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# SUPPLEMENTAL MATERIALS

# for

## Novel (*E*)-3-(1-substituted-1*H*-indazol-5-yl)-*N*-hydroxypropenamides as Histone Deacetylase Inhibitors: Design, Synthesis and Structure-Activity Relationships

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### *1. Chemistry*

Thin layer chromatography which was performed using Whatman® 250 μm Silica Gel GF Uniplates and visualized under UV light at 254 and 365 nm, was used to check the progress of reactions and preliminary evaluation of compounds' homogeneity. Melting points were measured using a **Gallenkamp Melting Point Apparatus (LabMerchant,** London, United Kingdom) and are uncorrected. Purification of compounds was carried out using crystallization methods and/or open silica gel column flash chromatography employing Merck silica gel 60 (240 to 400 mesh) as stationary phase. Nuclear magnetic resonance spectra ($^1$H NMR) were recorded on a Bruker 500 MHz spectrometer with DMSO-$d_6$ as solvent unless otherwise indicated. Tetramethylsilane was used as an internal standard. Chemical shifts are reported in parts per million (ppm), downfield from tetramethylsilane. Mass spectra with different ionization modes including electron ionization (EI), Electrospray ionization (ESI), were recorded using PE Biosystems API2000 (Perkin Elmer, Palo Alto, CA, USA) and Mariner® (Azco Biotech, Inc. **Oceanside, CA, USA)** mass spectrometers, respectively. The elemental (C, H, N) analyses were performed on a Perkin Elmer model 2400 elemental analyzer. All reagents and solvents were purchased from Aldrich or Fluka Chemical Corp. (Milwaukee, WI, USA) or Merck unless noted otherwise. Solvents were used directly as purchased unless otherwise indicated.

## 2. Biology

### *2.1. Cytotoxicity assay*

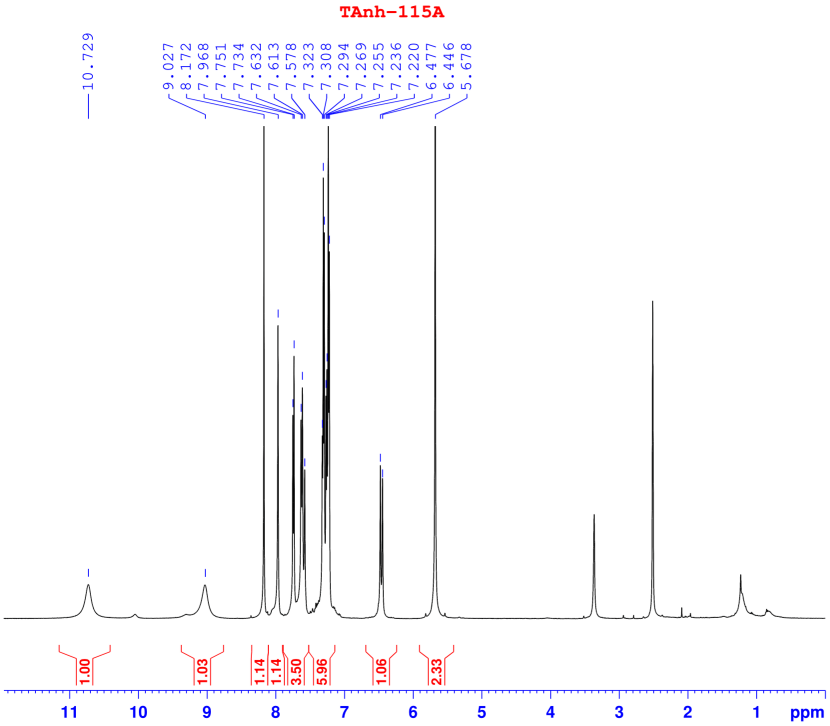
The cytotoxicity of the synthesized compounds was evaluated against three human cancer cell lines, including SW620 (colon cancer), PC3 (prostate cancer), and NCI-H23 (lung cancer). The cell lines were purchased from a Cancer Cell Bank at the Korea Research Institute of Bioscience and Biotechnology (KRIBB). The media, sera and other reagents that were used for cell culture in this assay were obtained from GIBCO Co. Ltd. (Grand Island, New York, USA). The cells were culture in DMEM (Dulbecco's Modified Eagle Medium) until confluence. The cells were then trypsinized and suspended at $3 \times 10^4$ cells/mL of cell culture medium. On day 0, each well of the 96-well plates was seeded with 180 μL of cell suspension. The plates were then incubated in a 5% $CO_2$ incubator at 37 ºC for 24 h. Compounds were initially dissolved in dimethyl sulfoxide (DMSO) and diluted to appropriate concentrations by culture medium. Then 20 μL of each compounds' samples, which were prepared as described above, were added to each well of the 96-well plates, which had been seeded with cell suspension and incubated for 24-h, at various concentrations. The plates were further incubated for 48 h. Cytotoxicity of the compounds was measured by the colorimetric method, as described previously [34] with slight modifications.[35-37] The $IC_{50}$ values were calculated using a Probits method [38] and were averages of three independent determinations (SD ≤ 10%).

### *2.2. HDAC enzymes assay*

The HDAC enzymes (Hela cell nuclear extract) were purchased from Enzo Life Sciences Inc. (Farmingdale, New York, USA). The HDAC enzymatic assay was performed using a Fluorogenic HDAC Assay Kit (Enzo Life Sciences Inc.) according to the manufacturer's instructions. The testing protocol was similar to that previously reported elsewhere.[39-40] Briefly, HDAC enzymes were incubated with vehicle or various concentrations of the assayed samples or SAHA for 30 min at 37ºC in the presence of an HDAC fluorimetric substrate. The HDAC assay developer (which produces a fluorophore in reaction mixture) was added, and the fluorescence was measured using VICTOR (PerkinElmer, Waltham, MA, USA) with excitation at 360 nm and emission at 460 nm. The measured activities were subtracted by the vehicle-treated control enzyme activities and $IC_{50}$ values were calculated using GraphPad Prism (GraphPad Software, San Diego, CA, USA).

## 3. ALL $^1$H & $^{13}$C NMR SPECTRA OF THE COMPOUNDS

**$^{1}$H NMR of compound 5a**

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NUC1                         1H
P1                         9.80 usec
PLW1               24.00000000 W

F2 - Processing parameters
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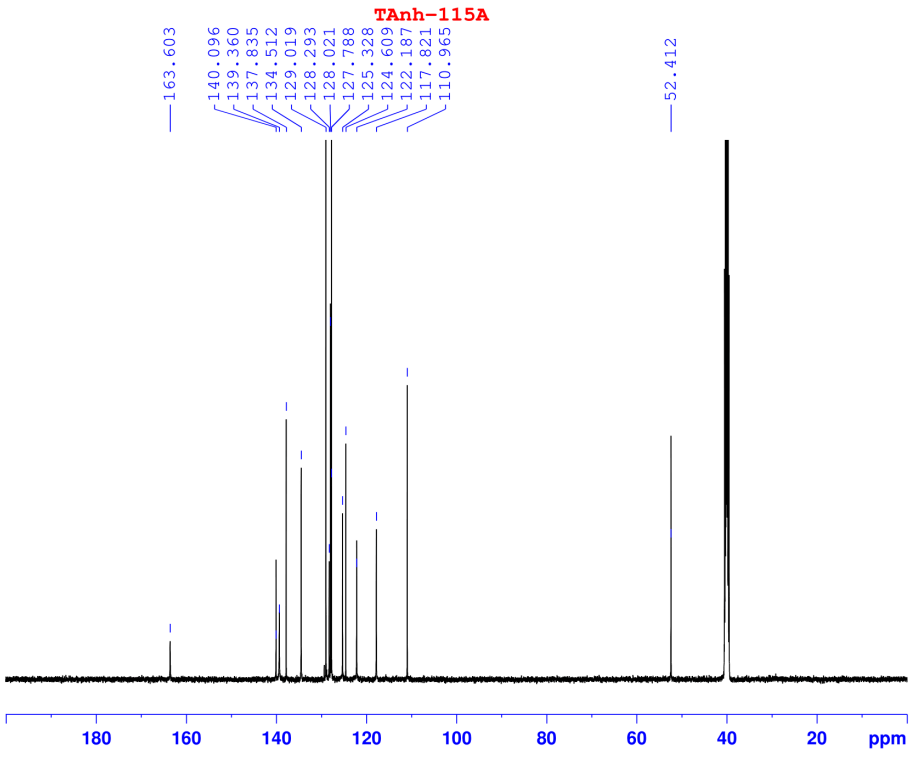


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FIDRES             0.476837 Hz
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RG                    191.38
DW                   16.000 usec
DE                    6.50 usec
TE                    301.0 K
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D11                0.03000000 sec
TD0                           1

======== CHANNEL f1 ========
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NUC1                        13C
P1                         9.50 usec
PLW1               90.00000000 W

======== CHANNEL f2 ========
SFO2               500.1320005 MHz
NUC2                         1H
CPDPRG[2               waltz16
PCPD2                     80.00 usec
PLW2               24.00000000 W
PLW12               0.36015001 W
PLW13               0.23050000 W

F2 - Processing parameters
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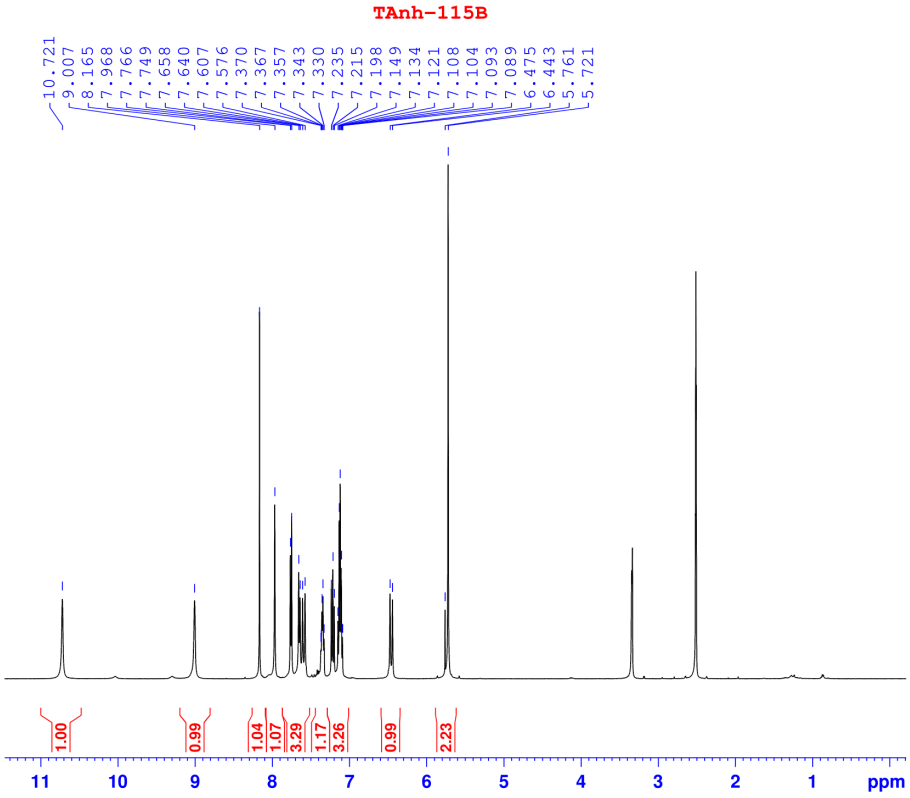
**$^{1}$H NMR of compound 5b**





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SOLVENT                 DMSO
NS                        16
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AQ                 3.2767999 sec
RG                    191.38
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DE                     6.50 usec
TE                    300.4 K
D1                1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
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NUC1                        1H
P1                       9.80 usec
PLW1             24.00000000 W

F2 - Processing parameters
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PC                       1.00
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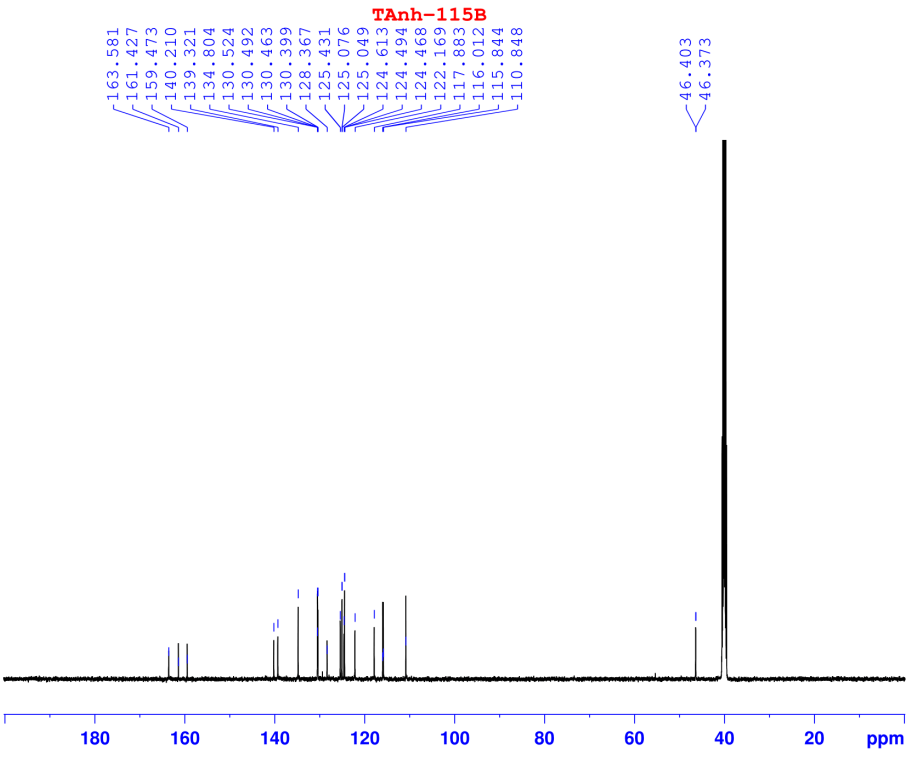
**$^{13}$C NMR of compound 5b**





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NS                      1741
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FIDRES             0.476837 Hz
AQ                 1.0485760 sec
RG                    191.38
DW                    16.000 usec
DE                     6.50 usec
TE                    301.1 K
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D11               0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
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NUC1                       13C
P1                       9.50 usec
PLW1             90.00000000 W

======== CHANNEL f2 ========
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NUC2                        1H
CPDPRG[2                waltz16
PCPD2                   80.00 usec
PLW2             24.00000000 W
PLW12             0.36015001 W
PLW13             0.23050000 W

F2 - Processing parameters
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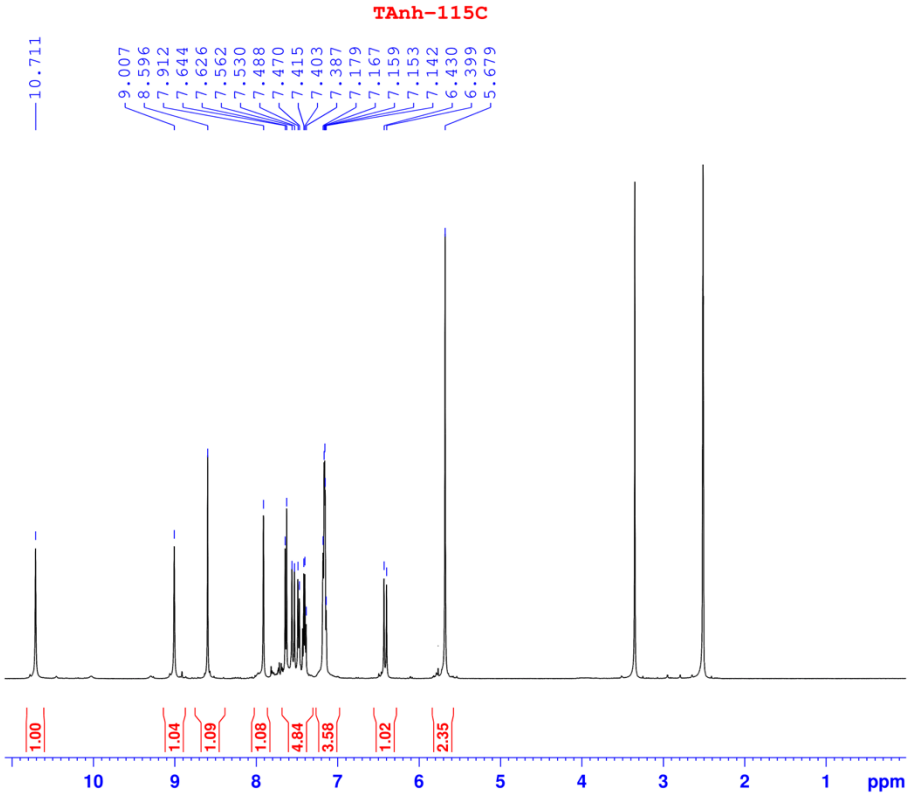
**$^{1}$H NMR of compound 5c**

