Supporting Information for:

Stereocontrolled access to δ-lactone-fused-γ-lactams bearing angular benzylic quaternary stereocenters

Timothy K. Beng, Morgan J. Rodriguez, and Claire Borg*

Department of Chemistry, Central Washington University,
Ellensburg, WA 98926, USA
Timothy.beng@cwu.edu

Contents:

1. General Experimental Information and Procedures S2

2. Scheme 1 Results S4

3. References S63

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.

The 1,3-azadienes were prepared as previously reported by us.[1]

General Procedure A: Synthesis and *6-endo*-bromolactonization of lactam acid 3[2]

A 10 mL screw-cap vial was flame-dried, evacuated and flushed with nitrogen. A solution of 1,3-azadiene **2** (1.0 mL, 0.10 M in freshly distilled 2-MeTHF) was added to the vial at room temperature followed by anhydride **1** (176.2 mg, 1 mmol, 1 equiv) and sodium sulfate (0.10 g). The contents were placed in a pre-heated oil bath thermostatted at the desired temperature (usually 23 – 40 ^{o}C). After complete conversion (as judged by TLC and NMR), the mixture/suspension was cooled to room temperature. It was then filtered to remove the sodium sulfate, while washing with THF. The solvents were removed *in vacuo* and the residue was washed several times with petroleum ether, affording the crude acid **3**. The lactam acid was then charged (in air) in an oven-dried 10 mL screw-cap vial equipped with a stir bar and DCM (5 mL) was added. Then, NBS (196 mg, 1.1 mmol, 1.1 equiv) and $Ph_3P{=}S$ (14.7 mg, 5 mol%) were added. The reaction mixture was stirred at room temperature until TLC and GC-MS showed full conversion. Then, the reaction mixture was diluted with DCM (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: Synthesis and *6-endo*-iodolactonization of lactam acid 3

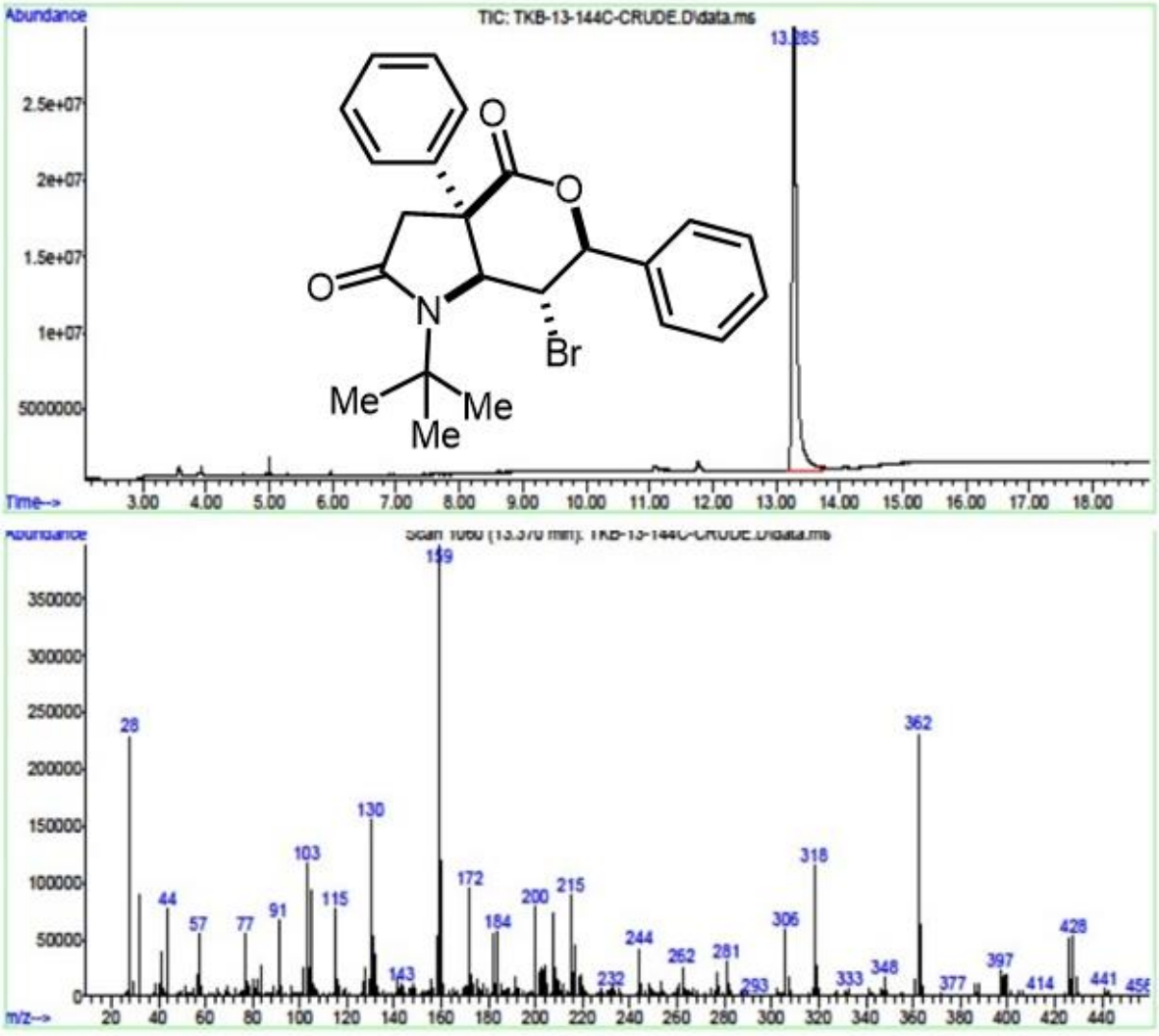
A 10 mL screw-cap vial was flame-dried, evacuated and flushed with nitrogen. A solution of 1,3-azadiene **2** (1.0 mL, 0.10 M in freshly distilled 2-MeTHF) was added to the vial at room temperature followed by anhydride **1** (176.2 mg, 1 mmol, 1 equiv) and sodium sulfate (0.10 g). The contents were placed in a pre-heated oil bath thermostatted at the desired temperature (usually 23 – 40 ^oC). After complete conversion (as judged by TLC and NMR), the mixture/suspension was cooled to room temperature. It was then filtered to remove the sodium sulfate, while washing with THF. The solvents were removed *in vacuo* and the residue was washed several times with petroleum ether, affording the crude acid **3**. The lactam acid was then charged (in air) in an oven-dried 10 mL screw-cap vial equipped with a stir bar and DCM (5 mL) was added. Then, NIS (247.5 mg, 1.1 mmol, 1.1 equiv) and $Ph_3P{=}S$ (14.7 mg, 5 mol%) were added at 0 ^oC. The reaction mixture was stirred at 0 ^oC until TLC and GC-MS showed full conversion. Then, the reaction mixture was 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.

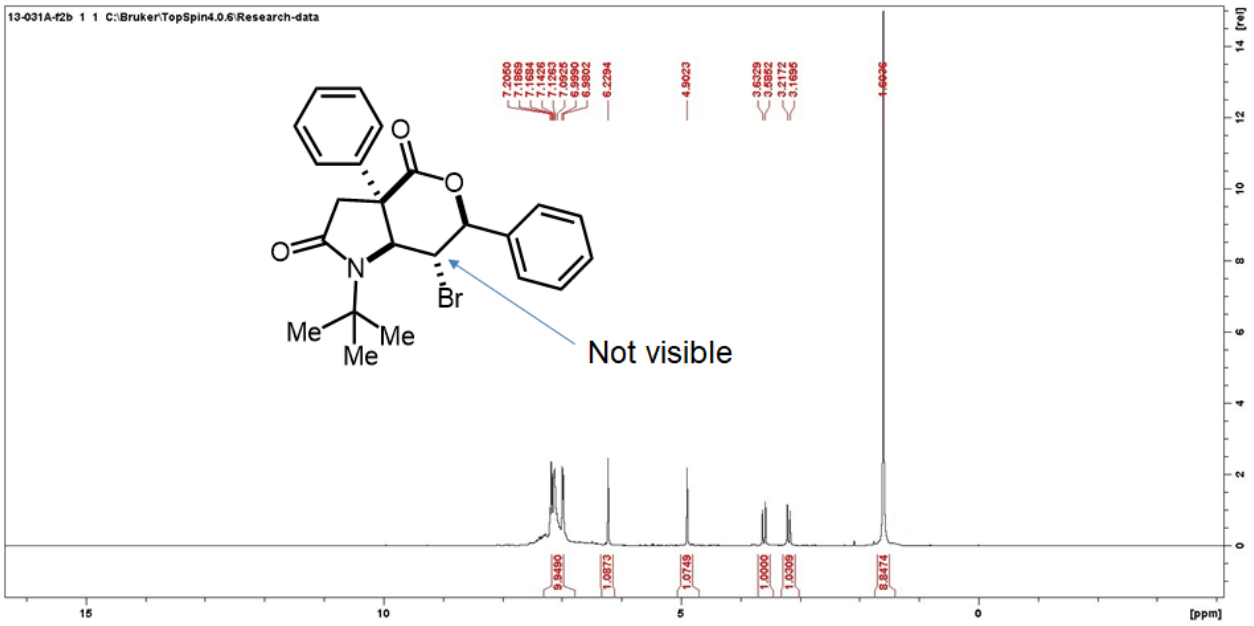
Scheme 1 Results

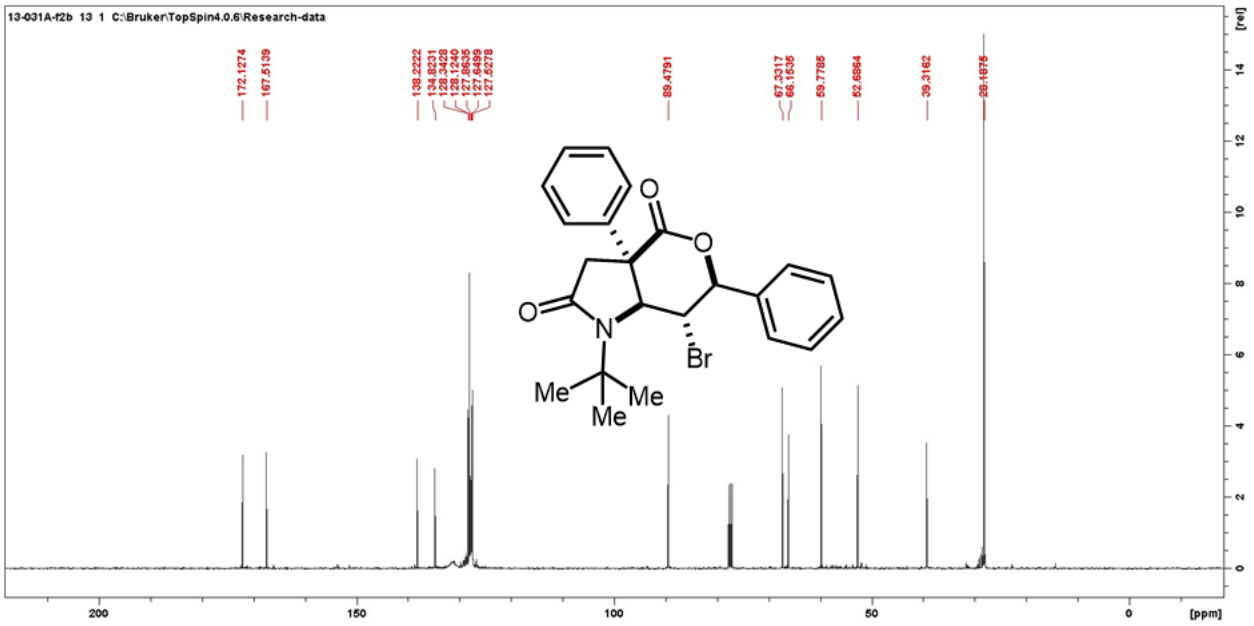
Compound 4a

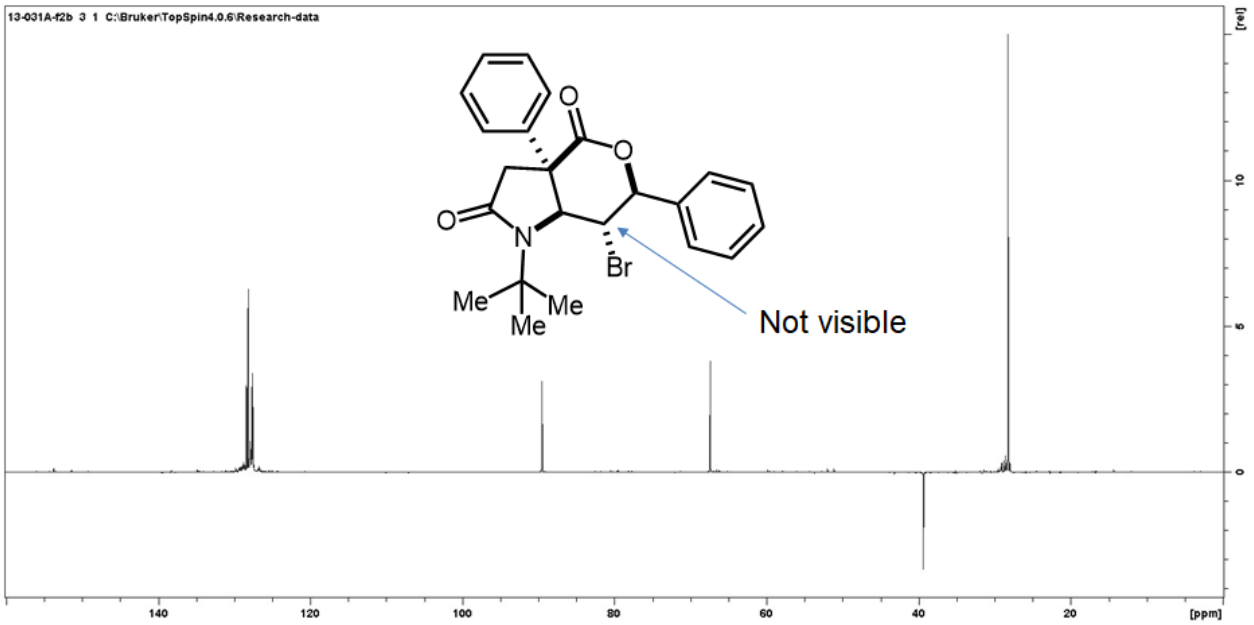
Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Amorphous solid. Yield = 383.7 mg, 87%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 – 6.98 (m, 10H), 6.23 (d, *J* = 1.9 Hz, 1H), 4.90 (s, 1H), 3.60 (d, *J* = 16.4 Hz, 1H), 3.21 (d, *J* = 16.4 Hz, 1H), 1.60 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 167.5, 138.2, 134.8, 128.4, 128.1, 127.9, 127.7, 127.5, 89.5, 67.3, 66.2, 59.8, 52.7, 39.3, 28.2. FTIR (KBr): 2976.1, 2927.2, 1721.8, 1650.2, 1492.0, 1438.5, 1362.3, 1320.5, 1290.1, 1206.3, 1180.3, 1146.7, 1132.4, 995.8, 918.9, 700.1. HRMS calc for $C_{23}H_{24}BrNO_3$ 441.0940, found 441.0946.

```
File       :C:\GCMS\Beng Research\Data\TKB-13-144C-CRUDE.D
Operator   : Beng
Acquired   :  8 Sep 2021  19:36     using AcqMethod 180-280C-20190419.M
Instrument :    Instrument #1
Sample Name:
Misc Info  :
Vial Number: 1
```




13-031A-f2b 1 1 C:\Bruker\TopSpin4.0.6\Research-data
Not visible
[ppm]

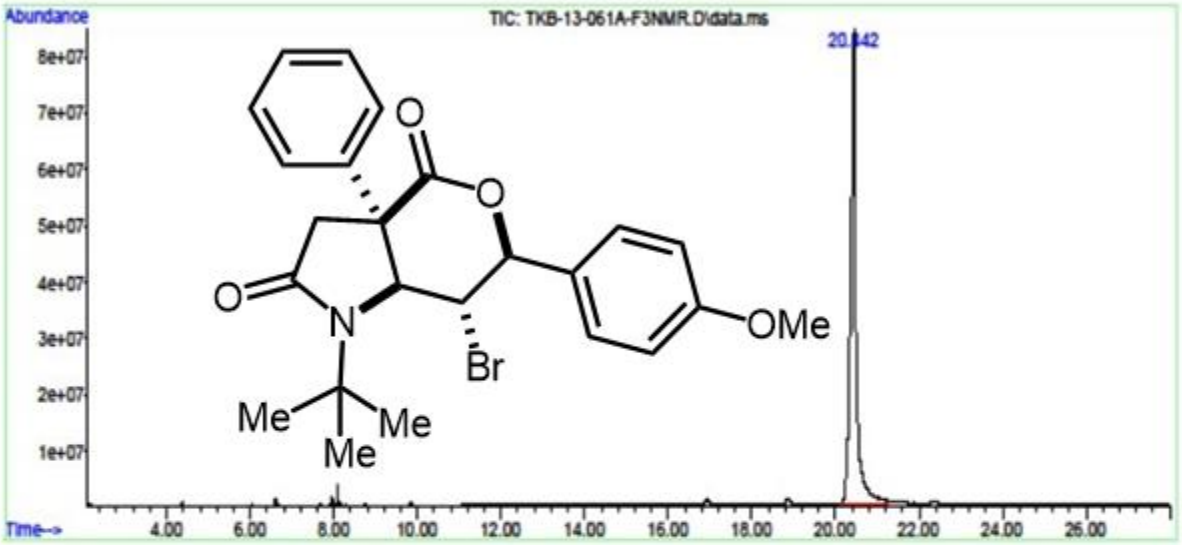

13-031A-f2b 13 1 C:\Bruker\TopSpin4.0.6\Research-data
[ppm]

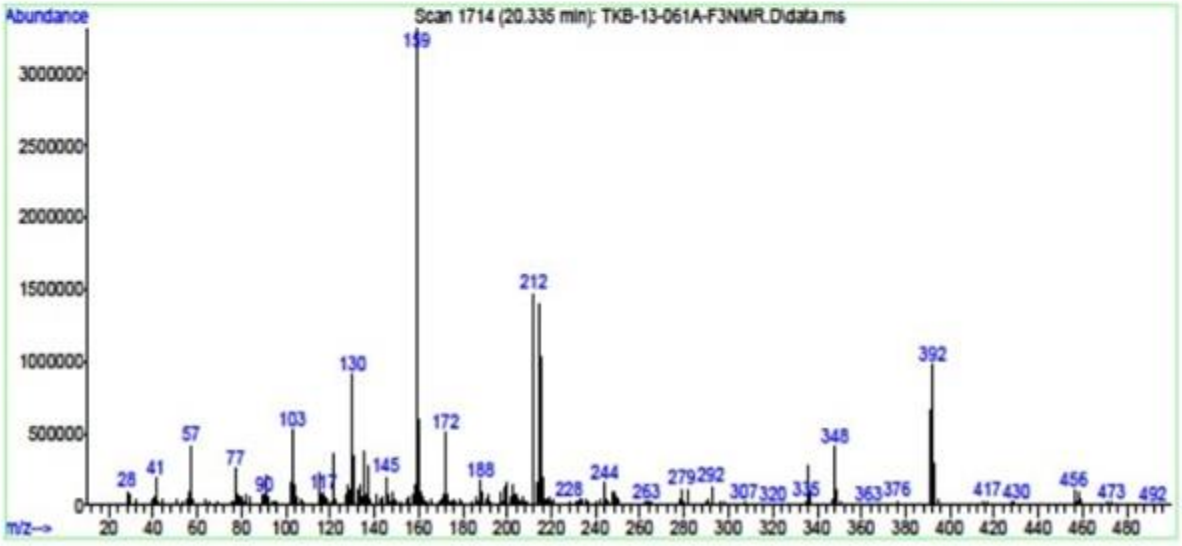


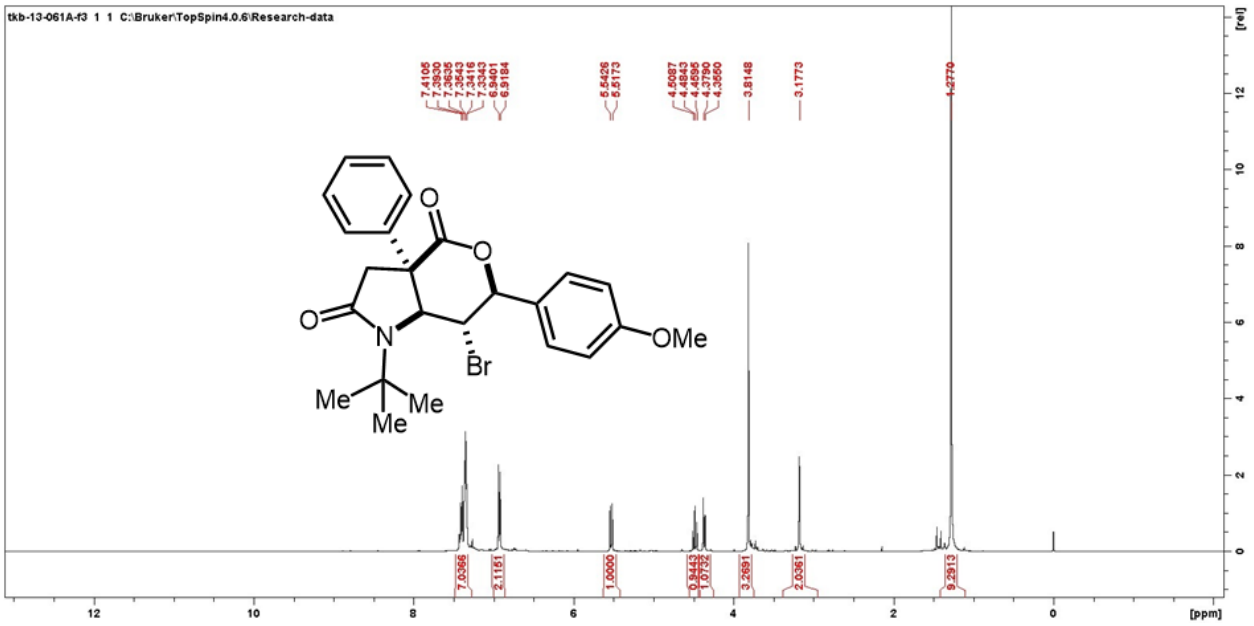
Compound 4b

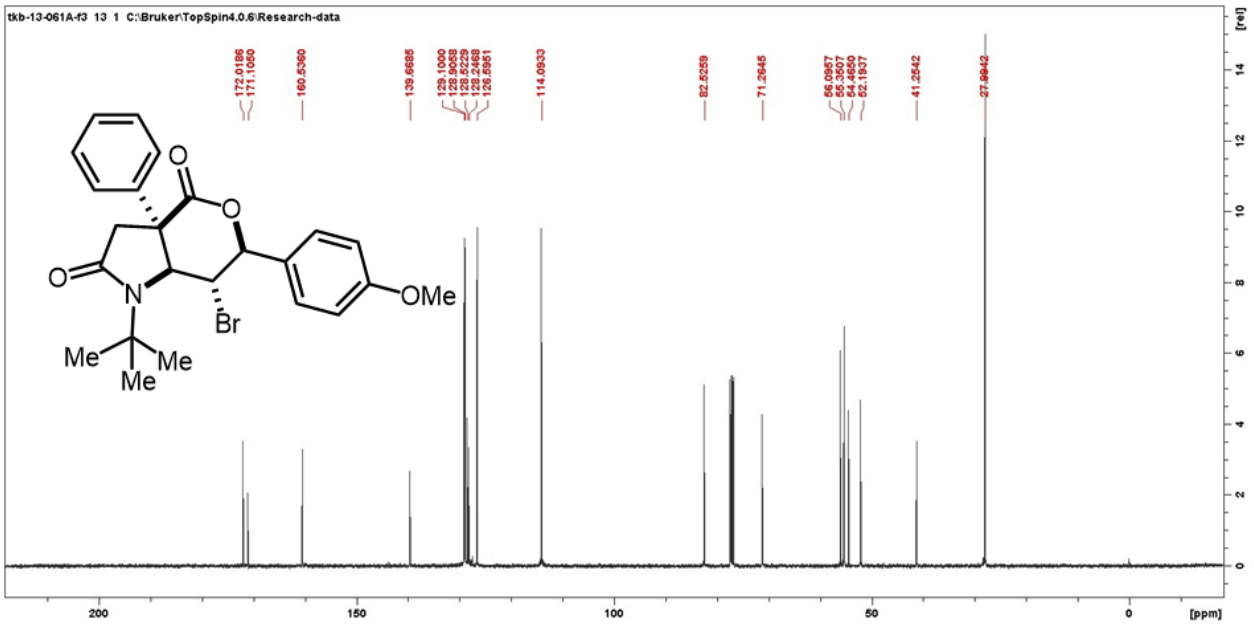
Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Amorphous solid. Yield = 387.1 mg, 82%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.26 (m, 7H), 6.95 (d, *J* = 6.7 Hz, 2H), 5.51 (d, *J* = 9.7 Hz, 1H), 4.42 (t, *J* = 9.6 Hz, 1H), 4.36 (d, *J* = 9.5 Hz, 1H), 3.84 (s, 3H), 3.22 (d, *J* = 17.7 Hz, 1H), 3.12 (d, *J* = 17.7 Hz, 1H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 171.0, 160.6, 139.6, 129.1, 128.8, 128.6, 128.2, 126.6, 114.1, 82.6, 56.2, 55.4, 54.4, 52.2, 41.3, 28.0. FTIR (KBr):2930.9, 1721.7, 1664.2, 1606.9, 1576.9, 1511.8, 1422.4, 1359.3, 1300.0, 1250.9, 1175.8, 1113.2, 1031.2, 996.3, 970.3, 923.7, 826.6, 764.9. HRMS calc for $C_{24}H_{26}BrNO_4$ 471.1045, found 471.1049.

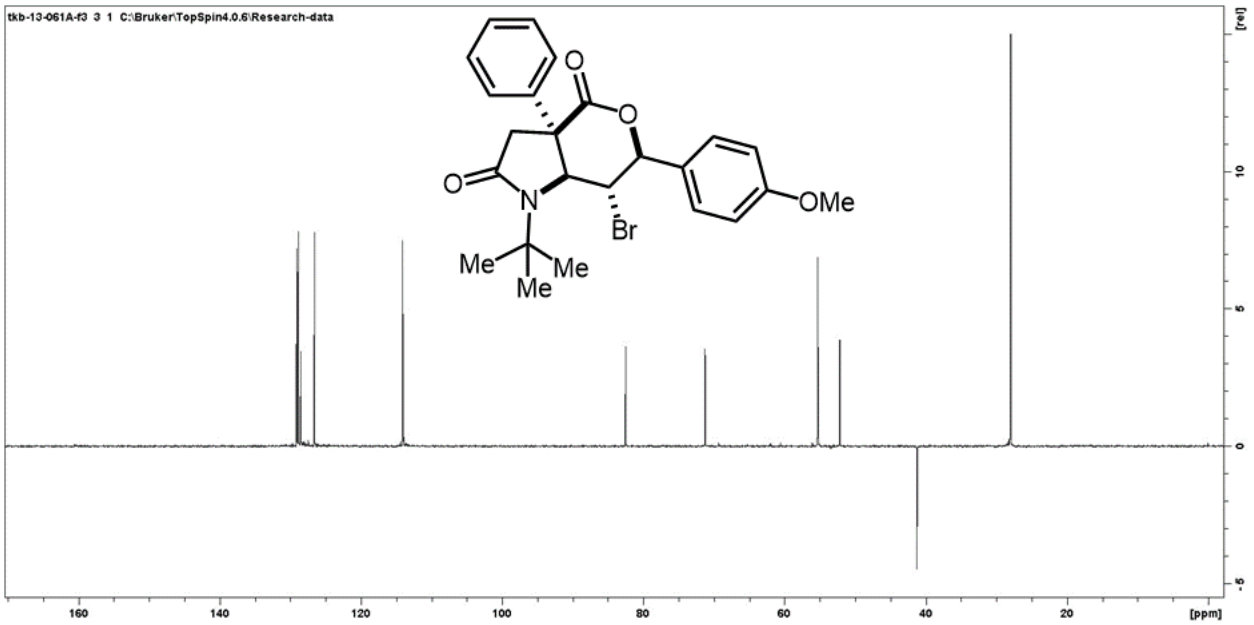
```
File       :C:\GCMS\Beng Research\Data\TKB-13-061A-F3NMR.D
Operator   : Beng
Acquired   : 18 Feb 2021  18:04     using AcqMethod 180-280C-20190419.M
Instrument :    Instrument #1
Sample Name:
Misc Info  :
Vial Number: 1
```

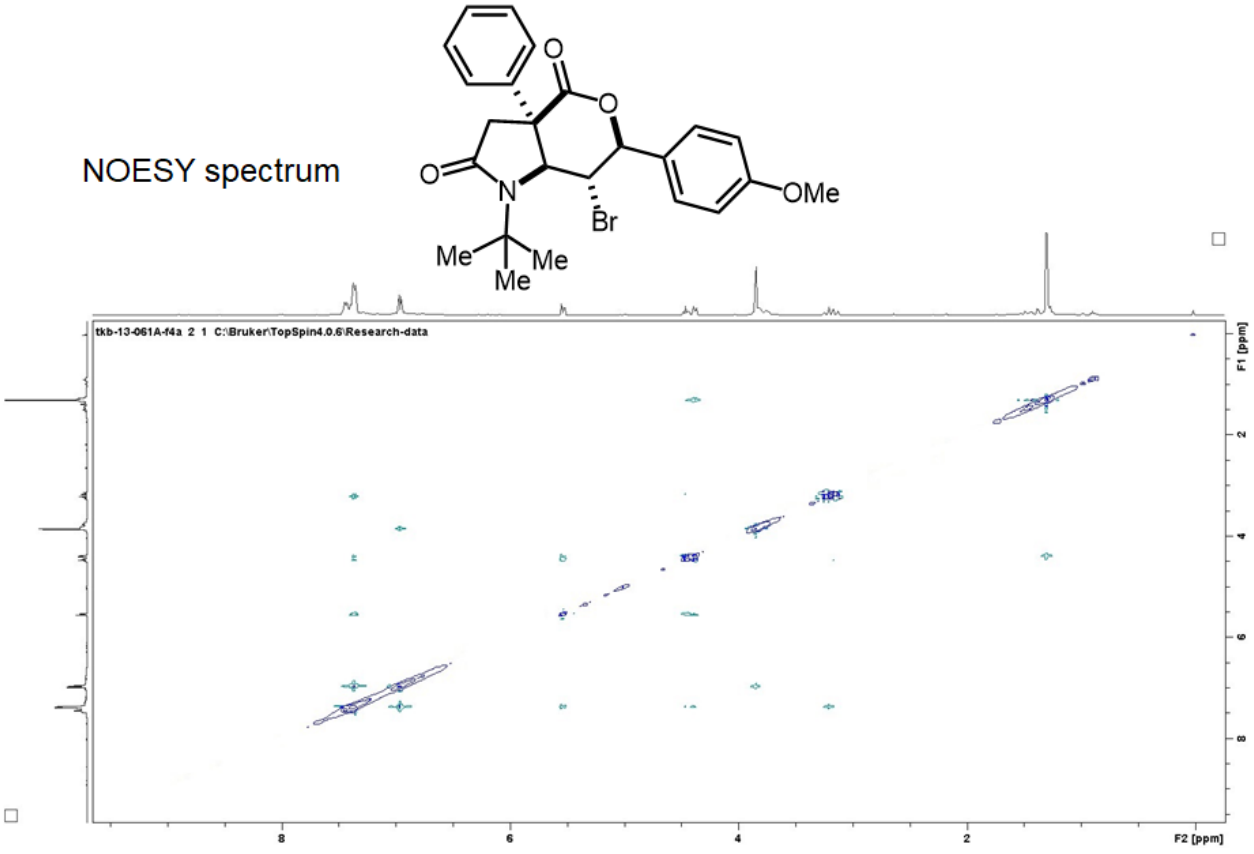





tkb-13-061A-f3 1 1 C:\Bruker\TopSpin4.0.6\Research-data
7.4105
7.3930
7.3635
7.3543
7.3416
7.3343
6.9401
6.9184
5.5426
5.5173
4.5087
4.4843
4.4586
4.3760
4.3560
3.8148
3.1773
1.2770
7.0366
2.1161
1.0000
0.9443
1.0132
3.2691
2.0361
9.2913
O
O
O
N
Br
OMe
Me
Me
Me
12
10
8
6
4
2
0
[ppm]
[rel]

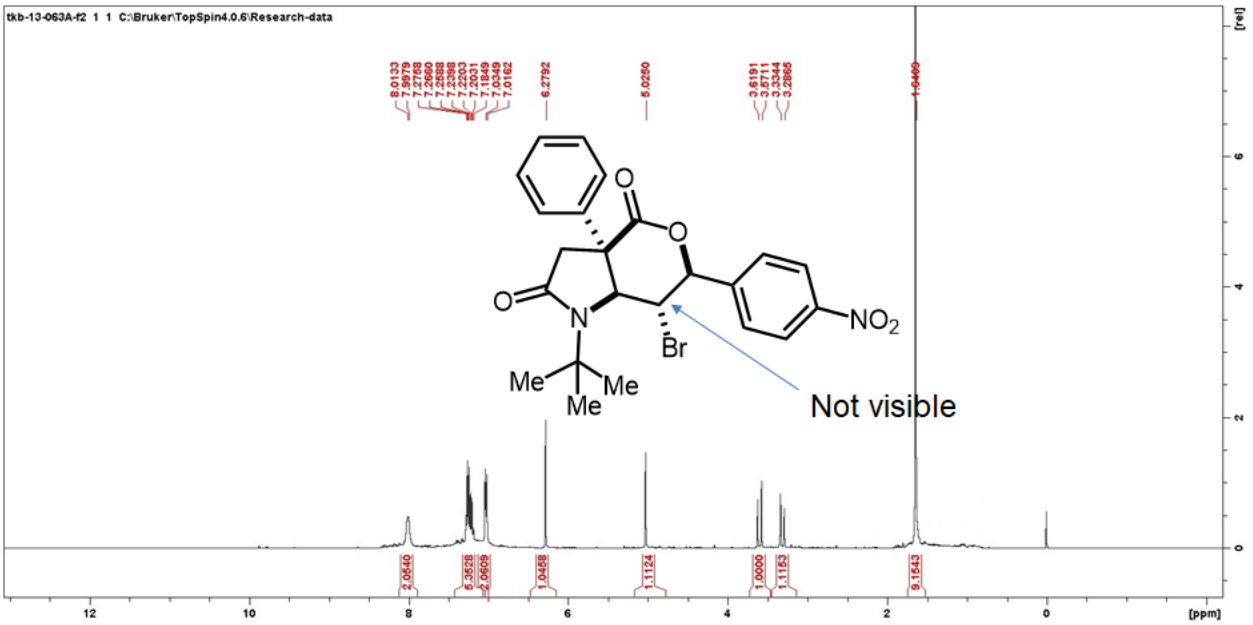

tkb-13-061A-f3 13 1 C:\Bruker\TopSpin4.0.6\Research-data
172.0186
171.1050
160.5360
139.6685
129.1000
128.9058
128.8229
128.2468
126.5951
114.0933
82.5259
71.2645
56.0957
55.3507
54.4850
52.1937
41.2542
27.6842
O
O
O
N
Br
OMe
Me
Me
Me
200
150
100
50
0
[ppm]
[rel]

