Supporting Information for:

Leveraging the 1,3-azadiene-anhydride reaction for the synthesis of functionalized piperidines bearing up to five contiguous stereocenters

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Contents:

1. General Experimental Information and Procedures S2

2. Scheme 1 results (1,3-azadiene-anhydride reaction) S5

3. Scheme 2 results (Formation of activated enamines) S50

4. Scheme 3 results (Halolactonization) S80

5. Scheme 4 results (Cascade epoxy-amidation and epoxy-esterification) S95

6. Scheme 5 results (Reduction and CCR with phenylsuccinic anhydride) S106

7. Scheme 6 results (Denitrative alkenylation) S112

8. Scheme 7 results (Catalytic alkynylation of chloroenamines) S119

9. References S126

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 1,4-dioxane was stored under 4 A^{o} molecular sieves for several days prior to use. THF was distilled from sodium benzophenone ketyl. All amines, alkenes and enals 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) or CAM, *p*-anisaldehyde, or $KMnO_4$ stain. All reported temperatures were internal to a reaction vessel. Unless otherwise indicated, ^{1}H, ^{13}C, and DEPT-135 spectra were acquired using $CDCl_3$ 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). Brine solutions are saturated solutions of aqueous sodium chloride. Representative GC-MS traces are provided.

General Procedure A: Reaction of 1,3-azadienes[1] with anhydride 1c: 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 2-MeTHF) was added to the vial at room temperature followed by anhydride **1c** (5 mmol, 1.0 equiv). The contents were placed in a pre-heated oil bath thermostatted 80 ^{o}C. After complete consumption of the 1,3-azadiene (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 lactam acid.

Methyl esterification of the lactam acid: To a stirring suspension of the acid (1 mmol), dissolved in DMF (5 mL), and K_2CO_3 (3 equiv) was added methyl iodide (2 equiv) under a nitrogen atmosphere. The reaction mixture was stirred for 12 h (TLC monitoring). After complete conversion, it was diluted with water and extracted with EtOAc (2×10 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 B: Vilsmeier-Haack functionalization[2]: To a solution of DMF (4 mmol, 4 equiv) in CH_2Cl_2 (5 mL) at 0 ^oC was added dropwise, phosphorus oxychloride (2 mmol, 2 equiv). The resulting pale yellow mixture was refluxed for 60 min. A solution of the lactam ester (1.0 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 GC-MS monitoring was used to follow the extent of the reaction). Upon completion, the mixture was poured into a flask containing crushed ice. After stirring at room temperature for 60 min, the layers were separated (the majority of the product stays in the DCM layer). Powdered K_2CO_3 was added slowly to the aqueous layer 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 two times with CH_2Cl_2. The combined organic layers (three in total, one *before* and two after addition of K_2CO_3) were washed with brine and dried over Na_2SO_4 for 30 min. The mixture was filtered and concentrated under reduced pressure to give the desired product as an oily salt, which was immediately subjected to flash chromatography on silica pretreated with 1% Et_3N.

General Procedure C: *6-endo*-halolactonization of 3: The lactam-bearing alkenoic acid (0.5 mmol, 1 equiv) was charged (in air) in an oven-dried 10 mL screw-cap vial equipped with a stir bar and DCM (2 mL) was added. Then, NBS (98 mg, 0.55 mmol, 1.1 equiv) were added. The reaction mixture was stirred at room temperature until TLC and GC-MS showed full conversion. Then, the reaction mixture was diluted with DCM (10 mL) and quenched with 10% aqueous sodium sulfite (5 mL). The layers were separated and the aqueous layer was extracted once with DCM. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to give the desired lactam-lactone, which was purified by flash chromatography on silica.

General Procedure D: *5-exo*-bromolactonization of 3c: The lactam-bearing alkenoic acid (0.5 mmol, 1 equiv) was charged (in air) in an oven-dried 10 mL screw-cap vial equipped with a stir bar and DMF (2 mL) was added. Then, NBS (98 mg, 0.55 mmol, 1.1 equiv) were added. The reaction mixture was stirred at room temperature until TLC and GC-MS showed full conversion. Then, the reaction mixture was diluted with EtOAc (10 mL) and quenched with 10% aqueous sodium sulfite (5 mL). The layers were separated and the aqueous layer was extracted once with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and

concentrated *in vacuo* to give the desired lactam-lactone, which was purified by flash chromatography on silica.

General Procedure E: Deconstructive epoxy-amidation and epoxy-esterification: To an oven-dried 5 mL screw-cap vial equipped with a stir bar dissolved lactam-bromolactone **5** (0.25 mmol, 1 equiv) in DMF (2 mL). Cs_2CO_3 (0.75 mmol, 3 equiv) and the corresponding nucleophile (0.50 mmol, 2 equiv) were added. The reaction mixture was stirred at room temperature until TLC and GC-MS showed full conversion (~18 h). Then, the reaction mixture was diluted with EtOAc (10 mL) and washed successively with water and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the desired product, which was purified by flash chromatography on silica.

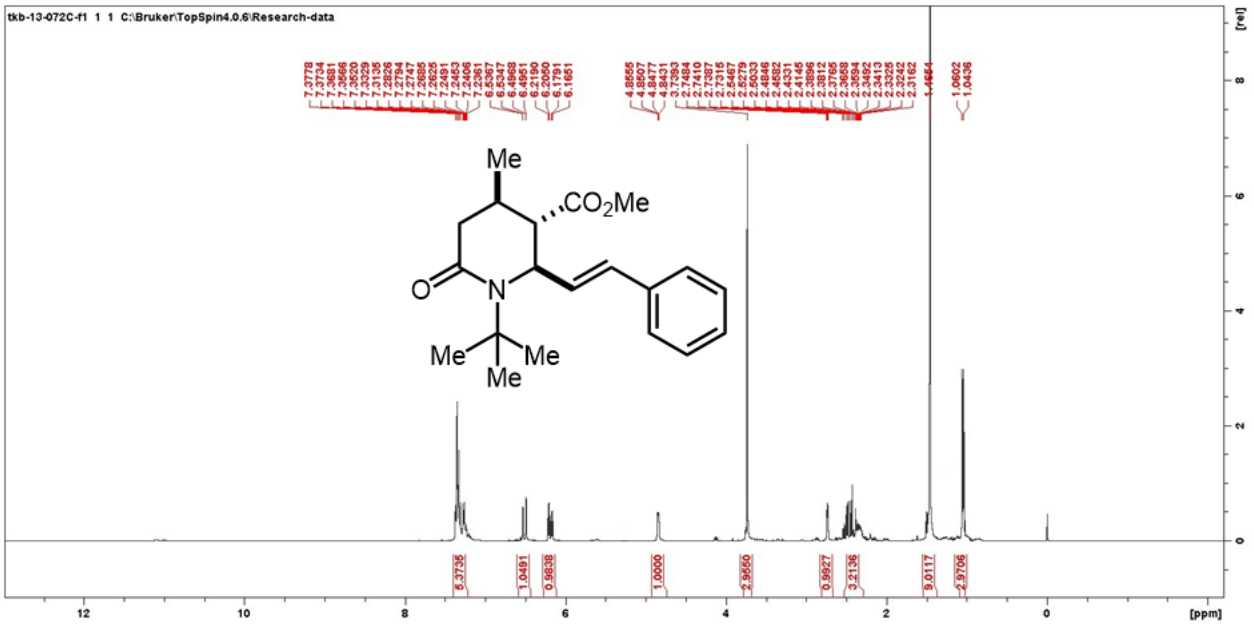
General Procedure F: Catalytic hydrogenation: EtOAc (10 mL) was added to a flask containing 10% Pd/C (100 mg) at room temperature. The flask was degassed and placed under an inert atmosphere of nitrogen. A solution of the unsaturated lactam in EtOAc (10 mL) was added. After complete addition, the nitrogen line was cut off and then replaced with a balloon of hydrogen. After complete consumption of the unsaturated lactam (based on LC-MS and TLC monitoring), the mixture was filtered through a plug of Celite and concentrated under reduced pressure.

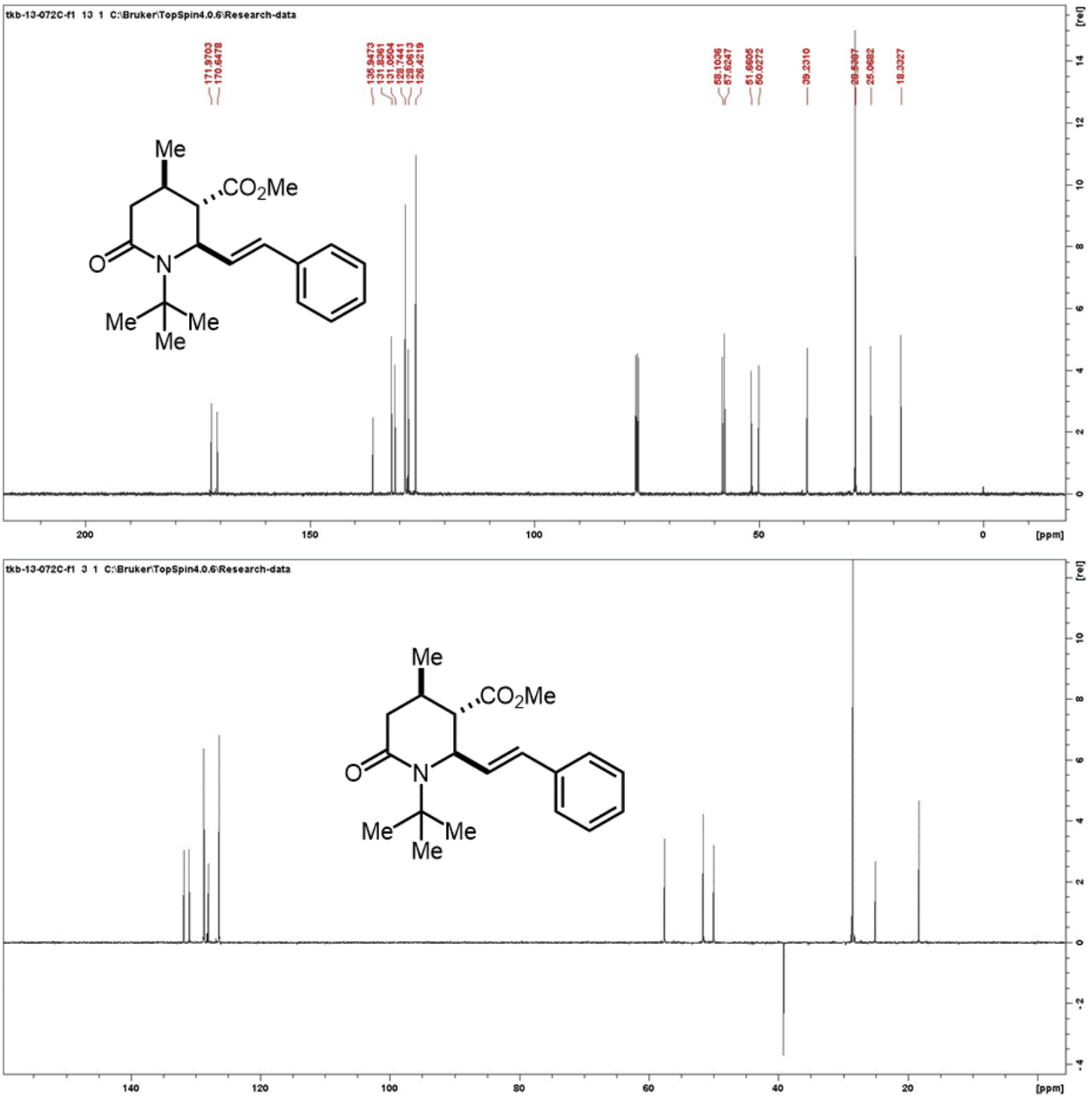
General Procedure G: Denitrative alkenylation: To an oven-dried tube equipped with a magnetic stirring bar were added sequentially nitroarene **3c11** (0.5 mmol) in 2-MeTHF (5.0 mL), the styrene derivative (0.75 mmol, 1.5 equiv), $Pd(acac)_2$ (7.5 mg, 5 mol%), Brettphos (53.5 mg, 20 mol%), and Rb_2CO_3 (0.3 mmol, 3 equiv) under N_2 atmosphere. The reaction mixture was stirred and heated at 100 °C for 18 h (TLC and GC-MS monitoring). The reaction mixture was cooled to room temperature, and then it was passed through a short pad of silica gel with EtOAc. The solution was concentrated *in vacuo* and immediately subjected to flash chromatography on silica pretreated with 1% Et_3N.

General Procedure H: Pd-catalyzed alkynylation[3]: To an oven dried Schlenk tube equipped with a stir bar was added the α-chloro enamine (0.25 mmol), dissolved in dioxane (1 mL), followed by 2,6-lupetidine (0.17 mL, 1.25 mmol, 5 equiv), CuI (5 mg, 0.025 mmol, 10 mol%) $PdCl_2(PhCN)_2$ (4.75 mg, 0.0125 mmol, 5 mol%) and the desired alkyne (0.50 mmol, 2 equiv), under nitrogen atmosphere. The reaction was stirred at room temperature until complete consumption of the enamine (GC-MS and TLC monitoring; typically 0.5 – 2 h).

Compound 3c1

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 263.6 mg, 80%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.23 (m, 5H), 6.52 (d, *J* = 15.9 Hz, 1H), 6.17 (dd, *J* = 16.0, 5.6 Hz, 1H), 4.85 (dd, *J* = 5.6, 2.7 Hz, 1H), 3.74 (s, 3H), 2.74 (dd, *J* = 4.3, 2.7 Hz, 1H), 2.55 – 2.31 (m, 3H), 1.47 (s, 9H), 1.07 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 170.7, 135.9, 131.8, 131.0, 128.8, 128.1, 126.4, 58.1, 57.6, 51.7, 50.0, 39.2, 28.5, 25.1, 18.3. **HRMS-EI^{+}** (*m/z*): calc for $C_{20}H_{27}NO_3$, 329.1991, found 329.1996. FTIR (KBr): 2976.0, 2927.2, 1721.7, 1650.1, 1492.0, 1438.4, 1362.2, 1320.5, 1290.1, 1206.3, 1180.3, 1146.7, 1132.3, 995.8, 918.8, 700.1

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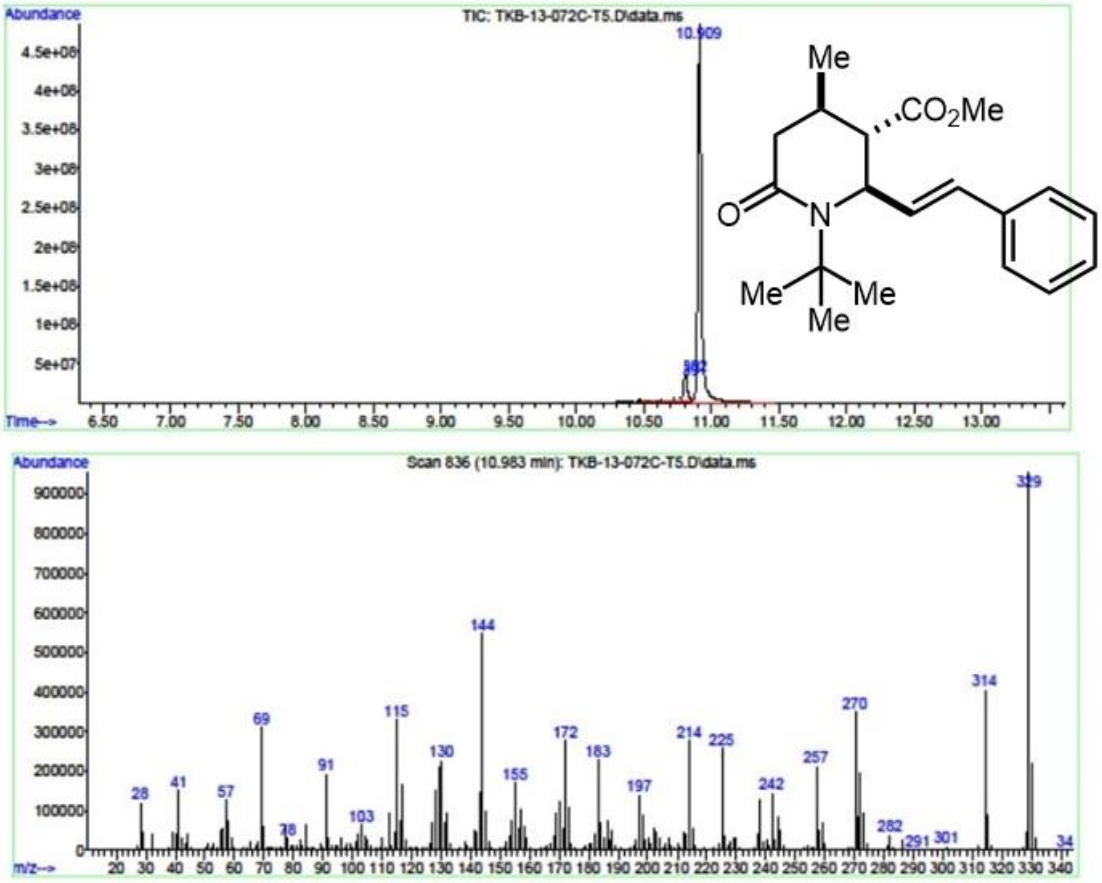
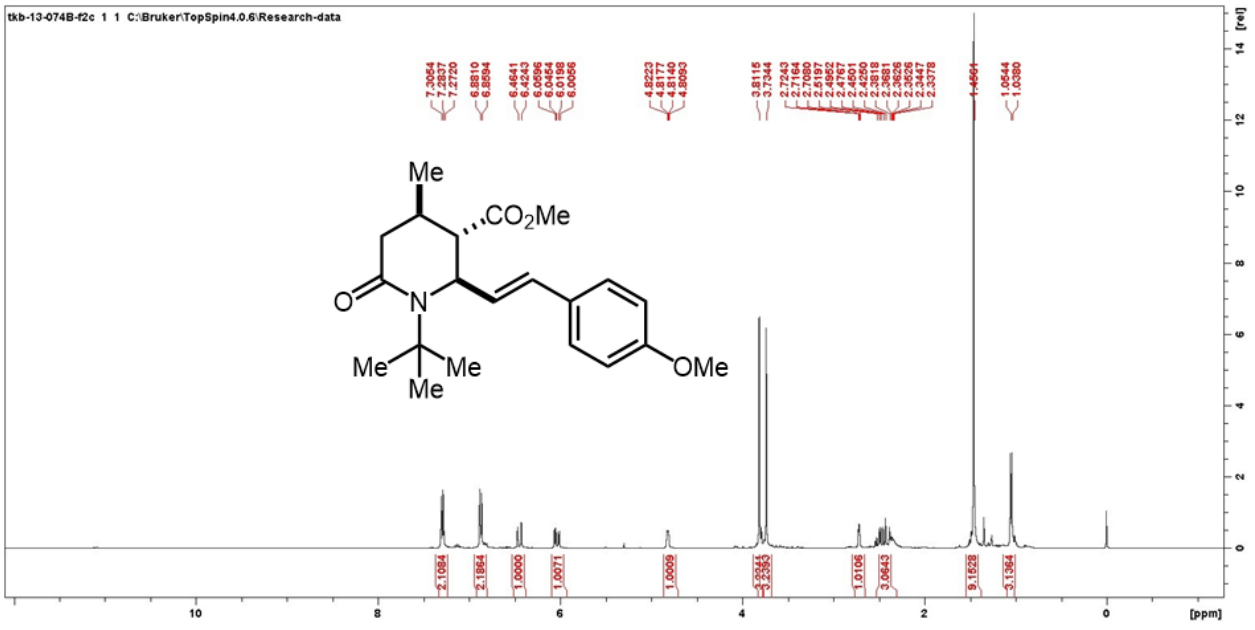


Compound 3c2

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 309.1 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 6.8 Hz, 2H), 6.88 (d, J = 6.8 Hz, 2H), 6.44 (d, J = 15.9 Hz, 1H), 6.03 (dd, J = 15.9, 5.7 Hz, 1H), 4.82 (dd, J = 5.7, 2.7 Hz, 1H), 3.81 (s, 3H), 3.73 (s, 3H), 2.72 (dd, J = 4.3, 2.7 Hz, 1H), 2.56 – 2.28 (m, 3H), 1.46 (s, 9H), 1.04 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 170.7, 159.6, 131.2, 128.7, 127.6, 114.2, 58.1, 57.7, 55.3, 51.6, 50.2, 39.2, 28.5, 25.0, 18.3. **HRMS-EI^{+}** (*m/z*): calc for $C_{21}H_{29}NO_4$, 359.2907, found 359.2911. FTIR (KBr): 2930.9, 1721.7, 1664.1, 1606.8, 1576.9, 1511.8, 1422.3, 1359.3, 1300.0, 1250.9, 1175.8, 1113.1, 1031.2, 996.2, 970.2, 923.7, 826.1, 764.8.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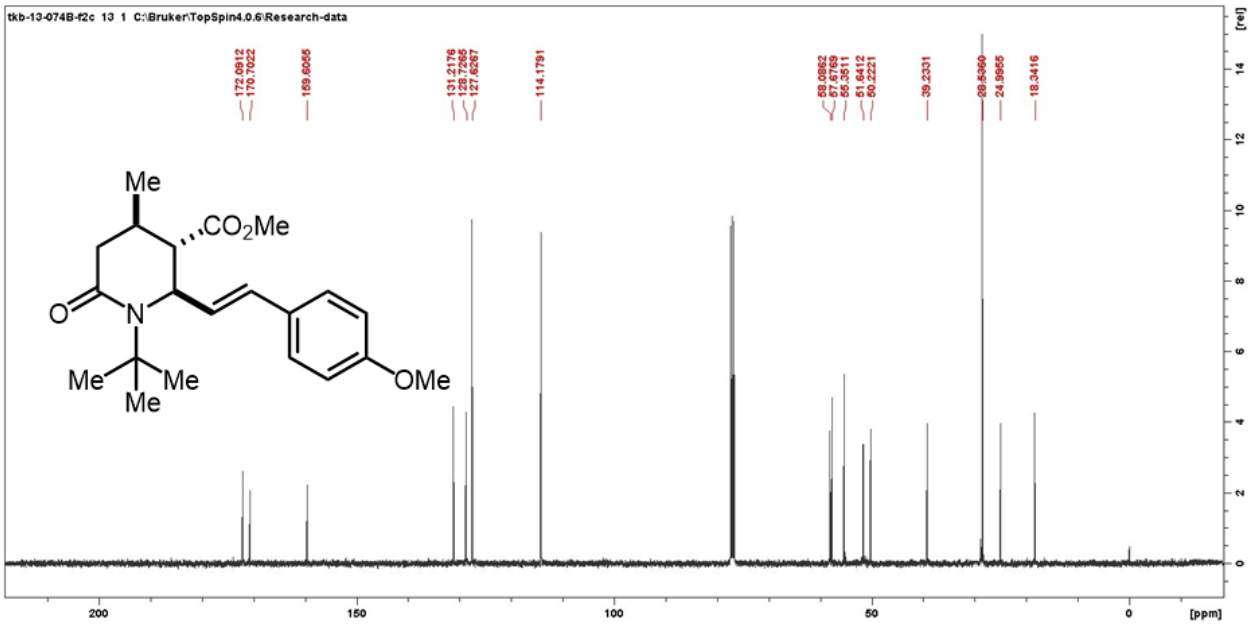
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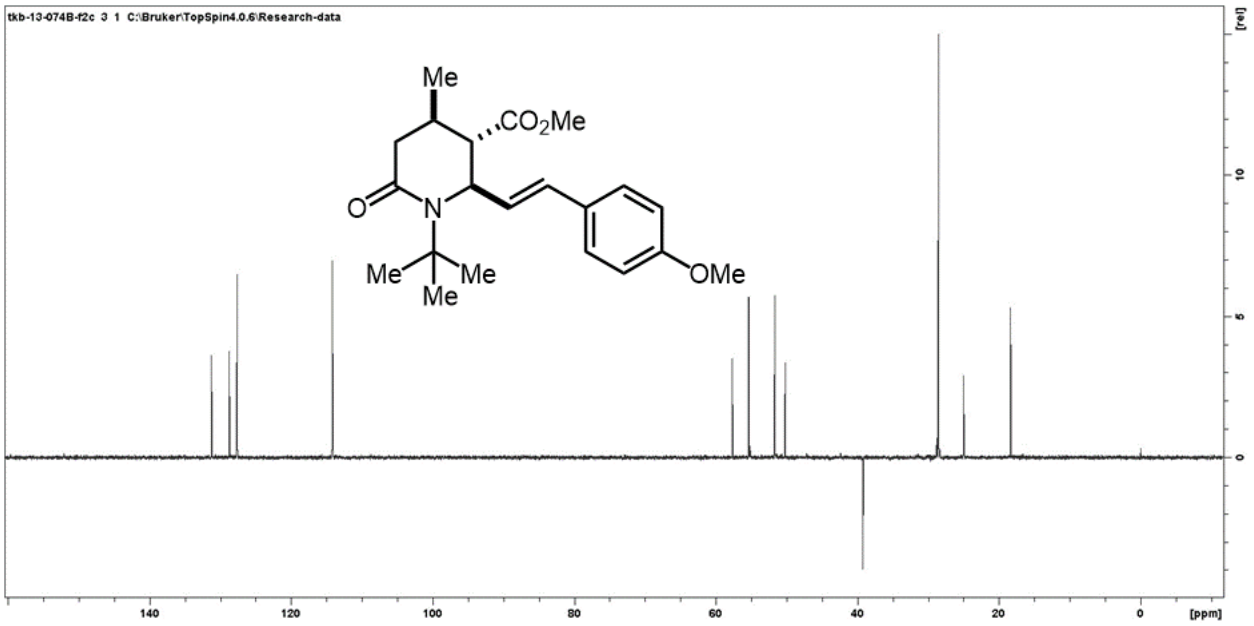


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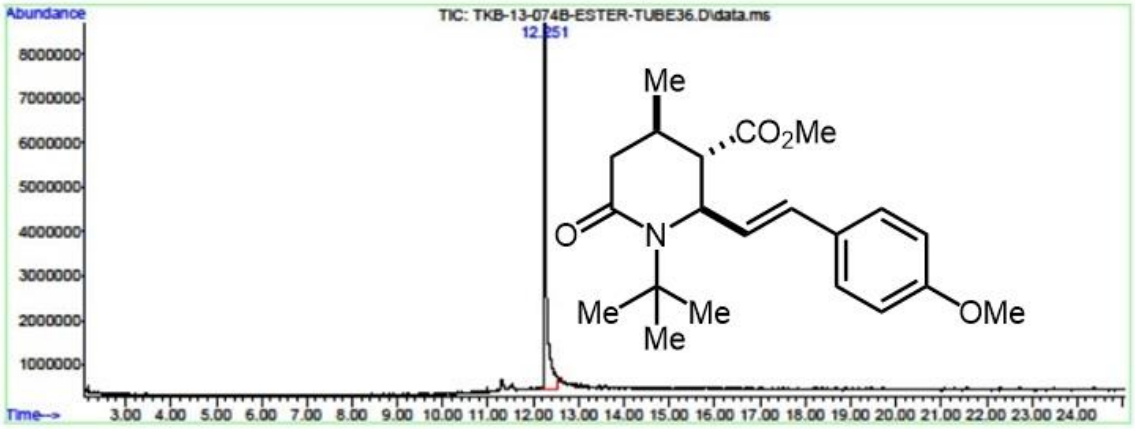
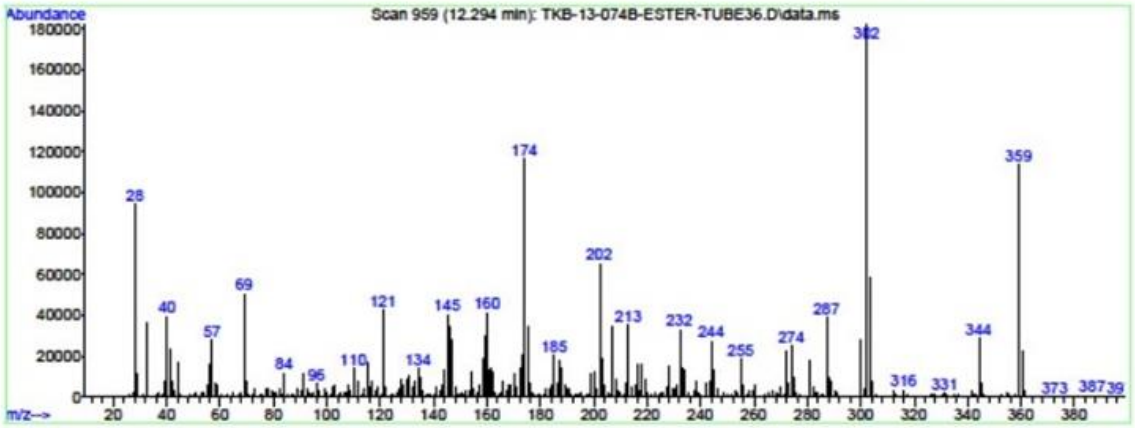
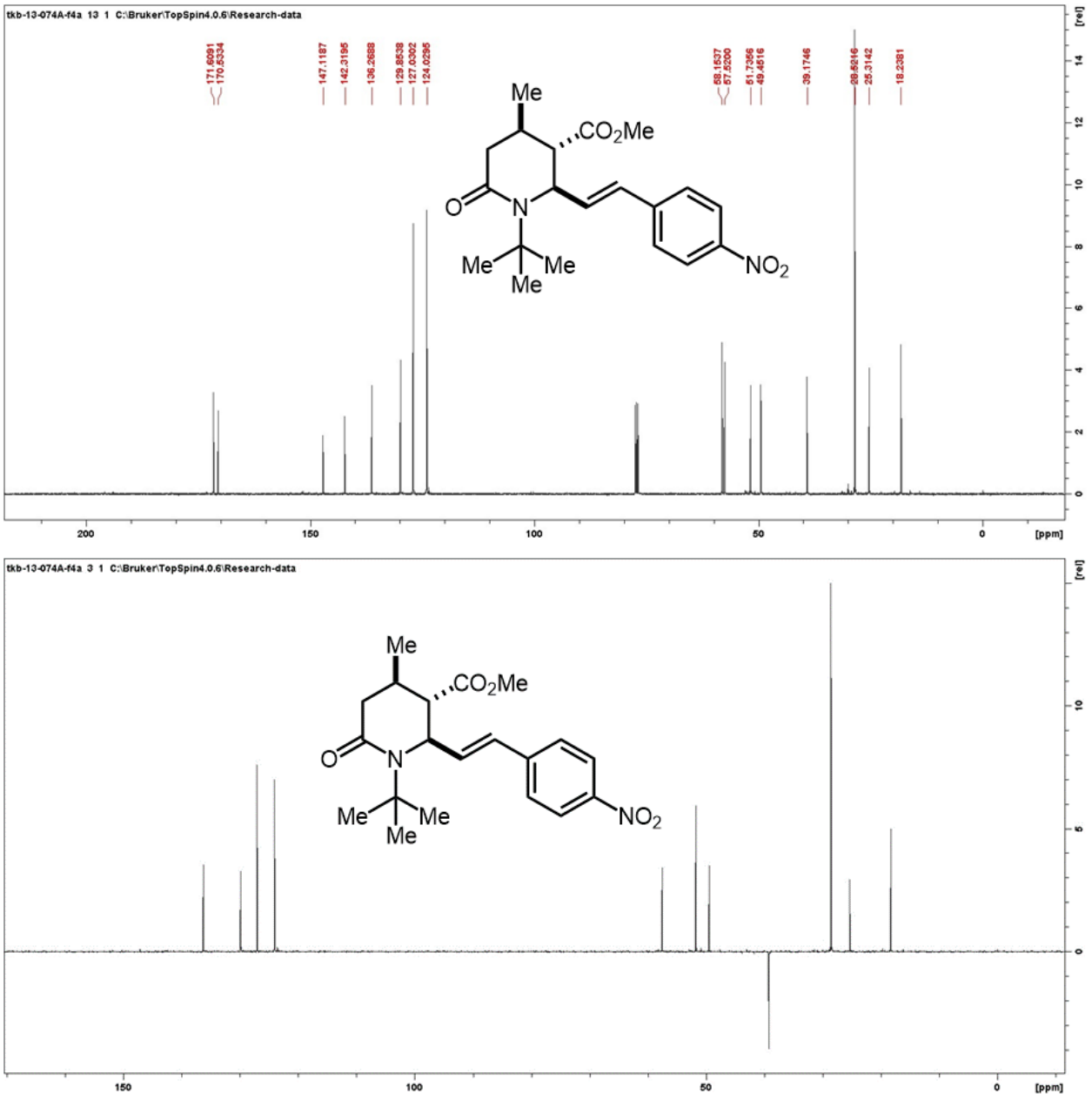




Compound 3c3

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (30:70). Oily substance. Yield = 288.3 mg, 77%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.2 Hz, 2H), 7.54 (d, *J* = 7.2 Hz, 2H), 6.63 (d, *J* = 16.0 Hz, 1H), 6.47 (dd, *J* = 16.0, 5.3 Hz, 1H), 4.95 (dd, *J* = 5.3, 2.0 Hz, 1H), 3.77 (s, 3H), 2.84 (dd, *J* = 4.9, 2.0 Hz, 1H), 2.56-2.31 (m, 3H), 1.49 (s, 9H), 1.09 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 170.5, 147.1, 142.3, 136.3, 129.9, 127.0, 124.0, 58.2, 57.5, 51.7, 49.5, 39.2, 28.5, 25.3, 18.2. **HRMS-EI^{+}** (*m/z*): calc for $C_{20}H_{26}N_2O_4$, 374.1842, found 374.1837.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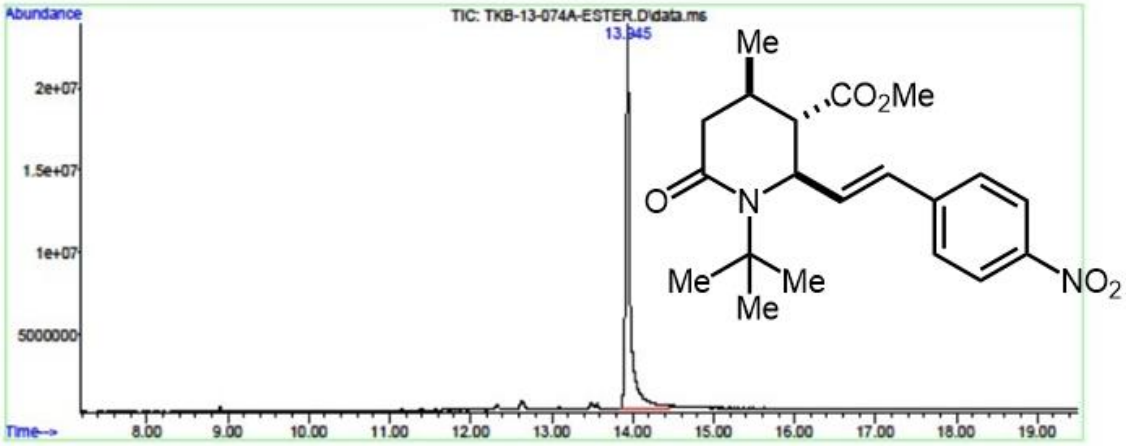
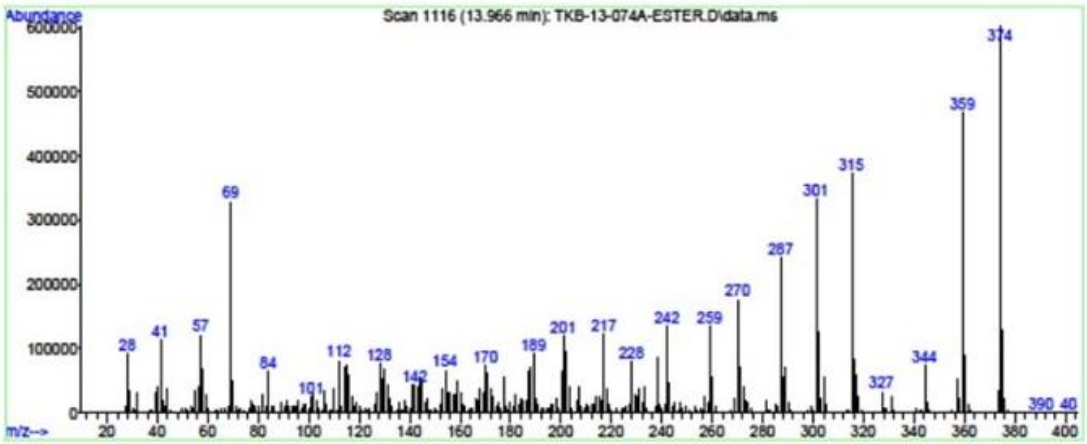
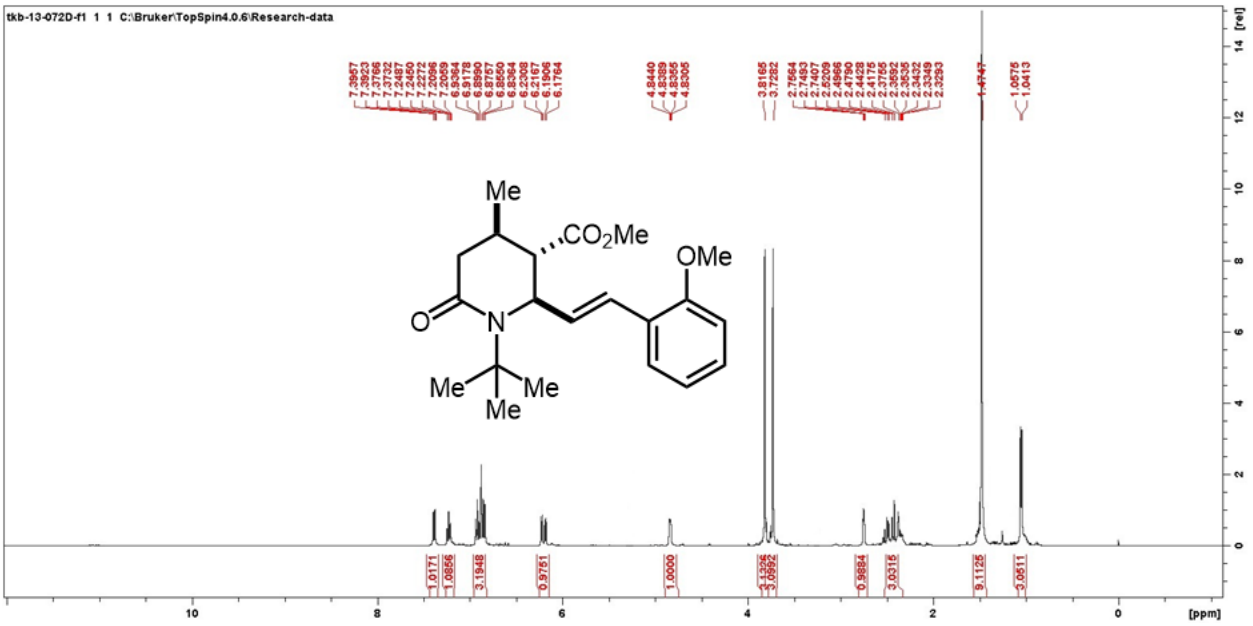




Compound 3c4

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 273.2 mg, 76%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.6 Hz, 1H), 7.27 – 7.15 (m, 1H), 6.93 – 6.83 (m, 3H), 6.20 (dd, *J* = 16.1, 5.7 Hz, 1H), 4.84 (dd, *J* = 5.7, 2.5 Hz, 1H), 3.81 (s, 3H), 3.73 (s, 3H), 2.75 (dd, *J* = 4.3, 2.5 Hz, 1H), 2.58 – 2.28 (m, 3H), 1.47 (s, 9H), 1.05 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 170.7, 156.8, 131.6, 129.0, 127.0, 126.9, 125.1, 120.6, 111.0 58.1, 55.4, 51.6, 50.3, 39.2, 28.5, 25.0, 18.4. **HRMS-EI^{+}** (*m/z*): calc for $C_{21}H_{29}NO_4$, 359.2907, found 359.2911.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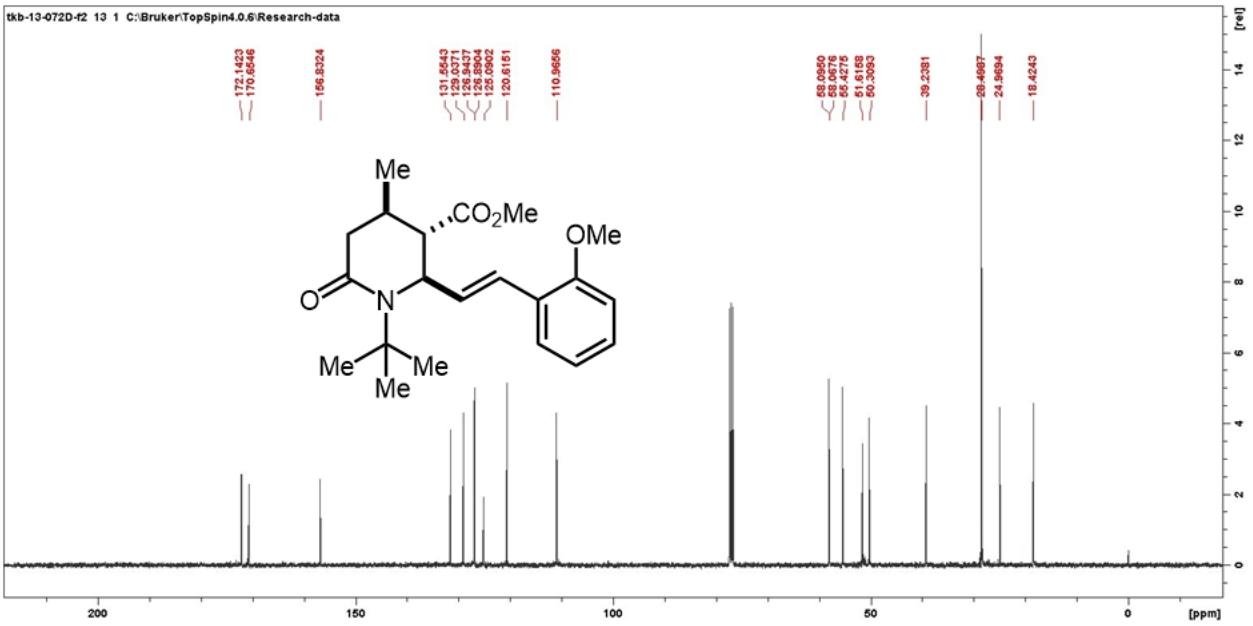
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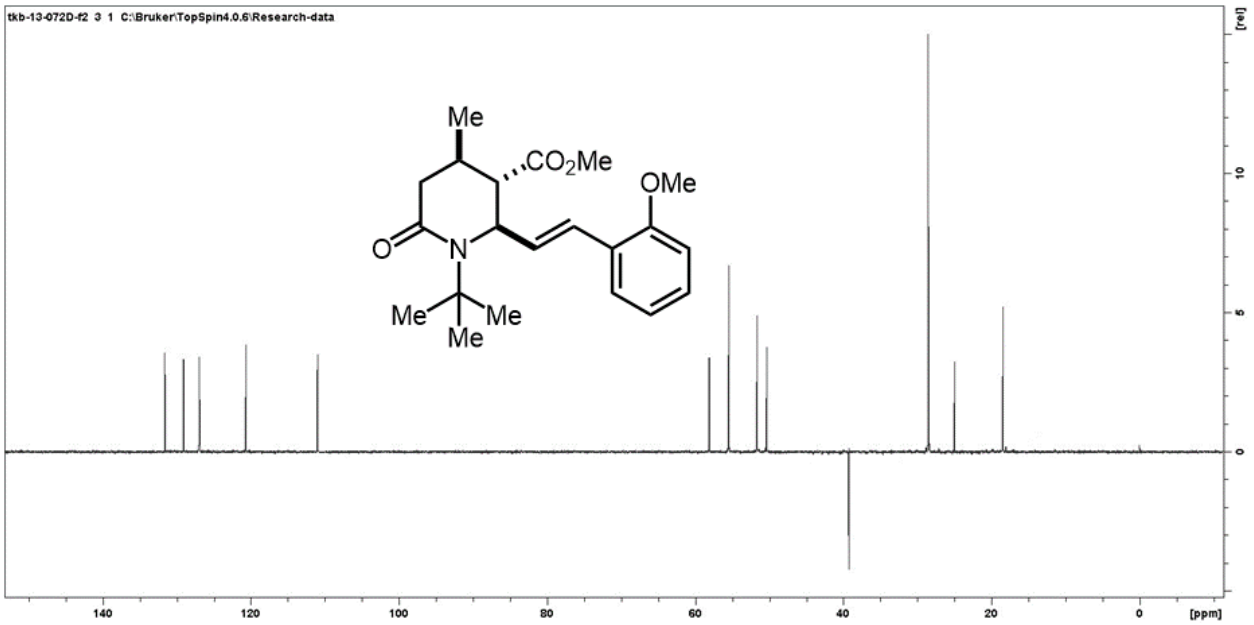


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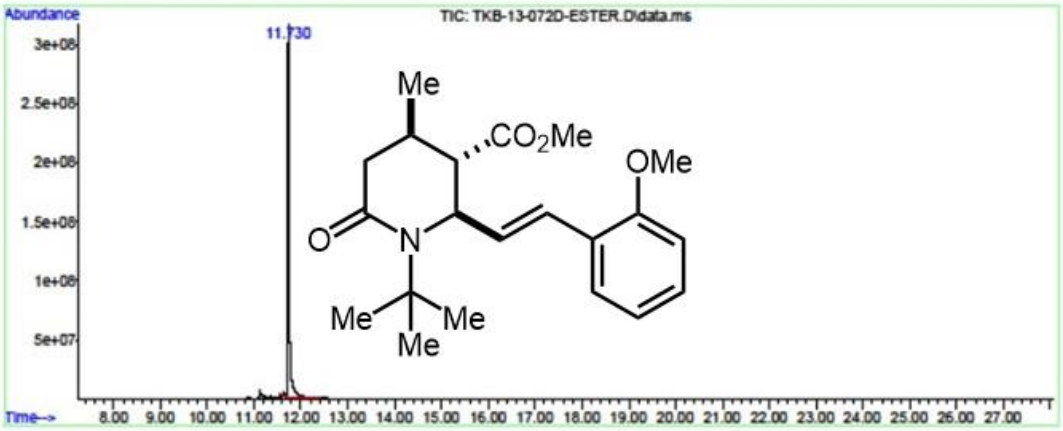
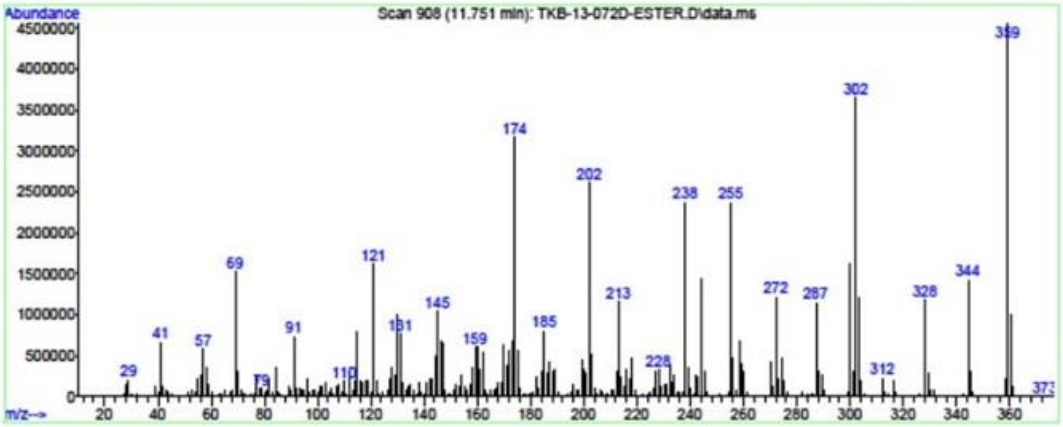
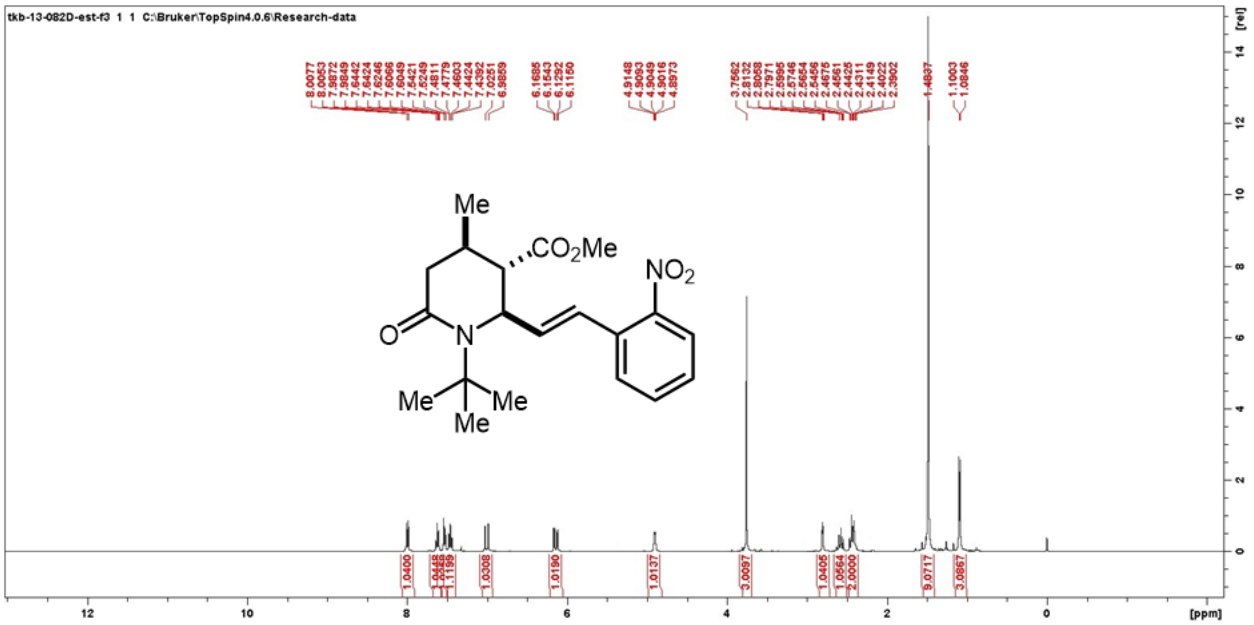
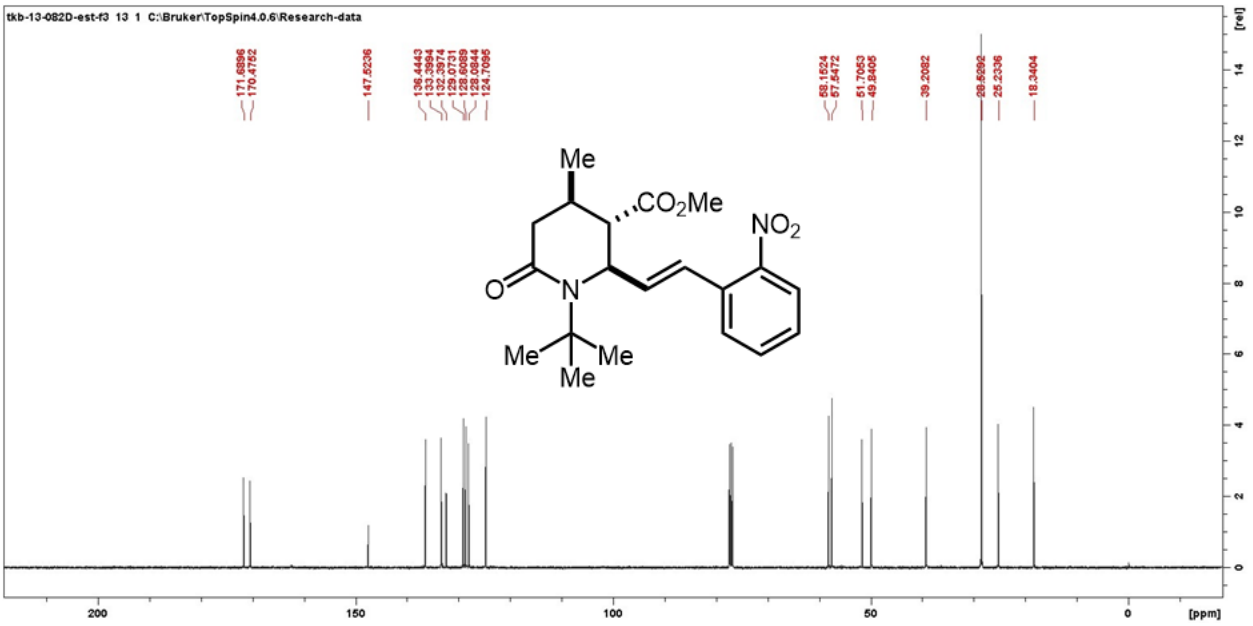




Compound 3c5

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (30:70). Oily substance. Yield = 262.1 mg, 70%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.1, 1.3 Hz, 1H), 7.62 (td, *J* = 7.6, 1.3 Hz, 1H), 7.53 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.46 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H), 7.01 (d, *J* = 15.8 Hz, 1H), 6.14 (dd, *J* = 15.8, 5.7 Hz, 1H), 4.90 (dd, *J* = 5.7, 2.7 Hz, 1H), 3.76 (s, 3H), 2.81 (dd, *J* = 4.1, 2.7 Hz, 1H), 2.65 – 2.52 (m, 1H), 2.49 – 2.35 (m, 2H), 1.48 (s, 9H), 1.09 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 170.5, 147.5, 136.4, 133.4, 132.4, 129.1, 128.6, 128.1, 124.7, 58.2, 57.5, 51.7, 49.8, 39.2, 28.5, 25.2, 18.3. **HRMS-EI^{+}** (*m/z*): calc for $C_{20}H_{26}N_2O_4$, 374.1842, found 374.1837.

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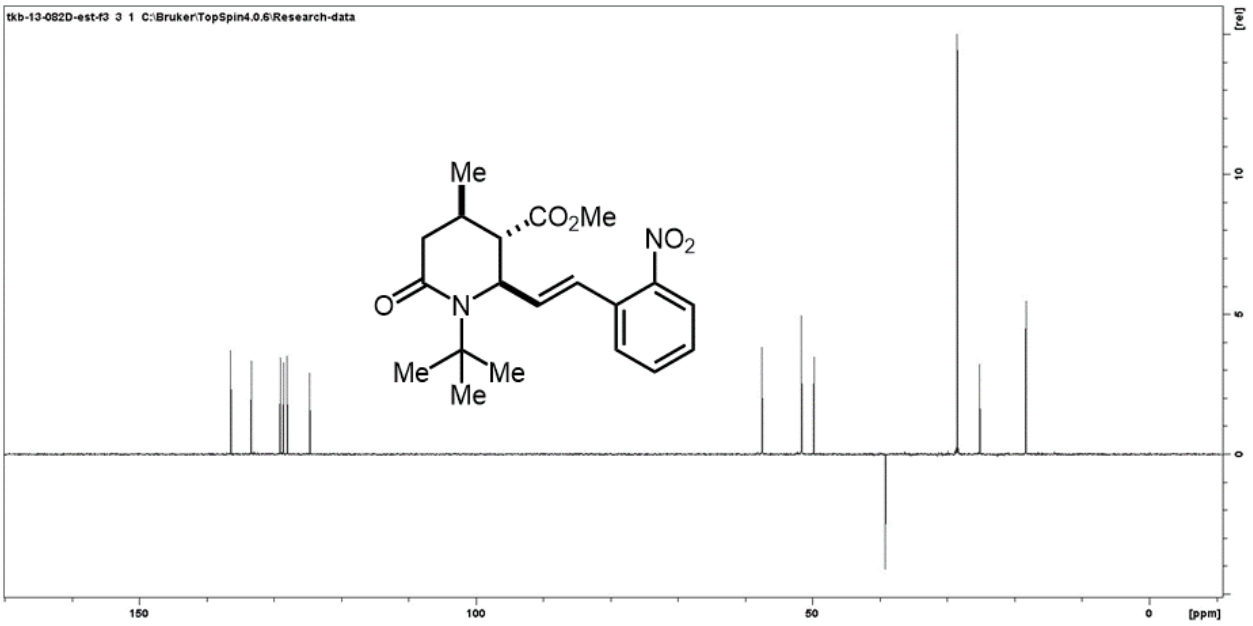
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NO2
O
N
Me
Me
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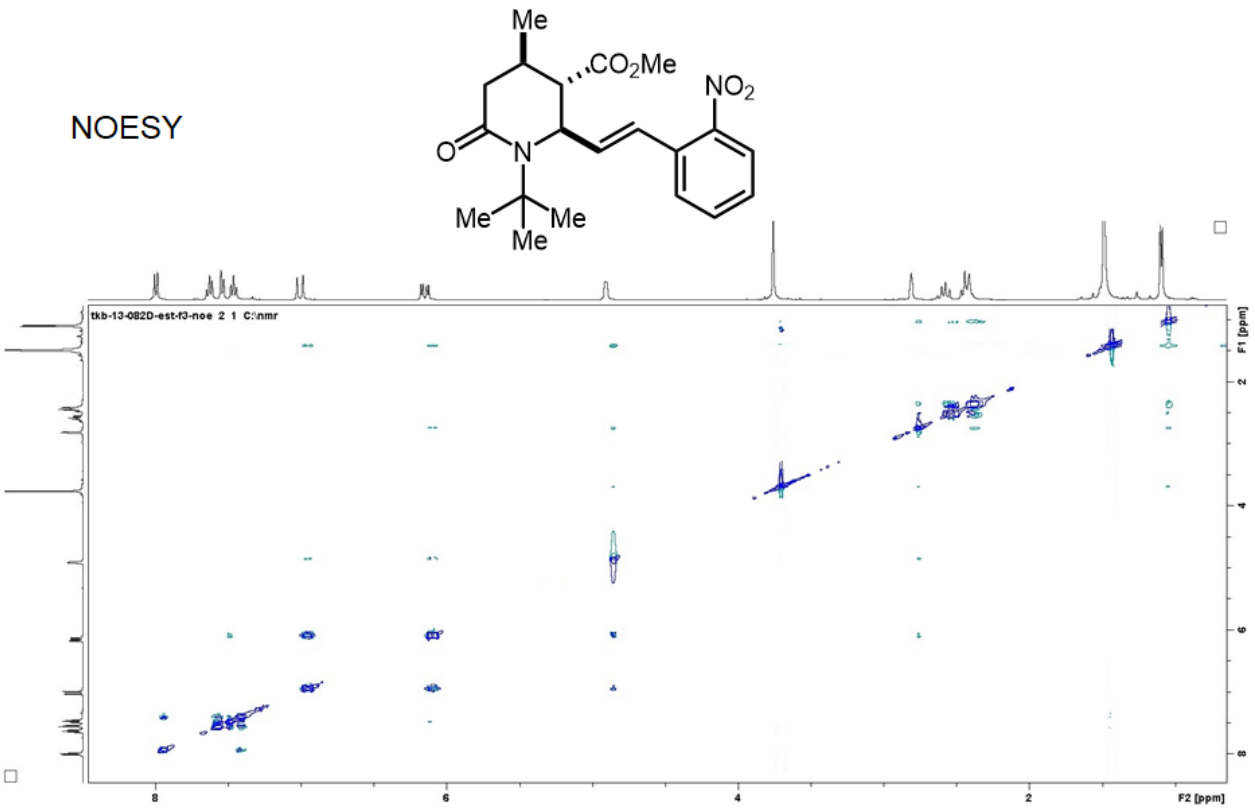
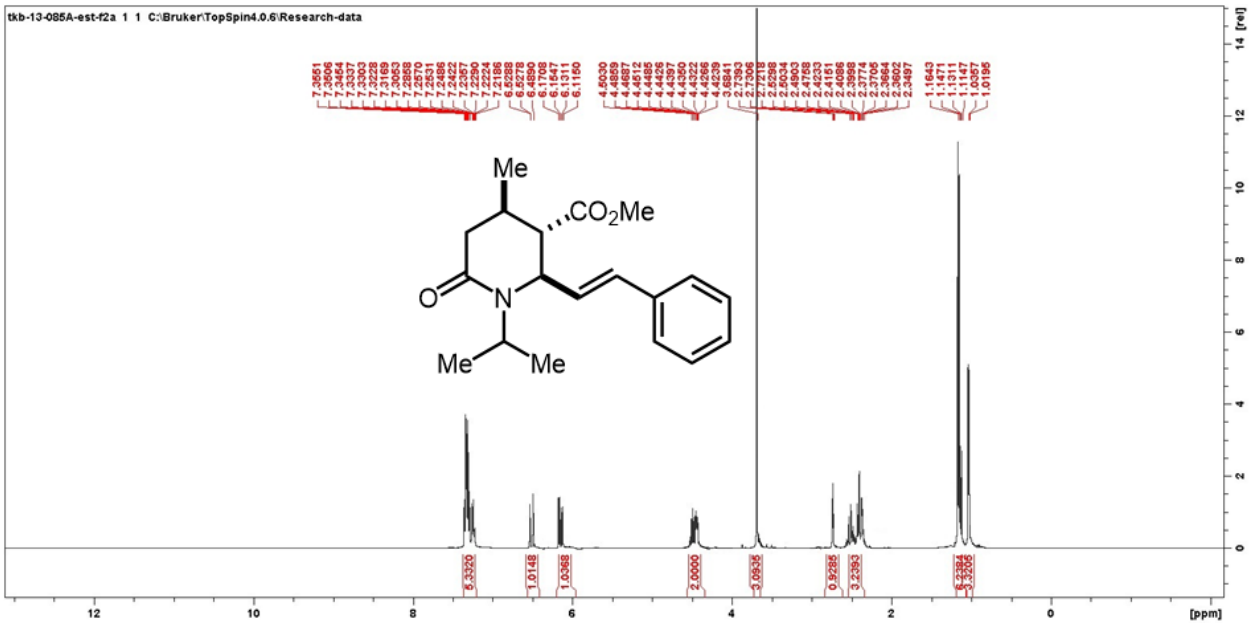


Compound 3c6

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 242.9 mg, 77%, 93:7 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.21 (m, 5H), 6.55 (d, J = 15.9 Hz, 1H), 6.14 (dd, J = 15.9, 6.4 Hz, 1H), 4.50 – 4.42 (m, 2H), 3.68 (s, 3H), 2.73 (t, J = 3.5 Hz, 1H), 2.53 – 2.35 (m, 3H), 1.16-1.14 (overlapping doublets, 6H), 1.03 (d, J = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 169.4, 135.9, 132.1, 130.2, 128.7, 128.1, 126.4, 57.0, 51.7, 49.7, 47.4, 37.8, 25.3, 20.2, 19.8, 17.9. **HRMS-EI^{+}** (*m/z*): calc for $C_{19}H_{25}NO_3$, 315.1834, found 315.1839.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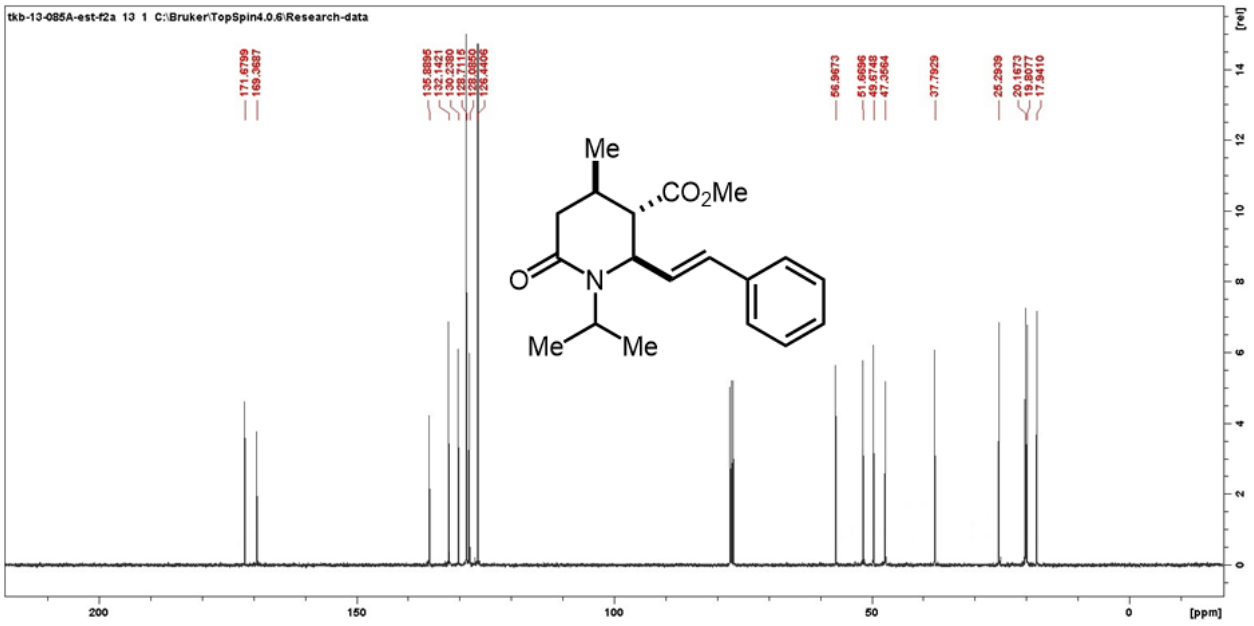
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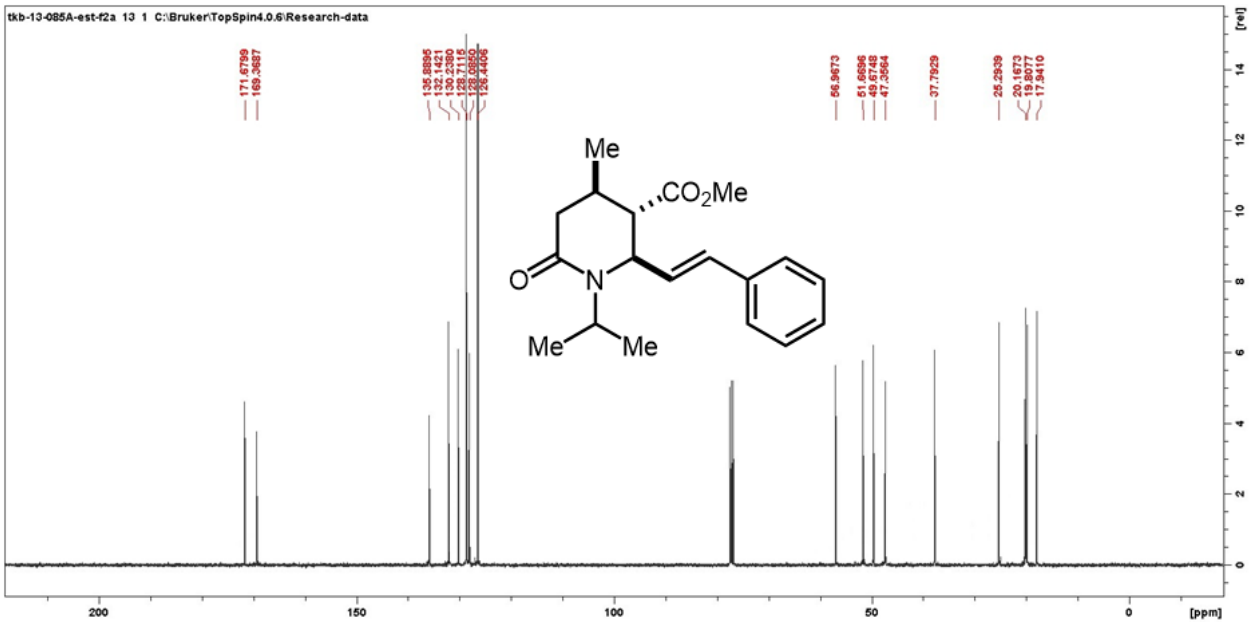
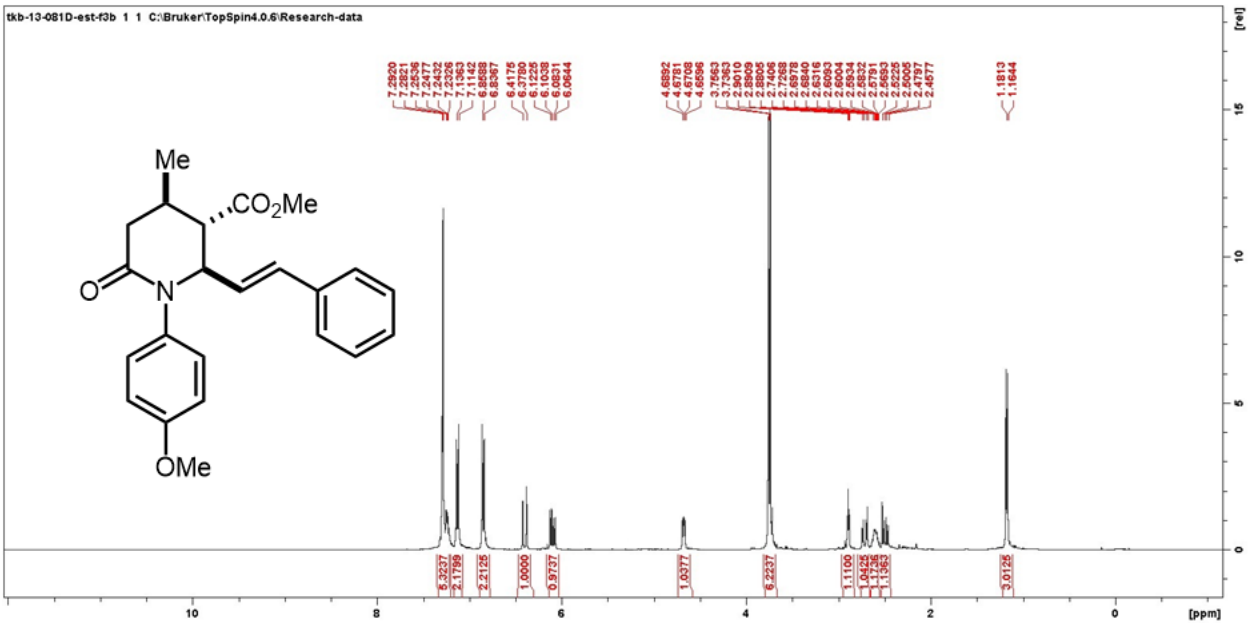