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PULPROG                 zg30
TD                     65536
SOLVENT                 DMSO
NS                        16
DS                         2
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FIDRES             0.152588 Hz
AQ                 3.2767999 sec
RG                    191.38
DW                    50.000 usec
DE                     6.50 usec
TE                    297.6 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
SFO1              500.1330885 MHz
NUC1                      1H
P1                      9.80 usec
PLW1              24.00000000 W

F2 - Processing parameters
SI                     65536
SF                500.1300000 MHz
WDW                       EM
SSB          0
LB                     0.30 Hz
GB           0
PC                     1.00
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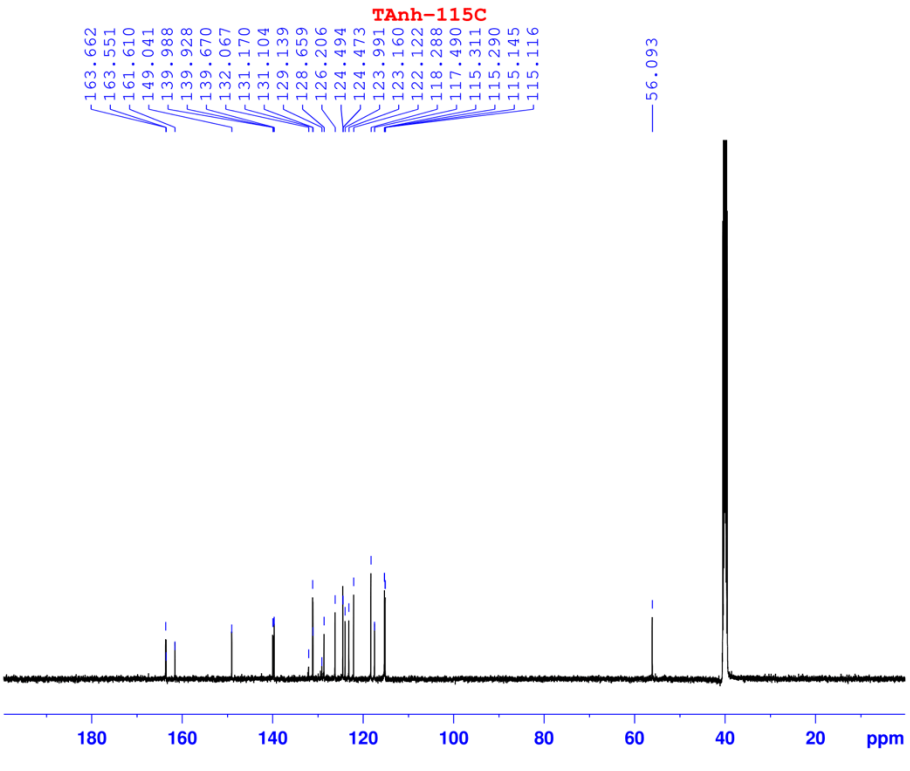
**$^{13}$C NMR of compound 5c**

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PROCNO                       1

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NS                      1742
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FIDRES             0.476837 Hz
AQ                 1.0485760 sec
RG                    191.38
DW                    16.000 usec
DE                     6.50 usec
TE                    298.6 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                        1

======== CHANNEL f1 ========
SFO1              125.7703637 MHz
NUC1                     13C
P1                      9.50 usec
PLW1              90.00000000 W

======== CHANNEL f2 ========
SFO2              500.1320005 MHz
NUC2                      1H
CPDPRG[2              waltz16
PCPD2                  80.00 usec
PLW2              24.00000000 W
PLW12              0.36015001 W
PLW13              0.23050000 W

F2 - Processing parameters
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WDW                       EM
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LB                     1.00 Hz
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PC                     1.40
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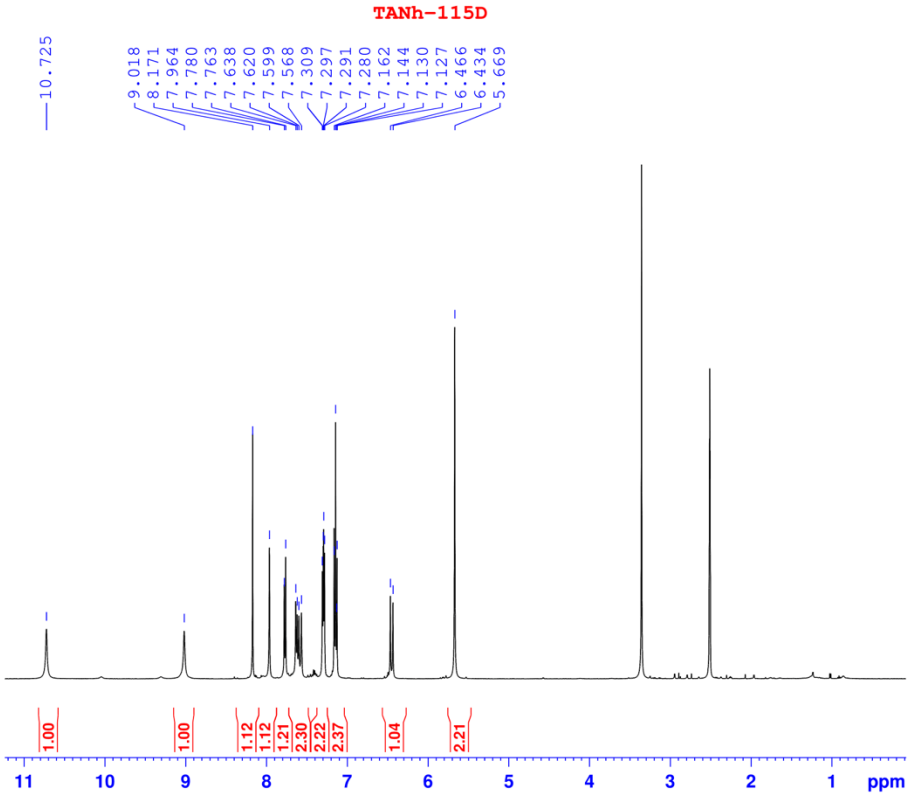
**$^{1}$H NMR of compound 5d**

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PULPROG                  zg30
TD                      65536
SOLVENT                  DMSO
NS                         16
DS                          2
SWH                 10000.000 Hz
FIDRES                0.152588 Hz
AQ                    3.2767999 sec
RG                       191.38
DW                       50.000 usec
DE                        6.50 usec
TE                       297.8 K
D1                  1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
SFO1                500.1330885 MHz
NUC1                        1H
P1                        9.80 usec
PLW1                24.00000000 W

F2 - Processing parameters
SI                      65536
SF                  500.1300000 MHz
WDW                        EM
SSB                 0
LB                        0.30 Hz
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PC                        1.00
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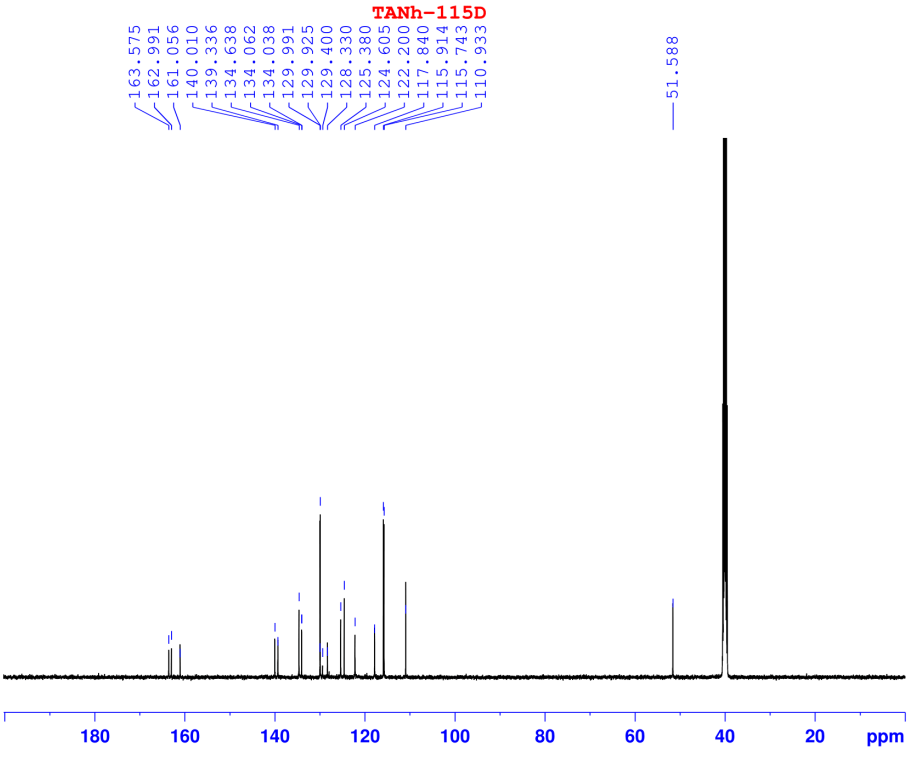
**$^{13}$C NMR of compound 5d**

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FIDRES                0.476837 Hz
AQ                    1.0485760 sec
RG                       191.38
DW                       16.000 usec
DE                        6.50 usec
TE                       298.8 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                           1

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NUC1                        13C
P1                        9.50 usec
PLW1                90.00000000 W

======== CHANNEL f2 ========
SFO2                500.1320005 MHz
NUC2                        1H
CPDPRG[2                waltz16
PCPD2                     80.00 usec
PLW2                24.00000000 W
PLW12                0.36015001 W
PLW13                0.23050000 W

F2 - Processing parameters
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SSB                 0
LB                        1.00 Hz
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PC                        1.40
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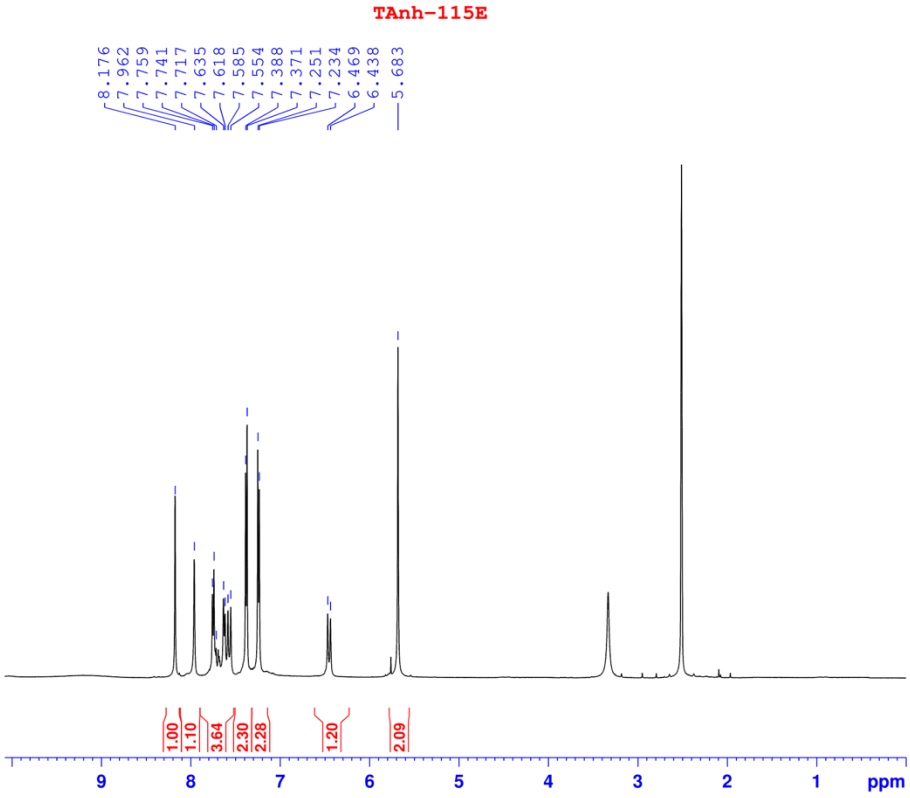
**$^{1}$H NMR of compound 5e**

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PULPROG                 zg30
TD                     65536
SOLVENT                 DMSO
NS                        16
DS                         2
SWH                10000.000 Hz
FIDRES             0.152588 Hz
AQ                 3.2767999 sec
RG                    191.38
DW                    50.000 usec
DE                     6.50 usec
TE                    300.8 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
SFO1              500.1330885 MHz
NUC1                      1H
P1                     9.80 usec
PLW1              24.00000000 W

F2 - Processing parameters
SI                     65536
SF                500.1300000 MHz
WDW                       EM
SSB          0
LB                     0.30 Hz
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PC                     1.00
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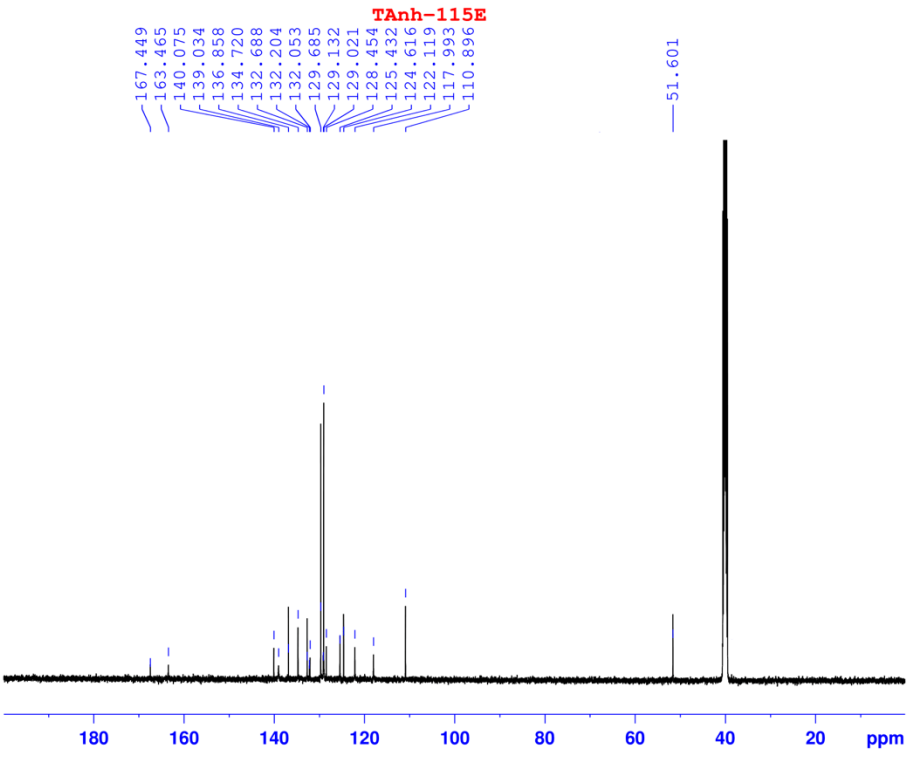
**$^{13}$C NMR of compound 5e**

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PROCNO                       1

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PULPROG              zgpg30
TD                     65536
SOLVENT                 DMSO
NS                      2048
DS                         4
SWH                31250.000 Hz
FIDRES             0.476837 Hz
AQ                 1.0485760 sec
RG                    191.38
DW                    16.000 usec
DE                     6.50 usec
TE                    301.2 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                        1

======== CHANNEL f1 ========
SFO1              125.7703637 MHz
NUC1                     13C
P1                     9.50 usec
PLW1              90.00000000 W

======== CHANNEL f2 ========
SFO2              500.1320005 MHz
NUC2                      1H
CPDPRG[2             waltz16
PCPD2                 80.00 usec
PLW2              24.00000000 W
PLW12              0.36015001 W
PLW13              0.23050000 W

