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Supporting Information for:

Contra-thermodynamic halolactonization of lactam-tethered 5-aryl-4(*E*)-pentenoic acids for the flexible and stereocontrolled synthesis of fused lactam-halolactones

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Contents:

2. Experimental Section

All experiments involving air and moisture-sensitive reagents were carried out under an inert atmosphere of nitrogen and using freshly distilled solvents. Freshly purchased toluene and DMF were stored under 4 A^{o} molecular sieves for several days prior to use. THF was distilled from sodium benzophenone ketyl. All amines 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 electron spray ionization (ESI) or electron impact (EI) techniques. High-resolution ESI was obtained on an LTQ-FT (ion trap; analyzed using Excalibur). High resolution EI was obtained on an Autospec (magnetic sector; analyzed using MassLynx). Brine solutions are saturated solutions of aqueous sodium chloride.

Phenylsuccinic anhydride was obtained from Fisher Scientific. All other anhydrides were obtained from Sigma-millipore.

The lactam acids depicted in Scheme 3 were prepared as previously reported by us.[1]

The lactam acids depicted in Schemes 1 and 2 were prepared as being reported by us.[3]

Some of the lactam acids were characterized as the ester, for ease of purification.

Some of the lactam acids were advanced to the halolactonization step prior to extensive characterization.

General Procedure A: Bromolactonization of lactam acid 1

To an oven-dried 10 mL screw-cap vial, equipped with a stir bar, was added lactam-tethered alkenoic acid **1** (1.0 mmol), dissolved in DMF (1 mL). Then, NBS (196 mg, 1.1 mmol, 1.1 equiv) and *N*-methylmorpholine oxide (5.9 mg, 5 mol%) were added. The reaction mixture was stirred at room temperature until TLC and GC-MS showed full conversion. The reaction mixture was then diluted with DCM (20 mL) and quenched with 10% aqueous sodium sulfite (10 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.

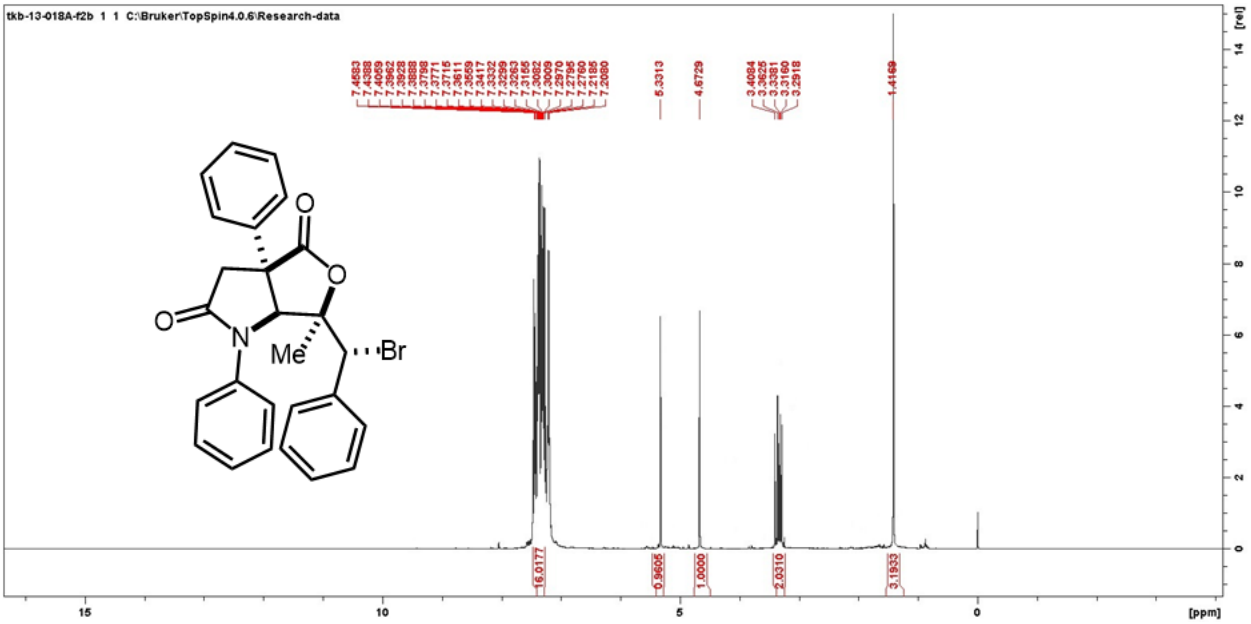
General Procedure B: Iodolactonization of lactam acid 1

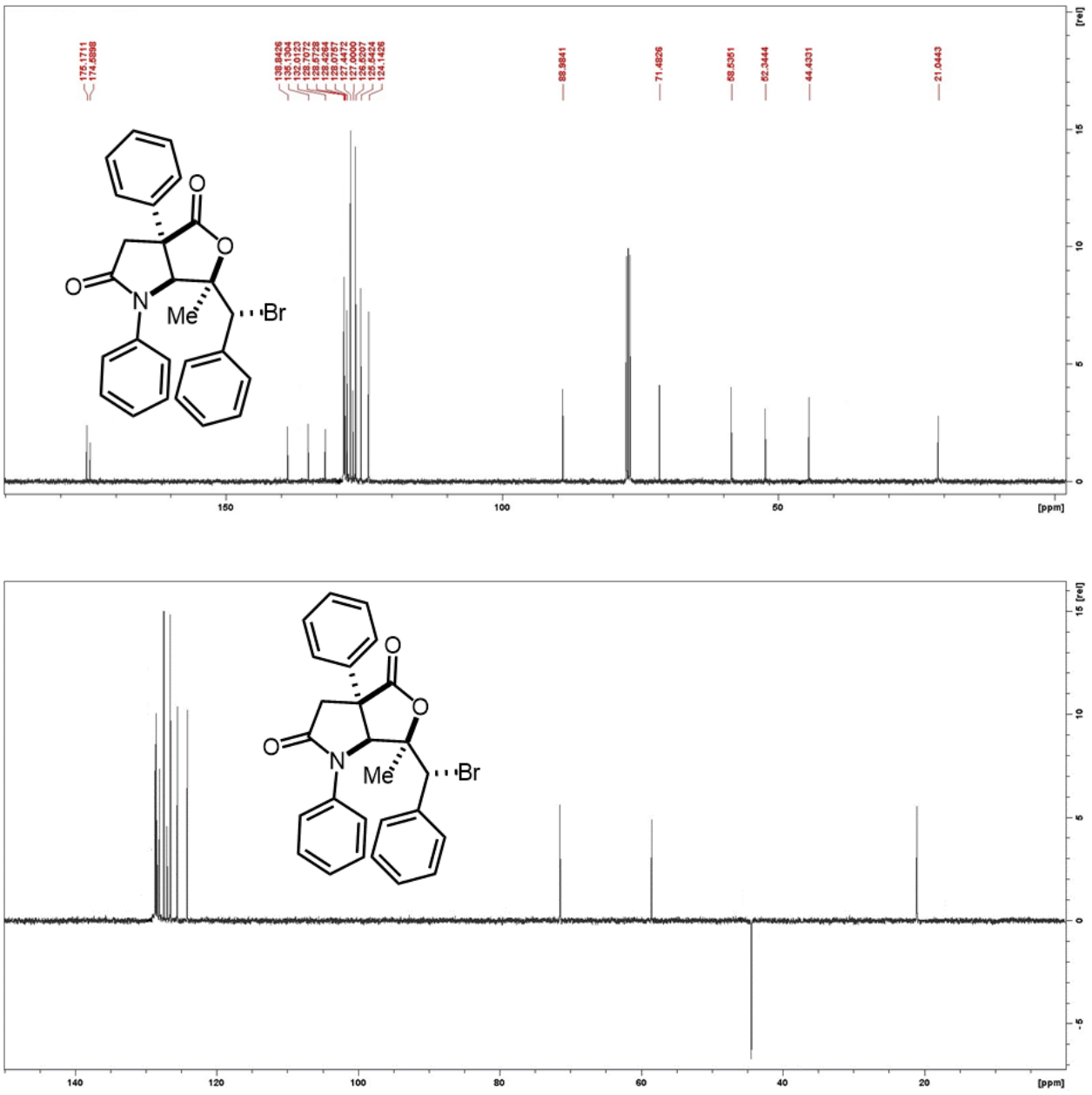
To an oven-dried 10 mL screw-cap vial equipped with a stir bar was added lactam-tethered alkenoic acid **1** (1.0 mmol), dissolved in DMF (1 mL). NIS (247.5 mg, 1.1 mmol, 1.1 equiv) and *N*-methylmorpholine oxide (5.9 mg, 5 mol%) were then added. The reaction mixture was stirred at 0 ^{o}C until TLC and GC-MS showed full conversion. The reaction mixture was then diluted with DCM (20 mL) and quenched with 10% aqueous sodium sulfite (10 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.

Scheme 1 Results

Compound 2a

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Yellowish oil. Yield = 404.6 mg, 85%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.20 (m, 15H), 5.33 (s, 1H), 4.67 (s, 1H), 3.40 – 3.29 (m, 2H), 1.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.2, 174.6, 138.9, 135.1, 132.0, 128.7, 128.6, 128.4, 128.1, 127.4, 127.0, 126.5, 125.6, 124.1, 89.0, 71.5, 58.5, 52.3, 44.4, 21.0. FTIR (KBr): 2965.4, 1727.5, 1696.3, 1604.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1135.9, 1031.8, 905.8, 839.0. **HRMS-EI^{+}** (*m/z*): calc for $C_{26}H_{22}BrNO_3$ $[M]^{+}$ 475.0783, found 475.0789.

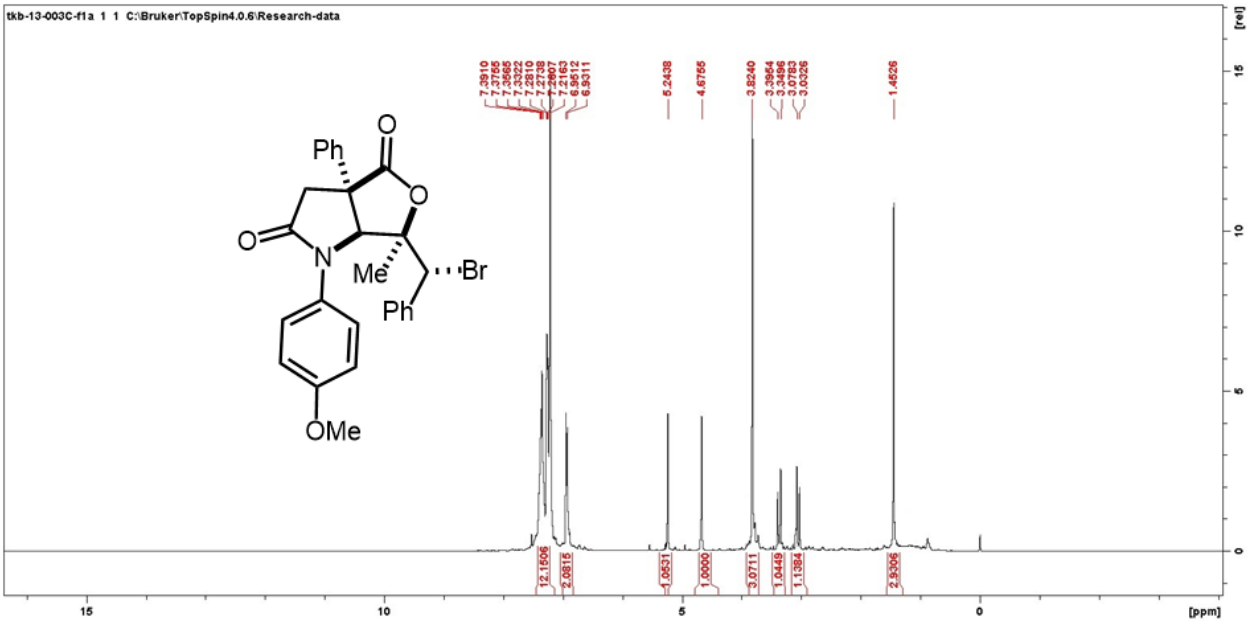


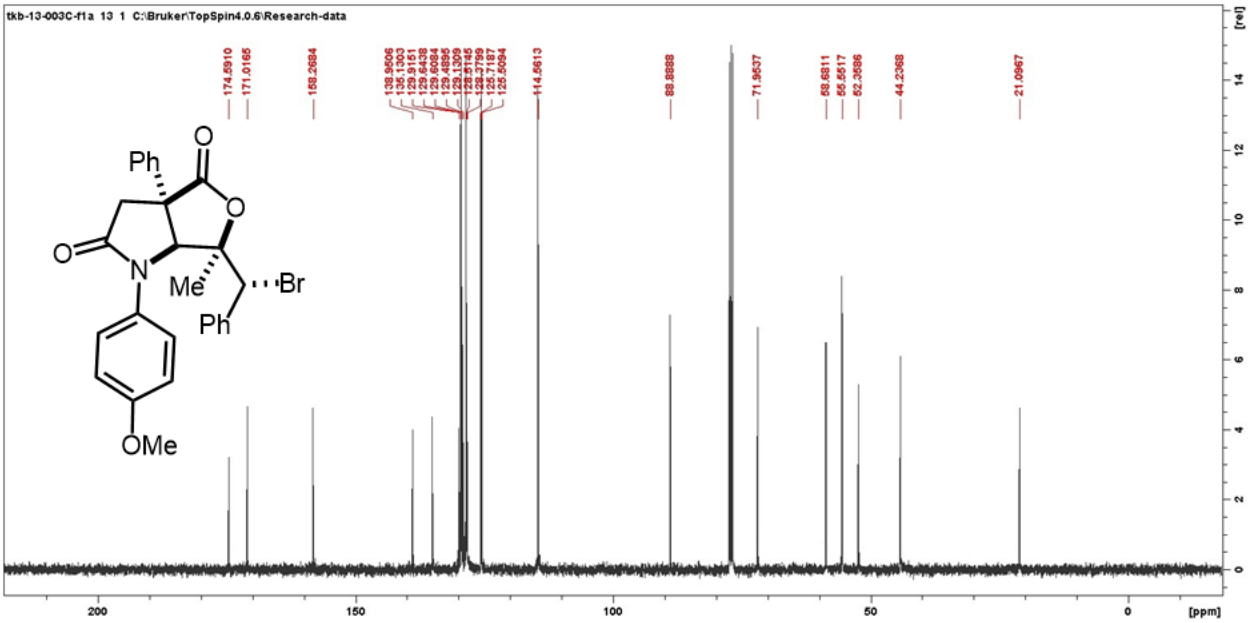


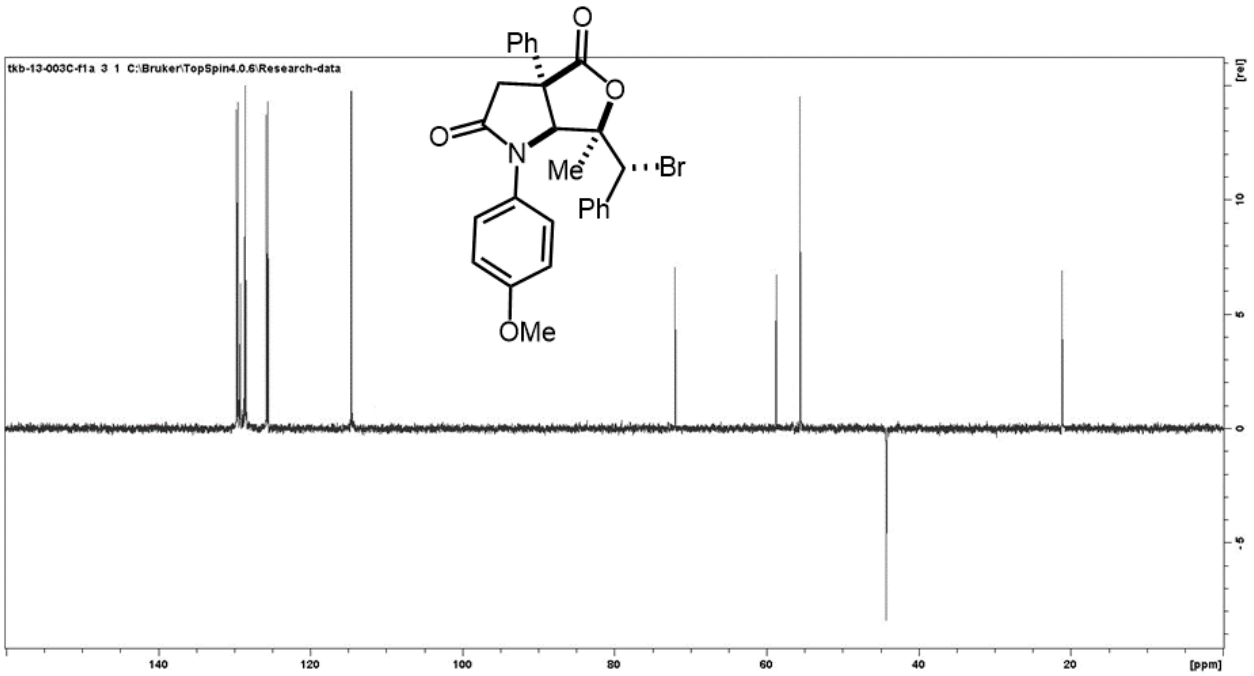
Compound 2b

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Orange oil. Yield = 450.7 mg, 89%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.21 (m, 12H), 6.94 (d, *J* = 6.9 Hz, 2H), 5.24 (s, 1H), 4.68 (s, 1H), 3.82 (s, 3H), 3.38 (d, *J* = 18.3 Hz, 1H), 3.05 (d, *J* = 18.3 Hz, 1H), 1.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 171.0, 158.3, 139.0, 135.1, 129.7, 129.5, 129.1, 128.5, 128.4, 125.7,

125.5, 114.6, 88.9, 72.0, 58.7, 55.6, 52.4, 44.2, 21.1. FTIR (KBr): 2984.1, 1733.5, 1654.3, 1606.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1299.7, 1242.5, 1179.3, , 1031.8, 994.9, 823.7, 735.2. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{27}H_{24}BrNO_4$ $[M]^{+}$ 505.0889, found 505.0894.

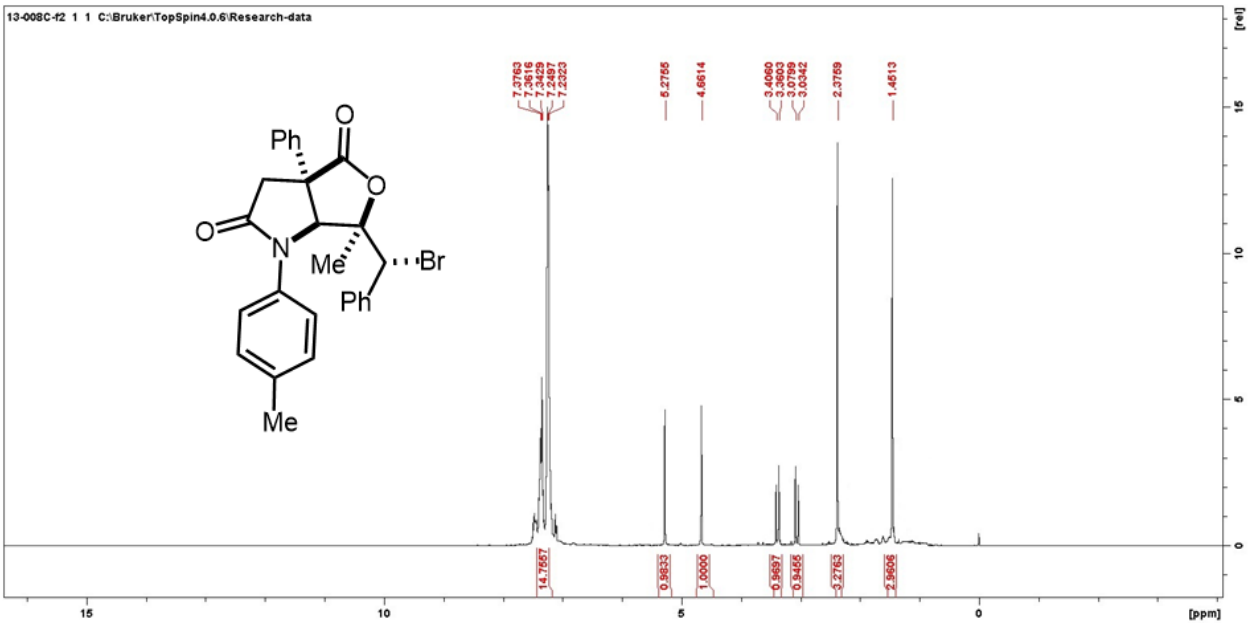






Compound 2c

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Pale yellow oil. Yield = 426.6 mg, 87%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.23 (m, 14H), 5.28 (s, 1H), 4.66 (s, 1H), 3.38 (d, *J* = 16.5 Hz, 1H), 3.05 (d, *J* = 16.5 Hz, 1H), 2.38 (s, 3H), 1.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 170.9, 138.9, 137.0, 135.2, 134.6, 129.9, 129.7, 129.5, 129.1, 128.6, 128.4, 125.5, 124.0, 88.9, 71.6, 58.5, 52.3, 44.4, 21.1. FTIR (KBr): 2939.4, 1723.5, 1696.3, 1604.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1135.9, 1031.8, 985.8, 833.0. **HRMS-EI^{+}** (*m/z*): calc for $C_{27}H_{24}BrNO_3$ $[M]^{+}$ 489.0940, found 489.0944.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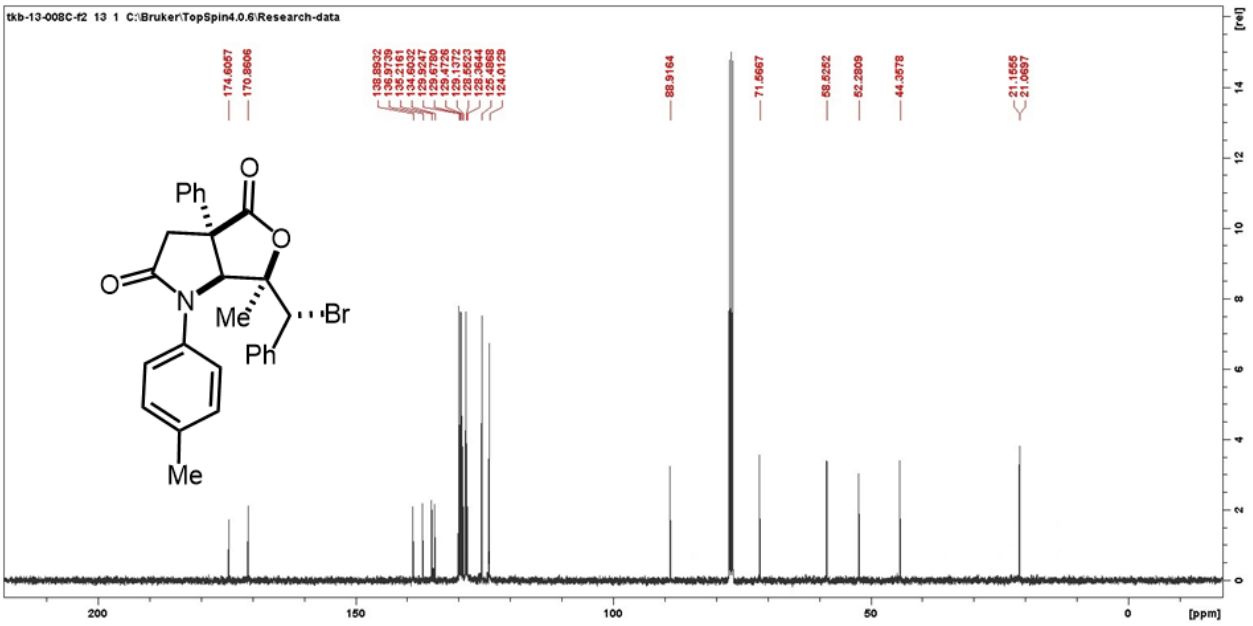
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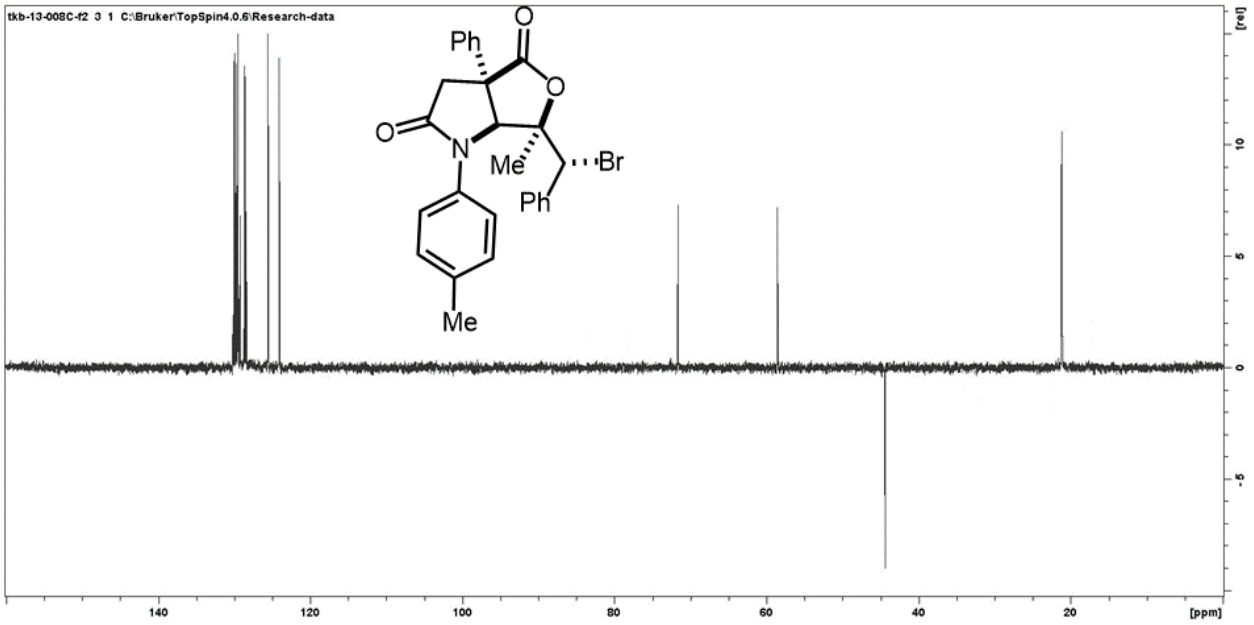
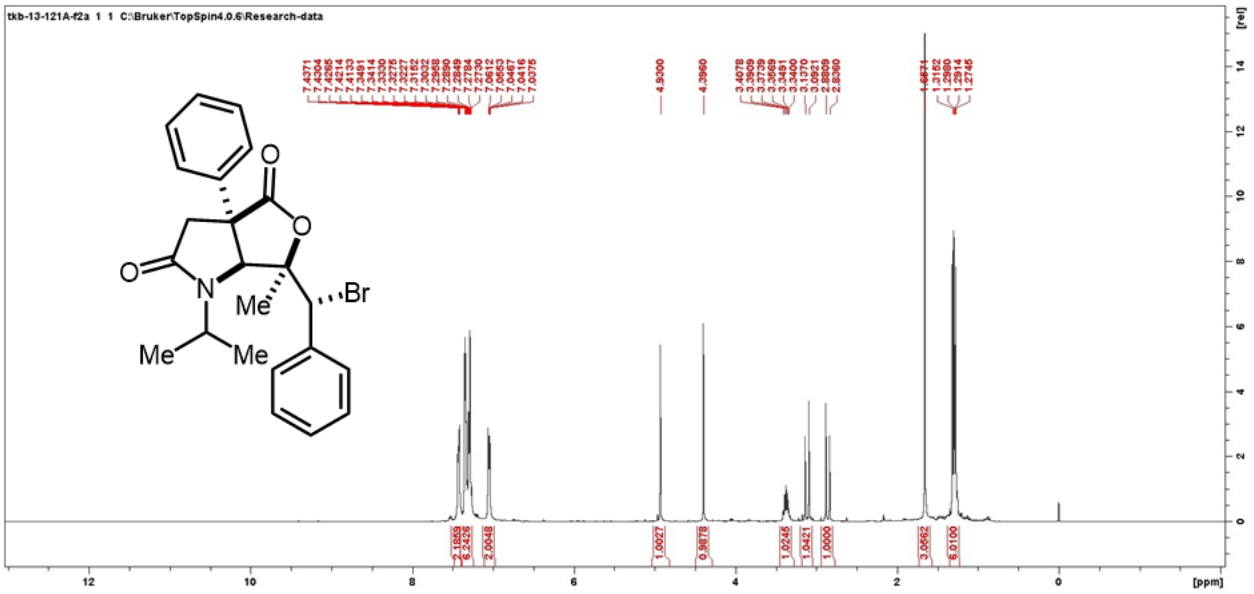


Compound 2d

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Reddish oily substance. Yield = 389.0 mg, 88%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.41 (m, 2H), 7.35 – 7.27 (m, 6H), 7.06 – 7.04 (m, 2H), 4.93 (s, 1H), 4.40 (s, 1H), 3.37 (dq, *J* = 14.6, 7.8, 7.3 Hz, 1H), 3.11 (d, *J* = 18.0 Hz, 1H), 2.86 (d, *J* = 18.0 Hz, 1H), 1.66 (s, 3H), 1.31 – 1.27 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 172.9, 139.2, 135.4, 129.9, 129.4, 129.2, 128.7, 128.1, 125.4, 88.1, 71.4, 59.6, 53.3, 48.2, 44.4, 21.8, 19.5, 19.3. FTIR (KBr): 2985.4, 1737.5, 1691.2, 1644.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1002.8, 925.8, 791.0. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{23}H_{24}BrNO_3$ $[M]^{+}$ 441.0940, found 441.0944.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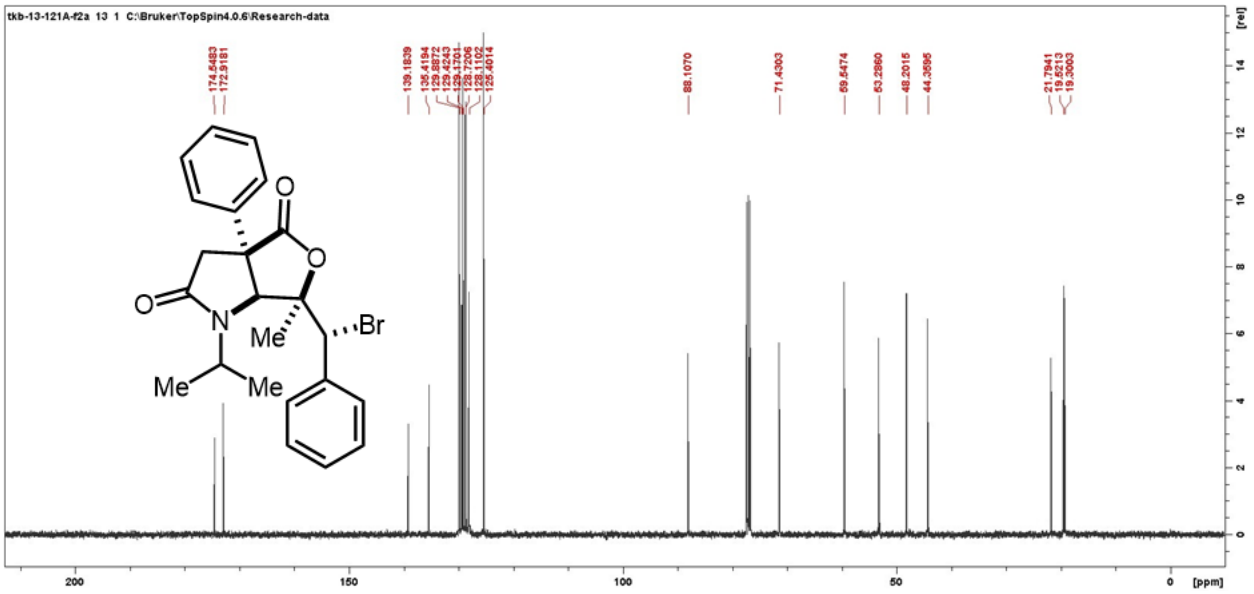
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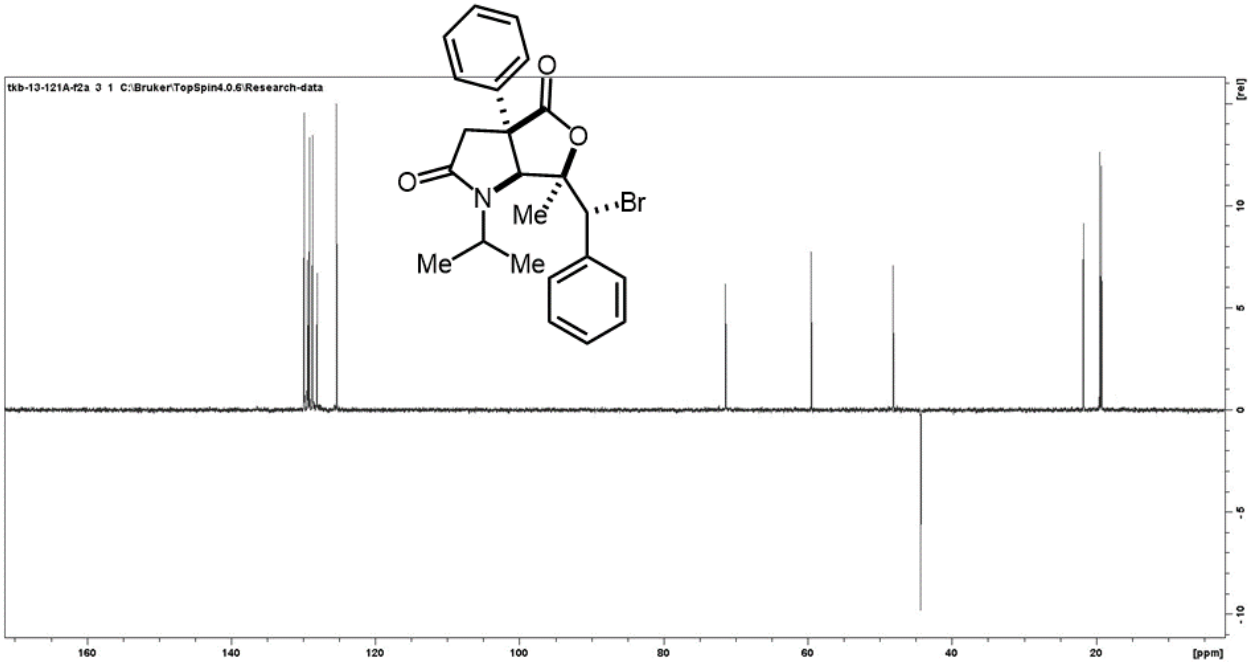

Compound 2e

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Yellowish oily substance. Yield = 356.4 mg, 81%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.24 (m, 10H), 5.77 – 5.64 (m, 1H), 5.32 – 5.24 (m, 2H), 4.95 (s, 1H), 4.68 (s, 1H), 4.41 (d, *J* = 4.7 Hz, 1H), 3.17 (d, 1H), 2.94 – 2.90 (m, 2H), 1.51 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 172.3, 139.0, 135.3, 131.3, 129.9, 129.5, 129.3, 128.8, 128.3, 125.7, 119.5, 88.3, 69.6, 60.0, 52.7, 45.0, 43.8, 21.0. FTIR (KBr): 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. **HRMS-EI$^+$** (*m/z*): calc for $C_{23}H_{22}BrNO_3$ $[M]^+$ 439.0783, found 439.0788.

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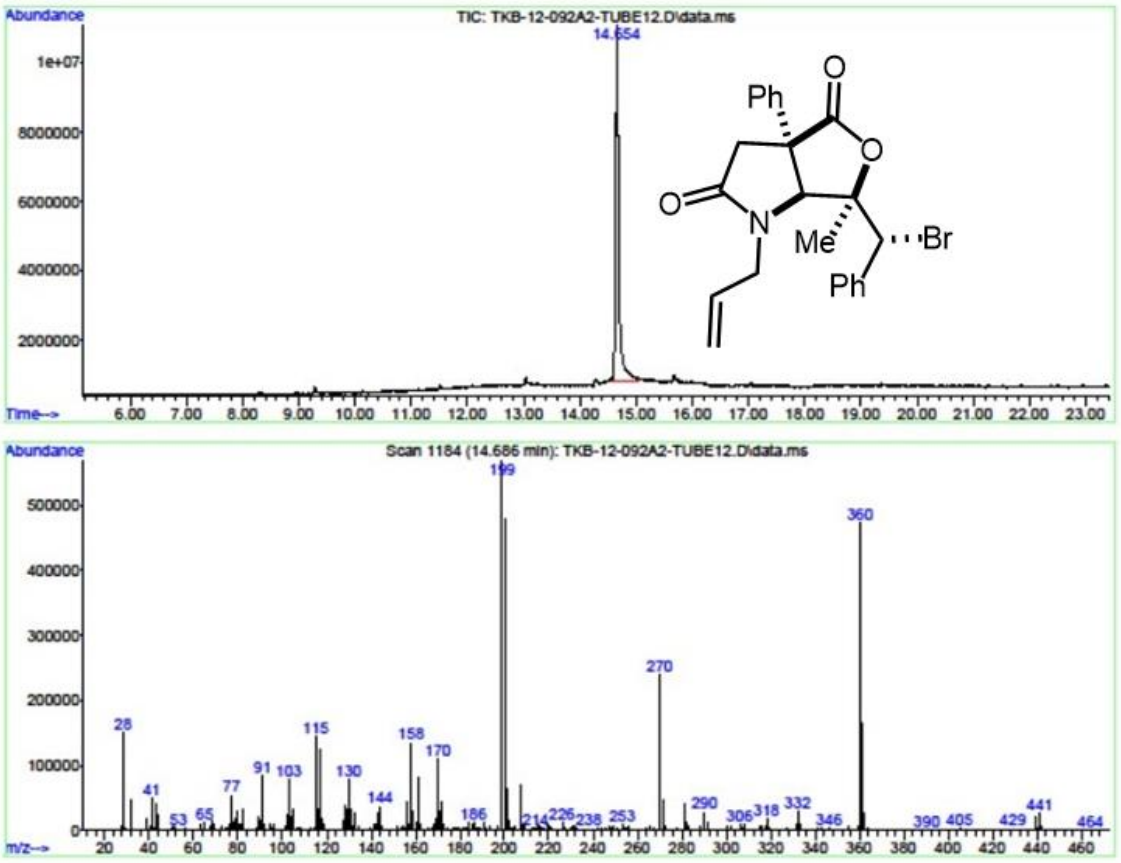

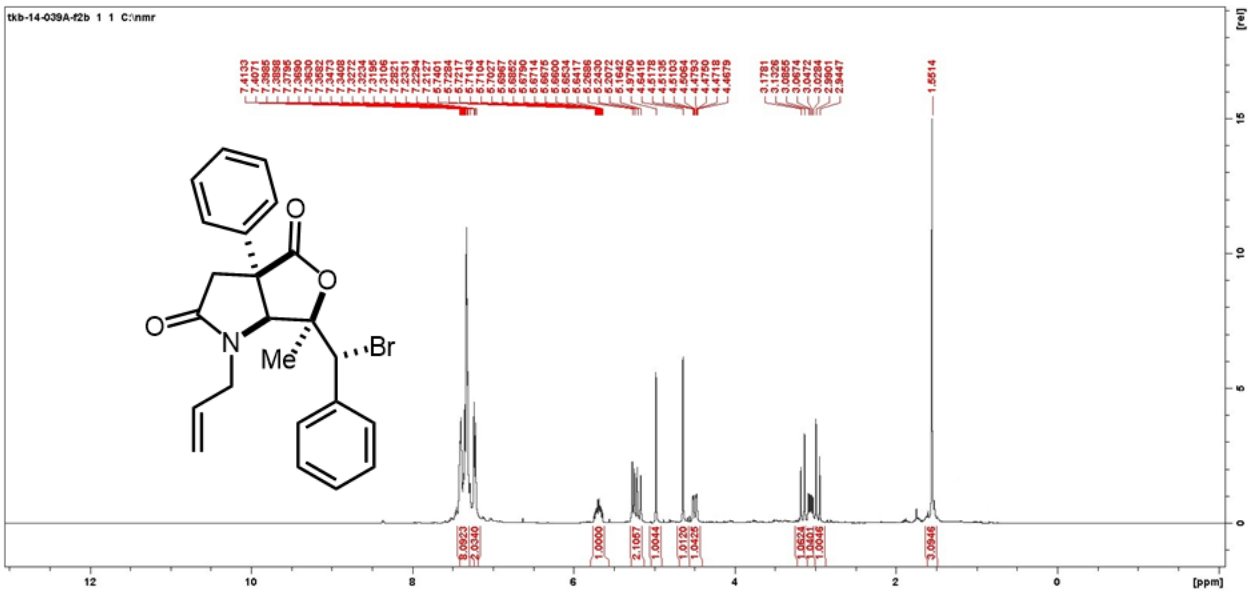

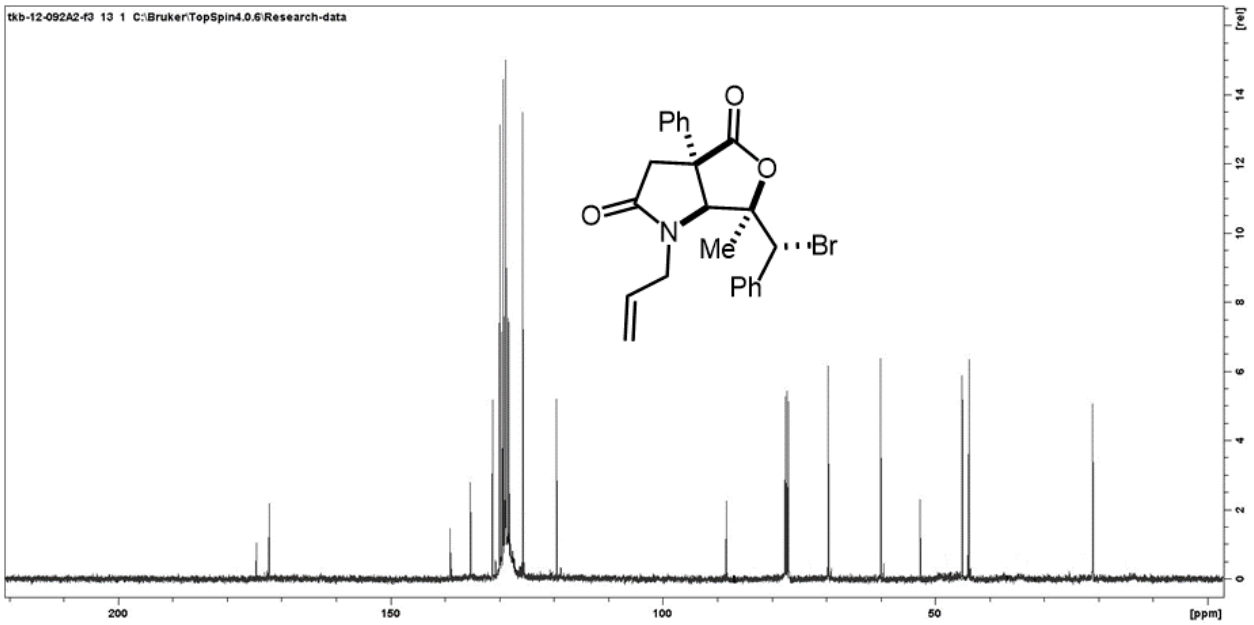

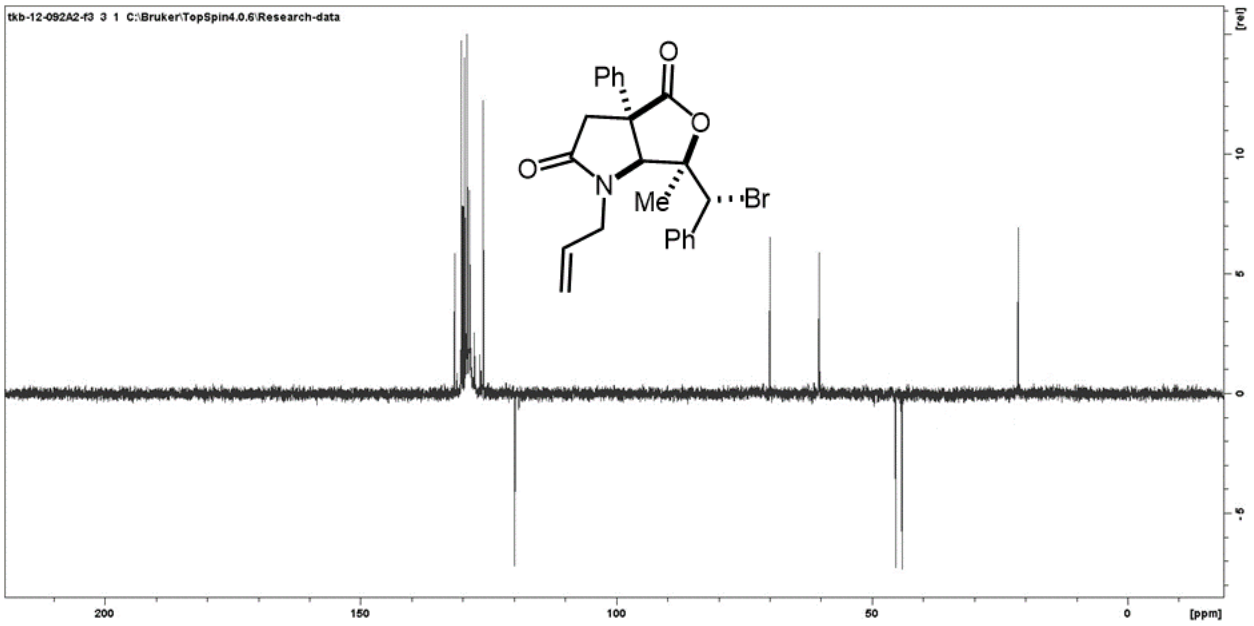

Compound 2f

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Pale yellow oil. Yield = 398.1 mg, 85%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.40 (m, 3H), 7.33 – 7.26 (m, 5H), 7.10 – 7.07 (m, 2H), 5.01 (s, 1H), 4.44 (s, 1H), 3.32 (p, *J* = 8.4 Hz, 1H), 3.08 (d, *J* = 18.0 Hz, 1H), 2.85 (d, *J* = 18.0 Hz, 1H), 2.05 – 1.71 (m, 6H), 1.63 (s, 3H), 1.58 – 1.40 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.5, 172.1 139.3, 135.4, 129.9, 129.5, 129.4, 129.1, 128.7, 128.0, 125.3, 88.1, 72.2, 59.8, 57.5,

52.8, 44.8, 29.6, 28.1, 24.5, 24.1, 22.0. FTIR (KBr): 2994.1, 1763.4, 1669.4, 1608.2, 1511.1, 1431.8, 1414.7, 1344.9, 1298.4, 1135.3, 1031.8, 996.7, 706.4. **HRMS-EI$^+$** (*m/z*): calc for $C_{25}H_{26}BrNO_3$ $[M]^+$ 467.1096, found 467.1092.

