SUPPLEMENTARY INFORMATION

Symmetrical di-substituted phenylamino-*s*-triazine derivatives as anticancer agents: *In vitro* and *in silico* approach

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MOLECULAR DOCKING

CONF EGFR

```
receptor = receptor.pdbqt
ligand = ligand.pdbqt


center_x = 22.0137
center_y = 0.252828
center_z = 52.794

size_x = 40
size_y = 40
size_z = 40

exhaustiveness = 8
num_modes = 10
energy_range = 4
```

CONF DHFR

```
receptor = receptor.pdbqt
ligand = ligand.pdbqt


center_x = -1.65679
center_y = 22.0285
center_z = 23.0763

size_x = 40
size_y = 40
size_z = 40

exhaustiveness = 8
num_modes = 10
energy_range = 4
```

CONF CDK2

```
receptor = receptor.pdbqt
ligand = ligand.pdbqt


center_x = 100.865
center_y = 101.747
center_z = 79.8926

size_x = 40
size_y = 40
size_z = 40

exhaustiveness = 8
num_modes = 10
energy_range = 4
```

CONF VEGFR2

```
receptor = receptor.pdbqt
ligand = ligand.pdbqt


center_x = 20.8237
center_y = 25.5351
center_z = 39.4596

size_x = 40
size_y = 40
size_z = 40

exhaustiveness = 8
num_modes = 10
energy_range = 4
```

CONF mTOR

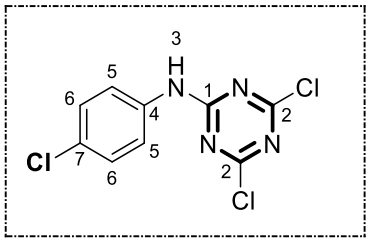
```
receptor = receptor.pdbqt
ligand = ligand.pdbqt


center_x = 50.1244
center_y = -1.7953
center_z = -45.9034

size_x = 40
size_y = 40
size_z = 40

exhaustiveness = 8
num_modes = 10
energy_range = 4
```

CONF PI3K

```
receptor = receptor.pdbqt
ligand = ligand.pdbqt


center_x = 21.3492
center_y = -4.07429
center_z = 20.8696

size_x = 40
size_y = 40
size_z = 40

exhaustiveness = 8
num_modes = 10
energy_range = 4
```

NMR DATA

COMPOUND 1a



Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	10.91 (1H, s)	-NH-
5	7.60 (2H, d, *J* = 9.0 Hz)	H_{Ar}
6	7.42 (2H, d, *J* = 8.5 Hz)	H_{Ar}

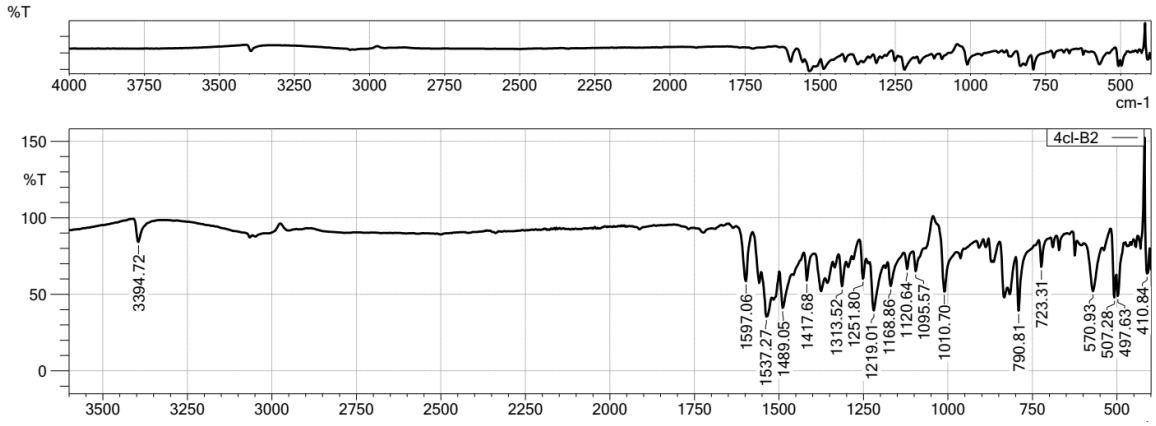
^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 163.8 (>C=, C_1), 154.1 (>C=, C_2), 135.9 (>C=, C_4), 128.8 (>C=, C_6), 128.4 (>C=, C_7), 123.1 (>C=, C_5).

LC-MS (*m/z*)

Expected formula: $C_9H_5Cl_3N_4$ Exact mass: 273.9580

$[M+H]^+$ calcd: 274.9653 $[M+H]^+$ found: 274.9405

IR (1a)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3250
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2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1
4cl-B2
150
%T
100
50
0
3394.72
1597.06
1537.27
1489.05
1417.68
1313.52
1251.80
1219.01
1168.86
1120.64
1095.57
1010.70
790.81
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570.93
507.28
497.63
410.84

MS (1a)

==== Shimadzu LCMSsolution Data Report ====

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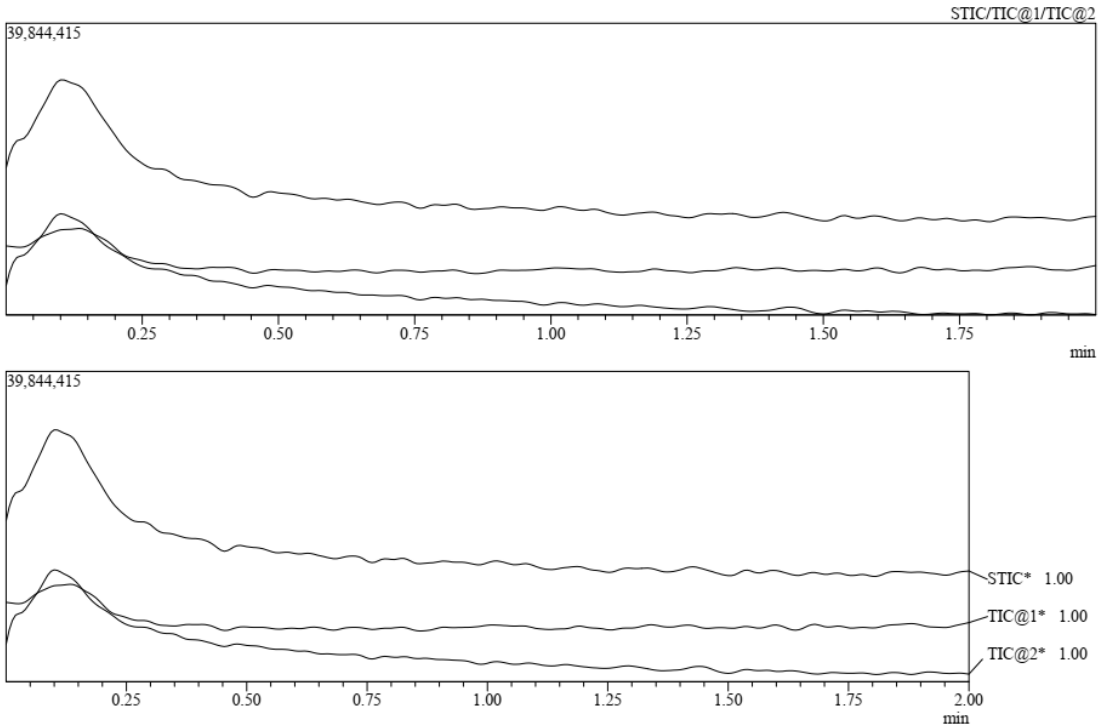
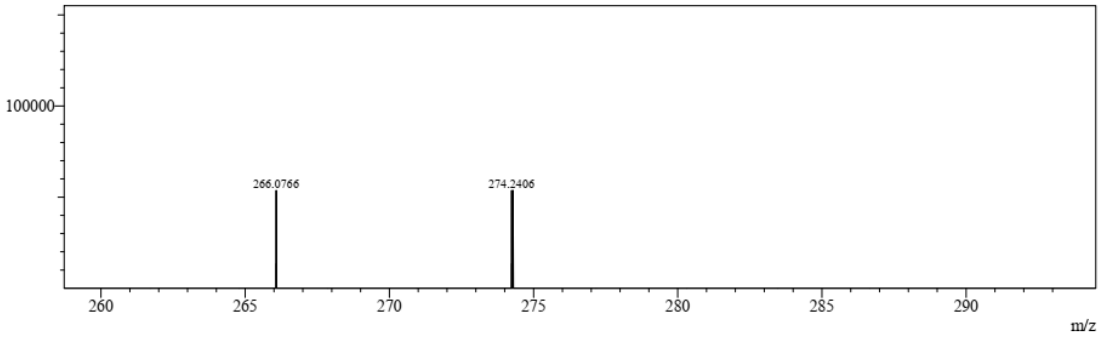
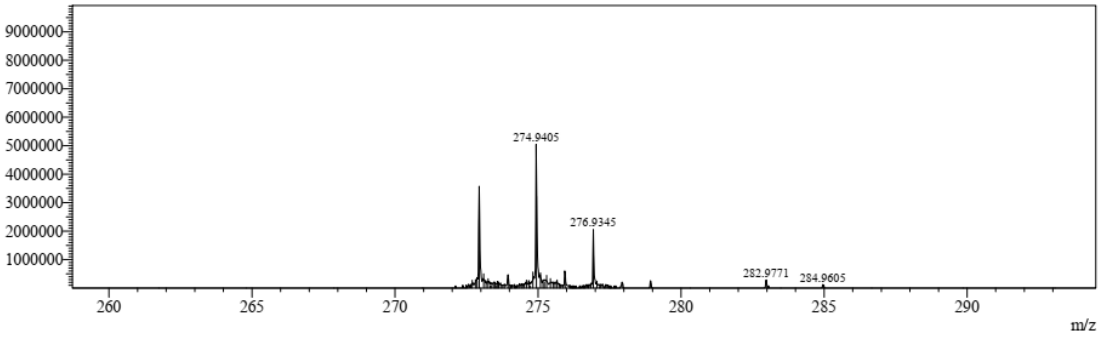


<Spectrum>

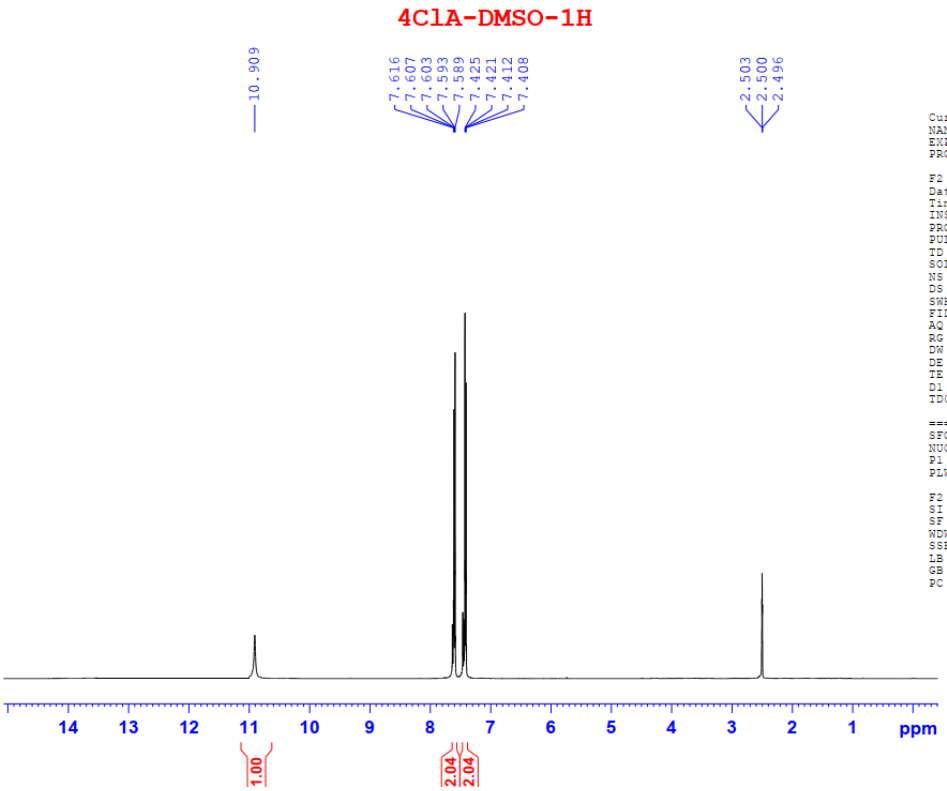
MSMS: Precursor m/z ----- /+ Base Peak 353.23(5416622)



MSMS: Precursor m/z ----- /- Base Peak 274.94(3223711)



^{1}H NMR (1a)

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EXPNO                       10
PROCNO                       1

F2 - Acquisition Parameters
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Time                    9.02
INSTRUM                spect
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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                       157.35
DW                       50.000 usec
DE                        6.50 usec
TE                      303.0 K
D1                 1.00000000 sec
TD0                         1

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

F2 - Processing parameters
SI                     65536
SF                 500.2390052 MHz
WDW                       EM
SSB                  0
LB                        0.30 Hz
GB                   0
PC                        1.00
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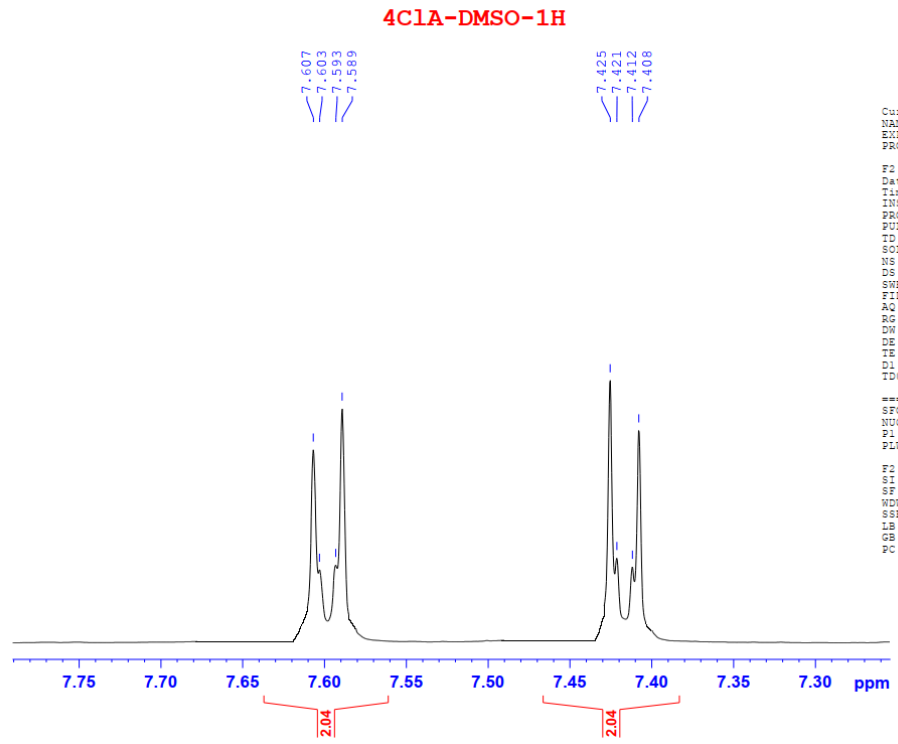


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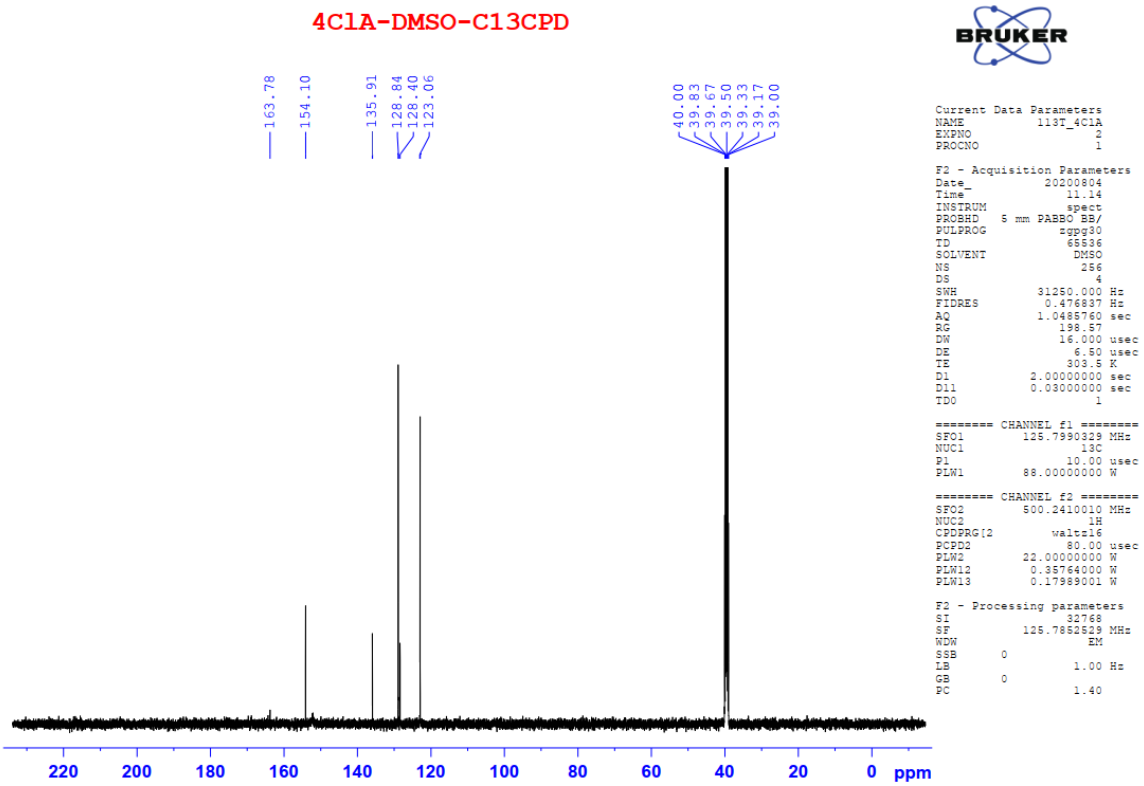
Current Data Parameters
NAME                 113T_4ClA
EXPNO                       10
PROCNO                       1

F2 - Acquisition Parameters
Date_               20200804
Time                    9.02
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                       157.35
DW                       50.000 usec
DE                        6.50 usec
TE                      303.0 K
D1                 1.00000000 sec
TD0                         1

