Supplementary Information for:

Catalytic, selective, and stereocontrolled construction of C4 quaternary and homobenzylic dihydroisoquinolones by sp^3 C–H benzylation

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2. Experimental Section

All experiments involving air and moisture sensitive reagents such as organolithium reagents were carried out under an inert atmosphere of nitrogen and using freshly distilled solvents. Column chromatography was performed on silica gel (230-400 mesh). Thin-layer chromatography (TLC) was performed using Silicycle SiliaplateTM glass backed plates (250 μm thickness, 60 Å porosity, F-254 indicator) and visualized using UV (254 nm) or $KMnO_4$ stain. Unless otherwise indicated, ^1H, ^{13}C, and DEPT-135 NMR, and NOESY spectra were acquired using $CDCl_3$ 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). Representative GC-MS traces are provided to substantiate the diastereomeric ratios. The dihydroisoquinolone (DHIQ) precursors employed in these studies (see below) were prepared using a previously reported protocol.[1] Newly synthesized DHIQs were advanced without extensive characterization.

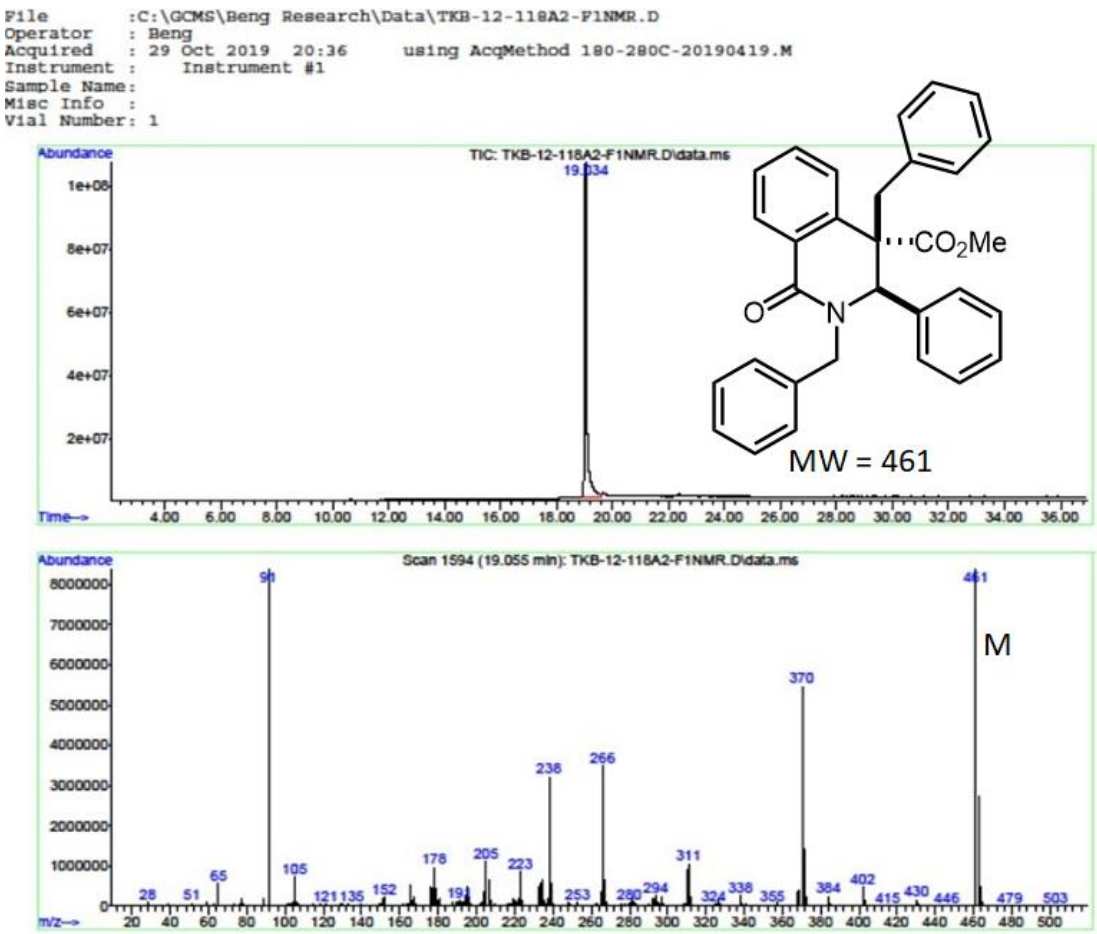
General Procedure A: Benzylation of vicinally functionalized dihydroisoquinolones

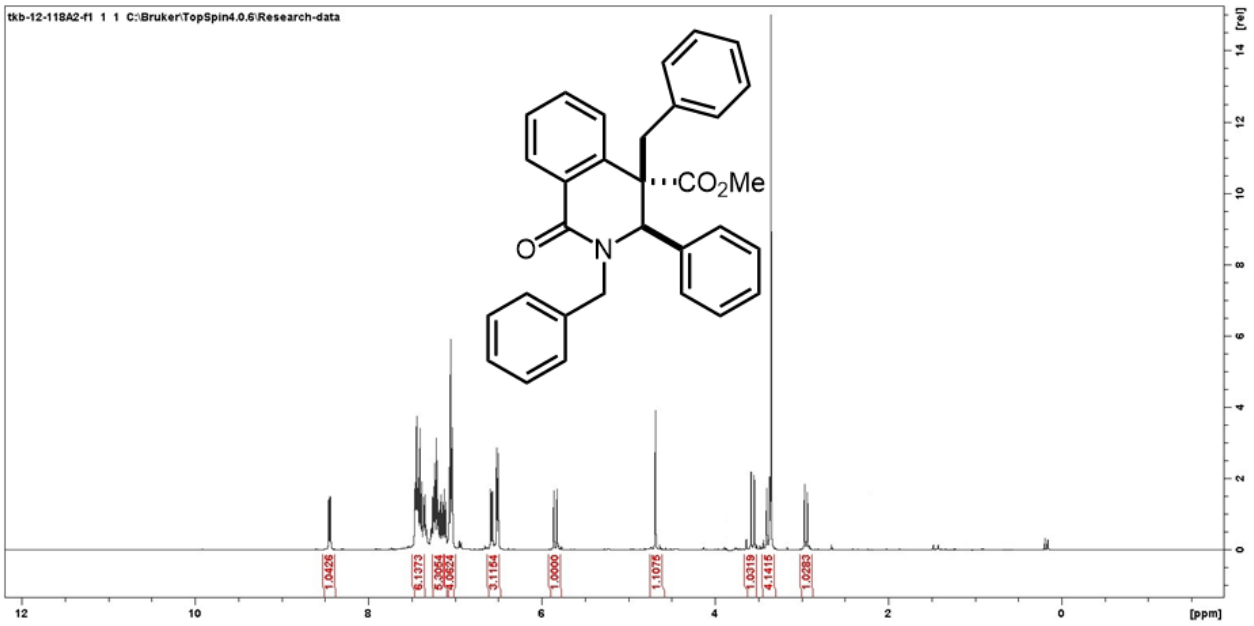
$Pd(OAc)_2$ (11.25 mg, 0.05 mmol, 5 mol%), *rac*-BINAP (37.25 mg, 0.06 mmol, 6 mol%) and Cs_2CO_3 (391 mg, 1.2 mmol, 1.2 equiv) were added to a dry and degassed vial at room temperature. *N*,*N*-dimethylformamide (1.0 mL) was added and after 10 minutes of stirring at room temperature the benzyl carbonate (1.0 mmol, 1.0 equiv), the DHIQ dissolved in 1 mL DMF (1.0 mmol, 1.0 equiv). The contents were heated to 90 ºC for 10 or 18 h (TLC and GC-MS monitoring). After cooling to room temperature, the reaction was filtered through Celite® and the solvent evaporated under reduced pressure. The crude mixture was purified by flash chromatography on silica eluting with hexanes/EtOAc.

General Procedure B: Chemoselective ester reduction: To a stirred suspension of LiCl (42.39 mg, 1.0 mmol) and KBH_4 (53.94 mg, 1.0 mmol) in dry THF (2 mL), a solution of quaternary ester **2** (0.25 mmol) in dry THF (10 mL) was added dropwise for 5 min. The reaction mixture was stirred at room temperature for 22 h. The solvent was removed under reduced pressure and the residue was poured into water (20 mL). The suspension was extracted with ethyl acetate and the organic phase was dried (Na_2SO_4). After removal of the solvent, the residue was purified by flash chromatography on silica.

Compound 2a

Prepared from ester **1a** (371.4 mg, 1.0 mmol) and benzyl 4-nitrophenylcarbonate (273.24, 1 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Yield = 406 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 1.5 Hz, 1H), 7.44 – 7.33 (m, 6H), 7.32 – 7.24 (m, 5H), 7.28 – 7.15 (m, 4H), 6.51 (dd, *J* = 8.0, 1.1 Hz, 1H), 6.44 (dt, *J* = 7.1, 1.4 Hz, 2H), 5.77 (d, *J* = 14.5 Hz, 1H), 4.62 (s, 1H), 3.49 (d, *J* = 14.5 Hz, 1H), 3.31 (d, *J* = 13.1 Hz, 1H), 3.28 (s, 3H), 2.88 (d, *J* = 13.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.12, 163.15, 136.79, 136.61, 135.93, 135.10, 131.26, 130.75, 130.63, 129.40, 128.96, 128.90, 128.69, 128.49, 128.17, 128.09, 128.05, 127.86, 127.83, 126.93, 67.12, 58.19, 51.81, 48.43, 45.99. FTIR (KBr): 2976.0754, 2927.2335, 1721.7979, 1650.1792, 1492.0415, 1438.4625, 1362.2698, 1320.5399, 1290.1484, 1206.364, 1180.3512, 1146.7618, 1132.397, 995.8166, 918.8793, 700.1334. HRMS calc for $C_{31}H_{27}NO_3$ 461.1991, found 461.1208.

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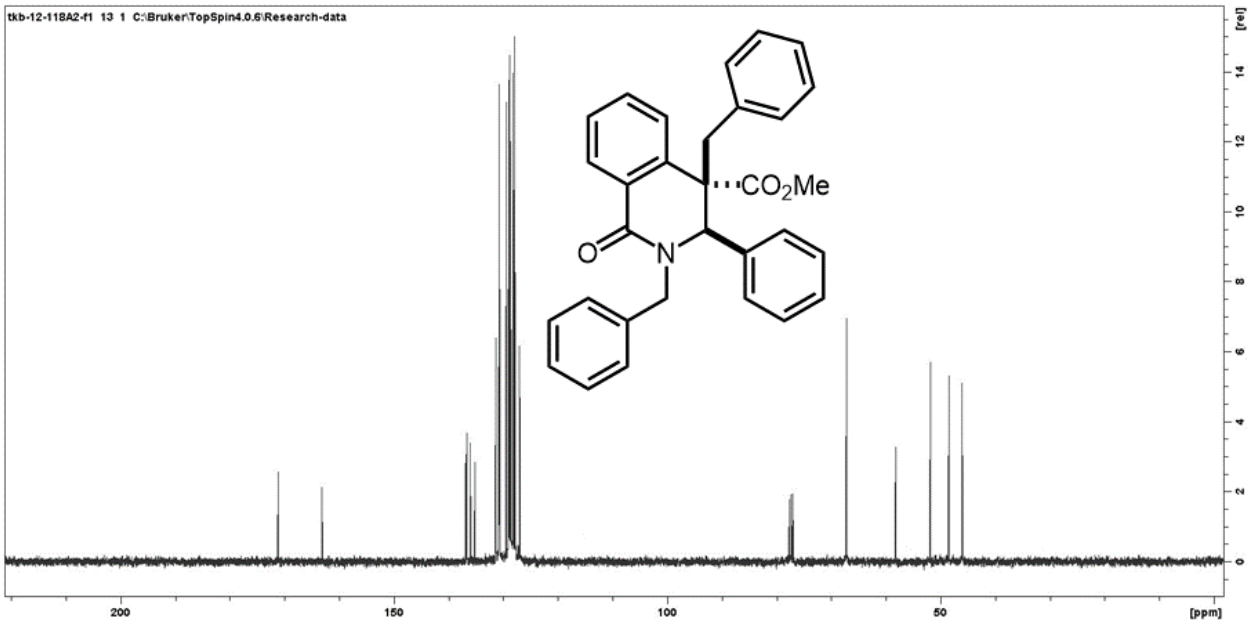
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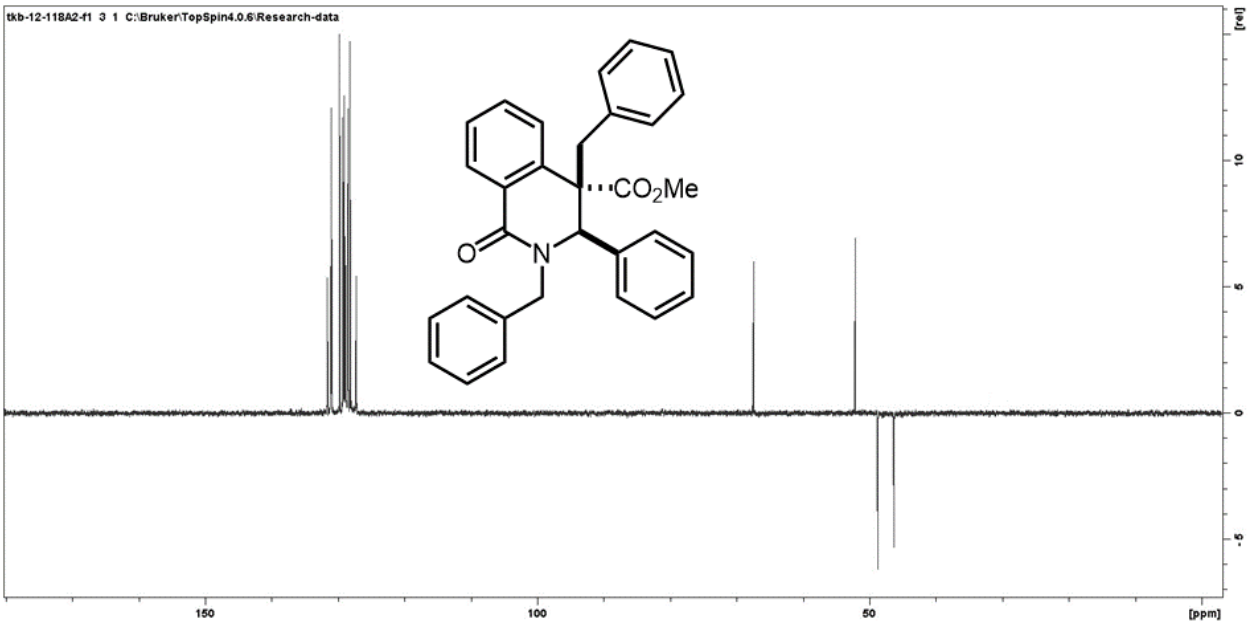
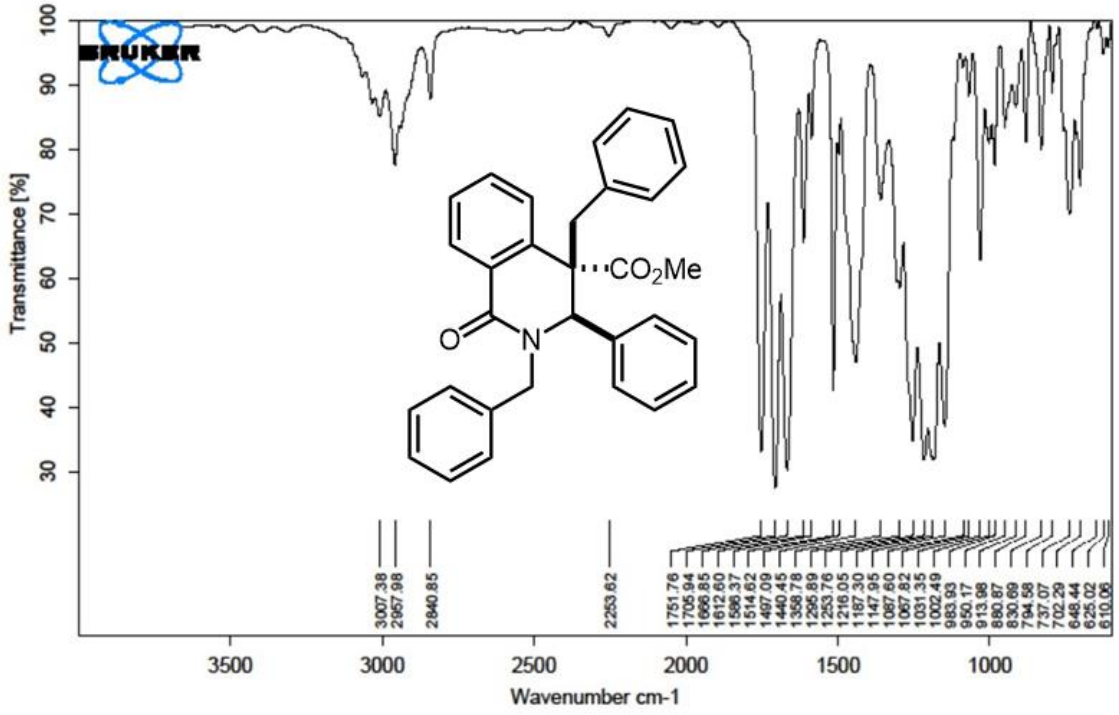
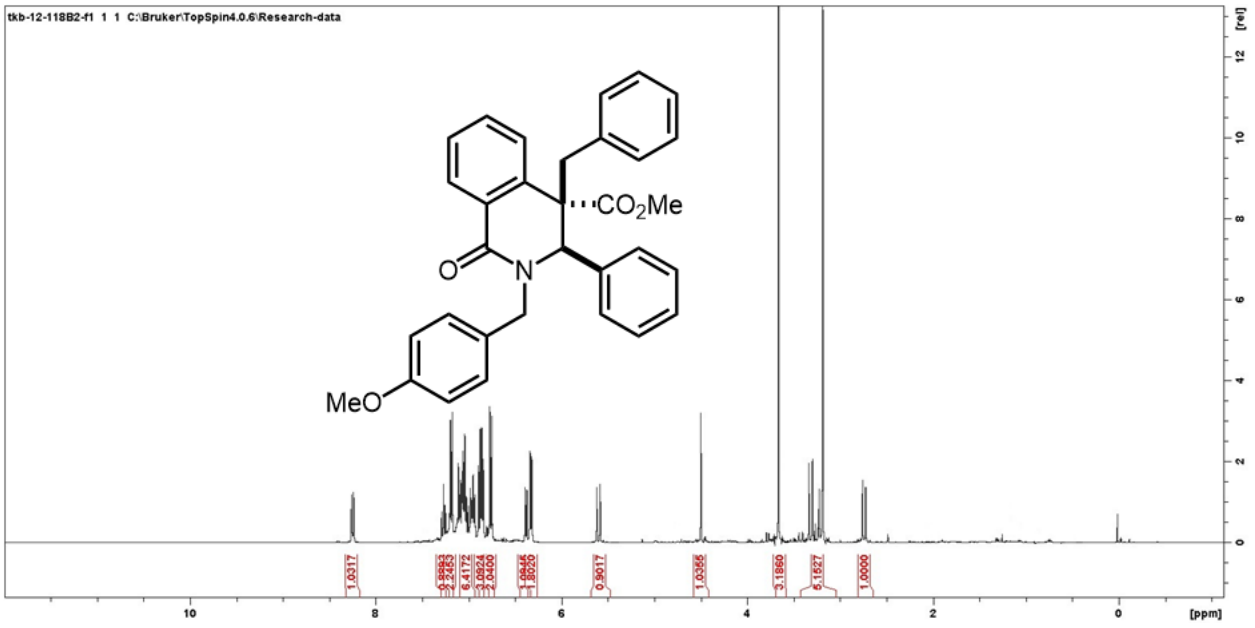


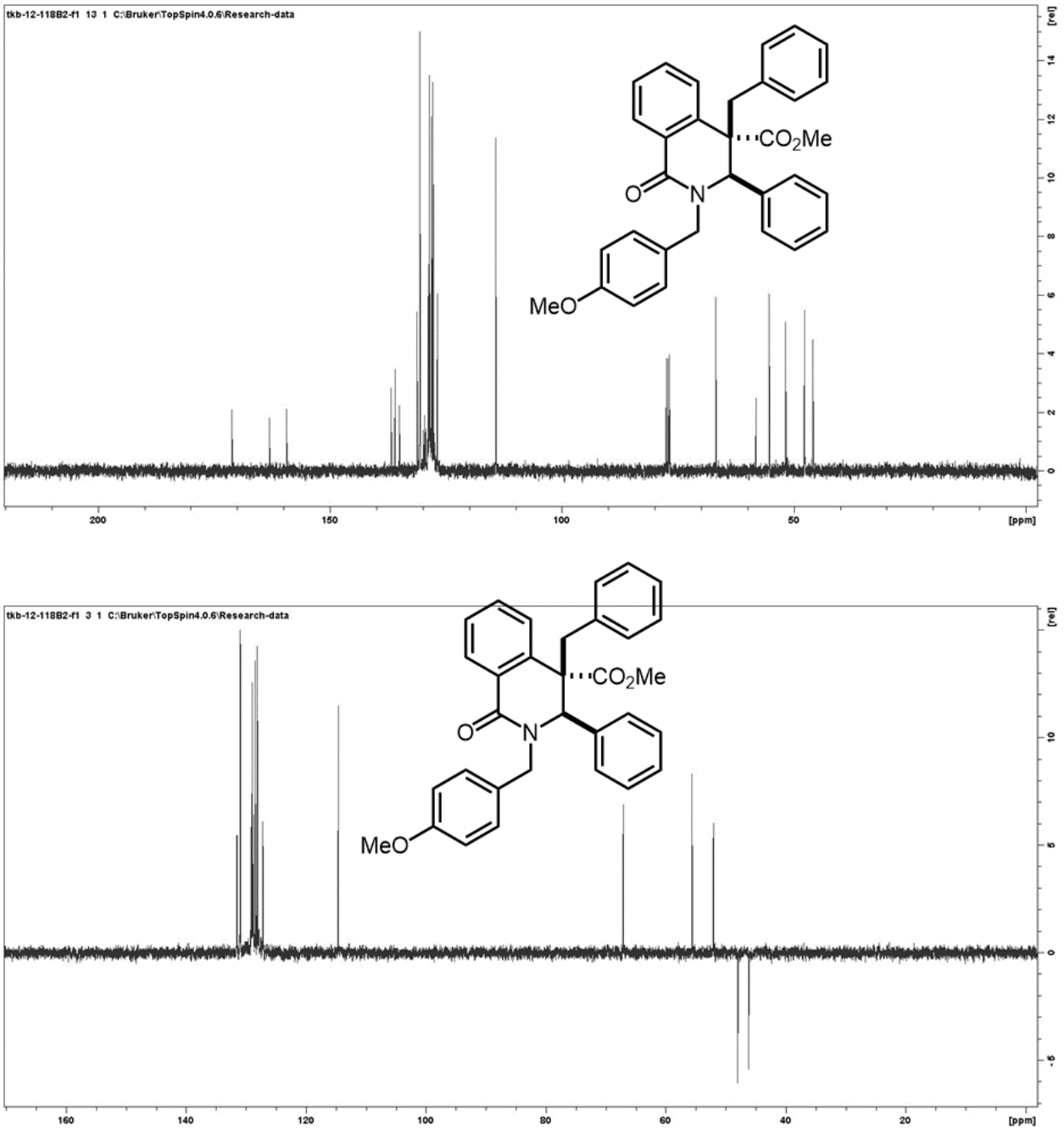


Compound 2b

Prepared from ester **1b** (401 mg, 1.0 mmol) and benzyl 4-nitrophenylcarbonate (273.24, 1 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yield = 418 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (dd, 1H), 7.46 – 7.30 (m, 3H), 7.33 – 7.21 (m, 6H), 7.14 – 6.86 (m, 3H), 6.75 (d, J = 6.5 Hz, 2H), 6.35 – 6.29 (m,

3H), 5.60 (d, J = 14.4 Hz, 1H), 4.50 (s, 1H), 3.66 (s, 3H), 3.64 (d, J = 14.4 Hz, 1H), 3.33 (d, J = 13.0 Hz, 1H). 3.28 (s, 3H), 2.74 (d, J = 13.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.17, 163.03, 159.39, 136.81, 135.96, 135.03, 131.20, 130.69, 130.67, 130.63, 128.83, 128.72, 128.65, 128.55, 128.44, 128.19, 128.15, 128.10, 128.03, 127.83, 127.78, 127.76, 126.88, 114.29, 66.82, 58.20, 55.36, 51.77, 47.70, 45.92. FTIR (KBr): 2930.9333, 1721.7229, 1664.1745, 1606.8615, 1576.9493, 1511.8758, 1422.3889, 1359.3077, 1300.0014, 1250.9591, 1175.8146, 1113.165, 1031.2694, 996.2804, 970.248, 923.7263, 826.1509, 764.8959. HRMS calc for $C_{32}H_{29}NO_4$ 491.2097, found 491.2092.