F2 - Processing parameters
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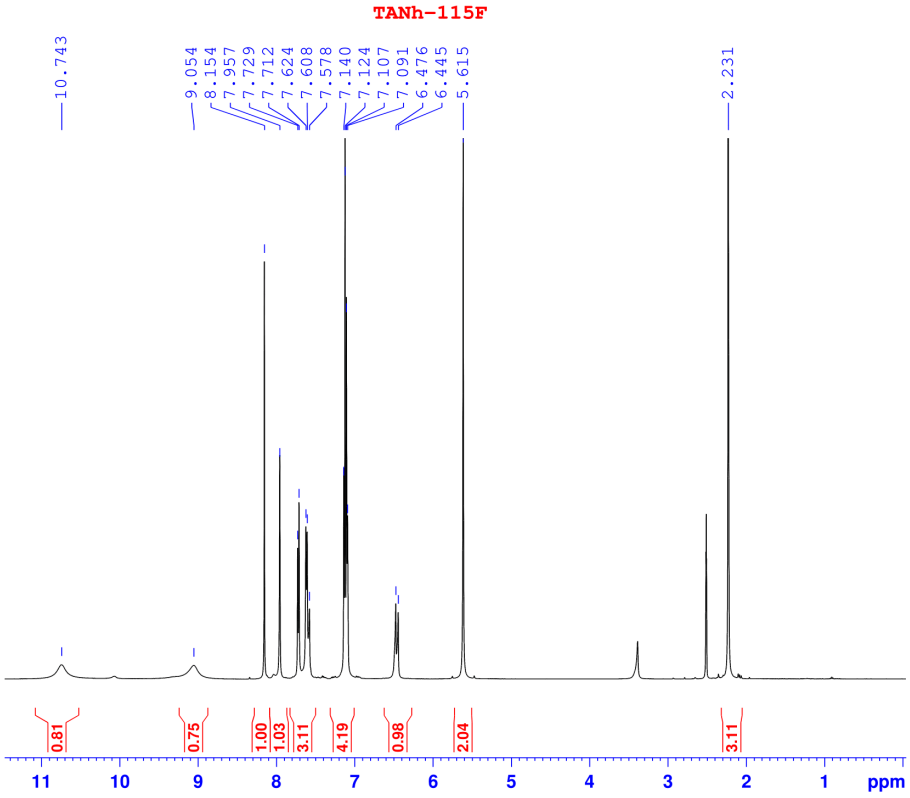
**$^{1}$H NMR of compound 5f**

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PROCNO                       1

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PULPROG                 zg30
TD                     65536
SOLVENT                 DMSO
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FIDRES             0.152588 Hz
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RG                     95.24
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DE                     6.50 usec
TE                    297.9 K
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TD0                          1

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NUC1                        1H
P1                        9.80 usec
PLW1              24.00000000 W

F2 - Processing parameters
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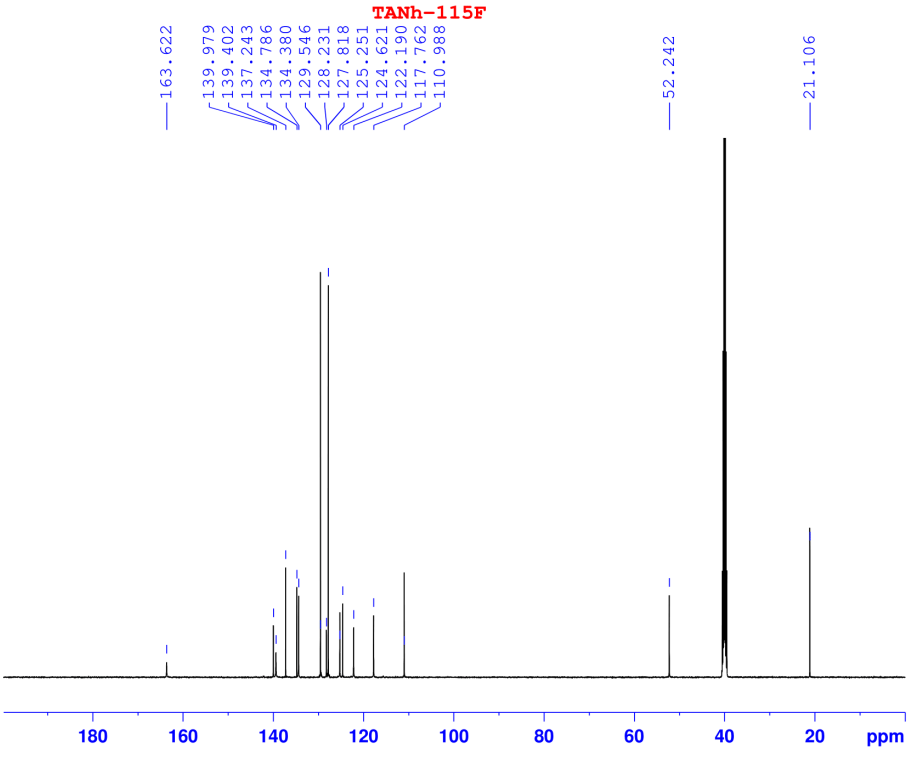
**$^{13}$C NMR of compound 5f**

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PROCNO                       1

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PULPROG              zgpg30
TD                     65536
SOLVENT                 DMSO
NS                        2048
DS                           4
SWH                31250.000 Hz
FIDRES             0.476837 Hz
AQ                 1.0485760 sec
RG                     191.38
DW                    16.000 usec
DE                     6.50 usec
TE                    298.7 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1              125.7703637 MHz
NUC1                       13C
P1                        9.50 usec
PLW1              90.00000000 W

======== CHANNEL f2 ========
SFO2              500.1320005 MHz
NUC2                        1H
CPDPRG[2                waltz16
PCPD2                    80.00 usec
PLW2              24.00000000 W
PLW12              0.36015001 W
PLW13              0.23050000 W

F2 - Processing parameters
SI                         65536
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WDW                           EM
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LB                        1.00 Hz
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PC                        1.40
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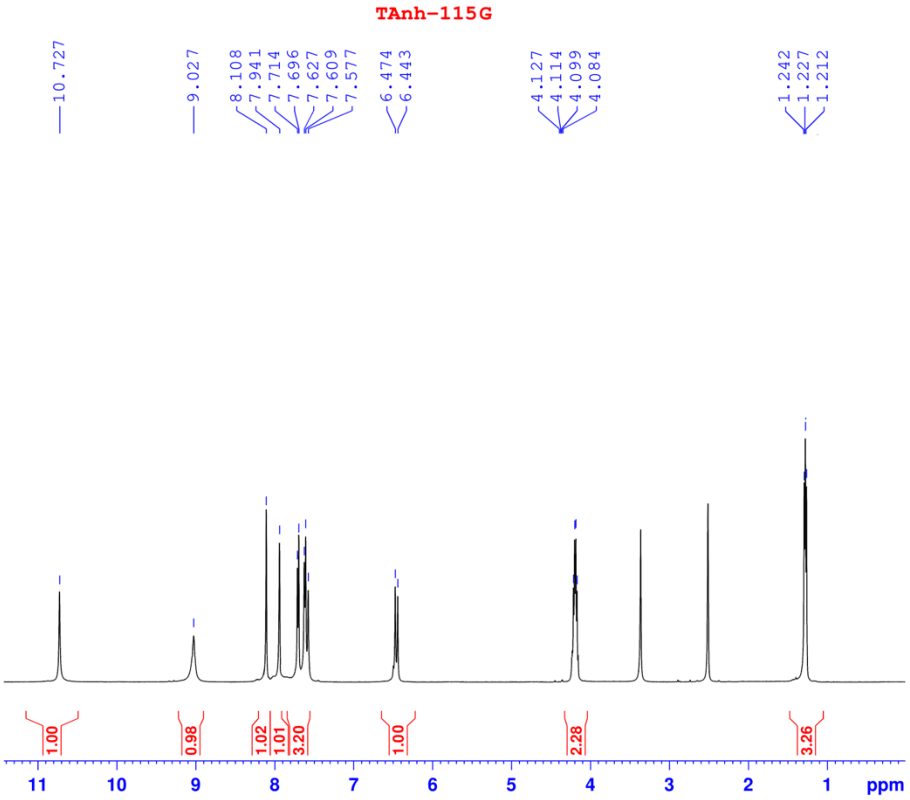
**$^{1}$H NMR of compound 5g**

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PROCNO                  1

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Time                14.27
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PROBHD    5 mm PABBO BB/
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH             10000.000 Hz
FIDRES          0.152588 Hz
AQ              3.2767999 sec
RG                 191.38
DW                 50.000 usec
DE                  6.50 usec
TE                 300.9 K
D1            1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1          500.1330885 MHz
NUC1                   1H
P1                   9.80 usec
PLW1         24.00000000 W

F2 - Processing parameters
SI                  65536
SF            500.1300000 MHz
WDW                    EM
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LB                   0.30 Hz
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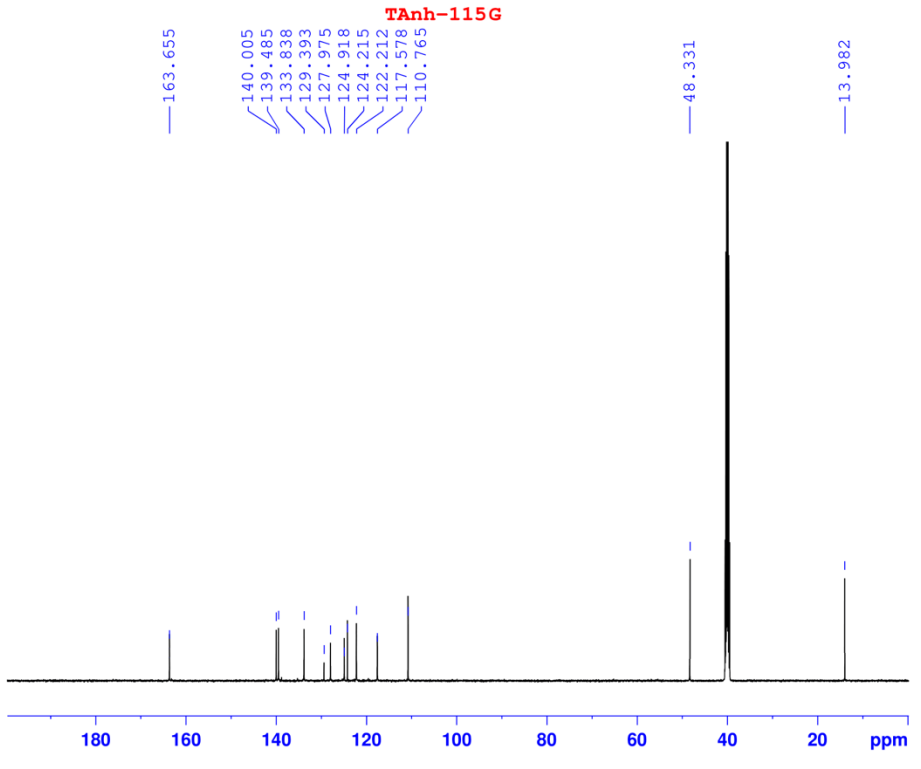
**$^{13}$C NMR of compound 5g**

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PROCNO                  1

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Time                 8.26
INSTRUM             spect
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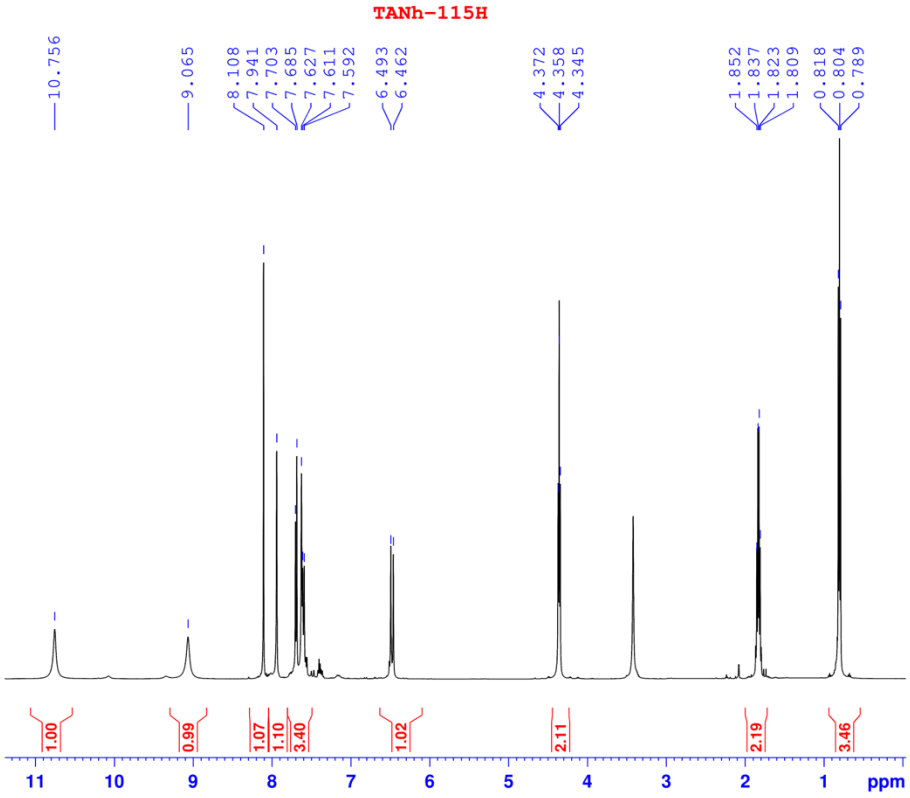
PULPROG           zgpg30
TD                  65536
SOLVENT              DMSO
NS                   1404
DS                      4
SWH             31250.000 Hz
FIDRES          0.476837 Hz
AQ              1.0485760 sec
RG                 191.38
DW                 16.000 usec
DE                  6.50 usec
TE                 301.7 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1          125.7703637 MHz
NUC1                  13C
P1                   9.50 usec
PLW1         90.00000000 W

======== CHANNEL f2 ========
SFO2          500.1320005 MHz
NUC2                   1H
CPDPRG[2           waltz16
PCPD2                80.00 usec
PLW2         24.00000000 W
PLW12         0.36015001 W
PLW13         0.23050000 W

F2 - Processing parameters
SI                  65536
SF            125.7577885 MHz
WDW                    EM
SSB       0
LB                   1.00 Hz
GB        0
PC                   1.40
```

**$^{1}$H NMR of compound 5h**



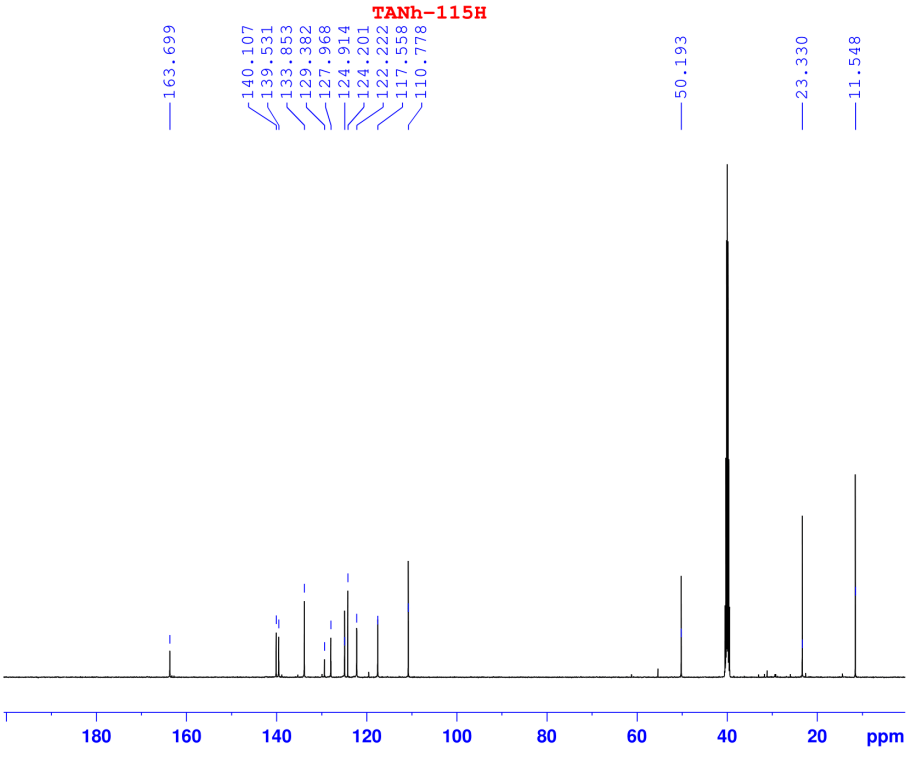

```
Current Data Parameters
NAME                 TANh-115H
EXPNO                       80
PROCNO                       1

F2 - Acquisition Parameters
Date_               20201230
Time                   16.28
INSTRUM                spect
PROBHD     5 mm PABBO BB/
PULPROG                 zg30
TD                     65536
SOLVENT                 DMSO
NS                        16
DS                         2
SWH                10000.000 Hz
FIDRES             0.152588 Hz
AQ                 3.2767999 sec
RG                     77.23
DW                    50.000 usec
DE                     6.50 usec
TE                    297.8 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
SFO1              500.1330885 MHz
NUC1                      1H
P1                      9.80 usec
PLW1              24.00000000 W