Compound 3c7

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 318.7 mg, 84%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 5H), 7.12 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 6.40 (d, J = 15.8 Hz, 1H), 6.09 (dd, J = 15.8, 7.5 Hz, 1H), 4.71 – 4.64 (m, 1H), 3.78 – 3.59 (m, 6H), 2.89 (t, J = 4.1 Hz, 1H), 2.71 (dd, J = 17.1, 5.6 Hz, 1H), 2.65 – 2.54 (m, 1H), 2.49 (dd, J = 17.1, 8.9 Hz, 1H), 1.17 (d, J = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 169.5, 158.4, 135.9, 134.6, 133.4, 128.8, 128.6, 128.1, 127.9, 126.5, 114.4, 63.5, 55.3, 51.9, 49.3, 38.0, 26.8, 17.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{25}NO_4$, 379.1784, found 379.1788. FTIR (KBr): 2932.4, 1721.5, 1666.3, 1606.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1135.9, 1031.8, 995.8, 968.9, 919.9, 831.0, 750.2, 694.7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OMe
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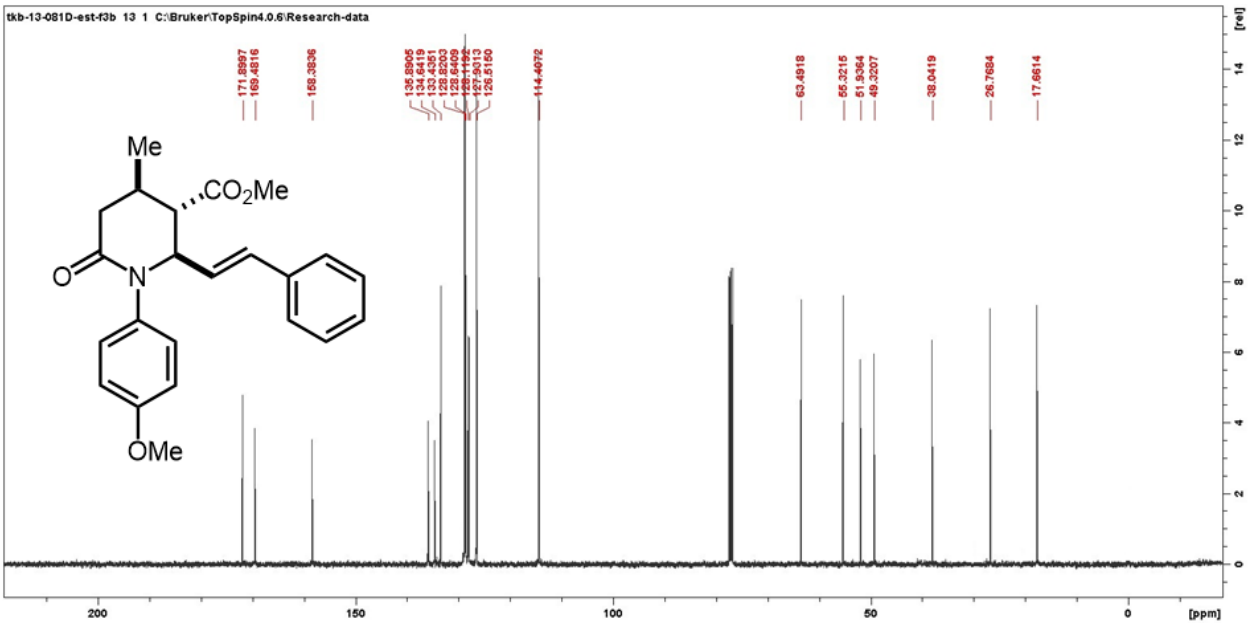
[ppm]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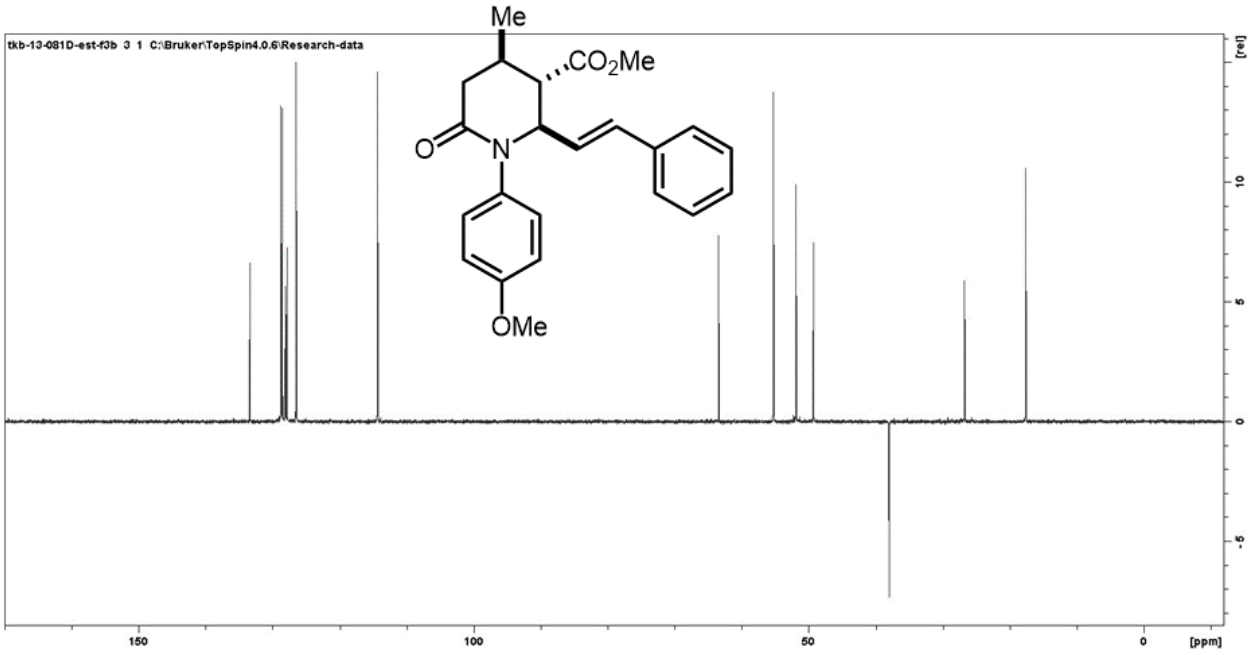
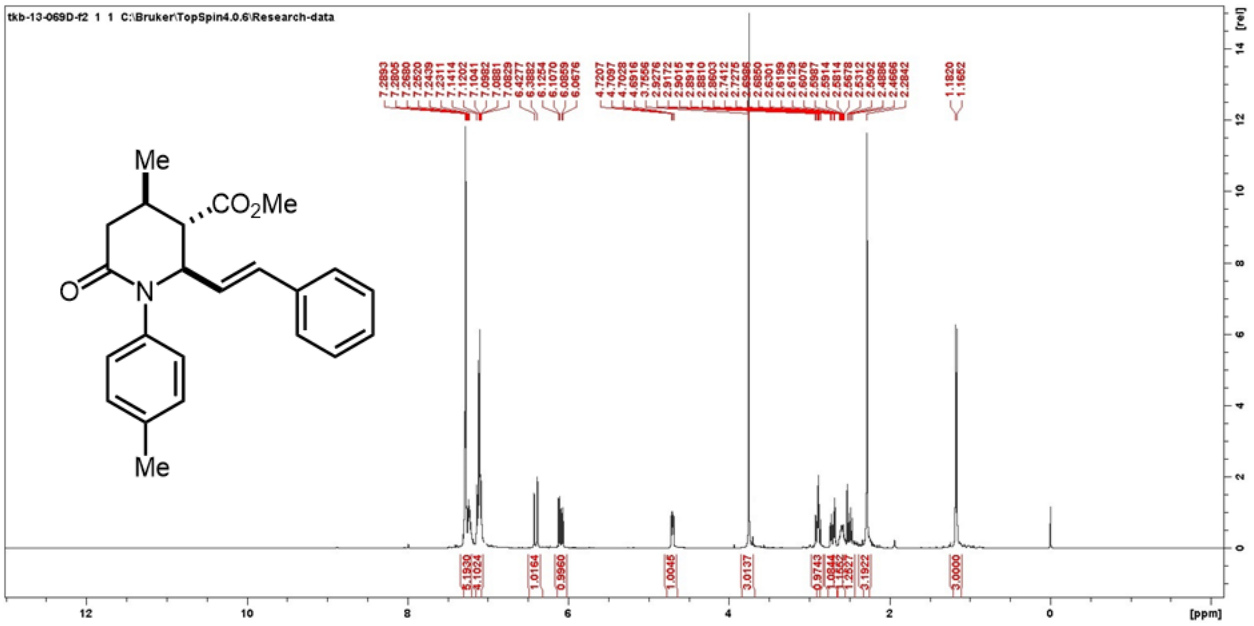


Compound 3c8

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 294.4 mg, 81%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 5H), 7.14 – 7.08 (m, 4H), 6.41 (d, *J* = 15.8 Hz, 1H), 6.09 (dd, *J* = 15.8, 7.4 Hz, 1H), 4.71 (dd, *J* = 7.4, 4.4 Hz, 1H), 3.76 (s, 3H), 2.93 – 2.86 (m, 1H), 2.71 (dd, *J* = 17.1, 5.5 Hz, 1H), 2.66 – 2.53 (m, 1H), 2.51 – 2.47 (m, 1H), 2.28 (s, 3H), 1.18 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 169.3, 139.3, 137.0, 135.9, 133.4, 129.8, 128.7, 128.5, 128.1, 127.9, 127.5, 126.6, 126.5, 63.3, 52.0, 49.4, 38.1, 26.8, 21.1, 17.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{25}NO_3$, 363.1834, found 363.1837.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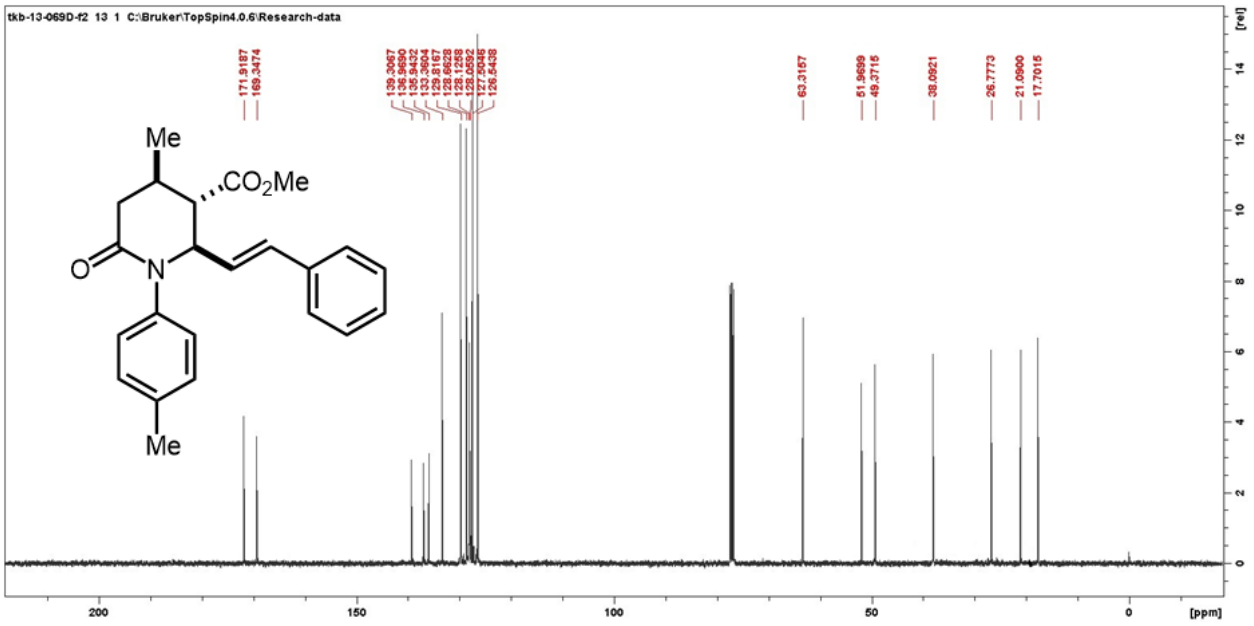
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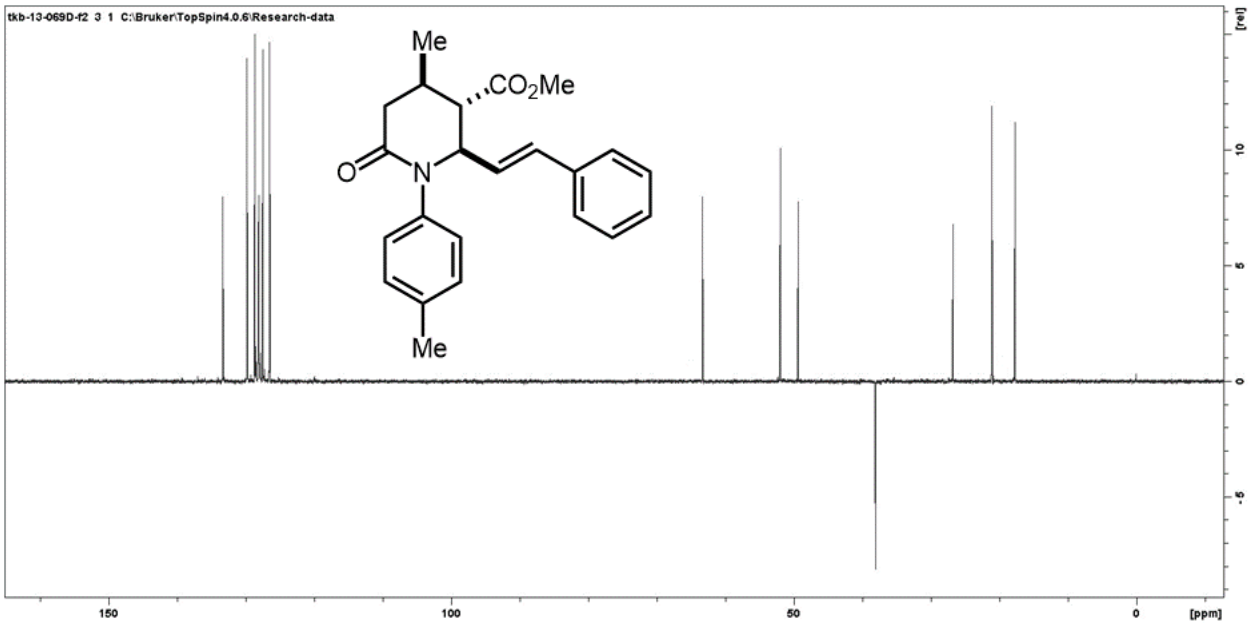
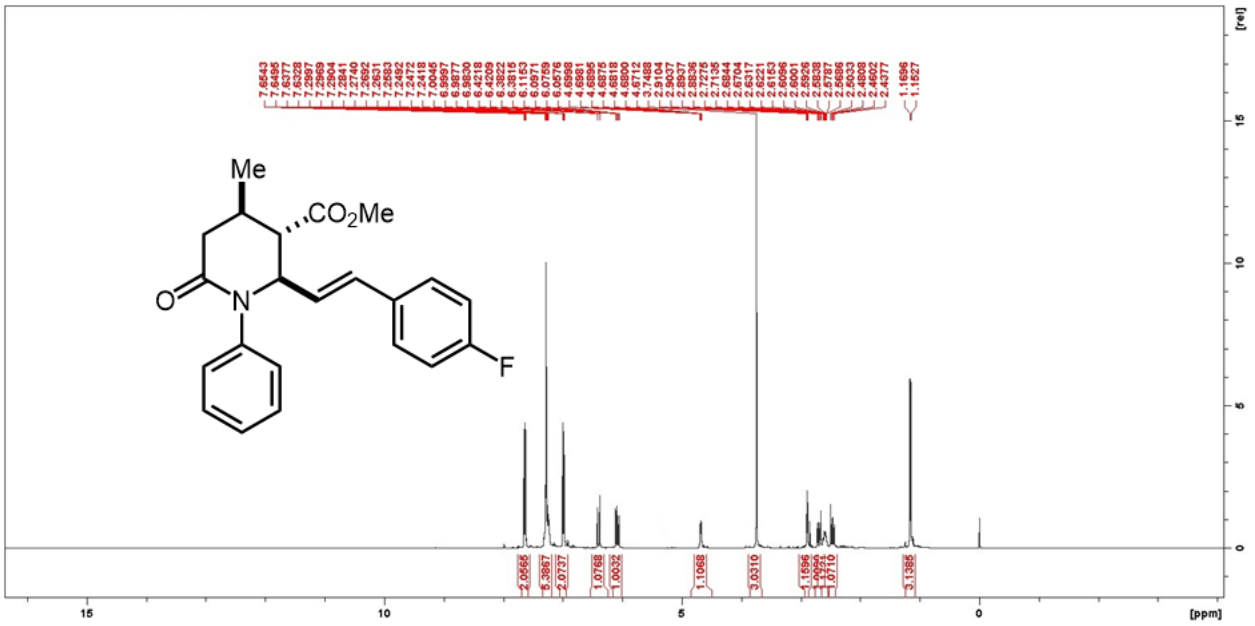


Compound 3c9

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 279.2 mg, 76%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, 2H), 7.30 – 7.24 (m, 5H), 6.98 (d, 2H), 6.42 (d, J = 15.8 Hz, 1H), 6.09 (dd, J = 15.8, 7.5 Hz, 1H), 4.69 (dd, J = 7.5, 4.6 Hz, 1H), 3.75 (s, 3H), 2.95 – 2.80 (m, 1H), 2.77 – 2.53 (m, 1H), 2.56 – 2.45 (m, 1H), 2.48 – 2.17 (m, 1H), 1.15 (d, J = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 169.5, 162.6, 160.2, 137.8, 135.7, 134.0, 133.8, 130.2, 130.1, 129.9, 129.8, 129.6, 129.5, 128.7, 128.6, 128.3, 128.2, 127.5, 126.6, 126.5, 126.4, 116.2, 115.9, 63.5, 52.0, 49.2, 38.0, 26.8, 17.7. **HRMS-EI$^+$** (*m/z*): calc for $C_{22}H_{22}FNO_3$, 367.1584, found 367.1589.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F
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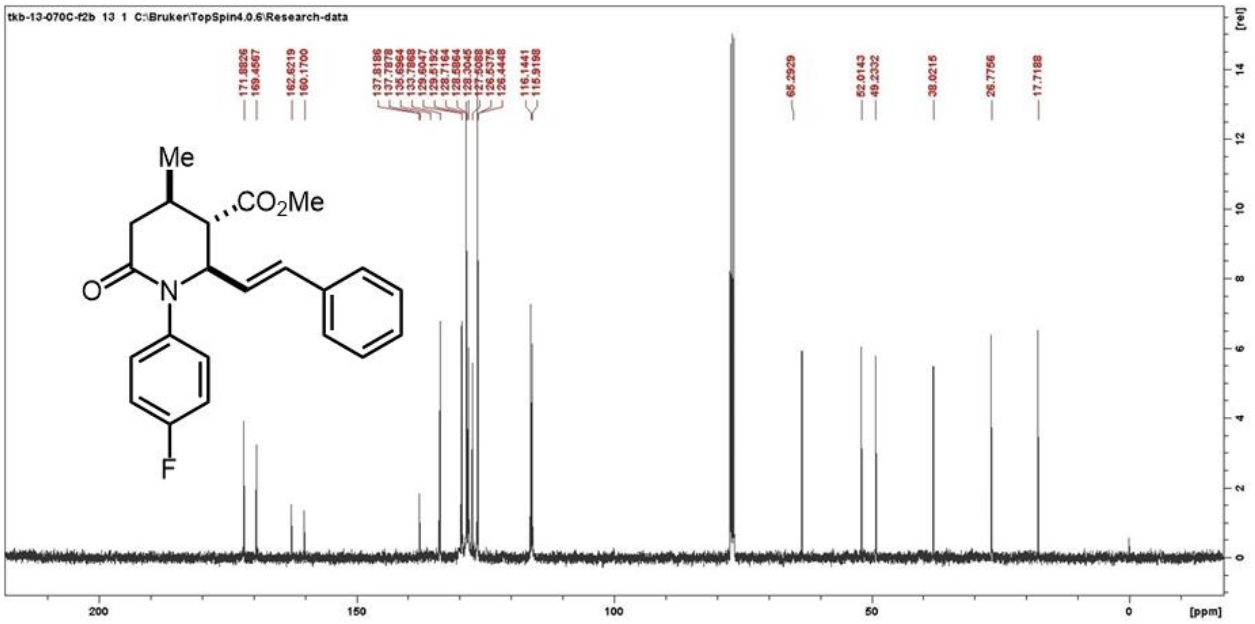
[ppm]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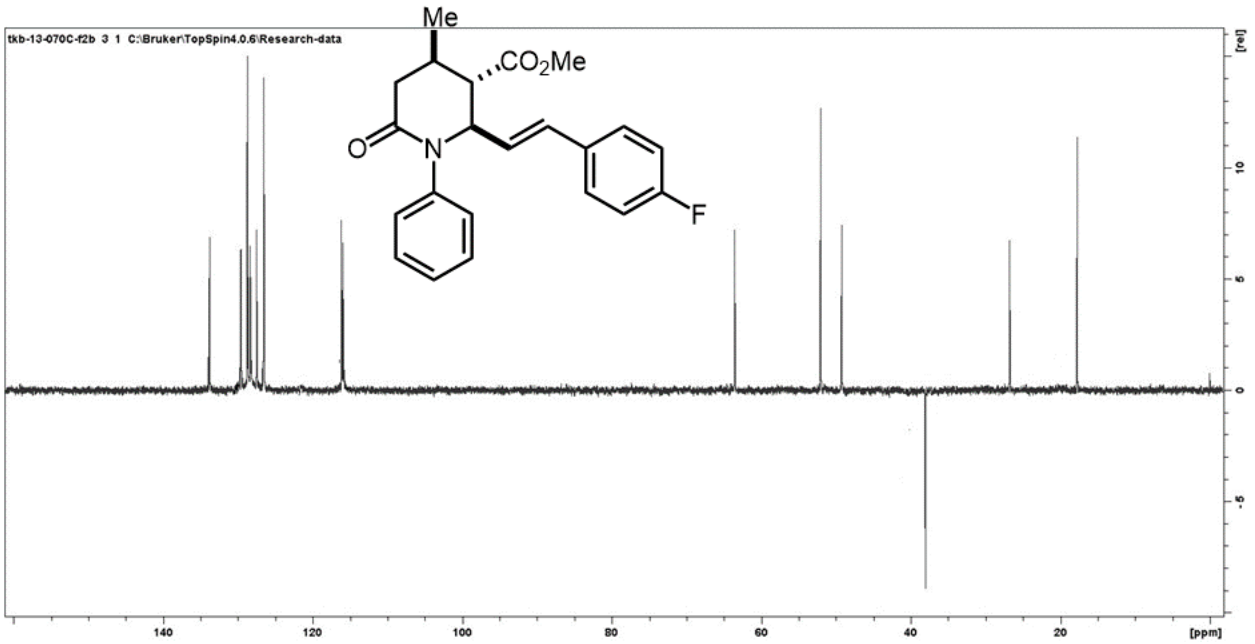
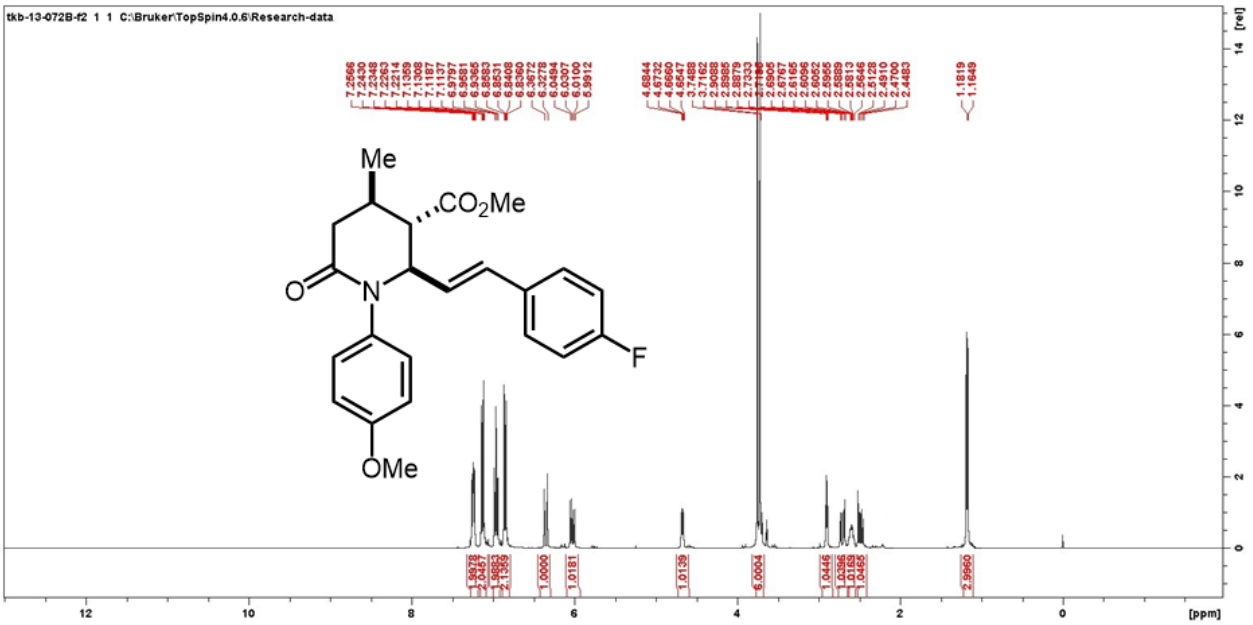


Compound 3c10

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 302.1 mg, 76%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.20 (m, 2H), 7.17 – 7.03 (m, 2H), 7.01 – 6.90 (m, 2H), 6.92 – 6.77 (m, 2H), 6.35 (d, *J* = 15.8 Hz, 1H), 6.02 (dd, *J* = 15.8, 7.5 Hz, 1H), 4.71 (dd, *J* = 7.5, 4.2 Hz, 1H), 3.73 – 3.71 (s,s, 6H), 2.90 (t, *J* = 4.2 Hz, 1H), 2.71 (dd, *J* = 17.1, 5.6 Hz, 1H), 2.67 – 2.53 (m, 1H), 2.51 – 2.43 (m, 1H), 1.17 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 169.4, 163.8, 161.3, 158.4, 134.7, 132.2, 132.1, 132.1, 128.9, 128.2, 128.1, 127.8, 115.7, 115.4, 115.4, 63.4, 55.3, 51.9, 49.3, 38.1, 26.8, 17.6. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{24}FNO_4$, 397.1689, found 397.1694.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F
OMe
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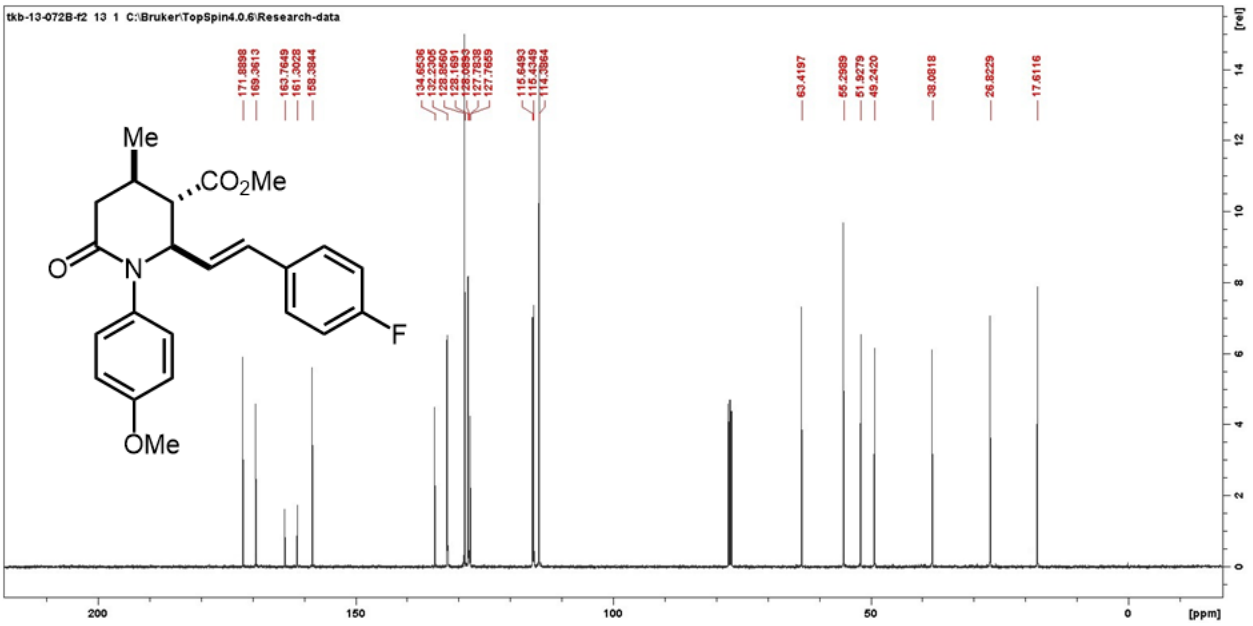
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115.4349
114.3864
63.4197
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CO2Me
O
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F
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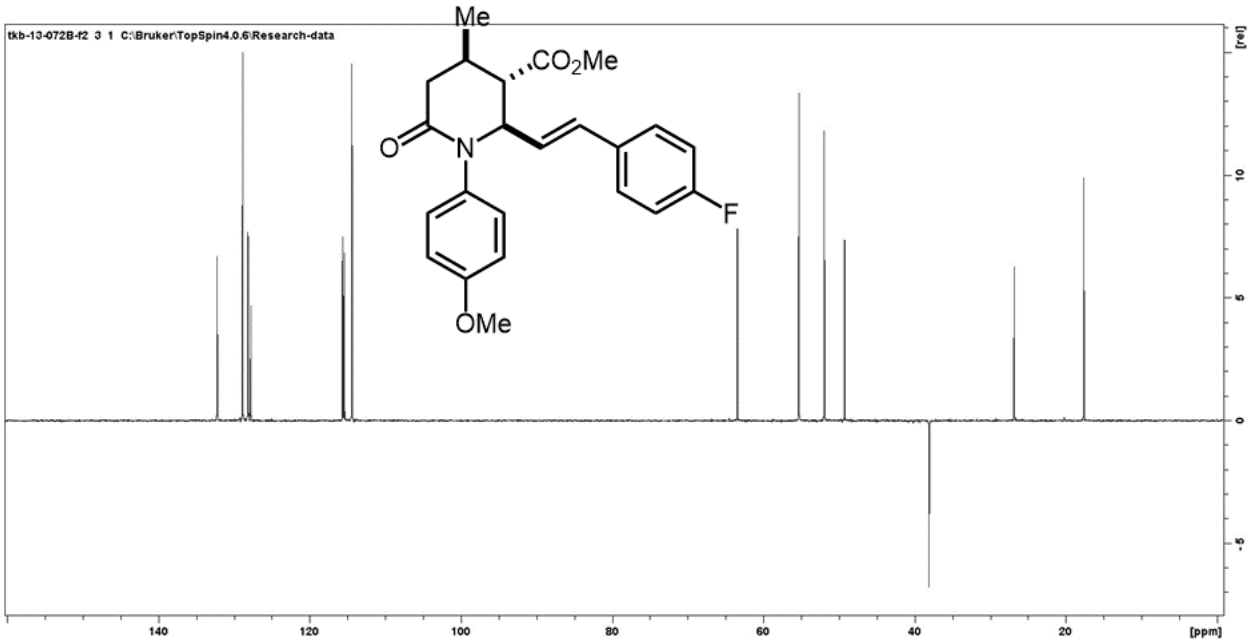
[ppm]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OMe
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80
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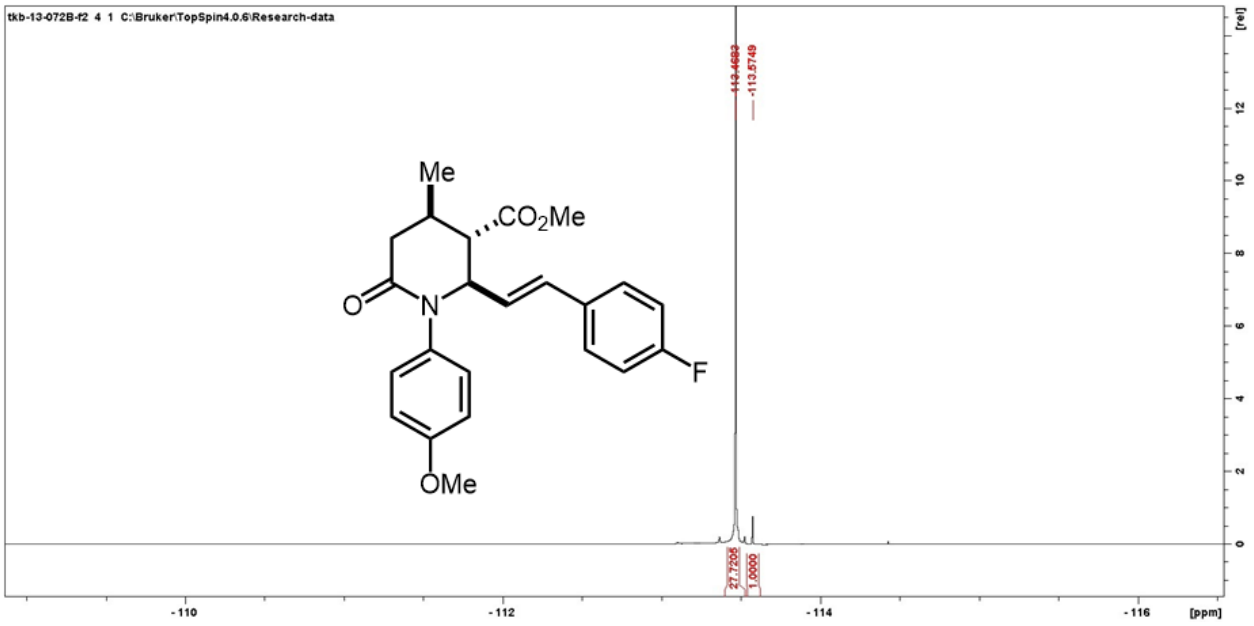
40
20
[ppm]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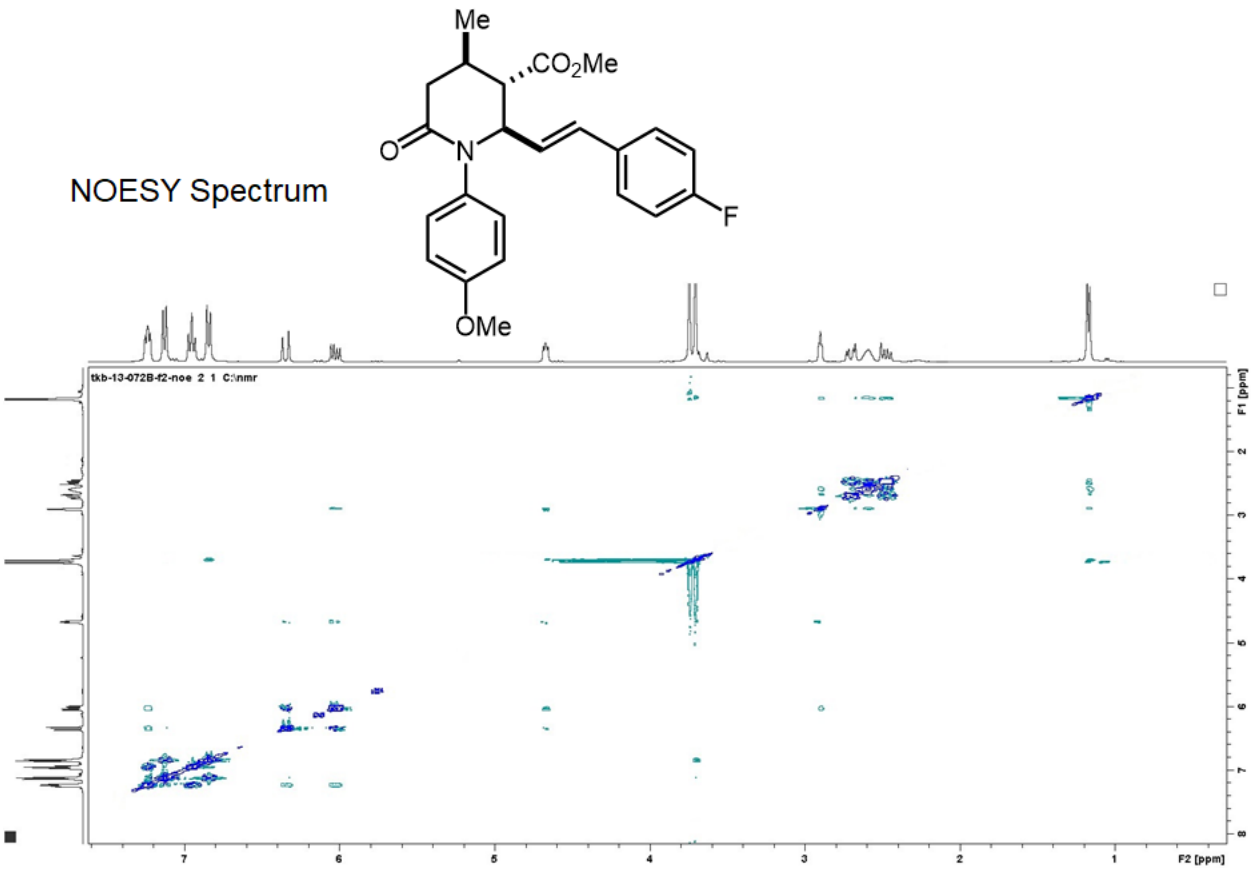
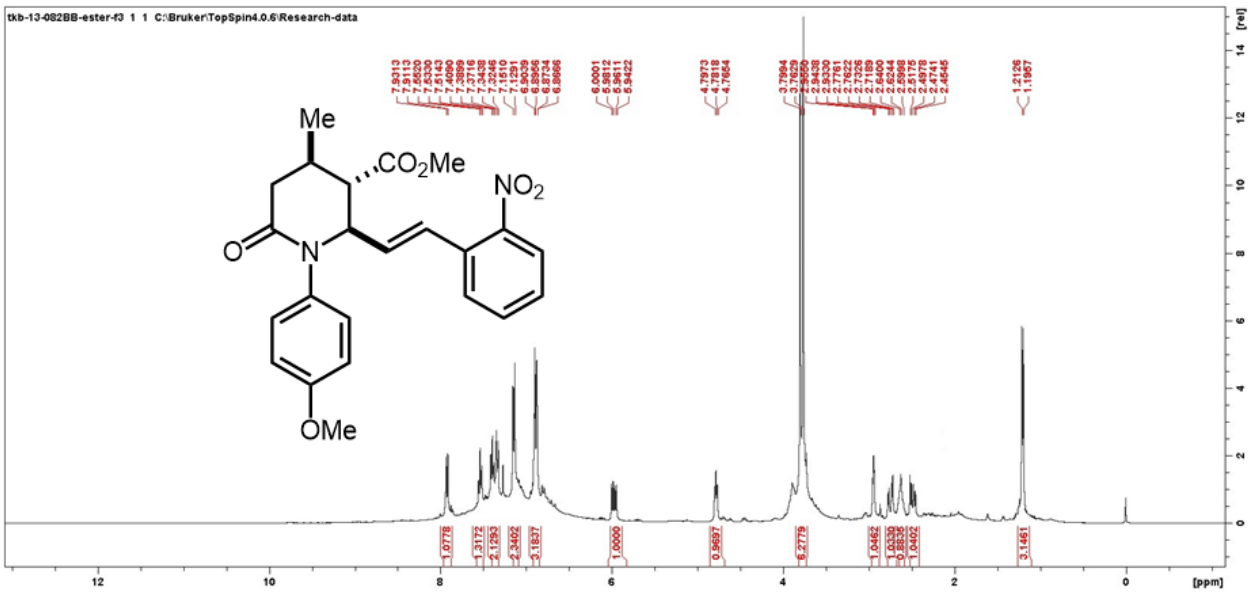


Compound 3c11

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 301.4 mg, 71%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.44 – 7.30 (m, 2H), 7.14 (d, *J* = 8.7 Hz, 2H), 6.91 – 6.87 (m, 3H), 5.97 (dd, *J* = 15.6, 7.6 Hz, 1H), 4.78 (dd, *J* = 7.6, 5.4 Hz, 1H), 3.80 - 3.77 (m, 6H), 2.98 – 2.93 (m, 1H), 2.75 (dd, *J* = 17.4, 5.6 Hz, 1H), 2.63 (q, *J* = 10.5, 9.1 Hz, 1H), 2.49 (dd, *J* = 17.3, 7.9 Hz, 1H), 1.20 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 169.3, 158.5, 147.6, 134.3, 133.2, 132.2, 129.6, 129.0, 128.9, 128.6, 124.6, 114.5, 62.8, 55.4, 52.1, 49.2, 38.3, 27.2, 17.3. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{24}N_2O_6$, 424.1634, found 424.1639.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OMe
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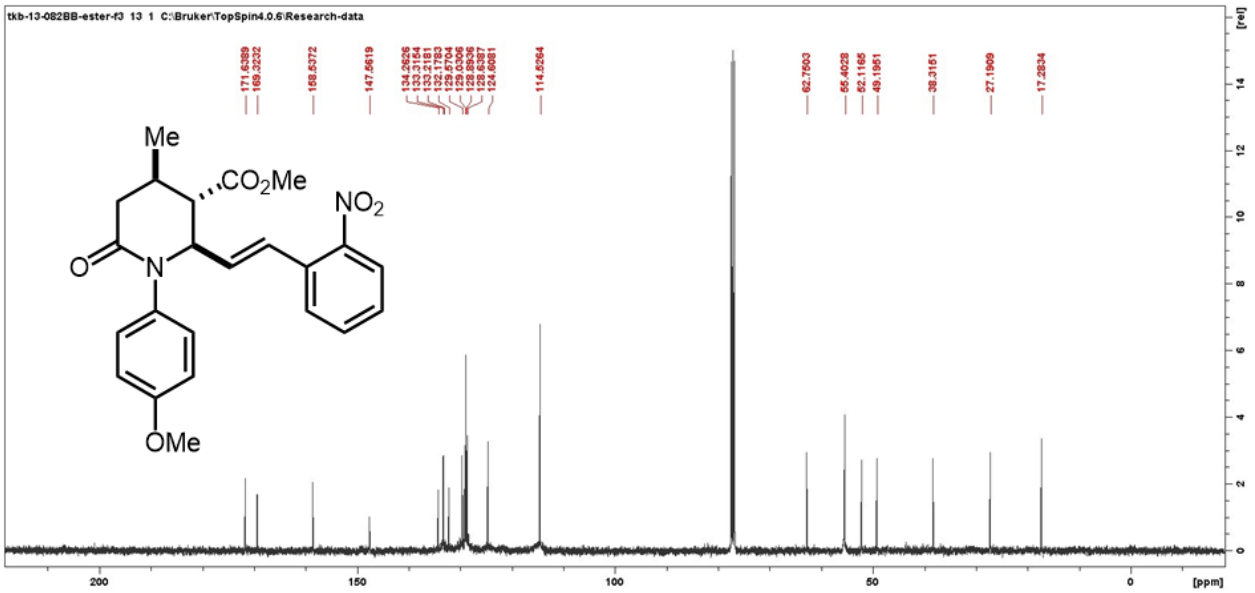
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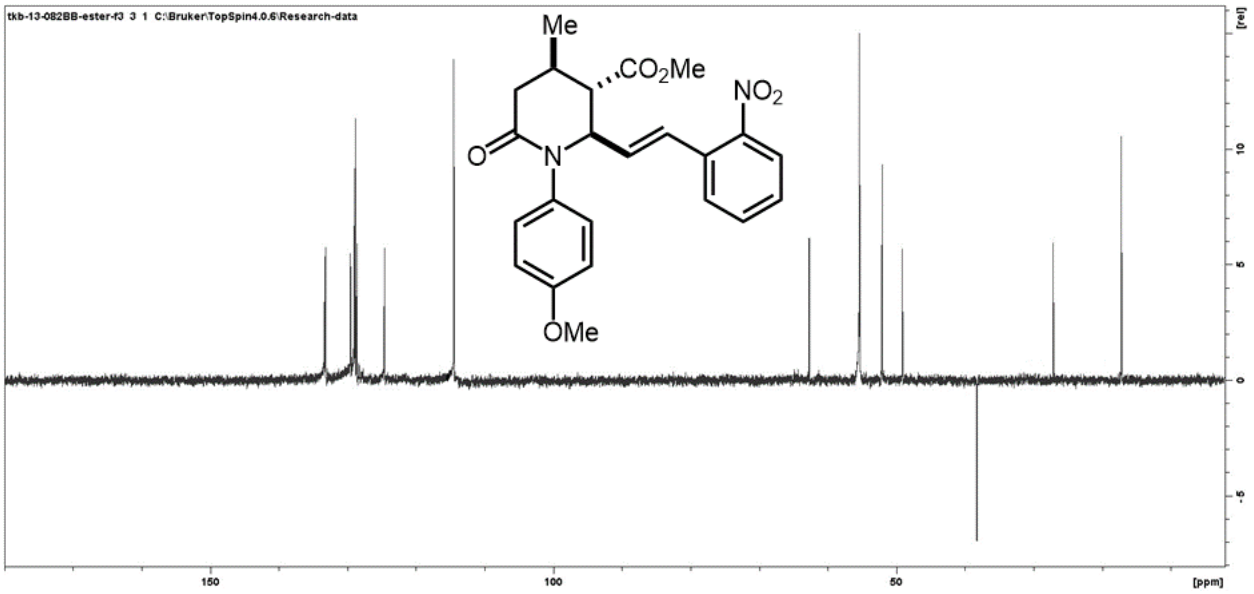
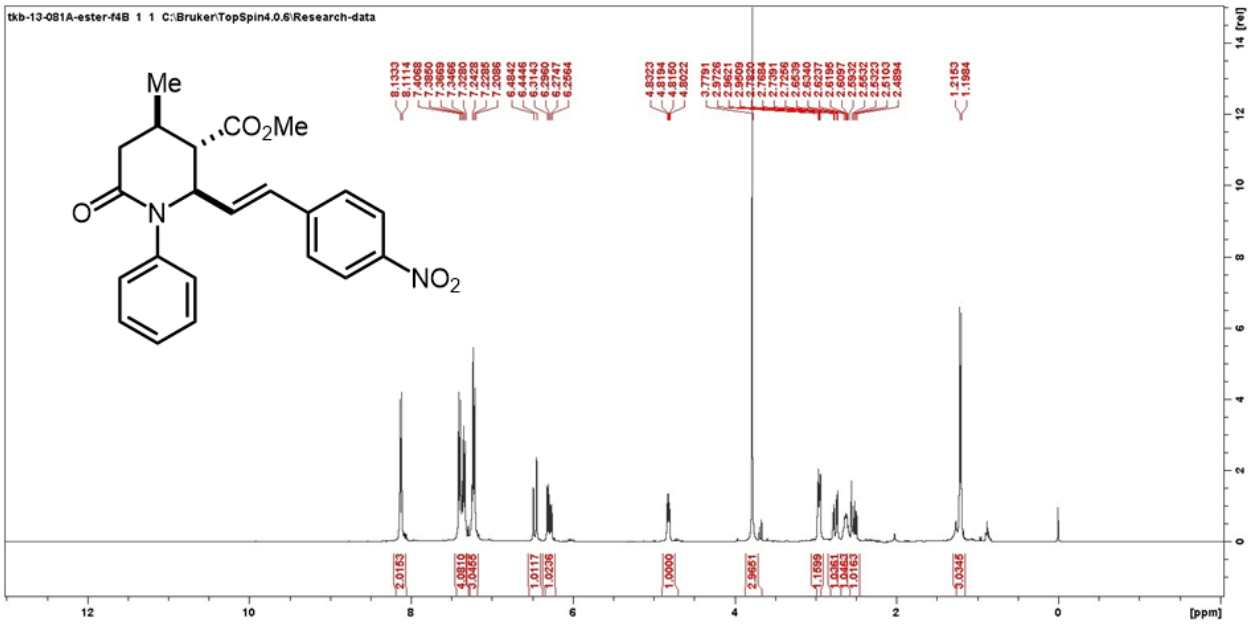
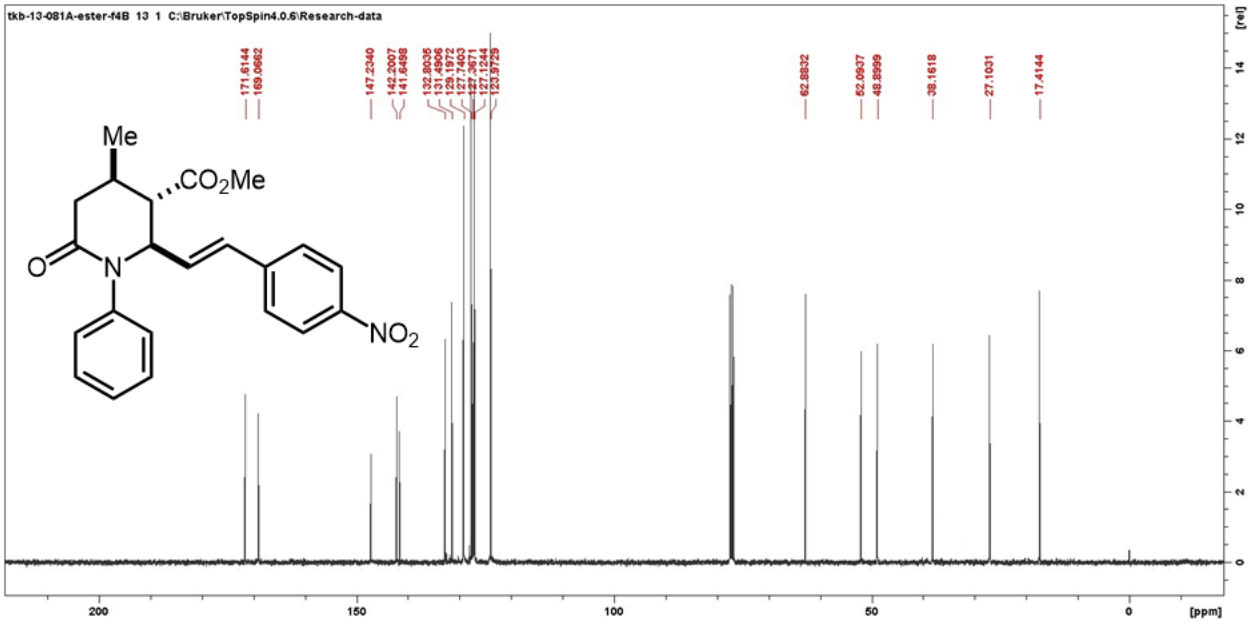
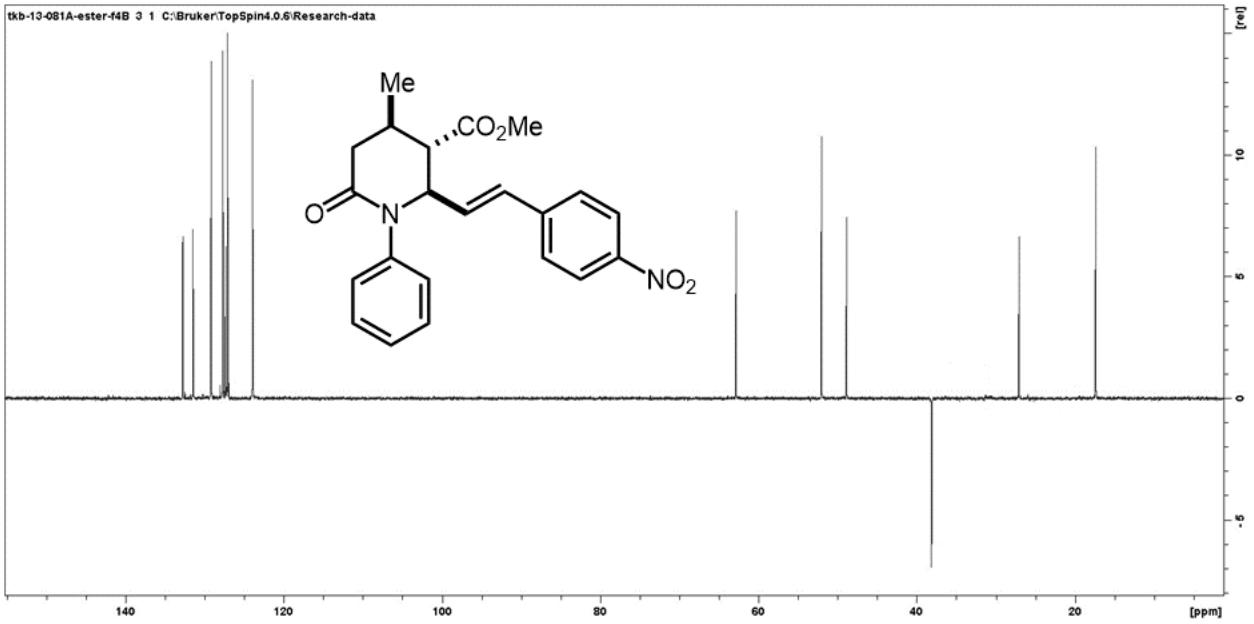


Compound 3c12

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 287.9 mg, 73%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, 2H), 7.41 – 7.32 (m, 4H), 7.24 – 7.21 (m, 2H), 6.46 (d, *J* = 15.8 Hz, 1H), 6.29 (dd, *J* = 15.8, 7.4 Hz, 1H), 3.78 (s, 3H), 3.00 – 2.95 (m, 1H), 2.75 (dd, *J* = 17.2, 5.4 Hz, 1H), 2.69 – 2.56 (m, 1H), 2.52 (dd, *J* = 17.2, 8.4 Hz, 1H), 1.21 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.62, 169.07, 147.24, 142.20, 141.65, 132.81, 131.49, 129.20, 127.74, 127.37, 127.13, 123.98, 62.89, 52.10, 48.90, 38.17, 27.11, 17.42. **HRMS-EI$^+$** (*m/z*): calc for $C_{22}H_{22}N_2O_5$, 394.1529, found 394.1533.



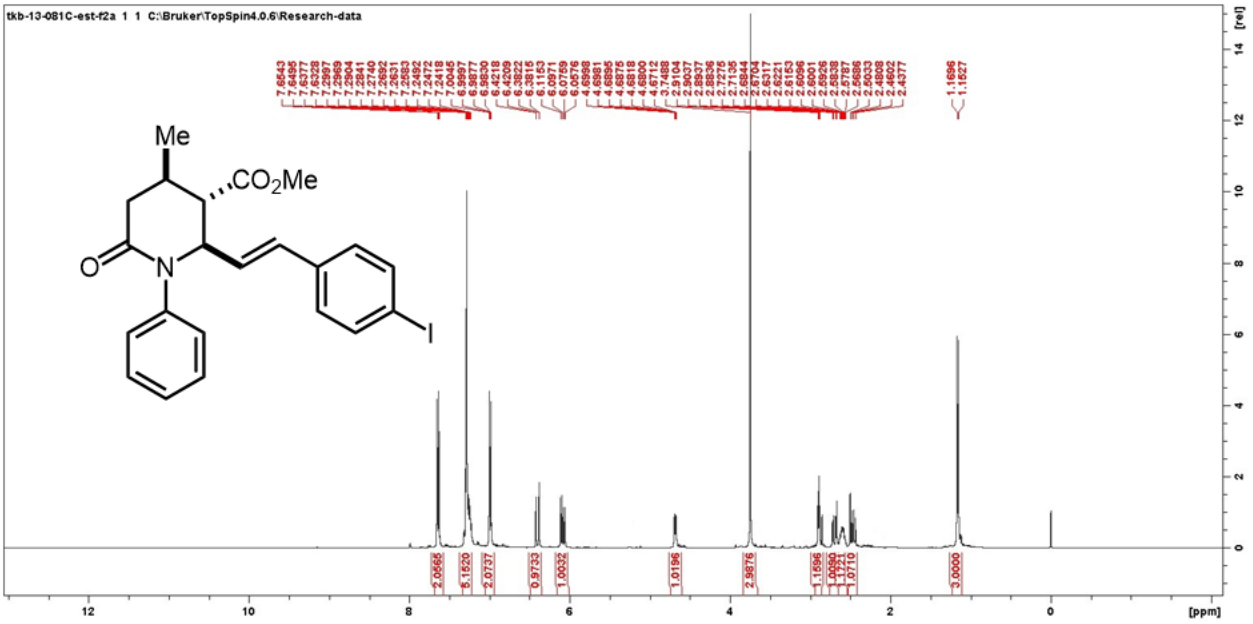


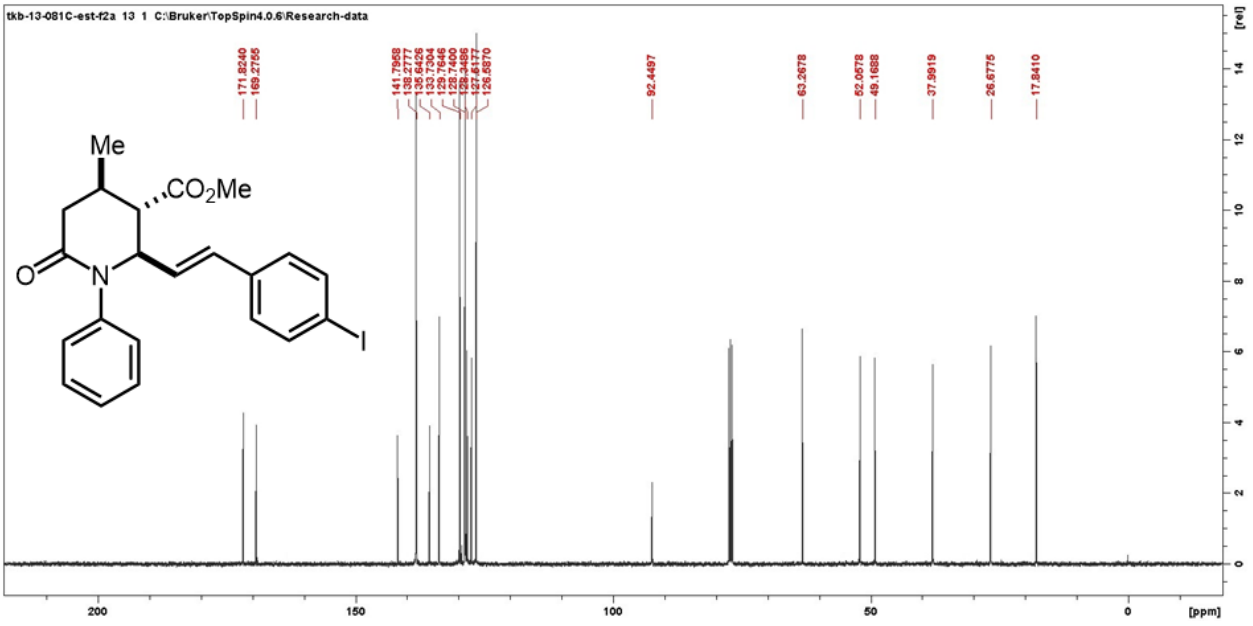


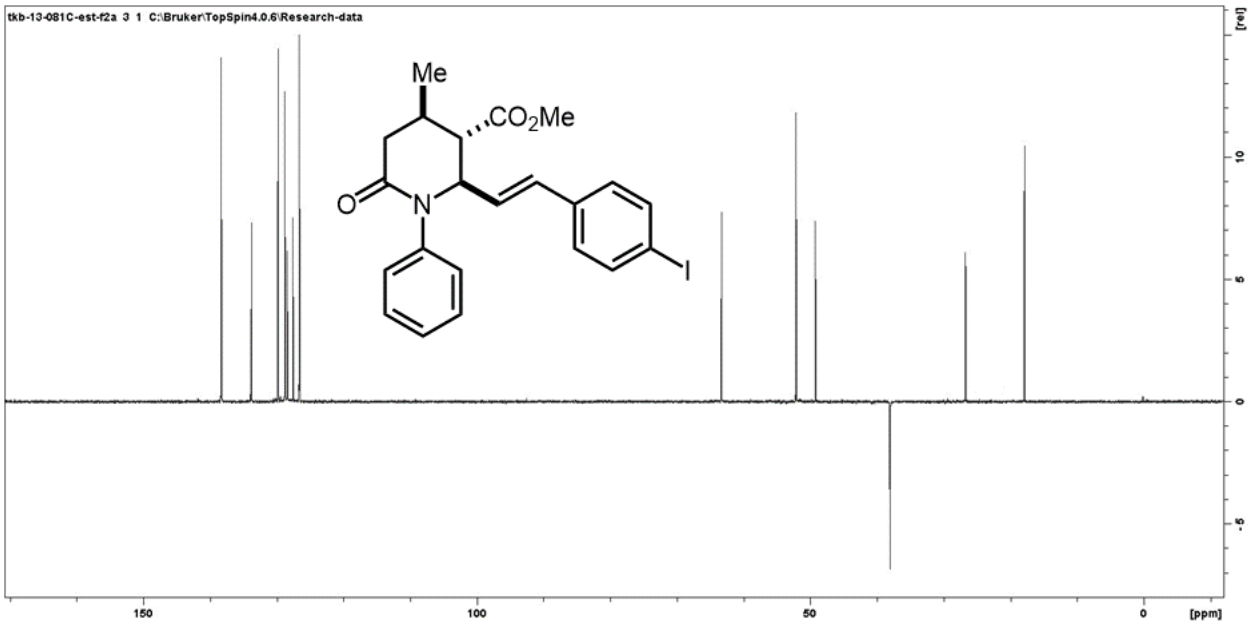
Compound 3c13

Prepared in 5 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 1876 mg, 79%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.3 Hz, 2H), 7.30 – 7.24 (m, 5H), 7.00 (d, J = 7.3 Hz, 2H), 6.40 (d, J = 15.8 Hz, 1H), 6.09 (dd, J = 15.8, 7.3 Hz, 1H), 4.68 (dd, J = 7.3, 4.2 Hz, 1H), 3.75 (s, 3H), 2.93 – 2.83 (m, 1H), 2.70 (dd, J = 17.2, 5.6 Hz, 1H), 2.67 – 2.53 (m, 1H), 2.47 (dd, J = 17.2,

9.0 Hz, 1H), 1.17 (d, J = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 169.3, 141.8, 138.3, 135.6, 133.7, 129.8, 128.7, 128.3, 127.5, 126.6, 92.4, 63.3, 52.1, 49.2, 38.0, 26.7, 17.8. **HRMS-EI$^+$** (m/z): calc for $C_{22}H_{22}INO_3$, 475.0644, found 475.0649.

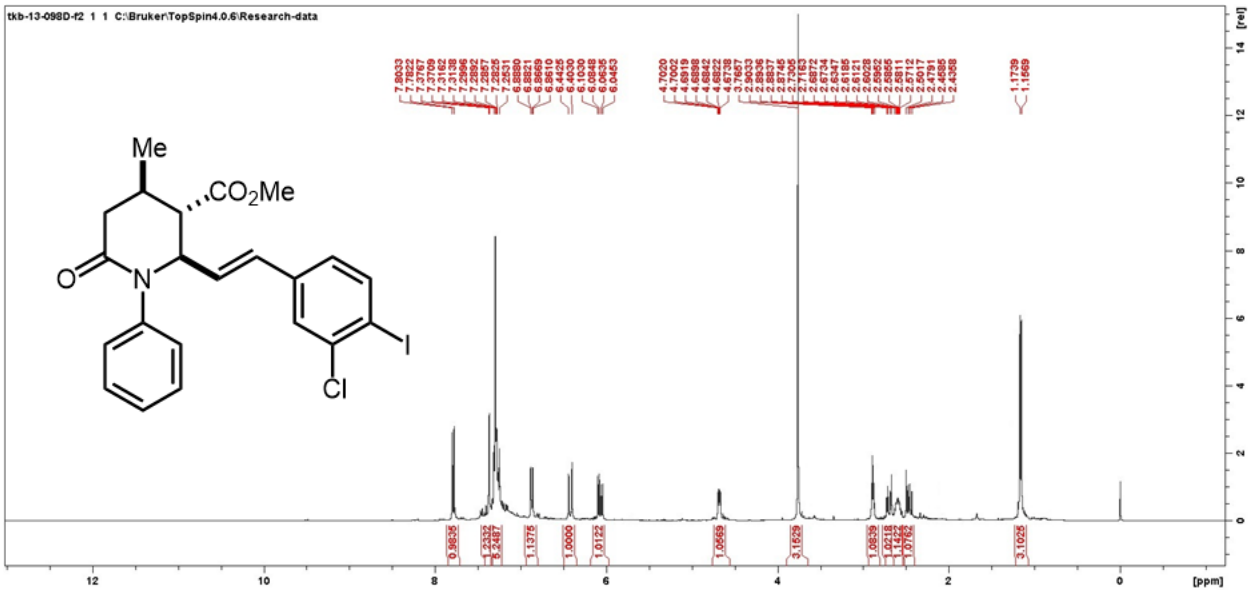


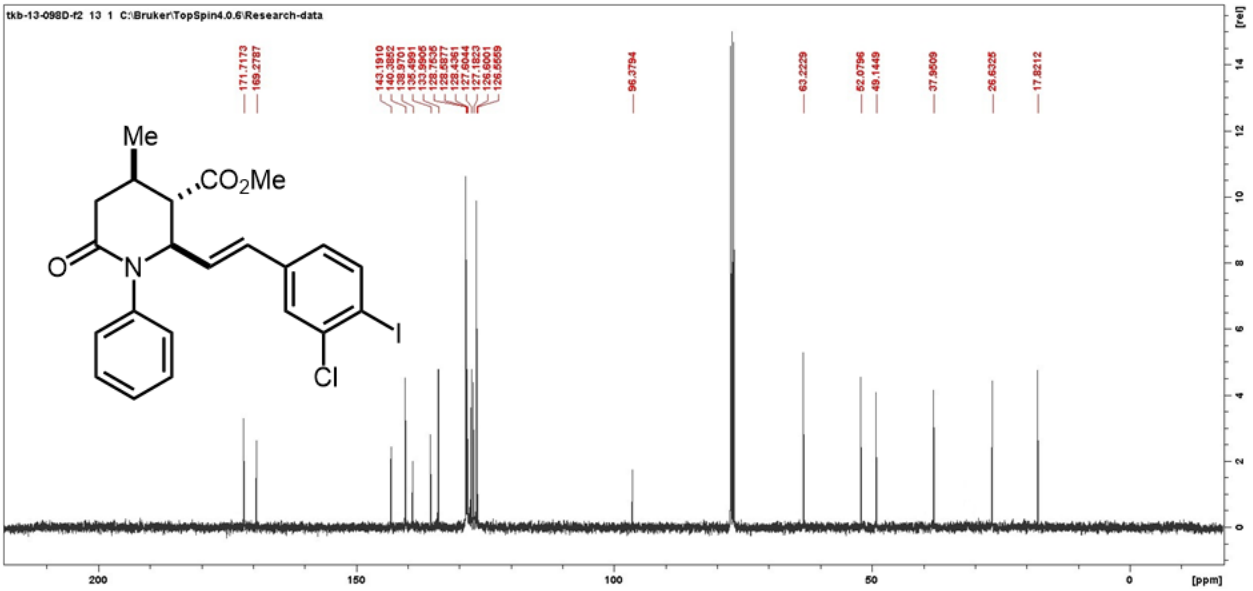


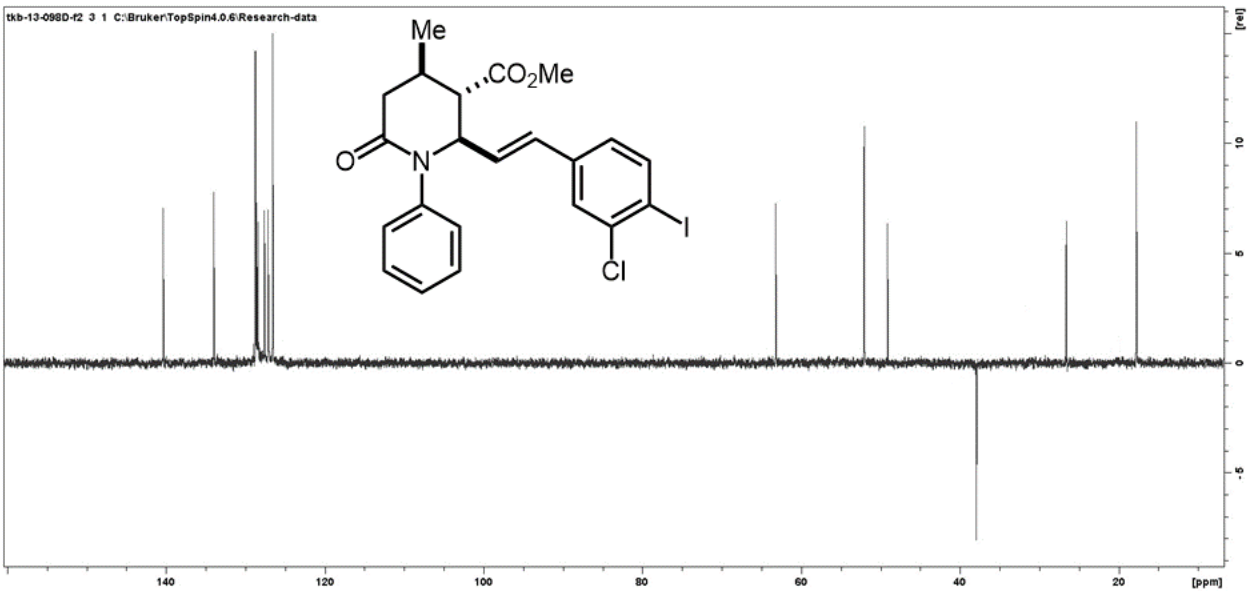


Compound 3c14

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 372.1 mg, 73%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.4 Hz, 1H), 7.38 – 7.25 (m, 6H), 6.87 (d, J = 8.4 Hz, 1H), 6.40 (d, J = 15.8 Hz, 1H), 6.07 (dd, J = 15.8, 7.3 Hz, 1H), 4.73 – 4.62 (m, 1H), 3.77 (s, 3H), 2.89 (q, J = 3.8 Hz, 1H), 2.70 (dd, J = 17.2, 5.6 Hz, 1H), 2.65 – 2.53 (m, 1H), 2.47 (dd, J = 17.3, 9.1 Hz, 1H), 1.17 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 169.3, 143.2, 140.4, 138.9, 135.5, 134.0, 128.8, 128.6, 128.4, 127.6, 127.2, 126.6, 96.4, 63.2, 52.1, 49.1, 37.9, 26.6, 17.8. **HRMS-EI^{+}** (*m/z*): calc for $C_{22}H_{21}ClINO_3$, 509.0255, found 509.0258.