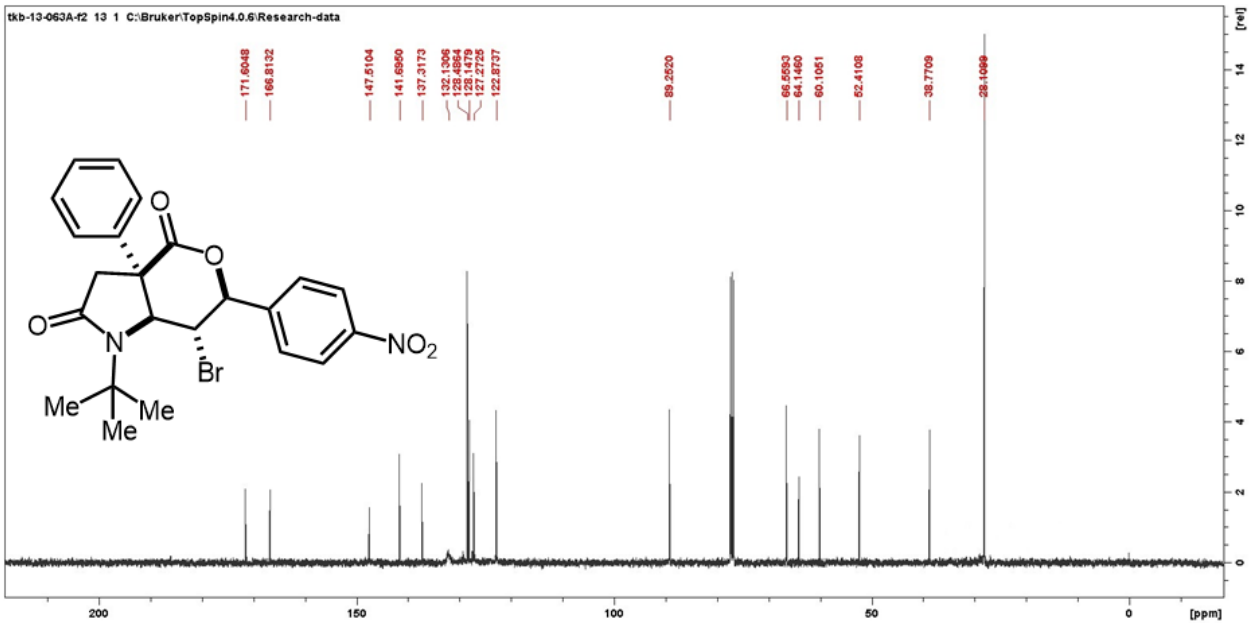

tkb-13-061A-f3 3 1 C:\Bruker\TopSpin4.0.6\Research-data
O
O
O
N
Br
OMe
Me
Me
Me
160
140
120
100
80
60
40
20
[ppm]

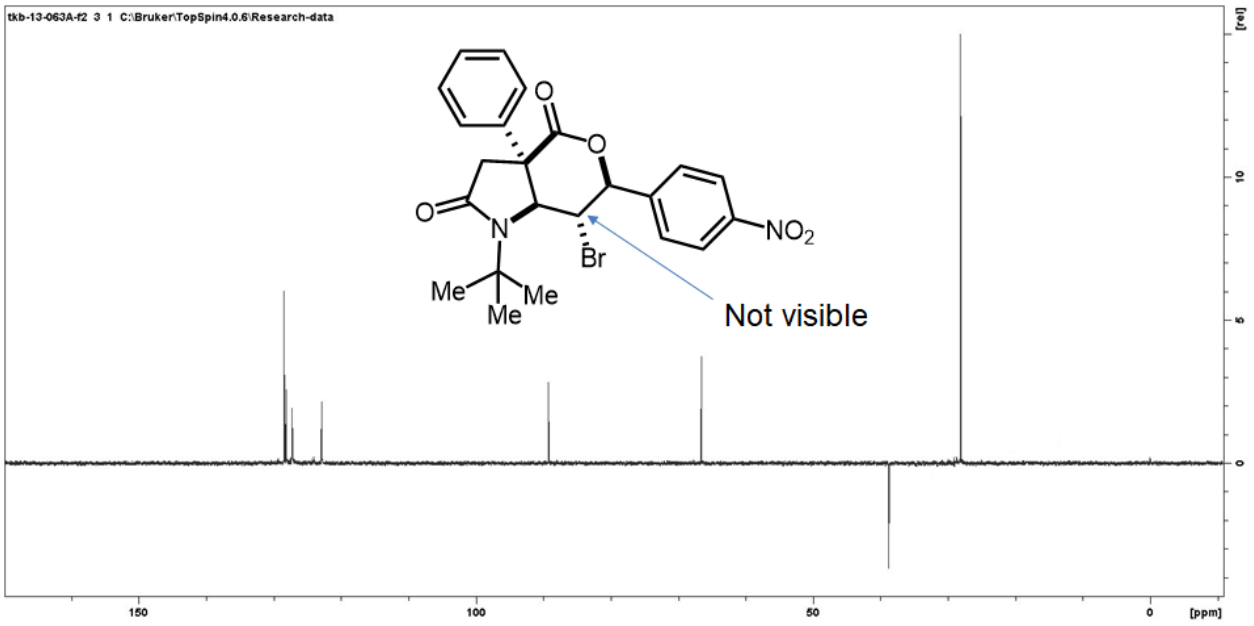

NOESY spectrum
O
O
O
N
Br
OMe
Me
Me
Me
tkb-13-061A-f4a 2 1 C:\Bruker\TopSpin4.0.6\Research-data
F1 [ppm]
F2 [ppm]
8
6
4
2

Compound 4c

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (40:60). Amorphous solid. Yield = 443.2 mg, 91%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (br s, 2H), 7.30 – 7.15 (m, 5H), 7.03 (d, *J* = 7.6 Hz, 2H), 6.28 (s, 1H), 5.03 (s, 1H), 3.59 (d, *J* = 19.2 Hz, 1H), 3.31 (d, *J* = 19.2 Hz, 1H), 1.64 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 166.8, 147.5, 141.7, 137.3, 128.5, 128.2, 127.3, 122.9, 89.3, 66.6, 64.2, 60.1, 52.4, 38.8, 28.1. FTIR (KBr): 2976.0, 1721.7, 1650.1, 1492.0, 1438.4, 1362.2, 1320.5, 1290.1, 1206.3, 1180.3, 1146.7, 1132.1, 995.8, 918.8, 700.1. HRMS calc for $C_{23}H_{23}BrN_2O_5$ 486.0790, found 486.0797.





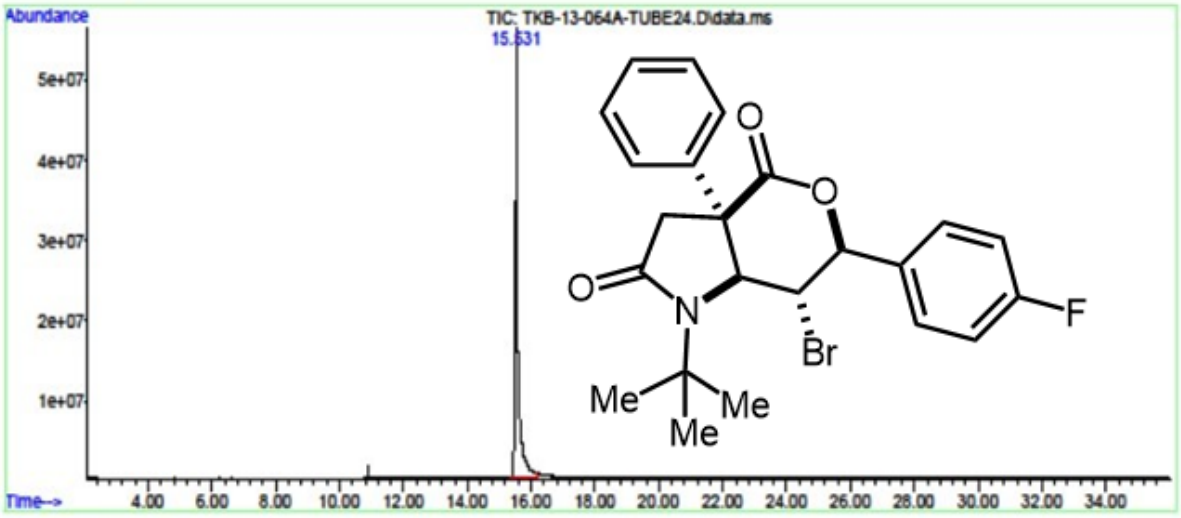


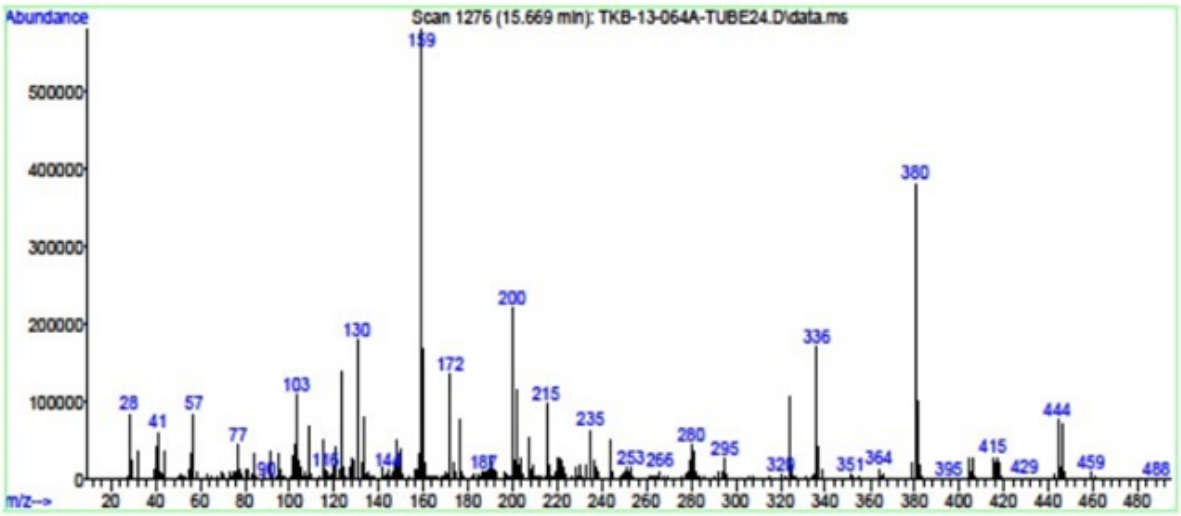
Compound 4d

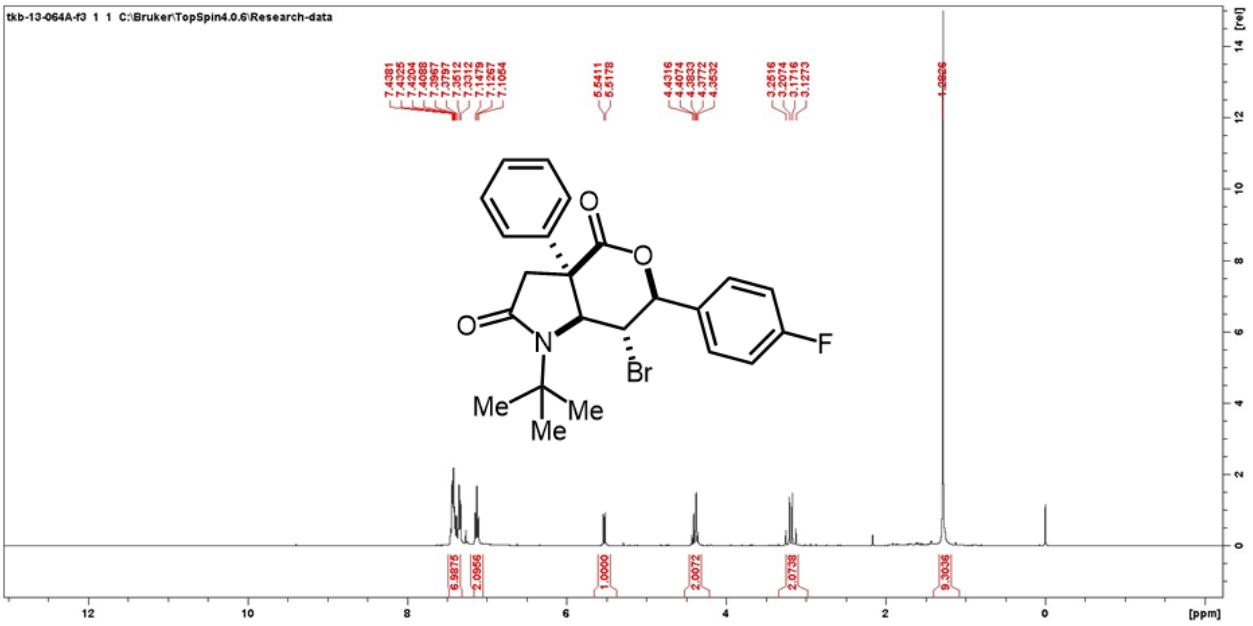
Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 404.8 mg, 88%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.33 (m, 7H), 7.13 (t, J = 8.4 Hz, 2H), 5.53 (d, J = 9.3 Hz, 1H), 4.45 – 4.33 (m, 2H), 3.23 (d, J = 17.7 Hz, 1H), 3.15 (d, J = 17.7 Hz, 1H), 1.28 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 170.8, 164.6, 162.1, 139.4, 132.1, 132.0, 129.6, 129.5, 129.2, 128.7,

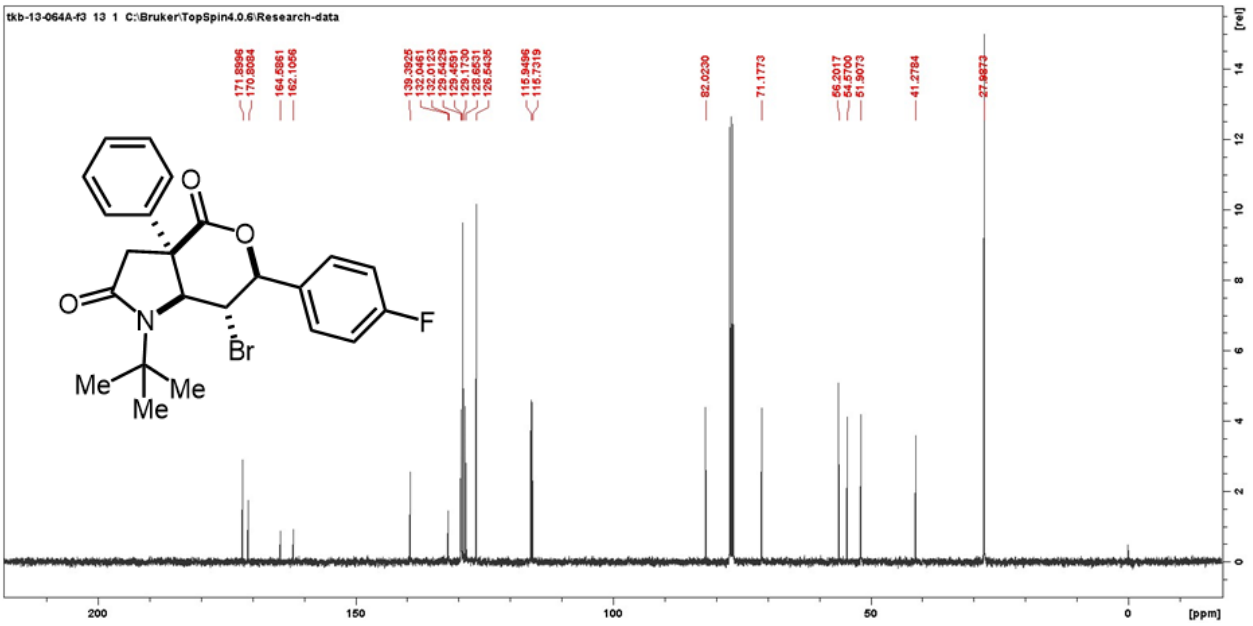
126.6, 116.0, 115.7, 82.0, 71.2, 56.2, 54.6, 51.9, 41.3, 28.0. FTIR (KBr): 2932.4, 1721.5, 1666.3, 1606.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1135.9, 1031.8, 995.8, 831.0, 750.2, 694.7. HRMS calc for $C_{23}H_{23}BrFNO_3$ 459.0845, found 459.0840.

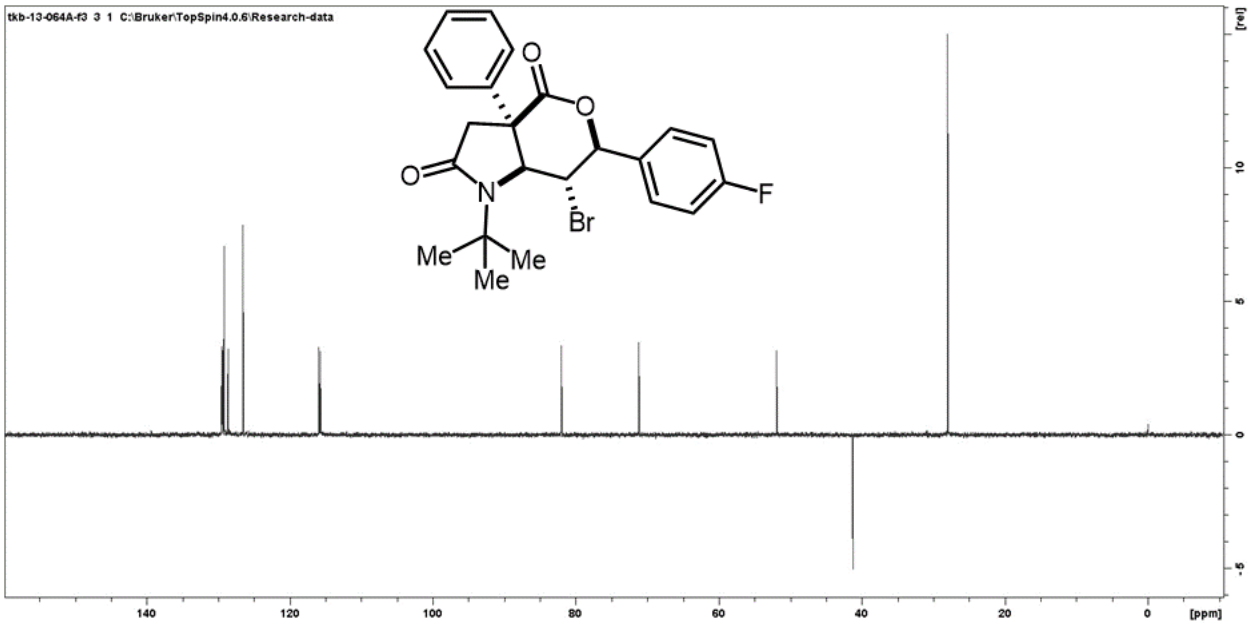
```
File       :C:\GCMS\Beng Research\Data\TKB-13-064A-TUBE24.D
Operator   : Beng
Acquired   :  1 Mar 2021  18:43     using AcqMethod 180-280C-20190419.M
Instrument :    Instrument #1
Sample Name:
Misc Info  :
Vial Number: 1
```

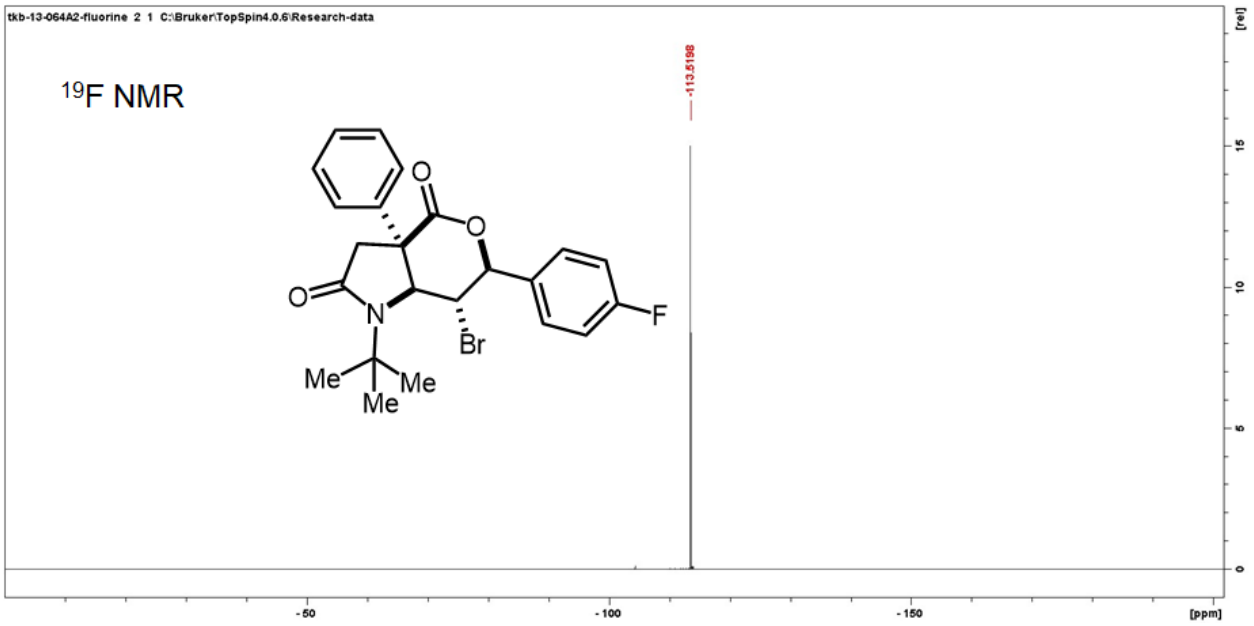





tkb-13-064A-f3 1 1 C:\Bruker\TopSpin4.0.6\Research-data
7.4381
7.4325
7.4094
7.4088
7.3967
7.3797
7.3512
7.3312
7.1479
7.1267
7.1064
5.5411
5.5178
4.4316
4.4074
4.3953
4.3772
4.3532
3.2516
3.2074
3.1716
3.1273
1.0826
6.9675
2.0956
1.0000
2.0072
2.0738
9.3036
O
O
O
N
F
Br
Me
Me
Me
12
10
8
6
4
2
0
[ppm]


tkb-13-064A-f3 13 1 C:\Bruker\TopSpin4.0.6\Research-data
171.8996
170.8084
164.5861
162.1056
139.3925
132.0461
132.0123
129.5429
129.4451
129.1730
128.6531
126.5436
115.9496
115.7319
82.0230
71.1773
56.2017
54.5700
51.9073
41.2784
27.6873
O
O
O
N
F
Br
Me
Me
Me
200
150
100
50
0
[ppm]



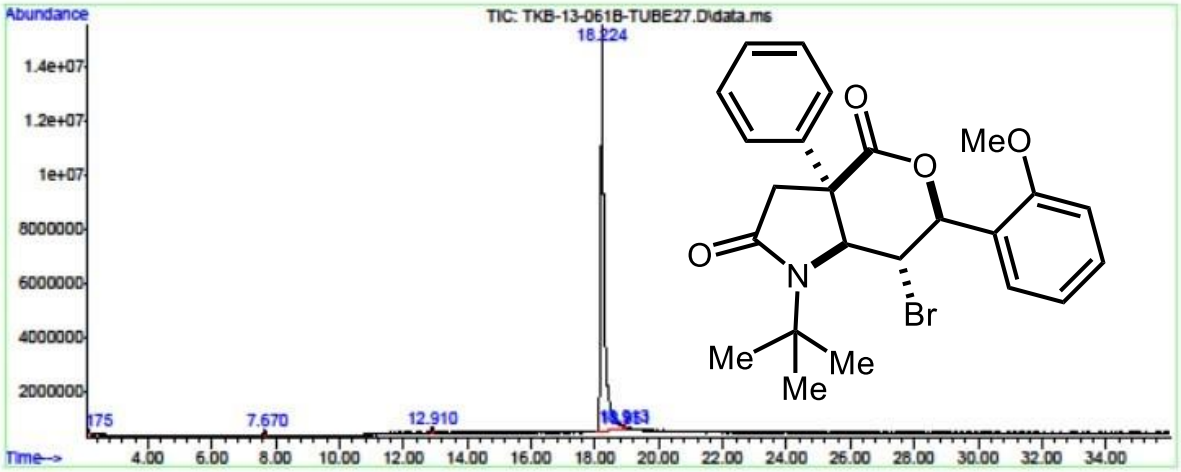


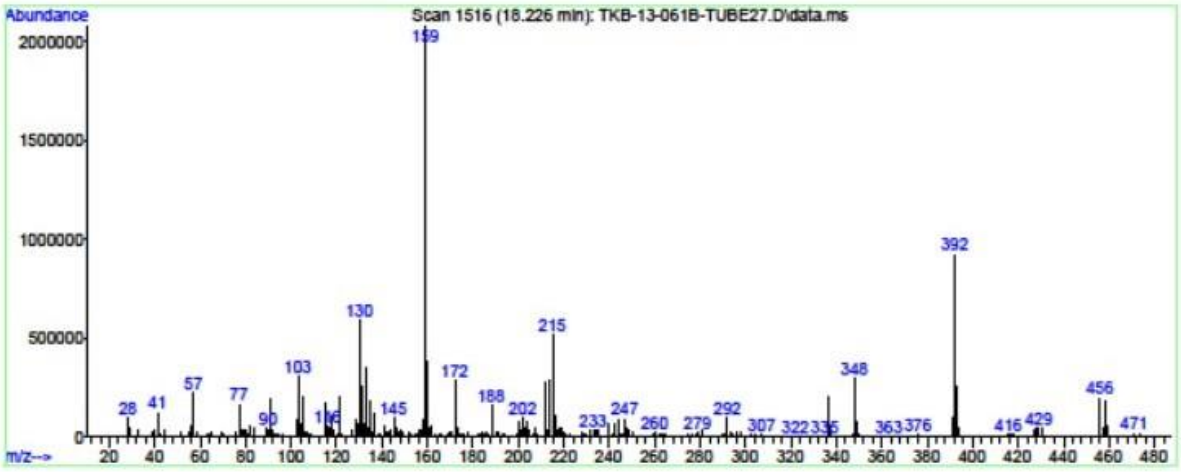
Compound 4e

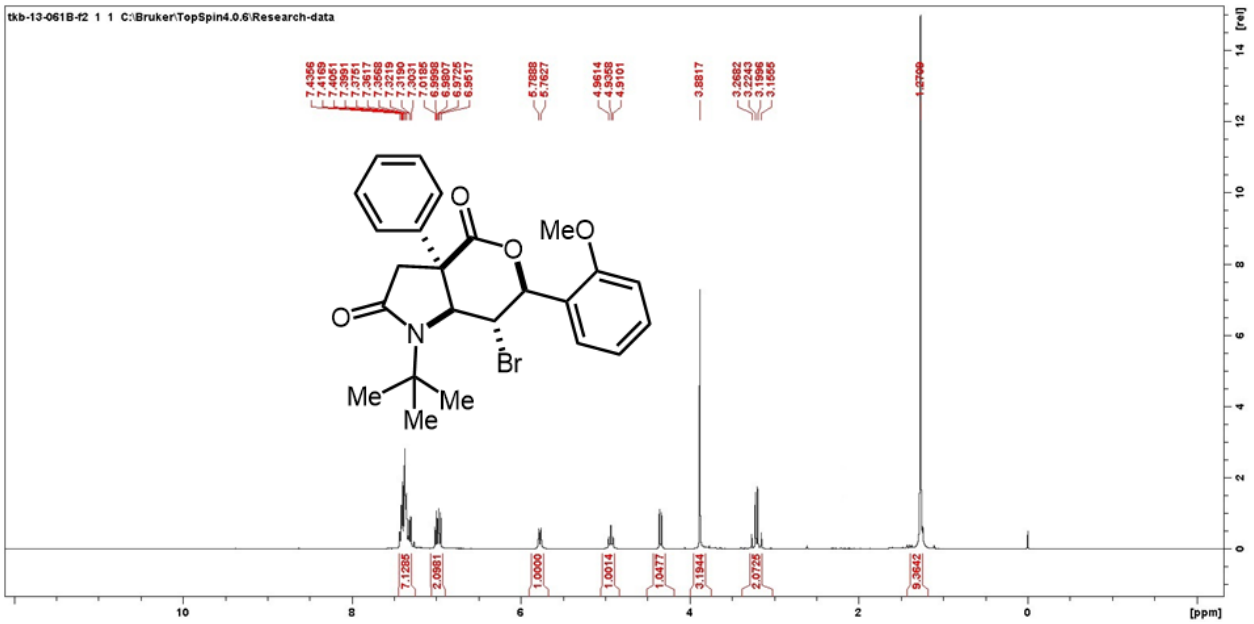
Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Amorphous solid. Yield = 358.7 mg, 76%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.24 (m, 7H), 7.04 – 6.93 (m, 2H), 5.78 (d, J = 10.4 Hz, 1H), 4.94 (t, J = 10.3 Hz, 1H), 4.35 (d, J = 10.1 Hz, 1H), 3.88 (s, 3H), 3.25 (d, J = 17.6 Hz, 1H), 3.18 (d, J = 17.6 Hz, 1H), 1.27 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2, 171.2, 157.5, 139.9, 131.1, 129.1, 128.5, 126.5, 124.0, 120.7, 111.6, 80.8, 70.9, 56.0, 55.9, 54.6, 50.2 40.9, 28.0. FTIR

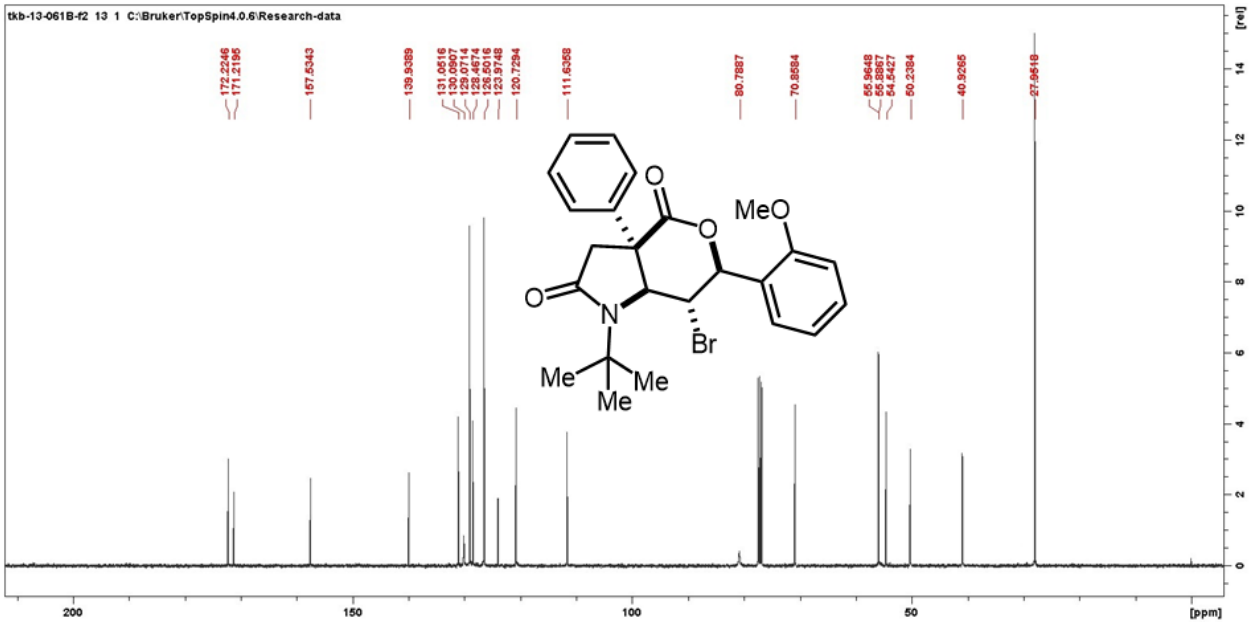
(KBr): 2932.5, 1721.4, 1665.4, 1607.2, 1511.1, 1431.8, 1414.7, 1344.9, 1298.4, 1245.6, 1179.4, 1135.3, 1031.8, 996.7, 921.8, 832.1, 701.6. HRMS calc for $C_{24}H_{26}BrNO_4$ 471.1045, found 471.1049.

