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Supporting Information

Synthesis of Optically Pure (*S*)-2-Amino-5-arylpent-4-ynoic acids by Sonogashira Reactions and their Potential Use as Highly Selective Potent Inhibitors of Aldose Reductase

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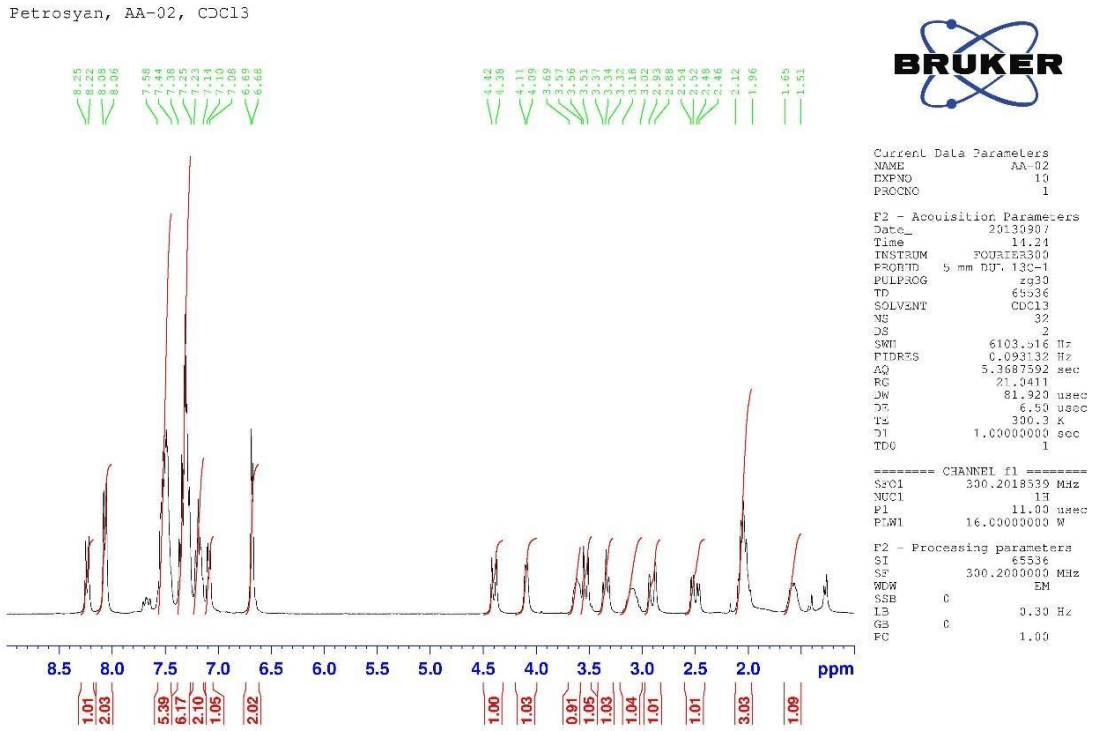
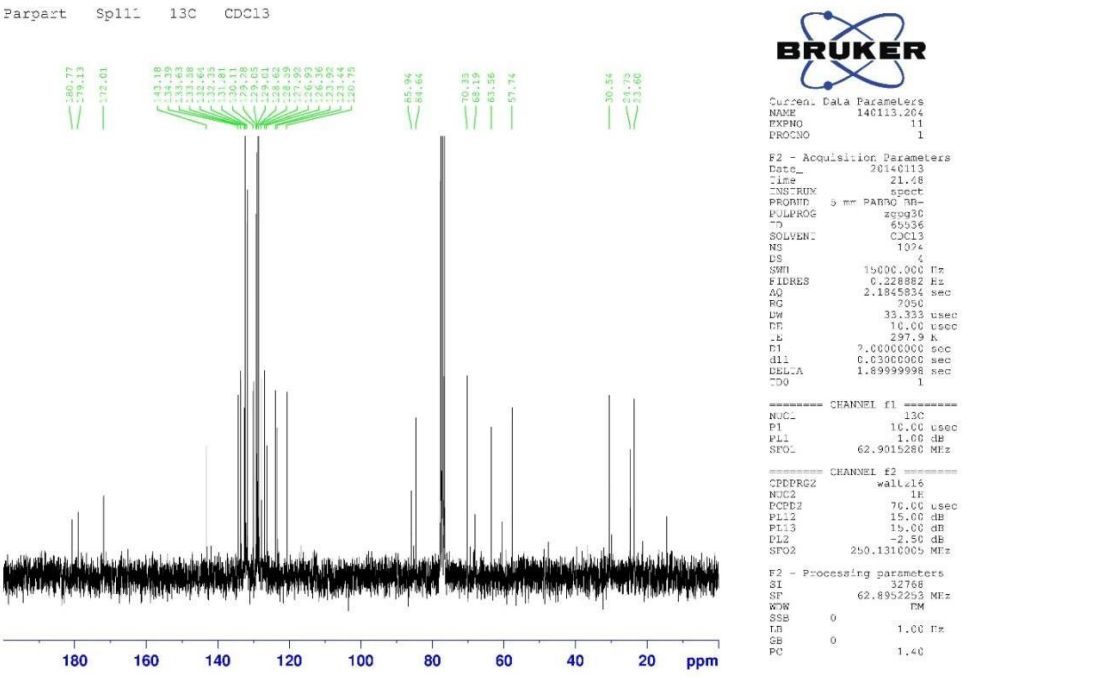
[e] Centre for Advanced Drug Research, COMSATS Institute of Information Technology, Abbottabad-22060, Pakistan

Content

1 NMR spectras

1.1 (*S*)-2-Amino-5-[phenyl]pent-4-insäure-Ni-(*S*)-BPBP (2a):





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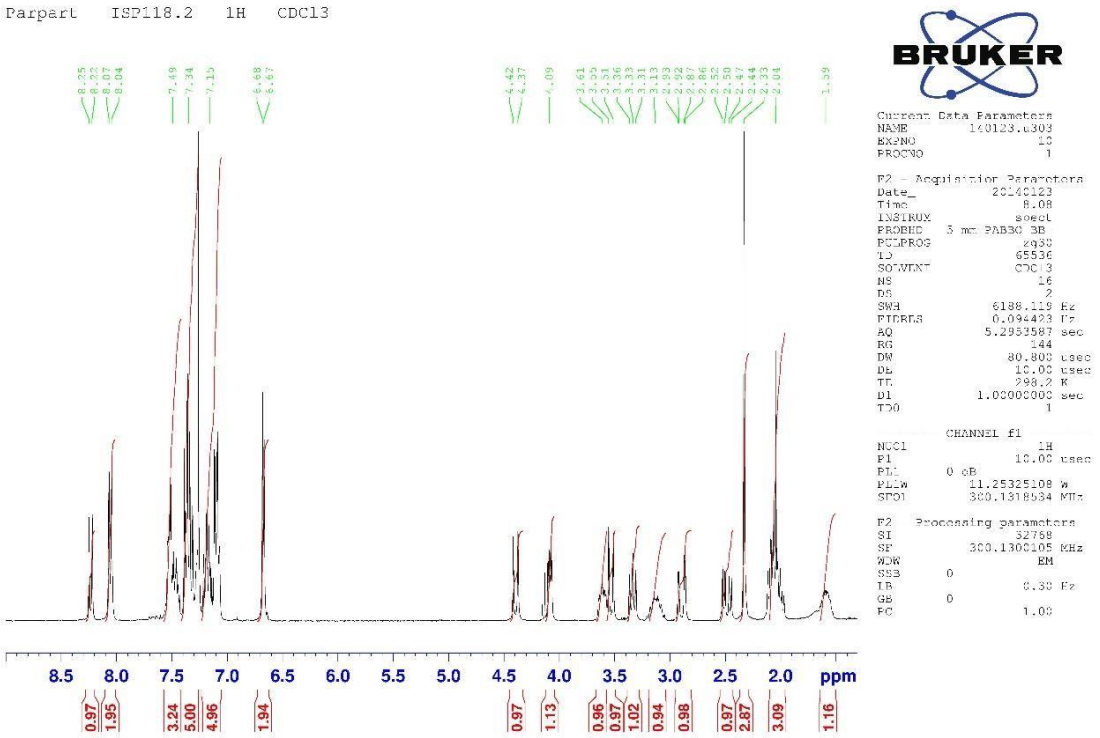

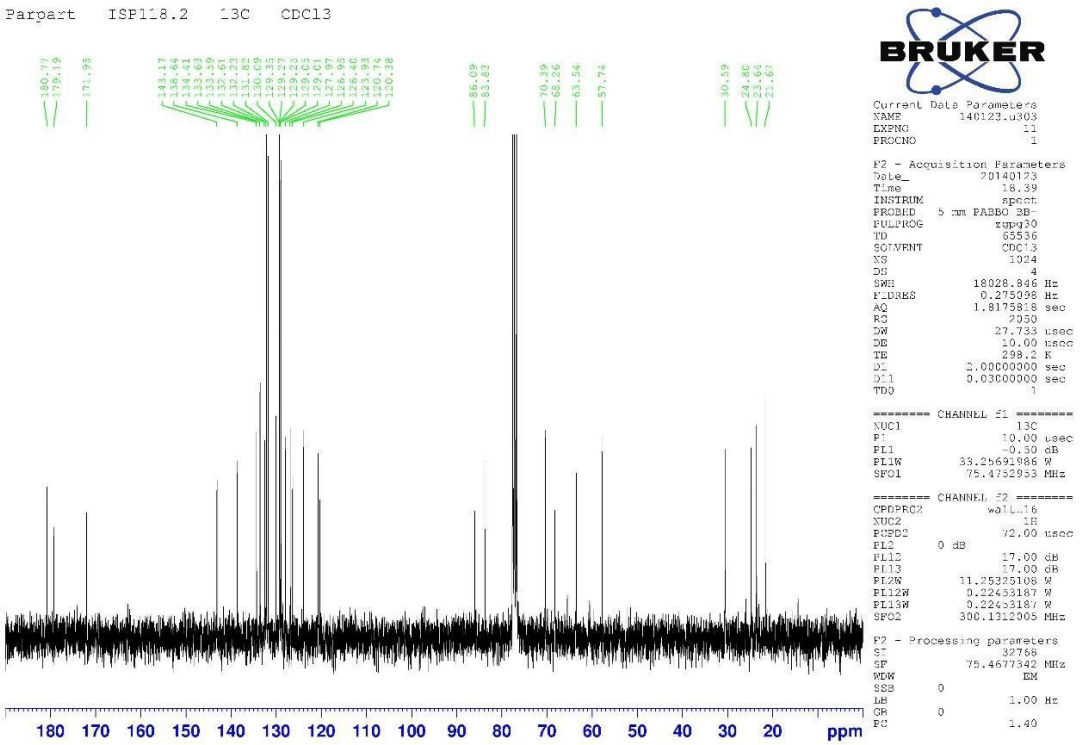

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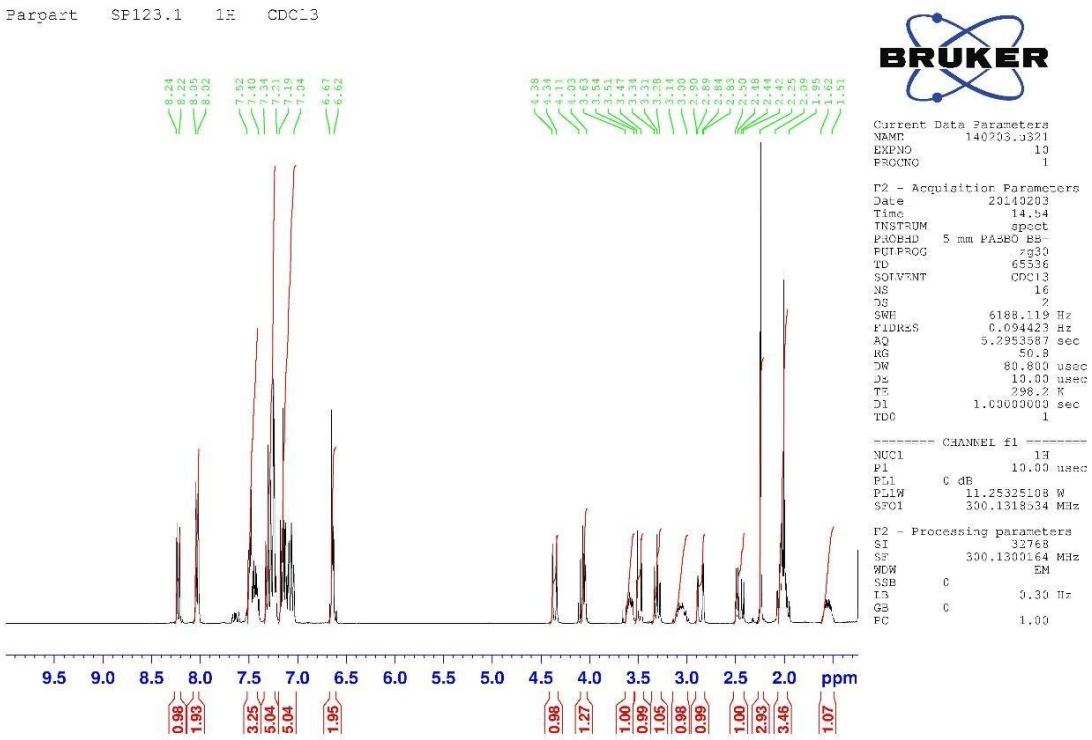

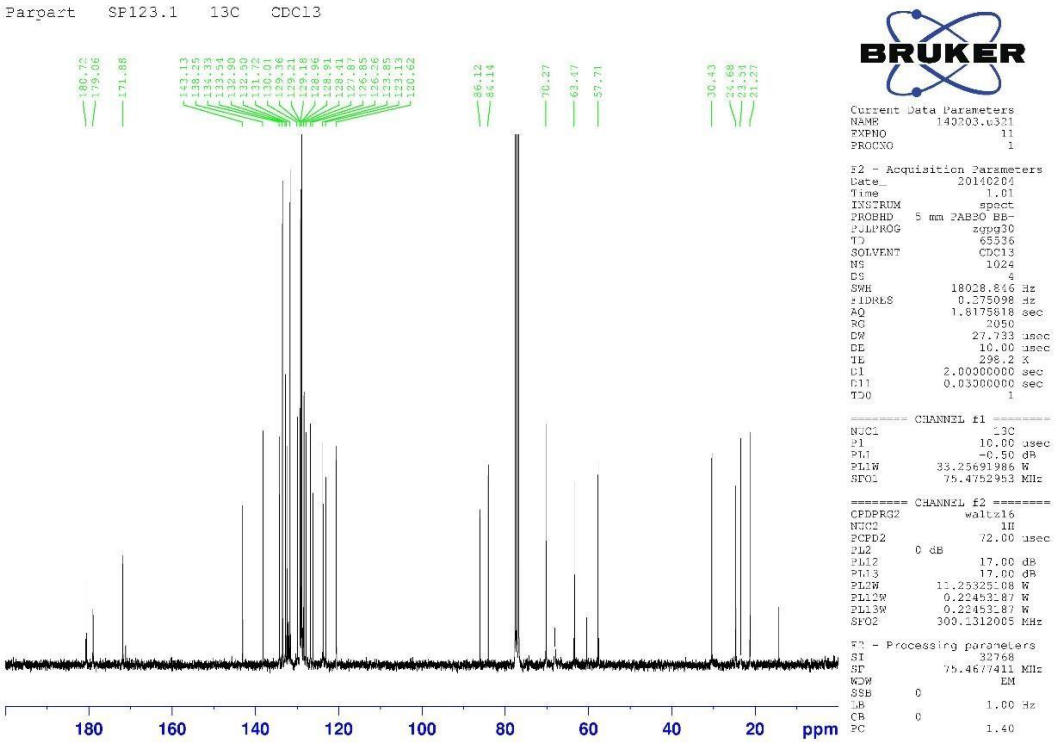

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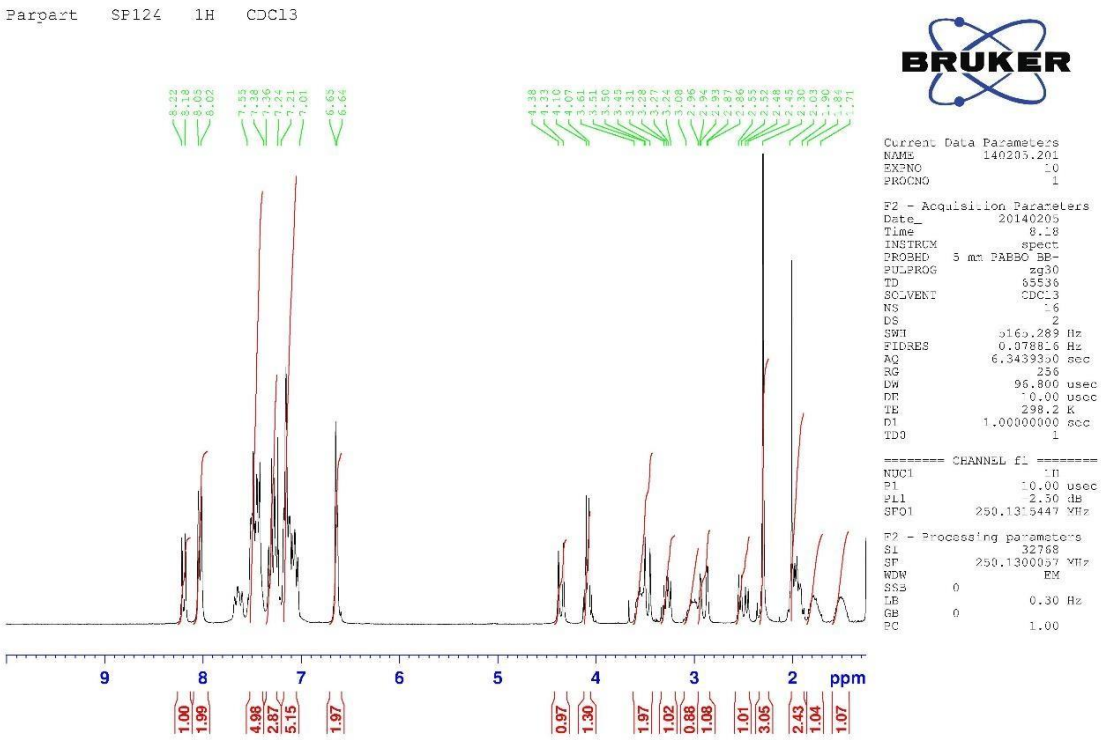