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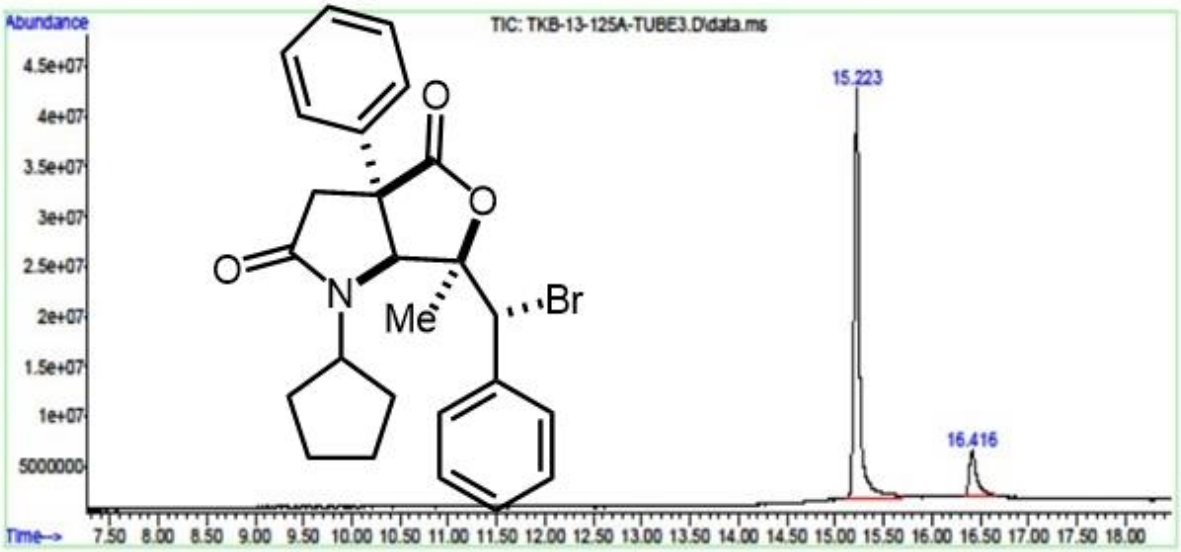

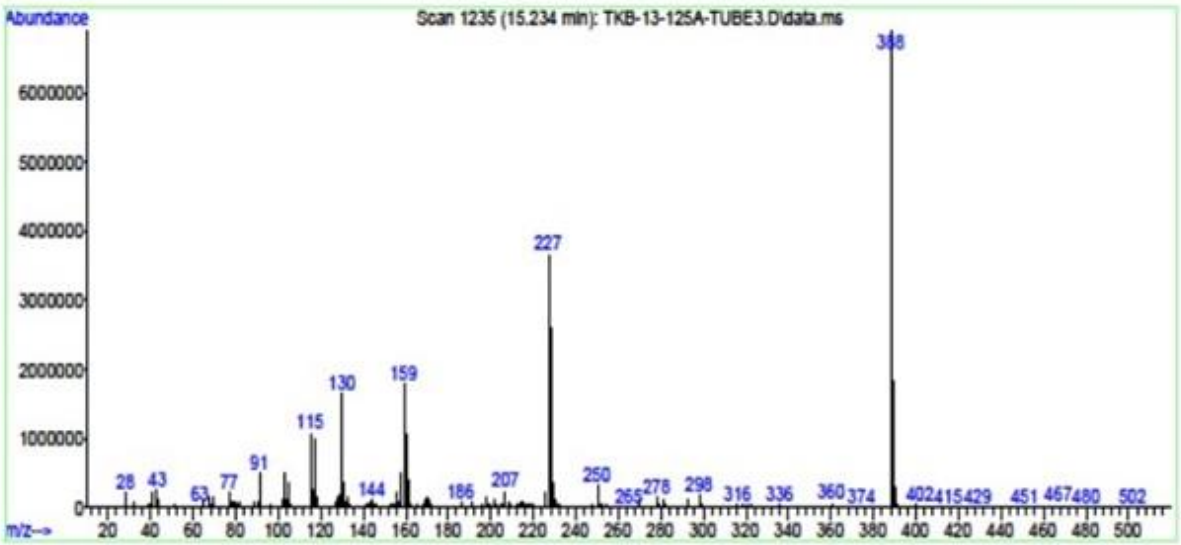

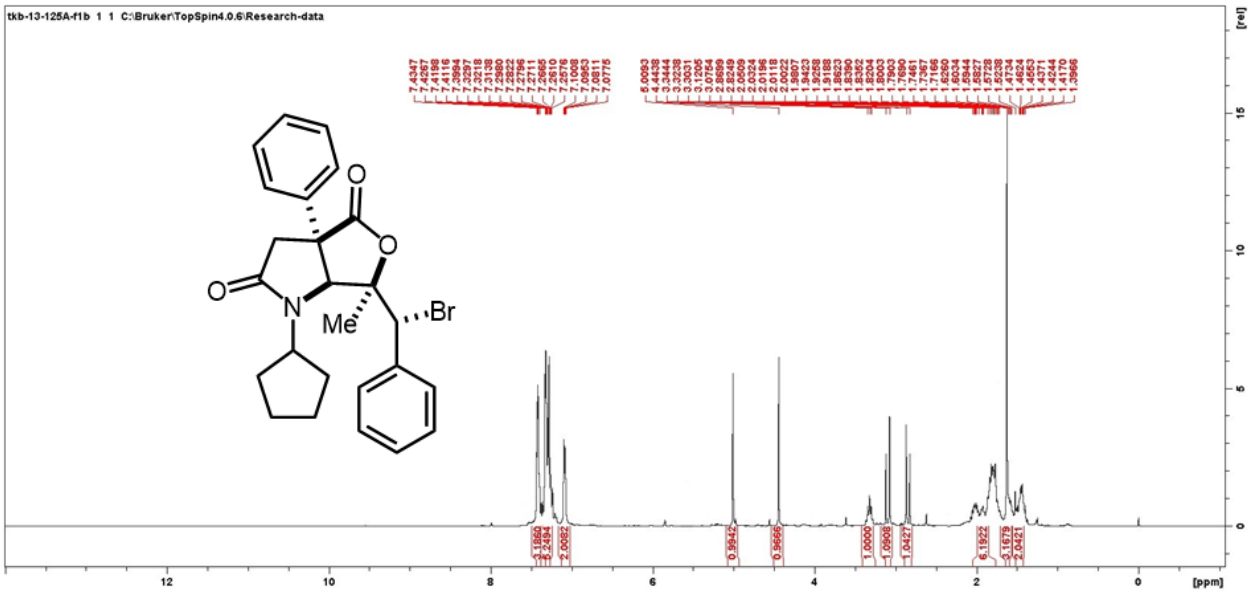
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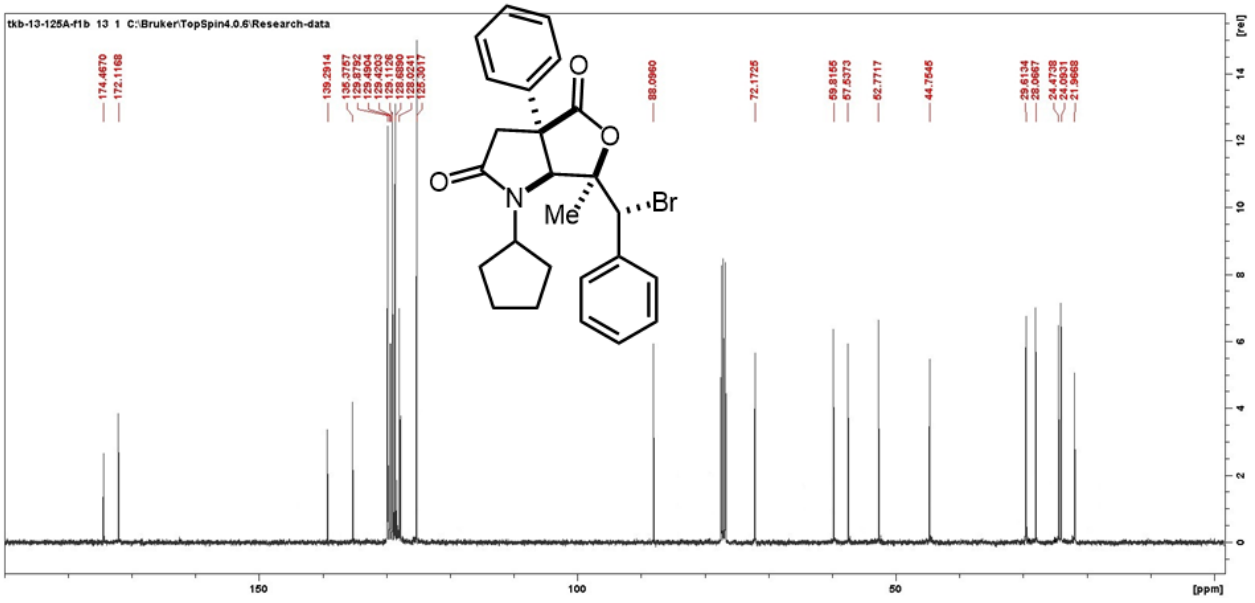
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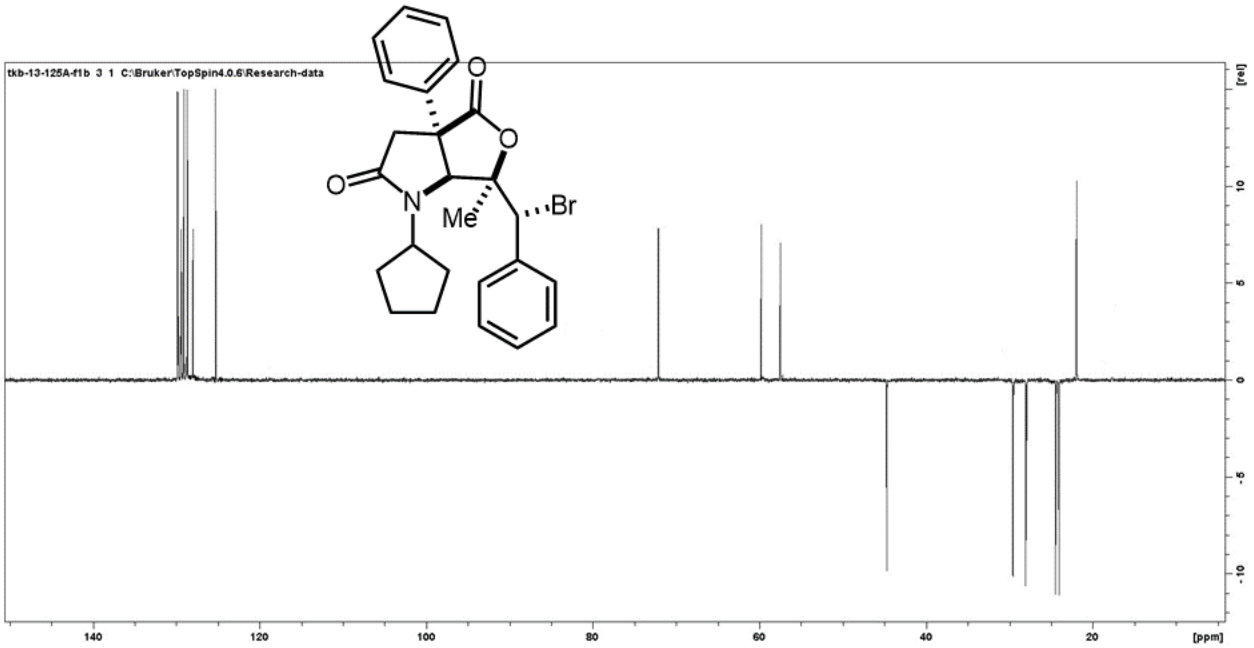
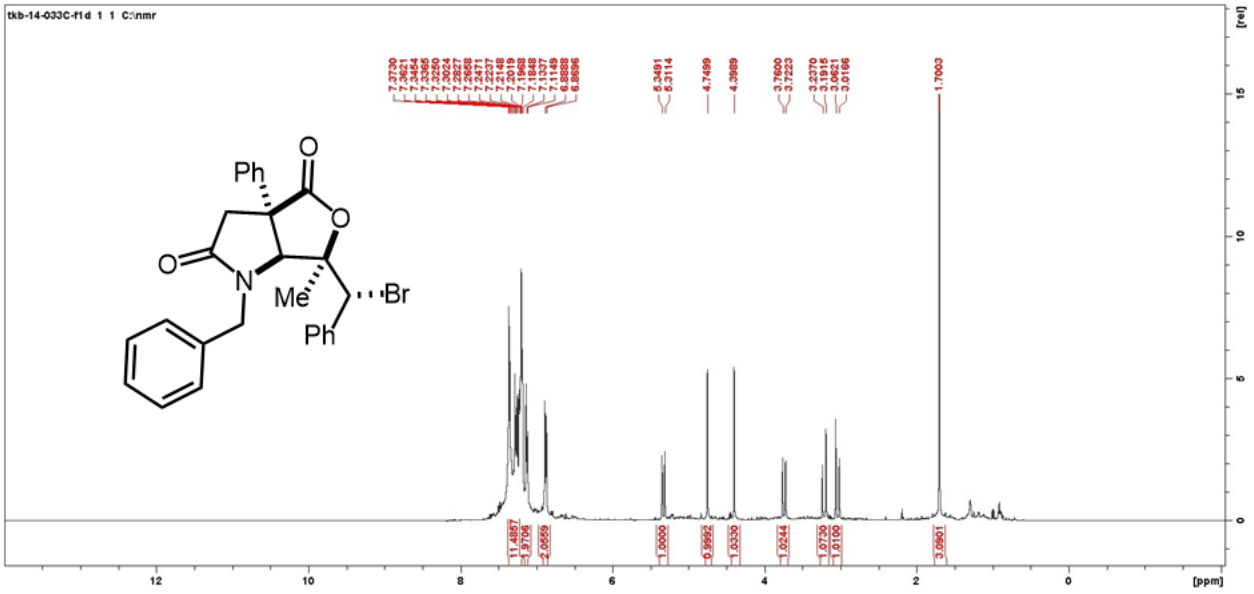
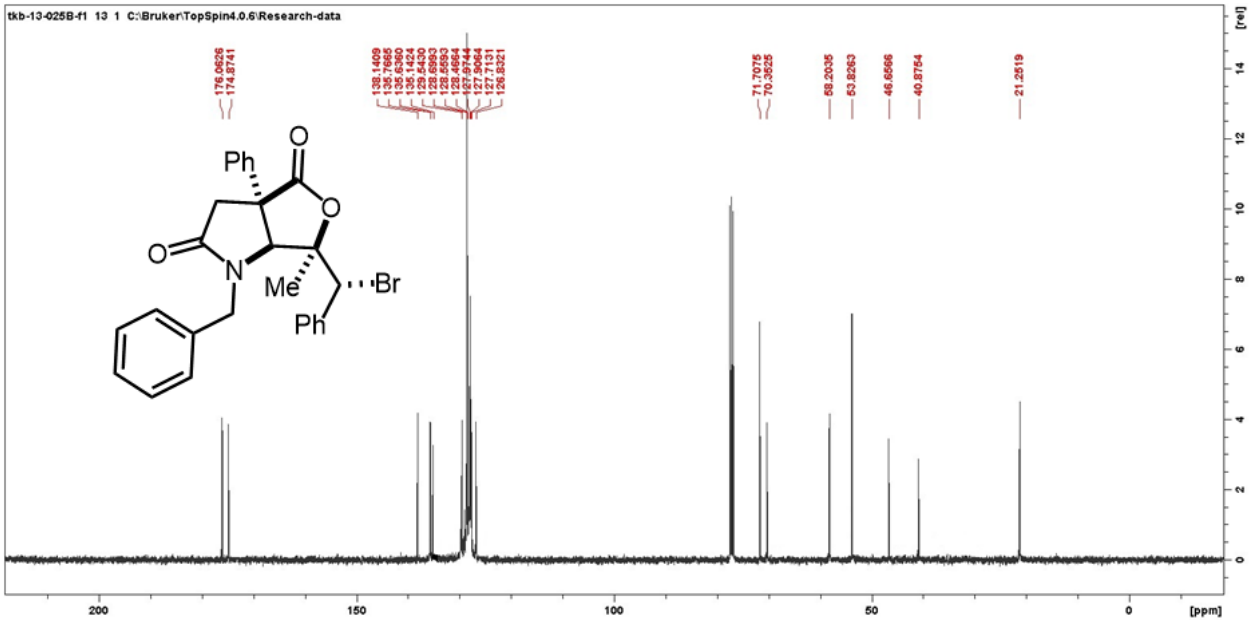
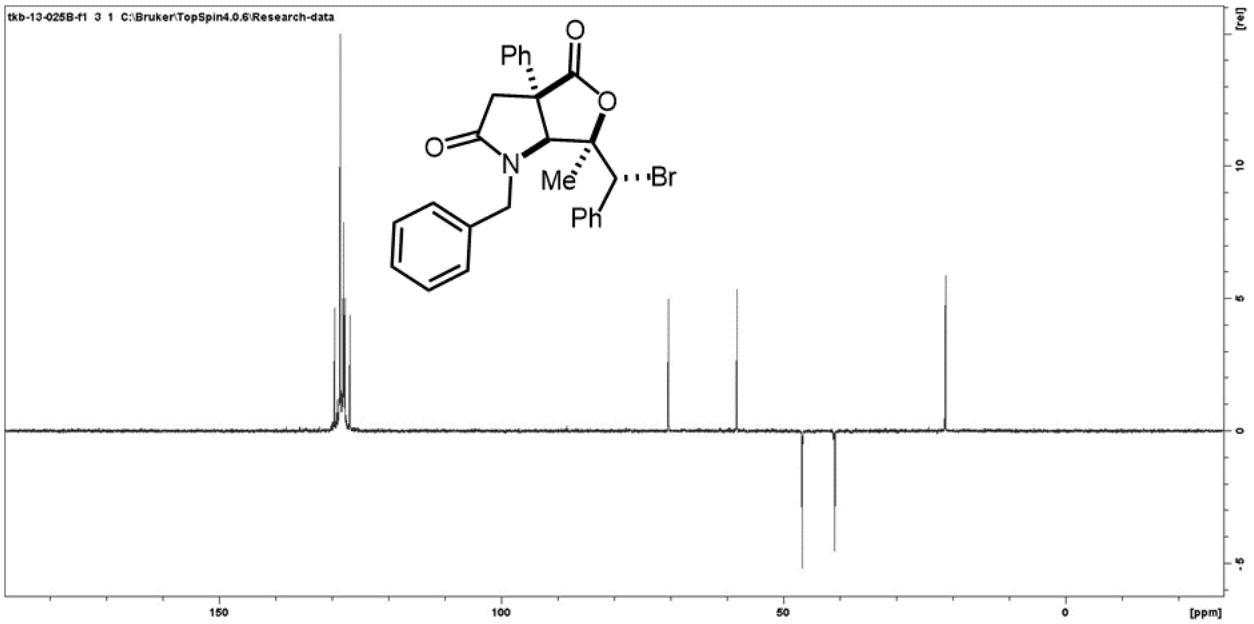


Compound 2g

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Off-white amorphous substance. Yield = 377.3 mg, 77%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.02 (m, 14H), 6.78 (d, 1H), 5.32 (d, J = 14.9 Hz, 1H), 4.75 (s, 1H), 4.40 (s, 1H), 3.74 (d, J = 17.3 Hz, 1H), 3.21 (d, J = 17.3 Hz, 1H), 3.00 (d, J = 17.3 Hz, 1H), 1.70 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.1, 174.9, 138.1, 135.8, 135.6, 135.2, 129.6, 128.6, 128.5, 128.0, 127.9, 127.7, 126.8, 71.7, 70.4, 58.2, 53.8, 46.7, 40.9, 21.3. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{27}H_{24}BrNO_3$ $[M]^+$ 489.0940, found 489.0947.



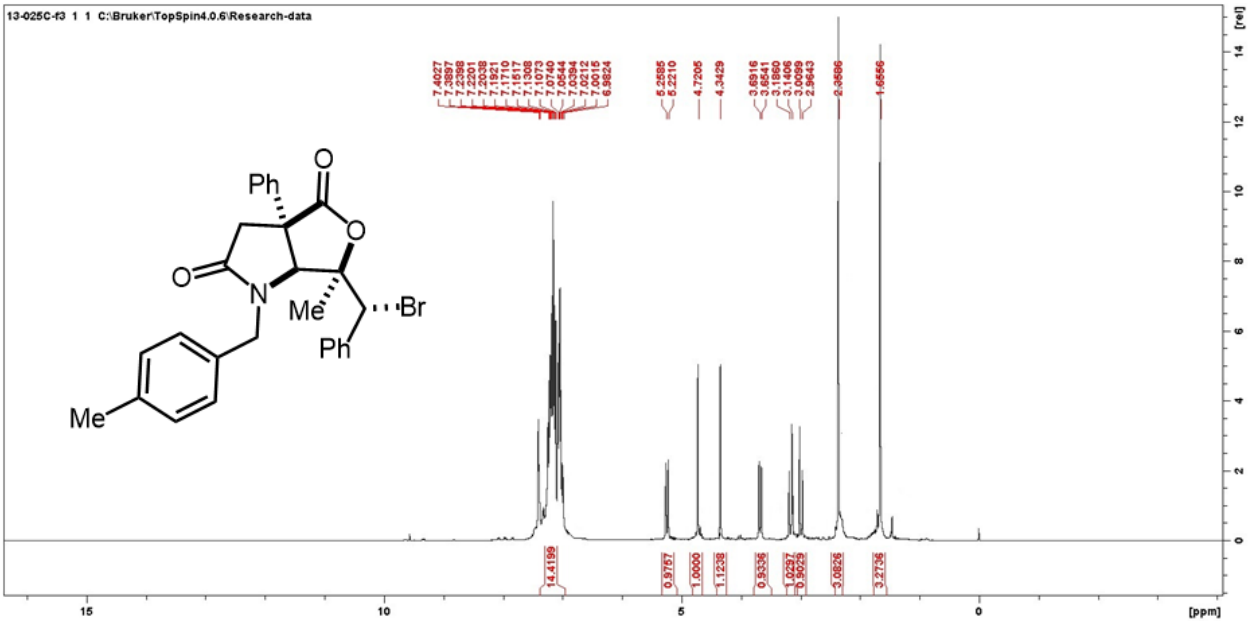


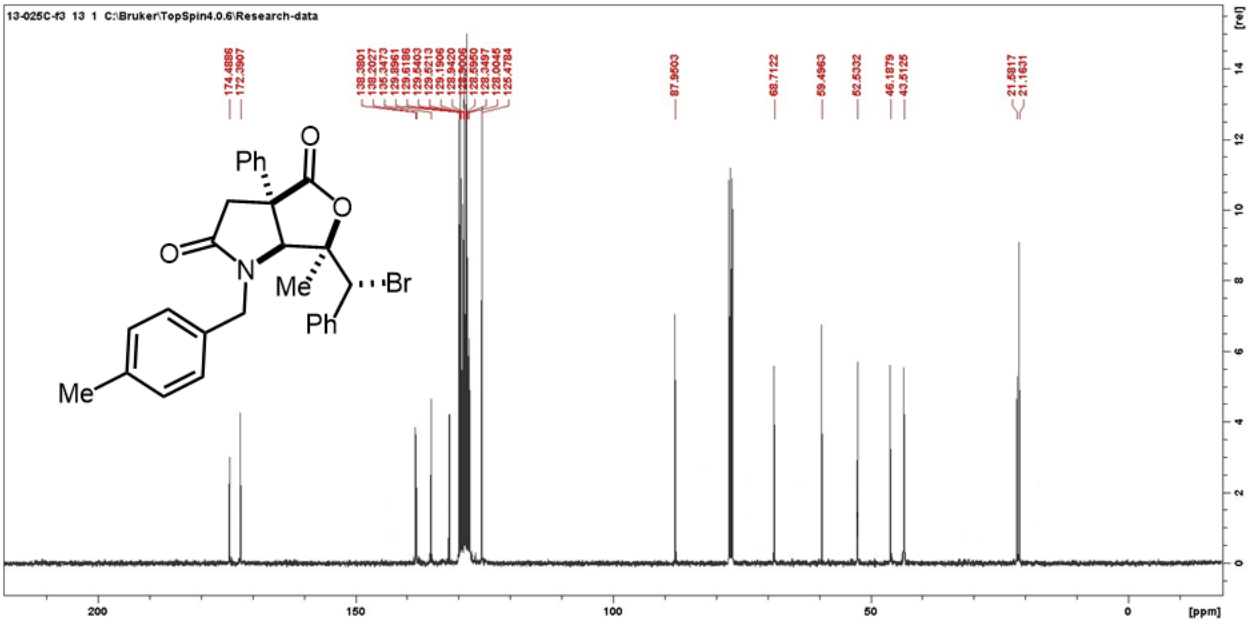


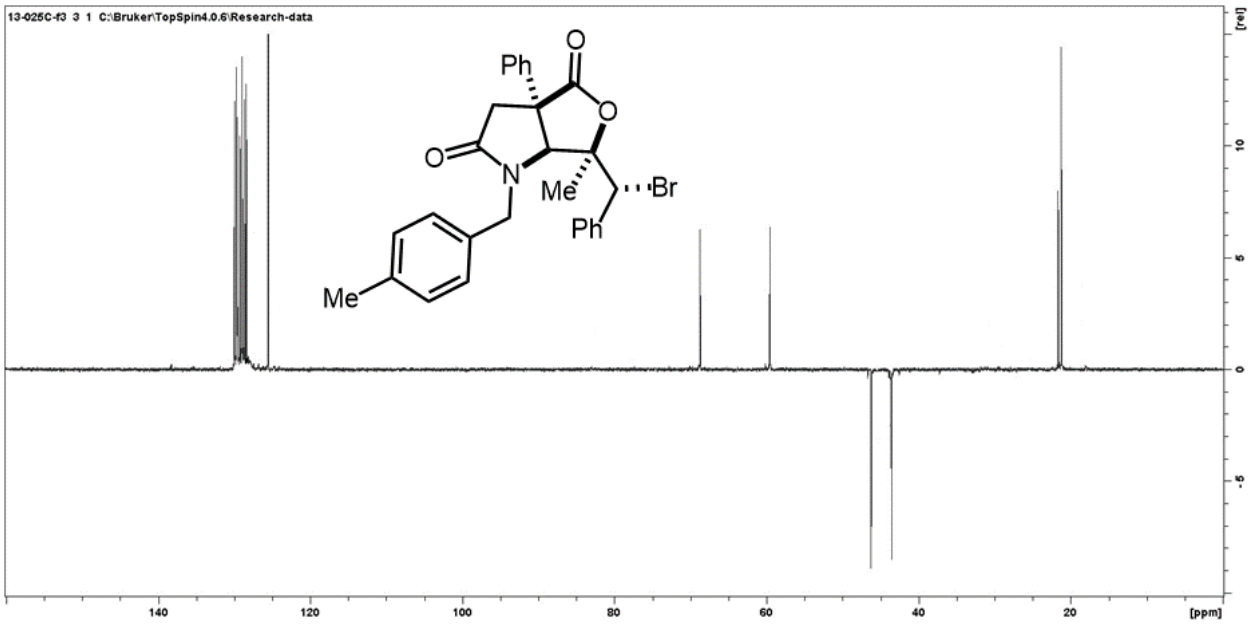
Compound 2h

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yellowish oil. Yield = 413.6 mg, 82%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 –6.98 (m, 14H), 5.24 (d, *J* = 15.0 Hz, 1H), 4.72 (s, 1H), 4.34 (d, *J* = 1.7 Hz, 1H), 3.67 (d, *J* = 15.0 Hz, 1H), 3.14 (d, *J* = 18.2 Hz, 1H), 2.99 (d, *J* = 18.2 Hz, 1H), 2.33 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.5, 172.4, 138.2, 135.4, 129.9,

129.6, 129.6, 129.5, 129.2, 129.0, 128.9, 128.6, 128.4, 128.0, 125.5, 88.0, 68.7, 59.5, 52.5, 46.2, 43.5, 21.6, 21.2. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{28}H_{26}BrNO_3$ $[M]^{+}$ 503.1096, found 503.1090.

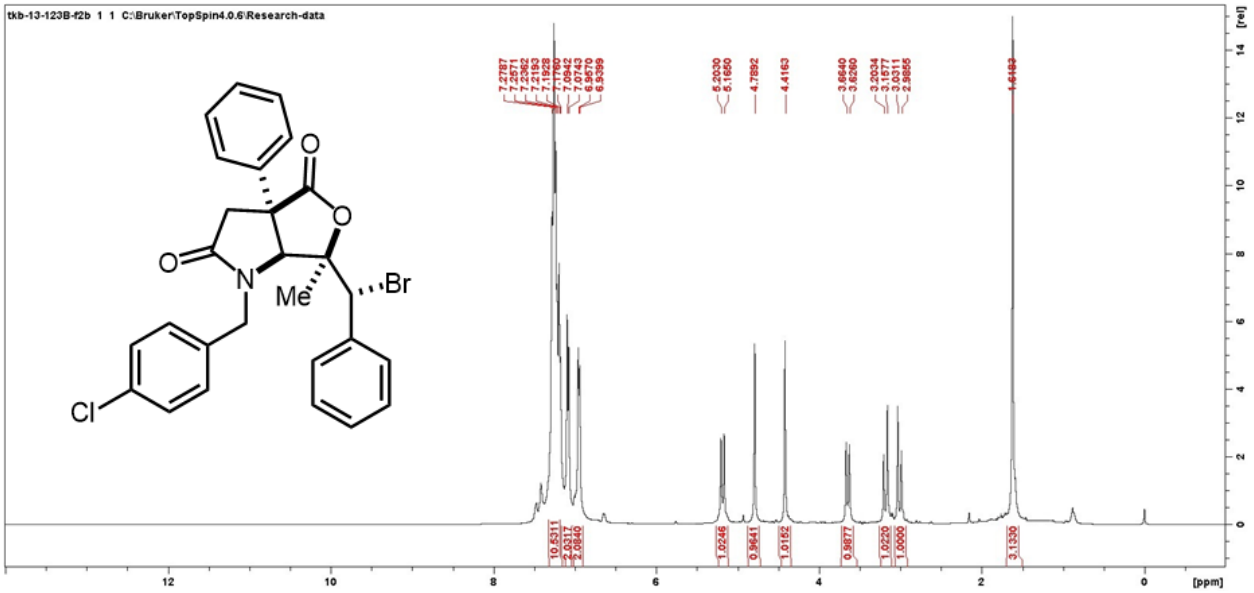


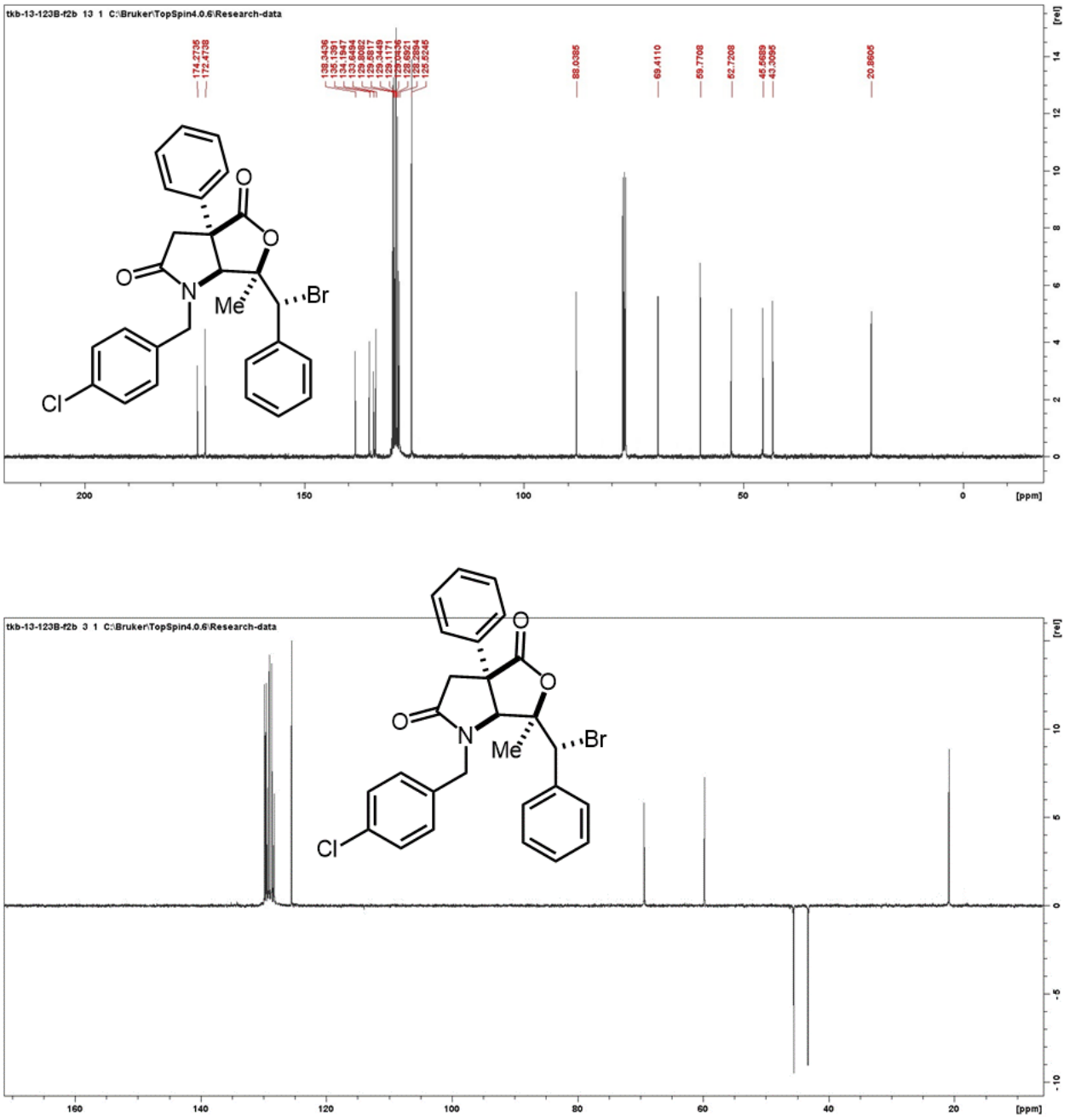




Compound 2i

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yellowish oil. Yield = 451.5 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.18 (m, 10H), 7.08 (d, *J* = 8.1 Hz, 2H), 6.95 (d, *J* = 7.2 Hz, 2H), 5.18 (d, *J* = 15.2 Hz, 1H), 4.79 (s, 1H), 4.42 (s, 1H), 3.65 (d, *J* = 15.2 Hz, 1H), 3.18 (d, *J* = 17.6 Hz, 1H), 3.01 (d, *J* = 17.6 Hz, 1H), 1.61 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 172.5, 138.4, 135.1, 134.2, 133.7, 129.8, 129.6, 129.4, 129.1, 129.1, 128.7, 128.3, 125.5, 88.0, 69.4, 59.8, 52.7, 45.6, 43.3, 20.9. **HRMS-EI^{+}** (*m/z*): calc for $C_{27}H_{23}BrClNO_3$ $[M]^{+}$ 523.0550, found 523.0555.

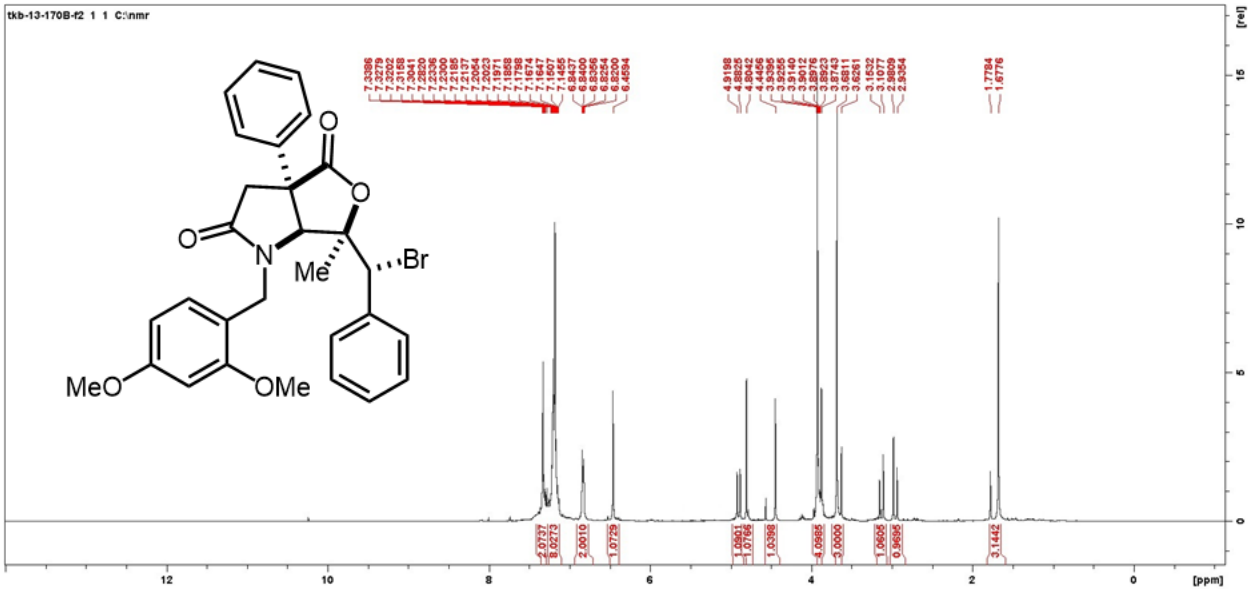


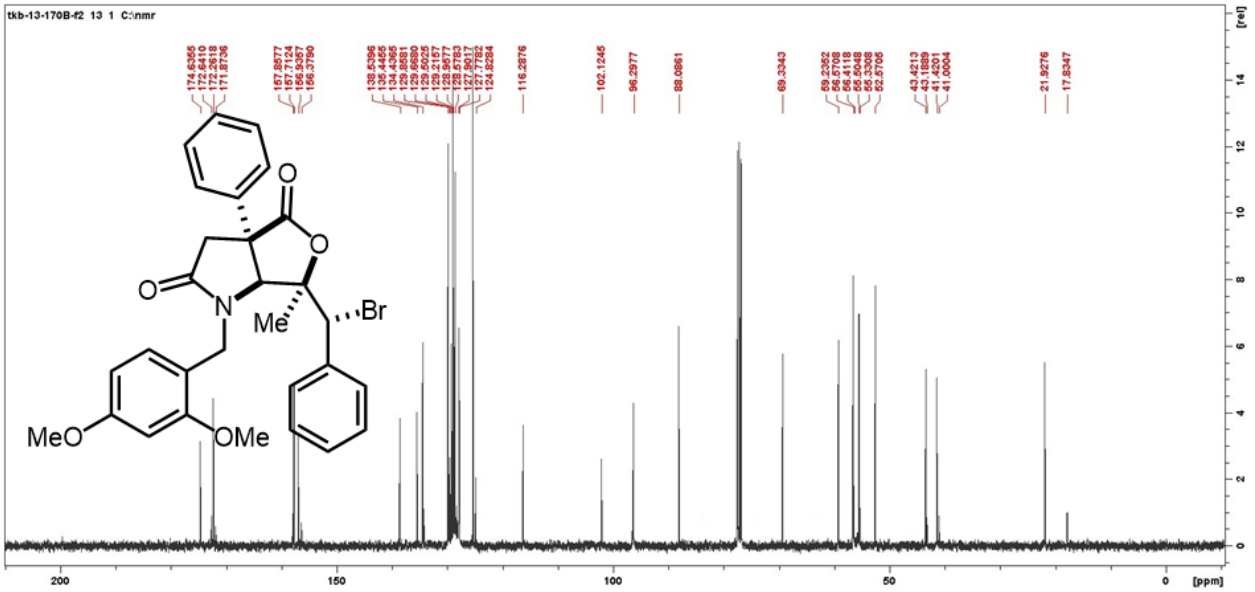


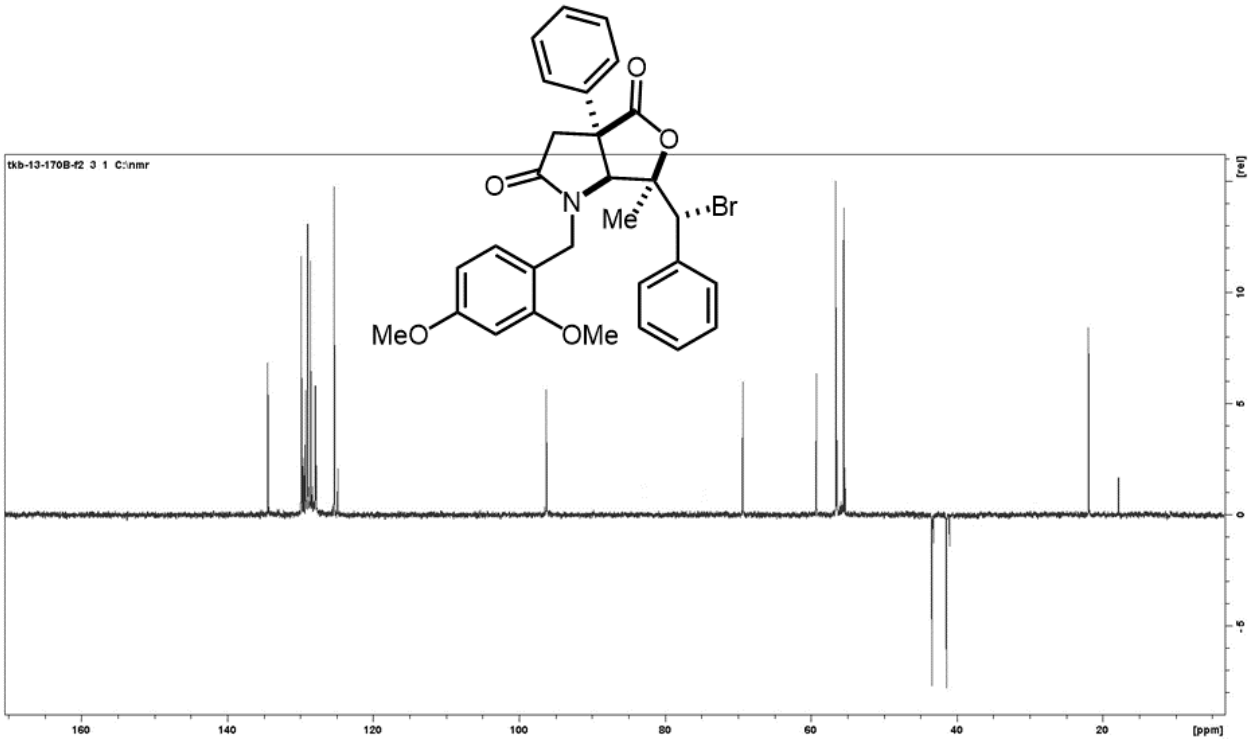
Compound 2j

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Yellowish oil. Yield = 467.5 mg, 85%, 85:15 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.11 (m, 10H), 6.85 – 6.82 (m, 2H), 6.46 (s, 1H), 4.90 (d, J = 14.9 Hz, 1H), 4.80 (s, 1H), 4.45 (s, 1H), 3.93 – 3.87 (m, 4H), 3.68 (s, 3H), 3.17 (d, J = 13.6 Hz, 1H), 2.95 (d, J = 13.6 Hz, 1H), 1.68 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 172.6, 157.9,

156.9, 138.5, 135.4, 134.4, 129.9, 129.2, 128.9, 128.6, 127.9, 125.3, 116.3, 102.1, 96.3, 88.1, 69.3, 63.8, 59.2, 56.6, 56.4, 55.5, 55.3, 52.6, 43.4, 43.2, 41.4, 41.0, 21.9, 17.8. **HRMS-EI$^+$** (*m/z*): calc for $C_{29}H_{28}BrNO_5$ $[M]^+$ 549.1151, found 549.1157.

