Supporting Information

Synthesis of diazatricycloundecane scaffold via gold(I)-catalysed Conia-ene-type 5-*exo-dig* cyclization and stepwise substituent assembly for construction of sp^3-rich compound library

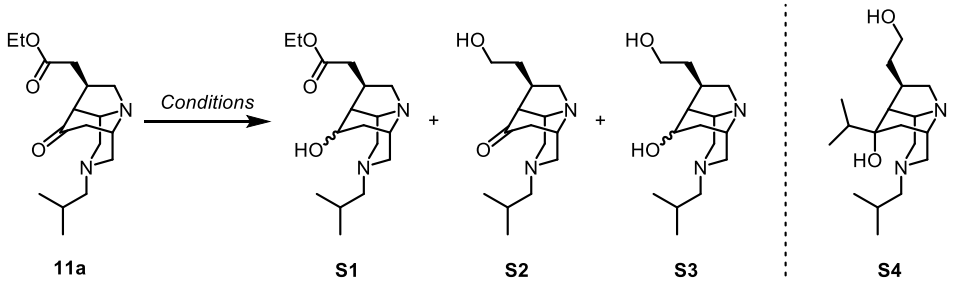
Tomoya Doi,[1] Kohei Umedera,[1] Kazuki Miura,[1,2] Taiki Morita,[1,2] Hiroyuki Nakamura*[1,2]

1) School of Life Science and Technology, Tokyo Institute of Technology, 4259 Nagatsuta-cho, Midori-ku, Yokohama 226-8503, Japan.
2) Laboratory for Chemistry and Life Science, Institute of Innovative Research, Tokyo Institute of Technology, 4259 Nagatsuta-cho, Midori-ku, Yokohama 226-8503, Japan.

Table of contents

1. Investigation on reduction of ketones

Table S1. Investigation of reduction of ketone **11a**

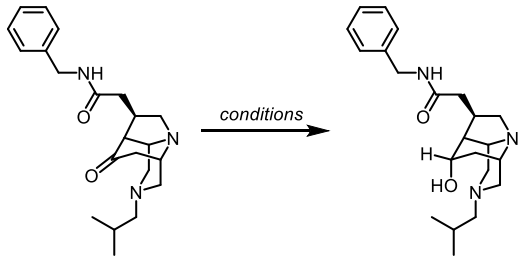


11a **S1** **S2** **S3** **S4**

Entry	Reagent	Solvent	Temp.	Time	Yield (%) of S1/S2/S3/S4
1	$NaBH_4$ (5.7 eq.)	EtOH	rt to 50 °C	28 h	0/31/0/-
2	Red-Al® (2.6 eq.)	Et_2O	0 °C	6.5 h	0/58/0/-
3	*i*-PrMgCl (4 eq.)	THF	0 °C to rt	7 h	0/-/-/0
4	$LiAlH_4$ (7 eq.)	Et_2O	0 °C to rt	2 h	0/trace/< 93[a]/-

[a] diol **S3** was obtained as a mixture of unidentified byproducts.

Table S2. Ketone-selective reduction of **12a** with various reductants



12a **13a**

Entry	Reagent	Solvent	Temp.	Time (h)	Yield (%)
1	$LiAlH_4$ (7 eq.)	Et_2O	0 °C	2	8
2	$NaBH_4$ (5 eq) $CeCl_3 \cdot 7H_2O$ (5 eq.)	MeOH	0 °C to 40 °C	5	8
3	$LiBH_4$ (4 eq.)	Et_2O	0 °C	1	Not detected
4	$NaBH_4$ (15 eq.)	EtOH	0 °C to reflux	Overnight	Not detected
5	L-selectride® (4 eq.)	THF	-78 °C to rt	12	No reaction
6	DIBAL-H (6 eq.)	THF	-78 °C to rt	Overnight	Complex mixture
7	Al(O*i*-Pr)$_3$ (10 eq.)	*i*-PrOH	reflux	10	No reaction
8	SmI_2 (3 eq.) H_2O (30 eq.)	THF	-78 °C	2	71