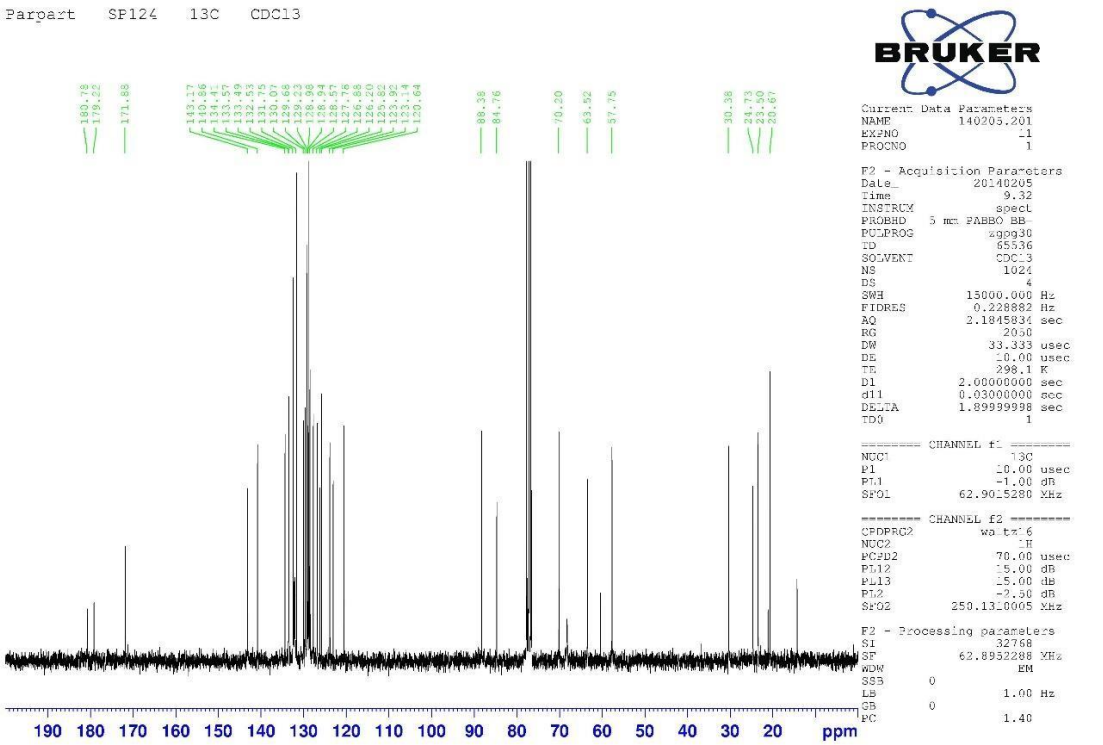

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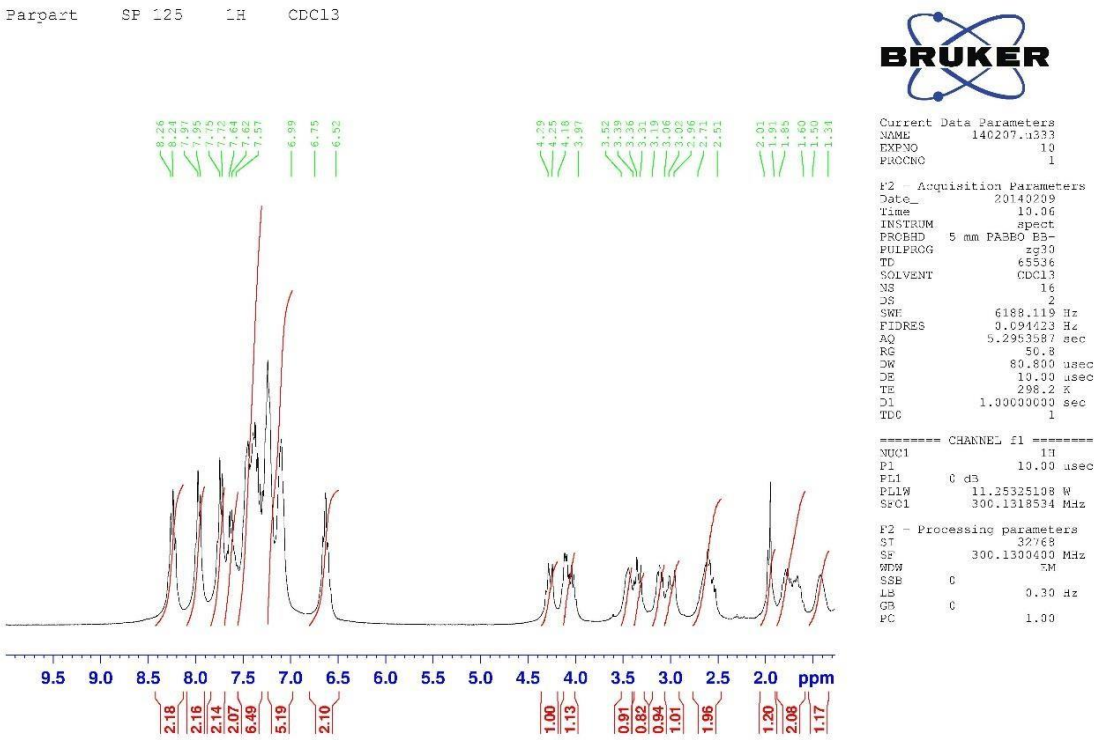

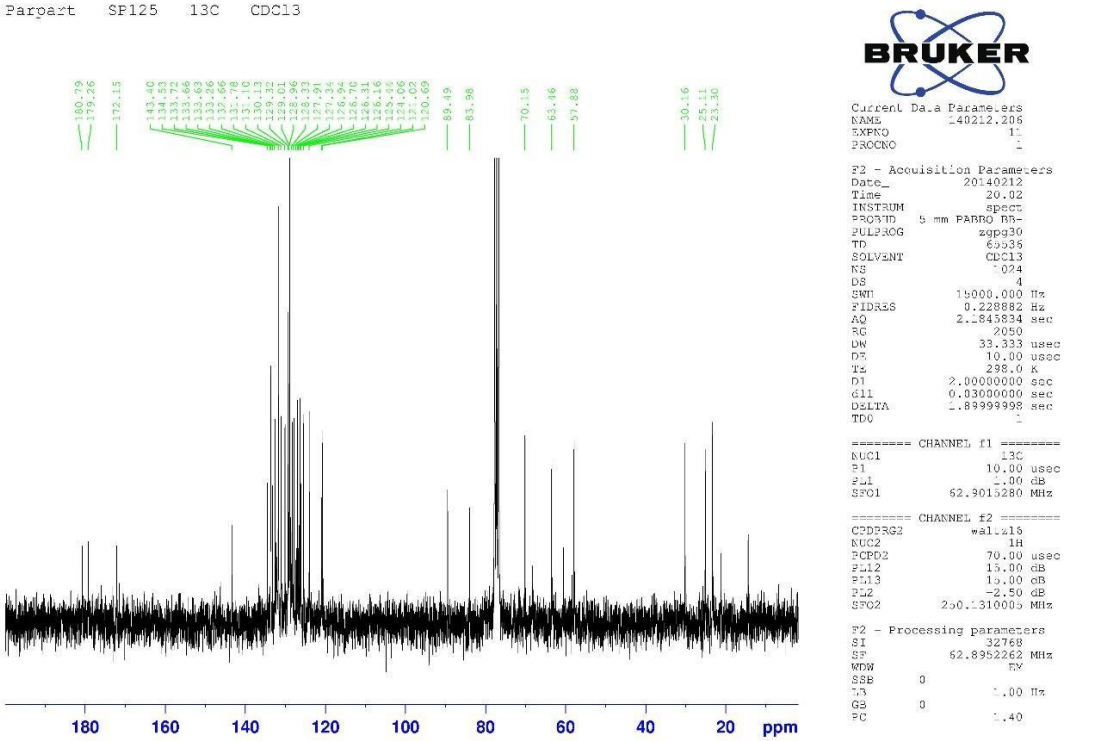

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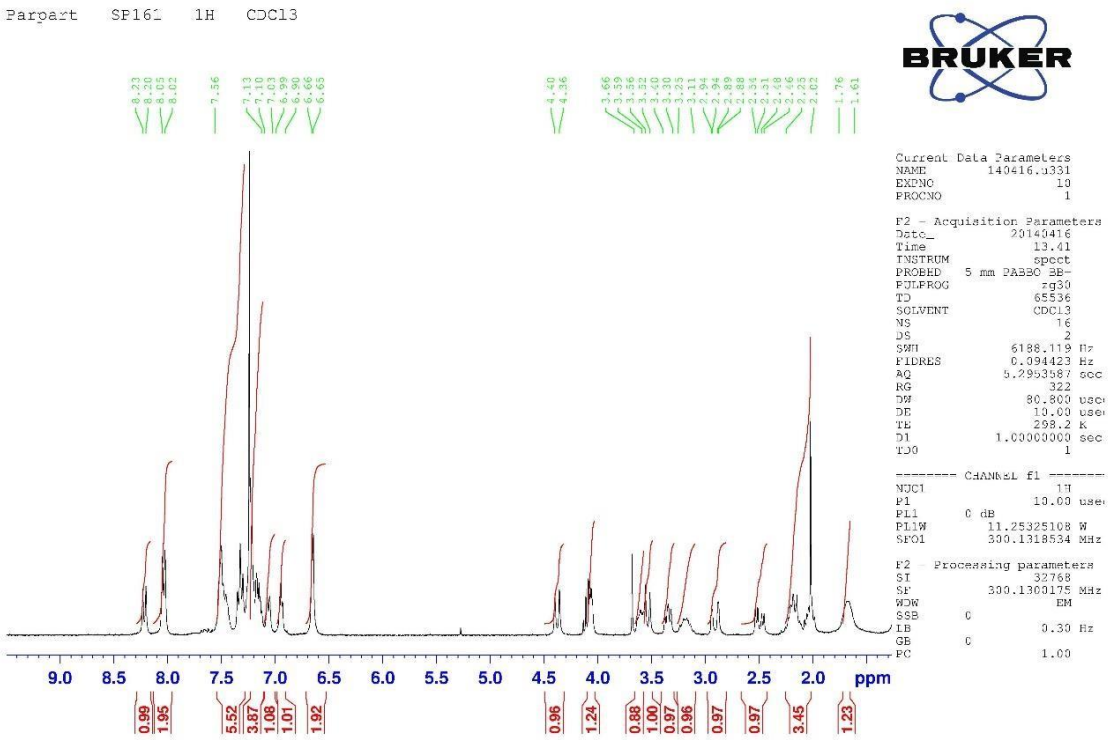

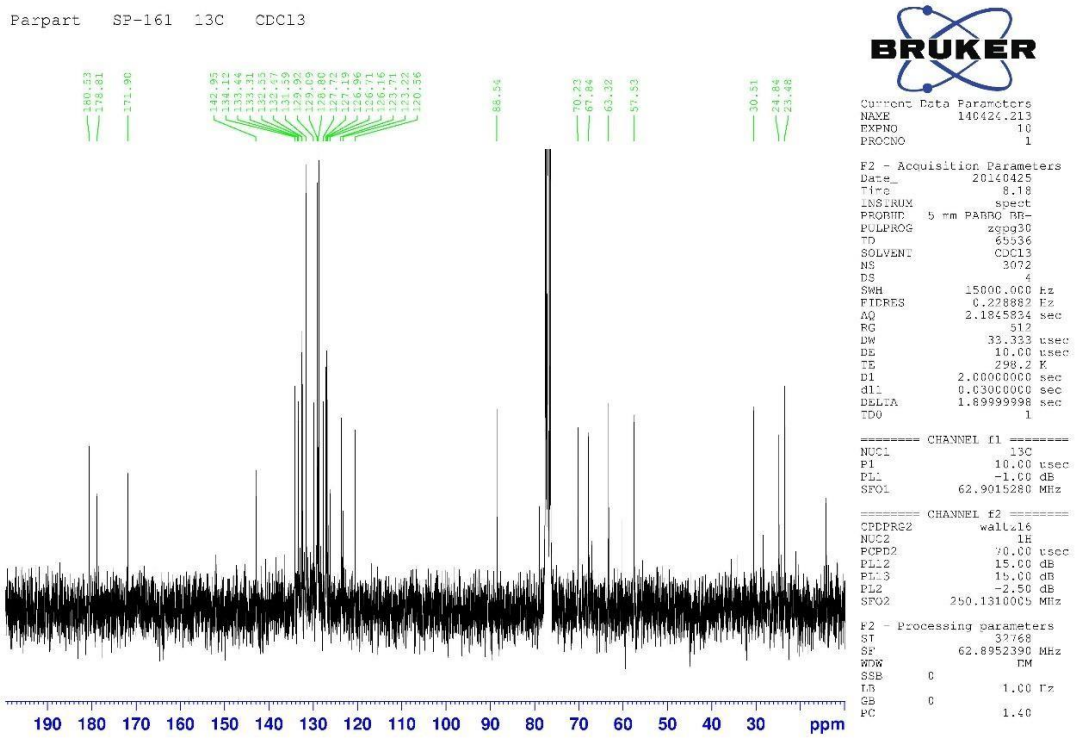

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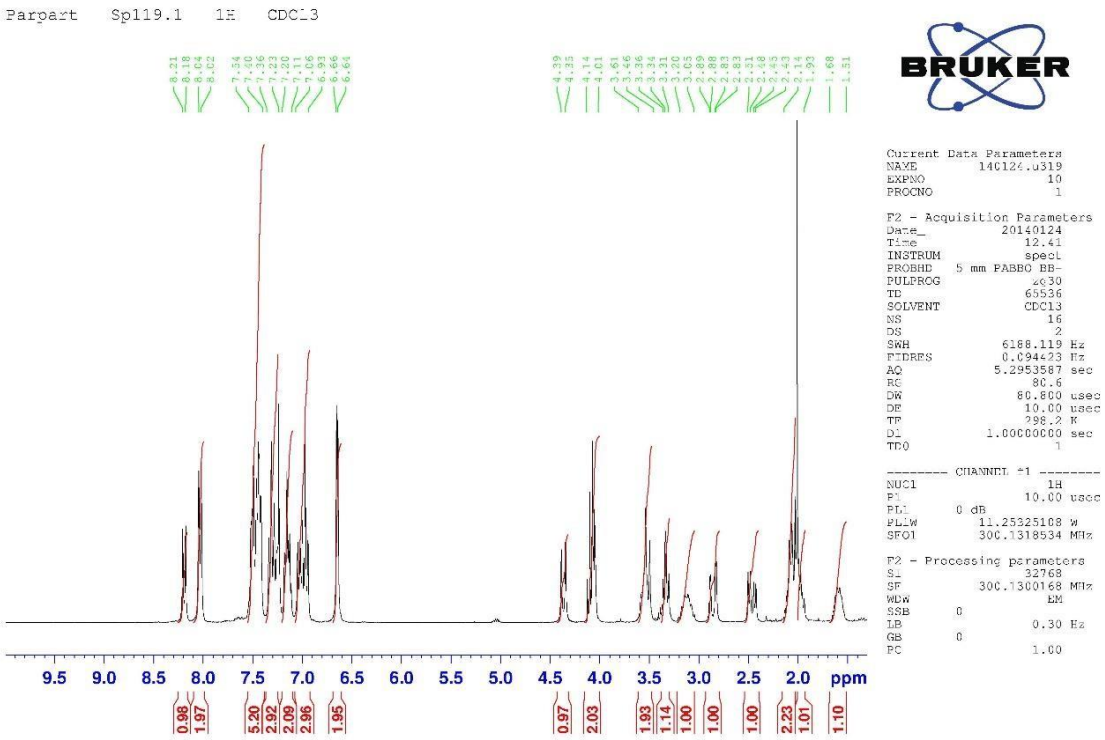
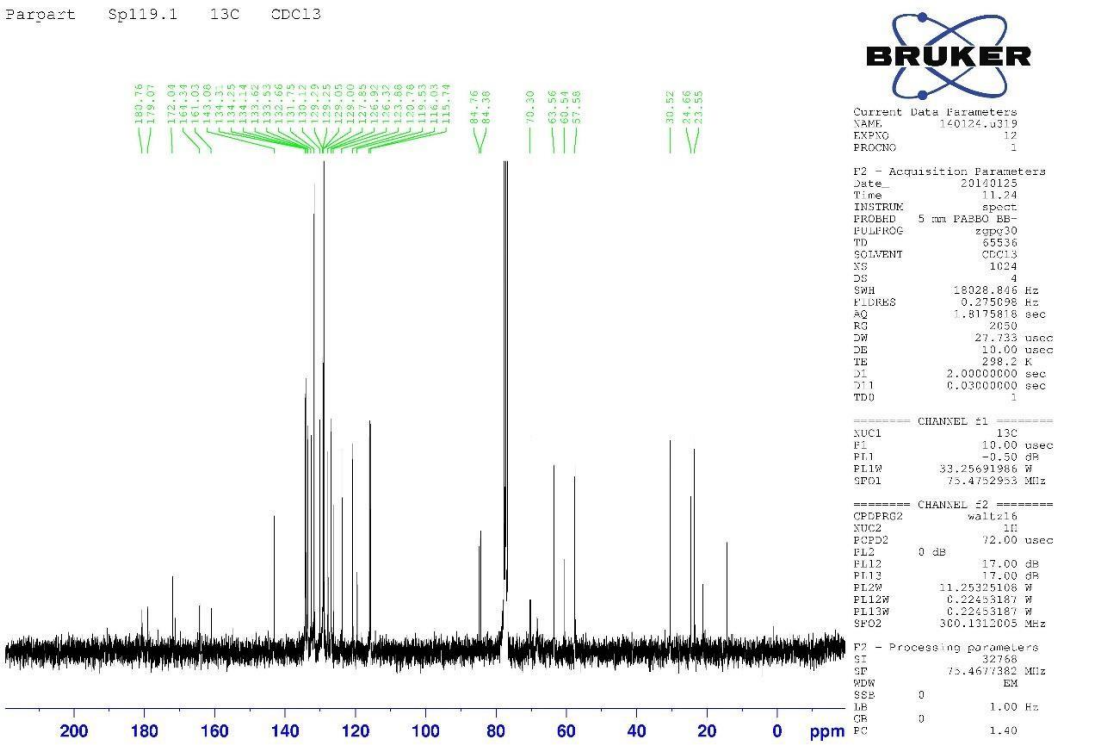
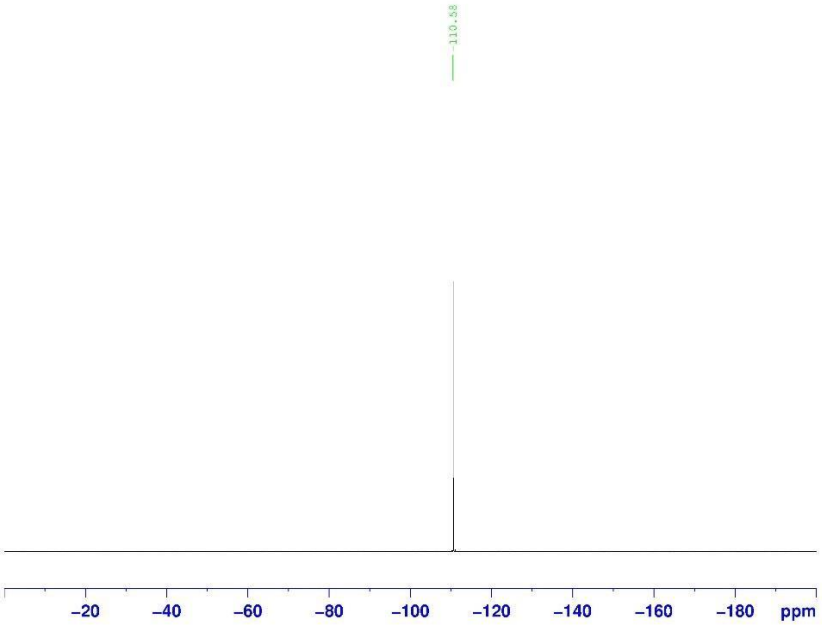




