Convenient Access to 5-Membered Cyclic Iminium Ions: Evidence for a Stepwise [4+2] Cycloaddition Mechanism

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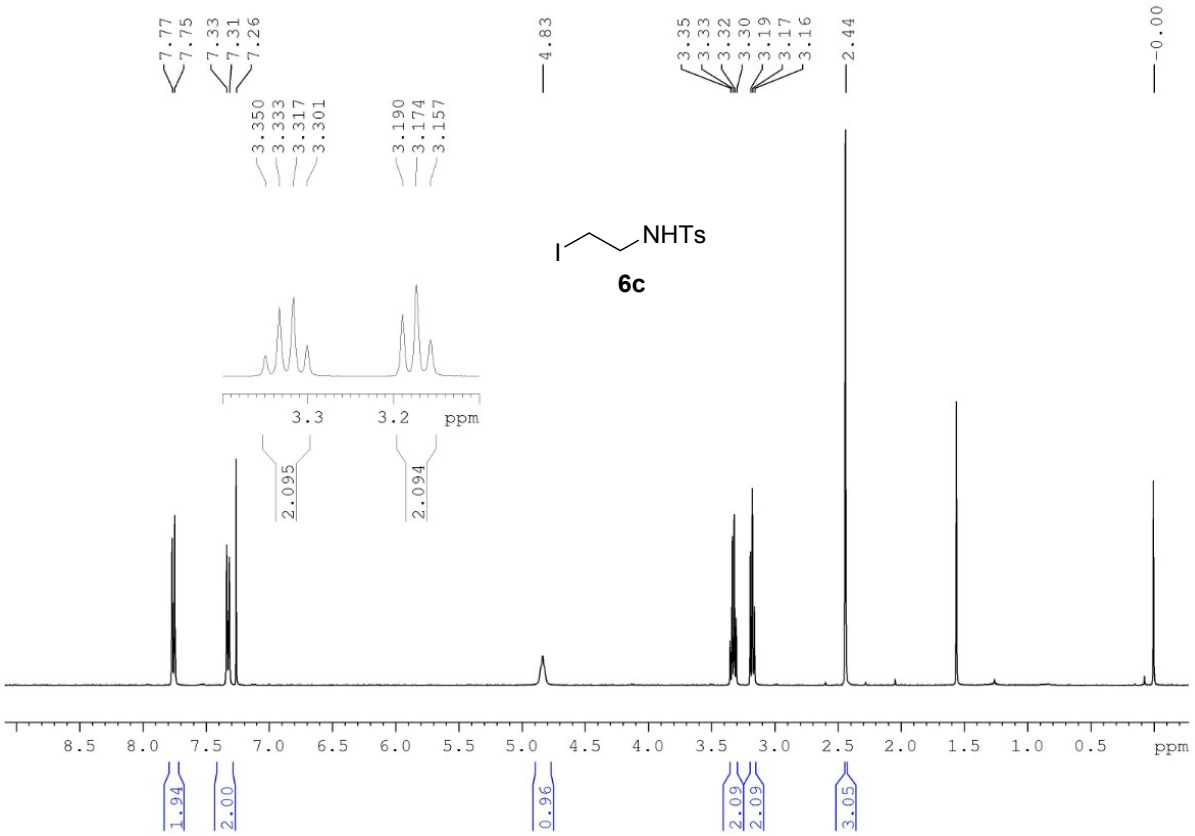
Supporting Information

Iodide 6c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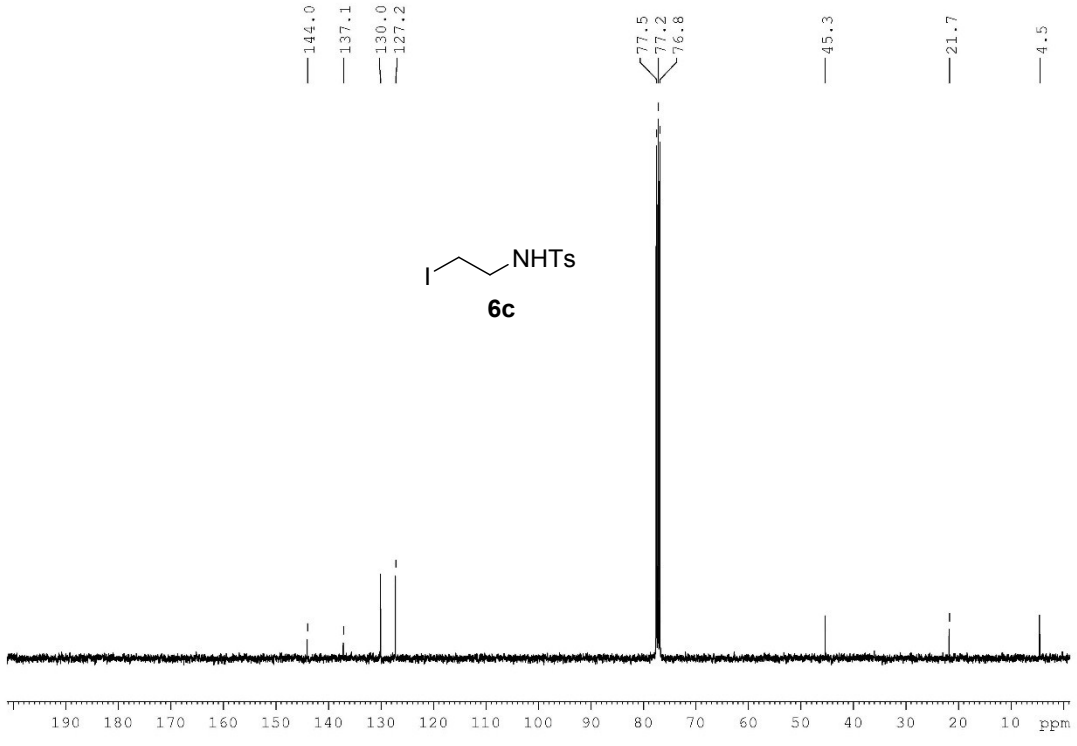
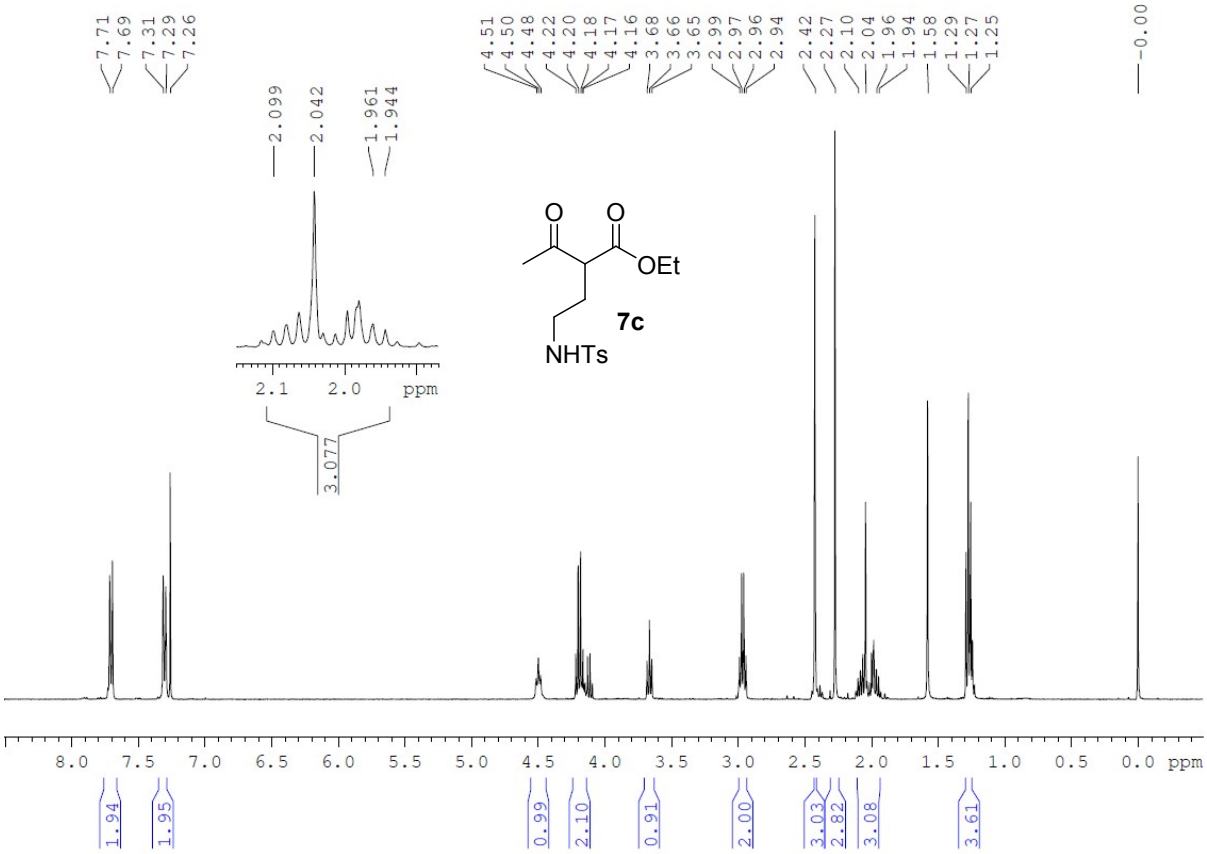
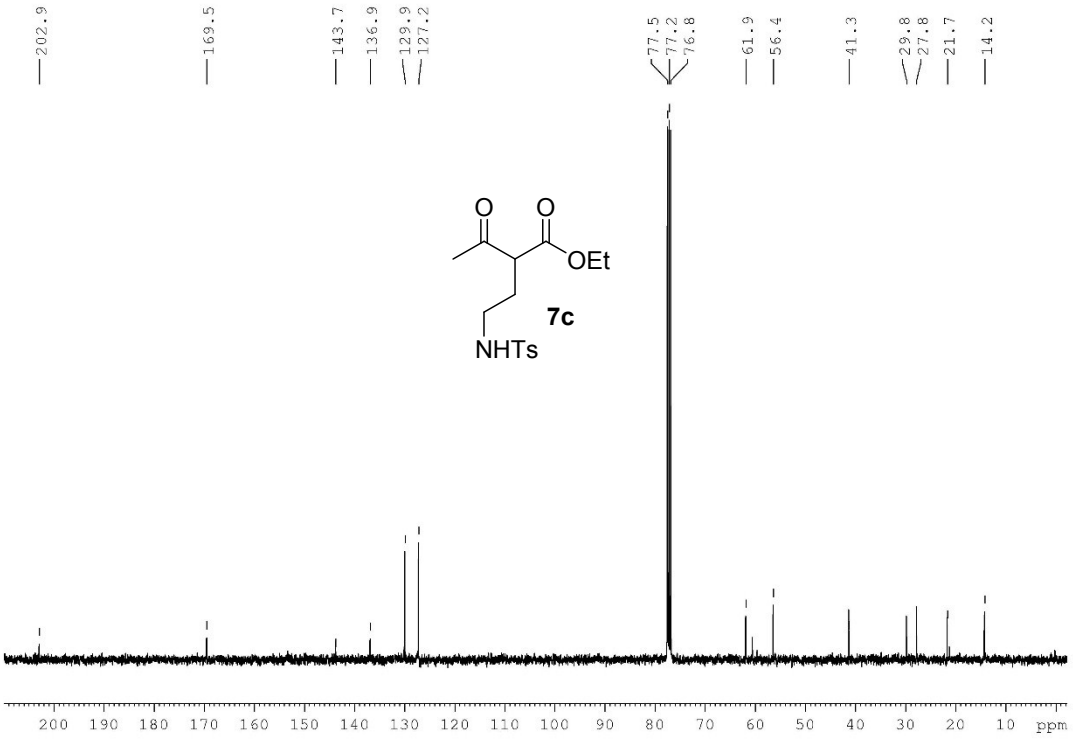
7.75
7.33
7.31
7.26
4.83
3.35
3.33
3.32
3.30
3.19
3.17
3.16
2.44
0.00
3.350
3.333
3.317
3.301
3.190
3.174
3.157
NHTs
6c
3.3
3.2
ppm
2.095
2.094
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.94
2.00
0.96
2.09
2.09
3.05

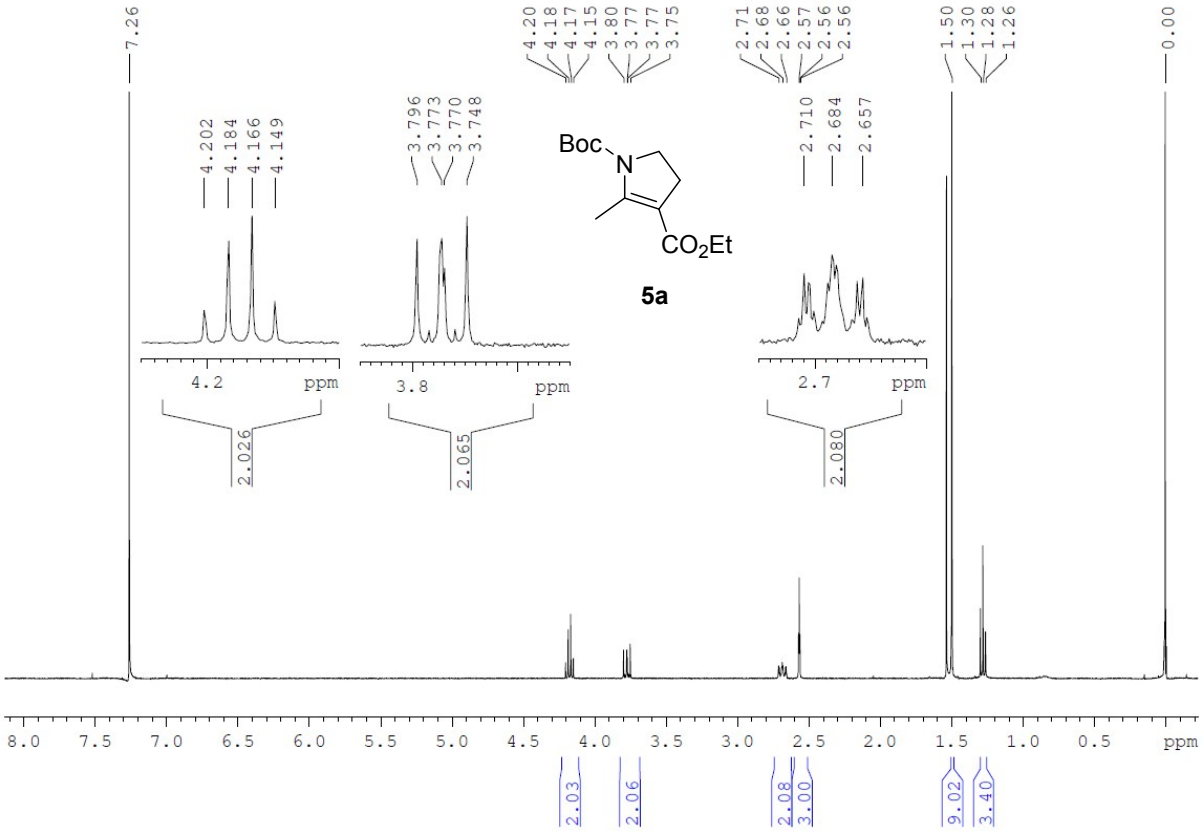

144.0
137.1
130.0
127.2
77.5
77.2
76.8
45.3
21.7
4.5
NHTs
6c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