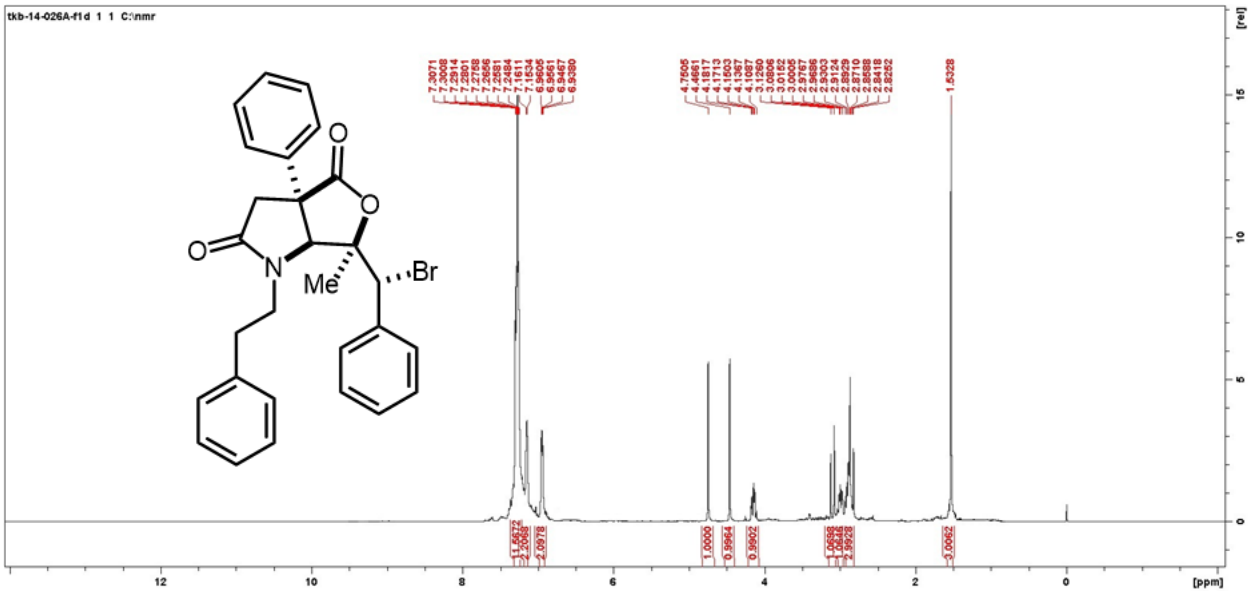






Compound 2k

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Pale yellow oil. Yield = 428.8 mg, 85%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.15 (m, 13H), 6.96 – 6.94 (m, 2H), 4.75 (s, 1H), 4.47 (s, 1H), 4.15 (td, J = 12.0, 6.7 Hz, 1H), 3.12 – 2.82 (m, 5H), 1.52 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.8, 172.2, 139.0, 137.8, 135.0, 129.8, 129.3, 128.9, 128.8, 128.6, 128.1, 126.8, 125.6, 88.7, 71.5, 59.7, 52.8, 44.3, 43.9, 32.9, 20.0. **HRMS-EI^{+}** (*m/z*): calc for $C_{28}H_{26}BrNO_3$ $[M]^{+}$ 503.1096, found 503.1092.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O
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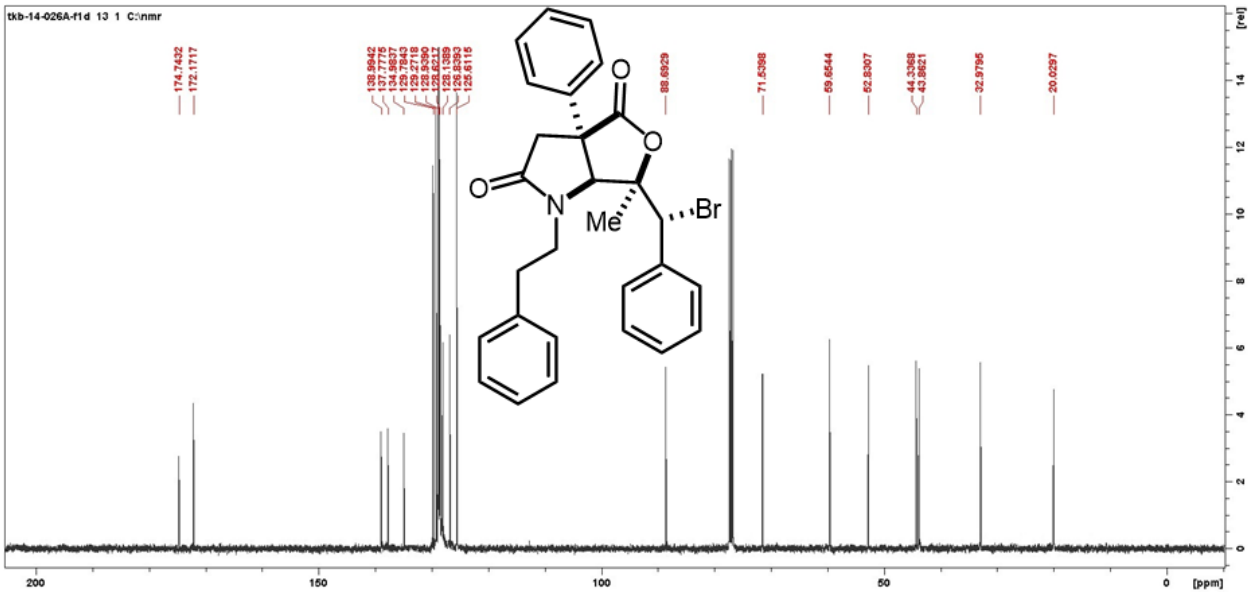
N
Me
Br
[rel]
[ppm]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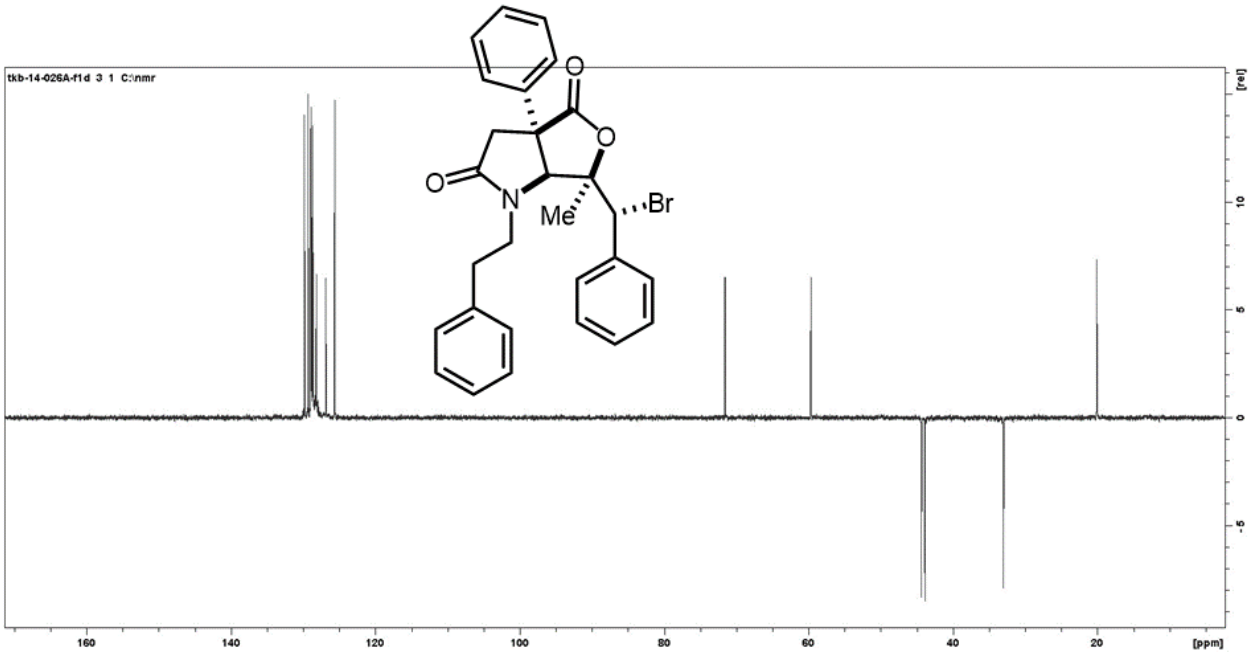
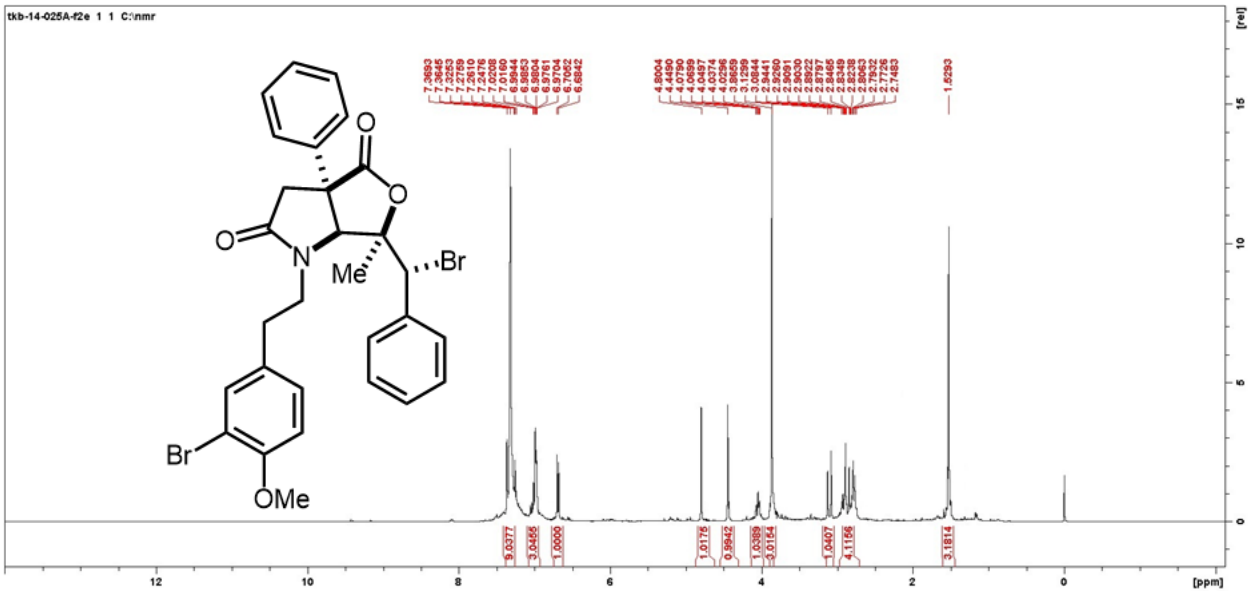
[rel]
[ppm]



Compound 2l

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 269.9 mg, 88%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.25 (m, 9H), 7.02 – 6.97 (m, 3H), 6.69 (d, *J* = 8.4 Hz, 1H), 4.81 (s, 1H), 4.43 (s, 1H), 4.16 – 3.98 (m, 1H), 3.86 (s, 3H), 3.10 (d, 1H), 2.94 – 2.75 (m, 4H), 1.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7, 172.1, 154.8, 138.9, 135.0, 133.5, 131.2, 129.8, 129.4, 129.3, 129.0, 128.7, 128.2, 125.6, 112.1, 111.87, 88.8, 71.4, 59.8, 56.2, 52.8, 44.3, 43.7, 31.7, 20.3. **HRMS-EI^{+}** (*m/z*): calc for $C_{29}H_{27}Br_2NO_4$ $[M]^{+}$ 611.0307, found 611.0313.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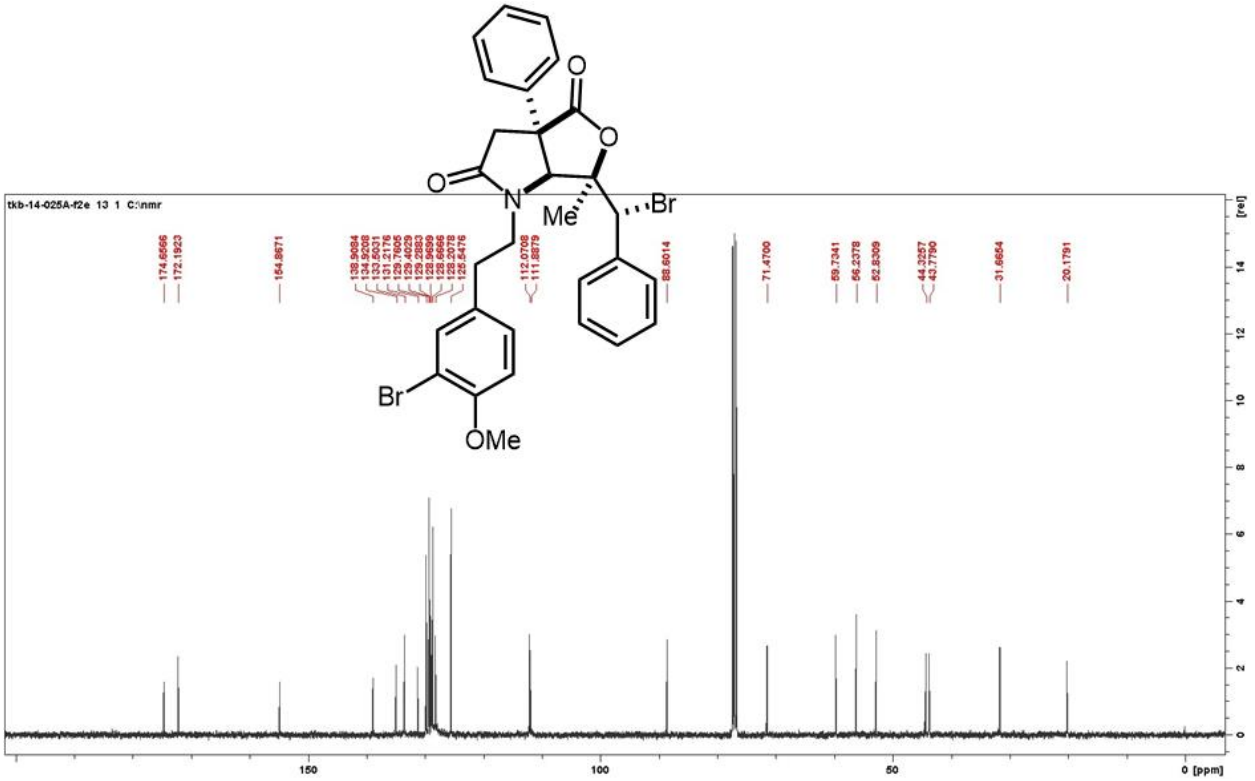
[ppm]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Br
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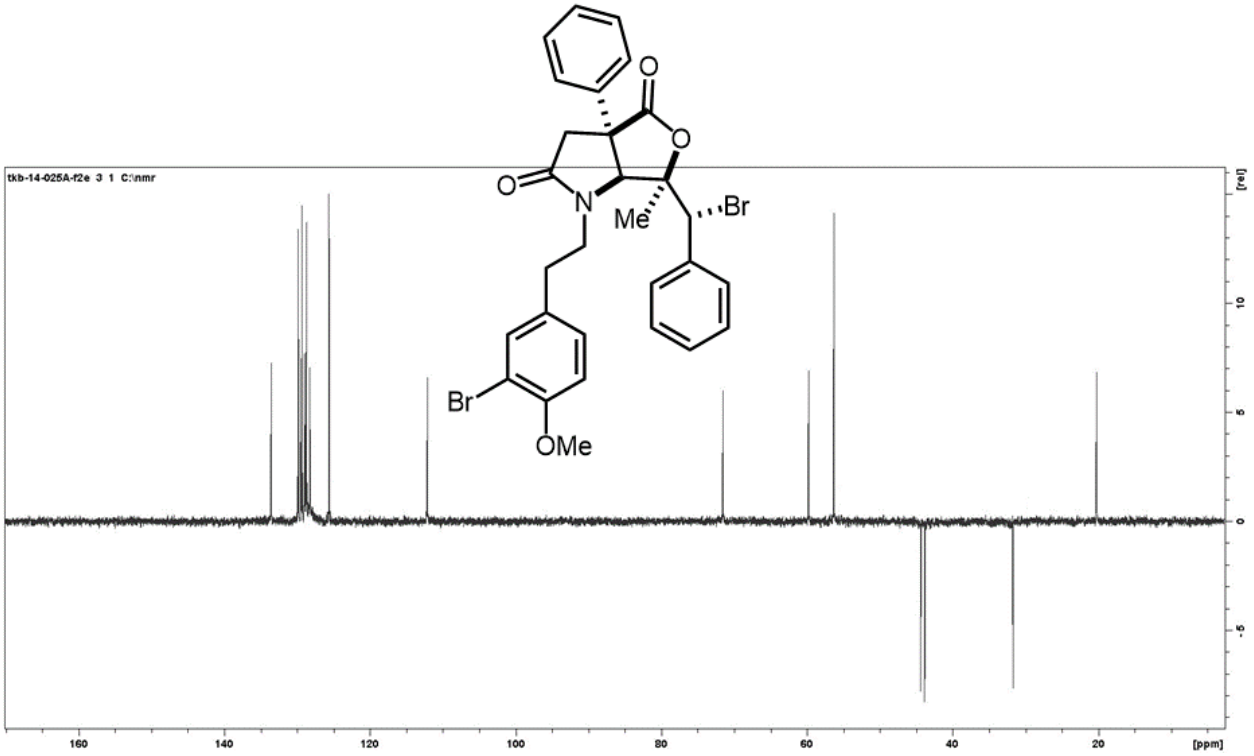
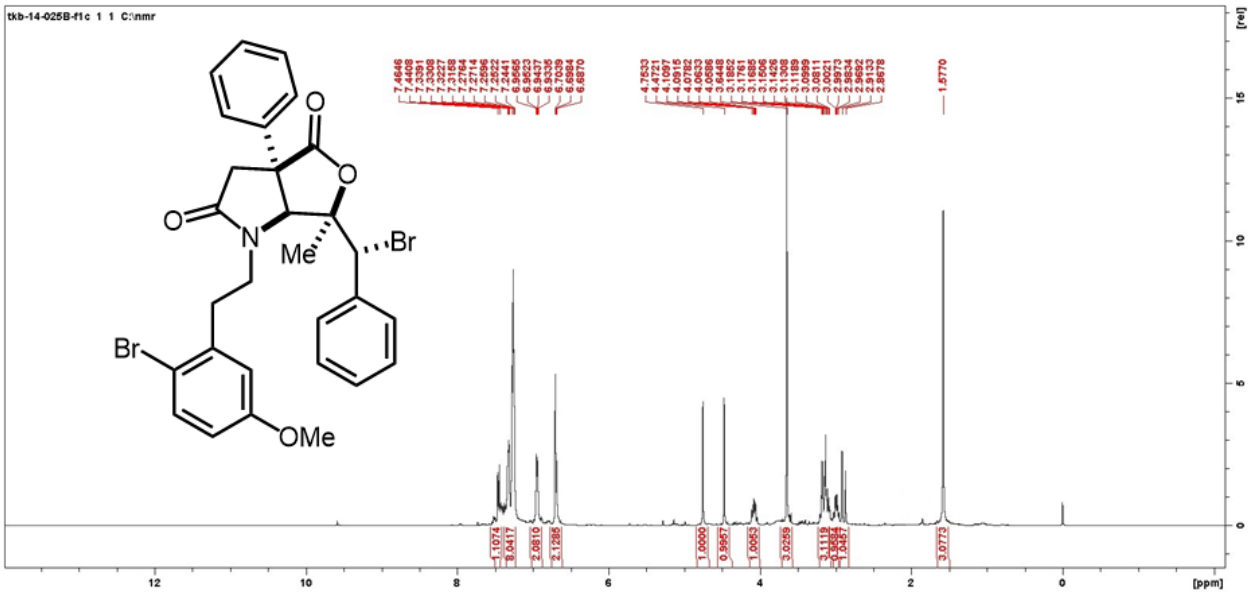


Compound 2m

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Pale yellow oil. Yield = 257.6 mg, 84%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.24 (m, 9H), 6.96 – 6.93 (m, 2H), 6.70 – 6.69 (m, 2H), 4.75 (s, 1H), 4.47 (s, 1H), 4.13 – 4.01 (m, 1H), 3.65 (s, 3H), 3.23 – 3.04 (m, 3H), 3.04 – 2.93 (m, 1H), 2.89 (d, *J* = 18.2 Hz, 1H), 1.58 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7, 172.2, 159.2, 138.6, 138.2, 135.1, 133.7, 129.8, 129.2, 128.6, 128.1, 125.4, 116.7, 114.8, 114.5, 88.7, 71.0, 59.0, 55.4, 52.8, 44.1, 43.0, 33.5, 20.4. **HRMS-EI^{+}** (*m/z*): calc for $C_{29}H_{27}Br_2NO_4$ $[M]^{+}$ 611.0307, found 611.0313.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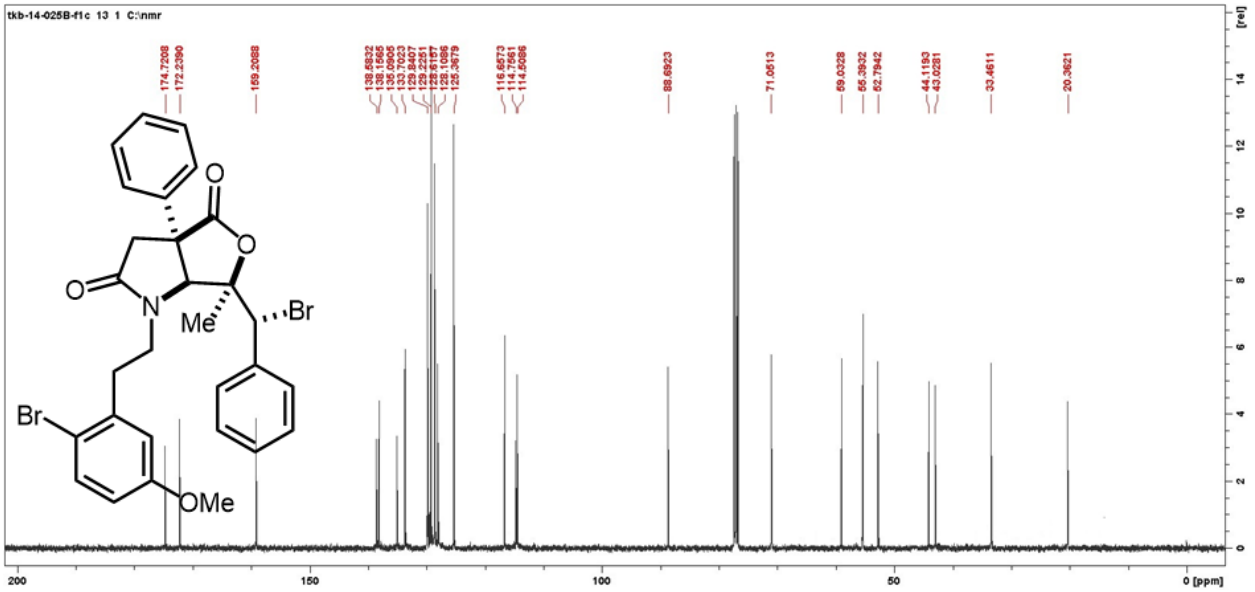
Br
Br
OMe
[rel]
[ppm]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125.3679
116.6573
114.7581
114.2088
88.8923
71.0513
69.0328
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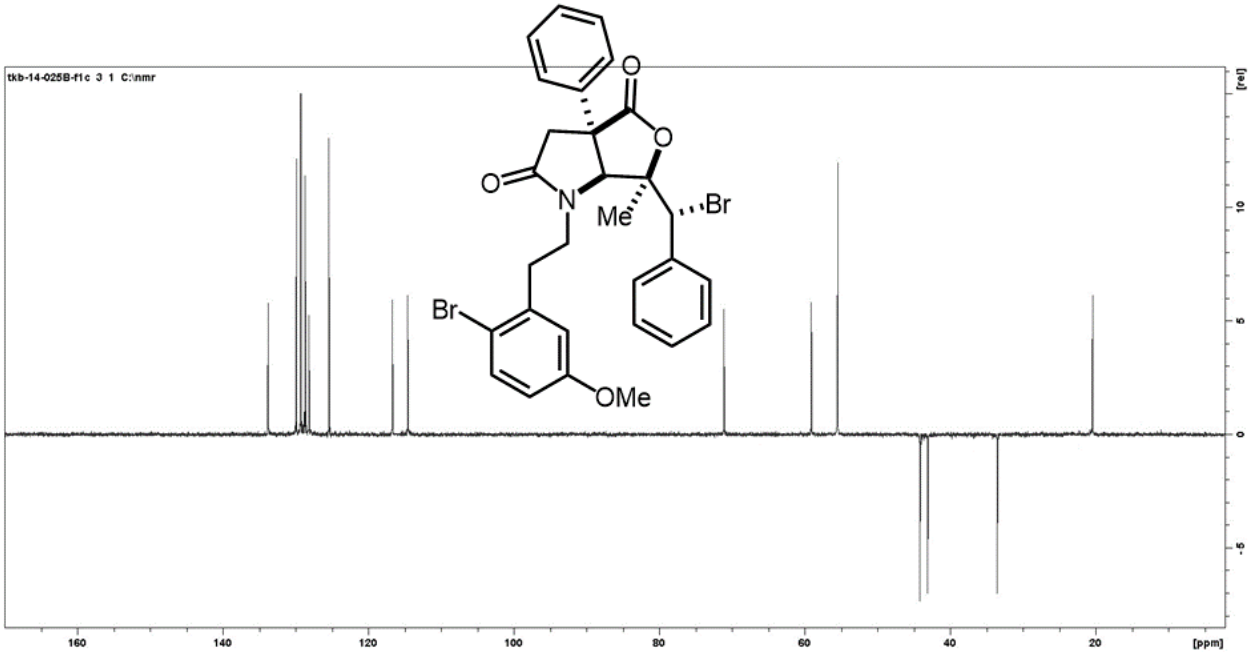
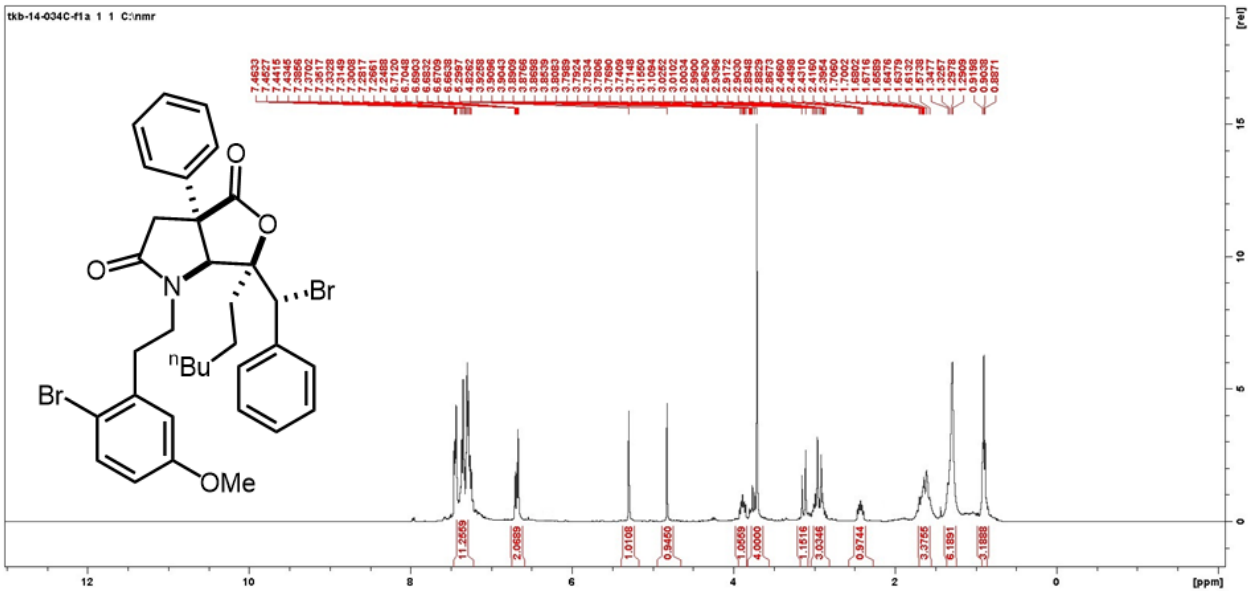


Compound 2n

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yellowish oil. Yield = 246.1 mg, 72%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.24 (m, 11H), 6.71 – 6.66 (m, 2H), 5.30 (s, 1H), 4.83 (s, 1H), 3.92 – 3.85 (m, 4H), 3.80 – 3.71 (m, 4H), 3.01 (d, *J* = 18.7 Hz, 1H), 2.96 – 2.87 (m, 3H), 2.43 (dd, *J* = 11.7, 9.6 Hz, 1H), 1.70 – 1.57 (m, 3H), 1.34 – 1.29 (m, 6H), 0.90 (t, *J* = 8.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 172.4, 159.1, 139.3, 138.0, 135.2, 133.4, 129.5, 129.2, 129.1, 128.9, 128.0, 125.6, 116.3, 114.9, 114.1, 89.5, 70.4, 58.3, 55.4, 52.3, 44.6, 42.5, 33.6, 33.2, 31.5, 29.7, 23.1, 22.5, 14.0. **HRMS-EI^{+}** (*m/z*): calc for $C_{34}H_{37}Br_2NO_4$ $[M]^{+}$ 681.1089, found 689.1093.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Br
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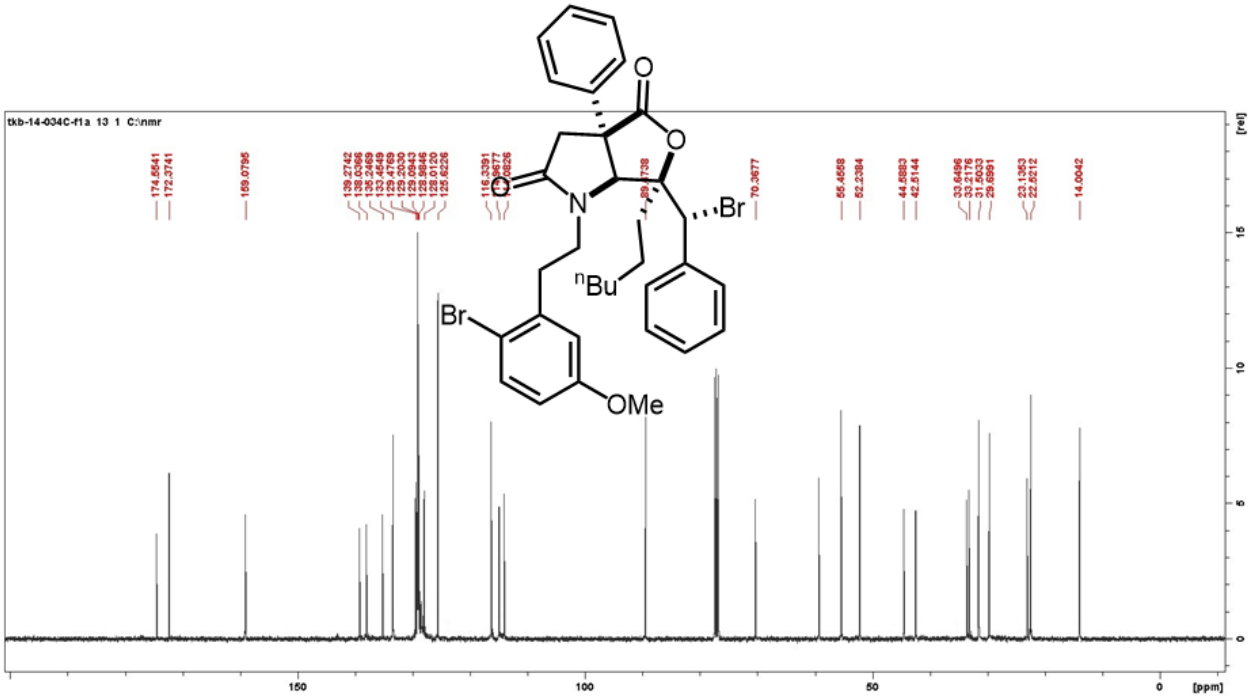
Br
OMe
[rel]
[ppm]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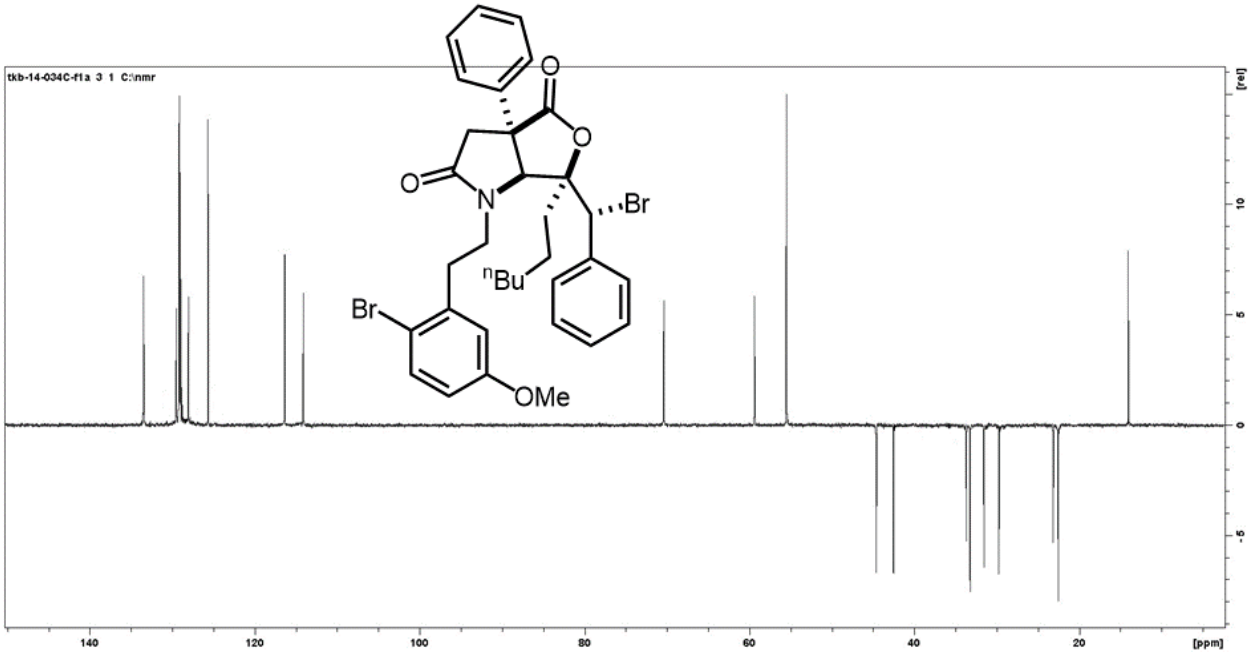
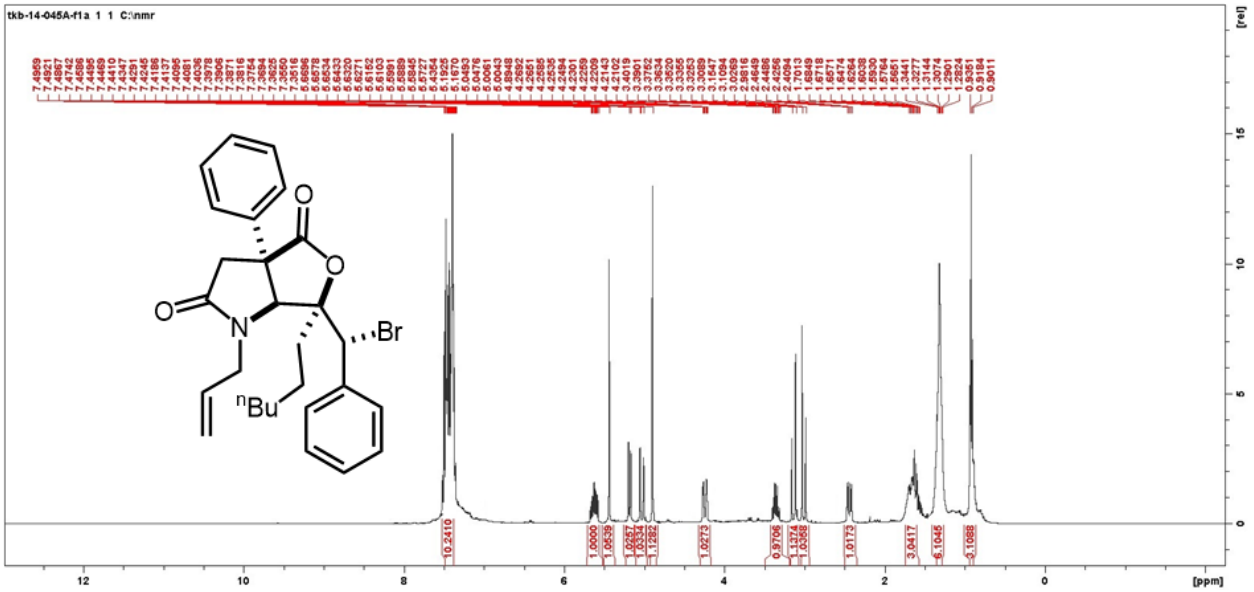
N
Br
nBu
Br
OMe
[rel]
[ppm]

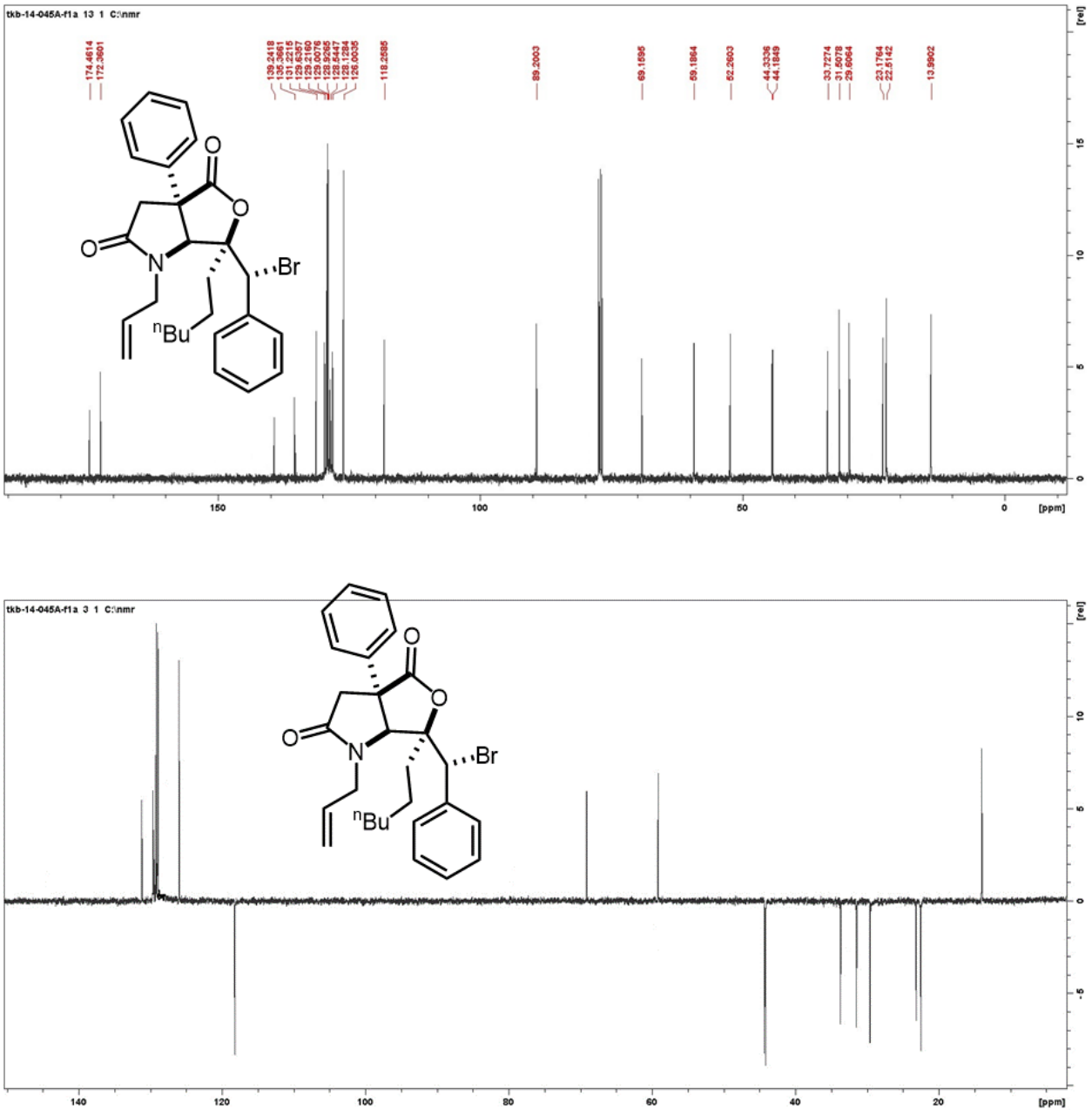


Compound 2o

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Yellowish oil. Yield = 178.7 mg, 70%, 95:5 dr.

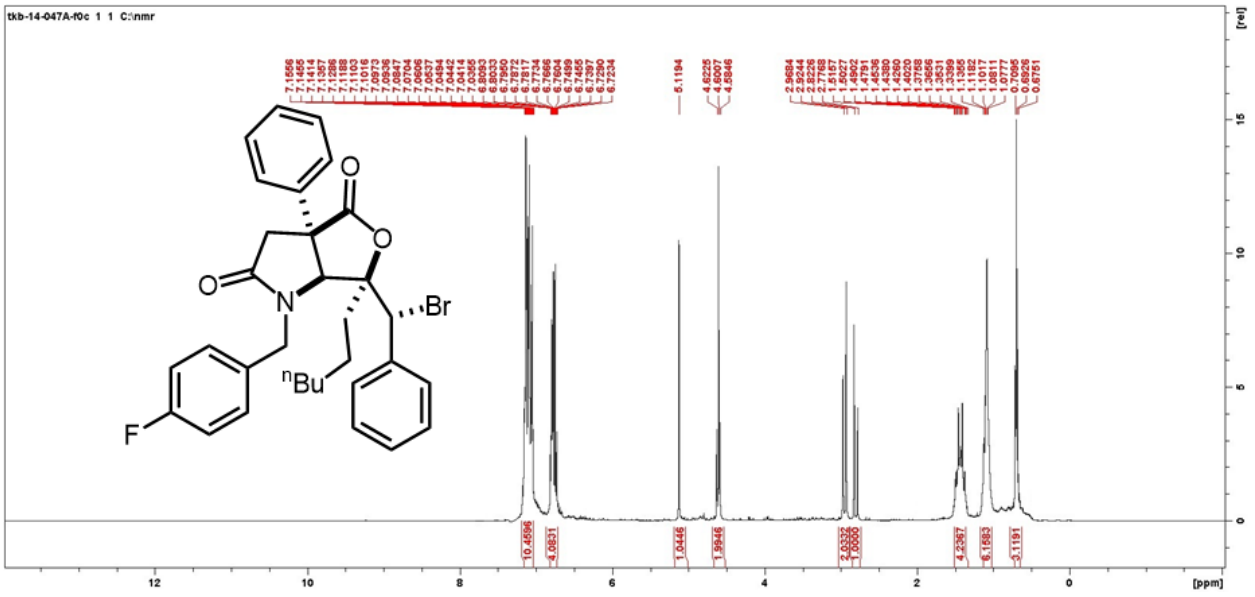
HRMS-EI$^+$ (*m/z*): calc for $C_{28}H_{32}BrNO_3$ $[M]^+$ 509.1566, found 509.1569.





