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Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Design of Substituted Tetrahydrofuran Derivatives for HIV-1 Protease Inhibitors: Synthesis, Biological Evaluation, and X-ray Structural Studies

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General Methods.

All chemicals and reagents were purchased from commercial suppliers and used without further purification unless otherwise noted. The following reaction solvents were distilled prior to use: dichloromethane from calcium hydride, diethyl ether and tetrahydrofuran from Na/benzophenone, methanol and ethanol from activated magnesium under argon. All reactions were carried out under an argon atmosphere in either flame or oven-dried (120 °C) glassware. TLC analysis was conducted using glass-backed Thin-Layer Silica Gel Chromatography Plates (60 Å, 250 μm thickness, F-254 indicator). Column chromatography was performed using 230-400 mesh, 60 Å pore diameter silica gel. ^{1}H and ^{13}C NMR spectra were recorded at room temperature on a Bruker AV800, DRX-500 and ARX-400. Chemical shifts (δ values) are reported in parts per million, and are referenced to the deuterated residual solvent peak. NMR data is reported as: δ value (chemical shift, *J*-value (Hz), integration, where s = singlet, d = doublet, t = triplet, q = quartet, brs = broad singlet). Optical rotations were recorded on a Perkin Elmer 341 polarimeter. HRMS and LRMS spectra were recorded at the Purdue University Department of Chemistry Mass Spectrometry Center. HPLC analysis and purification was done an on Agilent 1100 series instrument using a YMC Pack ODS-A column of 4.6 mm ID for analysis and either 10 mm ID or 20 mm ID for purification. The purity of test compounds was determined by HRMS and HPLC analysis. All test compounds showed ≥90% purity.

Expression and purification of protease species

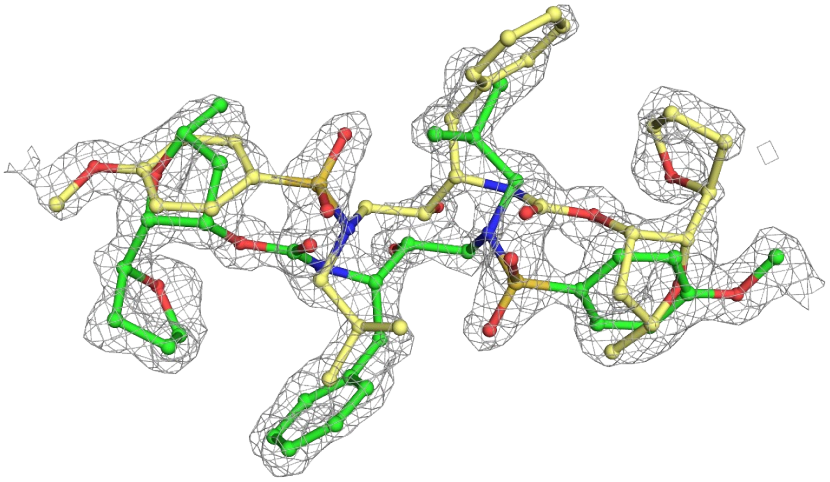
Expression and purification of protease were carried out as previously described [1]. Briefly, Rosetta (DE3) pLysS strain (Novagen) was transformed with an expression vector (pET-30a), which contained the genes of wild-type HIV-1^{NL4-3}-PR (PR^{WT}) using heat-shock. The culture was grown in a shake flask containing 30 mL of Luria broth plus kanamycin and chloramphenicol (LB$^{Km+/Cp+}$) at 37°C overnight. In the expression of PR^{WT}, twenty milliliter of the grown culture was added to 1 L of ZYM-10052 [1.0% N-Z amine, 0.5% yeast extract, 25 mM disodium hydrogenphosphate, 25 mM potassium dihydrogenphosphate, 50 mM ammonium chloride, 5 mM sodium sulfate, 1.0% glycerol, 0.05% glucose, 0.2% α-lactose, 2 mM magnesium sulphate] plus kanamycin and chloramphenicol (ZYM-10052$^{Km+/Cp+}$). The ZYM-10052$^{Km+/Cp+}$ culture was further continued at 37°C for 20~22 hours. Then the culture was spun down for pellet collection, and thus-obtained pellets were stored at −80 °C until use. For purification of PR^{WT}, the pellet was resuspended in buffer A [20 mM Tris, 1 mM EDTA, and 1 mM DTT] and lysed with sonication. The cell lysates were separated into a supernatant fraction and an inclusion body fraction with centrifugation. PR^{WT} was confirmed to be present in the inclusion body fraction, which was washed five times with buffer A containing 2 M urea and then with buffer A without urea. The twice-washed pellet was solubilized and PRs were unfolded with 100 mM formic acid (pH 2.8). The unfolded PRs were purified using the fast protein liquid chromatography system (ÄKTA pure 25; GE Healthcare) and separated using the reverse phase chromatography column (RESOURS RPC 3 mL; GE Healthcare) using the gradient of buffer B [1.0% formic acid, 2.0% acetonitrile] and buffer C [1% formic acid, 70% acetonitrile]. The flow rate was set to 1.0 mL min^{-1} and the column was equilibrated with 75% buffer B and 25% buffer C. Then, the amount of buffer C was increased to 75% over a 30 min period (10-time the column volume). PR^{WT} was eluted with 35~50% buffer C. After the elution, buffer C amount was increased to 100% in 6 min and returned to the starting condition over the next 6 min. The peak fractions including PR^{WT} were collected and three-time diluted with buffer B. The diluted PR^{WT} solution was injected into the ÄKTA pure 25 again and the targeted PR^{WT} was purified using the same purification step as described above. The collected fractions containing PR^{WT} were subjected to desalting (HiTrap Desalting; GE Healthcare) and the eluted solution was equilibrated using 100 mM formic acid and stored at -80 °C until use.

The unfolded PR^{WT} was refolded with the addition of a neutralizing buffer A [100 mM ammonium acetate pH 6.0, 0.005% Tween-20], making the final pH 5.0 to 5.2. The PR^{WT}-containing solution was run through Amicon Ultra-15 10K centrifugal filter units (Millipore), giving a solution containing PR (5~8 mg/ml) in 10 mM ammonium acetate pH 5.0 and 0.005% Tween-20. Occasionally, twice greater concentrations of a test compound were used for crystalization. After centrifugation, the supernatants were collected and subjected to crystallization using the hanging-drop vapor diffusion method. Nextal Tubes ProComplex Suite (QIAGEN) and Wizard Crystallization Screen Series (Emerald BioSystems) were used for the first screening to determine the optimum crystallization condition.

Table S1: Crystallographic Data Collection and Refinement Statistics

	PR/compound **4l** (GRL-072-17A)
Space group	$P2_12_12$
Unit cell dimensions: (Å)	
a	58.57
b	85.88
c	46.31
Resolution range (Å)	50-1.32 (1.37-1.32)
Redundancy (final shell)	5.8 (4.8)
Unique reflections	51438 (3856)
Completeness (%) overall (final shell)	93.6 (71.5)
R_{merge} (%) overall (final shell)	8.9 (51.2)
I/σ(I) overall (final shell)	17.1 (3.9)
Refinement	
R (%)	13.2
R_{free} (%)	16.4
No. of solvent atoms	232
RMS deviation from ideality	
Bonds (Å)	0.019
Angle (degree)	2.2
Average B-factors ($Å^2$)	
Whole chain atoms	16.4
Inhibitor	13.5
Solvent	25.4

Figure S1: **2Fo-Fc electron density map showing two alternative conformations of inhibitor 4l.** The 2Fo-Fc electron density map (gray) for inhibitor **4I** in the X-ray structure with HIV protease is contoured at a level of 1 sigma. The carbon atoms are shown in green for conformation A and in yellow for conformation B of inhibitor with relative occupancies of 0.55 and 0.45.



Geometric Criteria for Weak Interactions.

Hydrogen bond interactions are defined by standard geometrical criteria as described in [1, 2]. The geometric criteria for weak interactions are: C-H...O (distance between C and O<=3.5 Å, angle >=90°), O-H...π (distance<=4.3 Å to centroid of π system, angle >=120°), C-H...π (distance<=4.5 Å, angle >=120°) [1-3], lone pair (n)-π as C=O...π (distance is between 2.8 to 3.8 Å to center of π system, angle between two planes <=90°) [4] and π-π stacking [5].

References

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HIV-1 Protease inhibitory assay. The assay is based upon reported procedure (1). Fluorescence measurements were made using PerkinElmer LS-50B Luminescence Spectrophotometer. Ten microliters of a stock solution (0.05 mg/mL) of HIV protease were incubated with five different concentrations of substrate 2-(aminobenzoyl)-Thr-Ile-Nle-Phe(p-$N0_2$)-Gln-ArgNH_2 (Km = 37 at 37 °C with the increase in fluorescence monitored. A stock solution of 1 mM substrate in DMSO was diluted to 0.1 mM with assay buffer and used for the assay. All kcat and Km values were obtained employing standard data fitting techniques for a reaction obeying Michaelis-Menten kinetics. The data curves were fitted using SigmaPlot. The active enzyme concentrations were calculated from the intercept of the linear fit to the IC_{50} versus [S] plots with the IC_{50} axis. The K_i values were obtained from the IC_{50} values estimated from an inhibitor dose-response curve with the spectroscopic assay using the equation $K_i = (IC_{50}–[E]/2)/(1+ [S]/Km)$, where [E] and [S] are the PR and substrate concentrations, respectively. The K_i values were measured at four to five substrate concentrations. The measurements were repeated at least three times to produce the average values given in Table 3.

Cells, viruses, and antiviral agents. The MT-2 cells were obtained from the NIH AIDS Reagent Program, NIAID, NIH, Bethesda, MD, USA (2). Human $CD4^+$ MT-2 cells were grown in RPMI-1640-based culture medium supplemented with 10% fetal calf serum (FCS: JRH Biosciences, Lenexa, MD), 50 unit/mL penicillin, and 100 µg/mL of kanamycin (3,4). Darunavir (DRV) was synthesized as previously described (5).

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(2) Haertle, T., et al. "Metabolism and Anti-Human Immunodeficiency Virus-1 Activity of 2-Halo-2', 3'-Dideoxyadenosine Derivatives." J. Biol. Chem. **1988**, *263,* 5870-5875.
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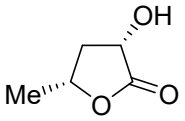
^{1}H NMR (500 MHz, $CDCl_3$)



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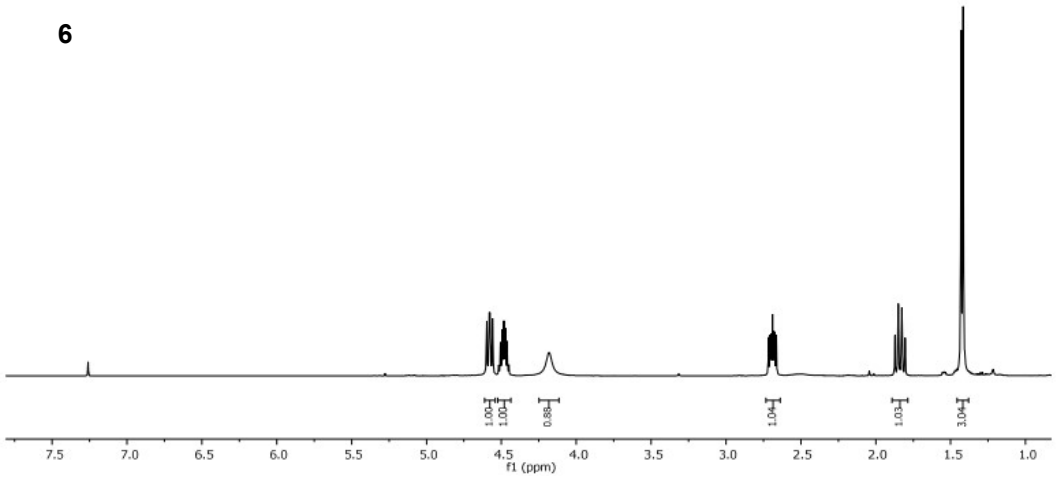

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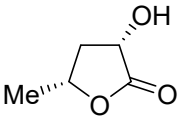

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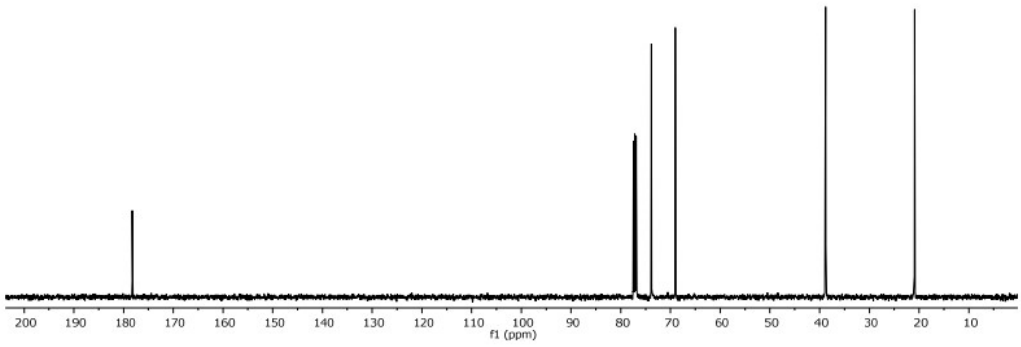

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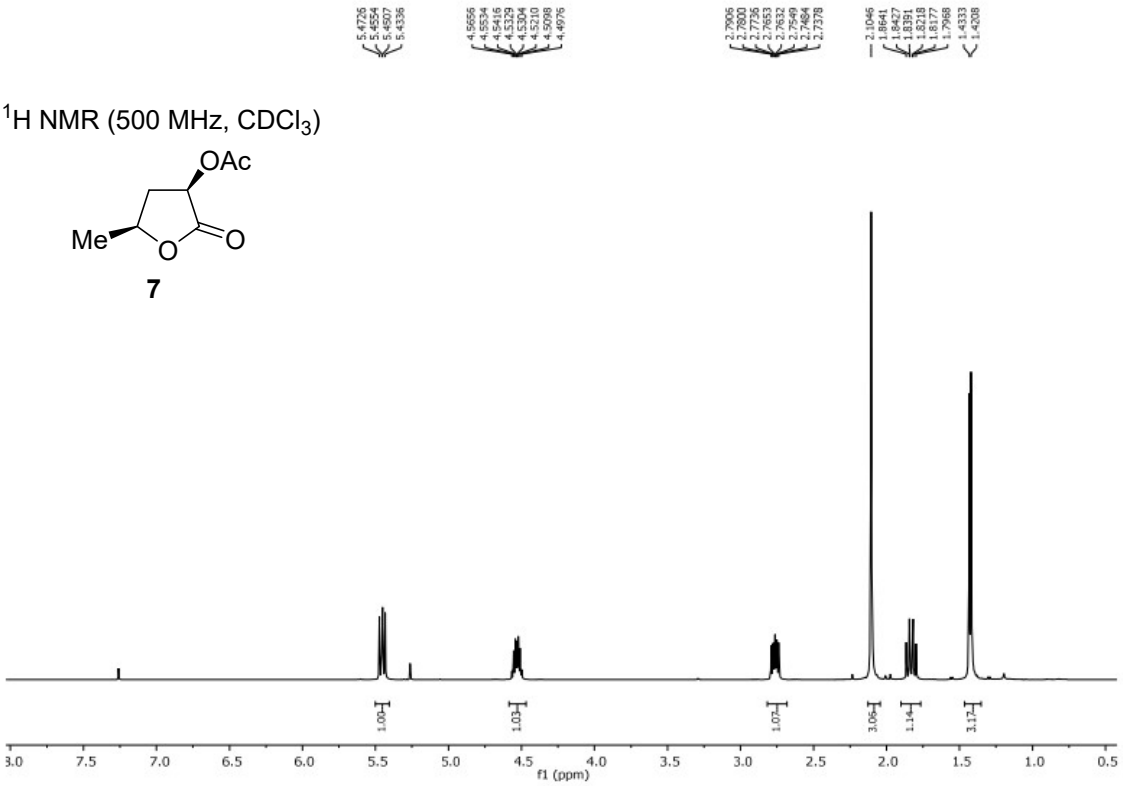

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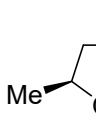

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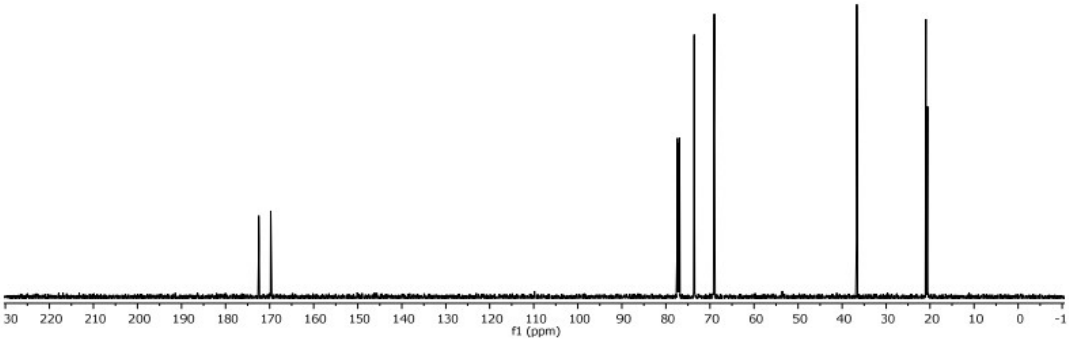

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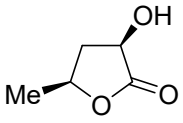

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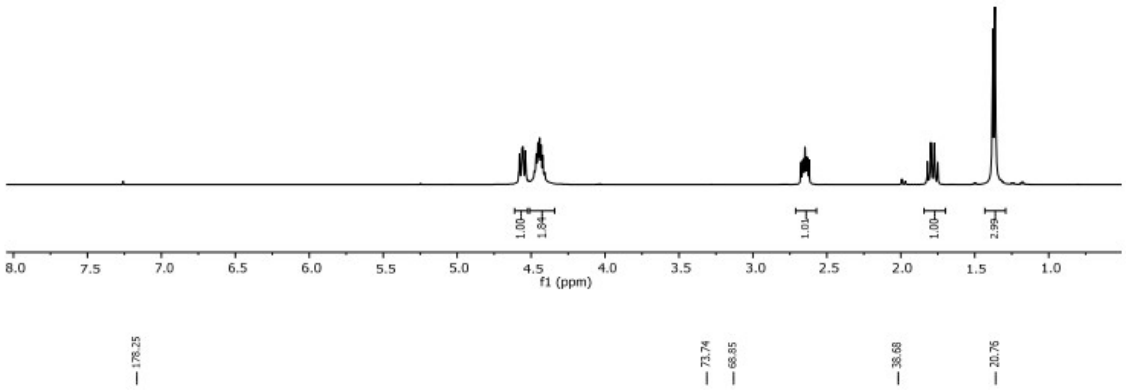

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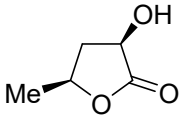

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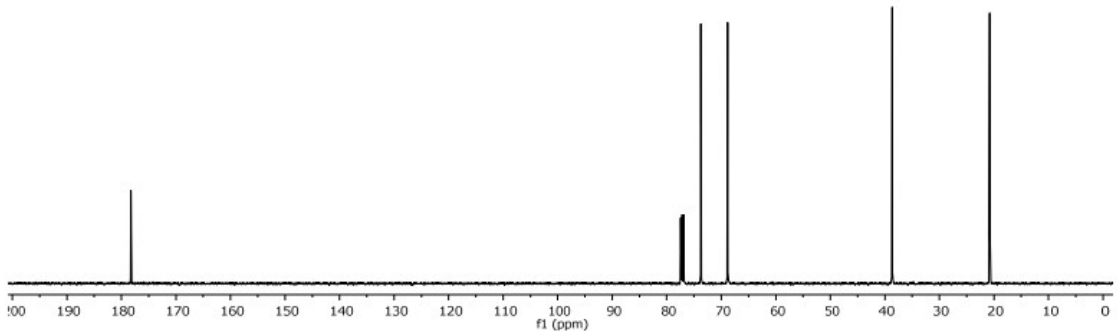

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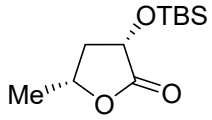

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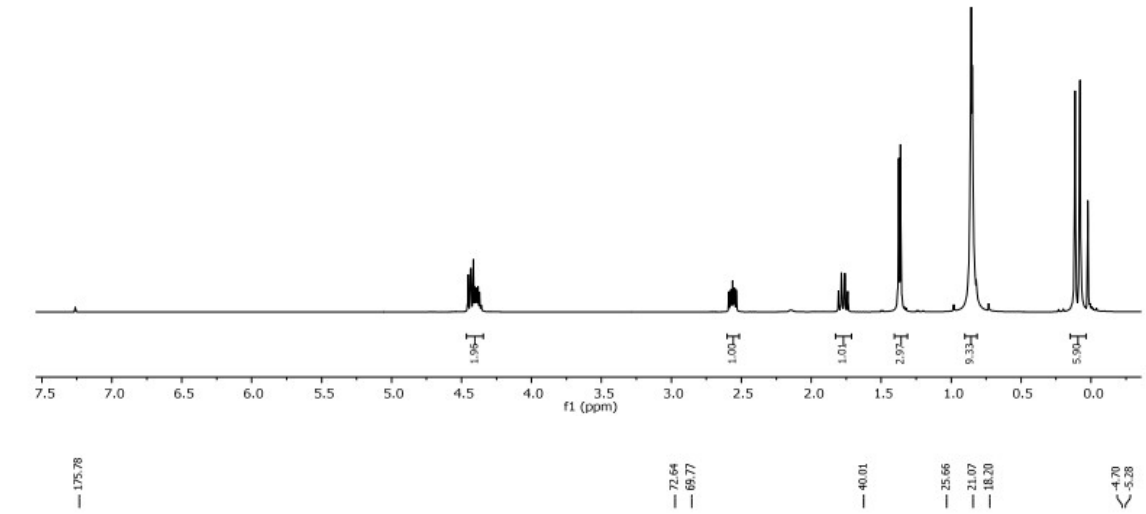

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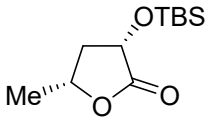

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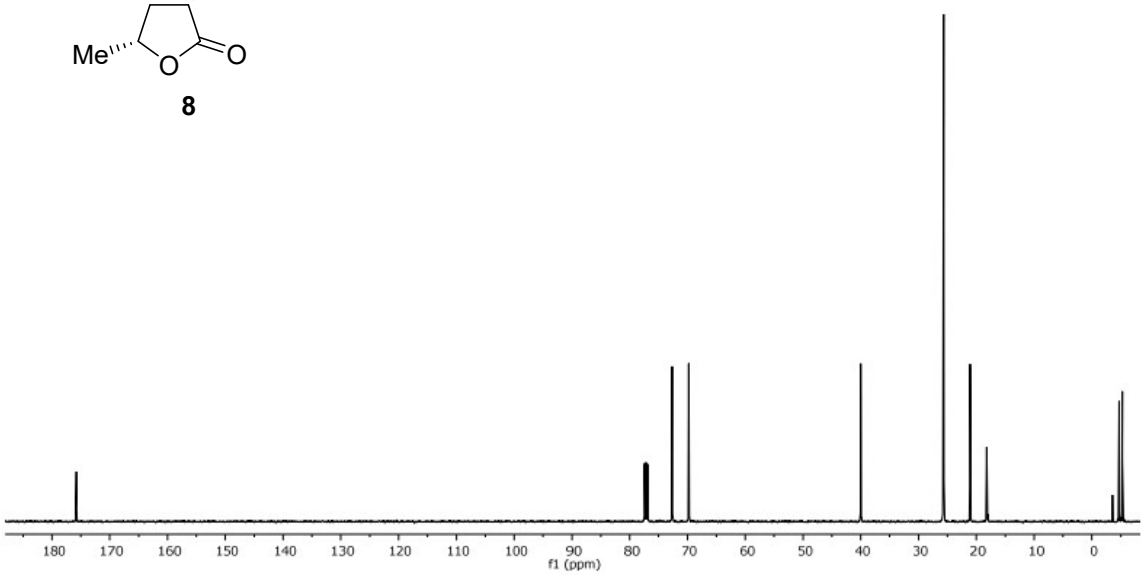

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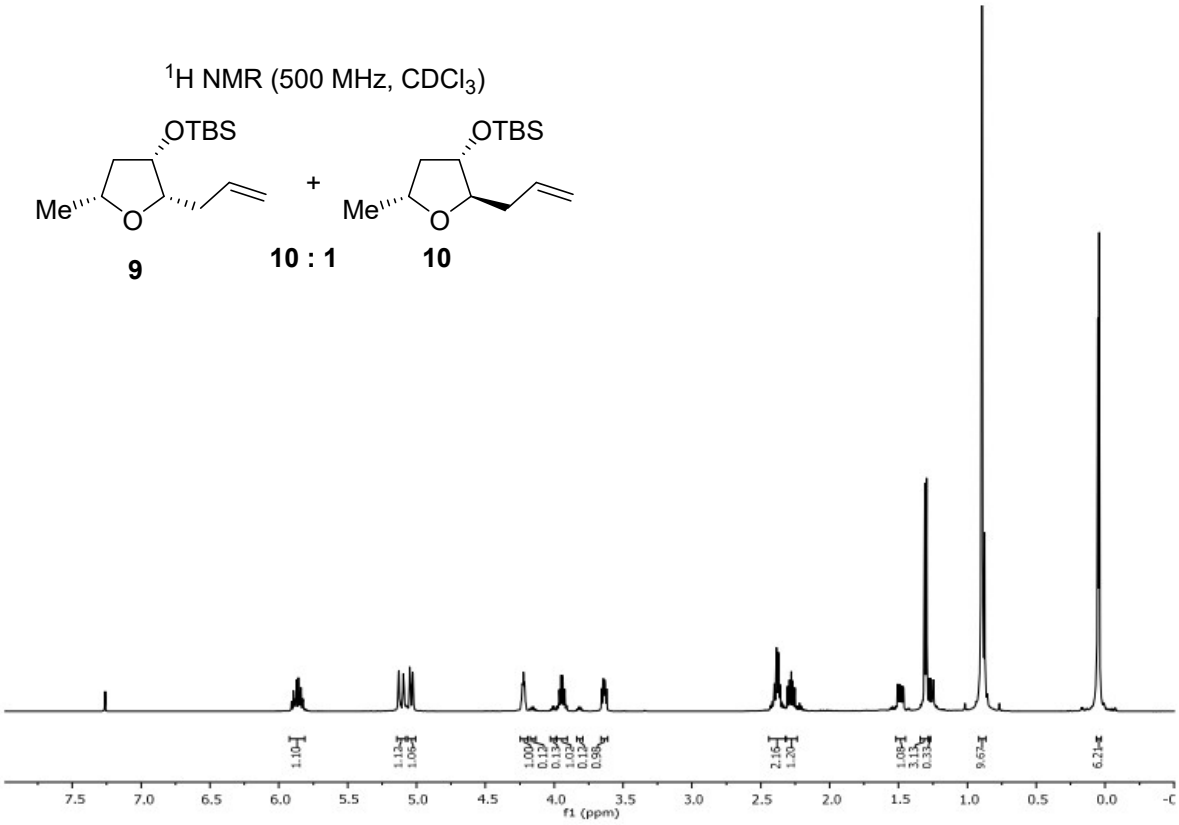

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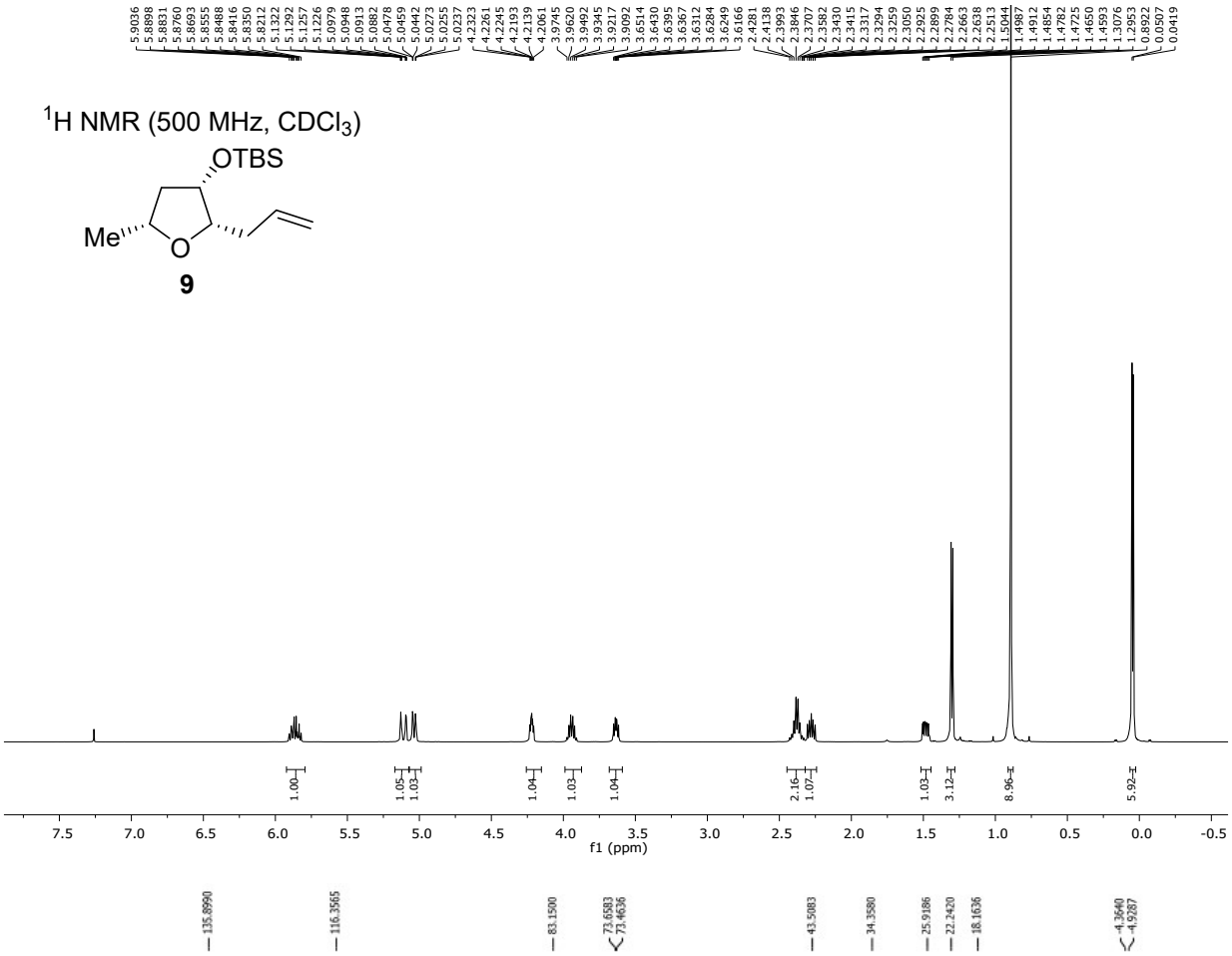

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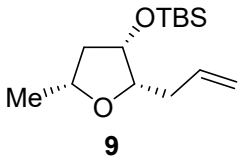

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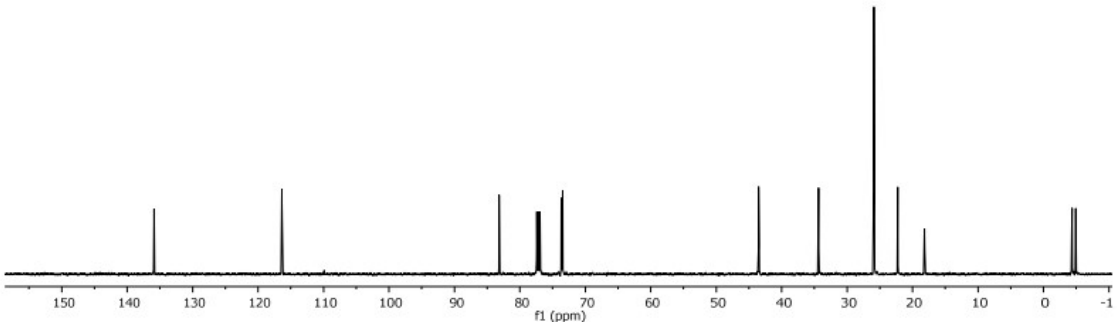

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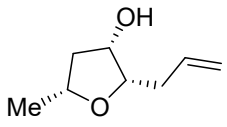

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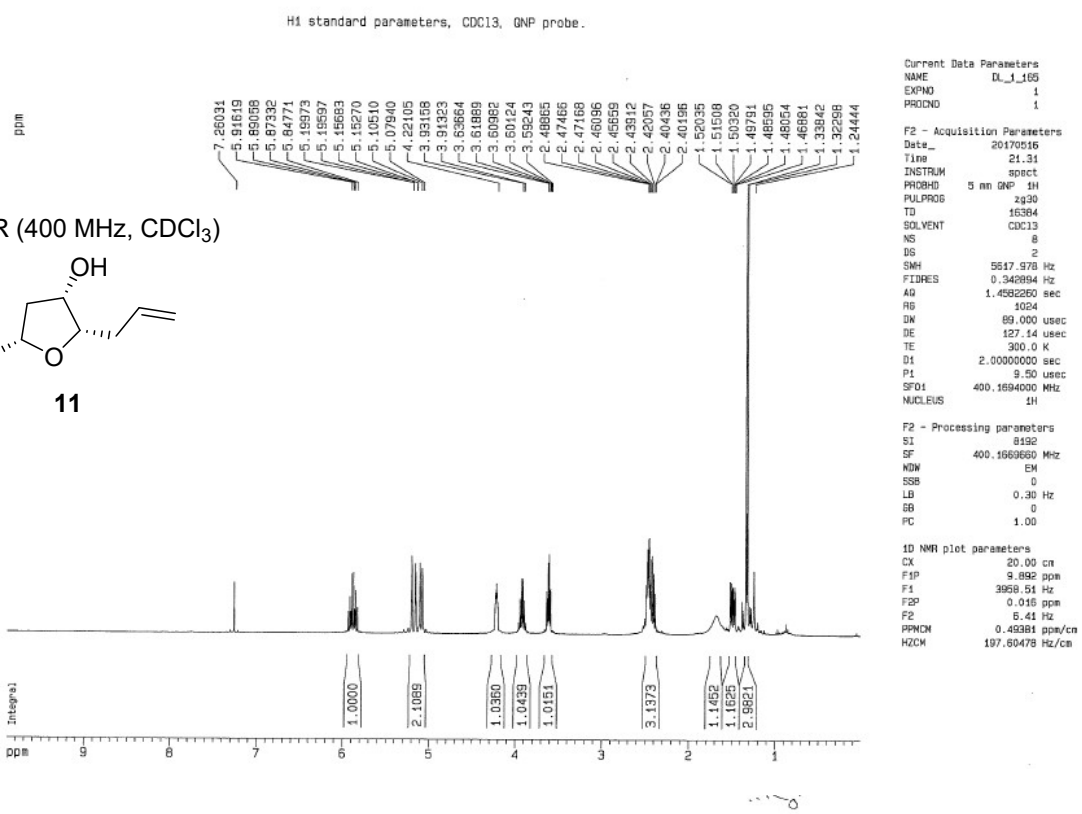

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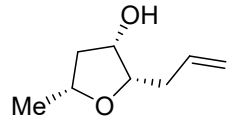

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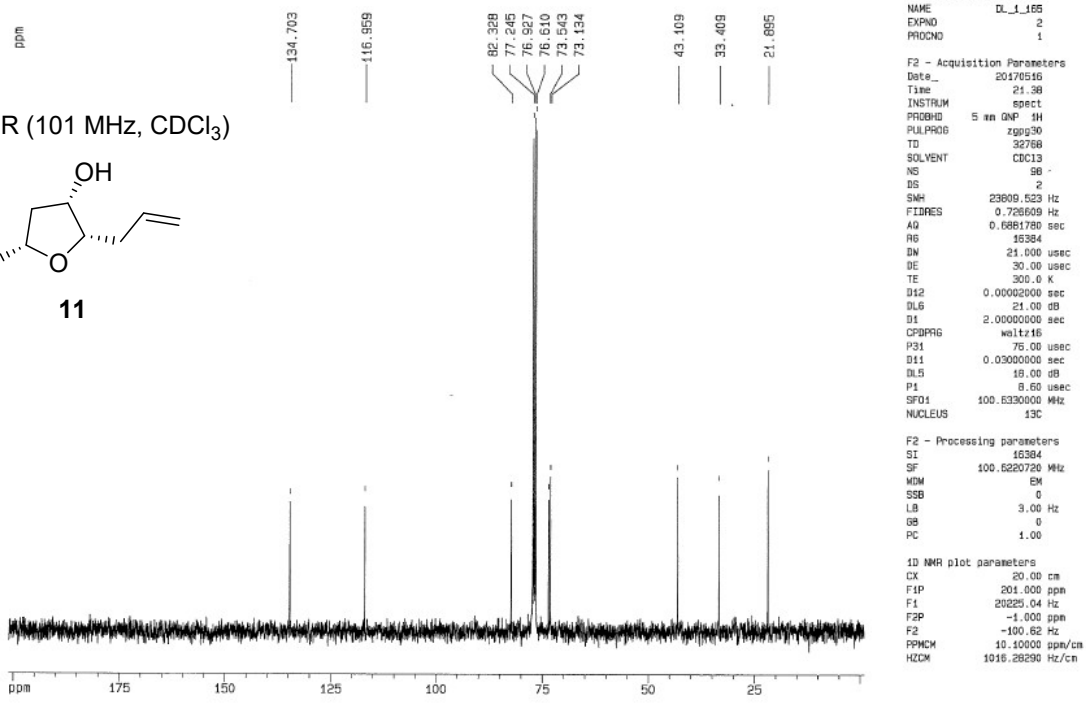

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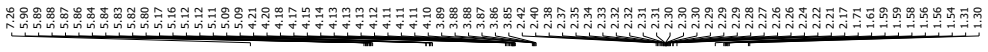

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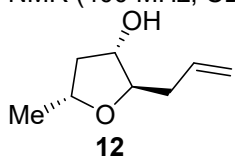

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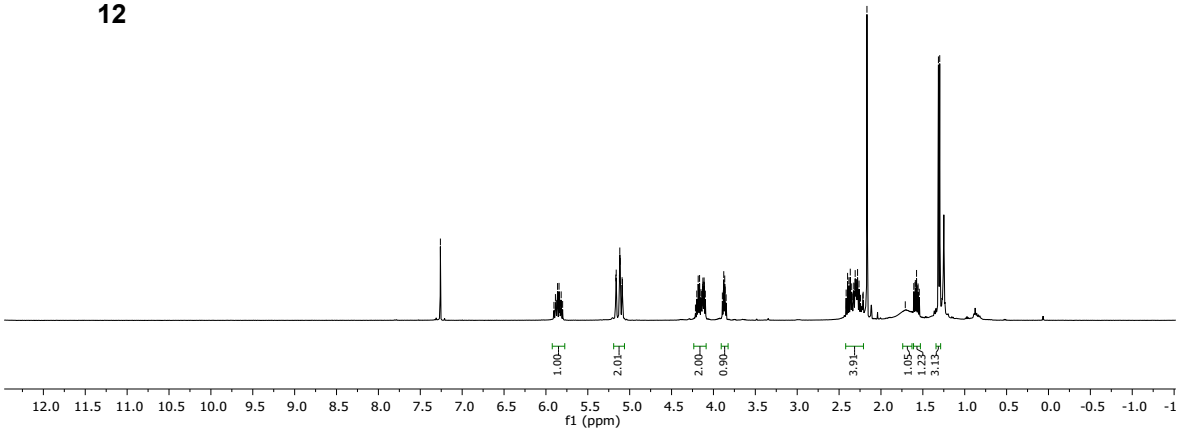

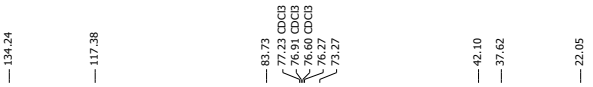

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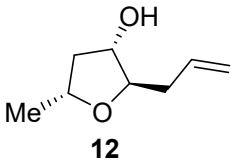

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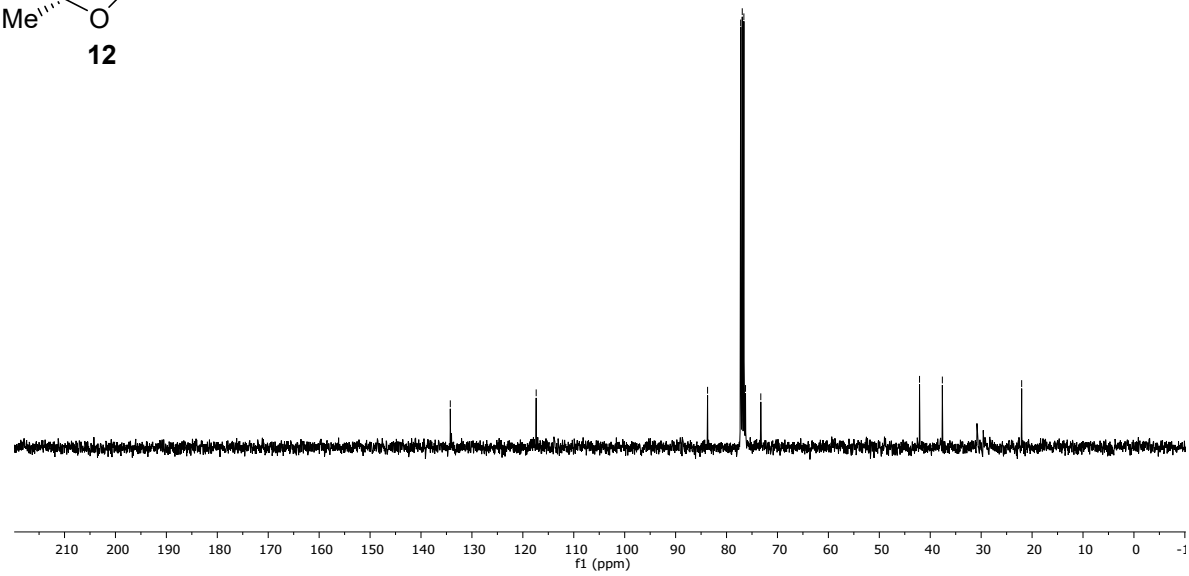
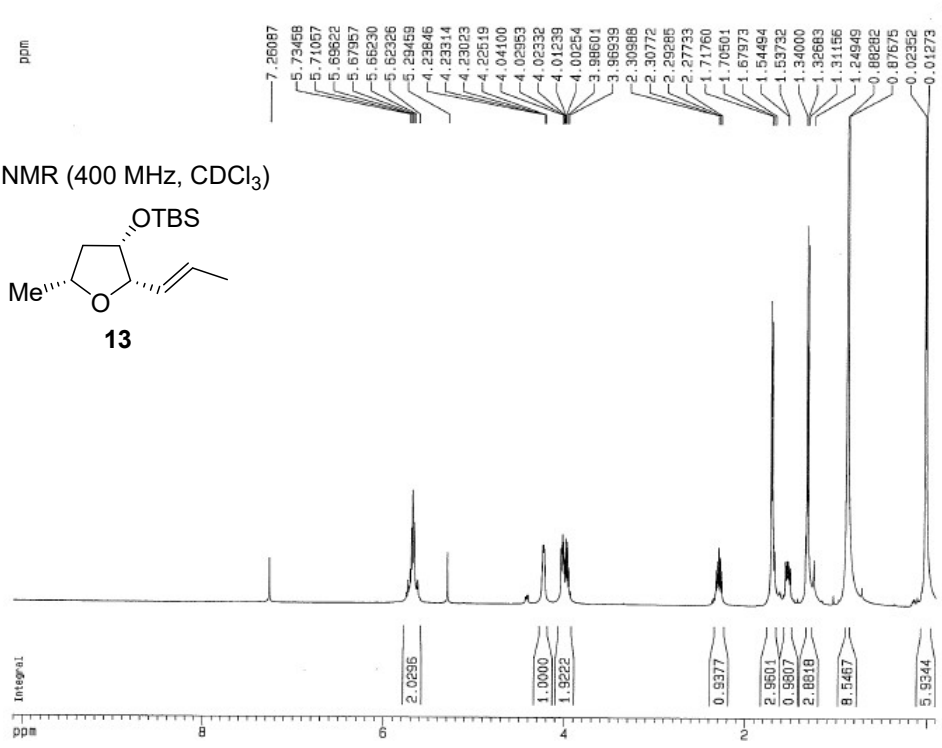


^{1}H NMR (400 MHz, $CDCl_3$)

13

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Current Data Parameters
NAME                  DL_1_151
EXPNO                        1
PROCNO                       1

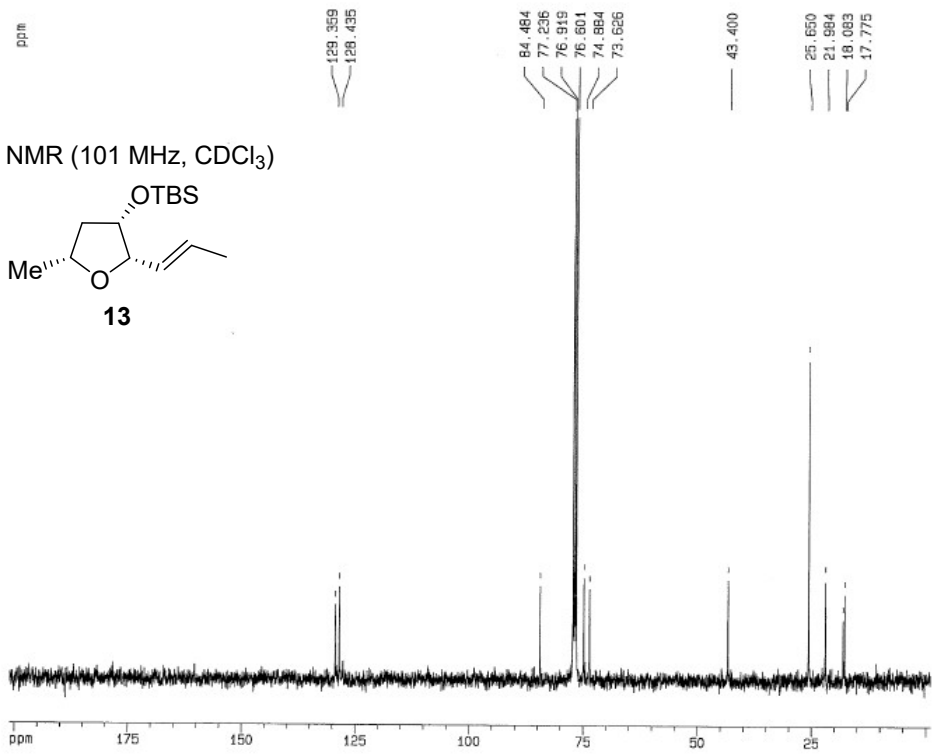
F2 - Acquisition Parameters
Date_               20170417
Time                   17.16
INSTRUM                spect
PROBHD     5 mm QNP  1H
PULPROG                zg30
TD                    16384
SOLVENT               CDCl3
NS                        8
DS                        2
SWH                5617.978 Hz
FIDRES             0.342894 Hz
AQ                 1.4582260 sec
RG                      715
DW                   89.000 usec
DE                   127.14 usec
TE                    300.0 K
D1                 2.00000000 sec
P1                    9.50 usec
SFO1               400.1694000 MHz
NUCLEUS                  1H

F2 - Processing parameters
SI                       8192
SF                 400.1669660 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00