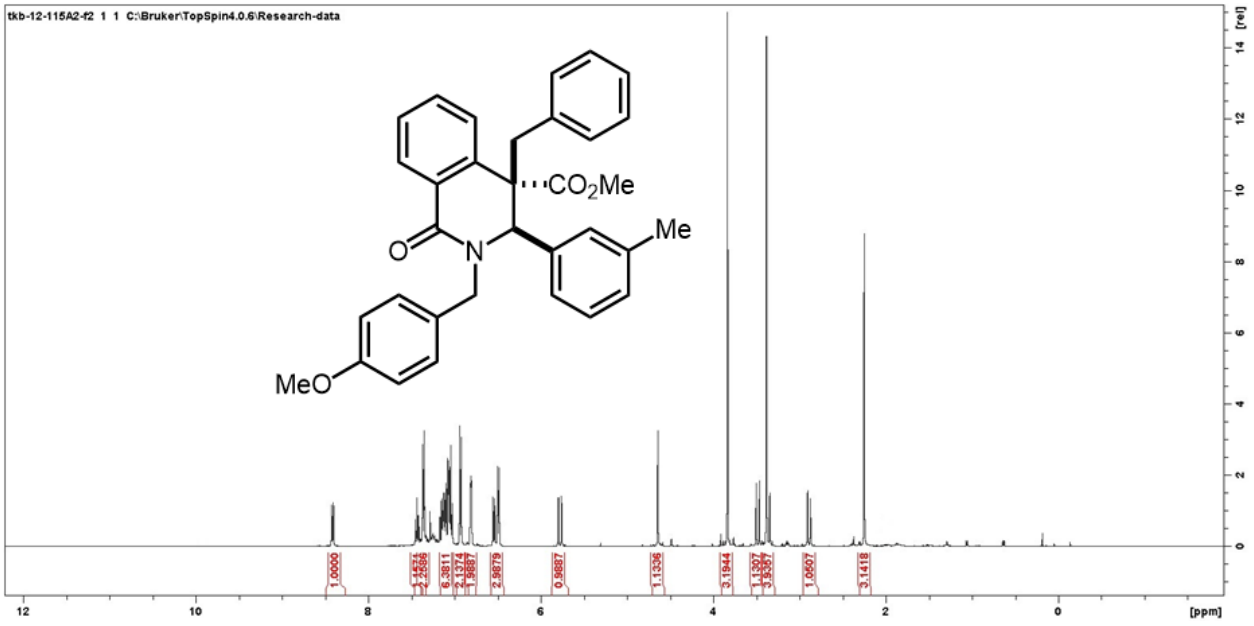


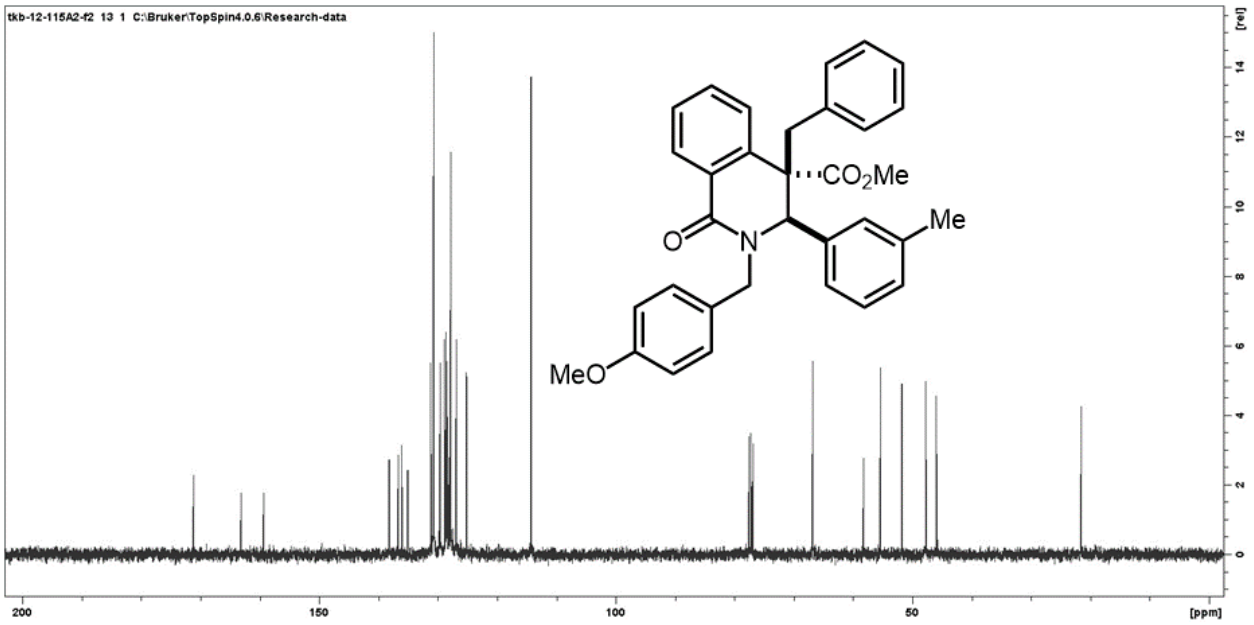


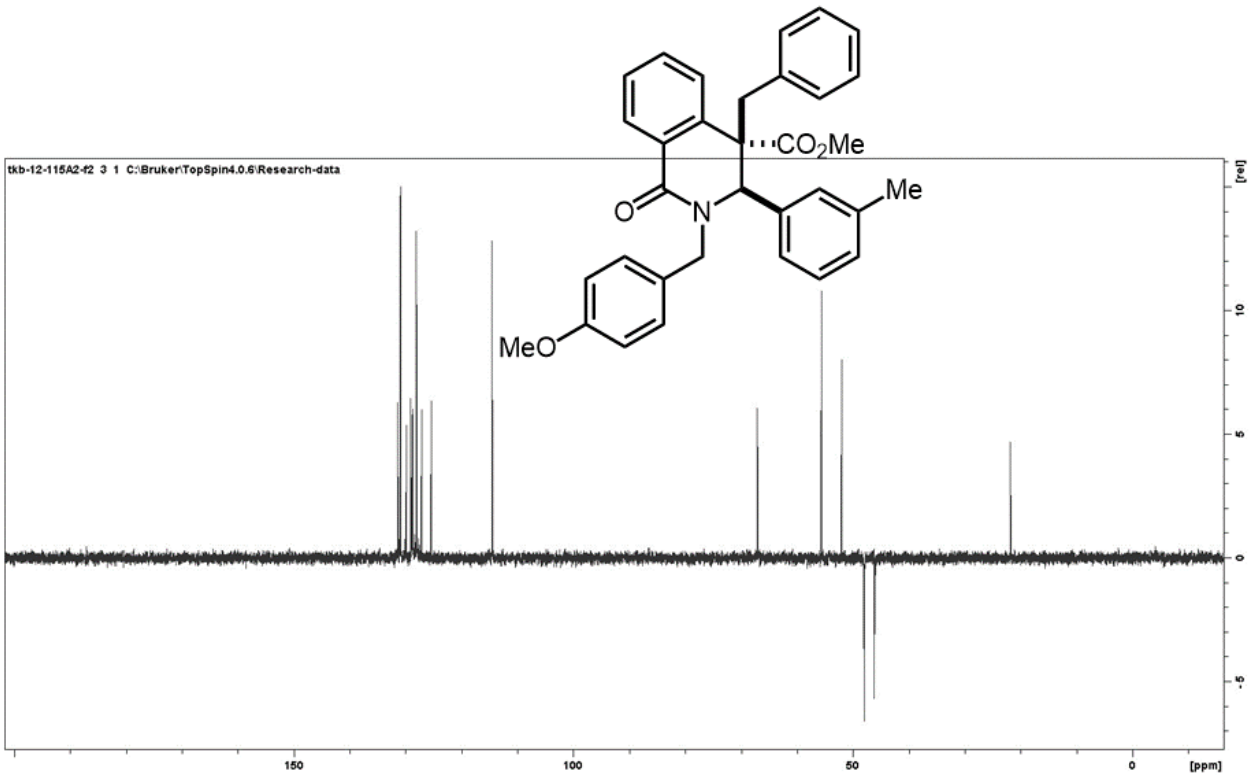
Compound 2c

Prepared from ester **1c** (415.5 mg, 1.0 mmol) and benzyl 4-nitrophenylcarbonate (273.24, 1 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yield = 450 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.42 – 7.21 (m, 3H), 7.14 – 7.01 (m, 6H), 6.91 – 6.81 (m, 2H), 6.73 (dp, *J* = 3.7, 1.8 Hz, 2H), 6.47 (dd, *J* = 7.9, 1.1 Hz, 1H), 6.47 – 6.38 (m, 2H), 5.70 (d, *J* = 14.4 Hz, 1H), 4.57 (s, 1H),

3.76 (s, 3H), 3.41 (d, J = 14.4 Hz, 1H), 3.31 (s, 3H), 3.28 (d, J = 13.0 Hz, 1H), 2.81 (d, J = 13.0 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.17, 163.11, 159.35, 138.16, 136.65, 136.00, 135.04, 131.15, 130.68, 130.65, 130.64, 129.58, 128.81, 128.62, 128.56, 128.39, 127.81, 127.75, 126.86, 125.12, 114.24, 66.78, 58.22, 55.35, 51.74, 47.70, 45.91, 21.54. FTIR (KBr): 2932.4213, 1721.5204, 1666.3806, 1606.9472, 1511.0233, 1448.5693, 1414.7191, 1384.979, 1357.4641, 1298.7878, 1247.5543, 1179.3944, 1135.9684, 1031.8974, 995.8644, 968.9312, 919.9415, 831.0313, 750.2581, 694.7613. HRMS calc for $C_{33}H_{31}NO_4$ 505.2253, found 505.2258.

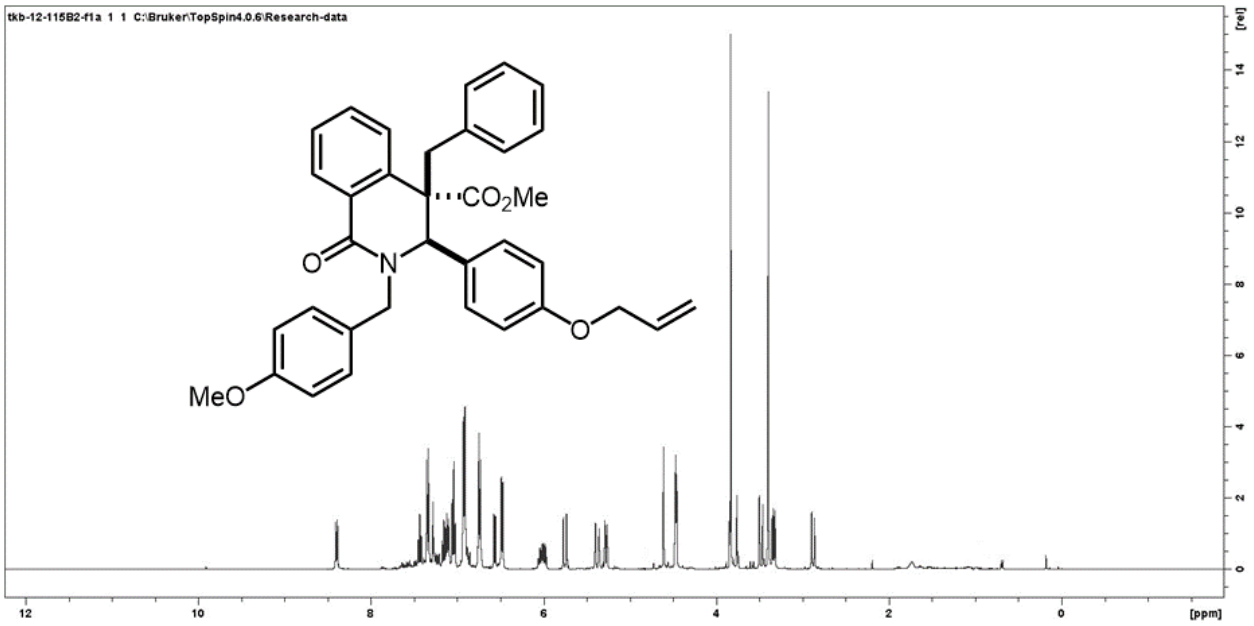






Compound 2d

Prepared from ester **1d** (228.8 mg, 0.5 mmol) and benzyl 4-nitrophenylcarbonate (136.62, 0.5 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yield = 224.5 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (dd, 1H), 7.35 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.24 (d, 2H), 7.04 – 6.88 (m, 2H), 6.91 – 6.82 (m, 2H), 6.71 – 6.62 (m, 4H), 6.59 (dd, *J* = 8.0, 1.2 Hz, 2H), 6.41 (dt, *J* = 7.1, 1.4 Hz, 1H), 6.31 – 6.22 (m, 2H), 5.82 – 5.77 (m, 1H), 5.60 (d, *J* = 17.2 Hz, 1H), 5.20 (d, *J* = 17.2 Hz, 1H), 5.16 (dq, *J* = 10.5, 1.5 Hz, 1H), 4.43 (s, 1H), 4.39 (ddt, *J* = 5.3, 3.2, 1.6 Hz, 2H), 3.66 (s, 3H), 3.35 – 3.26 (m, 1H), 3.22 (s, 3H), 3.20 – 3.12 (m, 1H), 2.70 (d, *J* = 13.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.23, 162.97, 159.34, 158.85, 136.00, 135.06, 133.07, 131.24, 130.66, 130.58, 129.32, 128.81, 128.60, 128.42, 128.07, 127.82, 127.75, 127.73, 126.86, 117.90, 114.73, 114.69, 114.25, 68.78, 66.19, 58.18, 55.35, 51.83, 47.53, 45.87. FTIR (KBr): 2932.5571, 1721.483, 1665.4081, 1607.2449, 1511.11, 1431.8598, 1414.7076, 1344.99, 1298.4941, 1245.6515, 1179.4413, 1135.306, 1031.8607, 996.7789, 921.8434, 832.167, 701.6744.HRMS calc for $C_{35}H_{33}NO_5$ 547.2359, found 547.2363.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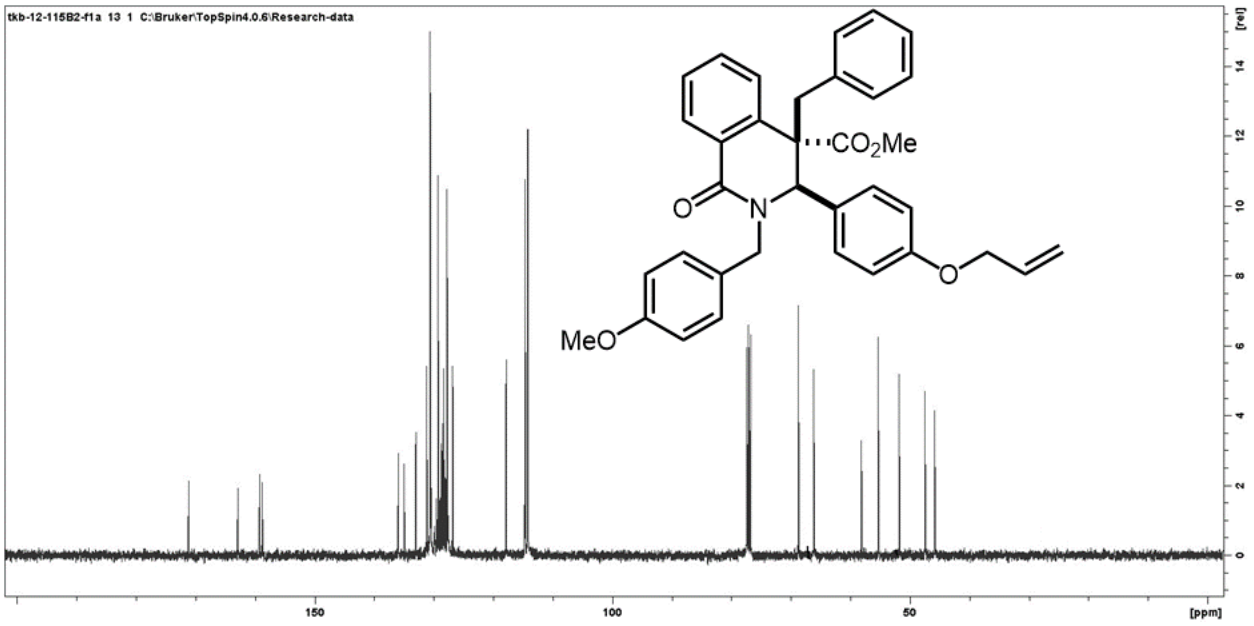
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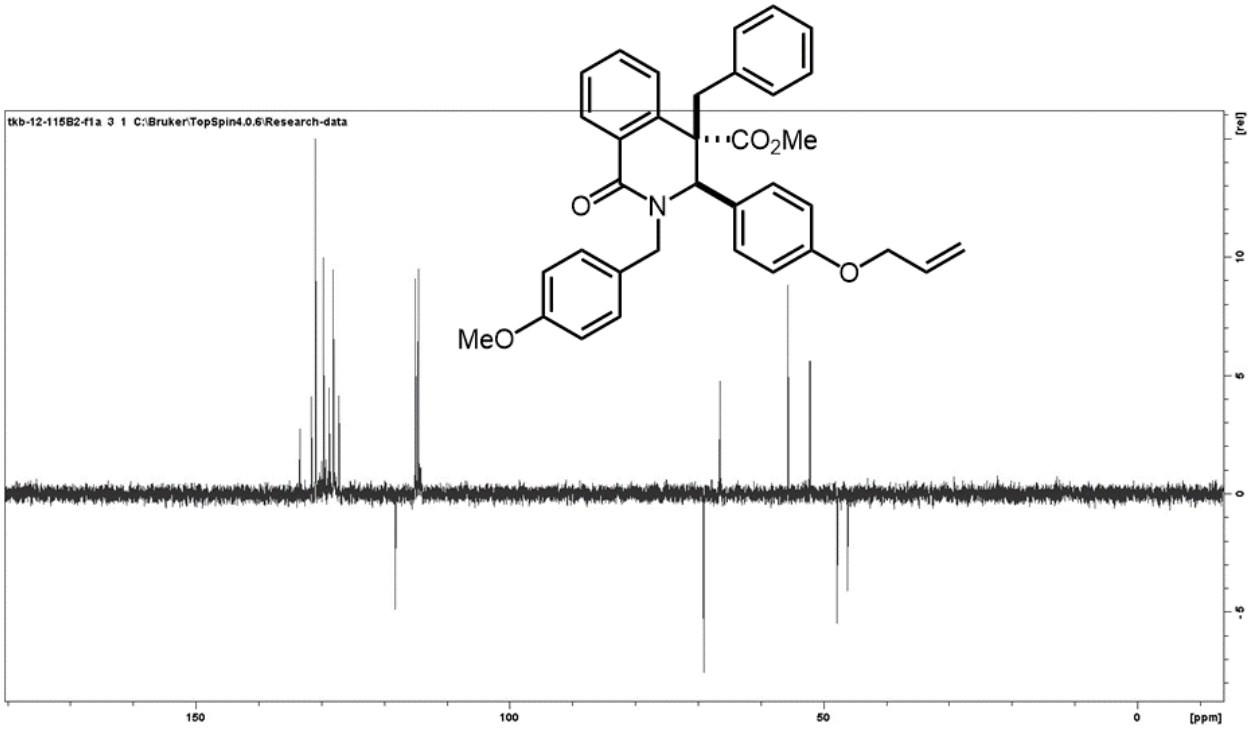
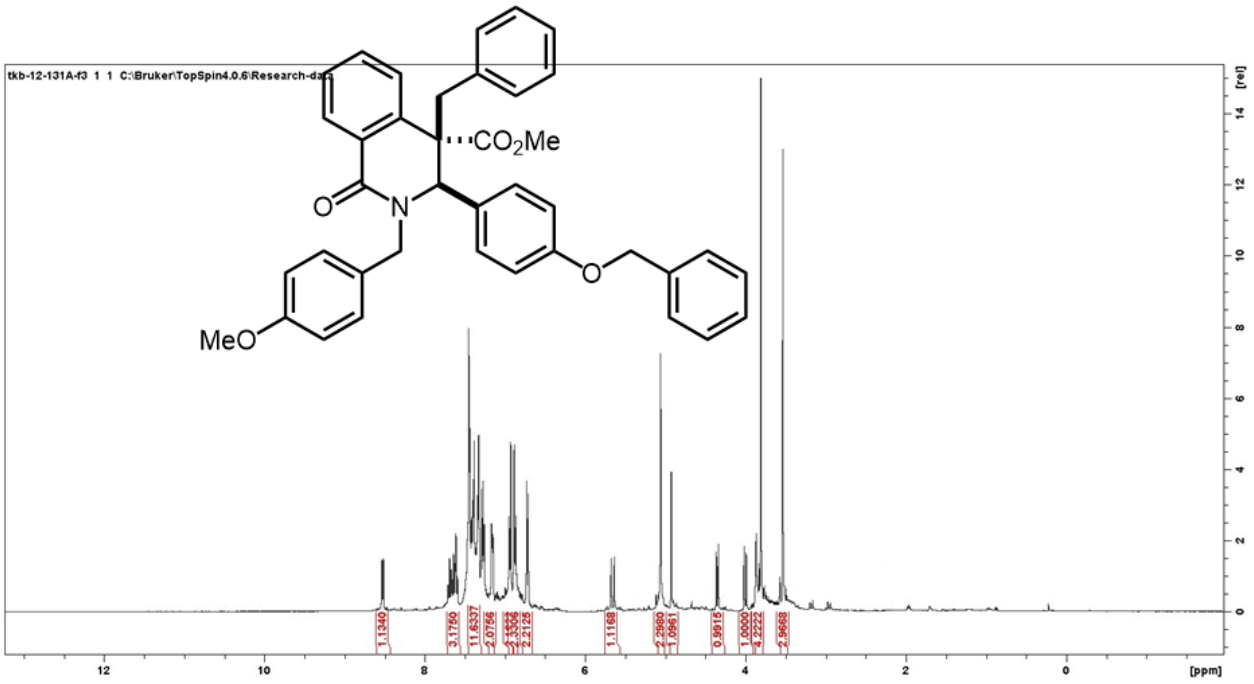


Compound 2e

Prepared from ester **1e** (253.8 mg, 0.5 mmol) and benzyl 4-nitrophenylcarbonate (136.62, 0.5 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yield = 254 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.67 – 7.59 (m, 3H), 7.53 – 7.35 (m, 10H), 7.31 – 7.20 (m, 1H), 7.03 – 6.80 (m, 2H), 6.93 – 6.74 (m, 4H), 6.74 – 6.54 (m, 2H), 5.64 (d, *J* = 15.1 Hz, 1H), 5.04 (s, 2H), 4.91 (s, 1H), 4.34 (d, *J* = 10.3 Hz, 1H), 3.99 (d, *J* = 10.3 Hz, 1H), 3.84 – 3.69 (m, 1H), 3.80 (s, 3H), 3.52 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.67, 162.37, 159.20, 158.92, 137.32, 136.73, 131.30, 129.98, 129.89, 129.59, 129.39, 129.26, 128.74, 128.72, 128.69, 128.34, 128.21, 128.18, 127.76, 127.65, 127.61, 127.59, 127.22, 115.02, 113.92, 83.03, 70.02, 67.53, 67.24, 55.28, 52.45, 47.59. FTIR (KBr): 2965.2971, 2872.3128, 1716.4748, 1650.8904, 1612.9884, 1585.9456, 1513.1051, 1455.3449, 1359.3702, 1304.1365, 1251.3997, 1177.4761, 1135.5369, 1033.8548, 996.7497, 896.0777, 833.6912, 804.9269. HRMS calc for $C_{39}H_{35}NO_5$ 597.2515, found 597.2510.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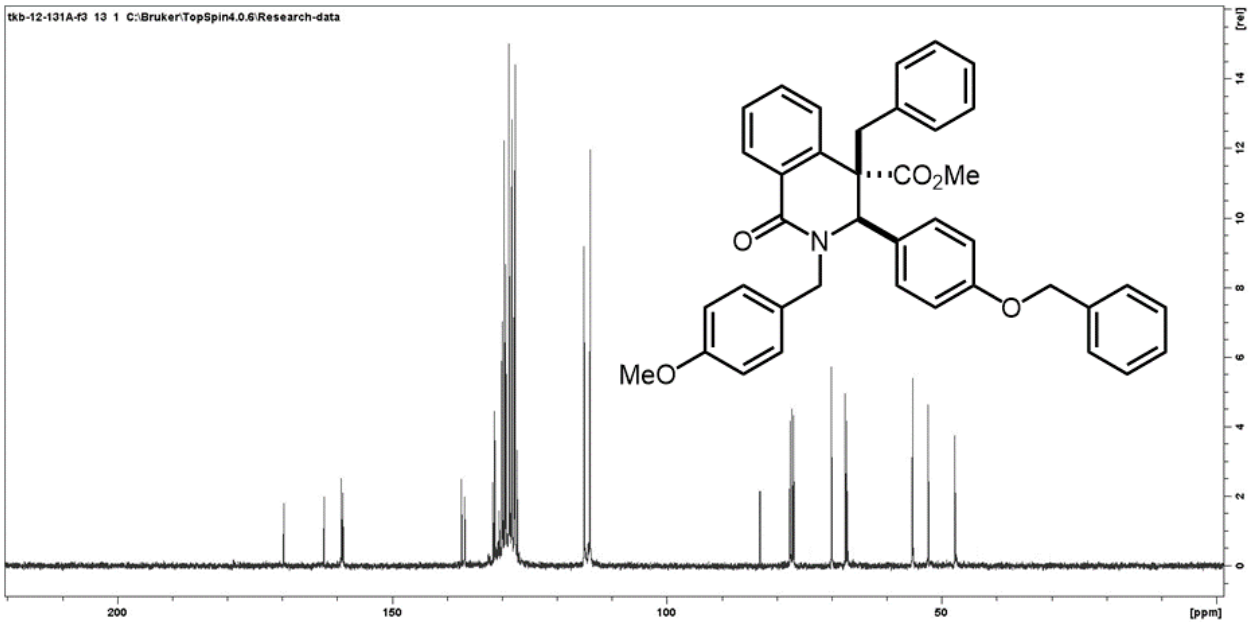
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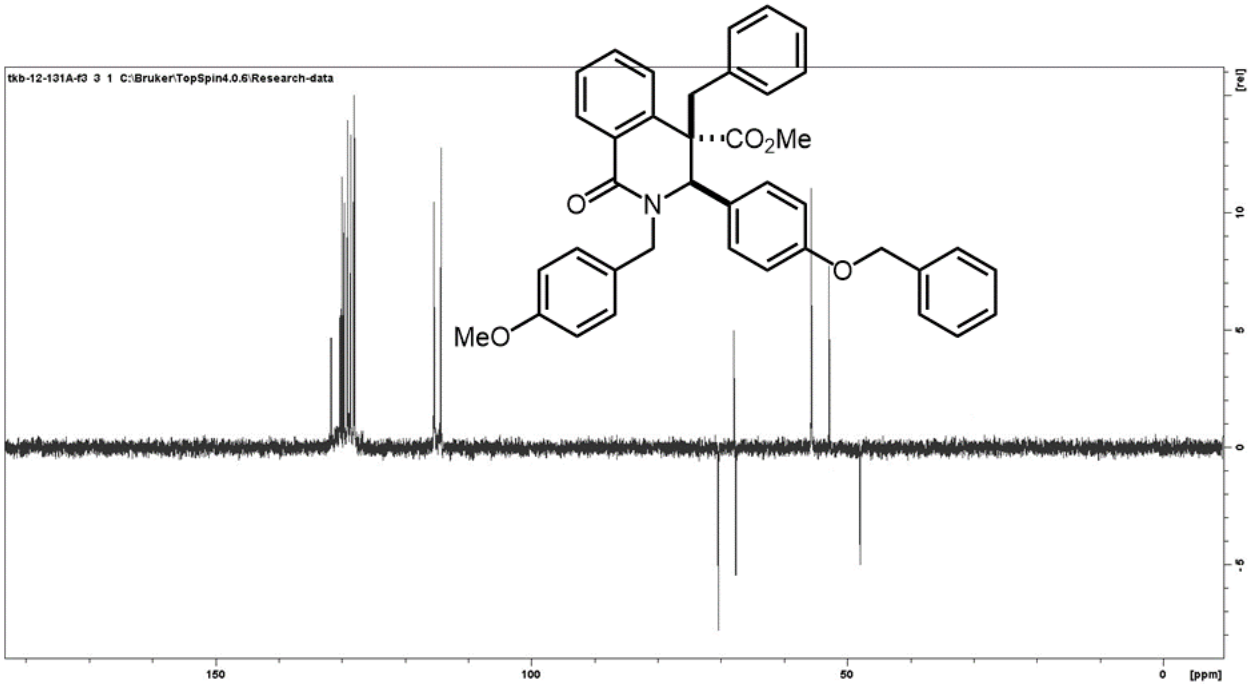
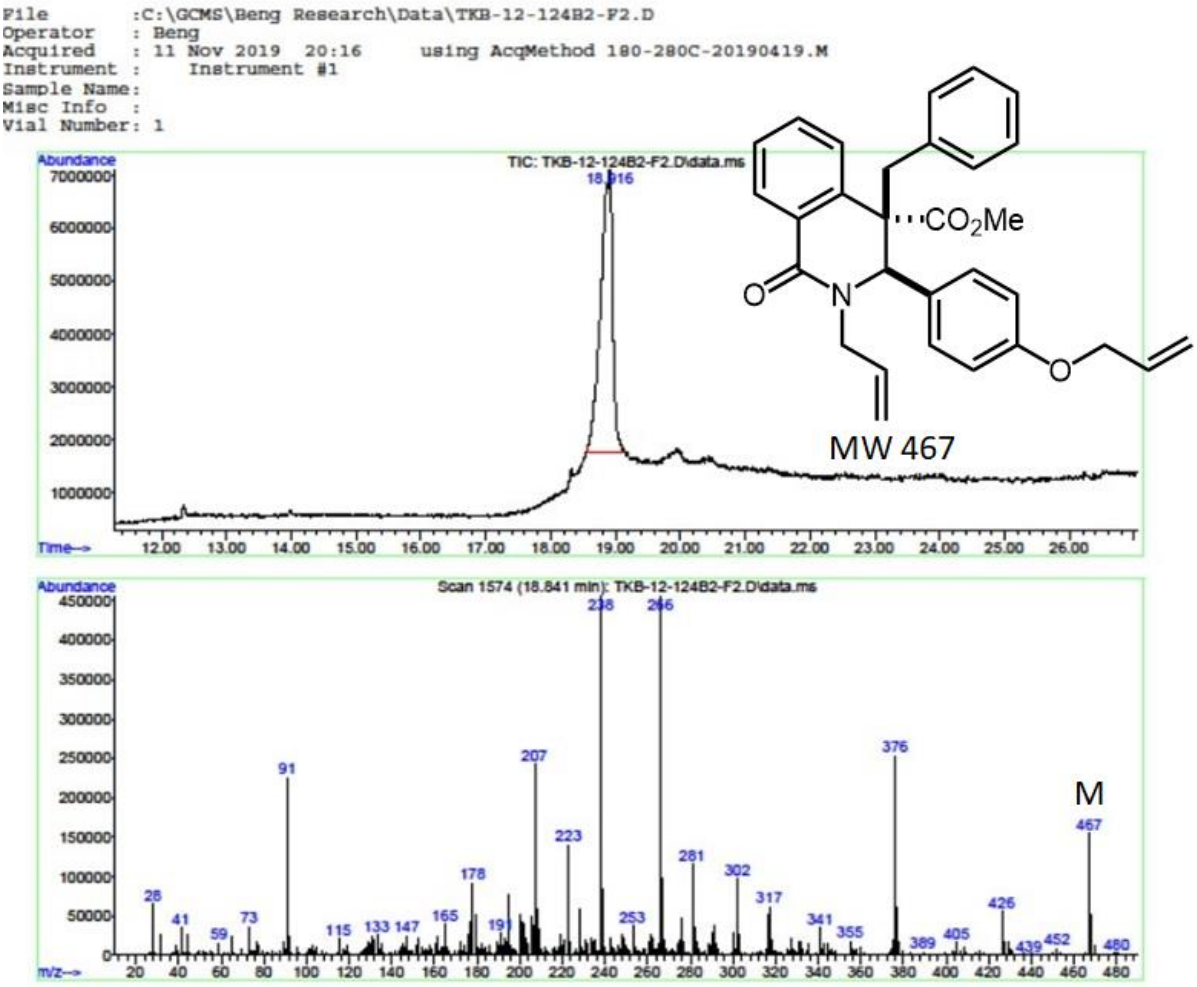


