# An Asymmetric Ugi Three-Component Reaction Induced by Chiral Cyclic Imines: Synthesis of Morpholin- or Piperazine-keto-Carboxamide Derivatives

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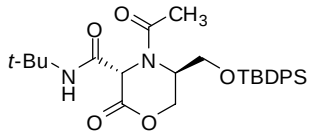
SUPPORTING INFORMATION

Solvents for reaction were distilled prior to use: Tetrahydrofuran was distilled from Na/benzophenone, $CH_2Cl_2$ and toluene from $CaH_2$, Methanol was distilled from magnesium turnings. All reagents were obtained from commercial suppliers unless otherwise stated. IR spectra were recorded on a commercial spectrophotometer. Optical rotations were reported as follows: $[\alpha]_D^T$ (c: g/100 mL, in solvent). $^1$H-NMR spectra were recorded on commercial instruments (400 or 600 MHz) with TMS as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constants (Hz), integration. $^{13}$C-NMR data were collected on commercial instruments (100 or 150 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. HR-ESIMS spectra were recorded using a commercial apparatus and methanol or Dichloromethane was used to dissolve the sample.


O
CH3
t-Bu
N
H
O
N
OTBDPS
O
O

**4a**


8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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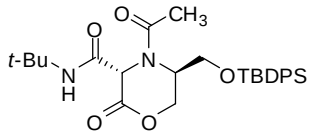
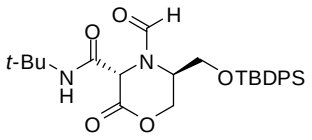
0.0
ppm


O
CH3
t-Bu
N
H
O
N
OTBDPS
O
O

**4a**


180
160
140
120
100
80
60
40
20


O
H
O
t-Bu
N
H
N
OTBDPS
O
O

**4b**


8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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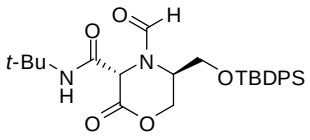
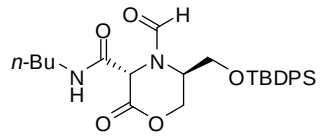
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


O
H
O
t-Bu
N
H
N
OTBDPS
O
O

**4b**


180
160
140
120
100
80
60
40
20


O
H
O
n-Bu
N
H
N
OTBDPS
O
O

**4c**


8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.0
3.5
3.0
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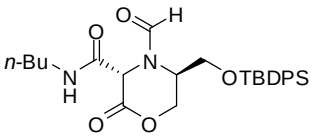
1.5
1.0
0.5
0.0
ppm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H
O
n-Bu
N
H
N
OTBDPS
O
O

**4c**


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140
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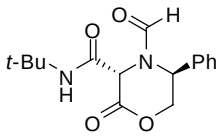
100
80
60
40
20


O
H
O
t-Bu
N
H
N
Ph
O
O

**4d**


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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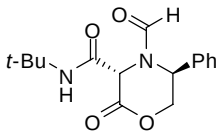
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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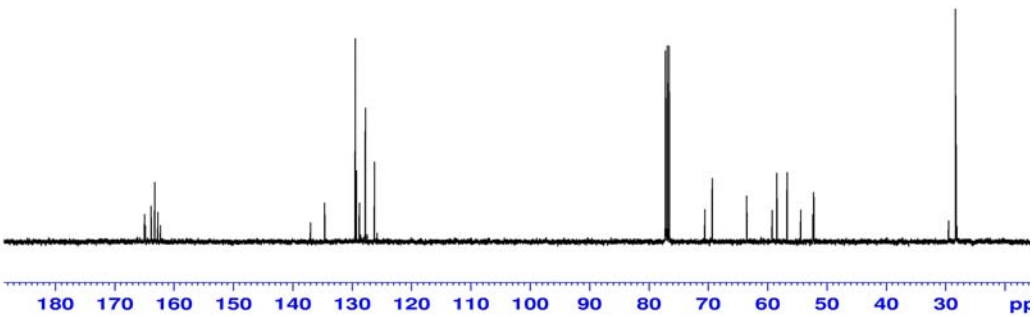
H
O
t-Bu
N
H
N
Ph
O
O

**4d**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100
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80
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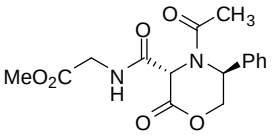
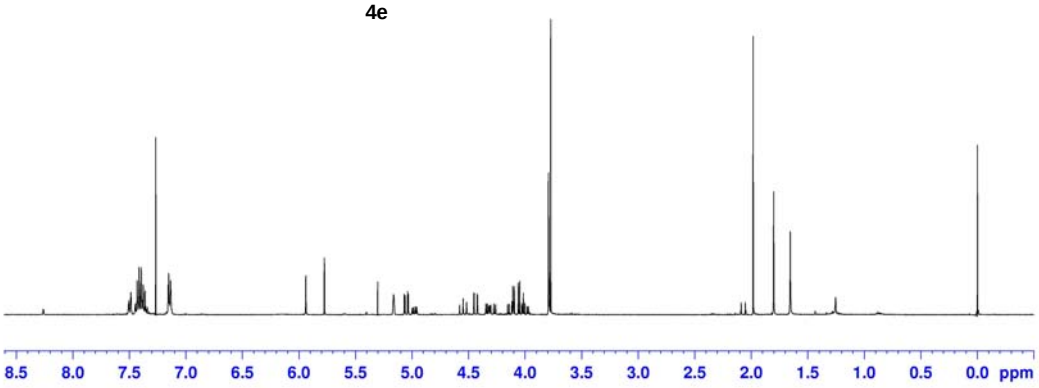
60
50
40
30



**4e**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7.5
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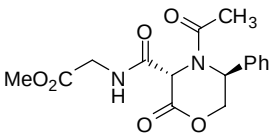
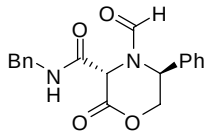
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm



**4e**


180
160
140
120
100
80
60
40
20



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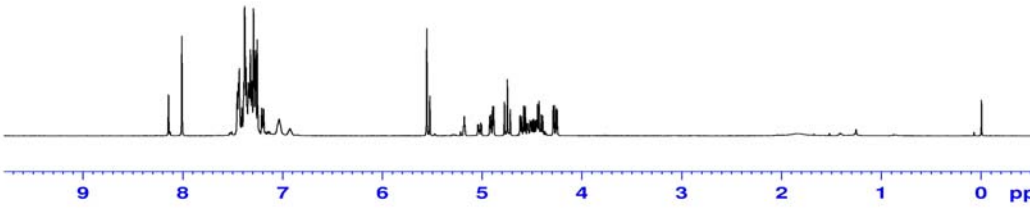
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4
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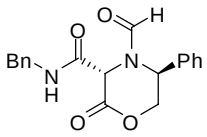
2
1
0
pp



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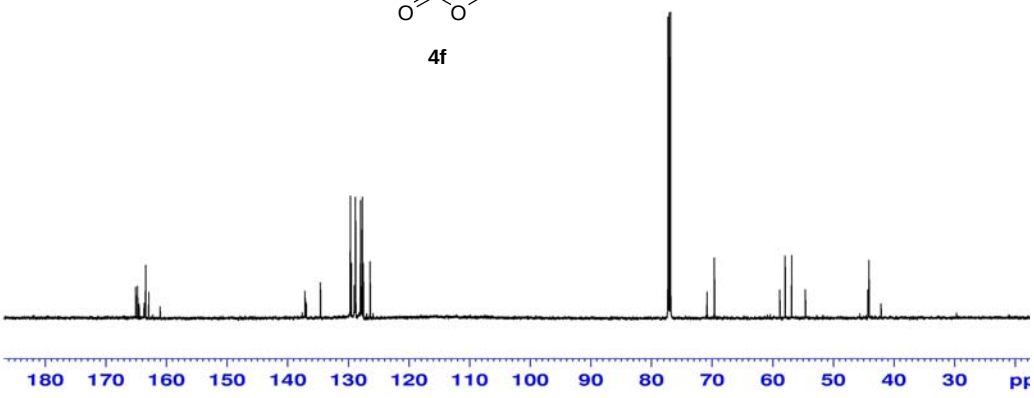
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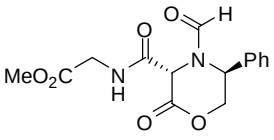
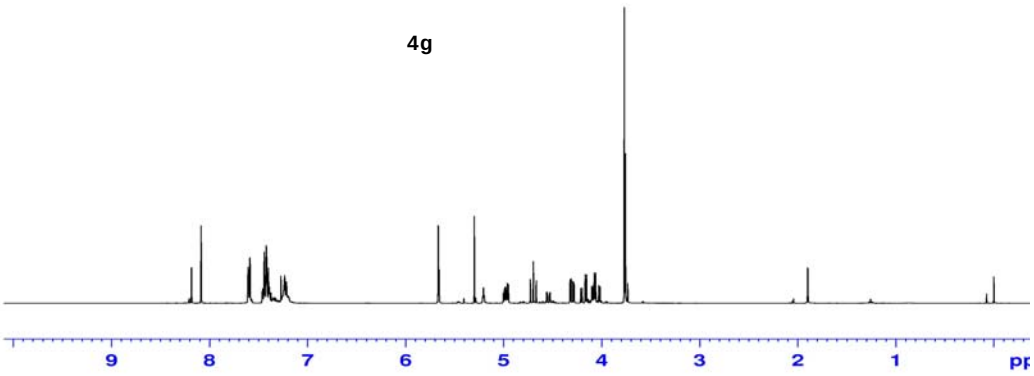
30
pp



**4g**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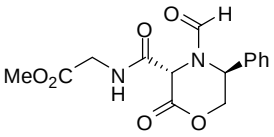
pp



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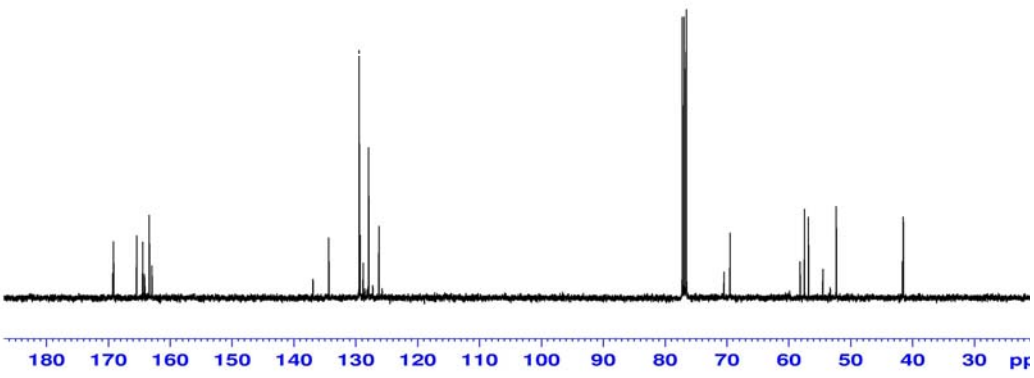
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50
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30
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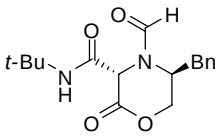
O
H
O
t-Bu
N
H
N
Bn
O
O

**4h**


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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0.5
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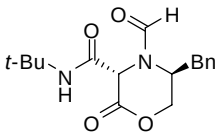
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H
O
t-Bu
N
H
N
Bn
O
O

**4h**


180
160
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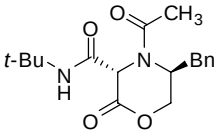
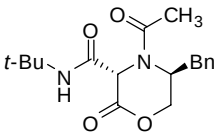
100
80
60
40
20


O
CH3
t-Bu
N
H
N
Bn
O
O

**4i**


9
8
7
6
5
4
3
2
1
0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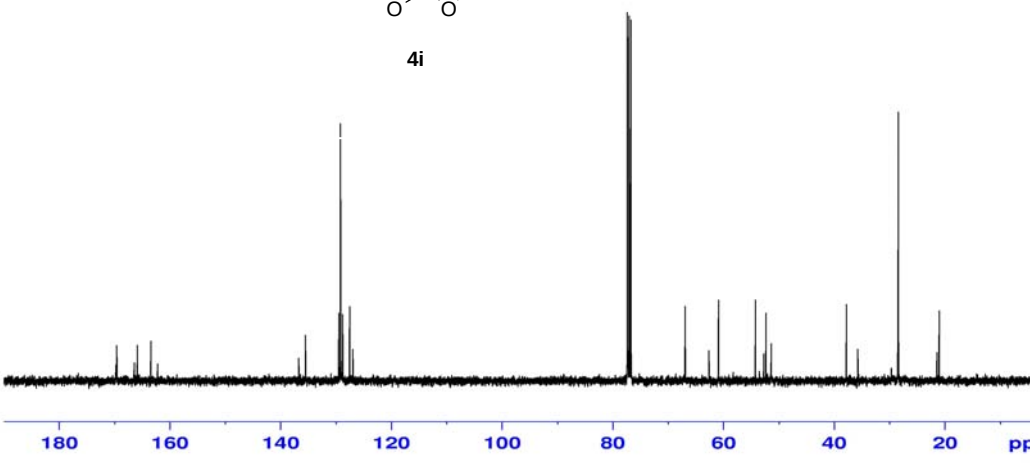
t-Bu
N
H
N
Bn
O
O

**4i**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40
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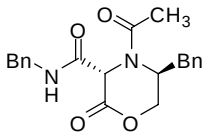
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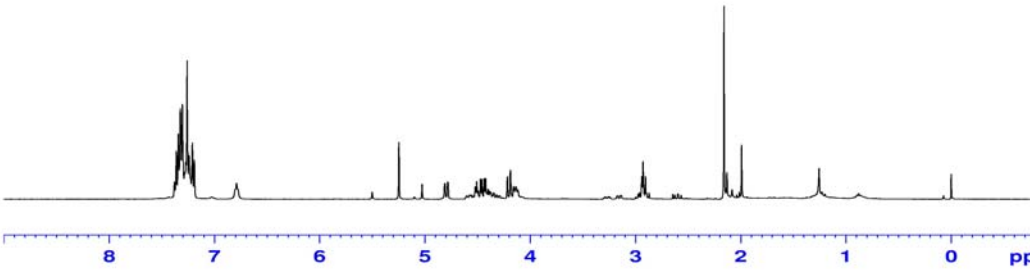
CH3
O
Bn
N
H
N
Bn
O
O

**4j**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4
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2
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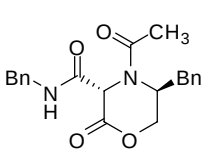
0
pp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CH3
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Bn
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N
Bn
O
O

