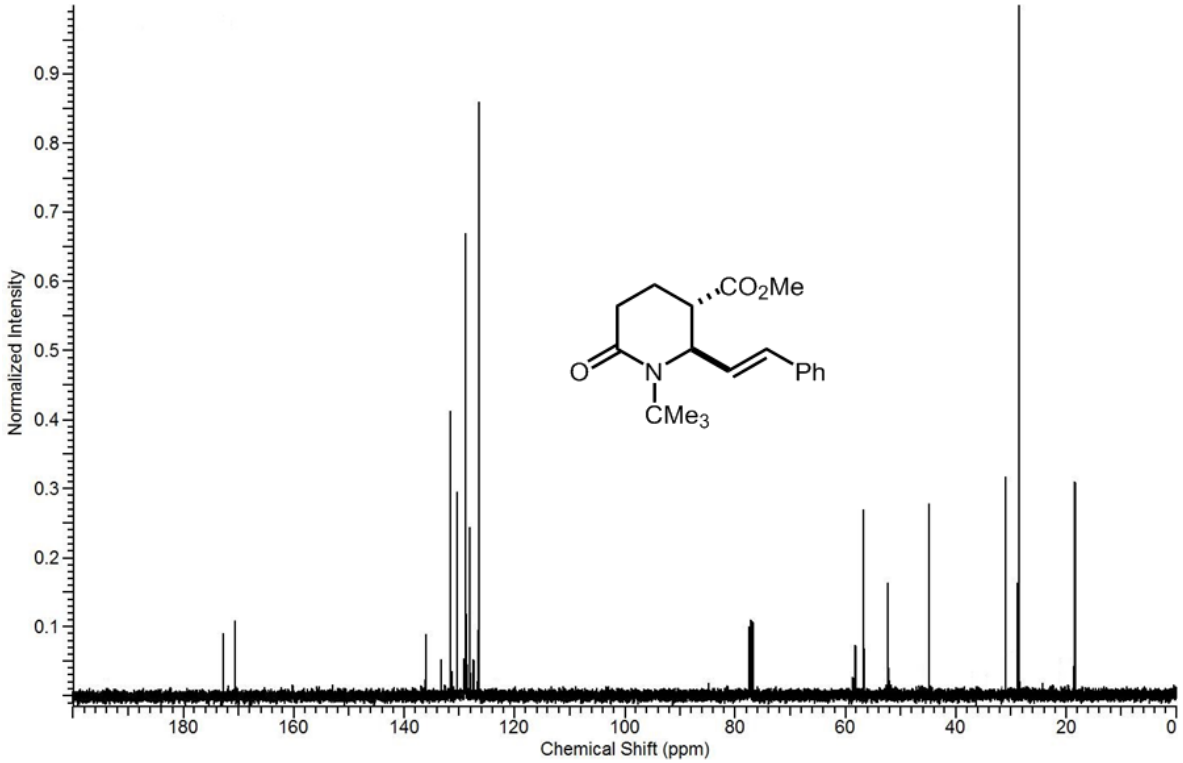

DB-202B2-ester-rerun.013.esp
Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2Me
O
N
Ph
Me

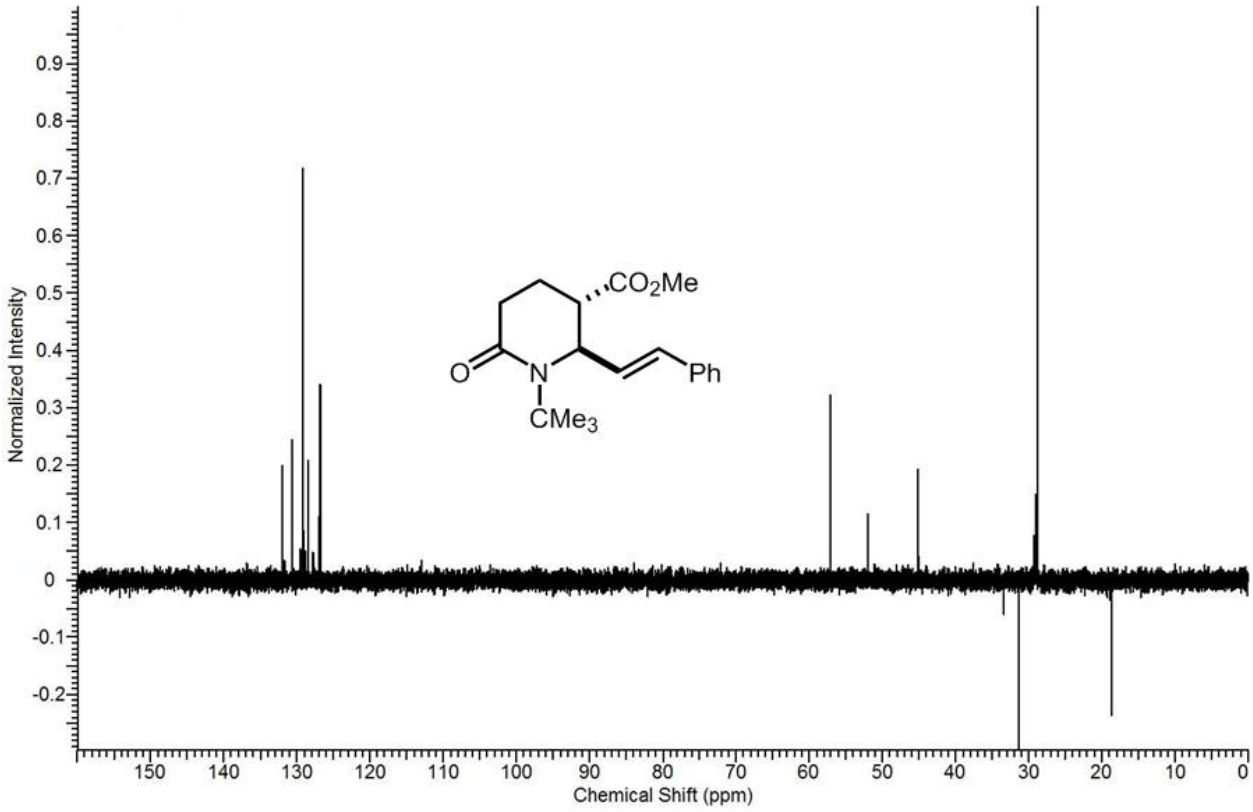


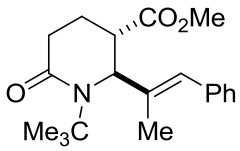
7o2

Prepared from imine **4n** (187 mg, 1.0 mmol) and glutaric anhydride (114 mg, 1.0 equiv), using General Procedures B and C. Temp = 100 ^{o}C, time = 12 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 258 mg, 82% over 2 steps, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 to 7.14 (5H, m), 6.52 to 6.49 (1H, d), 6.19 to 6.07 (1H, dd), 5.03 to 5.01 (1H, dd), 3.78 (3H, s), 2.92 to 2.81 (1H, m), 2.53 to 2.31 (2H, m), 2.15 to 1.90 (2H, m), 1.47 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 170.6, 136.0, 133.2, 129.1, 128.7, 128.1, 127.9, 126.4, 58.7, 58.2, 51.6, 44.7, 31.0, 28.5, 18.6. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{19}H_{25}NO_3$ 315.1834; found 315.1839.



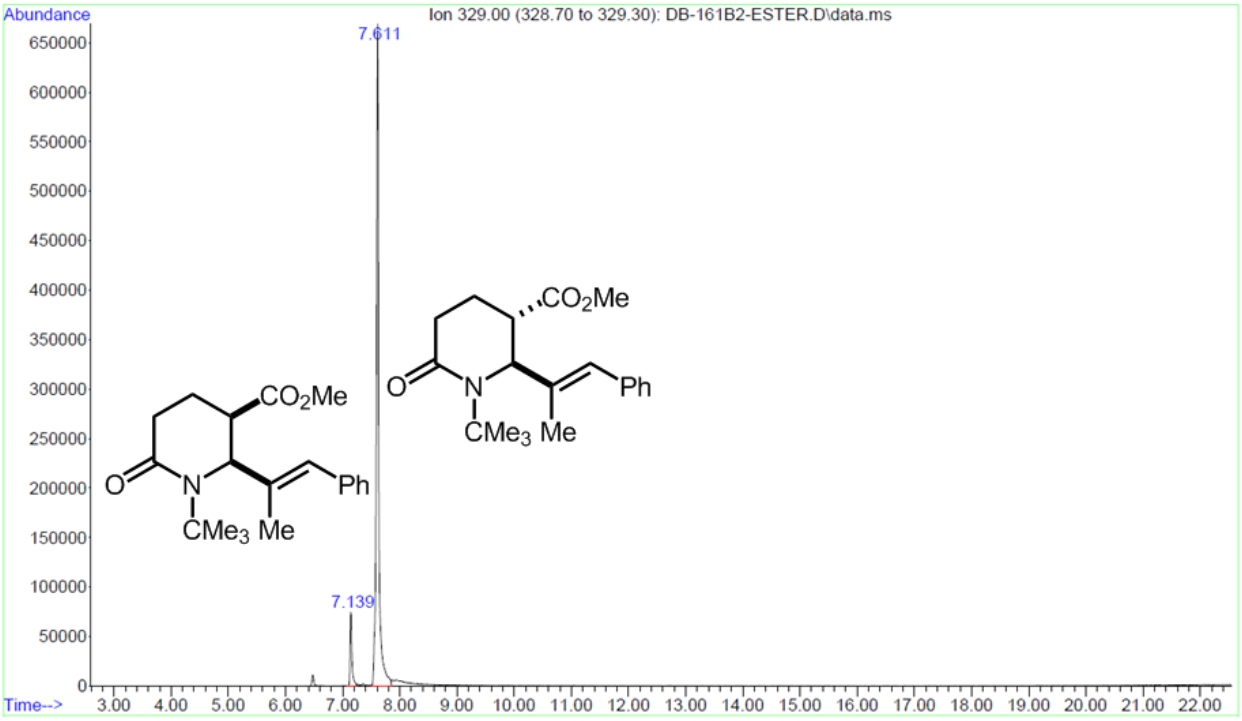

Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
CMe3
O
N

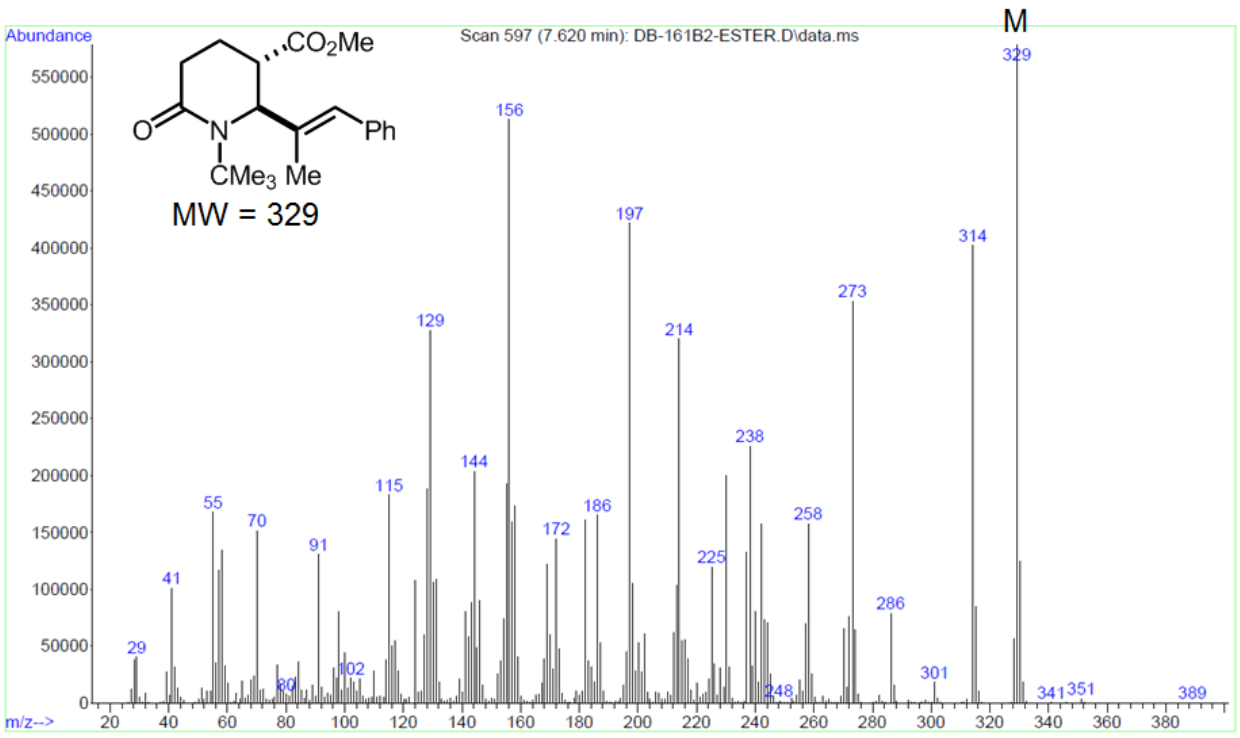

Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
CMe3
O
N

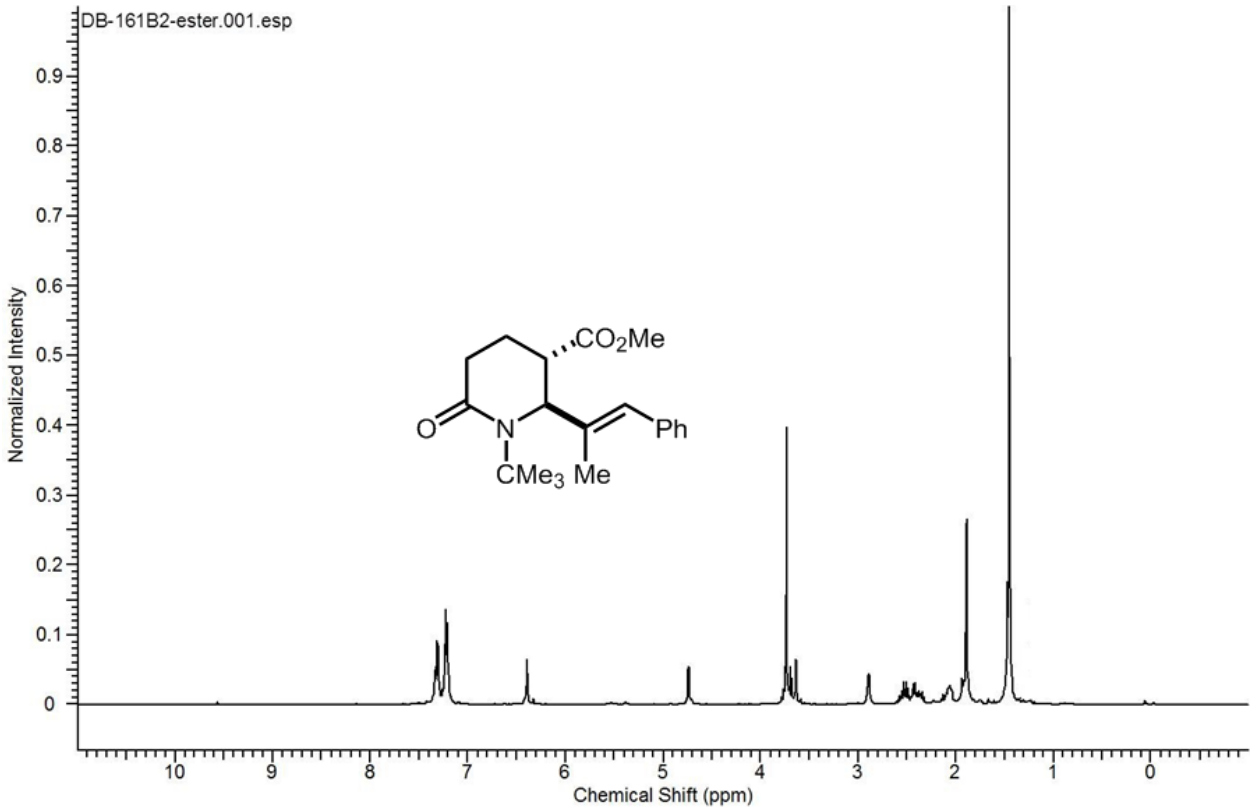


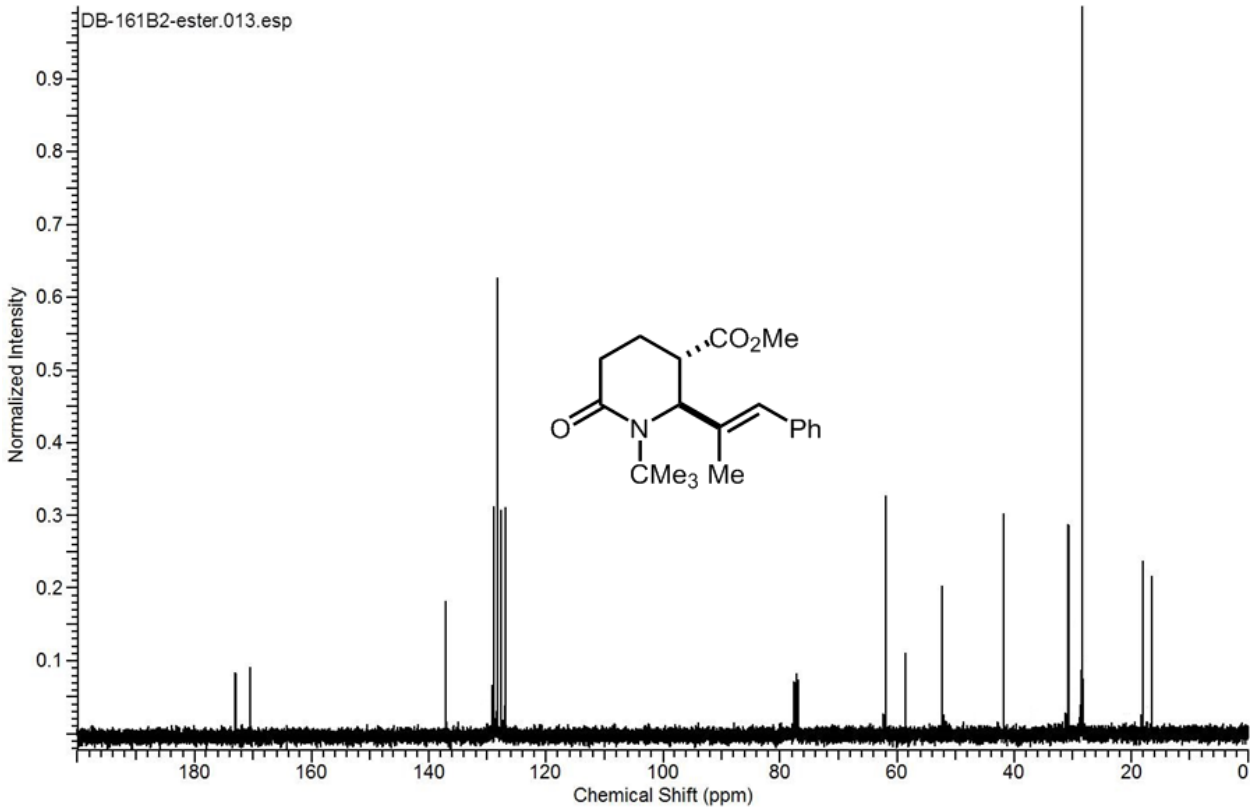
7p2

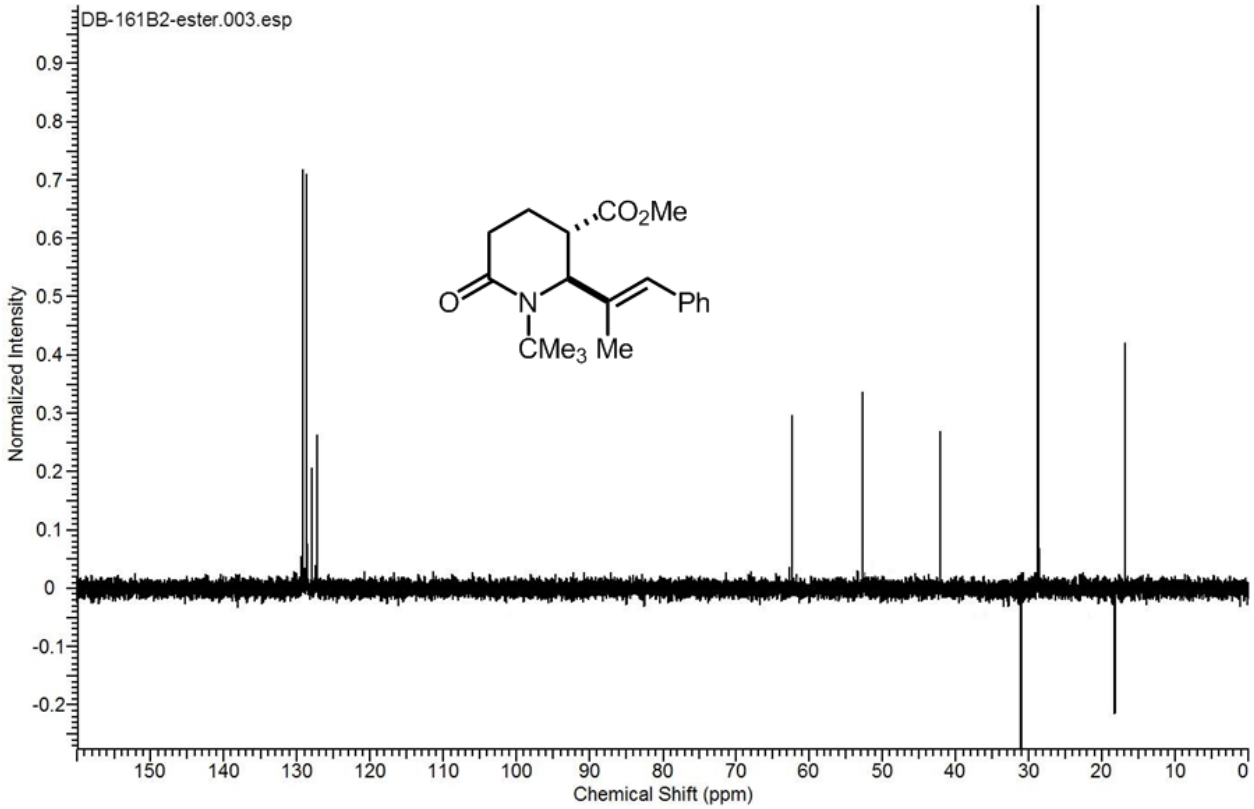
Prepared from imine **4o** (201 mg, 1.0 mmol) and glutaric anhydride (114 mg, 1.0 equiv), using General Procedures B and C. Temp = 100 ^{o}C, time = 18 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 250 mg, 76% over 2 steps, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 to 7.17 (5H, m), 6.39 (1H, s), 4.71 (1H, d), 3.76 (3H, s), 2.92 to 2.88 (1H, m), 2.55 to 2.32 (3H, m), 2.23 to 1.82 (4H, m), 1.49 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 170.5, 136.9, 129.0, 128.8, 128.2, 127.6, 127.2, 126.9, 62.3, 58.6, 55.3, 41.7, 31.1, 28.8, 19.4, 17.9. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{20}H_{27}NO_3$ 329.1991; found 329.1995.

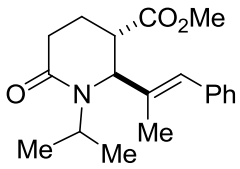



Abundance
Scan 597 (7.620 min): DB-161B2-ESTER.D\data.ms
M
329
CO2Me
O
N
Ph
CMe3 Me
MW = 329
156
197
314
273
129
214
238
144
115
186
258
55
70
172
225
91
41
286
29
102
80
301
248
341
351
389
m/z-->


DB-161B2-ester.001.esp
CO2Me
O
N
Ph
CMe3 Me
Normalized Intensity
Chemical Shift (ppm)

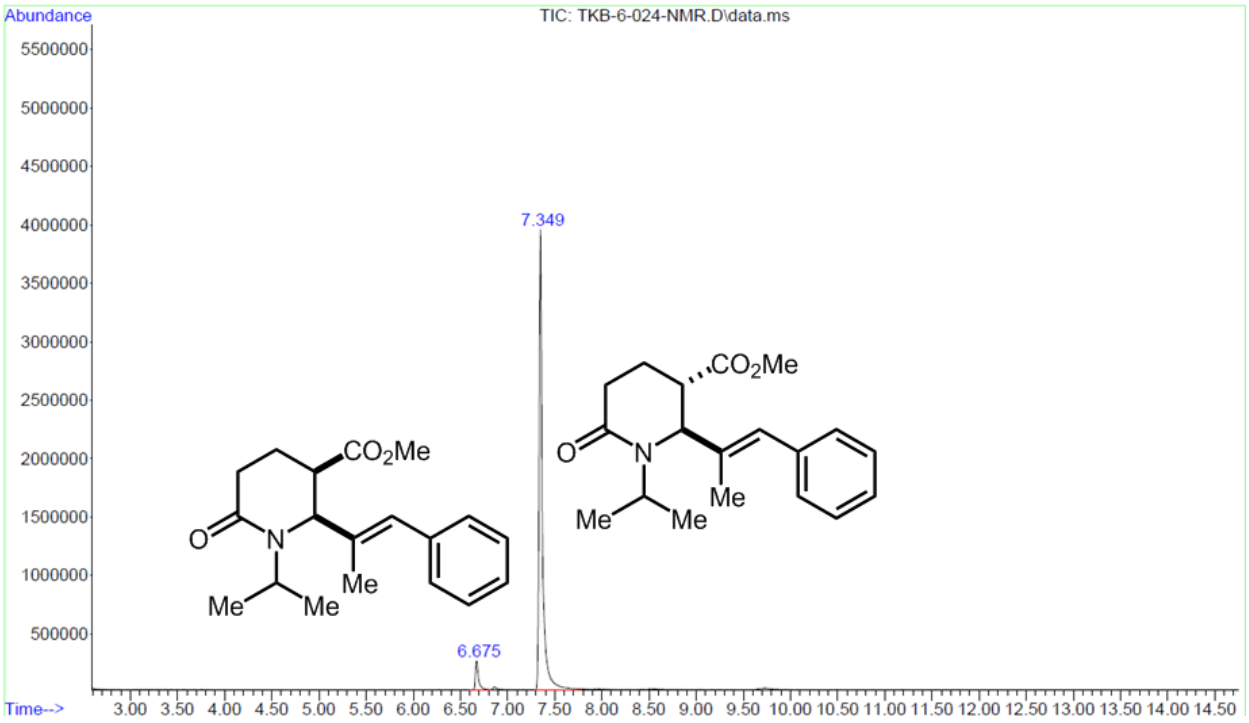

DB-161B2-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
N
O
CMe3
Me

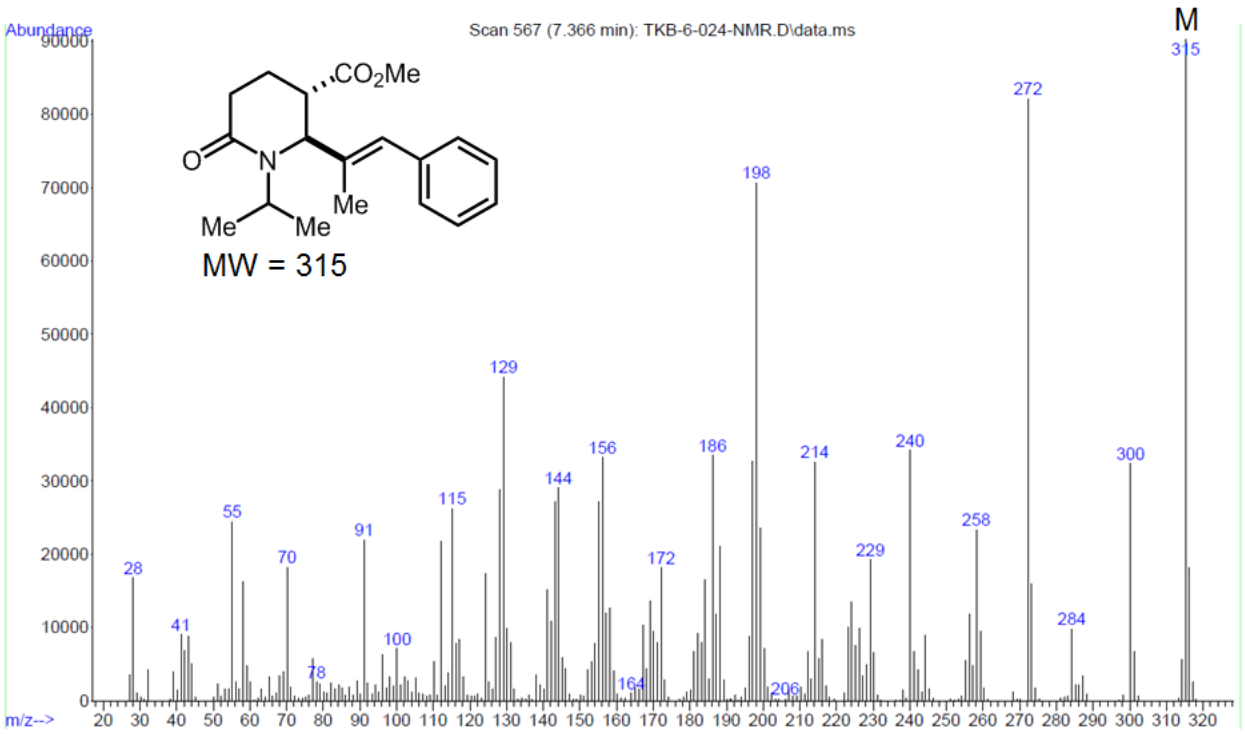

DB-161B2-ester.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
N
O
CMe3
Me

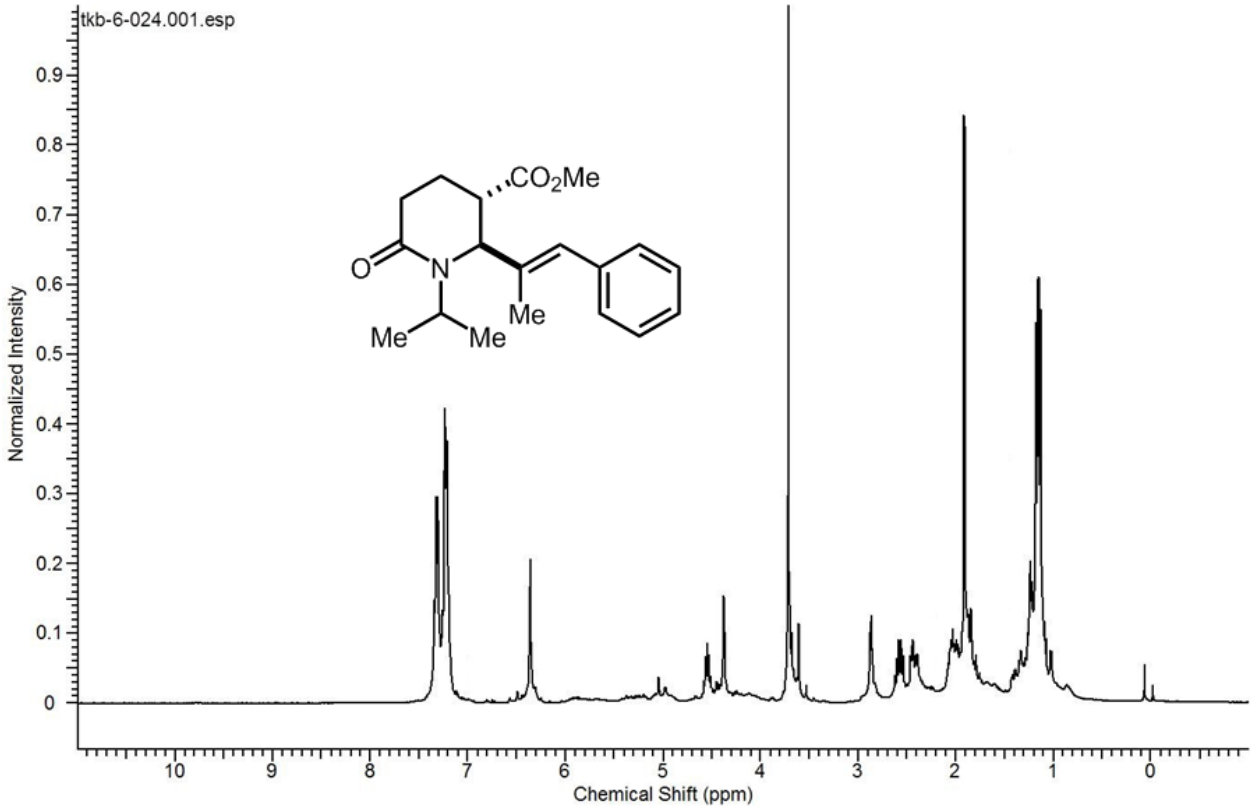


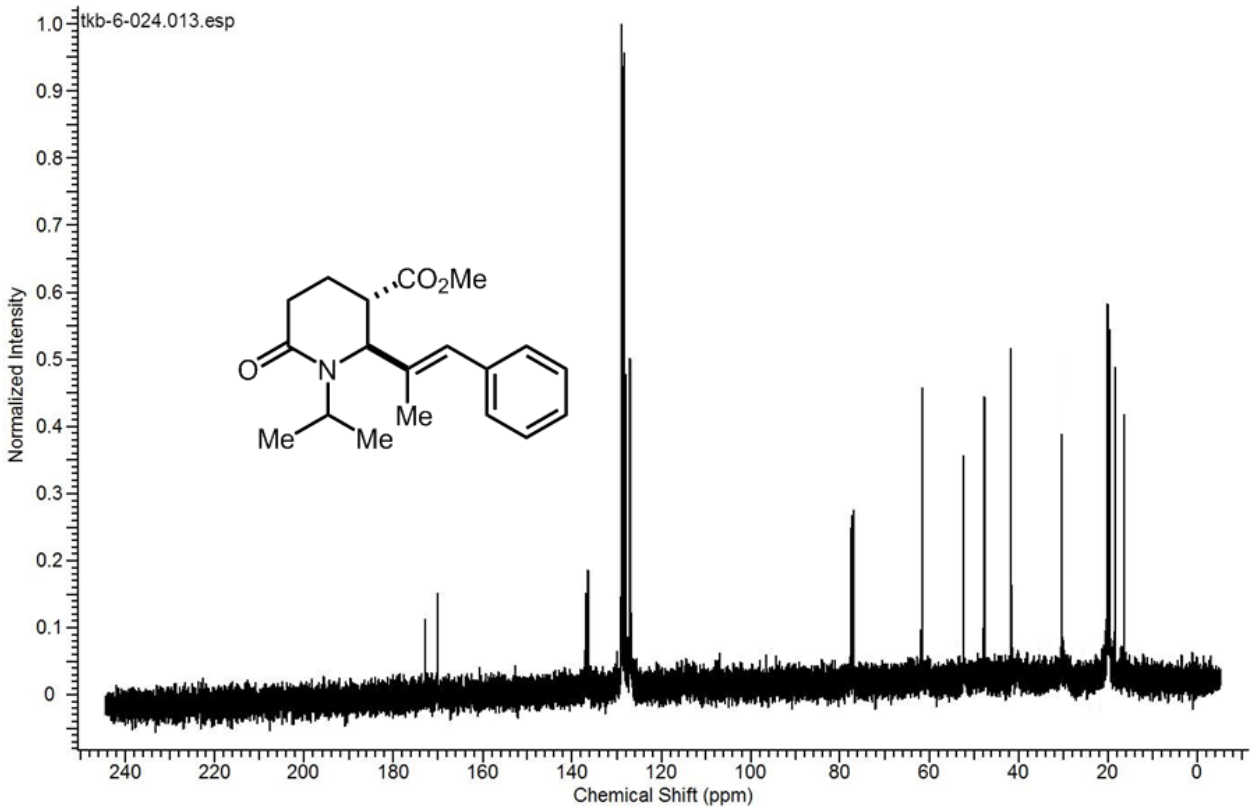
7q2

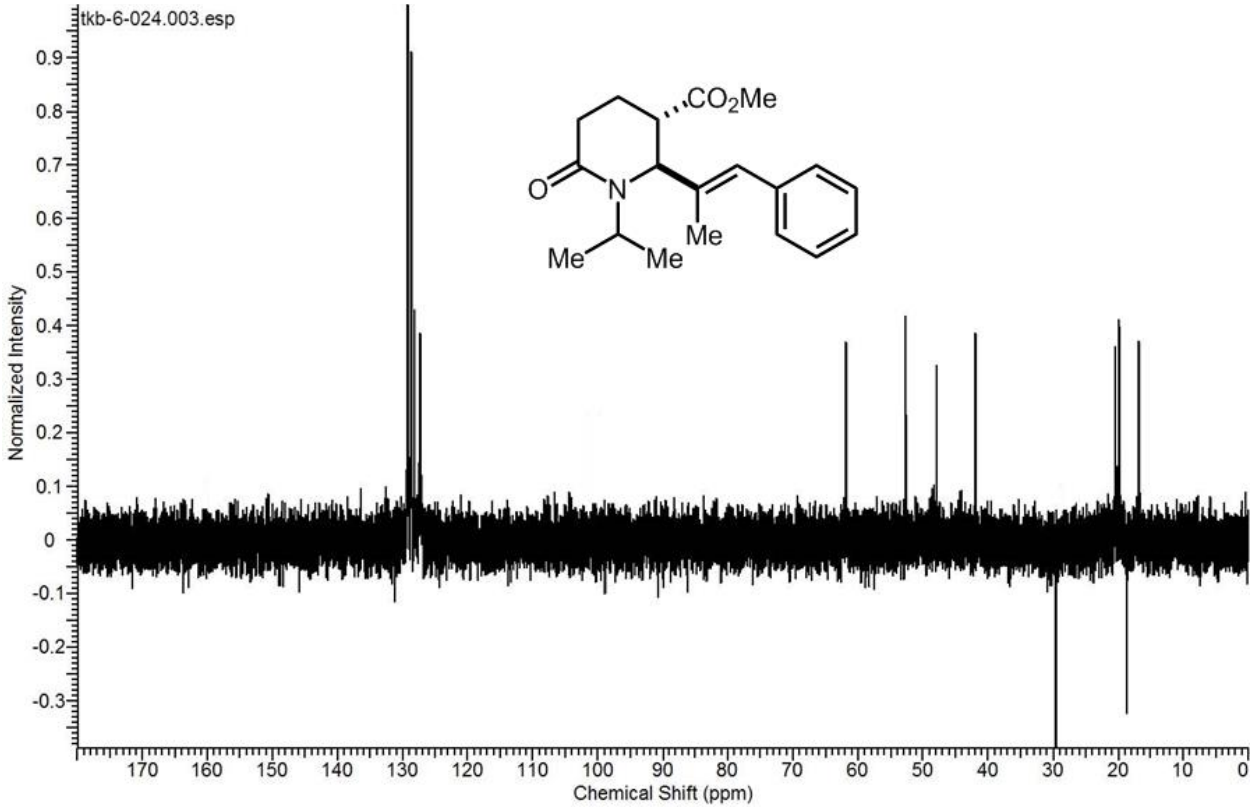
Prepared from imine **4q** (187 mg, 1.0 mmol) and glutaric anhydride (114 mg, 1.0 equiv), using General Procedures B and C. Temp = 100 ^{o}C, time = 18 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 250 mg, 76% over 2 steps, 90:10 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 to 7.21 (5H, m), 6.39 (1H, s), 4.55 to 4.37 (2H, m), 3.77 (3H, s), 2.88 to 2.82 (1H, m), 2.63 to 2.37 (2H, m), 2.08 to 1.76 (5H, m), 1.41 to 1.26 (6H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.82, 170.14, 137.03, 136.84, 136.42, 129.88, 128.87, 127.88, 126.98, 125.56, 61.80, 55.02, 47.93, 41.67, 30.38, 20.95, 20.16, 19.52, 18.86. **HRMS-EI**$^{+}$ (*m/z*): calc'd for $C_{19}H_{25}NO_3$ 315.1834; found 315.1839.