Compound 2f

Prepared from ester **1f** (188.7 mg, 0.5 mmol) and benzyl 4-nitrophenylcarbonate (136.62, 0.5 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Yield = 184.7 mg, 79%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.23 (td, *J* = 7.6, 1.2 Hz, 1H), 7.03 – 6.83 (m, 4H), 6.80 – 6.69 (m, 2H), 6.60 – 6.49 (m, 2H), 6.45 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.45 – 6.36 (m, 2H), 5.88 – 5.67 (m, 2H), 5.23 – 5.12 (m, 3H), 5.12 – 5.03 (m, 1H), 4.83 (ddt, *J* = 14.6, 4.7, 1.6 Hz, 1H), 4.61 (s, 1H), 4.26 (dt, *J* = 5.3, 1.6 Hz, 2H), 3.63 (d, *J* = 12.9 Hz, 1H), 3.28 (s, 3H), 3.08 (dd, *J* = 14.7, 8.8 Hz, 1H), 3.01 (d, *J* = 12.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.28, 162.71, 158.83, 135.98, 135.19, 133.09, 132.86, 131.21, 130.67, 130.55, 129.27, 128.97, 128.30, 128.16, 127.89, 127.72, 126.94, 119.84, 117.82, 114.68, 68.74, 66.86, 58.42, 51.89, 47.98, 46.11. FTIR (KBr): 2960.2931, 2872.3128, 1716.4748, 1650.8904, 1612.9884, 1585.9456, 1513.1051, 1455.3449, 1359.3702, 1304.1365, 1251.3997, 1177.4761, 1135.5369, 1033.8548, 996.7497. HRMS calc for $C_{30}H_{29}NO_4$ 467.2097, found 467.2084.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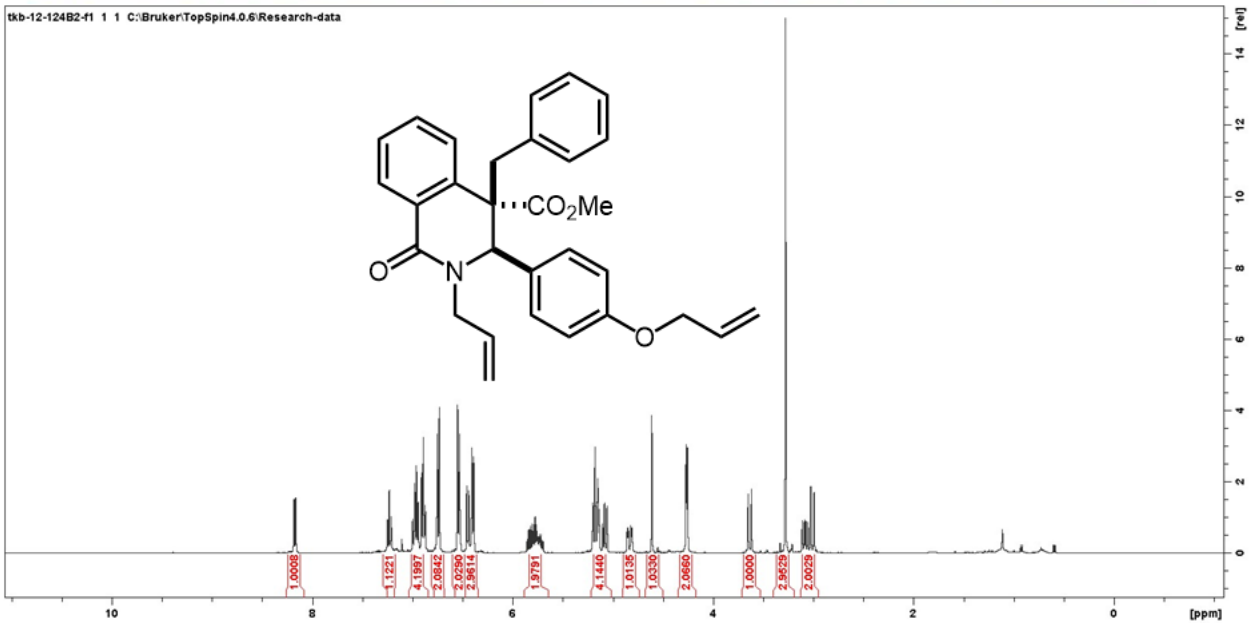
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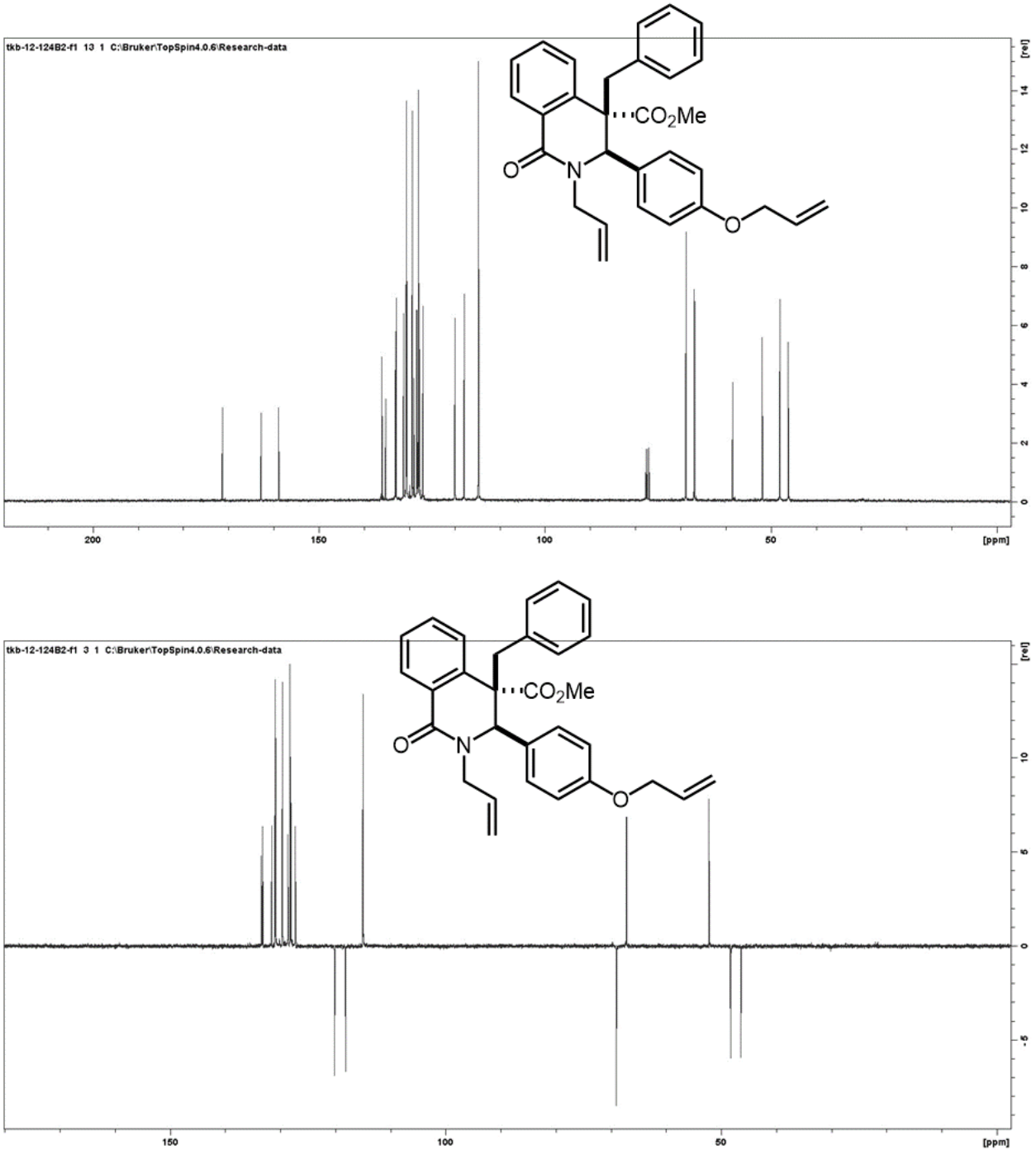
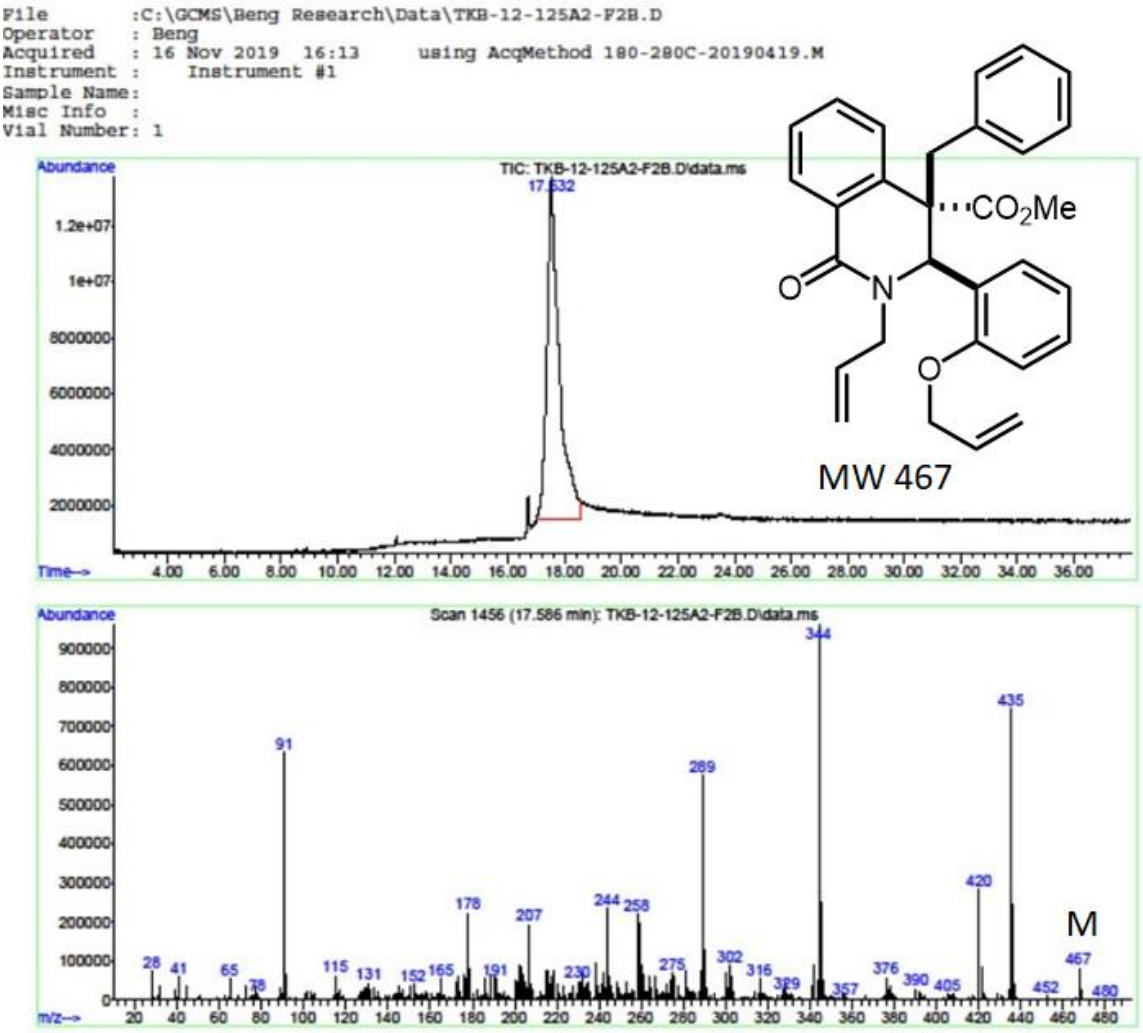
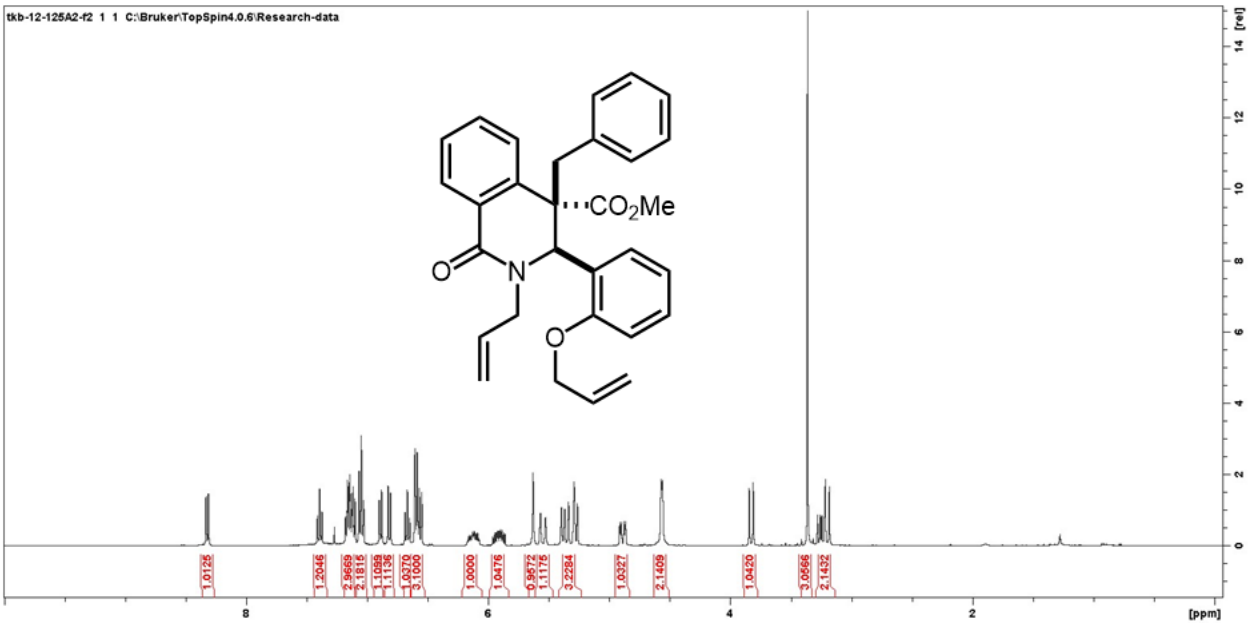


Compound 2g

Prepared from ester **1g** (188.7 mg, 0.5 mmol) and benzyl 4-nitrophenylcarbonate (136.62, 0.5 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Yield = 191.5 mg, 82%.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.33 (td, *J* = 7.6, 1.2 Hz, 1H), 7.17 – 6.89 (m, 5H), 6.83 (dd, *J* = 7.8, 1. 7 Hz,

1H), 6.75 (dd, *J* = 8.3, 1.1 Hz, 1H), 6.60 (td, *J* = 7.6, 1.1 Hz, 1H), 6.59 – 6.46 (m, 3H), 6.16 (ddt, *J* = 17.2, 10.3, 4.9 Hz, 1H), 5.85 (dddd, *J* = 17.1, 10.0, 8.7, 5.0 Hz, 1H), 5.57 (s, 1H), 5.48 (dq, *J* = 17.3, 1.7 Hz, 1H), 5.32 (dq, *J* = 10.6, 1.5 Hz, 1H), 5.30 – 5.17 (m, 2H), 4.83 (ddt, *J* = 14.4, 4.9, 1.5 Hz, 1H), 4.53 (d, *J* = 4.6 Hz, 2H), 3.76 (d, *J* = 13.0 Hz, 1H), 3.30 (s, 3H), 3.27 – 3.15 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.16, 162.79, 155.75, 136.21, 136.06, 133.12, 132.68, 130.83, 130.72, 130.63, 129.68, 128.95, 128.30, 128.18, 127.76, 127.59, 126.79, 125.98, 121.20, 119.68, 117.38, 111.50, 69.08, 58.16, 57.51, 51.64, 48.27, 46.02. FTIR (KBr): 2965.2981, 2876.3125, 1716.4748, 1650.8904, 1612.9884, 1585.9456, 1513.1051, 1455.3449, 1359.3702, 1304.1365, 1251.3997, 1177.4761, 1135.5369, 1033.8548, 996.7497. HRMS calc for $C_{30}H_{29}NO_4$ 467.2097, found 467.2084.

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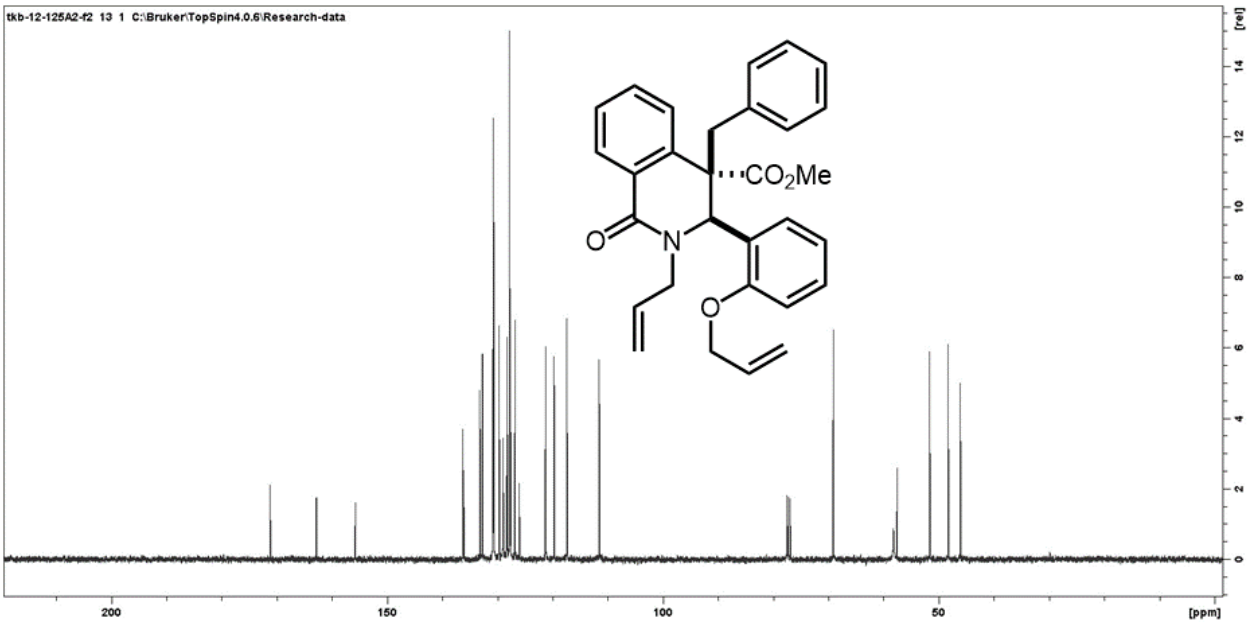
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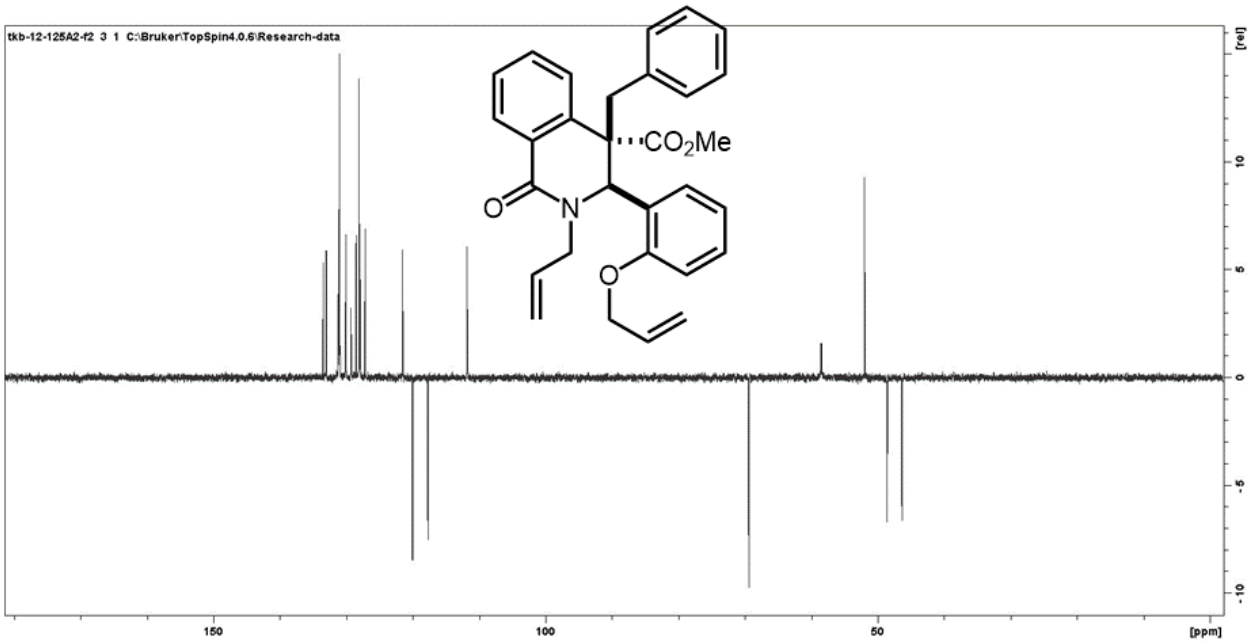

Compound 2h

Prepared from ester **1h** (200 mg, 0.5 mmol) and benzyl 4-nitrophenylcarbonate (136.62, 0.5 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Yield = 210.7 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.51 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.46 (td, *J* = 7.6, 1.2 Hz, 1H), 7.18 – 6.96 (m, 7H), 6.62 – 6.54 (m, 3H), 5.84 (dddd, *J* = 17.1, 10.1, 8.4, 5.0 Hz, 1H), 5.53 (s, 1H), 5.47 – 5.34 (m, 1H), 5.27 – 5.19 (m, 1H), 4.76 (ddt, *J* = 14.7, 5.1, 1.5 Hz, 1H), 3.79 (d, *J* = 13.0 Hz, 1H), 3.39 (s, 3H), 3.40 – 3.21 (m, 1H), 3.15 (d, *J* = 13.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.70, 162.19, 137.09, 135.71, 135.56, 132.99, 132.31, 130.97, 130.92, 130.65, 130.28, 129.52, 128.34, 128.29, 127.91, 127.89, 127.02, 124.41, 119.87, 64.54, 57.33, 51.99, 48.43, 46.41. FTIR (KBr): 2969.2955, 2872.3128, 1715.4747, 1650.8904, 1585.9456, 1513.1051, 1455.3449, 1359.3702, 1304.1365, 1251.3997, 1177.4761, 1135.5369, 1033.8548, 993.7422. HRMS calc for $C_{27}H_{24}BrNO_3$ 489.0940, found 489.0949.