1D NMR plot parameters
CX                      20.00 cm
F1P                    10.100 ppm
F1                   4041.69 Hz
F2P                   -0.100 ppm
F2                    -40.02 Hz
PPMCM                 0.51000 ppm/cm
HZCM                204.08516 Hz/cm
```

^{13}C NMR (101 MHz, $CDCl_3$)

13

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Current Data Parameters
NAME                  DL_1_151
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_               20170417
Time                   17.20
INSTRUM                spect
PROBHD     5 mm QNP  1H
PULPROG              zgpg30
TD                    32768
SOLVENT               CDCl3
NS                      161
DS                        2
SWH               23809.523 Hz
FIDRES             0.726609 Hz
AQ                 0.6881780 sec
RG                    16384
DW                   21.000 usec
DE                   30.00 usec
TE                    300.0 K
D12                0.00002000 sec
DL6                  21.00 dB
D1                 2.00000000 sec
CPDPRG                waltz16
P31                  76.00 usec
D11                0.03000000 sec
DL5                  18.00 dB
P1                    8.60 usec
SFO1               100.6330000 MHz
NUCLEUS                  13C

F2 - Processing parameters
SI                       16384
SF                 100.6220720 MHz
WDW                        EM
SSB                         0
LB                       3.00 Hz
GB                          0
PC                       1.00

1D NMR plot parameters
CX                      20.00 cm
F1P                   201.000 ppm
F1                   20225.04 Hz
F2P                   -1.000 ppm
F2                    -100.62 Hz
PPMCM                10.10000 ppm/cm
HZCM               1016.28290 Hz/cm
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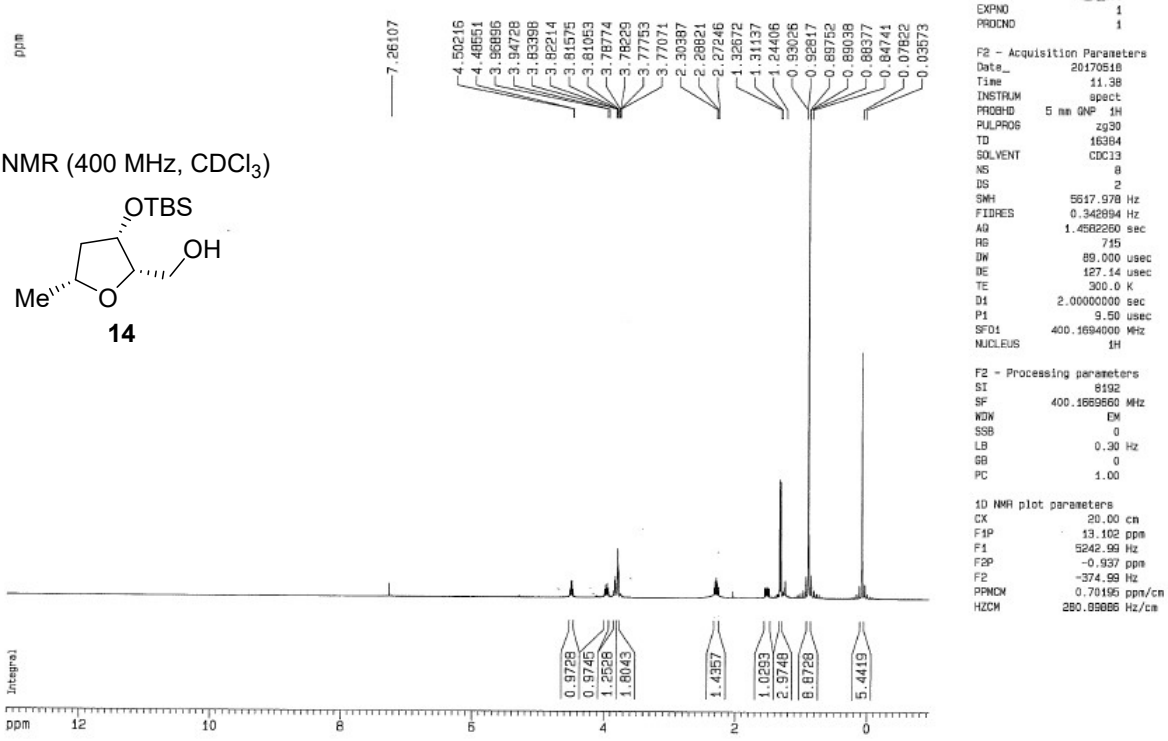
^{1}H NMR (400 MHz, $CDCl_3$)

14



Current Data Parameters
NAME DL_1_166
EXPNO 1
PROCNO 1

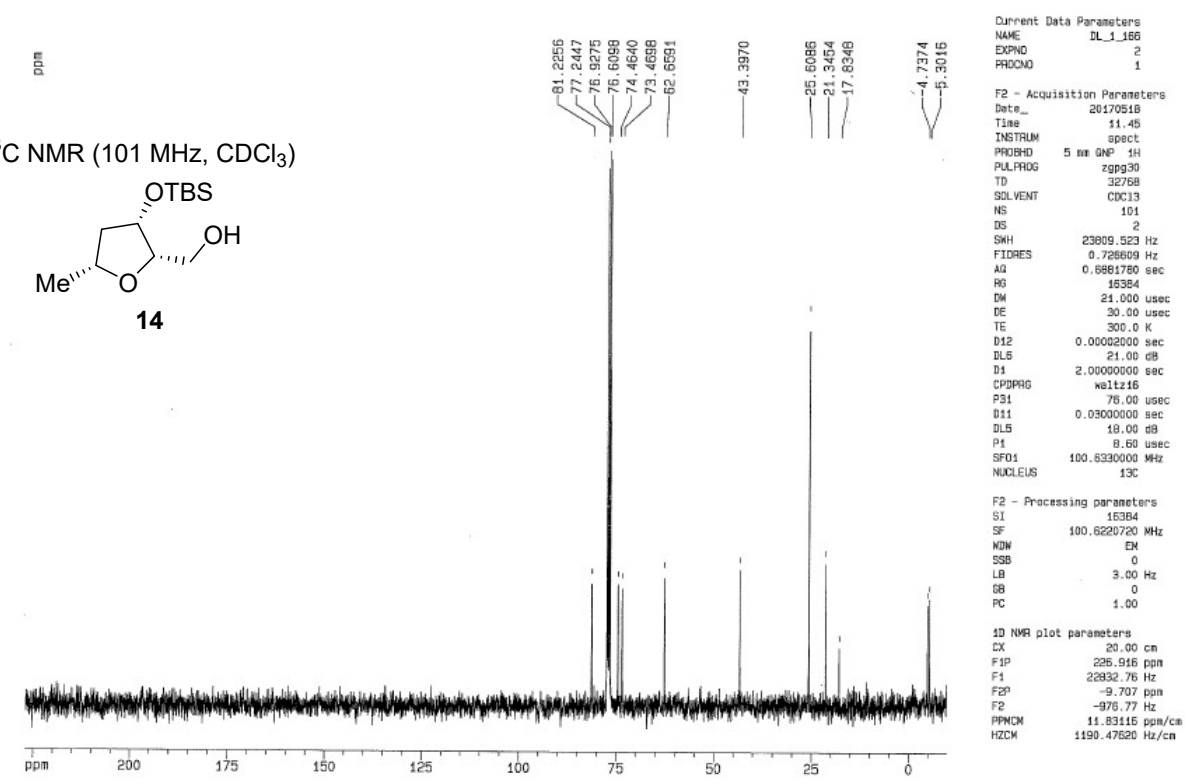
F2 - Acquisition Parameters
Date_ 20170518
Time 11.38
INSTRUM spect
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 16384
SOLVENT CDCl3
NS 8
DS 2
SWH 5617.978 Hz
FIDRES 0.342894 Hz
AQ 1.4582260 sec
RG 715
DW 89.000 usec
DE 127.14 usec
TE 300.0 K
D1 2.00000000 sec
P1 9.50 usec
SFO1 400.1694000 MHz
NUCLEUS 1H

F2 - Processing parameters
SI 8192
SF 400.1669860 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 13.102 ppm
F1 5242.99 Hz
F2P -0.937 ppm
F2 -374.99 Hz
PPMCM 0.70195 ppm/cm
HZCM 280.88086 Hz/cm

^{13}C NMR (101 MHz, $CDCl_3$)

14



Current Data Parameters
NAME DL_1_166
EXPNO 2
PROCNO 1

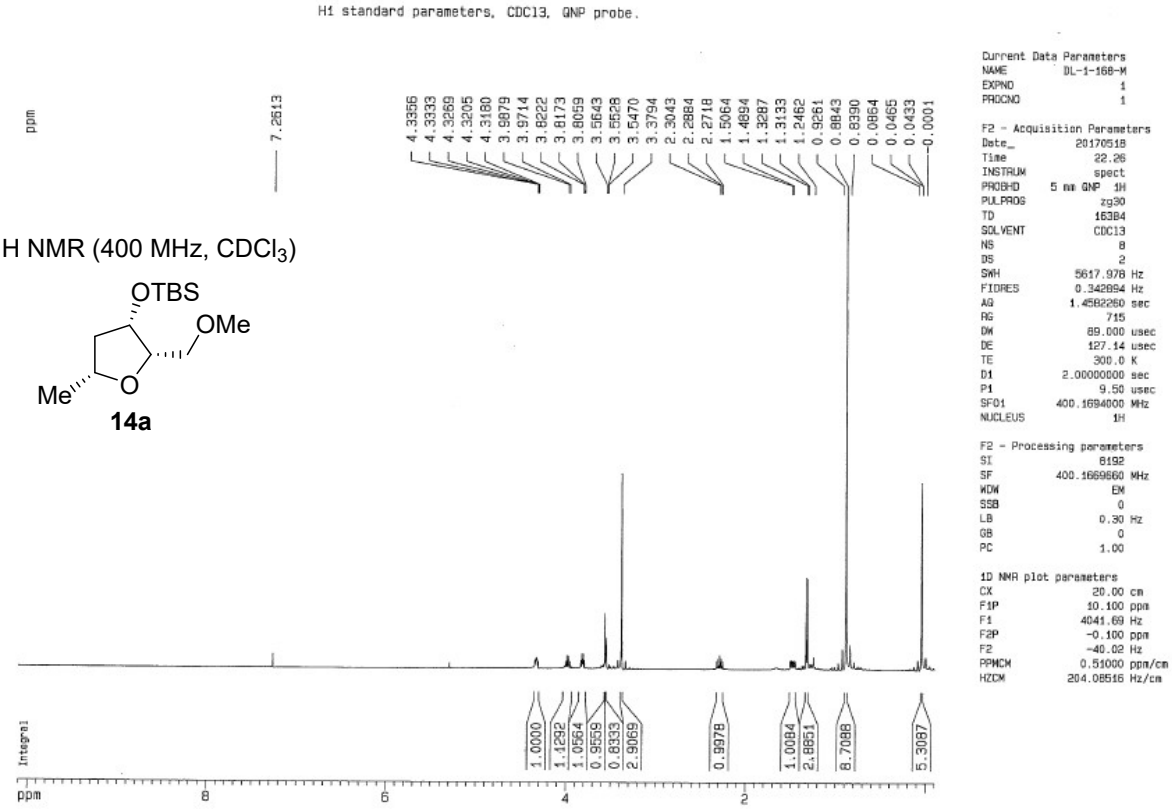
F2 - Acquisition Parameters
Date_ 20170518
Time 11.45
INSTRUM spect
PROBHD 5 mm QNP 1H
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 101
DS 2
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 0.6881780 sec
RG 16384
DW 21.000 usec
DE 30.00 usec
TE 300.0 K
D12 0.00002000 sec
DL6 21.00 dB
D1 2.00000000 sec
CPDPRG waltz16
P31 76.00 usec
D11 0.03000000 sec
DL5 18.00 dB
P1 8.60 usec
SFO1 100.6330000 MHz
NUCLEUS 13C

F2 - Processing parameters
SI 16384
SF 100.6220720 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 226.916 ppm
F1 22832.76 Hz
F2P -9.707 ppm
F2 -976.77 Hz
PPMCM 11.83116 ppm/cm
HZCM 1190.47620 Hz/cm

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

14a



Current Data Parameters
NAME DL-1-168-M
EXPNO 1
PROCNO 1

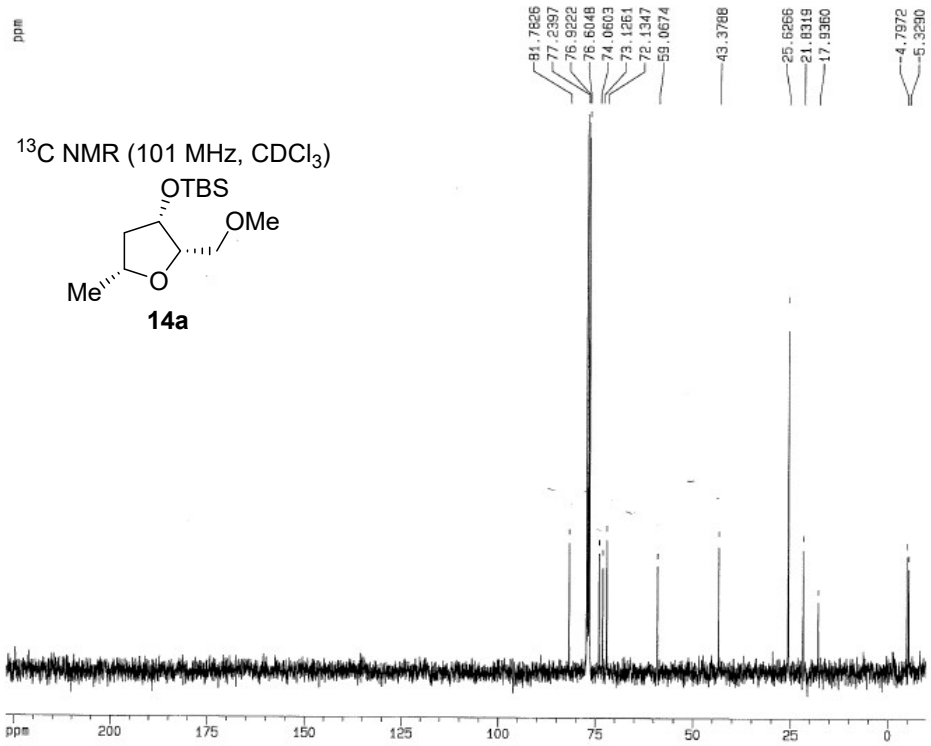
F2 - Acquisition Parameters
Date_ 20170518
Time 22.26
INSTRUM spect
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 16384
SOLVENT CDCl3
NS 8
DS 2
SWH 5617.978 Hz
FIDRES 0.342894 Hz
AQ 1.4582260 sec
RG 715
DW 89.000 usec
DE 127.14 usec
TE 300.0 K
D1 2.00000000 sec
P1 9.50 usec
SFO1 400.1694000 MHz
NUCLEUS 1H

F2 - Processing parameters
SI 8192
SF 400.1669660 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 10.100 ppm
F1 4041.69 Hz
F2P -0.100 ppm
F2 -40.02 Hz
PPMCM 0.51000 ppm/cm
HZCM 204.08516 Hz/cm

^{13}C NMR (101 MHz, $CDCl_3$)

14a



Current Data Parameters
NAME DL-1-168-M
EXPNO 2
PROCNO 1

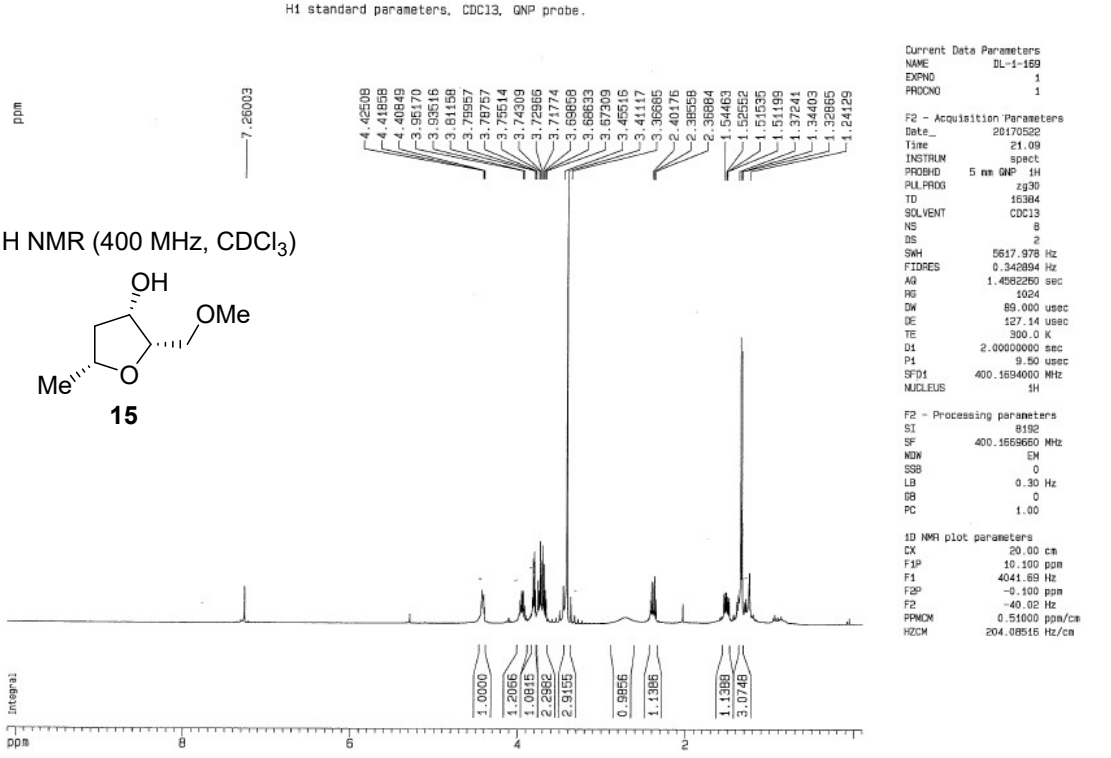
F2 - Acquisition Parameters
Date_ 20170518
Time 22.32
INSTRUM spect
PROBHD 5 mm QNP 1H
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 101
DS 2
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 0.6881780 sec
RG 16384
DW 21.000 usec
DE 30.00 usec
TE 300.0 K
D12 0.00002000 sec
DL6 21.00 dB
D1 2.00000000 sec
CPDPRG waltz16
P31 76.00 usec
D11 0.03000000 sec
DL5 18.00 dB
P1 8.60 usec
SFO1 100.6330000 MHz
NUCLEUS 13C

F2 - Processing parameters
SI 16384
SF 100.6220720 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 226.916 ppm
F1 22832.75 Hz
F2P -9.707 ppm
F2 -975.77 Hz
PPMCM 11.83116 ppm/cm
HZCM 1190.47620 Hz/cm

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

15




```
Current Data Parameters
NAME            DL-1-169
EXPNO                  1
PROCNO                 1

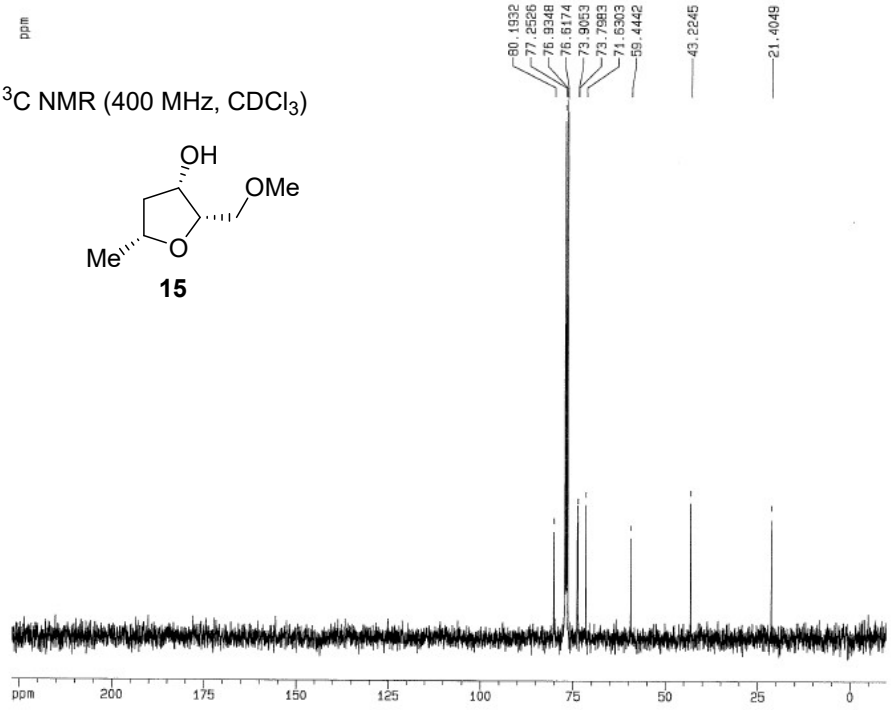
F2 - Acquisition Parameters
Date_           20170522
Time               21.09
INSTRUM            spect
PROBHD     5 mm QNP  1H
PULPROG            zg30
TD                16384
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             5617.978 Hz
FIDRES          0.342894 Hz
AQ              1.4582250 sec
RG                  1024
DW                89.000 usec
DE                127.14 usec
TE                300.0 K
D1              2.00000000 sec
P1                 9.50 usec
SFO1          400.1694000 MHz
NUCLEUS               1H

F2 - Processing parameters
SI                  8192
SF            400.1669650 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                 20.00 cm
F1P               10.100 ppm
F1               4041.69 Hz
F2P               -0.100 ppm
F2                -40.02 Hz
PPMCM             0.51000 ppm/cm
HZCM            204.08516 Hz/cm
```

^{13}C NMR (400 MHz, $CDCl_3$)

15




```
Current Data Parameters
NAME            DL-1-169
EXPNO                  2
PROCNO                 1

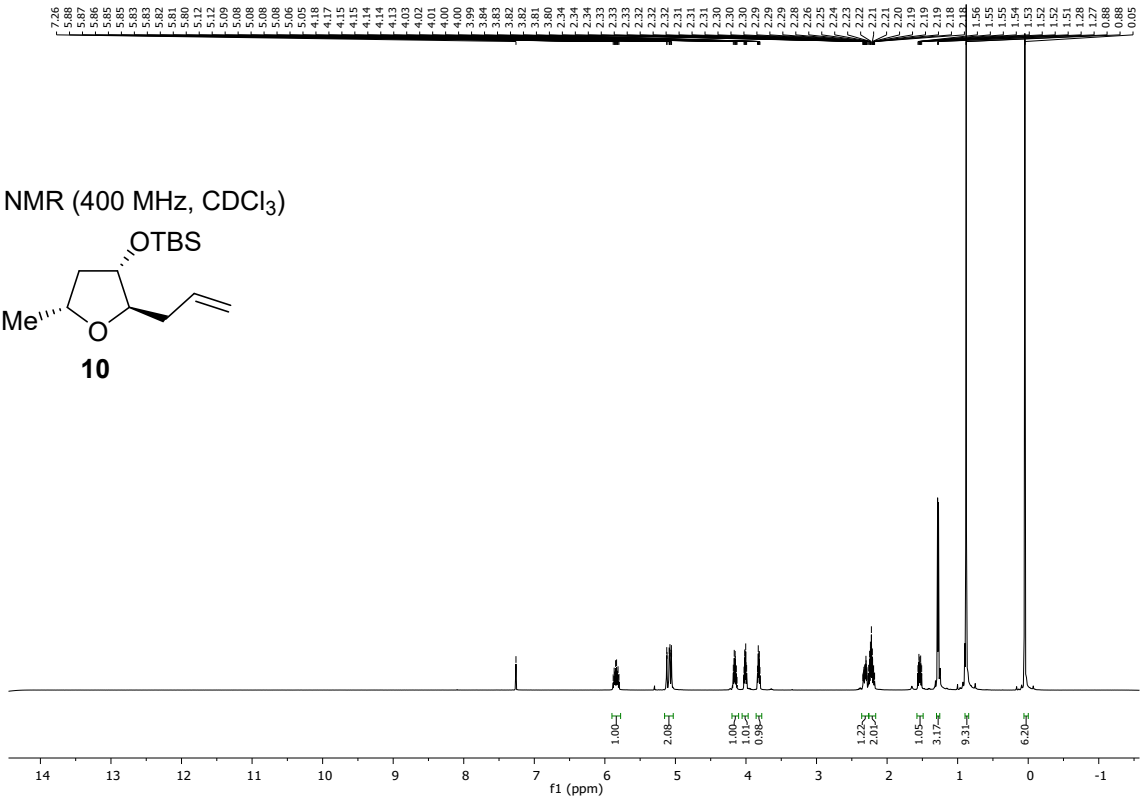
F2 - Acquisition Parameters
Date_           20170522
Time               21.13
INSTRUM            spect
PROBHD     5 mm QNP  1H
PULPROG          zgpg30
TD                32768
SOLVENT            CDCl3
NS                    77
DS                     2
SWH            23809.523 Hz
FIDRES          0.726609 Hz
AQ              0.6881780 sec
RG                 16384
DW                21.000 usec
DE                30.00 usec
TE                300.0 K
D12             0.00002000 sec
DL6               21.00 dB
D1              2.00000000 sec
CPDPRG            waltz16
P31               76.00 usec
D11             0.03000000 sec
DL5               18.00 dB
P1                 8.50 usec
SFO1          100.6330000 MHz
NUCLEUS               13C