**4j**


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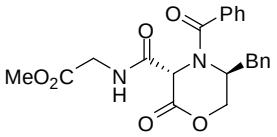
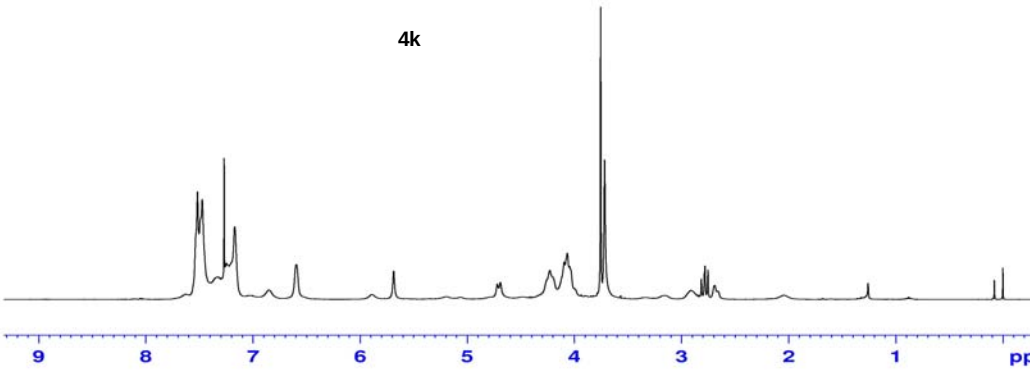
40
20
pp


O
Ph
O
N
Bn
MeO2C
N
H
O
O

**4k**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4
3
2
1
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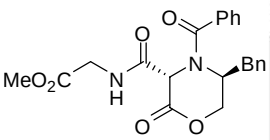
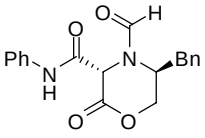

O
Ph
O
N
Bn
MeO2C
N
H
O
O

**4k**


190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
pp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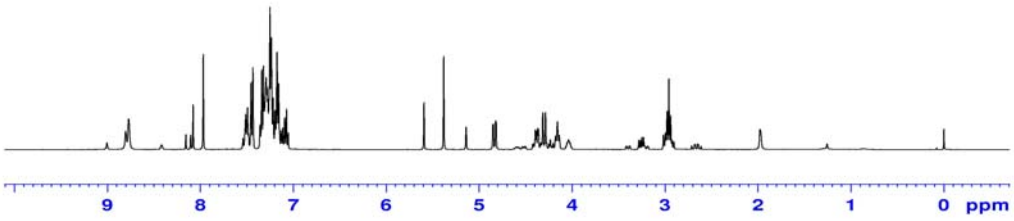
H
O
Ph
N
H
N
Bn
O
O

**4l**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4
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2
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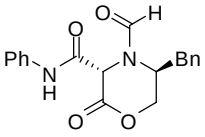
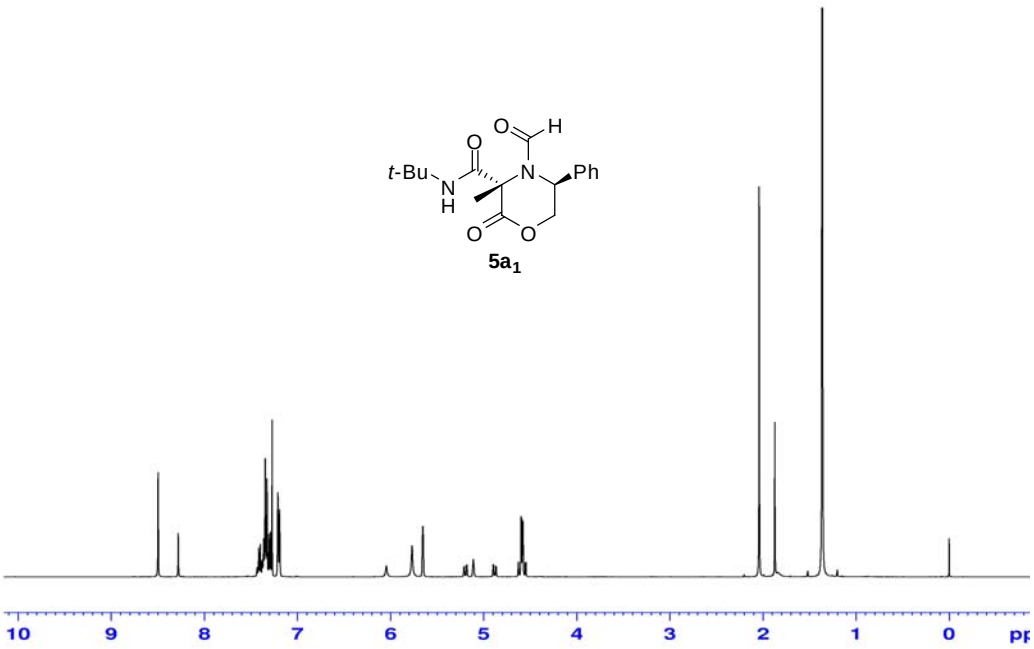
0
ppm

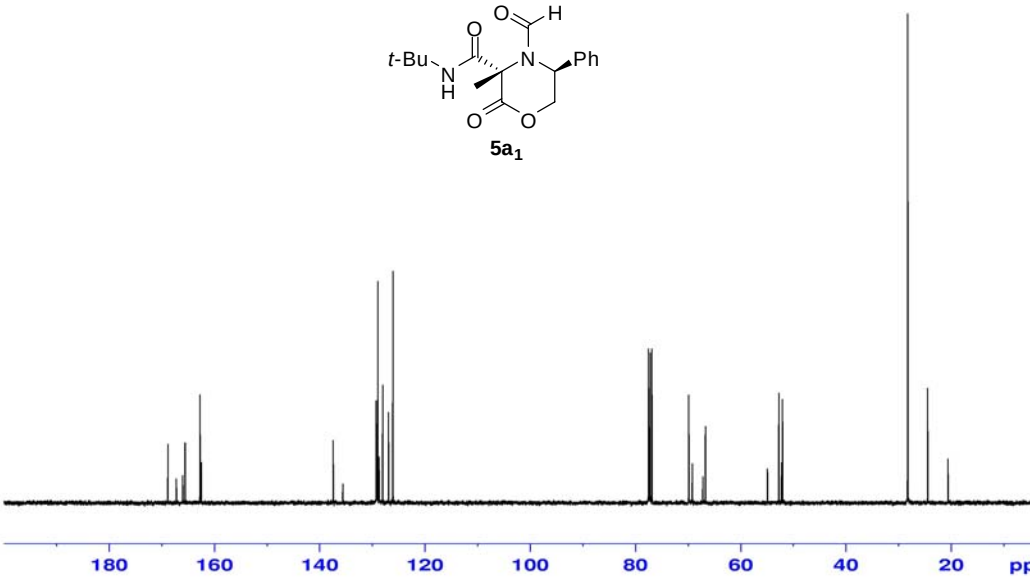

O
H
O
Ph
N
H
N
Bn
O
O

**4l**

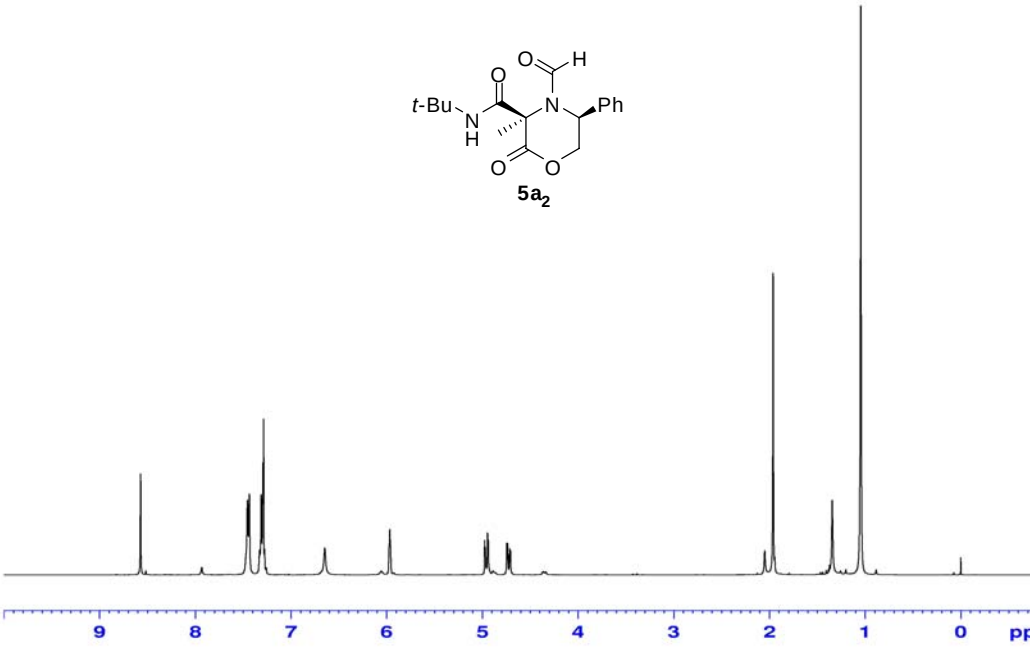

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30


O
H
O
t-Bu
N
H
N
Ph
O
O
10
9
8
7
6
5
4
3
2
1
0

**5a$_1$**


O
H
O
t-Bu
N
H
N
Ph
O
O
180
160
140
120
100
80
60
40
20

**5a$_1$**

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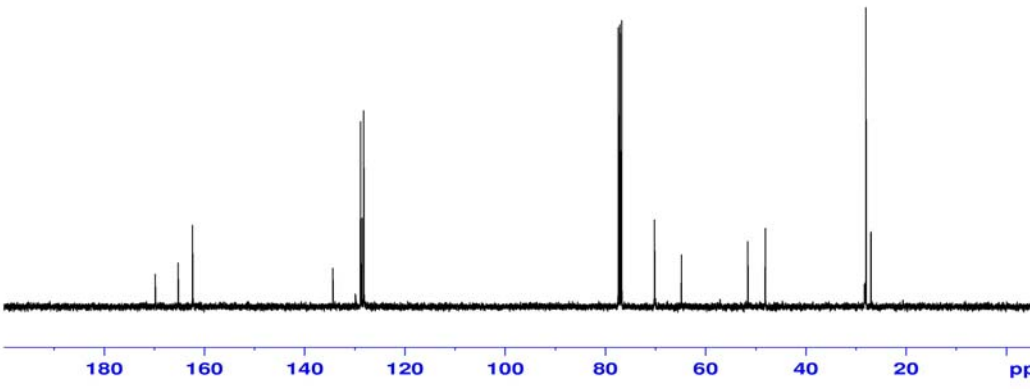
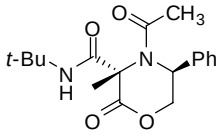
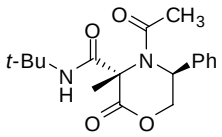


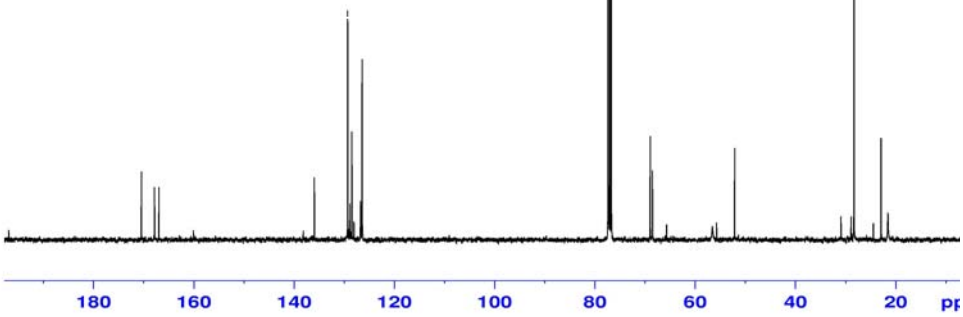

O
CH3
t-Bu
N
H
N
Ph
O
O
O

**5b**


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm


O
CH3
t-Bu
N
H
N
Ph
O
O
O

**5b**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100
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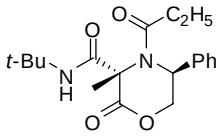
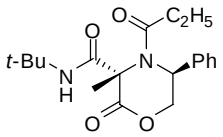
60
40
20
pp

