

## Synthesis, Molecular Docking Analysis and *in Vitro* Evaluation of New Heterocyclic Hybrids of 4-Aza-Podophyllotoxin as Potent Cytotoxic Agents

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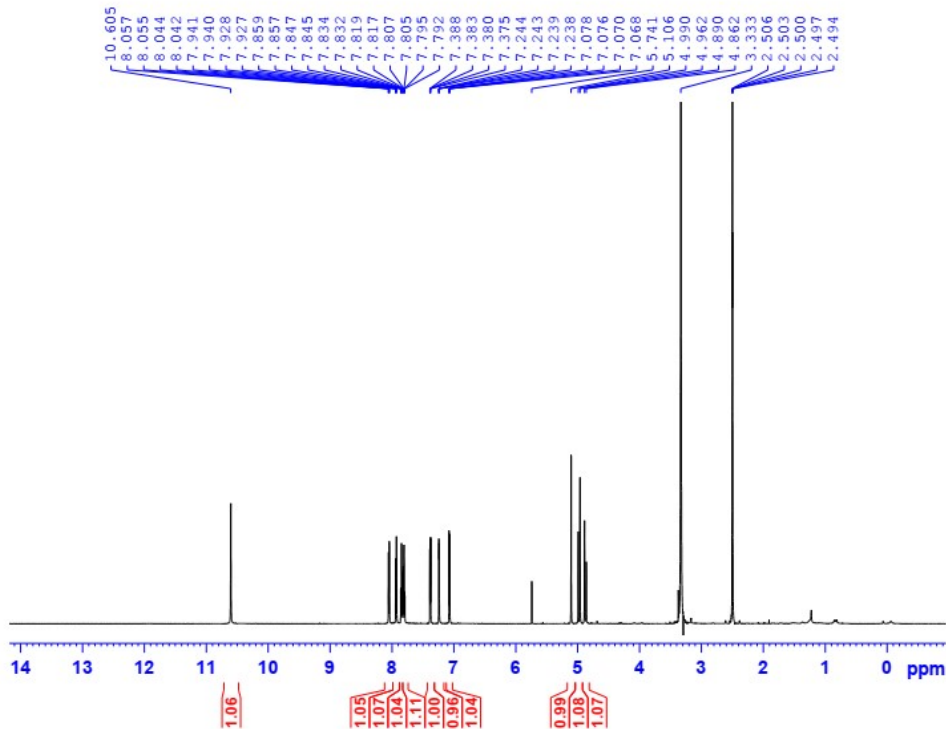
### LIST OF CONTENT

<b>SPECTRUM SECTION</b> .....	2
11-(Thiophen-3-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline-1,5,10(3 <i>H</i> )-trione ( <b>13a</b> ) .....	2
11-(Furan-3-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline-1,5,10(3 <i>H</i> )-trione ( <b>13b</b> ) .....	5
11-(Furan-2-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline-1,5,10(3 <i>H</i> )-trione ( <b>13c</b> ) .....	7
11-(5-Bromofuran-2-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline-1,5,10(3 <i>H</i> )-trione ( <b>13d</b> ) ....	8
11-(Benzo[b]thiophen-3-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline-1,5,10(3 <i>H</i> )-trione ( <b>13e</b> ) .....	10
11-(Benzofuran-3-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline-1,5,10(3 <i>H</i> )-trione ( <b>13f</b> ).....	11
11-(Benzo[b]thiophen-2-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline-1,5,10(3 <i>H</i> )-trione ( <b>13g</b> ) .....	13
11-(2-Chlorothiazol-5-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline-1,5,10(3 <i>H</i> )-trione ( <b>13h</b> )	14
11-(1,5-Dimethyl-1 <i>H</i> -pyrazol-4-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline-1,5,10(3 <i>H</i> )- trione ( <b>13i</b> ).....	16
11-(1 <i>H</i> -pyrazol-5-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline-1,5,10(3 <i>H</i> )-trione ( <b>13j</b> ) .....	17
11-(2-Methoxypyridin-4-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline-1,5,10(3 <i>H</i> )-trione ( <b>13k</b> ) .....	19
11-(3-Fluoropyridin-2-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline-1,5,10(3 <i>H</i> )-trione ( <b>13l</b> )	20
11-(2-Methoxy-5-(trifluoromethyl)pyridin-3-yl)-4,11-dihydrobenzo[g]furo[3,4- <i>b</i> ]quinoline- 1,5,10(3 <i>H</i> )-trione ( <b>13m</b> ) .....	22
<b>Table 1.</b> Estimated of binding energy of docking complexes for 13a-m, podophyllotoxin and colchicine.* .....	24

# SPECTRUM SECTION

## 11-(Thiophen-3-yl)-4,11-dihydrobenzo[g]furo[3,4-b]quinoline-1,5,10(3H)-trione (13a)

HP245.39-DMSO-1H

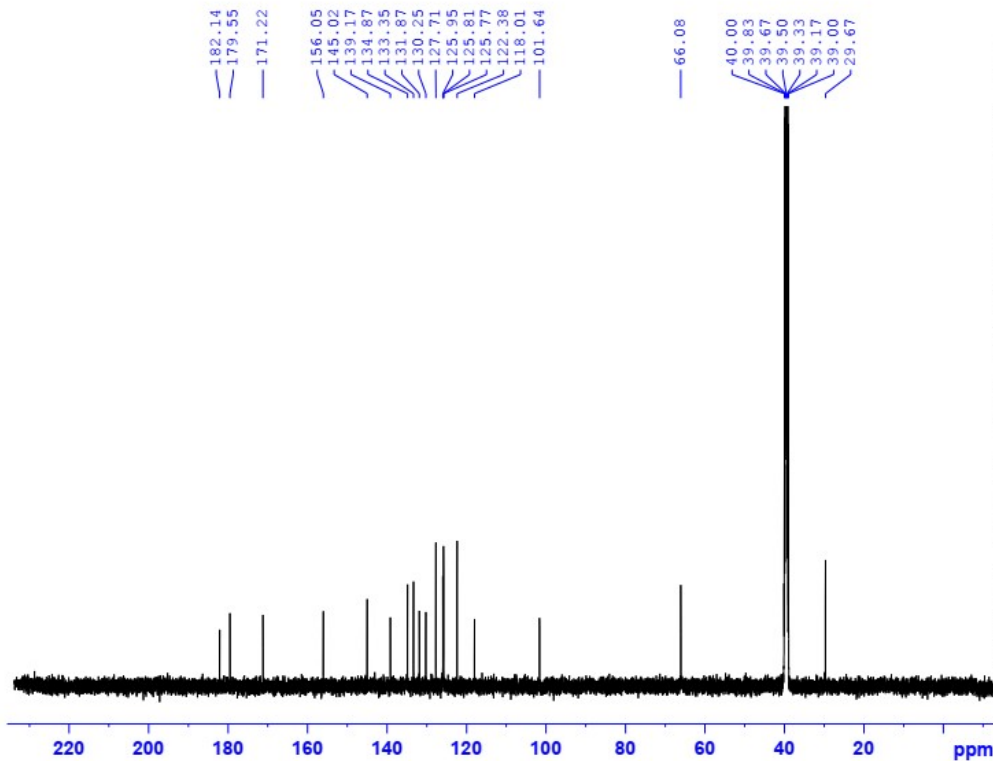


Current Data Parameters  
NAME HP245.39  
EXPNO 10  
PROCNO 1

F2 - Acquisition Parameters  
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Time 16.24 h  
INSTRUM AvanceNeo\_600MHz  
PROBHD E114607\_0862 ( )  
PULPROG zg30  
TD 65536  
SOLVENT DMSO  
NS 16  
DS 3  
SWH 11904.762 Hz  
FIDRES 0.368304 Hz  
AQ 2.7525120 sec  
RG 97.1264  
WDW 42.000 usec  
SSB 0.71 usec  
LB 203.2 Hz  
D1 1.00000000 sec  
TDO 1  
SFO1 600.4087078 MHz  
NUC1  
P0 3.50 usec  
P1 10.50 usec  
PLW1 27.08700066 W

F2 - Processing parameters  
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SF 600.4000042 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

HP245.39-DMSO-C13CPD



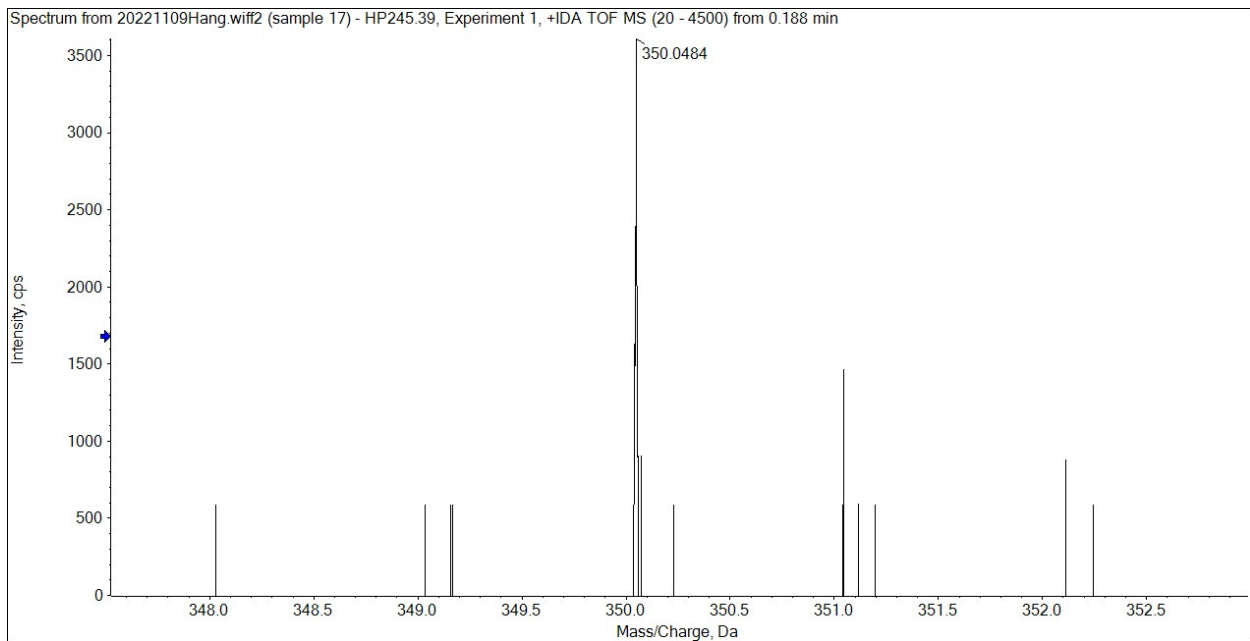
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NAME HP245.39  
EXPNO 2  
PROCNO 1

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Date\_ 20220808  
Time 13.55  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zgpg30  
TD 65536  
SOLVENT DMSO  
NS 1024  
DS 4  
SWH 21250.000 Hz  
FIDRES 0.476827 Hz  
AQ 1.0485760 sec  
RG 198.57  
WDW 16.000 usec  
SSB 6.50 usec  
LB 203.9 Hz  
D1 2.00000000 sec  
D11 0.02000000 sec  
TDO 1

===== CHANNEL #1 =====  
SFO1 125.7990230 MHz  
NUC1 13C  
P1 10.00 usec  
PLW1 88.00000000 W

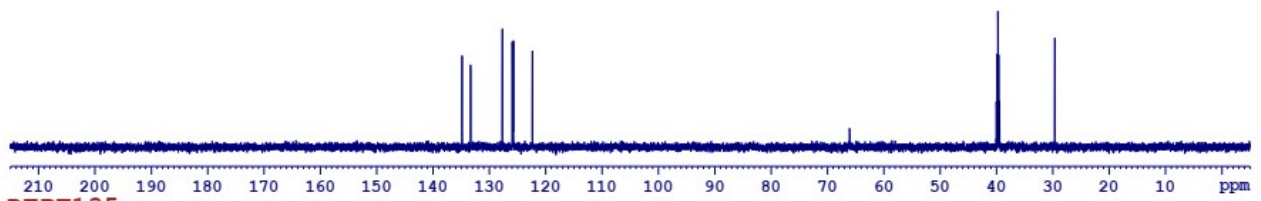
===== CHANNEL #2 =====  
SFO2 500.2410010 MHz  
NUC2 1H  
CPDPRG[2] waltz16  
PCPD2 80.00 usec  
PLW2 22.00000000 W  
PLW12 0.38764000 W  
PLW13 0.17989001 W

F2 - Processing parameters  
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SF 125.7852608 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40