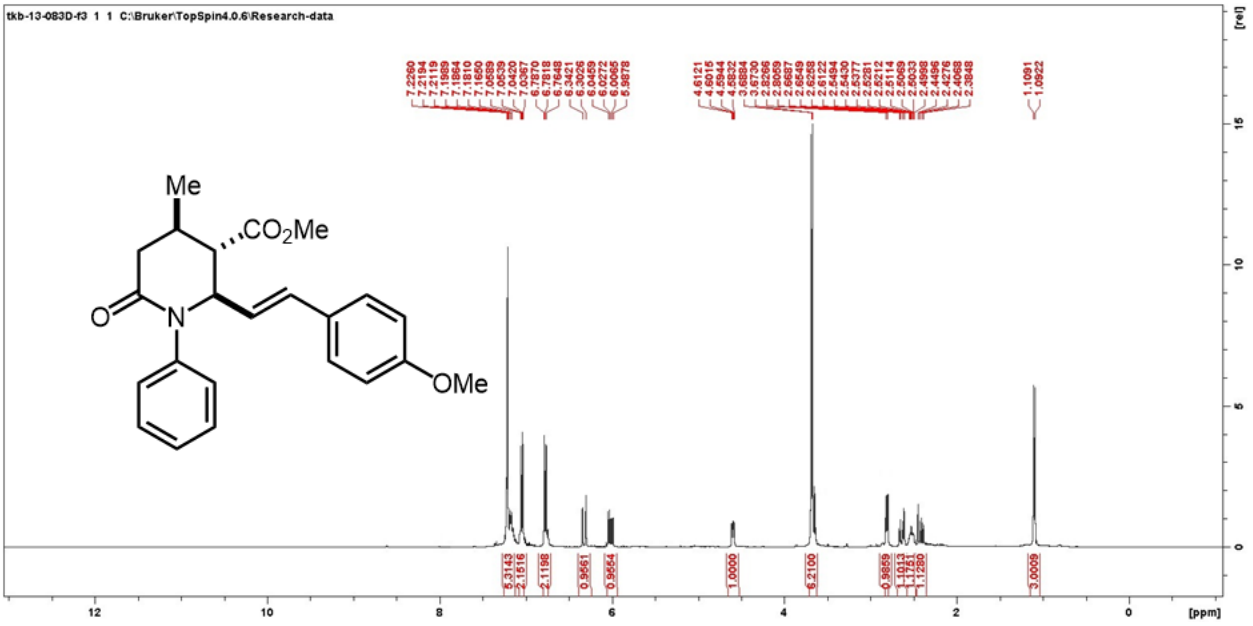


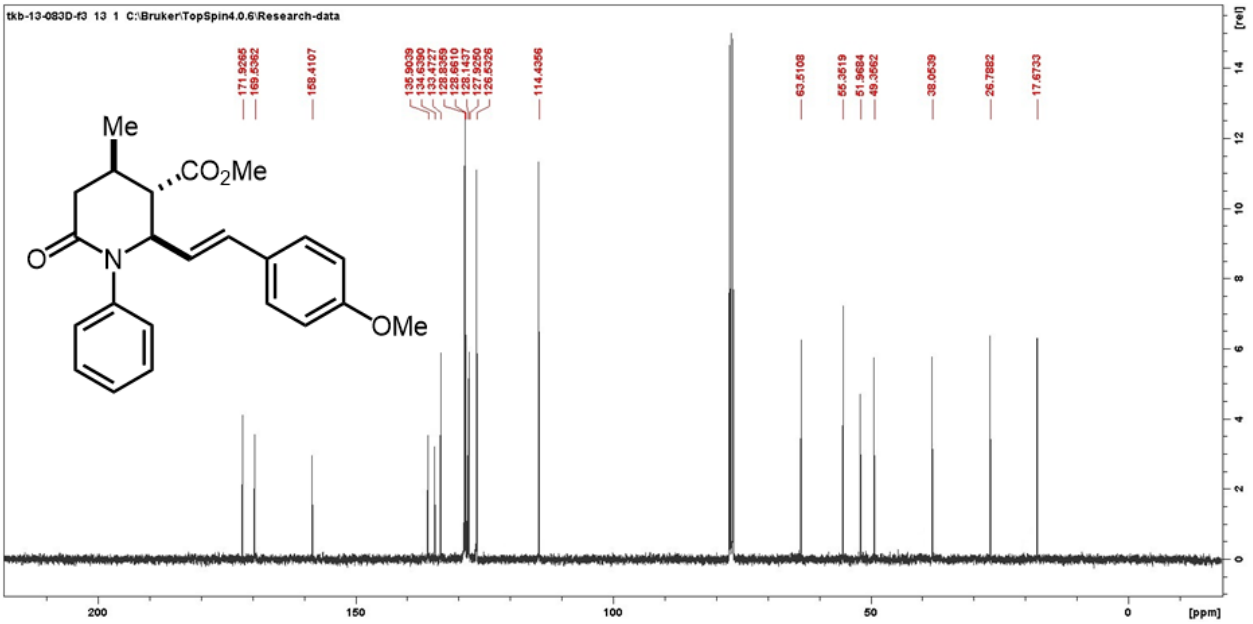


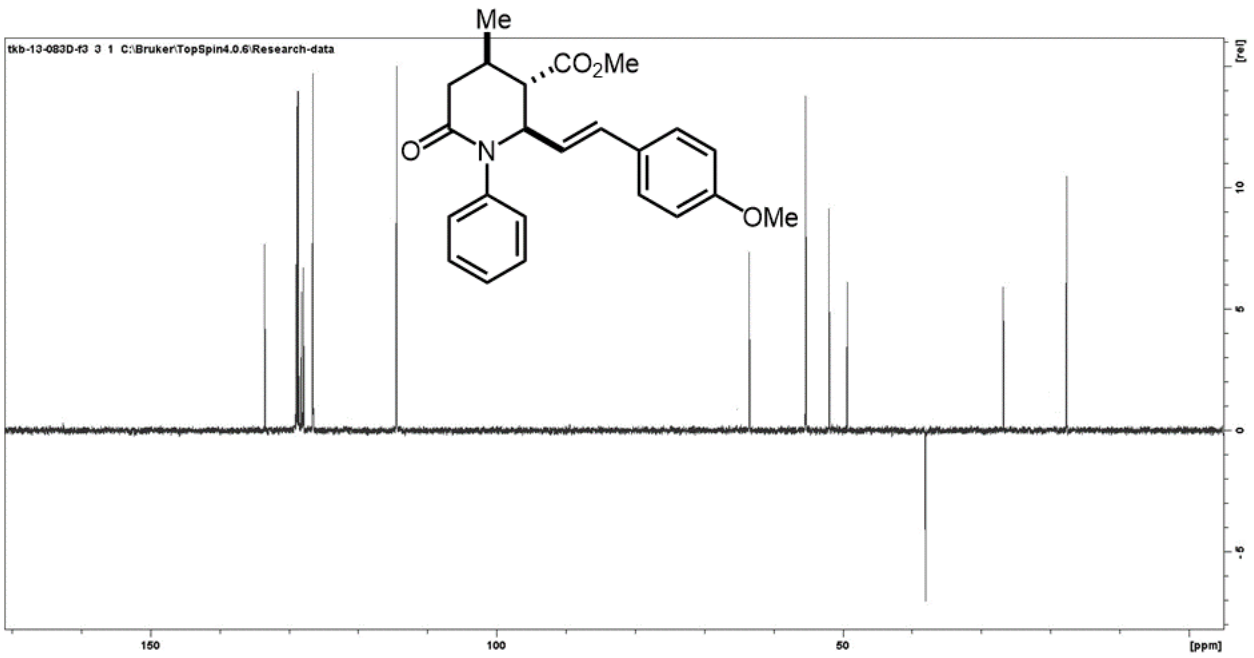
Compound 3c15

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 311.1 mg, 82%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 5H), 7.12 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.40 (d, *J* = 15.8 Hz, 1H), 6.09 (dd, *J* = 15.8, 7.5 Hz, 1H), 4.71 – 4.64 (m, 1H), 3.78 – 3.59 (m, 6H), 2.89 (t, *J* = 4.1 Hz, 1H), 2.71 (dd, *J* = 17.1, 5.6 Hz, 1H), 2.65 – 2.54 (m, 1H), 2.49 (dd, *J* = 17.1, 8.9 Hz, 1H), 1.17 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.90, 169.49, 158.39,

135.89, 134.65, 133.44, 128.82, 128.64, 128.12, 127.93, 126.52, 114.41, 63.50, 55.32, 51.94, 49.32, 38.05, 26.77, 17.66. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{23}H_{25}NO_4$, 379.1784, found 379.1789. FTIR (KBr): 2932.5, 1721.4, 1665.4, 1607.2, 1511.1, 1431.8, 1414.7, 1344.9, 1298.4, 1245.6, 1179.4, 1135.3, 1031.8, 996.7, 921.8, 832.1, 701.6.

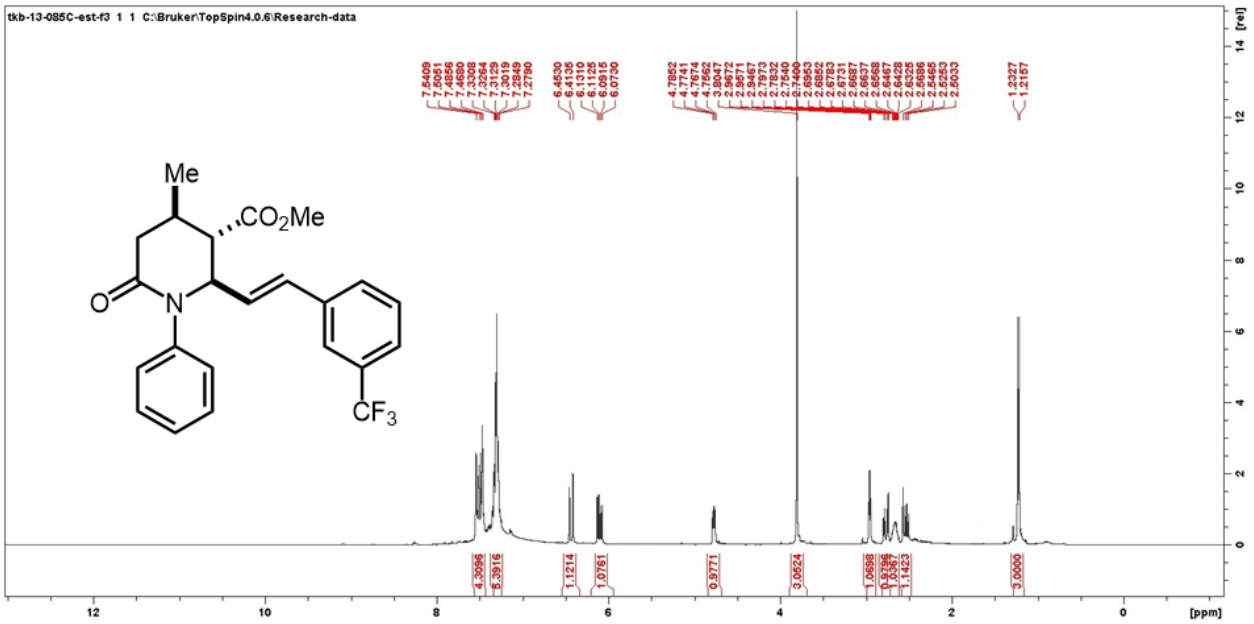






Compound 3c16

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 292.2 mg, 70%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.46 (m, 4H), 7.33 – 7.28 (m, 5H), 6.44 (d, *J* = 15.8 Hz, 1H), 6.10 (dd, *J* = 15.8, 7.4 Hz, 1H), 4.79 – 4.76 (m, 1H), 3.80 (s, 3H), 2.96 (t, *J* = 4.2 Hz, 1H), 2.77 (dd, *J* = 17.3, 5.7 Hz, 1H), 2.73 – 2.59 (m, 1H), 2.54 (dd, *J* = 17.3, 8.8 Hz, 1H), 1.22 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.73, 169.40, 142.42, 135.57, 134.09, 131.53, 129.60, 128.71, 128.36, 127.26, 126.53, 124.70, 124.66, 124.05, 124.02, 63.26, 52.06, 49.21, 38.04, 26.78, 17.71. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{22}F_3NO_3$, 417.1552, found 417.1555.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O
N
CF3
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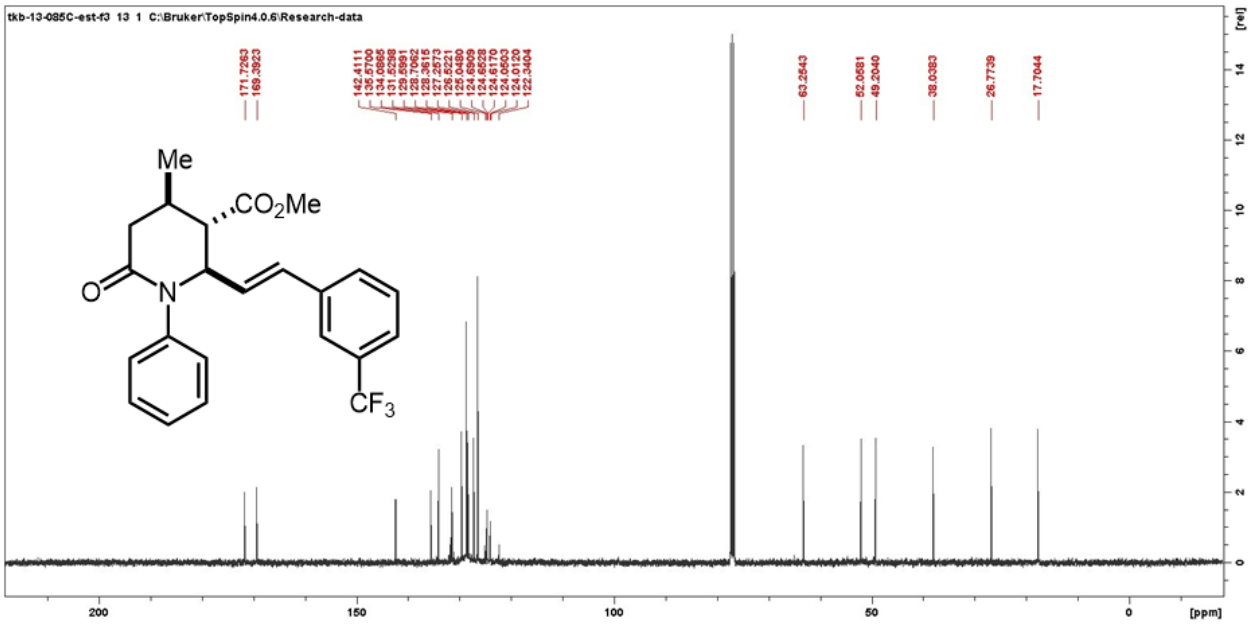
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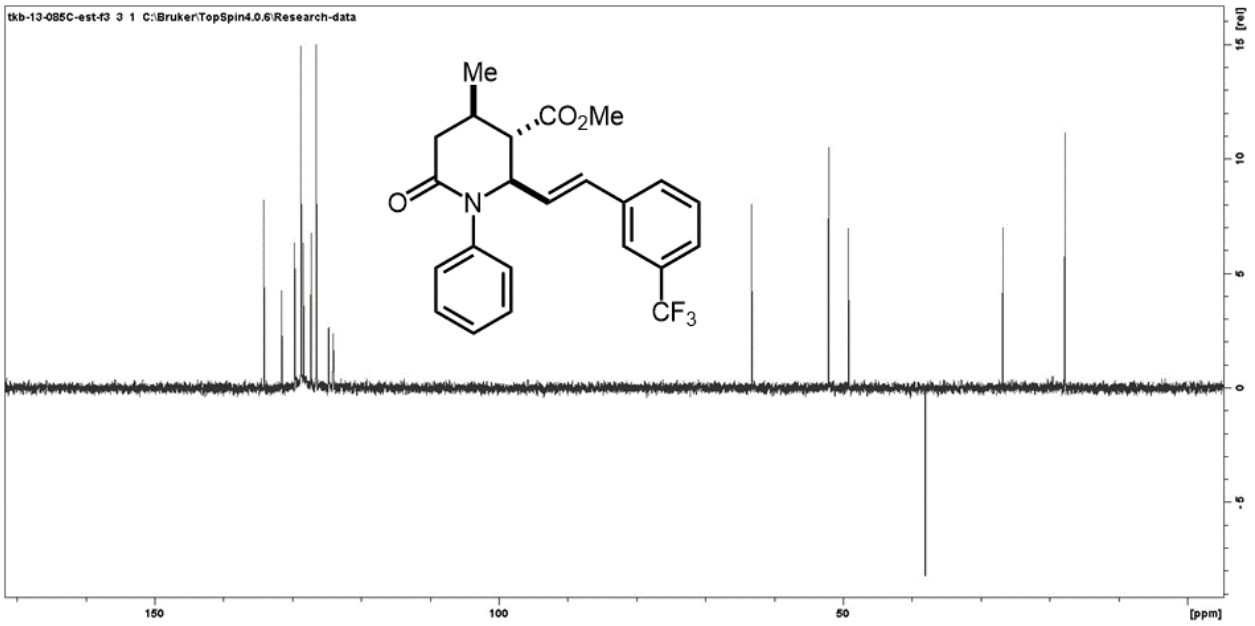
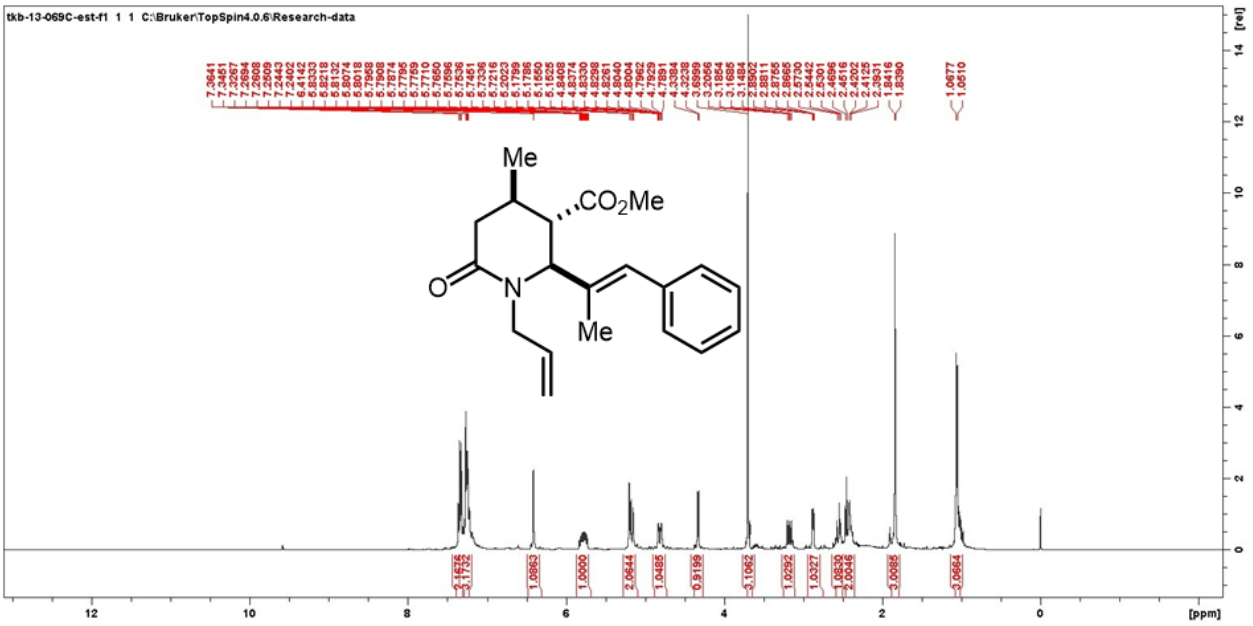


Compound 3c17

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 261.9 mg, 80%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.24 (m, 5H), 6.41 (s, 1H), 5.78 (dddd, *J* = 16.9, 10.4, 8.0, 4.6 Hz, 1H), 5.25 – 5.10 (m, 2H), 4.81 (ddt, *J* = 14.8, 4.6, 1.7 Hz, 1H), 4.32 (d, *J* = 4.4 Hz 1H), 3.70 (s, 3H), 3.17 (dt, *J* = 14.8, 7.3 Hz, 1H), 2.90 – 2.87 (t, 1H), 2.57 – 2.39 (m, 3H), 1.84 (s, 3H), 1.05 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.97, 169.28, 136.72, 134.10, 132.60, 129.20, 128.91, 128.82, 128.79, 128.29, 128.27, 128.25, 127.01, 118.13, 63.44, 51.83, 46.93, 46.70, 37.91, 26.72, 16.71, 14.74. **HRMS-EI^{+}** (*m/z*): calc for $C_{20}H_{25}NO_3$, 327.1834, found 327.1839.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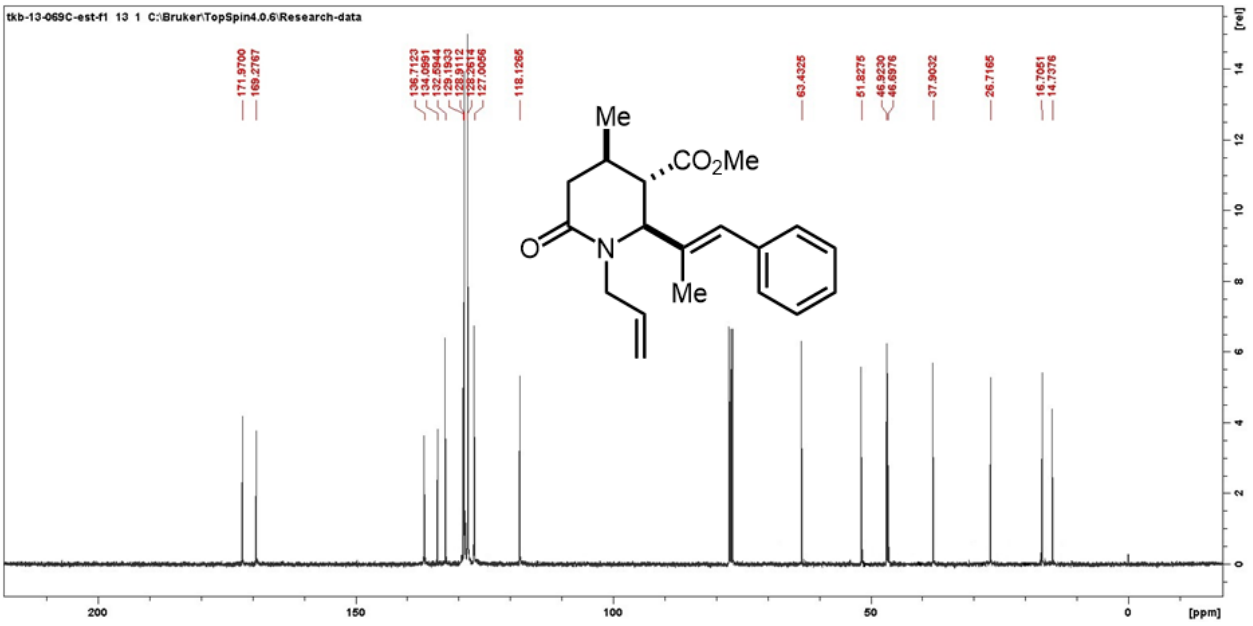
N
Me
[ppm]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63.4325
51.8275
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CO2Me
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Me
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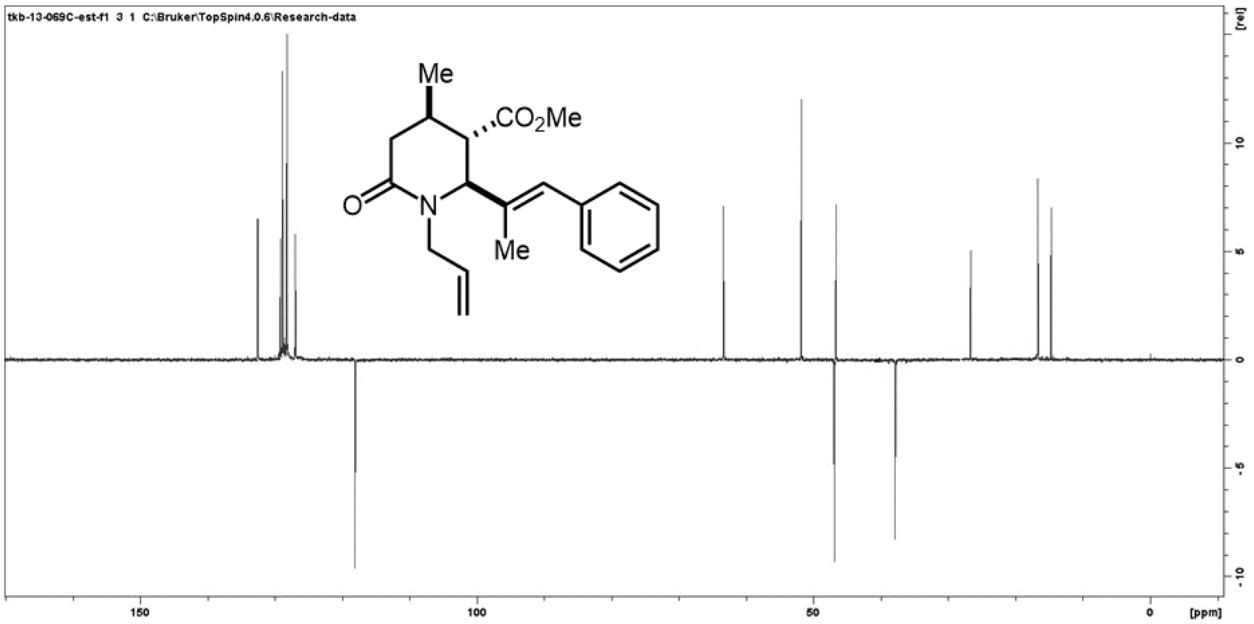
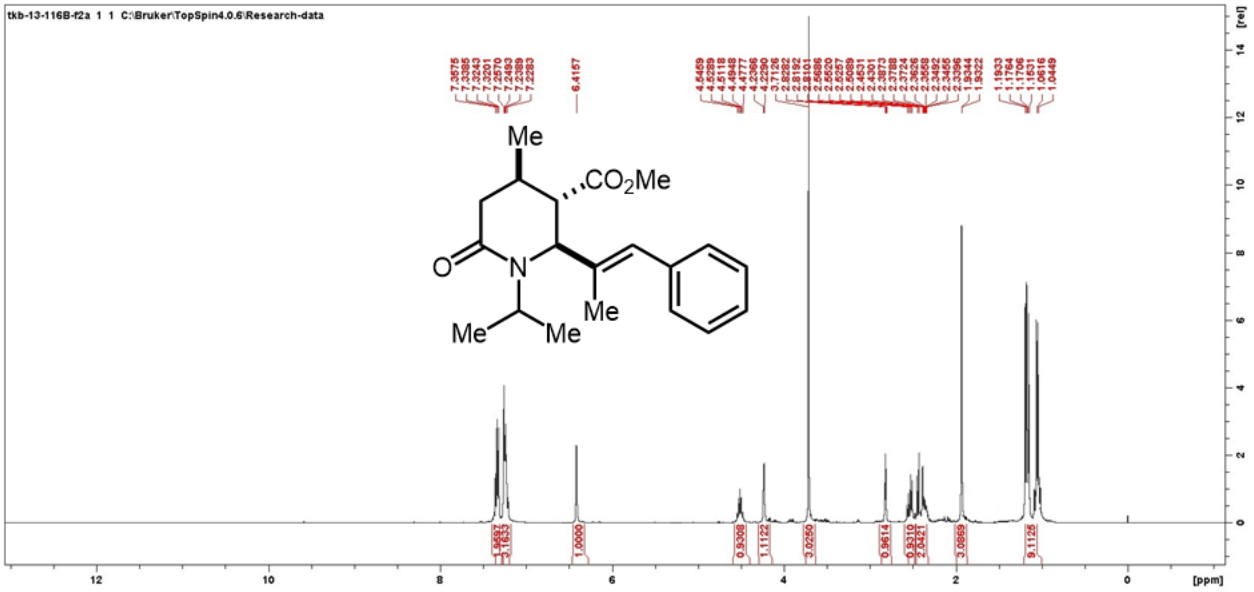
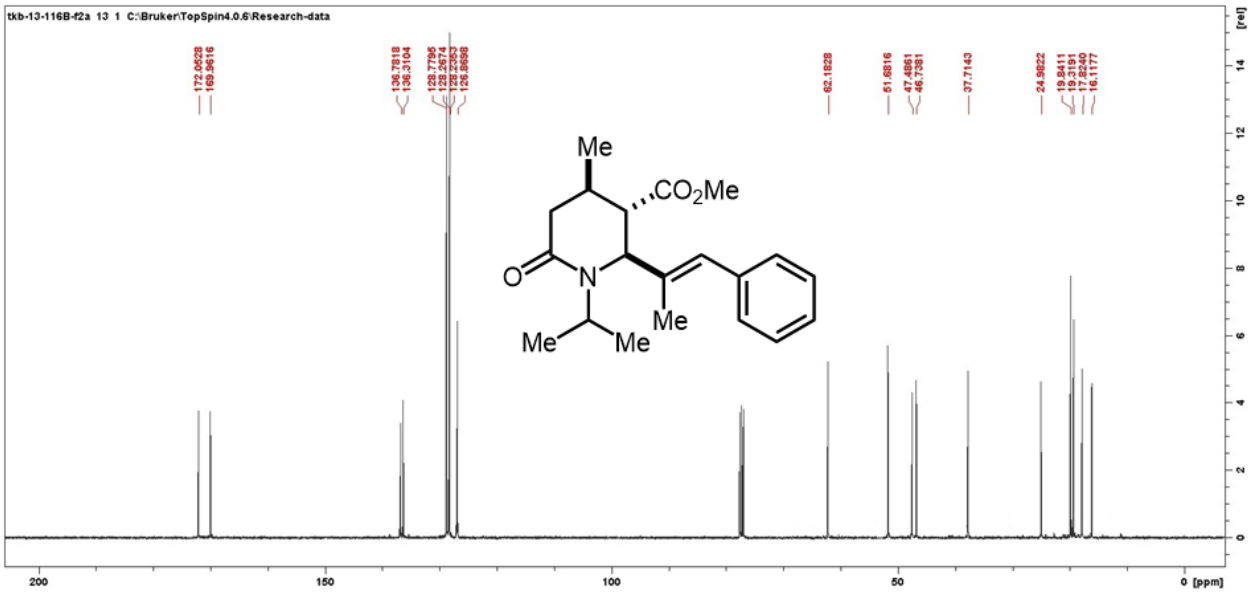
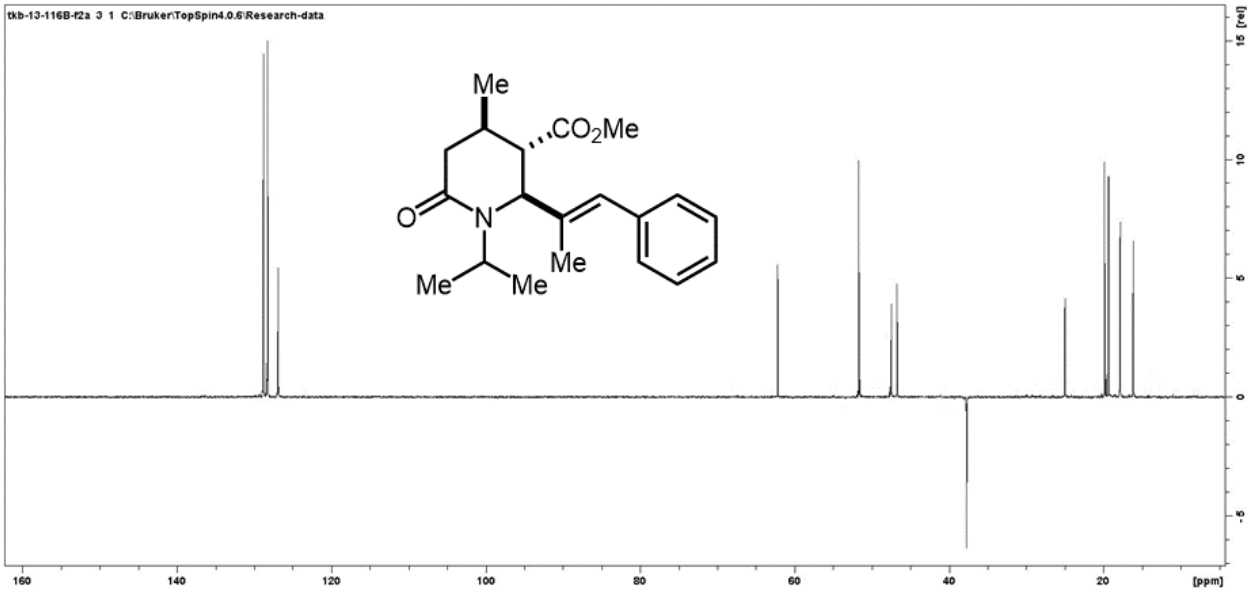


Compound 3c18

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 266.8 mg, 81%, 95:5 dr. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{20}H_{27}NO_3$, 329.1991, found 329.1998.

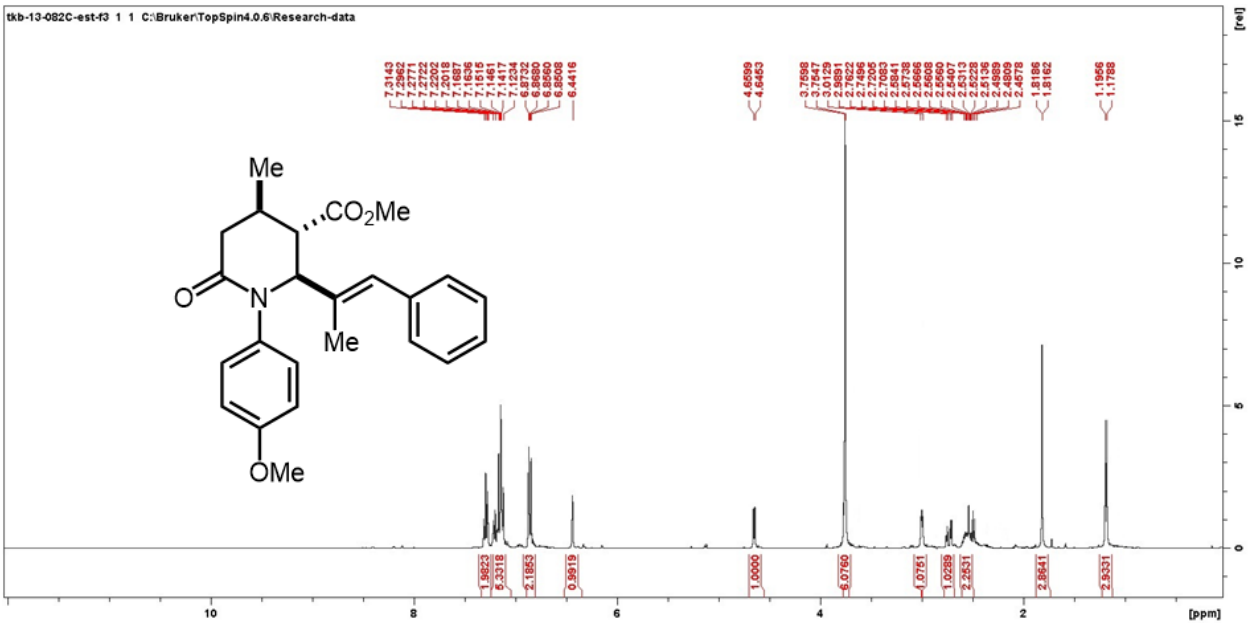






Compound 3c19

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 299.0 mg, 76%, 95:5 dr. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{24}H_{27}NO_4$, 393.1940, found 393.1945.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OMe
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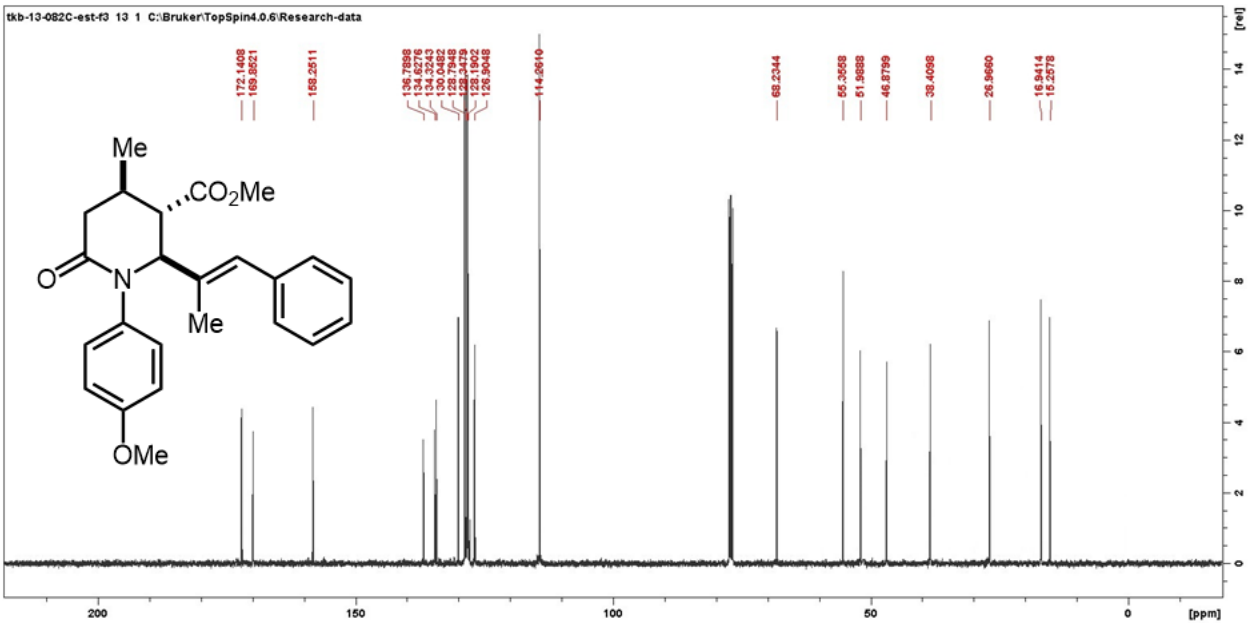
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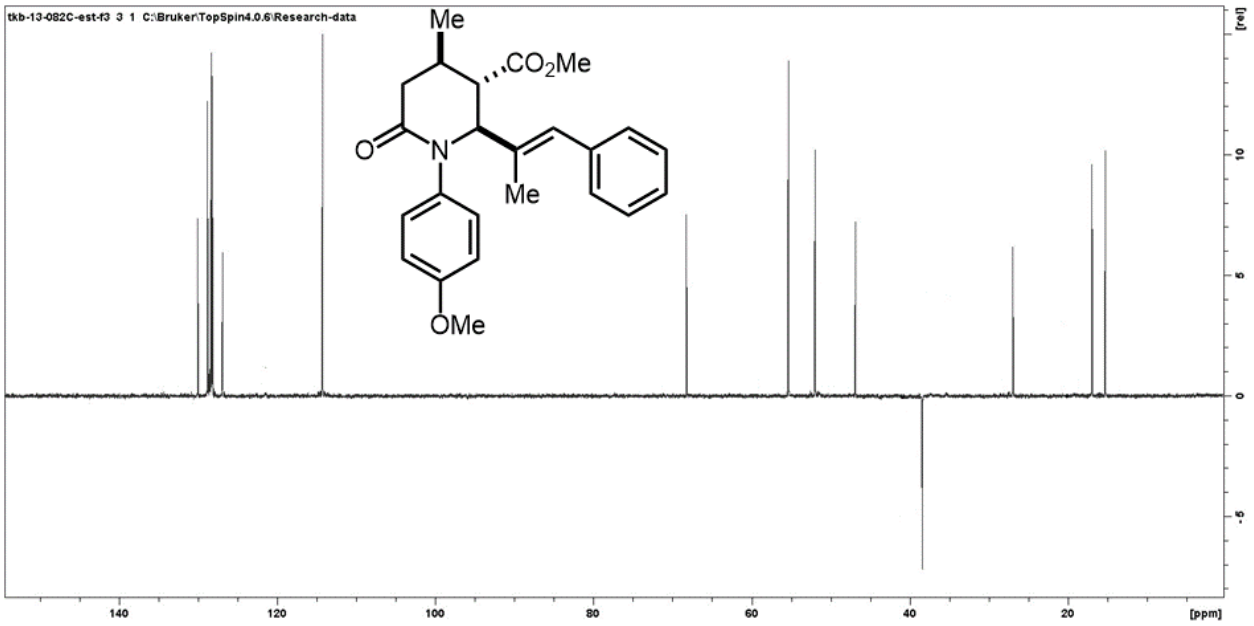
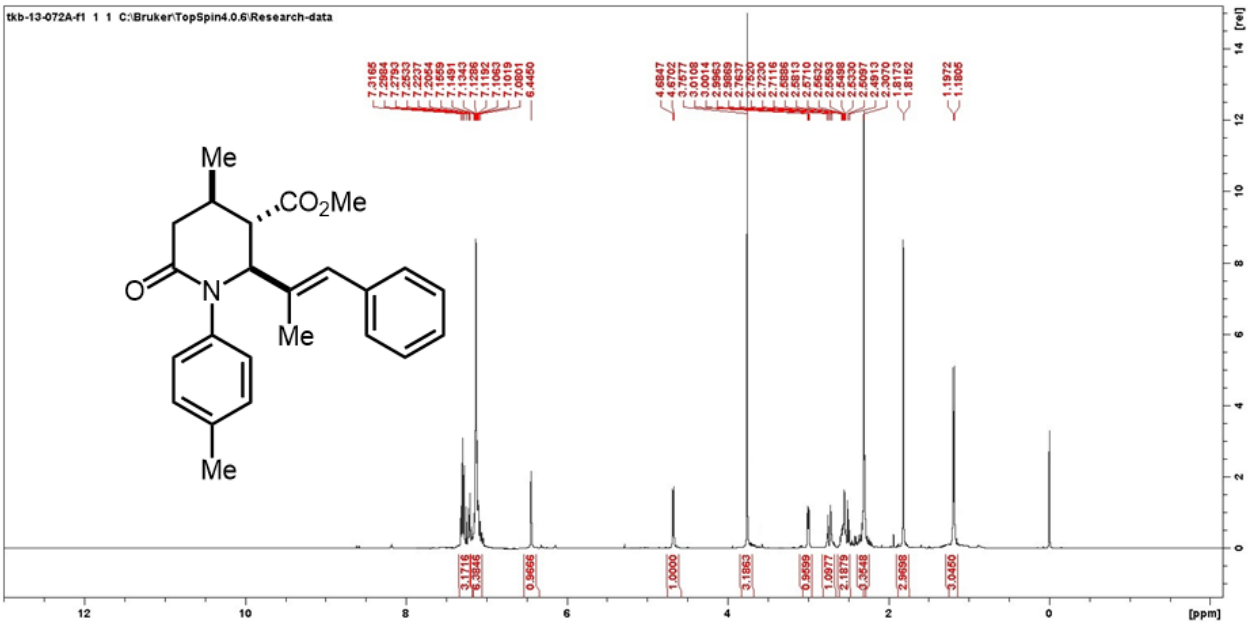


Compound 3c20

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 271.8 mg, 72%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.20 (m, 3H), 7.16 – 7.09 (m, 6H), 6.45 (s, 1H), 4.68 (d, J = 5.9 Hz, 1H), 3.76 (s, 3H), 3.00 (dd, J = 5.9, 3.7 Hz, 1H), 2.80 – 2.67 (m, 1H), 2.64 – 2.49 (m, 2H), 2.31 (s, 3H), 1.82 (s, 3H), 1.19 (d, J = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.16, 169.76, 139.21, 136.83, 136.81, 134.32, 130.03, 129.64, 129.38, 128.82, 128.19, 127.05, 126.90, 68.08, 52.02, 46.92, 38.43, 26.95, 21.07, 16.98, 15.29. **HRMS-EI^{+}** (*m/z*): calc for $C_{24}H_{27}NO_3$, 377.1991, found 377.1996.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N
Me
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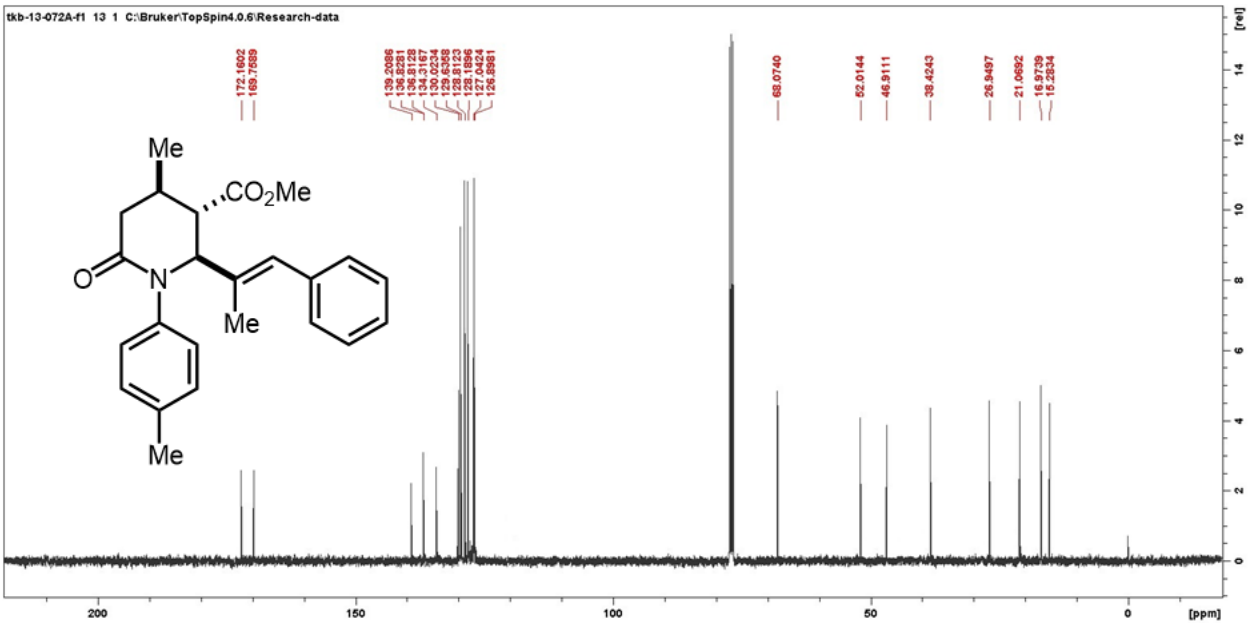
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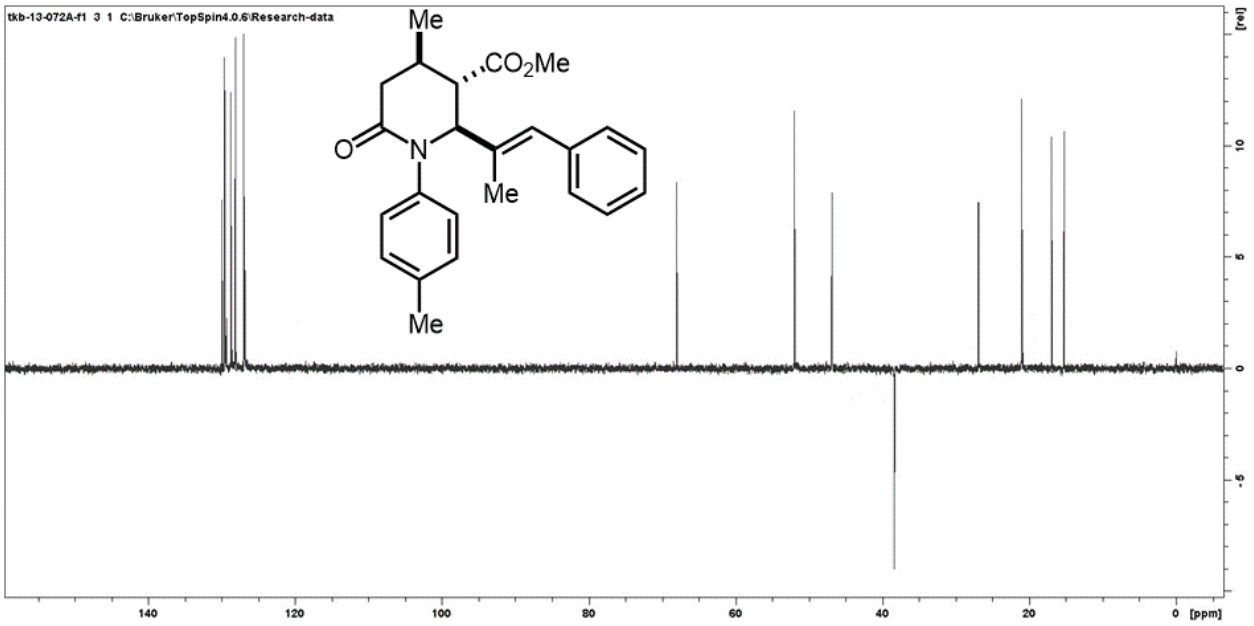
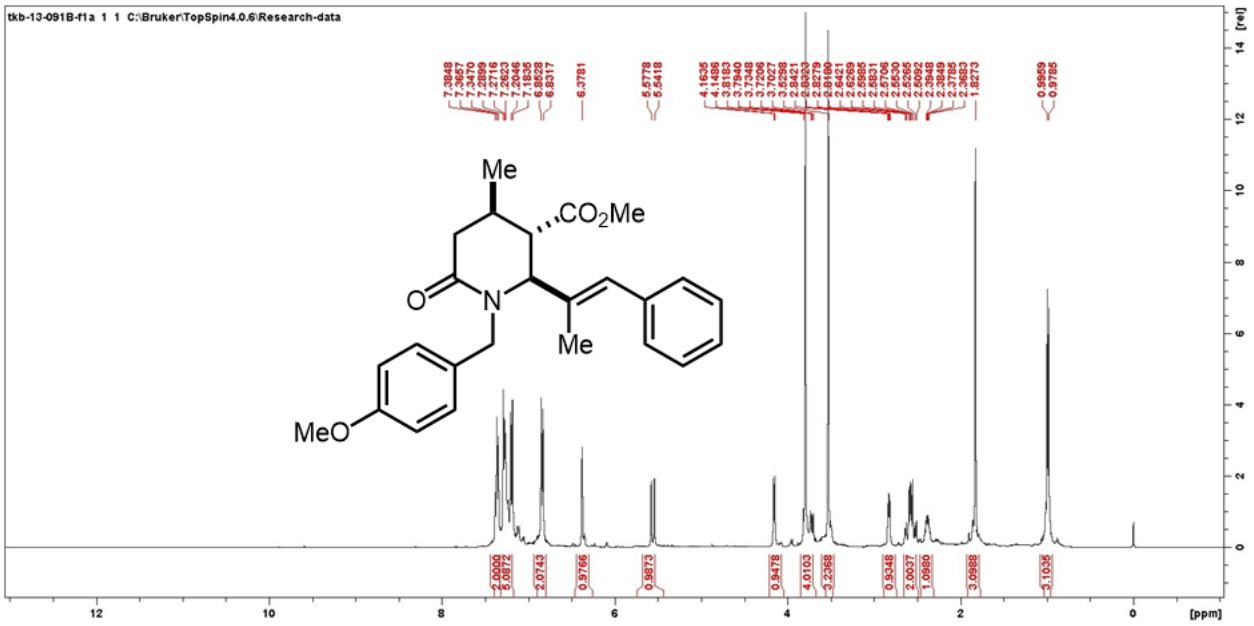


Compound 3c21

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 354.5 mg, 87%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.18 (m, 7H), 6.84 (d, J = 7.3 Hz, 2H), 6.38 (s, 1H), 5.56 (d, J = 14.4 Hz, 1H), 4.16 (d, J = 6.0 Hz, 1H), 3.81 – 3.70 (m, 4H), 3.51 (s, 3H), 2.83 (dd, J = 6.0, 3.8 Hz, 1H), 2.67 – 2.43 (m, 2H), 2.39 (pd, J = 7.0, 4.4 Hz, 1H), 1.83 (s, 3H), 0.99 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 169.7, 159.0, 136.8, 133.9, 130.1, 129.0, 128.9, 128.3, 127.1, 113.8, 63.0, 55.3, 51.7, 46.7, 46.5, 38.0, 26.6, 16.6, 14.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{25}H_{29}NO_4$, 407.2097, found 407.2092.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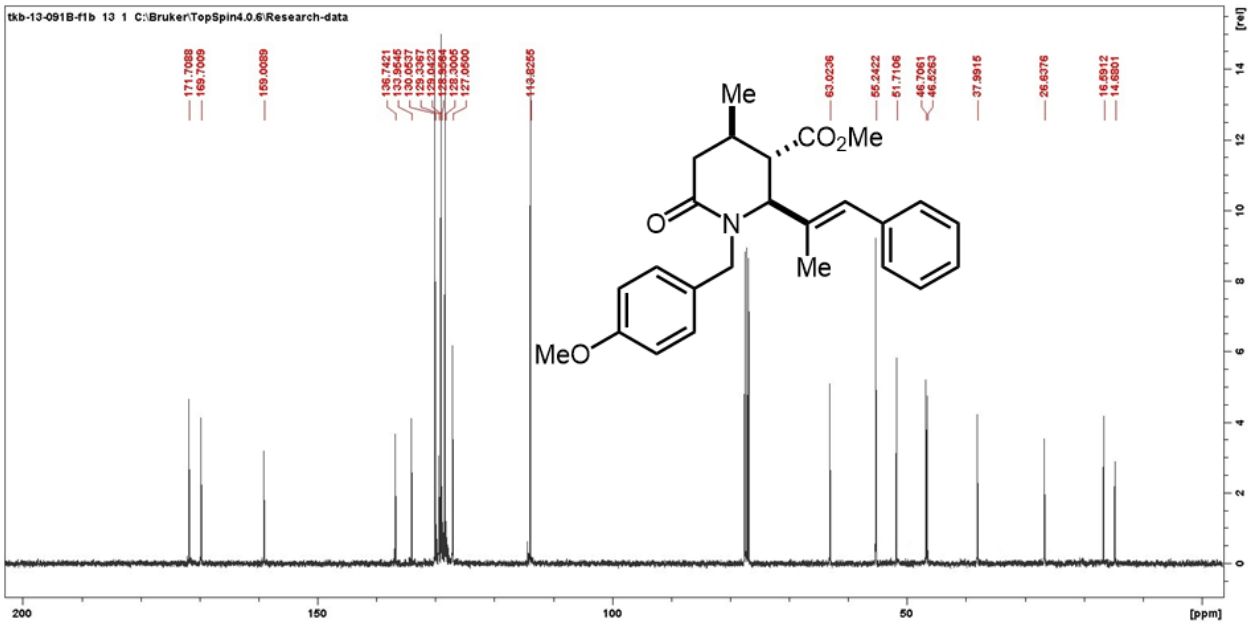
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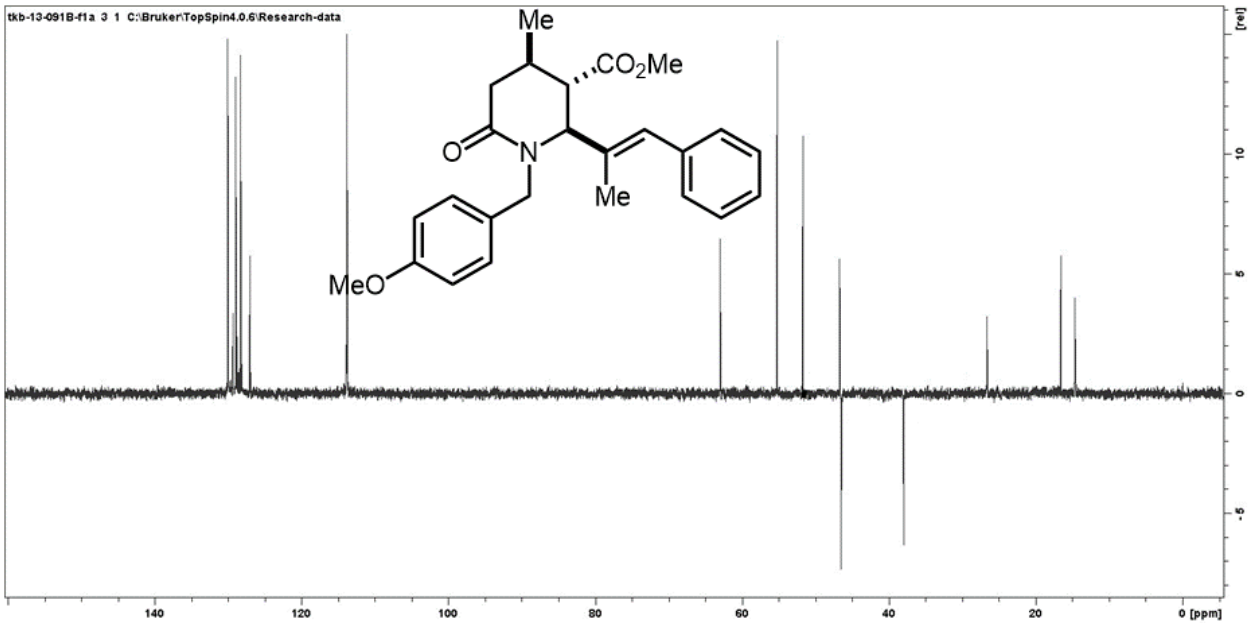
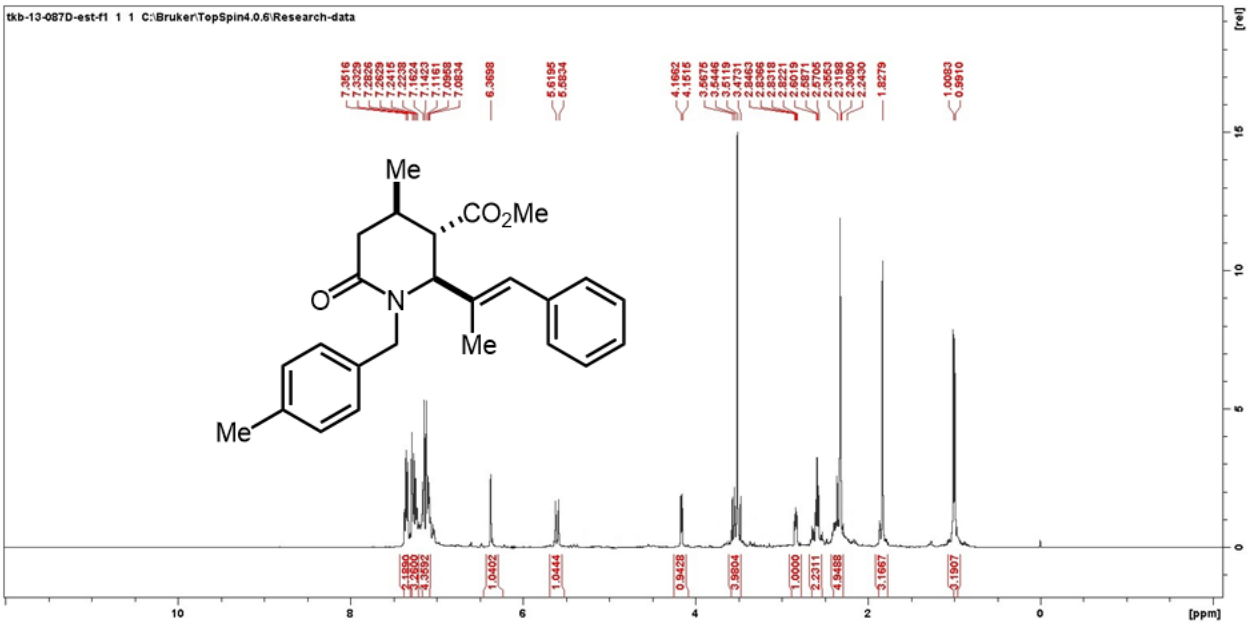


Compound 3c22

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Oily substance. Yield = 324.9 mg, 83%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.08 (m, 9H), 6.37 (s, 1H), 5.60 (d, *J* = 14.5 Hz, 1H), 4.16 (d, *J* = 5.9 Hz, 1H), 3.57 – 3.47 (m, 4H), 2.83 (dd, *J* = 6.0, 3.8 Hz, 1H), 2.69 – 2.45 (m, 2H), 2.45 – 2.24 (m, 5H), 1.83 (s, 3H), 1.00 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 169.7, 137.0, 136.8, 133.9, 133.9, 129.1, 129.0, 128.7, 128.3, 127.0, 63.1, 51.7, 46.9, 46.7, 37.9, 26.6, 21.1, 16.7, 14.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{25}H_{29}NO_3$, 391.2147, found 391.2153.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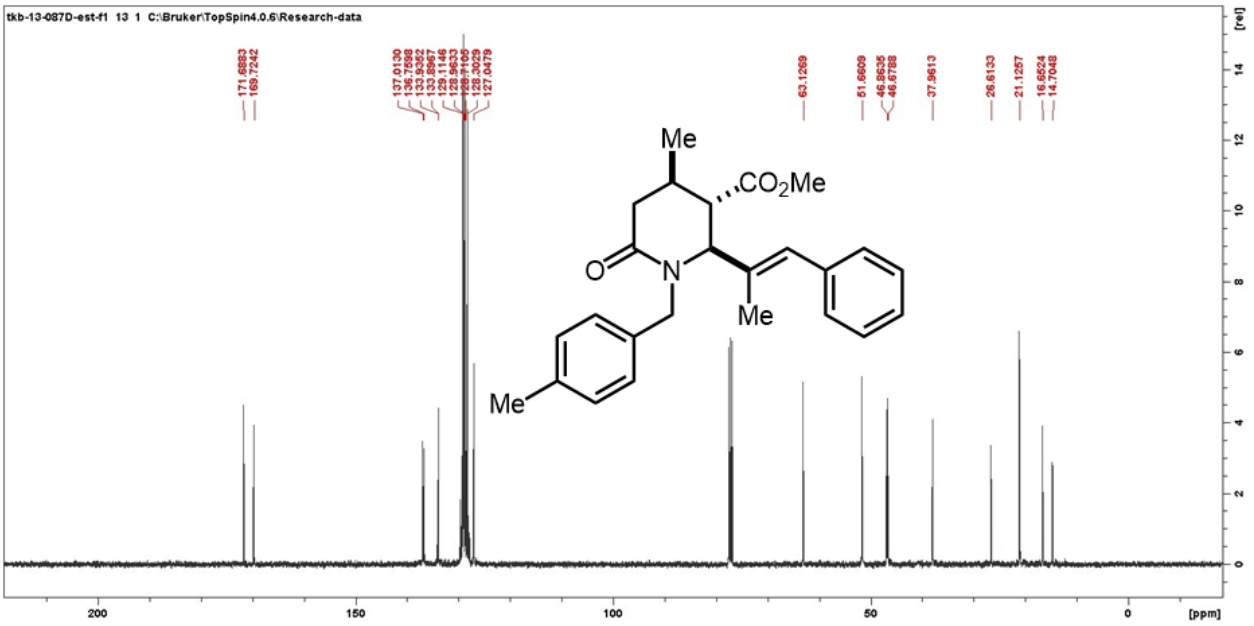
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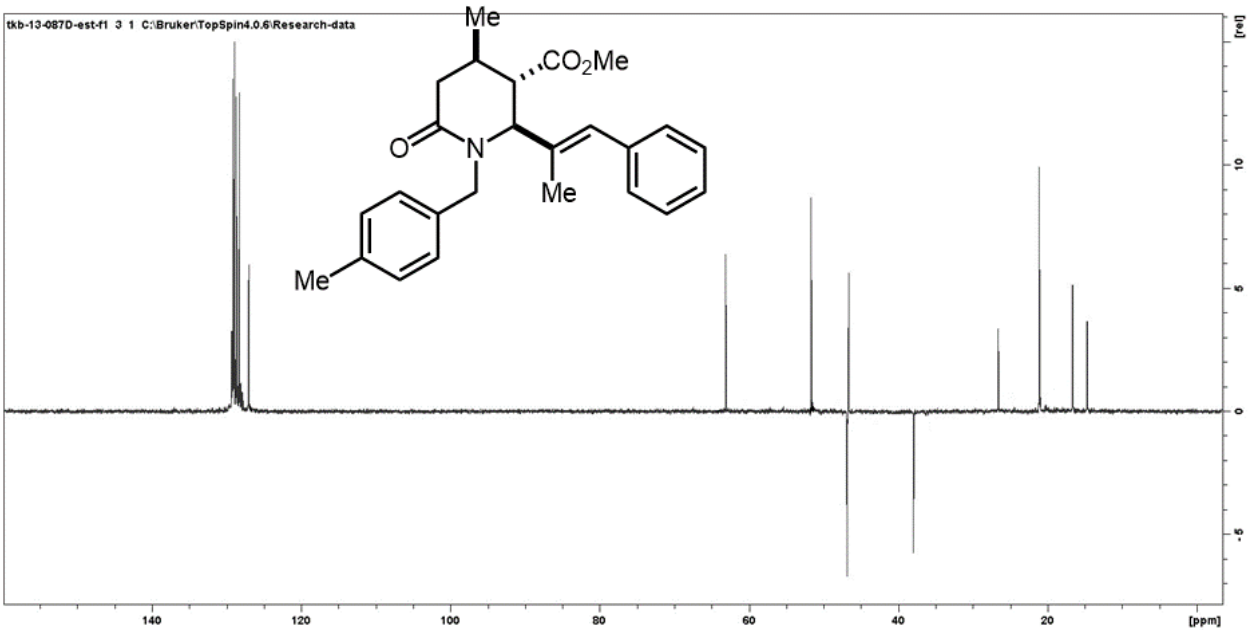
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N
Me
Me
[rel]
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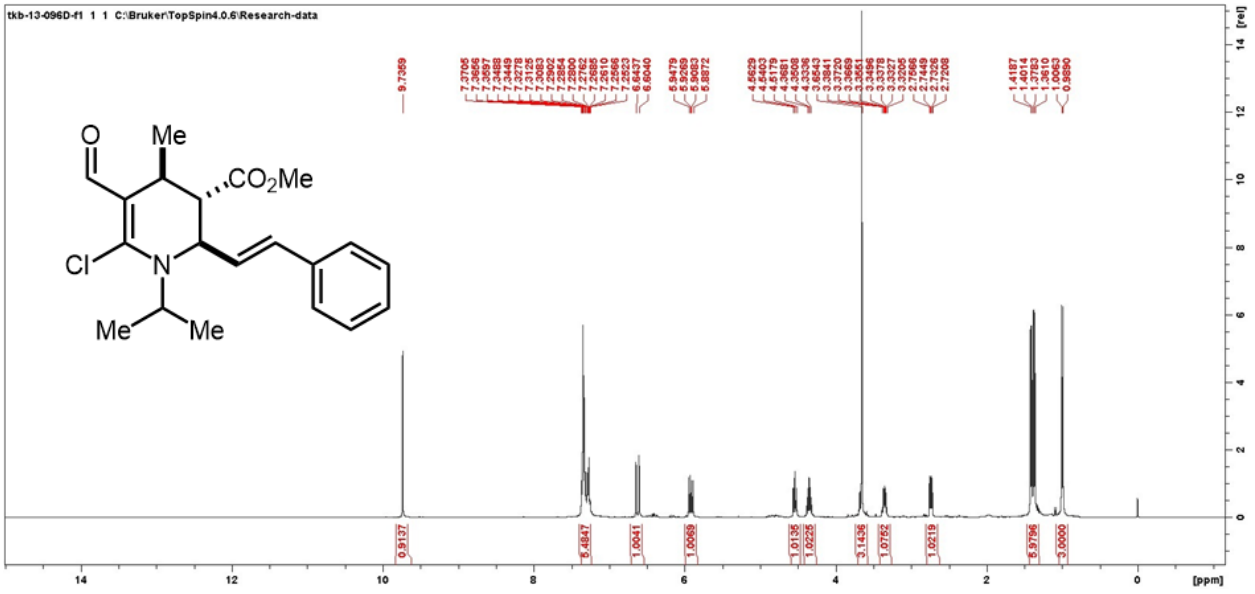
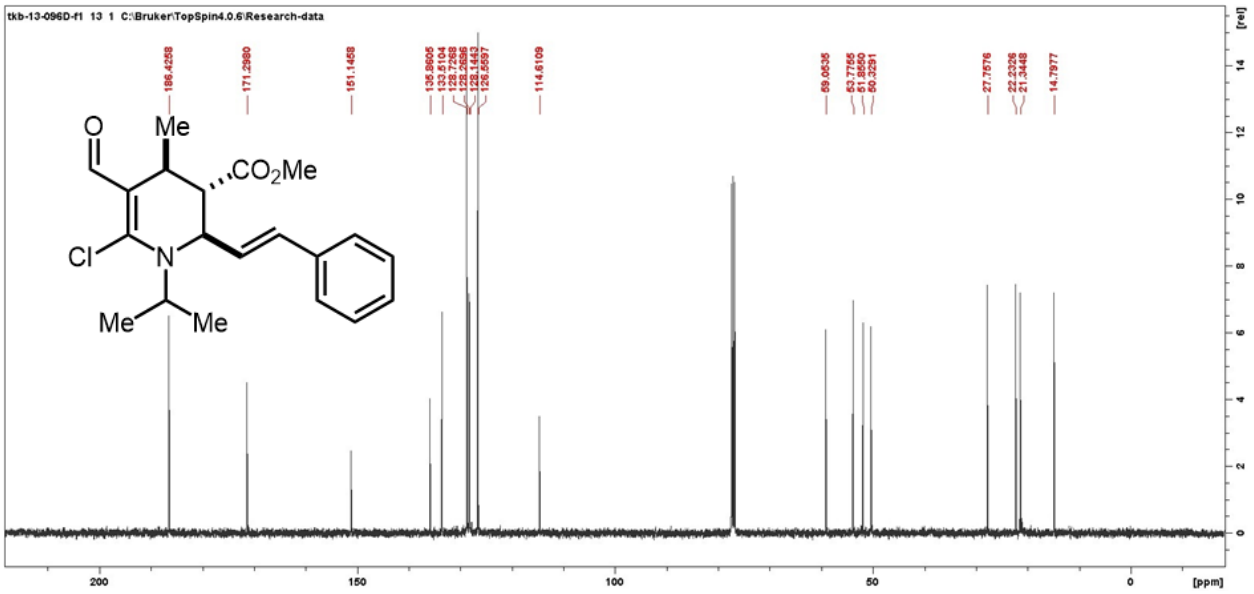
0
-5
140
120
100
80
60
40
20
[ppm]

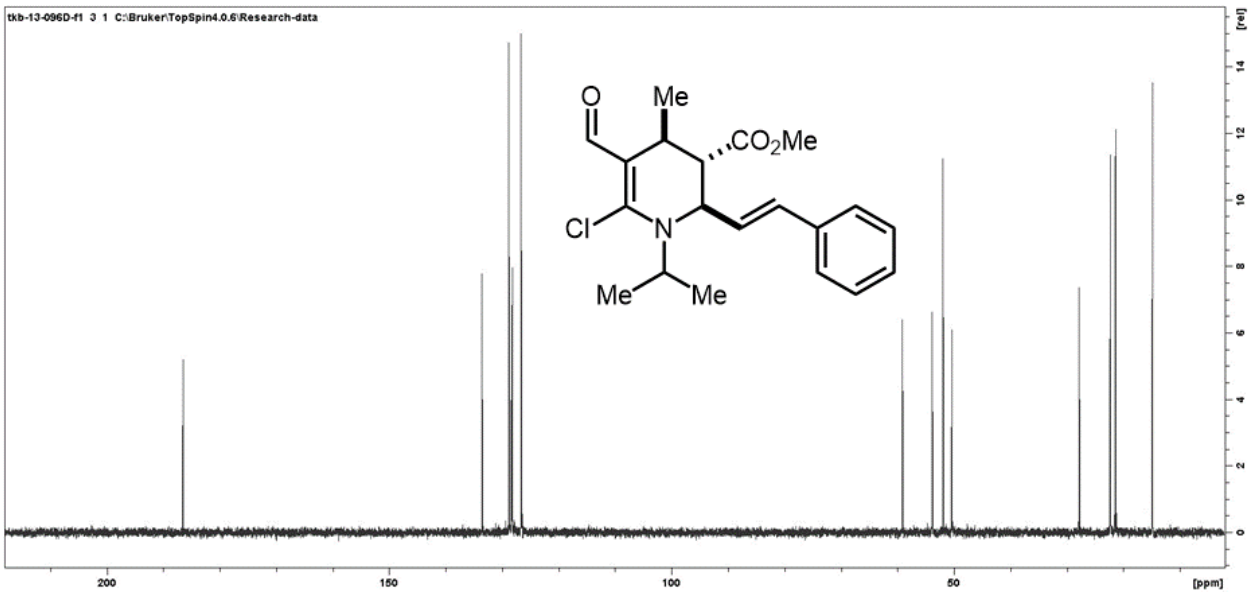
Scheme 2 Results

Compound 4a

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (85:15). Oily substance. Yield = 168.3 mg, 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.39 – 7.20 (m, 5H), 6.62 (d, *J* = 15.9 Hz, 1H), 5.92 (dd, *J* = 15.9, 8.5 Hz, 1H), 4.54 (t, *J* = 9.0 Hz, 1H), 4.35 (hept, *J* = 6.9 Hz, 1H), 3.65 (s, 3H), 3.35 (qd, *J* = 6.9, 4.6 Hz, 1H), 2.74 (dd, *J* = 9.6, 4.7 Hz, 1H), 1.39 (dd, *J* = 16.2, 6.9 Hz, 6H), 1.00 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.4, 171.3, 151.1, 135.9, 133.5, 128.7, 128.3, 128.1, 126.6, 114.6, 59.1, 53.8, 51.9, 50.3, 27.8, 22.2, 21.3, 14.8. **HRMS-EI$^+$** (*m/z*): calc for $C_{20}H_{24}ClNO_3$, 361.1445, found 361.1449. FTIR (KBr): 2924.8, 1642.2, 1494.9, 1448.8, 1427.0, 1393.4, 1361.6, 1328.7, 1289.7, 1223.6, 1198.9, 1130.0, 1074.1, 1030.4, 988.5, 966.1, 925.5, 741.6, 693.4.