F2 - Processing parameters
SI                     65536
SF                500.1300000 MHz
WDW                       EM
SSB          0
LB                     0.30 Hz
GB           0
PC                     1.00
```

**$^{13}$C NMR of compound 5h**




```
Current Data Parameters
NAME                 TANh-115H
EXPNO                       81
PROCNO                       1

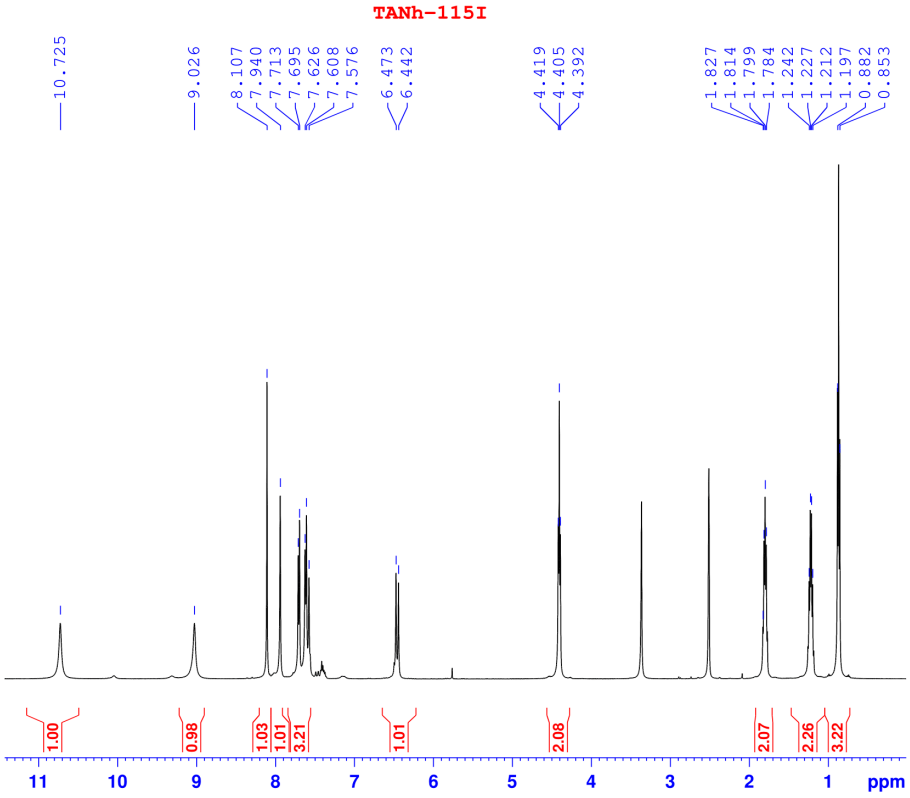
F2 - Acquisition Parameters
Date_               20201231
Time                    4.16
INSTRUM                spect
PROBHD     5 mm PABBO BB/
PULPROG              zgpg30
TD                     65536
SOLVENT                 DMSO
NS                      2048
DS                         4
SWH                31250.000 Hz
FIDRES             0.476837 Hz
AQ                 1.0485760 sec
RG                    191.38
DW                    16.000 usec
DE                     6.50 usec
TE                    298.6 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                        1

======== CHANNEL f1 ========
SFO1              125.7703637 MHz
NUC1                     13C
P1                      9.50 usec
PLW1              90.00000000 W

======== CHANNEL f2 ========
SFO2              500.1320005 MHz
NUC2                      1H
CPDPRG[2             waltz16
PCPD2                  80.00 usec
PLW2              24.00000000 W
PLW12              0.36015001 W
PLW13              0.23050000 W

F2 - Processing parameters
SI                     65536
SF                125.7577885 MHz
WDW                       EM
SSB          0
LB                     1.00 Hz
GB           0
PC                     1.40
```

**$^{1}$H NMR of compound 5i**



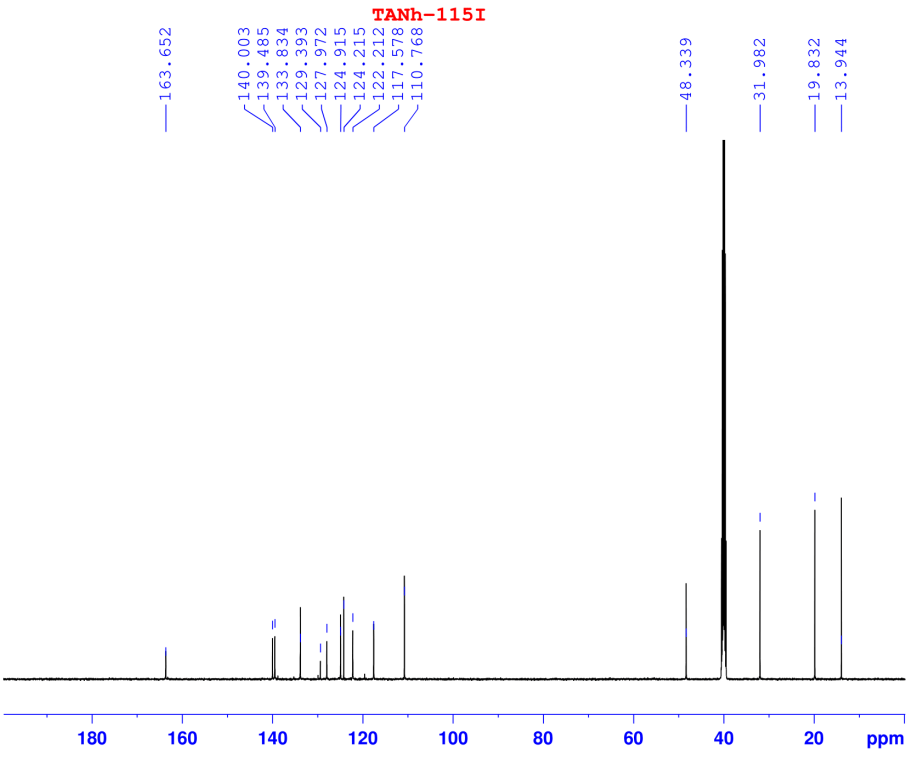

```
Current Data Parameters
NAME            TANh-115I
EXPNO                  30
PROCNO                  1

F2 - Acquisition Parameters
Date_            20201230
Time                16.00
INSTRUM             spect
PROBHD    5 mm PABBO BB/
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH             10000.000 Hz
FIDRES          0.152588 Hz
AQ              3.2767999 sec
RG                 138.87
DW                 50.000 usec
DE                  6.50 usec
TE                 297.8 K
D1            1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1          500.1330885 MHz
NUC1                   1H
P1                  9.80 usec
PLW1         24.00000000 W

F2 - Processing parameters
SI                  65536
SF            500.1300000 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

**$^{13}$C NMR of compound 5i**




```
Current Data Parameters
NAME            TANh-115I
EXPNO                  31
PROCNO                  1

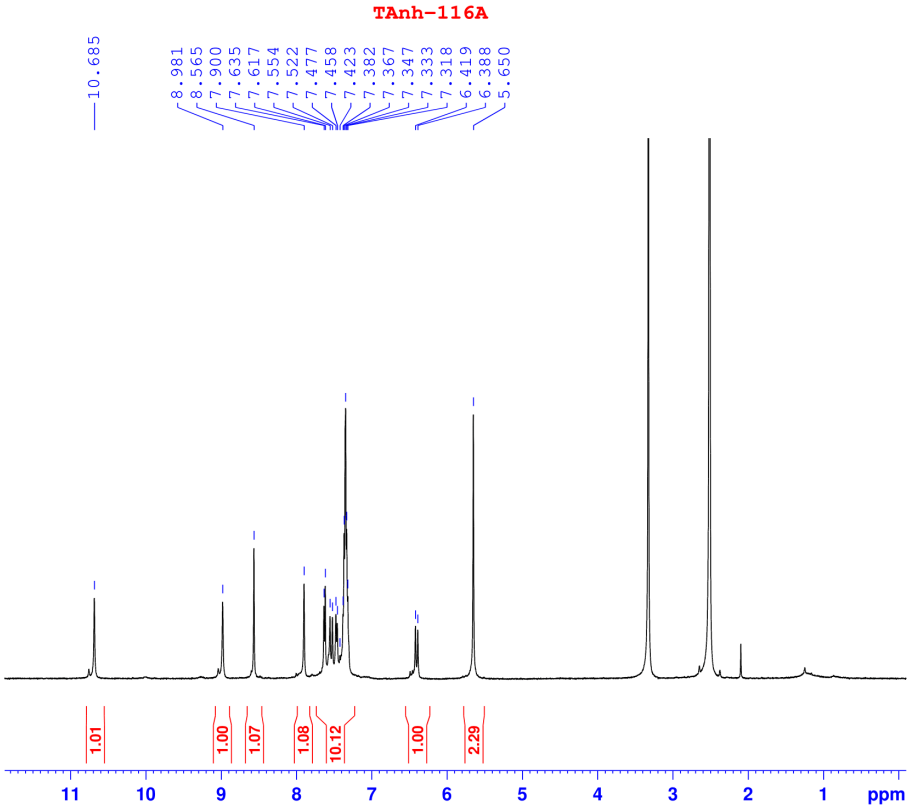
F2 - Acquisition Parameters
Date_            20201230
Time                22.09
INSTRUM             spect
PROBHD    5 mm PABBO BB/
PULPROG           zgpg30
TD                  65536
SOLVENT              DMSO
NS                   2048
DS                      4
SWH             31250.000 Hz
FIDRES          0.476837 Hz
AQ              1.0485760 sec
RG                 191.38
DW                 16.000 usec
DE                  6.50 usec
TE                 298.7 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1          125.7703637 MHz
NUC1                   13C
P1                  9.50 usec
PLW1         90.00000000 W

======== CHANNEL f2 ========
SFO2          500.1320005 MHz
NUC2                   1H
CPDPRG[2           waltz16
PCPD2                80.00 usec
PLW2         24.00000000 W
PLW12         0.36015001 W
PLW13         0.23050000 W

F2 - Processing parameters
SI                  65536
SF            125.7577885 MHz
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

**$^{1}$H NMR of compound 7a**



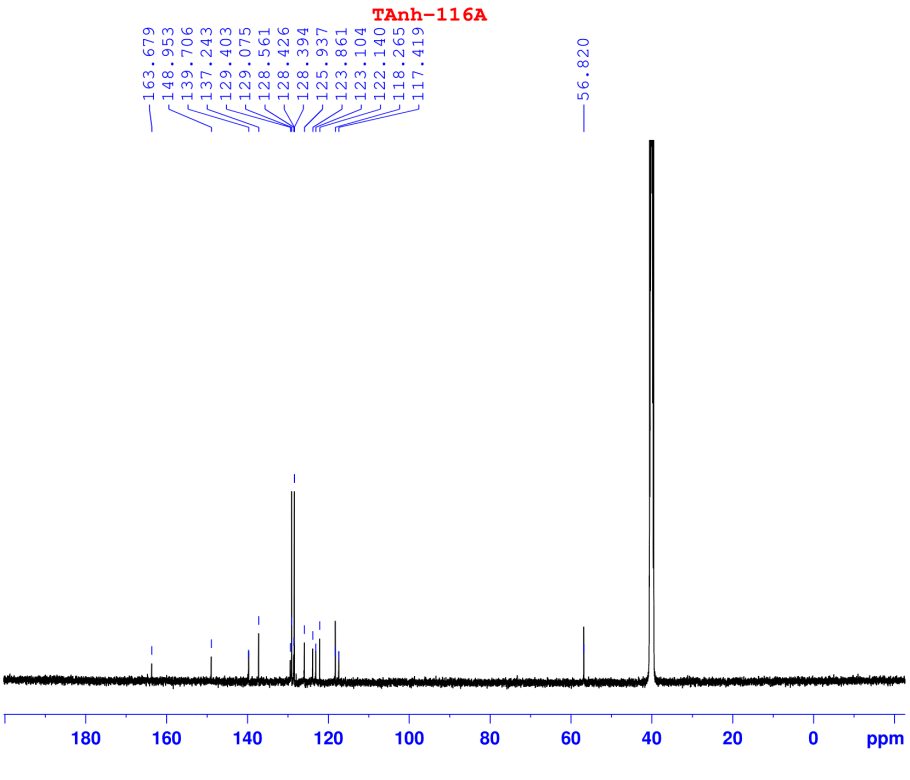

```
Current Data Parameters
NAME                 TAnh-116A
EXPNO                       30
PROCNO                       1

F2 - Acquisition Parameters
Date_               20201208
Time                   17.07
INSTRUM                spect
PROBHD    5 mm PABBO BB/
PULPROG                 zg30
TD                     65536
SOLVENT                 DMSO
NS                        16
DS                         2
SWH                10000.000 Hz
FIDRES             0.152588 Hz
AQ                 3.2767999 sec
RG                    191.38
DW                    50.000 usec
DE                     6.50 usec
TE                    300.4 K
D1                 1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1            500.1330885 MHz
NUC1                       1H
P1                       9.80 usec
PLW1            24.00000000 W

F2 - Processing parameters
SI                     65536
SF              500.1300000 MHz
WDW                       EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```

**$^{13}$C NMR of compound 7a**




```
Current Data Parameters
NAME                 TAnh-116A
EXPNO                       34
PROCNO                       1

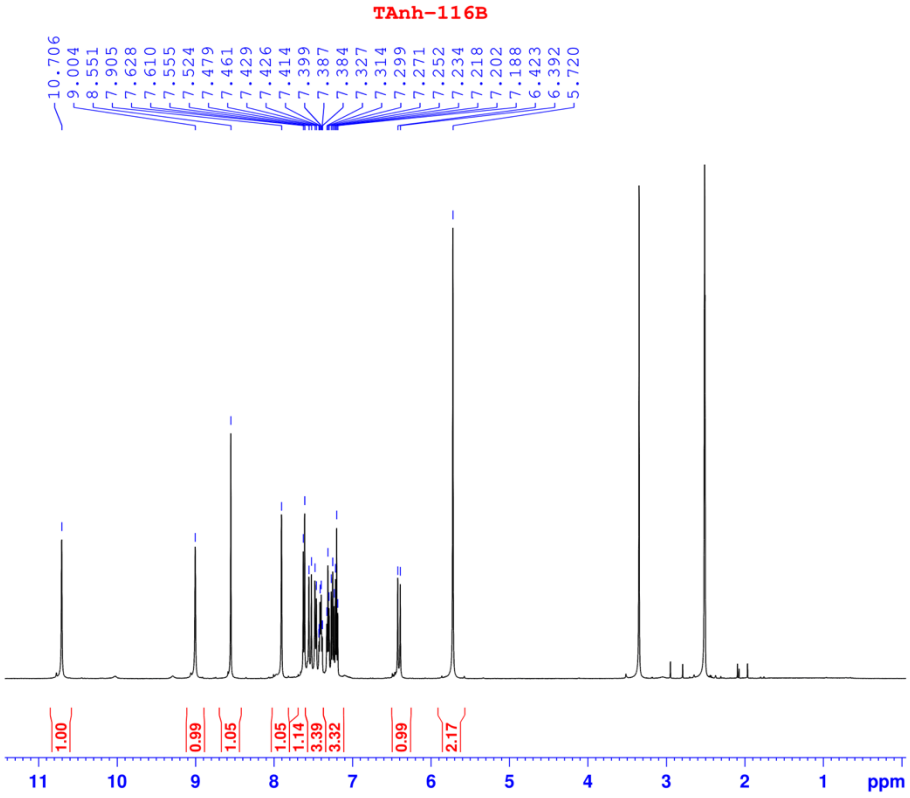
F2 - Acquisition Parameters
Date_               20201209
Time                   19.31
INSTRUM                spect
PROBHD    5 mm PABBO BB/
PULPROG              zgpg30
TD                     65536
SOLVENT                 DMSO
NS                      8192
DS                         4
SWH                31250.000 Hz
FIDRES             0.476837 Hz
AQ                 1.0485760 sec
RG                    191.38
DW                    16.000 usec
DE                     6.50 usec
TE                    301.2 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                          1

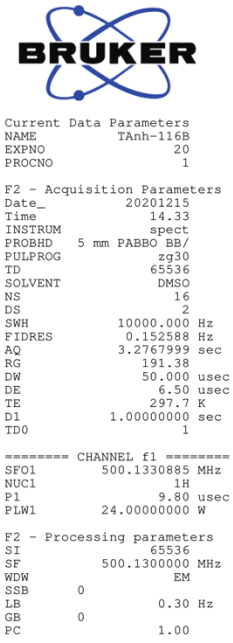
======== CHANNEL f1 ========
SFO1            125.7703637 MHz
NUC1                      13C
P1                       9.50 usec
PLW1            90.00000000 W

======== CHANNEL f2 ========
SFO2            500.1320005 MHz
NUC2                       1H
CPDPRG[2             waltz16
PCPD2                 80.00 usec
PLW2            24.00000000 W
PLW12            0.36015001 W
PLW13            0.23050000 W

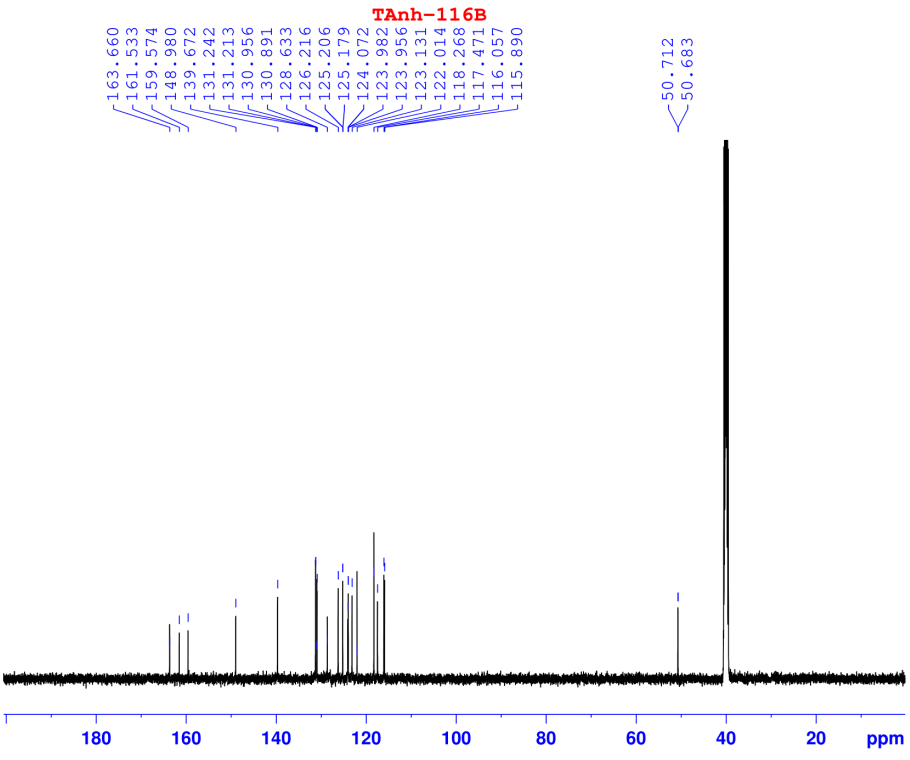
F2 - Processing parameters
SI                     65536
SF              125.7577885 MHz
WDW                       EM
SSB          0
LB                    1.00 Hz
GB           0
PC                    1.40
```