Compound 2p

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yellowish oil. Yield = 202.5 mg, 70%, 95:5 dr. **HRMS-EI**$^+$ (*m/z*): calc for $C_{32}H_{33}BrFNO_3$ $[M]^+$ 577.1628, found 577.1633.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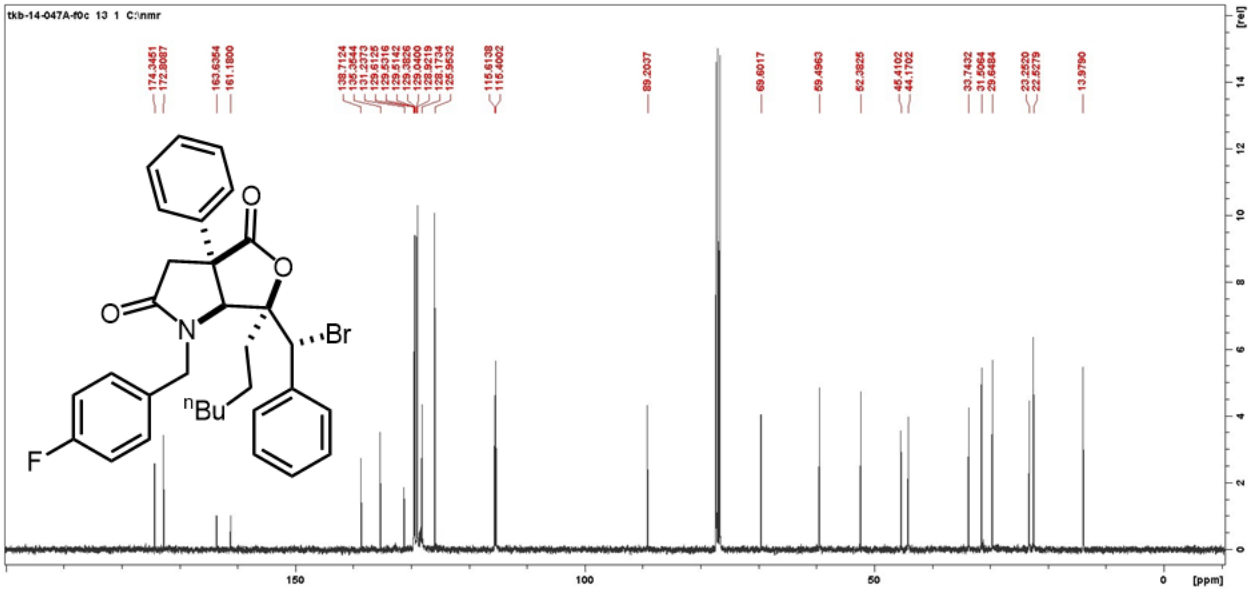
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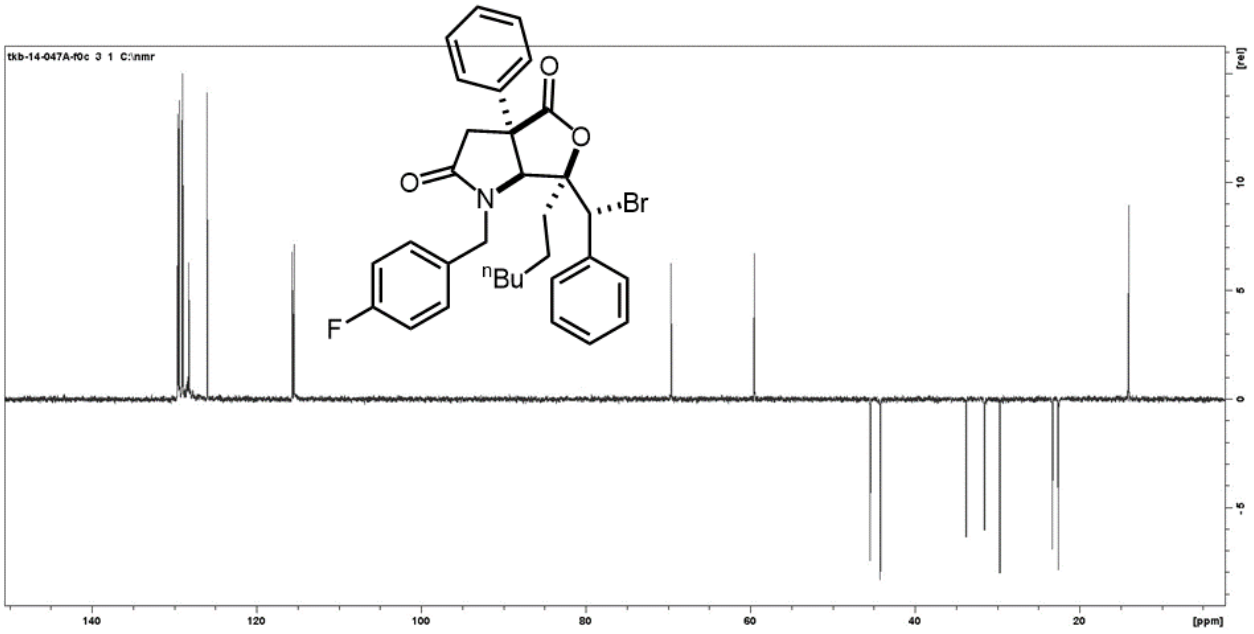
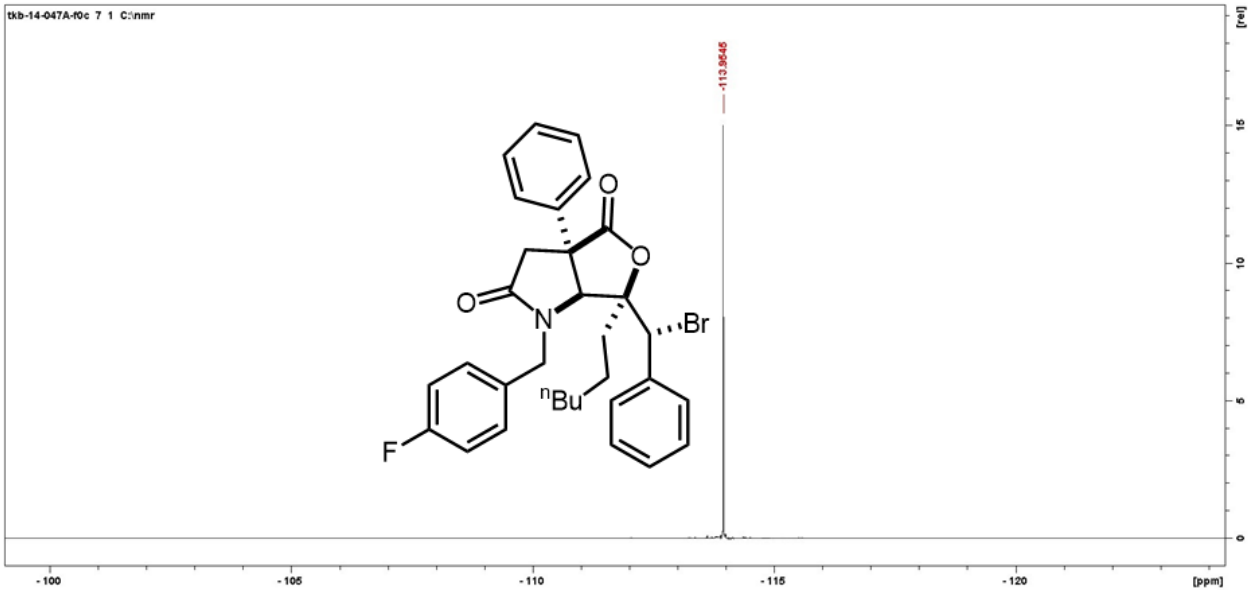


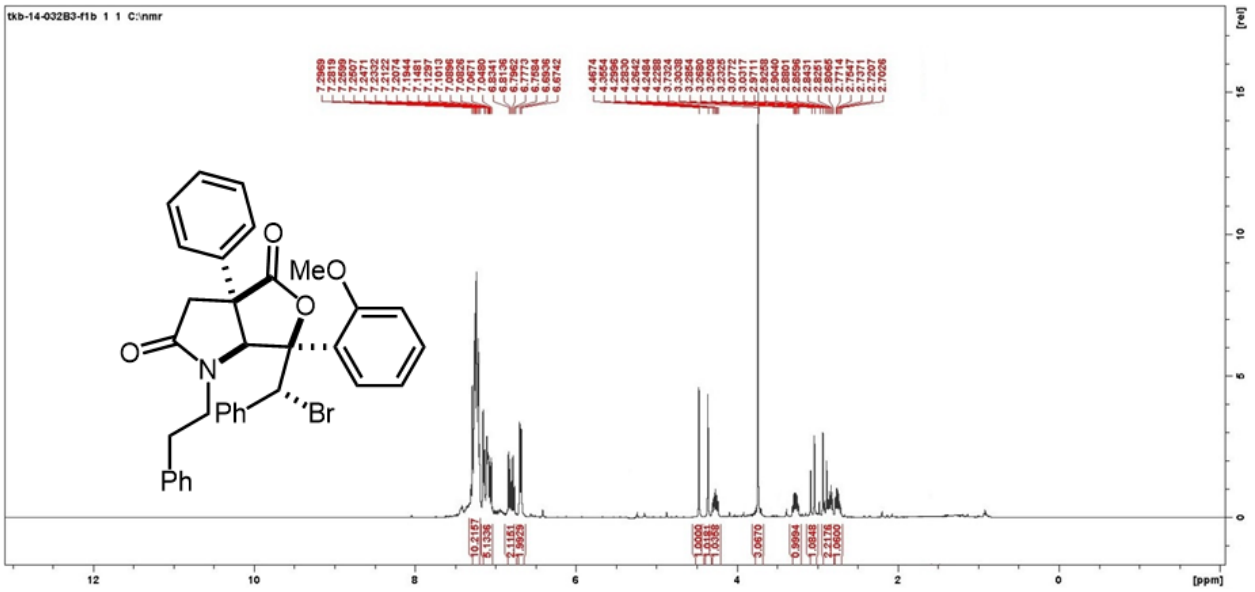
^{19}F NMR

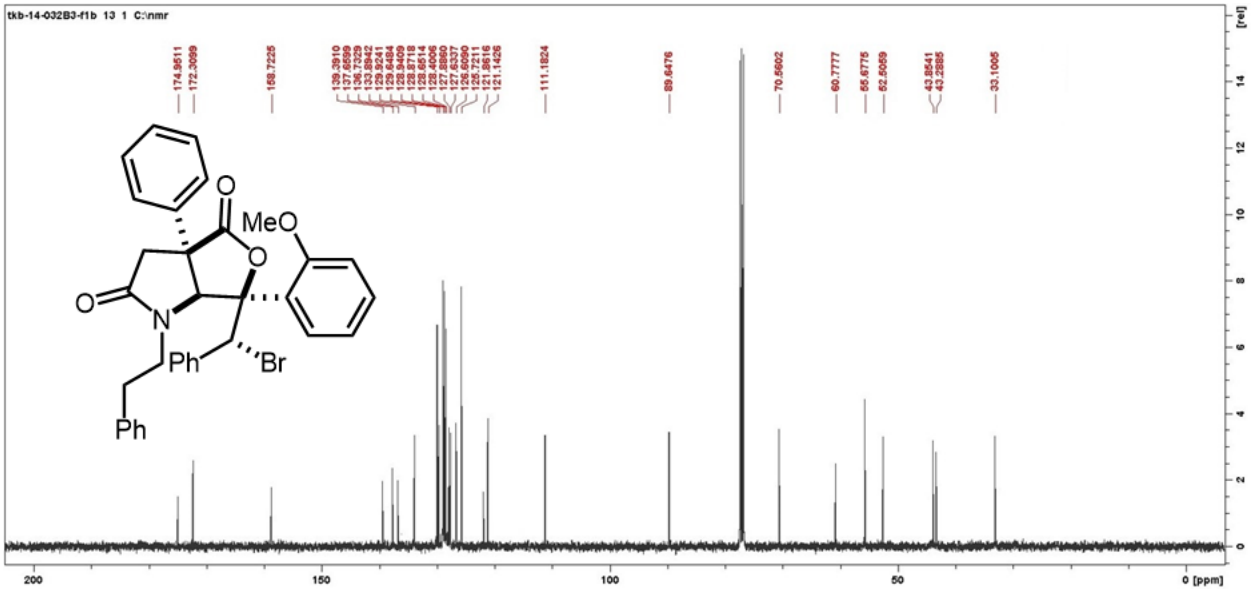


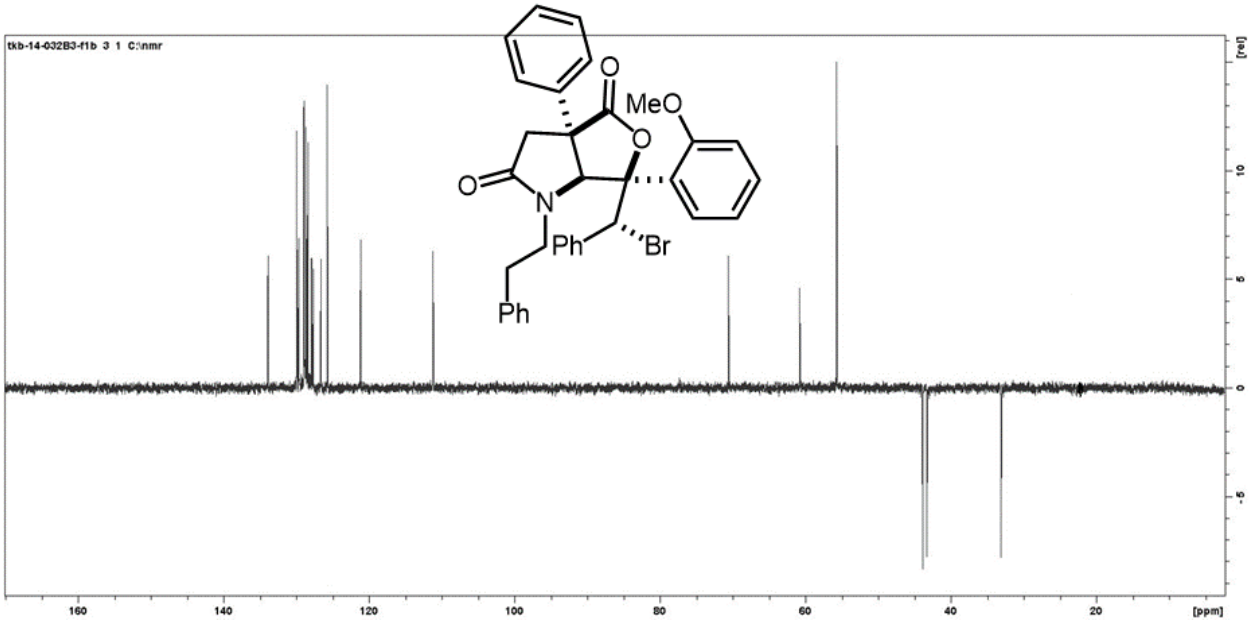
Compound 2q

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yellowish oil. Yield = 173.0 mg, 58%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.19 (m, 10H), 7.15 – 7.04 (m, 5H), 6.83 – 6.76 (m, 2H), 6.68 (dd, J = 7.7, 1.9 Hz, 2H), 4.47 (s, 1H), 4.36 (s, 1H), 4.26 (ddd, J = 14.2, 8.3, 6.2 Hz, 1H), 3.73 (s,

3H), 3.27 (dt, *J* = 14.3, 7.4 Hz, 1H), 3.03 (d, *J* = 18.3 Hz, 1H), 2.95 – 2.79 (m, 2H), 2.74 (dt, *J* = 13.8, 7.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9, 172.3, 158.7, 139.4, 137.7, 136.7, 133.9, 129.9, 129.6, 128.9, 128.6, 128.4, 127.9, 127.6, 126.6, 125.7, 121.9, 121.2, 111.2, 89.7, 70.6, 60.8, 55.7, 52.5, 43.9, 43.3, 33.1. **HRMS-EI$^+$** (*m/z*): calc for $C_{34}H_{30}Br_2NO_4$ $[M]^+$ 595.1358, found 595.1365.

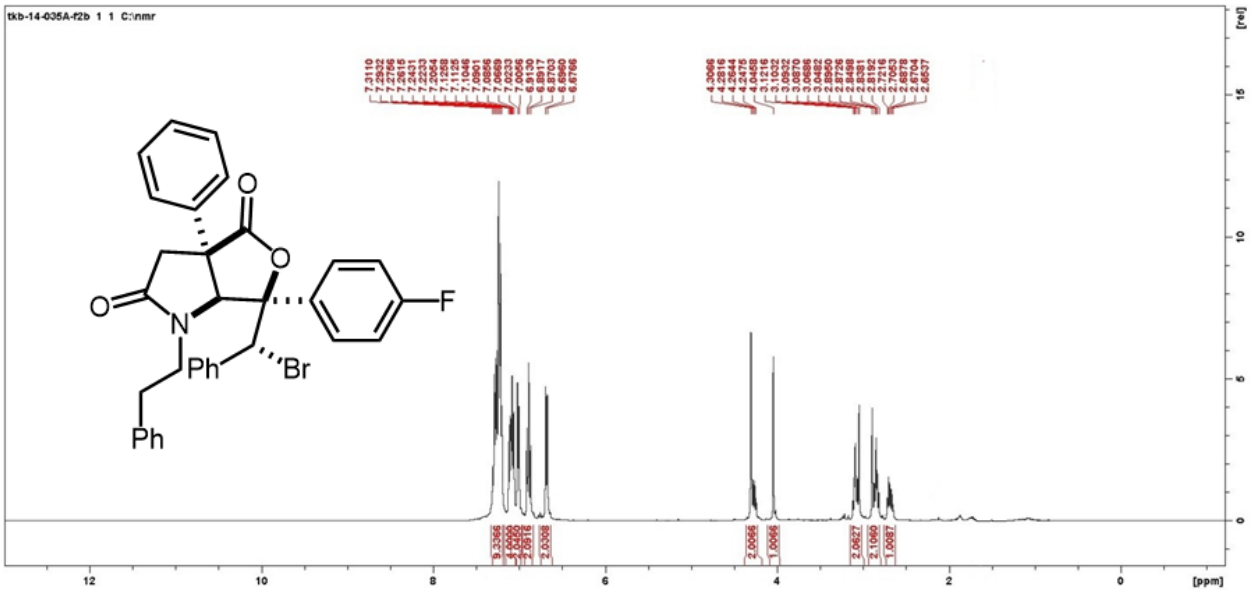


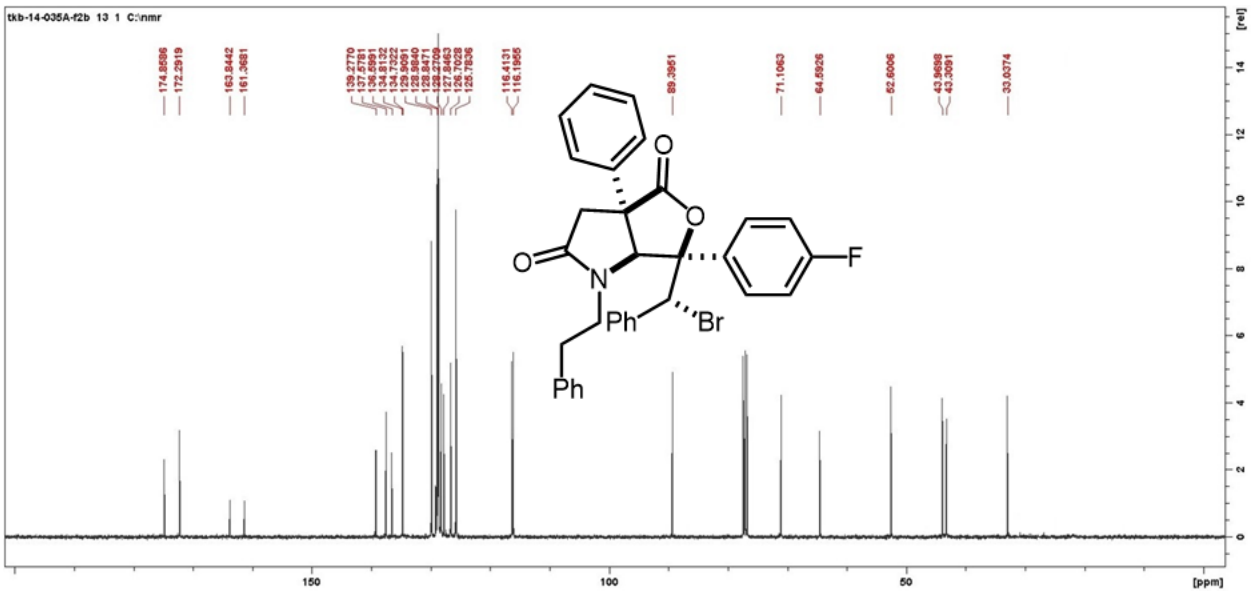




Compound 2r

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yellowish oil. Yield = 181.2 mg, 62%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.20 (m, 9H), 7.12 – 7.07 (m, 6H), 6.89 (t, *J* = 8.5 Hz, 2H), 6.69 (d, *J* = 7.8 Hz, 2H), 4.31 (s, 1H), 4.28 (dt, *J* = 13.8, 6.9 Hz, 1H), 4.05 (s, 1H), 3.14 – 3.01 (m, 2H), 2.93 – 2.78 (m, 2H), 2.69 (dt, *J* = 13.8, 6.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9, 172.3, 163.8, 161.4, 139.3, 137.6, 136.6, 134.8, 134.7, 129.9, 129.0, 128.8, 128.8, 128.8, 128.7, 128.3, 127.8, 126.7, 125.8, 116.4, 116.2, 89.4, 71.1, 64.6, 52.6, 44.0, 43.3, 33.0. **HRMS-EI^{+}** (*m/z*): calc for $C_{33}H_{27}BrFNO_3$ $[M]^{+}$ 583.1158, found 583.1161.

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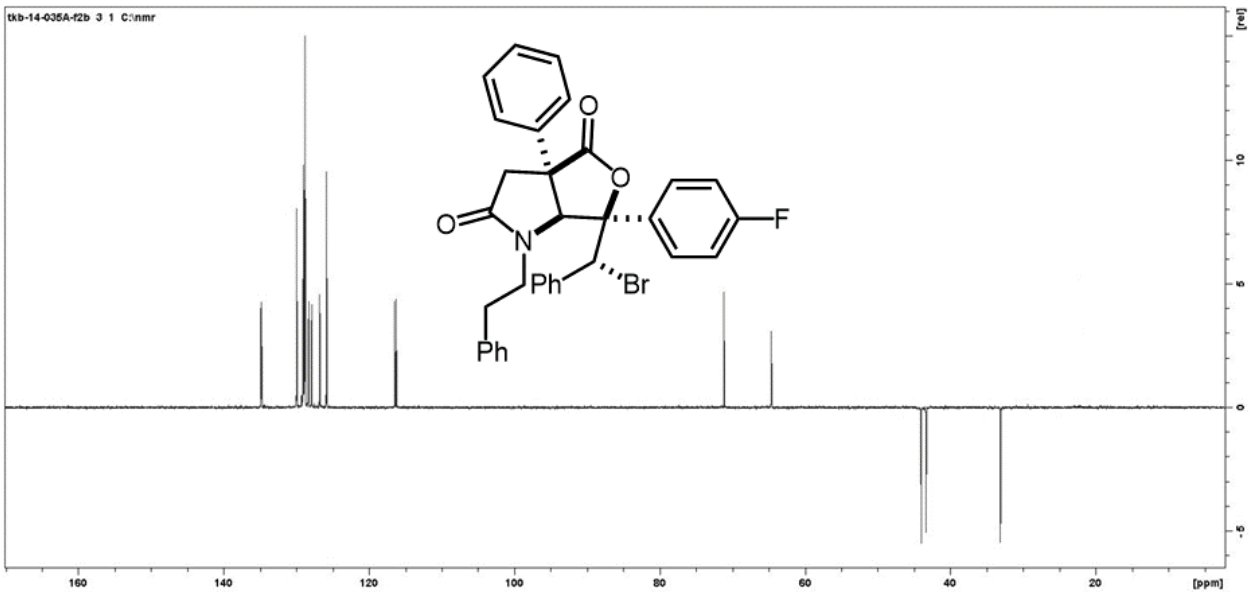
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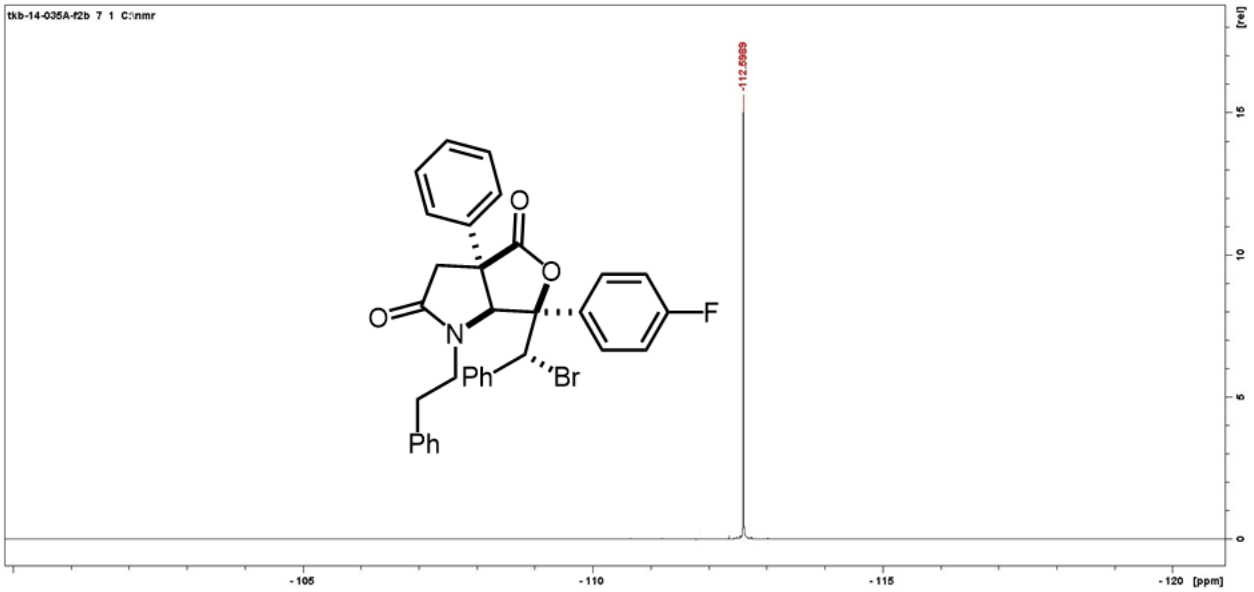
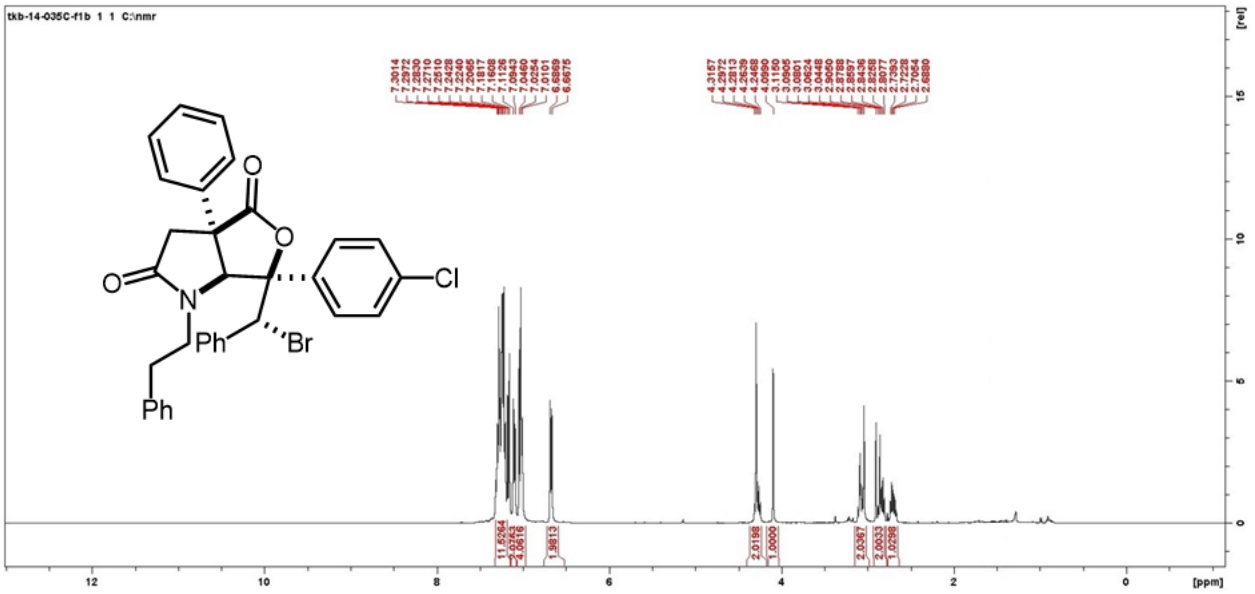
^{19}F NMR



Compound 2s

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Orange oil. Yield = 180.3 mg, 60%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.16 (m, 11H), 7.10 (d, *J* = 7.1 Hz, 2H), 7.04 – 7.01 (m, 4H), 6.68 (d, *J* = 7.5 Hz, 2H), 4.32 – 4.25 (m, 2H), 4.10 (s, 1H), 3.11 – 3.04 (m, 2H), 2.91 – 2.81 (m, 2H), 2.74 – 2.69 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7, 172.3, 139.2, 137.6, 136.4, 134.1, 133.2, 132.7, 129.9, 129.3, 129.0, 128.8, 128.7, 128.3, 127.8, 126.7, 125.7, 89.3, 71.0, 63.9, 52.6, 43.99, 43.3, 33.1. **HRMS-EI$^+$** (*m/z*): calc for $C_{33}H_{27}BrClNO_3$ $[M]^+$ 599.0863, found 599.0868.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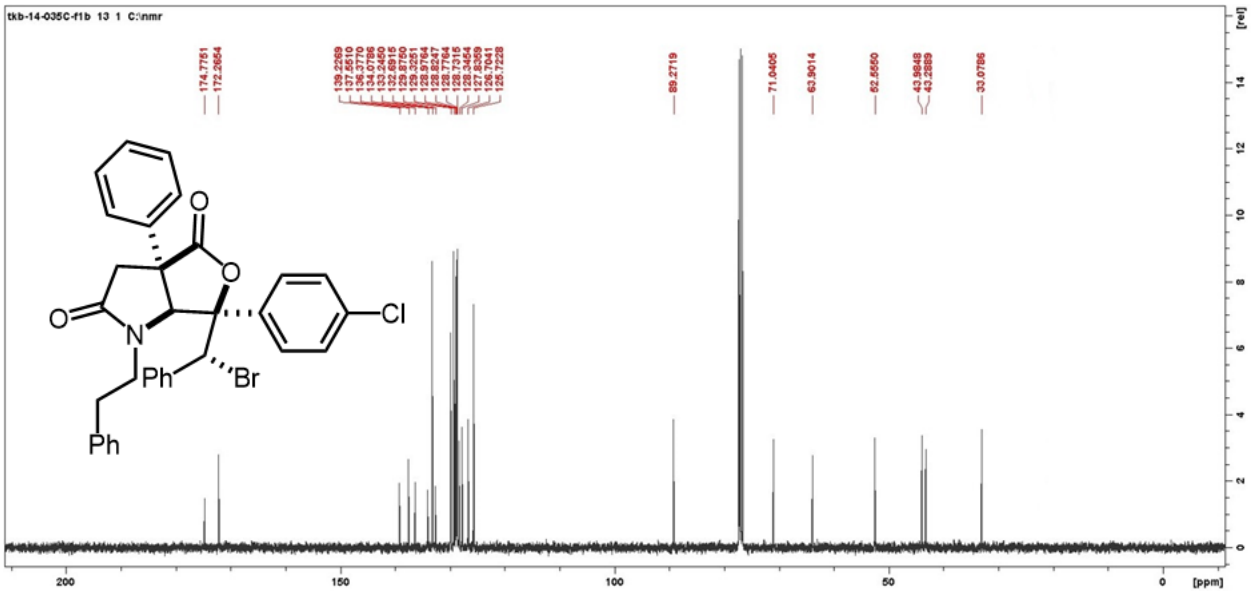
[ppm]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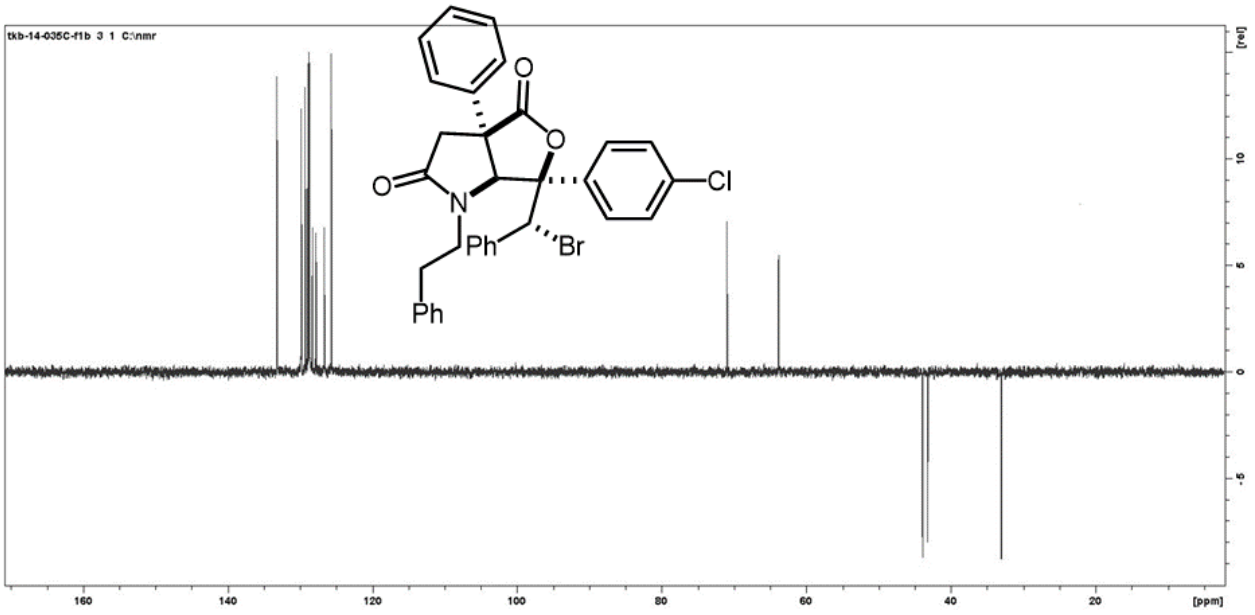
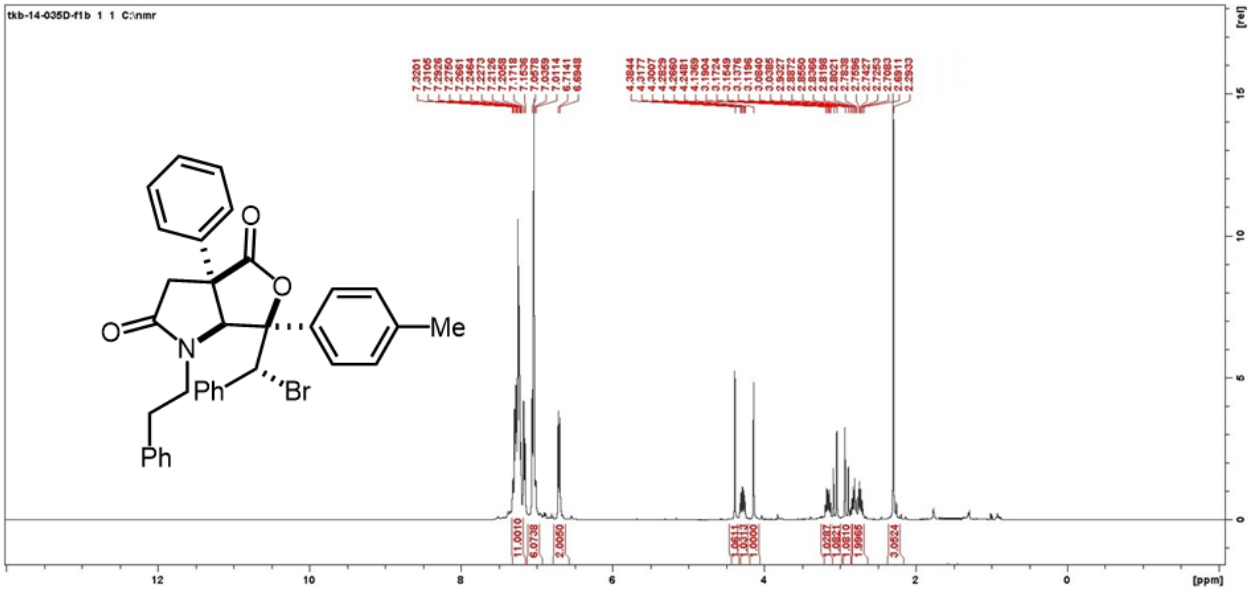
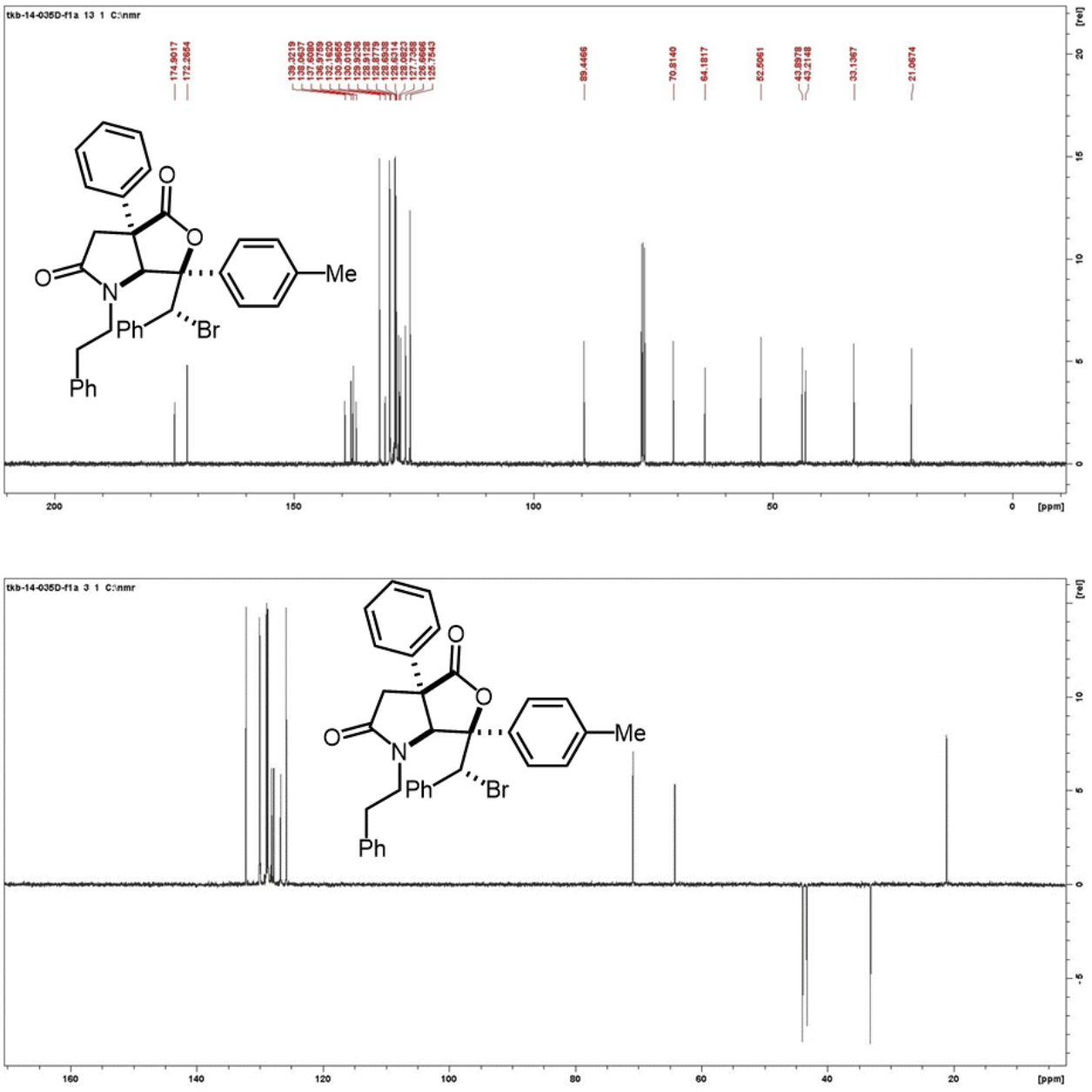


Compound 2t

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Orange oil. Yield = 188.7 mg, 65%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.20 (m, 11H), 7.17 – 7.01 (m, 6H), 6.70 (d, *J* = 7.7 Hz, 2H), 4.38 (s, 1H), 4.28 (dt, *J* = 14.0, 7.0 Hz, 1H), 4.14 (s, 1H), 3.19 – 3.04 (m, 2H), 2.93 – 2.69 (m, 3H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.90, 172.27, 139.33, 138.07, 137.61, 136.98, 132.17, 130.97, 130.01, 129.93, 128.92, 128.88, 128.70, 128.63, 128.09, 127.74, 126.67, 125.76, 89.45, 70.82, 64.19, 52.51, 43.90, 43.22, 33.14, 21.07. **HRMS-EI$^+$** (*m/z*): calc for $C_{34}H_{30}BrNO_3$ $[M]^+$ 579.1408, found 579.1411.