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

F2 - Processing parameters
SI                     65536
SF                 500.2390052 MHz
WDW                       EM
SSB                  0
LB                        0.30 Hz
GB                   0
PC                        1.00
```

^{13}C NMR (1a)

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Current Data Parameters
NAME                  113T_4ClA
EXPNO                         2
PROCNO                        1

F2 - Acquisition Parameters
Date_                  20200804
Time                      11.14
INSTRUM                   spect
PROBHD     5 mm PABBO BB/
PULPROG                zgpg30
TD                        65536
SOLVENT                    DMSO
NS                          256
DS                            4
SWH                   31250.000 Hz
FIDRES                0.476837 Hz
AQ                    1.0485760 sec
RG                       198.57
DW                       16.000 usec
DE                        6.50 usec
TE                       303.5 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                           1

======== CHANNEL f1 ========
SFO1                125.7990329 MHz
NUC1                        13C
P1                       10.00 usec
PLW1                88.00000000 W

======== CHANNEL f2 ========
SFO2                500.2410010 MHz
NUC2                        1H
CPDPRG[2                waltz16
PCPD2                    80.00 usec
PLW2                22.00000000 W
PLW12                0.35764000 W
PLW13                0.17989001 W

F2 - Processing parameters
SI                          32768
SF                  125.7852529 MHz
WDW                            EM
SSB                 0
LB                        1.00 Hz
GB                  0
PC                        1.40
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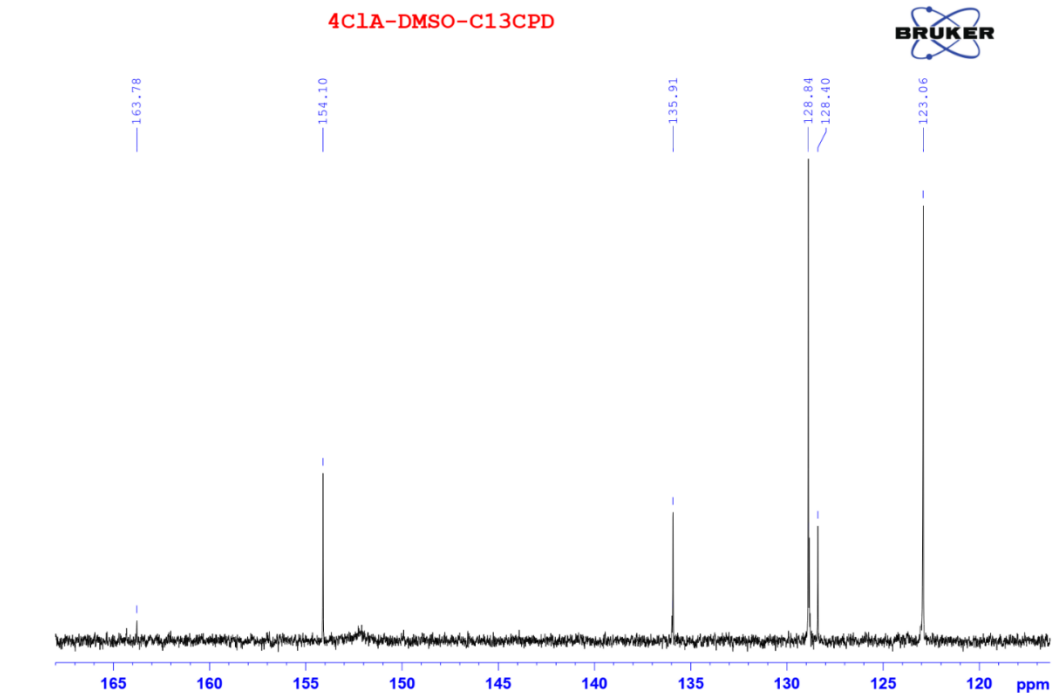
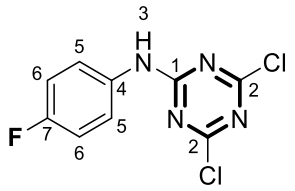


COMPOUND 1b



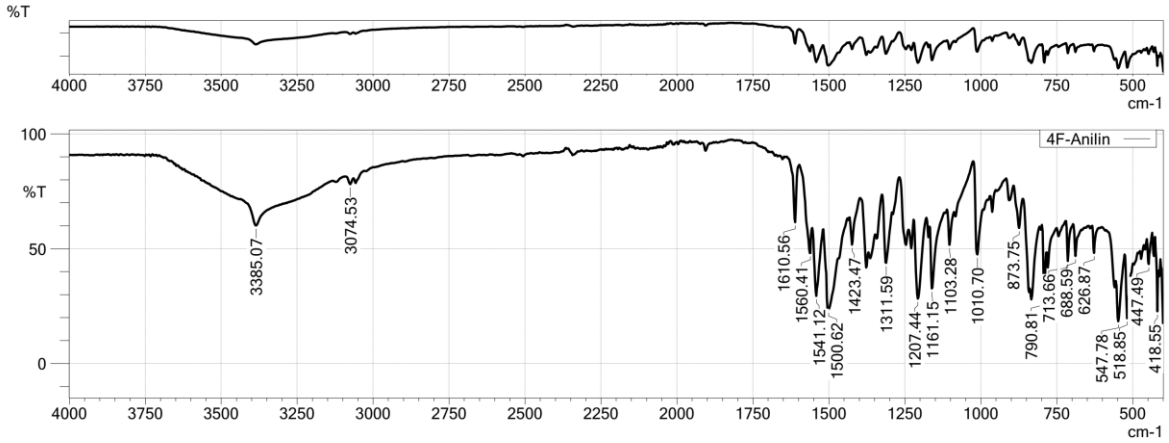
Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	11.13 (1H, s)	-NH-
5	7.58 (2H, d, *J* = 9.0 Hz)	H_{Ar}
6	7.20 (2H, d, *J* = 9.0 Hz)	H_{Ar}

^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 164.0 (>C=, C_1), 161.19 and 159.26 (>C=, J_{C-F} = 241.25 Hz, C_7), 154.0 (>C=, C_2), 133.40 and 133.38 (>C=, J_{C-F} = 2.5 Hz, C_4), 125.53 and 125.47 (>C=, J_{C-F} = 7.5 Hz, C_5), 116.33 and 116.15 (>C=, J_{C-F} = 22.5 Hz, C_6).

LC-MS (*m/z*)

Expected formula: $C_9H_5Cl_2FN_4$	Exact mass: 257.9875
$[M+H]^+$ calcd: 258.9948	$[M+H]^+$ found: 258.9718
$[M-H]^-$ calcd: 256.9803	$[M-H]^-$ found: 257.0161

IR (1b)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cm-1
100
%T
50
0
4F-Anilin
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3074.53
1610.56
1560.41
1541.12
1500.62
1423.47
1311.59
1207.44
1161.15
1103.28
1010.70
873.75
790.81
713.66
688.59
626.87
547.78
518.85
447.49
418.55
4000 3750 3500 3250 3000 2750 2500 2250 2000 1750 1500 1250 1000 750 500
cm-1

MS (1b)

==== Shimadzu LCMSsolution Data Report ====

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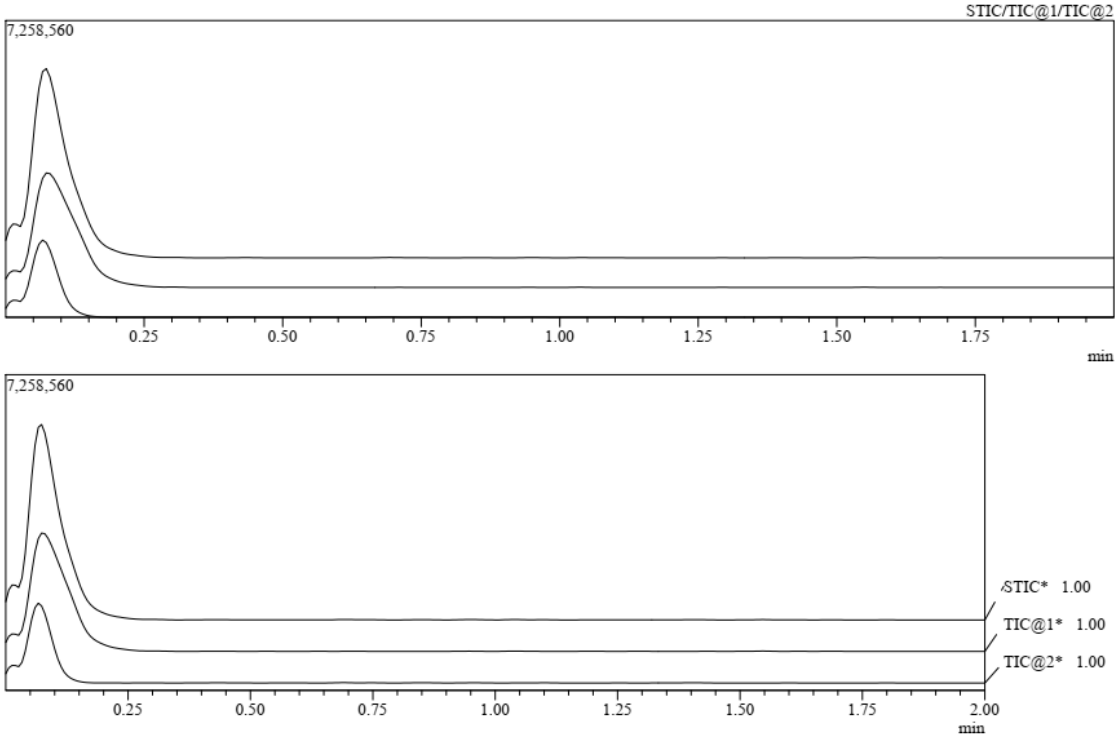
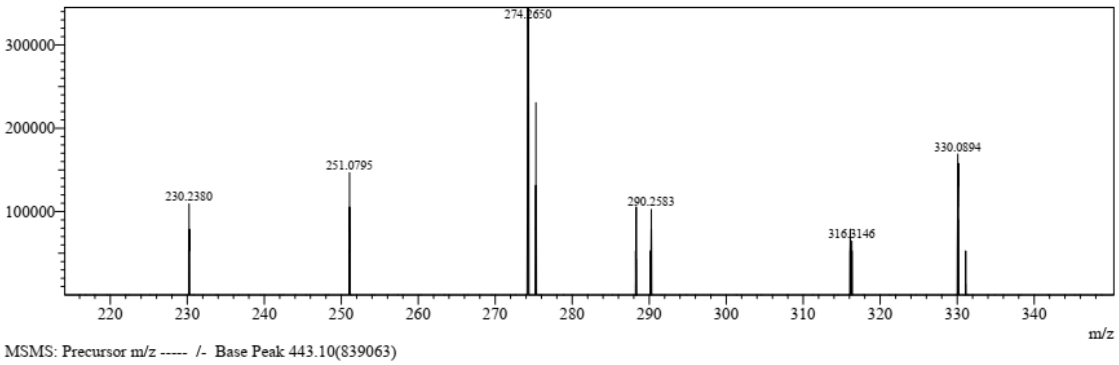
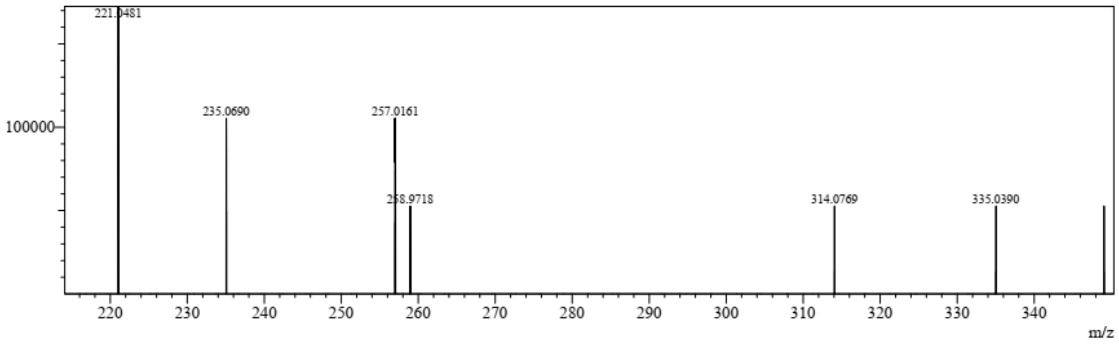


<Spectrum>

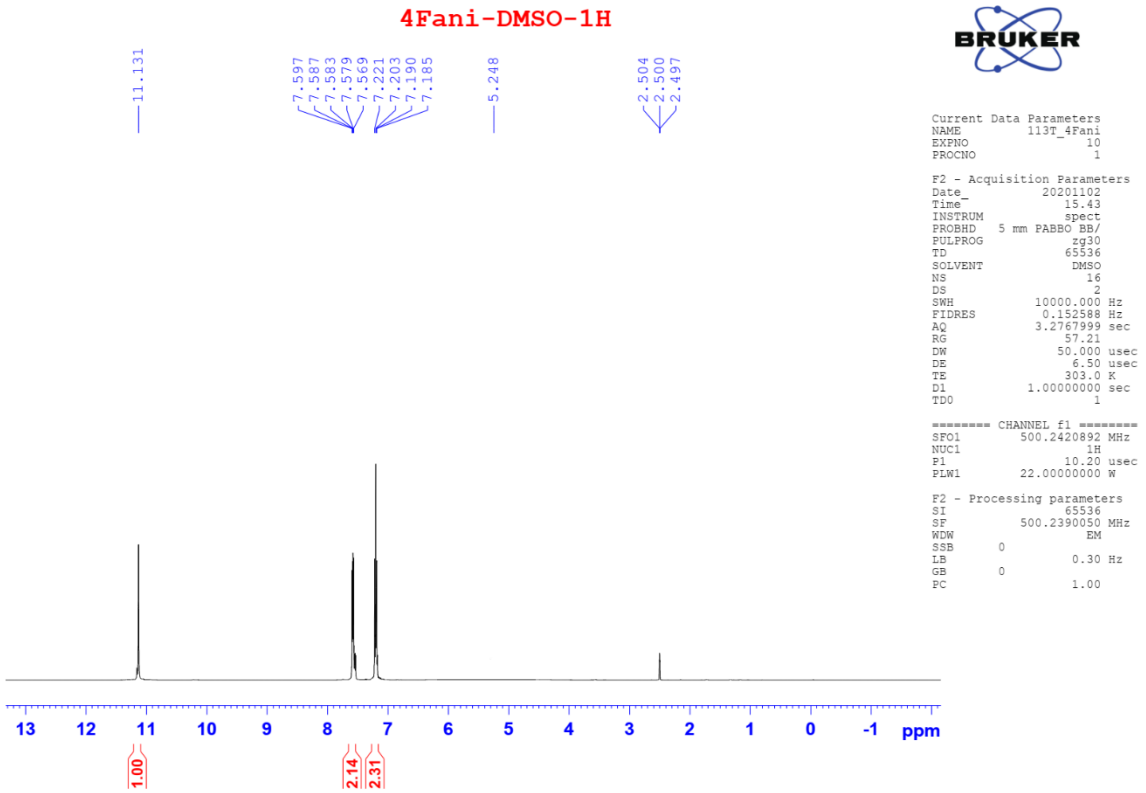
MSMS: Precursor m/z ----- /+ Base Peak 274.26(1281963)



MSMS: Precursor m/z ----- /- Base Peak 443.10(839063)



^{1}H NMR (1b)

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EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20201102
Time              15.43
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                57.21
DW               50.000 usec
DE                6.50 usec
TE                303.0 K
D1            1.00000000 sec
TD0                    1

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

F2 - Processing parameters
SI                 65536
SF            500.2390050 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
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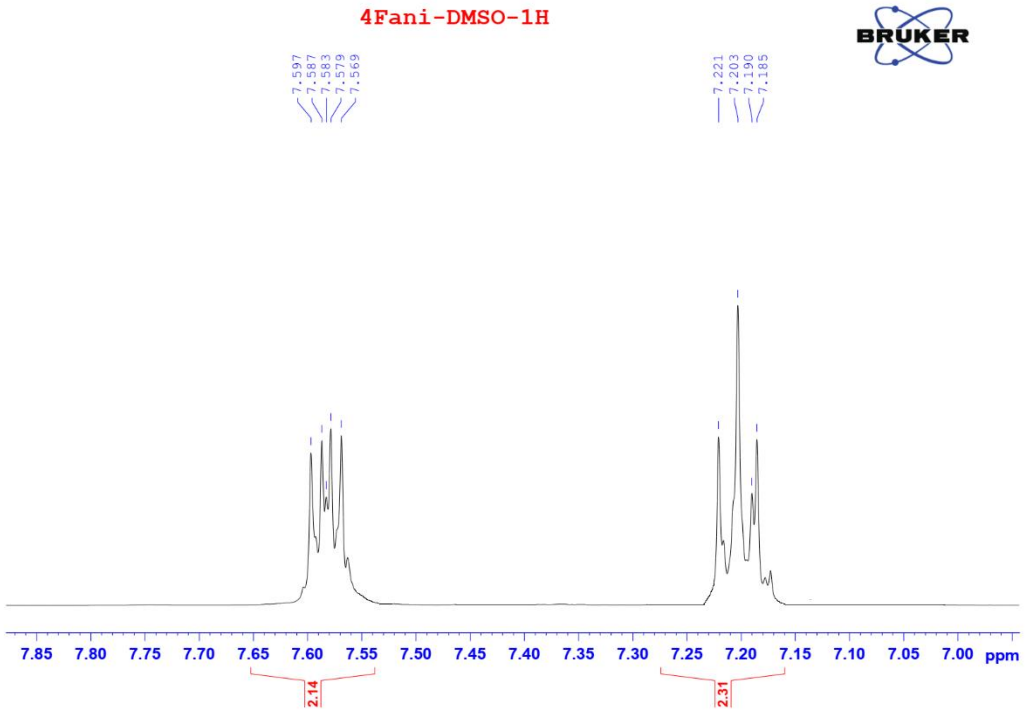
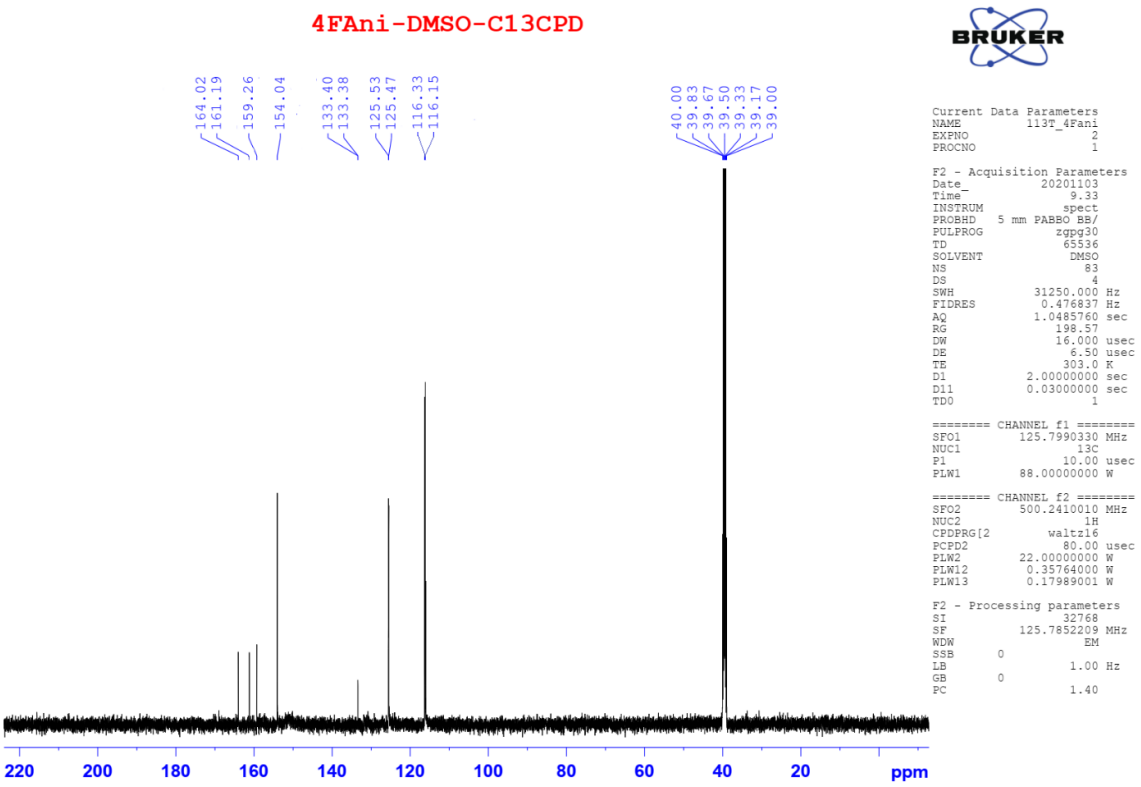


^{13}C NMR (1b)



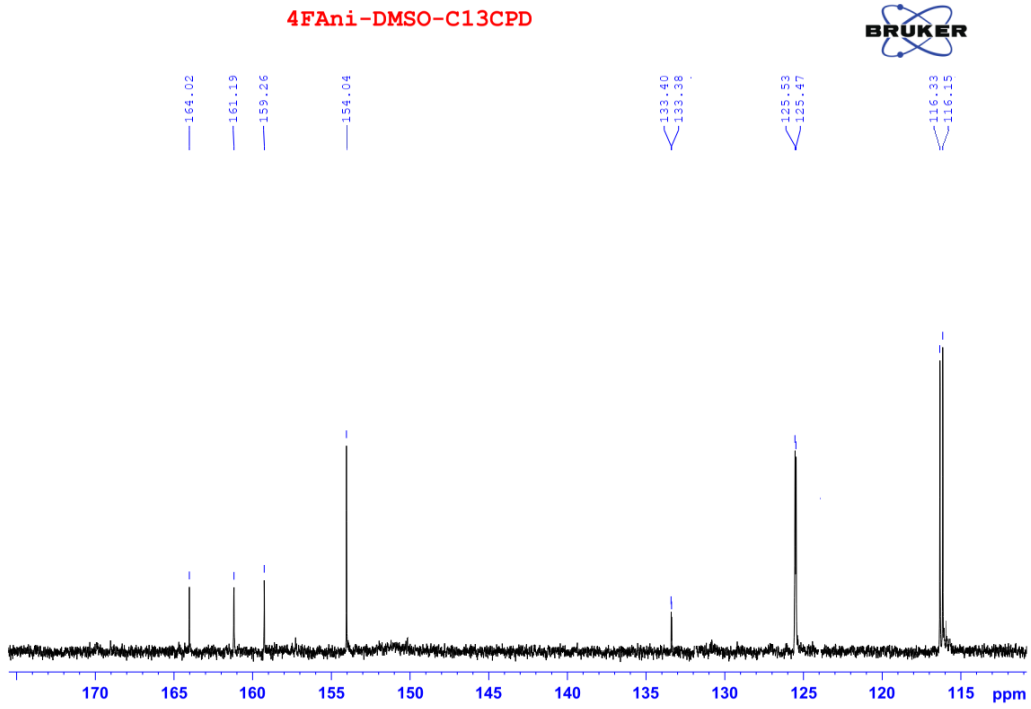

```
Current Data Parameters
NAME          113T_4Fani
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20201103
Time               9.33
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG         zgpg30
TD               65536
SOLVENT            DMSO
NS                   83
DS                    4
SWH           31250.000 Hz
FIDRES        0.476837 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
TD0                   1

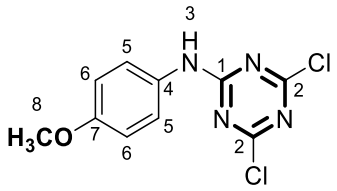
======== CHANNEL f1 ========
SFO1        125.7990330 MHz
NUC1                13C
P1                10.00 usec
PLW1        88.00000000 W

======== CHANNEL f2 ========
SFO2        500.2410010 MHz
NUC2                 1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2        22.00000000 W
PLW12        0.35764000 W
PLW13        0.17989001 W

F2 - Processing parameters
SI                32768
SF          125.7852209 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```



COMPOUND 1c



Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	10.97 (1H, s)	-NH-
5	7.42 (2H, d, *J* = 9.0 Hz)	H_{Ar}
6	6.95 (2H, d, *J* = 9.0 Hz)	H_{Ar}
8	3.10 (3H, s)	-OCH_3

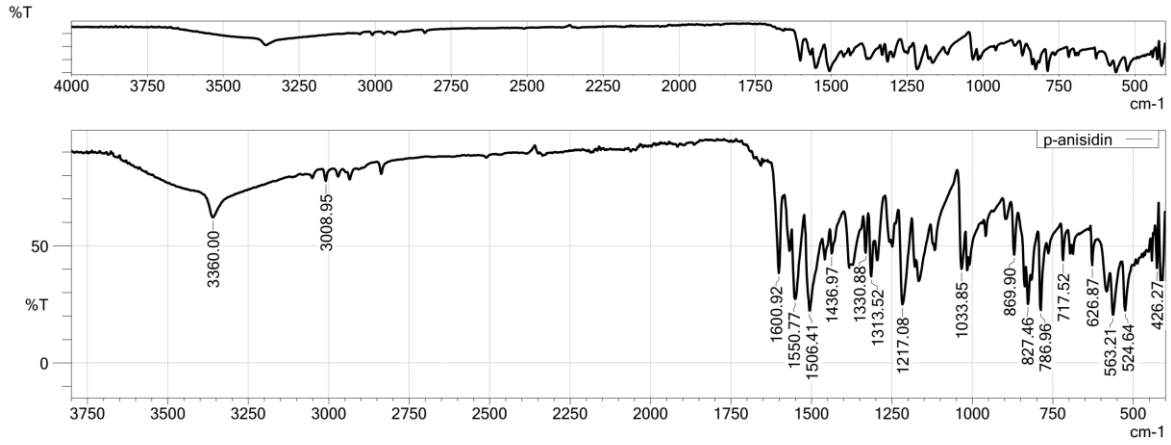
^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 157.8 (>C=, C_1), 153.7 (>C=, C_2), 150.0 (>C=, C_7), 127.8 (>C=, C_4), 125.3 (>C=, C_5), 114.6 (>C=, C_6), 55.5 (-OCH_3, C_8).

LC-MS (*m/z*)

Expected formula: $C_{10}H_8Cl_2N_4O$ Exact mass: 270.0075

$[M-H]^-$ calcd: 269.0002 $[M-H]^-$ found: 268.9938

IR (1b)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3250
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2250
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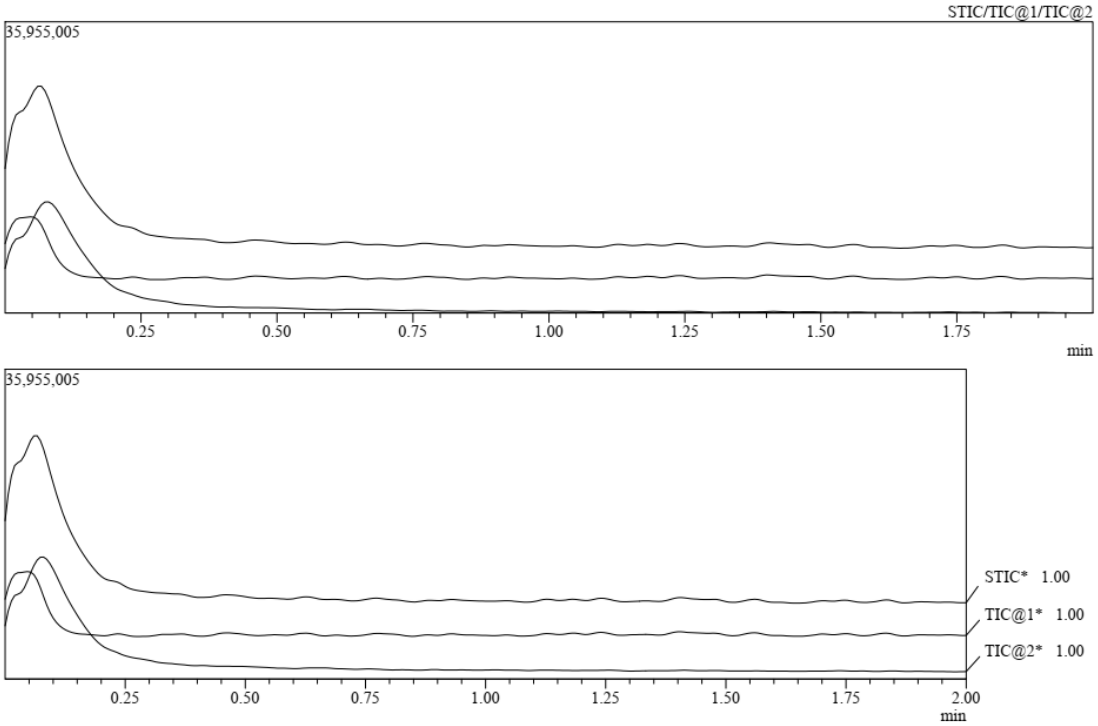
1500
1250
1000
750
500
cm-1
p-anisidin
50
%T
0
3360.00
3008.95
1600.92
1550.77
1506.41
1436.97
1330.88
1313.52
1217.08
1033.85
869.90
827.46
786.96
717.52
626.87
563.21
524.64
426.27

MS (1c)

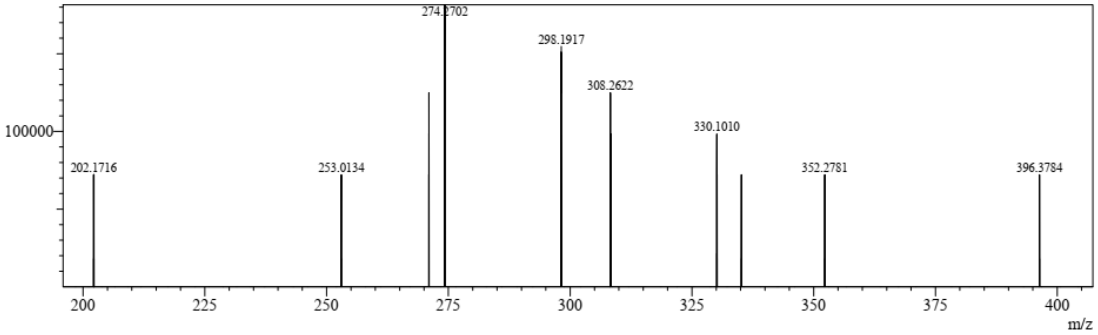
==== Shimadzu LCMSsolution Data Report ====

<Chromatogram>

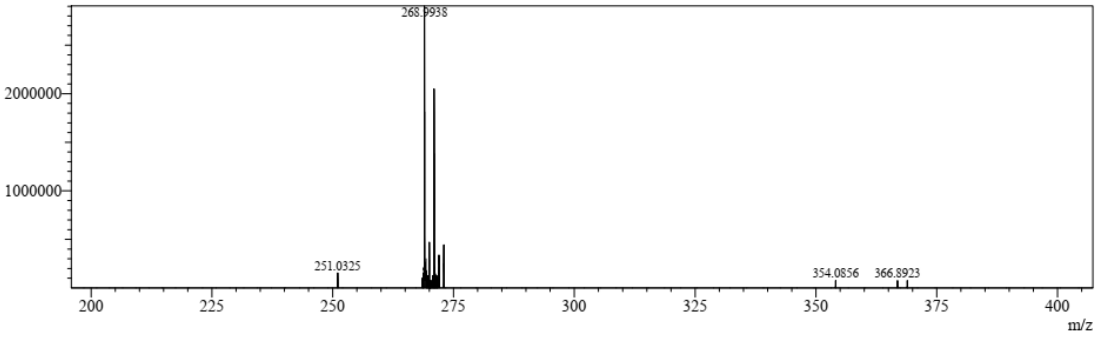


<Spectrum>

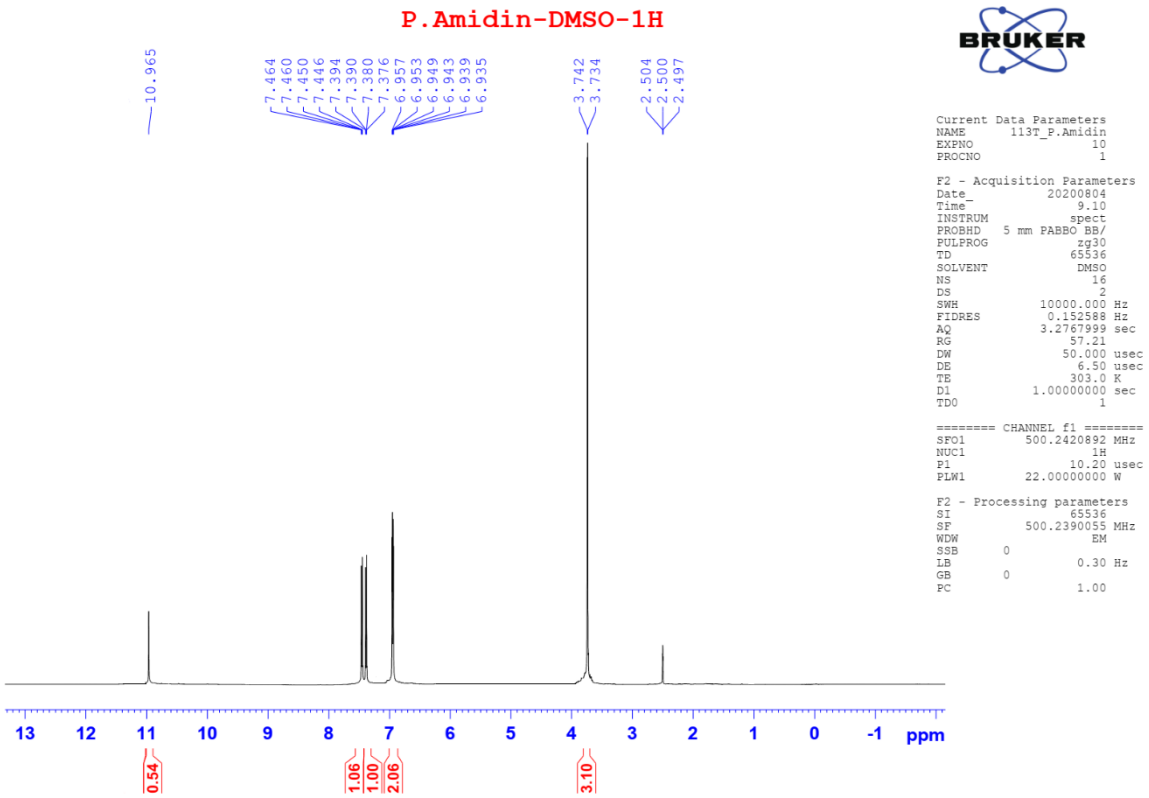
MSMS: Precursor m/z ----- /+ Base Peak 274.27(422405)