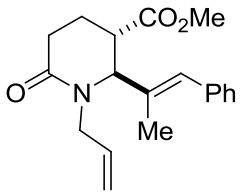



Abundance
Scan 567 (7.366 min): TKB-6-024-NMR.D\data.ms
M
315
272
198
129
156
186
214
240
300
144
115
55
91
258
229
70
172
28
284
41
100
78
164
206
m/z-->
MW = 315


tkb-6-024.001.esp
Normalized Intensity
Chemical Shift (ppm)

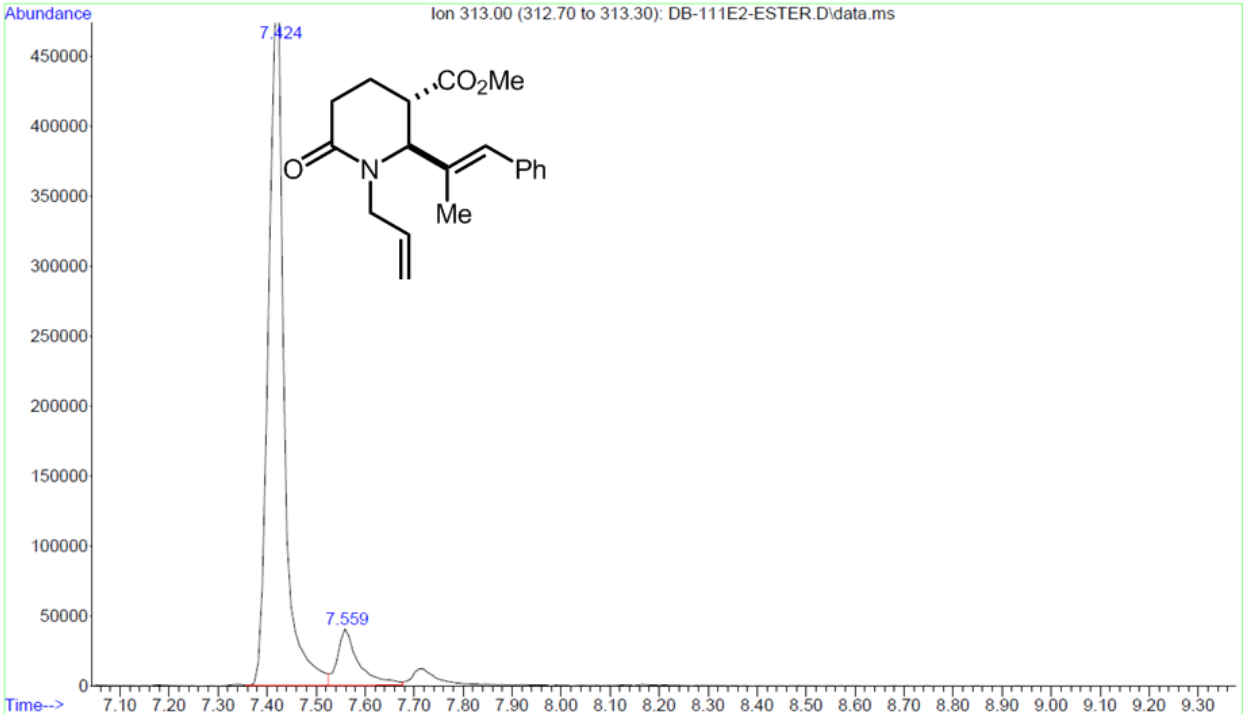

tkb-6-024.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
O
N
Me
Me
Me

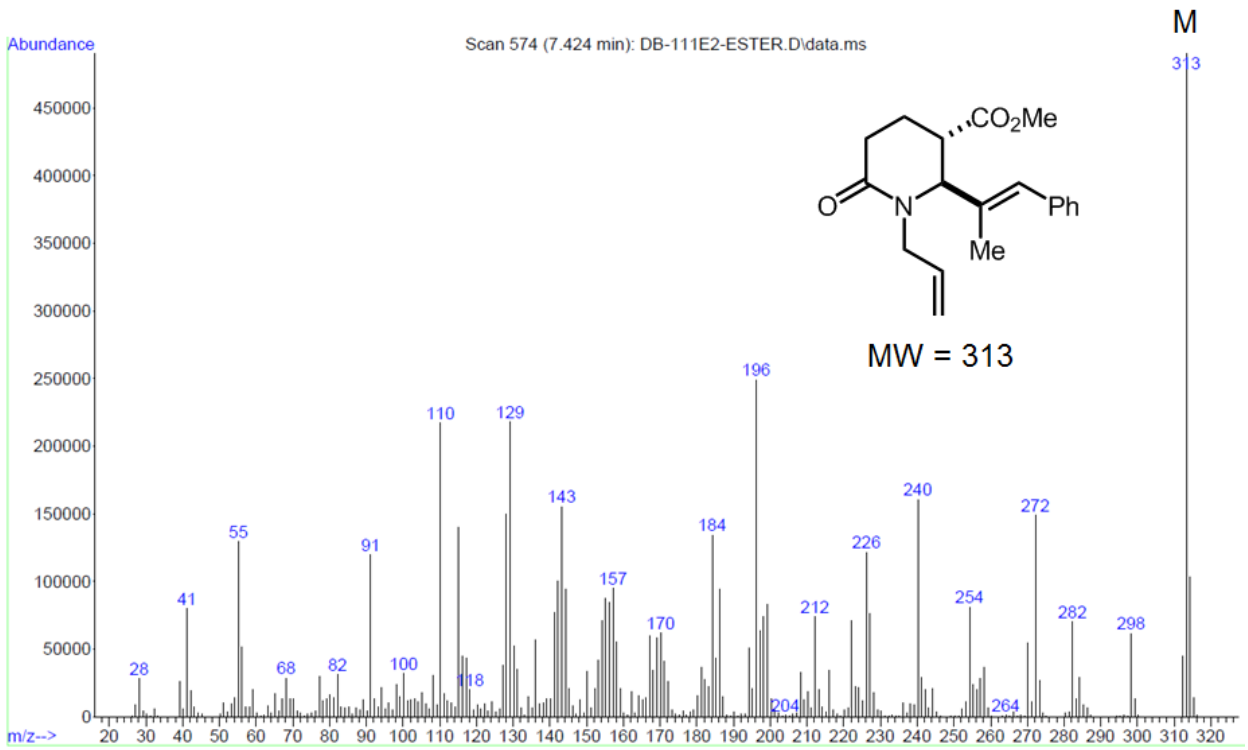

tkb-6-024.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
O
N
Me
Me
Me

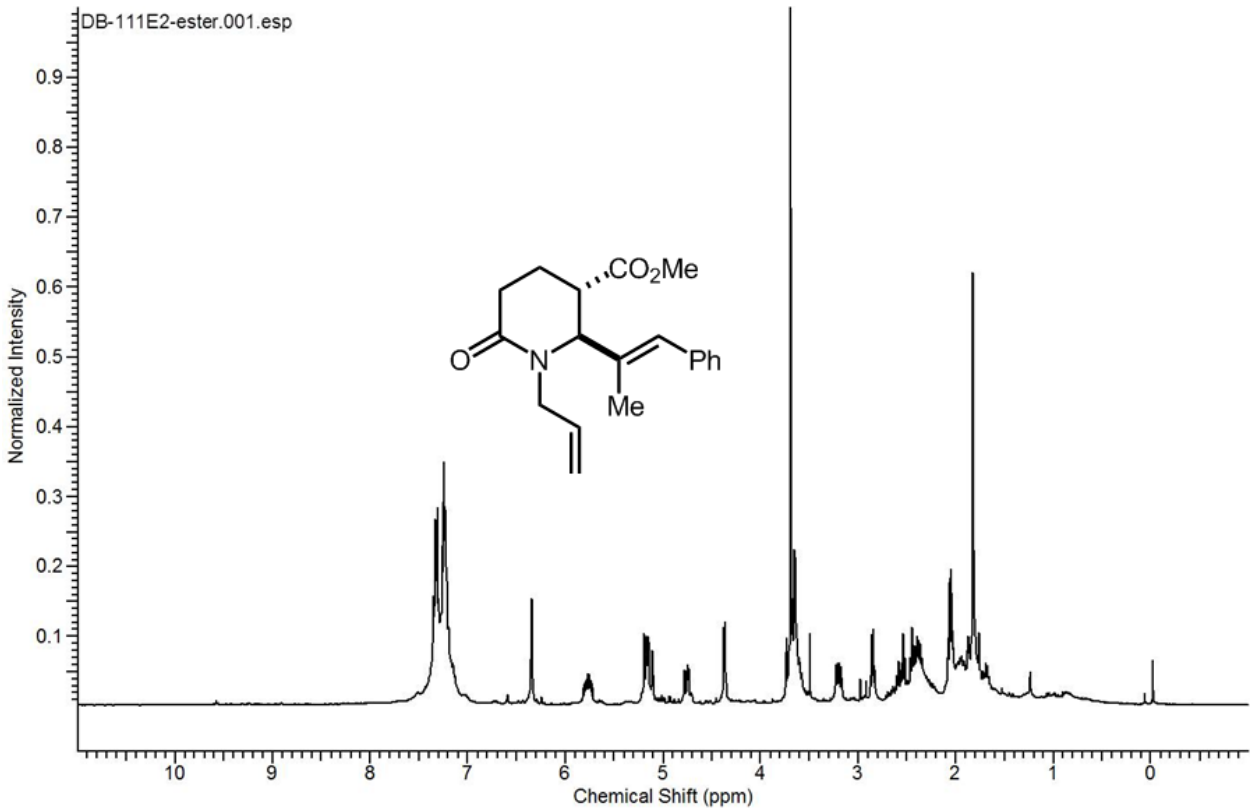


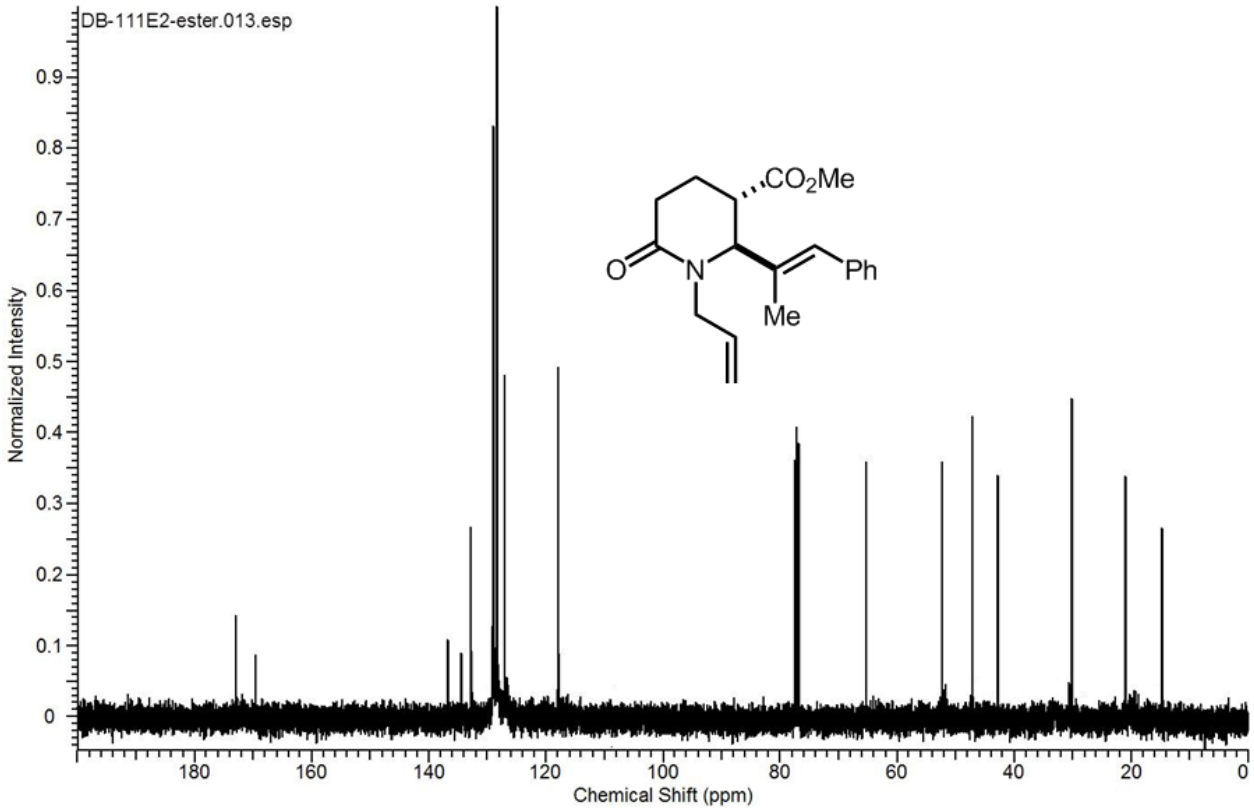
7r2

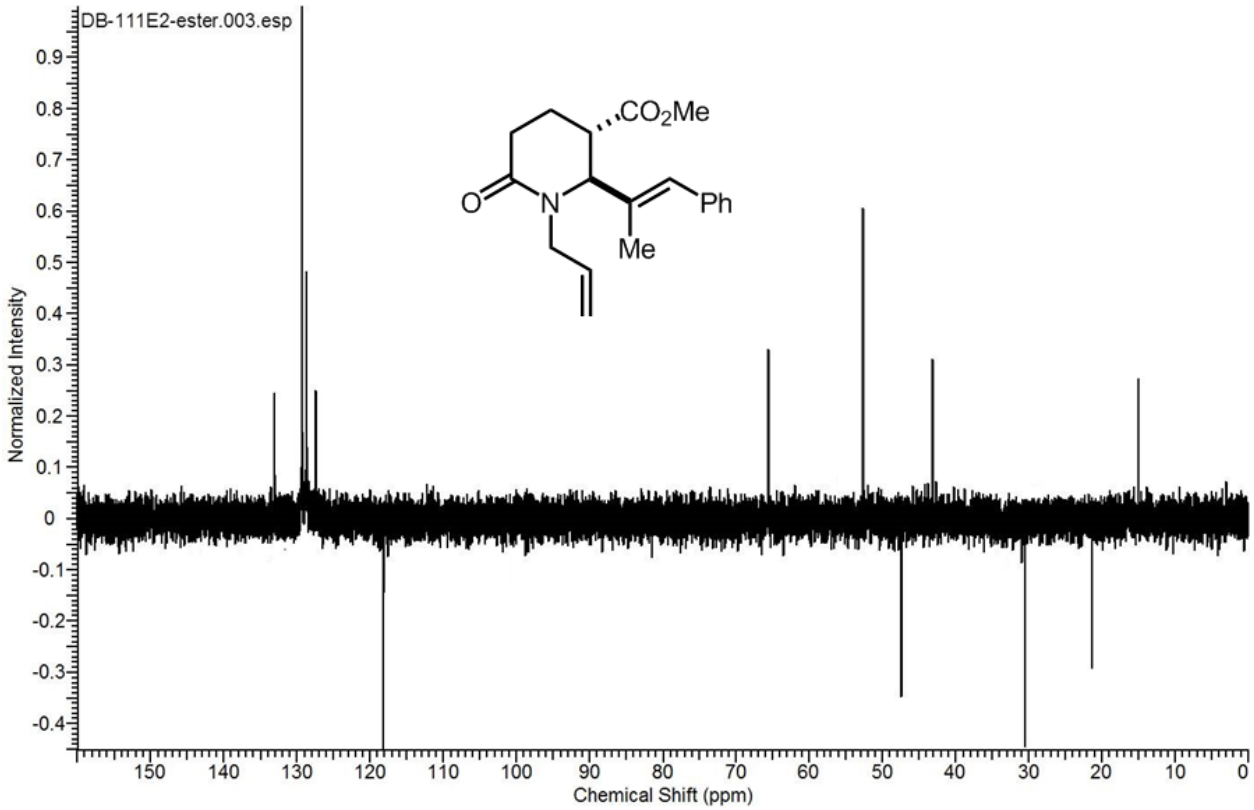
Prepared from imine **4v** (185 mg, 1.0 mmol) and glutaric anhydride (114 mg, 1.0 equiv), using General Procedures B and C. Temp = 100 ^{o}C, time = 18 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 235 mg, 75% over 2 steps, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 to 7.02 (5H, m), 6.34 (1H, s), 5.82 to 5.72 (1H, m), 5.13 to 5.05 (2H, m), 4.75 to 4.70 (1H, dd), 4.38 (1H, d), 3.72 to 3.60 (4H, m), 3.28 to 3.21 (1H, dd), 2.87 to 2.80 (1H, m), 2.49 to 2.20 (2H, m), 2.03 to 1.69 (5H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 169.6, 136.7, 134.4, 132.7, 129.1, 128.9, 128.3, 127.0, 118.0, 65.2, 52.2, 46.3, 42.6, 30.1, 21.0, 16.1. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{19}H_{23}NO_3$ 313.1678; found 313.1684.



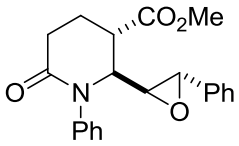

Abundance
Scan 574 (7.424 min): DB-111E2-ESTER.D\data.ms
M
313
CO2Me
O
N
Ph
Me
MW = 313
196
110
129
143
184
240
272
55
91
226
157
212
254
282
41
170
298
28
68
82
100
118
204
264
m/z-->


DB-111E2-ester.001.esp
Normalized Intensity
CO2Me
O
N
Ph
Me
Chemical Shift (ppm)


DB-111E2-ester.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
Me
N
O

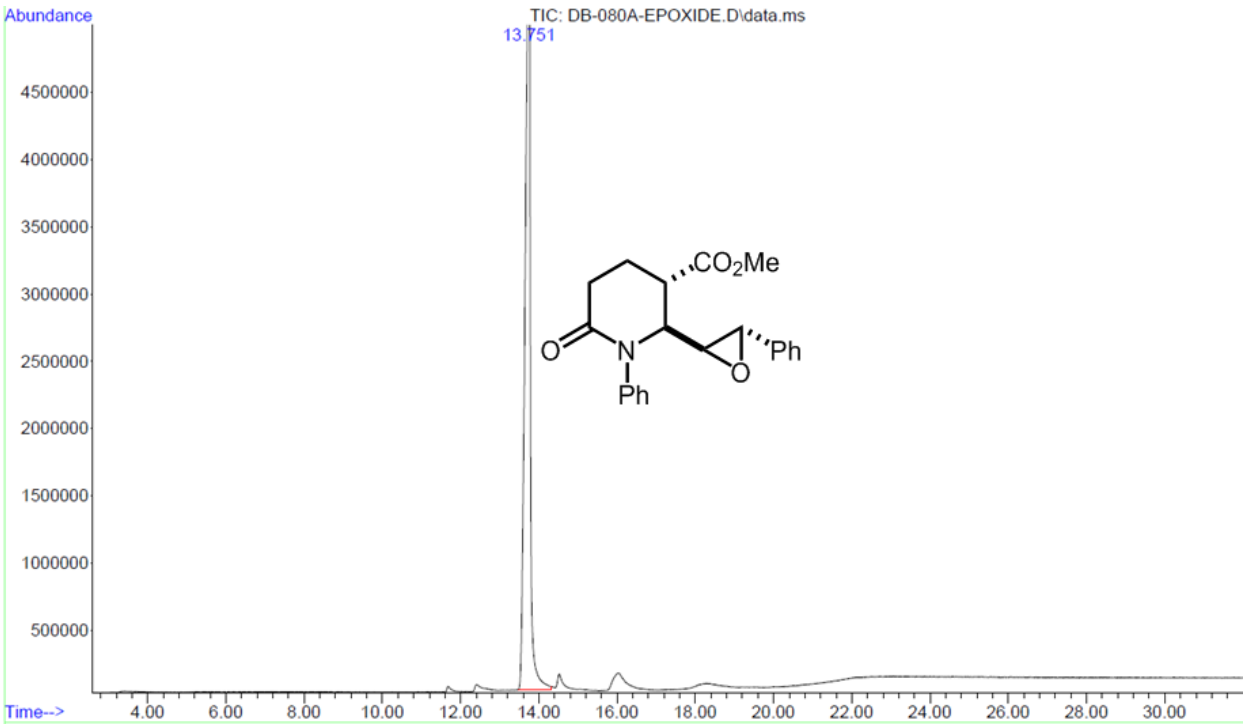

DB-111E2-ester.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
Me
N
O

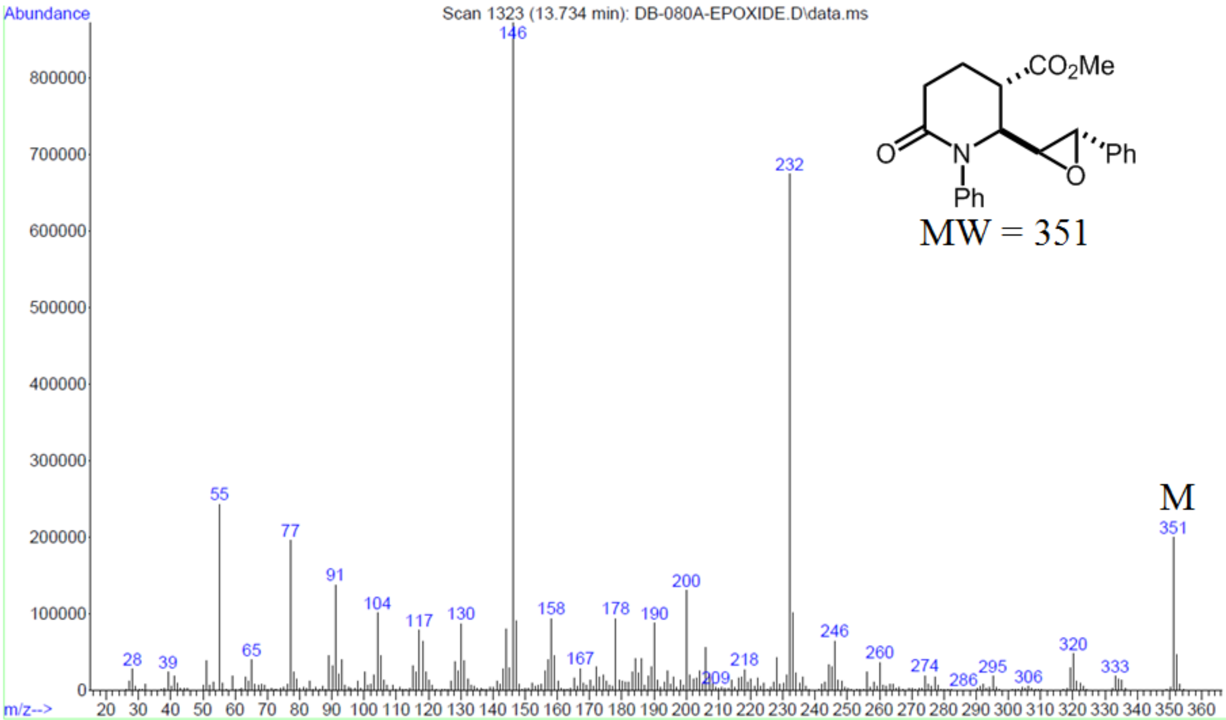
Epoxidation:



11a, 88%, >99:1 dr

Prepared from allylic lactam **7a2** (0.50 mmol) using General Procedure F. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 155 mg, 88%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 to 7.10 (8H, m), 6.91 to 6.86 (2H, d), 4.01 (1H, d), 3.81 (3H, s), 3.28 to 3.25 (1H, d), 3.17 to 3.15 (1H, dd), 2.69 to 2.35 (4H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 168.4, 141.5, 135.5, 133.2, 129.7, 129.6, 129.3, 128.6, 128.5, 128.4, 128.0, 127.6, 125.3, 63.7, 61.9, 60.3, 52.7, 40.7, 29.5, 20.0. **HRMS-EI**$^{+}$ (*m/z*): calc'd for $C_{21}H_{21}NO_4$ 351.1471; found 351.1475.





Abundance
Scan 1323 (13.734 min): DB-080A-EPOXIDE.D\data.ms
146
232
55
77
91
104
117
130
158
167
178
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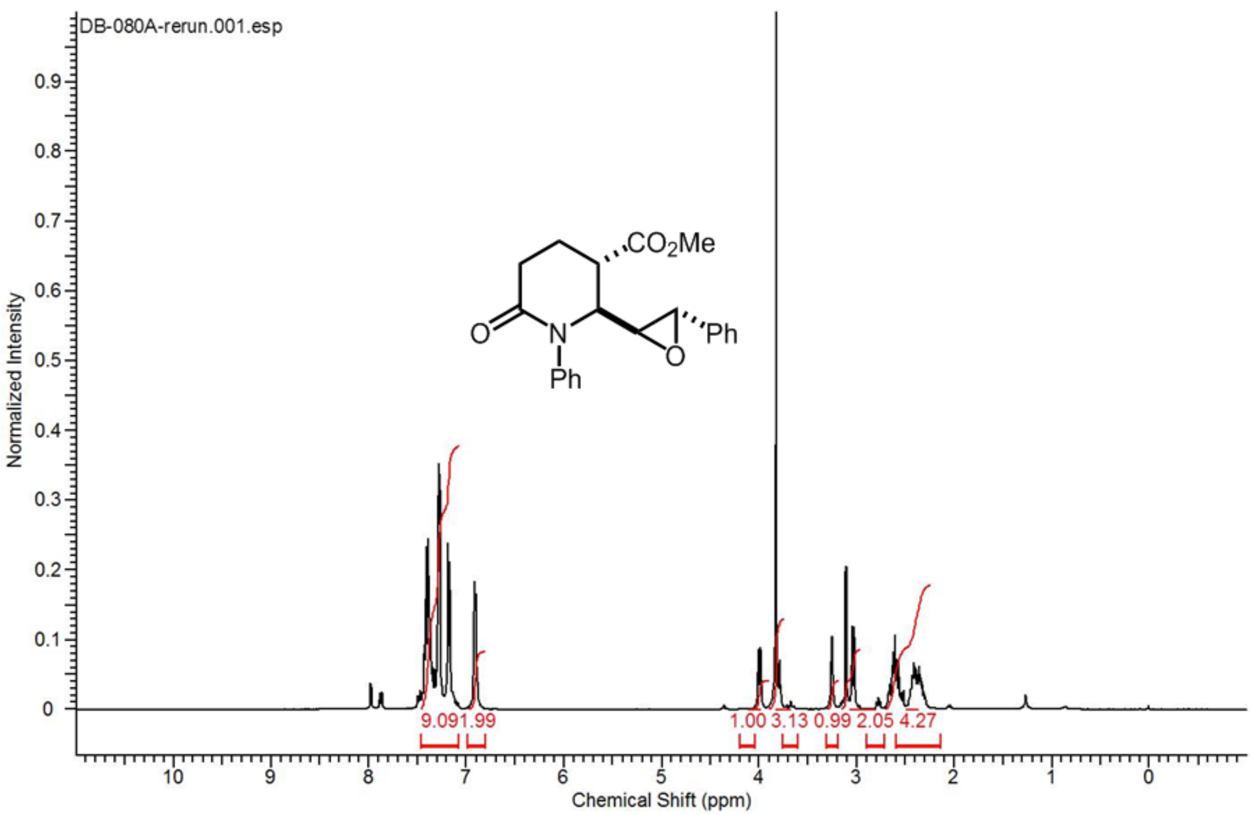
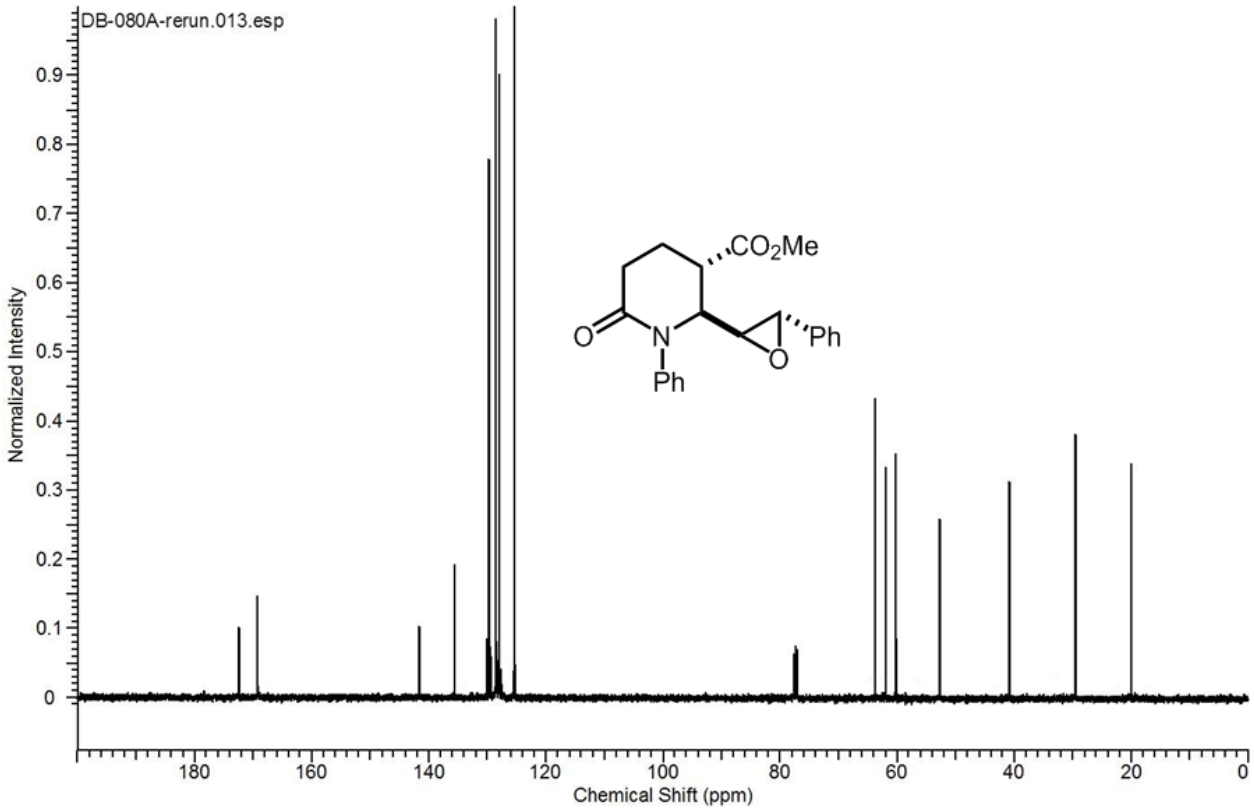
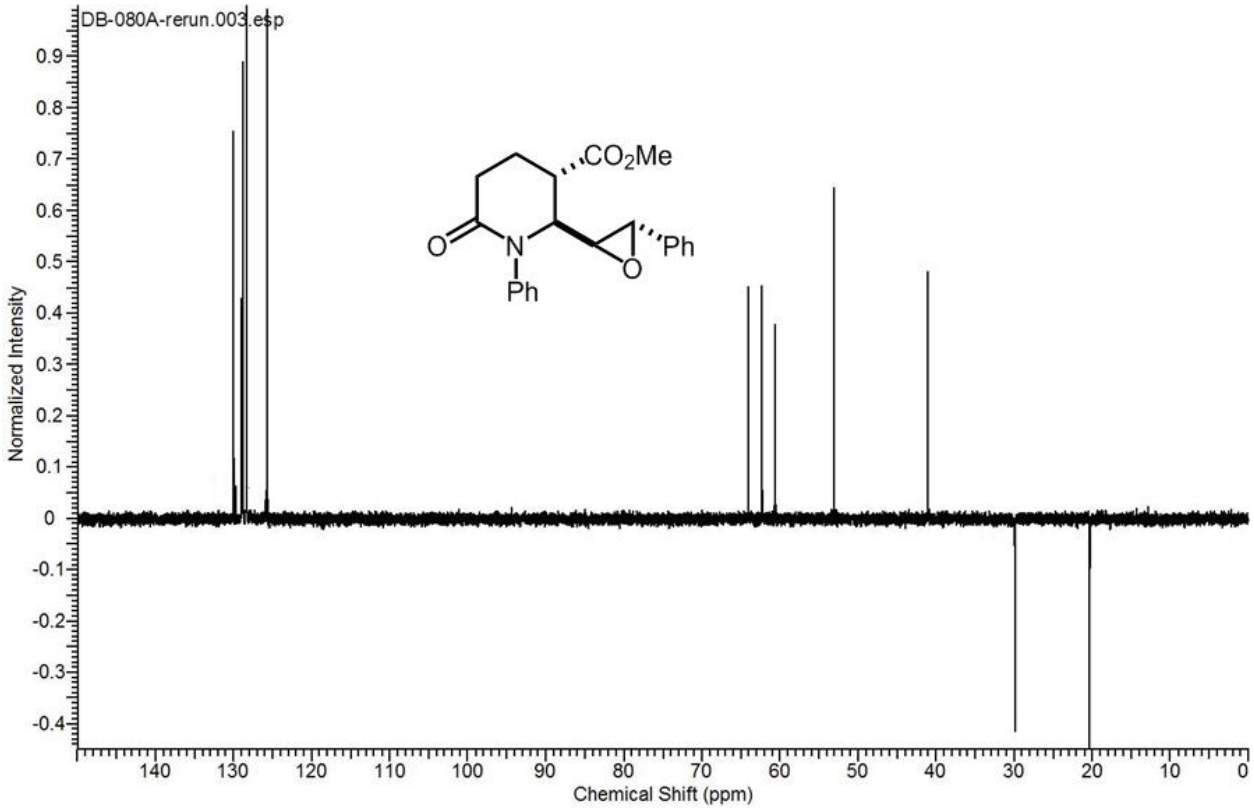
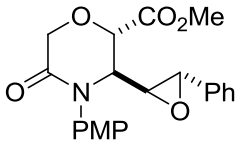
200
209
218
246
260
274
286
295
306
320
333
M
351
m/z-->
CO2Me
O
N
Ph
Ph
O
MW = 351



