Supporting Information for:

Stereocontrolled four-carbon homologation of vicinally functionalized allylic pyrrolidines to highly customized azonines bearing remote benzylic stereocenters

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Contents:

2. Experimental Section

All experiments involving air and moisture-sensitive reagents were carried out under an inert atmosphere of nitrogen and using freshly distilled solvents. Freshly purchased 2,2,5,5-tetramethyloxolane (TMO) and hexafluoroisopropanol (HFIP) were stored under 4 A^{o} molecular sieves for several days prior to use. Tetrahydrofuran (THF) and and 2-methyltetrahydrofuran (2-MeTHF) were distilled from sodium benzophenone ketyl. Other reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. All amines, enals, Grignard reagents, and potassium carbonate were newly purchased and used without further purification. 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). Unless otherwise indicated, ^{1}H NMR spectral data were acquired using $CDCl_3$ as solvent, at room temperature. Chemical shifts are quoted in parts per million (ppm) referenced to 0.00 ppm for TMS. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants, J, were reported in Hertz unit (Hz). ^{13}C NMR spectra were recorded on Bruker DRX-400 was fully decoupled by broadband proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 77.16 ppm of $CDCl_3$. HRMS-EI^{+} data were obtained using either electron spray 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). The 1,3-azadienes employed in General Procedure A were prepared as previously reported.[1]

General Procedure A: Reaction of 1,3-azadienes with succinic anhydride[2]: A 20 mL screw-cap vial was flame-dried, evacuated and flushed with nitrogen. A solution of the 1,3-azadiene (5.0 mL, 0.10 M in freshly distilled TMO) was added to the vial at room temperature followed by succinic anhydride (500 mg, 5 mmol, 1.0 equiv). The contents were placed in a pre-heated oil bath thermostatted 90 ^{o}C. After complete consumption of the 1,3-azadiene (as judged by TLC, GC-MS, 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 lactam acid.

General Procedure B: LAH reduction: To a 10 mL round-bottomed flask equipped with a magnetic stir bar under a N_2 atmosphere, in a 0 °C ice/water bath, was added the lactam (1.0 mmol) and THF (50 mL). $LiAlH_4$ (220 mg, 5.6 mmol) was then added portion-wise. The reaction mixture was allowed to warm to room temperature overnight (judged complete by GC-MS analysis). After this time (typically 18 h), the reaction mixture was cooled to 0 °C and quenched by slow addition of a solution of 2 N $NaOH_{(aq)}$ (1 mL). The organic layer was decanted into a clean flask. The aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were placed in a separatory funnel and washed with brine, then dried over anhydrous Na_2SO_4. It was filtered and concentrated *in vacuo* to yield the crude tertiary amine as an oil, which was subjected to column chromatography on silica gel eluting with hexanes/acetone.

General procedure C: Methyl esterification of the lactam acid: To a stirring suspension of the acid (1 mmol), dissolved in DMF (5 mL), and K_2CO_3 (414.6 mg, 3 mmol, 3 equiv) was added methyl iodide (0.12 mL, 2 mmol, 2 equiv) under a nitrogen atmosphere. The reaction mixture was stirred for 18 h (TLC monitoring). After complete conversion, it was diluted with water and extracted with EtOAc (3×20 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to give the desired ester, which was purified by flash chromatography on silica.

General procedure D: Grignard addition: To a stirred solution of lactam-ester (1.0 mmol, 1.0 equiv) in dry THF (10 mL) cooled to −78 °C, was added a solution of the corresponding Grignard reagent (2.2 mmol, 2.2 equiv) dropwise. After stirring for 10 min at −78 °C, the reaction mixture was warmed to room temperature and stirred for 5 h. After the reaction was complete, as ascertained by GC-MS or TLC, the reaction mixture was quenched with saturated aqueous NH_4Cl, and diluted with EtOAc. The layers were separated and the aqueous later was extracted with EtOAc. The combined organic layers with dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Where it was necessary (most of the Grignard reagents employed in these studies did not require further purification before the next step), flash chromatography on silica gel (hexane/AcOEt) afforded the lactam-tethered alkenols.

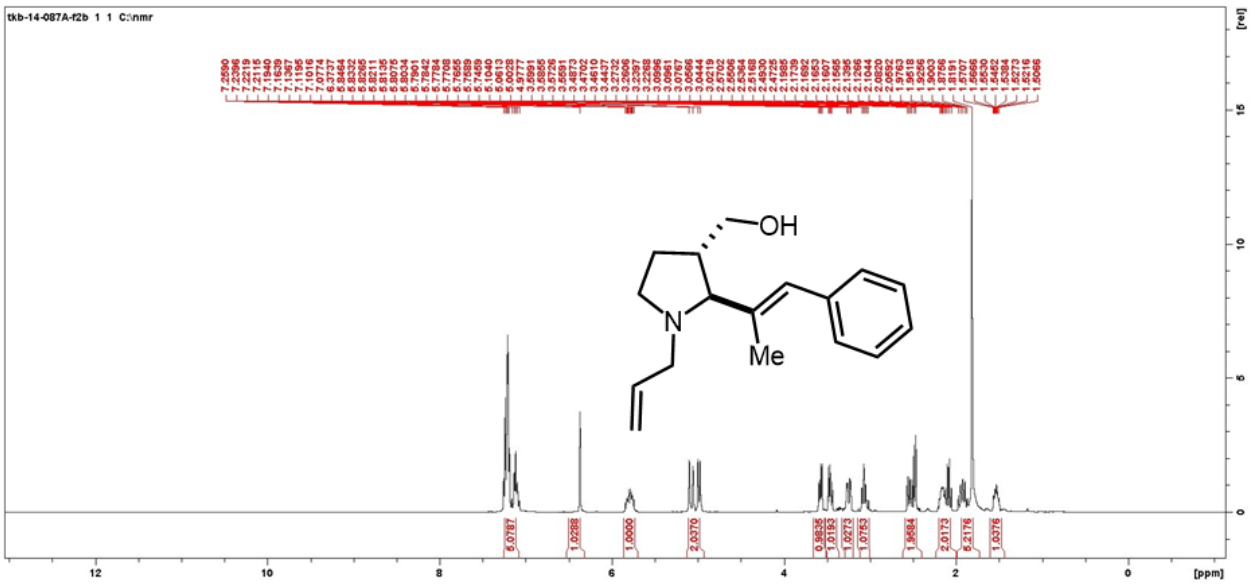
General procedure E: Four-carbon ring expansion of allylic pyrrolidine methanols: To a stirred solution of allylic pyrrolidine methanol **6/7** (1.0 mmol, 1.0 equiv) in HFIP (5 mL), was added the terminal alkyne (methyl propiolate or ethyl propiolate, 2.0 equiv) in one portion. The reaction mixture was stirred at room temperature. After the reaction was complete, as ascertained by GC-MS and/or TLC (usually 2 or 3 days), the reaction mixture was concentrated *in vacuo* to

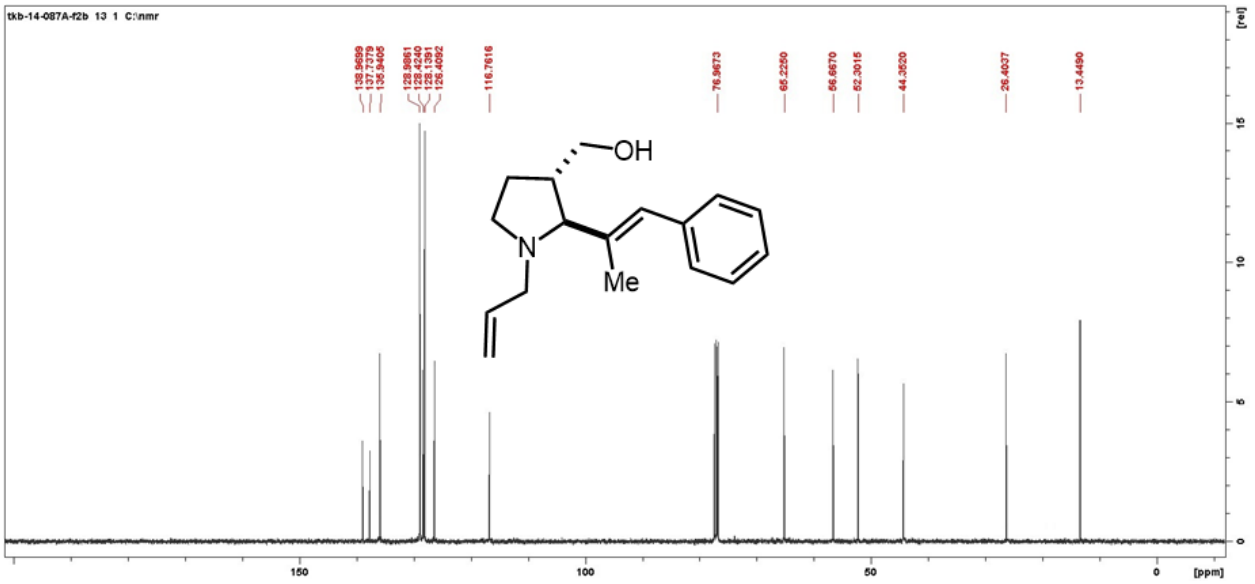
remove the HFIP. The crude product was then redissolved in DCM and directly subjected to flash chromatography on silica gel (hexanes/acetone) to afford the desired 9-membered ring azaheterocycles (*i.e.,* **8**).

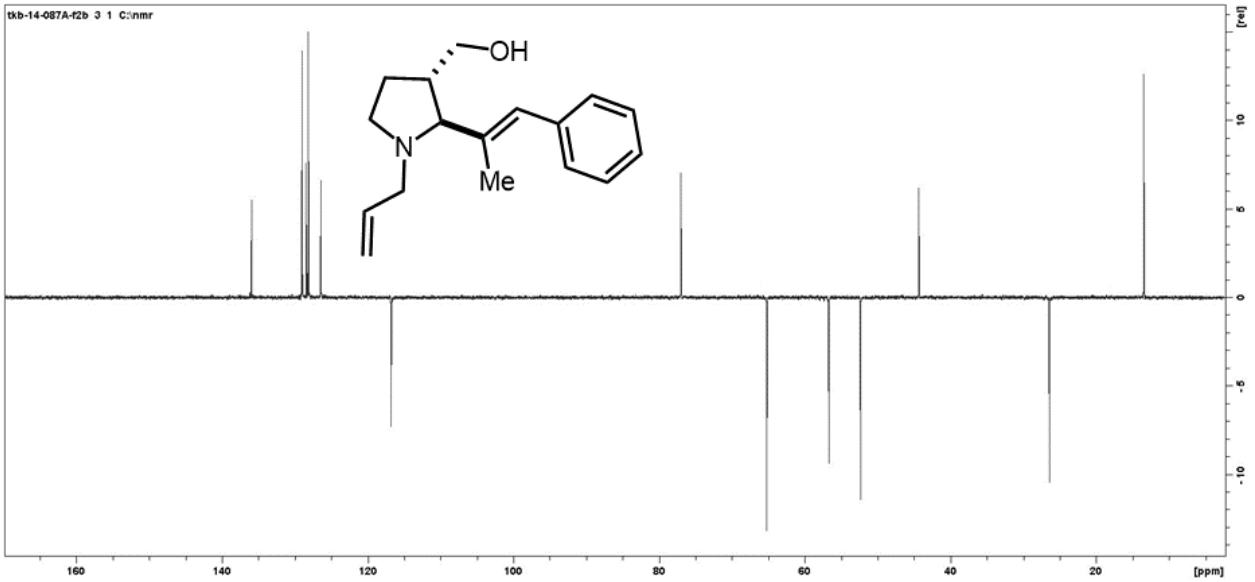
Scheme 1 results

Compound 6a

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Greenish-yellow oil. Yield = 453.0 mg, 88%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.08 (m, 5H), 6.37 (s, 1H), 5.83 (dddd, J = 17.6, 10.1, 7.8, 5.2 Hz, 1H), 5.10 (dq, J = 17.0, 1.6 Hz, 1H), 5.00 (dt, J = 10.0, 1.7 Hz, 1H), 3.58 (dd, J = 10.7, 5.6 Hz, 1H), 3.55 (dd, J = 10.7, 6.7 Hz, 1H), 3.47 – 3.23 (m, 1H), 3.09 – 3.02 (m, 1H), 2.61 – 2.50 (m, 2H), 2.36 – 2.16 (m, 2H), 2.05 (dtd, J = 12.4, 9.8, 8.0 Hz, 1H), 1.87 (d, J = 1.5 Hz, 3H), 1.54 (dddd, J = 13.1, 8.0, 5.1, 2.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 137.7, 136.0, 129.0, 128.4, 128.1, 126.4, 116.7, 77.0, 65.4, 56.6, 52.3, 44.3, 26.7, 13.4. **HRMS-EI^{+}** (*m/z*): calc for $C_{17}H_{23}NO$ $[M]^{+}$ 257.1780, found 257.1788.

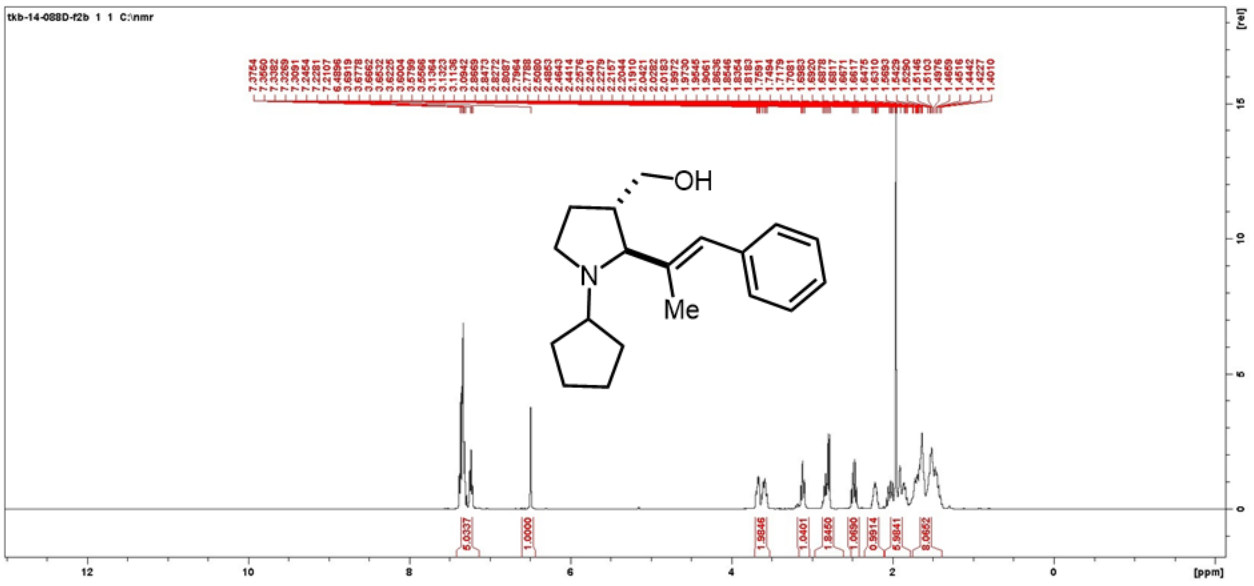






Compound 6b

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellow oil. Yield = 513.0 mg, 90%, 95:5 dr. 1H NMR (400 MHz, CDCl3) δ 7.37 – 7.21 (m, 5H), 6.49 (s, 1H), 3.72 – 3.53 (m, 2H), 3.11 (ddd, J = 9.7, 8.0, 2.2 Hz, 1H), 2.81 (dd, J = 19.9, 7.5 Hz, 2H), 2.53 – 2.42 (m, 1H), 2.22 (dtt, J = 9.9, 6.8, 5.0 Hz, 1H), 2.04 – 1.82 (m, 6H), 1.76 – 1.40 (m, 8H). ^{13}C NMR (101 MHz, CDCl3) δ 141.0, 138.0, 128.9, 128.2, 128.1, 126.8, 126.2, 76.3, 65.4, 64.4, 49.7, 45.3, 31.4, 31.2, 28.2, 26.6, 24.2, 24.1, 23.7, 14.3. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{19}H_{27}NO$ $[M]^{+}$ 285.2093, found 285.2097.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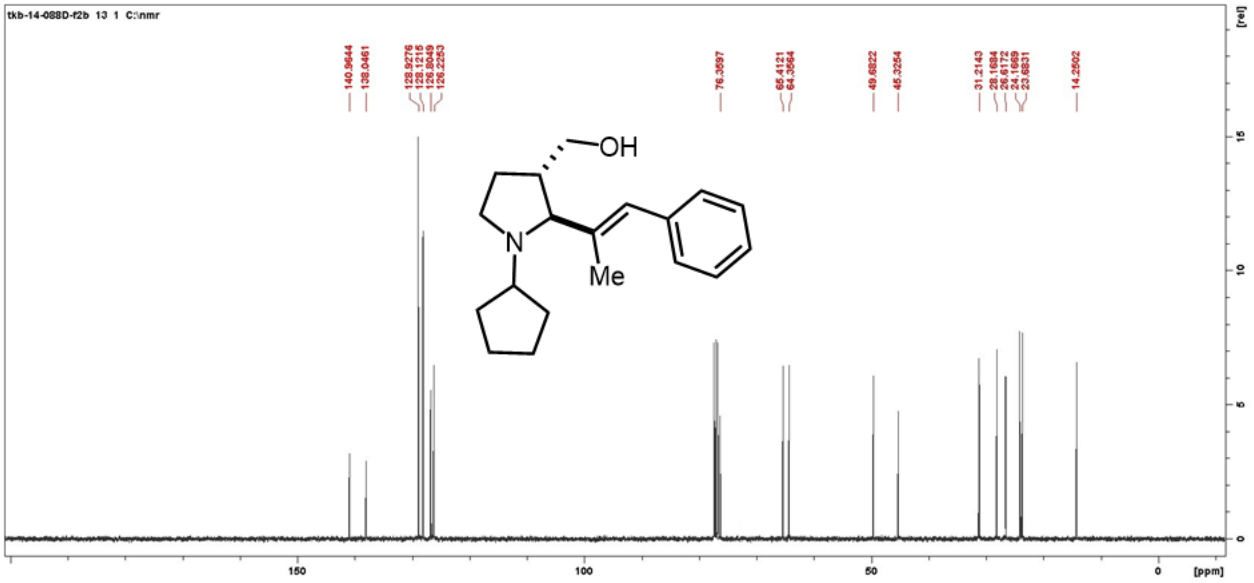
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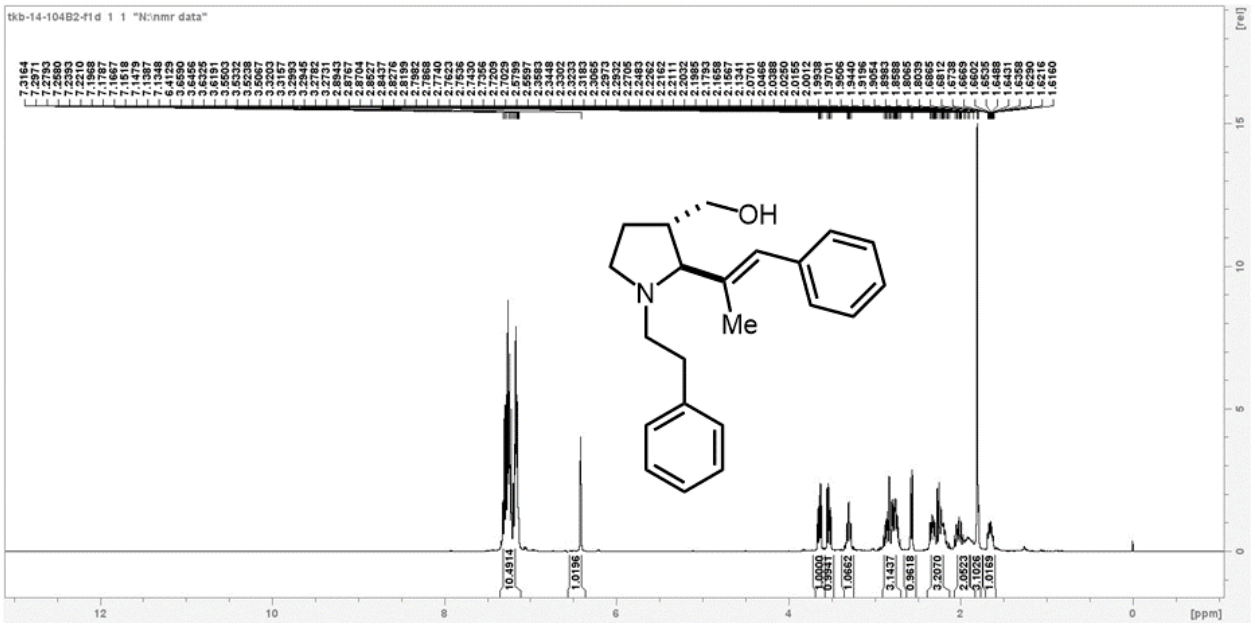
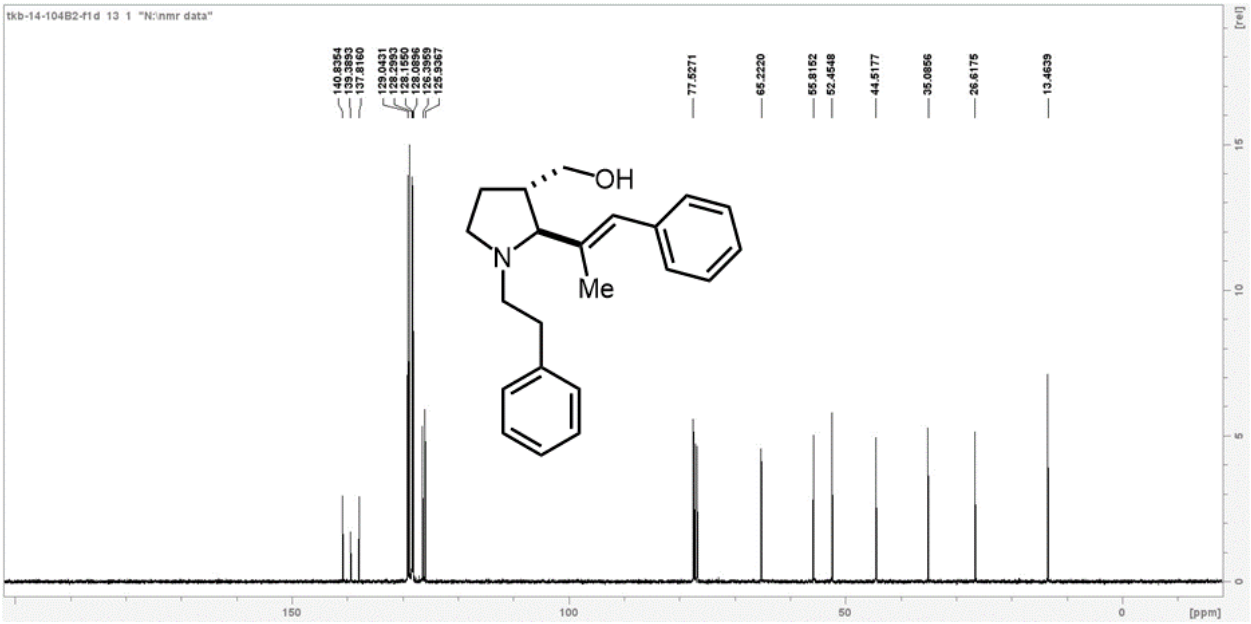
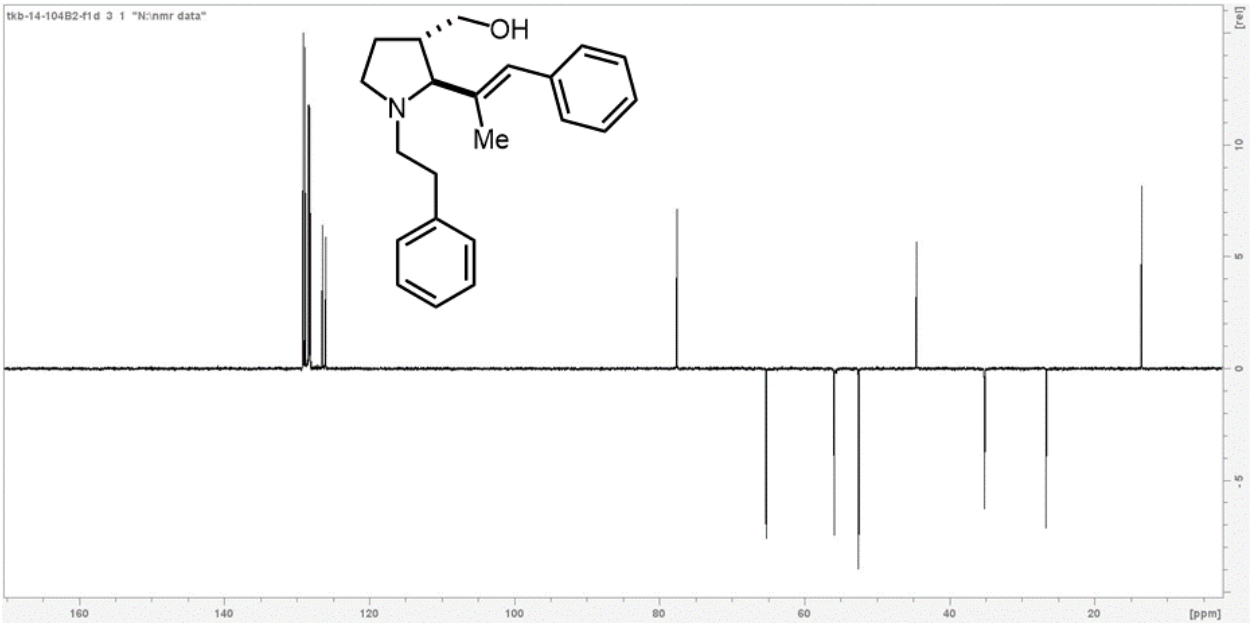
Compound 6c

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 60:40). Pale yellow oil. Yield = 546.5 mg, 85%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.09 (m, 10H), 6.41 (s, 1H), 3.64 (dd, *J* = 10.6, 5.4 Hz, 1H), 3.53 (dd, *J* = 10.6, 6.8 Hz, 1H), 3.37 – 3.22 (m, 1H), 2.94 – 2.67 (m, 3H), 2.57 (d, *J* = 8.0 Hz, 1H), 2.39 – 2.09 (m, 3H), 2.09 – 1.88 (m, 1H), 1.81 (s, 3H), 1.65 (dddd, *J* = 12.9, 8.0, 5.2, 2.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.8, 139.4, 137.8, 129.1, 128.8, 128.3, 128.2, 126.4, 125.9, 77.5, 65.2, 55.8, 52.5, 44.5, 35.1, 26.6, 13.5. **HRMS-EI$^+$** (*m/z*): calc for $C_{22}H_{27}NO$ $[M]^+$ 321.2093, found 321.2099.



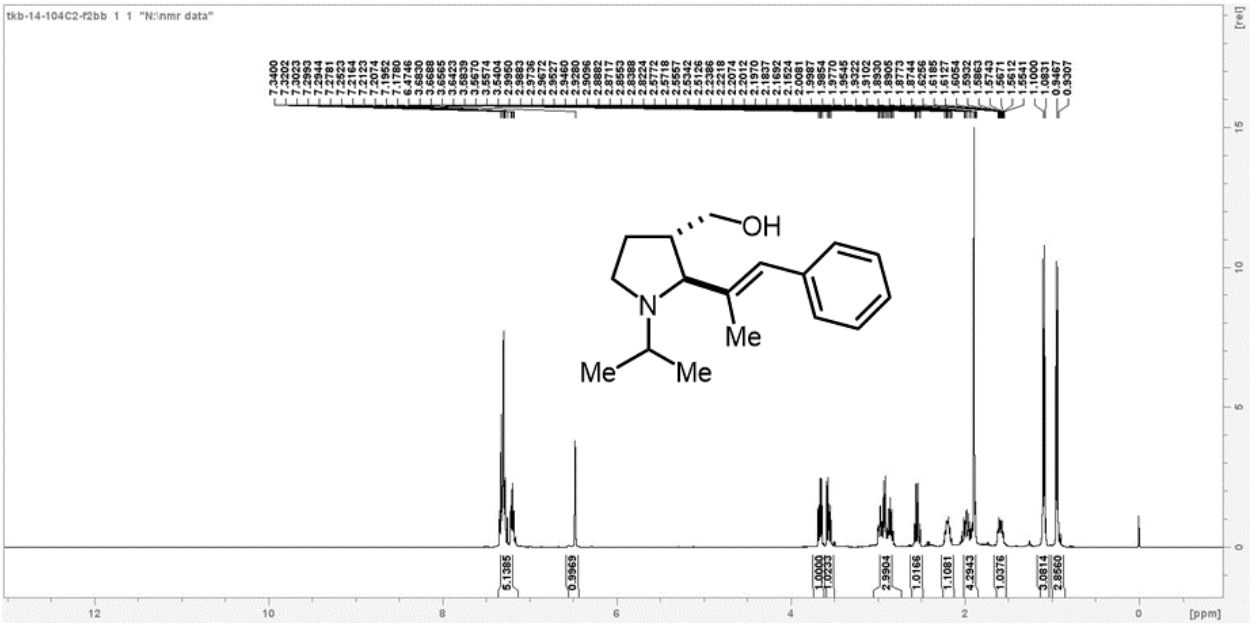


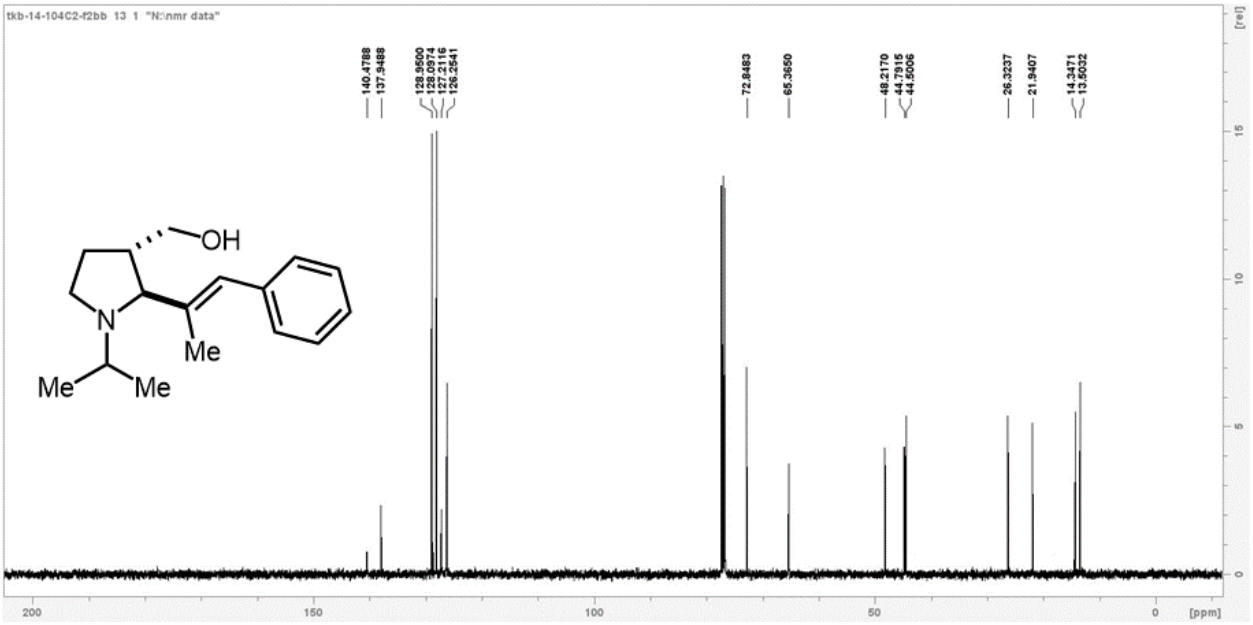


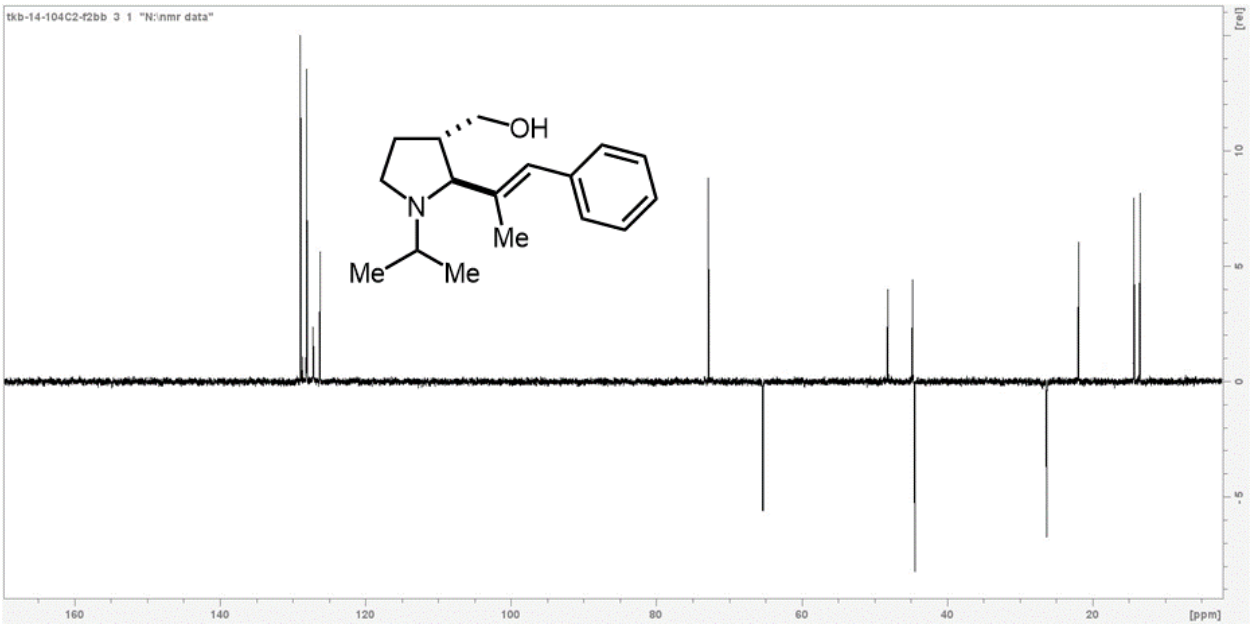
Compound 6d

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Pale yellow oil. Yield = 461.7 mg, 89%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.25 (m, 4H), 7.24 – 7.14 (m, 1H), 6.47 (s, 1H), 3.66 (dd, J = 10.6, 5.7 Hz, 1H), 3.56 (dd, J = 10.6, 6.8 Hz, 1H), 3.02 – 2.78 (m, 3H), 2.55 (q, J = 8.7 Hz, 1H), 2.26 – 2.13 (m, 1H), 1.98 (dq, J = 12.6, 8.8 Hz, 1H), 1.89 (s, 3H), 1.59

(dddd, J = 12.9, 8.1, 5.2, 2.9 Hz, 1H), 1.09 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.5, 137.9, 129.0, 128.1, 127.2, 126.3, 72.8, 65.4, 48.2, 44.8, 44.5, 26.3, 21.9, 14.3, 13.5. **HRMS-EI$^+$** (*m/z*): calc for $C_{17}H_{25}NO$ $[M]^+$ 259.1936, found 259.1939.

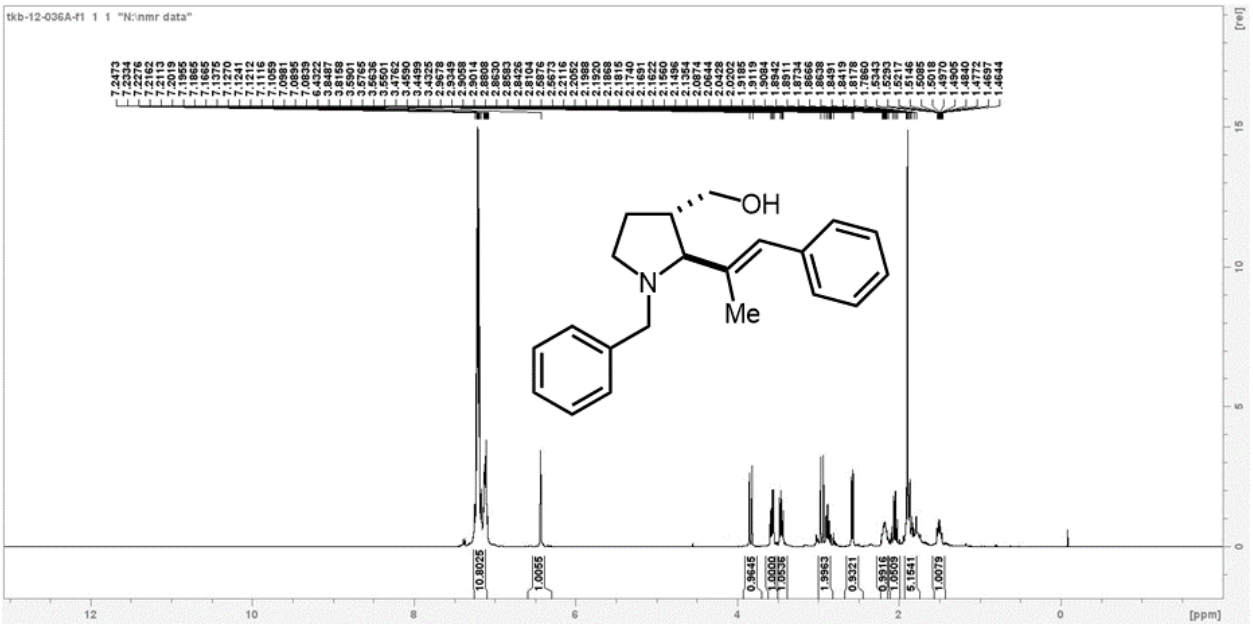






Compound 6e

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Pale yellow oil. Yield = 528.7 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.08 (m, 10H), 6.43 (d, *J* = 1.6 Hz, 1H), 3.83 (d, *J* = 13.2 Hz, 1H), 3.57 (dd, *J* = 10.6, 5.4 Hz, 1H), 3.45 (dd, *J* = 10.6, 6.9 Hz, 1H), 2.97 – 2.75 (m, 2H), 2.58 (d, *J* = 8.1 Hz, 1H), 2.25 – 2.09 (m, 1H), 2.05 (q, *J* = 9.0 Hz, 1H), 1.98 – 1.70 (m, 5H), 1.50 (dddd, *J* = 13.0, 7.9, 5.1, 2.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 139.3, 129.1, 128.8, 128.7, 128.3, 126.9, 126.6, 77.3, 65.4, 58.2, 52.4, 44.5, 26.6, 13.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{21}H_{25}NO$ $[M]^{+}$ 307.1936, found 307.1939.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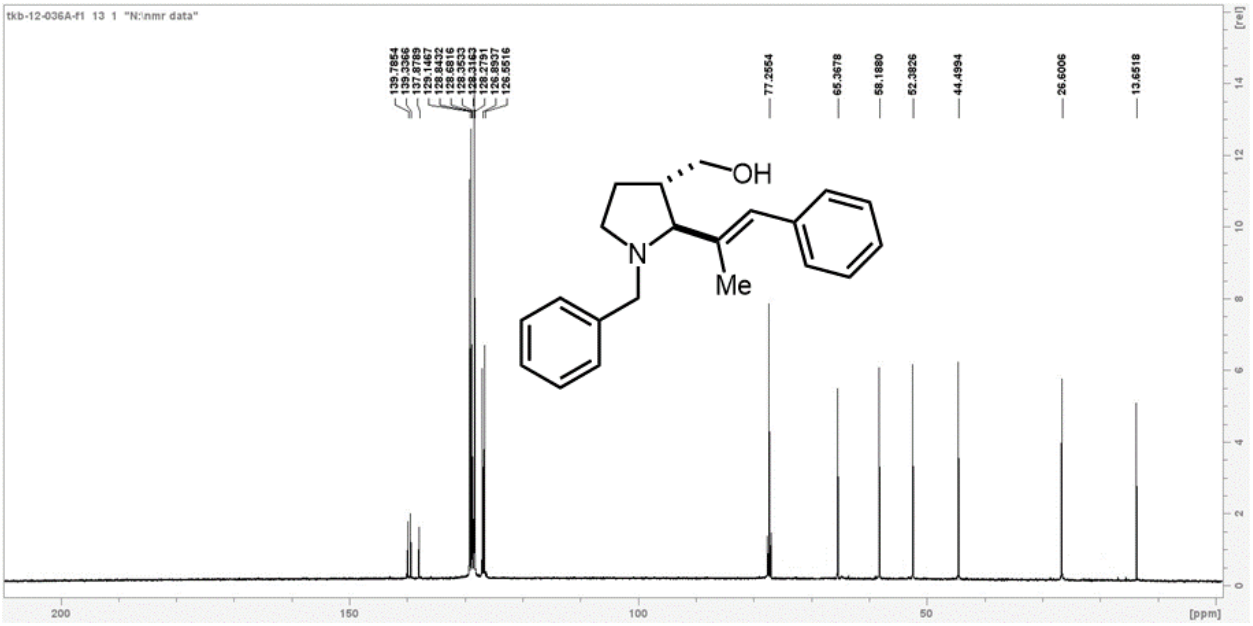
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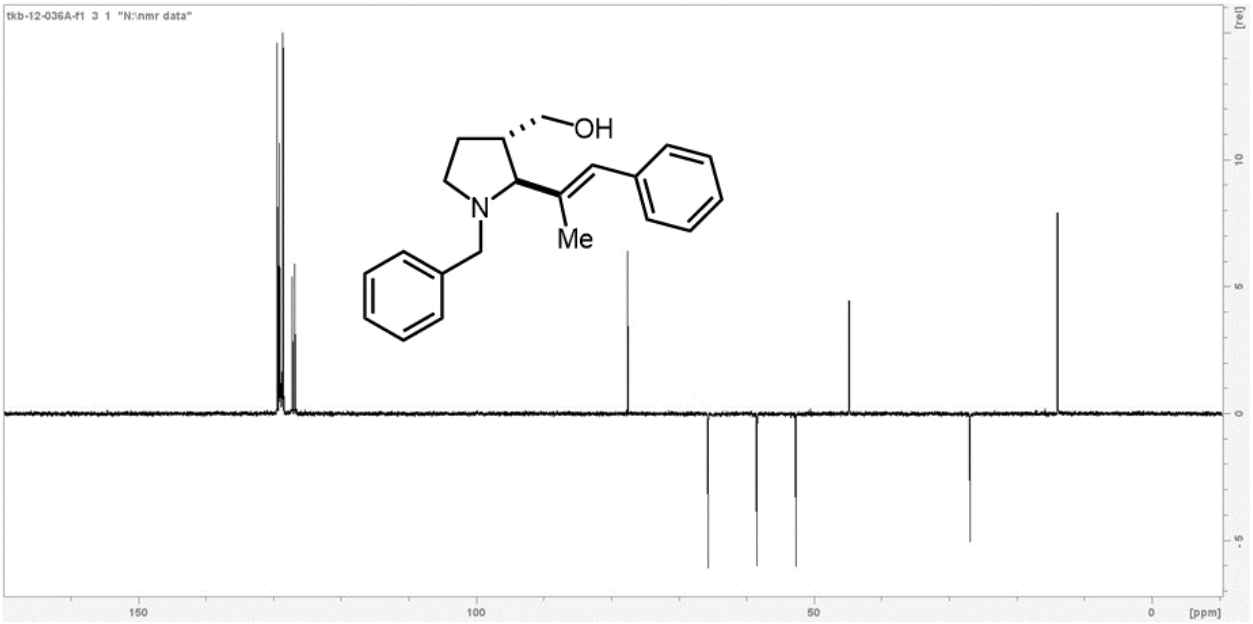

Compound 6f

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Pale yellow oil. Yield = 600.7 mg, 89%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.35 (m, 4H), 7.27 – 7.24 (m, 3H), 6.89 (d, J = 7.6 Hz, 2H), 6.58 (d, J = 1.6 Hz, 1H), 3.91 (d, J = 12.9 Hz, 1H), 3.83 (s, 3H), 3.73 (dd, J = 10.6, 5.4 Hz, 1H), 3.61 (dd, J = 10.6, 6.9 Hz, 1H), 3.11 – 2.98 (m, 2H), 2.71 (d, J = 8.1 Hz, 1H), 2.33 (dddt, J = 10.3, 8.1, 7.0, 5.3 Hz, 1H), 2.26 – 2.13 (m, 1H), 2.09 – 1.94 (m, 4H), 1.65 (dddd, J = 12.9, 8.2, 5.0, 2.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 139.3, 137.9, 131.8, 129.9, 129.0, 128.4, 128.1, 126.4, 113.6, 77.0, 65.1, 57.4, 55.3, 52.2, 44.5, 26.5, 13.6. **HRMS-EI$^+$** (*m/z*): calc for $C_{22}H_{27}NO_2$ $[M]^+$ 337.2042, found 337.2048.