2. X-ray structural analysis of 13a (crl71127)

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) crl71127_auto

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: crl71127_auto

```
Bond precision:   C-C = 0.0022 A          Wavelength=1.54184

Cell:             a=16.4271(3)     b=9.6289(2)         c=12.6774(2)
                  alpha=90         beta=96.421(2)      gamma=90
Temperature:      90 K

                  Calculated                  Reported
Volume            1992.67(6)                  1992.67(6)
Space group       P 21/c                      P 1 21/c 1
Hall group        -P 2ybc                     -P 2ybc
Moiety formula    C22 H33 N3 O2               C22 H33 N3 O2
Sum formula       C22 H33 N3 O2               C22 H33 N3 O2
Mr                371.51                      371.51
Dx,g cm-3         1.238                       1.238
Z                 4                           4
Mu (mm-1)         0.628                       0.628
F000              808.0                       808.0
F000'             810.21
h,k,lmax          20,12,15                    20,11,15
Nref              4176                        4044
Tmin,Tmax         0.919,0.992                 0.807,1.000
Tmin'             0.919

Correction method= # Reported T Limits: Tmin=0.807 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.968          Theta(max)= 76.633

R(reflections)= 0.0497( 3610)                wR2(reflections)=
                                             0.1213( 4044)
S = 1.069                 Npar= 247
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

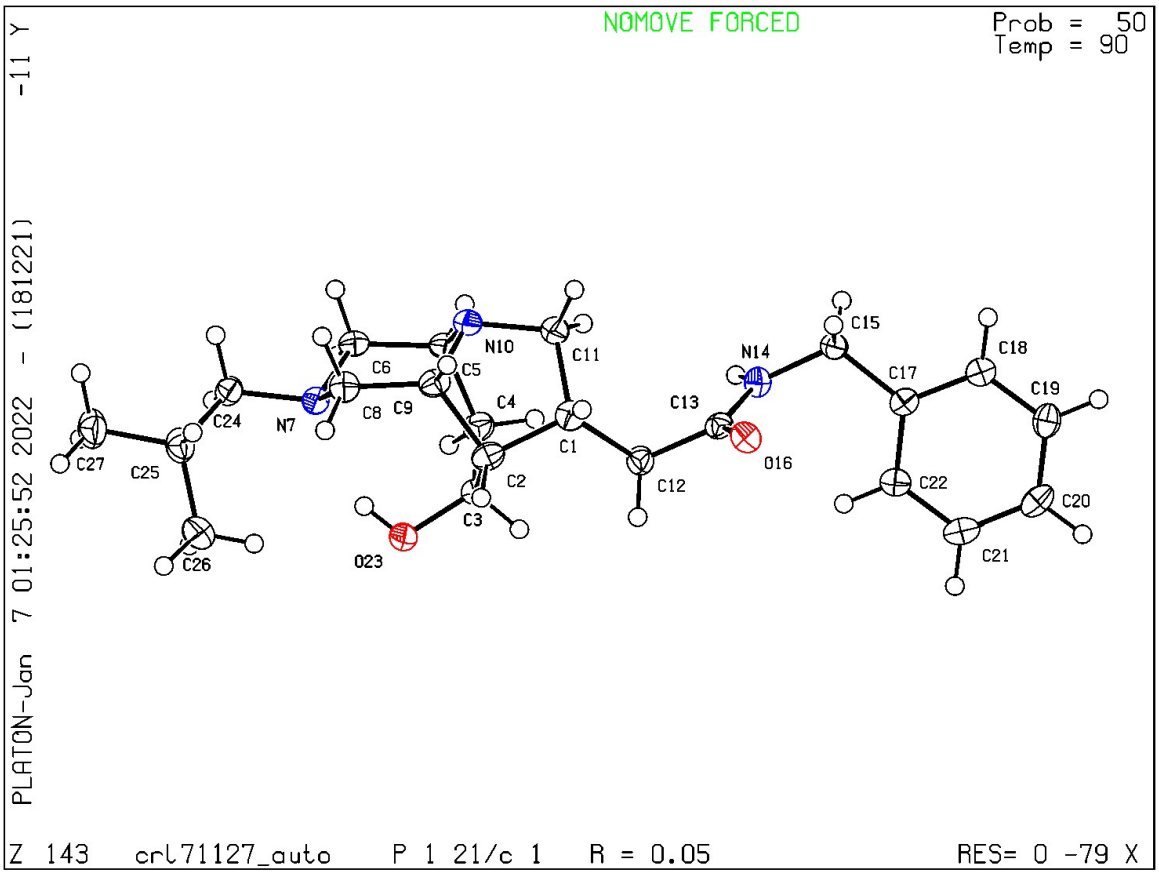
DIFMX02_ALERT_1_C The maximum difference density is > 0.1*ZMAX*0.75
The relevant atom site should be identified.
PLAT094_ALERT_2_C Ratio of Maximum / Minimum Residual Density .... 3.01 Report
PLAT097_ALERT_2_C Large Reported Max. (Positive) Residual Density 0.75 eA-3
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ..... 5.237 Check

Alert level G

PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms ..... 2 Report
PLAT793_ALERT_4_G Model has Chirality at C1 (Centro SPGR) R Verify
PLAT793_ALERT_4_G Model has Chirality at C2 (Centro SPGR) S Verify
PLAT793_ALERT_4_G Model has Chirality at C3 (Centro SPGR) S Verify
PLAT793_ALERT_4_G Model has Chirality at C5 (Centro SPGR) S Verify