Parpart Sp119.1 19F CDCl3

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TD                 131072
SOLVENT             CDCl3
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DS                      4
SWH              66964.289 Hz
FIDRES           0.510897 Hz
AQ               0.9787210 sec
RG                    2050
DW                7.467 usec
DE                10.00 usec
TE                298.2 K
D1           1.00000000 sec
D11          0.03000000 sec
D12          0.00002000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   19F
P1                10.00 usec
PL1                -3.00 dB
PL1W         15.53680420 W
SFO1         282.3761148 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                   1H
PCPD2             72.00 usec
PL2          0 dB
PL12               17.00 dB
PL2W         11.25325108 W
PL12W         0.22453187 W
SFO2         300.1312005 MHz

F2 - Processing parameters
SI                  65536
SF           282.4043550 MHz
WDW                    EM
SSB          0
LB                  0.30 Hz
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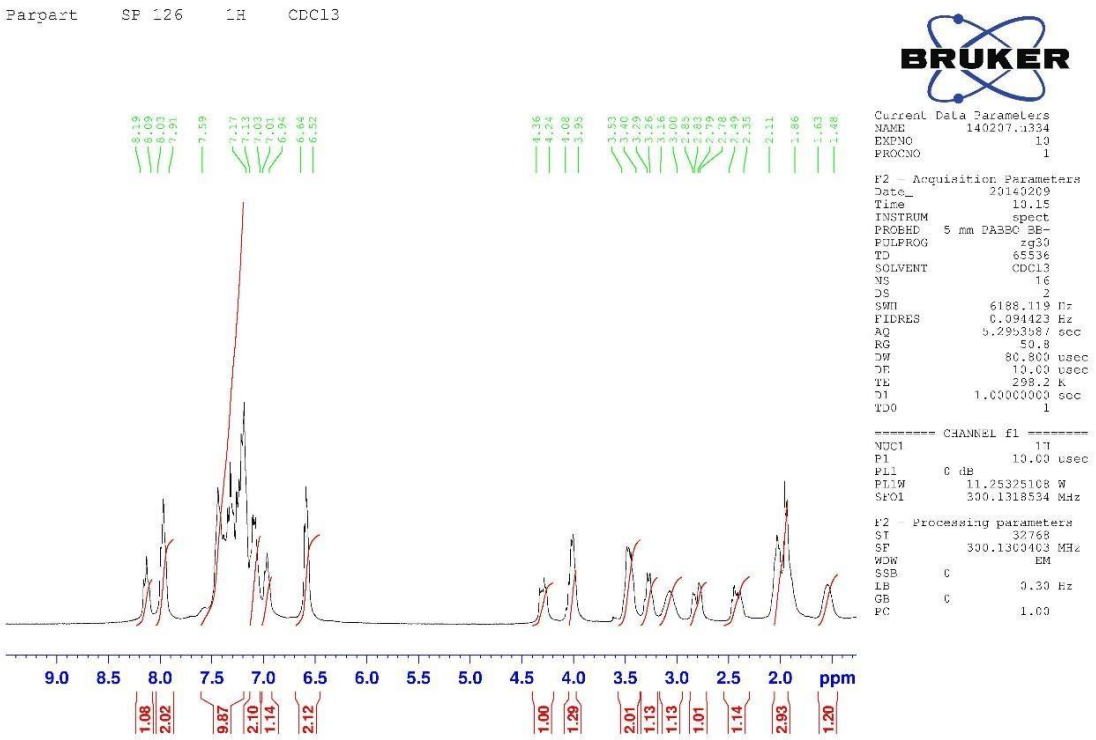

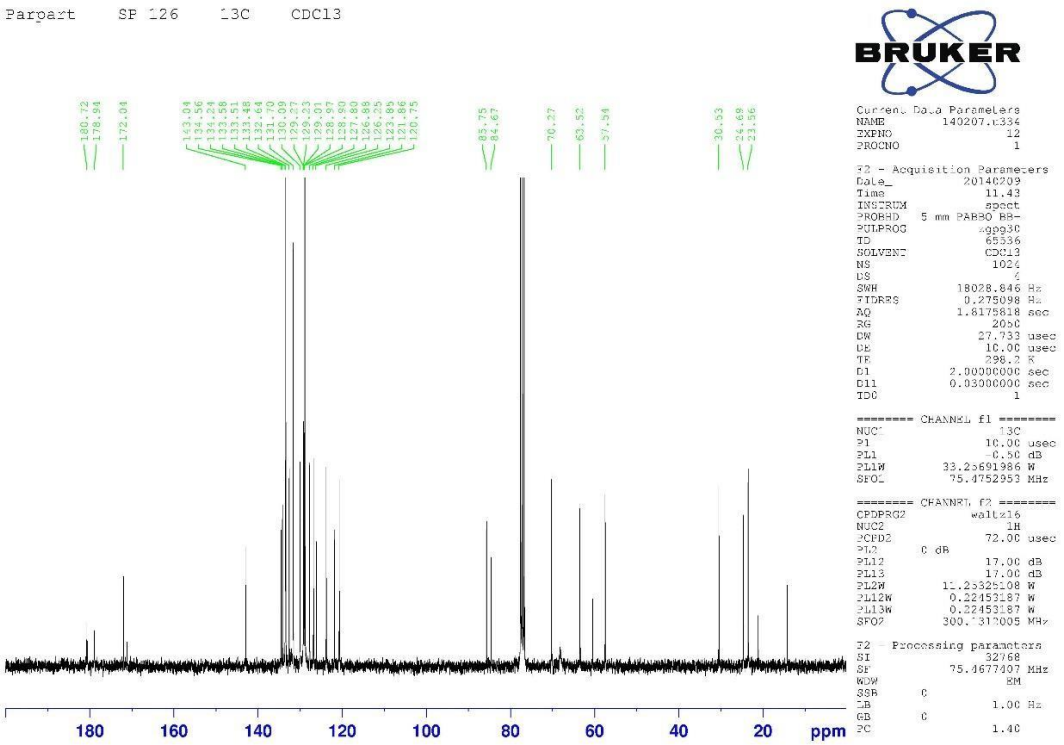

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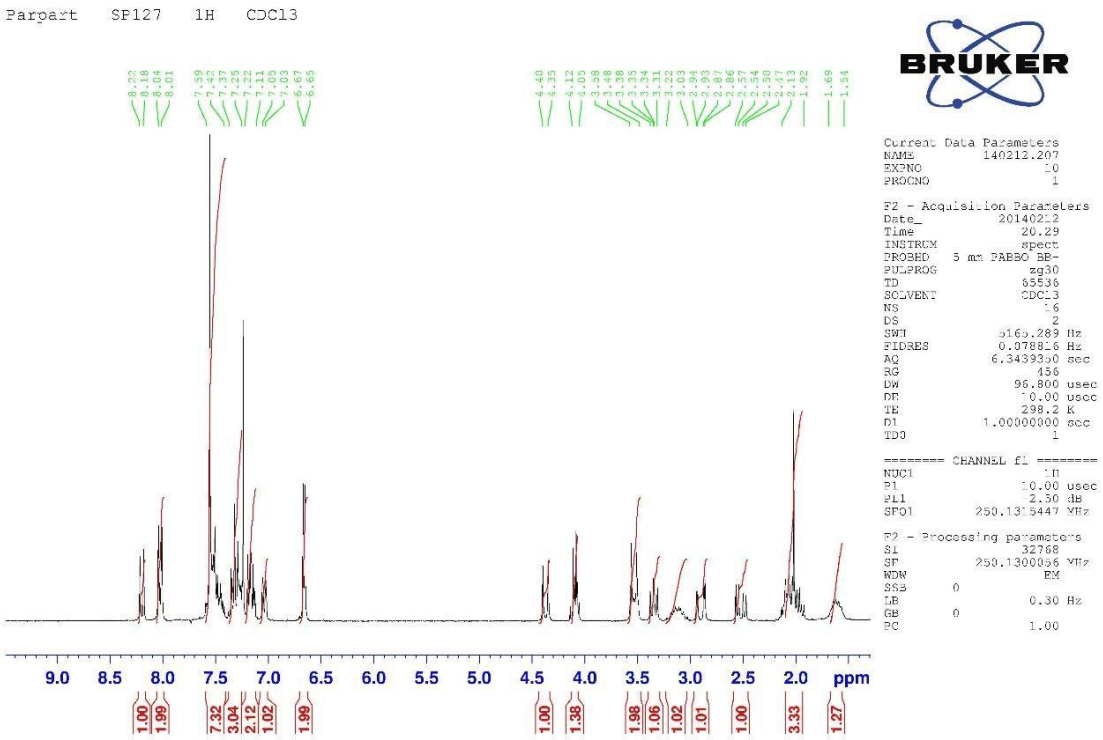

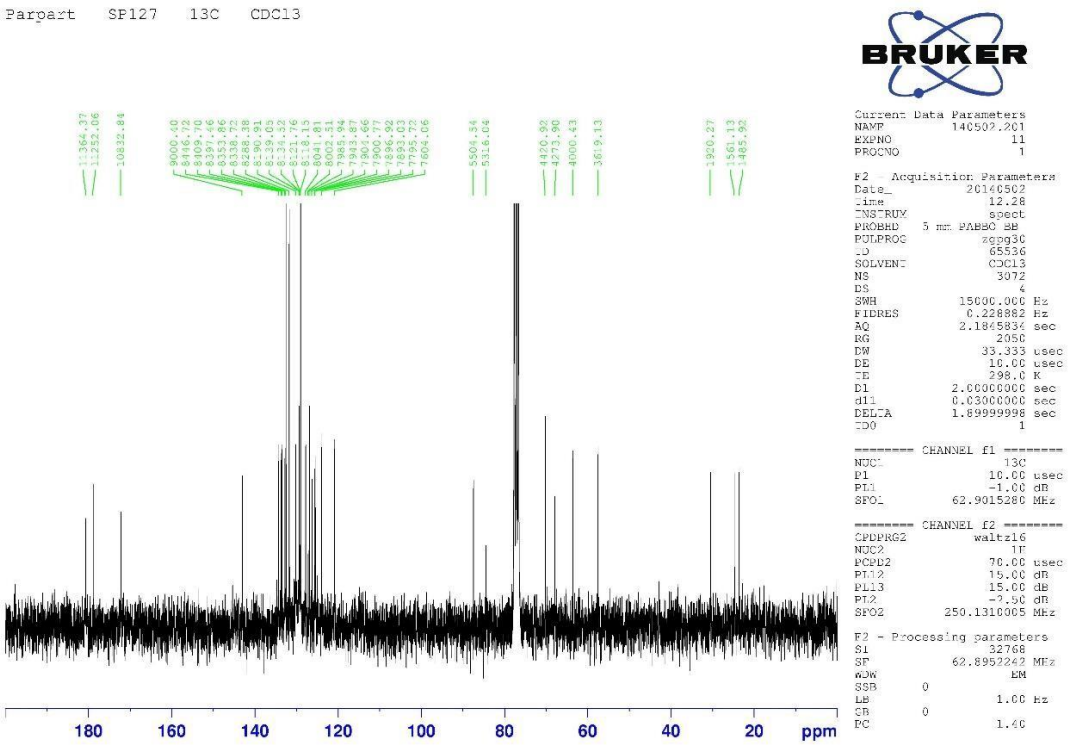

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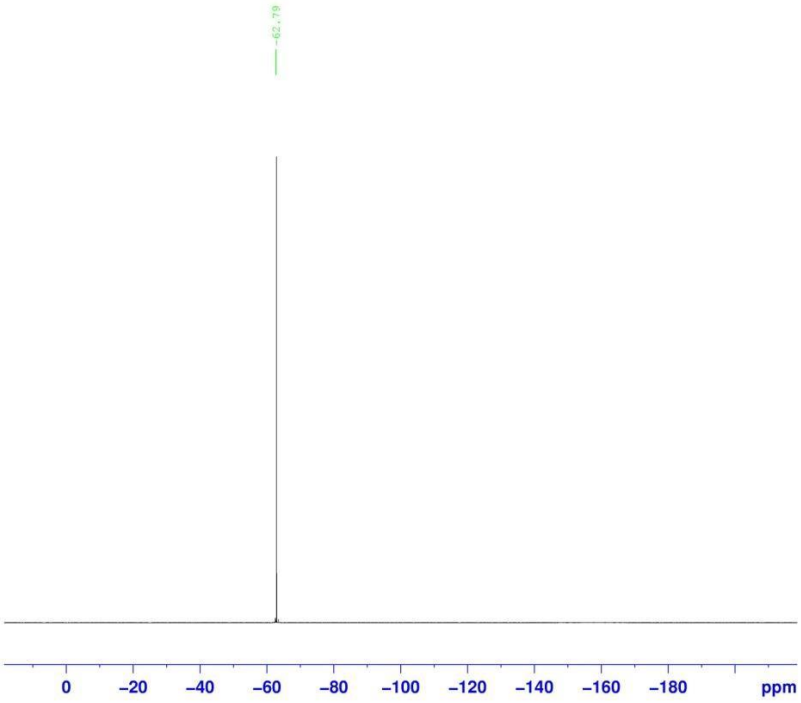


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DS                      4
SWH             66964.289 Hz
FIDRES          0.510897 Hz
AQ              0.9787210 sec
RG                   2050
DW                7.467 usec
DE                10.00 usec
TE                298.2 K
D1             1.00000000 sec
D11            0.03000000 sec
D12            0.00002000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   19F
P1                  10.00 usec
PL1                 -3.00 dB
PL1W          15.53680420 W
SFO1         282.3761148 MHz

======== CHANNEL f2 ========
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NUC2                    1H
PCPD2                72.00 usec
PL2         0 dB
PL12                17.00 dB
PL2W          11.25325108 W
PL12W          0.22453187 W
SFO2         300.1312005 MHz

F2 - Processing parameters
SI                     65536
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WDW                       EM
SSB         0
LB                   0.30 Hz
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PC                   1.00
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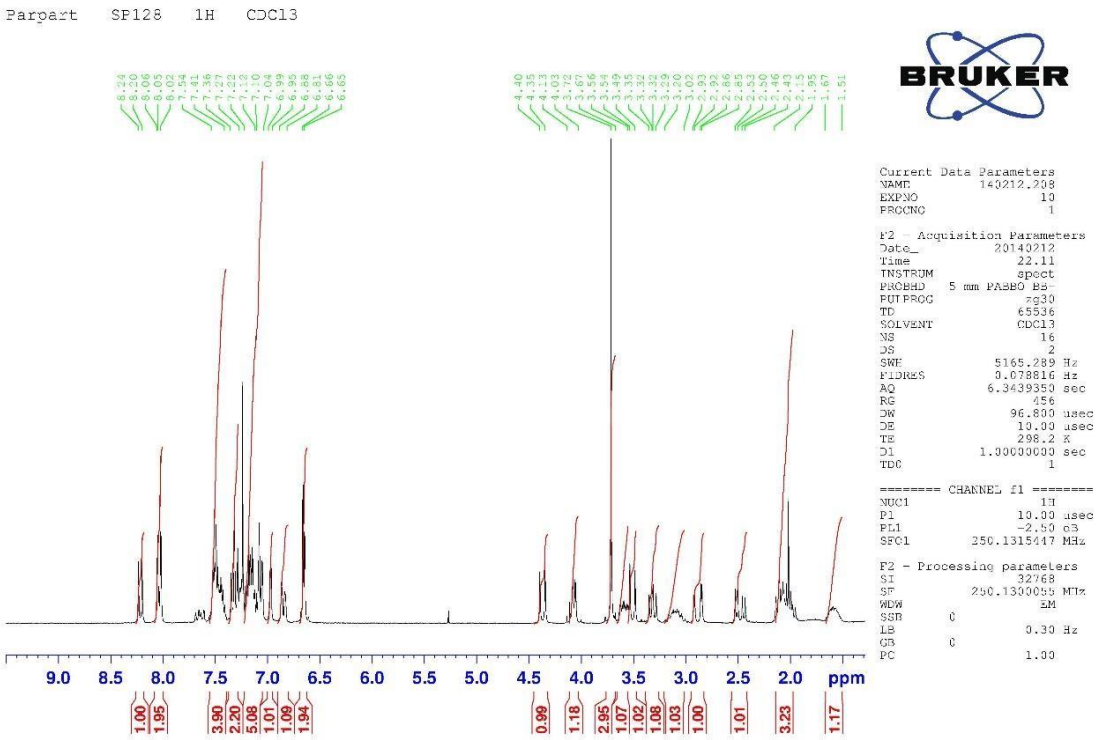