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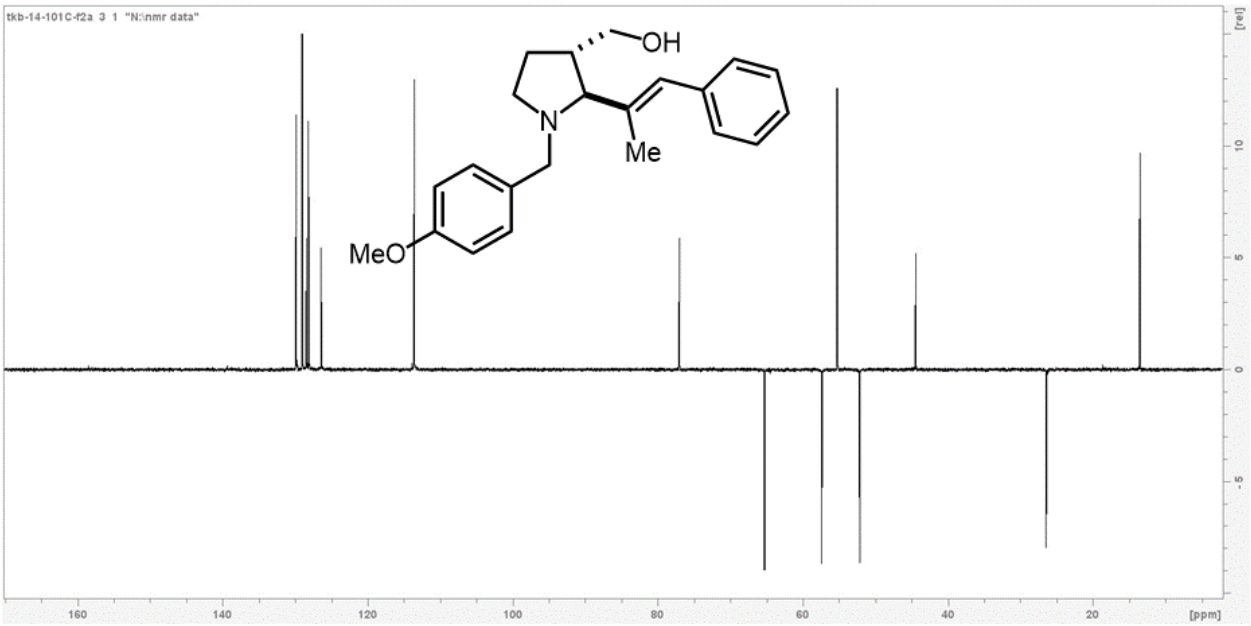
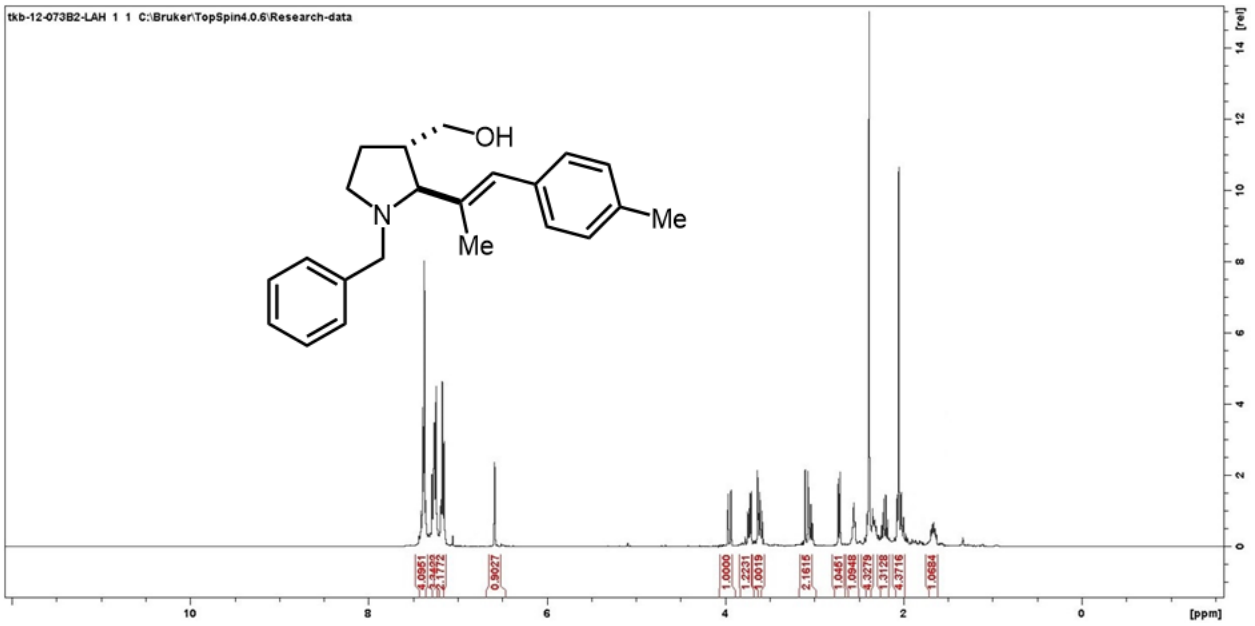


Compound 6g

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 60:40). Pale yellow oil. Yield = 552.9 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.12 (m, 9H), 6.42 (d, *J* = 1.6 Hz, 1H), 3.78 (d, *J* = 13.1 Hz, 1H), 3.56 (dd, *J* = 10.6, 5.4 Hz, 1H), 3.03 – 2.73 (m, 2H), 2.55 (d, *J* = 8.1 Hz, 1H), 2.45 – 2.35 (m, 1H), 2.20 – 2.06 (m, 4H), 2.04 (td, *J* = 9.3, 8.2 Hz, 1H), 1.96 – 1.84 (m, 4H), 1.66 (h, *J* = 3.9, 3.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4, 137.9, 136.7, 136.4, 129.1, 129.0, 128.8, 128.6, 128.3, 126.5, 77.2, 65.3, 57.9, 52.3, 44.6, 26.6, 21.3, 13.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{22}H_{27}NO$ $[M]^{+}$ 321.2093, found 321.2098.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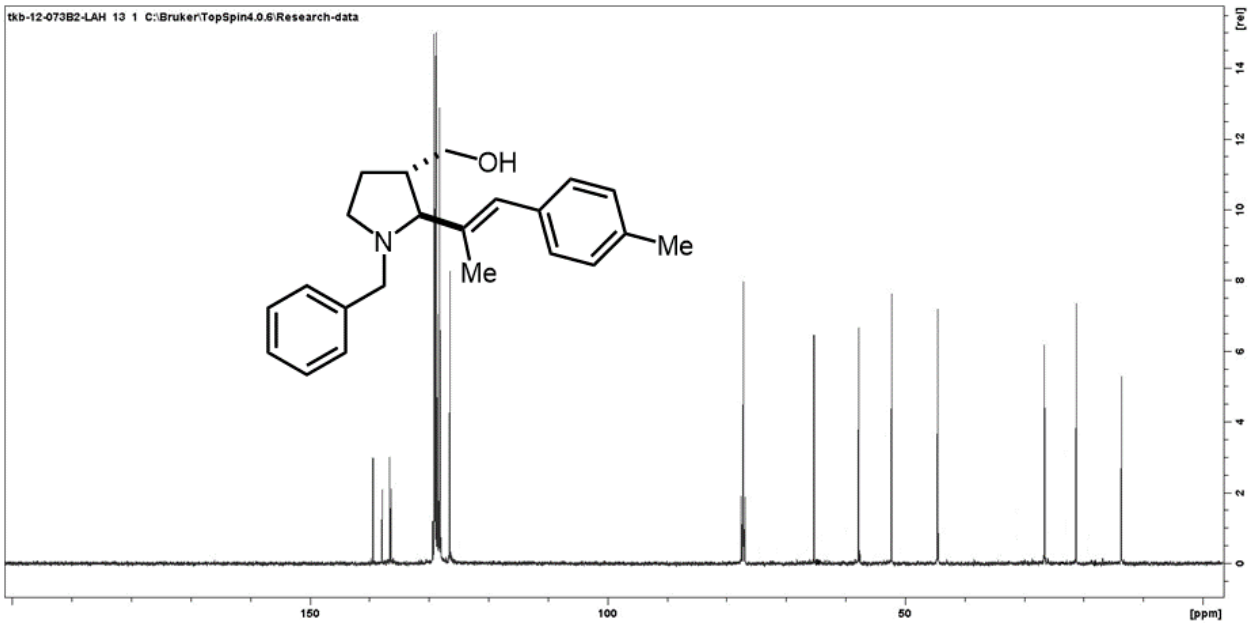
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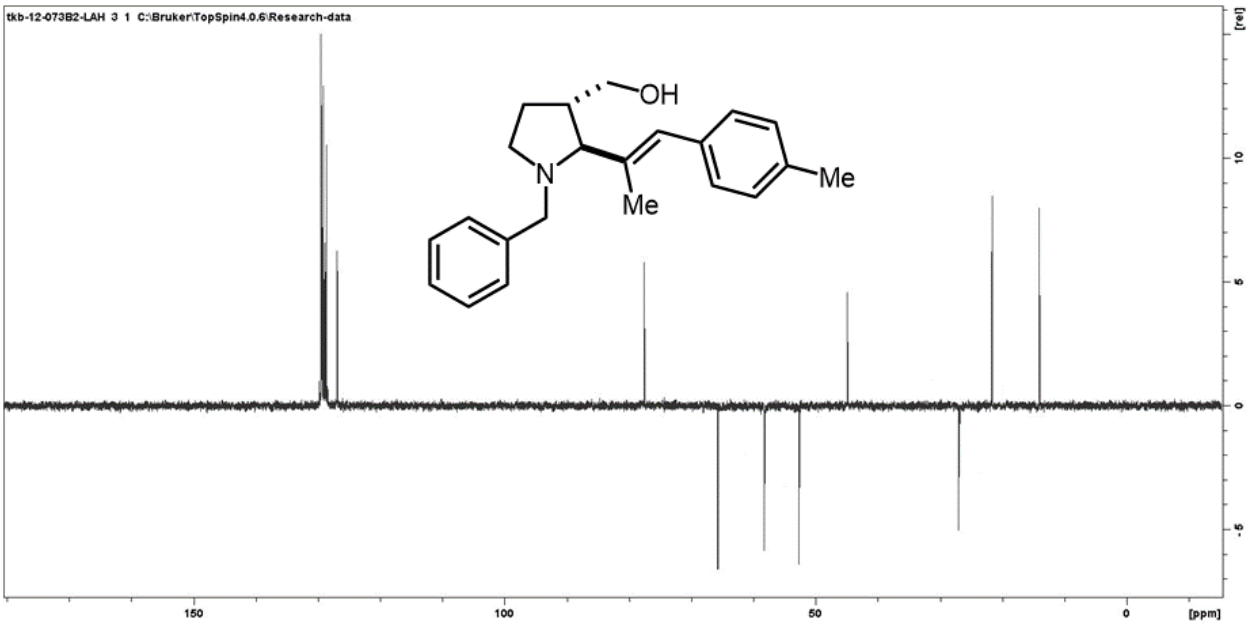
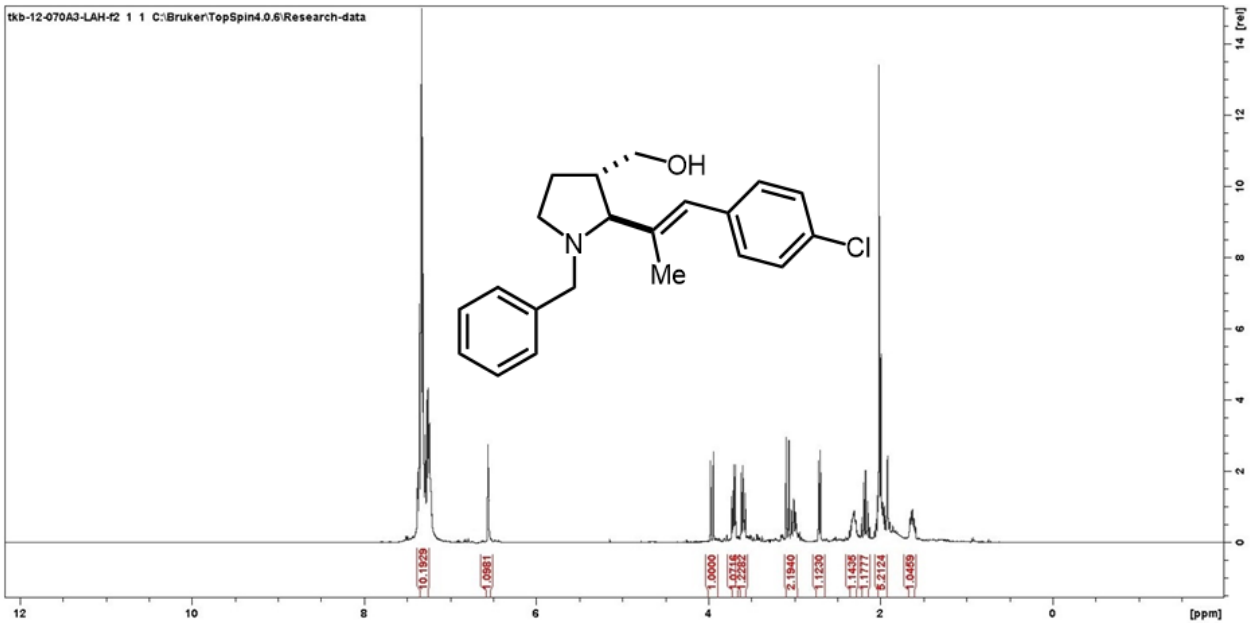


Compound 6h

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 567.5 mg, 83%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.02 (m, 9H), 6.40 (d, *J* = 1.6 Hz, 1H), 3.78 (d, *J* = 13.3 Hz, 1H), 3.56 (dd, *J* = 10.6, 5.5 Hz, 1H), 3.04 – 2.73 (m, 2H), 2.56 (dd, *J* = 8.1, 2.1 Hz, 1H), 2.27 – 2.10 (m, 1H), 2.10 – 1.94 (m, 1H), 1.94 – 1.80 (m, 5H), 1.58 (dddd, *J* = 12.9, 8.3, 5.0, 2.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 139.3, 137.8, 130.1, 129.1, 128.8, 128.7, 128.4, 128.3, 128.2, 126.9, 126.5, 77.3, 65.4, 58.1, 52.4, 44.5, 26.6, 13.6. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{21}H_{24}ClNO$ $[M]^{+}$ 341.1546, found 341.1552.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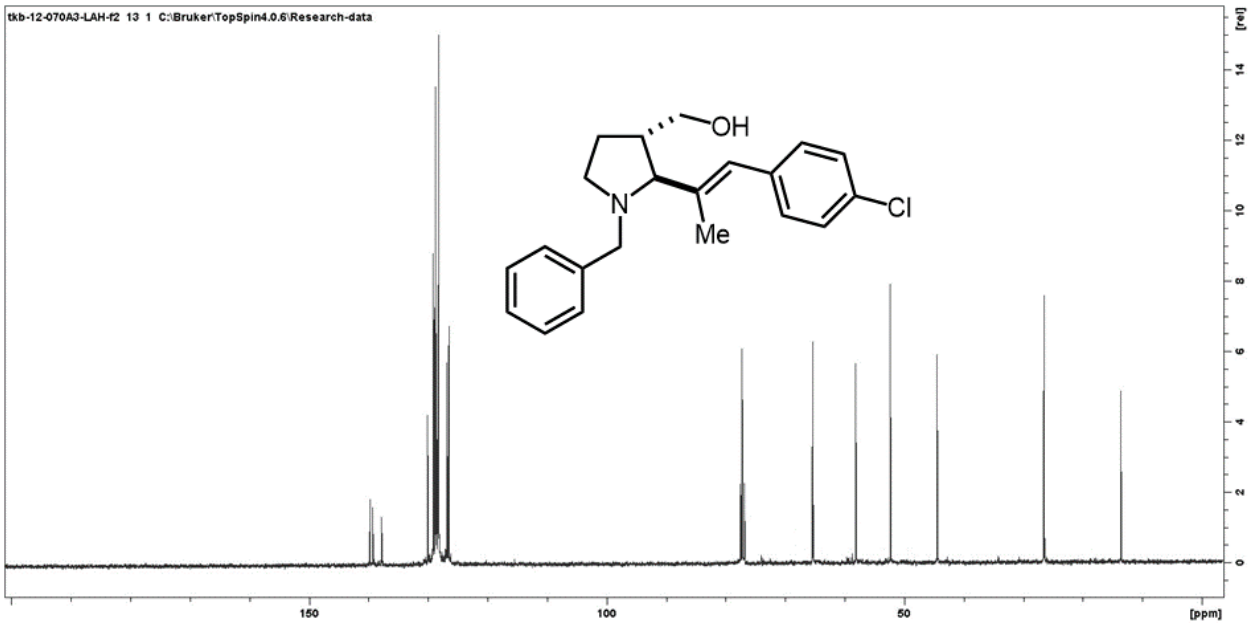
tkb-12-070A3-LAH-f2 13 1 C:\Bruker\TopSpin4.0.6\Research-data
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N
Me
Cl
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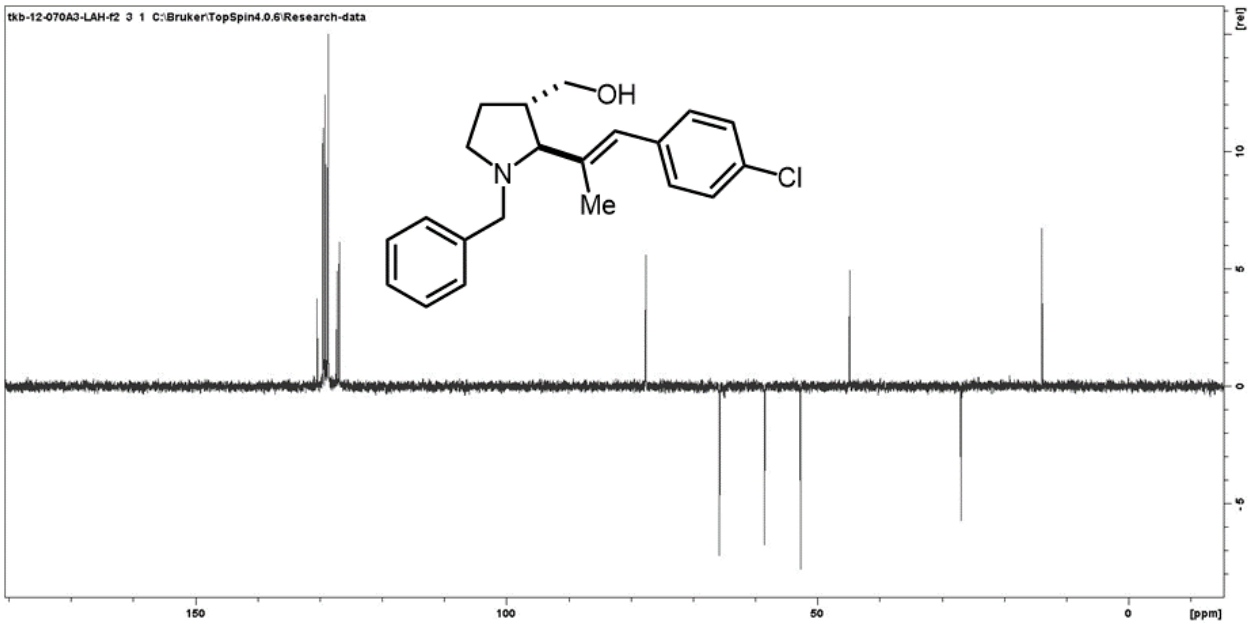
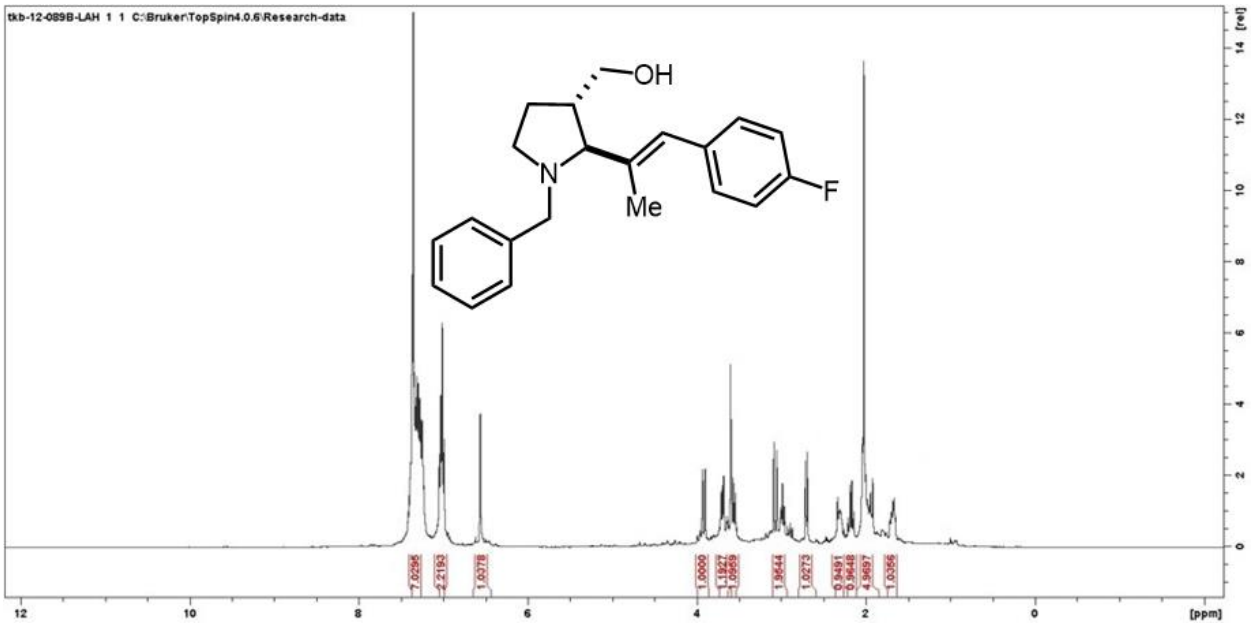
100
50
[ppm]
[rel]



Compound 6i

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 559.7 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.13 (m, 7H), 7.08 – 7.02 (m, 2H), 6.51 (d, *J* = 1.7 Hz, 1H), 3.88 (d, *J* = 12.3 Hz, 1H), 3.72 – 3.54 (m, 3H), 3.02 – 2.88 (m, 2H), 2.65 (d, *J* = 8.1 Hz, 1H), 2.57 (td, *J* = 5.5, 4.3, 2.9 Hz, 1H), 2.34 – 2.20 (m, 1H), 2.13 (q, *J* = 8.9 Hz, 1H), 2.06 – 1.91 (m, 5H), 1.73 – 1.67 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 160.7, 139.1, 137.9, 135.6, 135.5, 130.3, 130.2, 129.1, 128.7, 128.3, 126.6, 115.1, 114.9, 77.0, 64.9, 57.5, 54.1, 52.3, 44.6, 23.5, 13.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{21}H_{24}FNO$ $[M]^{+}$ 325.1842, found 325.1848.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Me
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1.0000
1.1922
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0.9648
4.9697
1.0356
12
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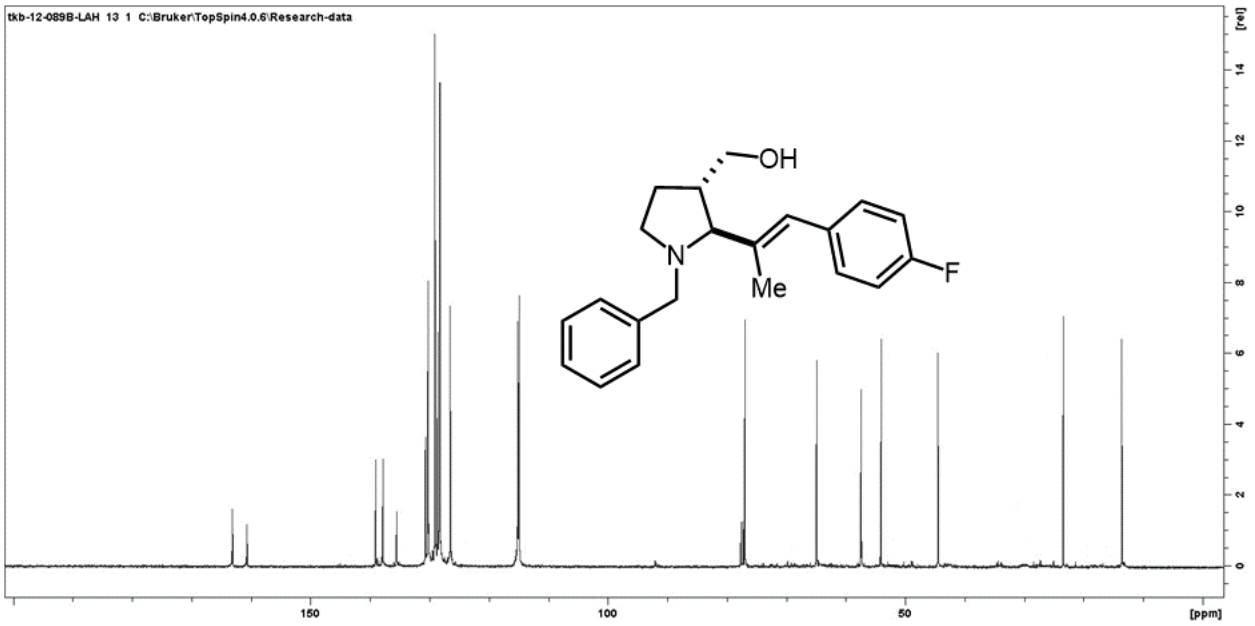
8
6
4
2
0
[ppm]
[rel]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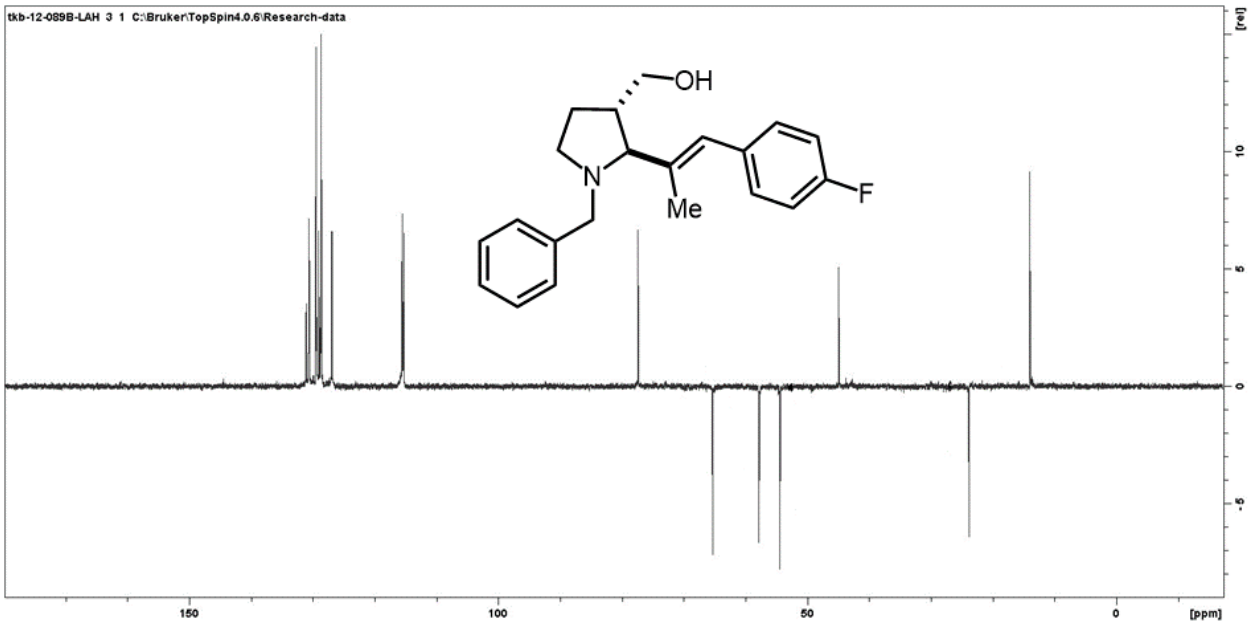
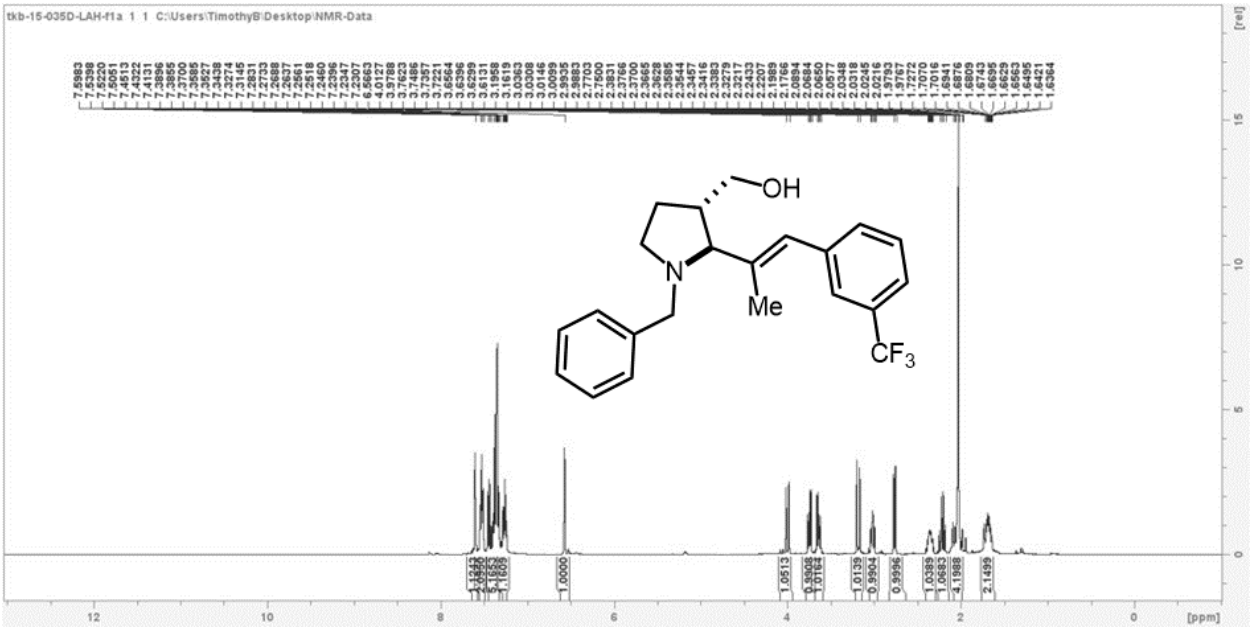
N
Me
F
150
100
50
[ppm]
[rel]



Compound 6j

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 80:20). Amorphous solid. Yield = 593.2 mg, 79%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.56 – 7.21 (m, 8H), 6.57 (d, *J* = 1.7 Hz, 1H), 4.00 (d, *J* = 13.6 Hz, 1H), 3.74 (dd, *J* = 10.6, 5.5 Hz, 1H), 3.63 (dd, *J* = 10.6, 6.7 Hz, 1H), 3.18 (d, *J* = 13.6 Hz, 1H), 3.01 (td, *J* = 8.5, 2.3 Hz, 1H), 2.76 (d, *J* = 8.1 Hz, 1H), 2.35 (dddt, *J* = 10.2, 8.1, 6.6, 5.3 Hz, 1H), 2.21 (q, *J* = 8.9 Hz, 1H), 2.14 – 1.91 (m, 5H), 1.68 (dddd, *J* = 13.1, 10.6, 6.8, 1.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.8, 138.9, 137.6, 131.9, 130.7, 130.4, 129.0, 128.9, 128.8, 128.6, 128.4, 128.2, 128.2, 126.5, 125.7, 125.2, 125.1, 123.7, 123.6, 122.9, 77.0, 65.2, 57.6, 52.4, 44.3, 26.4, 13.5. **HRMS-EI^{+}** (*m/z*): calc for $C_{22}H_{24}F_3NO$ $[M]^+$ 375.1810, found 375.1818.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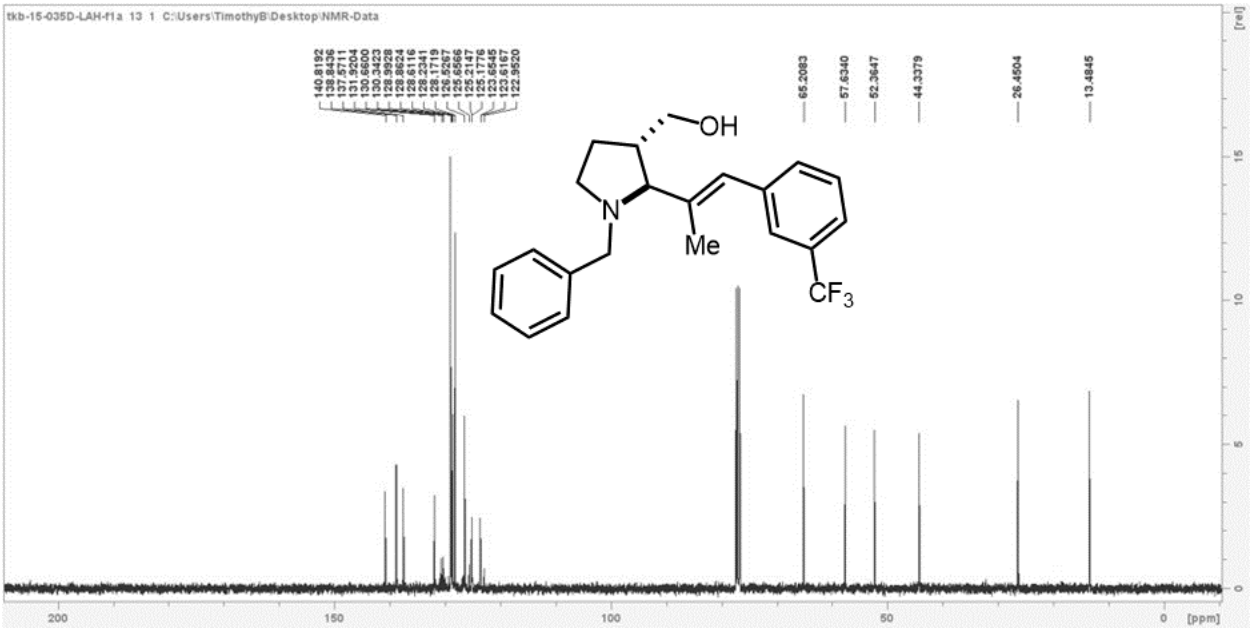
N
Me
CF3
[ppm]


tkb-15-035D-LAH-f1a 13 1 C:\Users\TimothyB\Desktop\NMR-Data
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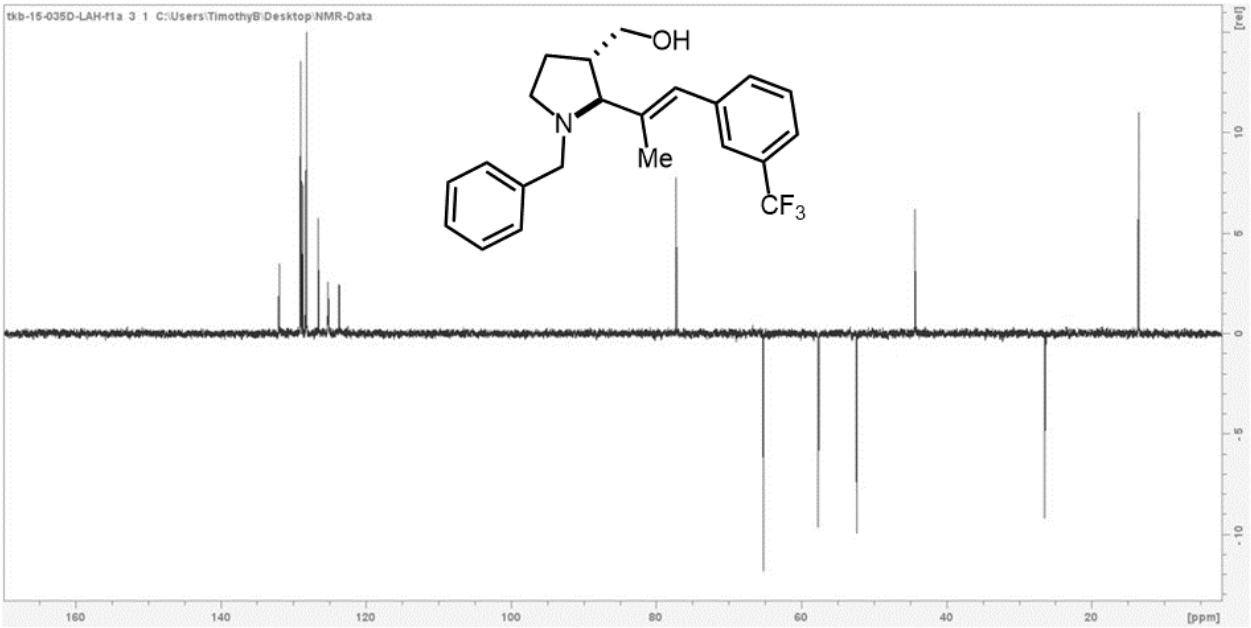
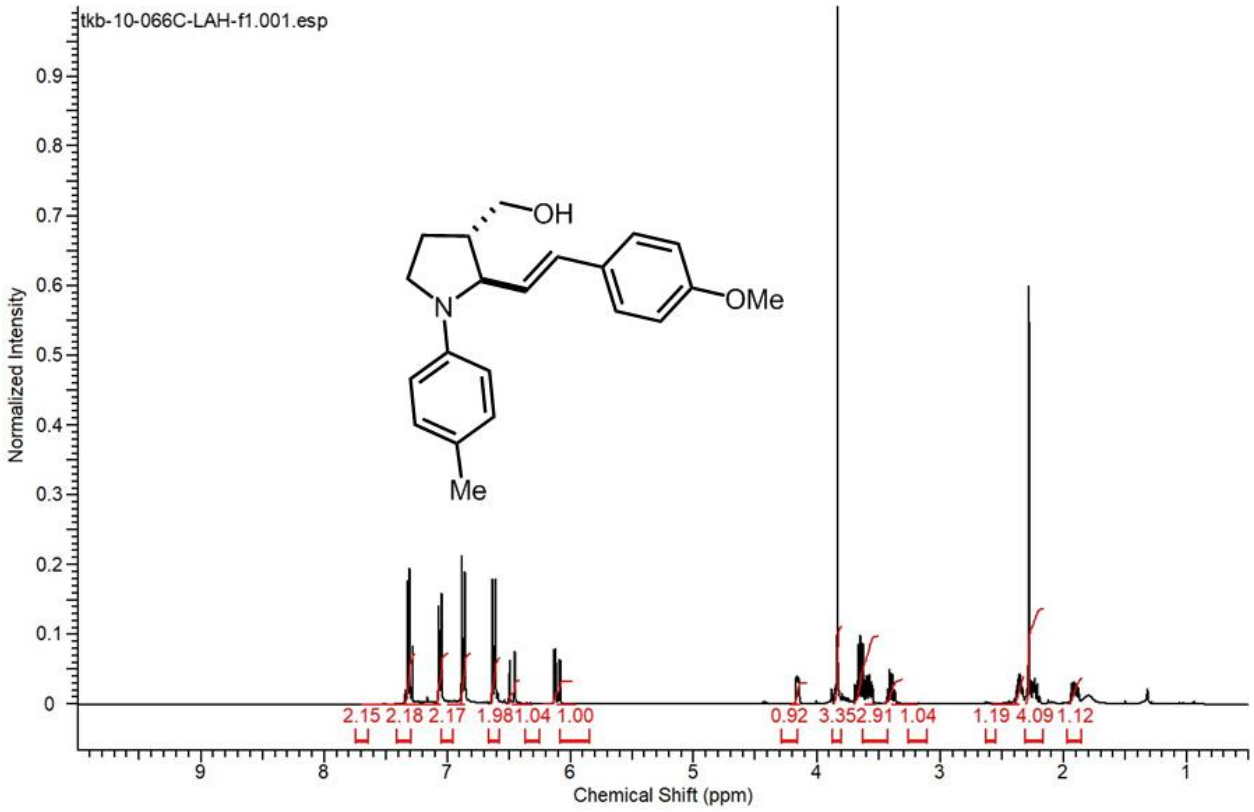
44.3379
26.4504
13.4845
OH
N
Me
CF3
[ppm]



Compound 6k

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Amorphous solid. Yield = 452.7 mg, 70%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.1 Hz, 2H), 7.01 (d, *J* = 8.1 Hz, 2H), 6.89 (d, *J* = 7.6 Hz, 2H), 6.68 (d, *J* = 7.6 Hz, 2H), 6.47 (d, *J* = 15.9 Hz, 1H), 6.11 (dd, *J* = 15.8, 5.9 Hz, 1H), 4.16 (dd, *J* = 5.9, 3.1 Hz, 1H), 3.83 (s, 3H), 3.71 – 3.53 (m, 3H), 3.45 – 3.32 (m, 1H), 2.36 (ddq, *J* = 10.6, 6.9, 3.4 Hz, 1H), 2.28 (s, 3H), 2.29 – 2.17 (m, 1H), 1.91 (ddt, *J* = 12.7, 7.4, 3.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 145.5, 129.8, 129.6, 129.3, 127.6, 125.0, 114.0, 112.6, 64.2, 63.3, 55.4, 48.3, 47.6, 25.7, 20.4. **HRMS-EI^{+}** (*m/z*): calc for $C_{21}H_{25}NO_2$ $[M]^{+}$ 323.1885, found 323.1889.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Chemical Shift (ppm)
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N
Me
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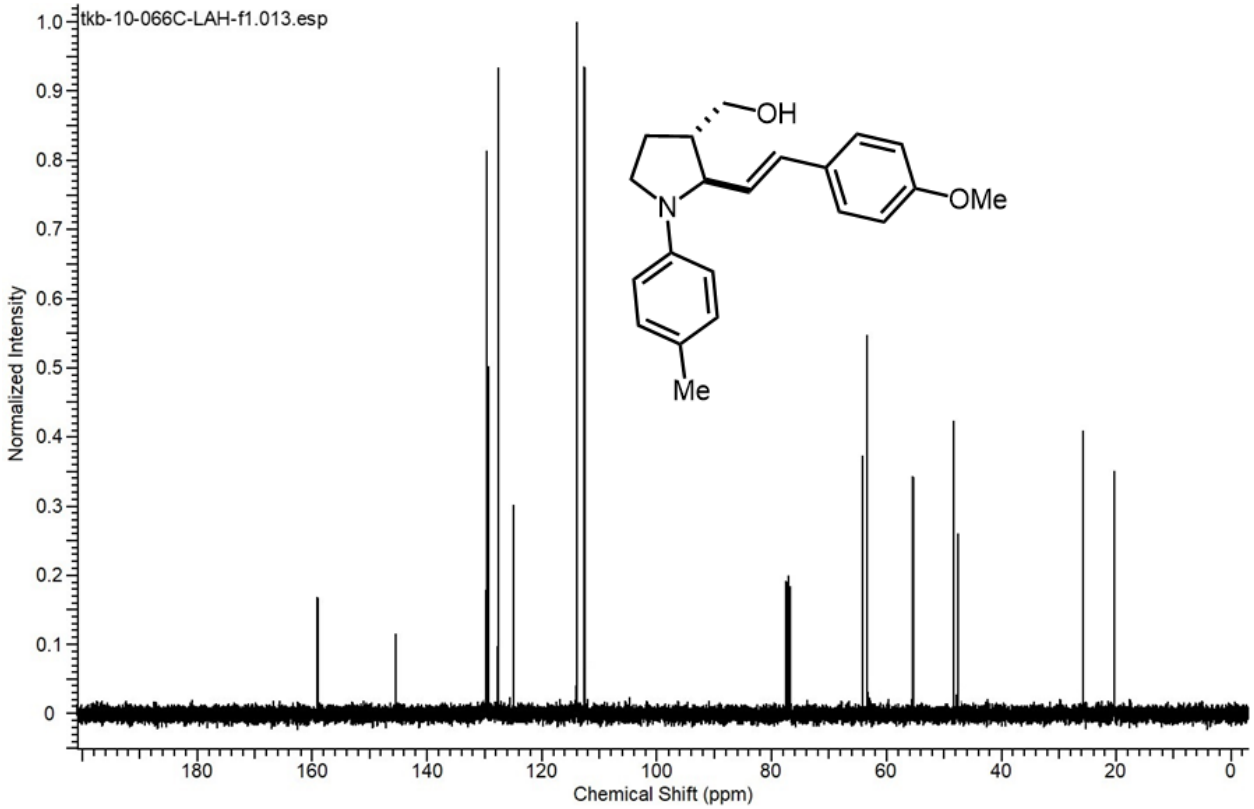
0.92 3.35 2.91 1.04
1.19 4.09 1.12


tkb-10-066C-LAH-f1.013.esp
Normalized Intensity
Chemical Shift (ppm)
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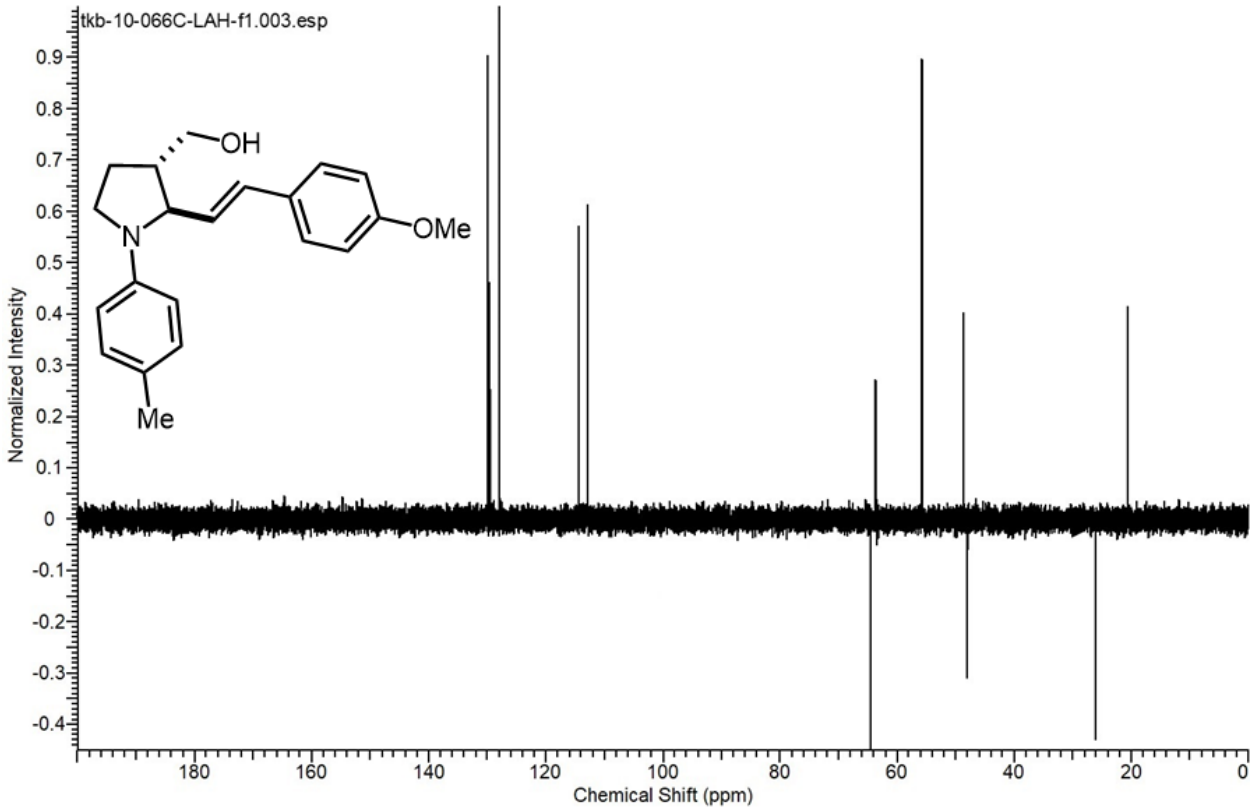
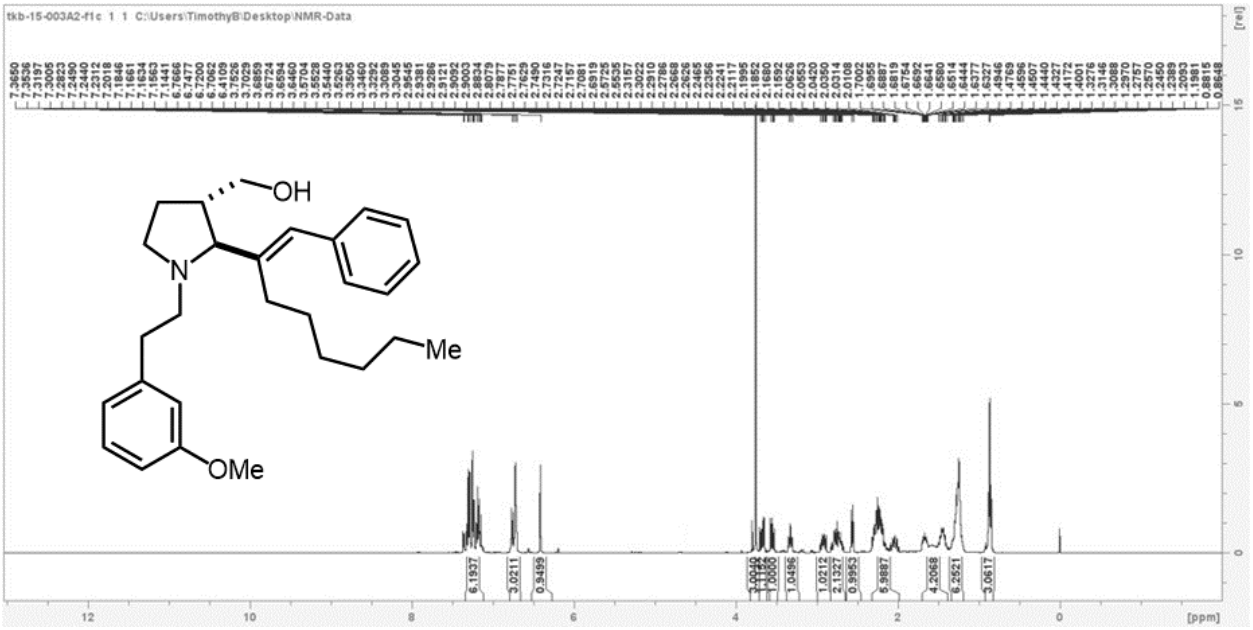
OMe
N
Me