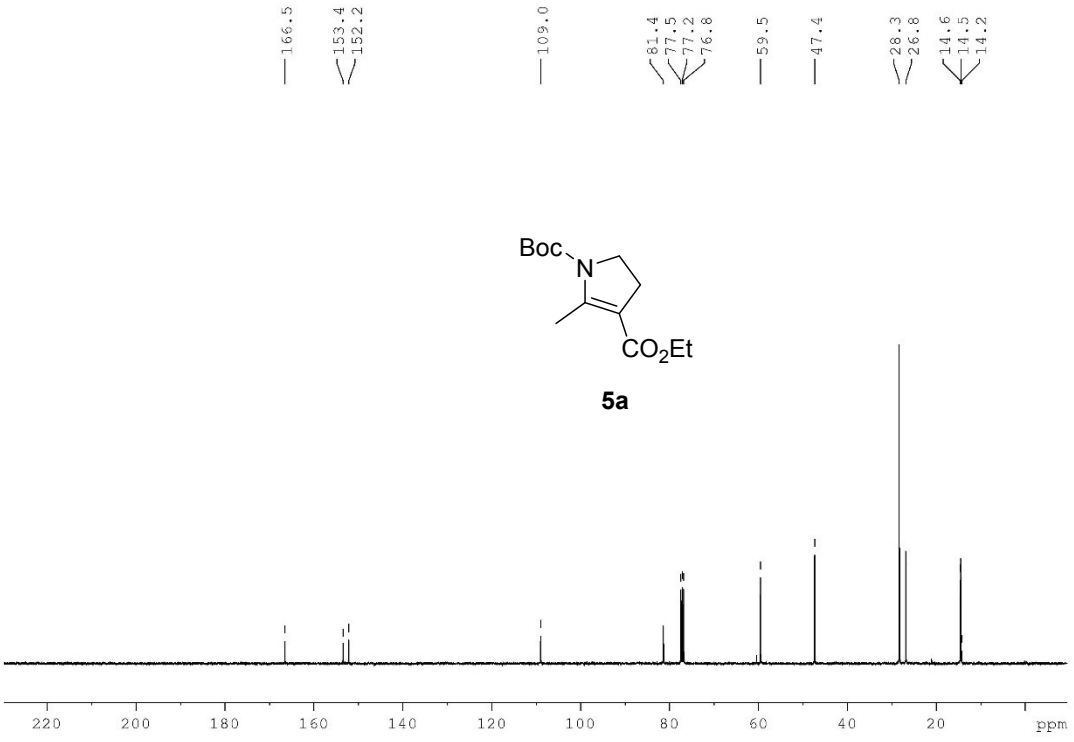
Keto Ester 7c



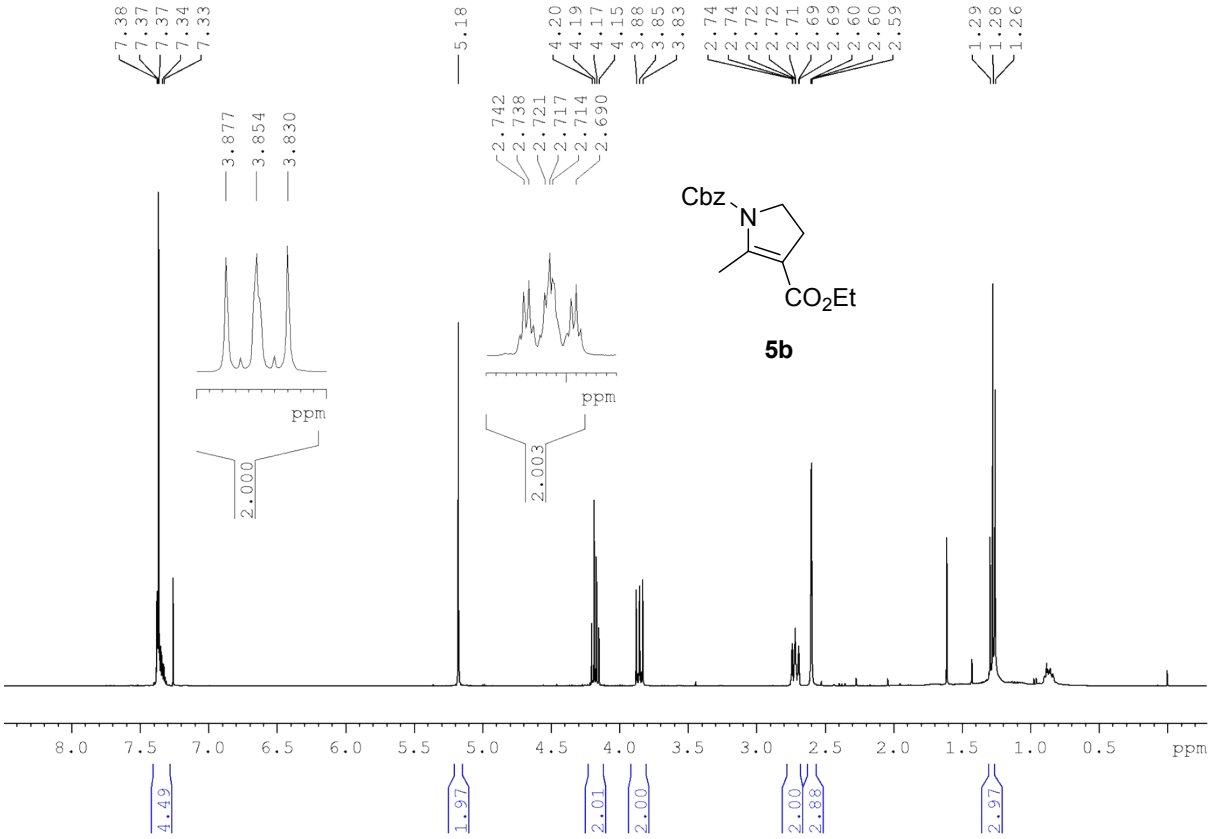


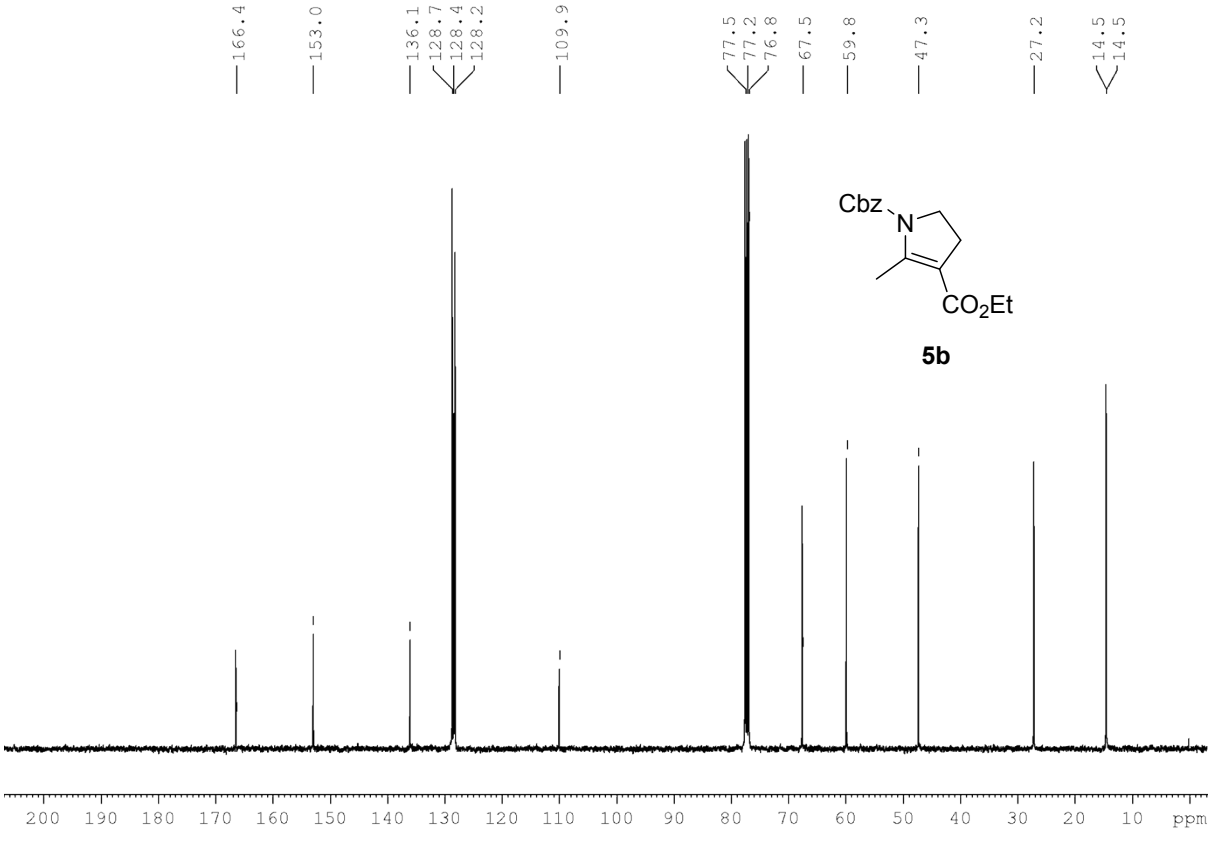
***N*-Boc Ester 5a**





_N_-Cbz Ester 5b





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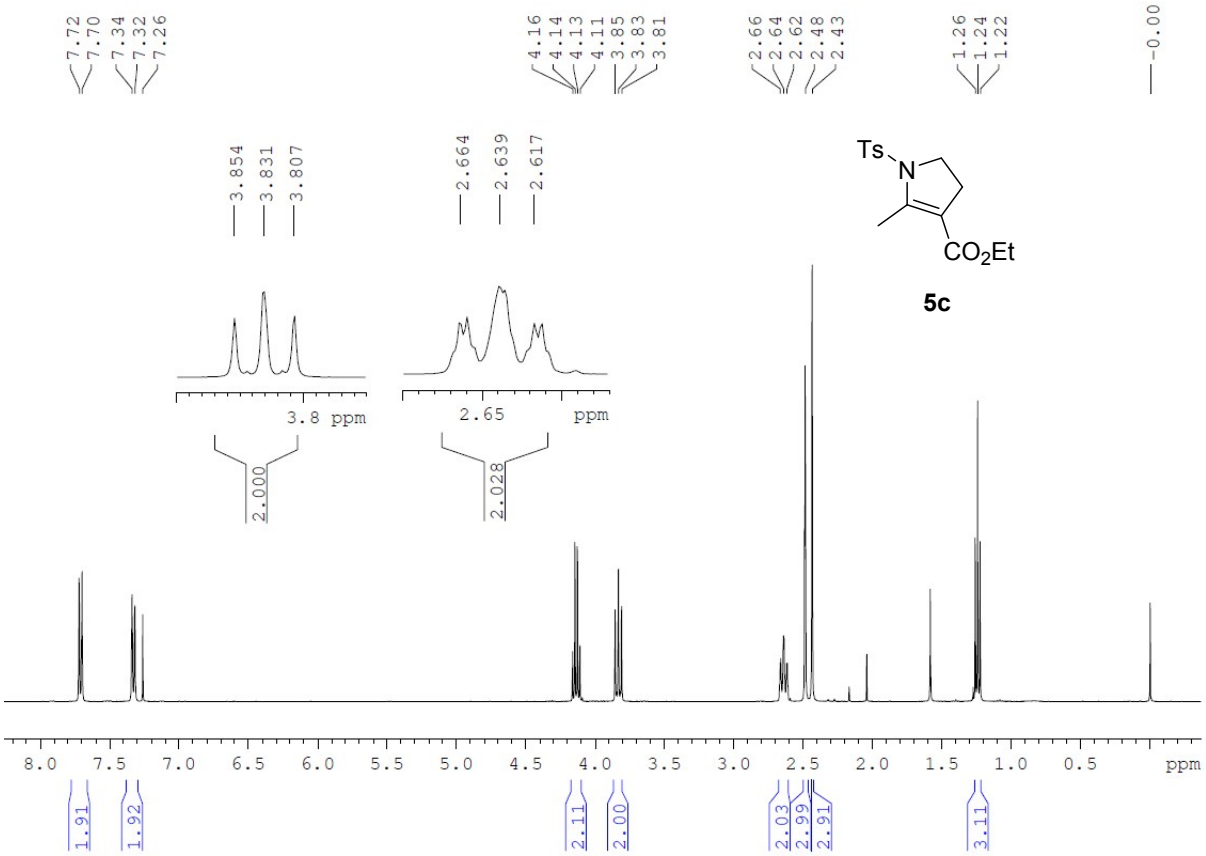
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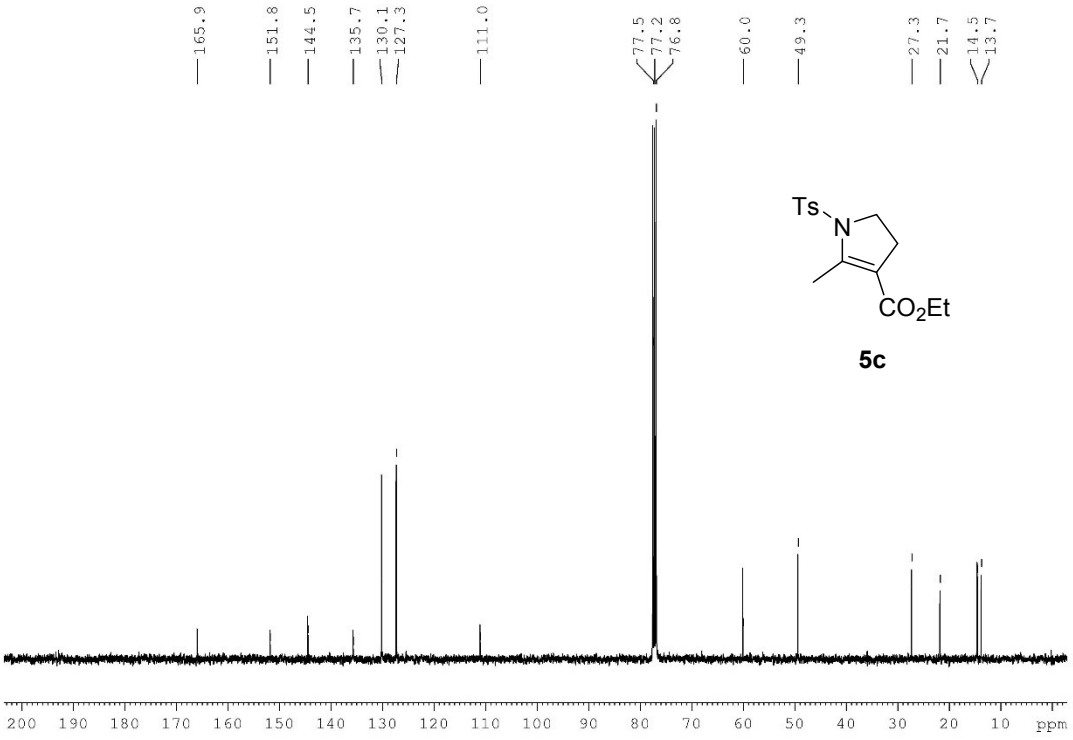
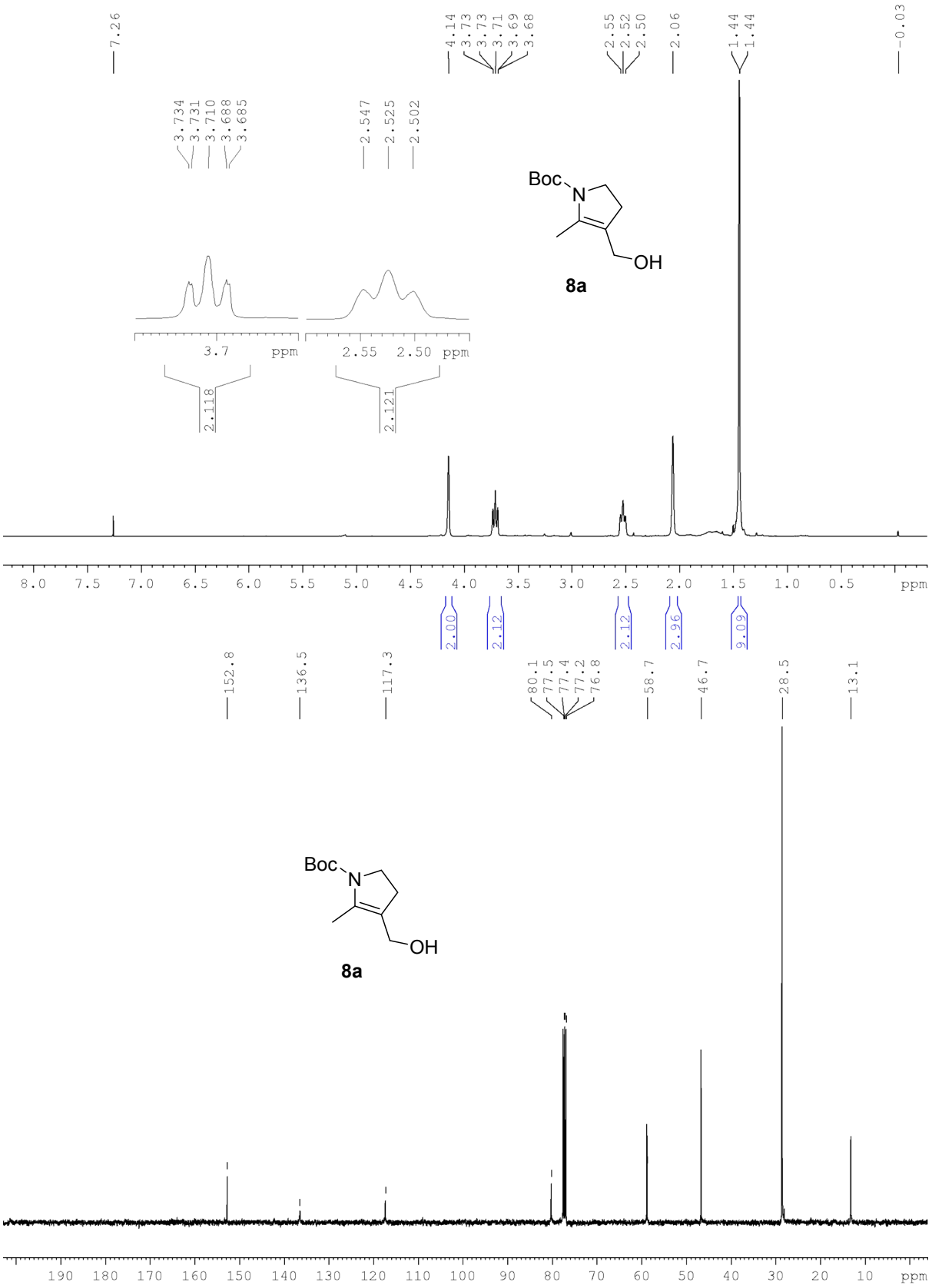
7.70
7.34
7.32
7.26
4.16
4.14
4.13
4.11
3.85
3.83
3.81
2.66
2.64
2.62
2.48
2.43
1.26
1.24
1.22
0.00
3.854
3.831
3.807
2.664
2.639
2.617
Ts
N
CO2Et
5c
3.8 ppm
2.65 ppm
2.000
2.028
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.91
1.92
2.11
2.00
2.03
2.99
2.91
3.11


165.9
151.8
144.5
135.7
130.1
127.3
111.0
77.5
77.2
76.8
60.0
49.3
27.3
21.7
14.5
13.7
Ts
N
CO2Et
5c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Alcohol 8a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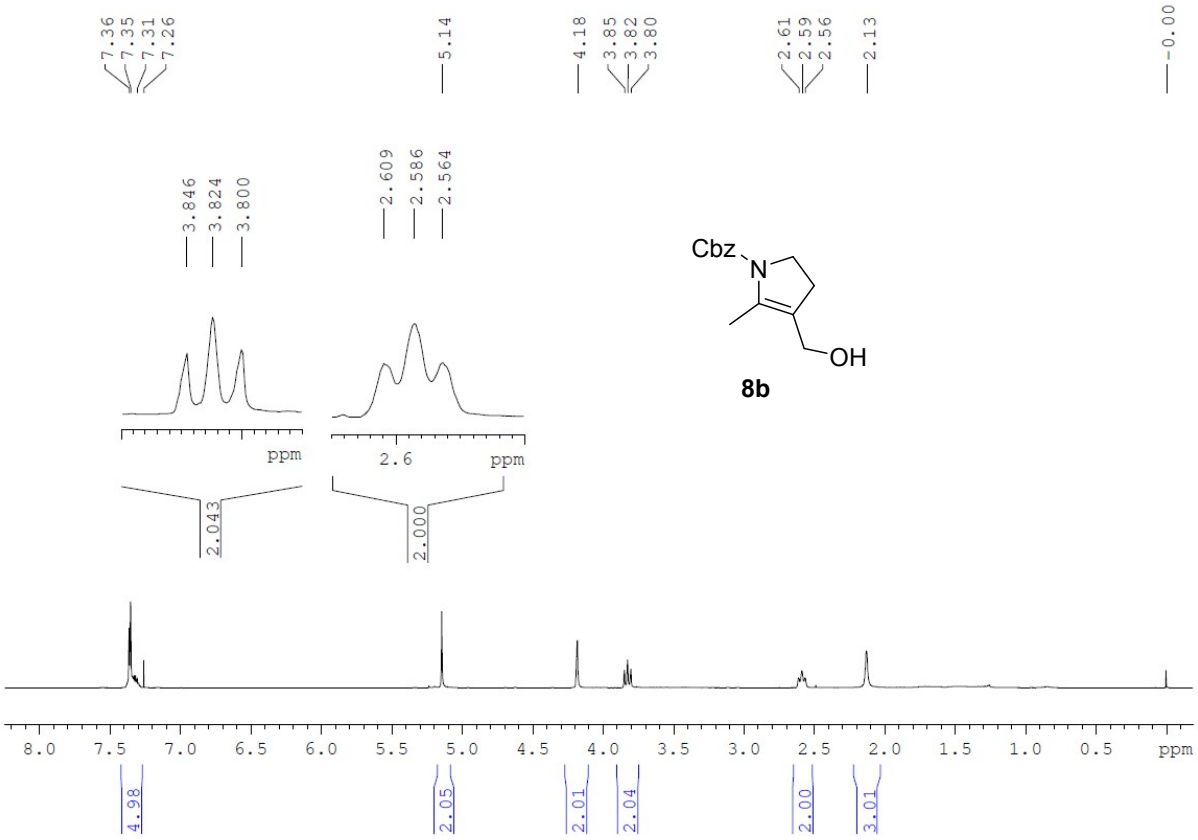
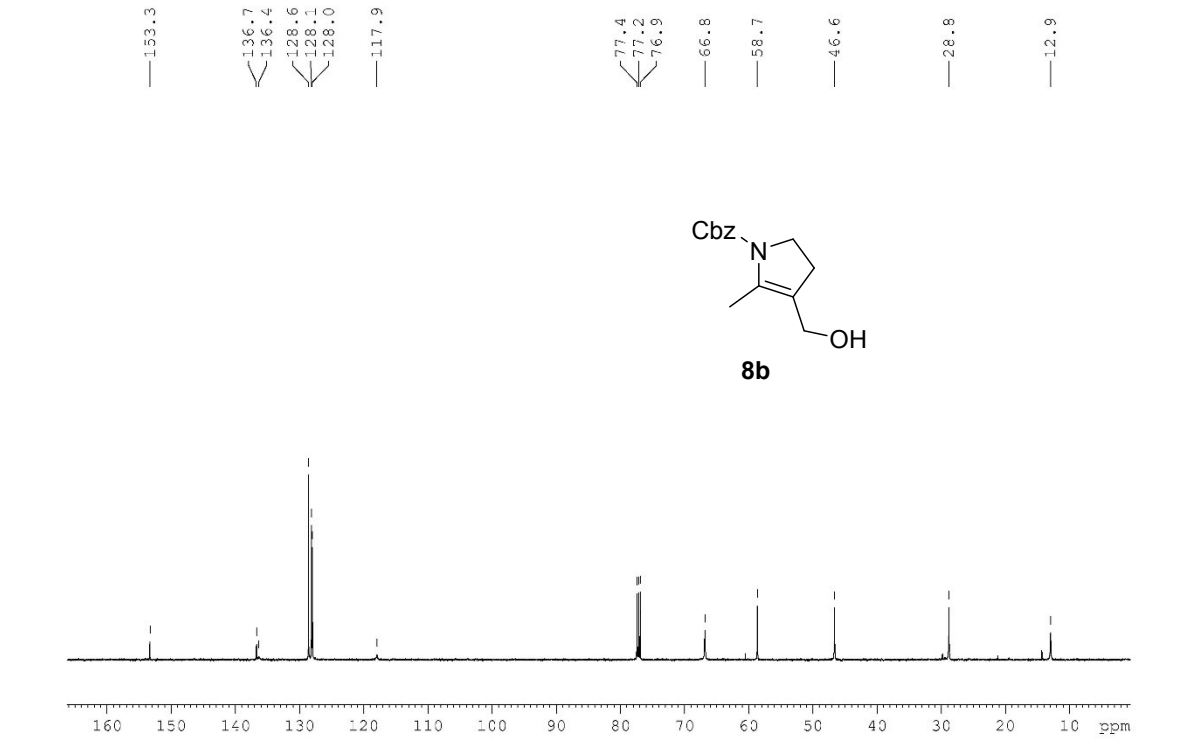
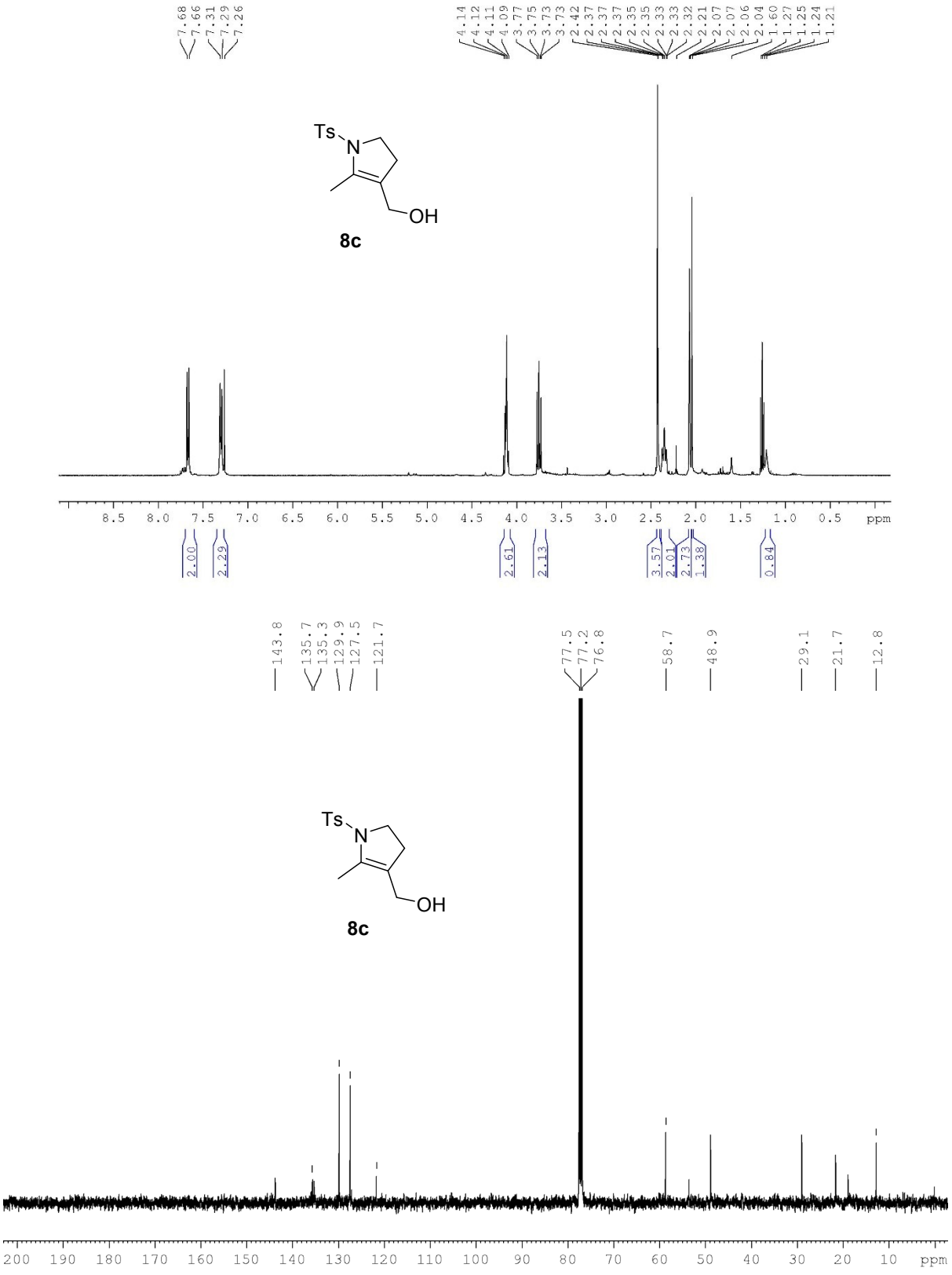
4.14
3.73
3.73
3.71
3.69
3.68
2.55
2.52
2.50
2.06
1.44
1.44
0.03
3.734
3.731
3.710
3.688
3.685
2.547
2.525
2.502
Boc
N
OH
8a
3.7 ppm
2.55 2.50 ppm
2.118
2.121
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.00
2.12
2.12
2.96
9.09
152.8
136.5
117.3
80.1
77.5
77.4
77.2
76.8
58.7
46.7
28.5
13.1
Boc
N
OH
8a
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Alcohol 8b


7.36
7.35
7.31
7.26
5.14
4.18
3.85
3.82
3.80
2.61
2.59
2.56
2.13
0.00
3.846
3.824
3.800
2.609
2.586
2.564
Cbz
N
OH
8b
ppm
2.6
ppm
2.043
2.000
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
4.98
2.05
2.01
2.04
2.00
3.01


153.3
136.7
136.4
128.6
128.1
128.0
117.9
77.4
77.2
76.9
66.8
58.7
46.6
28.8
12.9
Cbz
N
OH
8b
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