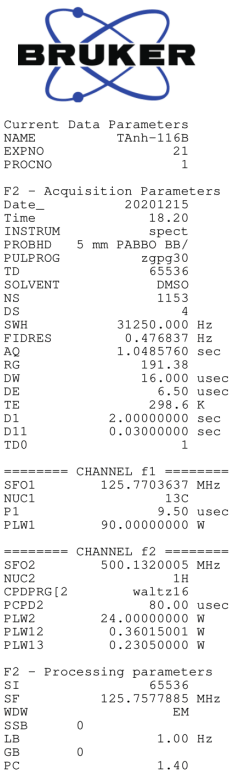
**$^{1}$H NMR of compound 7b**



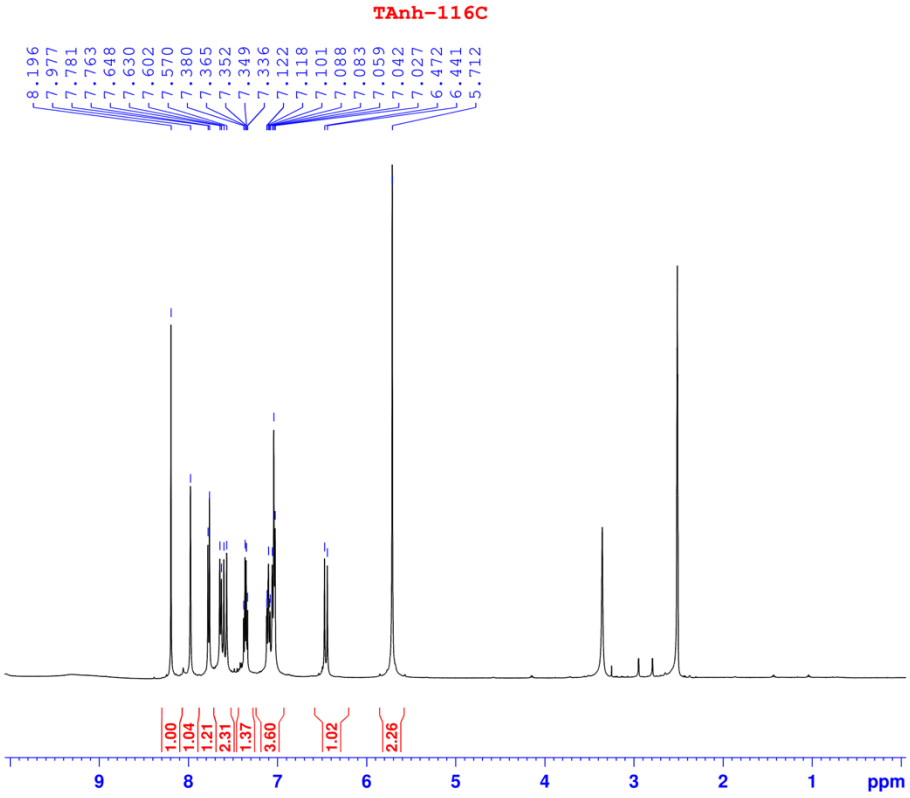




**$^{13}$C NMR of compound 7b**



**$^{1}$H NMR of compound 7c**



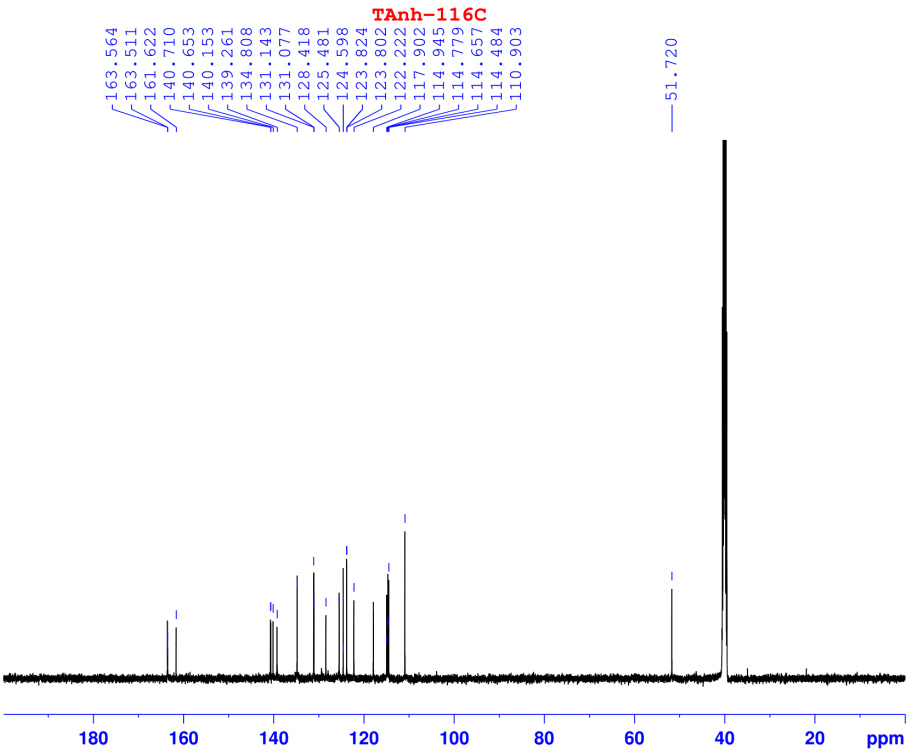

```
Current Data Parameters
NAME                 TAnh-116C
EXPNO                       30
PROCNO                       1

F2 - Acquisition Parameters
Date_               20201215
Time                   14.37
INSTRUM                spect
PROBHD    5 mm PABBO BB/
PULPROG                 zg30
TD                     65536
SOLVENT                 DMSO
NS                        16
DS                         2
SWH                10000.000 Hz
FIDRES             0.152588 Hz
AQ                 3.2767999 sec
RG                    191.38
DW                    50.000 usec
DE                     6.50 usec
TE                    297.5 K
D1                 1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1            500.1330885 MHz
NUC1                       1H
P1                       9.80 usec
PLW1            24.00000000 W

F2 - Processing parameters
SI                     65536
SF              500.1300000 MHz
WDW                       EM
SSB          0
LB                     0.30 Hz
GB           0
PC                     1.00
```

**$^{13}$C NMR of compound 7c**




```
Current Data Parameters
NAME                 TAnh-116C
EXPNO                       31
PROCNO                       1

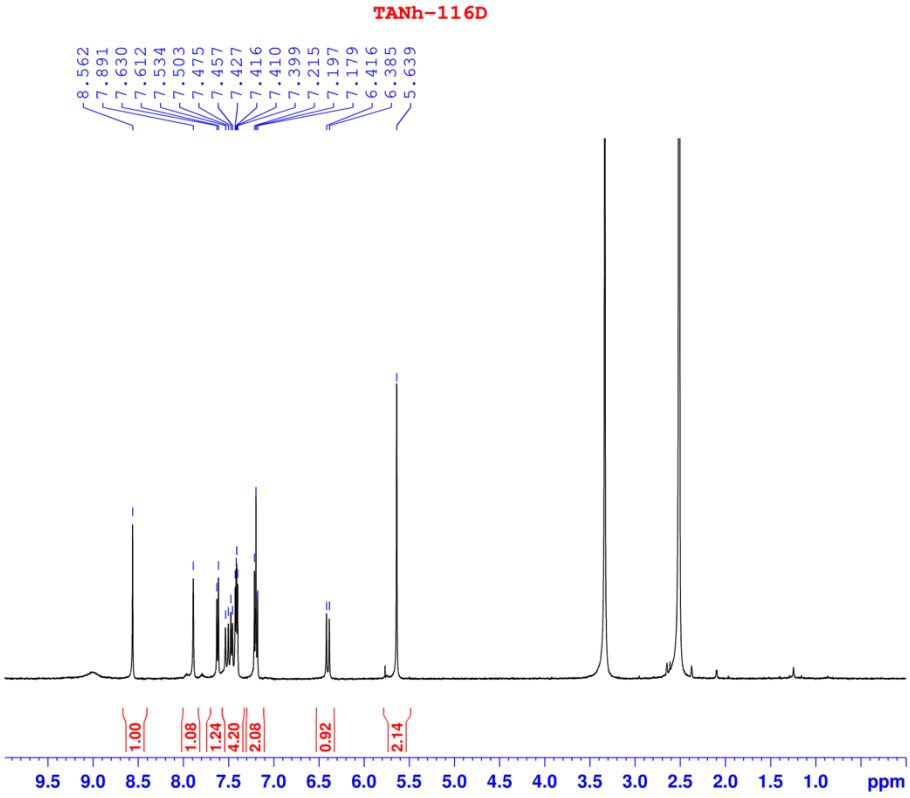
F2 - Acquisition Parameters
Date_               20201215
Time                   19.46
INSTRUM                spect
PROBHD    5 mm PABBO BB/
PULPROG              zgpg30
TD                     65536
SOLVENT                 DMSO
NS                      1001
DS                         4
SWH                31250.000 Hz
FIDRES             0.476837 Hz
AQ                 1.0485760 sec
RG                    191.38
DW                    16.000 usec
DE                     6.50 usec
TE                    298.5 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1            125.7703637 MHz
NUC1                      13C
P1                       9.50 usec
PLW1            90.00000000 W

======== CHANNEL f2 ========
SFO2            500.1320005 MHz
NUC2                       1H
CPDPRG[2             waltz16
PCPD2                  80.00 usec
PLW2            24.00000000 W
PLW12            0.36015001 W
PLW13            0.23050000 W

F2 - Processing parameters
SI                     65536
SF              125.7577885 MHz
WDW                       EM
SSB          0
LB                     1.00 Hz
GB           0
PC                     1.40
```

**$^{1}$H NMR of compound 7d**



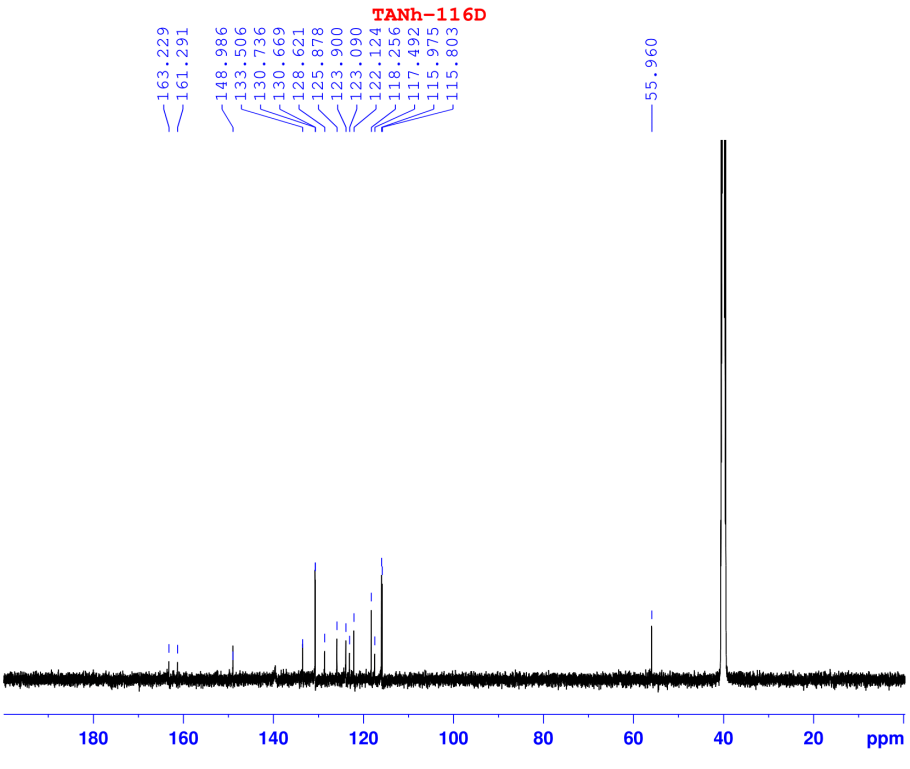

```
Current Data Parameters
NAME                  TANh-116D
EXPNO                        40
PROCNO                        1

F2 - Acquisition Parameters
Date_                 20201230
Time                      16.05
INSTRUM                   spect
PROBHD    5 mm PABBO BB/
PULPROG                   zg30
TD                       65536
SOLVENT                   DMSO
NS                           16
DS                            2
SWH                  10000.000 Hz
FIDRES                0.152588 Hz
AQ                    3.2767999 sec
RG                       191.38
DW                       50.000 usec
DE                        6.50 usec
TE                       297.9 K
D1                    1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
SFO1                500.1330885 MHz
NUC1                        1H
P1                        9.80 usec
PLW1                24.00000000 W

F2 - Processing parameters
SI                       65536
SF                  500.1300000 MHz
WDW                         EM
SSB                  0
LB                        0.30 Hz
GB                   0
PC                        1.00
```