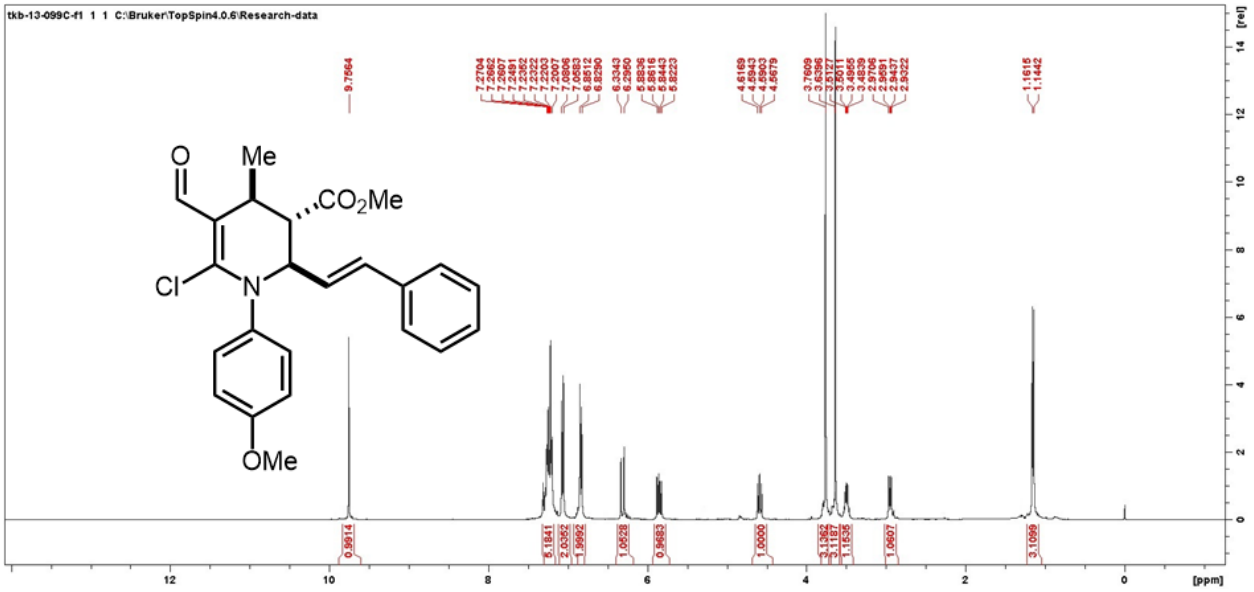


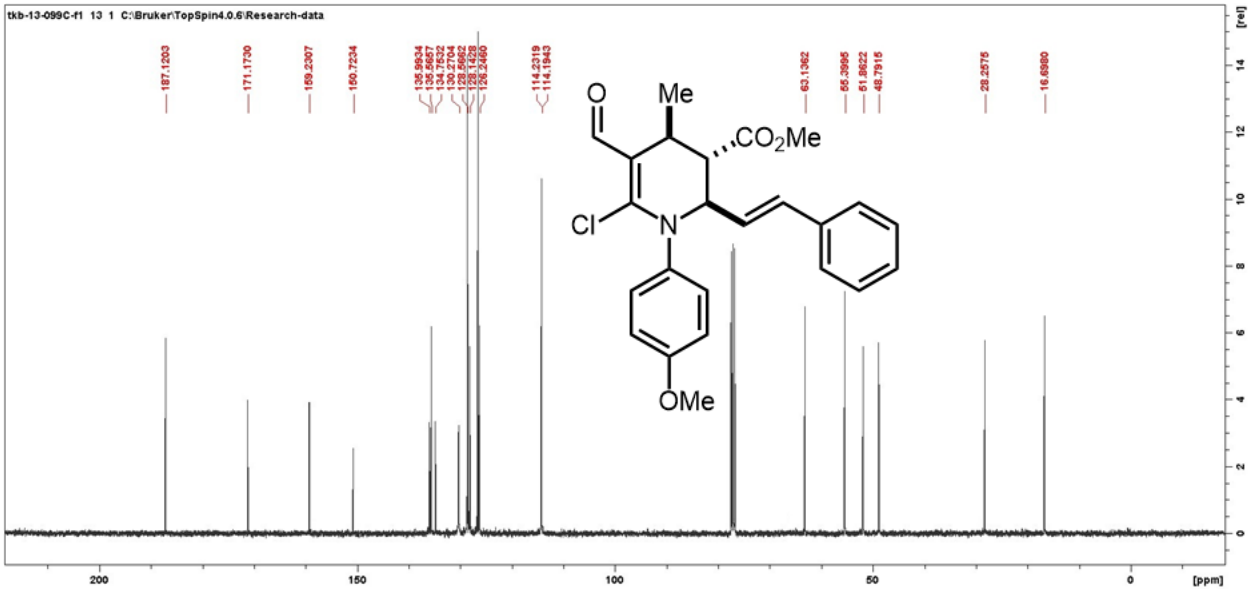


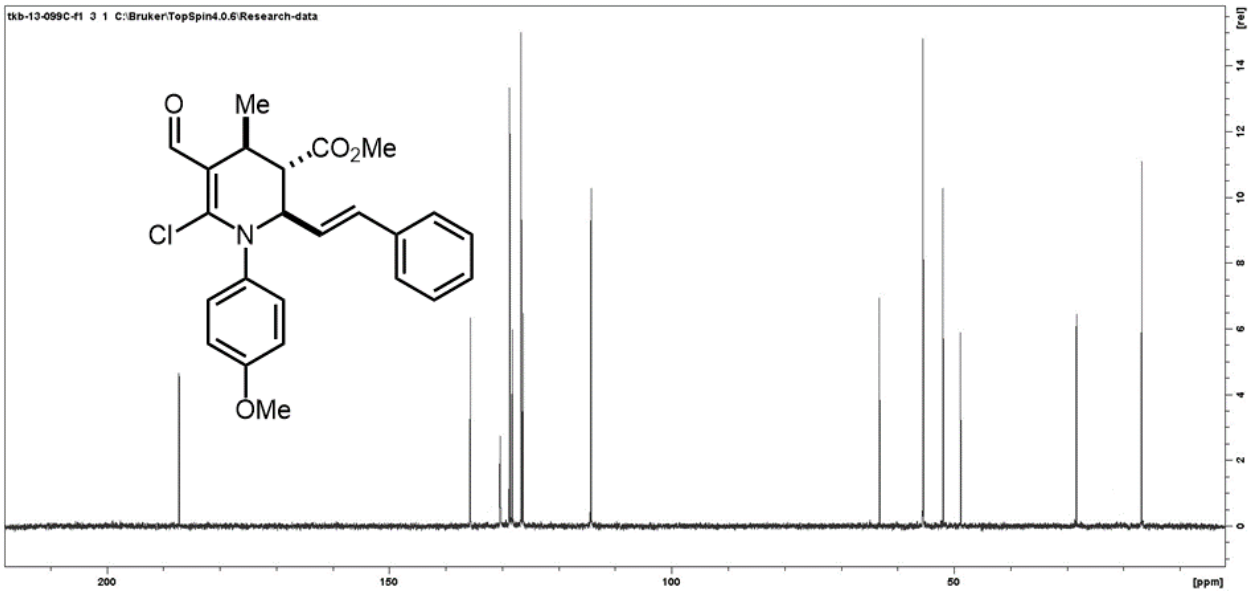
Compound 4b

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (75:25). Oily substance. Yield = 181.0 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.27 – 7.20 (m, 5H), 7.07 (d, 2H), 6.83 (d, 2H), 6.31 (d, *J* = 15.7 Hz, 1H), 5.85 (dd, *J* = 15.7, 8.8 Hz, 1H), 4.59 (dd, *J* = 10.8, 8.8 Hz, 1H), 3.76 (s, 3H), 3.64 (s, 3H), 3.50 (qd, *J* = 6.9, 4.4 Hz, 1H), 2.95 (dd, *J* = 10.8, 4.6 Hz, 1H), 1.15 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.1, 171.1, 159.2, 150.7, 136.0, 135.5, 134.7,

130.2, 128.5, 128.1, 126.5, 126.2, 114.2, 114.2, 63.1, 55.4, 51.8, 48.7, 28.2, 16.7. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{24}H_{24}ClNO_4$, 425.1394, found 425.1398.

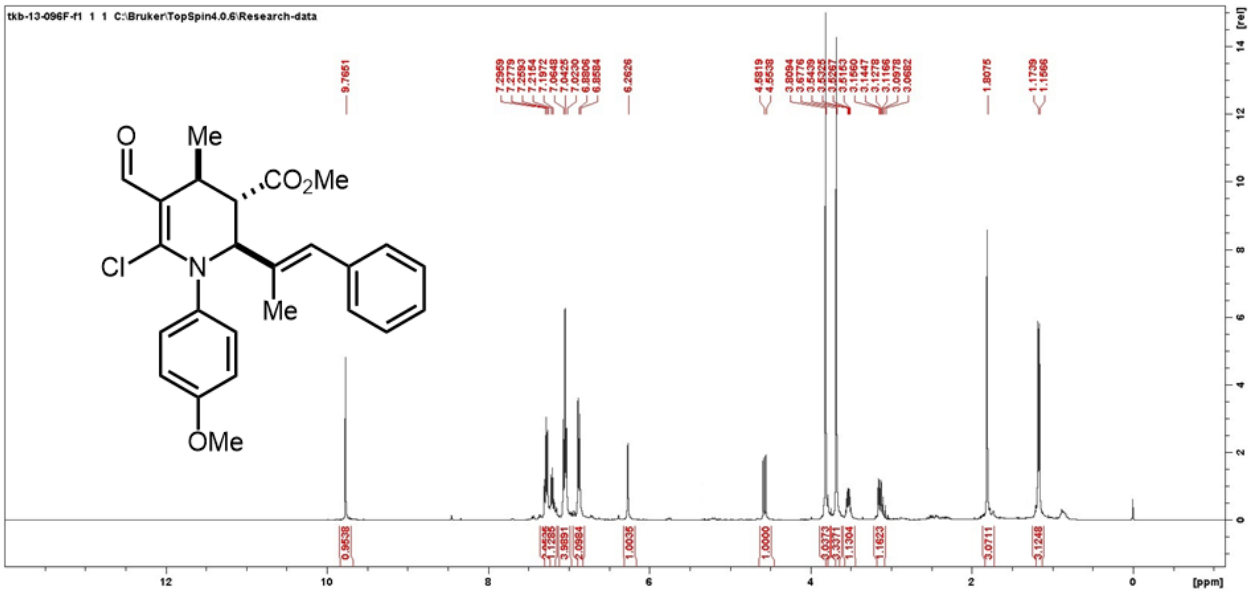






Compound 4c

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (75:25). Oily substance. Yield = 193.6 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.29 – 7.19 (m, 3H), 7.06 – 7.02 (m, 4H), 6.87 (d, 2H), 6.26 (s, 1H), 4.57 (d, J = 11.2 Hz, 1H), 3.81 (s, 3H), 3.68 (s, 3H), 3.53 (qd, J = 6.9, 4.5 Hz, 1H), 3.18 – 3.05 (m, 1H), 1.81 (s, 3H), 1.17 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.1, 171.3, 159.2, 151.3, 136.8, 134.9, 133.0, 132.9, 129.5, 128.7, 128.1, 126.9, 115.4, 114.2, 68.8, 55.5, 51.9, 46.9, 28.1, 16.6, 13.9. HRMS calc for $C_{25}H_{26}ClNO_4$, 439.1550, found 439.1555. FTIR (KBr): 2965.2, 2872.3, 1716.4, 1650.8, 1612.9, 1585.9, 1513.1, 1455.3, 1359.3, 1304.1, 1251.3, 1177.4, 1135.5, 1033.8, 996.7, 896.0, 833.6, 804.9. **HRMS-EI$^+$** (*m/z*): calc for $C_{23}H_{31}NO_4$ 385.2253, found 385.2257.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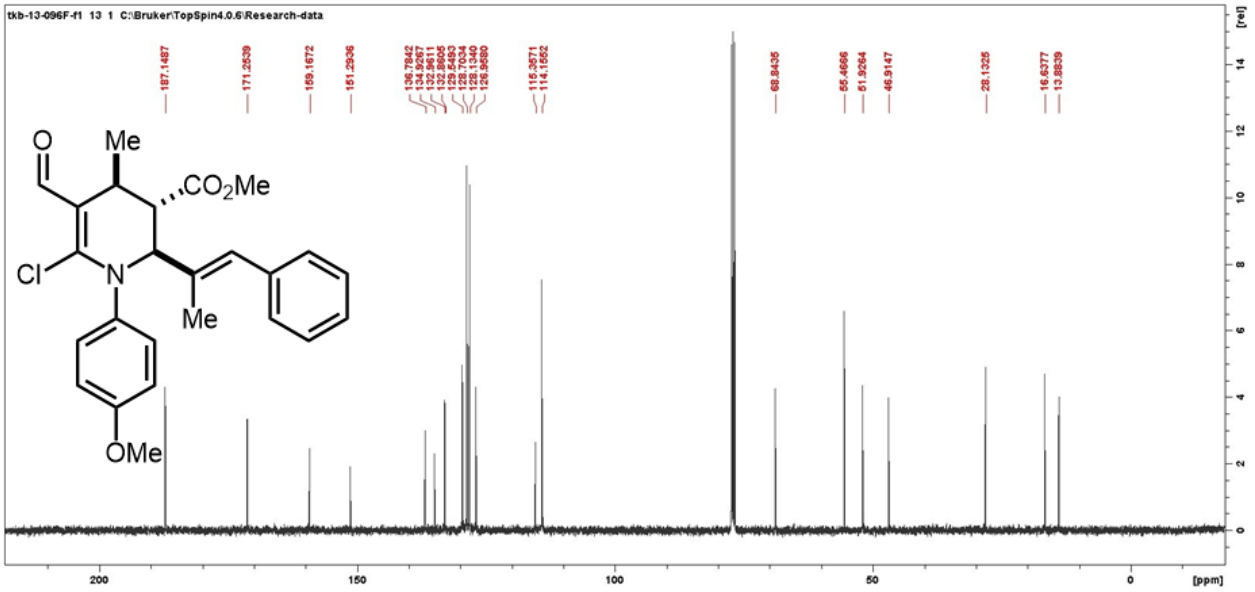
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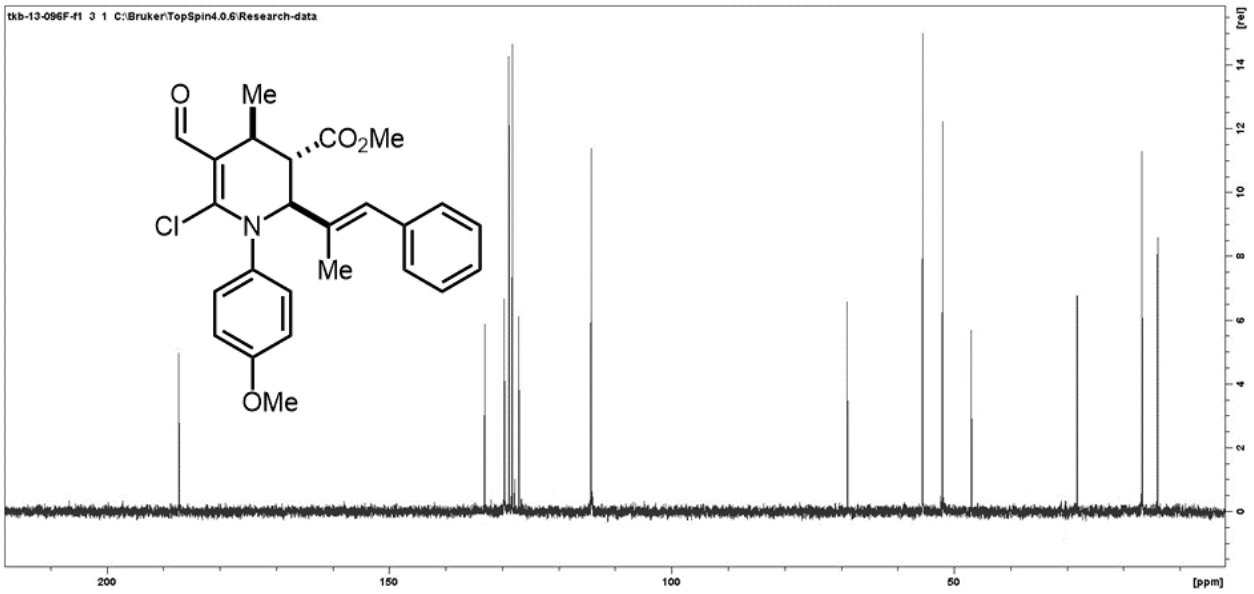
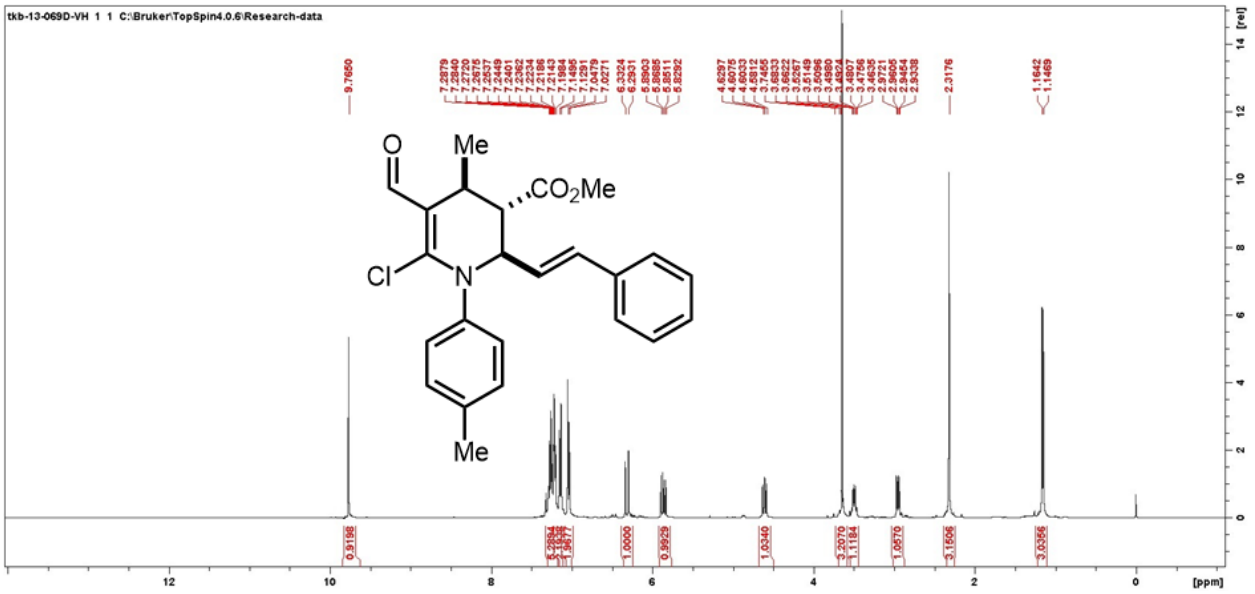


Compound 4d

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (90:10). Oily substance. Yield = 184.5 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.29 – 7.13 (m, 7H), 7.02 (d, *J* = 7.0 Hz, 2H), 6.31 (d, *J* = 15.7 Hz, 1H), 5.86 (dd, *J* = 15.7, 8.7 Hz, 1H), 4.61 (dd, *J* = 10.7, 8.7 Hz, 1H), 3.64 (s, 3H), 3.50 (qd, *J* = 6.9, 4.5 Hz, 1H), 2.95 (dd, *J* = 10.7, 4.7 Hz, 1H), 2.32 (s, 3H), 1.16 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.17, 171.18, 150.39, 139.50, 138.38, 136.03, 135.40, 129.73, 128.84, 128.56, 128.12, 126.55, 126.33, 114.44, 63.04, 51.86, 48.93, 28.26, 21.13, 16.65. **HRMS-EI$^+$** (*m/z*): calc for $C_{24}H_{24}ClNO_3$, 409.1445, found 409.1449.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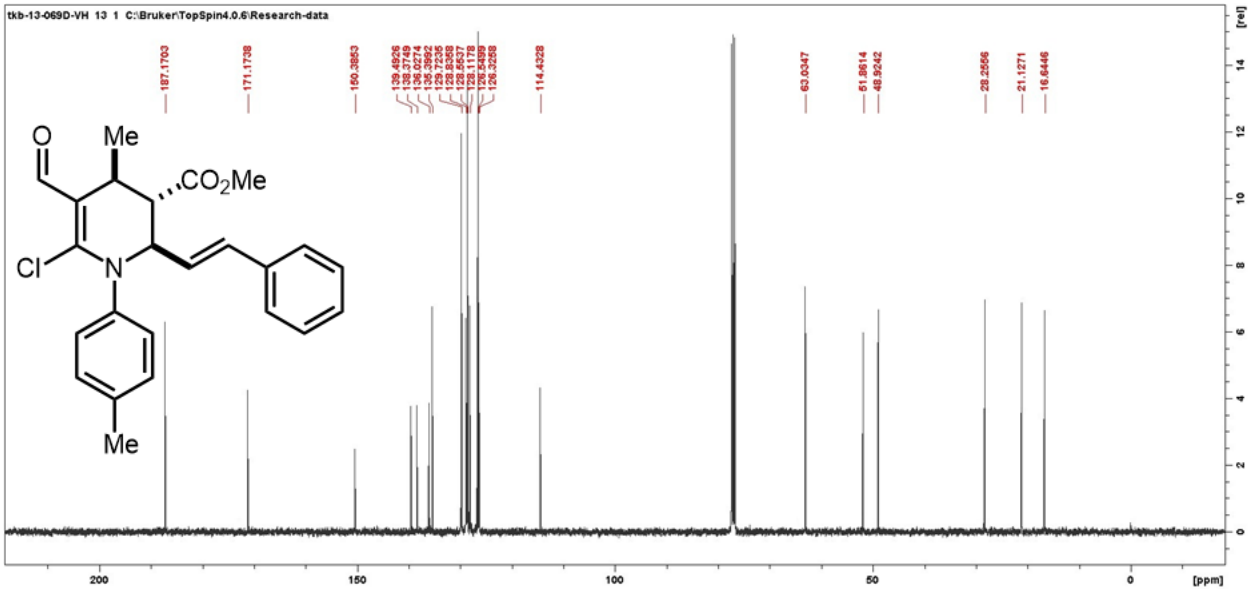
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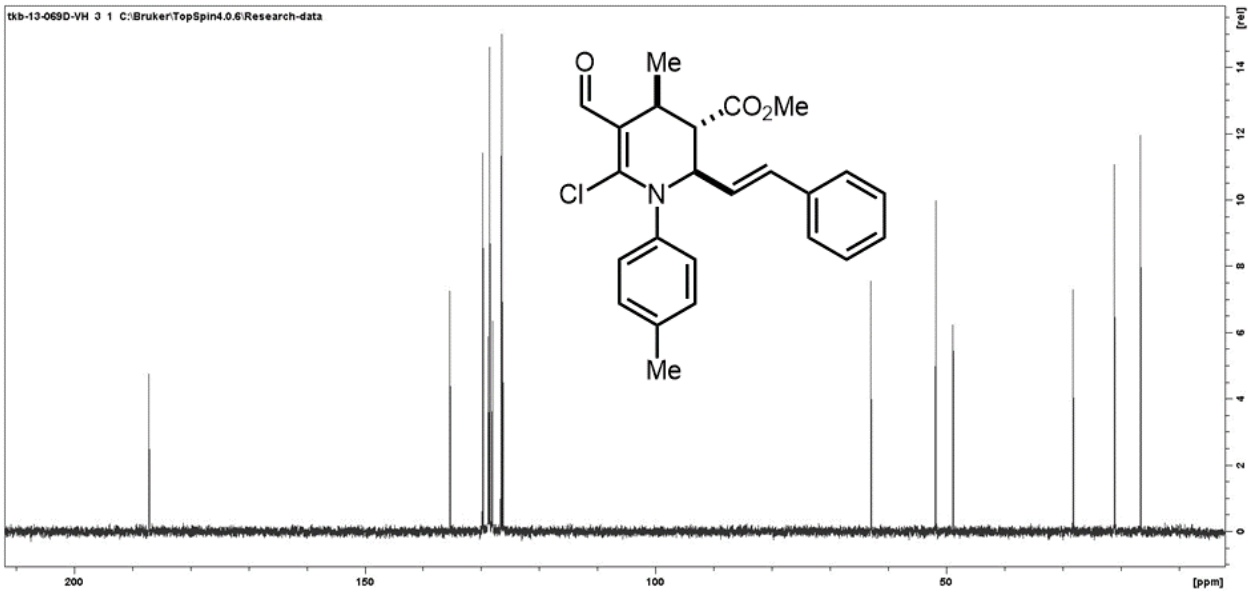
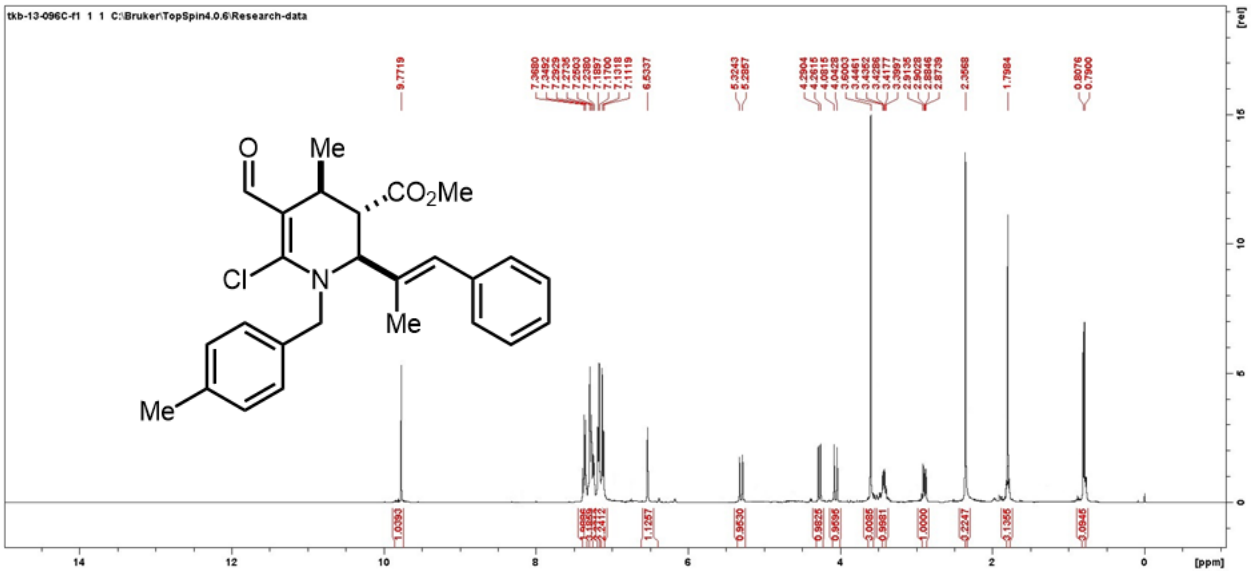
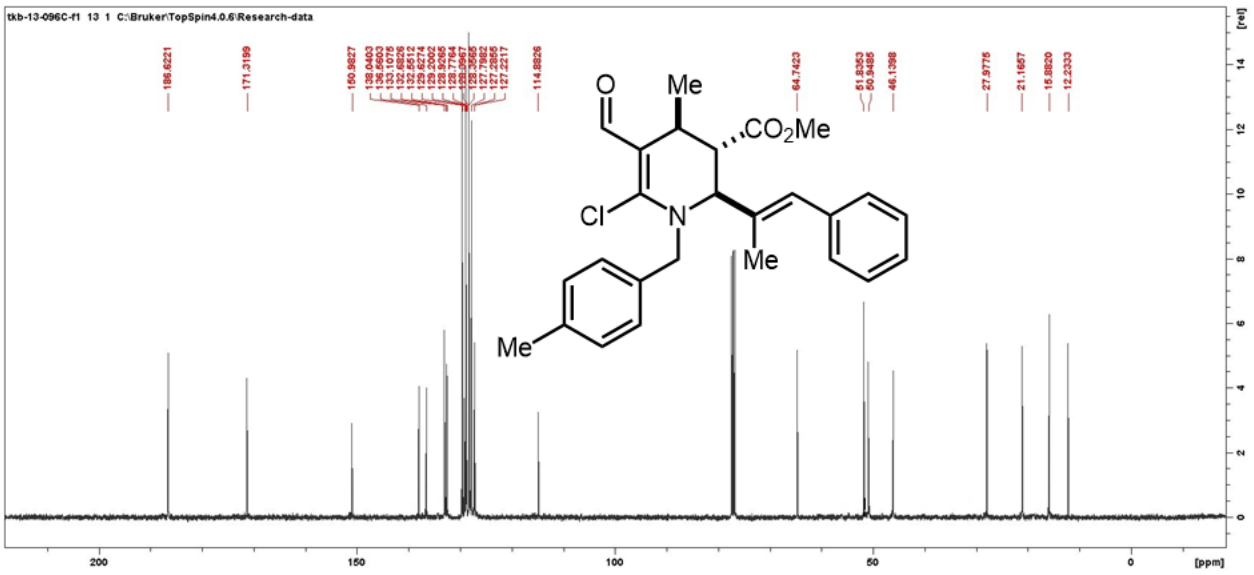
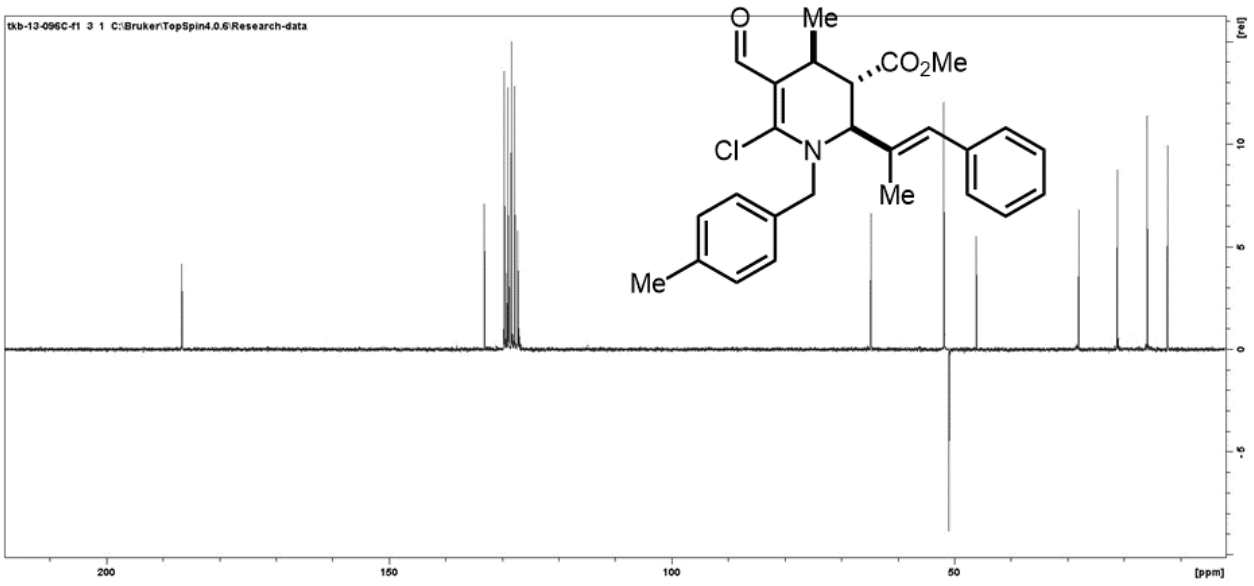


Compound 4e

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (80:20). Oily substance. Yield = 190.5 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.36 – 7.11 (m, 9H), 6.53 (s, 1H), 5.31 (d, *J* = 15.5 Hz, 1H), 4.28 (d, *J* = 11.6 Hz, 1H), 4.09 (dd, *J* = 25.2, 15.8 Hz, 1H), 3.60 (s, 3H), 3.54 – 3.41 (m, 1H), 2.95 – 2.84 (m, 1H), 2.36 (s, 3H), 1.80 (s, 3H), 0.79 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.6, 171.3, 151.0, 138.0, 136.6, 133.1, 132.7, 132.5, 129.6, 129.2, 128.9, 128.4, 127.8, 127.3, 127.2, 114.9, 64.8, 51.8, 50.9, 46.1, 27.9, 21.2, 15.9, 12.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{26}H_{28}ClNO_3$, 437.1758, found 437.1762.



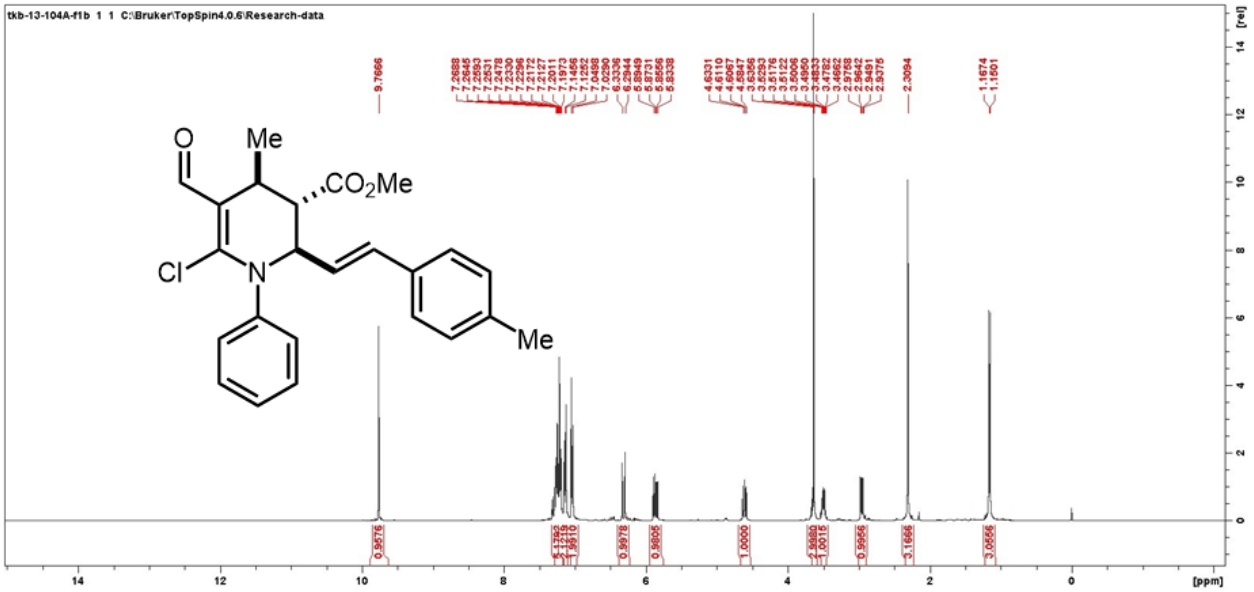


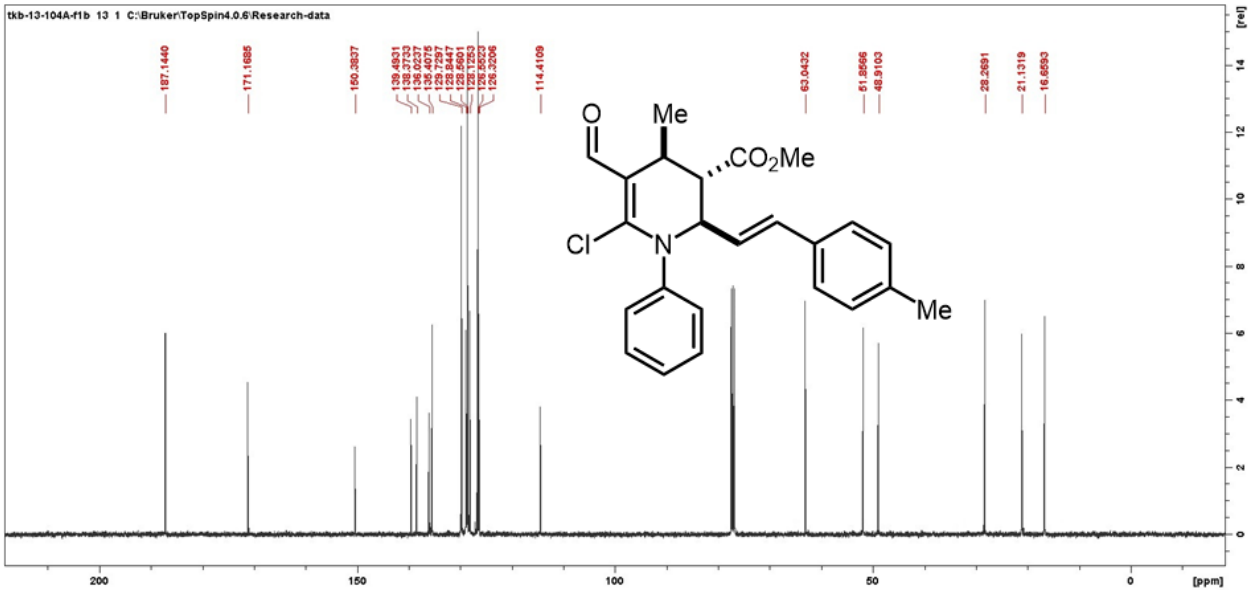


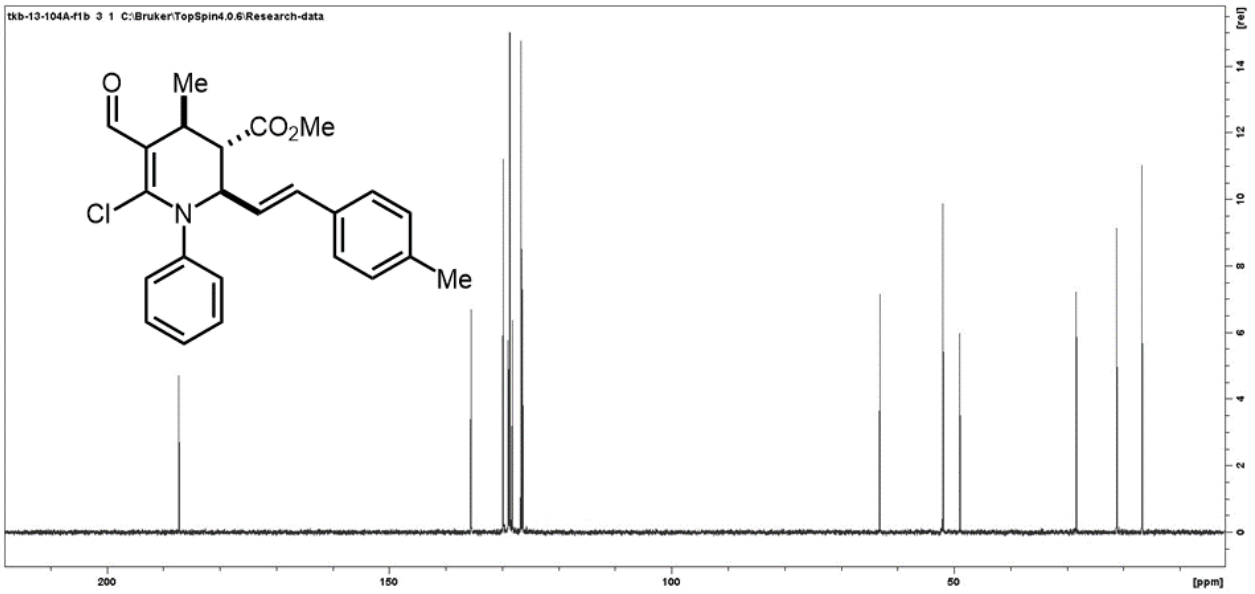
Compound 4f

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (80:20). Oily substance. Yield = 186.5 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.27 – 7.19 (m, 5H), 7.14 – 7.11 (m, 2H), 7.03 (d, J = 7.7 Hz, 2H), 6.31 (d, J = 15.7 Hz, 1H), 5.86 (dd, J = 15.7, 8.7 Hz, 1H), 4.61 (dd, J = 10.7, 8.7 Hz, 1H), 3.64 (s, 3H), 3.50 (qd, J = 6.9, 4.5 Hz, 1H), 2.96 (dd, J = 10.7, 4.7 Hz, 1H), 2.31 (s, 3H), 1.16 (d, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.1, 171.2, 150.4, 139.5,

138.4, 136.0, 135.4, 129.7, 128.8, 128.6, 128.1, 126.6, 126.3, 114.4, 63.0, 51.9, 48.9, 28.3, 21.1, 16.7. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{24}H_{24}ClNO_3$, 409.1445, found 409.1449.

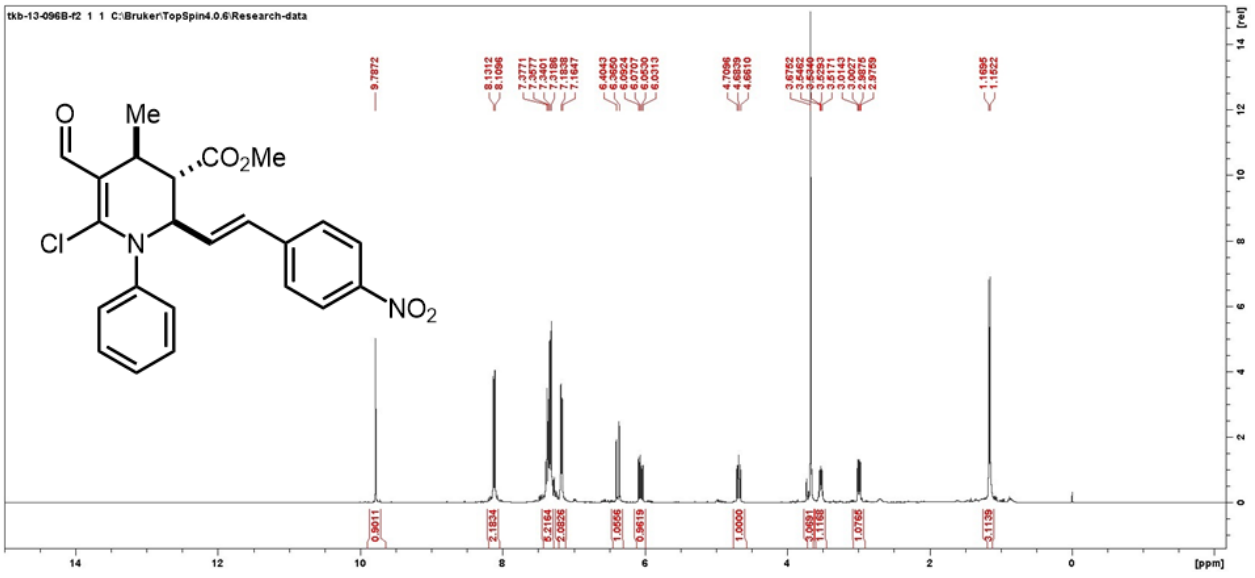






Compound 4g

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (50:50). Oily substance. Yield = 191.8 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.38 – 7.32 (m, 5H), 7.14 (d, *J* = 7.9 Hz, 2H), 6.38 (d, *J* = 15.7 Hz, 1H), 6.06 (dd, *J* = 15.8, 8.7 Hz, 1H), 4.69 (dd, *J* = 10.7, 8.7 Hz, 1H), 3.68 (s, 3H), 3.59 – 3.48 (m, 1H), 3.00 (dd, *J* = 10.7, 4.7 Hz, 1H), 1.16 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.22, 170.99, 149.87, 147.34, 142.12, 141.91, 133.42, 131.05, 129.25, 129.05, 128.58, 127.07, 123.97, 114.75, 62.58, 52.03, 48.51, 28.30, 16.69. **HRMS-EI$^+$** (*m/z*): calc for $C_{23}H_{21}ClN_2O_5$, 440.1139, found 440.1145.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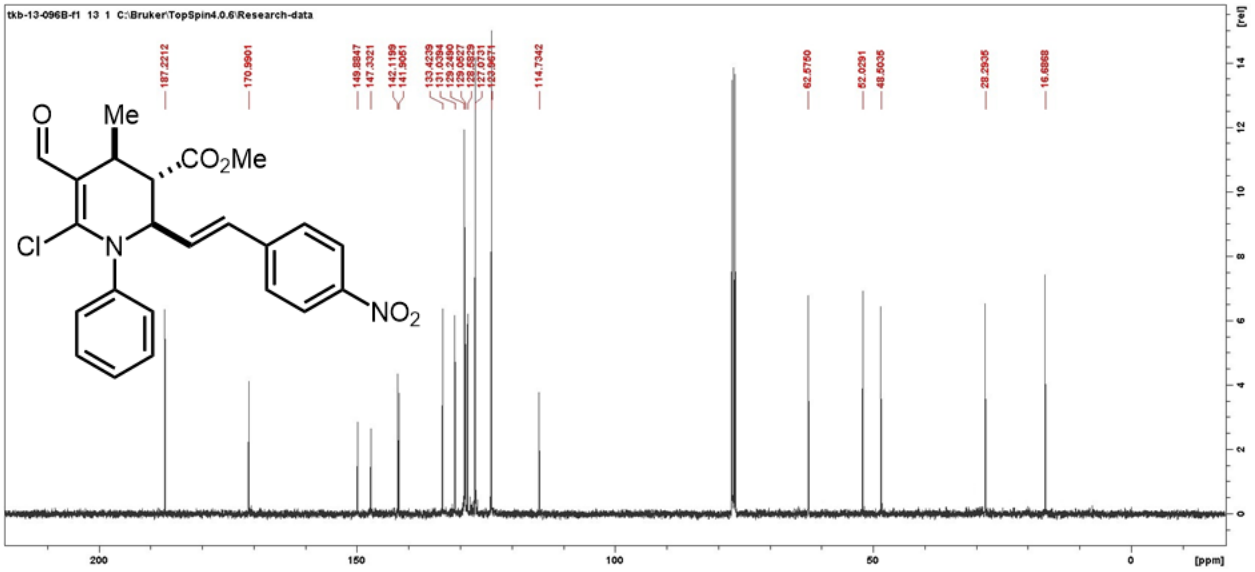
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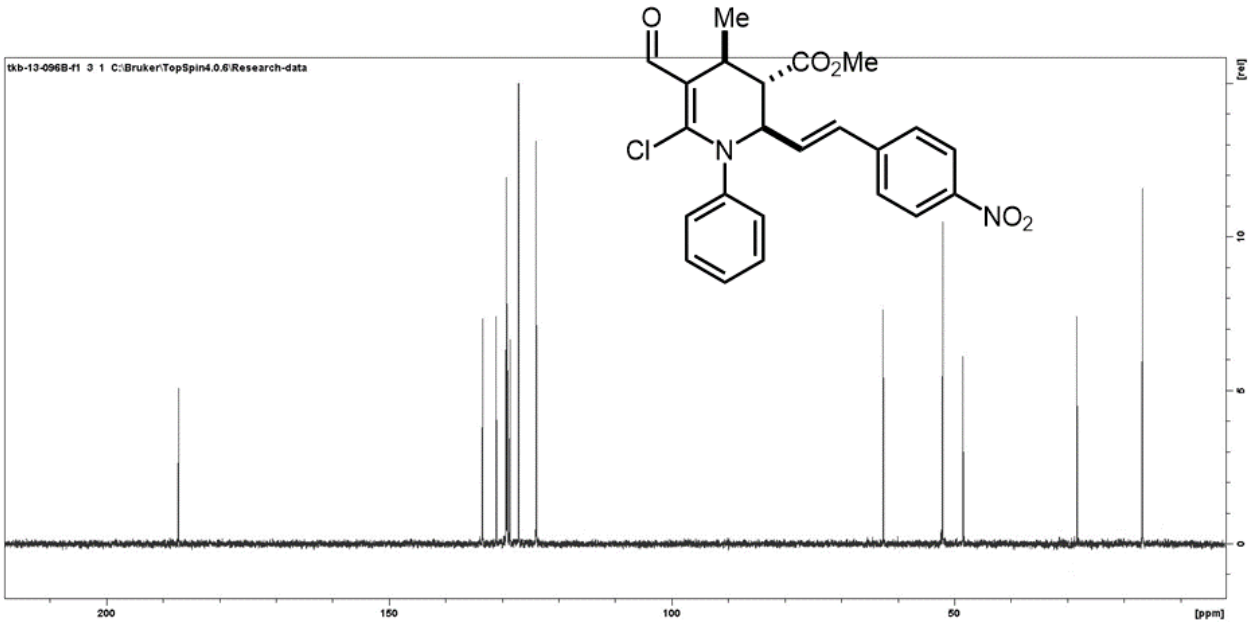
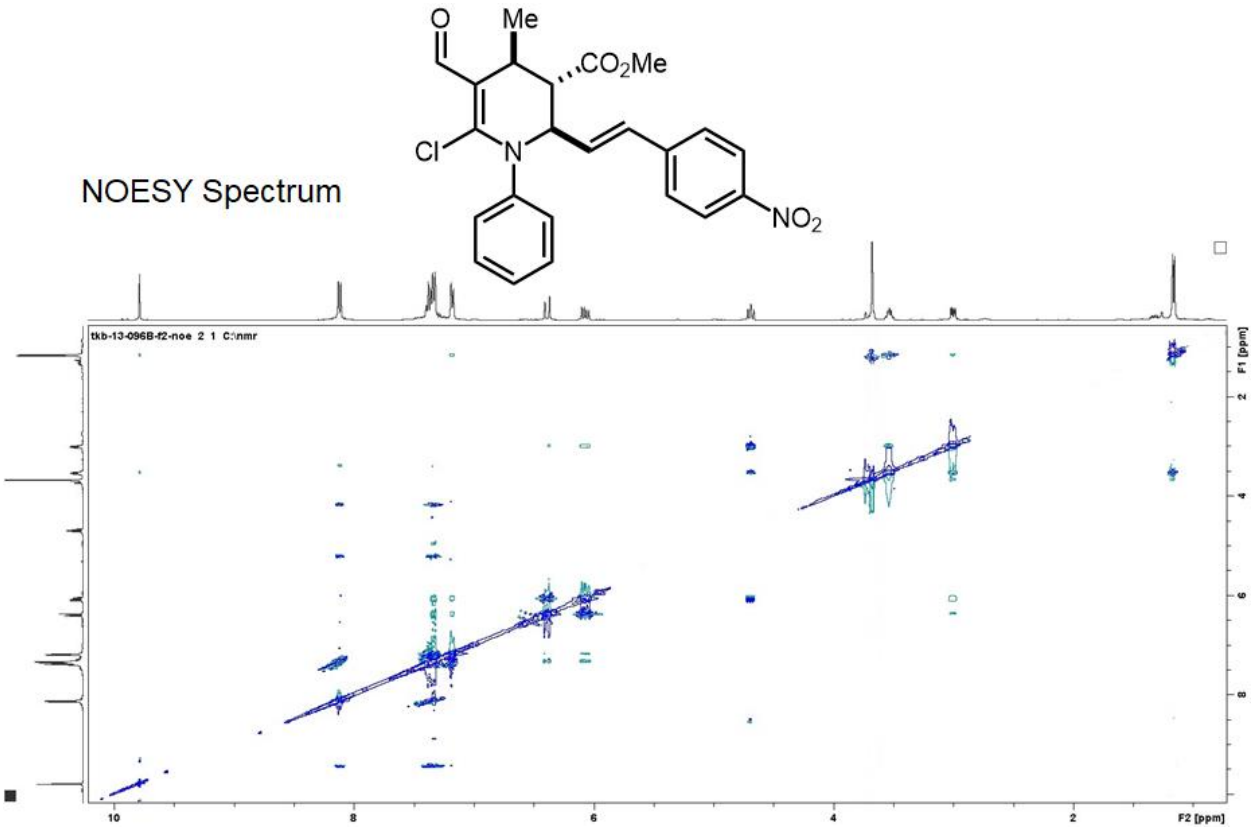
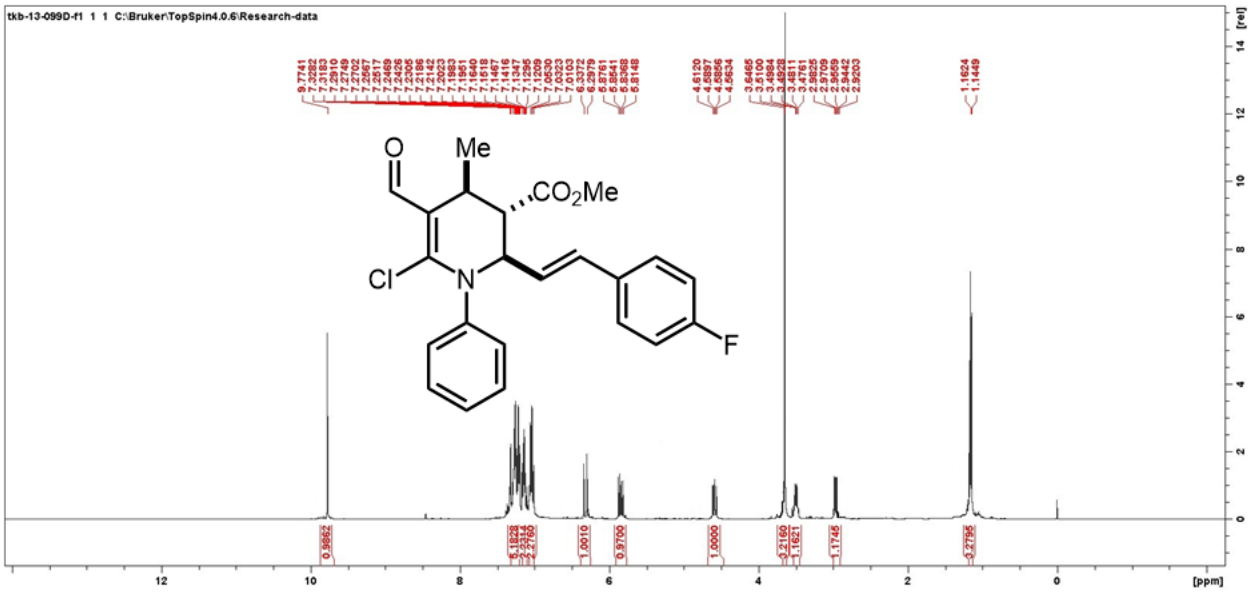


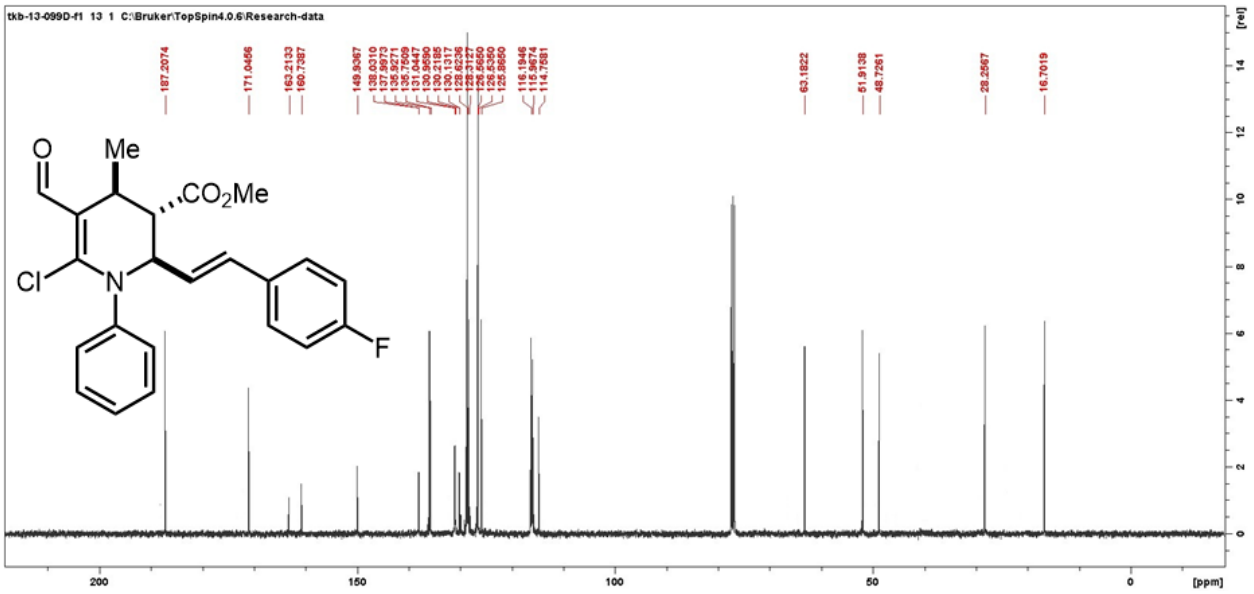


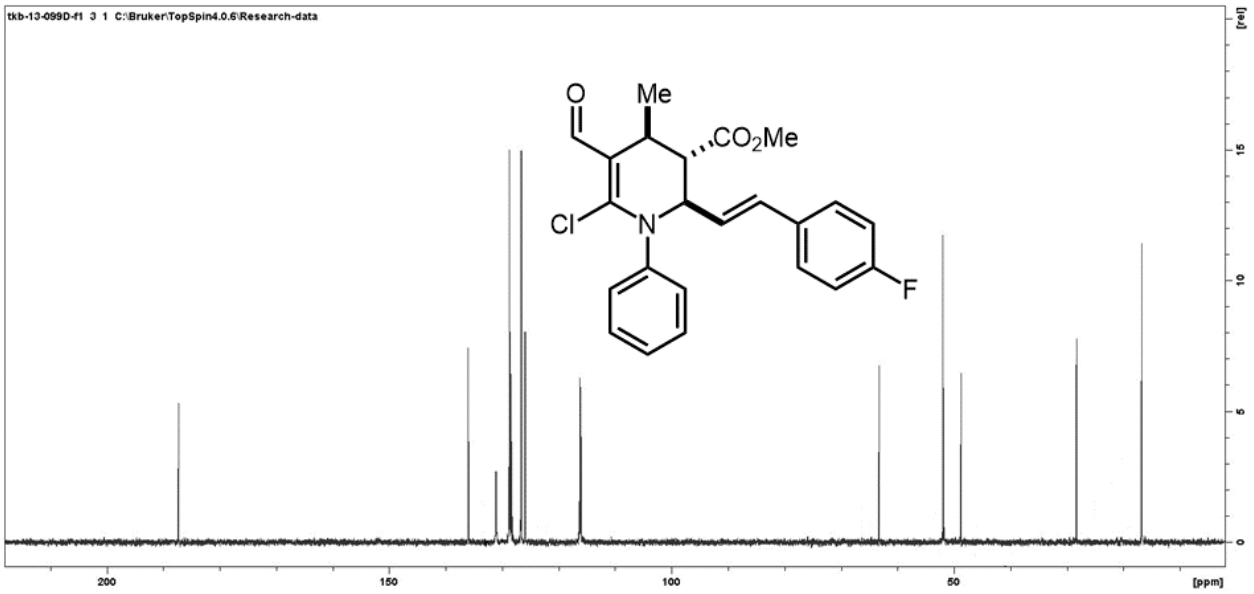
Compound 4h

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (90:10). Oily substance. Yield = 173.8

mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.33 – 7.01 (m, 9H), 6.32 (d, *J* = 15.7 Hz, 1H), 5.85 (dd, *J* = 15.7, 8.8 Hz, 1H), 4.59 (dd, *J* = 10.7, 8.8 Hz, 1H), 3.66 (s, 3H), 3.57 – 3.44 (m, 1H), 3.02 – 2.83 (m, 2H), 1.15 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.2, 171.0, 163.2, 160.7, 149.9, 138.0, 135.9, 135.7, 131.0, 130.9, 130.2, 130.1, 128.8, 128.7, 128.6, 128.3, 126.7, 126.6, 126.5, 125.9, 116.3, 116.2, 116.1, 115.9, 114.7, 63.2, 51.9, 48.7, 28.3, 16.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{21}ClFNO_3$, 413.1194, found 413.1198.

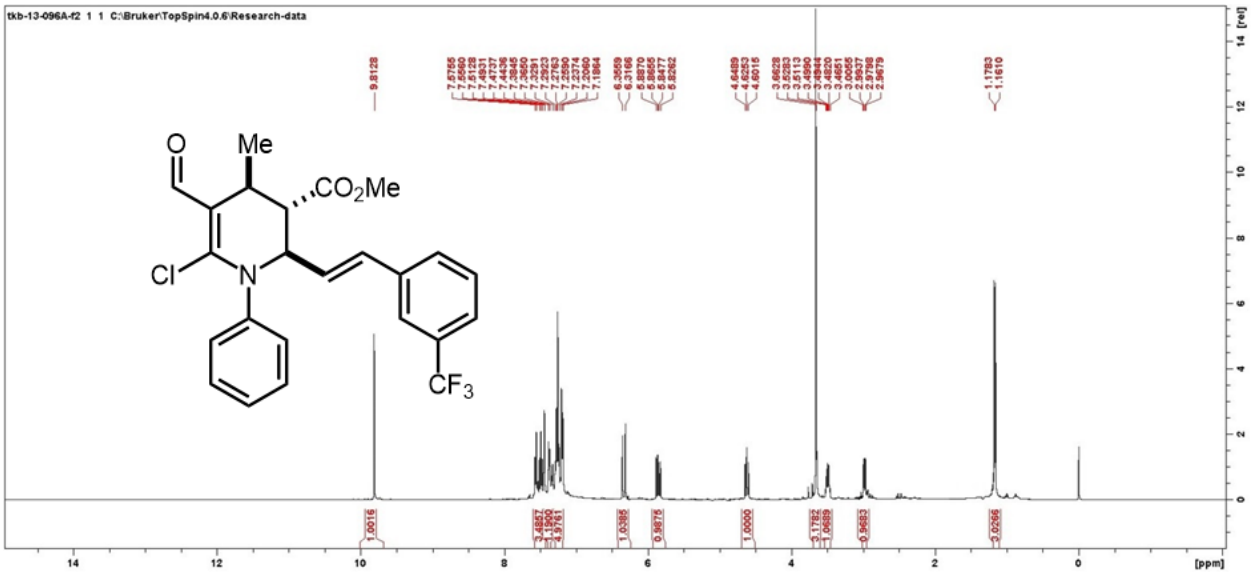


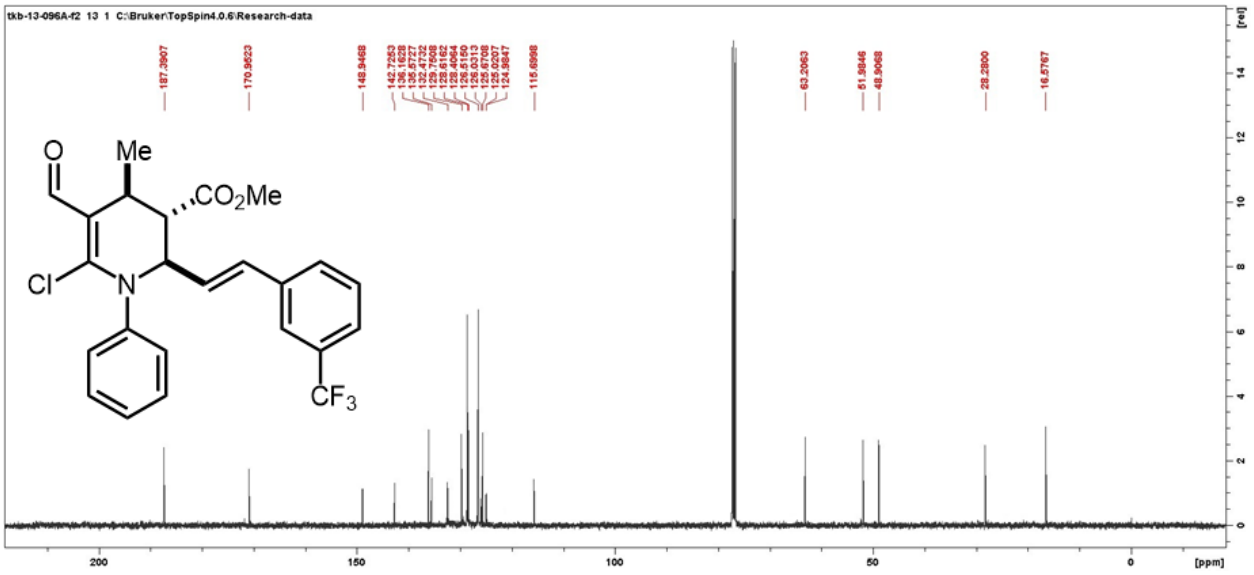




Compound 4i

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (90:10). Oily substance. Yield = 197.1 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.57 – 7.19 (m, 9H), 6.34 (d, *J* = 15.7 Hz, 1H), 5.86 (dd, *J* = 15.7, 8.6 Hz, 1H), 4.63 (dd, *J* = 10.3, 8.6 Hz, 1H), 3.66 (s, 3H), 3.55 – 3.44 (m, 1H), 3.06 – 2.86 (m, 1H), 1.17 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.4, 170.9, 148.9, 142.7, 136.2, 135.6, 132.4, 129.7, 128.6, 128.4, 126.5, 125.6, 115.7, 63.2, 51.9, 48.9, 28.3, 16.6. **HRMS-EI$^+$** (*m/z*): calc for $C_{24}H_{21}ClF_3NO_3$, 463.1162, found 463.1168.