Alcohol 8c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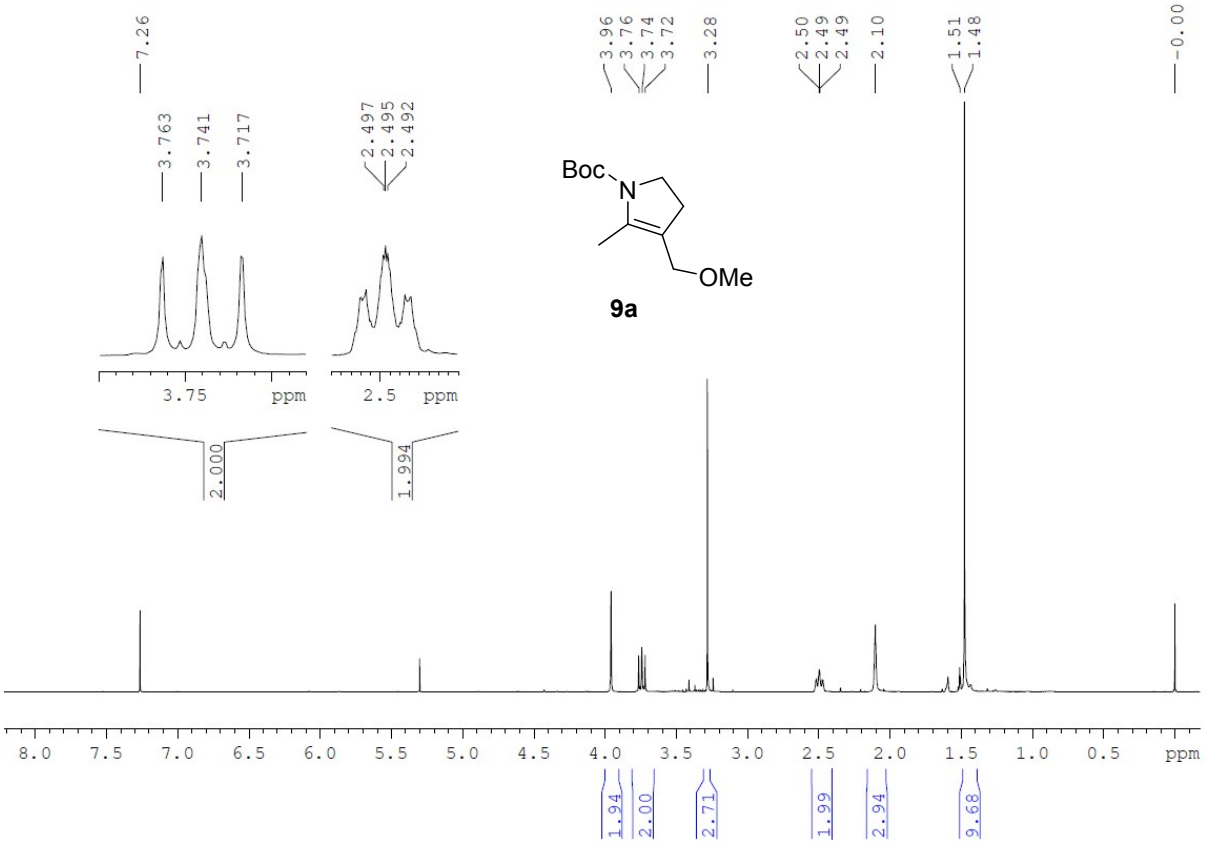
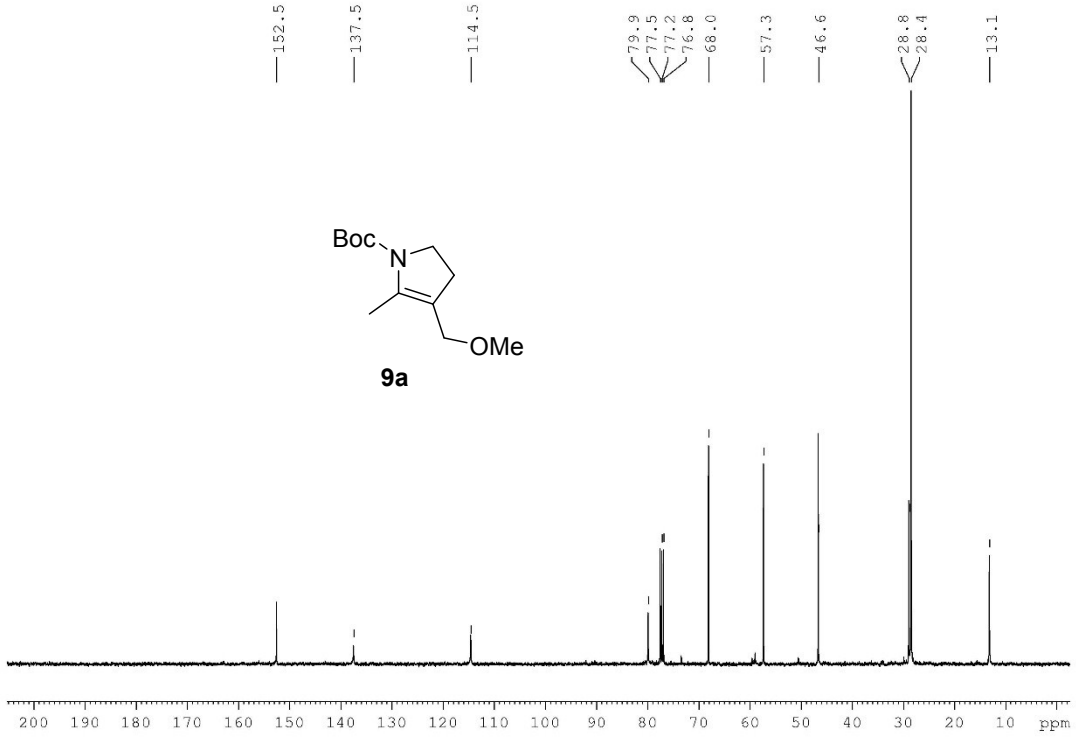
7.66
7.31
7.29
7.26
4.14
4.12
4.11
4.09
3.77
3.75
3.73
3.73
2.42
2.37
2.37
2.37
2.35
2.33
2.33
2.32
2.21
2.07
2.07
2.06
2.04
1.60
1.27
1.25
1.24
1.21
Ts
N
OH
8c
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.00
2.29
2.61
2.13
3.57
2.01
2.73
1.38
0.84
143.8
135.7
135.3
129.9
127.5
121.7
77.5
77.2
76.8
58.7
48.9
29.1
21.7
12.8
Ts
N
OH
8c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Methyl ether 9a





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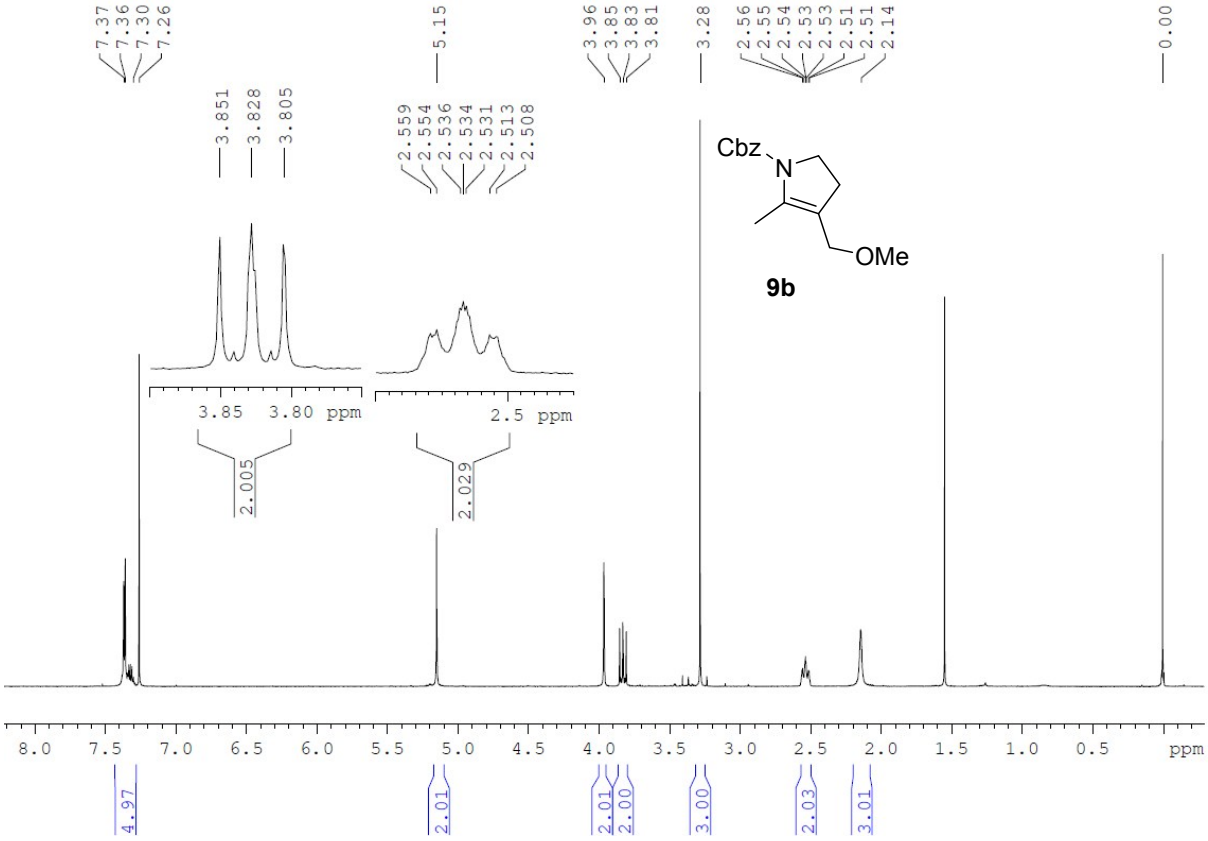
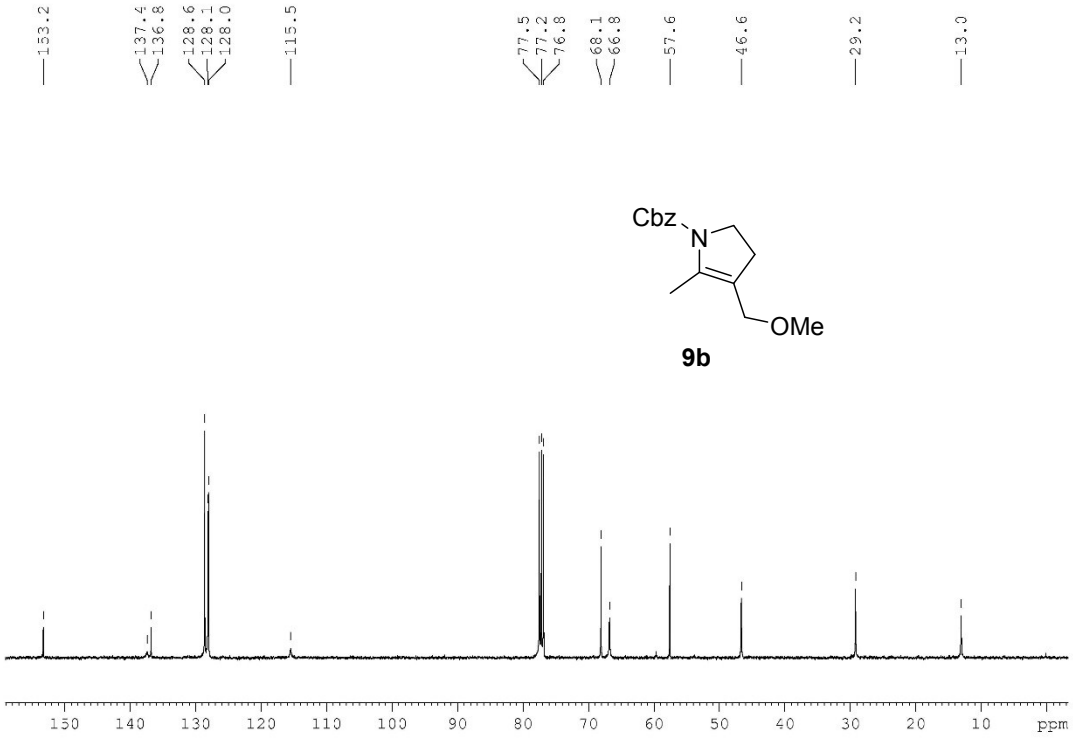
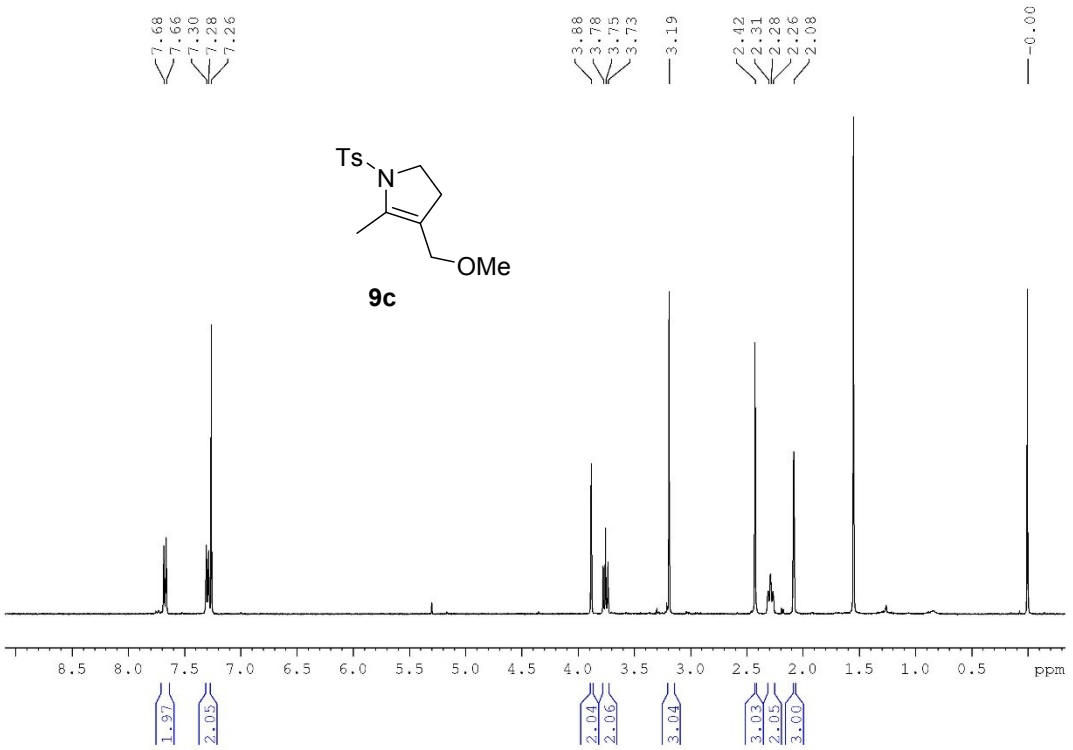
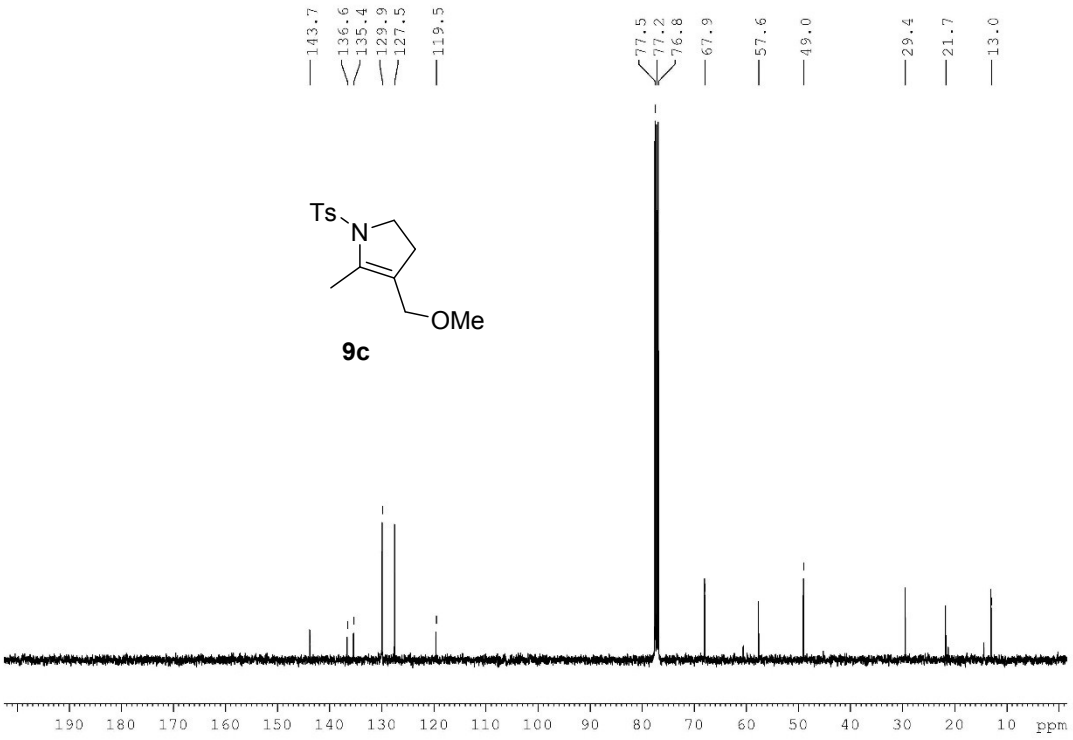