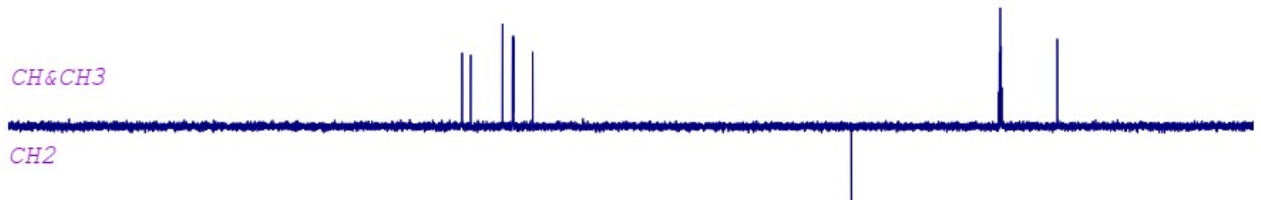


**HP245.39-DMSO-C13CPD&DEPT**

**DEPT90**



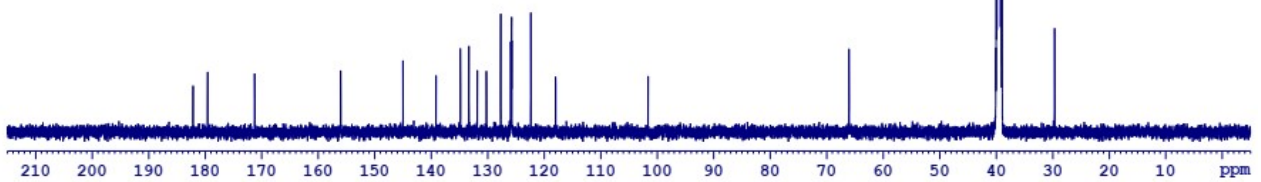
**DEPT135**



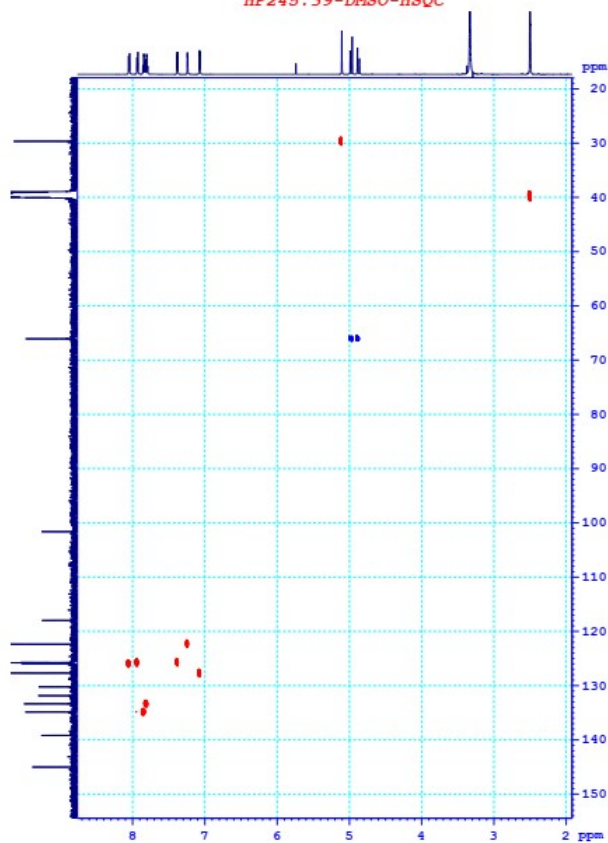
*CH&CH3*

*CH2*

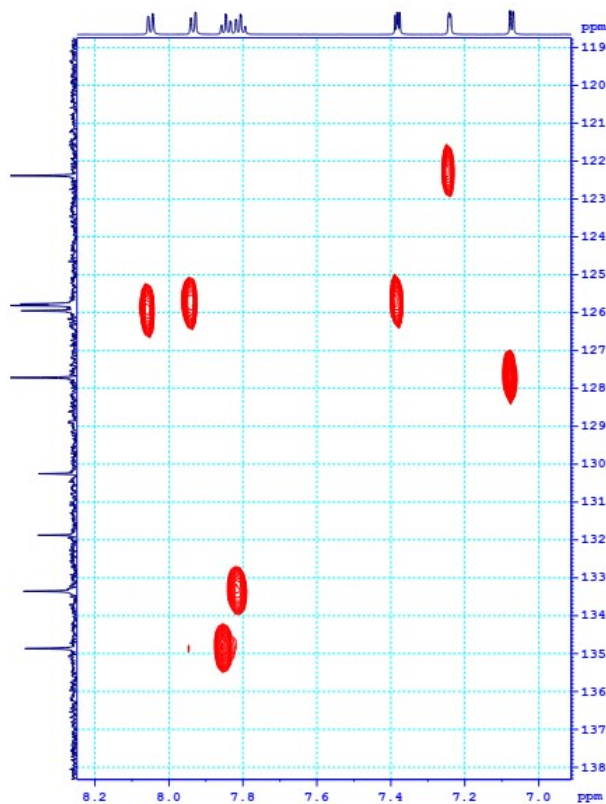
**C13CPD**



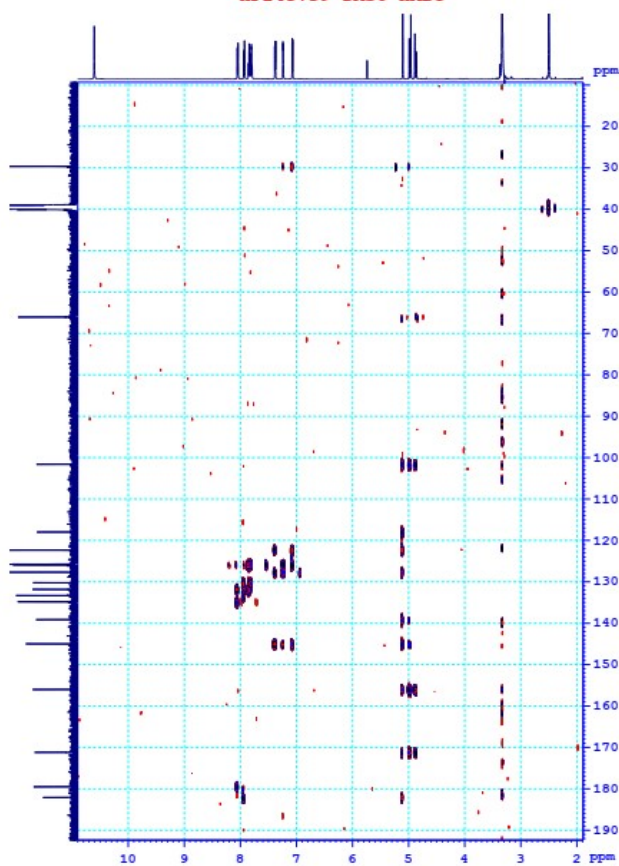
HP245.39-DMSO-HSQC



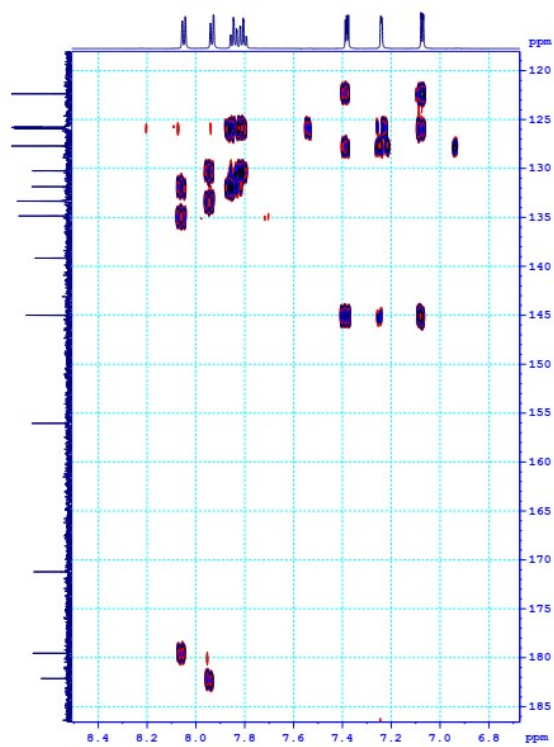
HP245.39-DMSO-HSQC



HP245.39-DMSO-HMBC



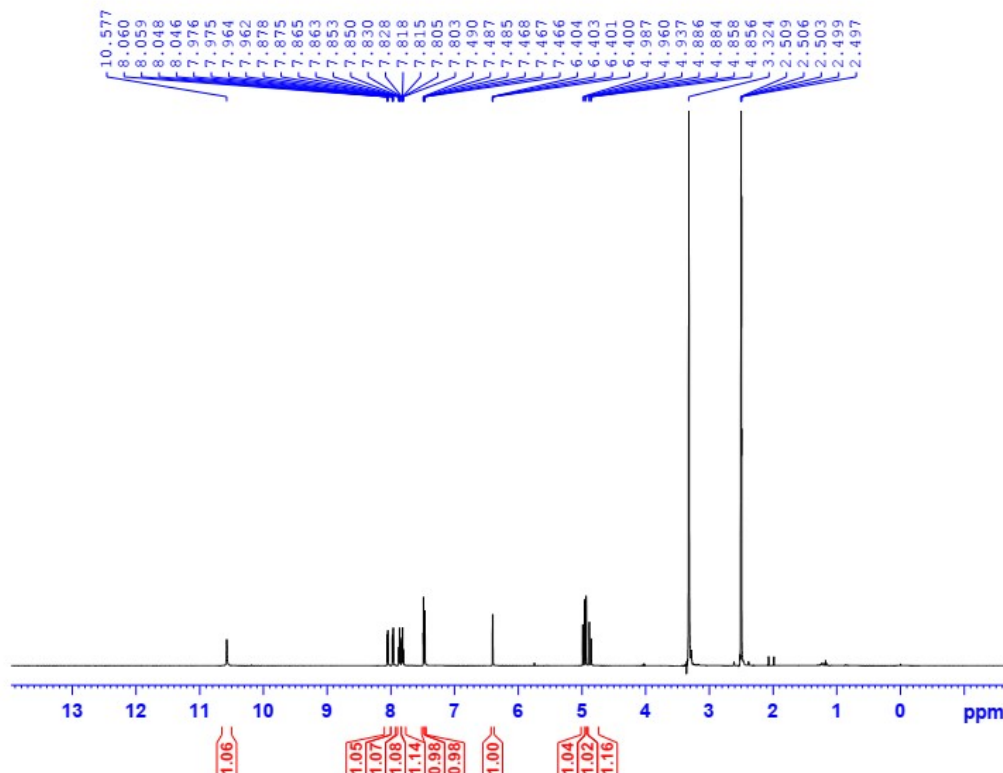
HP245.39-DMSO-HMBC





# 11-(Furan-3-yl)-4,11-dihydrobenzo[g]furo[3,4-b]quinoline-1,5,10(3H)-trione (13b)

TK245.89-DMSO-1H



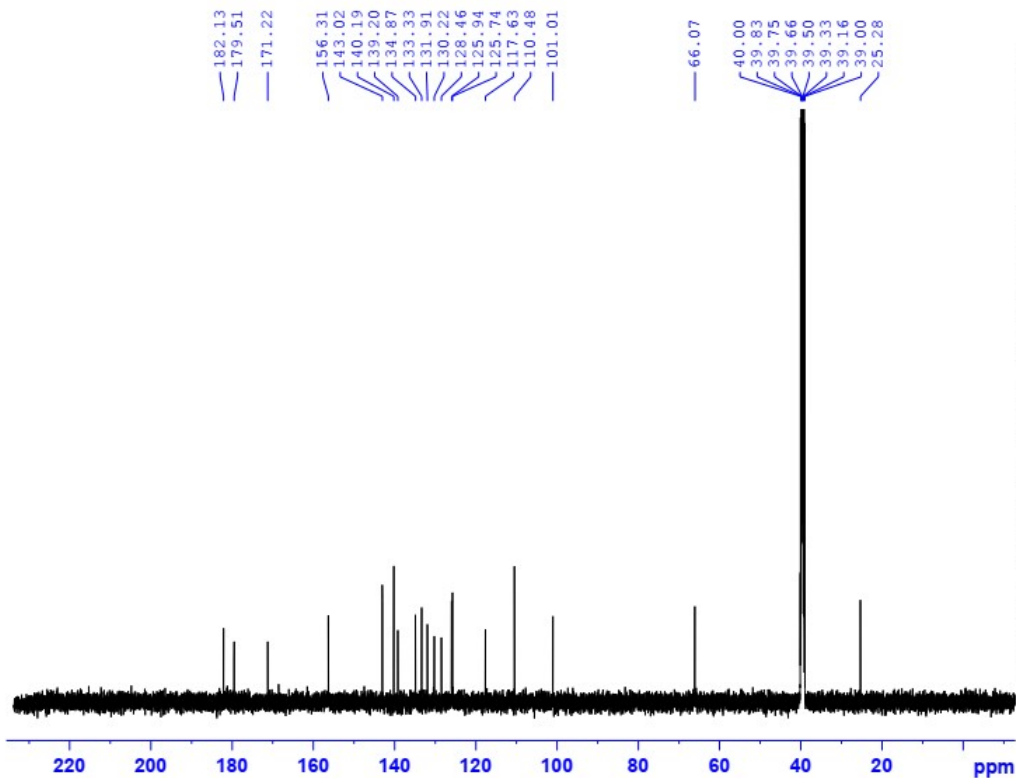
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EXPNO    10
PROCNO   1

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Date_    20221012
Time     17.44 h
INSTRUM  AvanceNeo_600MHz
PROBHD   Z114607_0862 (
PULPROG  zg30
TD        65536
SOLVENT  DMSO
NS        16
DS        2
SINH      11904.762 Hz
FIDRES    0.362304 Hz
AQ        2.7525120 sec
RG        101
DN        42.000 usec
DE        8.71 usec
TE        303.2 K
D1        1.00000000 sec
TDO       1
SF01      600.4037075 MHz
NUC1      1H
P1        8.50 usec
PL1       10.50 usec
PLW1      27.03700066 W

F2 - Processing parameters
SI        65536
SF        600.4000038 MHz
WDW       EM
SSB       0
LB        0.20 Hz
GB        0
PC        1.00
    
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TK245.89-DMSO-C13CPD



```

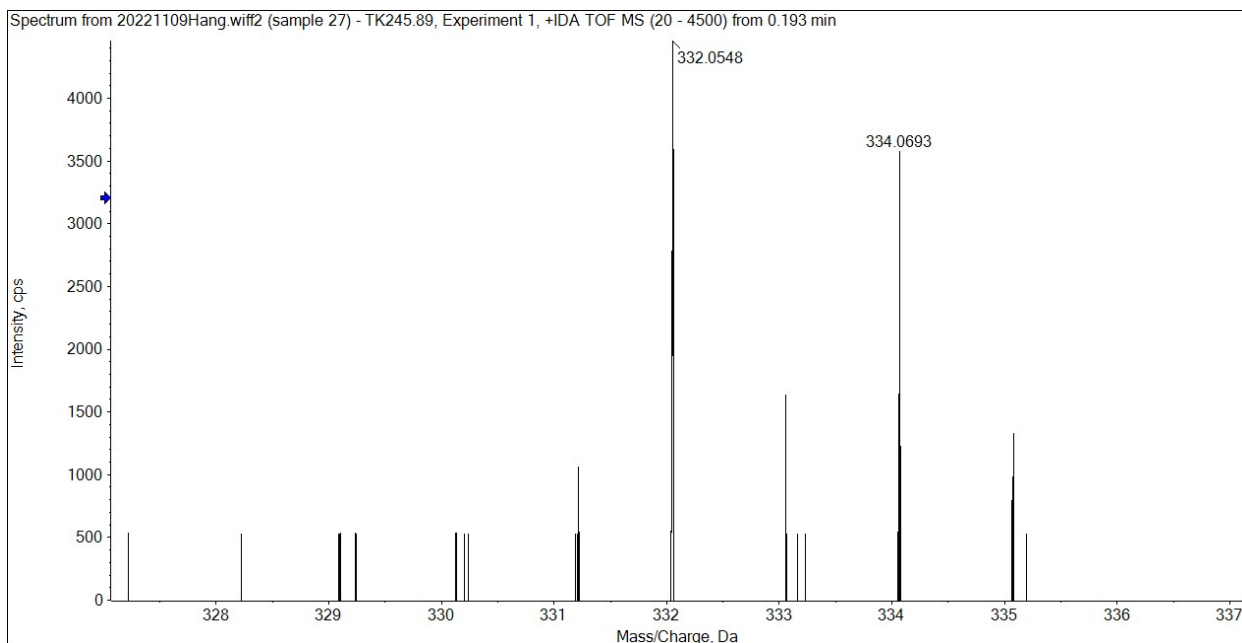
Current Data Parameters
NAME      6TK245.89
EXPNO    3
PROCNO   1

F2 - Acquisition Parameters
Date_    20221014
Time     10.10
INSTRUM  spect
PROBHD   5 mm PABBO BB/
PULPROG  zgpg30
TD        65536
SOLVENT  DMSO
NS        812
DS        4
SINH      31250.000 Hz
FIDRES    0.476897 Hz
AQ        1.0485760 sec
RG        198.57
DN        16.000 usec
DE        6.50 usec
TE        303.0 K
D1        2.00000000 sec
D11      0.02000000 sec
TDO       1

===== CHANNEL f1 =====
SF01      125.7990230 MHz
NUC1      13C
P1        10.00 usec
PLW1      88.00000000 W

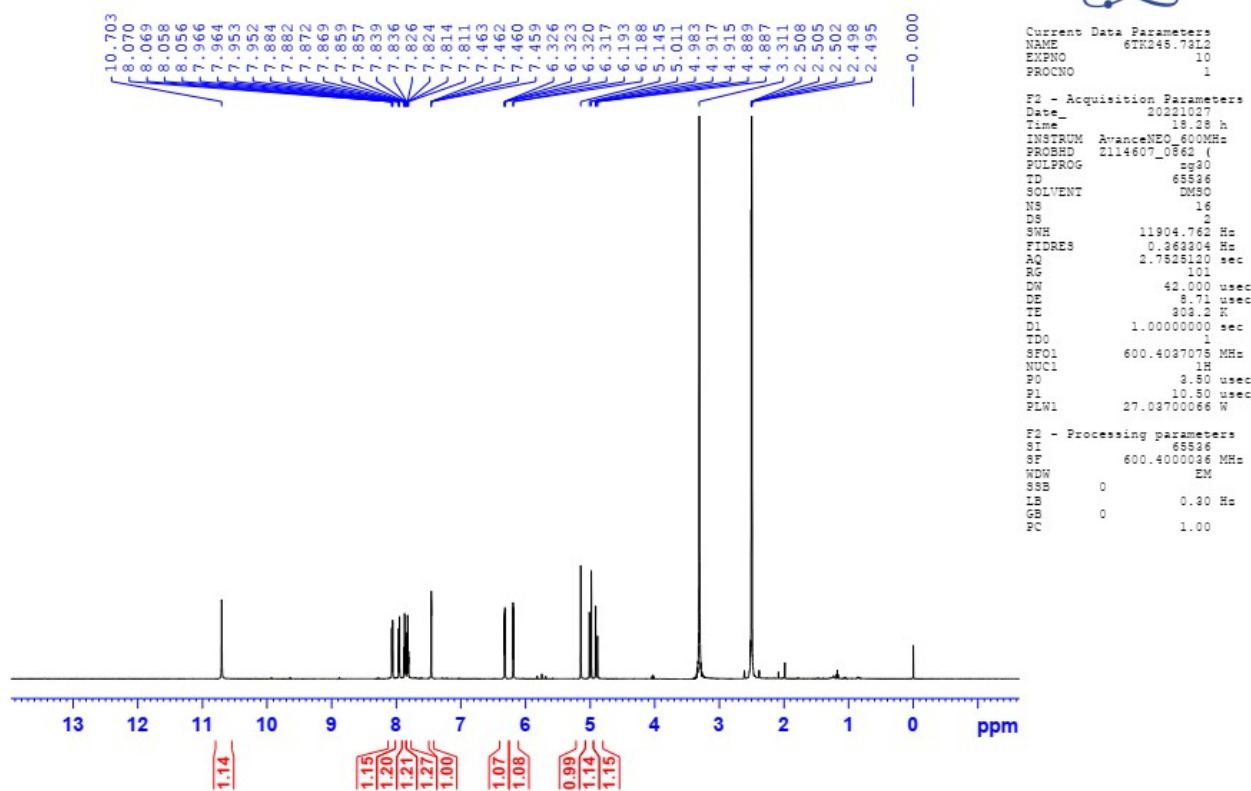
===== CHANNEL f2 =====
SF02      500.2410010 MHz
NUC2      1H
CPDPRG2  waltz16
PCPD2    80.00 usec
PLW2     22.00000000 W
PLW12    0.28764000 W
PLW13    0.17989001 W

F2 - Processing parameters
SI        32768
SF        125.7852614 MHz
WDW       EM
SSB       0
LB        1.00 Hz
GB        0
PC        1.40
    
```