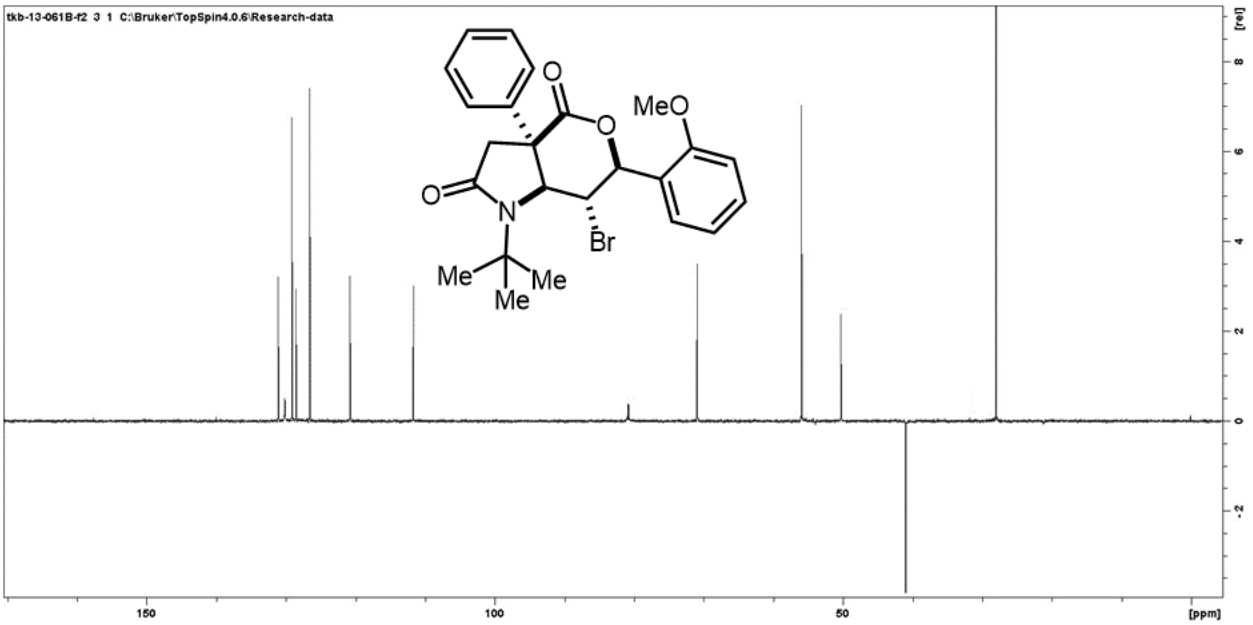
```
File       :C:\GCMS\Beng Research\Data\TKB-13-061B-TUBE27.D
Operator   : Beng
Acquired   : 20 Feb 2021  11:08     using AcqMethod 180-280C-20190419.M
Instrument :    Instrument #1
Sample Name:
Misc Info  :
Vial Number: 1
```





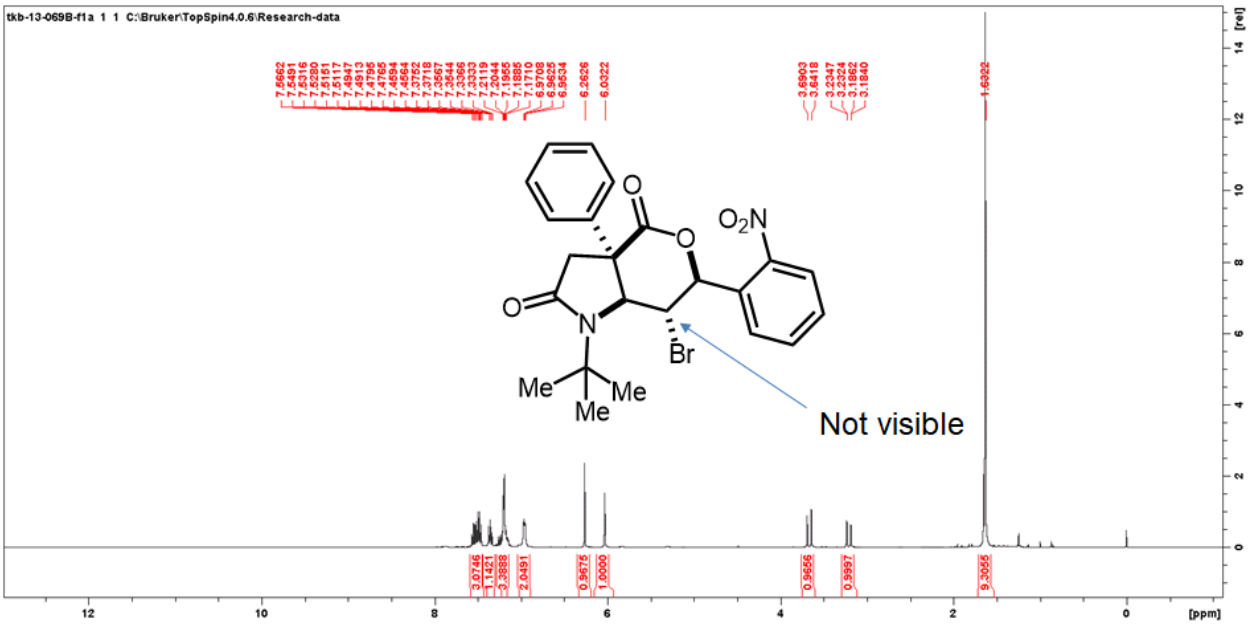

tkb-13-061B-f2 1 1 C:\Bruker\TopSpin4.0.6\Research-data
MeO
O
O
N
Br
Me
Me
Me
[ppm]

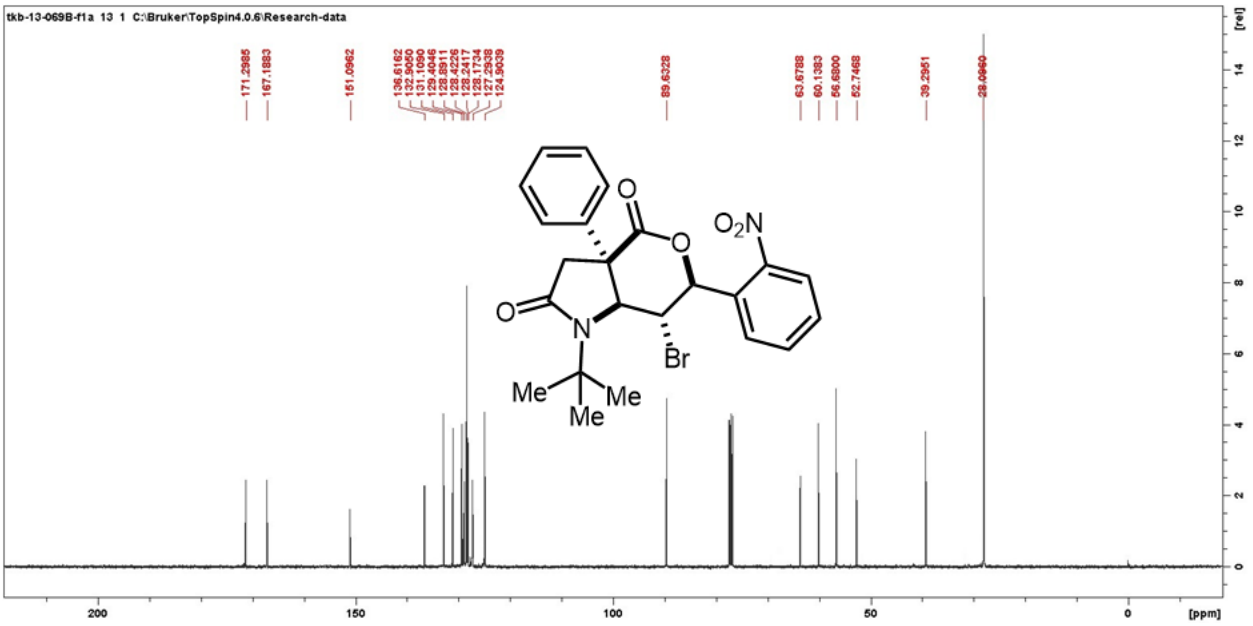

tkb-13-061B-f2 13 1 C:\Bruker\TopSpin4.0.6\Research-data
MeO
O
O
N
Br
Me
Me
Me
[ppm]

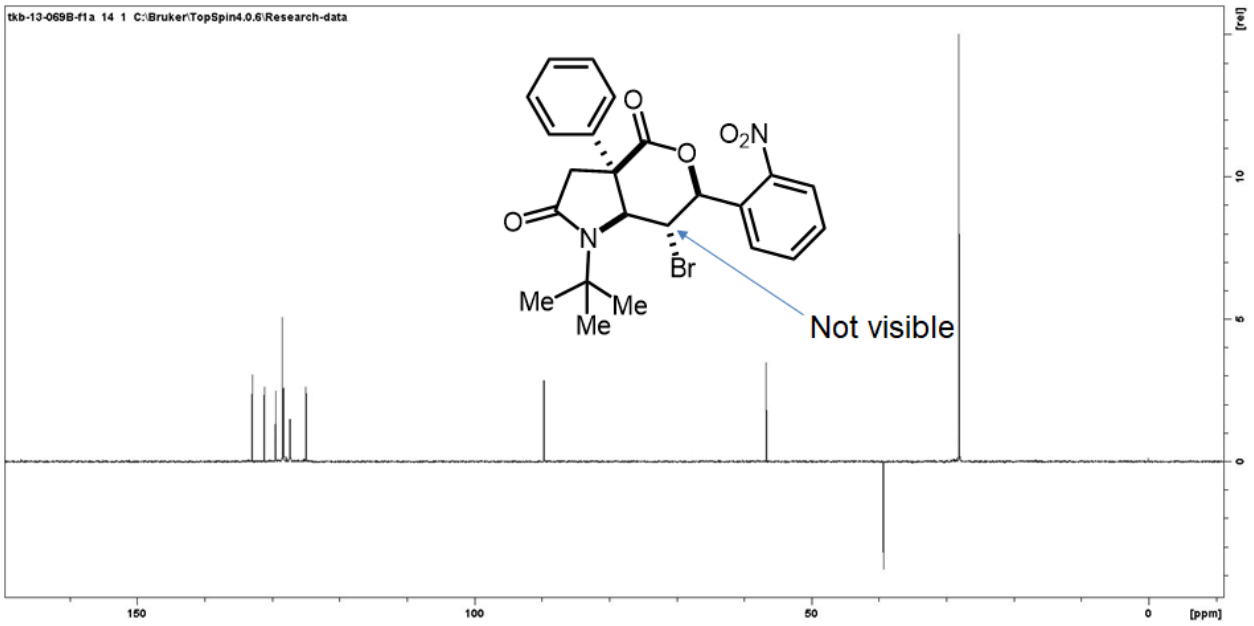


Compound 4f

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Amorphous solid. Yield = 418 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.45 (m, 3H), 7.37 – 7.33 (m, 1H), 7.21 – 7.17 (m, 3H), 6.96 (dt, *J* = 6.1, 3.4 Hz, 2H), 6.26 (s, 1H), 6.03 (d, *J* = 1.1 Hz, 1H), 3.67 (d, *J* = 17.3 Hz, 1H), 3.20 (d, *J* = 17.3 Hz, 1H), 1.63 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 167.2, 151.1, 136.6, 132.9, 131.1, 129.4, 128.9, 128.4, 128.2, 127.3, 124.9, 89.6, 63.7, 60.1, 56.7, 52.8, 39.3, 28.1. FTIR (KBr): 2972.8, 1728.5, 1669.3, 1606.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1135.9, 1031.8, 992.8, 833.0, 755.2. HRMS calc for $C_{23}H_{23}BrN_2O_5$ 486.0790, found 486.0797.

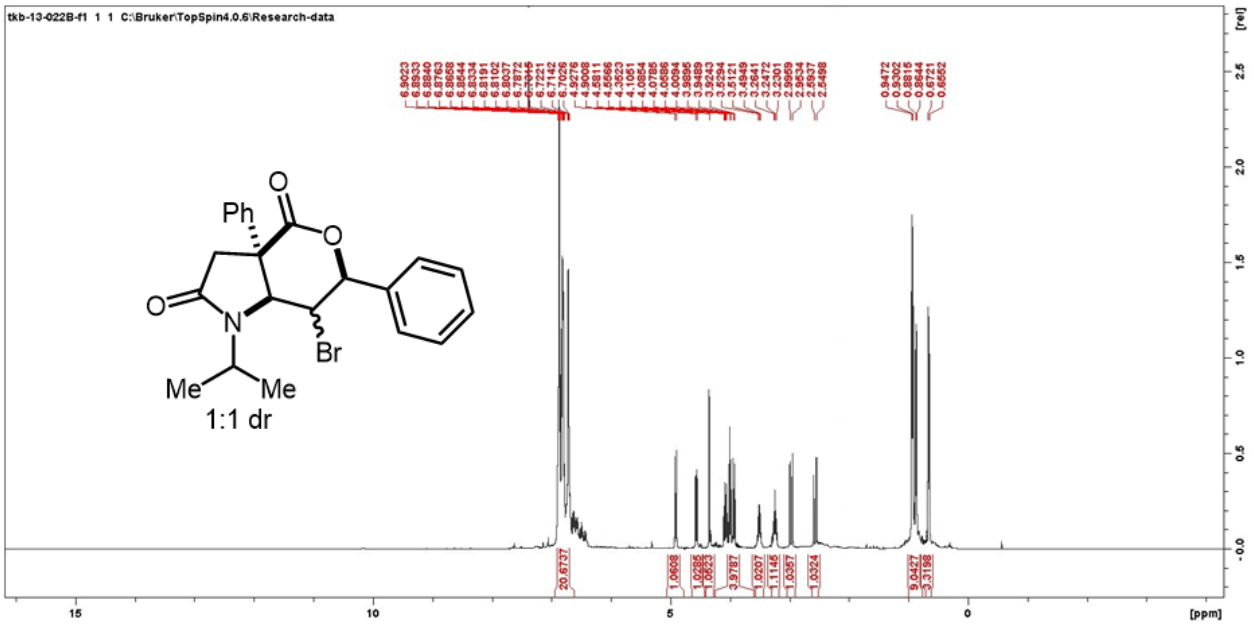

tkb-13-069B-f1a 1 1 C:\Bruker\TopSpin4.0.6\Research-data
Not visible
[ppm]

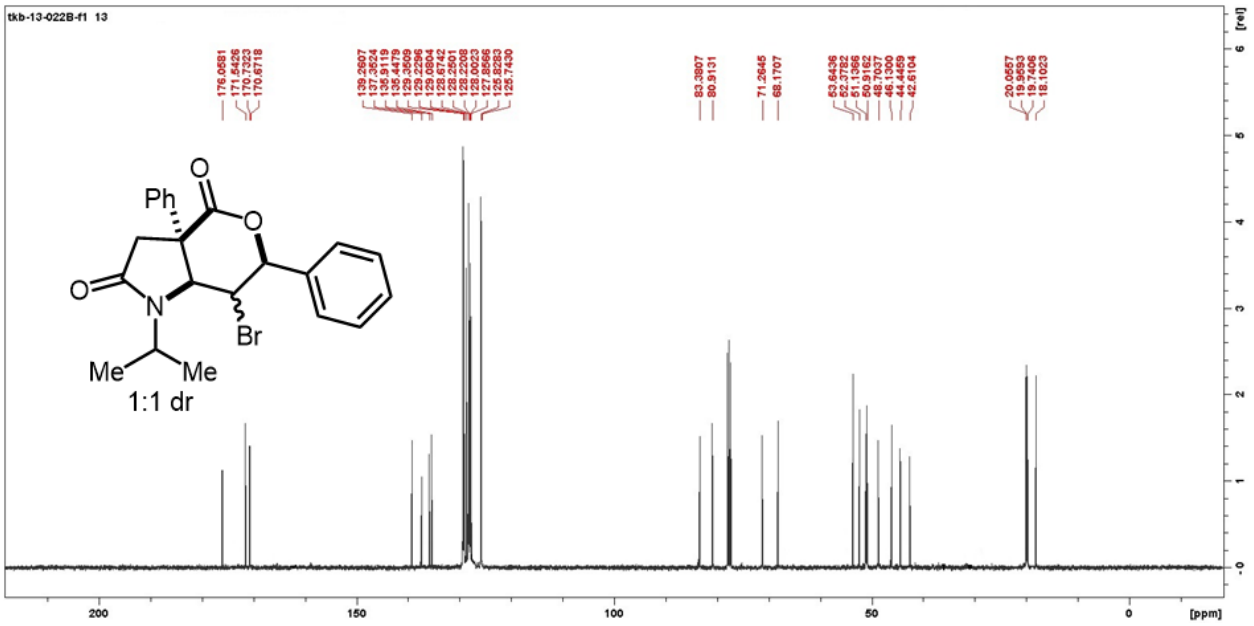

tkb-13-069B-f1a 13 1 C:\Bruker\TopSpin4.0.6\Research-data
[ppm]

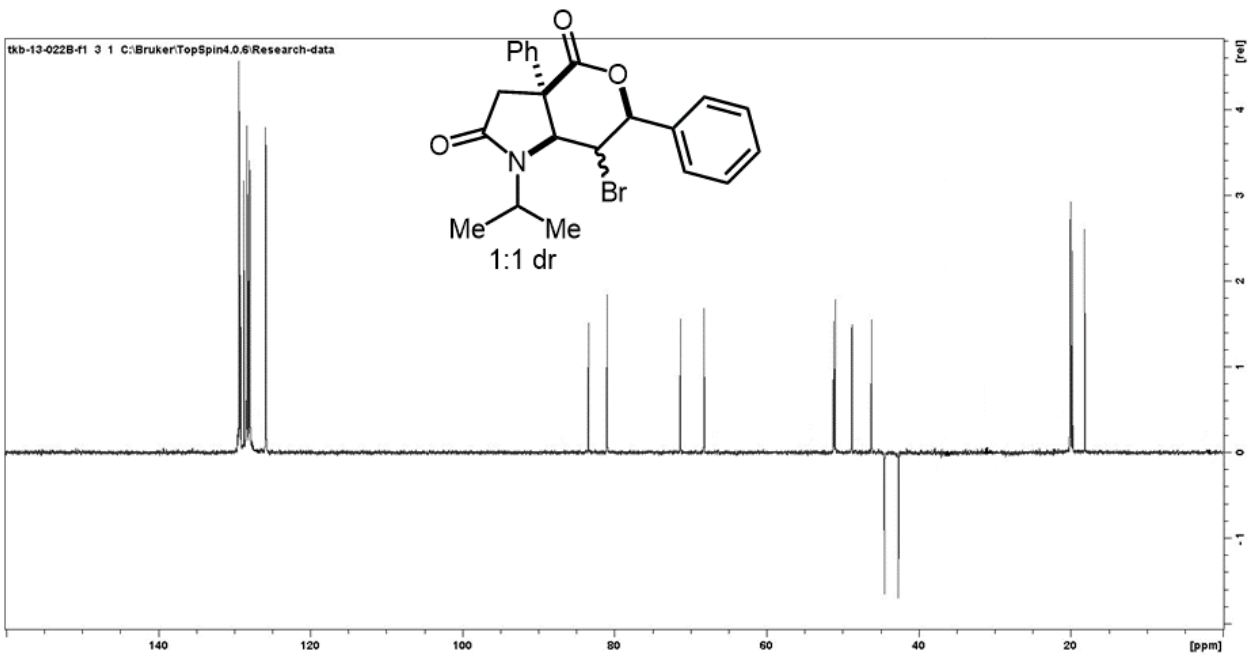


Compound 4g

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (85:15). Oily substance. Yield = 346.7 mg, 81%, 50:50 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 – 6.70 (m, 20H), 4.91 (d, *J* = 10.7 Hz, 1H), 4.57 (d, *J* = 9.8 Hz, 1H), 4.35 (s, 1H), 4.13 – 3.90 (m, 4H), 3.51 (p, *J* = 6.9 Hz, 1H), 3.25 (p, *J* = 6.8 Hz, 1H), 2.97 (d, *J* = 17.0 Hz, 1H), 2.57 (d, *J* = 17.5 Hz, 1H), 0.94 – 0.86 (m, 9H), 0.66 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.1, 171.6, 170.7, 170.7, 139.3, 137.4, 135.9, 135.5, 129.4, 129.2, 129.1, 128.7, 128.3, 128.3, 128.2, 128.0, 127.9, 125.8, 125.8, 83.4, 80.9, 71.3, 68.2, 53.7, 52.4, 51.1, 50.9, 48.7, 46.1, 44.5, 42.6, 20.1, 20.0, 19.7, 18.1. FTIR (KBr): 2934.6, 1721.8, 1669.4, 1608.2, 1511.1, 1431.8, 1414.7, 1344.9, 1298.4, 1245.6, 1179.4, 1135.3, 1031.8, 996.7, 921.8, 832.1, 701.9. HRMS calc for $C_{22}H_{22}BrNO_3$ 427.0783, found 427.0715.

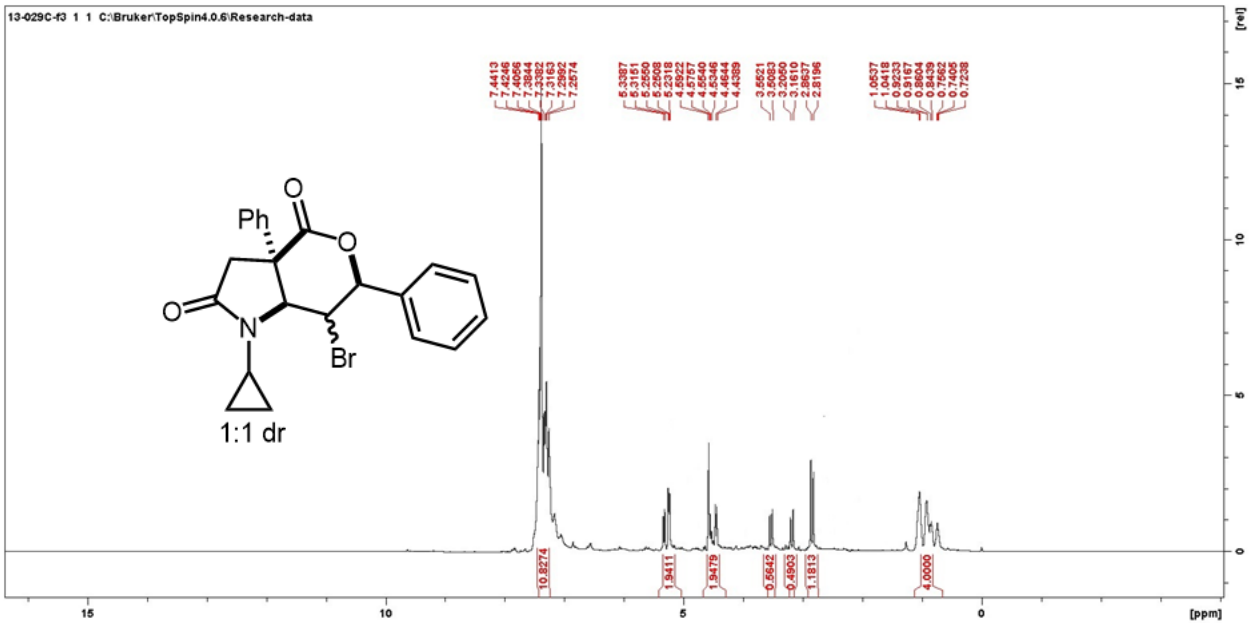

tkb-13-022B-f1 1 1 C:\Bruker\TopSpin4.0.6\Research-data
Ph
O
O
N
Br
Me
Me
1:1 dr
[ppm]

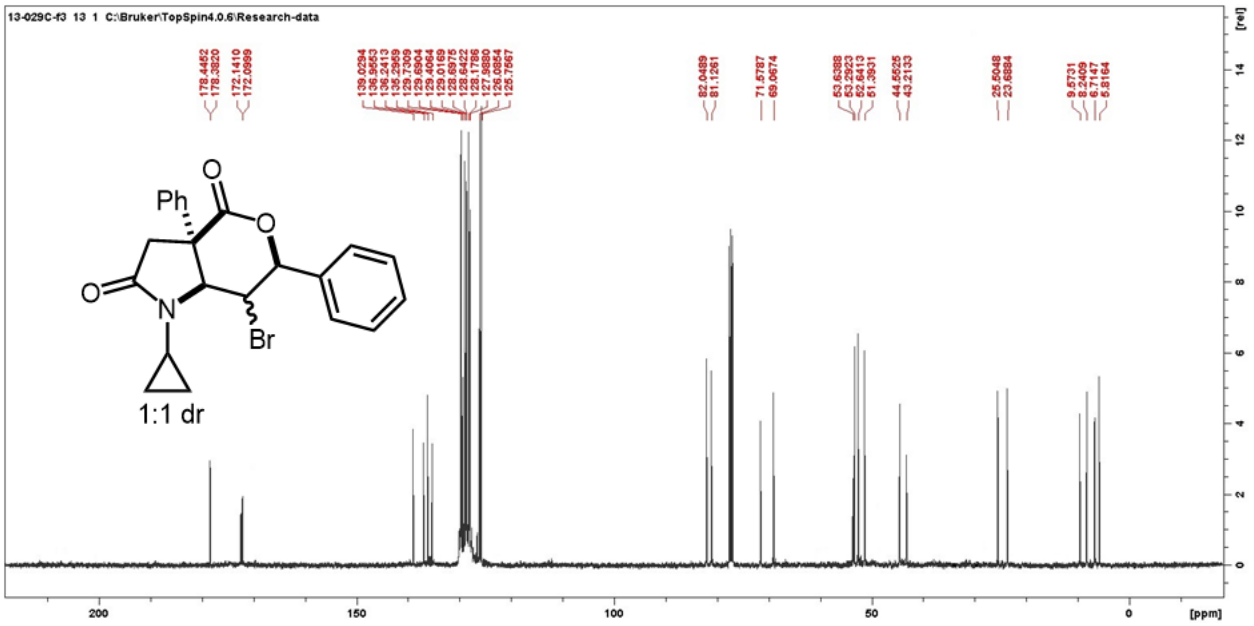

tkb-13-022B-f1 13
Ph
O
O
N
Br
Me
Me
1:1 dr
[ppm]

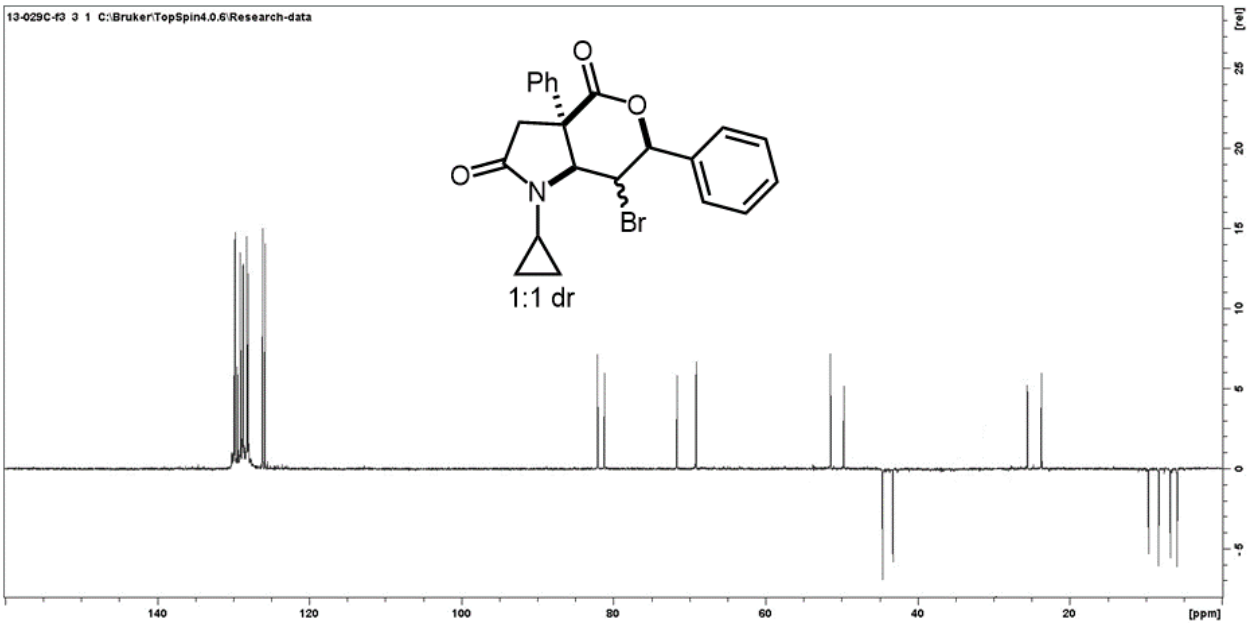


Compound 4h

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (85:15). Oily substance. Yield = 328.3 mg, 77%, 50:50 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.26 (m, 10H), 5.34 – 5.23 (m, 2H), 4.59 – 4.43 (m, 2H), 3.53 (dd, *J* = 17.6, 2.5 Hz, 0.5H), 3.19 (dd, *J* = 17.6, 2.6 Hz, 0.5H), 2.84 (dd, *J* = 17.6, 2.5 Hz, 1H), 1.05 – 0.72 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5, 178.4, 172.1, 172.1, 139.0, 137.0, 136.2, 135.3, 129.7, 129.7, 129.4, 129.0, 128.7, 128.7, 128.2, 128.0, 126.1, 125.8, 82.1, 81.1, 77.7, 77.6, 77.3, 77.3, 77.0, 77.0, 71.6, 69.1, 53.3, 52.6, 51.4, 49.7, 49.7, 44.6, 43.2, 25.5, 23.7, 9.6, 8.2, 6.7, 5.8. FTIR (KBr): 2984.1, 1723.4, 1669.4, 1608.2, 1511.1, 1431.8, 1414.7, 1344.9, 1298.4, 1135.3, 1031.8, 996.7, 702.4. HRMS calc for $C_{22}H_{20}BrNO_3$ 425.0627, found 425.0622.

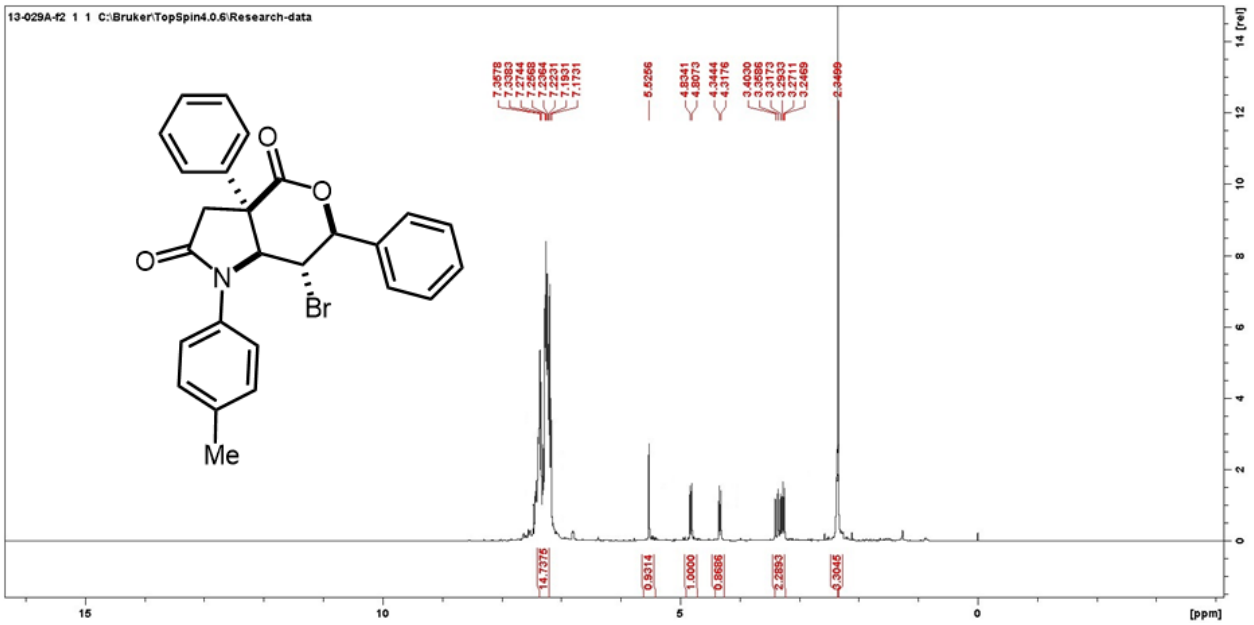

13-029C-f3 1 1 C:\Bruker\TopSpin4.0.6\Research-data
Ph
O
O
N
Br
1:1 dr
[ppm]

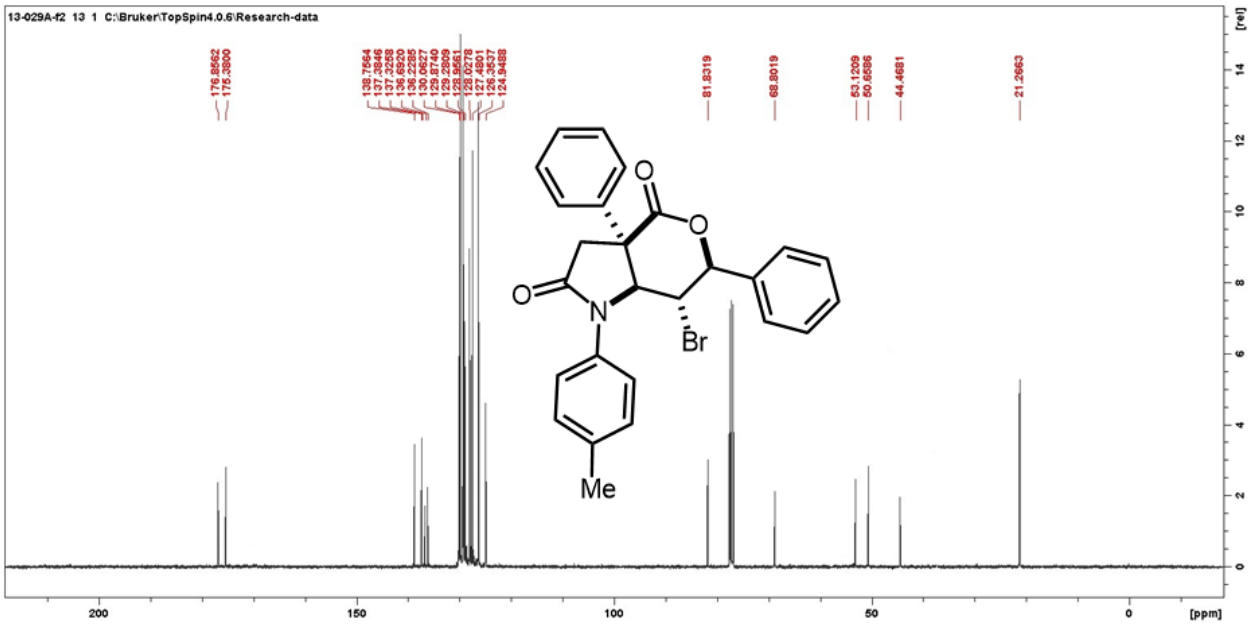

13-029C-f3 13 1 C:\Bruker\TopSpin4.0.6\Research-data
Ph
O
O
N
Br
1:1 dr
[ppm]

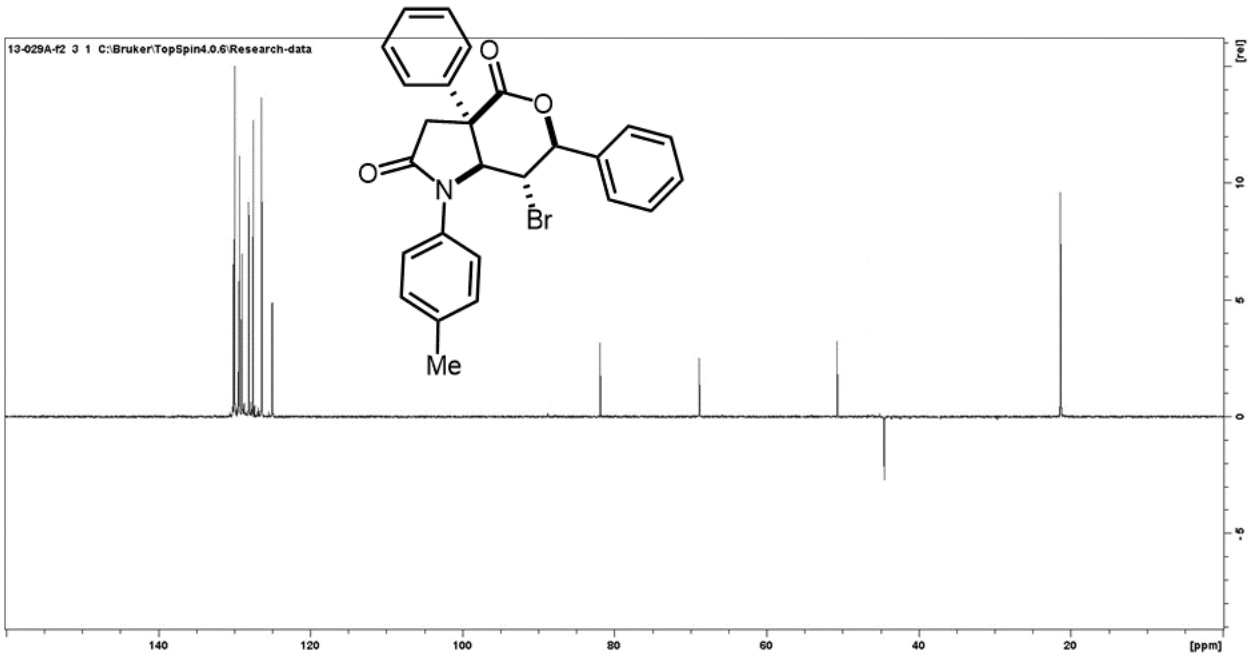


Compound 4i

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 385.6 mg, 81%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.11 (m, 14H), 5.52 (s, 1H), 4.82 (d, *J* = 10.8 Hz, 1H), 4.33 (d, *J* = 10.8 Hz, 1H), 4.11 (dd, *J* = 9.8, 4.7 Hz, 2H), 3.38 (d, *J* = 17.7 Hz, 1H), 3.28 (d, *J* = 17.7 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.9, 175.4, 138.8, 137.4, 137.3, 136.7, 136.2, 130.1, 129.9, 129.9, 129.3, 129.0, 128.0, 128.0, 127.5, 126.4, 126.3, 125.0, 68.8, 53.1, 50.7, 44.5, 21.3. FTIR (KBr): 2935.4, 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, 995.8, 831.0. HRMS calc for $C_{26}H_{22}BrNO_3$ 475.0783, found 475.0788.