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N
CF3
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100
50
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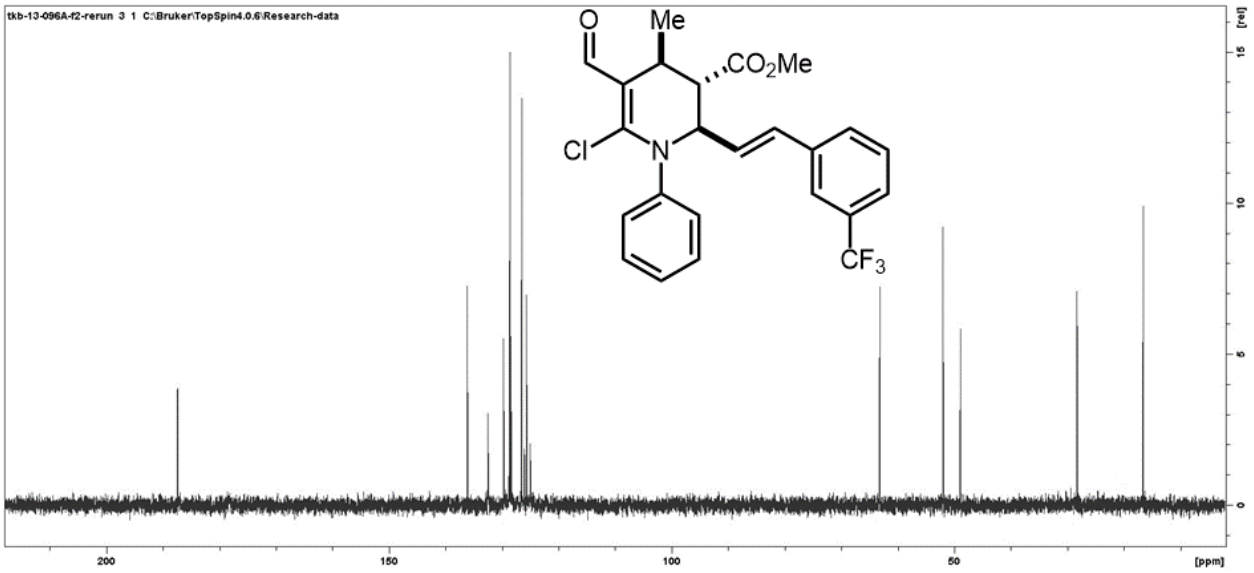
[ppm]
[rel]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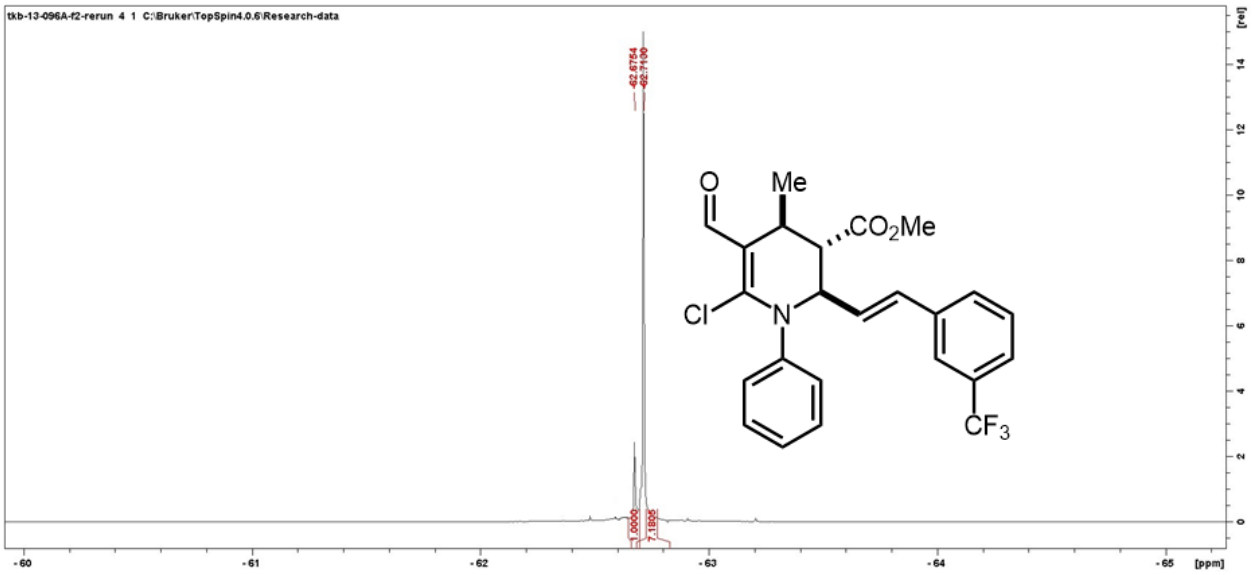
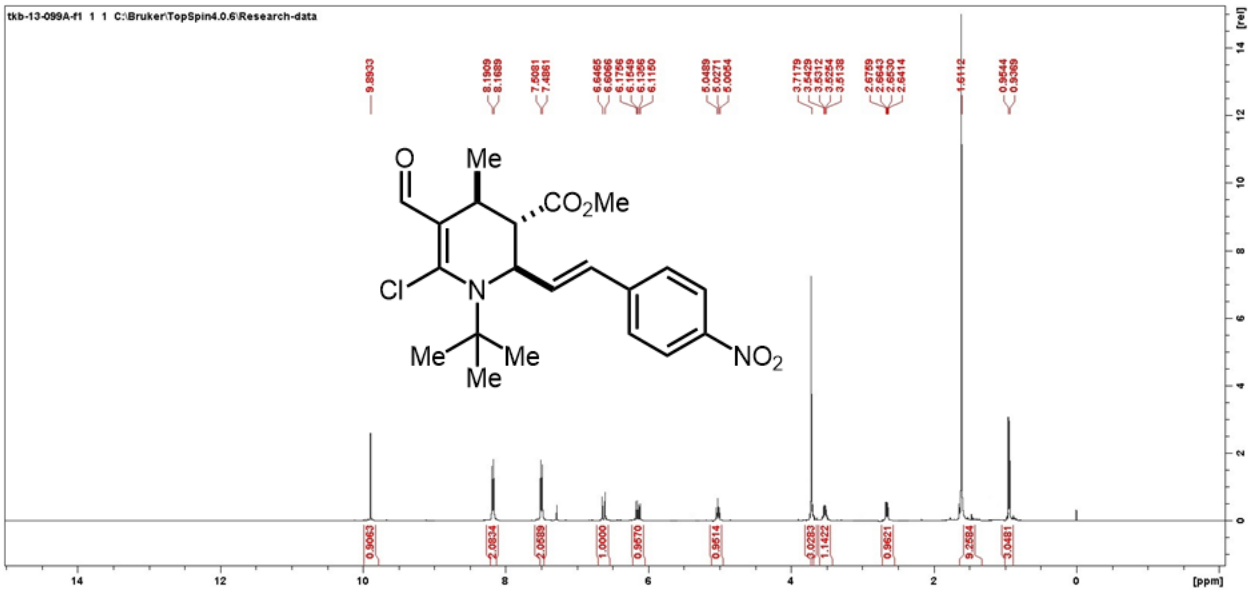
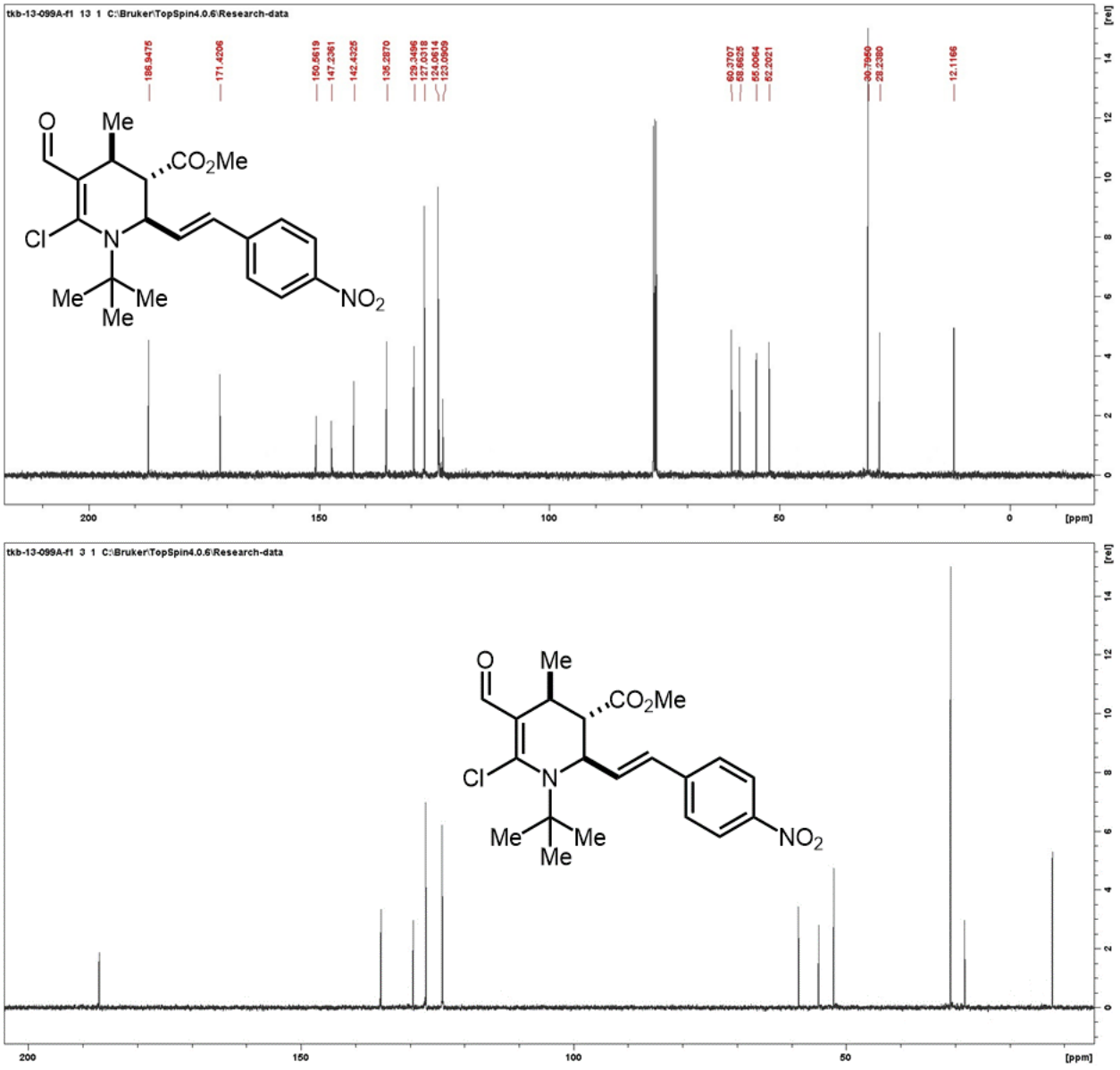


Compound 4j

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (95:5). Oily substance. Yield = 195.7 mg, 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.18 (d, *J* = 7.2 Hz, 2H), 7.49 (d, *J* = 7.2 Hz, 2H), 6.63 (d, *J* = 16.0 Hz, 1H), 6.15 (dd, *J* = 16.0, 7.7 Hz, 1H), 5.03 (t, *J* = 8.7 Hz, 1H), 3.72 (s, 3H), 3.53 (qd, *J* = 7.0, 4.5 Hz, 1H), 2.66 (dd, *J* = 9.2, 4.6 Hz, 1H), 1.61 (s, 9H), 0.96 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.9, 171.4, 150.6, 147.2, 142.4, 135.3, 129.5, 129.3, 127.2, 127.0, 124.1, 124.0, 123.1, 60.4, 58.7, 55.0, 52.2, 30.8, 28.2, 12.1. **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{25}ClN_2O_5$, 420.1452, found 420.1458.

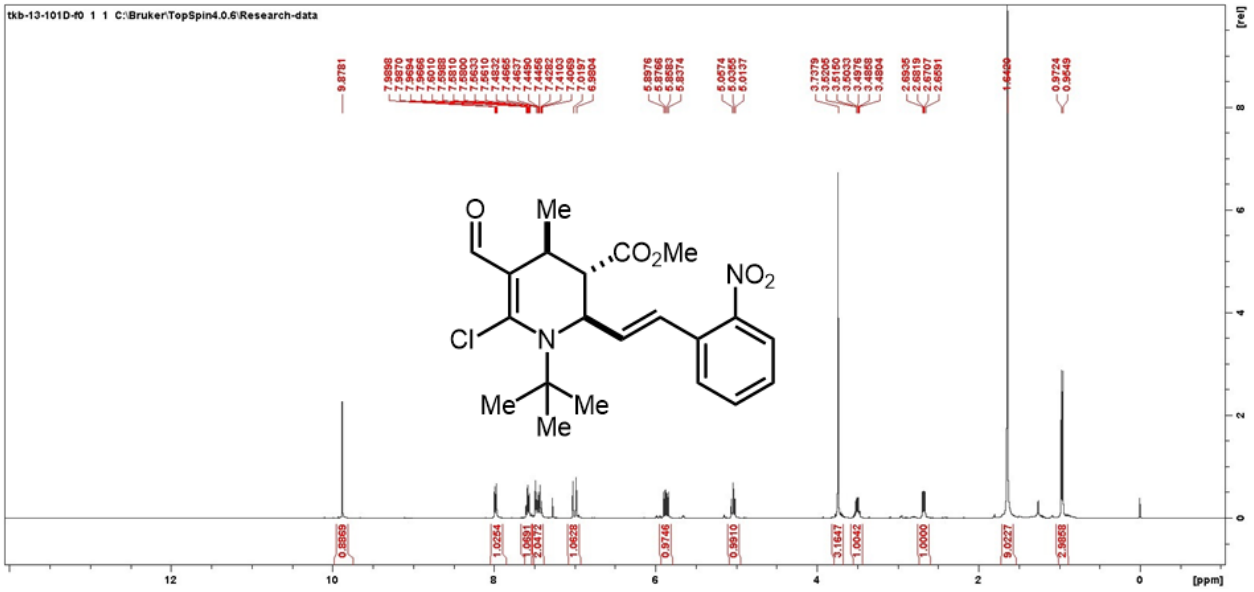


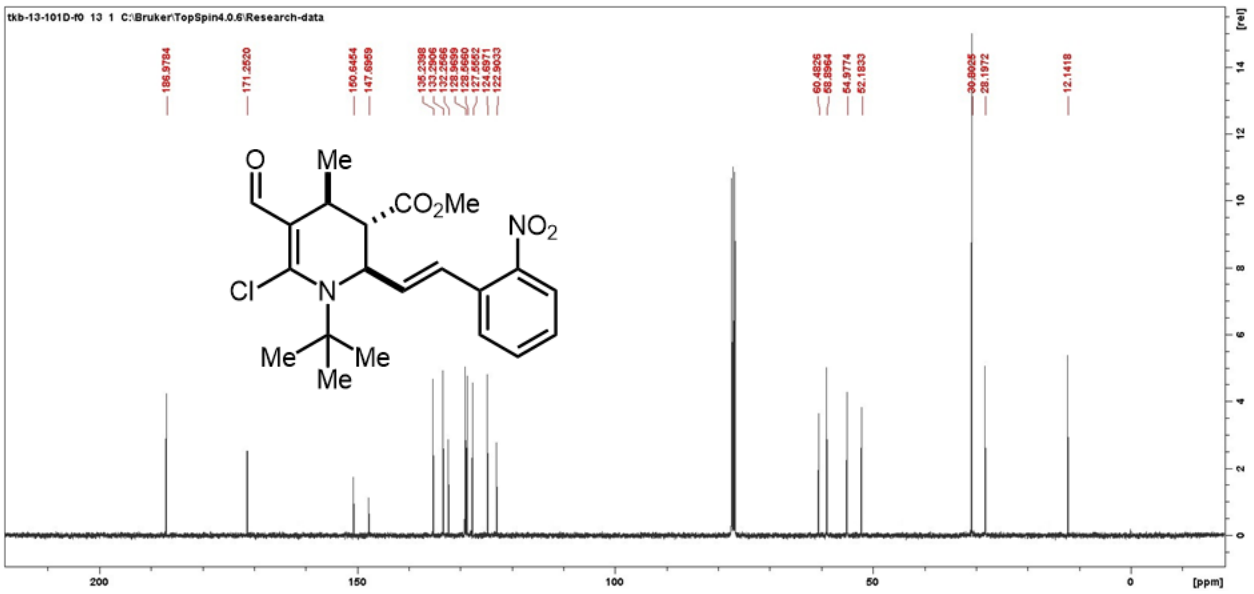


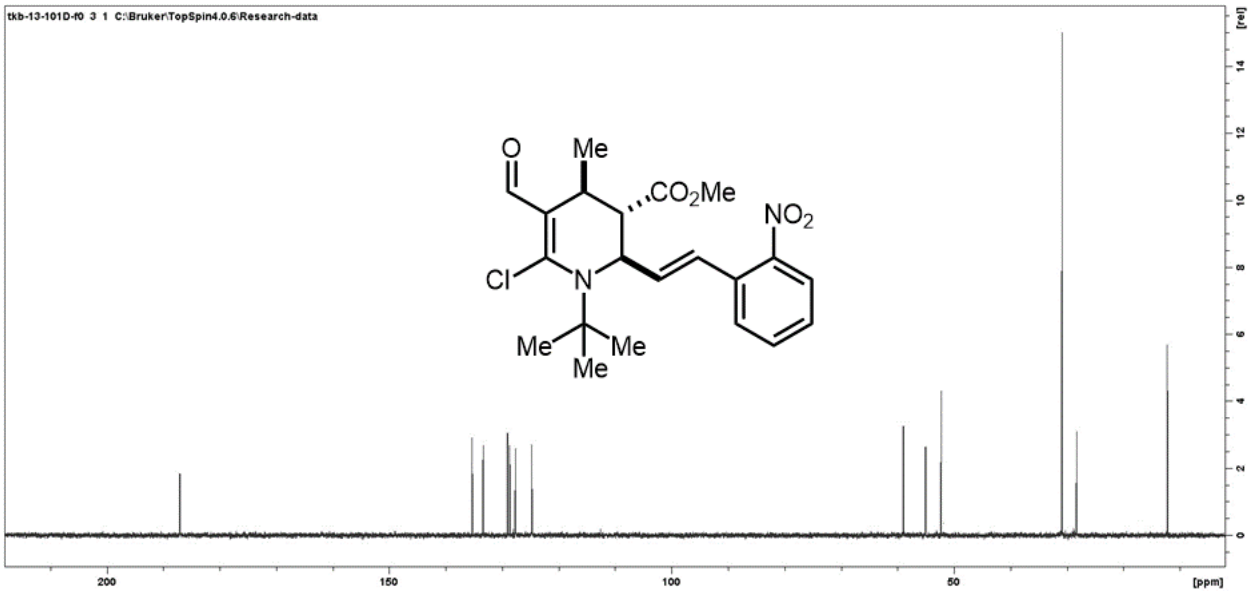
Compound 4k

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (95:5). Oily substance. Yield = 189.4 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 7.98 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.58 (td, *J* = 7.6, 1.3 Hz, 1H), 7.54 – 7.38 (m, 2H), 7.00 (d, *J* = 15.7 Hz, 1H), 5.87 (dd, *J* = 15.7, 8.4 Hz, 1H), 5.04 (t, *J* = 8.7 Hz, 1H), 3.74 (s, 3H), 3.50 (qd, *J* = 7.0, 4.6 Hz, 1H), 2.68 (dd, *J* = 9.1, 4.7 Hz, 1H), 1.64 (s, 9H), 0.96 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.0, 171.2, 150.6, 147.7, 135.2,

133.3, 132.3, 128.9, 128.6, 127.6, 124.7, 122.9, 60.5, 58.9, 55.0, 52.2, 30.8, 28.2, 12.1. **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{25}ClN_2O_5$, 420.1452, found 420.1458.

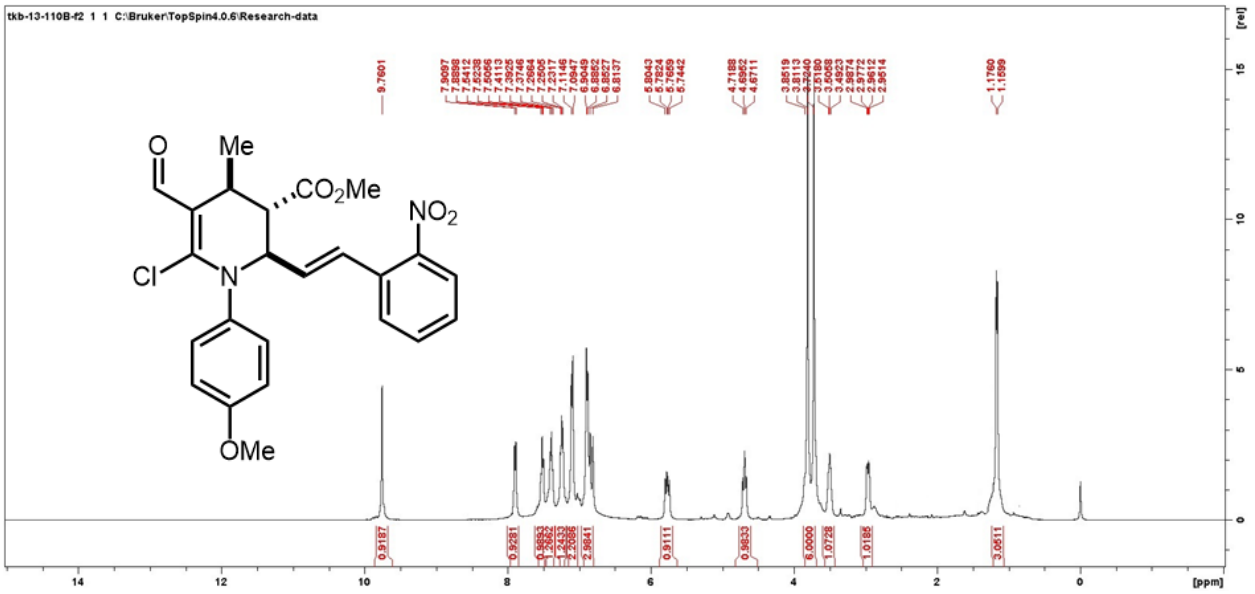






Compound 4l

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (75:25). Oily substance. Yield = 209.6 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.40 (q, J = 9.5, 7.7 Hz, 1H), 7.29 – 7.21 (m, 2H), 6.90 – 6.81 (m, 3H), 5.77 (dd, J = 15.6, 8.7 Hz, 1H), 4.70 (t, J = 9.8 Hz, 1H), 3.81 (s, 3H), 3.72 (s, 3H), 3.51 (p, J = 6.5 Hz, 1H), 2.97 (dd, J = 10.8, 4.7 Hz, 1H), 1.17 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.2, 170.9, 159.4, 150.5, 147.6, 134.6, 133.2, 132.0, 131.6, 131.4, 130.2, 128.9, 128.7, 124.5, 114.3, 114.1, 62.4, 55.5, 52.0, 48.6, 28.4, 16.8. **HRMS-EI$^+$** (*m/z*): calc for $C_{24}H_{23}ClN_2O_6$, 470.1245, found 470.1253.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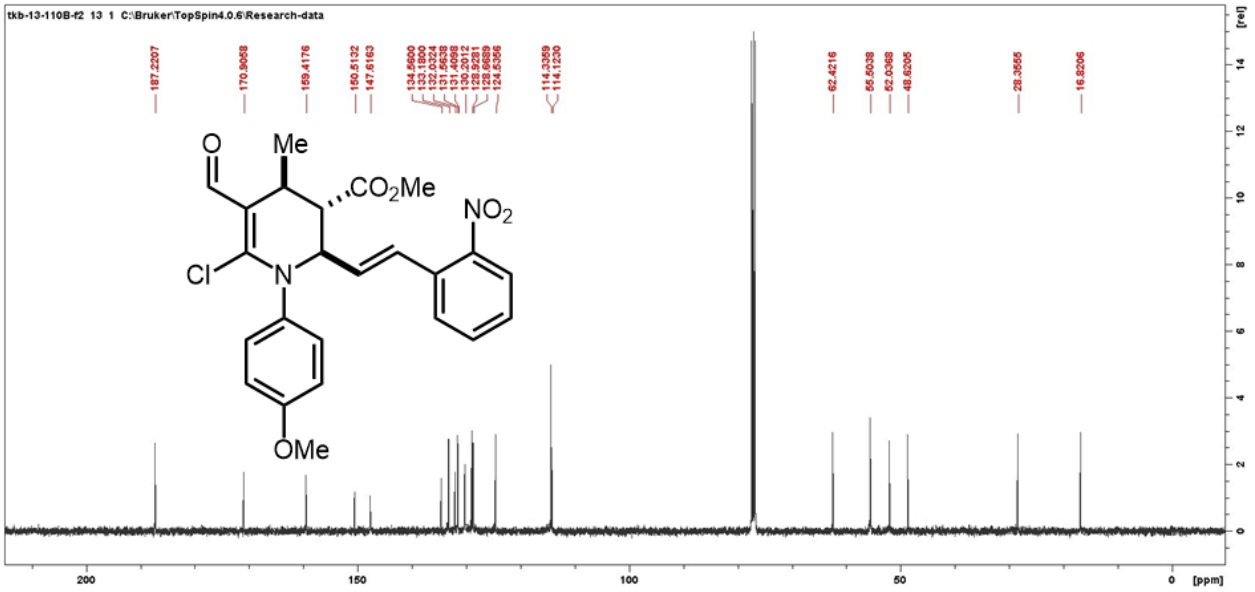
CO2Me
NO2
Cl
N
OMe
[ppm]
[rel]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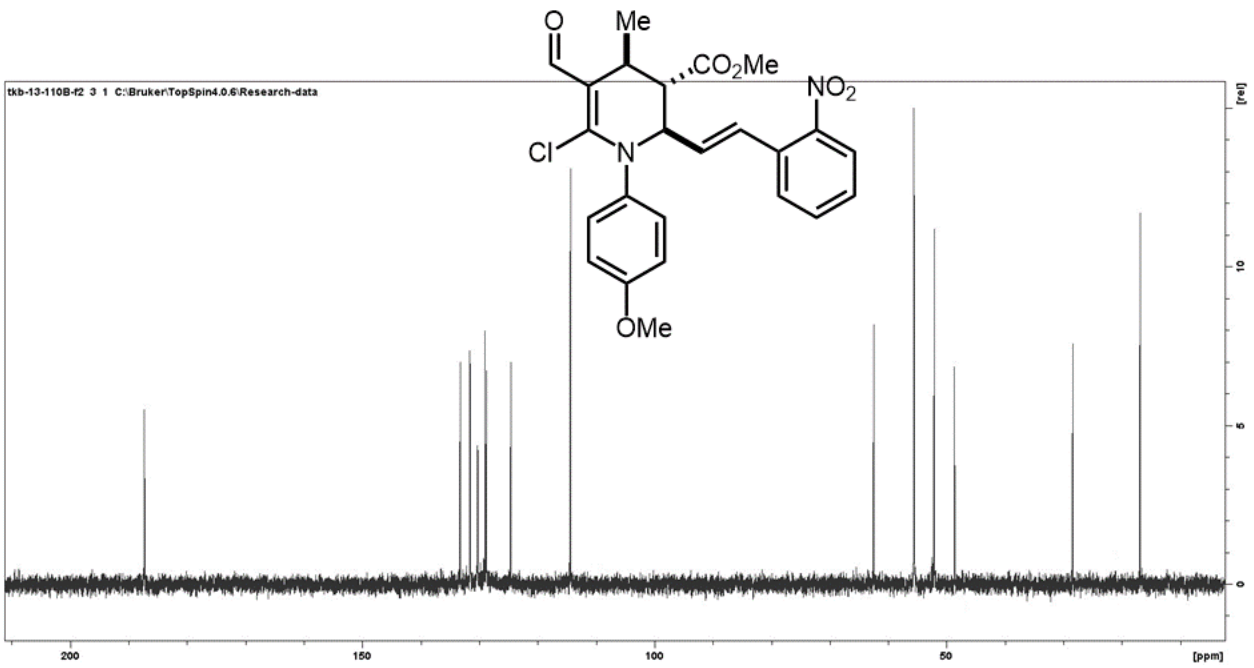
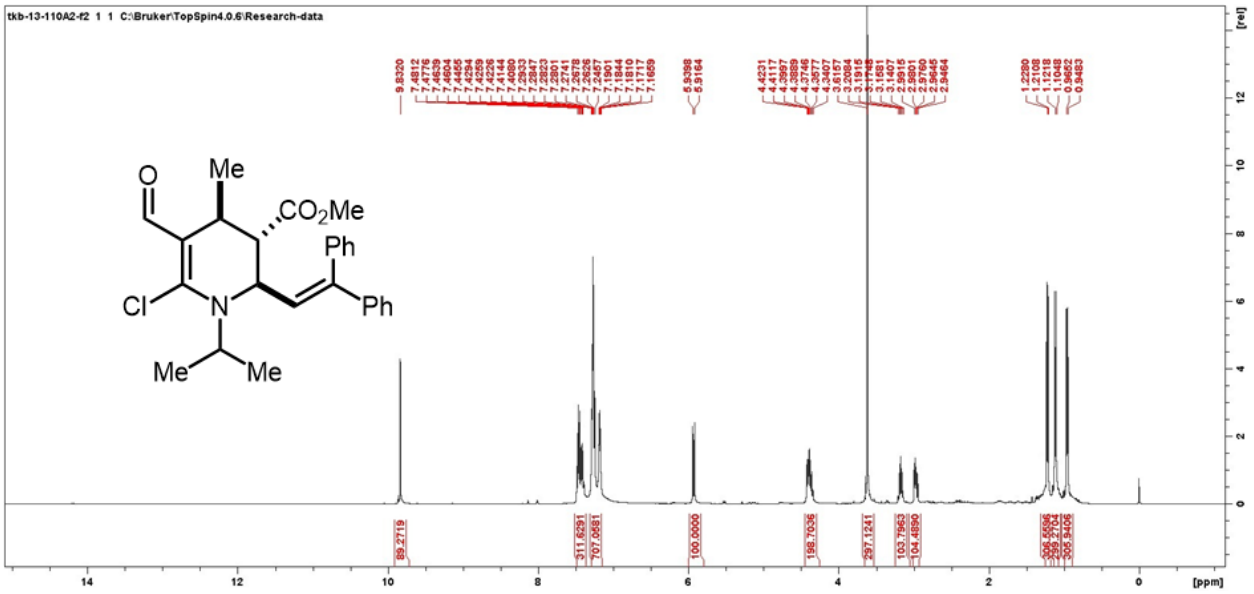


Compound 4m

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (75:25). Oily substance. Yield = 199.3 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.83 (s, 1H), 7.48 – 7.41 (m, 3H), 7.29 – 7.17 (m, 7H), 5.93 (d, *J* = 9.4 Hz, 1H), 4.46 – 4.30 (m, 2H), 3.62 (s, 3H), 3.17 (p, *J* = 6.9 Hz, 1H), 3.01 – 2.92 (m, 1H), 1.22 (d, *J* = 6.9 Hz, 3H), 1.11 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.73, 171.14, 150.82, 144.45, 141.11, 138.43, 129.41, 128.61, 128.36, 128.16, 128.13, 127.58, 125.27, 112.23, 54.87, 52.14, 51.56, 51.14, 27.82, 21.45, 20.74, 14.86. **HRMS-EI$^+$** (*m/z*): calc for $C_{26}H_{28}ClNO_3$, 437.1758, found 437.1763.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Ph
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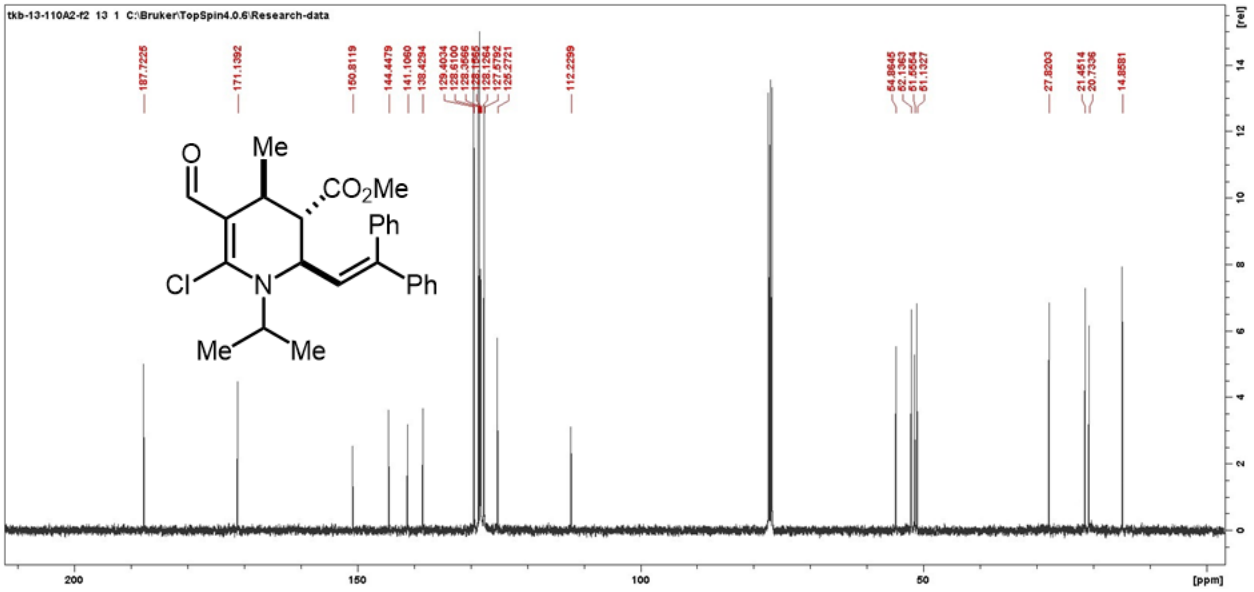
[ppm]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O
CO2Me
Ph
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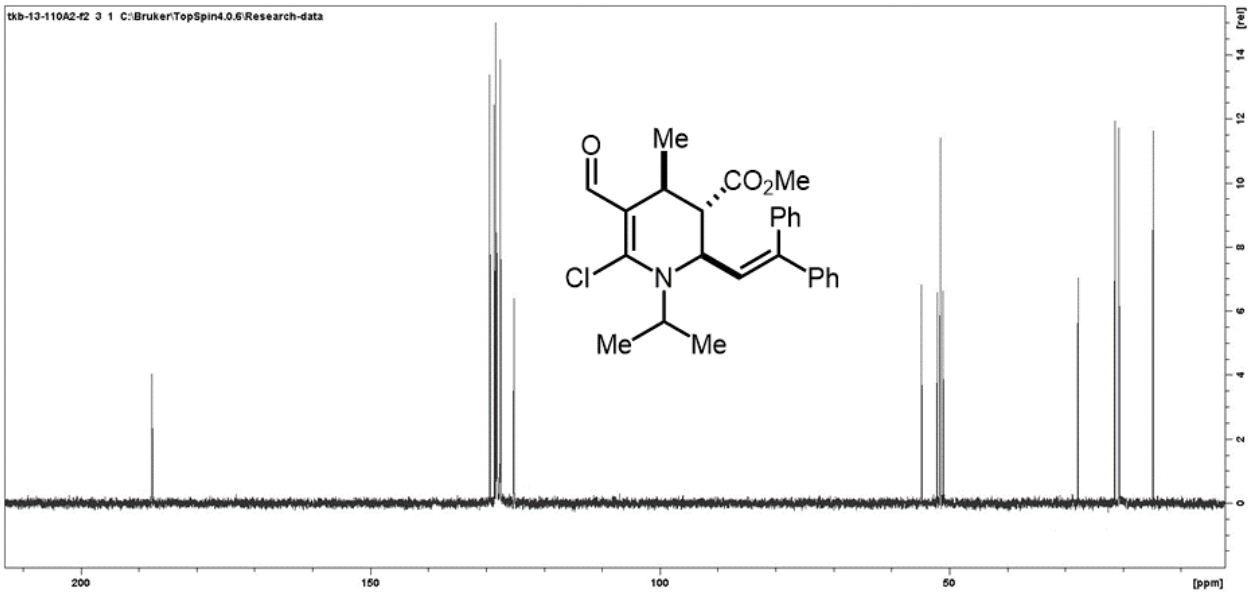
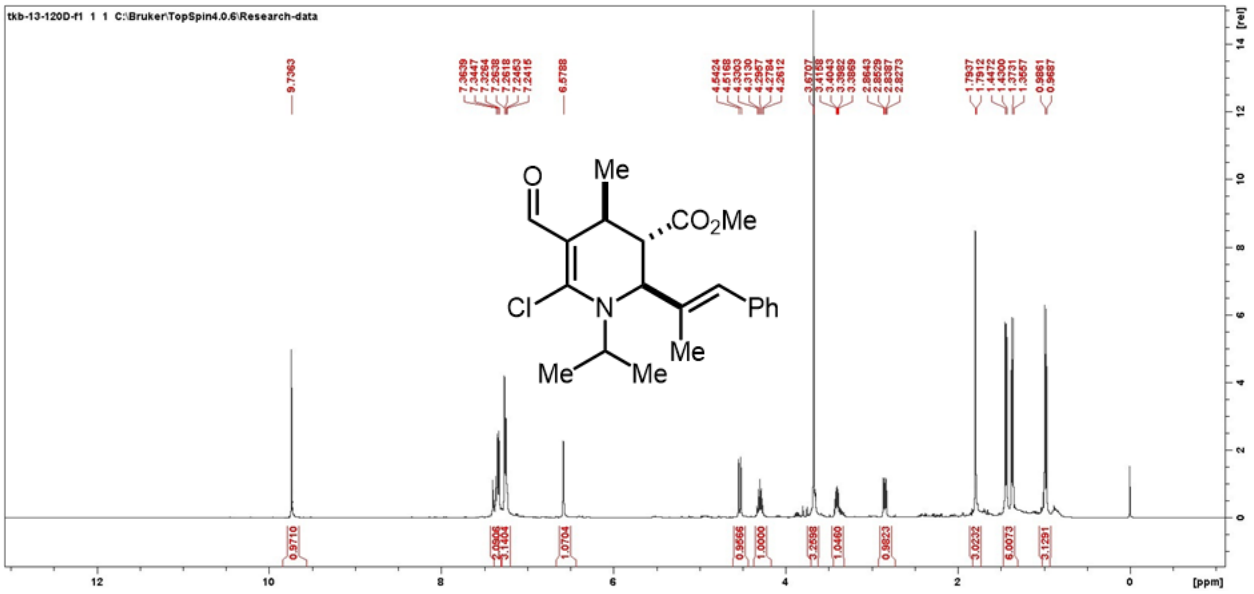


Compound 4n

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (75:25). Oily substance. Yield = 176.7 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.36 – 7.32 (m, 2H), 7.26 – 7.22 (m, 3H), 6.58 (s, 1H), 4.53 (d, *J* = 10.2 Hz, 1H), 4.30 (hept, *J* = 6.9 Hz, 1H), 3.66 (s, 3H), 3.46 – 3.31 (m, 1H), 2.85 (dd, *J* = 10.3, 4.6 Hz, 1H), 1.79 (s, 3H), 1.44 (d, *J* = 6.9 Hz, 3H), 1.36 (d, *J* = 7.0 Hz, 3H), 0.98 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.4, 171.5, 151.9, 136.8, 135.0, 130.6, 128.8, 128.3, 127.1, 116.2, 64.7, 54.2, 51.9, 48.9, 27.7, 21.2, 21.1, 14.7, 13.1. **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{26}ClNO_3$, 375.1601, found 375.1605.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4.3303
4.3130
4.2957
4.2784
4.2612
3.4707
3.4168
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2.8643
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2.8273
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1.7912
1.4472
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1.3557
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0.9687
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Cl
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Ph
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Me
Me
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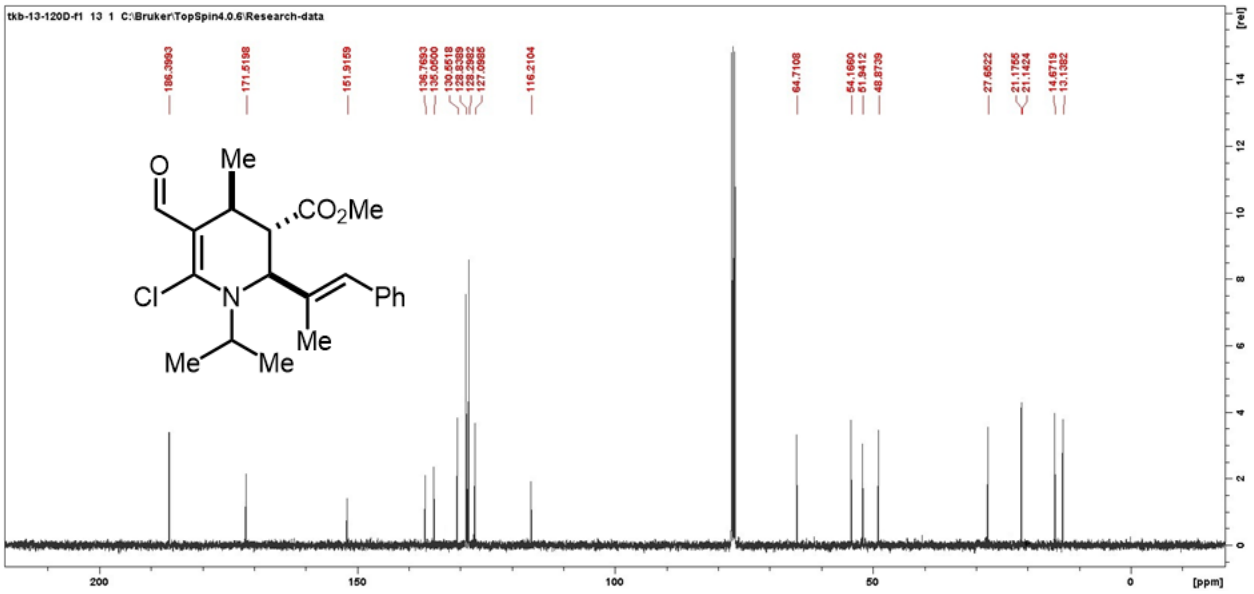
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54.1660
51.3412
48.8739
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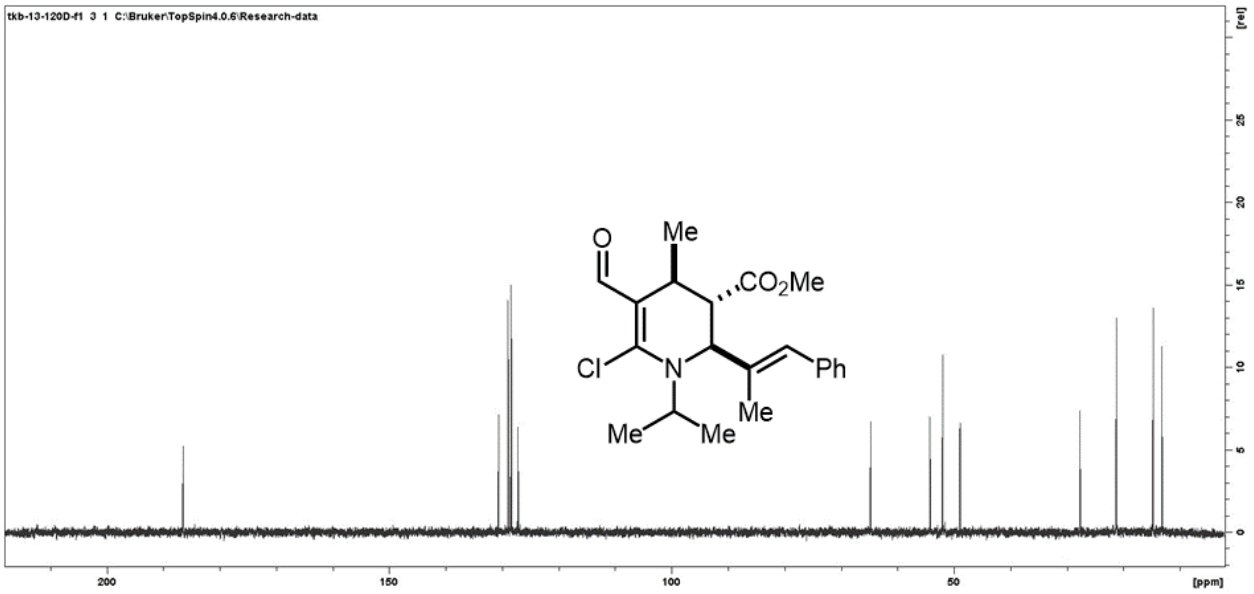
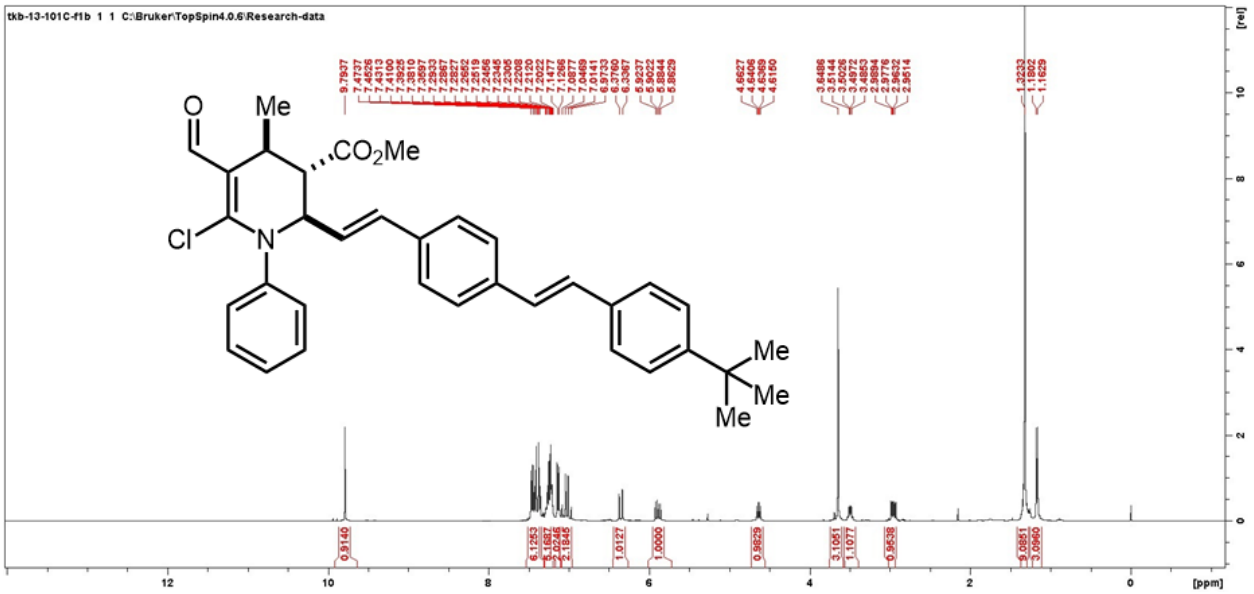
[rel]
[ppm]



Compound 4o

Prepared in 0.25 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (75:25). Oily substance. Yield = 119.2 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 7.47 – 7.35 (m, 6H), 7.29 – 7.20 (m, 5H), 7.15 – 7.12 (m, 2H), 7.04 – 7.01 (m, 2H), 6.36 (d, *J* = 15.8 Hz, 1H), 5.89 (dd, *J* = 15.7, 8.6 Hz, 1H), 4.64 (dd, *J* = 10.5, 8.6 Hz, 1H), 3.65 (s, 3H), 3.50 (qd, *J* = 6.9, 4.6 Hz, 1H), 3.01 – 2.91 (m, 1H), 1.32 (s, 9H), 1.17 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.2, 171.1, 151.2, 150.0, 141.0, 137.6, 135.9, 135.5, 134.1, 129.9, 129.1, 128.6, 128.2, 126.9, 126.6, 126.5, 126.3, 126.2, 125.6, 114.9, 63.1, 51.9, 49.0, 34.6, 31.2, 28.2, 16.6. **HRMS-EI$^+$** (*m/z*): calc for $C_{35}H_{36}ClNO_3$, 553.2384, found 553.2395.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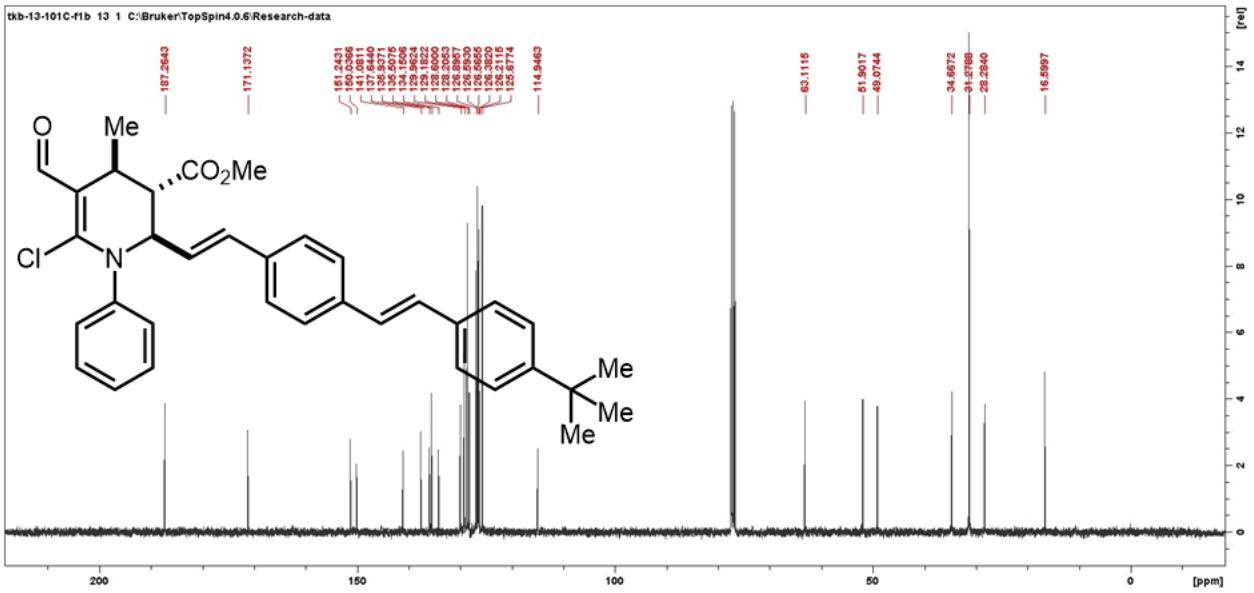
CO2Me
Cl
N
Me
Me
Me
[ppm]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Cl
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Me
Me
Me
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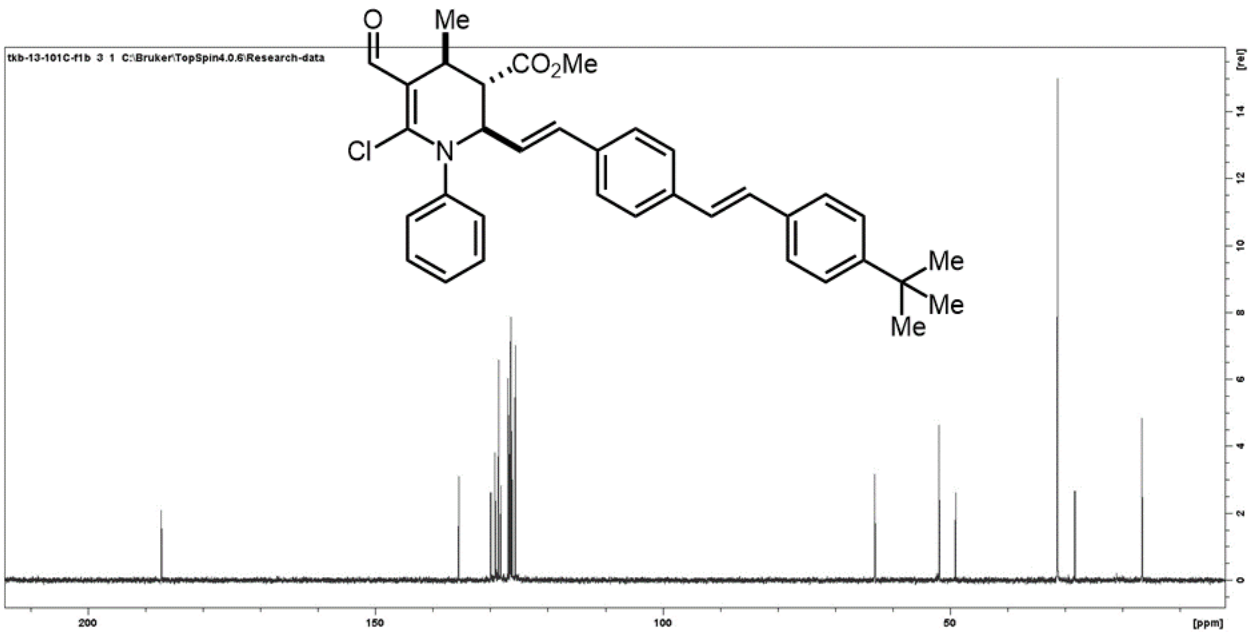
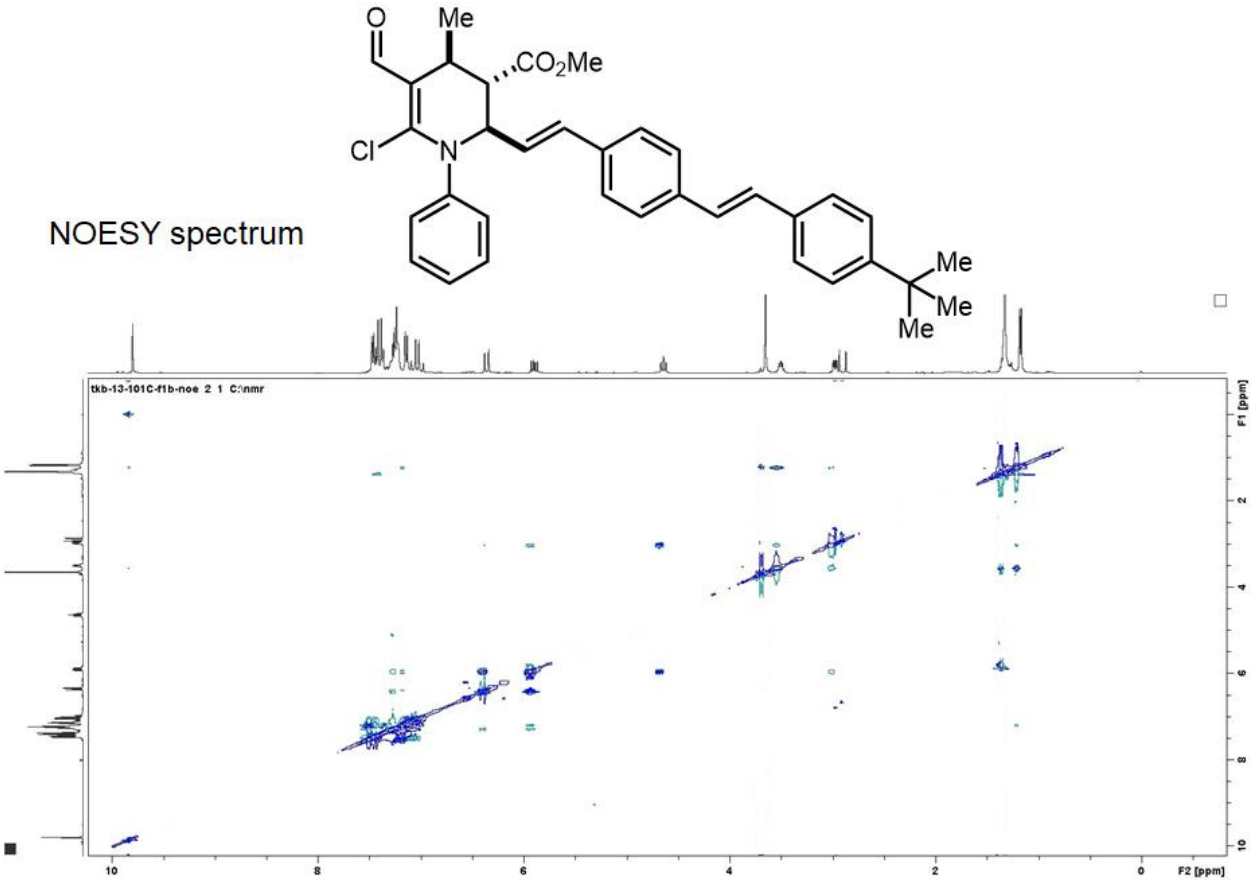
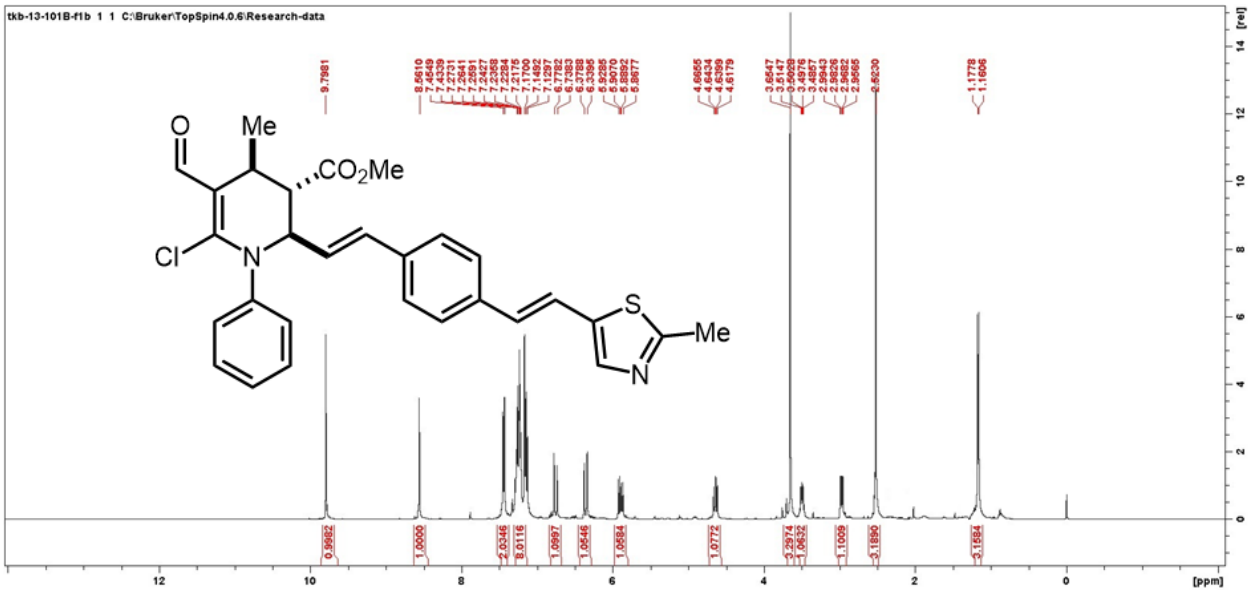


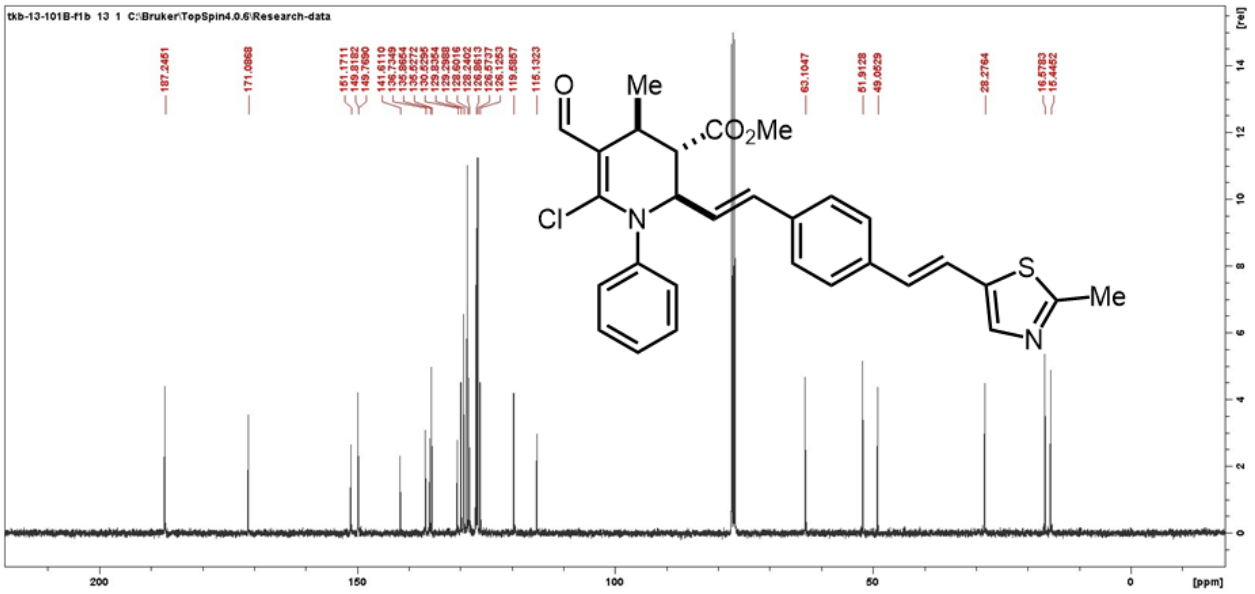


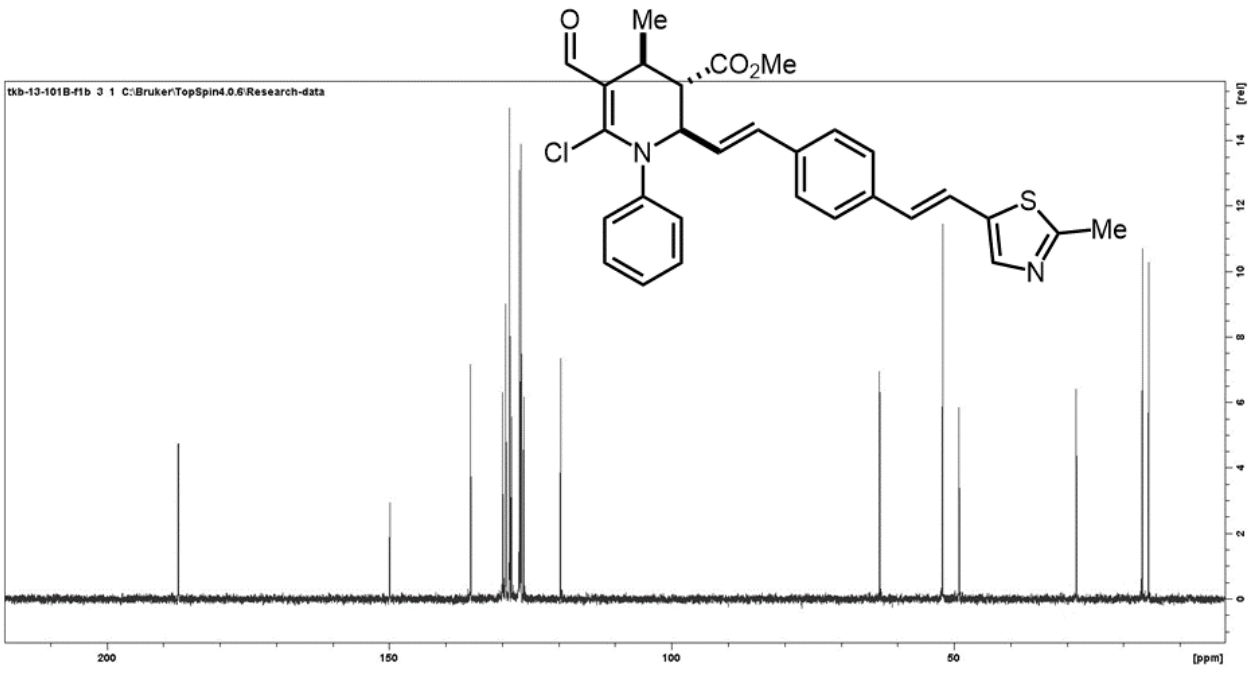
Compound 4p

Prepared in 0.25 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica (pretreated with Et_3N), eluting with hexane/EtOAc (75:25). Oily substance. Yield = 107.7

mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.56 (s, 1H), 7.44 (d, 2H), 7.27 – 7.21 (m, 8H), 6.76 (d, J = 15.9 Hz, 1H), 6.36 (d, J = 15.7 Hz, 1H), 5.90 (dd, J = 15.7, 8.6 Hz, 1H), 4.64 (dd, J = 10.5, 8.6 Hz, 1H), 3.65 (s, 3H), 3.51 – 3.49 (m, 1H), 2.98 (dd, J = 10.5, 4.7 Hz, 1H), 2.52 (s, 3H), 1.17 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.2, 171.1, 151.2, 149.8, 141.6, 136.7, 135.9, 135.5, 130.5, 129.8, 129.3, 128.6, 128.2, 126.9, 126.6, 126.1, 119.6, 115.1, 63.1, 51.9, 49.1, 28.3, 16.6, 15.4. **HRMS-EI^{+}** (*m/z*): calc for $C_{29}H_{27}ClN_2O_3S$, 518.1431, found 518.1438.





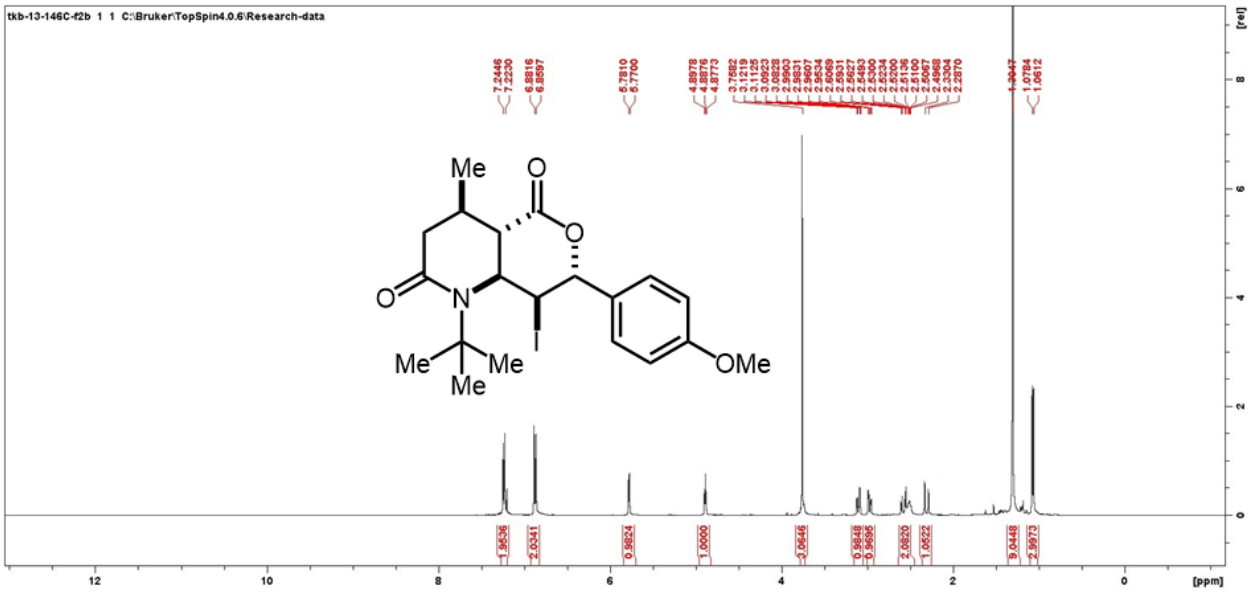

tkb-13-101B-f1b 3 1 C:\Bruker\TopSpin4.0.6\Research-data
O
Me
CO2Me
Cl
N
S
Me
N
200
150
100
50
[ppm]

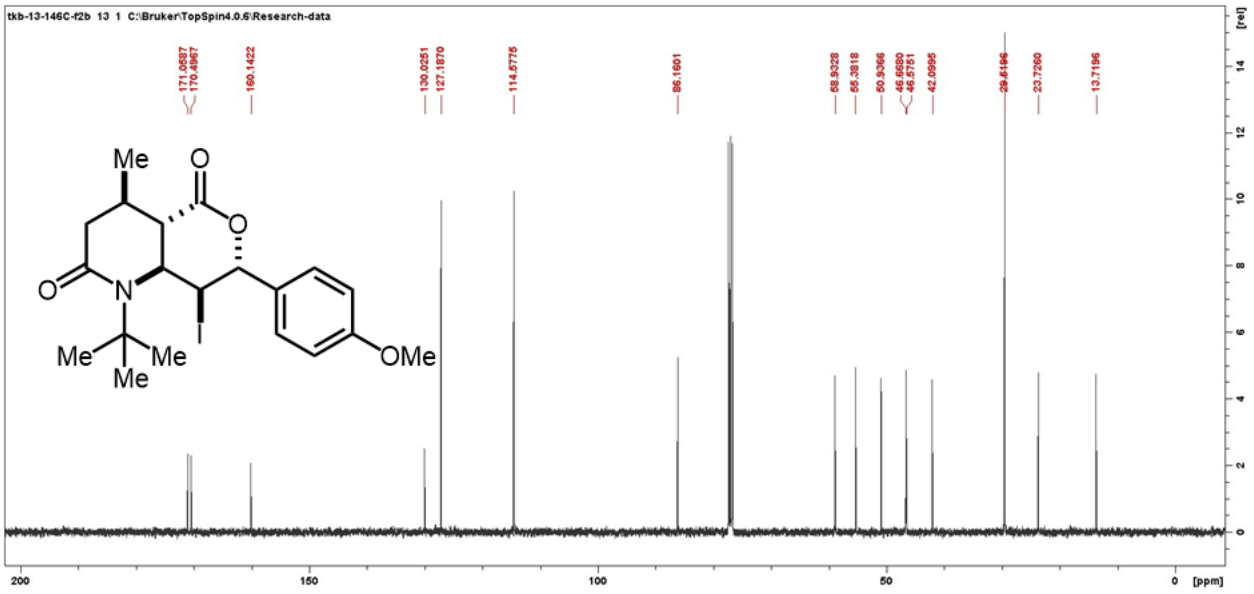
Scheme 3 Results

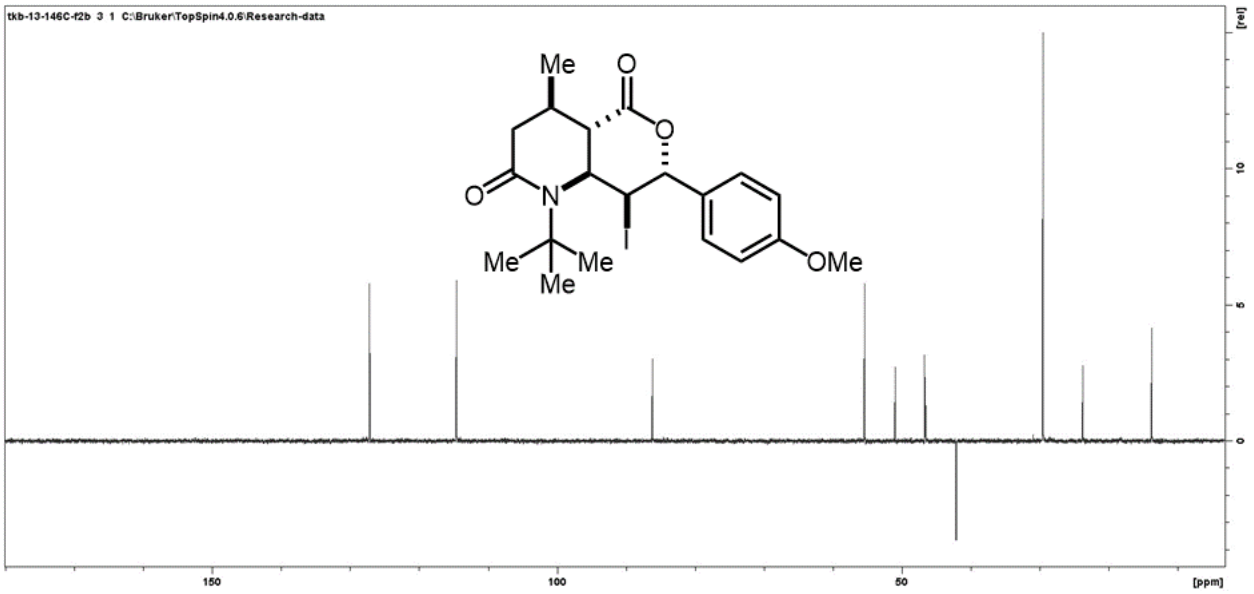
Compound 5a

Prepared in 0.50 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Oily substance. Yield = 226.2 mg, 96%.