MSMS: Precursor m/z ----- /- Base Peak 268.99(1813064)



^{1}H NMR (1c)



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EXPNO 10
PROCNO 1

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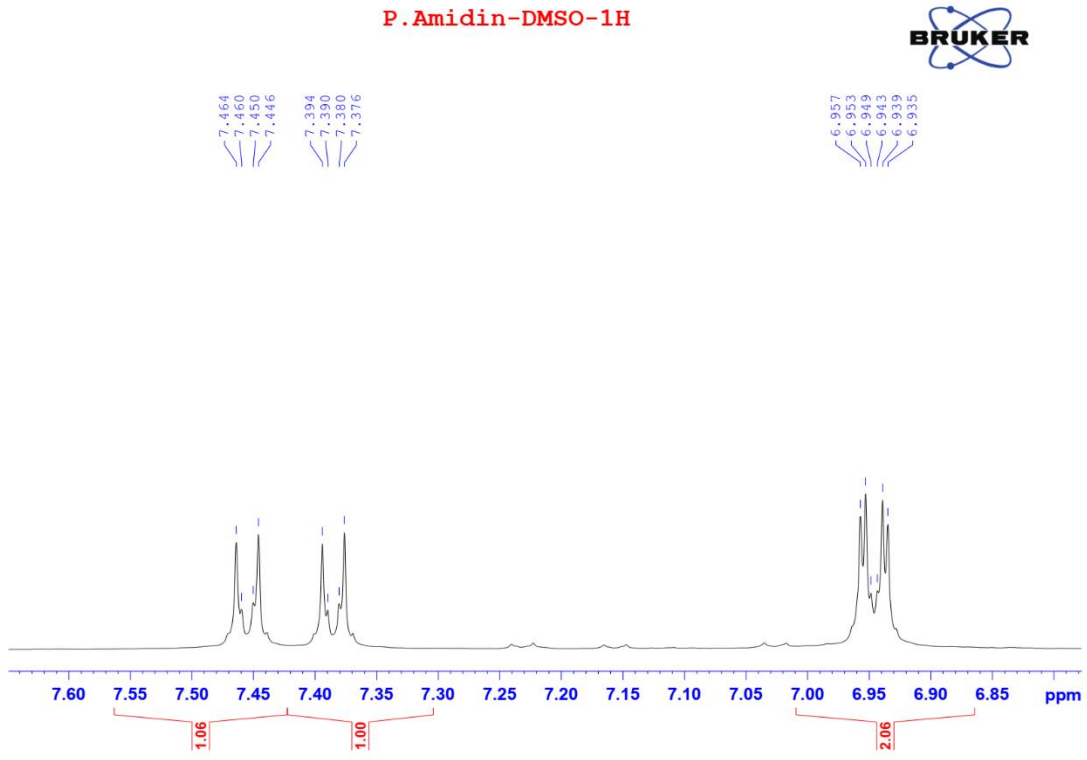
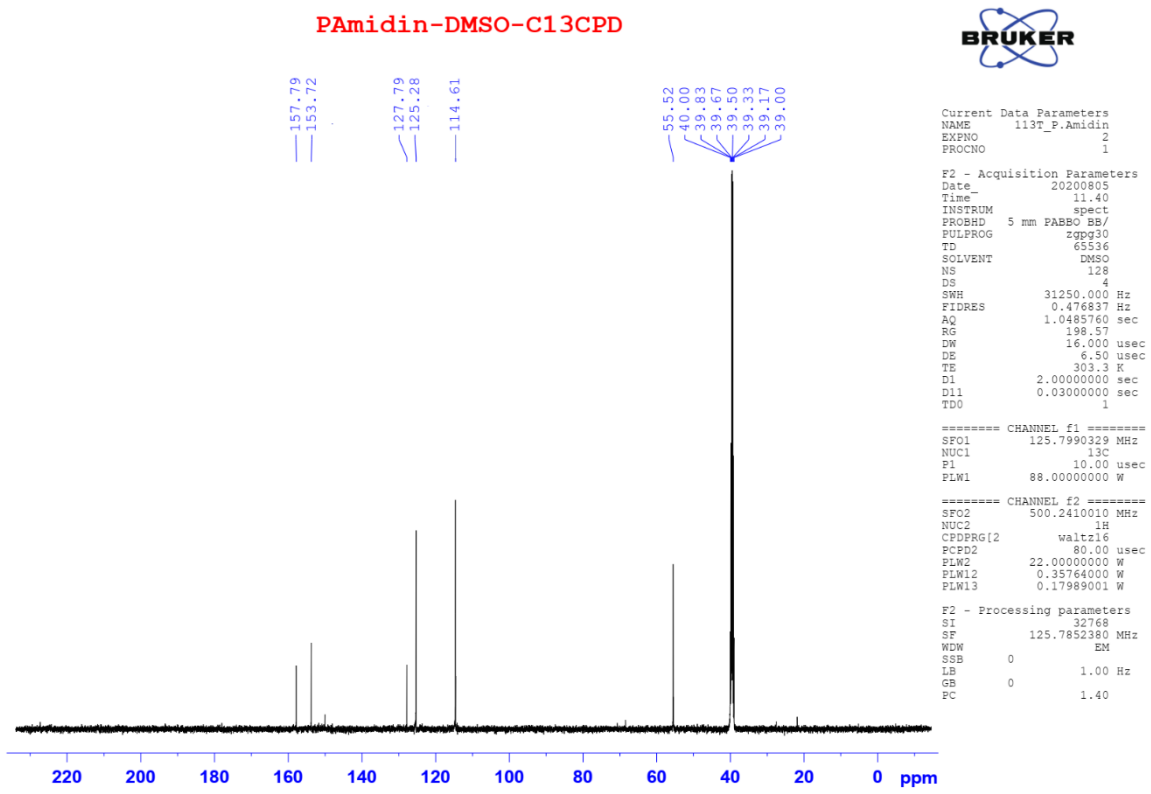
Time 9.10
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 57.21
DW 50.000 usec
DE 6.50 usec
TE 303.0 K
D1 1.00000000 sec
TD0 1

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

F2 - Processing parameters
SI 65536
SF 500.2390055 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



^{13}C NMR (1c)

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Current Data Parameters
NAME       113T_P.Amidin
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200805
Time              11.40
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                 128
DS                   4
SWH          31250.000 Hz
FIDRES        0.476837 Hz
AQ            1.0485760 sec
RG              198.57
DW              16.000 usec
DE               6.50 usec
TE              303.3 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1         125.7990329 MHz
NUC1               13C
P1               10.00 usec
PLW1        88.00000000 W

======== CHANNEL f2 ========
SFO2         500.2410010 MHz
NUC2               1H
CPDPRG[2        waltz16
PCPD2            80.00 usec
PLW2        22.00000000 W
PLW12        0.35764000 W
PLW13        0.17989001 W

F2 - Processing parameters
SI                32768
SF           125.7852380 MHz
WDW                EM
SSB       0
LB               1.00 Hz
GB        0
PC               1.40
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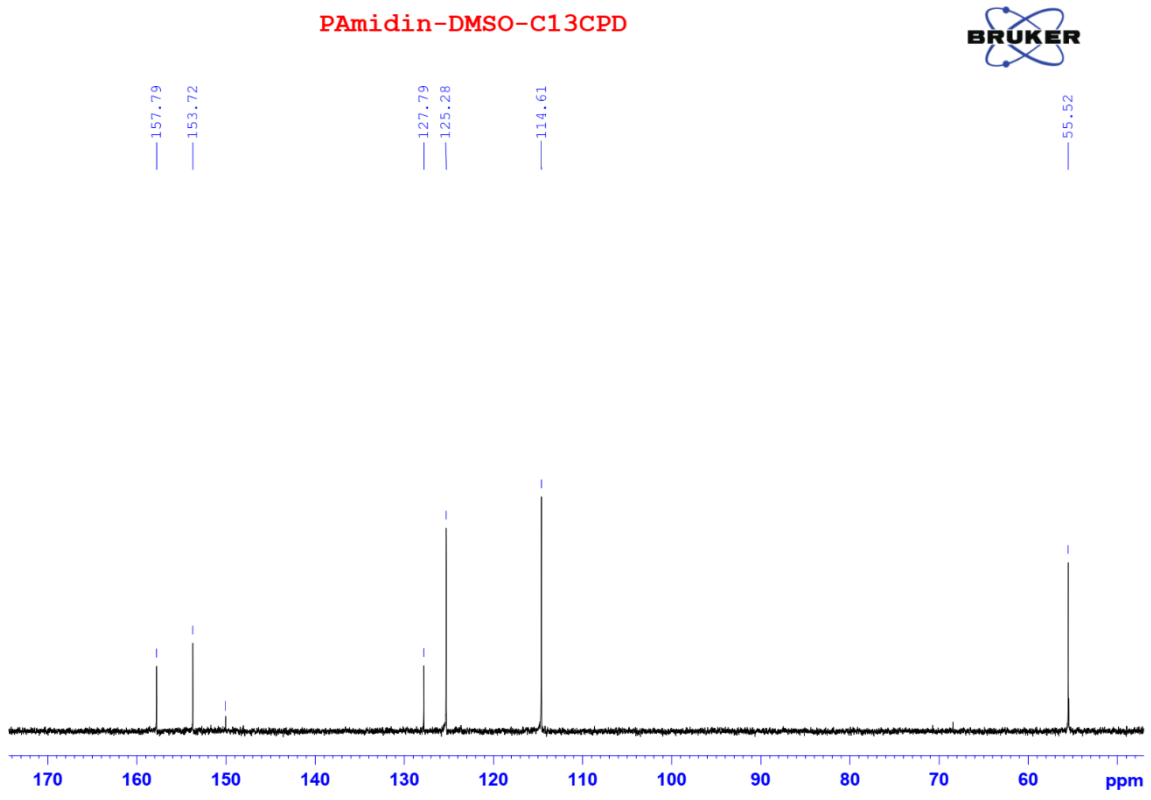
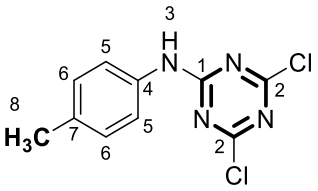


COMPOUND 1d



Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	11.03 (1H, s)	-NH-
5	7.46 (2H, d, *J* = 8.5 Hz)	H_{Ar}
6	7.17 (2H, d, *J* = 8.5 Hz)	H_{Ar}
8	2.27 (3H, s)	-CH_3

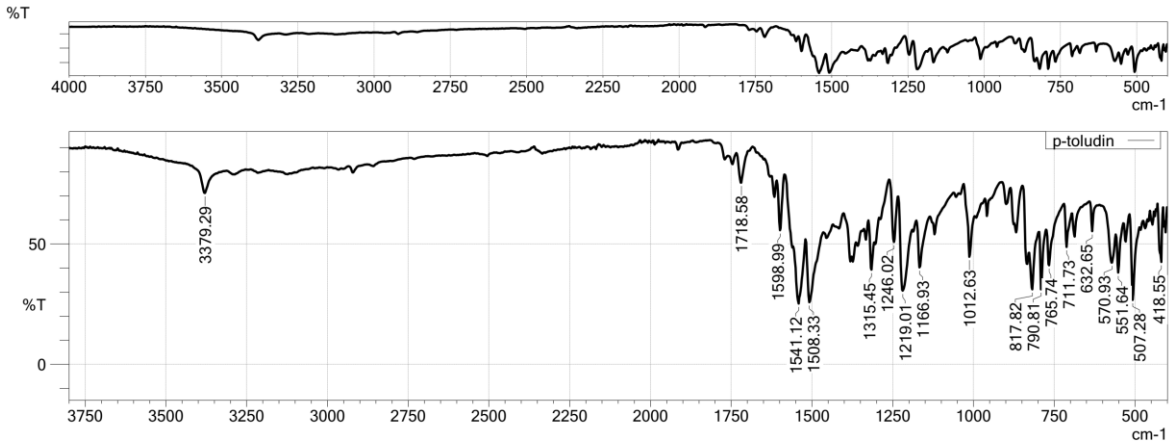
^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 163.8 (>C=, C_1), 153.8 (>C=, C_2), 134.4 (>C=, C_4), 130.4 (>C=, C_7), 129.7 (>C=, C_6), 121.8 (>C=, C_5), 20.6 (-CH_3, C_8).

LC-MS (*m/z*)

Expected formula: $C_{10}H_8Cl_2N_4$ Exact mass: 254.0126

$[M-H]^-$ calcd: 253.0053 $[M-H]^-$ found: 253.0039

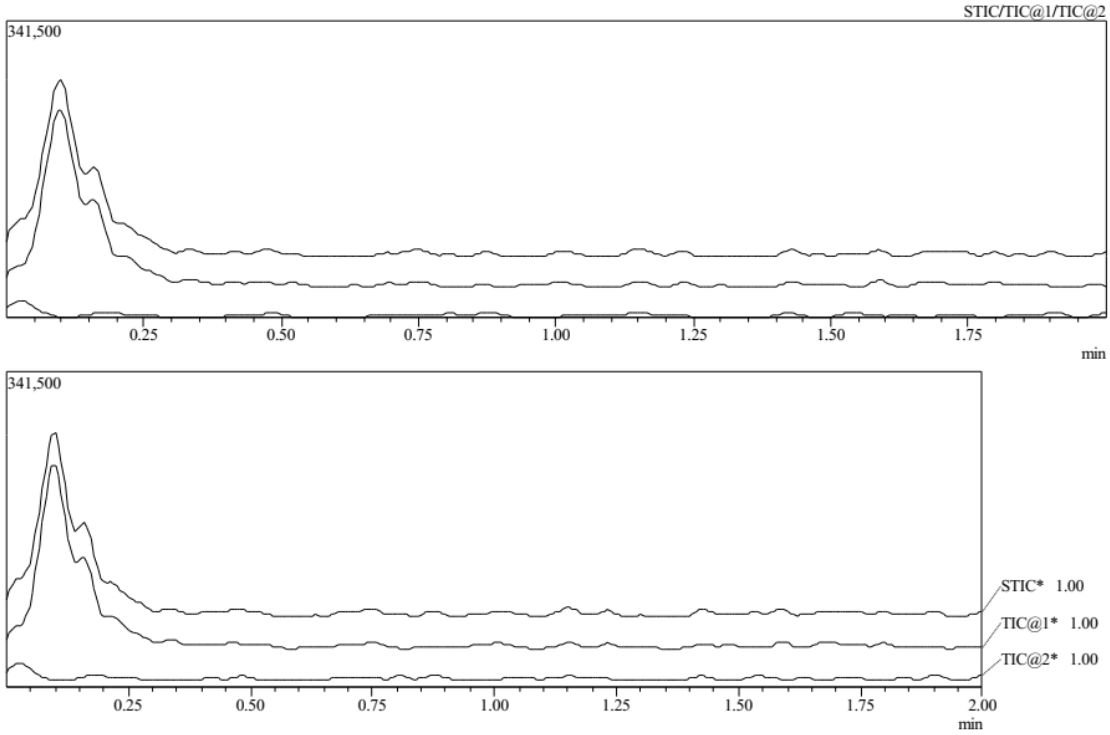
IR (1d)


%T
4000
3750
3500
3250
3000
2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1
p-toludin
3379.29
1718.58
1598.99
1541.12
1508.33
1315.45
1246.02
1219.01
1166.93
1012.63
817.82
790.81
765.74
711.73
632.65
570.93
551.64
507.28
418.55
50
%T
0
3750
3500
3250
3000
2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1

MS (1d)

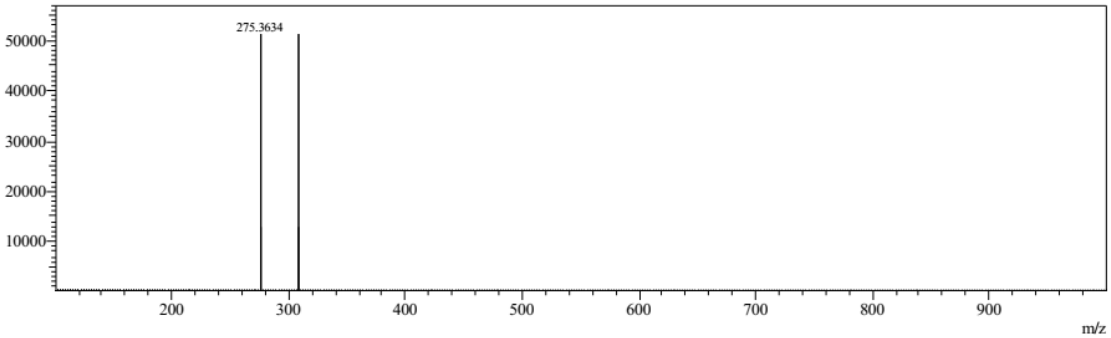
==== Shimadzu LCMSsolution Data Report ====

<Chromatogram>

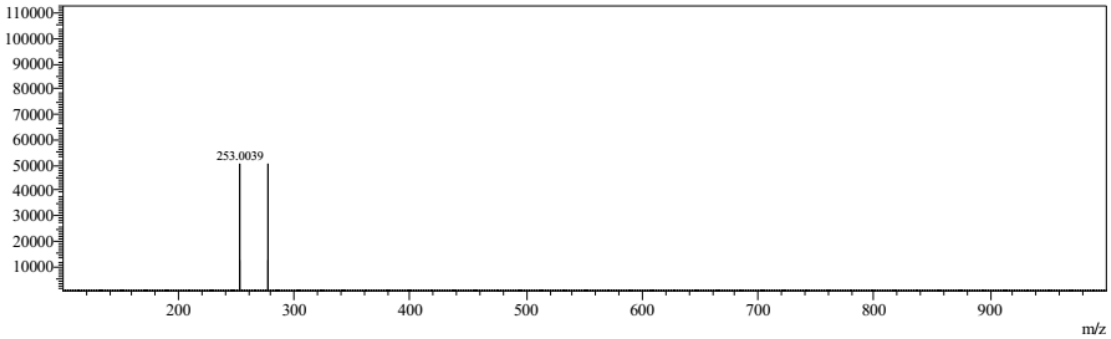


<Spectrum>

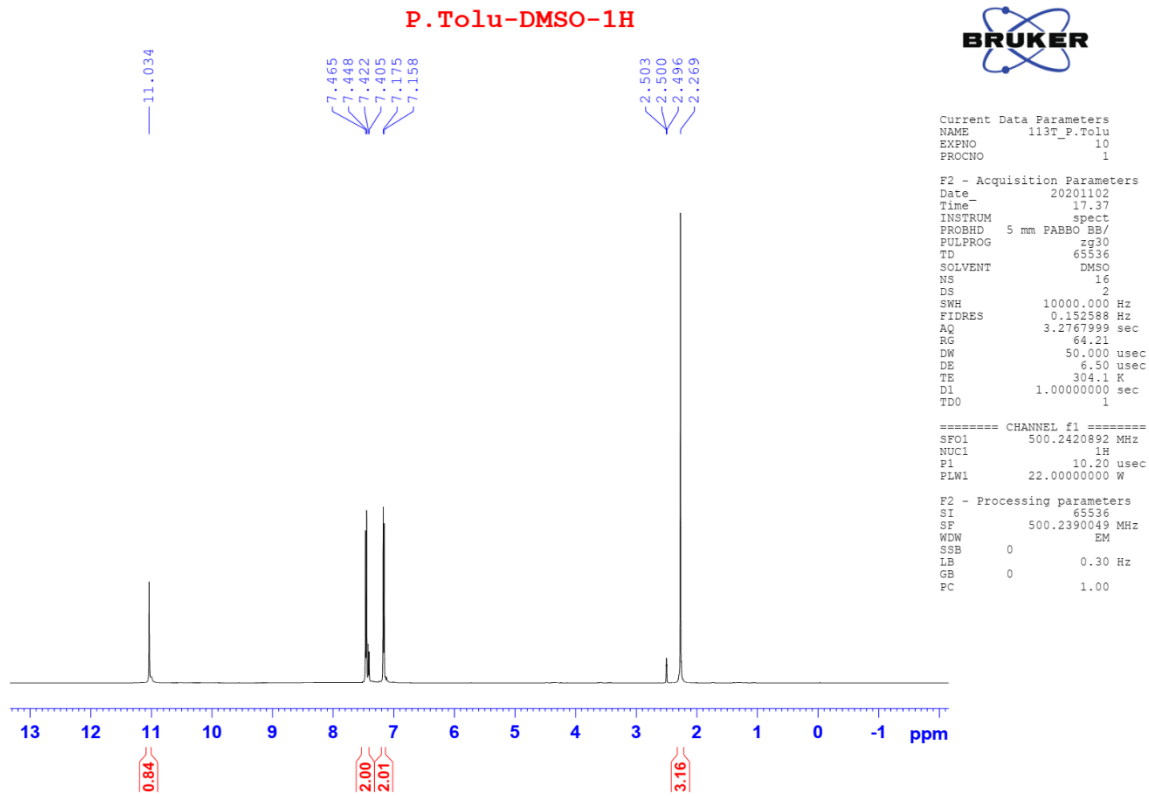
MSMS: Precursor m/z ----- /+ Base Peak 275.36(12800)



MSMS: Precursor m/z ----- /- Base Peak 253.00(12672)



^{1}H NMR (1d)

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Current Data Parameters
NAME          113T_P.Tolu
EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_           20201102
Time               17.37
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                 64.21
DW                50.000 usec
DE                 6.50 usec
TE                304.1 K
D1             1.00000000 sec
TD0                    1

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

F2 - Processing parameters
SI                 65536
SF            500.2390049 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```
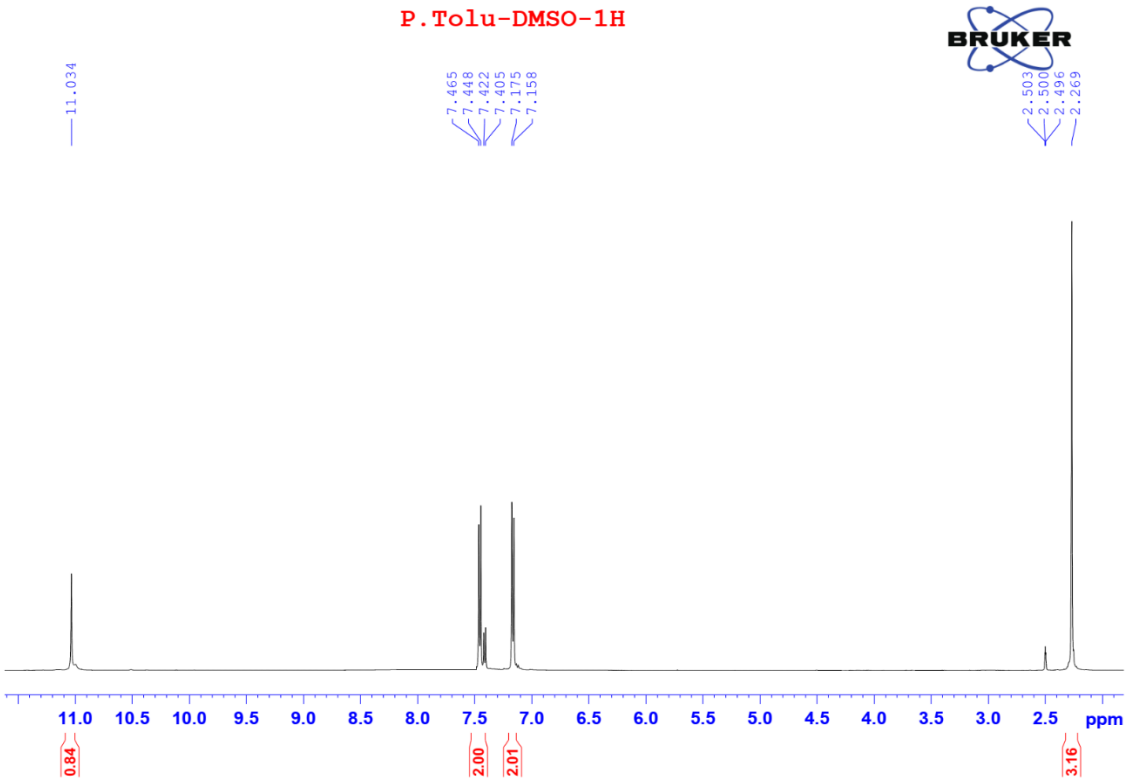
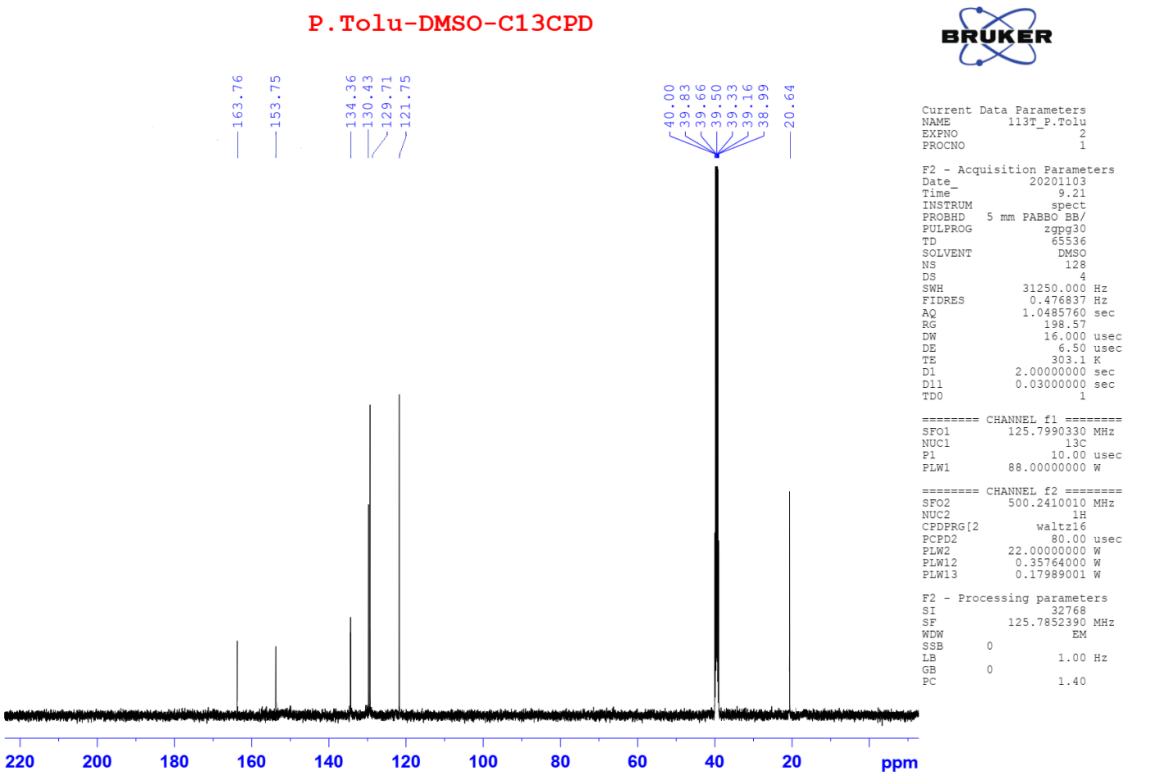
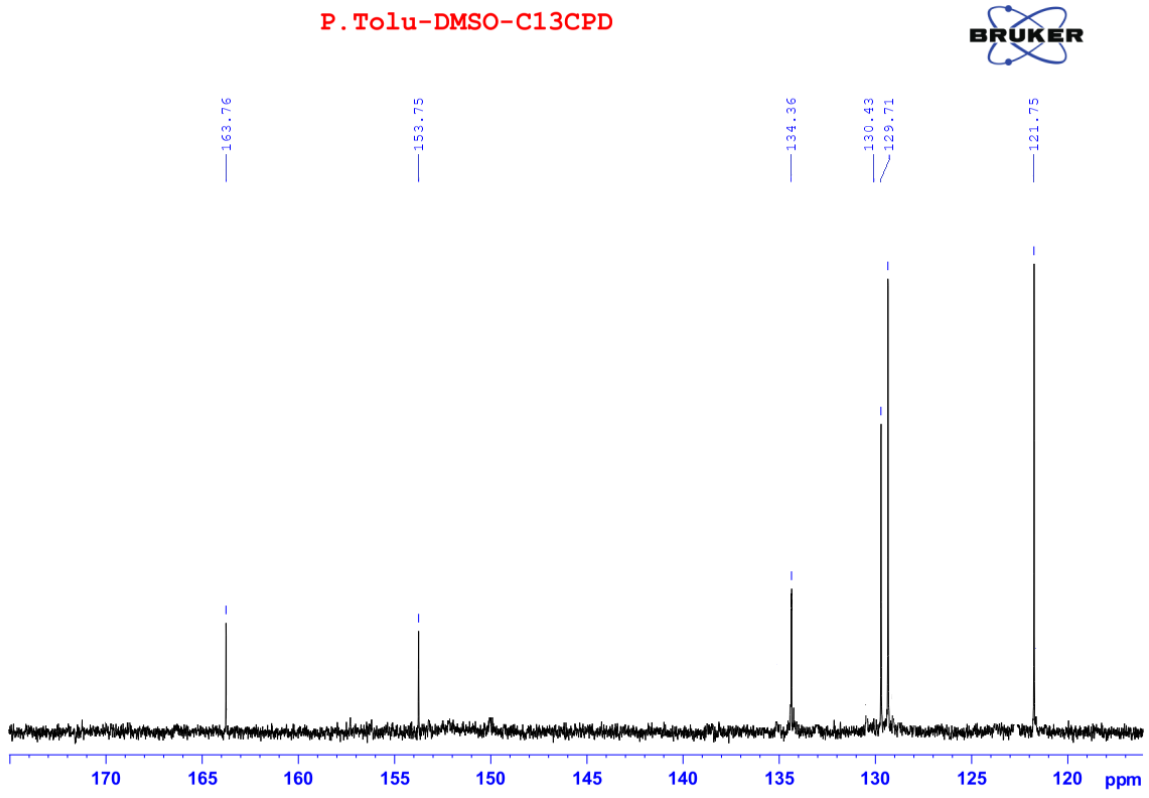
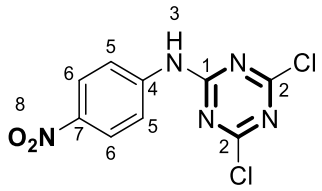