PLAT793_ALERT_4_G Model has Chirality at C9 (Centro SPGR) R Verify
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 117 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 12 Info

0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
4 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
8 **ALERT level G** = General information/check it is not something unexpected

1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
3 ALERT type 2 Indicator that the structure model may be wrong or deficient
1 ALERT type 3 Indicator that the structure quality may be low
6 ALERT type 4 Improvement, methodology, query or suggestion
1 ALERT type 5 Informative message, check


NOMOVE FORCED
Prob = 50
Temp = 90
-11 Y
PLATON-Jan 7 01:25:52 2022 - (181221)
Z 143 crl71127_auto P 1 21/c 1 R = 0.05
RES= 0 -79 X
N10
C11
C6
C5
C15
N14
C18
C17
C19
C13
C24
N7
C8
C9
C4
C1
C27
C25
C2
C12
O16
C22
C20
C3
O23
C21
C26

3. PMI analysis of diazatricyclic compounds

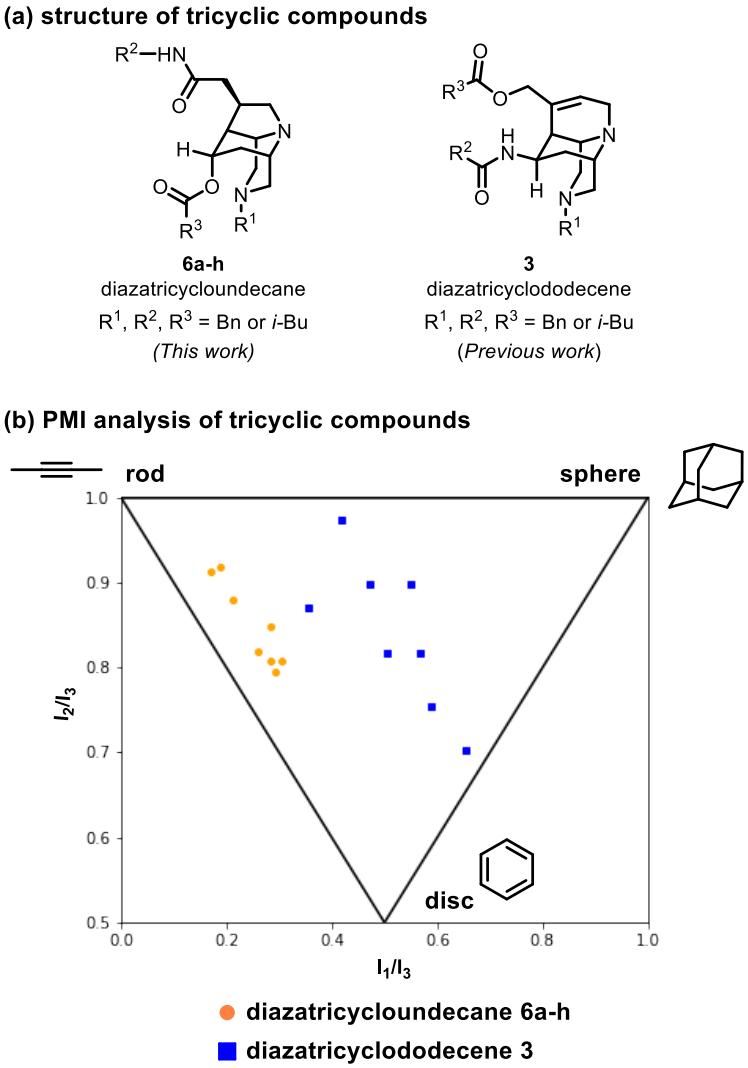


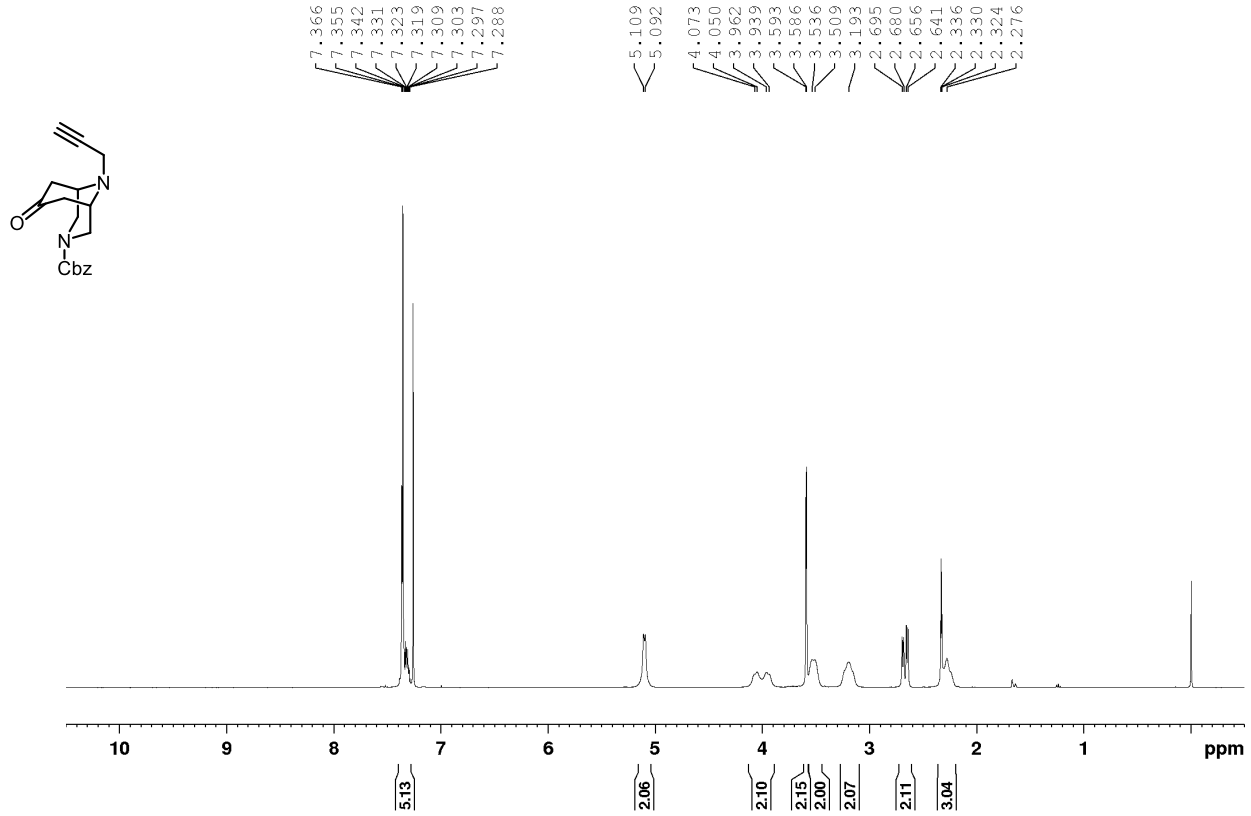