HRMS-EI^{+} (*m/z*): calc for $C_{20}H_{26}INO_4$, 471.0907, found 471.0912.



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Me
Me
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5
0
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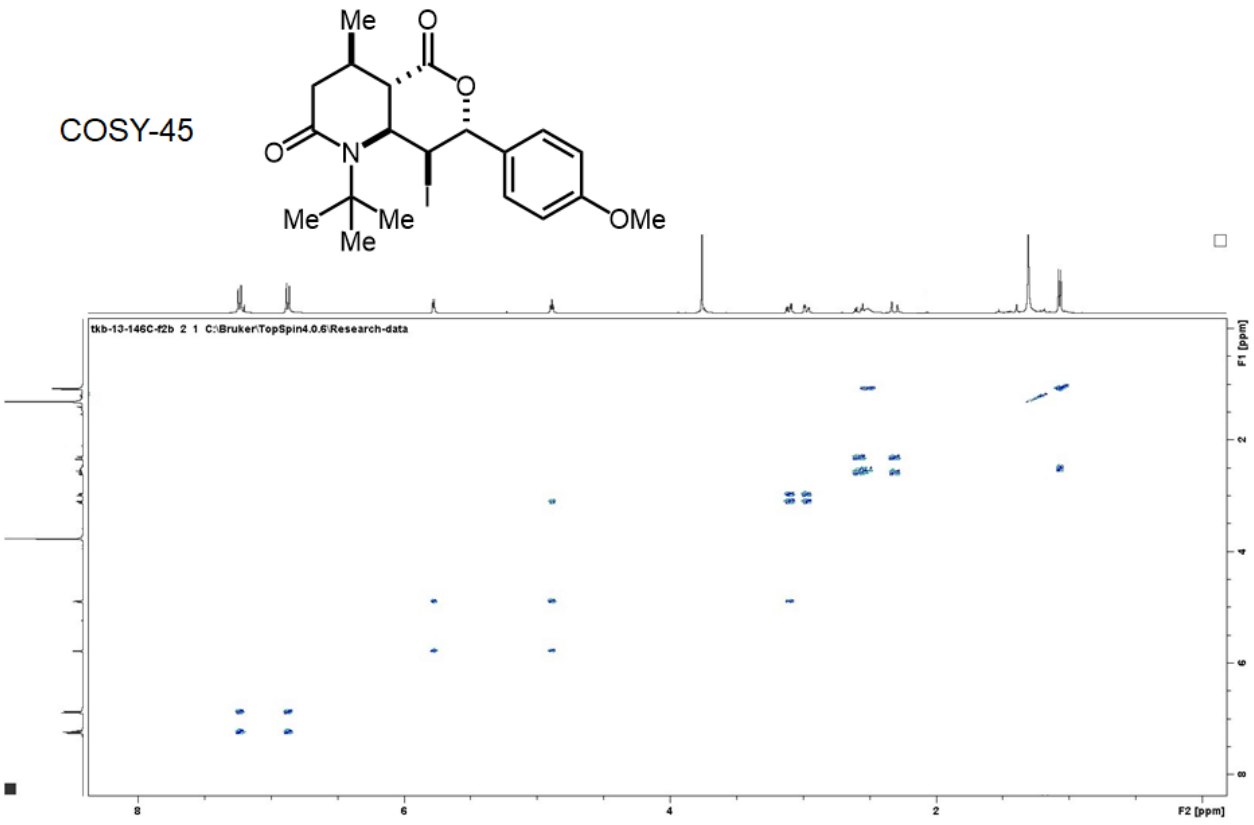
50
[ppm]

COSY-45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4
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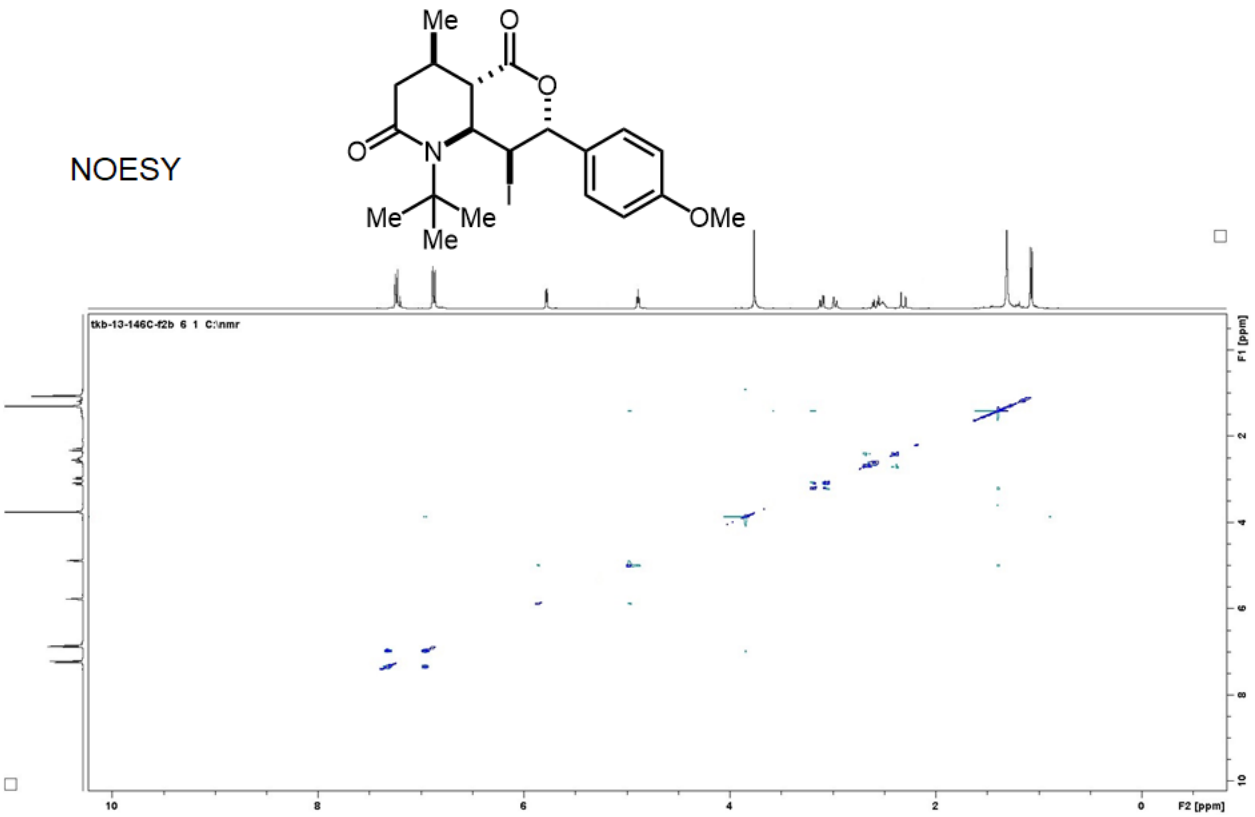
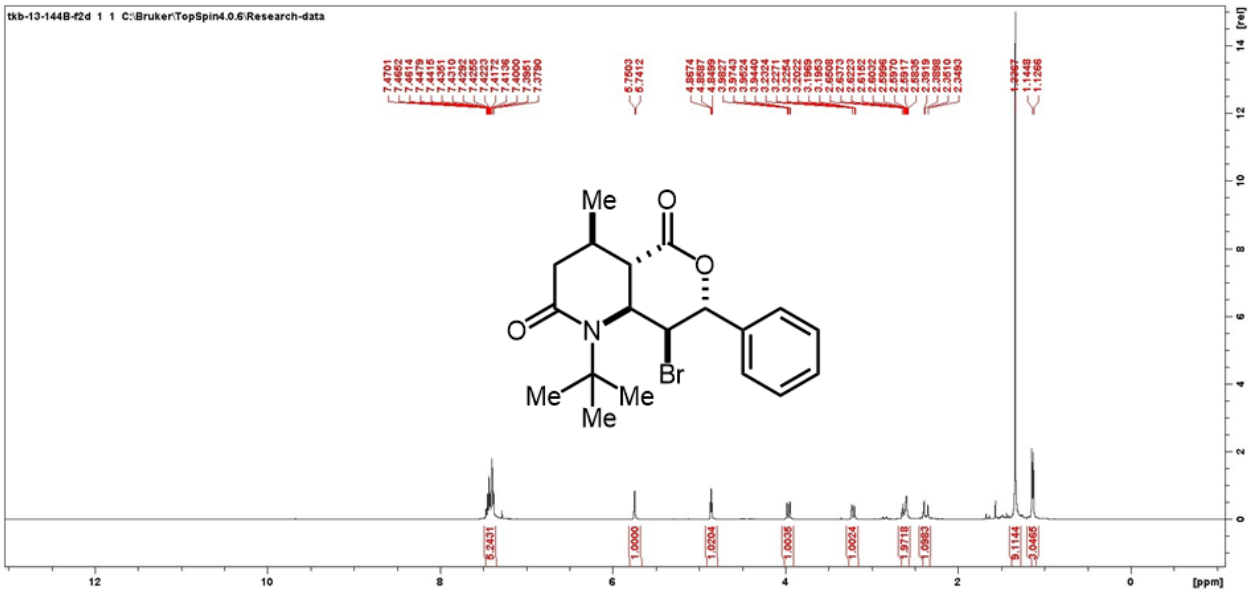


Compound 5b

Prepared in 0.50 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Oily substance. Yield = 185.3 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.38 (m, 5H), 5.75 (d, *J* = 3.7 Hz, 1H), 4.86 (t, *J* = 3.5 Hz, 1H), 3.96 (dd, *J* = 12.1, 3.4 Hz, 1H), 3.21 (ddd, *J* = 12.1, 2.9, 1.0 Hz, 1H), 2.67 – 2.54 (m, 2H), 2.42 – 2.32 (m, 1H), 1.34 (s, 9H), 1.13 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 170.0, 137.8, 129.3 129.2, 125.5, 84.9, 60.8, 58.6, 50.5, 43.8, 42.0, 29.2, 23.6, 13.4. **HRMS-EI^{+}** (*m/z*): calc for $C_{19}H_{24}BrNO_3$, 393.0940, found 393.0944.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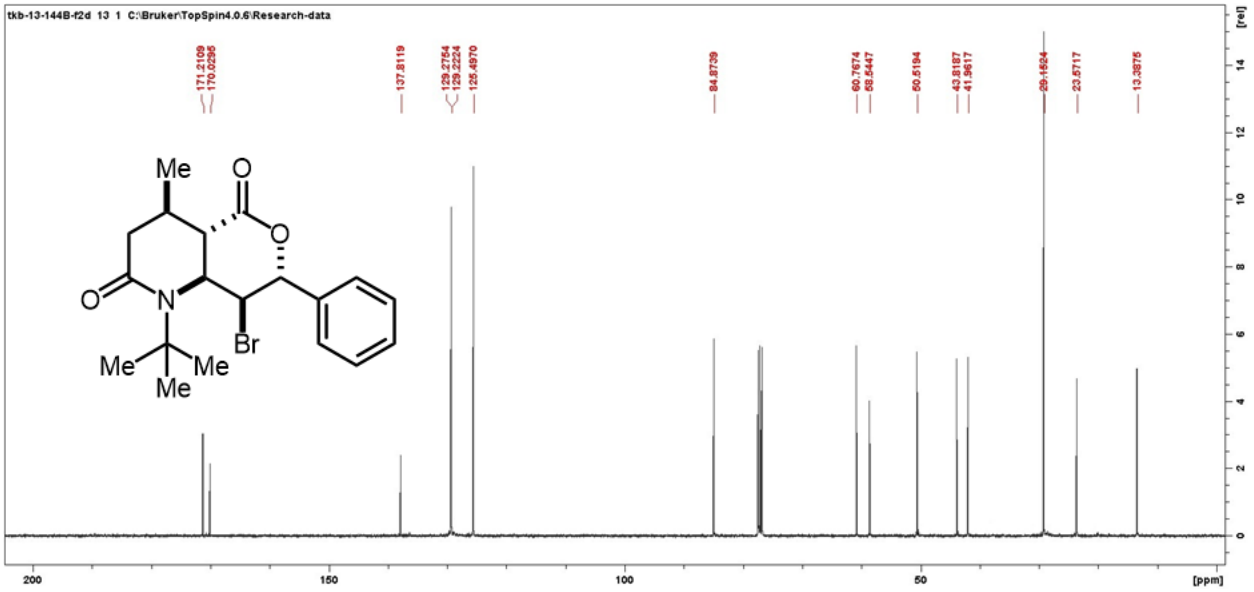
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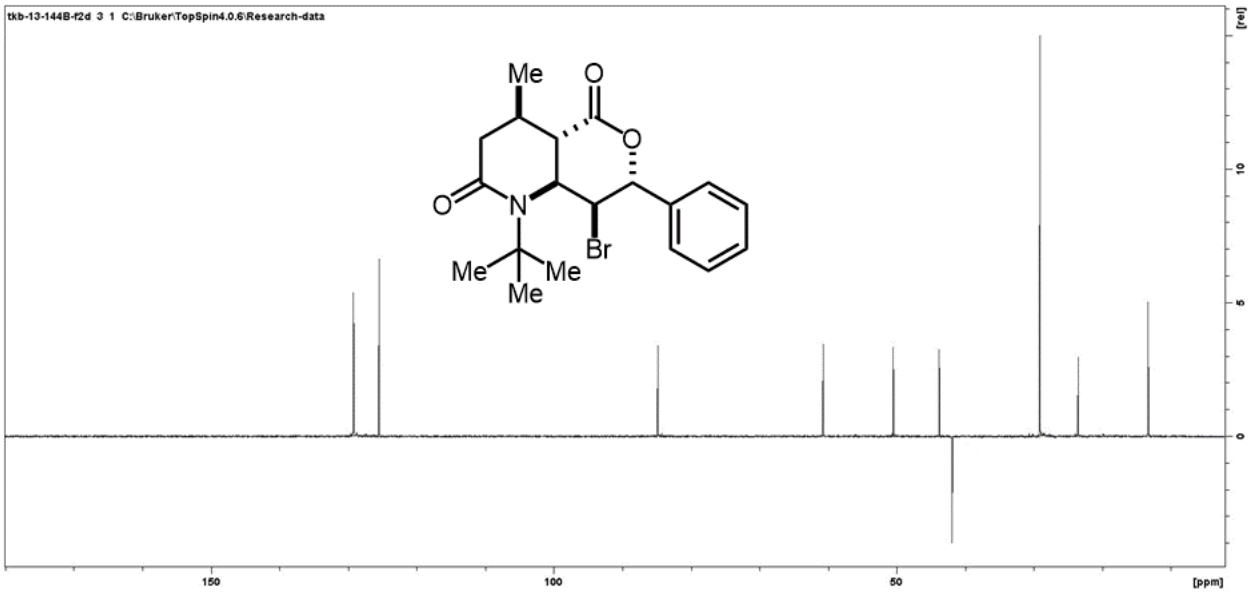
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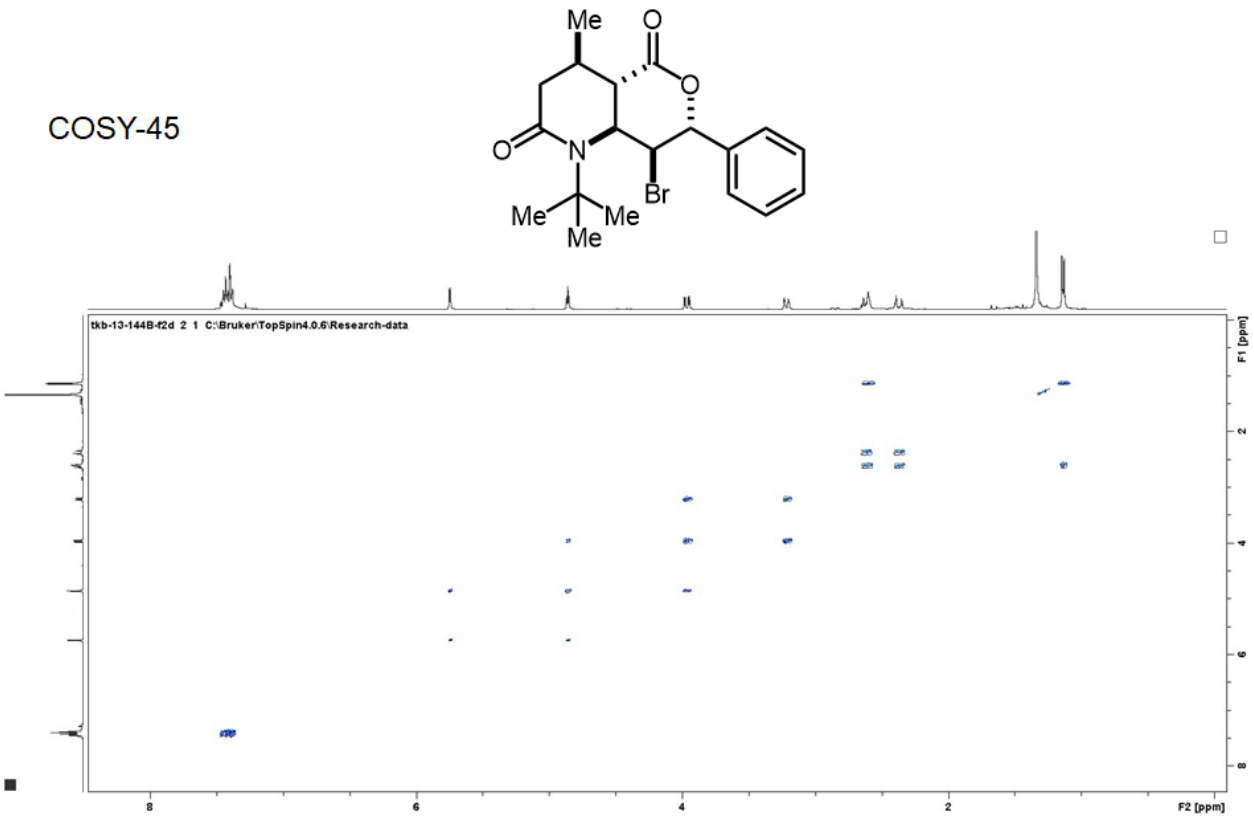
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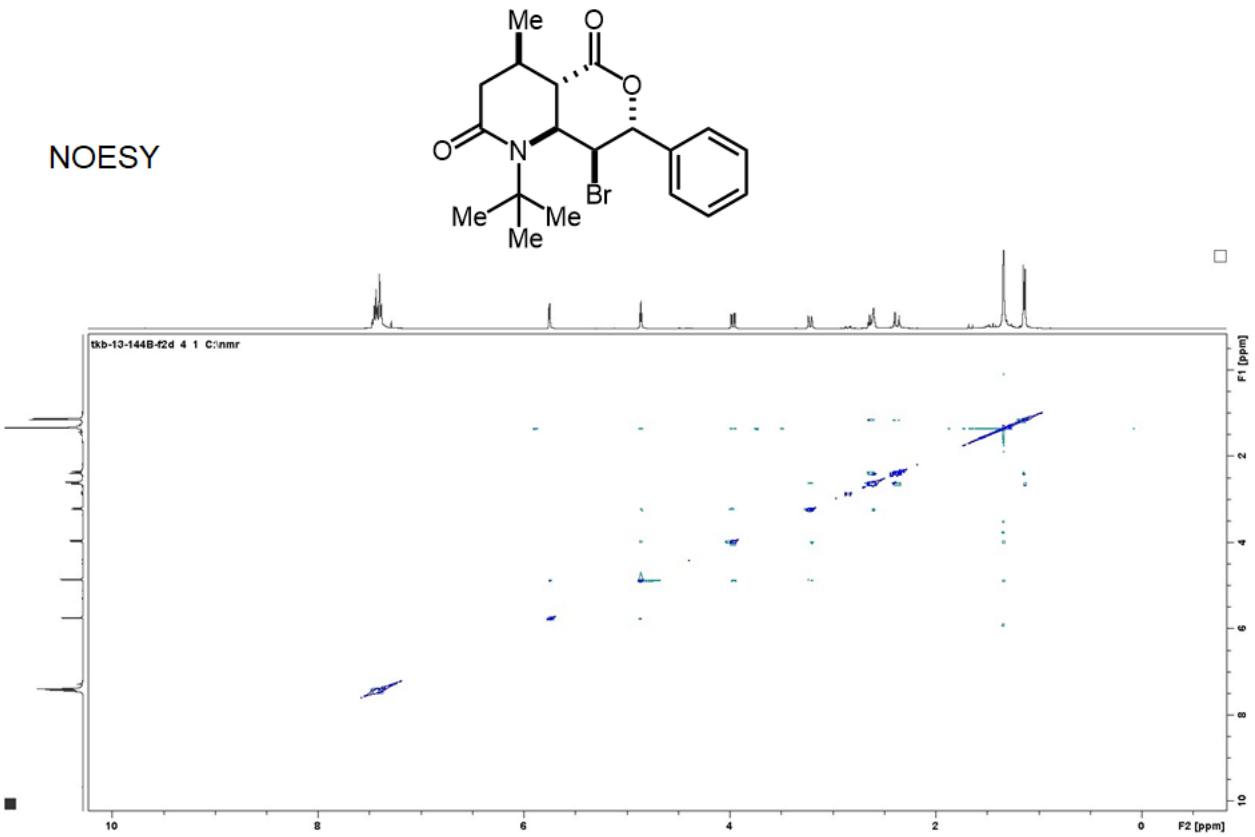
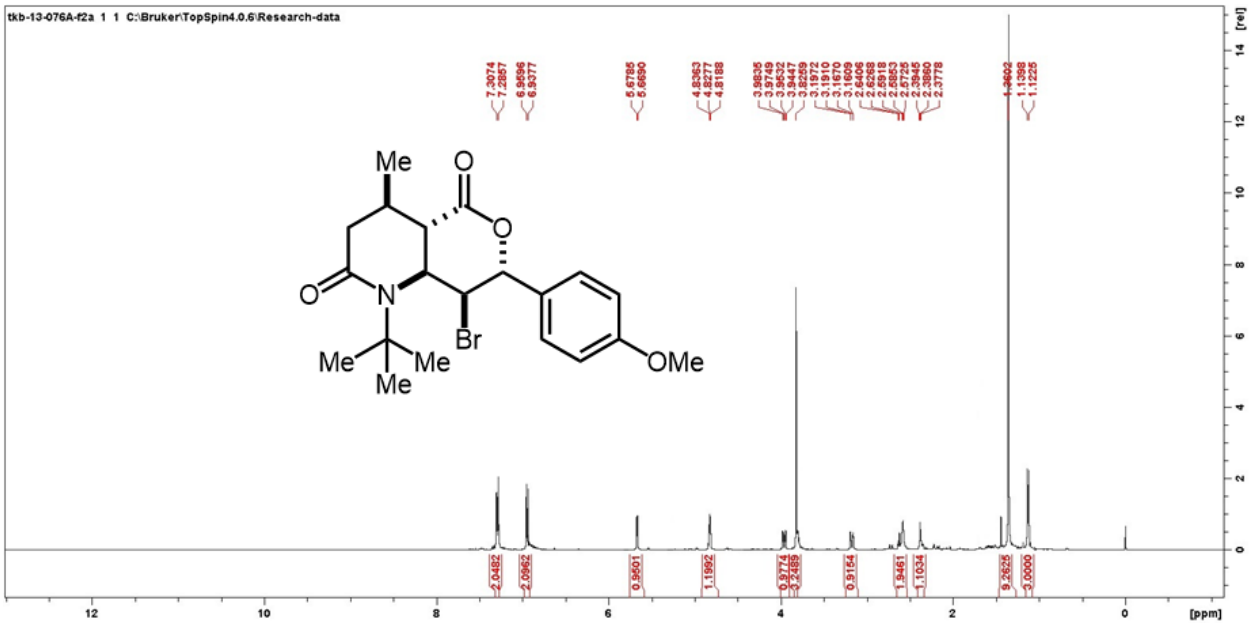


Compound 5c

Prepared in 0.50 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 195.2 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 7.2 Hz, 2H), 6.94 (d, *J* = 7.2 Hz, 2H), 5.67 (d, *J* = 3.9 Hz, 1H), 4.83 (q, *J* = 3.8 Hz, 1H), 3.96 (dd, *J* = 12.1, 3.5 Hz, 1H), 3.82 (s, 3H), 3.18 (dd, *J* = 12.1, 2.8 Hz, 1H), 2.60 (ddt, *J* = 8.4, 6.2, 4.3 Hz, 2H), 2.40 – 2.38 (m, 1H), 1.37 (s, 9H), 1.10 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 170.2, 160.1, 129.6, 127.0, 114.6, 84.7, 61.1, 58.6, 55.4, 50.7, 43.7, 42.0, 29.2, 23.6, 13.3. **HRMS-EI^{+}** (*m/z*): calc for $C_{20}H_{26}BrNO_4$, 423.1045, found 423.1049.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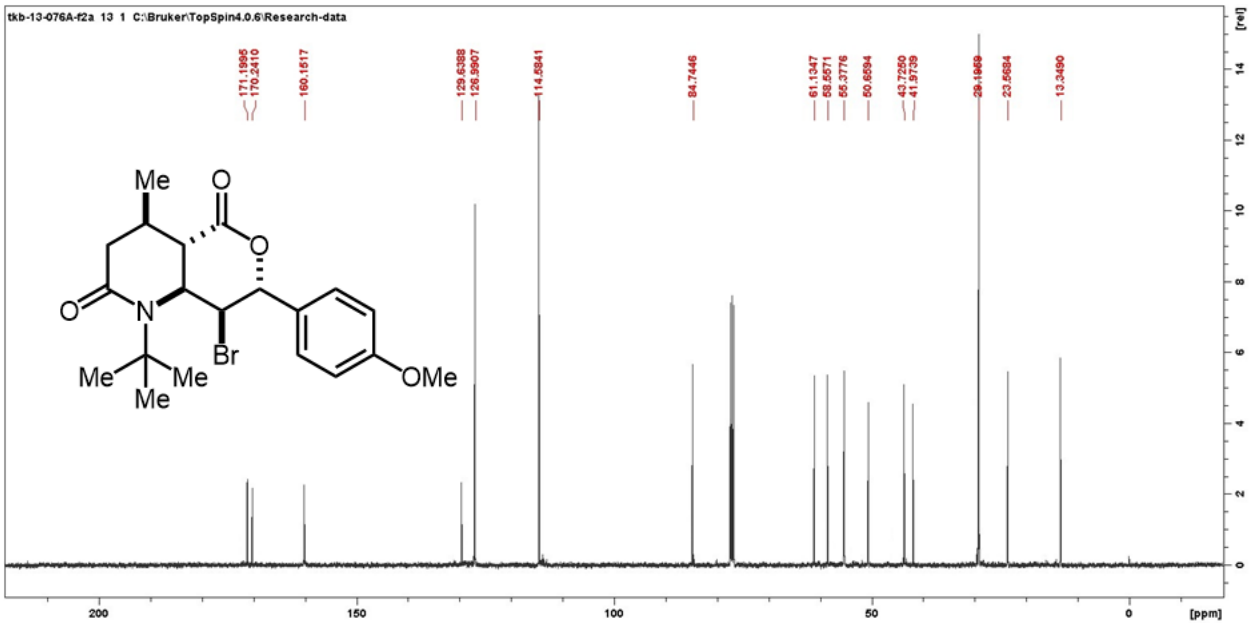
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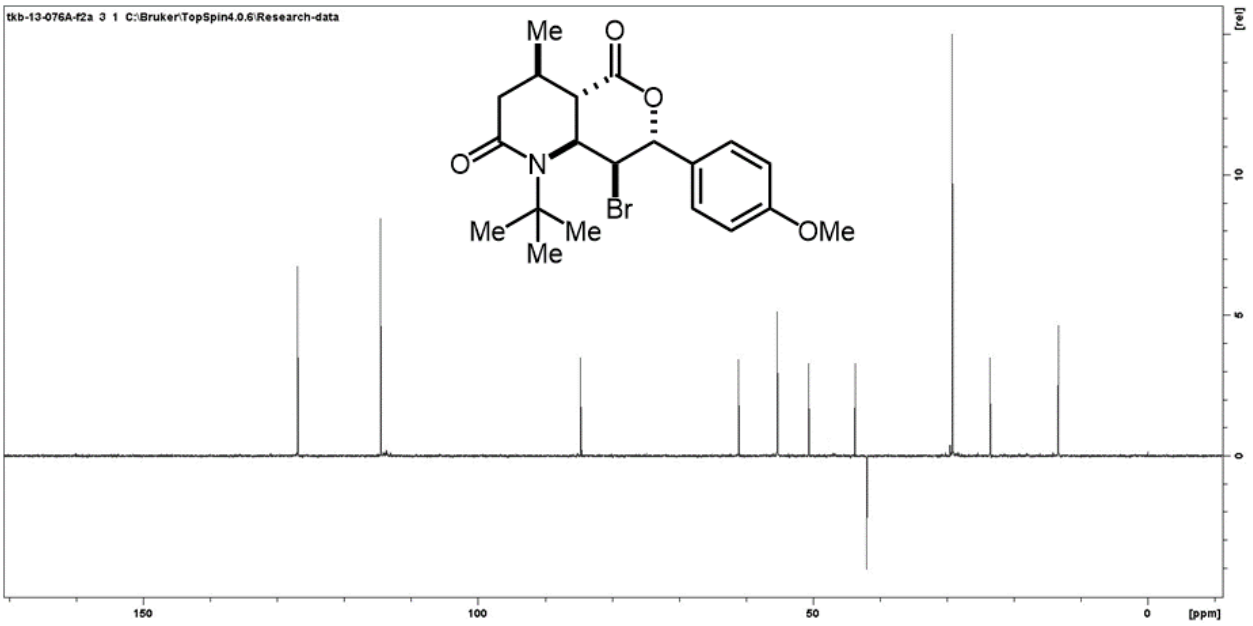
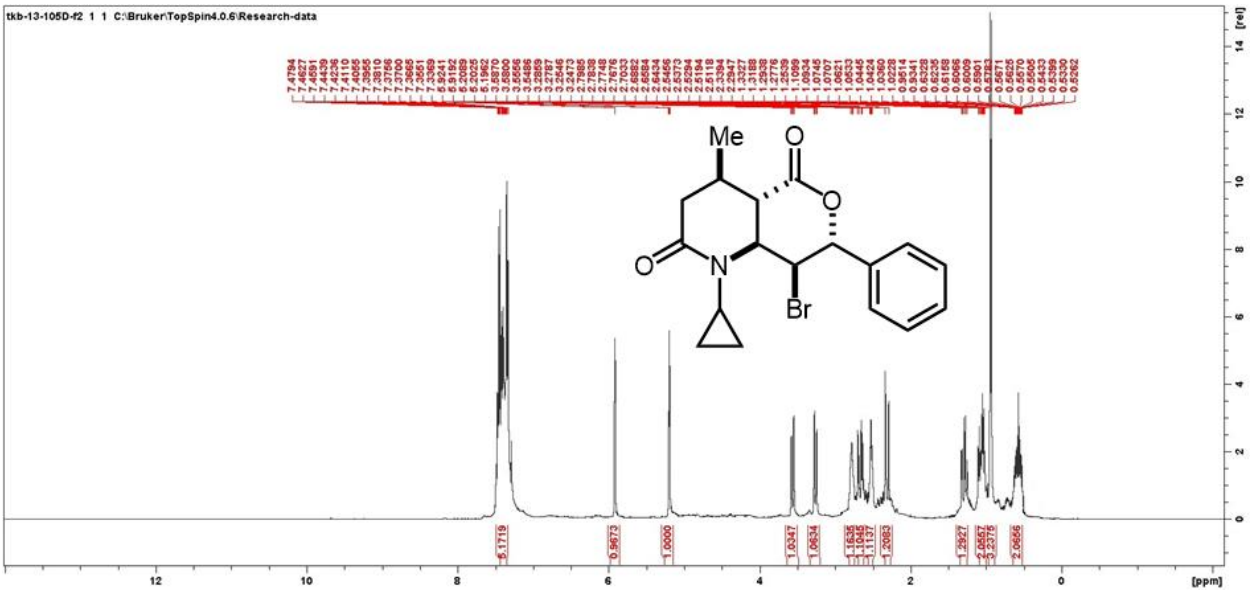
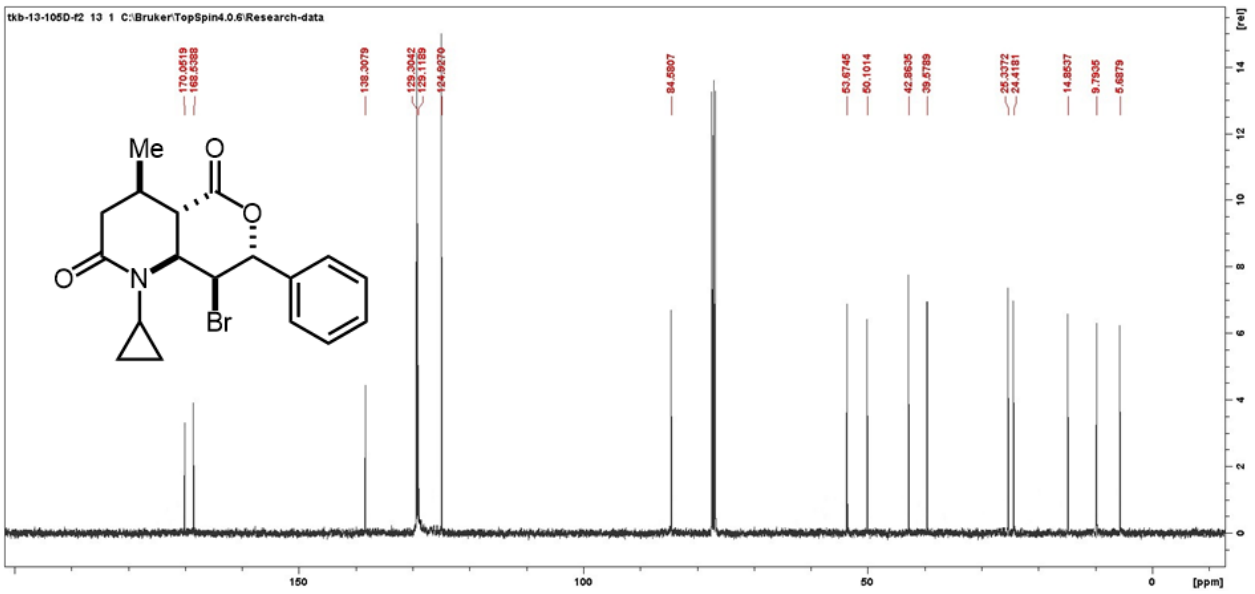
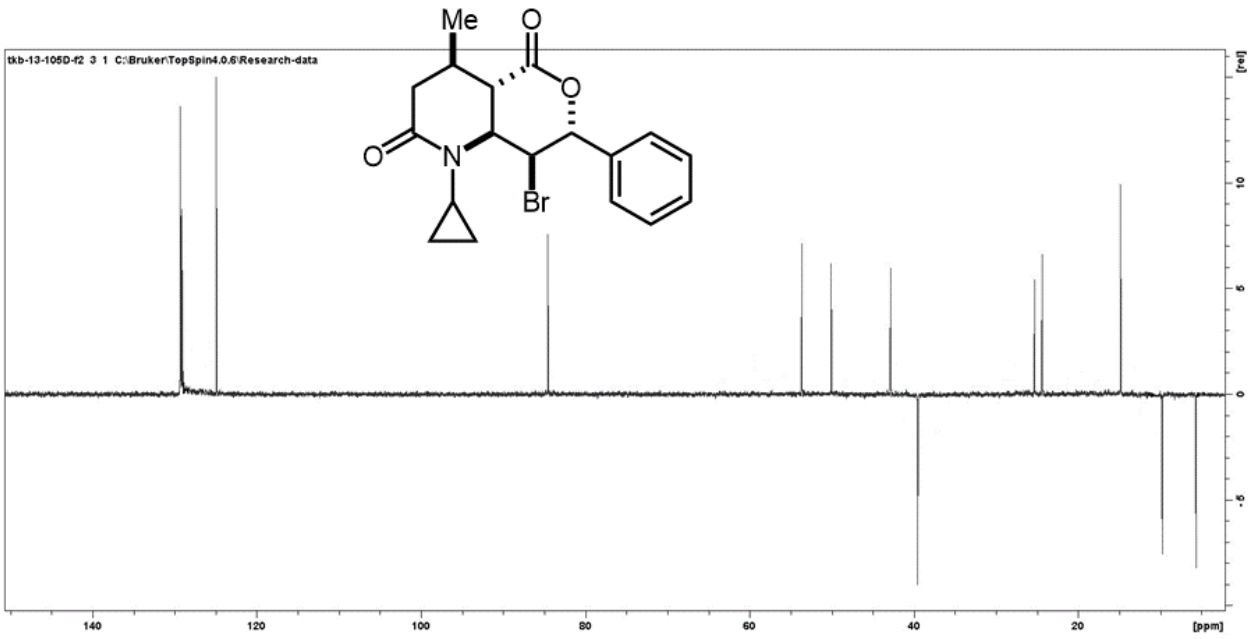


Compound 5d

Prepared in 0.50 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 162.7 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.34 (m, 5H), 5.92 (d, *J* = 2.4 Hz, 1H), 5.21 (d, 1H), 3.57 (dd, *J* = 12.5, 2.9 Hz, 1H), 3.27 (dd, *J* = 12.6, 3.0 Hz, 1H), 2.95 – 2.47 (m, 3H), 2.47 – 2.26 (m, 1H), 1.44 – 1.18 (m, 1H), 1.15 – 0.99 (m, 5H), 0.63 – 0.53 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 168.5, 138.3, 129.3, 129.1, 124.9, 84.6, 53.7, 50.1, 42.9, 39.6, 25.3, 24.4, 14.9, 9.8, 5.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{18}H_{20}BrNO_3$, 377.0627, found 377.0632.



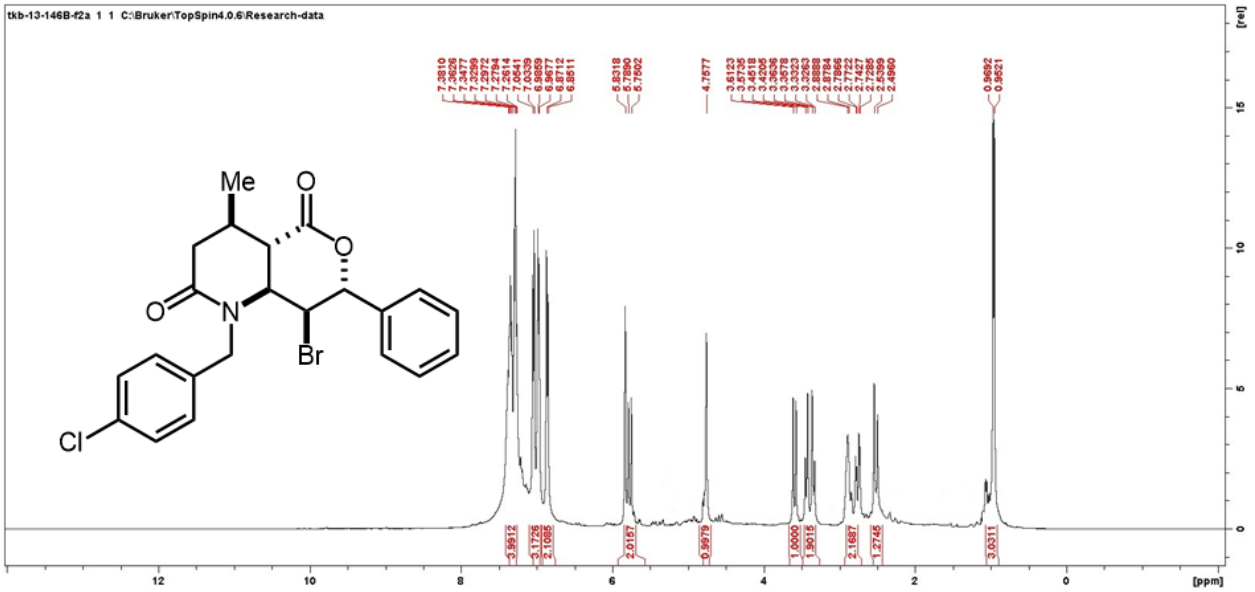


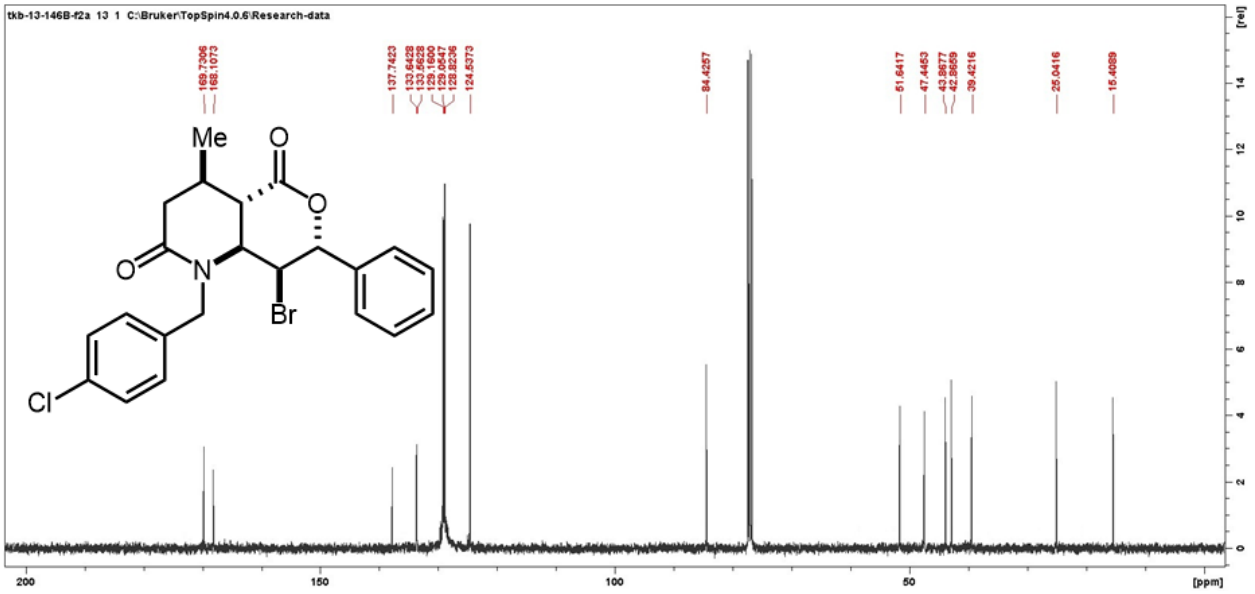


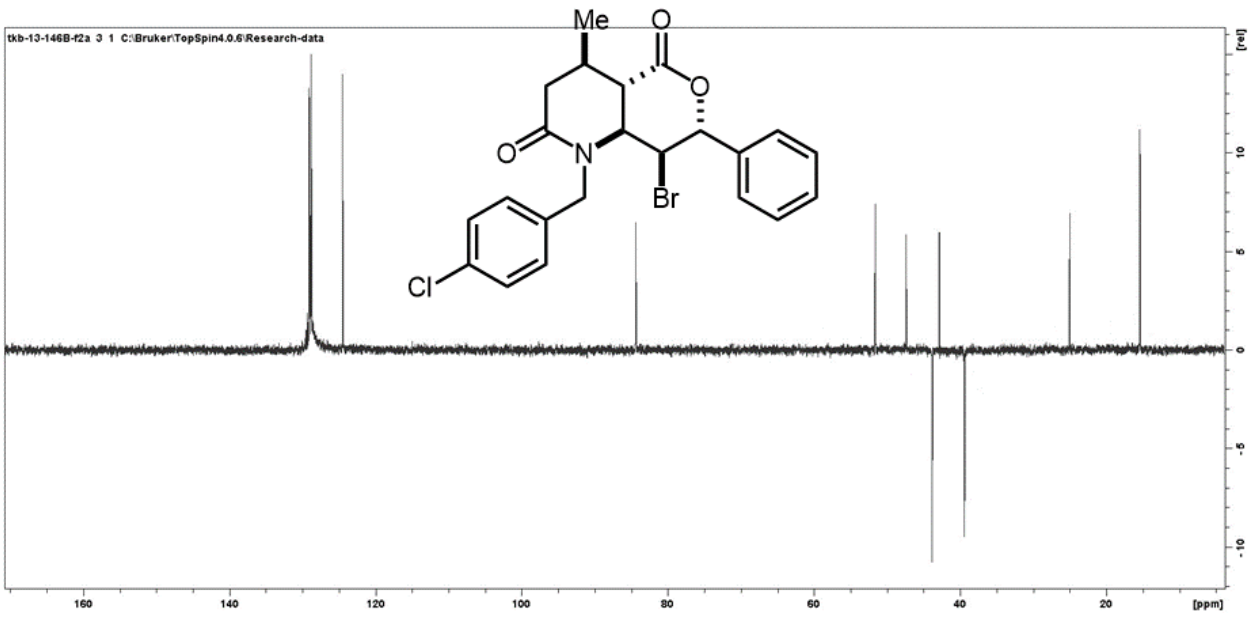
Compound 5e

Prepared in 0.50 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 192.0 mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 4H), 7.04 (d, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 2H), 6.86 (d, *J* = 8.0 Hz, 2H), 5.83 (s, 1H), 5.77 (d, *J* = 15.6 Hz, 1H), 4.76 (s, 1H), 3.59 (d, *J* = 15.5 Hz, 1H), 3.43

(dd, J = 12.5, 2.6 Hz, 1H), 3.35 (dd, J = 12.5, 3.1 Hz, 1H), 2.89 – 2.87 (m, 1H), 2.76 (dd, J = 17.6, 6.0 Hz, 1H), 2.52 (d, J = 17.7 Hz, 1H), 0.96 (d, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 168.1, 137.7, 133.6, 129.2, 129.1, 129.0, 128.8, 124.5, 84.4, 51.6, 47.4, 43.9, 42.9, 39.4, 25.0, 15.4. **HRMS-EI**$^+$ (*m/z*): calc for $C_{22}H_{21}BrClNO_3$, 461.0393, found 461.0398.

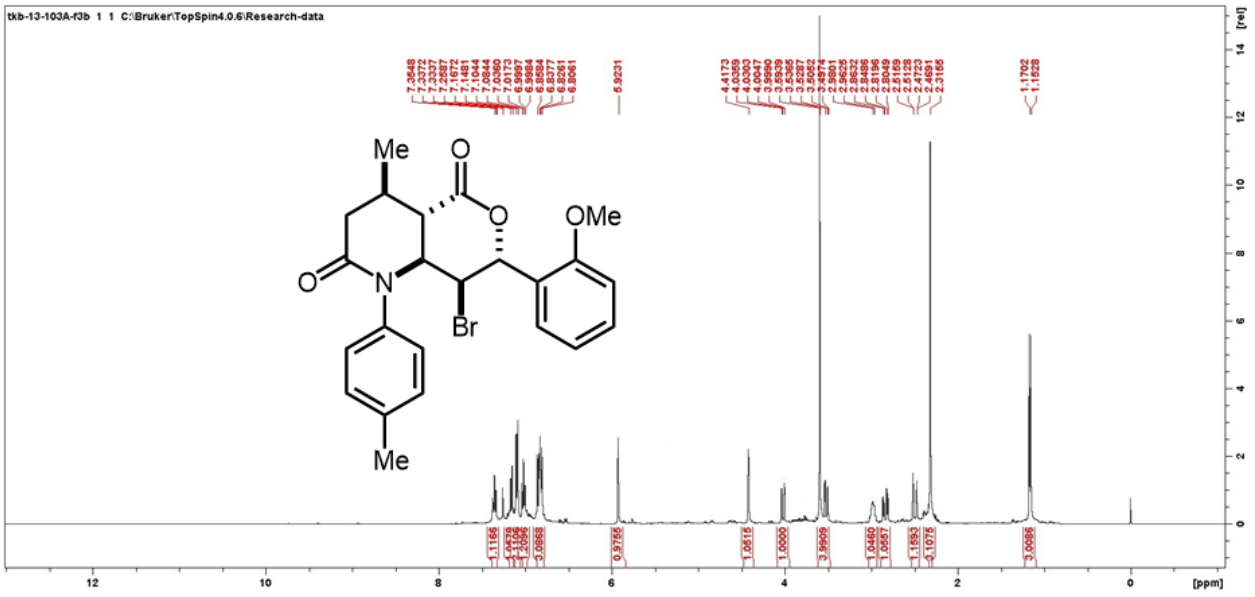






Compound 5f

Prepared in 0.50 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 204 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.33 (m, 1H), 7.26 – 7.08 (m, 4H), 6.86 – 6.81 (m, 3H), 5.92 (d, *J* = 1.0 Hz, 1H), 4.41 (t, *J* = 2.6 Hz, 1H), 4.02 (dd, *J* = 12.5, 2.4 Hz, 1H), 3.59 (s, 3H), 3.52 (dd, *J* = 12.5, 3.2 Hz, 1H), 3.04 – 2.91 (m, 1H), 2.83 (dd, *J* = 17.5, 5.9 Hz, 1H), 2.49 (dd, *J* = 17.5, 1.7 Hz, 1H), 2.32 (s, 3H), 1.16 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 168.7, 155.1, 137.7, 135.1, 130.4, 129.8, 127.3, 126.1, 126.0, 121.1, 111.0, 82.4, 55.2, 52.0, 51.2, 43.7, 39.8, 25.3, 21.1, 15.6. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{24}BrNO_4$, 457.0889, found 457.0883.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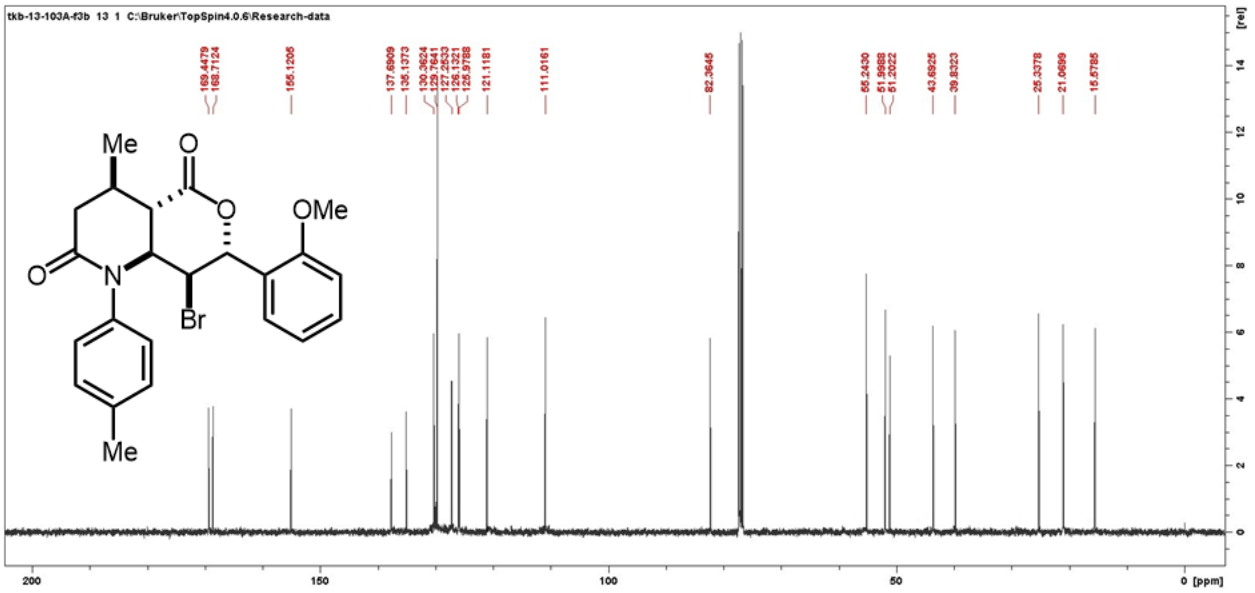
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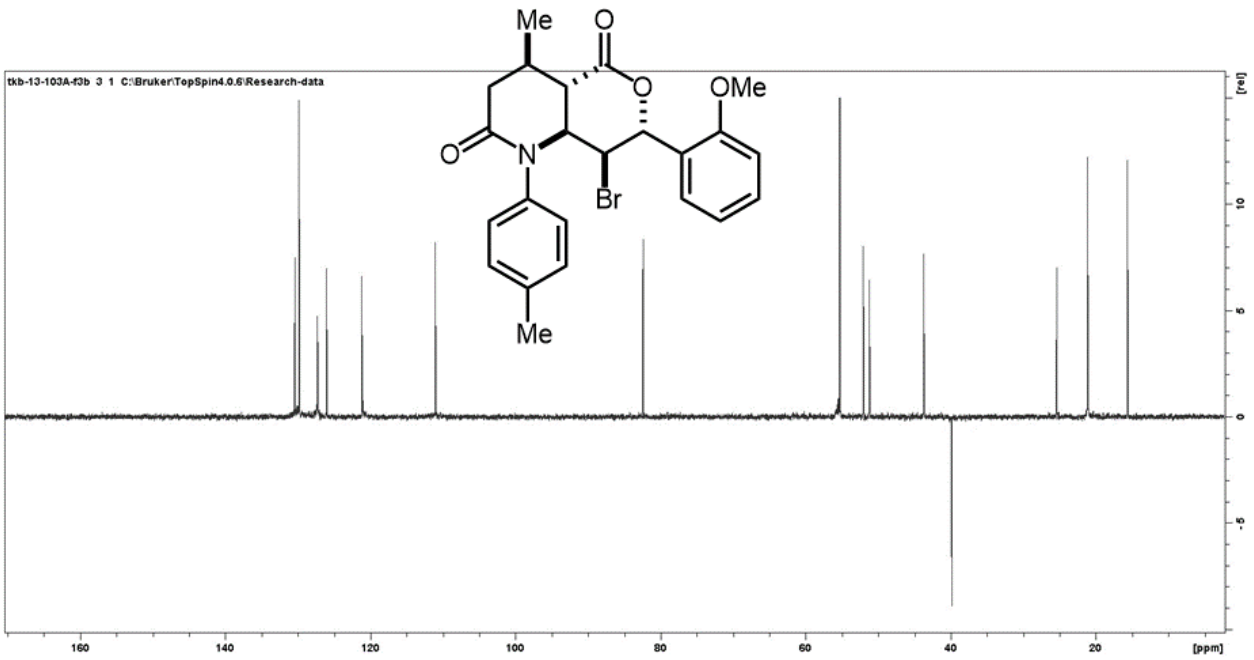
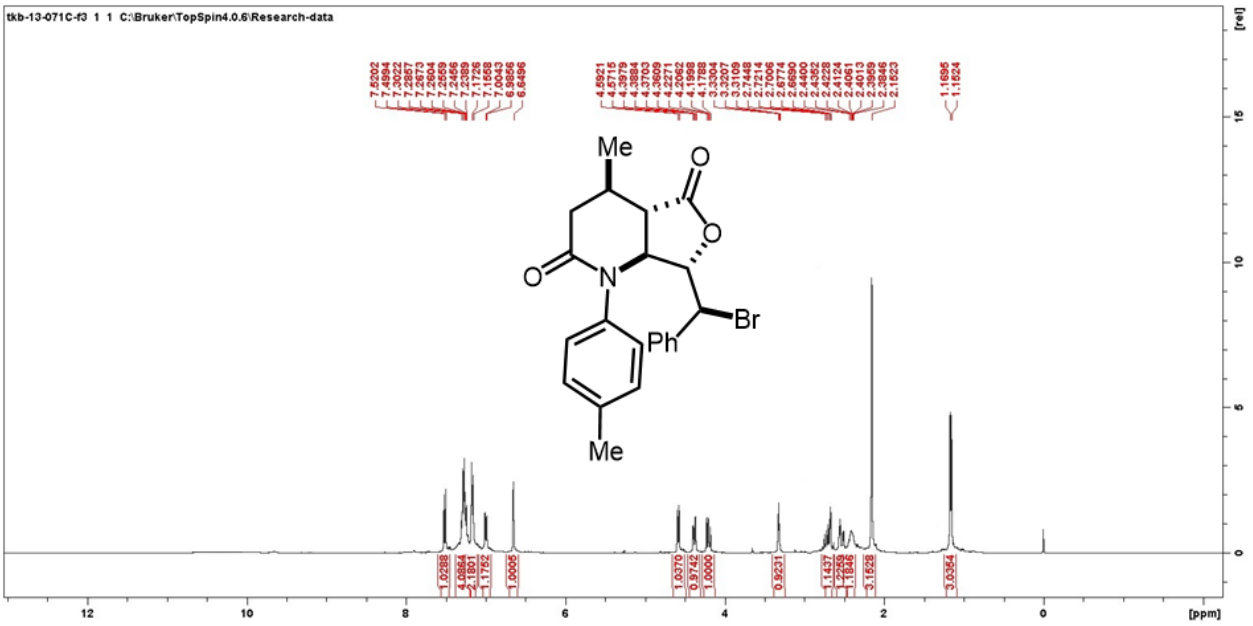


Compound 6a

Prepared in 0.50 mmol scale using **General Procedure D.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 173.5 mg, 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.3 Hz, 1H), 7.38 – 7.19 (m, 4H), 7.22 – 7.10 (m, 2H), 7.00 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.65 (s, 1H), 4.58 (d, *J* = 8.3 Hz, 1H), 4.38 (dd, *J* = 11.1, 3.8 Hz, 1H), 4.19 (dd, *J* = 11.1, 8.3 Hz, 1H), 3.33 (t, *J* = 4.1 Hz, 1H), 2.77 – 2.66 (m, 1H), 2.54 (dd, *J* = 17.5, 5.0 Hz, 1H), 2.49 – 2.36 (m, 1H), 2.16 (s, 3H), 1.16 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.4, 168.9, 163.4, 142.9, 136.0, 135.8, 131.9, 129.8, 128.8, 127.5, 127.4, 125.4, 61.6, 59.2, 56.3, 47.0, 38.0, 36.9, 31.8, 26.5, 20.9, 17.3. **HRMS-EI^{+}** (*m/z*): calc for $C_{22}H_{22}BrNO_3$, 427.0783, found 427.0788.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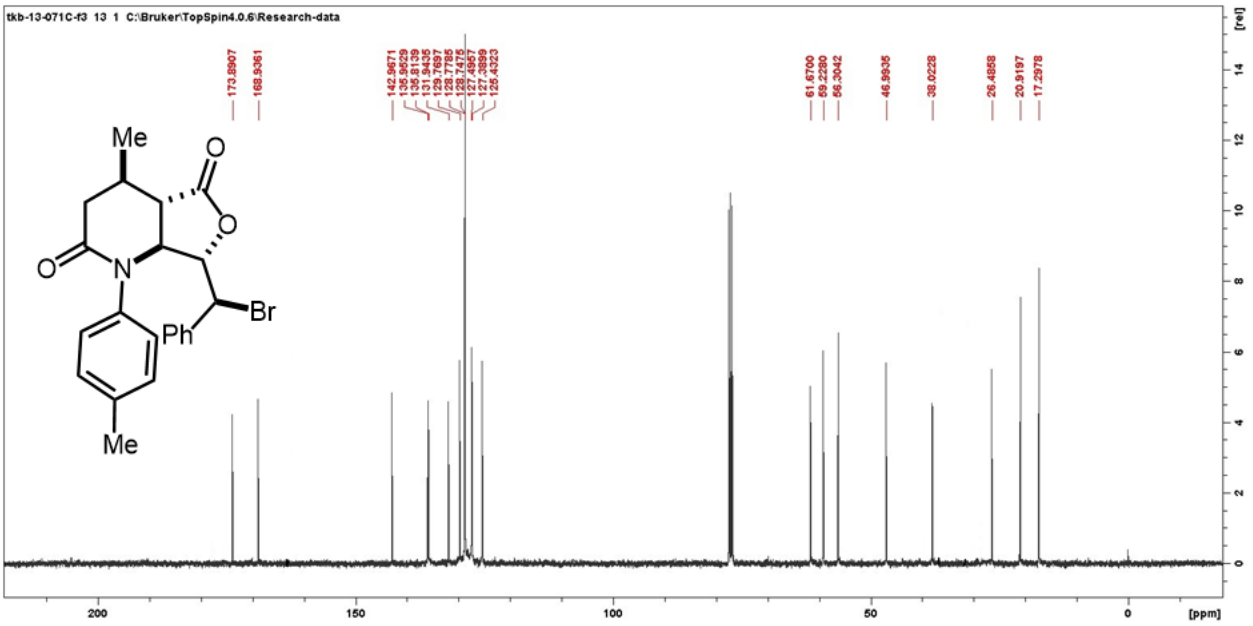
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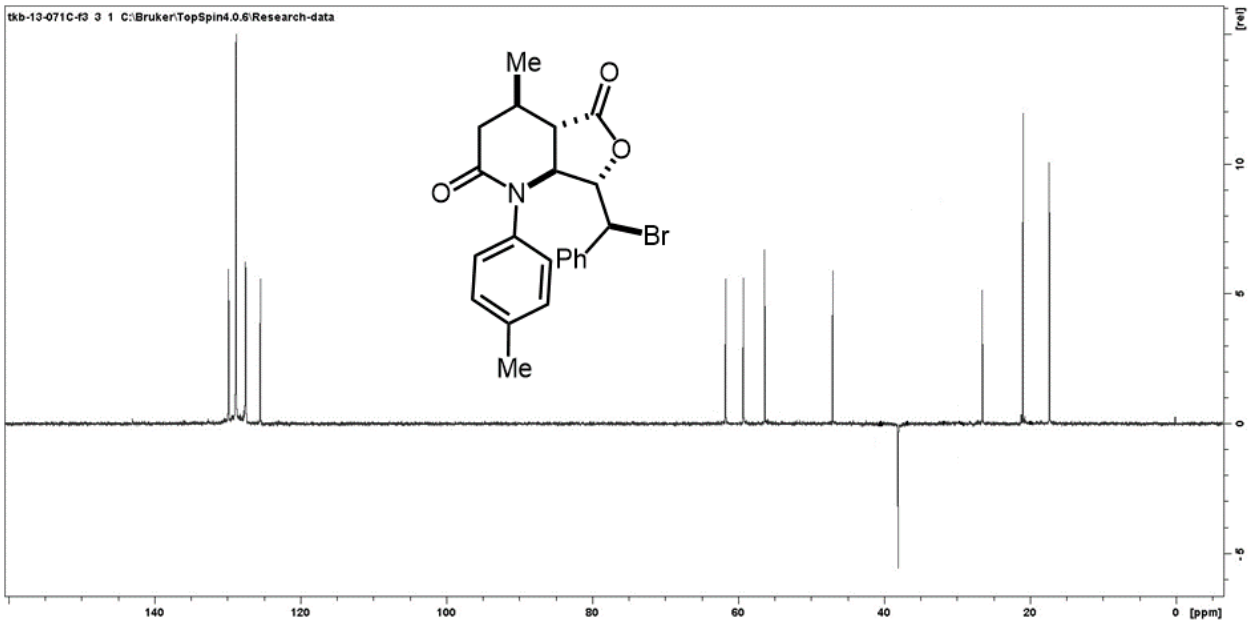
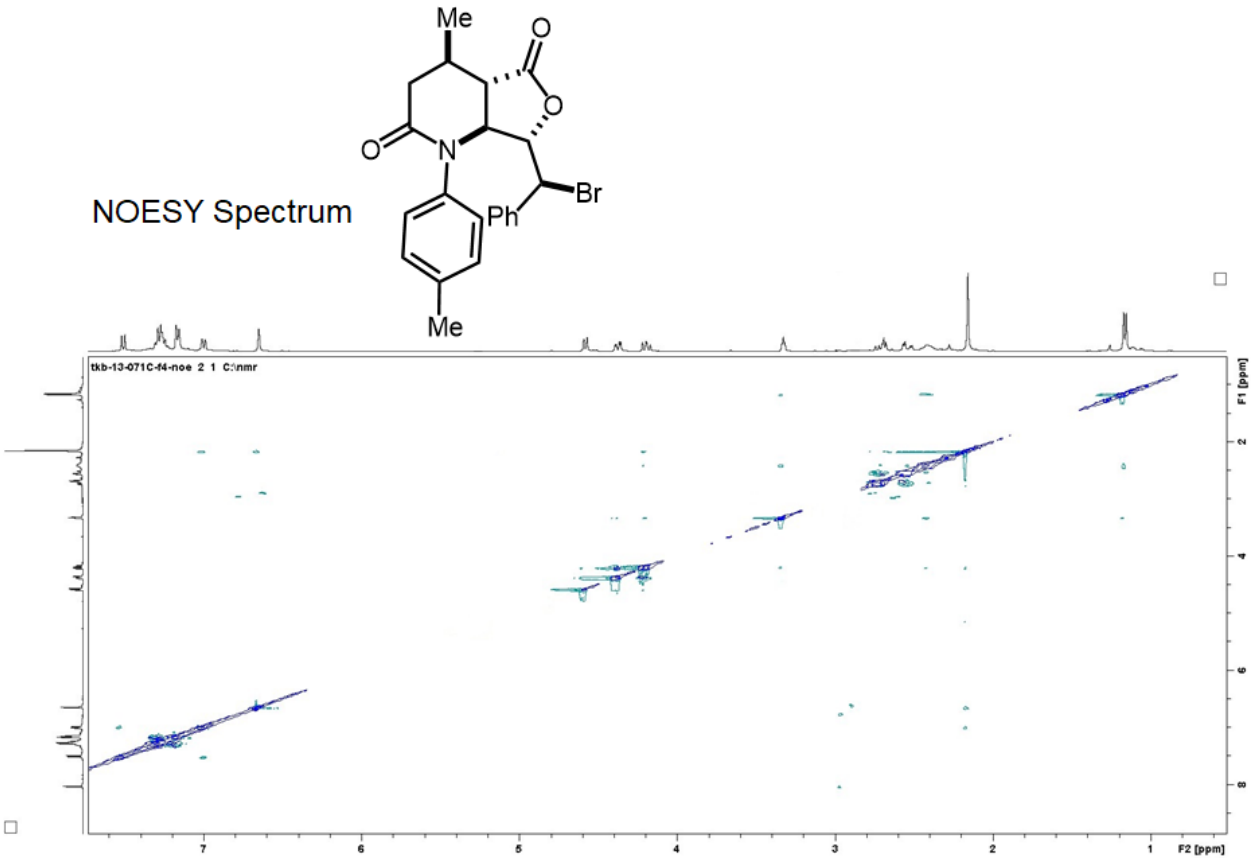


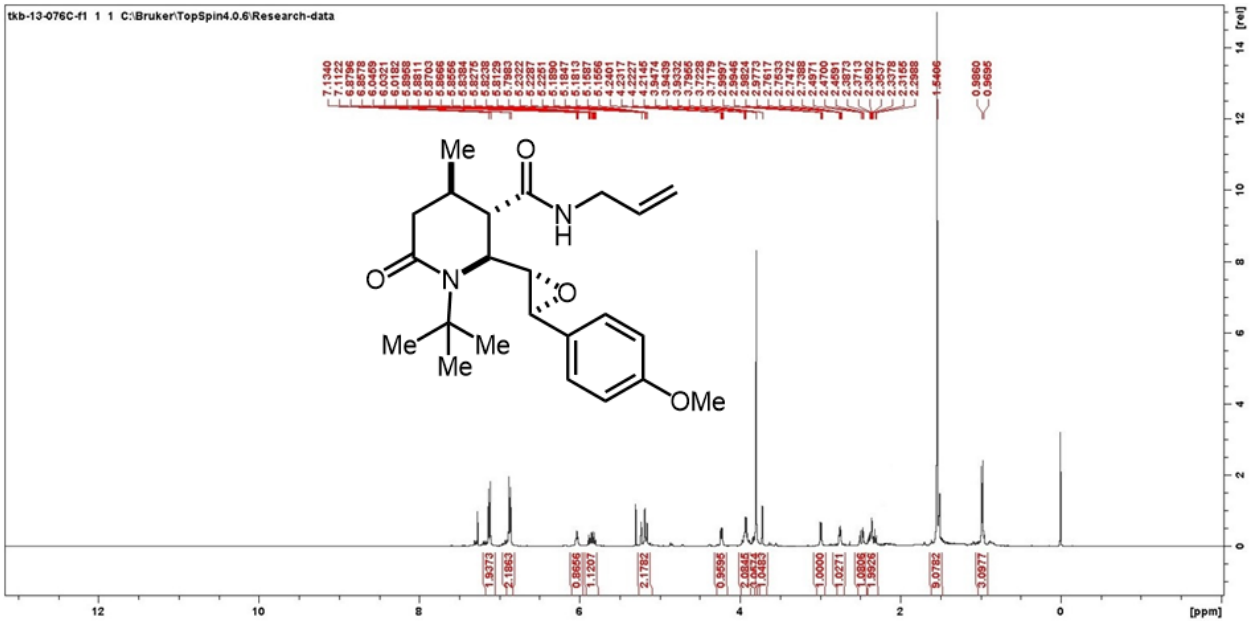
NOESY Spectrum

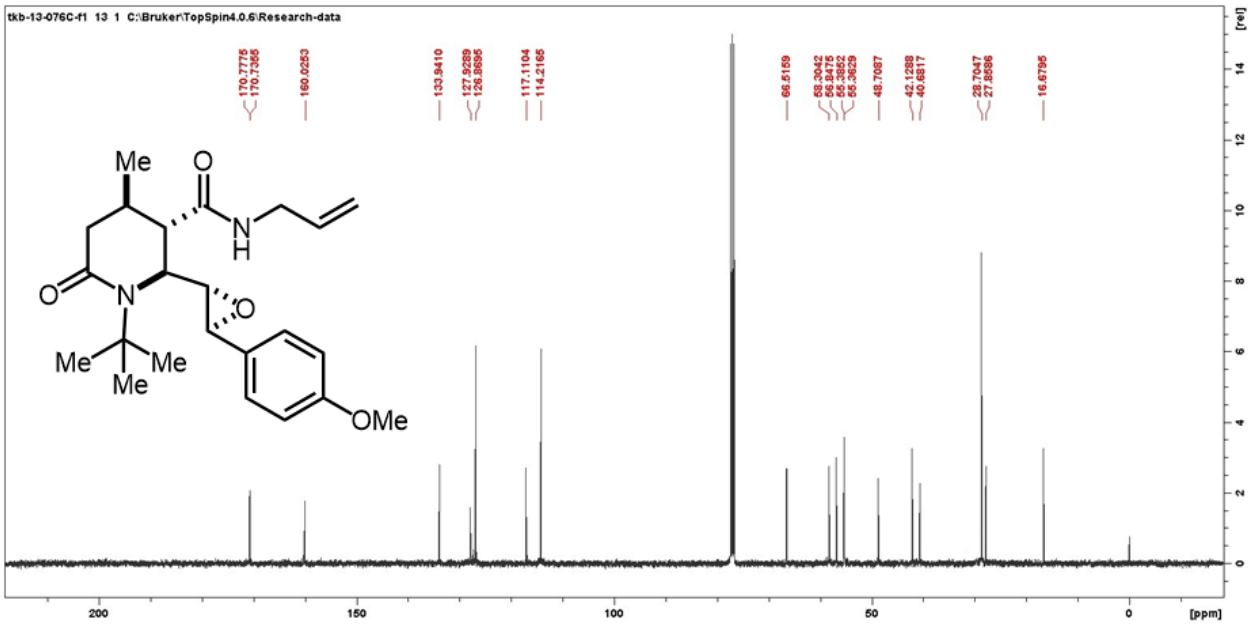


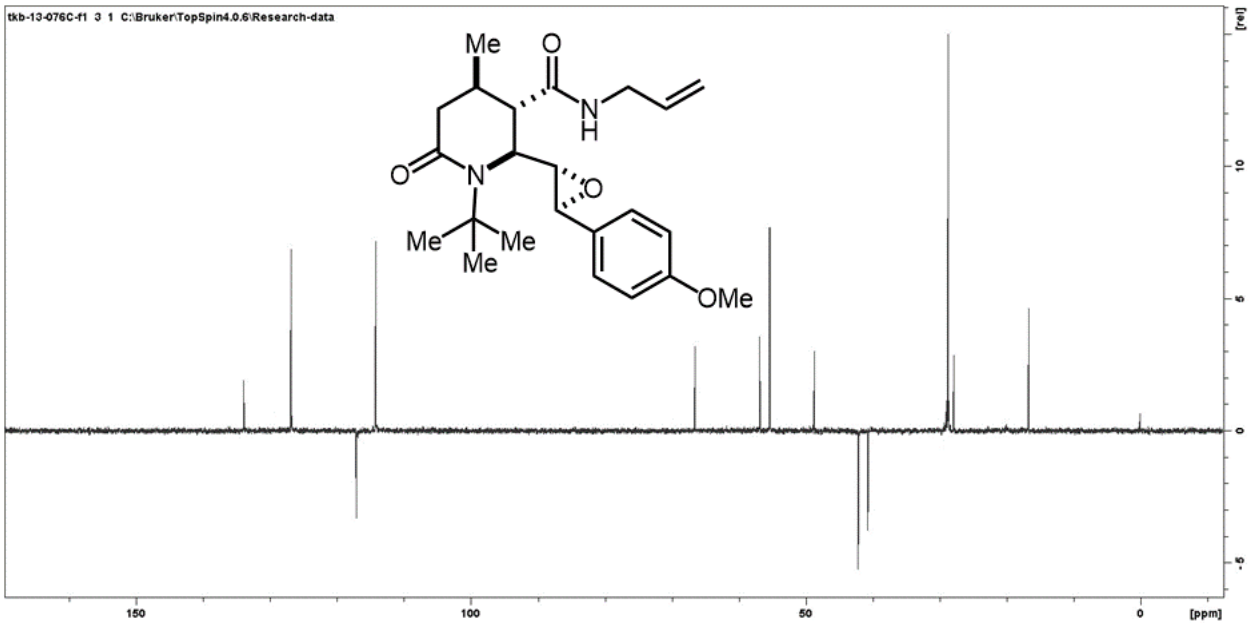
Scheme 4 Results

Compound 7a

Prepared in 0.50 mmol scale using **General Procedure E**, using allylamine (1 mmol, 2 equiv) as the nucleophile. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 164 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 7.7 Hz, 2H), 6.87 (d, *J* = 7.7 Hz, 2H), 6.00 (dd, *J* = 5.7, 3.0 Hz, 1H), 5.90 – 5.80 (m, 1H), 5.26 – 5.12 (m, 2H), 4.22 (dd, *J* = 7.0, 3.3 Hz, 1H), 4.02 – 3.84 (m, 2H), 3.80 (s, 3H), 3.72 (d, *J* = 2.1 Hz, 1H), 3.00 (dd, *J* = 7.0, 2.1 Hz, 1H), 2.75 (dd, *J* = 5.9, 3.3 Hz, 1H), 2.56 – 2.44 (m, 1H), 2.44 – 2.28 (m, 2H), 1.55 (s, 9H), 0.97 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 160.0, 133.9, 127.9, 126.9, 117.2, 114.2, 66.5, 58.3, 56.9, 55.4, 55.3, 48.8, 42.1, 40.7, 28.7, 27.9, 16.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{32}N_2O_4$, 400.2362, found 400.2369. FTIR (KBr): 3384.3, 3009.7, 2933.6, 1647.7, 1607.2, 1577.1, 1512.0, 1454.2, 1427.6, 1359.8, 1299.2, 1250.9, 1176.0, 1151.5, 1119.6, 1031.3, 990.3, 927.8, 825.4, 765.0, 749.7.