13-029A-f2 1 1 C:\Bruker\TopSpin4.0.6\Research-data
7.3678
7.3383
7.2744
7.2568
7.2364
7.1931
7.1731
5.5256
4.8341
4.8073
4.3444
4.3176
3.4030
3.3586
3.3173
3.2933
3.2711
3.2469
2.3469
14.7375
0.9314
1.0000
0.9686
2.2693
0.3046
O
O
O
N
Br
Me
15
10
5
0
[ppm]

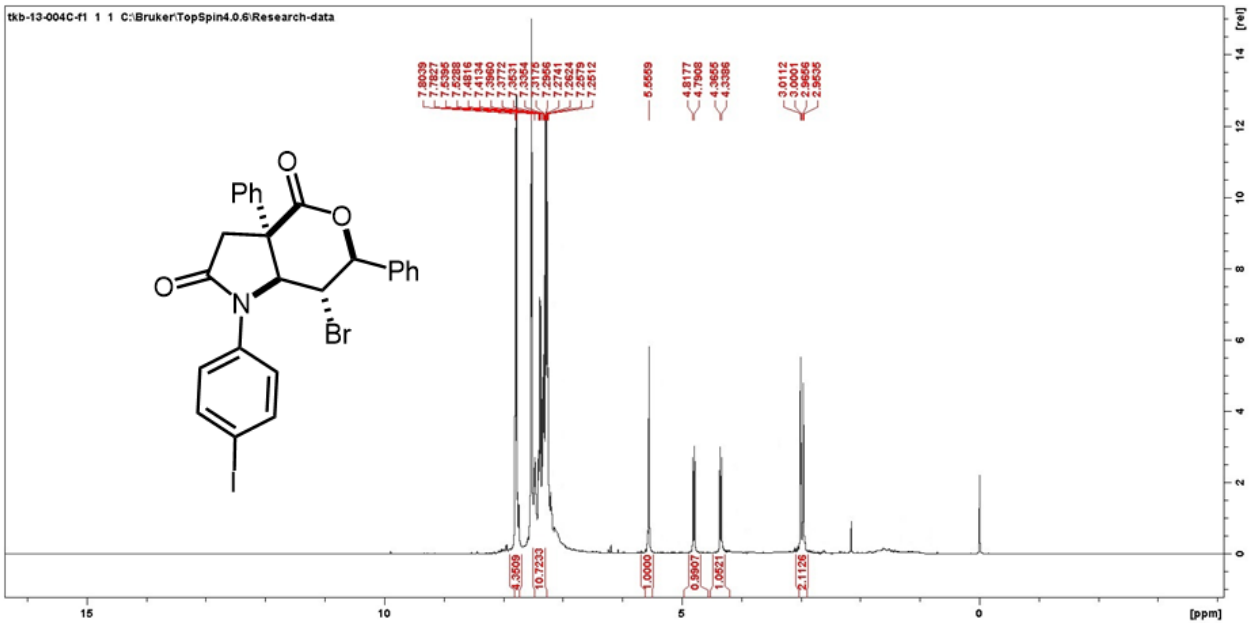

13-029A-f2 13 1 C:\Bruker\TopSpin4.0.6\Research-data
176.8562
175.3800
138.7564
137.3846
137.3268
136.6920
136.2265
130.0627
129.8740
129.2809
128.9681
128.8278
127.4801
126.3537
124.9488
81.8319
68.8019
53.1209
50.6586
44.4681
21.2663
O
O
O
N
Br
Me
200
150
100
50
0
[ppm]

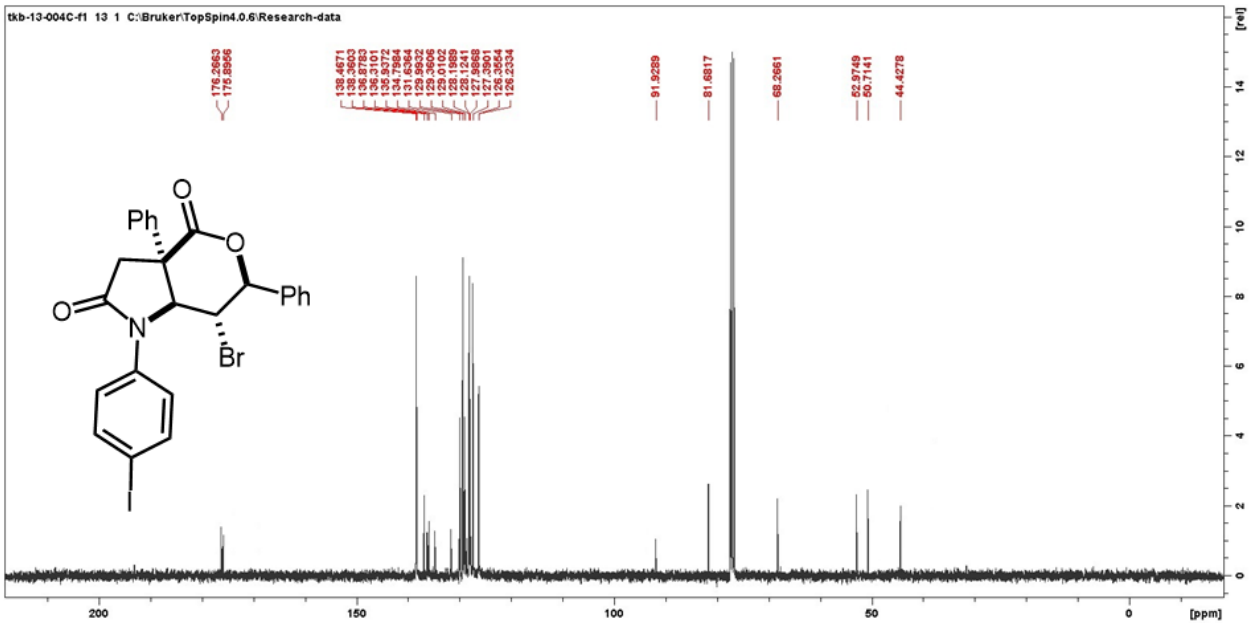


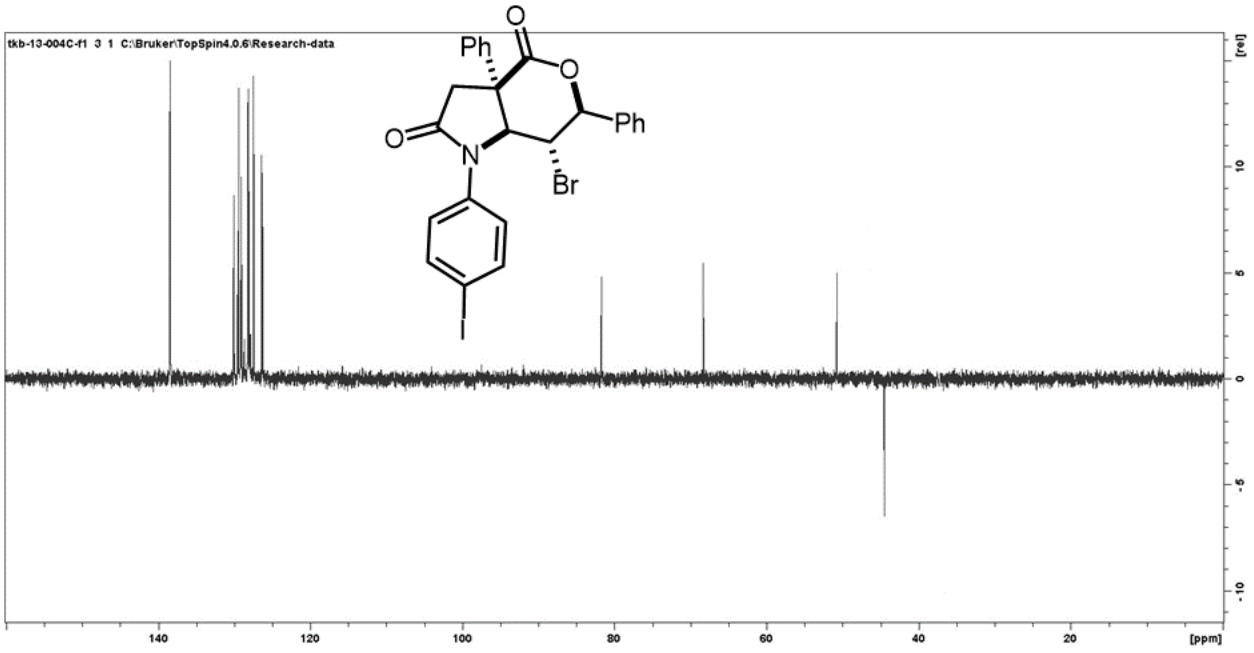
Compound 4j

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 464.5 mg, 79%, 95:5 dr.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.77 (m, 4H), 7.53 – 7.25 (m, 10H), 5.56 (s, 1H), 4.80 (d, *J* = 10.8 Hz, 1H), 4.35 (d, *J* = 10.8 Hz, 1H), 3.01-2.96 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.3, 175.9, 138.5, 138.4, 136.9, 136.3, 135.9, 134.8, 130.0, 129.4, 129.0, 128.1, 128.0, 127.4, 126.4, 126.2, 91.9, 81.7, 68.3, 53.0, 50.7. FTIR (KBr): 2924.8, 1642.2, 1494.9, 1448.8, 1427.0, 1393.4, 1361.6, 1328.7, 1289.7, 1223.6, 1198.9, 1130.1, 1074.1, 1030.4, 988.5, 966.1, 925.5, 741.6, 693.4. HRMS calc for $C_{25}H_{19}BrINO_3$ 586.9593, found 586.9588.


tkb-13-004C-f1 1 1 C:\Bruker\TopSpin4.0.6\Research-data
Ph
O
O
Ph
O
N
Br
I
[rel]
[ppm]

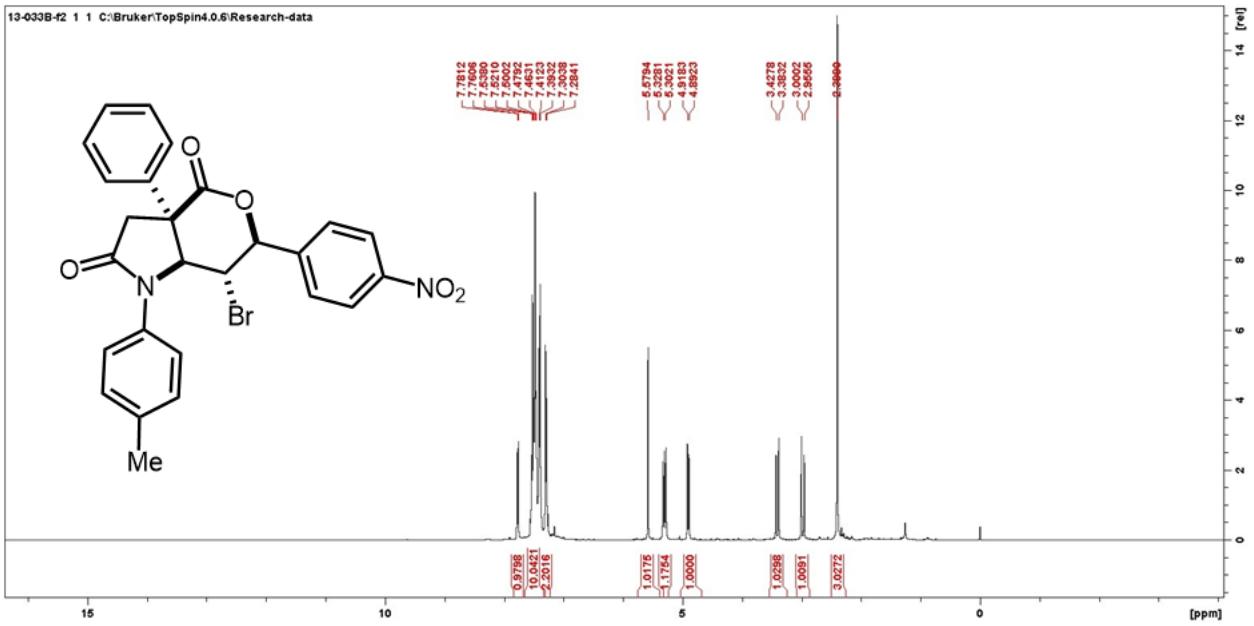

tkb-13-004C-f1 13 1 C:\Bruker\TopSpin4.0.6\Research-data
Ph
O
O
Ph
O
N
Br
I
[rel]
[ppm]

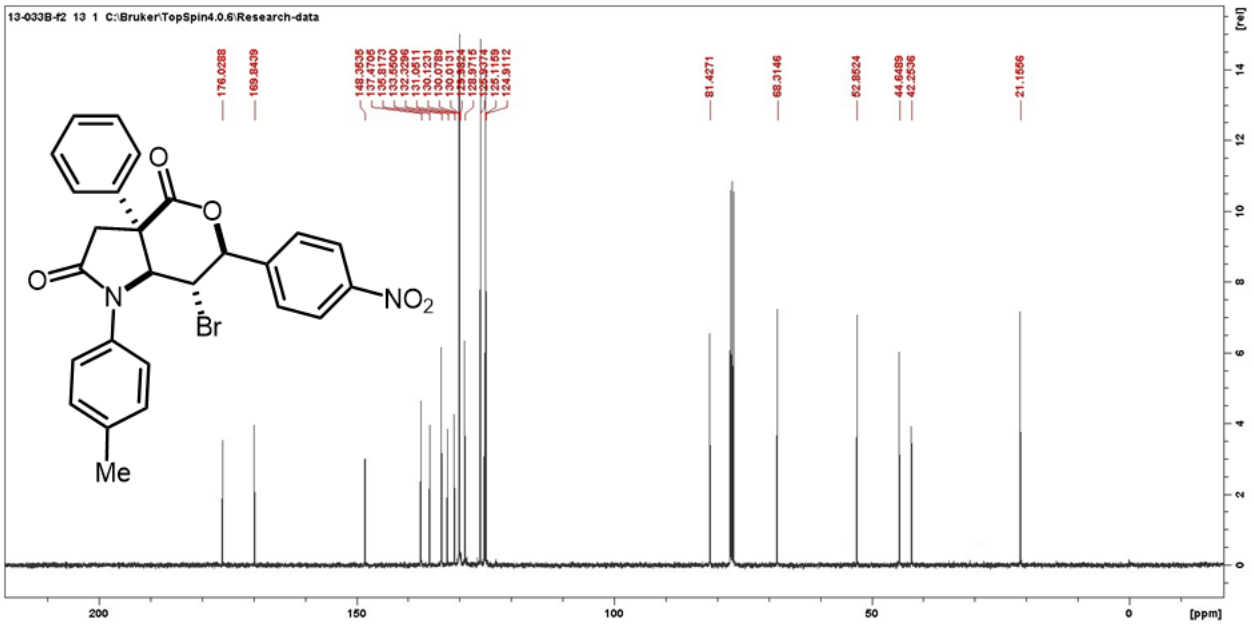


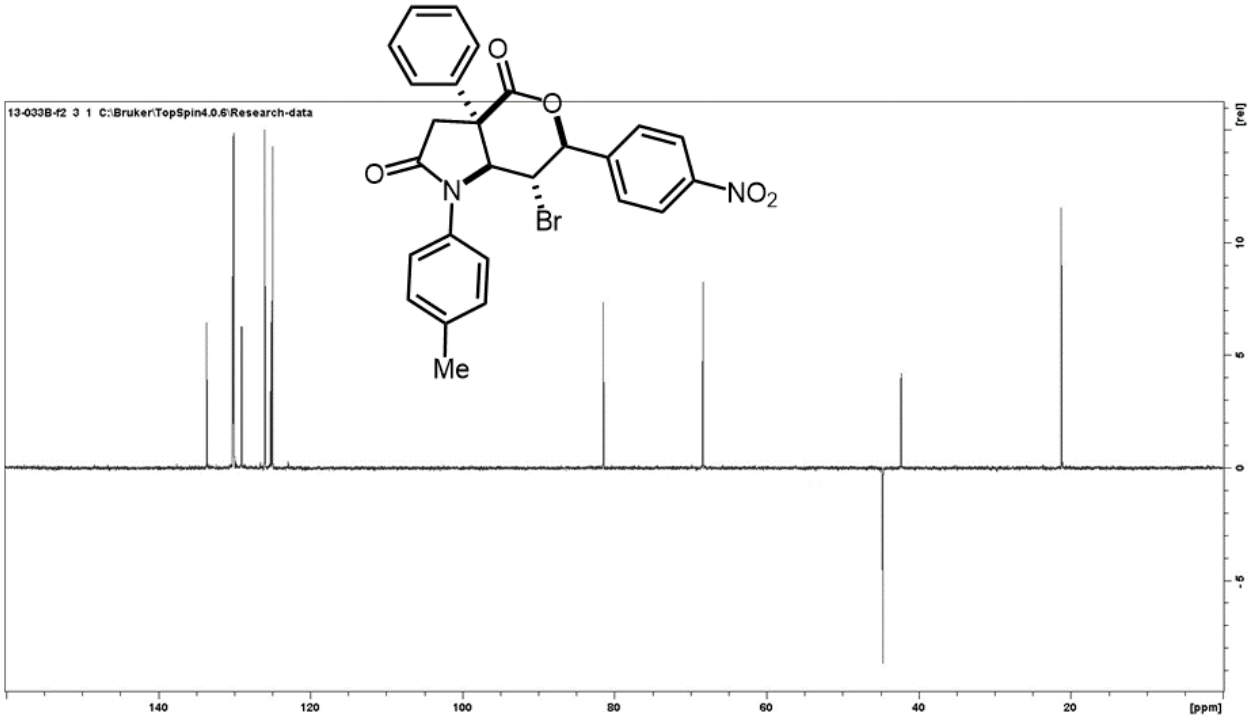
Compound 4k

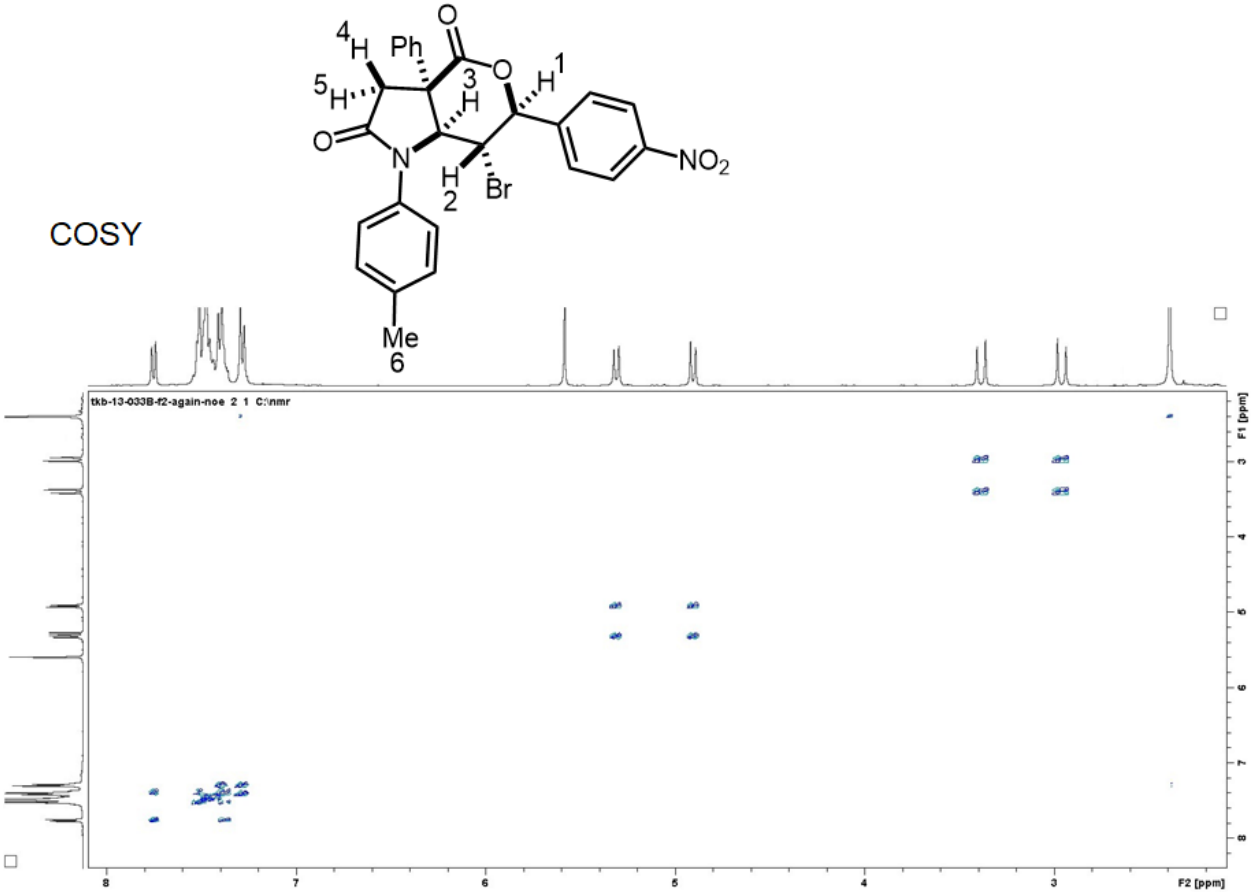
Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 453.3 mg, 87%, 95:5 dr.

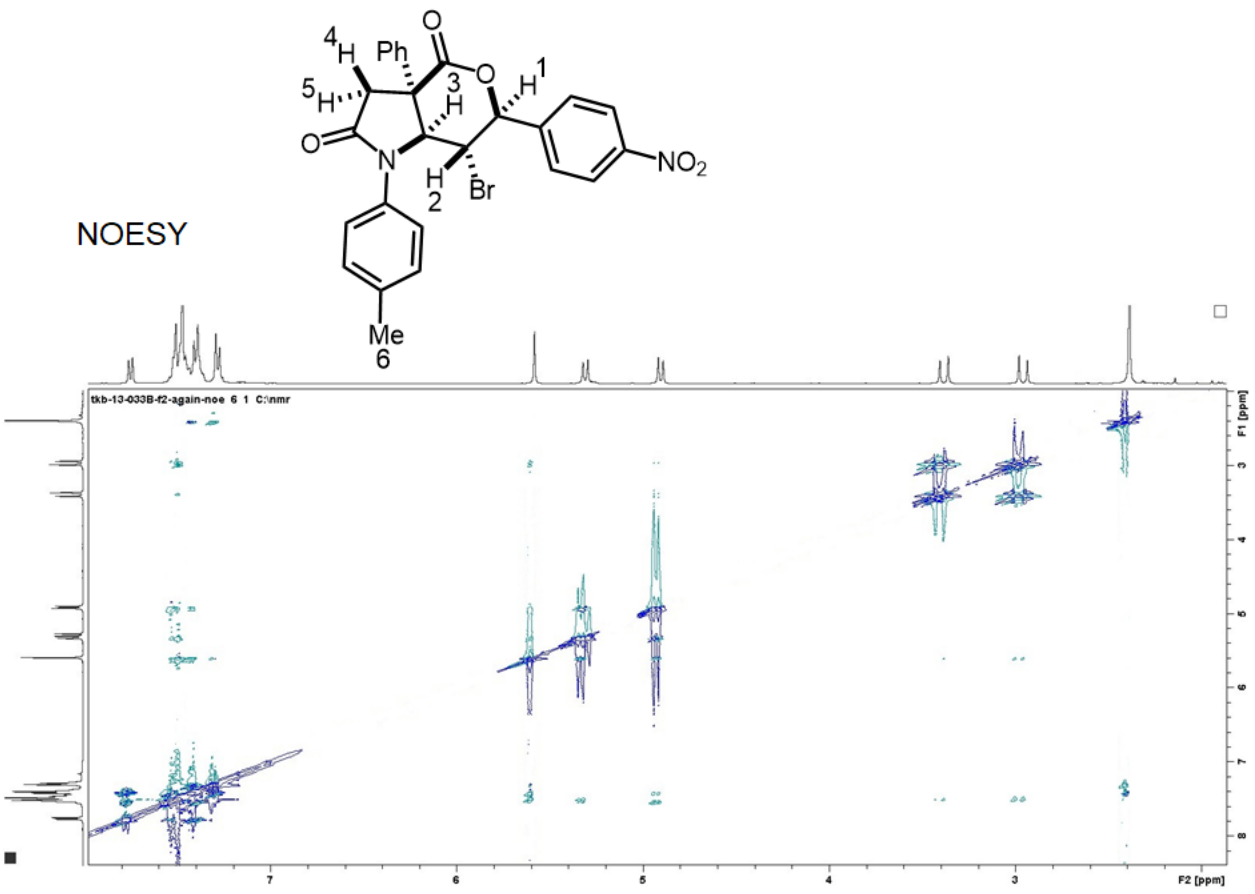
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.2 Hz, 1H), 7.58 – 7.35 (m, 10H), 7.29 (d, *J* = 8.0 Hz, 2H), 5.58 (s, 1H), 5.35 – 5.25 (m, 2H), 4.91 (d, *J* = 10.4 Hz, 1H), 3.41 (d, *J* = 17.9 Hz, 1H), 2.98 (d, *J* = 17.9 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.0, 169.9, 148.4, 137.5, 135.8, 133.6, 132.3, 131.1, 130.1, 130.1, 130.0, 130.0, 129.0, 125.9, 125.1, 124.9, 81.4, 68.3, 52.9, 44.7, 42.3, 21.2. FTIR (KBr): 2965.2, 2872.3, 1716.4, 1650.8, 1612.9, 1585.9, 1513.1, 1455.3, 1359.3, 1304.1, 1251.3, 1177.4, 1135.5, 1033.8, 996.7, 896.0, 833.6, 804.9. HRMS calc for $C_{26}H_{21}BrN_2O_5$ 520.0634, found 520.0634.

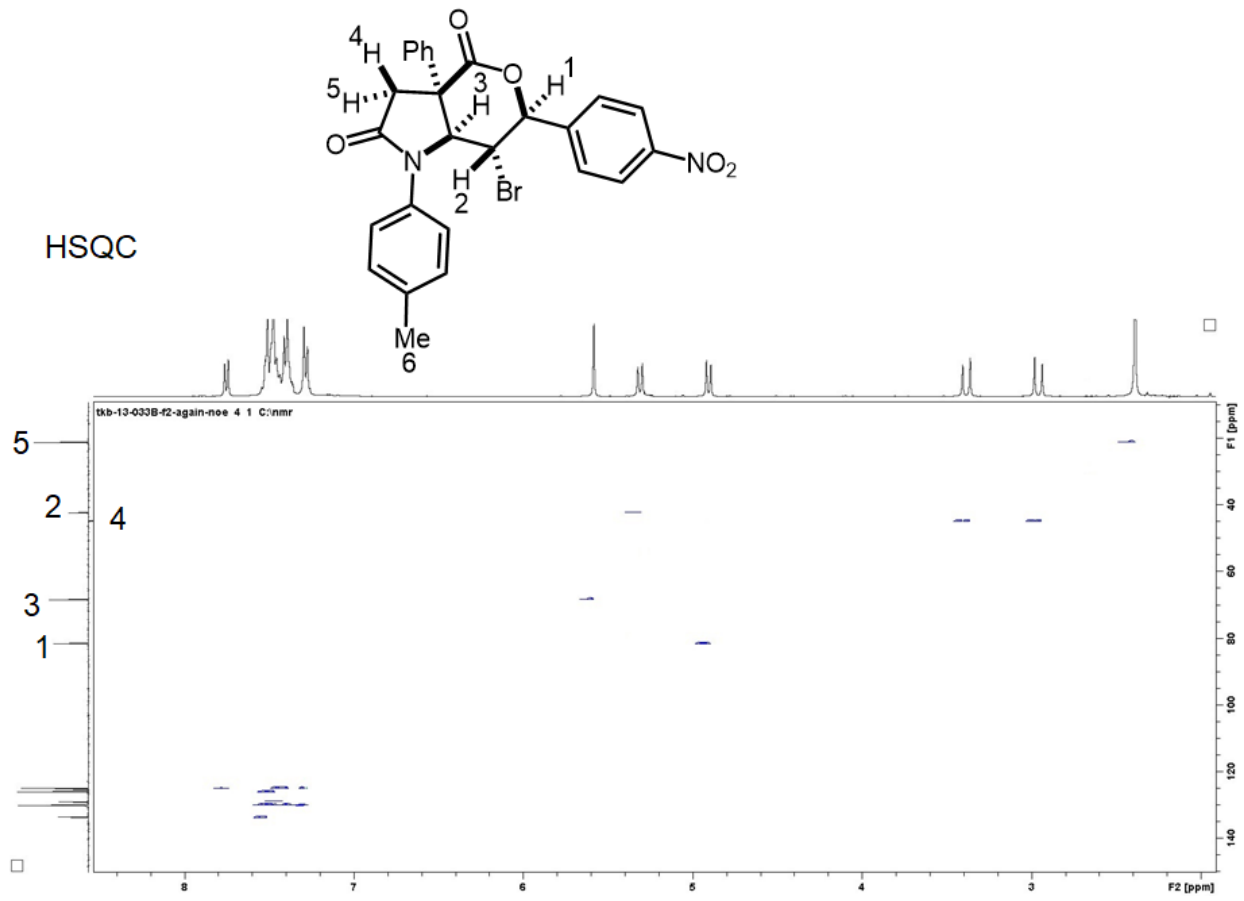

13-033B-f2 1 1 C:\Bruker\TopSpin4.0.6\Research-data
7.7812
7.7606
7.6390
7.6310
7.5602
7.4792
7.4631
7.4123
7.3932
7.3038
7.2841
5.5794
5.3281
5.3021
4.9183
4.8923
3.4278
3.3832
3.0002
2.9565
0.9798
10.0421
2.2016
1.0175
1.1754
1.0000
1.0298
1.0091
3.0272
O
O
O
N
Br
NO2
Me
15
10
5
0
[ppm]
[rel]


13-033B-f2 13 1 C:\Bruker\TopSpin4.0.6\Research-data
176.0288
169.8439
148.3536
135.8173
133.5500
132.3296
131.0611
130.1131
130.0789
130.0131
128.9716
125.1169
124.9112
81.4271
68.3146
52.8524
44.6489
42.2536
21.1556
O
O
O
N
Br
NO2
Me
200
150
100
50
0
[ppm]
[rel]


13-033B-f2 3 1 C:\Bruker\TopSpin4.0.6\Research-data
O
O
N
Br
NO2
Me
140
120
100
80
60
40
20
[ppm]

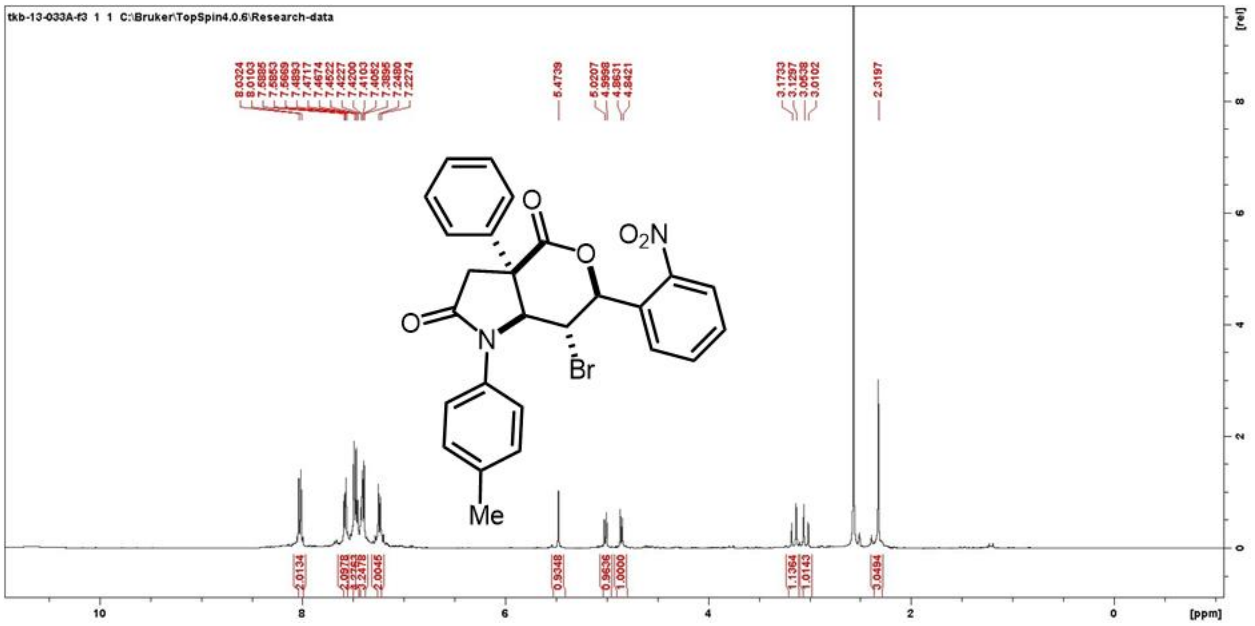

4H
Ph
5H
3H
O
O
H1
N
H2
Br
NO2
Me
6
COSY
tkb-13-033B-f2-again-noe 2 1 C:\nmr
F1 [ppm]
F2 [ppm]

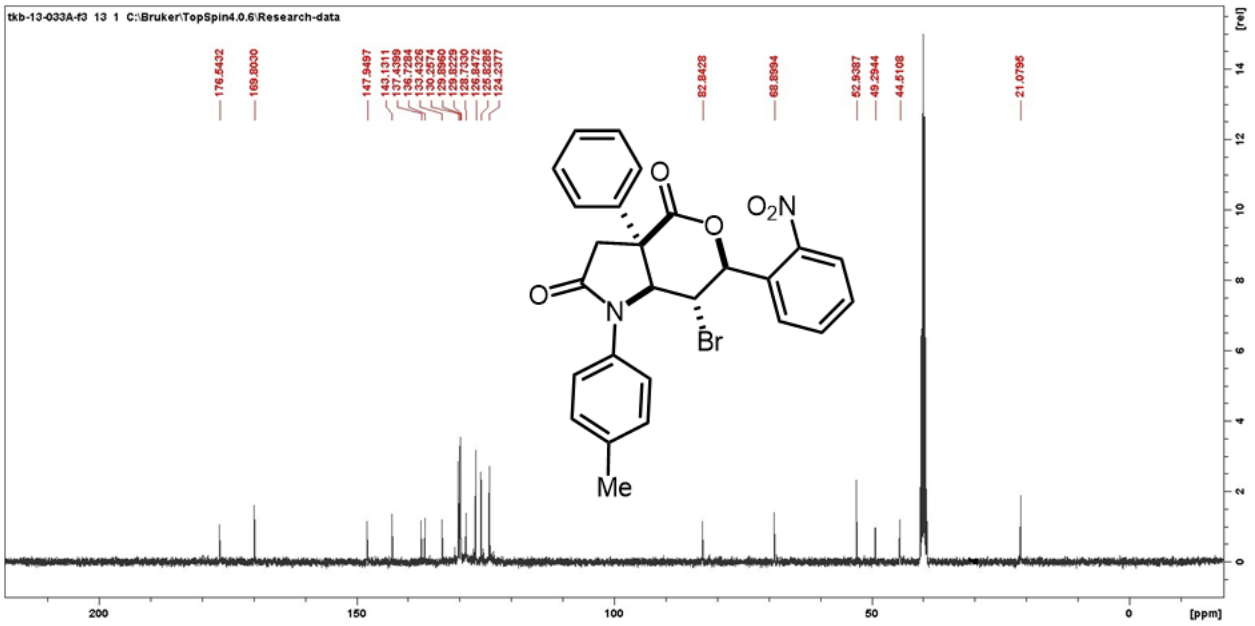

NOESY
4H
Ph
O
3
O
H1
5H
H
O
N
H
2
Br
NO2
Me
6
tkb-13-033B-f2-again-noe 6 1 C:\nmr
F1 [ppm]
F2 [ppm]
7
6
5
4
3

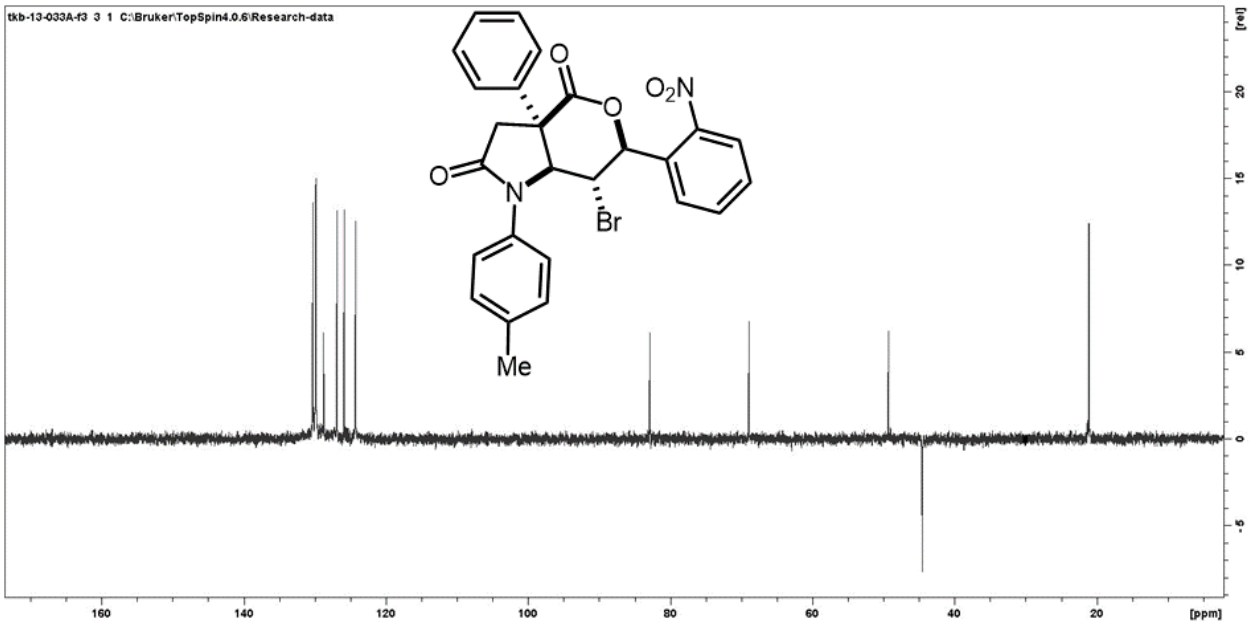


Compound 4l

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 422.3 mg, 81%, 95:5 dr. ^{1}H NMR (400 MHz, DMSO) δ 8.01 (d, *J* = 1.9 Hz, 2H), 7.63 – 7.54 (m, 2H), 7.57 – 7.43 (m, 7H), 7.24 – 7.22 (m, 2H), 5.47 (d, *J* = 1.0 Hz, 1H), 5.00 (d, *J* = 10.0 Hz, 1H), 4.86 ((d, *J* = 10.0 Hz, 1H), 3.17 – 2.99 (m, 2H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 176.6, 169.8, 148.0, 143.1, 137.4, 136.7, 133.4, 130.3, 129.9, 129.8, 128.7, 126.9, 125.8, 124.2, 82.9, 68.9, 52.9, 49.3, 44.5, 21.1. FTIR (KBr): 2933.4, 1721.5, 1666.3, 1606.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1137.9, 1033.8, 995.8, 831.7. HRMS calc for $C_{26}H_{21}BrN_2O_5$ 520.0634, found 520.0634.