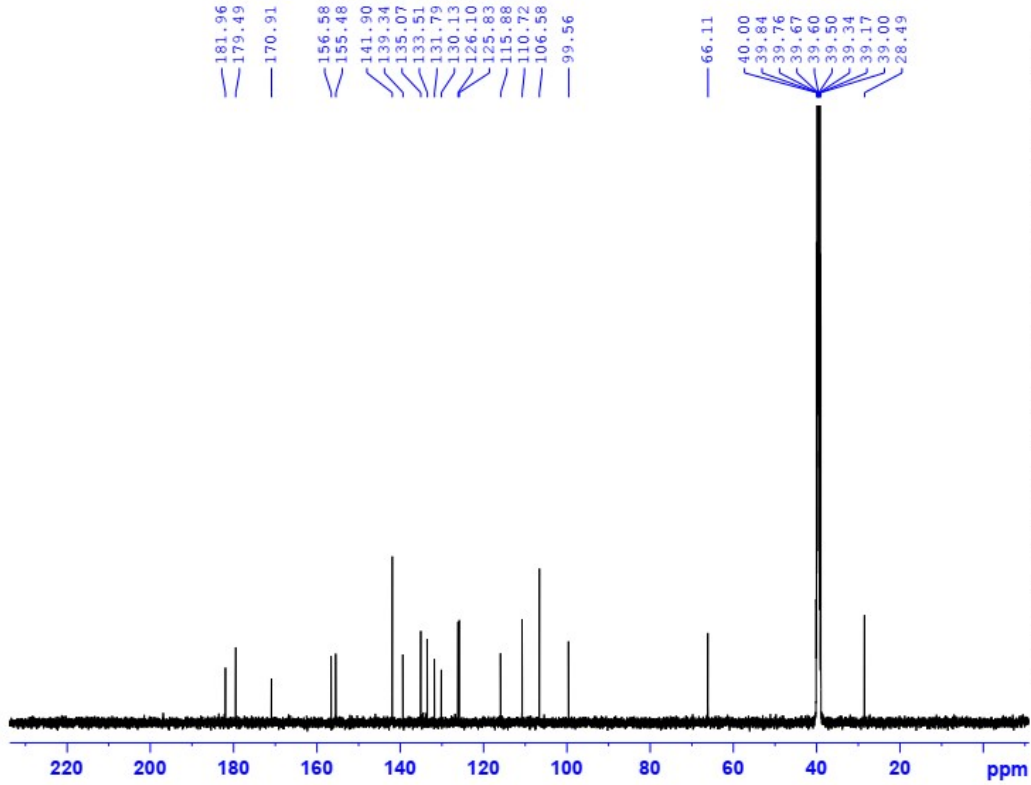


**11-(Furan-2-yl)-4,11-dihydrobenzo[g]furo[3,4-b]quinoline-1,5,10(3H)-trione (13c)**

**TK245.73L2-DMSO-1H**



TK245.73L2-DMSO-C13CPD



```

Current Data Parameters
NAME      6TK245.73L2
EXPNO    1
PROCNO   1

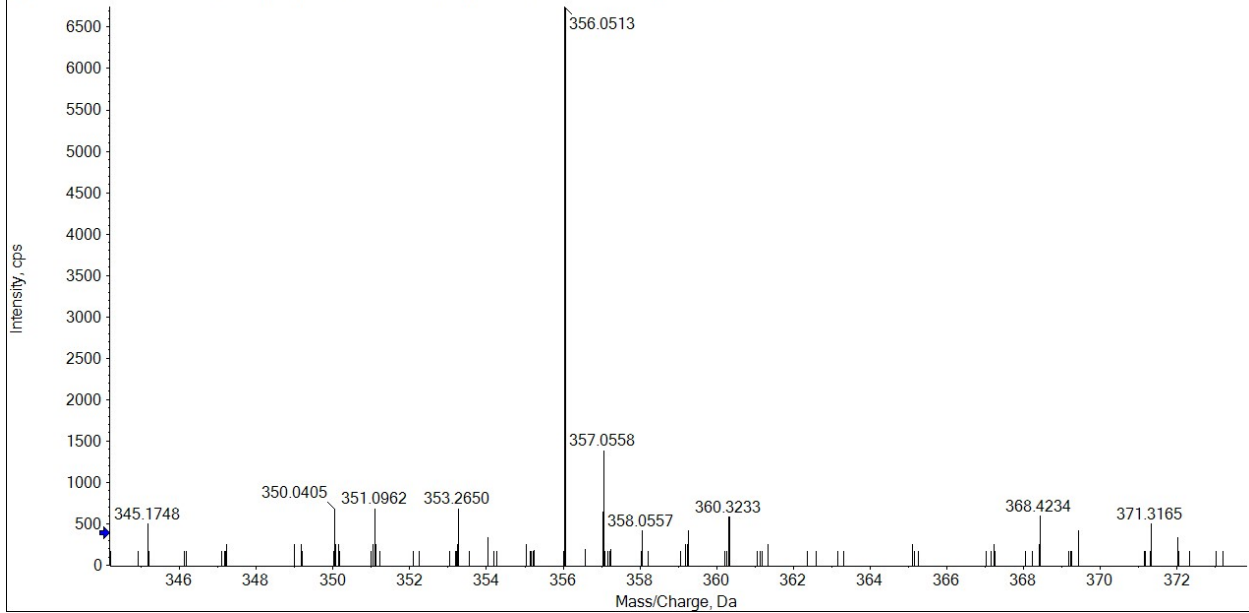
F2 - Acquisition Parameters
Date_    20221101
Time     7.40
INSTRUM  spect
PROBHD   5 mm PABBO BB/
PULPROG  zgpg30
TD       65526
SOLVENT  DMSO
NS       4
DS       4
SWH      31250.000 Hz
FIDRES   0.476837 Hz
AQ       1.0488760 sec
RG       198.57
DN       16.000 usec
DE       6.50 usec
TE       303.0 K
D1       2.00000000 sec
D11      0.02000000 sec
TDO      1

===== CHANNEL f1 =====
SF01    125.7990230 MHz
NUC1    13C
P1      10.00 usec
PLW1    88.00000000 W

===== CHANNEL f2 =====
SF02    800.2410010 MHz
NUC2    1H
CPDPRG2  waltz16
PCPD2   80.00 usec
PLM2    22.00000000 W
PLM12   0.35764000 W
PLM13   0.17889001 W

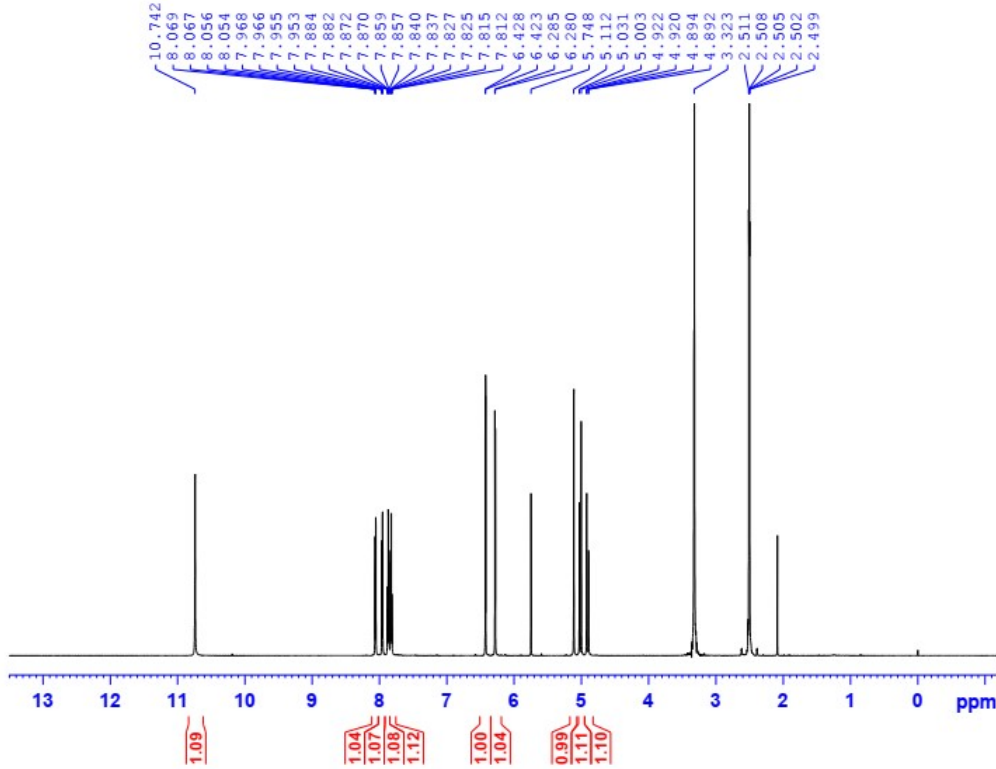
F2 - Processing parameters
SI      32768
SF      125.7852870 MHz
WDW     EM
SSB     0
LB      1.00 Hz
GB      0
PC      1.40
    
```

Spectrum from 20221109Hang.wiff2 (sample 21) - HP245.73, Expenment 1, +IDA TOF MS (20 - 4500) from 0.356 min



11-(5-Bromofuran-2-yl)-4,11-dihydrobenzo[g]furo[3,4-b]quinoline-1,5,10(3H)-trione  
(13d)

TK245.75L2-DMSO-1H

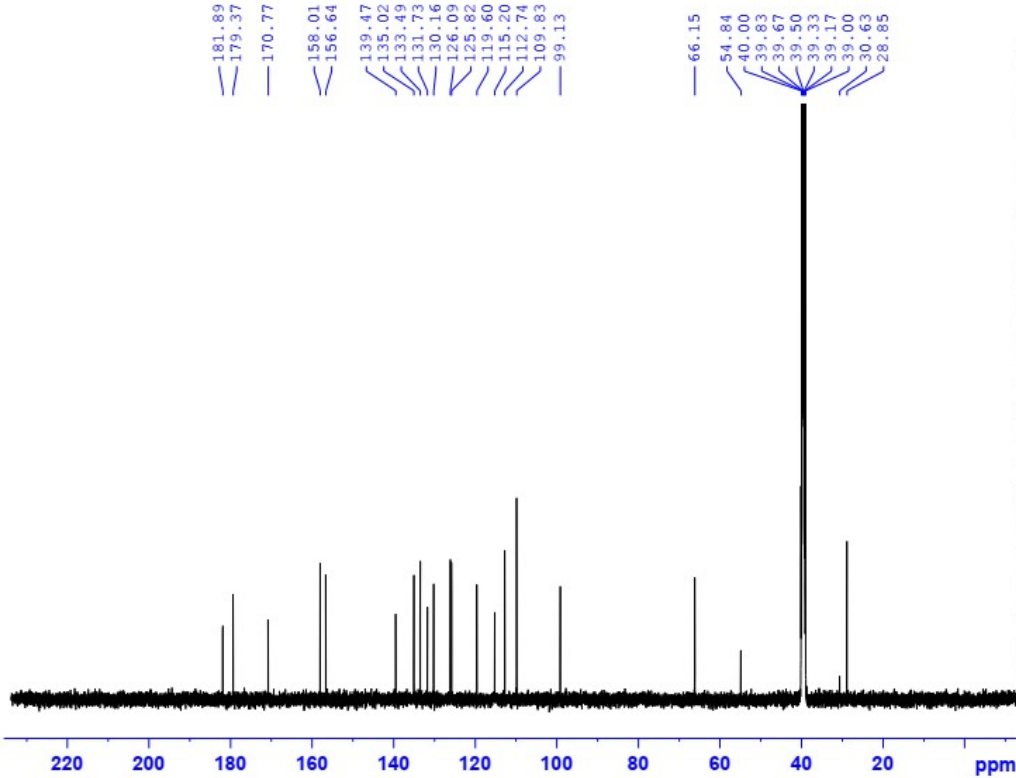


```
Current Data Parameters
NAME      6TK245.75L2
EXPNO    10
PROCNO   1

F2 - Acquisition Parameters
Date_    20221102
Time     17.55 h
INSTRUM  AvanceNEO.600MHz
PROBHD   Z114607_0562 (
PULPROG  zgpg30
TD        65536
SOLVENT  DMSO
NS        16
DS        2
SWH       11904.762 Hz
FIDRES    0.368304 Hz
AQ        2.7529120 sec
RG        99.4118
DM        42.000 usec
DE        8.71 usec
TE        303.1 K
D1        1.00000000 sec
TD0       1
SF01      600.4037075 MHz
NUC1      1H
P0        3.50 usec
P1        10.50 usec
PLW1     27.03700066 W

F2 - Processing parameters
SI        65536
SF        600.4000013 MHz
WDW       EM
SSB       0
LB        0.20 Hz
GB        0
PC        1.00
```

TK245.75L2-DMSO-C13CPD



```
Current Data Parameters
NAME      6TK245.75L2
EXPNO    1
PROCNO   1

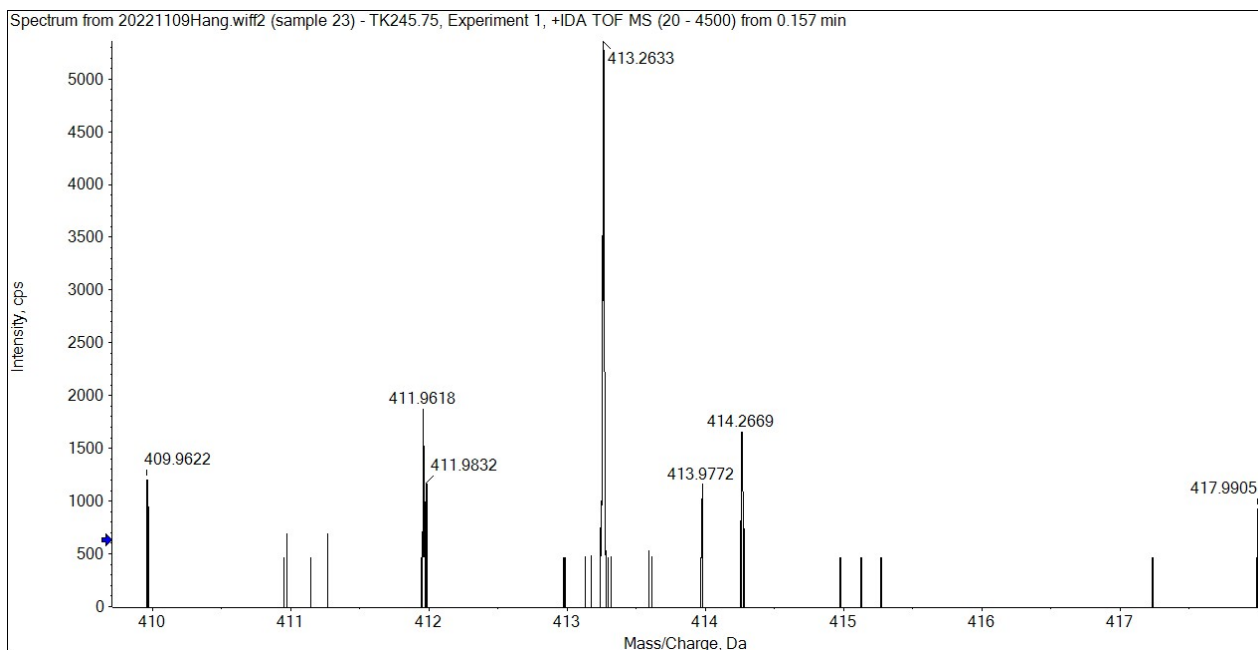
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Time     7.10
INSTRUM  spect
PROBHD   5 mm PABBO BB/
PULPROG  zgpg30
TD        65536
SOLVENT  DMSO
NS        2048
DS        4
SWH       31250.000 Hz
FIDRES    0.476837 Hz
AQ        1.0488760 sec
RG        198.37
DM        16.000 usec
DE        6.50 usec
TE        303.0 K
D1        2.00000000 sec
D11       0.02000000 sec
TD0       1

===== CHANNEL f1 =====
SF01      125.7990280 MHz
NUC1      13C
P1        10.00 usec
PLW1     88.00000000 W

===== CHANNEL f0 =====
SF02      800.2410010 MHz
NUC2      1H
CPDPRG2  waltz16
PCPD2    80.00 usec
PLN2     22.00000000 W
PLN12    0.35764000 W
PLN13    0.17989001 W

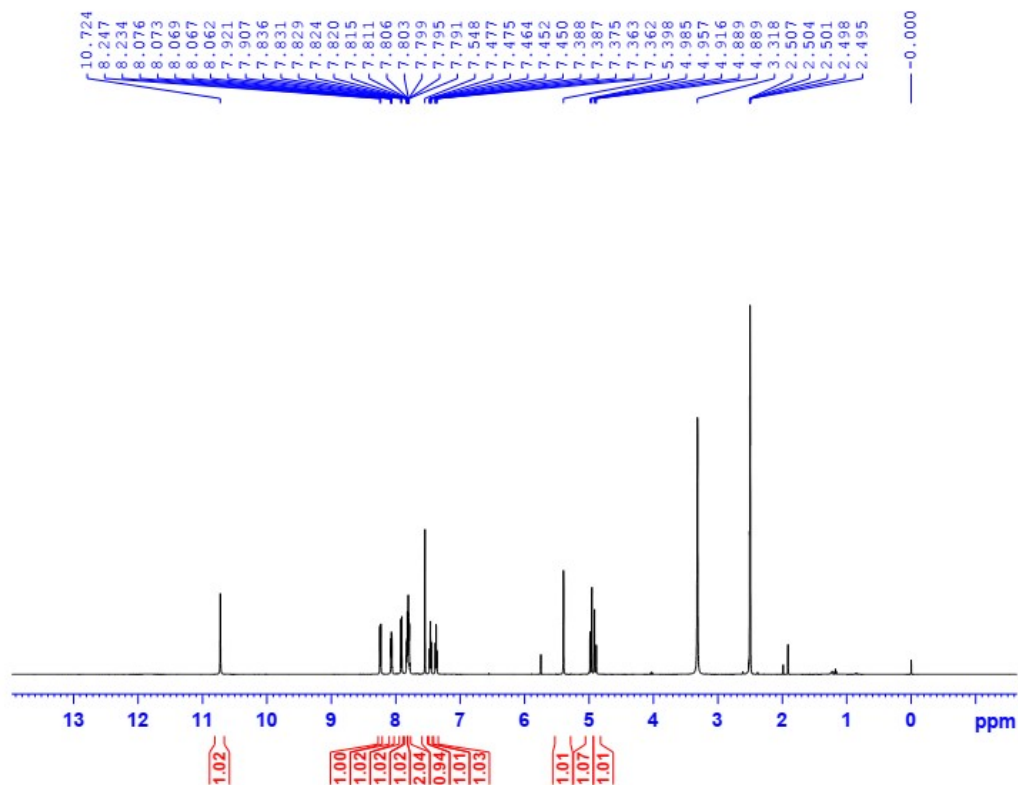
F2 - Processing parameters
SI        32768
SF        125.7852617 MHz
WDW       EM
SSB       0
LB        1.00 Hz
GB        0
PC        1.40
```