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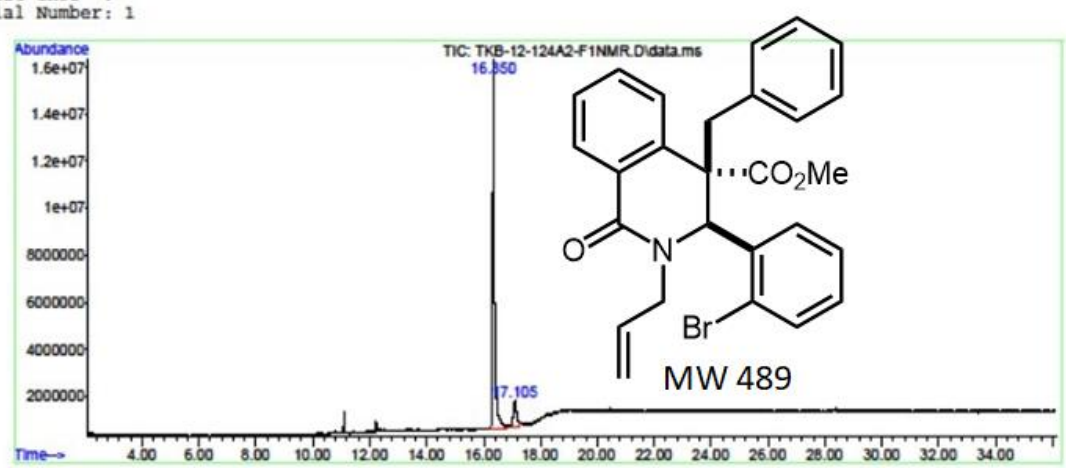
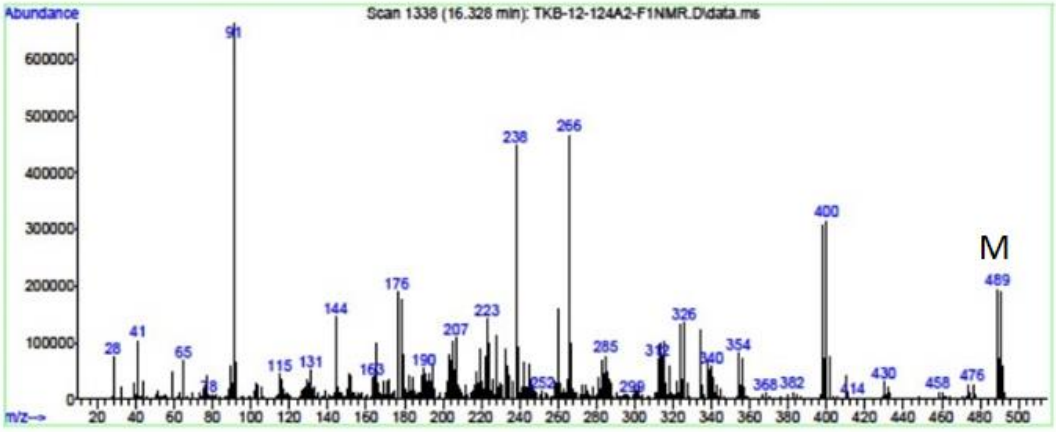
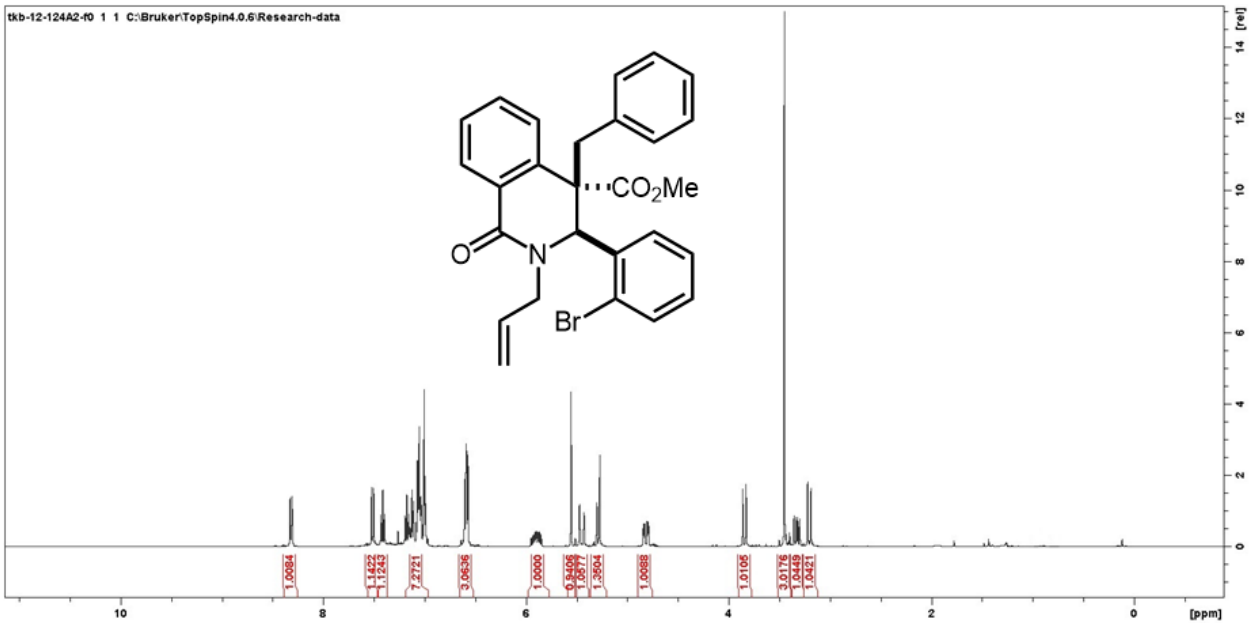
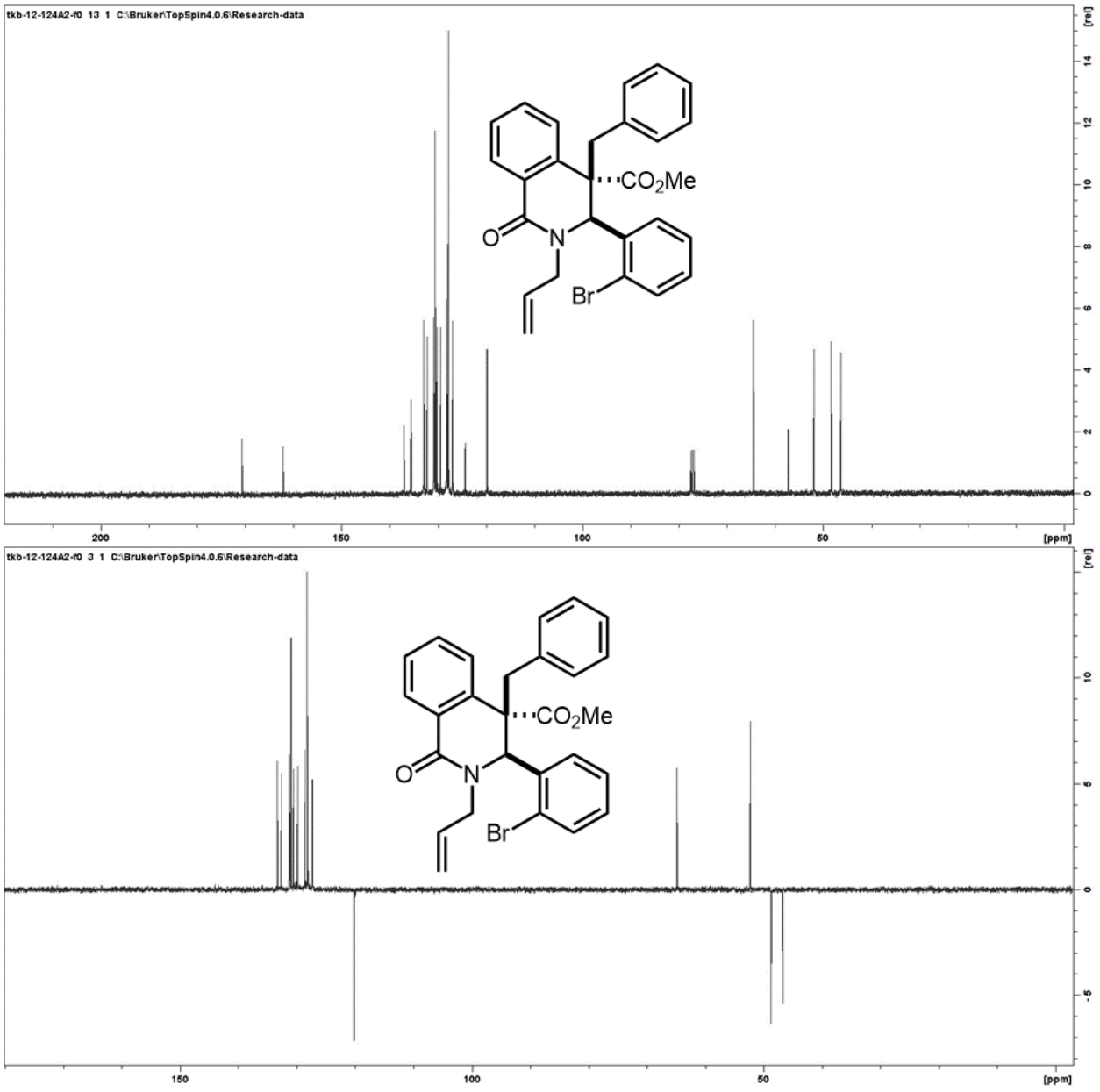




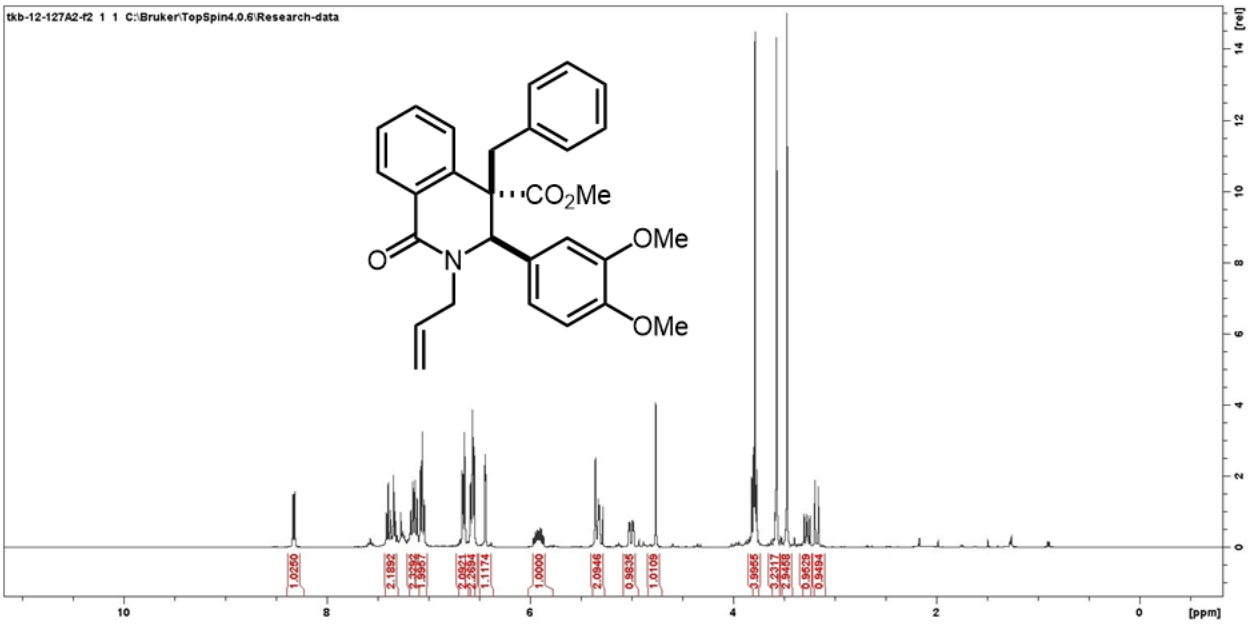


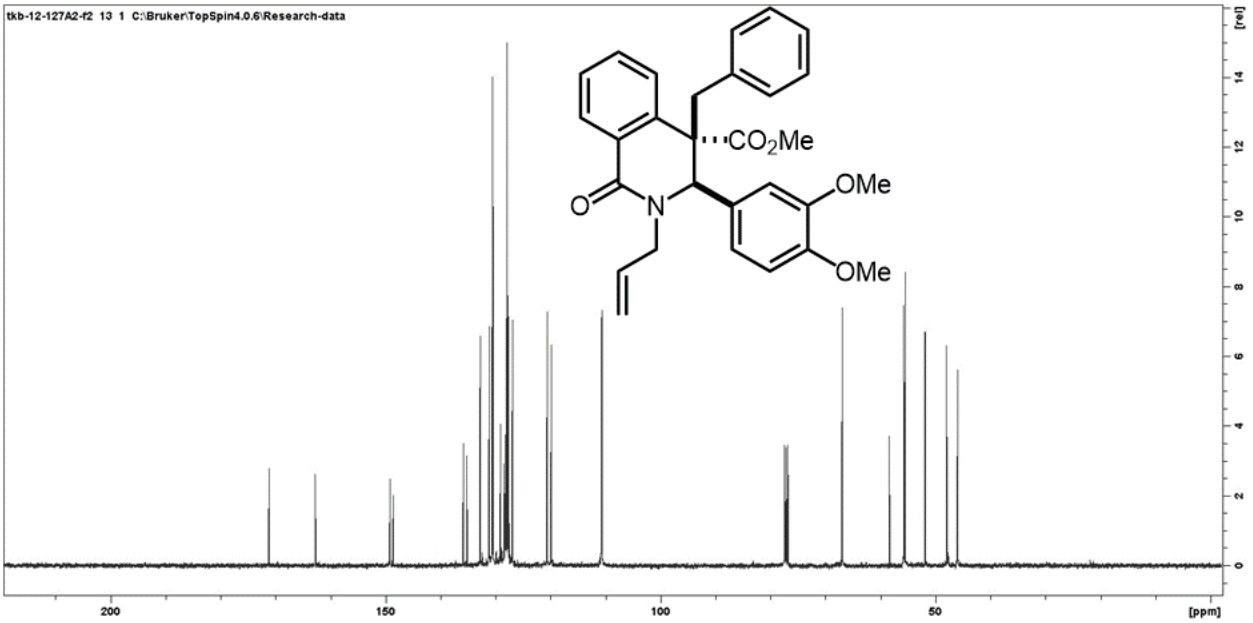


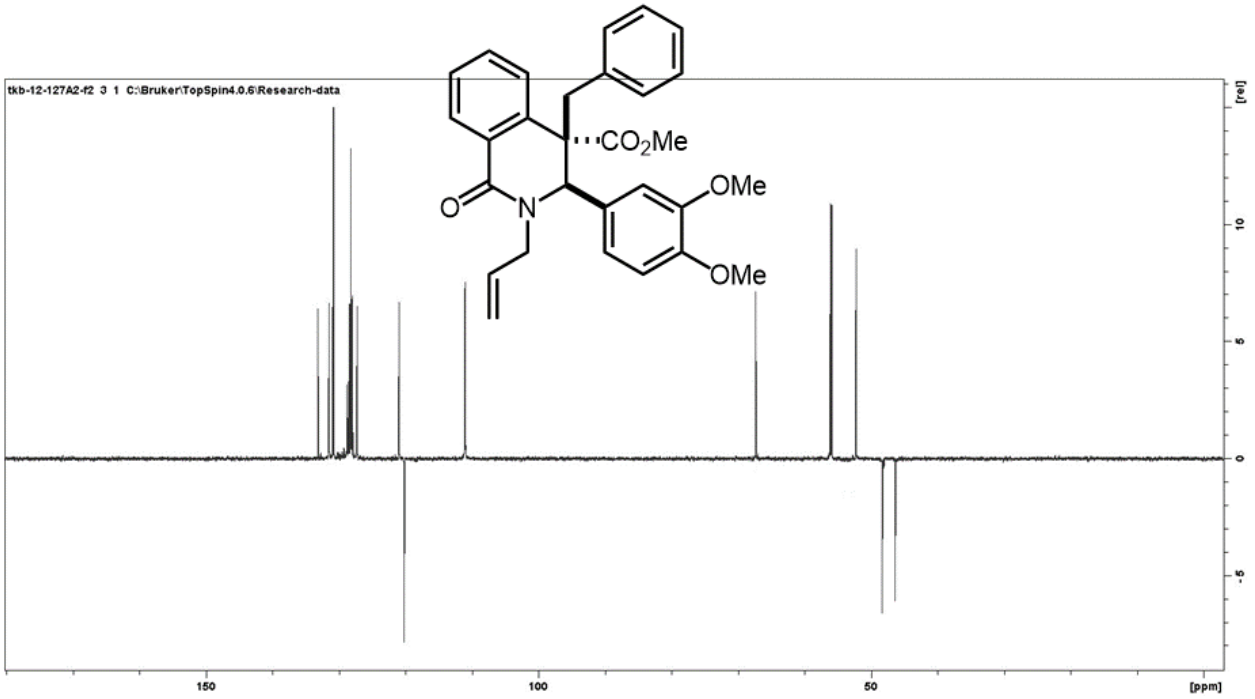
Compound 2i

Prepared from ester **1i** (190.7 mg, 0.5 mmol) and benzyl 4-nitrophenylcarbonate (136.62, 0.5 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (30:70). Yield = 207.5 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, J = 7.8, 1.5 Hz, 1H), 7.38 – 7.33 (m, 2H), 7.31 – 7.02 (m, 4H), 6.67 – 6.61 (m, 2H), 6.60 (dd, J = 8.4, 6.6 Hz, 2H), 6.37 (d, J = 2.2 Hz, 1H), 5.85 (dtd, J = 18.0, 9.1, 4.7 Hz, 1H), 5.29 (d, J = 2.2 Hz, 1H), 5.25 (d, J = 4.7 Hz, 1H), 4.94 (ddt, J = 14.8, 4.9, 1.6 Hz, 1H), 4.69 (s, 1H), 3.84 – 3.68 (m, 1H), 3.72 (s, 3H), 3.51 (s, 3H), 3.40 (s, 3H), 3.21 (dd, J = 14.8, 8.8 Hz, 1H), 3.11 (d, J = 12.9 Hz,

1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.25, 162.80, 149.20, 148.68, 135.89, 135.26, 132.85, 131.19, 130.70, 130.53, 129.16, 128.49, 128.27, 128.23, 128.11, 127.90, 127.73, 126.96, 120.67, 119.89, 110.82, 110.72, 67.01, 58.41, 55.80, 55.59, 51.94, 48.01, 46.05. FTIR (KBr): 2944.2832, 2872.3100, 1717.4743, 1655.8901, 1585.9456, 1513.1051, 1455.3449, 1359.3702, 1304.1365, 1251.3997, 1177.4761, 1135.5369, 1033.8548, 993.7411, 893.7422. HRMS calc for $C_{29}H_{29}NO_5$ 471.2046, found 471.2044.







Compound 2j

Prepared from ester **1j** (166.7 mg, 0.5 mmol) and benzyl 4-nitrophenylcarbonate (136.62, 0.5 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Yield = 167.3 mg, 79%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, 1H), 7.57 – 7.42 (m, 3H), 7.36 – 7.30 (m, 4H), 7.28 – 7.14 (m, 4H), 6.89 (d, *J* = 1.7 Hz, 2H), 5.68 (d, *J* = 14.5 Hz, 1H), 4.38 (s, 1H), 3.42 (d, *J* = 14.5 Hz, 1H), 3.29 (s, 3H), 2.66 (d, *J* = 16.1 Hz, 1H), 2.47 (d, *J* = 16.1 Hz, 1H), 1.57 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.88, 162.98, 136.75, 136.51, 135.50, 131.29, 130.37, 129.22, 128.89, 128.67, 128.40, 128.12, 128.04, 127.94, 80.45, 74.27, 66.33, 56.01, 52.13, 48.22, 31.77, 3.54. FTIR (KBr): 2965.2971, 2872.3128, 1716.4748, 1650.8904, 1612.9884, 1585.9456, 1513.1051, 1455.3449, 1359.3702, 1304.1365, 1251.3997, 1177.4761, 1135.5369, 1033.8548, 996.7497, 896.0777, 833.6912, 804.9269. HRMS calc for $C_{28}H_{25}NO_3$ 423.1834, found 423.1838.

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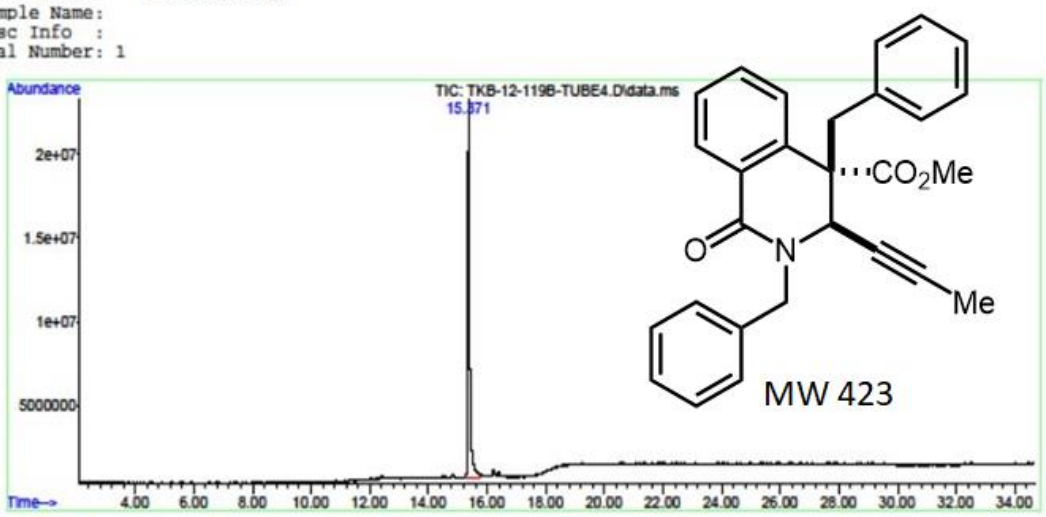
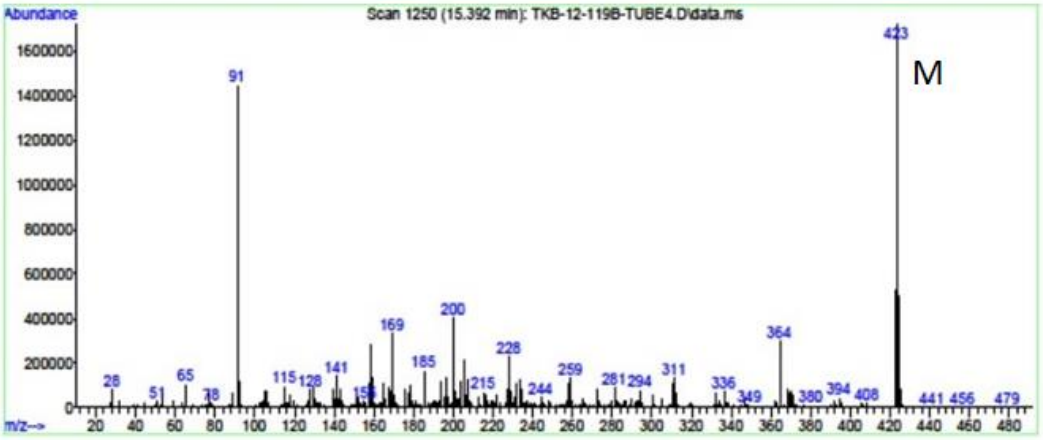
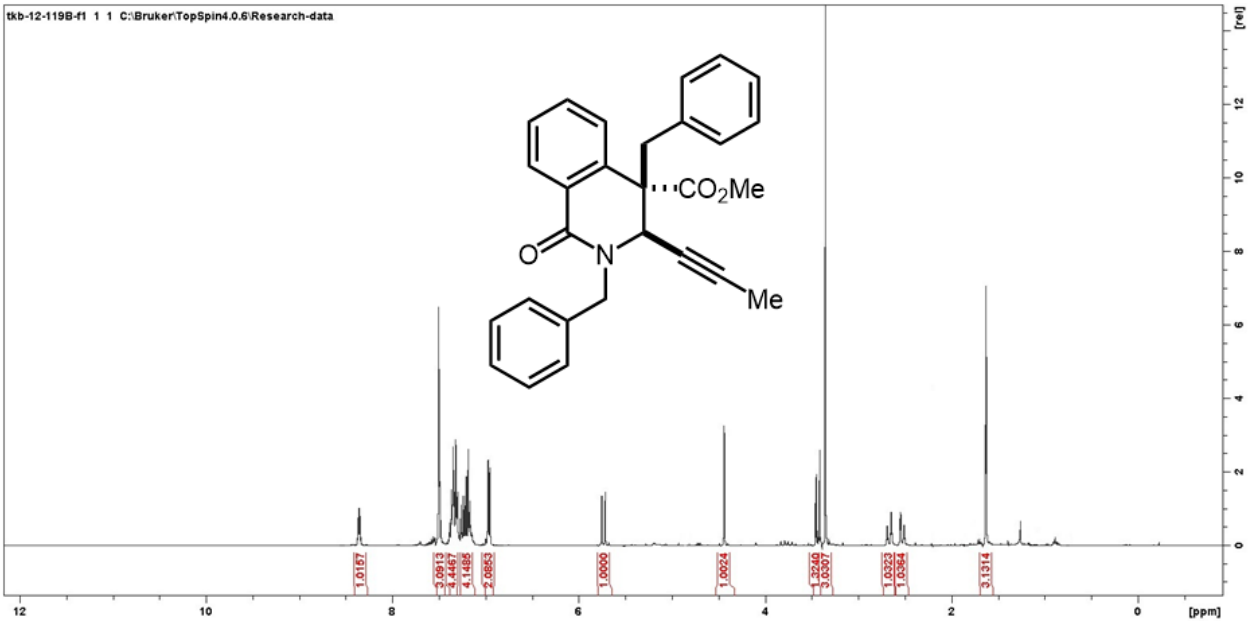
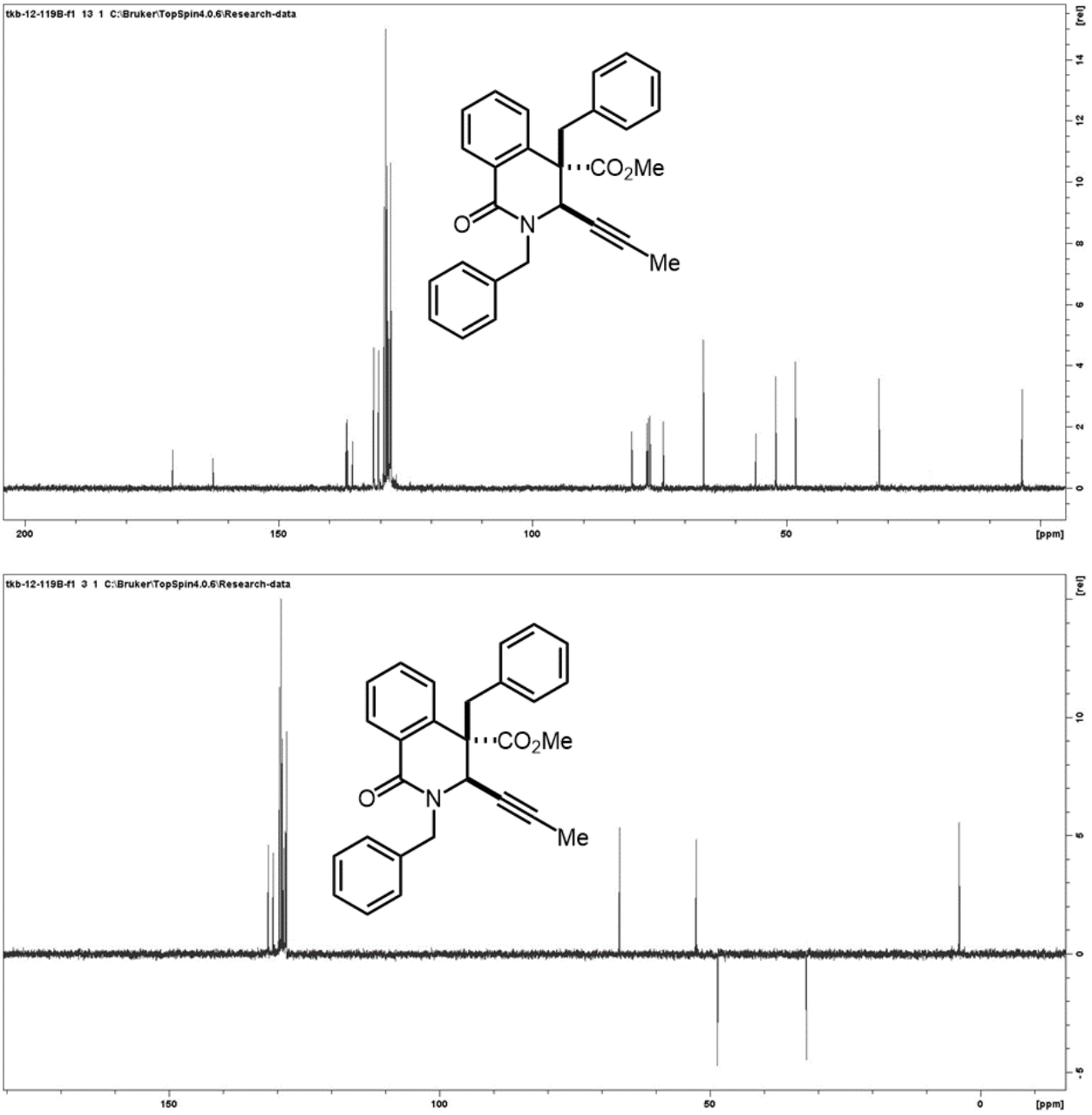