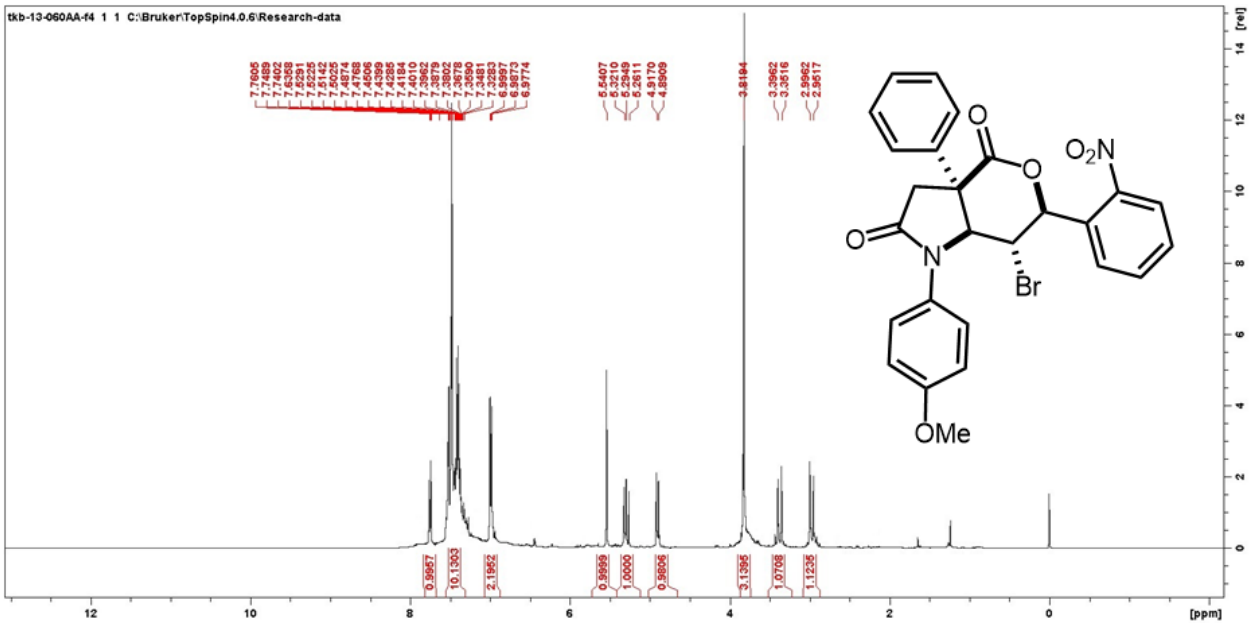

tkb-13-033A-f3 1 1 C:\Bruker\TopSpin4.0.6\Research-data
8.0324
8.0103
7.5885
7.5663
7.4893
7.4717
7.4674
7.4522
7.4227
7.4200
7.4103
7.4062
7.3886
7.2490
7.2274
5.4739
5.0207
4.9968
4.8631
4.8421
3.1733
3.1297
3.0838
3.0102
2.3197
O
O
O2N
O
N
Br
Me
2.0134
2.0978
4.3478
2.0045
0.9348
0.9636
1.0000
1.1364
1.0143
3.0494
10
8
6
4
2
0
[ppm]
[rel]

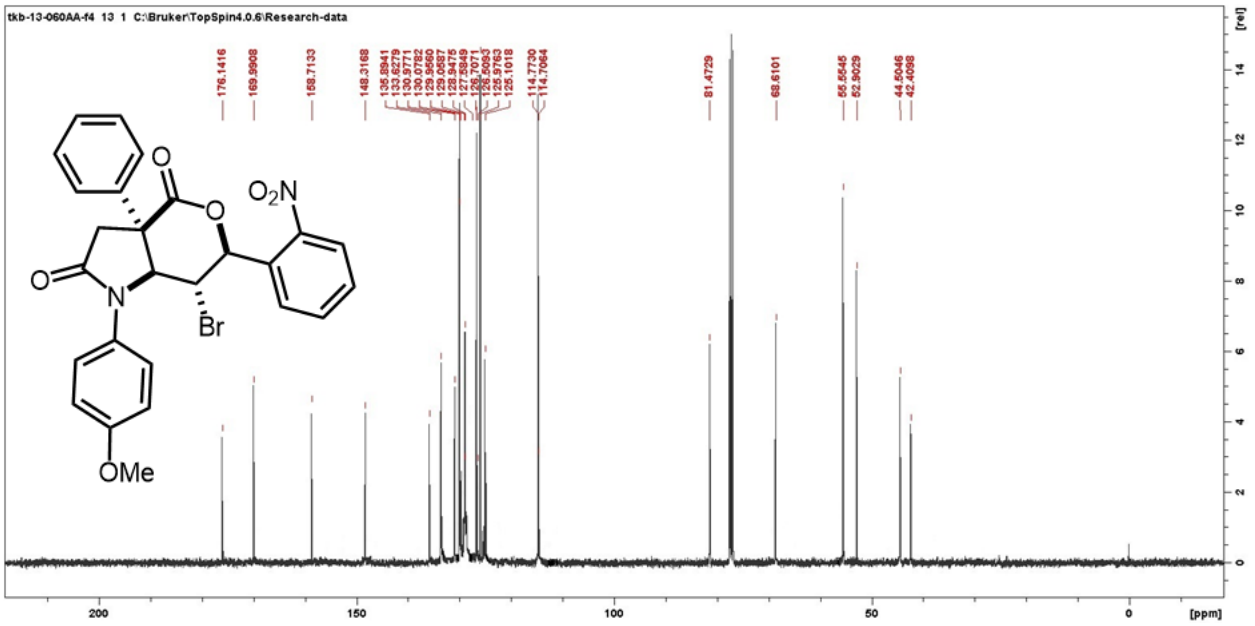

tkb-13-033A-f3 13 1 C:\Bruker\TopSpin4.0.6\Research-data
176.5432
169.8030
147.9497
143.1311
137.4399
136.7284
133.4326
130.2574
129.8259
129.6529
128.7330
126.8472
125.8285
124.2377
82.8428
68.8994
52.9387
49.2944
44.5108
21.0795
O
O
O2N
O
N
Br
Me
200
150
100
50
0
[ppm]
[rel]

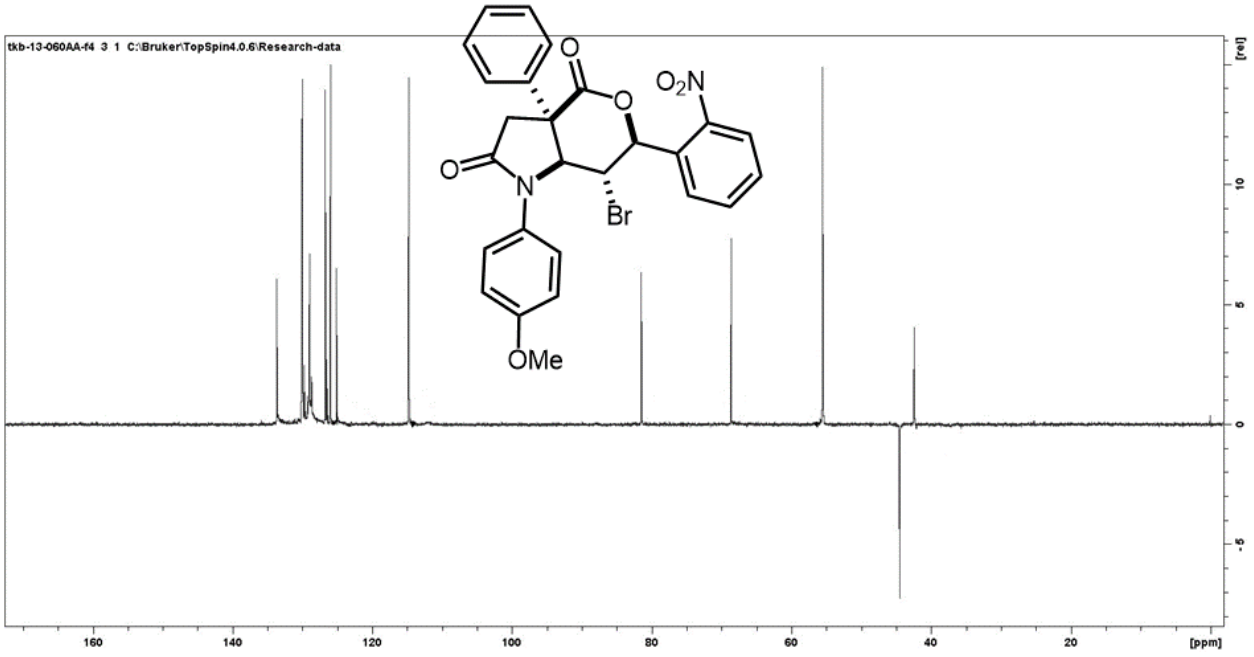


Compound 4m

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 451.1 mg, 84%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz,1), 7.63 – 7.32 (m, 10H), 7.03 – 6.98 (m, 2H), 5.54 (s, 1H), 5.30 (d, *J* = 10.5 Hz, 1H), 4.90 (dd, *J* = 10.5, 5.0 Hz, 1H), 3.82 (s, 3H), 3.35 (d, *J* = 3.1 Hz, 1H), 2.97 (d, *J* = 3.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.1, 170.0, 158.7, 148.3, 135.9, 133.6, 131.0, 130.1, 130.0, 129.0, 127.6, 126.7, 126.0, 125.1, 114.8, 81.5, 68.6, 55.6, 52.9, 44.5, 42.4. FTIR (KBr): 2944.4, 1736.5, 1658.3, 1606.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1135.9, 1031.8, 995.9, 833.7, 755.2. HRMS calc for $C_{26}H_{21}BrN_2O_6$ 536.0583, found 536.0589.

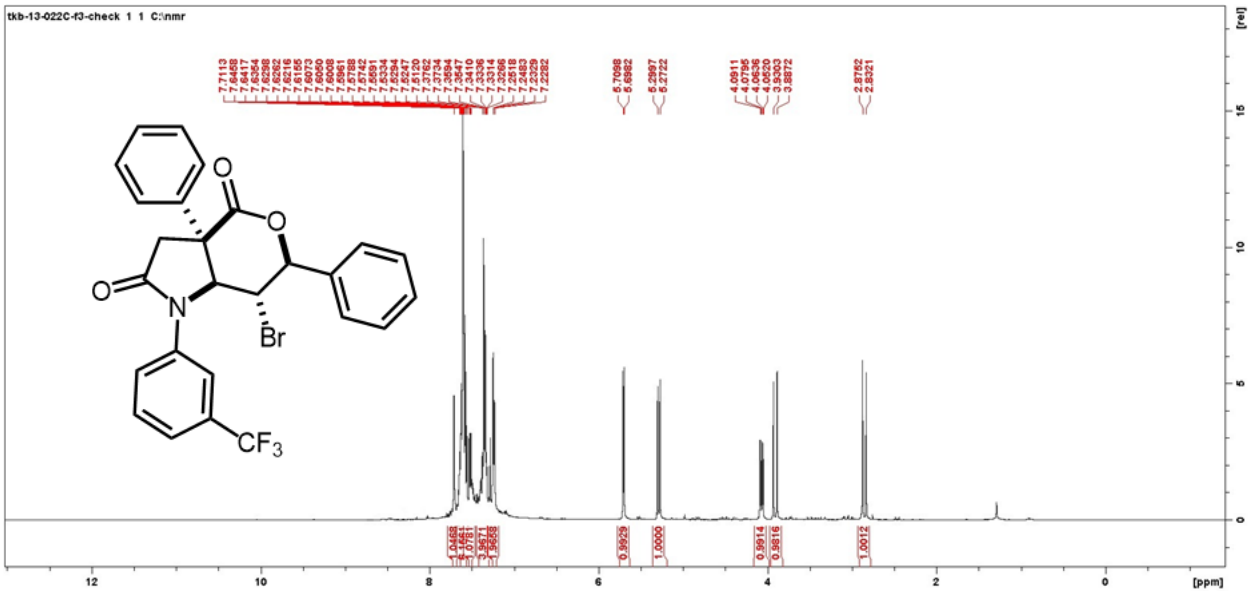

tkb-13-060AA-f4 1 1 C:\Bruker\TopSpin4.0.6\Research-data
O2N
O
N
Br
OMe
[ppm]

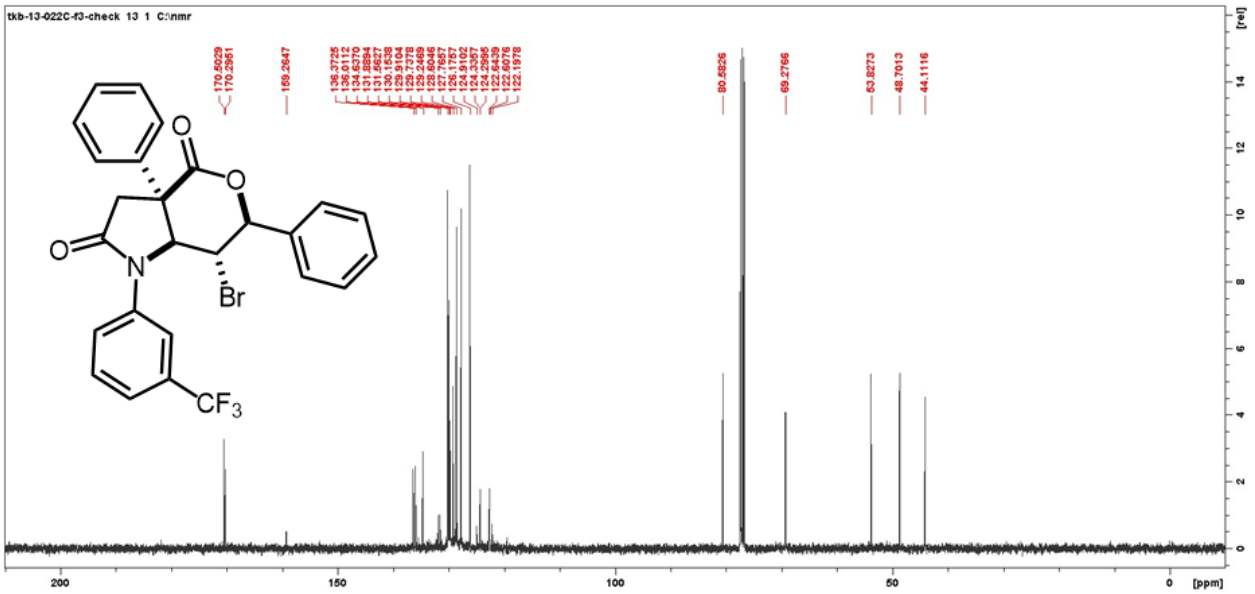

tkb-13-060AA-f4 13 1 C:\Bruker\TopSpin4.0.6\Research-data
O2N
O
N
Br
OMe
[ppm]

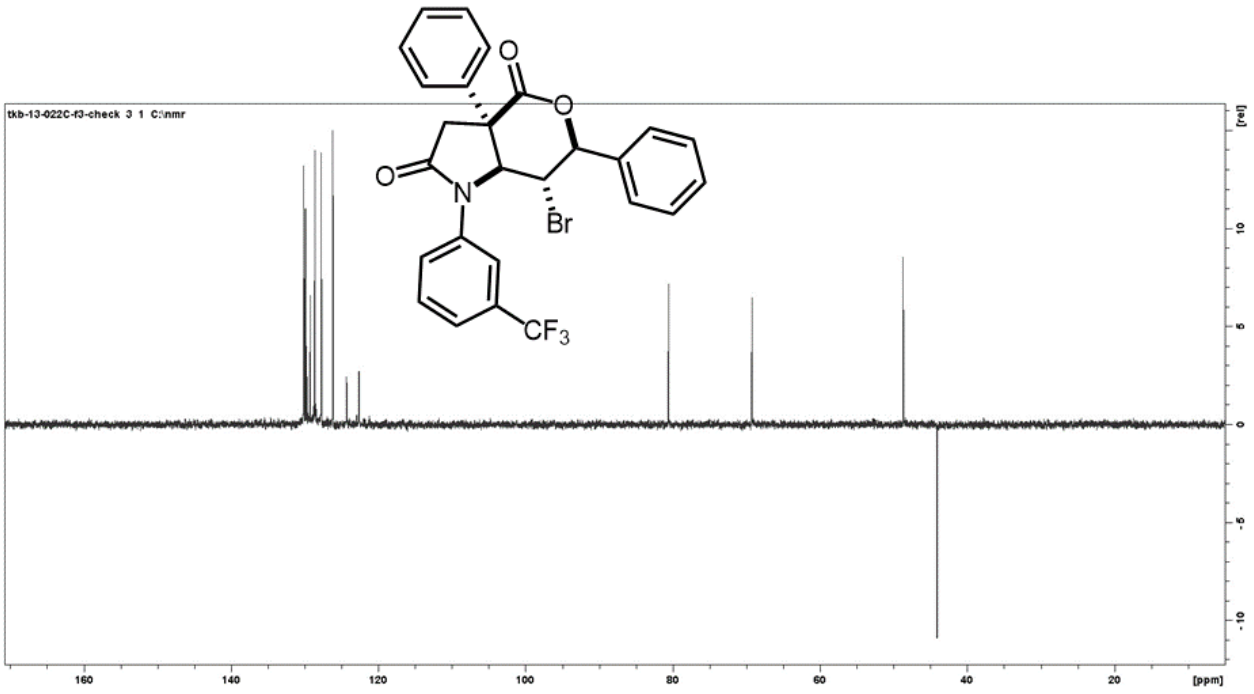


Compound 4n

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 408.1 mg, 77%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.66 – 7.54 (m, 7H), 7.41 – 7.14 (m, 6H), 5.68 (d, J = 4.7 Hz, 1H), 5.26 (d, J = 11.0 Hz, 1H), 4.05 (dd, J = 11.0, 4.6 Hz, 1H), 3.88 (d, J = 17.3 Hz, 1H), 2.82 (d, J = 17.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 170.3, 159.1, 136.4, 136.0, 134.7, 130.1, 129.9, 129.9, 129.2, 128.6, 127.8, 126.2, 124.3, 124.3, 122.6, 122.6, 80.6, 69.3, 53.8, 48.7, 44.1. FTIR (KBr): 3027.4, 2924.0, 1724.2, 1646.3, 1474.3, 1452.8, 1361.9, 1342.0, 1205.6, 1140.2, 1071.7, 1028.3, 996.4, 735.4. HRMS calc for $C_{26}H_{19}BrF_3NO_3$ 529.0500, found 529.0504.

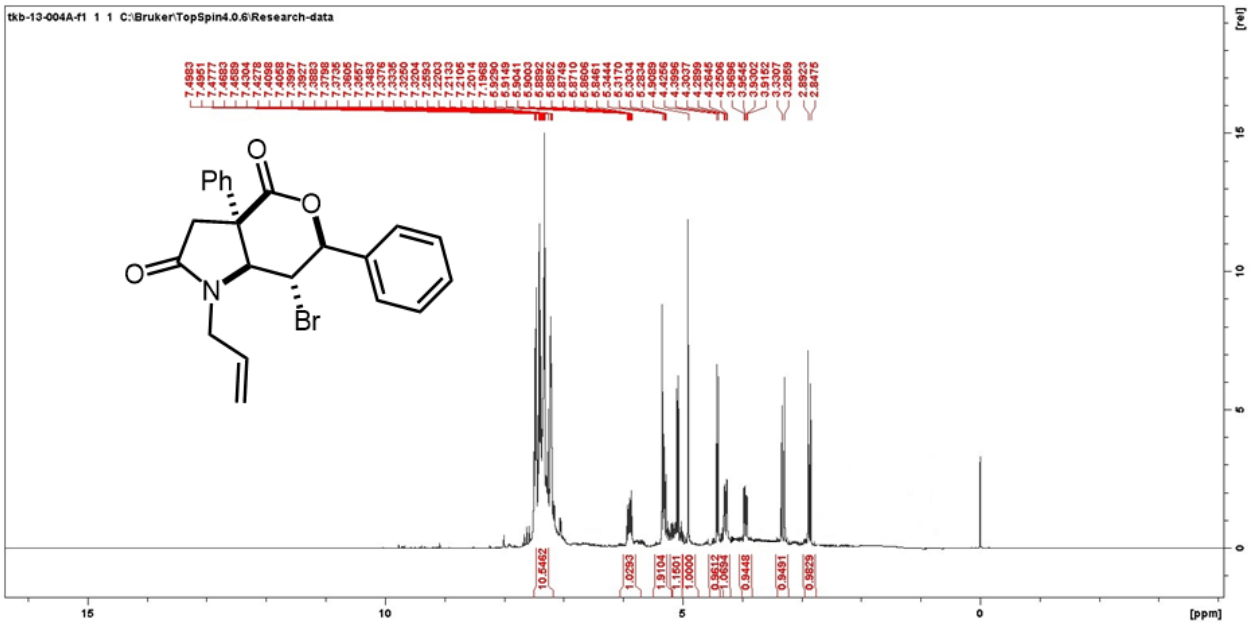

tkb-13-022C-f3-check 1 1 C6nmr
7.7113
7.6458
7.6417
7.6354
7.6298
7.6282
7.6216
7.6156
7.6073
7.6060
7.6008
7.5961
7.5788
7.5742
7.5691
7.5634
7.5294
7.5247
7.5120
7.5076
7.4734
7.3694
7.3547
7.3410
7.3330
7.3314
7.3296
7.2818
7.2483
7.2329
7.2282
5.7098
5.6982
5.2997
5.2722
4.0911
4.0795
4.0536
4.0420
3.9023
3.8872
2.8752
2.8321
1.0468
1.1661
1.0767
1.0000
0.9929
1.0000
0.9914
0.9816
1.0012
O
O
O
N
Br
CF3
12
10
8
6
4
2
0
[ppm]
[rel]

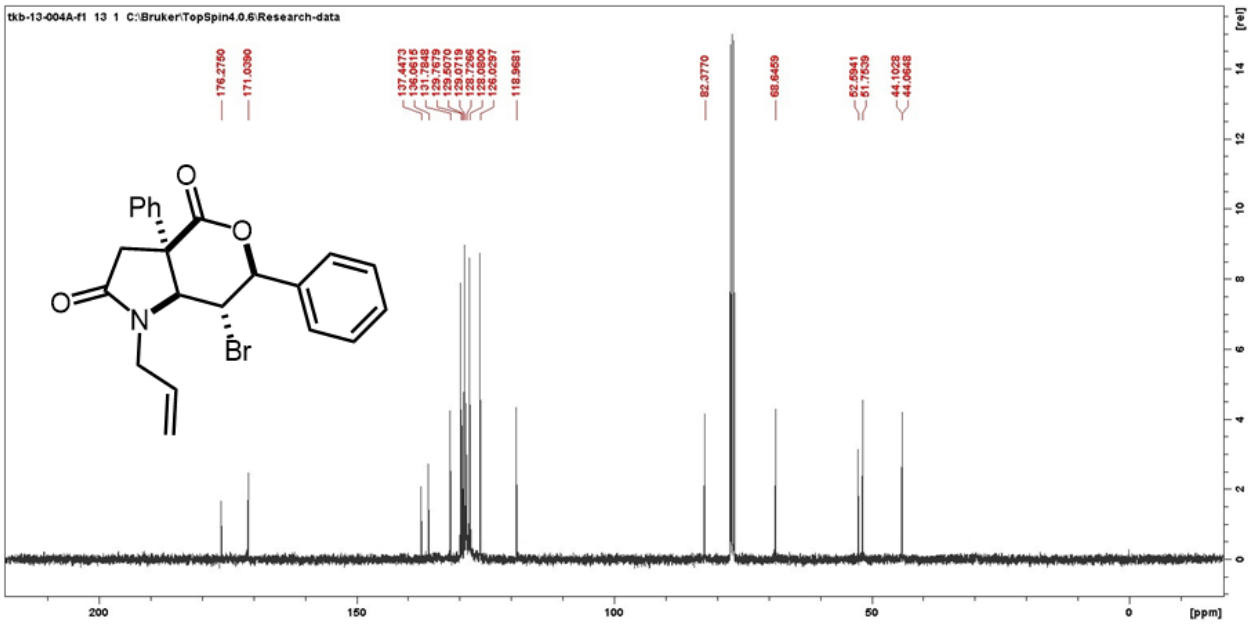

tkb-13-022C-f3-check 13 1 C6nmr
170.5029
170.2561
169.2647
136.3725
136.0112
134.5770
131.8894
131.5627
130.1538
129.9014
129.7378
129.2469
128.6046
127.1767
127.1357
124.9102
124.3357
124.2395
122.6459
122.6076
122.1978
80.5826
69.2766
53.8273
48.7013
44.1116
O
O
O
N
Br
CF3
200
150
100
50
0
[ppm]
[rel]

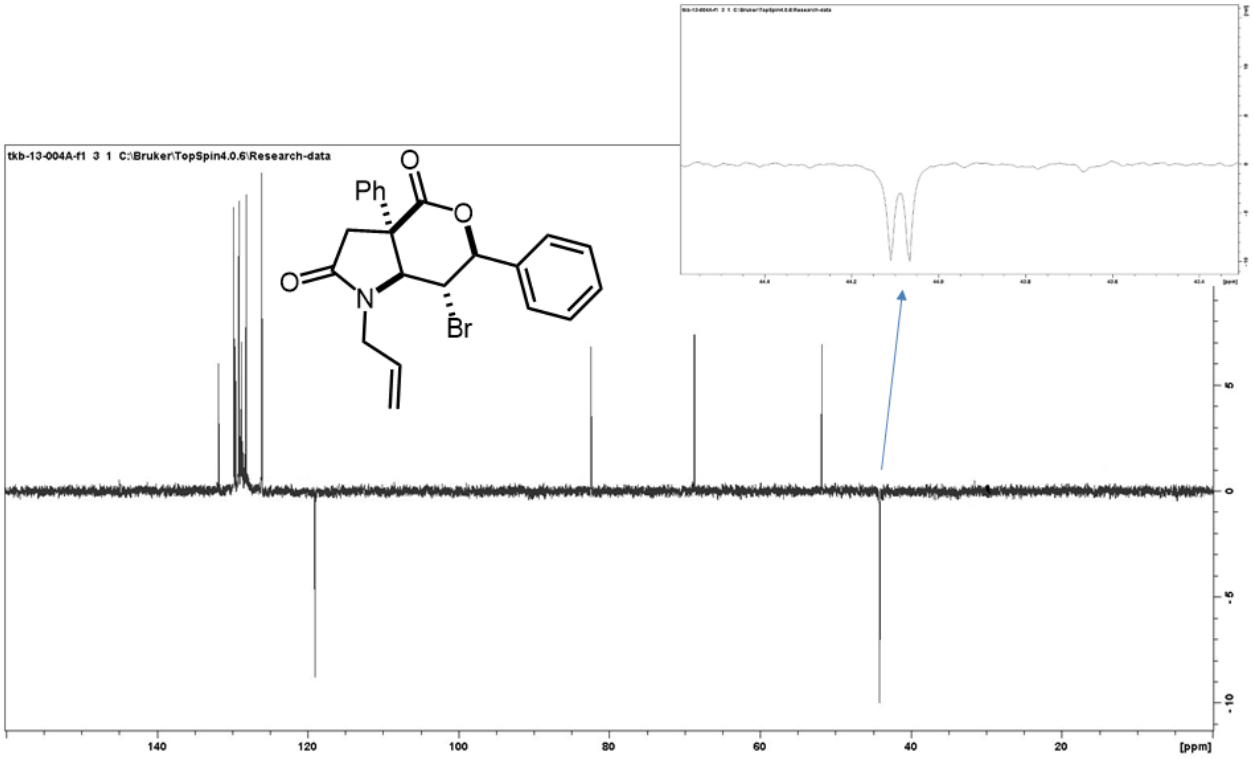


Compound 4o

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 366.9 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.20 (m, 10H), 5.89 (ddt, *J* = 17.5, 9.8, 5.8 Hz, 1H), 5.34 (s, 1H), 5.31 (dd, *J* = 6.3, 1.3 Hz, 1H), 5.08 – 5.00 (m, 1H), 4.91 (s, 1H), 4.45 – 4.20 (m, 2H), 3.97 – 3.92 (m, 1H), 3.30 (d, *J* = 17.3 Hz, 1H), 2.86 (d, *J* = 17.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.3, 171.0, 137.5, 136.1, 131.8, 129.8, 129.5, 129.1, 128.7, 128.1, 126.0, 119.0, 82.4, 68.7, 52.6, 51.8, 44.1, 44.1. 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 calc for $C_{22}H_{20}BrNO_3$ 425.0627, found 425.0631.


tkb-13-004A-f1 1 1 C:\Bruker\TopSpin4.0.6\Research-data
Ph
O
O
N
Br
[ppm]
[rel]

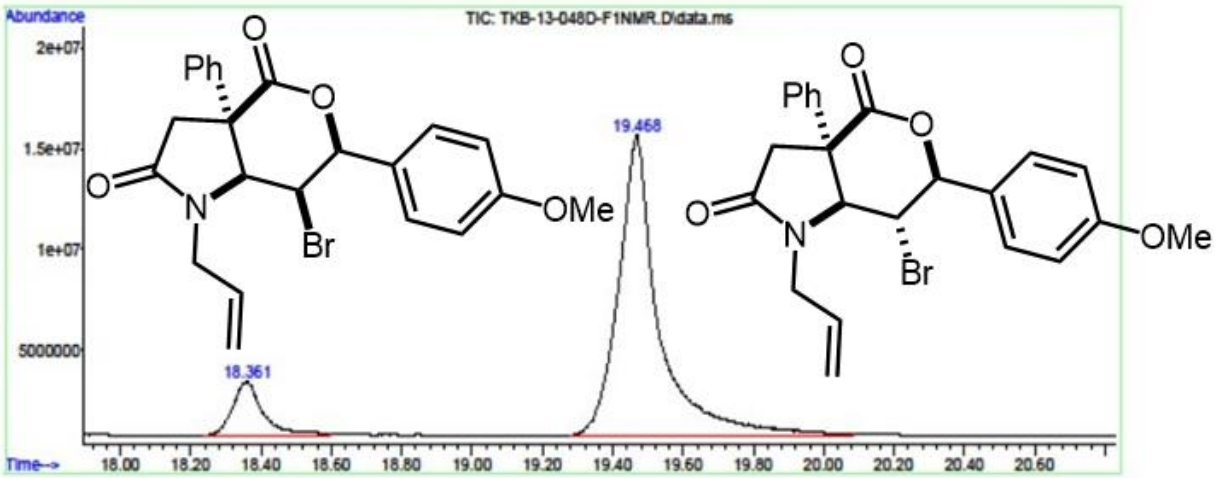

tkb-13-004A-f1 13 1 C:\Bruker\TopSpin4.0.6\Research-data
176.2760
171.0390
137.4473
134.6645
131.7948
129.7679
129.5070
129.0719
128.7266
128.0890
126.0297
118.9681
82.3770
68.6459
62.5941
51.7539
44.1028
44.0648
Ph
O
O
N
Br
[ppm]
[rel]