F2 - Processing parameters
SI                 16384
SF            100.6220720 MHz
WDW                   EM
SSB                    0
LB                  3.00 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                 20.00 cm
F1P              226.916 ppm
F1             22832.76 Hz
F2P               -9.707 ppm
F2              -976.77 Hz
PPMCM            11.83115 ppm/cm
HZCM          1190.47620 Hz/cm
```

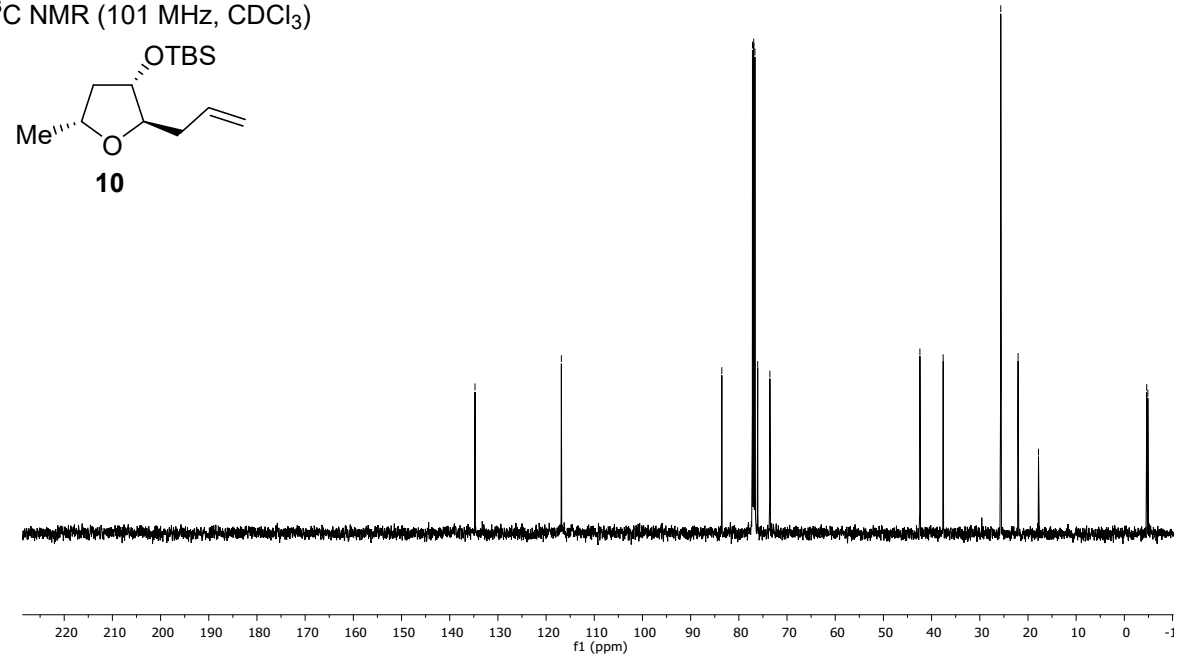
^{1}H NMR (400 MHz, $CDCl_3$)

10



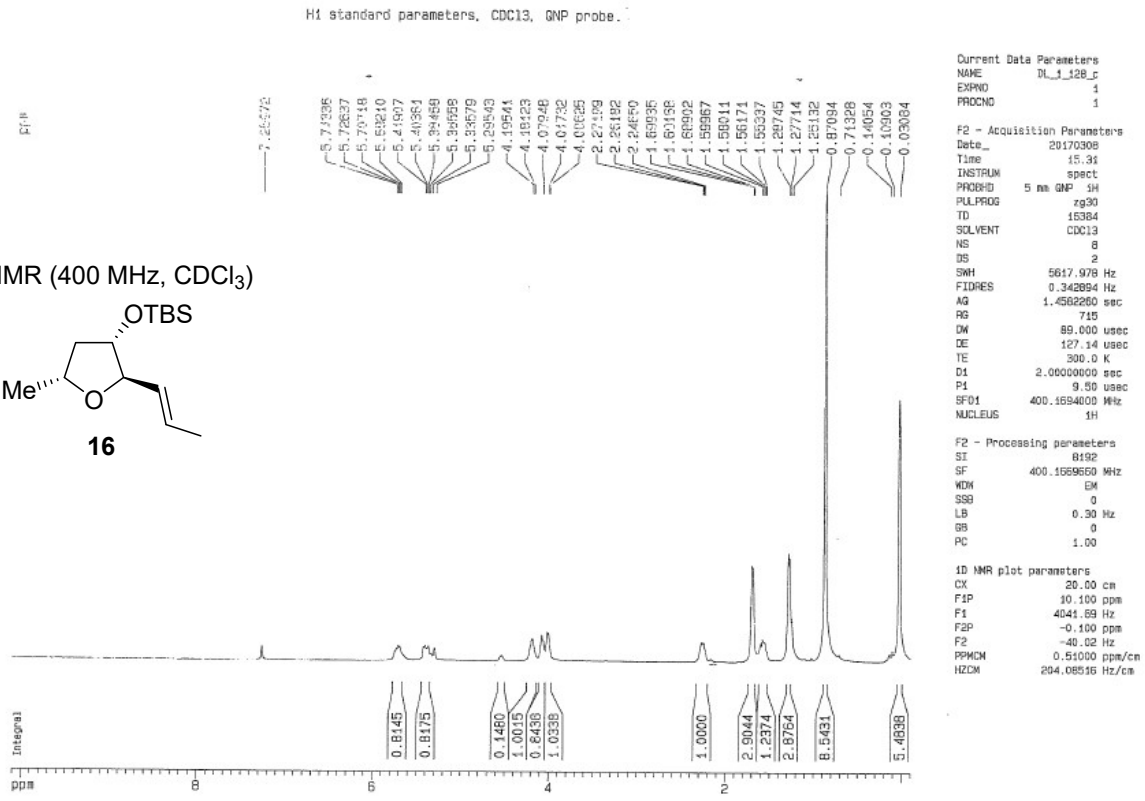
^{13}C NMR (101 MHz, $CDCl_3$)

10



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

16



Current Data Parameters
NAME DL_1_128_c
EXPNO 1
PROCNO 1

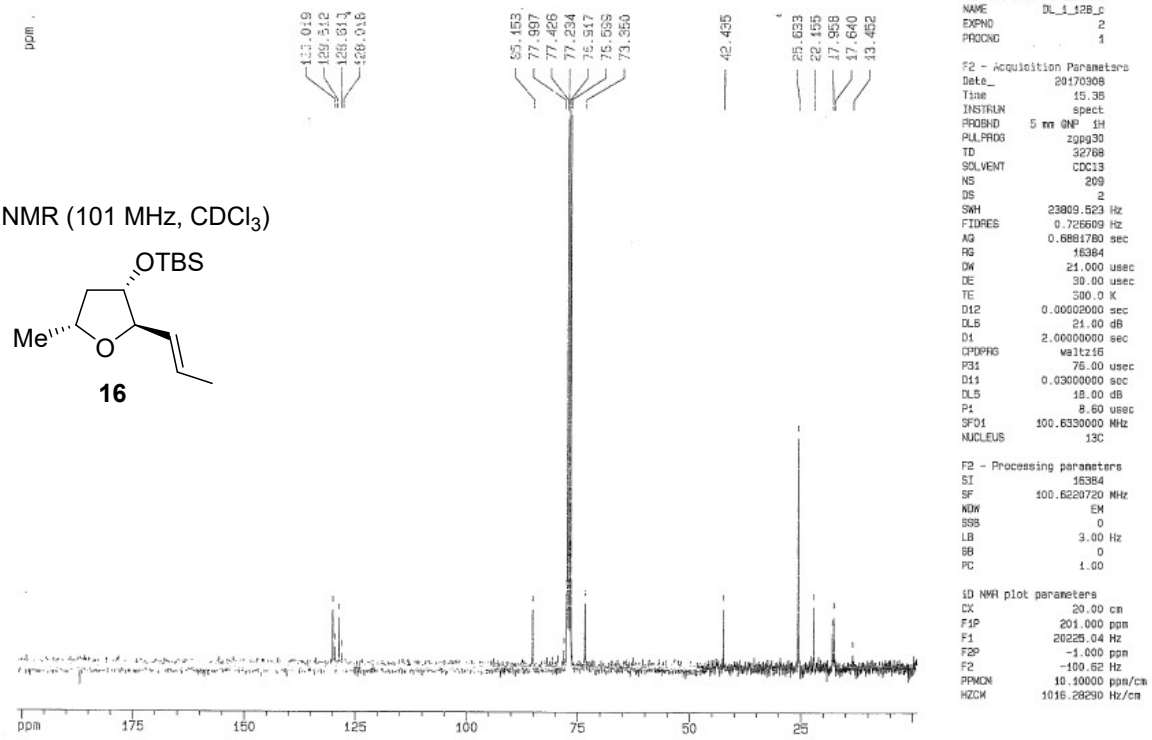
F2 - Acquisition Parameters
Date_ 20170308
Time 15.31
INSTRUM spect
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 15384
SOLVENT CDCl3
NS 8
DS 2
SWH 5617.978 Hz
FIDRES 0.342894 Hz
AQ 1.4582260 sec
RG 715
DW 89.000 usec
DE 127.14 usec
TE 300.0 K
D1 2.00000000 sec
P1 9.50 usec
SFO1 400.1694000 MHz
NUCLEUS 1H

F2 - Processing parameters
SI 8192
SF 400.1569650 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 10.100 ppm
F1 4041.69 Hz
F2P -0.100 ppm
F2 -40.02 Hz
PPMCM 0.51000 ppm/cm
HZCM 204.08516 Hz/cm

^{13}C NMR (101 MHz, $CDCl_3$)

16



Current Data Parameters
NAME DL_1_128_c
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20170308
Time 15.35
INSTRUM spect
PROBHD 5 mm QNP 1H
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 209
DS 2
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 0.6881780 sec
RG 16384
DW 21.000 usec
DE 30.00 usec
TE 300.0 K
D12 0.00002000 sec
DL6 21.00 dB
D1 2.00000000 sec
CPDPRG waltz16
P31 76.00 usec
D11 0.03000000 sec
DL5 18.00 dB
P1 8.60 usec
SFO1 100.6330000 MHz
NUCLEUS 13C

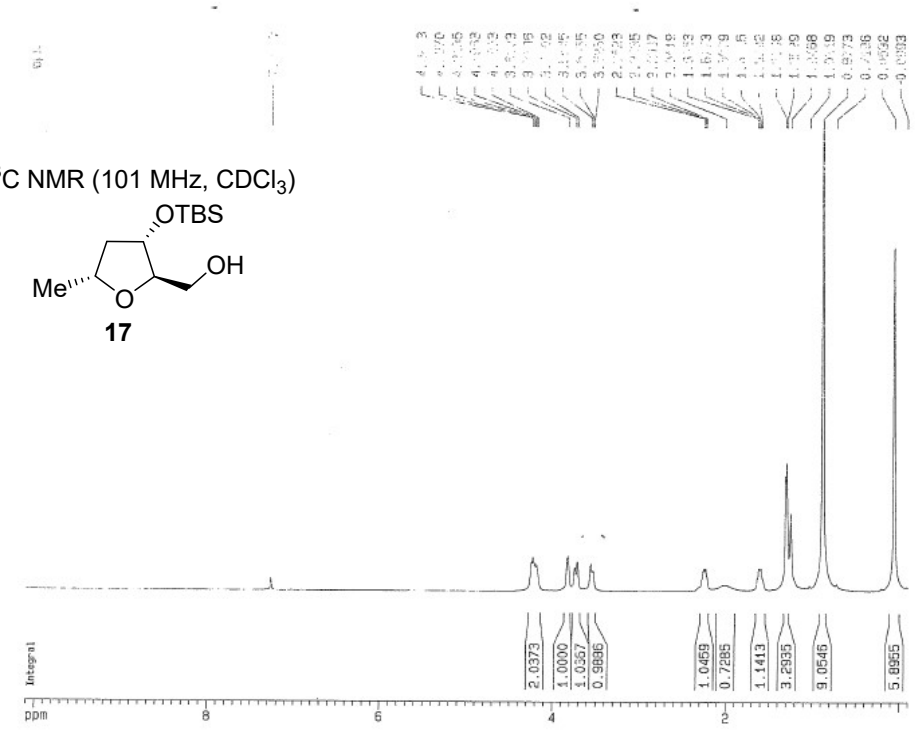
F2 - Processing parameters
SI 16384
SF 100.6220720 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 201.000 ppm
F1 20225.04 Hz
F2P -1.000 ppm
F2 -100.62 Hz
PPMCM 10.10000 ppm/cm
HZCM 1016.28290 Hz/cm

H1 standard parameters, CDCl3, QNP probe.

^{13}C NMR (101 MHz, $CDCl_3$)

17



Current Data Parameters
NAME DL_1_130
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20170313
Time 15.37
INSTRUM spect
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 16384
SOLVENT CDCl3
NS 34
DS 2
SWH 5617.978 Hz
FIDRES 0.342894 Hz
AQ 1.4582260 sec
RG 715
DW 89.000 usec
DE 127.14 usec
TE 300.0 K
D1 2.00000000 sec
P1 9.50 usec
SFO1 400.1694000 MHz
NUCLEUS 1H

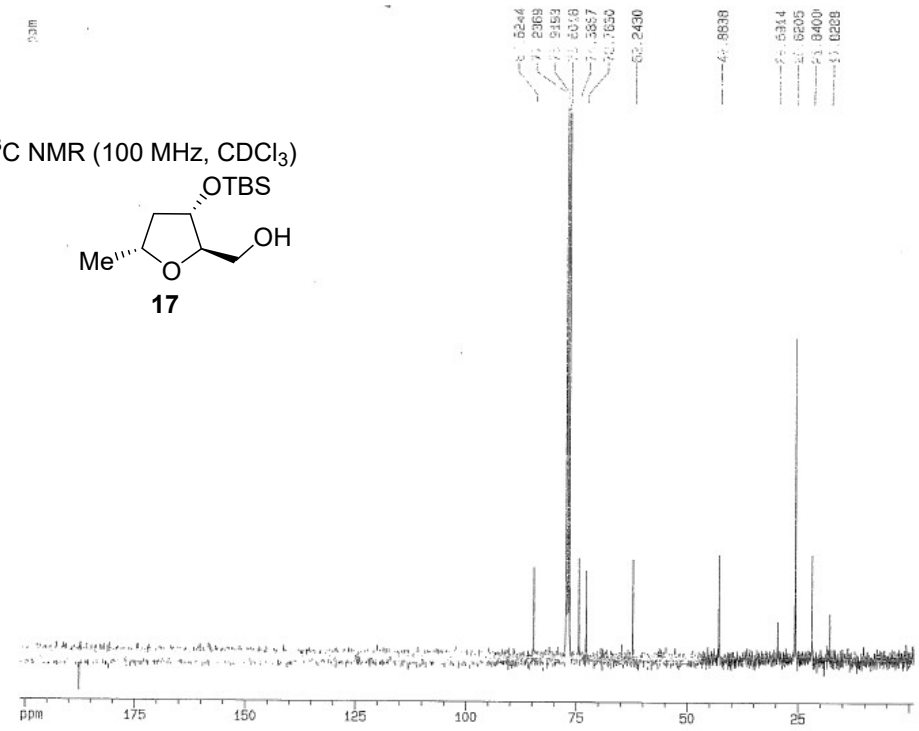
F2 - Processing parameters
SI 8192
SF 400.1689860 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 10.100 ppm
F1 4041.69 Hz
F2P -0.100 ppm
F2 -40.02 Hz
PPMCM 0.51000 ppm/cm
HZCM 204.08516 Hz/cm

C13 standard parameters, CDCl3, QNP probe.

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

17



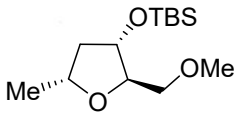
Current Data Parameters
NAME DL_1_130
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20170313
Time 18.12
INSTRUM spect
PROBHD 5 mm QNP 1H
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 177
DS 2
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 0.6881780 sec
RG 15384
DW 21.000 usec
DE 30.00 usec
TE 300.0 K
D12 0.00002000 sec
DL6 21.00 dB
D1 2.00000000 sec
CPDPRG waltz16
P31 76.00 usec
D11 0.03000000 sec
DL5 18.00 dB
P1 8.60 usec
SFO1 100.6330000 MHz
NUCLEUS 13C

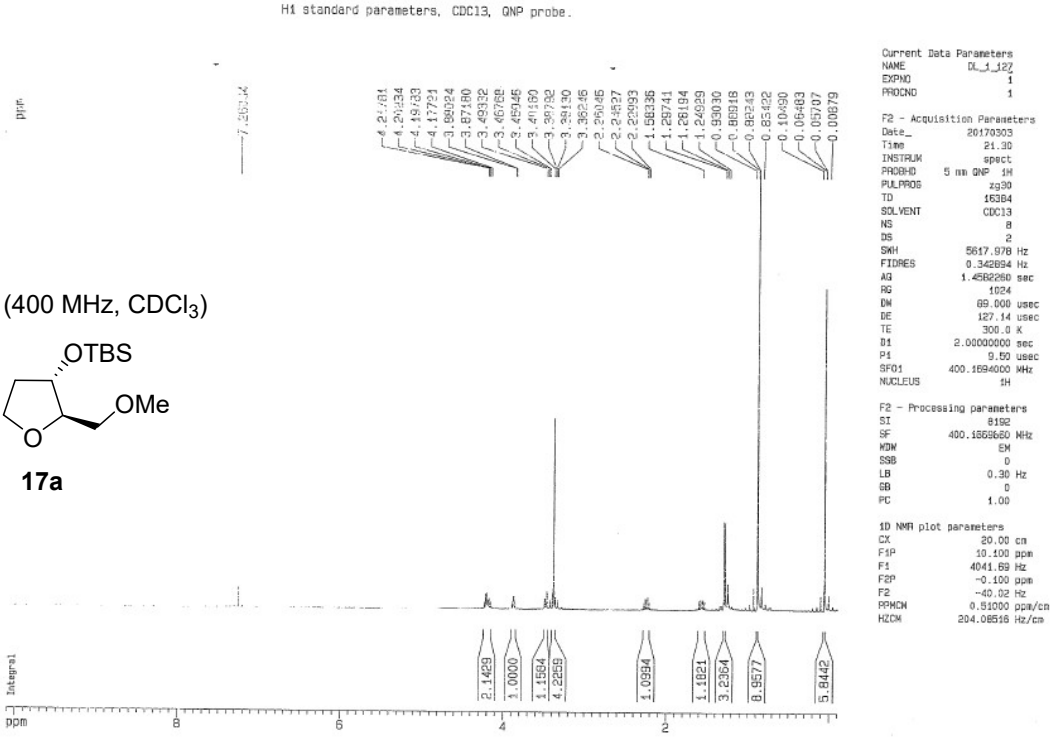
F2 - Processing parameters
SI 16384
SF 100.6220720 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 201.000 ppm
F1 20225.04 Hz
F2P -1.000 ppm
F2 -100.62 Hz
PPMCM 10.10000 ppm/cm
HZCM 1016.28290 Hz/cm

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

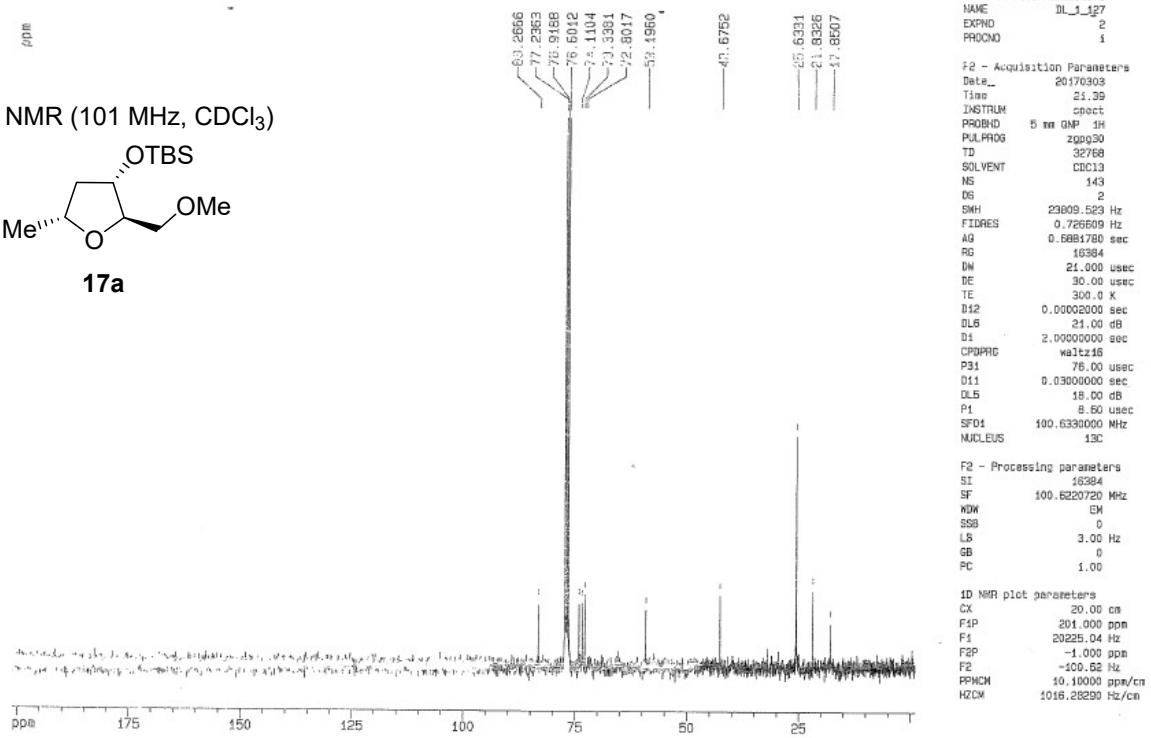


17a

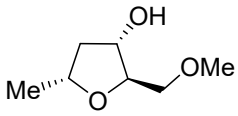


^{13}C NMR (101 MHz, $CDCl_3$)

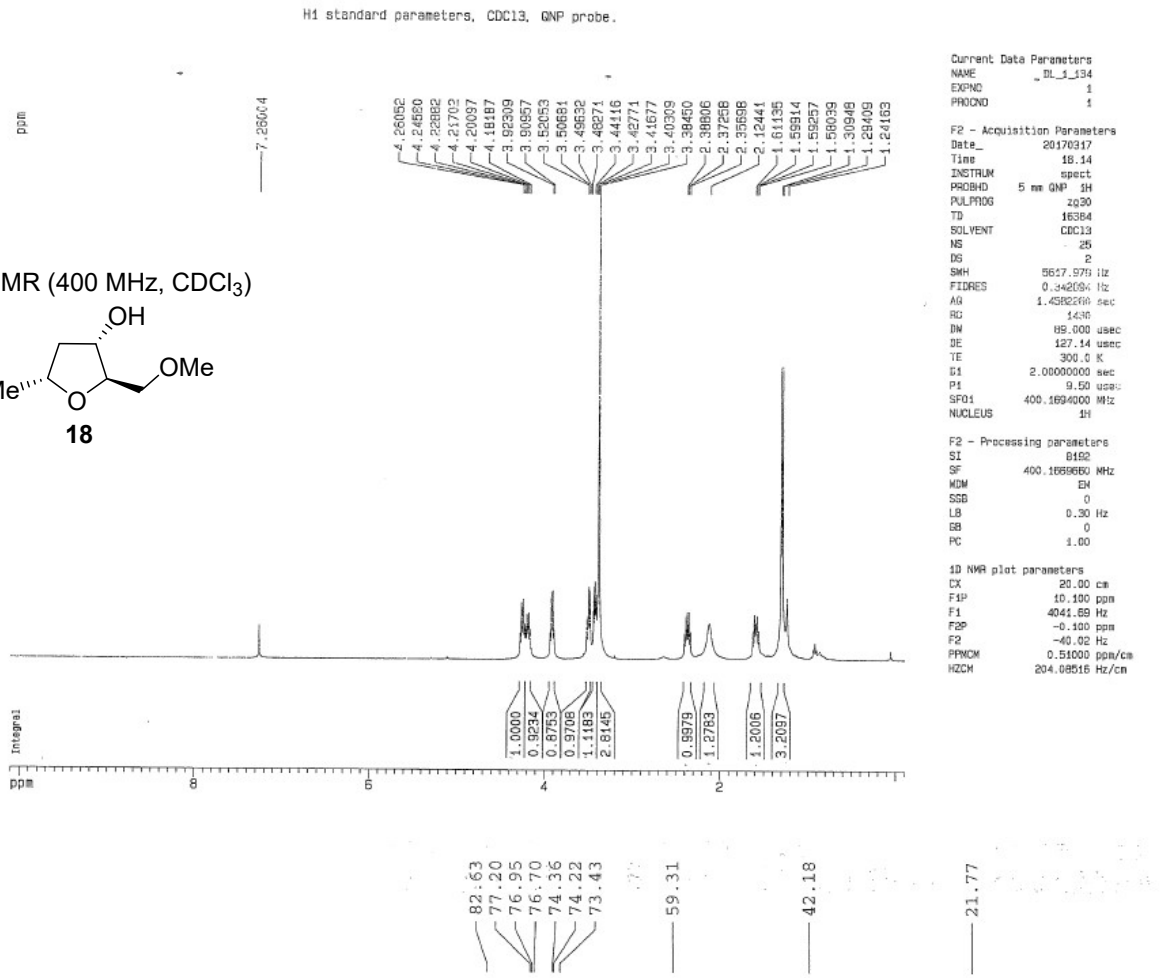
17a



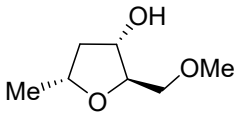
^{1}H NMR (400 MHz, $CDCl_3$)



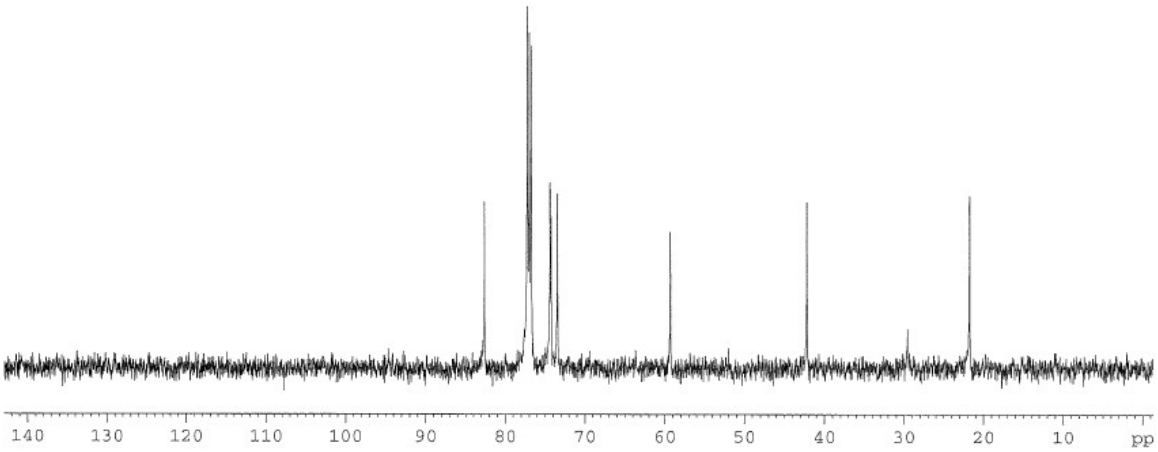
18

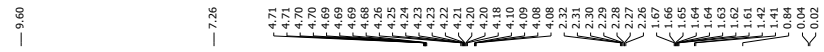


^{13}C NMR (101 MHz, $CDCl_3$)

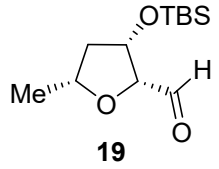


18

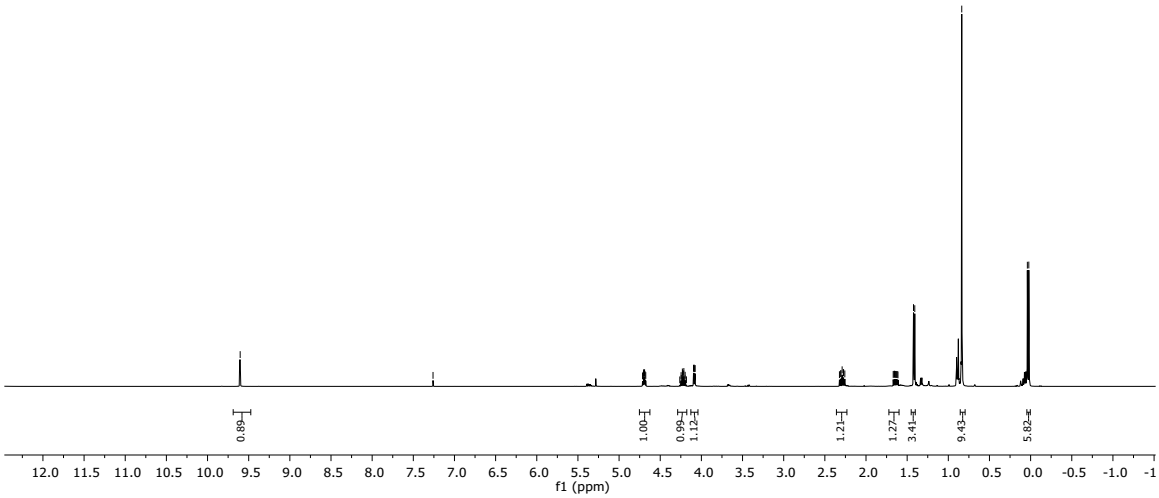




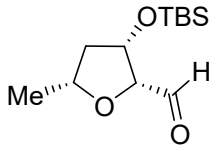
^{1}H NMR (400 MHz, $CDCl_3$)



19



^{13}C NMR (101 MHz, $CDCl_3$)



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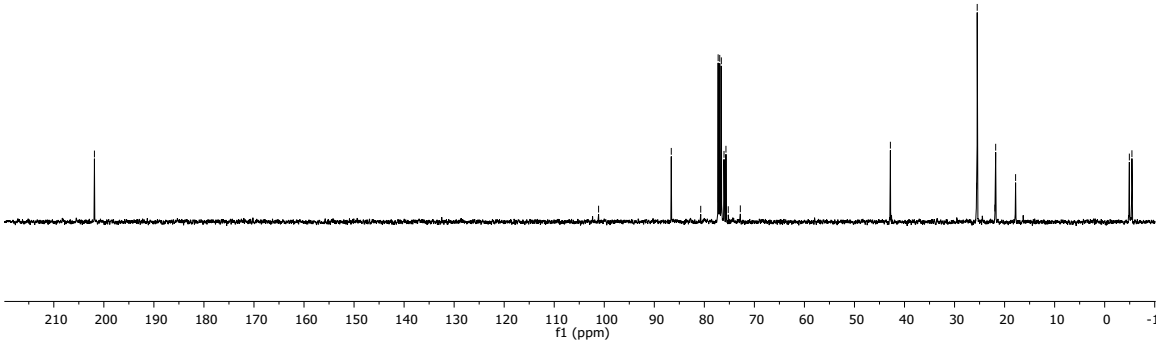
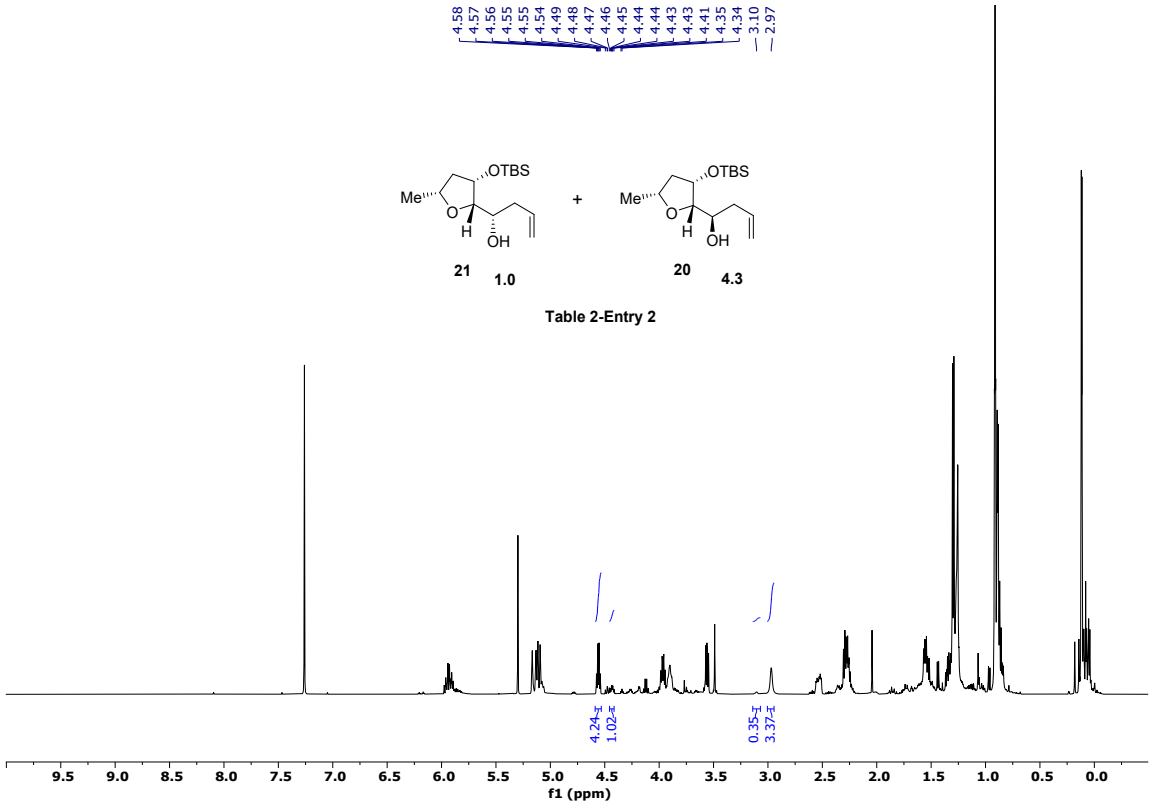
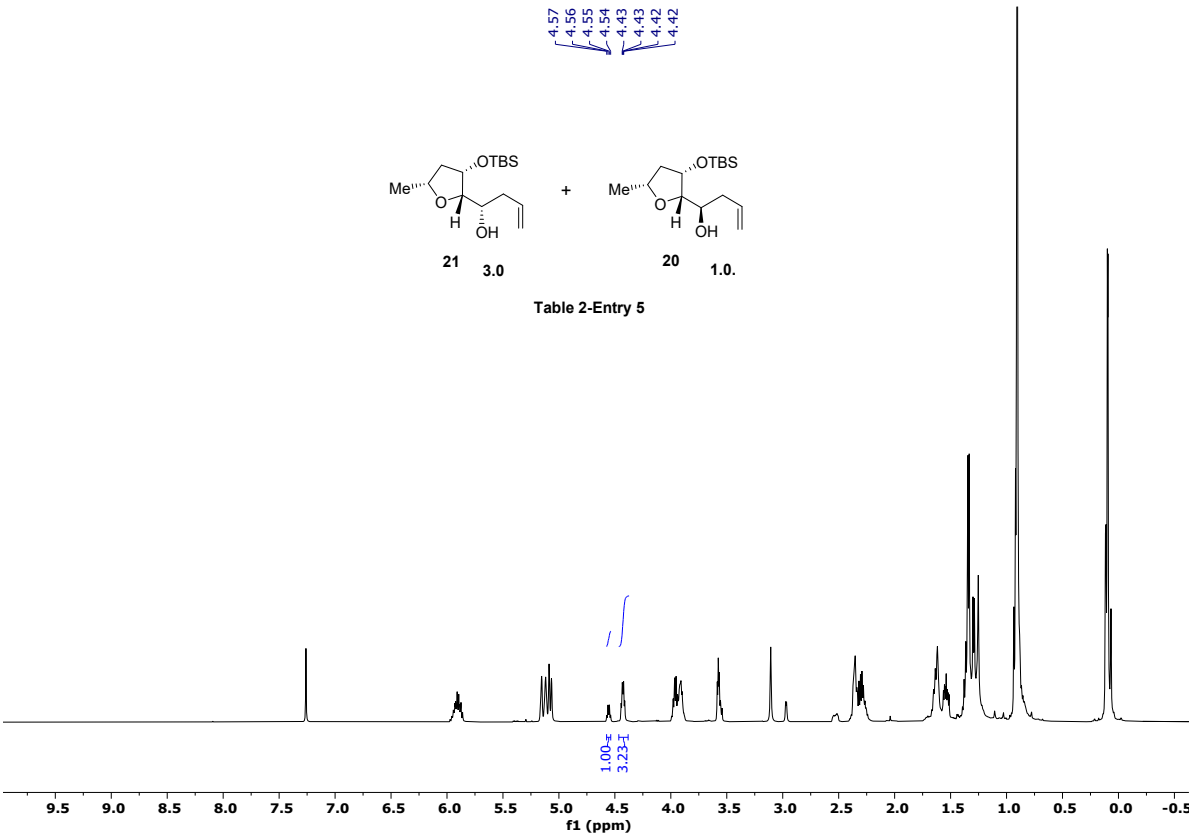




21 **1.0** **20** **4.3**

Table 2-Entry 2

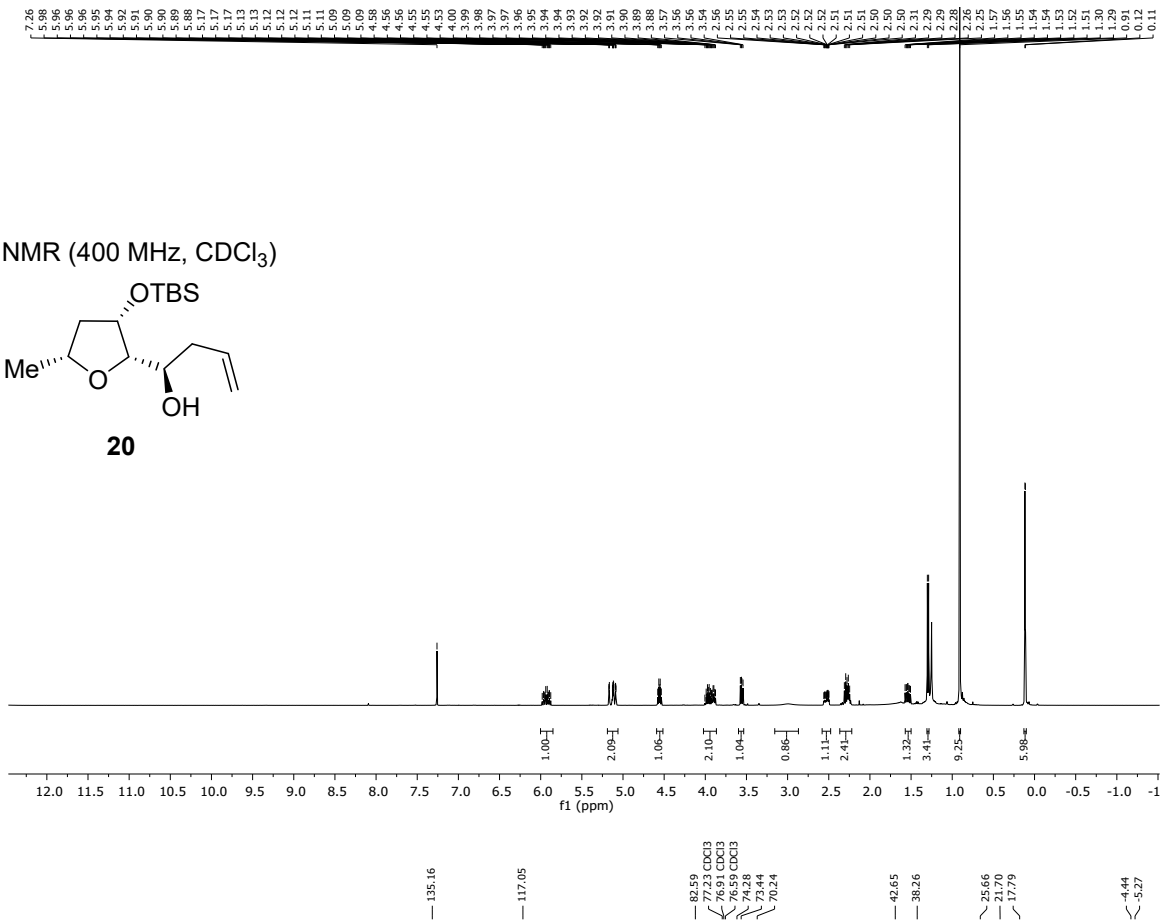


21 **3.0** **20** **1.0.**

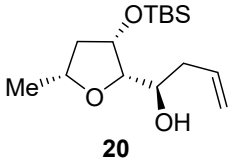
Table 2-Entry 5

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

20



^{13}C NMR (101 MHz, $CDCl_3$)



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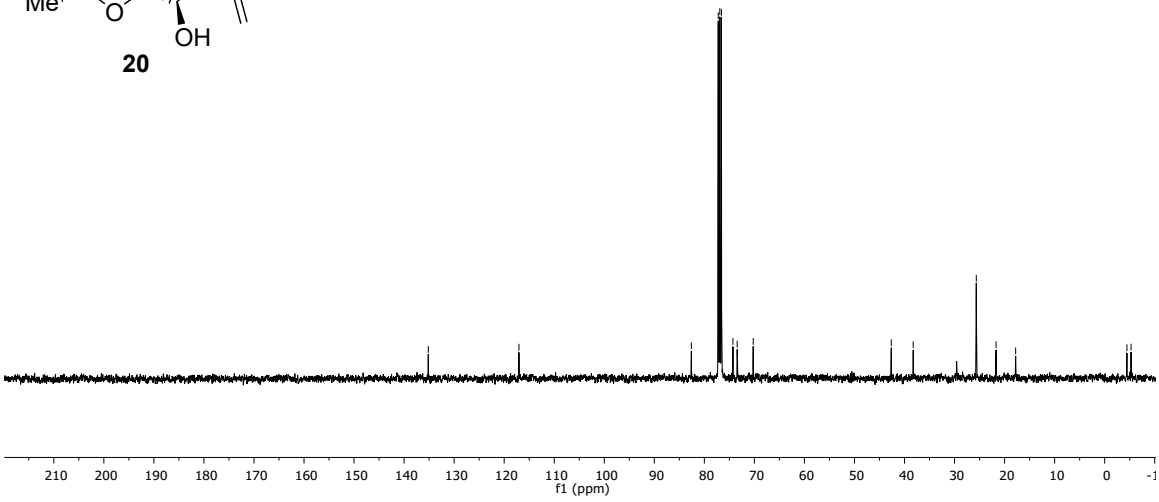
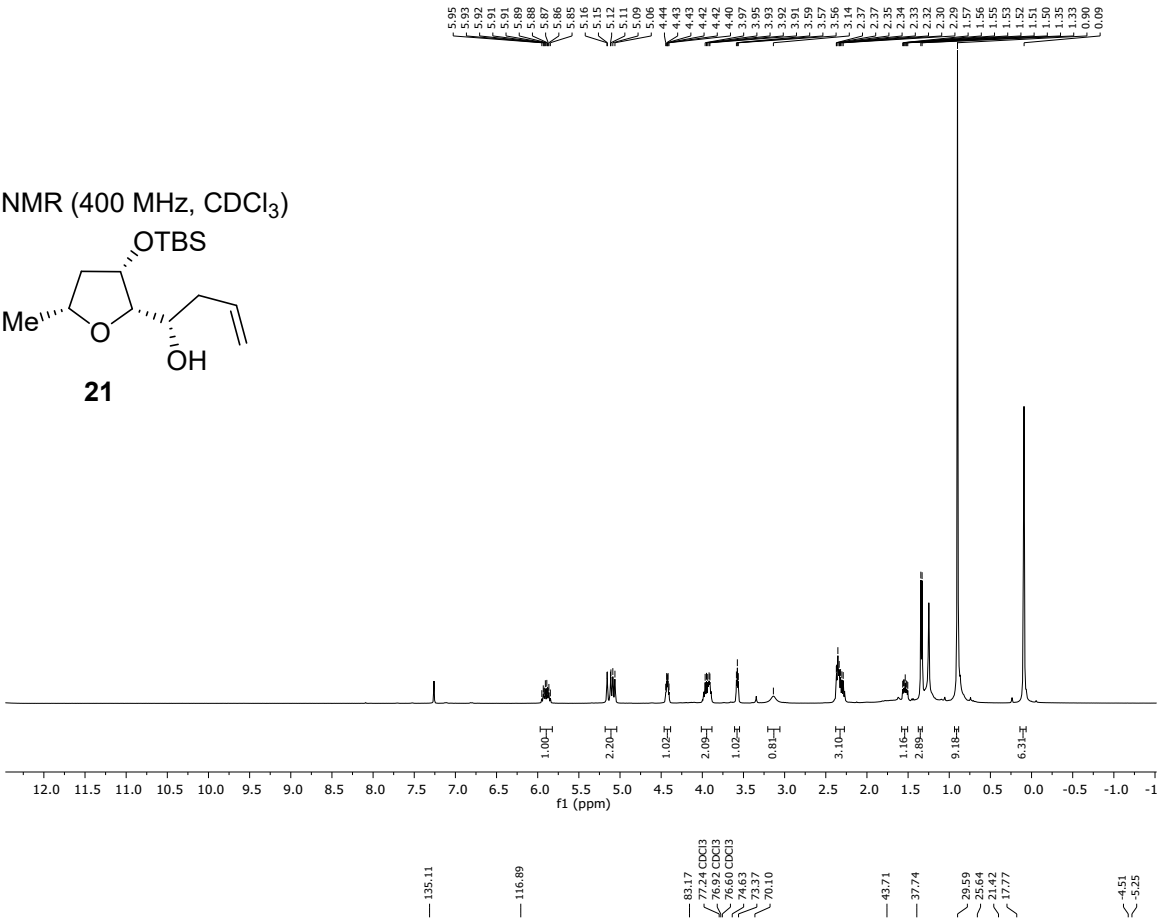
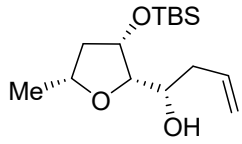


^{1}H NMR (400 MHz, $CDCl_3$)

21



^{13}C NMR (101 MHz, $CDCl_3$)



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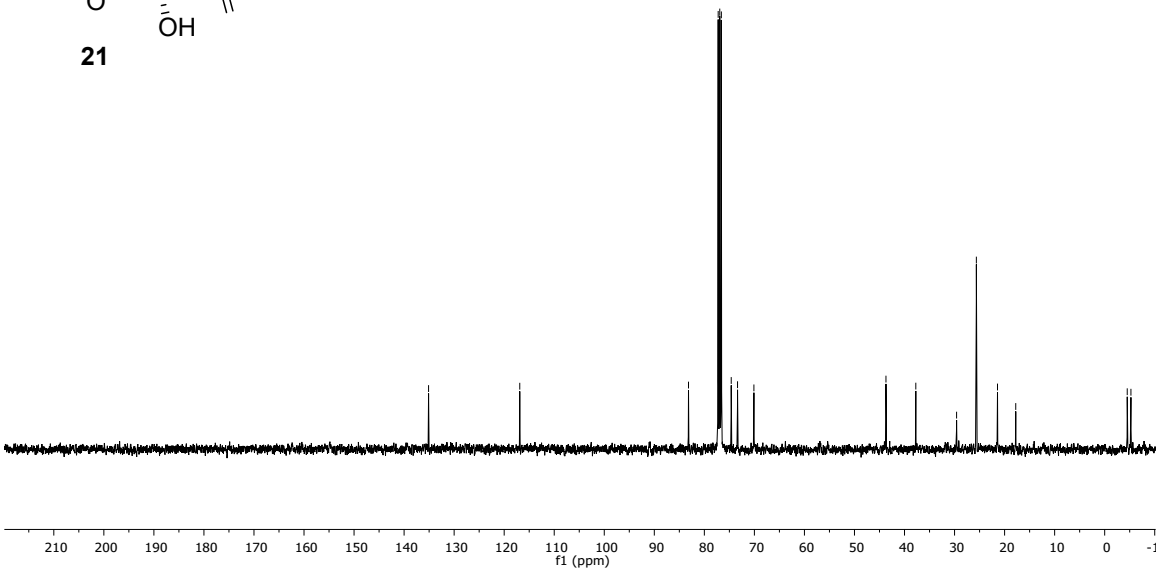
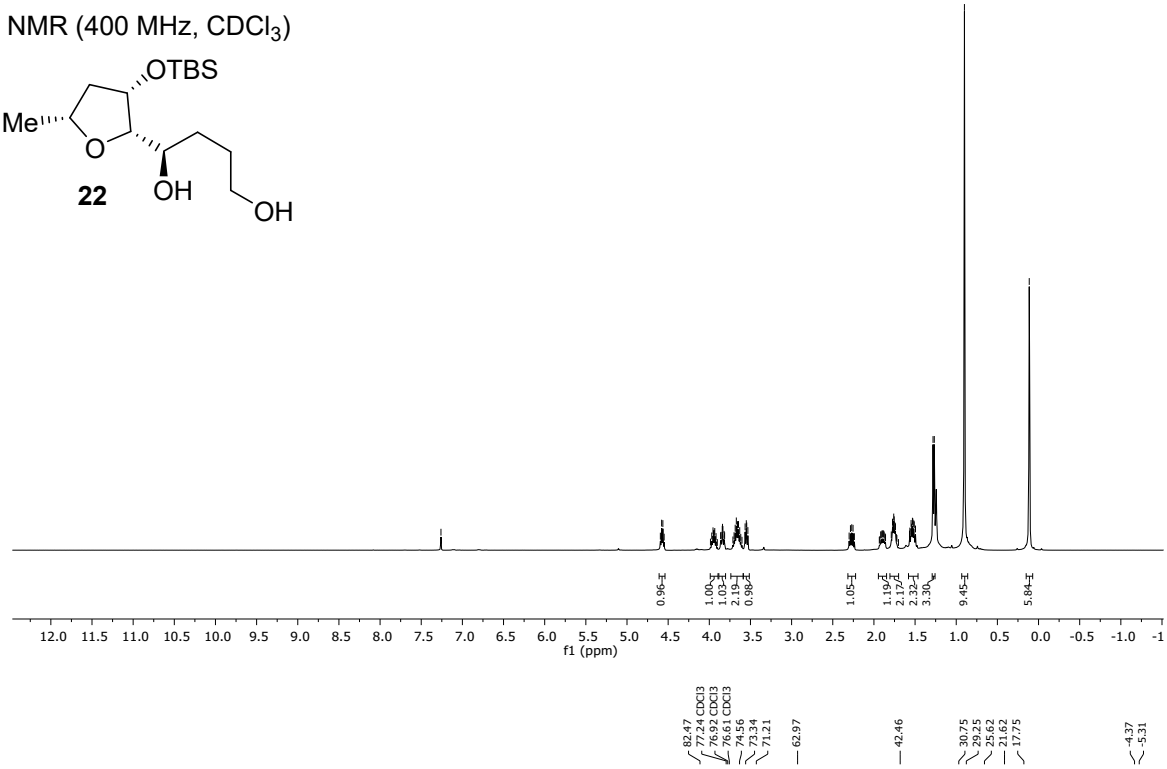
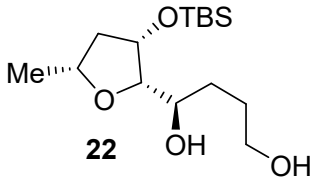
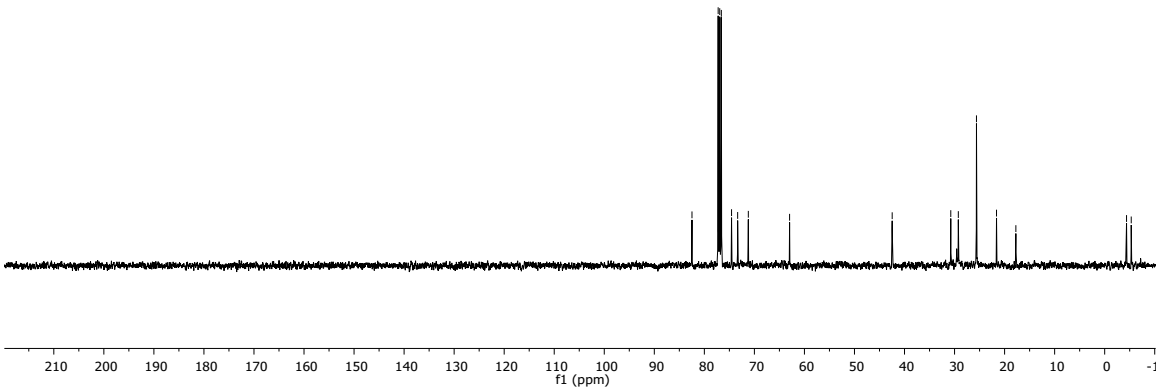


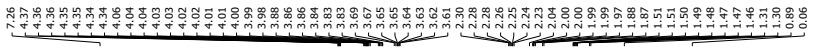
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

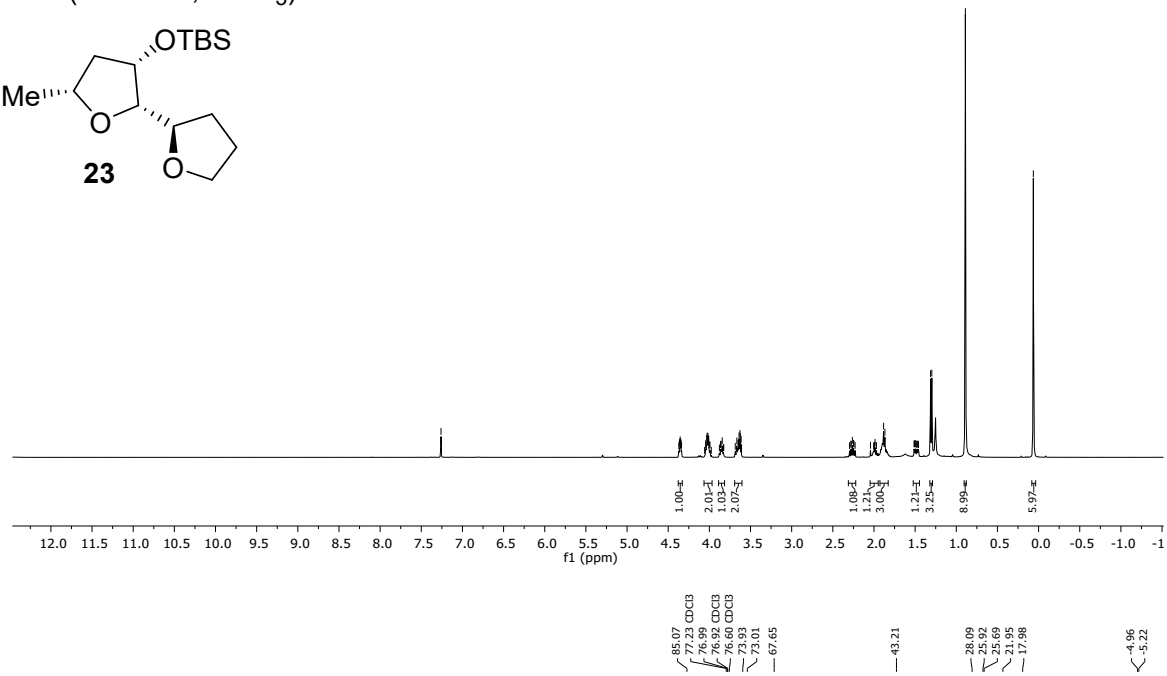




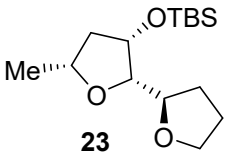


^{1}H NMR (400 MHz, $CDCl_3$)

23



^{13}C NMR (101 MHz, $CDCl_3$)



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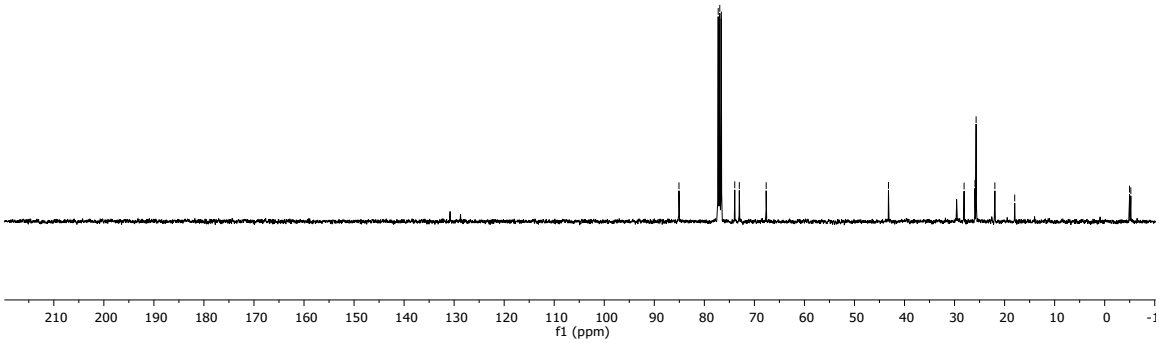
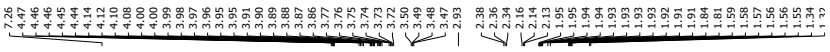
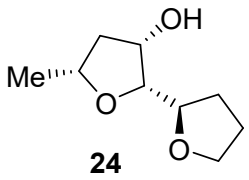




^{1}H NMR (400 MHz, $CDCl_3$)



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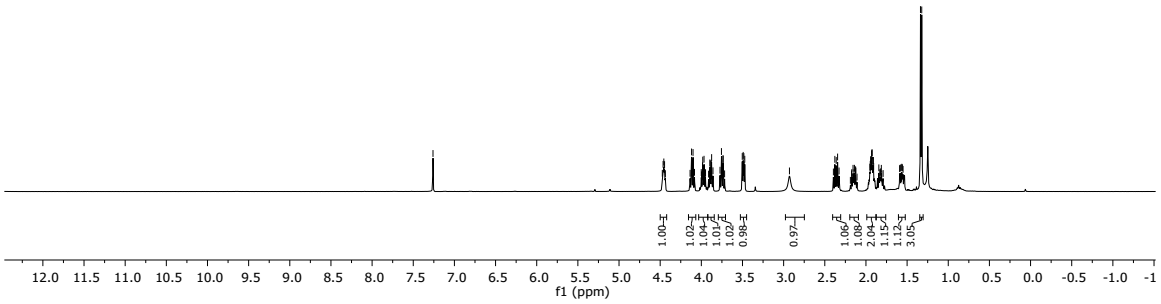
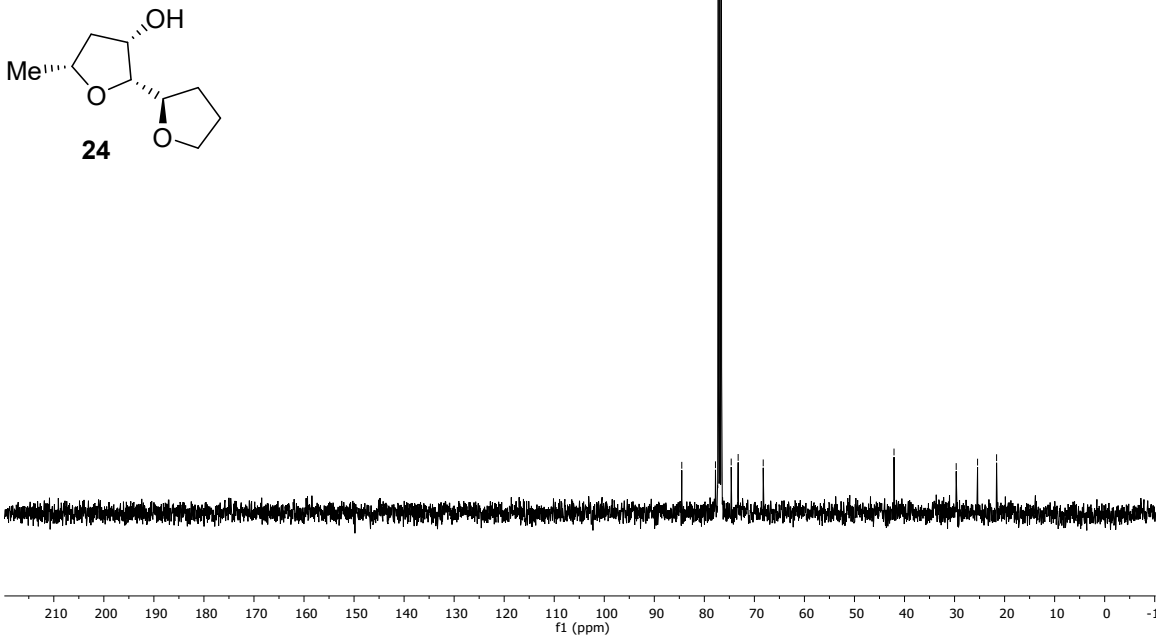


^{13}C NMR (101 MHz, $CDCl_3$)



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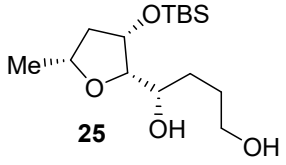
^{1}H NMR (400 MHz, $CDCl_3$)



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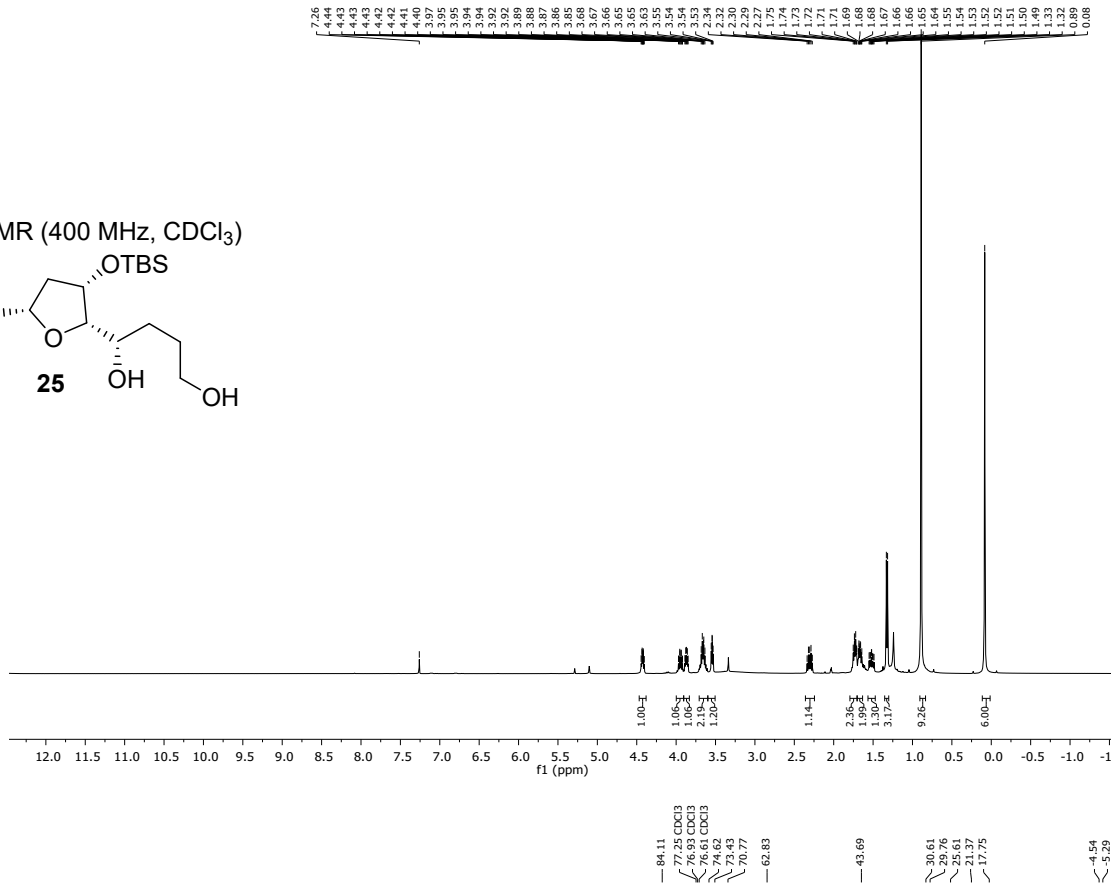
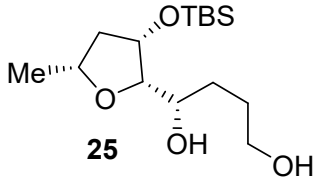


^{13}C NMR (101 MHz, $CDCl_3$)



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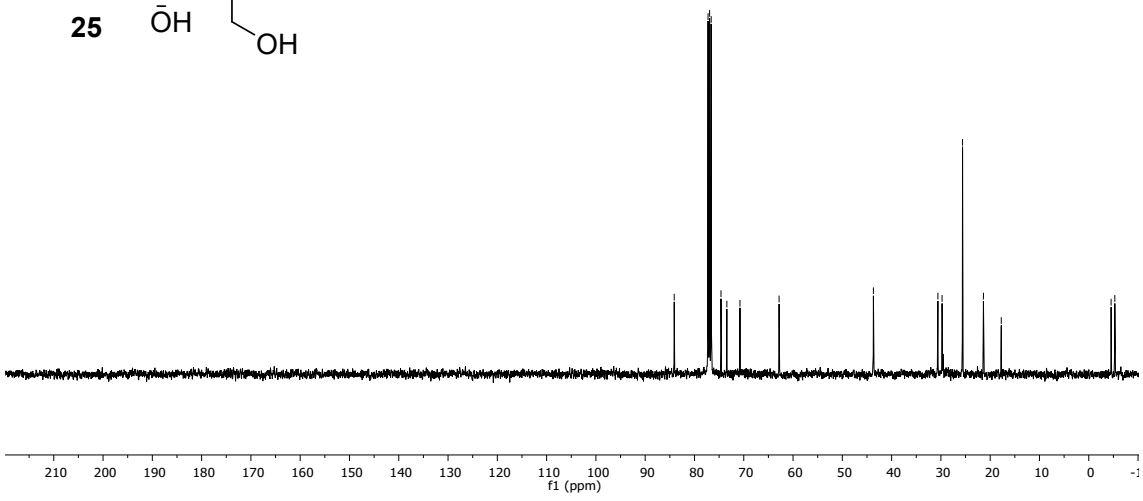
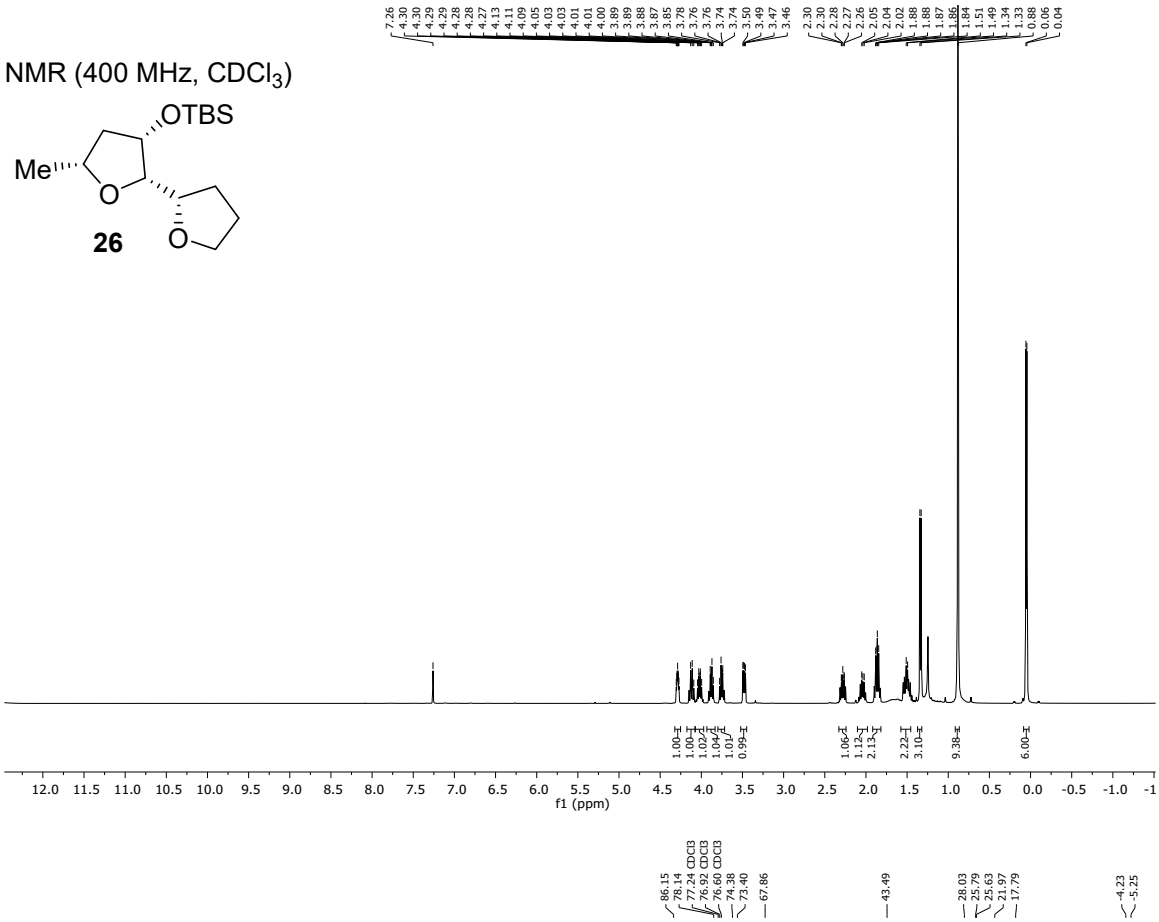


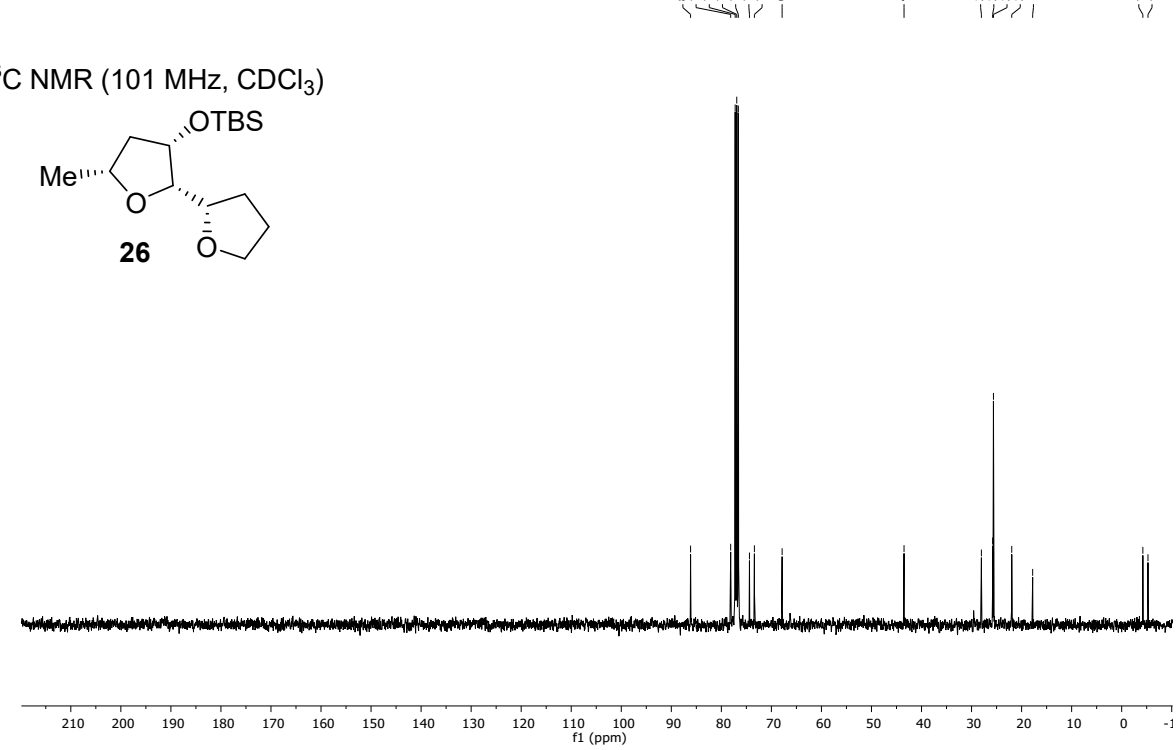
^{1}H NMR (400 MHz, $CDCl_3$)

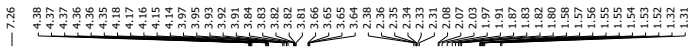
26



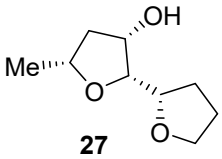
^{13}C NMR (101 MHz, $CDCl_3$)

26





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



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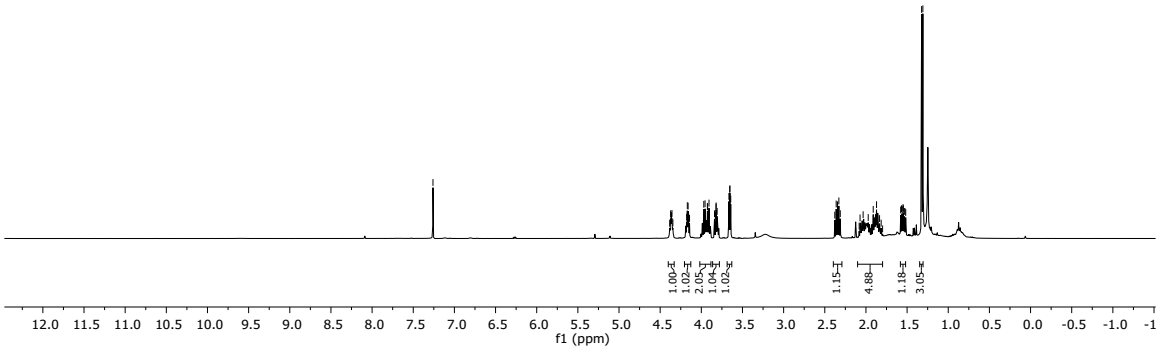

^{13}C NMR (101 MHz, $CDCl_3$)

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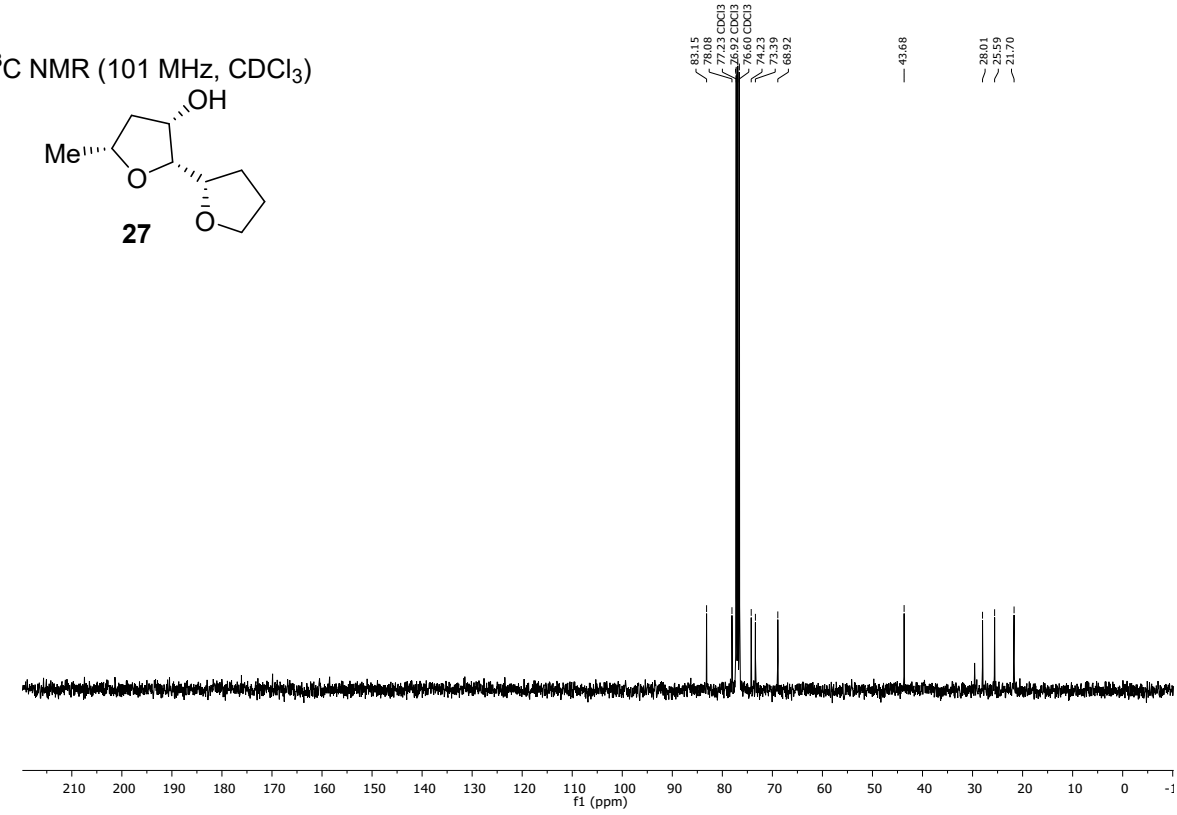
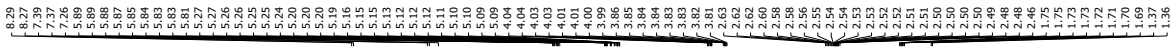
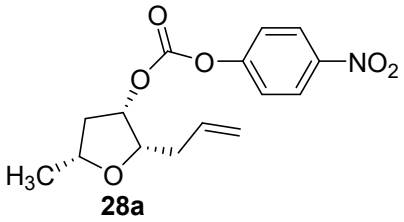




^{1}H NMR (400 MHz, $CDCl_3$)



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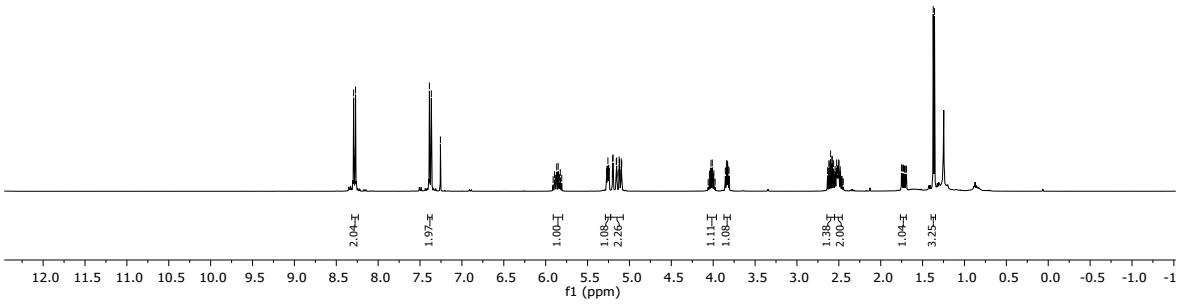
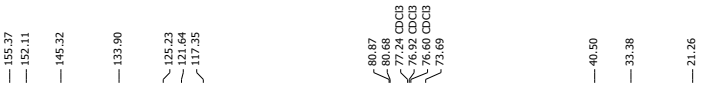
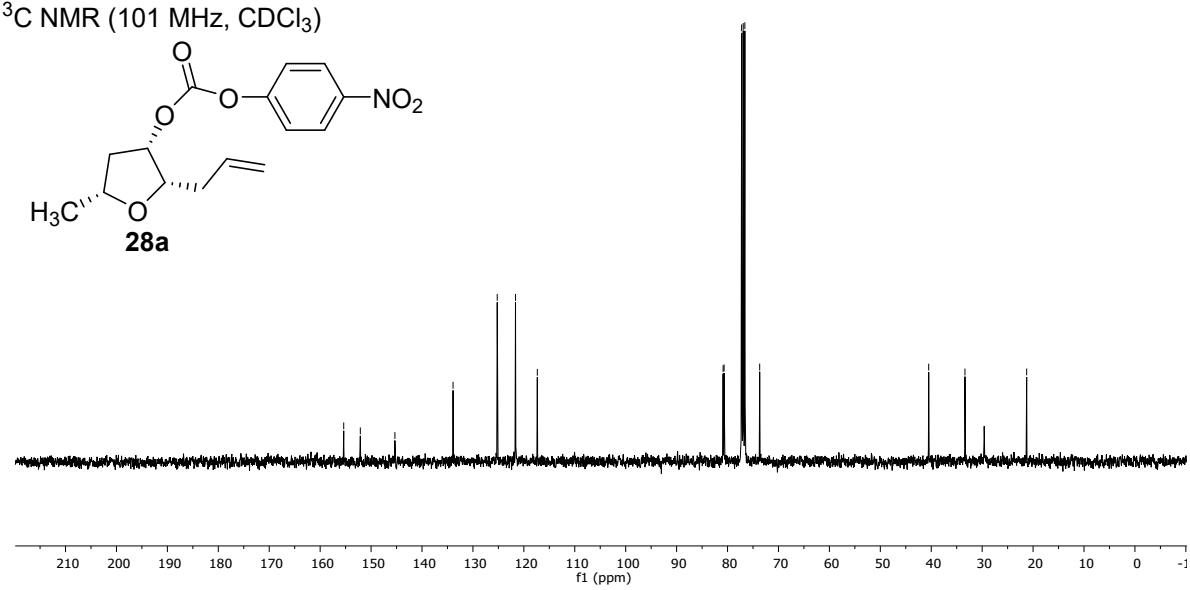
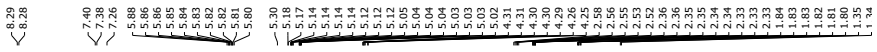




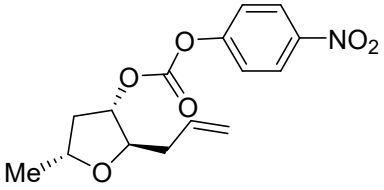
^{13}C NMR (101 MHz, $CDCl_3$)

28a





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



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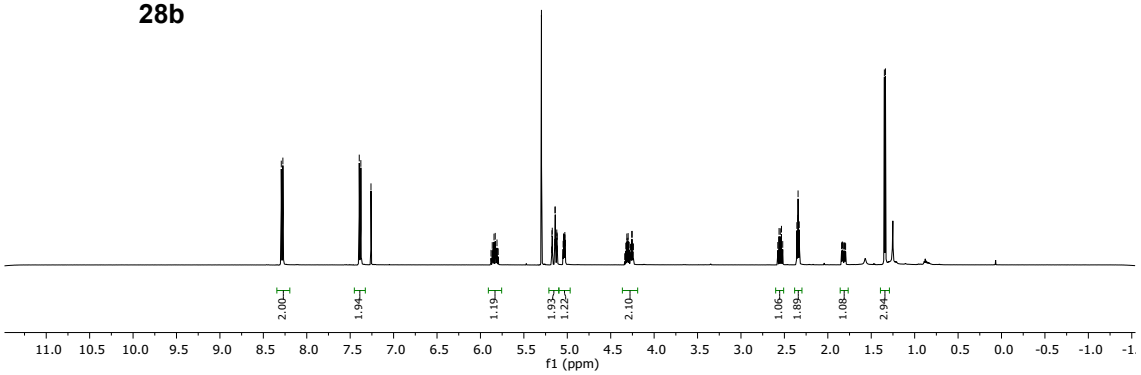
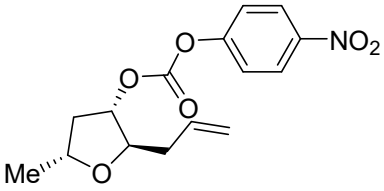


^{13}C NMR (126 MHz, $CDCl_3$)



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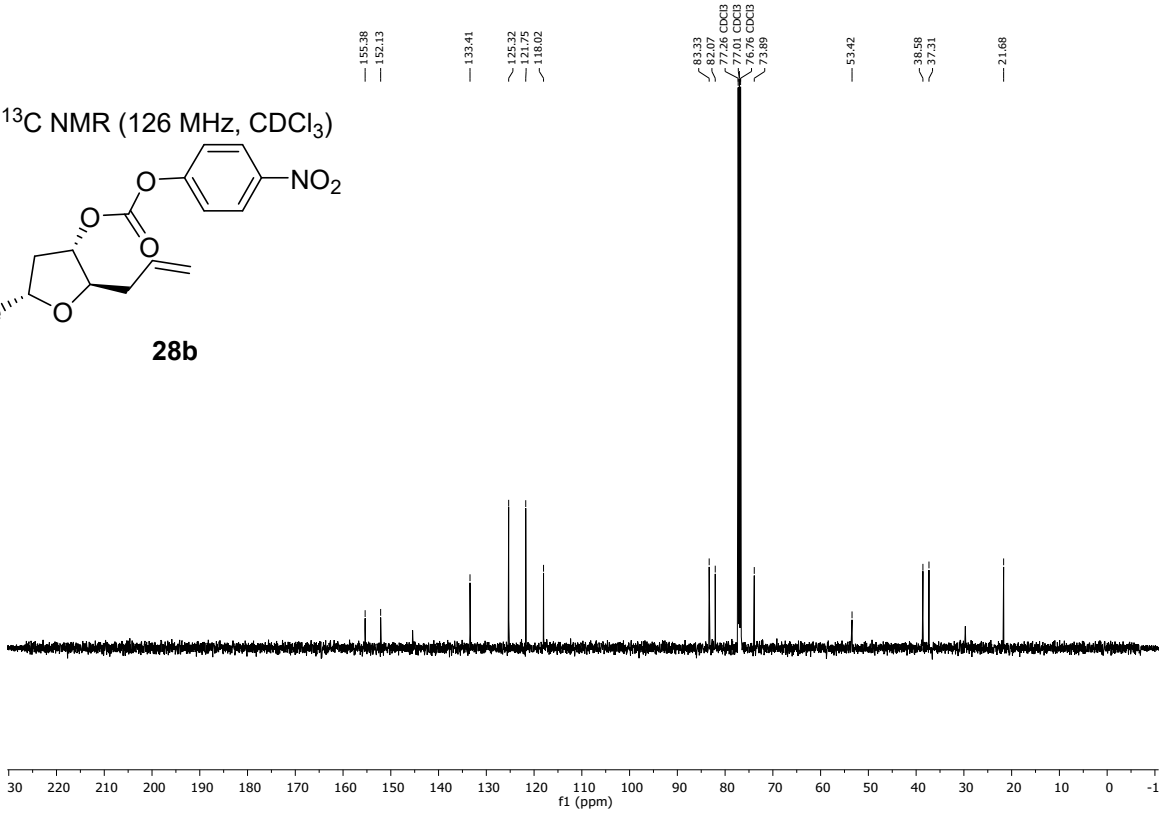

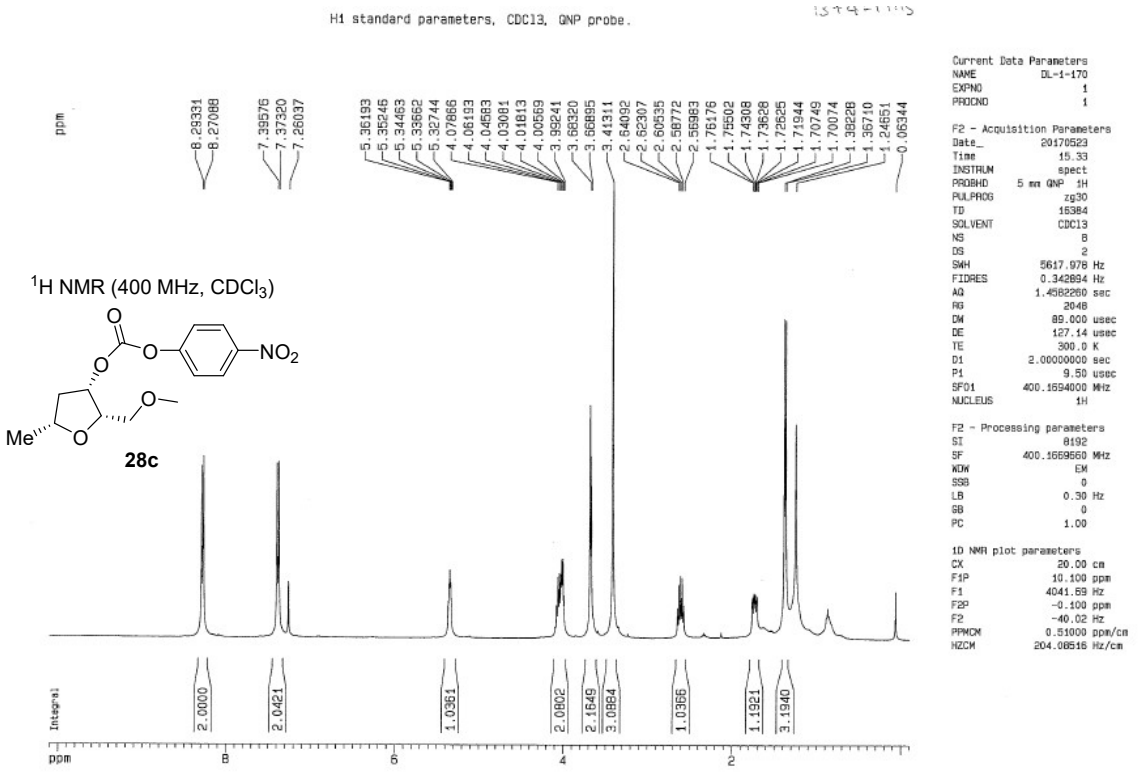
H1 standard parameters, CDCl3, QNP probe.
^{1}H NMR (400 MHz, CDCl$_3$)
28c
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PROCNO 1
F2 - Acquisition Parameters
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Time 15.33
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PULPROG zg30
TD 16384
SOLVENT CDCl3
NS 8
DS 2
SWH 5617.978 Hz
FIDRES 0.342894 Hz
AQ 1.4582260 sec
RG 2048
DW 89.000 usec
DE 127.14 usec
TE 300.0 K
D1 2.00000000 sec
P1 9.50 usec
SF01 400.1694000 MHz
NUCLEUS 1H
F2 - Processing parameters
SI 8192
SF 400.1669560 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 20.00 cm
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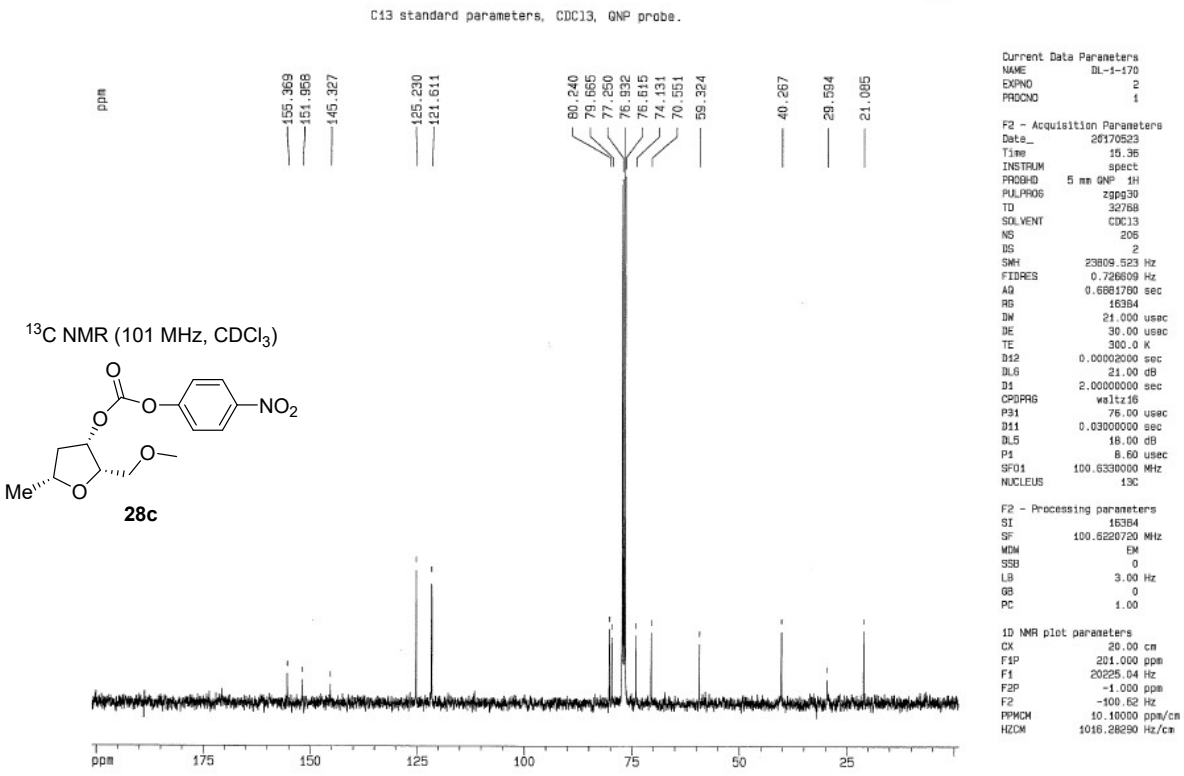
F1 4041.69 Hz
F2P -0.100 ppm
F2 -40.02 Hz
PPMCM 0.51000 ppm/cm
HZCM 204.08516 Hz/cm


C13 standard parameters, CDCl3, QNP probe.
^{13}C NMR (101 MHz, CDCl$_3$)
28c
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PROCNO 1
F2 - Acquisition Parameters
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Time 15.36
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TD 32768
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DS 2
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 0.6881780 sec
RG 16384
DW 21.000 usec
DE 30.00 usec
TE 300.0 K
D12 0.00002000 sec
DL6 21.00 dB
D1 2.00000000 sec
CPDPRG waltz16
P31 76.00 usec
D11 0.03000000 sec
DL5 18.00 dB
P1 8.60 usec
SF01 100.6330000 MHz
NUCLEUS 13C
F2 - Processing parameters
SI 16384
SF 100.6220720 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 20.00 cm
F1P 201.000 ppm
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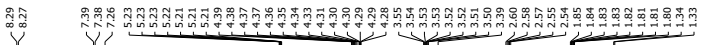
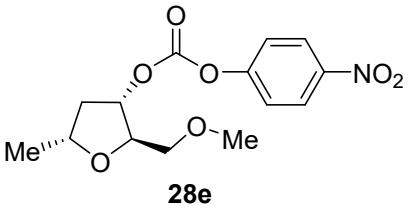
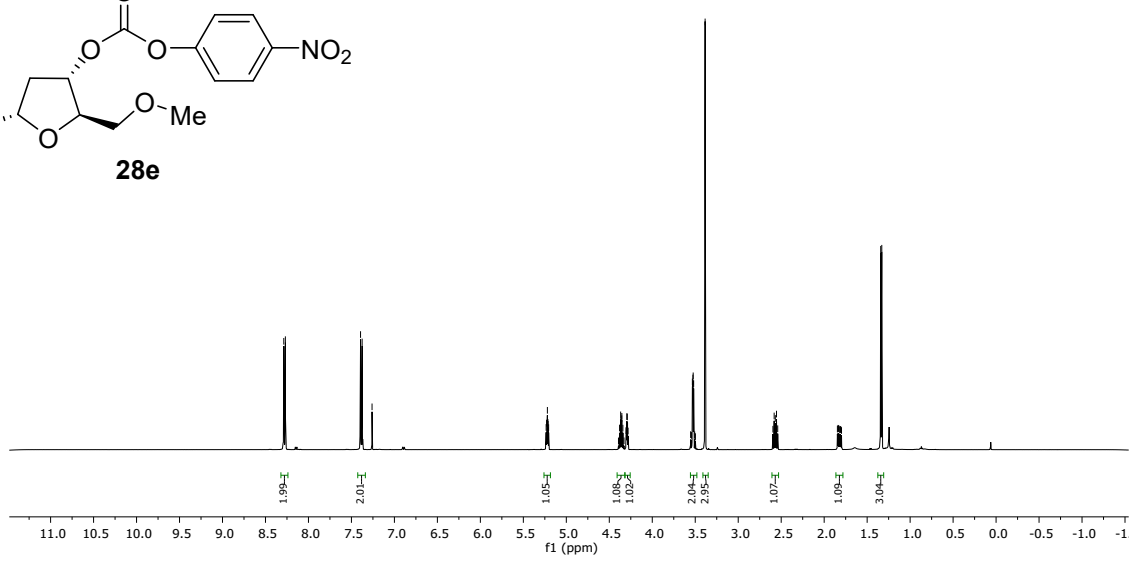
F2P -1.000 ppm
F2 -100.62 Hz
PPMCM 10.10000 ppm/cm
HZCM 1016.28290 Hz/cm

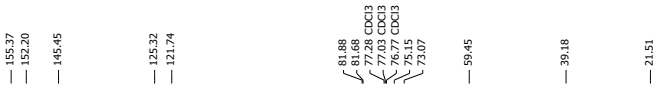


^{1}H NMR (500 MHz, $CDCl_3$)

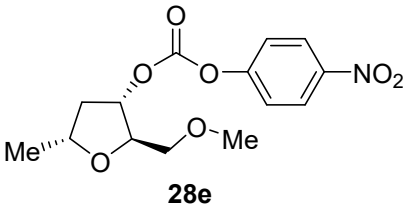


28e





^{13}C NMR (126 MHz, $CDCl_3$)



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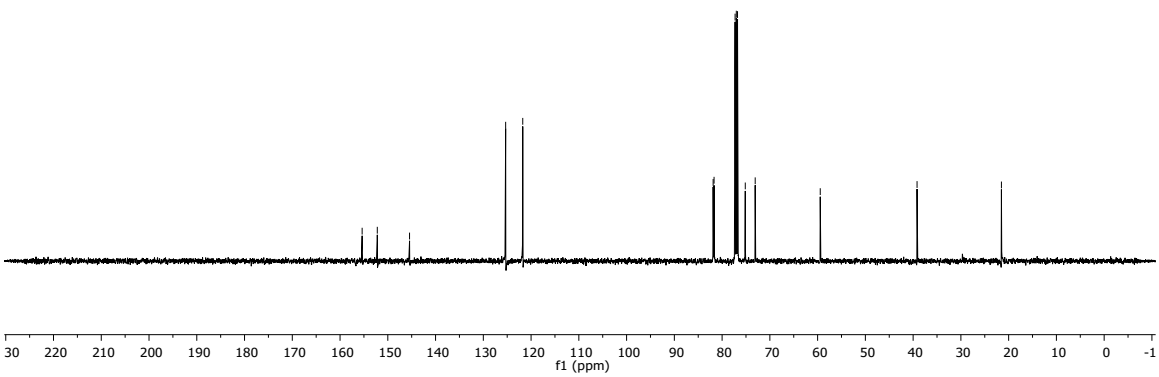
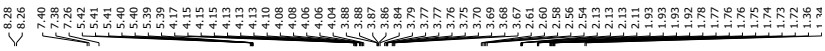
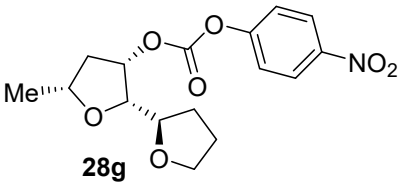
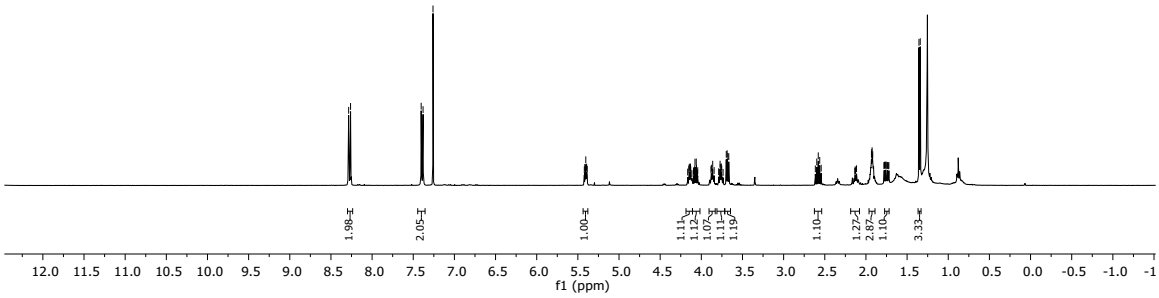




^{1}H NMR (400 MHz, $CDCl_3$)

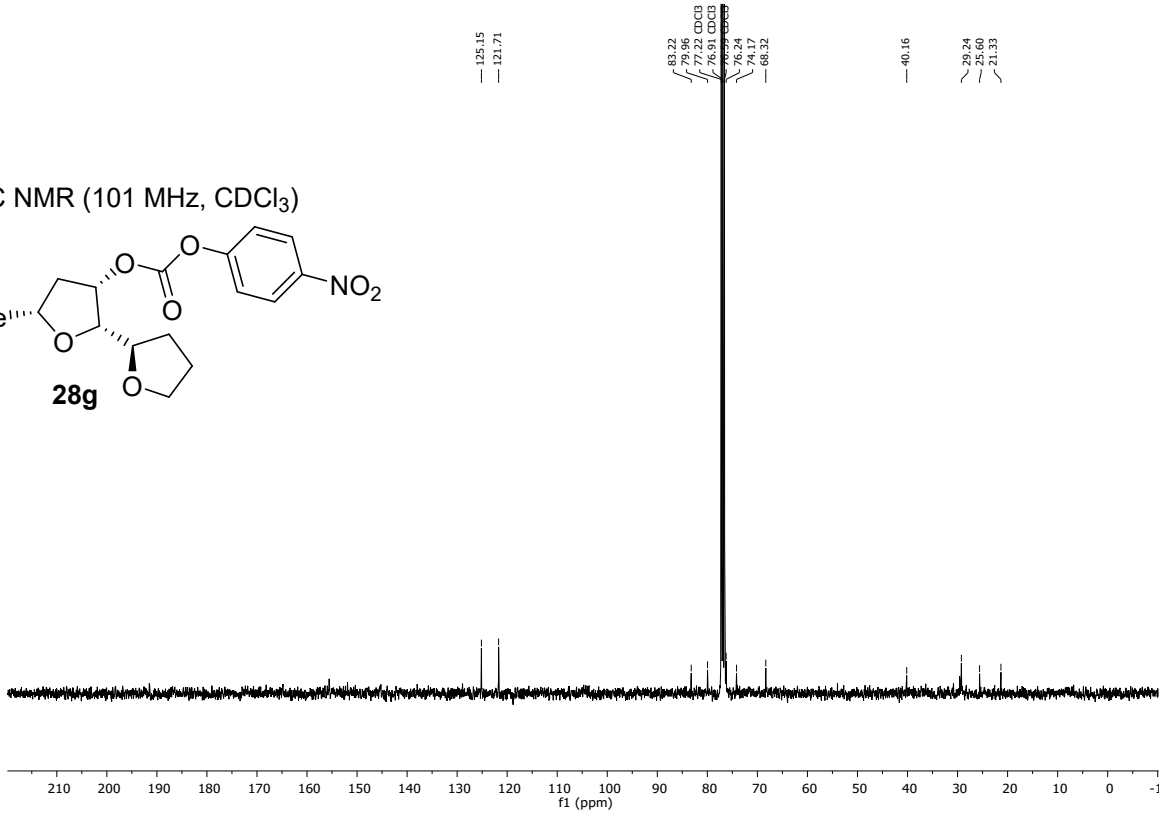


28g

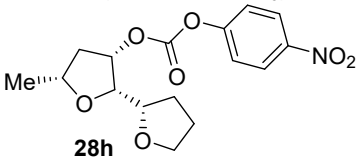


^{13}C NMR (101 MHz, $CDCl_3$)

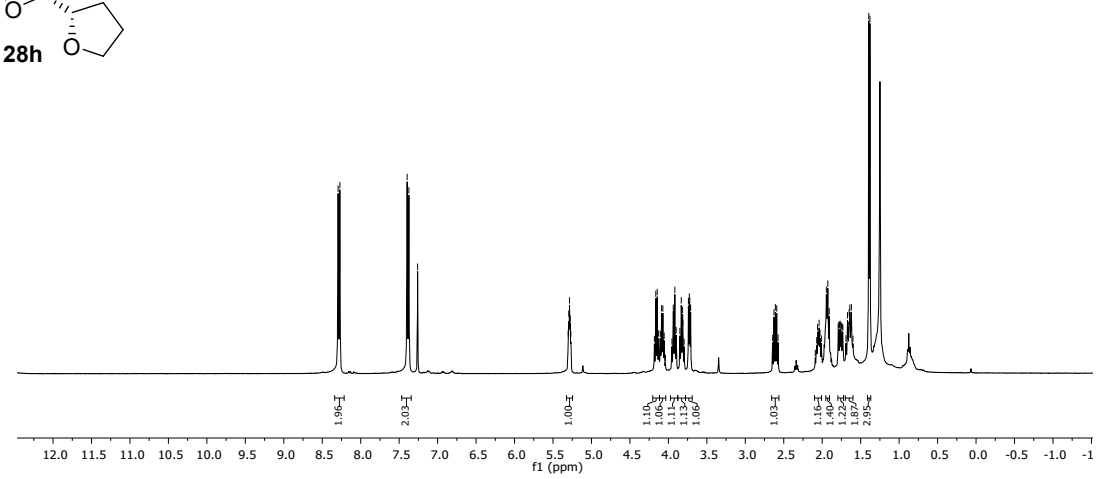
28g



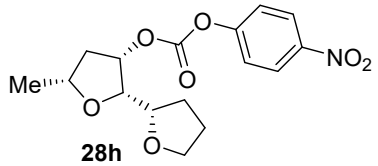
^{1}H NMR (400 MHz, $CDCl_3$)



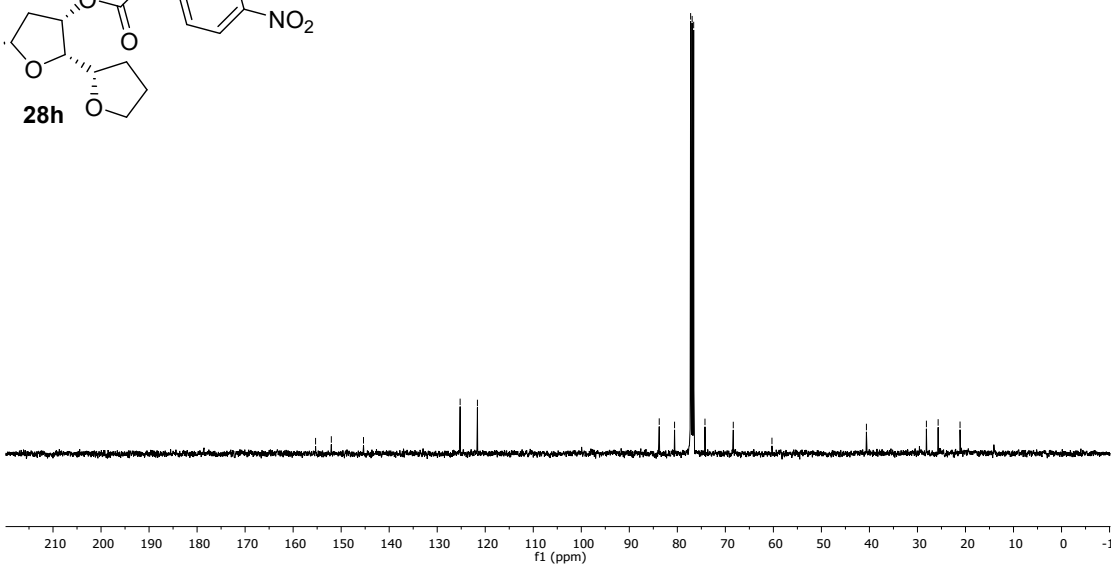
28h

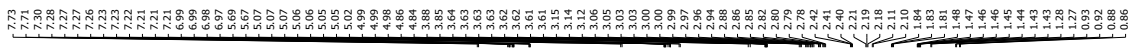


^{13}C NMR (101 MHz, $CDCl_3$)



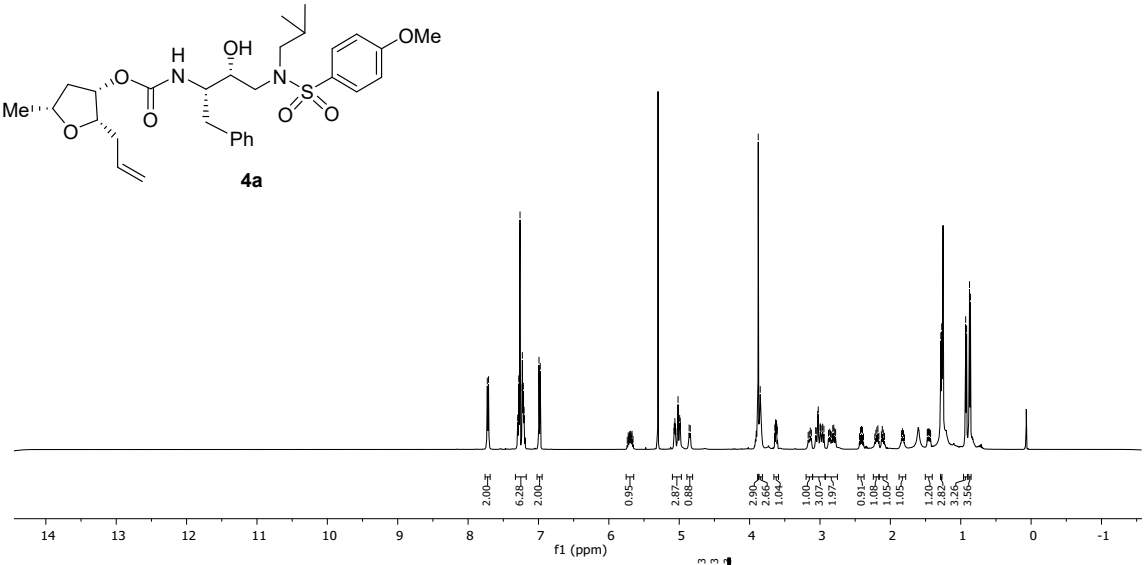
28h





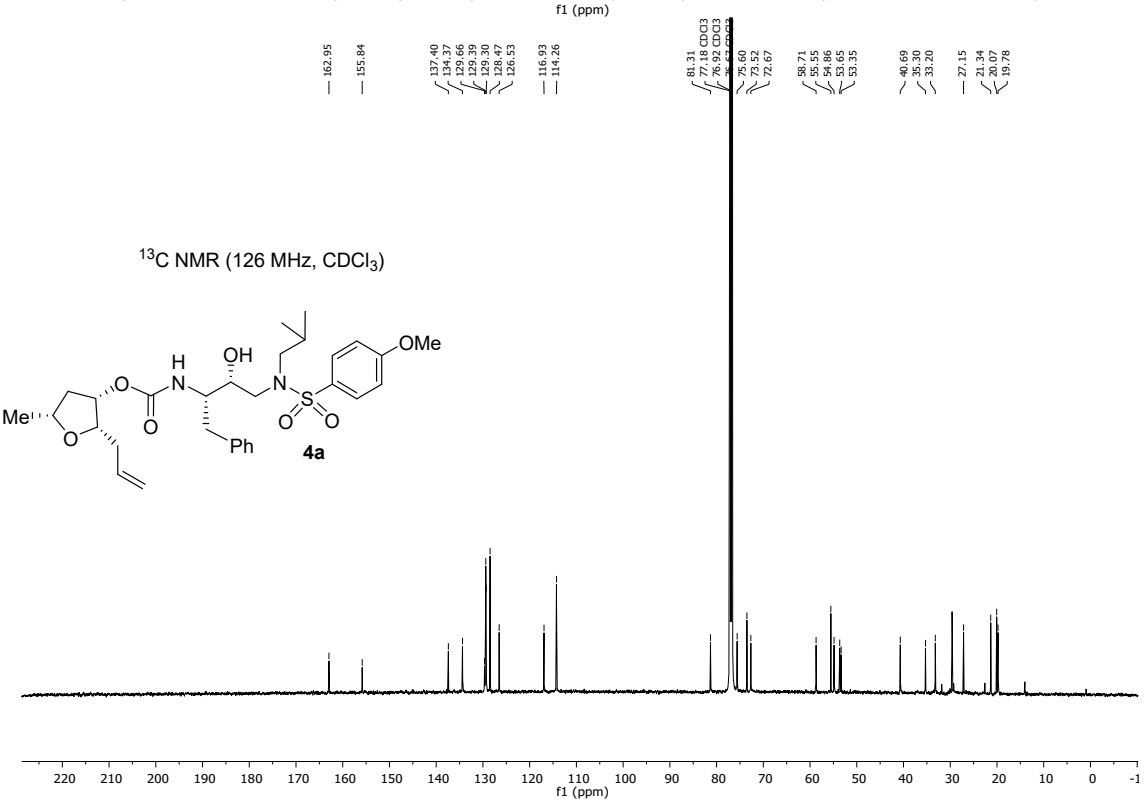
^{1}H NMR (500 MHz, $CDCl_3$)

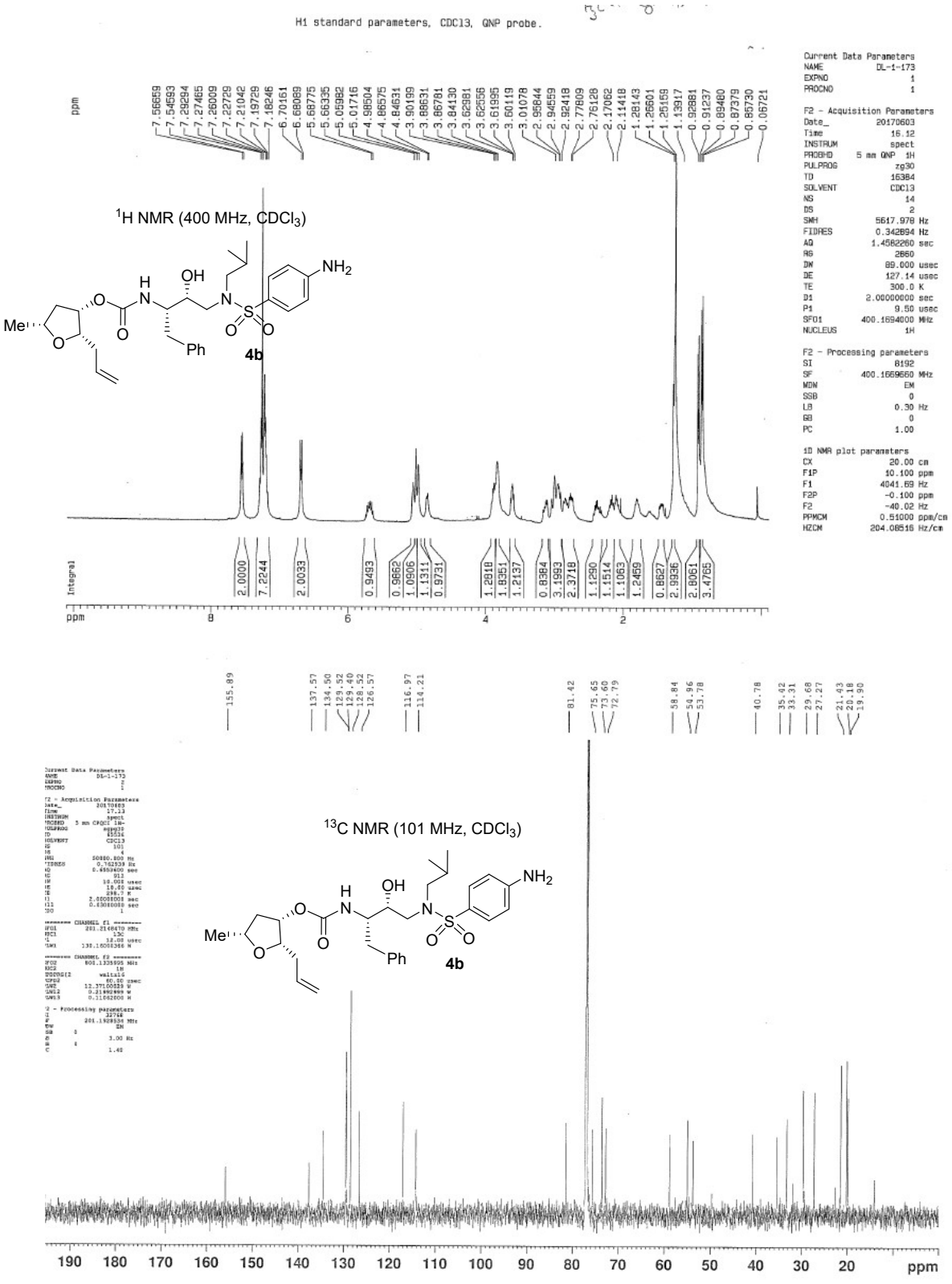
4a

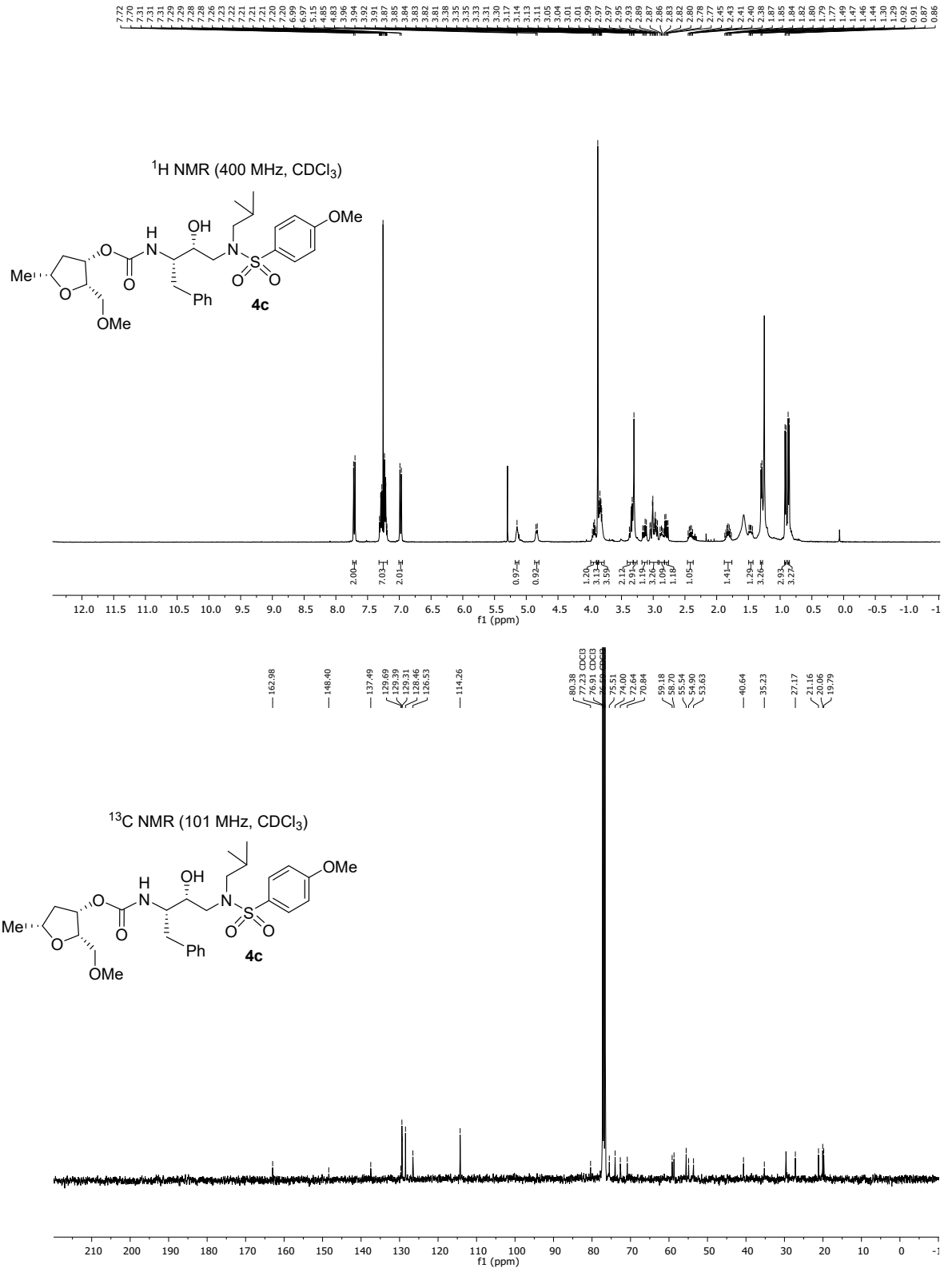


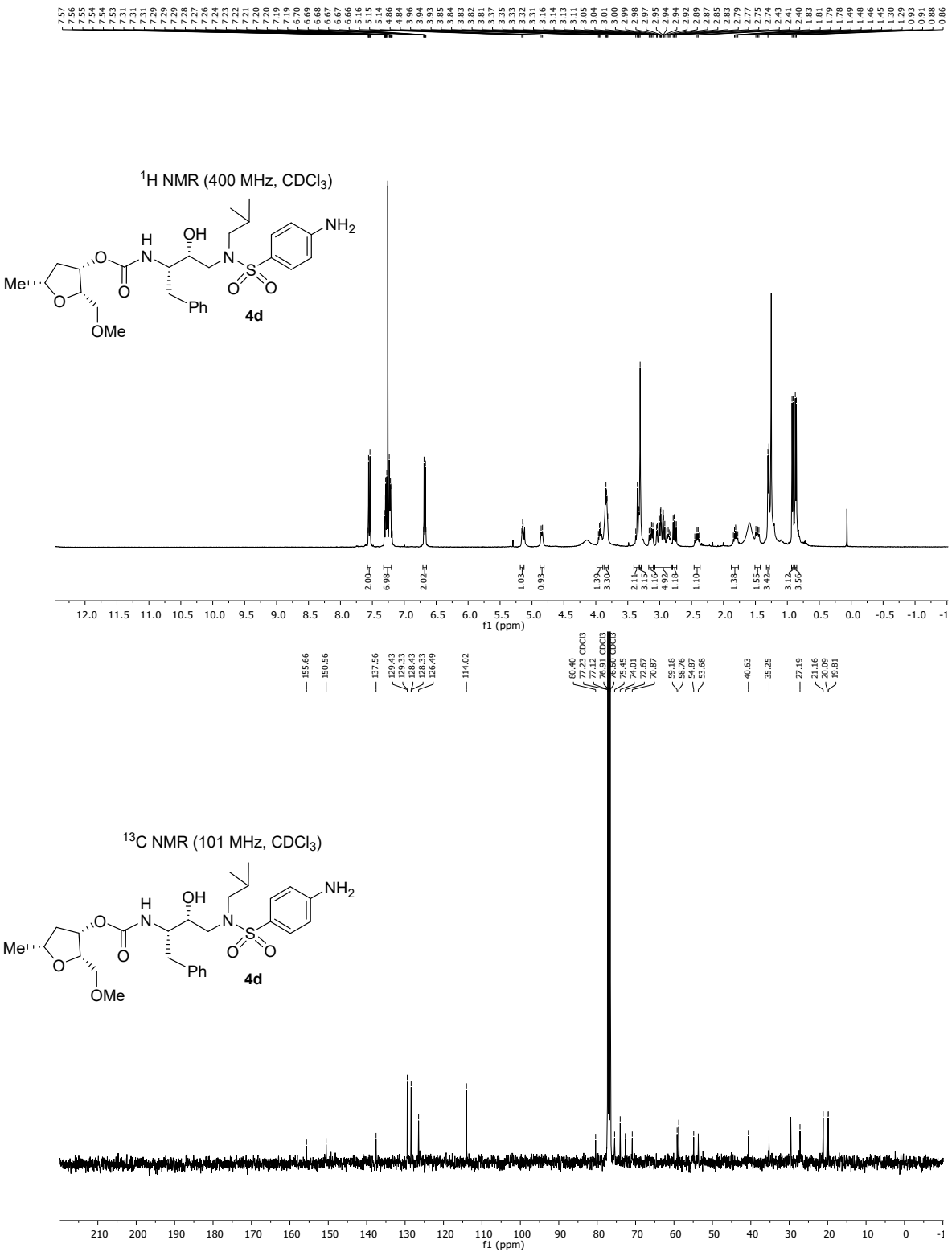
^{13}C NMR (126 MHz, $CDCl_3$)

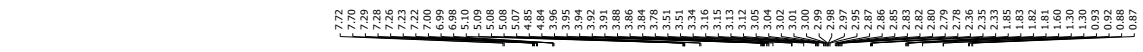
4a



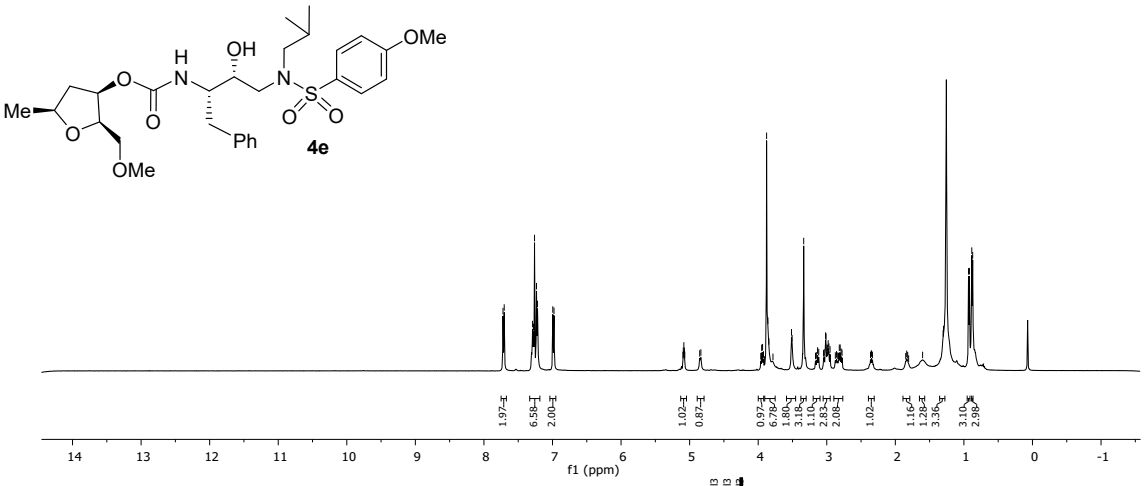

H1 standard parameters, CDCl3, QNP probe.
^{1}H NMR (400 MHz, $CDCl_3$)
^{13}C NMR (101 MHz, $CDCl_3$)
4b
Me
Ph
OH
NH$_2$
ppm

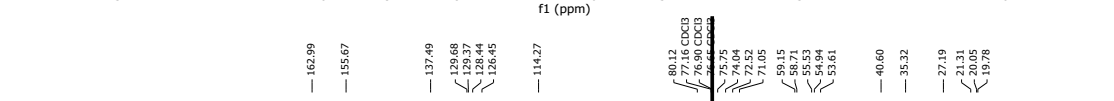

^{1}H NMR (400 MHz, $CDCl_3$)
OMe
OH
H
N
O
N
S
O
O
Me
O
O
Ph
OMe
4c
f1 (ppm)
^{13}C NMR (101 MHz, $CDCl_3$)
OMe
OH
H
N
O
N
S
O
O
Me
O
O
Ph
OMe
4c
f1 (ppm)


^{1}H NMR (400 MHz, $CDCl_3$)
^{13}C NMR (101 MHz, $CDCl_3$)
4d
f1 (ppm)

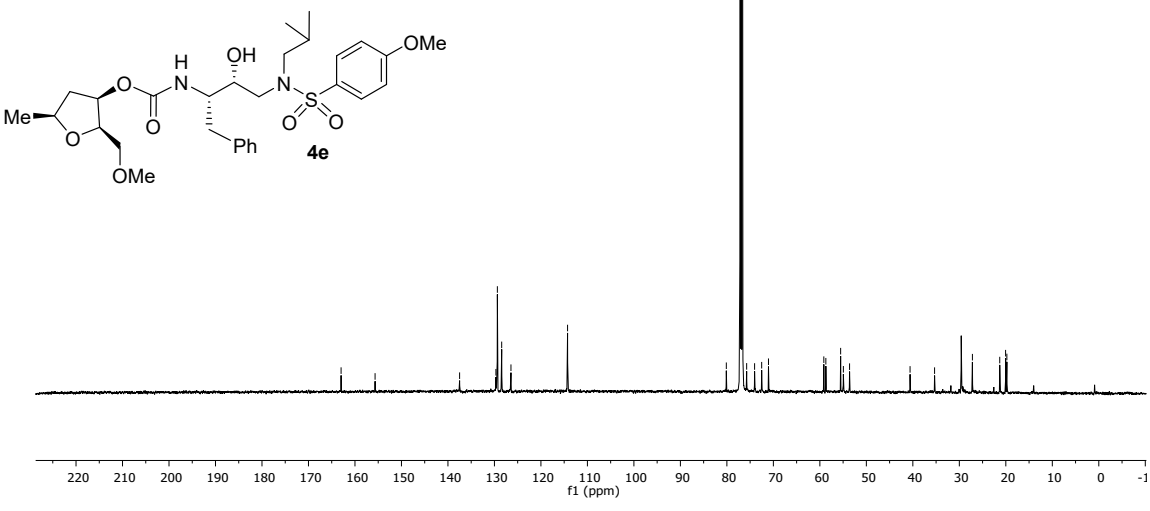


^{1}H NMR (500 MHz, $CDCl_3$)

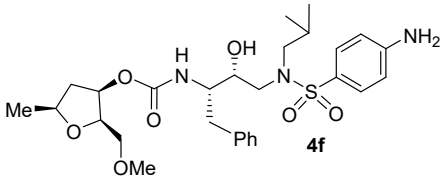




^{13}C NMR (126 MHz, $CDCl_3$)



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



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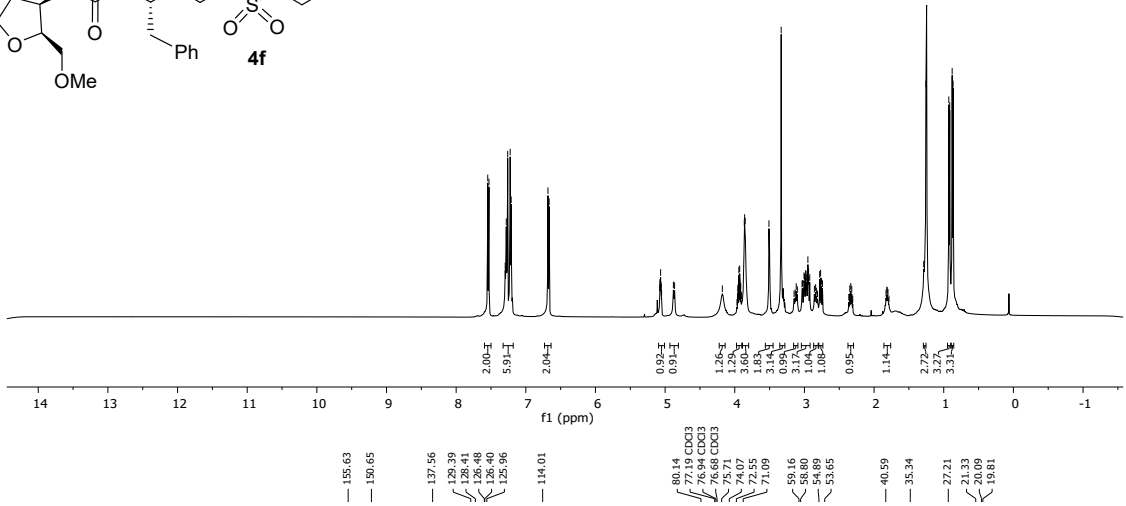
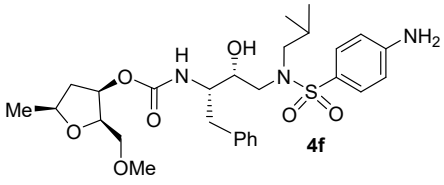


^{13}C NMR (126 MHz, $CDCl_3$)



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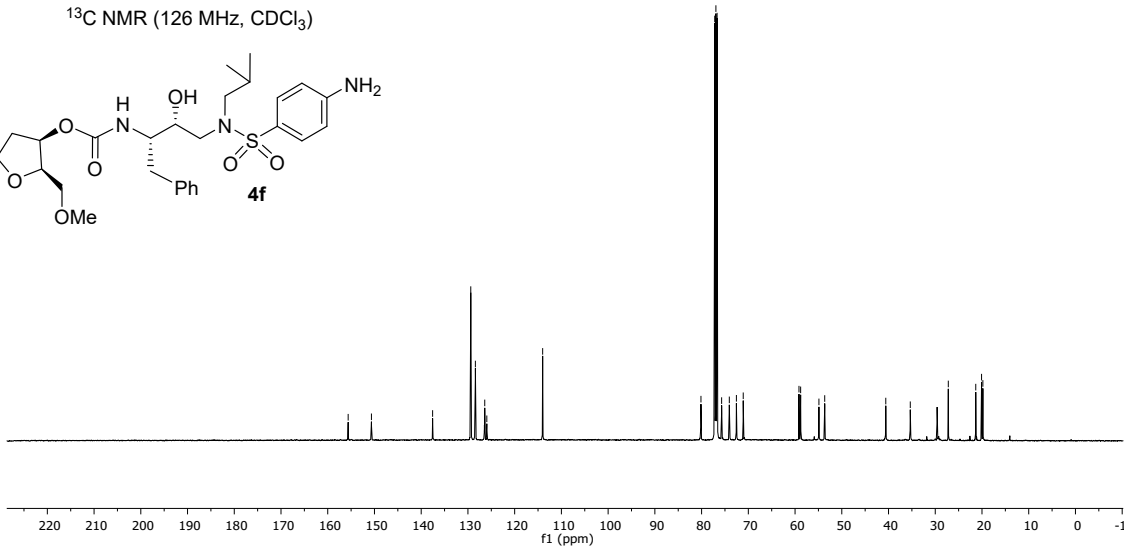
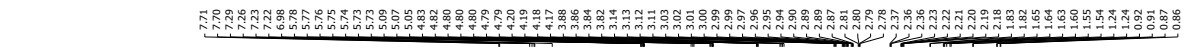
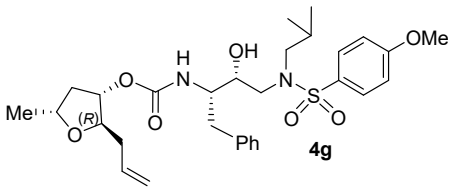
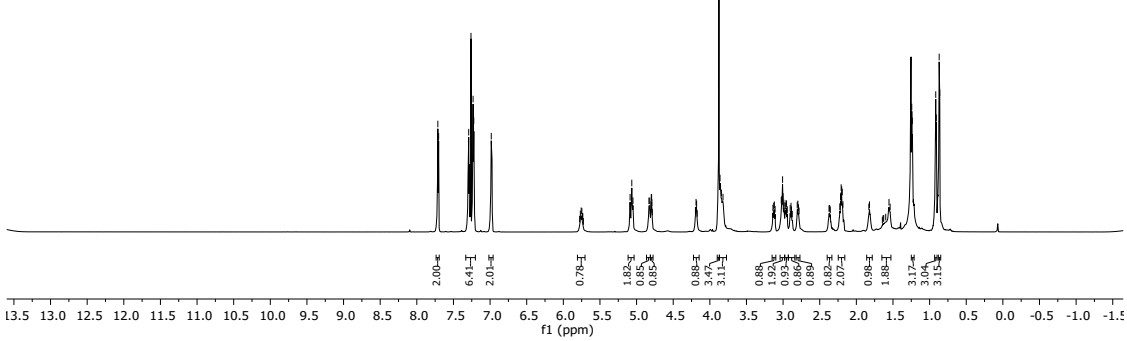




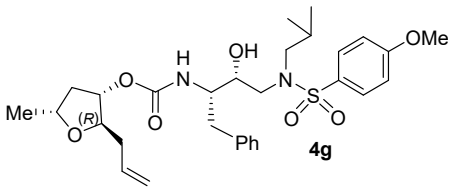
^{1}H NMR (800 MHz, $CDCl_3$)



4g



^{13}C NMR (201 MHz, $CDCl_3$)



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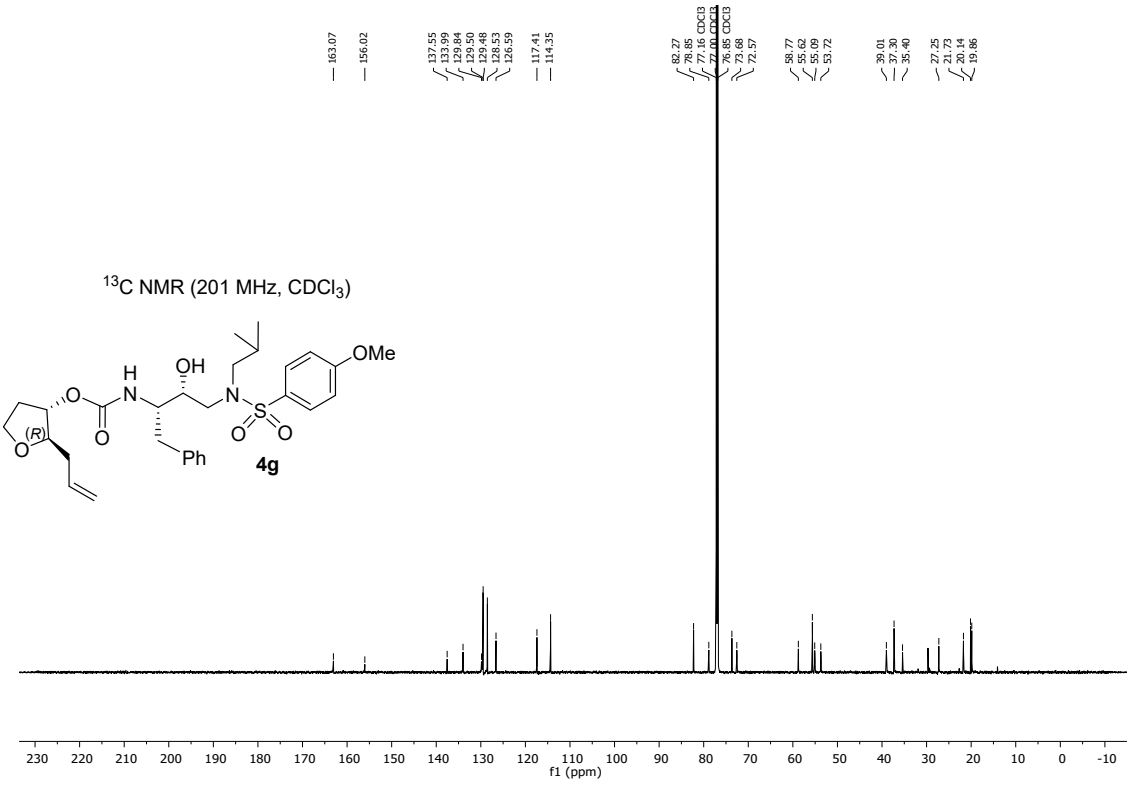
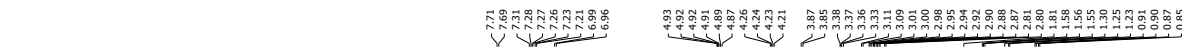
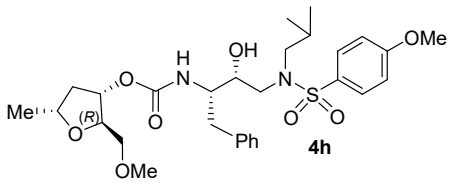
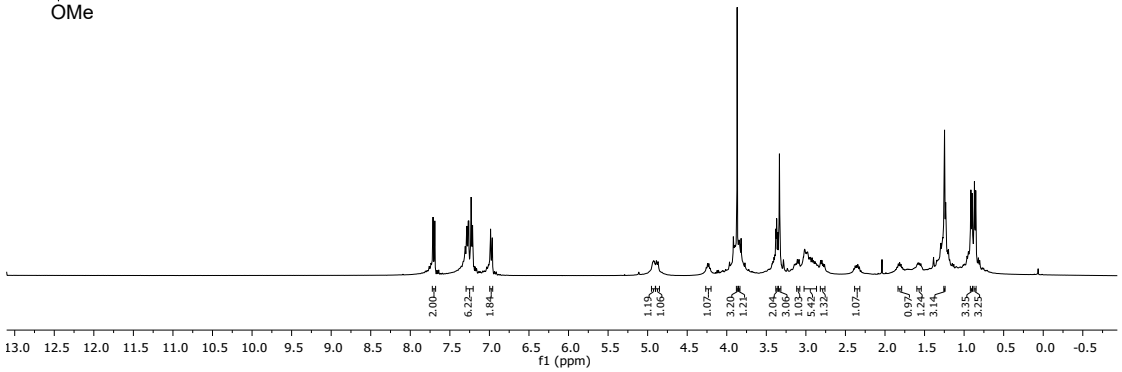


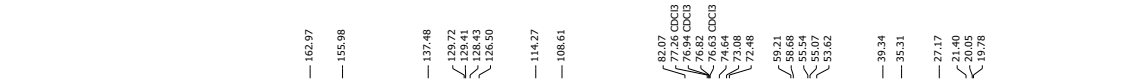


^{1}H NMR (400 MHz, $CDCl_3$)

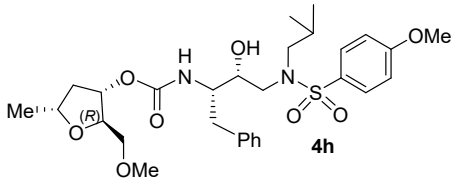


4h





^{13}C NMR (101 MHz, $CDCl_3$)



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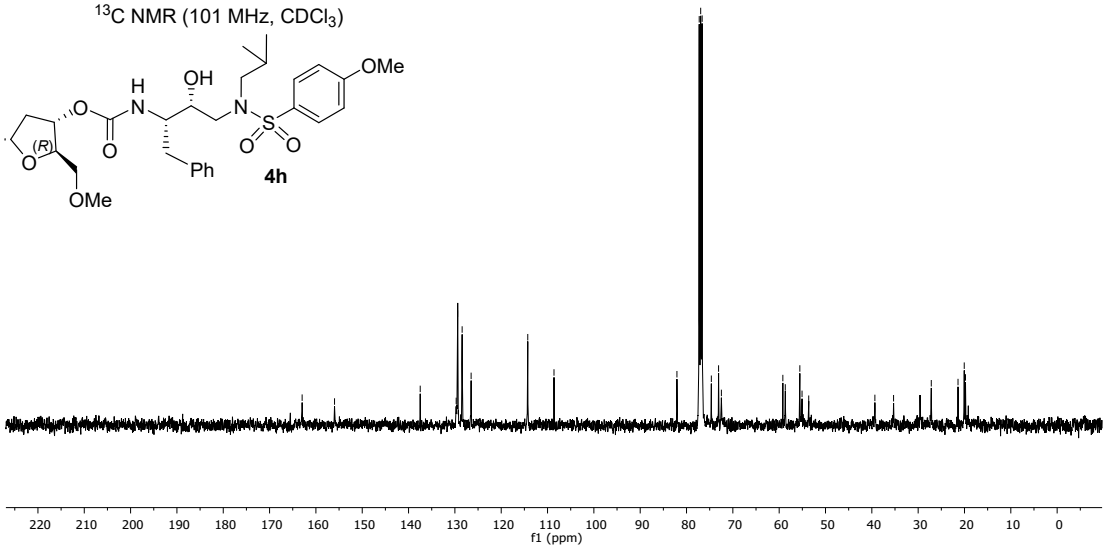
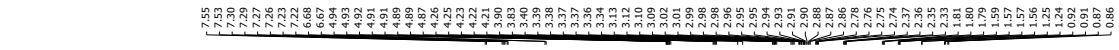
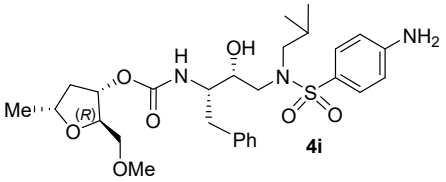
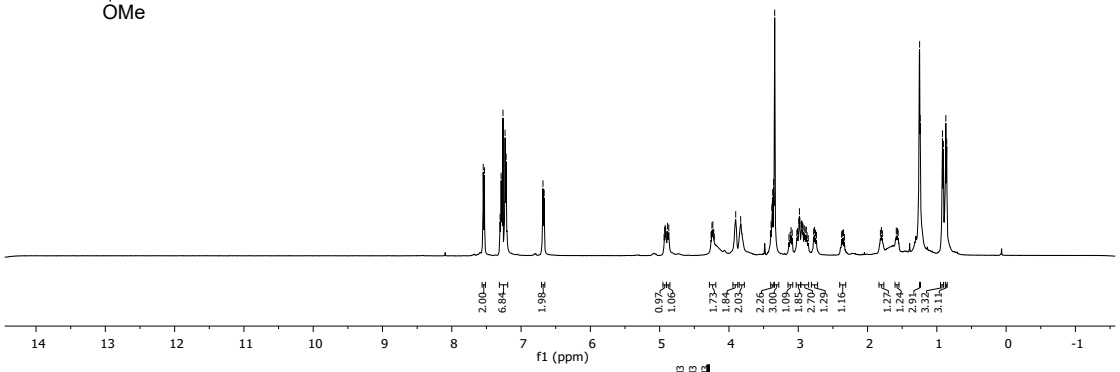
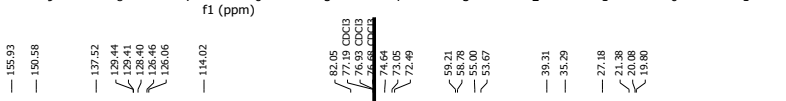




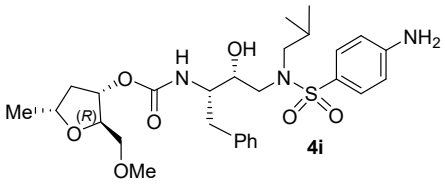
^{1}H NMR (500 MHz, $CDCl_3$)

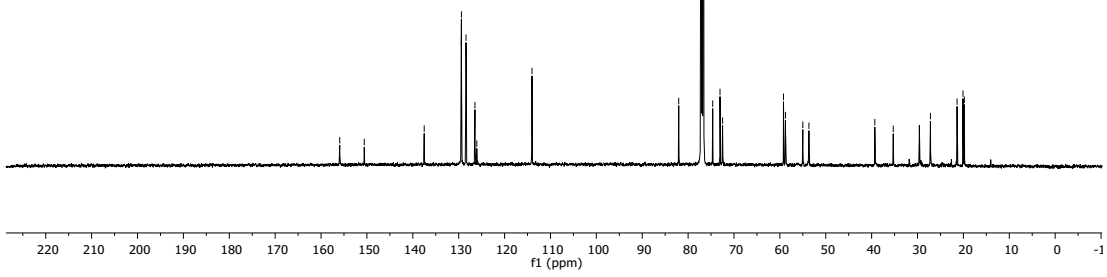


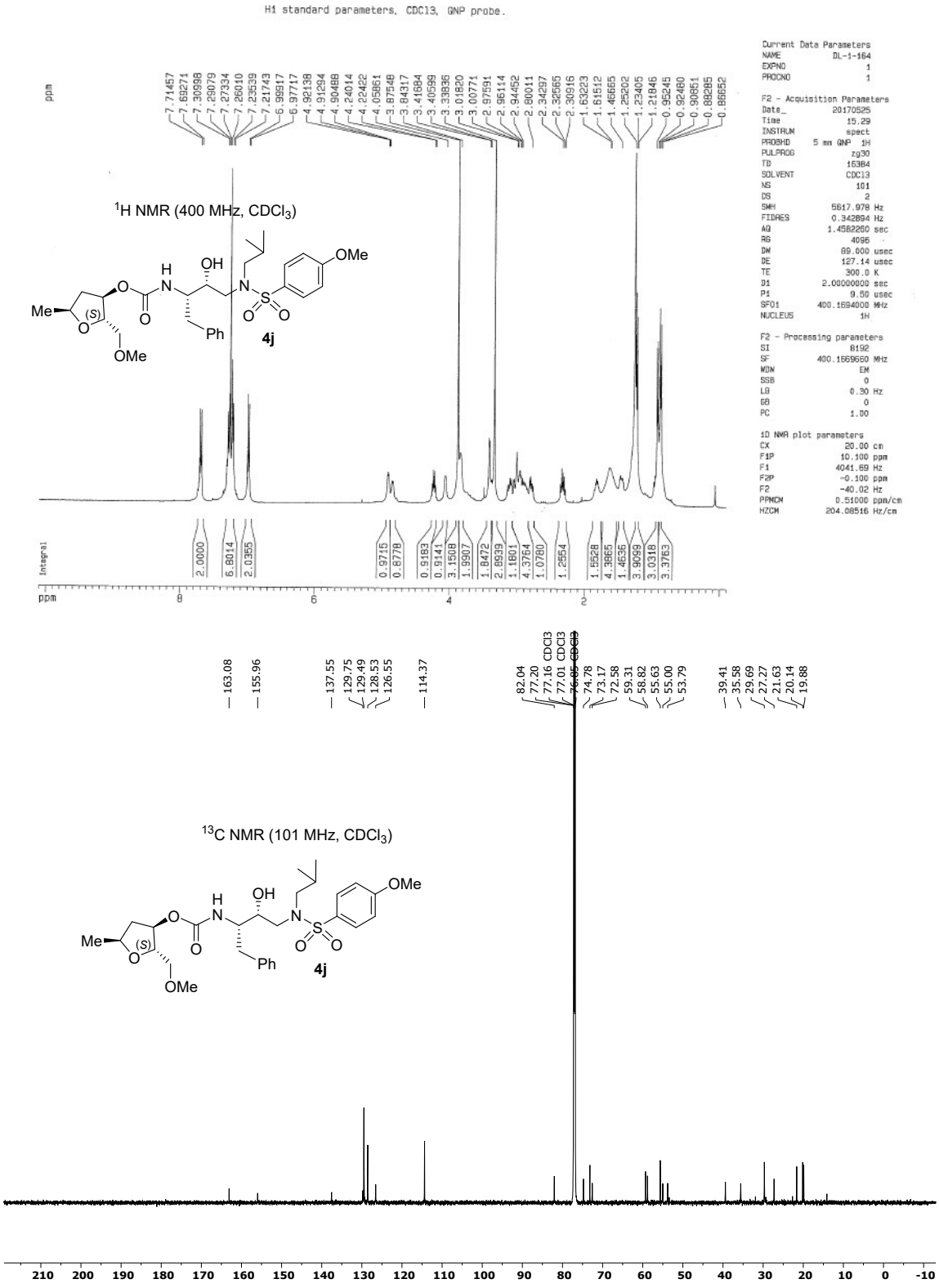


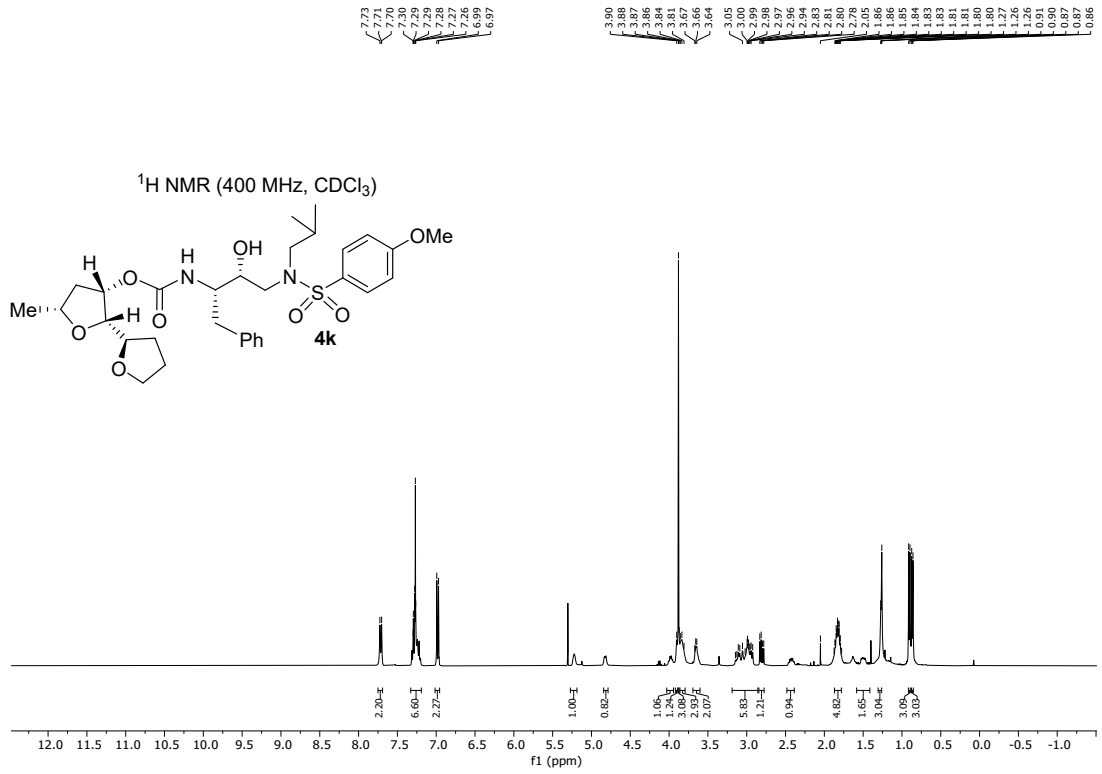


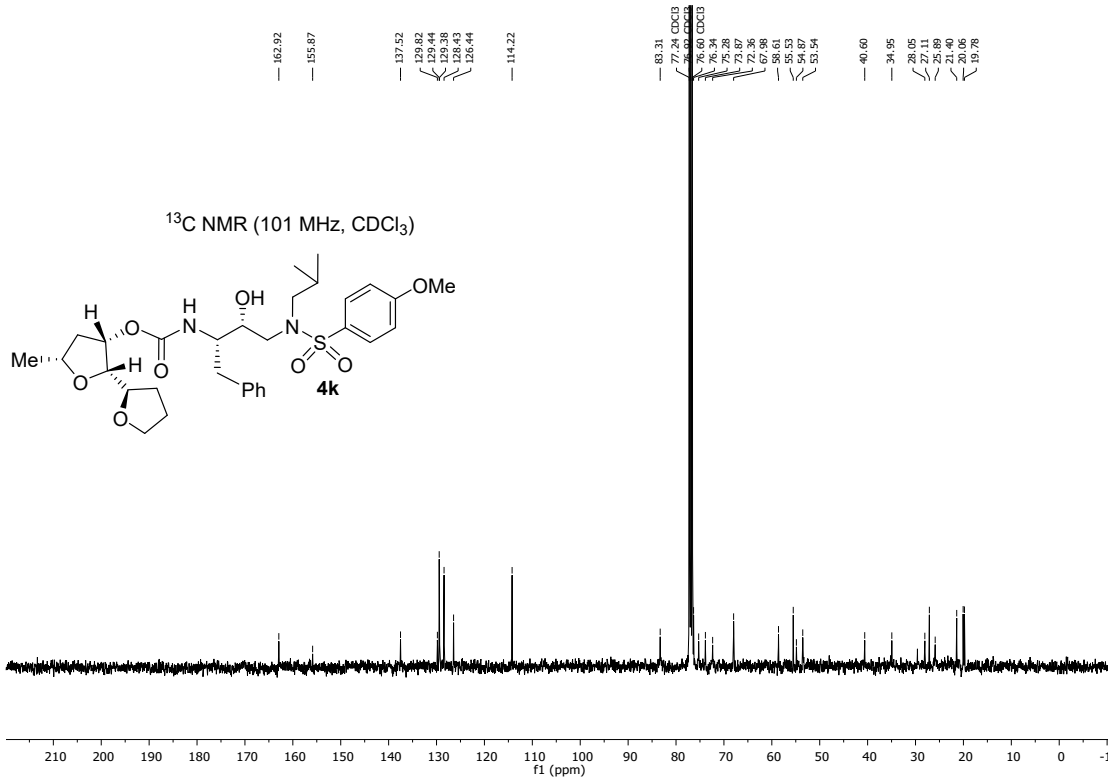
^{13}C NMR (126 MHz, $CDCl_3$)

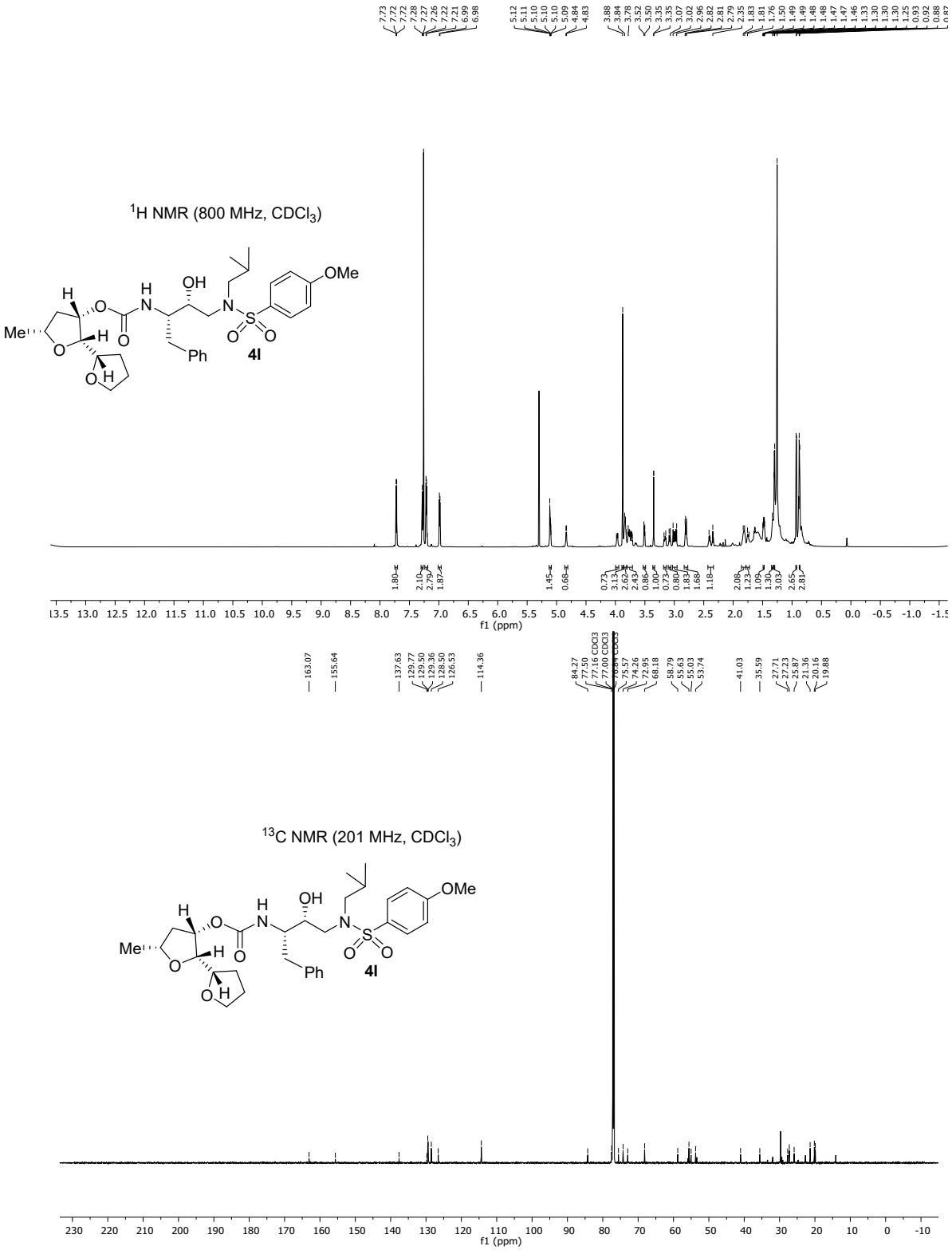




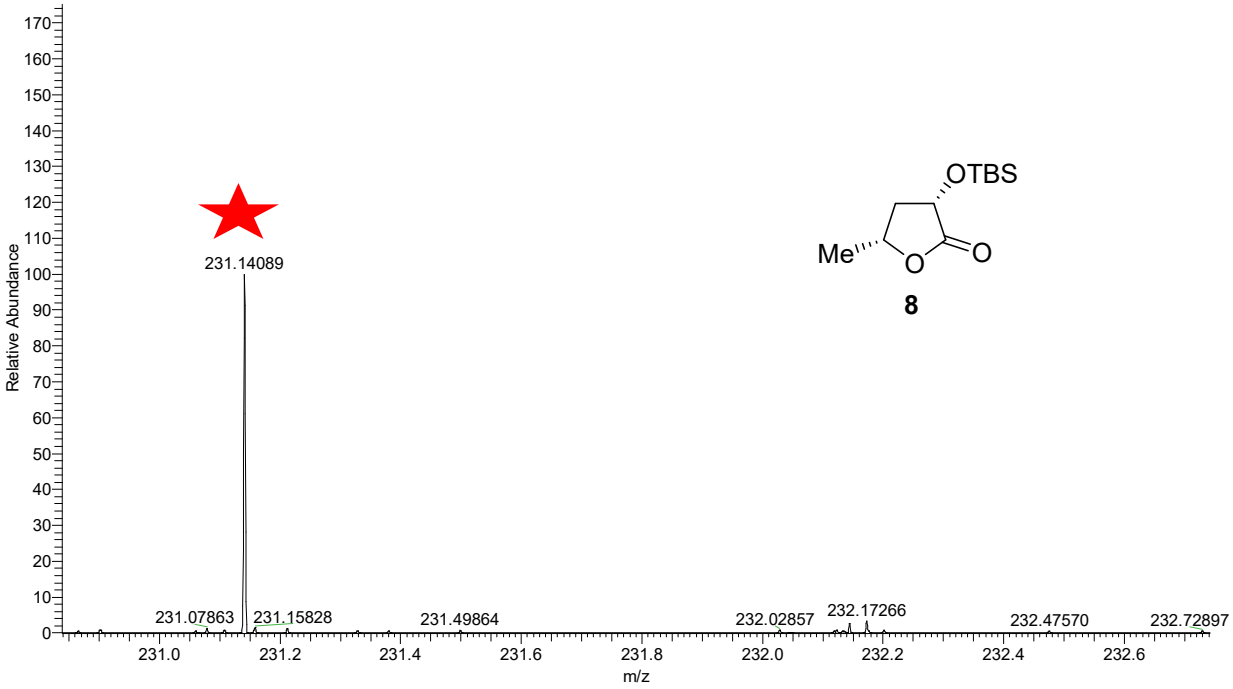

H1 standard parameters, CDCl3, QNP probe.
^{1}H NMR (400 MHz, $CDCl_3$)
4j
^{13}C NMR (101 MHz, $CDCl_3$)
4j


^{1}H NMR (400 MHz, $CDCl_3$)
OMe
OH
H
N