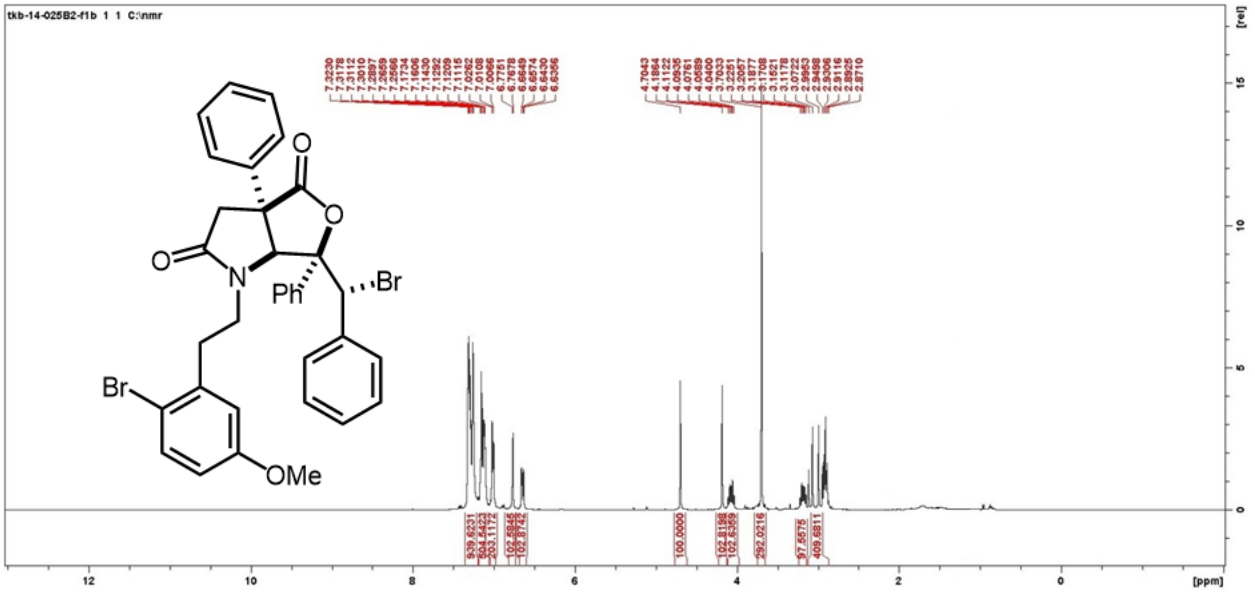


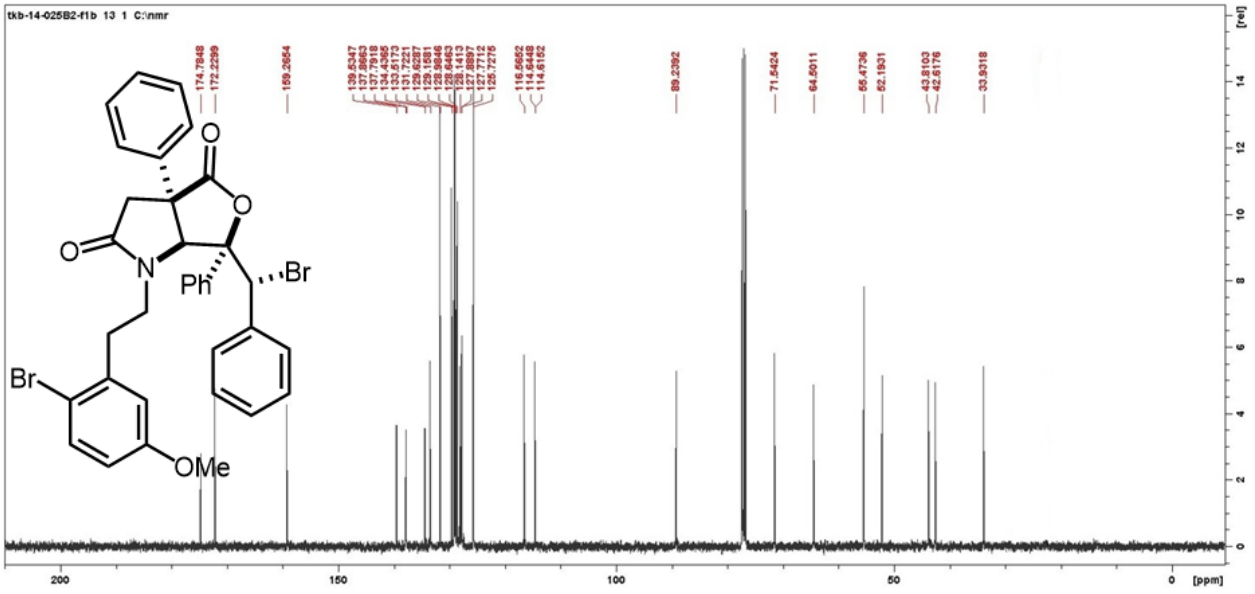


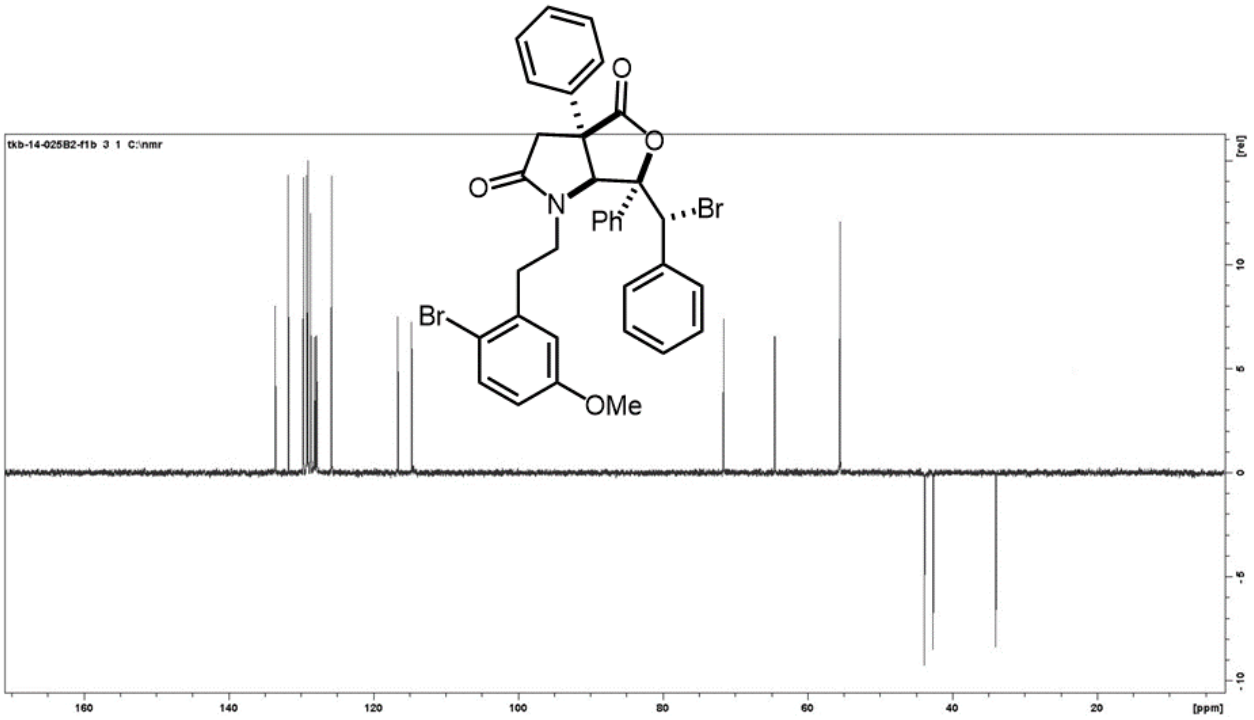
Compound 2u

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Reddish-brown oil. Yield = 216.1 mg, 64%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 9H), 7.17 – 7.11 (m, 5H),, 7.02 – 7.00 (m, 2H), 6.77 (d, *J* = 3.1 Hz, 1H), 6.65 (dd, *J* = 8.8, 3.1 Hz, 1H), 4.70 (s, 1H), 4.19 (s, 1H), 4.08 (dt, *J* = 14.4, 7.5 Hz, 1H), 3.70 (s, 3H), 3.25 – 3.10 (m, 1H), 3.07 (d, *J* = 18.4 Hz, 1H), 2.93 (d, *J* = 18.4

Hz, 1H), 2.91 – 2.87 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.8, 172.2, 159.3, 139.5, 137.9, 137.8, 134.4, 133.5, 131.7, 129.6, 129.2, 129.0, 128.6, 128.1, 127.9, 127.8, 125.7, 116.6, 114.6, 114.6, 89.2, 71.6, 64.5, 55.5, 52.2, 43.8, 42.6, 33.9. **HRMS-EI$^+$** (*m/z*): calc for $C_{34}H_{29}Br_2NO_4$ $[M]^+$ 673.0463, found 673.0468.



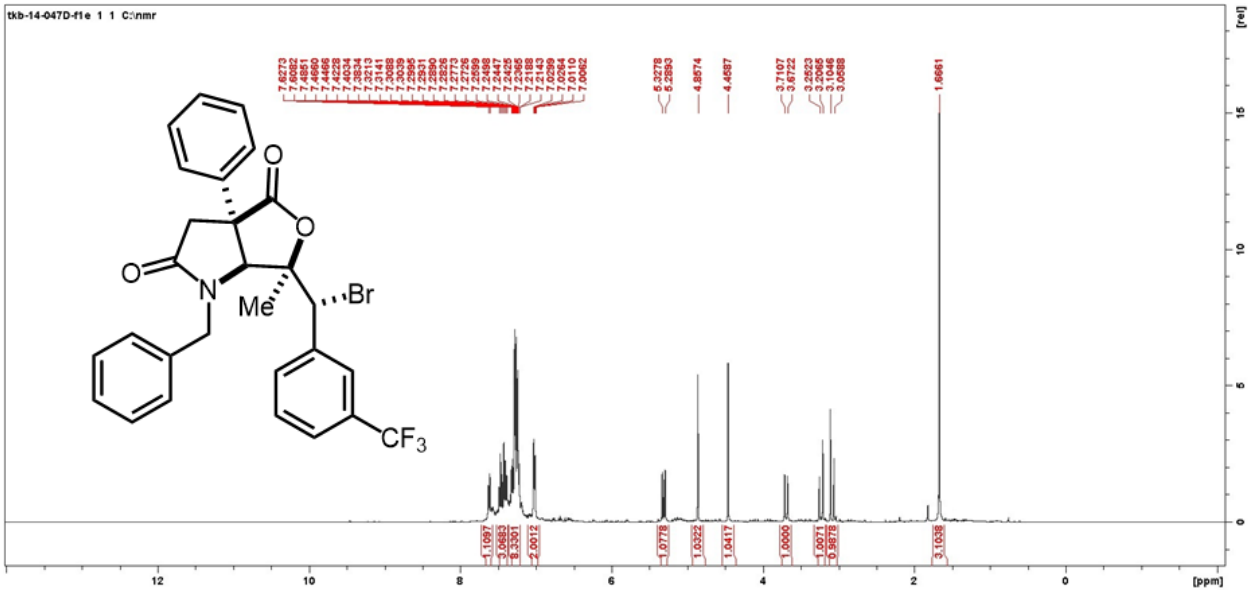


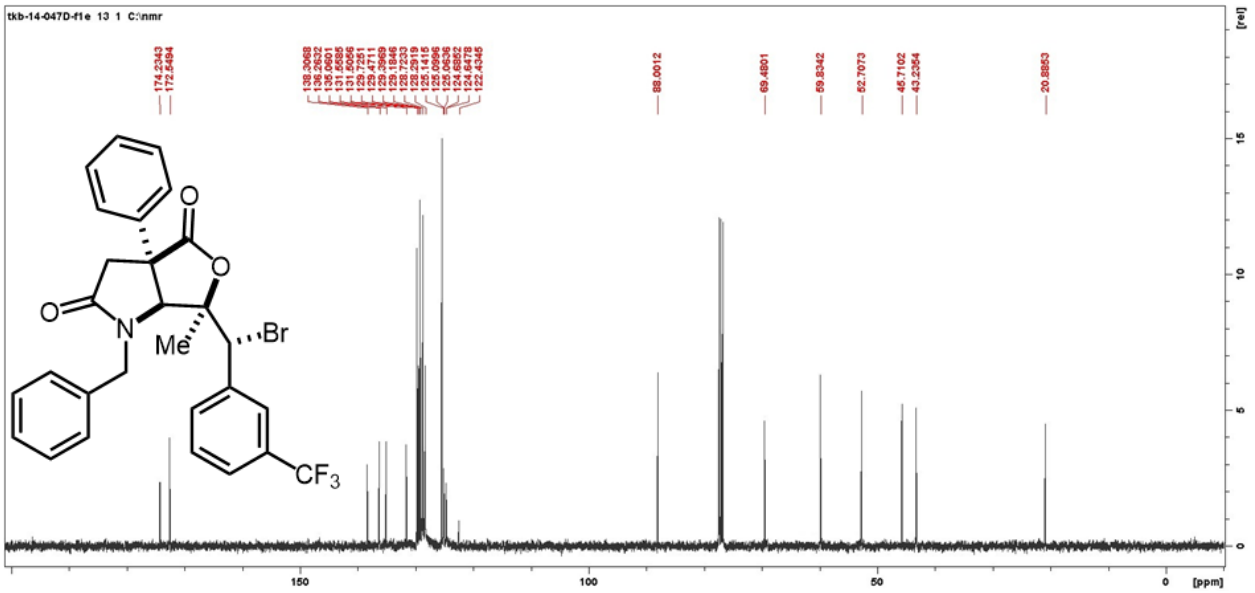


Compound 2v

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Yellowish oil. Yield = 223.4 mg, 80%, 95:5 dr.

HRMS-EI^{+} (*m/z*): calc for $C_{28}H_{23}BrF_3NO_3$ $[M]^{+}$ 557.0813, found 557.0816.

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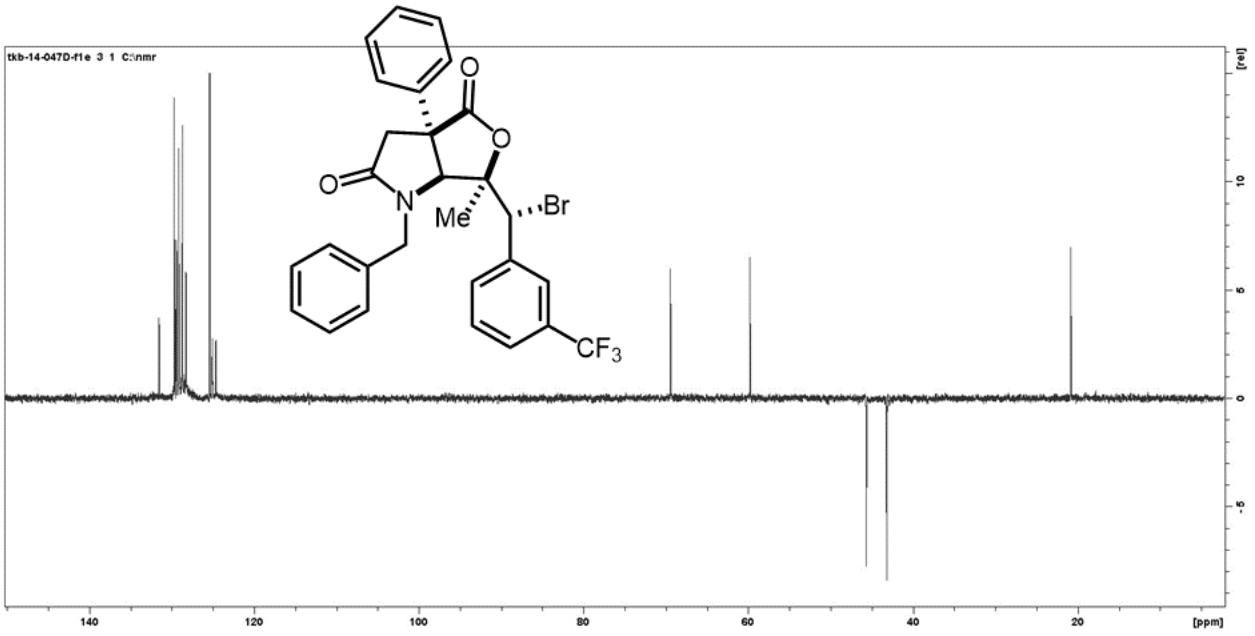
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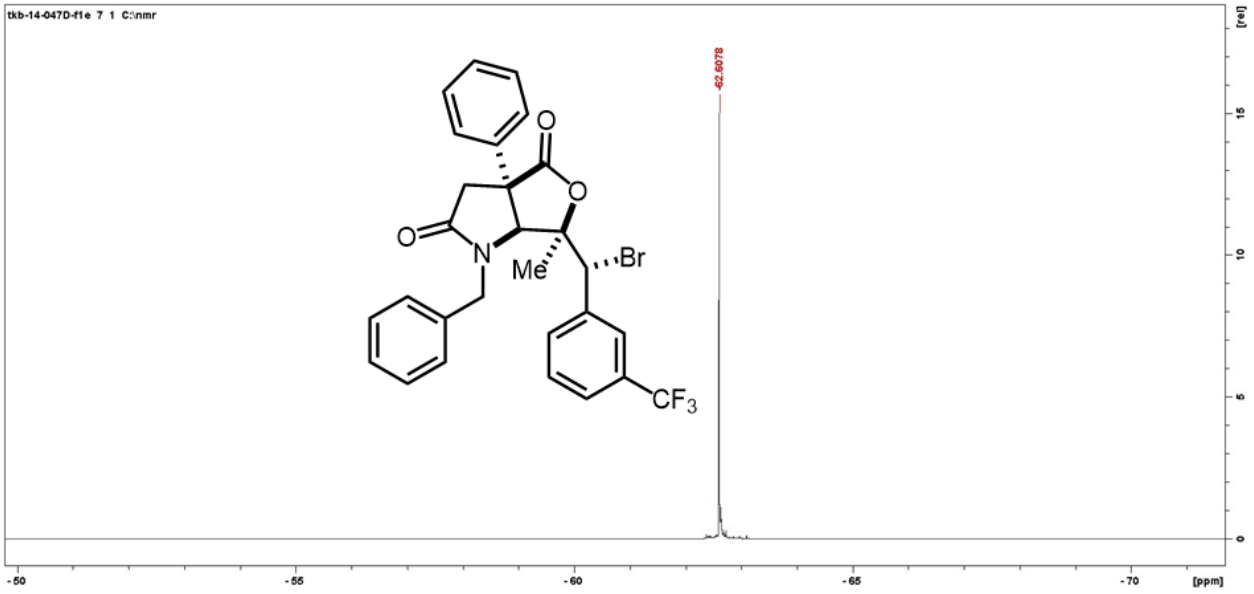
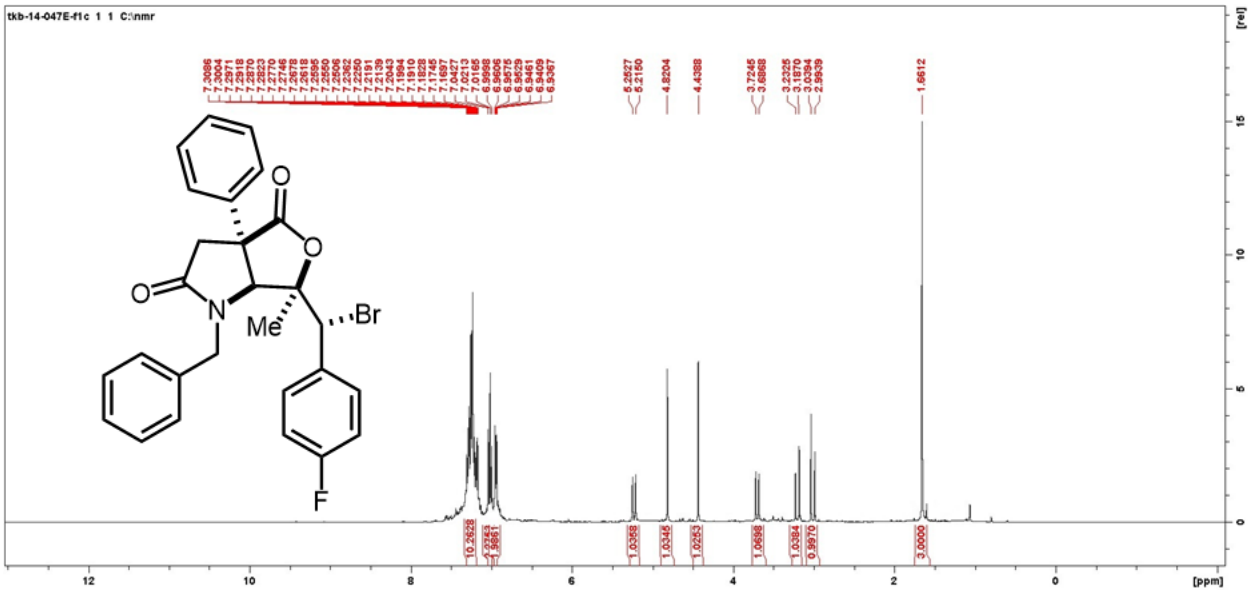
^{19}F NMR

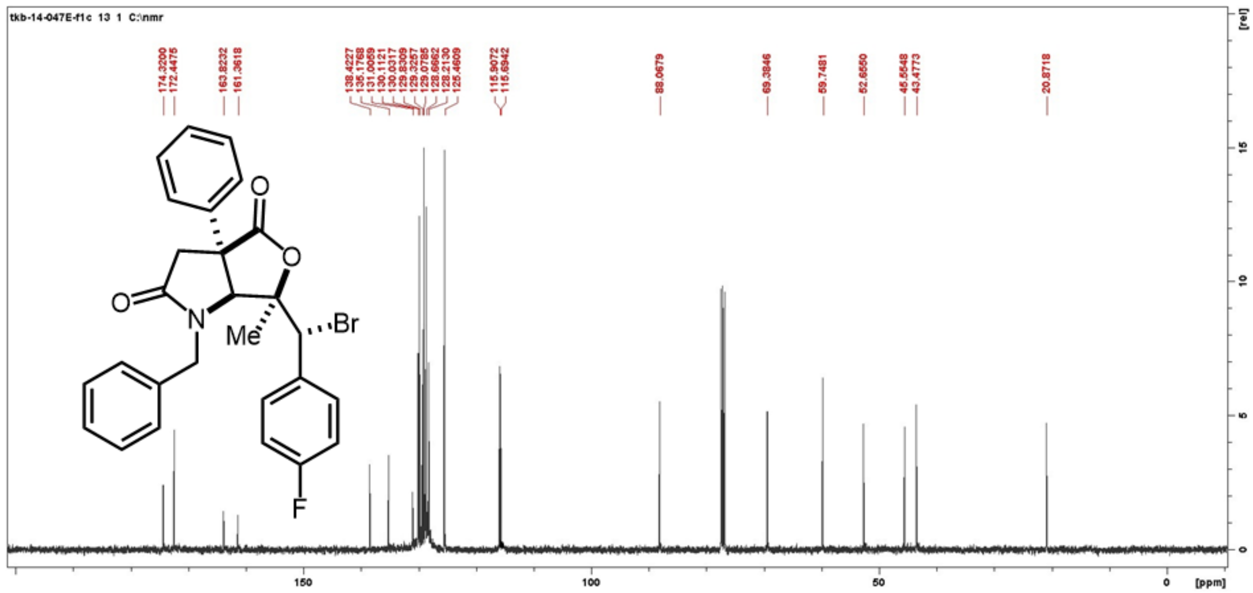


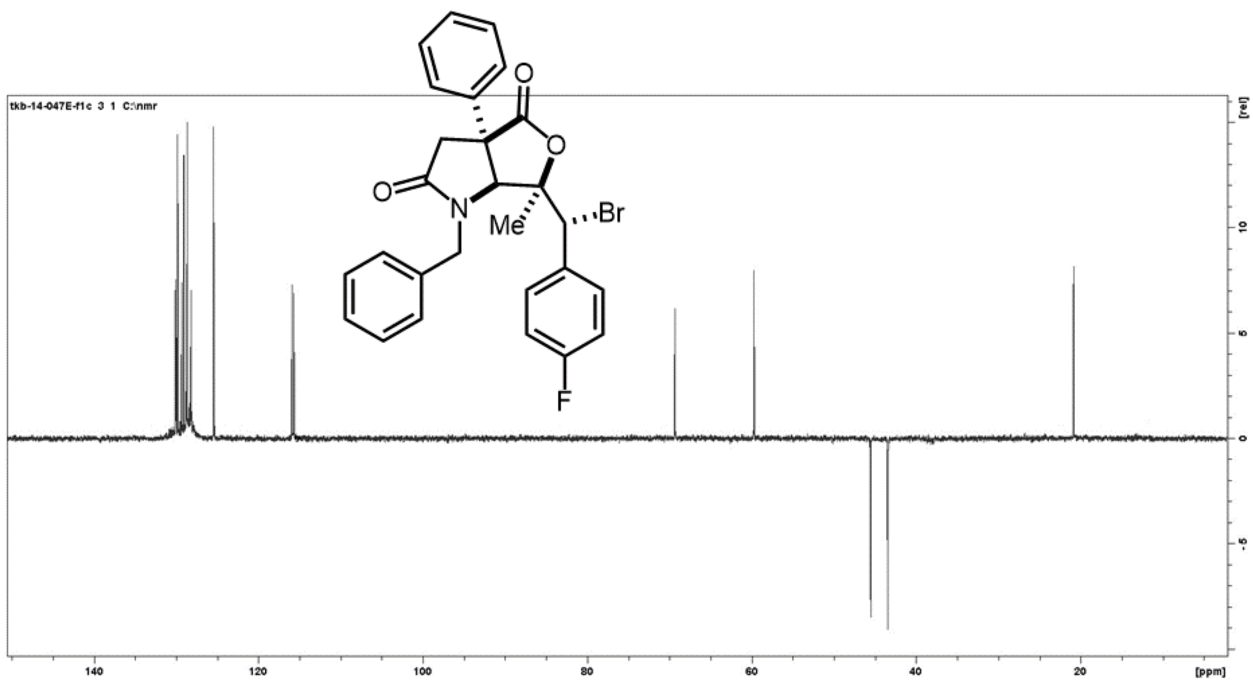
Compound 2w

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Yellowish oil. Yield = 208.4 mg, 82%, 95:5 dr.

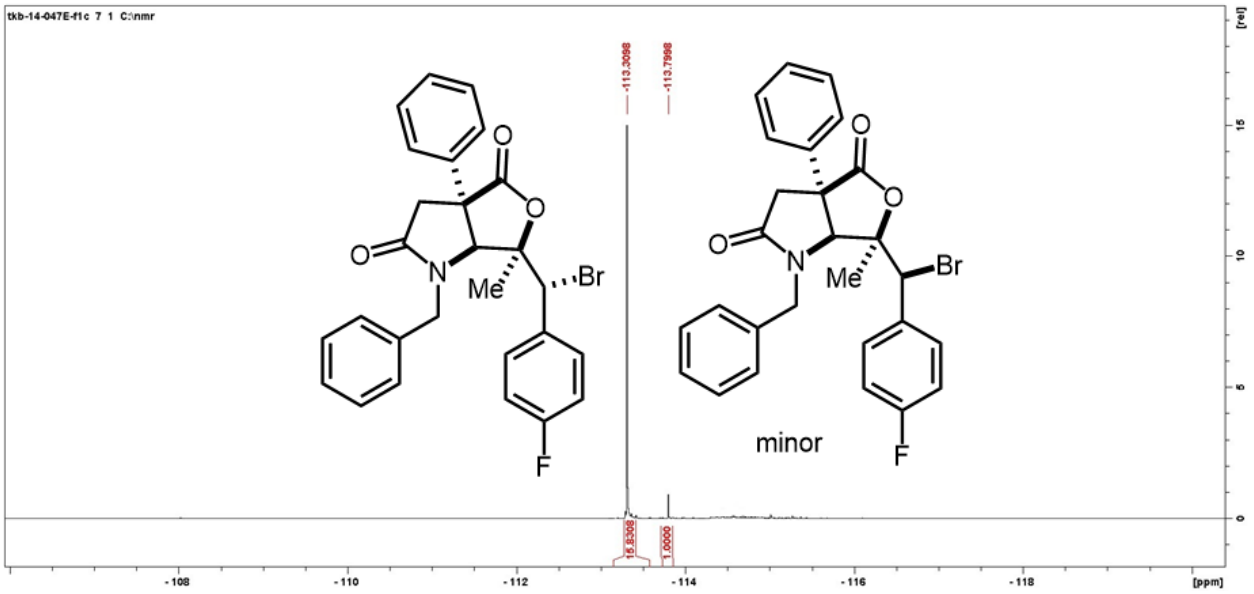
HRMS-EI$^+$ (*m/z*): calc for $C_{27}H_{23}BrFNO_3$ $[M]^+$ 507.0845, found 507.0849.





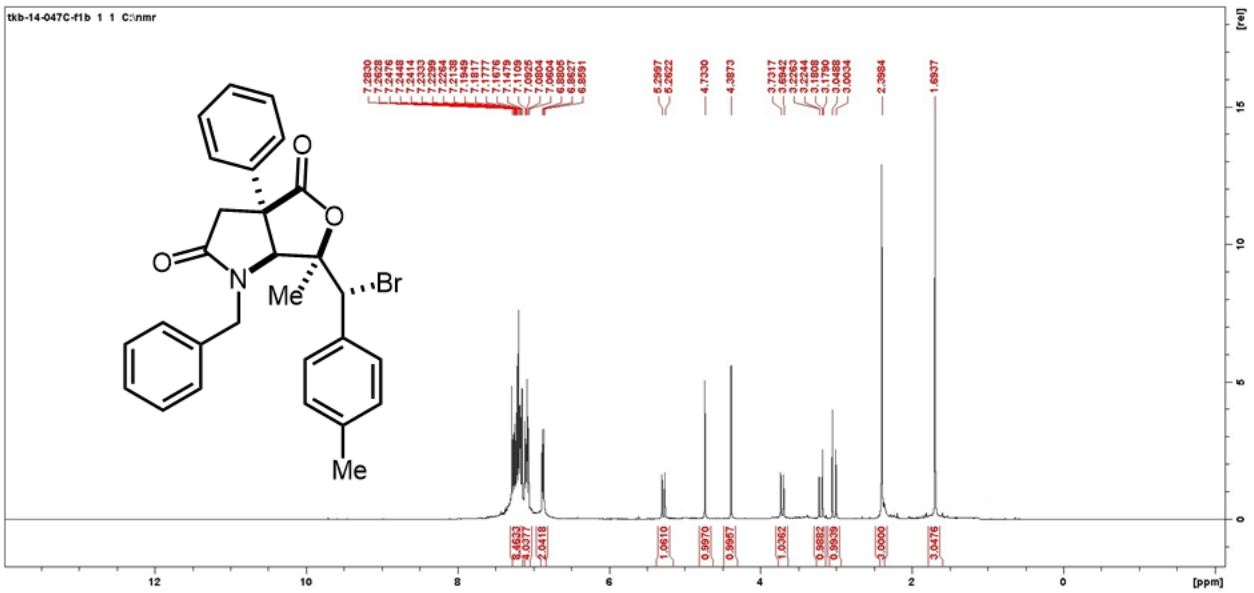


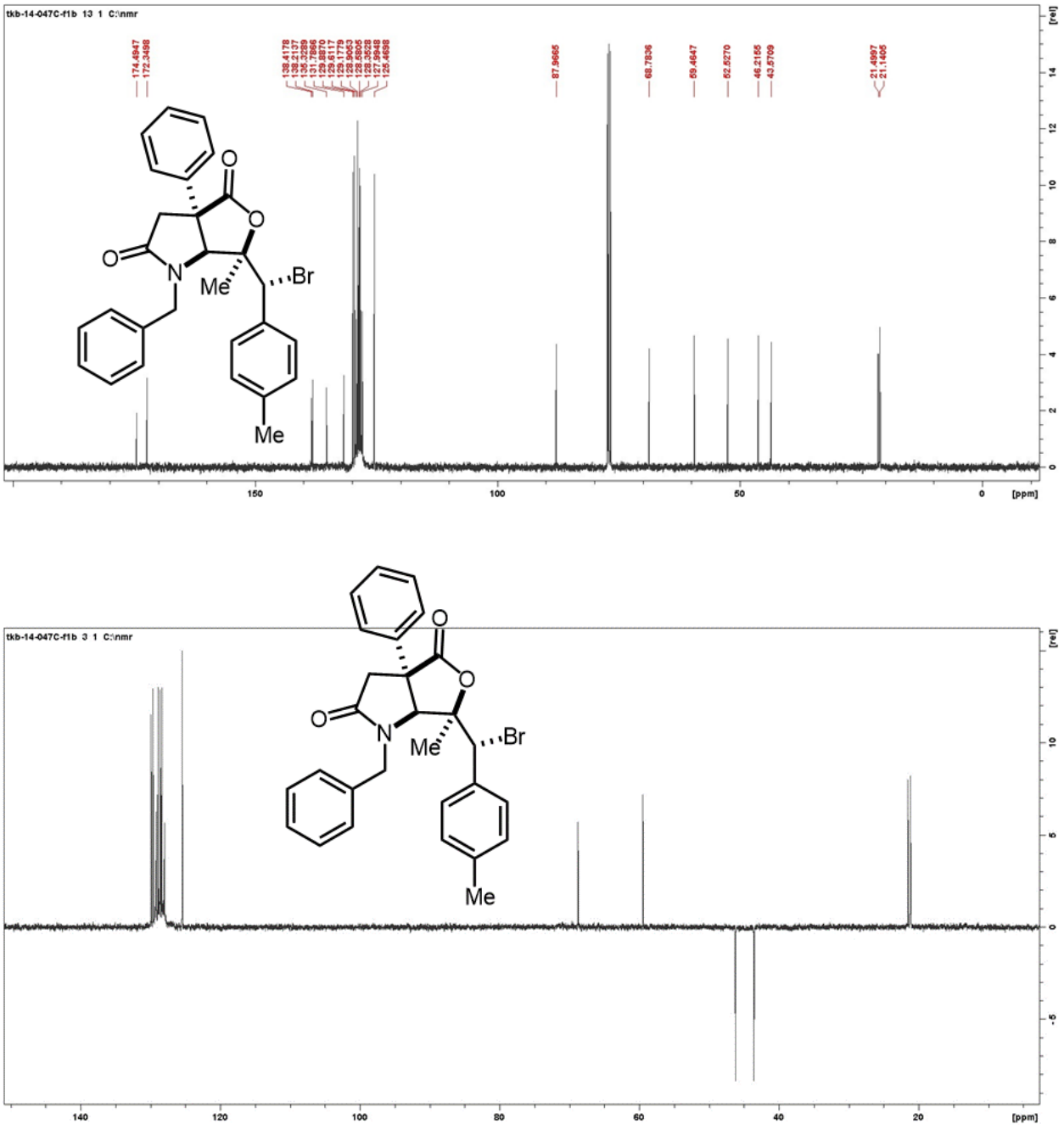
^{19}F NMR



Compound 2x

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (40:60). Pale-yellow oil. Yield = 194.2 mg, 77%, 95:5 dr. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{28}H_{26}BrNO_3$ $[M]^+$ 503.1096, found 503.1099.

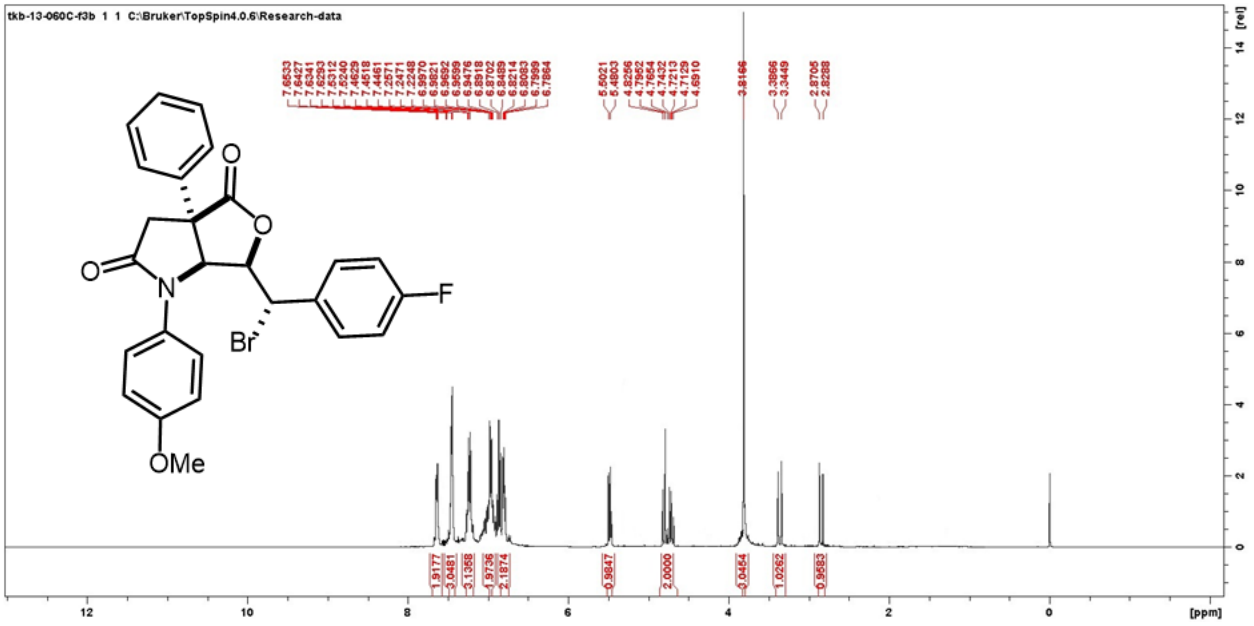


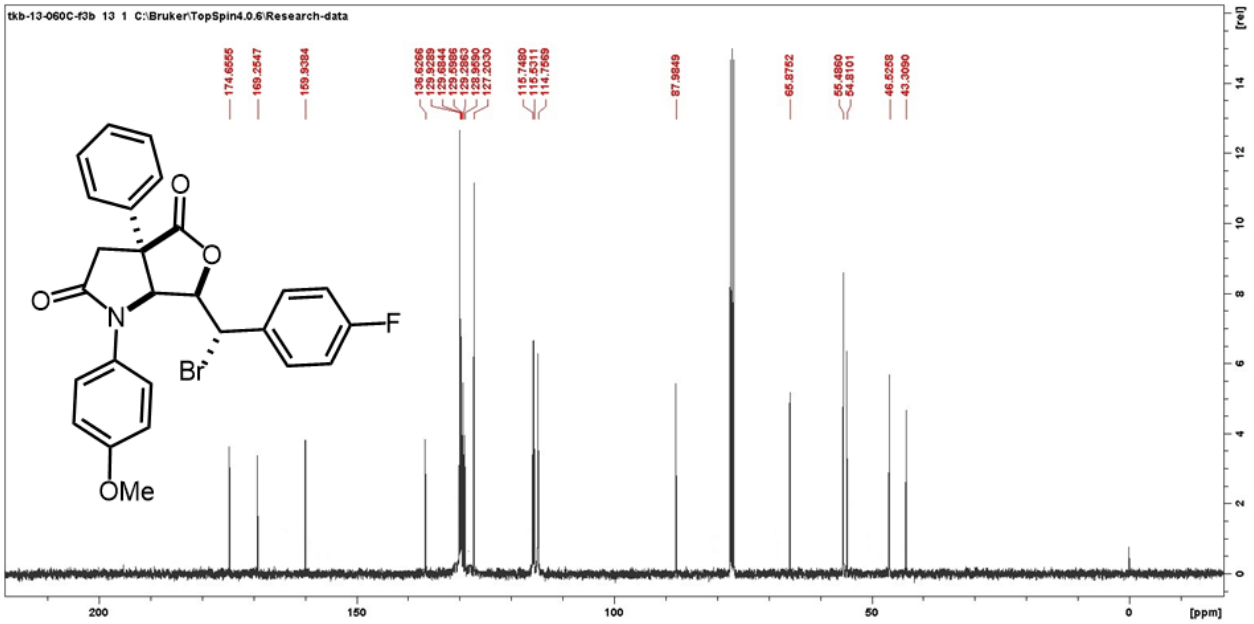


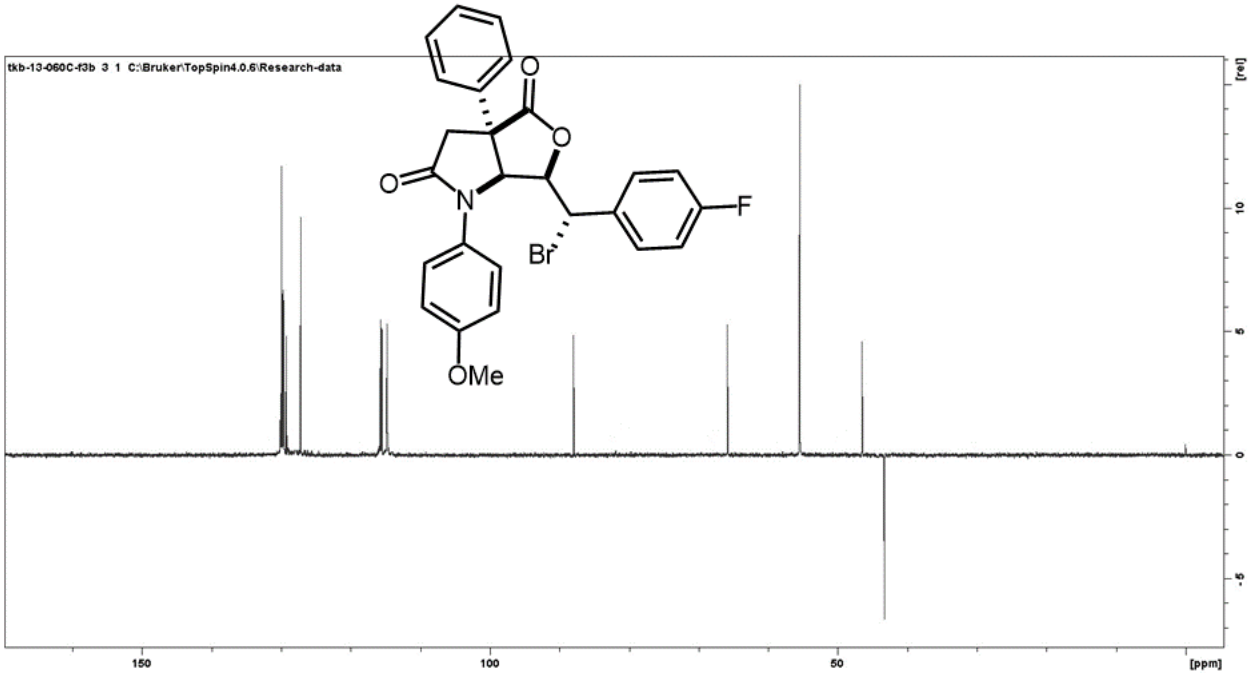
Compound 2y

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Greenish-yellow oil. Yield = 413.1 mg, 81%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.62 (m, 2H), 7.53 – 7.42 (m, 3H), 7.46 – 7.44 (m, 3H), 7.25 – 7.15 (m, 2H), 7.00 – 6.78 (m, 2H), 5.58 – 5.44 (m, 1H), 4.85 – 4.67 (m, 2H), 3.81 (s, 3H), 3.39 (d, *J* =17.2 Hz, 1H), 2.82 (d, *J* = 17.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7, 169.3, 159.9, 136.6, 129.9, 129.7, 129.6, 129.3, 129.0, 127.2, 115.8, 115.5, 114.8, 88.0, 65.9, 55.5, 54.8,

46.5, 43.3. FTIR (KBr): 3037.4, 2924.0, 1724.2, 1646.3, 1474.3, 1452.8, 1361.9, 1342.0, 1205.6, 1140.2, 1078.7, 1022.3, 996.4, 715.1. **HRMS-EI**$^+$ (*m/z*): calc for $C_{26}H_{21}BrFNO_4$ $[M]^+$ 509.0638, found 509.0644.