Compound 6l

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellow oil. Yield = 708.3 mg, 84%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.09 (m, 6H), 6.76 (dt, *J* = 7.5, 1.2 Hz, 1H), 6.71 (qd, *J* = 4.1, 1.9 Hz, 2H), 6.41 (s, 1H), 3.75 (s, 3H), 3.73 – 3.62 (m, 1H), 3.55 (dd, *J* = 10.6, 7.0 Hz, 1H), 3.33 (td, *J* = 8.4, 2.2 Hz, 1H), 2.92 (ddd, *J* = 11.7, 10.1, 6.6 Hz, 1H), 2.84 – 2.65 (m, 2H), 2.56 (d, *J* = 7.6 Hz, 1H), 2.34 – 2.09 (m, 5H), 2.04 (dtd, *J* = 12.5, 9.6, 7.9 Hz, 1H), 1.67 (dddd, *J* = 14.8, 7.6, 4.6, 2.1 Hz, 1H), 1.52 – 1.37 (m, 1H), 1.37 – 1.16 (m, 6H), 0.87 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 144.0, 142.4, 137.9, 129.2, 128.6, 128.2, 128.0, 126.3, 121.2, 114.6, 111.2, 65.4, 56.1, 55.1, 52.4, 45.8, 35.4, 31.5, 29.9, 29.2, 28.5, 26.6, 22.6, 14.1. **HRMS-EI^{+}** (*m/z*): calc for $C_{28}H_{39}NO_2$ $[M]^{+}$ 421.2981, found 421.2987.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OMe
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1.0212
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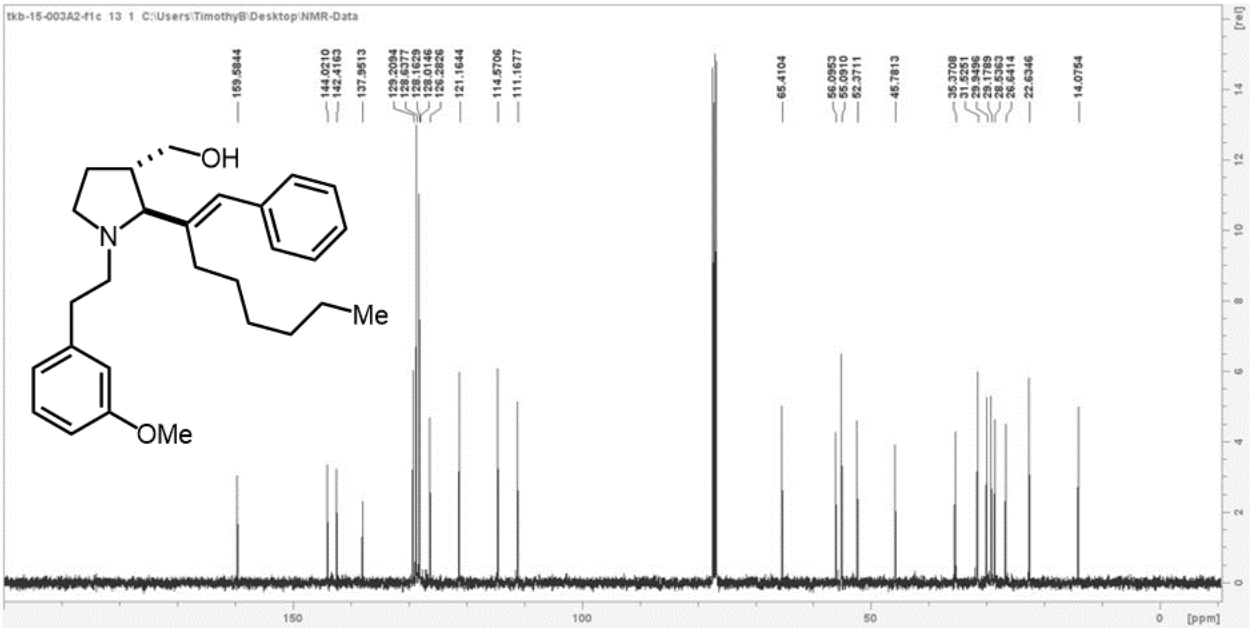
6.2521
3.0617
12
10
8
6
4
2
0
[ppm]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OMe
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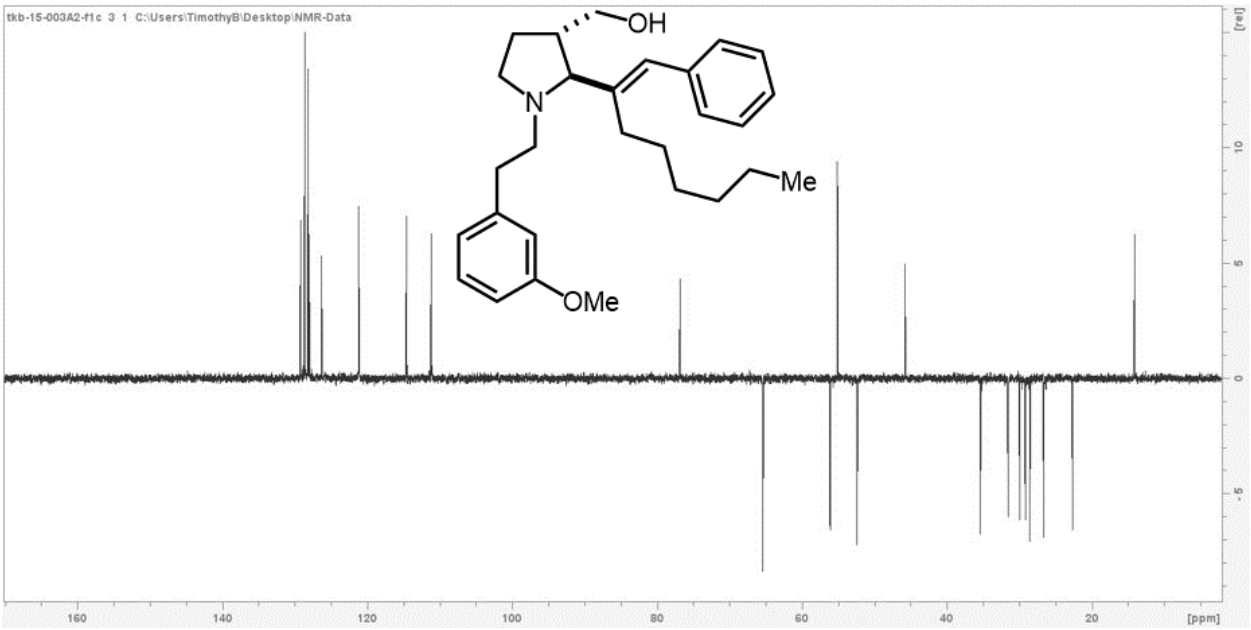
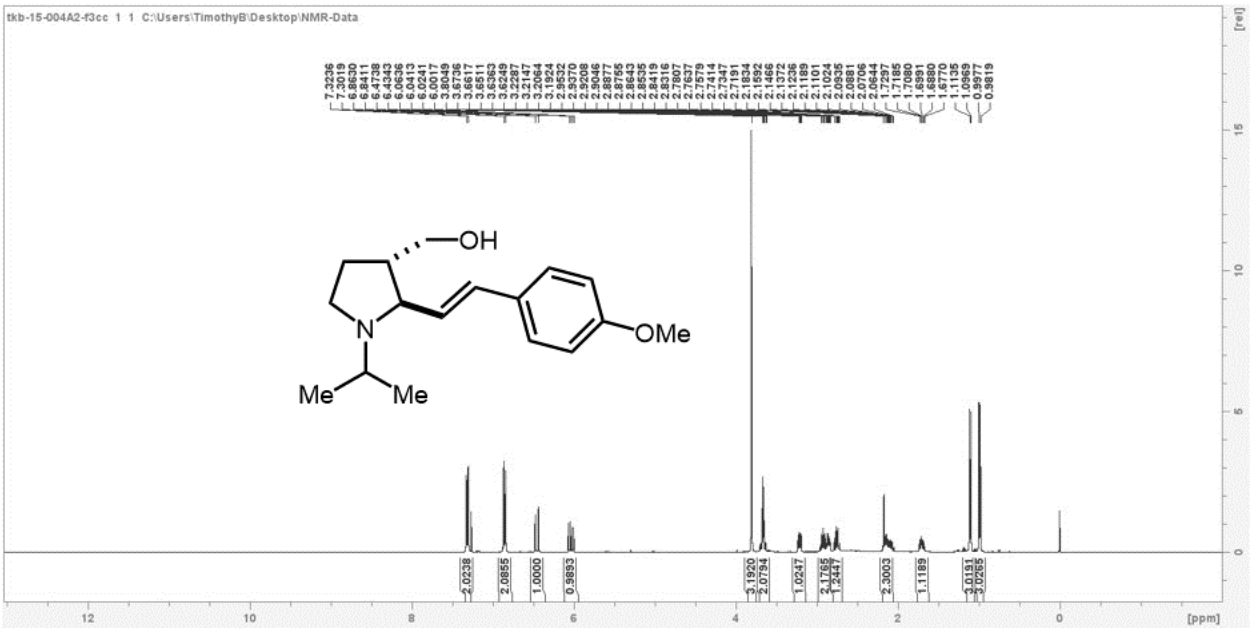
50
0
[ppm]



Compound 6m

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Greenish-yellow oil. Yield = 484.7 mg, 88%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.8 Hz, 2H), 6.85 (d, *J* = 15.8 Hz, 2H), 6.45 (d, *J* = 15.8 Hz, 1H), 6.03 (dd, *J* = 15.8, 8.9 Hz, 1H), 3.81 (s, 3H), 3.72 – 3.60 (m, 2H), 3.21 (dd, *J* = 8.9, 5.5 Hz, 1H), 2.99 – 2.81 (m, 2H), 2.75 (td, *J* = 9.0, 6.4 Hz, 1H), 2.22 – 2.02 (m, 2H), 1.70 (ddd, *J* = 12.5, 8.9, 4.6 Hz, 1H), 1.11 (d, *J* = 6.6 Hz, 3H), 0.99 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 131.2, 129.7, 128.4, 127.5, 114.0, 67.1, 65.8, 55.3, 48.6, 46.3, 45.6, 26.0, 22.3, 16.4. **HRMS-EI$^+$** (*m/z*): calc for $C_{17}H_{25}NO_2$ $[M]^+$ 275.1885, found 275.1888.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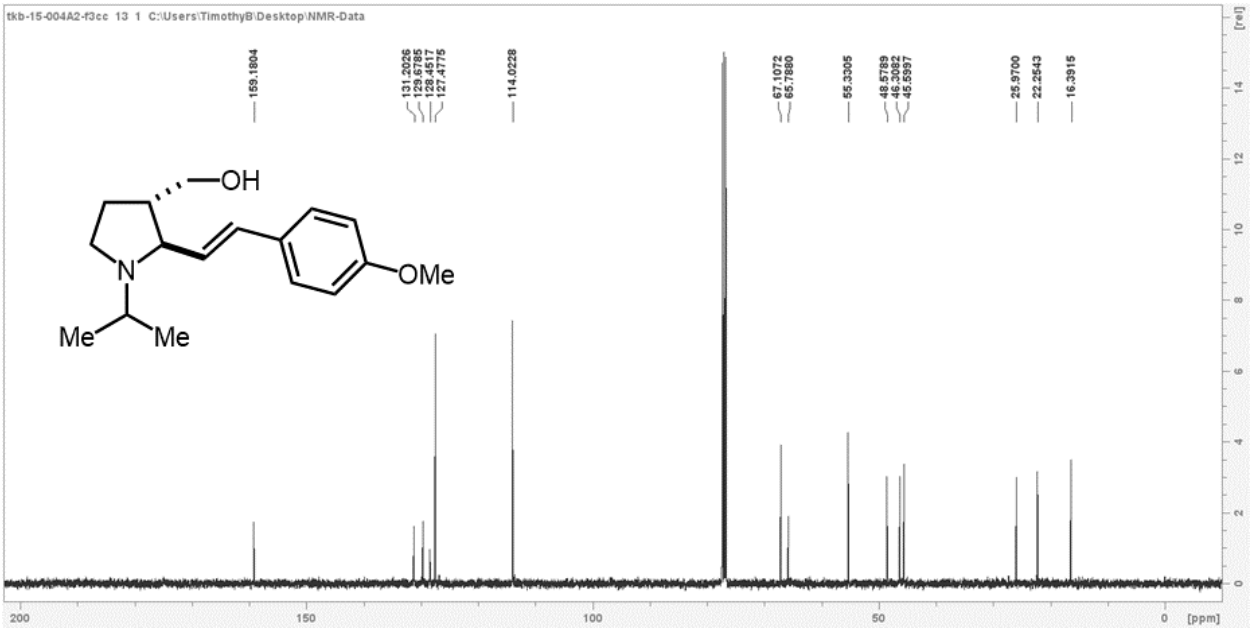
N
OMe
Me
Me
[ppm]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Me
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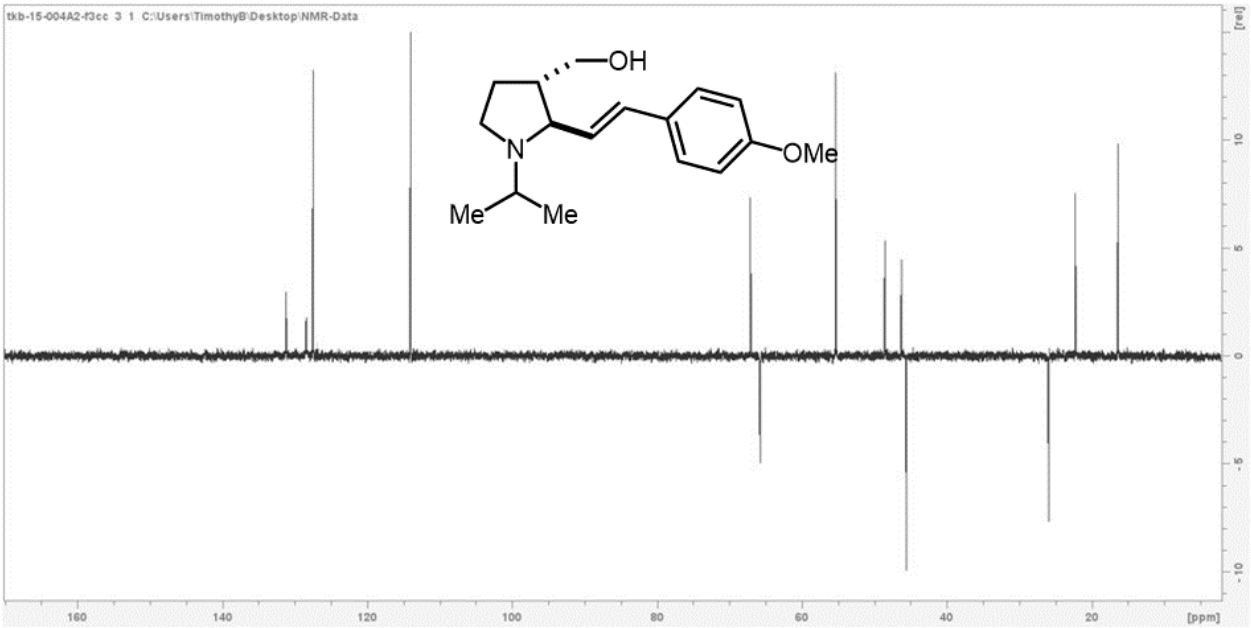
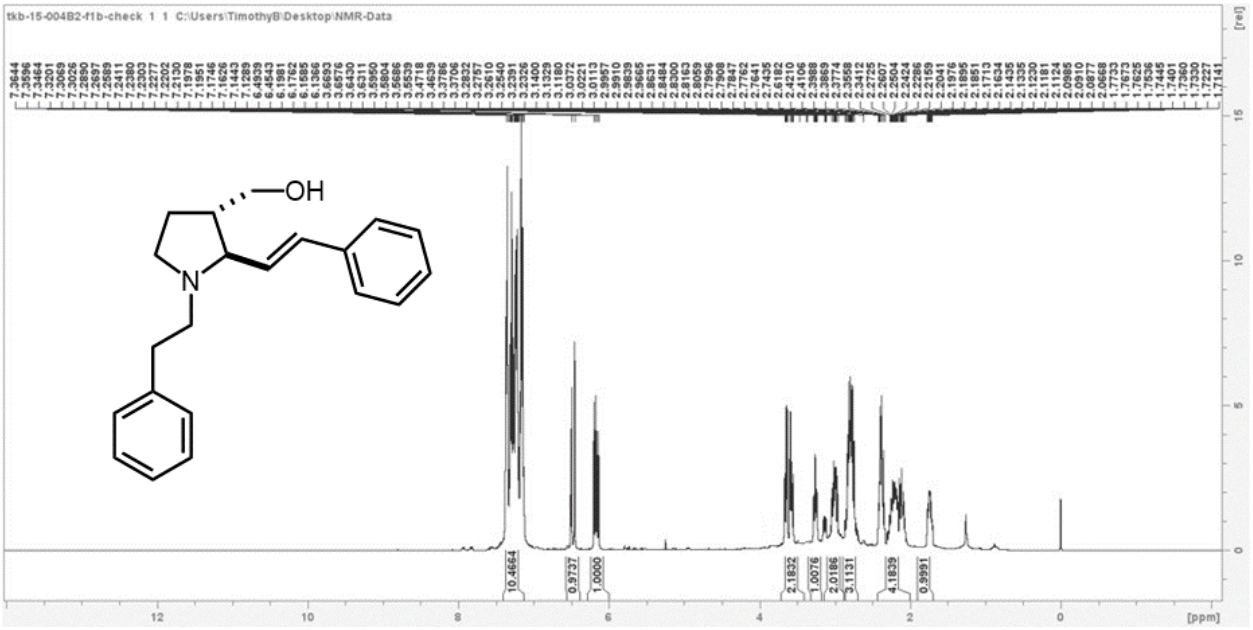


Compound 6n

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Greenish-yellow oil. Yield = 510.3 mg, 83%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.13 (m, 10H), 6.50 (d, *J* = 15.8 Hz, 1H), 6.17 (dd, *J* = 15.8, 8.8 Hz, 1H), 3.65 (dd, *J* = 10.6, 4.7 Hz, 1H), 3.57 (dd, *J* = 10.6, 5.8 Hz, 1H), 3.51 – 3.31 (m, 1H), 3.26 (td, *J* = 8.7, 3.0 Hz, 1H), 3.18 – 2.90 (m, 2H), 2.89 – 2.66 (m, 3H), 2.44 – 2.03 (m, 4H), 1.80 – 1.68 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.3, 136.7, 132.9, 128.7, 128.6, 128.4, 127.7, 126.5, 126.1, 71.3, 64.6, 64.5, 55.8, 52.6, 46.7, 35.1, 26.2. **HRMS-EI^{+}** (*m/z*): calc for $C_{21}H_{25}NO$ $[M]^{+}$ 307.1936, found 307.1942.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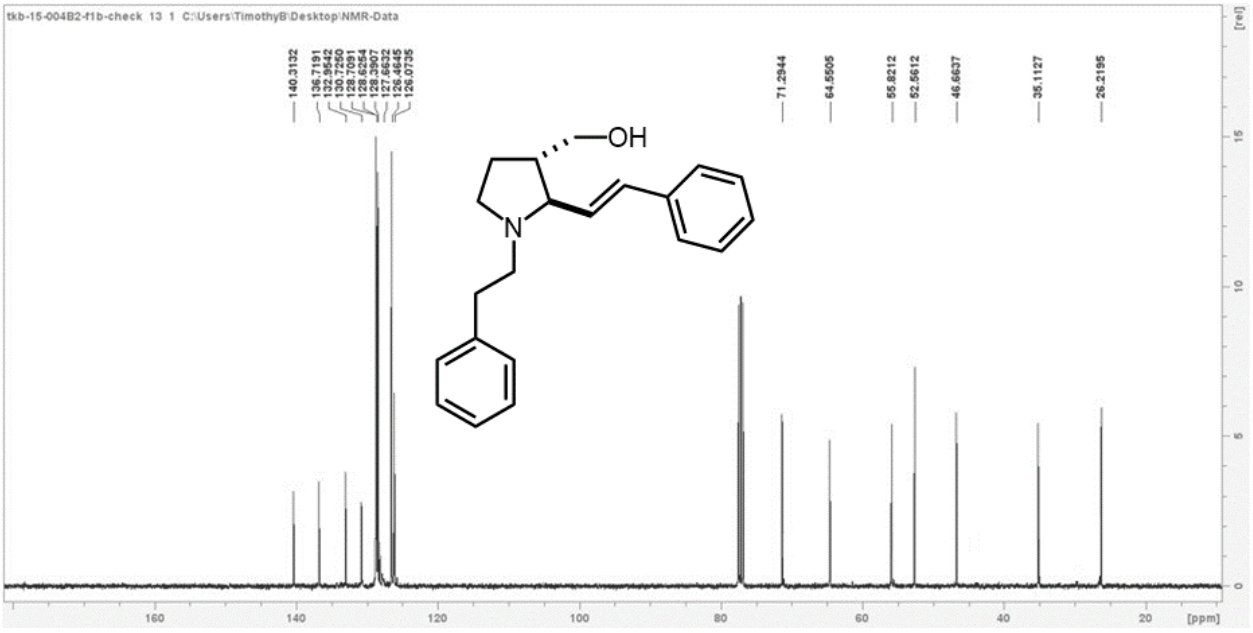
[ppm]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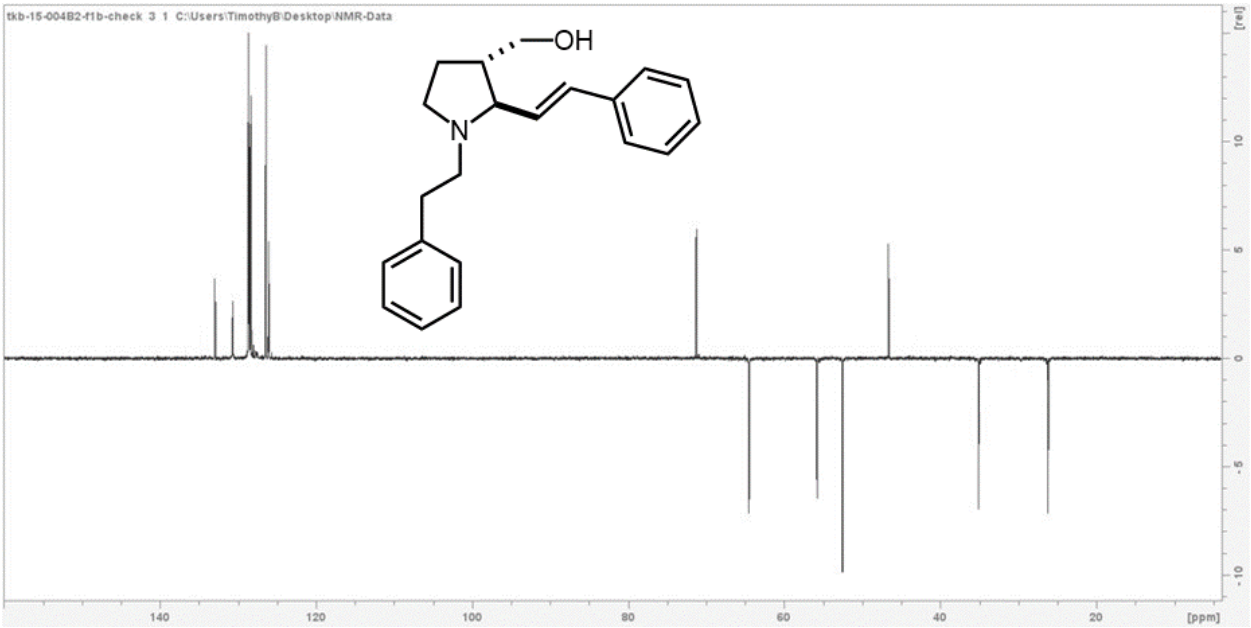
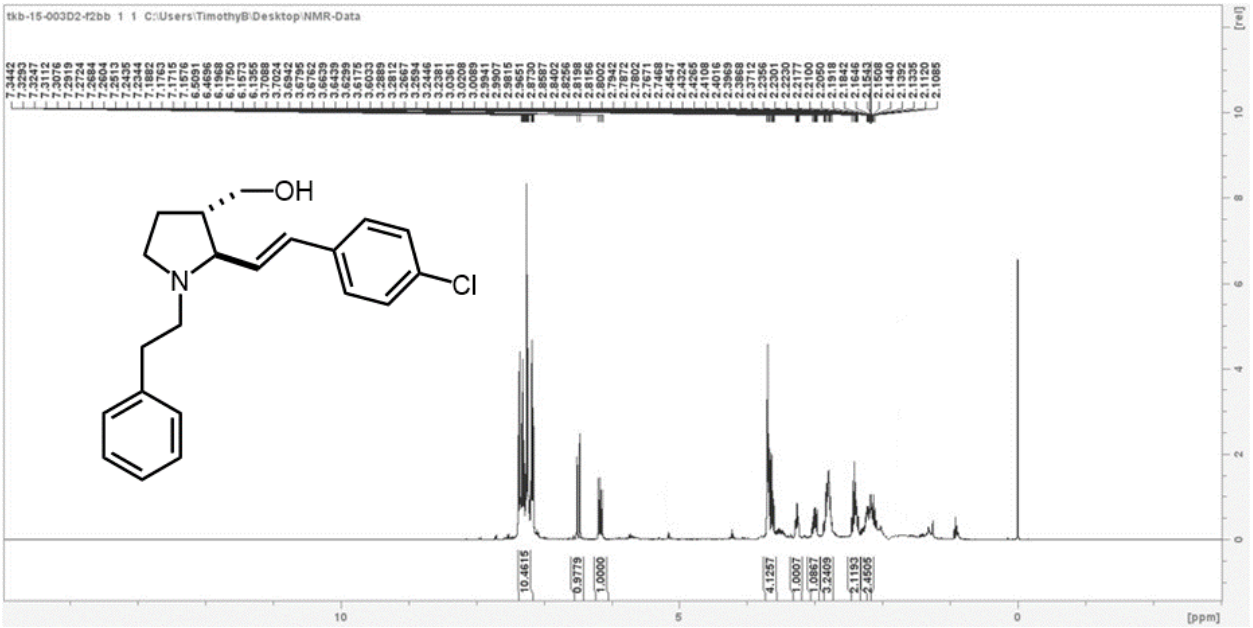
[ppm]



Compound 6o

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 540.2 mg, 79%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.11 (m, 9H), 6.49 (d, *J* = 15.8 Hz, 1H), 6.17 (dd, *J* = 15.8, 8.8 Hz, 1H), 3.90 – 3.80 (m, 1H), 3.74 – 3.62 (m, 3H), 3.65 – 3.49 (m, 1H), 3.26 (td, *J* = 8.8, 3.1 Hz, 1H), 3.00 (ddd, *J* = 11.7, 10.3, 6.4 Hz, 1H), 2.90 – 2.70 (m, 4H), 2.39 – 2.19 (m, 2H), 2.21 – 2.07 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.3, 136.7, 132.9, 128.7, 128.6, 128.3, 127.6, 126.4, 126.0, 71.3, 62.8, 55.7, 52.5, 46.6, 29.9, 26.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{24}ClNO$ $[M]^+$ 341.1546, found 341.1542.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0
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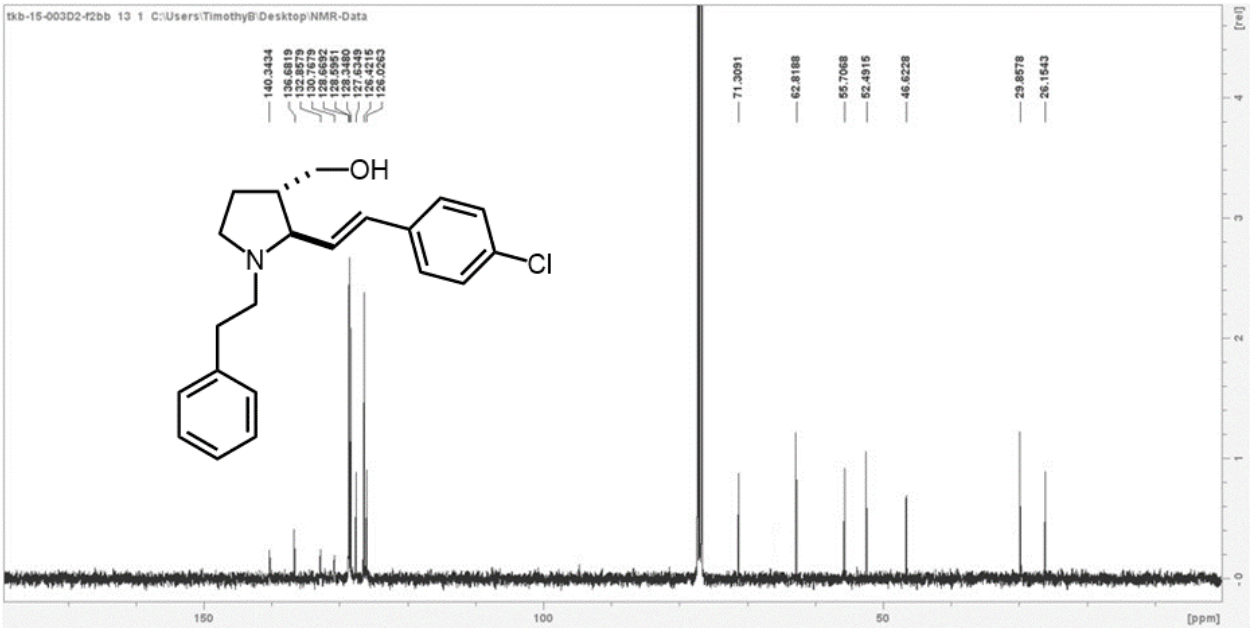
[rel]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N
Cl
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50
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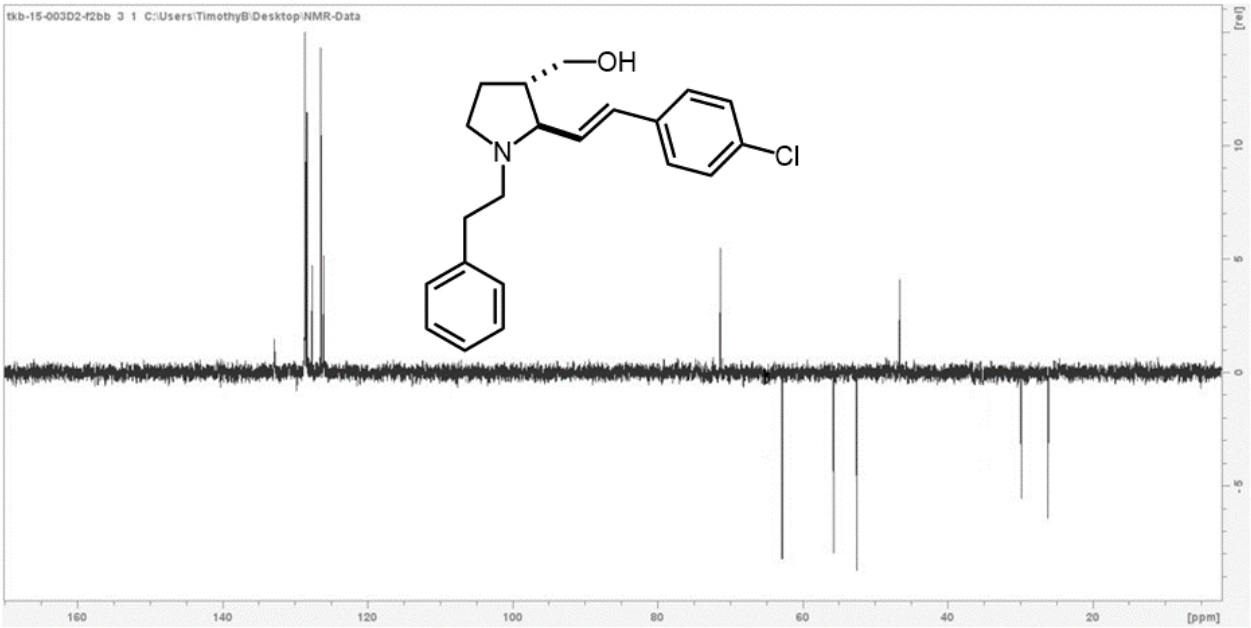
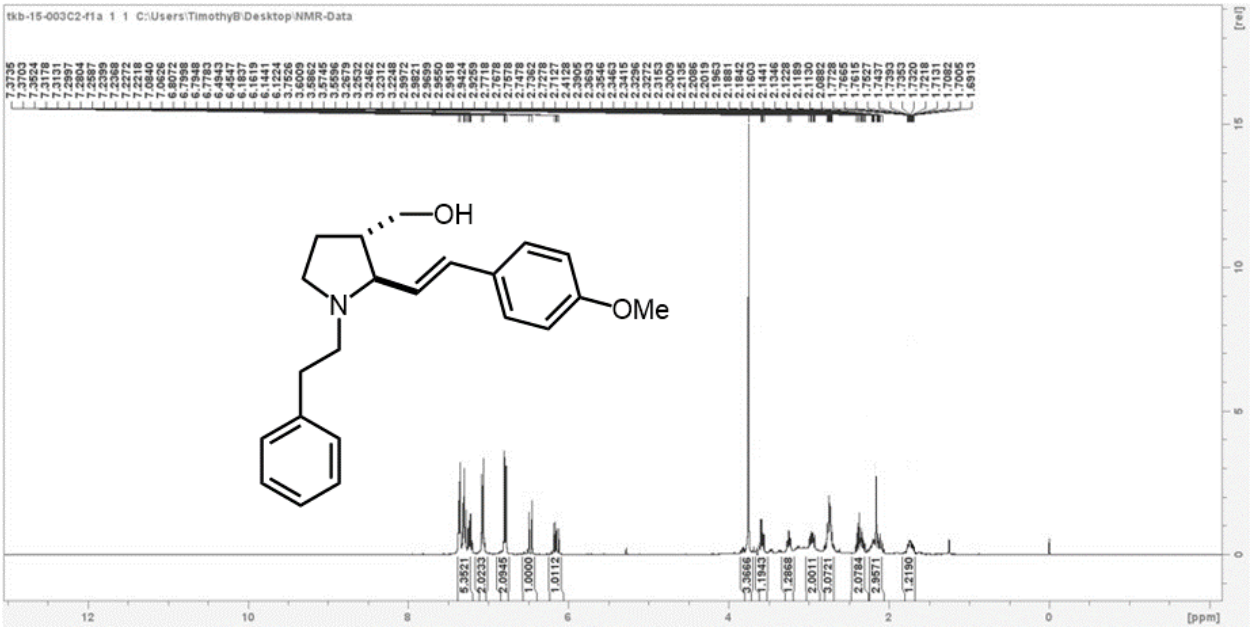


Compound 6p

Prepared in 2.0 mmol scale using **General Procedures A** and **B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellow oil. Yield = 580.4 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.22 (m, 5H), 7.13 – 7.01 (m, 2H), 6.85 – 6.75 (m, 2H), 6.47 (d, *J* = 15.8 Hz, 1H), 6.15 (dd, *J* = 15.8, 8.7 Hz, 1H), 3.75 (s, 3H), 3.58 (dd, *J* = 10.6, 5.9 Hz, 1H), 3.25 (td, *J* = 8.7, 2.9 Hz, 1H), 3.18 (s, 3H), 2.96 (ddd, *J* = 11.8, 10.3, 6.2 Hz, 1H), 2.83 – 2.64 (m, 3H), 2.44 – 2.29 (m, 2H), 2.29 – 2.04 (m, 2H), 1.65 (d, *J* = 2.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9, 136.7, 132.4, 130.7, 129.6, 128.6, 127.6, 126.43, 113.8, 71.3, 64.6, 56.1, 55.2, 52.6, 46.6, 34.2, 26.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{22}H_{27}NO_2$ $[M]^+$ 337.2042, found 337.2047.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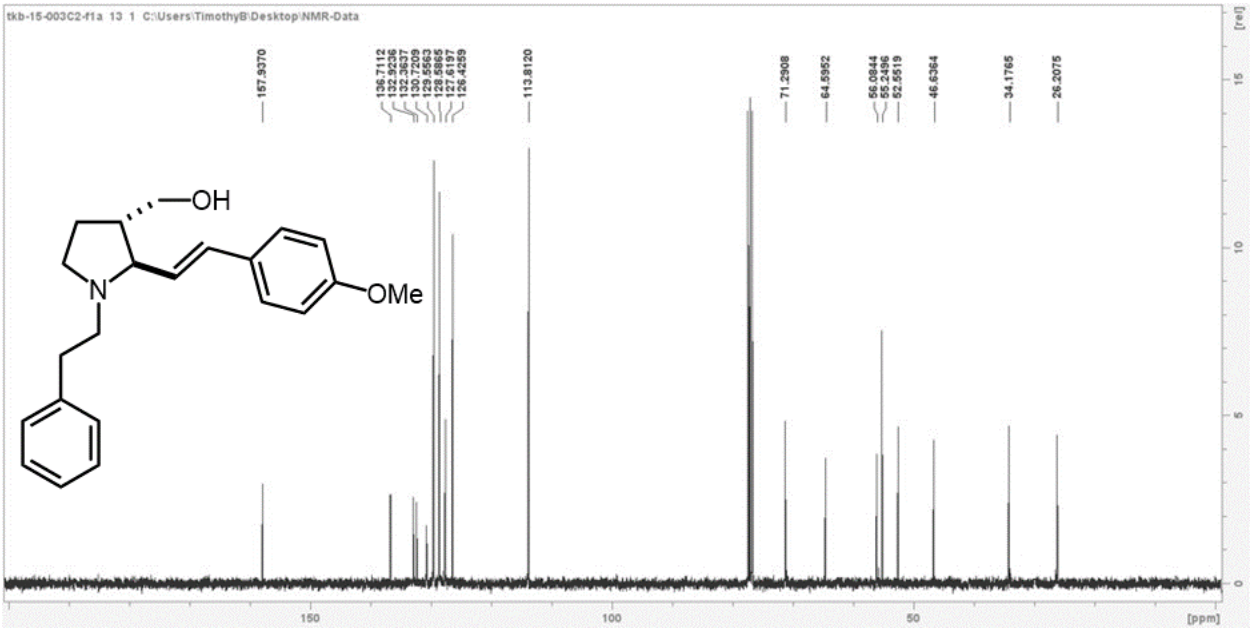
2.0784
2.9571
1.2190
[ppm]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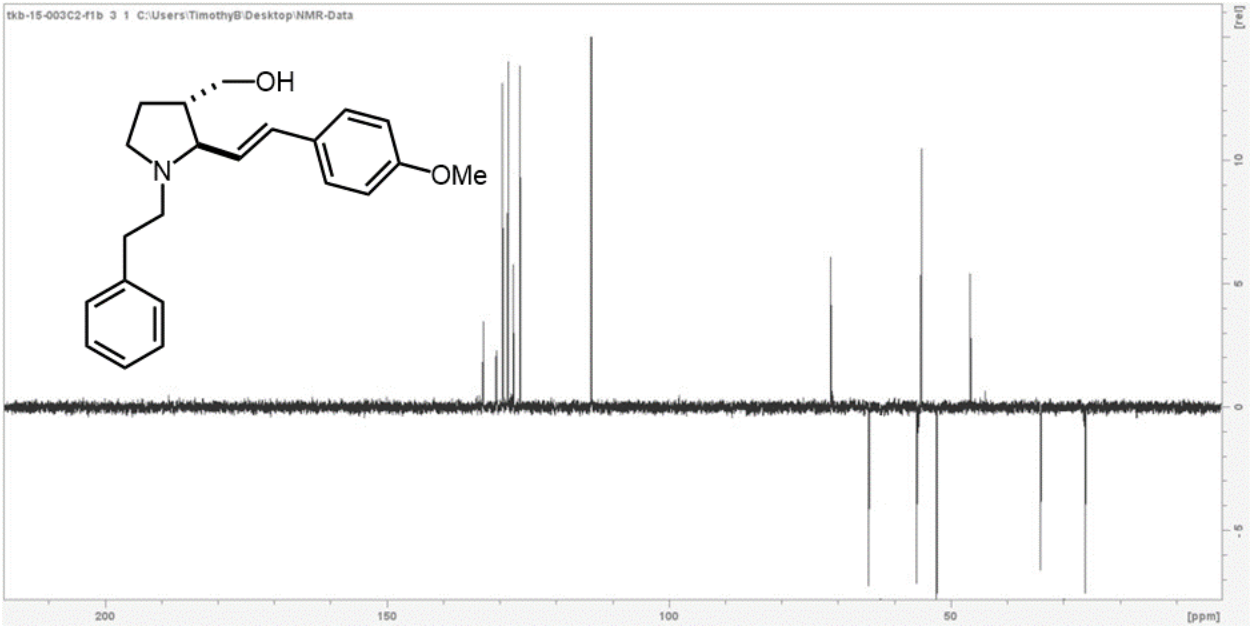
OMe
[ppm]


tkb-15-003C2-f1b 3 1 C:\Users\TimothyB\Desktop\NMR-Data
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OMe
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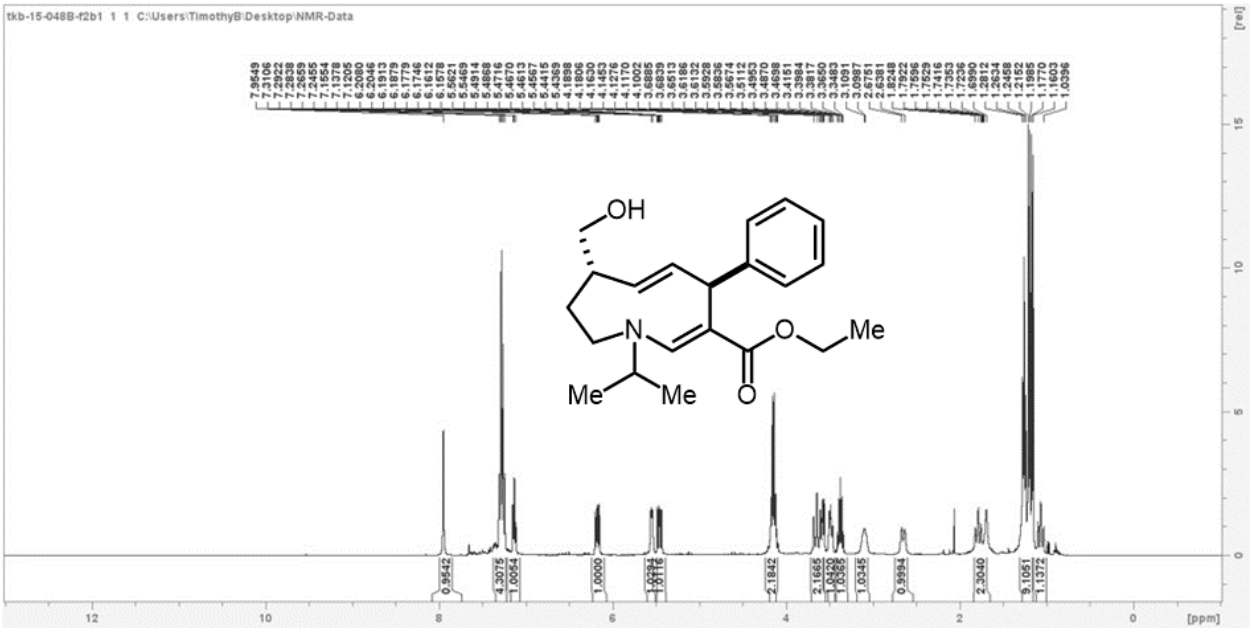
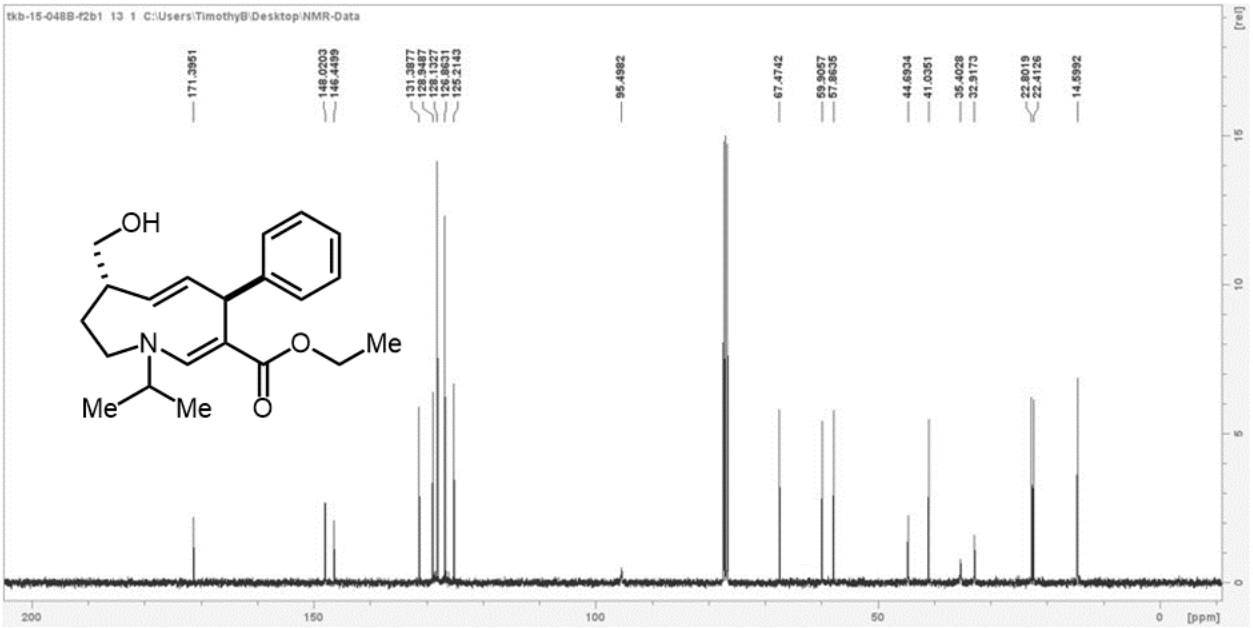
150
100
50
[ppm]

Scheme 2 Results: Ring expansion of allylic pyrrolidine methanols

Compound 8a

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 309.1 mg, 90%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.41 – 7.21 (m, 4H), 7.14 (ddt, *J* = 9.1, 7.4, 1.7 Hz, 1H), 6.18 (dd, *J* = 12.1, 6.7 Hz, 1H), 5.55 (d, *J* = 6.7 Hz, 1H), 5.46 (dd, *J* = 12.1, 7.9 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.73 – 3.54 (m, 2H), 3.49 (dd, *J* = 10.3, 6.5 Hz, 1H), 3.38 (hept, *J* = 6.7 Hz, 1H), 3.17 – 3.06 (m, 1H), 2.66 (d, *J* = 15.4 Hz, 1H), 1.88 – 1.64 (m, 2H), 1.28 – 1.21 (m, 1H), 1.13 – 1.02 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 148.0, 146.4, 131.4, 128.9, 128.1, 126.9, 125.2, 95.5, 67.5, 59.9, 57.9, 44.7, 41.0, 35.4, 32.9, 22.8, 22.4, 14.6. **HRMS-EI^{+}** (*m/z*): calc for $C_{21}H_{29}NO_3$ $[M]^+$ 343.2147, found 343.2152.