S
O
Me
Ph
4k
f1 (ppm)


^{13}C NMR (101 MHz, $CDCl_3$)
OMe
OH
H
N
S
O
Me
Ph
4k
f1 (ppm)

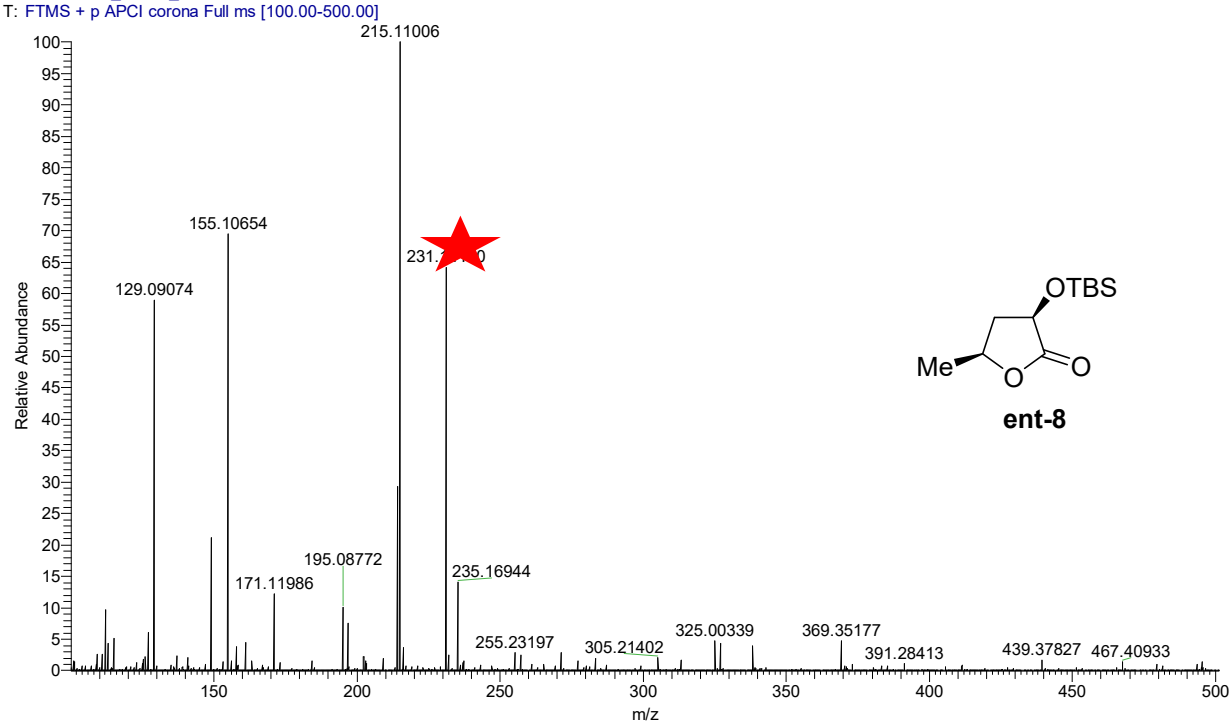

^{1}H NMR (800 MHz, $CDCl_3$)
4l
^{13}C NMR (201 MHz, $CDCl_3$)
4l
f1 (ppm)

RIC-AS-12455_ESI+_ACN+H2O_DL-01-114-8 #1-36 RT: 0.00-0.50 AV: 36 NL: 3.37E5
T: FTMS + p ESI Full ms [100.00-800.00]



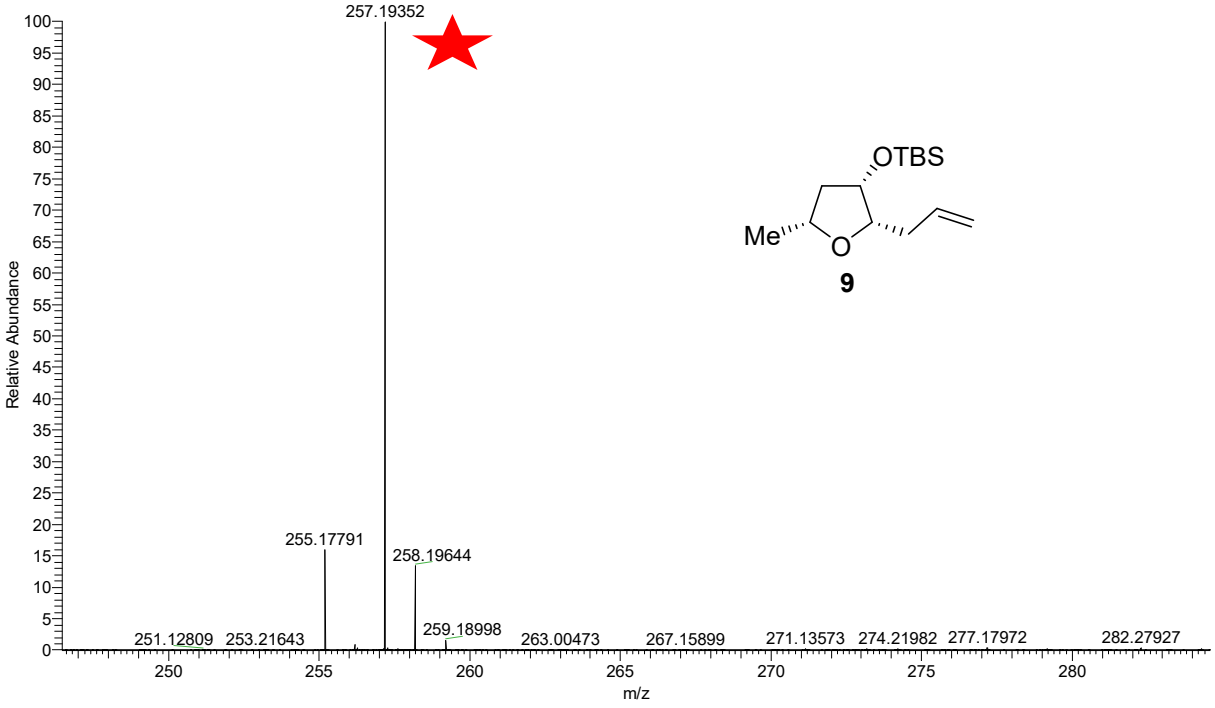
8

RIC-AS-12464_APCI+_ASH-OBC-ENT-8 #1-30 RT: 0.01-0.45 AV: 30 NL: 1.01E6
T: FTMS + p APCI corona Full ms [100.00-500.00]



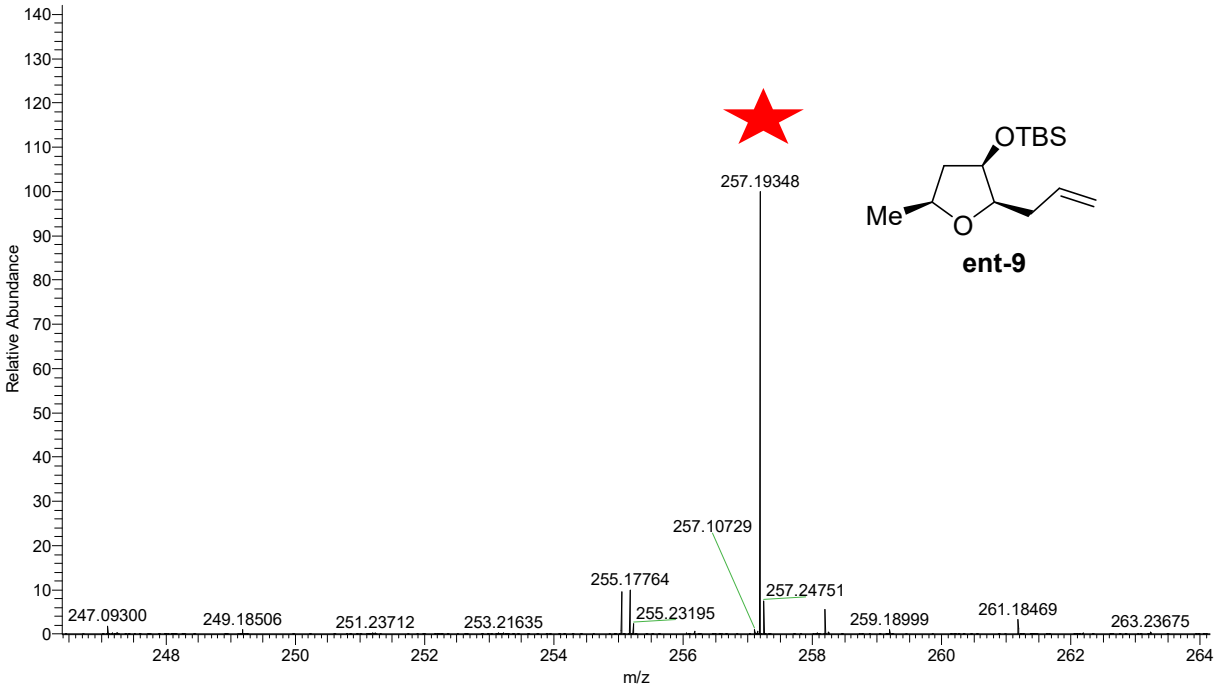
ent-8

RIC-AS-12455_APCI+_ACN+H2O_ASH-OBC-9 #1-35 RT: 0.00-0.50 AV: 35 NL: 8.98E6
T: FTMS + p APCI corona Full ms [100.00-800.00]



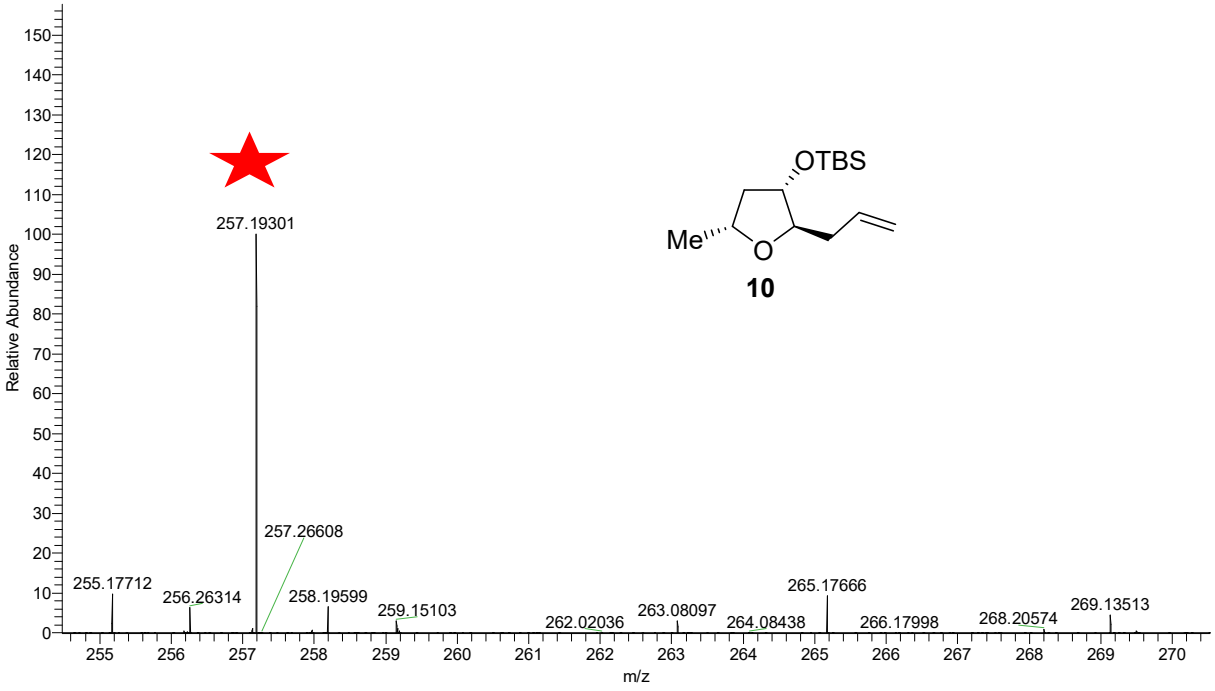
9

RIC-AS-12472_APCI+_MeOH_ASH-OBC-ent-9 #1-30 RT: 0.00-0.44 AV: 30 NL: 3.82E5
T: FTMS + p APCI corona Full ms [100.00-500.00]



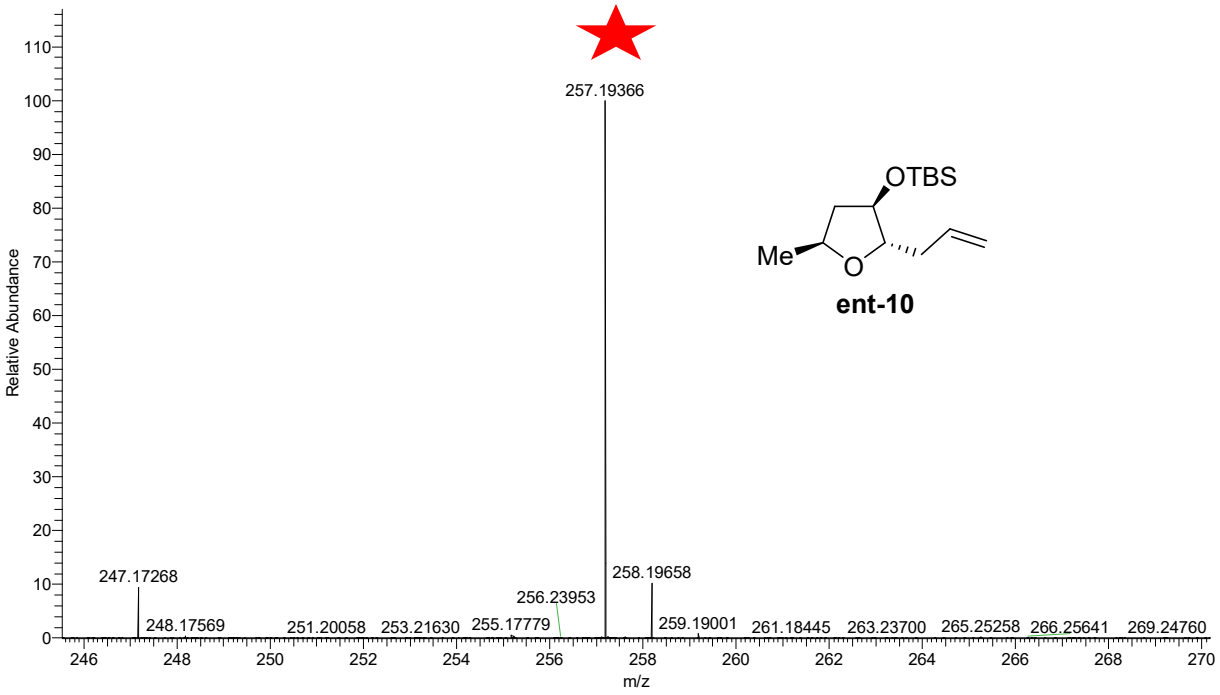
ent-9

RIC-AS-12455_ESI+_ACN+H2O_DL-01-125-10 #1-36 RT: 0.00-0.50 AV: 36 NL: 7.71E6
T: FTMS + p ESI Full ms [100.00-800.00]



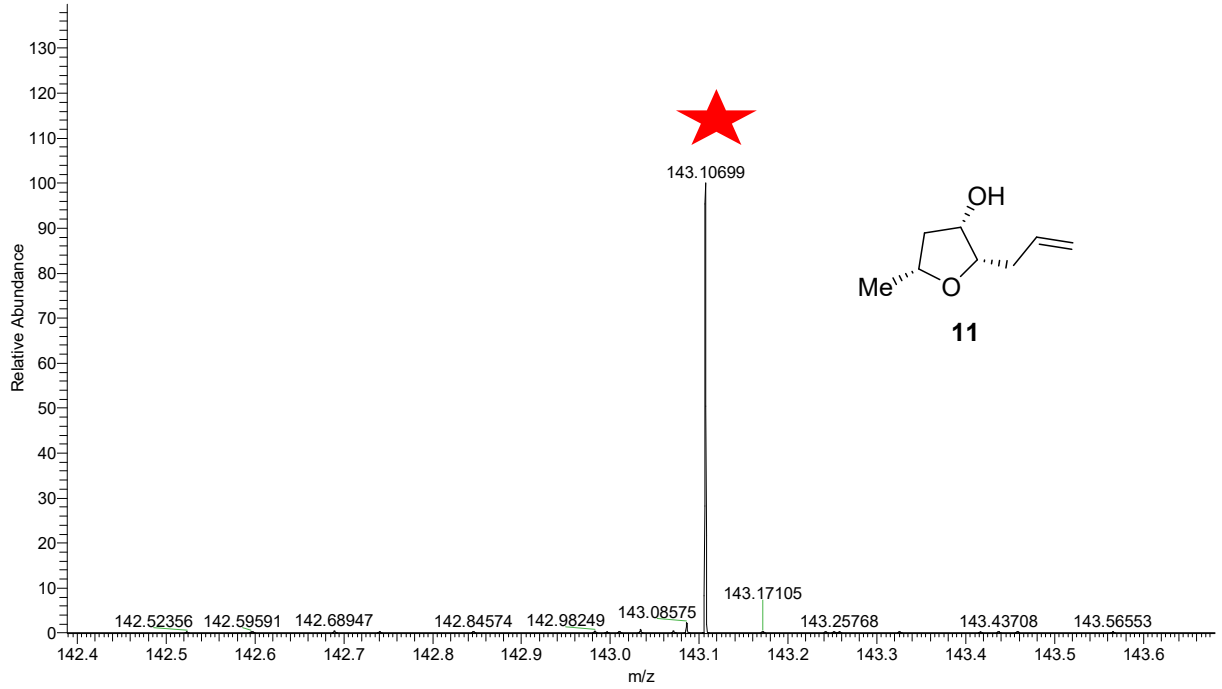
10

RIC-AS-12472_APCI+_MeOH_ASH-OBC-ent-10 #1-30 RT: 0.01-0.43 AV: 30 NL: 6.21E6
T: FTMS + p APCI corona Full ms [100.00-500.00]



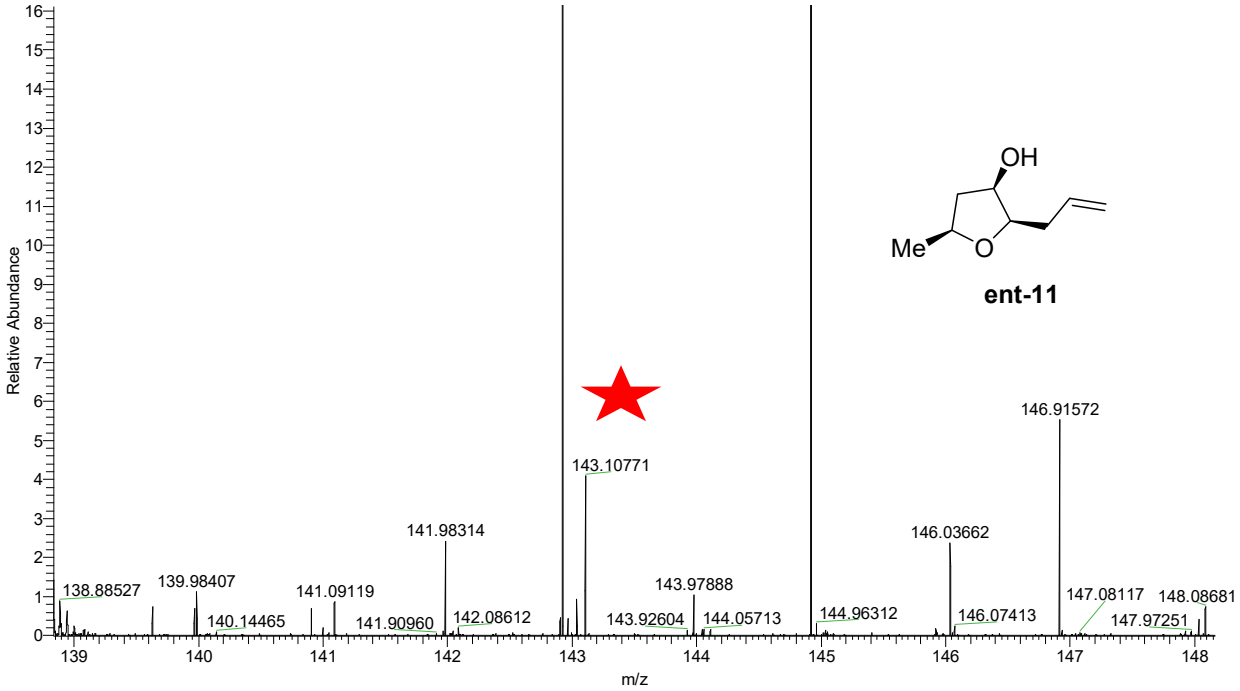
ent-10

RIC-AS-12464_APCI+_ASH-OBC-11 #1-30 RT: 0.01-0.45 AV: 30 NL: 2.85E4
T: FTMS + p APCI corona Full ms [105.00-195.00]



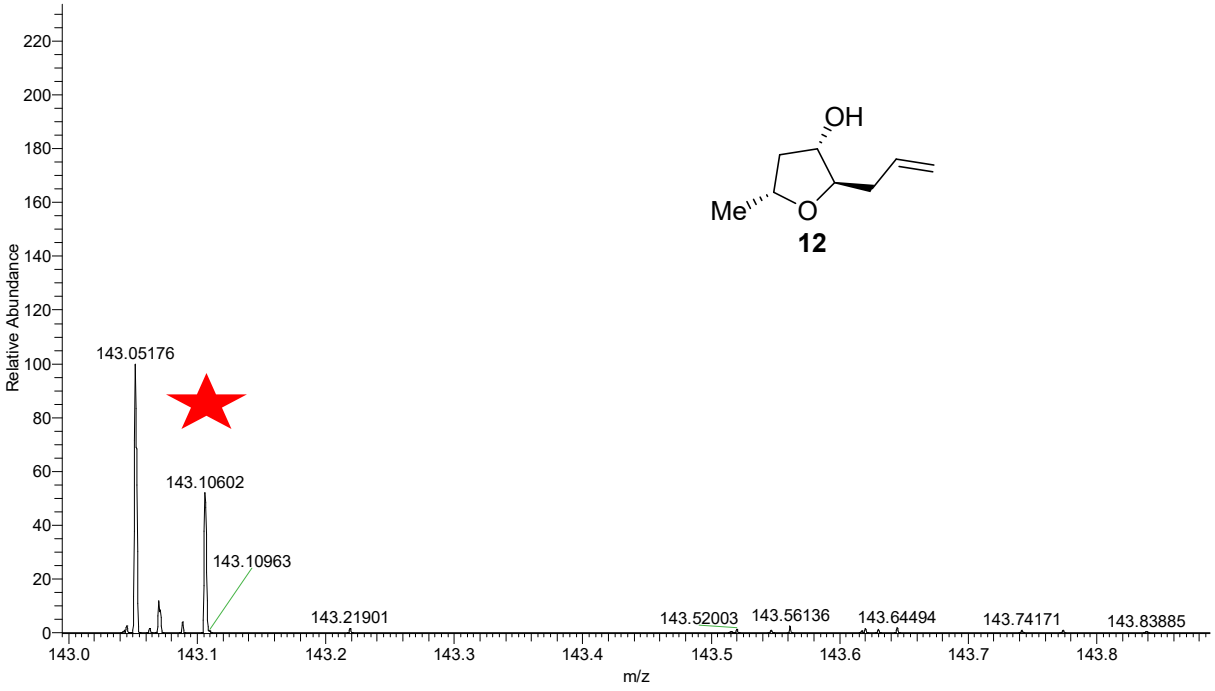
11

RIC-AS-12464_APCI+_ASH-OBC-Ent-11 #1-30 RT: 0.01-0.44 AV: 30 NL: 6.21E5
T: FTMS + p APCI corona Full ms [105.00-195.00]



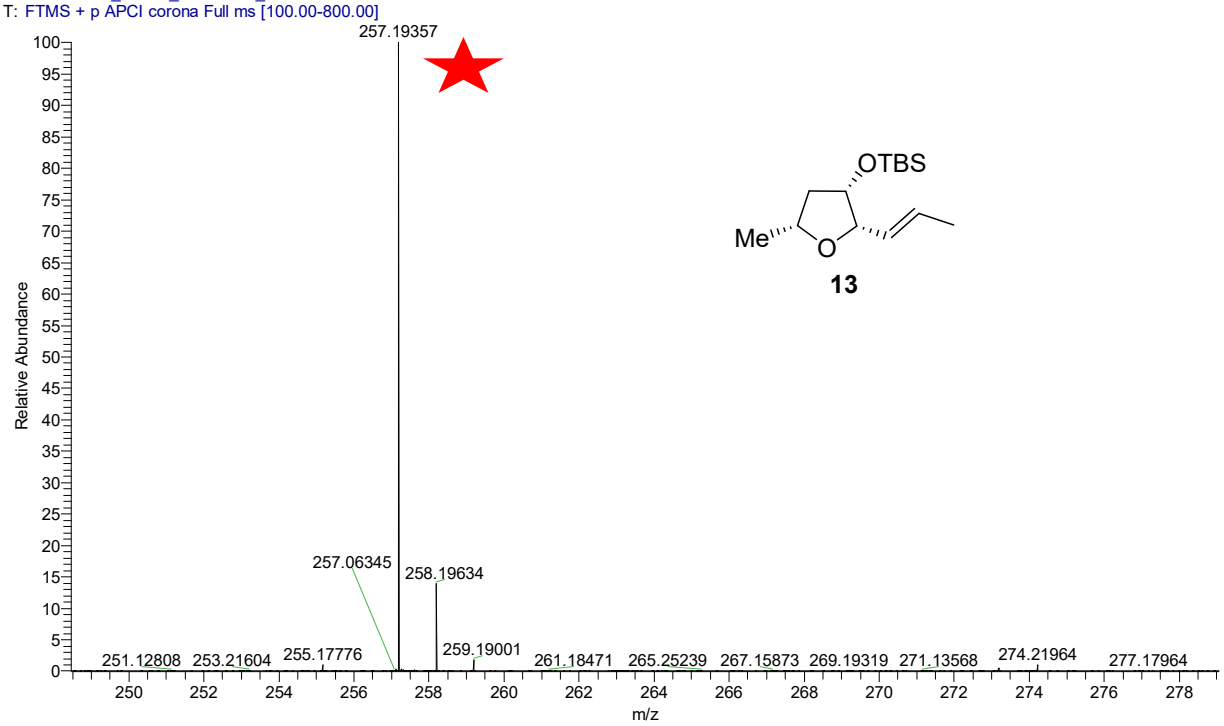
ent-11

RIC-AS-12455_APCI+_ACN+H2O_DL-01-123-12 #1-35 RT: 0.01-0.49 AV: 35 NL: 1.14E5
T: FTMS + p APCI corona Full ms [100.00-800.00]

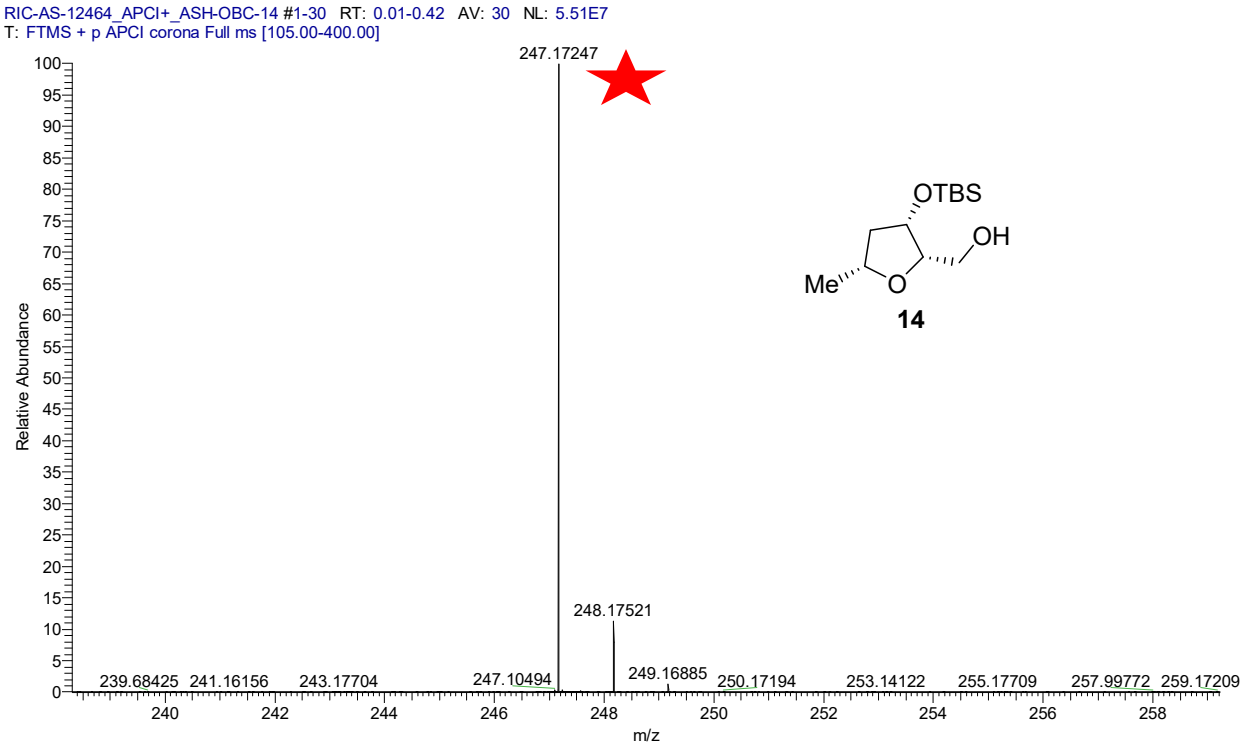


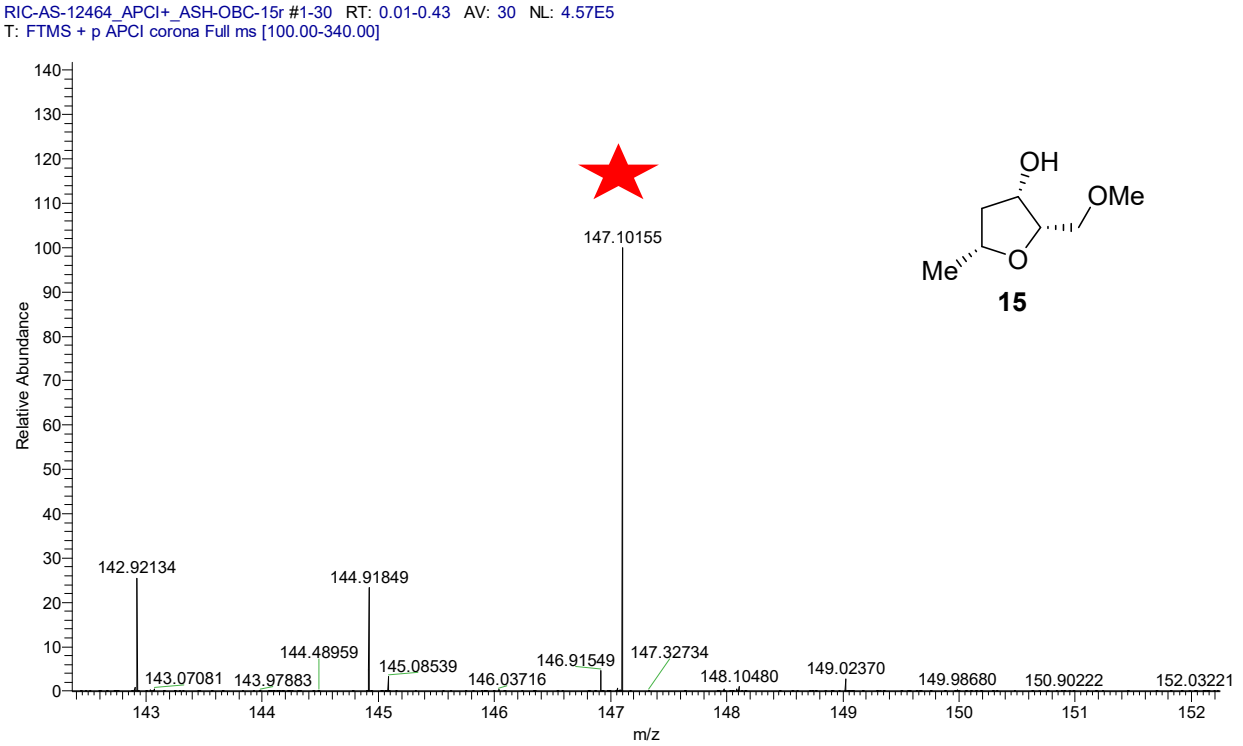
12

RIC-AS-12455_APCI+_ACN+H2O_ASH-OBC-13 #1-34 RT: 0.01-0.49 AV: 34 NL: 2.40E7
T: FTMS + p APCI corona Full ms [100.00-800.00]

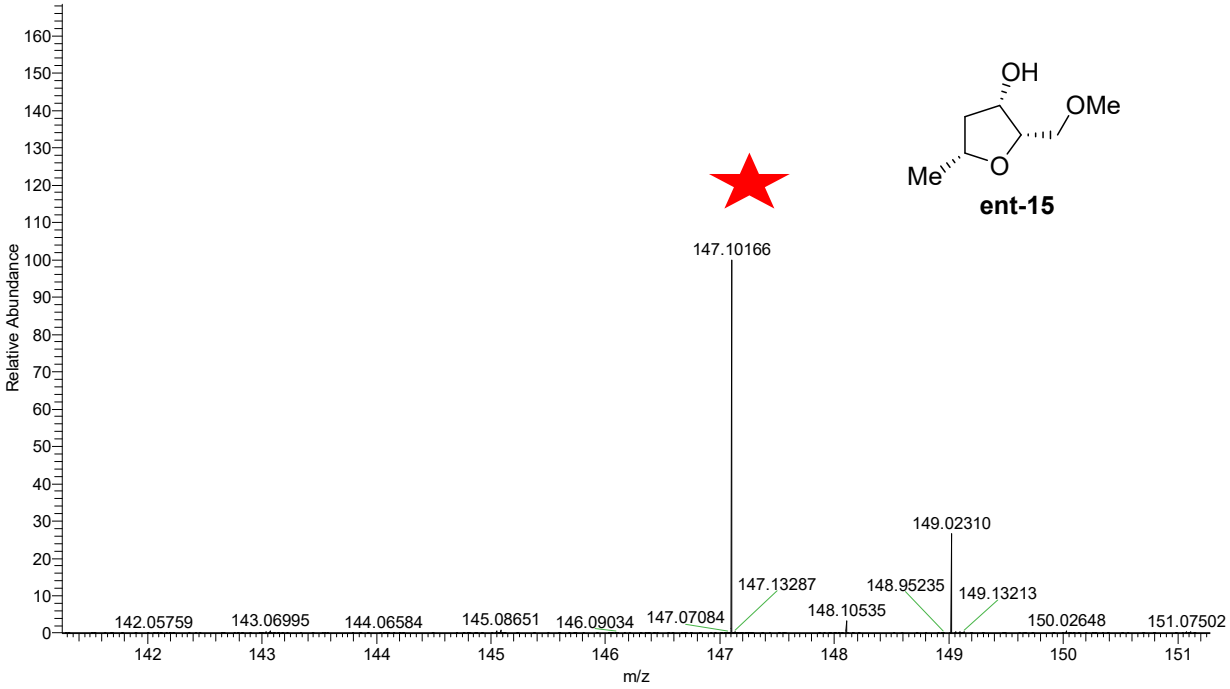


13

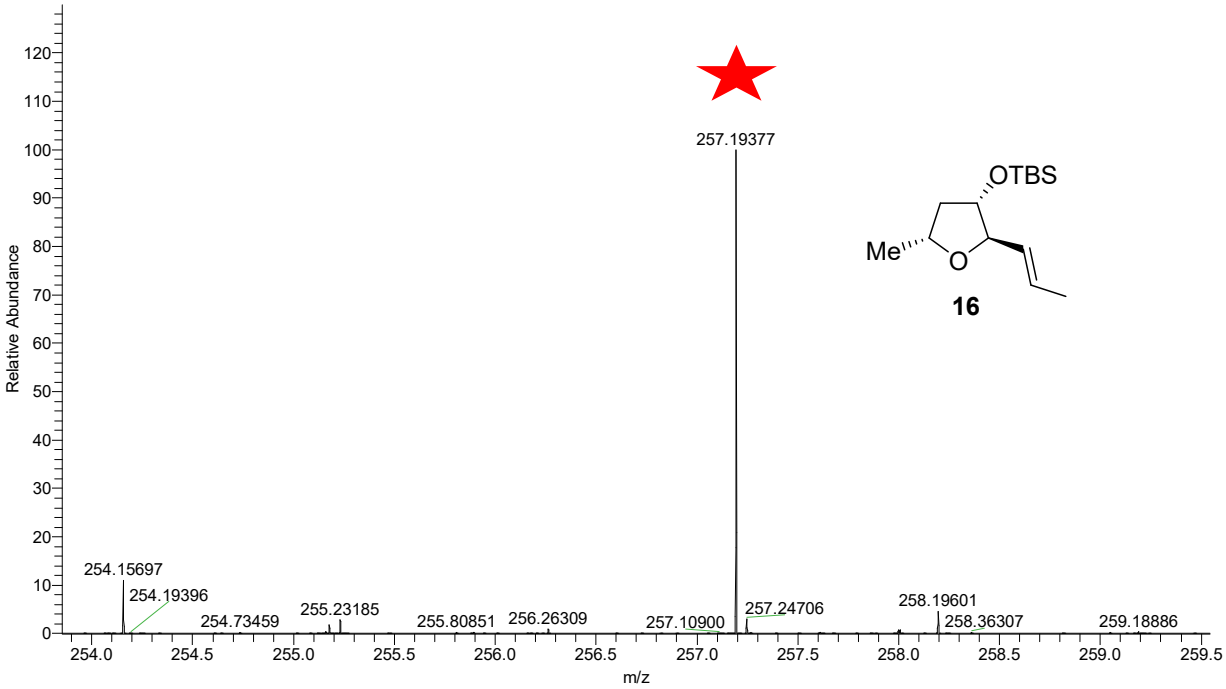

RIC-AS-12464_APCI+_ASH-OBC-14 #1-30 RT: 0.01-0.42 AV: 30 NL: 5.51E7
T: FTMS + p APCI corona Full ms [105.00-400.00]
247.17247
248.17521
239.68425
241.16156
243.17704
247.10494
249.16885
250.17194
253.14122
255.17709
257.99772
259.17209
Relative Abundance
m/z
OTBS
OH
Me
O
14


RIC-AS-12464_APCI+_ASH-OBC-15r #1-30 RT: 0.01-0.43 AV: 30 NL: 4.57E5
T: FTMS + p APCI corona Full ms [100.00-340.00]
147.10155
142.92134
144.91849
144.48959
143.07081
143.97883
145.08539
146.03716
146.91549
147.32734
148.10480
149.02370
149.98680
150.90222
152.03221
Relative Abundance
m/z
OH
OMe
Me
O
15

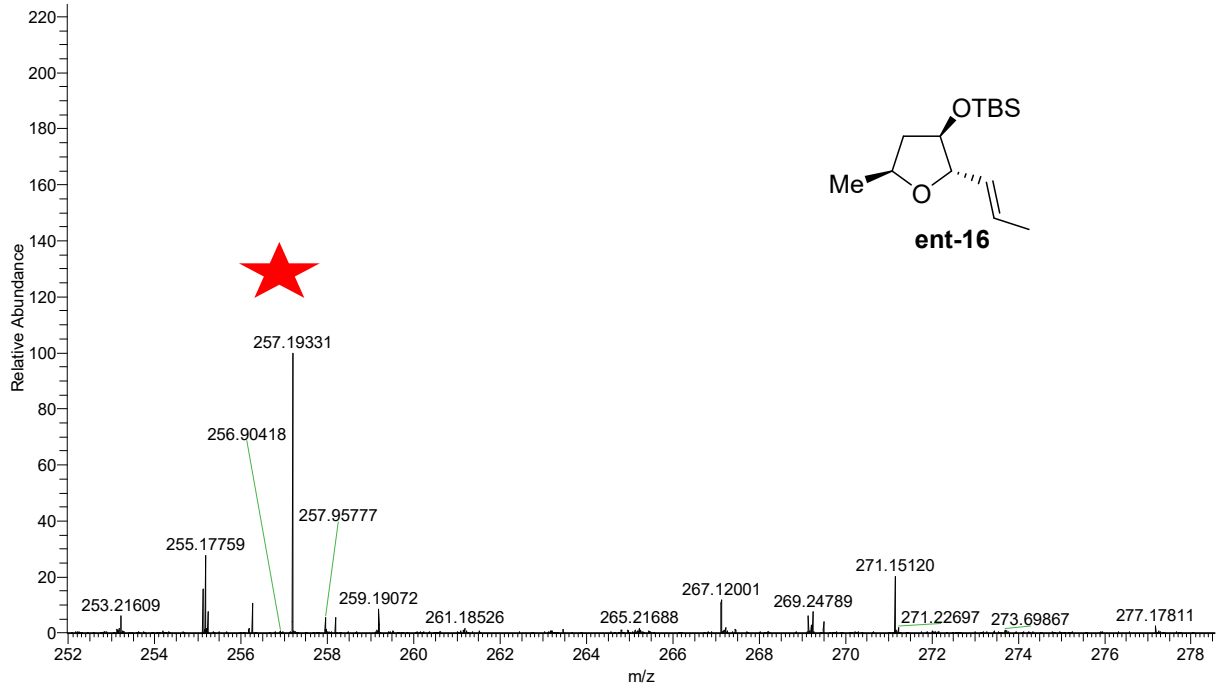
RIC-AS-12472_APCI+_MeOH_ASH-OBC-ent-15 #1-30 RT: 0.00-0.44 AV: 30 NL: 5.36E5
T: FTMS + p APCI corona Full ms [100.00-500.00]



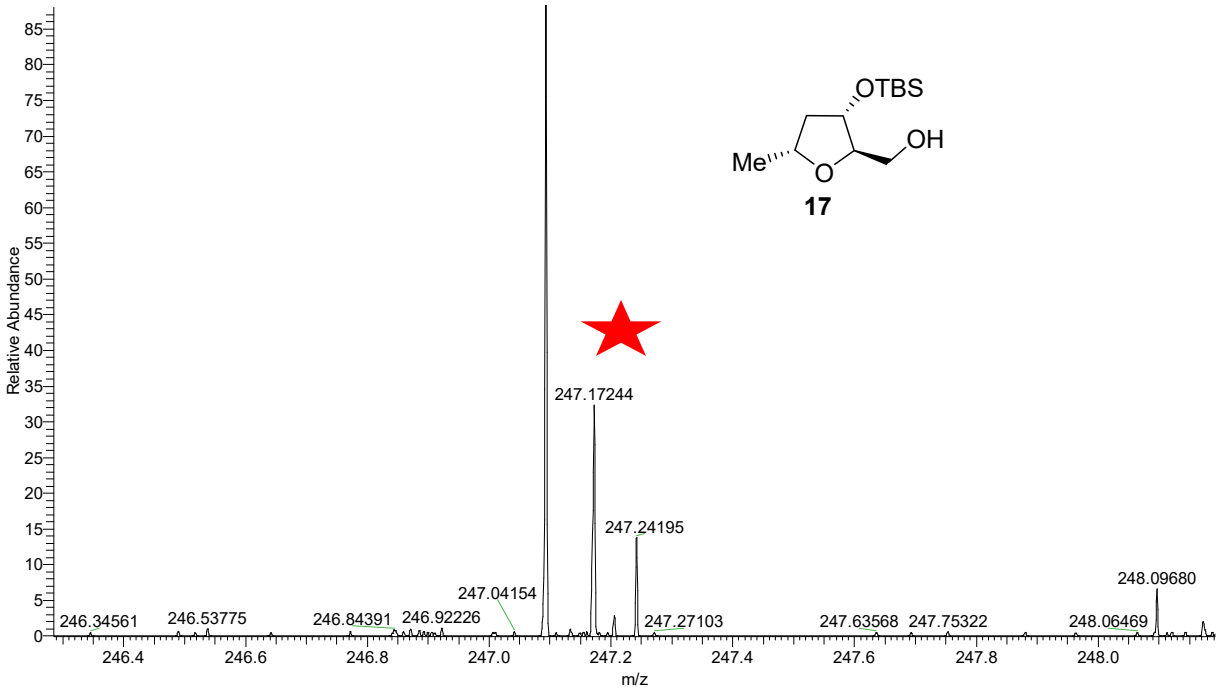
RIC-AS-12464_APCI+_ASH-OBC-16 #1-30 RT: 0.01-0.44 AV: 30 NL: 3.88E5
T: FTMS + p APCI corona Full ms [160.00-500.00]



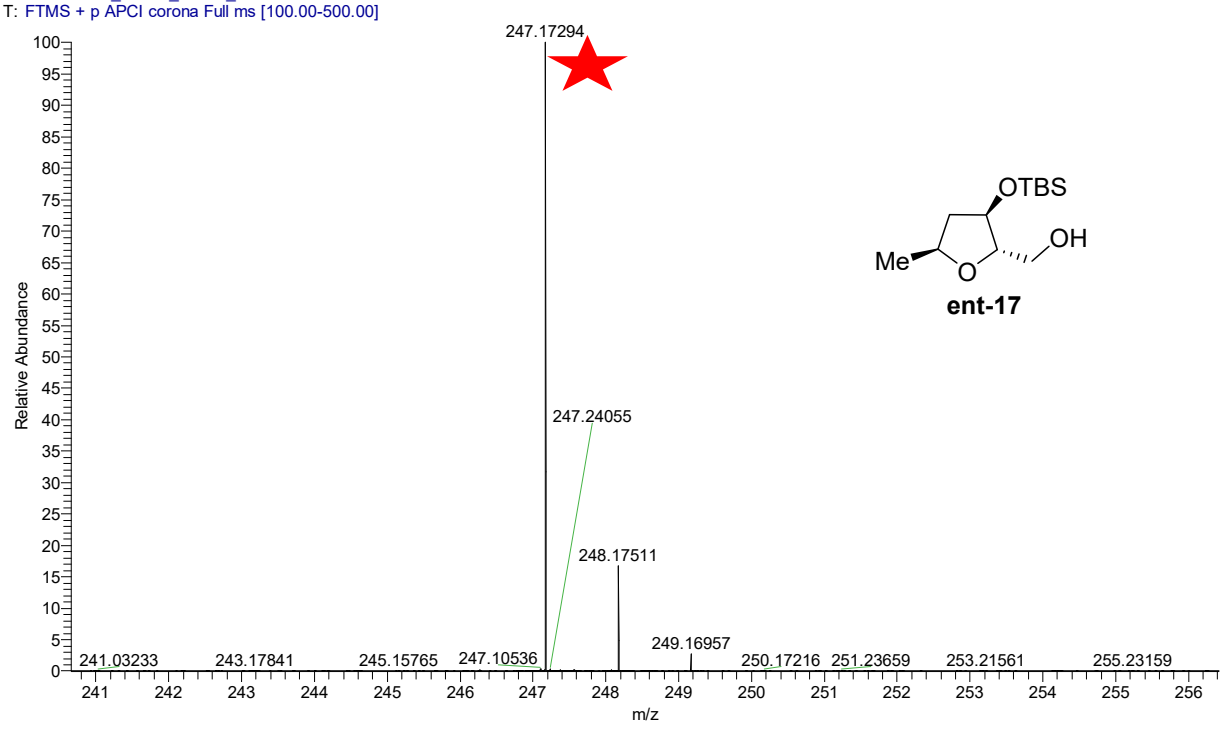
RIC-AS-12455_ESI+_ACN+H2O_DL-01-159-ENT-16 #1-34 RT: 0.01-0.49 AV: 34 NL: 1.41E5
T: FTMS + p ESI Full ms [100.00-800.00]



RIC-AS-12464_APCI+_ASH-OBC-17 #1-30 RT: 0.01-0.45 AV: 30 NL: 1.52E4
T: FTMS + p APCI corona Full ms [105.00-400.00]

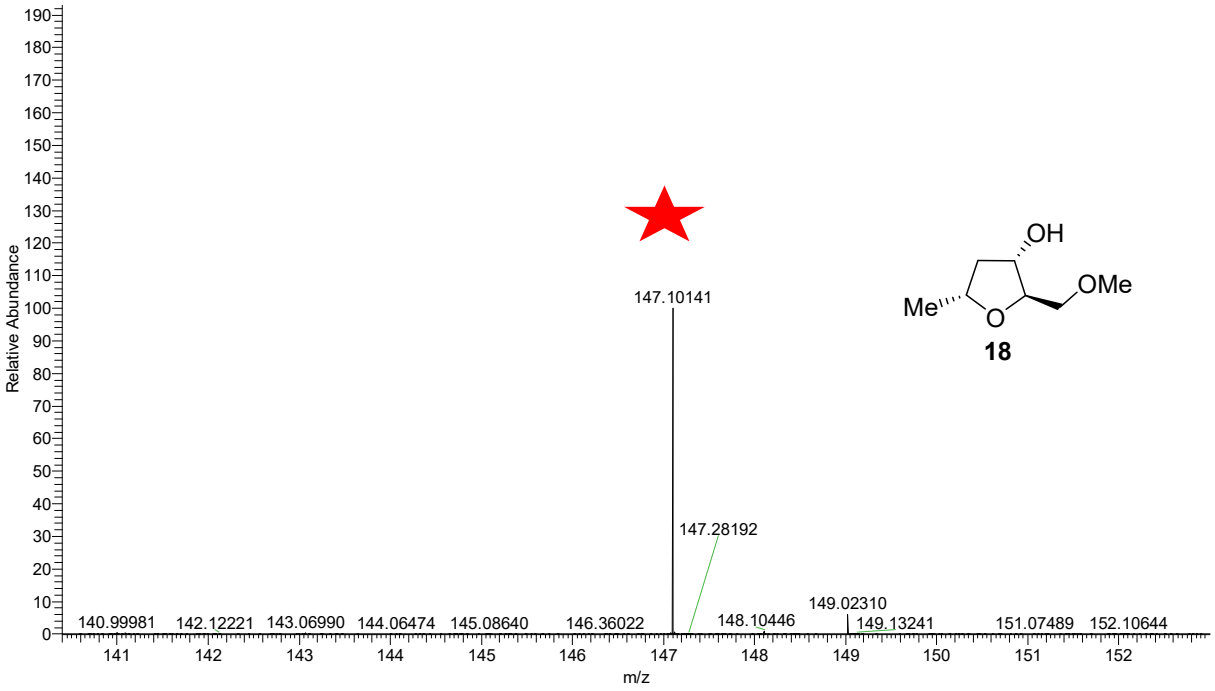


RIC-AS-12472_APCI+_MeOH_ASH-OBC-ent-17 #1-30 RT: 0.01-0.43 AV: 30 NL: 3.75E7
T: FTMS + p APCI corona Full ms [100.00-500.00]



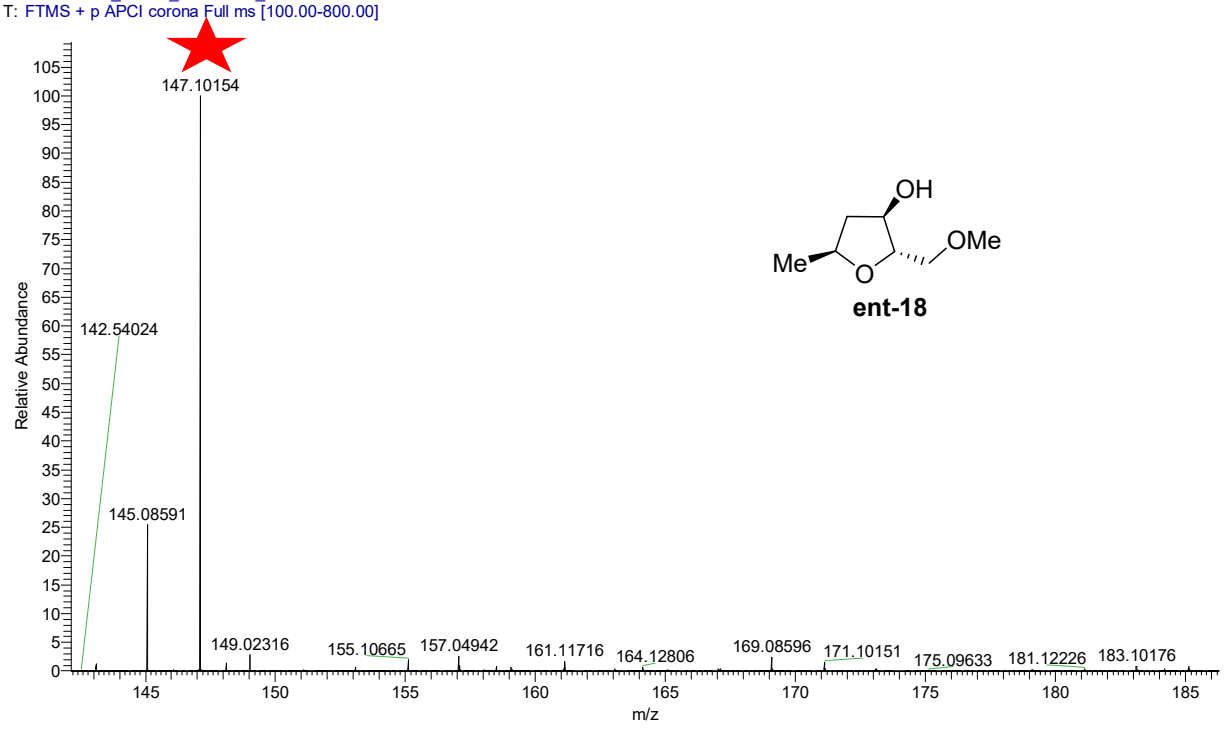
ent-17

RIC-AS-12464_APCI+_ASH-OBC-18 #1-30 RT: 0.00-0.42 AV: 30 NL: 1.43E6
T: FTMS + p APCI corona Full ms [100.00-500.00]



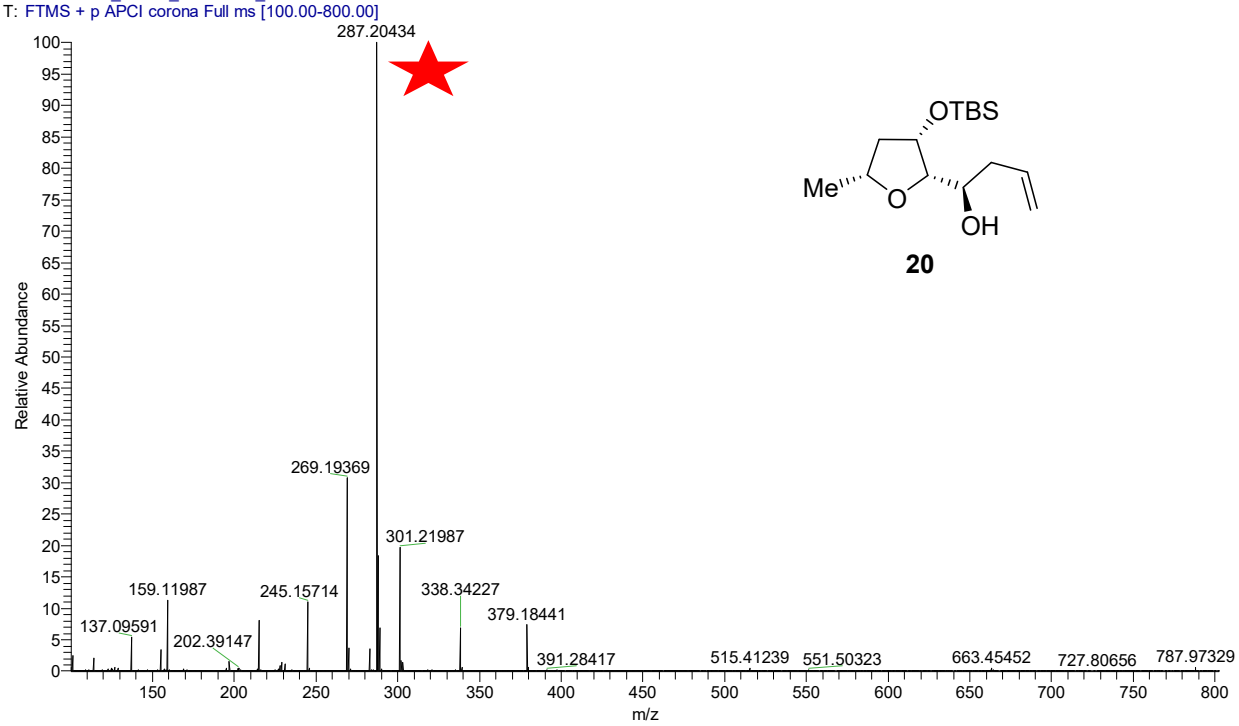
18

RIC-AS-12455_APCI+_ACN+H2O_DL-01-081-ENT-18 #1-34 RT: 0.01-0.49 AV: 34 NL: 2.59E6
T: FTMS + p APCI corona Full ms [100.00-800.00]

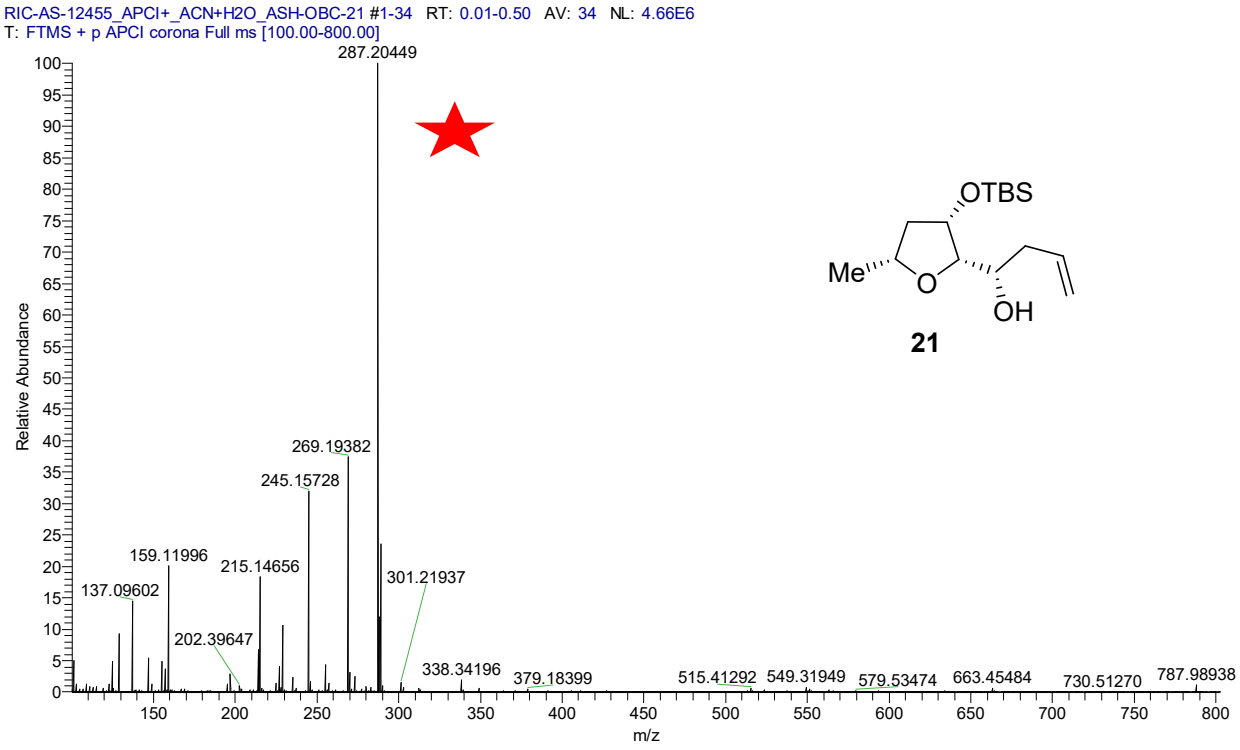


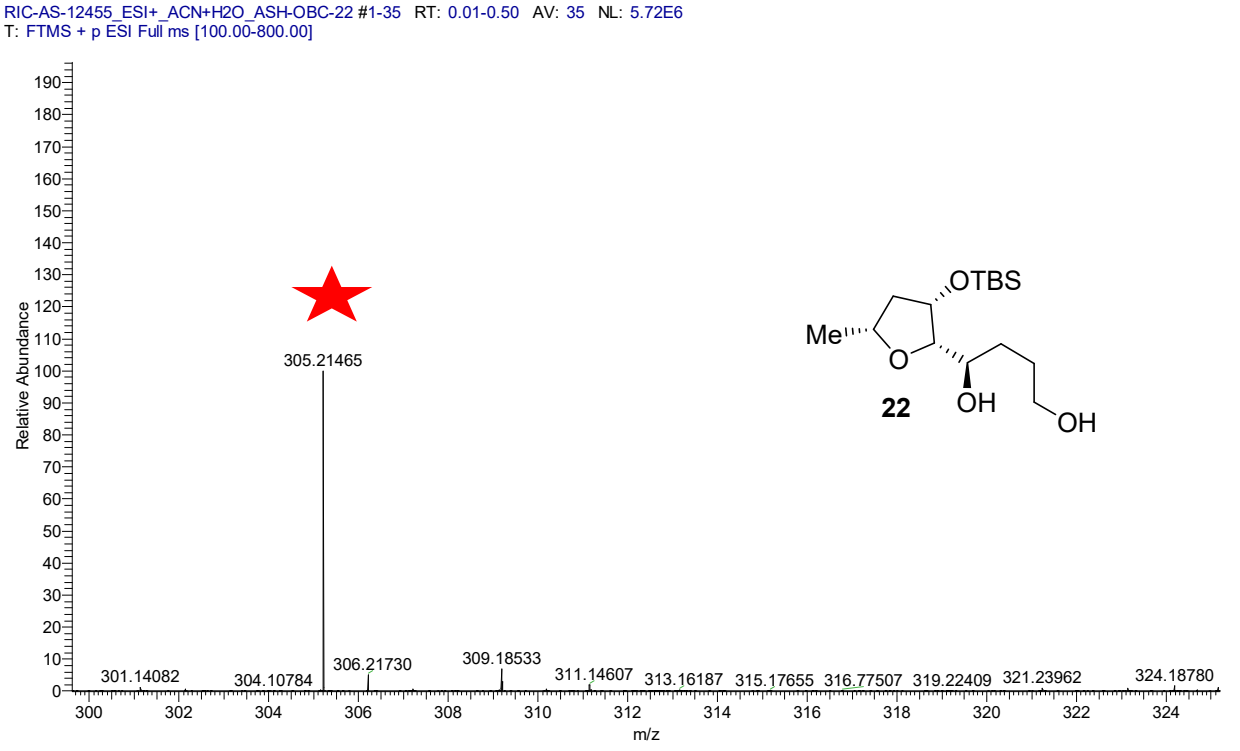
ent-18

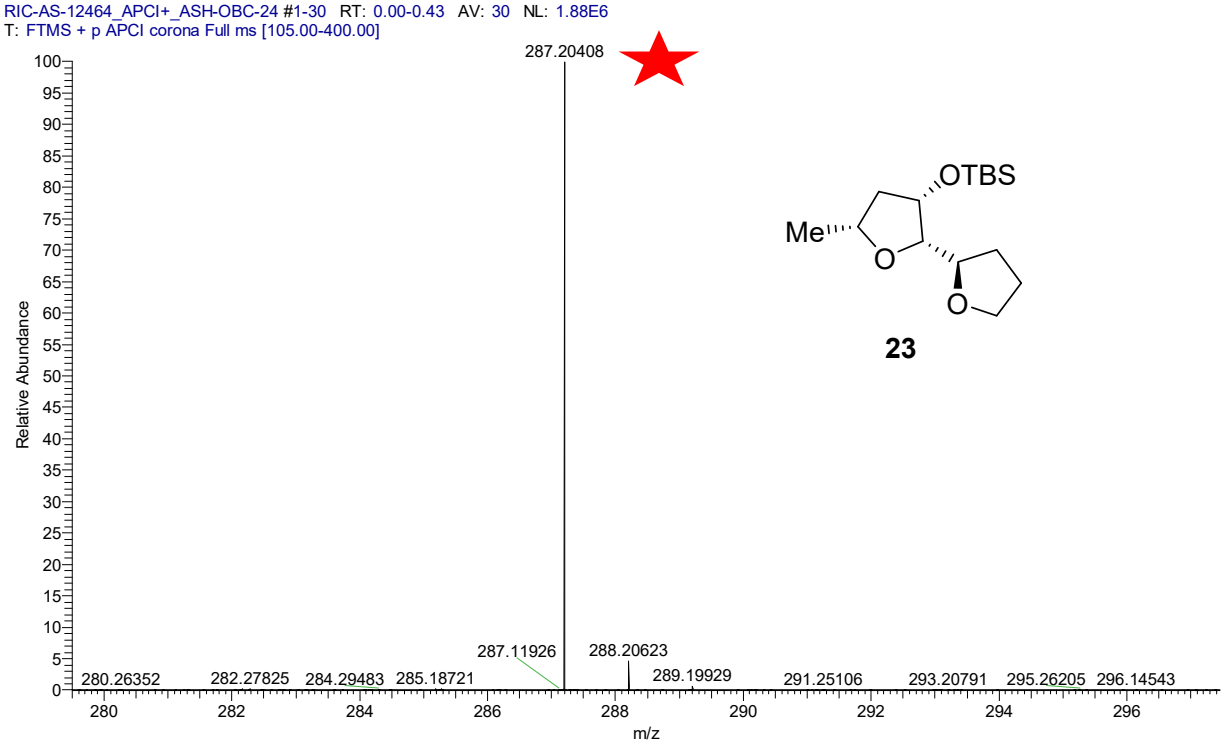
RIC-AS-12455_APCI+_ACN+H2O_ASH-OBC-20 #1-35 RT: 0.01-0.50 AV: 35 NL: 2.69E7
T: FTMS + p APCI corona Full ms [100.00-800.00]

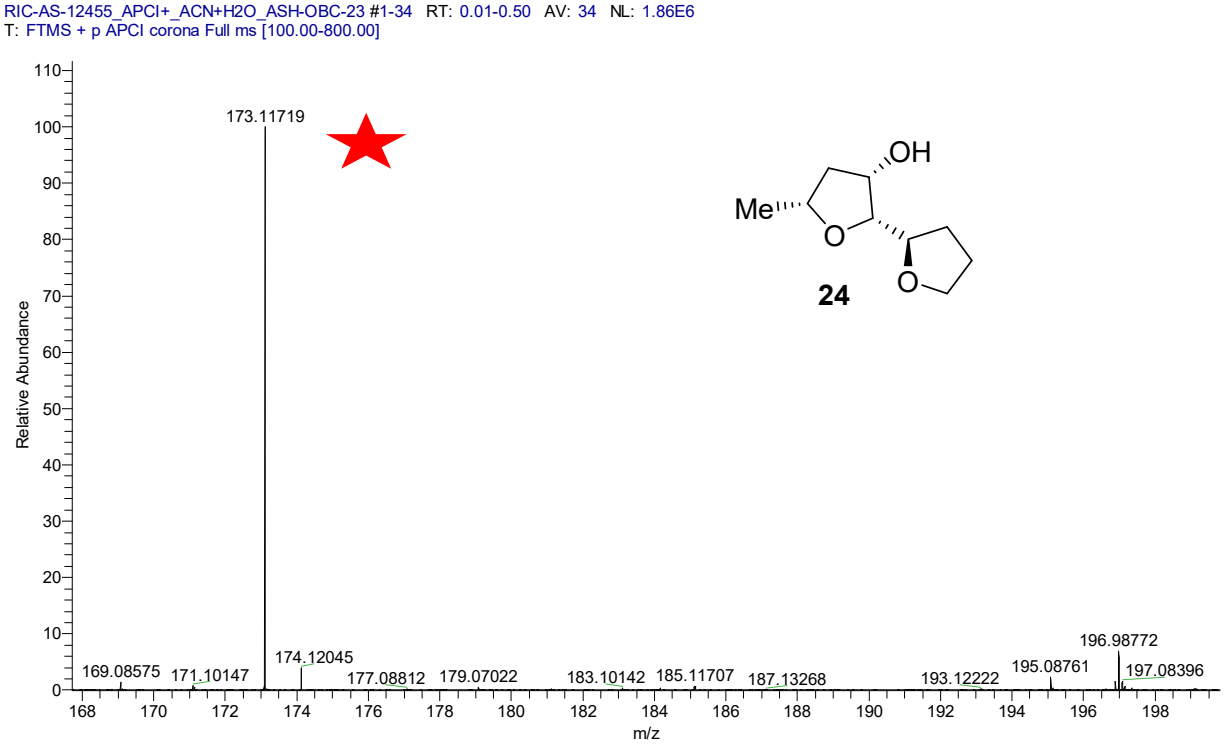


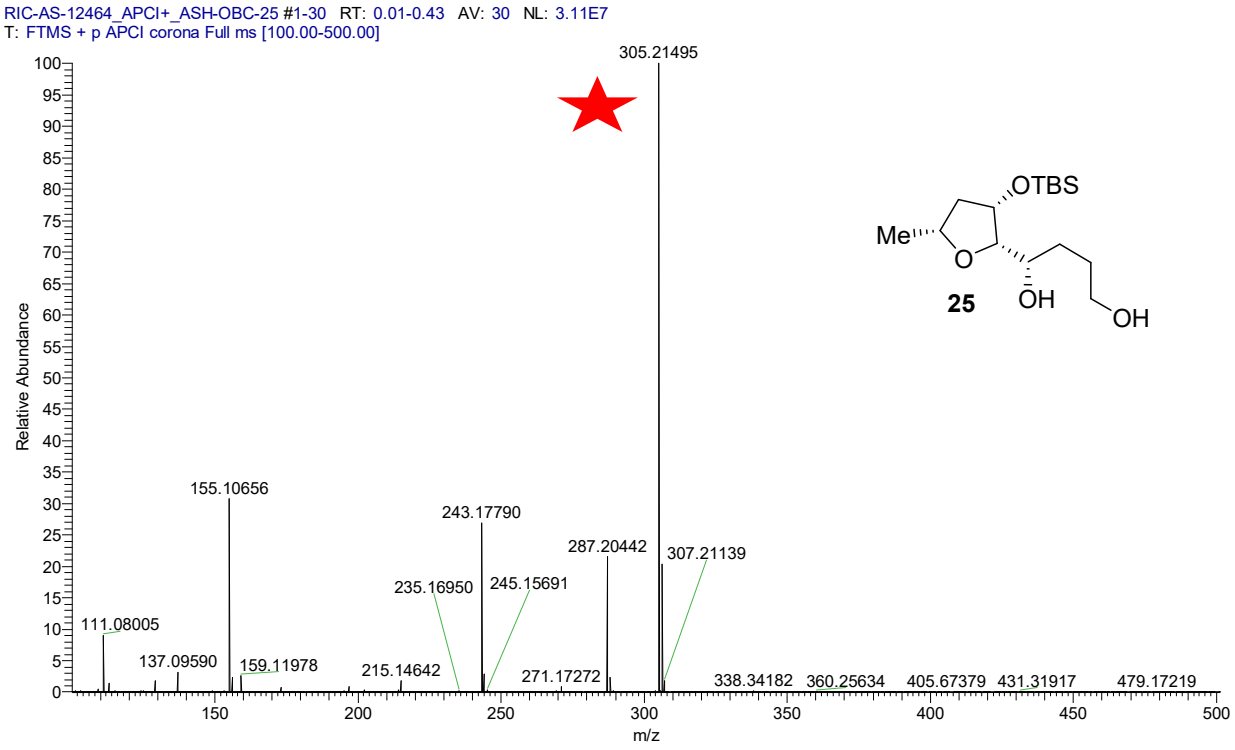
20

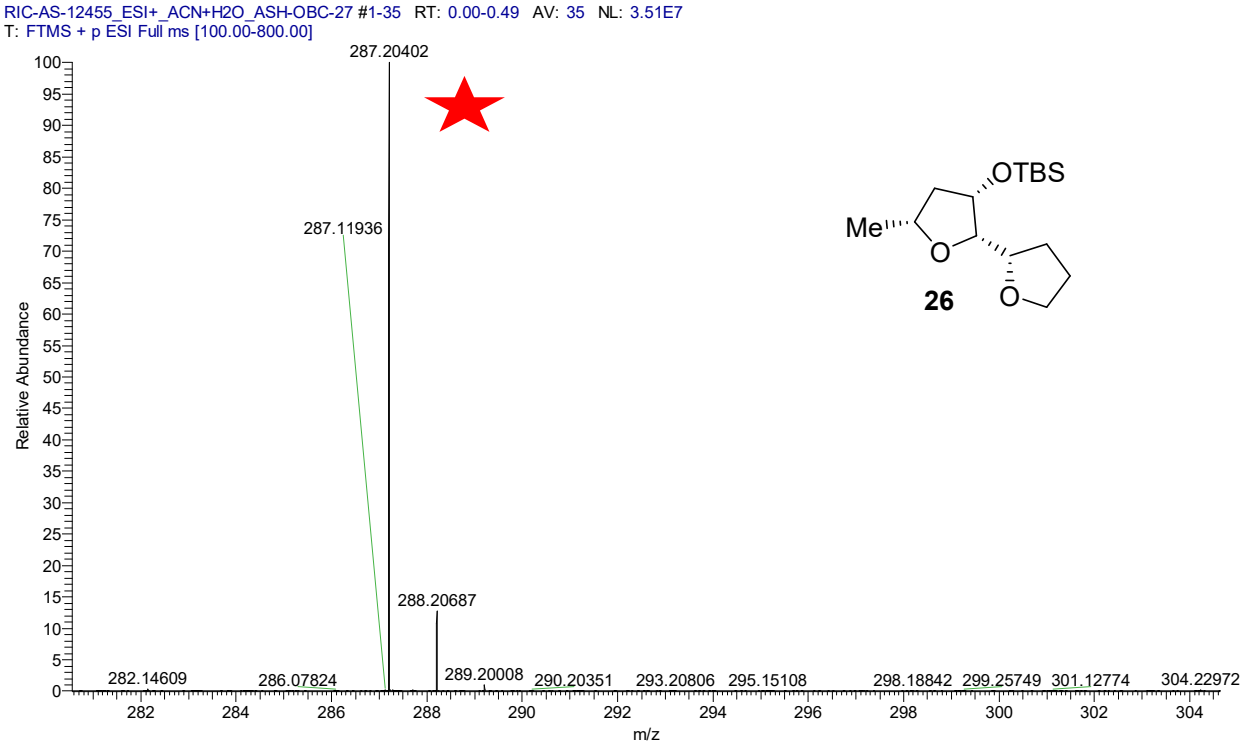

RIC-AS-12455_APCI+_ACN+H2O_ASH-OBC-21 #1-34 RT: 0.01-0.50 AV: 34 NL: 4.66E6
T: FTMS + p APCI corona Full ms [100.00-800.00]
287.20449
269.19382
245.15728
159.11996
215.14656
137.09602
301.21937
202.39647
338.34196
379.18399
515.41292
549.31949
579.53474
663.45484
730.51270
787.98938
Relative Abundance
m/z
OTBS
Me
O
OH
21


RIC-AS-12455_ESI+_ACN+H2O_ASH-OBC-22 #1-35 RT: 0.01-0.50 AV: 35 NL: 5.72E6
T: FTMS + p ESI Full ms [100.00-800.00]
305.21465
301.14082
304.10784
306.21730
309.18533
311.14607
313.16187
315.17655
316.77507
319.22409
321.23962
324.18780
Relative Abundance
m/z
OTBS
Me
O
OH
OH
22

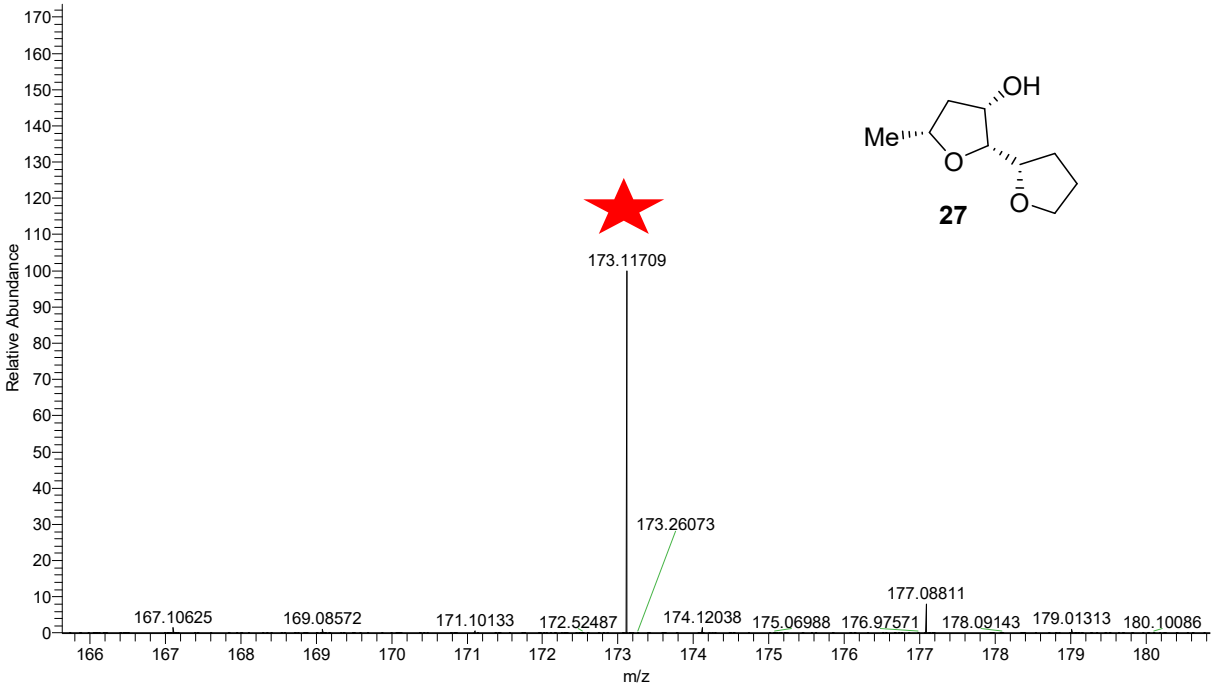

RIC-AS-12464_APCI+_ASH-OBC-24 #1-30 RT: 0.00-0.43 AV: 30 NL: 1.88E6
T: FTMS + p APCI corona Full ms [105.00-400.00]
287.20408
OTBS
Me
O
O
23
Relative Abundance
287.11926
288.20623
280.26352
282.27825
284.29483
285.18721
289.19929
291.25106
293.20791
295.26205
296.14543
m/z


RIC-AS-12455_APCI+_ACN+H2O_ASH-OBC-23 #1-34 RT: 0.01-0.50 AV: 34 NL: 1.86E6
T: FTMS + p APCI corona Full ms [100.00-800.00]
173.11719
OH
Me
O
O
24
Relative Abundance
169.08575
171.10147
174.12045
177.08812
179.07022
183.10142
185.11707
187.13268
193.12222
195.08761
196.98772
197.08396
m/z

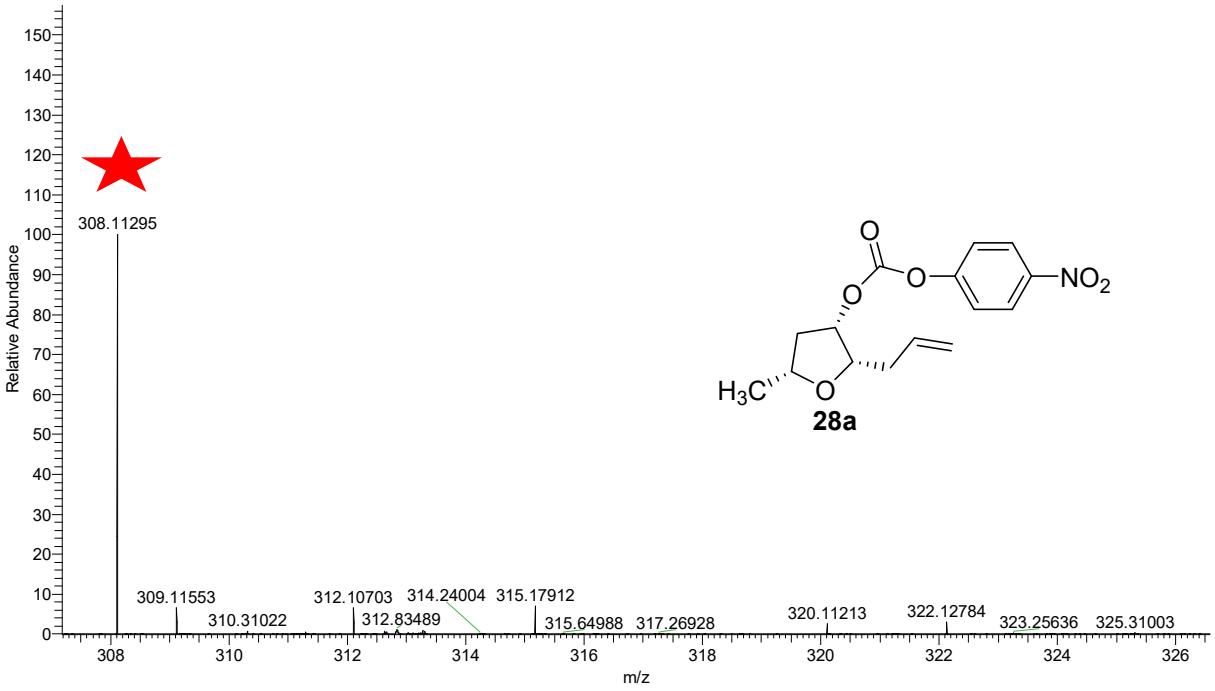

RIC-AS-12464_APCI+_ASH-OBC-25 #1-30 RT: 0.01-0.43 AV: 30 NL: 3.11E7
T: FTMS + p APCI corona Full ms [100.00-500.00]
305.21495
155.10656
243.17790
287.20442
307.21139
235.16950
245.15691
111.08005
137.09590
159.11978
215.14642
271.17272
338.34182
360.25634
405.67379
431.31917
479.17219
Relative Abundance
m/z
OTBS
Me
O
OH
OH
25

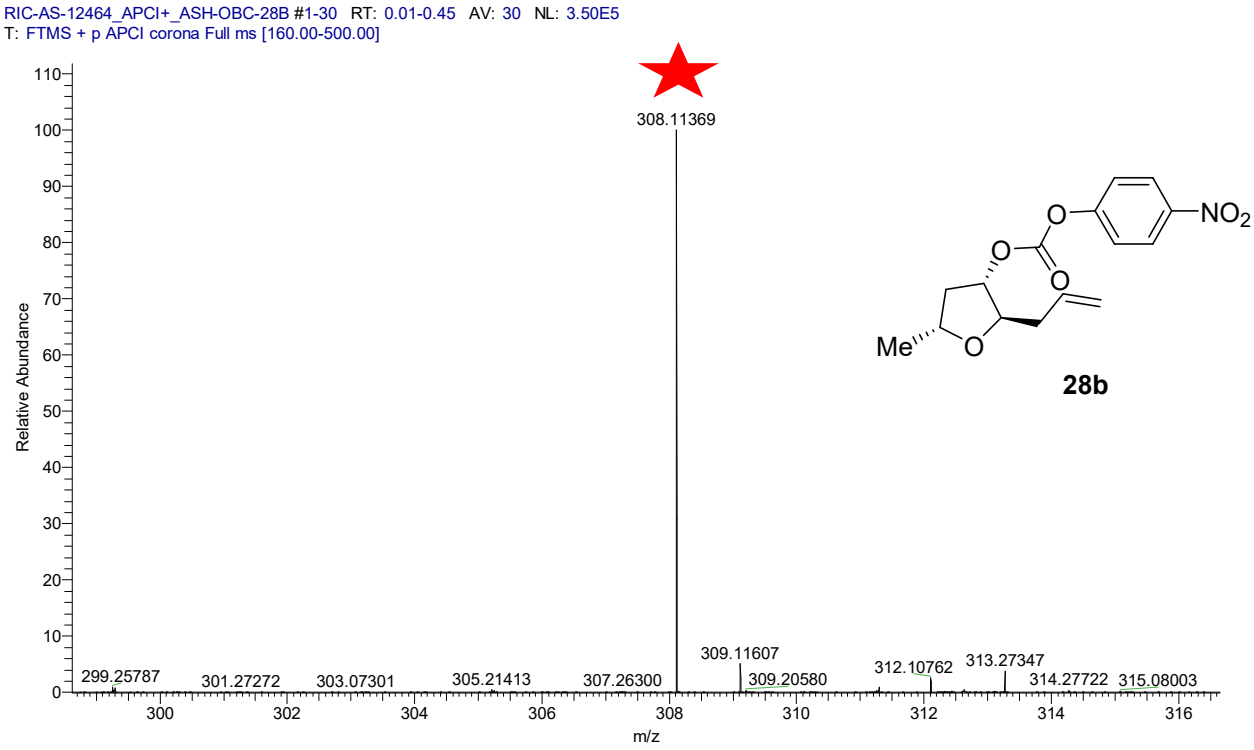

RIC-AS-12455_ESI+_ACN+H2O_ASH-OBC-27 #1-35 RT: 0.00-0.49 AV: 35 NL: 3.51E7
T: FTMS + p ESI Full ms [100.00-800.00]
287.20402
287.11936
288.20687
282.14609
286.07824
289.20008
290.20351
293.20806
295.15108
298.18842
299.25749
301.12774
304.22972
Relative Abundance
m/z
OTBS
Me
O
O
26

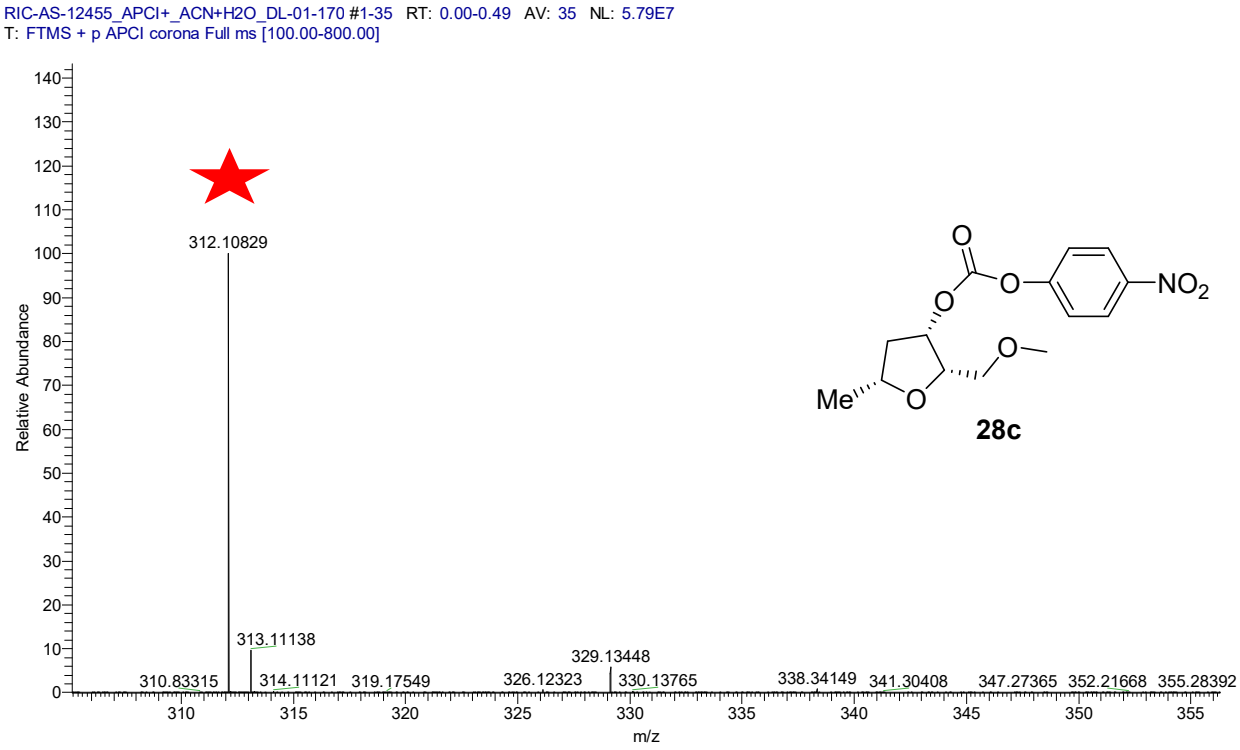
RIC-AS-12464_APCI+_ASH-OBC-27 #1-30 RT: 0.01-0.42 AV: 30 NL: 4.94E6
T: FTMS + p APCI corona Full ms [105.00-400.00]



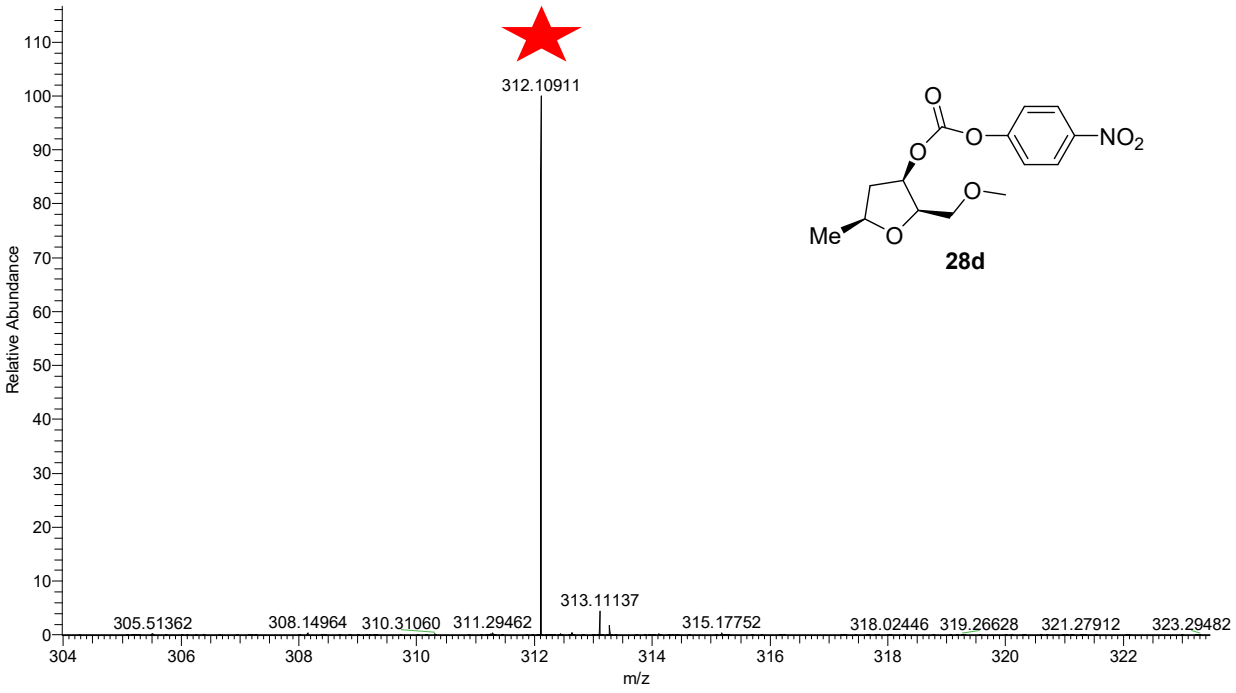
RIC-AS-12455_APCI+_ACN+H2O_DL-01-090 #1-35 RT: 0.01-0.50 AV: 35 NL: 2.30E6
T: FTMS + p APCI corona Full ms [100.00-800.00]




RIC-AS-12464_APCI+_ASH-OBC-28B #1-30 RT: 0.01-0.45 AV: 30 NL: 3.50E5
T: FTMS + p APCI corona Full ms [160.00-500.00]
308.11369
309.11607
299.25787
301.27272
303.07301
305.21413
307.26300
309.20580
312.10762
313.27347
314.27722
315.08003
Relative Abundance
m/z
NO2
Me
28b

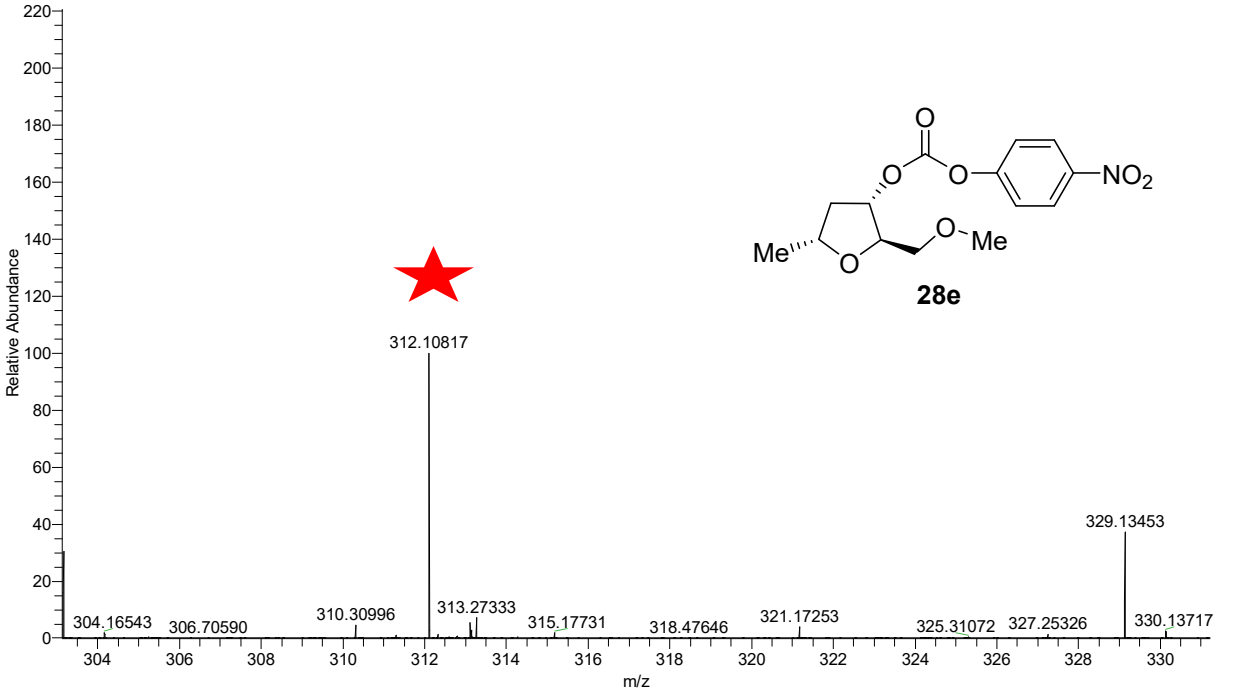

RIC-AS-12455_APCI+_ACN+H2O_DL-01-170 #1-35 RT: 0.00-0.49 AV: 35 NL: 5.79E7
T: FTMS + p APCI corona Full ms [100.00-800.00]
312.10829
313.11138
310.83315
314.11121
319.17549
326.12323
329.13448
330.13765
338.34149
341.30408
347.27365
352.21668
355.28392
Relative Abundance
m/z
NO2
Me
28c

RIC-AS-12464_APCI+_ASH-OBC-28D #1-30 RT: 0.00-0.43 AV: 30 NL: 8.36E5
T: FTMS + p APCI corona Full ms [160.00-500.00]

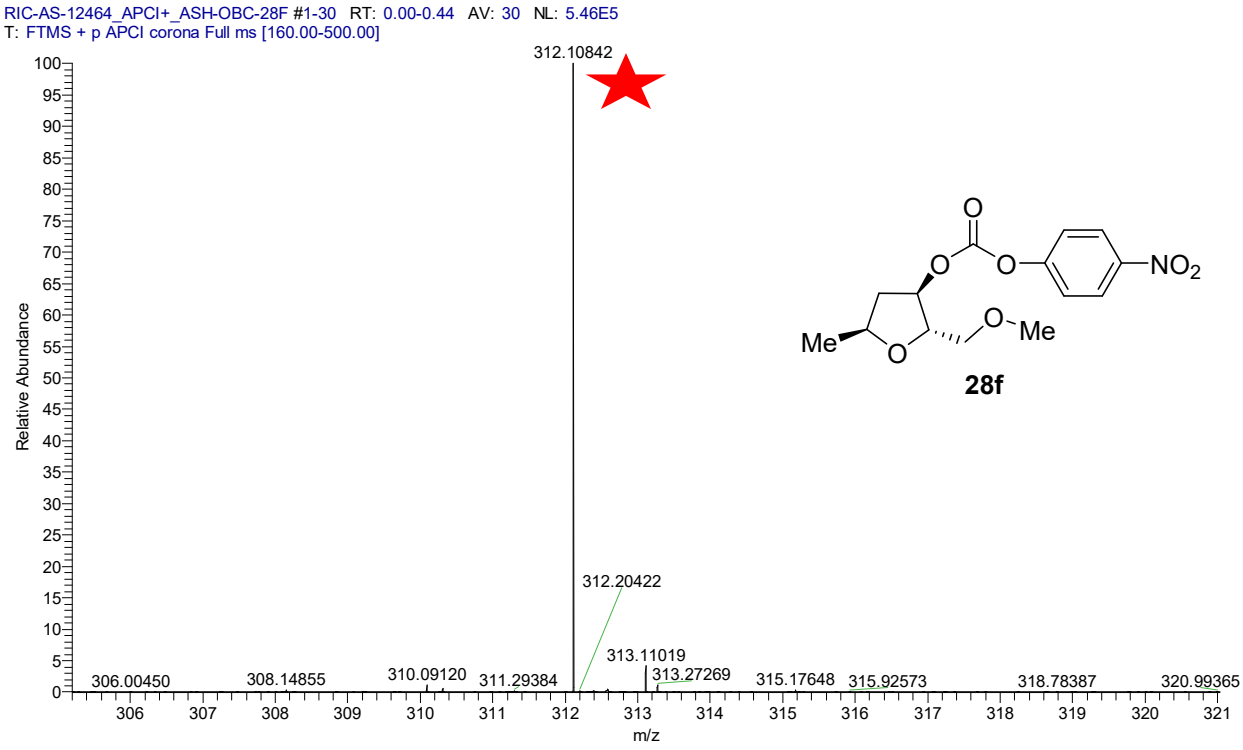


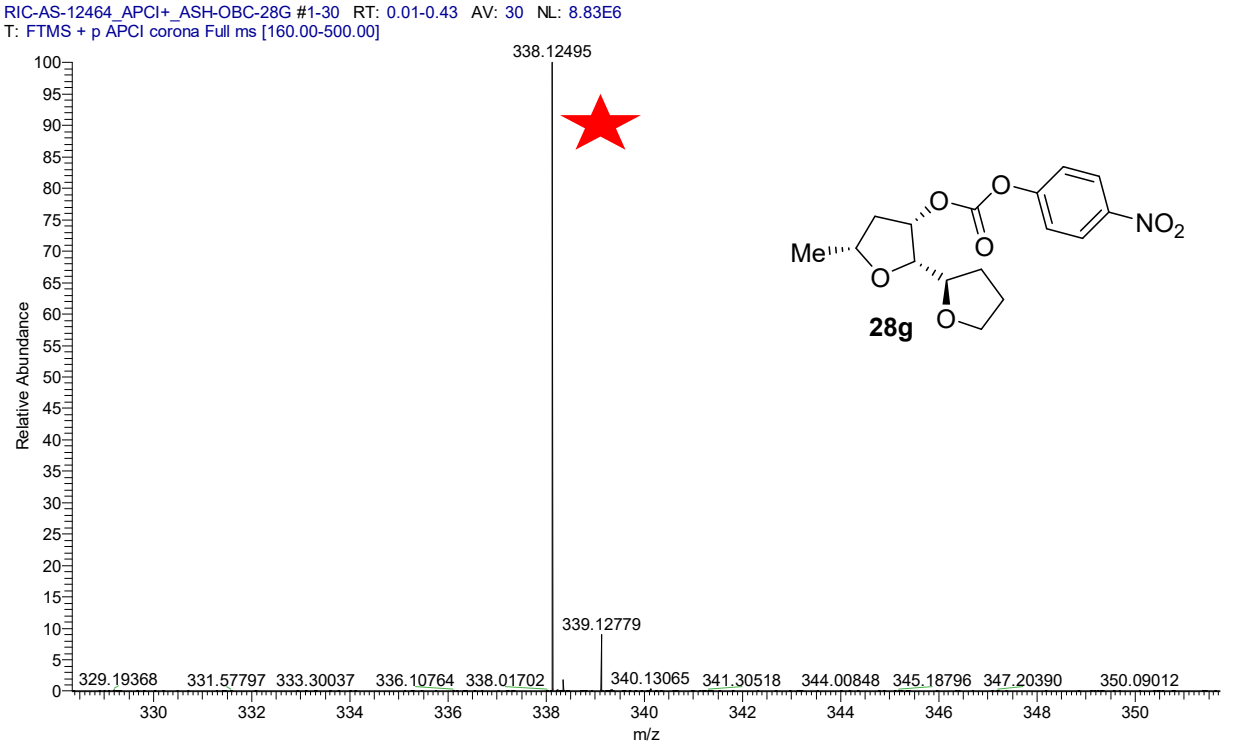
28d

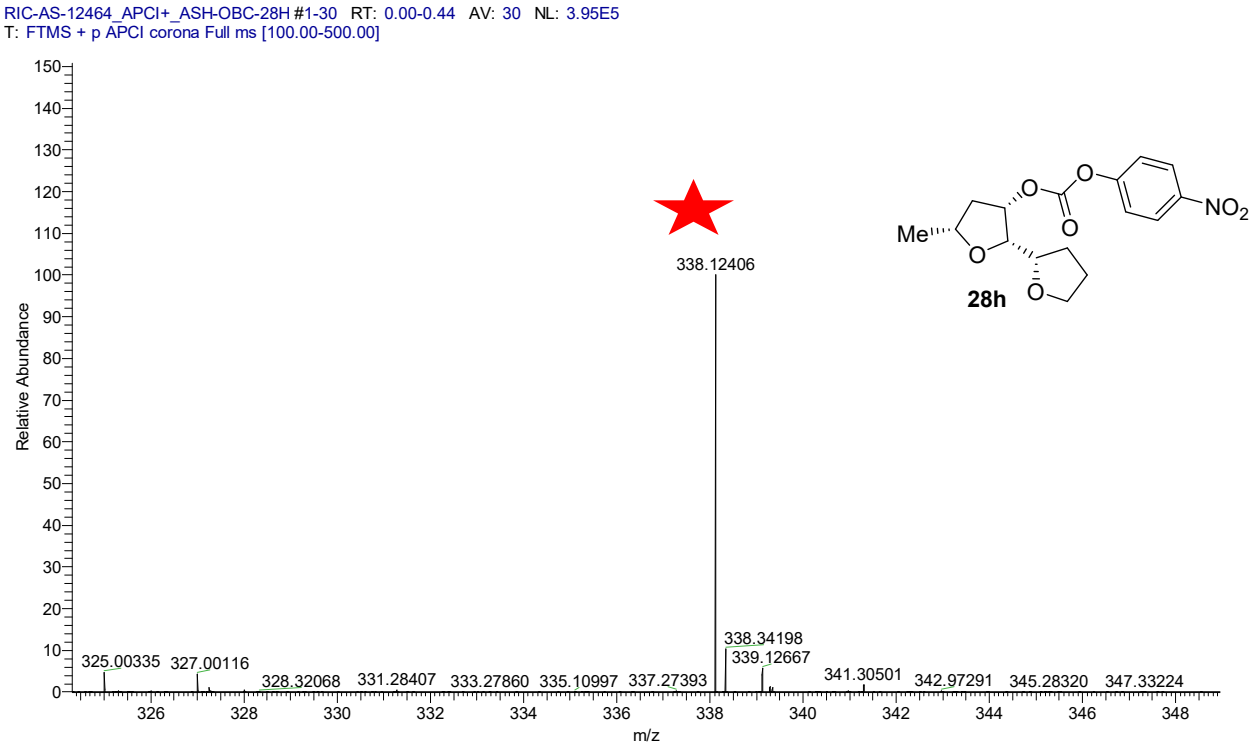
RIC-AS-12455_APCI+_ACN+H2O_DL-03-064 #1-33 RT: 0.01-0.49 AV: 33 NL: 2.87E5
T: FTMS + p APCI corona Full ms [100.00-800.00]

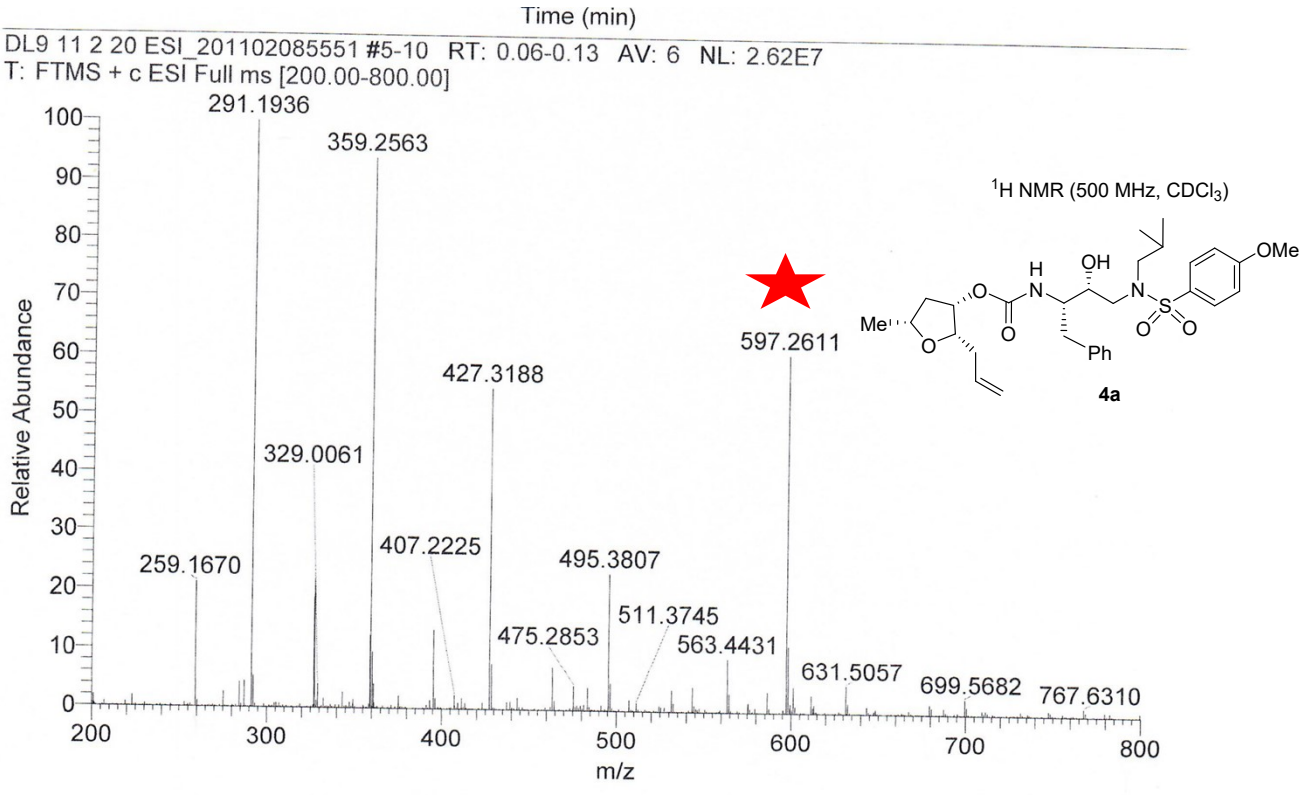


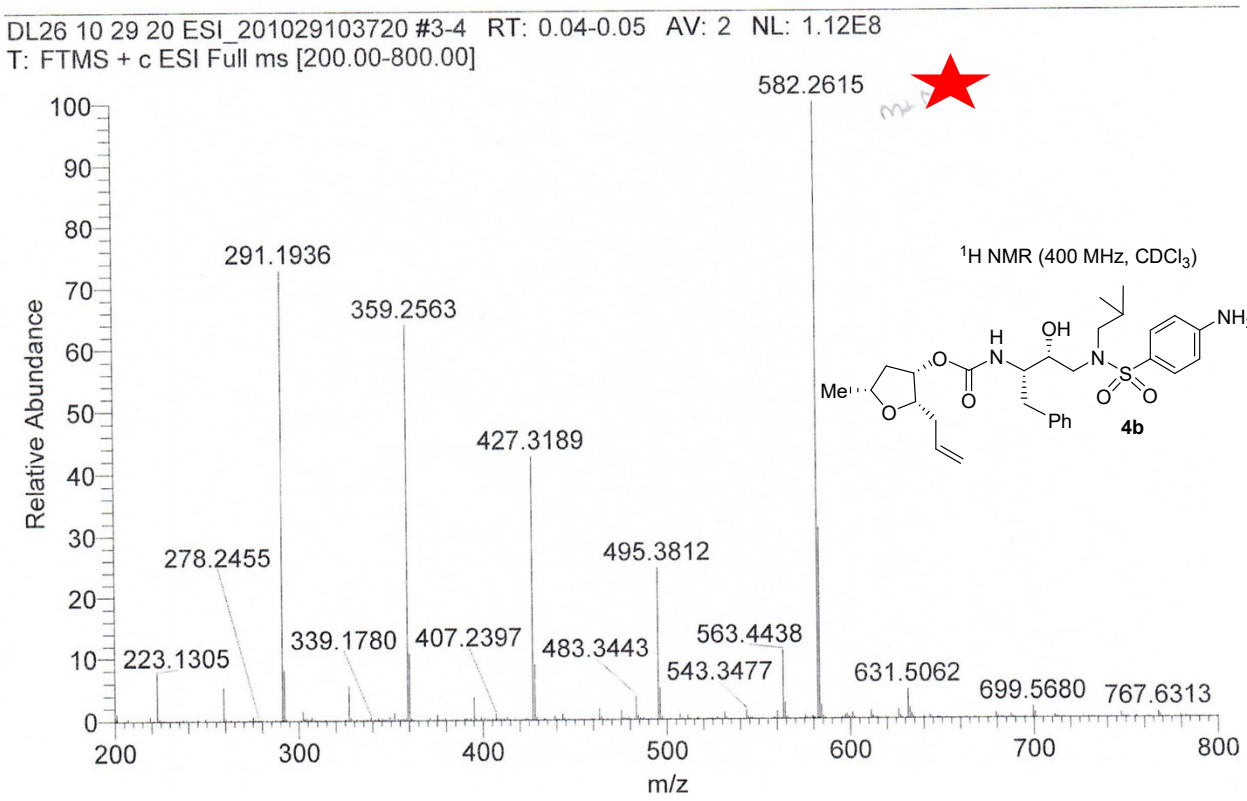
28e

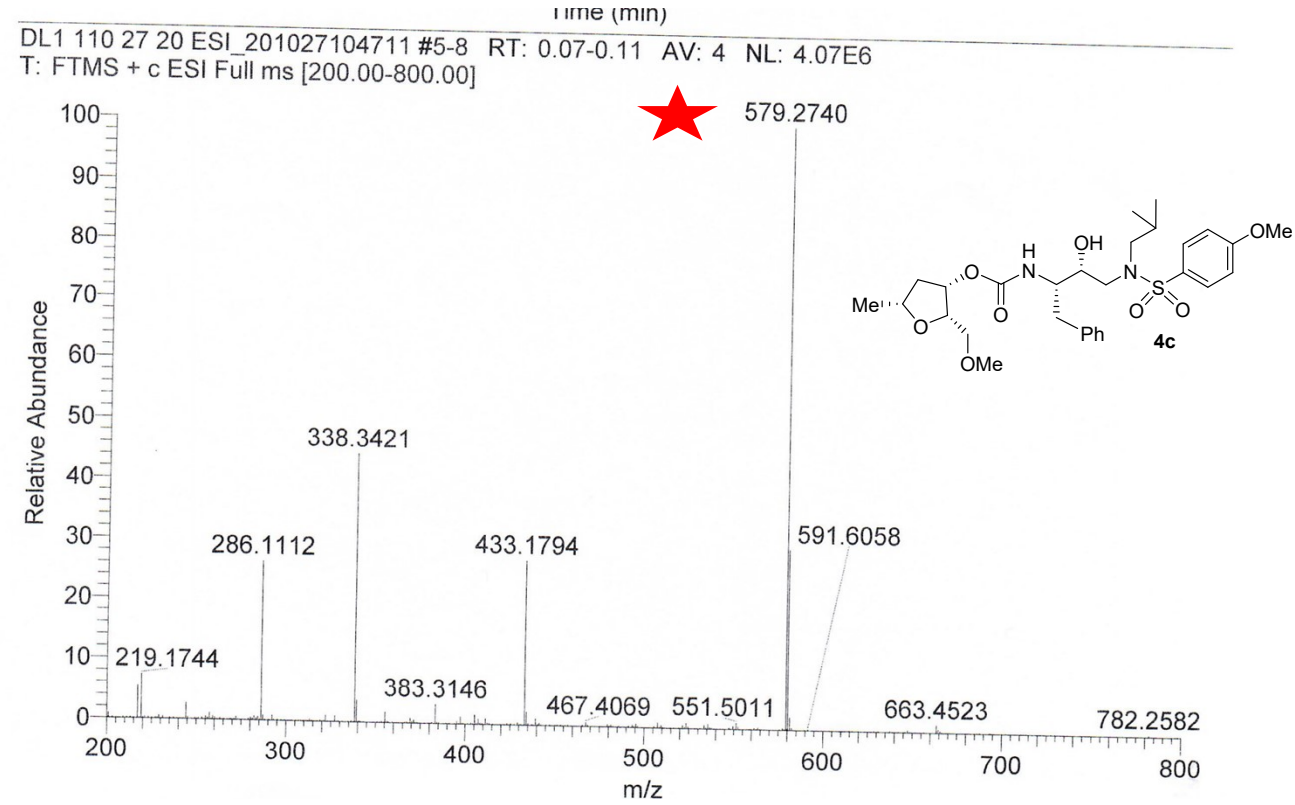

RIC-AS-12464_APCI+_ASH-OBC-28F #1-30 RT: 0.00-0.44 AV: 30 NL: 5.46E5
T: FTMS + p APCI corona Full ms [160.00-500.00]
312.10842
312.20422
313.11019
313.27269
306.00450
308.14855
310.09120
311.29384
315.17648
315.92573
318.78387
320.99365
Relative Abundance
m/z
28f

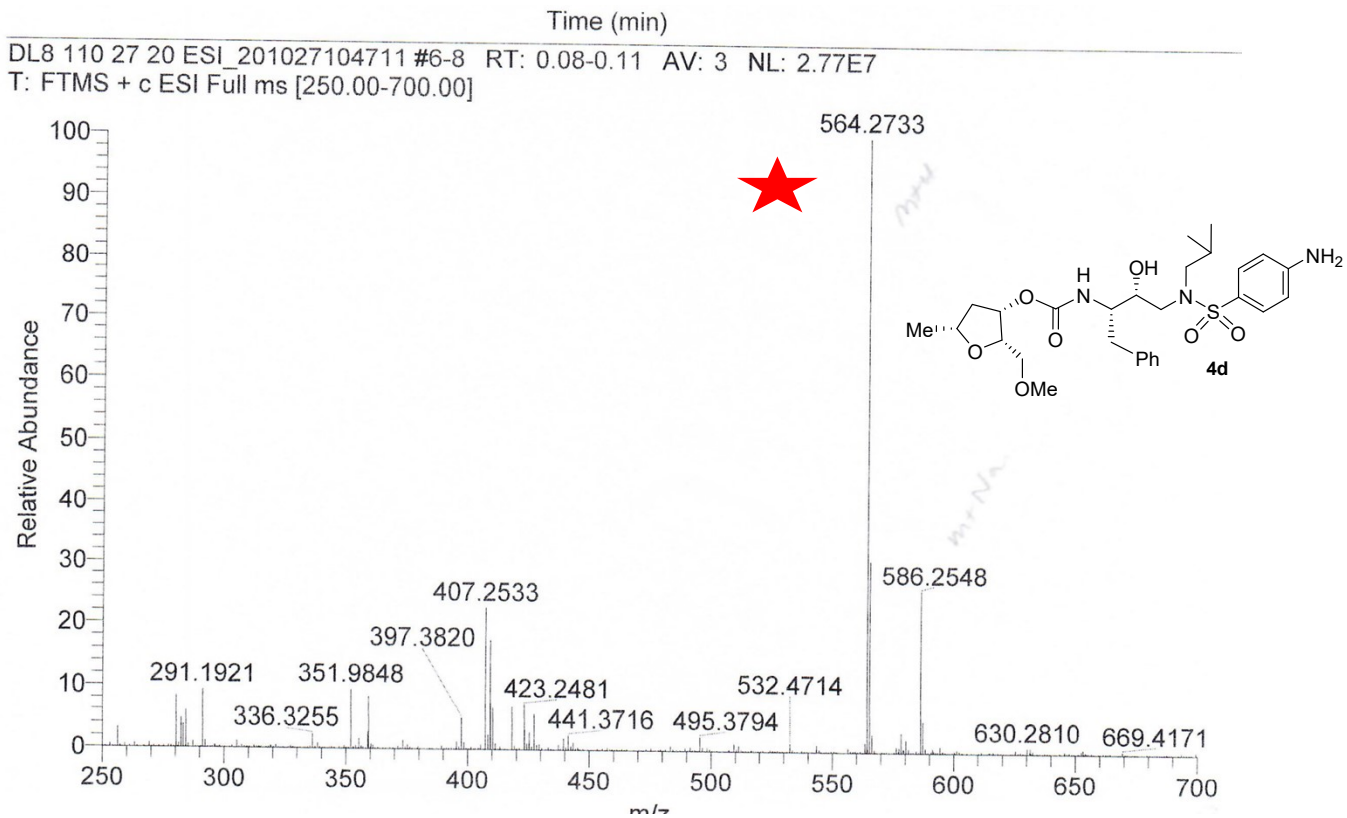

RIC-AS-12464_APCI+_ASH-OBC-28G #1-30 RT: 0.01-0.43 AV: 30 NL: 8.83E6
T: FTMS + p APCI corona Full ms [160.00-500.00]
338.12495
339.12779
329.19368
331.57797
333.30037
336.10764
338.01702
340.13065
341.30518
344.00848
345.18796
347.20390
350.09012
Relative Abundance
m/z
28g

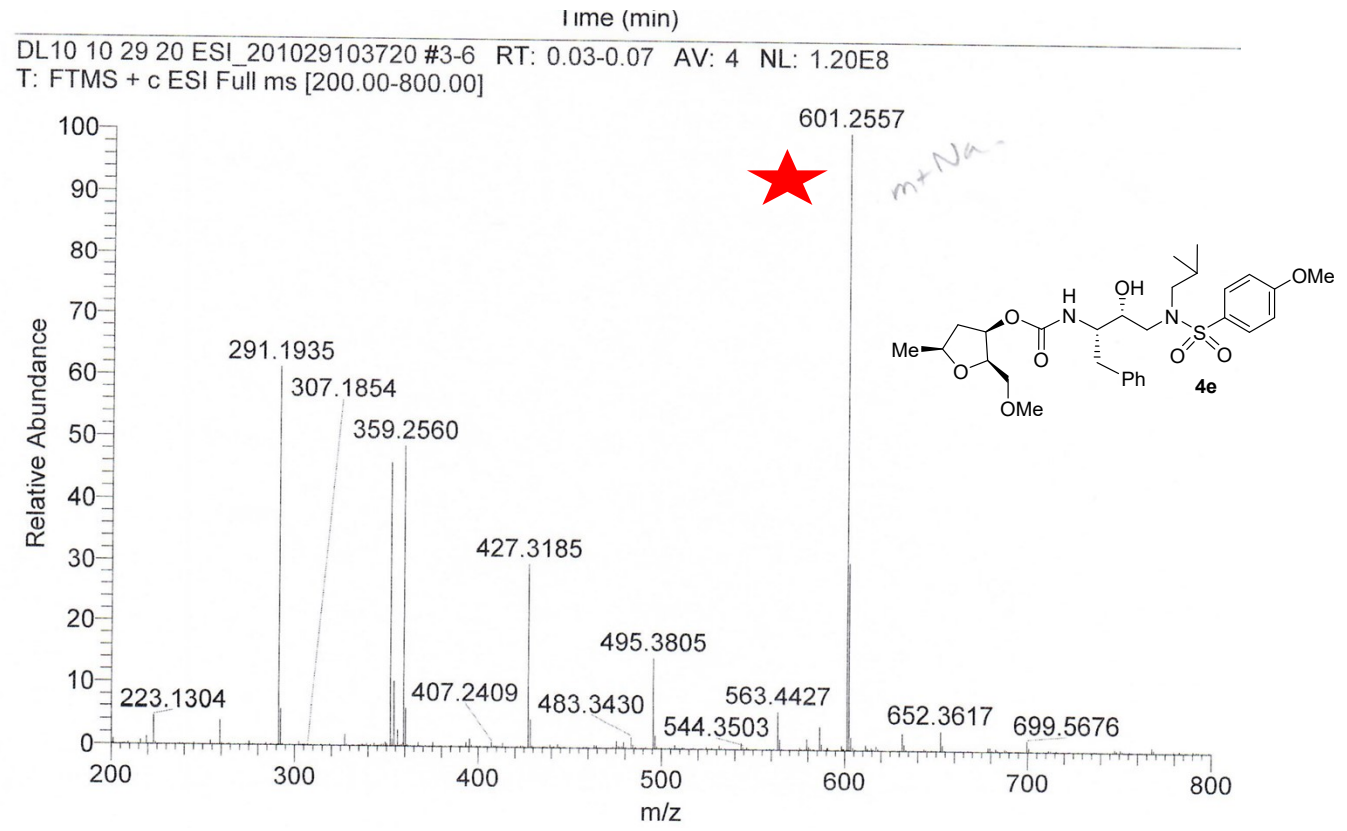

RIC-AS-12464_APCI+_ASH-OBC-28H #1-30 RT: 0.00-0.44 AV: 30 NL: 3.95E5
T: FTMS + p APCI corona Full ms [100.00-500.00]
Relative Abundance
m/z
338.12406
325.00335
327.00116
328.32068
331.28407
333.27860
335.10997
337.27393
338.34198
339.12667
341.30501
342.97291
345.28320
347.33224
Me
NO2
28h

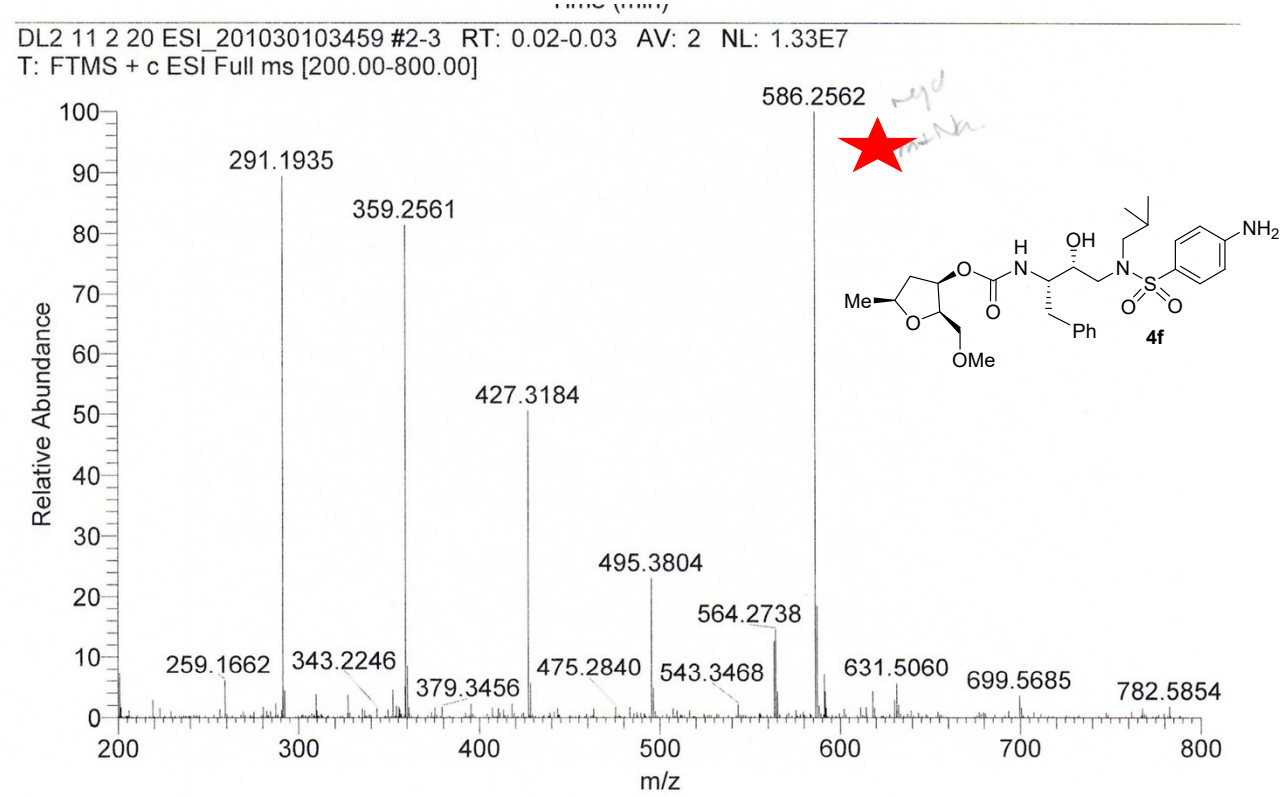

Time (min)
DL9 11 2 20 ESI_201102085551 #5-10 RT: 0.06-0.13 AV: 6 NL: 2.62E7
T: FTMS + c ESI Full ms [200.00-800.00]
Relative Abundance
m/z
291.1936
359.2563
427.3188
329.0061
259.1670
407.2225
495.3807
511.3745
475.2853
563.4431
597.2611
631.5057
699.5682
767.6310
1H NMR (500 MHz, CDCl3)
OMe
OH
Ph
Me
4a

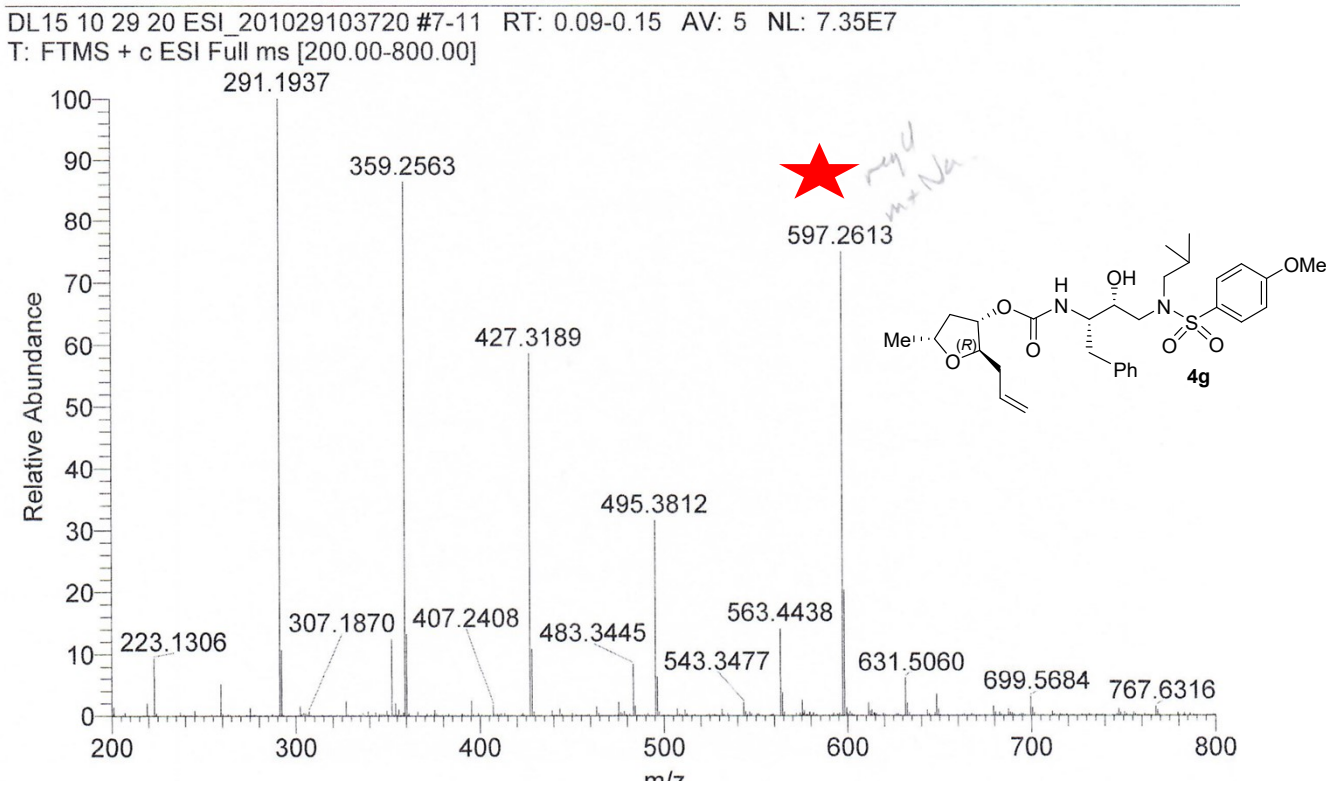

DL26 10 29 20 ESI_201029103720 #3-4 RT: 0.04-0.05 AV: 2 NL: 1.12E8
T: FTMS + c ESI Full ms [200.00-800.00]
582.2615
291.1936
359.2563
427.3189
278.2455
495.3812
223.1305
339.1780
407.2397
483.3443
563.4438
543.3477
631.5062
699.5680
767.6313
Relative Abundance
m/z
^{1}H NMR (400 MHz, CDCl$_3$)
4b

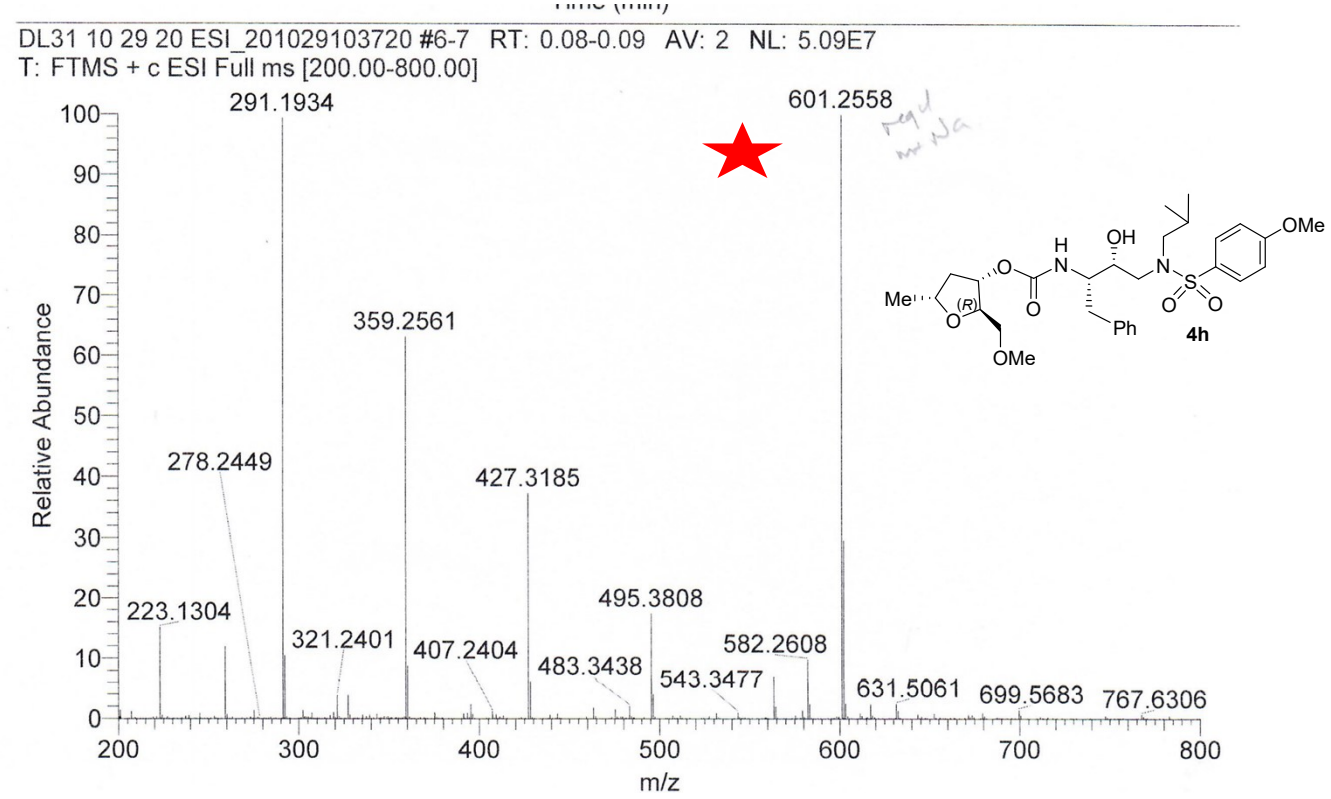

DL1 110 27 20 ESI_201027104711 #5-8 RT: 0.07-0.11 AV: 4 NL: 4.07E6
T: FTMS + c ESI Full ms [200.00-800.00]
579.2740
338.3421
286.1112
433.1794
591.6058
219.1744
383.3146
467.4069
551.5011
663.4523
782.2582
Relative Abundance
m/z
4c

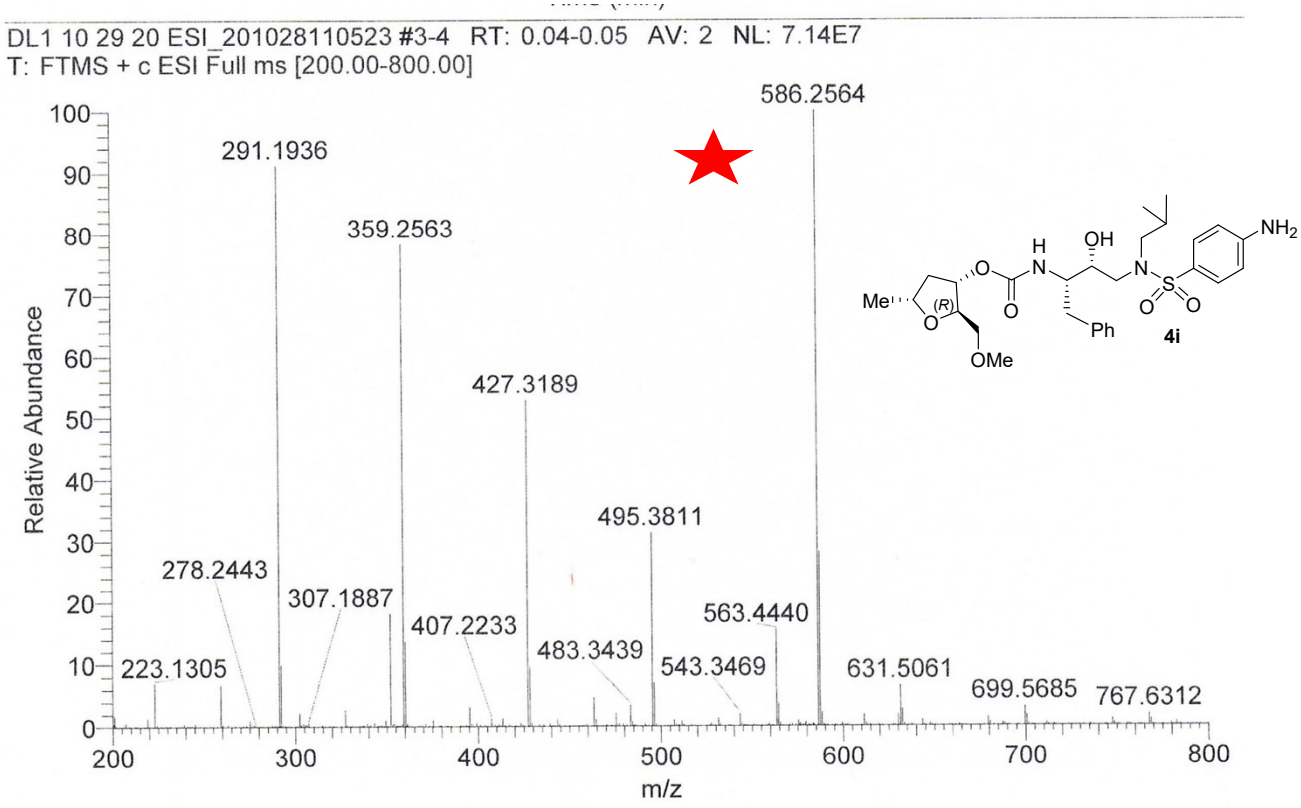

Time (min)
DL8 110 27 20 ESI_201027104711 #6-8 RT: 0.08-0.11 AV: 3 NL: 2.77E7
T: FTMS + c ESI Full ms [250.00-700.00]
Relative Abundance
564.2733
586.2548
407.2533
397.3820
291.1921
351.9848
423.2481
532.4714
336.3255
441.3716
495.3794
630.2810
669.4171
m/z
4d

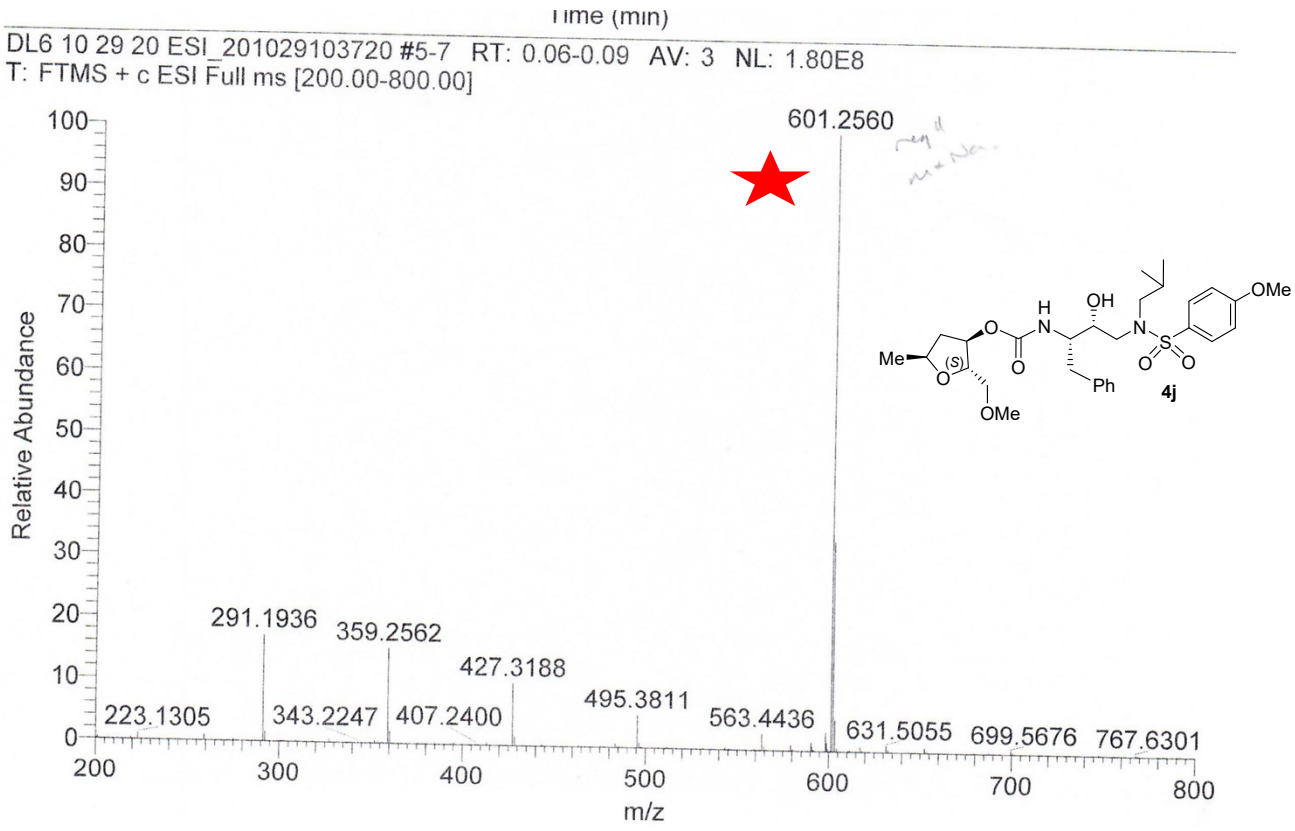

Time (min)
DL10 10 29 20 ESI_201029103720 #3-6 RT: 0.03-0.07 AV: 4 NL: 1.20E8
T: FTMS + c ESI Full ms [200.00-800.00]
Relative Abundance
601.2557
291.1935
307.1854
359.2560
427.3185
495.3805
223.1304
407.2409
483.3430
563.4427
544.3503
652.3617
699.5676
m/z
4e

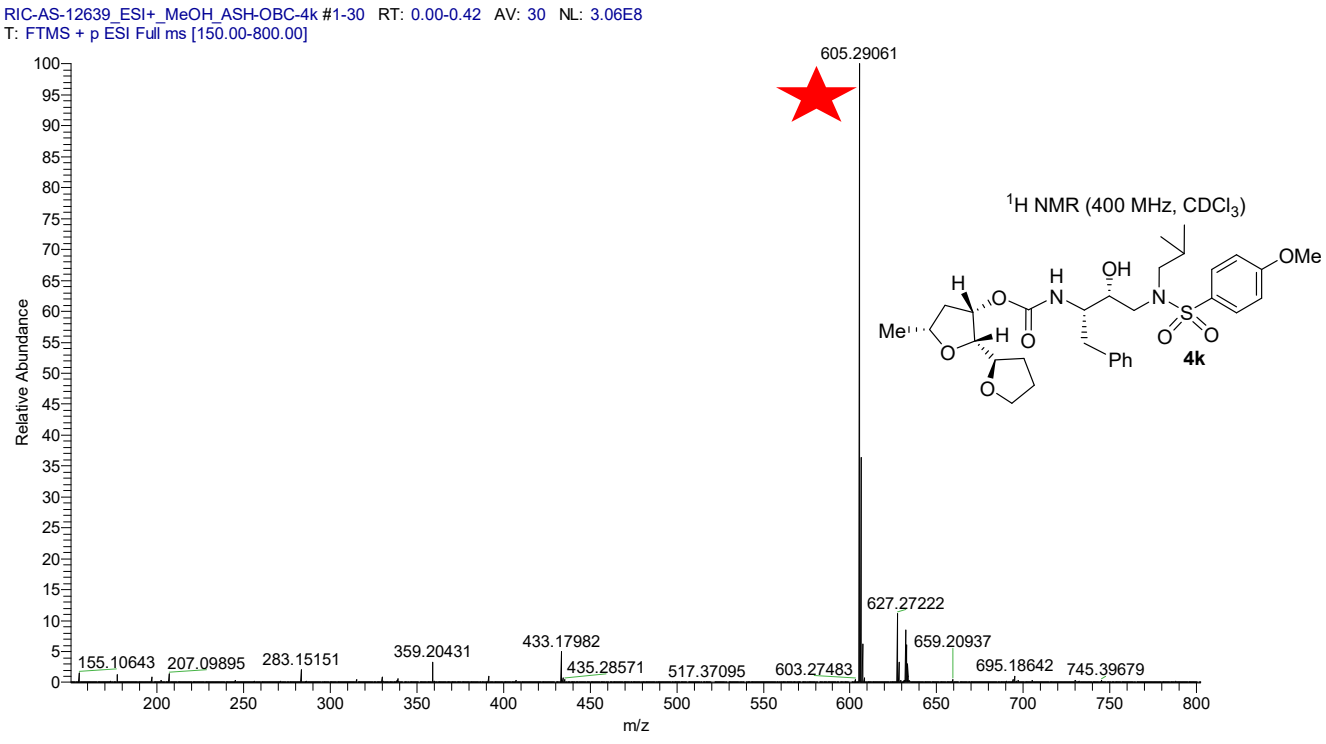

DL2 11 2 20 ESI_201030103459 #2-3 RT: 0.02-0.03 AV: 2 NL: 1.33E7
T: FTMS + c ESI Full ms [200.00-800.00]
586.2562
291.1935
359.2561
427.3184
495.3804
564.2738
259.1662
343.2246
379.3456
475.2840
543.3468
631.5060
699.5685
782.5854
Relative Abundance
m/z
4f

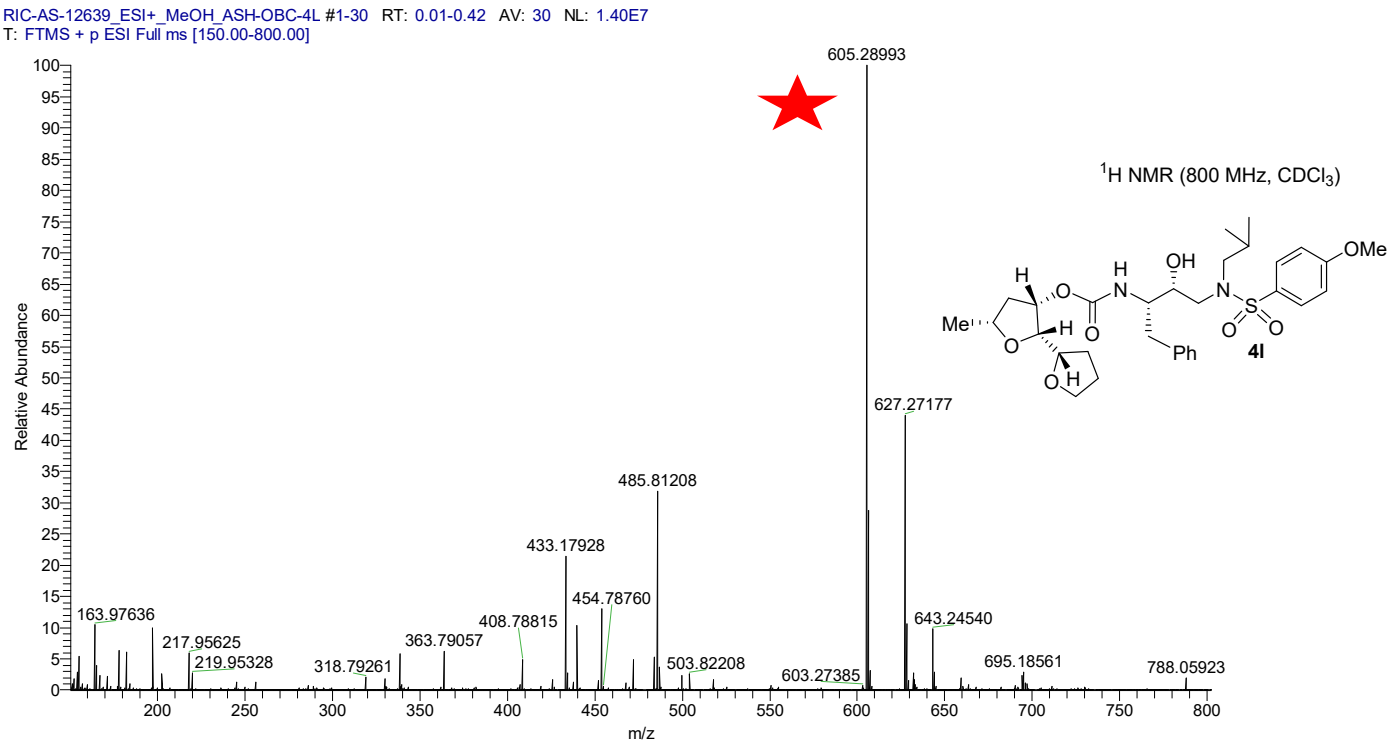

DL15 10 29 20 ESI_201029103720 #7-11 RT: 0.09-0.15 AV: 5 NL: 7.35E7
T: FTMS + c ESI Full ms [200.00-800.00]
291.1937
359.2563
597.2613
427.3189
495.3812
223.1306
307.1870
407.2408
483.3445
543.3477
563.4438
631.5060
699.5684
767.6316
Relative Abundance
4g


DL31 10 29 20 ESI_201029103720 #6-7 RT: 0.08-0.09 AV: 2 NL: 5.09E7
T: FTMS + c ESI Full ms [200.00-800.00]
291.1934
601.2558
359.2561
278.2449
427.3185
223.1304
321.2401
407.2404
483.3438
495.3808
543.3477
582.2608
631.5061
699.5683
767.6306
Relative Abundance
m/z
4h


DL1 10 29 20 ESI_201028110523 #3-4 RT: 0.04-0.05 AV: 2 NL: 7.14E7
T: FTMS + c ESI Full ms [200.00-800.00]
586.2564
291.1936
359.2563
427.3189
495.3811
278.2443
307.1887
407.2233
483.3439
563.4440
543.3469
223.1305
631.5061
699.5685
767.6312
Relative Abundance
m/z
4i


Time (min)
DL6 10 29 20 ESI_201029103720 #5-7 RT: 0.06-0.09 AV: 3 NL: 1.80E8
T: FTMS + c ESI Full ms [200.00-800.00]
601.2560
291.1936
359.2562
427.3188
495.3811
223.1305
343.2247
407.2400
563.4436
631.5055
699.5676
767.6301
Relative Abundance
m/z
4j


RIC-AS-12639_ESI+_MeOH_ASH-OBC-4k #1-30 RT: 0.00-0.42 AV: 30 NL: 3.06E8
T: FTMS + p ESI Full ms [150.00-800.00]
605.29061
627.27222
659.20937
695.18642
745.39679
433.17982
359.20431
435.28571
517.37095
603.27483
155.10643
207.09895
283.15151
Relative Abundance
m/z
1H NMR (400 MHz, CDCl3)
4k


RIC-AS-12639_ESI+_MeOH_ASH-OBC-4L #1-30 RT: 0.01-0.42 AV: 30 NL: 1.40E7
T: FTMS + p ESI Full ms [150.00-800.00]
Relative Abundance
m/z
605.28993
627.27177
485.81208
433.17928
454.78760
408.78815
363.79057
318.79261
163.97636
217.95625
219.95328
503.82208
603.27385
643.24540
695.18561
788.05923
^{1}H NMR (800 MHz, CDCl$_3$)
OMe
OH
Me
Ph
4l

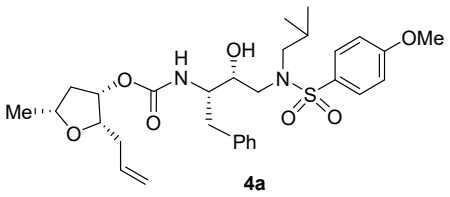
HPLC purity (Table 2, SI) data of inhibitors **4a-l**.

S.NO	Inhibitor	HPLC Purity
1	4a	94%
2	4b	92%
3	4c	92%
4	4d	92%
5	4e	93%
6	4f	92%
7	4g	92%
8	4h	92%
9	4i	92%
10	4j	92%
11	4k	92%
12	4l	93%

Data File C:\Chem32\1\Data\ASH-OBC-4A-254 504.D
Sample Name: ASH-OBC-4A-254

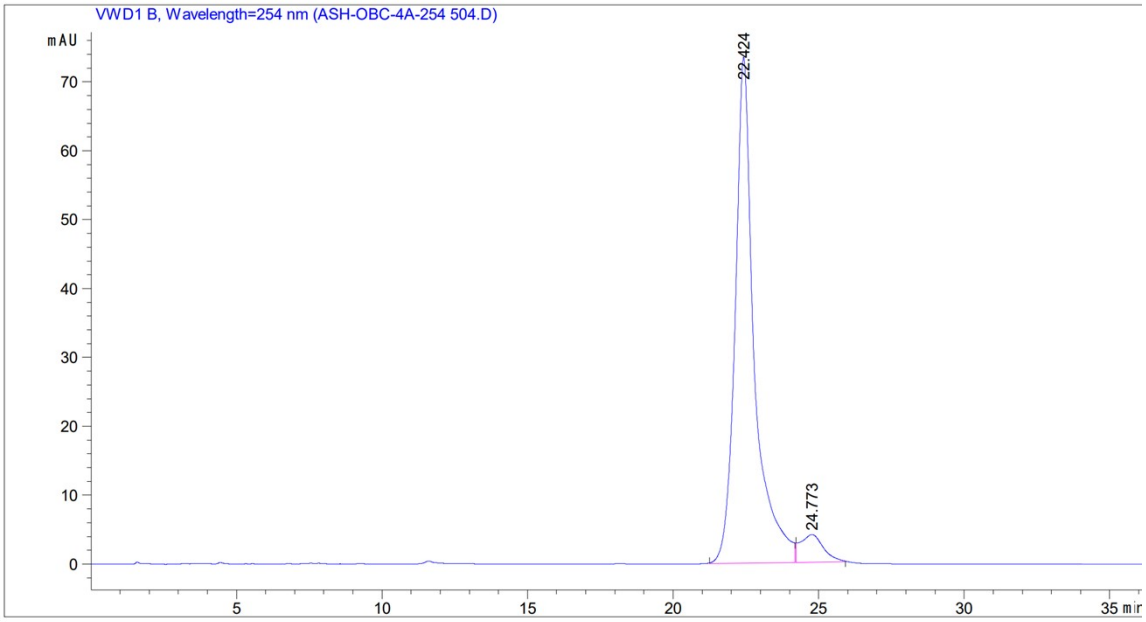
```
==========================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 6/7/2024 3:42:32 PM
                                             Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/7/2024 3:39:35 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/7/2024 4:19:03 PM by SYSTEM
                  (modified after loading)
Method Info     : Pump leak test method