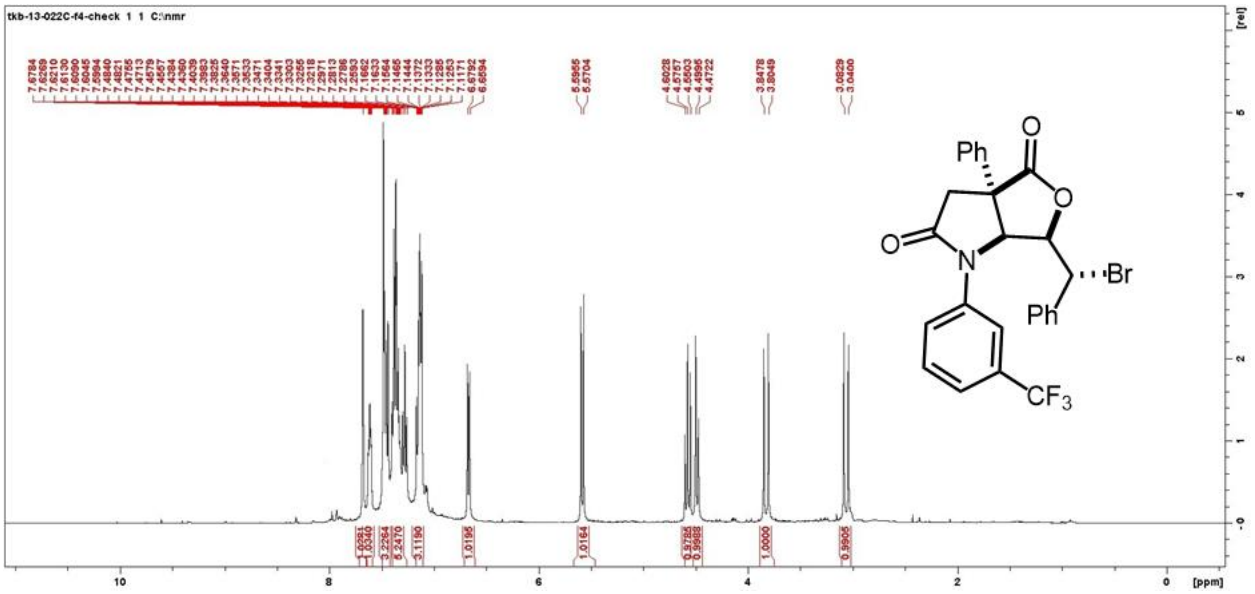






Compound 2z

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Pale yellow oil. Yield = 445.2 mg, 84%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 2.1 Hz, 1H), 7.57 (dq, *J* = 6.8, 2.3 Hz, 1H), 7.48 – 7.28 (m, 7H), 7.27 – 7.8 (m, 3H), 6.63 (dd, *J* = 7.9, 1.2 Hz, 1H), 5.54 (d, *J* = 10.1 Hz, 1H), 4.54 (t, *J* = 10.5 Hz, 1H), 4.45 (d, *J* = 11.0 Hz, 1H), 3.78 (d, *J* = 17.1 Hz, 1H), 3.01 (d, *J* = 17.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 171.9, 163.9, 141.3, 139.3, 136.7, 130.1, 129.3, 128.8, 128.2, 128.0, 127.7, 127.3, 69.5, 56.7, 54.0, 53.6, 43.0. **HRMS-EI$^+$** (*m/z*): calc for $C_{26}H_{19}BrF_3NO_3$ $[M]^+$ 529.0500, found 529.0506.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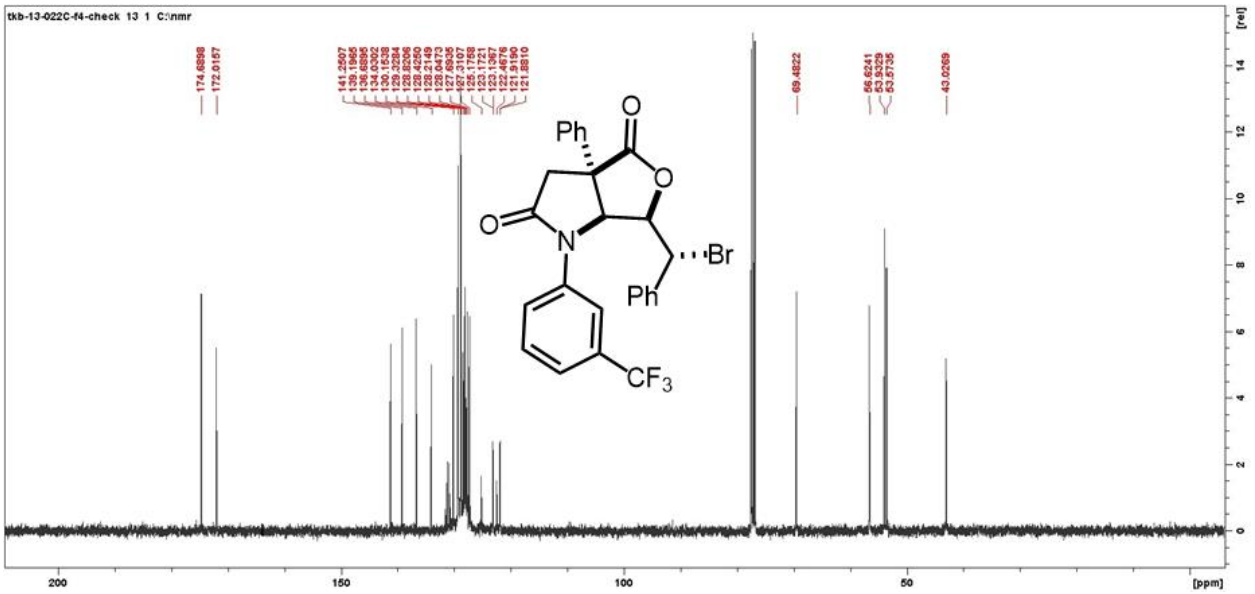
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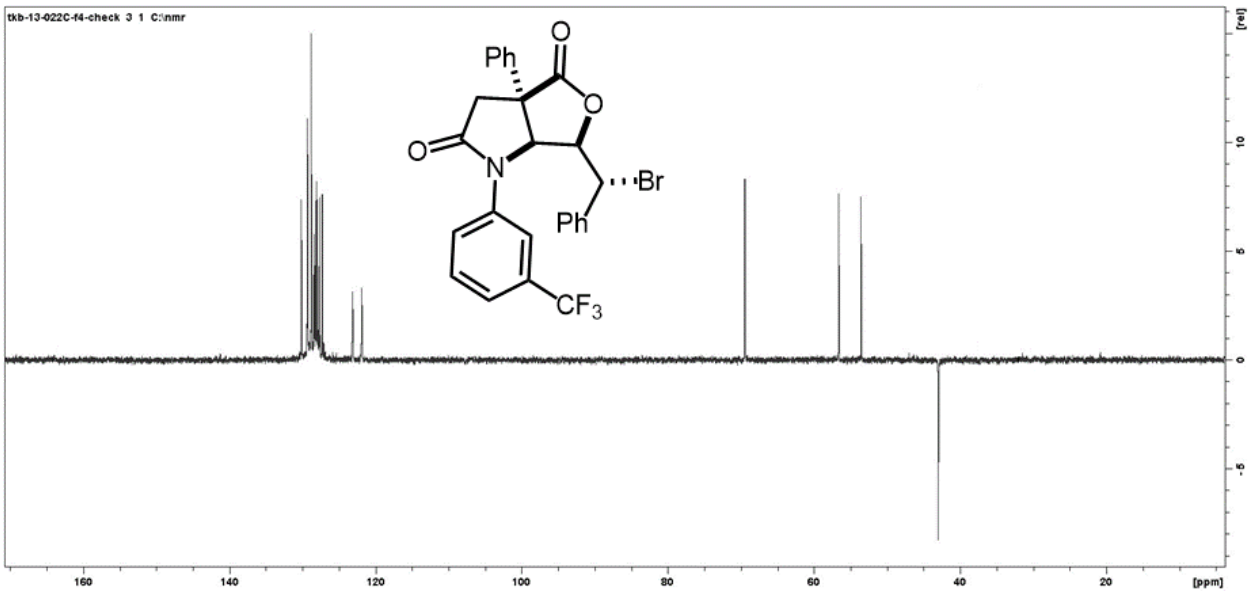
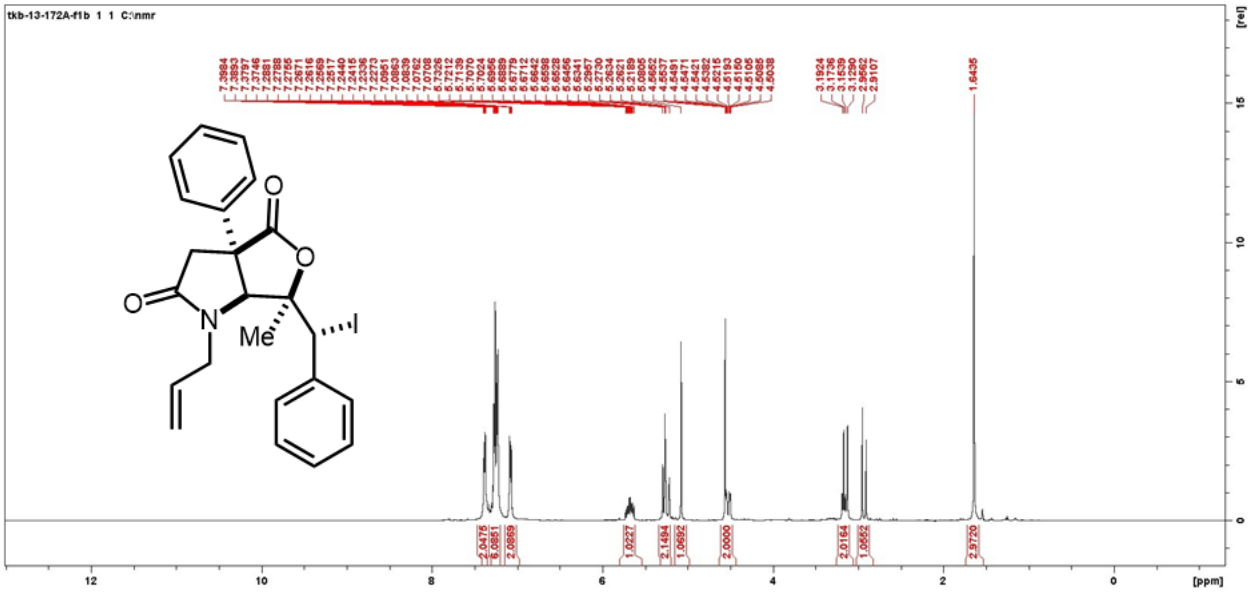
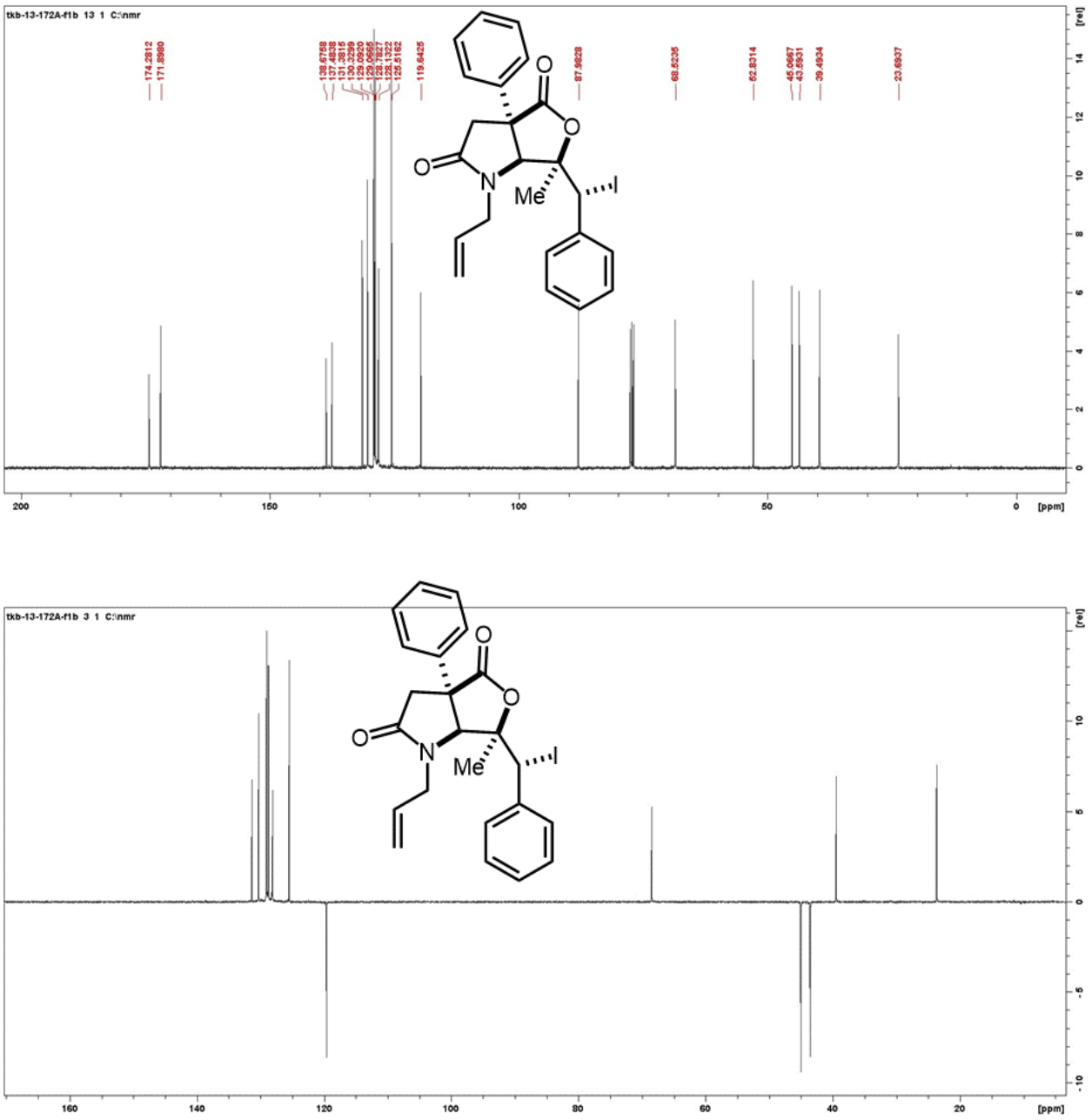


Scheme 2 Results

Compound 2z1

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Pale-yellowish oil. Yield = 457.8 mg, 94%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 8H), 7.09 – 7.07 (m, 2H), 5.68 (dddd, *J* = 17.5, 10.2, 7.5, 4.6 Hz, 1H), 5.33 – 5.19 (m, 2H), 5.08 (s, 1H), 4.56 – 4.50 (m, 2H), 3.17 – 3.12 (m, 2H), 2.94 (d, 1H), 1.64 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 171.9, 138.7, 137.5, 131.4, 130.3, 129.1, 128.8, 128.1, 125.5, 119.6, 88.0, 68.5, 52.8, 45.1, 43.6, 39.5, 23.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{22}INO_3$ $[M]^{+}$ 487.0644, found 487.0649.

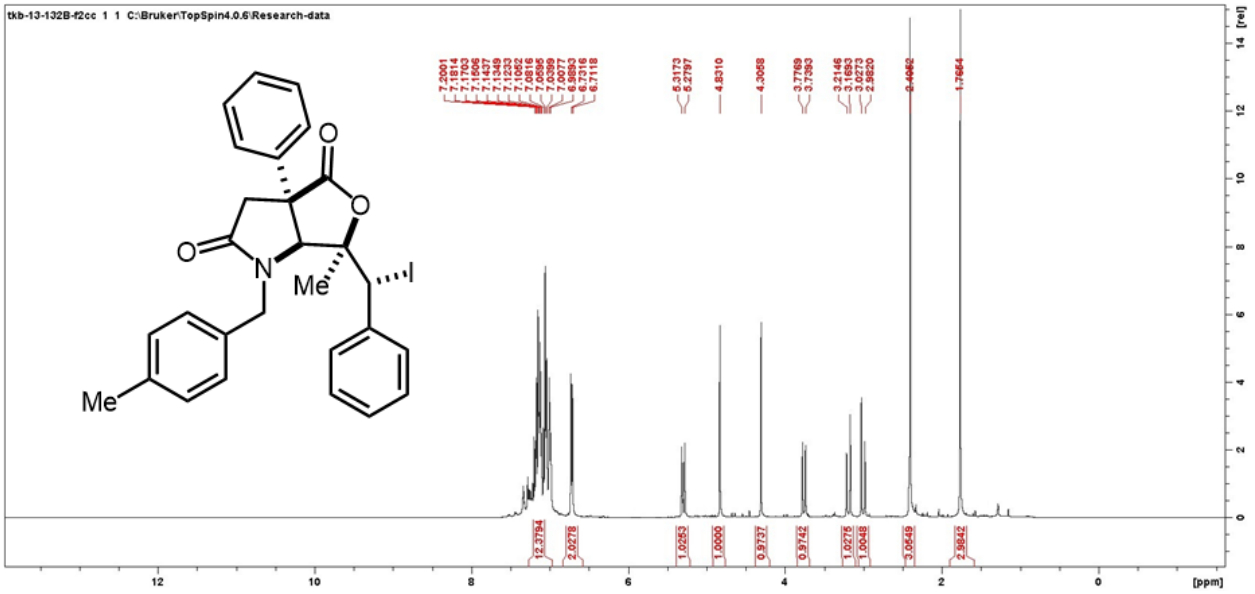


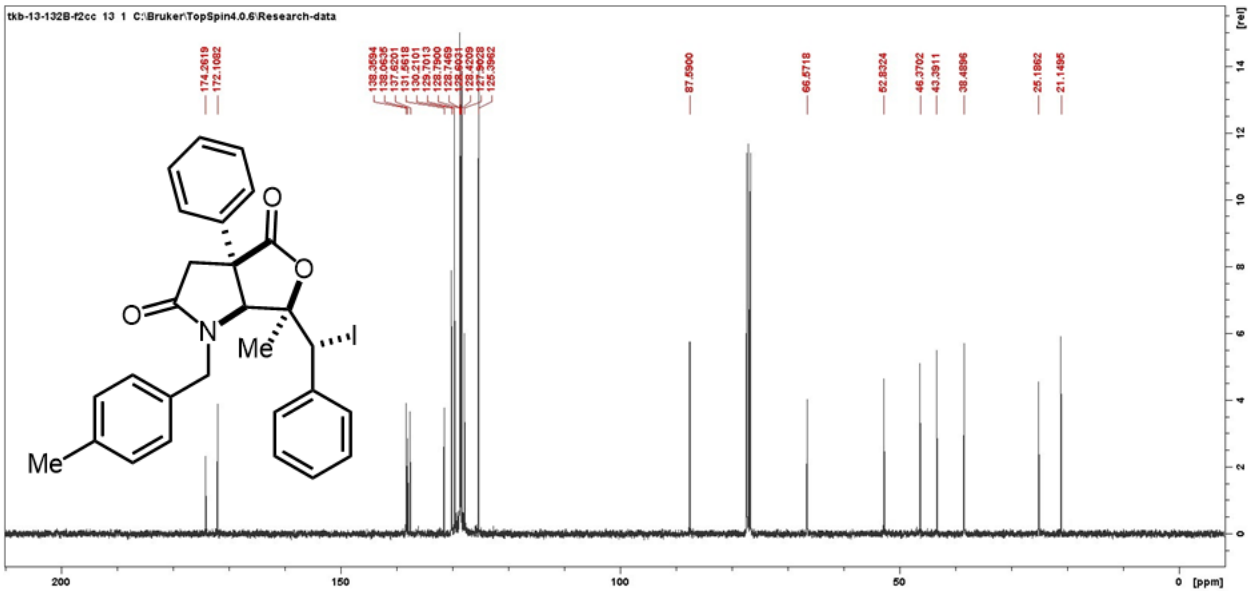


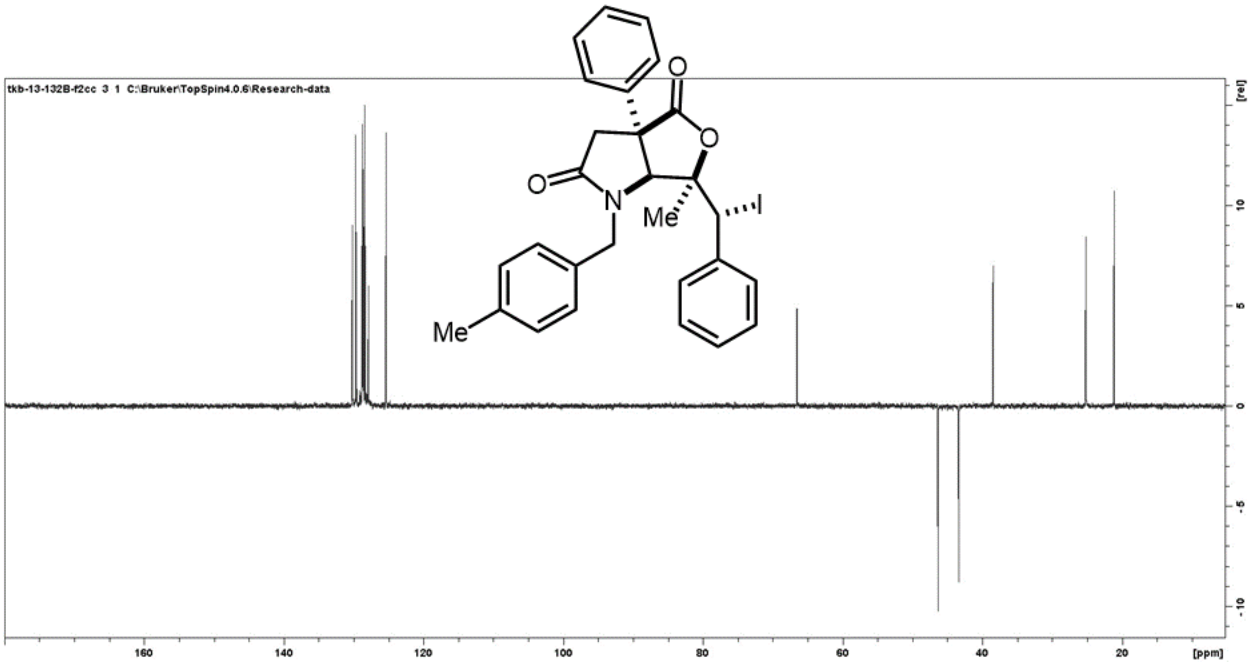
Compound 2z2

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yellowish oil. Yield = 507.3 mg, 92%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 – 6.99 (m, 12H), 6.72 (dd, J = 7.8, 1.8 Hz, 2H), 5.30 (d, J = 15.0 Hz, 1H), 4.83 (s, 1H), 4.31 (s, 1H), 3.76 (d, J = 15.1 Hz, 1H), 3.18 (d, J = 17.1 Hz, 1H), 3.00 (d, J = 17.1 Hz, 1H), 2.41 (s, 3H), 1.77 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 172.1, 138.4,

137.6, 131.6, 130.2, 129.7, 128.8, 128.8, 128.6, 128.4, 127.9, 125.4, 87.6, 66.6, 52.8, 46.4, 43.4, 38.5, 25.2, 21.2. FTIR (KBr): 3057.1, 2924.0, 1764.2, 1666.3, 1494.3, 1361.2, 1225.6, 1180.2, 1091.7, 1032.3, 996.4, 775.4. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{28}H_{26}INO_3$ $[M]^{+}$ 551.0957, found 551.0963.

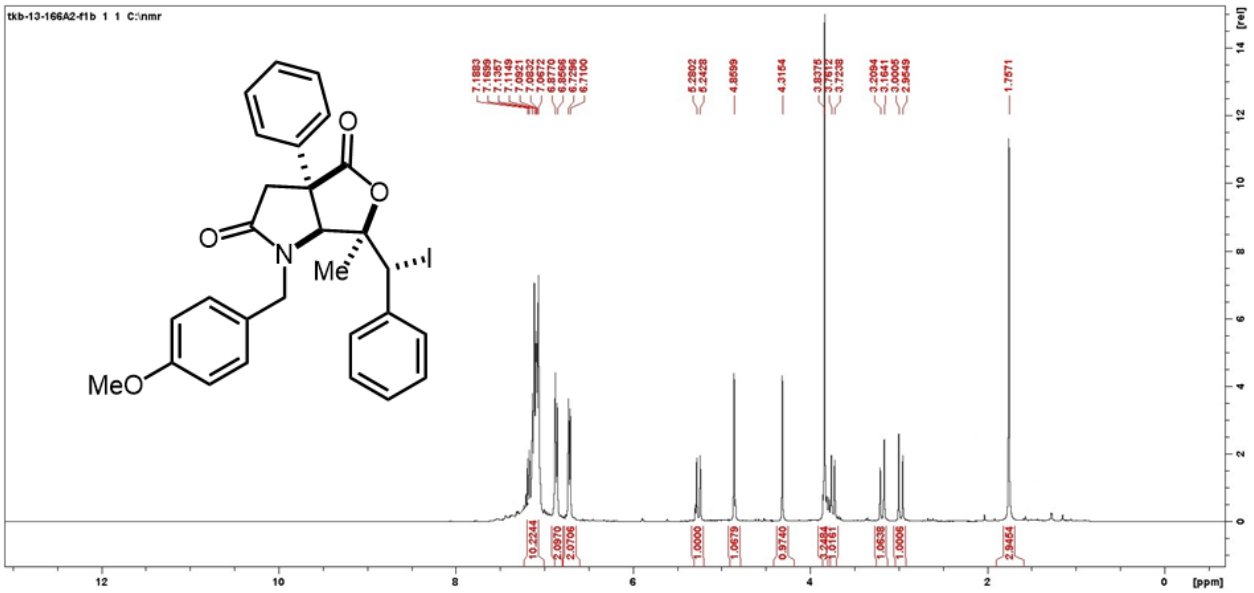






Compound 2*z*3

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yellowish oil. Yield = 488.0 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 – 7.07 (m, 10H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.71 (d, *J* = 8.0 Hz, 2H), 5.26 (d, *J* = 15.0 Hz, 1H), 4.86 (s, 1H), 4.32 (s, 1H), 3.84 (s, 3H), 3.74 (d, *J* = 15.0 Hz, 1H), 3.19 (d, *J* = 18.1 Hz, 1H), 3.00 (d, *J* = 18.1 Hz, 1H), 1.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 172.1, 159.8, 138.1, 137.6, 130.2, 129.8, 128.8, 128.8, 128.6, 127.9, 126.7, 125.4, 114.4, 87.6, 66.7, 55.4, 52.8, 46.0, 43.5, 38.6, 25.0. **HRMS-EI^{+}** (*m/z*): calc for $C_{28}H_{26}INO_4$ $[M]^{+}$ 567.0907, found 567.0912.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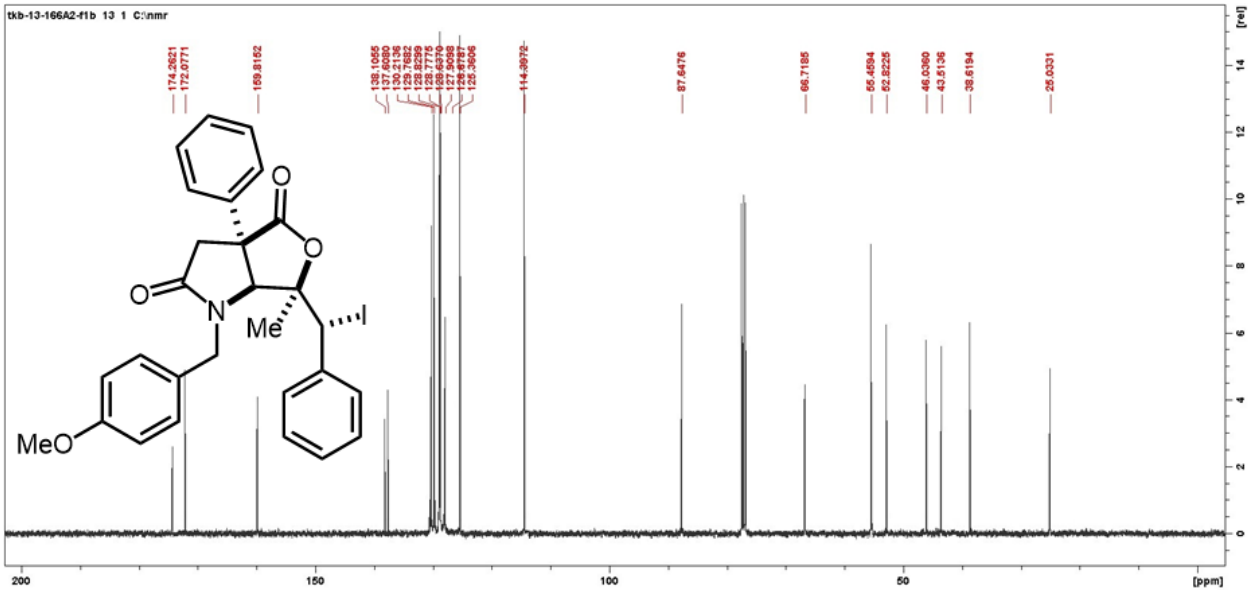
Me
I
[ppm]
[rel]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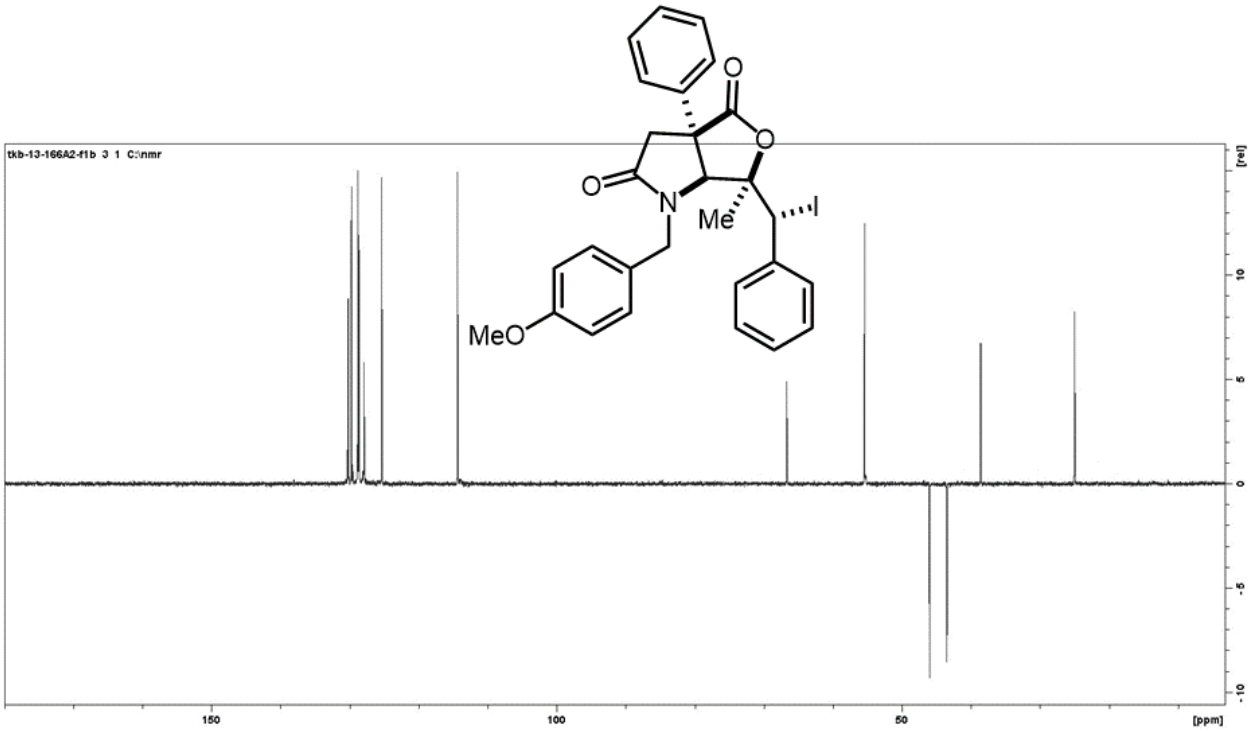
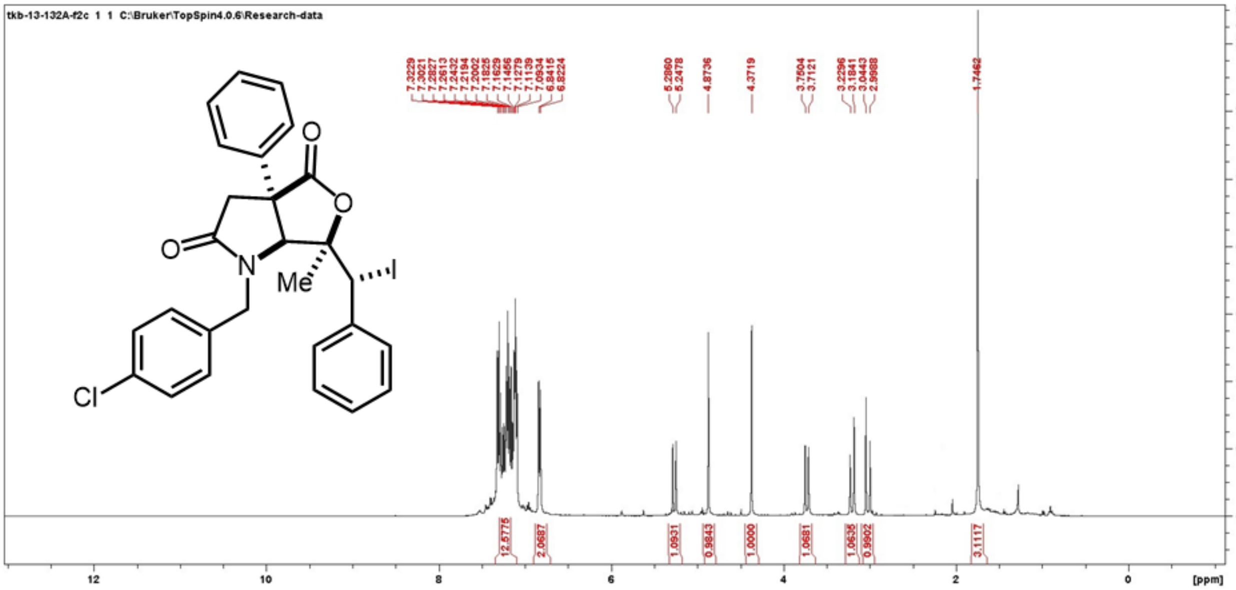


Compound 2*z*4

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Greenish-yellow oil. Yield = 514.6 mg, 90%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.09 (m, 12H), 6.83 (d, *J* = 7.4 Hz, 2H), 5.26 (d, *J* = 15.4 Hz, 1H), 4.87 (s, 1H), 4.37 (s, 1H), 3.73 (d, *J* = 15.4 Hz, 1H), 3.20 (d, *J* = 17.4 Hz, 1H), 2.99 (d, *J* = 17.4 Hz, 1H), 1.75 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 172.3, 138.0, 137.4, 134.4, 133.4, 130.2, 129.6, 129.2, 129.0, 129.0, 128.8, 128.2, 125.5, 87.7, 67.7, 53.0, 45.8, 43.2, 38.9, 24.1. FTIR (KBr): 2998.4, 2924.0, 1734.2, 1668.3, 1474.3, 1452.8, 1361.9, 1342.0, 1205.6, 1144.2, 1081.7, 1038.3, 986.4, 705.2. **HRMS-EI^{+}** (*m/z*): calc for $C_{27}H_{23}ClINO_3$ $[M]^{+}$ 571.0411, found 571.0405.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3.7121
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3.0443
2.9988
1.7462
12.5775
2.0687
1.0931
0.9843
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1.0636
0.9902
3.1117
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Cl
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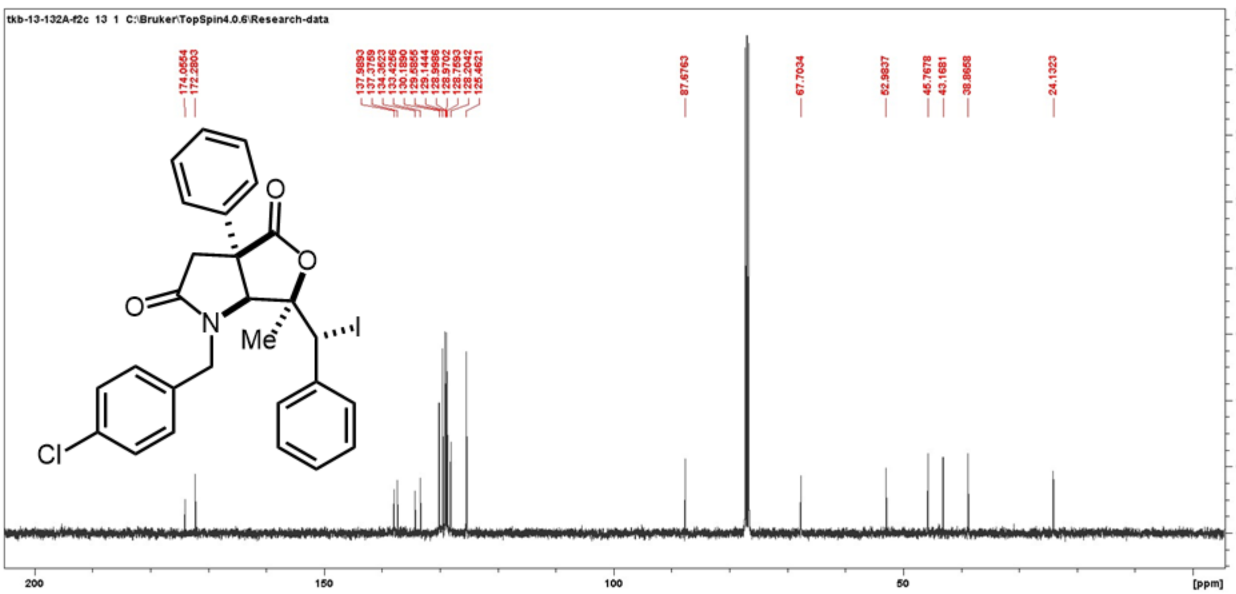
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Cl
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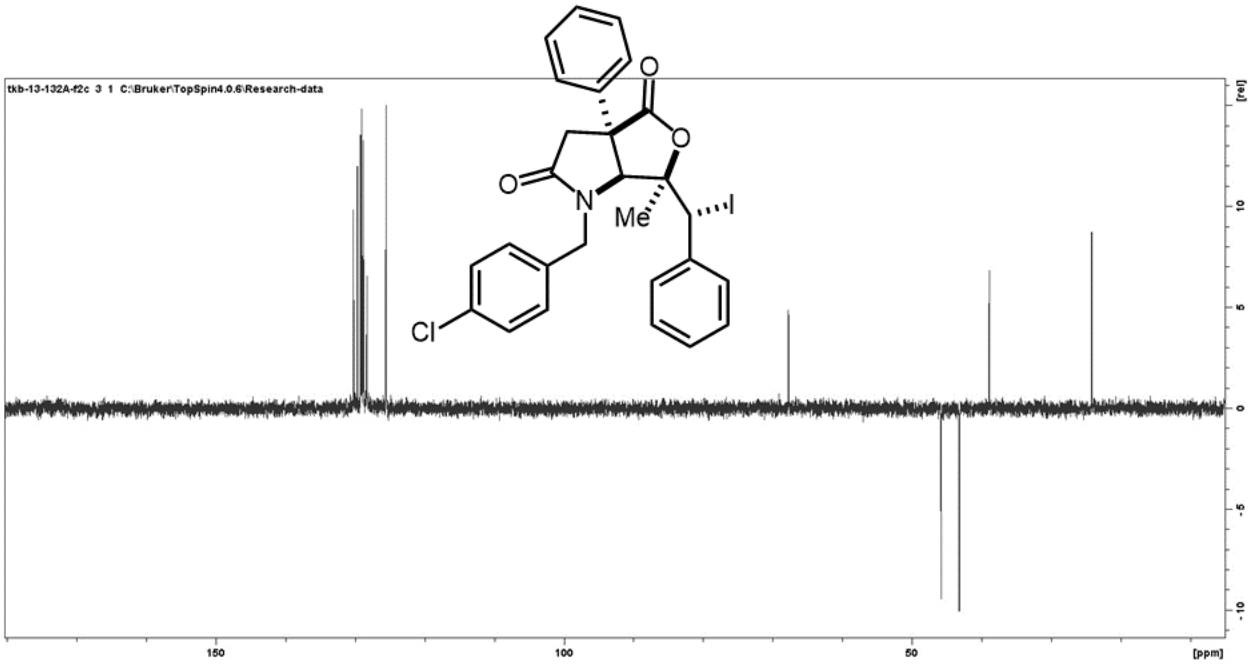
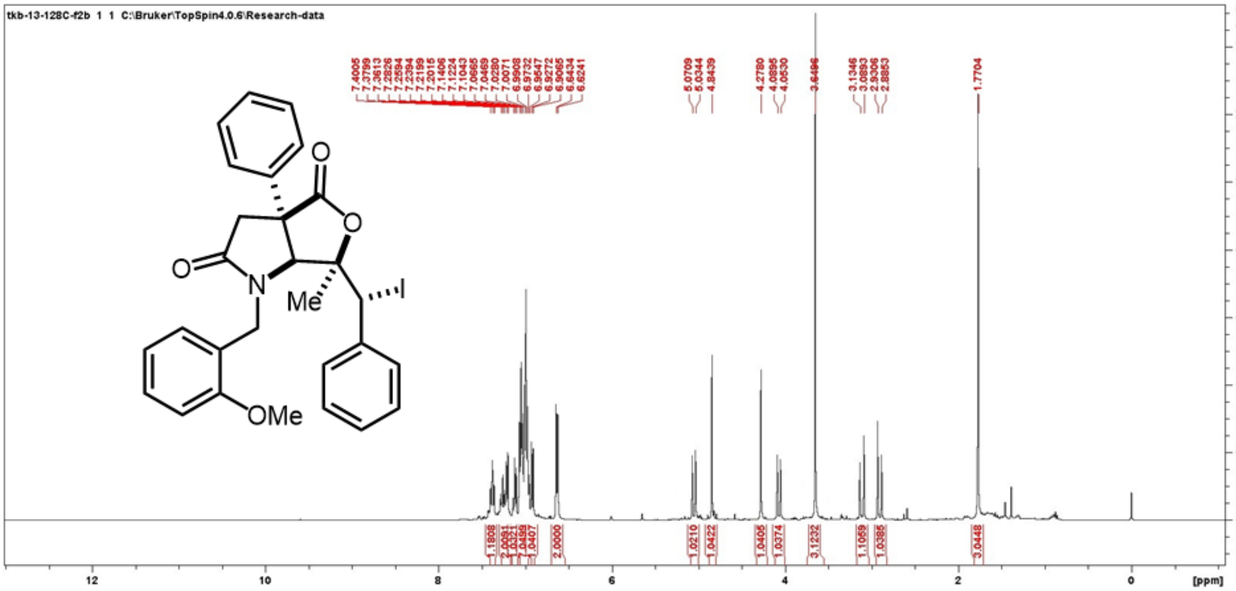


Compound 2z5

Prepared in 1 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Yellowish oil. Yield = 510.7 mg, 90%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (td, *J* = 7.9, 1.7 Hz, 1H), 7.27 (d, *J* = 9.4 Hz, 2H), 7.26 – 7.16 (m, 8H), 6.92 (d, *J* = 8.3 Hz, 1H), 6.63 (dd, *J* = 7.6, 1.8 Hz, 2H), 5.05 (d, *J* = 14.6 Hz, 1H), 4.84 (s, 1H), 4.28 (s, 1H), 4.07 (d, *J* = 14.6 Hz, 1H), 3.65 (s, 3H), 3.10 (d, *J* = 17.6 Hz, 1H), 2.90 (d, *J* = 17.6 Hz, 1H), 1.77 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.5, 171.8, 157.6, 138.5, 137.8, 131.3, 130.3, 130.2, 128.7, 128.5, 128.5, 127.6, 125.3, 122.6, 121.1, 110.8, 87.8, 67.1, 55.2, 52.8, 43.5, 42.5, 38.0, 26.0. FTIR (KBr): 2994.1, 1763.4, 1669.4, 1608.2, 1511.1, 1431.8, 1414.7, 1344.9, 1298.4, 1135.3, 1031.8, 996.7, 706.4. **HRMS-EI^{+}** (*m/z*): calc for $C_{28}H_{26}INO_4$ $[M]^{+}$ 567.0907, found 567.0900.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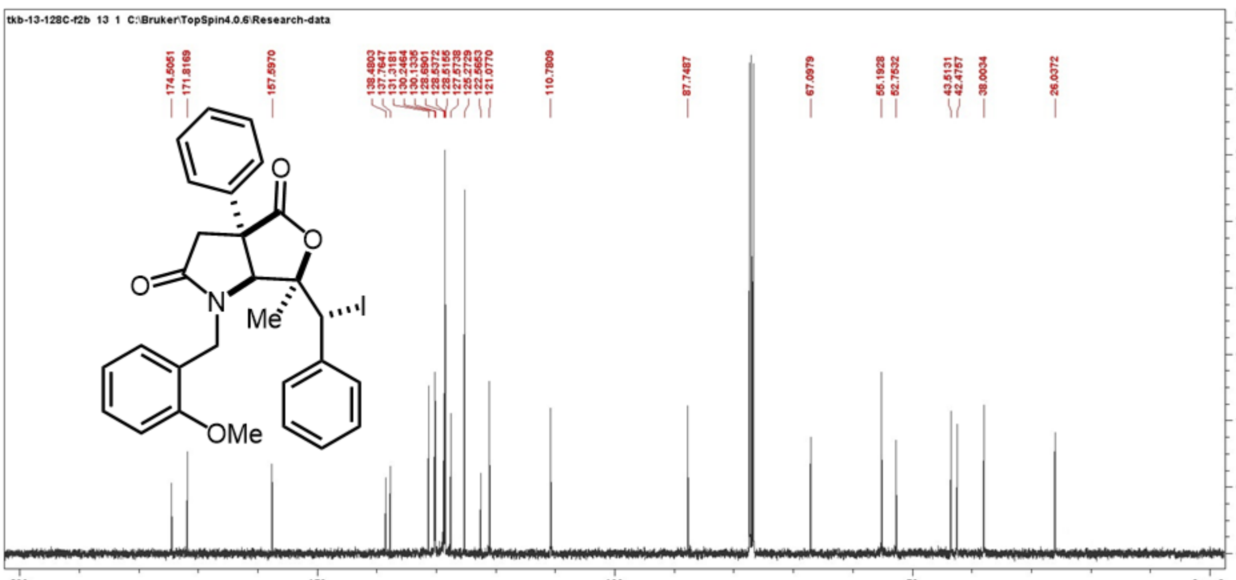
OMe
[ppm]
[rel]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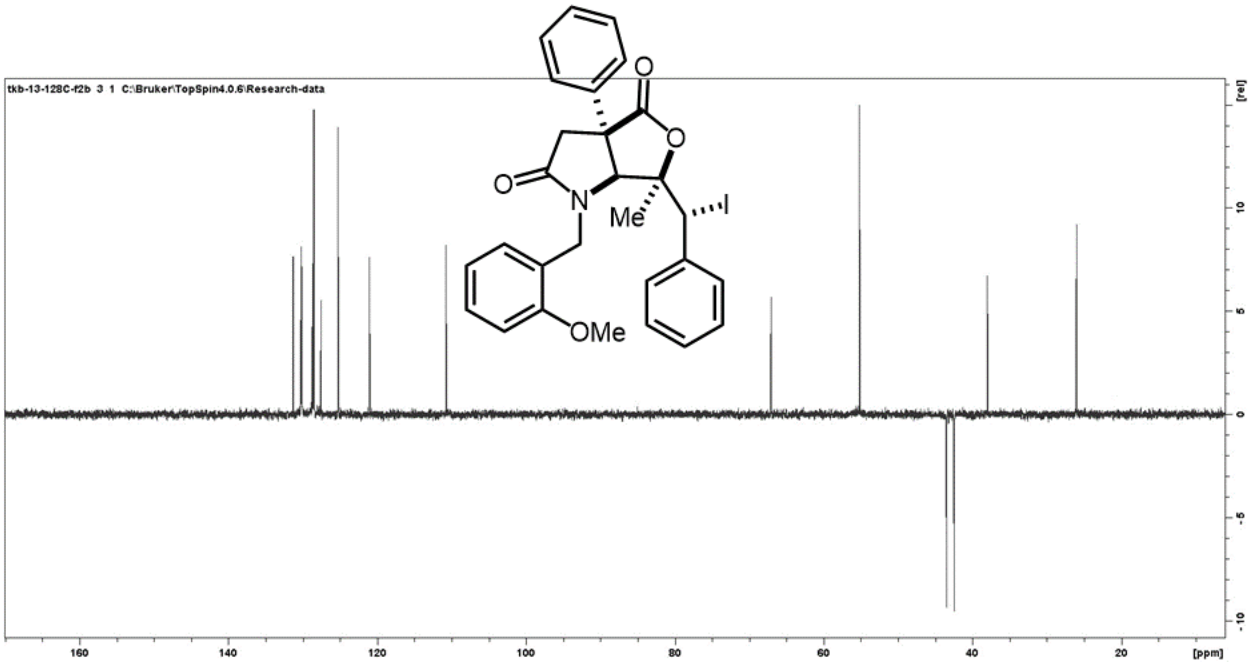
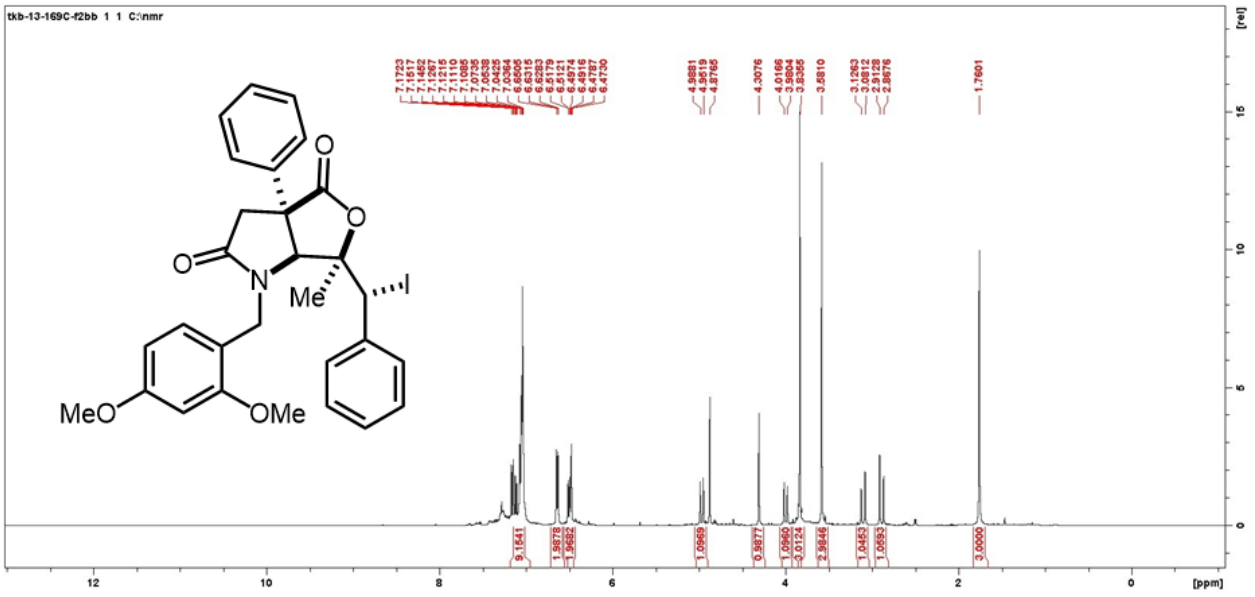