DB-080A-rerun.001.esp
Normalized Intensity
Chemical Shift (ppm)
9.09
1.99
1.00
3.13
0.99
2.05
4.27
CO2Me
O
N
Ph
Ph
O

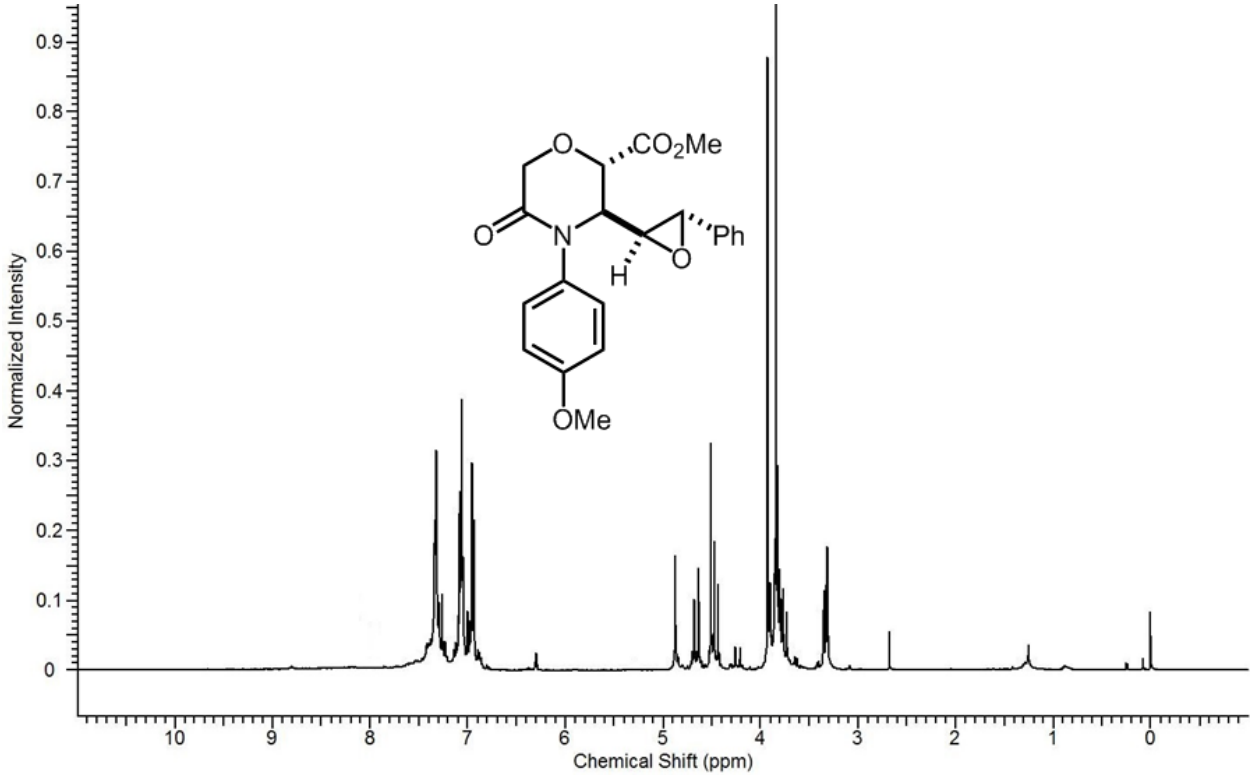

DB-080A-rerun.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
N
O
Ph

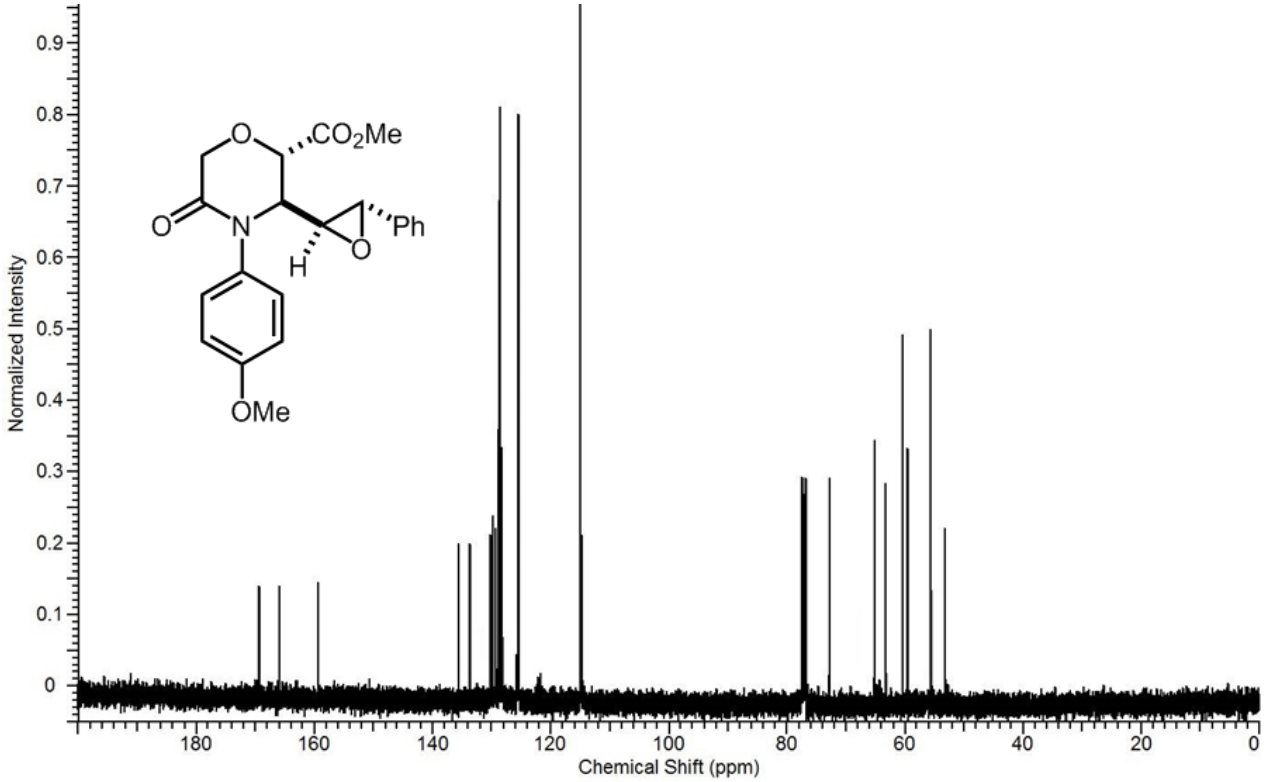

DB-080A-rerun.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
N
O
Ph

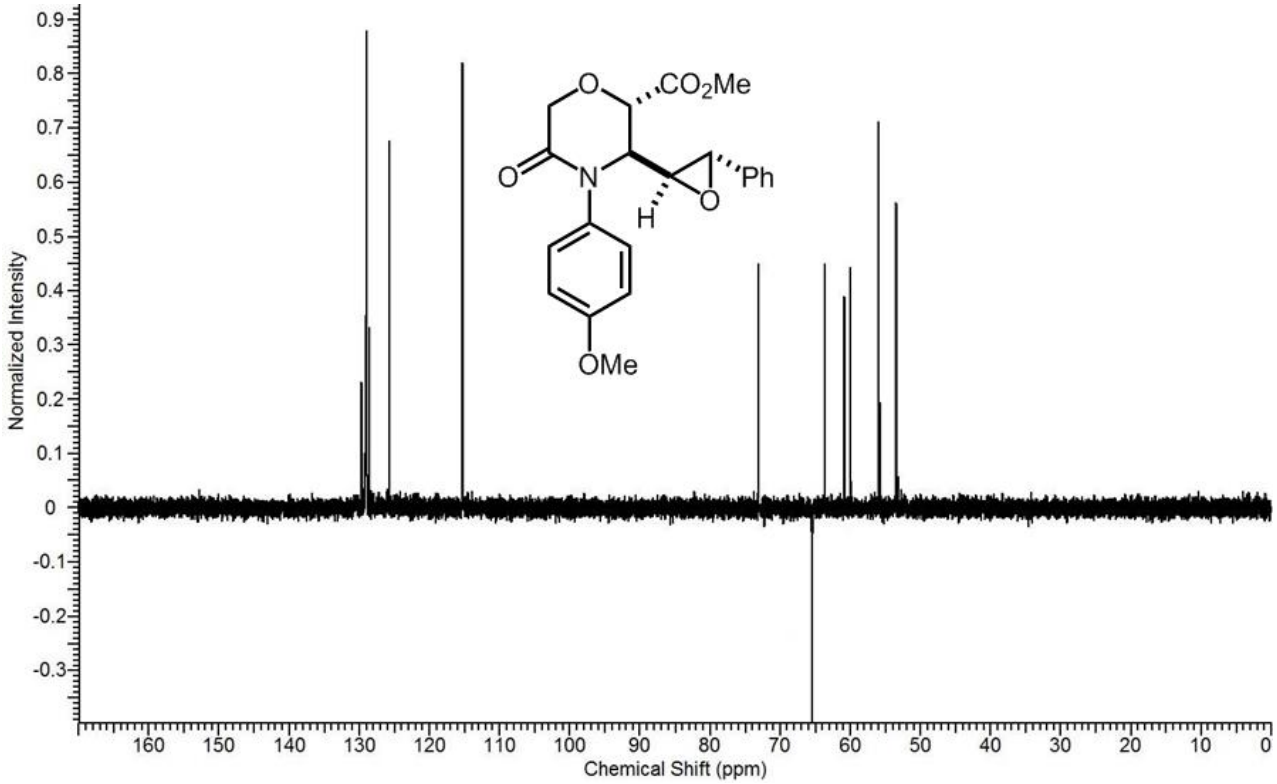


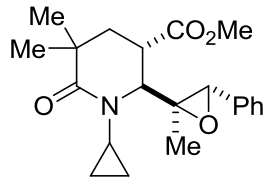
11b, 77%, >99:1 dr

Prepared from allylic lactam **5c2** (0.50 mmol) using General Procedure F. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75 to 0:100). Yield = 148 mg, 77%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 to 6.96 (9H, m), 4.87 (1H, d), 4.71 to 4.61 (1H, d), 4.52 to 4.28 (2H, m), 3.89 to 3.72 (6H, m), 3.35 to 3.31 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.38, 165.97, 159.37, 136.43, 134.64, 129.84, 128.80, 126.86, 125.73, 114.98, 72.88, 65.11, 64.30, 63.32, 60.49, 59.63, 55.53. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{21}H_{21}NO_6$ 383.1369; found 383.1366.



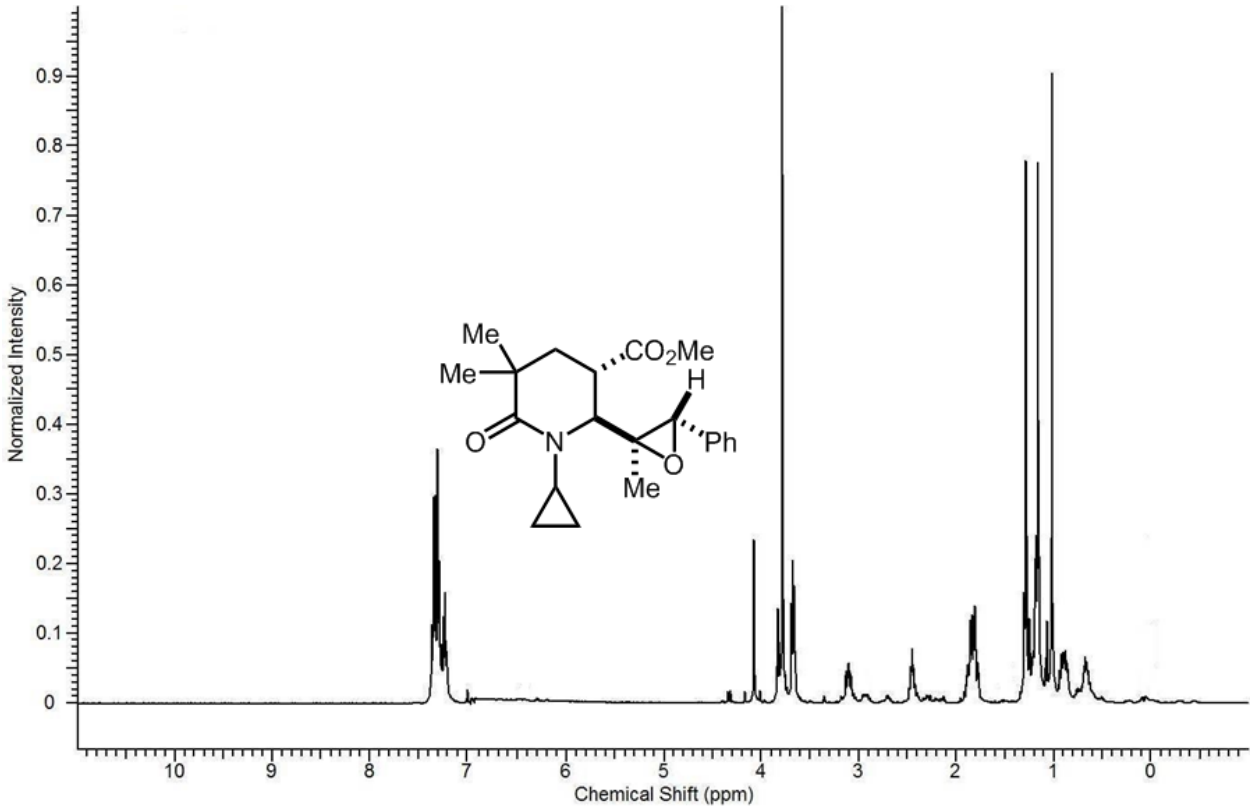

Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
OMe

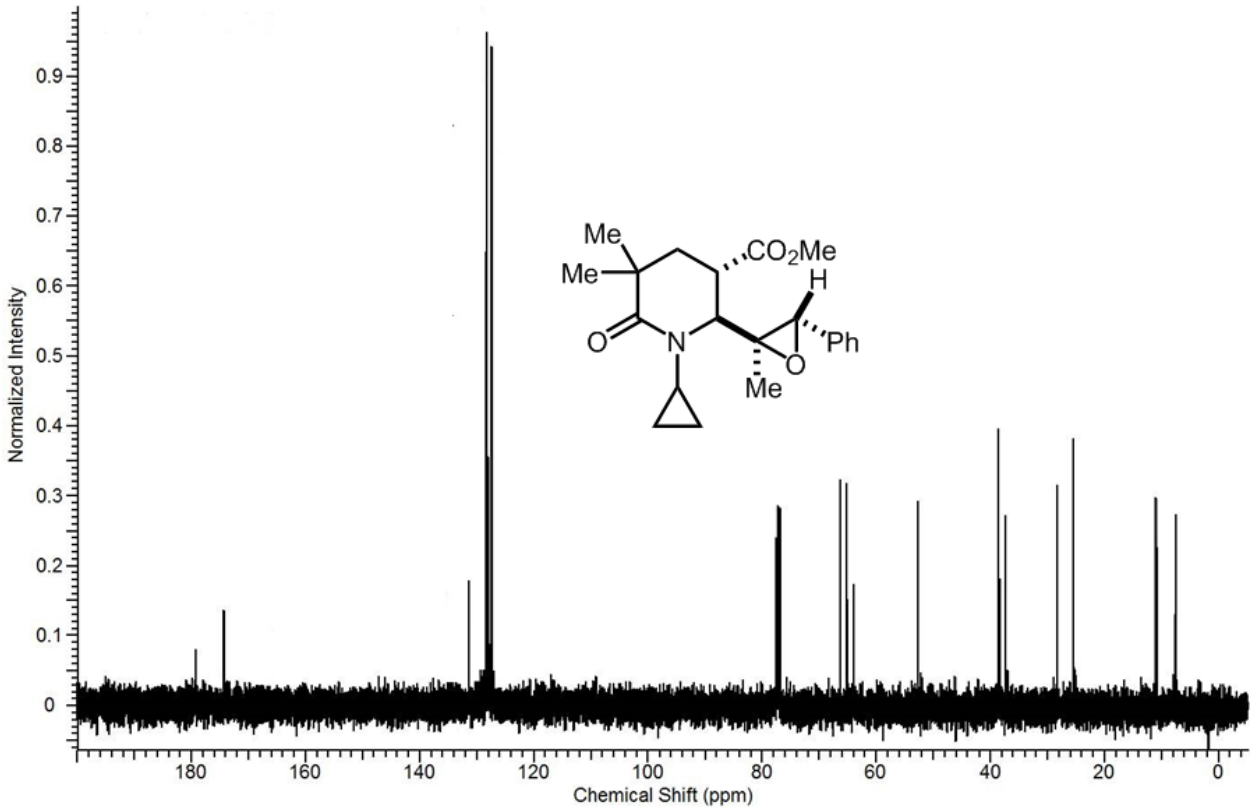

Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
OMe

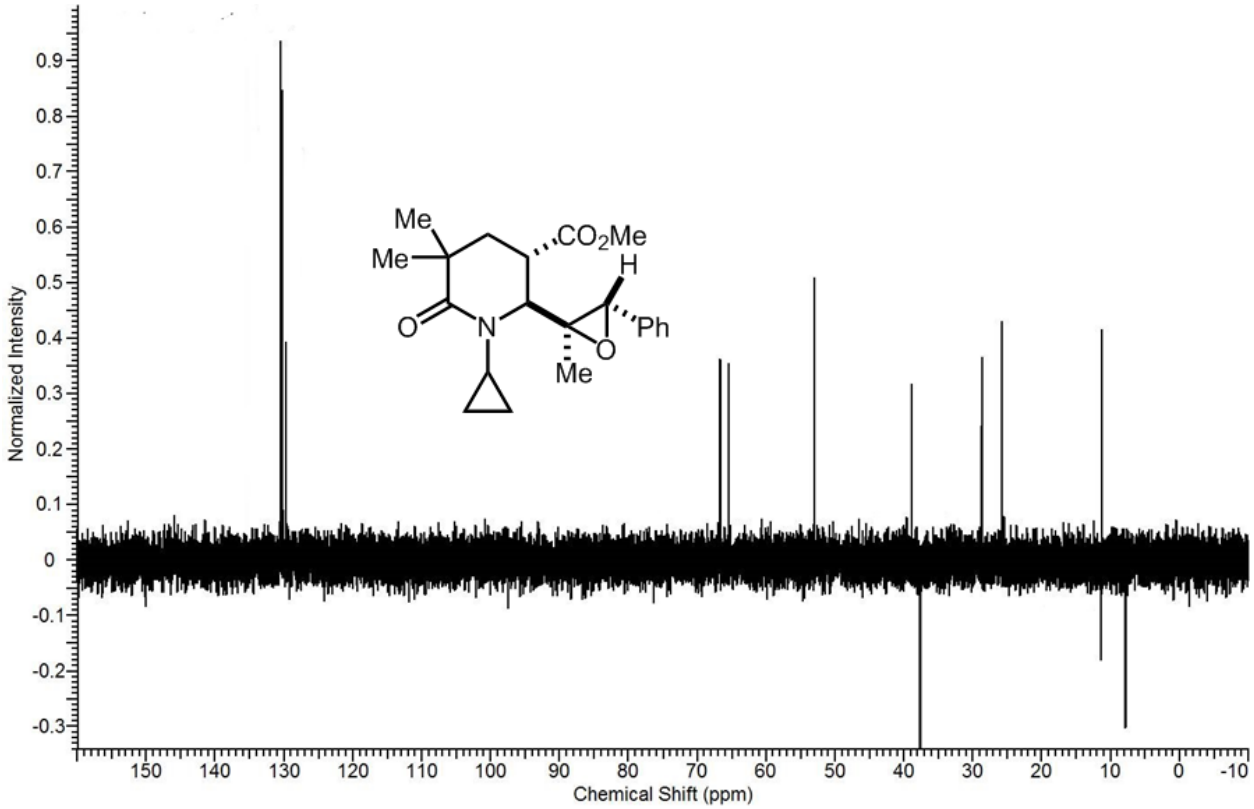


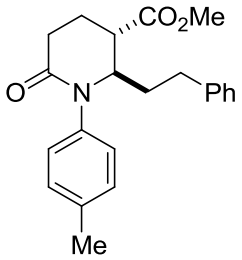
11c, 84%, >99:1 dr

Prepared from allylic lactam **7n2** (0.50 mmol) using General Procedure F. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75 to 0:100). Yield = 150 mg, 84%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 to 7.20 (5H, m), 4.17 (1H, s), 3.83 to 3.65 (5H, m), 3.13 to 3.03 (1H, m), 2.48 to 2.39 (1H, t), 1.89 to 1.80 (2H, m), 1.32 to 0.62 (10H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.1, 174.2, 131.3, 129.8, 128.3, 127.5, 126.2, 68.2, 65.1, 63.8, 52.6, 38.5, 38.2, 28.3, 25.2, 10.9, 7.9. **HRMS-EI**$^{+}$ (*m/z*): calc'd for $C_{21}H_{27}NO_4$ 357.1940; found 357.1945.



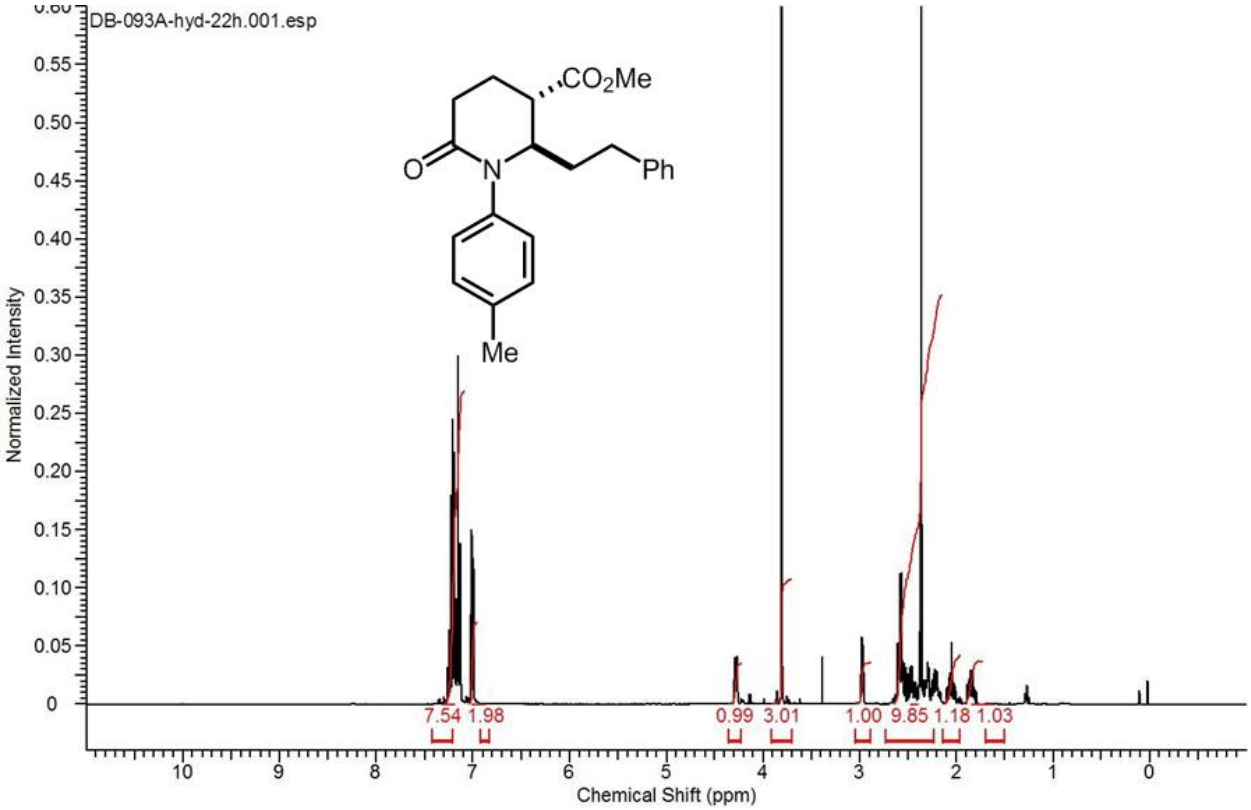

Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2Me
H
Ph
O
N
O
Me

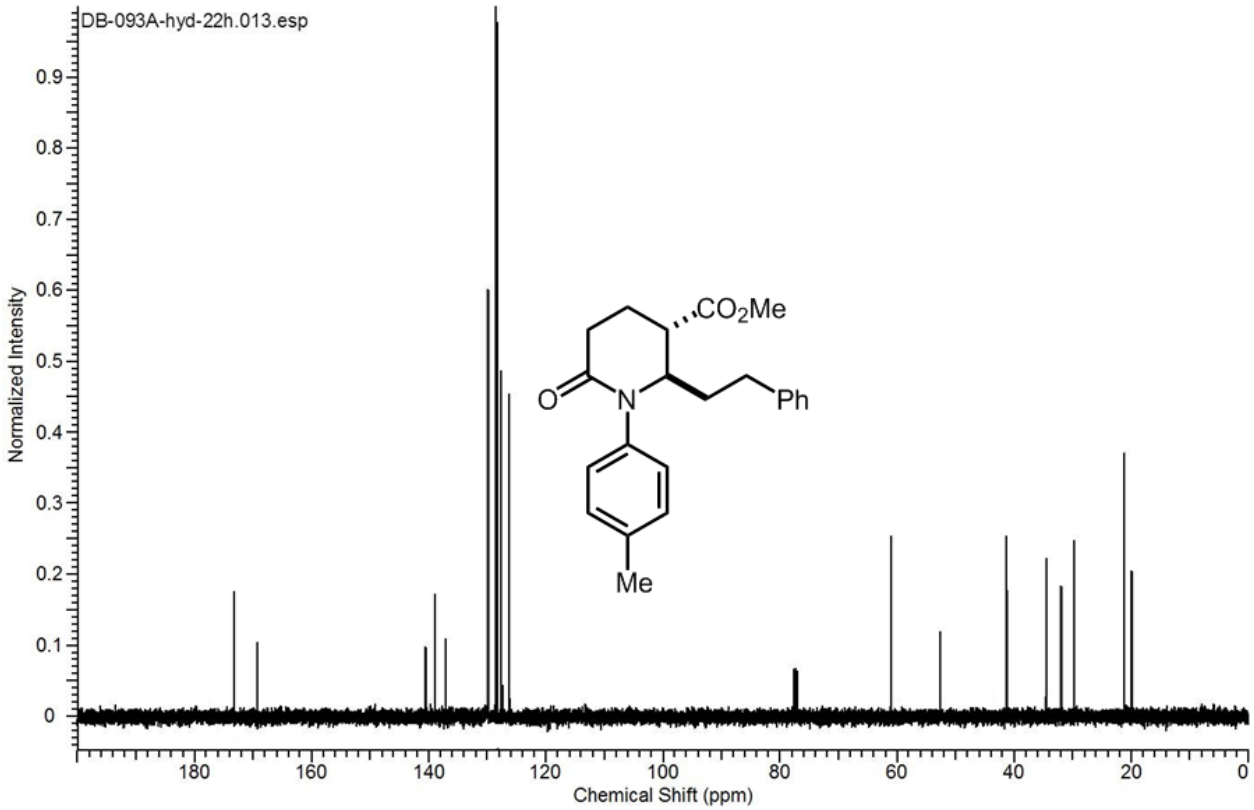

Normalized Intensity
Chemical Shift (ppm)
Me
Me
CO2Me
H
Ph
O
N
O
Me



12a

Prepared from alkene **7b2** (0.50 mmol) using General Procedure E. Yield = 167 mg, 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 to 7.13 (7H, m), 7.02 (2H, d), 4.30 to 4.20 (1H, m), 3.79 (3H, s), 2.80 to 2.71 (1H, t), 2.65 to 2.16 (9H, m), 2.10 to 1.979 (1H, m), 1.83 to 1.79 (1H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 169.1, 140.5, 138.9, 137.0, 129.9 129.9, 128.5, 128.4, 128.2, 128.1, 127.6, 127.3, 126.2, 126.1, 61.0, 52.5, 41.3, 34.6, 31.9, 29.7, 21.2, 19.9. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{22}H_{25}NO_3$ 351.1834; found 351.1839.