**11-(Benzo[b]thiophen-3-yl)-4,11-dihydrobenzo[g]furo[3,4-b]quinoline-1,5,10(3*H*)-trione (13e)**

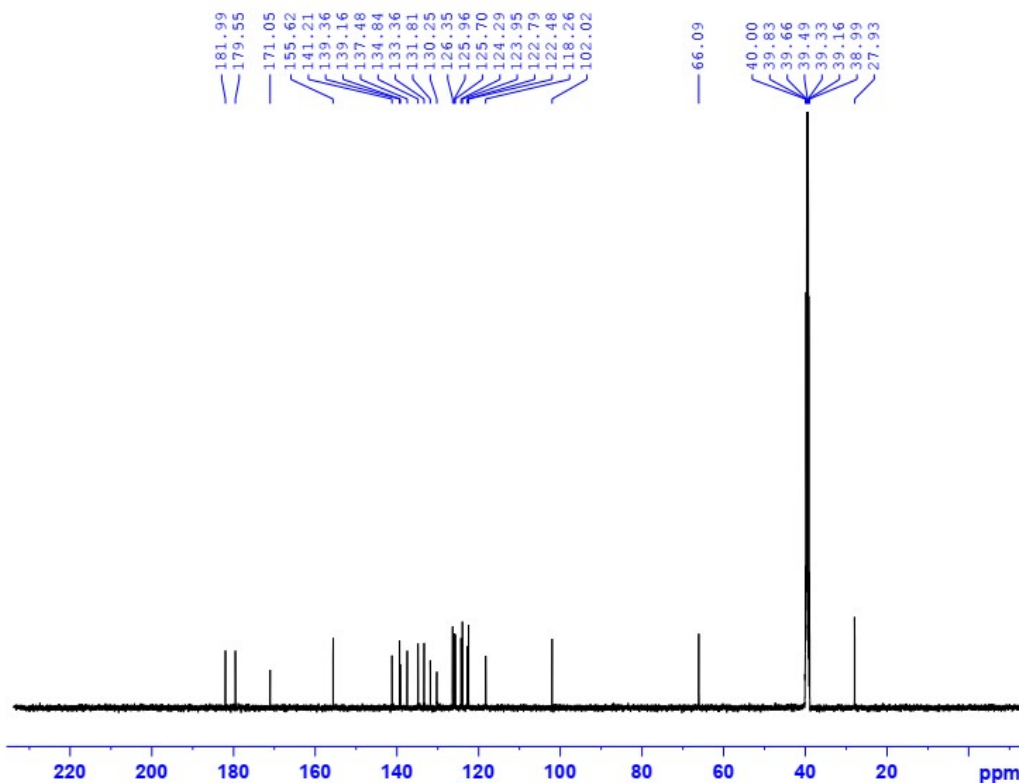
HP245.68-DMSO-1H



Current Data Parameters  
 Date\_ 20220912  
 Time\_ 20.11 h  
 INSTRUM AvanceNEO\_600MHz  
 PROBHD B1H4607\_0862 ( )  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT DMSO  
 NS 16  
 DS 2  
 SWH 11904.762 Hz  
 FIDRES 0.362304 Hz  
 AQ 2.7525120 sec  
 RG 101  
 DW 42.000 usec  
 DE 8.71 usec  
 TE 302.1 K  
 D1 1.00000000 sec  
 TDO 1  
 SFO1 600.4037075 MHz  
 NUC1 1H  
 P0 3.50 usec  
 P1 10.50 usec  
 PLW1 27.03700066 W

F2 - Processing parameters  
 SI 65536  
 SF 600.4000037 MHz  
 WDW EM  
 SSB 0  
 GB 0 0.20 Hz  
 PC 1.00

HP245.68-DMSO-C13CPD



```

Current Data Parameters
NAME      6HP245.68
EXPNO    2
PROCNO   1

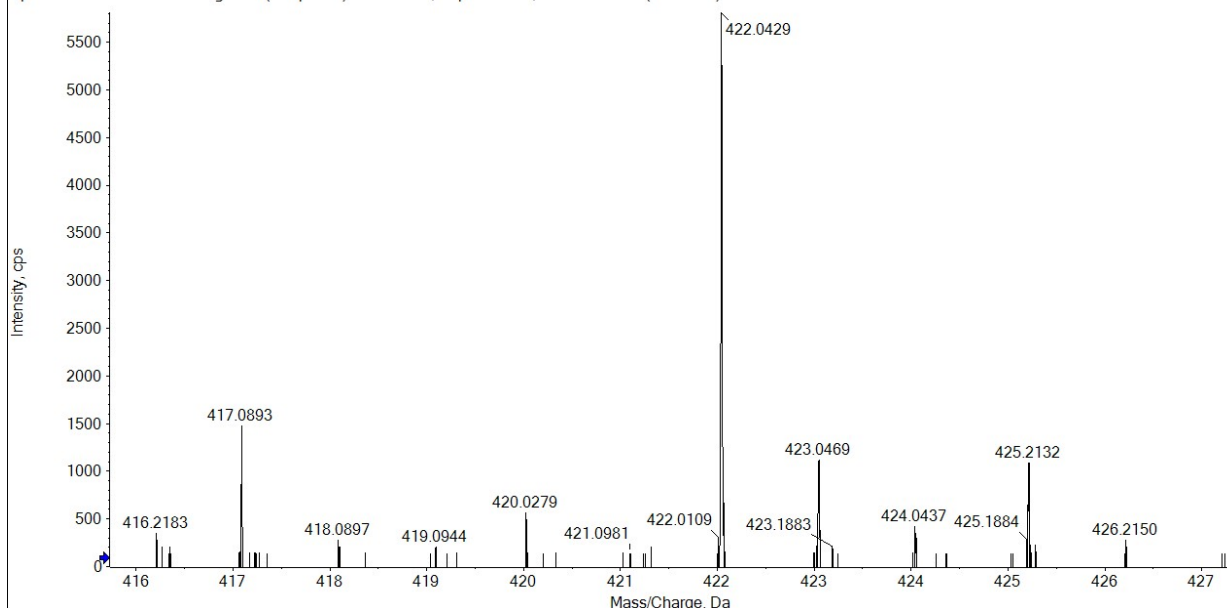
F2 - Acquisition Parameters
Date_    20220916
Time     8.21
INSTRUM  spect
PROBHD   5 mm PABBO BB/
PULPROG  zgpg30
TD        65536
SOLVENT  DMSO
NS        1024
DS         4
SWH       31250.000 Hz
FIDRES    0.476827 Hz
AQ         1.0488760 sec
RG         198.57
DW         16.000 usec
DE         6.50 usec
TE         304.0 K
D1         2.00000000 sec
D11        0.03000000 sec
TDO        1

===== CHANNEL f1 =====
SFO1      125.7990330 MHz
NUC1       13C
P1         10.00 usec
PLW1      88.00000000 W

===== CHANNEL f2 =====
SFO2      500.2410010 MHz
NUC2       1H
CPDPRG2   waltz16
PCPD2      80.00 usec
PLW2      22.00000000 W
PLW12     0.35764000 W
PLW13     0.17889001 W

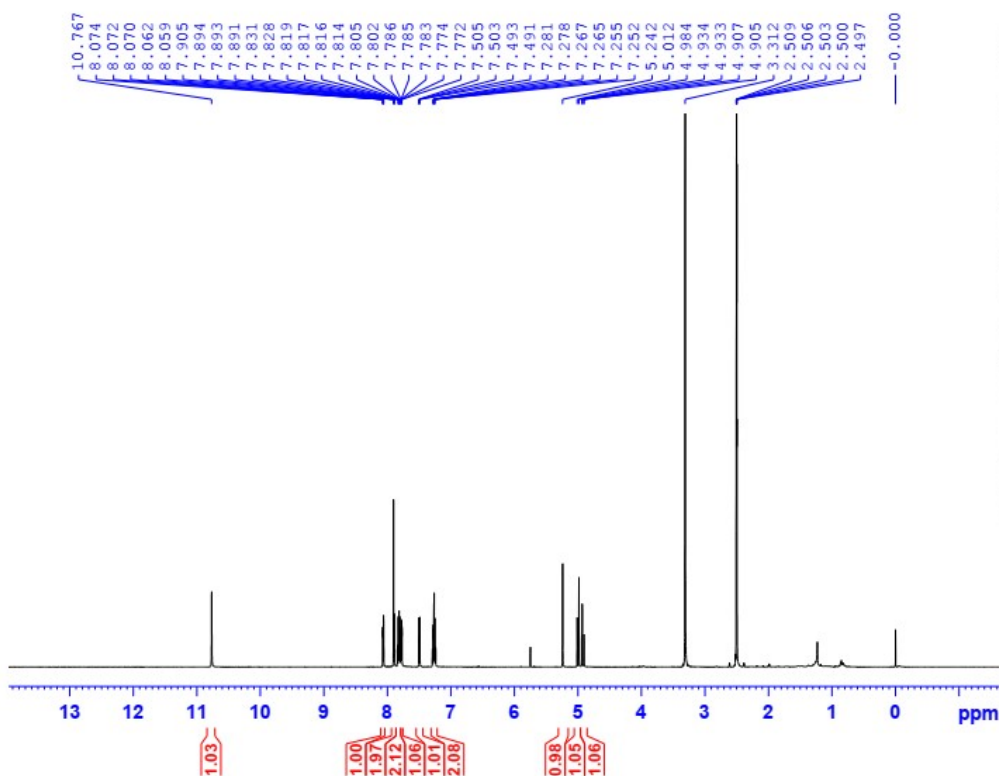
F2 - Processing parameters
SI         32768
SF         125.7852609 MHz
WDW        EM
SSB         0
LB          1.00 Hz
GB          0
PC          1.40
    
```

Spectrum from 20221109Hang.wiff2 (sample 18) - HP245.68, Experiment 1, +IDA TOF MS (20 - 4500) from 0.143 min



# 11-(Benzofuran-3-yl)-4,11-dihydrobenzo[g]furo[3,4-b]quinoline-1,5,10(3H)-trione (13f)

HP254.70-DMSO-1H



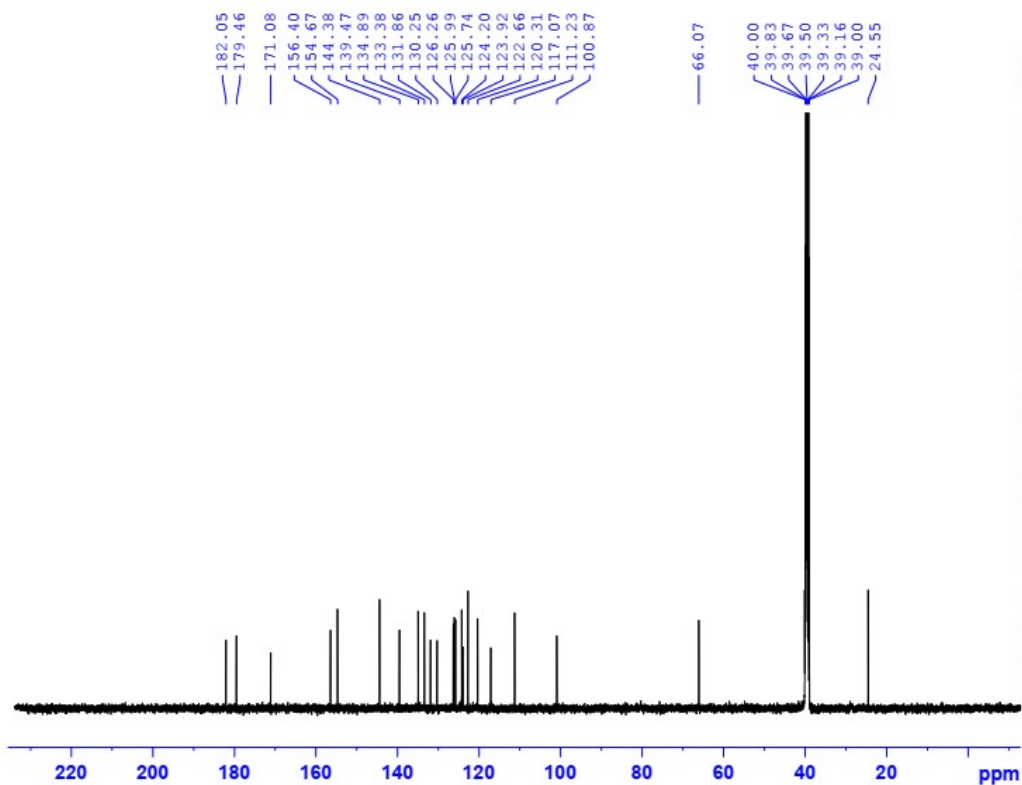
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Current Data Parameters
NAME      6HP254.70
EXPNO    10
PROCNO   1

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Date_    20220916
Time     0.49 h
INSTRUM  AvanceNEO 600MHz
PROBHD   Z114607_0562 (
PULPROG  zg30
TD        65536
SOLVENT  DMSO
NS        16
DS        2
SWH       11904.762 Hz
FIDRES    0.369304 Hz
AQ        2.7525120 sec
RG         101
DM        42.000 usec
DE         8.71 usec
TE        303.1 K
D1        1.00000000 sec
TDO       1
SFO1      600.4037078 MHz
NUC1      1H
PC        3.50 usec
P1        10.50 usec
PLW1     27.02700066 W

F2 - Processing parameters
SI        65536
SF        600.4000027 MHz
WDW       EM
SSB       0
LB        0.30 Hz
GB        0
PC        1.00
    
```

HP254.70-DMSO-C13CPD



```

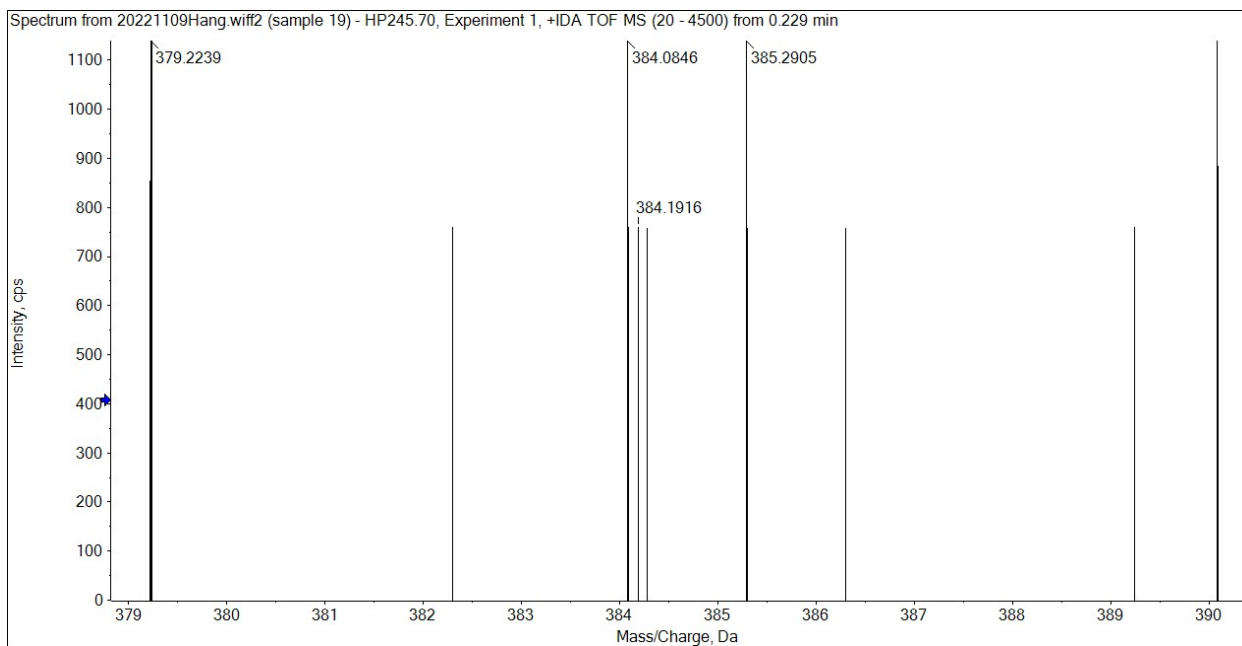
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NAME      6HP254.70
EXPNO    2
PROCNO   1

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Date_    20220920
Time     3.28
INSTRUM  spect
PROBHD   5 mm PABBO BB/
PULPROG  zgpg30
TD        65536
SOLVENT  DMSO
NS        2048
DS        4
SWH       21250.000 Hz
FIDRES    0.476827 Hz
AQ        1.0485760 sec
RG        198.57
DM        16.000 usec
DE         6.50 usec
TE        304.0 K
D1        2.00000000 sec
D11       0.02000000 sec
TDO       1

===== CHANNEL f1 =====
SFO1     125.7690220 MHz
NUC1     13C
PC       10.00 usec
PLW1     88.00000000 W