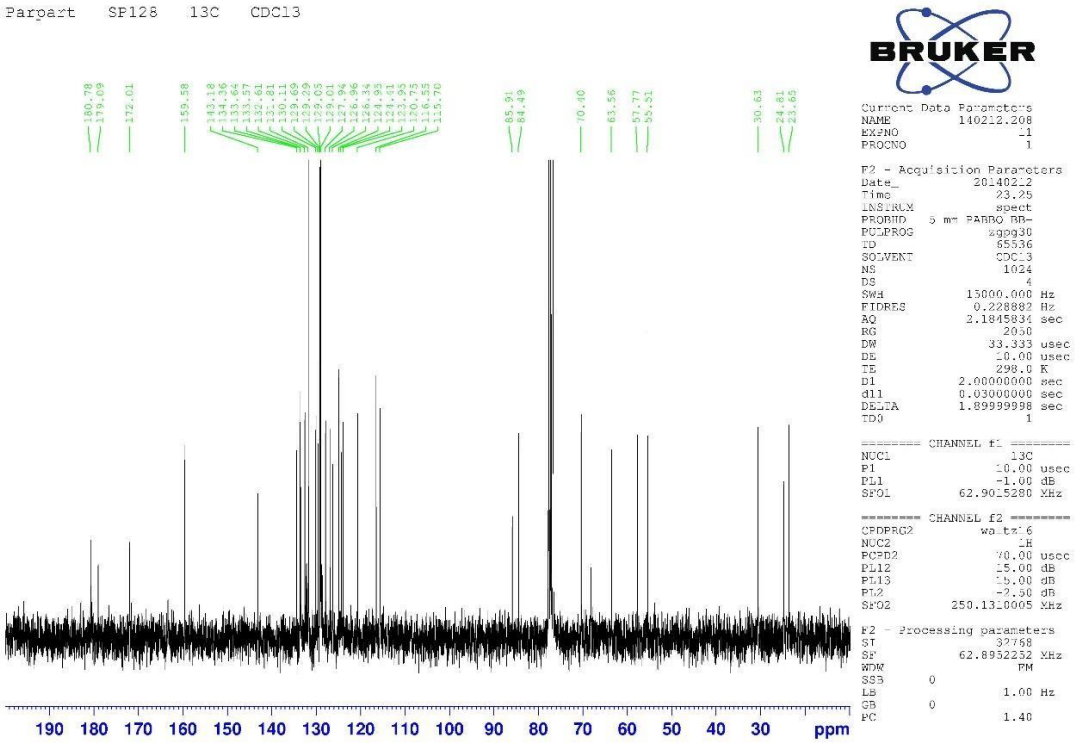

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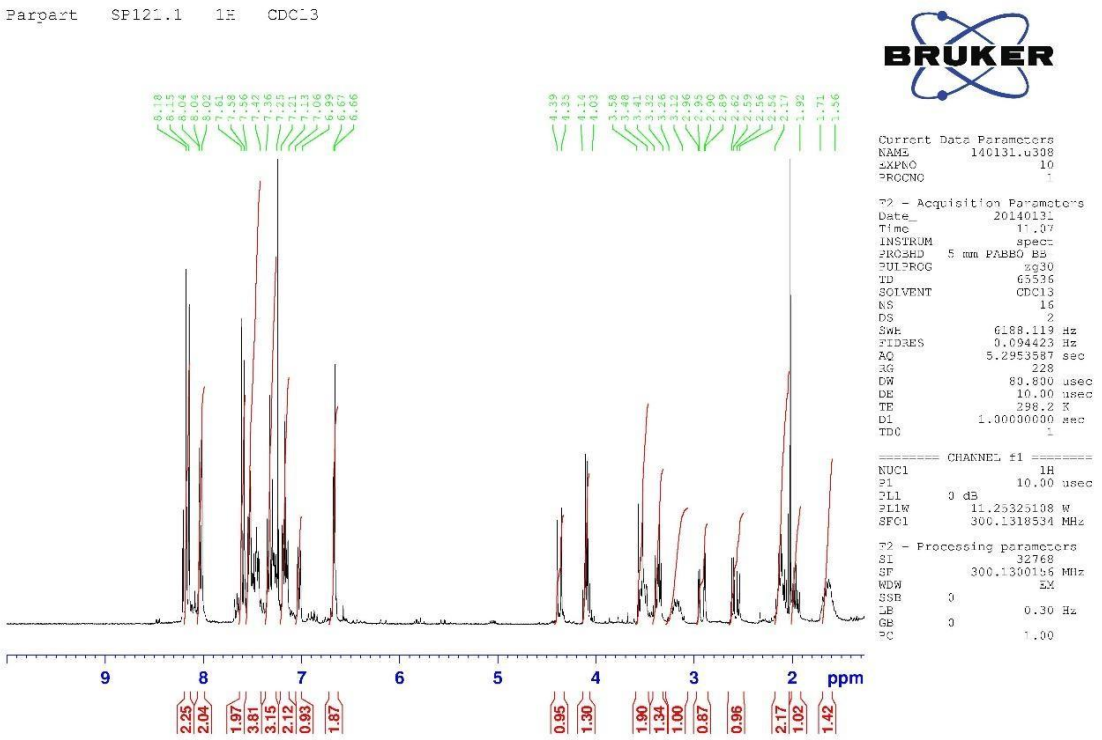

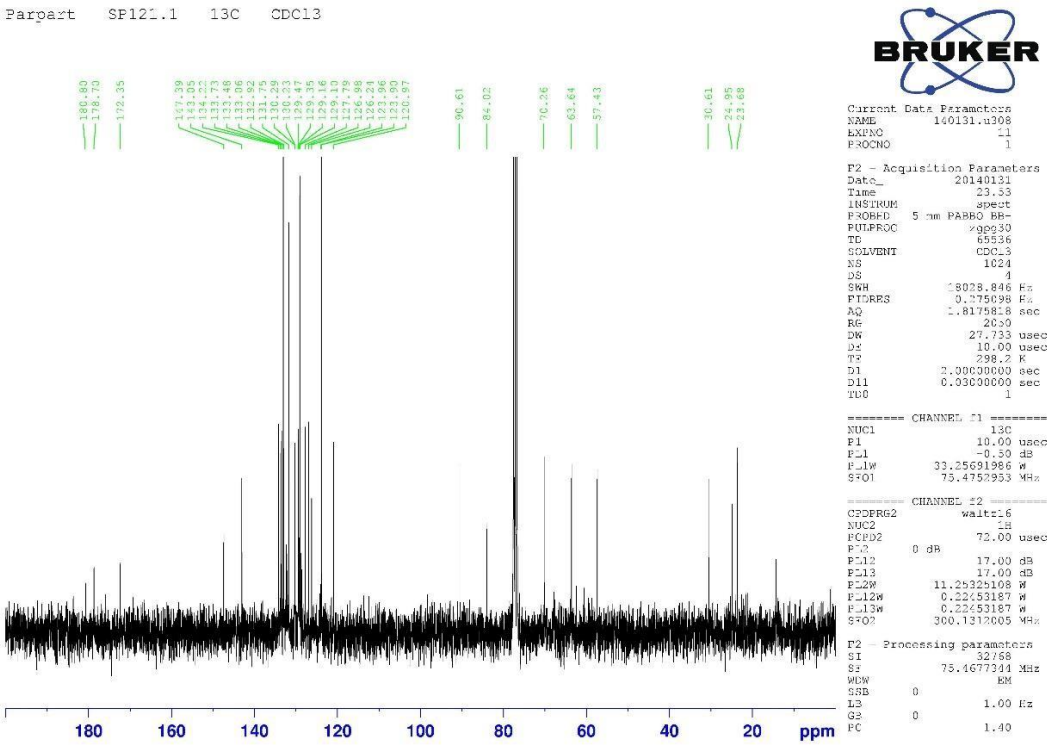

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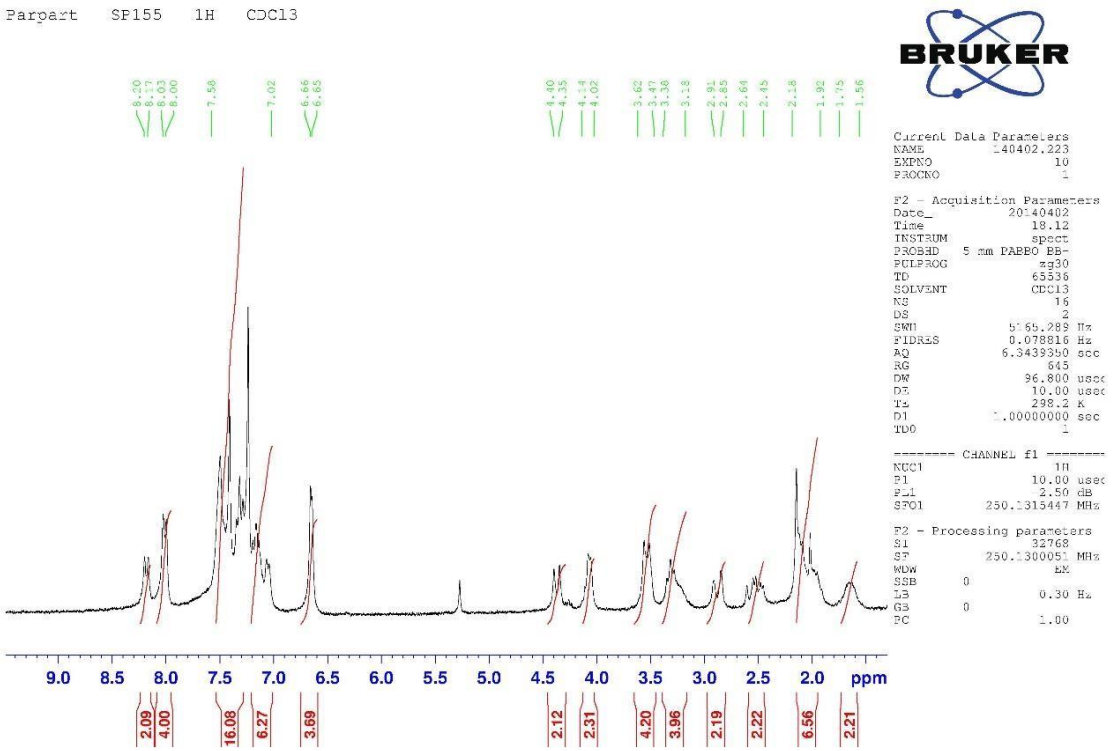
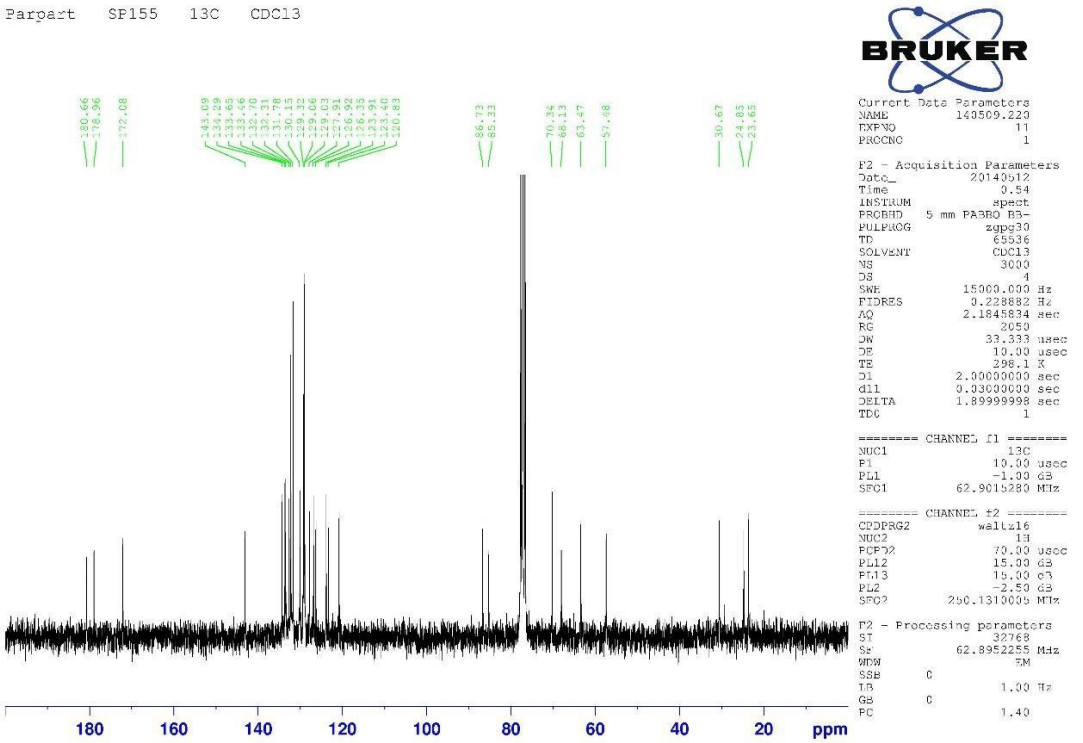
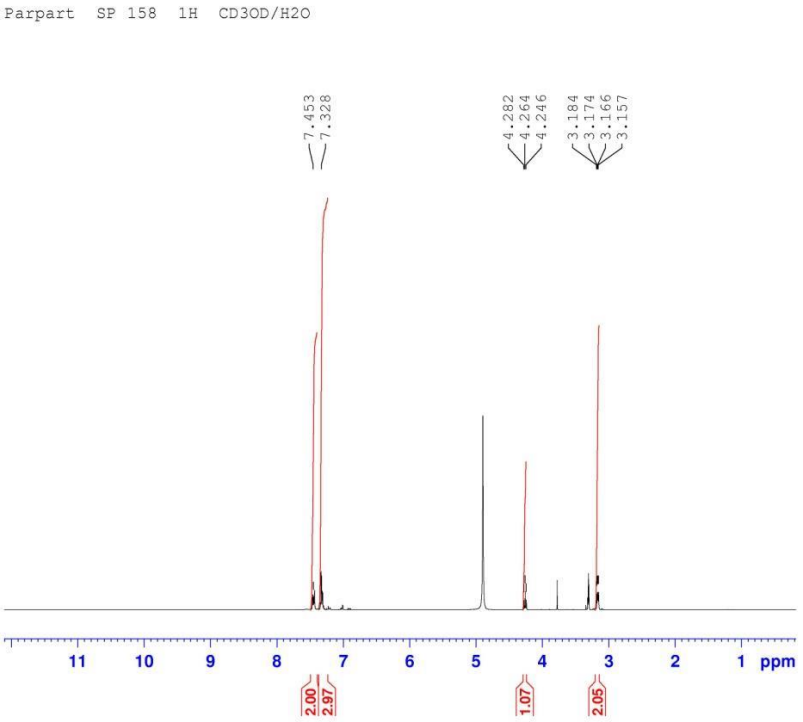




1.13 (*S*)-2-Amino-5-[phenyl]pent-4-insäure (3a):

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TD                 65536
SOLVENT             MeOD
NS                    16
DS                     2
SWH           6188.119 Hz
FIDRES        0.094423 Hz
AQ            5.2953587 sec
RG                   101
DW               80.800 usec
DE               10.00 usec
TE                298.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                10.00 usec
PL1        0 dB
PL1W        11.25325108 W
SFO1       300.1318534 MHz

F2 - Processing parameters
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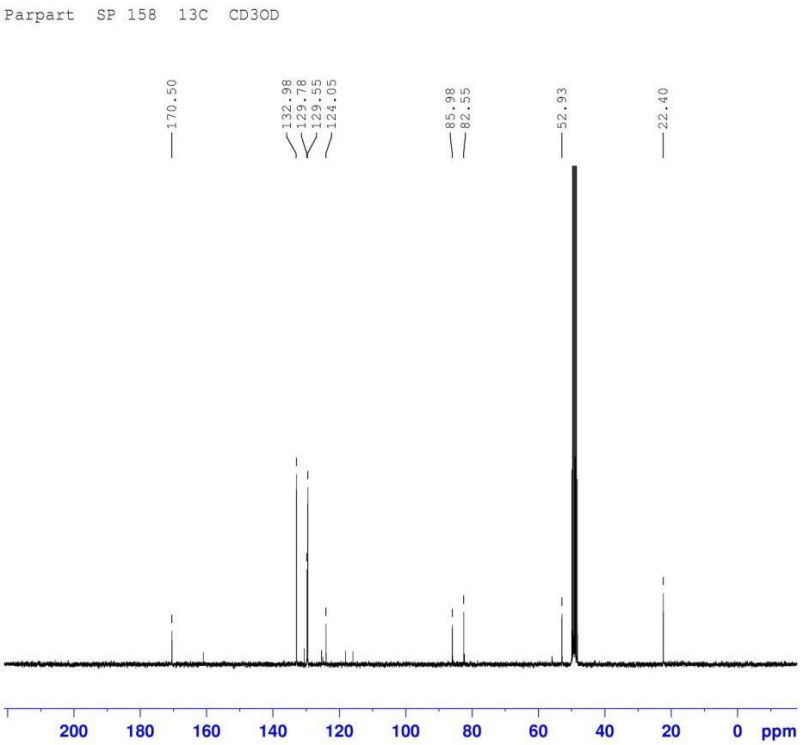