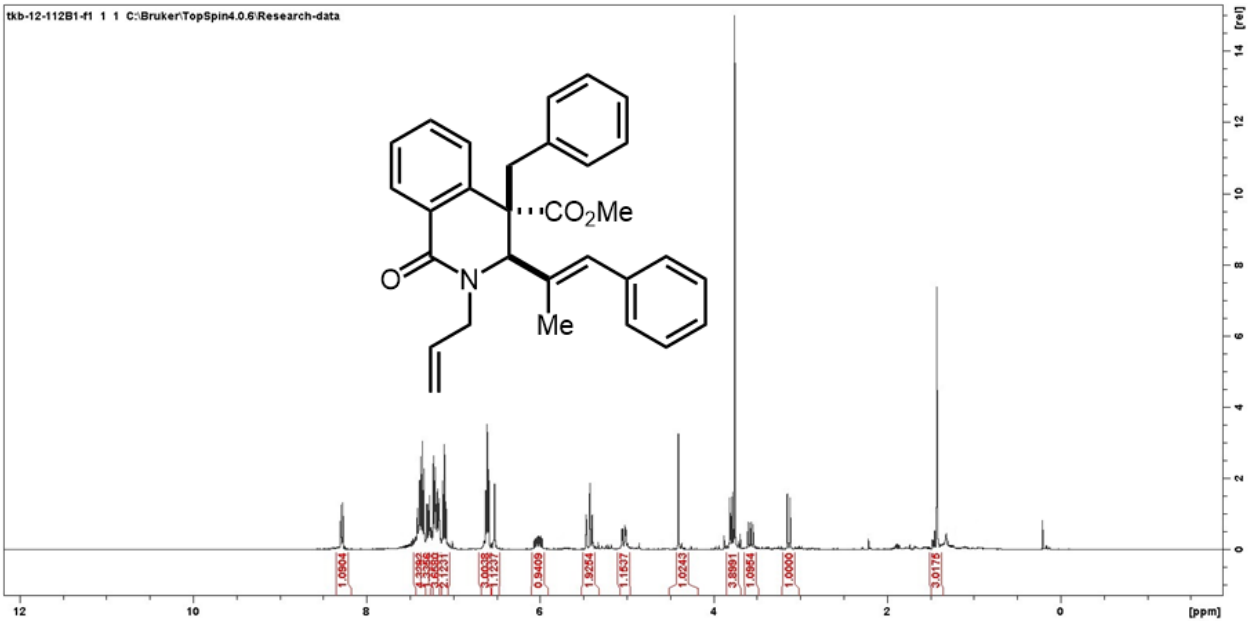


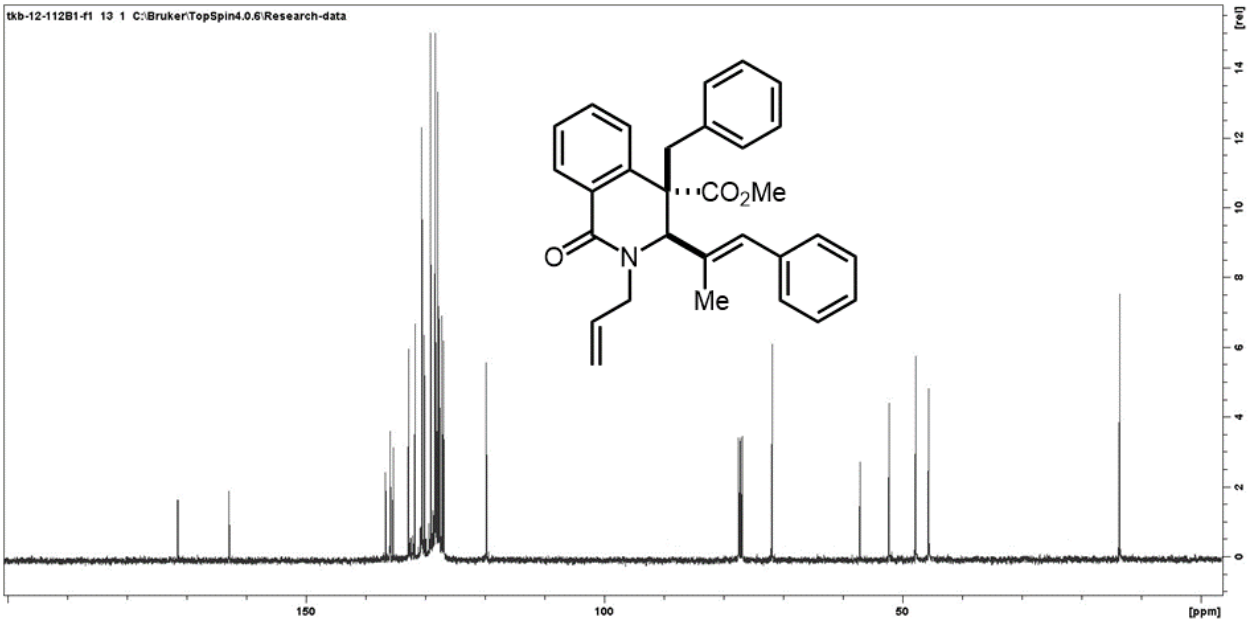


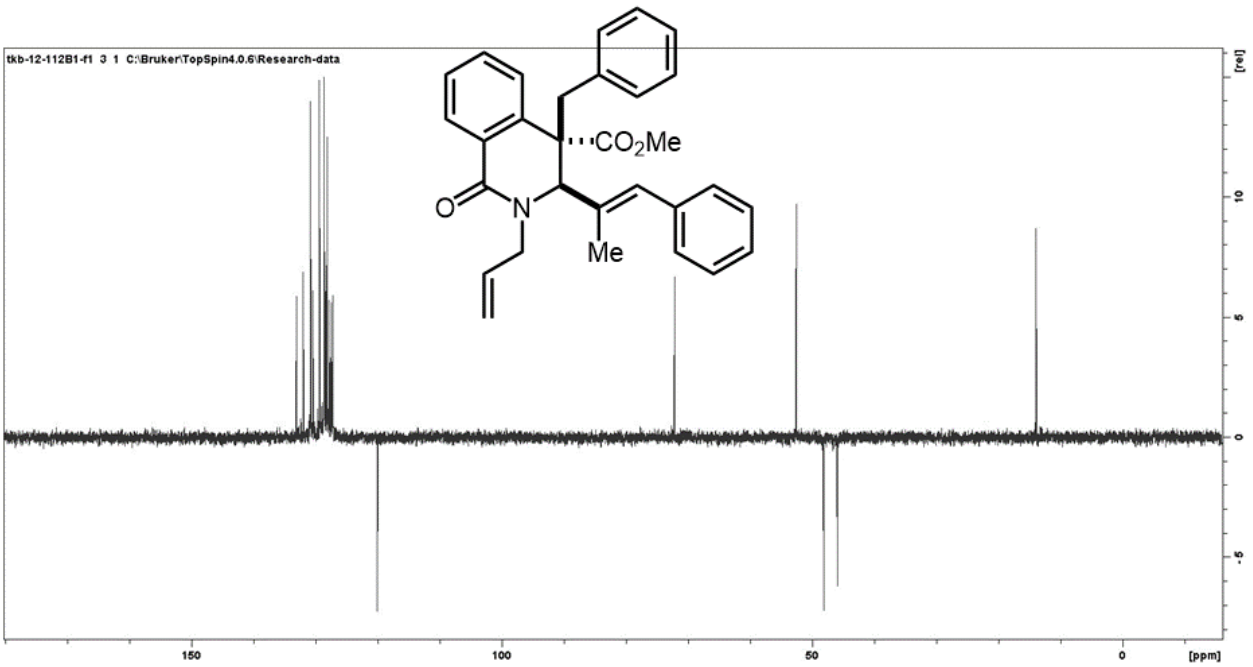
Compound 2k

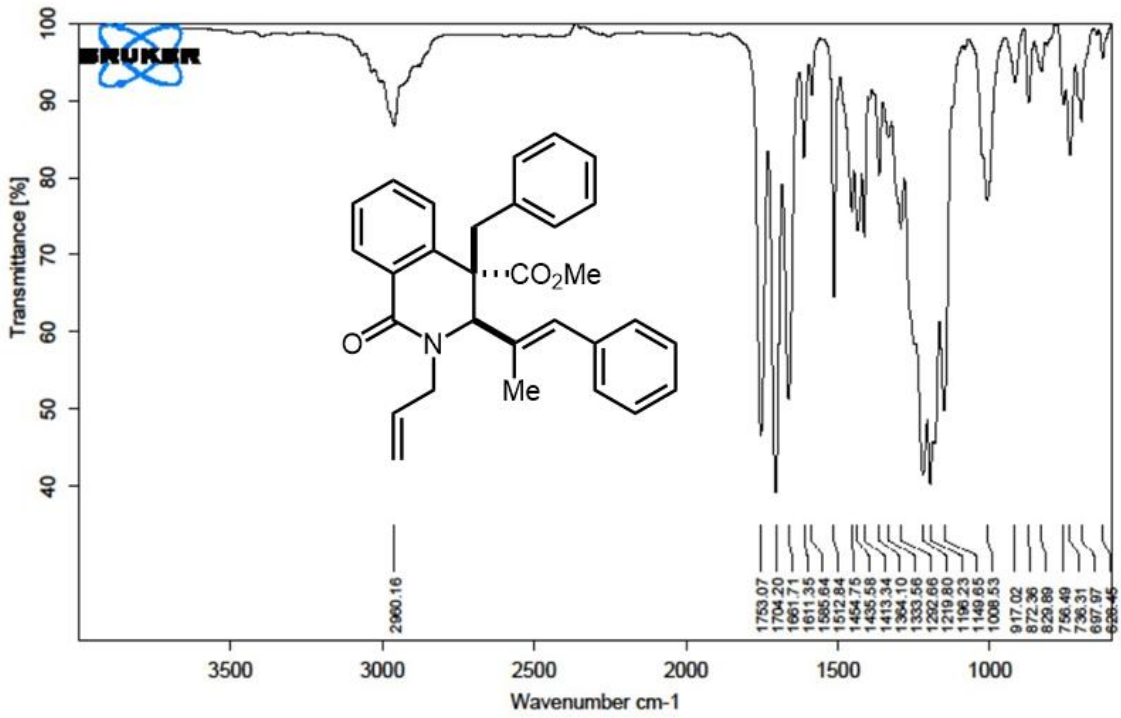
Prepared from ester **1k** (180.7 mg, 0.5 mmol) and benzyl 4-nitrophenylcarbonate (136.62, 0.5 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Yield = 201 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.48 – 7.01 (m, 10H), 6.58 – 6.49 (m, 3H), 6.43 (s, 1H), 6.02 (dddd, *J* = 17.1, 10.0, 8.6, 4.9 Hz, 1H), 5.40 – 5.30 (m, 2H), 4.94 (ddt, *J* = 14.6, 4.8, 1.5 Hz, 1H), 4.31 (s, 1H), 3.69

(dd, J = 12.9, 5.8 Hz, 1H), 3.66 (s, 3H), 3.64 – 3.40 (m, 1H), 3.14 (d, J = 12.9 Hz, 1H), 1.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.48, 162.86, 136.63, 135.93, 135.86, 135.36, 132.80, 131.72, 130.60, 130.55, 130.14, 129.09, 128.35, 128.32, 128.15, 128.13, 127.95, 127.87, 127.58, 127.23, 126.93, 119.77, 71.87, 57.15, 52.28, 47.82, 45.64, 13.64. FTIR (KBr): 2965.2981, 2876.3125, 1716.4748, 1650.8904, 1612.9884, 1585.9456, 1513.1051, 1455.3449, 1359.3702, 1304.1365, 1251.3997, 1177.4761, 1135.5369, 1033.8548, 996.7497. HRMS calc for $C_{30}H_{29}NO_3$ 451.2147, found 451.2153.





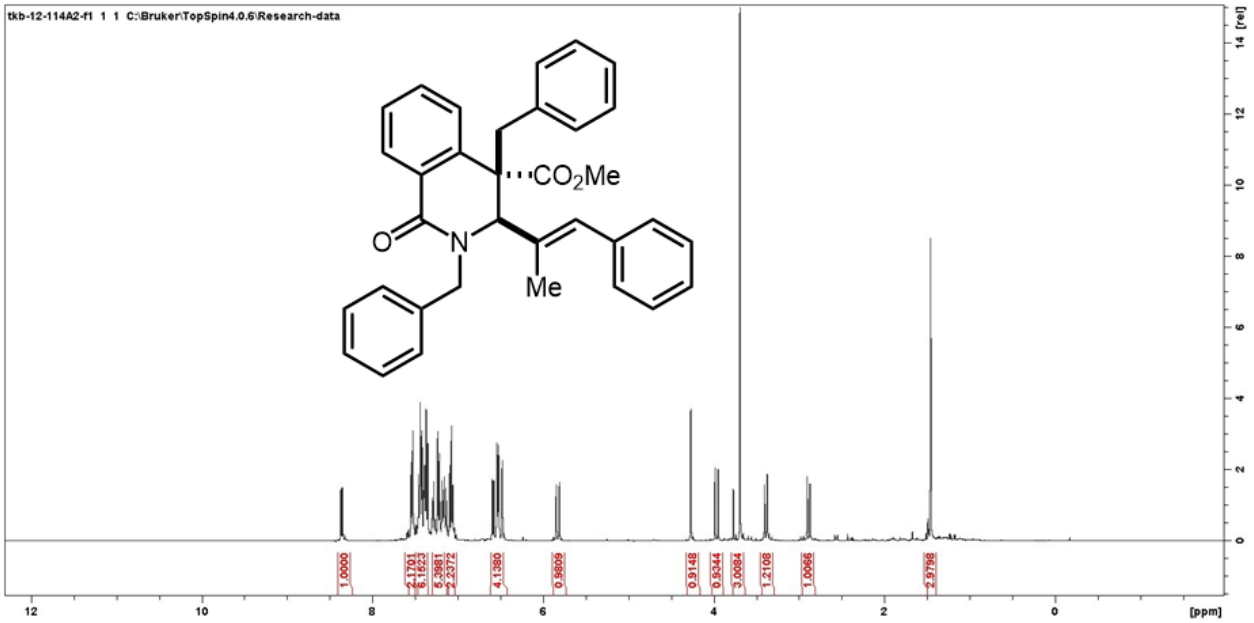


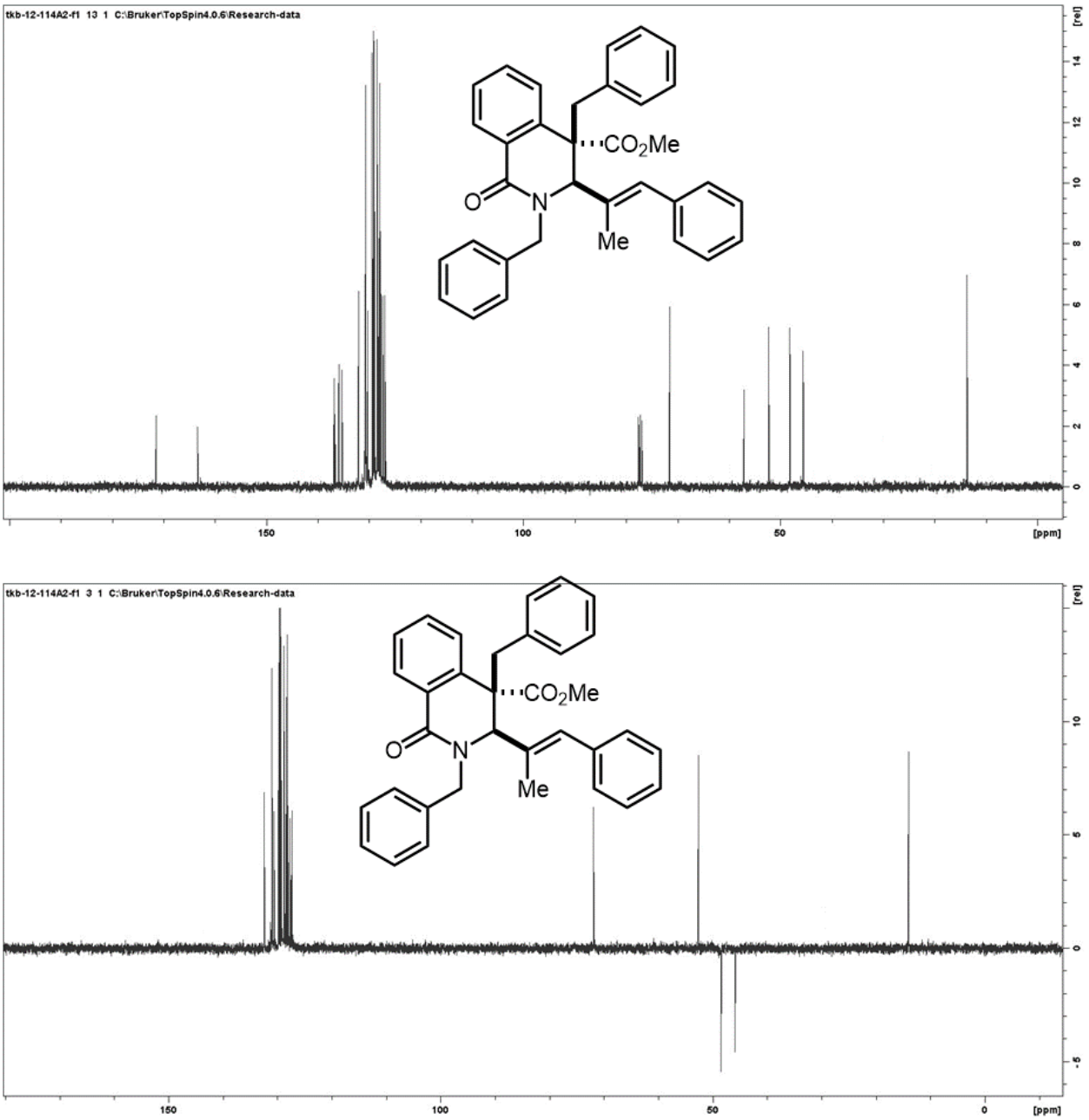


Compound 2l

Prepared from ester **1l** (205.8 mg, 0.5 mmol) and benzyl 4-nitrophenylcarbonate (136.62, 0.5 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting

with hexane/EtOAc (75:25). Yield = 210.7 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.53 – 7.13 (m, 13H), 7.17 – 7.01 (m, 2H), 6.59 – 6.46 (m, 3H), 6.39 (s, 1H), 5.74 (d, *J* = 14.4 Hz, 1H), 4.18 (s, 1H), 3.88 (d, *J* = 14.4 Hz, 1H), 3.61 (s, 3H), 3.34 (d, *J* = 13.0 Hz, 1H), 2.82 (d, *J* = 13.0 Hz, 1H), 1.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.40, 163.30, 136.80, 136.58, 135.92, 135.85, 135.21, 132.03, 130.64, 130.60, 130.24, 129.37, 129.13, 128.95, 128.93, 128.37, 128.33, 128.04, 127.84, 127.64, 127.29, 126.90, 71.48, 57.01, 52.24, 48.08, 45.49, 13.63. FTIR (KBr): 2930.9333, 1721.7229, 1664.1745, 1606.8615, 1576.9493, 1511.8758, 1422.3889, 1359.3077, 1300.0014, 1250.9591, 1175.8146, 1113.165, 1031.2694, 996.2804, 970.248, 923.7263, 826.1509, 764.8959. HRMS calc for $C_{34}H_{31}NO_3$ 501.2304, found 501.2309.

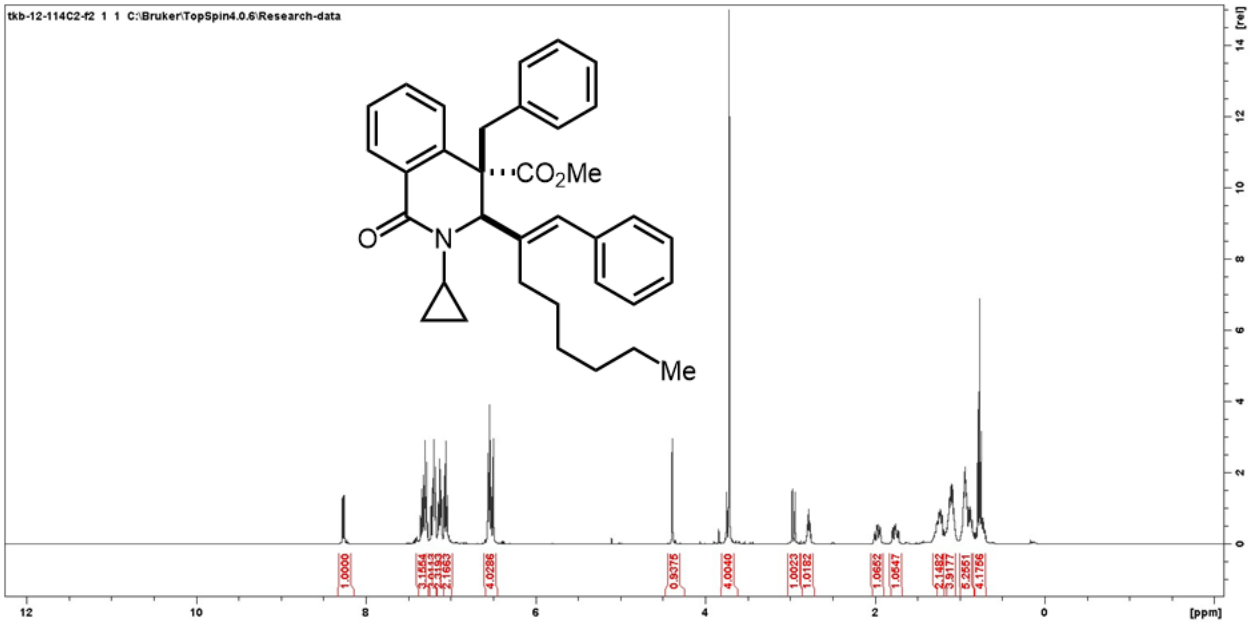


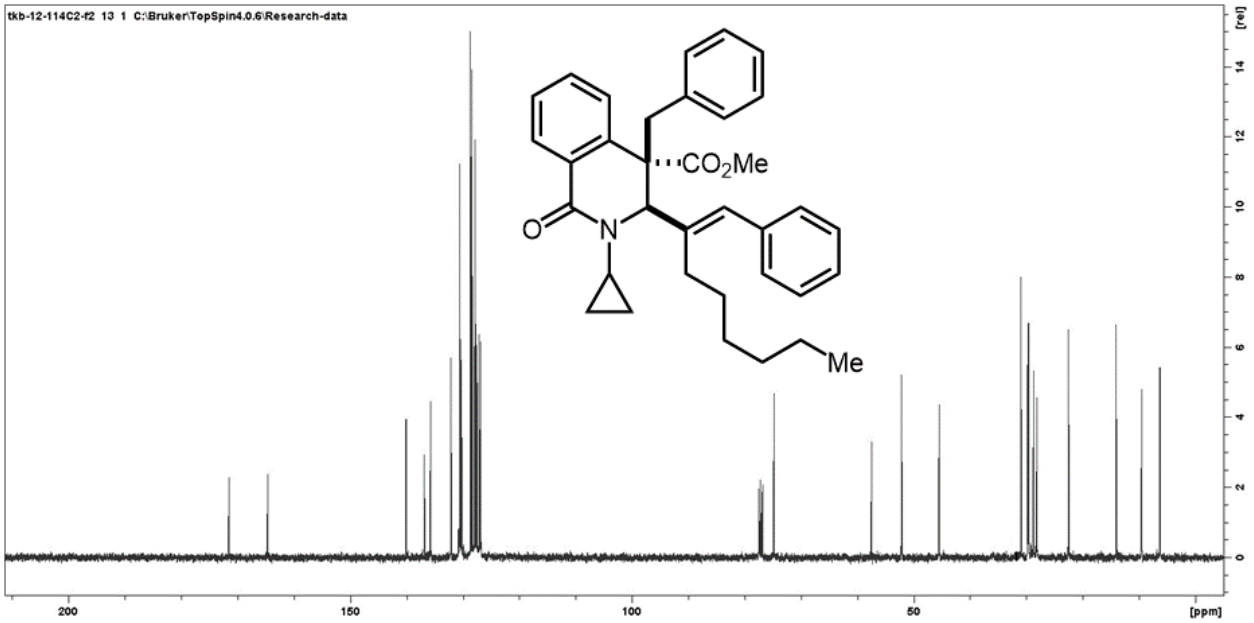


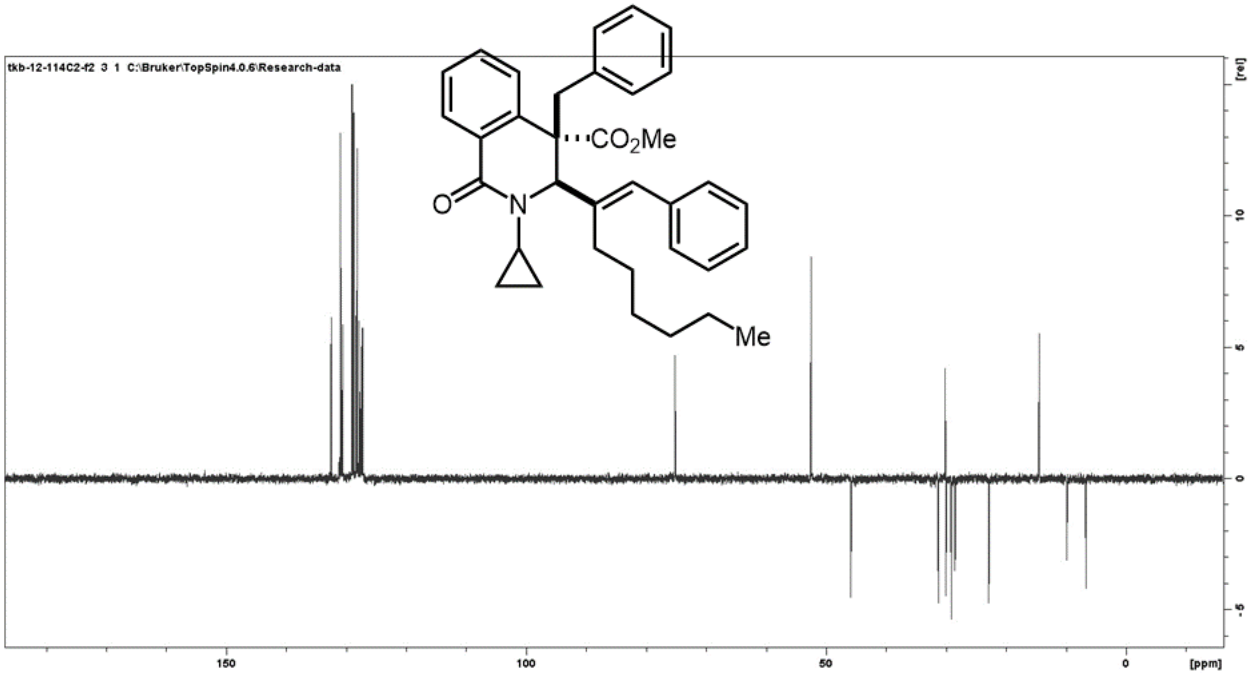
Compound 2m

Prepared from ester **1m** (215.8 mg, 0.5 mmol) and benzyl 4-nitrophenylcarbonate (136.62, 0.5 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (85:15). Yield = 213.9 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (dd, J = 7.8, 1.5 Hz, 1H), 7.41 – 7.10 (m, 10H), 6.48 – 6.43 (m, 4H), 4.33 (s, 1H), 3.59 – 3.55 (m, 4H), 2.89 (d, J = 12.8 Hz, 1H), 2.72 (tt, J = 7.0, 4.1 Hz, 1H), 1.91 (ddd, J = 14.0, 12.2, 4.7 Hz, 1H), 1.70 (ddd, J = 13.9, 12.0, 5.0 Hz, 1H), 1.27 – 1.05 (m, 6H), 0.85 – 0.72 (m, 9H). ^{13}C NMR (101

MHz, $CDCl_3$) δ 171.57, 164.69, 140.14, 136.87, 135.83, 135.80, 132.18, 130.64, 130.59, 130.28, 128.70, 128.43, 128.09, 128.05, 127.87, 127.55, 127.15, 126.95, 74.86, 57.50, 52.18, 45.54, 30.99, 29.82, 29.67, 28.79, 28.18, 22.54, 14.09, 9.57, 6.35. FTIR (KBr): 2965.2971, 2872.3128, 1716.4748, 1650.8904, 1612.9884, 1585.9456, 1513.1051, 1455.3449, 1359.3702, 1304.1365, 1251.3997, 1177.4761, 1135.5369, 1033.8548, 996.7497, 896.0777, 833.6912, 804.9269. HRMS calc for $C_{35}H_{39}NO_3$ 521.2930, found 521.2924.