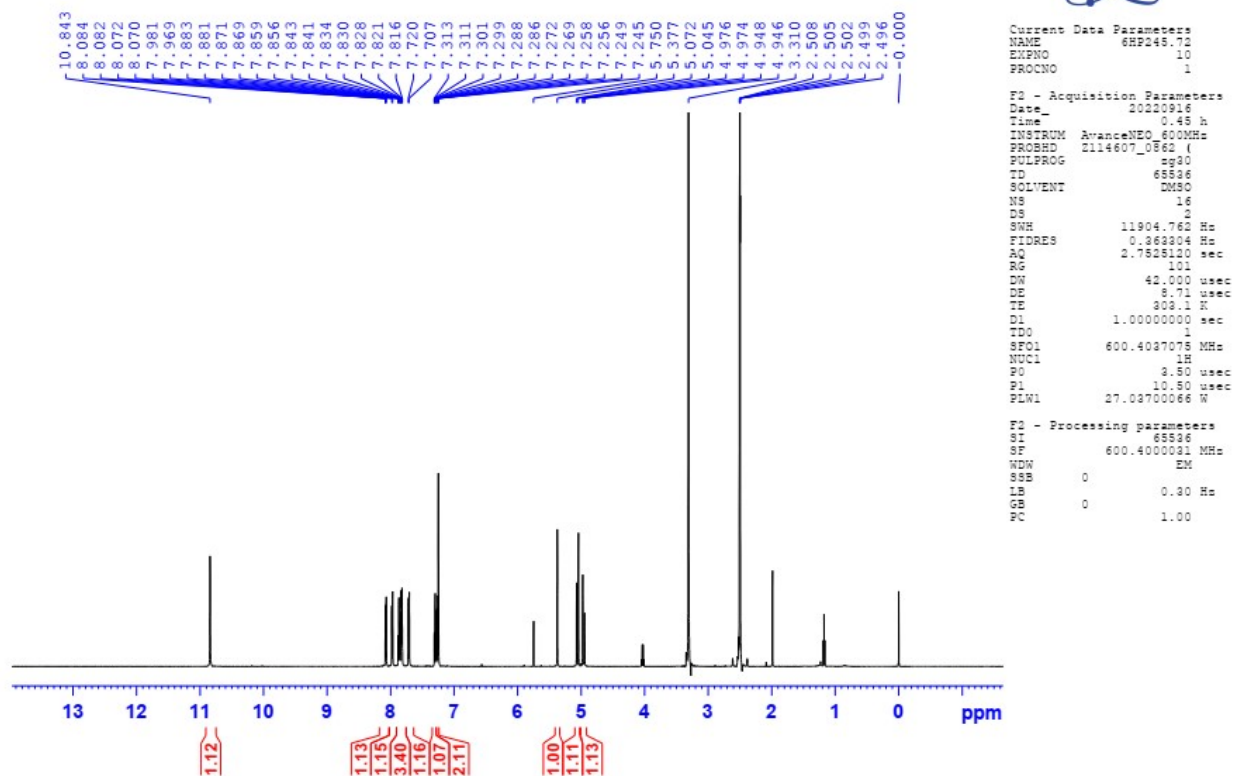
===== CHANNEL f2 =====
SFO2     300.2410010 MHz
NUC2     1H
CPDPRG2  waltz16
PCPD2    80.00 usec
PLW2     22.00000000 W
PLW12    0.28764000 W
PLW13    0.17989001 W

F2 - Processing parameters
SI        22768
SF        125.7652392 MHz
WDW       EM
SSB       0
LB        1.00 Hz
GB        0
PC        1.40
    
```

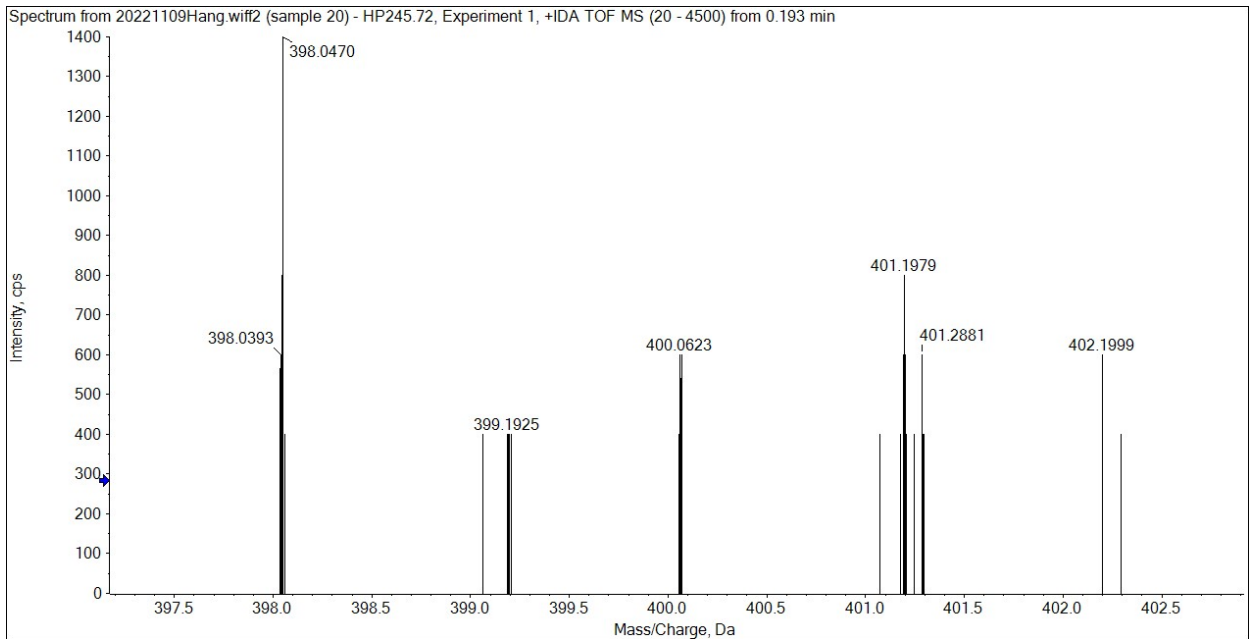
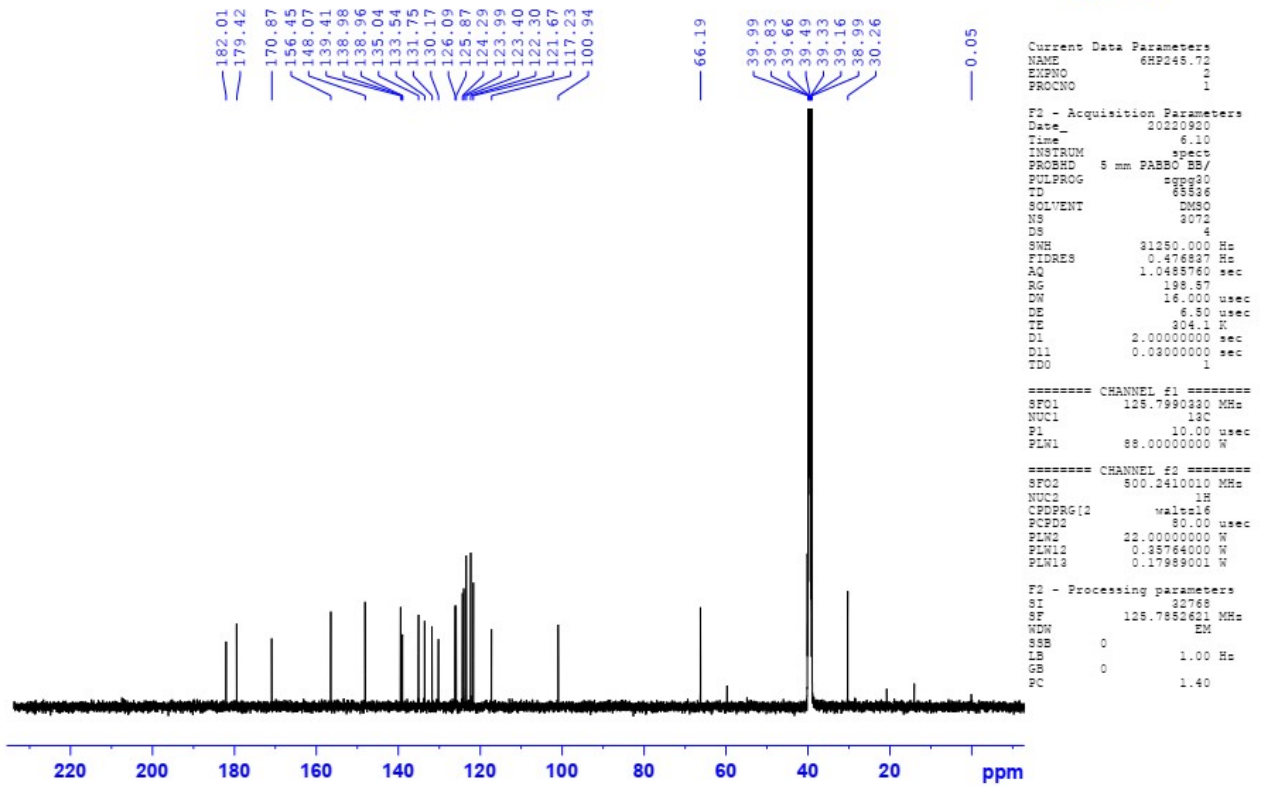


**11-(Benzo[b]thiophen-2-yl)-4,11-dihydrobenzo[g]furo[3,4-b]quinoline-1,5,10(3H)-trione (13g)**

HP245.72-DMSO-1H



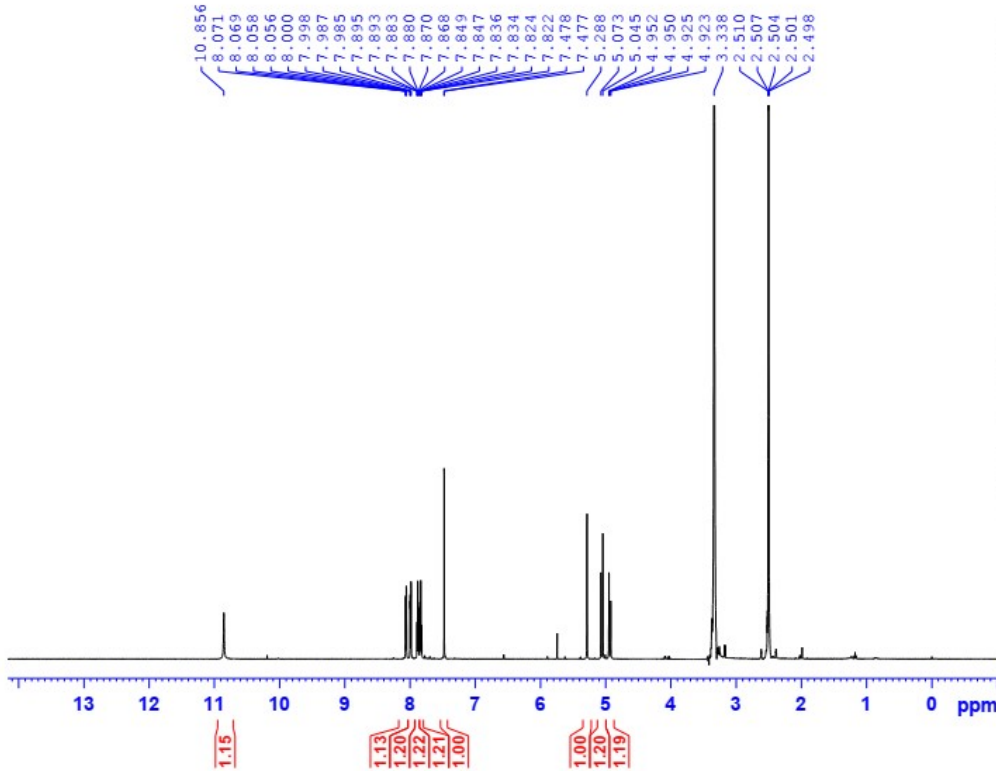
HP245.72-DMSO-C13CPD





11-(2-Chlorothiazol-5-yl)-4,11-dihydrobenzo[*g*]furo[3,4-*b*]quinoline-1,5,10(3*H*)-trione (13h)

DTA254.74-DMSO-1H

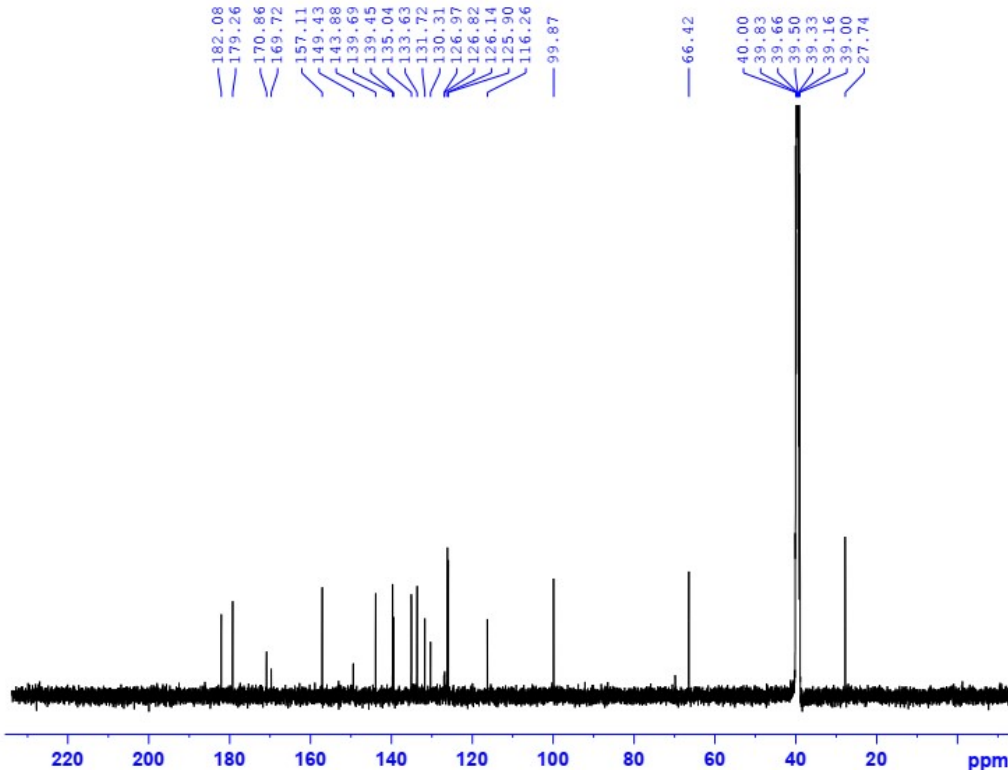


Current Data Parameters  
 NAME 6DTA254.74  
 EXPNO 10  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20220922  
 Time 17.47 h  
 INSTRUM AvanceNeo 600MHz  
 PROBRD Z114607\_0862 (1  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT DMSO  
 NS 16  
 DS 2  
 SWH 11904.762 Hz  
 FIDRES 0.362204 Hz  
 AQ 2.7528120 sec  
 RG 95.8865  
 DW 42.000 usec  
 DE 8.71 usec  
 TE 303.2 K  
 D1 1.00000000 sec  
 TDO 1  
 SFO1 600.4087078 MHz  
 NUC1 1H  
 P2 3.50 usec  
 P1 10.50 usec  
 PLW1 27.09700066 W

F2 - Processing parameters  
 SI 65536  
 SF 600.4000018 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

DTA254.74-DMSO-C13CPD



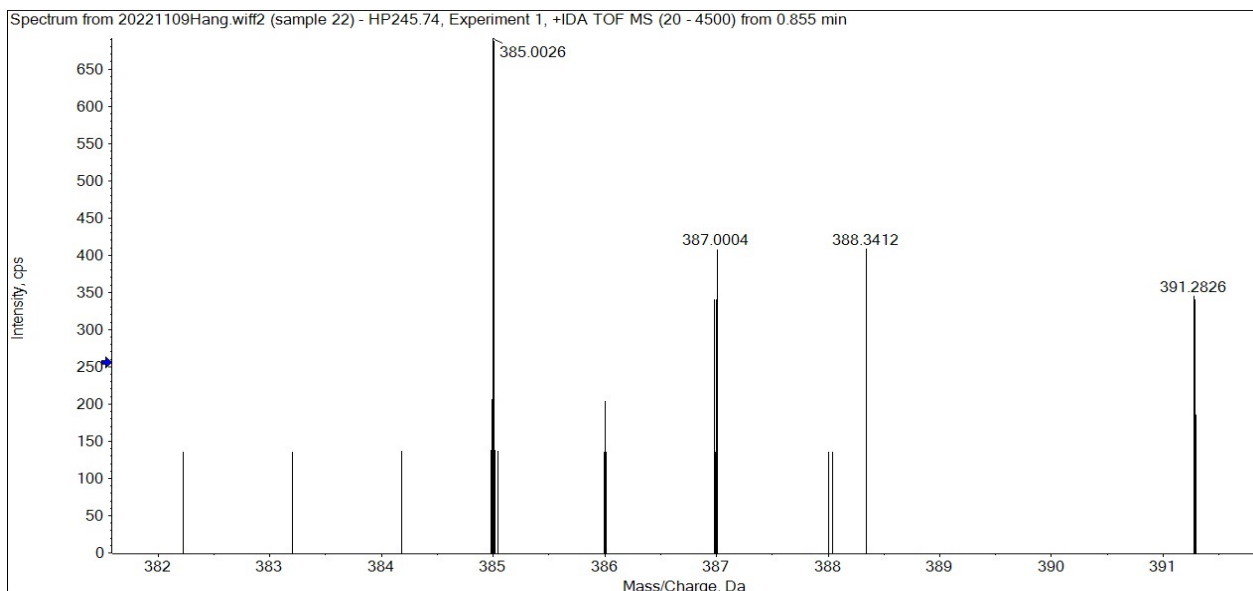
Current Data Parameters  
 NAME 6DTA254.74  
 EXPNO 2  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20220927  
 Time 4.26  
 INSTRUM spect  
 PROBRD 5 mm PABBO BBO  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT DMSO  
 NS 4  
 DS 4  
 SWH 31250.000 Hz  
 FIDRES 0.476827 Hz  
 AQ 1.0488760 sec  
 RG 198.87  
 DW 16.000 usec  
 DE 8.50 usec  
 TE 305.3 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TDO 1

===== CHANNEL #1 =====  
 SFO1 125.7990320 MHz  
 NUC1 13C  
 P1 10.00 usec  
 PLW1 88.00000000 W

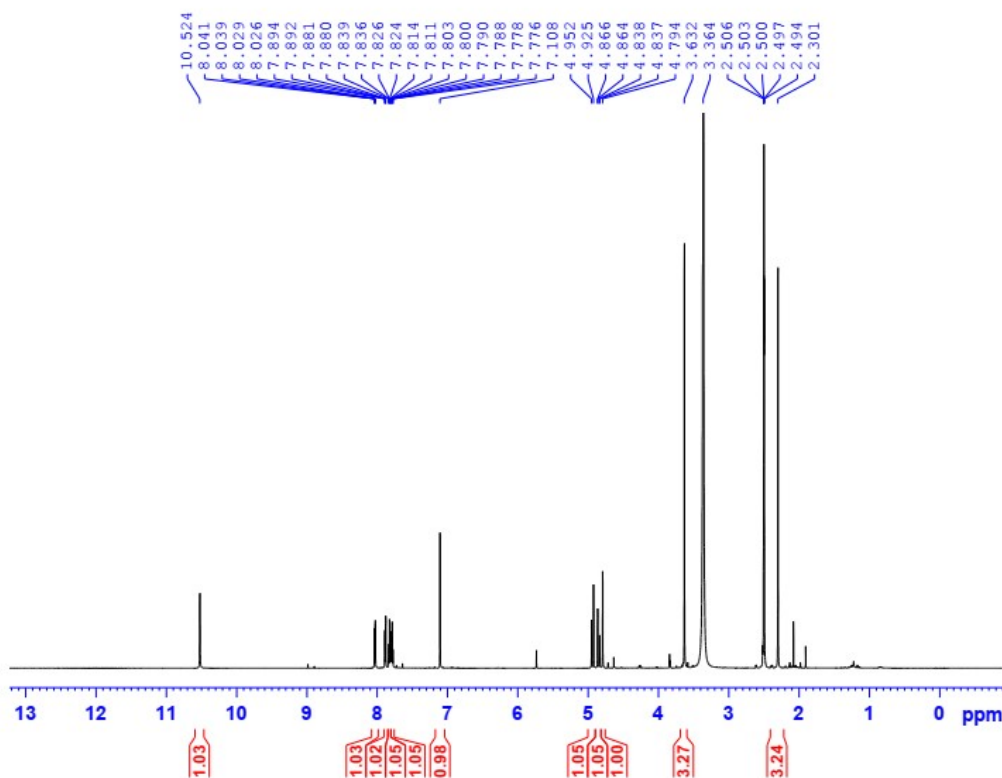
===== CHANNEL #2 =====  
 SFO2 500.2410010 MHz  
 NUC2 1H  
 CPDPRG12 waltz16  
 P2P2 80.00 usec  
 PLW2 22.00000000 W  
 PLW12 0.28764000 W  
 PLW13 0.17989001 W

F2 - Processing parameters  
 SI 32768  
 SF 125.7852559 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40

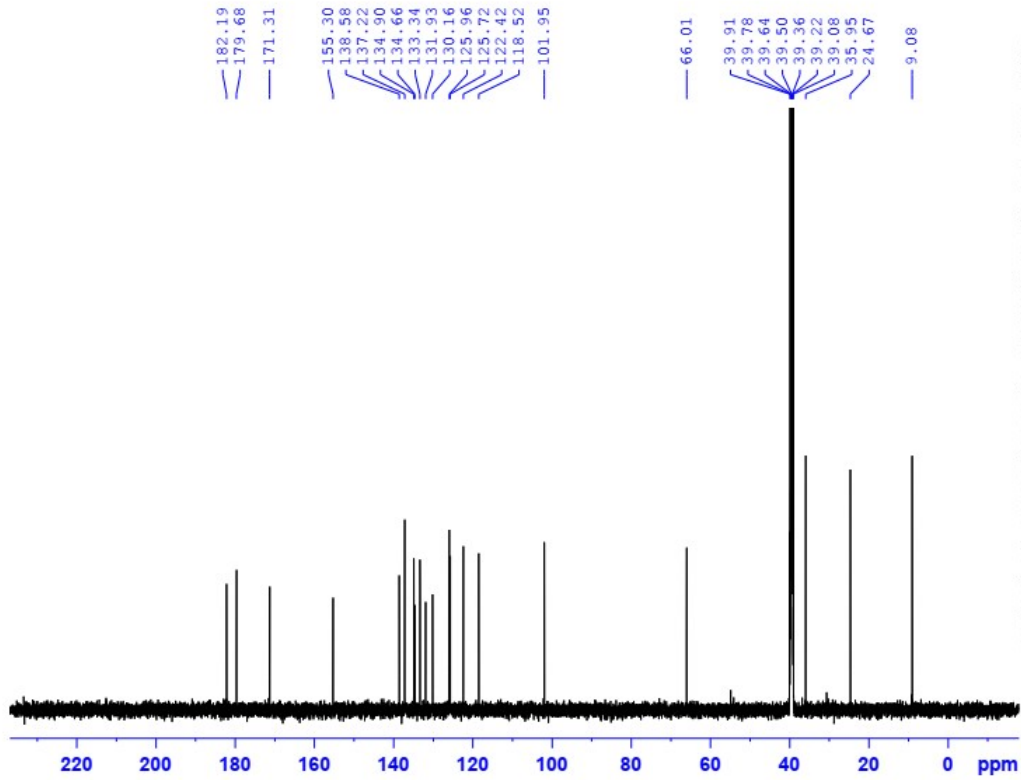


**11-(1,5-Dimethyl-1H-pyrazol-4-yl)-4,11-dihydrobenzo[g]furo[3,4-b]quinoline-1,5,10(3H)-trione (13i)**

TK245.79-DMSO-1H



TK245.79-DMSO-C13CPD



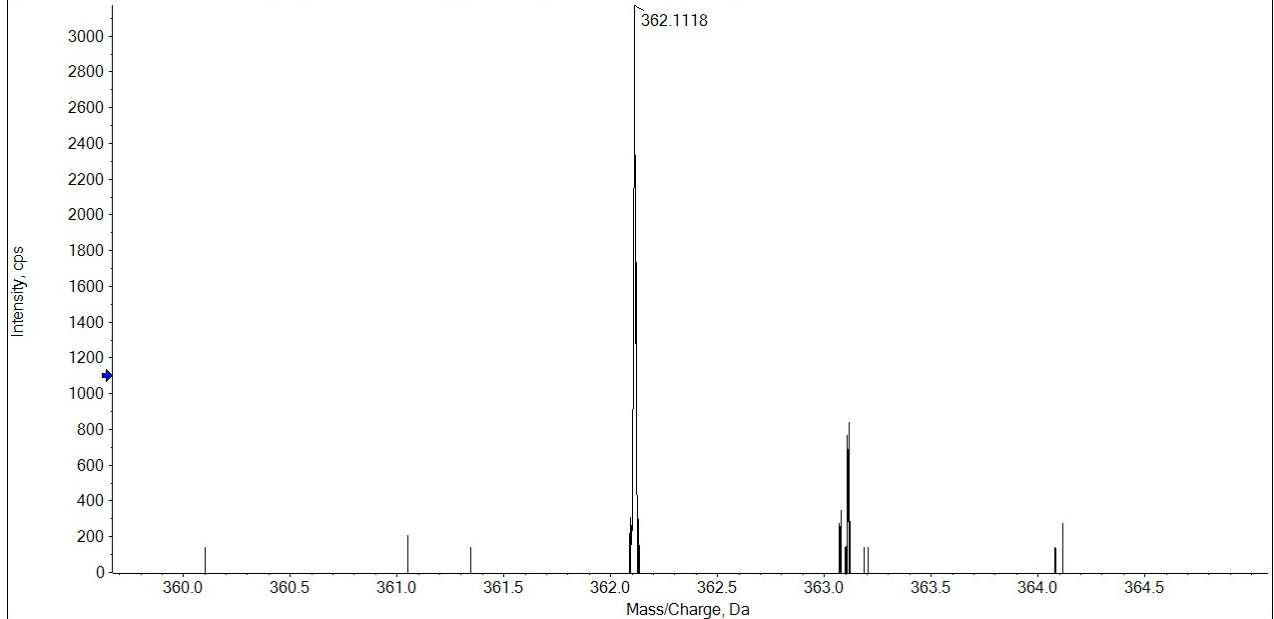
```