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57.8635
44.6934
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32.5173
22.8019
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Me
O
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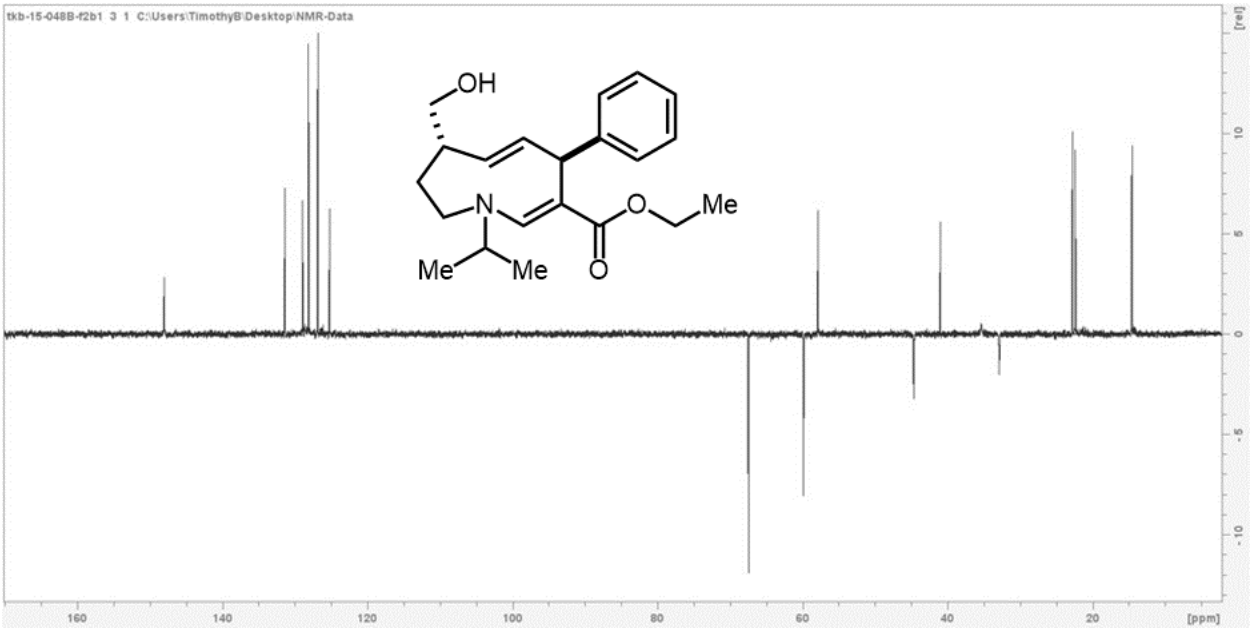
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Me
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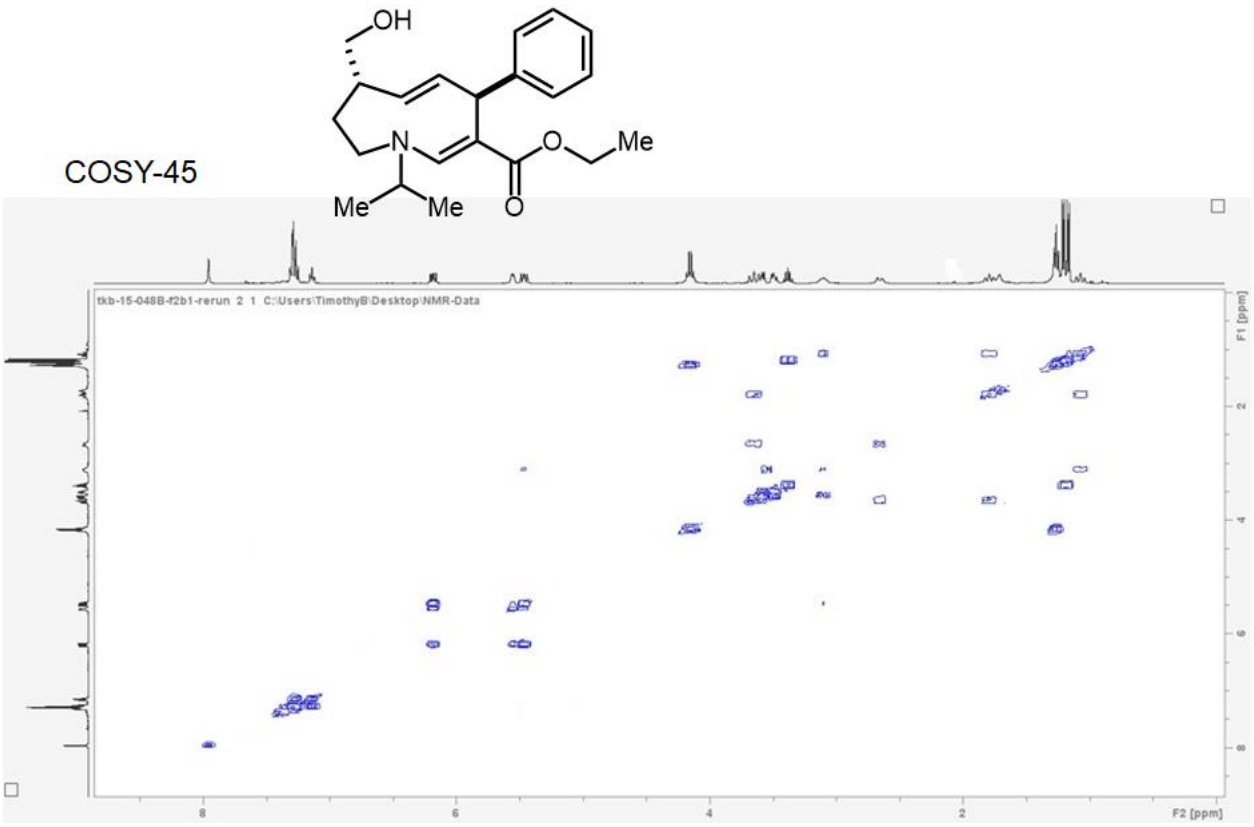
[ppm]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O
Me
Me
Me
O
COSY-45
tkb-15-048B-f2b1-rerun 2 1 C:\Users\TimothyB\Desktop\NMR-Data
F1 [ppm]
F2 [ppm]
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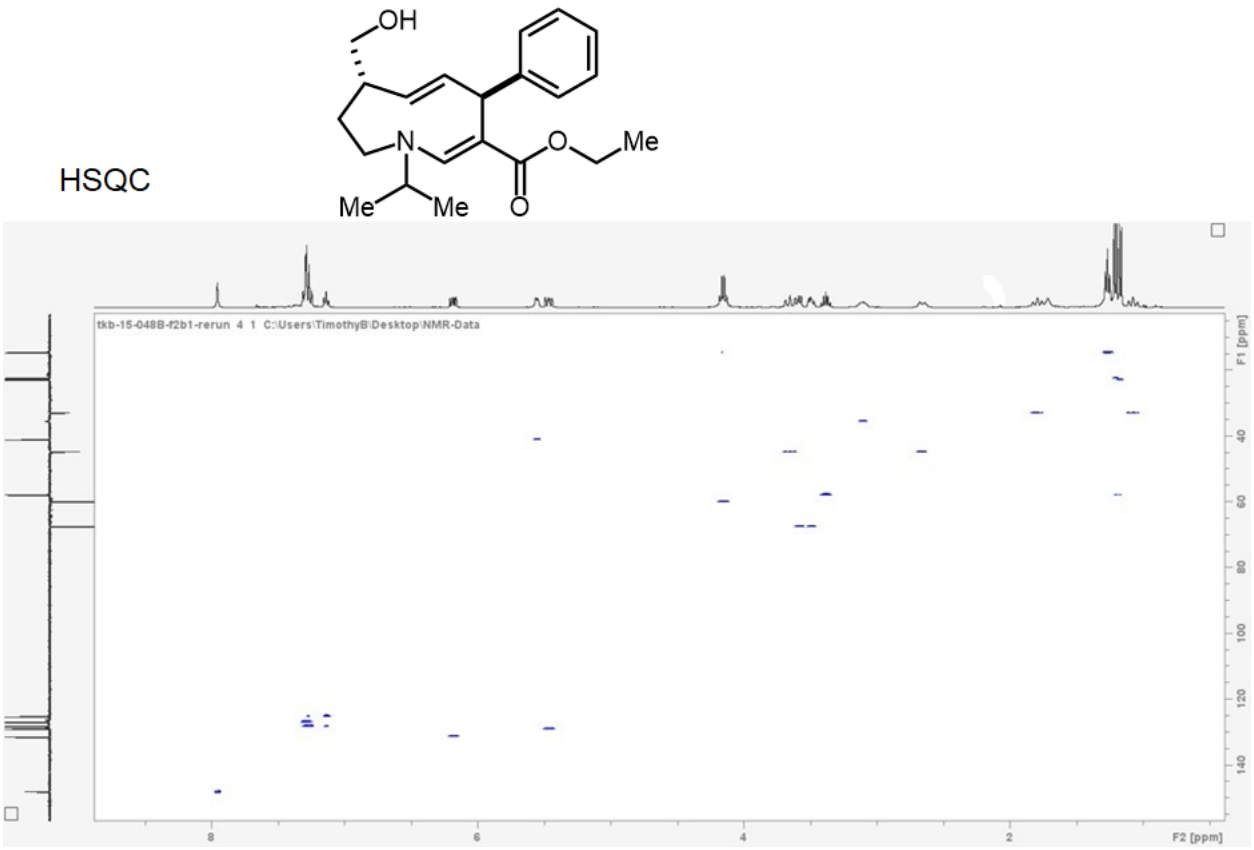
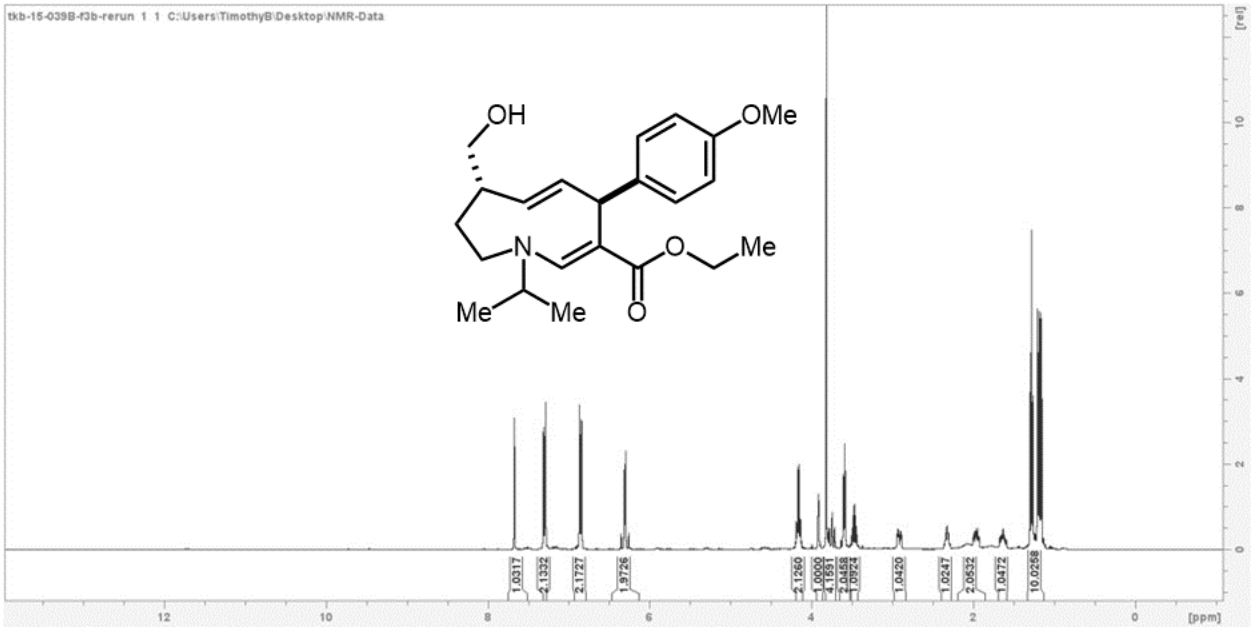
6
4
2



Compound 8b

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 60:40). Greenish-yellow oil. Yield = 351.1 mg, 94%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.30 (d, *J* = 7.1 Hz, 2H), 6.84 (d, *J* = 7.1 Hz, 2H), 6.35 – 6.25 (m, 2H), 4.15 (qd, *J* = 7.1, 1.1 Hz, 2H), 3.93 – 3.87 (m, 1H), 3.81 (s, 3H), 3.73 (ddd, *J* = 14.1, 11.8, 2.2 Hz, 1H), 3.58 (dd, *J* = 7.1, 2.1 Hz, 2H), 3.46 (hept, *J* = 6.6 Hz, 1H), 2.99 – 2.86 (m, 2H), 1.96 (dddd, *J* = 15.6, 7.9, 5.5, 2.2 Hz, 1H), 1.63 (dddd, *J* = 14.9, 11.8, 6.6, 3.1 Hz, 1H), 1.29 – 1.14 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 162.6, 158.6, 148.9, 134.7, 130.9, 128.1, 127.1, 113.9, 94.6, 66.7, 59.6, 58.0, 55.3, 44.0, 43.5, 38.9, 28.7, 21.4, 21.2, 14.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{22}H_{31}NO_4$ $[M]^{+}$ 373.2253, found 373.2257.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Me
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2.0458
1.0924
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10
8
6
4
2
0
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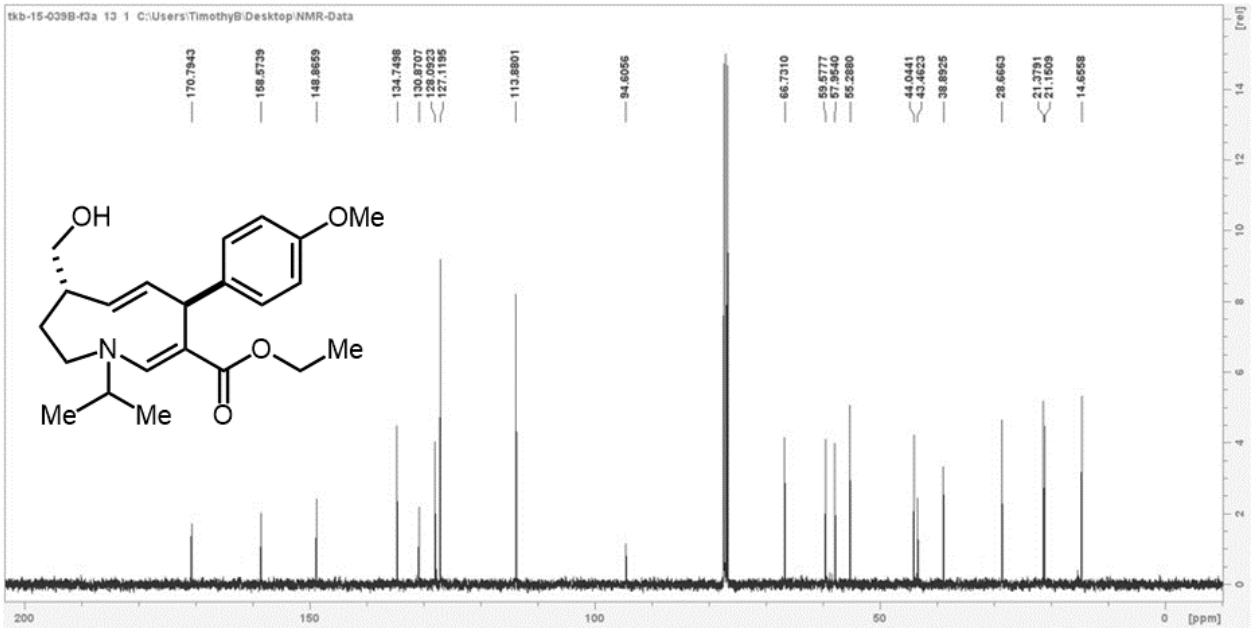
[rel]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66.7310
59.5777
57.9540
55.2880
44.0441
43.4623
38.8925
29.6663
21.3791
21.1509
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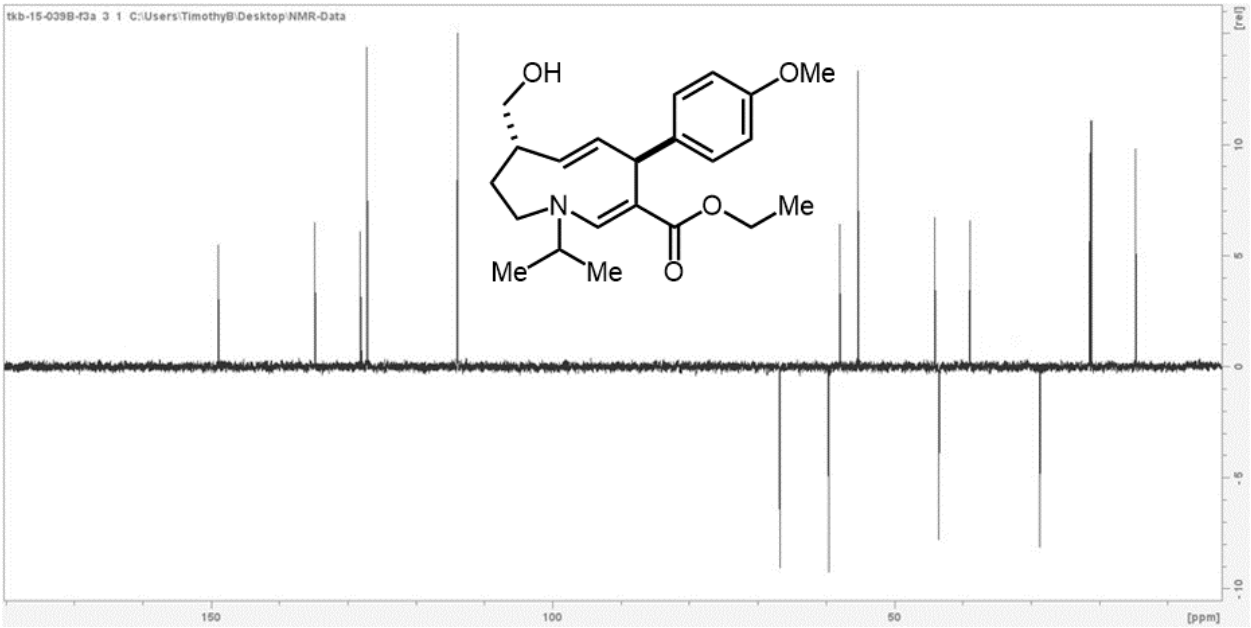
[rel]



Compound 8c

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 360.9 mg, 89%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.42 – 7.25 (m, 4H), 7.21 (ddt, *J* = 8.0, 4.9, 2.3 Hz, 4H), 6.97 – 6.90 (m, 2H), 6.17 (dd, *J* = 12.2, 6.4 Hz, 1H), 5.59 (d, *J* = 6.4 Hz, 1H), 5.46 (dd, *J* = 12.2, 8.1 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.67 (t, *J* = 13.8 Hz, 1H), 3.57 (dd, *J* = 10.3, 6.6 Hz, 1H), 3.47 (dq, *J* = 13.8, 6.4 Hz, 2H), 3.30 (dt, *J* = 13.8, 6.8 Hz, 1H), 3.12 (d, *J* = 12.0 Hz, 1H), 2.87 – 2.65 (m, 2H), 2.40 (d, *J* = 15.0 Hz, 1H), 1.78 (tt, *J* = 13.0, 3.1 Hz, 1H), 1.49 – 1.40 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.04 – 0.89 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.23, 150.85, 146.34, 138.21, 131.63, 128.97, 128.78, 128.57, 128.26, 127.16, 126.41, 125.37, 96.46, 67.52, 60.04, 59.03, 46.09, 40.93, 36.76, 35.15, 30.82, 14.63. **HRMS-EI^{+}** (*m/z*): calc for $C_{26}H_{31}NO_3$ $[M]^{+}$ 405.2304, found 405.2308.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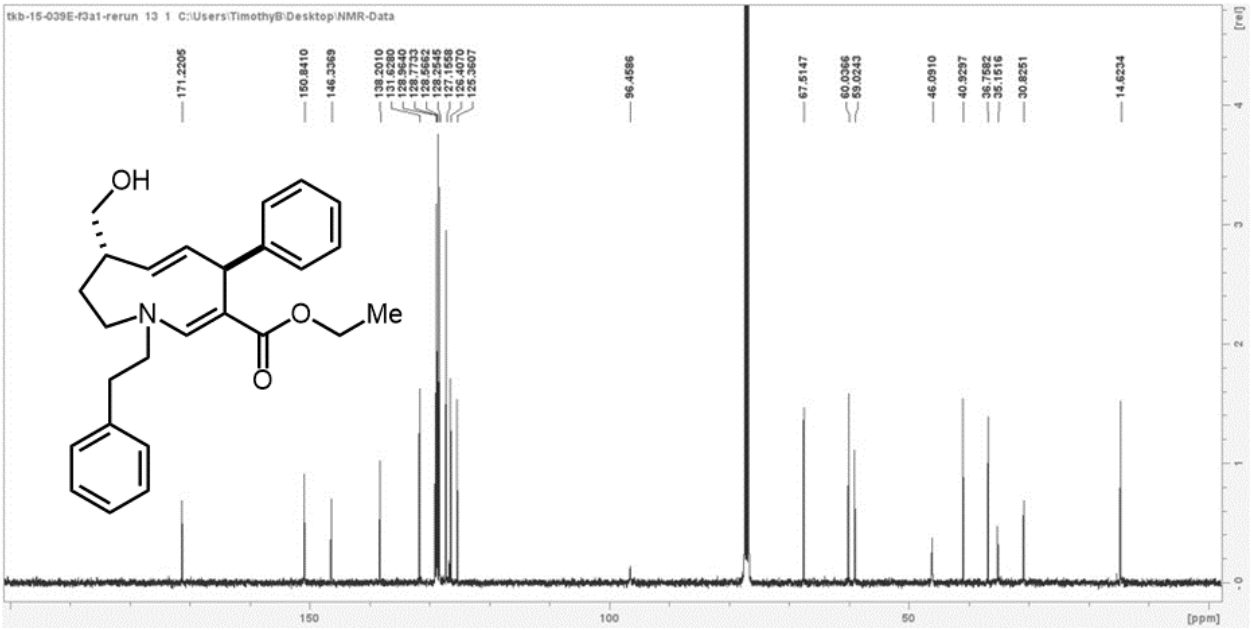
Me
O
[ppm]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128.2545
127.1558
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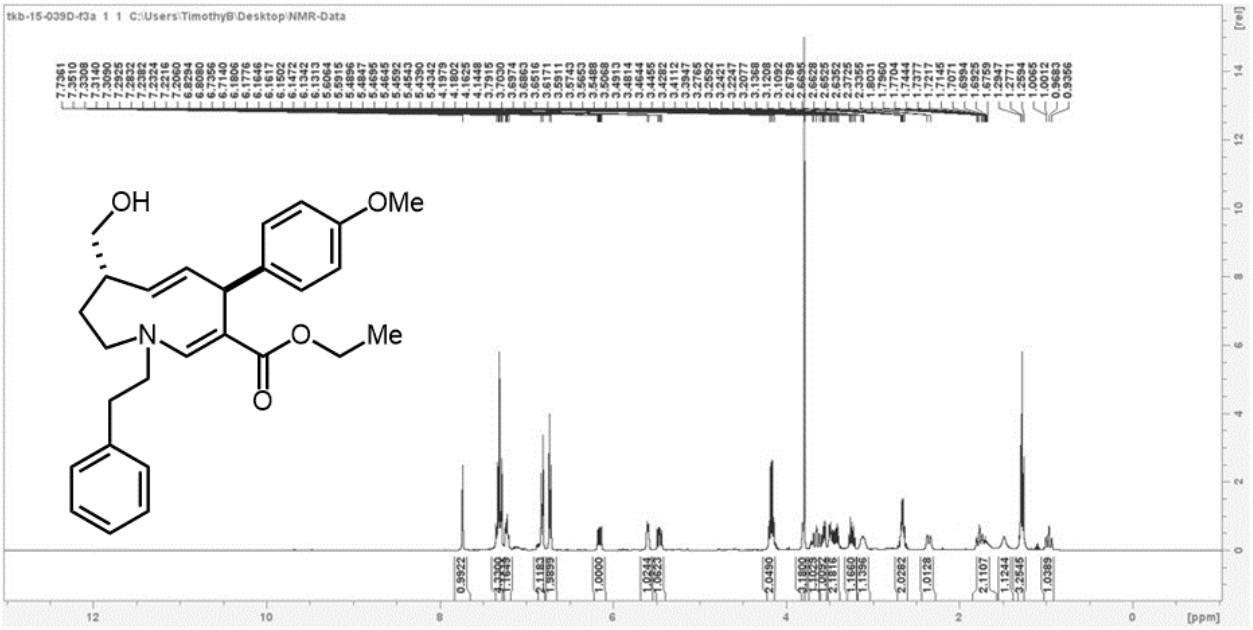
125.3607
96.4586
67.5147
60.0366
59.0243
46.0910
40.9297
36.7582
35.1616
30.8251
14.6234
OH
N
O
Me
O
150
100
50
[ppm]

Compound 8d

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Pale-yellow oil. Yield = 400.7 mg, 92%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.32 (h, *J* = 6.0 Hz, 4H), 7.22 (td, *J* = 6.9, 2.2 Hz, 1H), 6.82 (d, *J* = 7.2 Hz, 2H), 6.72 (d, *J* = 7.2 Hz, 2H), 6.16 (ddd, *J* = 12.2, 6.4, 1.5 Hz, 1H), 5.60 (d, *J* = 6.3 Hz, 1H), 5.46 (ddd, *J* = 12.2, 8.0, 2.0 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), 3.75 – 3.63 (m, 1H), 3.63 – 3.35 (m, 3H), 3.24 (dt, *J* = 13.8, 6.9 Hz, 1H), 3.12 (br s, 1H), 2.66 (td, *J* = 6.7, 4.0 Hz, 2H), 2.35 (d, *J* = 15.0 Hz, 1H), 1.80 – 1.68 (m, 2H), 1.30 (br. s, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.97 (tt, *J* = 13.2, 2.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.28, 158.13, 150.89, 146.46, 131.57, 130.22, 129.72, 129.03, 128.25, 127.21, 125.34, 113.96, 98.21, 67.52, 60.04, 59.21, 55.21, 46.14, 40.93, 35.89, 35.14, 30.81, 14.63. **HRMS-EI^{+}** (*m/z*): calc for $C_{27}H_{33}NO_4$ $[M]^{+}$ 435.2410, found 435.2414.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Me
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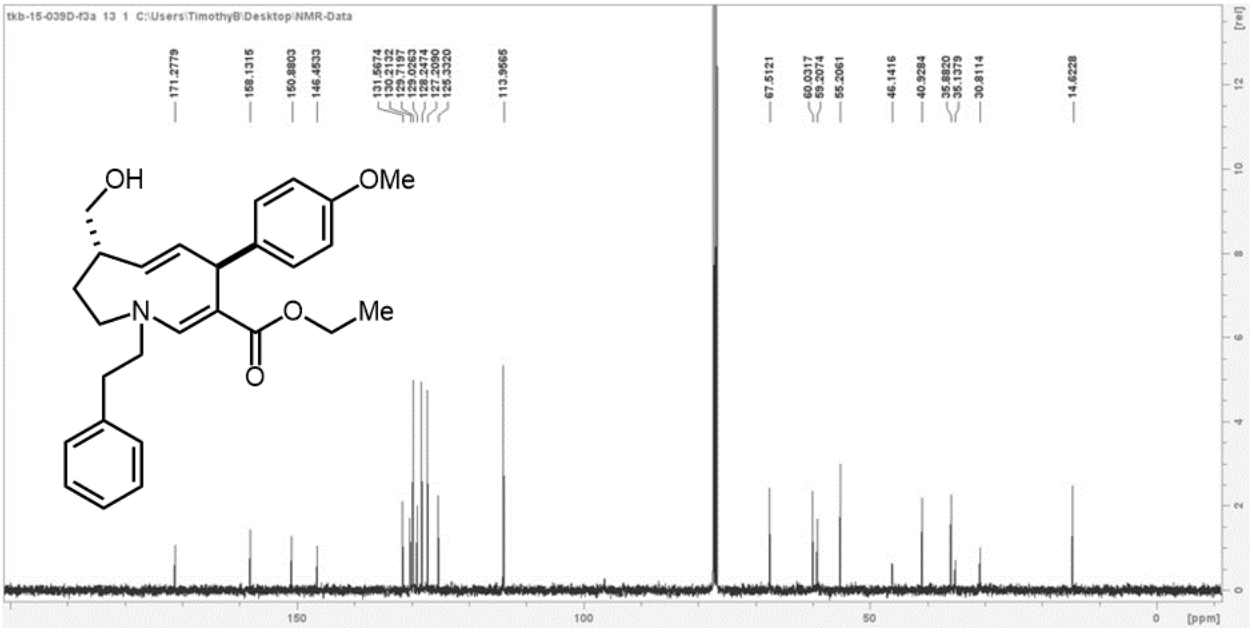
[ppm]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67.5121
60.0317
59.2074
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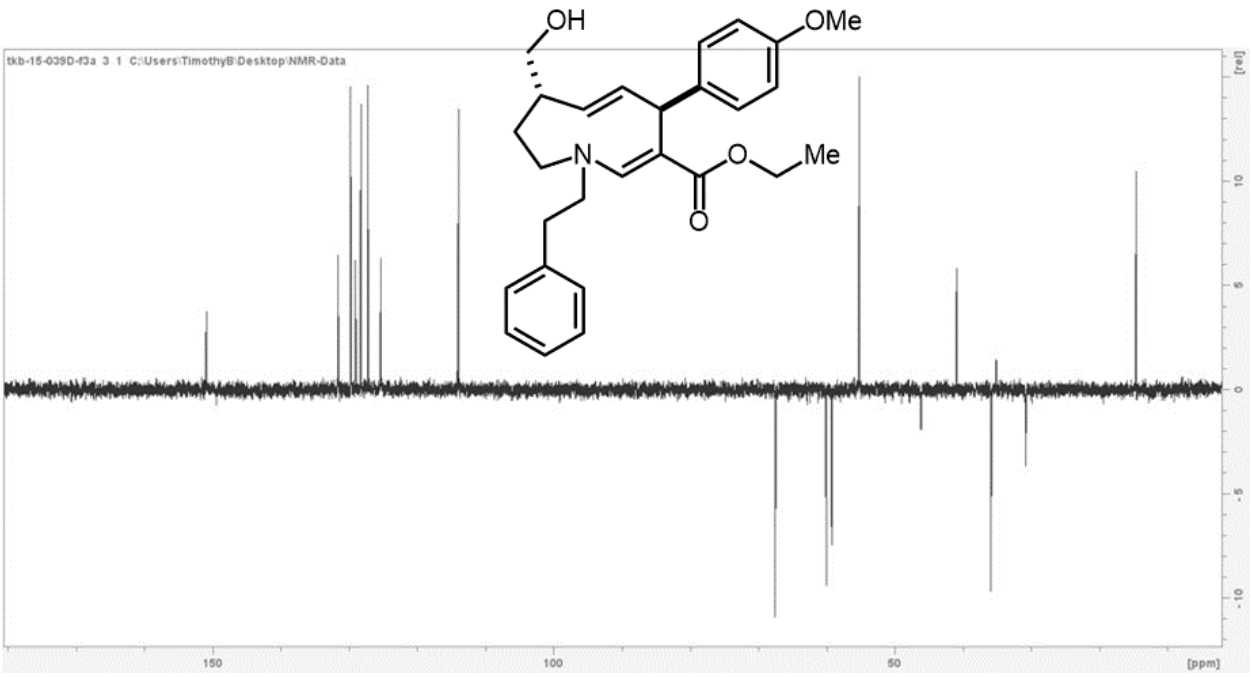
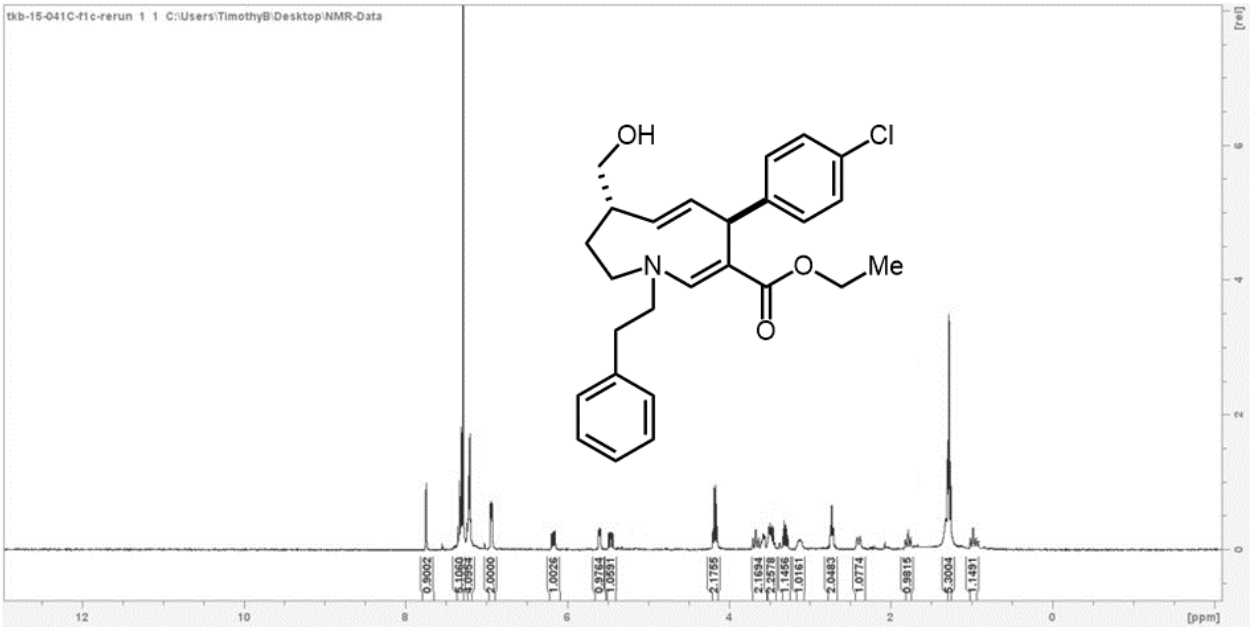


Compound 8e

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Amorphous solid. Yield = 378.4 mg, 86%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.37 – 7.28 (m, 5H), 7.26 – 7.16 (m, 2H), 6.93 (dd, *J* = 7.2, 2.3 Hz, 2H), 6.17 (ddd, *J* = 12.1, 6.4, 1.5 Hz, 1H), 5.60 (d, *J* = 6.4 Hz, 1H), 5.46 (ddd, *J* = 12.3, 8.0, 2.0 Hz, 1H), 4.22 – 4.12 (m, 2H), 3.66 (t, *J* = 13.8 Hz, 1H), 3.56 (d, *J* = 7.9 Hz, 1H), 3.47 (dt, *J* = 13.6, 6.9 Hz, 2H), 3.40 – 3.24 (m, 1H), 3.12 (br. s, 1H), 2.72 (td, *J* = 6.8, 2.6 Hz, 2H), 2.39 (d, *J* = 14.8 Hz, 1H), 1.78 (t, *J* = 13.1 Hz, 1H), 1.29 –1.22 (m, 5H), 1.03 – 0.86 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.22, 150.84, 146.34, 138.20, 131.66, 128.95, 128.78, 128.57, 128.26, 127.16, 126.41, 125.37, 67.53, 60.04, 59.03, 46.09, 40.93, 36.77, 30.82, 29.71, 14.63. **HRMS-EI^{+}** (*m/z*): calc for $C_{26}H_{30}ClNO_3$ $[M]^{+}$ 439.1914, found 439.1917.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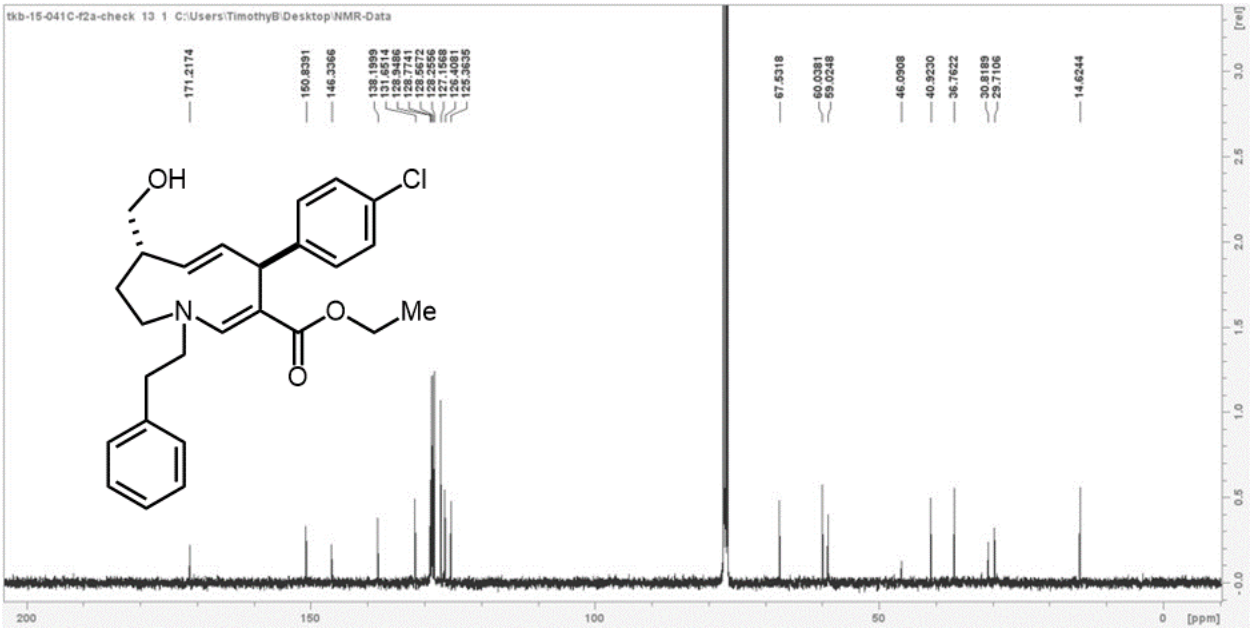
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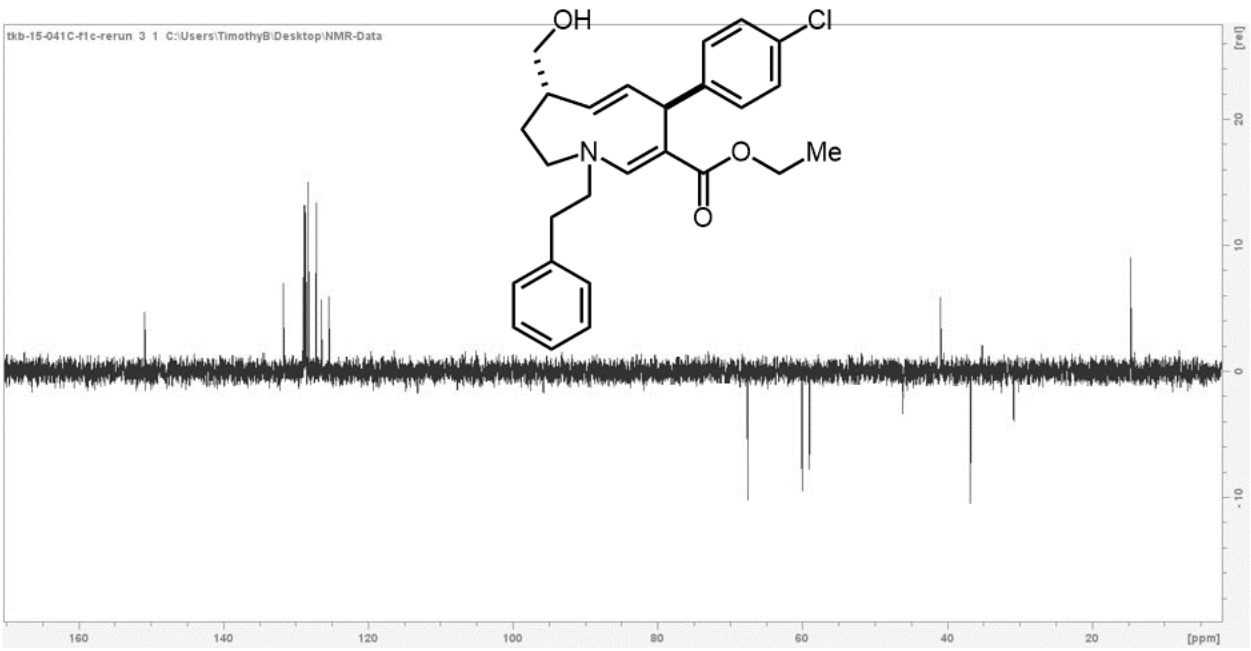
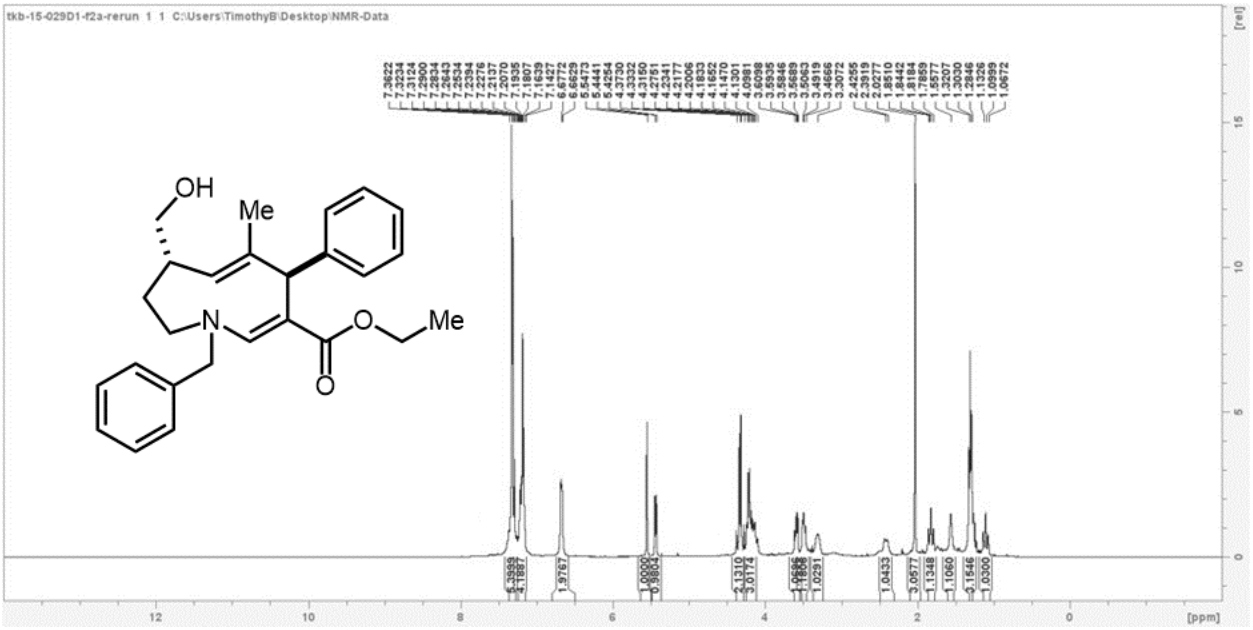