^{13}C NMR (1d)


P.Tolu-DMSO-C13CPD
BRUKER
163.76
153.75
134.36
130.43
129.71
121.75
40.00
39.83
39.66
39.50
39.33
39.16
38.99
20.64
220
200
180
160
140
120
100
80
60
40
20
ppm
Current Data Parameters
NAME 113T_P.Tolu
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201103
Time 9.21
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 128
DS 4
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0485760 sec
RG 198.57
DW 16.000 usec
DE 6.50 usec
TE 303.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 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
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 22.00000000 W
PLW12 0.35764000 W
PLW13 0.17989001 W
F2 - Processing parameters
SI 32768
SF 125.7852390 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40


P.Tolu-DMSO-C13CPD
BRUKER
163.76
153.75
134.36
130.43
129.71
121.75
170
165
160
155
150
145
140
135
130
125
120
ppm

COMPOUND 1e



Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	10.89 (1H, s)	-NH-
5	7.91 (2H, d, *J* = 9.0 Hz)	H_{Ar}
6	8.25 (2H, d, *J* = 9.0 Hz)	H_{Ar}

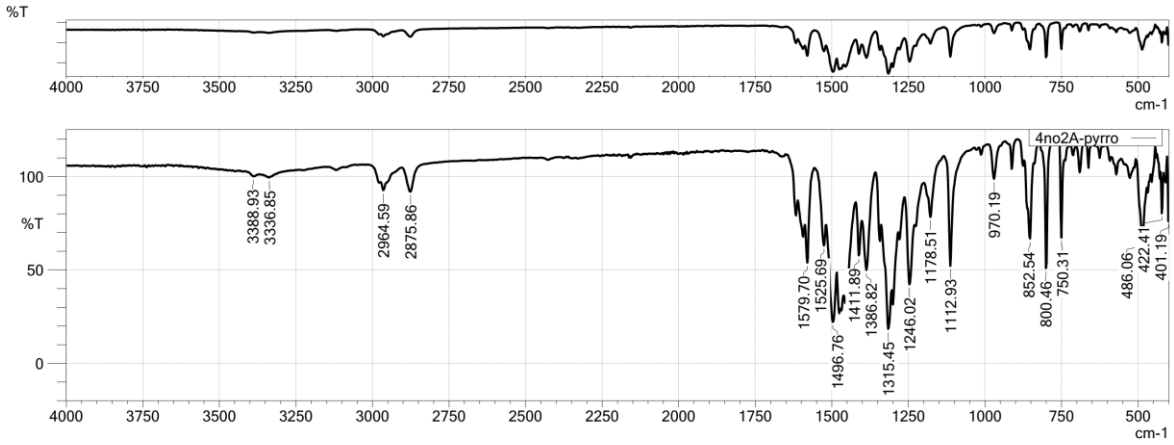
^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 160.7 (>C=, C_1), 154.2 (>C=, C_2), 144.2 (>C=, C_4), 142.5 (>C=, C_7), 125.0 (>C=, C_6), 119.8 (>C=, C_5).

LC-MS (*m/z*)

Expected formula: $C_9H_5Cl_2N_5O_2$ Exact mass: 284.9820

$[M-H]^-$ calcd: 283.9748 $[M-H]^-$ found: 283.9722

IR (1e)


%T
4000 3750 3500 3250 3000 2750 2500 2250 2000 1750 1500 1250 1000 750 500
cm-1
4no2A-pyrro
100
%T
50
0
3388.93
3336.85
2964.59
2875.86
1579.70
1525.69
1496.76
1411.89
1386.82
1315.45
1246.02
1178.51
1112.93
970.19
852.54
800.46
750.31
486.06
422.41
401.19
4000 3750 3500 3250 3000 2750 2500 2250 2000 1750 1500 1250 1000 750 500
cm-1

MS (1e)

==== Shimadzu LCMSsolution Data Report ====

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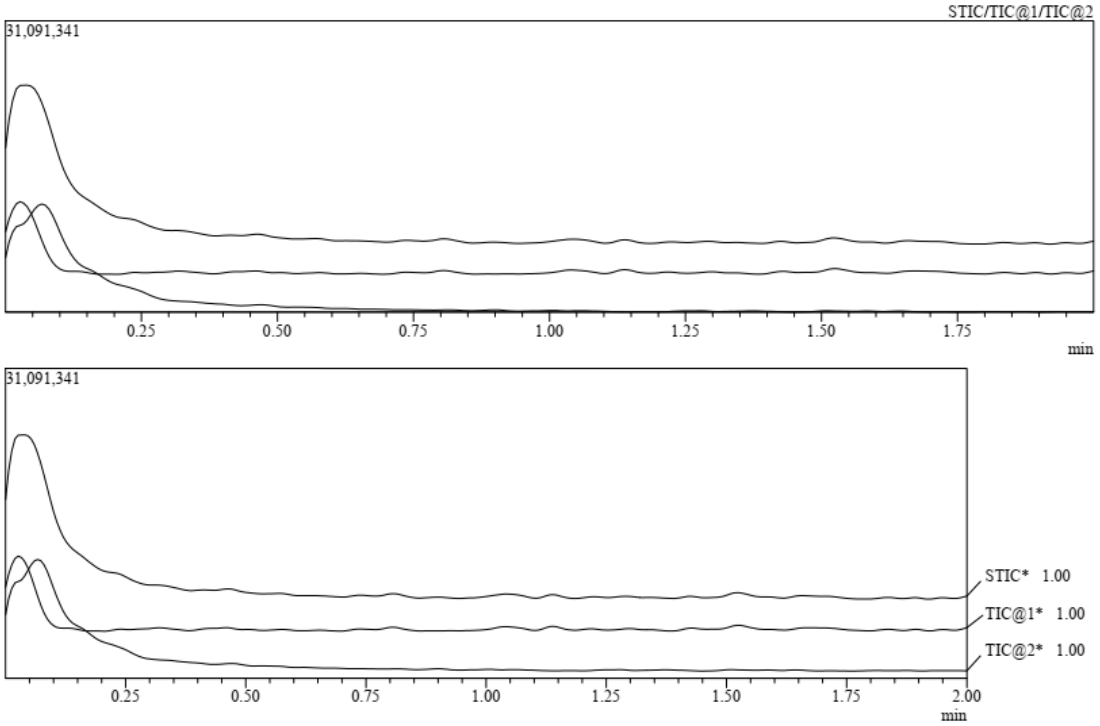
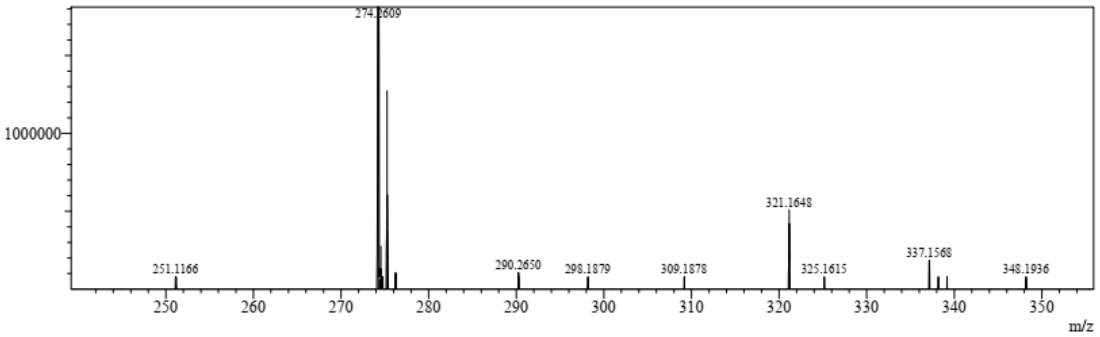
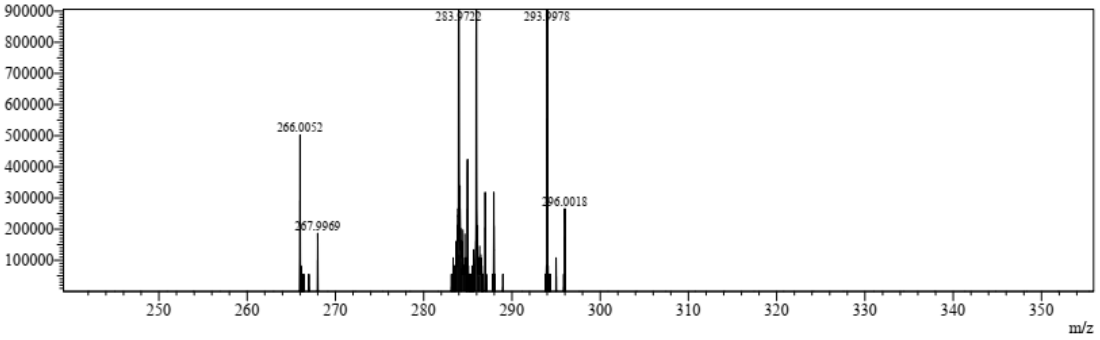


<Spectrum>

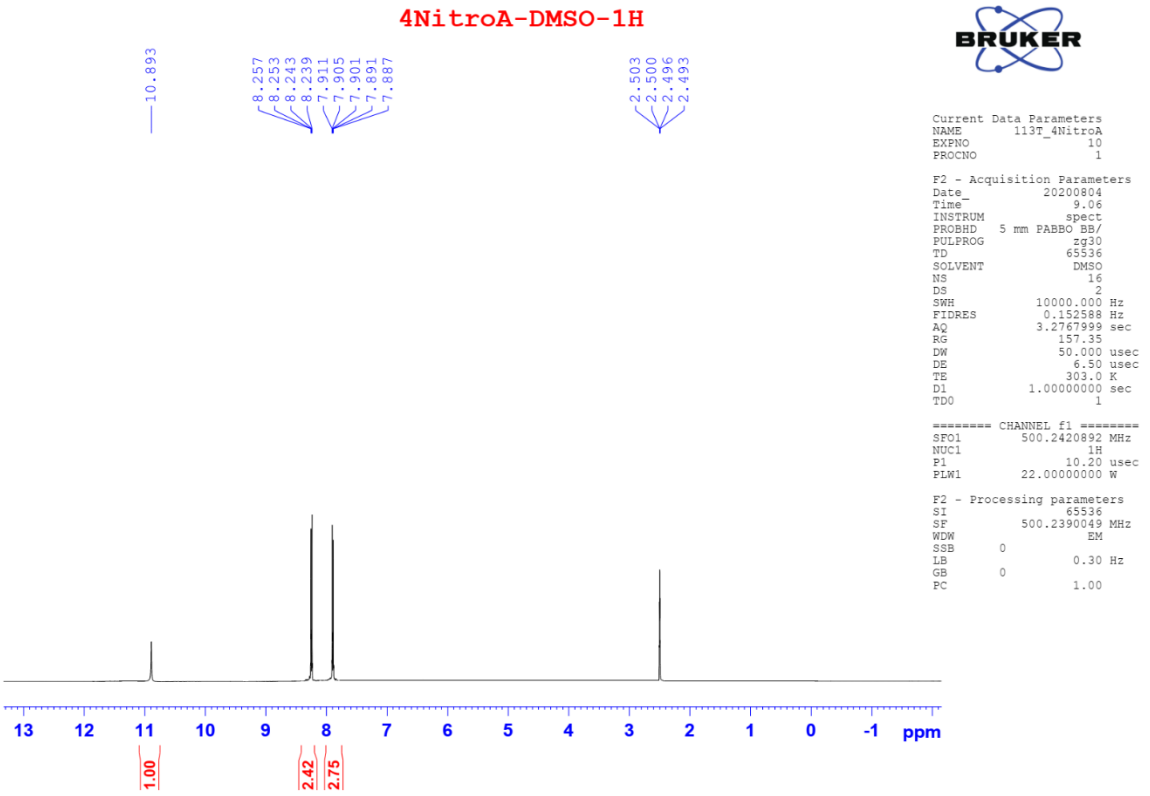
MSMS: Precursor m/z ----- /+ Base Peak 274.26(6856597)



MSMS: Precursor m/z ----- /- Base Peak 283.97(1729557)



^{1}H NMR (1e)

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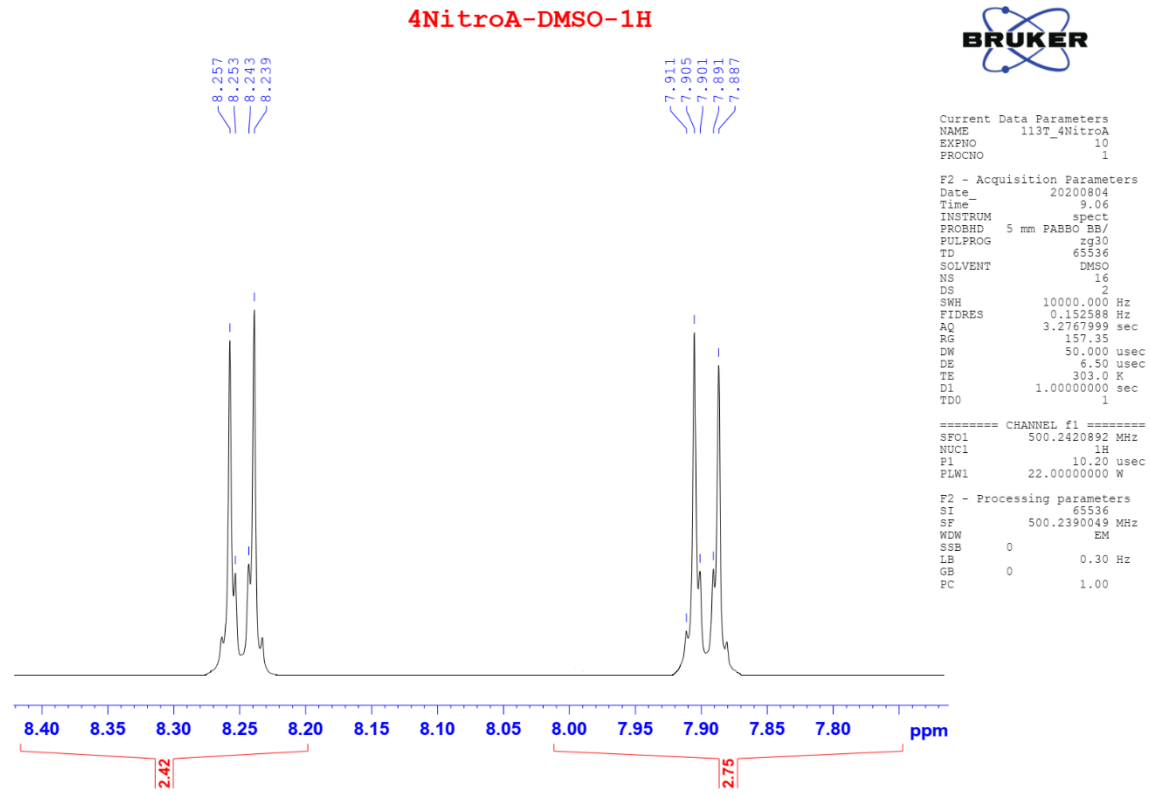
Current Data Parameters
NAME        113T_4NitroA
EXPNO               10
PROCNO               1

F2 - Acquisition Parameters
Date_          20200804
Time              9.06
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              157.35
DW              50.000 usec
DE               6.50 usec
TE              303.0 K
D1          1.00000000 sec
TD0                 1

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

F2 - Processing parameters
SI              65536
SF         500.2390049 MHz
WDW                EM
SSB       0
LB              0.30 Hz
GB        0
PC              1.00
```

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Current Data Parameters
NAME        113T_4NitroA
EXPNO               10
PROCNO               1

F2 - Acquisition Parameters
Date_          20200804
Time              9.06
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              157.35
DW              50.000 usec
DE               6.50 usec
TE              303.0 K
D1          1.00000000 sec
TD0                 1

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

F2 - Processing parameters
SI              65536
SF         500.2390049 MHz
WDW                EM
SSB       0
LB              0.30 Hz
GB        0
PC              1.00
```
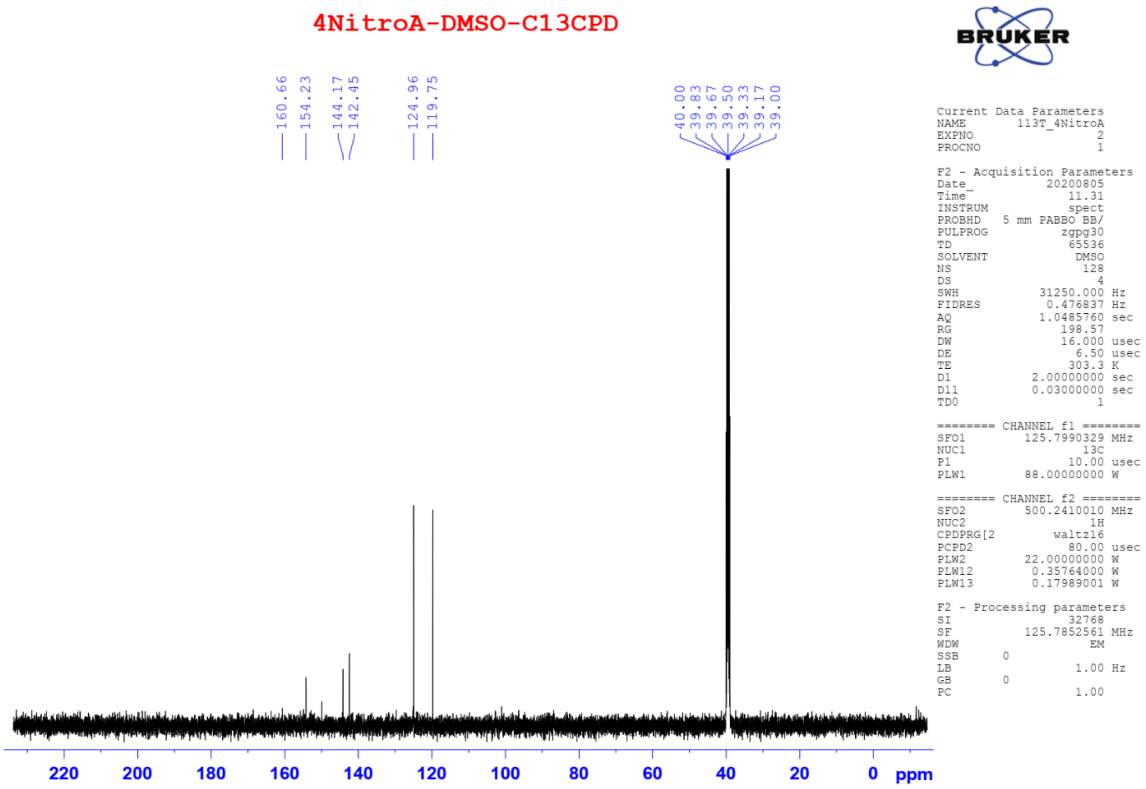