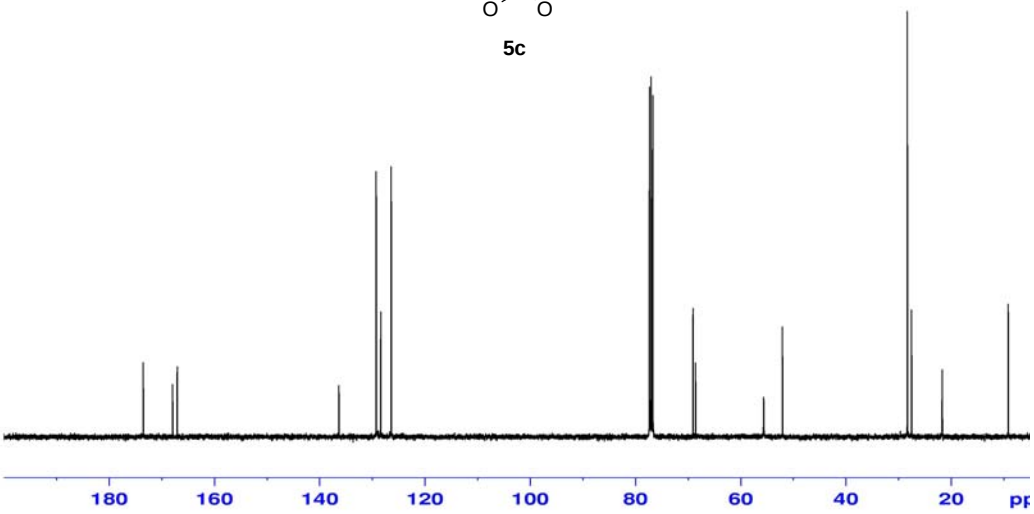


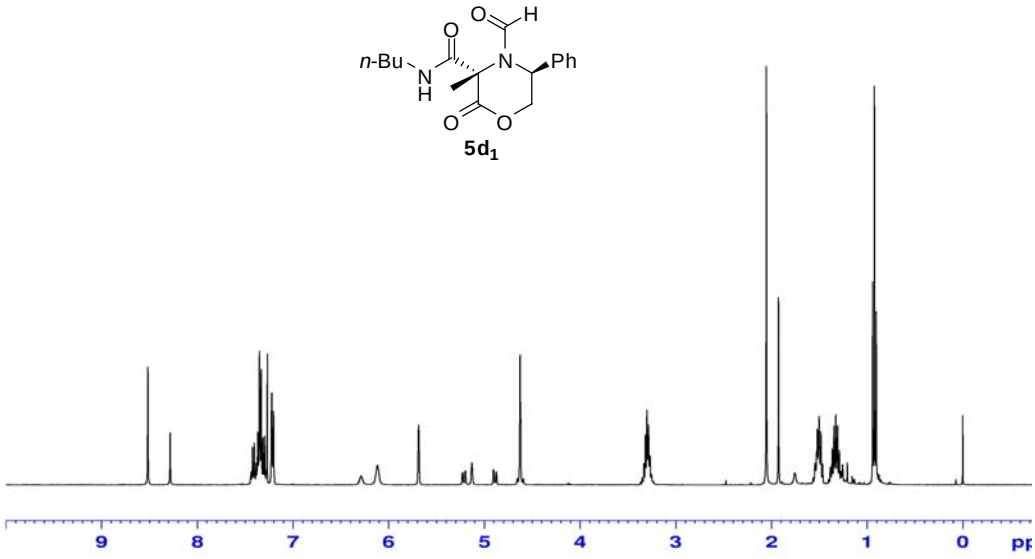
**5c**



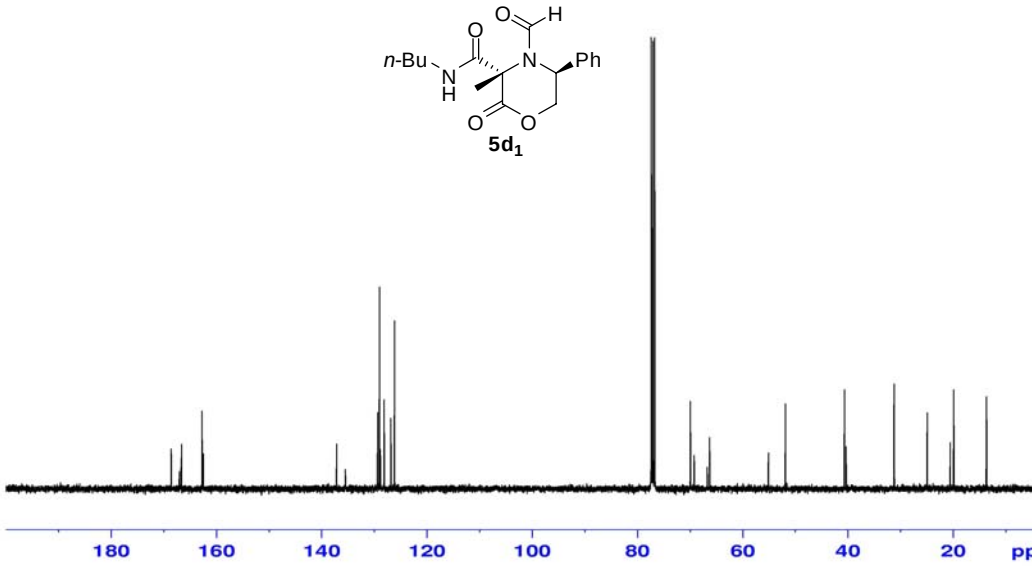



**5c**

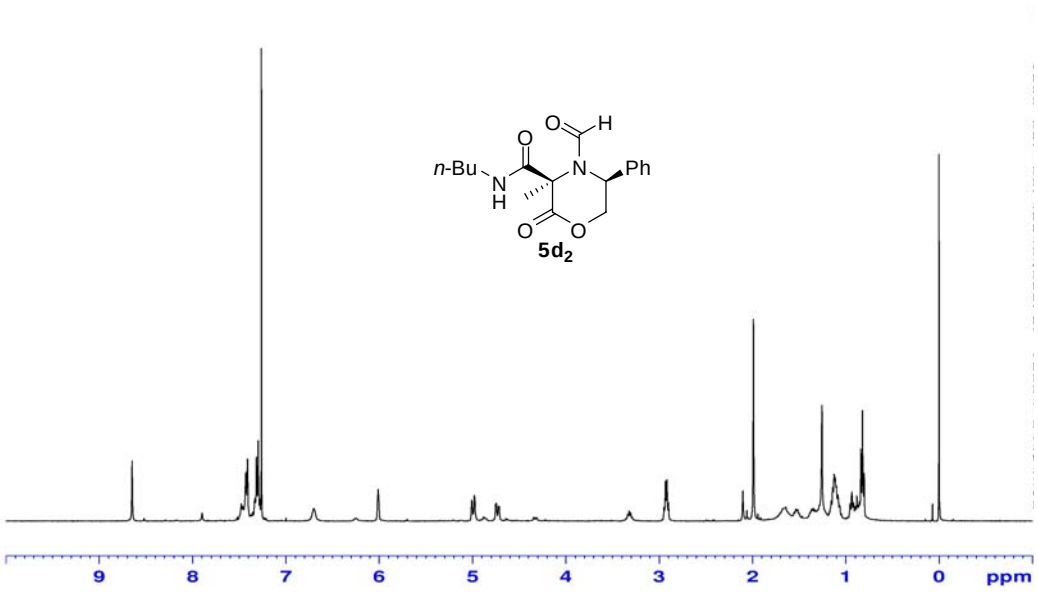


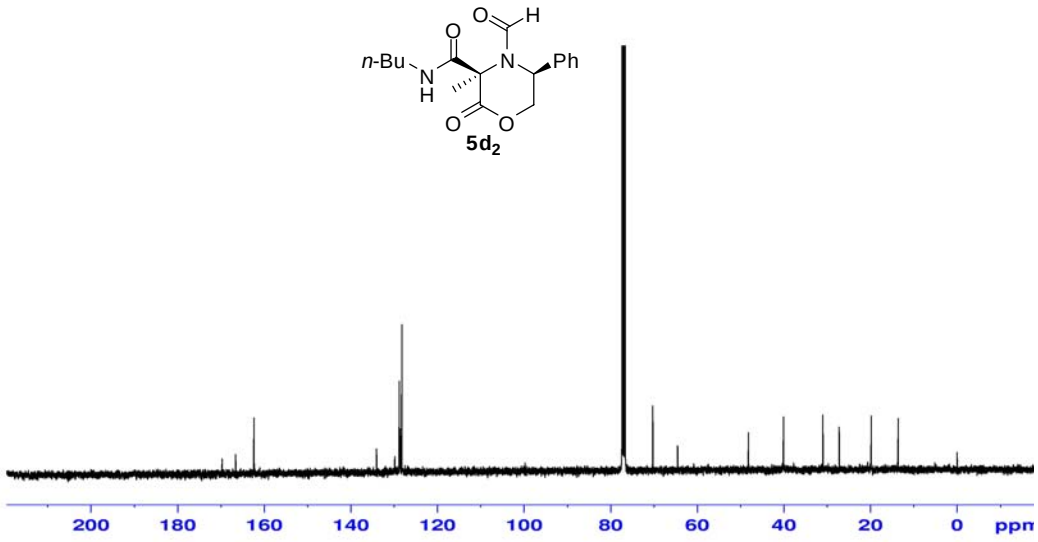

n-Bu
N
H
O
H
N
Ph
O
O
O
9
8
7
6
5
4
3
2
1
0

**5d$_1$**


n-Bu
N
H
O
H
N
Ph
O
O
O
180
160
140
120
100
80
60
40
20

**5d$_1$**


O
H
O
n-Bu
N
H
N
Ph
O
O
5d2
9
8
7
6
5
4
3
2
1
0
ppm


O
H
O
n-Bu
N
H
N
Ph
O
O
5d2
200
180
160
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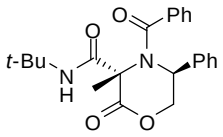
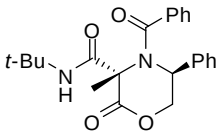
120
100
80
60
40
20
0
ppm

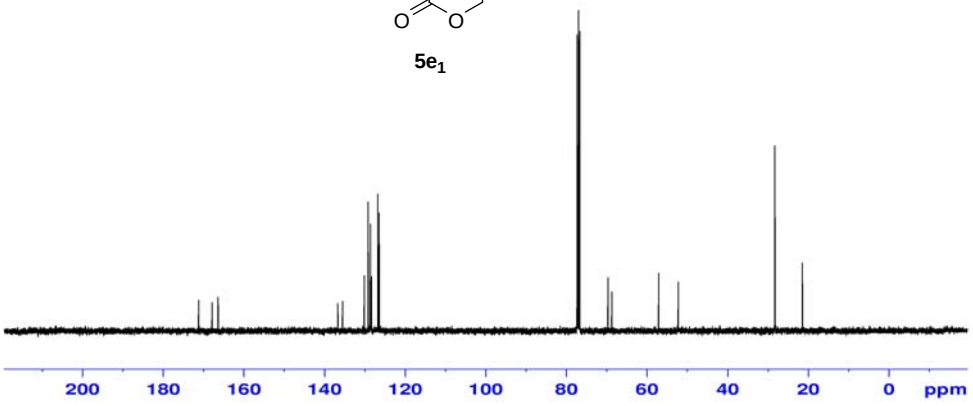

O
Ph
O
t-Bu
N
H
N
Ph
O
O

**5e$_1$**


8
7
6
5
4
3
2
1
0
ppm


O
Ph
O
t-Bu
N
H
N
Ph
O
O

**5e$_1$**


200
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100
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60
40
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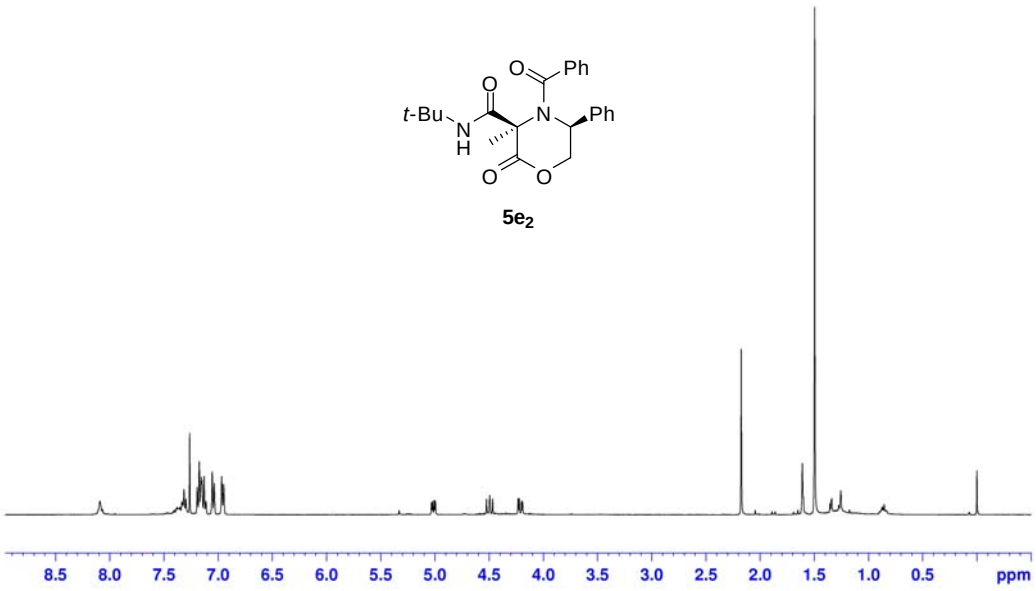
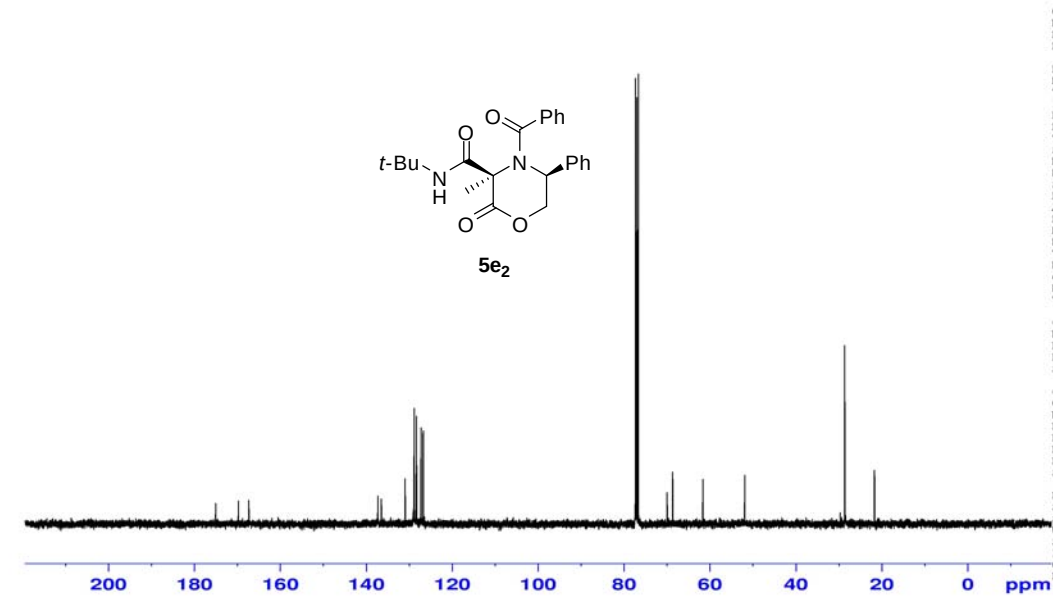
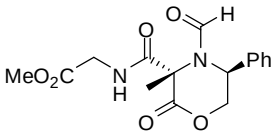
0
ppm