Current Data Parameters
NAME      TK245.79
EXPNO    2
PROCNO   1

F2 - Acquisition Parameters
Date_    20221001
Time     9.15 h
INSTRUM  Avance NEO 600MHz
PROBHD   1H14607_0662 (
PULPROG  zgpg30
TD       65536
SOLVENT  DMSO
NS       1024
DS       4
SNH      38461.539 Hz
FIDRES   1.173753 Hz
AQ        0.6519650 sec
RG        101
DM        13.000 usec
DE        6.50 usec
TE        303.1 K
D1        2.00000000 sec
D11       0.03000000 sec
TDD       1
SFO1      150.9873069 MHz
NUC1      13C
P0         4.20 usec
P1        12.60 usec
PLW1      66.92800393 W
SFO2      600.4014016 MHz
NUC2      1H
CPDPRG2   waltz65
PCPD2     80.00 usec
PLW2      27.03700066 W
PLW12     0.46875001 W
PLW13     0.30589001 W

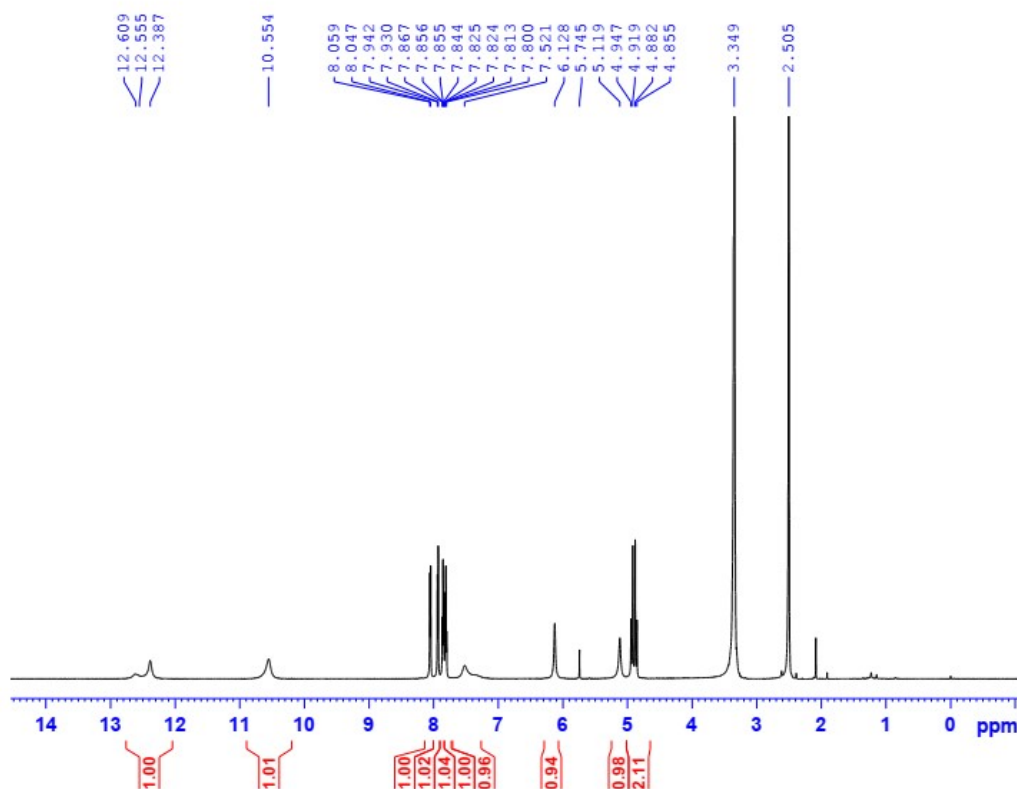
F2 - Processing parameters
SI        32768
SF        150.9707690 MHz
WDW       EM
SSB       0
LB        1.00 Hz
GB        0
PC        1.40
    