Figure S1. PMI analysis of compounds with diazatricyclic scaffolds. (a) chemical structures used for PMI analysis. (b) PMI plot[1] of diazatricycloundecanes **6a-h** (orange circle) and diazatricyclododecenes **3** with three isobutyl or benzyl groups (blue square). Conformers with the lowest energy generated by iCon[2] implemented in LigandScout 4.4.5 were used for the analysis. PMI = principal moment of inertia.

4. References

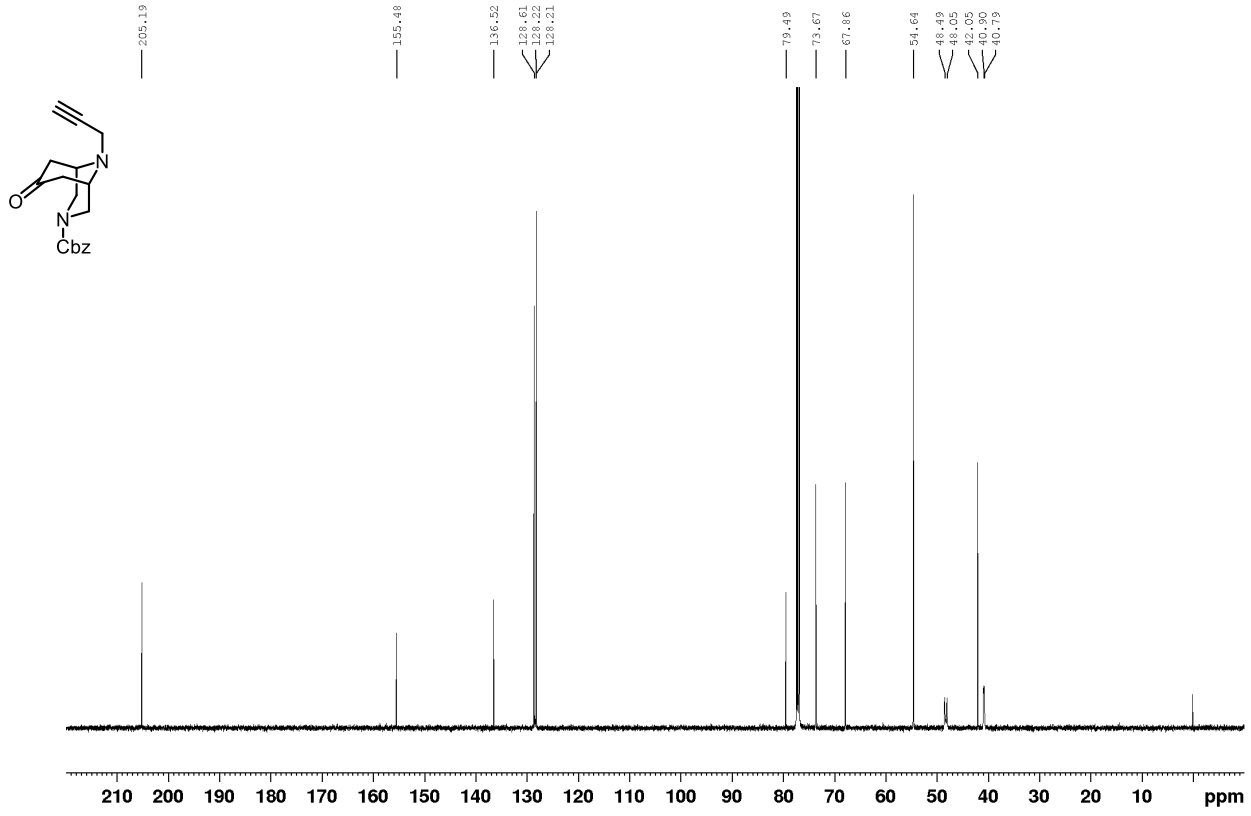
1. W. H. B. Sauer and M. K. Schwarz, *J. Chem. Inf. Comput. Sci.*, 2003, **43**, 987–1003.
2. G. Poli, T. Seidel and T. Langer, *Front Chem.*, 2018, **6**, 229.

5. NMR spectra

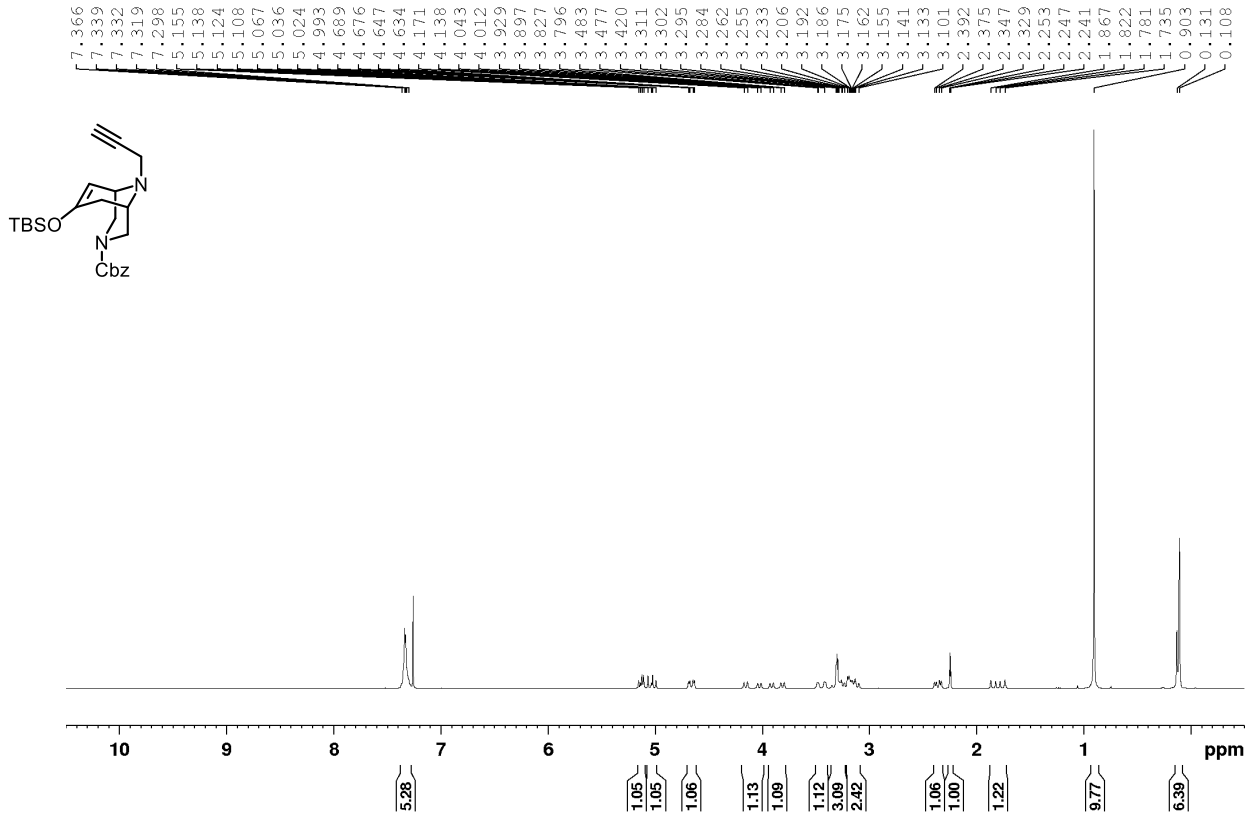
Ketone 8 (^{1}H NMR, $CDCl_3$, 400 MHz)



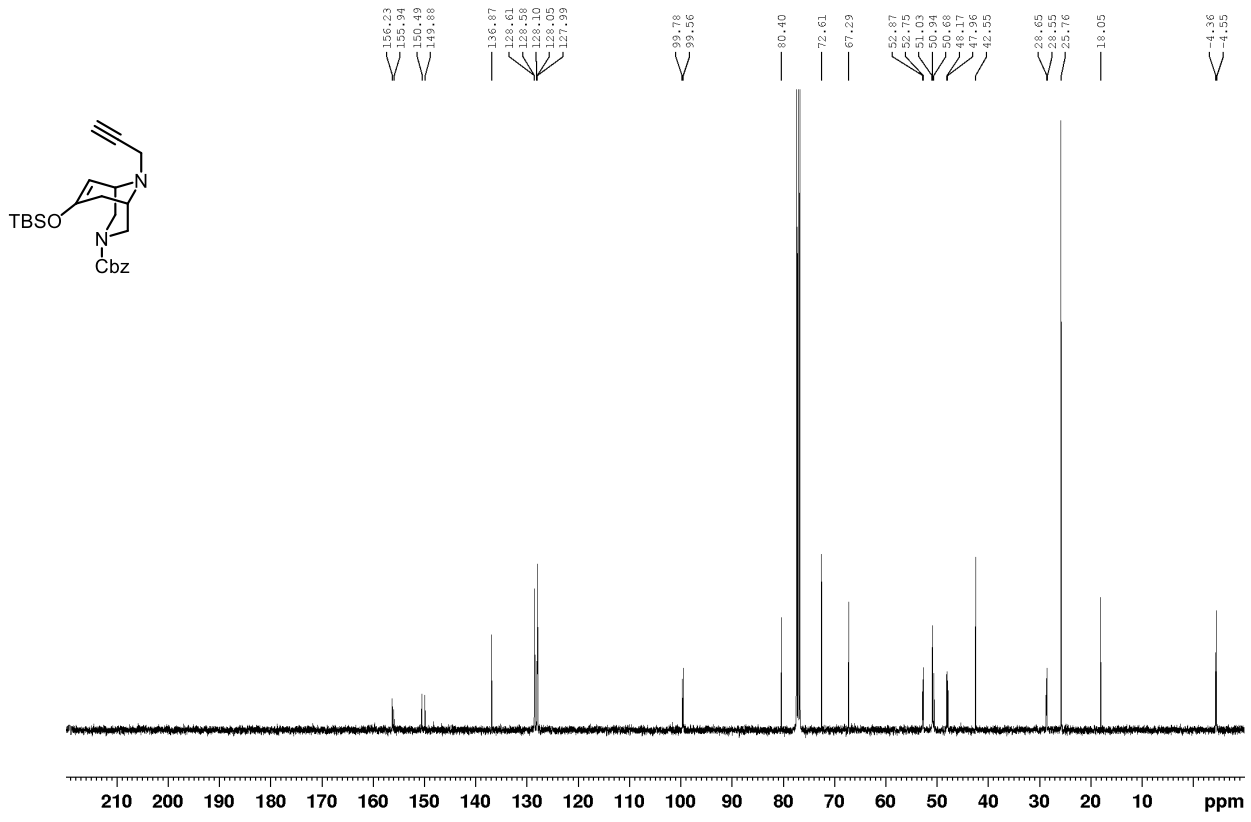
Ketone 8 (^{13}C NMR, $CDCl_3$, 125 MHz)



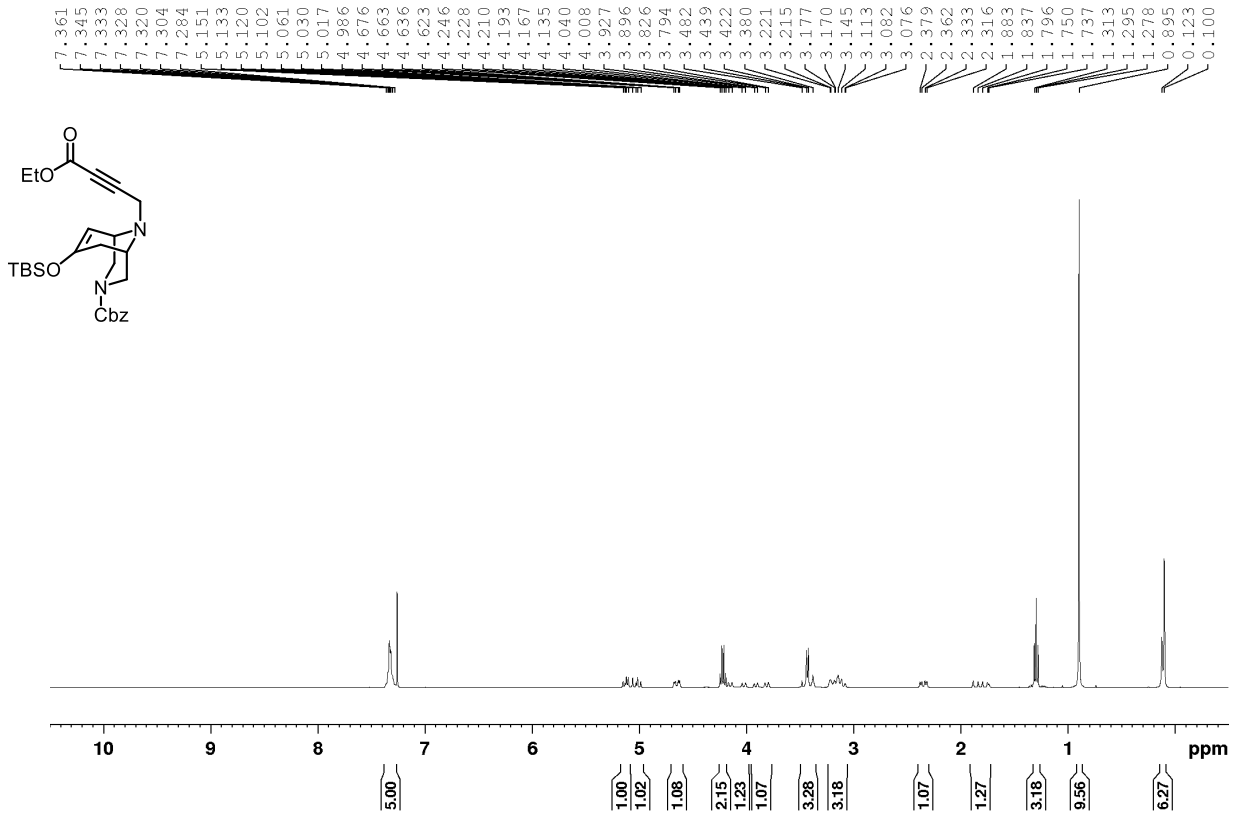
Silyl enol ether 9 (^{1}H NMR, $CDCl_3$, 400 MHz)



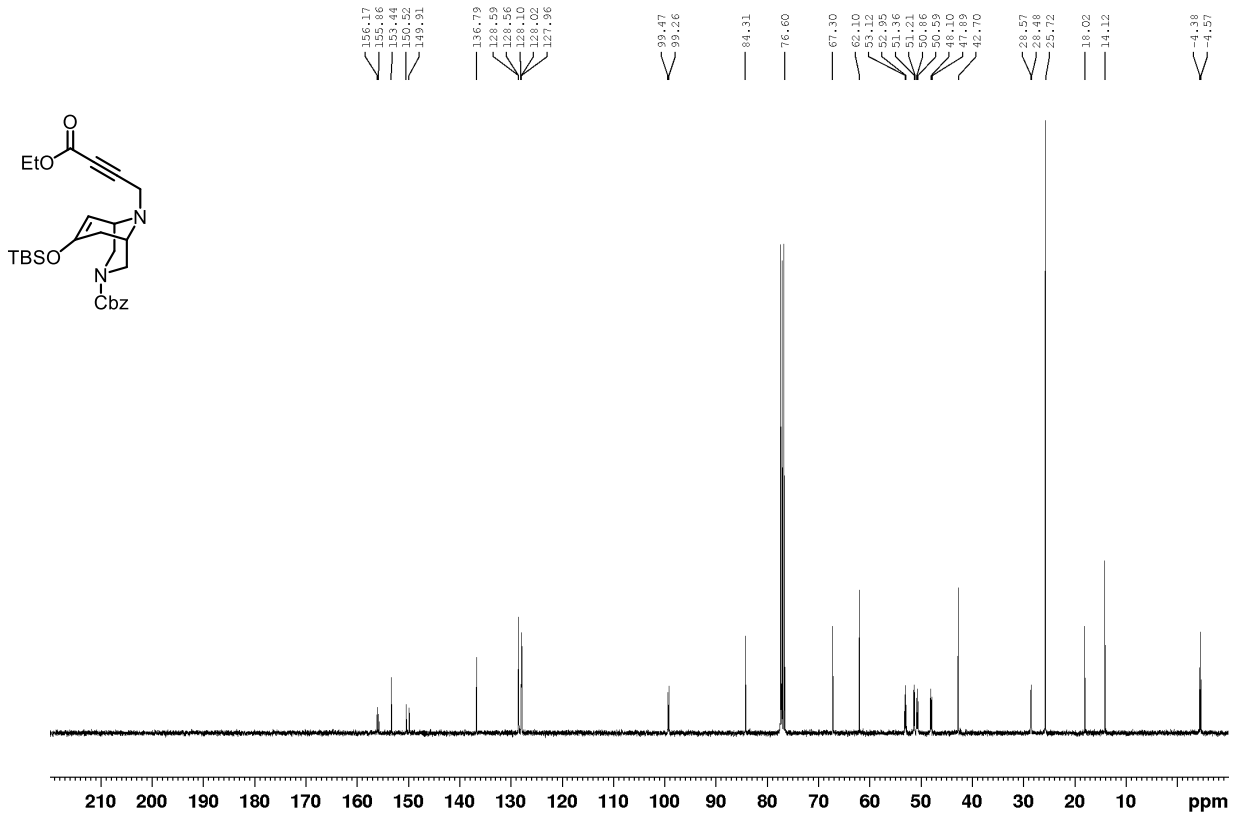
Silyl enol ether 9 (^{13}C NMR, $CDCl_3$, 100 MHz)



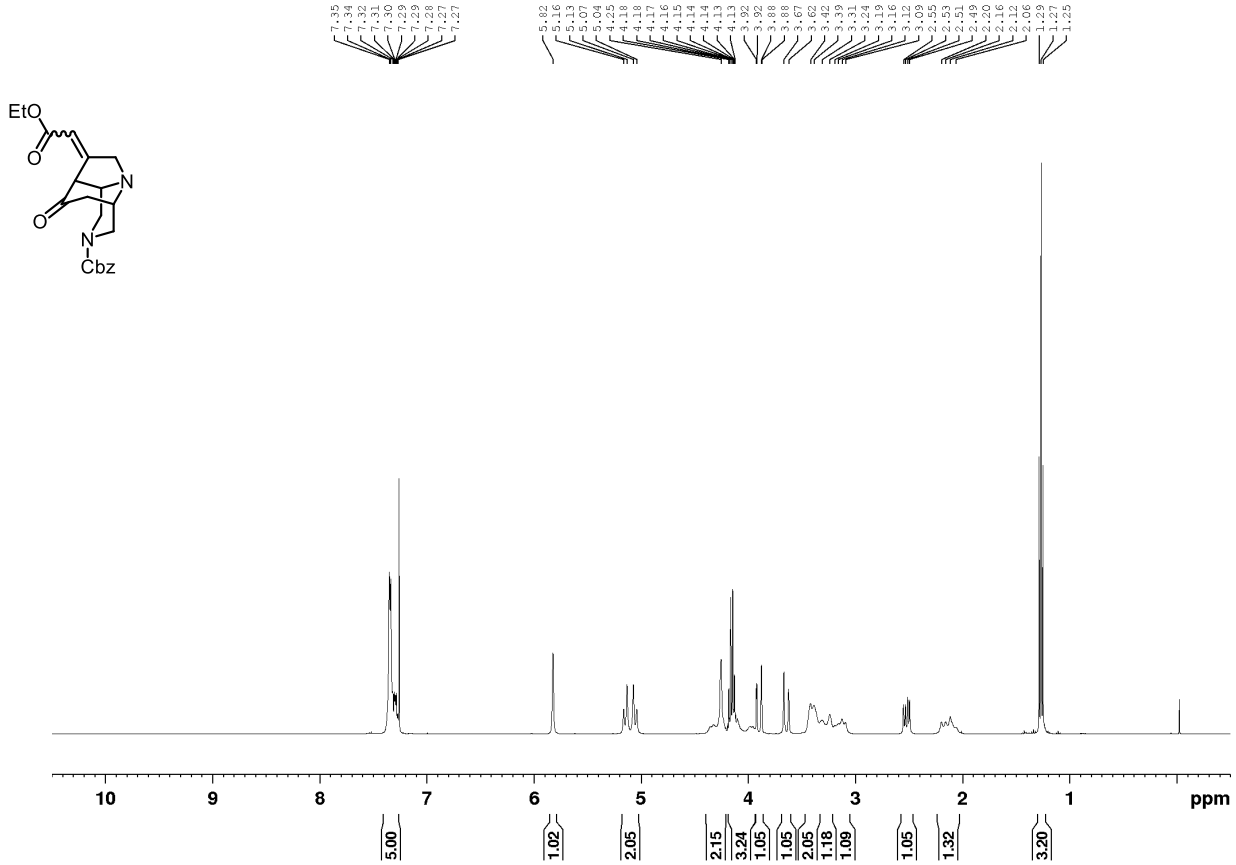
Ester 4 (^{1}H NMR, $CDCl_3$, 400 MHz)



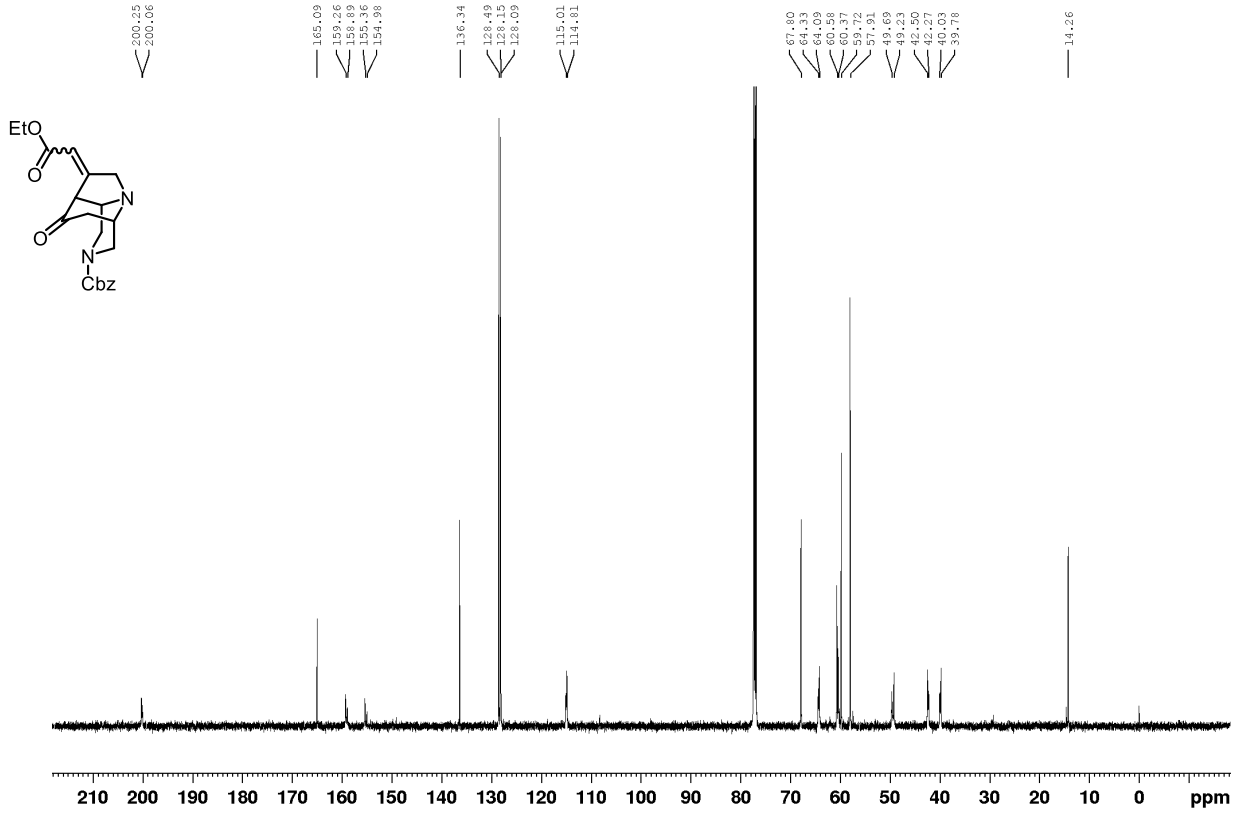
Ester 4 (^{13}C NMR, $CDCl_3$, 100 MHz)



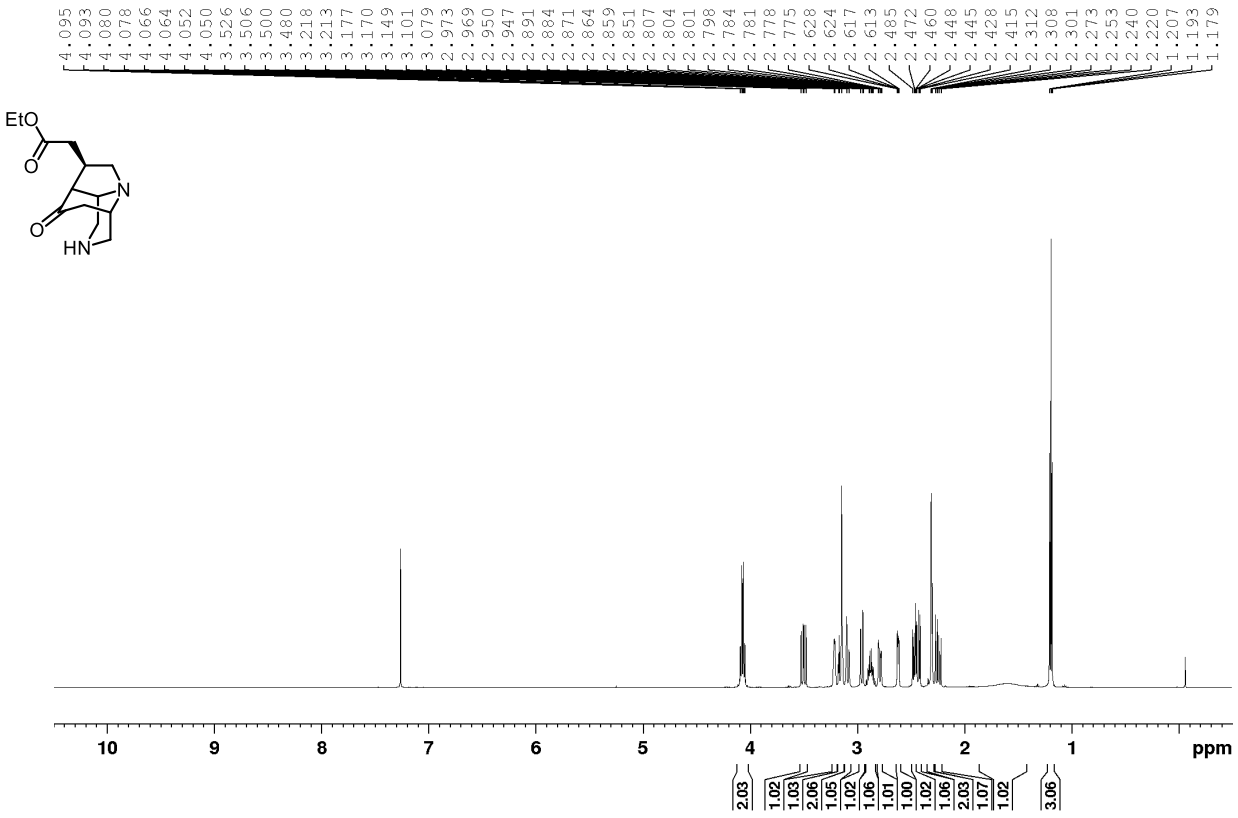