DB-093A-hyd-22h.013.esp
Normalized Intensity
Chemical Shift (ppm)
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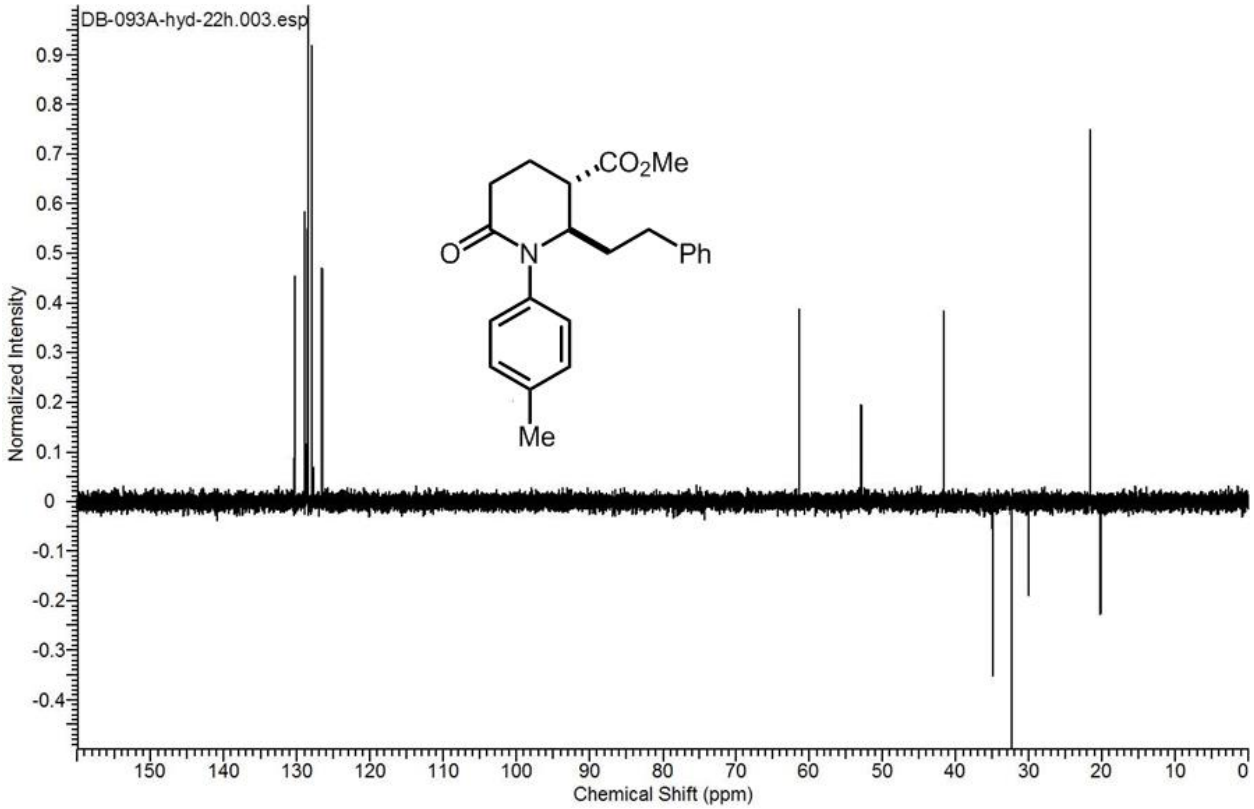
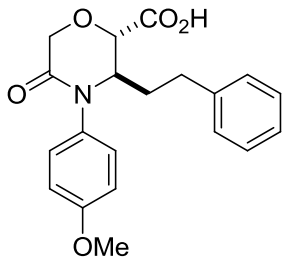
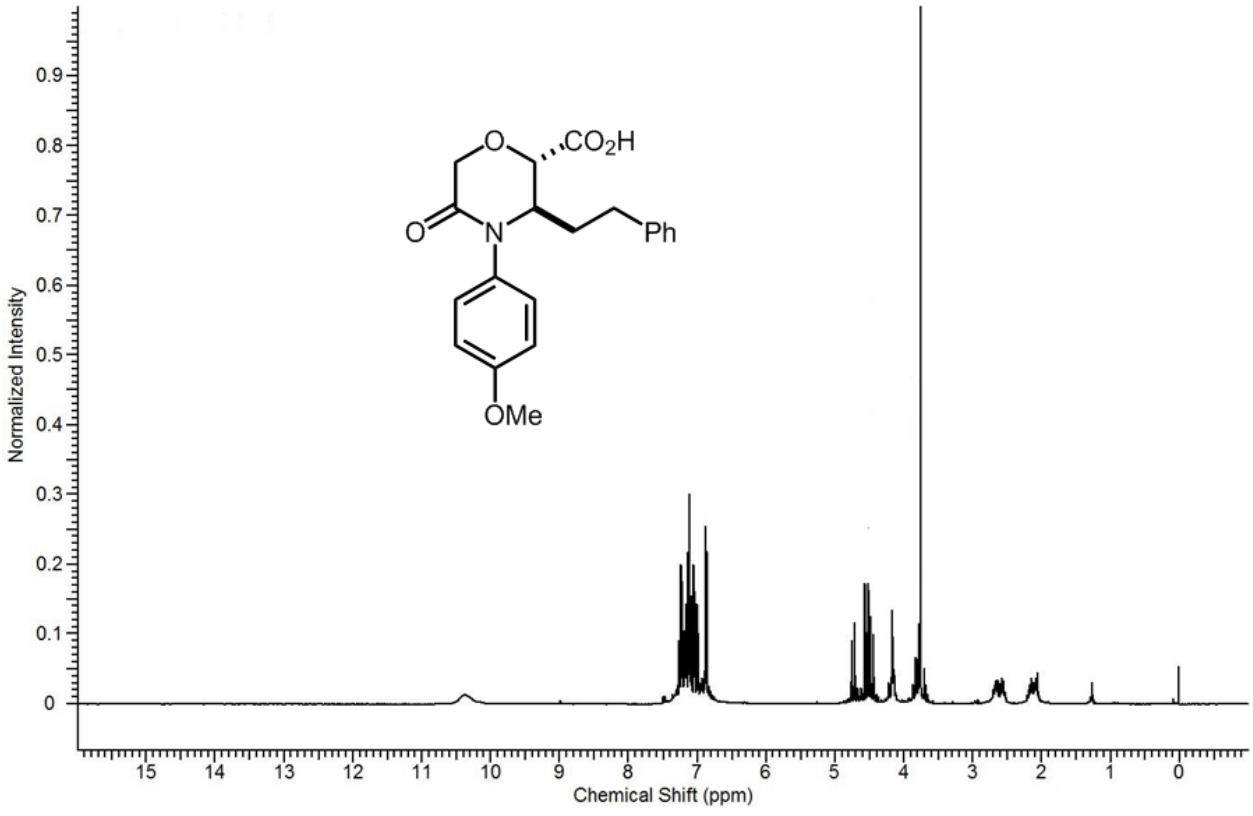
Ph
Me
O
N

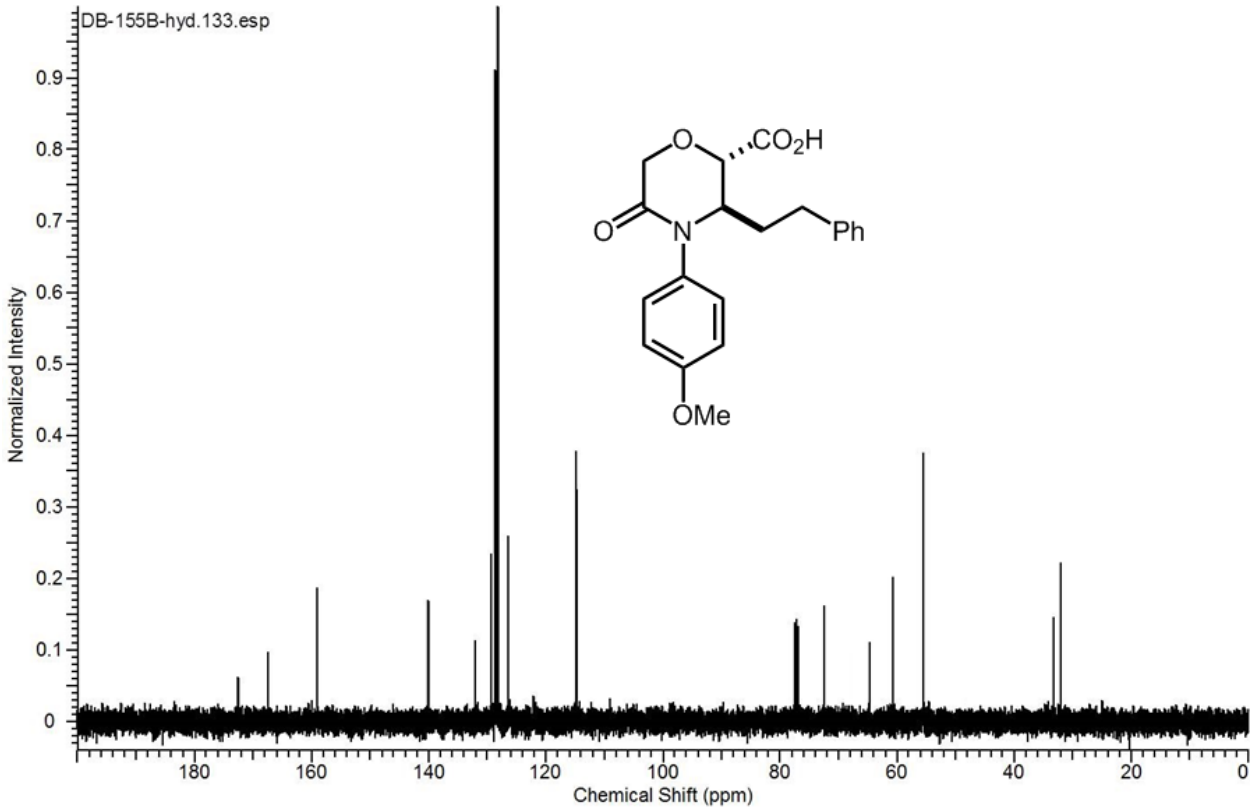

DB-093A-hyd-22h.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
Me
O
N



12b

Prepared from alkene **5c1** (0.50 mmol) using General Procedure E. Yield = 174 mg, 98%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.38 (1H, s, br), 7.37 to 6.76 (9H, m), 4.76 to 4.37 (3H, m), 4.18 (1H, d), 3.80 (3H, s), 2.70 to 2.52 (2H, m), 2.21 to 2.07 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.51, 167.42, 158.96, 140.15, 132.07, 129.34, 128.65, 128.49, 128.21, 128.20, 128.13, 126.39, 114.23, 72.54, 64.63, 60.74, 55.56, 33.29, 32.03. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{20}H_{21}NO_5$ 355.1420; found 355.1417.

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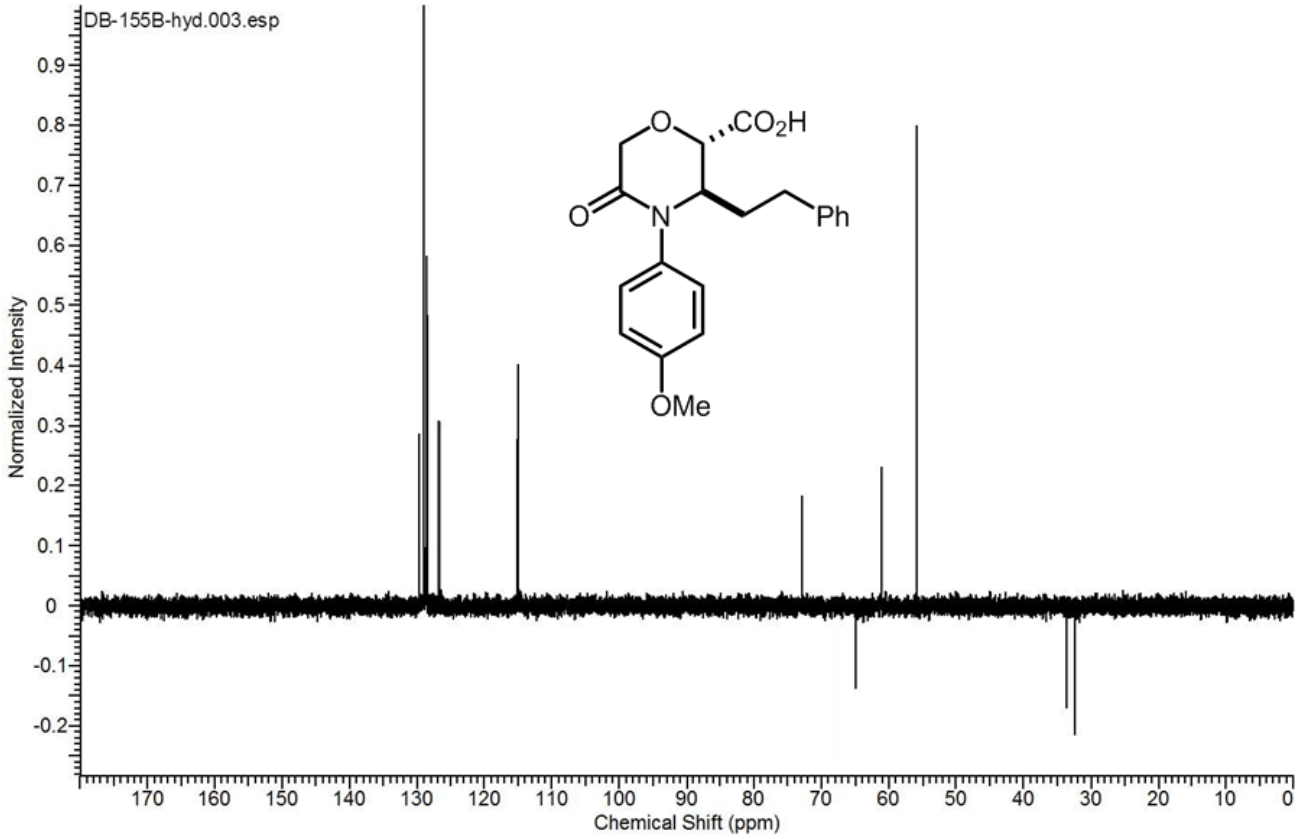
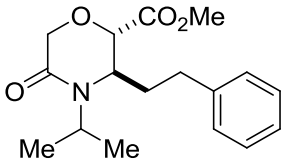
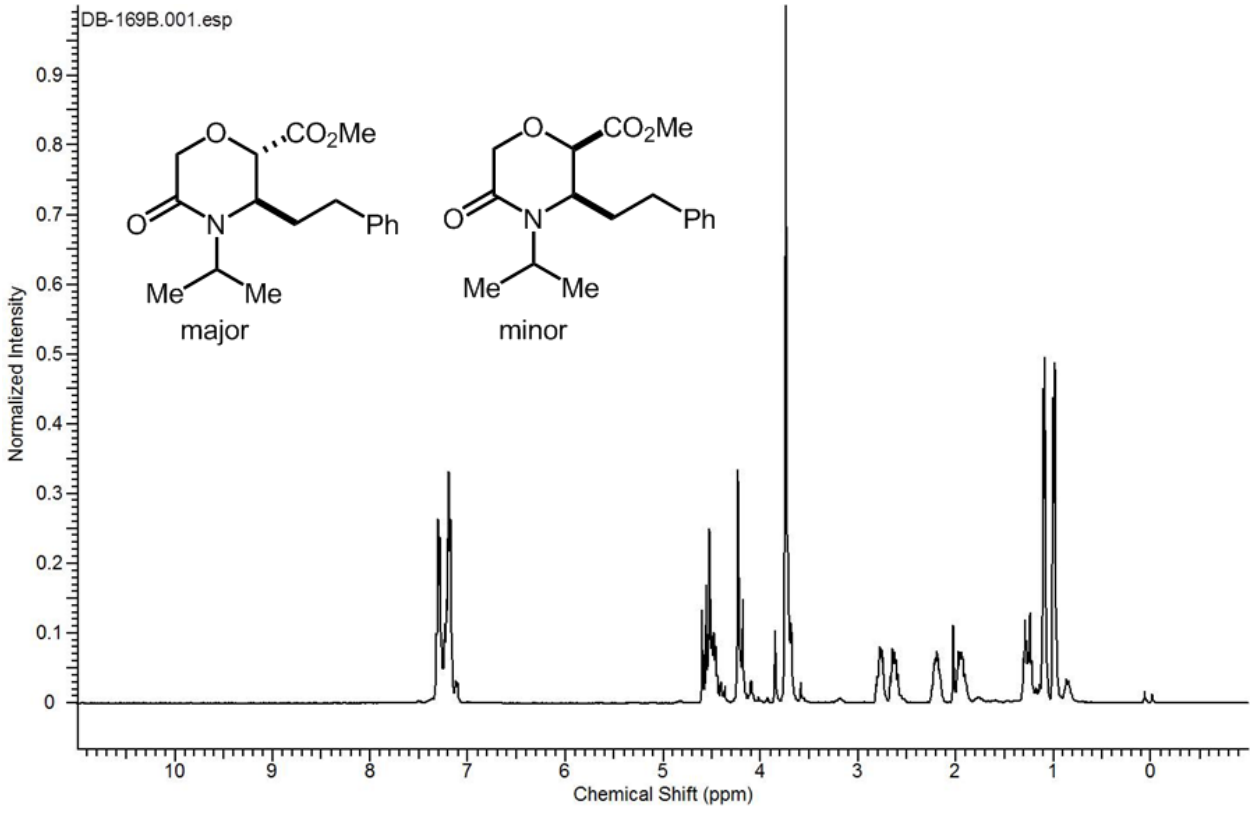
Normalized Intensity
Chemical Shift (ppm)
CO2H
Ph
OMe

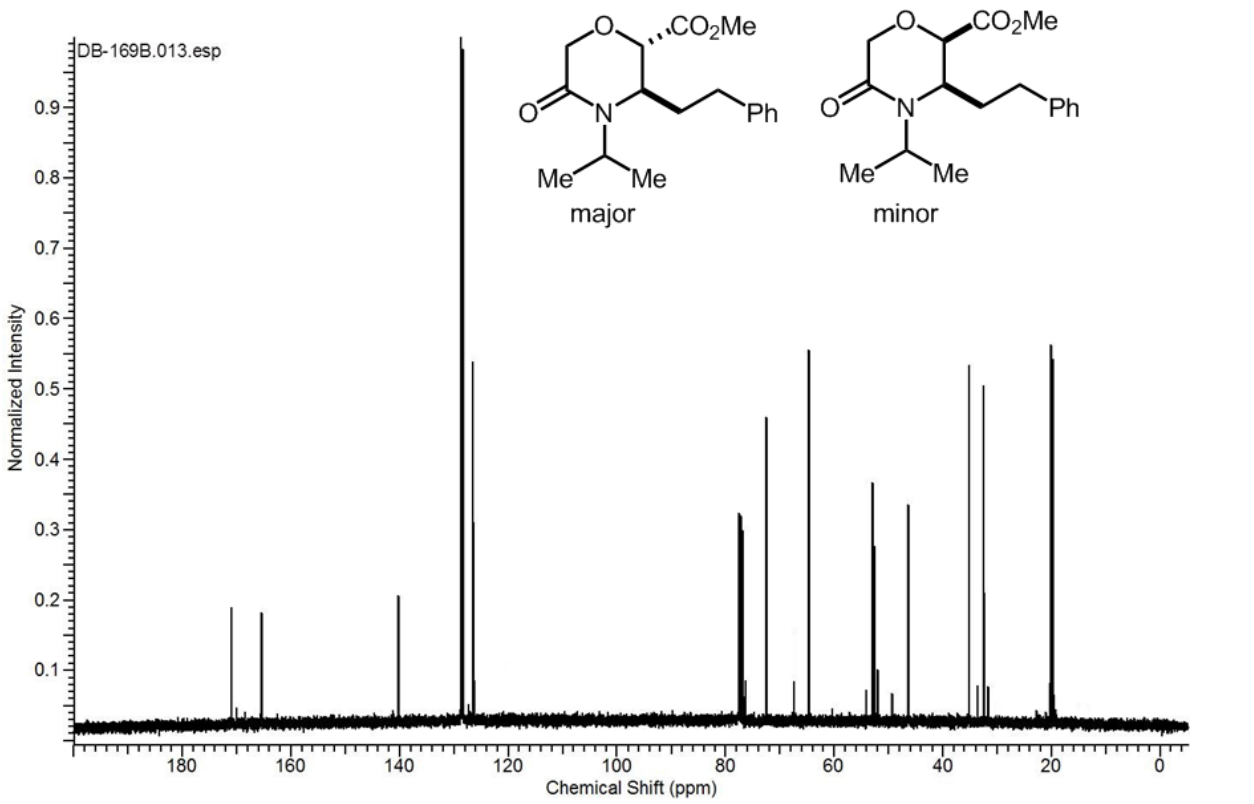

DB-155B-hyd.003.esp
Normalized Intensity
Chemical Shift (ppm)
CO2H
Ph
OMe



12c

Prepared from alkene **5q2** (0.25 mmol) using General Procedure E. Yield = 75 mg, 96%, 86:14 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 to 7.12 (5H, m), 4.61 to 4.09 (4H, m), 3.77 to 3.61 (4H, m), 2.83 to 2.61 (2H, m), 2.27 to 1.92 (2H, m), 1.32 to 1.02 (6H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 170.1, 168.4, 165.7, 165.4, 141.2, 140.2, 128.7, 128.6, 128.6, 128.4, 128.3, 127.3, 126.5, 126.3, 80.8, 77.5, 77.1, 76.8, 76.2, 72.5, 69.6, 68.1, 67.4, 64.7, 60.4, 54.0, 52.9, 52.6, 52.5, 52.0, 49.3, 46.4, 44.1, 39.0, 35.2, 33.7, 32.5, 31.7, 29.7, 22.7, 21.1, 20.4, 20.1, 19.9, 19.7, 19.2, 19.1, 14.2. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{17}H_{23}NO_4$ 305.1627; found 305.1622.

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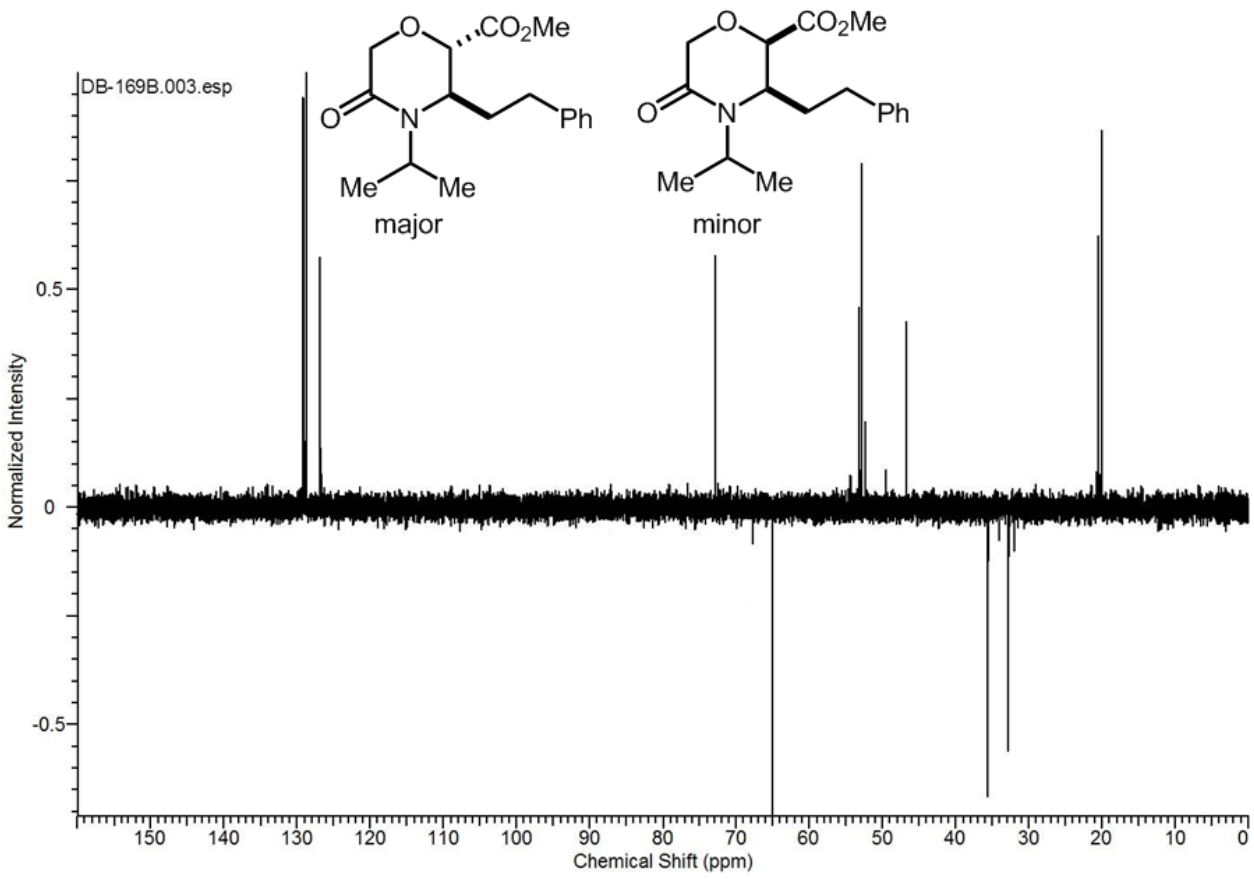
Normalized Intensity
Chemical Shift (ppm)
major
minor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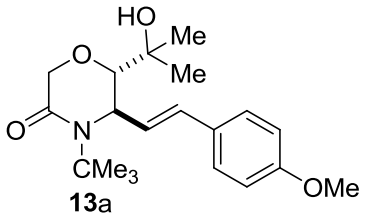
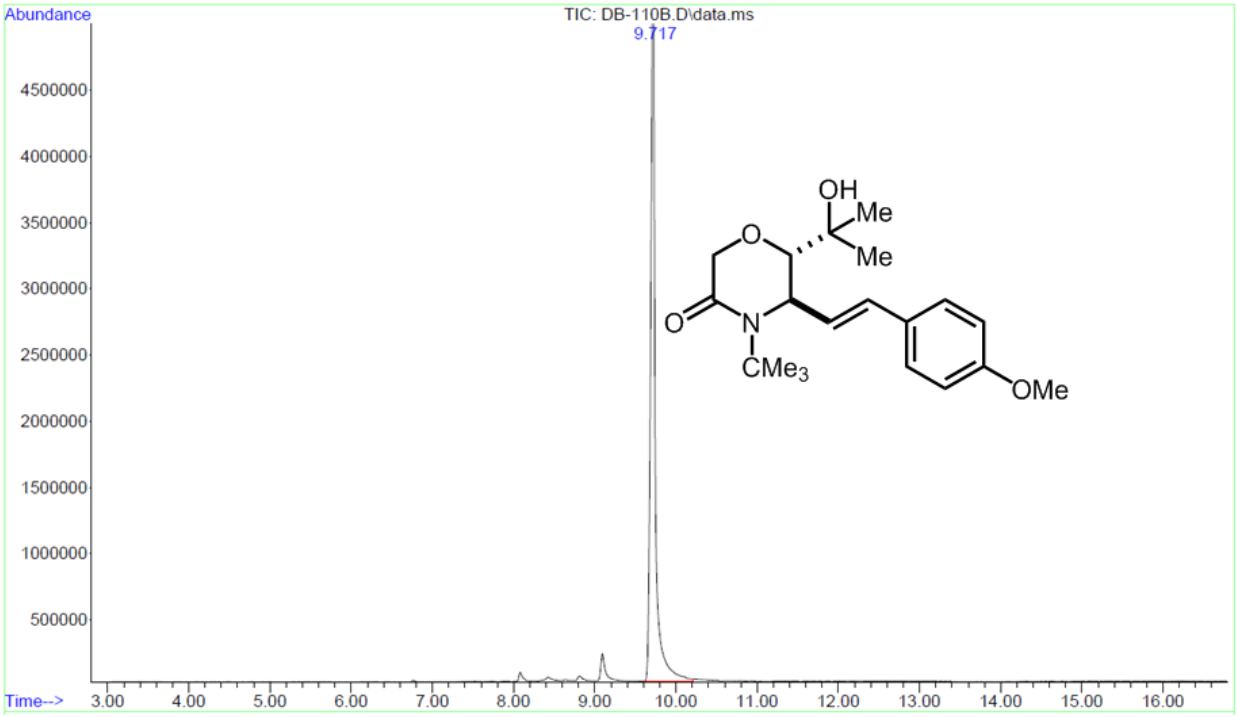
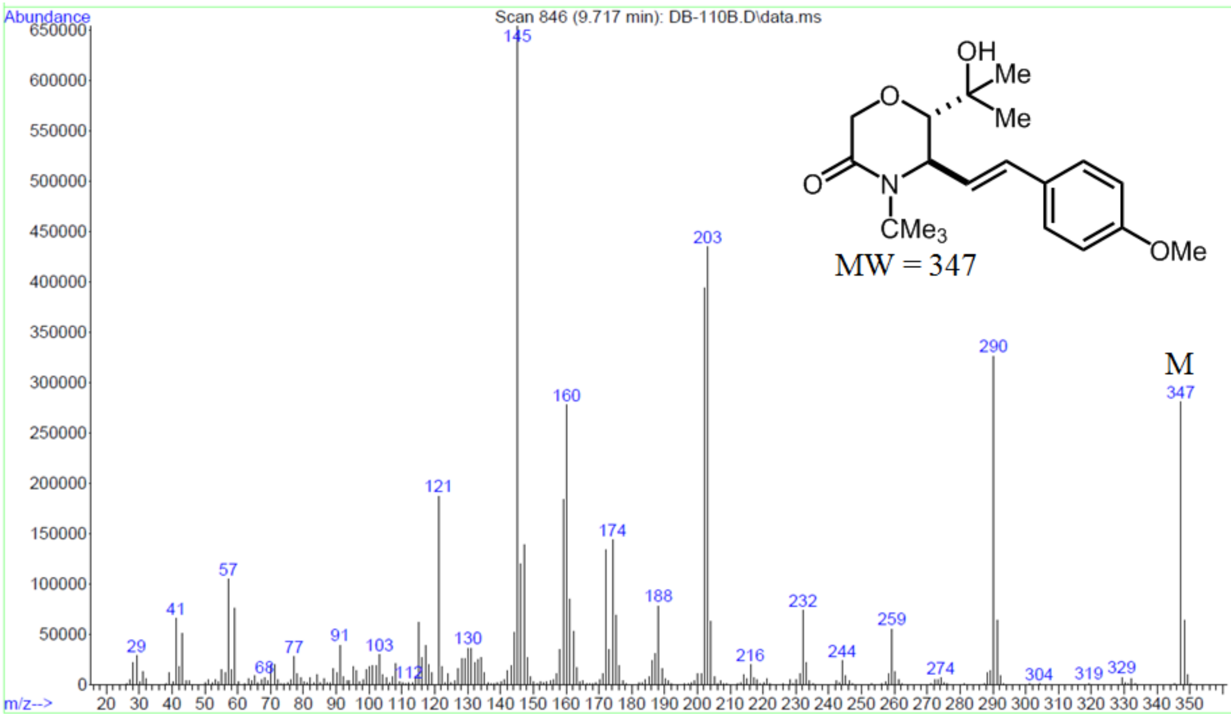
Normalized Intensity
Chemical Shift (ppm)
major
minor



13a

Prepared from ester **5p2** (0.50 mmol) and MeLi (1.42 mL, 1.4 M solution in THF, 2 mmol, 4 equiv) using General Procedure D. Yield = 151 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (2H, d), 6.84 (2H, d), 6.41 (1H, d), 5.97 to 5.91 (1H, dd), 4.69 to 4.66 (1H, dd), 4.17 (1H, d), 3.95 (1H, d), 3.79 (3H, s), 3.58 (1H, d), 2.29 (1H, s), 1.44 to 1.24 (9H, m). ^{13}C NMR (101 MHz, CDCl3) δ 171.3, 159.6, 132.0, 130.5, 130.4, 130.0, 128.7, 127.9, 127.8, 127.6, 125.6, 125.0, 114.2, 114.0, 113.7, 85.0, 84.1, 80.0, 77.4, 77.1, 76.8, 72.9, 71.2, 68.7, 68.0, 57.9, 55.7, 55.4, 55.2, 53.8, 30.4, 30.0, 28.8, 28.5, 28.4, 28.4, 28.0, 27.3, 26.7, 26.4, 26.2, 25.6, 14.3. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{20}H_{29}NO_4$ 347.2097; found 347.2095.

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203
290
M
347
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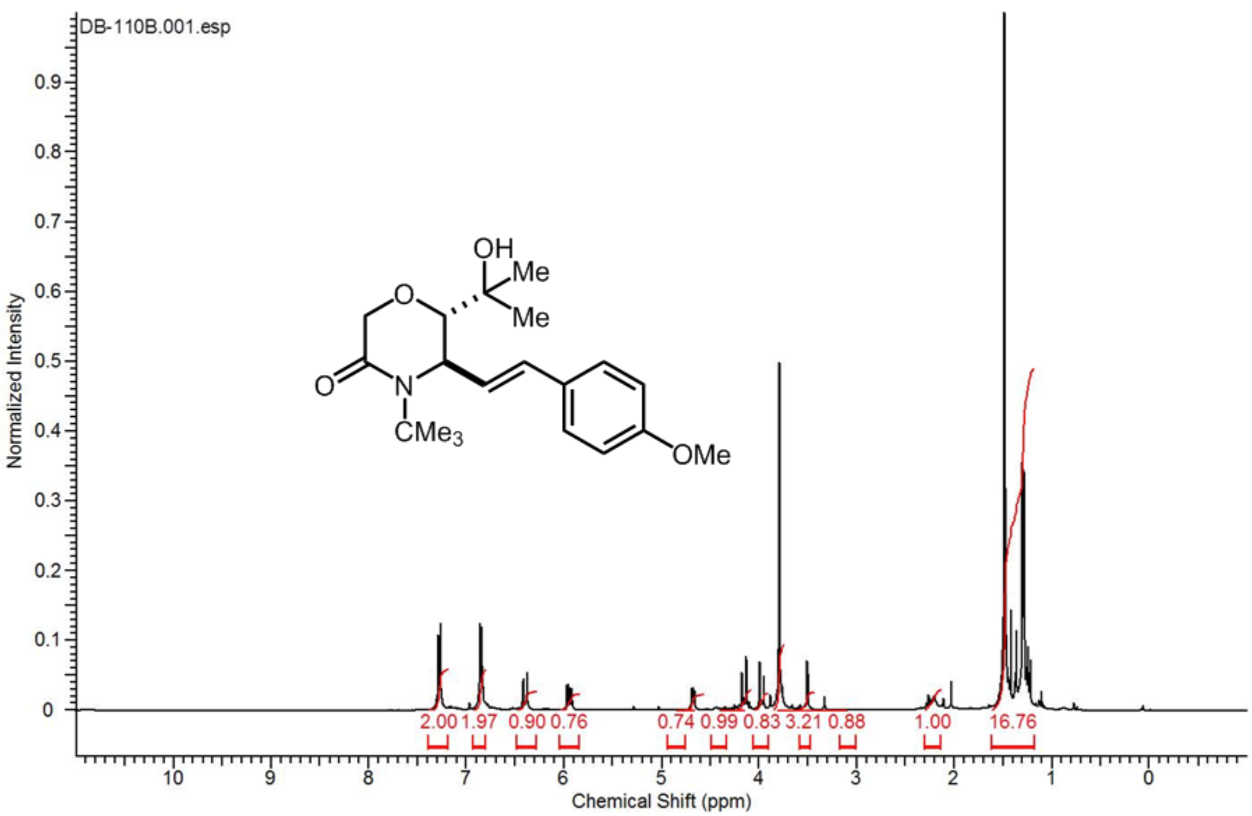
OH
Me
Me
O
N
CMe3
OMe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Normalized Intensity
Chemical Shift (ppm)
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1.00
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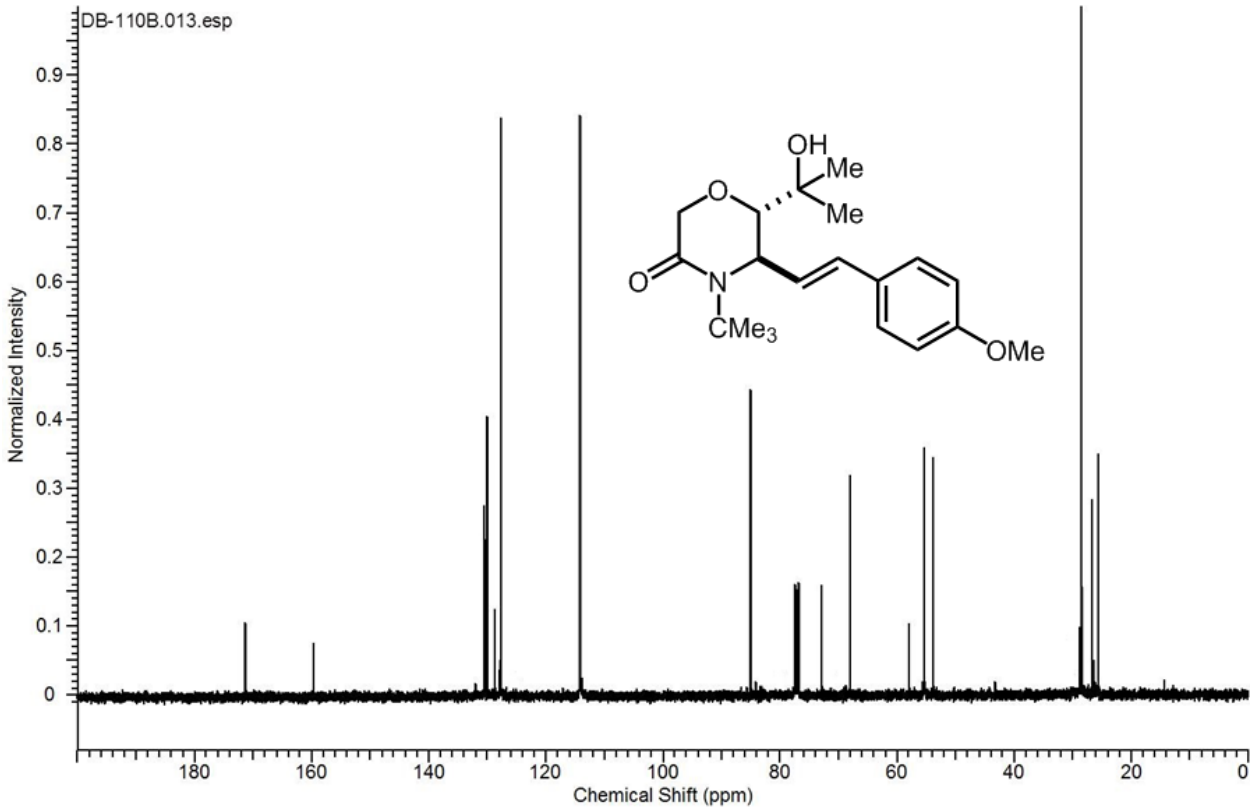
Me
O
N
CMe3
OMe