```

Spectrum from 20221109Hang.wif2 (sample 26) - TK245.79, Experiment 1, +IDA TOF MS (20 - 4500) from 0.942 min



# 11-(1H-pyrazol-5-yl)-4,11-dihydrobenzo[g]furo[3,4-b]quinoline-1,5,10(3H)-trione (13j)

TK254.62-DMSO-1H

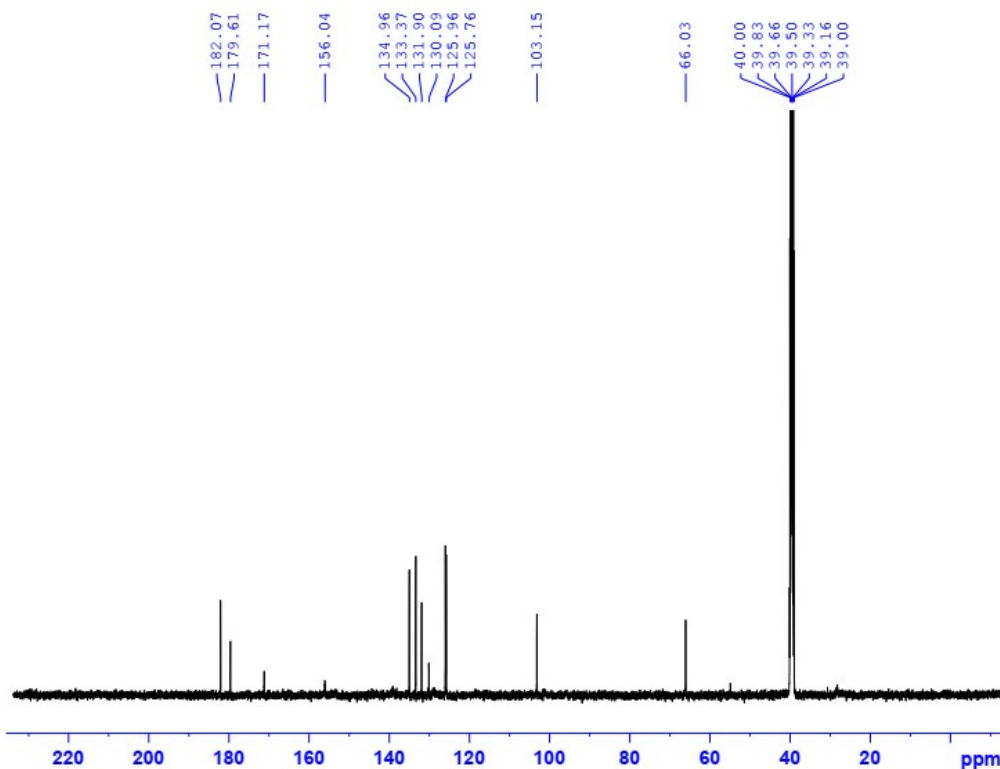


Current Data Parameters  
 NAME 6TH254.62  
 EXPNO 10  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20221031  
 Time 18.00 h  
 INSTRUM AvanceNeo 600MHz  
 PROBHD BBI4601\_0862 (4  
 FULPROG zgpg30  
 TD 65536  
 SOLVENT DMSO  
 NS 16  
 DS 2  
 SWH 11904.762 Hz  
 FIDRES 0.362304 Hz  
 AQ 2.7525120 sec  
 RG 34.8197  
 DW 42.000 usec  
 DE 8.71 usec  
 TE 303.1 K  
 D1 1.00000000 sec  
 TDO 1  
 SFO1 600.4037075 MHz  
 NUC1 1H  
 P0 3.50 usec  
 P1 10.50 usec  
 PLW1 27.03700066 W

F2 - Processing parameters  
 SI 65536  
 SF 600.4000017 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

TK254.62-DMSO-C13CPD



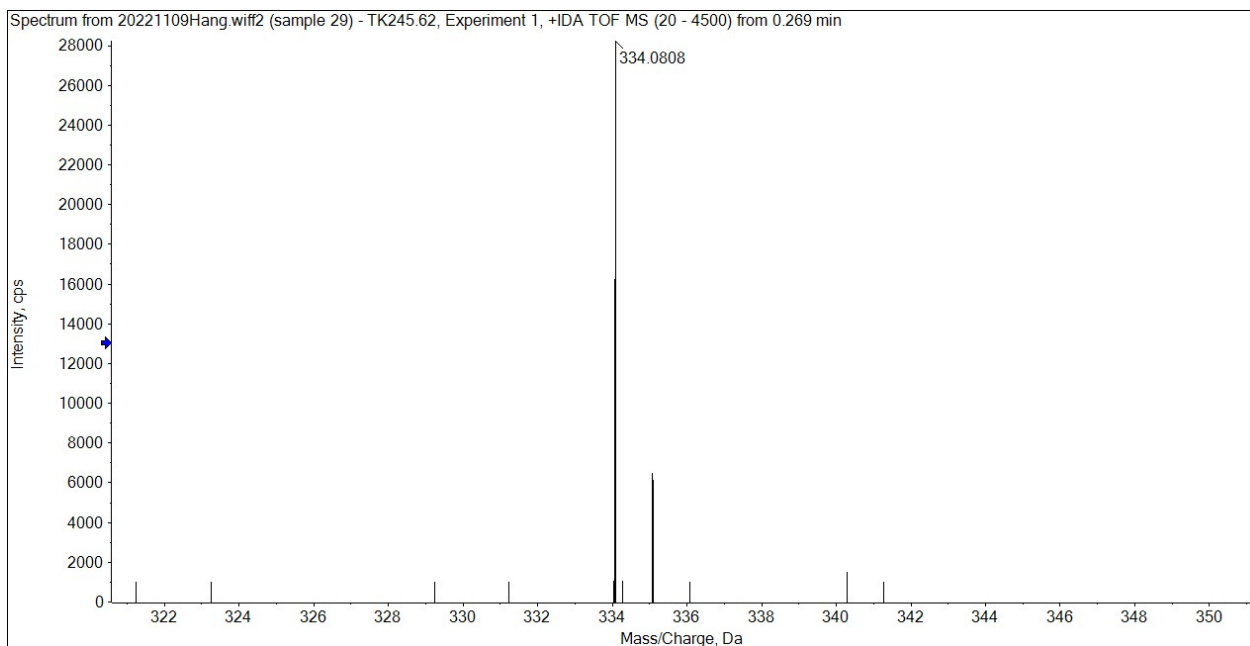
Current Data Parameters  
 NAME 6TH254.62  
 EXPNO 3  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20221102  
 Time 5.21  
 INSTRUM spect  
 PROBHD 5 mm F4BBO BB/  
 FULPROG zgpg30  
 TD 65536  
 SOLVENT DMSO  
 NS 2048  
 DS 4  
 SWH 31250.000 Hz  
 FIDRES 0.4766807 Hz  
 AQ 1.0485760 sec  
 RG 198.57  
 DW 16.000 usec  
 DE 6.50 usec  
 TE 303.0 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TDO 1

===== CHANNEL #1 =====  
 SFO1 125.7690240 MHz  
 NUC1 13C  
 P1 10.00 usec  
 PLW1 88.00000000 W

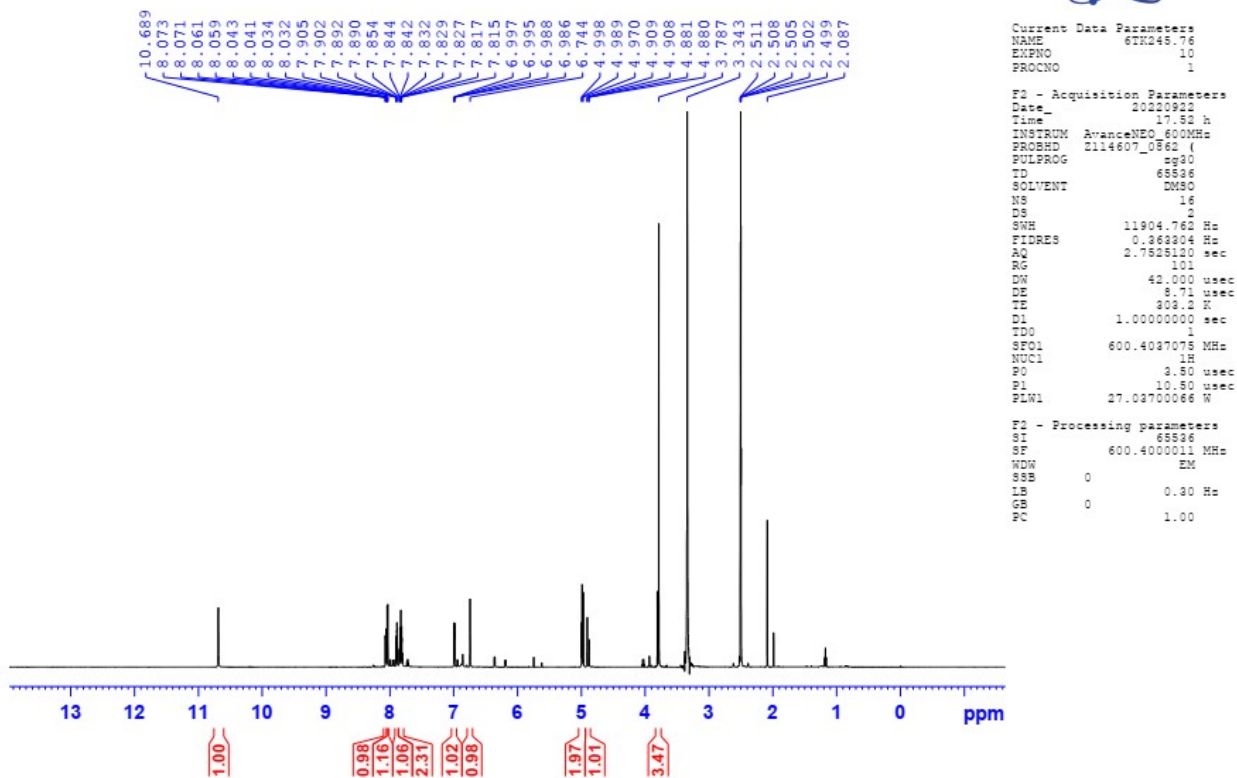
===== CHANNEL #2 =====  
 SFO2 500.2410010 MHz  
 NUC2 1H  
 CPDPRG12 waltz16  
 PCPD2 80.00 usec  
 P1M2 22.00000000 W  
 PLW12 0.35764000 W  
 PLW13 0.17989001 W

F2 - Processing parameters  
 SI 20736  
 SF 125.7652592 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40



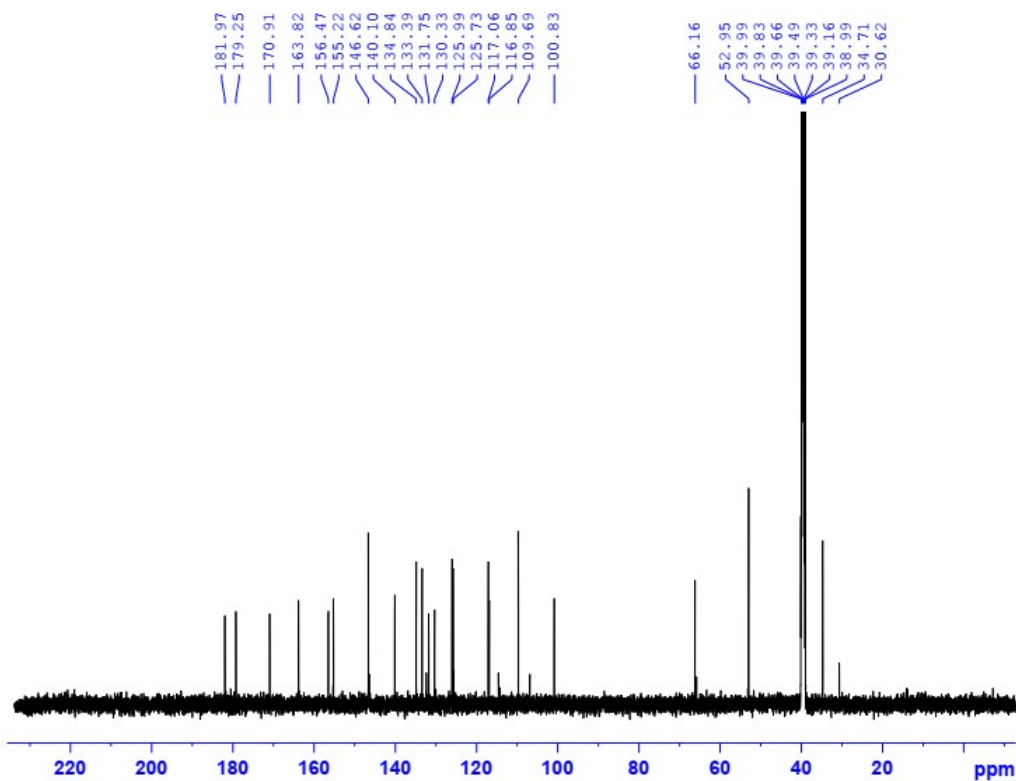
**11-(2-Methoxypyridin-4-yl)-4,11-dihydrobenzo[*g*]furo[3,4-*b*]quinoline-1,5,10(3*H*)-trione (13k)**

TK245.76-DMSO-1H





TK254.76-DMSO-C13CPD



```

Current Data Parameters
NAME      6TK254.76
EXPNO     2
PROCNO    1

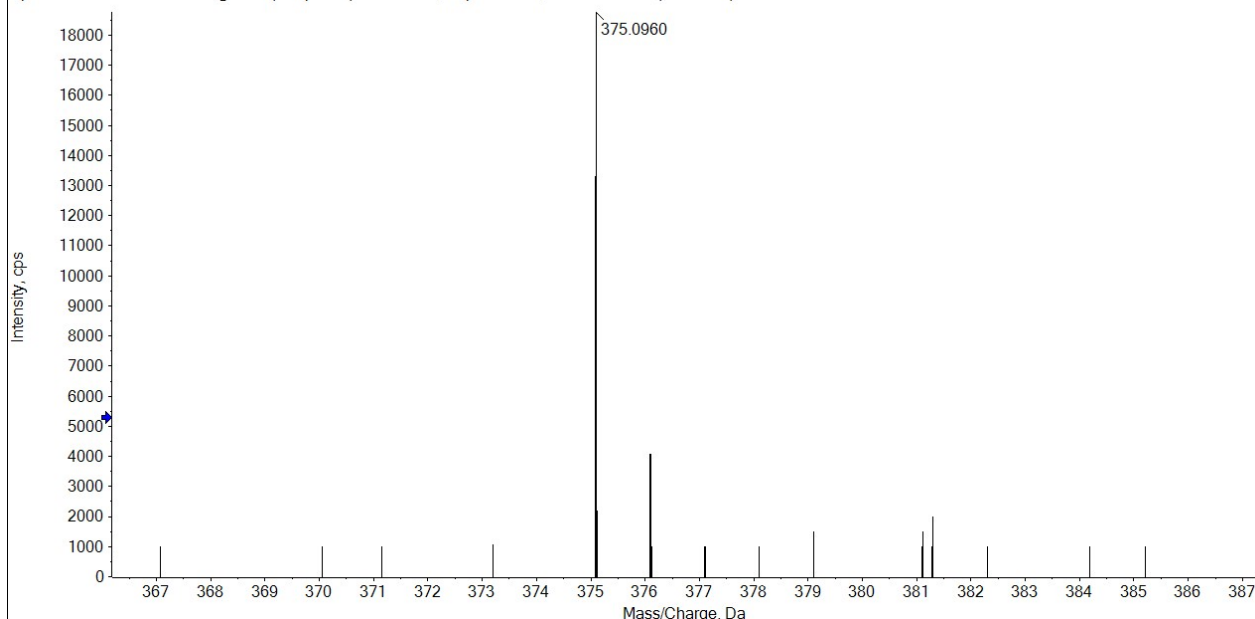
F2 - Acquisition Parameters
Date_     20220927
Time      5.50
INSTRUM   spect
PROBHD    5 mm BBO BB/
PULPROG   zgpg30
TD         65536
SOLVENT   DMSO
NS         1588
DS         4
SWH        31250.000 Hz
FIDRES     0.476837 Hz
AQ          1.0485760 sec
RG          198.87
DW          16.000 usec
DE          6.50 usec
TE          305.4 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0         1

===== CHANNEL #1 =====
SF01       125.7990330 MHz
NUC1        13C
P1          10.00 usec
PLW1        88.00000000 W

===== CHANNEL #2 =====
SF02       500.2410010 MHz
NUC2         1H
CPDPRG12   waltz16
PCPD2       80.00 usec
PLW2        20.00000000 W
PLW12       0.35764000 W
PLW13       0.17989001 W

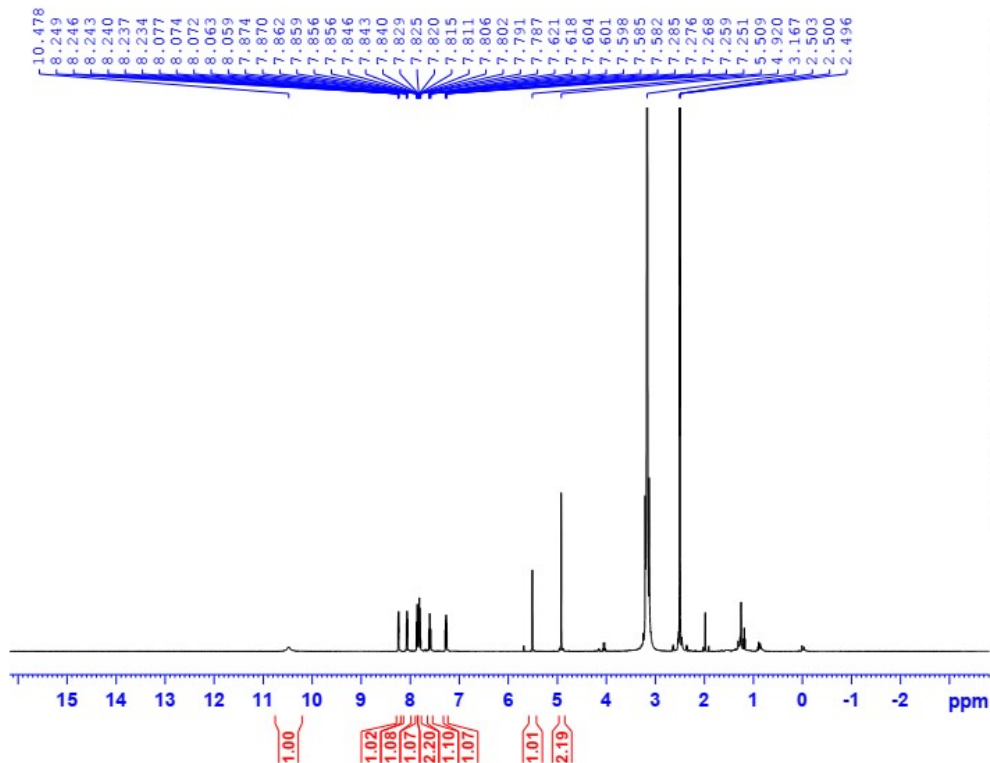
F2 - Processing parameters
SI          32768
SF          125.7852615 MHz
WDW         EM
SSB         0
LB          1.00 Hz
GB          0
PC          1.40
    
```

Spectrum from 20221109Hang.wiff2 (sample 24) - TK245.76, Experiment 1, +IDA TOF MS (20 - 4500) from 0.167 min



11-(3-Fluoropyridin-2-yl)-4,11-dihydrobenzo[g]furo[3,4-b]quinoline-1,5,10(3H)-trione  
(13l)

TK245.78.1-DMSO-1H



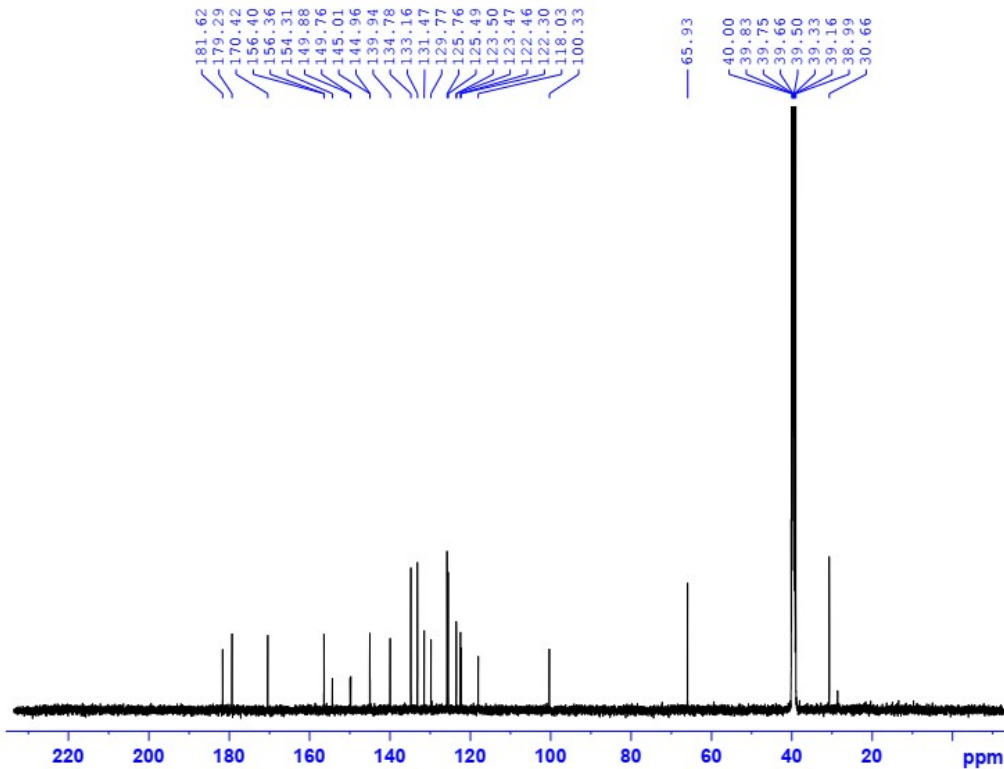
```
Current Data Parameters
NAME      6TK245.78.1
EXPNO    1
PROCNO   1