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TD                 65536
SOLVENT             MeOD
NS                  1024
DS                     4
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FIDRES        0.275098 Hz
AQ            1.8175818 sec
RG                  2050
DW               27.733 usec
DE               10.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                10.00 usec
PL1               -0.50 dB
PL1W        33.25691986 W
SFO1         75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2             72.00 usec
PL2        0 dB
PL12              17.00 dB
PL13              17.00 dB
PL2W        11.25325108 W
PL12W        0.22453187 W
PL13W        0.22453187 W
SFO2       300.1312005 MHz

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SI                 32768
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WDW                   EM
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LB                 1.00 Hz
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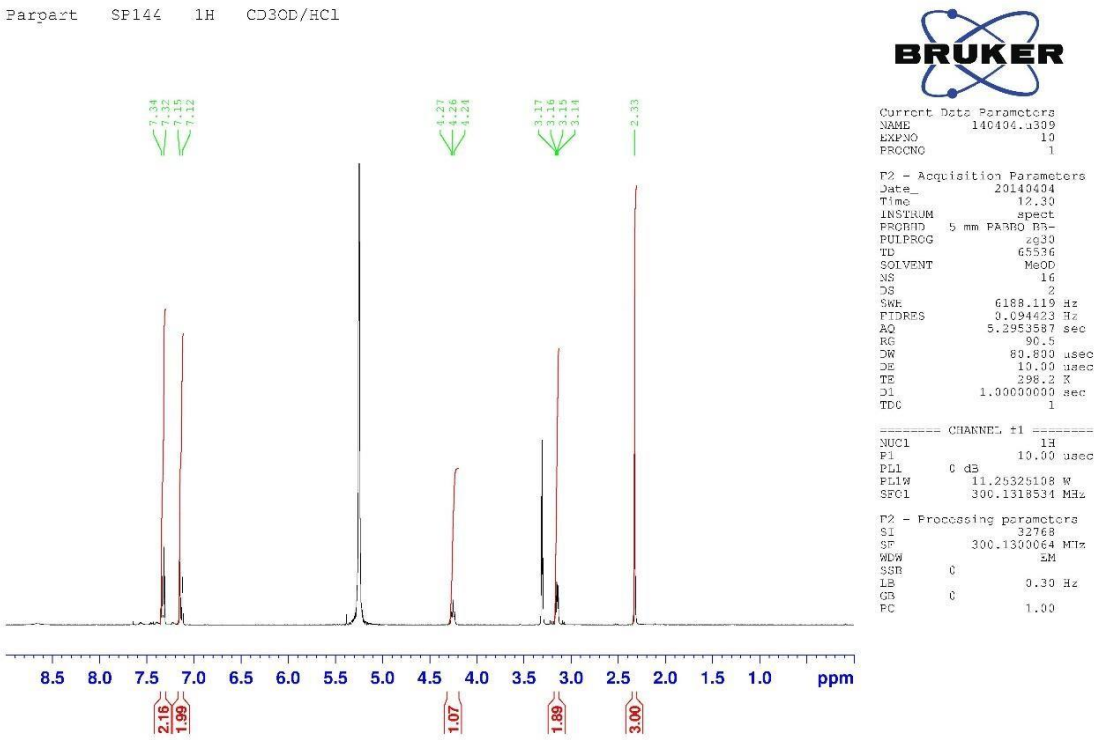

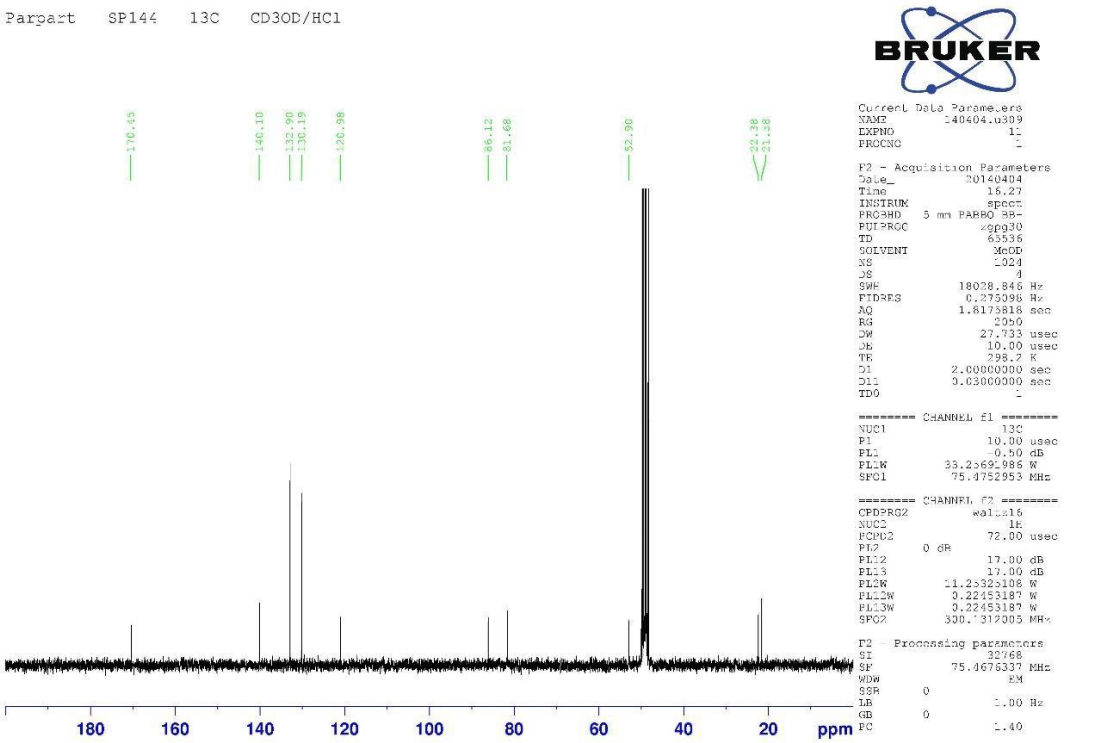

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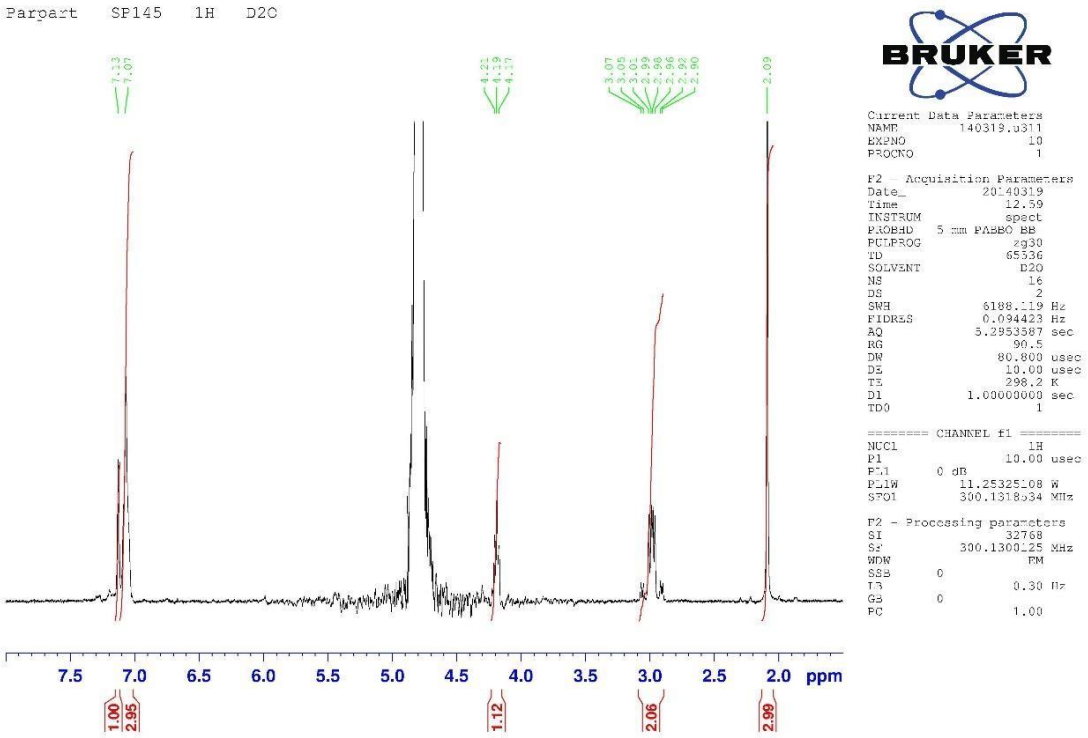

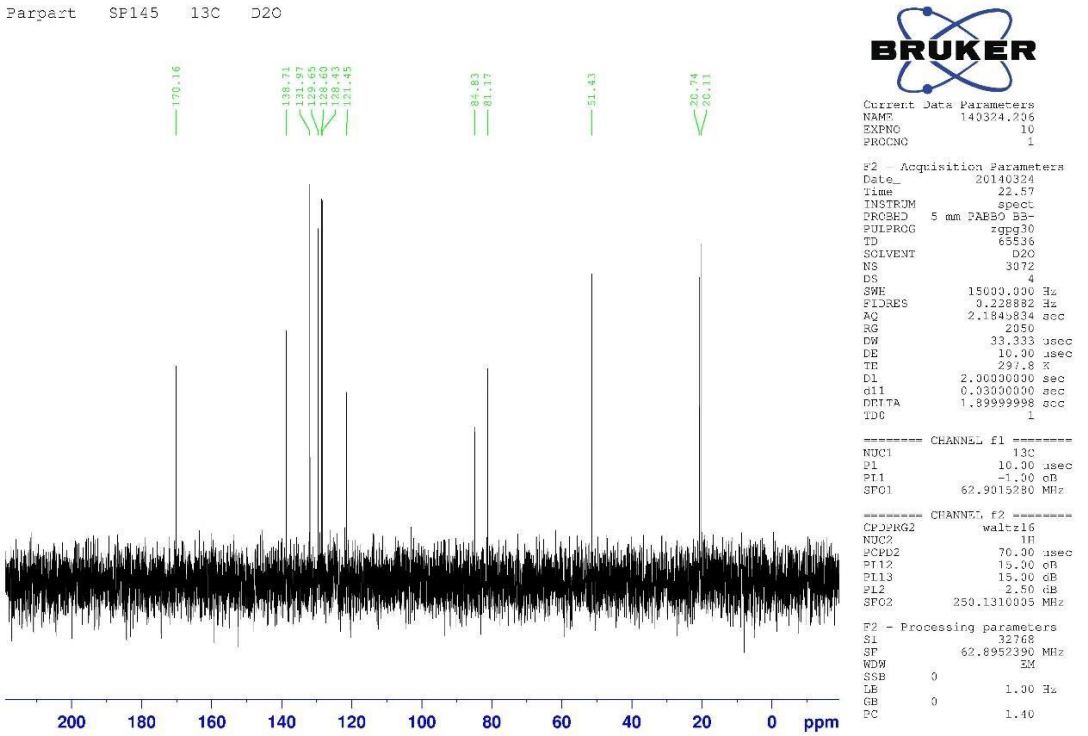

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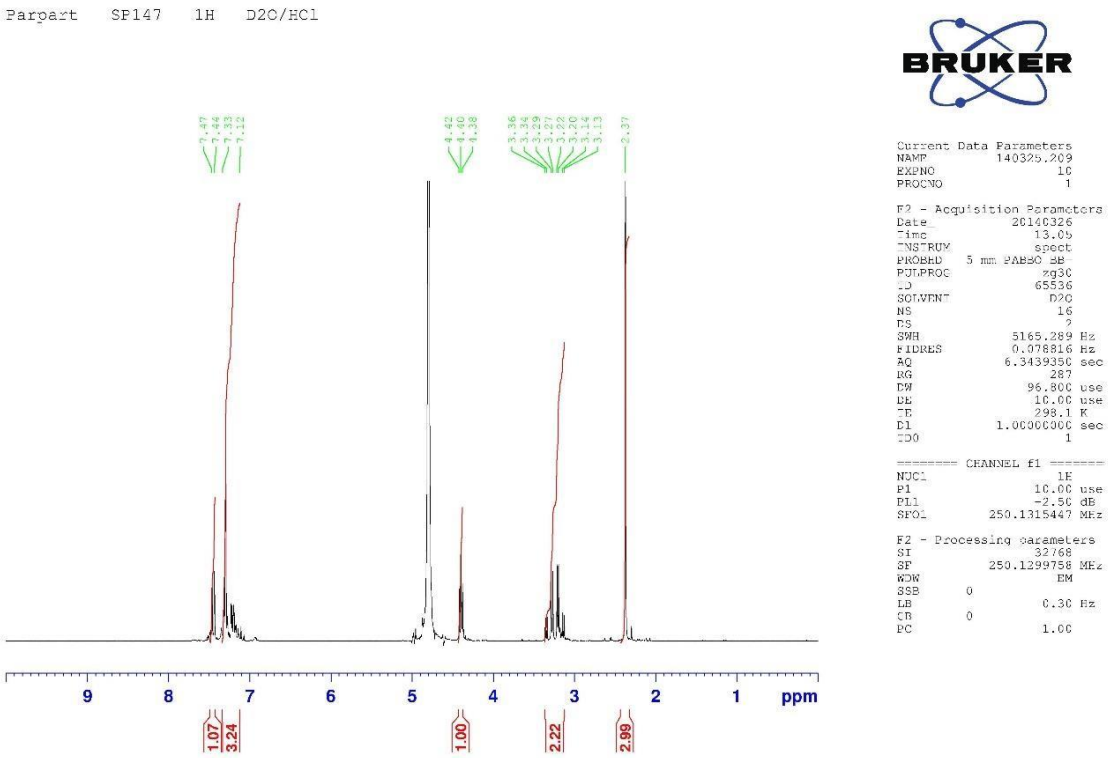

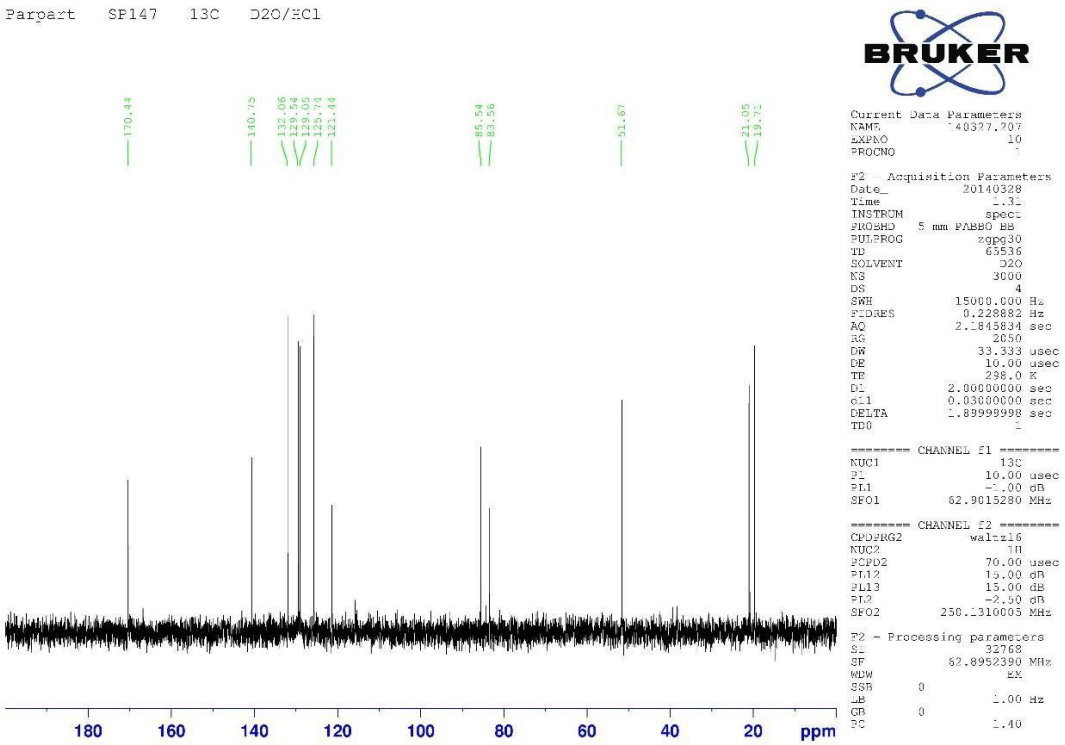

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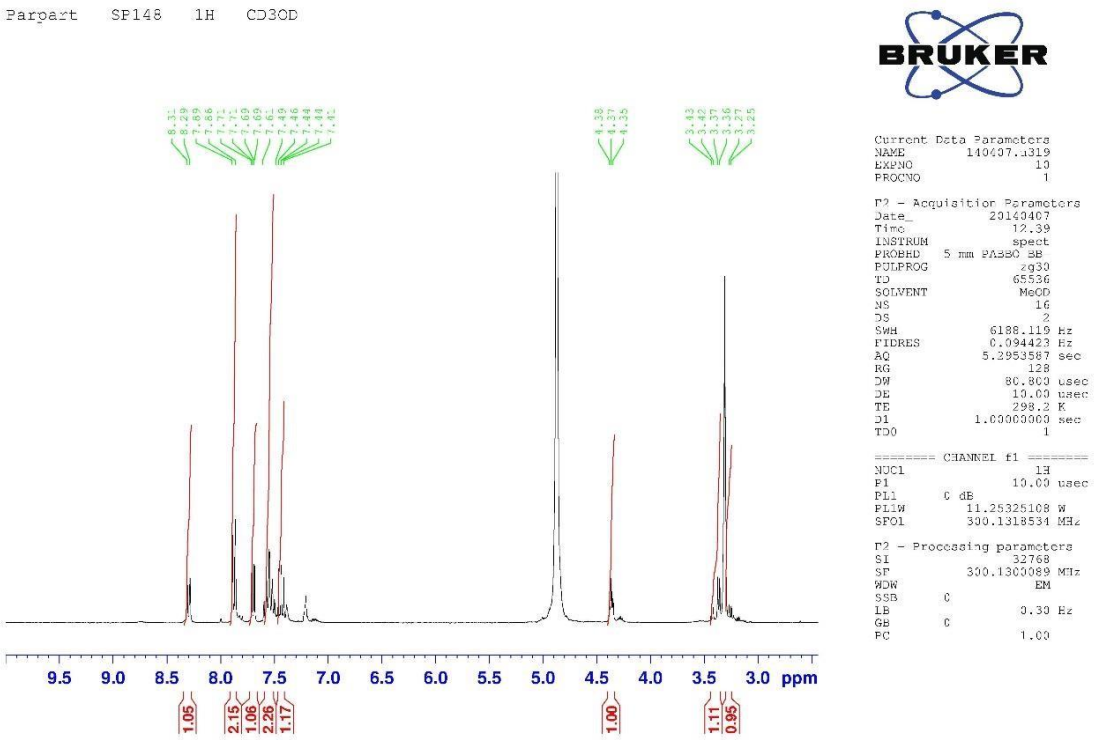