**$^{13}$C NMR of compound 7d**




```
Current Data Parameters
NAME                  TANh-116D
EXPNO                        42
PROCNO                        1

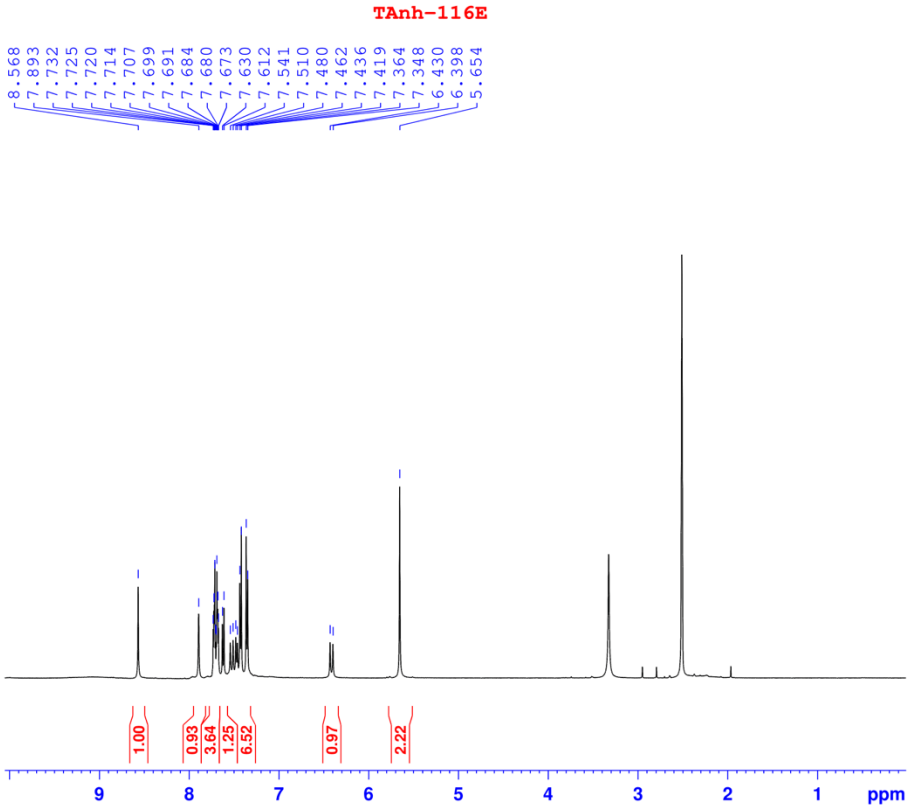
F2 - Acquisition Parameters
Date_                 20210101
Time                      3.02
INSTRUM                   spect
PROBHD    5 mm PABBO BB/
PULPROG                 zgpg30
TD                       65536
SOLVENT                   DMSO
NS                         8192
DS                            4
SWH                  31250.000 Hz
FIDRES                0.476837 Hz
AQ                    1.0485760 sec
RG                       191.38
DW                       16.000 usec
DE                        6.50 usec
TE                       298.2 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                           1

======== CHANNEL f1 ========
SFO1                125.7703637 MHz
NUC1                        13C
P1                        9.50 usec
PLW1                90.00000000 W

======== CHANNEL f2 ========
SFO2                500.1320005 MHz
NUC2                        1H
CPDPRG[2                waltz16
PCPD2                     80.00 usec
PLW2                24.00000000 W
PLW12                0.36015001 W
PLW13                0.23050000 W

F2 - Processing parameters
SI                       65536
SF                  125.7577885 MHz
WDW                         EM
SSB                  0
LB                        1.00 Hz
GB                   0
PC                        1.40
```

**$^{1}$H NMR of compound 7e**



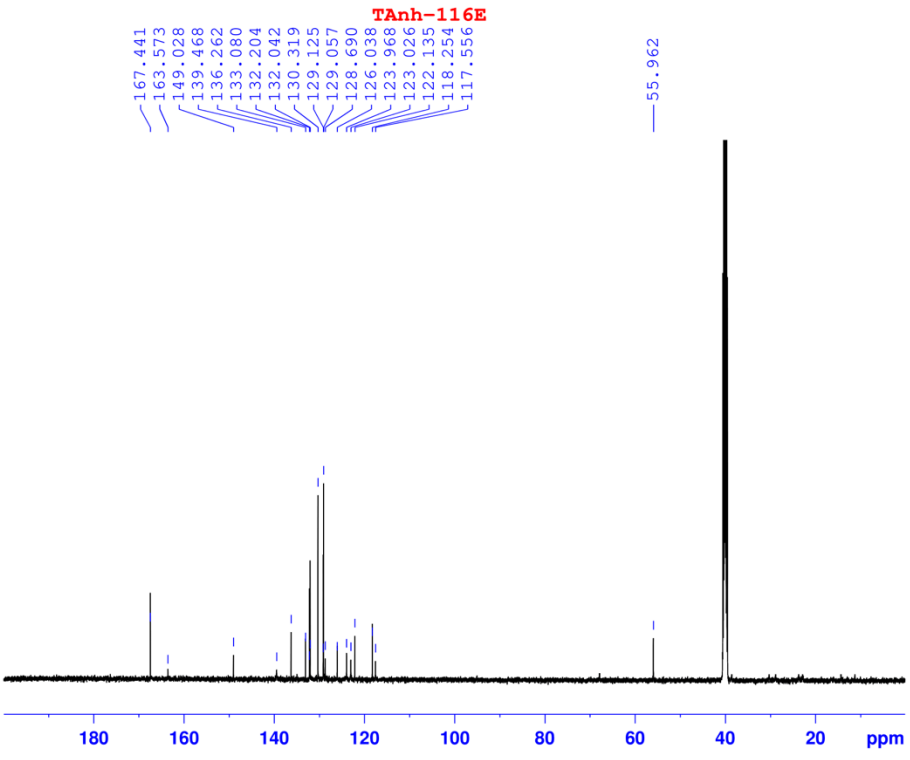

```
Current Data Parameters
NAME                 TAnh-116E
EXPNO                       20
PROCNO                       1

F2 - Acquisition Parameters
Date_               20201201
Time                   11.46
INSTRUM                spect
PROBHD    5 mm PABBO BB/
PULPROG                 zg30
TD                     65536
SOLVENT                 DMSO
NS                        16
DS                         2
SWH                10000.000 Hz
FIDRES             0.152588 Hz
AQ                 3.2767999 sec
RG                    191.38
DW                    50.000 usec
DE                     6.50 usec
TE                    301.0 K
D1                 1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1              500.1330885 MHz
NUC1                        1H
P1                       9.80 usec
PLW1              24.00000000 W

F2 - Processing parameters
SI                         65536
SF                500.1300000 MHz
WDW                          EM
SSB          0
LB                       0.30 Hz
GB           0
PC                       1.00
```

**$^{13}$C NMR of compound 7e**




```
Current Data Parameters
NAME                 TAnh-116E
EXPNO                       21
PROCNO                       1

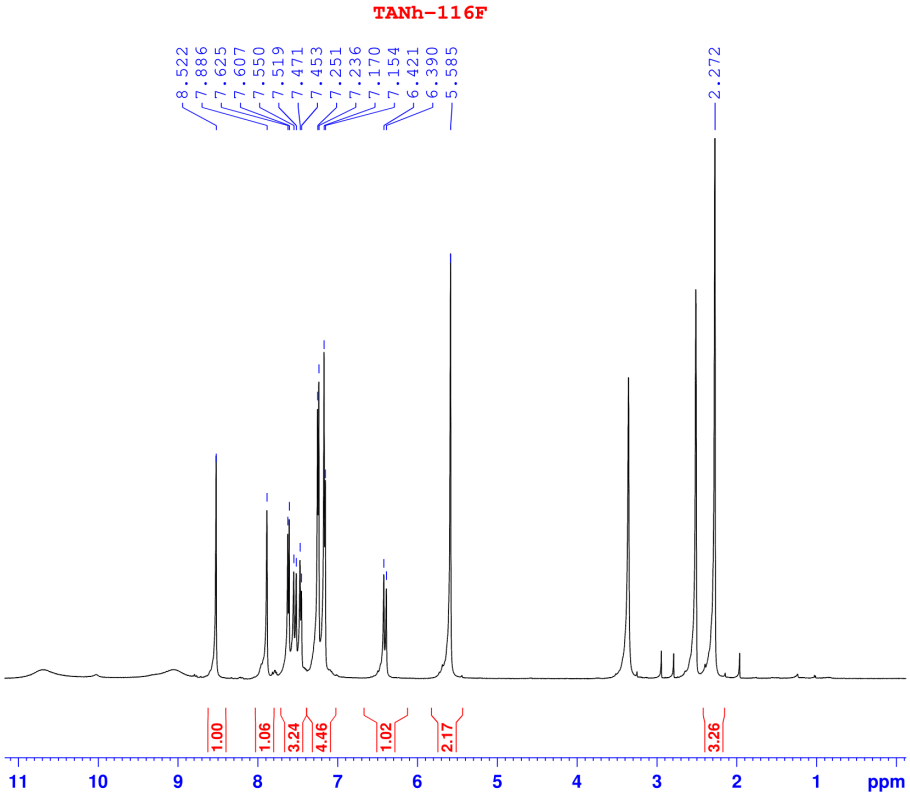
F2 - Acquisition Parameters
Date_               20201202
Time                   11.30
INSTRUM                spect
PROBHD    5 mm PABBO BB/
PULPROG              zgpg30
TD                     65536
SOLVENT                 DMSO
NS                        3072
DS                           4
SWH                31250.000 Hz
FIDRES             0.476837 Hz
AQ                 1.0485760 sec
RG                    191.38
DW                    16.000 usec
DE                     6.50 usec
TE                    301.6 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1              125.7703637 MHz
NUC1                       13C
P1                       9.50 usec
PLW1              90.00000000 W

======== CHANNEL f2 ========
SFO2              500.1320005 MHz
NUC2                        1H
CPDPRG[2                waltz16
PCPD2                   80.00 usec
PLW2              24.00000000 W
PLW12              0.36015001 W
PLW13              0.23050000 W

F2 - Processing parameters
SI                         65536
SF                125.7577885 MHz
WDW                          EM
SSB          0
LB                       1.00 Hz
GB           0
PC                       1.40
```

**$^{1}$H NMR of compound 7f**



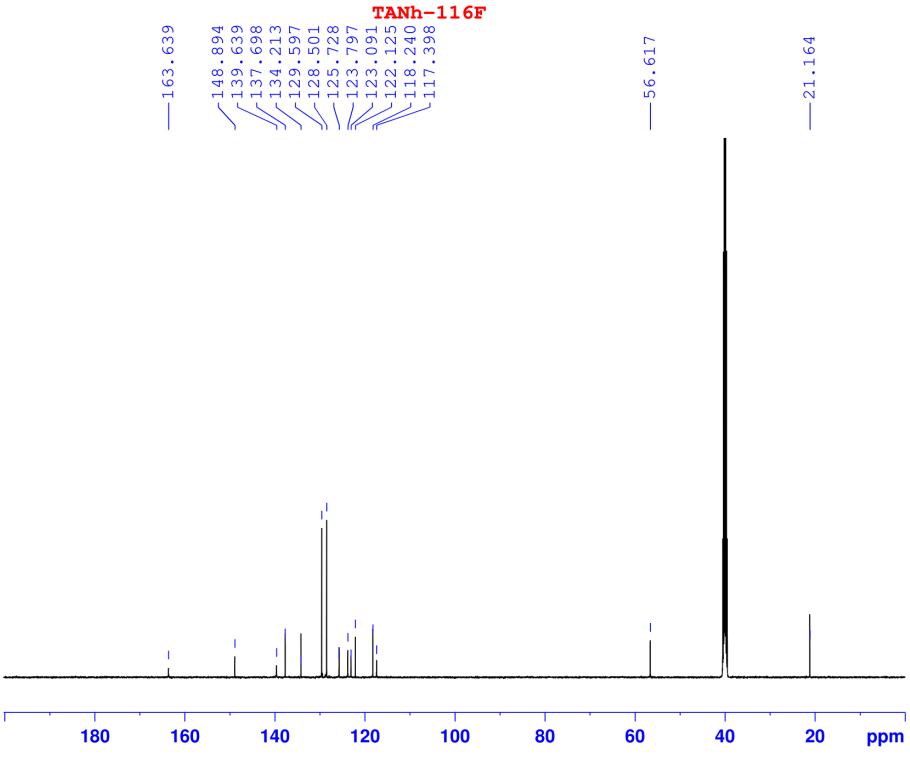

```
Current Data Parameters
NAME                 TANh-116F
EXPNO                      100
PROCNO                       1

F2 - Acquisition Parameters
Date_               20201230
Time                   16.43
INSTRUM                spect
PROBHD    5 mm PABBO BB/
PULPROG                 zg30
TD                     65536
SOLVENT                 DMSO
NS                        16
DS                         2
SWH                10000.000 Hz
FIDRES             0.152588 Hz
AQ                 3.2767999 sec
RG                    191.38
DW                    50.000 usec
DE                     6.50 usec
TE                    297.7 K
D1                 1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1              500.1330885 MHz
NUC1                        1H
P1                       9.80 usec
PLW1              24.00000000 W

F2 - Processing parameters
SI                         65536
SF                500.1300000 MHz
WDW                           EM
SSB          0
LB                       0.30 Hz
GB           0
PC                       1.00
```

**$^{13}$C NMR of compound 7f**




```
Current Data Parameters
NAME                 TANh-116F
EXPNO                      101
PROCNO                       1

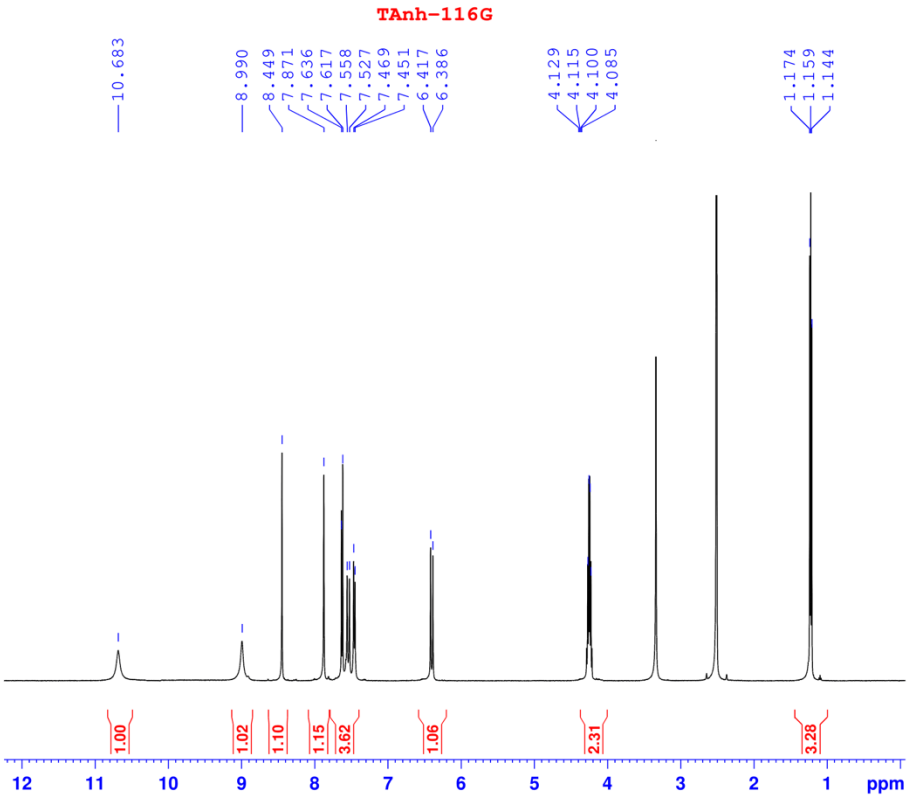
F2 - Acquisition Parameters
Date_               20201231
Time                    7.54
INSTRUM                spect
PROBHD    5 mm PABBO BB/
PULPROG               zgpg30
TD                     65536
SOLVENT                 DMSO
NS                      2048
DS                         4
SWH                31250.000 Hz
FIDRES             0.476837 Hz
AQ                 1.0485760 sec
RG                    191.38
DW                    16.000 usec
DE                     6.50 usec
TE                    298.5 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1              125.7703637 MHz
NUC1                       13C
P1                       9.50 usec
PLW1              90.00000000 W

======== CHANNEL f2 ========
SFO2              500.1320005 MHz
NUC2                        1H
CPDPRG[2               waltz16
PCPD2                   80.00 usec
PLW2              24.00000000 W
PLW12              0.36015001 W
PLW13              0.23050000 W

F2 - Processing parameters
SI                         65536
SF                125.7577885 MHz
WDW                           EM
SSB          0
LB                       1.00 Hz
GB           0
PC                       1.40
```