O
Ph
O
t-Bu
N
H
N
Ph
O
O
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

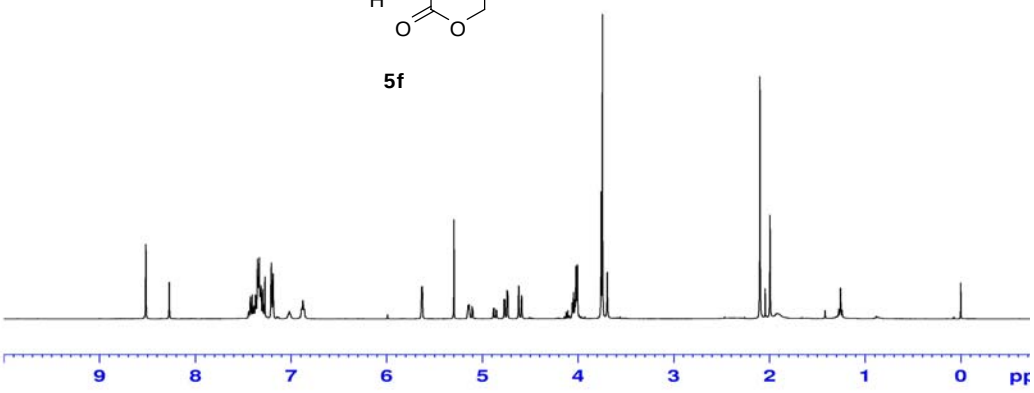
**5e$_2$**

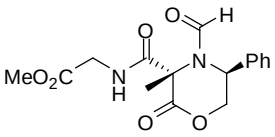

O
Ph
O
t-Bu
N
H
N
Ph
O
O
200
180
160
140
120
100
80
60
40
20
0
ppm

**5e$_2$**

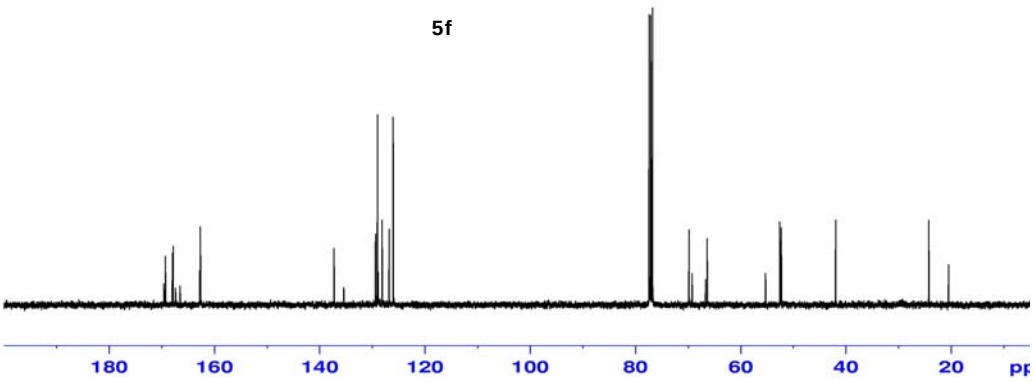

O
H
O
N
Ph
MeO2C
N
H
O
O

**5f**


9
8
7
6
5
4
3
2
1
0


O
H
O
N
Ph
MeO2C
N
H
O
O

**5f**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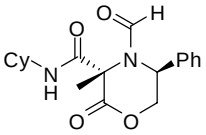
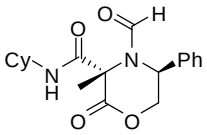
160
140
120
100
80
60
40
20

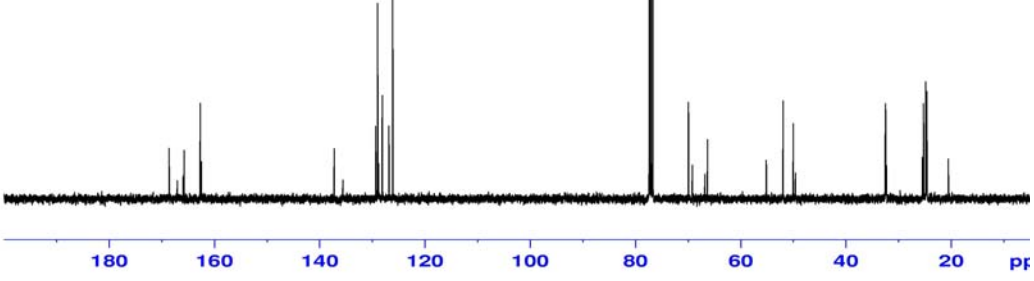

O
H
O
Cy
N
H
N
Ph
O
O

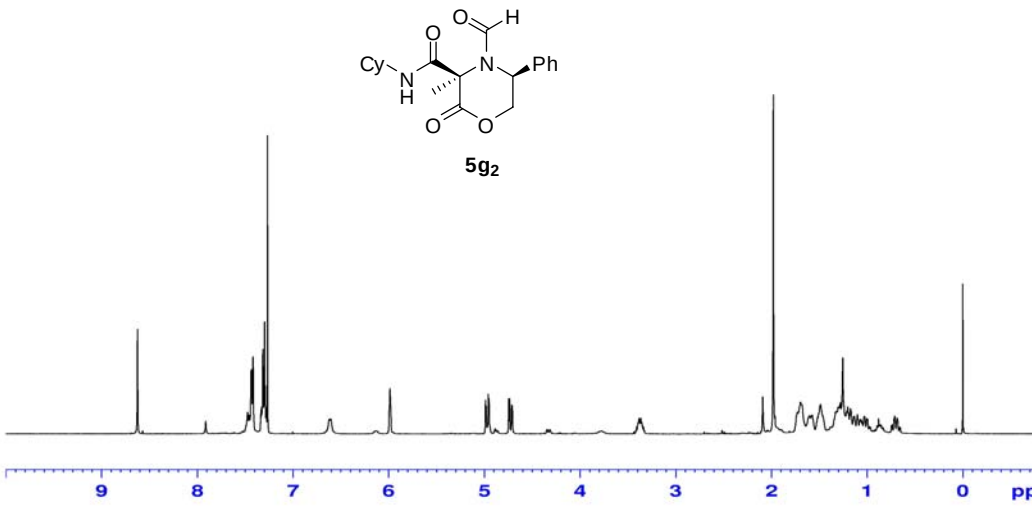
**5g$_1$**


9
8
7
6
5
4
3
2
1
0

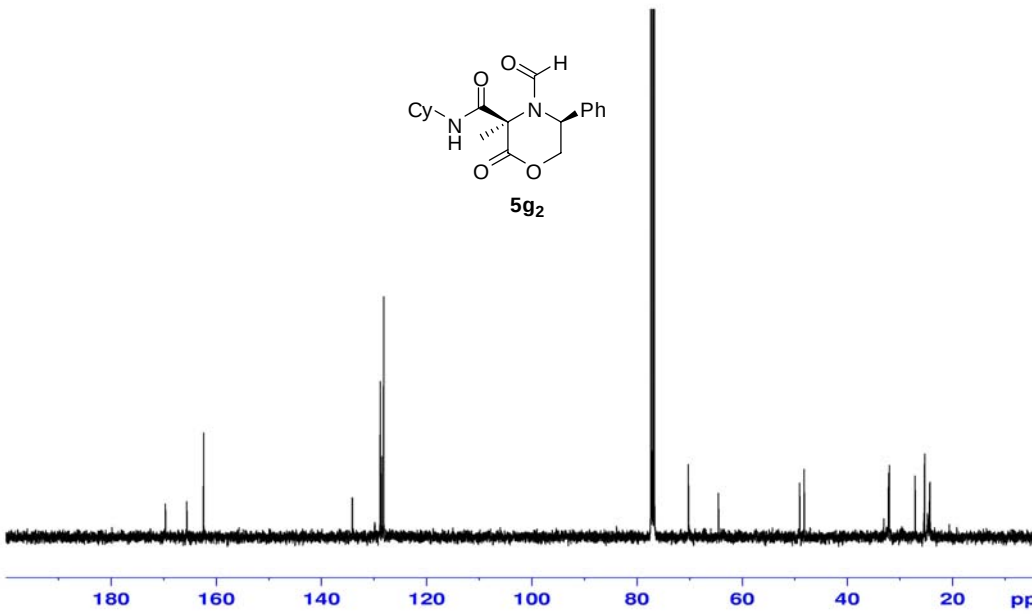

O
H
O
Cy
N
H
N
Ph
O
O

**5g$_1$**

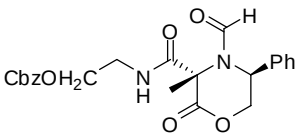

180
160
140
120
100
80
60
40
20


O
H
O
Cy
N
H
N
Ph
O
O
9
8
7
6
5
4
3
2
1
0
pp

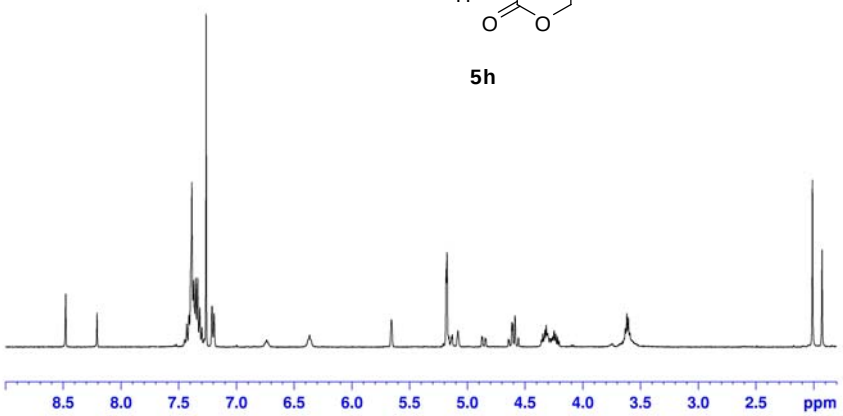
**5g$_2$**

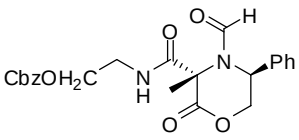

O
H
O
Cy
N
H
N
Ph
O
O
180
160
140
120
100
80
60
40
20
pp

**5g$_2$**

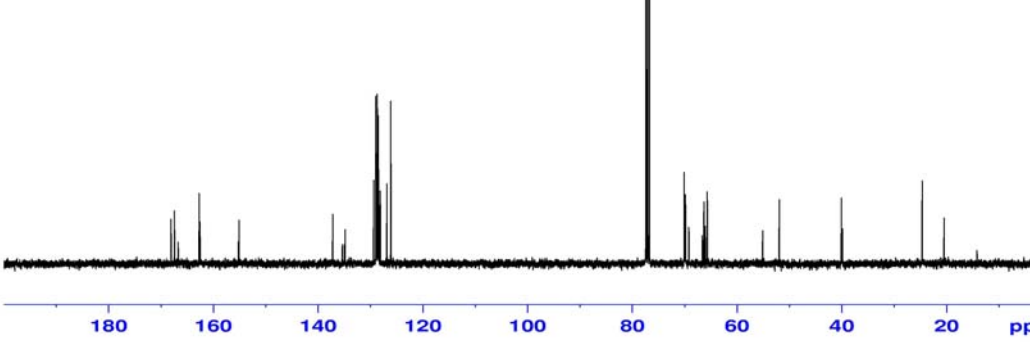

O
H
O
CbzOH2C
N
H
N
Ph
O
O

**5h**


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm


O
H
O
CbzOH2C
N
H
N
Ph
O
O

**5h**


180
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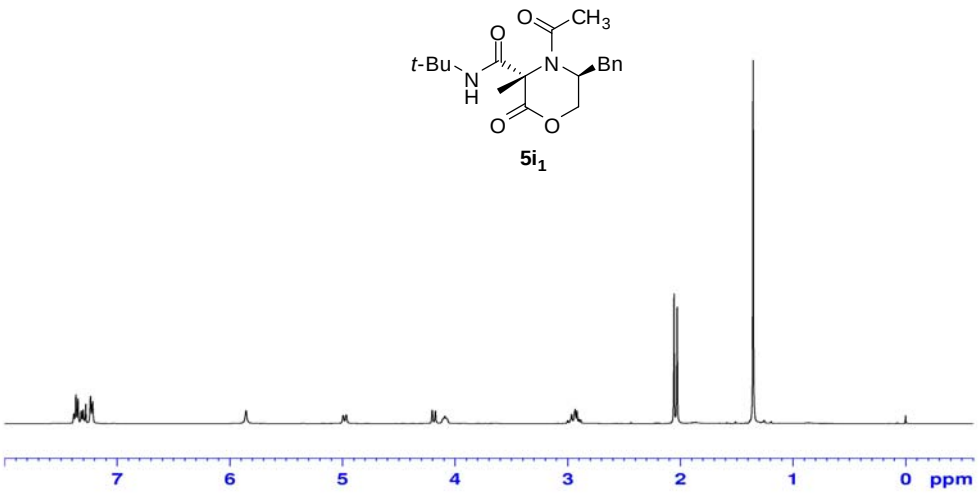
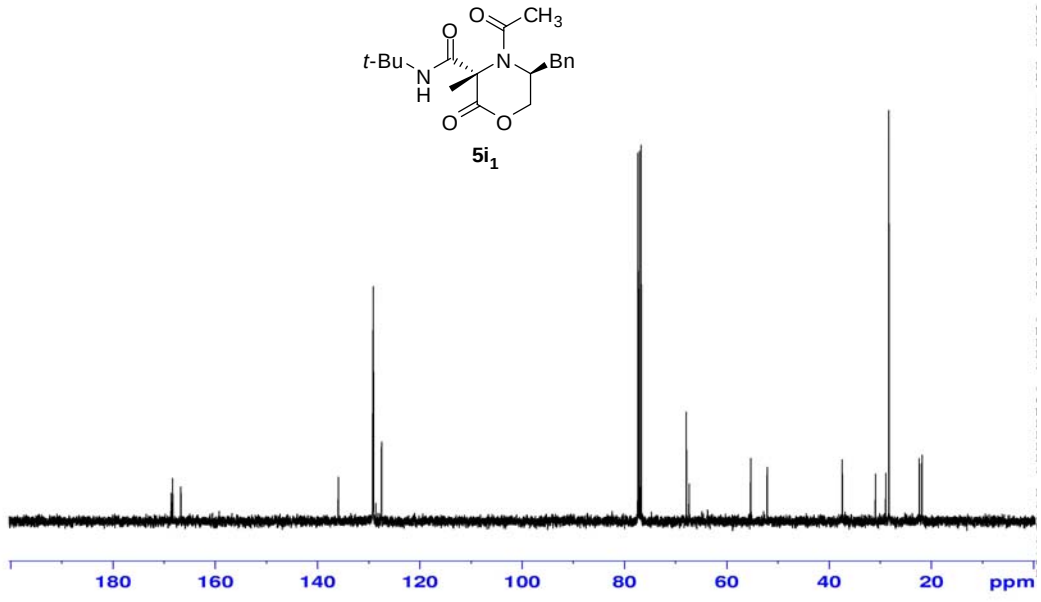
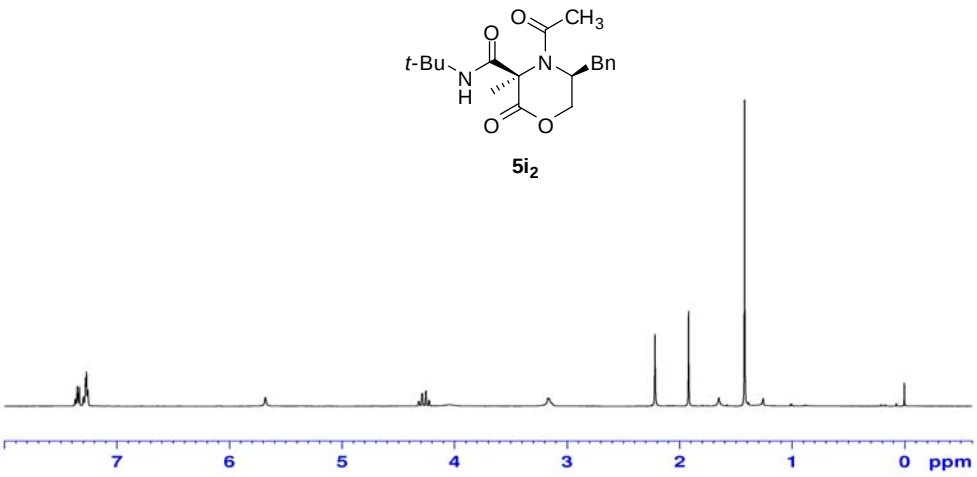
120
100
80
60
40
20