^{13}C NMR (1e)




```
Current Data Parameters
NAME        113T_4NitroA
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200805
Time              11.31
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                 128
DS                   4
SWH          31250.000 Hz
FIDRES        0.476837 Hz
AQ            1.0485760 sec
RG              198.57
DW              16.000 usec
DE               6.50 usec
TE              303.3 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1        125.7990329 MHz
NUC1               13C
P1               10.00 usec
PLW1        88.00000000 W

======== CHANNEL f2 ========
SFO2        500.2410010 MHz
NUC2               1H
CPDPRG[2        waltz16
PCPD2            80.00 usec
PLW2        22.00000000 W
PLW12        0.35764000 W
PLW13        0.17989001 W

F2 - Processing parameters
SI               32768
SF          125.7852561 MHz
WDW                 EM
SSB       0
LB               1.00 Hz
GB        0
PC               1.00
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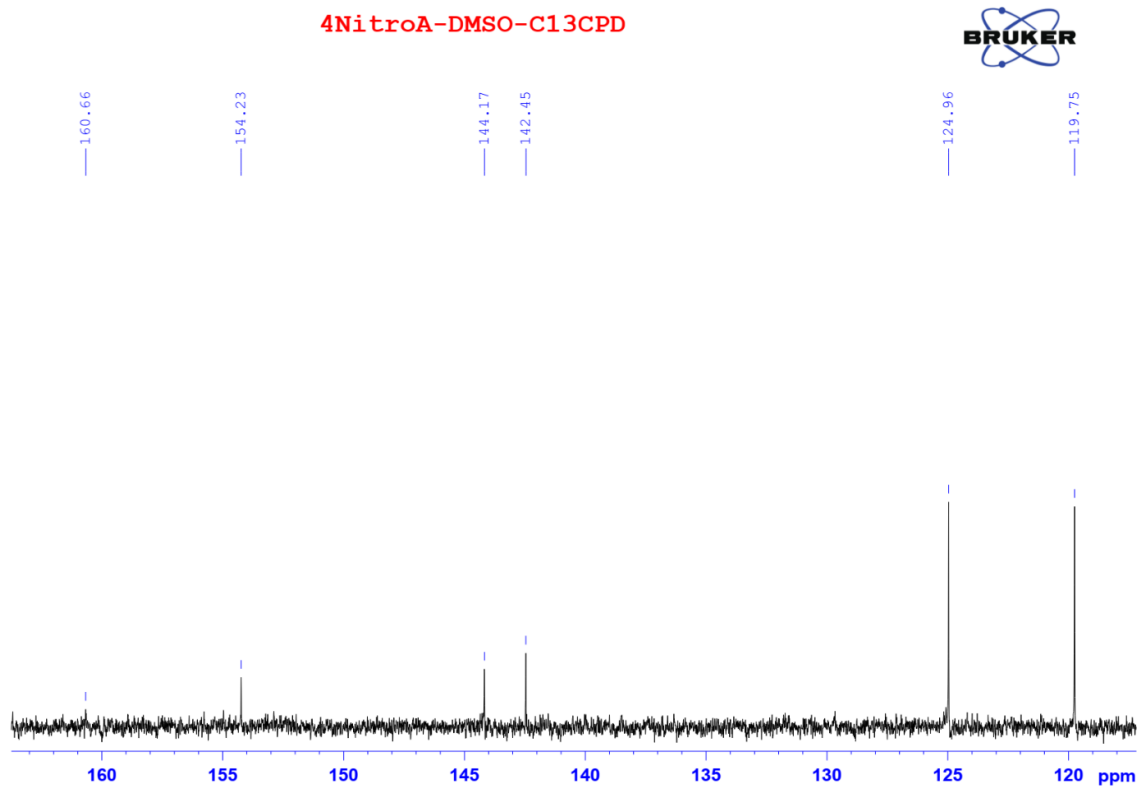
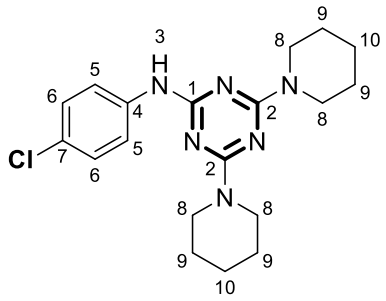


COMPOUND 2a



Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	8.96 (1H, s)	-NH-
5	7.69 (2H, d, *J* = 8.5 Hz)	H_{Ar}
6	7.07 (2H, d, *J* = 8.5 Hz)	H_{Ar}
8	3.69 (8H, t, *J* = 4.5 Hz)	-CH_2-
9	1.48 (8H, s)	-CH_2-
10	1.59 (4H, t, *J* = 4.5 Hz)	-CH_2-

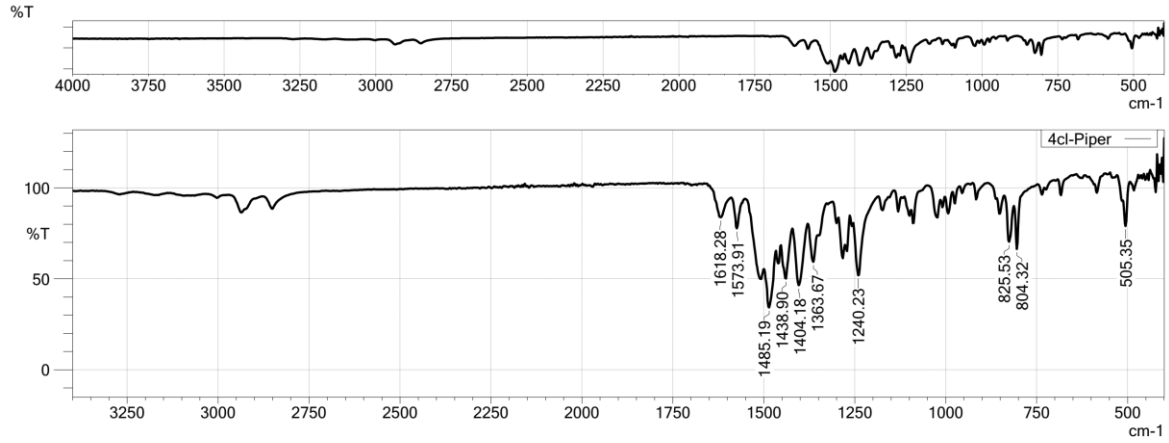
^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 164.4 (>C=, C_2), 155.9 (>C=, C_1), 136.9 (>C=, C_4), 128.0 (>C=, C_6), 124.6 (>C=, C_7), 120.7 (>C=, C_5), 43.5 (-CH_2-, C_8), 25.3 (-CH_2-, C_9), 24.3 (-CH_2-, C_{10}).

LC-MS (*m/z*)

Expected formula: $C_{19}H_{25}ClN_6$ Exact mass: 372.1829

$[M+H]^+$ calcd: 373.1902 $[M+H]^+$ found: 373.1898

IR (2a)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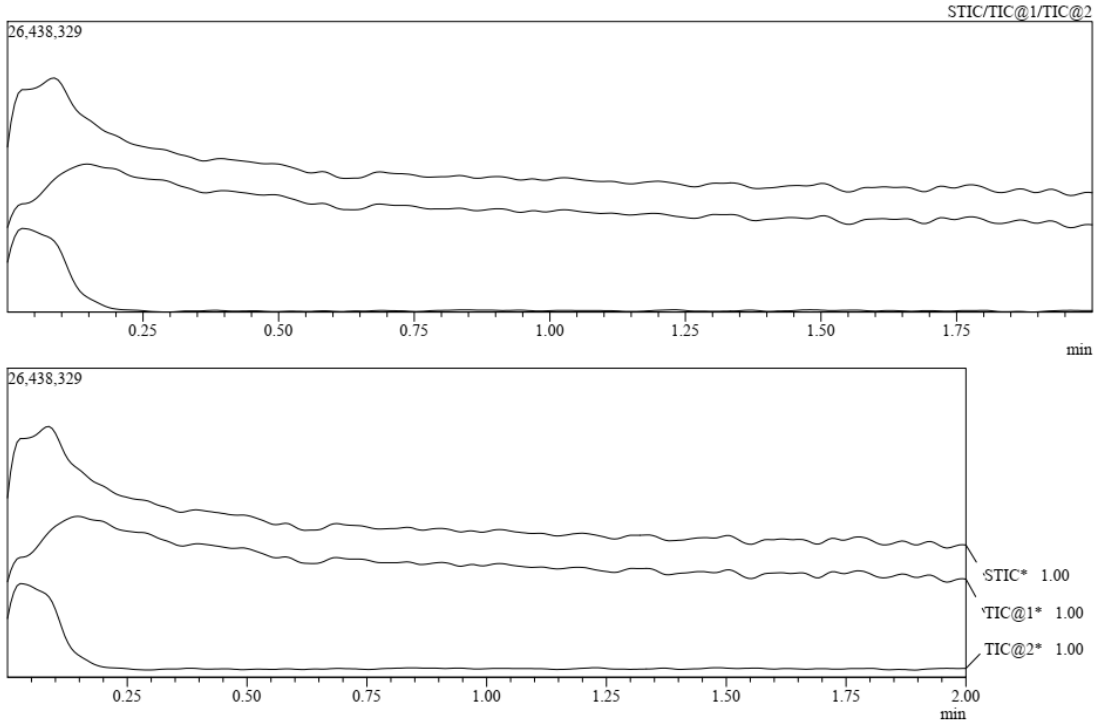
1500
1250
1000
750
500
cm-1
4cl-Piper
100
%T
50
0
1618.28
1573.91
1485.19
1438.90
1404.18
1363.67
1240.23
825.53
804.32
505.35
3250
3000
2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1

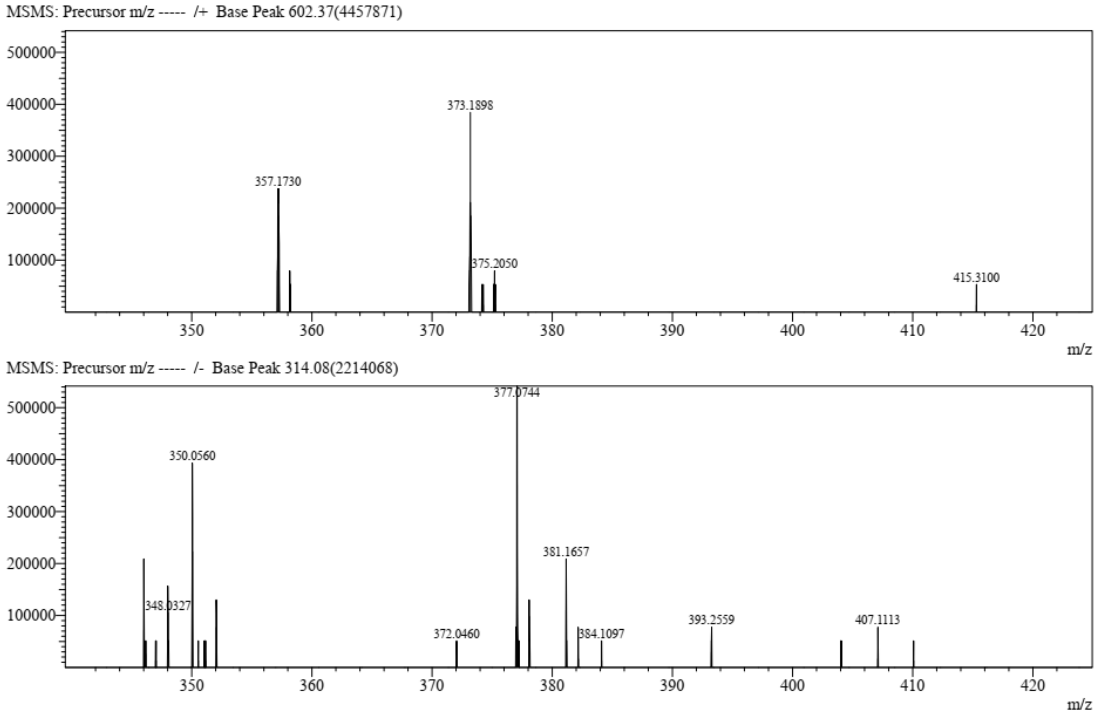
MS (2a)

==== Shimadzu LCMSsolution Data Report ====

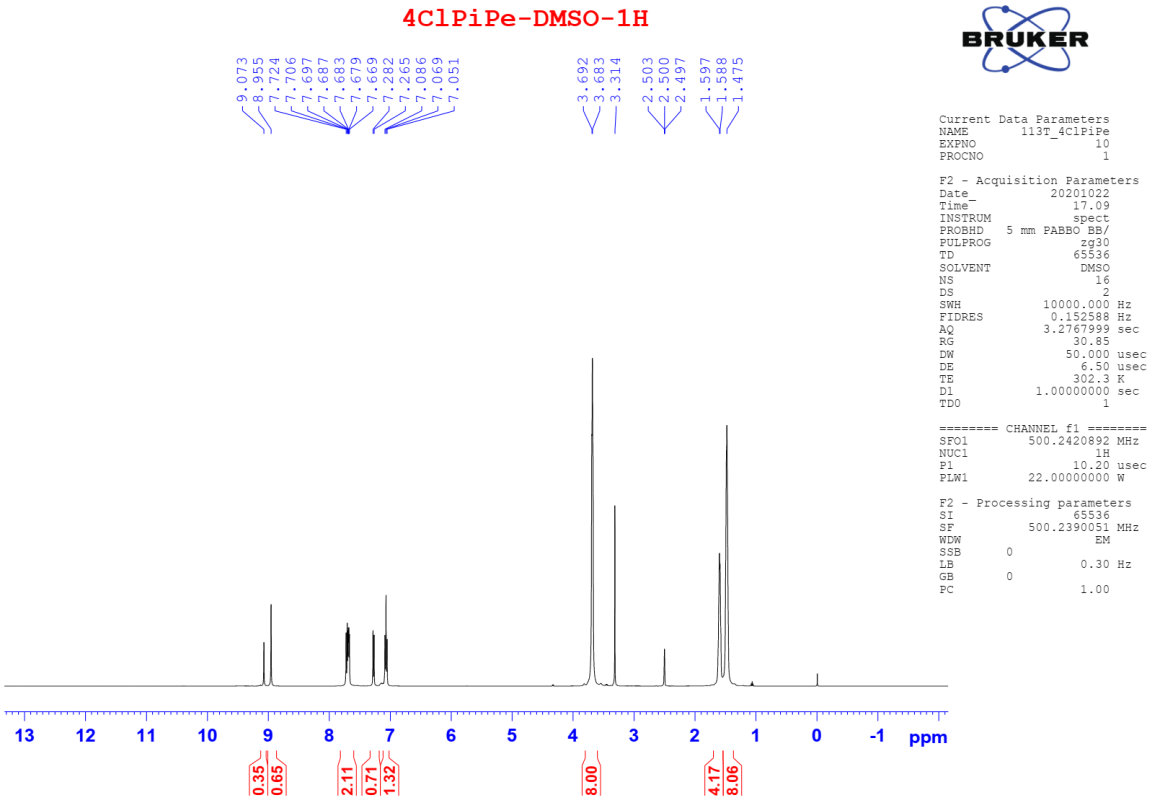
<Chromatogram>



<Spectrum>



^{1}H NMR (2a)

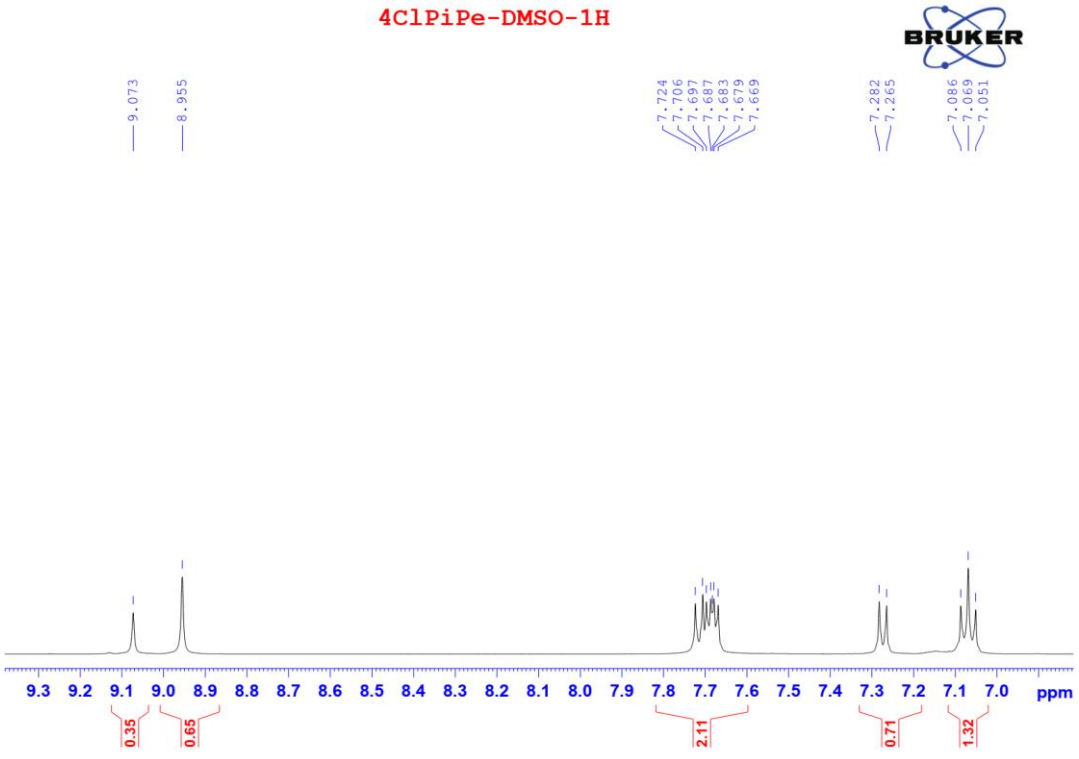


Current Data Parameters
NAME 113T_4ClPiPe
EXPNO 10
PROCNO 1

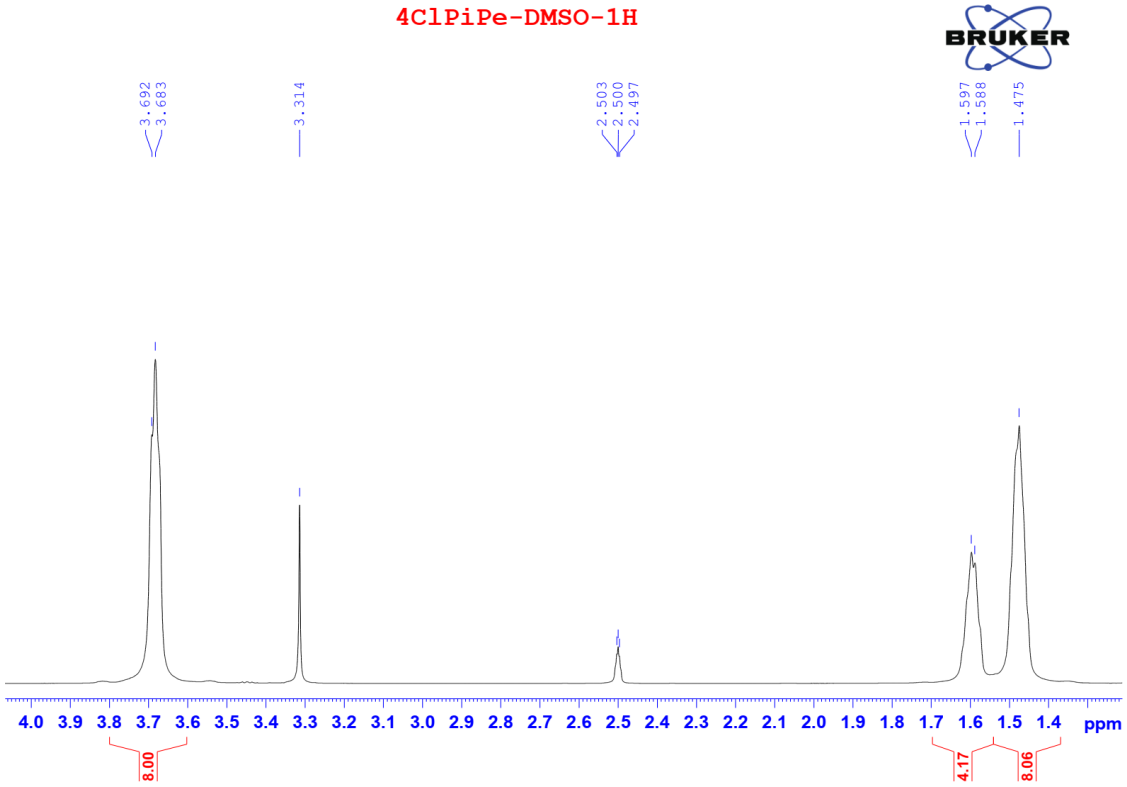
F2 - Acquisition Parameters
Date_ 20201022
Time 17.09
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 30.85
DW 50.000 usec
DE 6.50 usec
TE 302.3 K
D1 1.00000000 sec
TD0 1

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

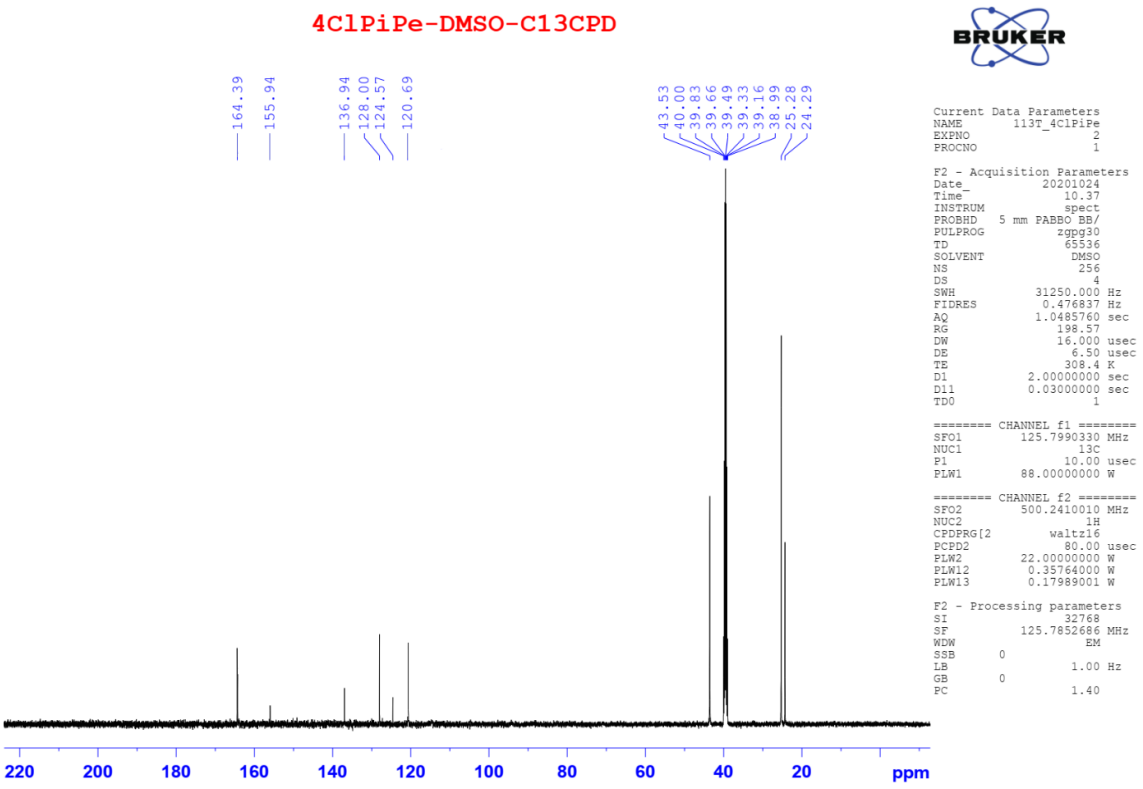
F2 - Processing parameters
SI 65536
SF 500.2390051 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



4ClPiPe-DMSO-1H



^{13}C NMR (2a)



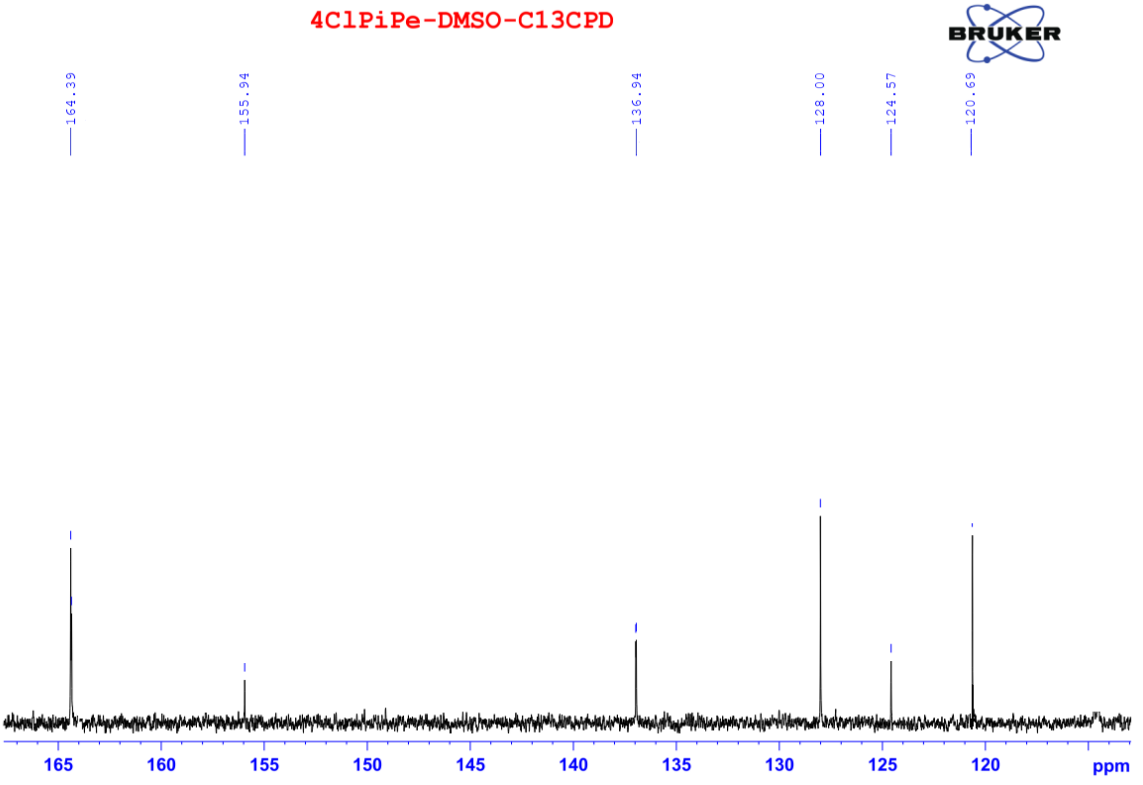

```
Current Data Parameters
NAME          113T_4ClPiPe
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_           20201024
Time               10.37
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG          zgpg30
TD                65536
SOLVENT             DMSO
NS                   256
DS                     4
SWH            31250.000 Hz
FIDRES          0.476837 Hz
AQ              1.0485760 sec
RG                198.57
DW                16.000 usec
DE                 6.50 usec
TE                308.4 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

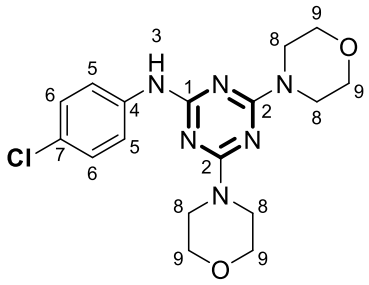
======== CHANNEL f1 ========
SFO1         125.7990330 MHz
NUC1                  13C
P1                  10.00 usec
PLW1         88.00000000 W

======== CHANNEL f2 ========
SFO2         500.2410010 MHz
NUC2                   1H
CPDPRG[2           waltz16
PCPD2               80.00 usec
PLW2         22.00000000 W
PLW12         0.35764000 W
PLW13         0.17989001 W

F2 - Processing parameters
SI                 32768
SF            125.7852686 MHz
WDW                   EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```



COMPOUND 3a



Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	8.82 (1H, s)	-NH-
5	7.65 (2H, d, *J* = 9.0 Hz)	H_{Ar}
6	7.01 (2H, d, *J* = 9.0 Hz)	H_{Ar}
8	3.70 (8H, t, *J* = 5.5 Hz)	-CH_2-
9	3.63 (8H, t, *J* = 5.0 Hz)	-CH_2-

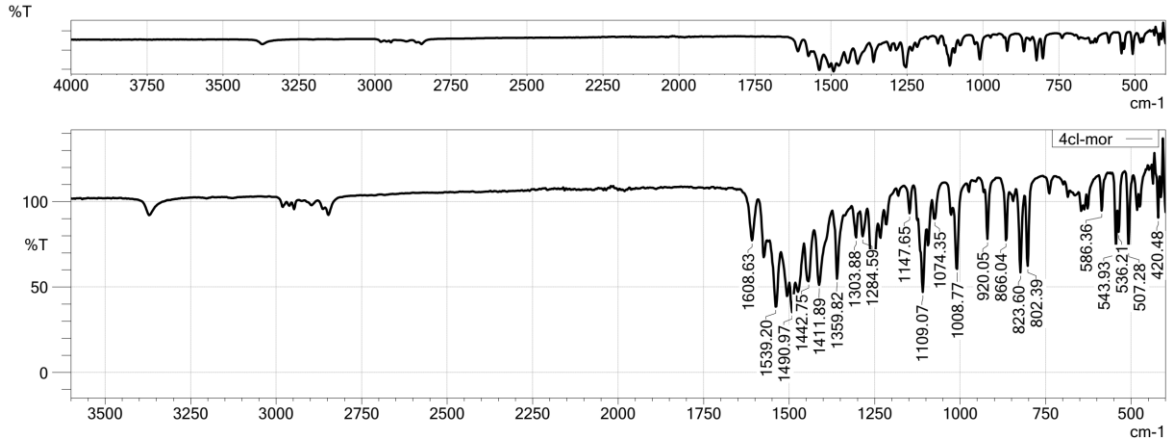
^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 164.7 (>C=, C_2), 156.1 (>C=, C_1), 136.3 (>C=, C_4), 121.2 (>C=, C_6), 121.1 (>C=, C_7), 114.4 (>C=, C_5), 65.6 (-CH_2-, C_9), 43.2 (-CH_2-, C_8).