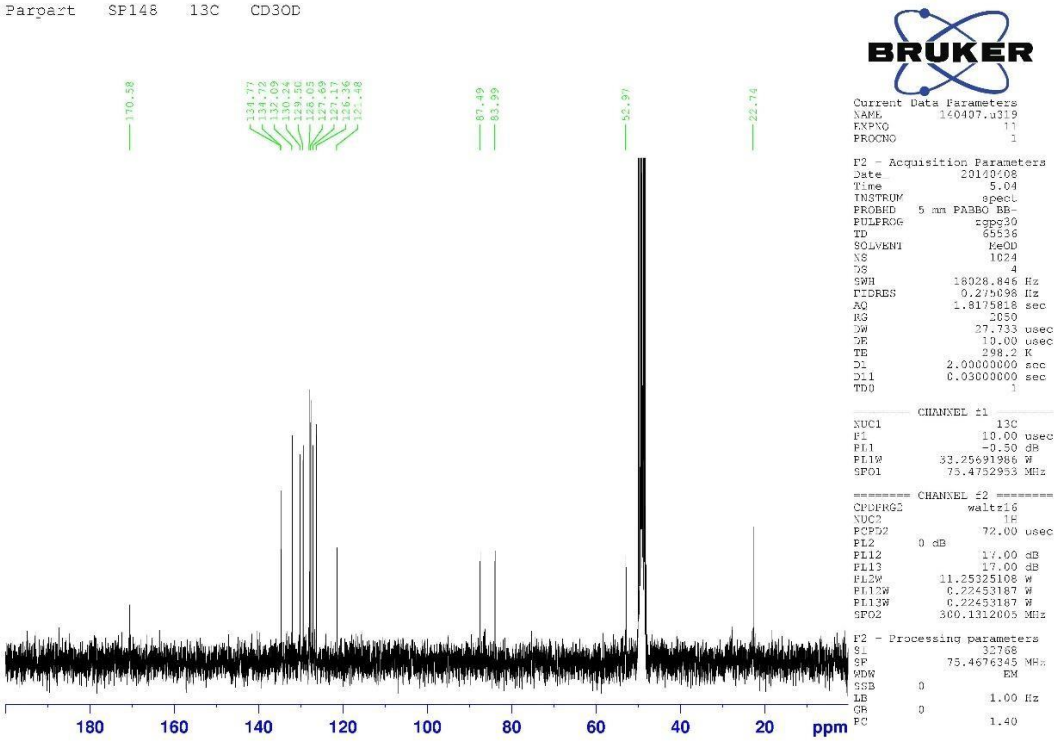

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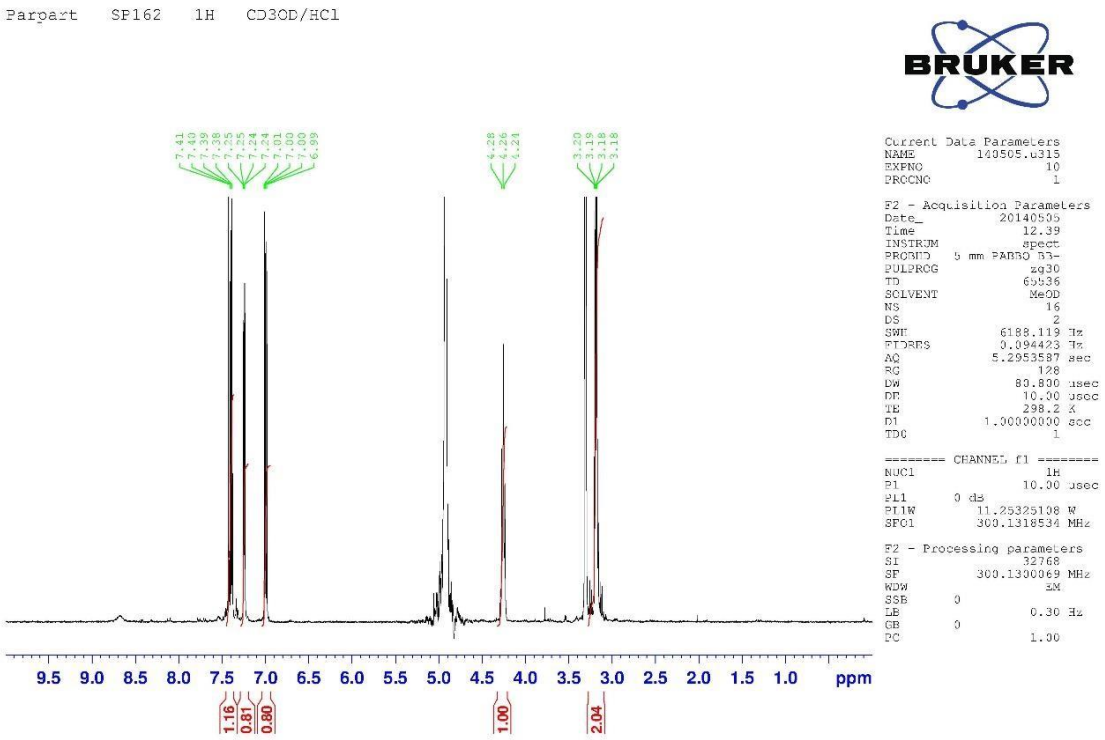

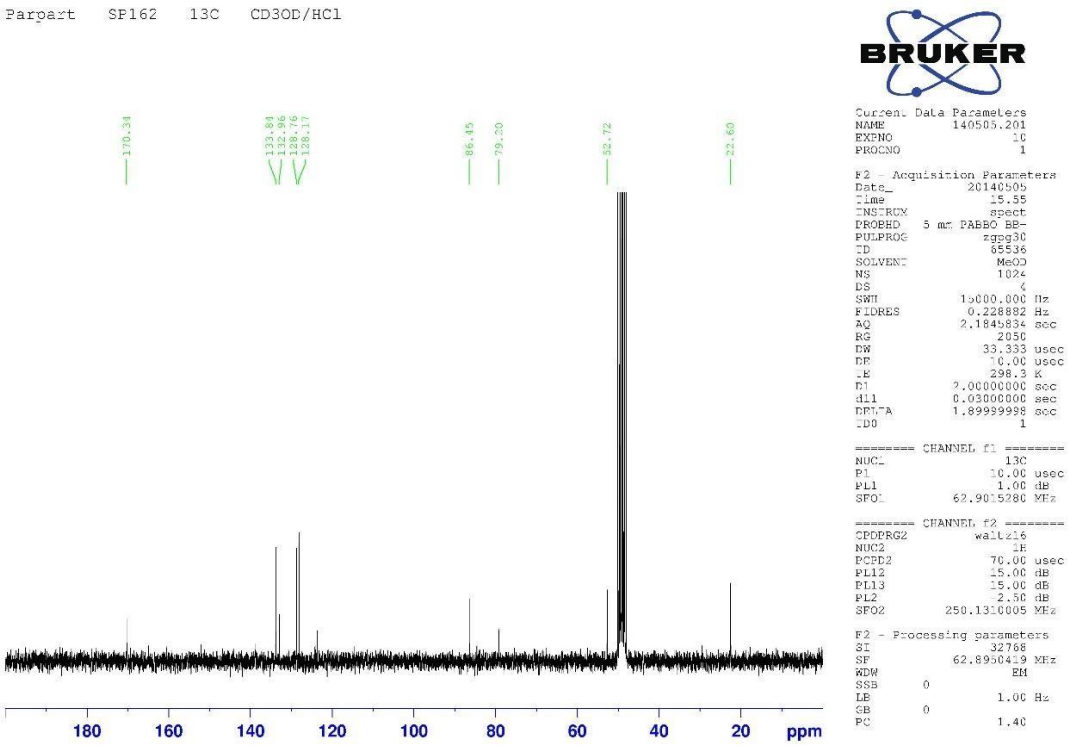

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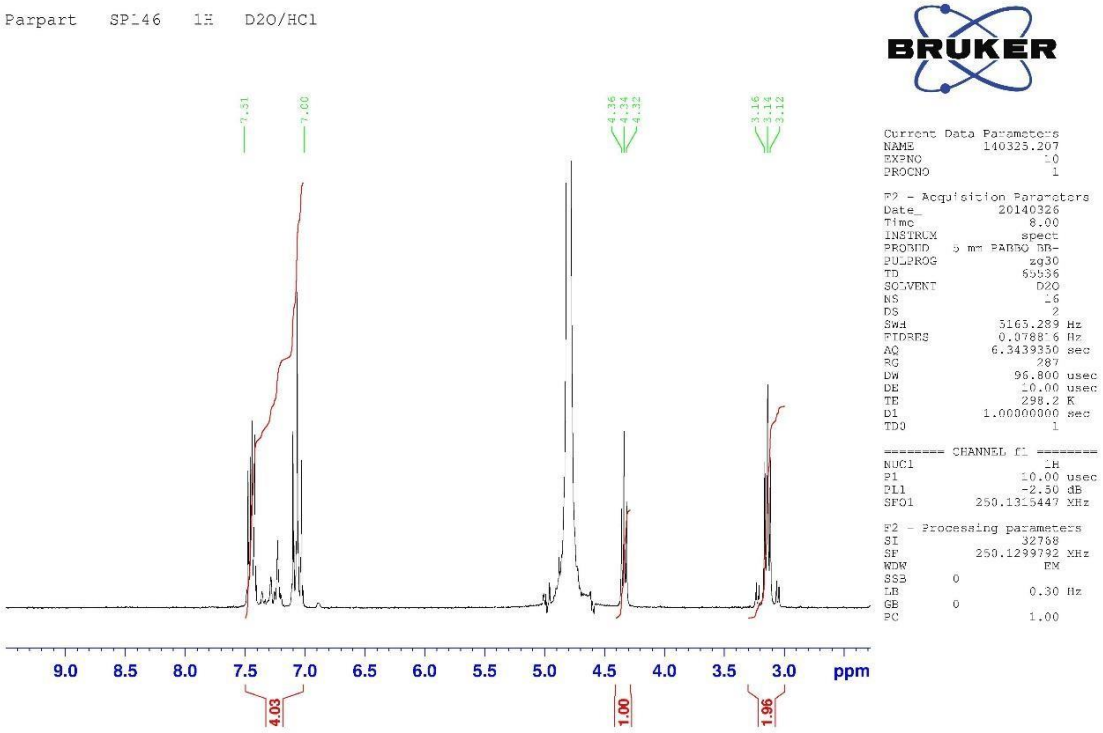
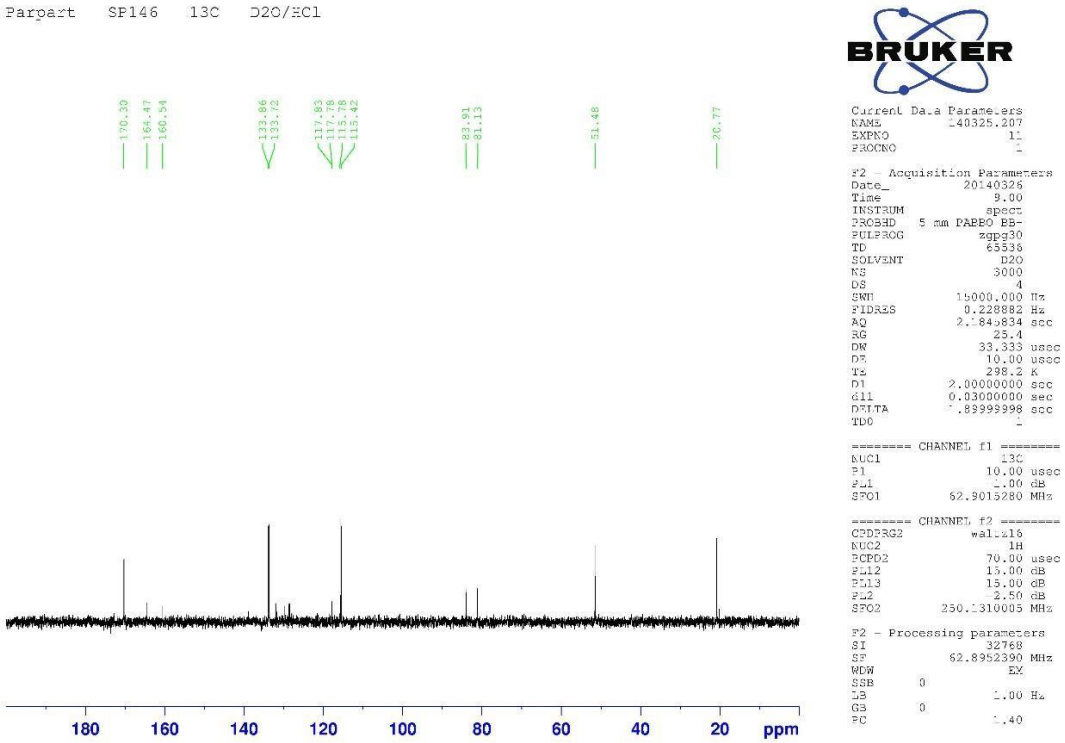
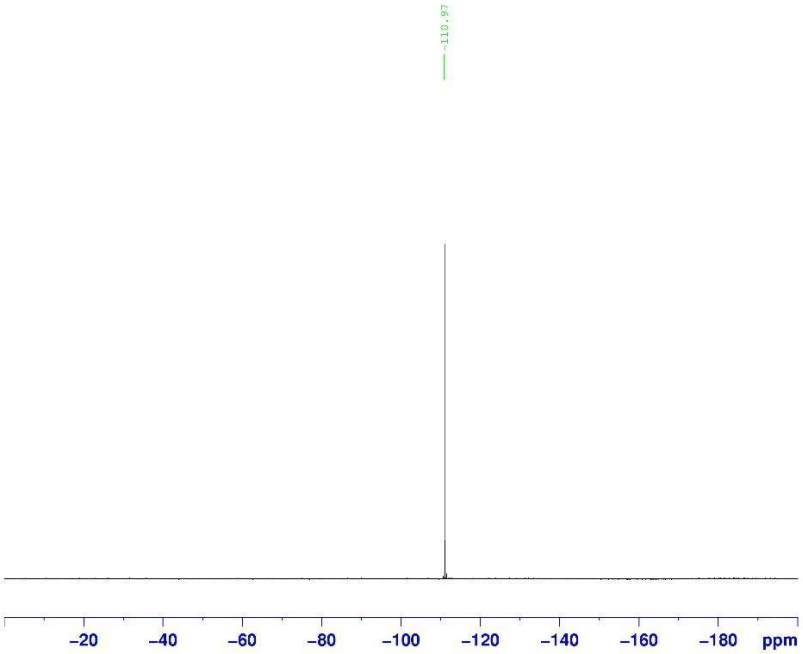




Parpart SP146 19F D2O/HCl



BRUKER

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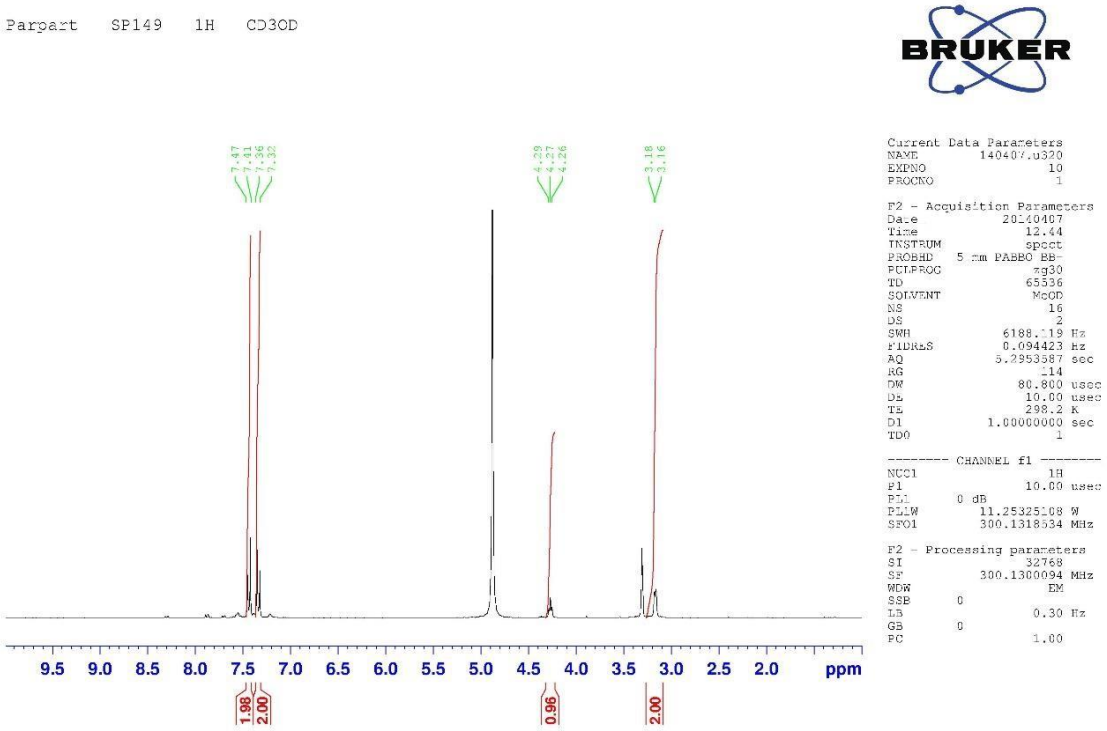
TD                         131072
SOLVENT                       D2O
NS                             64
DS                              4
SWH                     66964.289 Hz
FIDRES                   0.510897 Hz
AQ                       0.9787210 sec
RG                            2050
DW                           7.467 usec
DE                           10.00 usec
TE                          298.2 K
D1                      1.00000000 sec
D11                     0.03000000 sec
D12                     0.00002000 sec
TD0                             1