Sample Info     : 50% MeCN/H2O
                  1 mL/min
                  254 nm
                  5 uL inj.
                  1.0 mL/min
                  ymcpak-odsa
```



4a

Concentration = 1 mg/mL of compound in ACN : H_2O (1 : 1)




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:        :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\ASH-OBC-4A-254 504.D
Sample Name: ASH-OBC-4A-254

Signal 1: VWD1 B, Wavelength=254 nm

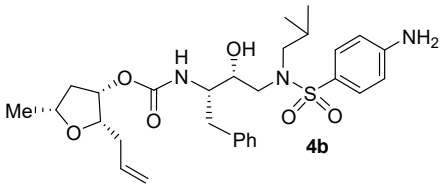
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.424	BB	0.6460	3347.90381	73.41902	93.7246
2	24.773	BB	0.7943	224.16246	4.02157	6.2754
Totals :				3572.06627	77.44059	

*** End of Report ***

Data File C:\Chem32\1\Data\ASH-OBC-4B-254-NEW-2 527.D
Sample Name: ASH-OBC-4B-254-NEW-2

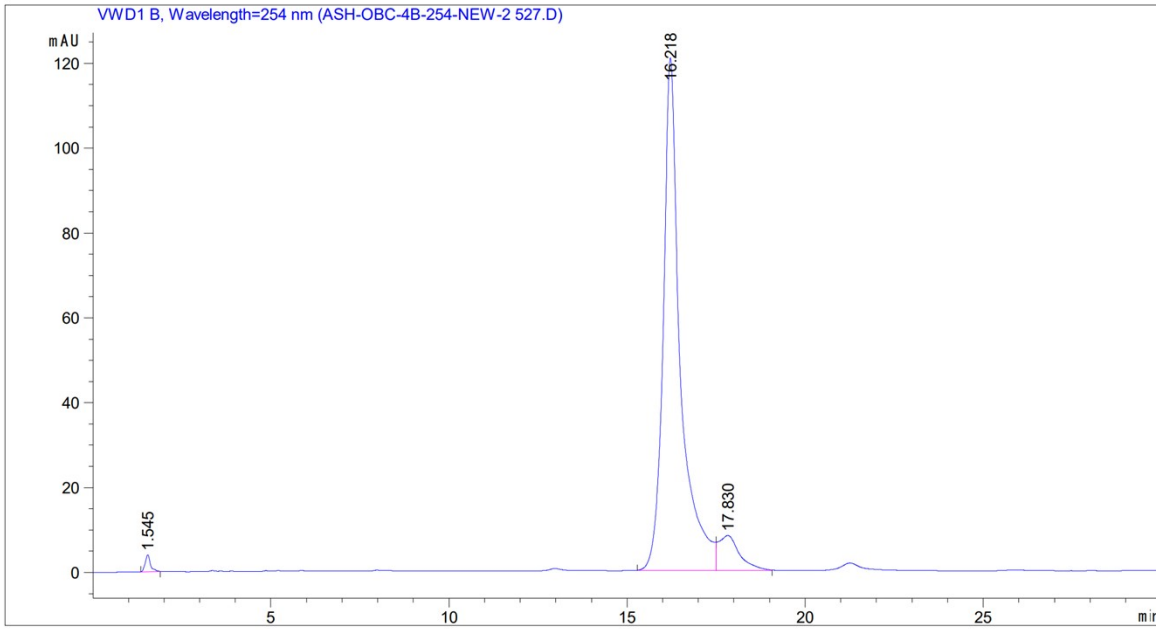
```
==========================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 6/10/2024 12:04:08 PM
                                               Inj Volume : 8.000 µl
Different Inj Volume from Sample Entry!  Actual Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/10/2024 11:56:18 AM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/10/2024 12:34:30 PM by SYSTEM
                  (modified after loading)
Method Info     : Pump leak test method