DB-110B.013.esp
Normalized Intensity
Chemical Shift (ppm)
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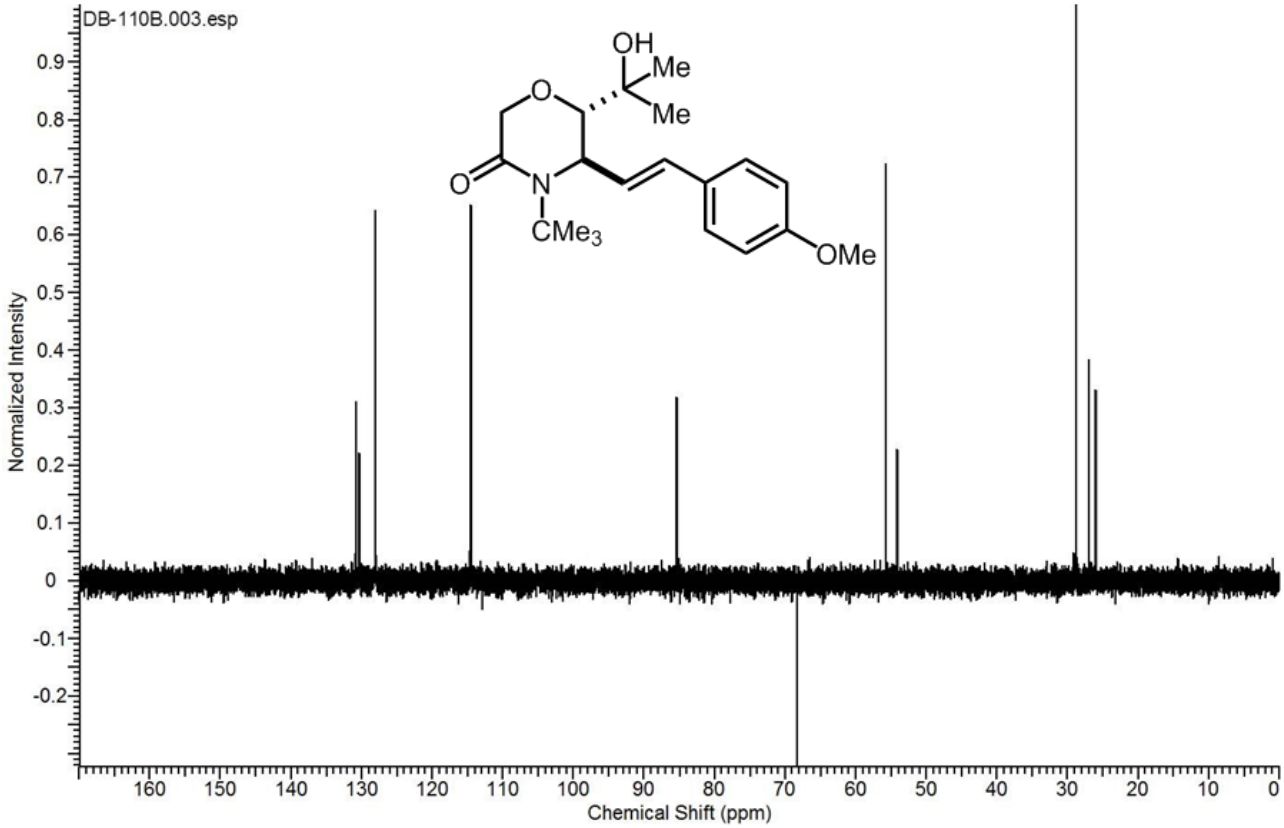
Me
Me
O
N
CMe3
OMe


DB-110B.003.esp
Normalized Intensity
Chemical Shift (ppm)
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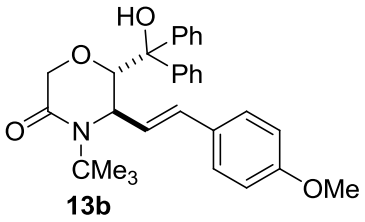
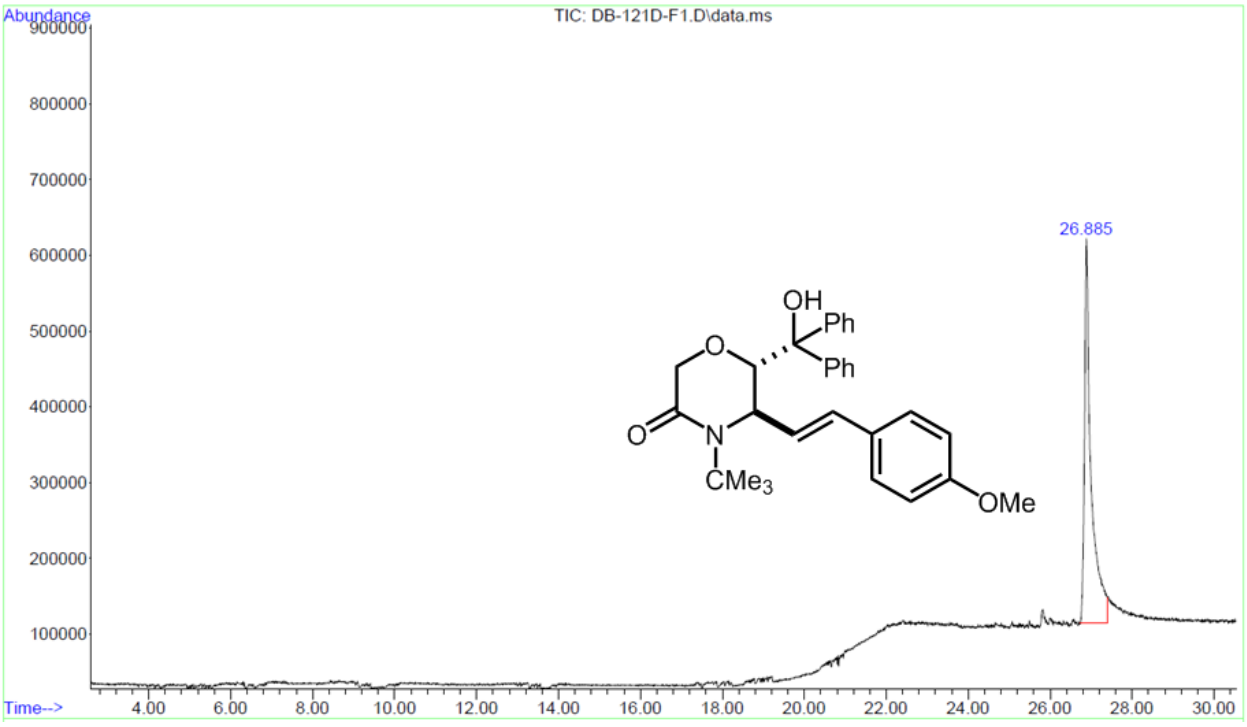
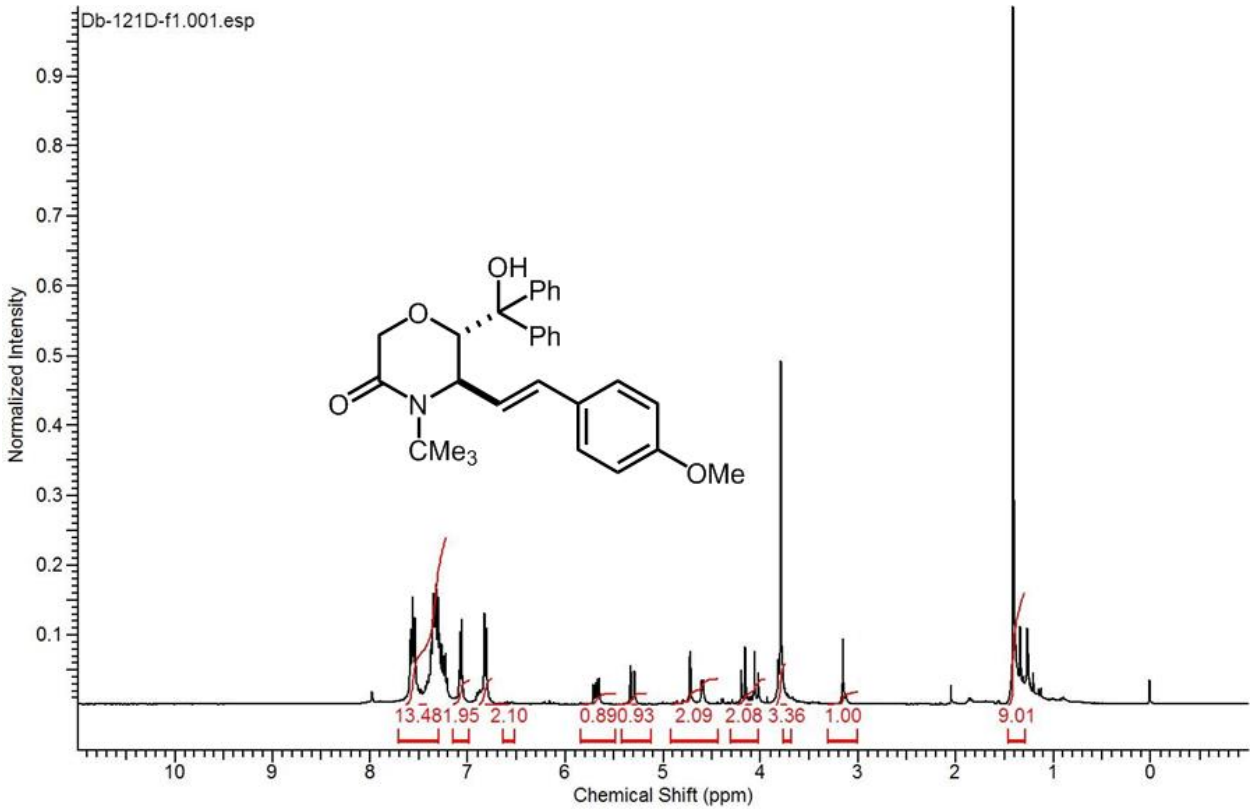
Me
O
N
CMe3
OMe



13b

Prepared from ester **5p2** (0.50 mmol) and phenyllithium (3.0 mL, 1.0 M solution in Et_2O, 3 mmol, 6 equiv) using General Procedure D. Yield = 200 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 to 7.21 (10H, m), 7.08 (2H, d), 6.83 (2H, d), 5.71 (1H, dd), 5.33 (1H, d), 4.79 to 4.58 (2H, m), 4.40 to 4.13 (2H, m), 3.79 (3H, s), 3.12 (1H, s), 1.31 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 159.5, 145.0, 142.8, 131.5, 130.4, 129.5, 128.7, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 127.8, 127.6, 127.4, 127.3, 126.5, 126.4, 126.2, 126.0, 126.0, 125.9, 125.3, 124.7, 114.2, 83.2, 80.2, 68.4, 59.3, 58.0, 57.7, 28.7. **HRMS-EI**$^+$ (*m/z*): calc'd for $C_{30}H_{33}NO_4$ 471.2410; found 471.2417.

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Chemical Shift (ppm)
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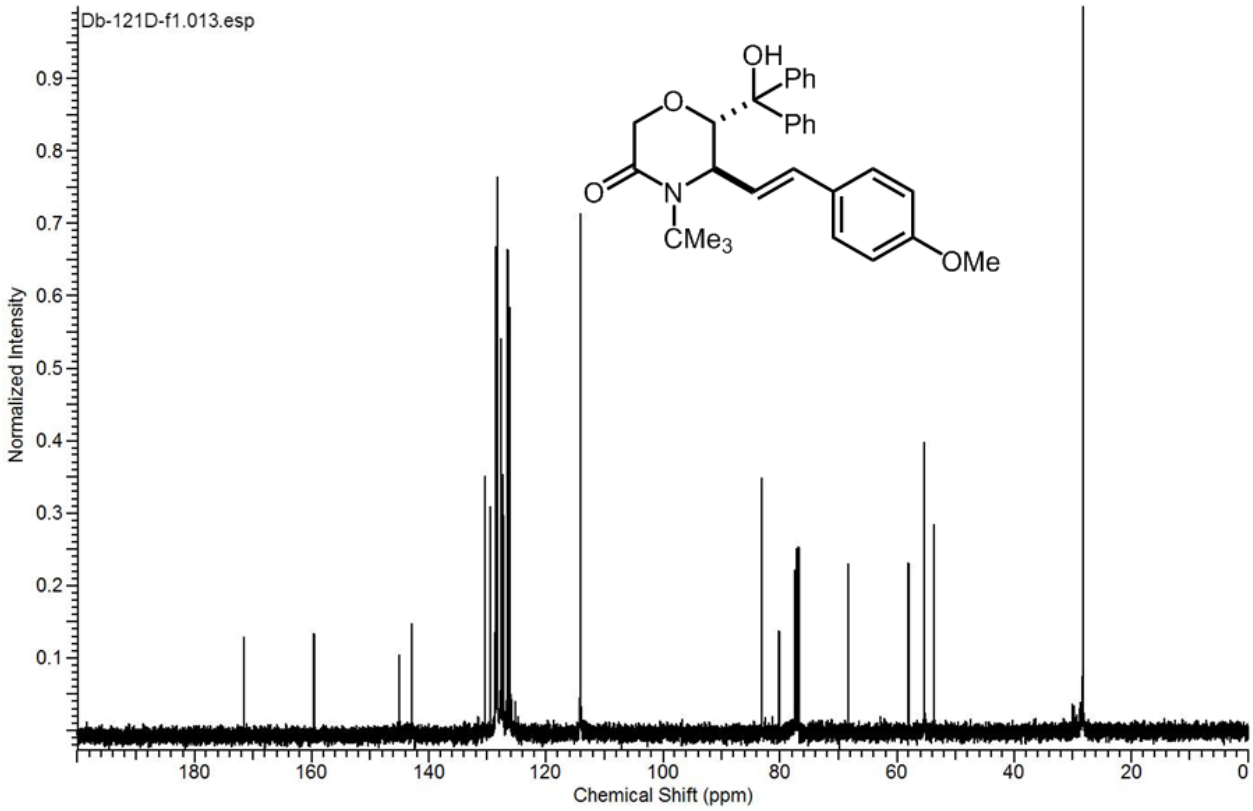
OH
Ph
Ph
O
N
CMe3
OMe


Db-121D-f1.013.esp
Normalized Intensity
Chemical Shift (ppm)
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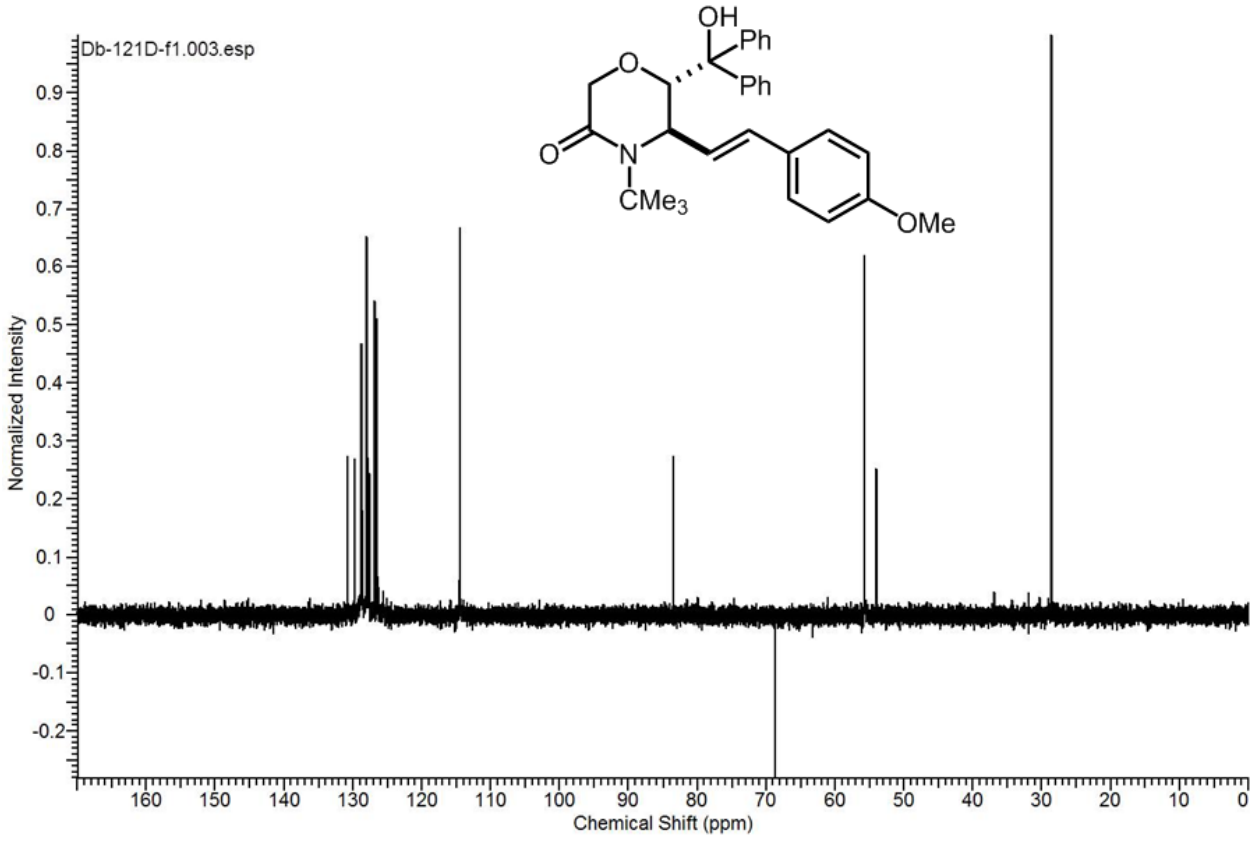
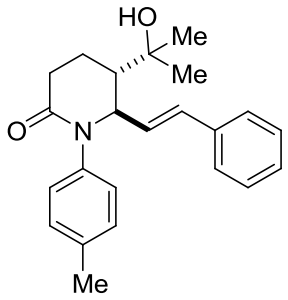
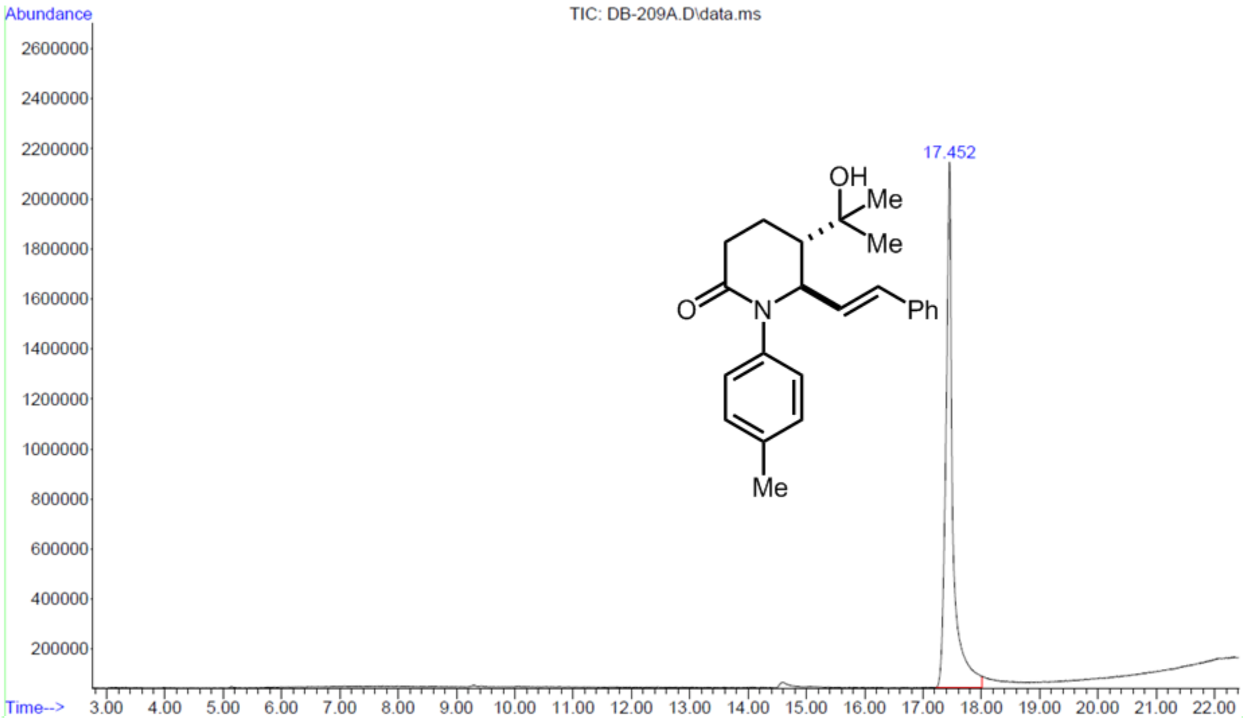
Ph
Ph
O
N
CMe3
OMe





13c

Prepared from ester **7b2** (0.50 mmol) and MeLi (1.42 mL, 1.4 M solution in THF, 2 mmol, 4 equiv) using General Procedure D. Yield = 154 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 to 7.11 (9H, m), 6.43 to 6.21 (2H, m), 4.64 (1H, dd), 2.58 to 2.05 (7H, m), 1.78 to 1.67 (2H, m), 1.44 to 1.39 (6H, s,s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 139.9, 136.3, 132.5, 129.7, 129.6, 128.7, 127.8, 126.5, 126.5, 126.1, 125.5, 72.9, 62.6, 50.6, 32.0, 29.1, 25.7, 22.2, 21.1. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{23}H_{27}NO_2$ 349.2042; found 349.2046.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Me
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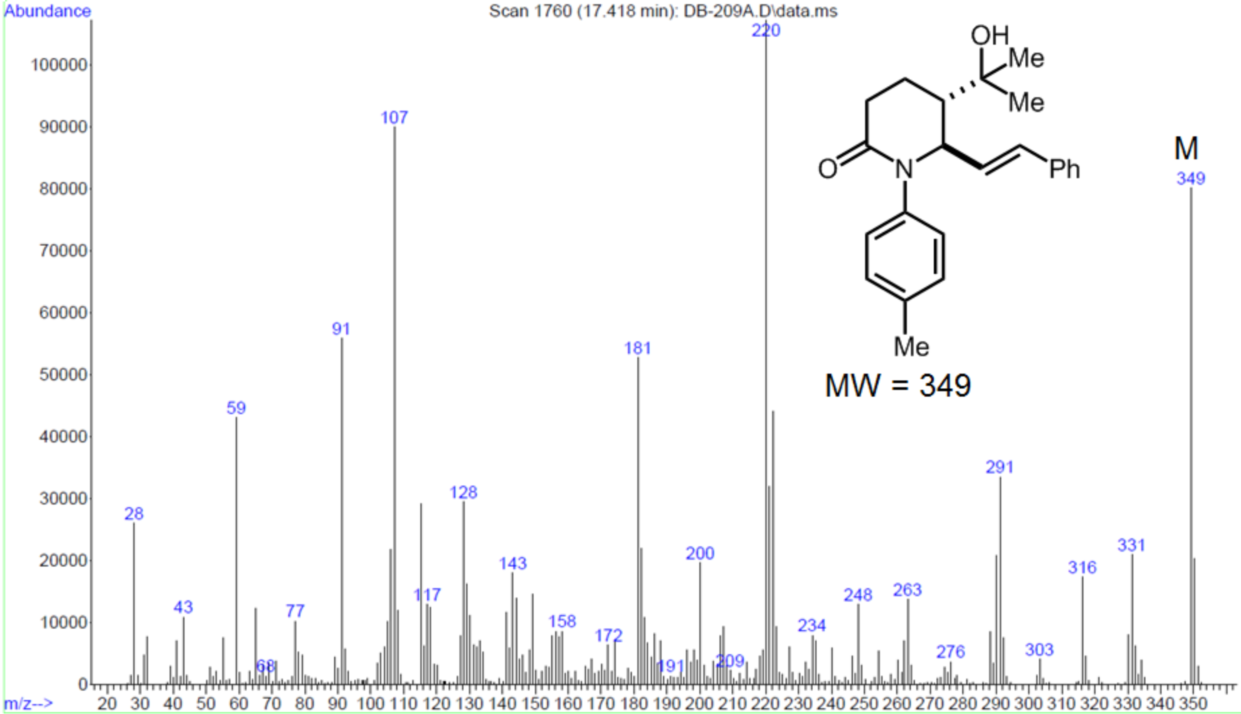
N
Ph
Me
Time-->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234
172
276
303
M
349
OH
Me
Me
O
N
Ph
Me
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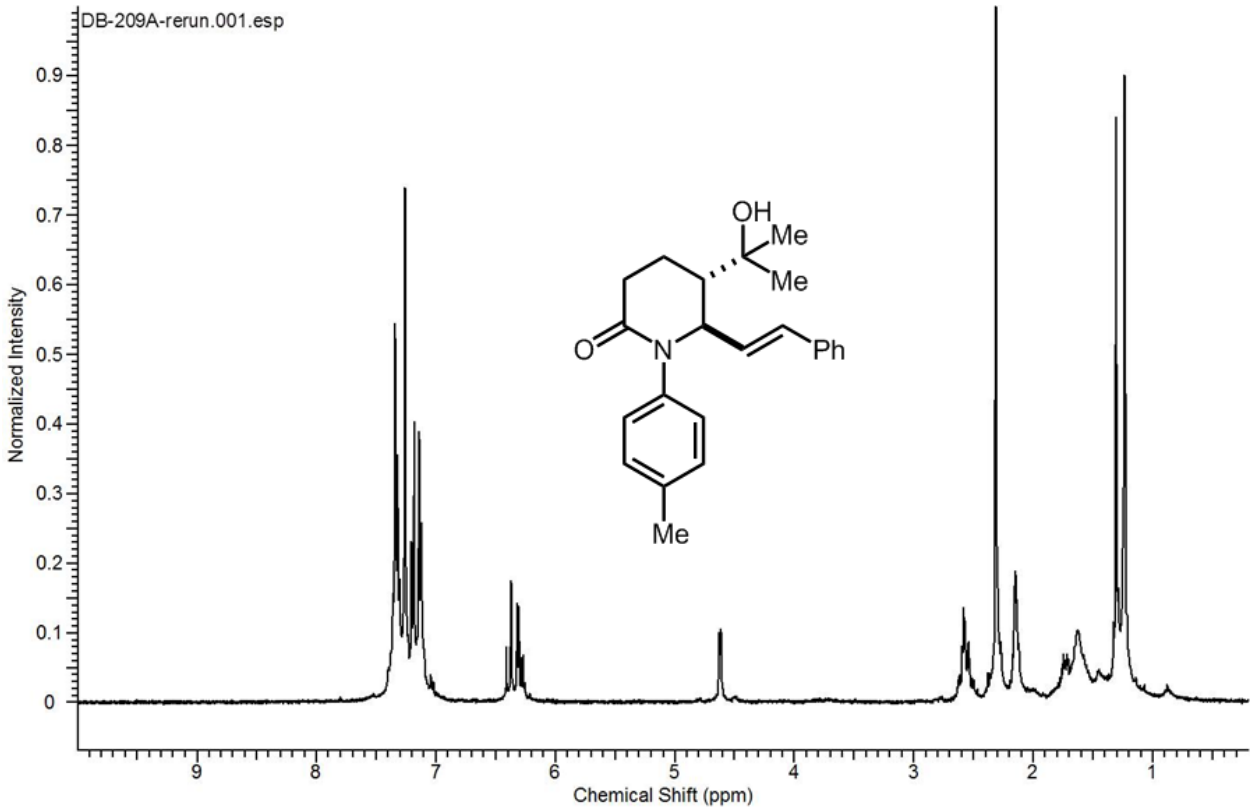
m/z-->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Normalized Intensity
Chemical Shift (ppm)
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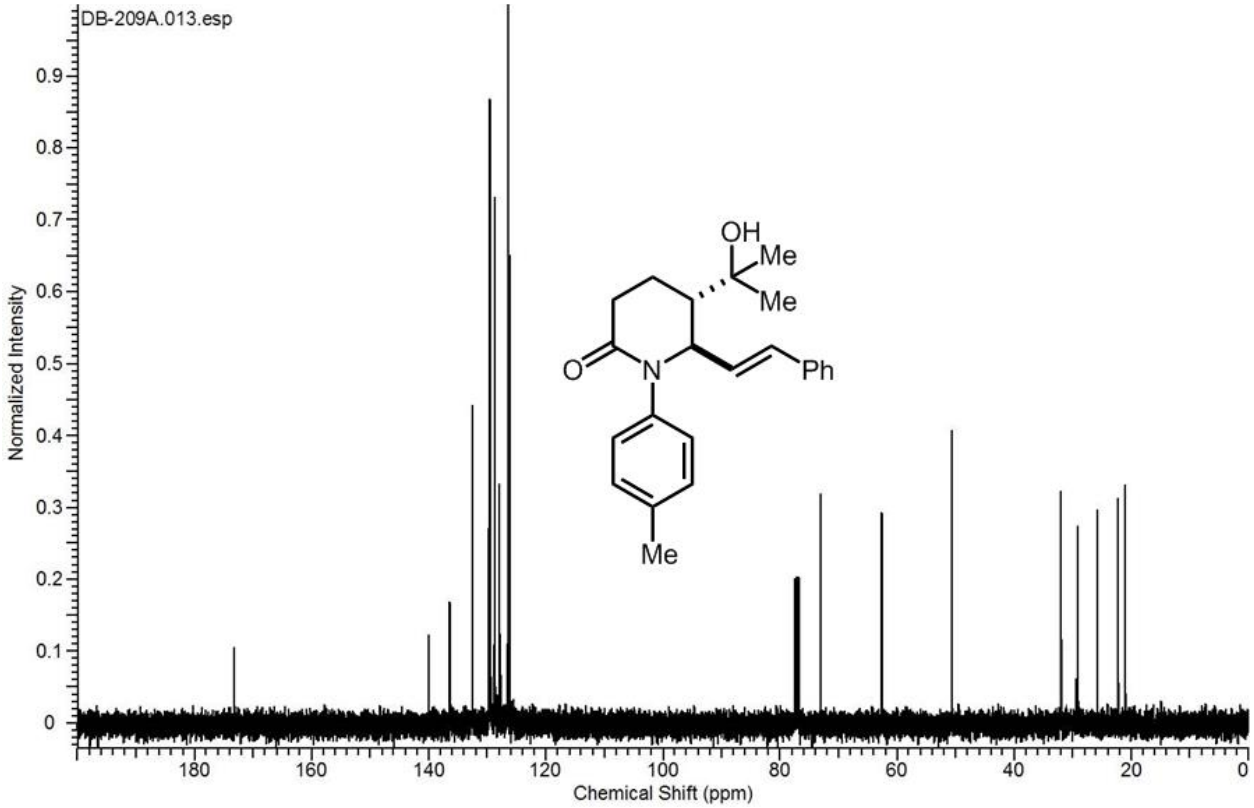
Me
O
N
Ph
Me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Normalized Intensity
Chemical Shift (ppm)
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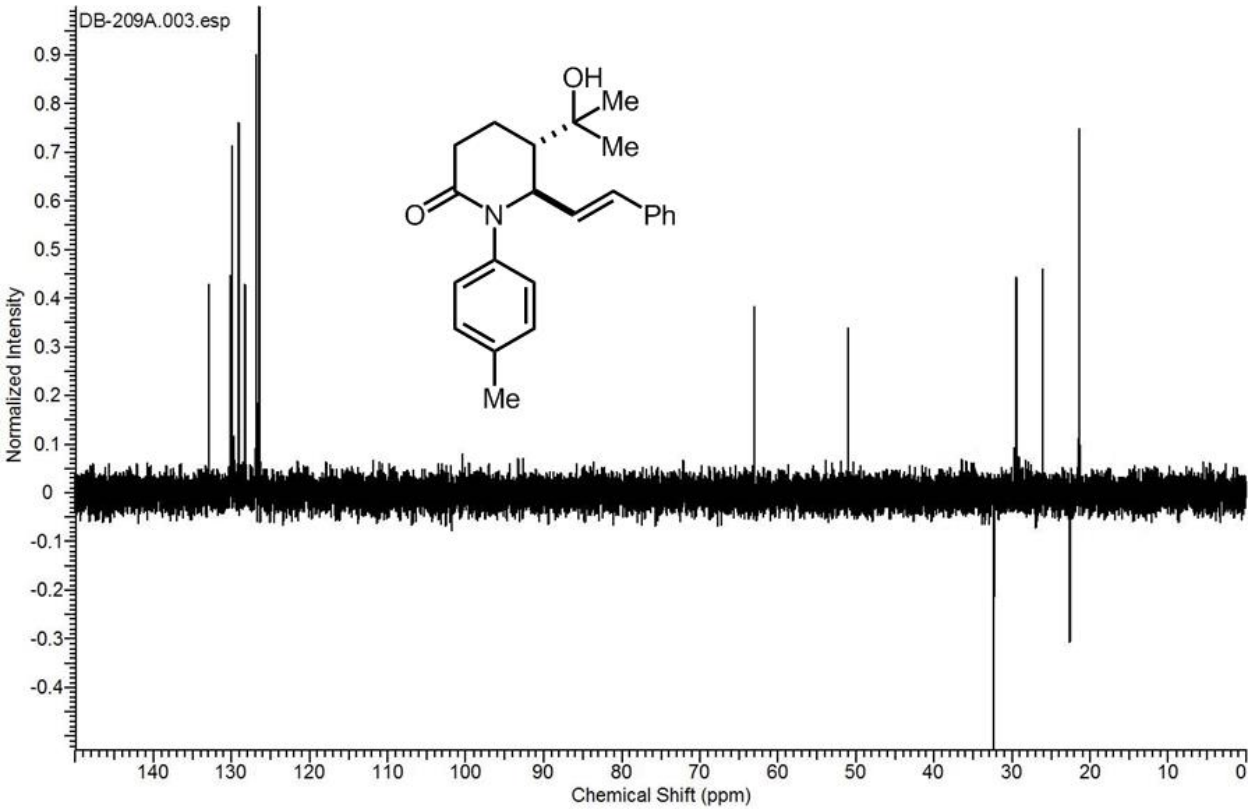
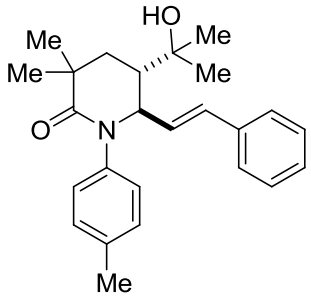
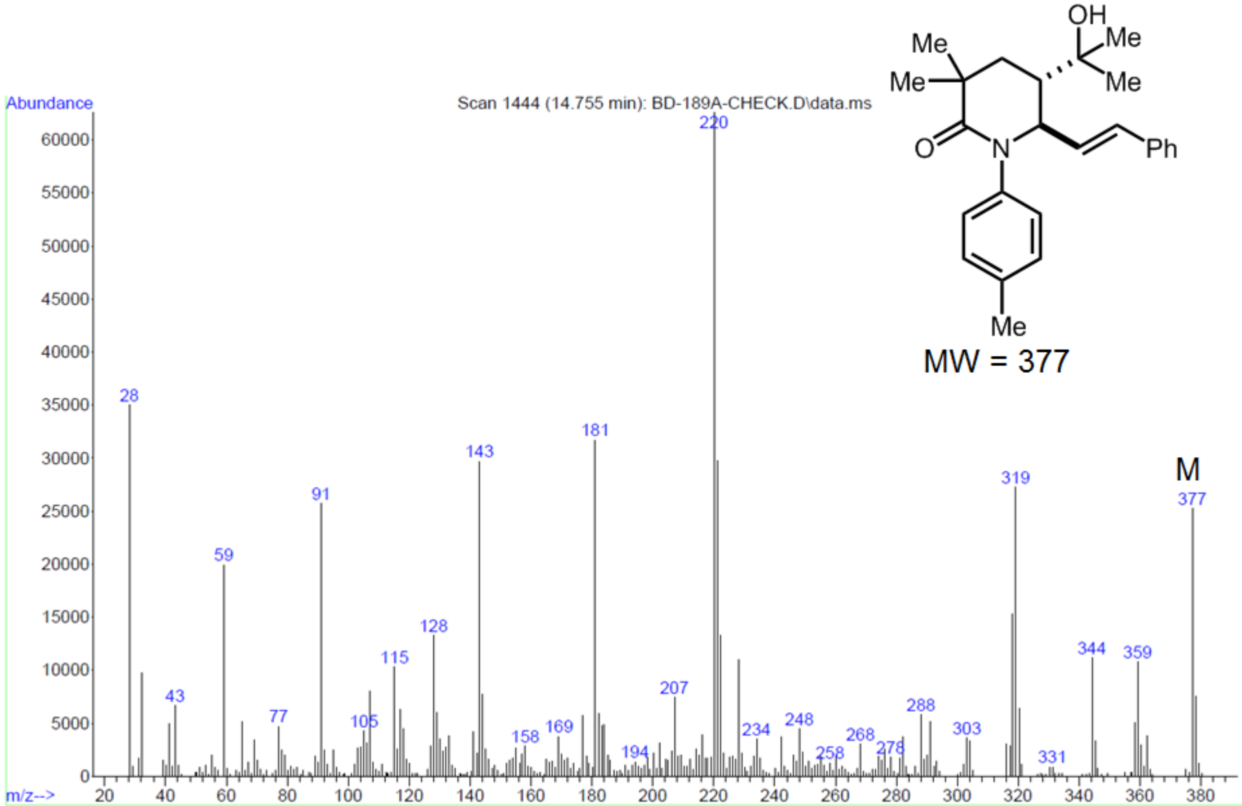
Me
O
N
Ph
Me





13d

Prepared from ester **7g2** (0.50 mmol) and MeLi (1.42 mL, 1.4 M solution in THF, 2 mmol, 4 equiv) using General Procedure D. Yield = 162 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 to 7.09 (9H, m), 6.19 to 6.10 (2H, m), 4.49 to 4.44 (1H, dd), 2.31 to 2.17 (5H, m), 1.84 to 1.73 (2H, m), 1.45 to 1.26 (12H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.9, 139.7, 136.4, 133.7, 130.8, 129.6, 128.7, 128.0, 127.9, 126.5, 125.6, 72.9, 65.5, 46.9, 38.9, 37.6, 30.1 28.9, 27.5, 25.2, 21.1. **HRMS-EI**$^{+}$ (*m/z*): calc'd for $C_{25}H_{31}NO_2$ 377.2355; found 377.2359.