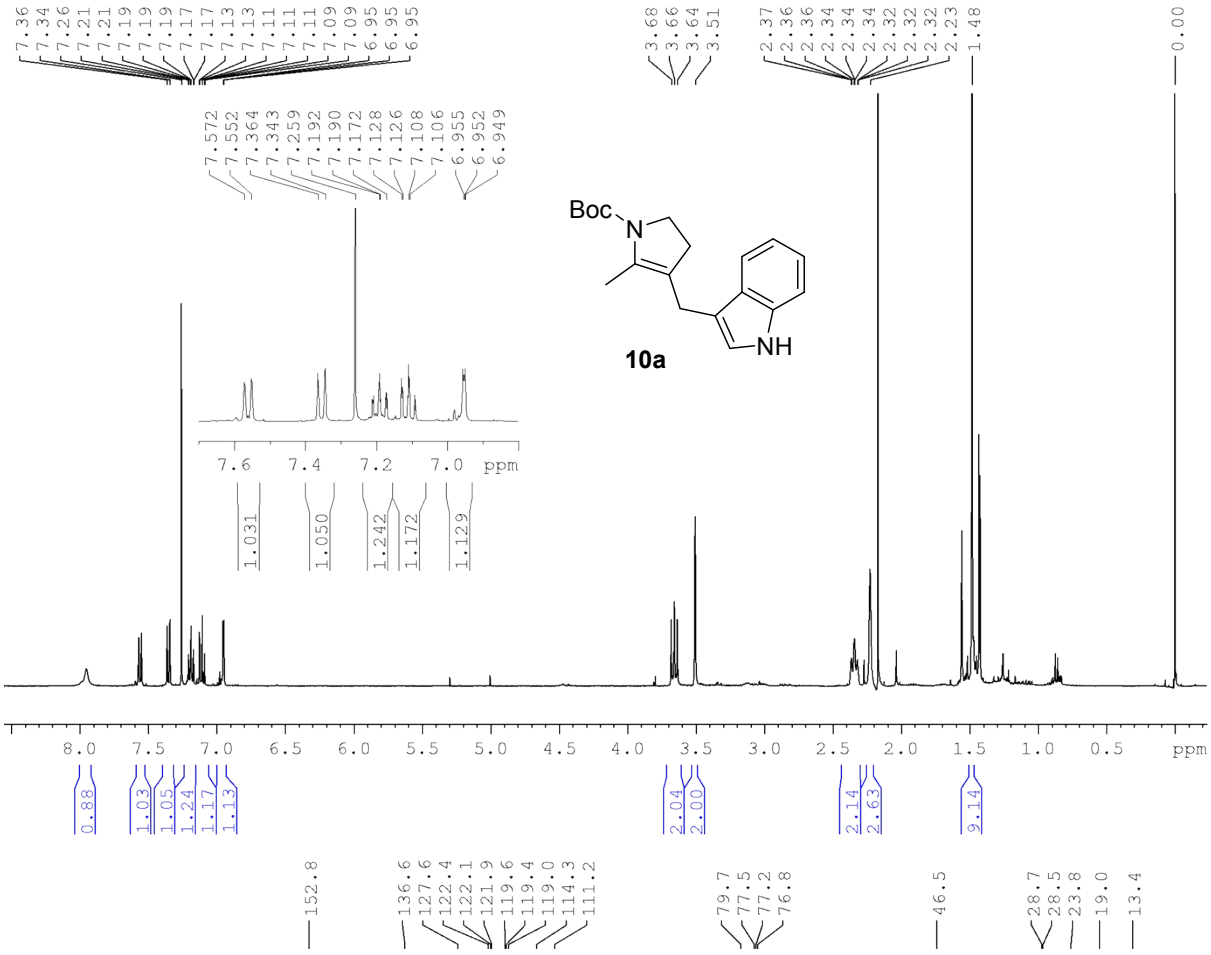


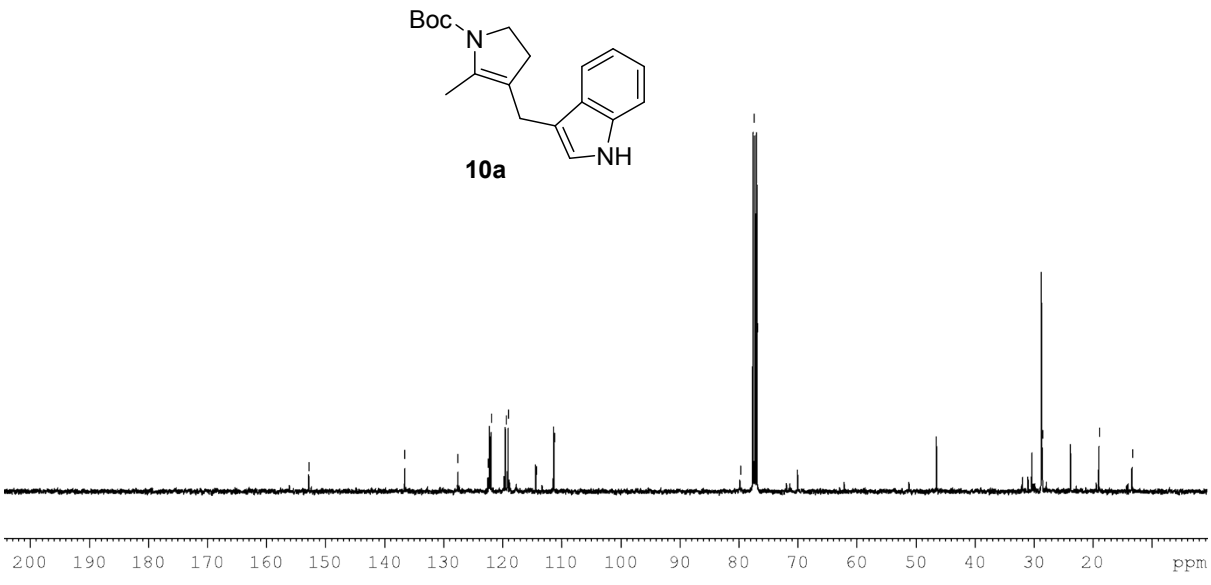
Methyl ether 9c





***N*-Boc enecarbamate 10a**





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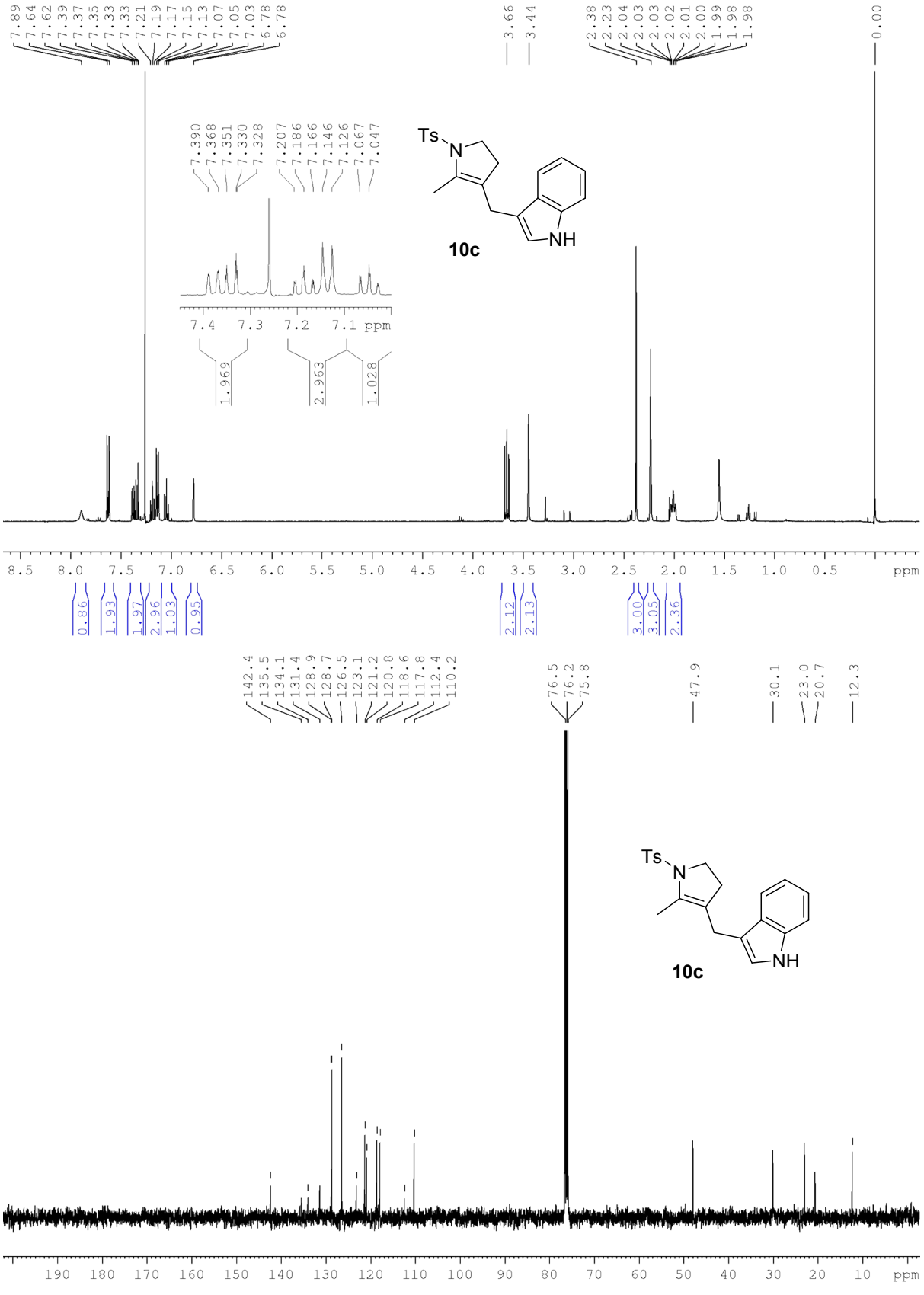
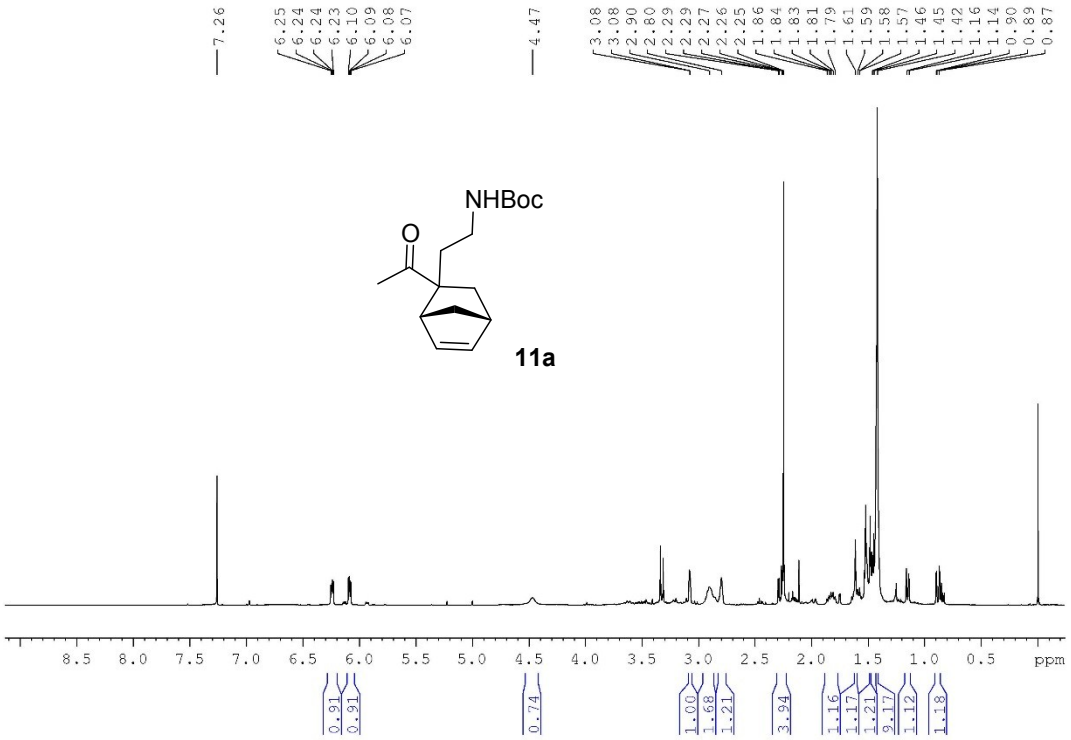
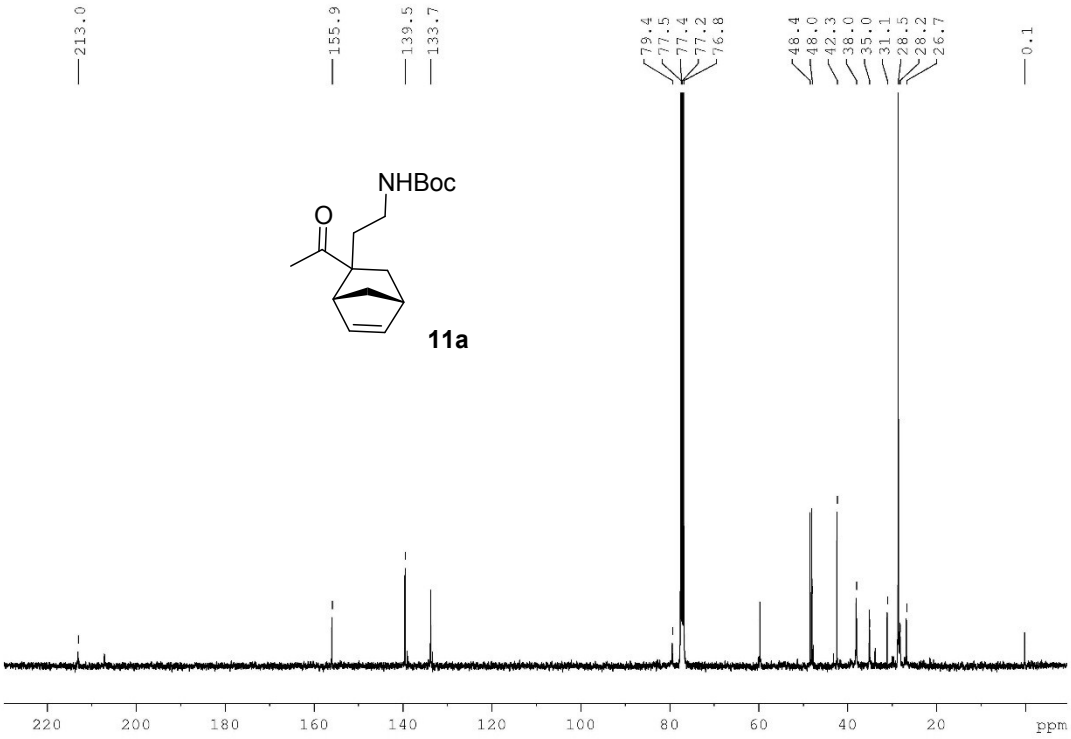
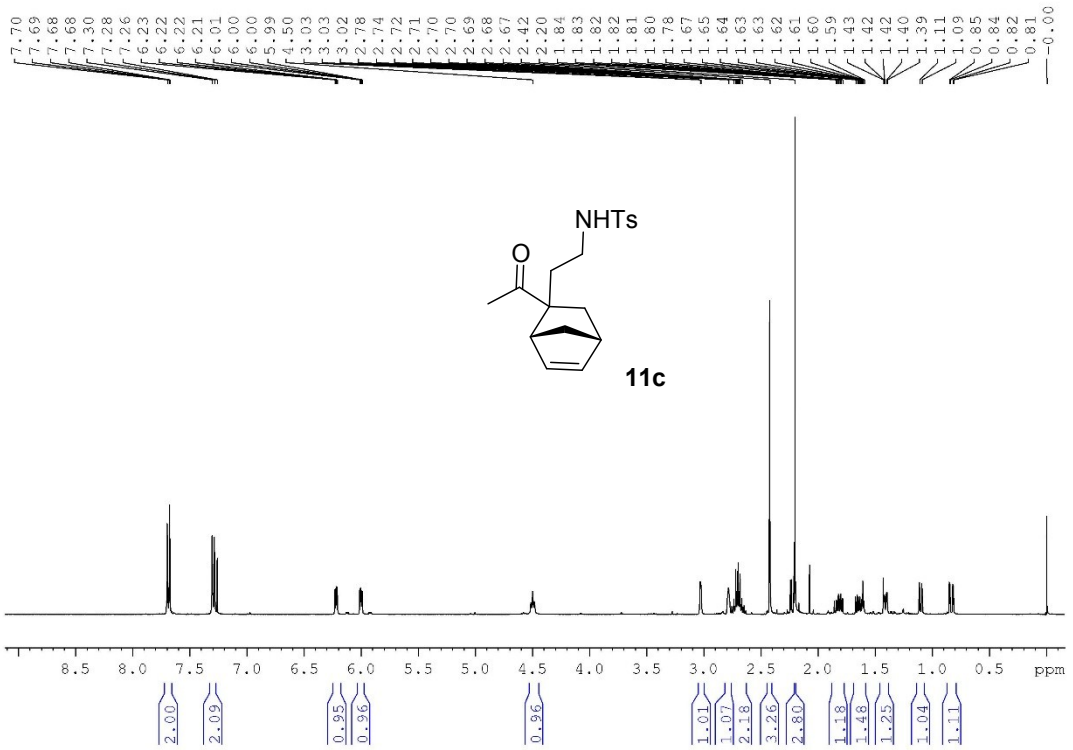


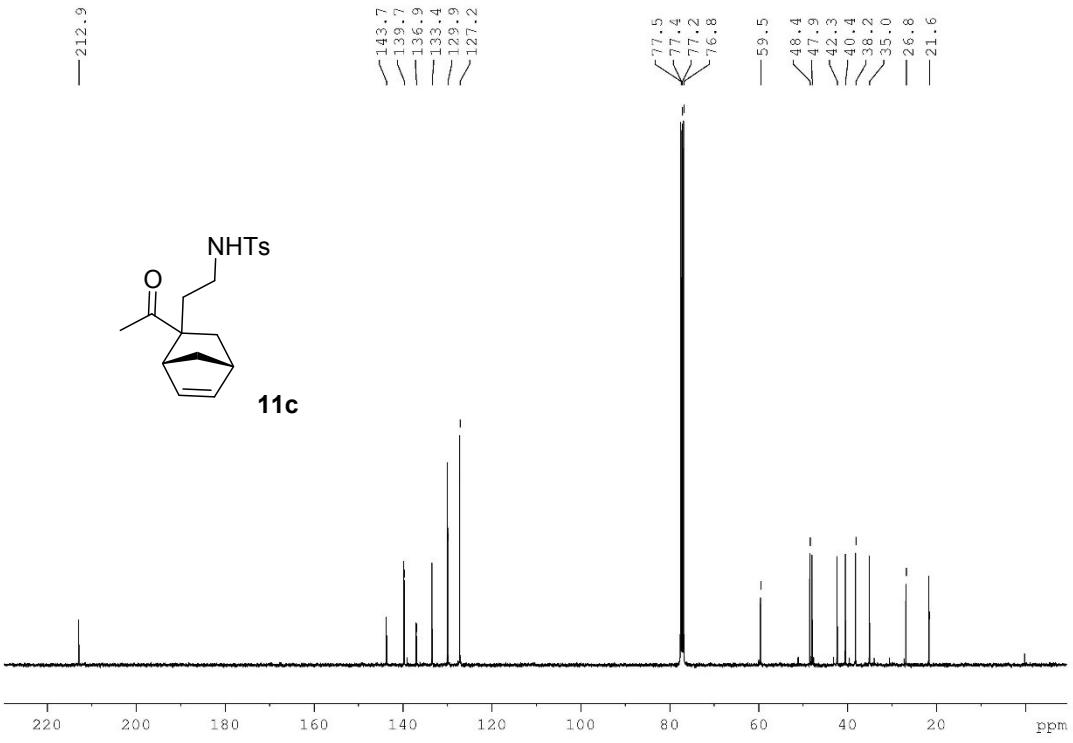
Diels-Alder adduct 11a



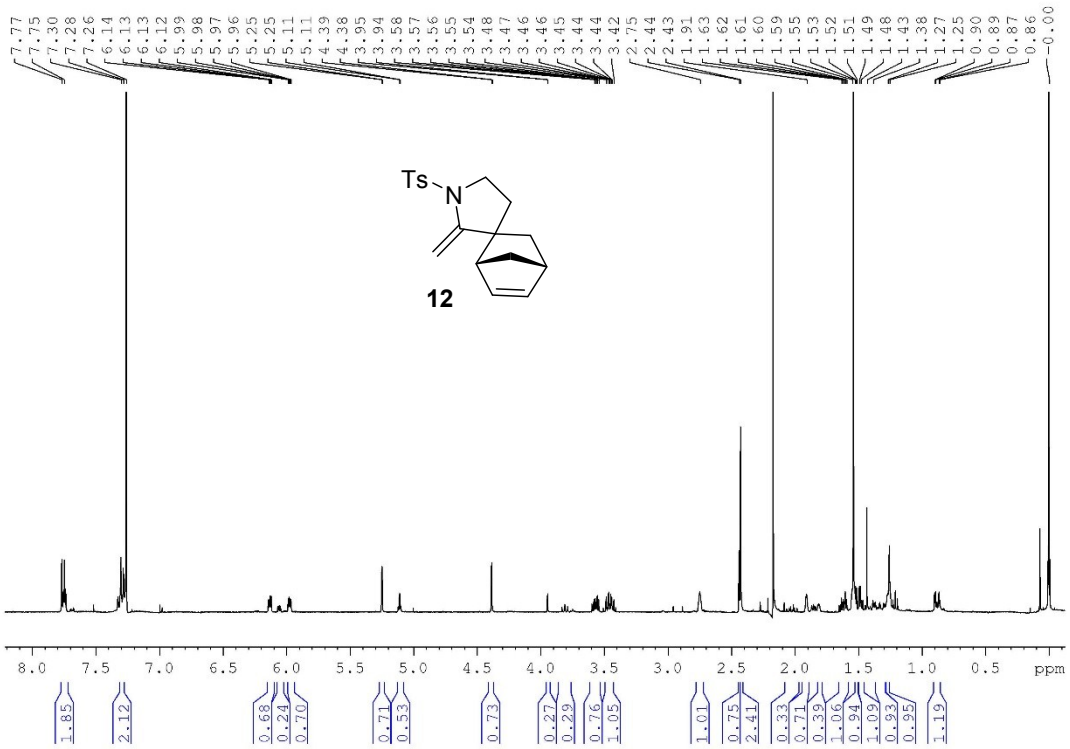


Diels-Alder adduct 11c





Adduct 12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6.14
6.13
6.13
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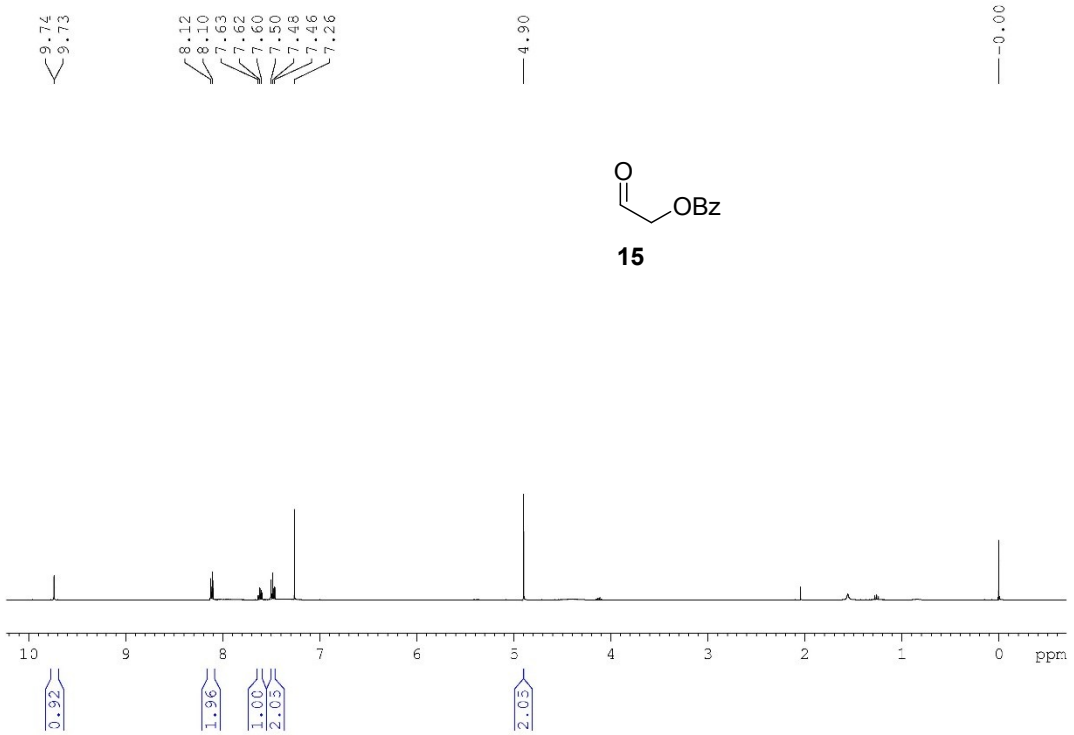
5.98
5.97
5.96
5.25
5.25
5.11
4.39
4.38
3.95
3.94
3.58
3.57
3.56
3.55
3.54
3.48
3.47
3.46
3.46
3.45
3.44
3.44
3.42
2.75
2.44
2.43
1.91
1.63
1.62
1.61
1.60
1.59
1.55
1.53
1.52
1.51
1.49
1.48
1.43
1.38
1.27
1.25
0.90
0.89
0.87
0.86
0.00
Ts
N
12
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.85
2.12
0.68
0.24
0.70
0.71
0.53
0.73
0.27
0.29
0.76
1.05
1.01
0.75
2.41
0.33
0.71
0.39
1.06
0.94
1.09
0.93
0.95
1.19