Compound 8f

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 373.1 mg, 92%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.14 (m, 9H), 6.68 – 6.66 (d, 2H), 5.55 (s, 1H), 5.43 (d, *J* = 7.5 Hz, 1H), 4.40 – 4.07 (m, 5H), 3.59 (dd, *J* = 10.3, 6.3 Hz, 1H), 3.49 (dd, *J* = 10.6, 6.3 Hz, 1H), 3.31 (br. s, 1H), 2.41 (d, *J* = 15.1 Hz, 1H), 2.03 (s, 3H), 1.82 (tt, *J* = 13.0, 3.2 Hz, 1H), 1.59 (br. s, 2H), 1.37 – 1.20 (m, 3H), 1.10 (tt, *J* = 13.1, 2.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.18, 151.78, 146.20, 137.38, 136.60, 128.57, 128.53, 128.42, 128.04, 127.28, 126.32, 125.19, 98.82, 68.09, 61.05, 60.08, 45.92, 35.81, 30.82, 27.83, 14.64, 12.55. **HRMS-EI^{+}** (*m/z*): calc for $C_{26}H_{31}NO_3$ $[M]^+$ 405.2304, found 405.2309.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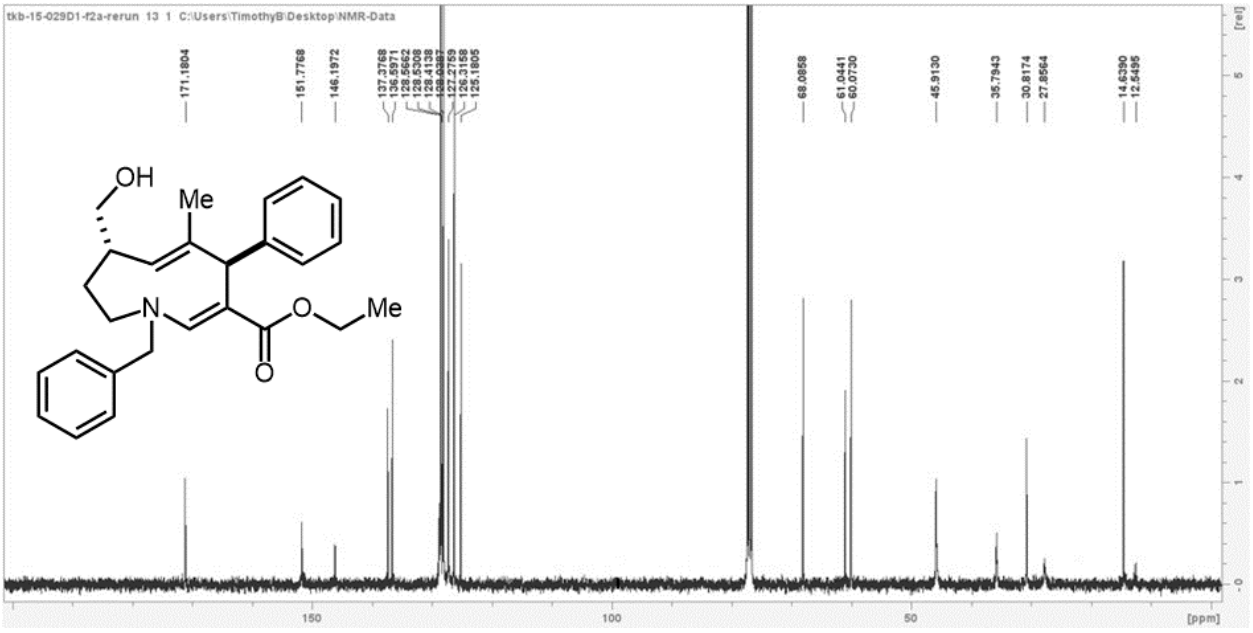
Me
N
O
Me
O
[ppm]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Me
O
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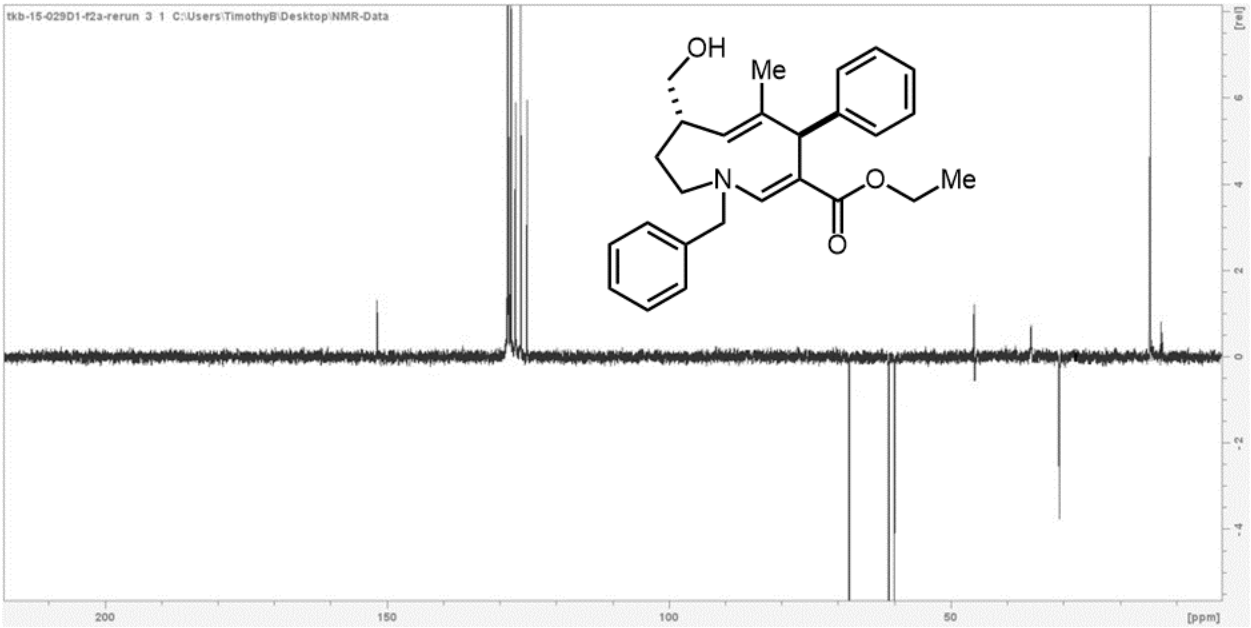
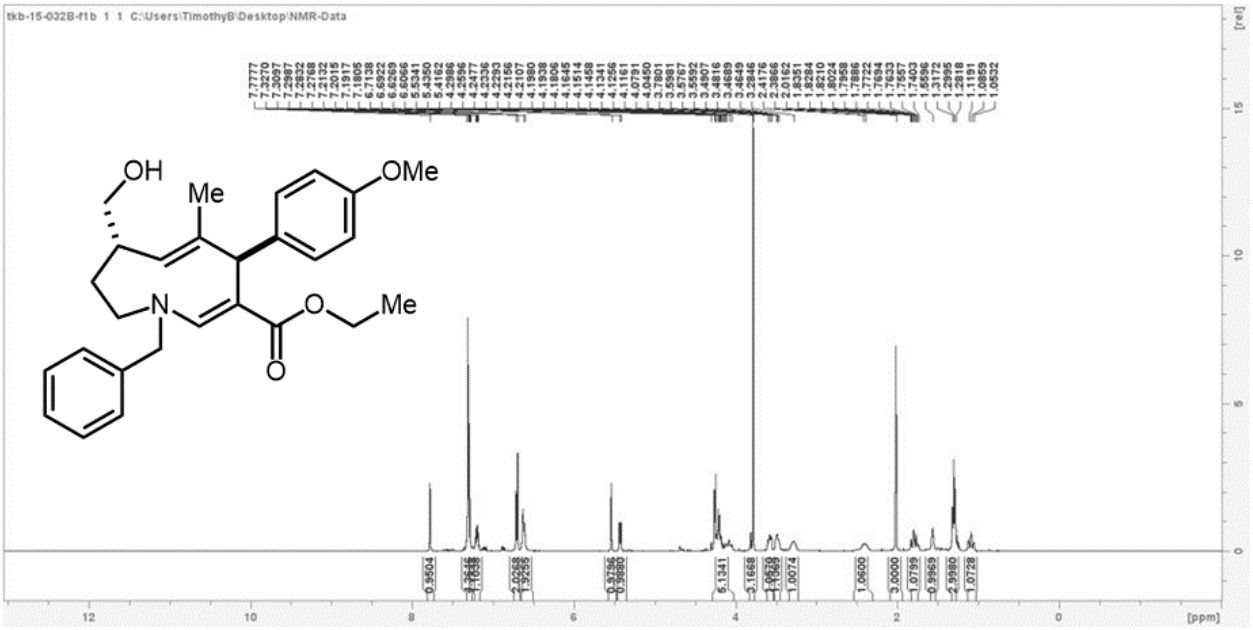


Compound 8g

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 60:40). Greenish-yellow oil. Yield = 413.8 mg, 95%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.30 (d, *J* = 4.4 Hz, 4H), 7.19 (ddd, *J* = 8.7, 5.1, 3.6 Hz, 1H), 6.74 – 6.66 (m, 2H), 6.62 (d, *J* = 8.3 Hz, 2H), 5.53 (s, 1H), 5.43 (dt, *J* = 7.7, 1.4 Hz, 1H), 4.32 – 4.12 (m, 5H), 3.78 (s, 3H), 3.58 (t, *J* = 8.9 Hz, 1H), 3.53 – 3.43 (m, 1H), 3.29 (d, *J* = 12.5 Hz, 1H), 2.40 (d, *J* = 14.6 Hz, 1H), 2.02 (s, 3H), 1.86 – 1.72 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.09 (tt, *J* = 13.0, 2.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.22, 158.89, 151.72, 146.22, 136.60, 129.29, 128.53, 128.41, 128.02, 127.66, 125.13, 113.91, 98.68, 68.09, 60.66, 60.05, 55.27, 45.93, 45.61, 35.83, 30.80, 14.64. **HRMS-EI^{+}** (*m/z*): calc for $C_{27}H_{33}NO_4$ $[M]^{+}$ 435.2410, found 435.2415.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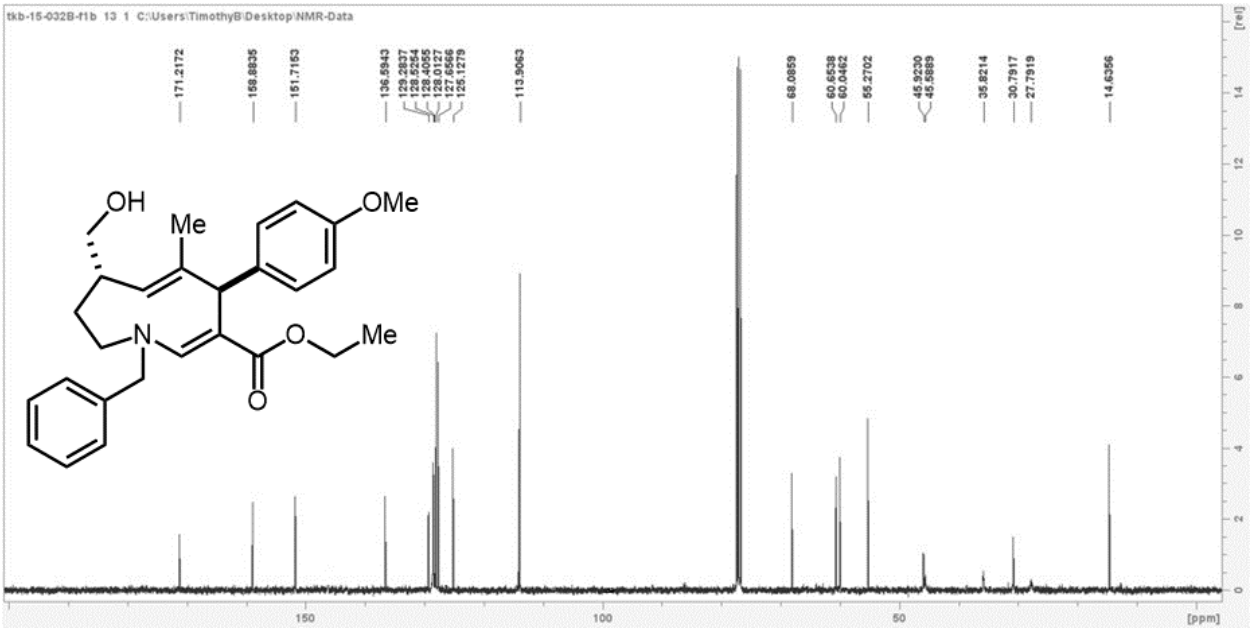
OMe
N
O
Me
O
[ppm]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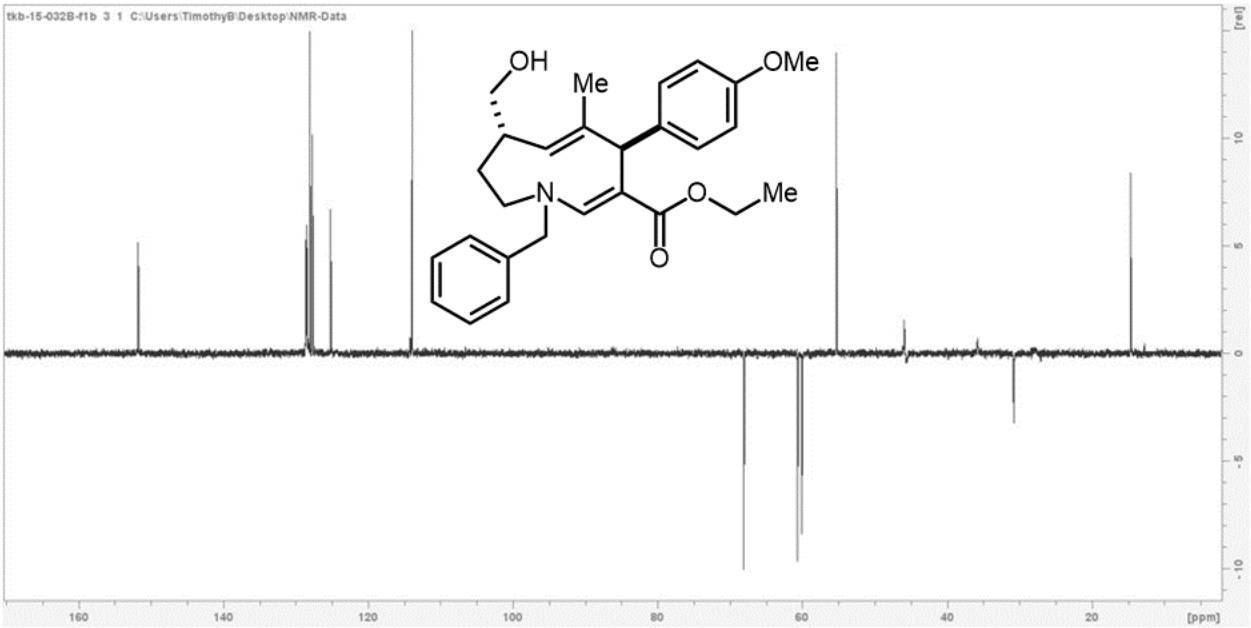

Compound 8h

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellow oil. Yield = 390.2 mg, 93%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.20 (m, 6H), 6.98 (d, *J* = 7.8 Hz, 2H), 6.57 (d, *J* = 7.8 Hz, 2H), 5.54 (s, 1H), 5.43 (d, *J* = 7.5 Hz, 1H), 4.35 – 4.05 (m, 5H), 3.58 (dd, *J* = 10.3, 6.3 Hz, 1H), 3.48 (dd, *J* = 10.4, 6.3 Hz, 1H), 3.34 – 3.25 (m, 1H), 2.44 – 2.34 (m, 1H), 2.30 (s, 3H), 2.02 (s, 3H), 1.81 (tt, *J* = 13.0, 3.2 Hz, 1H), 1.61 – 1.50 (m, 1H), 1.29 (t, *J* = 6.9 Hz, 3H), 1.15 – 0.96 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.23, 136.99, 136.63, 134.27, 129.20, 128.55, 128.41, 128.03, 127.95, 126.31, 125.16, 98.54, 68.10, 60.85, 60.04, 45.91, 35.80, 30.79, 27.86, 21.01, 14.65, 13.41. **HRMS-EI^{+}** (*m/z*): calc for $C_{27}H_{33}NO_3$ $[M]^{+}$ 419.2460, found 419.2466.


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Me
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0.9748
1.0524
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1.0618
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10
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6
4
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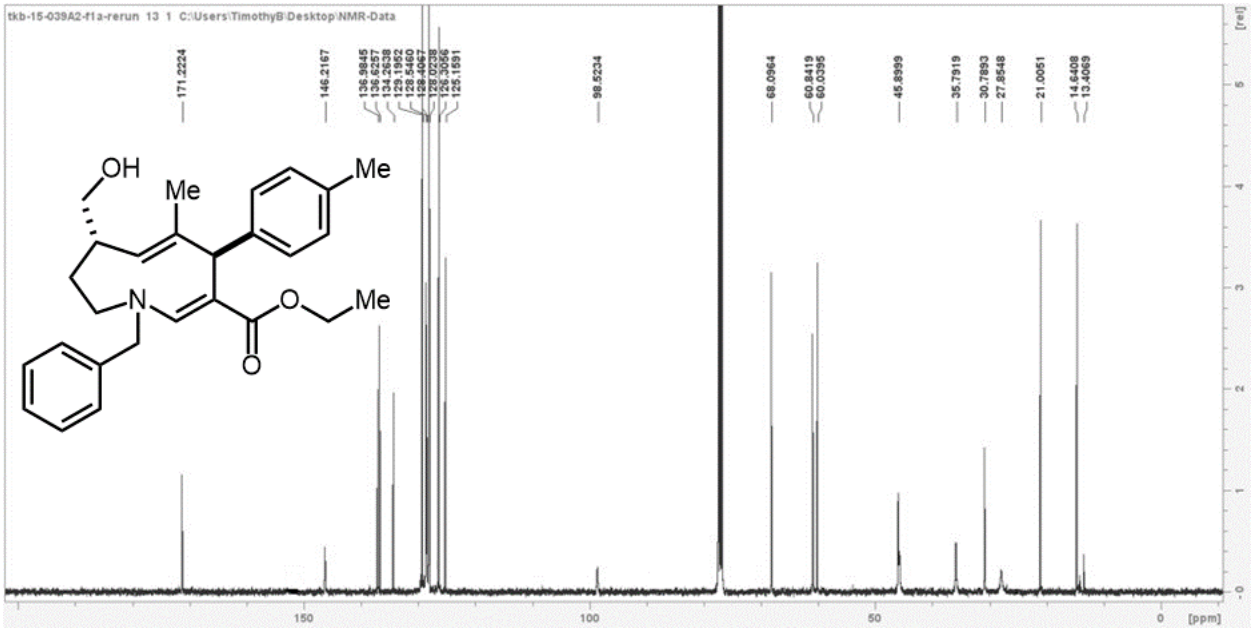
0
[ppm]


tkb-15-039A2-f1a-rerun 13 1 C:\Users\TimothyB\Desktop\NMR-Data
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68.0964
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60.0395
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35.7919
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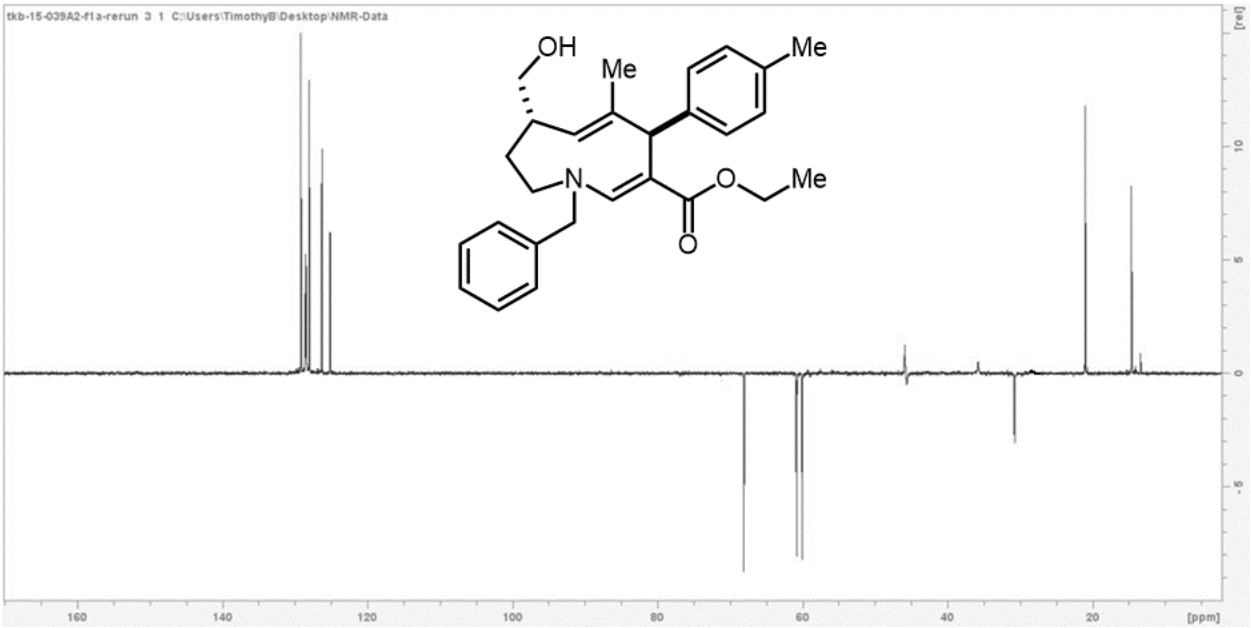
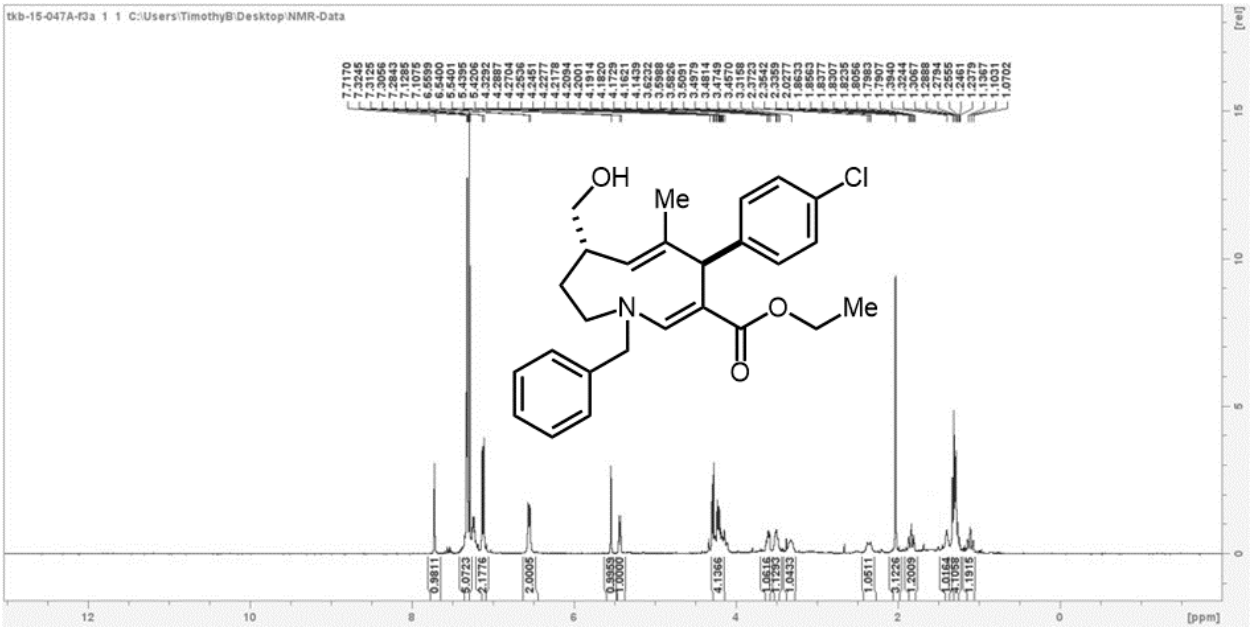


Compound 8i

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellow oil. Yield = 395.9 mg, 90%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.32 (q, *J* = 2.4 Hz, 4H), 7.28 – 7.20 (m, 1H), 7.24 – 7.05 (m, 2H), 6.55 (d, *J* = 8.0 Hz, 2H), 5.54 (s, 1H), 5.43 (d, *J* = 7.6 Hz, 1H), 4.35 – 4.14 (m, 4H), 3.62 – 3.58 (m, 1H), 3.50 (br s, 1H), 3.32 (br s, 1H), 2.35 (d, *J* = 15.2 Hz, 1H), 2.03 (s, 1H), 1.83 (tt, *J* = 13.0, 3.1 Hz, 1H), 1.35 – 1.21 (m, 5H), 1.13 – 1.04 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.01, 151.54, 146.09, 136.56, 135.92, 133.01, 128.66, 128.60, 128.37, 128.07, 127.61, 125.28, 68.09, 60.48, 60.17, 45.94, 35.84, 30.81, 29.71, 14.63. **HRMS-EI^{+}** (*m/z*): calc for $C_{26}H_{30}ClNO_3$ $[M]^{+}$ 439.1914, found 439.1917.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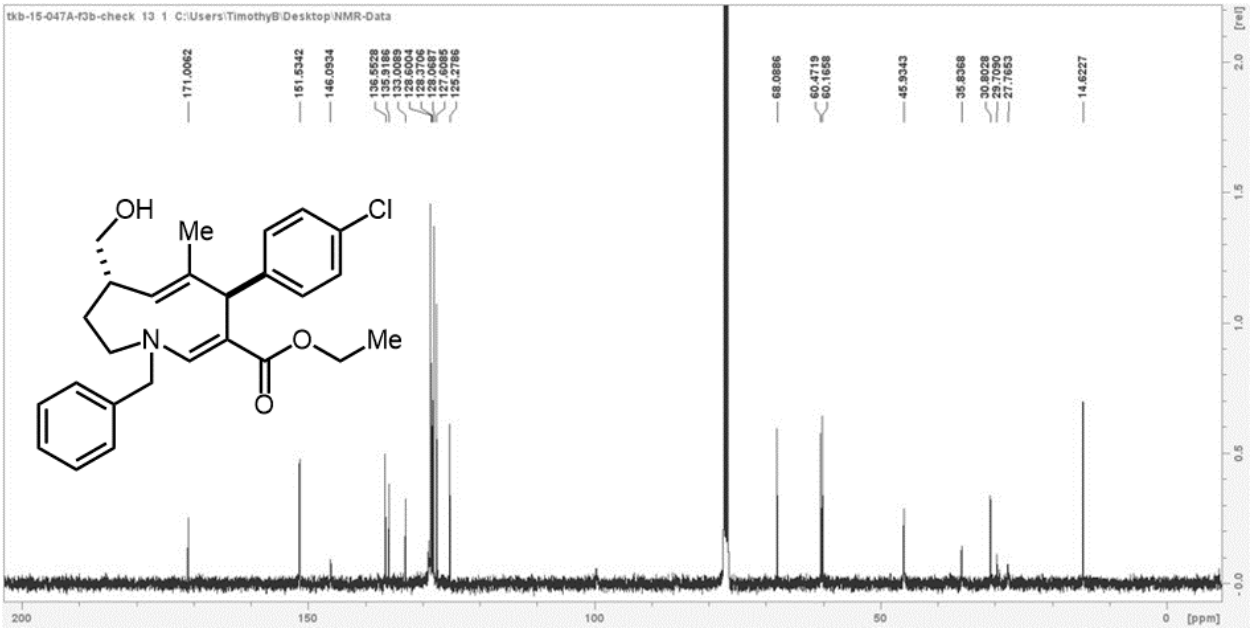
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O
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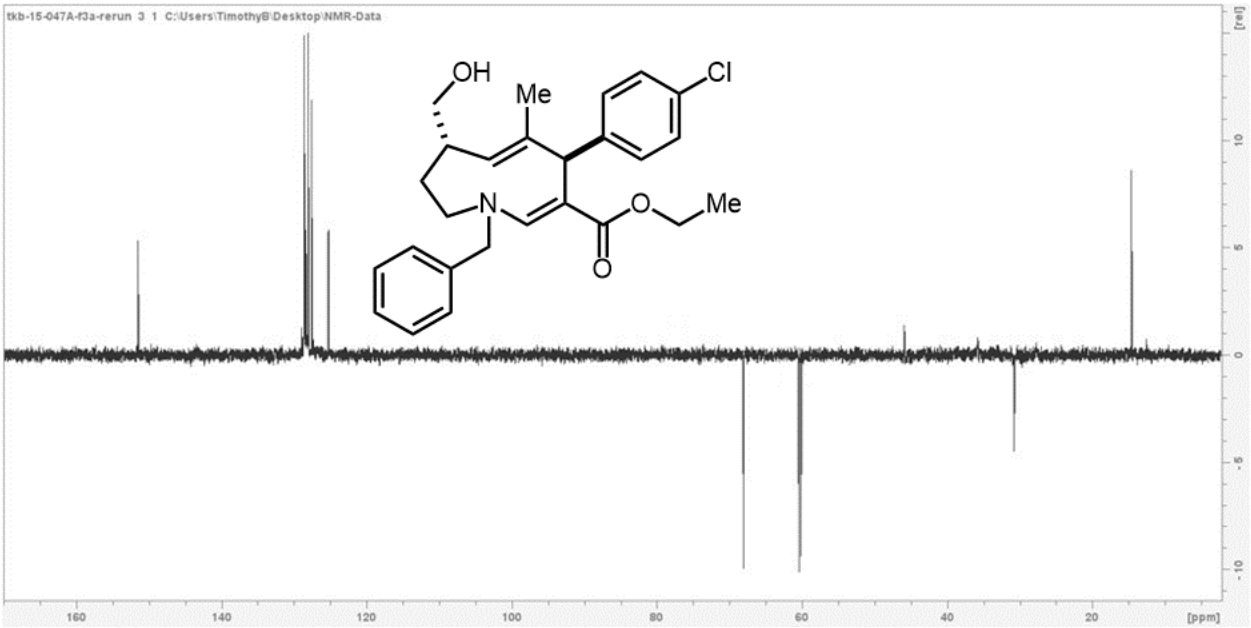
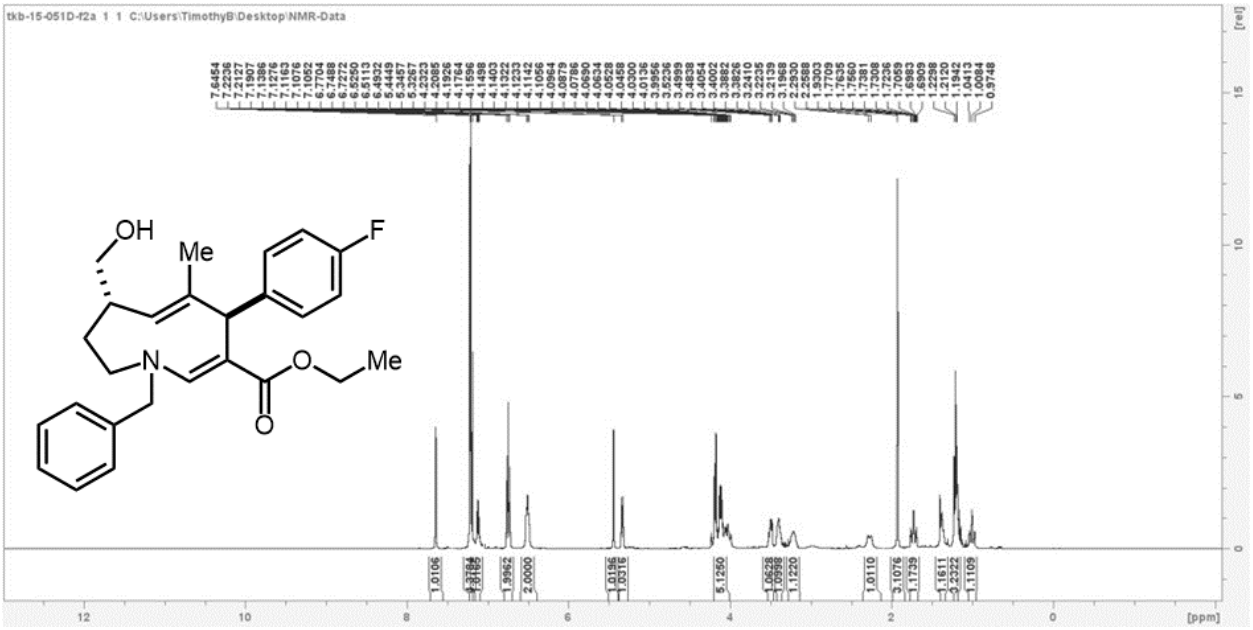


Compound 8j

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellow oil. Yield = 368.4 mg, 87%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.22 – 7.10 (m, 5H), 6.77 – 6.73 (m, 2H), 6.51 (dd, *J* = 8.4, 5.3 Hz, 2H), 5.45 (s, 1H), 5.34 (d, *J* = 7.6 Hz, 1H), 4.26 – 4.08 (m, 5H), 3.50 (dd, *J* = 10.1, 6.3 Hz, 1H), 3.44 – 3.33 (m, 2H), 2.28 (d, *J* = 15.0 Hz, 1H), 1.93 (s, 3H), 1.73 (tt, *J* = 13.0, 3.1 Hz, 1H), 1.25 – 1.10 (m, 4H), 1.10 – 0.95 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.06, 163.23, 160.79, 151.58, 146.13, 136.55, 133.00, 128.59, 128.38, 128.04, 127.94, 127.86, 126.37, 125.22, 115.48, 115.27, 99.43, 68.08, 60.46, 60.14, 45.94, 35.84, 30.81, 14.63, 12.59. **HRMS-EI^{+}** (*m/z*): calc for $C_{26}H_{30}FNO_3$ $[M]^{+}$ 423.2210, found 423.2215.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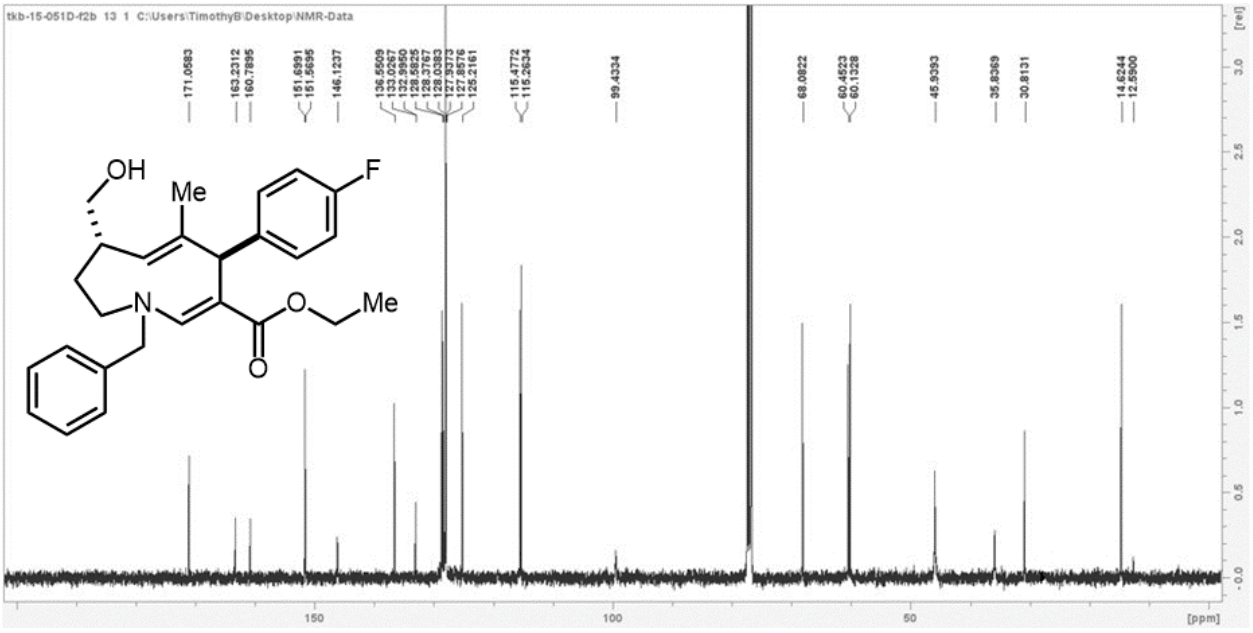
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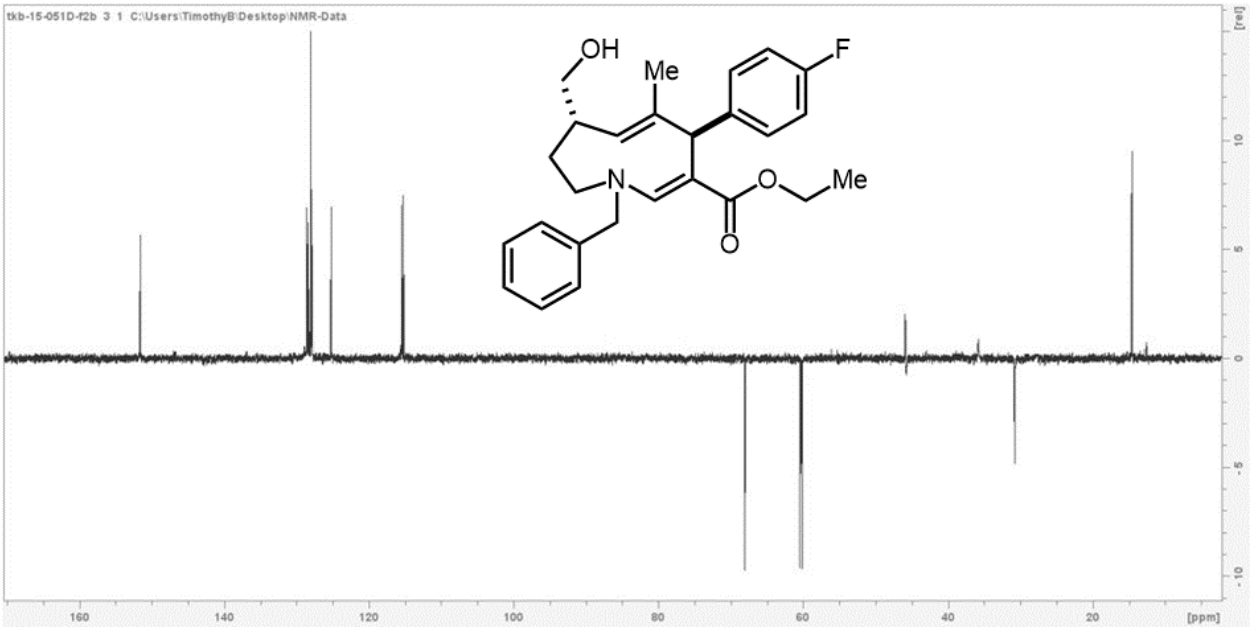
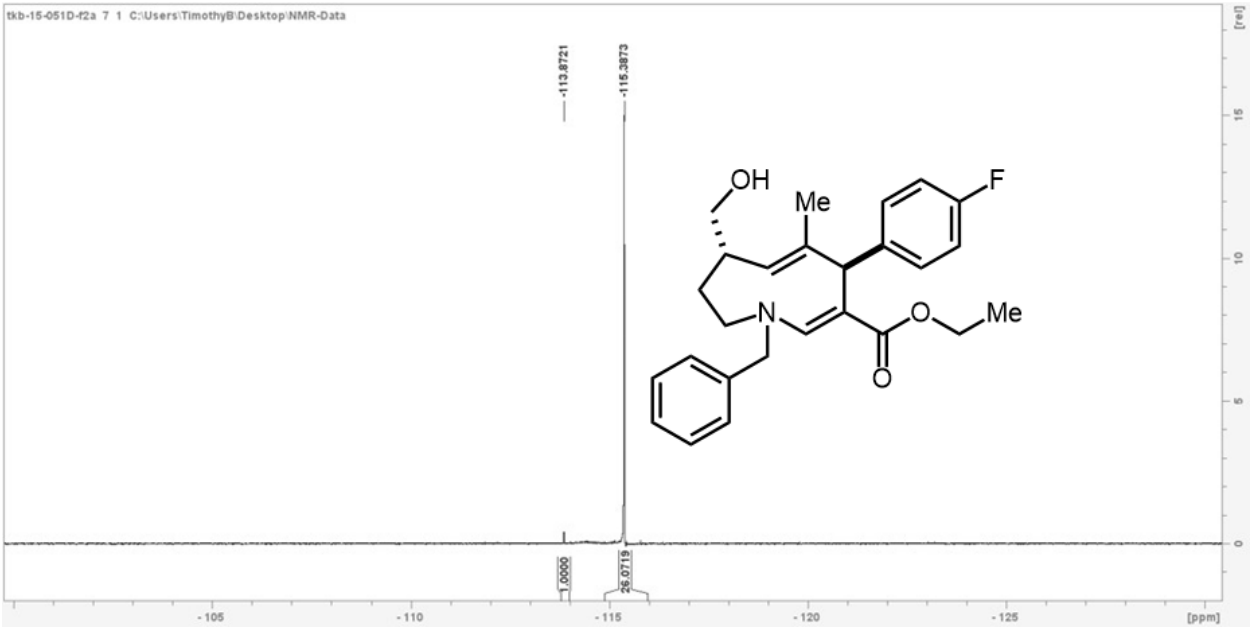


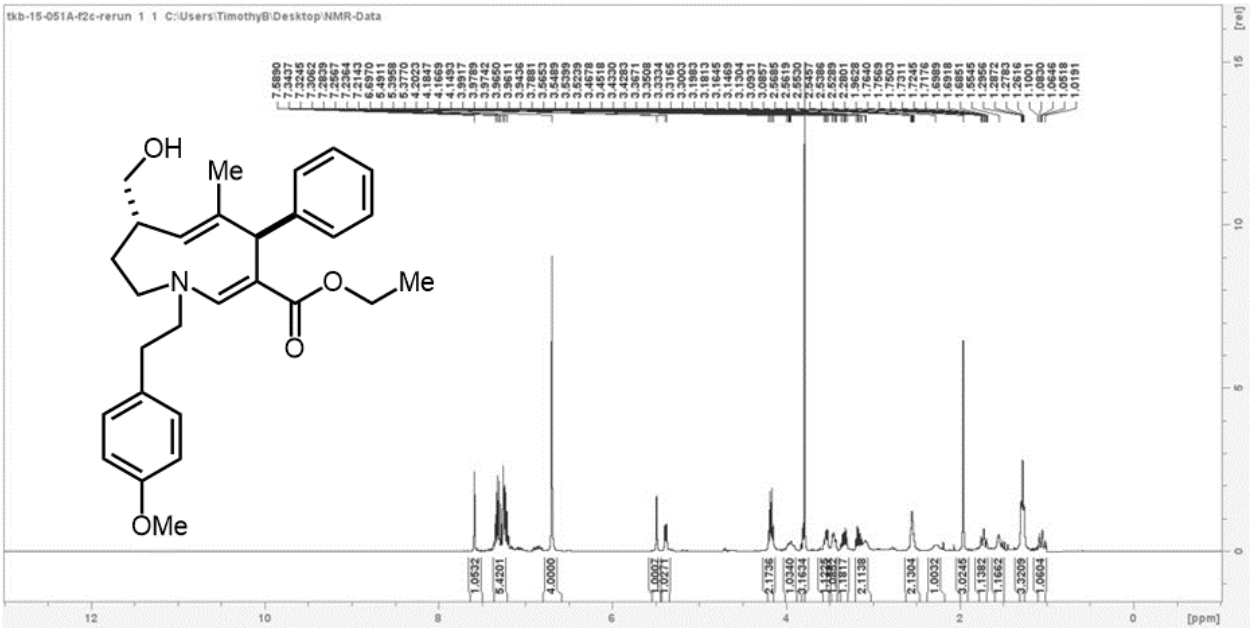
^{19}F NMR

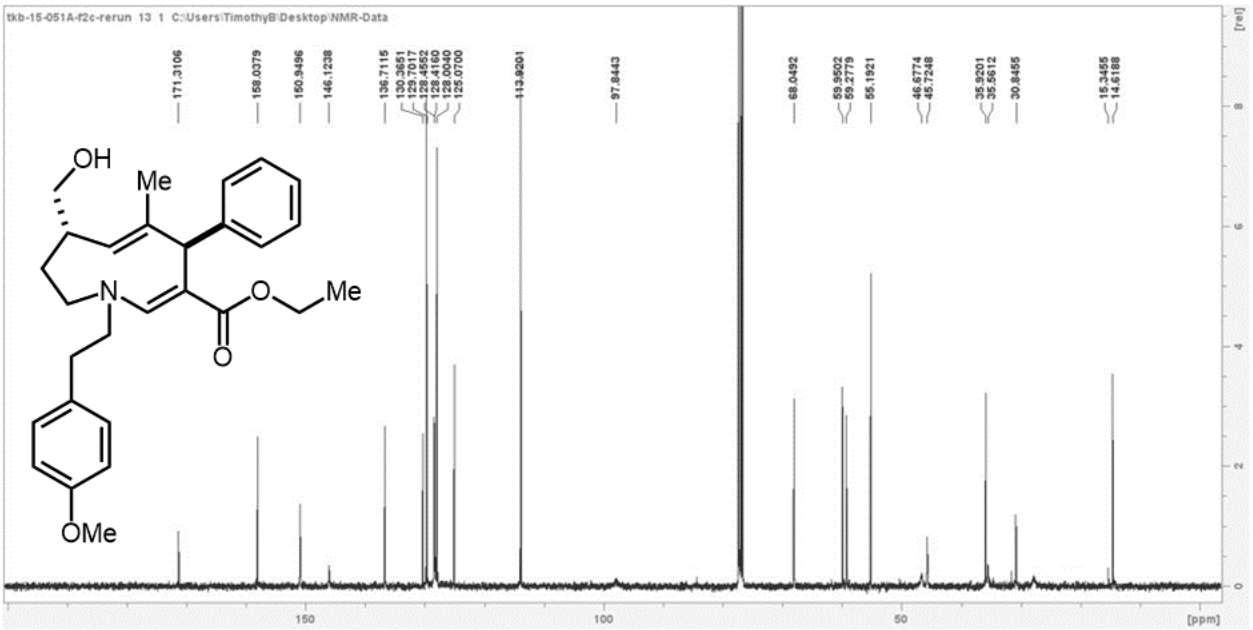


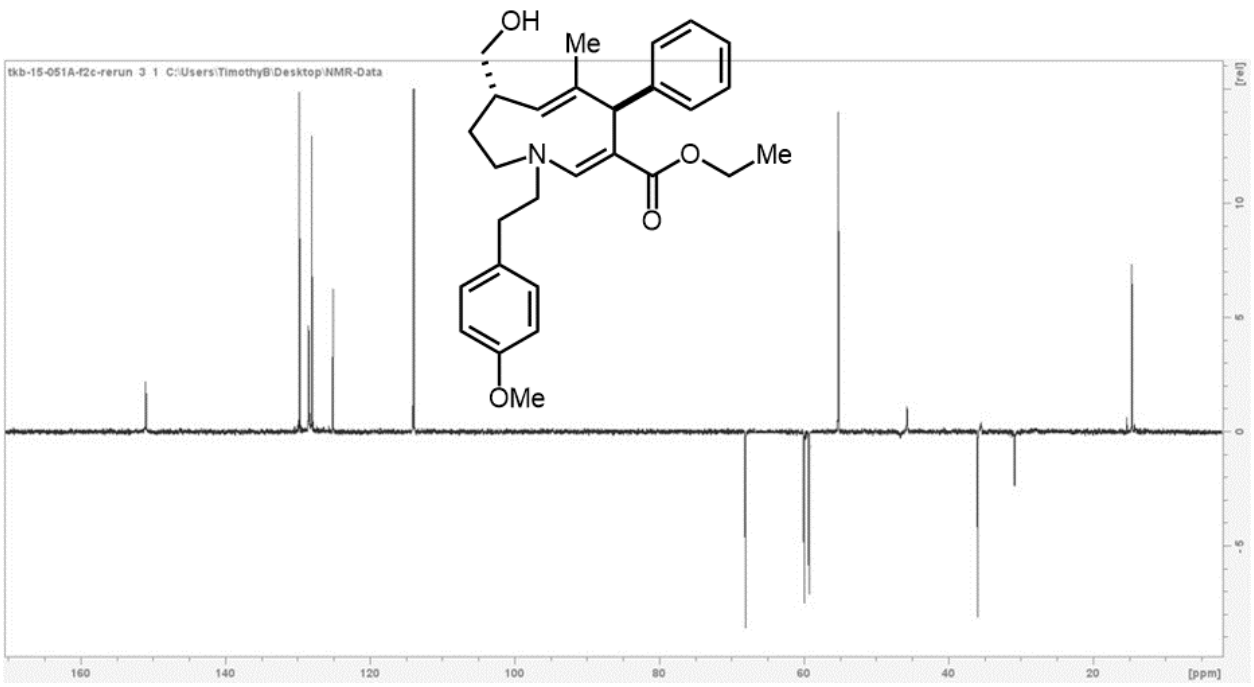
Compound 8k

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 60:40). Amorphous solid. Yield = 382.2 mg, 85%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.34 – 7.21 (m, 5H), 6.70 (s, 4H), 5.49 (s, 1H), 5.39 (d, *J* = 7.6 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.99 – 3.94 (m, 1H), 3.79 (s, 3H), 3.54 (dd, *J* = 10.3, 6.4 Hz, 1H), 3.45 (dd, *J* = 10.1, 6.1 Hz, 1H), 3.40 – 3.23 (m, 1H), 3.22 – 3.06 (m,

2H), 2.55 (td, J = 6.5, 3.2 Hz, 2H), 2.27 (s, 1H), 1.96 (s, 3H), 1.72 (tt, J = 13.0, 3.2 Hz, 1H), 1.54 (br s, 1H), 1.27 (t, J = 7.1 Hz, 3H), 1.16 – 0.96 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.31, 158.04, 150.95, 146.10, 136.71, 130.37, 129.71, 128.46, 128.42, 128.01, 125.07, 113.92, 97.84, 68.05, 59.95, 59.28, 55.20, 46.68, 45.73, 35.92, 30.85, 15.35, 14.62. **HRMS-EI$^+$** (*m/z*): calc for $C_{28}H_{35}NO_4$ $[M]^+$ 449.2566, found 449.2569.