Sample Info     : 50% MeCN/H2O
                  1.0 mL/min
                  254 nm
                  8 uL inj.
                  1.0 mL/min
                  ymcpak-odsa
```



4b

Concentration = 1 mg/mL of compound in ACN : H_2O (1 : 1)




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:        :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\ASH-OBC-4B-254-NEW-2 527.D
Sample Name: ASH-OBC-4B-254-NEW-2

Signal 1: VWD1 B, Wavelength=254 nm

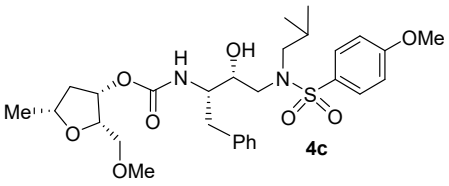
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.545	BB	0.1477	40.19727	3.98483	0.9102
2	16.218	BB	0.4717	4033.29370	120.75713	91.3297
3	17.830	BB	0.5817	342.69839	8.26544	7.7600
Totals :				4416.18937	133.00740	

*** End of Report ***

Data File C:\Chem32\1\Data\ASH-OBC-4C-254 503.D
Sample Name: ASH-OBC-4C-254

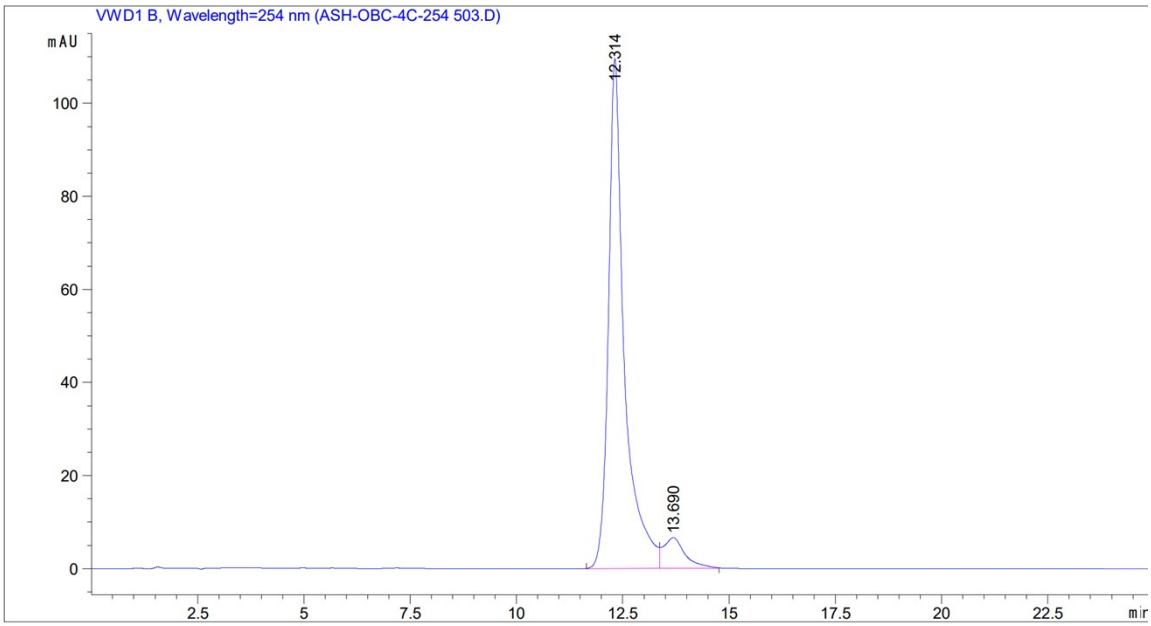
```
======================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 6/7/2024 3:14:24 PM
                                             Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/7/2024 3:03:25 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/7/2024 3:39:35 PM by SYSTEM
                  (modified after loading)
Method Info     : Pump leak test method