O
CH3
O
t-Bu
N
H
N
Bn
O
O
7
6
5
4
3
2
1
0
ppm

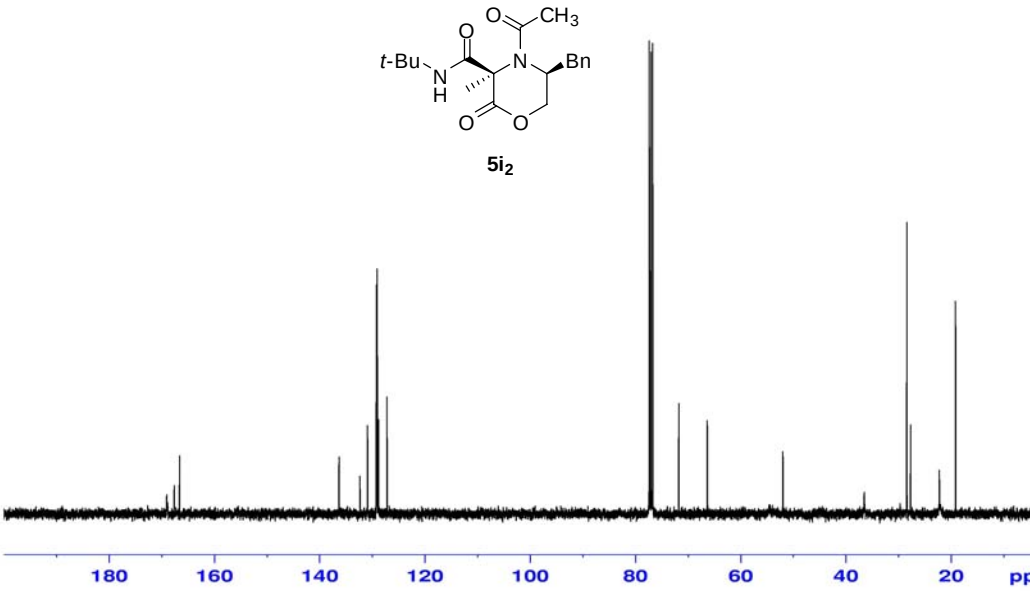
**5i$_1$**


O
CH3
O
t-Bu
N
H
N
Bn
O
O
180
160
140
120
100
80
60
40
20
ppm

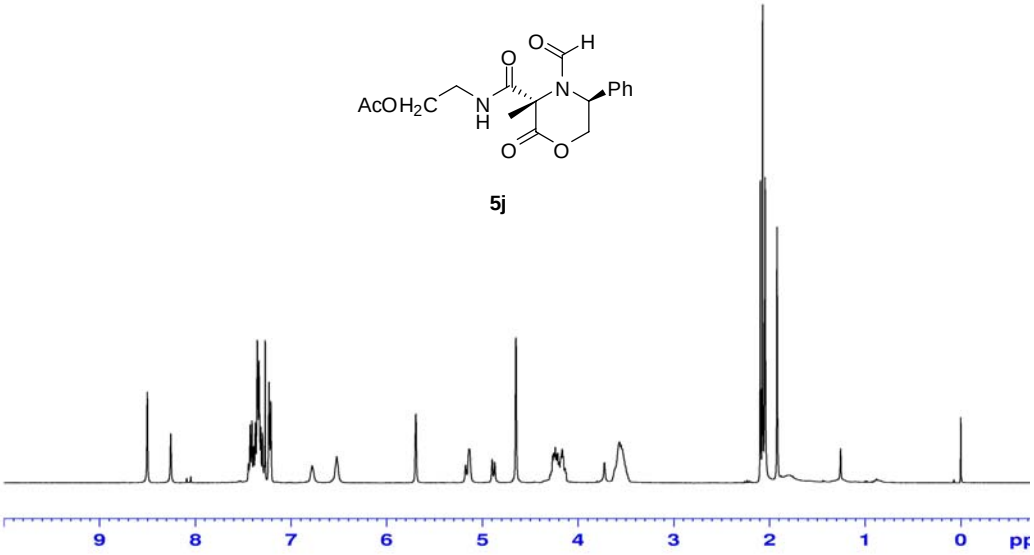
**5i$_1$**


O
CH3
O
t-Bu
N
H
N
Bn
O
O
7
6
5
4
3
2
1
0
ppm

**5i$_2$**


O
CH3
O
t-Bu
N
H
N
Bn
O
O
180
160
140
120
100
80
60
40
20

**5i$_2$**


AcOH2C
N
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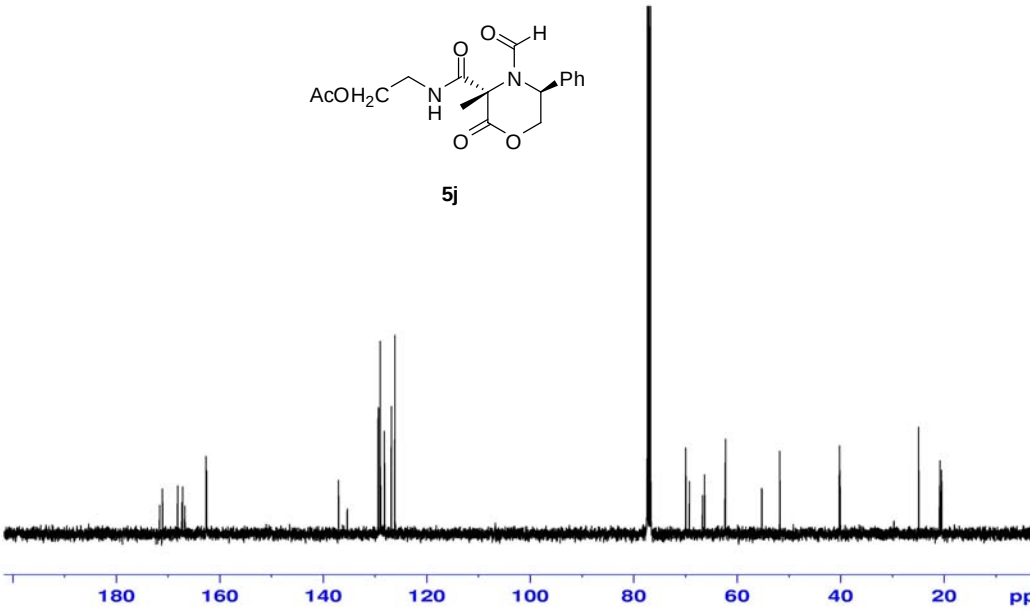
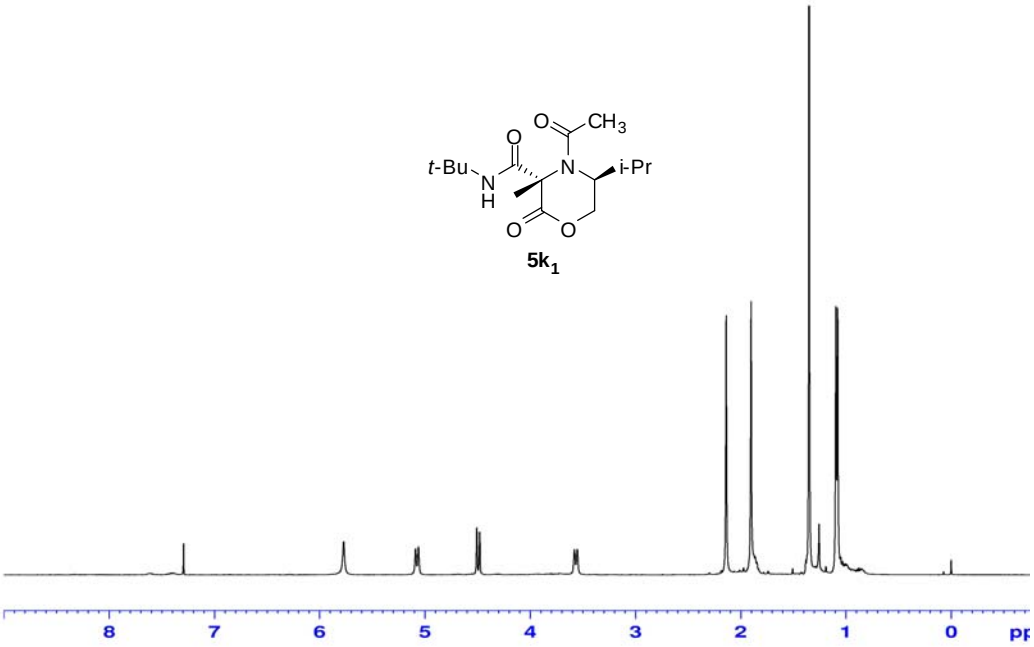
O
O
O
H
N
Ph
O
O
9
8
7
6
5
4
3
2
1
0