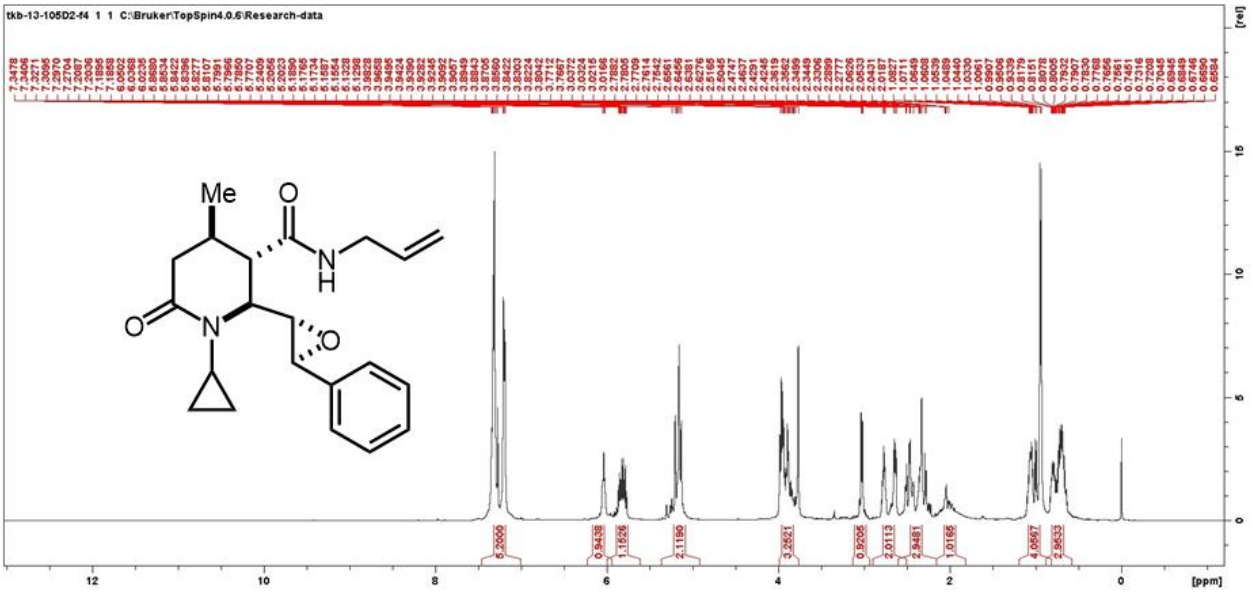


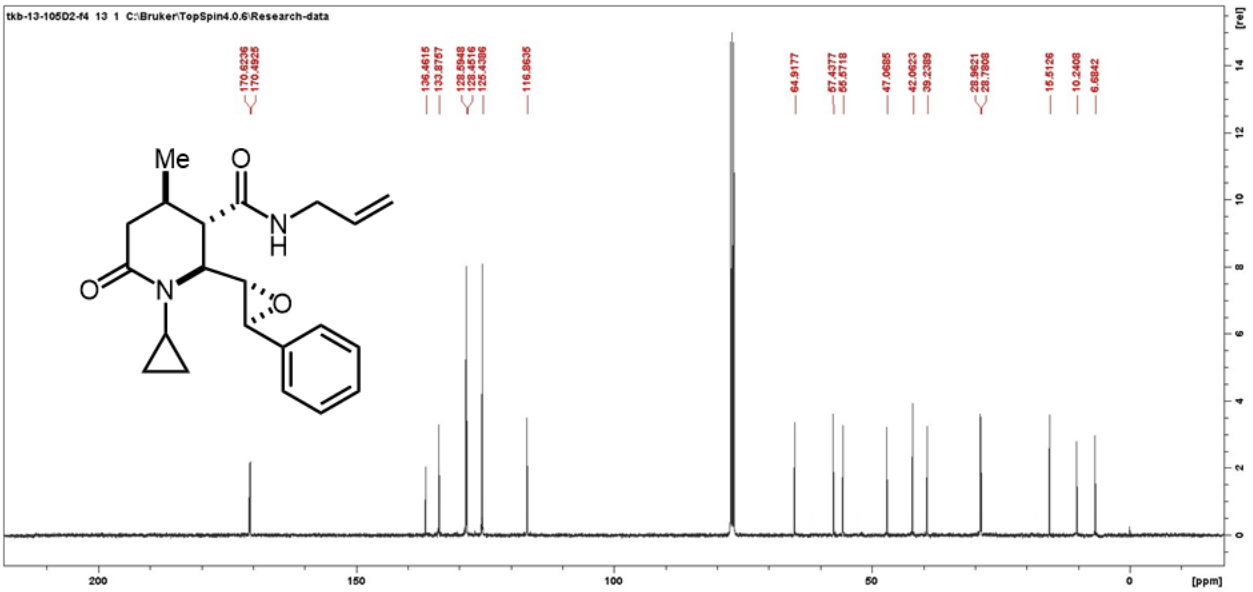


Compound 7b

Prepared in 0.50 mmol scale using **General Procedure E**, using allylamine (1 mmol, 2 equiv) as the nucleophile. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 140 mg, 79%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.18 (m, 5H), 6.04 (t, *J* = 5.8 Hz, 1H), 5.82 (ddt, *J* = 16.2, 10.9, 5.8 Hz, 1H), 5.33 – 5.09 (m, 2H), 3.98 – 3.89 (m, 3H), 3.04 (td, *J* = 7.2, 6.3, 2.1 Hz, 1H), 2.77 (tt, *J* = 7.2, 4.1 Hz, 1H), 2.71 – 2.61 (m, 1H), 2.49 (dd, *J* = 16.6, 4.7 Hz, 1H), 2.47 – 2.33 (m, 1H), 2.37 – 2.18 (m, 1H), 1.03 – 0.93 (m, 4H), 0.81 – 0.65 (m,

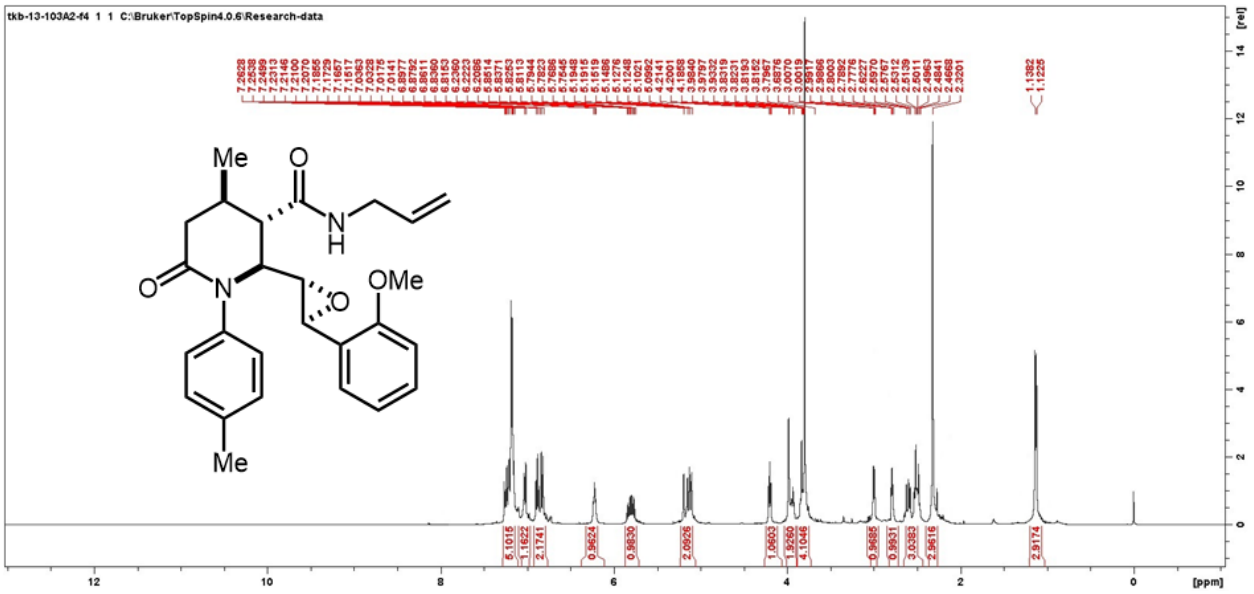
3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 170.5, 136.5, 133.9, 128.7, 128.6, 128.5, 125.4, 116.9, 64.9, 57.4, 55.6, 47.1, 42.1, 39.2, 29.0, 28.8, 15.5, 10.2, 6.7. **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{26}N_2O_3$, 354.1943, found 354.1948. FTIR (KBr): 3389.6, 2934.2, 1721.2, 1652.1, 1607.1, 1511.3, 1448.8, 1414.9, 1341.3, 1298.4, 1245.2, 1180.2, 1139.4, 1075.9, 1032.9, 999.4, 926.6, 832.0, 734.9, 702.6.





Compound 7c

Prepared in 0.50 mmol scale using **General Procedure E**, using allylamine (1 mmol, 2 equiv) as the nucleophile. Purification: Flash chromatography on silica eluting with hexane/EtOAc (20:80). Oily substance. Yield = 189 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.15 (m, 5H), 7.03 (dd, *J* = 7.5, 1.8 Hz, 1H), 6.90 – 6.82 (m, 2H), 6.22 (t, *J* = 5.7 Hz, 1H), 5.80 (ddt, *J* = 17.2, 10.2, 5.7 Hz, 1H), 5.17 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.11 (dt, *J* = 10.3, 1.5 Hz, 1H), 4.20 (t, *J* = 5.7 Hz, 1H), 3.98 – 3.93 (m, 2H), 3.83 – 3.69 (m, 4H), 3.00 – 2.96 (m, 1H), 2.80 – 2.78 (m, 1H), 2.67 – 2.56 (m, 3H), 2.32 (s, 3H), 1.13 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 169.7, 157.7, 139.2, 137.0, 134.2, 129.8, 129.1, 127.7, 125.6, 124.7, 120.7, 116.6, 110.1, 63.9, 62.0, 55.4, 51.6, 46.9, 42.0, 38.5, 28.6, 21.1, 17.0. **HRMS-EI^{+}** (*m/z*): calc for $C_{26}H_{30}N_2O_4$, 434.2206, found 434.2210. FTIR (KBr): 3384.5, 2972.9, 2932.8, 1638.2, 1449.1, 1364.7, 1290.2, 1270.3, 1247.8, 1206.5, 1179.9, 1131.1, 1071.4, 994.4, 924.8, 881.7, 797.4, 700.0.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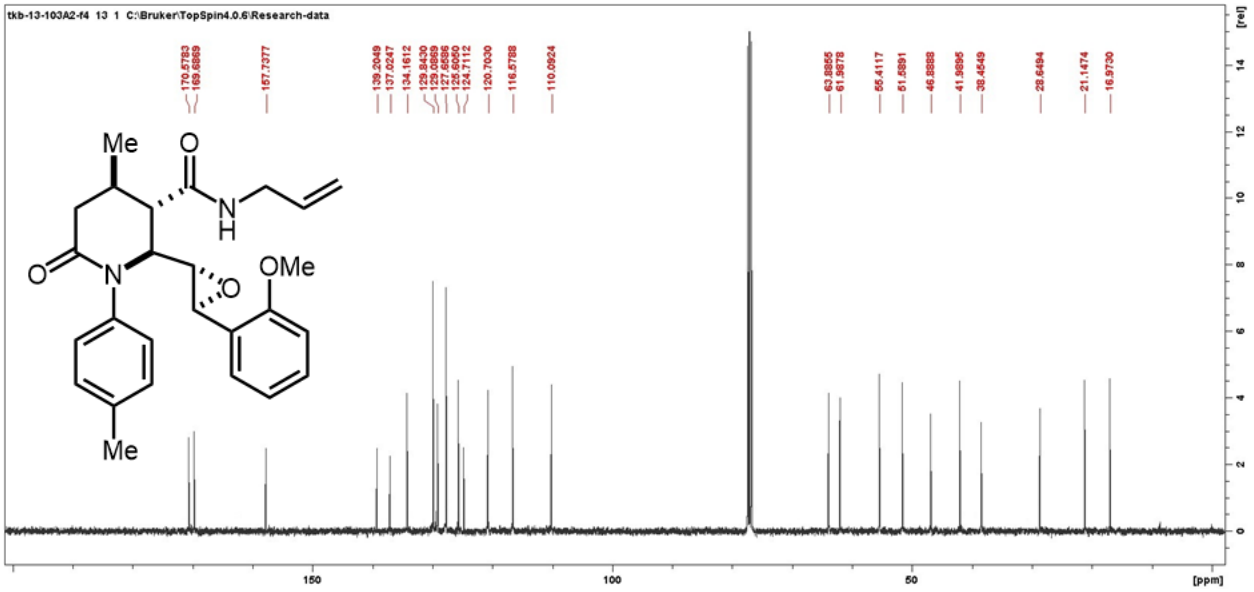
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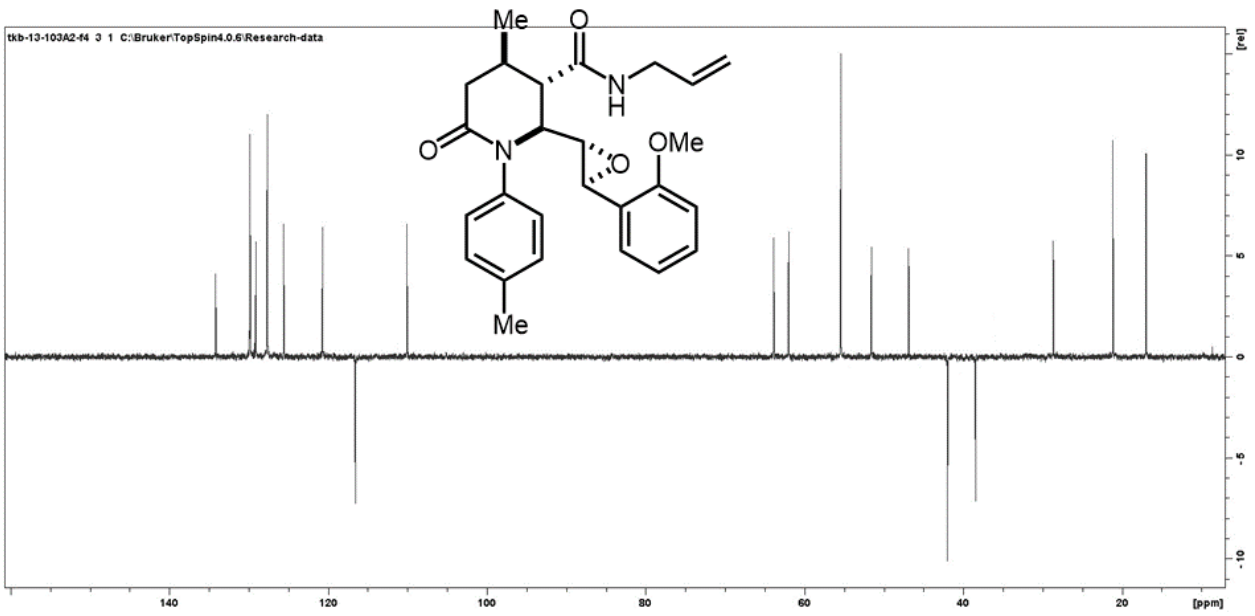
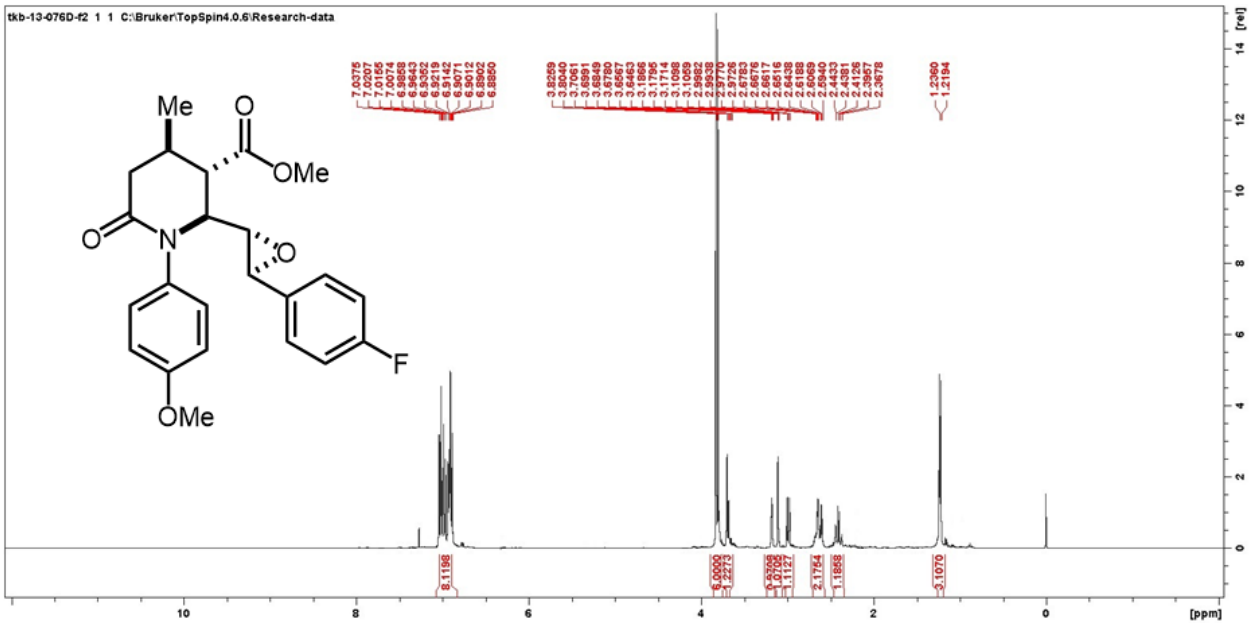


Compound 7d

Prepared in 0.50 mmol scale using **General Procedure E**, using MeOH (1 mmol, 2 equiv) as the nucleophile. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 190.2 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 – 6.89 (m, 9H), 3.82 – 3.80 (s,s, 6H), 3.71 – 3.65 (m, 1H), 3.18 (dt, *J* = 4.3, 2.0 Hz, 1H), 3.11 (d, *J* = 1.8 Hz, 1H), 3.03 – 2.95 (m, 1H), 2.73 – 2.56 (m, 2H), 2.49 – 2.34 (m, 1H), 1.22 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 169.3, 164.1, 161.6, 158.9, 134.3, 131.5, 131.4, 129.1, 127.1, 127.0, 115.5, 115.3, 114.8, 64.0, 62.2, 59.84 55.5, 52.1, 45.7, 37.5, 26.6, 18.2. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{24}FNO_5$, 413.1639, found 413.1644. FTIR (KBr): 2971.4, 2923.9, 1644.4, 1491.4, 1446.8, 1429.3, 1391.6, 1362.4, 1318.9, 1292.6, 1268.8, 1223.2, 1199.5, 1151.3, 1117.7, 993.1, 905.3, 744.2, 699.8.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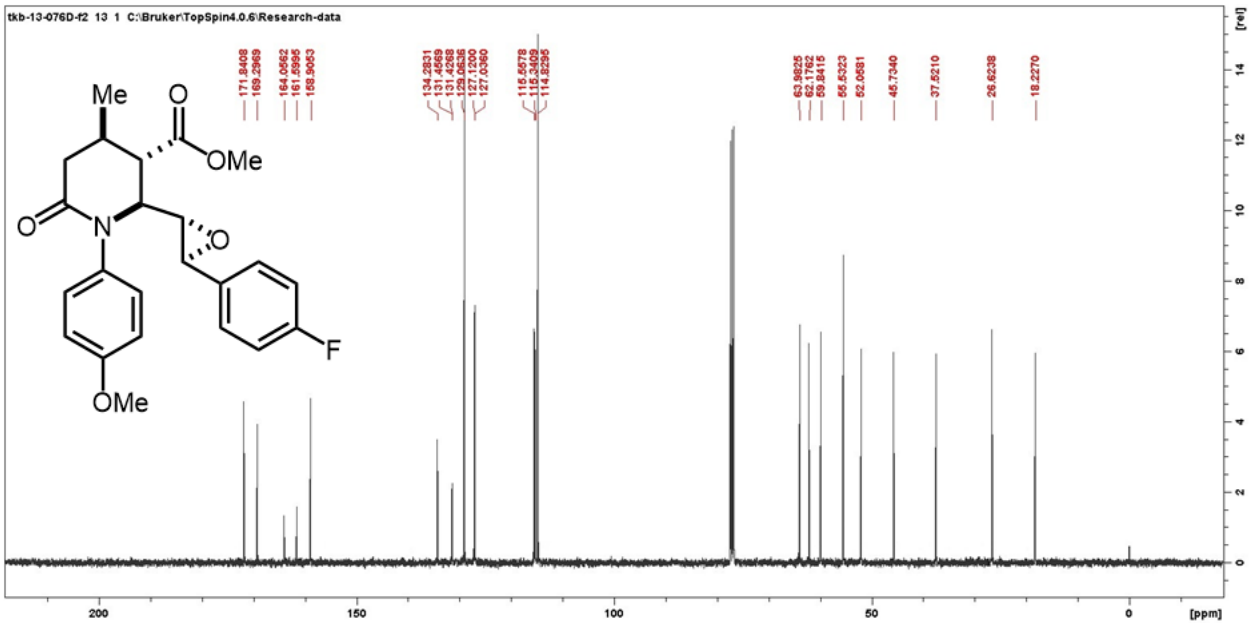
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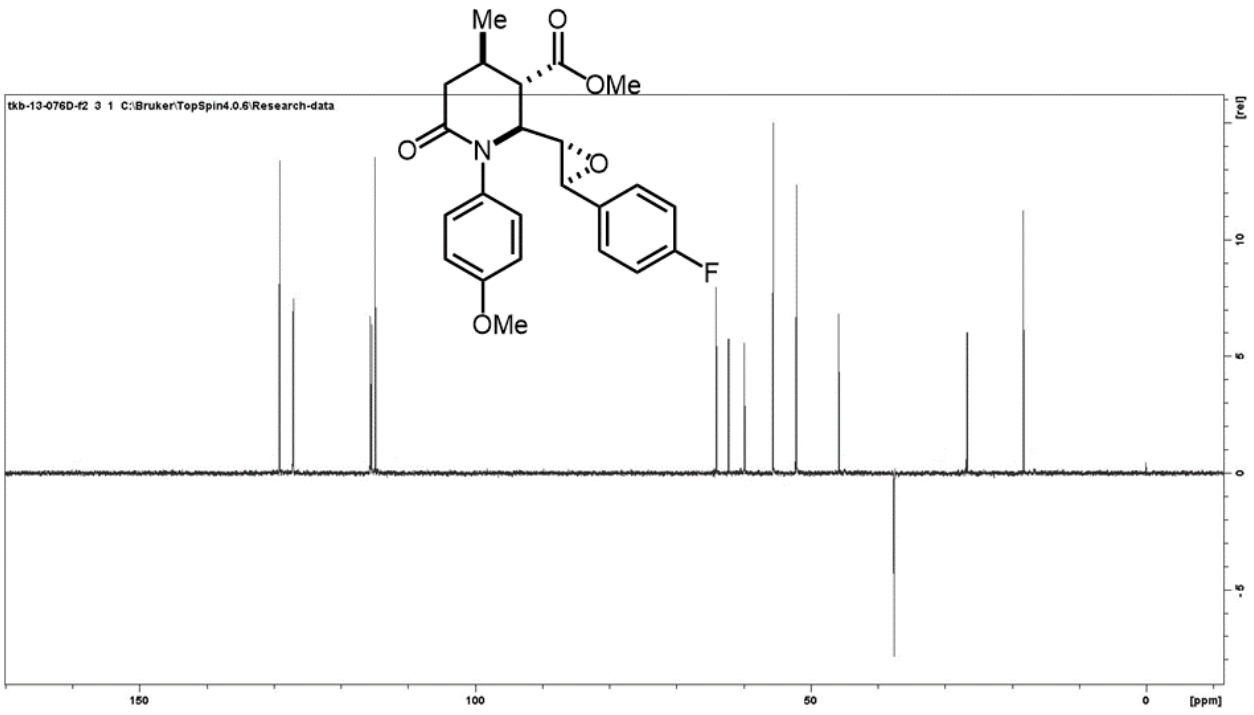
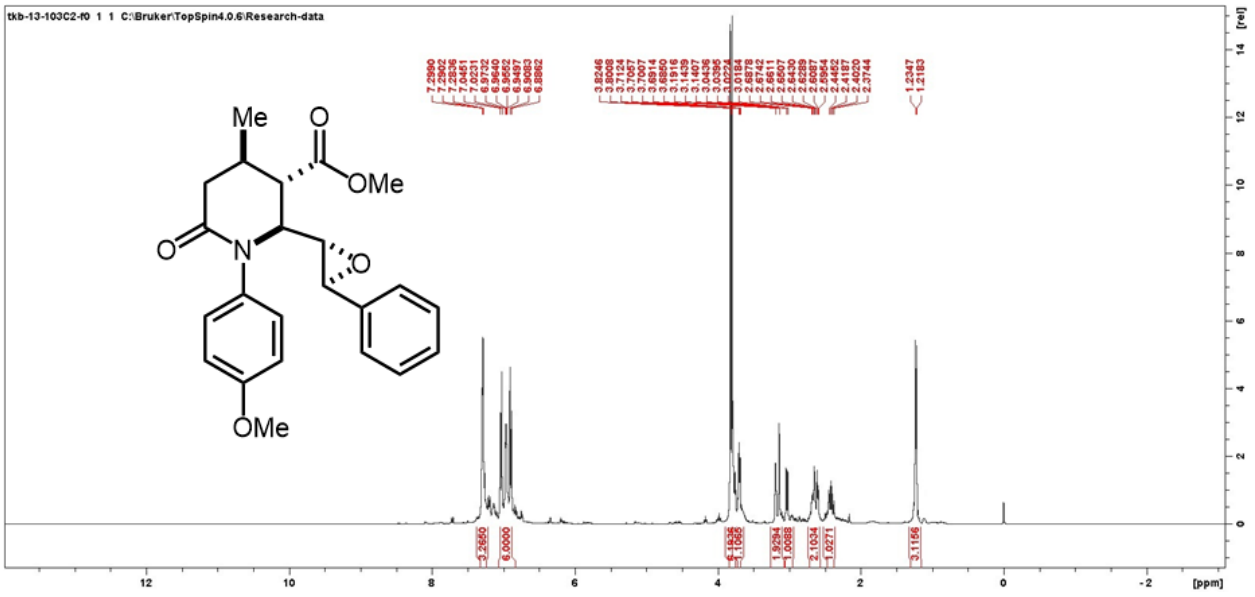


Compound 7e

Prepared in 0.50 mmol scale using **General Procedure E**, using MeOH (1 mmol, 2 equiv) as the nucleophile. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 177.8 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.28 (m, 3H), 7.04 – 6.89 (m, 6H), 3.82 – 3.69 (m, 7H), 3.22 – 3.07 (m, 2H), 3.07 – 2.92 (m, 1H), 2.75 – 2.54 (m, 2H), 2.44 – 2.37 (m, 1H), 1.23 (d, J = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 169.3, 158.9, 135.7, 134.4, 129.1, 128.5, 128.4, 125.4, 114.9, 64.1, 62.2, 60.4, 55.5, 52.0, 45.7, 37.5, 26.6, 18.3. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{25}NO_5$, 395.1733, found 395.1737.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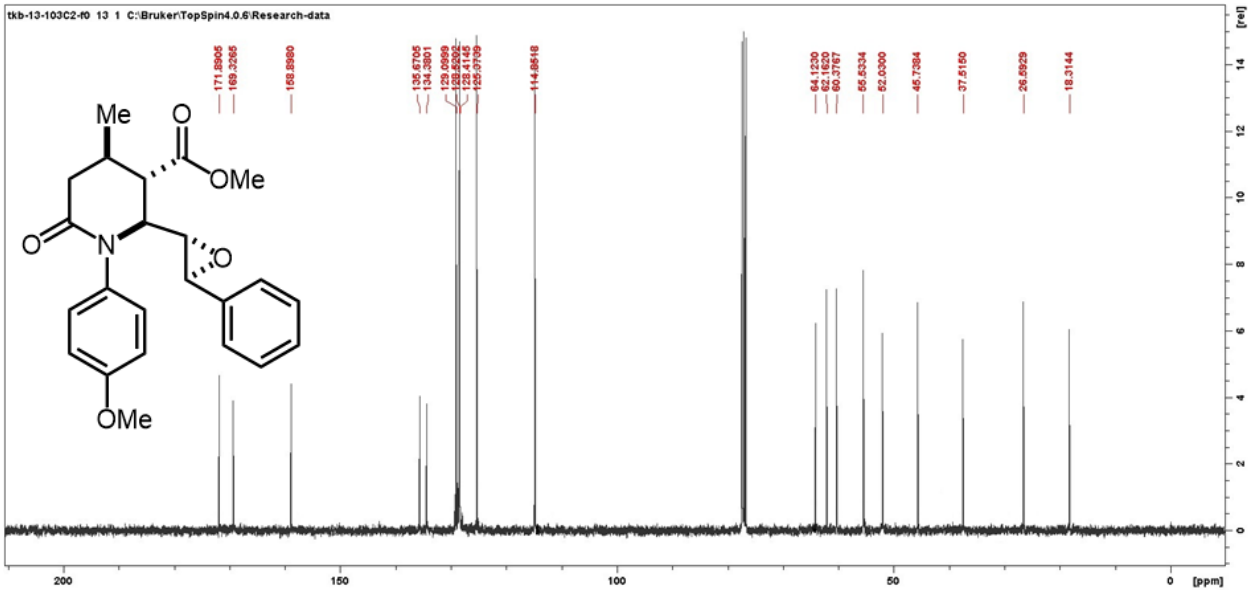
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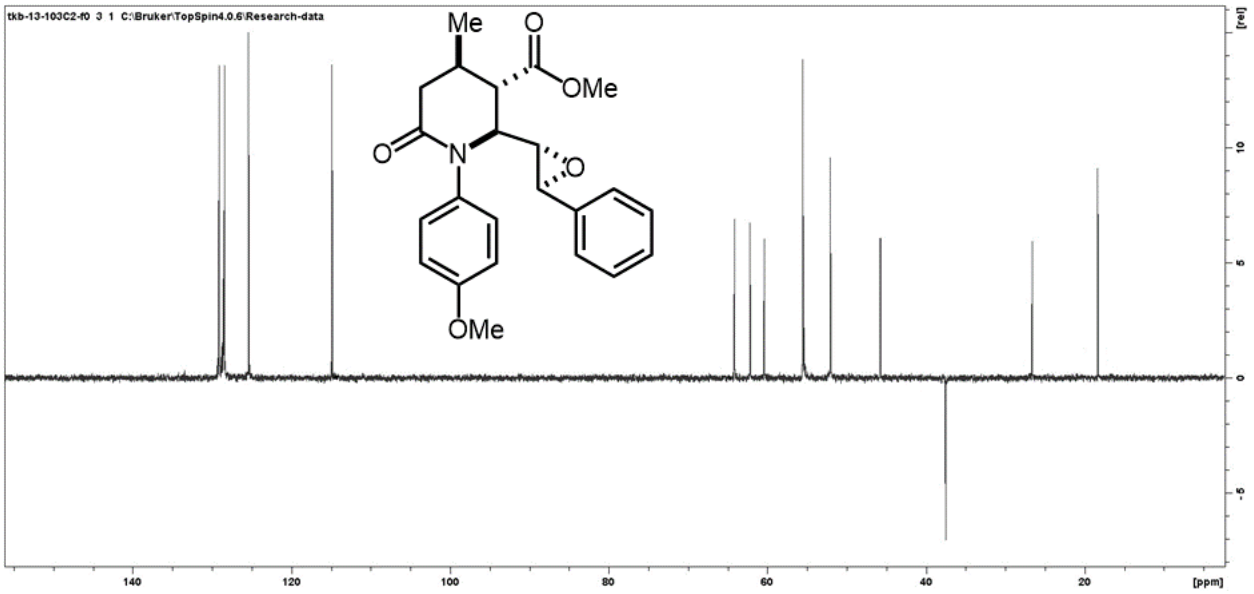
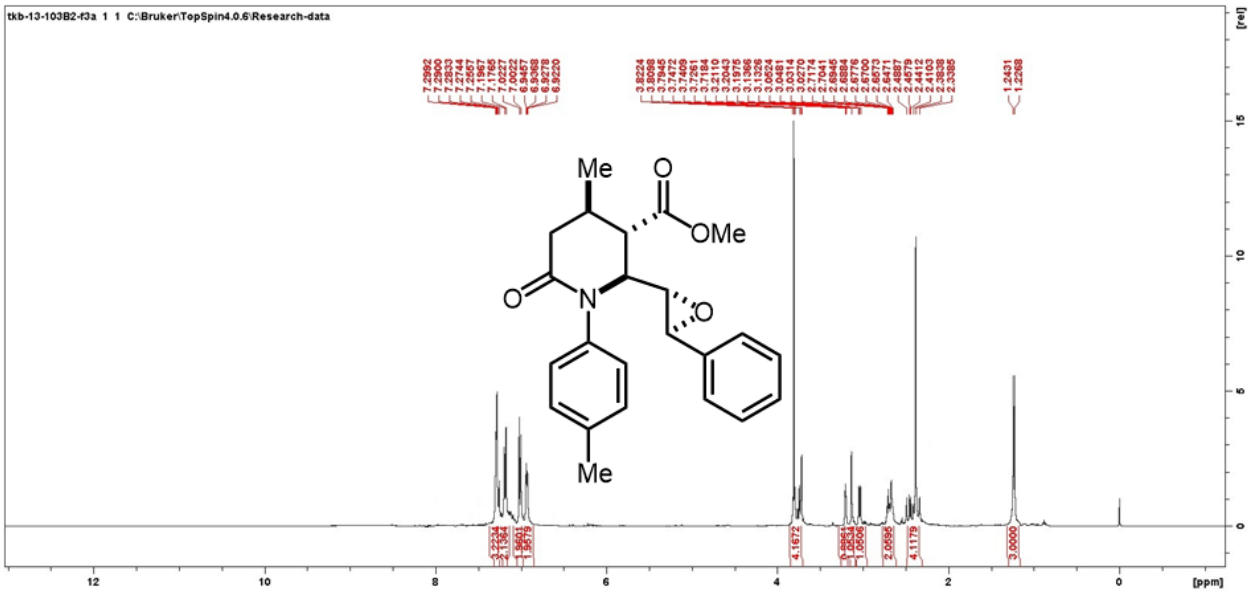


Compound 7f

Prepared in 0.50 mmol scale using **General Procedure E**, using MeOH (1 mmol, 2 equiv) as the nucleophile. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 168.9 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 3H), 7.20 – 7.17 (m, 2H), 6.94 (d, *J* = 3.4 Hz, 2H), 6.92 (d, *J* = 2.4 Hz, 1H), 3.81 (s, 3H), 3.79 – 3.71 (m, 1H), 3.24 – 3.17 (m, 1H), 3.13 (d, *J* = 1.9 Hz, 1H), 3.04 (dd, *J* = 8.5, 1.9 Hz, 1H), 2.72 – 2.65 (m, 2H), 2.49 – 2.34 (m, 1H), 1.24 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 169.8, 138.9, 137.8, 135.6, 133.3, 130.2, 130.1, 129.7, 128.5, 128.4, 128.2, 127.8, 125.3, 64.0, 62.1, 60.4, 52.1, 45.7, 37.4, 26.5, 21.1, 18.3. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{25}NO_4$, 379.1784, found 379.1789.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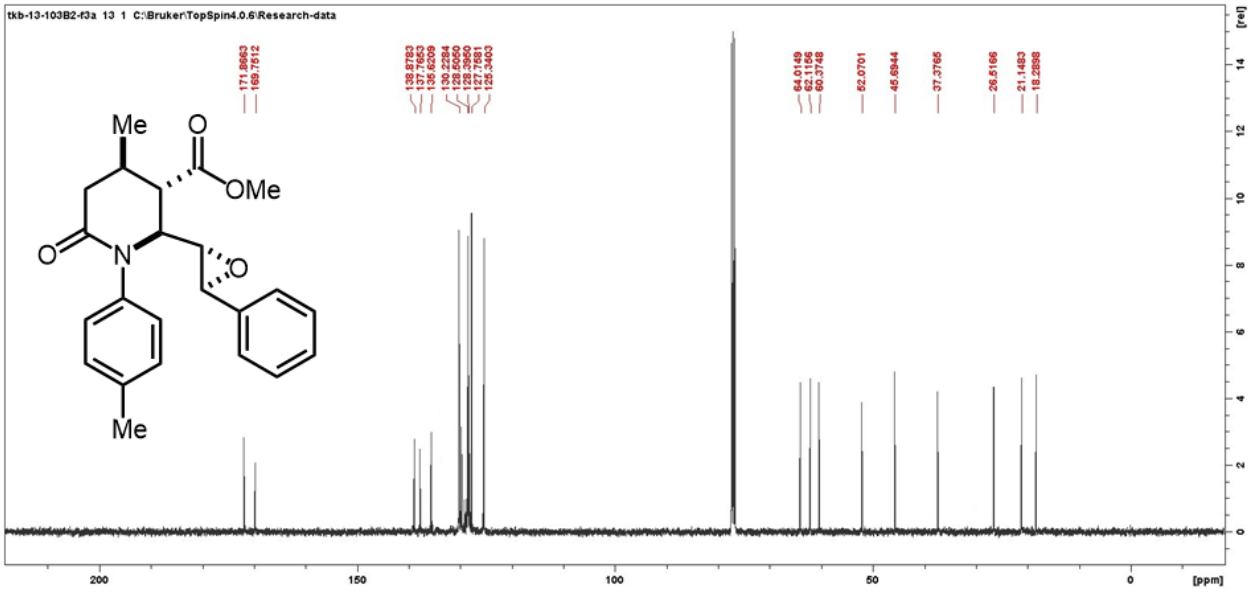
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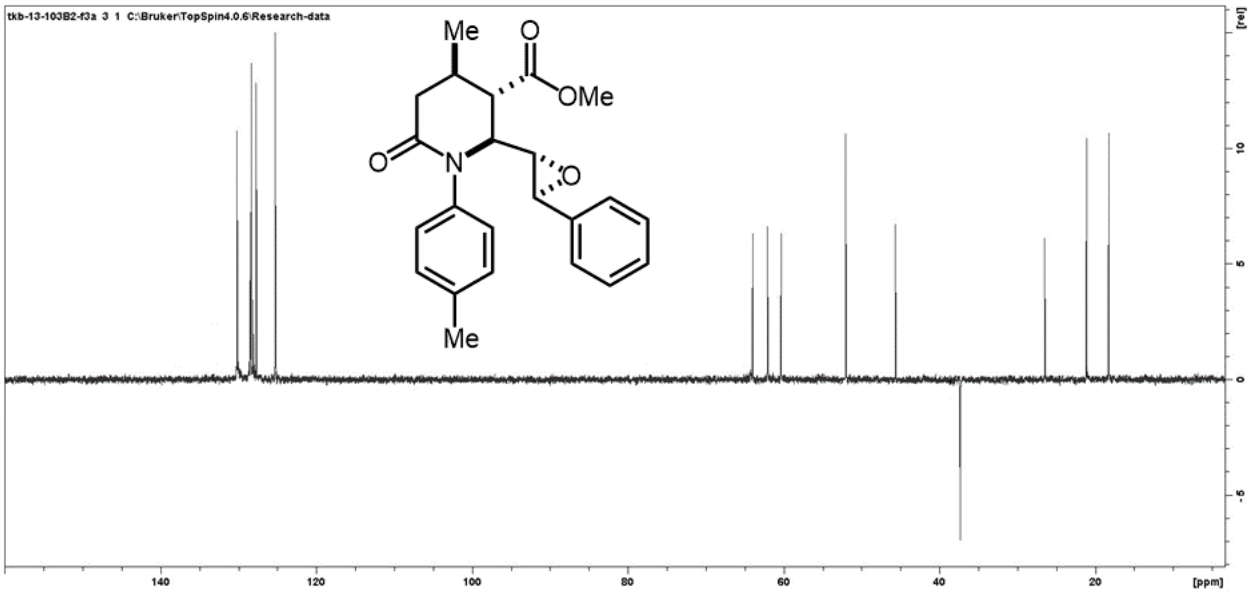
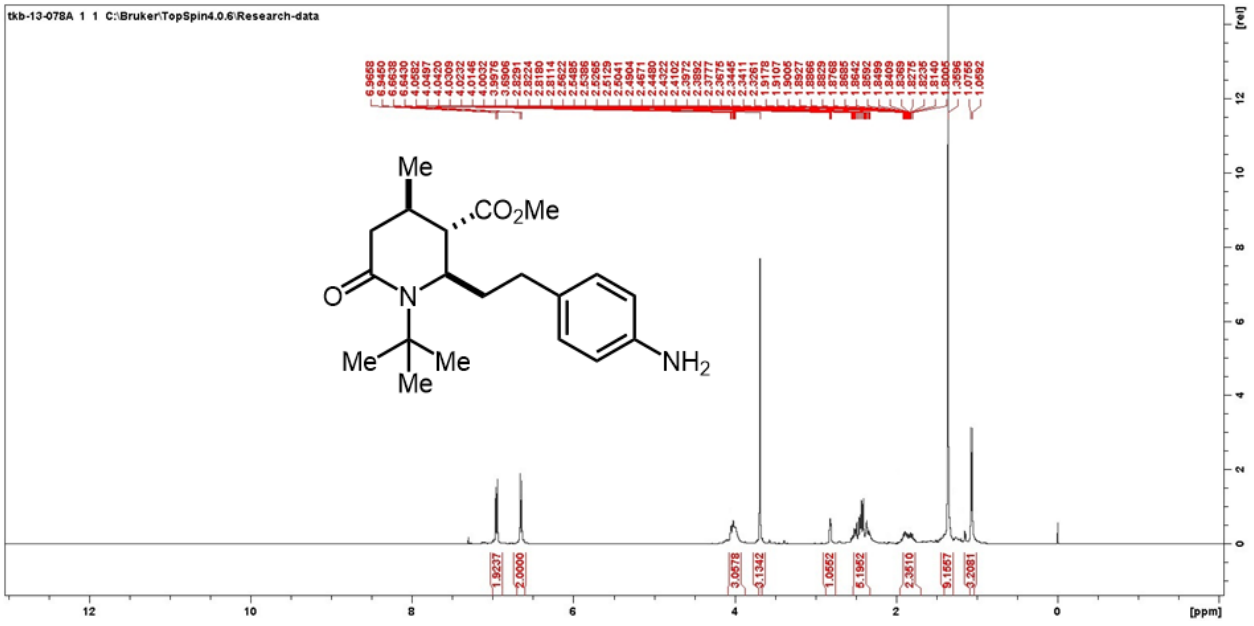
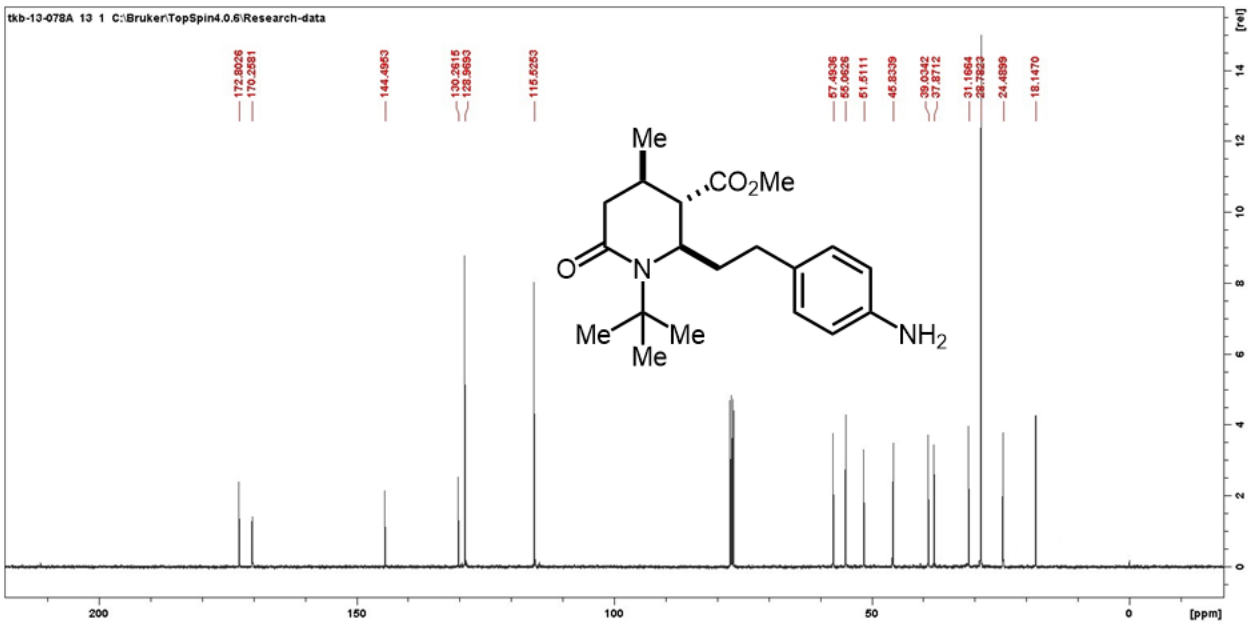


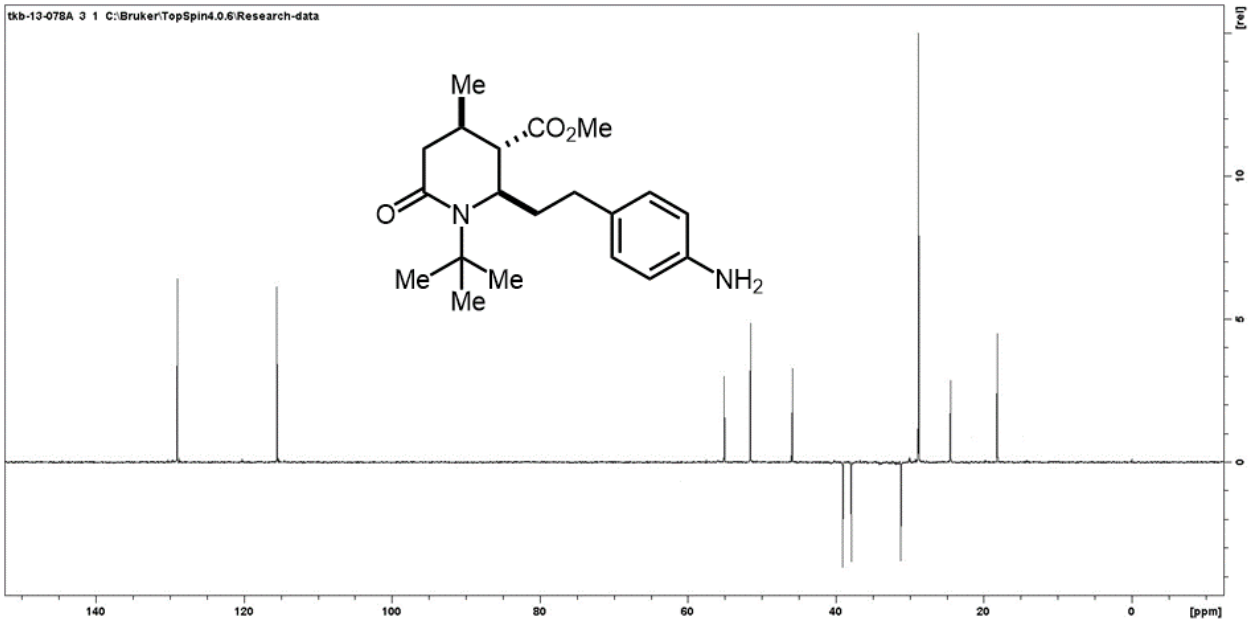
Scheme 5 Results

Compound 11a

Prepared in 0.50 mmol scale using **General Procedure F**. Yield = 168.1 mg, 97%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (d, *J* = 7.6 Hz, 2H), 6.65 (d, *J* = 7.6 Hz, 2H), 4.06 – 4.00 (m, 3H), 3.69 (s, 3H), 2.82 (dd, *J* = 4.7, 2.7 Hz, 1H), 2.56 – 2.33 (m, 5H), 1.91 – 1.80 (m, 2H), 1.36 (s, 9H), 1.07 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 170.3, 144.5, 130.3, 129.0, 115.5, 57.5, 55.1, 51.5, 45.8, 39.0, 37.9, 31.2, 28.8, 24.5, 18.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{20}H_{30}N_2O_3$, 346.2256, found 346.2260.



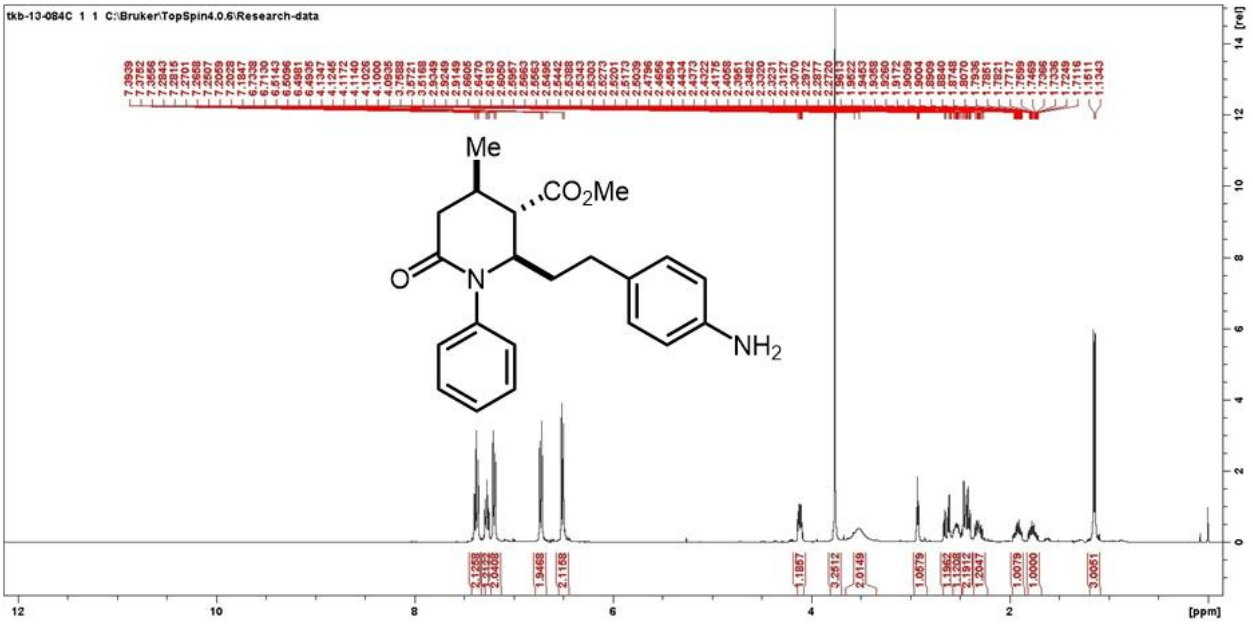


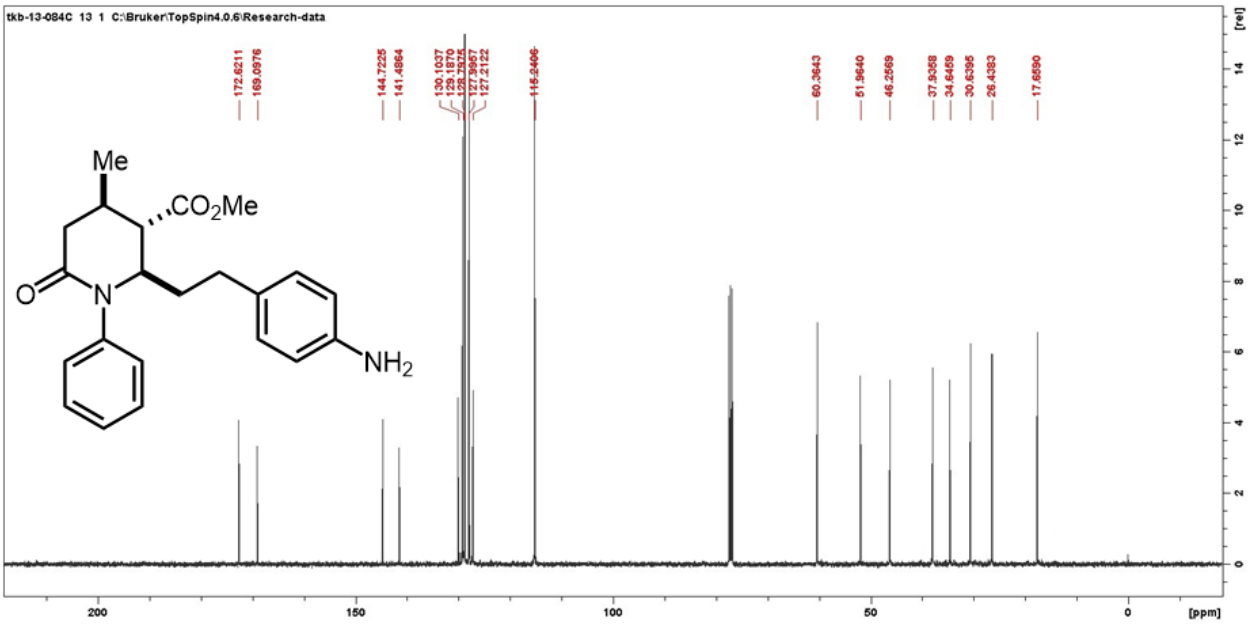


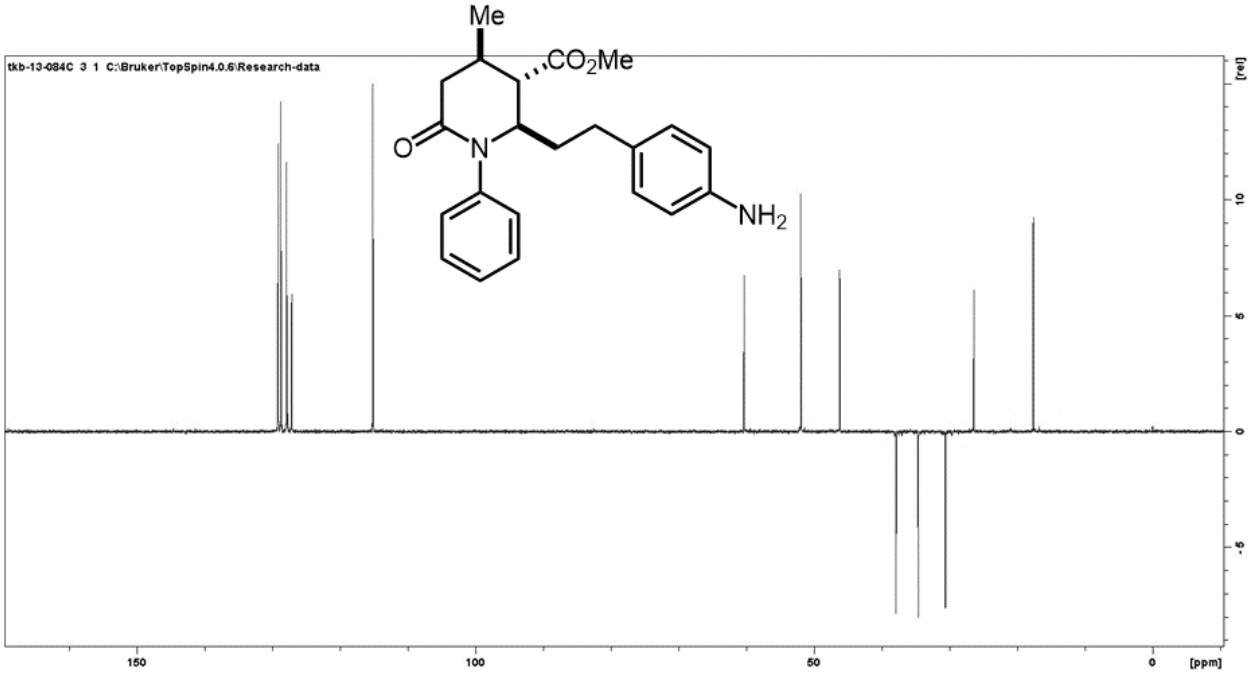
Compound 11b

Prepared in 0.50 mmol scale using **General Procedure F**. Yield = 170.1 mg, 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.35 (m, 2H), 7.28 – 7.25 (m, 1H), 7.20 – 7.18 (m, 2H), 6.73 (d, J = 7.1 Hz, 2H), 6.50 (d, J = 7.1 Hz, 2H), 4.11 (ddd, J = 8.5, 7.0, 4.3 Hz, 1H), 3.76 (s, 3H), 3.52 (br. s, 2H), 2.93 (t, J = 4.0 Hz, 1H), 2.68 – 2.37 (m, 4H), 2.31 (ddd, J = 14.0, 10.1, 6.4 Hz, 1H), 1.96 – 1.87 (m, 1H), 1.82 – 1.71 (m, 1H), 1.14 (d, J = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6,

169.1, 144.7, 141.5, 130.1, 129.2, 128.8, 128.0, 127.2, 115.2, 115.2, 60.4, 52.0, 46.3, 37.9, 34.7, 30.6, 26.4, 17.7. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{22}H_{26}N_2O_3$, 366.1943, found 366.1947.



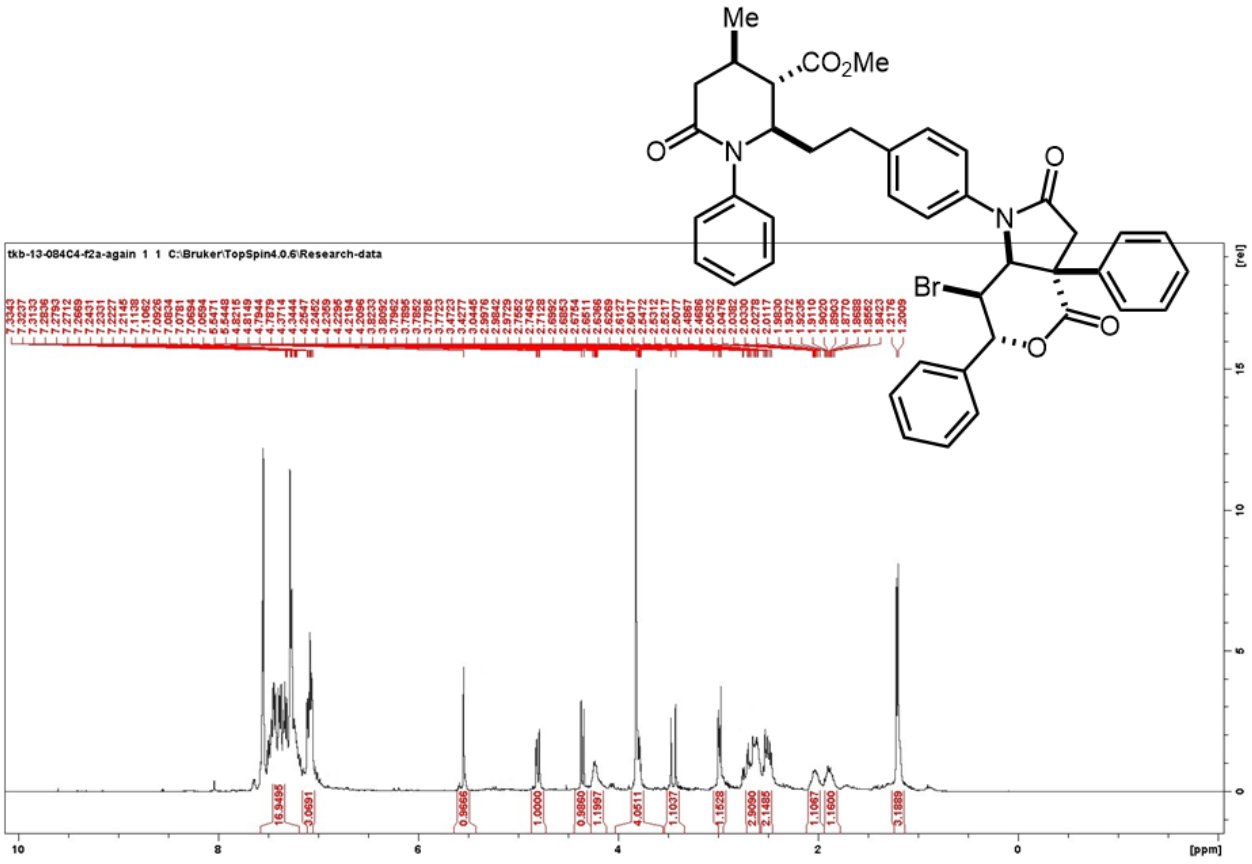


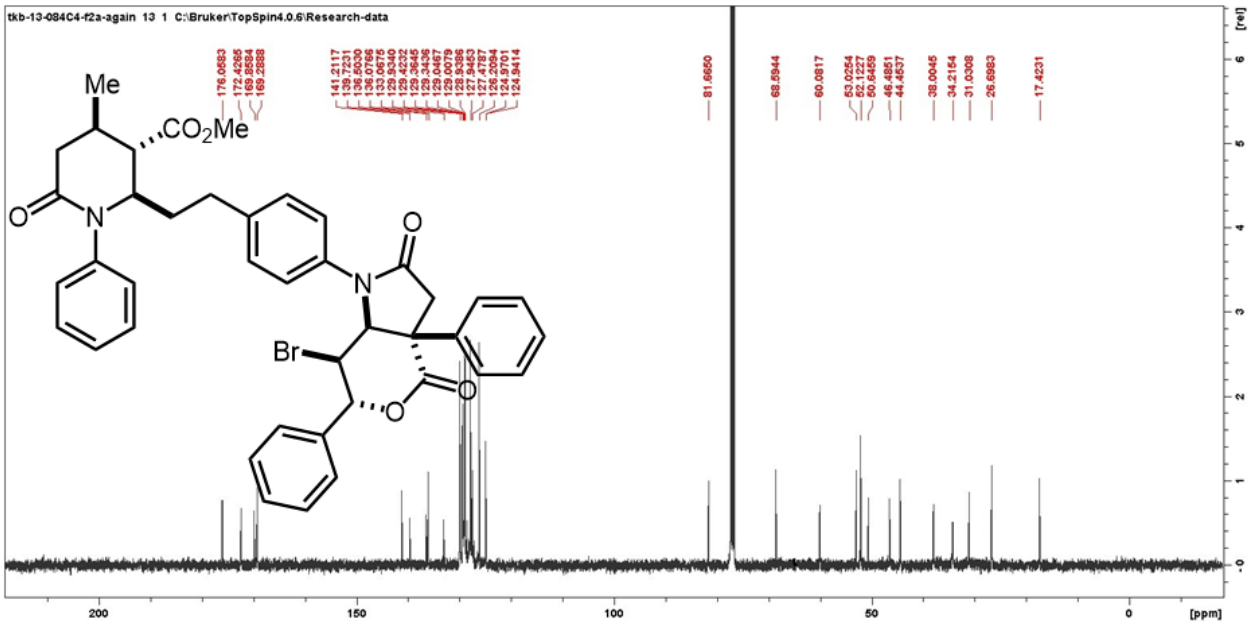


Compound 13

To a round-bottom flask equipped with a stir bar was added amine **11b** (0.5 mmol), *trans*-cinnamaldehyde (0.5 mmol, 1 equiv) benzene (2 mL), and anhydrous $MgSO_4$ (100 mg). The cloudy suspension was allowed to stir at room temperature. After complete consumption of the amine (based on TLC monitoring), the mixture was filtered and concentrated under reduced pressure to obtain the 1,3-azadiene. A 10 mL screw-cap vial was flame-dried, evacuated and flushed with nitrogen. A solution of the 1,3-azadiene in toluene (2.5 mL) was added to the vial at room temperature followed by phenylsuccinic anhydride **12** (88.1 mg, 0.5 mmol, 1 equiv). The contents were placed in a pre-heated oil bath thermostatted at 90 °C. After complete conversion (as judged by TLC and NMR), the mixture/suspension was cooled to room temperature and washed several times with petroleum ether, affording the alkenoic acid. DCM (2 mL) was added to the acid followed by NBS (98 mg, 0.6 mmol, 1.1 equiv). The reaction mixture was stirred at room temperature until TLC and GC-MS showed full conversion. Then, the reaction mixture was diluted with DCM (10 mL) and quenched with 10% aqueous sodium sulfite (5 mL). The layers were separated and the aqueous layer was extracted once with DCM. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to give lactam-lactone **13**, which was purified by flash chromatography on silica, eluting with hexane:EtOAc (1:1). Oily substance. Yield = 286.9 mg, 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.21 (m, 16H),

7.11 – 7.07 (m, 3H), 5.54 (s, 1H), 4.80 (dd, J = 10.9, 2.8 Hz, 1H), 4.36 (d, J = 10.8 Hz, 1H), 4.28 – 4.17 (m, 1H), 3.85 – 3.73 (m, 4H), 3.49 – 3.31 (m, 1H), 3.07 – 2.97 (m, 1H), 2.80 – 2.48 (m, 5H), 2.08 – 1.98 (m, 1H), 1.96 – 1.82 (m, 1H), 1.20 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.1, 172.4, 169.9, 169.8, 169.3, 141.2, 139.7, 136.1, 133.1, 129.9, 129.4, 129.0, 128.9, 128.0, 127.9, 126.2, 125.0, 124.9, 81.7, 68.6, 60.1, 53.0, 52.1, 50.7, 46.5, 44.5, 38.0, 34.3, 34.2, 31.0, 29.3, 26.7, 17.4, 17.4. **HRMS-EI**$^+$ (*m/z*): calc for $C_{41}H_{39}BrN_2O_6$, 734.1991, found 734.1998.