Aldehyde 15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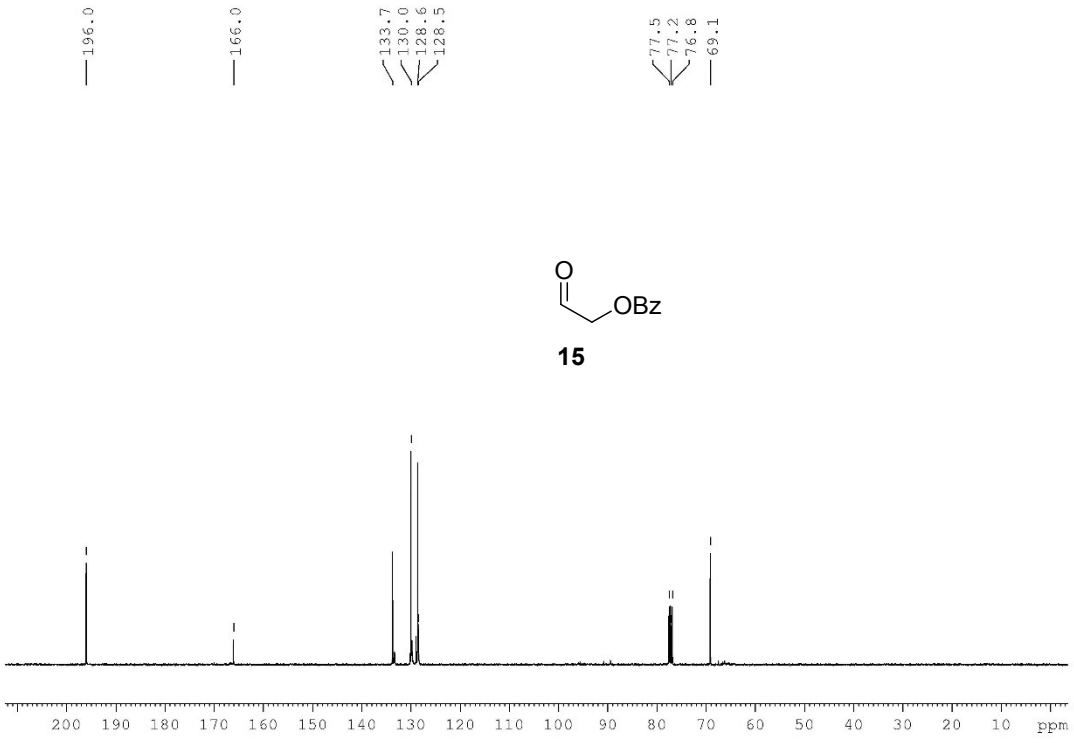
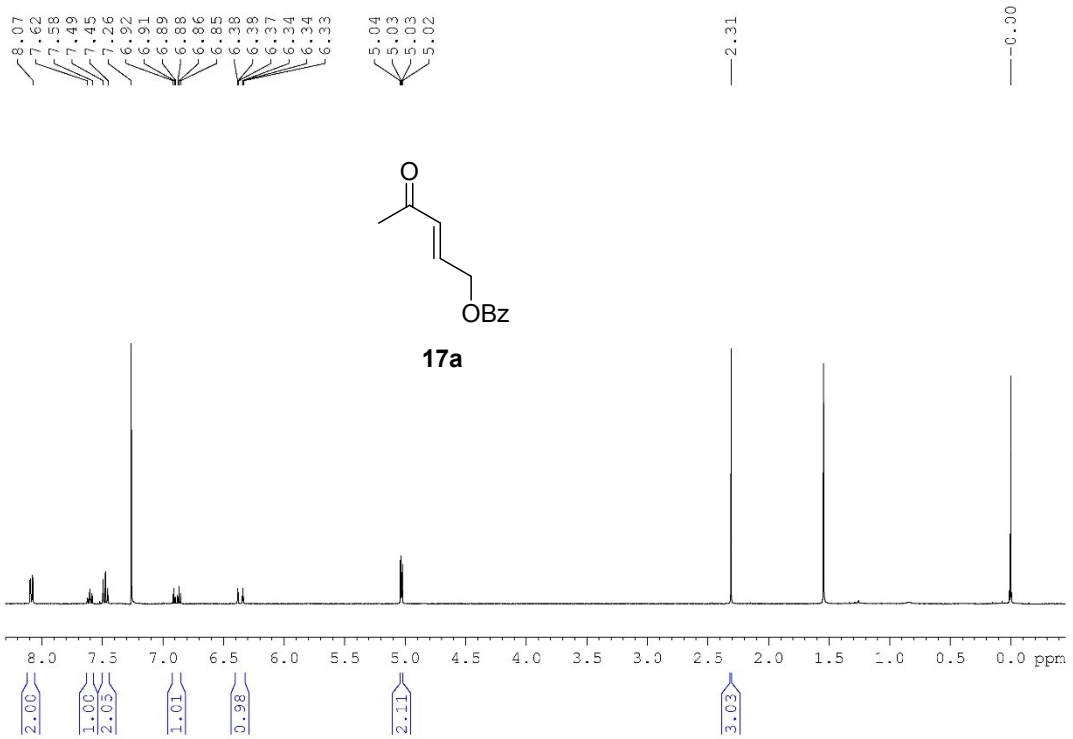
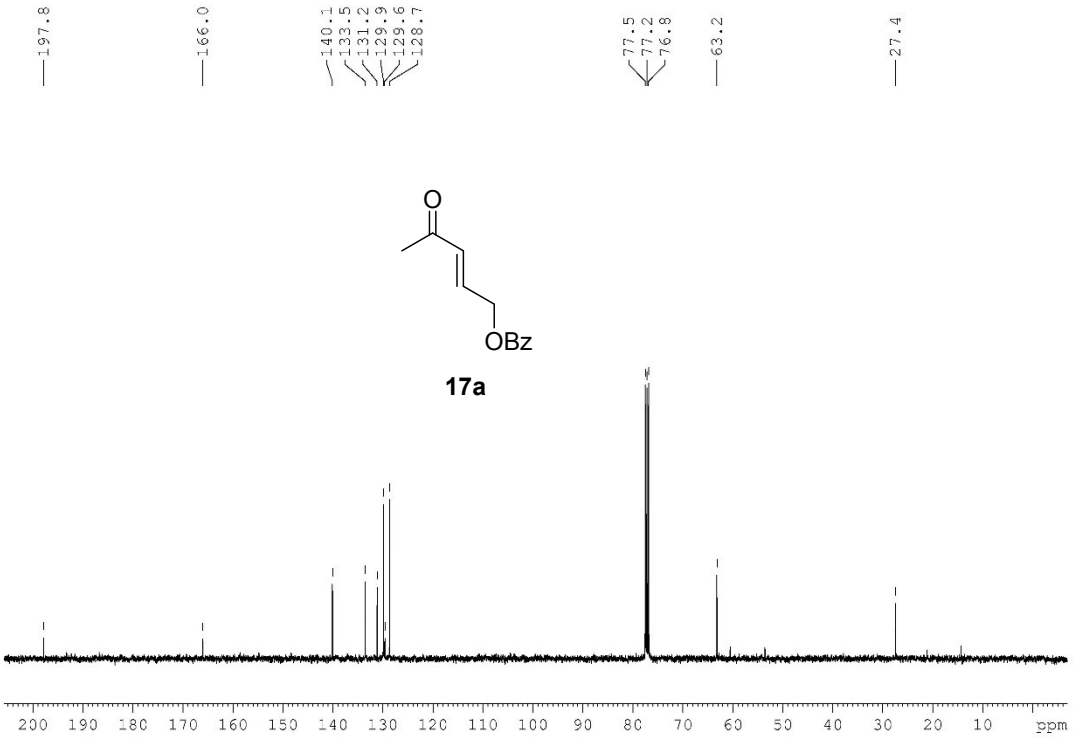
9.73
8.12
8.10
7.63
7.62
7.60
7.50
7.48
7.46
7.26
4.90
0.00
O
OBz
15
10
9
8
7
6
5
4
3
2
1
0
ppm
0.92
1.96
1.00
2.03
2.03

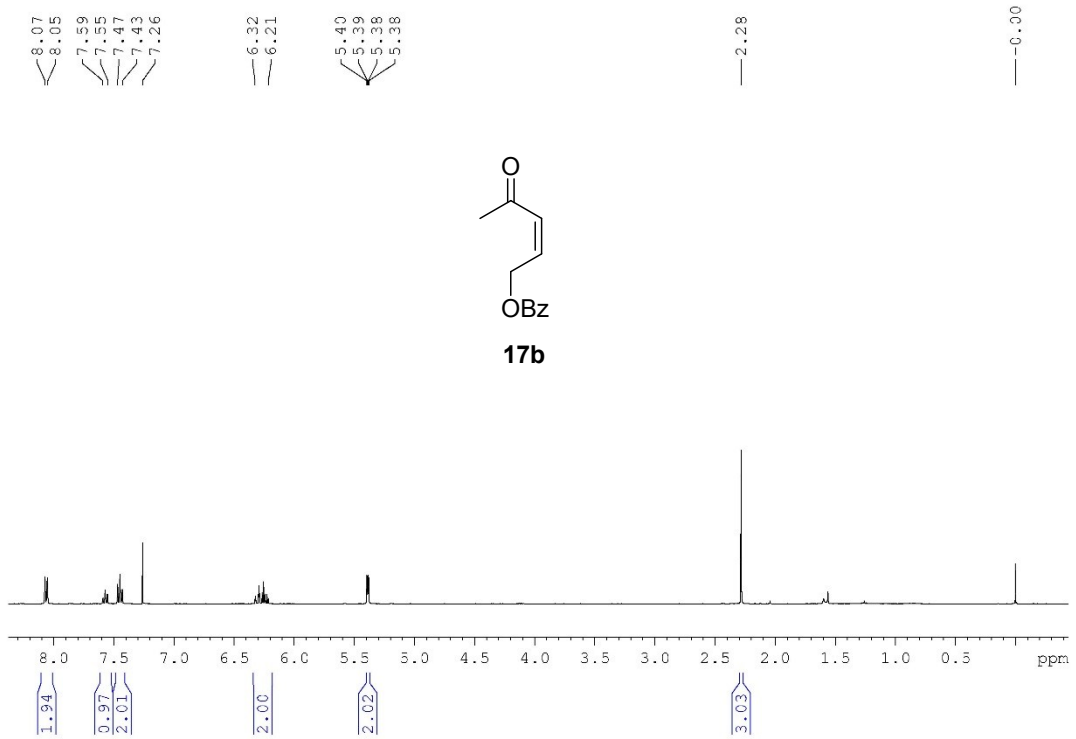

196.0
166.0
133.7
130.0
128.6
128.5
77.5
77.2
76.8
69.1
O
OBz
15
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

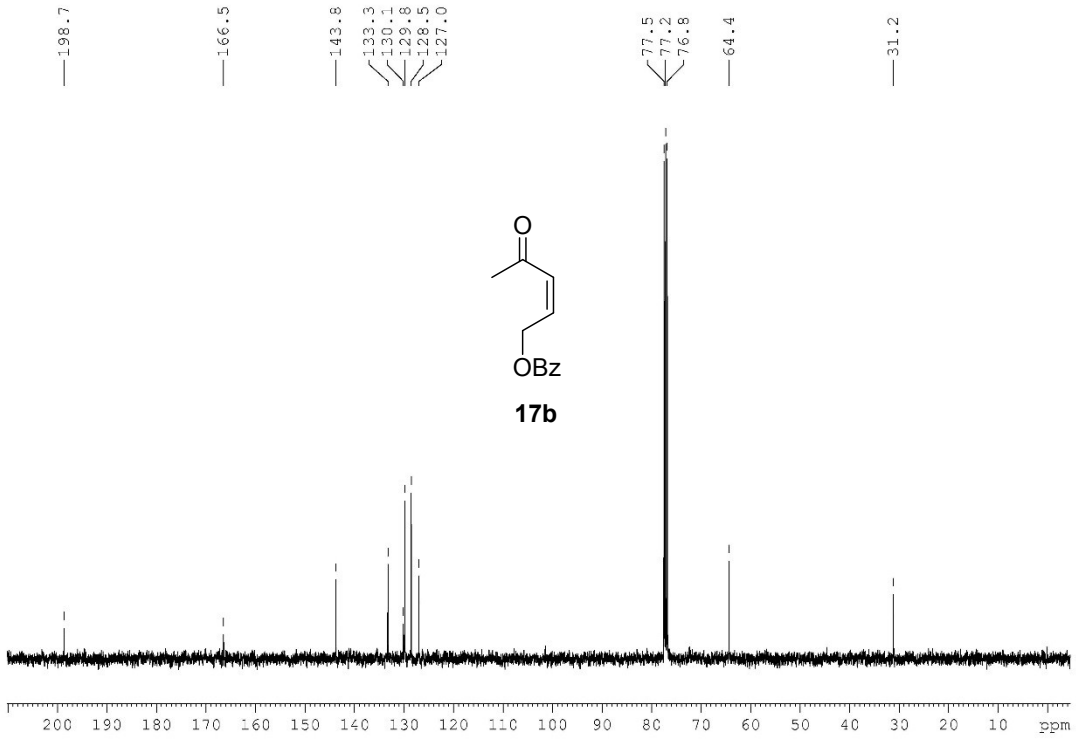
Enone 17a


8.07
7.62
7.58
7.49
7.45
7.26
6.92
6.91
6.89
6.88
6.86
6.85
6.38
6.38
6.37
6.34
6.34
6.33
5.04
5.03
5.03
5.02
2.31
0.00
O
OBz
17a
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
2.00
1.00
2.05
1.01
0.98
2.11
3.03

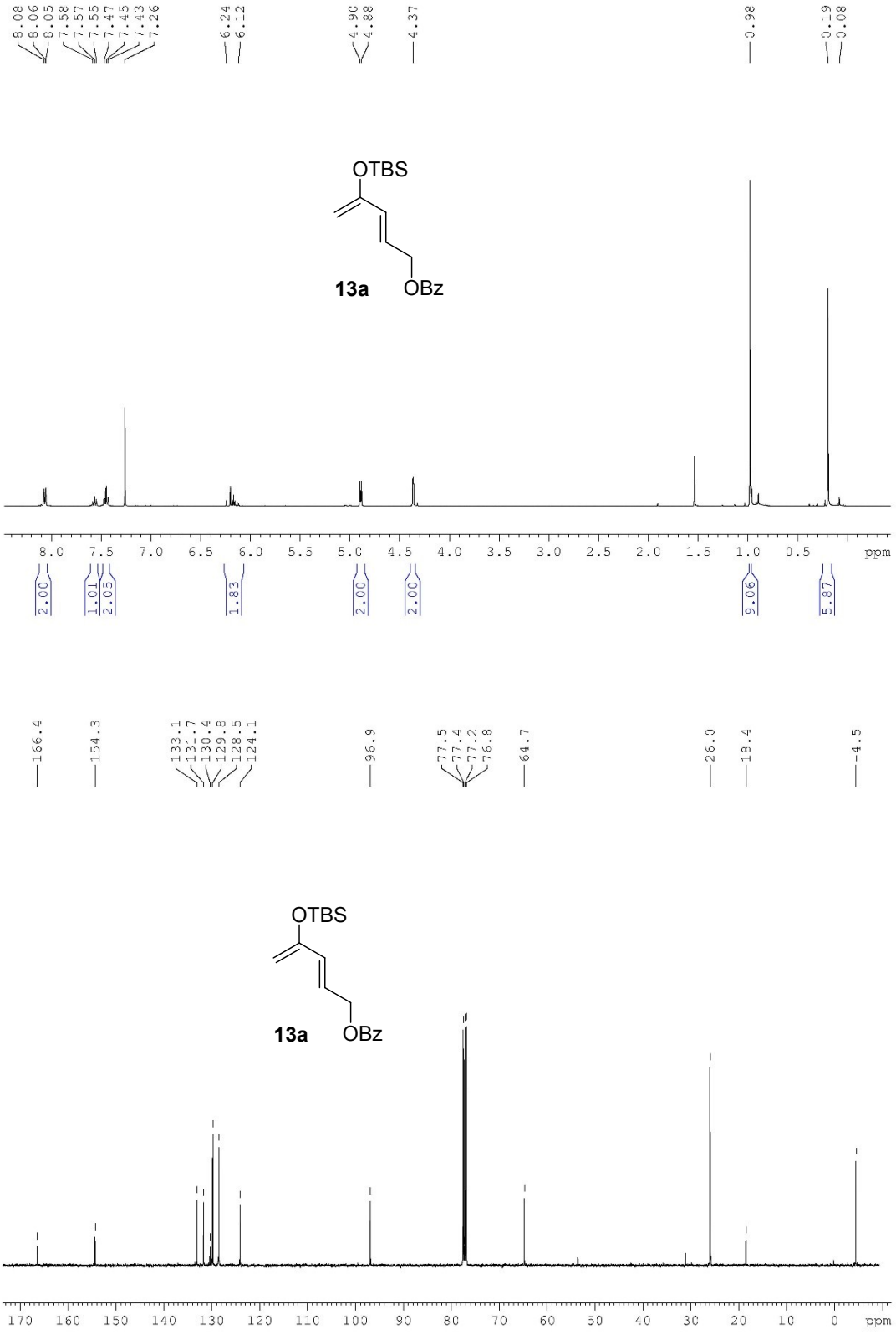

197.8
166.0
140.1
133.5
131.2
129.9
129.6
128.7
77.5
77.2
76.8
63.2
27.4
O
OBz
17a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

Enone 17b

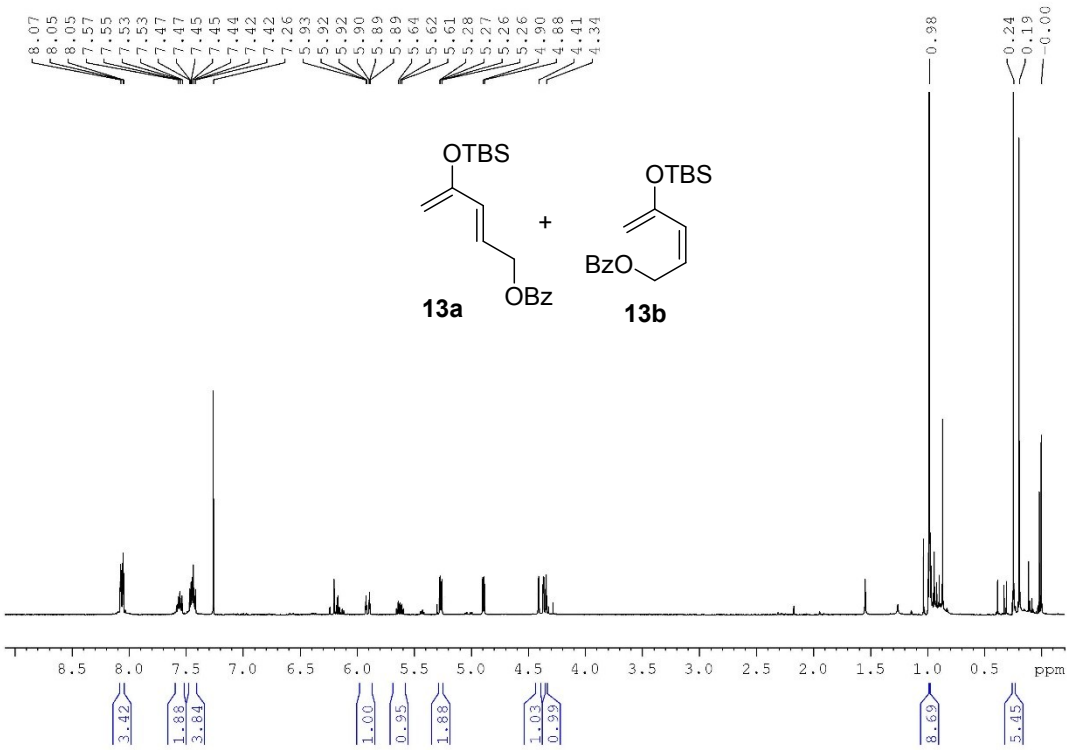

8.07
8.05
7.59
7.55
7.47
7.43
7.26
6.32
6.21
5.40
5.39
5.38
5.38
2.28
0.00
O
OBz
17b
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.94
0.97
2.01
2.00
2.02
3.03

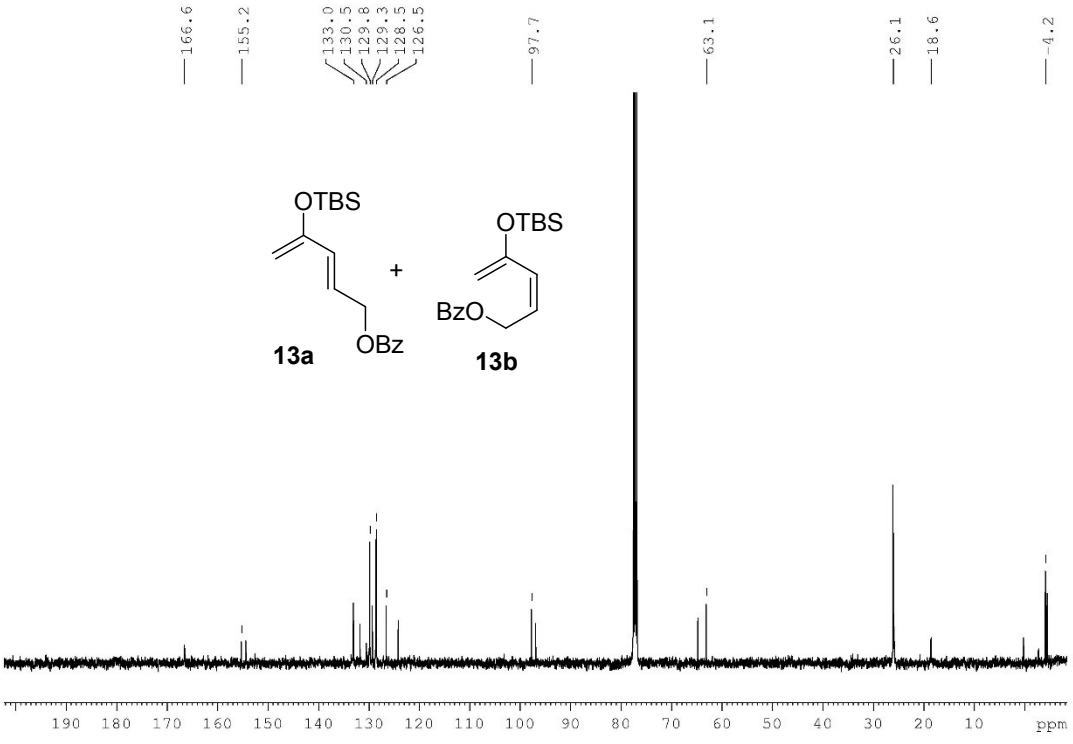

198.7
166.5
143.8
133.3
130.1
129.8
128.5
127.0
77.5
77.2
76.8
64.4
31.2
O
OBz
17b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