LC-MS (*m/z*)

Expected formula: $C_{17}H_{21}ClN_6O_2$ Exact mass: 376.1415

$[M+H]^+$ calcd: 377.1487 $[M+H]^+$ found: 377.1477

IR (3a)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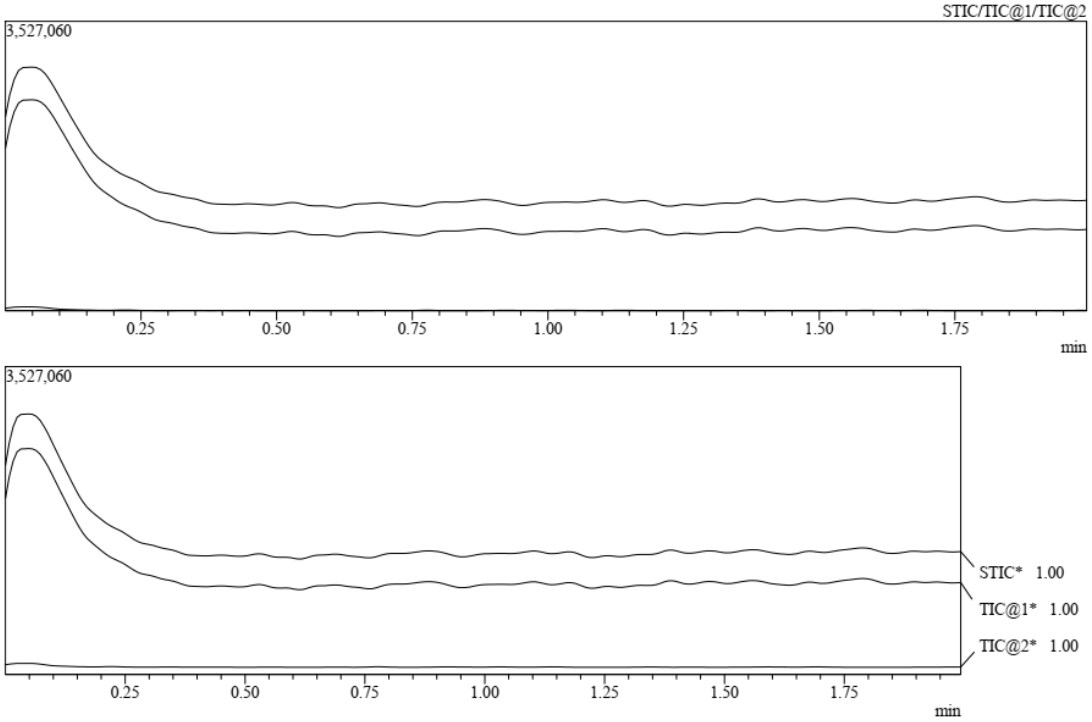
3250
3000
2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1
4cl-mor
100
%T
50
0
1608.63
1539.20
1490.97
1442.75
1411.89
1359.82
1303.88
1284.59
1147.65
1109.07
1074.35
1008.77
920.05
866.04
823.60
802.39
586.36
543.93
536.21
507.28
420.48
3500
3250
3000
2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1

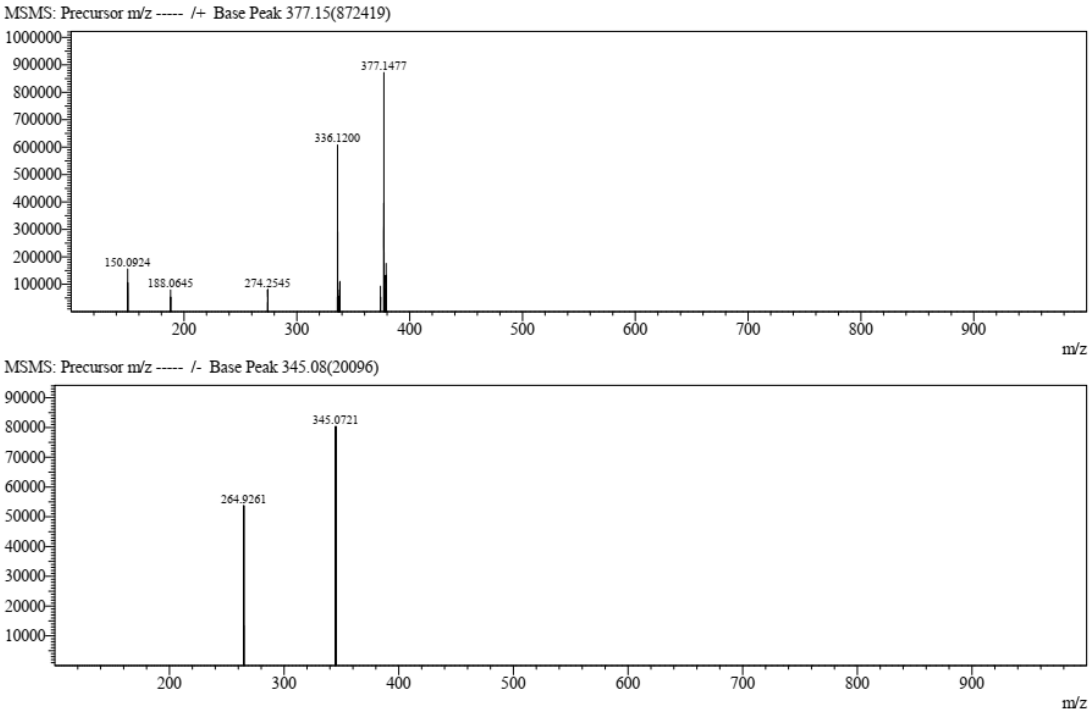
MS (3a)

==== Shimadzu LCMSsolution Data Report ====

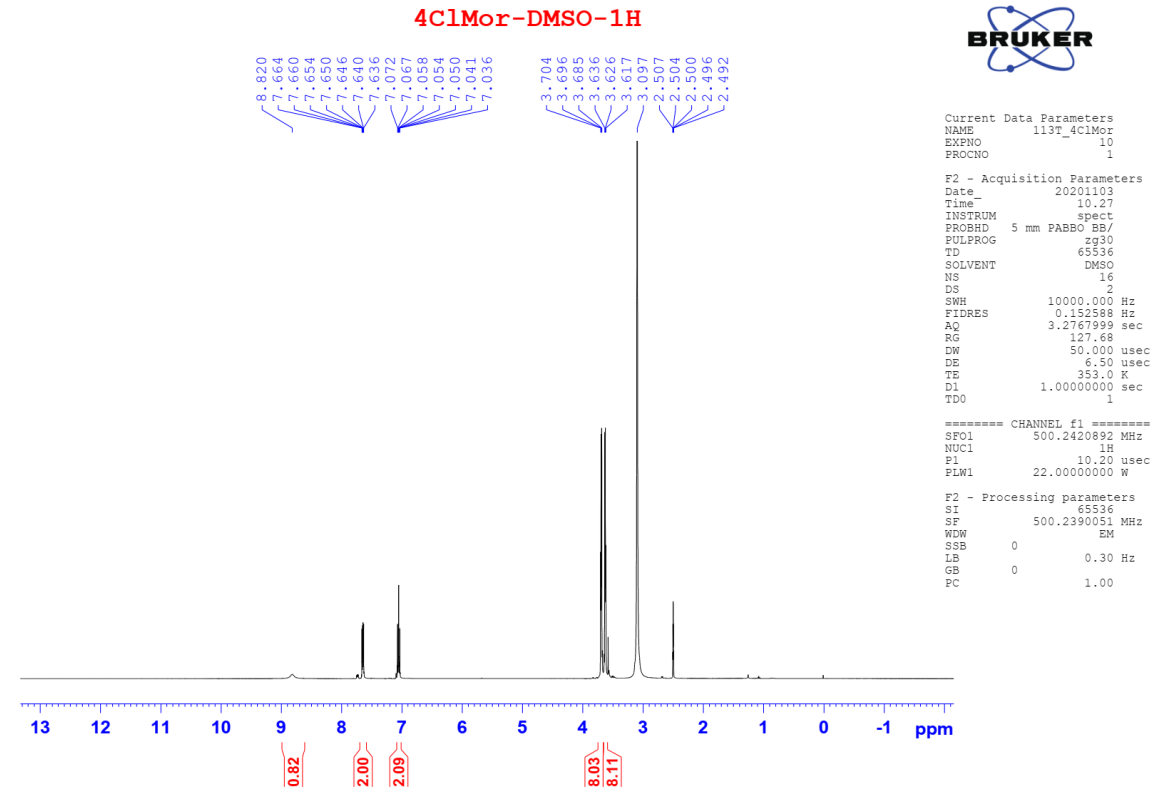
<Chromatogram>

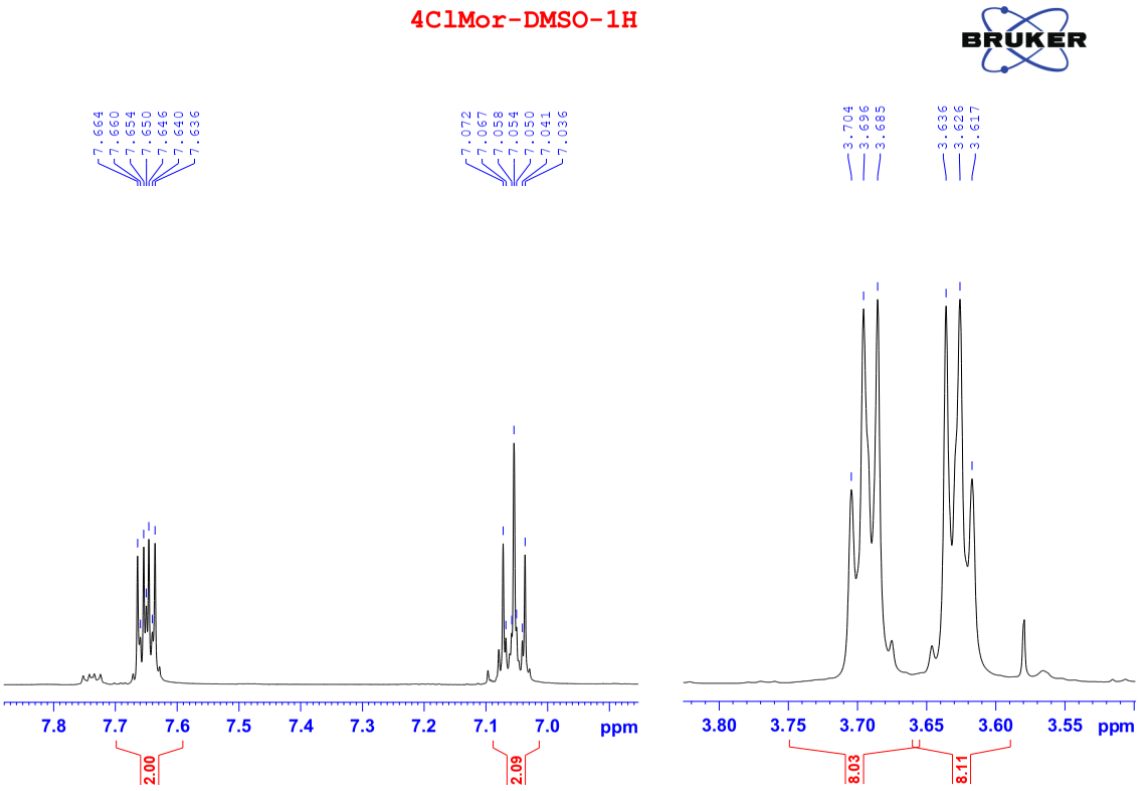


<Spectrum>

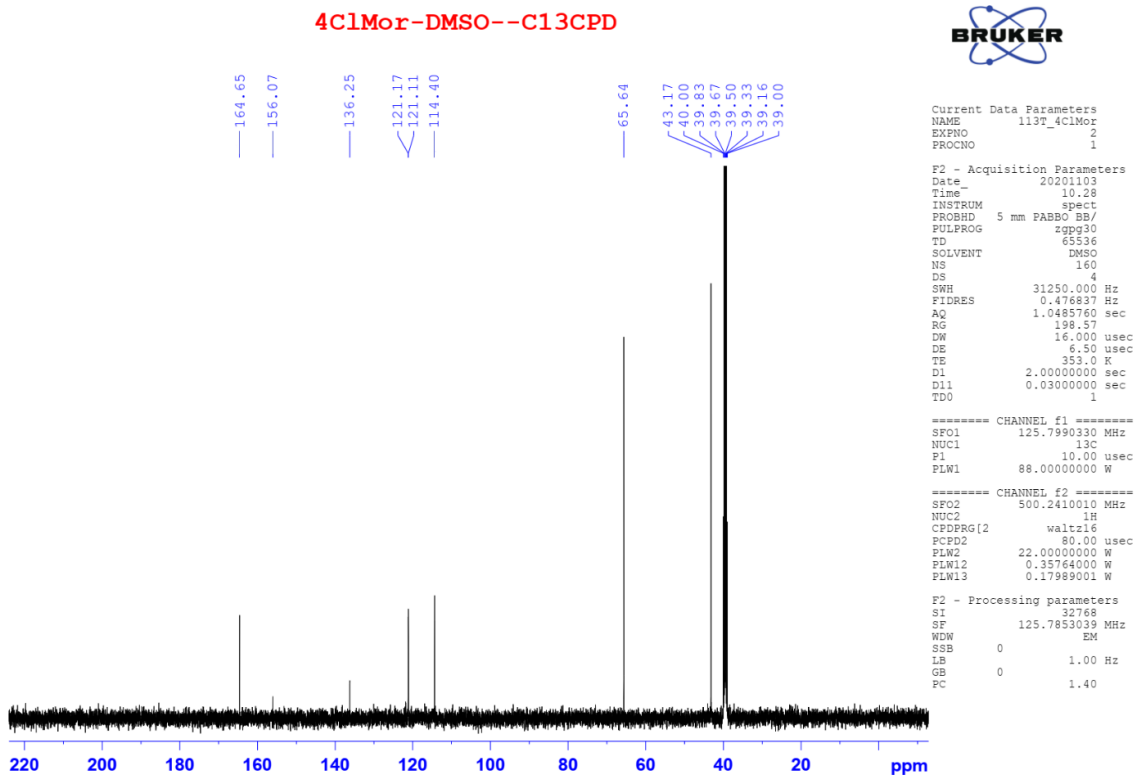


^{1}H NMR (3a)


4ClMor-DMSO-1H
BRUKER
8.820
7.664
7.660
7.654
7.650
7.646
7.640
7.636
7.072
7.067
7.058
7.054
7.050
7.041
7.036
3.704
3.696
3.685
3.636
3.626
3.617
3.097
2.507
2.504
2.500
2.496
2.492
Current Data Parameters
NAME 113T_4ClMor
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201103
Time 10.27
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 127.68
DW 50.000 usec
DE 6.50 usec
TE 353.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.2420892 MHz
NUC1 1H
P1 10.20 usec
PLW1 22.00000000 W
F2 - Processing parameters
SI 65536
SF 500.2390051 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 ppm
0.82
2.00
2.09
8.03
8.11


4ClMor-DMSO-1H
BRUKER
7.664
7.660
7.654
7.650
7.646
7.640
7.636
7.072
7.067
7.058
7.054
7.050
7.041
7.036
3.704
3.696
3.685
3.636
3.626
3.617
7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 ppm
2.00
2.09
3.80 3.75 3.70 3.65 3.60 3.55 ppm
8.03
8.11

^{13}C NMR (3a)

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Current Data Parameters
NAME         1137_4ClMor
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20201103
Time              10.28
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                 160
DS                   4
SWH          31250.000 Hz
FIDRES        0.476837 Hz
AQ            1.0485760 sec
RG              198.57
DW             16.000 usec
DE              6.50 usec
TE              353.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  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
CPDPRG[2        waltz16
PCPD2            80.00 usec
PLW2        22.00000000 W
PLW12        0.35764000 W
PLW13        0.17989001 W

F2 - Processing parameters
SI                32768
SF          125.7853039 MHz
WDW                EM
SSB       0
LB               1.00 Hz
GB        0
PC               1.40
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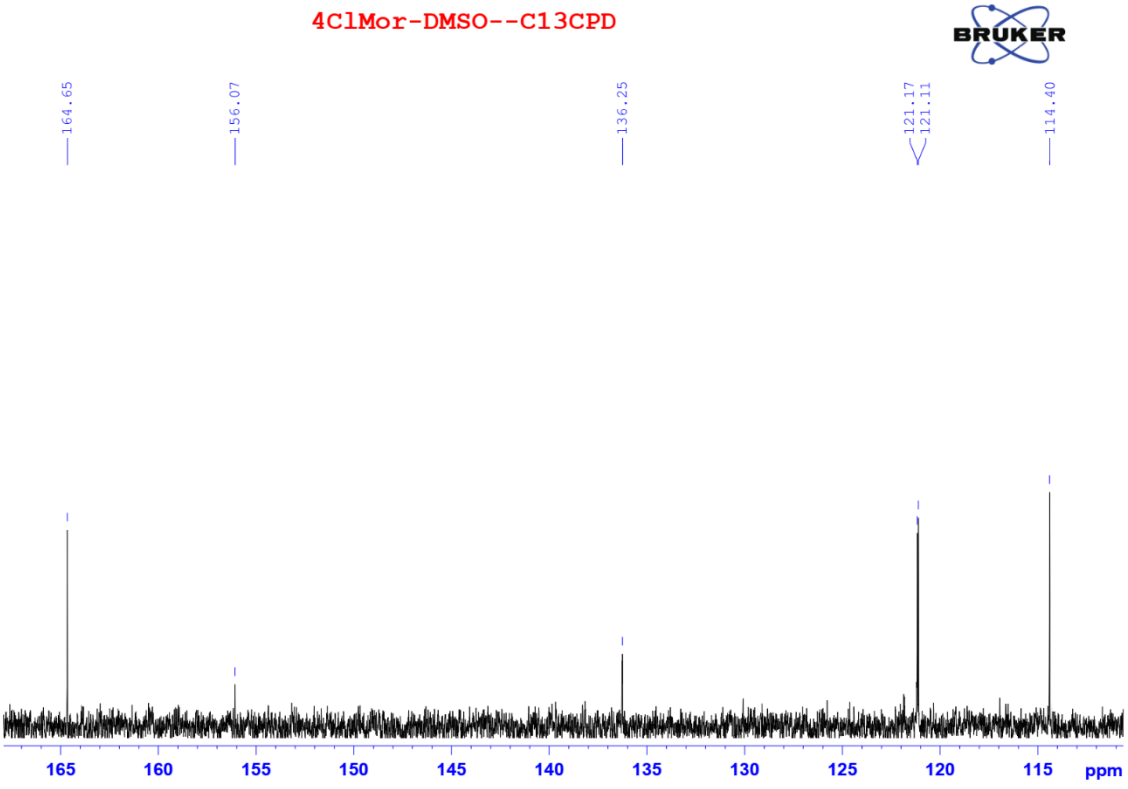
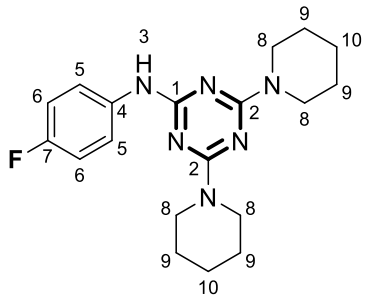


COMPOUND 2b



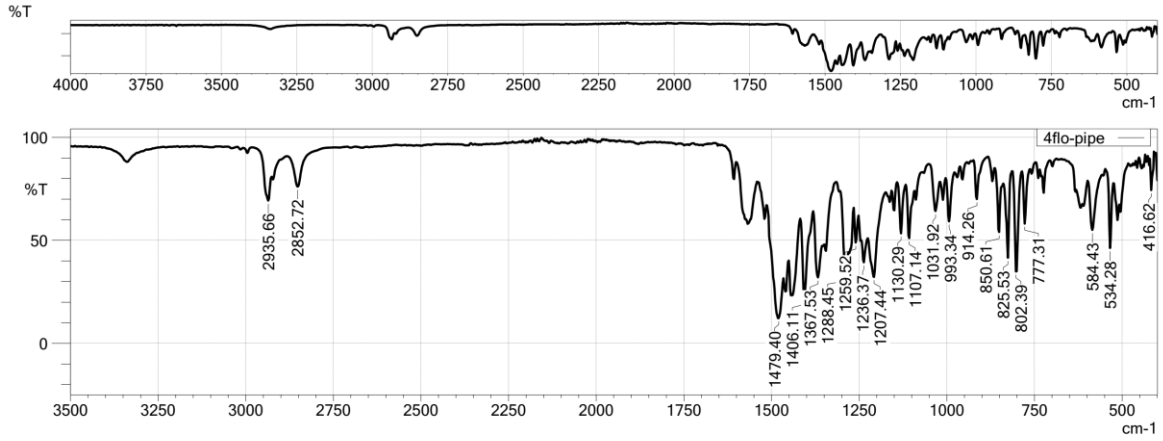
Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	8.66 (1H, s)	-NH-
5	7.68 (2H, d, *J* = 9.0 Hz)	H_{Ar}
6	7.04 (2H, d, *J* = 9.0 Hz)	H_{Ar}
8	3.70 (8H, t, *J* = 5.5 Hz)	-CH_2-
9	1.52 (8H, t, *J* = 4.0 Hz)	-CH_2-
10	1.62 (4H, t, *J* = 5.0 Hz)	-CH_2-

^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 164.4 (>C=, C_2), 164.0 (>C=, C_1), 157.86 and 155.98 (>C=, J_{C-F} = 235 Hz, C_7), 136.99 and 136.98 (>C=, J_{C-F} = 1.25 Hz, C_4), 120.78 and 120.72 (>C=, J_{C-F} = 7.5 Hz, C_5), 114.78 and 114.61 (>C=, J_{C-F} = 21.25 Hz, C_6), 43.6 (-CH_2-, C_8), 25.3 (-CH_2-, C_9), 24.3 (-CH_2-, C_{10}).

LC-MS (*m/z*)

Expected formula: $C_{19}H_{25}FN_6$	Exact mass: 356.2125
$[M+H]^+$ calcd: 357.2197	$[M+H]^+$ found: 357.2124

IR (2b)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2750
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1250
1000
750
500
cm-1
100
%T
50
0
4flo-pipe
2935.66
2852.72
1479.40
1406.11
1367.53
1288.45
1259.52
1236.37
1207.44
1130.29
1107.14
1031.92
993.34
914.26
850.61
825.53
802.39
777.31
584.43
534.28
416.62
3500
3250
3000
2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1

MS (2b)

==== Shimadzu LCMSsolution Data Report ====

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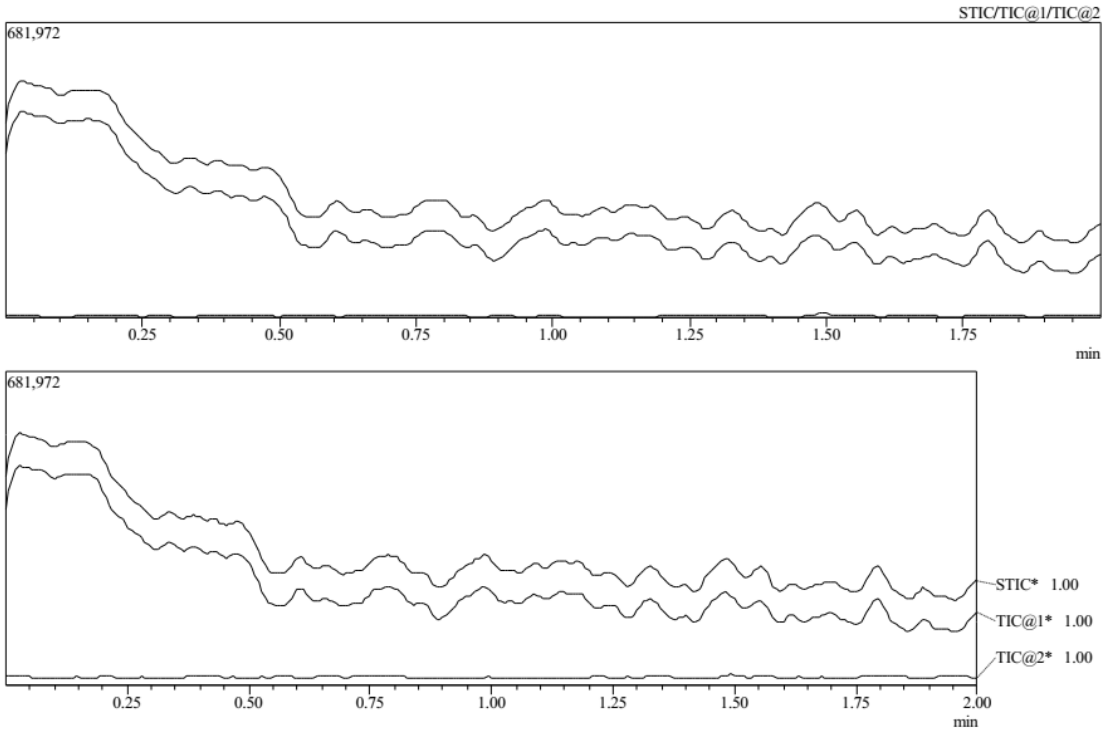