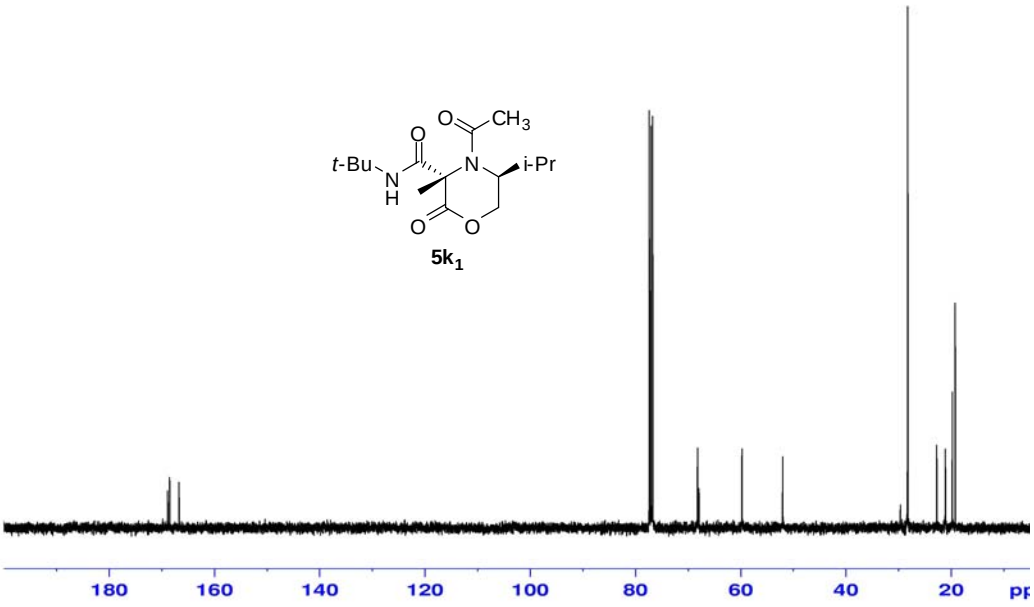
**5j**


AcOH2C
N
H
O
O
O
H
N
Ph
O
O
180
160
140
120
100
80
60
40
20

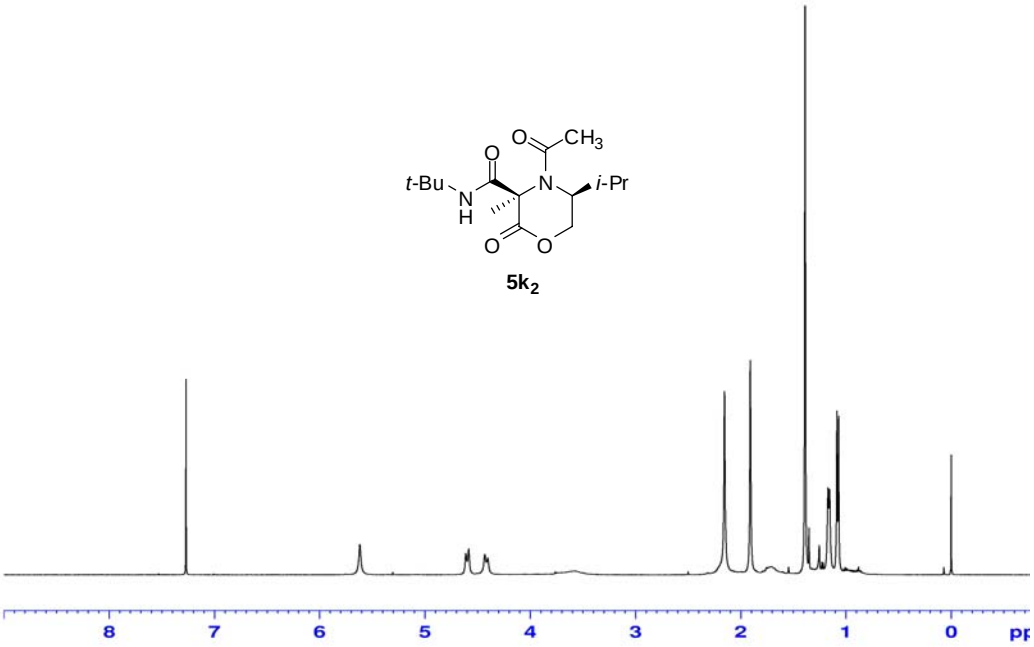
**5j**


O
CH3
O
t-Bu
N
H
N
i-Pr
O
O
8
7
6
5
4
3
2
1
0
pp

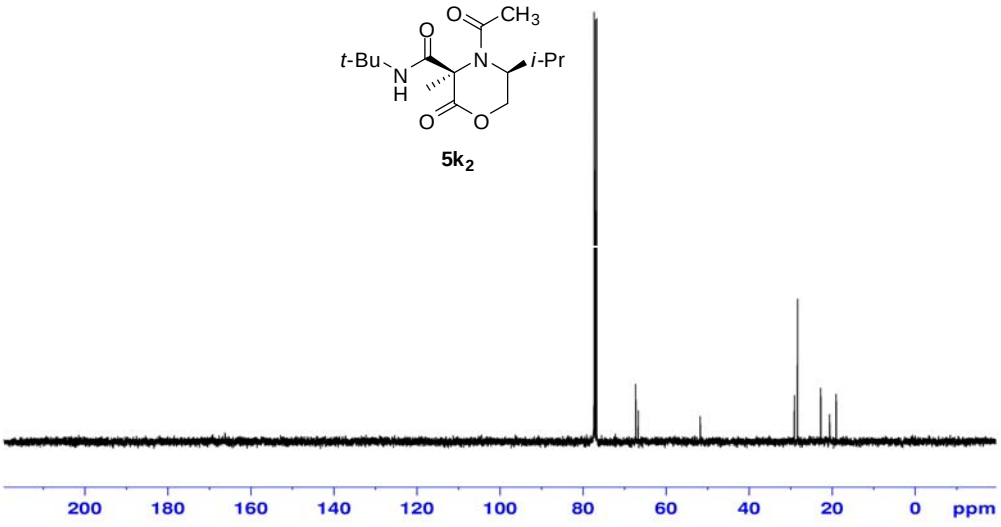
**5k$_1$**


O
CH3
O
t-Bu
N
H
N
i-Pr
O
O
180
160
140
120
100
80
60
40
20
pp

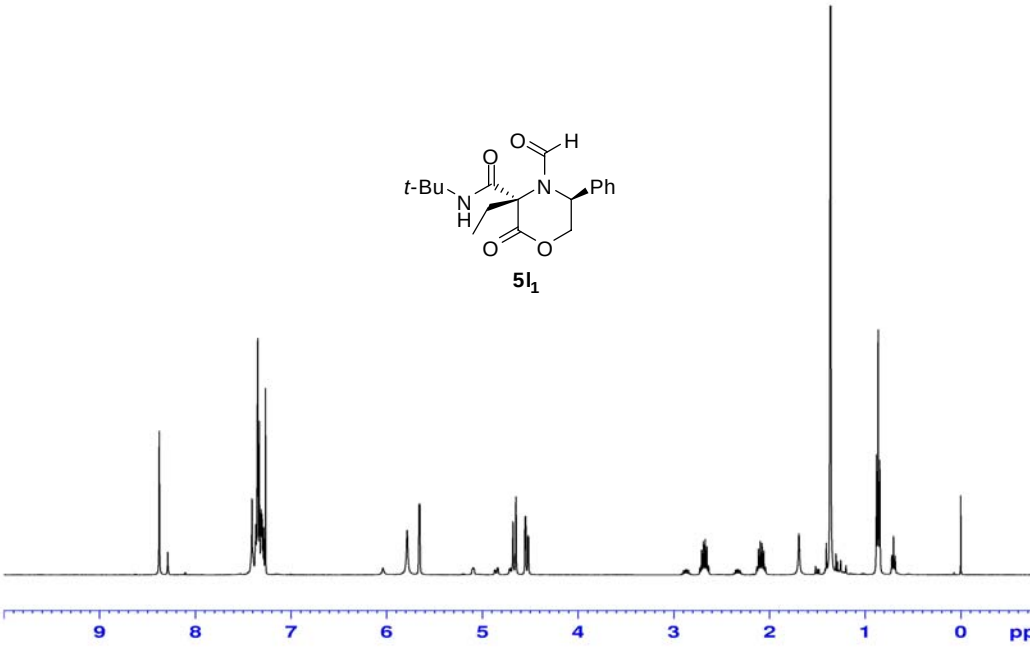
**5k$_1$**


O
CH3
O
t-Bu
N
H
N
i-Pr
O
O
8
7
6
5
4
3
2
1
0
pp

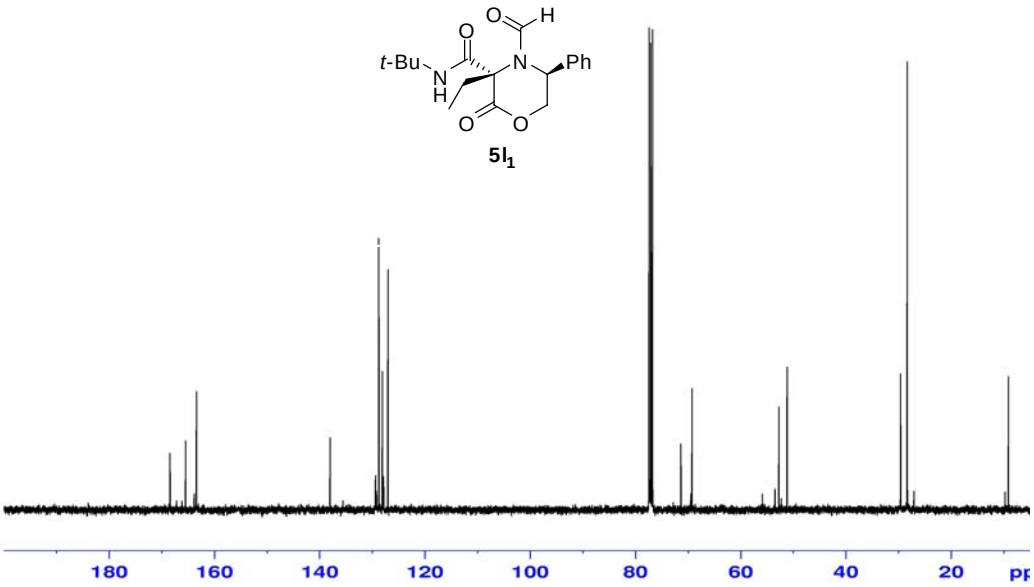
**5k$_2$**


O
CH3
O
t-Bu
N
H
N
i-Pr
O
O
200
180
160
140
120
100
80
60
40
20
0
ppm

**5k$_2$**


O
H
O
t-Bu
N
H
N
Ph
O
O
9
8
7
6
5
4
3
2
1
0
pp

**5l$_1$**


O
H
O
t-Bu
N
H
N
Ph
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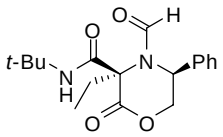
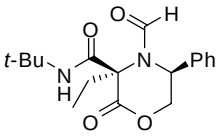
O
180
160
140
120
100
80
60
40
20
pp

**5l$_1$**


O
H
O
t-Bu
N
H
N
Ph
O
O

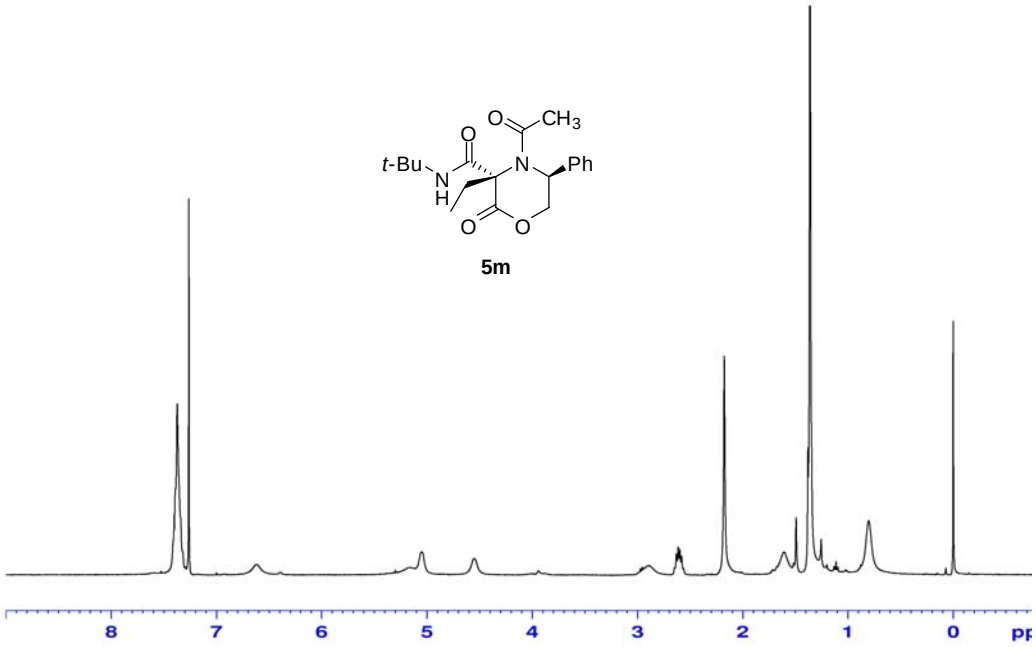
**5l$_2$**


9
8
7
6
5
4
3
2
1
0

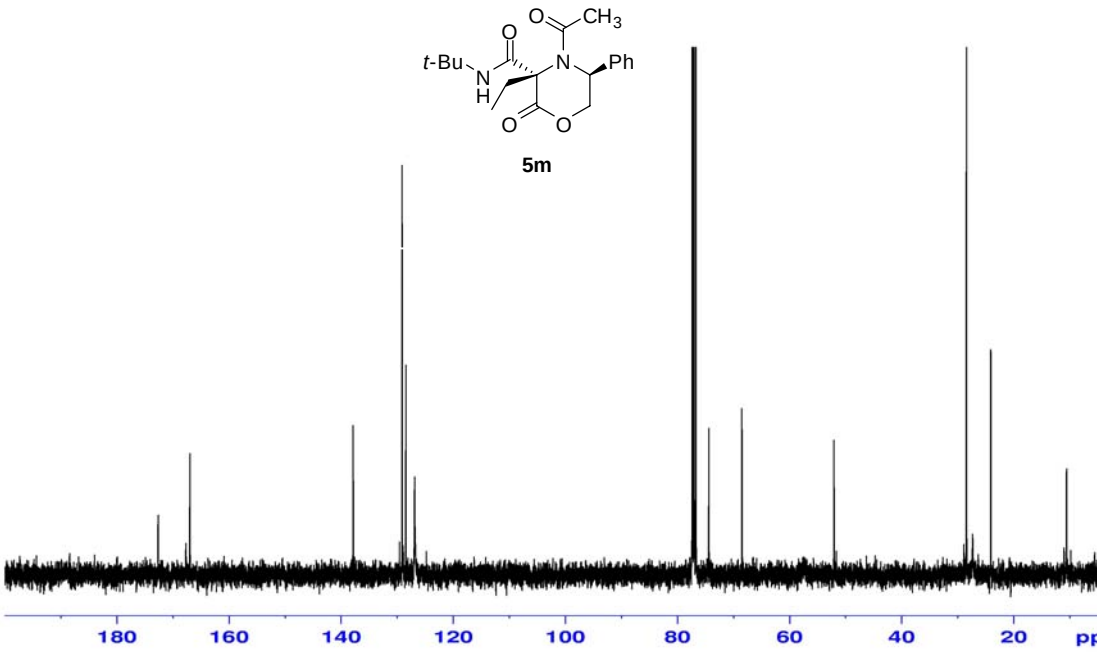

O
H
O
t-Bu
N
H
N
Ph
O
O

**5l$_2$**


200
180
160
140
120
100
80
60
40
20


O
CH3
O
t-Bu
N
H
N
Ph
O
O
8
7
6
5
4
3
2
1
0
pp

**5m**


O
CH3
O
t-Bu
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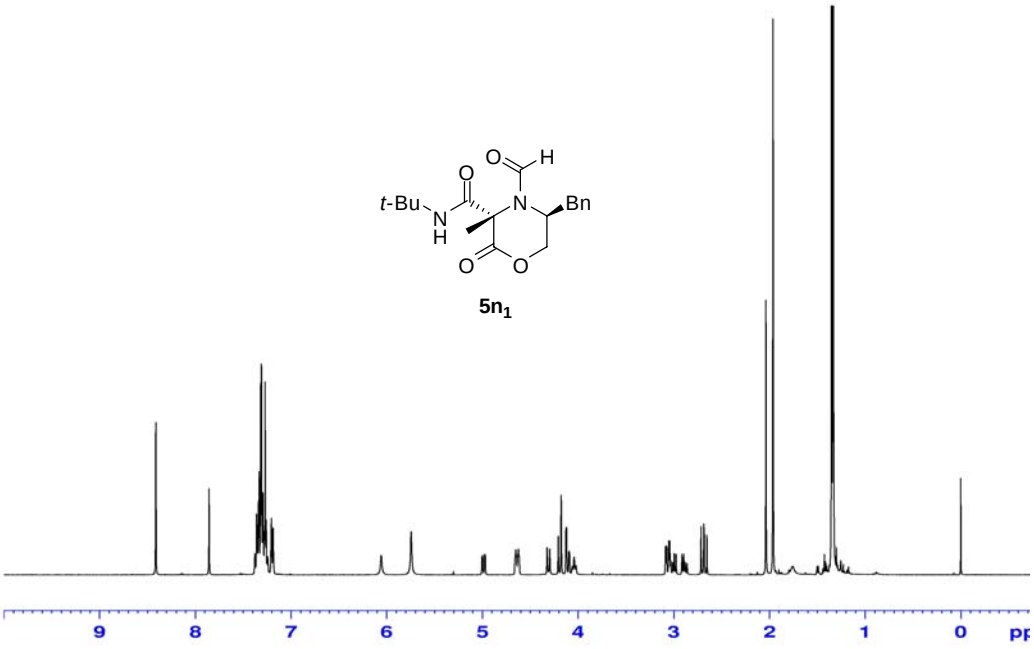
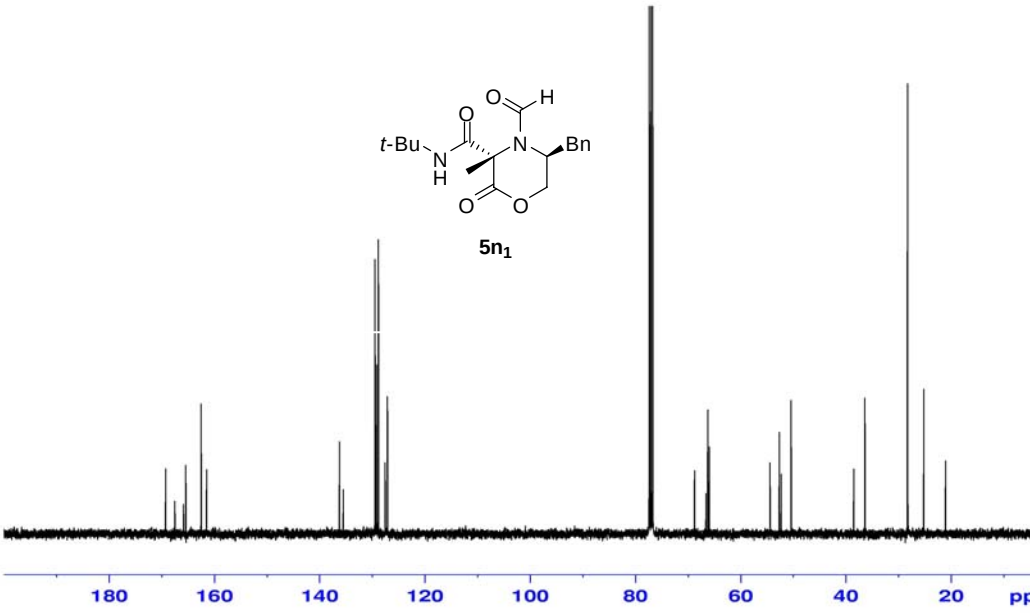
H
N
Ph
O
O
180
160
140
120
100
80
60
40
20
pp