Ester 10 (^{1}H NMR, $CDCl_3$, 400 MHz)



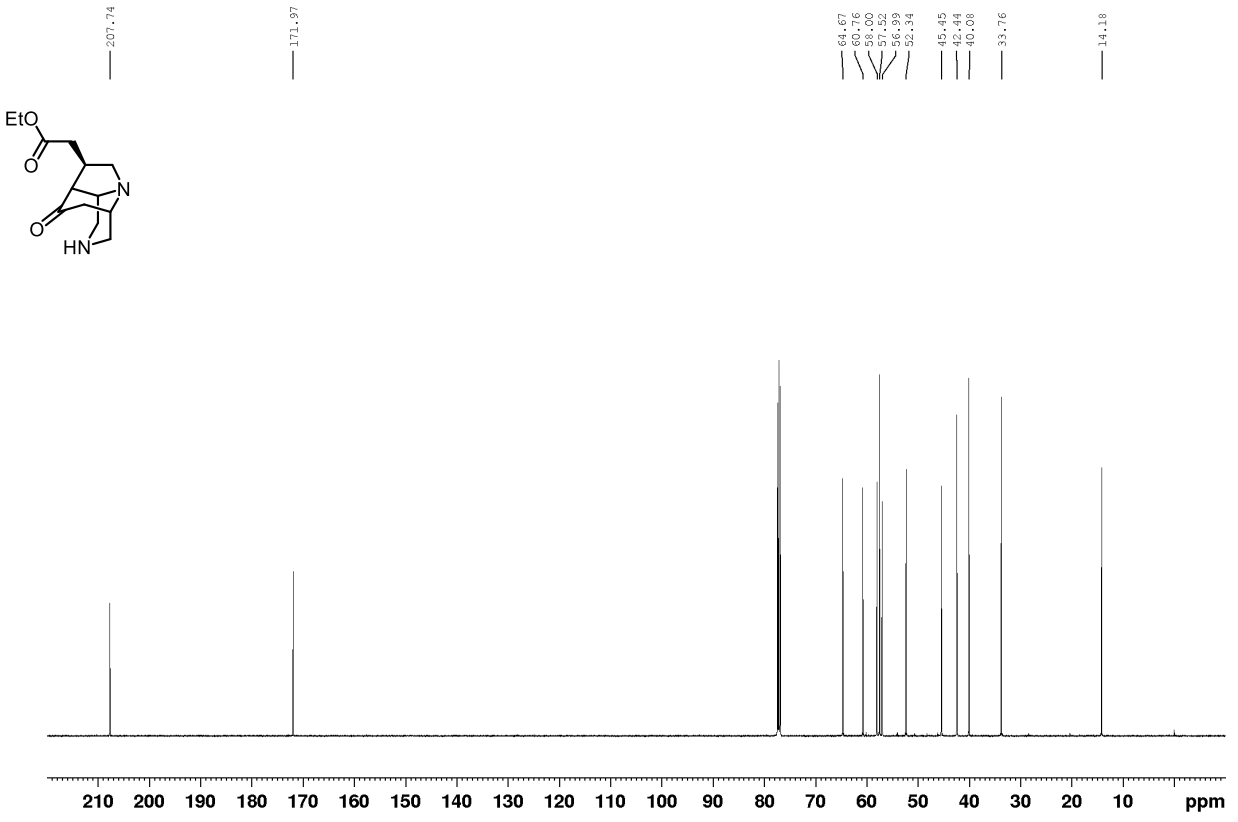
Ester 10 (^{13}C NMR, $CDCl_3$, 125 MHz)



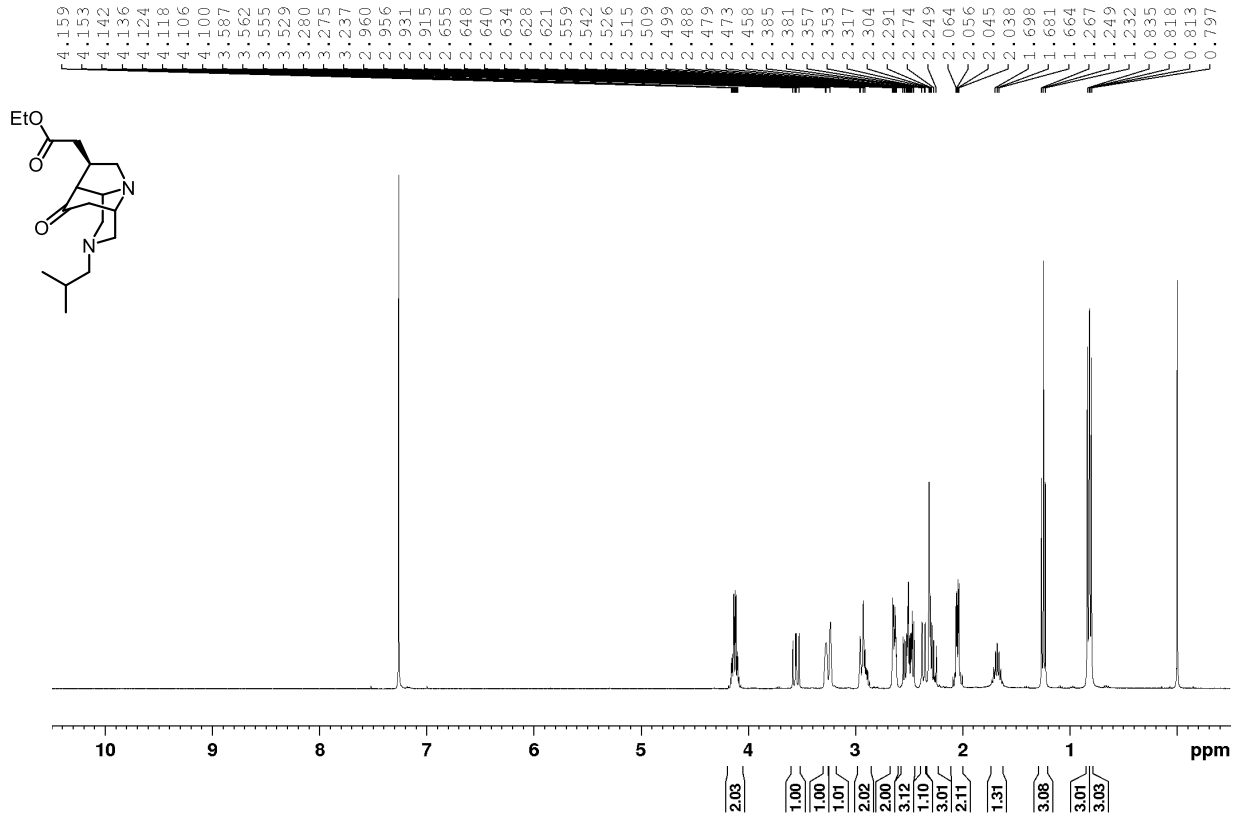
Diazatricycloundecane 5 (^{1}H NMR, $CDCl_3$, 500 MHz)



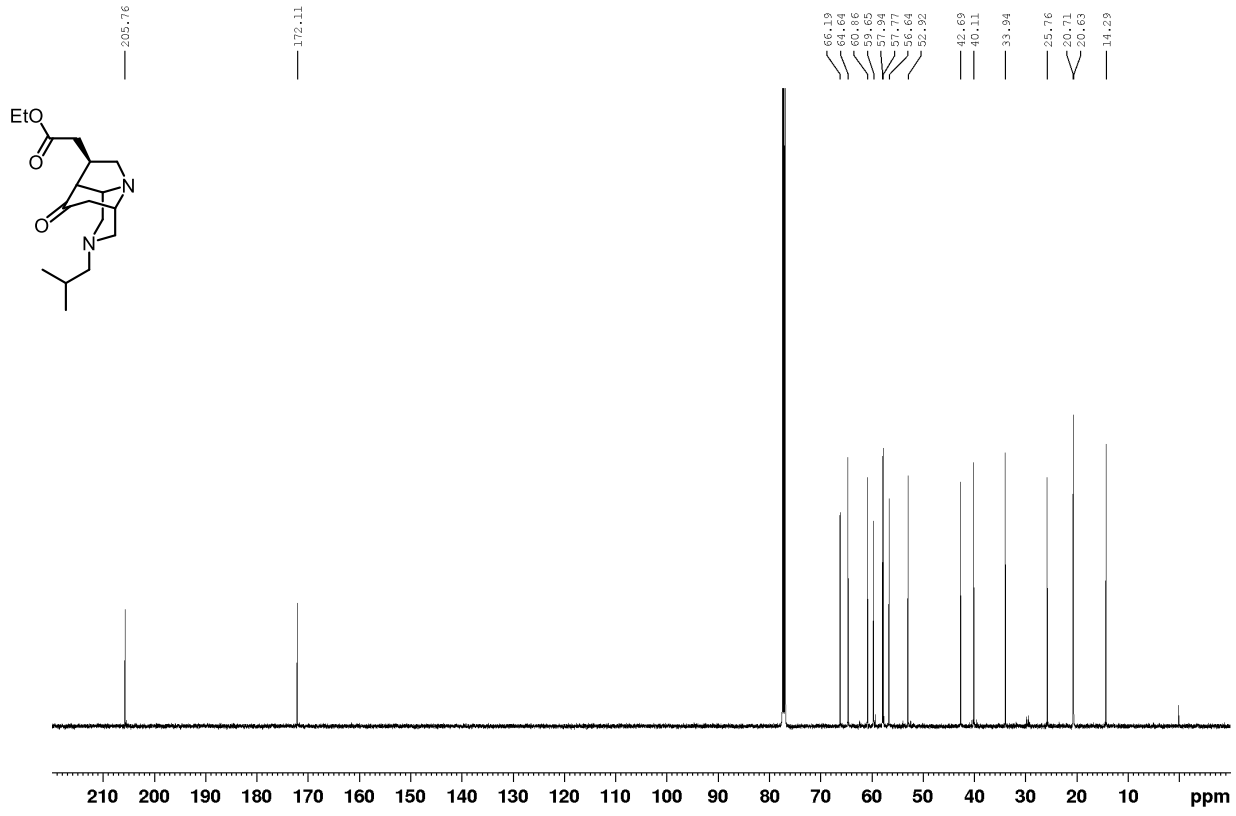
Diazatricycloundecane 5 (^{13}C NMR, $CDCl_3$, 125 MHz)



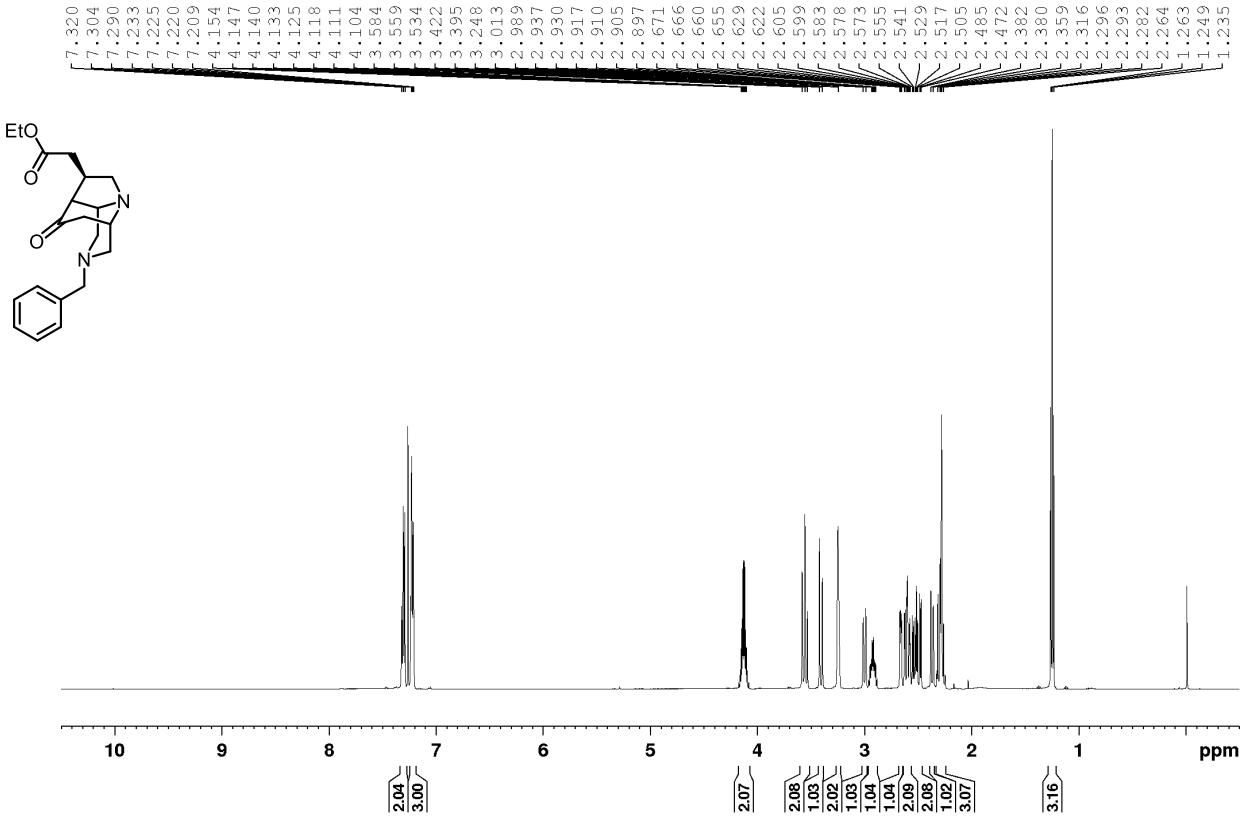
Ketone 11a (^{1}H NMR, $CDCl_3$, 400 MHz)



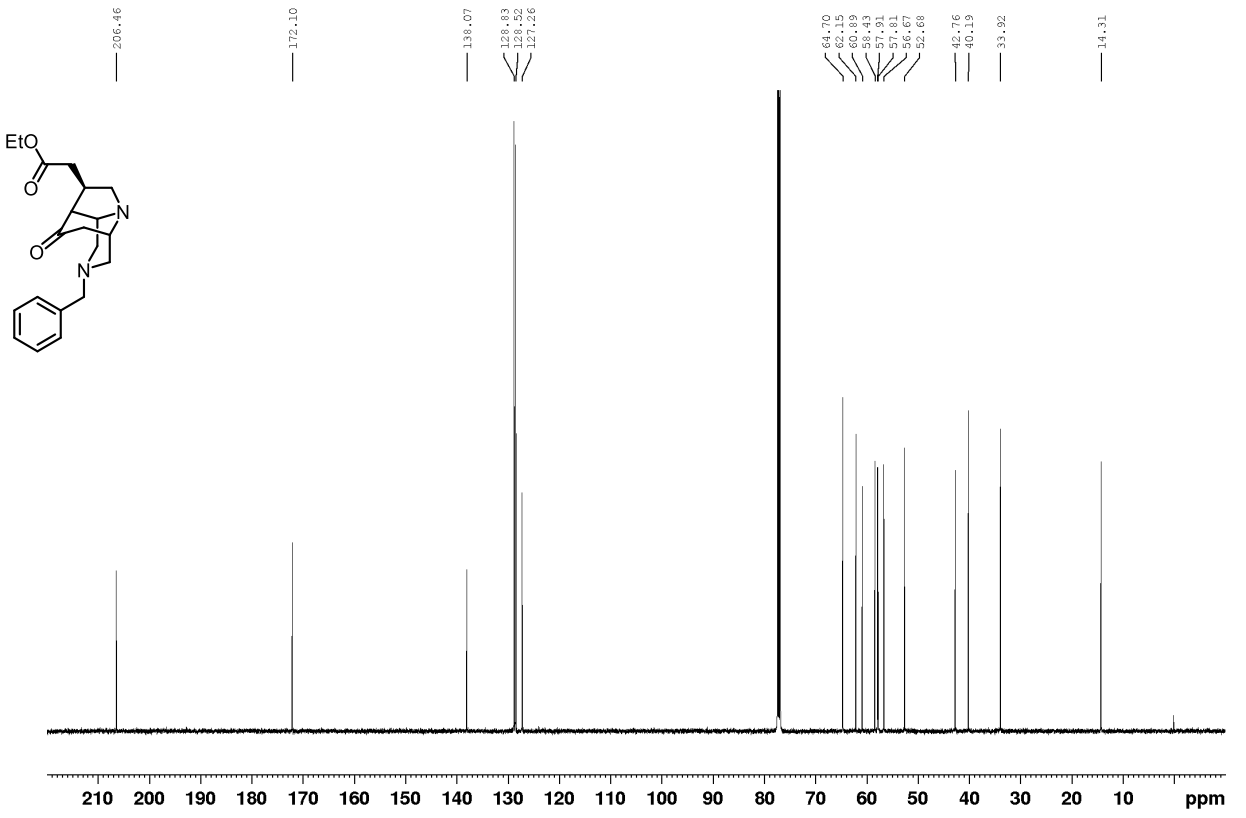
Ketone 11a (^{13}C NMR, $CDCl_3$, 125 MHz)



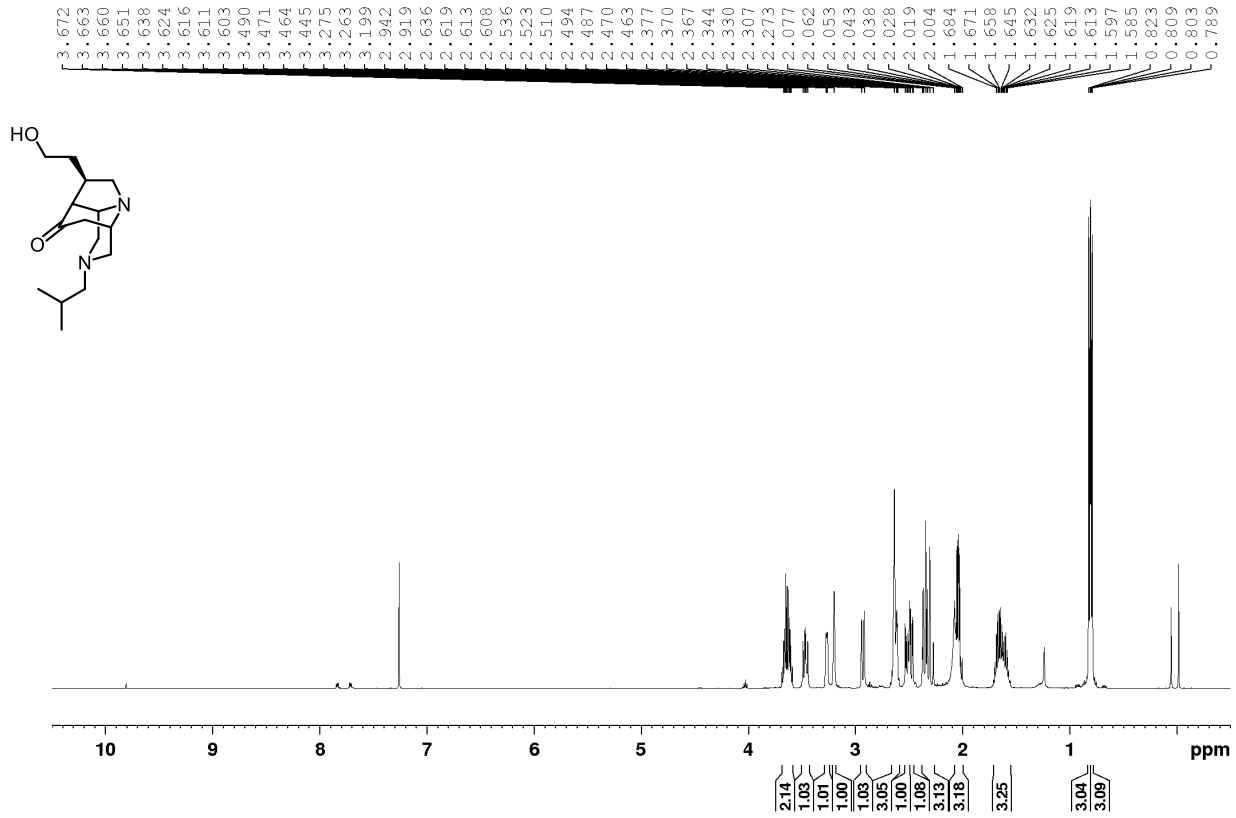
Ketone 11b (^{1}H NMR, $CDCl_3$, 500 MHz)



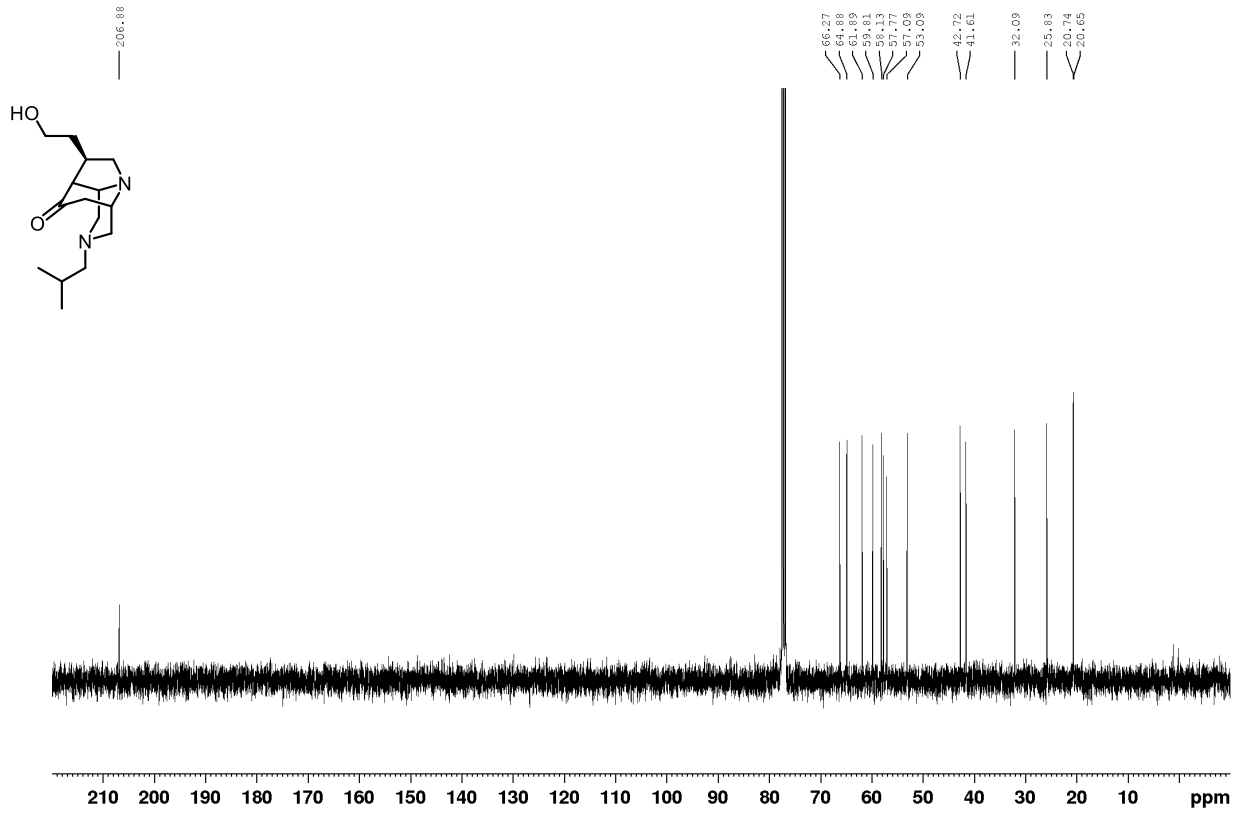
Ketone 11b (^{13}C NMR, $CDCl_3$, 125 MHz)



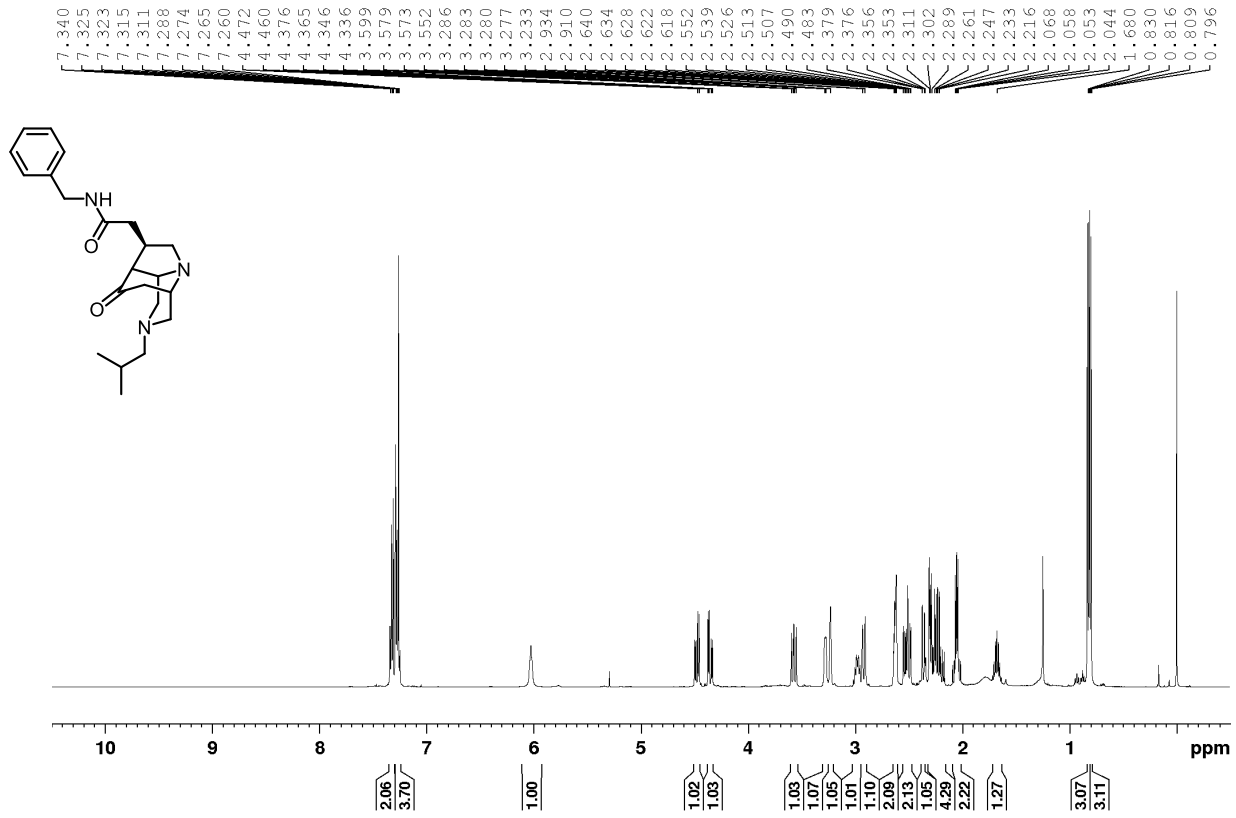
Alcohol S2 (^{1}H NMR, $CDCl_3$, 500 MHz)



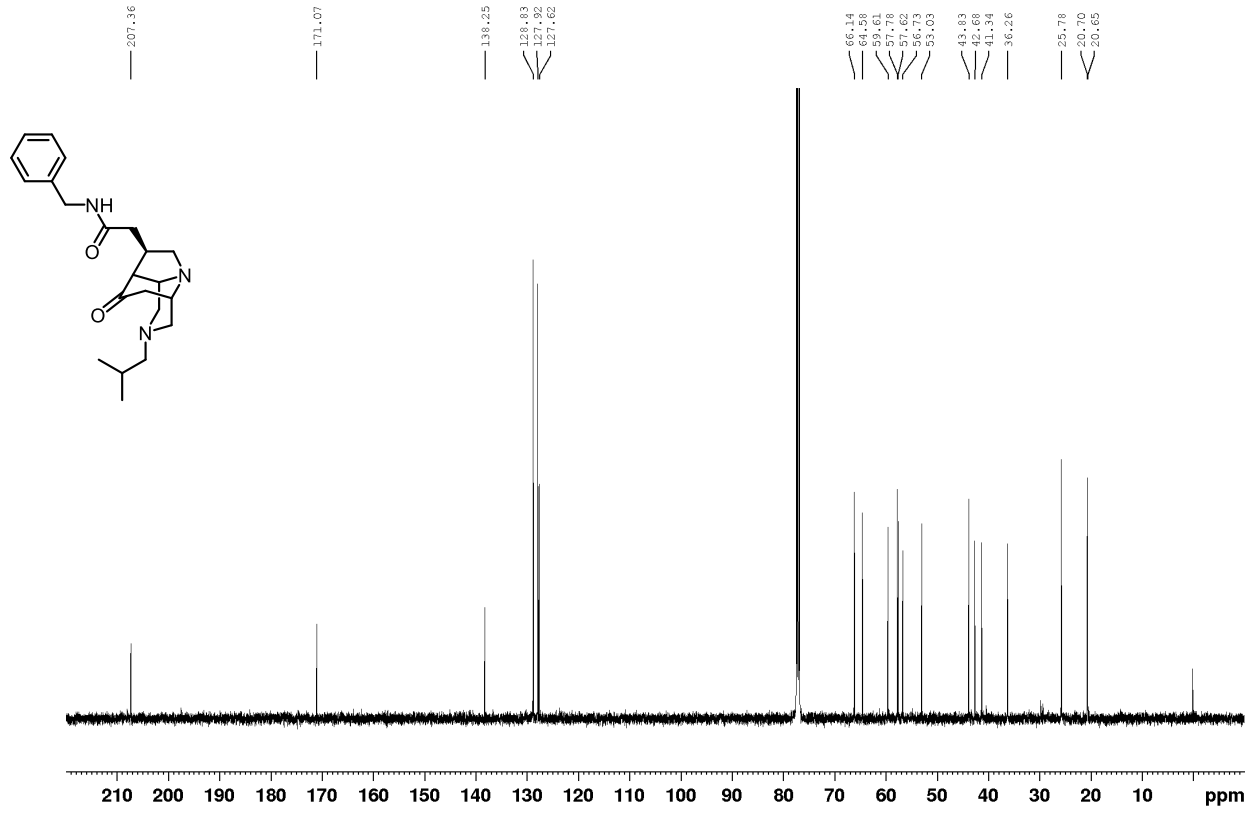
Alcohol S2 (^{13}C NMR, $CDCl_3$, 100 MHz)



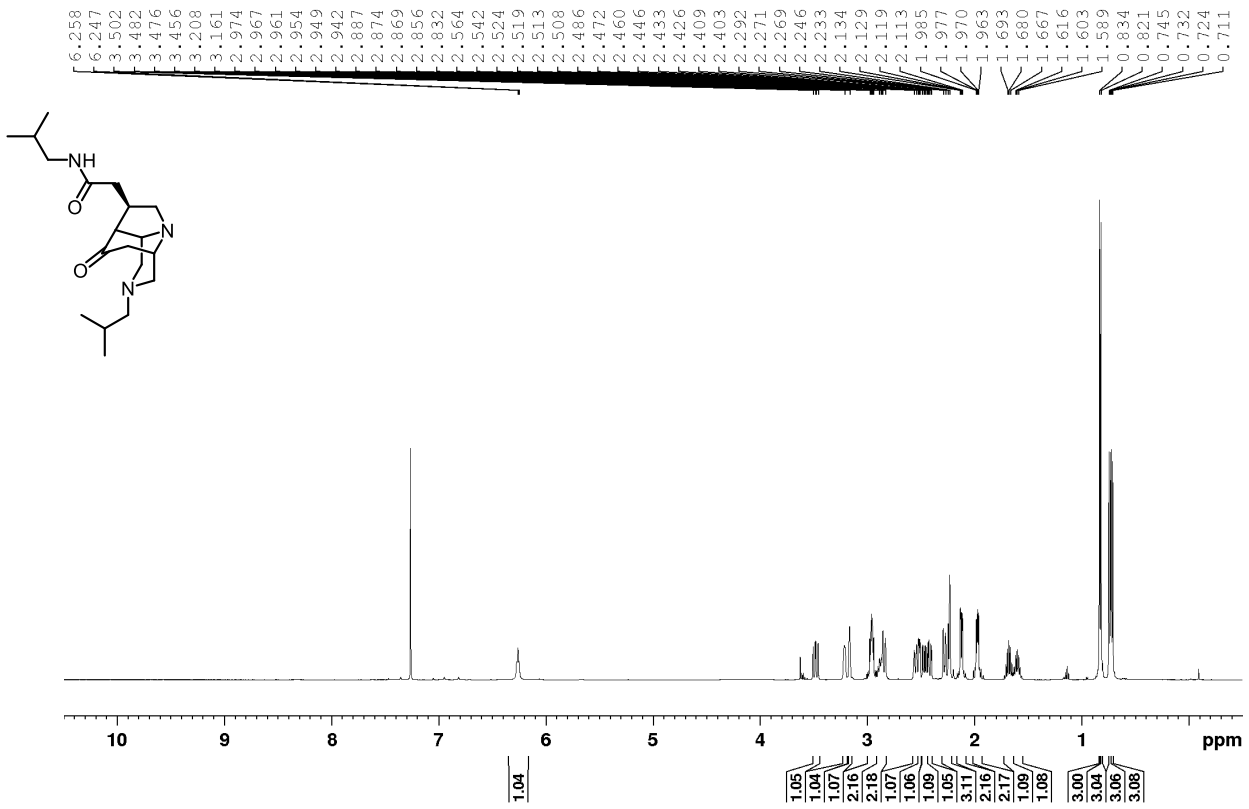
Amide 12a (^{1}H NMR, $CDCl_3$, 500 MHz)



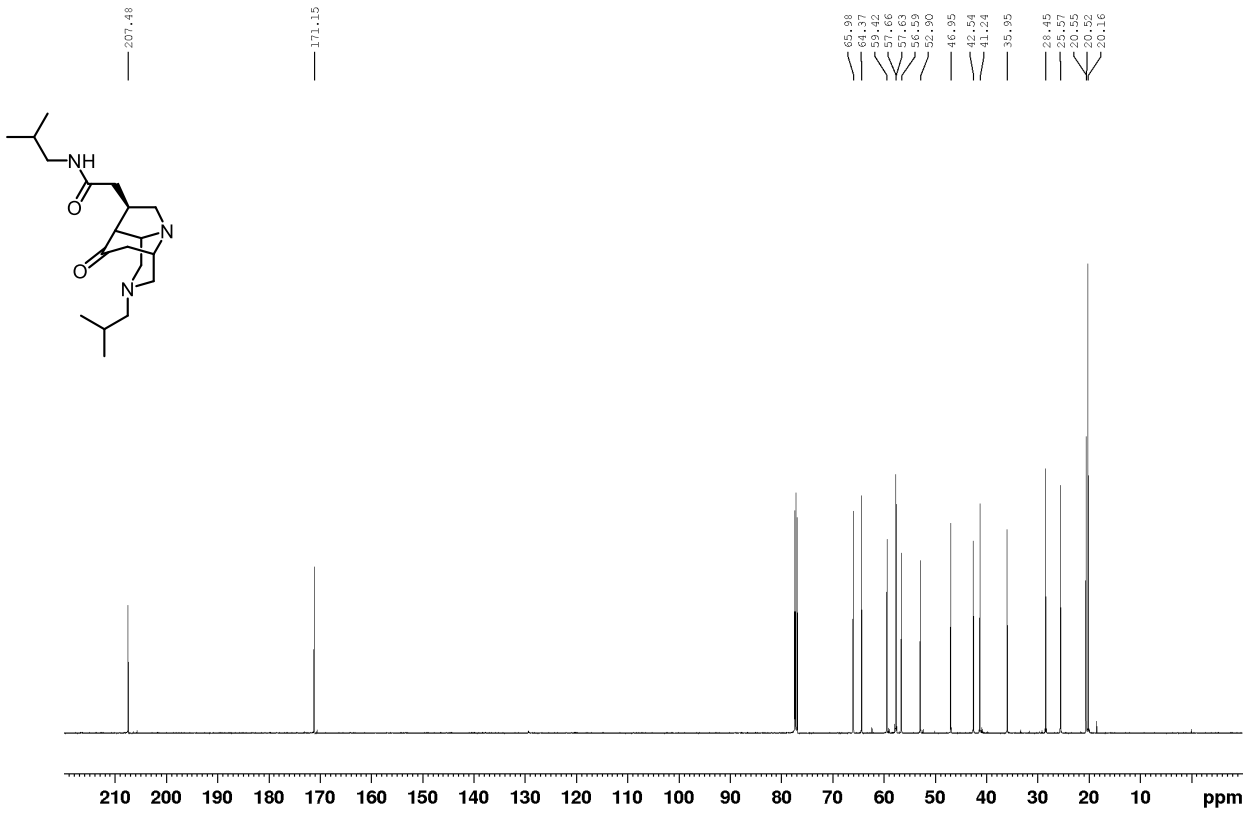
Amide 12a (^{13}C NMR, $CDCl_3$, 125 MHz)



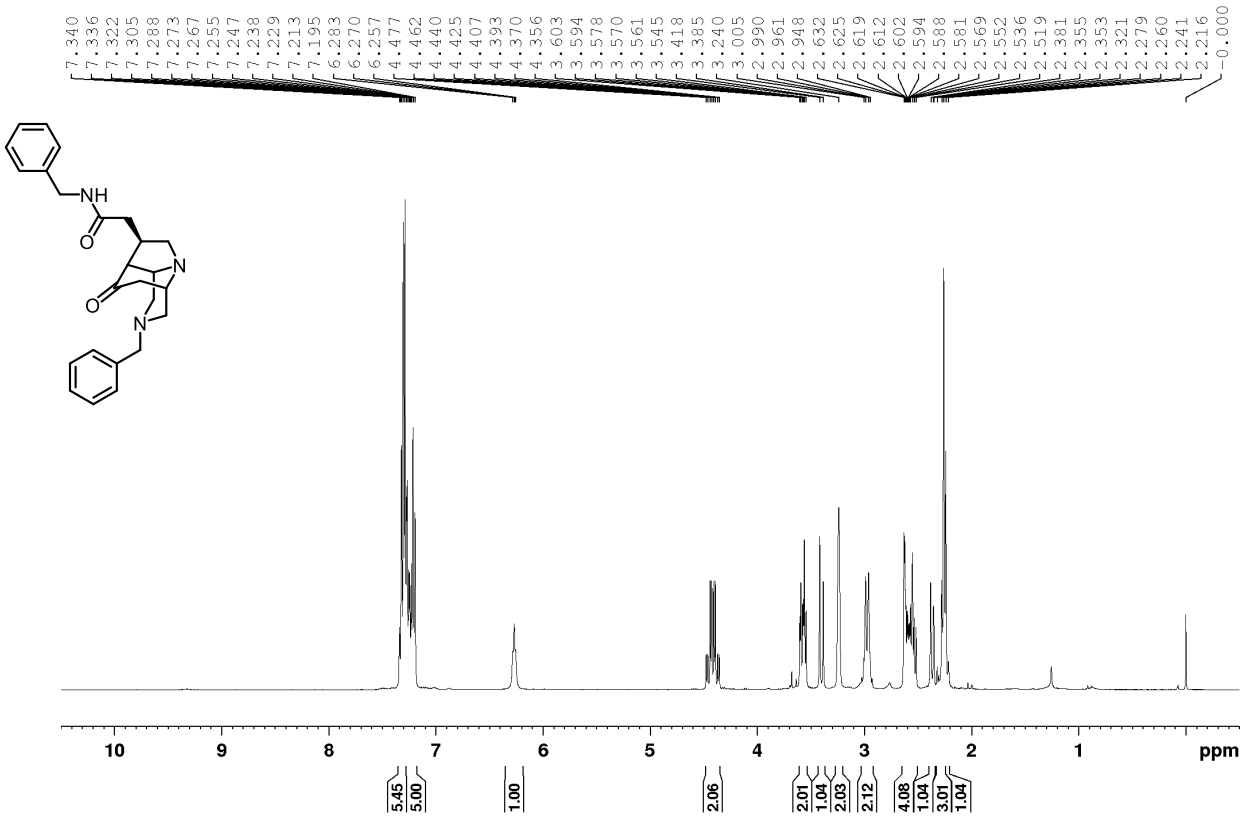
Amide 12b (^{1}H NMR, $CDCl_3$, 500 MHz)



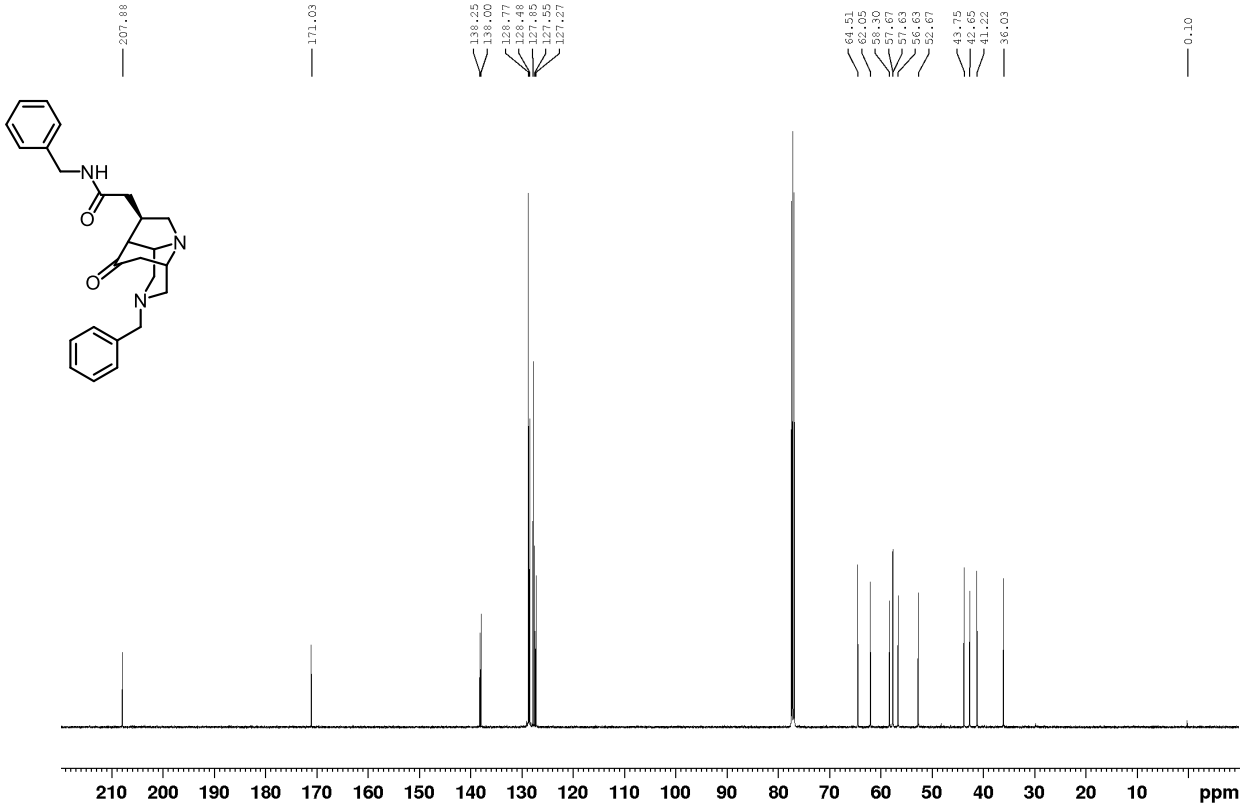