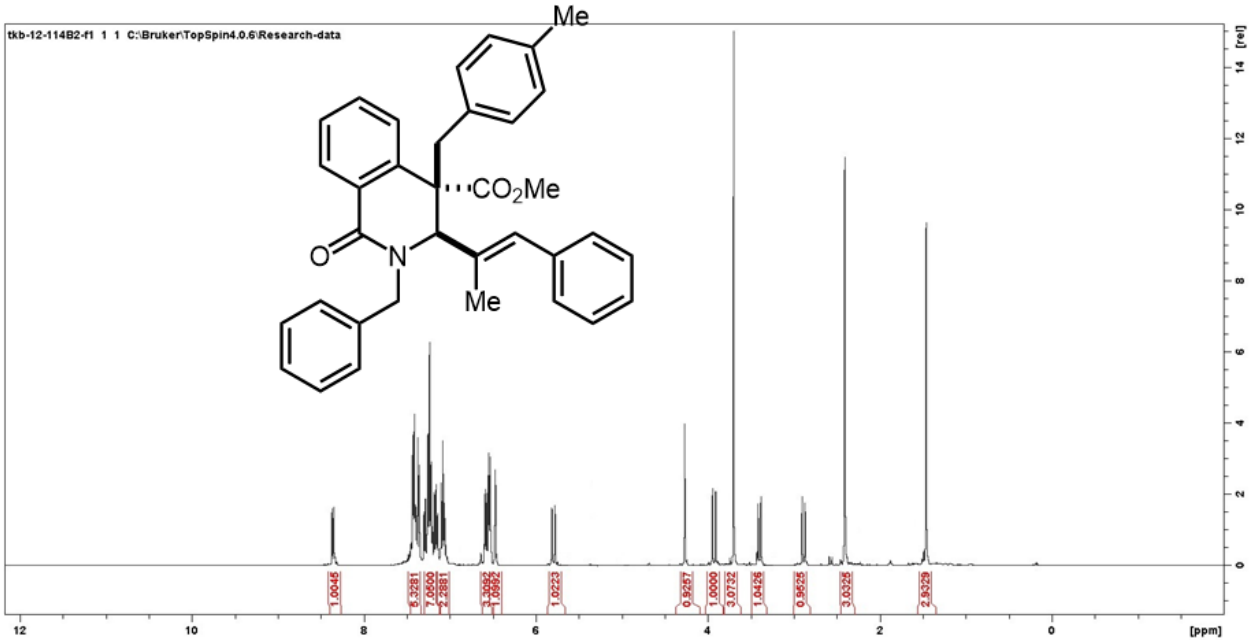




Scheme 2 results

Compound 2n

Prepared from ester **1l** (103 mg, 0.25 mmol) and carbonate **3b** (71.81, 0.25 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Yield = 110.9 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.40 – 7.26 (m, 5H), 7.24 – 7.16 (m, 7H), 7.14 (dd, *J* = 8.3, 6.7 Hz, 2H), 6.57 – 6.47 (m, 3H), 6.38 (s, 1H), 5.70 (d, *J* = 14.3 Hz, 1H), 4.18 (s, 1H), 3.83 (d, *J* = 14.4 Hz, 1H), 3.61 (s, 3H), 3.31 (d, *J* = 13.1 Hz, 1H), 2.79 (d, *J* = 13.0 Hz, 1H), 2.32 (s, 3H), 1.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.46, 163.22, 137.67, 136.63, 135.94, 135.92, 135.27, 133.68, 131.98, 130.66, 130.54, 130.22, 129.61, 129.34, 129.14, 129.10, 128.37, 128.32, 128.13, 127.84, 127.62, 127.26, 126.88, 71.32, 57.04, 52.22, 47.74, 45.47, 21.33, 13.64. HRMS calc for $C_{35}H_{33}NO_3$ 515.2460, found 515.2466.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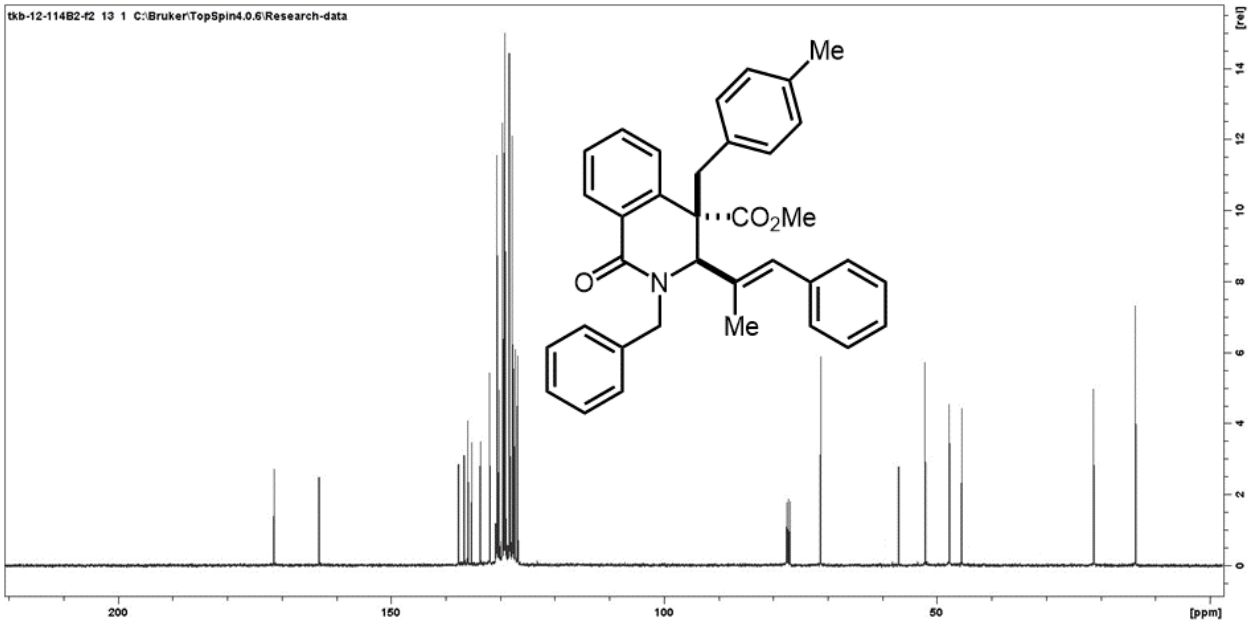
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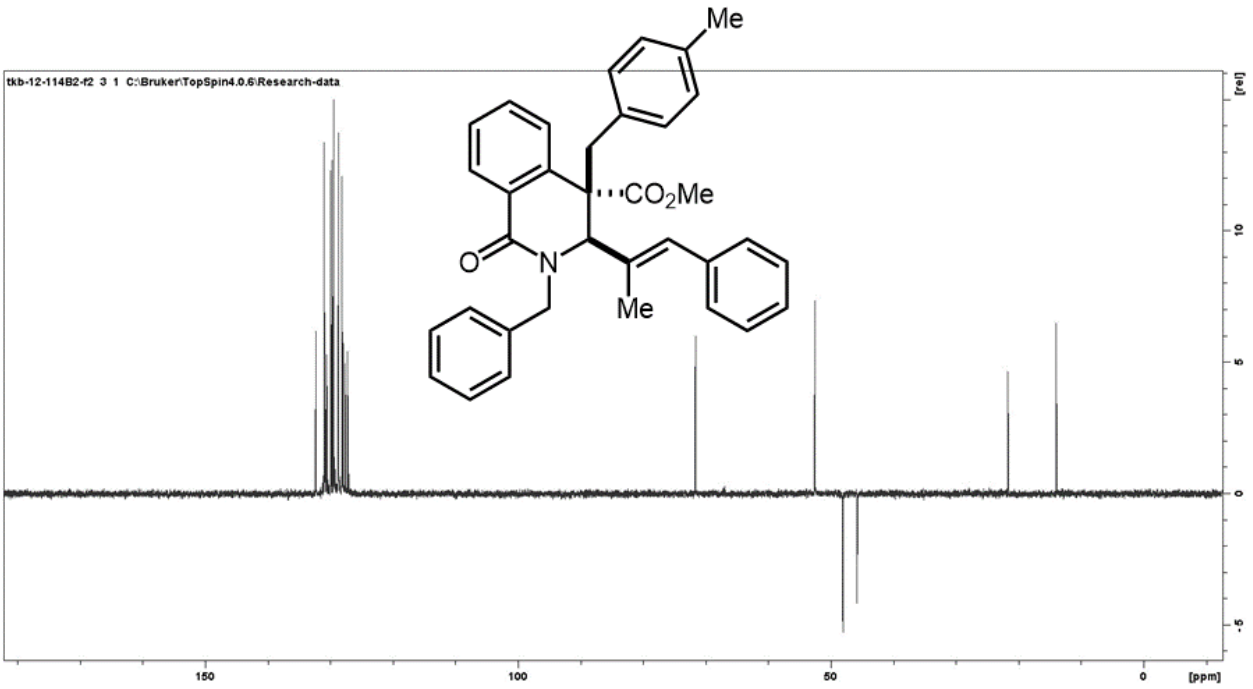
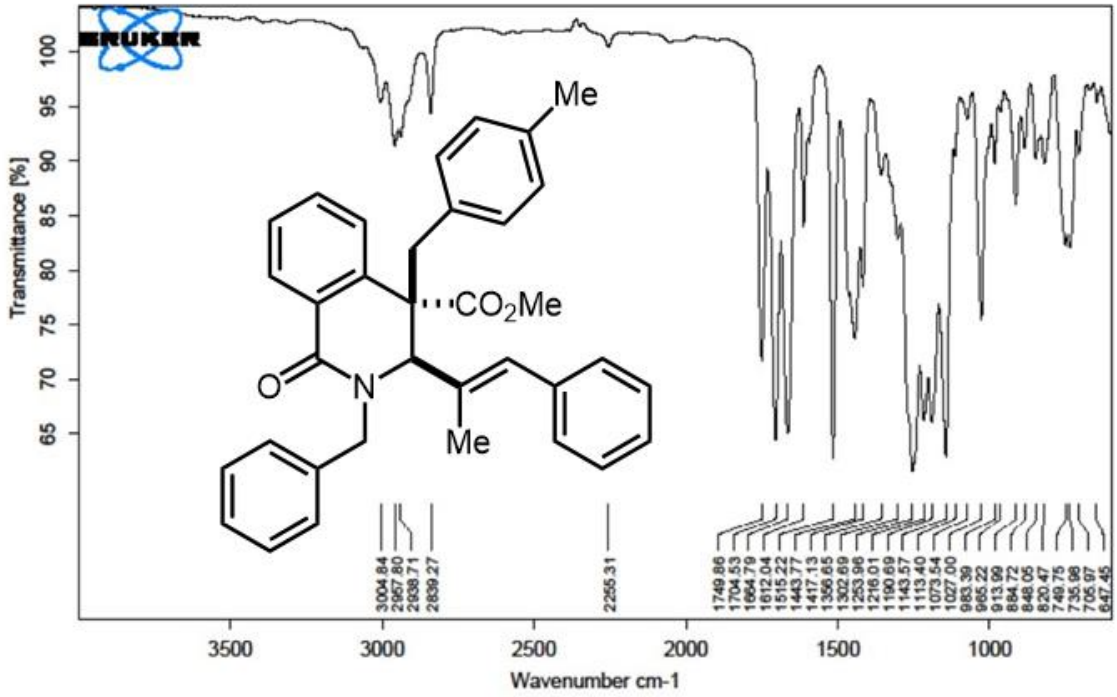
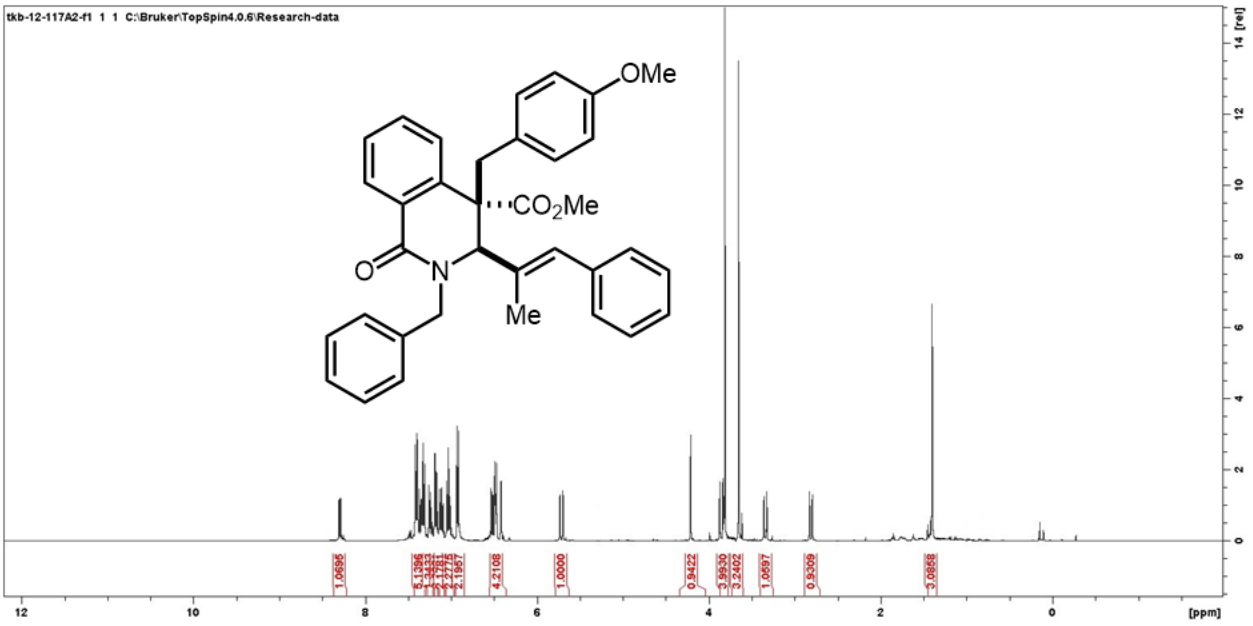


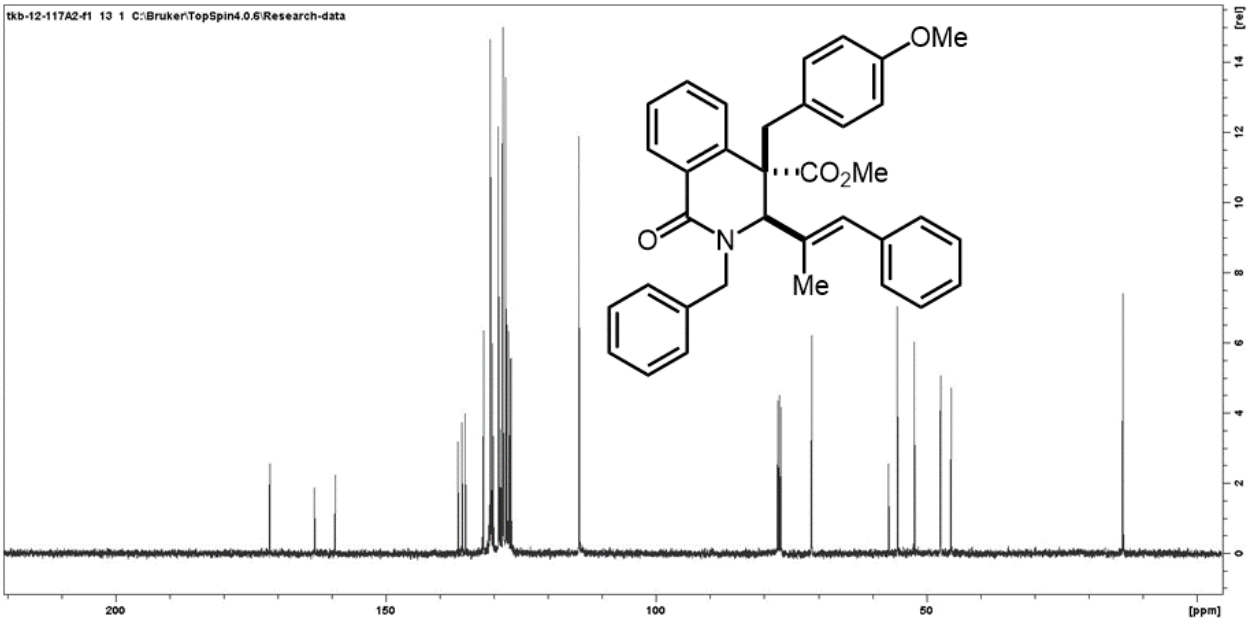


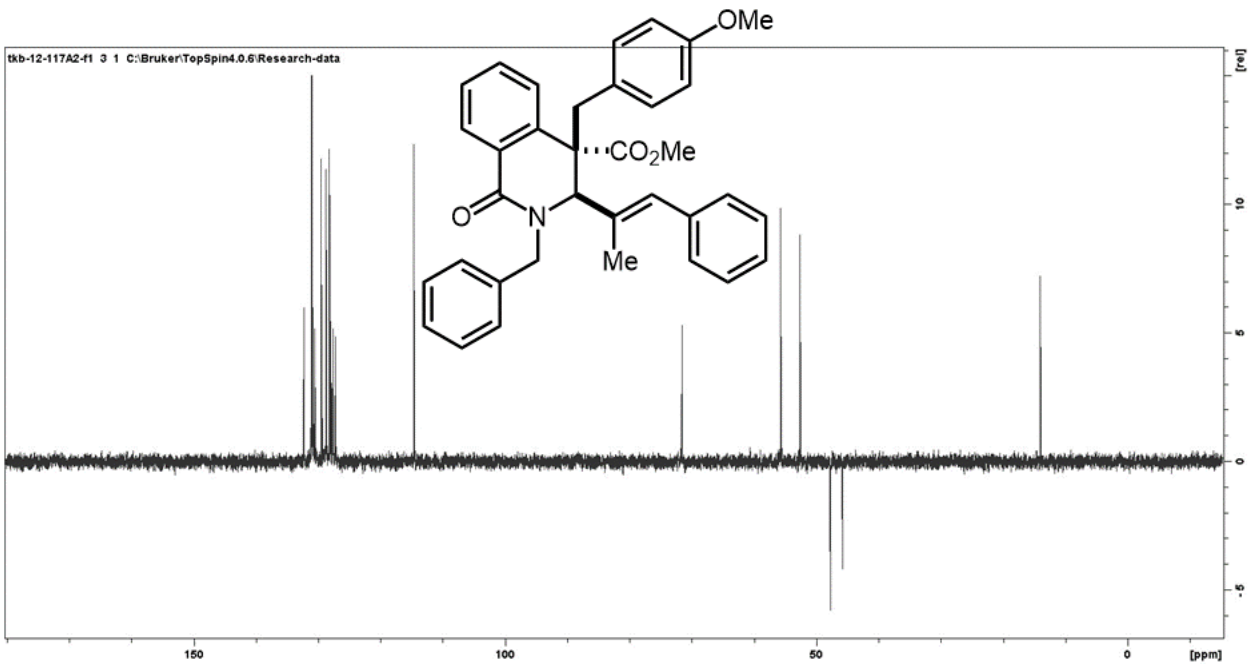
Compound 2o

Prepared from ester **1l** (103 mg, 0.25 mmol) and carbonate **3c** (75.81, 0.25 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Yield = 119.6 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (dd, *J* = 7.8, 1.5 Hz, 1H),

7.45 – 7.16 (m, 10H), 7.15 – 6.89 (m, 2H), 6.92 – 6.82 (m, 2H), 6.57 – 6.39 (m, 3H), 6.36 (s, 1H), 5.66 (d, J = 14.3 Hz, 1H), 4.16 (s, 1H), 3.84 (d, J = 14.3 Hz, 1H), 3.76 (s, 3H), 3.60 (s, 3H), 3.29 (d, J = 13.0 Hz, 1H), 2.76 (d, J = 13.0 Hz, 1H), 1.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.44, 163.17, 159.34, 136.60, 135.87, 135.85, 135.28, 131.89, 130.66, 130.64, 130.53, 130.19, 129.12, 128.74, 128.35, 128.28, 128.09, 127.82, 127.61, 127.25, 126.86, 114.25, 71.19, 57.01, 55.35, 52.23, 47.38, 45.42, 13.62. HRMS calc for $C_{35}H_{33}NO_4$ 531.2410, found 531.2417.