Silyloxy diene 13a

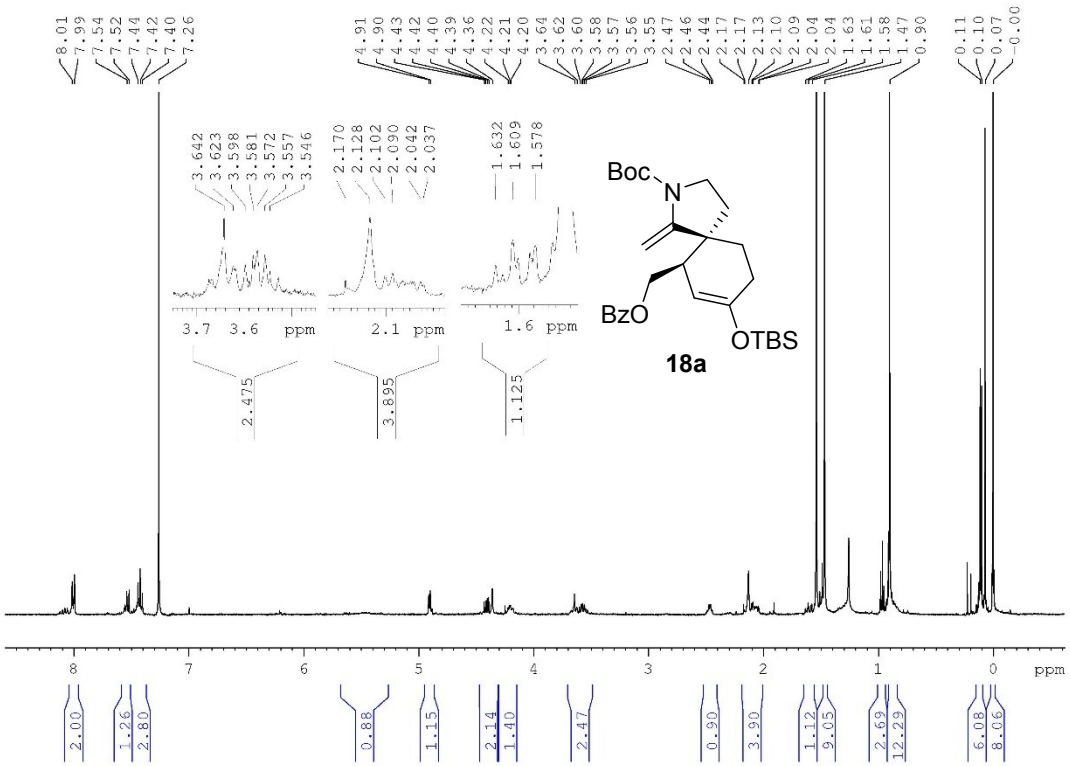


Mixture of Silyloxy dienes 13a-b

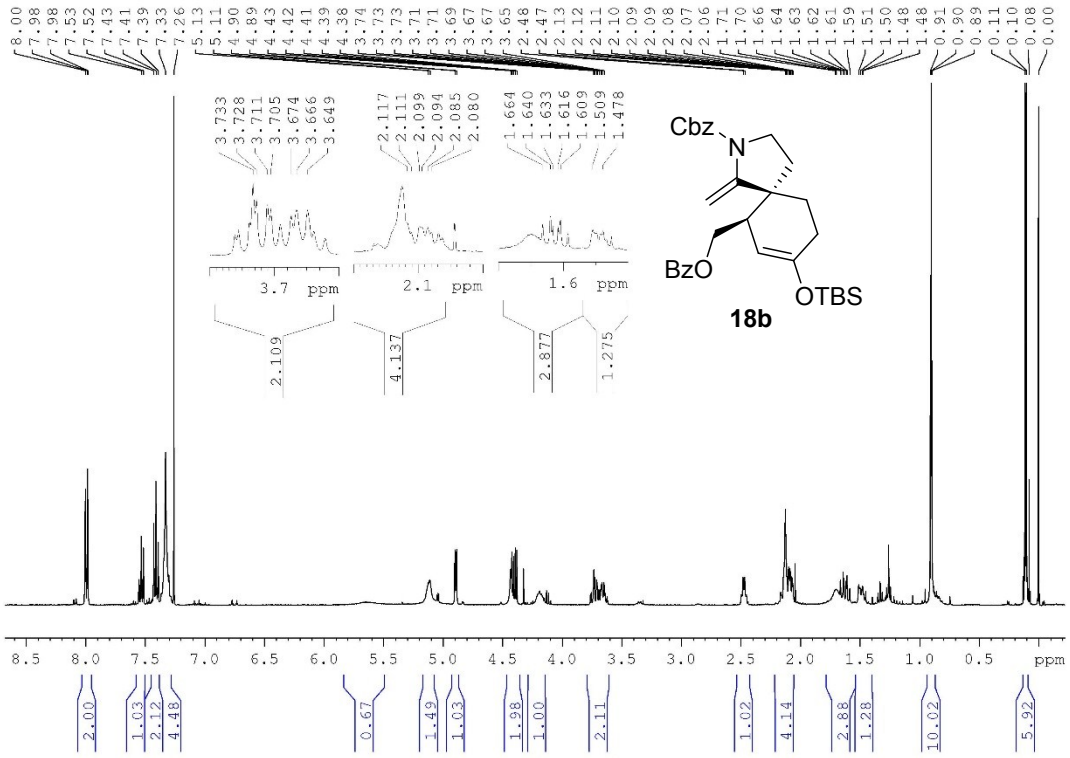


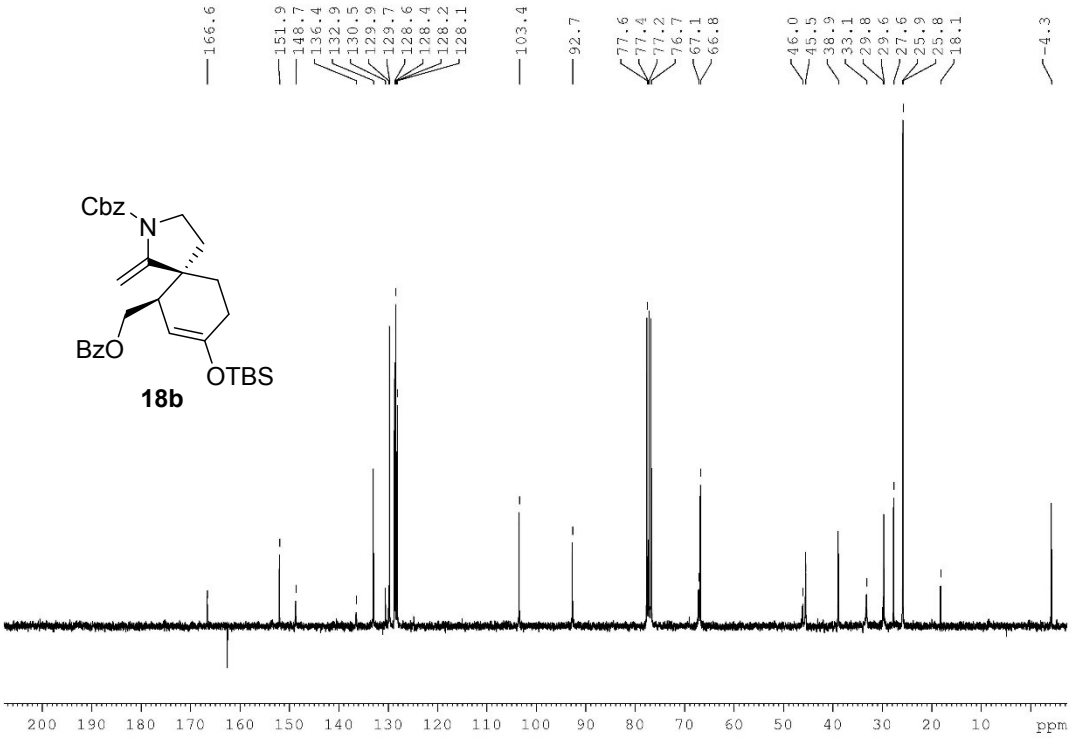


***N*-Boc enecarbamate adduct 18a**

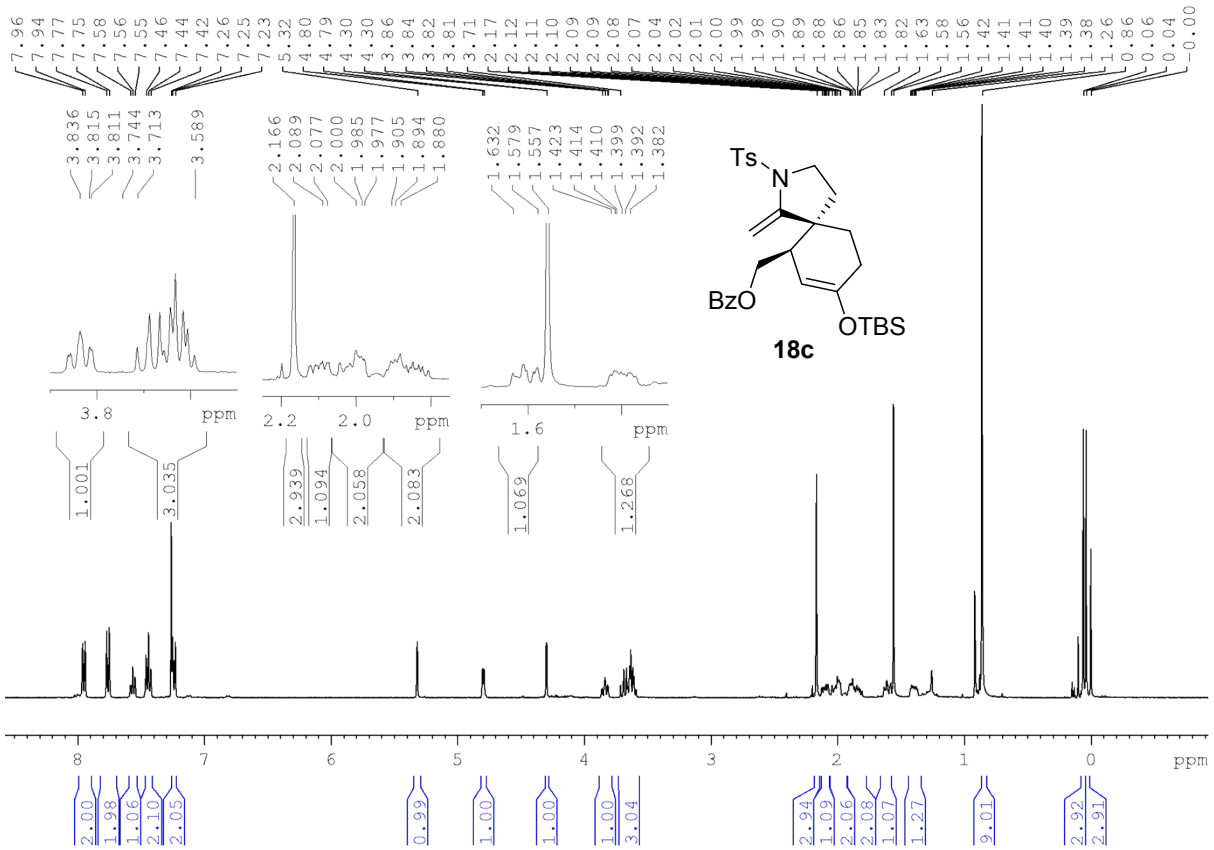


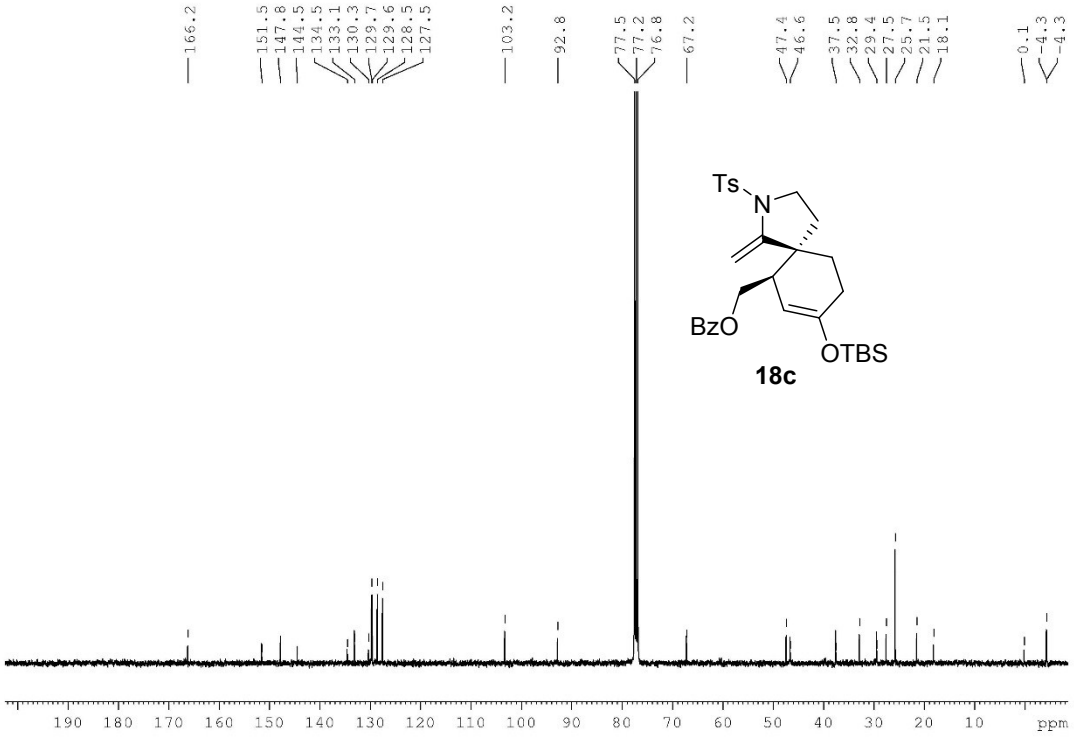
***N*-Cbz enecarbamate adduct 18b**



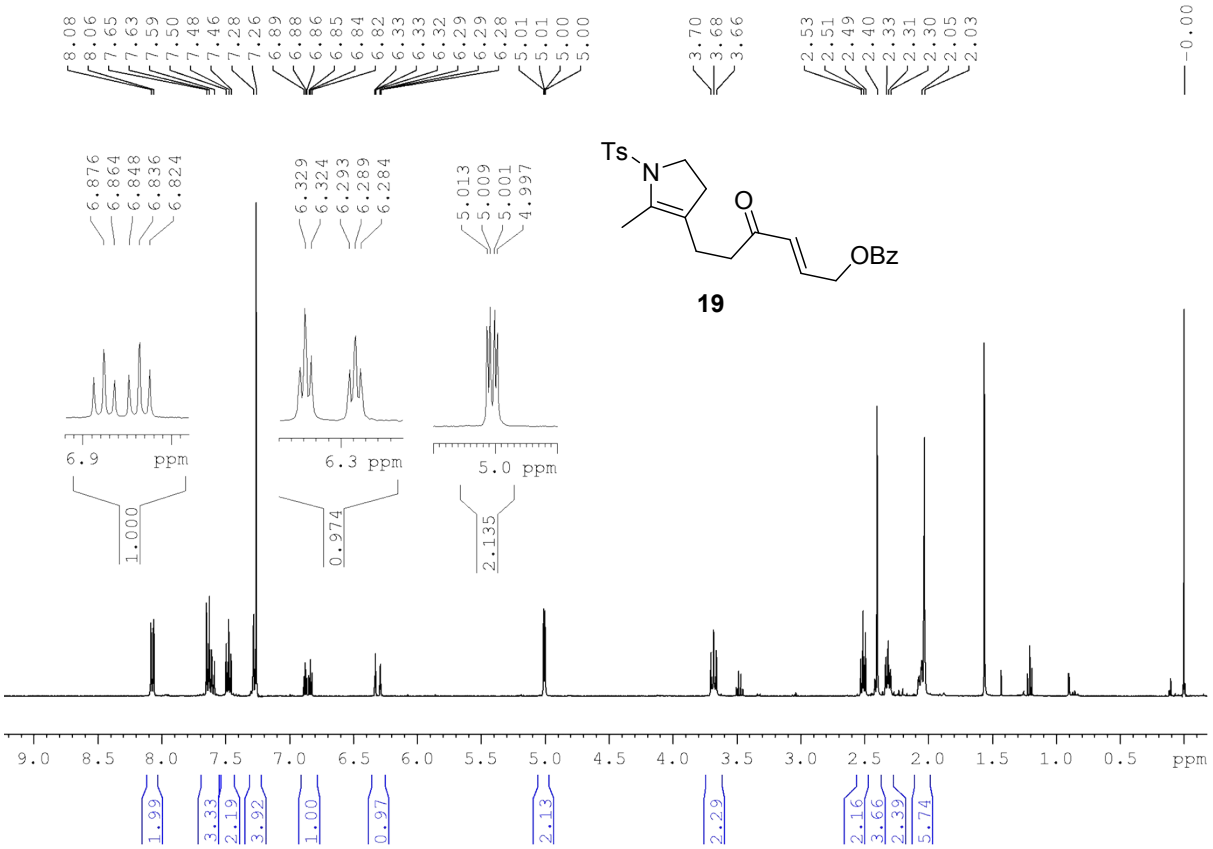


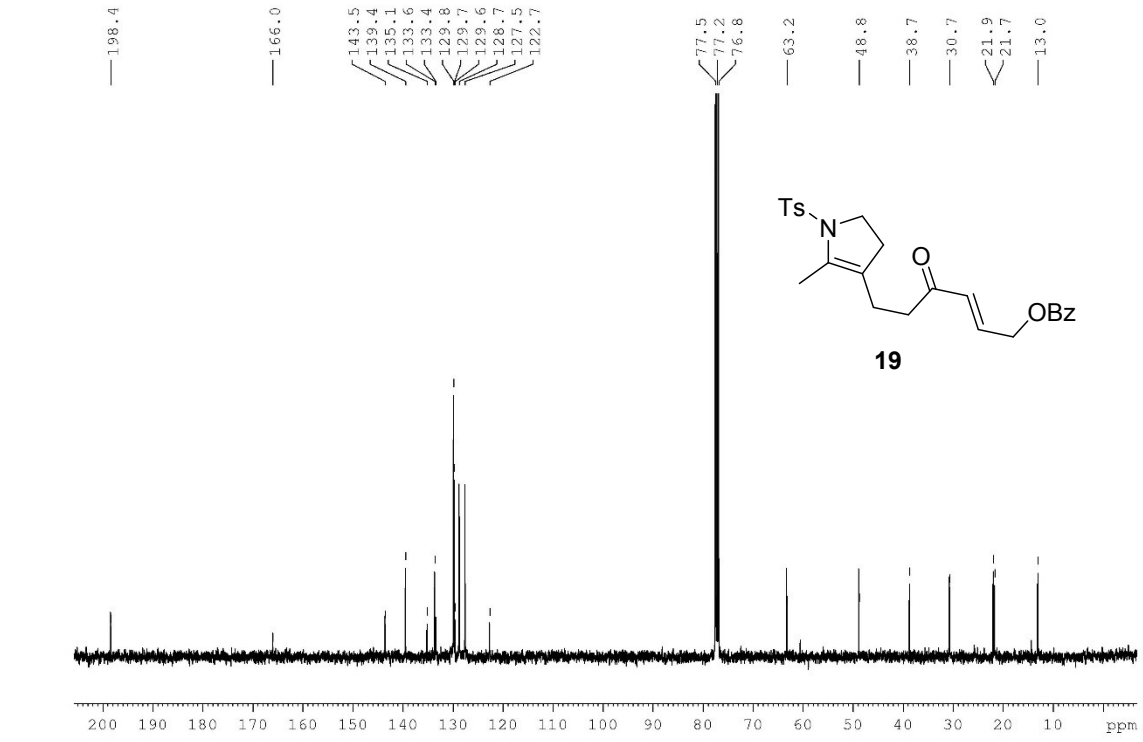
_N_-Ts enecarbamate adduct 18c



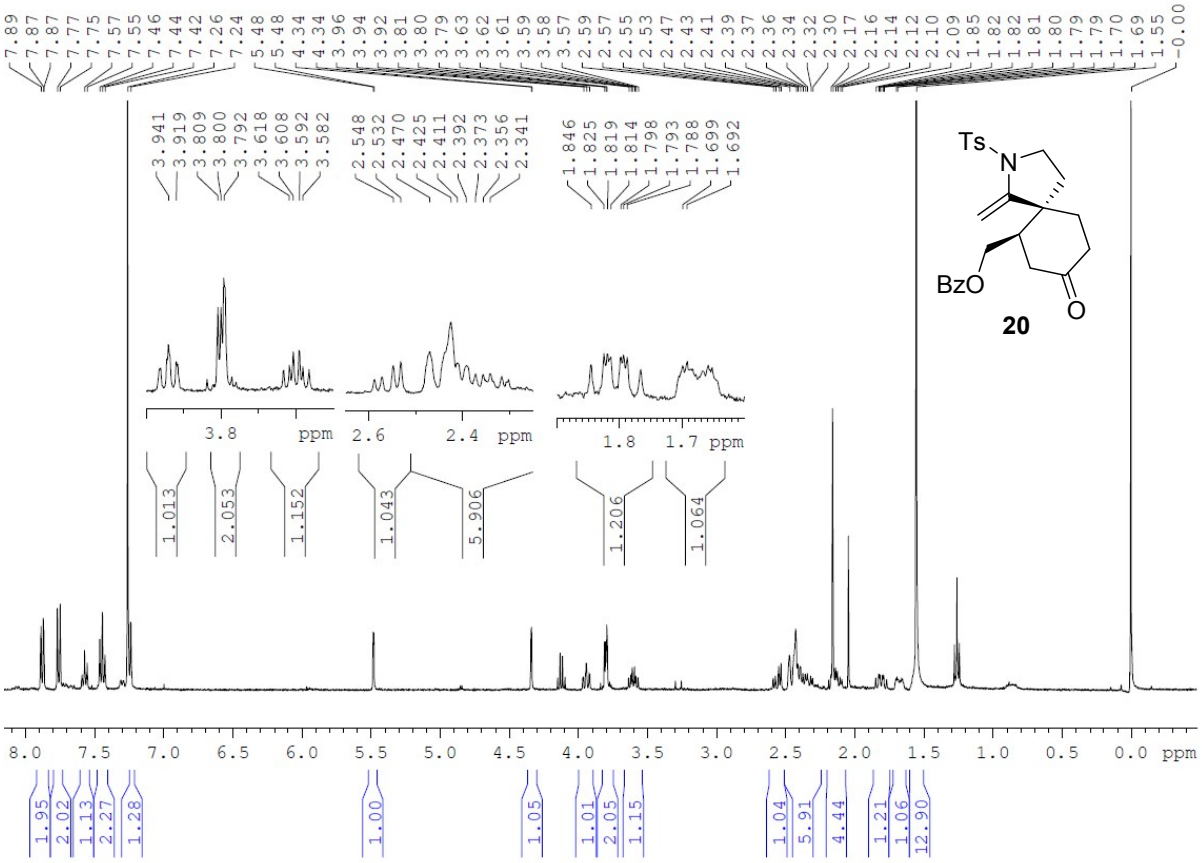


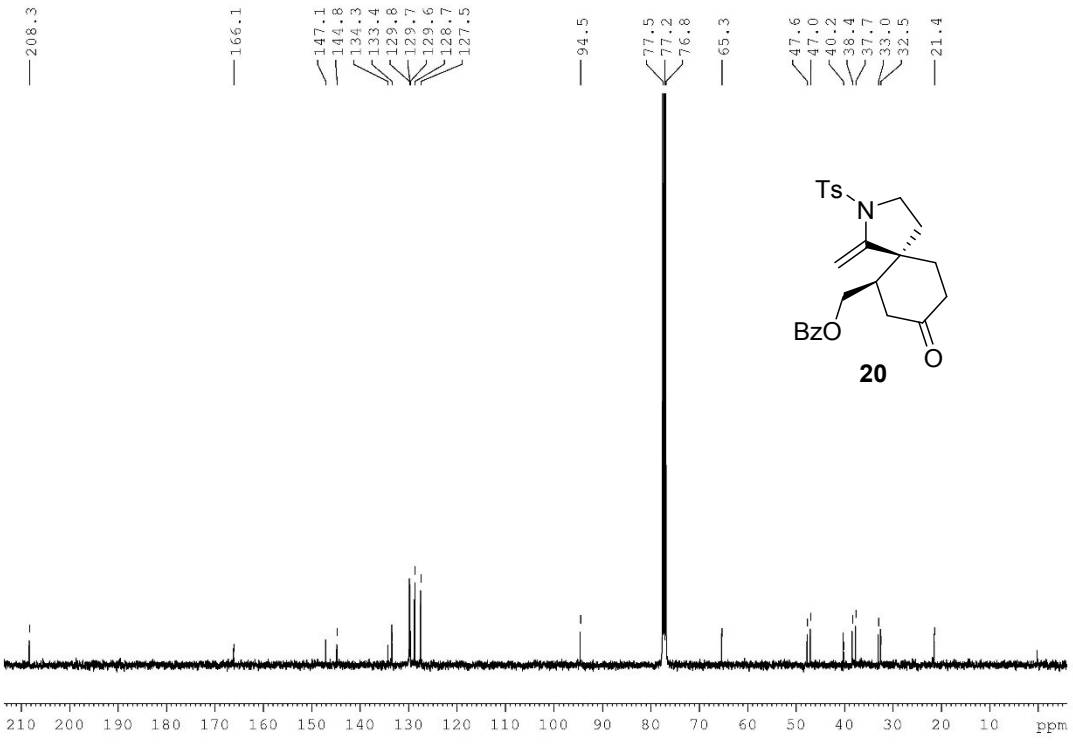
***N*-Ts enone 19**


8.08
8.06
7.65
7.63
7.59
7.50
7.48
7.46
7.28
7.26
6.89
6.88
6.86
6.85
6.84
6.82
6.33
6.33
6.32
6.29
6.29
6.28
5.01
5.01
5.00
5.00
3.70
3.68
3.66
2.53
2.51
2.49
2.40
2.33
2.31
2.30
2.05
2.03
0.00
6.876
6.864
6.848
6.836
6.824
6.329
6.324
6.293
6.289
6.284
5.013
5.009
5.001
4.997
Ts
N
O
OBz
19
6.9 ppm
6.3 ppm
5.0 ppm
1.000
0.974
2.135
9.0 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
1.99
3.33
2.19
3.92
1.00
0.97
2.13
2.29
2.16
3.66
2.39
5.74