Sample Info     : 50% MeCN/H2O
                  1 mL/min
                  254 nm
                  5 uL inj.
                  1.0 mL/min
                  ymcpak-odsa
```



4c

Concentration = 1 mg/mL of compound in ACN : H_2O (1 : 1)




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:        :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\ASH-OBC-4C-254 503.D
Sample Name: ASH-OBC-4C-254

Signal 1: VWD1 B, Wavelength=254 nm

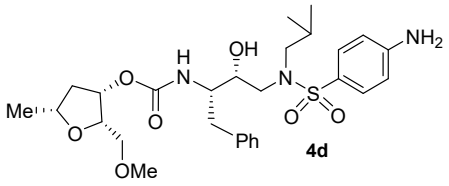
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.314	BV	0.3696	2850.65918	109.54819	92.4342
2	13.690	VB	0.4991	233.32800	6.59036	7.5658
Totals :				3083.98718	116.13856	

*** End of Report ***

Data File C:\Chem32\1\Data\ASH-OBC-4D-254 506.D
Sample Name: ASH-OBC-4D-254

```
======================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 6/7/2024 4:49:48 PM
                                             Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/7/2024 4:46:50 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/7/2024 5:17:39 PM by SYSTEM
                  (modified after loading)
Method Info     : Pump leak test method