Amide 12b (^{13}C NMR, $CDCl_3$, 125 MHz)



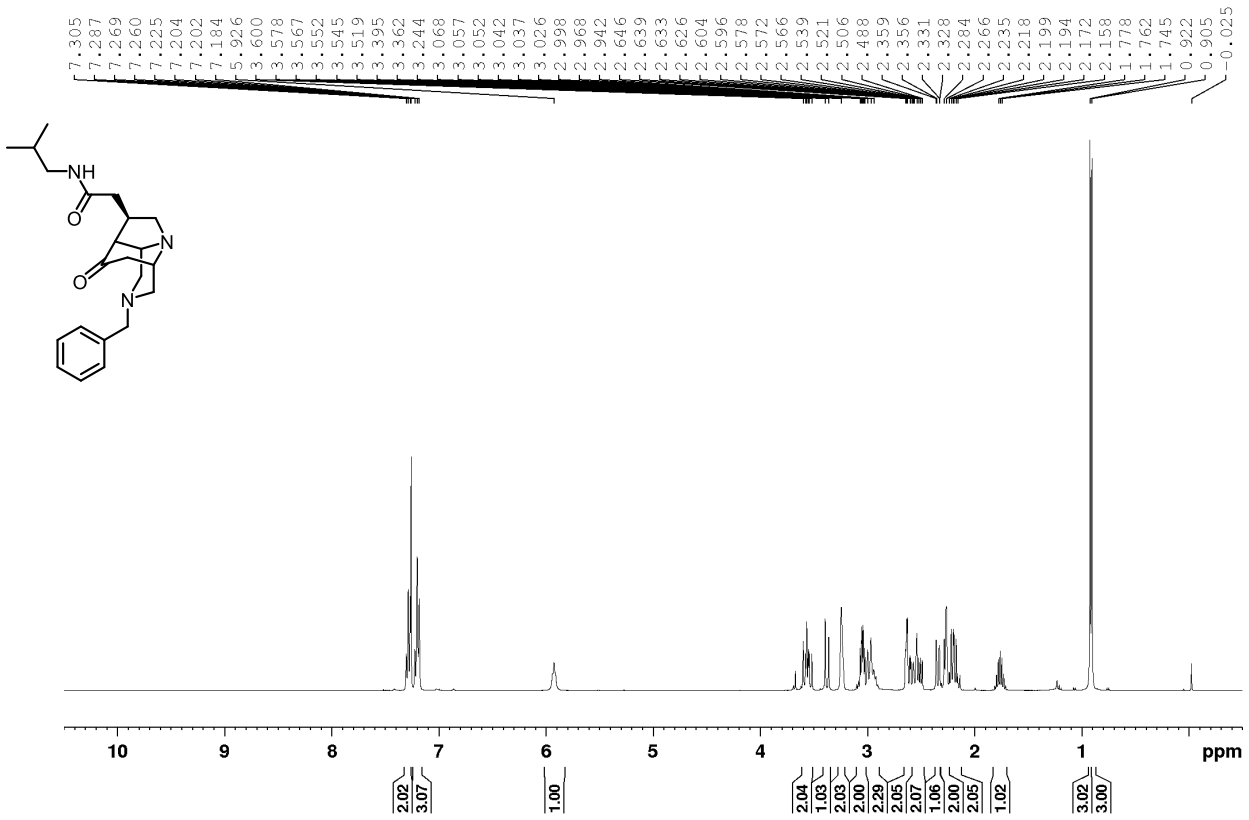
Amide 12c (^{1}H NMR, $CDCl_3$, 400 MHz)



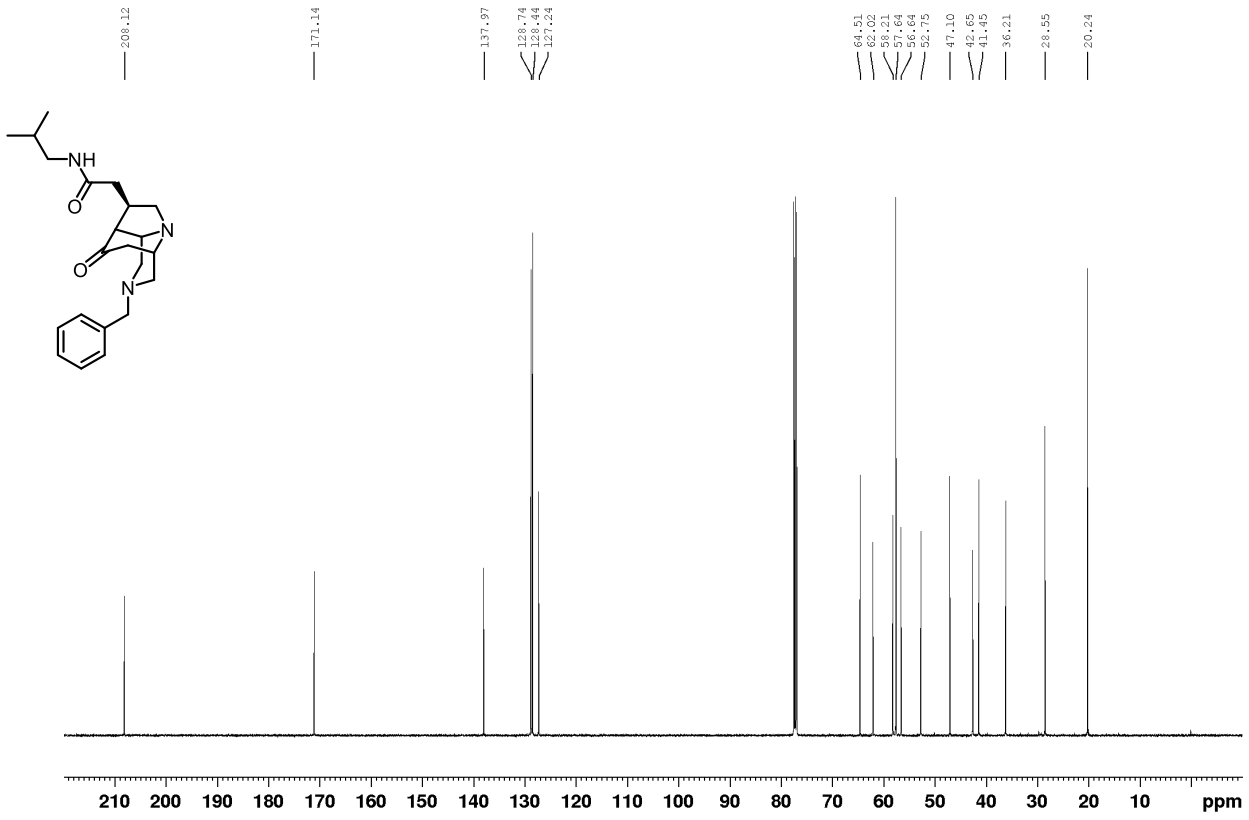
Amide 12c (^{13}C NMR, $CDCl_3$, 125 MHz)



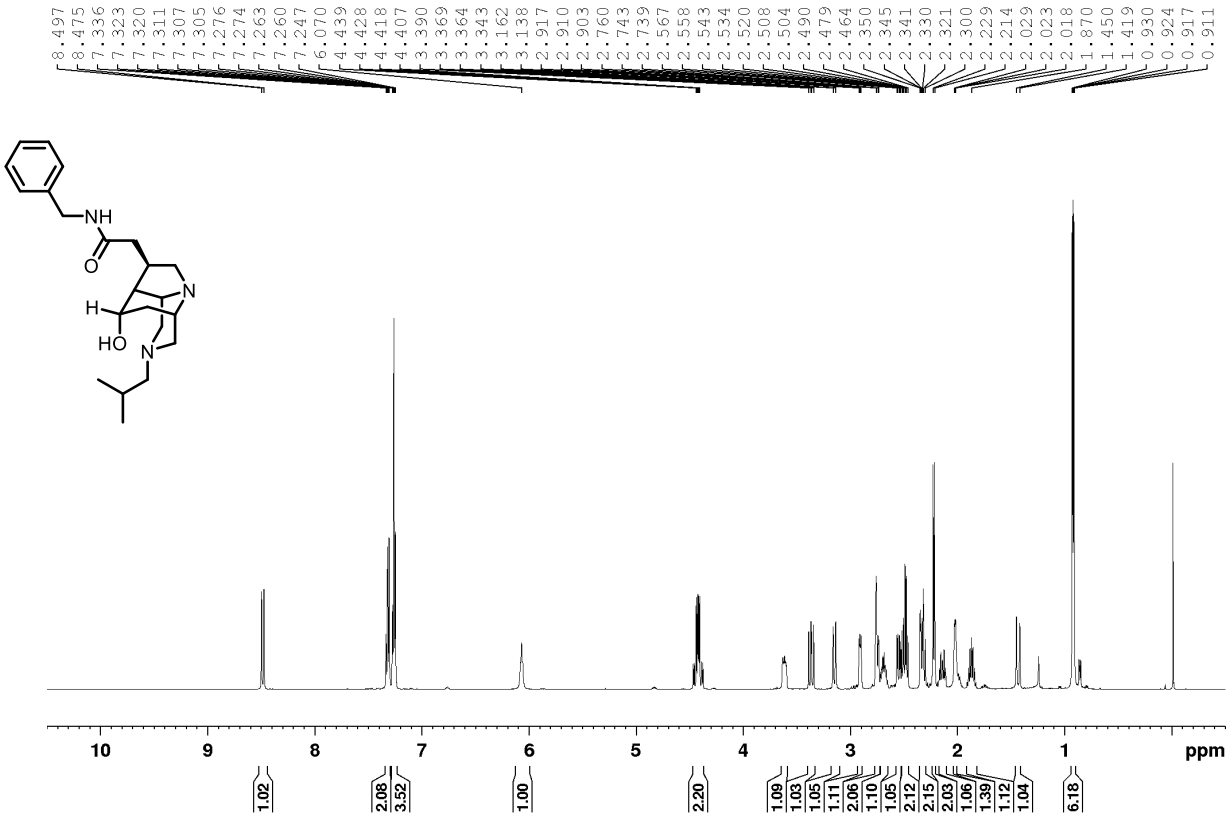
Amide 12d (^{1}H NMR, $CDCl_3$, 400 MHz)



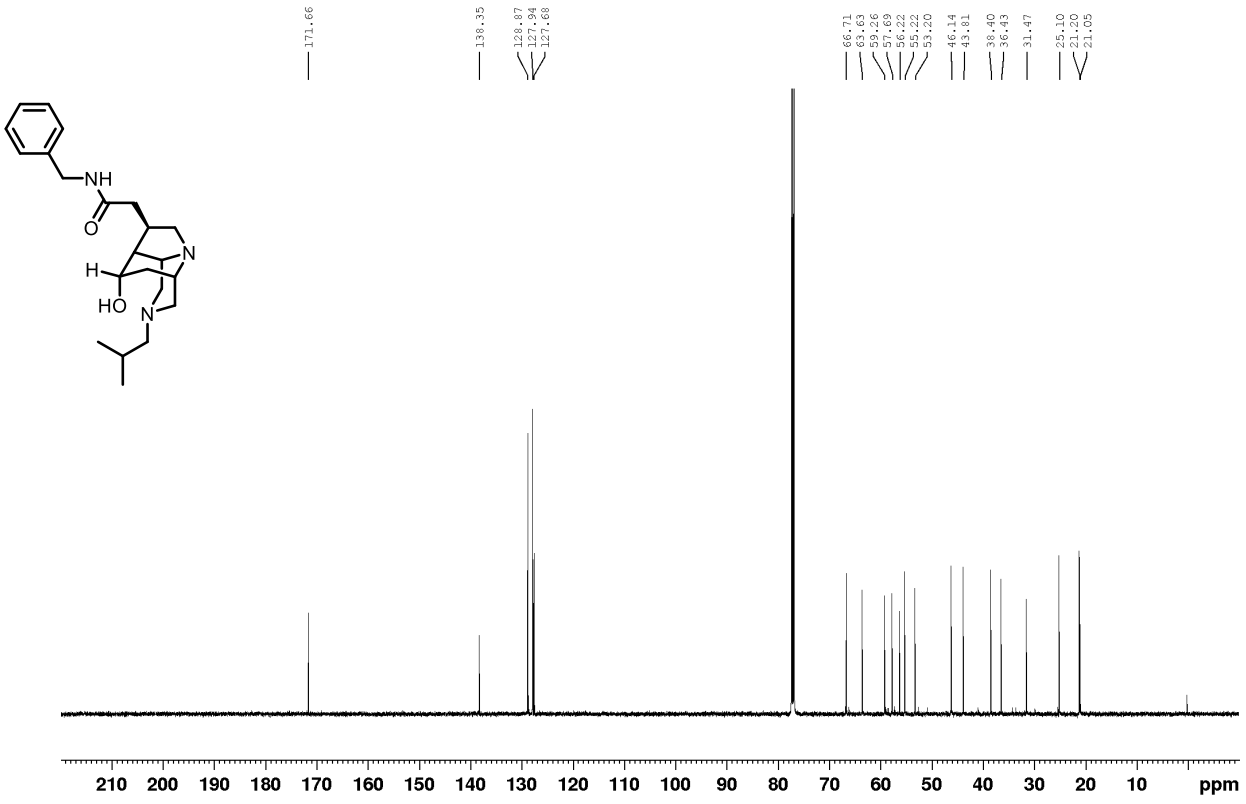
Amide 12d (^{13}C NMR, $CDCl_3$, 125 MHz)



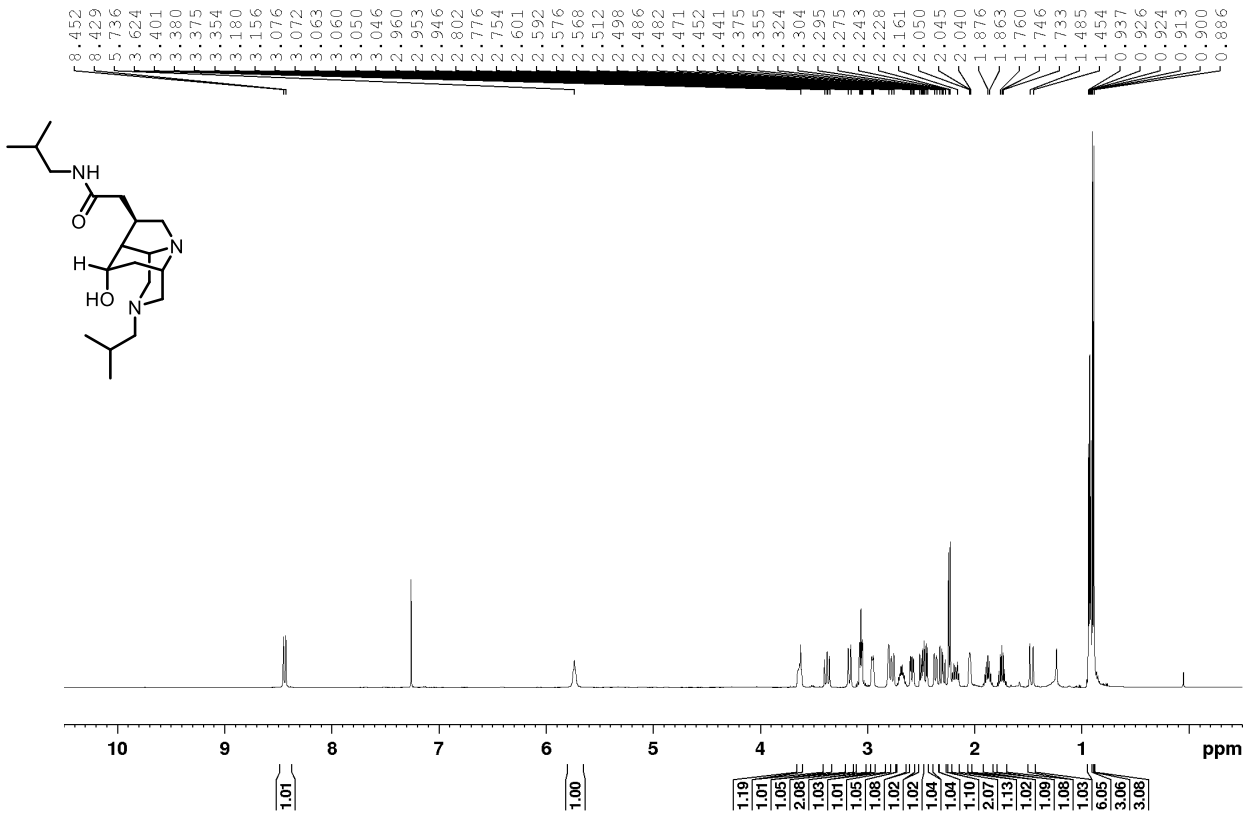
Alcohol 13a (^{1}H NMR, $CDCl_3$, 500 MHz)



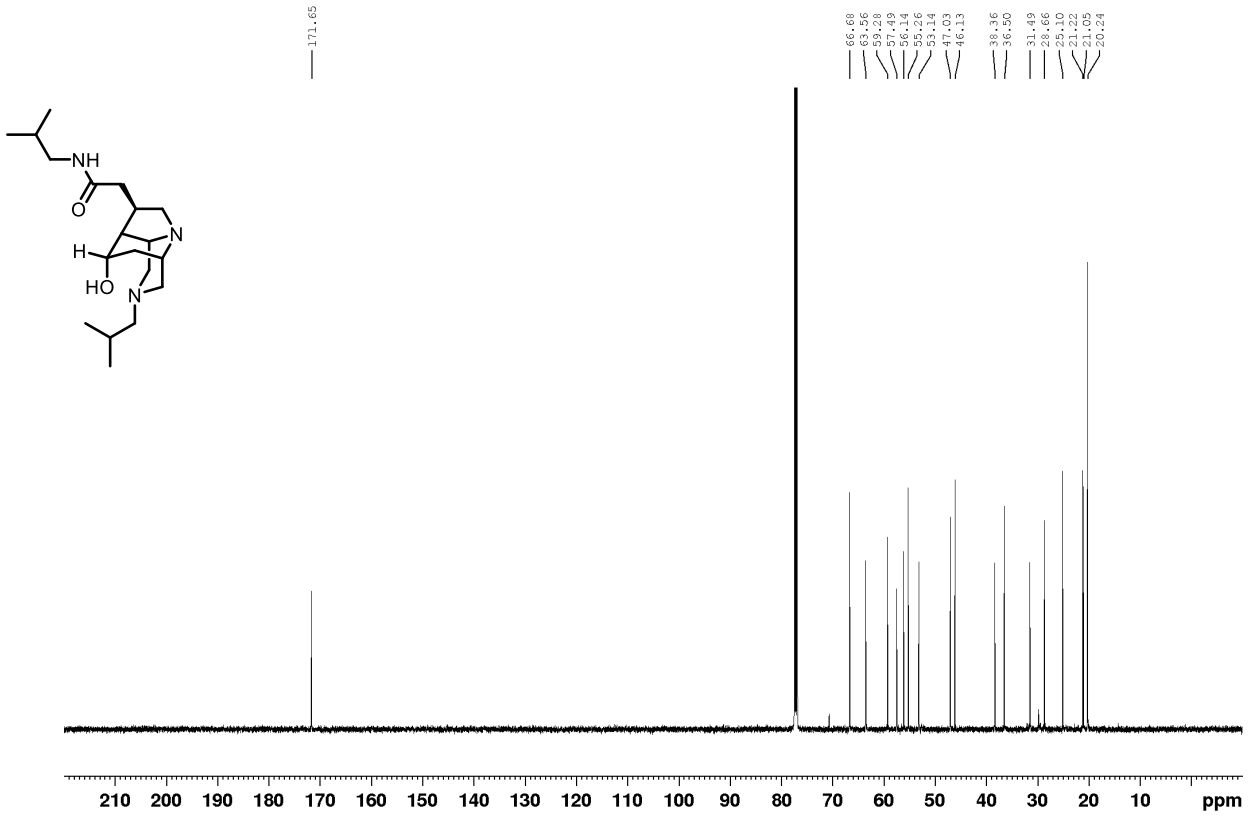
Alcohol 13a (^{13}C NMR, $CDCl_3$, 125 MHz)



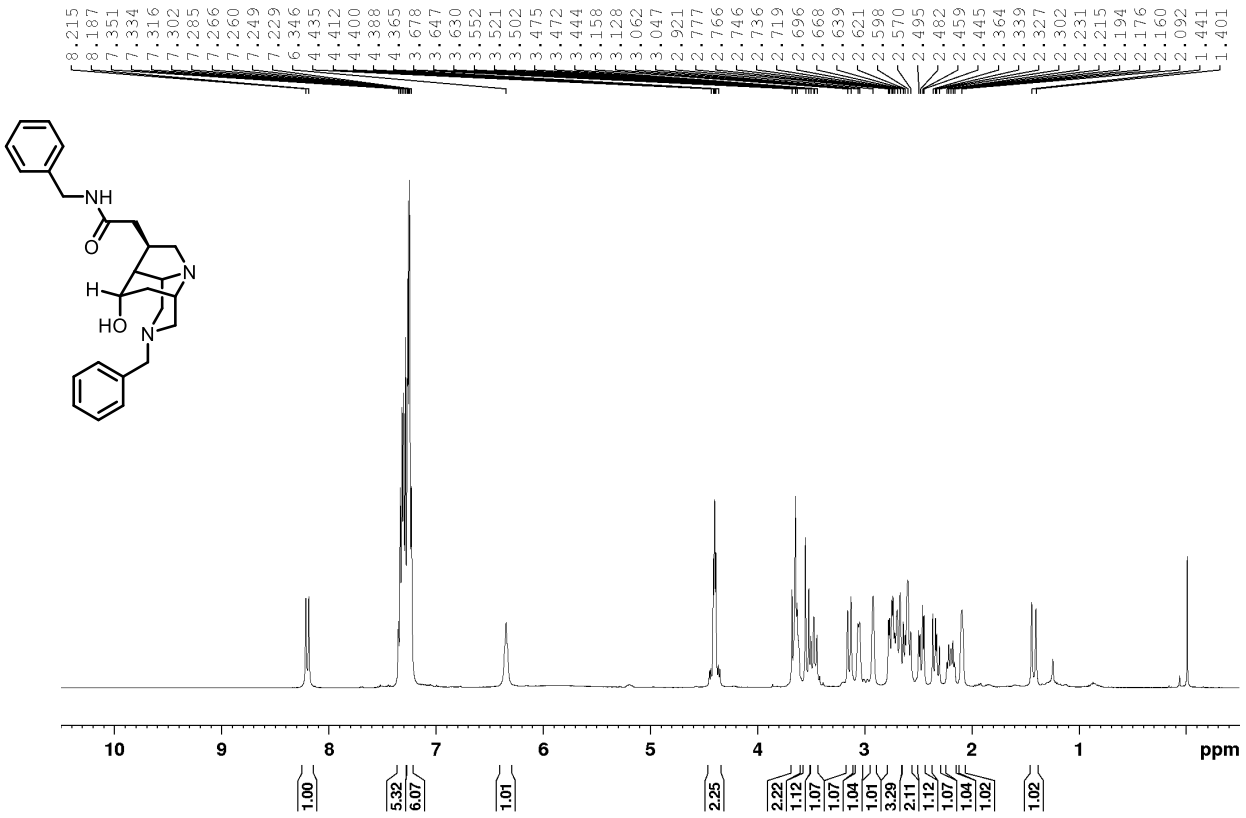
Alcohol 13b (^{1}H NMR, $CDCl_3$, 500 MHz)



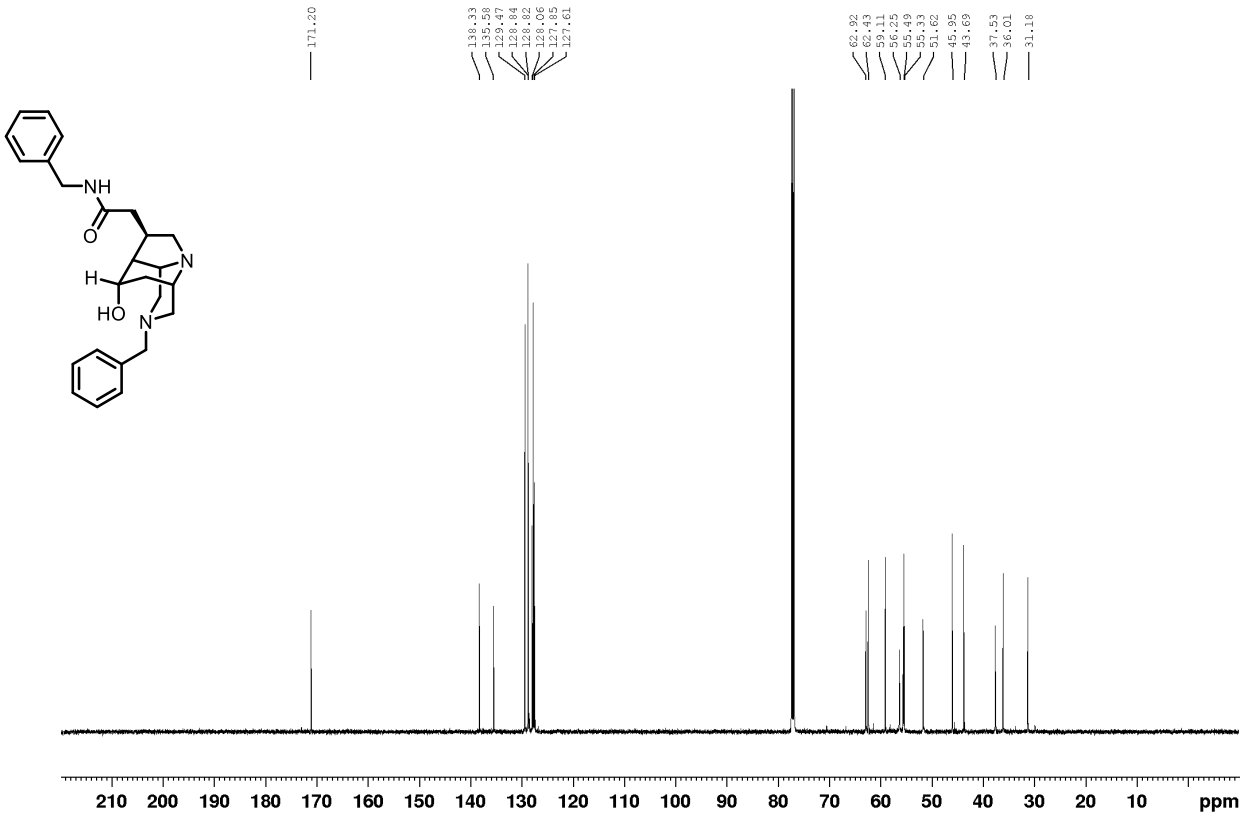
Alcohol 13b (^{13}C NMR, $CDCl_3$, 125 MHz)



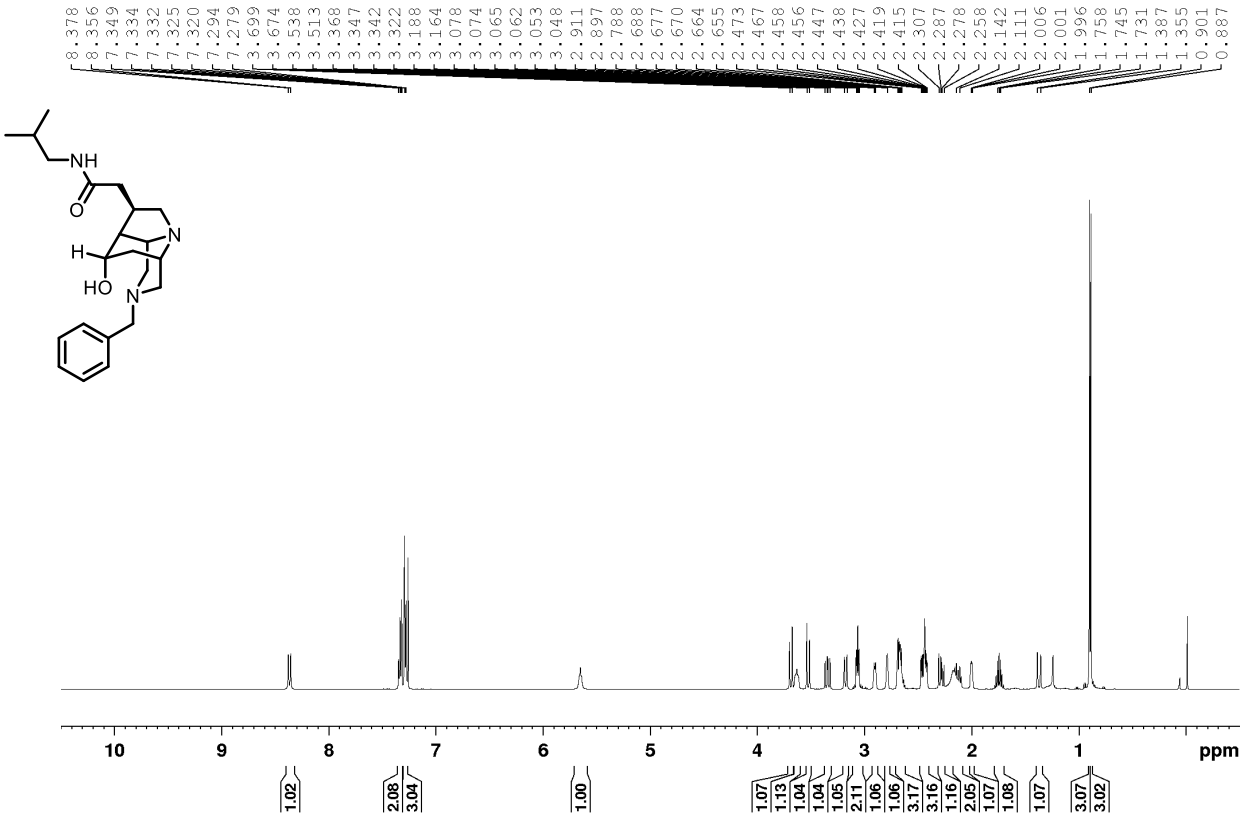
Alcohol 13c (^{1}H NMR, $CDCl_3$, 400 MHz)



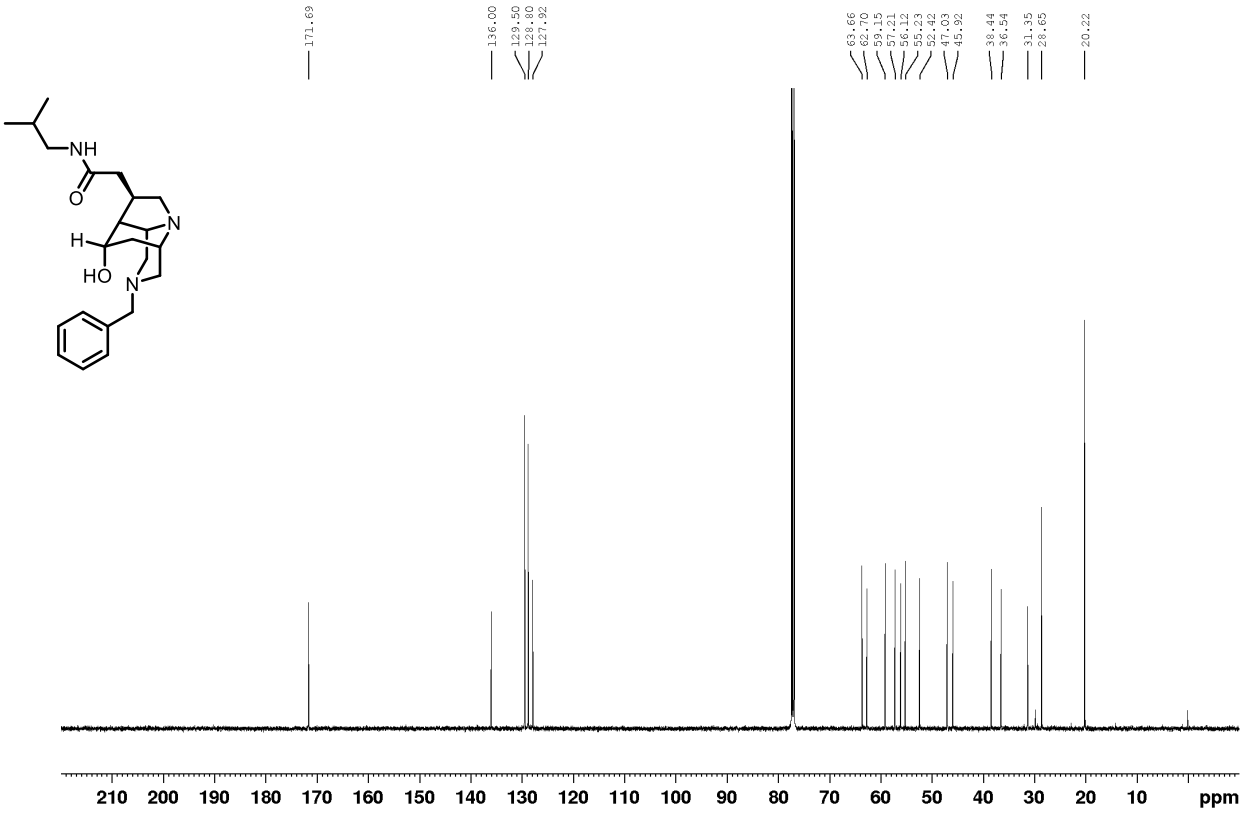
Alcohol 13c (^{13}C NMR, $CDCl_3$, 125 MHz)



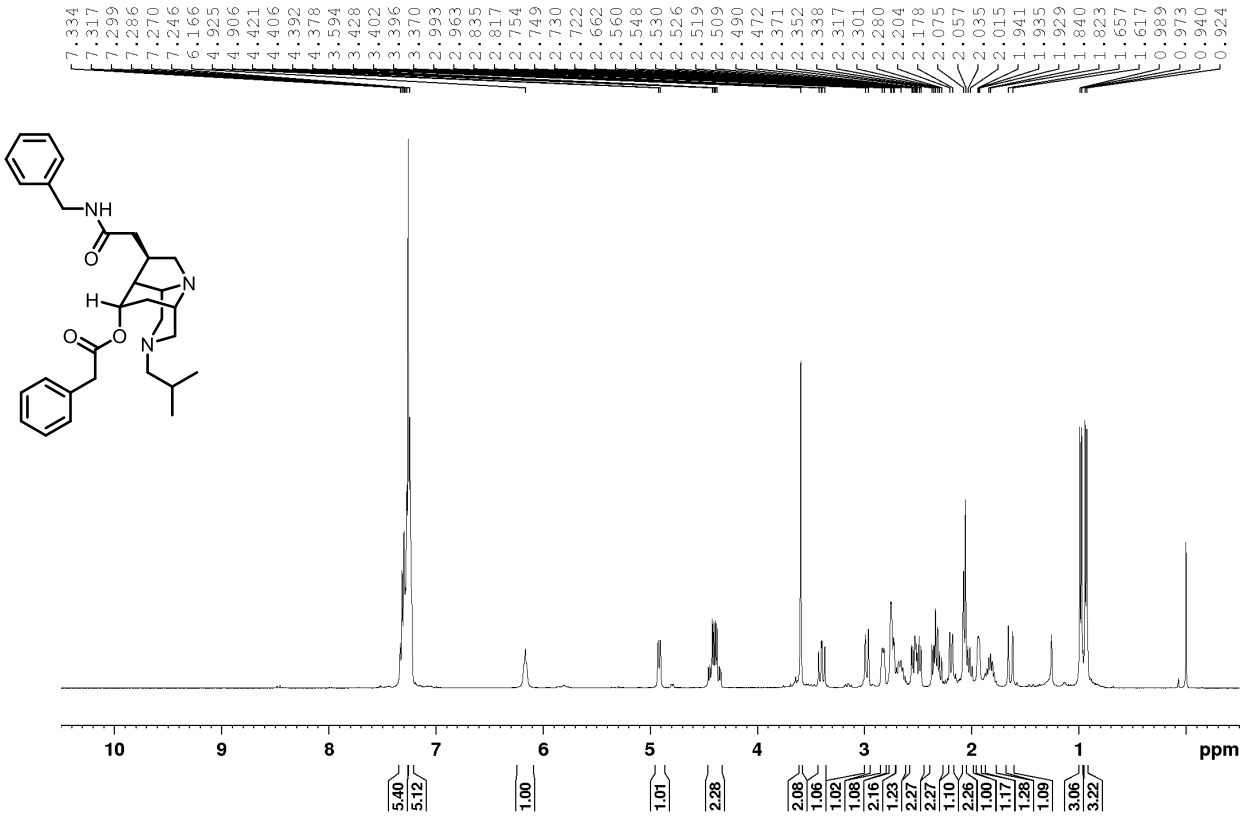
Alcohol 13d (^{1}H NMR, $CDCl_3$, 500 MHz)



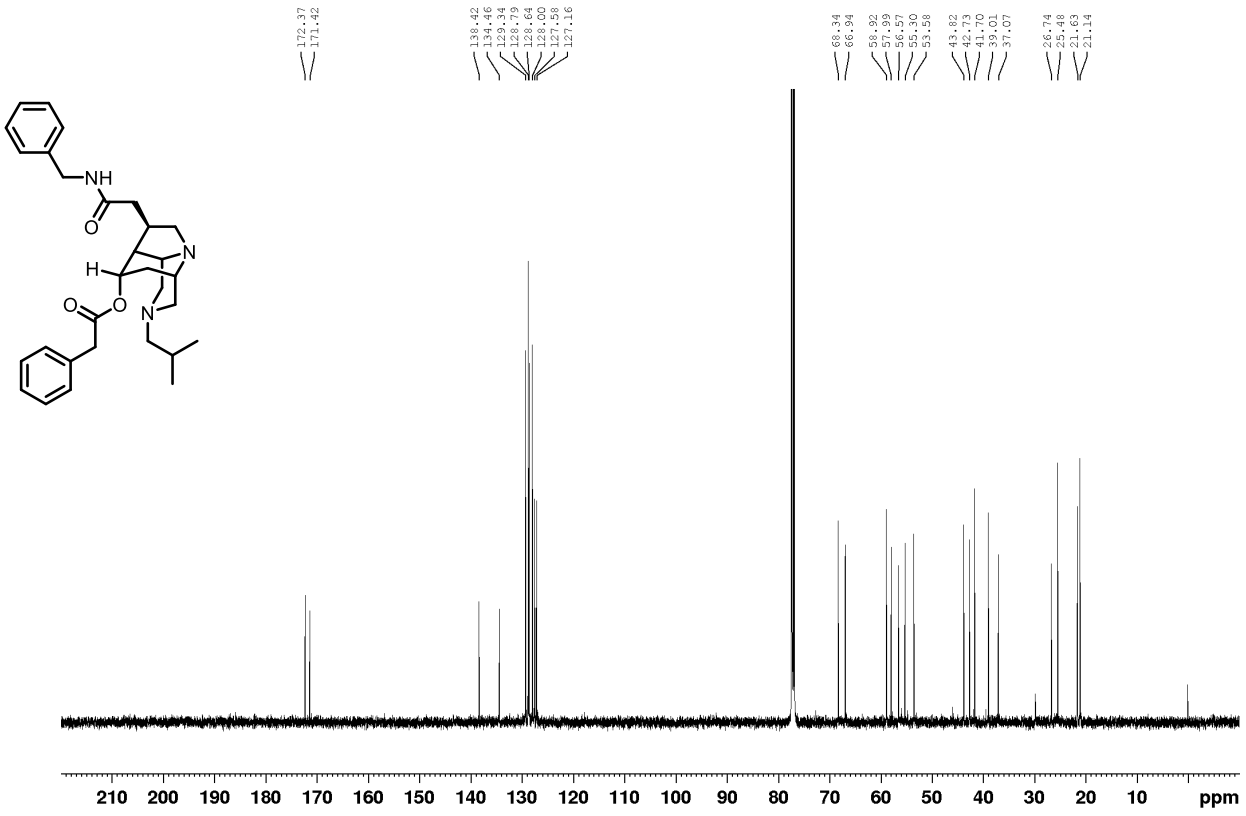
Alcohol 13d (^{13}C NMR, $CDCl_3$, 125 MHz)



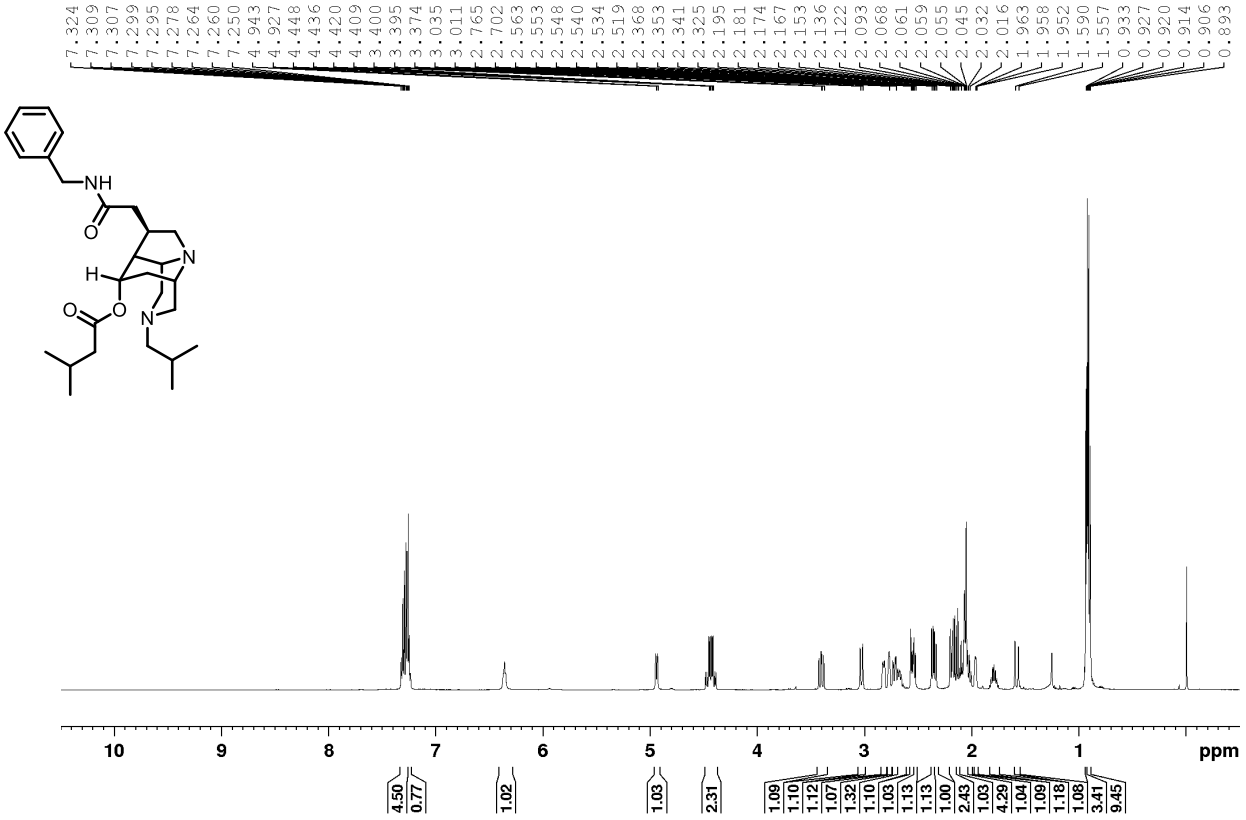
Ester 6a (^{1}H NMR, $CDCl_3$, 400 MHz)