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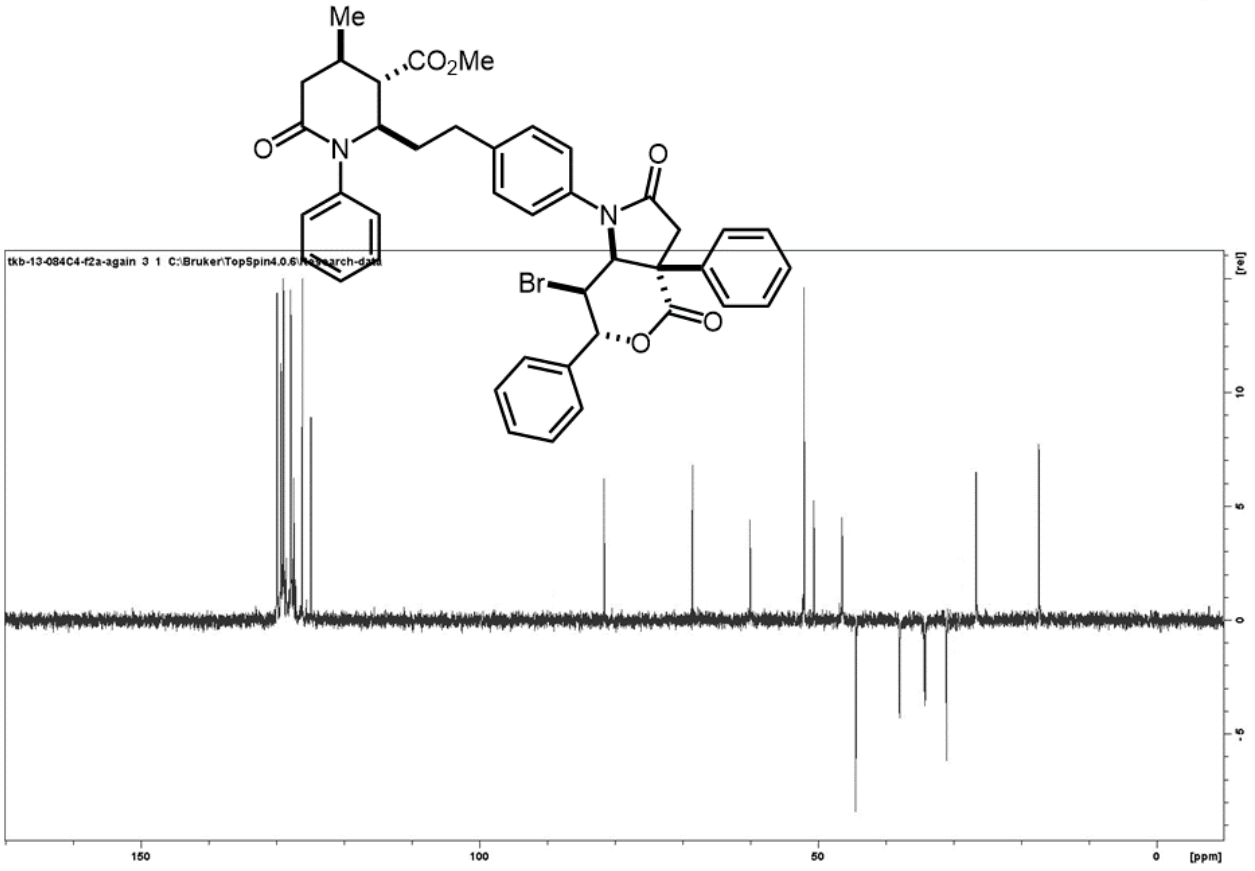
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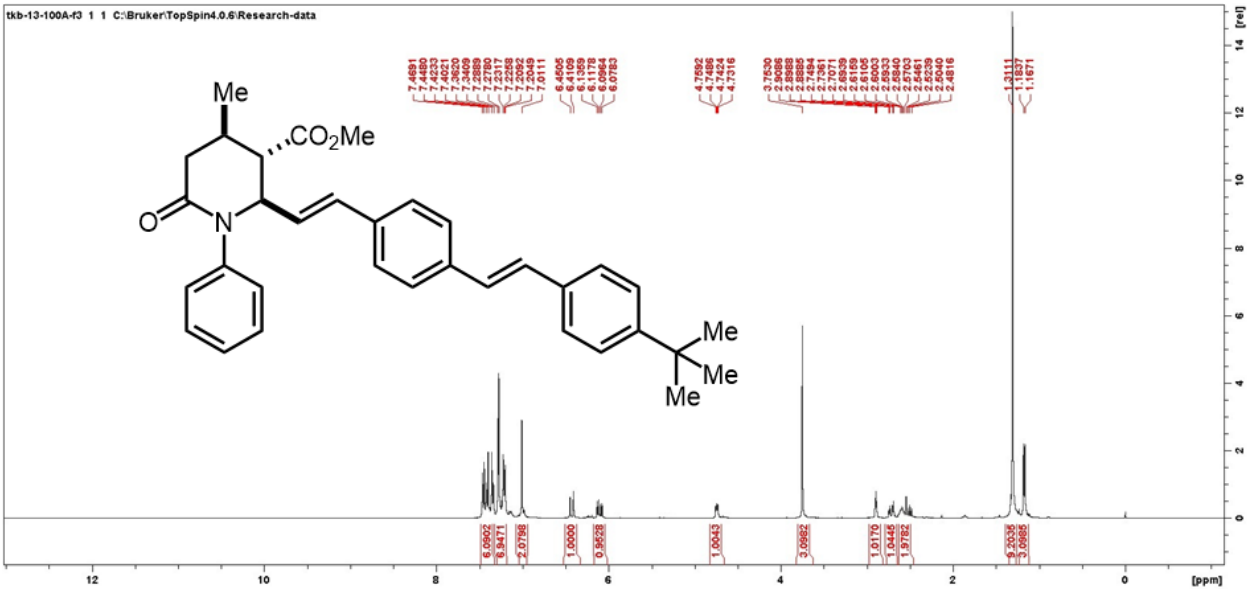
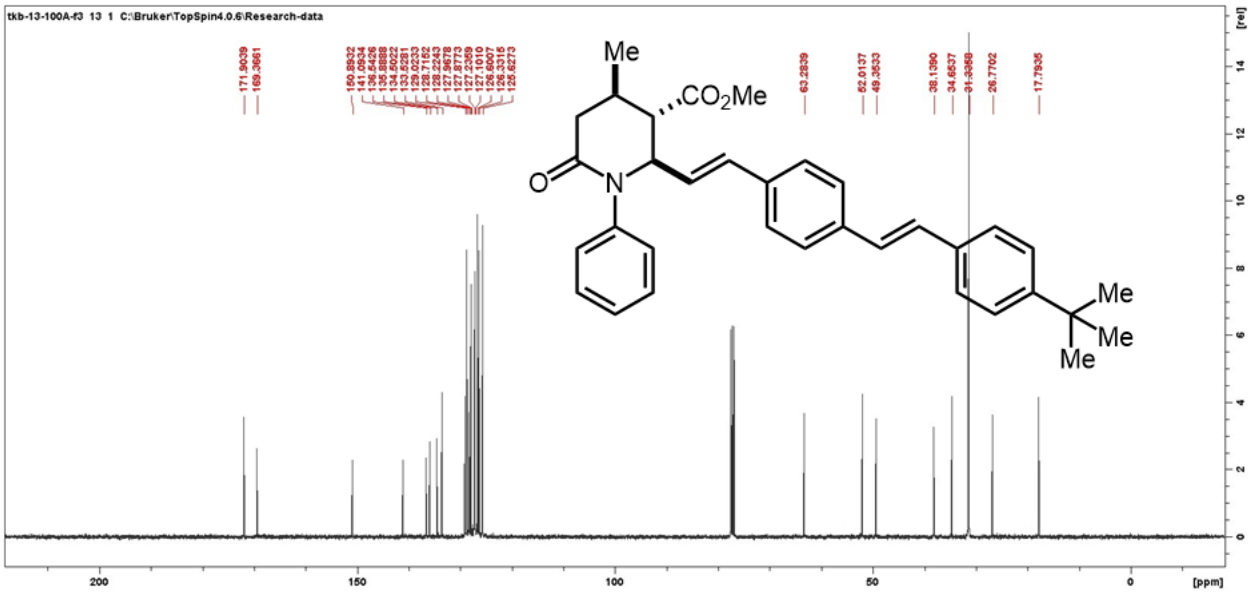
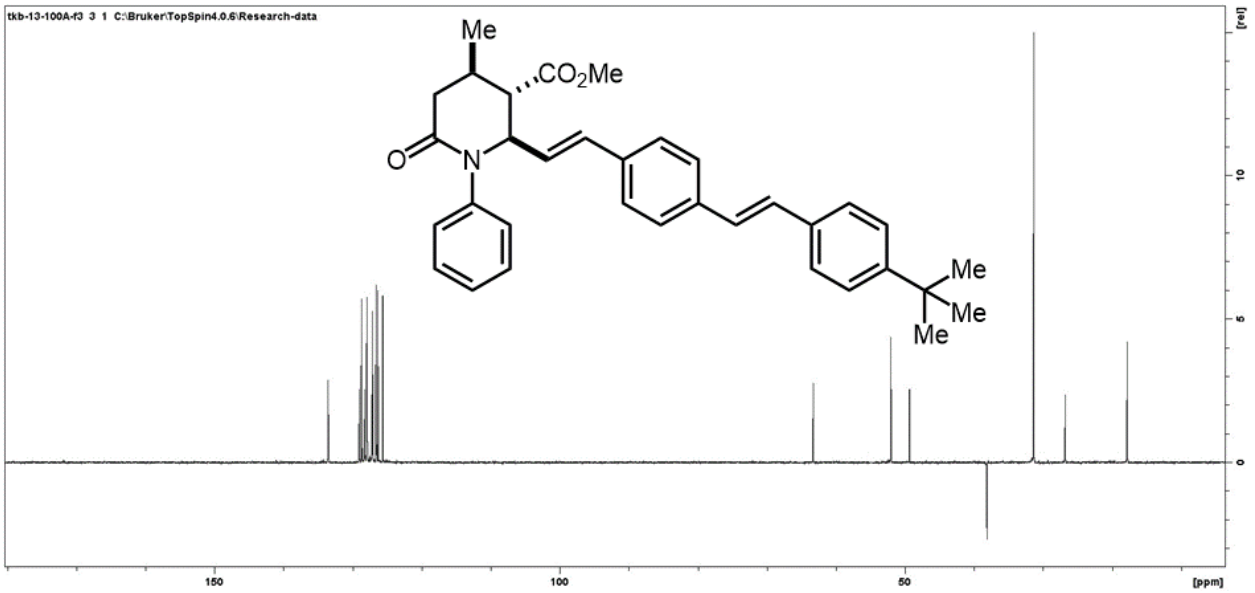
Scheme 6 Results (Denitrative alkenylation)

Compound 14a

Prepared in 0.50 mmol scale using **General Procedure G**, using 4-tert-butylstyrene (0.75 mmol, 1.5 equiv) as the alkene coupling partner. Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 225.9 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.20 (m, 13H), 7.01 (s, 2H), 6.43 (dd, *J* = 15.8, 1.1 Hz, 1H), 6.11 (dd, *J* = 15.8, 7.2 Hz, 1H), 4.78 – 4.71 (m, 1H), 3.75 (s, 3H), 2.90 (t, *J* = 4.1 Hz, 1H), 2.72 (dd, *J* = 16.9, 5.4 Hz, 1H), 2.66 – 2.56 (m, 1H), 2.59 – 2.46 (m, 1H), 1.31 (s, 9H), 1.18 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 169.4, 150.9, 141.1, 136.5, 135.9, 134.5, 133.5, 129.0, 128.7, 128.2, 128.0, 127.9, 127.2, 127.1, 126.6, 126.3, 125.6, 63.3, 52.0, 49.4, 38.1, 34.7, 31.3, 26.8, 17.8. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{34}H_{37}NO_3$, 507.2773, found 507.2779.



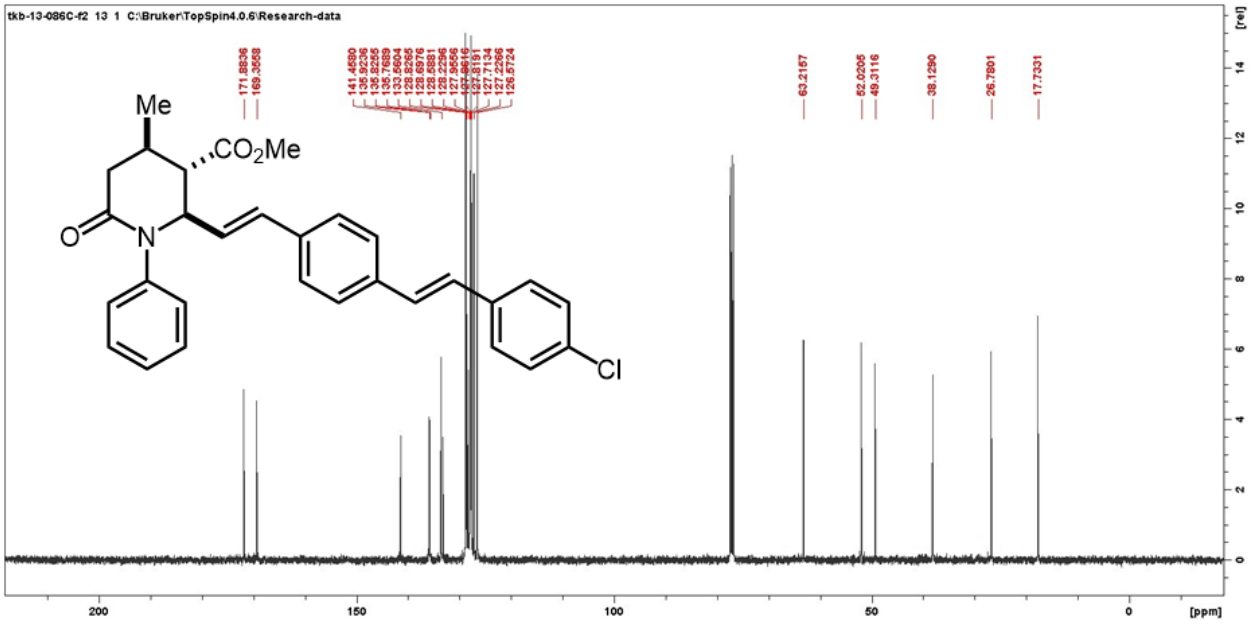


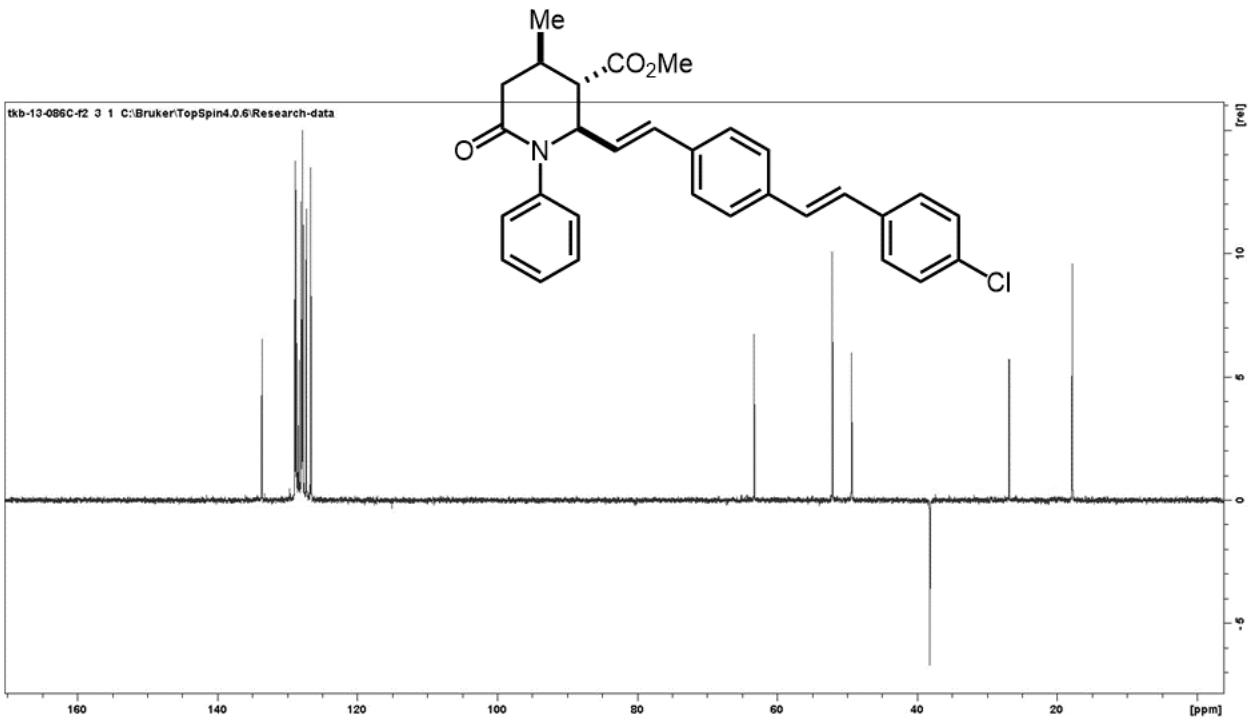


Compound 14b

Prepared in 0.50 mmol scale using **General Procedure G**, using 4-chlorostyrene (0.75 mmol, 1.5 equiv) as the alkene coupling partner. Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Oily substance. Yield = 201.7 mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.21 (m, 13H), 6.99 (s, 2H), 6.43 (d, J = 15.8 Hz, 1H), 6.11 (dd, J = 15.8, 7.3 Hz, 1H), 4.75 (dd, J = 7.3, 4.4 Hz, 1H), 3.77 (s, 3H), 2.91 (t, J = 4.1 Hz, 1H), 2.73 (dd, J = 17.1, 5.5 Hz, 1H), 2.67 – 2.56 (m, 1H), 2.52 (dd, J = 17.0, 8.8 Hz, 1H), 1.18 (d, J = 6.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 169.4, 141.5, 135.9, 135.8, 133.6, 133.2, 128.8, 128.7, 128.6, 128.2, 128.0, 127.9,

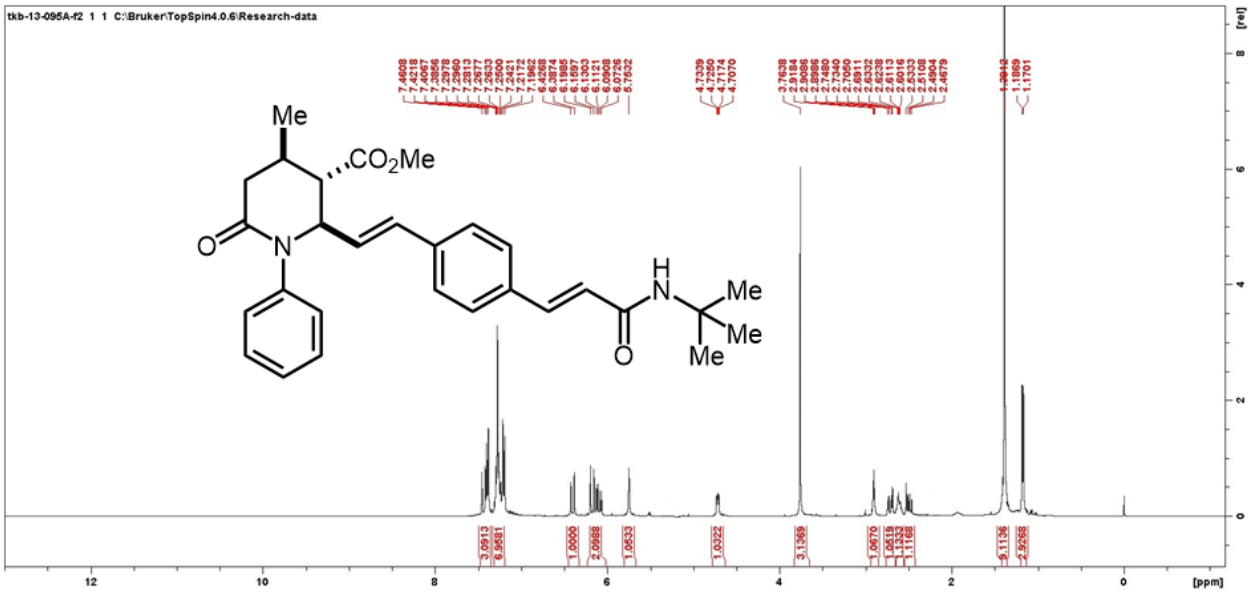
127.8, 127.7, 127.2, 126.6, 63.2, 52.0, 49.3, 38.1, 26.8, 17.7. **HRMS-EI$^+$** (*m/z*): calc for $C_{30}H_{28}ClNO_3$, 485.1758, found 485.1763.





Compound 14c

Prepared in 0.50 mmol scale using **General Procedure G**, using *N-tert*-butyl acrylamide (0.75 mmol, 1.5 equiv) as the alkene coupling partner. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 215.9 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 15.5 Hz, 1H), 7.40 (d, *J* = 2.0 Hz, 1H), 7.39 (s, 1H), 7.34 – 7.17 (m, 7H), 6.41 (dd, *J* = 15.7, 1.0 Hz, 1H), 6.18 (d, *J* = 15.6 Hz, 1H), 6.10 (dd, *J* = 15.8, 7.3 Hz, 1H), 5.75 (s, 1H), 4.72 (ddd, *J* = 7.3, 4.2, 1.1 Hz, 1H), 3.76 (s, 3H), 2.91 (t, *J* = 4.0 Hz, 1H), 2.72 (dd, *J* = 17.2, 5.6 Hz, 1H), 2.68 – 2.56 (m, 1H), 2.50 (dd, *J* = 17.2, 9.0 Hz, 1H), 1.39 (s, 9H), 1.18 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 169.5, 165.1, 142.8, 138.9, 135.7, 134.1, 133.7, 128.7, 128.5, 128.3, 127.9, 127.6, 126.5, 122.7, 63.3, 53.4, 52.0, 51.4, 49.2, 38.0, 28.8, 26.6, 17.8. **HRMS-EI^{+}** (*m/z*): calc for $C_{29}H_{34}N_2O_4$, 474.2519, found 474.2424.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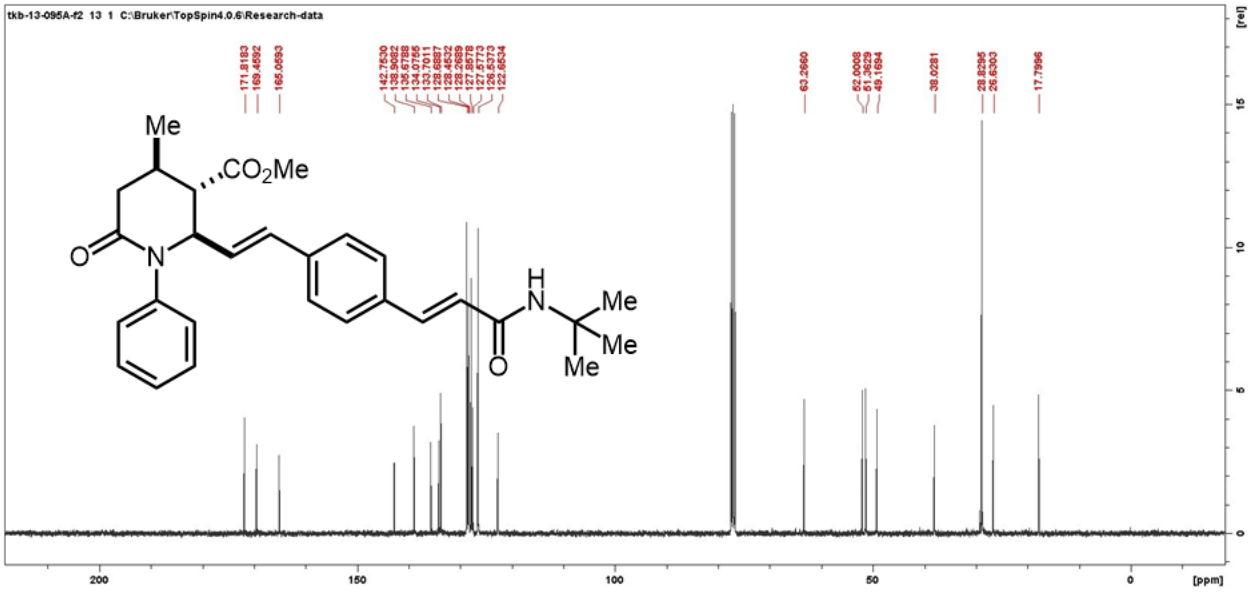
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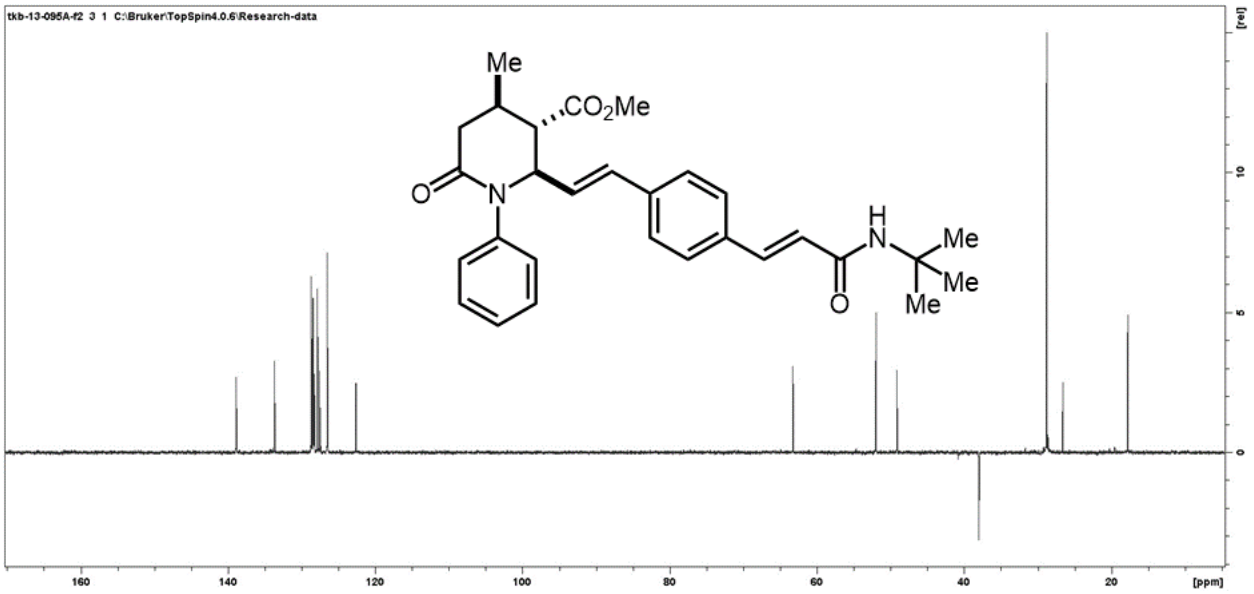

Compound 14d

Prepared in 0.50 mmol scale using **General Procedure G**, using *5-methylvinylthiazole* (0.75 mmol, 1.5 equiv) as the alkene coupling partner. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 193.8 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.43 (d, *J* = 6.4 Hz, 2H), 7.30 – 7.22 (m, 7H), 7.12 (d, 1H), 6.75 (d, *J* = 16.0 Hz, 1H), 6.42 (dd, *J* = 15.7, 1.0 Hz, 1H), 6.11 (dd, *J* = 15.8, 7.4 Hz, 1H), 4.75 (ddd, *J* = 7.4, 4.5, 1.1 Hz, 1H), 3.77 (s, 3H), 3.09 (q, *J* = 7.3 Hz, 1H), 2.74 (dd, *J* = 17.1, 5.5 Hz, 1H), 2.69 – 2.57 (m, 1H), 2.57 – 2.51 (m, 4H), 1.19 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 169.4, 150.7, 149.5, 141.5, 135.8, 135.7, 133.6, 130.8, 130.5, 128.7, 128.2, 128.0, 127.7, 127.0, 126.6, 118.7, 63.2, 52.0, 49.3, 38.1, 26.8, 17.7, 15.4. **HRMS-EI^{+}** (*m/z*): calc for $C_{28}H_{28}N_2O_3S$, 472.1821, found 472.1827.


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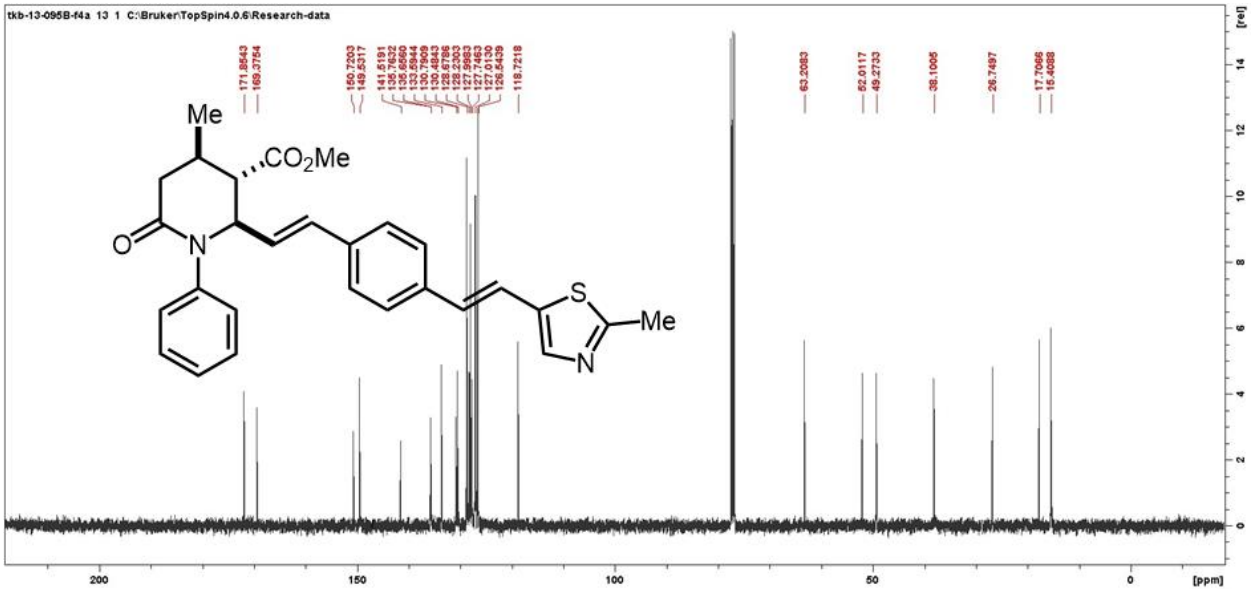
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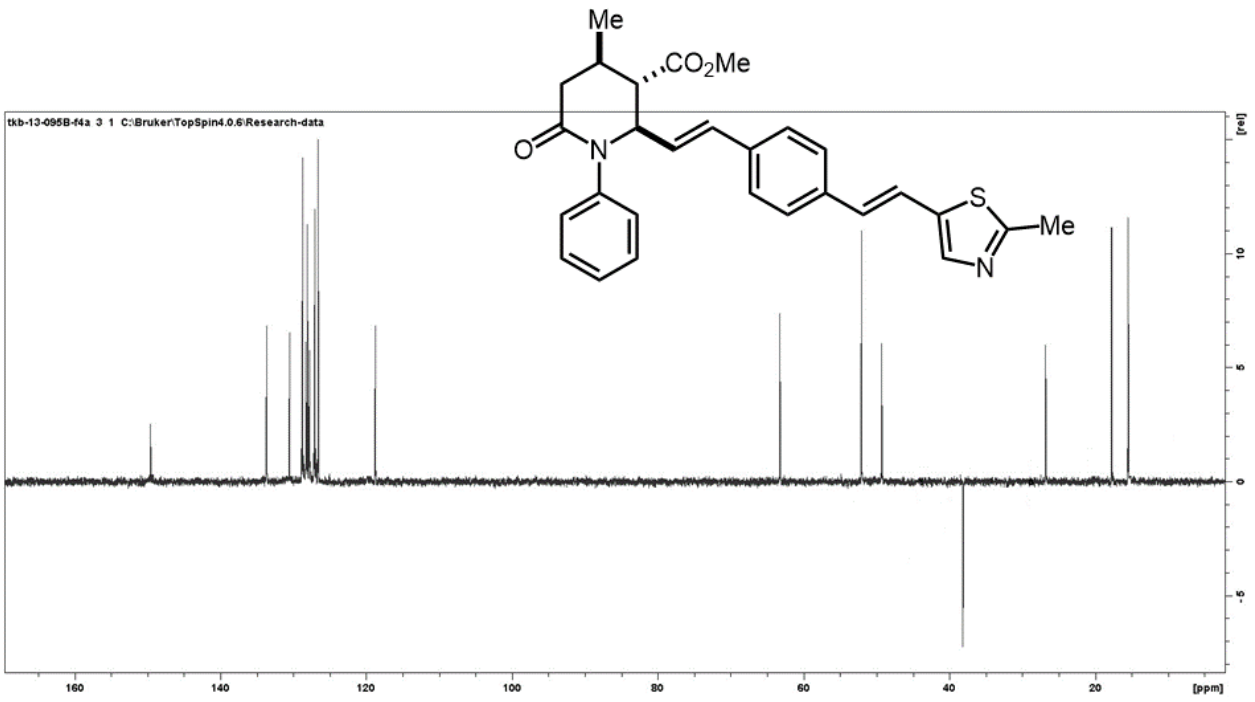
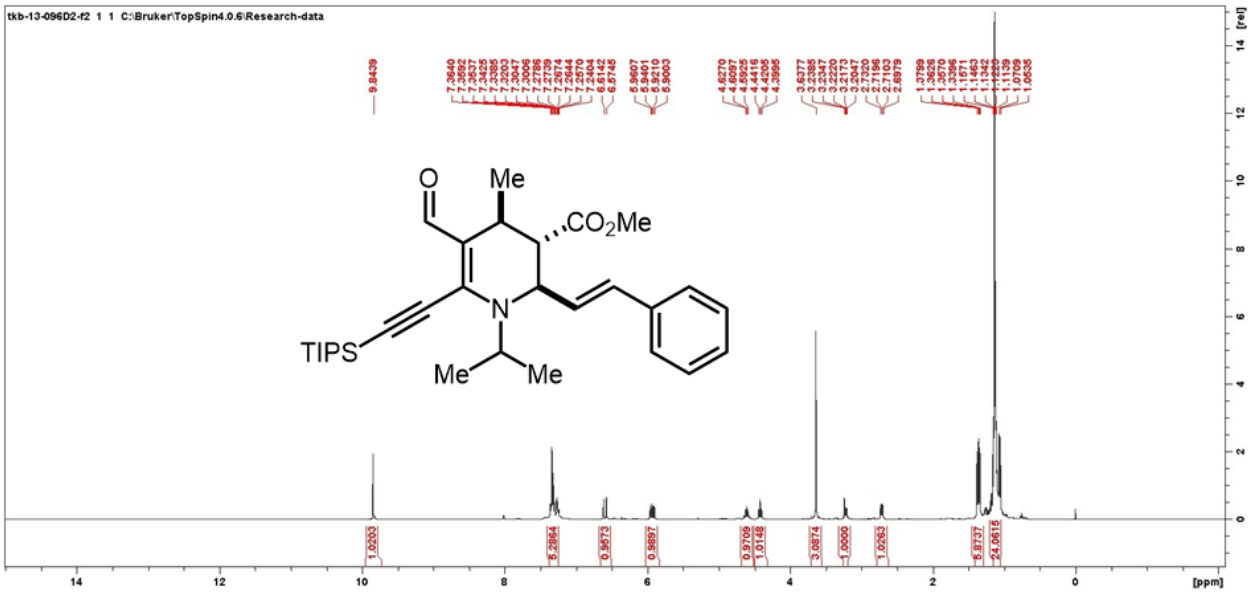


Scheme 7 Results

Compound 15a

Prepared in 0.25 mmol scale using **General Procedure H.** Purification: Flash chromatography on silica (pretreated with trimethylamine) eluting with hexane/EtOAc (90:10). Oily substance. Yield = 118.0 mg, 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 7.36 – 7.24 (m, 5H), 6.59 (d, *J* = 15.9 Hz, 1H), 5.93 (dd, *J* = 15.9, 8.2 Hz, 1H), 4.61 (hept, *J* = 7.0 Hz, 1H), 4.42 (t, *J* = 8.4 Hz, 1H), 3.64 (s, 3H), 3.27 – 3.17 (m, 1H), 2.72 (dd, *J* = 8.7, 5.0 Hz, 1H), 1.36 (dd, *J* = 9.2, 6.9 Hz, 6H), 1.15 – 1.05 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.8, 171.6, 143.5, 136.1, 133.0, 128.8, 128.7, 128.1, 126.5, 121.3, 104.2, 97.0, 55.8, 53.3, 51.6, 49.3, 26.0, 22.7, 20.6, 18.6, 15.3, 11.3. **HRMS-EI$^+$** (*m/z*): calc for $C_{31}H_{45}NO_3Si$, 507.3169, found 507.3175.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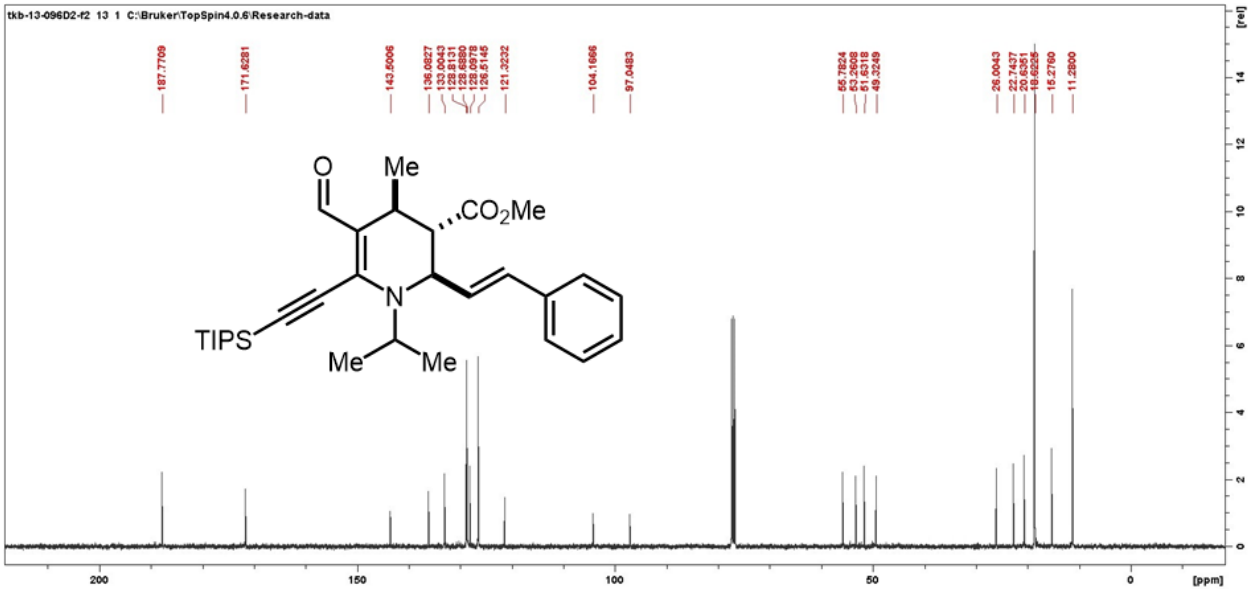
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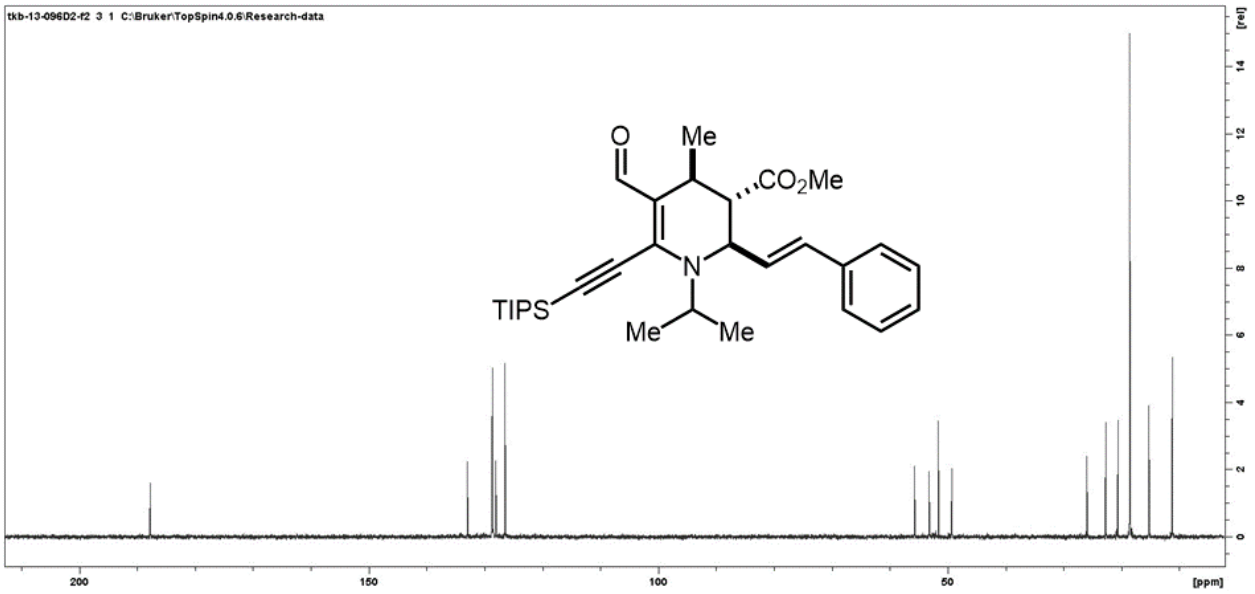
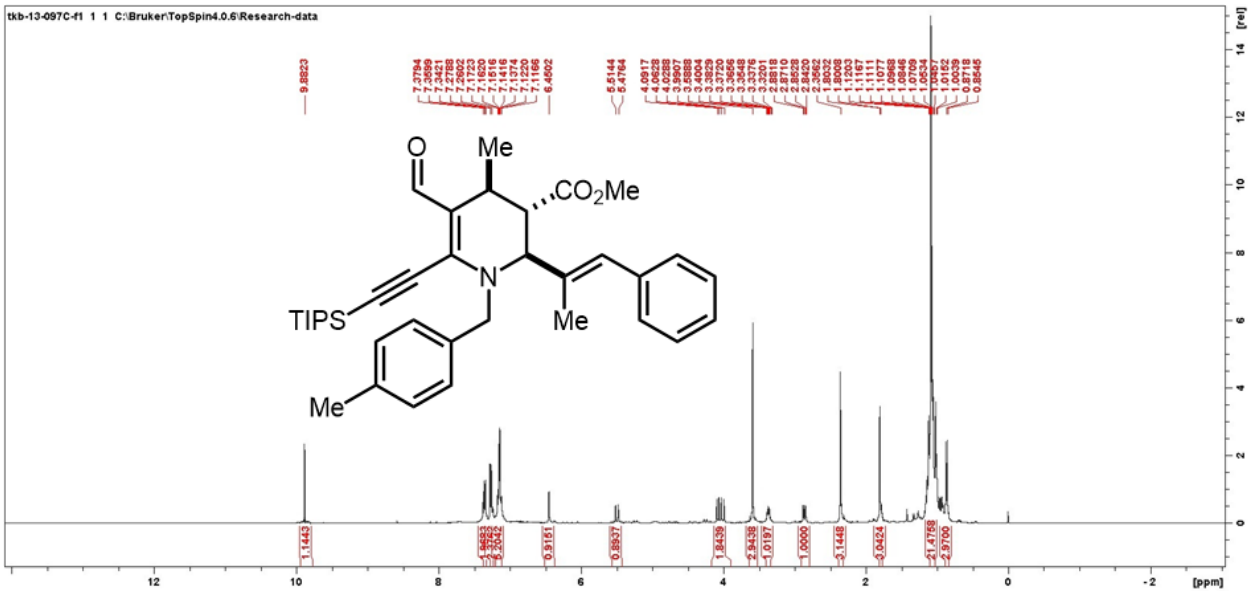


Compound 15b

Prepared in 0.25 mmol scale using **General Procedure H.** Purification: Flash chromatography on silica (pretreated with trimethylamine) eluting with hexane/EtOAc (90:10). Oily substance. Yield = 129.9 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 7.38 – 7.34 (m, 2H), 7.28 – 7.26 (m, 2H), 7.17 – 7.11 (m, 5H), 6.47 (s, 1H), 5.50 (d, *J* = 15.2 Hz, 1H), 4.08 (d, *J* = 11.6 Hz, 1H), 4.01 (d, *J* = 15.2 Hz, 1H), 3.59 (s, 3H), 3.36 (tt, *J* = 6.9, 3.6 Hz, 1H), 2.86 (dd, *J* = 11.6, 4.4 Hz, 1H), 2.36 (s, 3H), 1.80 (s, 3H), 1.12 – 0.85 (m, 24H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.8, 171.7, 144.1, 137.6, 136.8, 133.5, 133.1, 132.7, 129.4, 128.9, 128.3, 128.1, 127.7, 127.1, 126.7, 122.2, 104.2, 96.6, 61.4, 51.9, 51.7, 45.3, 26.2, 21.1, 18.6, 18.5, 16.3, 12.4, 11.2, 11.2, 11.1. **HRMS-EI^{+}** (*m/z*): calc for $C_{37}H_{49}NO_3Si$, 583.3482, found 583.3489.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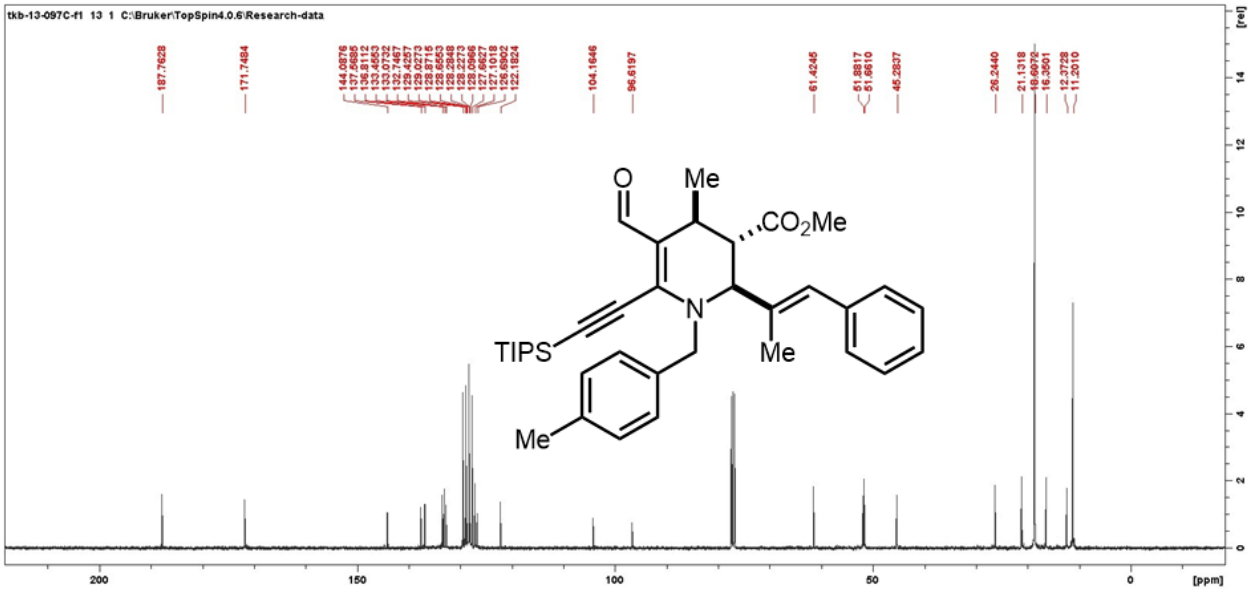
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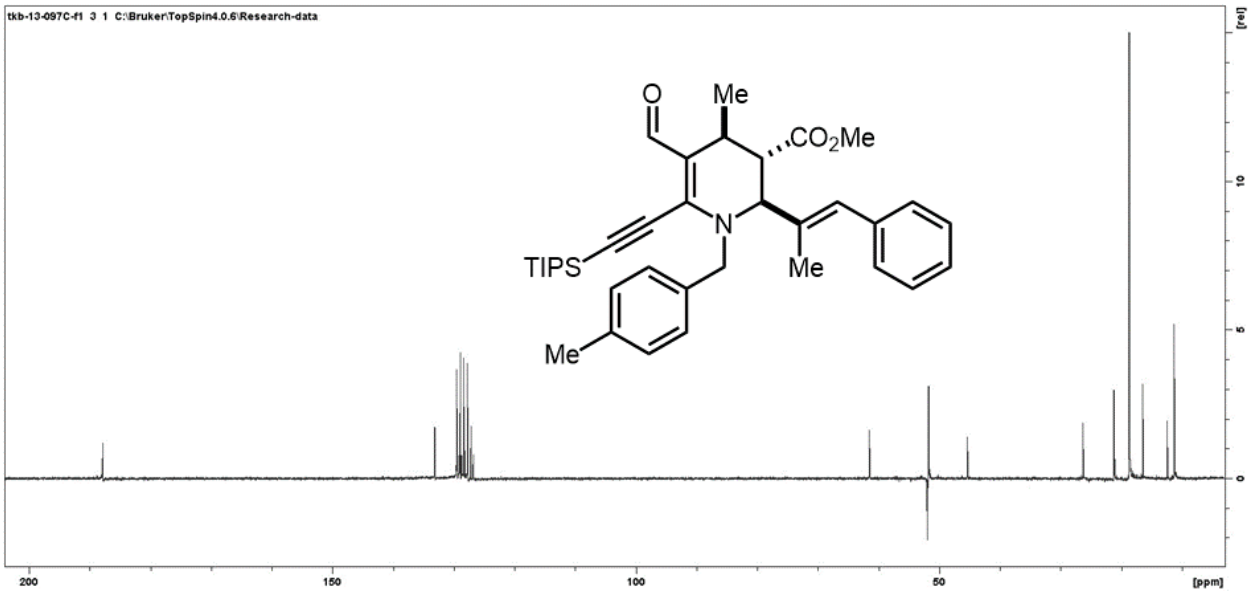
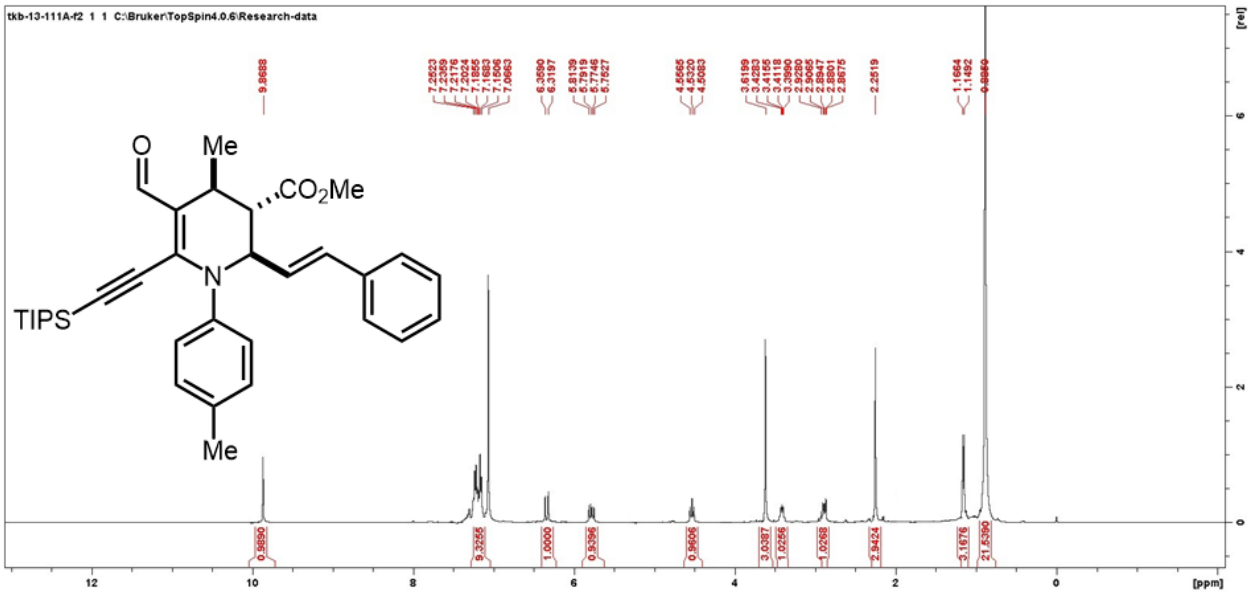
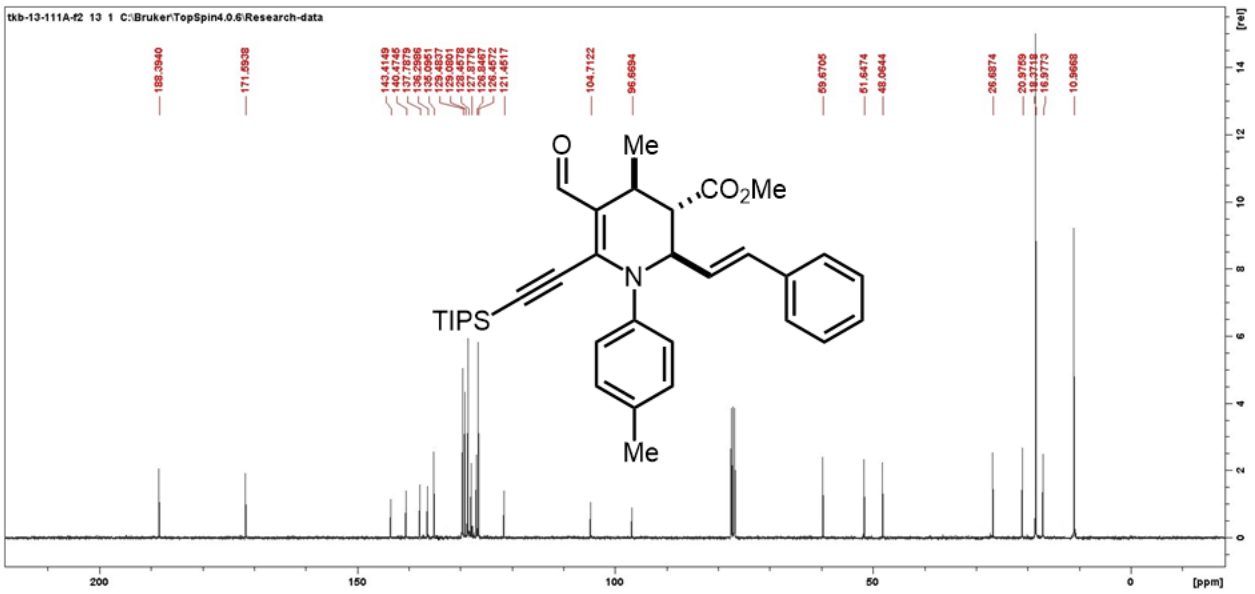
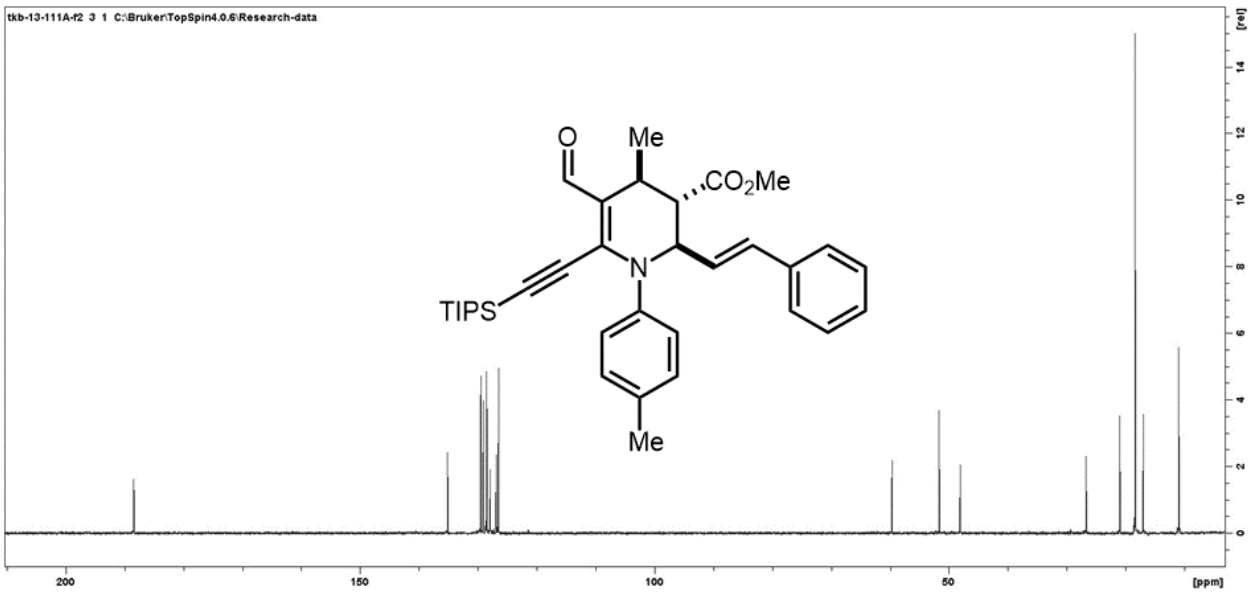


Compound 15c

Prepared in 0.25 mmol scale using **General Procedure H.** Purification: Flash chromatography on silica (pretreated with trimethylamine) eluting with hexane/EtOAc (80:20). Oily substance. Yield = 127.3 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (s, 1H), 7.25 – 7.06 (m, 9H), 6.34 (d, *J* = 15.7 Hz, 1H), 5.78 (dd, *J* = 15.7, 8.8 Hz, 1H), 4.53 (dd, *J* = 10.5, 8.8 Hz, 1H), 3.62 (s, 3H), 3.48 – 3.36 (m, 1H), 2.95 – 2.84 (m, 1H), 2.25 (s, 3H), 1.16 (d, *J* = 6.9 Hz, 3H), 0.89 (br. s, 21H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.4, 171.6, 143.4, 140.5, 137.8, 136.3, 135.1, 129.5, 129.1, 128.5, 127.9, 126.8, 126.5, 121.5, 104.7, 96.7, 59.7, 51.6, 48.1, 26.7, 21.0, 18.4, 17.0, 11.0. **HRMS-EI^{+}** (*m/z*): calc for $C_{35}H_{45}NO_3Si$, 555.3169, found 555.1362.



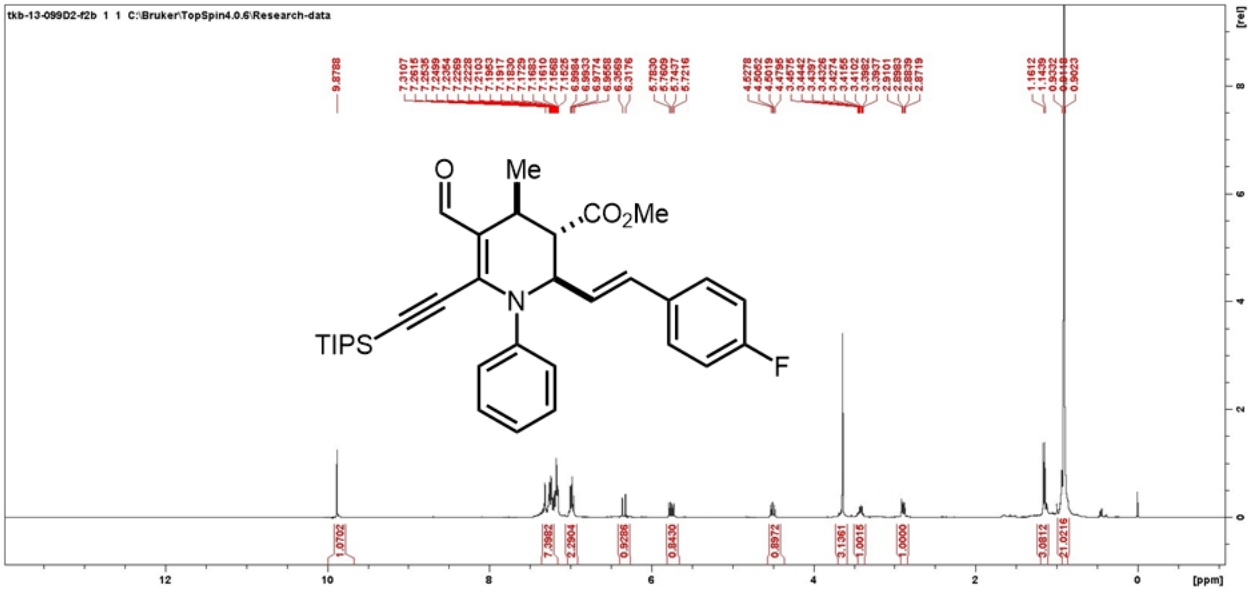


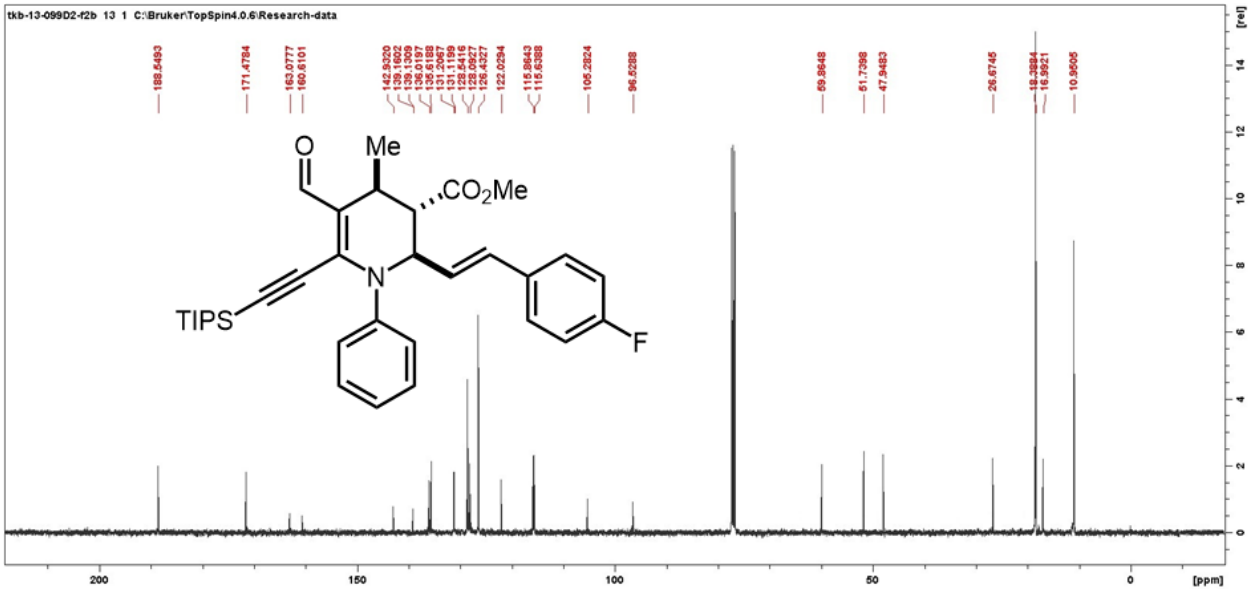


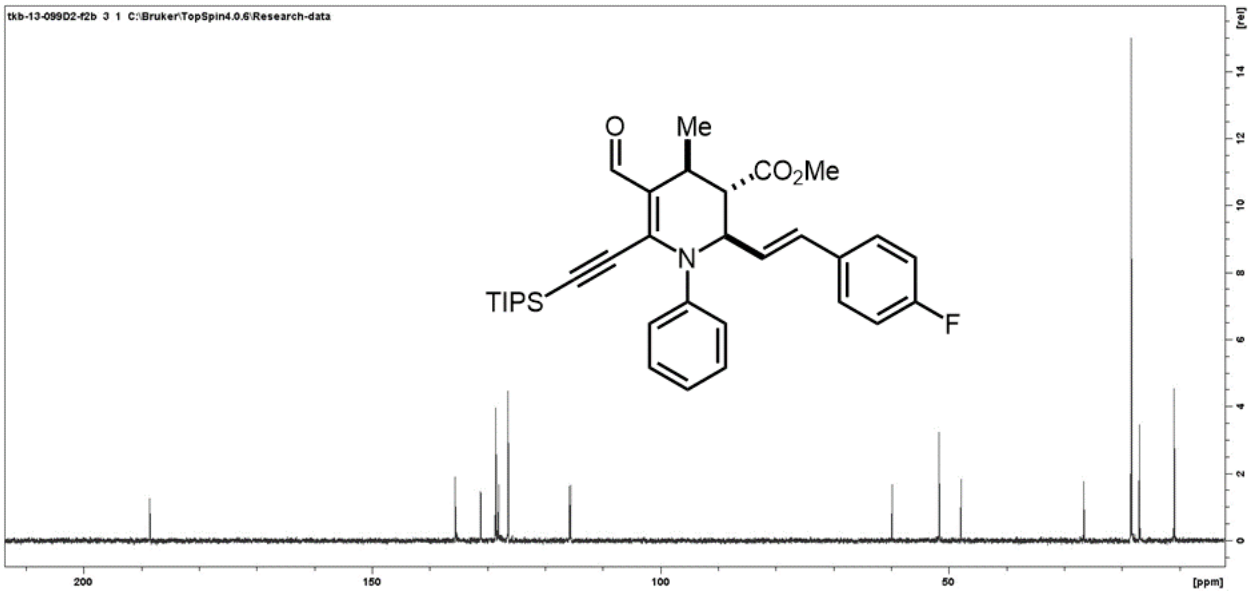
Compound 15d

Prepared in 0.25 mmol scale using **General Procedure H.** Purification: Flash chromatography on silica (pretreated with trimethylamine) eluting with hexane/EtOAc (80:20). Oily substance. Yield = 125.9 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 7.31 – 7.15 (m, 7H), 7.00 – 6.96 (m, 2H), 6.34 (d, *J* = 15.7 Hz, 1H), 5.75 (dd, *J* = 15.7, 8.8 Hz, 1H), 4.50 (dd, *J* = 10.5, 8.8 Hz, 1H), 3.64 (s, 3H), 3.41 (qd, *J* = 6.9, 4.6 Hz, 1H), 2.89 (dd, *J* = 10.5, 4.7 Hz, 1H), 1.15 (d, *J* = 6.9 Hz, 3H), 0.93 – 0.90 (m, 21H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.55, 171.48, 163.08, 160.61, 142.94,

139.16, 139.13, 136.02, 135.62, 131.21, 131.12, 128.75, 128.54, 128.10, 126.51, 126.44, 122.03, 115.87, 115.64, 105.29, 96.53, 59.87, 51.74, 47.95, 26.68, 18.39, 17.00, 10.95. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{34}H_{42}FNO_3Si$, 559.2918, found 559.2914.







References

(1) Braunstein, H.; Langevin, S.; Khim, M.; Adamson, J.; Hovenkotter, K.; Kotlarz, L.; Mansker, B.; Beng, T. K. *Org. Biomol. Chem.* **2016**, *14*, 8864.

(2) Beng, T. K.; Bassler, D. P., *Tetrahedron Lett.* **2014,** *55* (49), 6662-6664.

(3) Alami, M.; Crousse, B.; Ferri, F. *J. Organomet. Chem.* **2001**, *624*, 114.