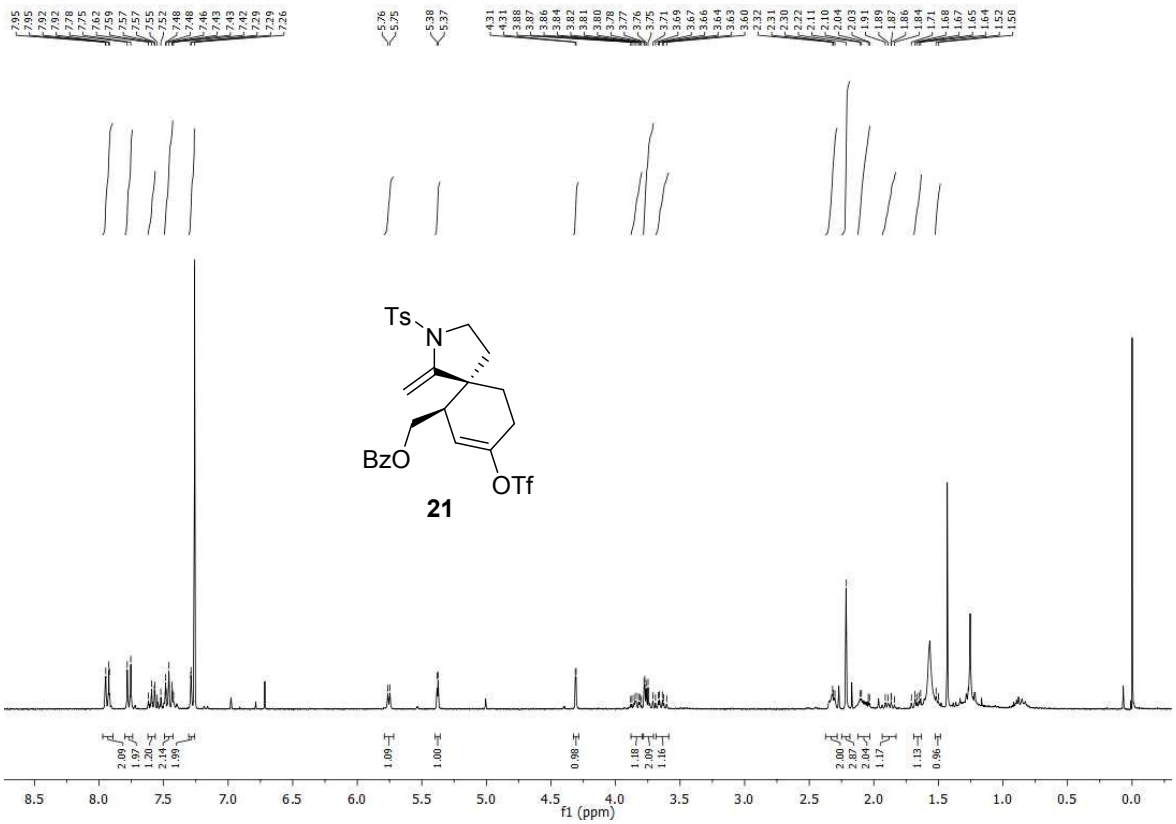

198.4
166.0
143.5
139.4
135.1
133.6
133.4
129.8
129.7
129.6
128.7
127.5
122.7
77.5
77.2
76.8
63.2
48.8
38.7
30.7
21.9
21.7
13.0
Ts
N
O
OBz
19
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

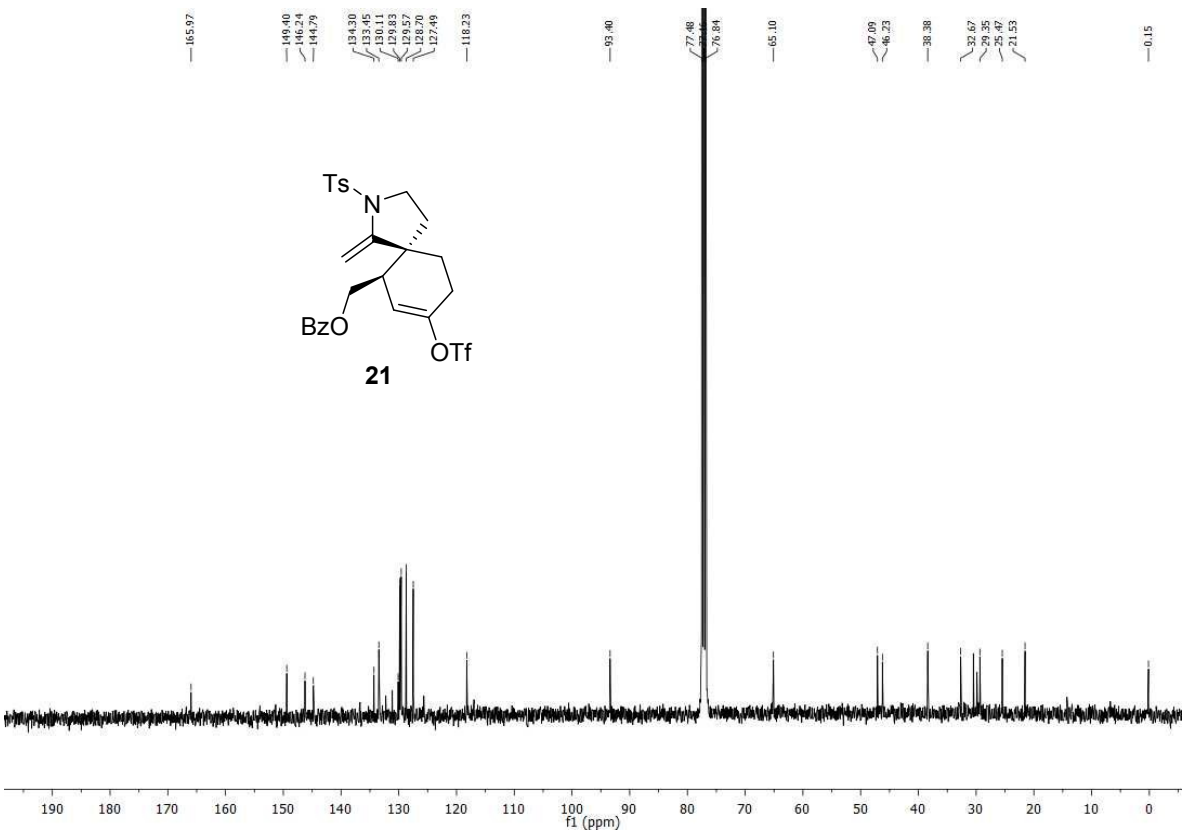
***N*-Ts bicyclic ketone 20**



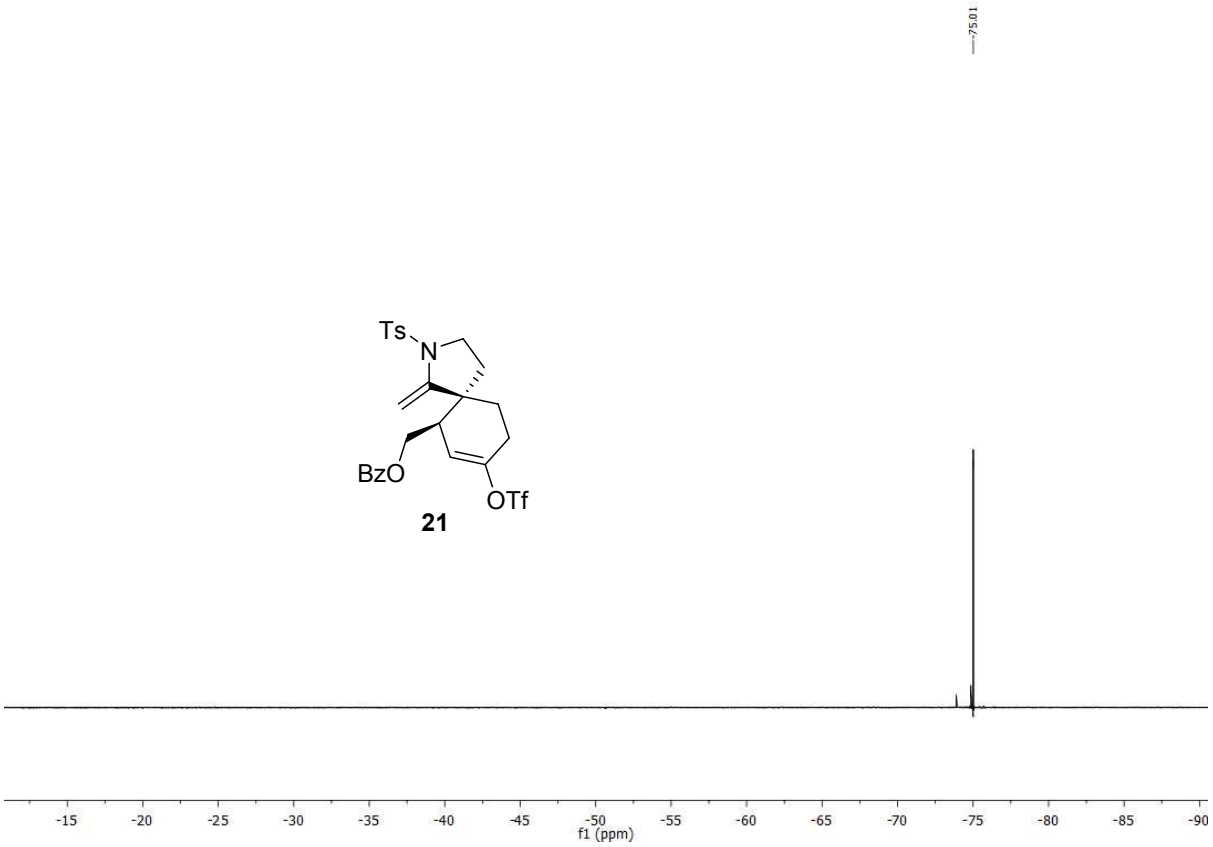


Vinyl triflate 21

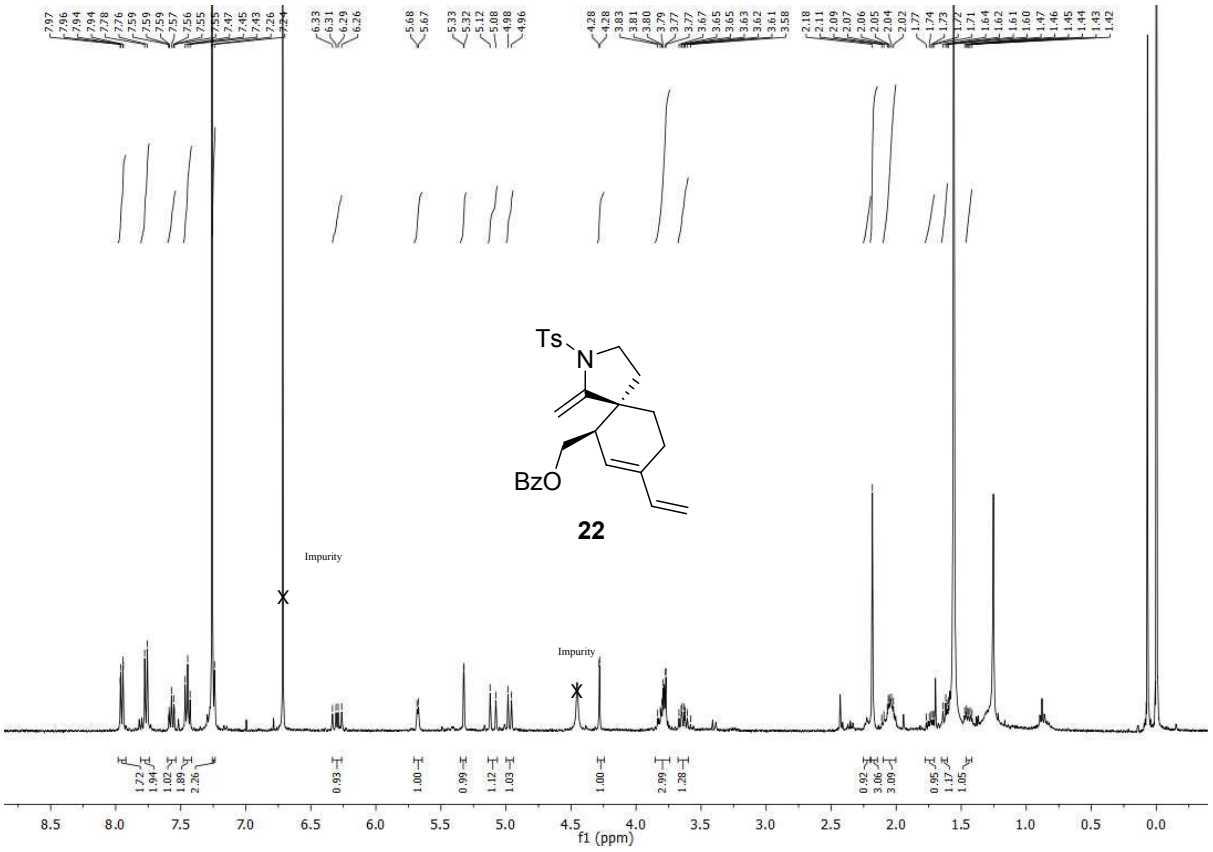


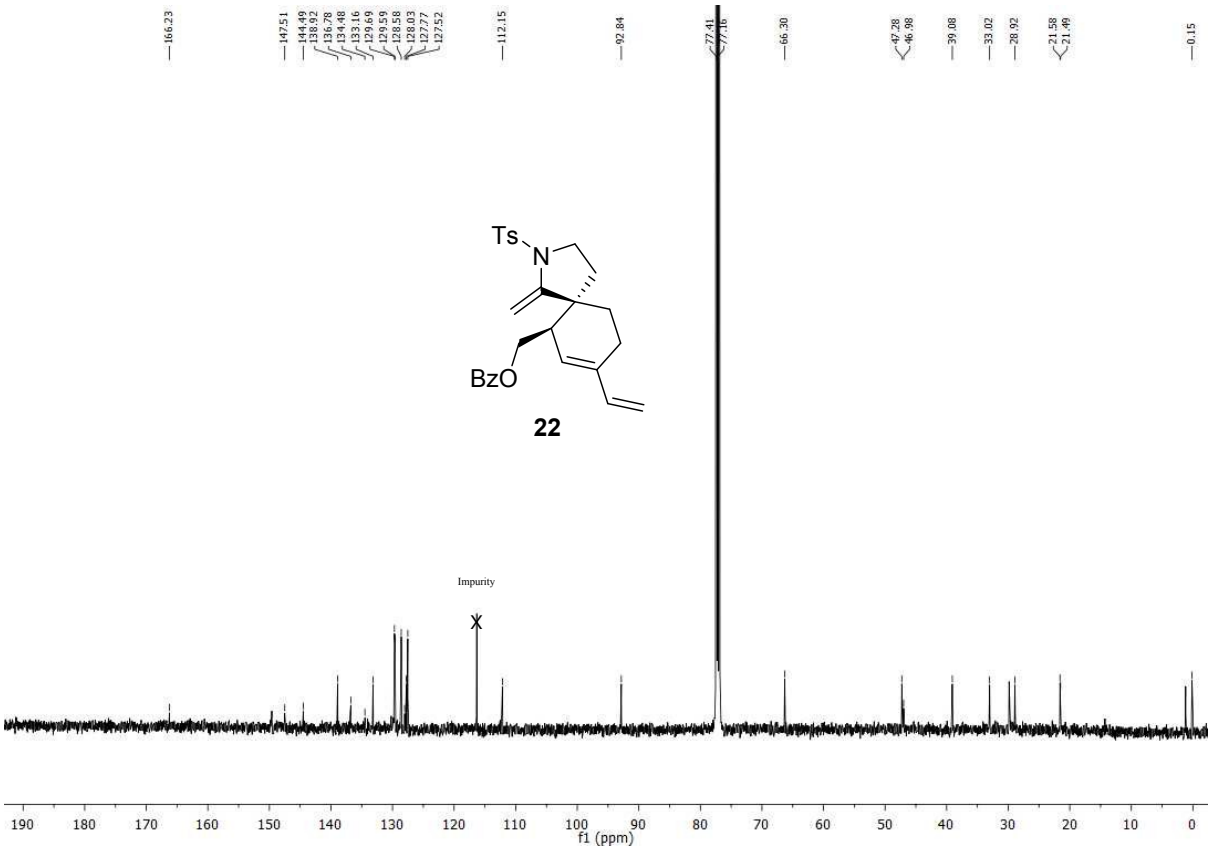


Vinyl triflate 21

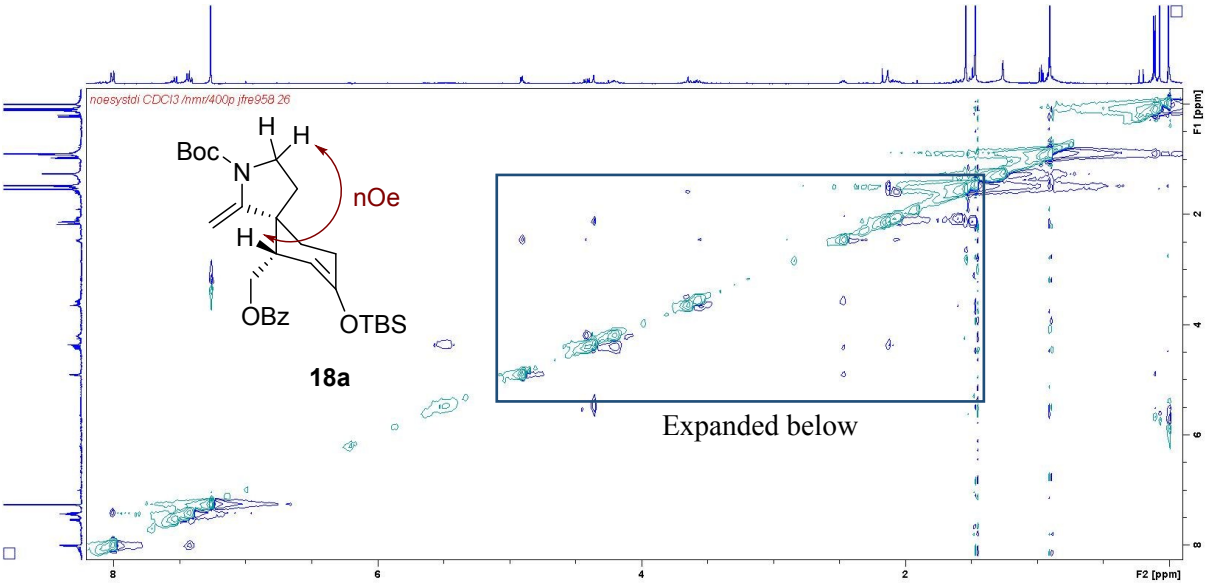


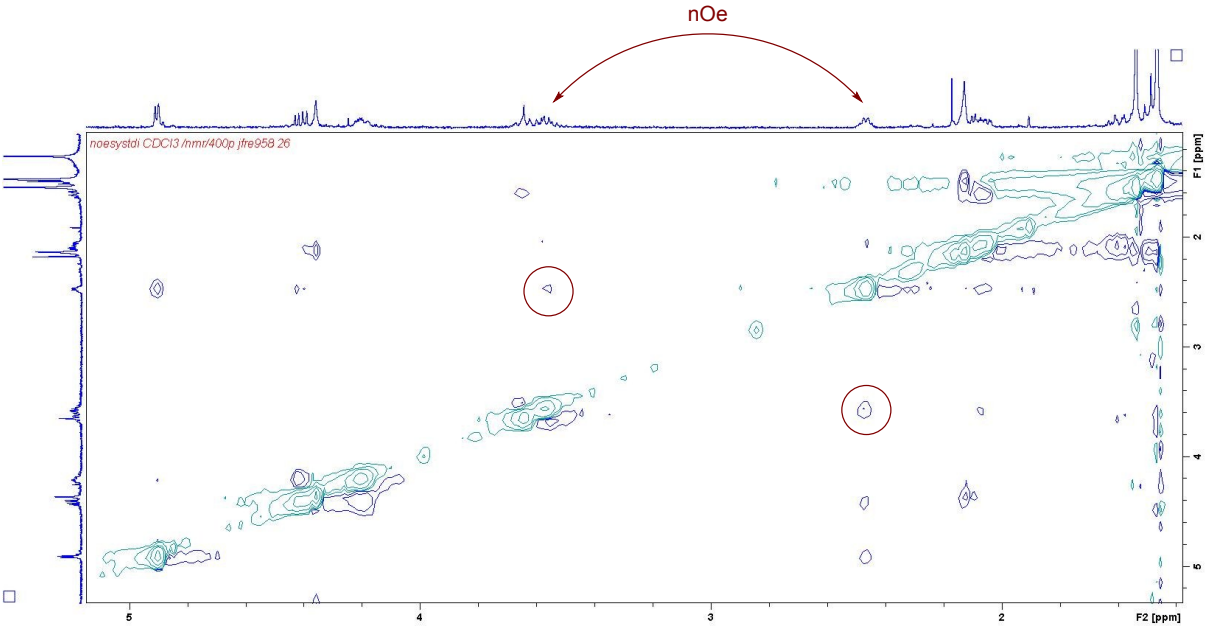
Enamine 22


Ts
N
BzO
22
Impurity
Impurity
f1 (ppm)