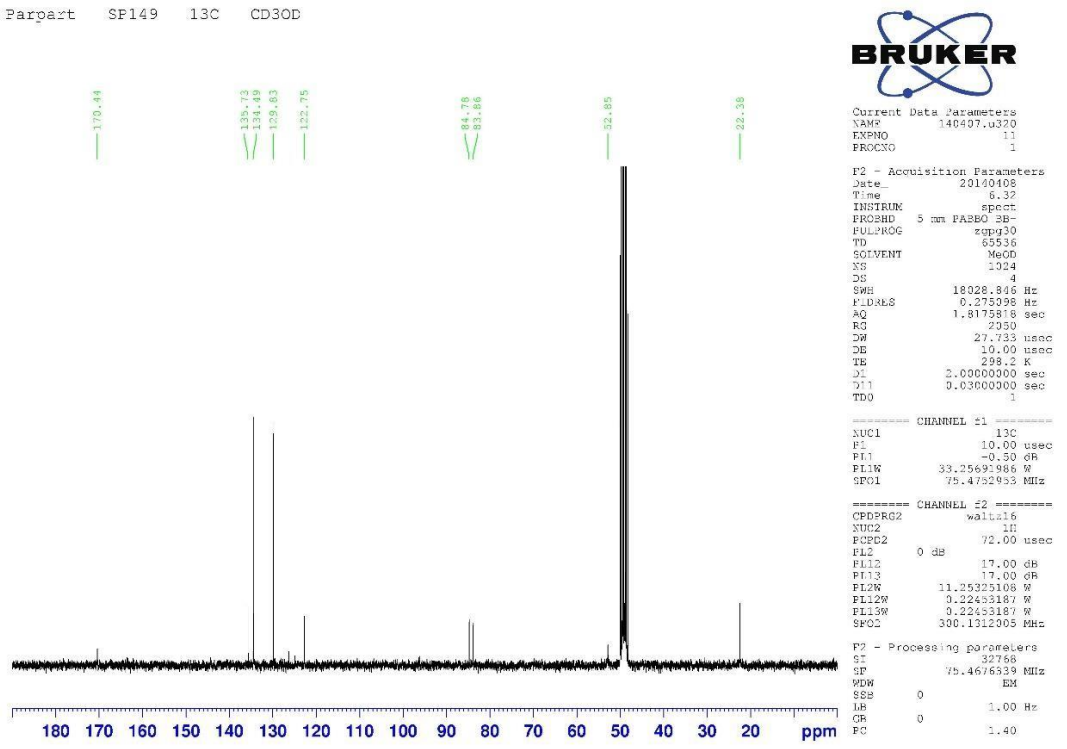
======== CHANNEL f1 ========
NUC1                          19F
P1                           10.00 usec
PL1                          -3.00 dB
PL1W                  15.53680470 W
SFO1                  282.3761148 MHz

======== CHANNEL f2 ========
CPDPRG2                   waltz16
NUC2                          1H
PCPD2                        72.00 usec
PL2                0 dB
PL12                         17.00 dB
PL2W                  11.25326108 W
PL12W                  0.22453187 W
SFO2                  300.1312005 MHz

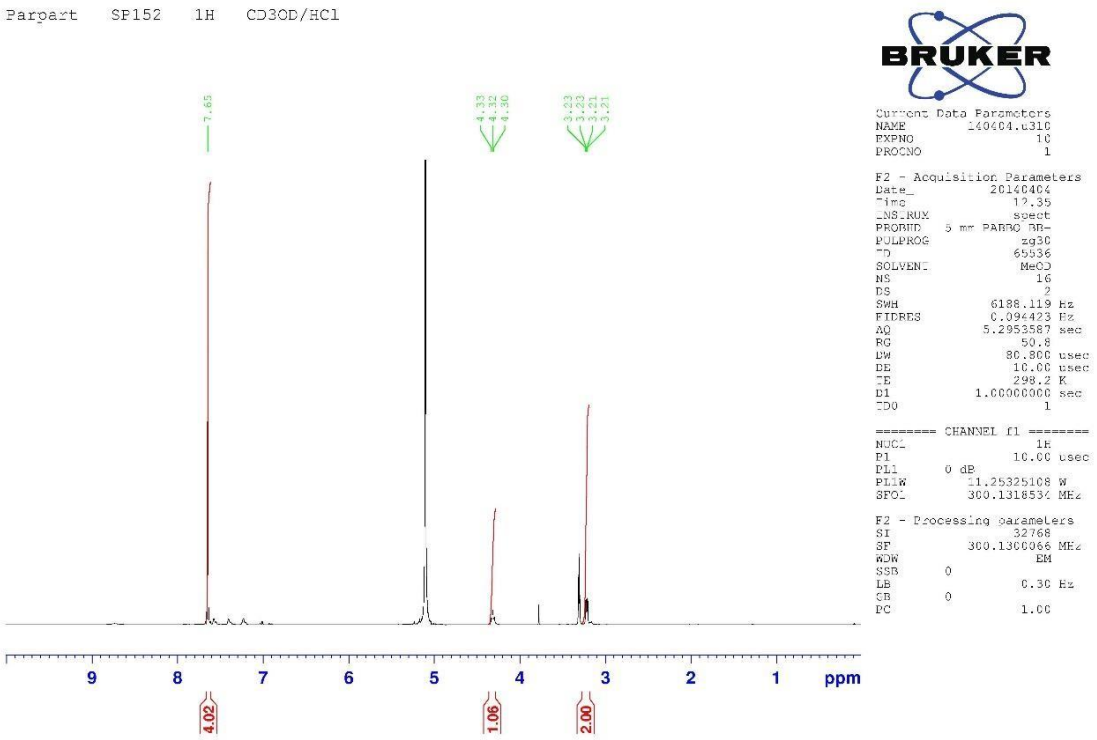
F2 - Processing parameters
SI                            65536
SF                    282.4043550 MHz
WDW                             EM
SSB                0
LB                            0.30 Hz
GB                 0
PC                            1.00
```

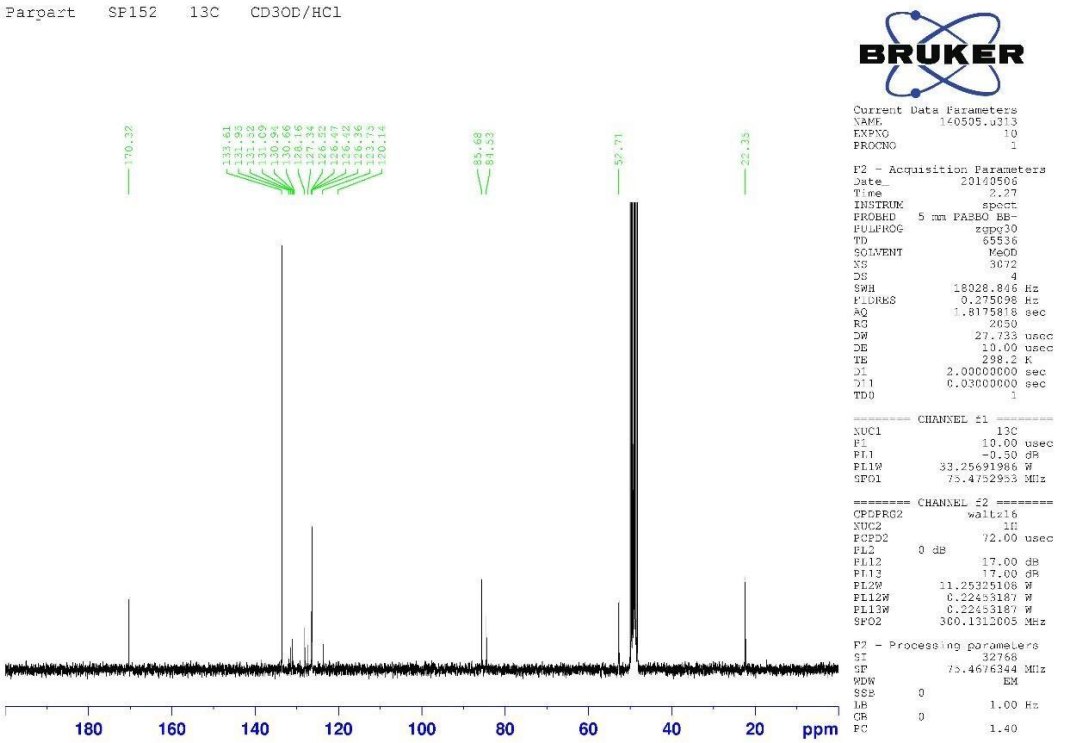
1.20 (*S*)-2-Amino-5-[4-chlorphenyl]pent-4-insäure (3h):



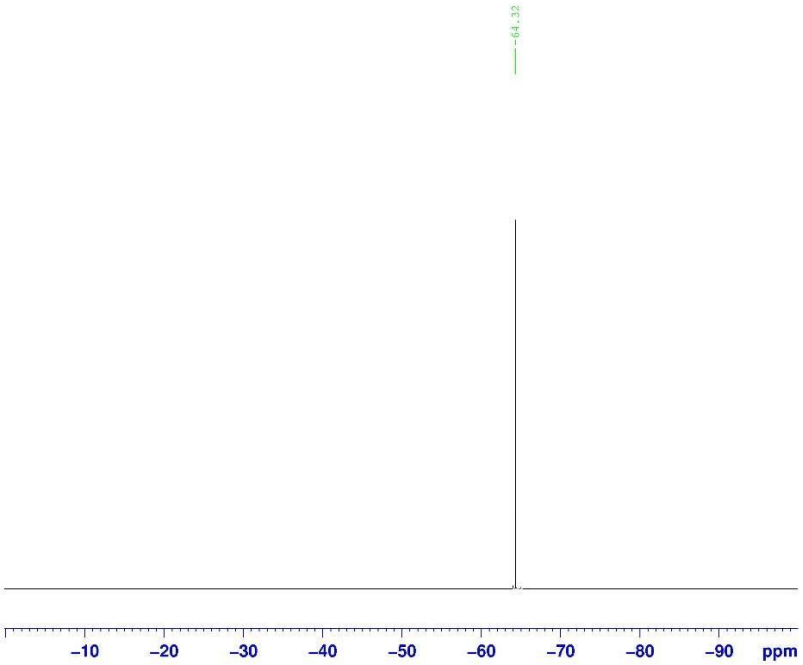


1.21 (*S*)-2-Amino-5-[4-trifluormethylphenyl]pent-4-insäure (3i):





Parpazt SP152 19F CD3OD/HCl




```
Current Data Parameters
NAME          140404.n310
EXPNO                  11
PROCNO                  1

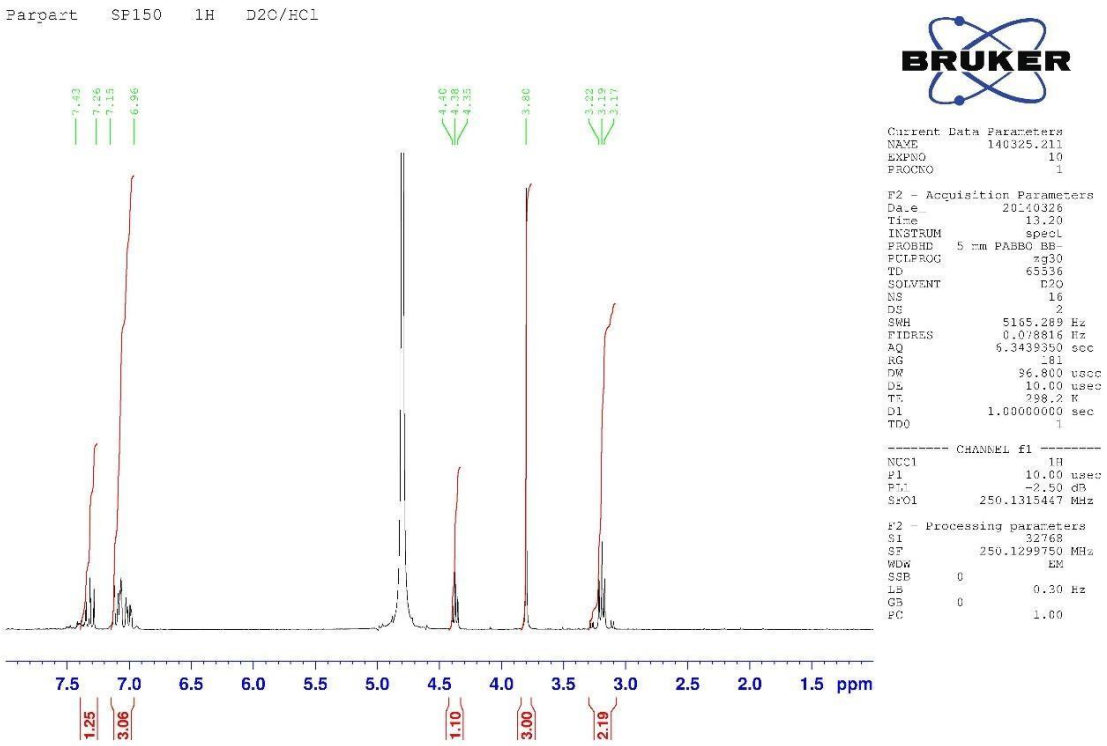
F2 - Acquisition Parameters
Date_              20140404
Time                  12.38
INSTRUM               spect
PROBHD  5 mm PABBO BB-
PULPROG          zgfhigqn
TD                 131072
SOLVENT               MeOD
NS                      64
DS                       4
SWH              66964.289 Hz
FIDRES           0.510897 Hz
AQ               0.9787210 sec
RG                    2050
DW                7.467 usec
DE                   10.00 usec
TE                  298.2 K
D1             1.00000000 sec
D11            0.03000000 sec
D12            0.00002000 sec
TD0                     1

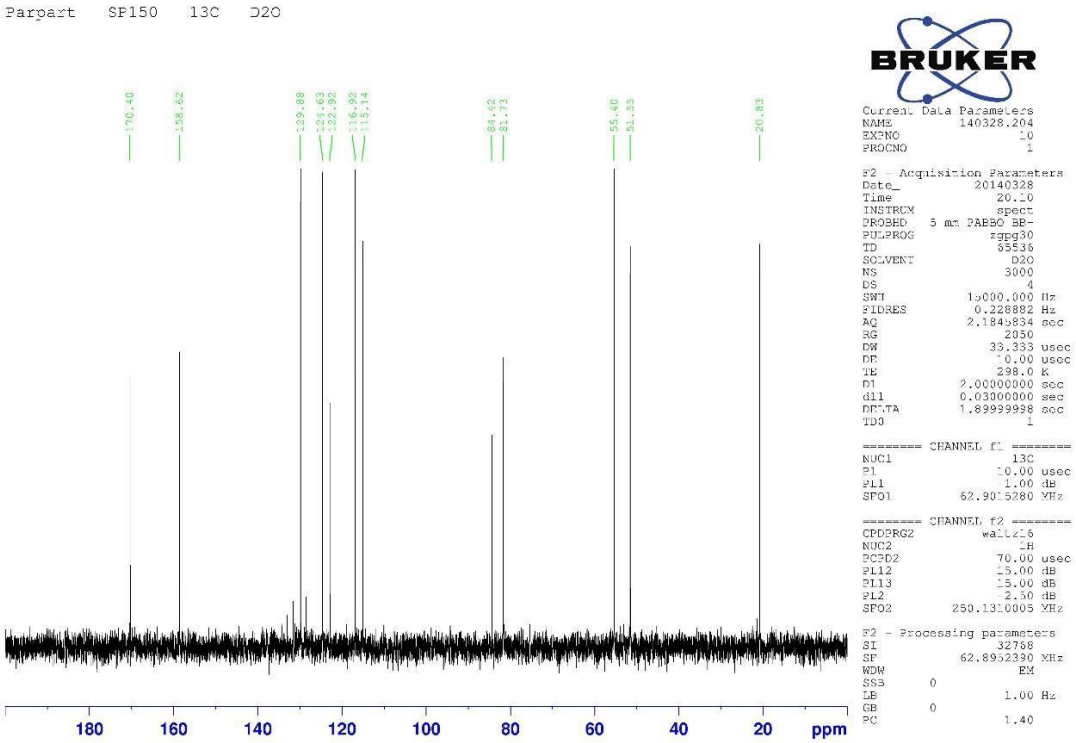
======== CHANNEL f1 ========
NUC1                   19F
P1                   10.00 usec
PL1                  -3.00 dB
PL1W          15.53680420 W
SFO1          282.3761748 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                72.00 usec
PL2       0 dB
PL12                 17.00 dB
PL2W          11.25325208 W
PL12W          0.22453287 W
SFO2          300.1312005 MHz