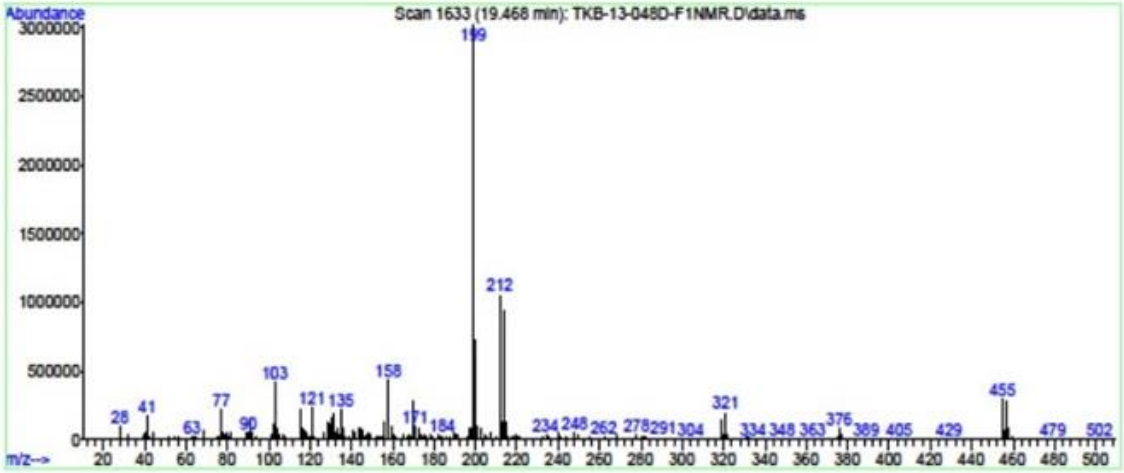


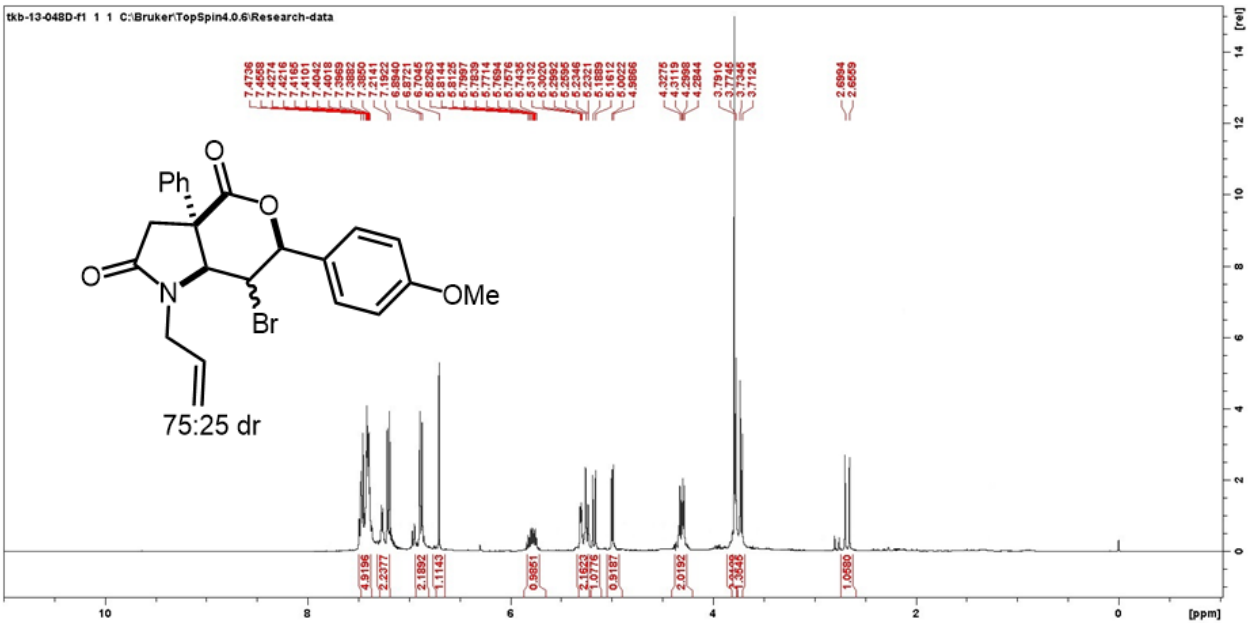
Compound 4p

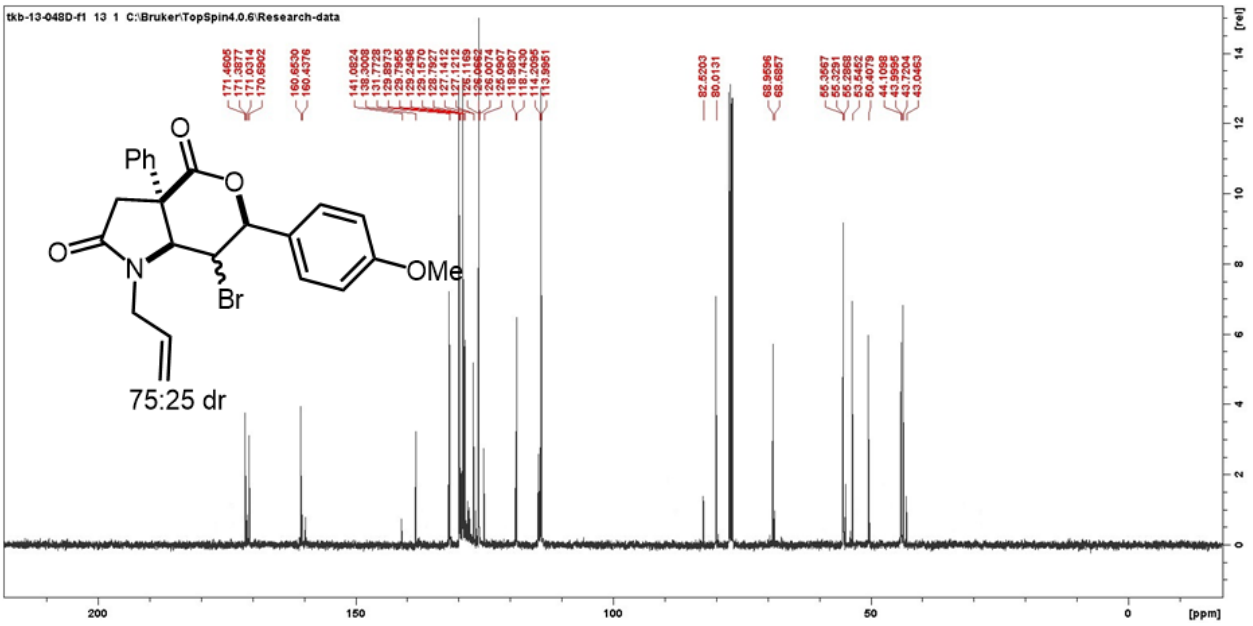
Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 369.4 mg, 81%, 75:25 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.38 (m, 5H), 7.21 – 7.19 (m, 2H), 6.89 – 6.87 (m, 2H), 6.70 (d, 1H), 5.83 – 5.74 (m, 1H), 5.38 – 5.23 (m, 2H), 5.21 – 5.04 (m, 1H), 4.99 (d, J = 6.3 Hz, 1H), 4.33 – 4.28 (m, 2H), 3.79 – 3.71 (m, 4H), 2.68 (d, J = 17.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 171.4, 170.7, 169.4, 160.7, 160.4, 141.1, 138.3, 131.8, 129.9, 129.8, 129.7, 129.3, 129.2, 128.8, 127.1, 127.1, 126.1, 126.1, 126.0, 125.1, 118.8, 114.5, 114.2, 114.0, 114.0, 82.5, 80.0, 69.0, 68.7, 55.4, 55.3, 55.3, 55.3, 54.9, 53.6, 50.4, 48.0, 44.1, 43.7. FTIR (KBr): 3009.7, 2933.6, 1647.4, 1607.2, 1577.1, 1512.0, 1454.2, 1427.6, 1359.8, 1299.2, 1250.9, 1176.0, 1151.5, 1119.6, 1031.3, 990.3, 927.8, 825.4, 765.0. HRMS calc for $C_{23}H_{22}BrNO_4$ 455.0732, found 455.0738.

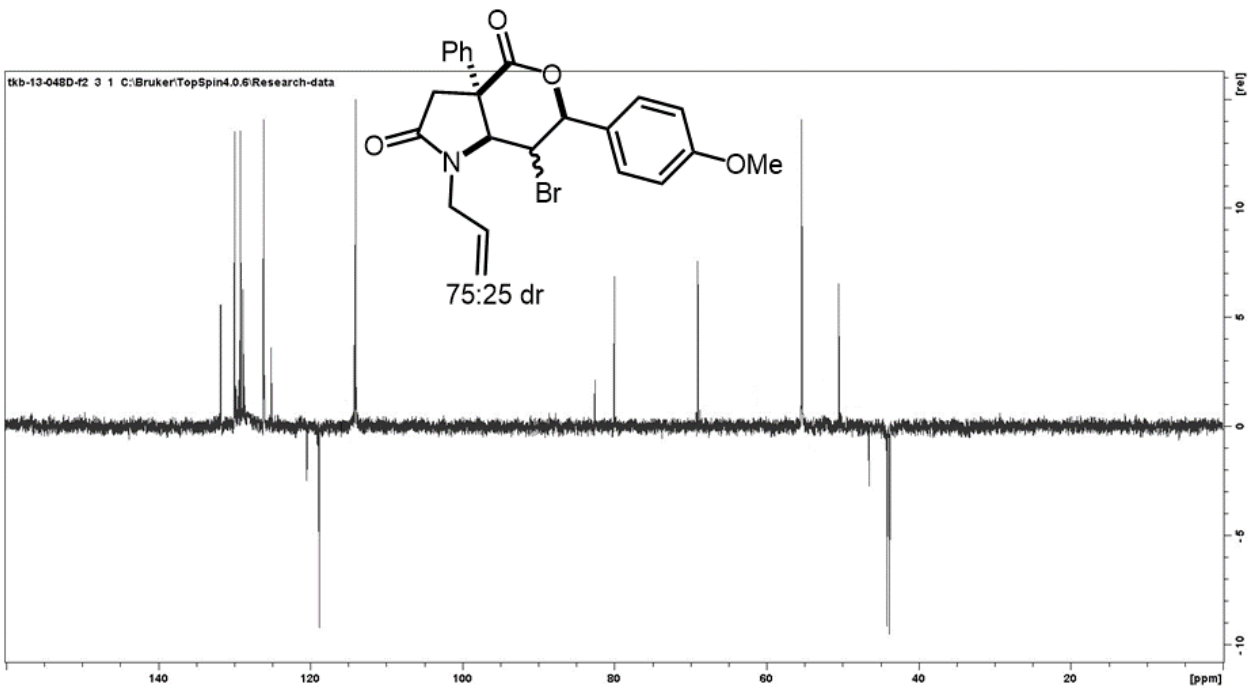
```
File       :C:\GCMS\Beng Research\Data\TKB-13-048D-F1NMR.D
Operator   : Beng
Acquired   : 26 Jan 2021  12:21     using AcqMethod 180-280C-20190419.M
Instrument :    Instrument #1
Sample Name:
Misc Info  :
Vial Number: 1
```





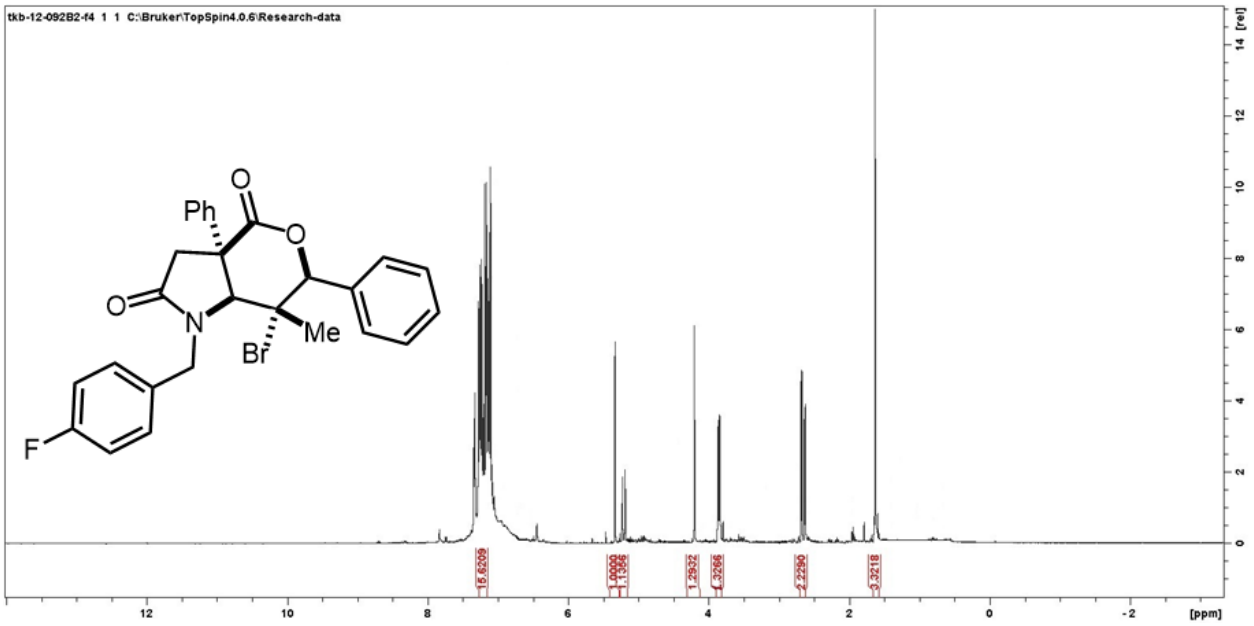

tkb-13-048D-f1 1 1 C:\Bruker\TopSpin4.0.6\Research-data
Ph
O
O
N
Br
OMe
75:25 dr
[ppm]
[rel]

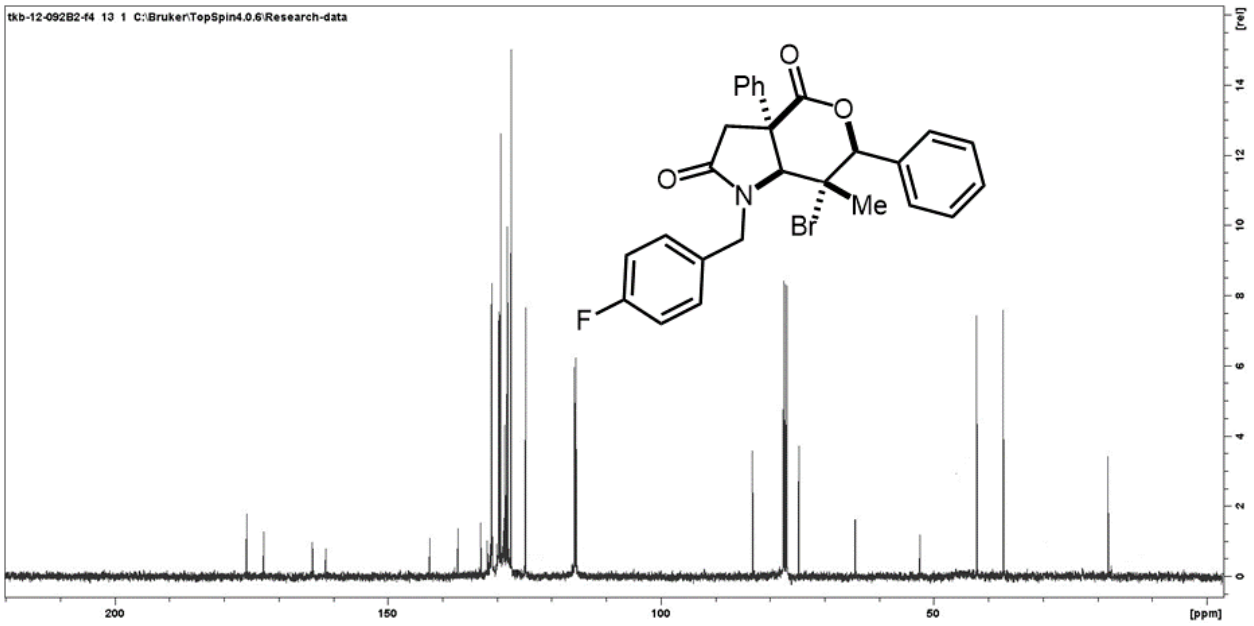

tkb-13-048D-f1 13 1 C:\Bruker\TopSpin4.0.6\Research-data
Ph
O
O
N
Br
OMe
75:25 dr
[ppm]
[rel]

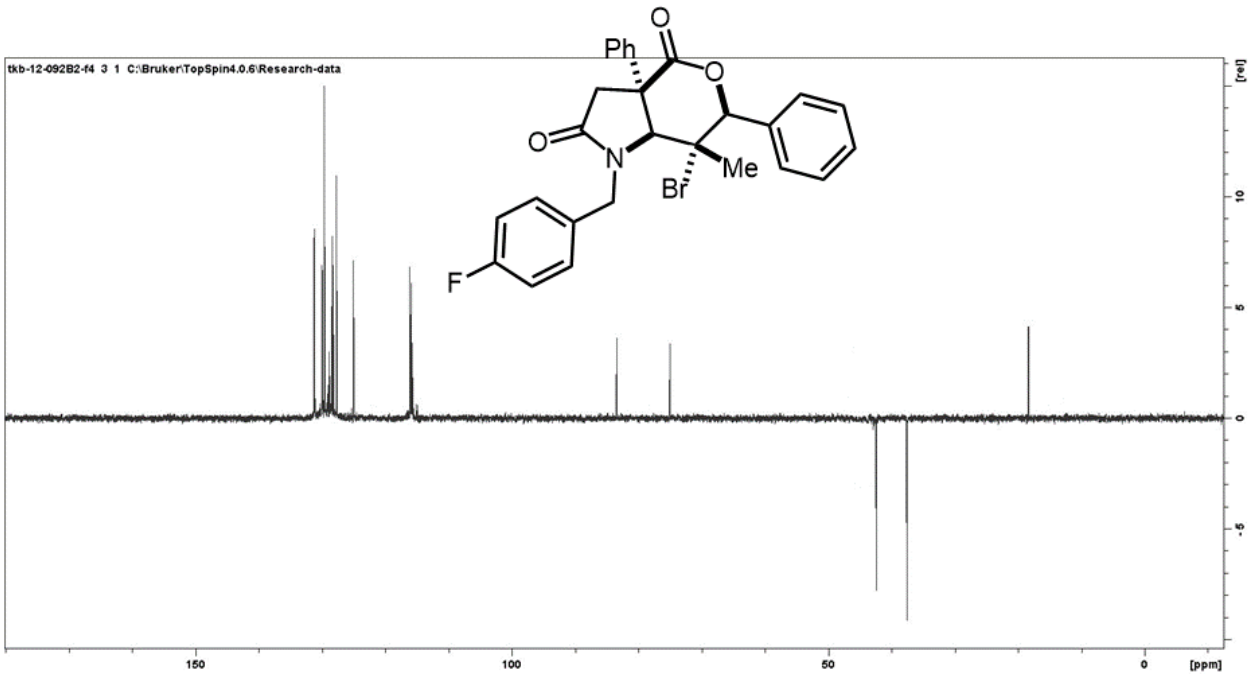


Compound 4q

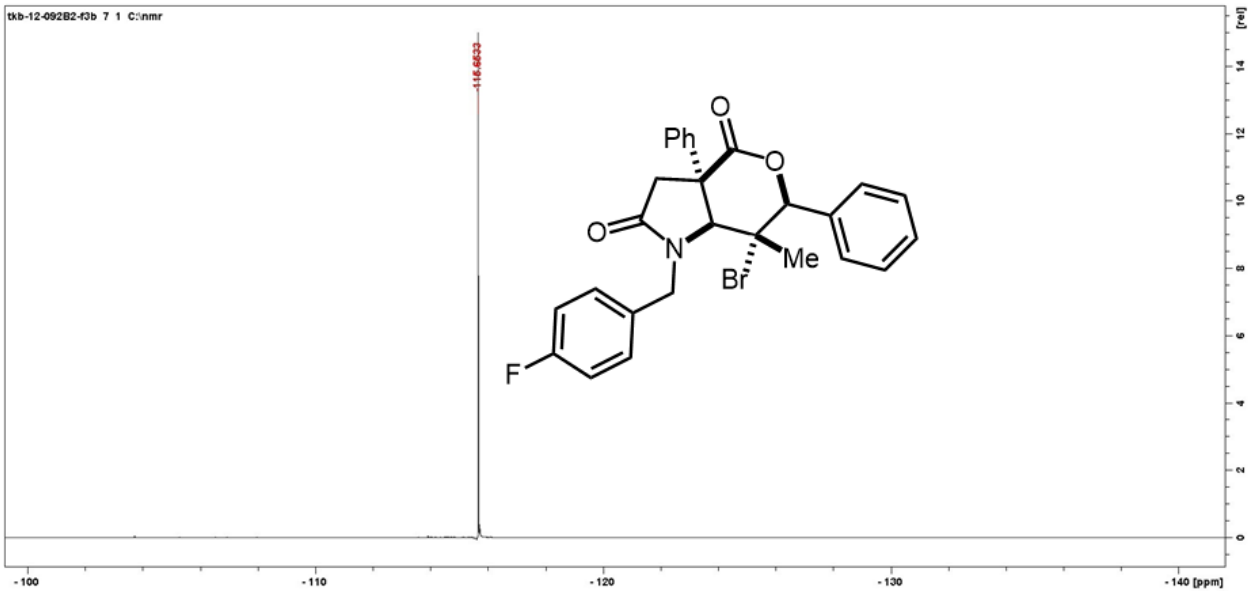
Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 421.9 mg, 83%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.07 (m, 14H), 5.34 (s, 1H), 5.21 (d, J = 14.8 Hz, 1H), 4.21 (s, 1H), 3.84 (d, J = 14.8 Hz, 1H), 2.74 – 2.56 (m, 2H), 1.60 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.5, 175.8, 163.8, 163.7, 161.4, 161.3, 142.3, 131.0, 130.9, 129.7, 129.6, 129.3, 128.1, 127.9, 127.4, 124.7, 115.8, 115.6, 83.1, 74.7, 64.4, 42.1, 37.2, 18.0. FTIR (KBr): 2934.2, 1721.2, 1652.1, 1511.3, 1448.8, 1414.9, 1341.3, 1298.4, 1245.2, 1139.4, 1075.9, 1032.9, 999.4, 832.0, 734.9. HRMS calc for $C_{27}H_{23}BrFNO_3$ 507.0845, found 507.0849.


tkb-12-092B2-f4 1 1 C:\Bruker\TopSpin4.0.6\Research-data
Ph
O
O
O
N
Me
Br
F
15.6209
1.0000
1.1058
1.2932
1.3266
2.2290
3.2118
12
10
8
6
4
2
0
-2
[ppm]
[rel]


tkb-12-092B2-f4 13 1 C:\Bruker\TopSpin4.0.6\Research-data
Ph
O
O
O
N
Me
Br
F
200
150
100
50
[ppm]
[rel]



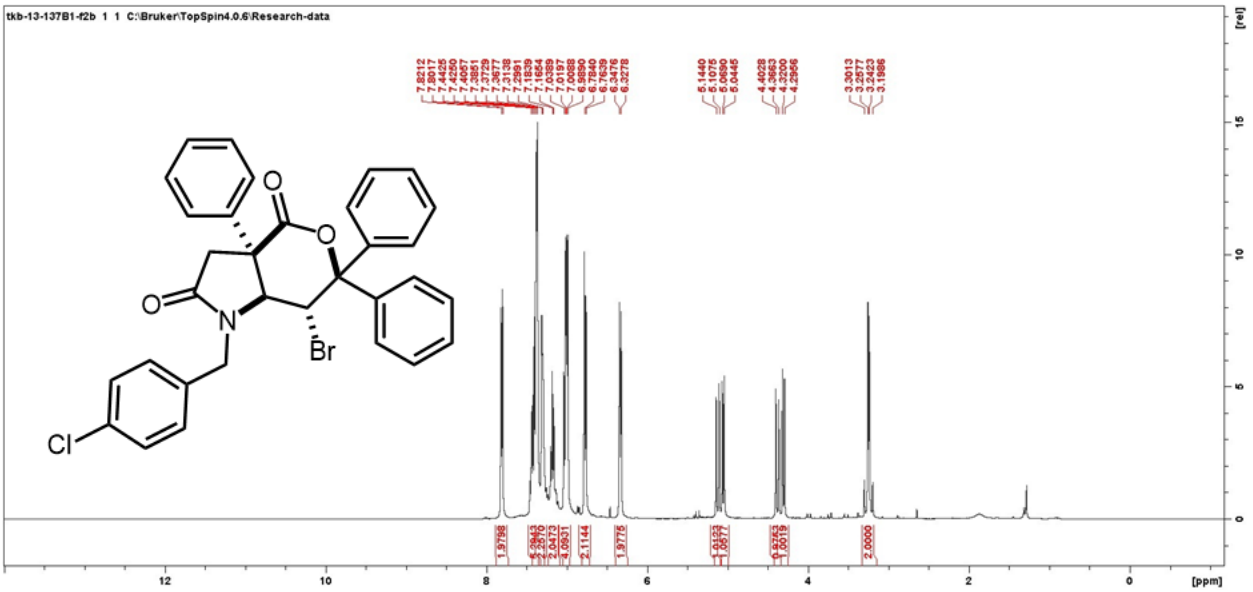
^{19}F NMR

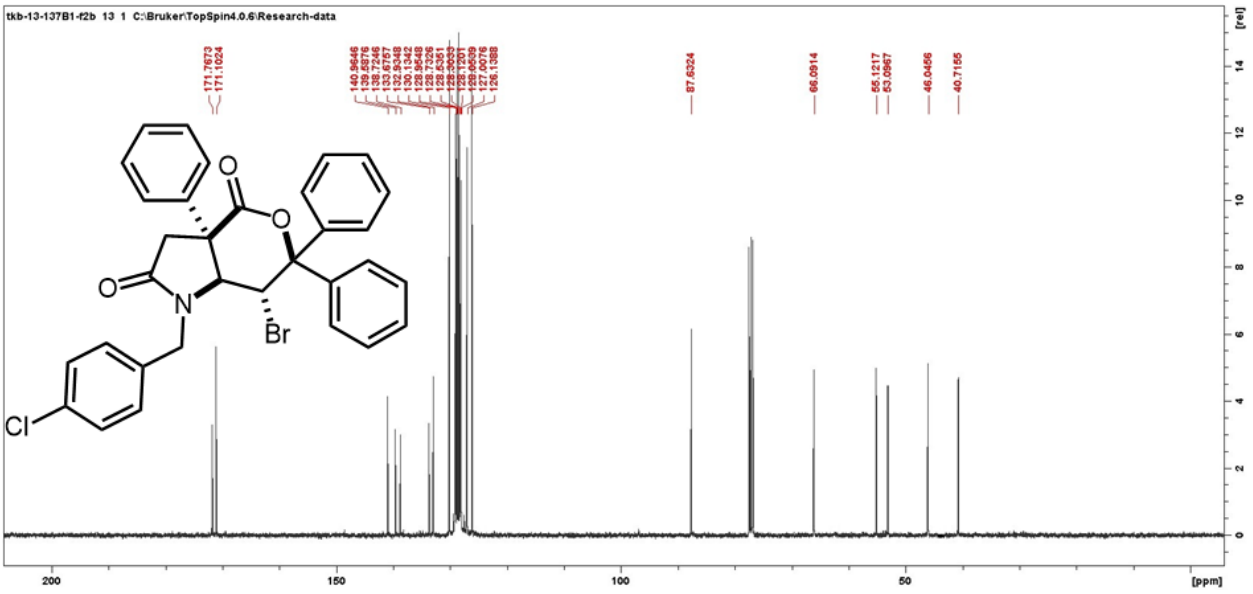


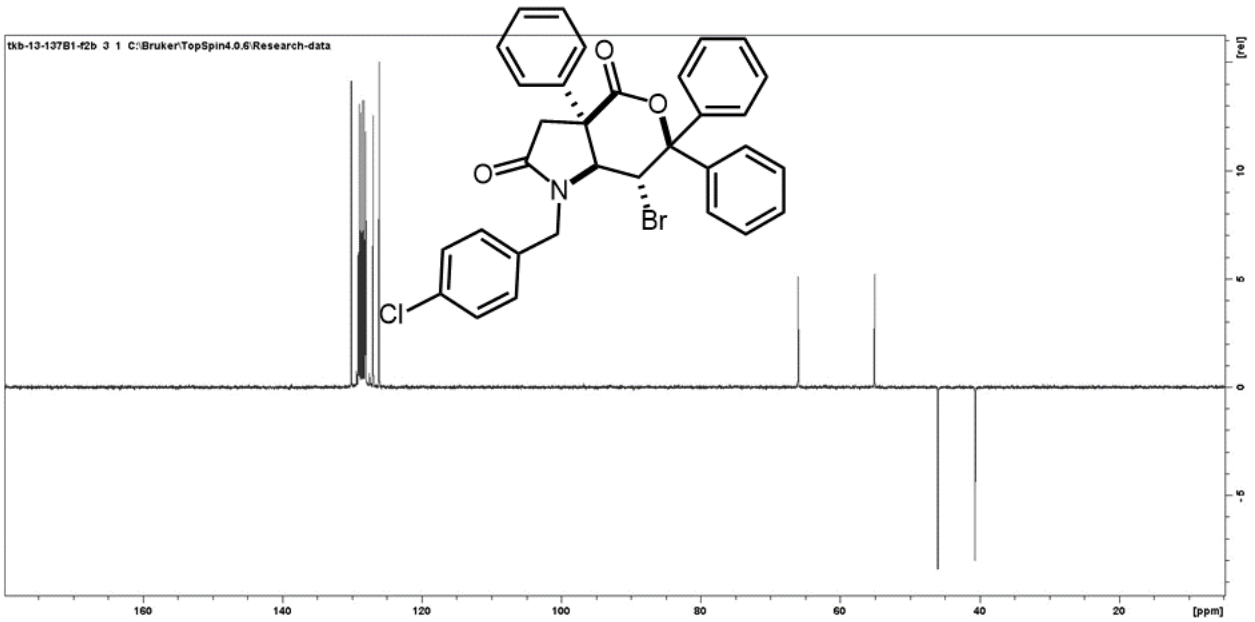
Compound 4r

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Oily substance. Yield = 557.6 mg, 95%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.6 Hz, 2H), 7.43 – 7.30 (m, 7H), 7.17 (q, J = 9.3, 8.3 Hz, 2H), 7.01 (dd, J = 12.3, 7.8 Hz, 4H), 6.77 (d, J = 8.0 Hz, 2H), 6.34 (d, J = 7.8 Hz, 2H), 5.13 (d, J = 14.6 Hz, 1H), 5.06 (d, J = 9.8 Hz, 1H), 4.38 (d, J = 14.6 Hz, 1H), 4.31 (d, J = 9.7 Hz, 1H), 3.32

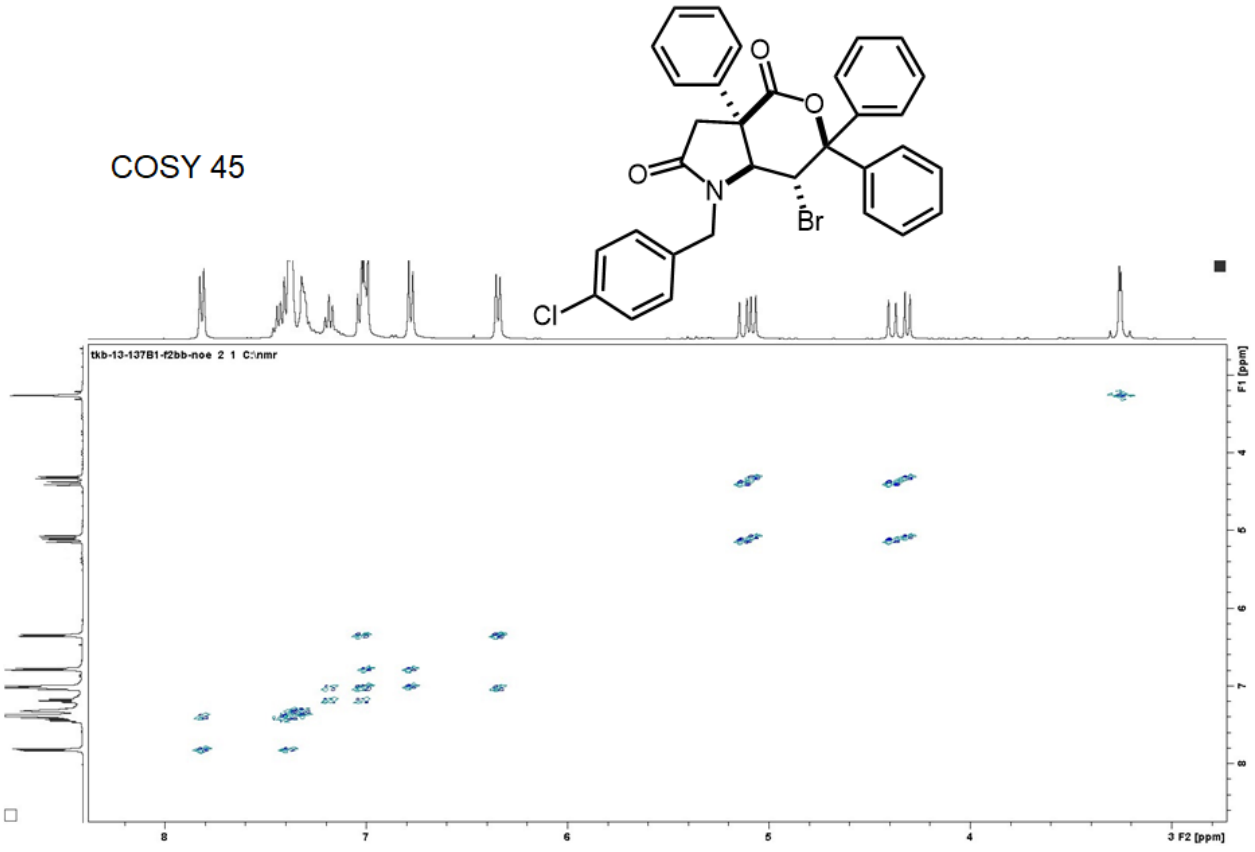
– 3.18 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 171.1, 141.0, 139.6, 138.7, 133.7, 132.9, 130.1, 129.2, 129.1, 129.0, 128.7, 128.5, 128.3, 128.1, 128.1, 127.0, 126.1, 87.6, 66.1, 55.1, 53.1, 46.1, 40.7. FTIR (KBr): 2971.4, 2923.9, 1644.4, 1491.4, 1446.8, 1429.3, 1391.6, 1362.4, 1318.9, 1292.6, 1268.8, 1223.0, 1199.5, 1151.3, 993.1, 905.3, 744.2. HRMS calc for $C_{32}H_{25}BrClNO_3$ 585.0706, found 585.0712.