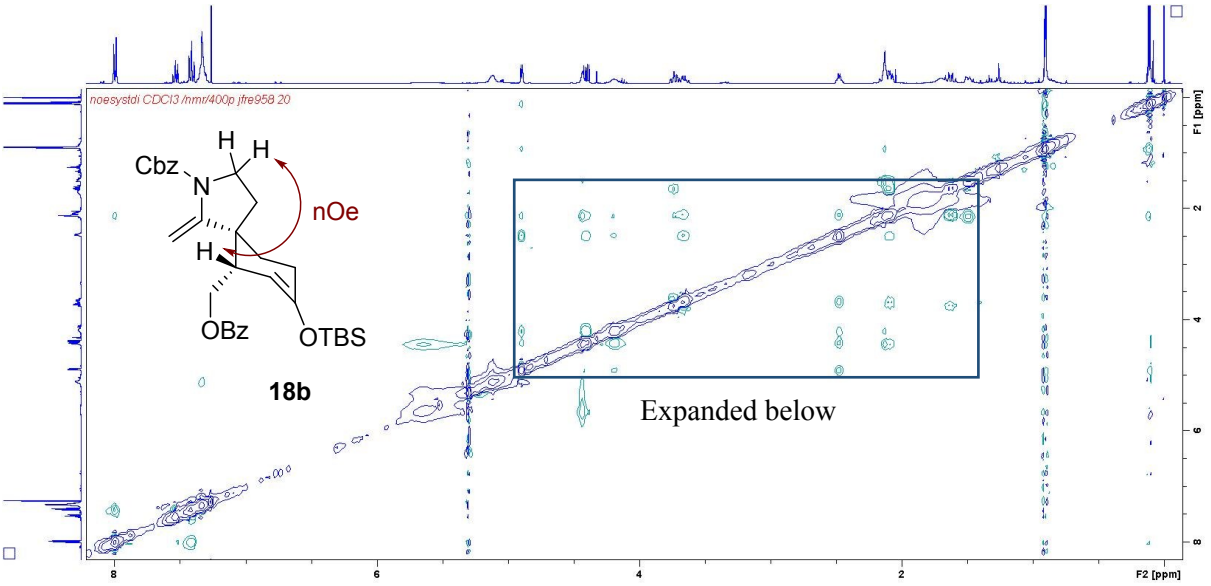

Ts
N
BzO
22
Impurity
f1 (ppm)

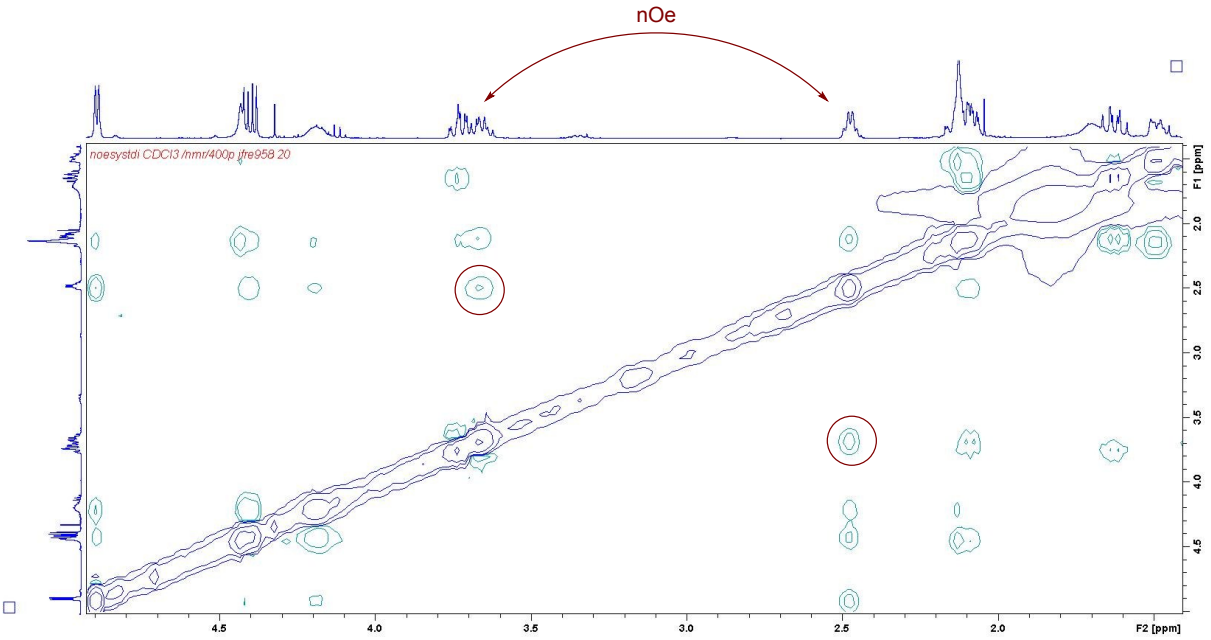
_N_-Boc Enecarbamate adduct 18a



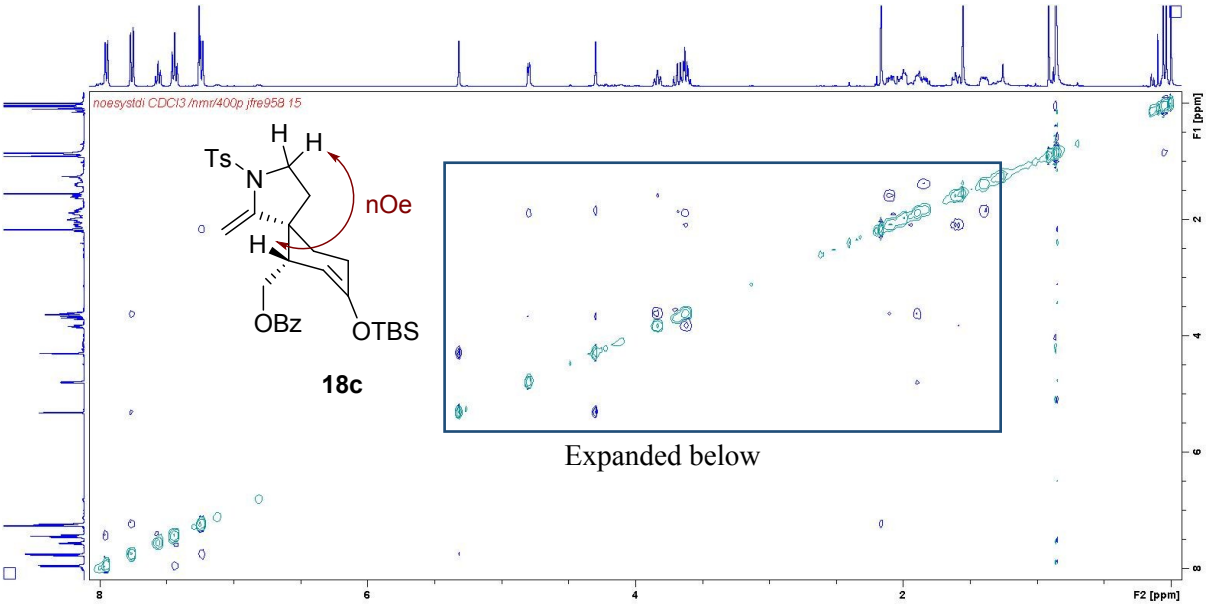


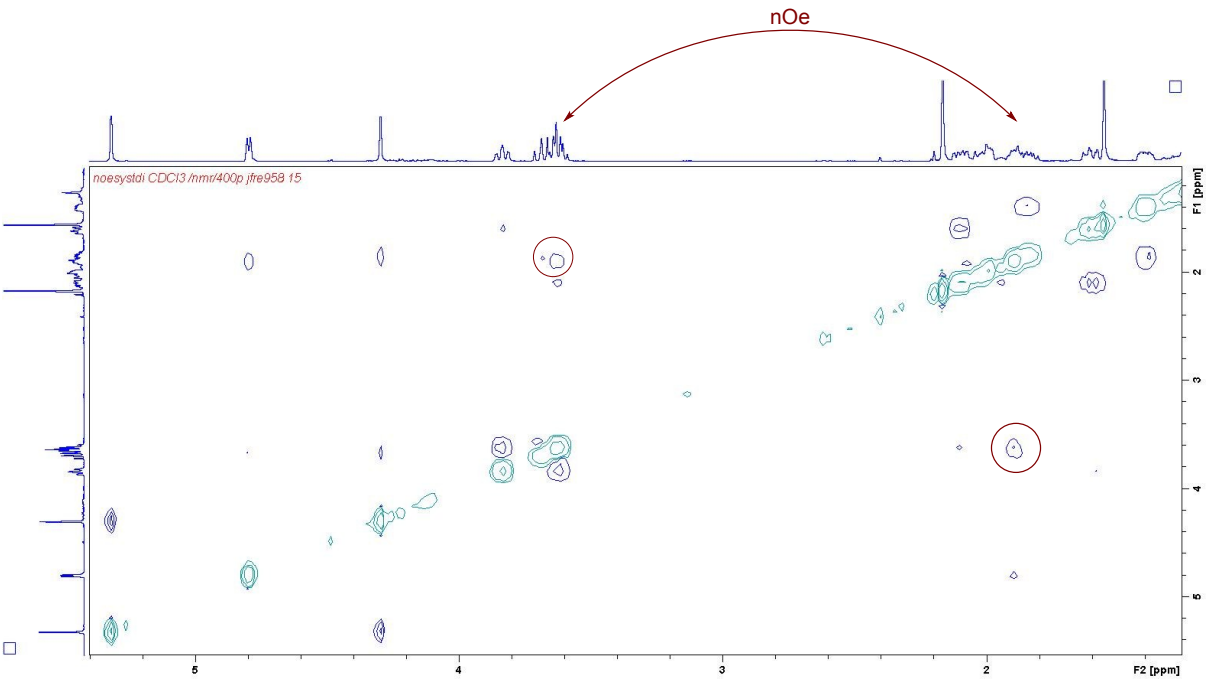
***N*-Cbz Enecarbamate adduct 18b**



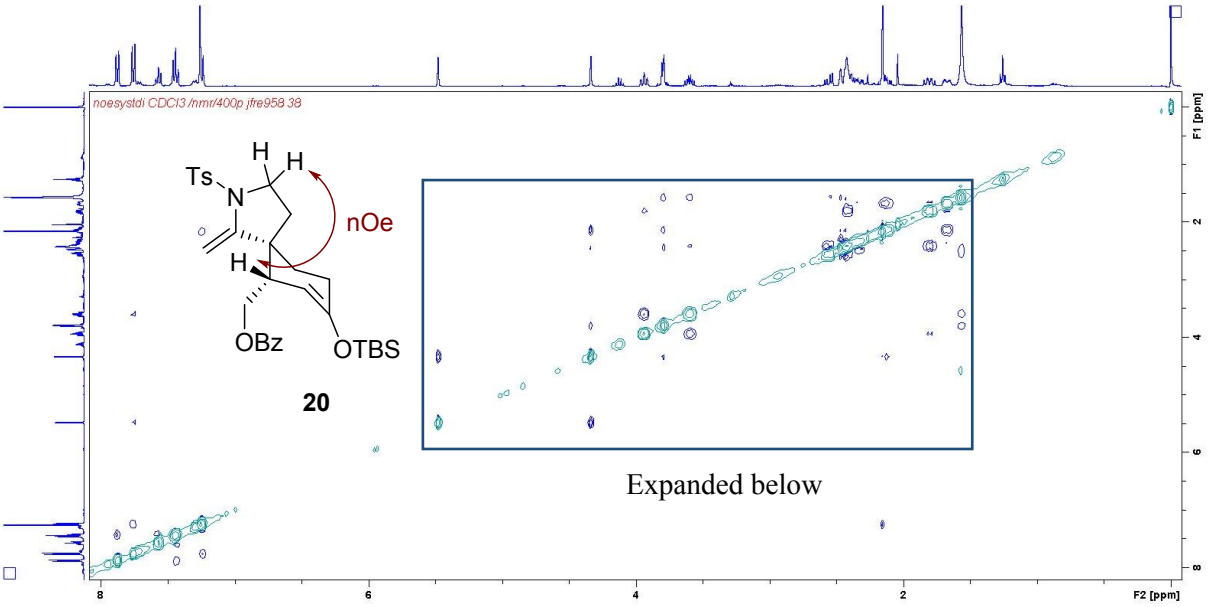


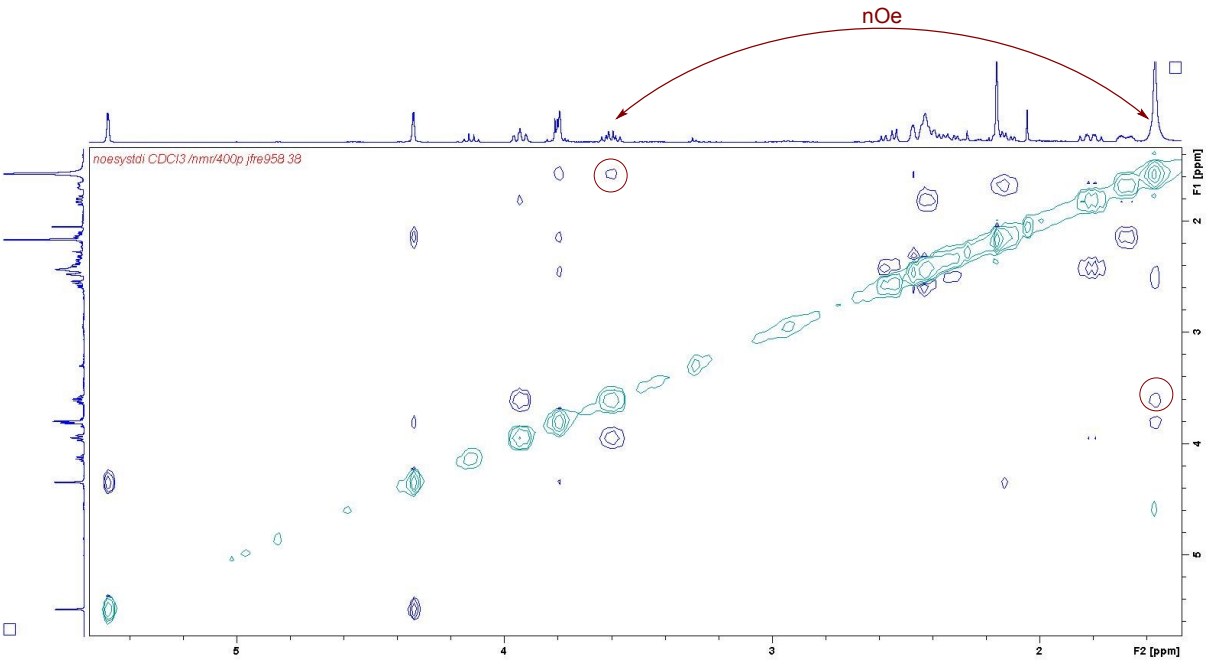
_N_-Ts Enecarbamate adduct 18c





***N*-Ts bicyclic ketone 20**





Crystallization. Single crystals of *N*-Ts bicyclic ketone (**20**) were obtained by slow recrystallization of a solution of the compound in ethyl acetate.

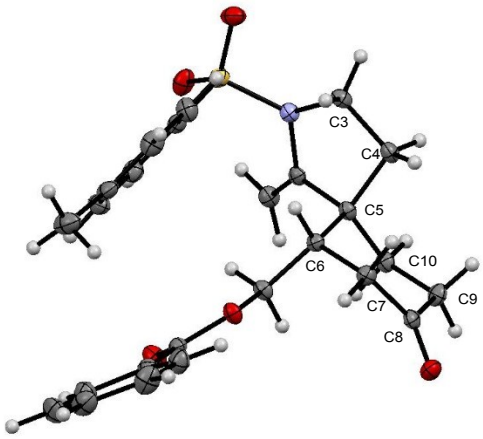


Figure S1. ORTEP diagram drawn with 50% ellipsoid probability of the crystal structure of *N*-Ts bicyclic ketone **20**.

Table S1. Crystal data and structure refinement details for *N*-Ts bicyclic ketone **20.**

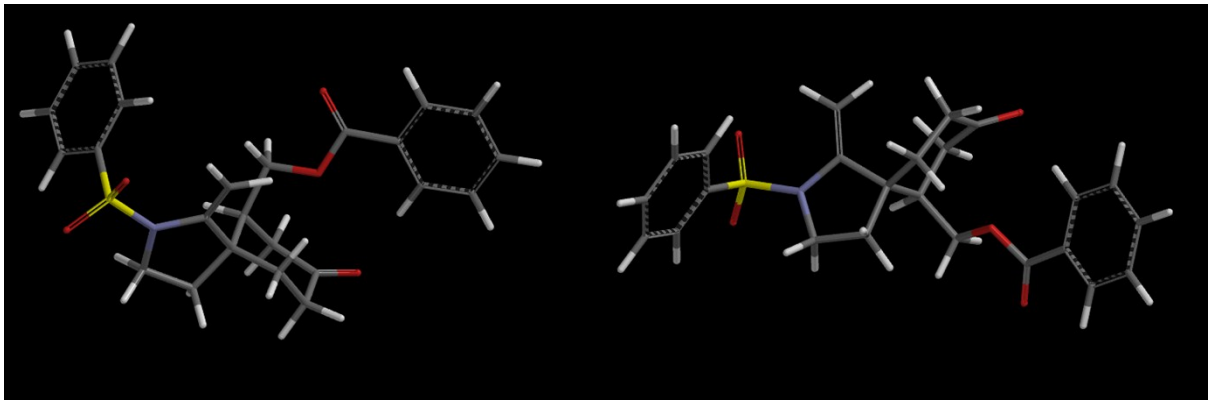
Empirical formula	$C_{24}H_{26}NO_6S$
Formula weight	456.52
Temperature (K)	293(2)
Wavelength (A)	1.54184
Crystal system	Monoclinic
Space group	P 21/c
a (Å)	11.1279(2)
b (Å)	6.76700(10)
c (Å)	29.5619(4)
α (°)	90.000
β (°)	97.0730(10)
γ (°)	90.000
V (Å^3)	2209.14(6)
Z	4
D_c (Mg/m^3)	1.373
F(000)	964
μ (mm^{-1})	1.655
θ_{max} (°)	67.734
Total reflections	22389
Unique reflections	3991
Reflections [$I > 2\sigma(I)$]]	3991
Parameters	298
R_{int}	0.0355
Goodness-of-fit	0.869
R [$F2 > 2\sigma(F2)$]	0.0325
wR (F2, all data)	0.0874

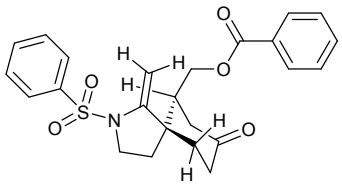
Calculations:

Assuming a late transition state, the relative energies of the possible formal *endo* and *exo* epimers, **20** and *epi*-**20**, should be indicative of the thermodynamically favoured product. For each epimer, point energies (HF, basis set 6-31+G*) were calculated for the equilibrium geometry (AM1) obtained after a conformer search (MMFF).

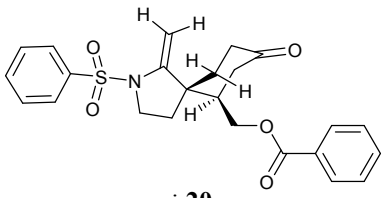
The results suggest that the observed isomer is 4.31 kcal/mol lower in energy than the potential epimer *epi*-**20**, that was not observed experimentally.

Figure S2. Calculated energies for possible formal *endo* and *exo* epimers, **20** and *epi*-**20**.





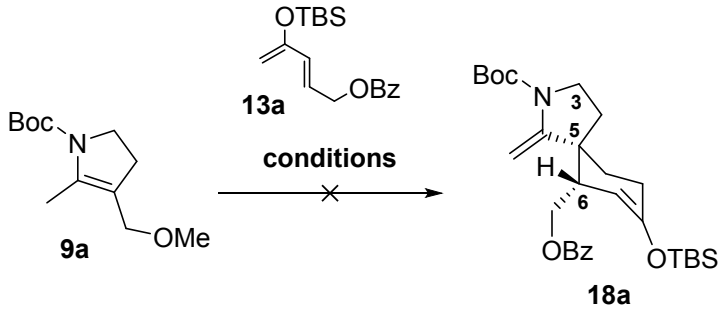
20



epi-**20**

	endo epimer (**20**)	*exo* epimer (*epi*-**20**)
Relative energy (kcal/mol)	0.00 *sole product*	4.31 *not observed*

Table S2. Attempted conditions for iminium Diels-Alder reaction of **9a**.



Entry	Lewis acid (equiv.)	Conditions	Result
1	$BF_3 \cdot OEt_2$ (1.1)[a,c]	CH_2Cl_2, −78 °C	-[e]
2	$BF_3 \cdot OEt_2$ (5)[a,c]	CH_2Cl_2, −78 °C	-[e]
3	$BF_3 \cdot OEt_2$ (10)[a,c]	CH_2Cl_2, −78 °C	**18a** (4%)
4	$BF_3 \cdot OEt_2$ (1.1)[b,c]	CH_2Cl_2, −78 °C	-[e]
5	$Sc(OTf)_3$ (0.1)[b,c]	CH_2Cl_2, −78 °C	-[e]
6	$Sc(OTf)_3$ (0.05)[b,c]	CH_2Cl_2, −78 °C	-[e]
7	$Sc(OTf)_3$ (0.05)[b,d]	CH_2Cl_2, 0 °C	-[e]
8	$Sc(OTf)_3$ (0.05)[b,d]	CH_3CN, −40 °C	-[e]
9	TMSOTf (0.2)[b,d]	CH_2Cl_2, −78 °C	-[e]
10	Et_2AlCl (0.2)[b,c]	CH_2Cl_2, −78 °C	-[e]
11	$LiBF_4$ (0.4)[a,d]	CH_2Cl_2, 0 °C	-[e]

[a] Method A: Lewis acid added to methyl ether **9a** and stirred for 5 min, prior to diene **13a** addition. [b] Method B: Lewis acid added to a mixture of methyl ether **9a** and diene **13a**. [c] Reaction quenched using TEA (10 equiv.) at −78 °C. [d] Reaction quenched using TEA (10 equiv.) at 0 °C. [e] Iminium precursor **9a** consumed; no desired product **18a** observed.