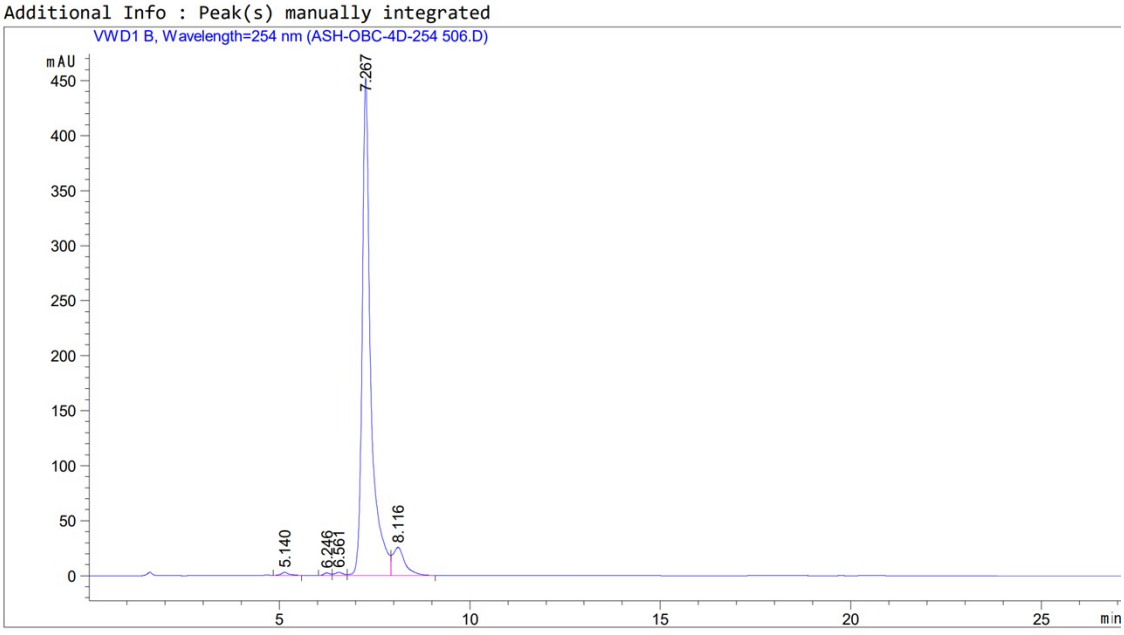
Sample Info     : 50% MeCN/H2O
                  1 mL/min
                  254 nm
                  5 uL inj.
                  1.0 mL/min
                  ymcpak-odsa
```



4d

Concentration = 1 mg/mL of compound in ACN : H_2O (1 : 1)

Additional Info : Peak(s) manually integrated




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:        :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\ASH-OBC-4D-254 506.D
Sample Name: ASH-OBC-4D-254

Signal 1: VWD1 B, Wavelength=254 nm

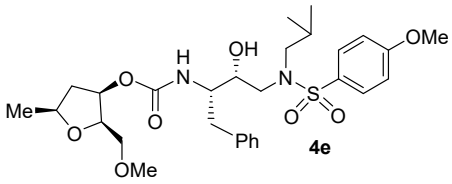
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.140	VB	0.2000	39.90999	2.80452	0.5154
2	6.246	BV	0.1628	25.37671	2.33571	0.3277
3	6.561	VV	0.2155	41.59143	2.79735	0.5371
4	7.267	VV	0.2244	7063.14893	451.75095	91.2196
5	8.116	VB	0.3196	572.98694	25.55422	7.4001
Totals :				7743.01400	485.24274	

*** End of Report ***

Data File C:\Chem32\1\Data\ASH-OBC-4E-254 507.D
Sample Name: ASH-OBC-4E-254

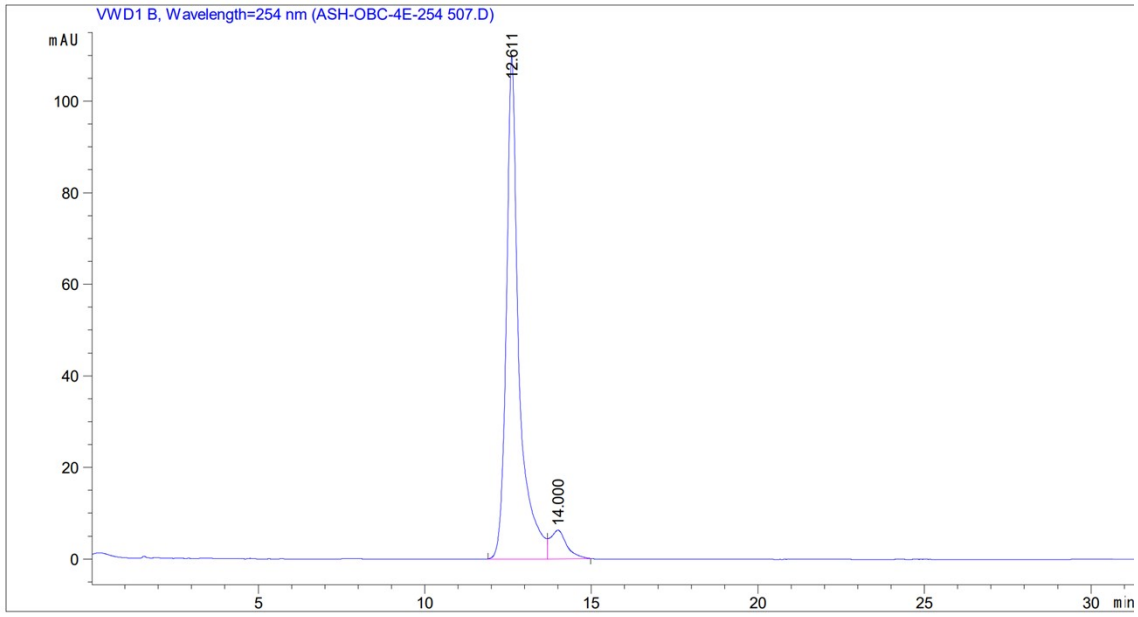
```
==========================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 6/7/2024 5:19:58 PM
                                             Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/7/2024 5:17:39 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/7/2024 5:51:34 PM by SYSTEM
                  (modified after loading)
Method Info     : Pump leak test method

Sample Info     : 50% MeCN/H2O
                  1 mL/min
                  254 nm
                  5 uL inj.
                  1.0 mL/min
                  ymcpak-odsa
```



4e

Concentration = 1 mg/mL of compound in ACN : H_2O (1 : 1)




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:                :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\ASH-OBC-4E-254 507.D
Sample Name: ASH-OBC-4E-254

Signal 1: VWD1 B, Wavelength=254 nm

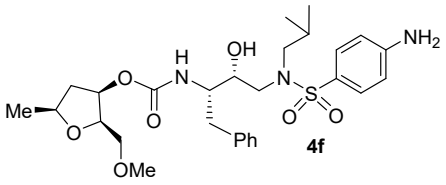
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.611	BV	0.3749	2883.74438	109.64135	92.9486
2	14.000	VB	0.4923	218.77094	6.28154	7.0514
Totals :				3102.51532	115.92289	

*** End of Report ***

Data File C:\Chem32\1\Data\ASH-OBC-4F-254-NEW-3 532.D
Sample Name: ASH-OBC-4F-254-NEW-3

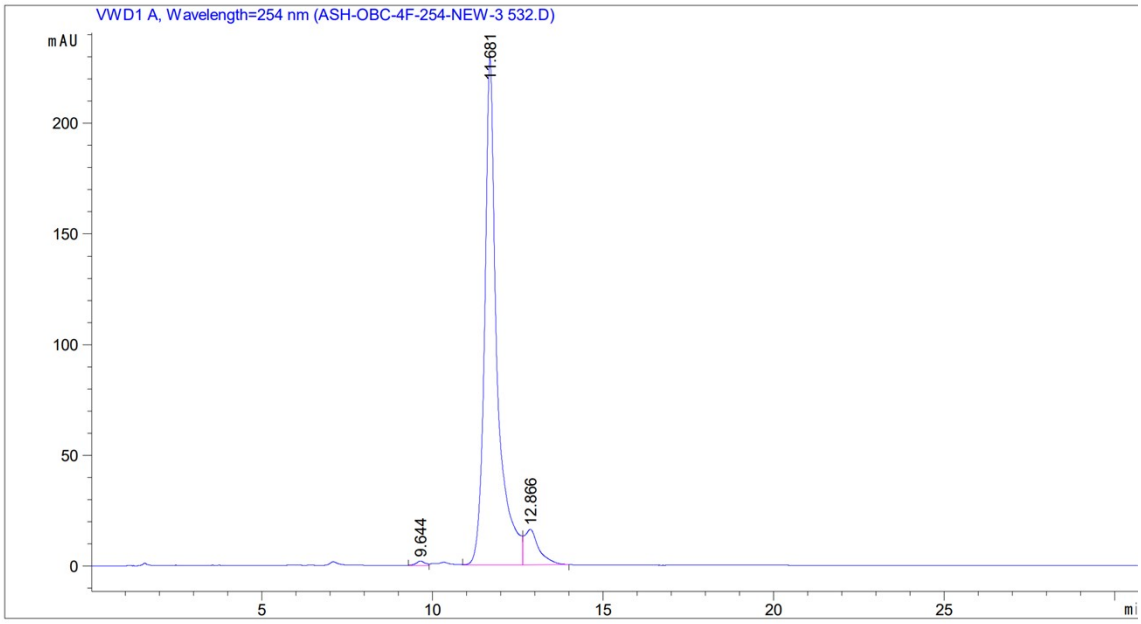
```
==========================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 6/10/2024 4:02:29 PM
                                             Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/10/2024 3:51:57 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/10/2024 4:33:40 PM by SYSTEM
                  (modified after loading)
Method Info     : Pump leak test method

Sample Info     : 45% MeCN/H2O
                  1.0 mL/min
                  254 nm
                  5 uL inj.
                  1.0 mL/min
                  ymcpak-odsa
```



4f

Concentration = 1 mg/mL of compound in ACN : H_2O (1 : 1)




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:                :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\ASH-OBC-4F-254-NEW-3 532.D
Sample Name: ASH-OBC-4F-254-NEW-3

Signal 1: VWD1 A, Wavelength=254 nm

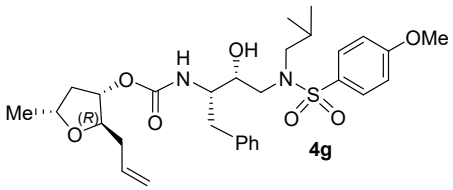
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.644	BV	0.2596	34.56042	1.94261	0.5452
2	11.681	VV	0.3583	5821.04443	229.20386	91.8309
3	12.866	VB	0.4174	483.26801	16.09259	7.6239
Totals :				6338.87286	247.23906	

*** End of Report ***

Data File C:\Chem32\1\Data\ASH-OBC-4G-254 511.D
Sample Name: ASH-OBC-4G-254

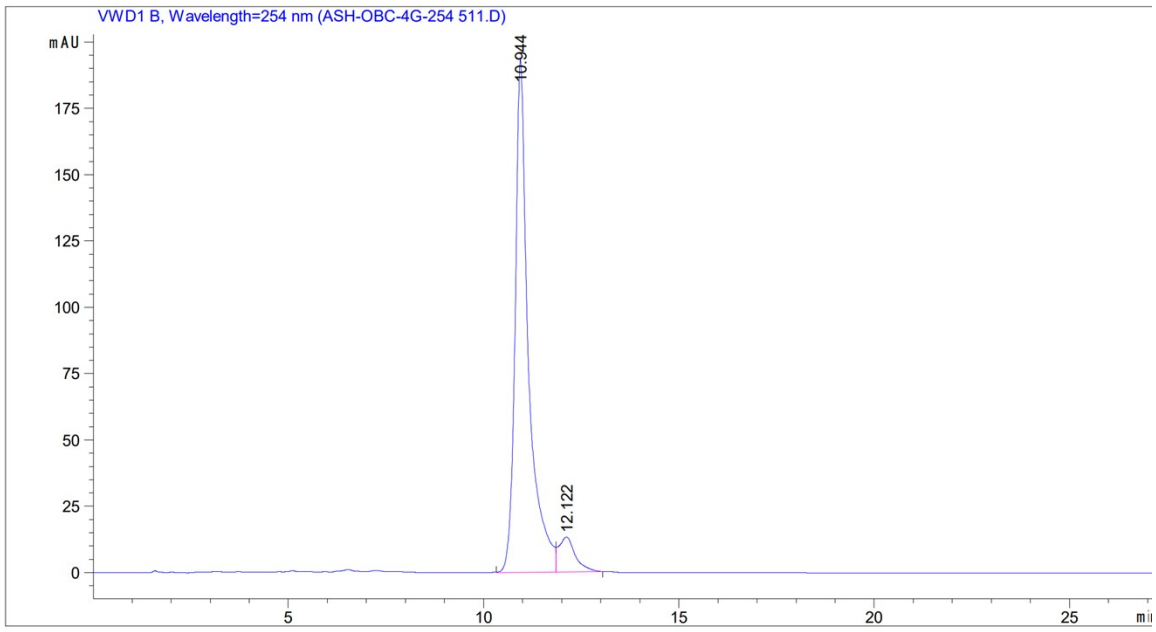
```
==========================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 6/7/2024 7:15:40 PM
                                               Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/7/2024 7:14:28 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/8/2024 1:06:11 PM by SYSTEM
                  (modified after loading)
Method Info     : Pump leak test method

Sample Info     : 60% MeCN/H2O
                  1 mL/min
                  254 nm
                  5 uL inj.
                  1.0 mL/min
                  ymcpak-odsa
```



4g

Concentration = 1 mg/mL of compound in ACN : H_2O (1 : 1)




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:        :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\ASH-OBC-4G-254 511.D
Sample Name: ASH-OBC-4G-254

Signal 1: VWD1 B, Wavelength=254 nm

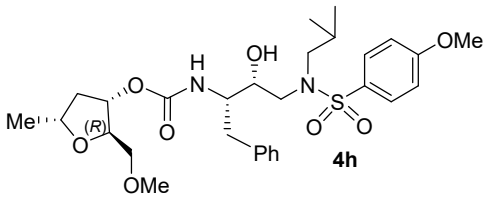
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.944	BV	0.3353	4591.29541	193.17729	92.2622
2	12.122	VB	0.4154	385.06030	13.15954	7.7378
Totals :				4976.35571	206.33683	

*** End of Report ***

Data File C:\Chem32\1\Data\ASH-OBC-4H-254 517.D
Sample Name: ASH-OBC-4H-254

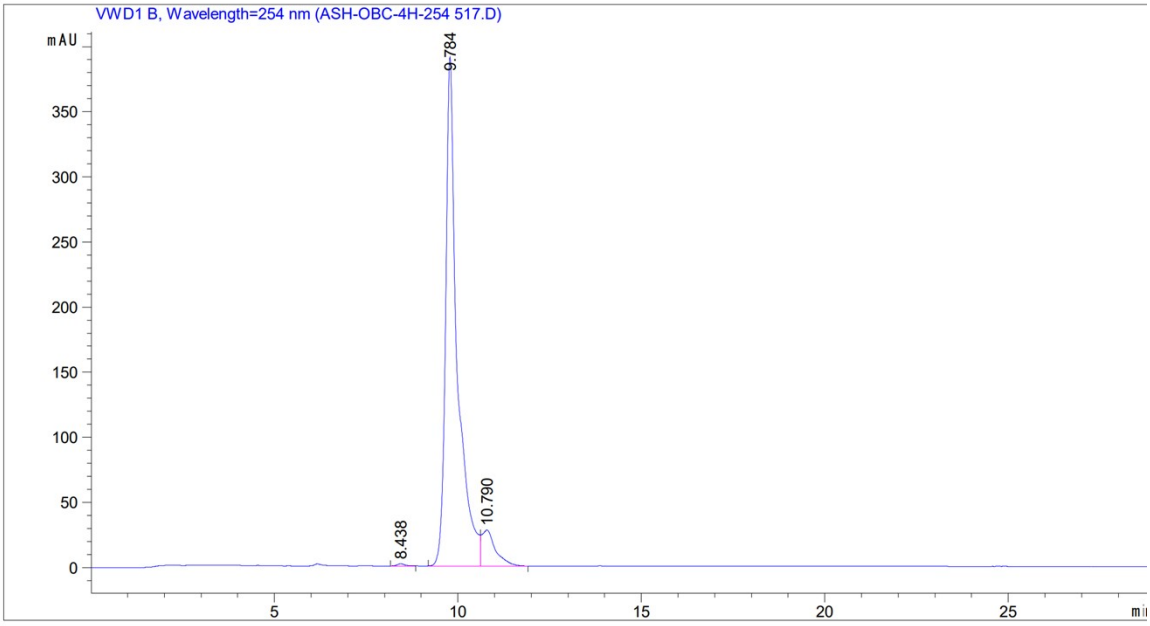
```
==========================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 6/8/2024 3:06:11 PM
                                             Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/8/2024 3:04:35 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/8/2024 3:35:26 PM by SYSTEM
                  (modified after loading)
Method Info     : Pump leak test method

Sample Info     : 55% MeCN/H2O
                  1 mL/min
                  254 nm
                  5 uL inj.
                  1.0 mL/min
                  ymcpak-odsa
```



4h

Concentration = 1 mg/mL of compound in ACN : H_2O (1 : 1)




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:        :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\ASH-OBC-4H-254 517.D
Sample Name: ASH-OBC-4H-254

Signal 1: VWD1 B, Wavelength=254 nm

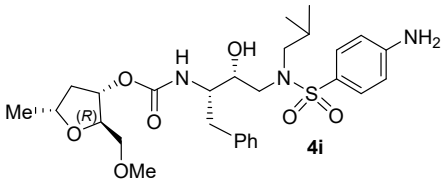
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.438	BB	0.2235	26.27509	1.72747	0.2791
2	9.784	BV	0.3103	8653.25684	390.81973	91.9159
3	10.790	VB	0.3718	734.78949	27.67530	7.8050
Totals :				9414.32142	420.22251	

*** End of Report ***

Data File C:\Chem32\1\Data\ASH-OBC-4I-254 518.D
Sample Name: ASH-OBC-4I-254

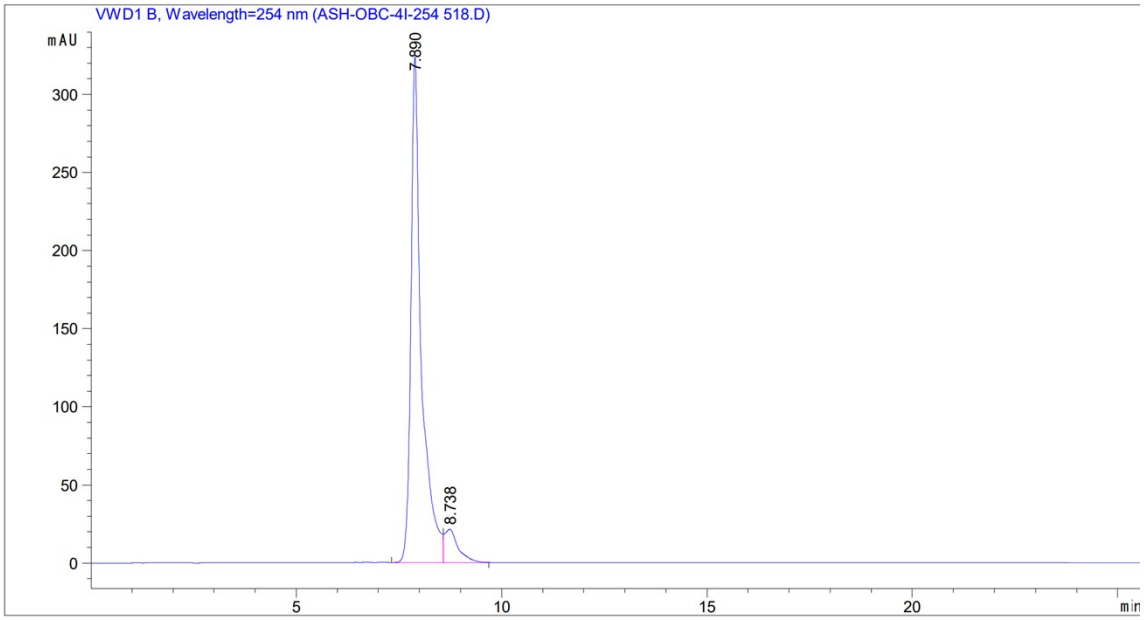
```
==========================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 6/8/2024 3:58:33 PM
                                             Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/8/2024 3:46:42 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/8/2024 4:24:31 PM by SYSTEM
                  (modified after loading)
Method Info     : Pump leak test method

Sample Info     : 50% MeCN/H2O
                  1 mL/min
                  254 nm
                  5 uL inj.
                  1.0 mL/min
                  ymcpak-odsa
```



4i

Concentration = 1 mg/mL of compound in ACN : H_2O (1 : 1)




```
==========================================================================
                      Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:        :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\ASH-OBC-4I-254 518.D
Sample Name: ASH-OBC-4I-254

Signal 1: VWD1 B, Wavelength=254 nm

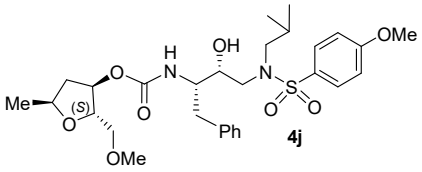
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.890	VV	0.2521	5774.38965	323.73325	92.0484
2	8.738	VB	0.3283	498.82303	21.36840	7.9516
Totals :				6273.21268	345.10165	

*** End of Report ***

Data File C:\Chem32\1\Data\ASH-OBC-4J-254 519.D
Sample Name: ASH-OBC-4J-254

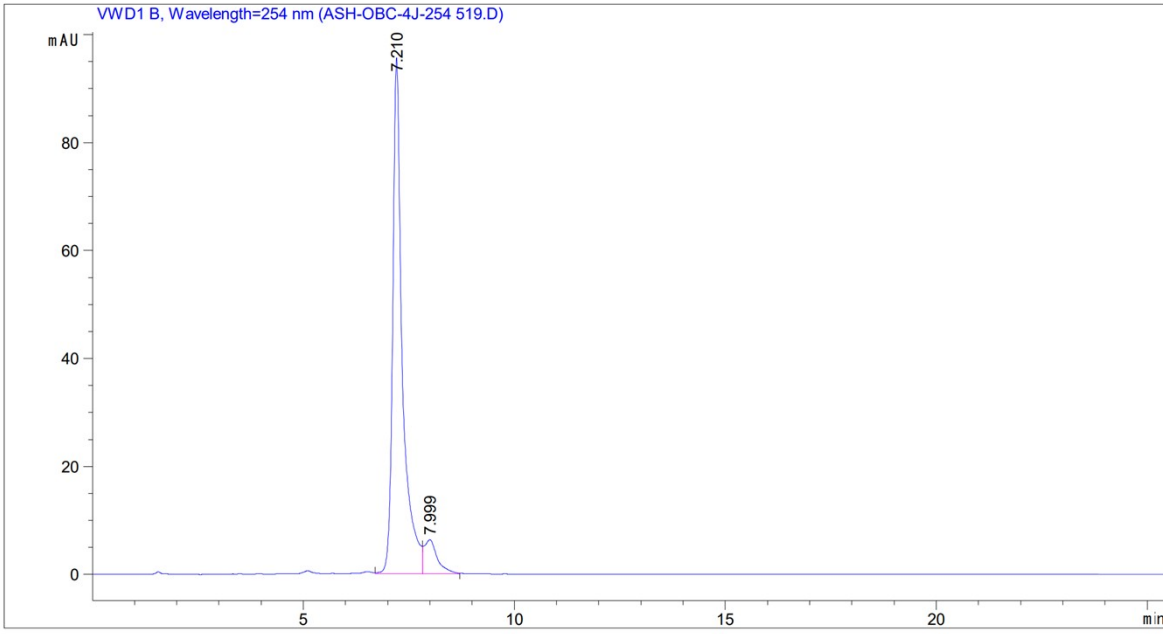
```
======================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 6/8/2024 4:41:09 PM
                                             Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/8/2024 4:24:31 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/8/2024 5:06:55 PM by SYSTEM
                  (modified after loading)
Method Info     : Pump leak test method

Sample Info     : 50% MeCN/H2O
                  1 mL/min
                  254 nm
                  5 uL inj.
                  1.0 mL/min
                  ymcpak-odsa
```



4j

Concentration = 1 mg/mL of compound in ACN : H_2O (1 : 1)




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:        :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\ASH-OBC-4J-254 519.D
Sample Name: ASH-OBC-4J-254

Signal 1: VWD1 B, Wavelength=254 nm

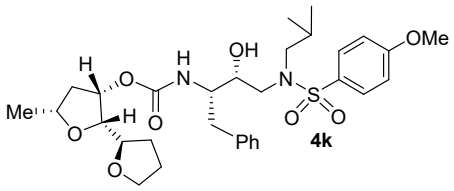
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.210	VV	0.2273	1518.76587	95.61581	91.7905
2	7.999	VB	0.3058	135.83417	6.29474	8.2095
Totals :				1654.60004	101.91054	

*** End of Report ***

Data File C:\Chem32\1\Data\ASH-OBC-4K-254-12 539.D
Sample Name: ASH-OBC-4K-254-12

```
==========================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 6/11/2024 12:20:39 PM
                                             Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/11/2024 12:19:49 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/11/2024 2:41:19 PM by SYSTEM
                  (modified after loading)
Method Info     : Pump leak test method

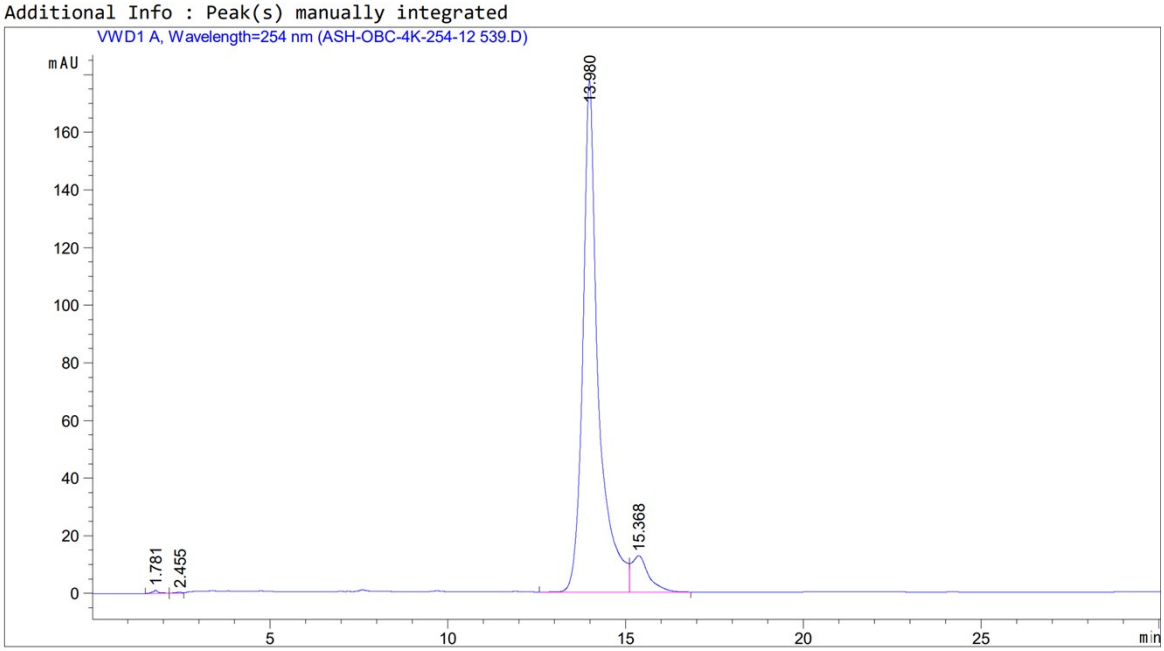
Sample Info     : 50% MeCN/H2O
                  1.0 mL/min
                  254 nm
                  5 uL inj.
                  1.0 mL/min
                  ymcpak-odsa
```



4k

Concentration = 0.8 mg/mL of compound in ACN : H_2O (1 : 1)

Additional Info : Peak(s) manually integrated




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:        :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\ASH-OBC-4K-254-12 539.D
Sample Name: ASH-OBC-4K-254-12

Signal 1: VWD1 A, Wavelength=254 nm

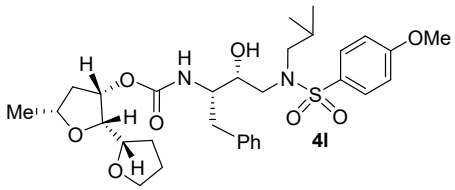
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.781	BB	0.1468	12.47250	1.11284	0.2138
2	2.455	BV	0.2072	4.74914	3.43689e-1	0.0814
3	13.980	VV	0.4281	5388.28711	177.54451	92.3706
4	15.368	VB	0.4793	427.82523	12.62603	7.3341
Totals :				5833.33398	191.62706	

*** End of Report ***

Data File C:\Chem32\1\Data\ASH-OBC-4L-254 520.D
Sample Name: ASH-OBC-4L-254

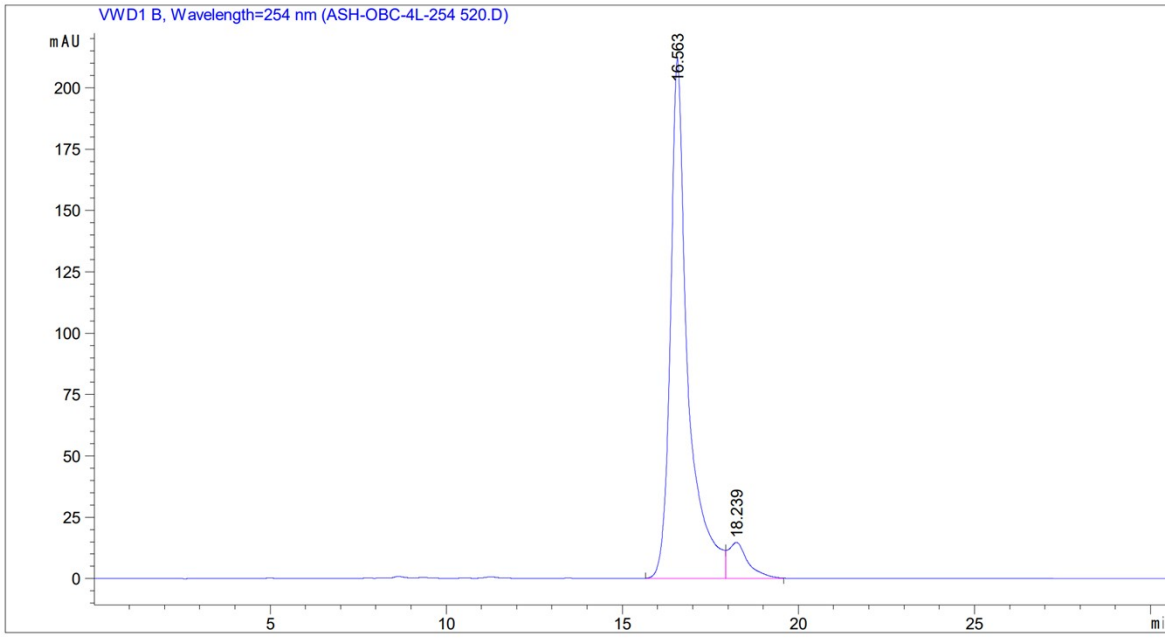
```
======================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 6/8/2024 5:21:35 PM
                                             Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/8/2024 5:06:55 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AB-02-34A.M
Last changed    : 6/8/2024 5:52:33 PM by SYSTEM
                  (modified after loading)
Method Info     : Pump leak test method

Sample Info     : 50% MeCN/H2O
                  1 mL/min
                  254 nm
                  5 uL inj.
                  1.0 mL/min
                  ymcpak-odsa
```



4l

Concentration = 1 mg/mL of compound in ACN : H_2O (1 : 1)




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:        :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\ASH-OBC-4L-254 520.D
Sample Name: ASH-OBC-4L-254

Signal 1: VWD1 B, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.563	BV	0.4878	7291.14063	211.69453	92.6870
2	18.239	VB	0.5549	575.26935	14.62415	7.3130
Totals :				7866.40997	226.31868	

*** End of Report ***