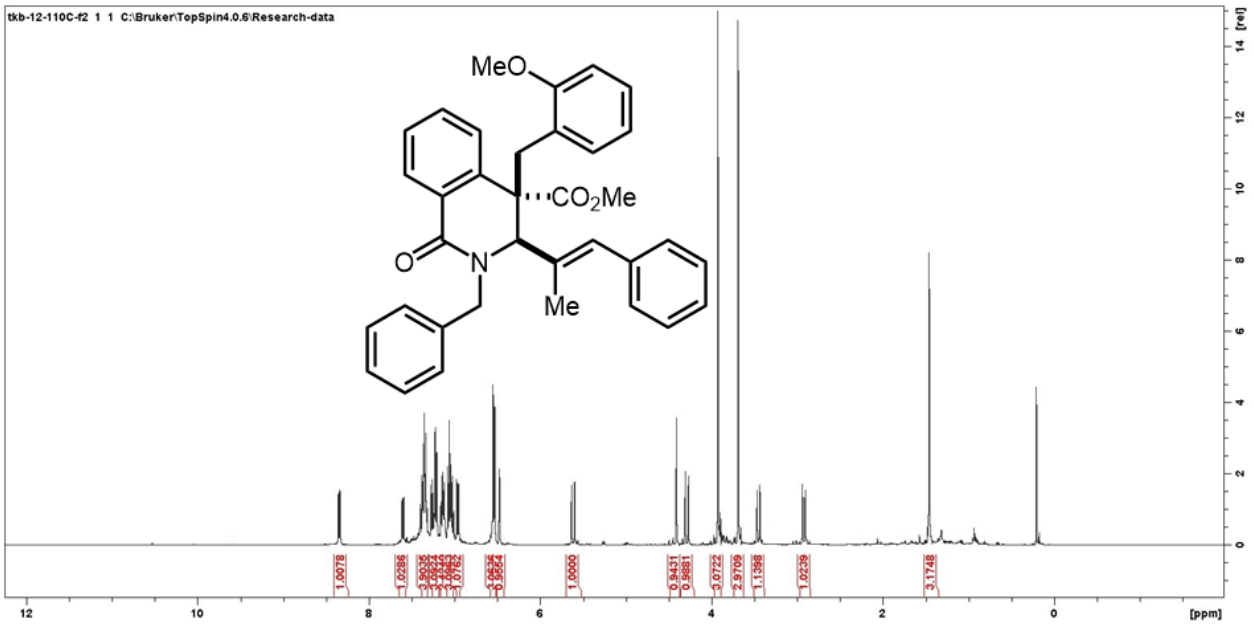






Compound 2p

Prepared from ester **1l** (103 mg, 0.25 mmol) and carbonate **3d** (75.81, 0.25 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Yield = 97 mg, 73%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.57 (d, 1H), 7.49 – 7.11 (m, 12H), 6.89 (dd, *J* = 8.3, 1.1 Hz, 1H), 6.58 – 6.43 (m, 3H), 6.41 (s, 1H), 5.54 (d, *J* = 14.2 Hz, 2H), 4.34 (s, 1H), 4.22 (d, *J* = 14.2 Hz, 1H), 3.85 (s, 3H), 3.62 (s, 3H), 3.42 (d, *J* = 13.0 Hz, 1H), 2.85 (d, *J* = 13.0 Hz, 1H), 1.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.71, 163.20, 157.93, 136.88, 136.20, 135.97, 135.47, 131.99, 131.77, 130.62, 130.38, 130.18, 129.44, 129.16, 128.36, 128.20, 127.85, 127.53, 127.17, 126.83, 124.88, 120.99, 110.66, 71.73, 57.25, 55.47, 52.25, 45.03, 43.14, 13.64. HRMS calc for $C_{35}H_{33}NO_4$ 531.2410, found 531.2417.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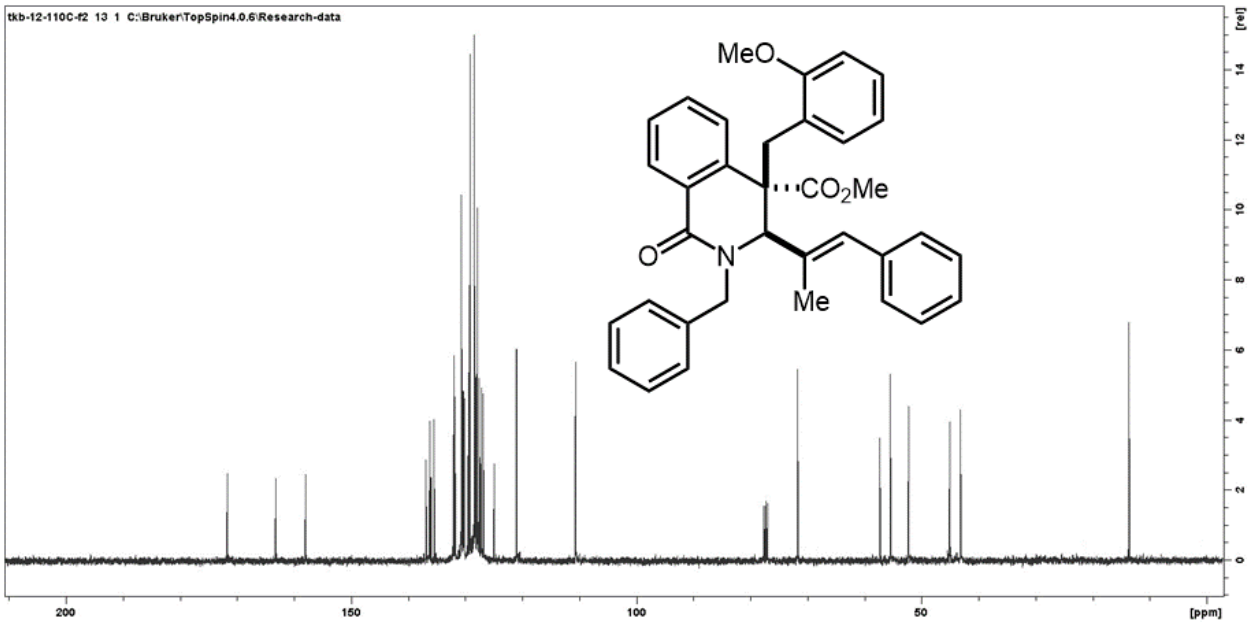
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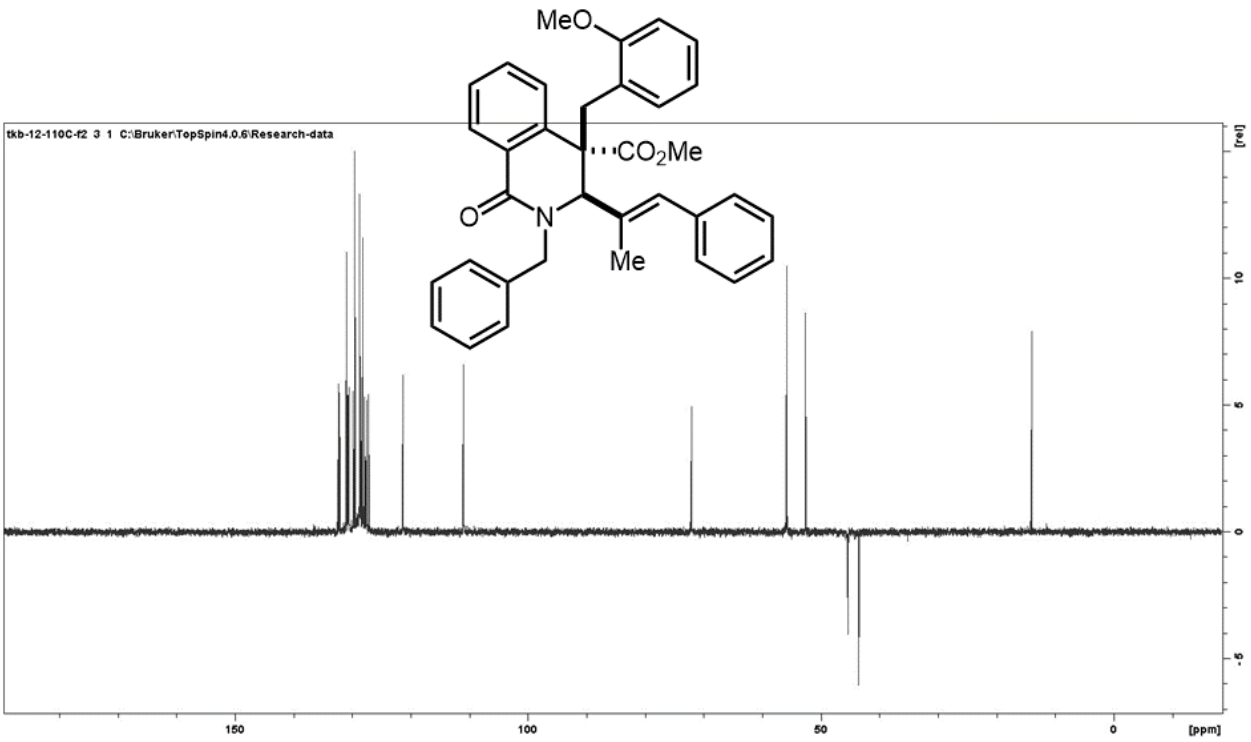
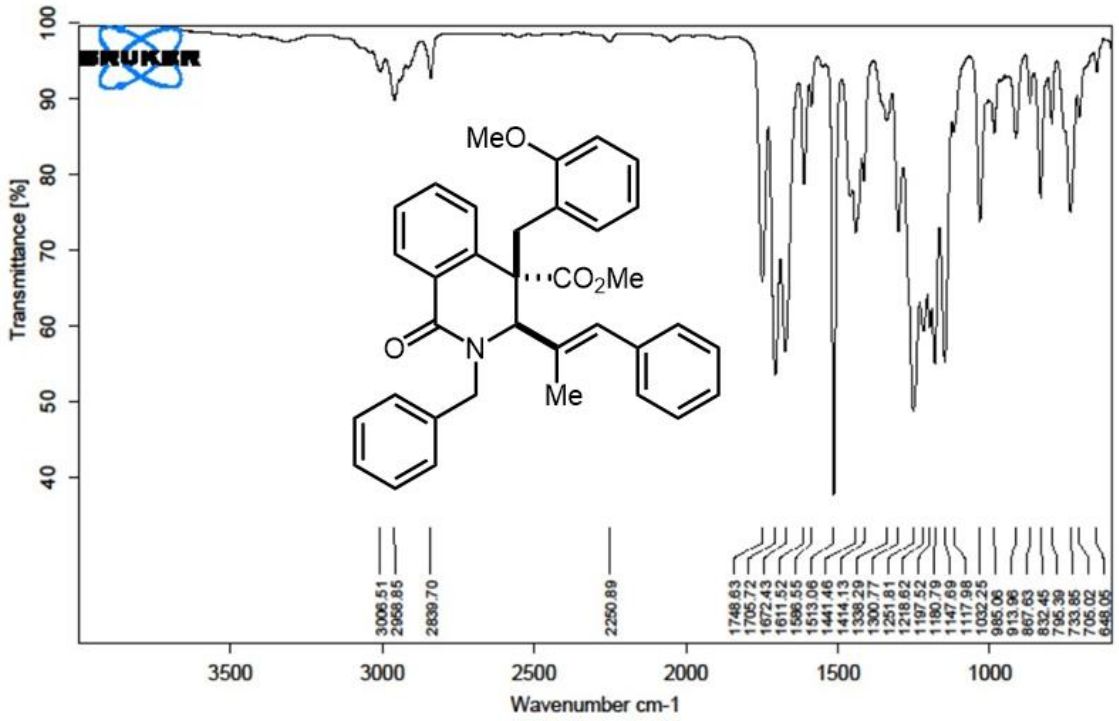
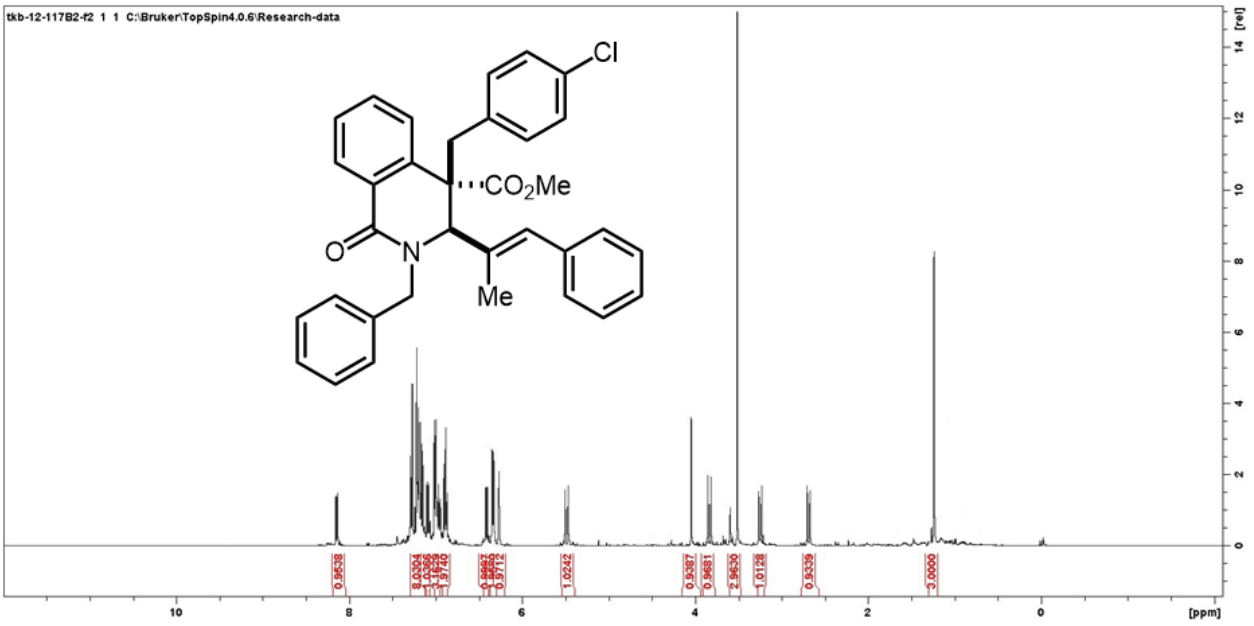


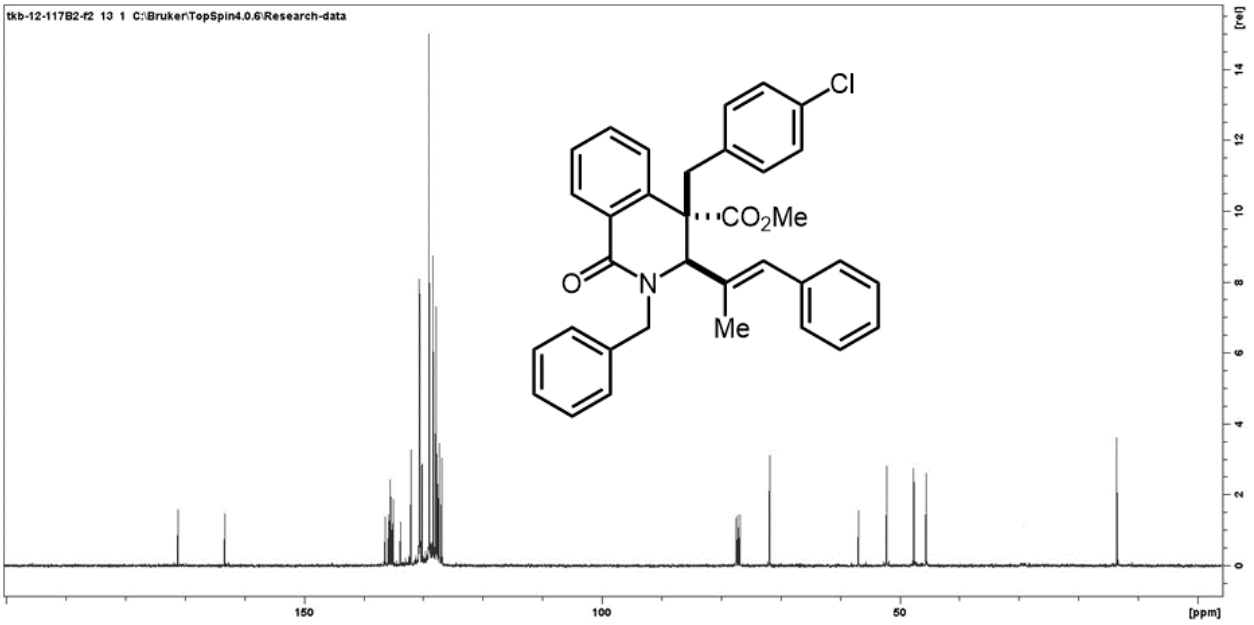


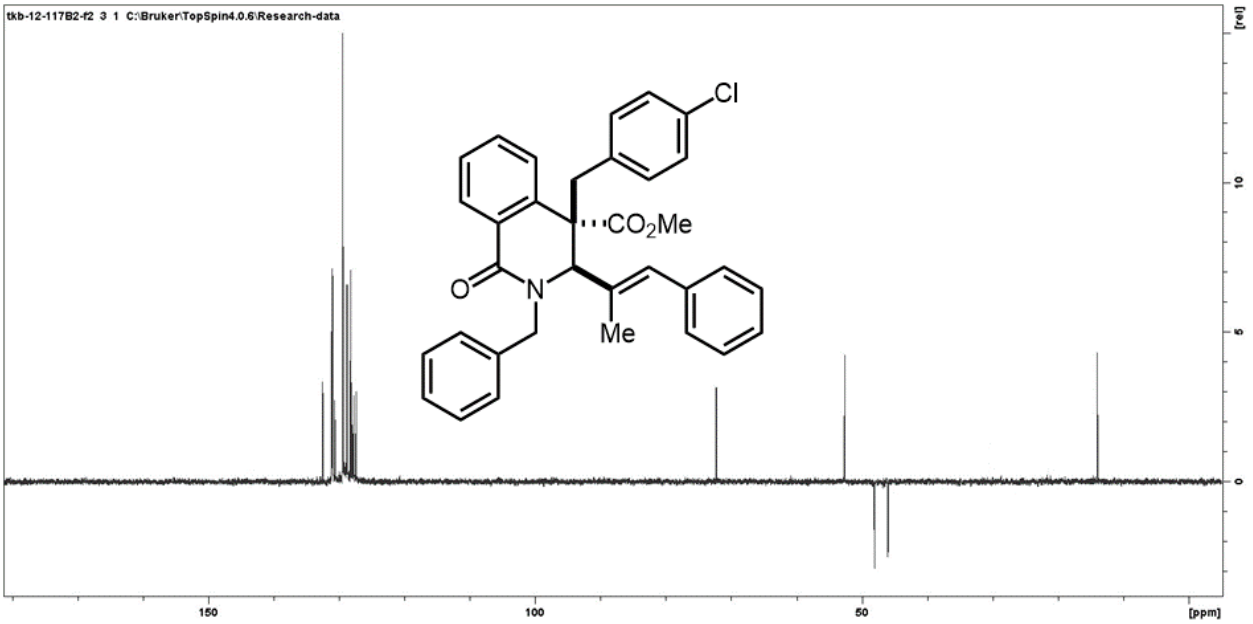
Compound 2q

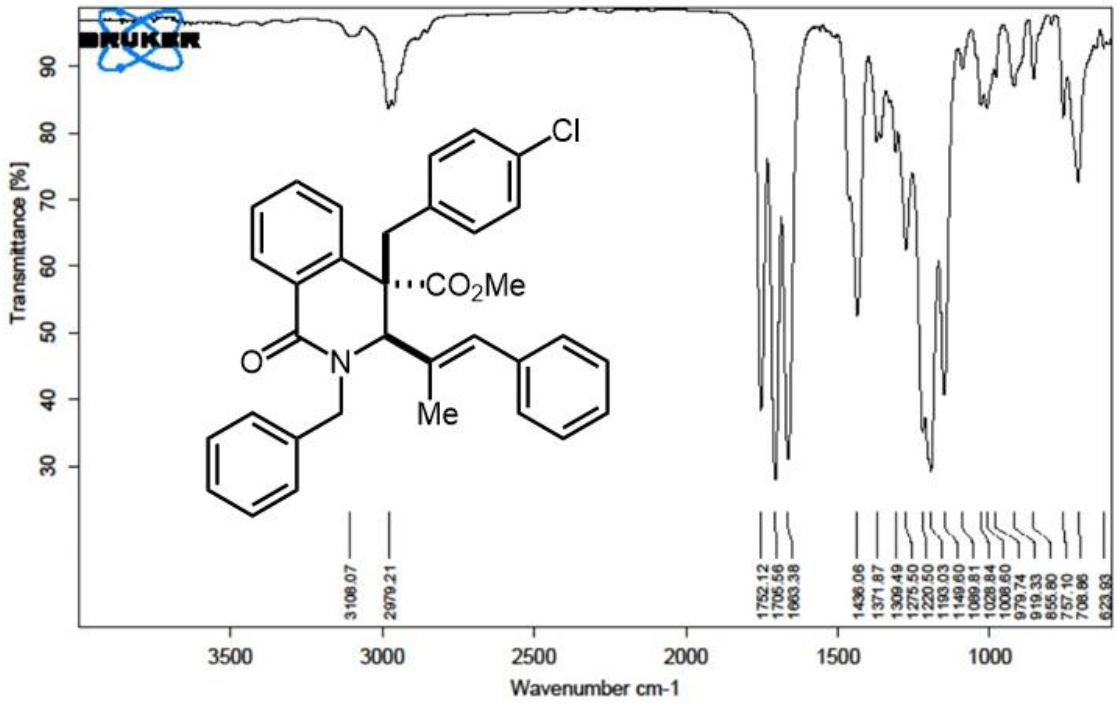
Prepared from ester **1l** (103 mg, 0.25 mmol) and carbonate **3e** (76.92, 0.25 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc

(80:20). Yield = 95 mg, 71%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.52 – 7.37 (m, 12H), 6.93 – 6.80 (m, 2H), 6.52 – 6.39 (m, 3H), 6.37 (s, 1H), 5.59 (d, *J* = 14.5 Hz, 2H), 4.15 (s, 1H), 3.84 (d, *J* = 14.5 Hz, 2H), 3.62 (s, 3H), 3.39 (d, *J* = 12.9 Hz, 1H), 2.69 (d, *J* = 12.9 Hz, 1H), 1.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.25, 163.35, 136.43, 135.92, 135.64, 135.44, 135.12, 132.11, 130.74, 130.70, 130.60, 130.26, 129.09, 128.40, 128.32, 127.88, 127.70, 127.36, 126.98, 71.92, 57.00, 52.27, 47.71, 45.65, 13.63. HRMS calc for $C_{34}H_{30}ClNO_3$ 535.1914, found 535.1918.





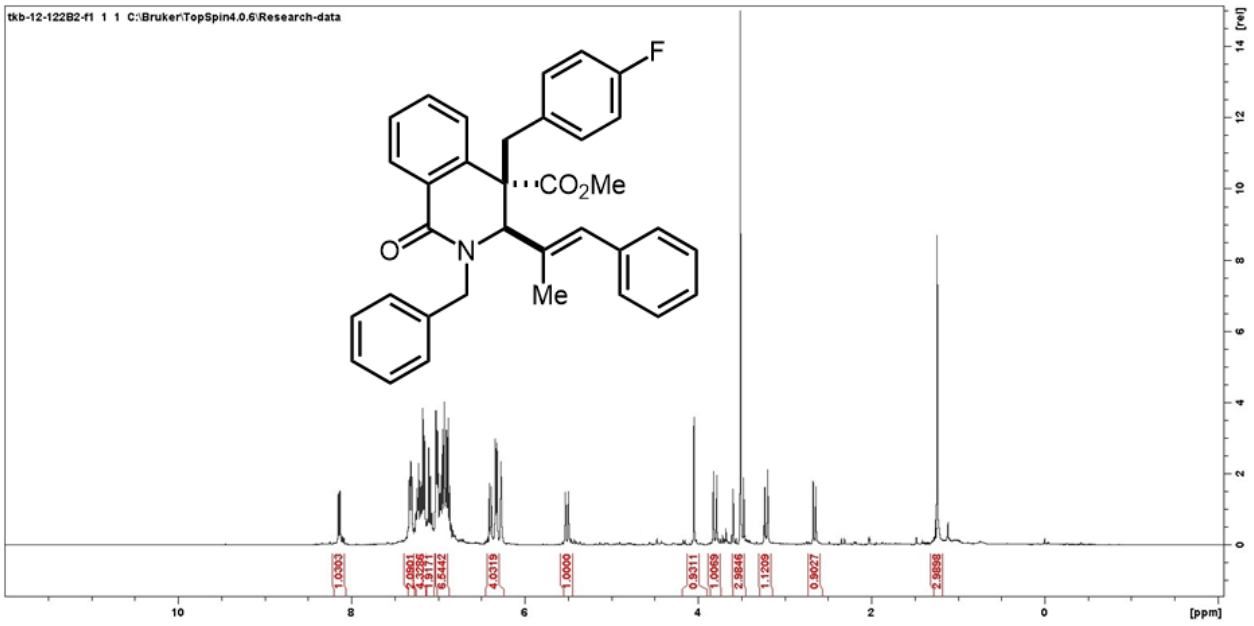


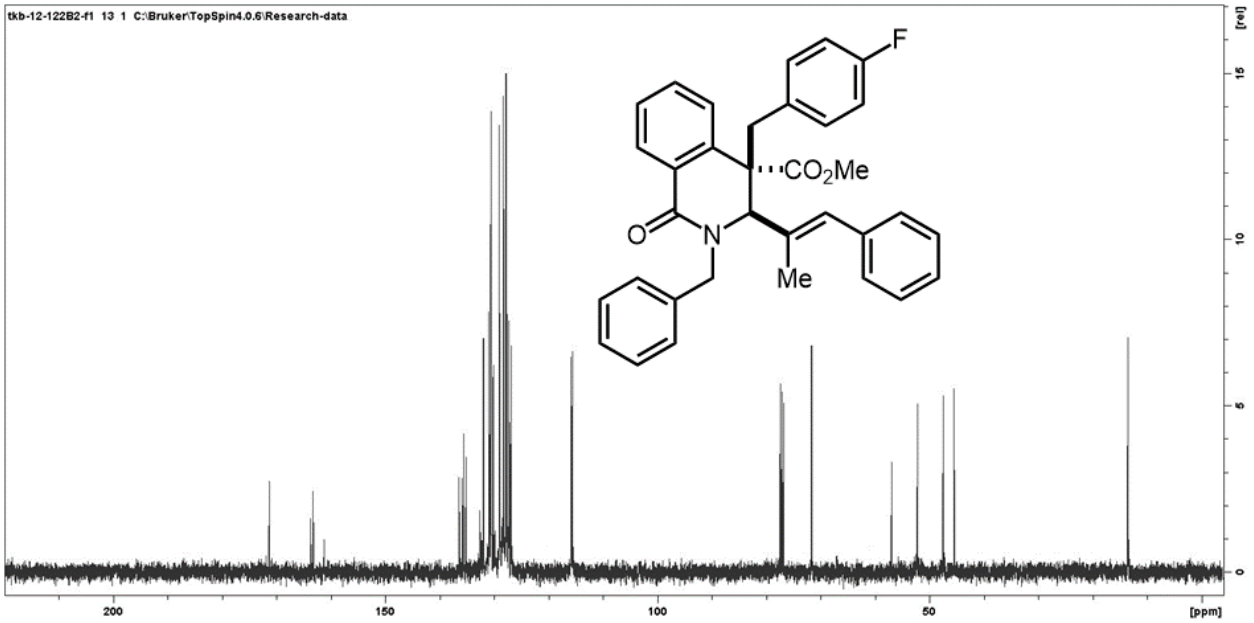


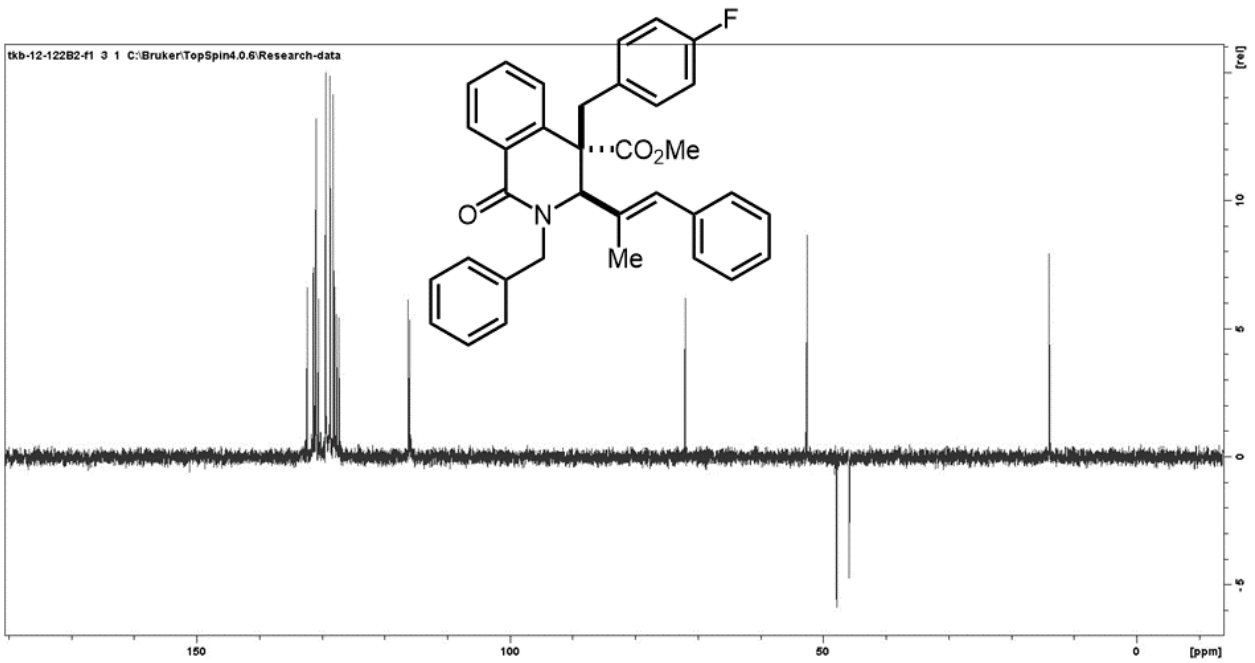
Compound 2r

Prepared from ester **1l** (103 mg, 0.25 mmol) and carbonate **3f** (72.81 mg, 0.25 mmol, 1 equiv) using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Yield = 89.6 mg, 69%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (dd, J = 7.8,

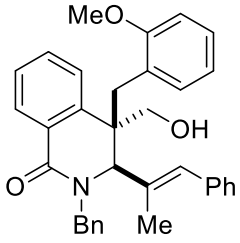
1.5 Hz, 1H), 7.39 – 7.05 (m, 8H), 7.09 – 6.76 (m, 6H), 6.47 – 6.36 (m, 4H), 5.55 (d, 1H), 4.14 (s, 1H), 3.80 (d, J = 14.4 Hz, 1H), 3.51 (s, 3H), 3.21 (d, J = 12.8 Hz, 1H), 2.65 (d, J = 12.8 Hz, 1H), 1.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.30, 163.75, 163.28, 161.30, 136.46, 135.87, 135.67, 135.19, 132.71, 132.67, 132.01, 131.07, 130.99, 130.82, 130.68, 130.59, 130.22, 129.09, 128.99, 128.95, 128.39, 128.30, 127.95, 127.85, 127.71, 127.67, 127.63, 127.33, 126.94, 119.66, 115.92, 115.70, 71.72, 57.01, 52.25, 47.53, 45.56, 13.62. HRMS calc for $C_{34}H_{30}FNO_3$ 519.2210, found 519.2216.