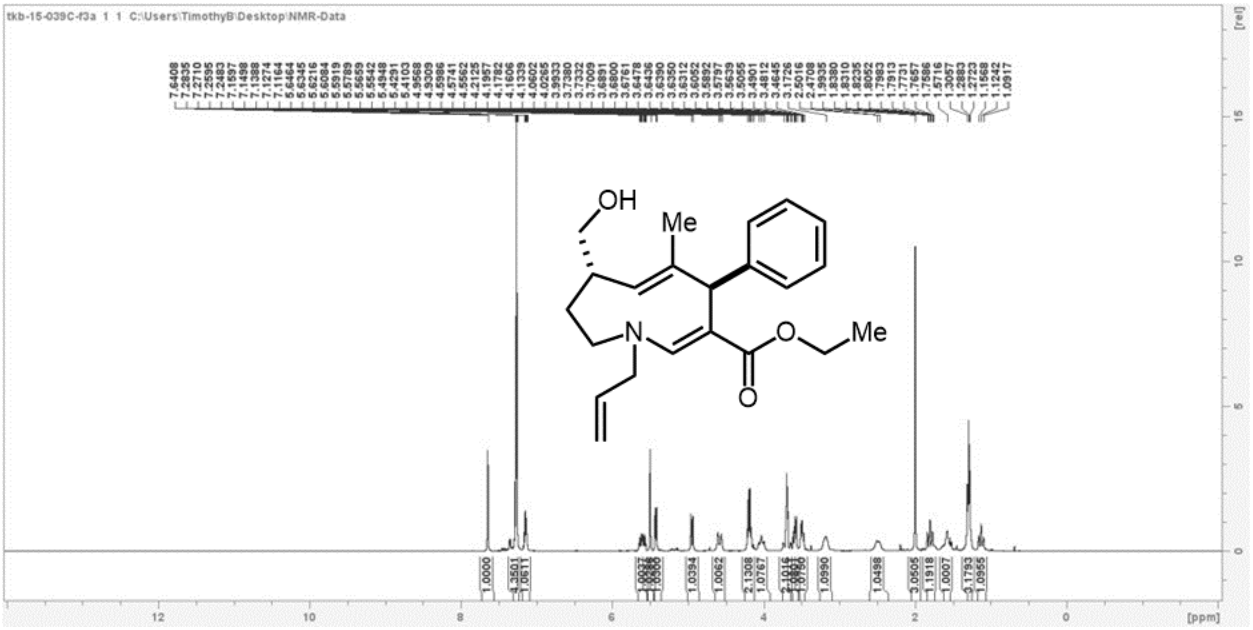






Compound 8l

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 75:25). Greenish-yellow oil. Yield = 312.8 mg, 88%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.28 – 7.25 (m, 4H), 7.16 – 7.11 (m, 1H), 5.60 (ddt, *J* = 17.1, 9.9, 4.8 Hz, 1H), 5.49 (s, 1H), 5.42 (dt, *J* = 7.6, 1.4 Hz, 1H), 4.94 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.59 (dd, *J* = 11.9, 8.4 Hz, 1H), 4.18 (pd, *J* = 8.4, 4.2 Hz, 2H), 4.03 (t, *J* = 13.8 Hz, 1H), 3.77 – 3.67 (m, 1H), 3.71 – 3.60 (m, 1H), 3.58 (dd, *J* = 10.3, 6.3 Hz, 1H), 3.49 (dd, *J* = 10.4, 6.3 Hz, 1H), 3.18 (br s, 1H), 2.48 (d, *J* = 15.1 Hz, 1H), 1.99 (s, 3H), 1.80 (tt, *J* = 13.0, 3.1 Hz, 1H), 1.57 (br. s, 1H), 1.28 (q, *J* = 6.8 Hz, 3H), 1.12 (tt, *J* = 13.3, 2.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.25, 151.18, 145.94, 136.68, 133.61, 128.37, 128.28, 127.96, 125.11, 116.42, 68.08, 60.01, 59.58, 45.74, 31.60, 30.91, 22.66, 14.61. **HRMS-EI^{+}** (*m/z*): calc for $C_{22}H_{29}NO_3$ $[M]^{+}$ 355.2147, found 355.2153.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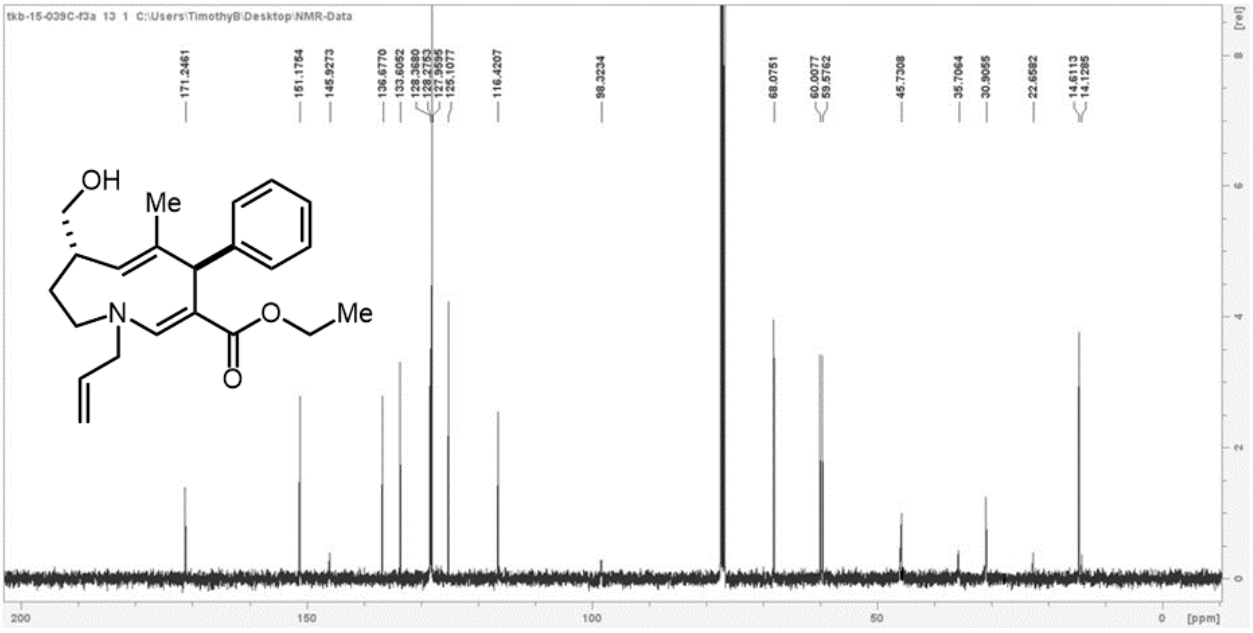
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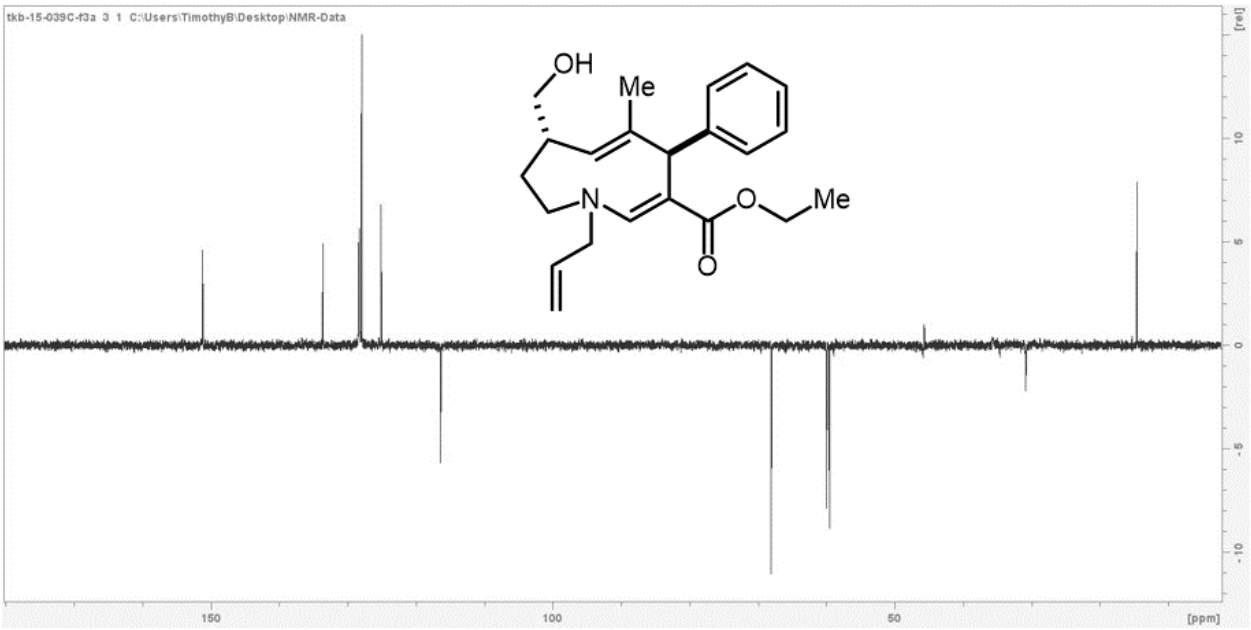
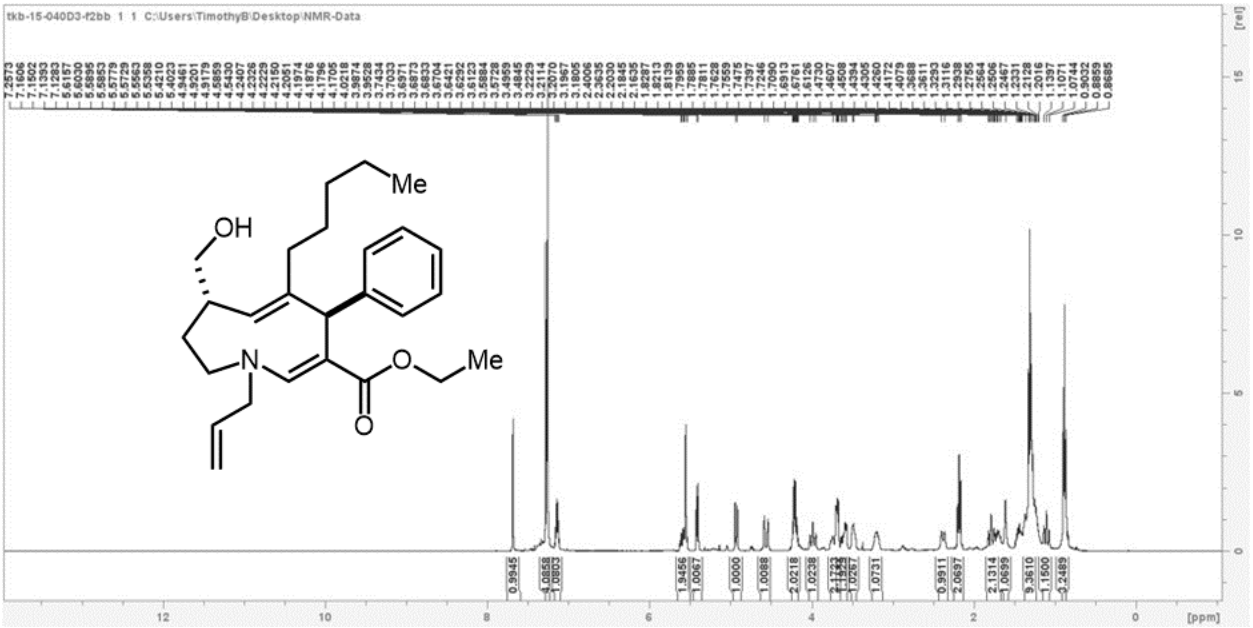


Compound 8m

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 75:25). Greenish-yellow oil. Yield = 349.5 mg, 85%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.26 (d, *J* = 4.4 Hz, 4H), 7.14 (p, *J* = 4.3 Hz, 1H), 5.65 – 5.51 (m, 2H), 5.41 (d, *J* = 7.5 Hz, 1H), 4.93 (dq, *J* = 10.4, 1.6 Hz, 1H), 4.56 (d, *J* = 17.1 Hz, 1H), 4.20 (dqt, *J* = 10.6, 6.9, 3.3 Hz, 2H), 3.99 (t, *J* = 13.9 Hz, 1H), 3.79 – 3.55 (m, 4H), 3.49 (q, *J* = 5.6 Hz, 1H), 3.27 – 3.15 (m, 1H), 2.38 (d, *J* = 15.0 Hz, 1H), 2.18 (dd, *J* = 9.3, 6.5 Hz, 2H), 1.76 – 1.63 (m, 2H), 1.57 (s, 1H), 1.33 – 1.21 (m, 9H), 1.11 (tt, *J* = 13.1, 2.5 Hz, 1H), 0.93 – 0.81 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.32, 151.39, 146.65, 141.77, 133.58, 128.36, 127.96, 127.86, 125.07, 116.36, 68.21, 60.00, 59.52, 45.74, 44.09, 35.33, 31.91, 30.67, 30.33, 22.59, 14.63, 14.14. **HRMS-EI^{+}** (*m/z*): calc for $C_{26}H_{37}NO_3$ $[M]^{+}$ 411.2773, found 411.2777.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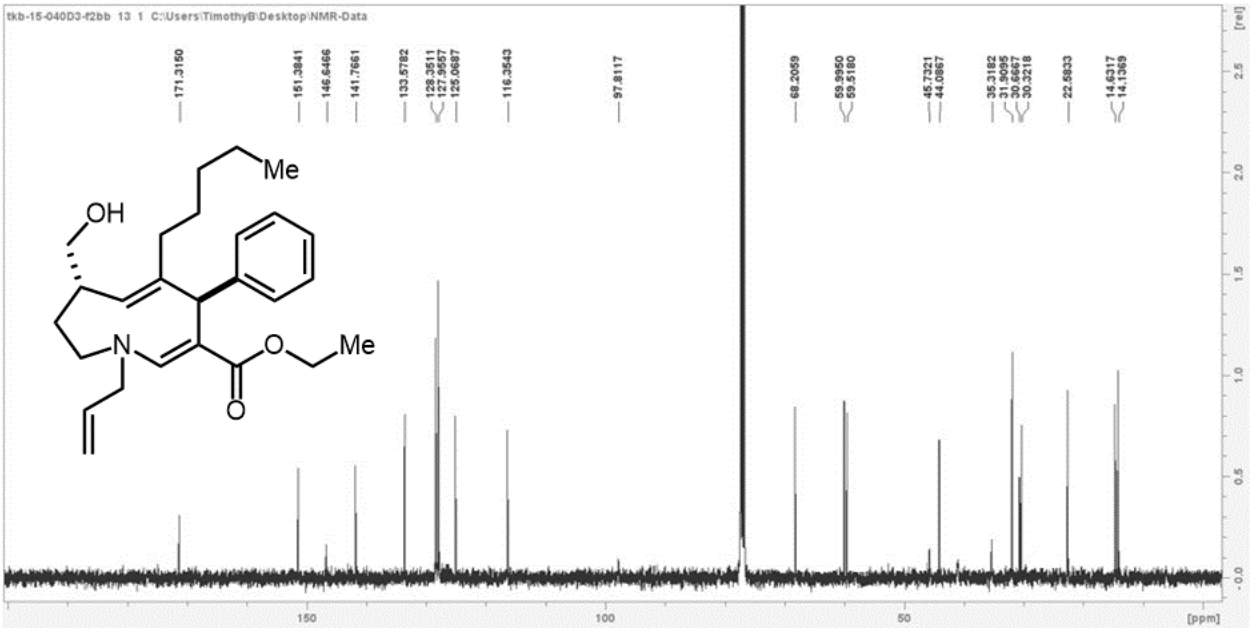
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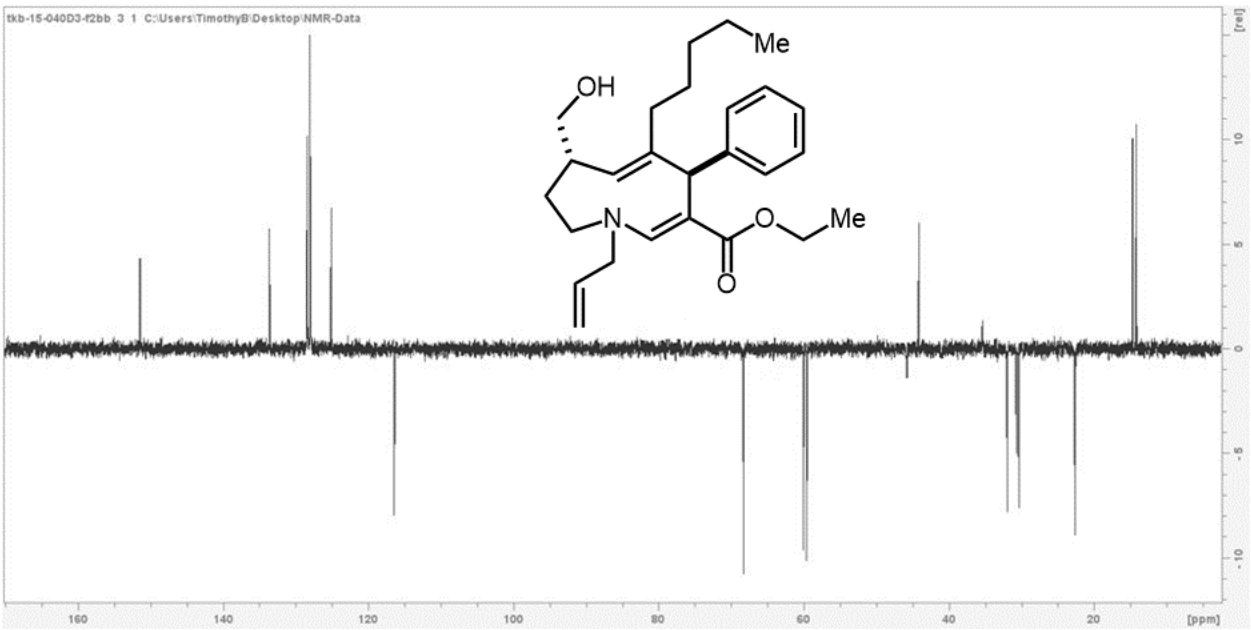
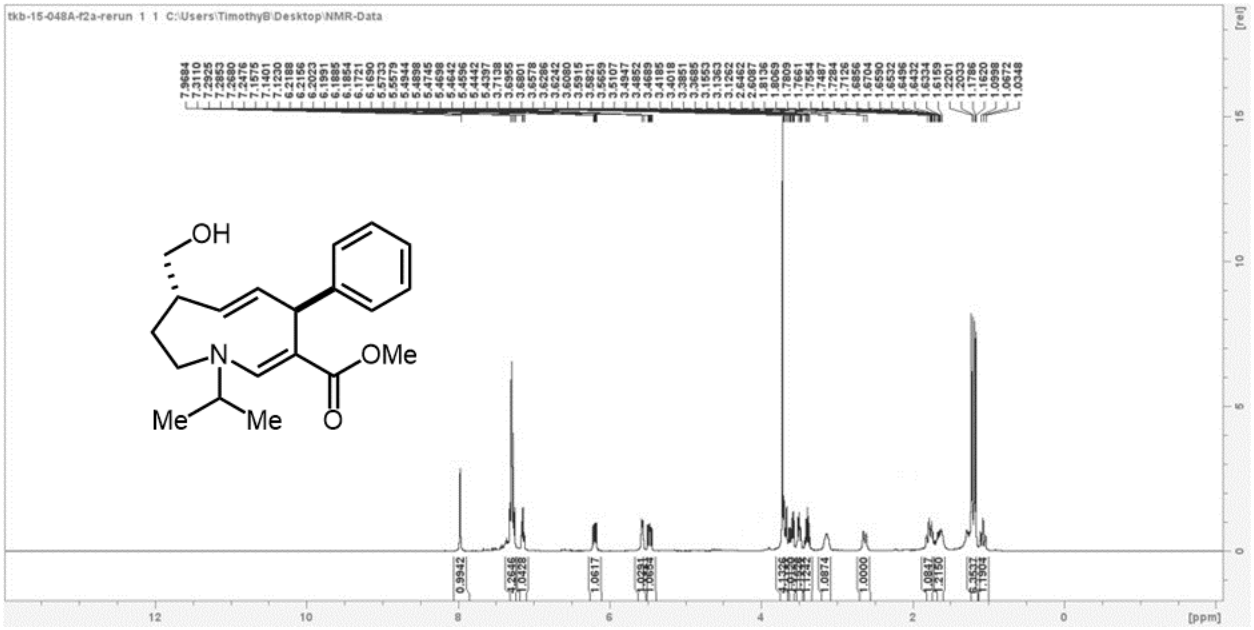


Compound 8n

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellowish oil. Yield = 296.5 mg, 90%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.41 – 7.23 (m, 4H), 7.14 (ddt, *J* = 9.0, 7.0, 1.7 Hz, 1H), 6.19 (dd, *J* = 12.1, 6.6 Hz, 1H), 5.57 (d, *J* = 6.6 Hz, 1H), 5.47 (dd, *J* = 12.1, 8.0 Hz, 1H), 3.74 – 3.54 (m, 5H), 3.49 (dd, *J* = 10.4, 6.4 Hz, 1H), 3.39 (hept, *J* = 6.7 Hz, 1H), 3.13 (t, *J* = 9.6 Hz, 1H), 2.63 (d, *J* = 15.2 Hz, 1H), 1.84 – 1.69 (m, 2H), 1.33 – 1.14 (m, 6H), 1.07 (tt, *J* = 12.9, 2.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.76, 148.29, 146.33, 131.33, 129.00, 128.17, 126.85, 125.27, 95.06, 67.48, 57.93, 51.47, 44.62, 41.14, 35.23, 32.78, 22.82, 22.44. **HRMS-EI$^+$** (*m/z*): calc for $C_{20}H_{27}NO_3$ $[M]^+$ 329.1991, found 329.1996.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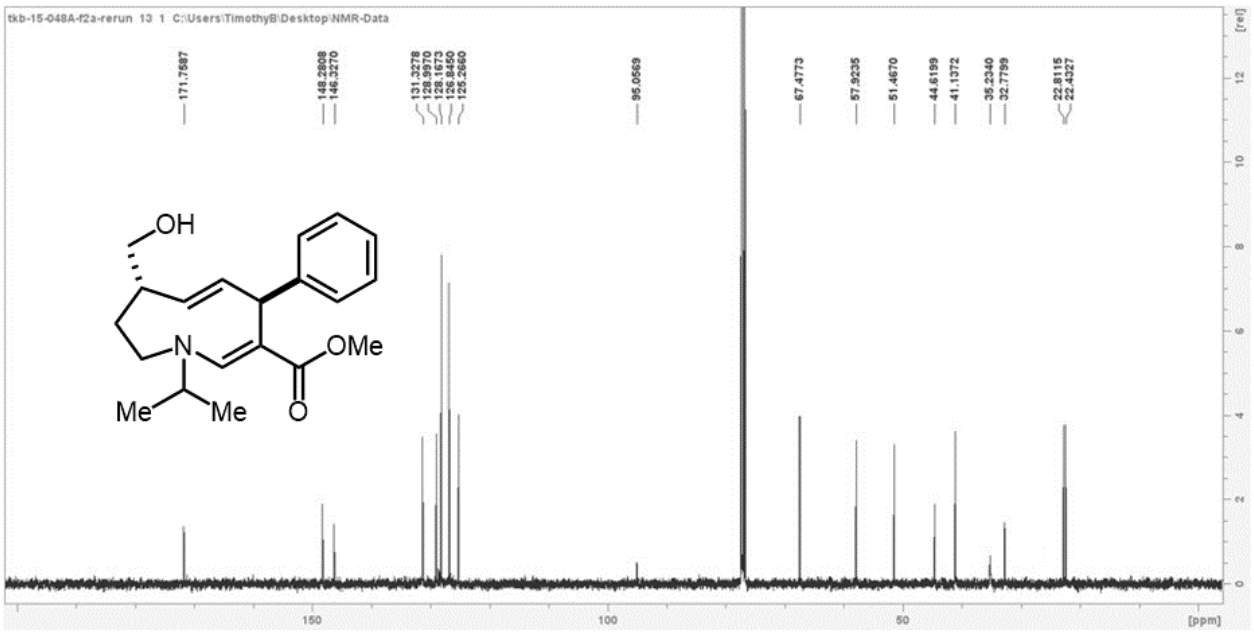
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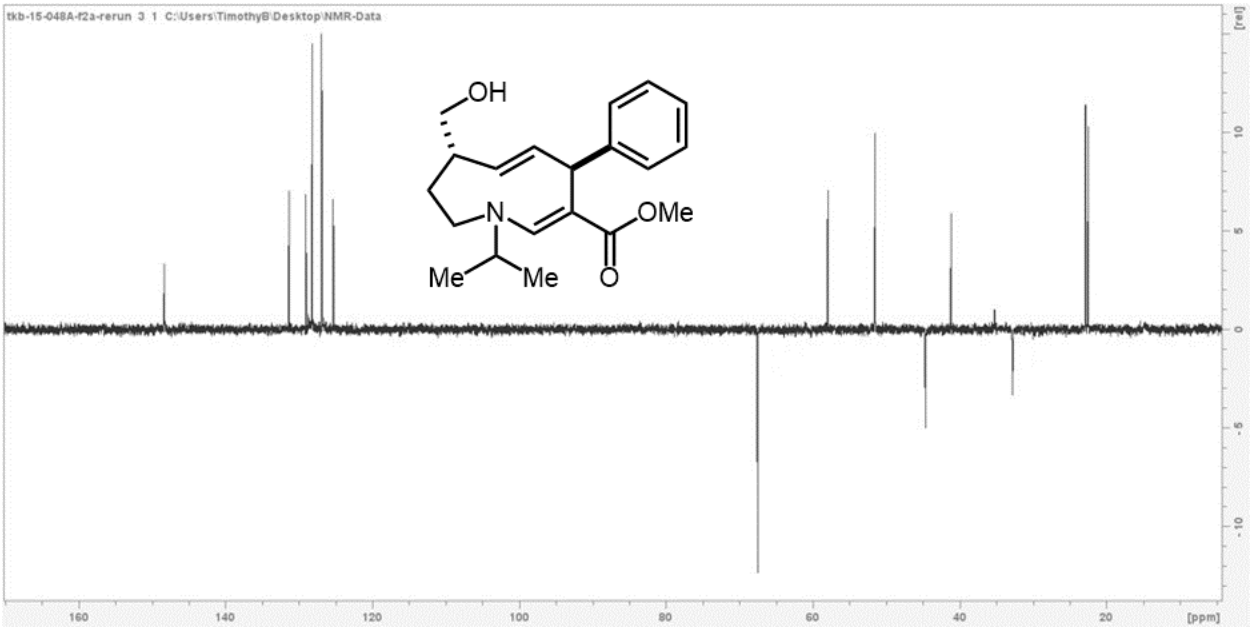
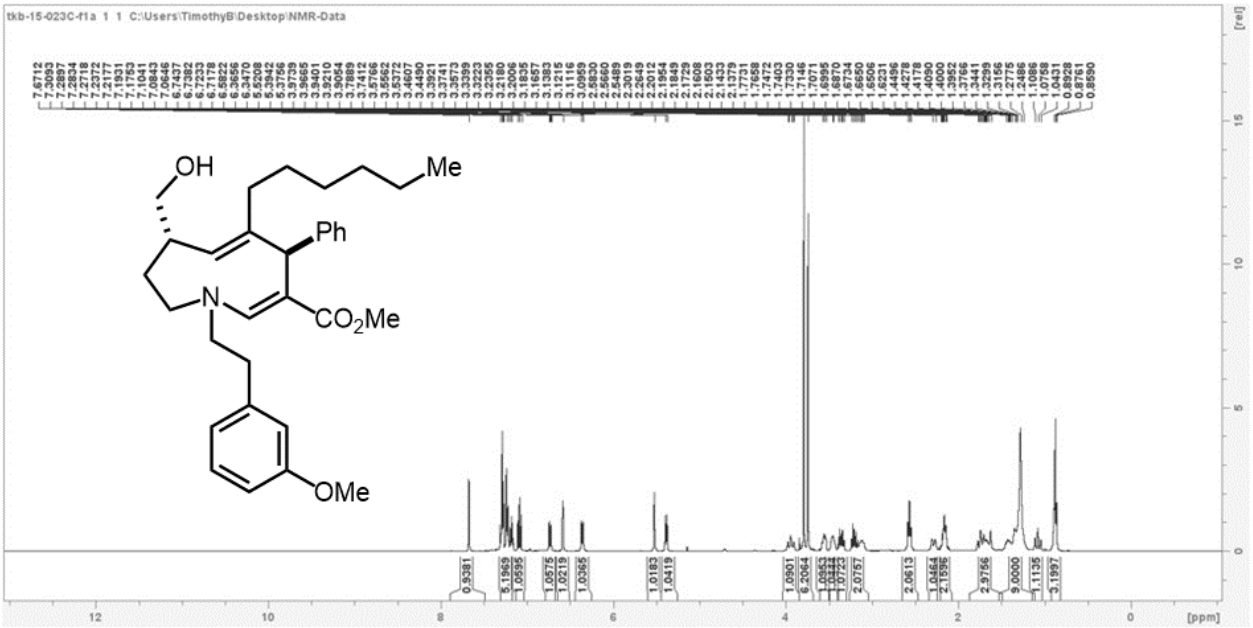


Compound 8o

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellowish oil. Yield = 429.8 mg, 85%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.30 – 7.17 (m, 5H), 7.08 (t, *J* = 7.9 Hz, 1H), 6.73 (dd, *J* = 8.3, 2.6 Hz, 1H), 6.58 (s, 1H), 6.36 (d, *J* = 7.5 Hz, 1H), 5.52 (s, 1H), 5.39 (d, *J* = 7.4 Hz, 1H), 3.94 (t, *J* = 13.9 Hz, 1H), 3.79 (s, 3H), 3.74 (s, 3H), 3.60 – 3.51 (m, 1H), 3.46 (d, *J* = 5.6 Hz, 1H), 3.36 (dt, *J* = 14.1, 7.1 Hz, 1H), 3.26 – 3.07 (m, 2H), 2.62 – 2.51 (m, 2H), 2.28 (d, *J* = 15.1 Hz, 1H), 2.24 – 2.08 (m, 2H), 1.80 – 1.60 (m, 3H), 1.37 – 1.22 (m, 9H), 1.08 (tt, *J* = 13.1, 2.5 Hz, 1H), 0.87 (t, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.65, 159.69, 150.99, 141.81, 139.77, 129.58, 128.31, 128.01, 127.83, 125.07, 121.24, 114.44, 111.49, 68.18, 59.02, 55.16, 51.40, 44.26, 36.82, 35.22, 31.77, 30.73, 30.51, 29.33, 22.69, 14.11. **HRMS-EI^{+}** (*m/z*): calc for $C_{32}H_{43}NO_4$ $[M]^{+}$ 505.3192, found 505.3197.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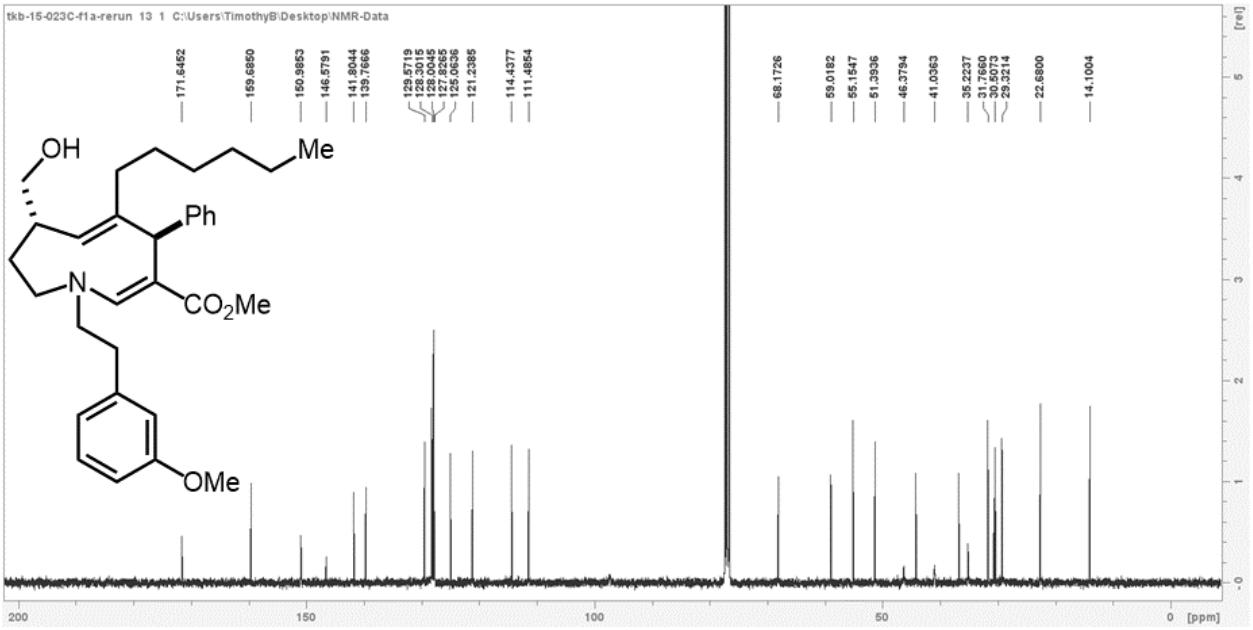
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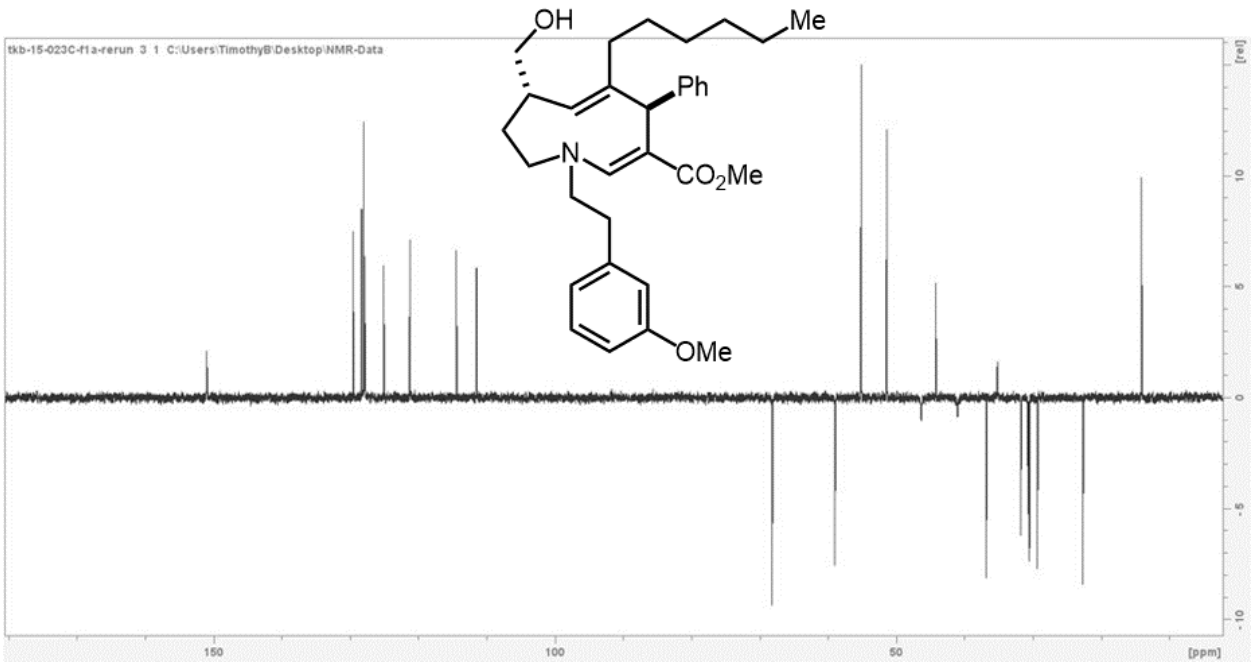
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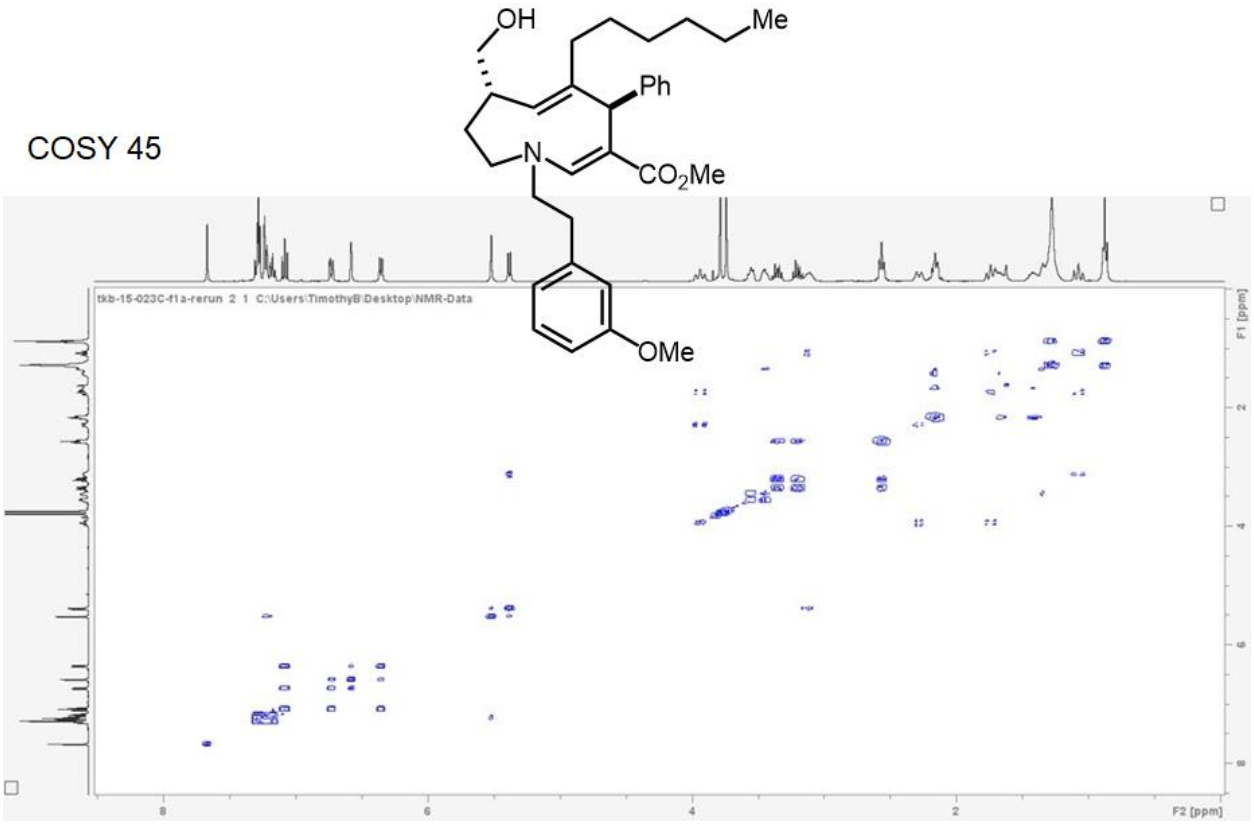
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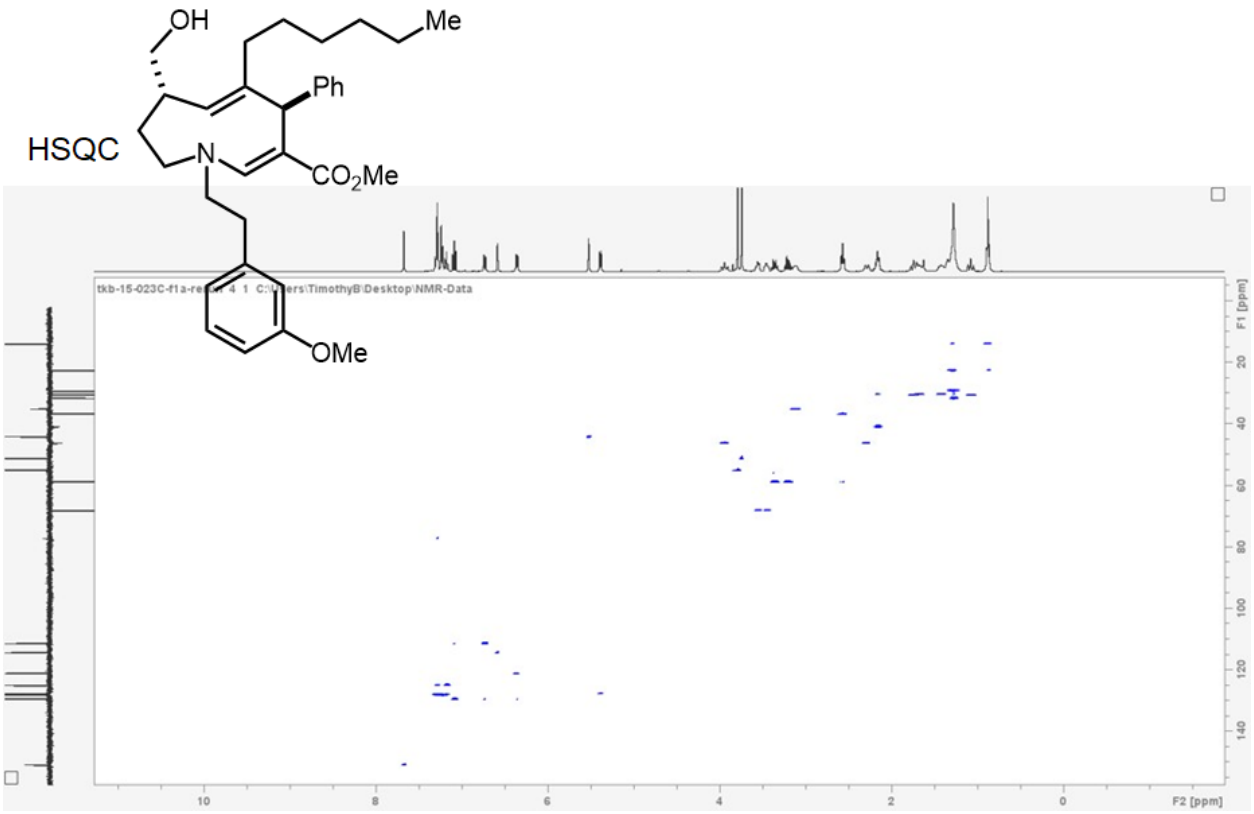
F2 [ppm]