**$^{1}$H NMR of compound 7g**



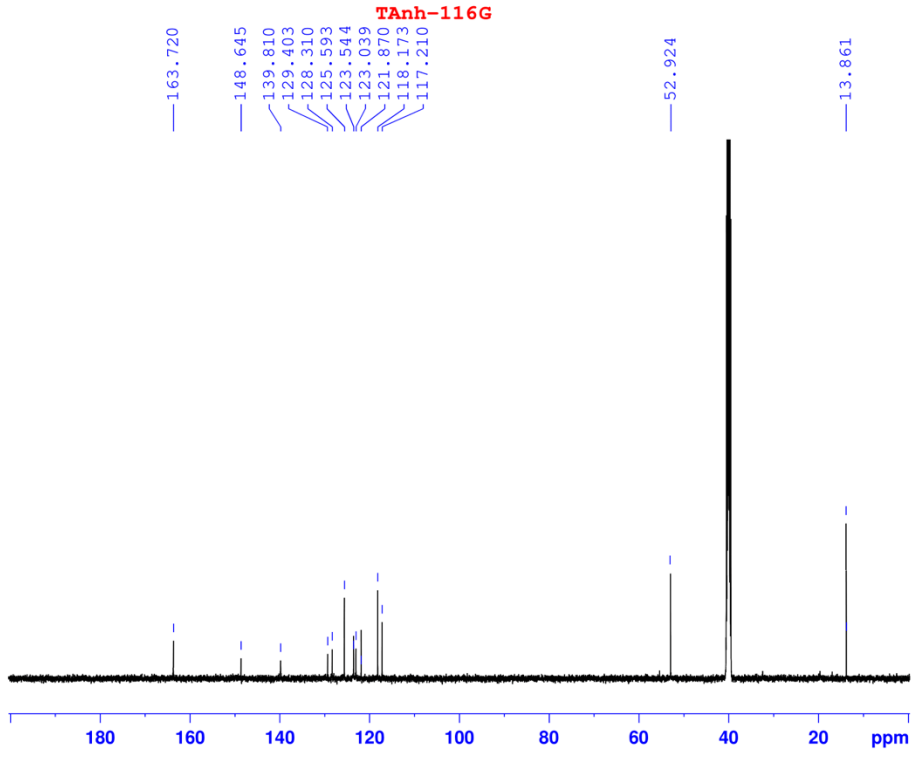

```
Current Data Parameters
NAME                 TAnh-116G
EXPNO                       20
PROCNO                       1

F2 - Acquisition Parameters
Date_               20201112
Time                   10.02
INSTRUM                spect
PROBHD     5 mm PABBO BB/
PULPROG                 zg30
TD                     65536
SOLVENT                 DMSO
NS                        16
DS                         2
SWH                10000.000 Hz
FIDRES             0.152588 Hz
AQ                 3.2767999 sec
RG                    191.38
DW                    50.000 usec
DE                     6.50 usec
TE                    300.7 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
SFO1              500.1330885 MHz
NUC1                      1H
P1                     9.80 usec
PLW1              24.00000000 W

F2 - Processing parameters
SI                     65536
SF                500.1300000 MHz
WDW                       EM
SSB          0
LB                     0.30 Hz
GB           0
PC                     1.00
```

**$^{13}$C NMR of compound 7g**




```
Current Data Parameters
NAME                 TAnh-116G
EXPNO                       10
PROCNO                       1

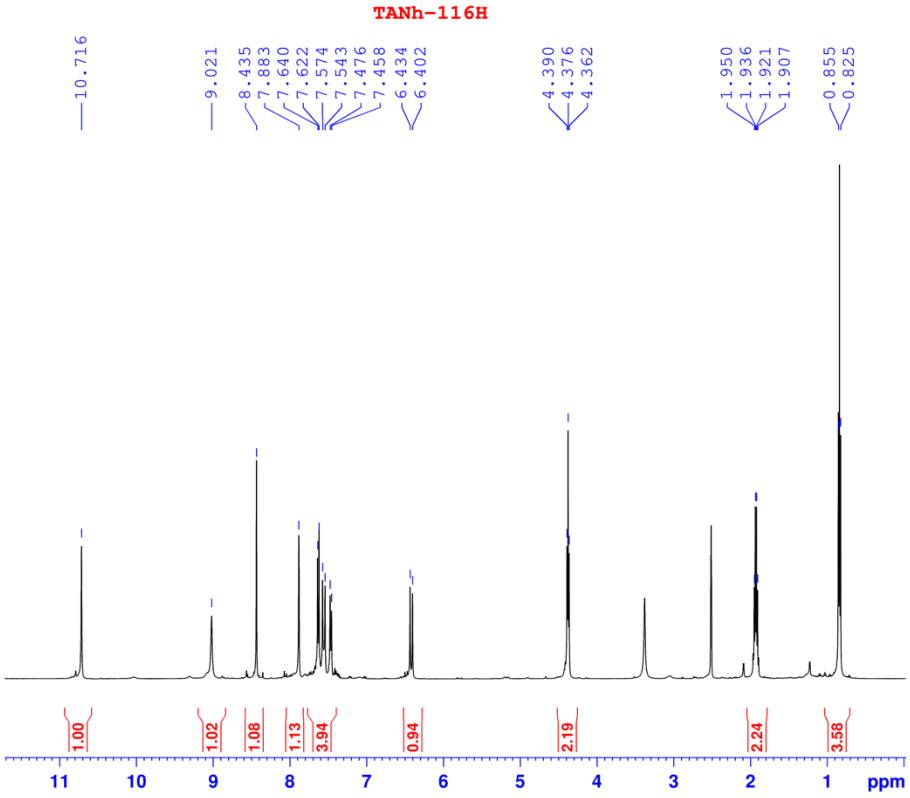
F2 - Acquisition Parameters
Date_               20201113
Time                   10.47
INSTRUM                spect
PROBHD     5 mm PABBO BB/
PULPROG              zgpg30
TD                     65536
SOLVENT                 DMSO
NS                      1626
DS                         4
SWH                31250.000 Hz
FIDRES             0.476837 Hz
AQ                 1.0485760 sec
RG                    191.38
DW                    16.000 usec
DE                     6.50 usec
TE                    301.5 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                        1

======== CHANNEL f1 ========
SFO1              125.7703637 MHz
NUC1                      13C
P1                     9.50 usec
PLW1              90.00000000 W

======== CHANNEL f2 ========
SFO2              500.1320005 MHz
NUC2                      1H
CPDPRG[2               waltz16
PCPD2                  80.00 usec
PLW2              24.00000000 W
PLW12              0.36015001 W
PLW13              0.23050000 W

F2 - Processing parameters
SI                     65536
SF                125.7577885 MHz
WDW                       EM
SSB          0
LB                     1.00 Hz
GB           0
PC                     1.40
```

**$^{1}$H NMR of compound 7h**



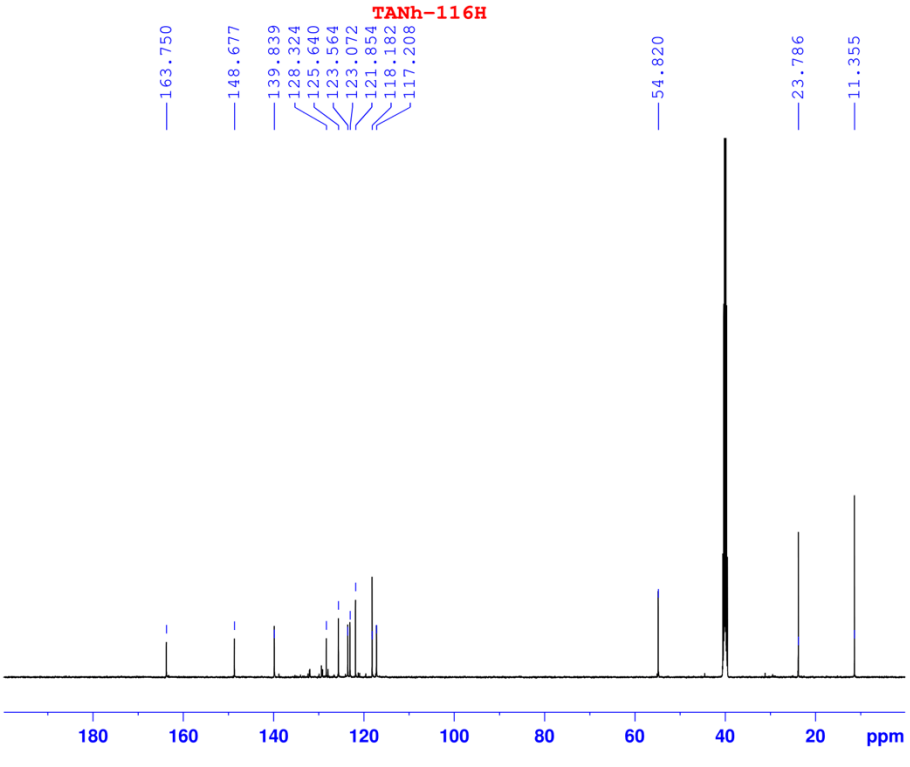

```
Current Data Parameters
NAME                  TANh-116H
EXPNO                        90
PROCNO                        1

F2 - Acquisition Parameters
Date_                 20201230
Time                      16.32
INSTRUM                   spect
PROBHD     5 mm PABBO BB/
PULPROG                   zg30
TD                       65536
SOLVENT                   DMSO
NS                           16
DS                            2
SWH                   10000.000 Hz
FIDRES                0.152588 Hz
AQ                    3.2767999 sec
RG                       123.67
DW                       50.000 usec
DE                         6.50 usec
TE                        297.8 K
D1                    1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
SFO1                500.1330885 MHz
NUC1                        1H
P1                         9.80 usec
PLW1                24.00000000 W

F2 - Processing parameters
SI                       65536
SF                  500.1300000 MHz
WDW                         EM
SSB                  0
LB                         0.30 Hz
GB                   0
PC                         1.00
```

**$^{13}$C NMR of compound 7h**




```
Current Data Parameters
NAME                  TANh-116H
EXPNO                        91
PROCNO                        1

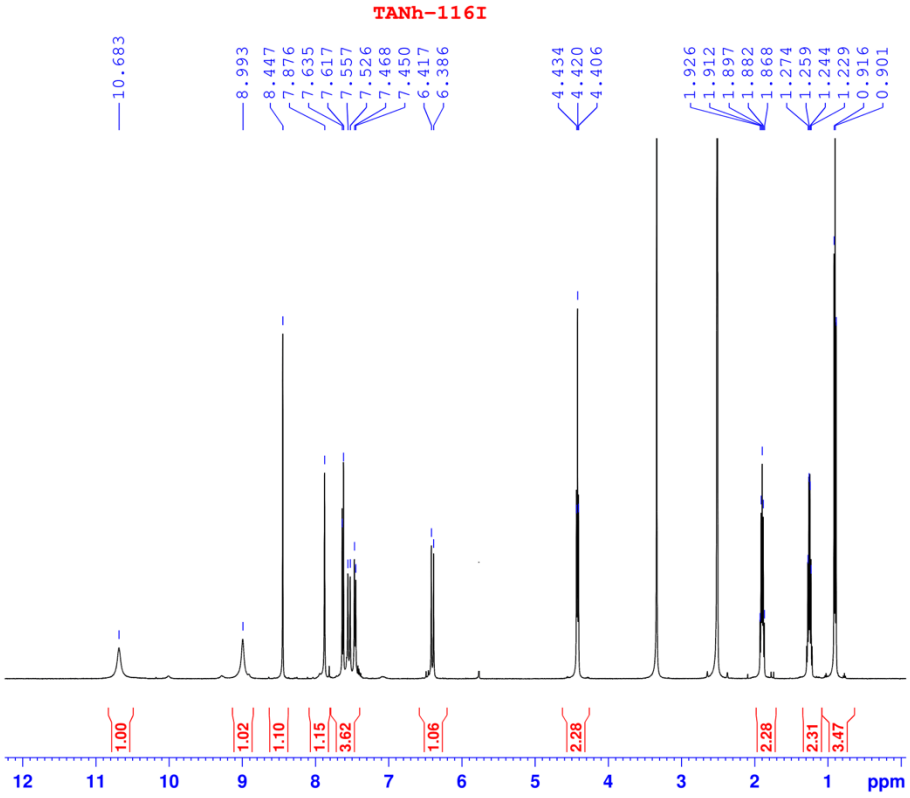
F2 - Acquisition Parameters
Date_                 20201231
Time                       6.05
INSTRUM                   spect
PROBHD     5 mm PABBO BB/
PULPROG                 zgpg30
TD                       65536
SOLVENT                   DMSO
NS                         2048
DS                            4
SWH                   31250.000 Hz
FIDRES                0.476837 Hz
AQ                    1.0485760 sec
RG                       191.38
DW                       16.000 usec
DE                         6.50 usec
TE                        298.5 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                           1

======== CHANNEL f1 ========
SFO1                125.7703637 MHz
NUC1                        13C
P1                         9.50 usec
PLW1                90.00000000 W

======== CHANNEL f2 ========
SFO2                500.1320005 MHz
NUC2                        1H
CPDPRG[2                waltz16
PCPD2                     80.00 usec
PLW2                24.00000000 W
PLW12                0.36015001 W
PLW13                0.23050000 W

F2 - Processing parameters
SI                       65536
SF                  125.7577885 MHz
WDW                         EM
SSB                  0
LB                         1.00 Hz
GB                   0
PC                         1.40
```

**$^{1}$H NMR of compound 7i**



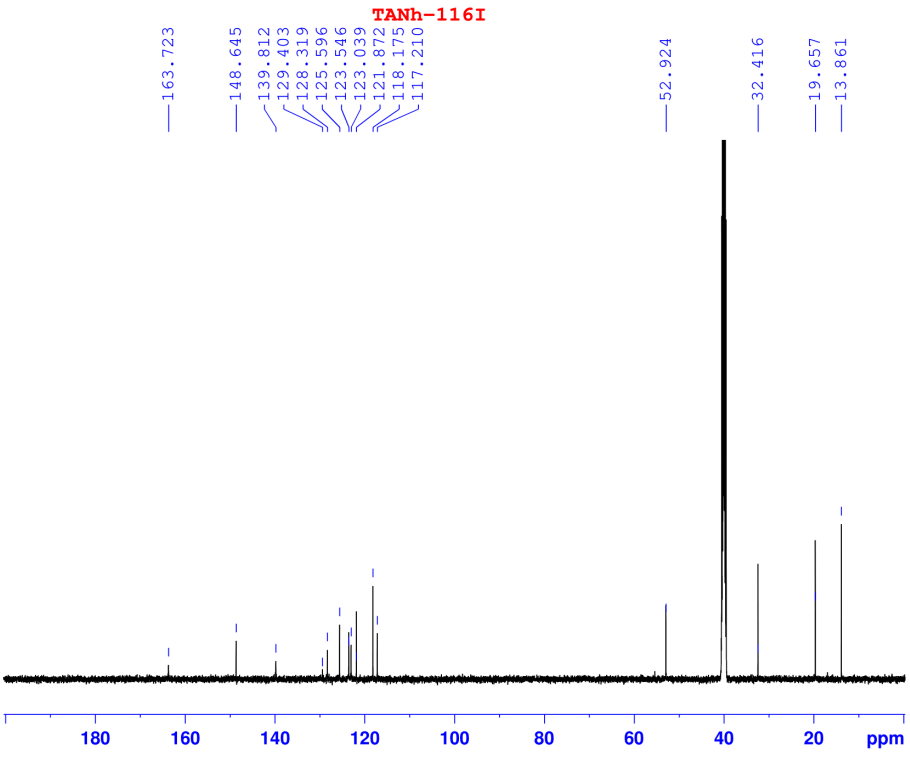

```
Current Data Parameters
NAME                  TANh-116I
EXPNO                        50
PROCNO                        1

F2 - Acquisition Parameters
Date_                 20201230
Time                      16.08
INSTRUM                   spect
PROBHD    5 mm PABBO BB/
PULPROG                   zg30
TD                       65536
SOLVENT                   DMSO
NS                           16
DS                            2
SWH                 10000.000 Hz
FIDRES                0.152588 Hz
AQ                    3.2767999 sec
RG                       191.38
DW                       50.000 usec
DE                         6.50 usec
TE                        297.8 K
D1                  1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
SFO1                500.1330885 MHz
NUC1                        1H
P1                         9.80 usec
PLW1                24.00000000 W

F2 - Processing parameters
SI                       65536
SF                  500.1300000 MHz
WDW                         EM
SSB                  0
LB                         0.30 Hz
GB                   0
PC                         1.00
```