Compound 2z6

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Amorphous viscous oil. Yield = 519.7 mg, 87%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 – 7.04 (m, 9H), 6.65 – 6.61 (m, 2H), 6.51 – 6.47 (m, 2H), 4.97 (d, *J* = 14.5 Hz, 1H), 4.88 (s, 1H), 4.31 (s, 1H), 4.00 (d, *J* = 14.5 Hz, 1H), 3.84 (s, 3H), 3.58 (s, 3H), 3.10 (d, *J* = 18.0 Hz, 1H), 3.90 (d, *J* = 18.0 Hz, 1H), 1.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.5, 171.7, 161.5, 158.6, 138.6, 137.8, 132.2, 130.3, 128.7, 128.5, 127.5, 125.2, 114.9, 104.5, 98.8, 87.8, 67.2, 55.6, 55.2, 52.7, 43.6, 42.4, 38.2, 26.2. **HRMS-EI^{+}** (*m/z*): calc for $C_{29}H_{28}INO_5$ $[M]^{+}$ 597.1012, found 597.1018.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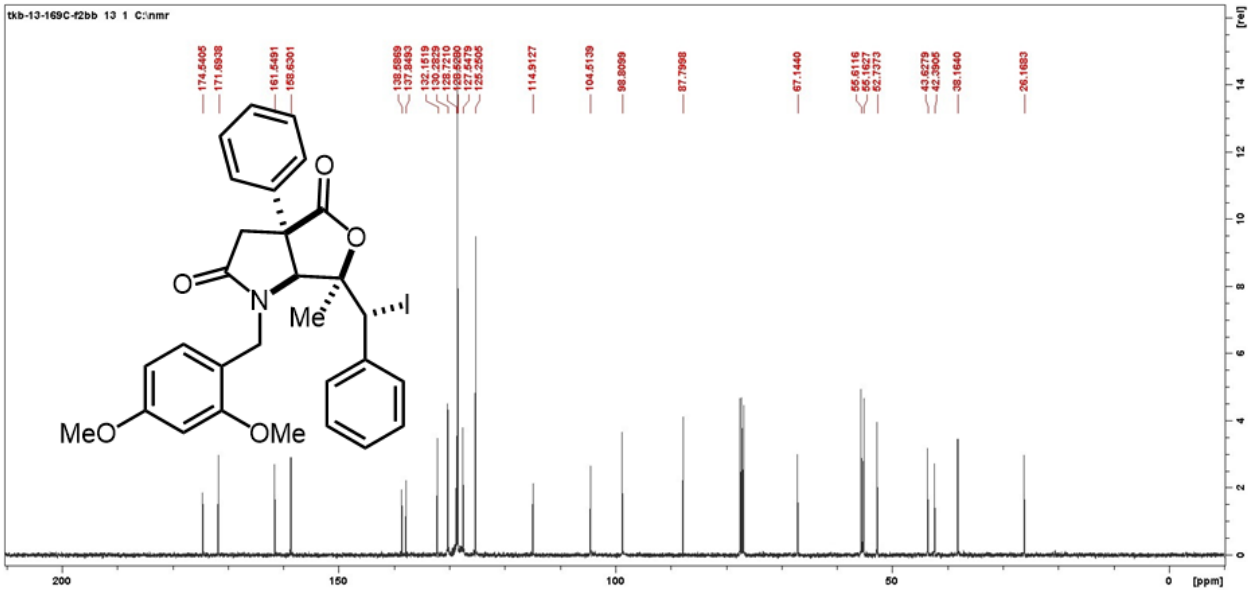
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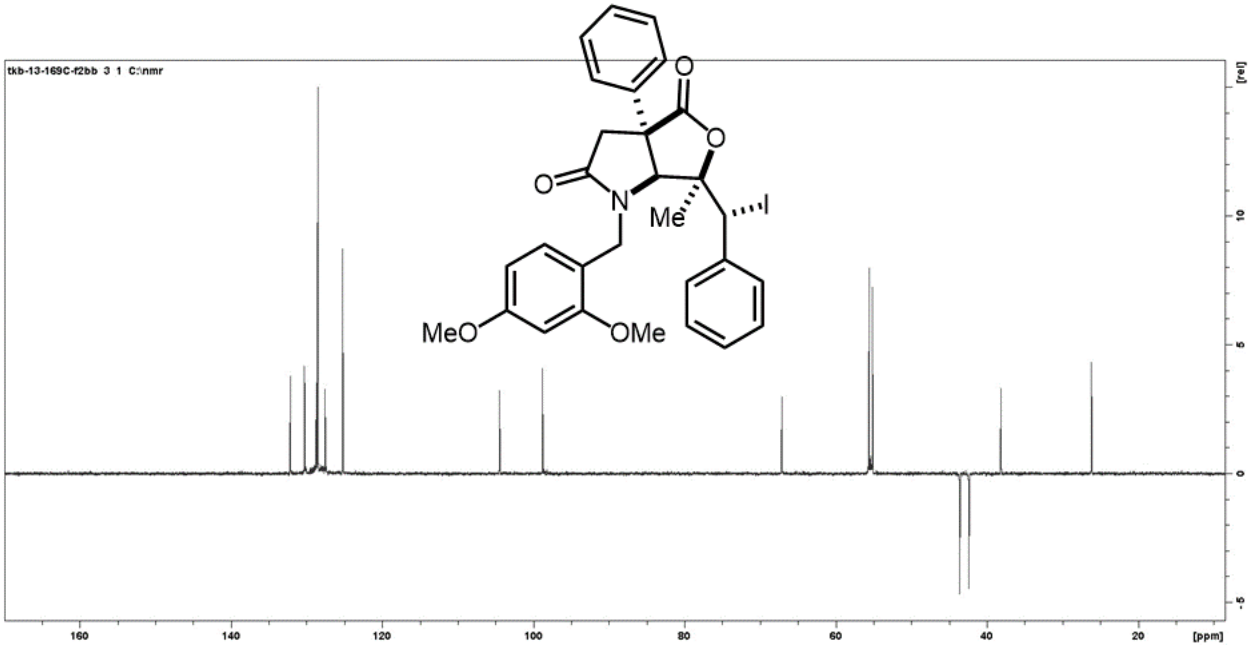
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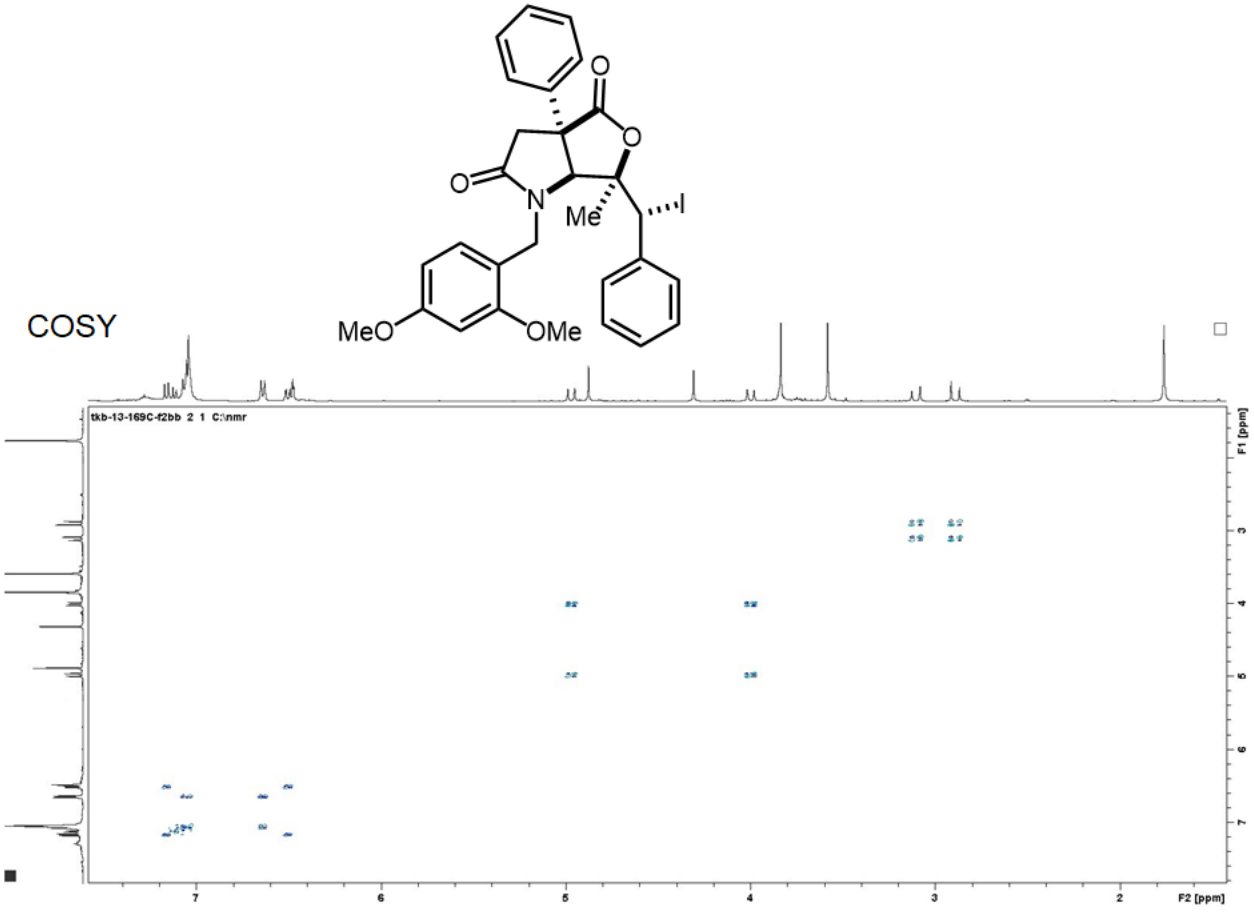
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N
Me
I
MeO
OMe
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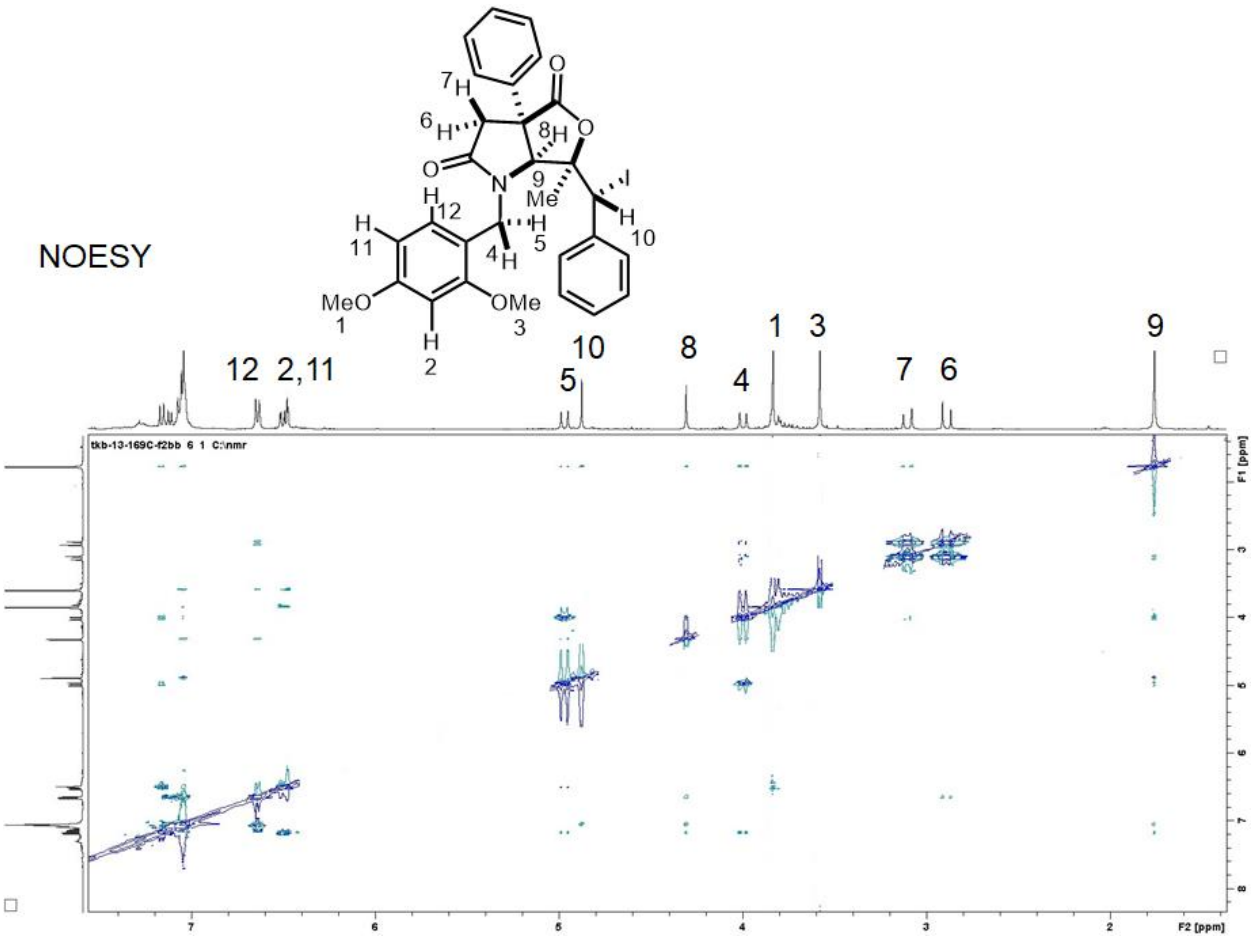
F2 [ppm]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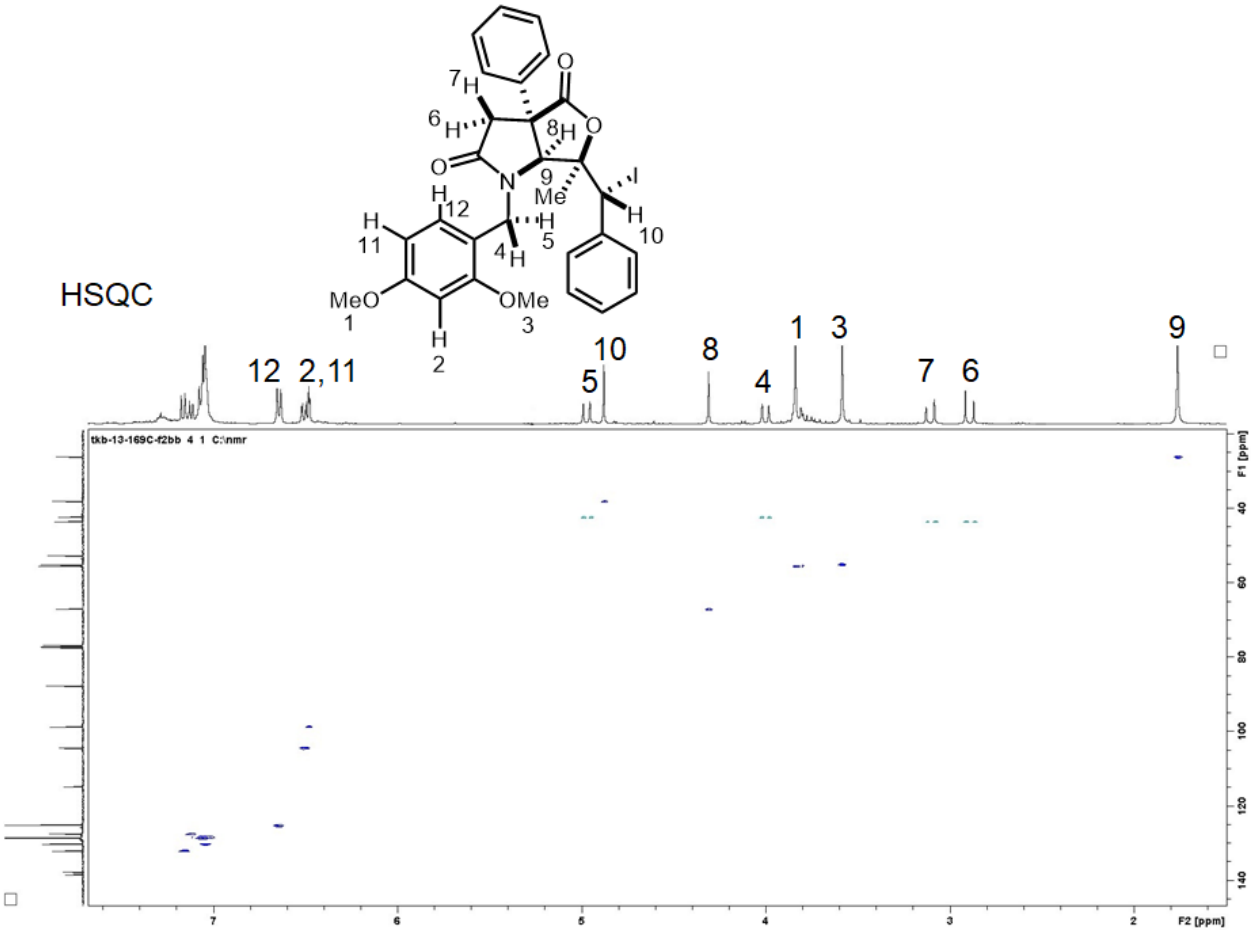
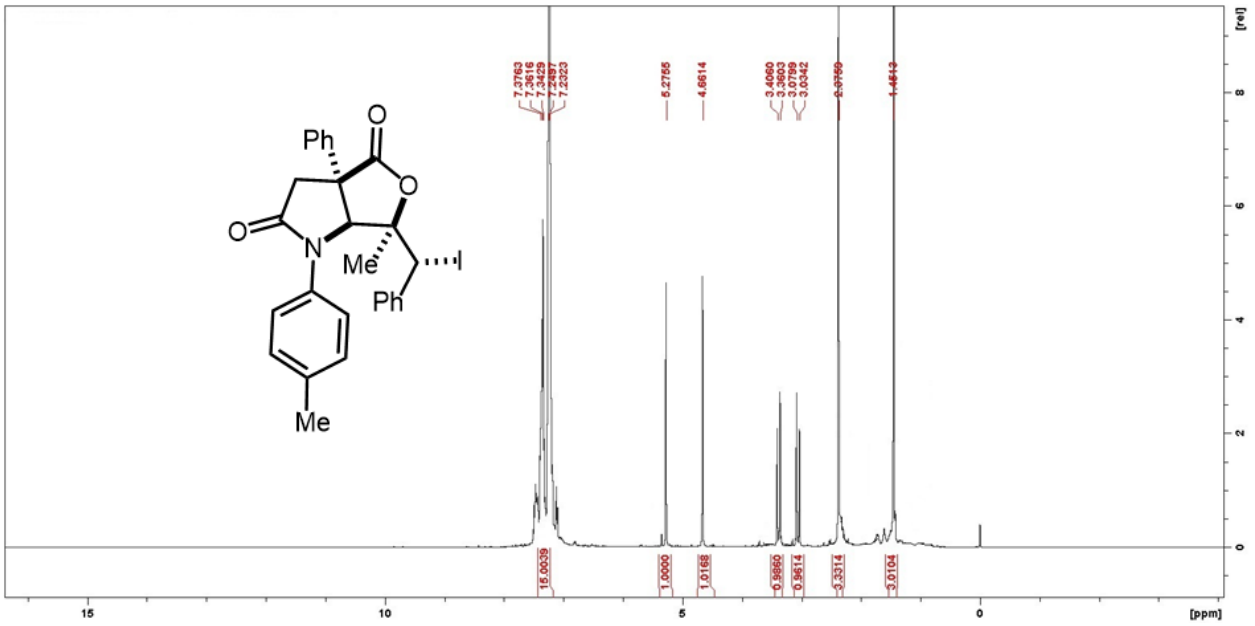
F2 [ppm]
F1 [ppm]



Compound 2z7

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Yellowish oil. Yield = 472.9 mg, 88%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.22 (m, 14H), 5.28 (s, 1H), 4.67 (s, 1H), 3.38 (d, *J* = 16.5 Hz, 1H), 3.05 (d, *J* = 16.5 Hz, 1H), 2.38 (s, 3H), 1.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 175.3, 138.8, 137.3, 129.9, 129.3, 129.3, 128.1, 127.4, 126.3, 88.6, 70.0, 46.0, 44.2, 37.3, 21.2. FTIR (KBr): 3020.0, 2834.3, 1724.9, 1646.3, 1474.3, 1452.8, 1361.9, 1342.0, 1205.6, 1140.2, 1077.7, 996.4, 766.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{27}H_{24}INO_3$ $[M]^+$ 537.0801, found 537.0805.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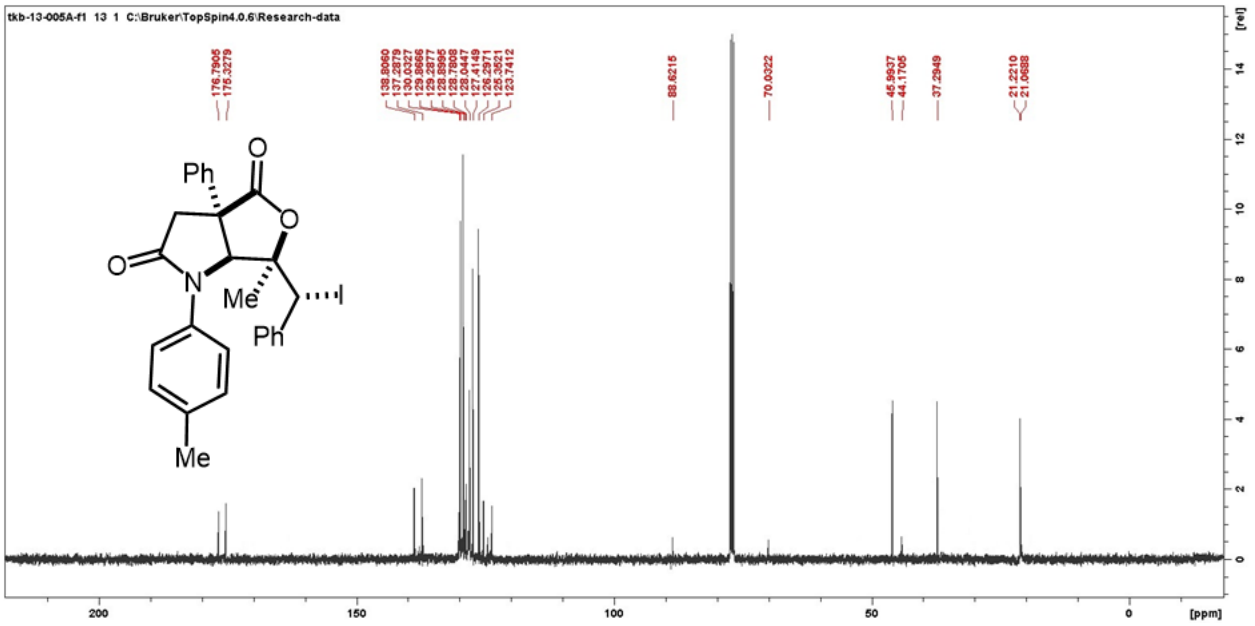
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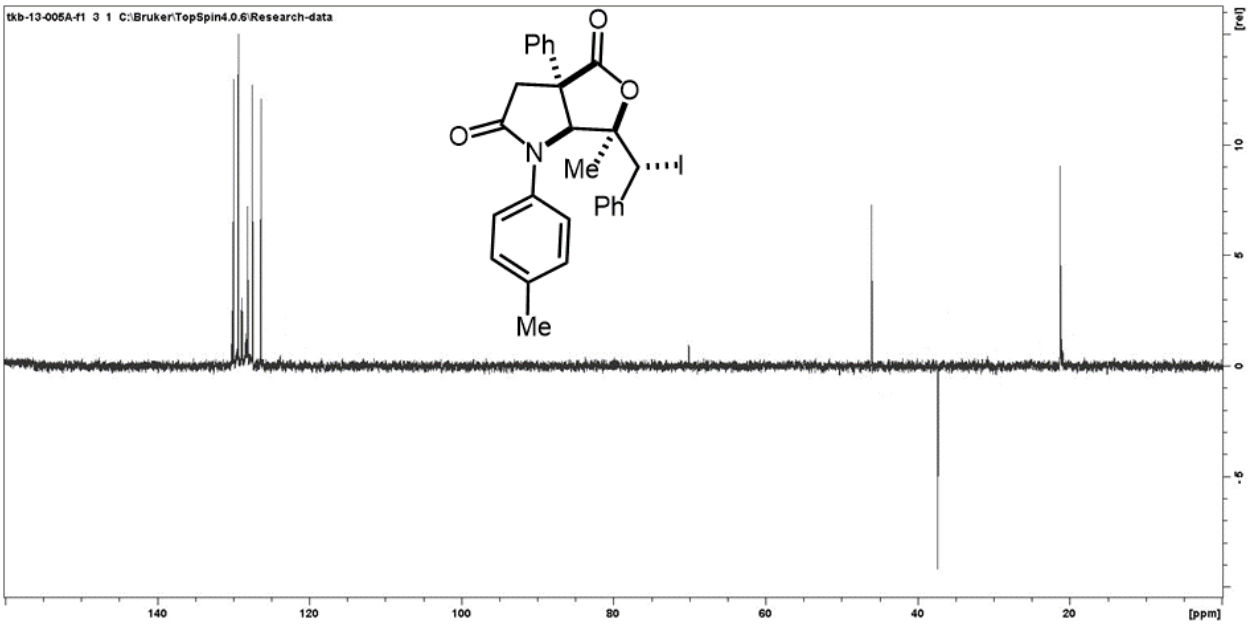


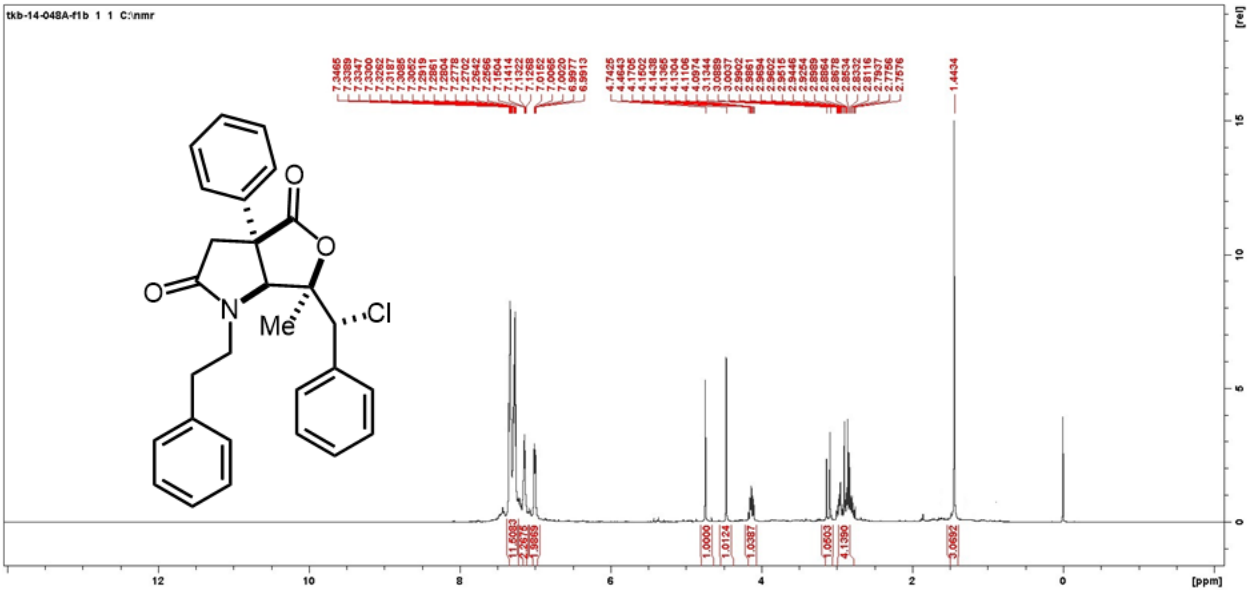
Compound 2z8

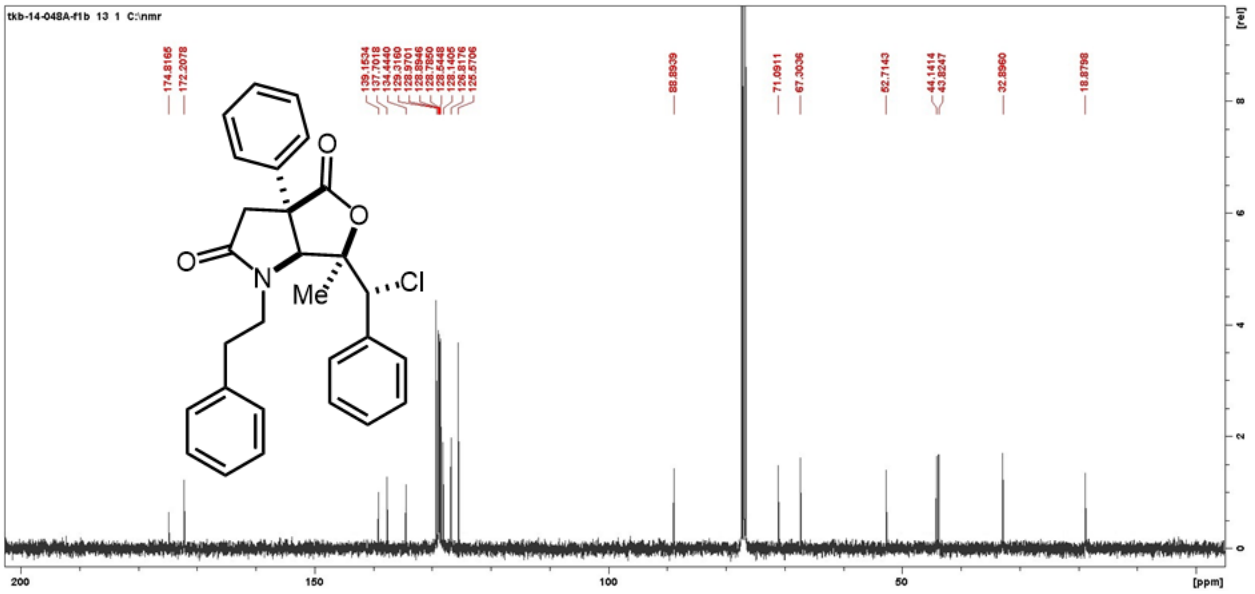
Prepared in 0.5 mmol scale using **General Procedure A**, but using NCS, at 60 ºC for 1 h.

Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yellowish oil.

Yield = 96.6 mg, 42%, >99:1 dr.

HRMS-EI^{+} (*m/z*): calc for $C_{28}H_{26}ClNO_3$ $[M]^{+}$ 459.1601, found 459.1604.

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52.7143
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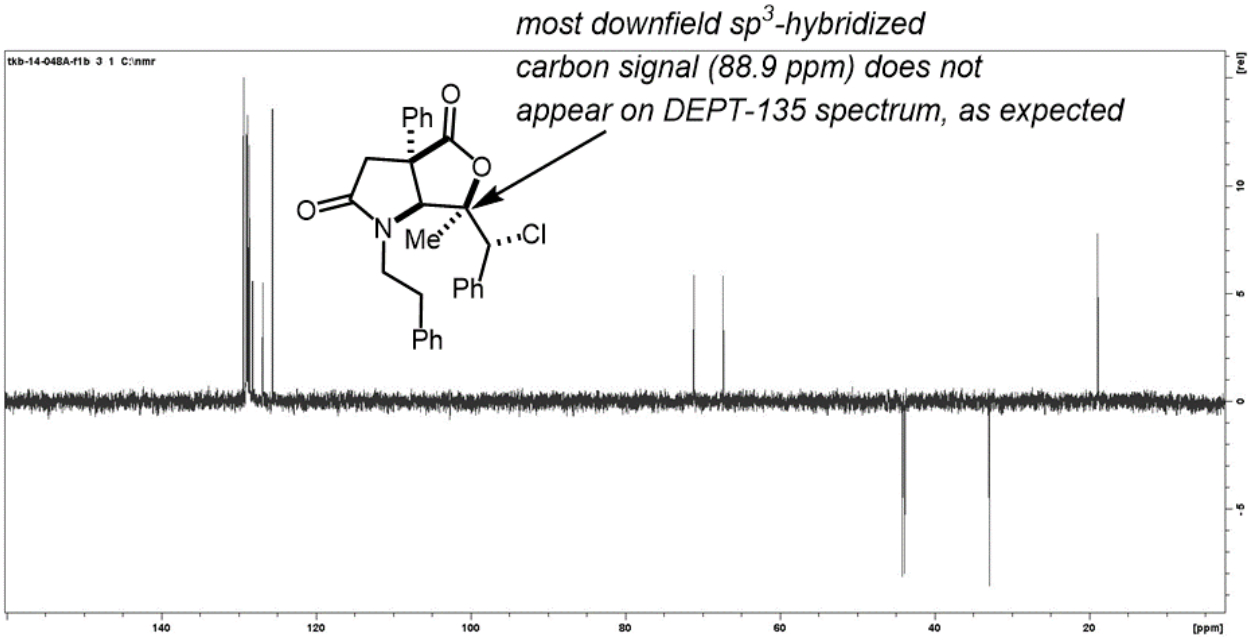
most downfield sp3-hybridized
carbon signal (88.9 ppm) does not
appear on DEPT-135 spectrum, as expected
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O
N
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Cl
Ph
Ph
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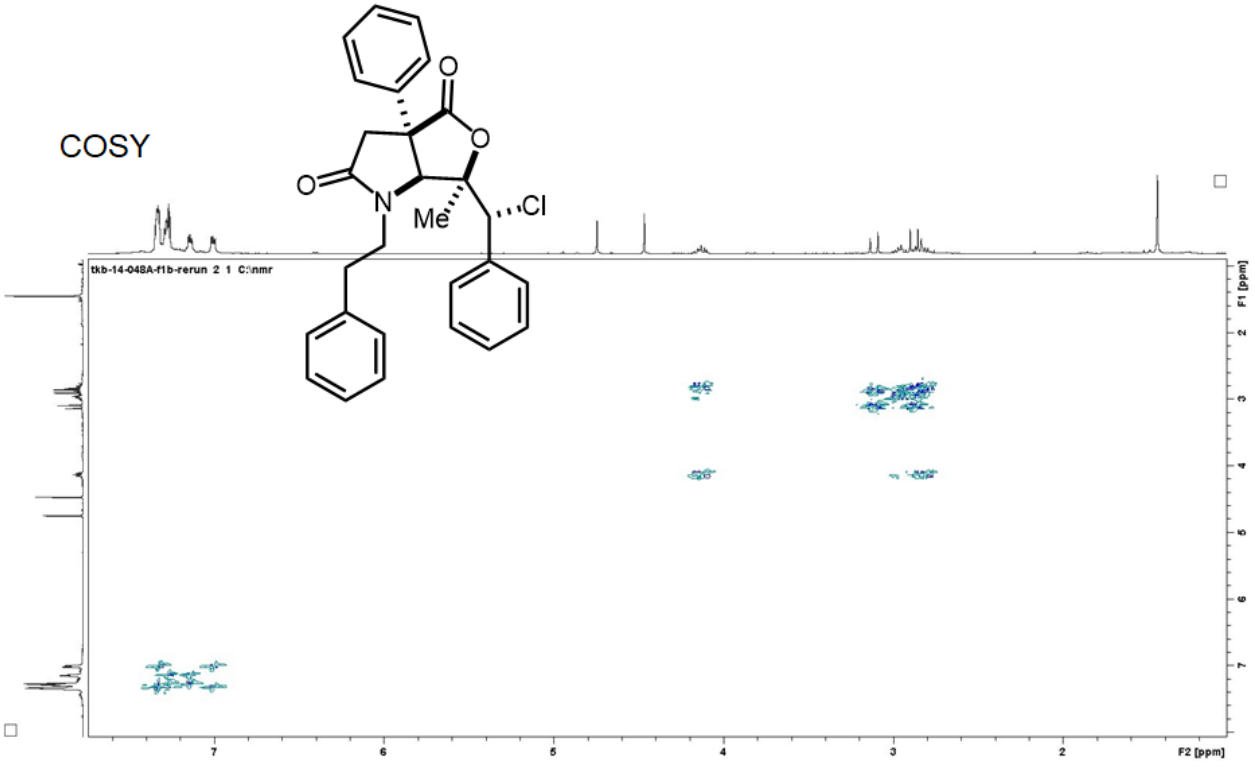
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O
O
N
Me
Cl
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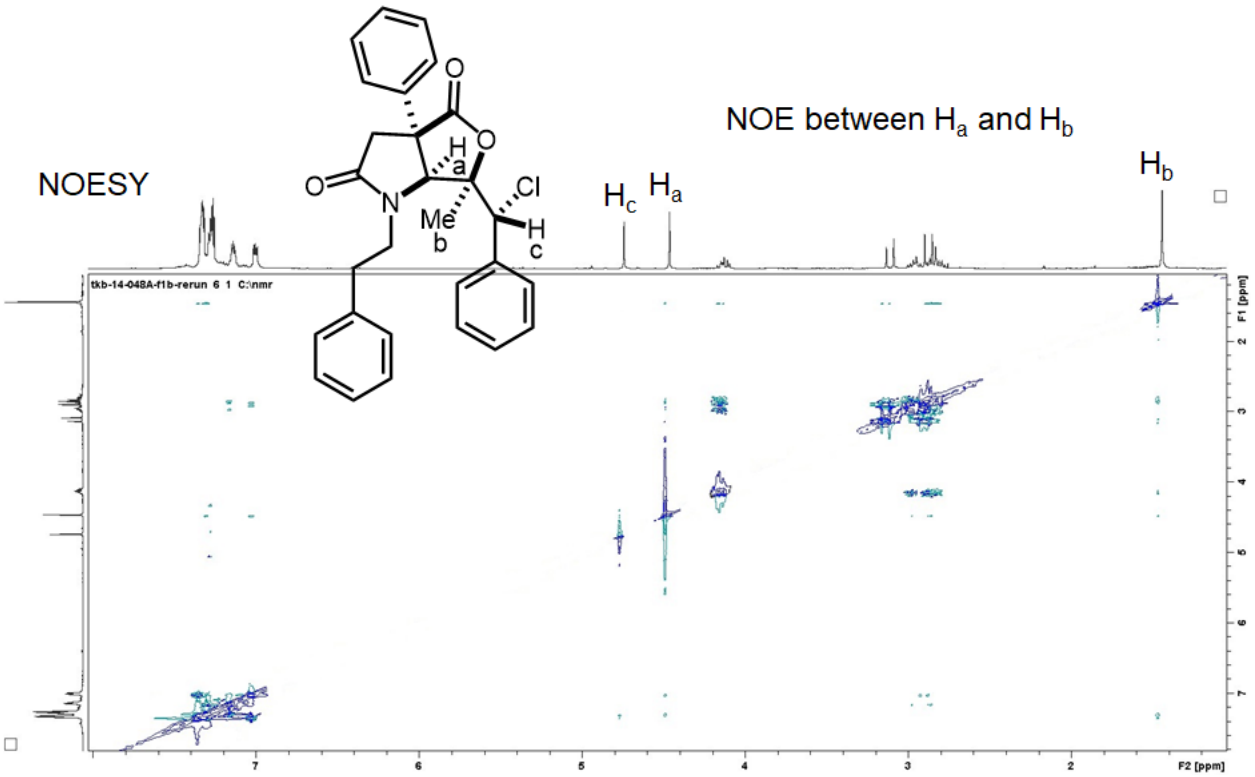
F1 [ppm]
F2 [ppm]


NOESY
NOE between Ha and Hb
O
O
O
N
Ha
Cl
Me
b
Hc
Hc Ha
Hb
tkb-14-048A-f1b-rerun 6 1 C:\nmr
F1 [ppm]
F2 [ppm]

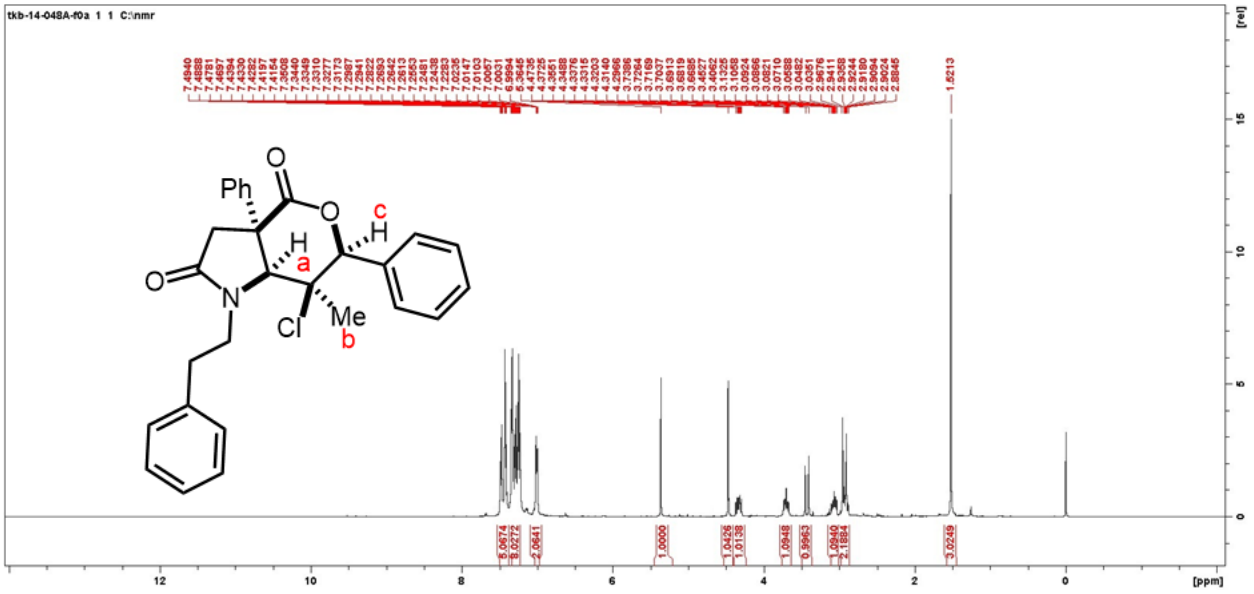
Compound 3b

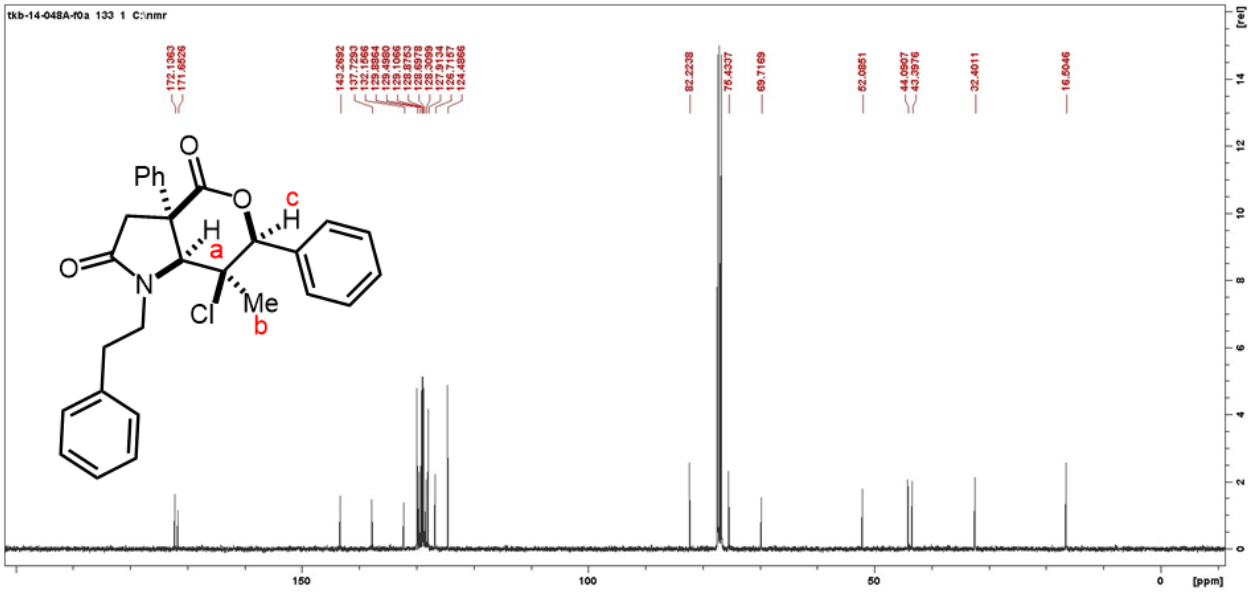
Prepared in 0.5 mmol scale using **General Procedure A**, but using NCS, at 60 ºC for 1 h.