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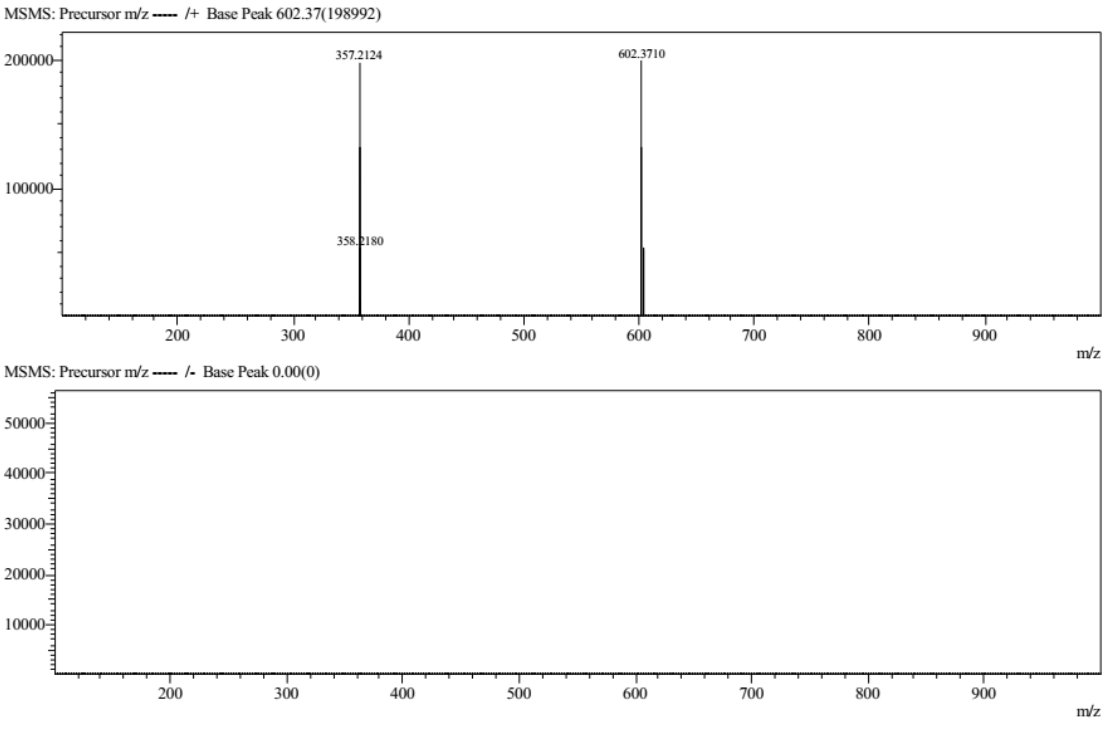
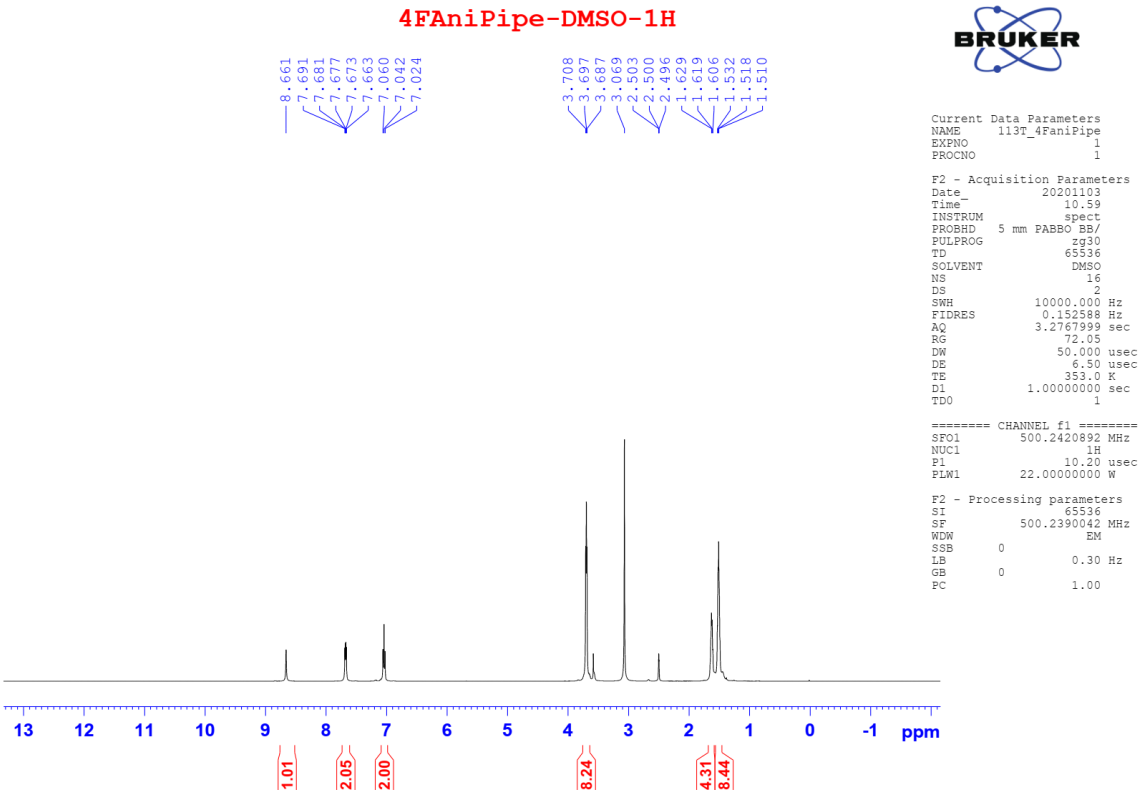


^{1}H NMR (2b)

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EXPNO                  1
PROCNO                 1

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Date_           20201103
Time_              10.59
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                 72.05
DW                50.000 usec
DE                 6.50 usec
TE                353.0 K
D1             1.00000000 sec
TD0                    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                 0.30 Hz
GB        0
PC                 1.00
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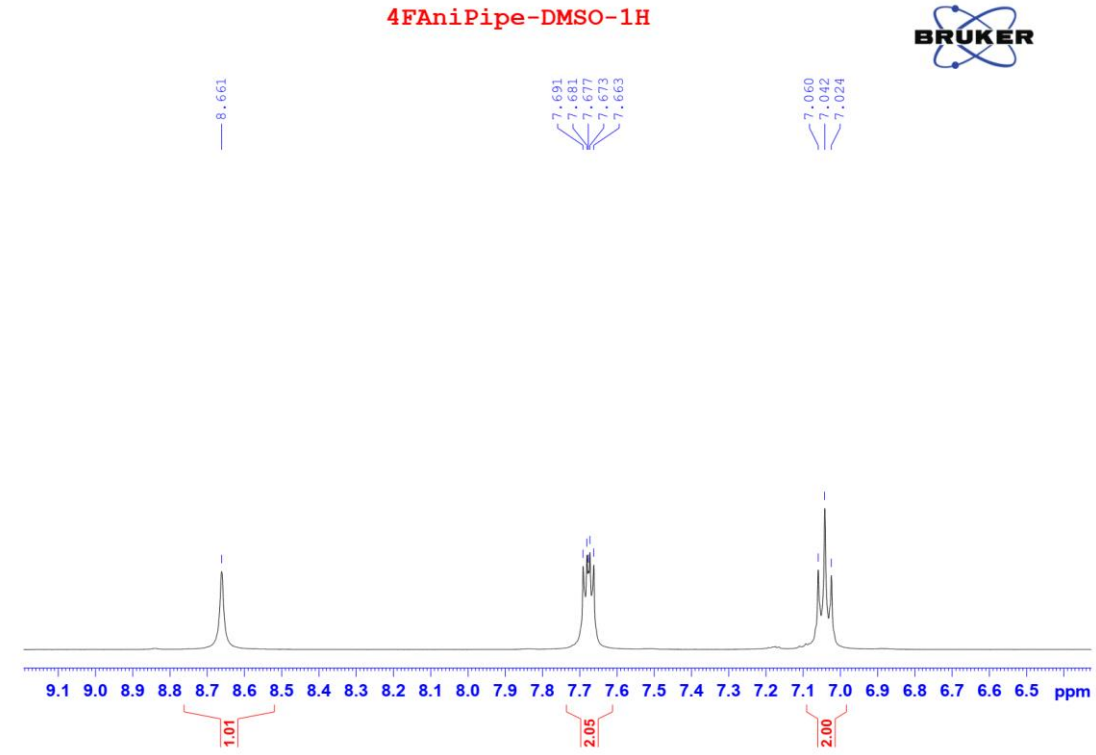
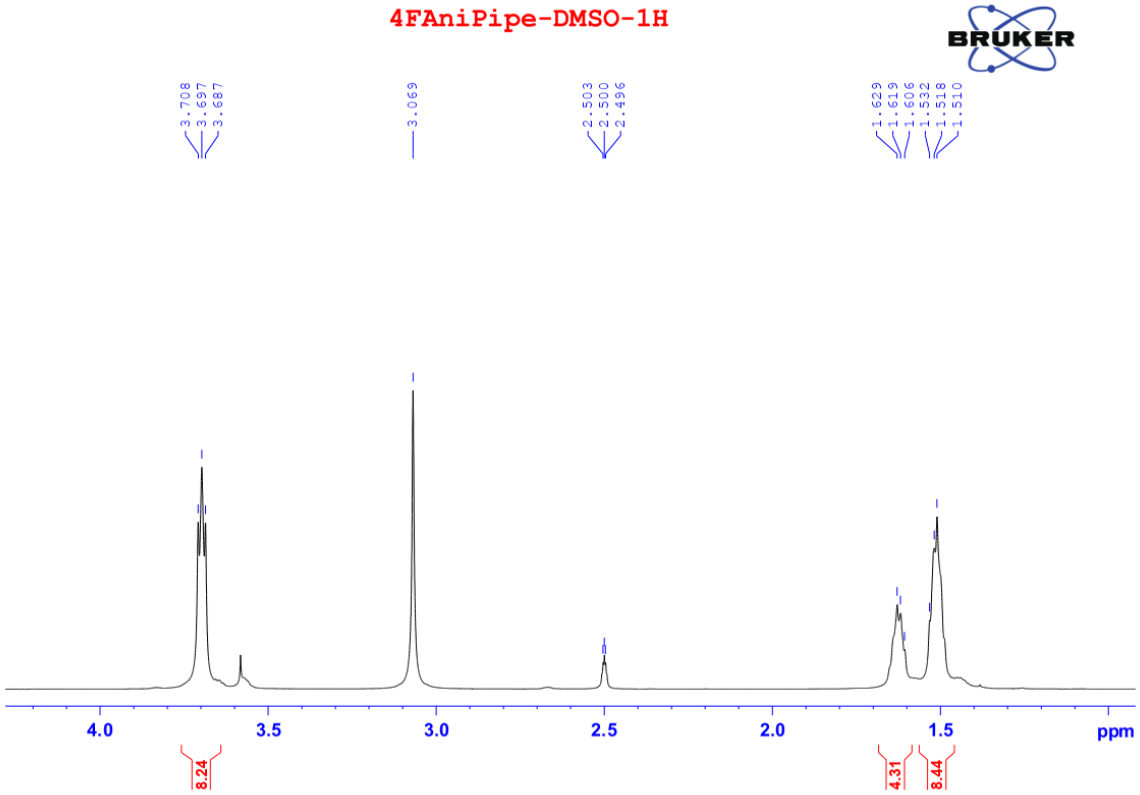
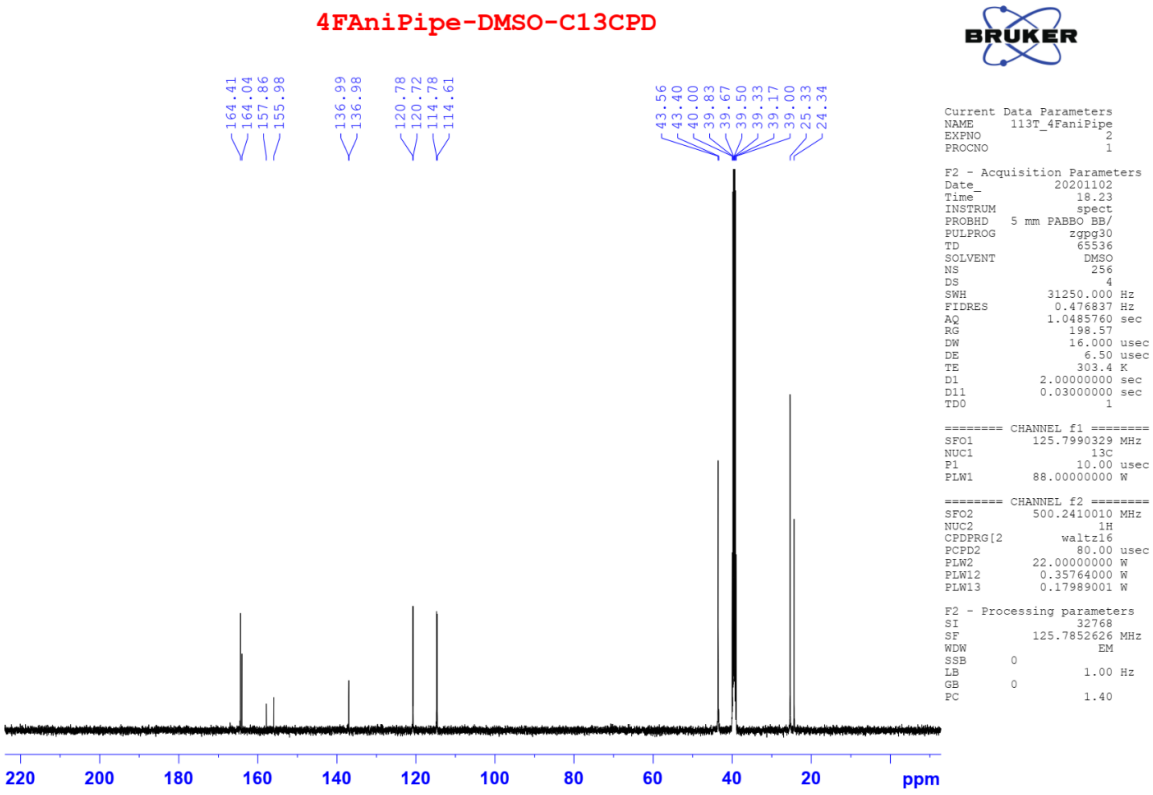


4FAniPipe-DMSO-1H



^{13}C NMR (2b)



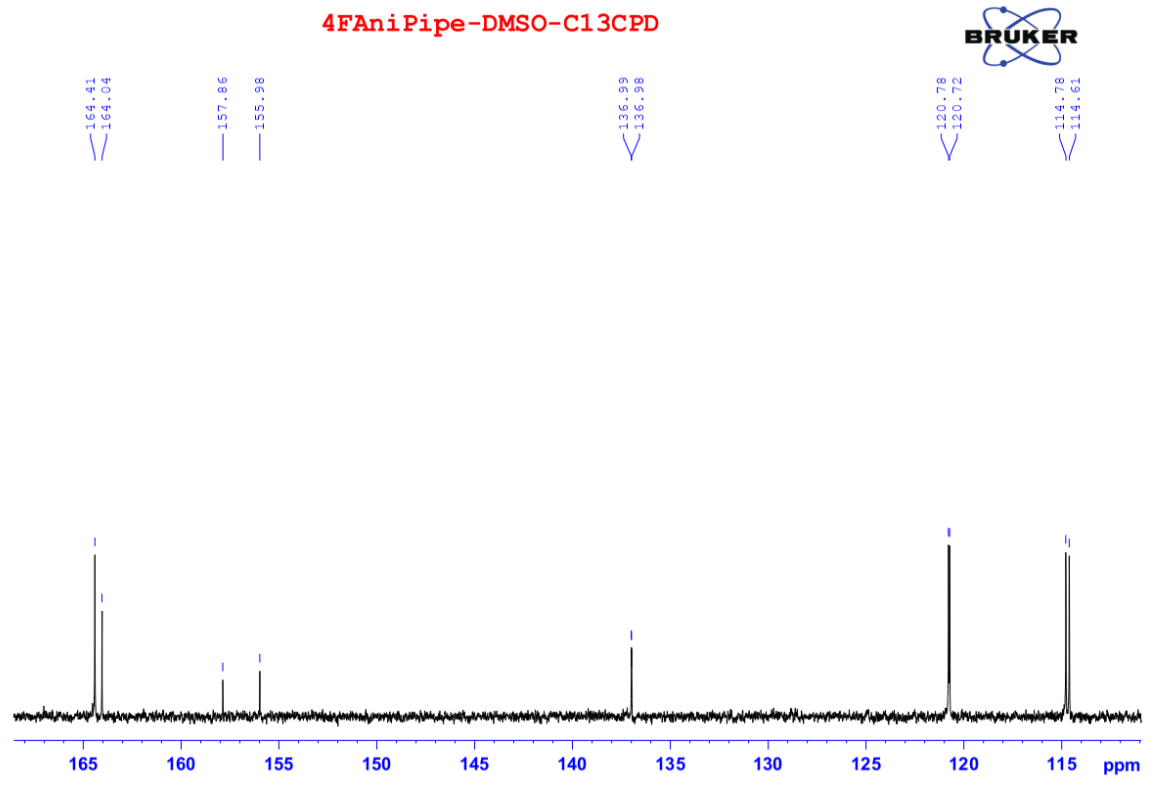

```
Current Data Parameters
NAME      113T_4FaniPipe
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20201102
Time              18.23
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                 256
DS                   4
SWH          31250.000 Hz
FIDRES        0.476837 Hz
AQ            1.0485760 sec
RG               198.57
DW              16.000 usec
DE               6.50 usec
TE              303.4 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1

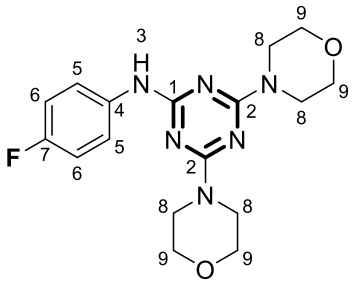
======== CHANNEL f1 ========
SFO1        125.7990329 MHz
NUC1               13C
P1               10.00 usec
PLW1        88.00000000 W

======== CHANNEL f2 ========
SFO2        500.2410010 MHz
NUC2               1H
CPDPRG[2        waltz16
PCPD2            80.00 usec
PLW2        22.00000000 W
PLW12        0.35764000 W
PLW13        0.17989001 W

F2 - Processing parameters
SI                32768
SF          125.7852626 MHz
WDW                EM
SSB       0
LB               1.00 Hz
GB        0
PC               1.40
```



COMPOUND 3b



Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	9.11 (1H, s)	-NH-
5	7.66 (2H, d, *J* = 9.0 Hz)	H_{Ar}
6	7.08 (2H, d, *J* = 9.0 Hz)	H_{Ar}
8	3.68 (8H, t, *J* = 5.0 Hz)	-CH_2-
9	3.61 (8H, t, *J* = 5.0 Hz)	-CH_2-

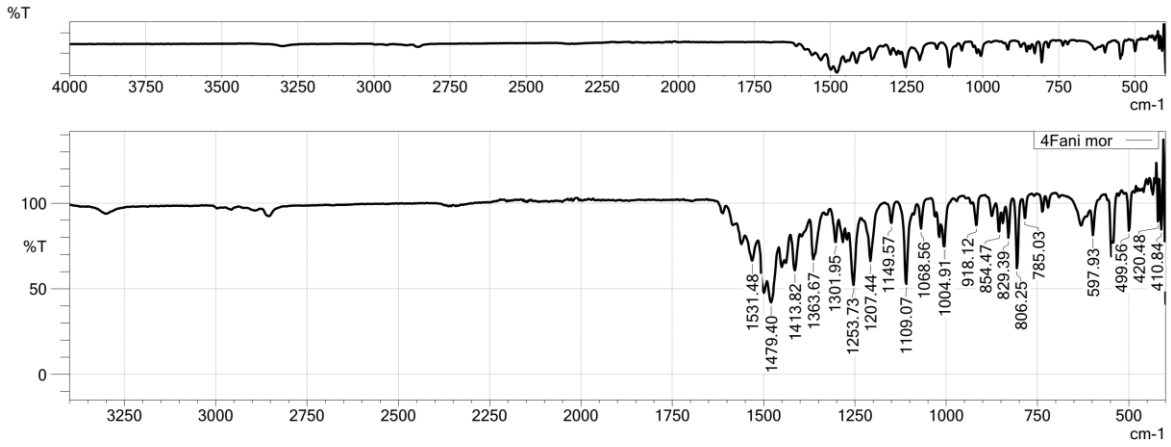
^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 164.7 (>C=, C_2), 163.9 (>C=, C_1), 158.09 and 156.20 (>C=, $J_{C\text{-}F}$ = 236.25 Hz, C_7), 136.6 (>C=, C_4), 121.19 and 121.13 (>C=, $J_{C\text{-}F}$ = 7.5 Hz, C_5), 114.90 and 114.73 (>C=, $J_{C\text{-}F}$ = 21.25 Hz, C_6), 66.0 (-CH_2-, C_9), 43.3 (-CH_2-, C_8).

LC-MS (*m/z*)

Expected formula: $C_{17}H_{21}FN_6O_2$ Exact mass: 360.1710

$[M+H]^+$ calcd: 361.1783 $[M+H]^+$ found: 361.1778

IR (3b)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2750
2500
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2000
1750
1500
1250
1000
750
500
cm-1
4Fani mor
100
%T
50
0
1531.48
1479.40
1413.82
1363.67
1301.95
1253.73
1207.44
1149.57
1109.07
1068.56
1004.91
918.12
854.47
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806.25
785.03
597.93
499.56
420.48
410.84
3250
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1250
1000
750
500
cm-1

MS (3b)

==== Shimadzu LCMSsolution Data Report ====

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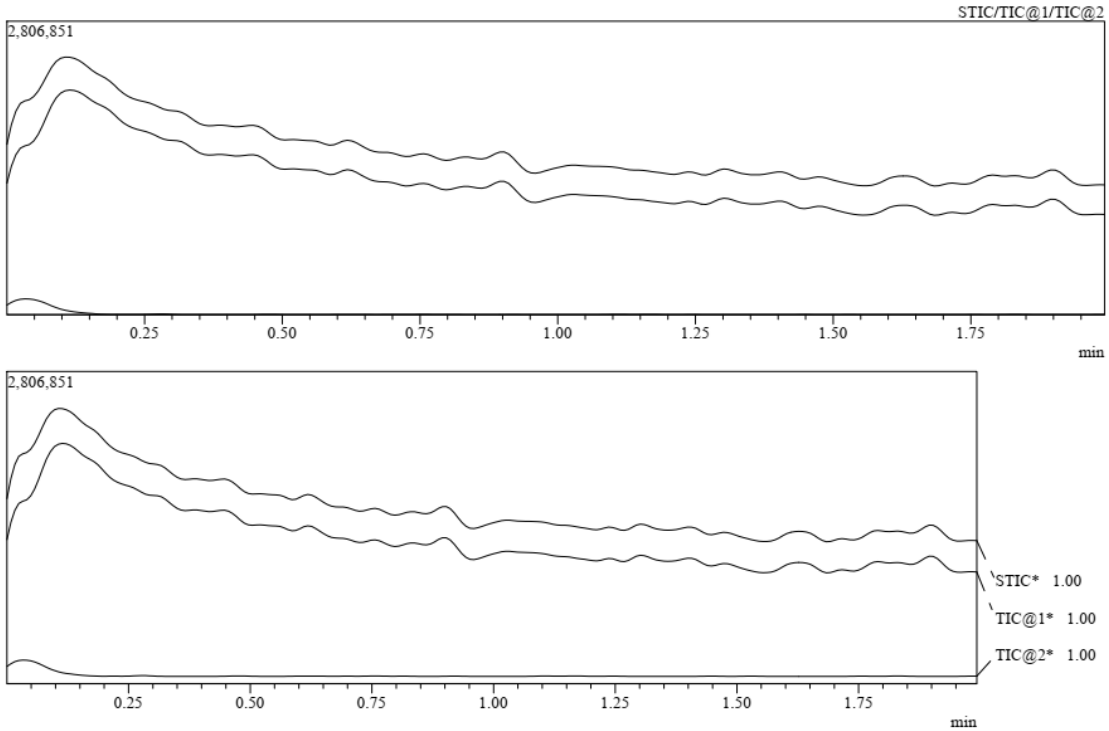

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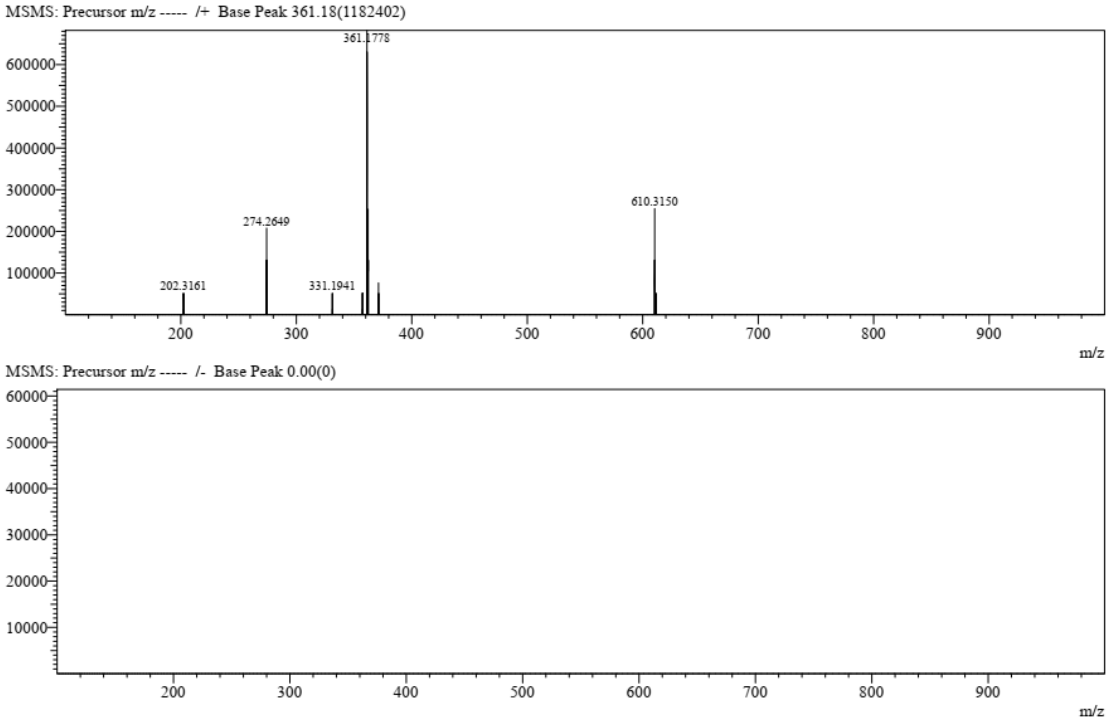
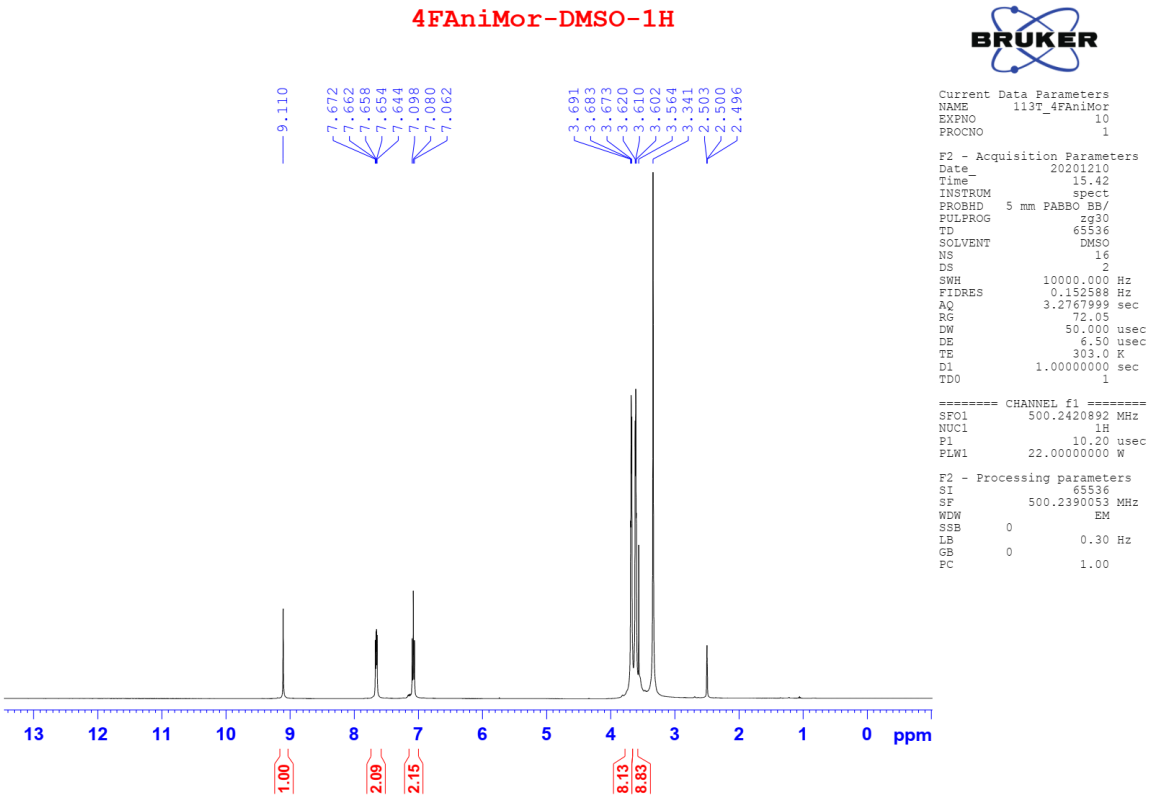