HSQC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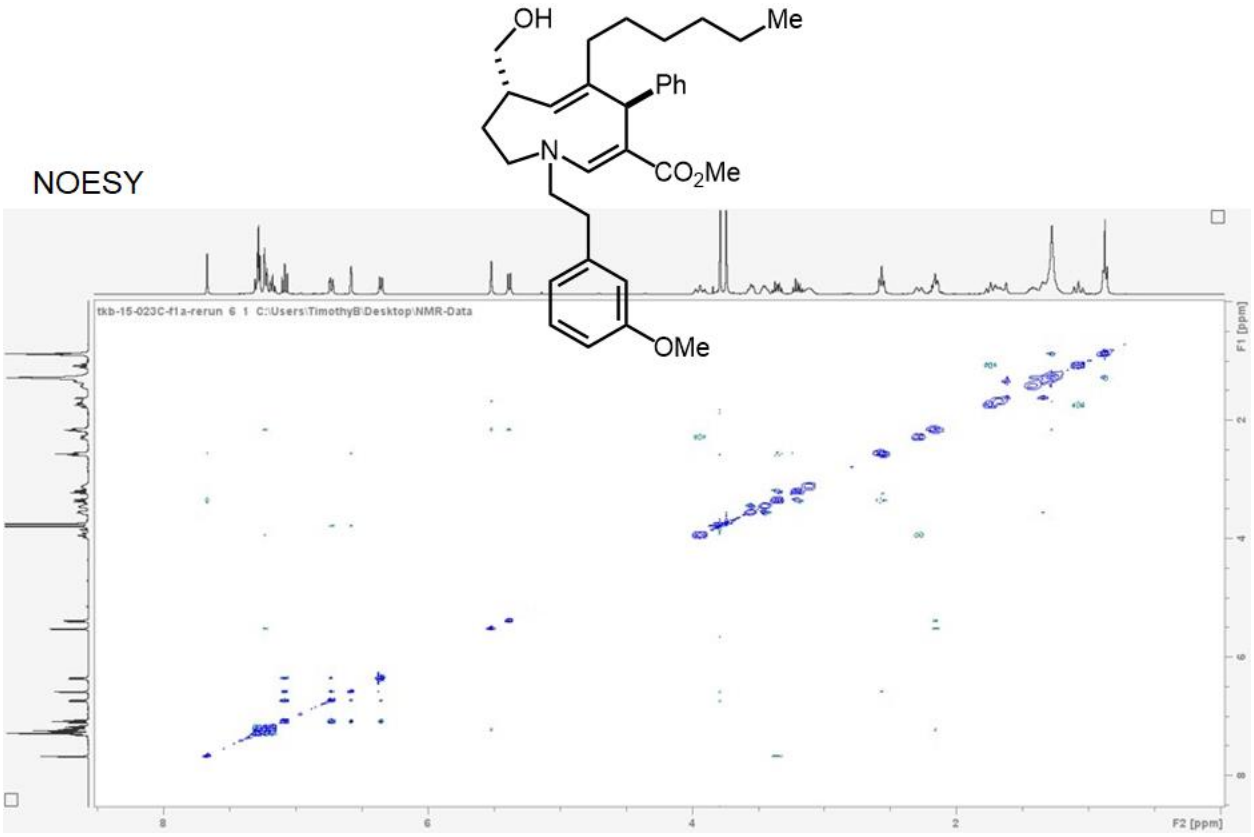
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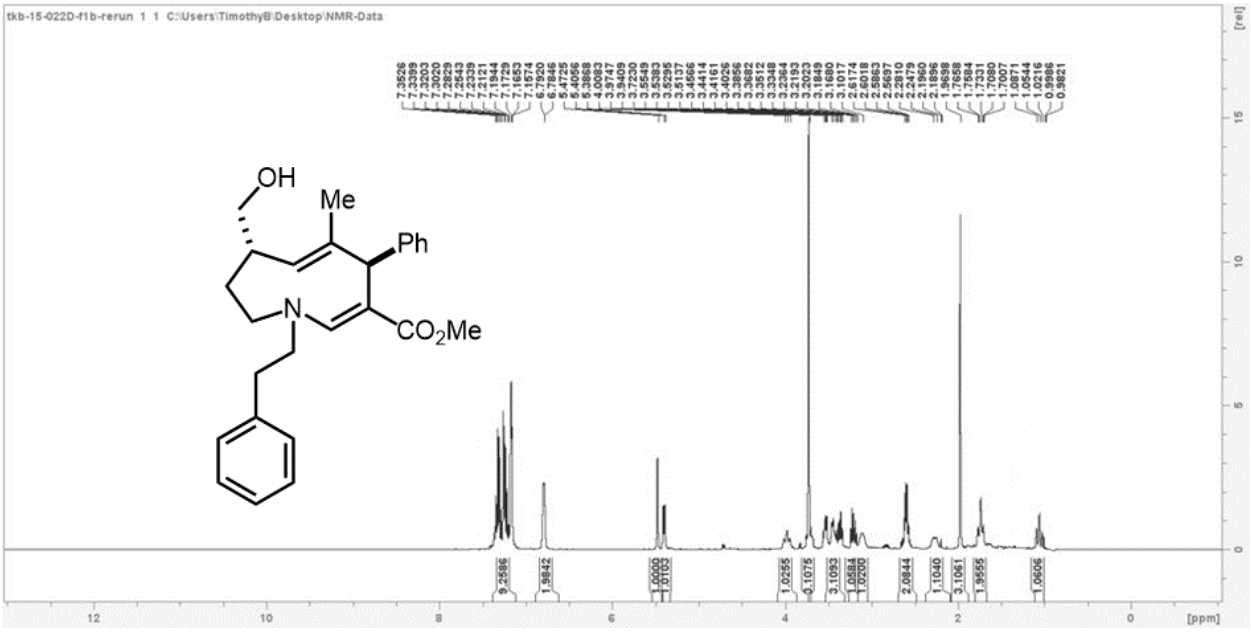
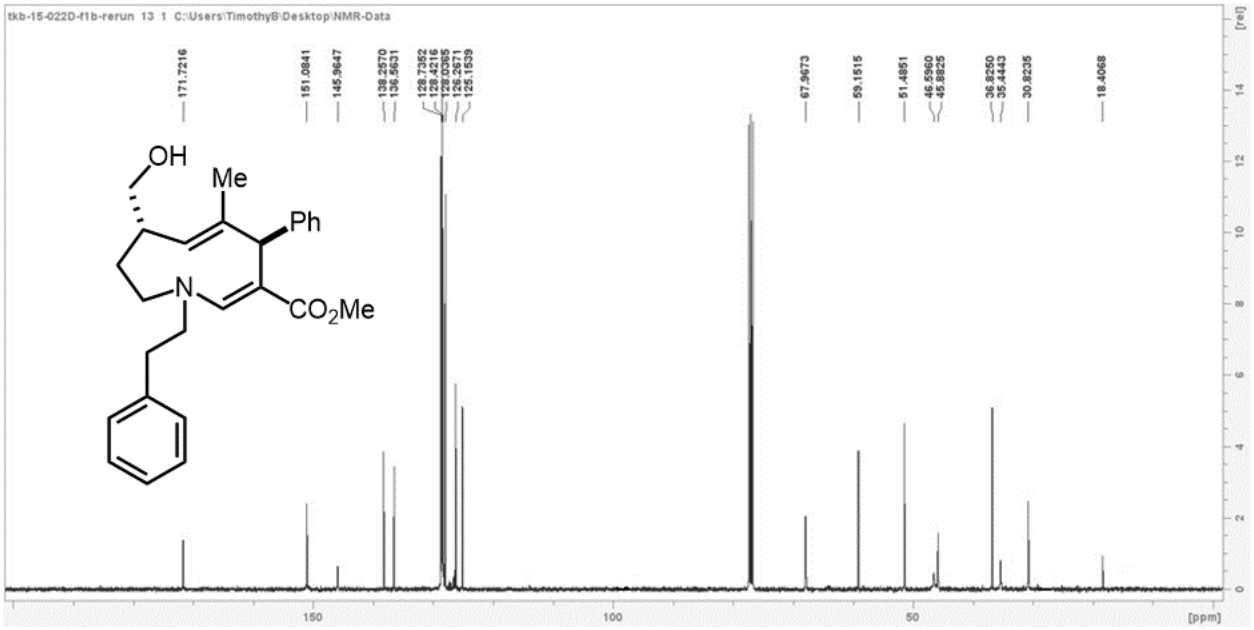
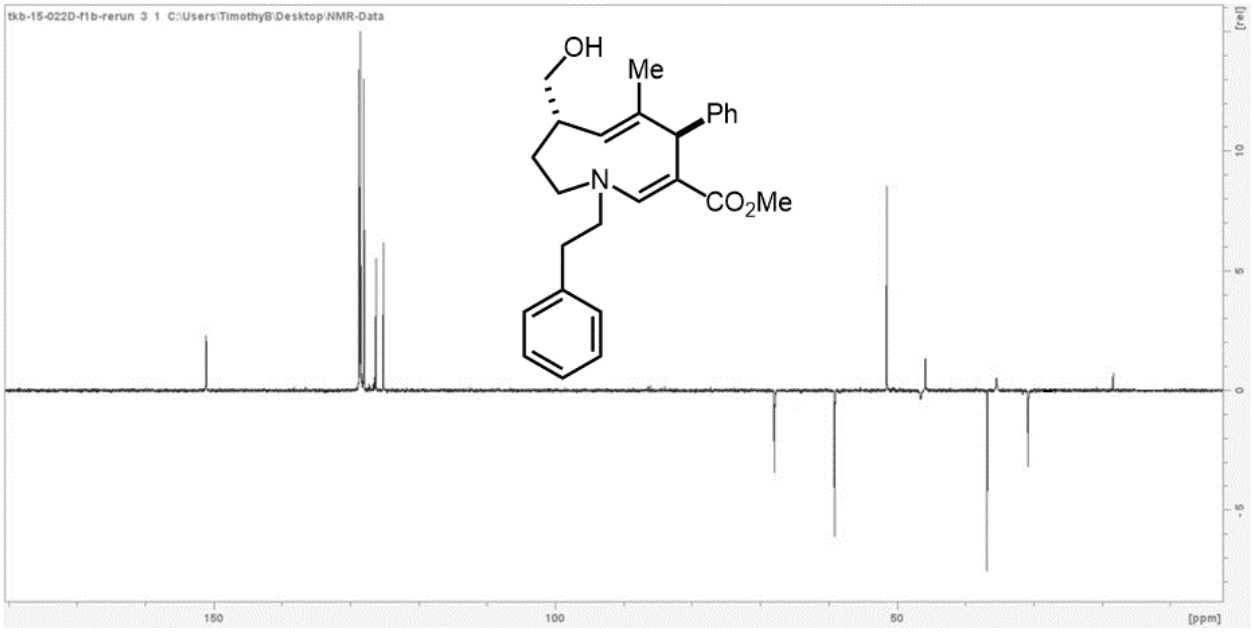
F1 [ppm]

Compound 8p

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 360.9 mg, 89%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.16 (m, 9H), 6.79 (dd, *J* = 6.5, 3.1 Hz, 2H), 5.47 (s, 1H), 5.40 (d, *J* = 7.5 Hz, 1H), 3.97 (t, *J* = 13.8 Hz, 1H), 3.72 (s, 3H), 3.53 (dd, *J* = 10.3, 6.4 Hz, 1H), 3.44 (t, *J* = 4.9 Hz, 1H), 3.44 – 3.31 (m, 1H), 3.20 (dt, *J* = 13.7, 6.8 Hz, 1H), 3.14 – 3.04 (m, 1H), 2.60 (hept, *J* = 6.7 Hz, 2H), 2.26 (d, *J* = 15.1 Hz, 1H), 1.97 (s, 3H), 1.80 – 1.59 (m, 2H), 1.12 – 0.96 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.72, 151.09, 145.97, 138.26, 136.57, 128.74, 128.56, 128.53, 128.43, 128.04, 126.27, 125.16, 97.75, 67.97, 59.16, 51.49, 46.56, 45.89, 36.83, 35.45, 30.83, 18.41. **HRMS-EI^{+}** (*m/z*): calc for $C_{26}H_{31}NO_3$ $[M]^{+}$ 405.2304, found 405.2308.



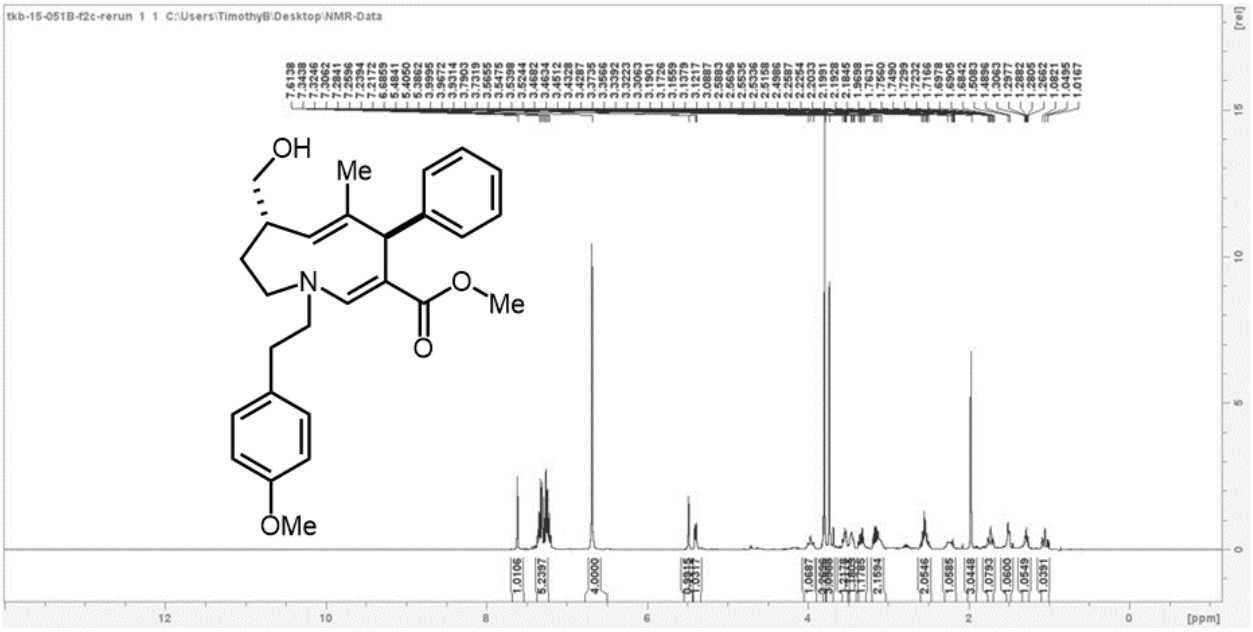


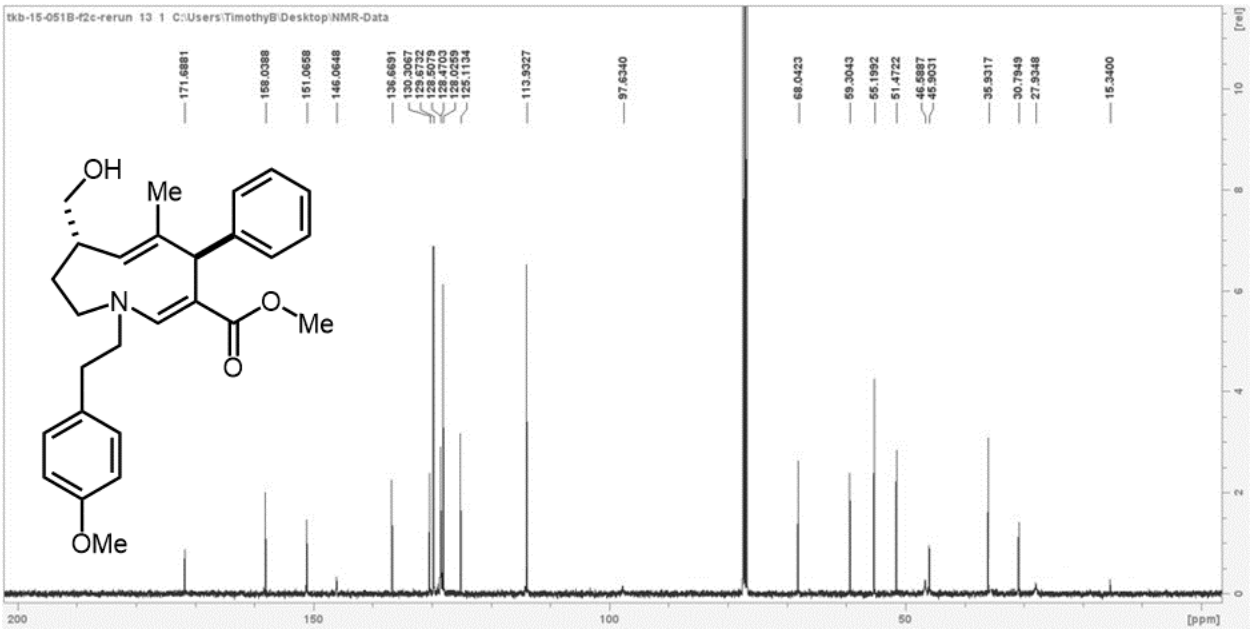


Compound 8q

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 379.0 mg, 87%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.42 – 7.15 (m, 5H), 6.69 (s, 4H), 5.48 (s, 1H), 5.40 (d, *J* = 7.5 Hz, 1H), 3.95 (q, *J* = 10.7 Hz, 1H), 3.79 (s, 3H), 3.73 (s, 3H), 3.54 (dd, *J* = 10.2, 6.5 Hz, 1H), 3.52 – 3.41 (m, 1H), 3.40 – 3.22 (m, 1H), 3.16 (ddd, *J* = 13.7, 7.3, 6.2 Hz, 2H), 2.55 (tq, *J* = 13.8, 6.6 Hz, 2H), 2.28 – 2.16 (m, 1H), 1.97 (s, 3H), 1.72 (tt, *J* = 13.0, 3.1 Hz,

1H), 1.55 – 1.41 (m, 1H), 1.28 (qd, J = 7.2, 4.8 Hz, 1H), 1.12 – 0.96 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.69, 158.04, 151.07, 146.06, 136.67, 130.31, 129.68, 128.51, 128.47, 128.03, 125.12, 113.94, 97.63, 68.05, 59.31, 55.20, 51.48, 46.59, 45.91, 35.94, 30.80, 15.34. **HRMS-EI$^+$** (*m/z*): calc for $C_{27}H_{33}NO_4$ $[M]^+$ 435.2410, found 435.2415.





Compound 8r

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 352.5 mg, 90%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.32 – 7.28 (m, 4H), 7.22 – 7.14 (m, 4H), 6.68 – 6.62 (m, 2H), 5.54 (s, 1H), 5.44 (dt, *J* = 7.6, 1.4 Hz, 1H), 4.39 – 4.25 (m, 2H), 4.15 (t, *J* = 14.0 Hz, 1H), 3.76 (s, 3H), 3.59 (dd, *J* = 10.3, 6.3 Hz, 1H), 3.49 (dt, *J* = 9.1, 4.0 Hz, 1H), 3.37 – 3.25 (m, 1H), 2.39 (d, *J* = 15.1 Hz, 1H), 2.03 (s, 3H), 1.81 (tt, *J* = 13.0, 3.1 Hz, 1H), 1.76 (s, 1H), 1.10 (tt, *J* = 13.3, 2.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.57, 152.00, 146.11, 137.31, 136.53, 128.61, 128.54, 128.50, 128.06, 127.29, 126.27, 125.24, 98.65, 68.06, 61.15, 51.57, 46.09, 45.81, 30.82, 15.33. **HRMS-EI^{+}** (*m/z*): calc for $C_{25}H_{29}NO_3$ $[M]^{+}$ 391.2147, found 391.2152.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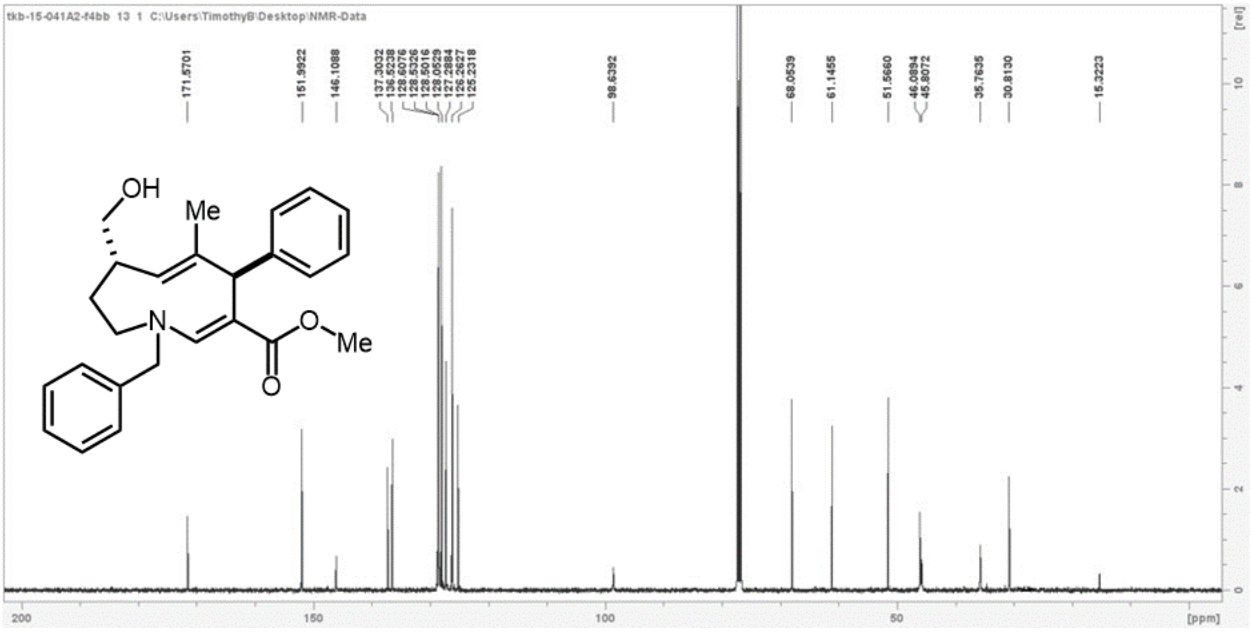
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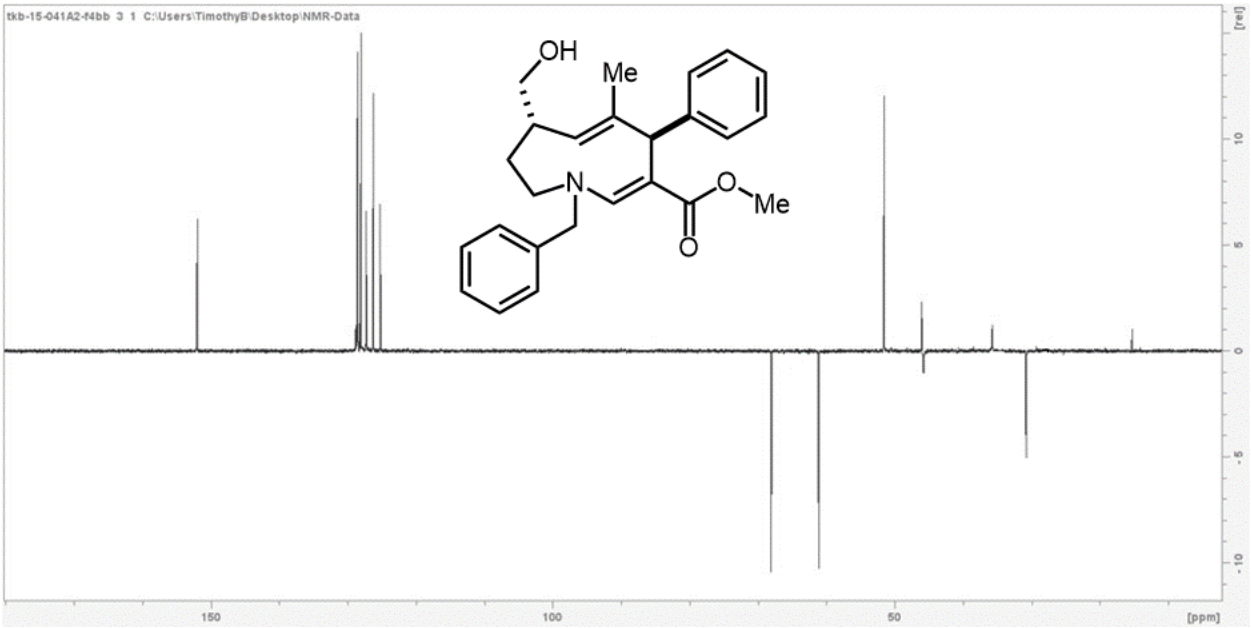
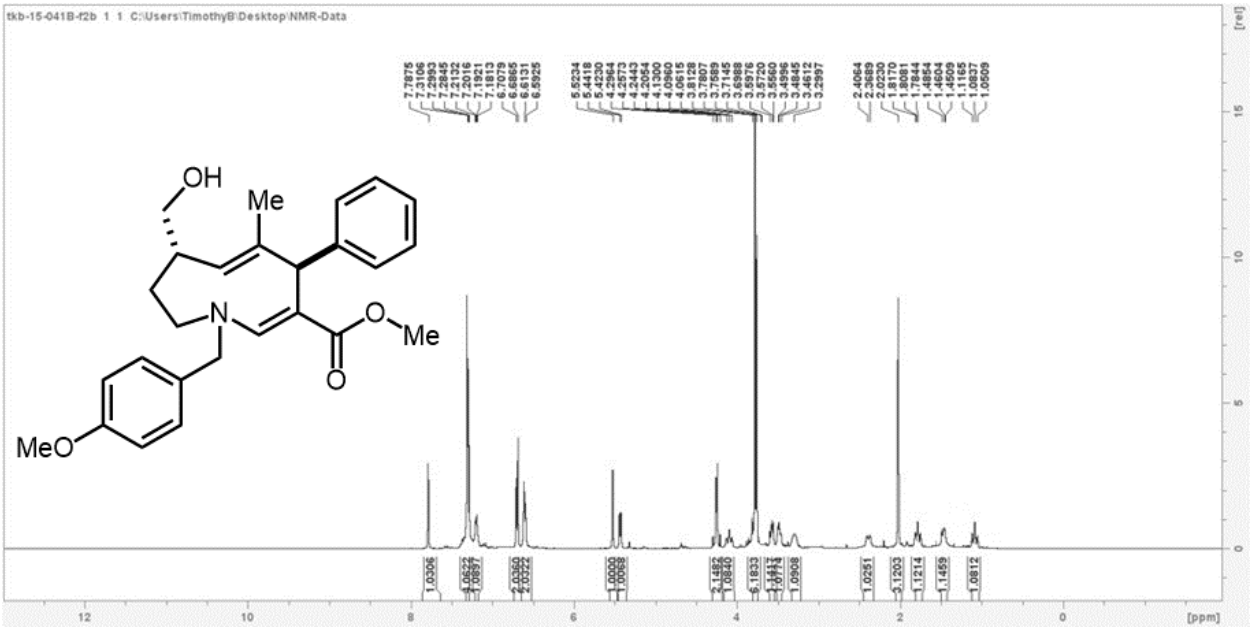


Compound 8s

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Amorphous solid. Yield = 396.2 mg, 94%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.31 – 7.19 (m, 5H), 6.73 – 6.66 (m, 2H), 6.60 (d, *J* = 8.2 Hz, 2H), 5.52 (s, 1H), 5.43 (d, *J* = 7.5 Hz, 1H), 4.32 – 4.18 (m, 2H), 4.10 (t, *J* = 13.9 Hz, 1H), 3.76 (s, 3H), 3.71 (s, 3H), 3.58 (dd, *J* = 10.3, 6.4 Hz, 1H), 3.48 (t, *J* = 8.2 Hz, 1H), 3.30 (s, 1H), 2.39 (d, *J* = 15.1 Hz, 1H), 2.02 (s, 3H), 1.78 (tt, *J* = 13.0, 3.1 Hz, 1H), 1.66 (s, 1H), 1.49 –1.45 (m, 1H), 1.09 (td, *J* = 13.1, 6.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.59, 158.89, 151.93, 136.59, 129.21, 128.57, 128.45, 128.03, 127.60, 125.18, 113.91, 68.09, 60.70, 55.27, 51.55, 46.07, 35.77, 30.78. **HRMS-EI$^+$** (*m/z*): calc for $C_{26}H_{31}NO_4$ $[M]^+$ 421.2253, found 421.2258.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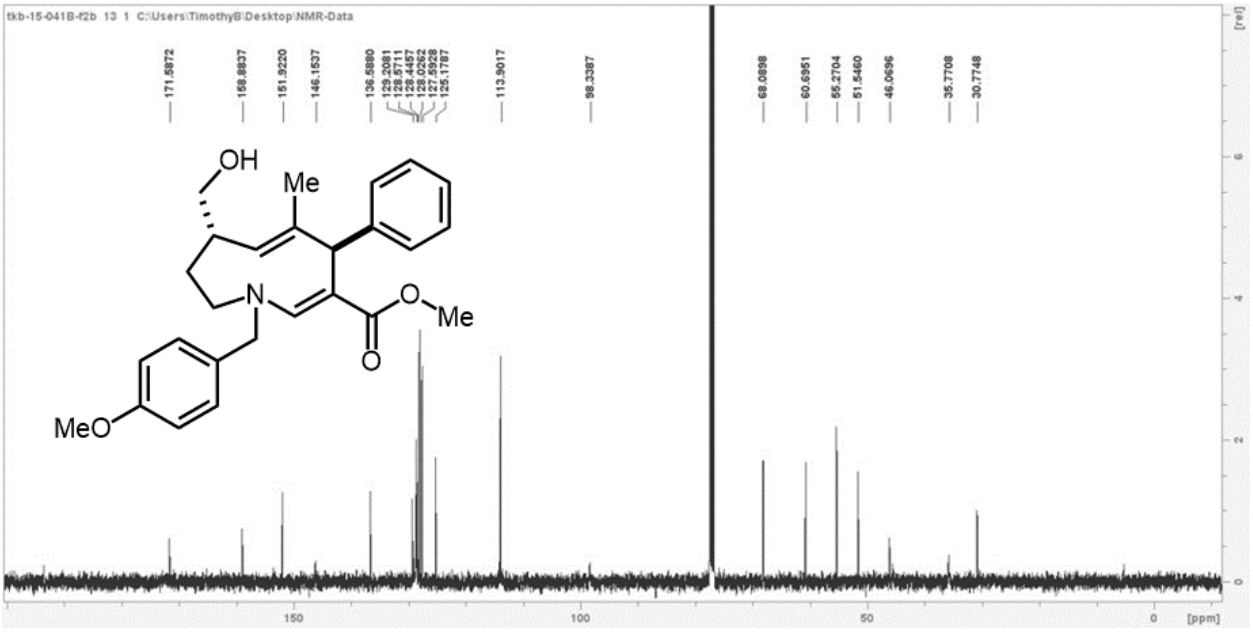
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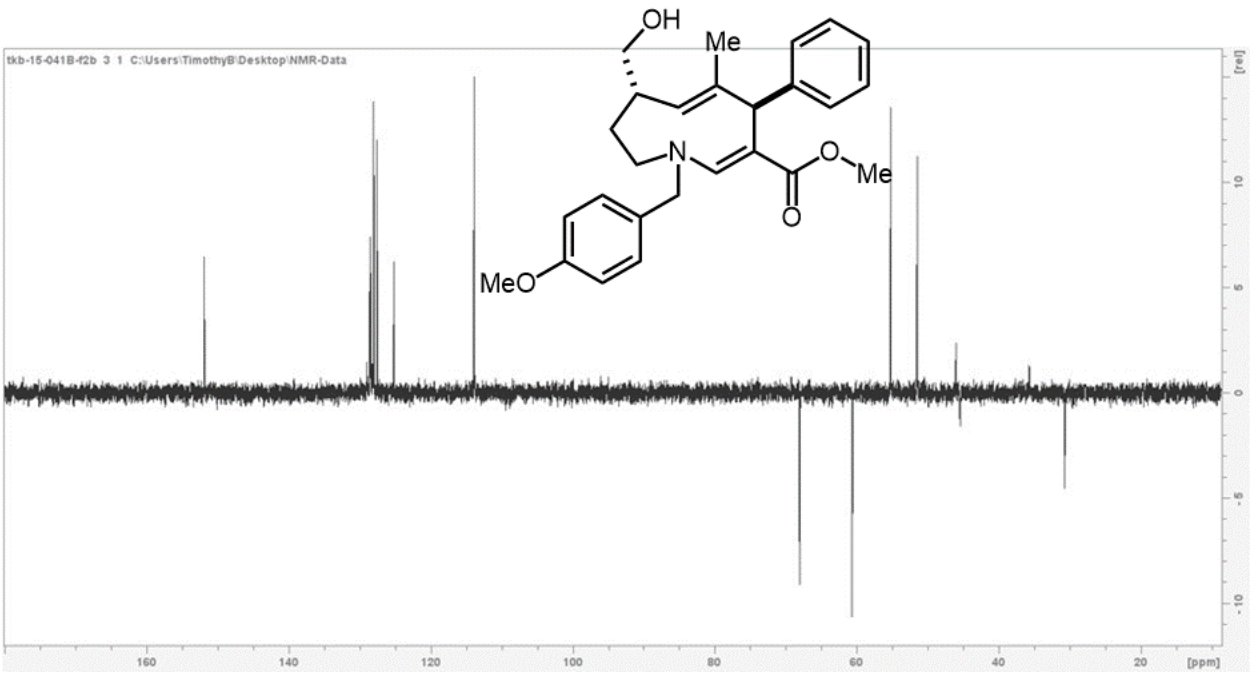
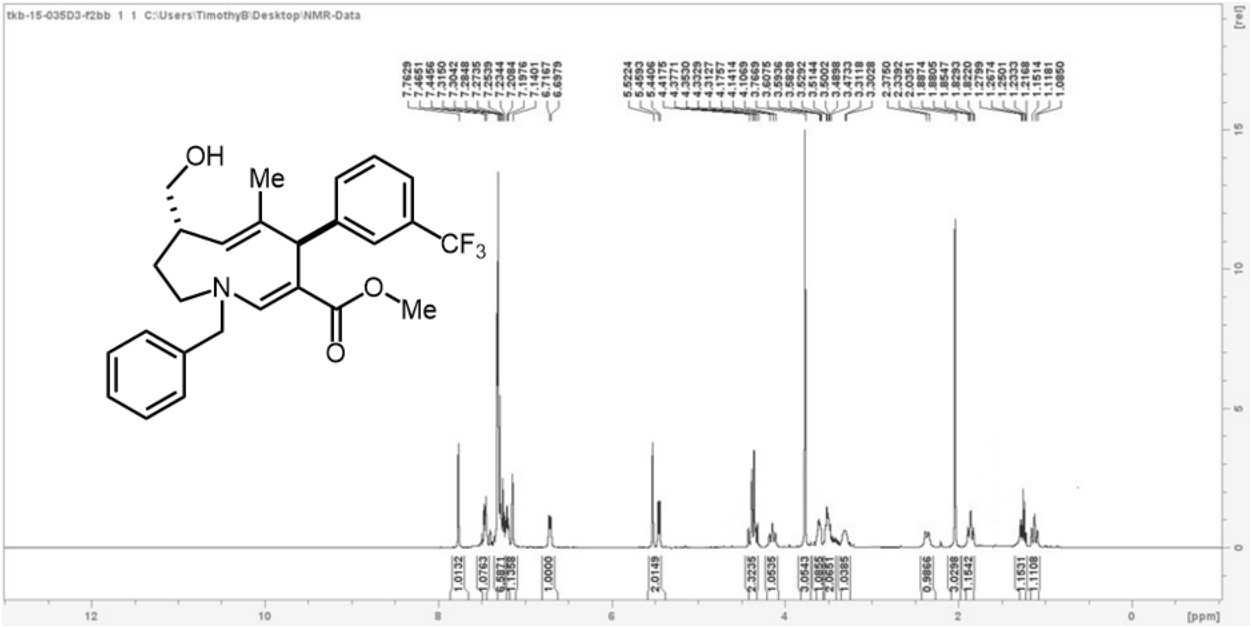


Compound 8t

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 390.6 mg, 85%, 90:10 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.45 – 7.41 (m, 1H), 7.31 – 7.20 (m, 6H), 7.14 (s, 1H), 6.71 (d, *J* = 7.7 Hz, 1H), 5.52 (s, 1H), 5.45 (d, *J* = 7.2 Hz, 1H), 4.44 – 4.27 (m, 2H), 4.14 (t, *J* = 14.0 Hz, 1H), 3.77 (s, 3H), 3.66 – 3.52 (m, 2H), 3.57 – 3.37 (m, 2H), 3.48 – 3.30 (m, 1H), 2.36 (d, *J* = 15.1 Hz, 1H), 2.04 (s, 3H), 1.85 (tt, *J* = 13.2, 3.3 Hz, 1H), 1.28 – 1.19 (m, 1H), 1.12 (tt, *J* = 13.0, 2.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.38, 151.61, 145.72, 138.52, 136.58, 129.56, 129.14, 128.44, 128.35, 128.24, 128.22, 128.13, 126.35, 125.41, 124.30, 124.26, 123.27, 123.23, 99.54, 68.04, 60.59, 51.65, 46.00, 35.73, 30.54, 27.89, 15.30. **HRMS-EI^{+}** (*m/z*): calc for $C_{26}H_{28}F_3NO_3$ $[M]^+$ 459.2021, found 459.2027.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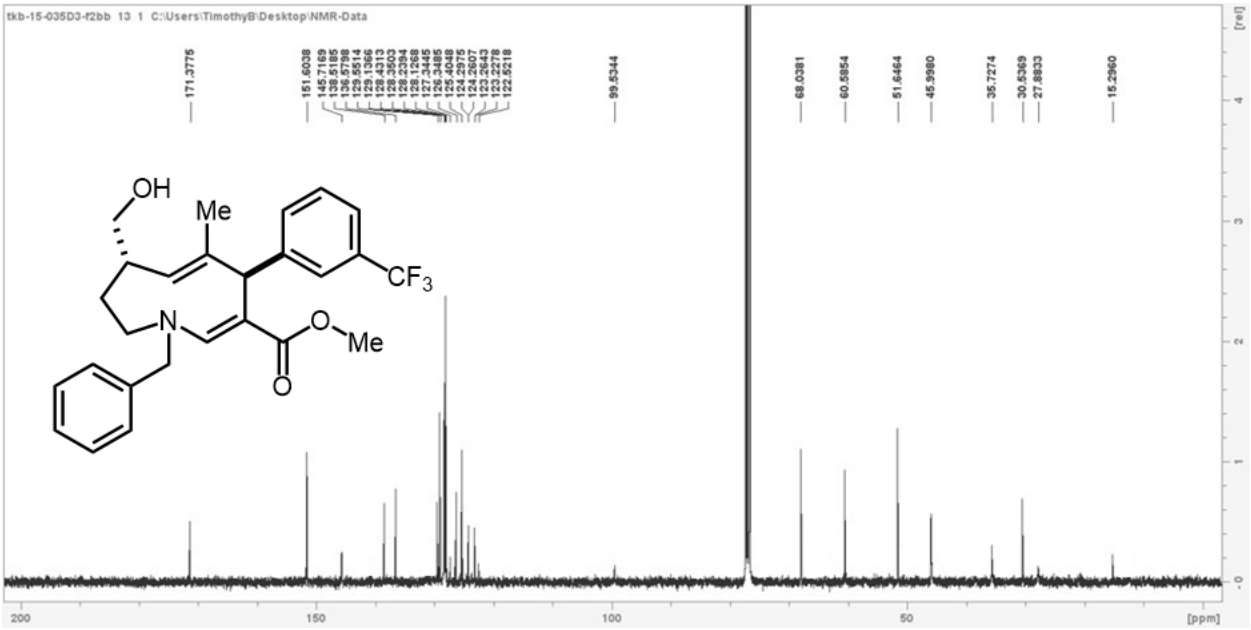
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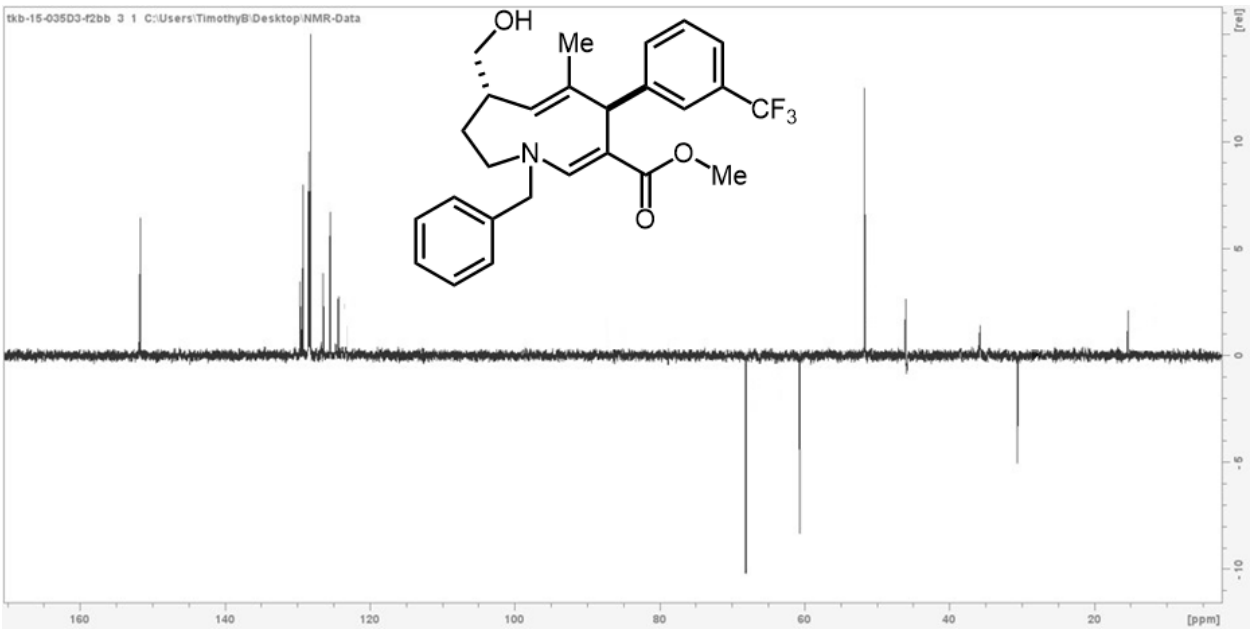
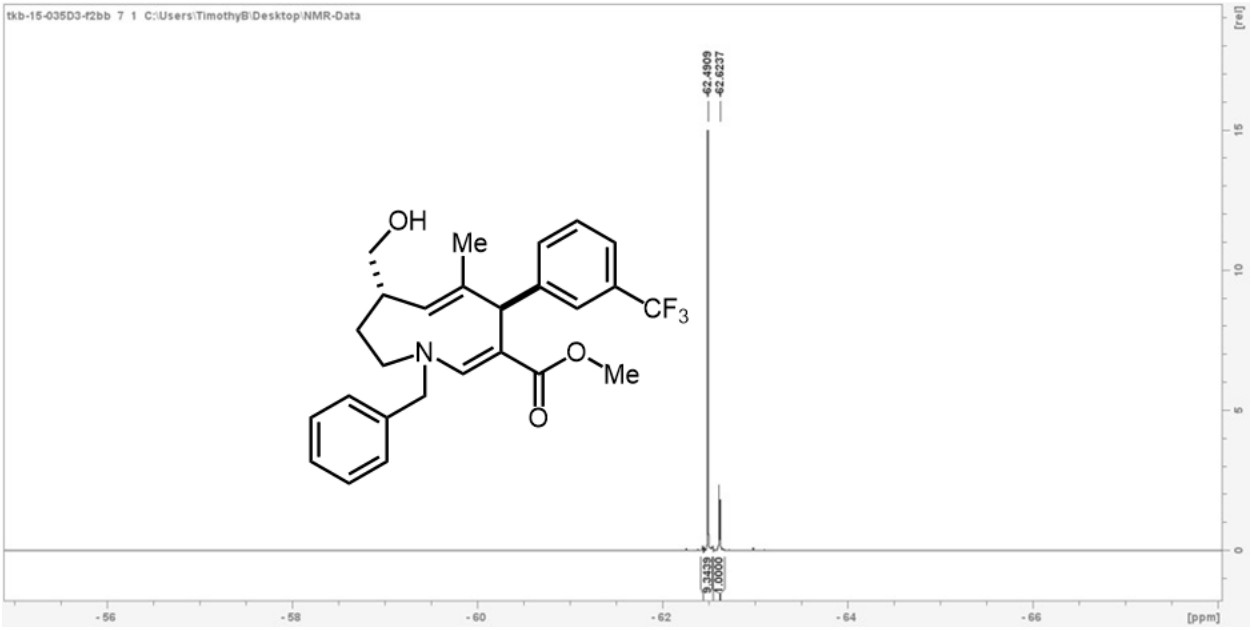


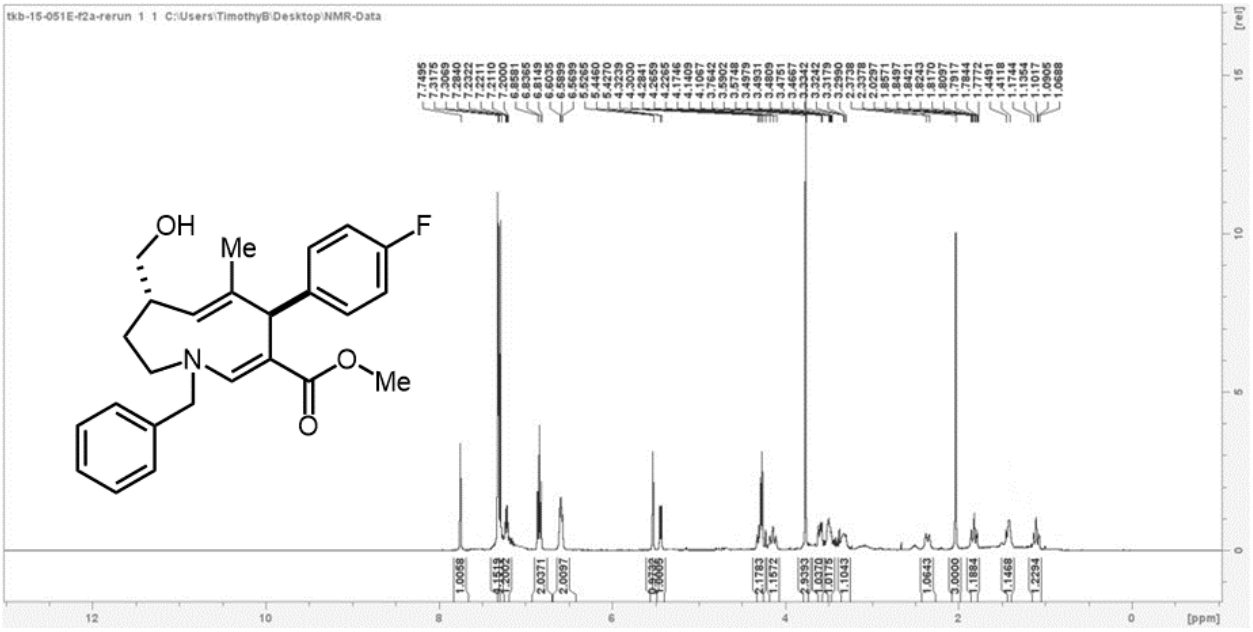
^{19}F NMR

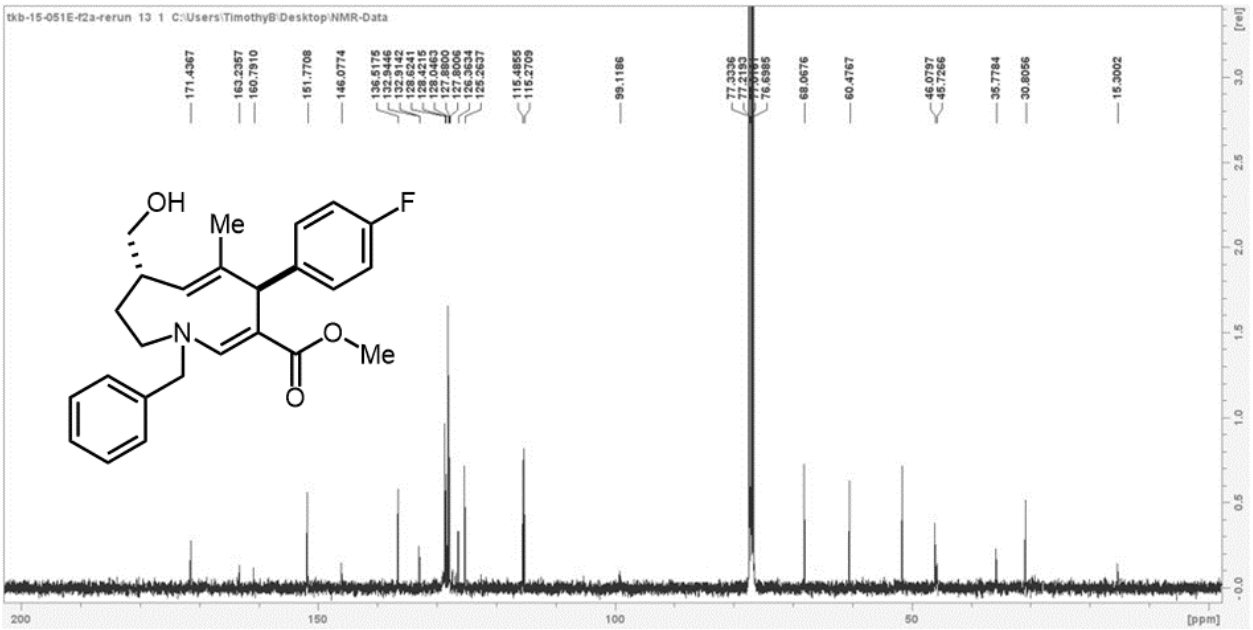


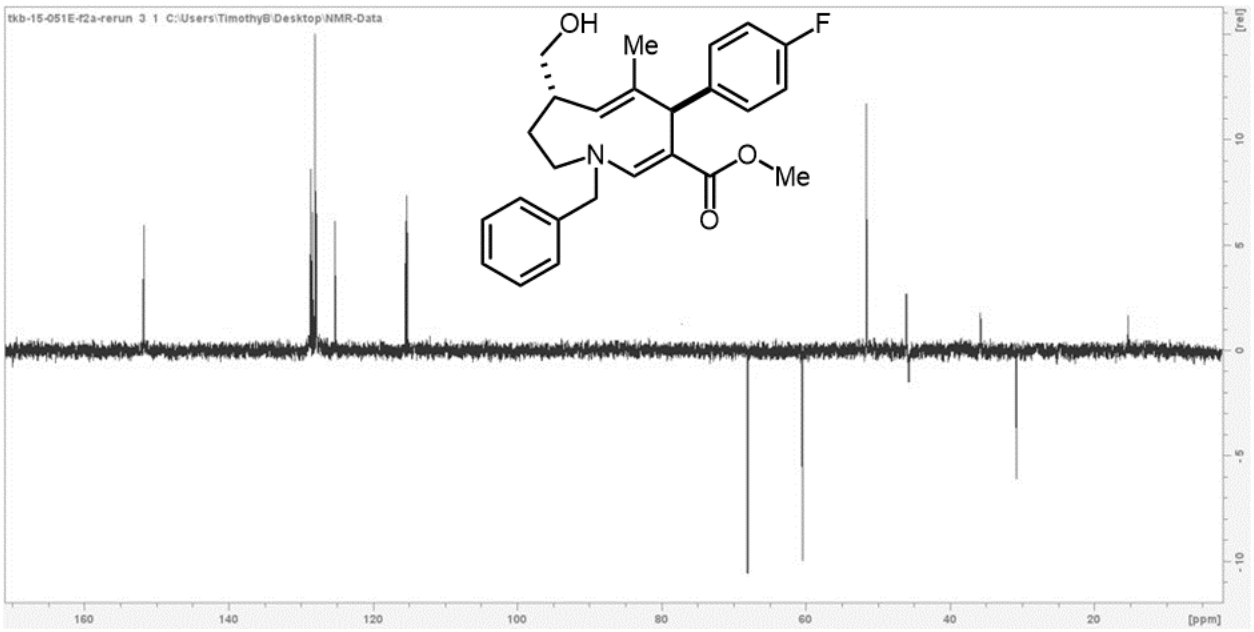
Compound 8u

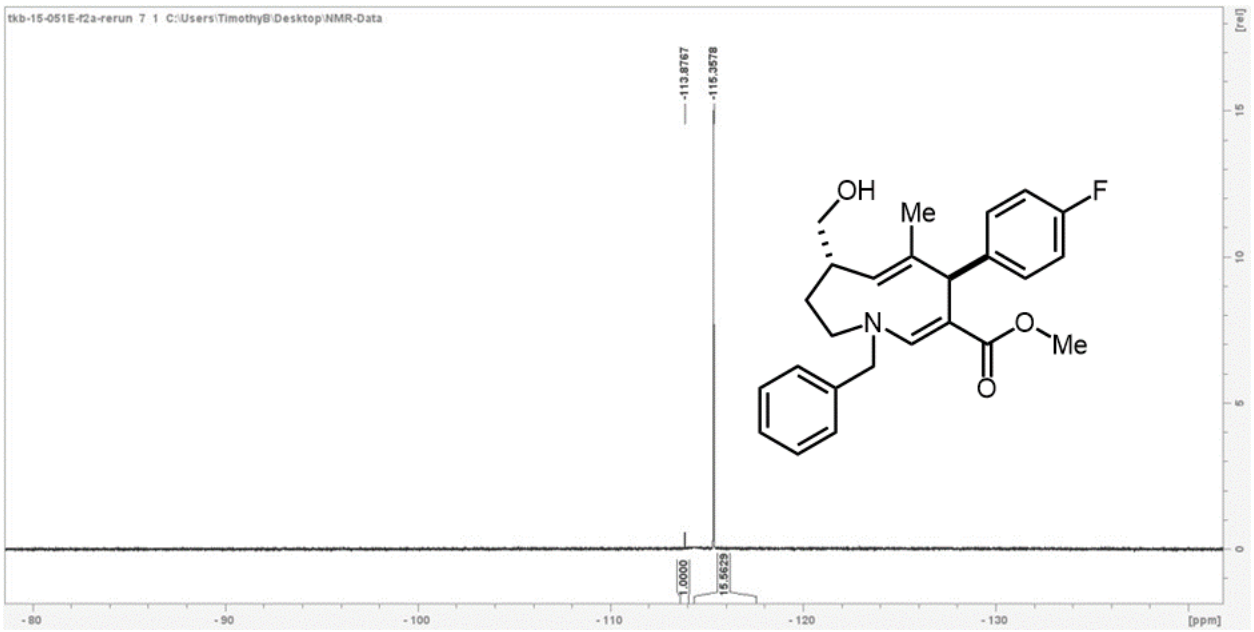
Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 372.6 mg, 91%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.32 – 7.20 (m, 5H), 6.89 – 6.78 (m, 2H), 6.59 (dd, *J* = 8.4, 5.2 Hz, 2H), 5.53 (s, 1H), 5.44 (dt, *J* = 7.6, 1.3 Hz, 1H), 4.35 – 4.20 (m, 2H), 4.14 (t, *J* = 13.8 Hz, 1H), 3.76 (s, 3H), 3.68 (d, *J* = 1.7 Hz, 1H), 3.64 – 3.56 (m, 1H), 3.49 (br s,

1H), 3.56 – 3.35 (m, 1H), 2.36 (d, *J* = 15.0 Hz, 1H), 2.02 (s, 3H), 1.82 (tt, *J* = 13.0, 3.1 Hz, 1H), 1.45 – 1.41 (m, 1H), 1.21 – 1.04 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.44, 163.24, 160.79, 151.78, 146.08, 136.52, 128.63, 128.43, 128.05, 127.88, 127.80, 125.27, 115.49, 115.27, 68.07, 60.48, 51.60, 46.08, 45.73, 35.78, 30.81, 15.31. **HRMS-EI**$^+$ (*m/z*): calc for $C_{25}H_{28}FNO_3$ $[M]^+$ 409.2053, found 409.2060.