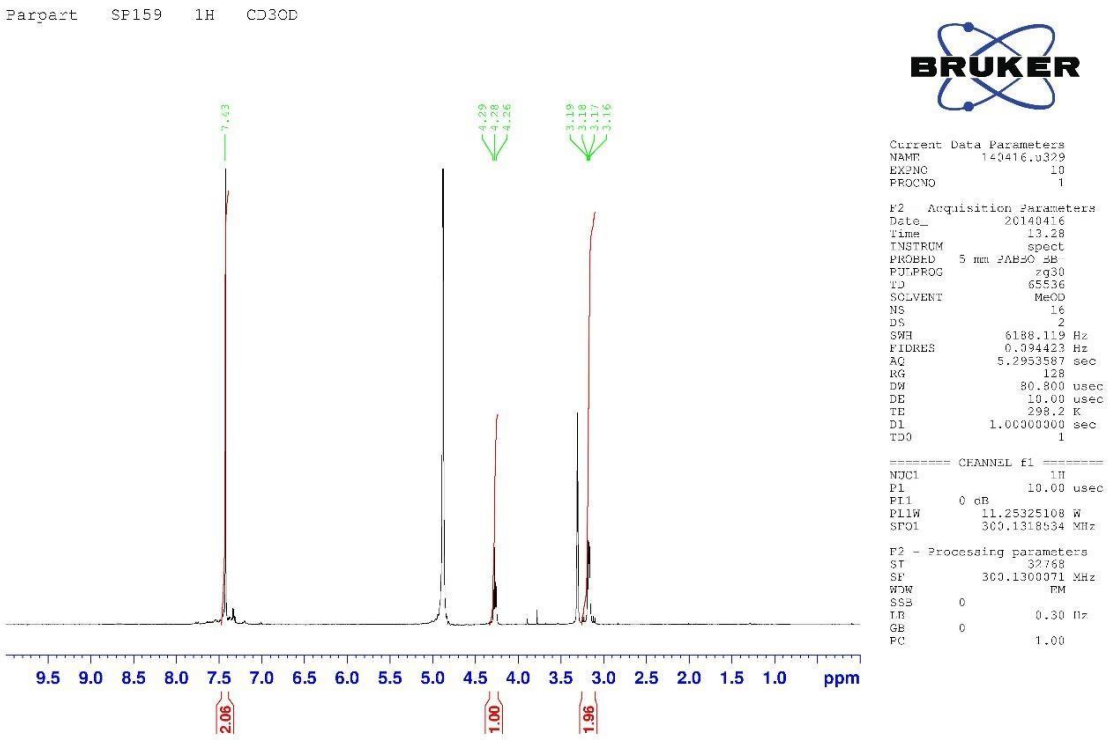
F2 - Processing parameters
SI                     65536
SF            282.4043550 MHz
WDW                       EM
SSB       0
LB                    0.30 Hz
GB        0
PC                    1.00
```

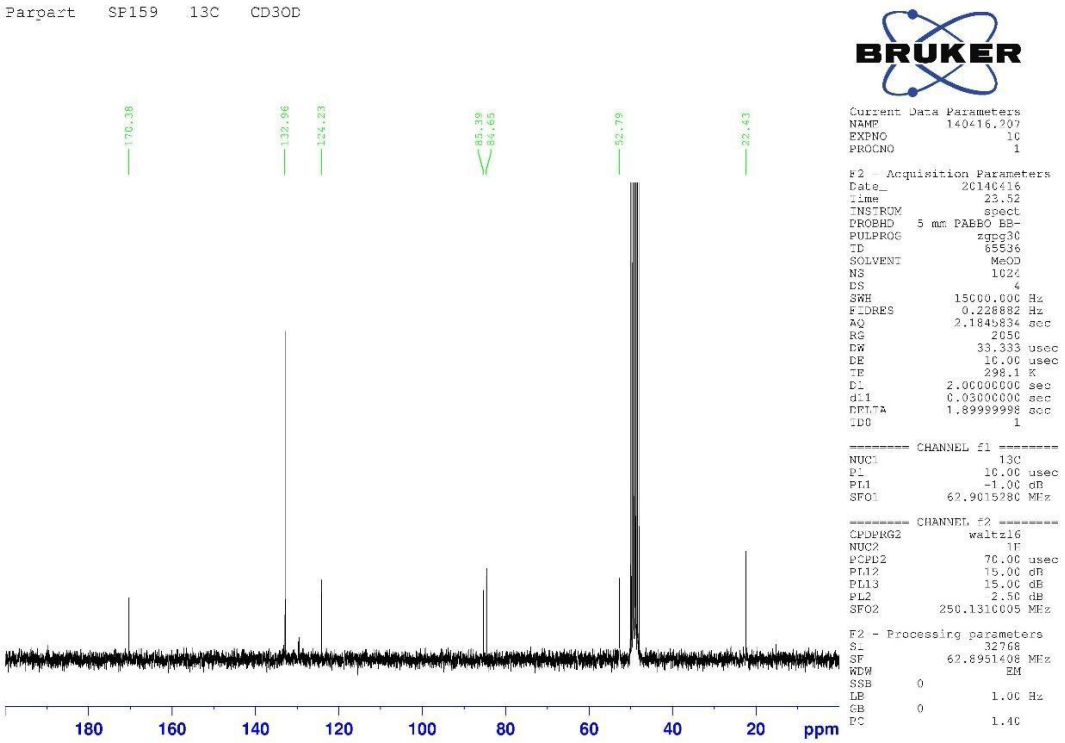
1.22 (*S*)-2-Amino-5-[3-methoxyphenyl]pent-4-insäure (3j):





1.23 5,5’-[1,4-phenyl]bis((*S*)-2-aminopent-4-insäure) (3l):





2 Chiral-HPLC

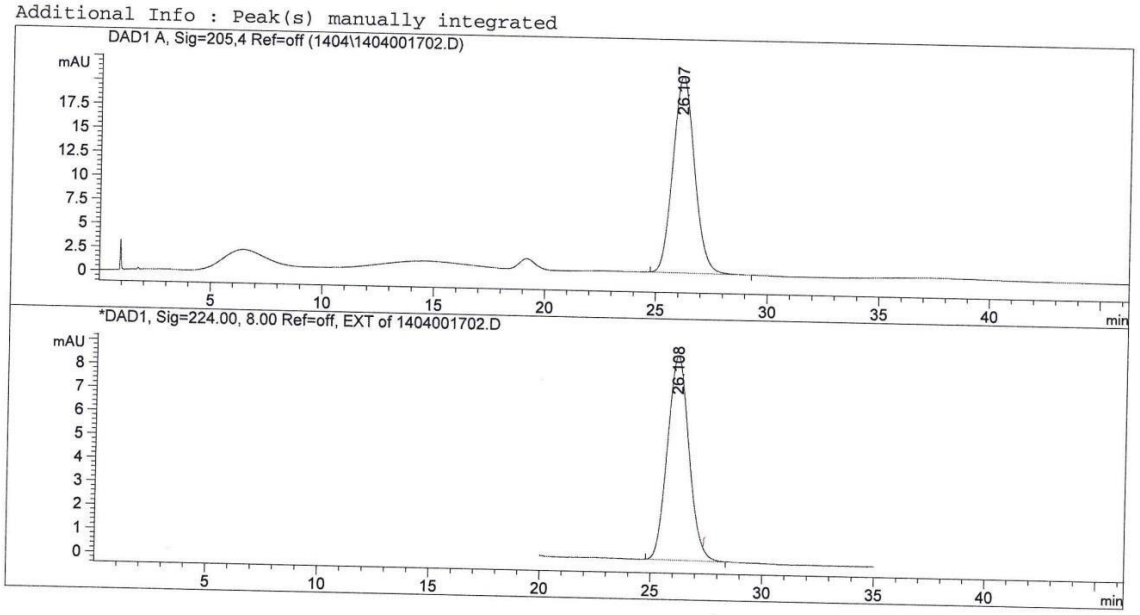
2.1 (*S*)-2-Amino-5-[4-fluorphenyl]pent-4-insäure (3g):

Data File C:\CHEM32\1\DATA\1404\1404001702.D
Sample Name: SP146

Parpart

```
Acq. Operator    : SYSTEM                                  Seq. Line :   3
Acq. Instrument  : LC4                                      Location : Vial 2
Injection Date   : 4/17/2014 11:07:00 AM                        Inj :   1
                                                          Inj Volume : 0.500 µl
Acq. Method      : C:\CHEM32\1\METHODS\PARPART.M
Last changed     : 4/17/2014 9:20:53 AM by SYSTEM
                   (modified after loading)
Analysis Method  : C:\CHEM32\1\METHODS\PARPART.M
Last changed     : 4/23/2014 10:28:42 AM by SYSTEM
                   (modified after loading)
Method Info      : Crownpak CR (-),  Perchlorsäure pH 2.0, 1ml/min, 40°C

Additional Info : Peak(s) manually integrated
```




```
                          Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=205,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1  26.107 BB    1.0054 1385.78687   20.48116 100.0000

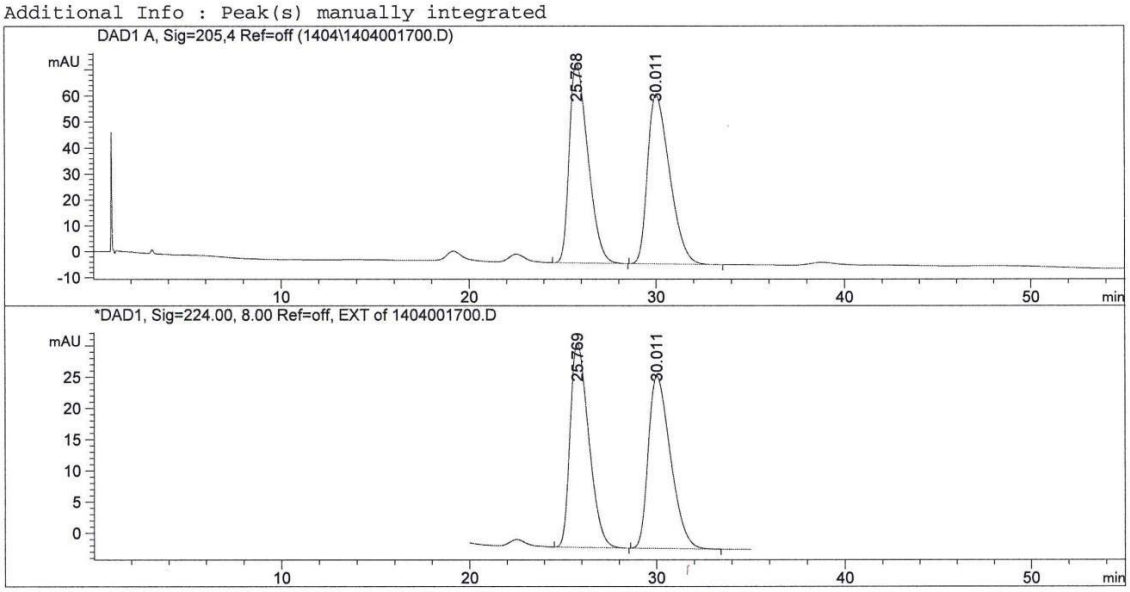
Totals :                  1385.78687   20.48116
```

Mehr als 99% ee.

Data File C:\CHEM32\1\DATA\1404\1404001700.D
Sample Name: SP154rac

```
==========================================================================
Acq. Operator   : SYSTEM                          Seq. Line :   1
Acq. Instrument : LC4                              Location : Vial 1
Injection Date  : 4/17/2014 9:15:20 AM                 Inj :   1
                                                  Inj Volume : 0.500 µl
Acq. Method     : C:\CHEM32\1\METHODS\PARPART.M
Last changed    : 4/17/2014 9:20:53 AM by SYSTEM
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\PARPART.M
Last changed    : 4/17/2014 9:14:28 AM by SYSTEM
Method Info     : Crownpak CR (-),  Perchlorsäure pH 2.0, 1ml/min, 40°C

Additional Info : Peak(s) manually integrated
```




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

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=205,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  25.768 BB    1.0709 5332.73926   76.90916  50.0389
   2  30.011 BB    1.2326 5324.43945   64.80263  49.9611

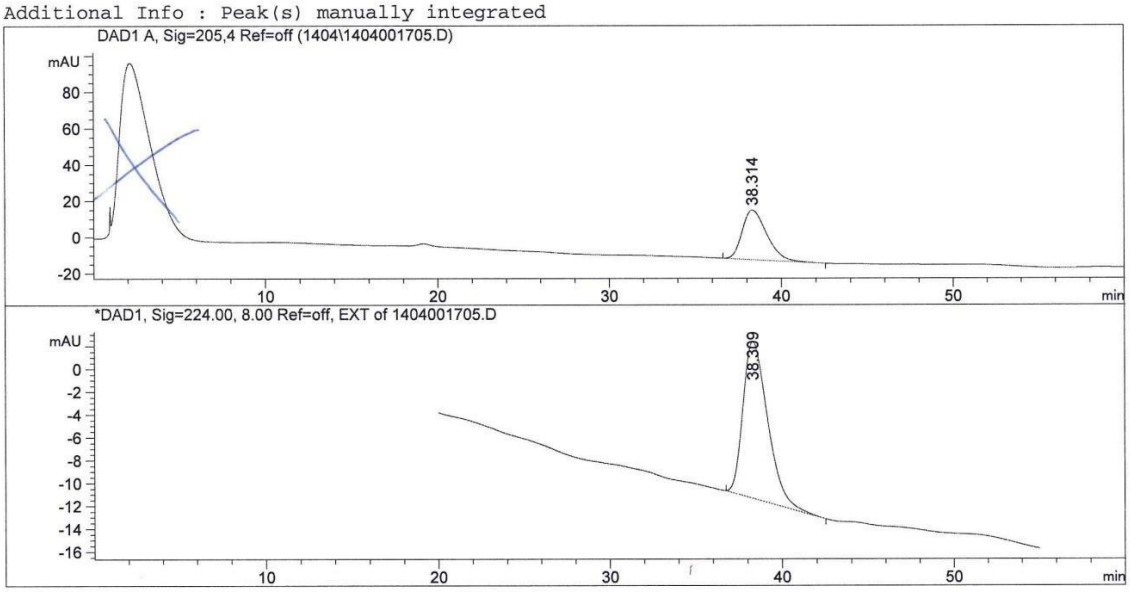
Totals :                  1.06572e4   141.71179
```

2.2 (*S*)-2-Amino-5-[3-methoxyphenyl]pent-4-insäure (3j):

```
Data File C:\CHEM32\1\DATA\1404\1404001705.D
Sample Name: SP150

==========================================================================
Acq. Operator   : SYSTEM                          Seq. Line :   3
Acq. Instrument : LC4                             Location : Vial 4
Injection Date  : 4/17/2014 1:17:10 PM                Inj :   1
                                                  Inj Volume : 0.500 µl
Acq. Method     : C:\CHEM32\1\METHODS\PARPART.M
Last changed    : 4/17/2014 1:55:29 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\PARPART.M
Last changed    : 5/7/2014 7:57:22 AM by SYSTEM
Method Info     : Crownpaki CR (-),  Perchlorsäure pH 2.0, 1ml/min, 40°C

Additional Info : Peak(s) manually integrated
```




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

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=205,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  38.314 BB    1.4392 2704.11328   27.35693 100.0000

Totals :                  2704.11328   27.35693

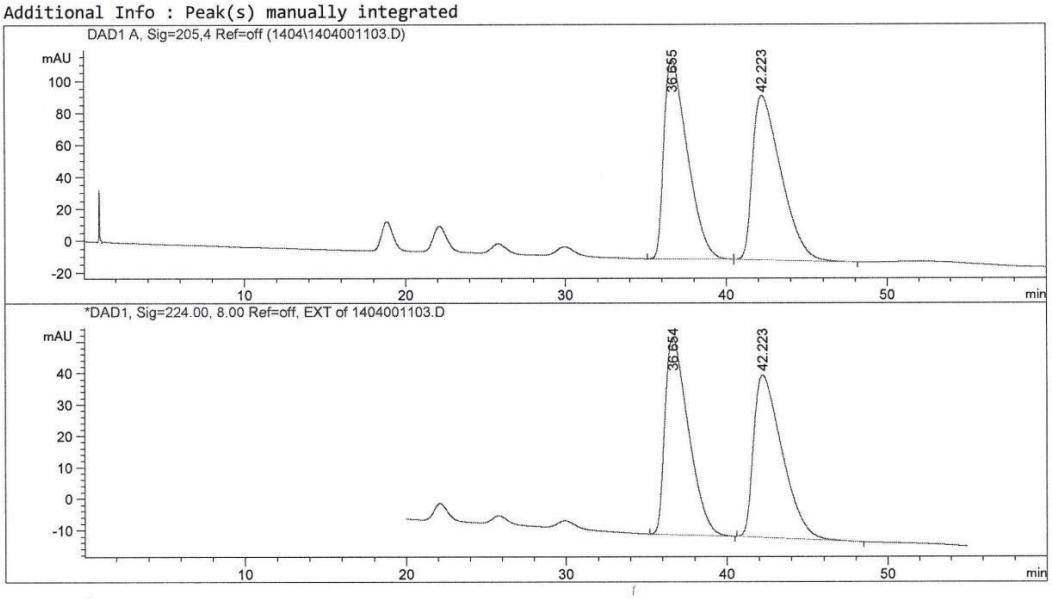
LC4 5/7/2014 11:45:07 AM SYSTEM                          Page   1 of 2
```

Data File C:\CHEM32\1\DATA\1404\1404001103.D
Sample Name: SP157

ParpaA

```
==========================================================================
Acq. Operator   : SYSTEM                          Seq. Line :   4
Acq. Instrument : LC4                              Location : Vial 2
Injection Date  : 4/11/2014 12:15:53 PM                Inj :   1
                                                  Inj Volume : 0.500 µl
Acq. Method     : C:\CHEM32\1\METHODS\PARPART.M
Last changed    : 4/11/2014 9:12:33 AM by SYSTEM
Analysis Method : C:\CHEM32\1\METHODS\PARPART.M
Last changed    : 5/7/2014 7:57:22 AM by SYSTEM
Method Info     : Crownpaki CR (-),  Perchlorsäure pH 2.0, 1ml/min, 40°C

Additional Info : Peak(s) manually integrated
```




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

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=205,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  36.655 BB    1.5196 1.25903e4   124.52320  49.9968
   2  42.223 BB    1.7604 1.25919e4   102.69941  50.0032

Totals :                  2.51823e4   227.22261
```