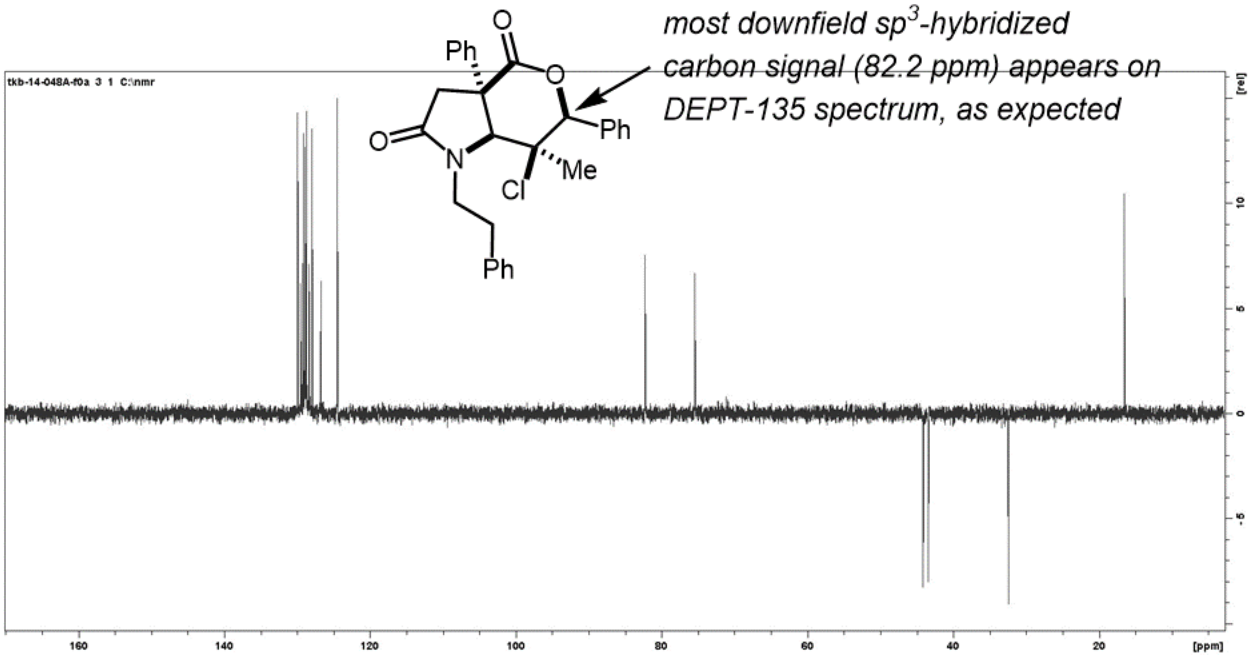
Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yellowish oil.

Yield = 80.5 mg, 35%, >99:1 dr.

HRMS-EI$^+$ (*m/z*): calc for $C_{28}H_{26}ClNO_3$ $[M]^+$ 459.1601, found 459.1604.






most downfield sp3-hybridized carbon signal (82.2 ppm) appears on DEPT-135 spectrum, as expected
Ph
O
O
Ph
O
N
Cl
Me
Ph
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120
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80
60
40
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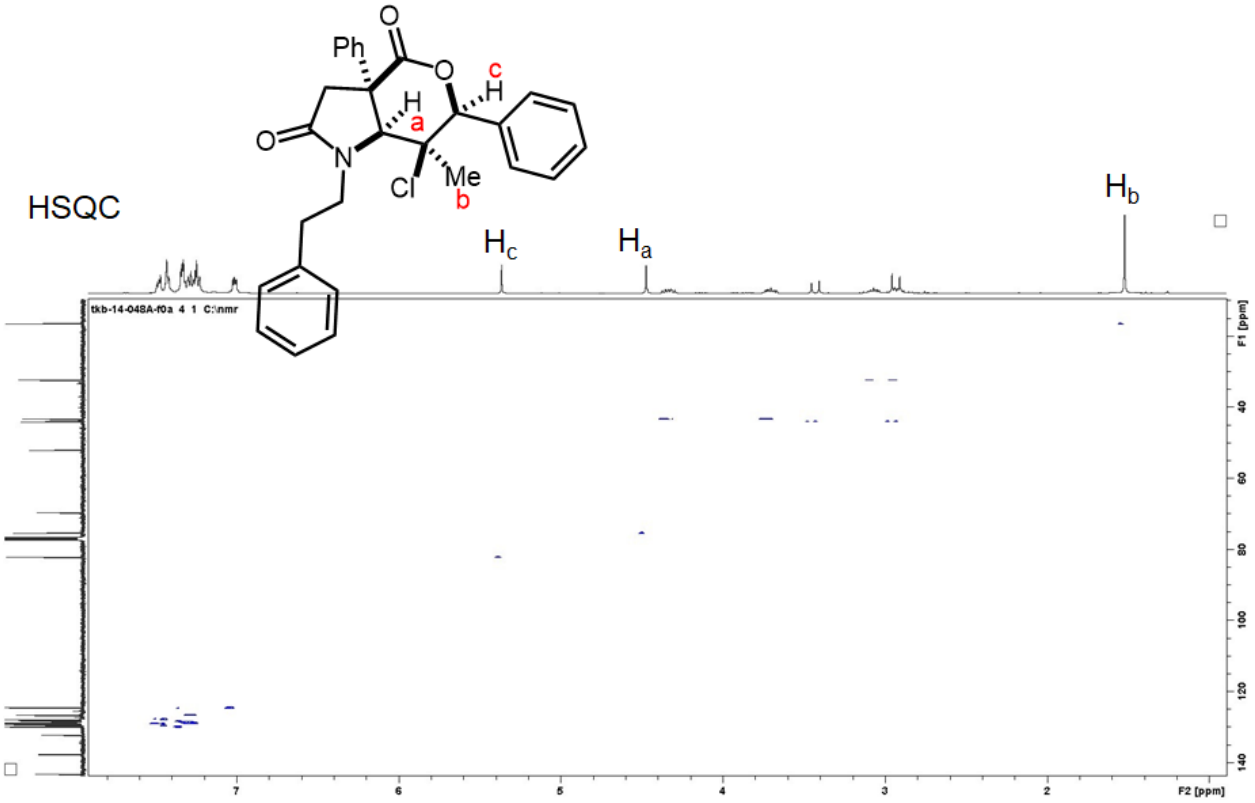
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Ha
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F1 [ppm]
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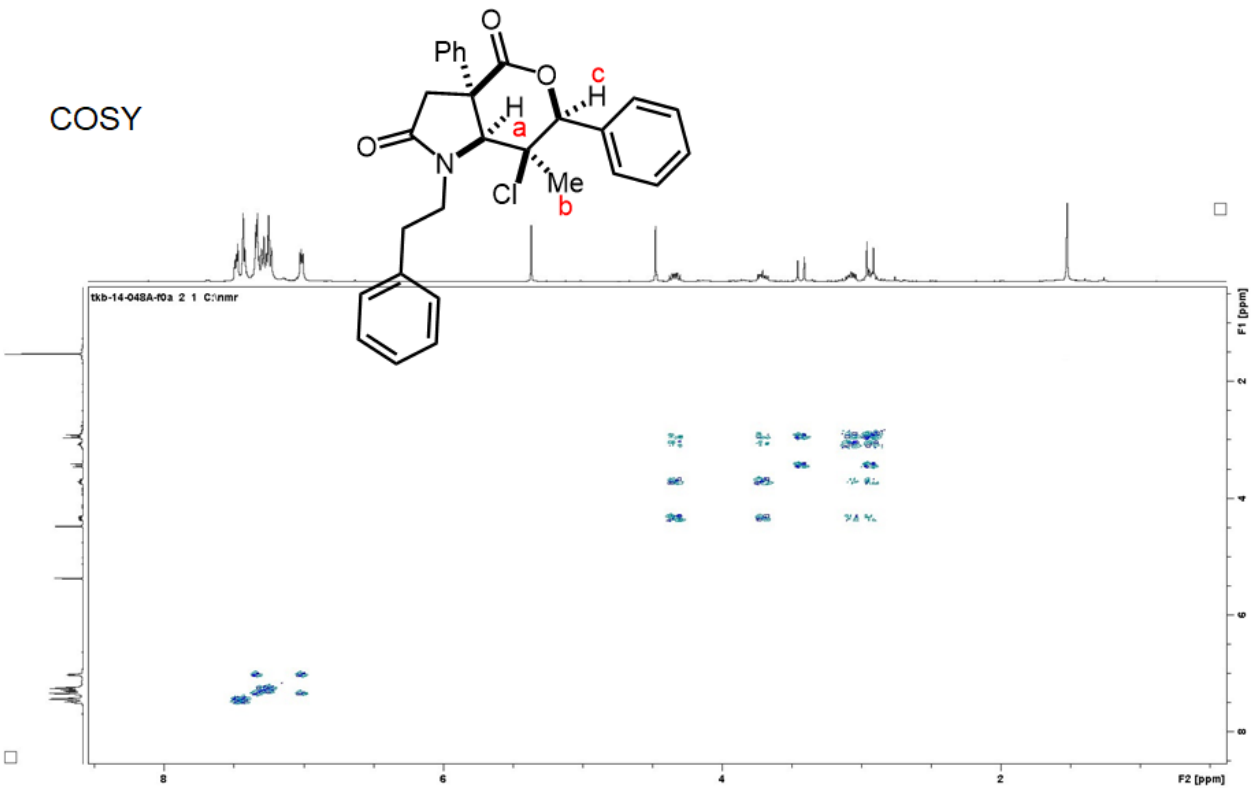
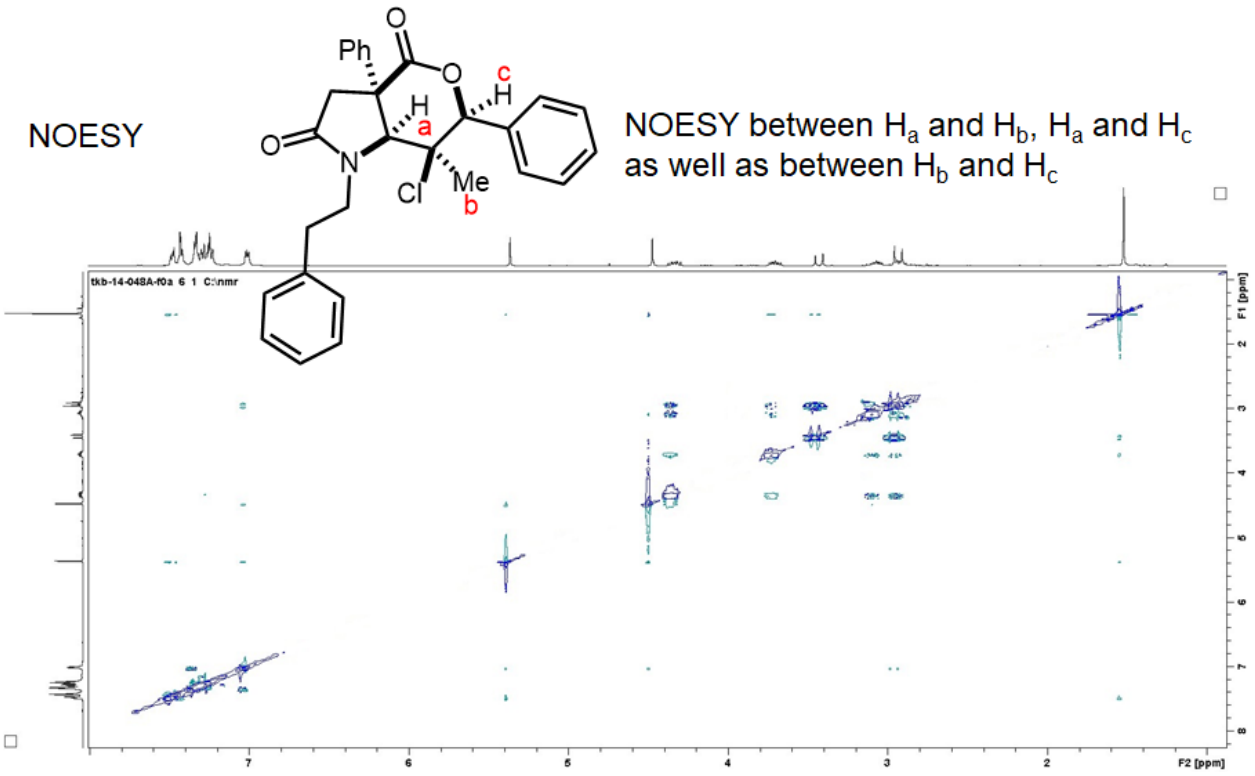
COSY



NOESY

NOESY between H_a and H_b, H_a and H_c as well as between H_b and H_c



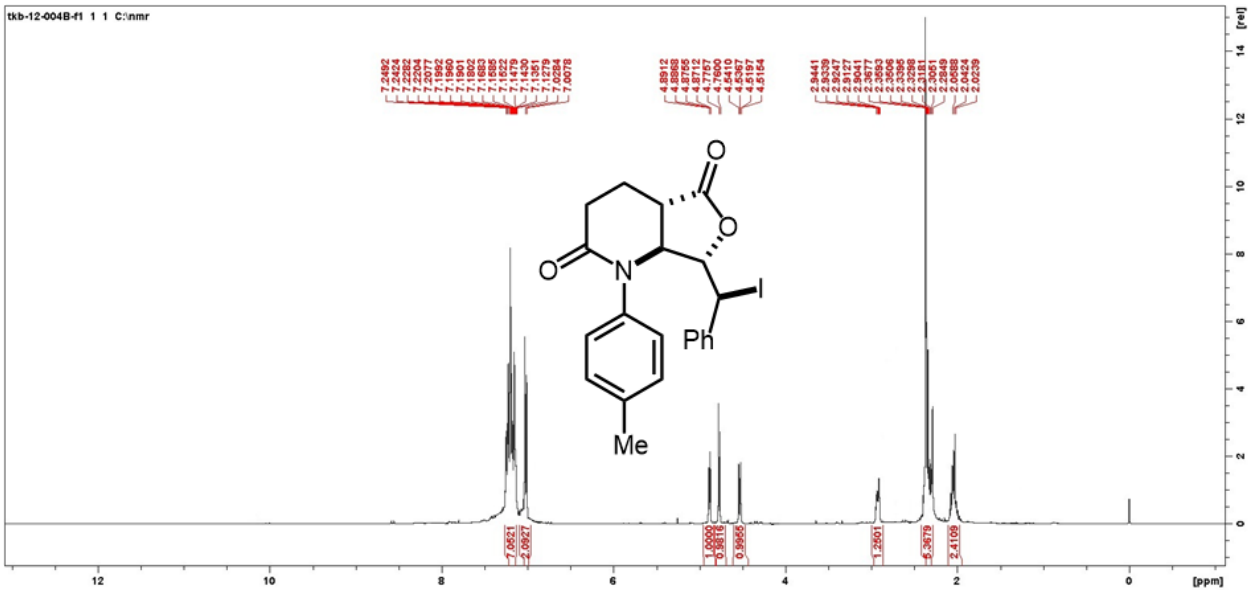
Scheme 3 Results

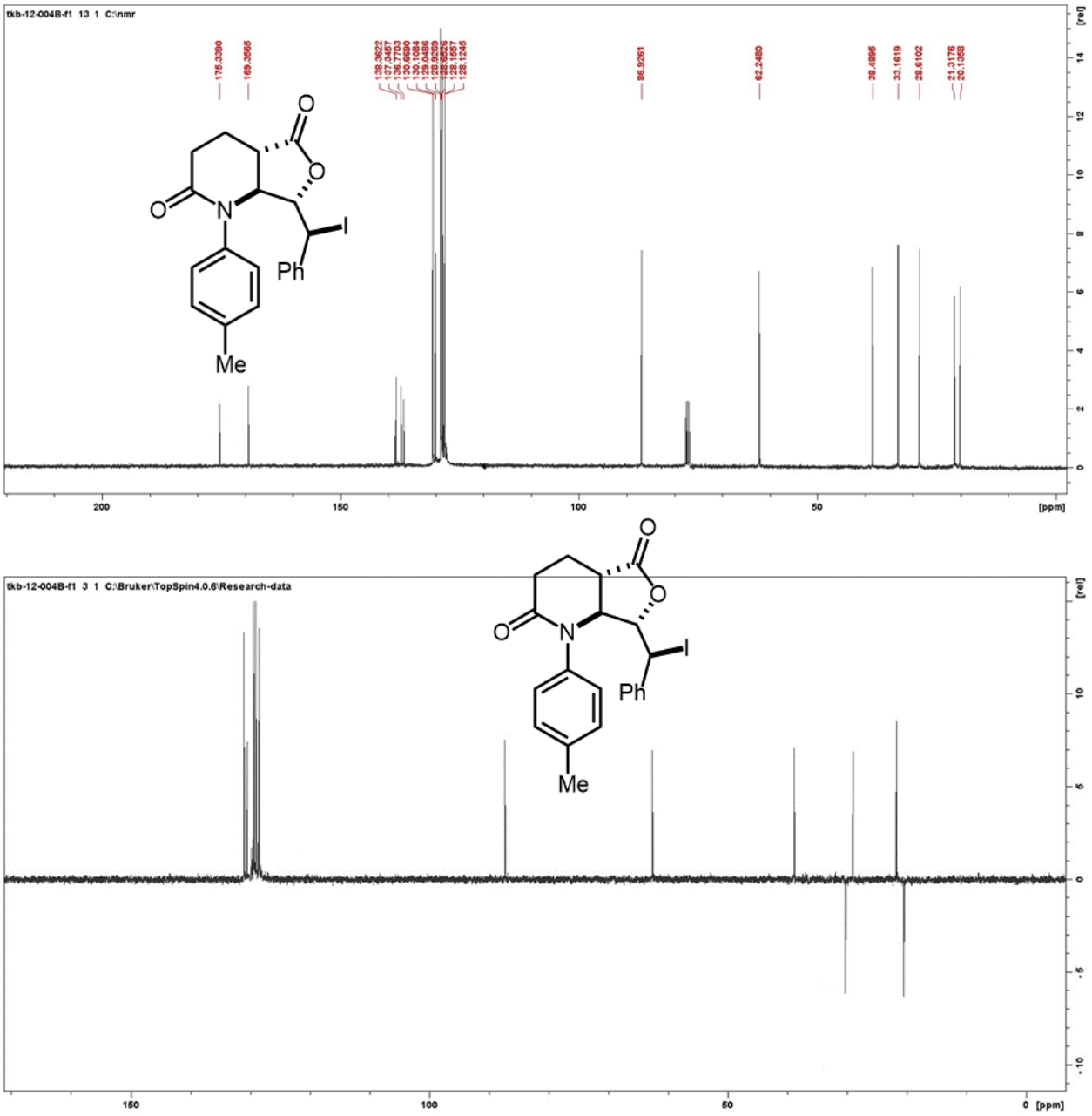
Compound 5a

Prepared in 0.50 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Reddish oil. Yield = 179.4 mg, 84%, 95:5 dr. ^{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 $C_{22}H_{22}BrNO_3$ $[M]^{+}$ 427.0783, found 427.0788. Data as previously reported.[2]

Compound 5b

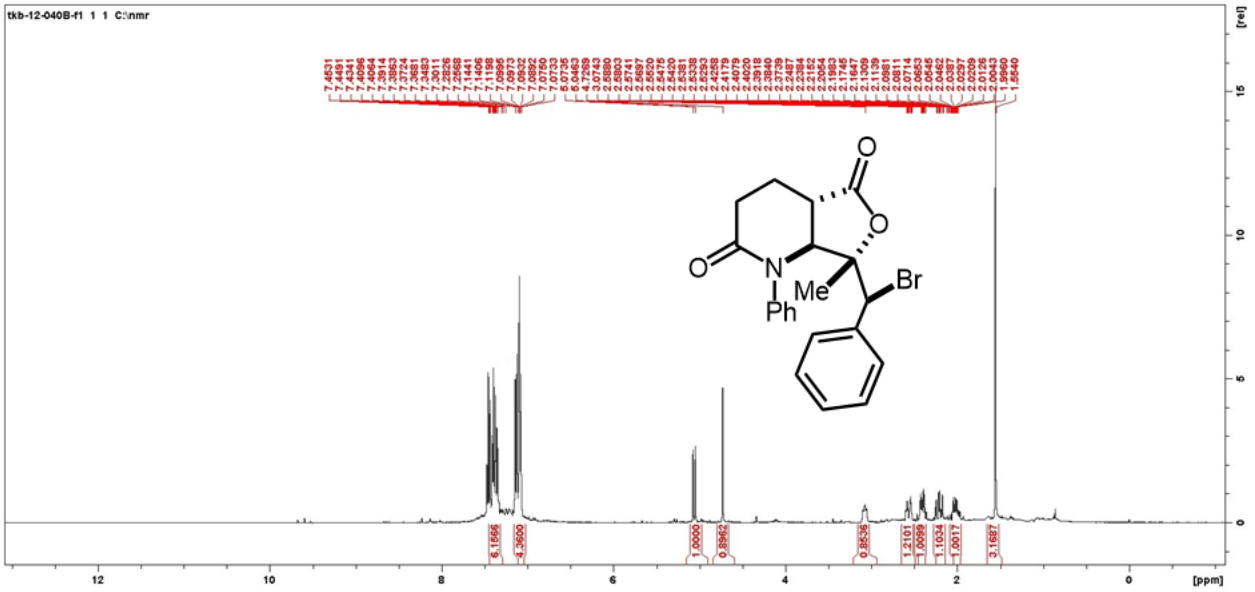
Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 405.9 mg, 88%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.20 (m, 7H), 7.12 – 6.98 (d, 2H), 4.88 (dd, *J* = 6.3, 1.8 Hz, 1H), 4.79 (d, *J* = 6.3 Hz, 1H), 4.53 (dd, *J* = 8.6, 1.8 Hz, 1H), 2.93 – 2.84 (m, 1H), 2.40 – 2.30 (m, 5H), 2.11 – 2.01 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.3, 169.4, 138.4, 137.3, 136.8, 130.7, 130.1, 129.0, 128.9, 128.7, 128.2, 128.1, 86.9, 62.2, 38.5, 33.2, 28.6, 21.3, 20.1. **HRMS-EI^{+}** (*m/z*): calc for $C_{21}H_{20}INO_3$ $[M]^{+}$ 461.0488, found 461.0493.





Compound 5c

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Pale yellow oil. Yield = 310.7 mg, 75%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.19 (m, 6H), 7.23 – 7.07 (m, 4H), 5.06 (d, J = 10.9 Hz, 1H), 4.74 (s, 1H), 3.17 – 3.02 (m, 1H), 2.66 (t, J = 6.5 Hz, 1H), 2.43 – 2.36 (m, 1H), 2.34 – 2.18 (m, 1H), 2.14 – 2.03 (m, 1H), 1.54 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 170.9, 141.3, 135.5, 129.4, 129.2, 128.9, 128.7, 128.5, 127.6, 127.5, 91.2, 62.9, 61.0, 41.0, 23.0, 22.9. **HRMS-EI^{+}** (*m/z*): calc for $C_{21}H_{20}BrNO_3$ $[M]^{+}$ 413.0627, found 413.0622.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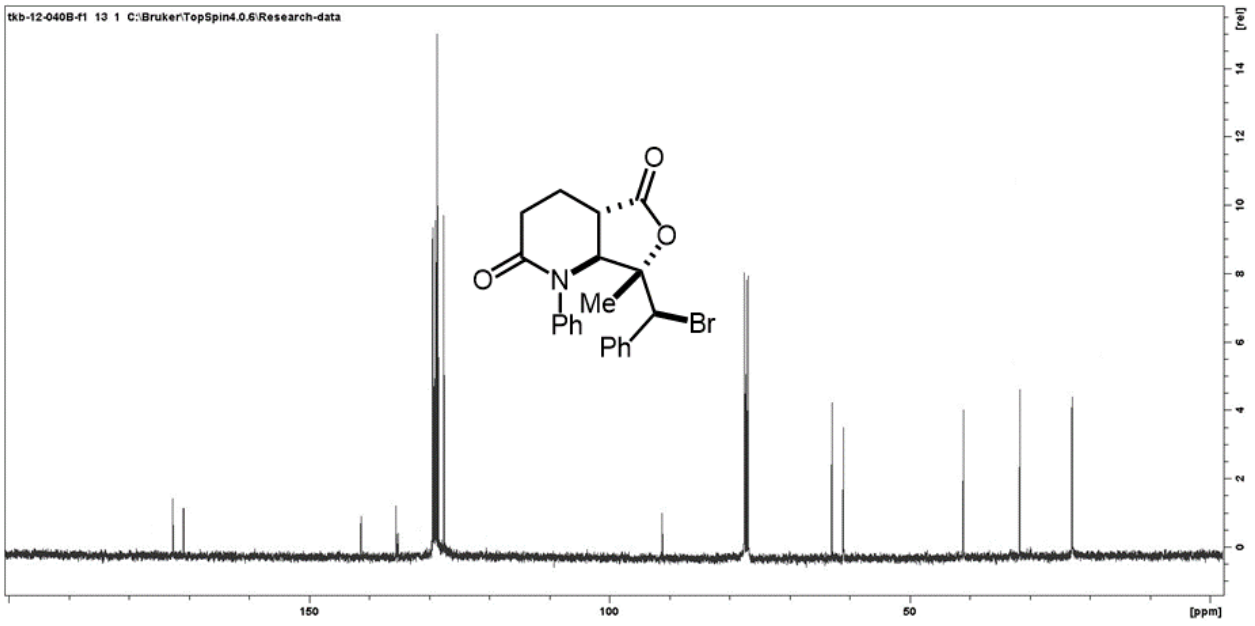
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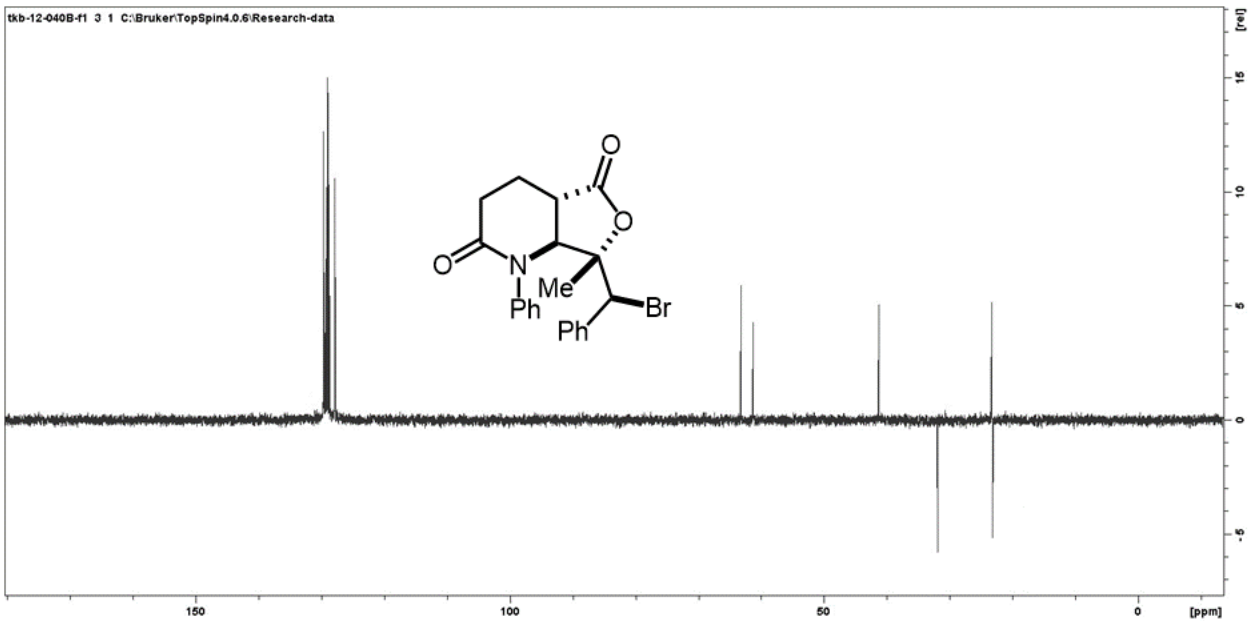
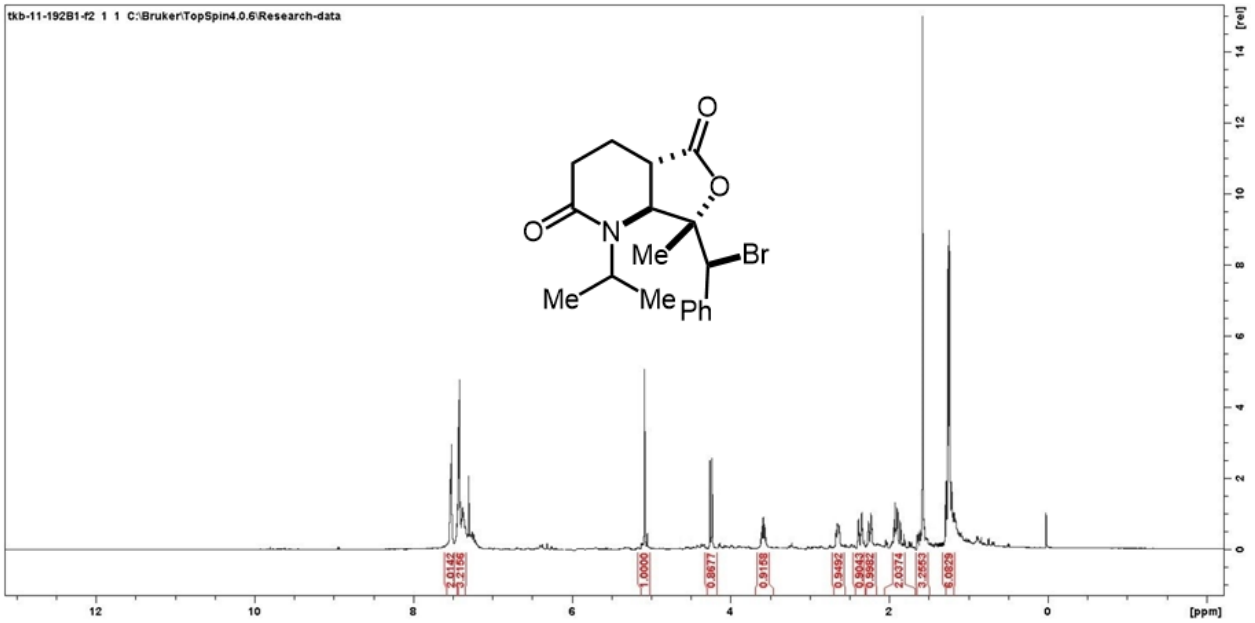
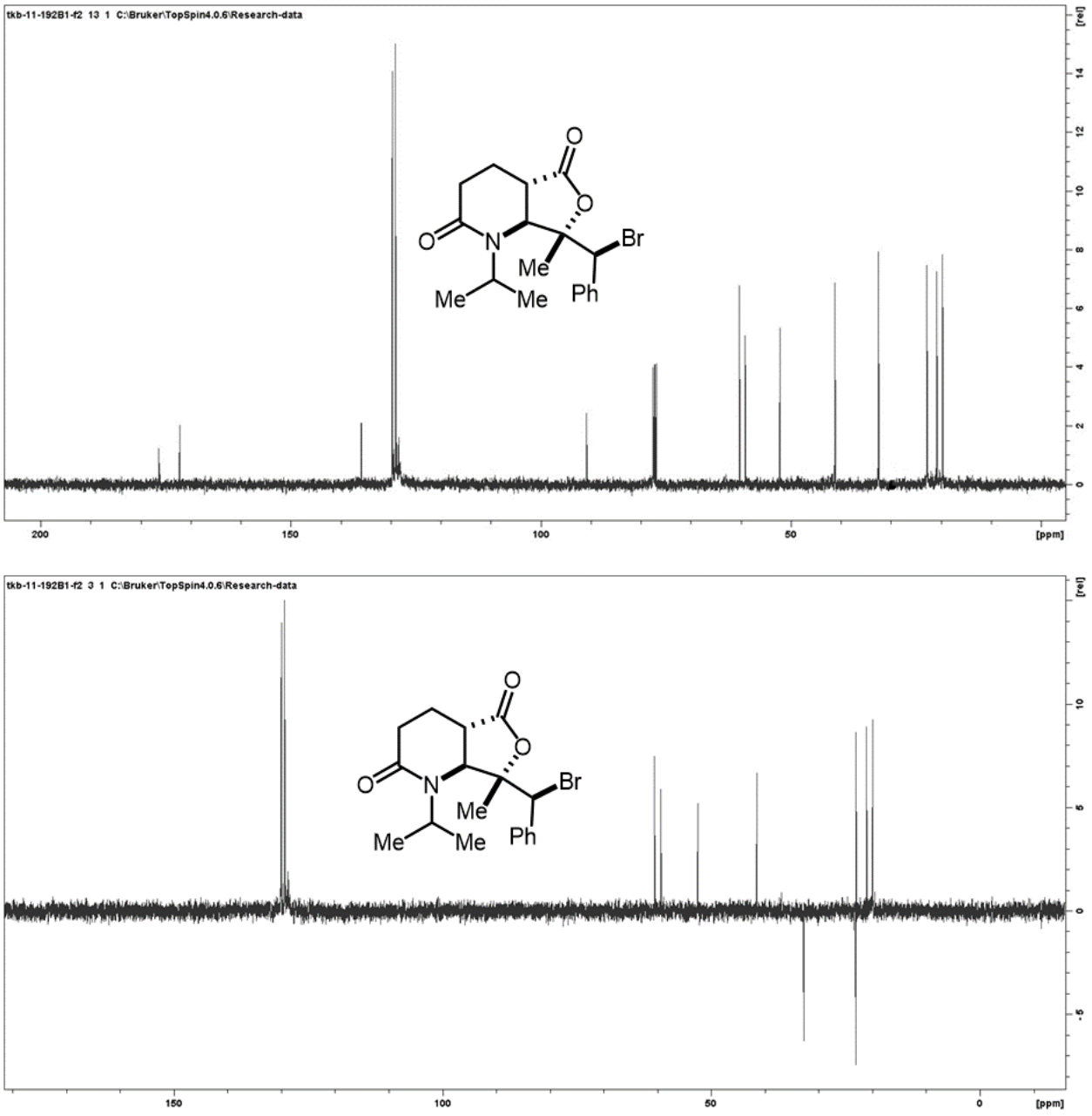


Compound 5d

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Yellowish oil. Yield = 251 mg, 66%, 90:10 dr. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 – 7.28 (m, 5H), 5.11 (s, 1H), 4.39 (d, *J* = 12.2 Hz, 1H), 3.66 – 3.54 (m, 1H), 2.64 (dd, *J* = 16.2, 7.4 Hz, 1H), 2.39 – 2.27 (m, 2H), 1.87 – 1.72 (m, 2H), 1.66 (s, 3H), 1.32 – 1.26 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.9, 173.8, 137.0, 129.4, 129.0, 128.1, 89.6, 61.1, 59.2, 53.4, 46.8, 42.3, 32.3, 22.7, 22.2, 21.0, 19.9. **HRMS-EI^{+}** (*m/z*): calc for $C_{18}H_{22}BrNO_3$ $[M]^+$ 379.0783, found 379.0788.

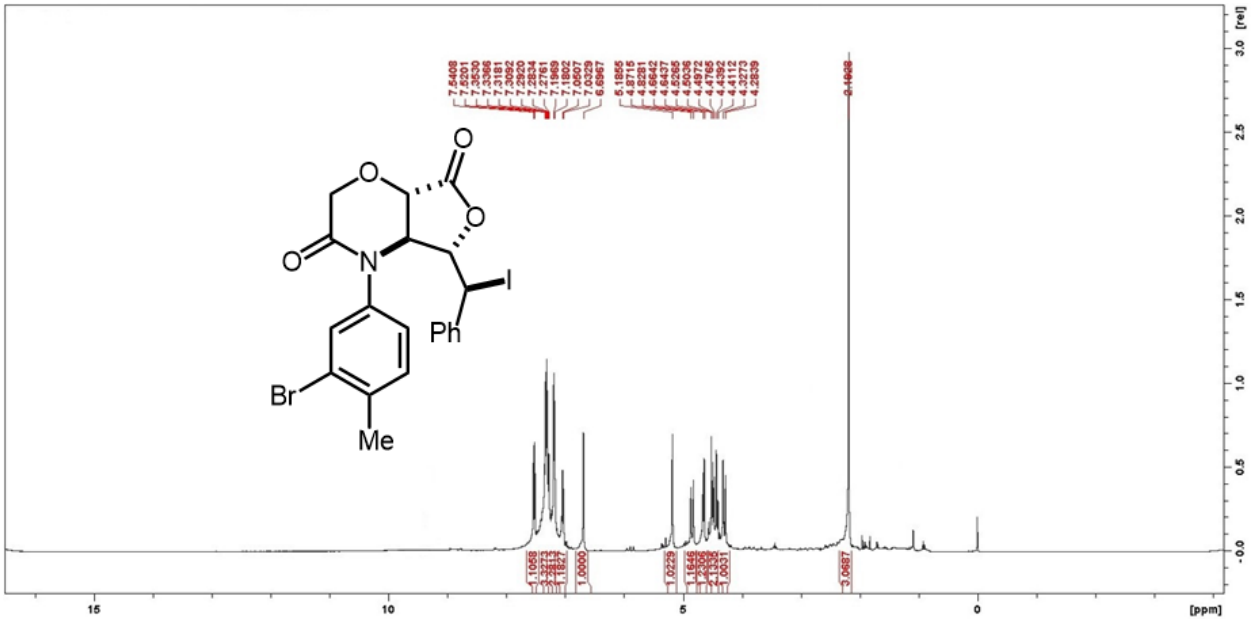


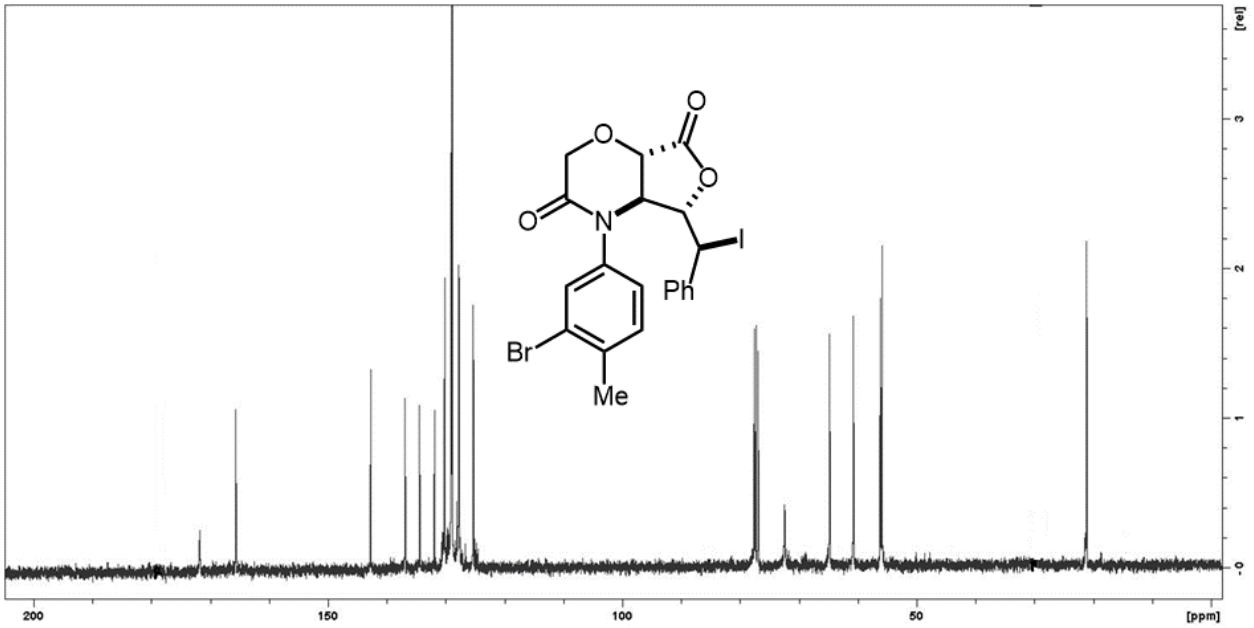


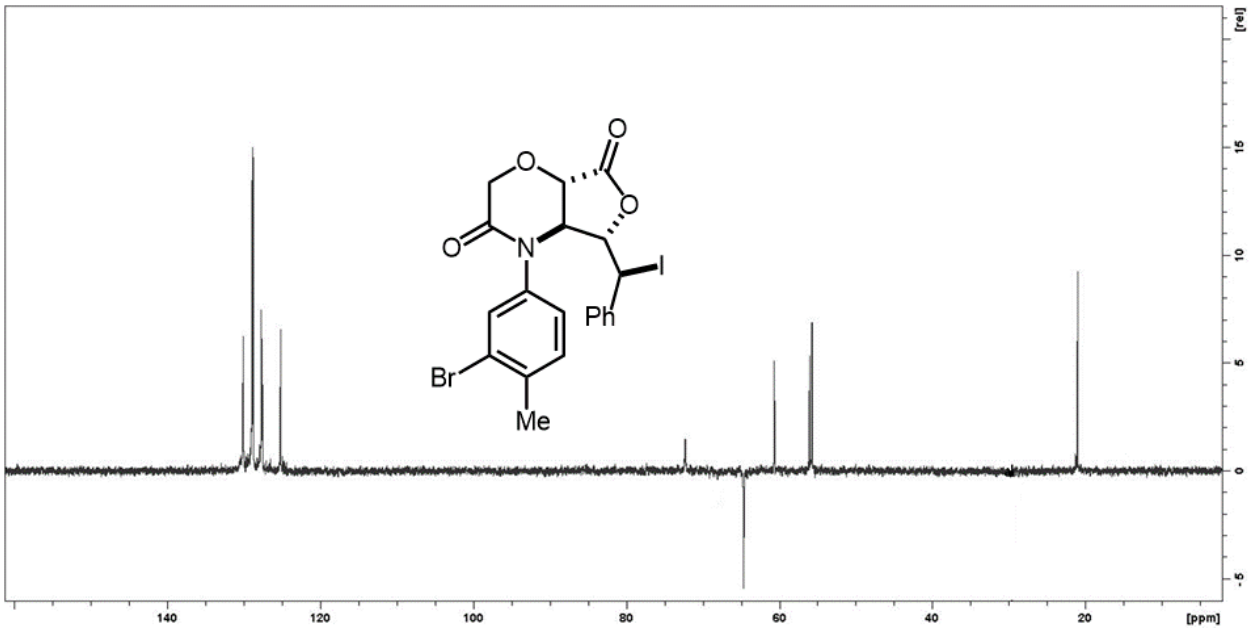
Compound 5e

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Orange oil. Yield = 417.5 mg, 77%, 95:5 dr. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 8.2 Hz, 1H), 7.41 – 7.22 (m, 3H), 7.25 – 7.14 (m, 2H), 7.09 – 7.01 (m, 1H), 6.70 (s, 1H), 5.19 (s, 1H), 4.85 (d, *J* = 17.4 Hz, 1H), 4.65 (d, *J* = 8.2 Hz, 1H), 4.59 – 4.46 (m, 1H), 4.50 – 4.39 (m, 1H), 4.37 – 4.26 (m, 1H), 2.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 165.6, 142.6, 136.8, 134.4, 131.9, 130.1, 129.0, 128.9, 128.8, 127.7,

127.6, 125.2, 72.4, 64.7, 60.7, 56.1, 55.8, 21.1. **HRMS-EI**$^+$ (*m/z*): calc for $C_{20}H_{17}BrINO_4$ $[M]^+$ 540.9386, found 540.9391.







References

(1) H. Braunstein, S. Langevin, M. Khim, J. Adamson, K. Hovenkotter, L. Kotlarz, B. Mansker and T. K. Beng, *Org. Biomol. Chem.*, 2016, **14**, 8864-8872.
(2) J. Garcia, J. Eichwald, J. Zesiger, and T. K. Beng, *RSC Adv.* 2022, **12**, 309−318.
(3) T. K. Beng, J. Fessenden, K. Quigley, J. Eichwald, and J. Zesiger, *New. J. Chem.*, revisions requested.