**$^{13}$C NMR of compound 7i**




```
Current Data Parameters
NAME                  TANh-116I
EXPNO                        51
PROCNO                        1

F2 - Acquisition Parameters
Date_                 20201231
Time                      0.38
INSTRUM                   spect
PROBHD    5 mm PABBO BB/
PULPROG                 zgpg30
TD                       65536
SOLVENT                   DMSO
NS                         2048
DS                            4
SWH                 31250.000 Hz
FIDRES                0.476837 Hz
AQ                    1.0485760 sec
RG                       191.38
DW                       16.000 usec
DE                         6.50 usec
TE                        298.6 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                           1

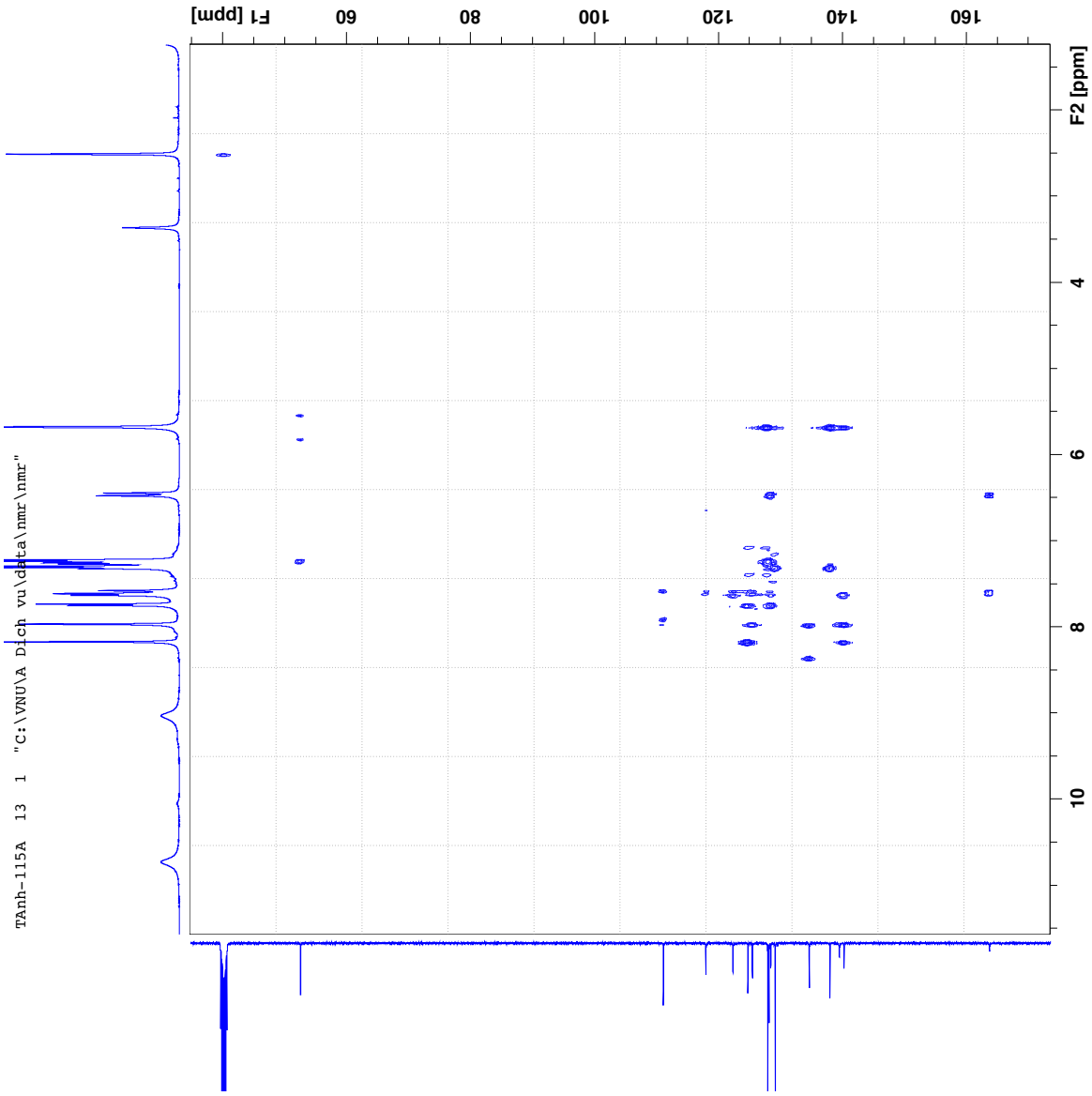
======== CHANNEL f1 ========
SFO1                125.7703637 MHz
NUC1                        13C
P1                         9.50 usec
PLW1                90.00000000 W

======== CHANNEL f2 ========
SFO2                500.1320005 MHz
NUC2                        1H
CPDPRG[2                waltz16
PCPD2                     80.00 usec
PLW2                24.00000000 W
PLW12                0.36015001 W
PLW13                0.23050000 W

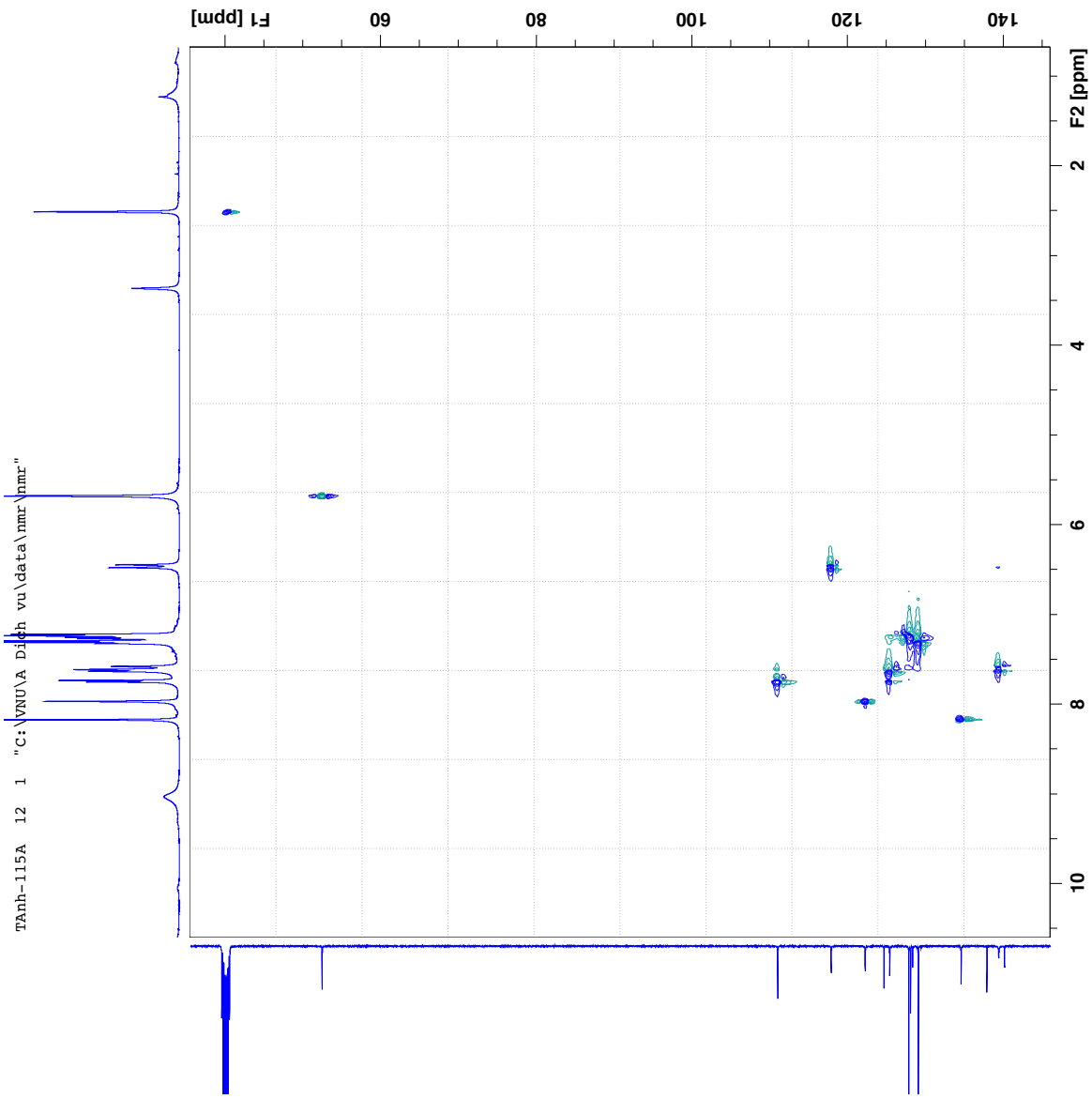
F2 - Processing parameters
SI                       65536
SF                  125.7577885 MHz
WDW                         EM
SSB                  0
LB                         1.00 Hz
GB                   0
PC                         1.40
```

**4. 2D NMR for representative final compound.**

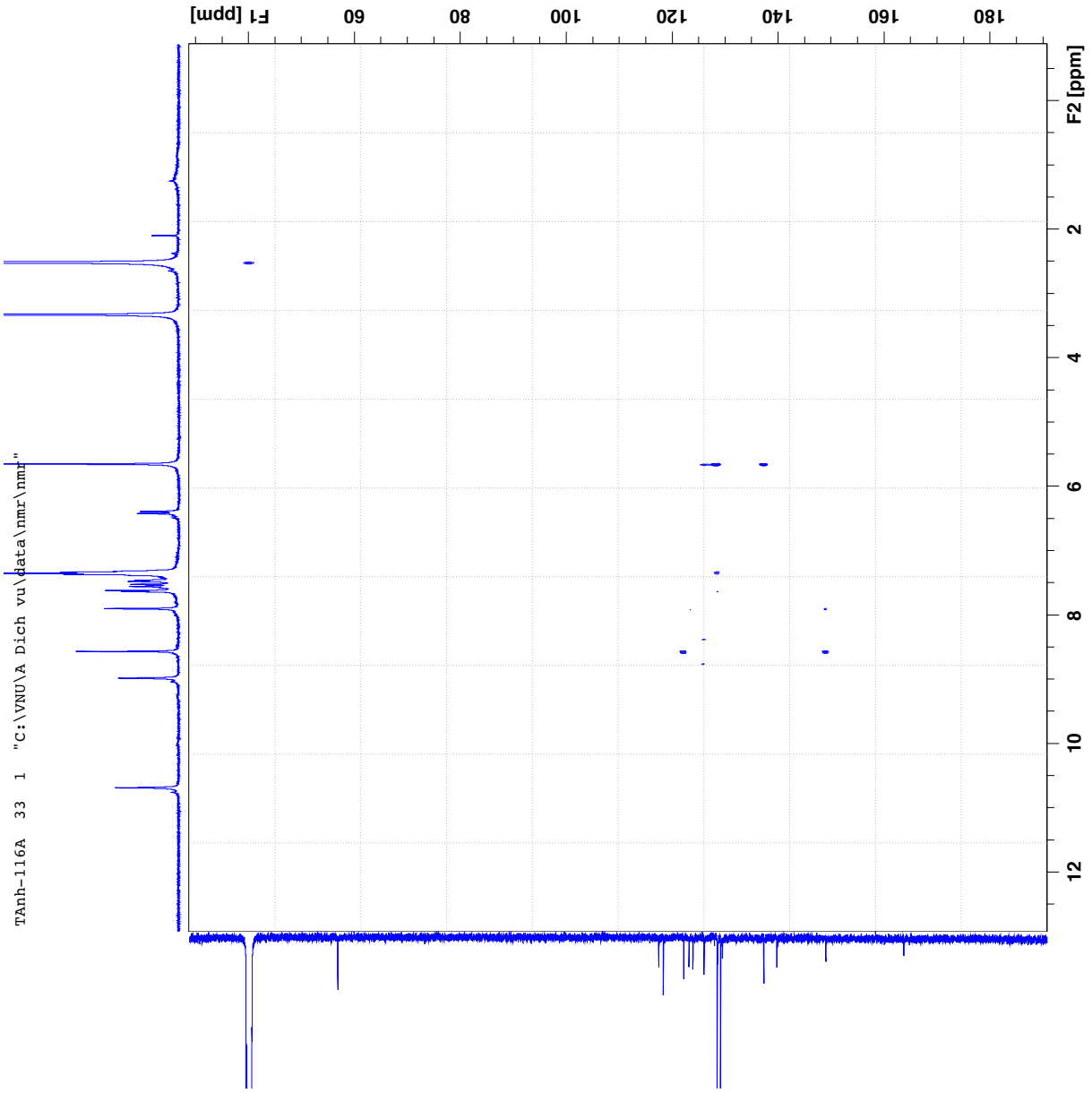
**HMBC of 5a**



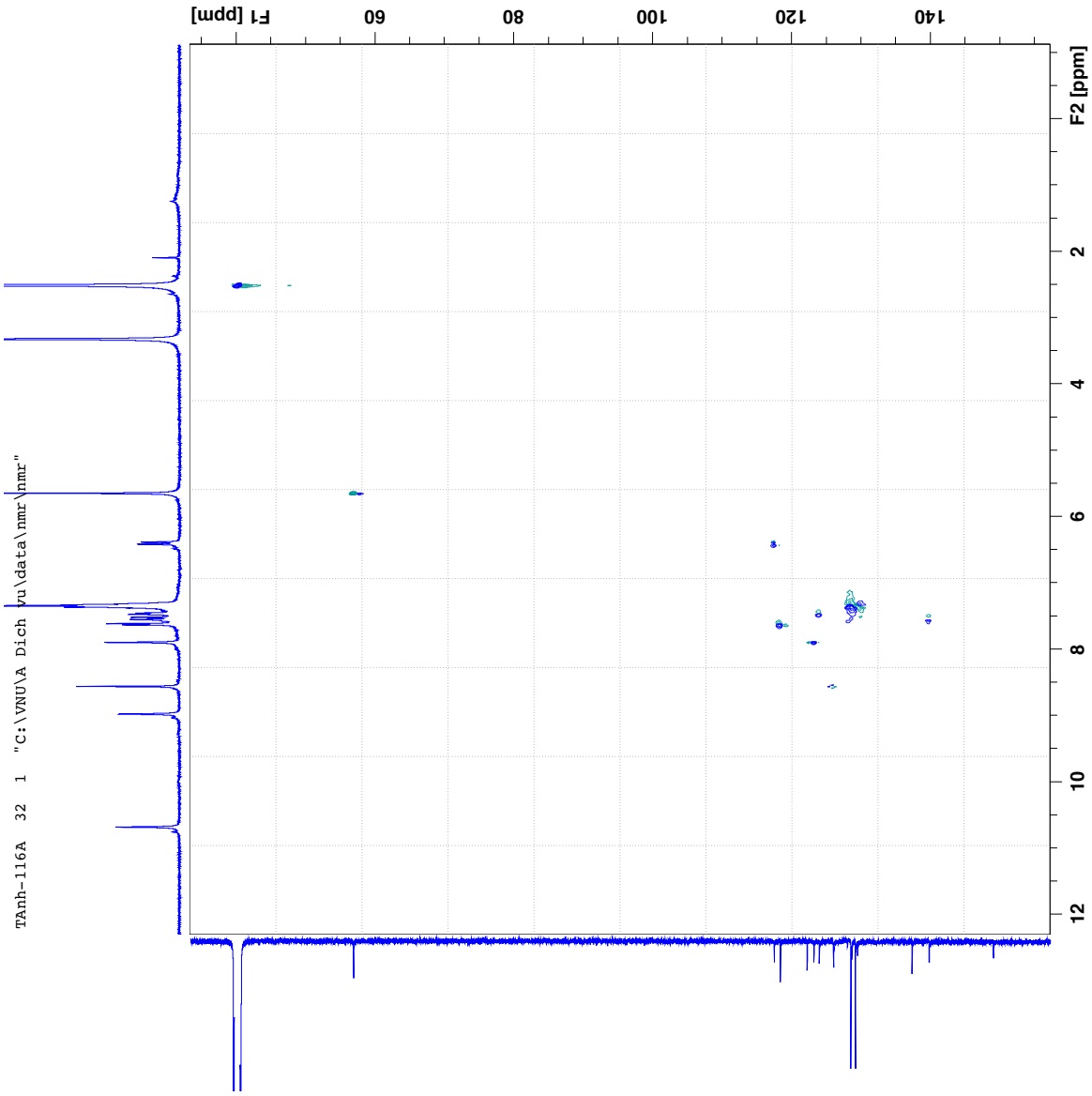
**HSQC of 5a**


F1 [ppm]
60
80
100
120
140
F2 [ppm]
2
4
6
8
10
TAnh-115A 12 1 "C:\VNU\A Dich vu\data\nmr\nmr"

**HMBC of 7a**


F1 [ppm]
60
80
100
120
140
160
180
F2 [ppm]
2
4
6
8
10
12
TAnh-116A 33 1 "C:\VNU\A Dich vu\data\nmr\nmr"

**HSQC of 7a**


F1 [ppm]
60
80
100
120
140
F2 [ppm]
2
4
6
8
10
12
TAnh-116A 32 1 "C:\VNU\A Dich vu\data\nmr\nmr"