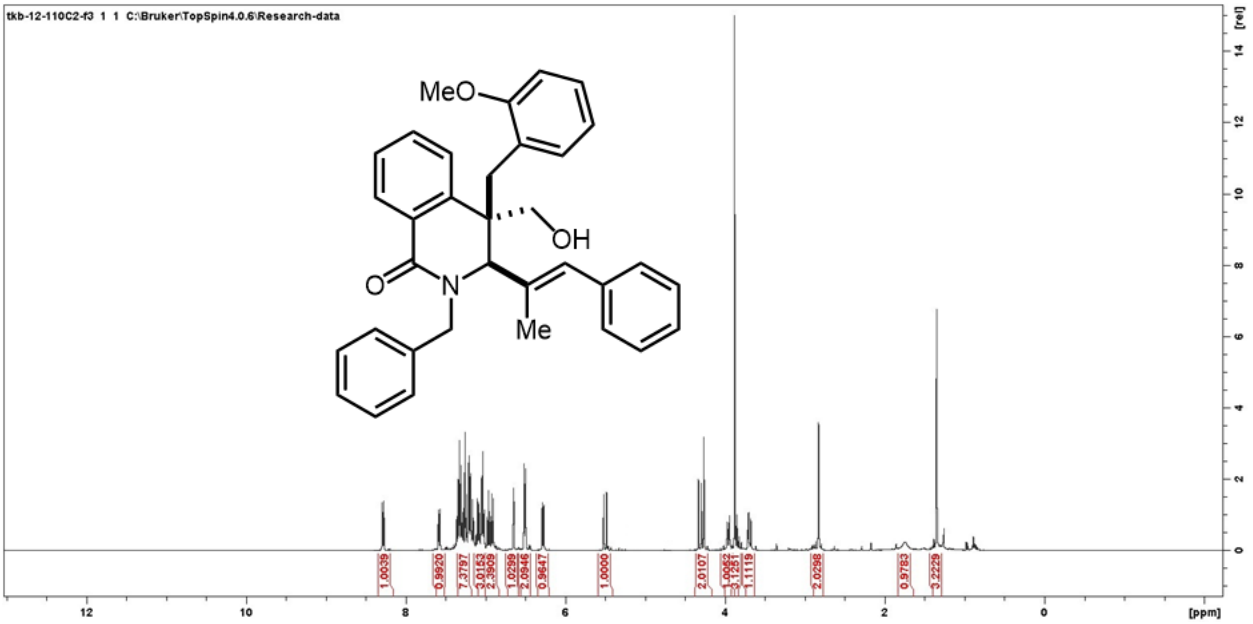


Scheme 3 results



6a, 91%

Prepared from quaternary ester **2p** (133 mg, 0.25 mmol) using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yield = 114.6 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.54 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.37 – 6.94 (m, 11H), 6.98 – 6.82 (m, 2H), 6.61 (s, 1H), 6.51 – 6.38 (m, 2H), 6.24 (dd, *J* = 7.9, 1.1 Hz, 1H), 5.46 (d, *J* = 14.2 Hz, 1H), 4.27 (d, *J* = 14.2 Hz, 1H), 4.22 (s, 1H), 3.91 (d, *J* = 11.3 Hz, 1H), 3.83 (s, 3H), 3.64 (d, *J* = 11.3 Hz, 1H), 2.88 – 2.73 (m, 2H), 1.78 (s, 1H) 1.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.87, 157.85, 139.53, 136.80, 136.45, 135.93, 131.97, 131.55, 131.26, 130.95, 129.21, 129.10, 128.68, 128.37, 127.59, 127.24, 127.16, 126.35, 125.25, 124.76, 120.99, 110.61, 70.54, 61.60, 55.47, 44.92, 42.64, 42.50, 14.48. FTIR (KBr): 3384.5368, 2972.9933, 2932.8937, 1638.2038, 1449.1308, 1364.7192, 1290.2159, 1270.3054, 1247.8533, 1206.5967, 1179.918, 1131.1074, 1071.4274, 994.4373, 924.8386, 881.7598, 797.4882, 700.0535. HRMS calc for $C_{34}H_{33}NO_3$ 503.2460, found 503.2463.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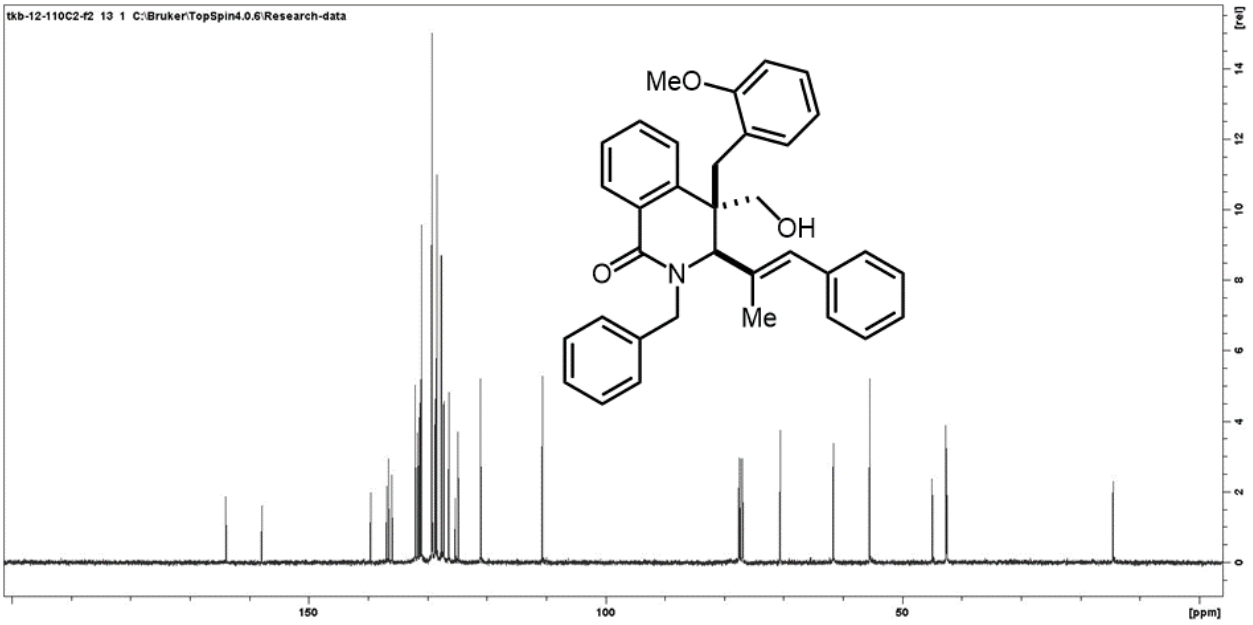
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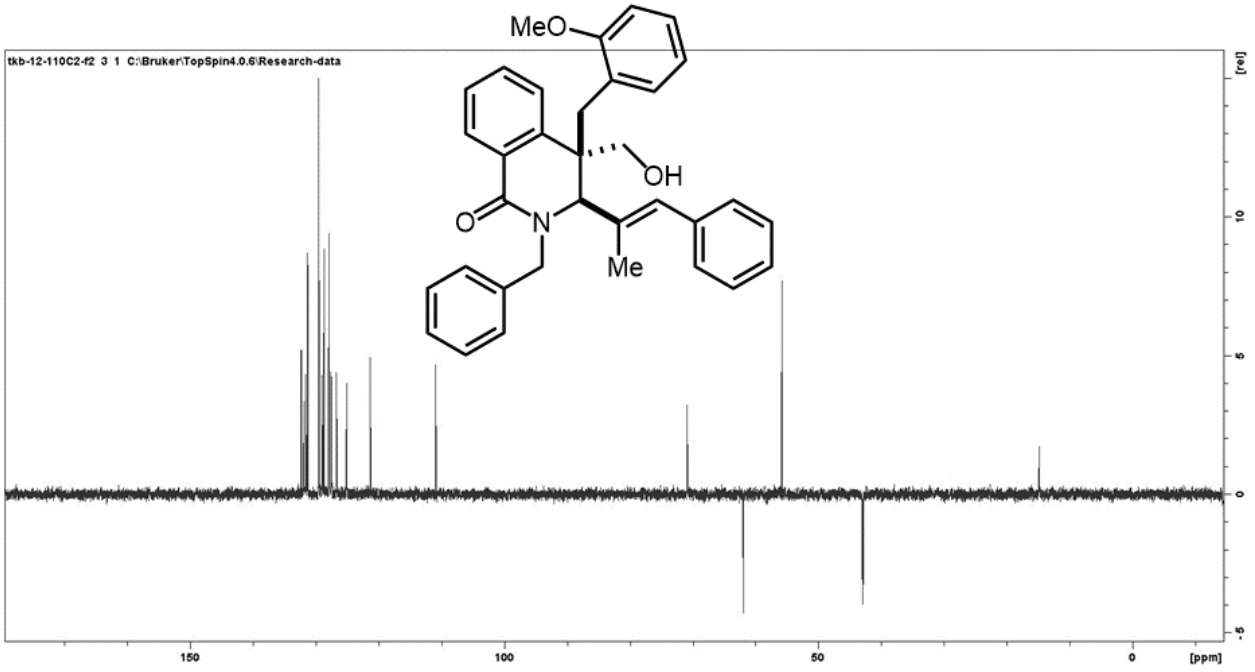
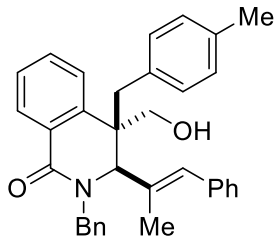
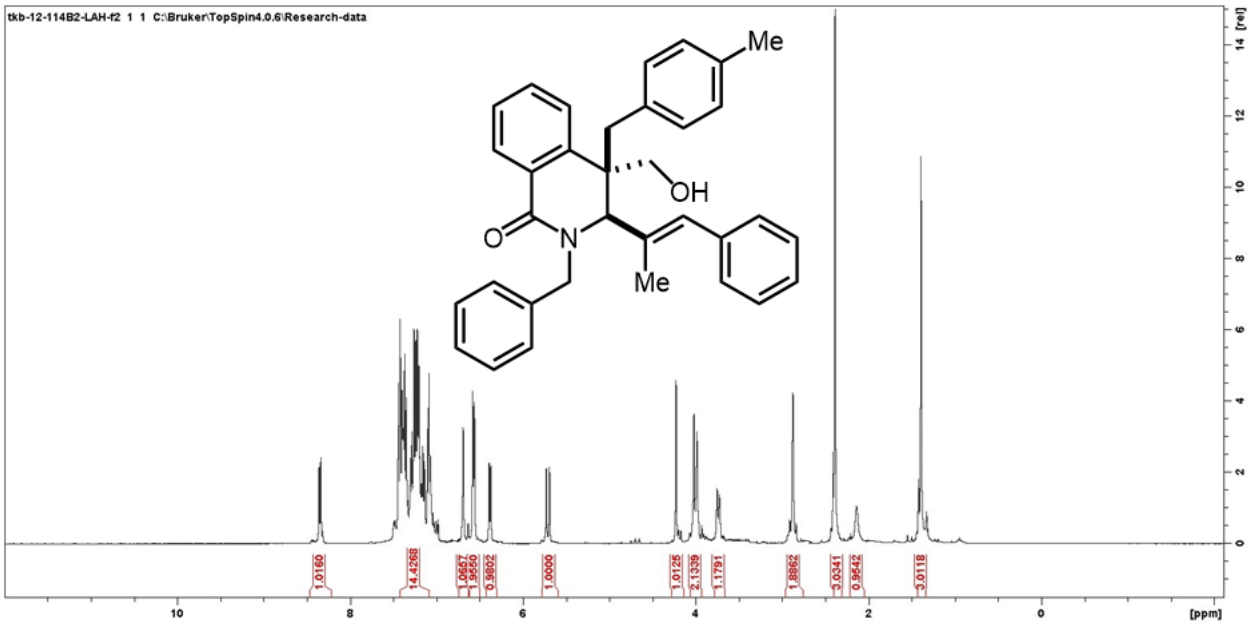




6b, 94%

Prepared from quaternary ester **2n** (129 mg, 0.25 mmol) using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (65:35). Yield = 114.5 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.44 – 7.05 (m, 14H), 6.61 (s, 1H), 6.52 – 6.46 (m, 2H), 6.30 (d, *J* = 7.7 Hz, 1H), 5.63 (d, *J* = 14.2 Hz, 1H), 4.15 (s, 1H), 3.93 (d, *J* = 11.0 Hz, 2H), 3.77 – 3.63 (m, 1H), 2.88 – 2.74 (m, 2H), 2.21 (s, 3H), 2.06 (s, 1H), 1.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.99, 139.67, 137.51, 136.68, 136.31, 135.42, 134.01, 131.85, 131.48, 131.03, 131.00, 129.57, 129.41, 129.32, 129.24, 129.19, 129.14, 128.93, 128.78, 128.39, 128.36, 127.78, 127.65, 127.34, 127.23, 126.44, 124.84, 70.27, 61.50, 47.82, 44.84, 43.00, 21.34, 14.51. FTIR (KBr): 3489.1994. 3391.272, 3060.2295, 3027.4261, 2924.038, 1724.2643, 1646.3958, 1494.2931, 1474.3358, 1452.8606, 1432.4058, 1361.9422, 1342.0932, 265.3056, 1205.6142, 1140.2378, 1071.7973, 1028.3461, 996.4523, 924.2151, 735.4288, 700.2396. HRMS calc for $C_{34}H_{33}NO_2$ 487.2511, found 487.2515.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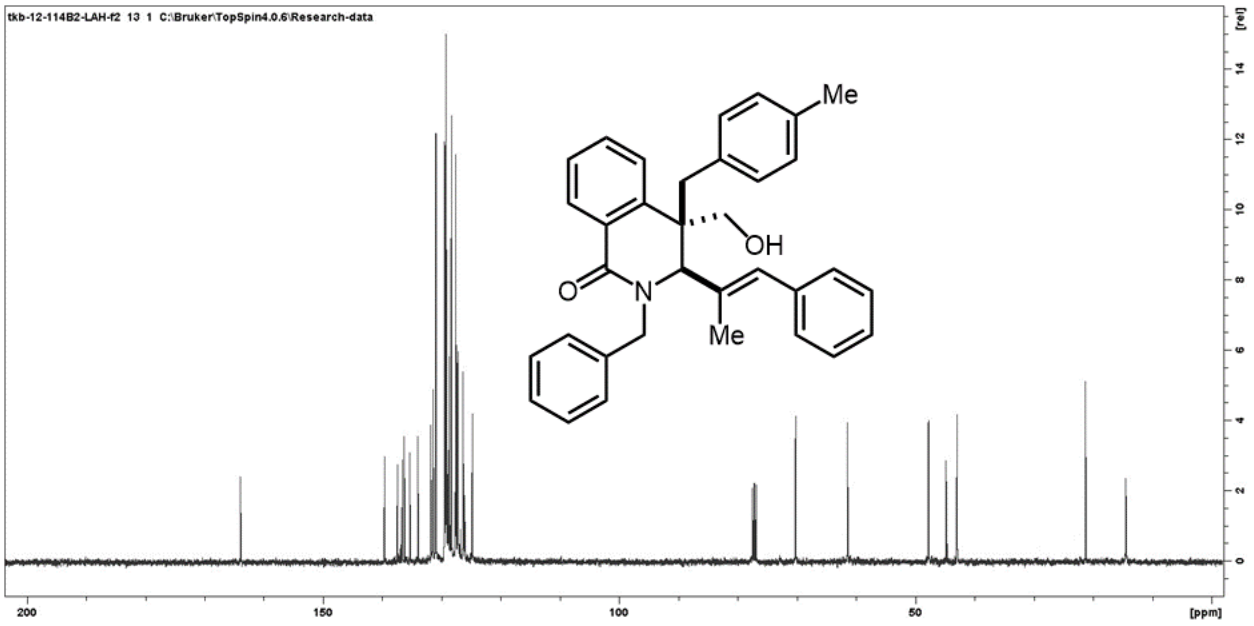
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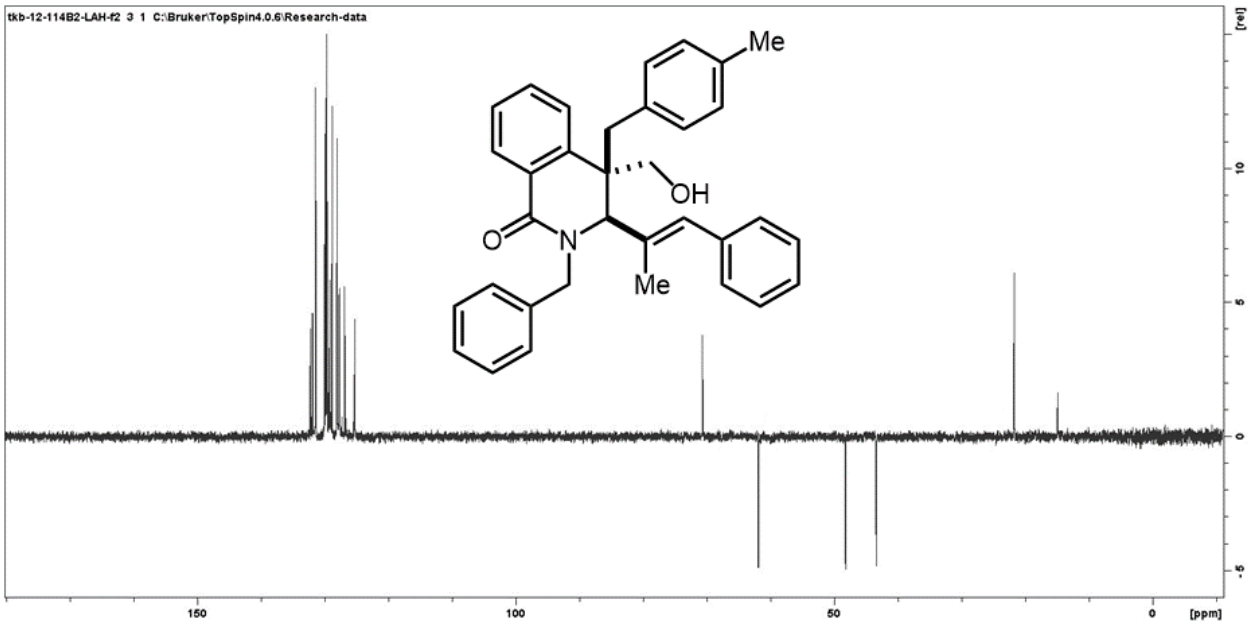
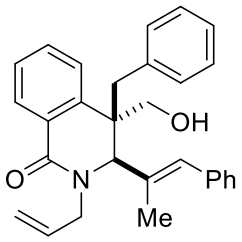
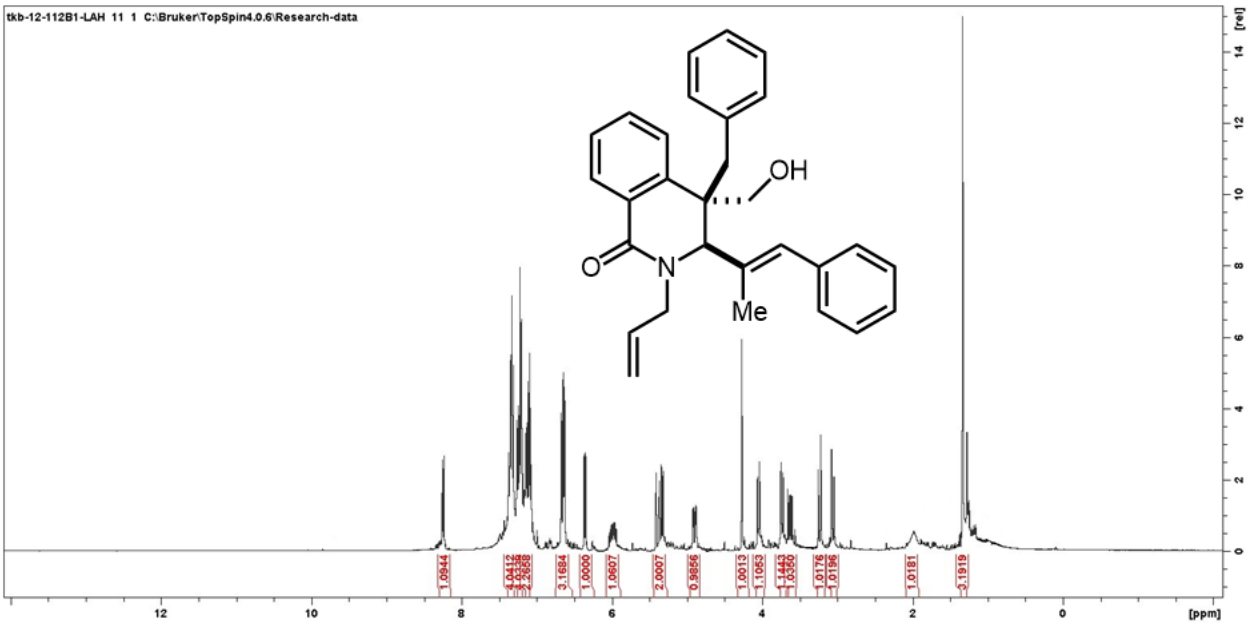




6c, 89%

Prepared from quaternary ester **2k** (112.9 mg, 0.25 mmol) using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (65:35). Yield = 94.1 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.38 – 7.08 (m, 10H), 6.62 – 6.52 (m, 3H), 6.31 (s, 1H), 5.93 (dddd, *J* = 17.2, 10.1, 8.4, 5.0 Hz, 1H), 5.33 – 5.29 (m, 2H), 4.84 – 4.71 (m, 1H), 4.21 (s, 1H), 4.08 (t, *J* = 10.2 Hz, 1H), 3.68 (d, *J* = 10.9 Hz, 1H), 3.55 (td, *J* = 14.8, 8.7 Hz, 1H), 3.28 (d, *J* = 12.9 Hz, 1H), 3.18 (d, *J* = 12.9 Hz, 1H), 1.99 (s, 1H), 1.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.56, 139.60, 136.65, 136.22, 135.58, 133.11, 131.54, 131.41, 130.95, 129.19, 129.17, 128.96, 128.62, 128.38, 127.70, 127.67, 127.32, 127.21, 126.50, 124.76, 119.41, 70.94, 61.57, 48.13, 45.06, 43.10, 14.50. FTIR (KBr): 3384.5506, 2924.8333, 1642.2515, 1494.9545, 1448.8548, 1427.0419, 1393.4602 1361.6968, 1328.7144, 1289.7737, 1223.6425, 1198.9141, 1130.0001, 1074.1578, 1030.4745, 988.561, 966.1662, 925.5022, 741.6755, 693.4562. HRMS calc for $C_{29}H_{29}NO_2$ 423.2198, found 423.2193.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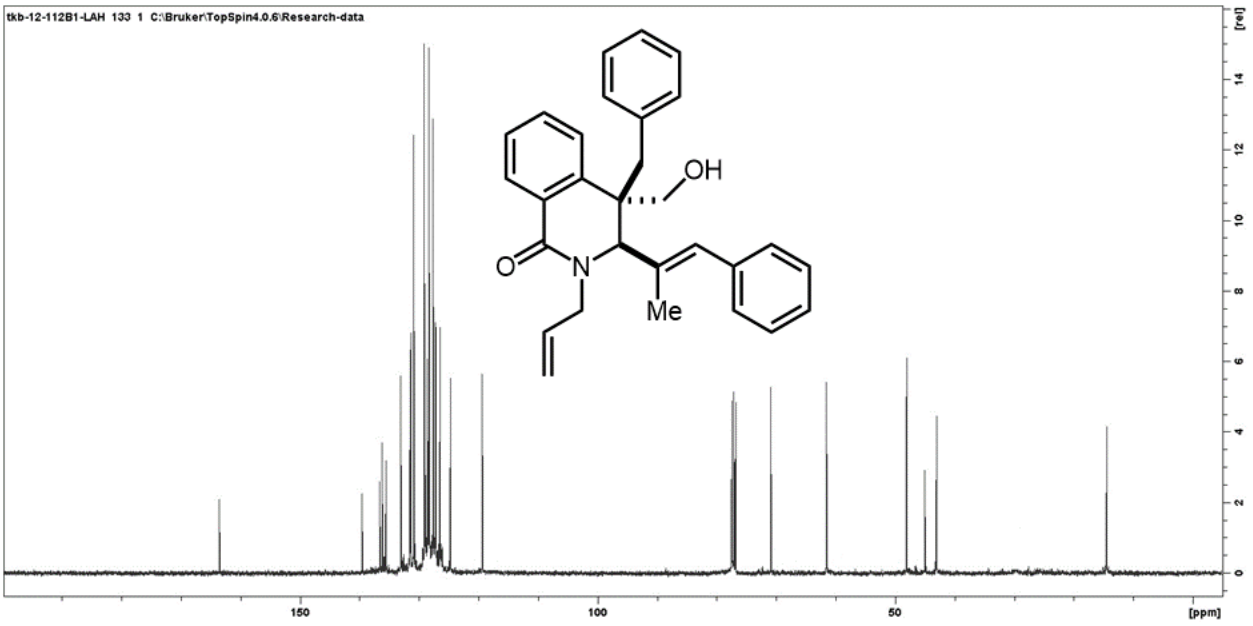
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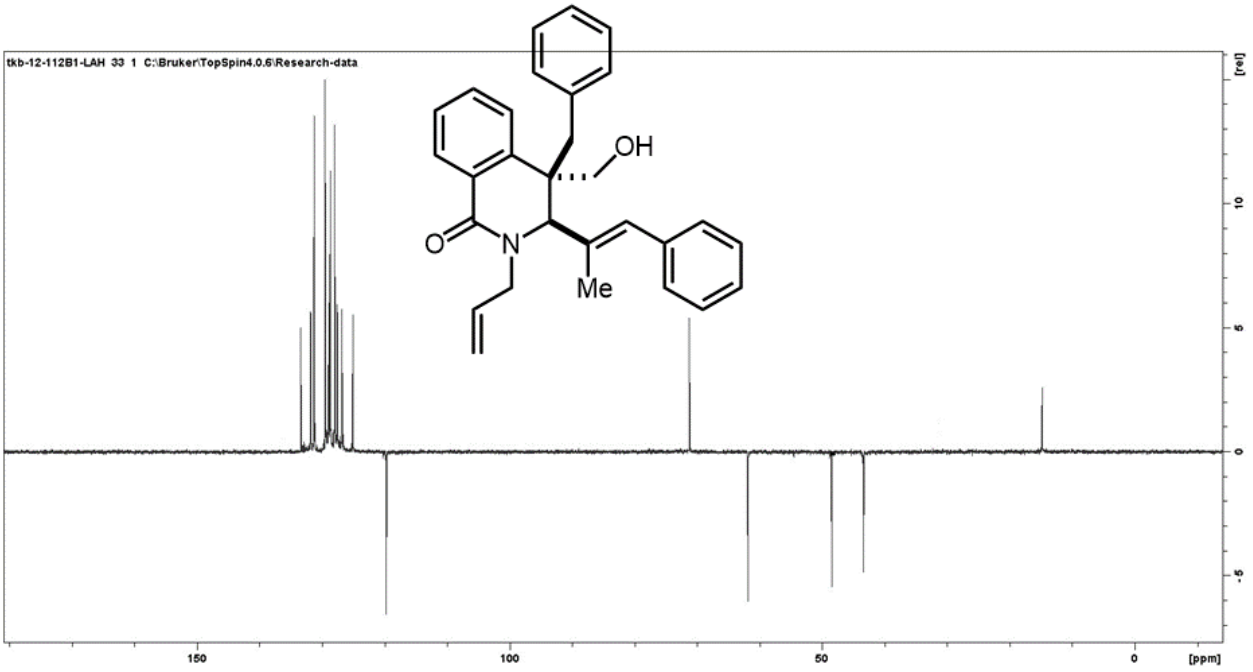

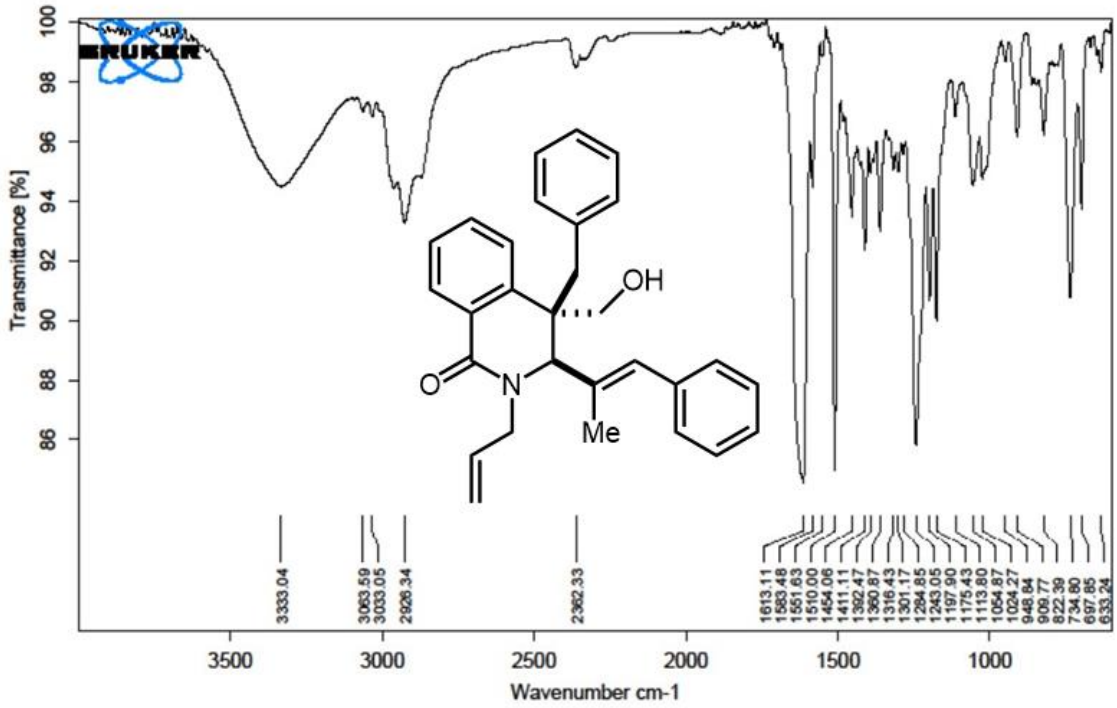

References

(1) Bonnaud, B.; Carlessi, A.; Bigg, D. C. H. J. Heterocycl. Chem. 1993, 30, 257.