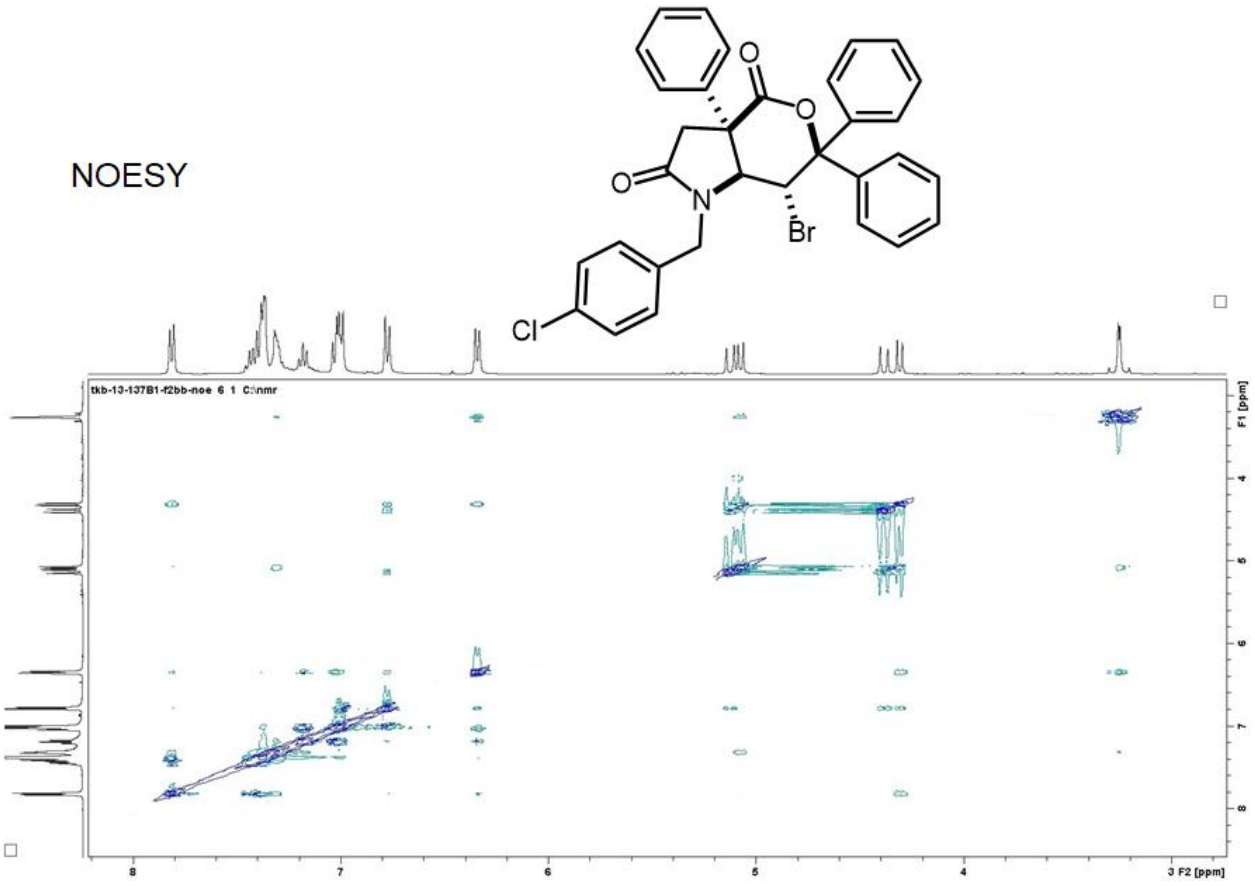





tkb-13-137B1-f2b 3 1 C:\Bruker\TopSpin4.0.6\Research-data
O
O
O
N
Br
Cl
160
140
120
100
80
60
40
20
[ppm]

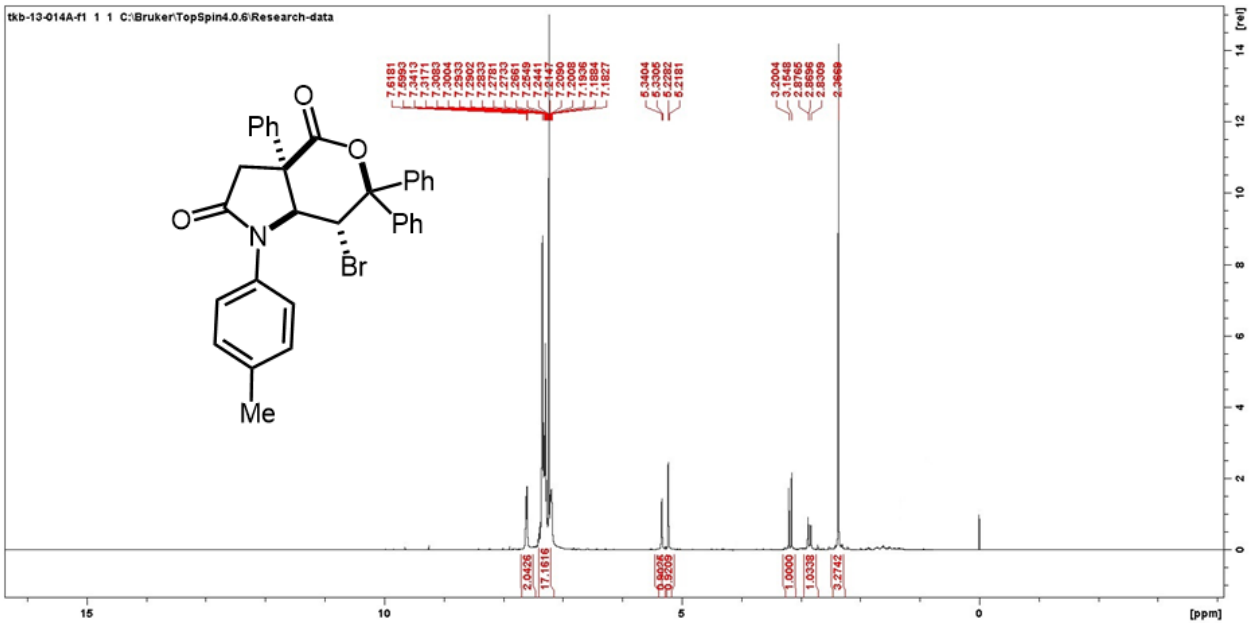
COSY 45

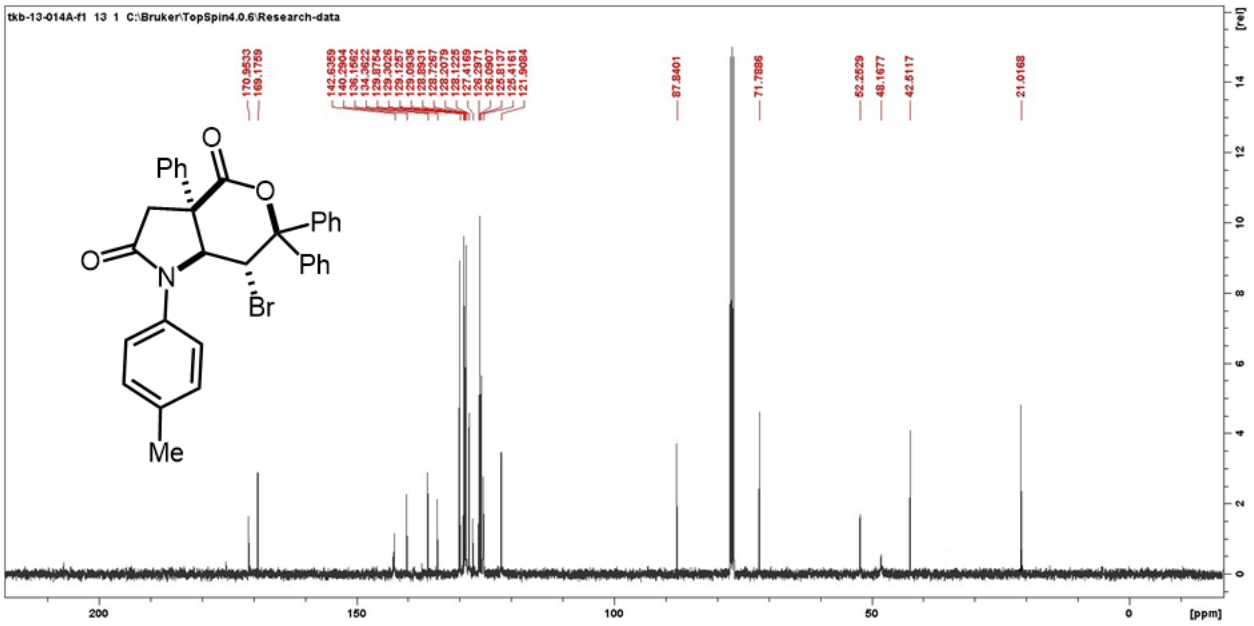

O
O
O
N
Br
Cl
tkb-13-137B1-f2bb-noe 2 1 C:\nmr
F1 [ppm]
8
7
6
5
4
3 F2 [ppm]

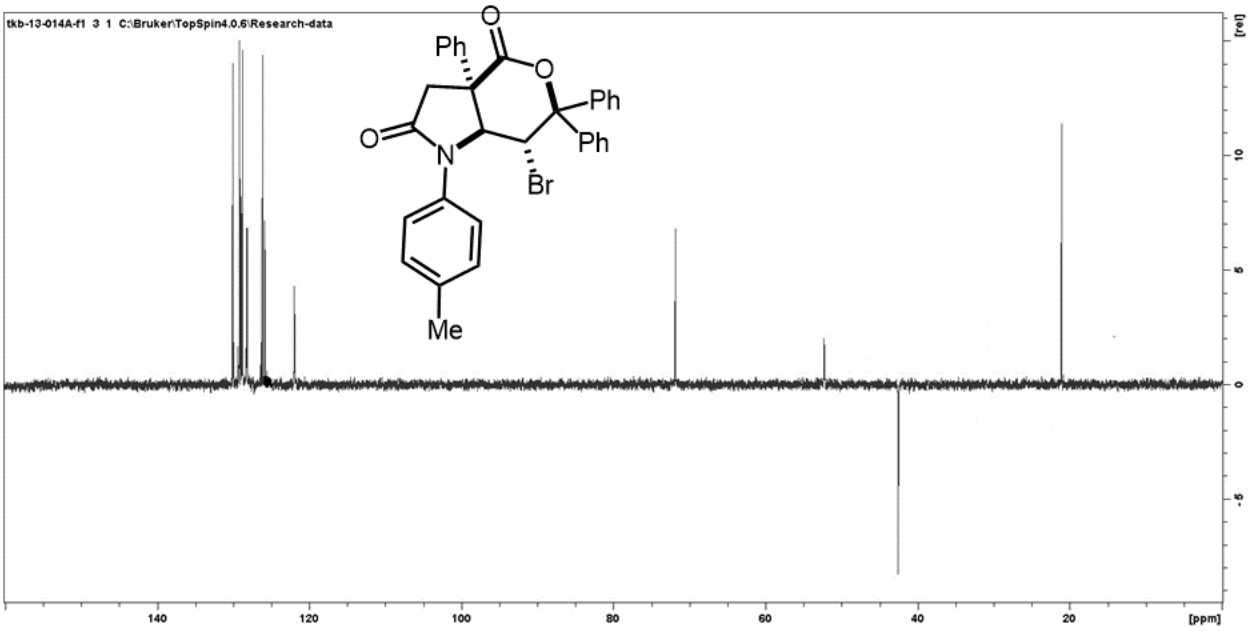


Compound 4s

Prepared in 1 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 508.3 mg, 92%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.7 Hz, 2H), 7.34 – 7.18 (m, 17H), 5.34 (d, *J* = 4.1 Hz, 1H), 5.29 – 5.20 (m, 1H), 3.15 (d, *J* = 17.2 Hz, 1H), 2.88 (d, *J* = 17.2 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 169.2, 142.6, 140.3, 136.2, 134.4, 130.0, 129.9, 129.3, 129.1, 129.1, 128.9, 128.7, 128.2, 128.1, 127.4, 126.3, 126.1, 125.8, 125.4, 121.9, 87.8, 76.8, 71.7, 52.3, 46.0, 42.5, 21.0. FTIR (KBr): 3029.4, 2924.0, 1724.9, 1646.3, 1474.3, 1452.8, 1361.9, 1342.0, 1205.6, 1140.2, 1071.7, 1028.3, 996.4, 775.4. HRMS calc for $C_{32}H_{26}BrNO_3$ 551.1096, found 551.1090.

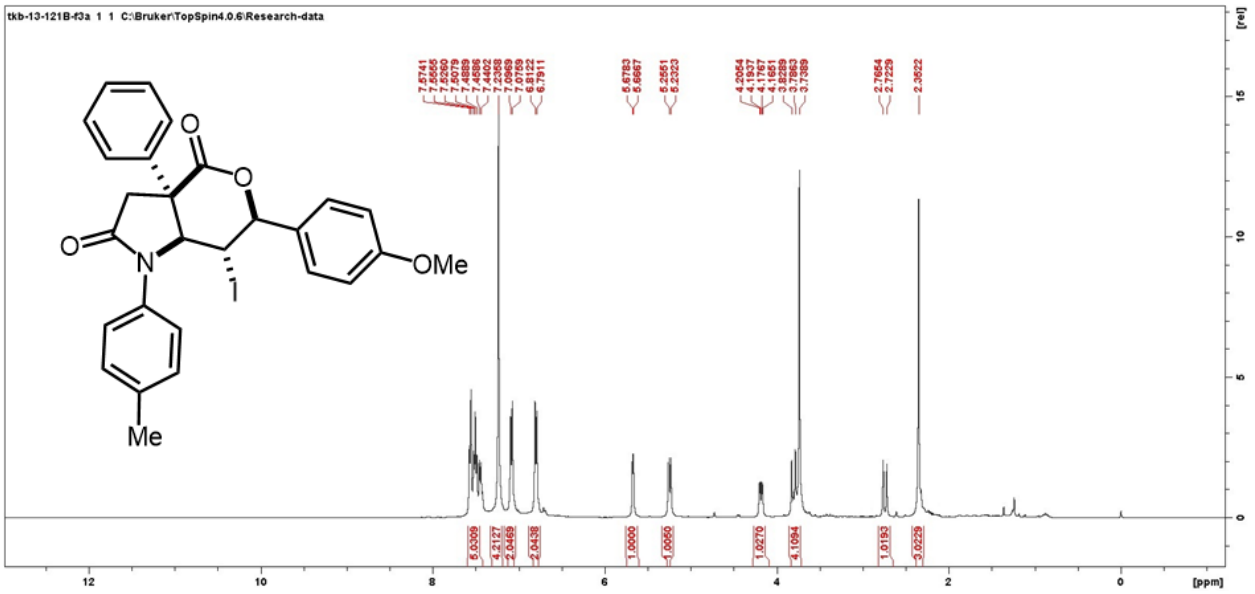

tkb-13-014A-f1 1 1 C:\Bruker\TopSpin4.0.6\Research-data
Ph
O
O
Ph
Ph
O
N
Br
Me
[rel]
[ppm]

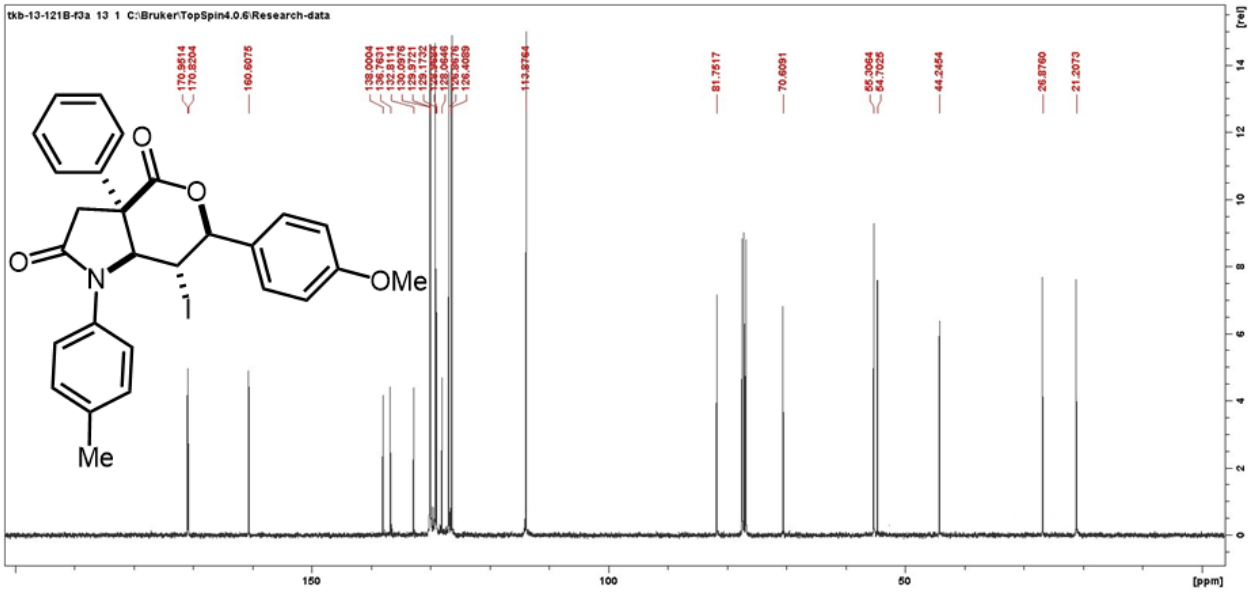

tkb-13-014A-f1 13 1 C:\Bruker\TopSpin4.0.6\Research-data
Ph
O
O
Ph
Ph
O
N
Br
Me
[rel]
[ppm]

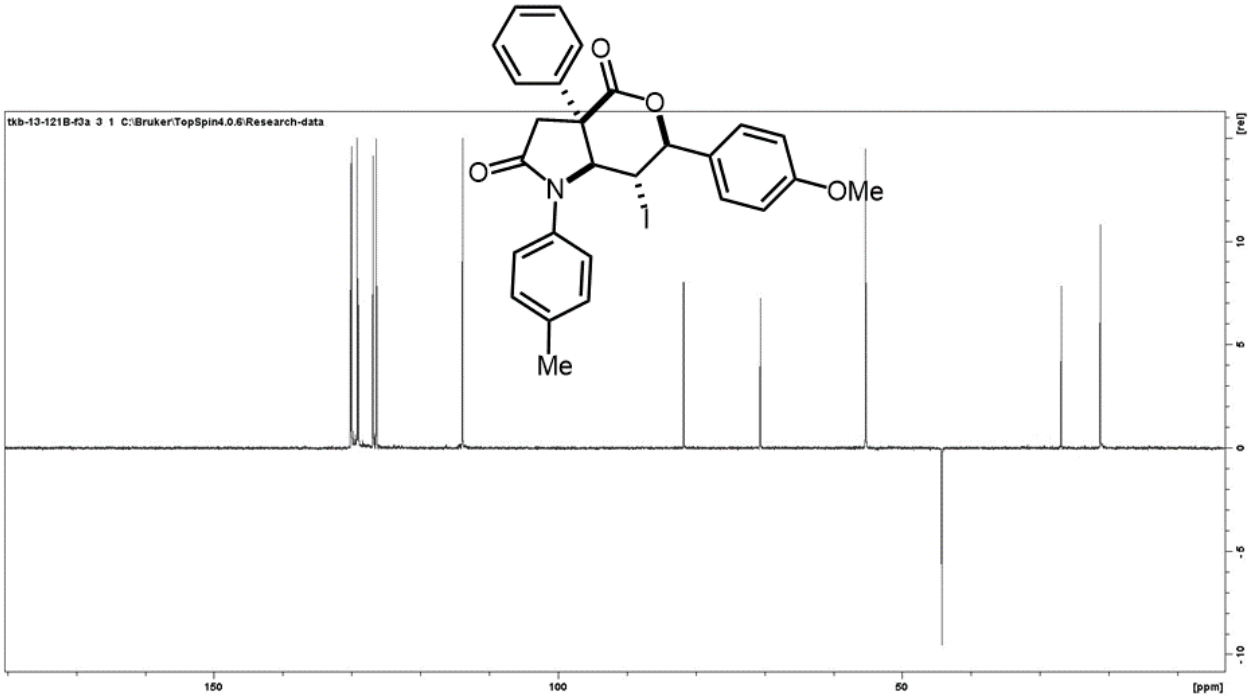


Compound 4t

Prepared in 1 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 492.5 mg, 89%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.44 (m, 5H), 7.27 – 7.23 (m, 4H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.67 (d, *J* = 4.8 Hz, 1H), 5.24 (d, *J* = 11.5 Hz, 1H), 4.19 (dd, *J* = 11.5, 4.8 Hz, 1H), 3.81 (d, *J* = 17.0 Hz, 1H), 3.74 (s, 3H), 2.74 (d, *J* = 17.0 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 170.8, 160.6, 138.0, 136.8, 132.8, 130.1, 130.0, 129.2, 129.0, 128.1, 126.9, 126.4, 113.9, 81.8, 70.6, 55.3, 54.7, 44.3, 26.9, 21.2. FTIR (KBr): 2944.8, 1642.2, 1494.9, 1448.8, 1427.0, 1393.4, 1361.6, 1328.7, 1289.7, 1223.6, 1198.9, 1130.1, 1074.1, 1030.4, 988.5, 966.1, 925.5, 741.8, 673.4. HRMS calc for $C_{27}H_{24}INO_4$ 553.0750, found 553.0756.


tkb-13-121B-f3a 1 1 C:\Bruker\TopSpin4.0.6\Research-data
OMe
Me
[ppm]
[rel]

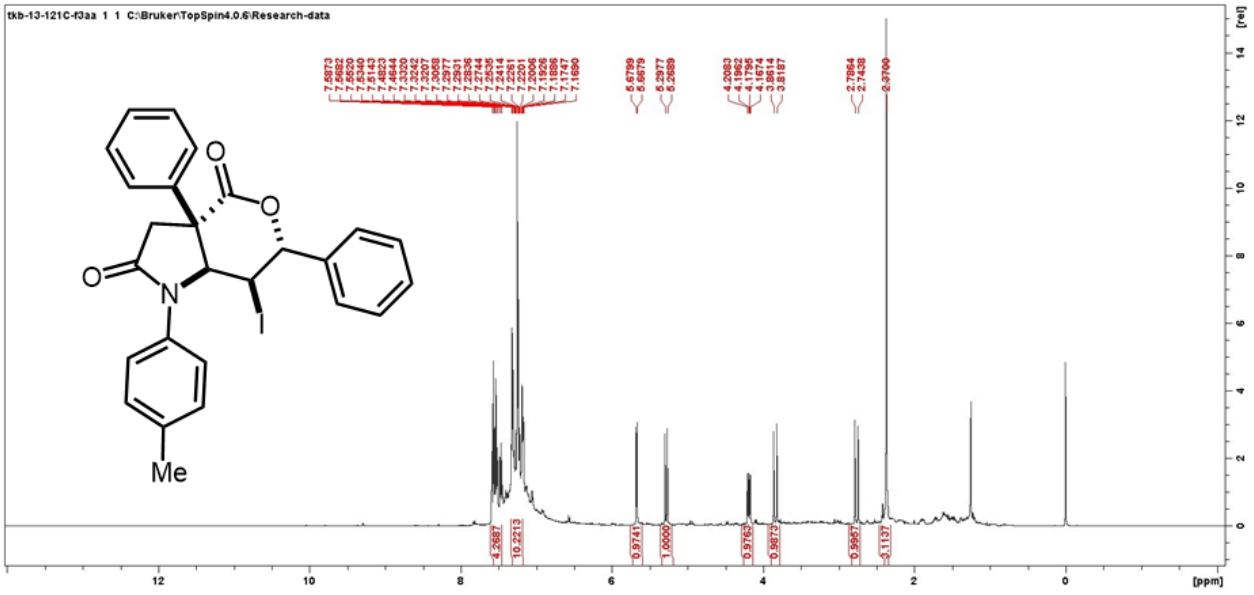

tkb-13-121B-f3a 13 1 C:\Bruker\TopSpin4.0.6\Research-data
OMe
Me
[ppm]
[rel]

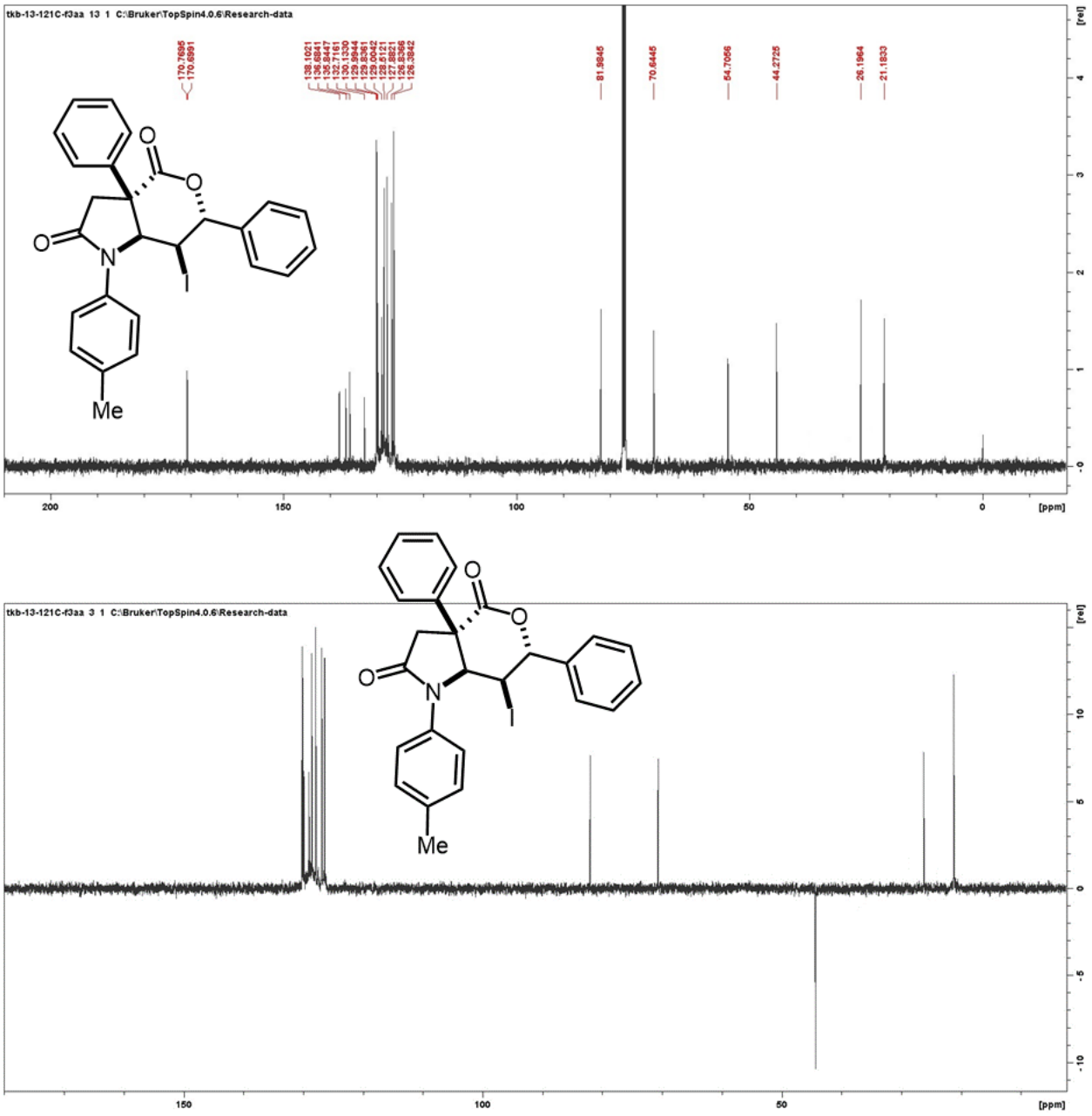


Compound 4u

Prepared in 1 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 481.5 mg, 92%, 95:5 dr.

FTIR (KBr): 3039.4, 2904.0, 1724.9, 1646.3, 1474.3, 1452.8, 1361.9, 1342.0, 1205.6, 1140.2, 1071.7, 986.4, 765.4. HRMS calc for $C_{26}H_{22}INO_3$ 523.0644, found 523.0649.

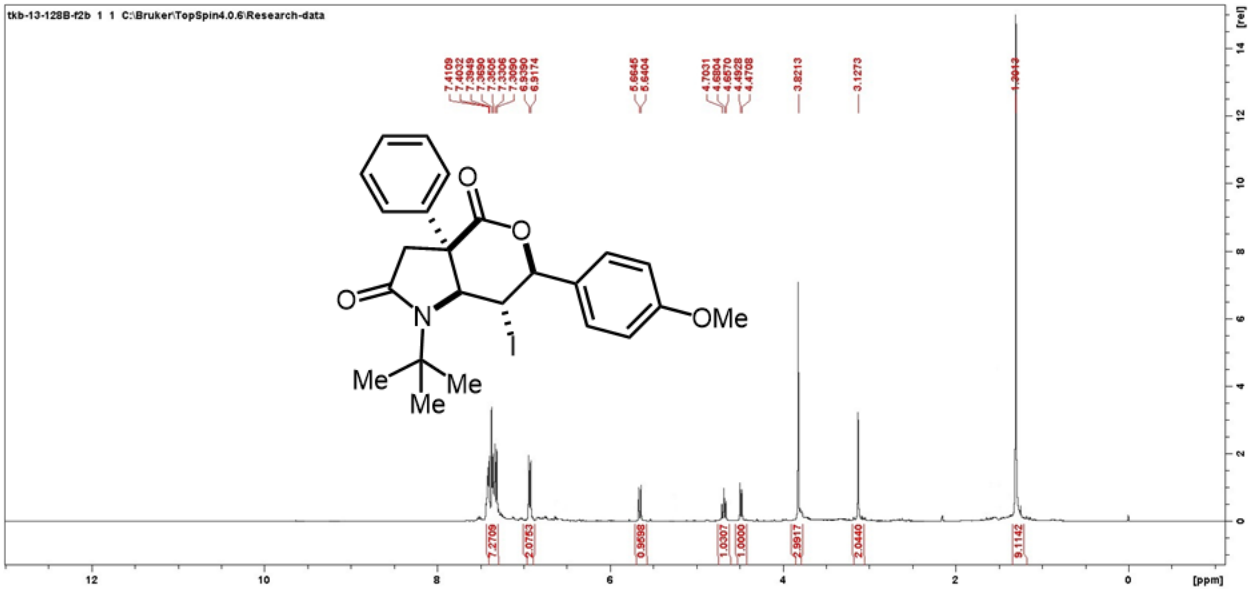


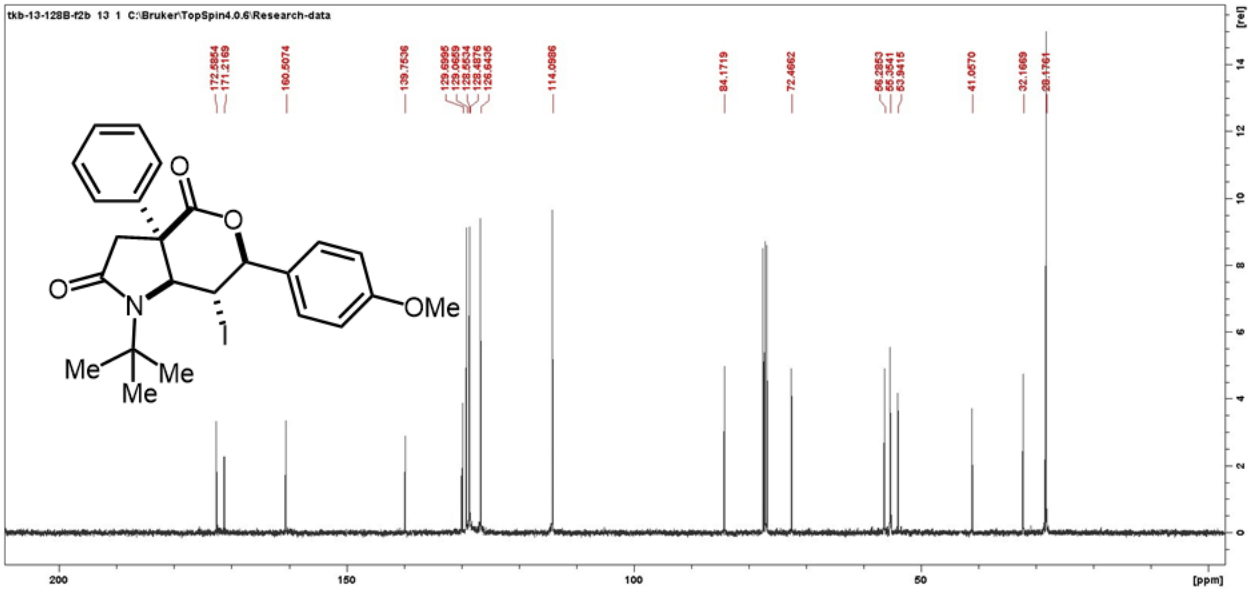


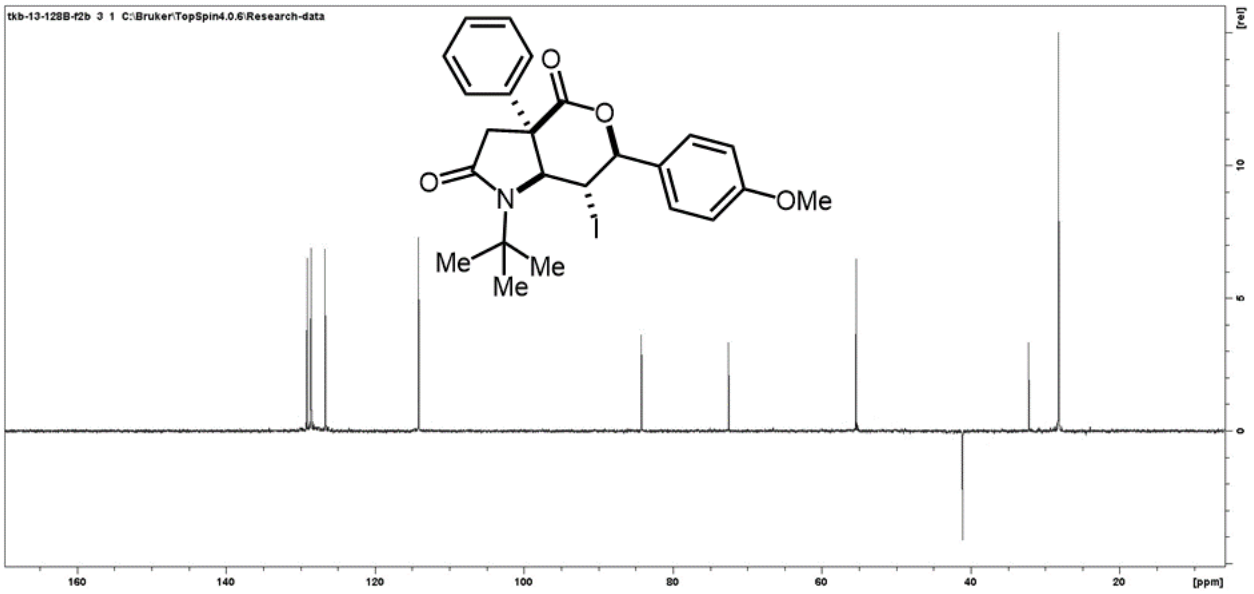
Compound 4v

Prepared in 1 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 488.2 mg, 94%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.30 (m, 7H), 6.93 (d, J = 7.2 Hz, 2H), 5.65 (d, J = 9.6 Hz, 1H), 4.68 (t, J = 9.2 Hz, 1H), 4.48 (d, J = 8.8 Hz, 1H), 3.80 (s, 3H), 3.13 (br. s, 2H), 1.30 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 171.2, 160.5, 139.8, 129.7, 129.1, 128.6, 128.5, 126.7, 114.1, 84.17, 72.47, 56.29, 55.36, 53.94, 41.06, 32.17, 28.18. FTIR (KBr): 3070.2, 2934.6, 2912.8,

2836.5, 1721.4, 1631.8, 1510.6, 1395.7, 1247.4, 1031.3, 820.5, 698.2. HRMS calc for $C_{24}H_{26}INO_4$ 519.0907, found 519.0911.