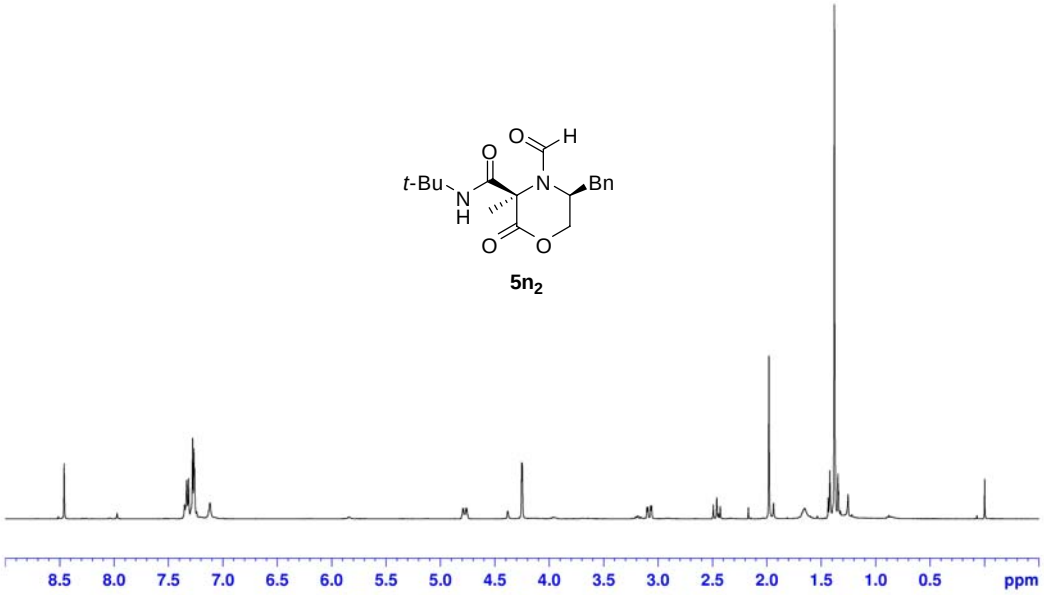
**5m**


O
H
O
t-Bu
N
H
N
Bn
O
O
9
8
7
6
5
4
3
2
1
0

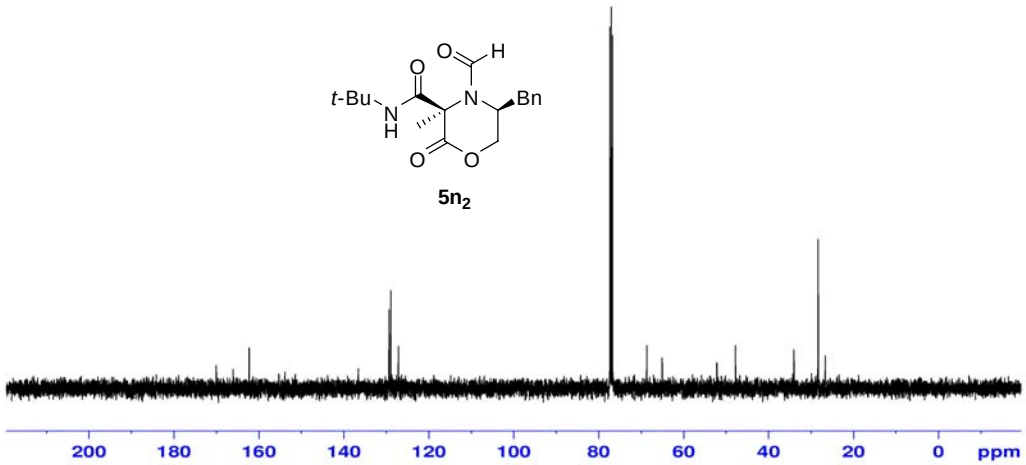
**5n$_1$**


O
H
O
t-Bu
N
H
N
Bn
O
O
180
160
140
120
100
80
60
40
20

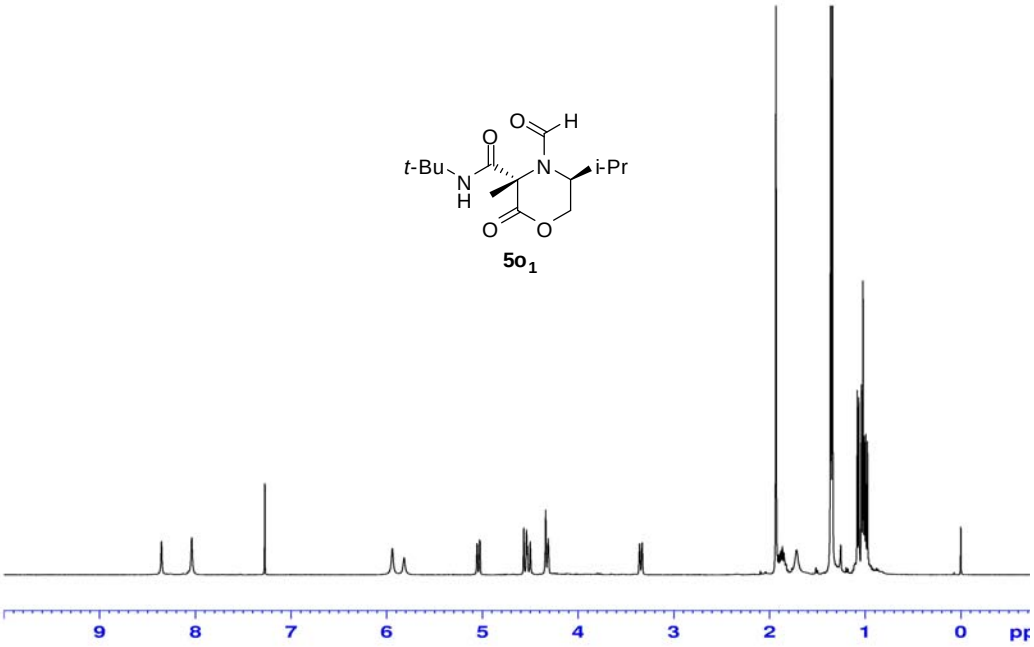
**5n$_1$**


O
H
O
t-Bu
N
H
N
Bn
O
O
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

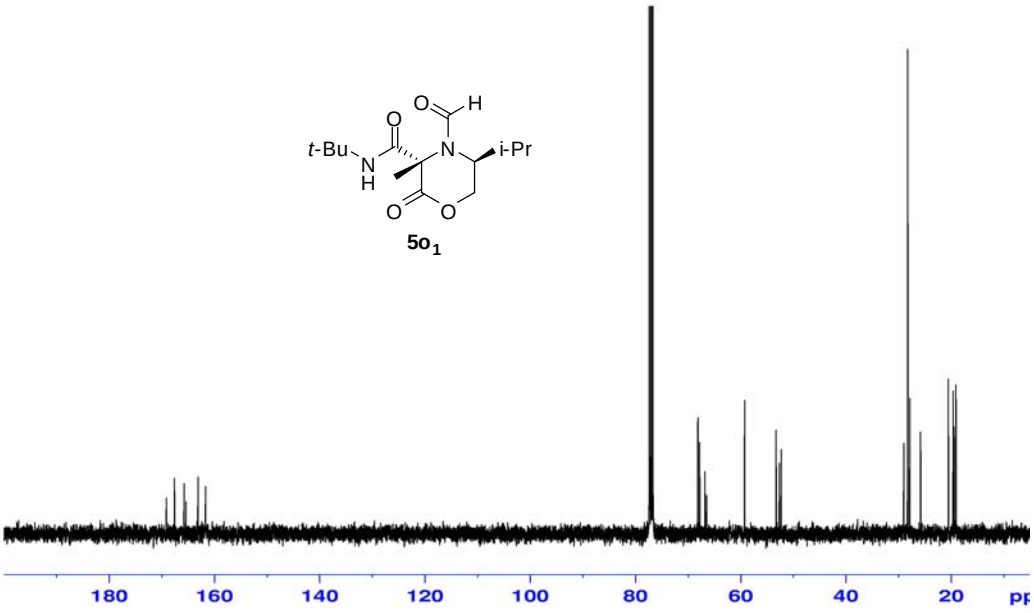
**5n$_2$**


O
H
O
t-Bu
N
H
N
Bn
O
O
200
180
160
140
120
100
80
60
40
20
0
ppm

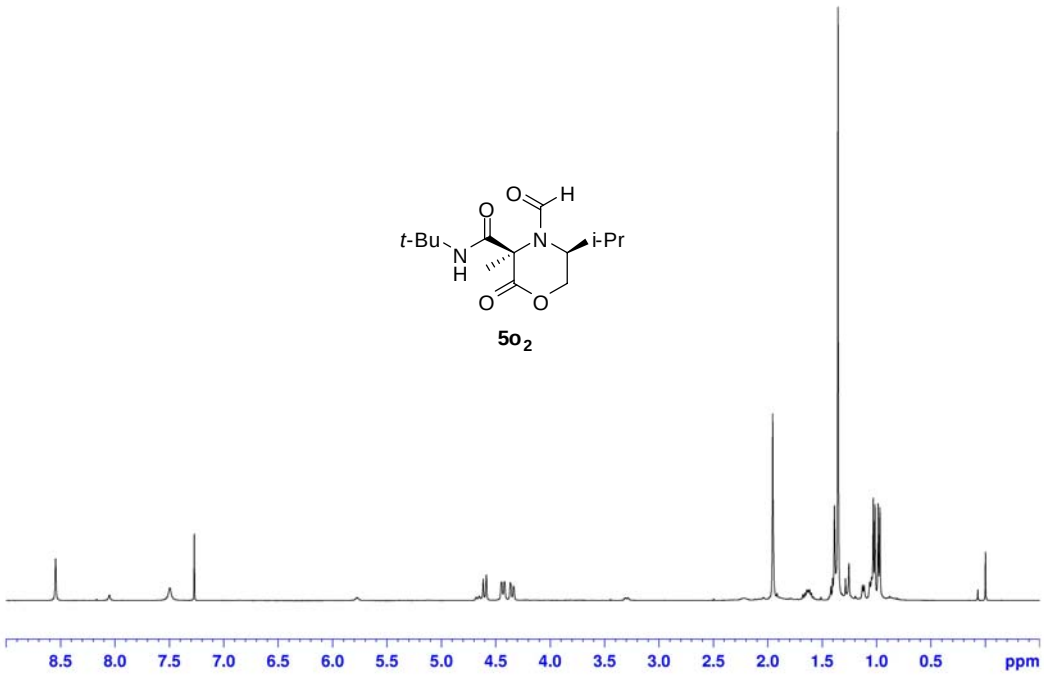
**5n$_2$**


O
H
O
t-Bu
N
H
N
i-Pr
O
O
9
8
7
6
5
4
3
2
1
0

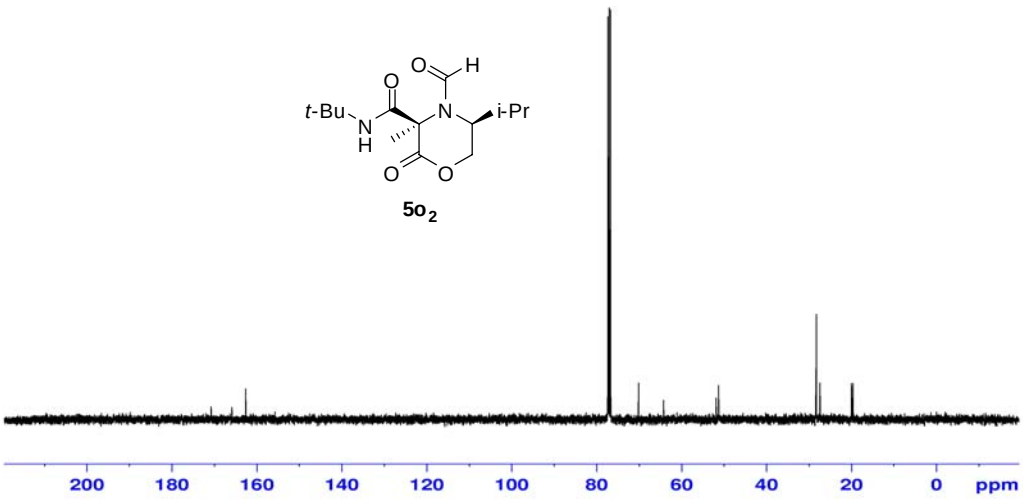
**5o$_1$**


O
H
O
t-Bu
N
H
N
i-Pr
O
O
180
160
140
120
100
80
60
40
20

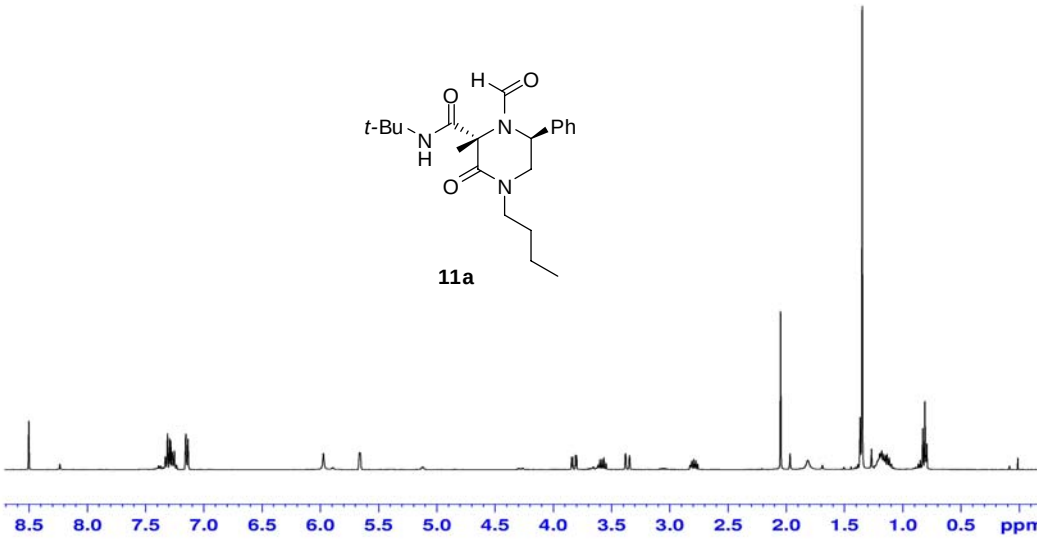
**5o$_1$**


O
H
O
t-Bu
N
H
N
i-Pr
O
O
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

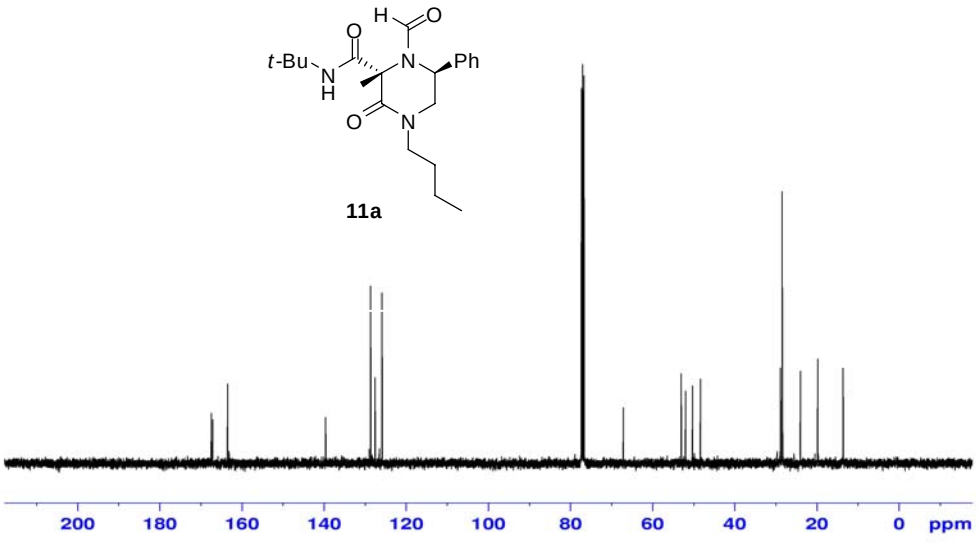
**5o$_2$**


O
H
O
t-Bu
N
H
N
i-Pr
O
O