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Me
Me
O
N
Ph
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59
77
91
105
115
128
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181
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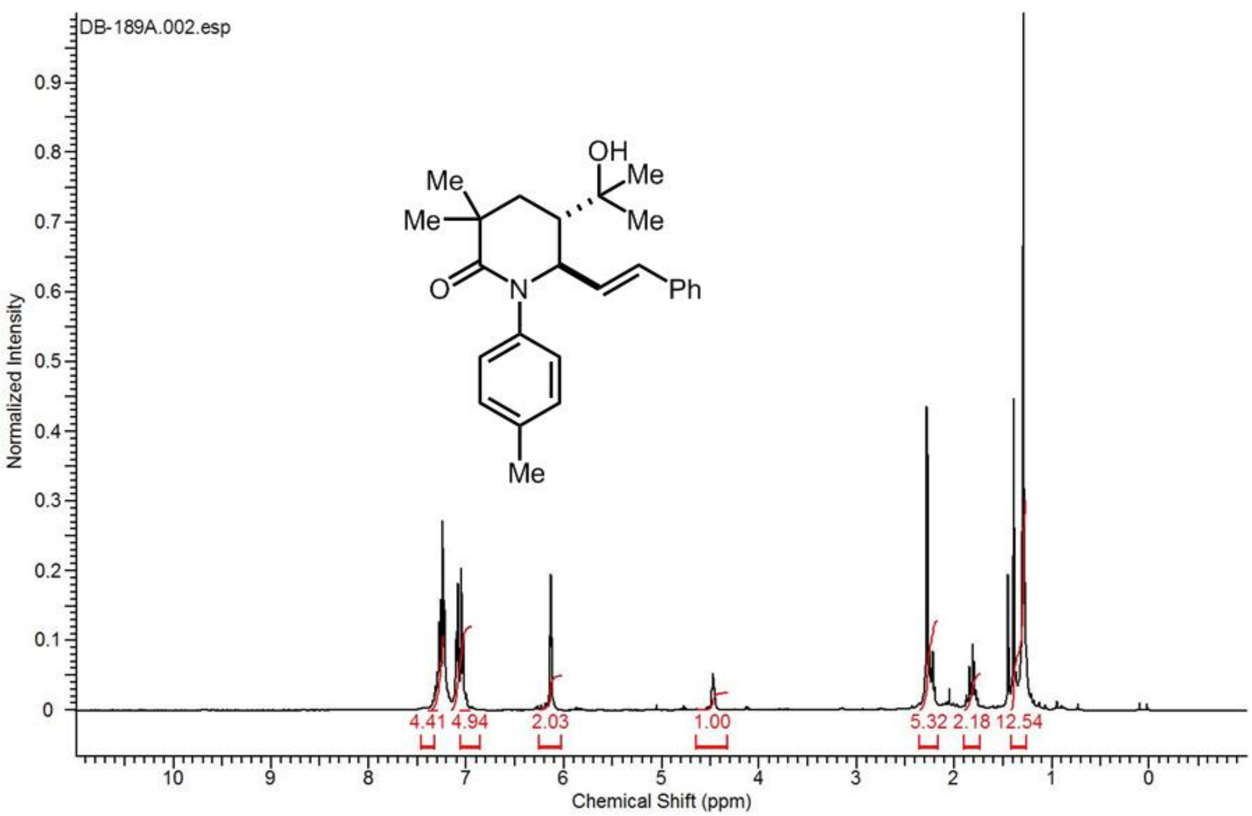
207
220
234
248
258
268
278
288
303
319
331
344
359
377



DB-189A.002.esp
Normalized Intensity
Chemical Shift (ppm)
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O
N
Ph
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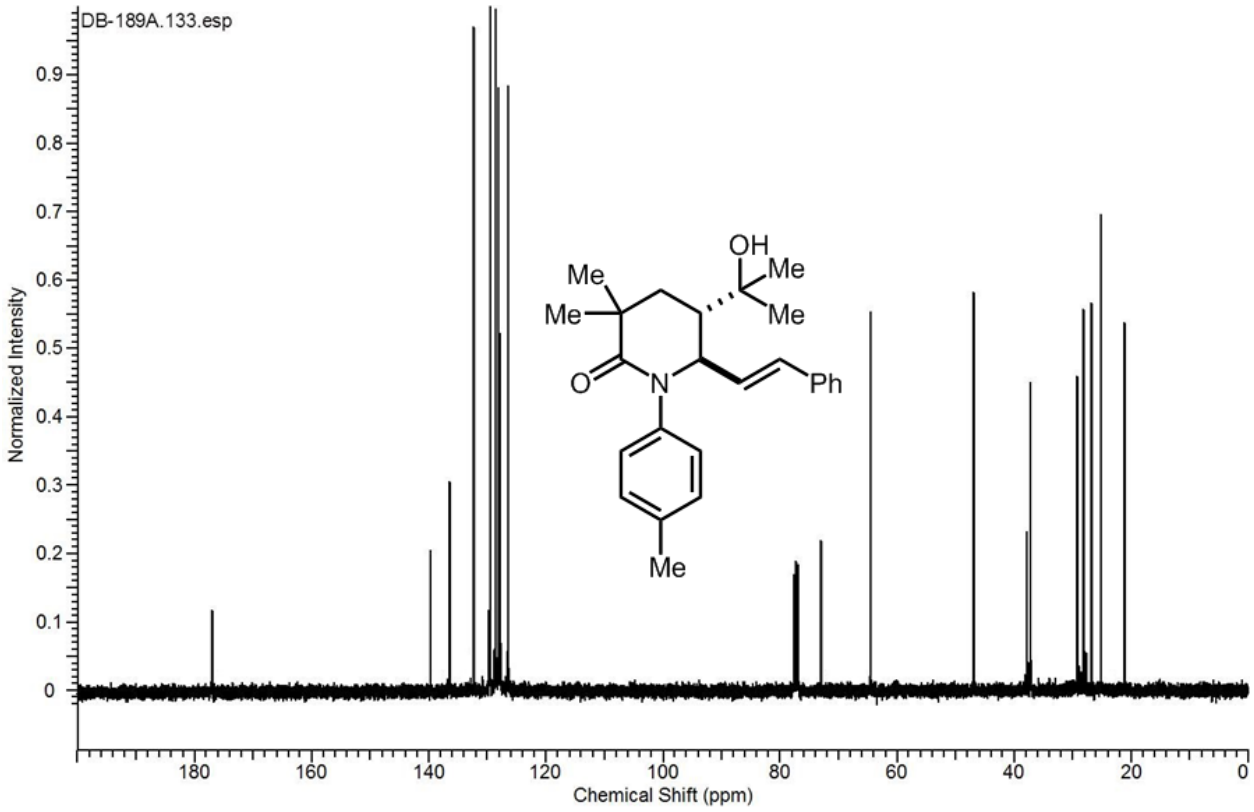
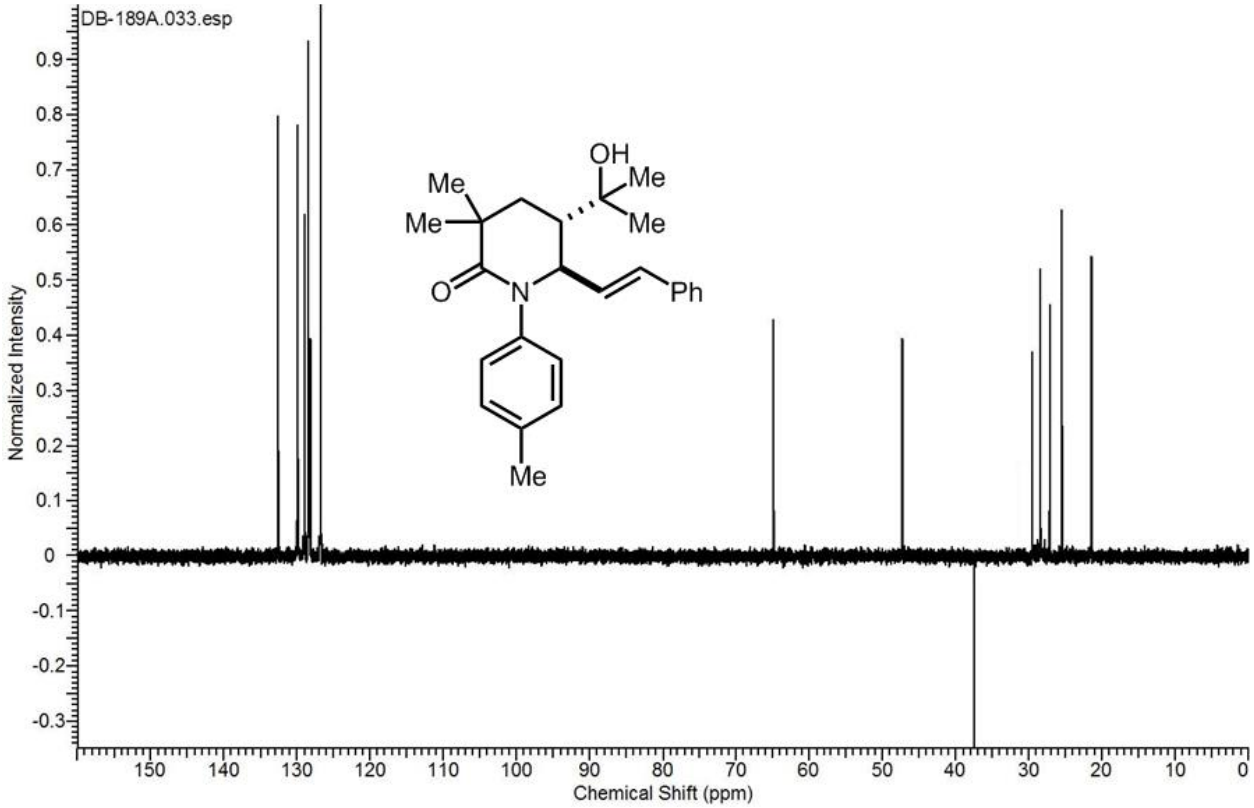
2.18
12.54


DB-189A.133.esp
Normalized Intensity
Chemical Shift (ppm)
OH
Me
Me
Me
Me
O
N
Ph
Me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Chemical Shift (ppm)
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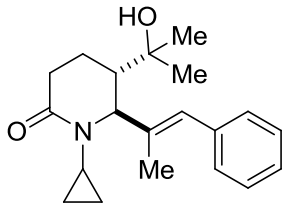
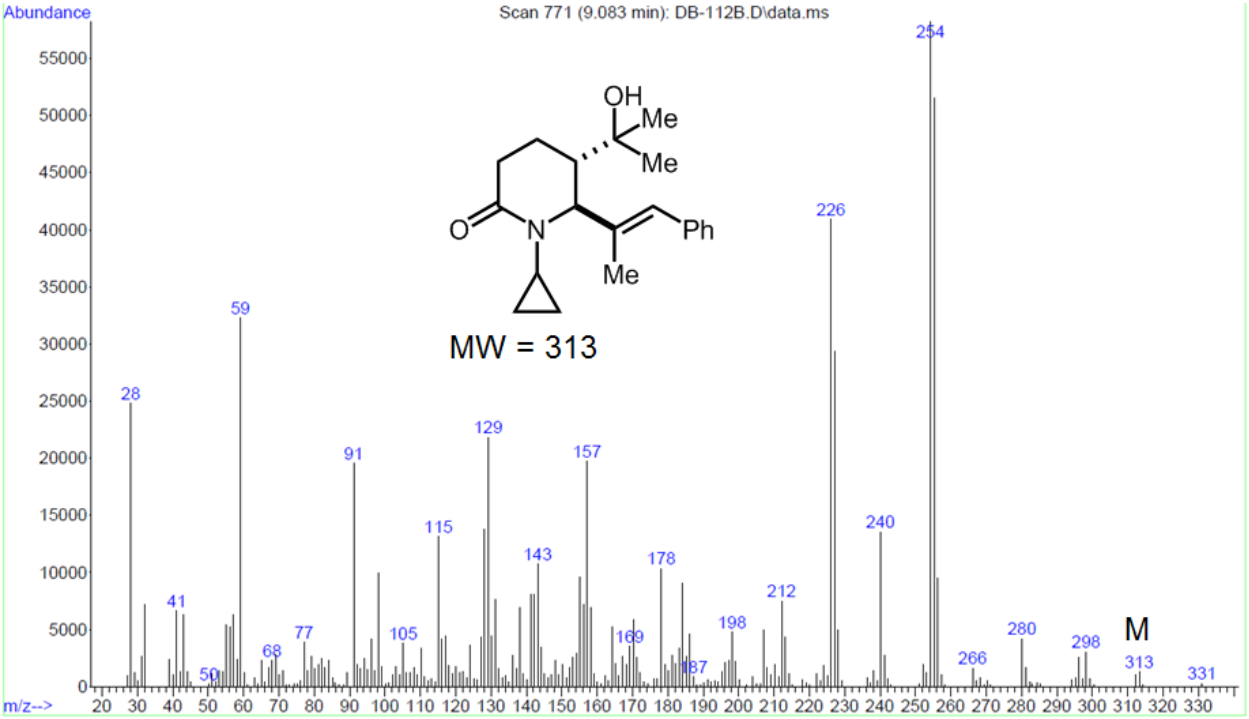
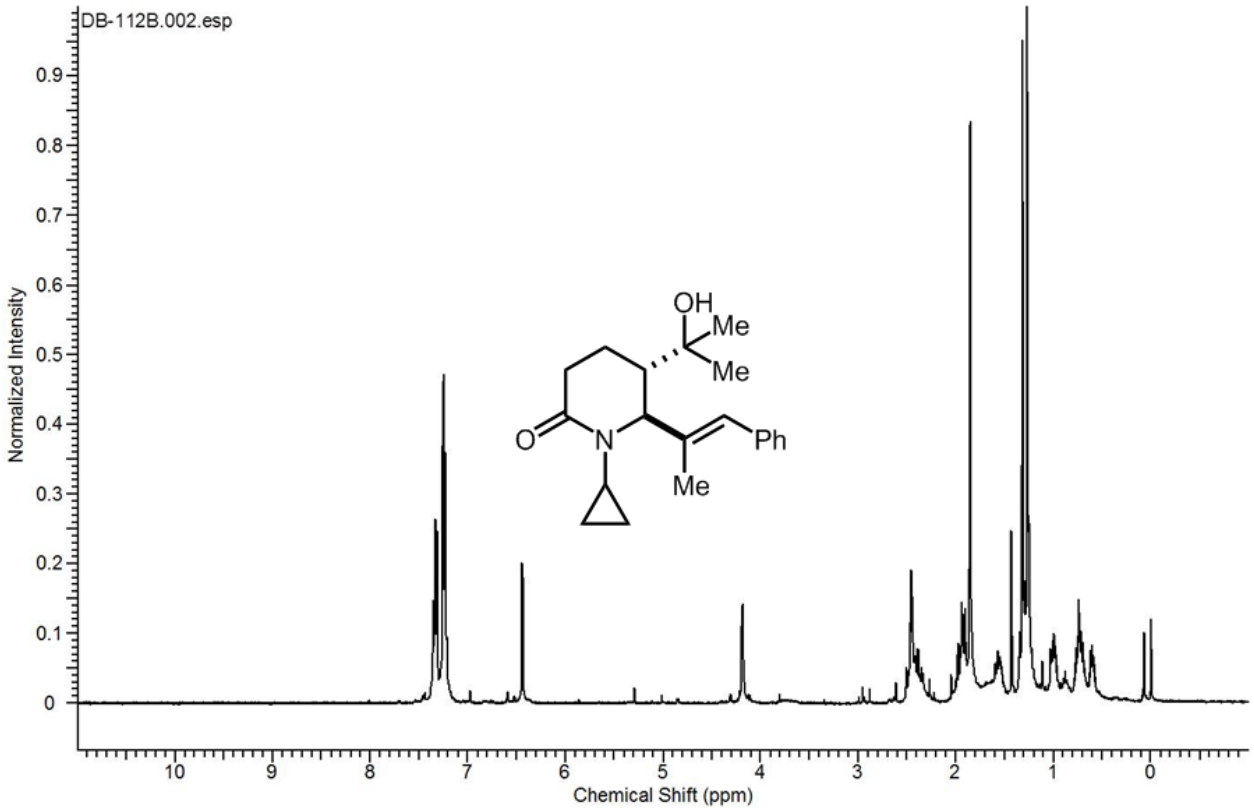
Me
Me
Me
O
N
Ph
Me



13e

Prepared from ester **7m2** (0.50 mmol) and MeLi (1.42 mL, 1.4 M solution in THF, 2 mmol, 4 equiv) using General Procedure D. Yield = 144 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 to 7.21 (5H, m), 4.21 to 4.18 (1H, d), 2.49 to 2.22 (2H, m), 1.98 to 1.85 (5H, m), 1.60 to 1.52 (1H, m), 1.35 to 1.22 (7H, s,s), 0.98 to 0.86 (1H, m), 0.79 to 0.56 (3H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.24, 138.18, 137.12, 128.95, 128.77, 128.39, 128.30, 126.86, 73.26, 66.40, 46.50, 31.81, 30.38, 29.48, 28.84, 26.94, 20.90, 14.69, 9.00, 6.31. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{20}H_{27}NO_2$ 313.2042; found 313.2037.

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Normalized Intensity
Chemical Shift (ppm)
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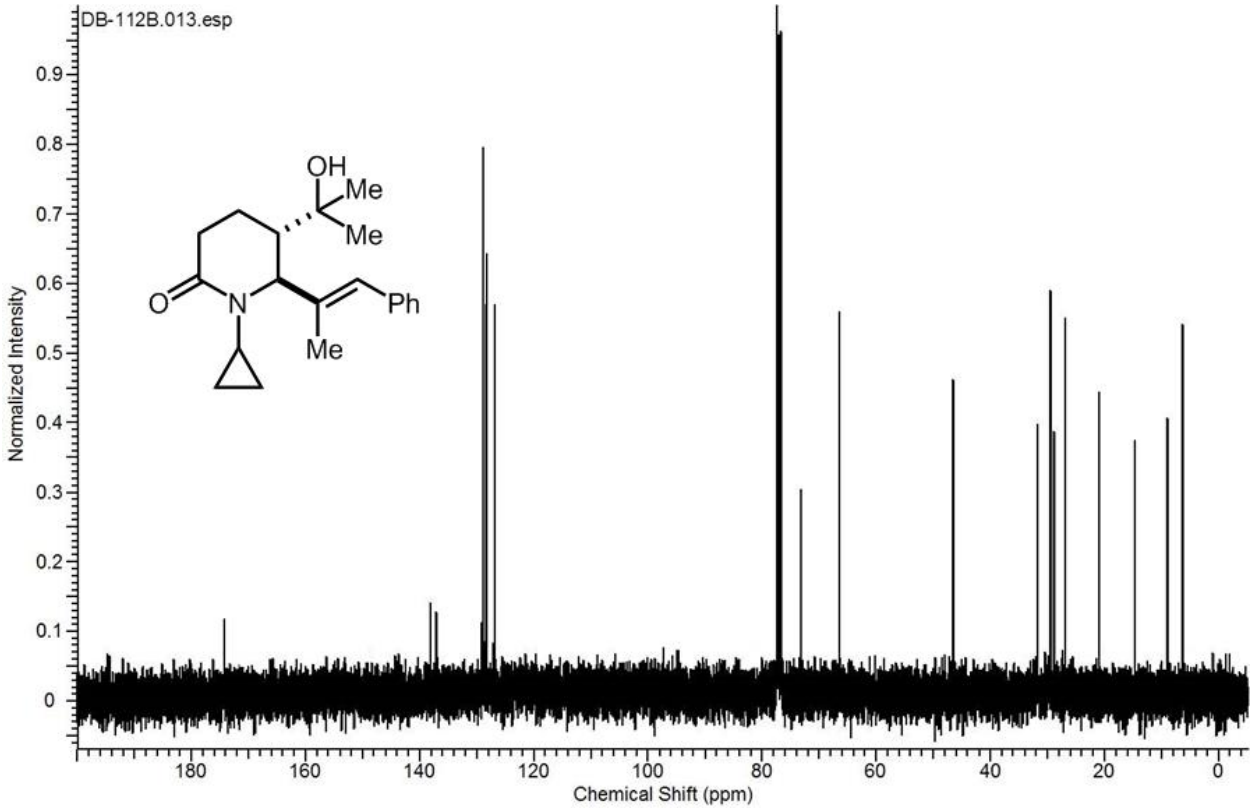
Me
Me
O
N
Ph
Me


DB-112B.013.esp
Normalized Intensity
Chemical Shift (ppm)
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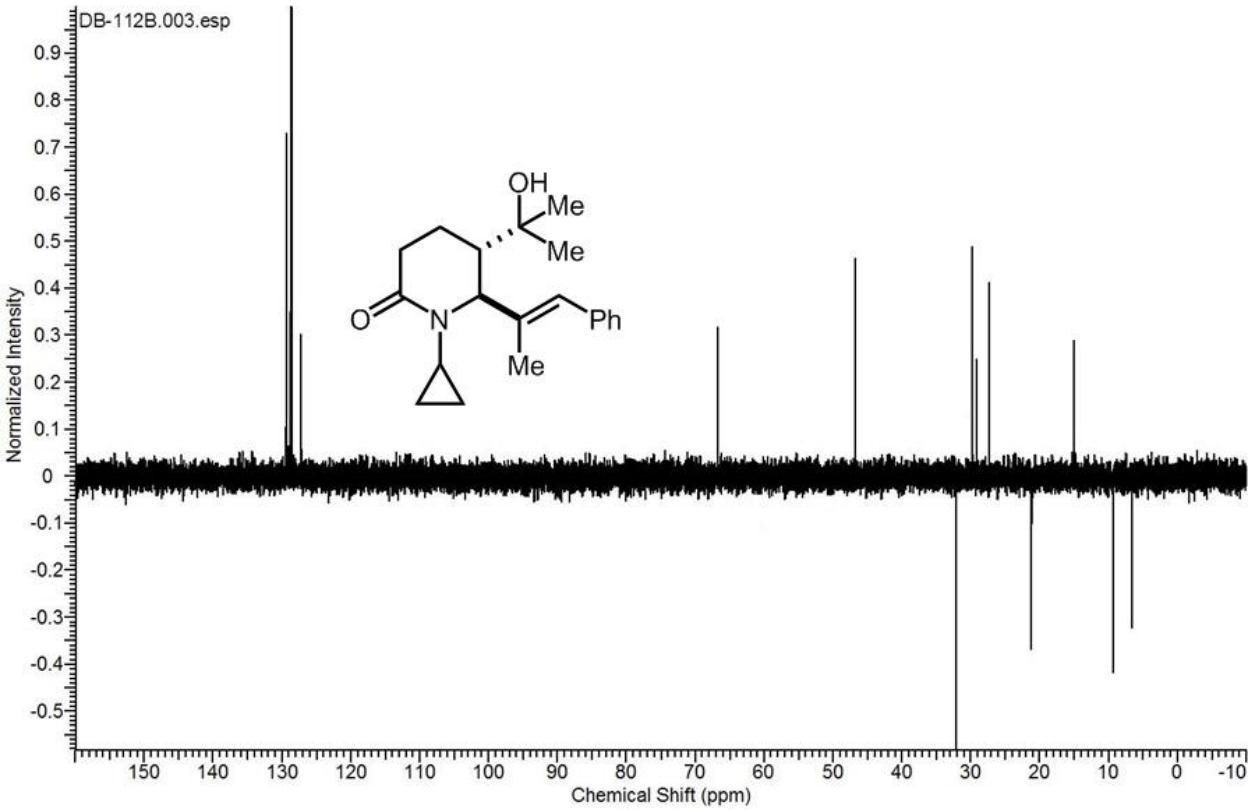
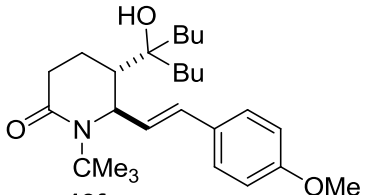
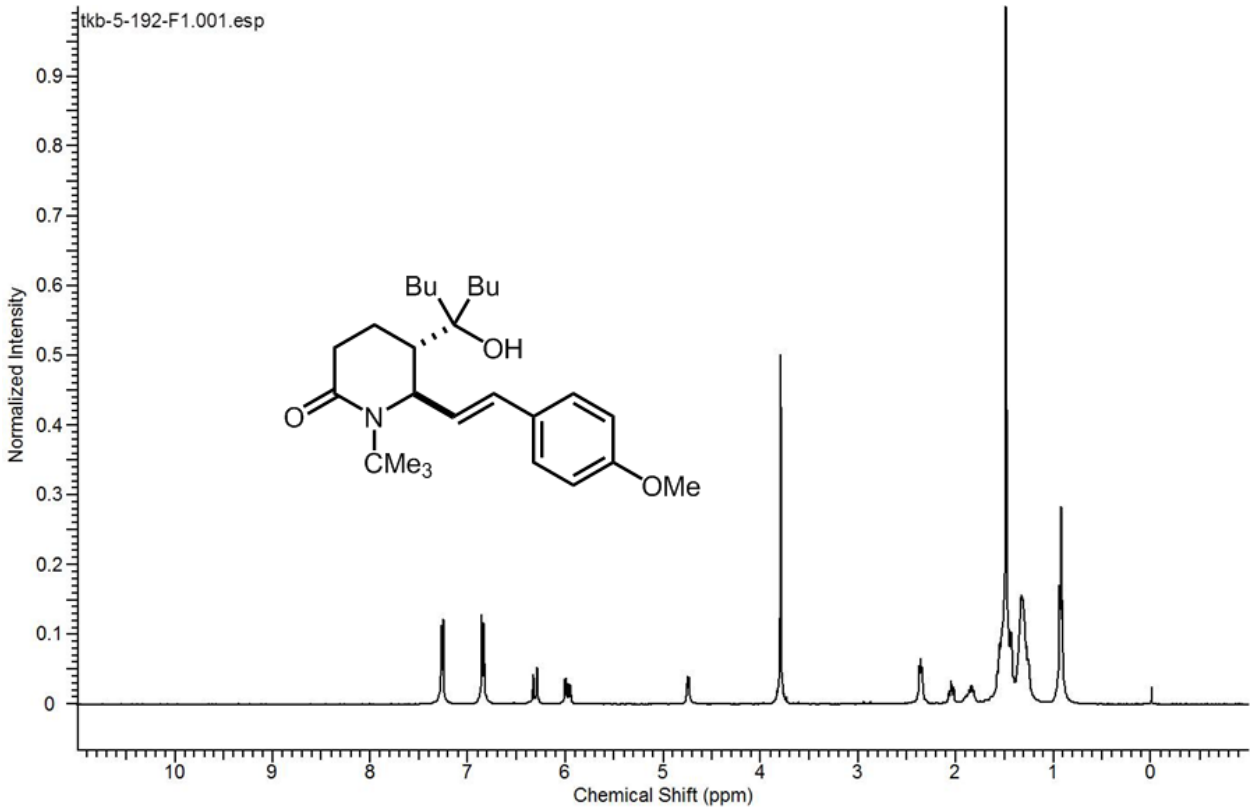
Me
O
N
Ph
Me