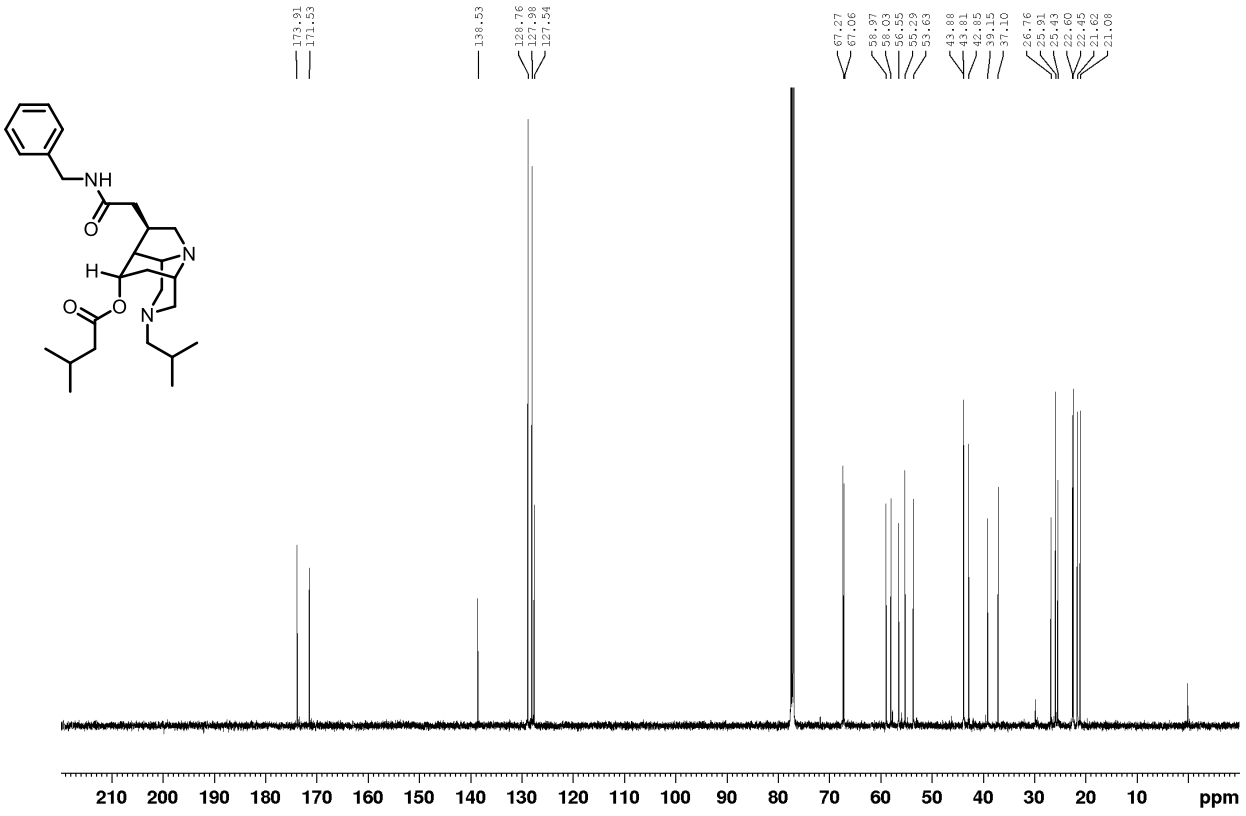
Ester 6a (^{13}C NMR, $CDCl_3$, 125 MHz)



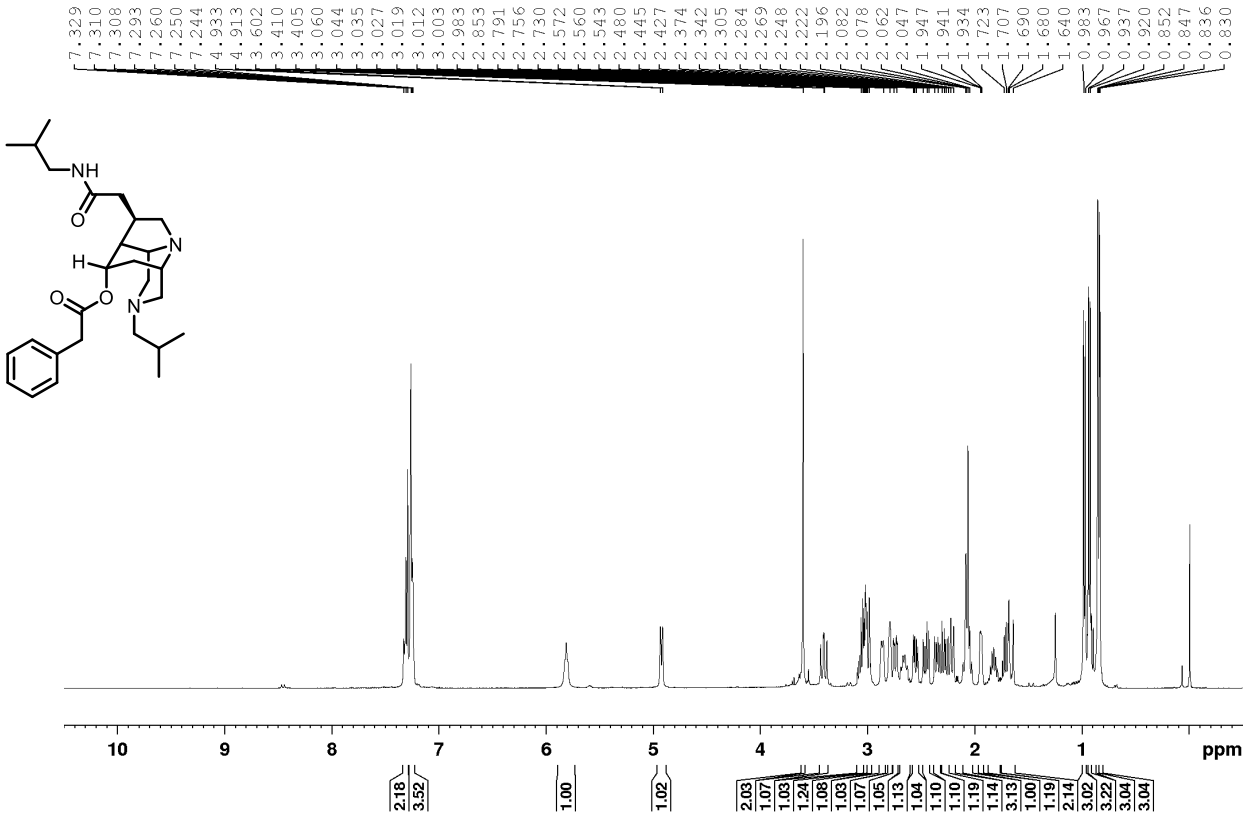
Ester 6b (^{1}H NMR, $CDCl_3$, 500 MHz)



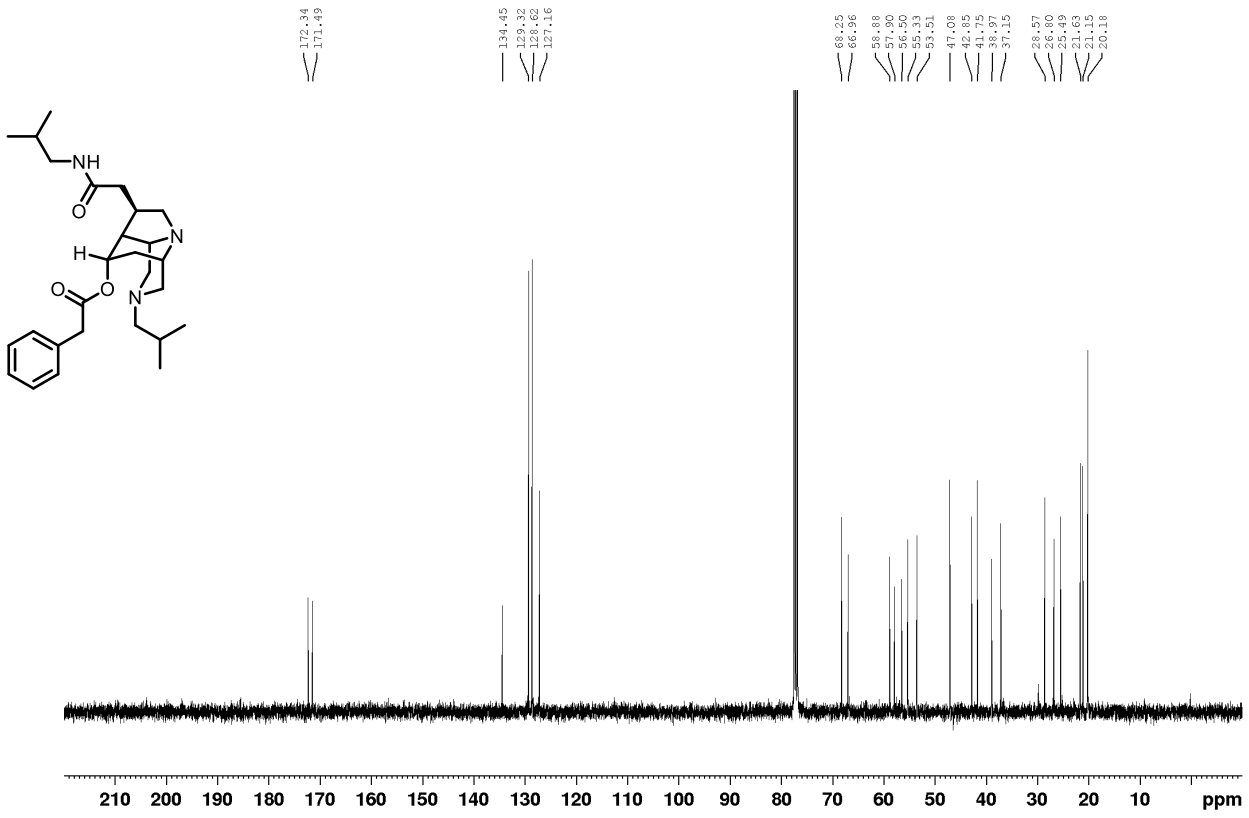
Ester 6b (^{13}C NMR, $CDCl_3$, 125 MHz)



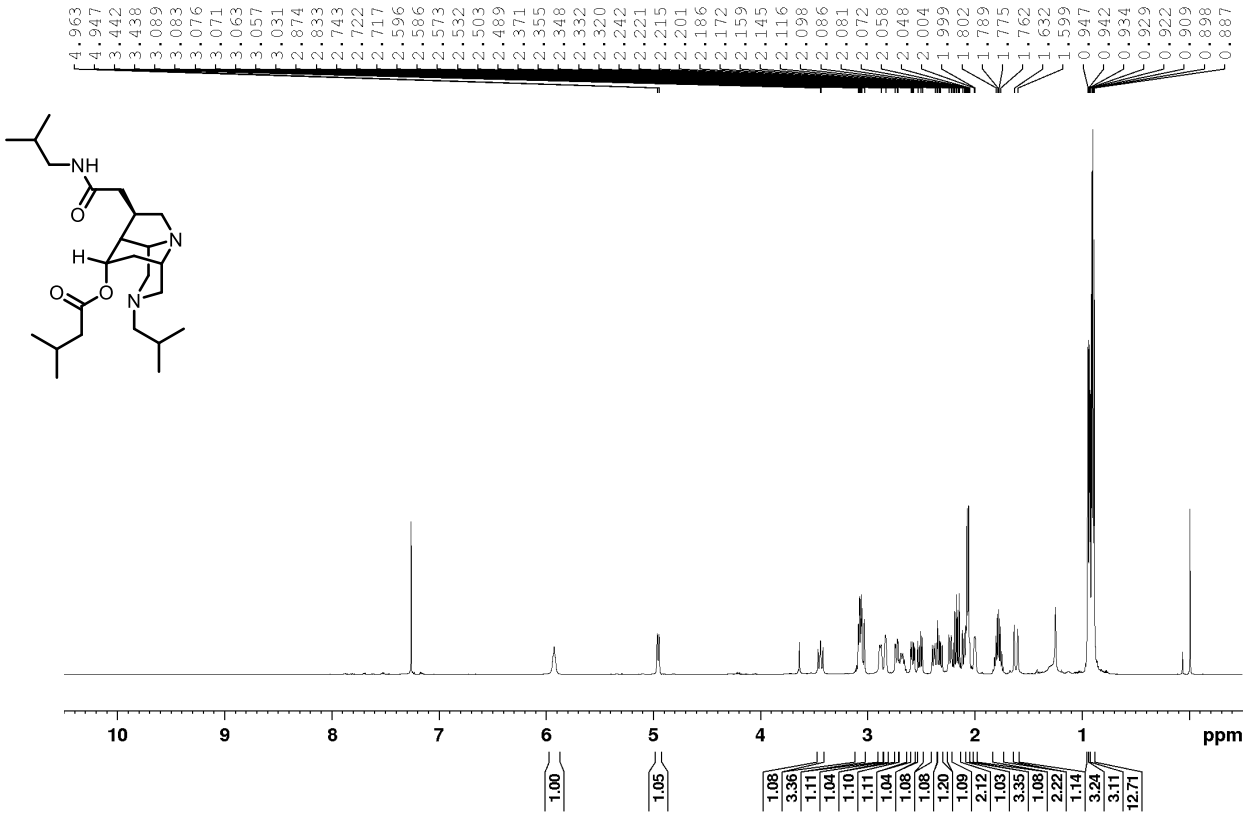
Ester 6c (^{1}H NMR, $CDCl_3$, 400 MHz)



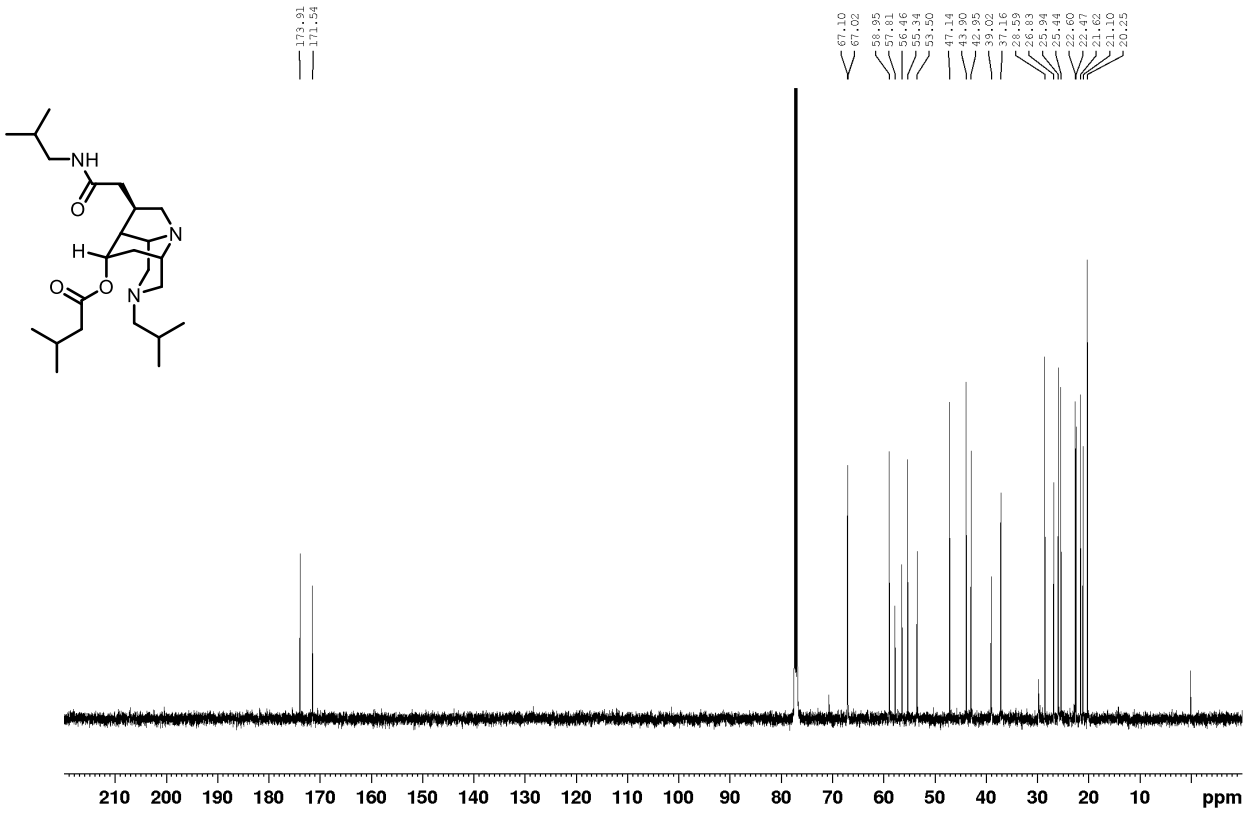
Ester 6c (^{13}C NMR, $CDCl_3$, 100 MHz)



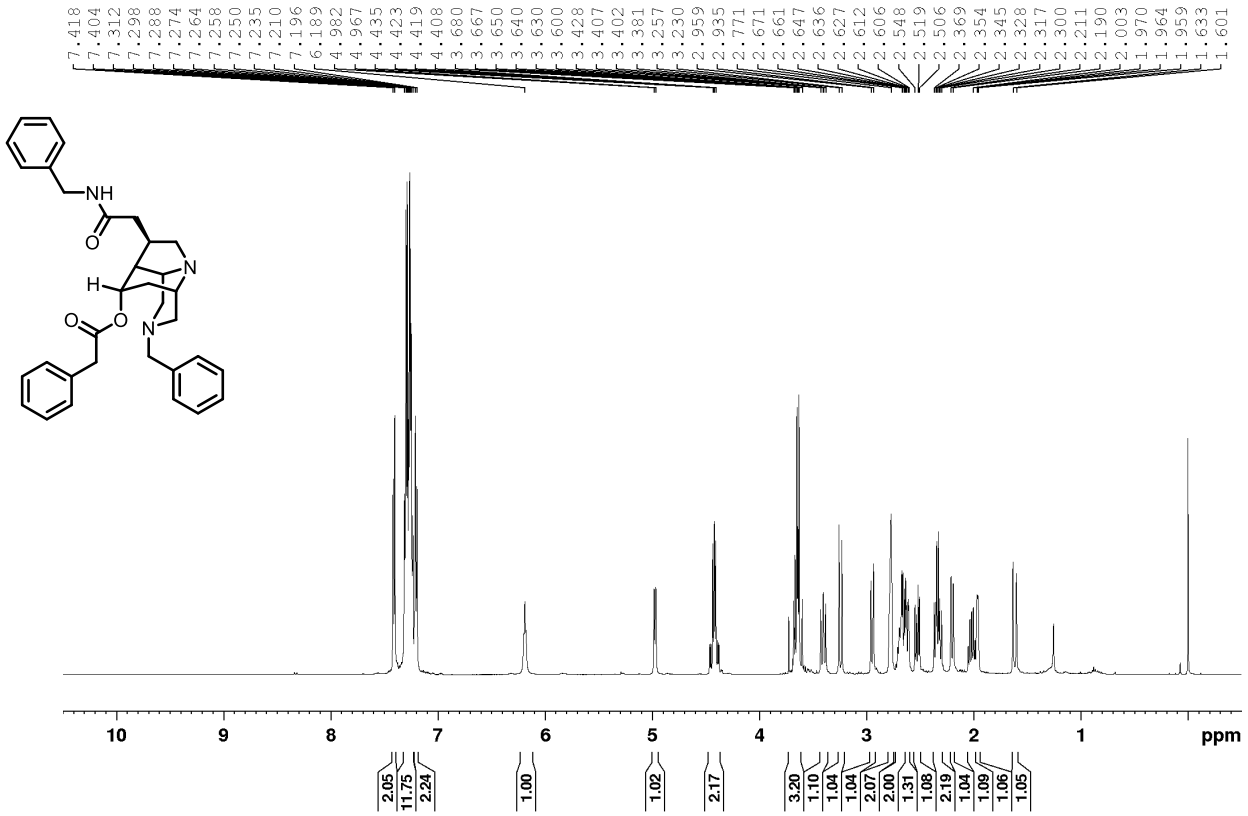
Ester 6d (^{1}H NMR, $CDCl_3$, 500 MHz)



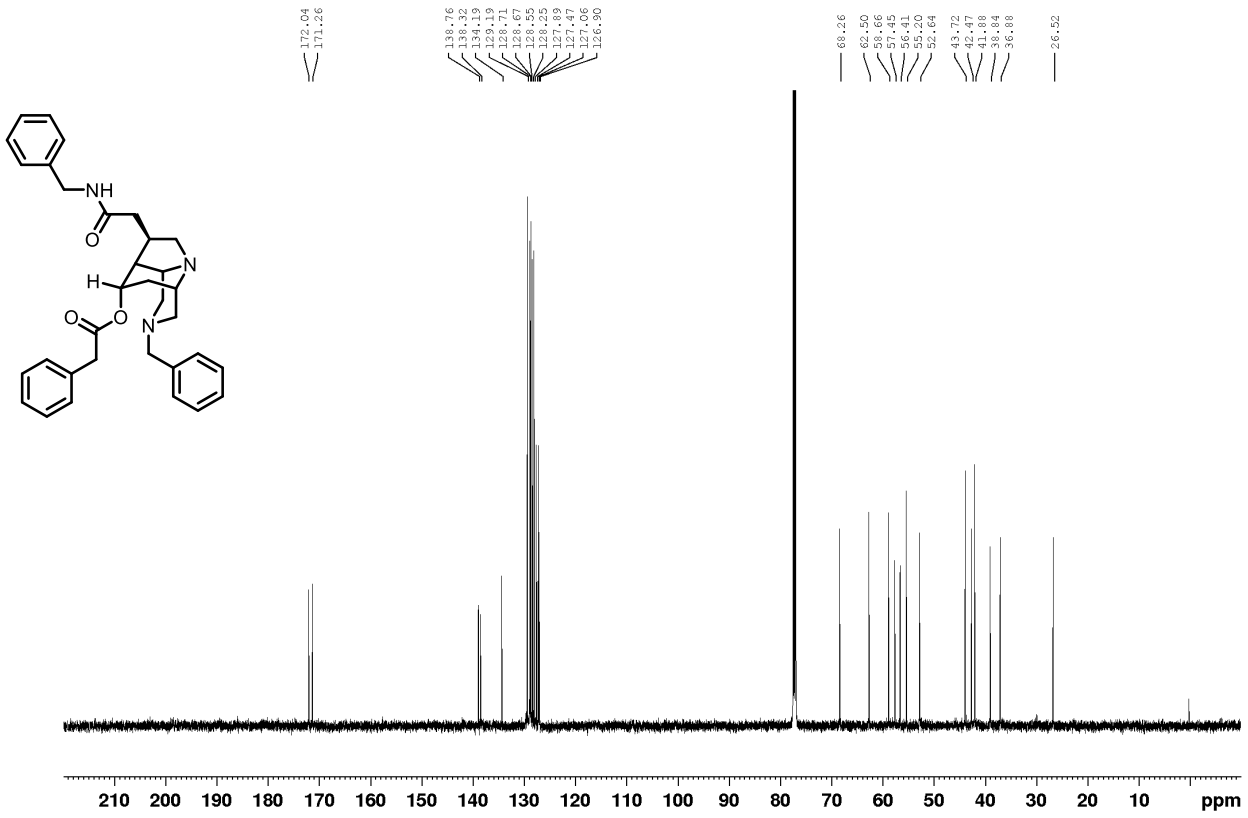
Ester 6d (^{13}C NMR, $CDCl_3$, 125 MHz)



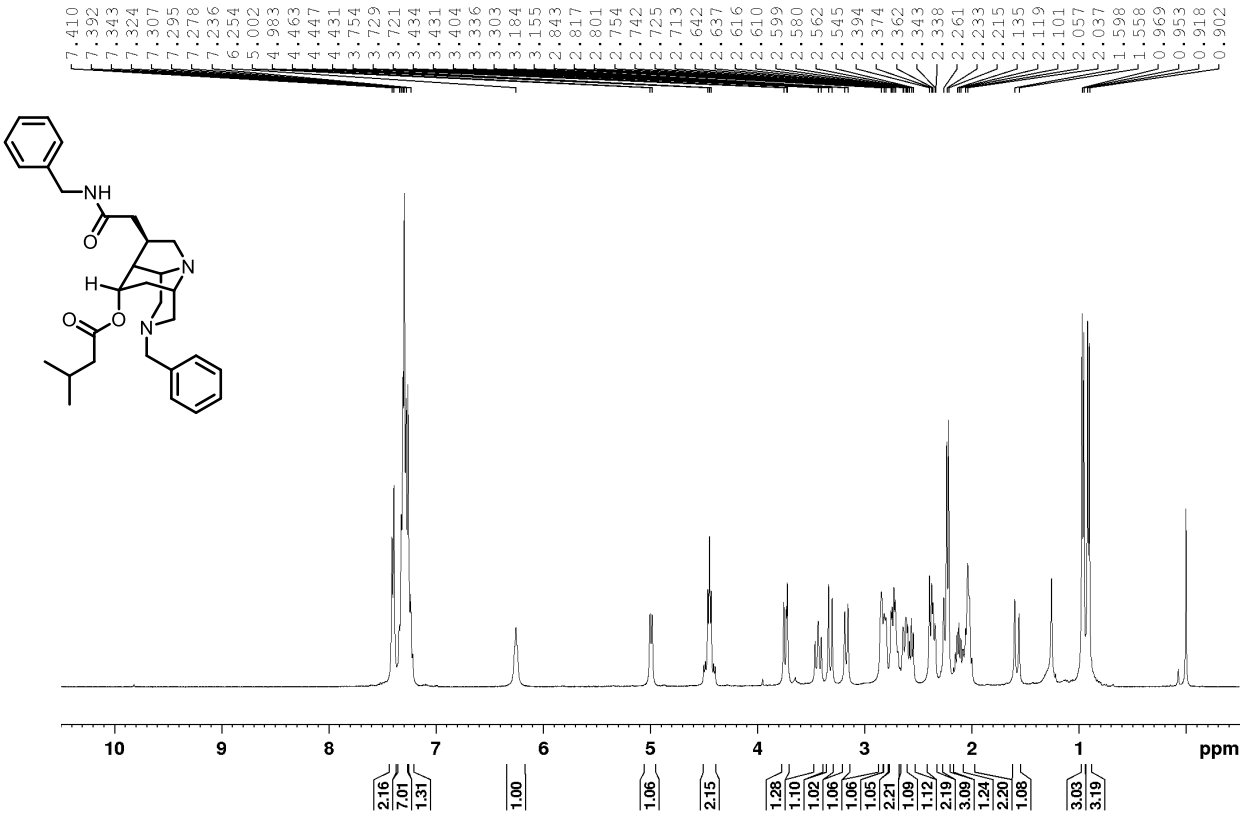
Ester 6e (^{1}H NMR, $CDCl_3$, 500 MHz)



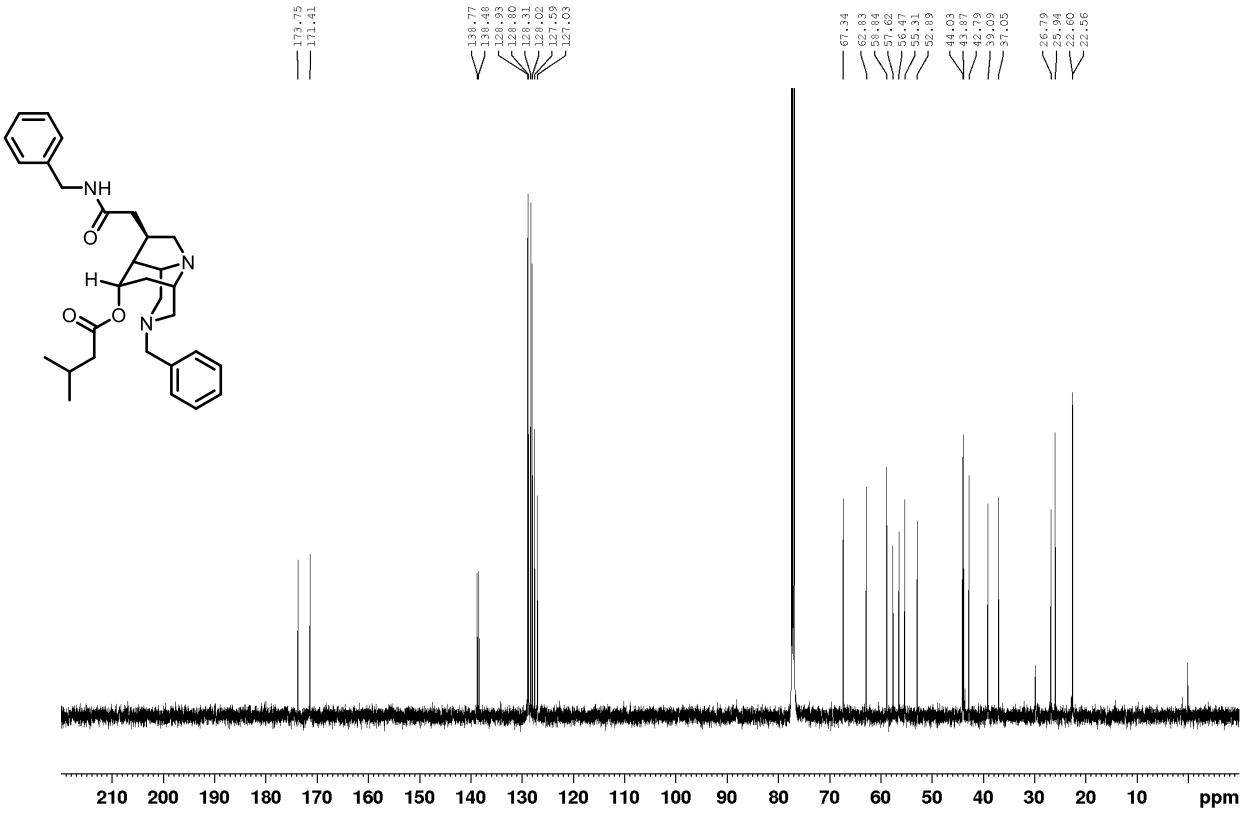
Ester 6e (^{13}C NMR, $CDCl_3$, 125 MHz)



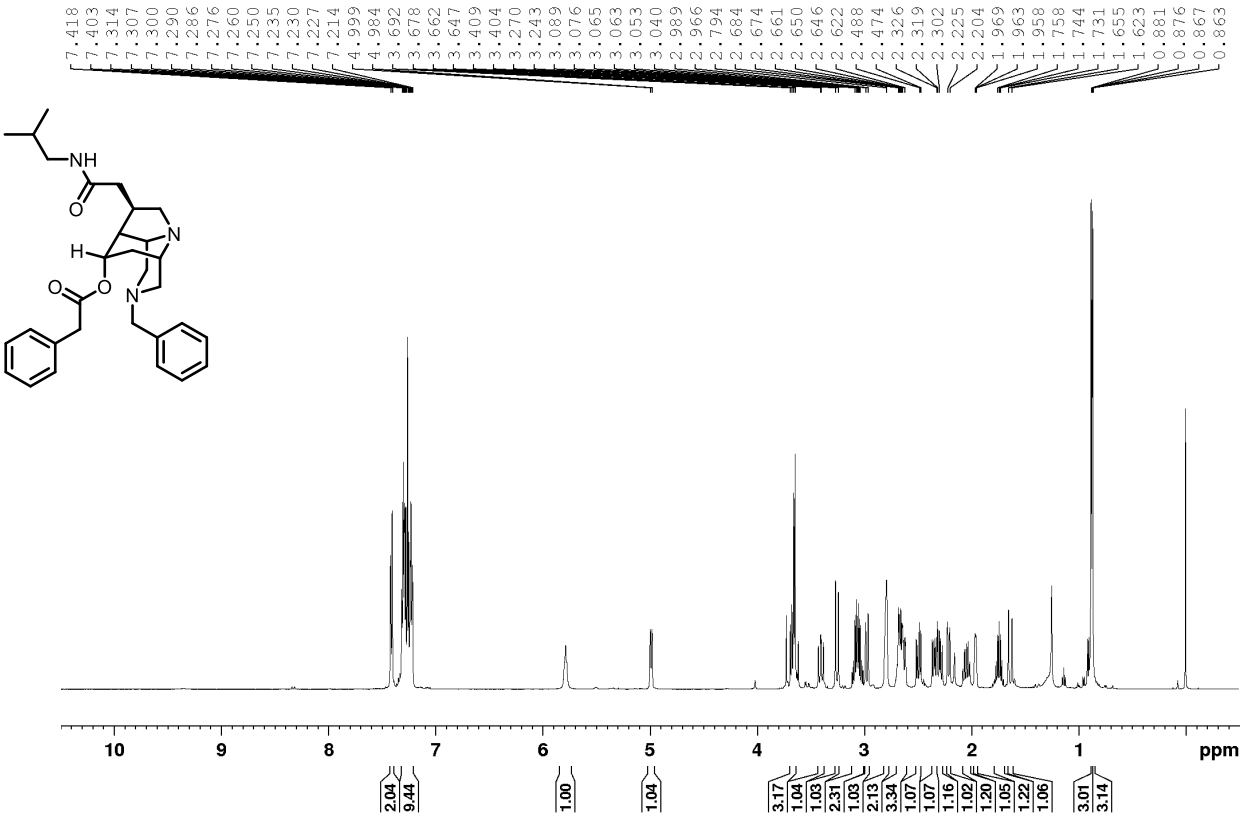
Ester 6f (^{1}H NMR, $CDCl_3$, 400 MHz)



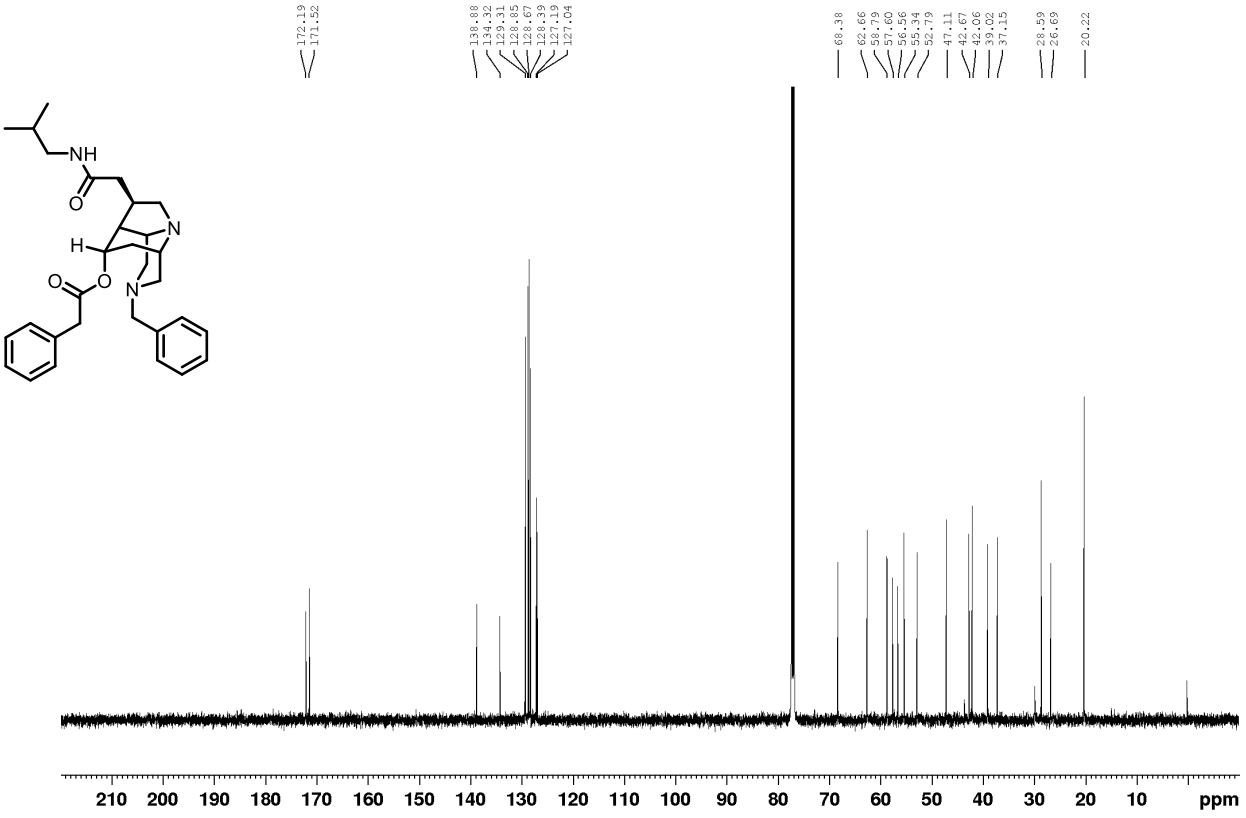
Ester 6f (^{13}C NMR, $CDCl_3$, 125 MHz)



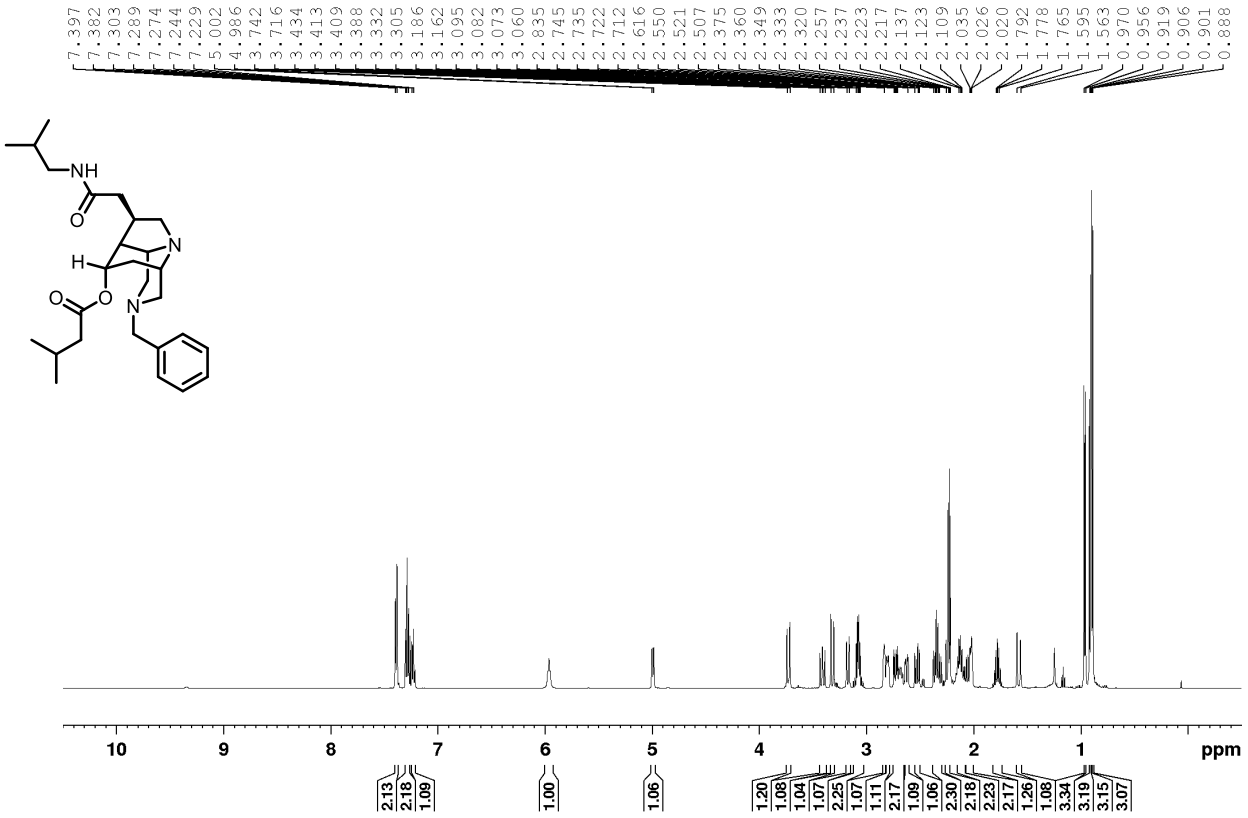
Ester 6g (^{1}H NMR, $CDCl_3$, 500 MHz)



Ester 6g (^{13}C NMR, $CDCl_3$, 125 MHz)



Ester 6h (^{1}H NMR, $CDCl_3$, 500 MHz)



Ester 6h (^{13}C NMR, $CDCl_3$, 125 MHz)