200 180 160 140 120 100 80 60 40 20 0 ppm

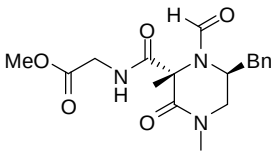
**5o$_2$**


H
O
O
t-Bu
N
H
N
Ph
O
N
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

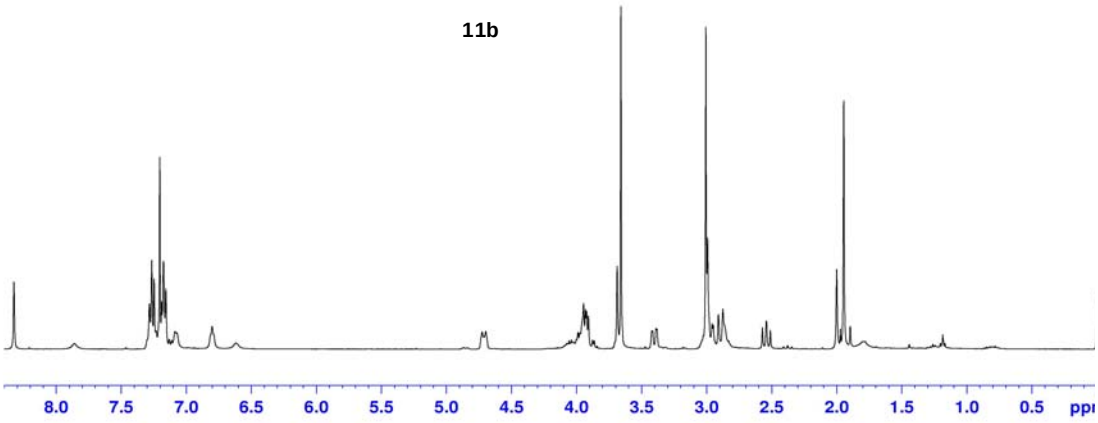
**11a**

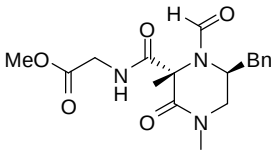

H
O
O
t-Bu
N
H
N
Ph
O
N
200 180 160 140 120 100 80 60 40 20 0 ppm

**11a**


H
O
O
MeO
N
H
N
Bn
O
O
N

**11b**

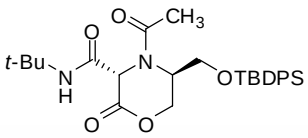

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5


H
O
O
MeO
N
H
N
Bn
O
O
N

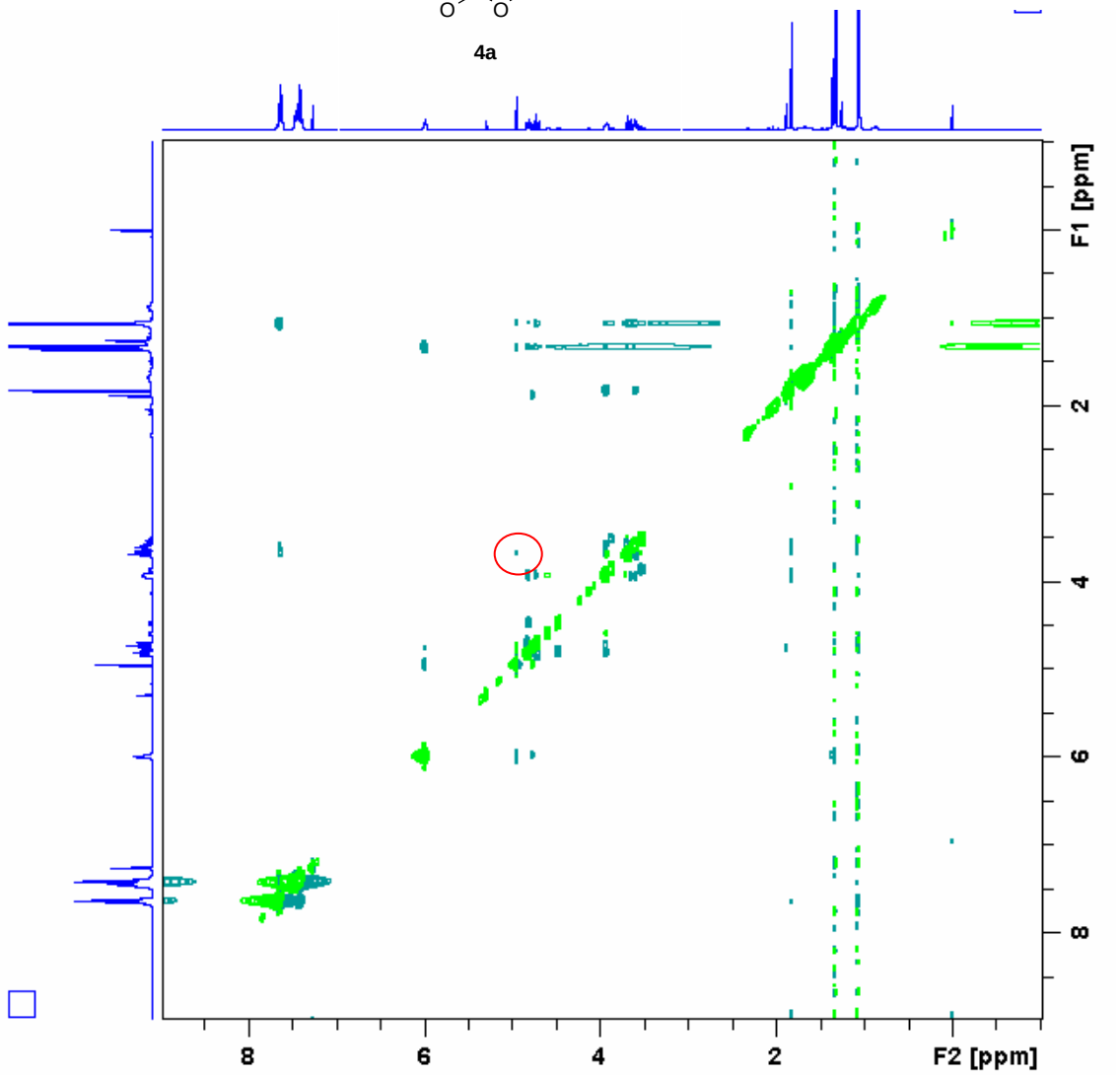
**11b**

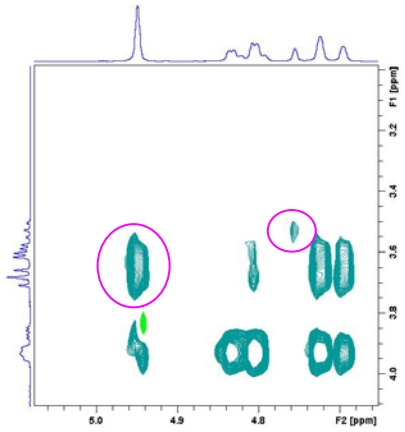

170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

NOESY spectrum of **4a**

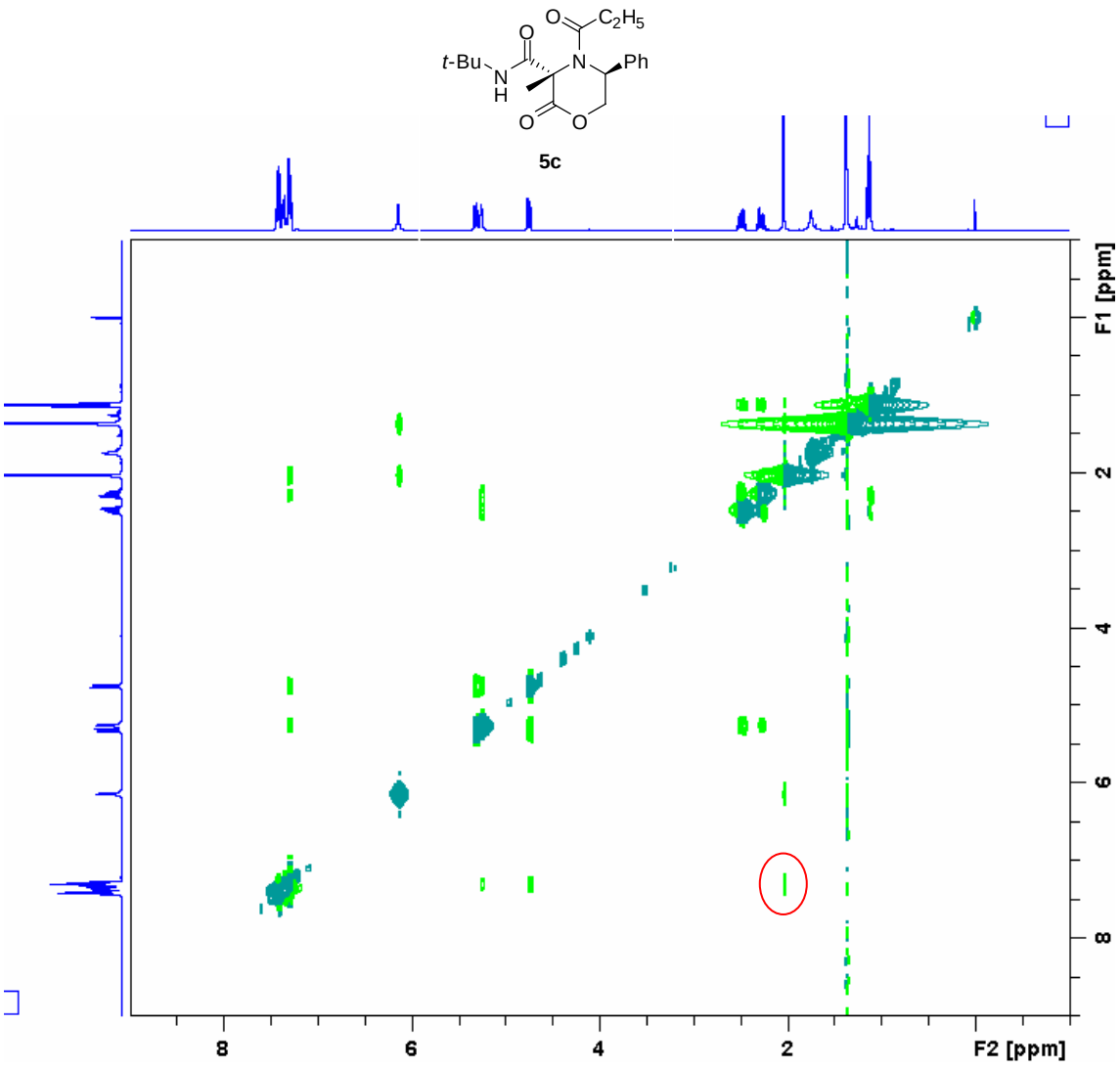


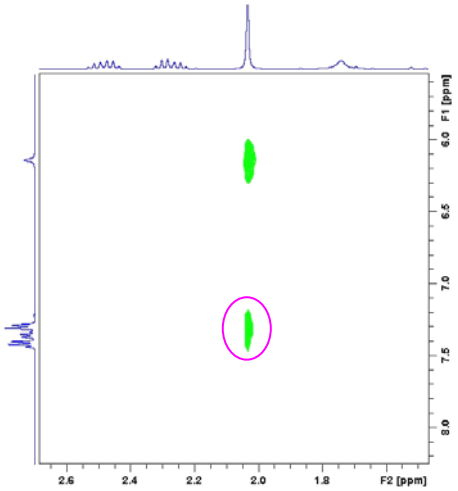

**4a**



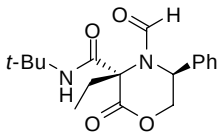



NOESY spectrum of **5c**



NOESY spectrum of **5l$_1$**




**5l$_1$**