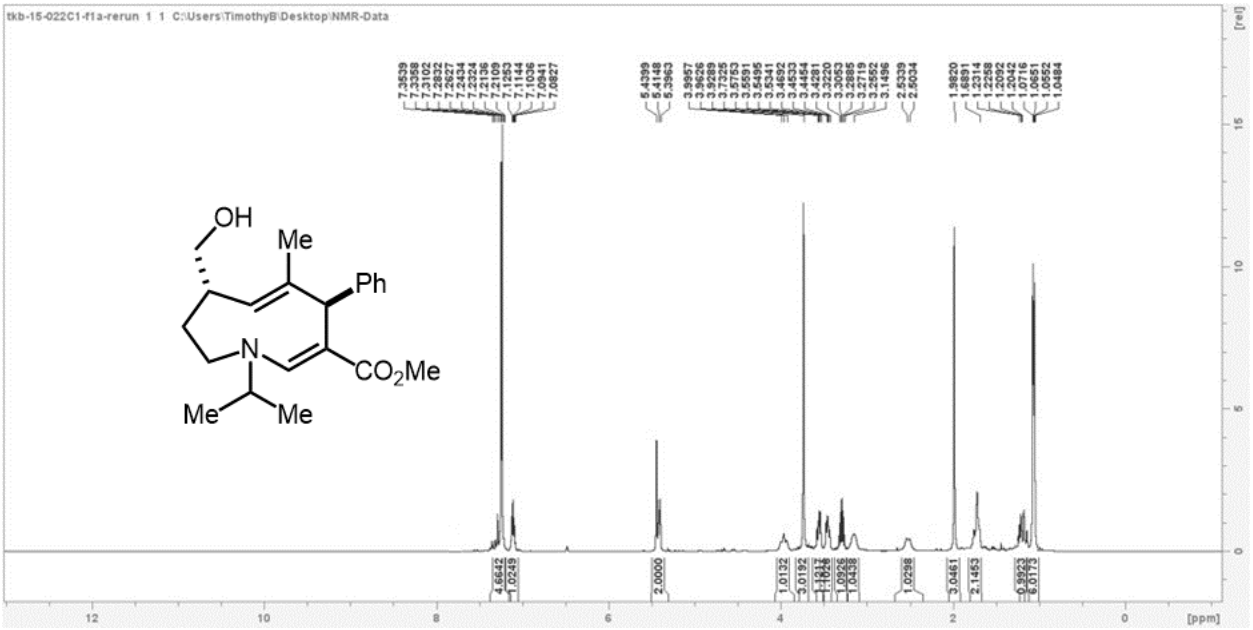


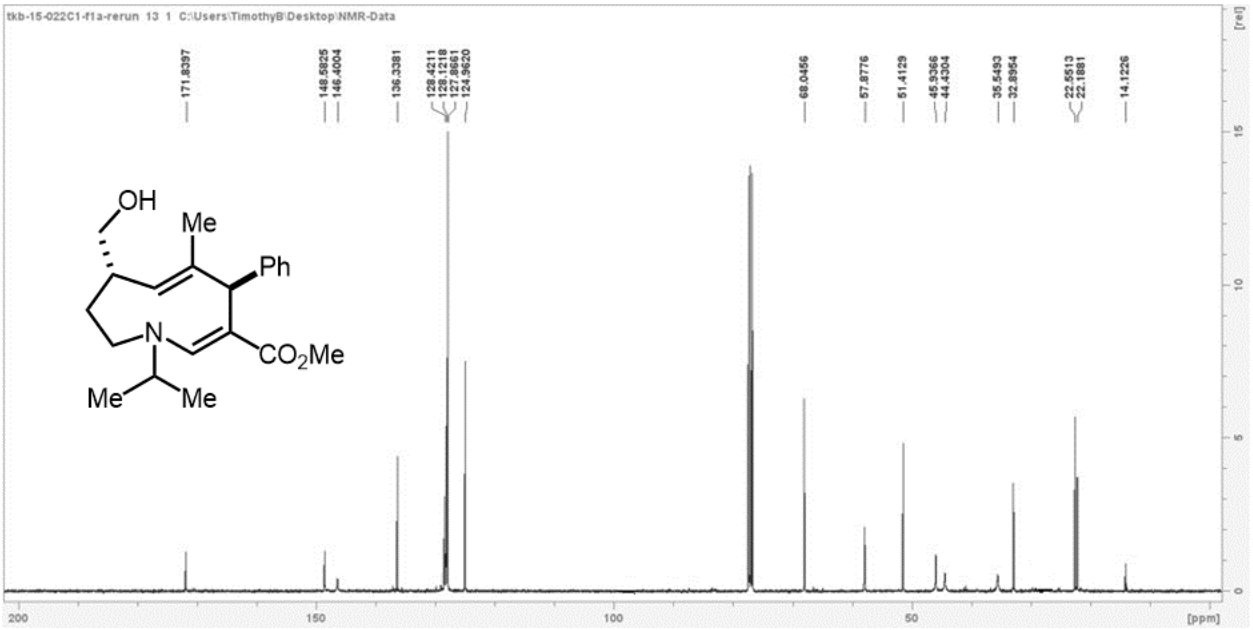


Compound 8v

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Amorphous solid. Yield = 291.9 mg, 85%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 4.4 Hz, 4H), 7.10 (dh, *J* = 7.7, 4.1 Hz, 1H), 5.46 – 5.37 (m, 2H), 3.96 (t, *J* = 14.0 Hz, 1H), 3.73 (s, 3H), 3.55 (dd, *J* = 10.3, 6.3 Hz, 1H), 3.45 (dd, *J* = 10.3, 6.4 Hz, 1H), 3.29 (hept, *J* = 6.9 Hz, 1H), 3.20 – 3.12 (m, 1H), 2.52 (d, *J* = 15.3 Hz,

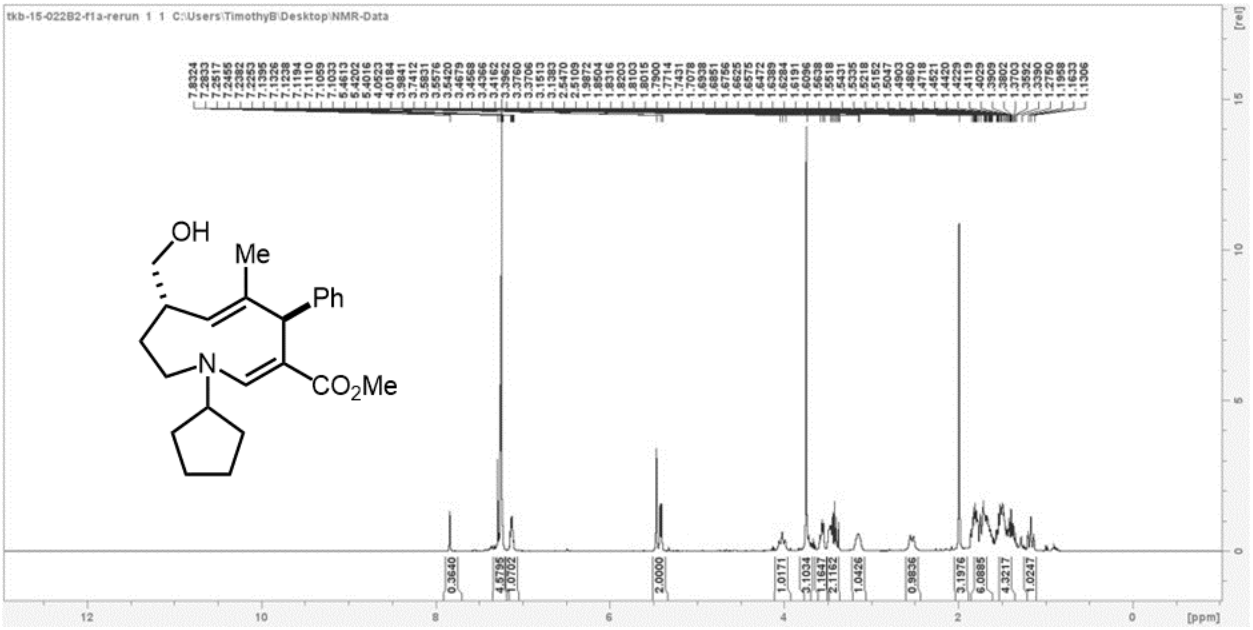
1H), 1.98 (s, 3H), 1.72 (tt, J = 12.7, 3.1 Hz, 2H), 1.23 – 1.20 (m, 2H), 1.07 – 1.05 (dd, 6H). **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{29}NO_3$ $[M]^+$ 343.2147, found 343.2142.





Compound 8w

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Amorphous solid. Yield = 321.5 mg, 87%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.28 – 7.22 (m, 5H), 7.12 (tdd, *J* = 5.4, 4.3, 2.6 Hz, 1H), 5.46 (s, 1H), 5.41 (dt, *J* = 7.4, 1.3 Hz, 1H), 4.02 (t, *J* = 14.0 Hz, 1H), 3.74 (s, 3H), 3.56 (dd, *J* = 10.4, 6.5 Hz, 1H), 3.43 (td, *J* = 19.3, 9.0 Hz, 2H), 3.15 (br. s, 1H), 2.53 (d, *J* = 15.0 Hz, 1H), 1.99 (s, 3H), 1.85 – 1.61 (m, 6H), 1.56 – 1.27 (m, 4H), 1.16 (tt, *J* = 13.1, 2.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.79, 148.86, 146.24, 136.61, 128.46, 128.18, 127.90, 124.98, 68.14, 67.47, 51.46, 45.96, 35.62, 32.41, 32.11, 32.06, 32.03, 29.88, 23.67, 23.42. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{31}NO_3$ $[M]^+$ 369.2304, found 369.2308.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10
8
6
4
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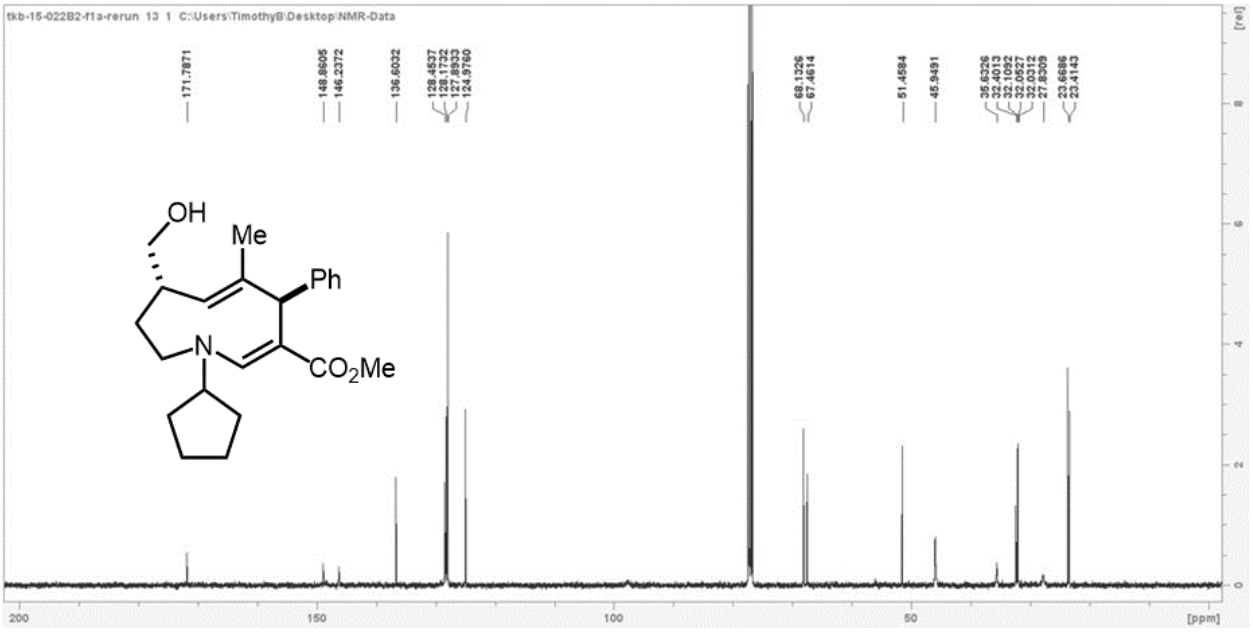
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124.9760
68.1326
67.4614
51.4584
45.9491
35.6326
32.4013
32.1092
32.0527
32.0312
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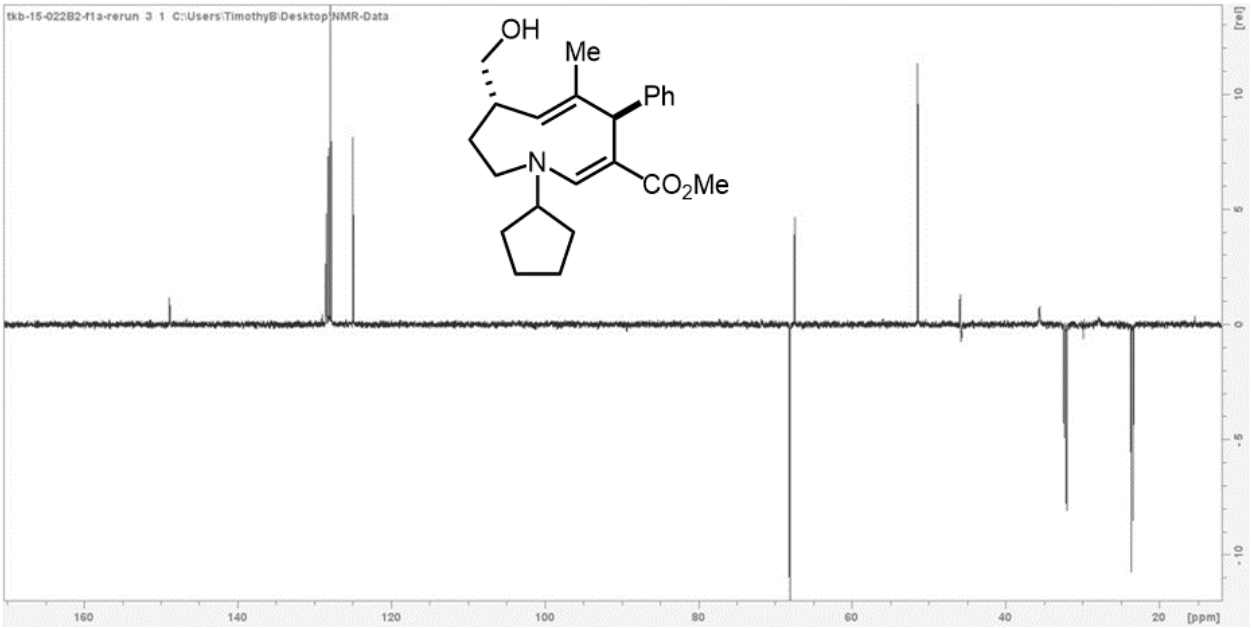
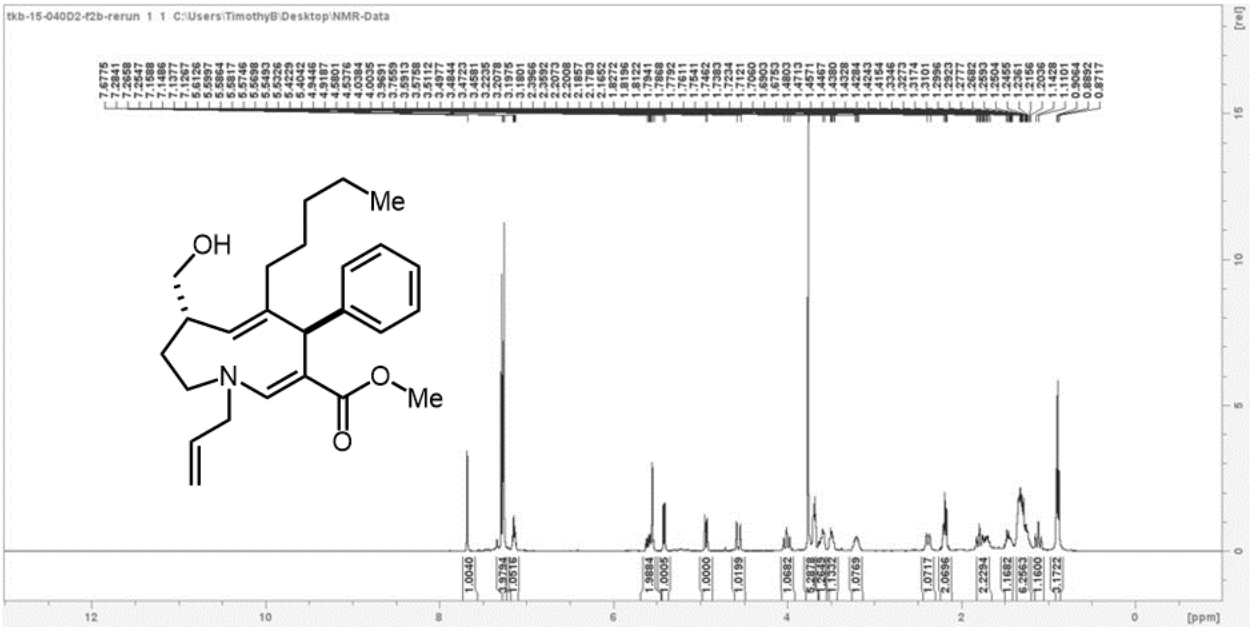
[ppm]



Compound 8x

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Light orange oil. Yield = 334.0 mg, 84%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.26 (d, *J* = 4.4 Hz, 4H), 7.14 (p, *J* = 4.3 Hz, 1H), 5.65 – 5.55 (m, 2H), 5.41 (d, *J* = 7.5 Hz, 1H), 4.93 (dt, *J* = 10.4, 1.7 Hz, 1H), 4.56 (d, *J* = 17.1 Hz, 1H), 4.00 (t, *J* = 13.9 Hz, 1H), 3.76 (s, 3H), 3.80 – 3.54 (m, 4H), 3.48 (dt, *J* = 9.2, 5.5 Hz, 1H), 3.24 – 3.15 (m, 1H), 2.38 (d, *J* = 15.0 Hz, 1H), 2.25 – 2.11 (m, 2H), 1.85 – 1.65 (m, 2H), 1.53 – 1.39 (m, 1H), 1.38 – 1.19 (m, 6H), 1.11 (tt, *J* = 13.1, 2.5 Hz, 1H), 0.89 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.62, 151.41, 146.57, 141.75, 133.50, 128.36, 127.97, 127.81, 125.10, 116.35, 97.67, 68.20, 59.53, 51.44, 45.72, 44.30, 35.32, 31.87, 30.69, 30.21, 22.58, 14.13. **HRMS-EI^{+}** (*m/z*): calc for $C_{25}H_{35}NO_3$ $[M]^{+}$ 397.2617, found 397.2622.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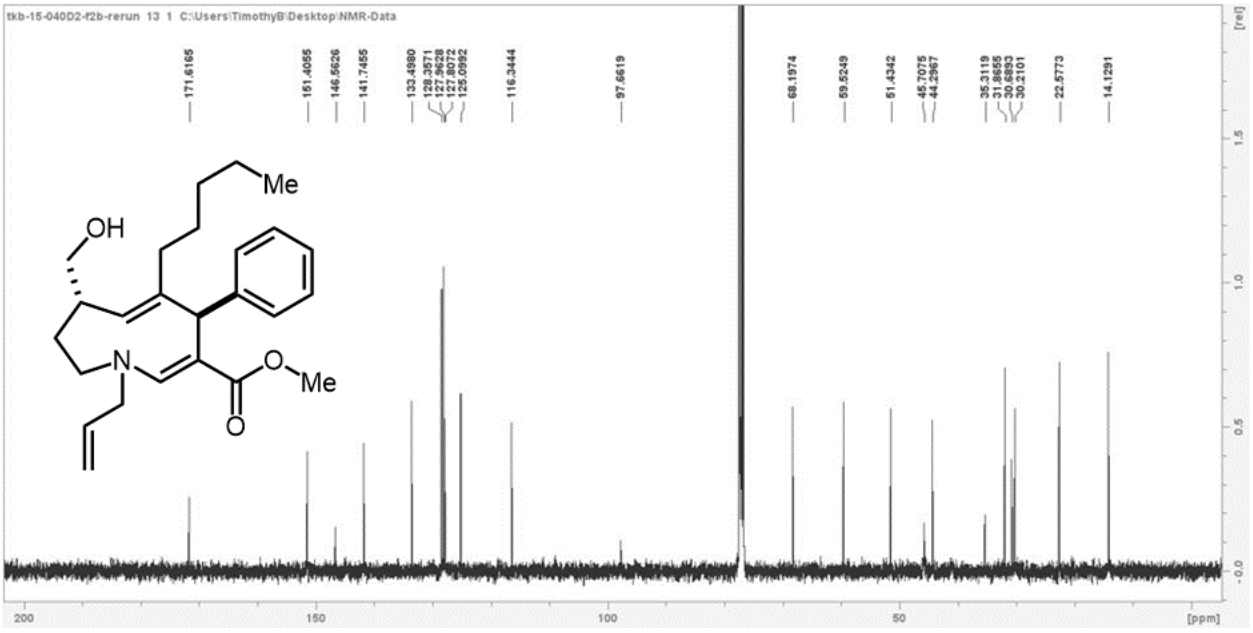
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44.2967
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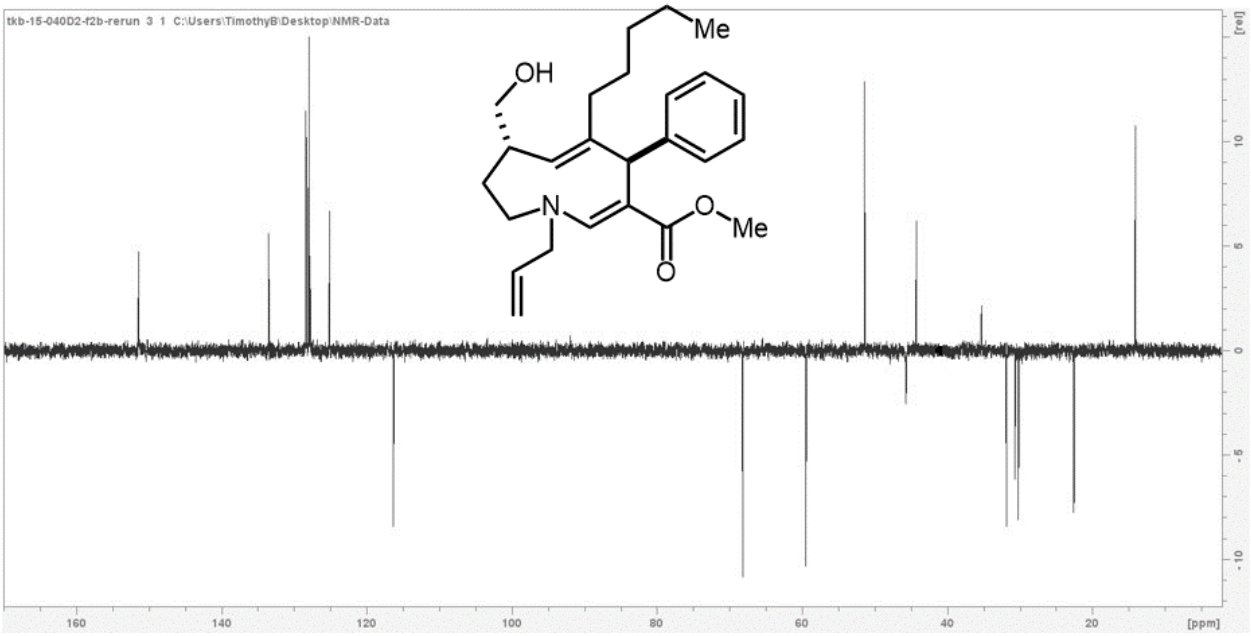
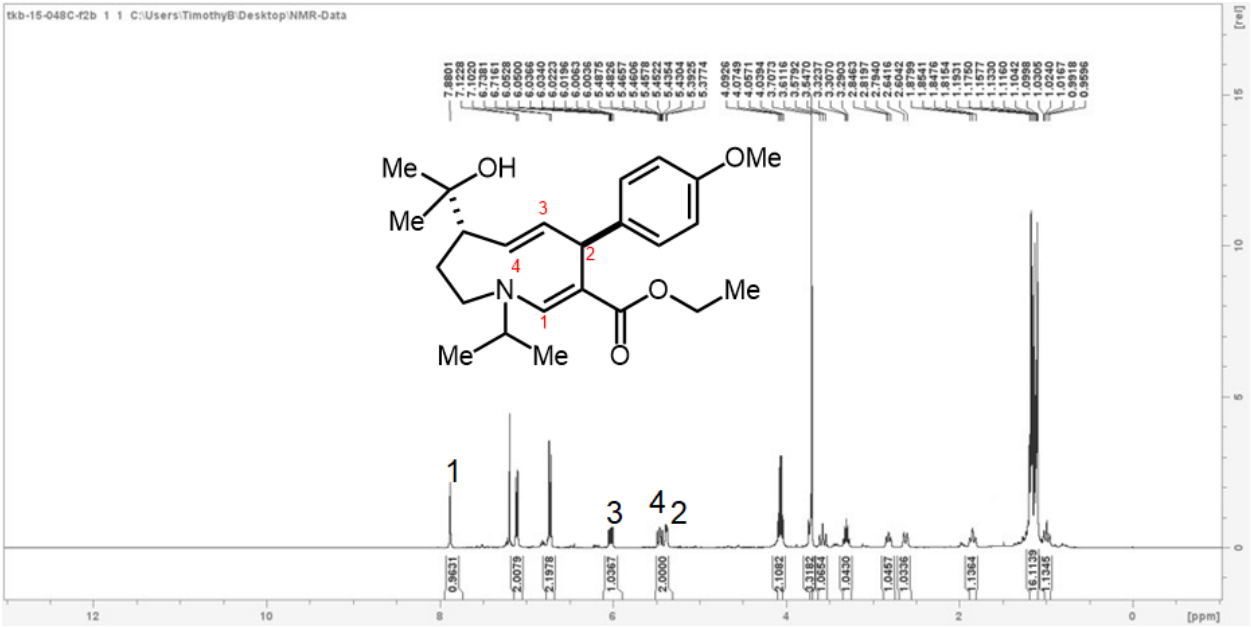


Compound 8y

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Greenish-yellow oil. Yield = 373.4 mg, 93%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.11 (d, *J* = 6.4 Hz, 2H), 6.72 (d, *J* = 6.4 Hz, 2H), 6.03 (dd, *J* = 12.1, 6.5 Hz, 1H), 5.46 (dd, *J* = 12.1, 8.7 Hz, 1H), 5.39 (d, *J* = 6.5 Hz, 1H), 4.07 (q, *J* = 7.1 Hz, 2H), 3.71 (s, 3H), 3.58 (ddd, *J* = 15.1, 12.7, 2.3 Hz, 1H), 3.31 (p, *J* = 6.7 Hz, 1H), 2.82 (t, *J* = 10.5 Hz, 1H), 2.62 (d, *J* = 15.0 Hz, 1H), 1.85 (td, *J* = 13.0, 6.6 Hz, 1H), 1.19 – 1.00 (m, 19H), 1.03 – 0.96 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.30, 157.22, 147.90, 138.81, 131.26, 127.84, 127.79, 113.50, 95.62, 72.27, 59.80, 57.76, 55.24, 45.44, 43.17, 40.29, 31.11, 28.46, 26.14, 23.01, 22.46, 14.63. **HRMS-EI^{+}** (*m/z*): calc for $C_{24}H_{35}NO_4$ $[M]^{+}$ 401.2566, found 401.2573.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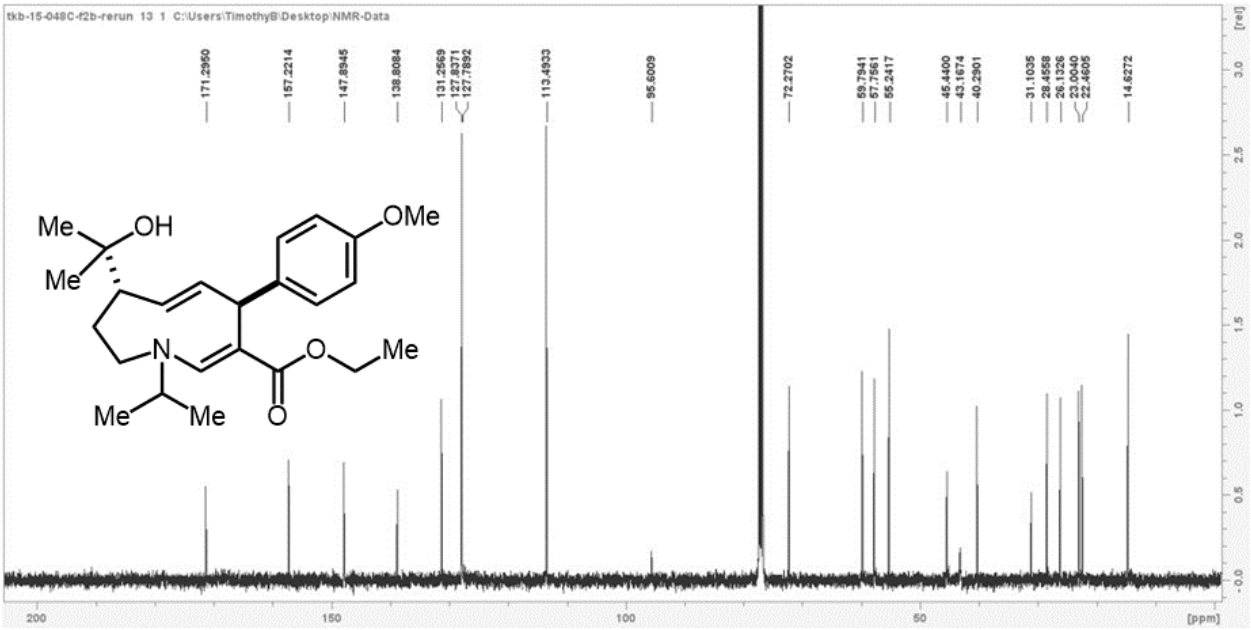
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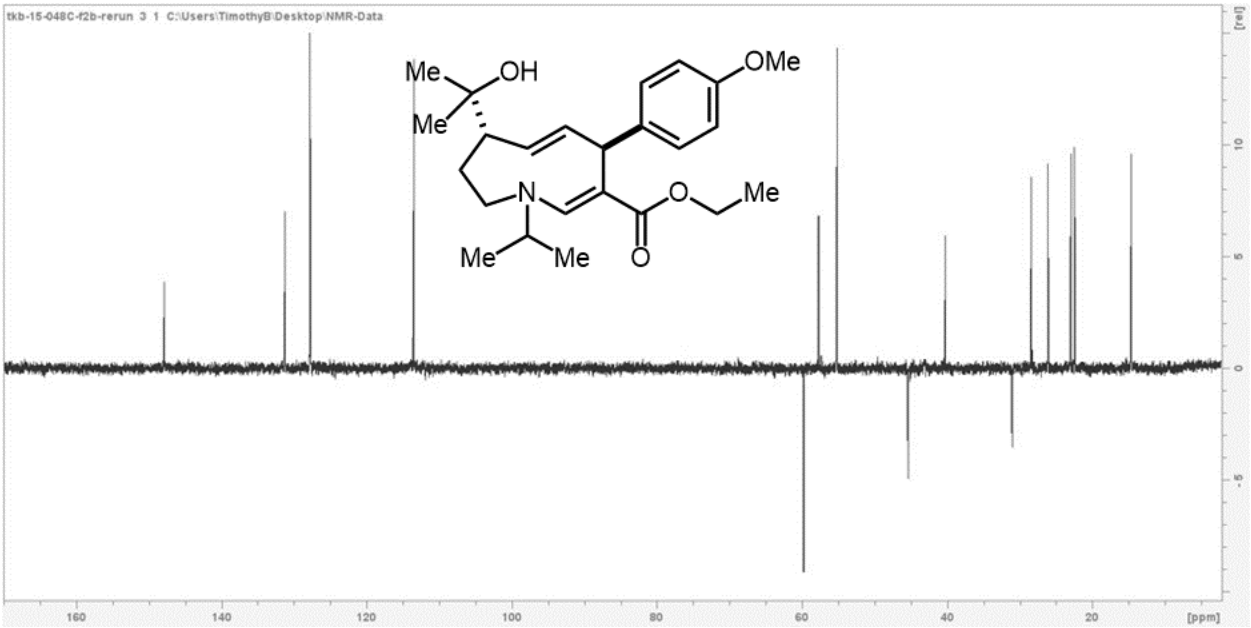
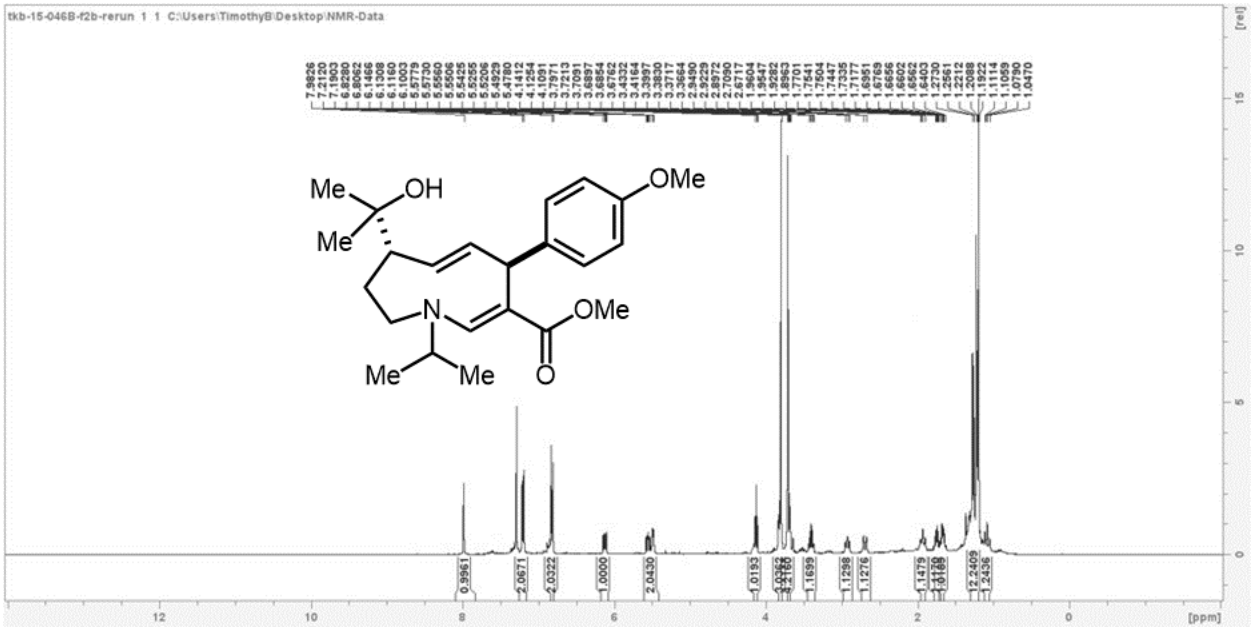


Compound 8z

Prepared in 1.0 mmol scale using **General Procedure E**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Greenish-yellow oil. Yield = 348.8 mg, 90%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.20 (d, *J* = 6.7 Hz, 2H), 6.81 (d, *J* = 6.7 Hz, 2H), 6.12 (dd, *J* = 12.3, 6.3 Hz, 1H), 5.60 – 5.46 (m, 2H), 4.22 – 4.09 (m, 1H), 3.80 (s, 3H), 3.76 – 3.62 (m, 4H), 3.40 (p, *J* = 6.7 Hz, 1H), 2.92 (t, *J* = 10.6 Hz, 1H), 2.69 (d, *J* = 14.7 Hz, 1H), 1.93 (tt, *J* = 12.9, 3.1 Hz, 1H), 1.81 – 1.60 (m, 1H), 1.30 – 1.13 (m, 12H), 1.16 – 1.02 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.73, 157.25, 148.15, 138.69, 131.17, 127.83, 113.52, 72.25, 57.82, 55.24, 51.43, 45.40, 40.39, 29.13, 28.44, 26.15, 25.10, 23.03, 22.47. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{33}NO_4$ $[M]^{+}$ 387.2410, found 387.2415.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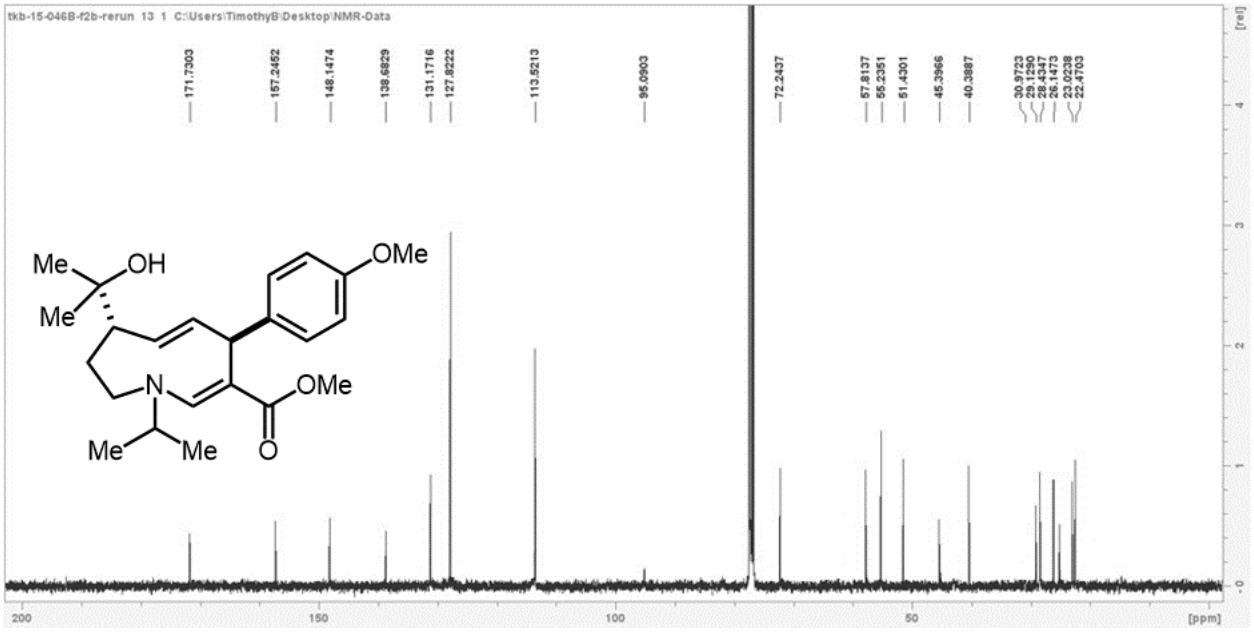
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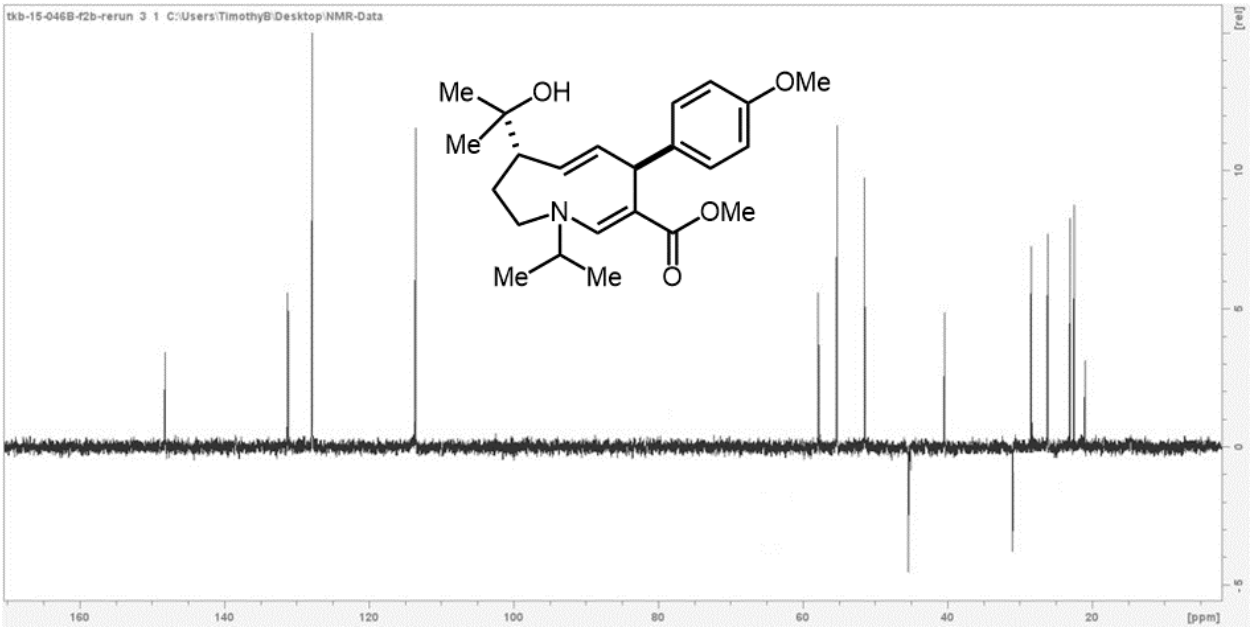

References

(1) H. Braunstein, S. Langevin, M. Khim, J. Adamson, K. Hovenkotter, L. Kotlarz, B. Mansker, T. K. Beng; *Org. Biomol. Chem.* 2016, **14**, 8864.
(2) I. S. Anosike and T. K. Beng, *RSC Adv.,* 2024, **14**, 18501-18507.