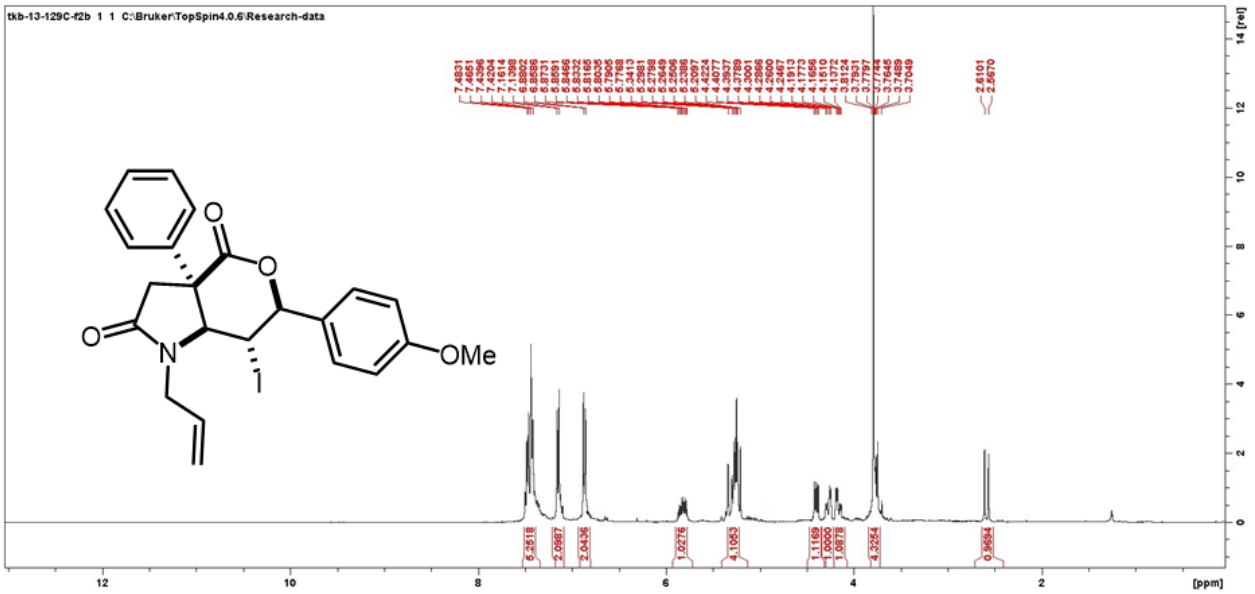


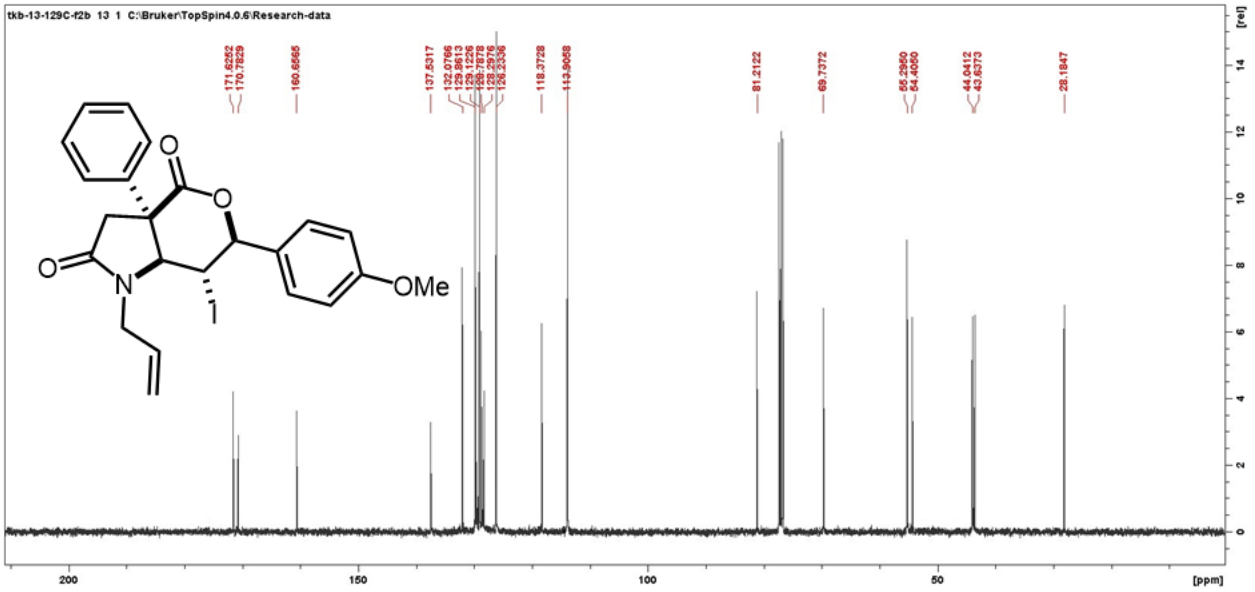


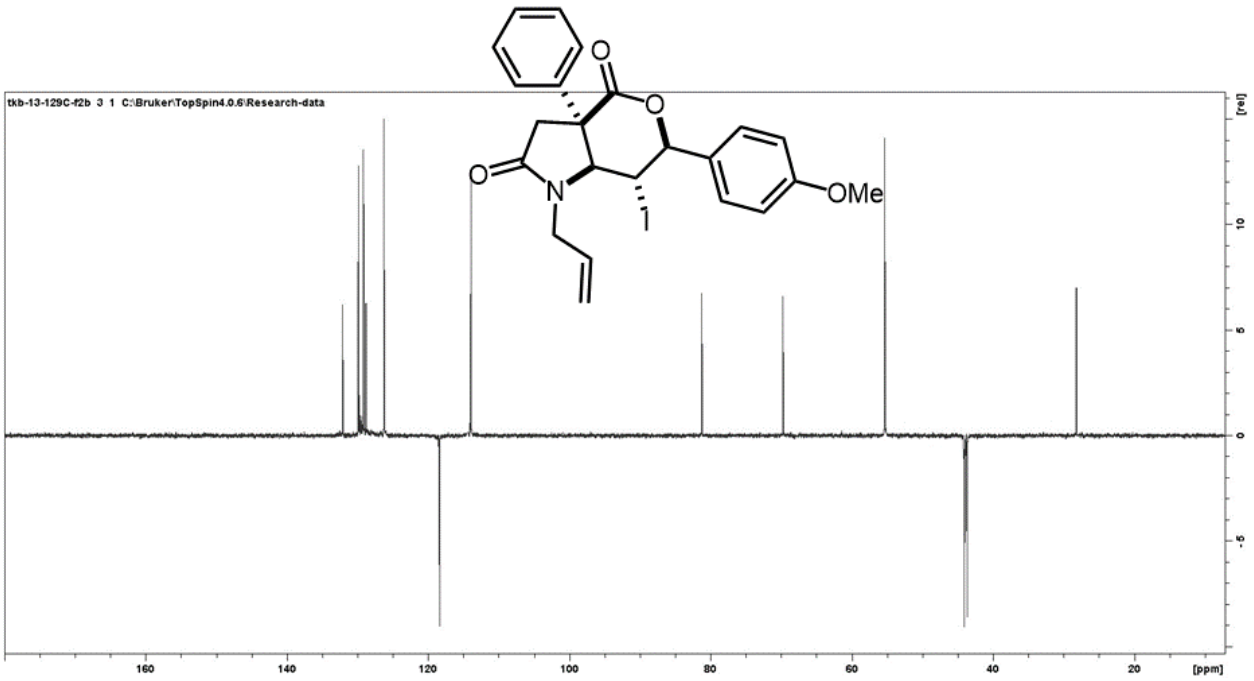


Compound 4w

Prepared in 1 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 442.6 mg, 88%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.42 (m, 5H), 7.14 (dd, *J* = 8.7, 6.7 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.83 (ddt, *J* = 16.3, 10.7, 5.6 Hz, 1H), 5.34 – 5.21 (m, 4H), 4.40 (dd, *J* = 11.6, 5.9 Hz, 1H), 4.27 (dd, *J* = 16.0, 5.4 Hz, 1H), 4.18 (d, *J* = 5.8 Hz, 1H), 4.13 (dd, *J* = 14.6, 5.9 Hz, 1H), 3.79 (s, 3H), 3.89 – 3.75 (m, 1H), 2.59 (d, *J* = 17.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 170.8, 160.7, 137.5, 132.1, 129.9, 129.1, 128.8, 128.3, 126.2, 118.4, 113.9, 81.2, 69.7, 55.3, 54.4, 44.0, 43.6, 28.2. FTIR (KBr): 2990.1, 2934.1, 2910.4, 2836.5, 1721.4, 1631.8, 1510.6, 1395.7, 1247.4, 1031.3, 833.5, 688.9. HRMS calc for $C_{23}H_{22}INO_4$ 503.0594, found 503.0599.


tkb-13-129C-f2b 1 1 C:\Bruker\TopSpin4.0.6\Research-data
OMe
[ppm]

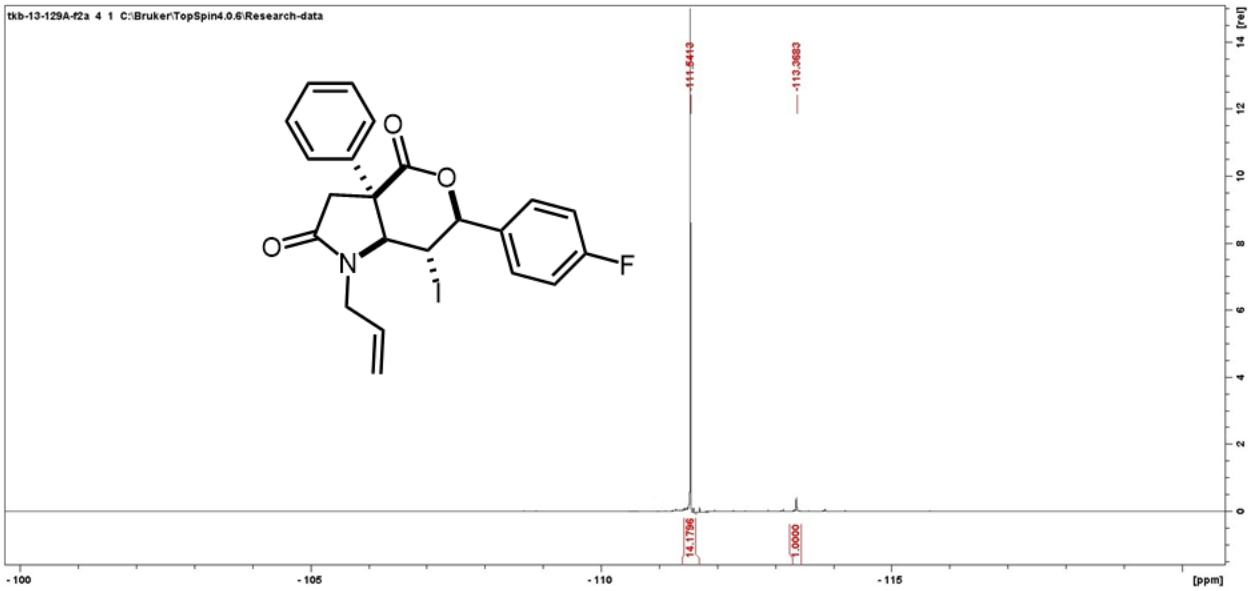

tkb-13-129C-f2b 13 1 C:\Bruker\TopSpin4.0.6\Research-data
OMe
[ppm]

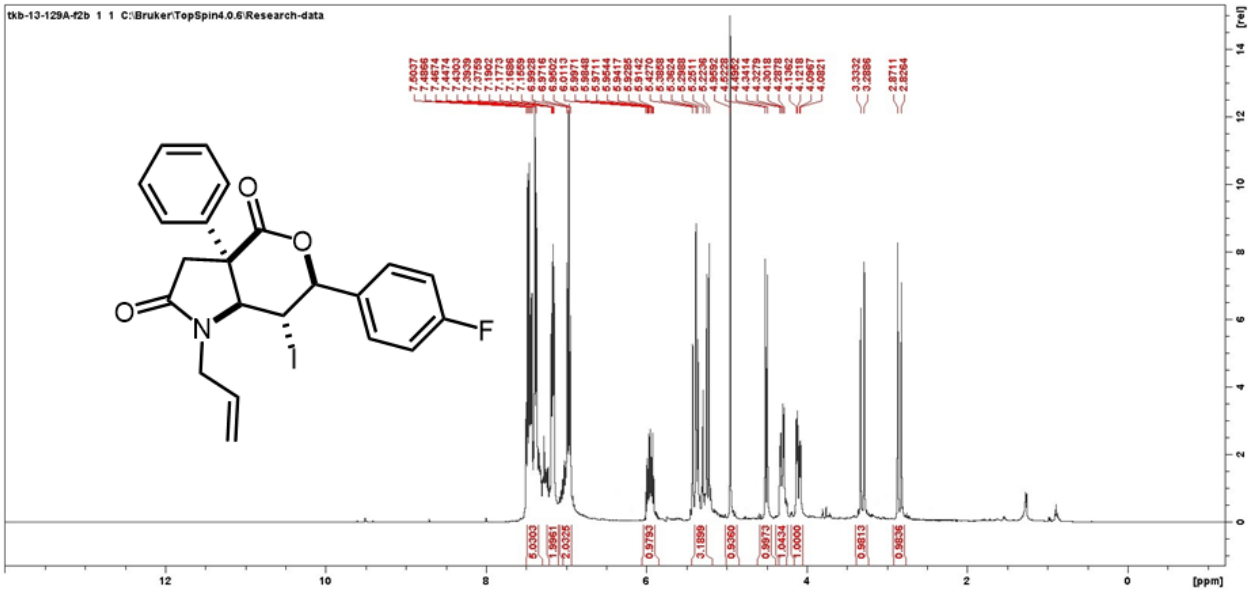


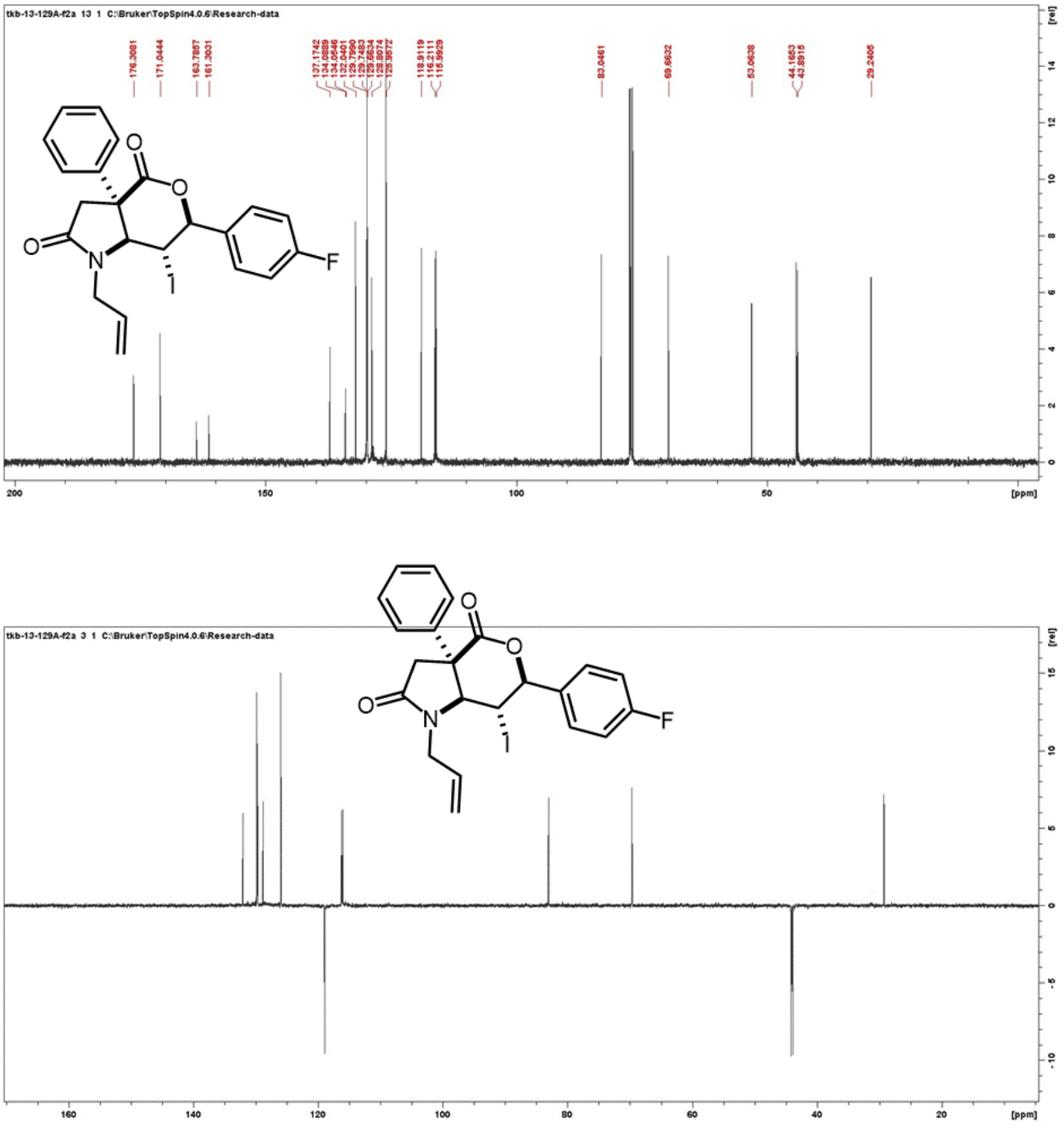
Compound 4x

Prepared in 1 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 471.6 mg, 96%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.43 (m, 5H), 7.19 – 7.16 (m, 2H), 6.99 – 6.95 (m, 2H), 5.97 (ddt, *J* = 16.2, 10.8, 5.7 Hz, 1H), 5.43 – 5.22 (m, 3H), 4.96 (s, 1H), 4.51 (d, *J* = 11.0 Hz, 1H), 4.32 (dd, *J* = 15.8, 5.5 Hz, 1H), 4.11 (dd, *J* = 15.9, 5.9 Hz, 1H), 3.32 (d, *J* = 17.8 Hz, 1H), 2.85 (d, *J* = 17.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.3, 171.1, 163.8, 161.3, 137.2, 134.1, 134.1, 132.1, 129.8, 129.8, 129.7, 128.8, 126.0, 118.9, 116.2, 116.0, 83.1, 69.7, 53.1, 44.2, 43.9, 29.2. FTIR (KBr): 3030.0, 2804.3, 1724.9, 1646.3, 1474.3, 1452.8, 1361.9, 1342.0, 1205.6, 1140.2, 1077.7, 996.4, 765.8. HRMS calc for $C_{22}H_{19}FINO_3$ 491.0394, found 491.0398.

^{19}F NMR


tkb-13-129A-f2a 4 1 C:\Bruker\TopSpin4.0.6\Research-data
-111.5413
-113.3683
14.1796
1.0000
-100
-105
-110
-115
[ppm]
[rel]

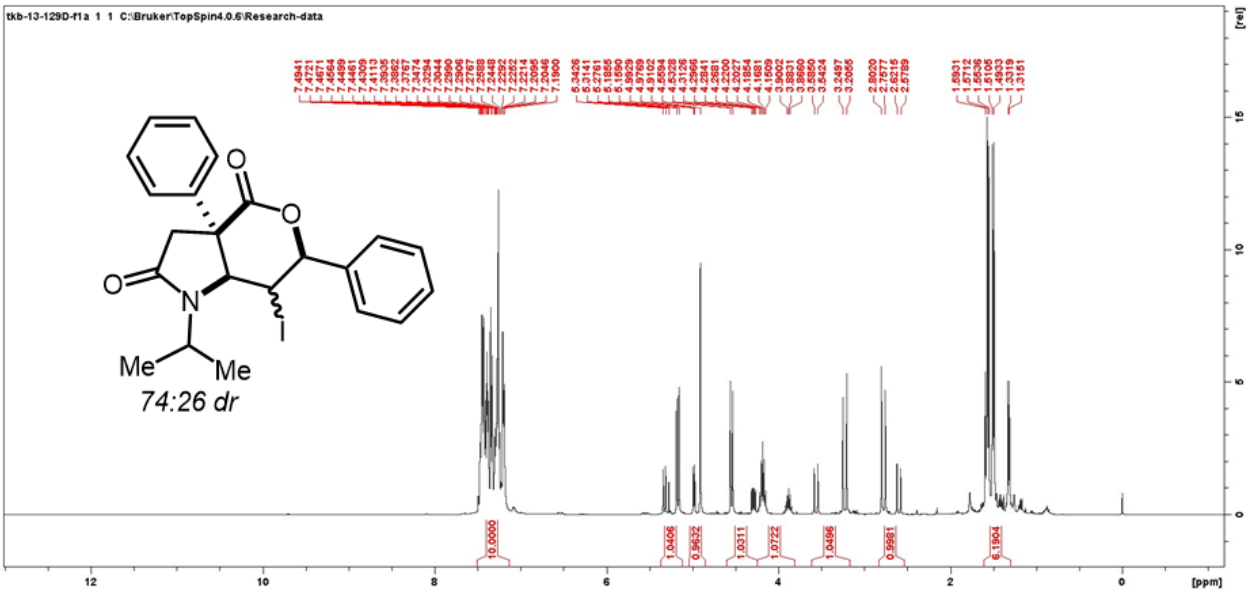

tkb-13-129A-f2b 1 1 C:\Bruker\TopSpin4.0.6\Research-data
5.0000
1.9961
2.0035
0.9753
3.1899
0.9360
0.9973
1.0434
1.0000
0.9613
0.9636
12
10
8
6
4
2
0
[ppm]
[rel]

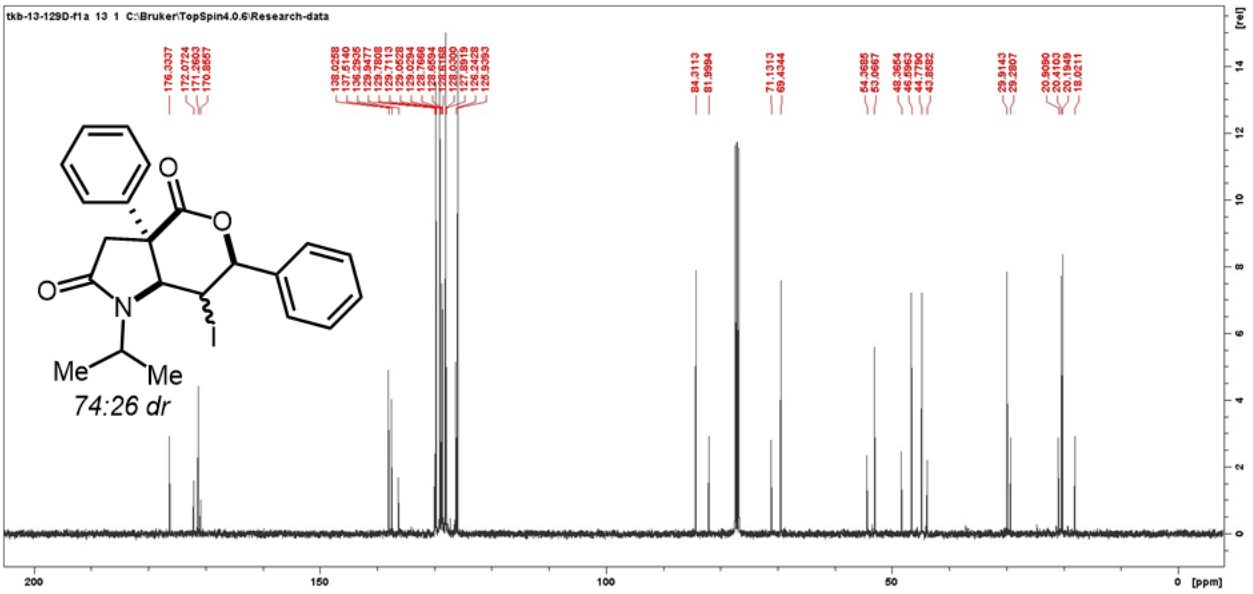


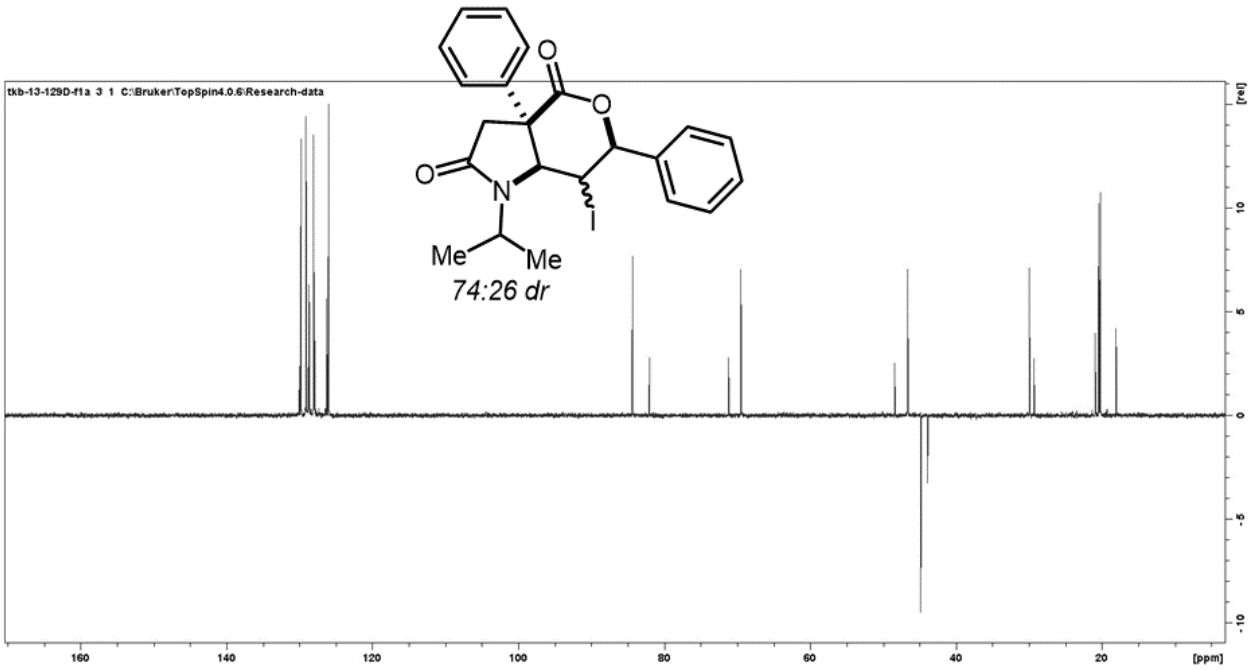
Compound 4y

Prepared in 1 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 427.5 mg, 90%, 74:26 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.19 (m, 10H), 5.32 + 5.17 (d, J = 10.6 Hz, 1H), 4.99 + 4.91 (s, 1H), 4.55 + 4.29 (d, J = 10.6 Hz, 1H), 4.19 + 3.88 (p, J = 7.0 Hz, 1H), 3.55 + 3.23 (d, J = 17.7 Hz, 1H), 2.78 + 2.59 (d, J = 17.7 Hz, 1H), 1.59 – 1.32 (m, 6H). ^{13}C NMR (101 MHz,

$CDCl_3$) δ 176.3, 172.1, 171.3, 170.9, 138.0, 138.0, 137.5, 136.3, 130.0, 129.8, 129.7, 129.1, 129.0, 128.8, 128.7, 128.6, 128.0, 127.9, 126.3, 125.9, 84.3, 82.0, 71.1, 69.4, 54.4, 53.1, 48.4, 46.6, 44.8, 43.9, 29.9, 29.3, 20.91, 20.4, 20.2, 18.0. FTIR (KBr): 2986.1, 2927.2, 1721.8, 1650.2, 1492.0, 1438.5, 1362.3, 1320.5, 1290.1, 1206.3, 1180.3, 1146.7, 1132.4, 985.8, 914.9, 703.1. HRMS calc for $C_{22}H_{22}INO_3$ 475.0644, found 475.0648.

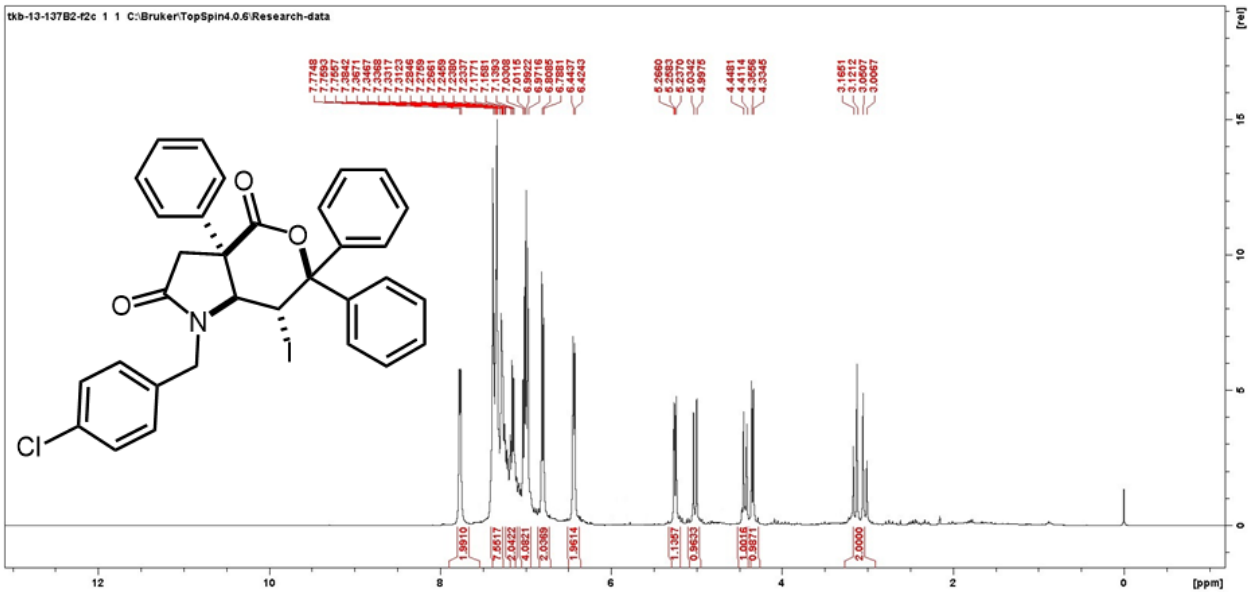


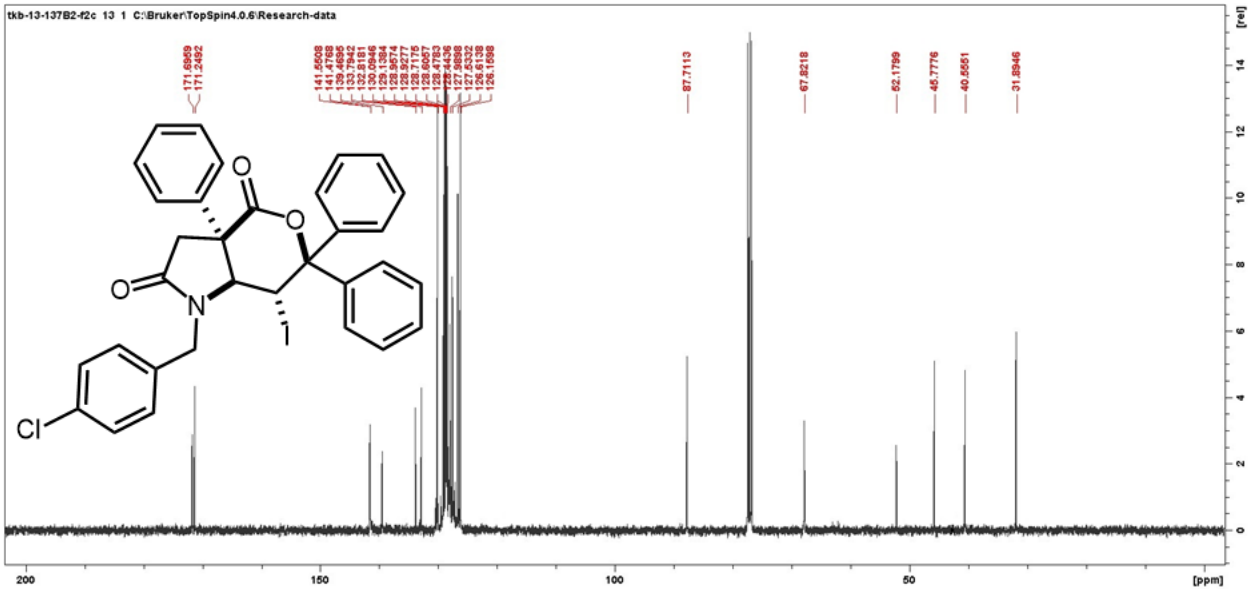


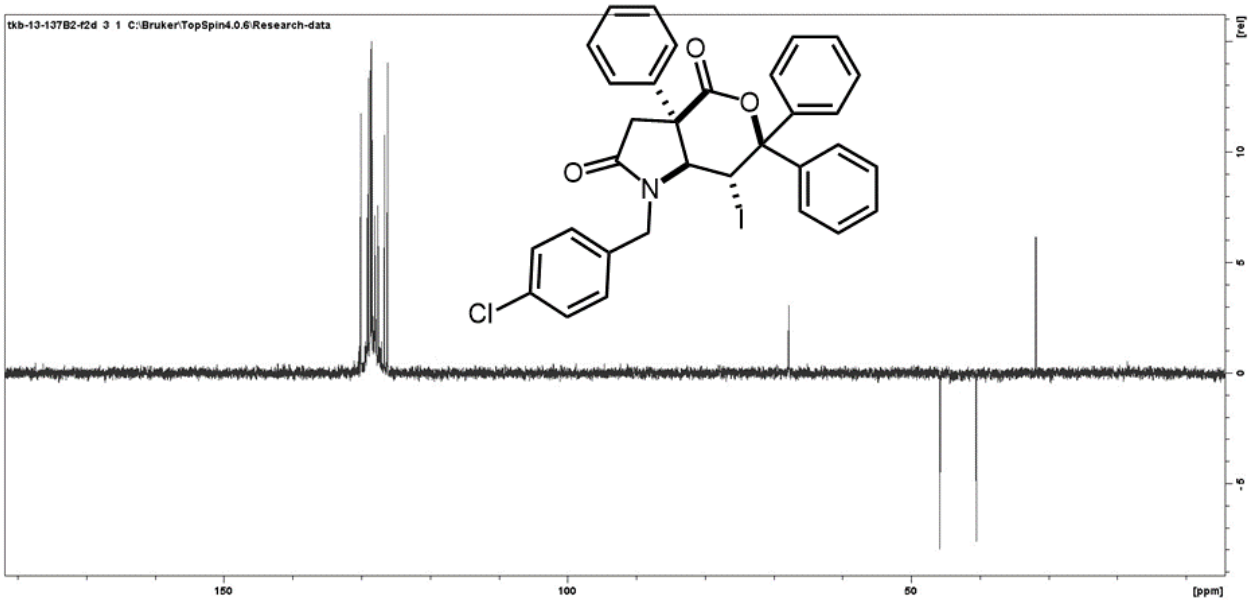


Compound 4z

Prepared in 1 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 608.6 mg, 96%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.8 Hz, 2H), 7.38 – 7.31 (m, 7H), 7.17 (q, *J* = 9.3, 8.3 Hz, 2H), 7.03 – 6.97 (m, 4H), 6.79 (d, *J* = 8.0 Hz, 2H), 6.43 (d, *J* = 7.8 Hz, 2H), 5.25 (d, *J* = 14.6 Hz, 1H), 5.00 (d, *J* = 9.8 Hz, 1H), 4.42 (d, *J* = 14.6 Hz, 1H), 4.34 (d, *J* = 9.7 Hz, 1H), 3.16 – 3.00 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 171.2, 141.5, 139.6, 138.7, 133.7, 132.9, 130.1, 129.2, 129.1, 129.0, 128.7, 128.5, 128.3, 128.1, 128.1, 127.0, 126.2, 87.7, 67.8, 52.2, 45.8, 40.5, 31.9. FTIR (KBr): 3002.5, 2958.9, 1764.3, 1707.5, 1678.7, 1601.0, 1539.9, 1511.3, 1464.4, 1435.3, 1414.9, 1369.5, 1286.5, 1268.5, 1246.0, 1197.2, 1154.7, 1121.6, 1035.6, 977.8, 908.1. HRMS calc for $C_{32}H_{25}ICINO_3$ 633.0568, found 633.0562.


tkb-13-137B2-f2c 1 1 C:\Bruker\TopSpin4.0.6\Research-data
[ppm]
[rel]


tkb-13-137B2-f2c 13 1 C:\Bruker\TopSpin4.0.6\Research-data
87.7113
67.8218
52.1799
45.7776
40.8661
31.8946
[ppm]
[rel]



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) T. K. Beng, J. Fessenden, K. Quigley, J. Eichwald, and J. Zesiger, *New J. Chem.,* under review.