F2 - Acquisition Parameters
Date_    20221006
Time     17.10
INSTRUM spect
PROBHD   5 mm PABBO BB/
PULPROG zgpg30
TD        65536
SOLVENT  DMSO
NS        2
DS        2
SFO1     10000.000 Hz
FIDRES   0.152588 Hz
AQ        3.2767999 sec
RG        89.68
DM        80.000 usec
DE        6.50 usec
TE        303.0 K
D1        1.00000000 sec
TDO       1

===== CHANNEL f1 =====
SFO1     500.2420892 MHz
NUC1      1H
P1        10.20 usec
PLW1     22.00000000 W

F2 - Processing parameters
SI        65536
SF        500.2390042 MHz
WDW       EM
SSB       0
LB        0.20 Hz
GB        0
PC        1.00
```

TK245.78.1-DMSO-C13CPD



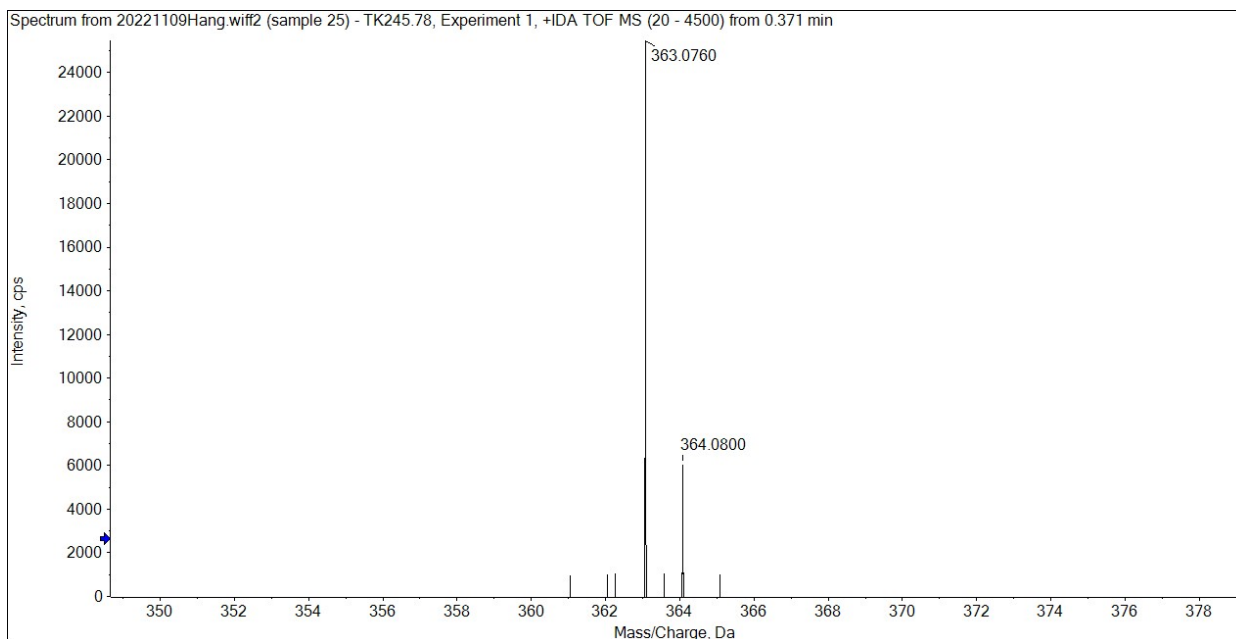
```
Current Data Parameters
NAME      6TK245.78.1
EXPNO    1
PROCNO   1

F2 - Acquisition Parameters
Date_    20221007
Time     7.22
INSTRUM spect
PROBHD   5 mm PABBO BB/
PULPROG zgpg30
TD        65536
SOLVENT  DMSO
NS        4
DS        4
SFO1     31250.000 Hz
FIDRES   0.476837 Hz
AQ        1.0485760 sec
RG        198.87
DM        16.000 usec
DE        6.50 usec
TE        303.0 K
D1        2.00000000 sec
D11      0.03000000 sec
TDO       1

===== CHANNEL f1 =====
SFO1     125.7690380 MHz
NUC1      13C
P1        10.00 usec
PLW1     88.00000000 W

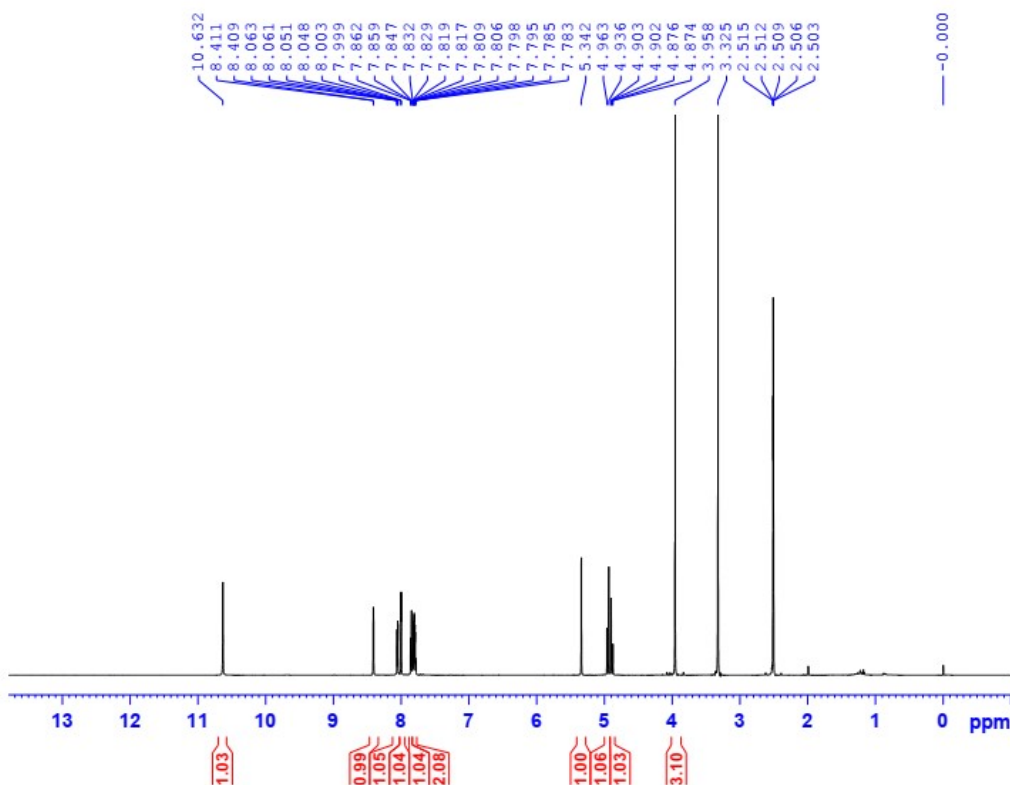
===== CHANNEL f2 =====
SFO2     500.2410010 MHz
NUC2      1H
PCPDPRG2 waltz16
PCPD2    80.00 usec
PLW2     22.00000000 W
PLW12    0.35764000 W
PLW13    0.17889001 W

F2 - Processing parameters
SI        32768
SF        125.7652923 MHz
WDW       EM
SSB       0
LB        1.00 Hz
GB        0
PC        1.40
```



**11-(2-Methoxy-5-(trifluoromethyl)pyridin-3-yl)-4,11-dihydrobenzo[g]furo[3,4-b]quinoline-1,5,10(3H)-trione (13m)**

**TK245.96-DMSO-1H**



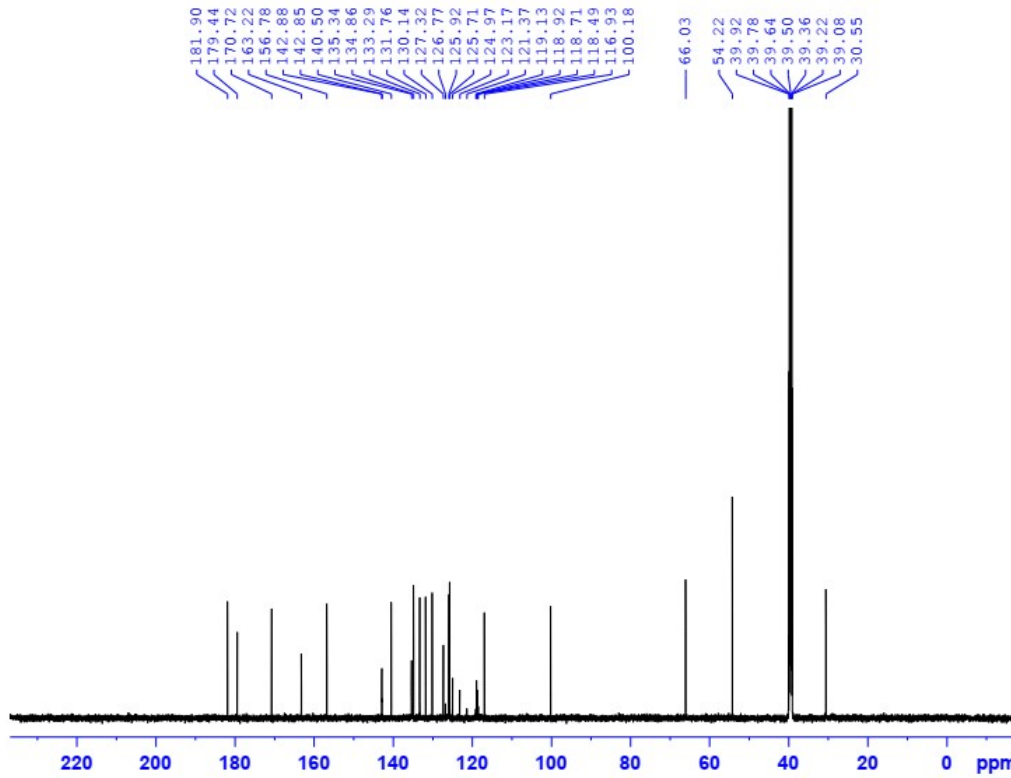
```

Current Data Parameters
NAME      6TK245.96
EXPNO    10
PROCNO   1

F2 - Acquisition Parameters
Date_    20221021
Time     15.41 h
INSTRUM  AvanceNEO_600MHz
PROBHD   Z114607_0862 (
PULPROG  zgpg
TD        65536
SOLVENT  DMSO
NS        16
DS        2
SWH       11904.762 Hz
FIDRES    0.262304 Hz
AQ        2.7525100 sec
RG        74.2857
DW        42.000 usec
DE        8.71 usec
TE        303.1 K
D1        1.00000000 sec
D11       1
TDO       1
SFO1      600.4027075 MHz
NUC1      1H
PQ        2.50 usec
PI        10.50 usec
PL1       27.03700066 W

F2 - Processing parameters
SI        65536
SF        600.3999991 MHz
WDW       EM
SSB       0
LB        0.30 Hz
GB        0
PC        1.00
  
```

TK245.96-DMSO-C13CPD

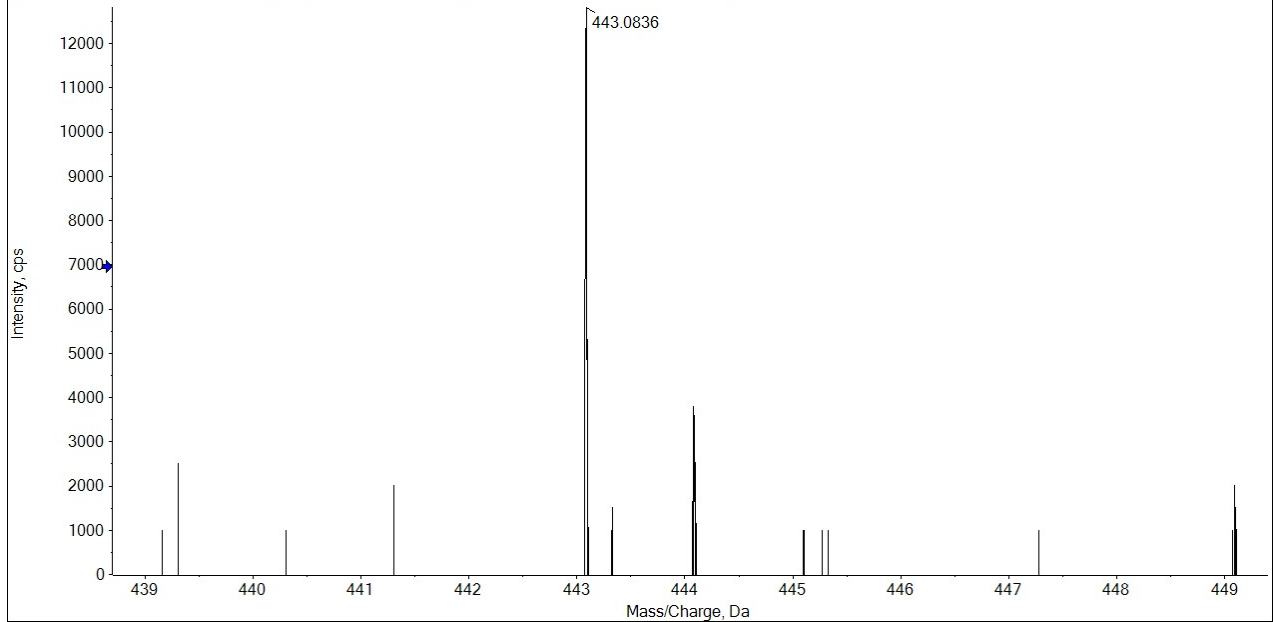


Current Data Parameters  
 NAME: TK245.96  
 EXPNO: 2  
 PROCNO: 1

F2 - Acquisition Parameters  
 Date\_: 20221022  
 Time: 5.18 h  
 INSTRUM: Avance NEO 600MHz  
 PROBHD: Z114607\_0862 (1  
 PULPROG: zgpg30  
 ID: 85826  
 SOLVENT: DMSO  
 NS: 1024  
 DS: 4  
 SWH: 28461.539 Hz  
 FIDRES: 1.179753 Hz  
 AQ: 0.8519680 sec  
 RG: 101  
 DW: 19.000 usec  
 DE: 6.50 usec  
 TE: 303.2 K  
 D1: 2.00000000 sec  
 D11: 0.03000000 sec  
 TDO: 1  
 SF01: 150.9873069 MHz  
 NUC1: 13C  
 P0: 4.20 usec  
 P1: 12.60 usec  
 PLW1: 66.32800299 W  
 SF02: 600.4024016 MHz  
 NUCC: 1H  
 CPDPRG2: waltz165  
 PCPD2: 80.00 usec  
 PLW2: 27.03700066 W  
 PLW12: 0.46575001 W  
 PLW13: 0.30599001 W

F2 - Processing parameters  
 SI: 32768  
 SF: 150.9707777 MHz  
 WDW: EM  
 SSB: 0  
 LB: 1.00 Hz  
 GB: 0  
 PC: 1.40

Spectrum from 20221109Hang.wiff2 (sample 28) - TK245.96, Experiment 1, +IDA TOF MS (20 - 4500) from 0.237 min



**Table S1.** Estimated of binding energy of docking complexes for **13a-m**, podophyllotoxin and colchicine.\*

Compounds	Binding energy	Hbond	Hphob	VwInt	Eintl	Dsolv	SolEl	mfScore	dTSsc
<b>13a</b>	-16.38	-3.064	-6.433	-25.42	17.12	10.230	11.46	-75.37	0.9014
<b>13b</b>	-13.79	-2.741	-5.399	-25.26	16.97	9.797	10.81	-76.93	0.8058
<b>13c</b>	-14.55	-2.851	-5.708	-24.54	15.64	9.732	11.74	-75.70	0.8152
<b>13d</b>	-15.29	-2.934	-6.015	-24.47	18.18	9.686	10.38	-80.66	0.8435
<b>13e</b>	-14.09	-1.143	-5.254	-26.30	20.77	10.580	12.15	-88.50	0.9600
<b>13f</b>	-16.45	-3.189	-6.794	-25.84	21.89	12.820	10.85	-93.06	0.9395
<b>13g</b>	-15.08	-2.684	-5.401	-25.16	14.61	10.260	15.23	-87.20	1.0070
<b>13h</b>	-17.86	-3.206	-7.434	-27.08	9.12	9.591	11.77	-102.91	0.9055
<b>13i</b>	-13.83	-1.905	-6.337	-24.90	11.67	14.110	18.42	-79.77	1.2020
<b>13j</b>	-15.64	-2.877	-5.179	-24.42	15.74	9.646	10.97	-80.76	0.7939
<b>13k</b>	-18.45	-3.159	-7.445	-27.87	8.42	9.007	11.80	-103.10	0.8863
<b>13l</b>	-15.78	-3.070	-6.207	-23.93	19.26	10.880	9.36	-71.60	0.8769
<b>13m</b>	-16.80	-1.996	-6.526	-26.86	9.32	10.360	10.88	-74.05	0.9259
Podophyllotoxin	-18.68	-1.611	-7.660	-28.16	9.21	10.143	10.68	-103.40	0.9565
Colchicine	-19.18	-1.418	-8.605	-28.34	9.71	10.690	9.05	-104.00	0.9576

\*Binding energy of tubulin-ligands (kcal/mol) computed via GBSA/MM-type scoring function; Hbond: Hbond is Hydrogen Bond energy; Hphob: the hydrophobic energy in exposing a surface to water; VwInt: the van der Waals interaction energy (sum of gc and gh van der waals); Eintl: internal conformation energy of the ligand; Dsolv: the desolvation of exposed H-bond donors and acceptors; SolEl: the solvation electrostatics energy change upon binding; mfScore: the potential of mean force score; mfScore: the potential of mean force score; dTSsc: Loss of entropy by the rotatable protein side-chains.