13f

Prepared from the corresponding ester (0.5 mmol) using General Procedure D. Yield = 204 mg, 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 to 7.26 (2H, d), 6.86 to 6.83 (2H, d), 6.36 to 6.29 (1H, d), 5.99 to 5.95 (1H, dd), 4.75 to 4.73 (1H, dd), 3.76 (3H, s), 2.39 to 2.30 (2H, m), 2.07 to 2.02 (1H, m), 1.90 to 1.80 (1H, m), 1.64 to 1.25 (22H, m), 0.98 to 0.90 (6H, t). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.60, 159.26, 132.81, 129.36, 127.86, 127.43, 114.12, 76.56, 57.75, 55.40, 54.76, 48.31, 36.88, 35.71, 34.36, 28.73, 25.62, 25.45, 23.51, 23.42, 21.37, 14.21. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{27}H_{43}NO_3$ 429.3243; found 429.3248.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Normalized Intensity
Chemical Shift (ppm)
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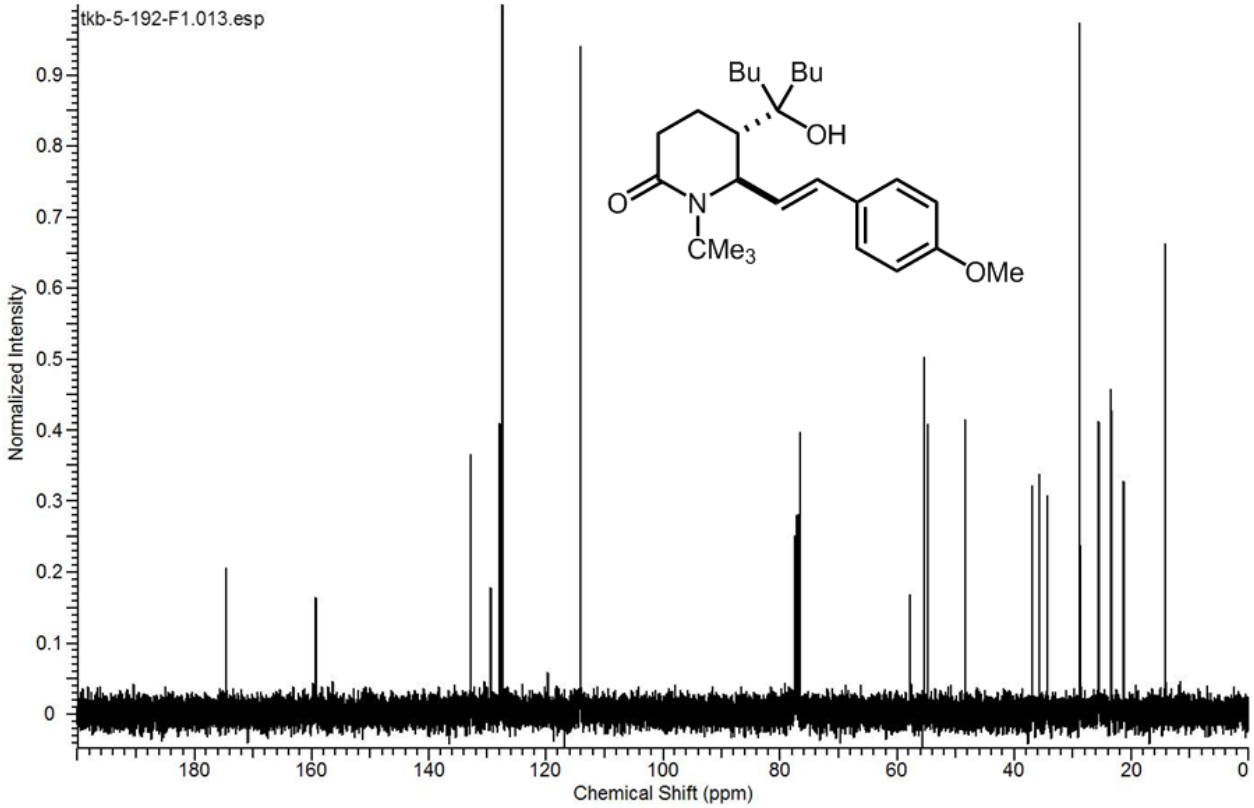
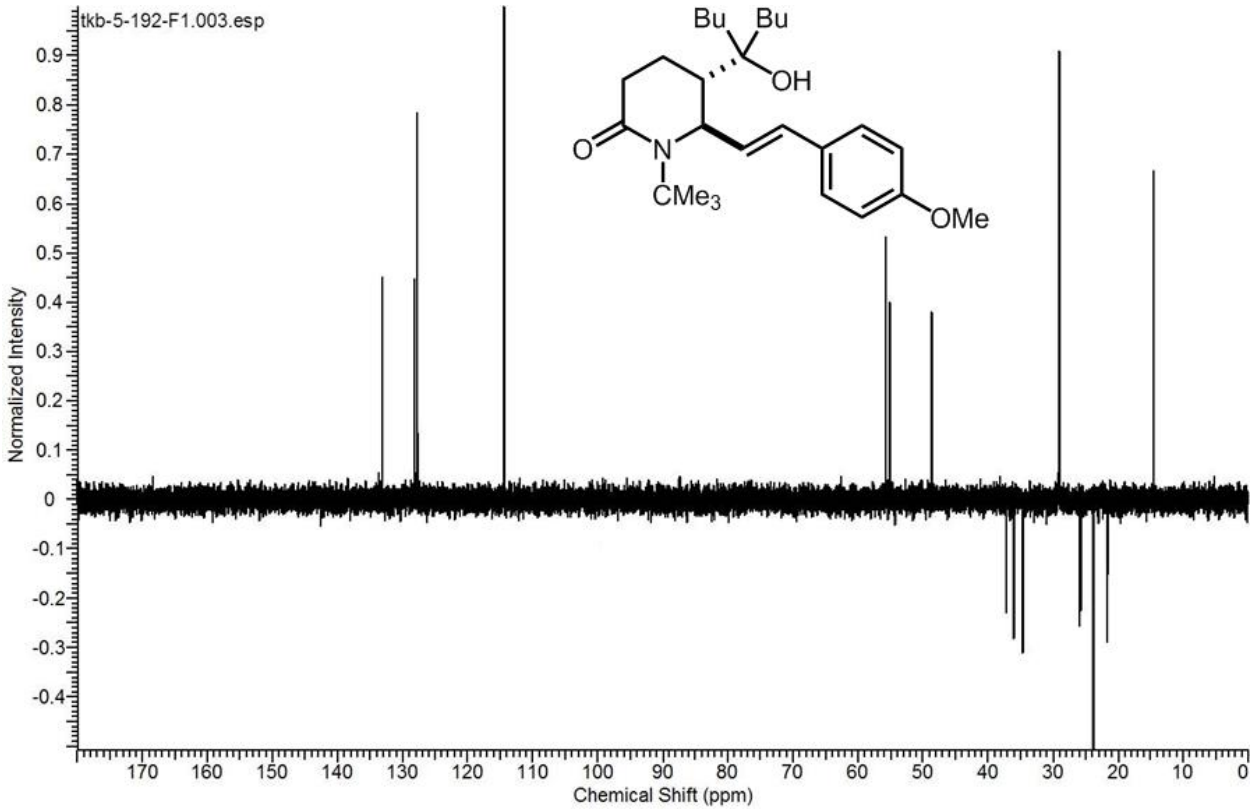
Bu
OH
O
N
CMe3
OMe


tkb-5-192-F1.013.esp
Normalized Intensity
Chemical Shift (ppm)
Bu
Bu
OH
O
N
CMe3
OMe


tkb-5-192-F1.003.esp
Bu
Bu
OH
O
N
CMe3
OMe
Normalized Intensity
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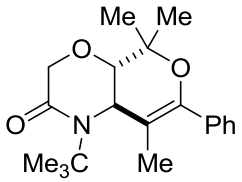
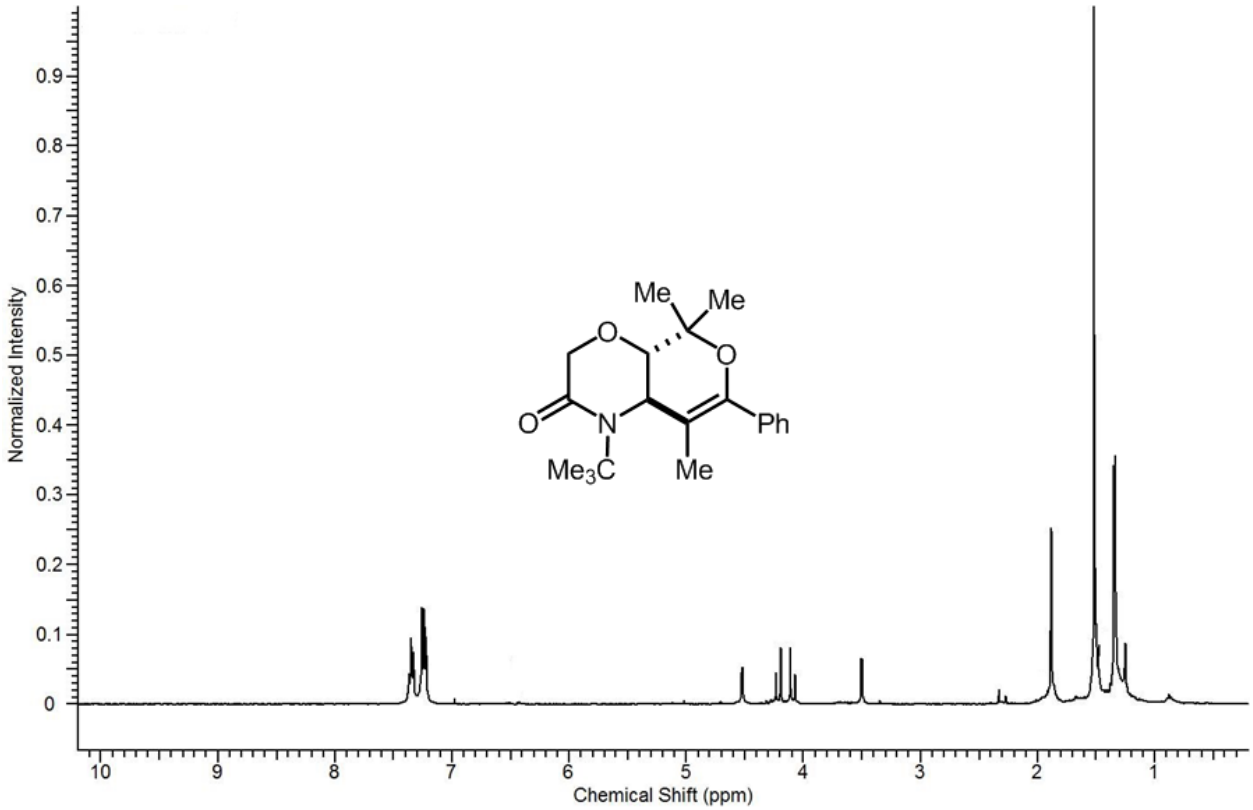
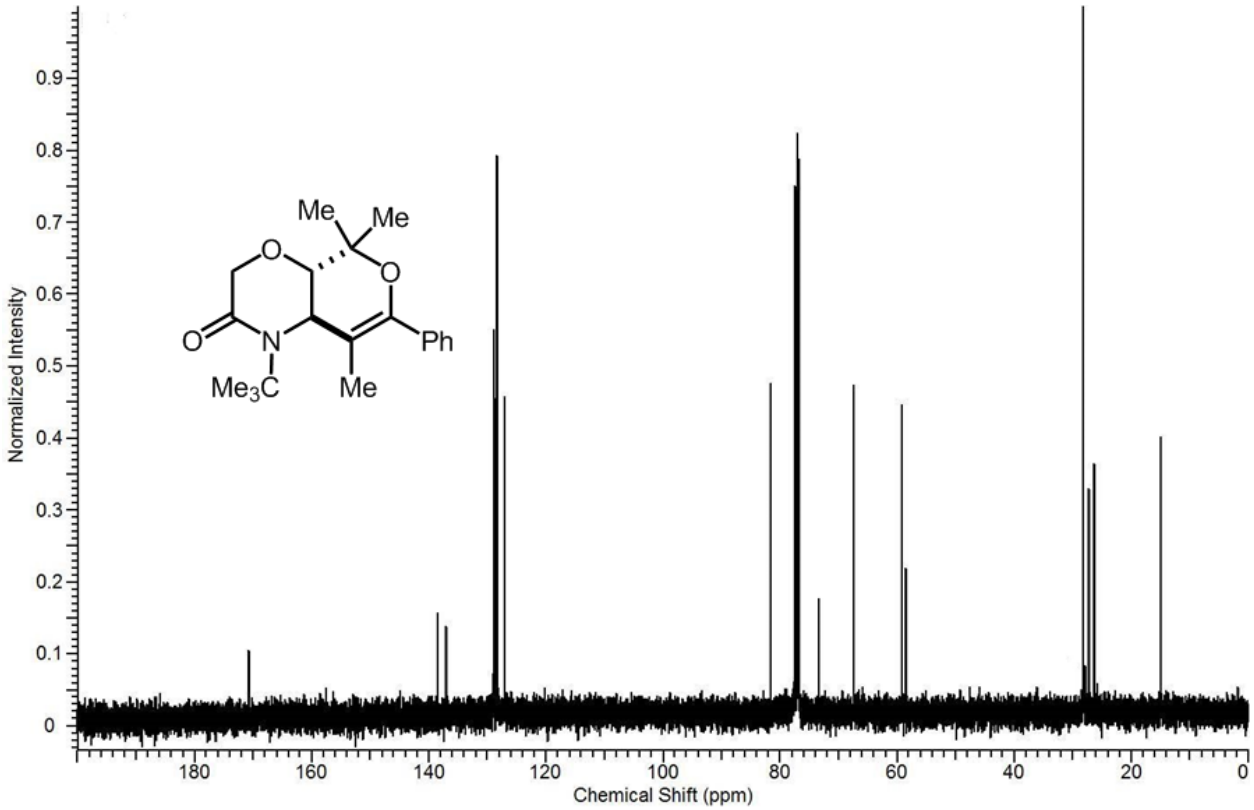
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)



14a

Prepared from ester **5o2** (0.50 mmol) using General Procedures D and G. Yield = 149 mg, 79%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 to 7.22 (5H, m), 4.53 (1H, d), 4.31 to 4.11 (2H, dd), 3.51 (1H, d), 1.88 (3H, s), 1.54 to 1.30 (15H, m). ^{13}C NMR (101 MHz, CDCl3) δ 170.7, 138.4, 137.0, 128.9, 128.5, 128.4, 128.3, 127.0, 81.5, 77.4, 77.3, 77.1, 76.8, 73.4, 67.4, 59.1, 58.5, 30.4, 29.8, 28.2, 27.8, 27.2, 26.3, 15.2. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{20}H_{27}NO_3$ 329.1991; found 329.1996.




Normalized Intensity
Chemical Shift (ppm)
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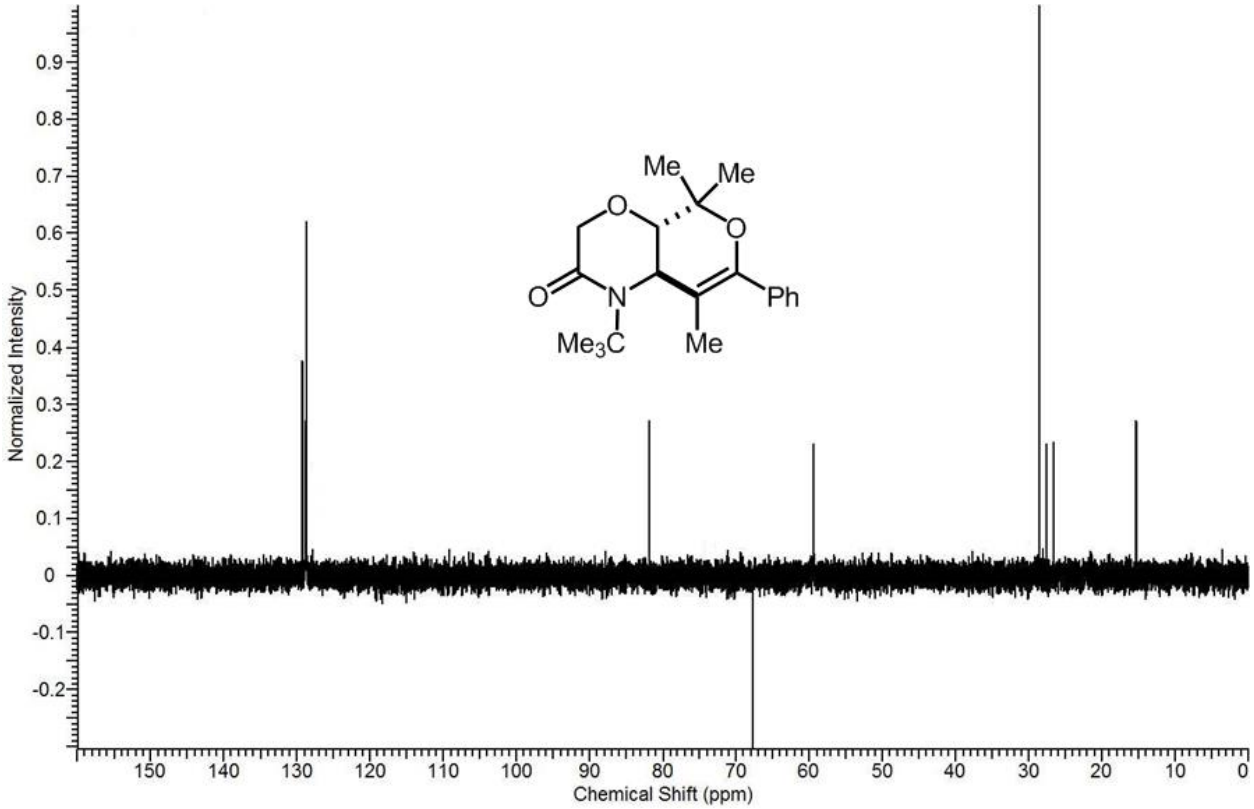
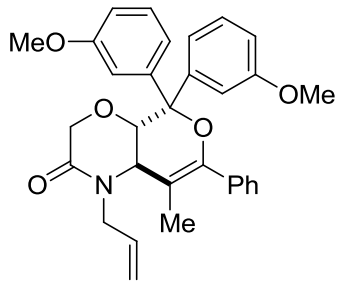
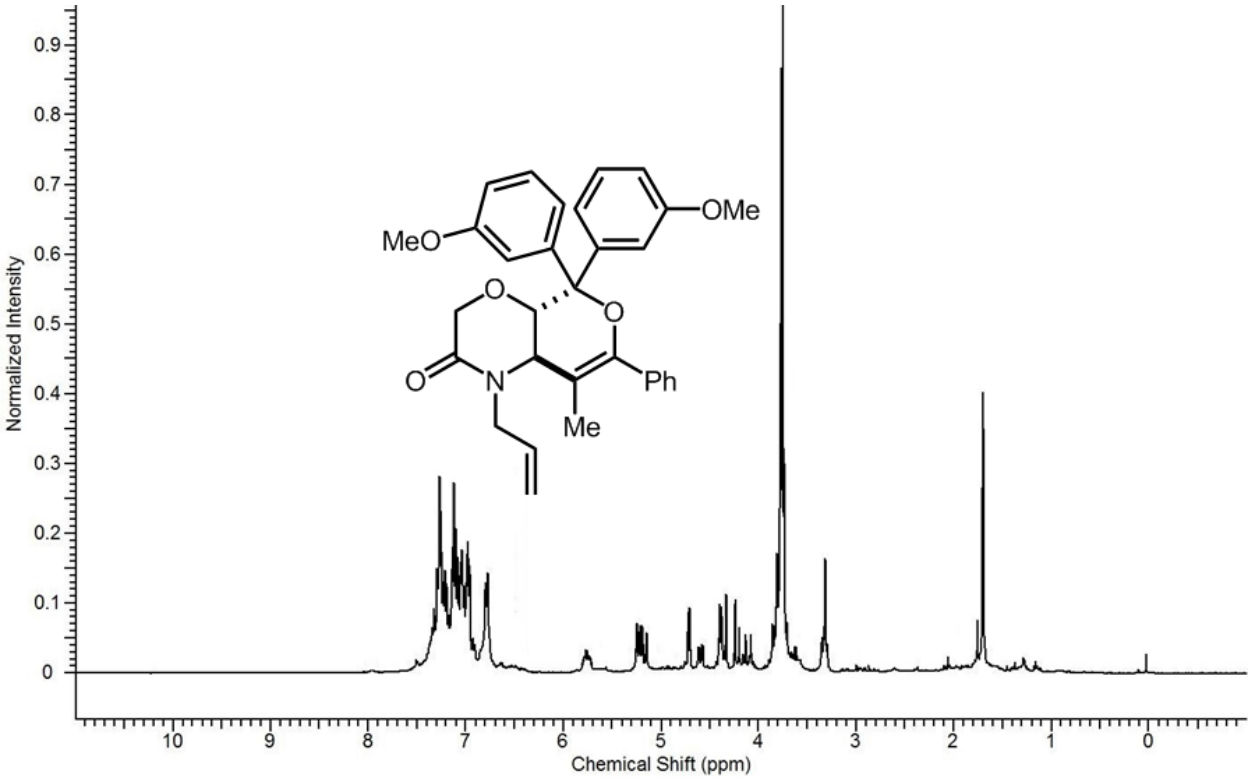
Me
O
O
O
N
Ph
Me3C
Me

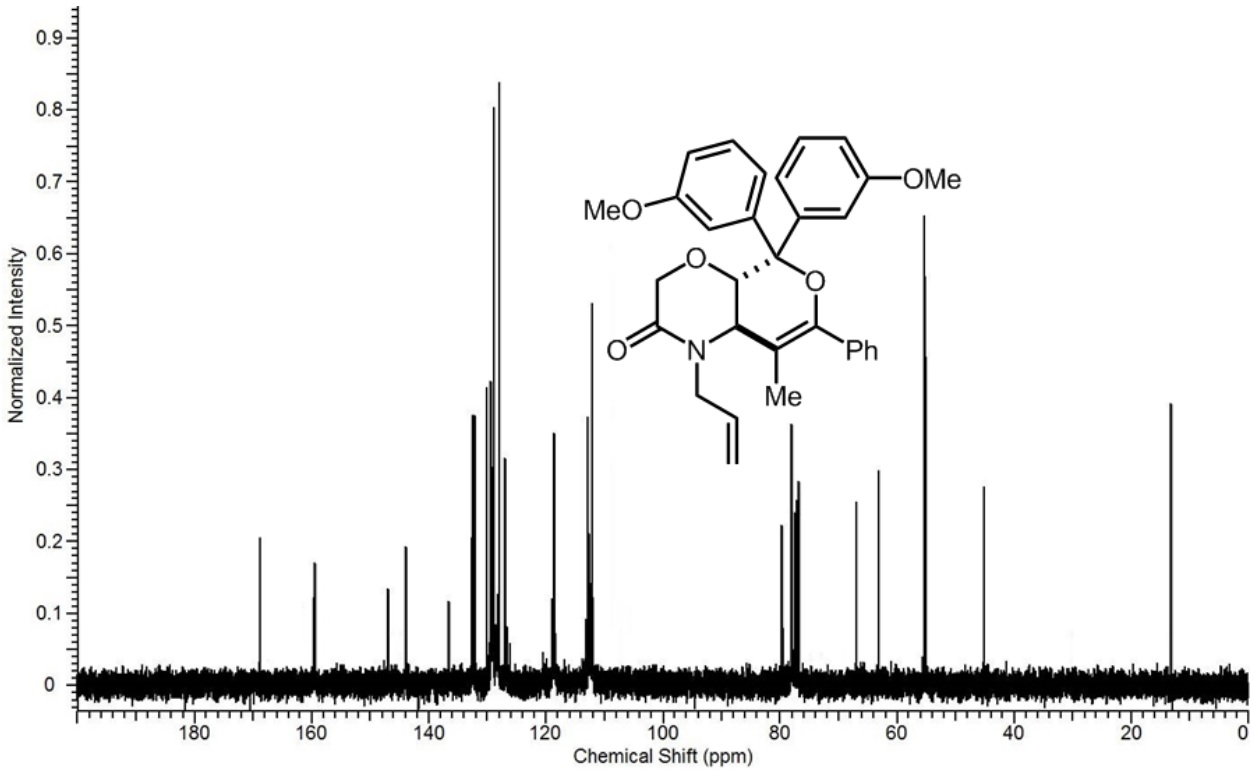

Normalized Intensity
Chemical Shift (ppm)
Me
Me
O
O
O
N
Ph
Me3C
Me



14b

Prepared from ester **5k2** (0.50 mmol) using General Procedures D and G. Yield = 206 mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 to 6.81 (13H, m), 5.78 to 5.71 (1H, m), 5.26 to 5.15 (2H, dd), 4.75 to 4.70 (1H, d), 4.62 to 4.58 (1H, dd), 4.44 to 4.10 (3H, m), 3.79 to 3.71 (6H, s,s), 3.33 to 3.00 (2H, m), 1.78 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.81, 160.93, 159.59, 146.92, 143.95, 136.56, 132.68, 132.44, 130.06, 129.58, 129.49, 129.42, 129.36, 129.30, 129.24, 129.14, 129.03, 128.91, 128.53, 128.45, 128.21, 127.98, 126.94, 126.62, 126.15, 118.98, 118.53, 113.06, 112.01, 79.66, 78.03, 66.97, 63.15, 55.27, 55.10, 45.1, 14.1. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{31}H_{31}NO_5$ 497.2202; found 497.2209.




Normalized Intensity
Chemical Shift (ppm)
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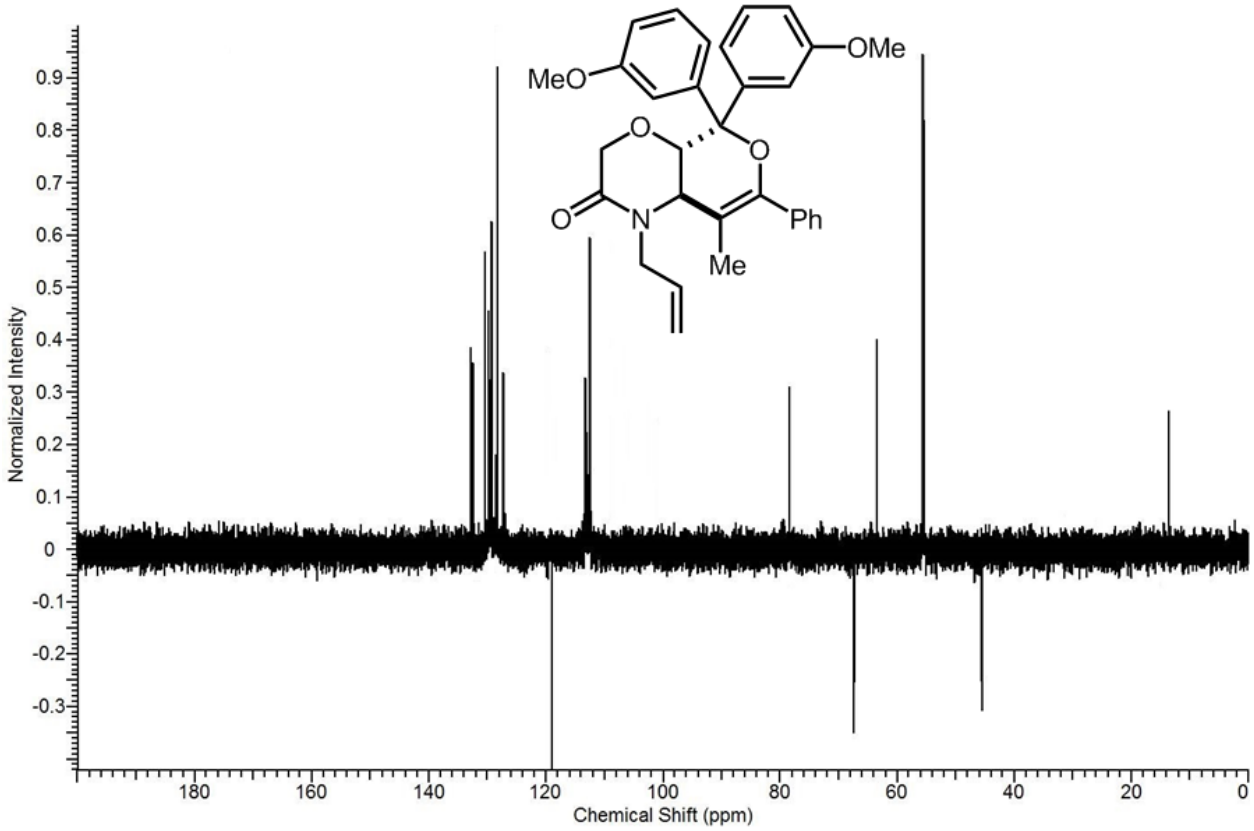
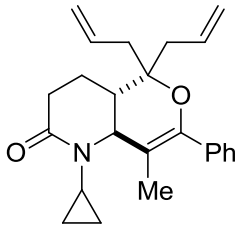
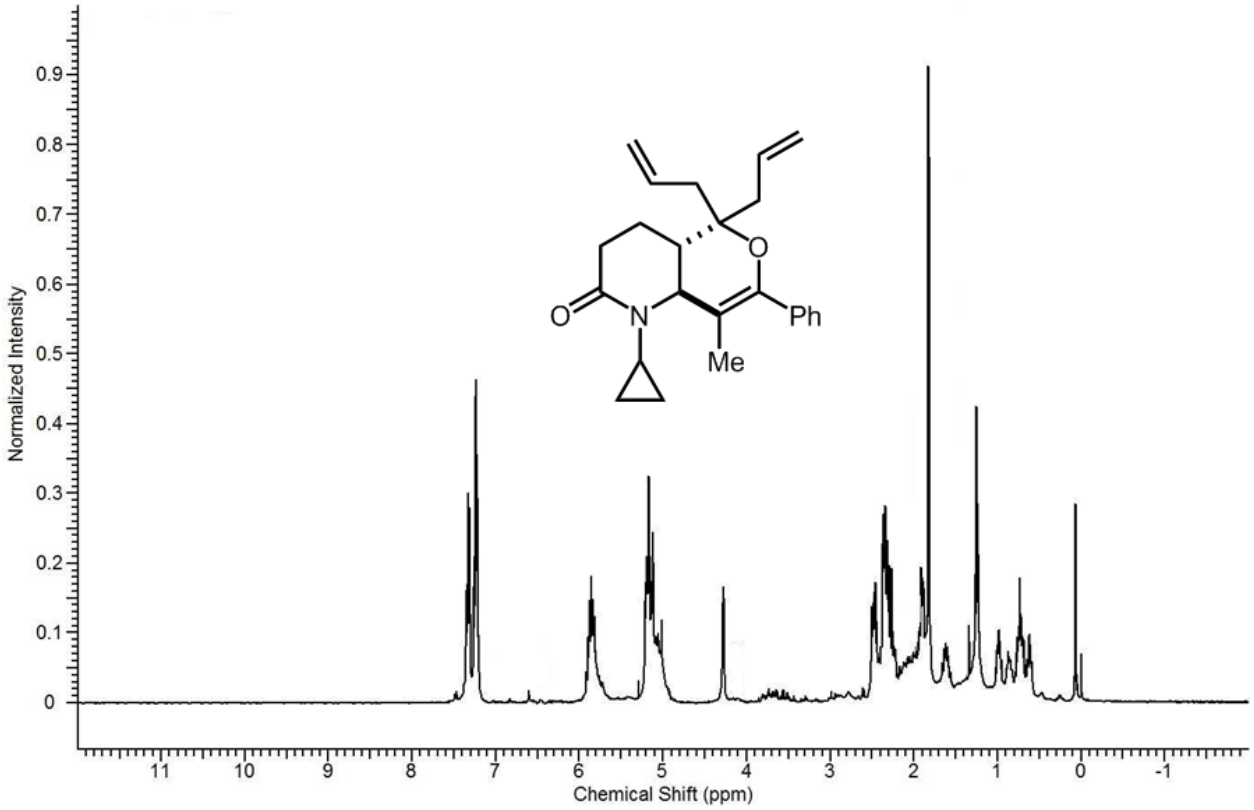
OMe
O
O
O
N
Ph
Me

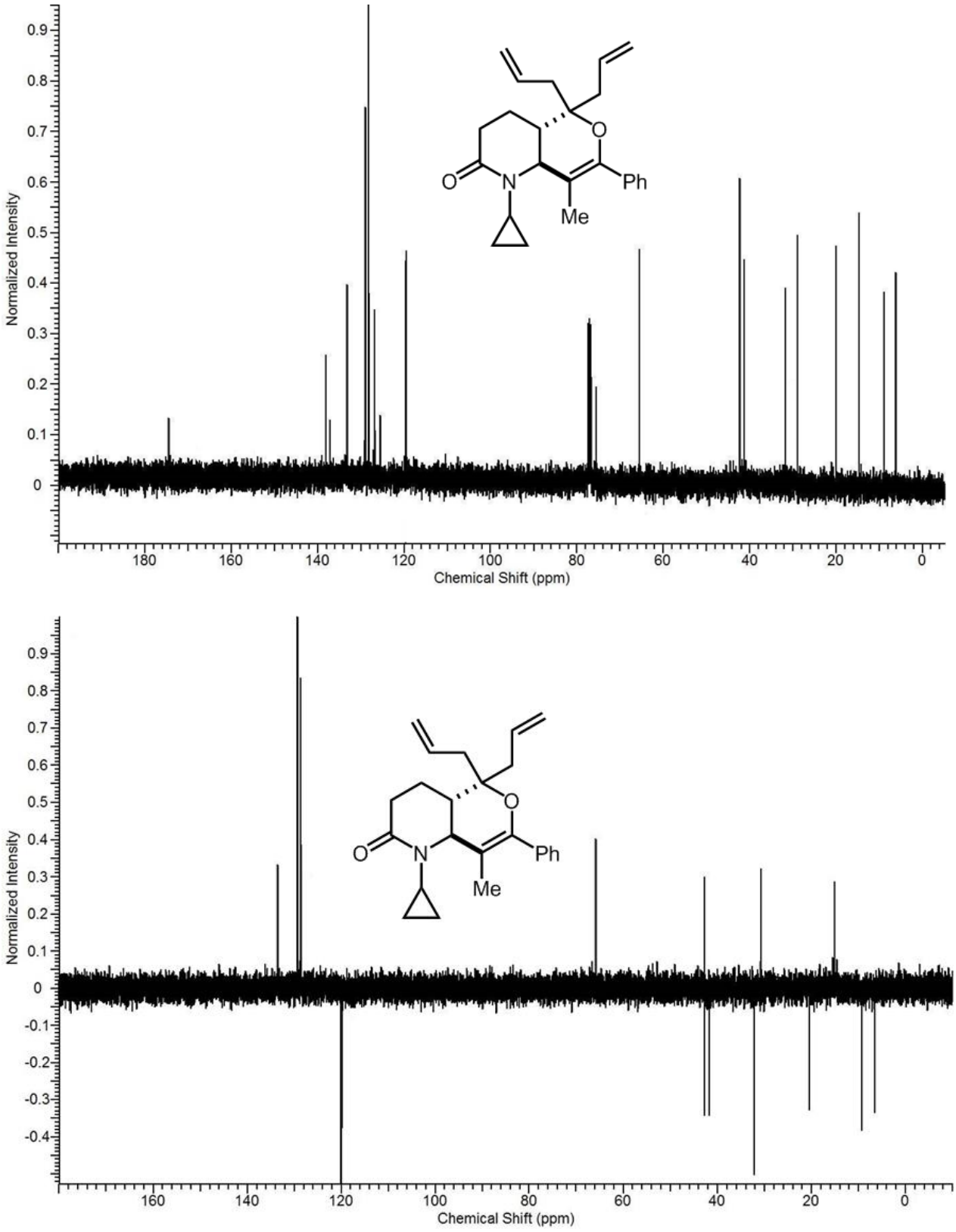

Normalized Intensity
Chemical Shift (ppm)
MeO
OMe
O
O
O
N
Ph
Me



14c

Prepared from ester **7n2** (0.50 mmol) using General Procedures D and G. Yield = 156 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 to 7.18 (5H, m), 5.92 to 5.72 (2H, m), 5.30 to 4.92 (4H, m), 4.30 to 4.27 (1H, br s), 2.59 to 0.60 (17H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.52, 138.08, 137.16, 133.16, 133.14, 129.08, 128.97, 128.87, 128.28, 128.16, 126.82, 125.57, 119.68, 75.56, 65.51, 41.33, 40.90, 31.82, 30.38, 29.76, 20.06, 14.74, 8.89, 6.18. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{24}H_{29}NO_2$ 363.2198; found 363.2202.




Normalized Intensity
Chemical Shift (ppm)
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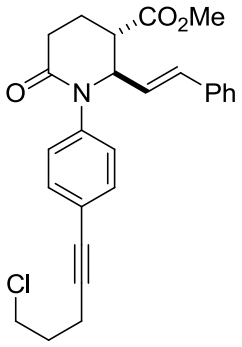
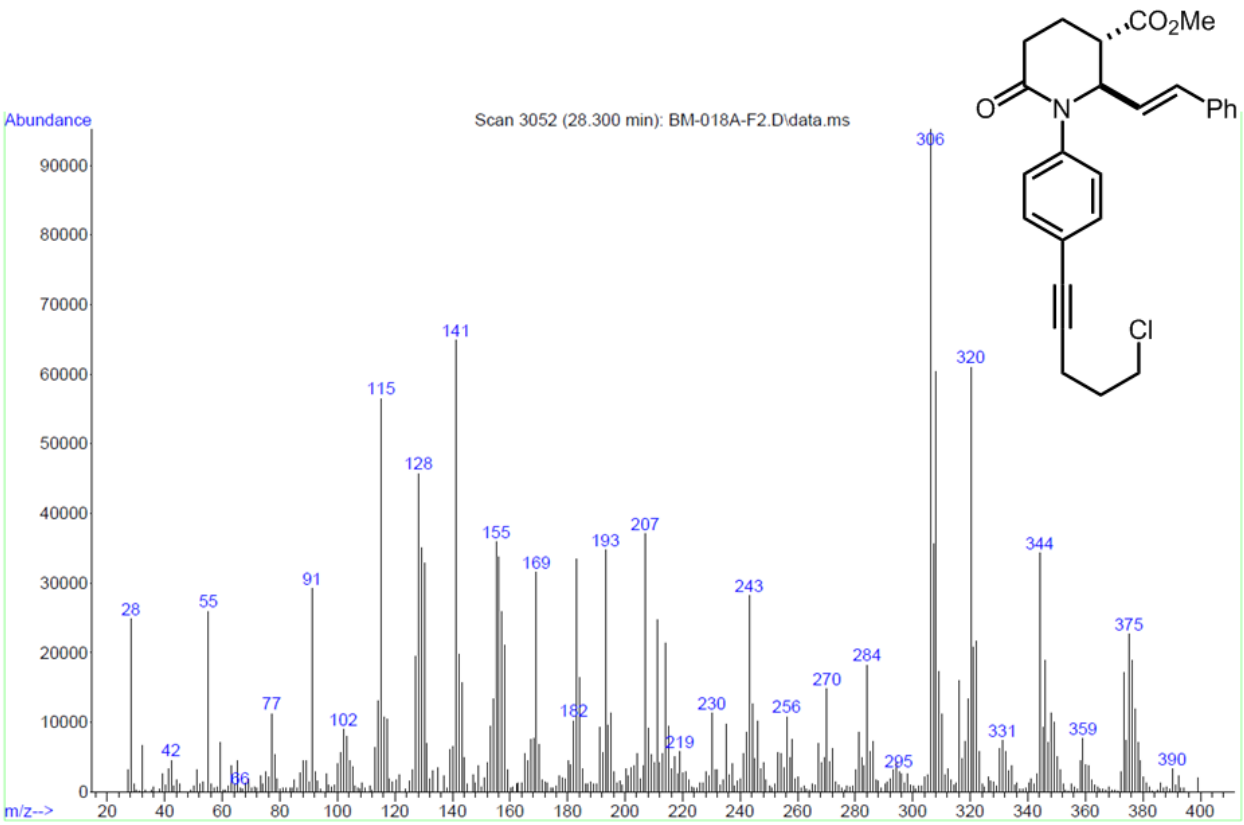
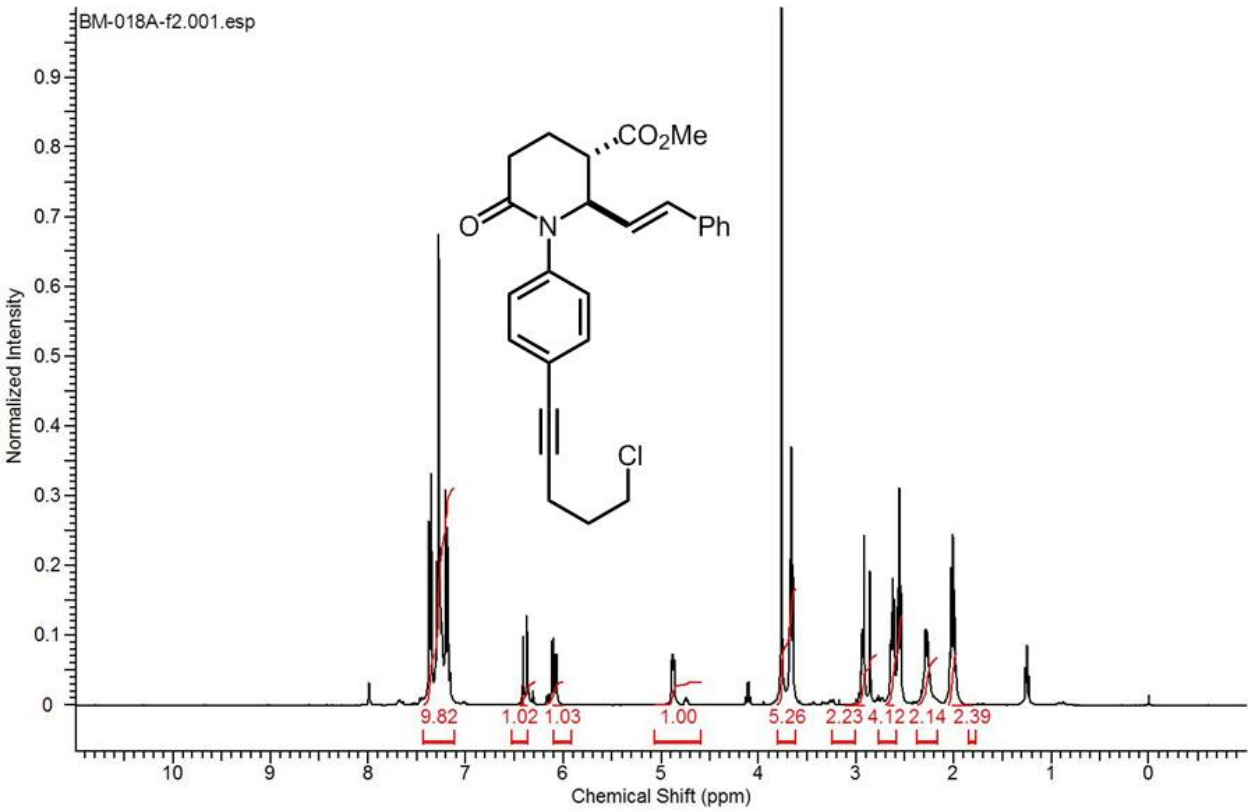
N
O
Ph
Me



15, 91%

To an oven-dried, septum-capped 2-neck-round bottom flask equipped with a stir bar, was added aryl iodide **7d2** (461 mg, 1 mmol, 1.0 equiv) in DMF/Et_3N (5:1 mL) and 5-chloro-1-pentyne (0.212 mL, 2 mmol, 2 equiv), under nitrogen atmosphere. After completely degassing the flask, $PdCl_2(PPh_3)_2$ (35 mg, 5 mol%) and CuI (10 mg, 5 mol%) were added rapidly and concurrently. The mixture was then stirred at room temperature for 22 h (as indicated by TLC and GC-MS). Upon completion, the mixture was concentrated under reduced pressure and directly subjected to flash chromatography on silica eluting with hexane/EtOAc. Yield = 396 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 to 7.16 (9H, m), 6.41 to 6.37 (1H, d), 6.18 to 6.06 (1H, dd), 4.89 to 4.86 (1H, dd), 3.78 to 3.63 (5H, m), 2.93 to 2.86 (2H, m), 2.65 to 2.51 (4H, m), 2.34 to 2.18 (2H, m), 2.03 to 1.97 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 169.2, 141.3, 135.7, 134.9, 133.4, 132.3, 128.7, 128.4, 127.5, 127.3, 126.7, 124.3, 122.5, 88.7, 81.1, 63.6, 52.5, 44.7, 43.8, 31.4, 29.7, 21.1, 16.9. **HRMS-EI$^+$** (*m/z*): calc'd for $C_{26}H_{26}ClNO_3$ 435.1601; found 435.1609.


Abundance
Scan 3052 (28.300 min): BM-018A-F2.D\data.ms
m/z-->
CO2Me
O
N
Ph
Cl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Normalized Intensity
Chemical Shift (ppm)
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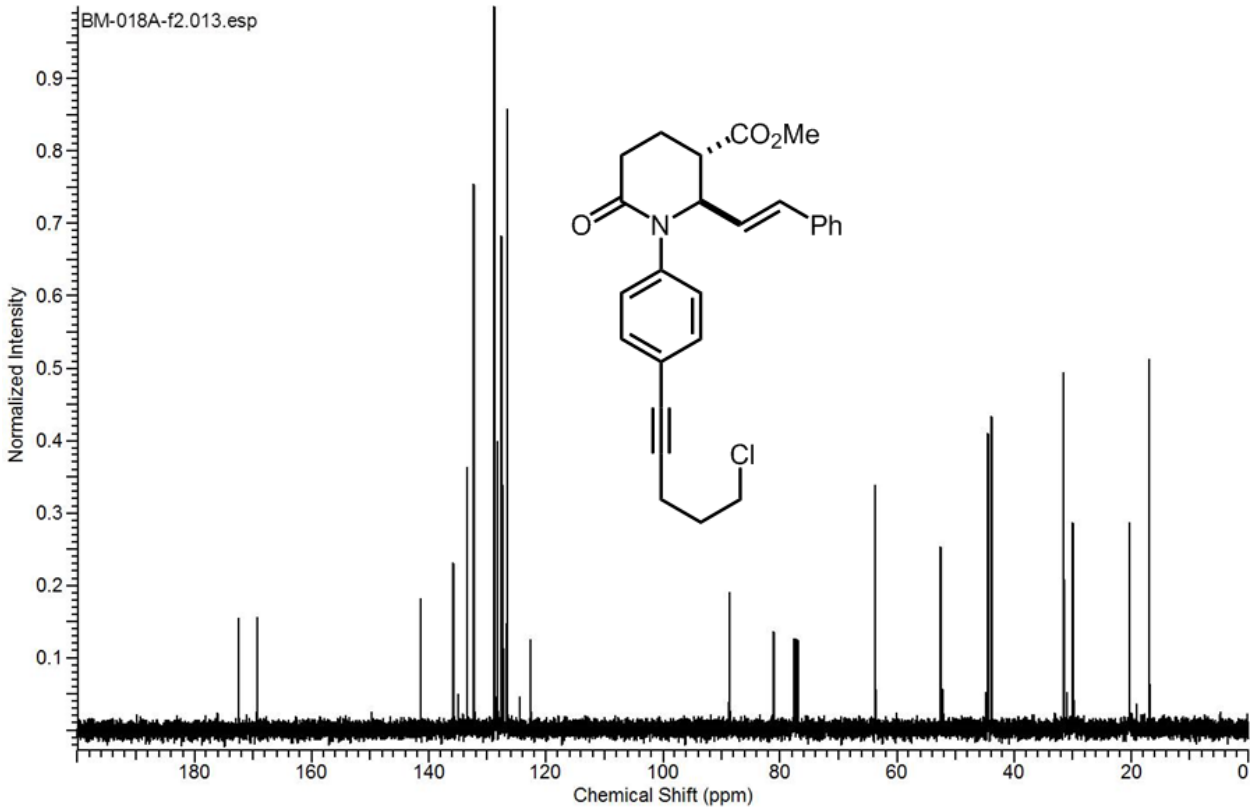
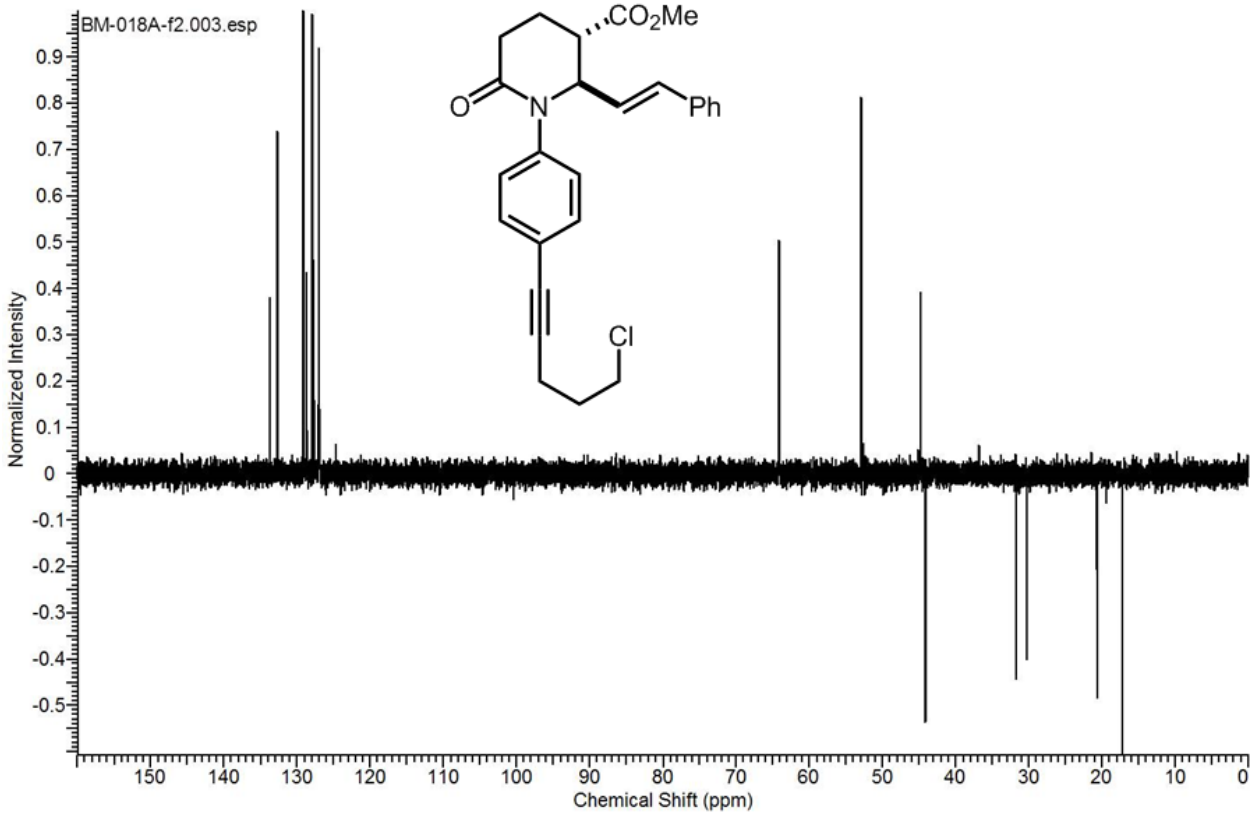
2.14
2.39
CO2Me
O
N
Ph
Cl


BM-018A-f2.013.esp
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
Cl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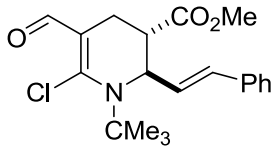
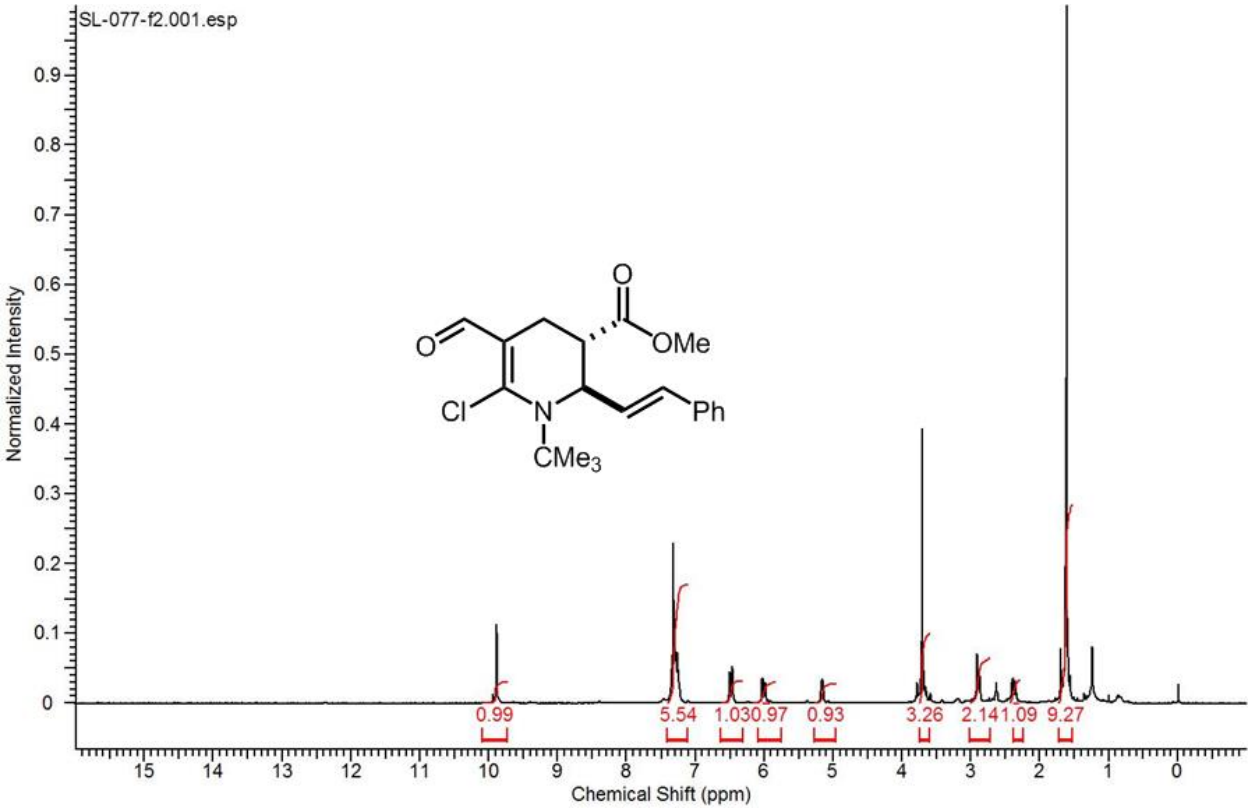
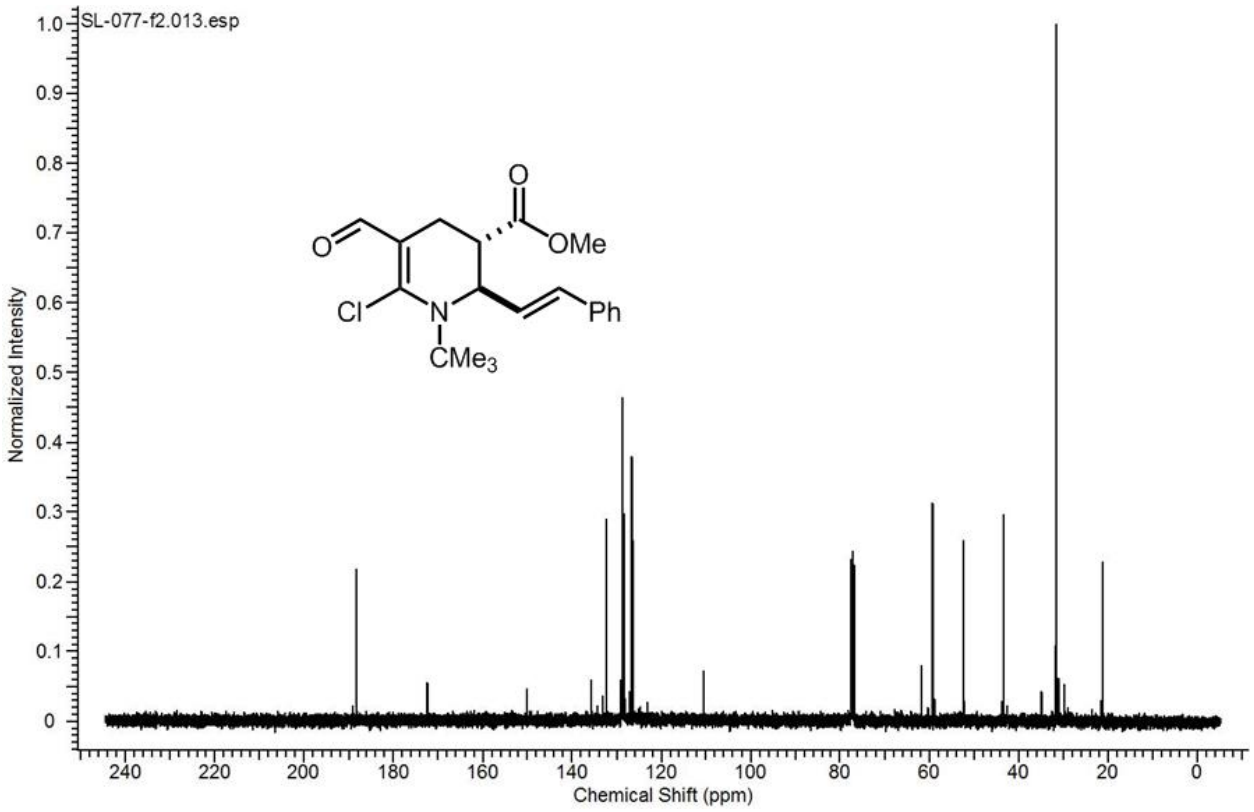
Normalized Intensity
Chemical Shift (ppm)
CO2Me
Ph
Cl

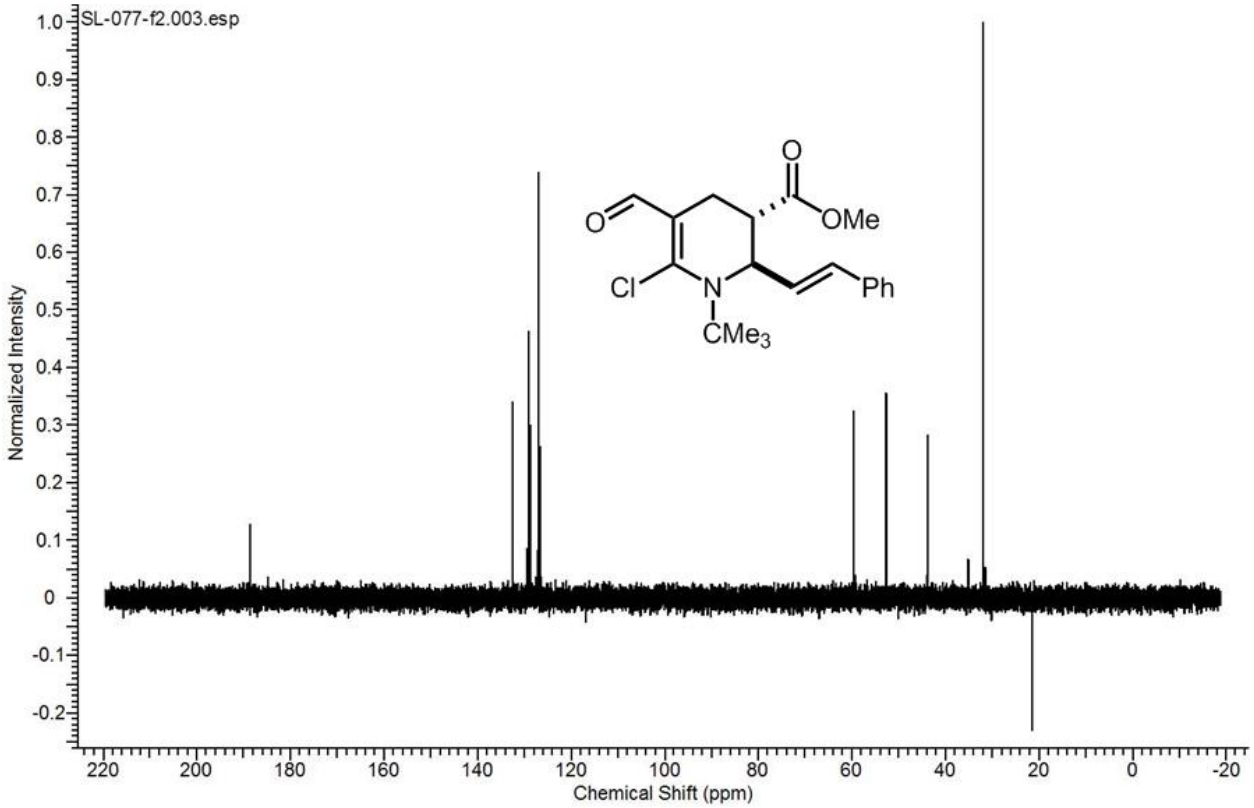


16a

Prepared from lactam **7o2** (1.0 mmol) using General Procedure H. Yield = 296 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (1H, s), 7.34 to 7.23 (5H, m), 6.47 to 6.44 (1H, d), 6.04 to 5.98 (1H, dd), 5.17 to 5.07 (1H, dd), 3.78 (3H, s), 2.90 to 2.87 (2H, m), 2.46 to 2.34 (1H, m), 1.56 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.08, 172.46, 150.04, 135.82, 134.20, 132.19, 128.96, 127.14, 126.67, 124.59, 110.54, 61.75, 59.26, 52.29, 43.59, 34.84, 31.64 21.08. **HRMS-EI^{+}** (*m/z*): calc'd for $C_{20}H_{24}ClNO_3$ 361.1145; found 361.1149.




SL-077-f2.013.esp
Normalized Intensity
Chemical Shift (ppm)
O
OMe
O
Cl
N
CMe3
Ph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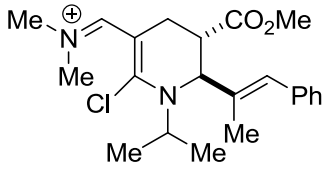
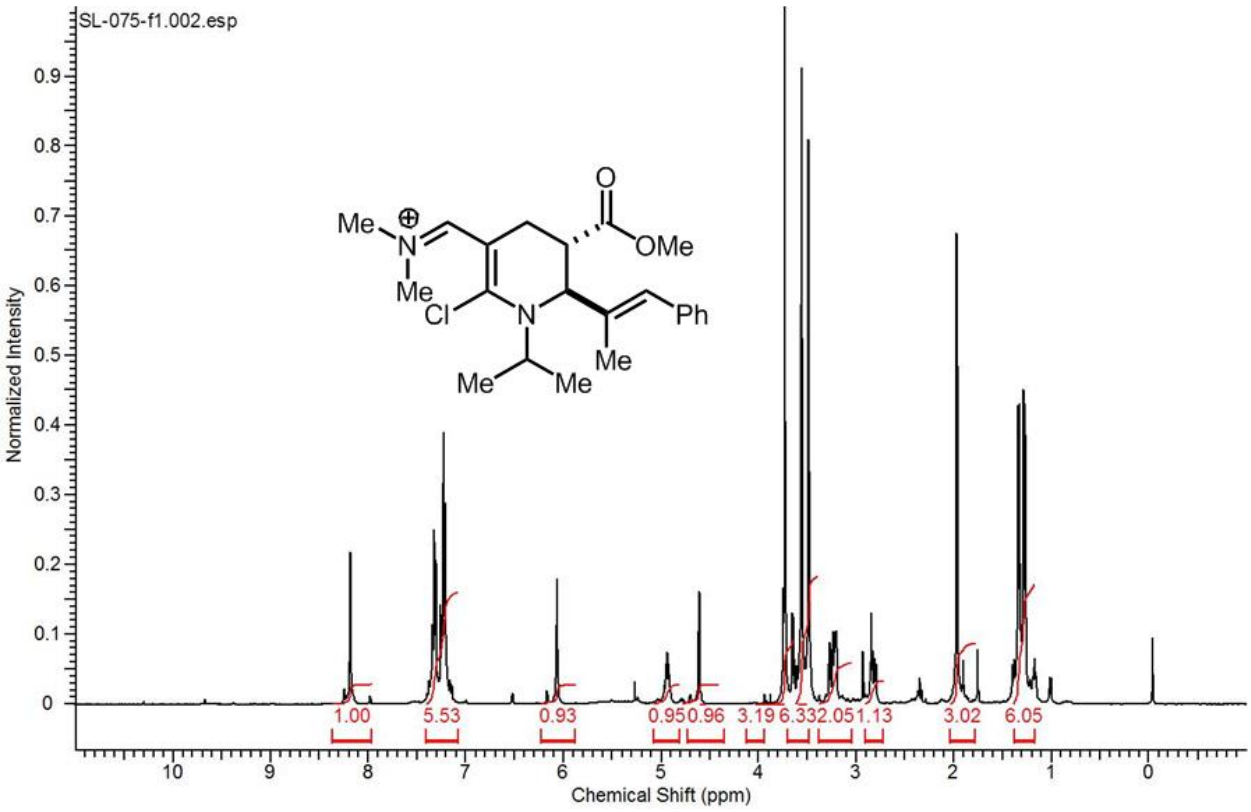
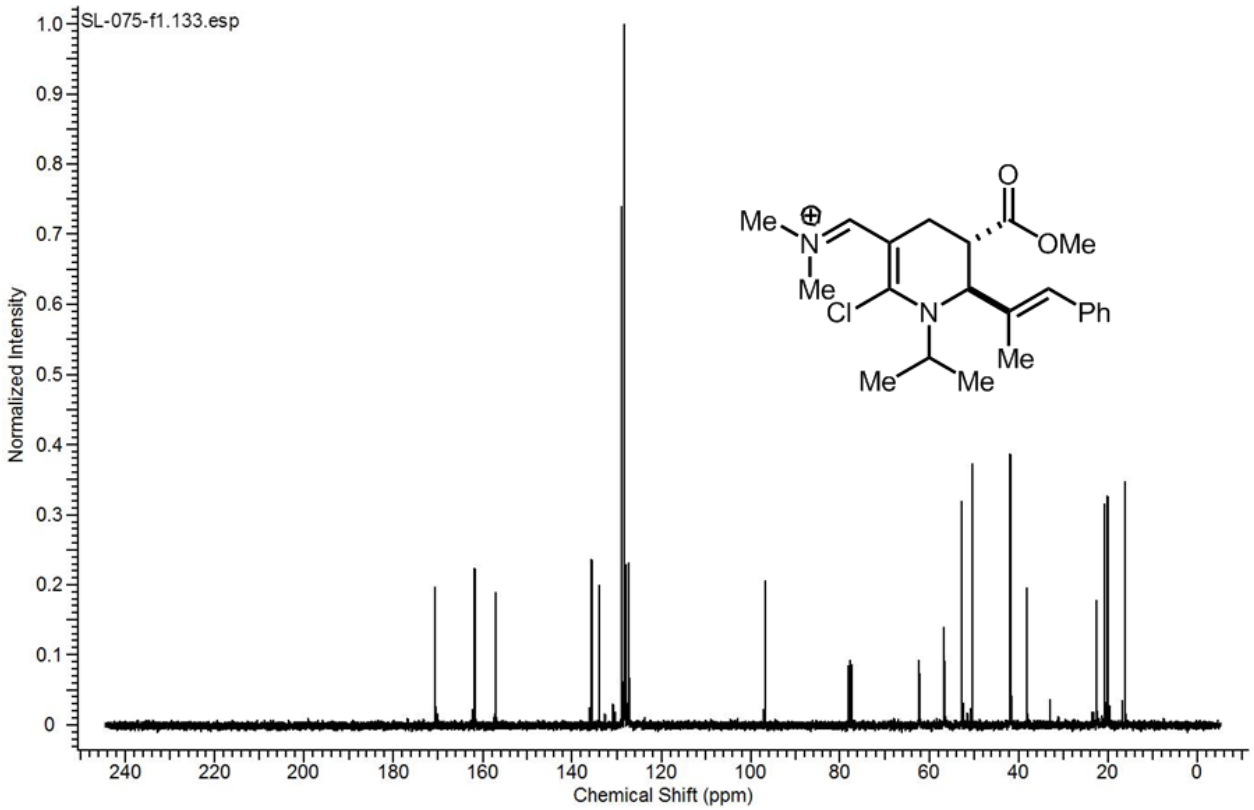
Normalized Intensity
Chemical Shift (ppm)
O
OMe
O
Cl
N
CMe3
Ph



16b

Prepared from lactam **7q2** (1.0 mmol) using General Procedure H, but hydrolysis was carried out for only 20 min and no basification was necessary. Yield = 342 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (1H, s), 7.38 to 7.21 (5H, m), 6.06 (1H, s), 4.98 to 4.90 (1H, m), 4.70 to 4.66 (1H, d), 3.76 to 3.61 (9H, m), 3.28 to 3.16 (2H, m), 2.86 to 2.80 (1H, dd), 1.88 (3H, s), 1.38 to 1.25 (6H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.70, 162.33, 157.46, 136.10, 135.47, 128.92, 128.10, 127.95, 127.42, 97.17, 62.27, 58.36, 56.65, 52.78, 41.94, 38.16, 23.18, 21.38, 20.09, 16.70. **HRMS-EI**$^{+}$ (*m/z*): calc'd for $C_{22}H_{30}Cl_2N_2O_2^{+}$ 381.1990; found 381.1994.

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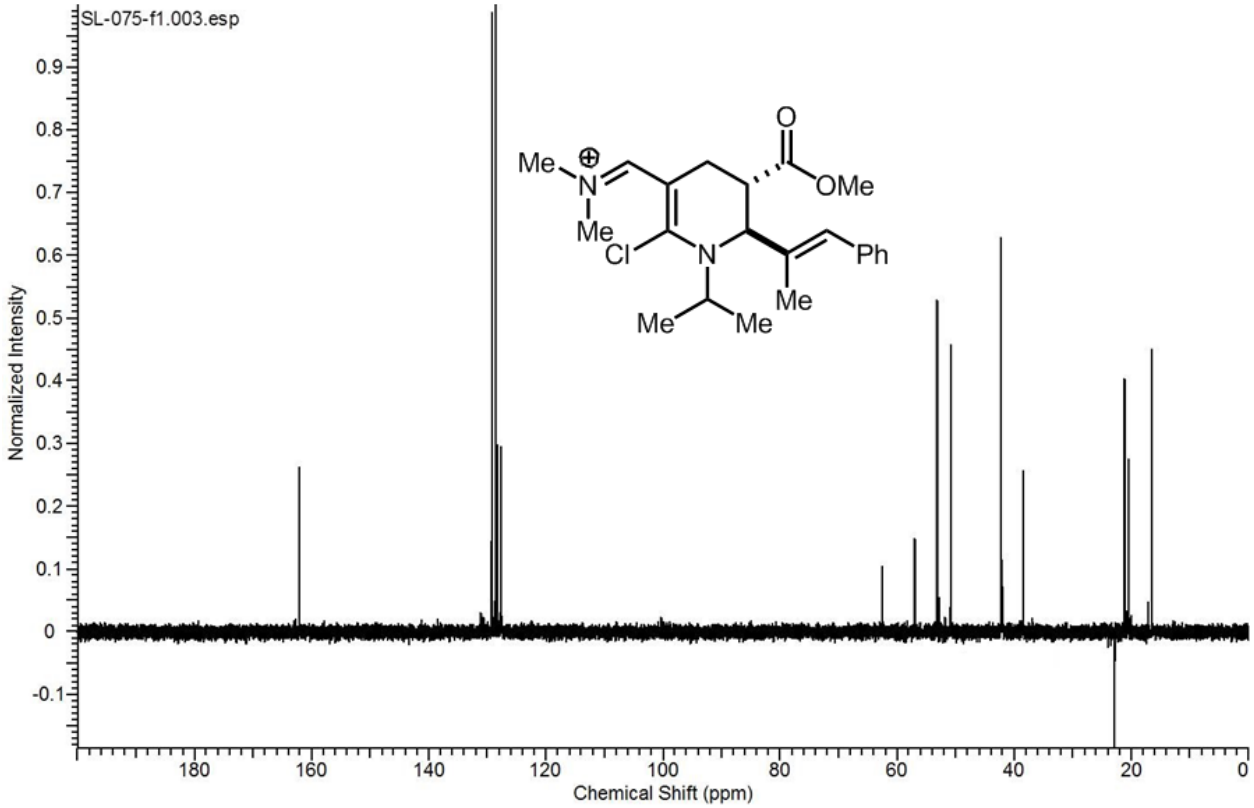
Normalized Intensity
Chemical Shift (ppm)
Me
N
Me
Cl
O
OMe
N
Ph
Me
Me
Me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Normalized Intensity
Chemical Shift (ppm)
Me
N
Me
Cl
O
OMe
N
Ph
Me
Me
Me

References

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