^{1}H NMR (3b)

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Current Data Parameters
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EXPNO                10
PROCNO                1

F2 - Acquisition Parameters
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Time              15.42
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                72.05
DW                50.000 usec
DE                 6.50 usec
TE               303.0 K
D1           1.00000000 sec
TD0                  1

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

F2 - Processing parameters
SI                65536
SF          500.2390053 MHz
WDW                EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
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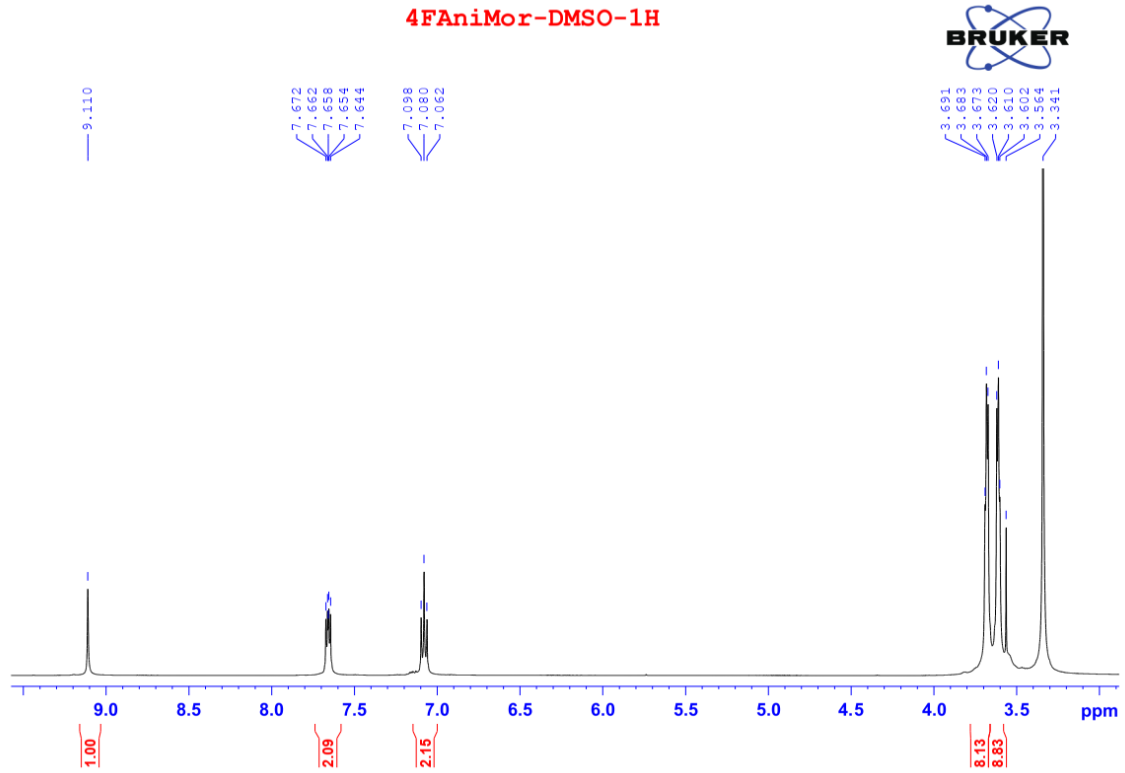
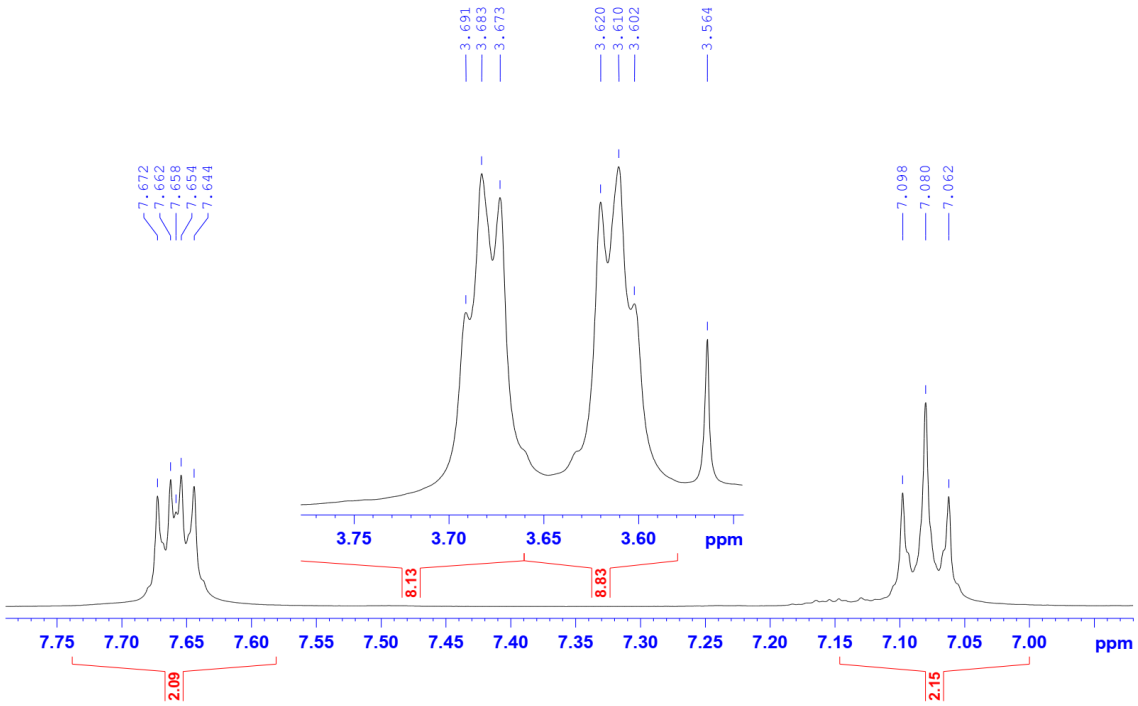
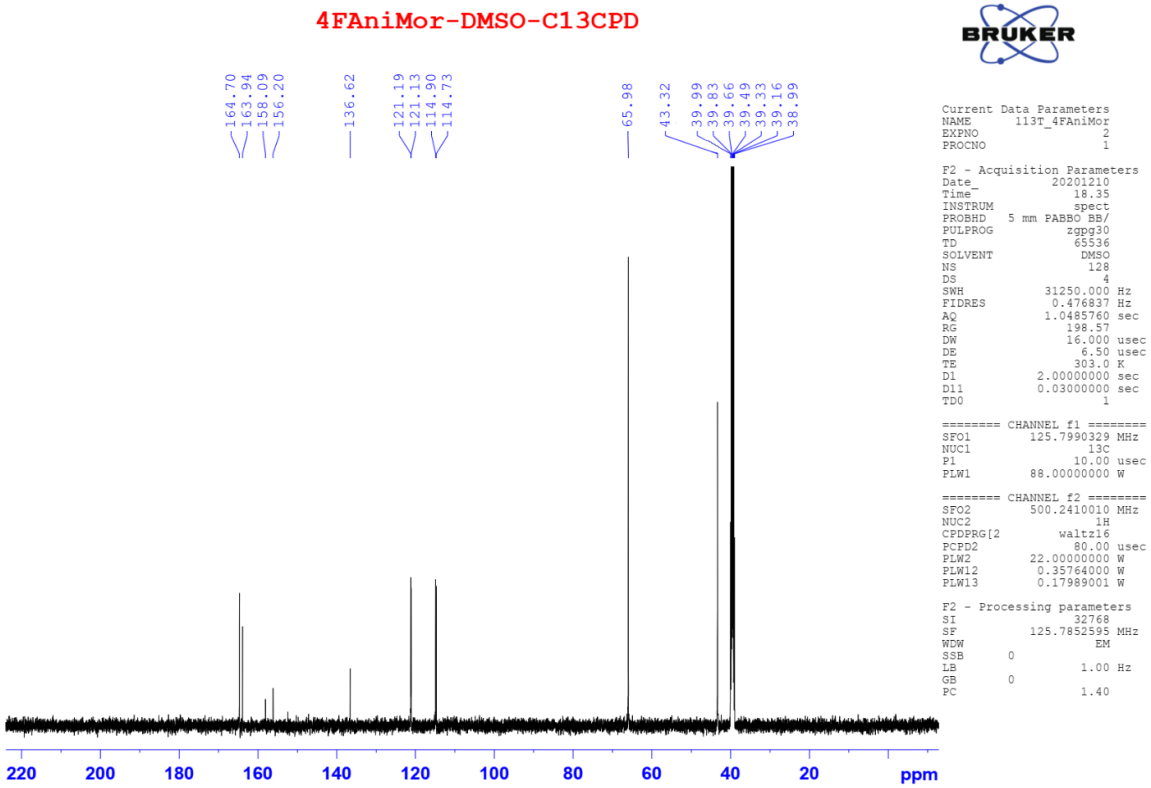
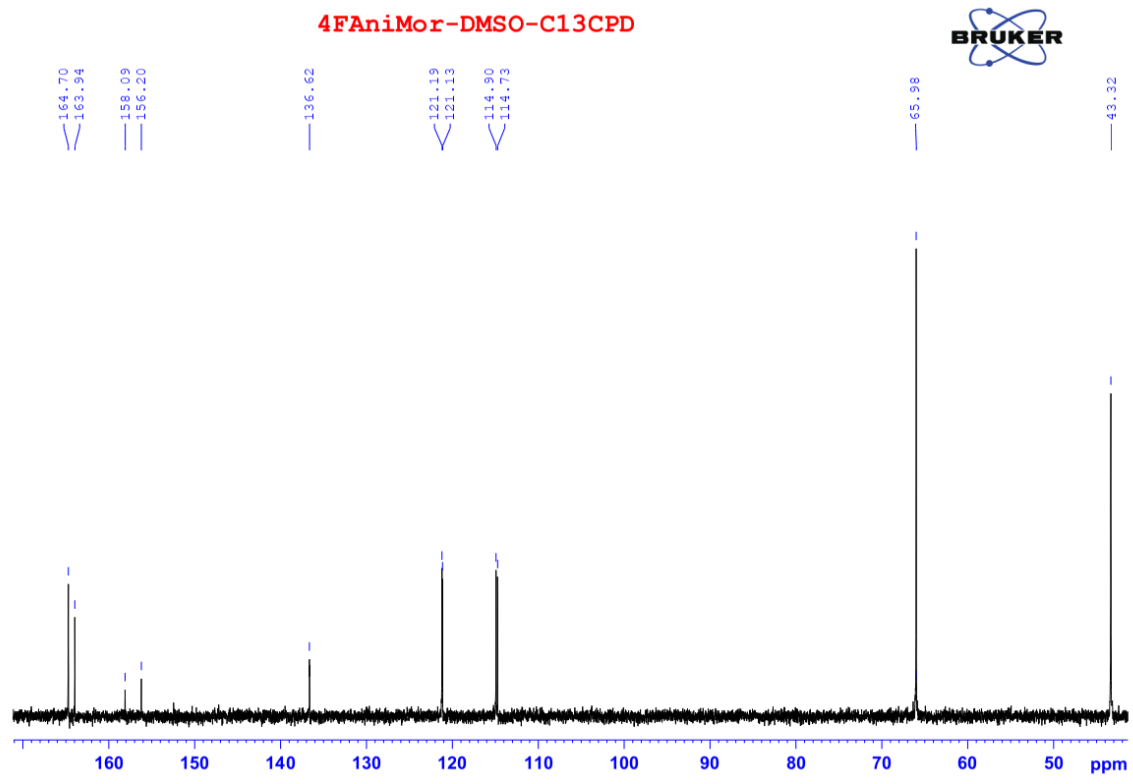


4FAniMor-DMSO-1H

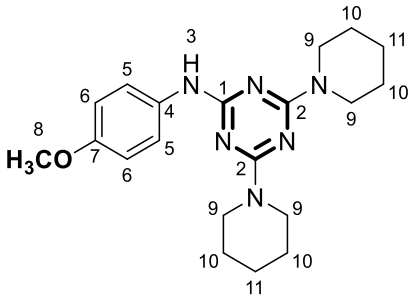


^{13}C NMR (3b)


4FAniMor-DMSO-C13CPD
BRUKER
164.70
163.94
158.09
156.20
136.62
121.19
121.13
114.90
114.73
65.98
43.32
39.99
39.83
39.66
39.49
39.33
39.16
38.99
220
200
180
160
140
120
100
80
60
40
20
ppm
Current Data Parameters
NAME 113T_4FAniMor
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201210
Time 18.35
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 128
DS 4
SWH 31250.000 Hz
FIDRES 0.476837 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
TD0 1
======== CHANNEL f1 ========
SFO1 125.7990329 MHz
NUC1 13C
P1 10.00 usec
PLW1 88.00000000 W
======== CHANNEL f2 ========
SFO2 500.2410010 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 22.00000000 W
PLW12 0.35764000 W
PLW13 0.17989001 W
F2 - Processing parameters
SI 32768
SF 125.7852595 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40


4FAniMor-DMSO-C13CPD
BRUKER
164.70
163.94
158.09
156.20
136.62
121.19
121.13
114.90
114.73
65.98
43.32
160
150
140
130
120
110
100
90
80
70
60
50
ppm

COMPOUND 2c



Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	8.72 (1H, s)	-NH-
5	7.57 (2H, d, *J* = 9.0 Hz)	H_{Ar}
6	6.83 (2H, d, *J* = 9.0 Hz)	H_{Ar}
8	3.70 (3H, s)	-OCH_3
9	3.68 (8H, t, *J* = 5.0 Hz)	-CH_2-
10	1.48 (8H, t, *J* = 3.5 Hz)	-CH_2-
11	1.59 (4H, t, *J* = 4.5 Hz)	-CH_2-

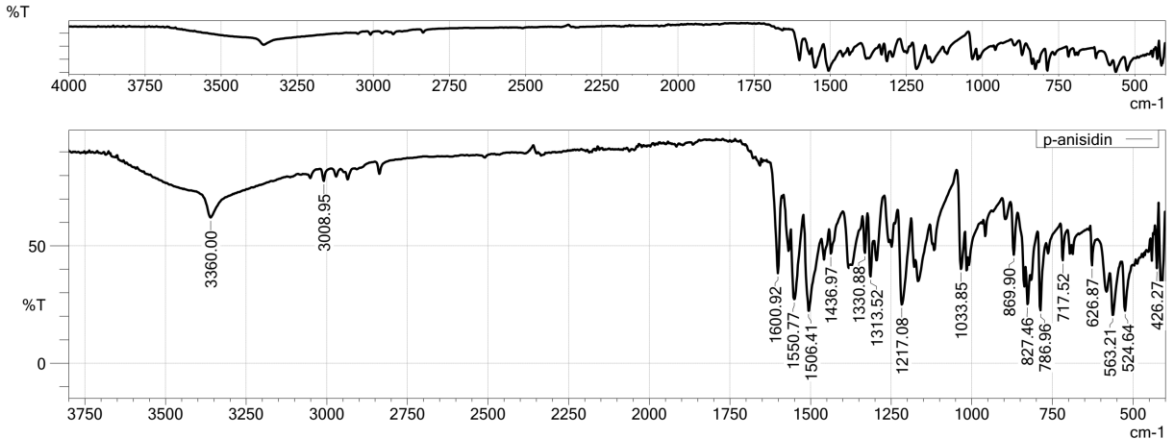
^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 164.5 (>C=, C_2), 164.0 (>C=, C_1), 154.0 (>C=, C_7), 133.8 (>C=, C_4), 120.8 (>C=, C_5), 113.5 (>C=, C_6), 55.1 (-OCH_3, C_8), 43.5 (-CH_2-, C_9), 25.4 (-CH_2-, C_{10}), 24.4 (-CH_2-, C_{11}).

LC-MS (*m/z*)

Expected formula: $C_{20}H_{28}N_6O$ Exact mass: 368.2325

$[M+H]^+$ calcd: 369.2397 $[M+H]^+$ found: 369.2299

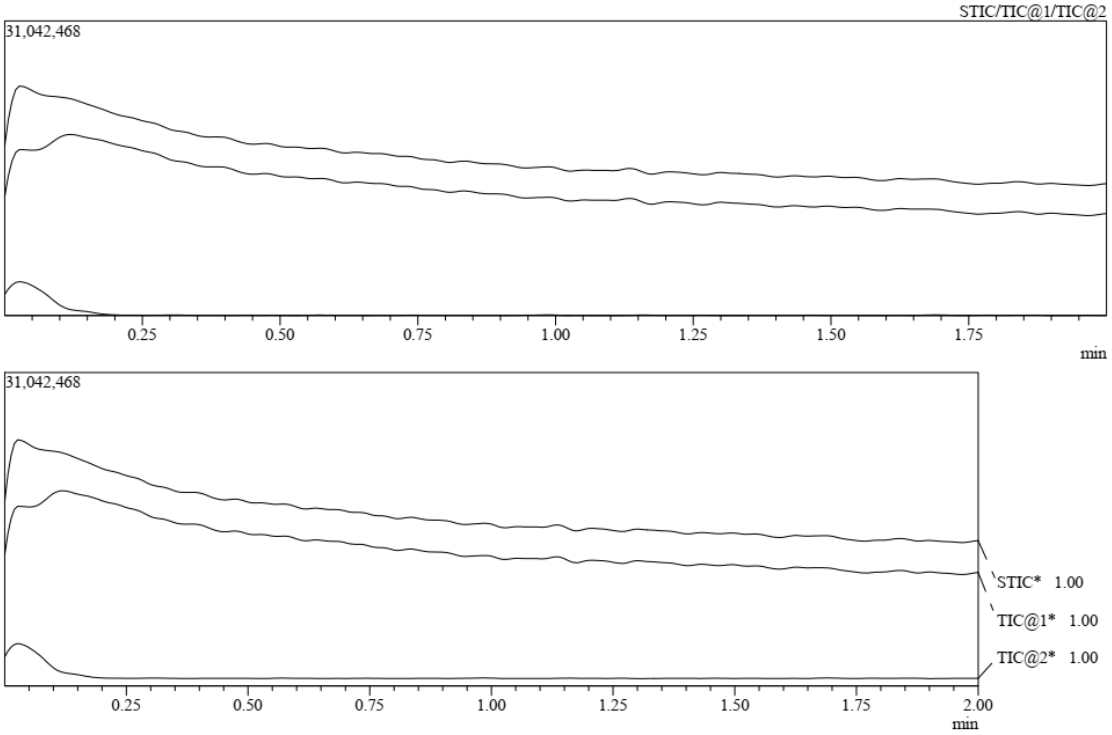
IR (2c)


%T
4000
3750
3500
3250
3000
2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1
p-anisidin
50
%T
0
3360.00
3008.95
1600.92
1550.77
1506.41
1436.97
1330.88
1313.52
1217.08
1033.85
869.90
827.46
786.96
717.52
626.87
563.21
524.64
426.27

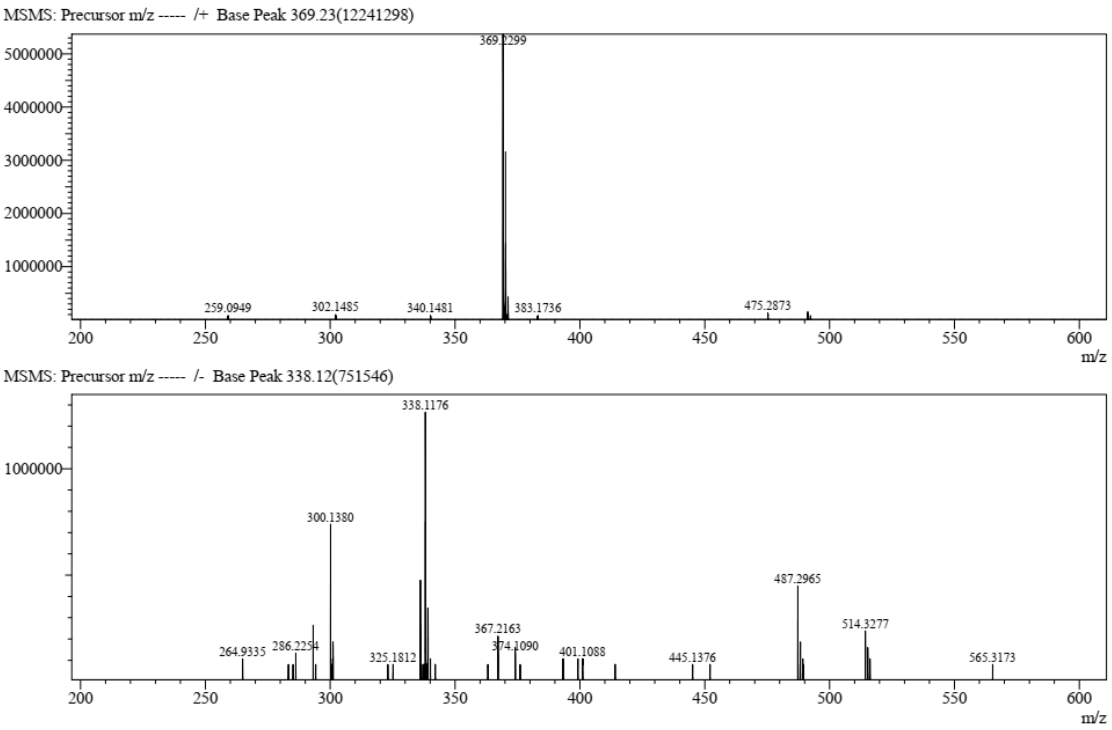
MS (2c)

==== Shimadzu LCMSsolution Data Report ====

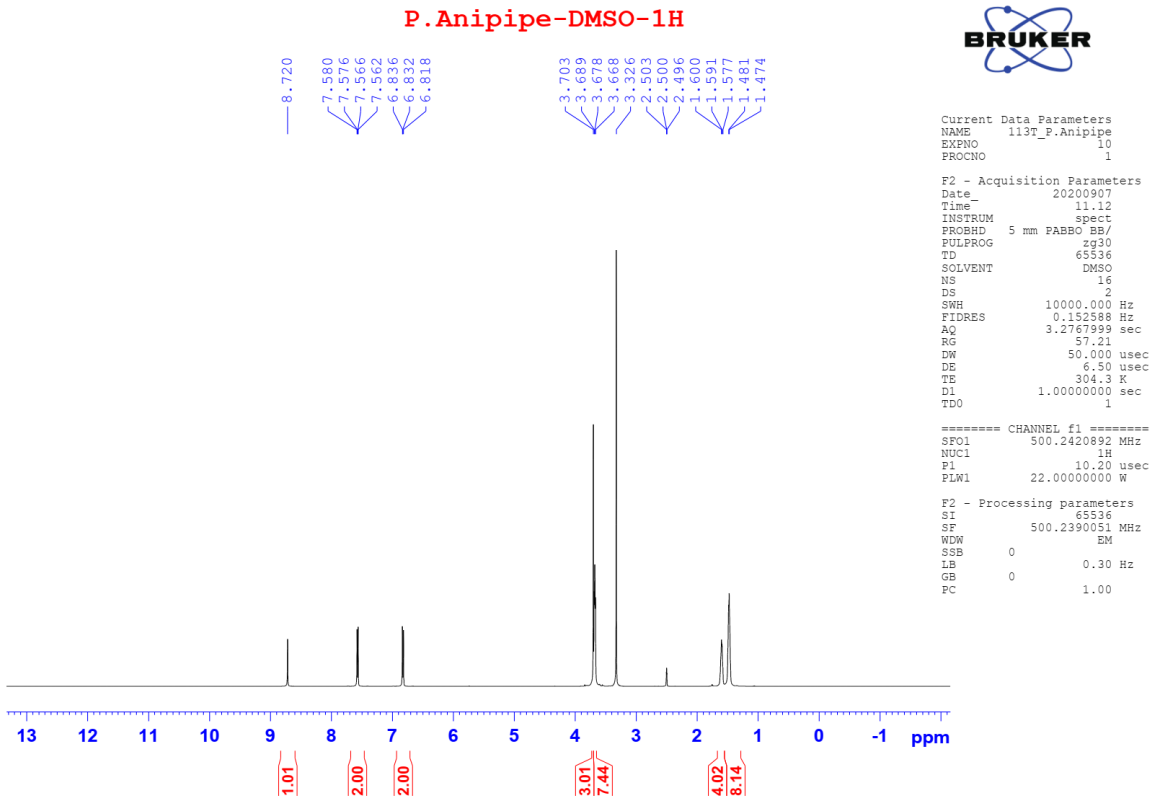
<Chromatogram>



<Spectrum>



^{1}H NMR (2c)

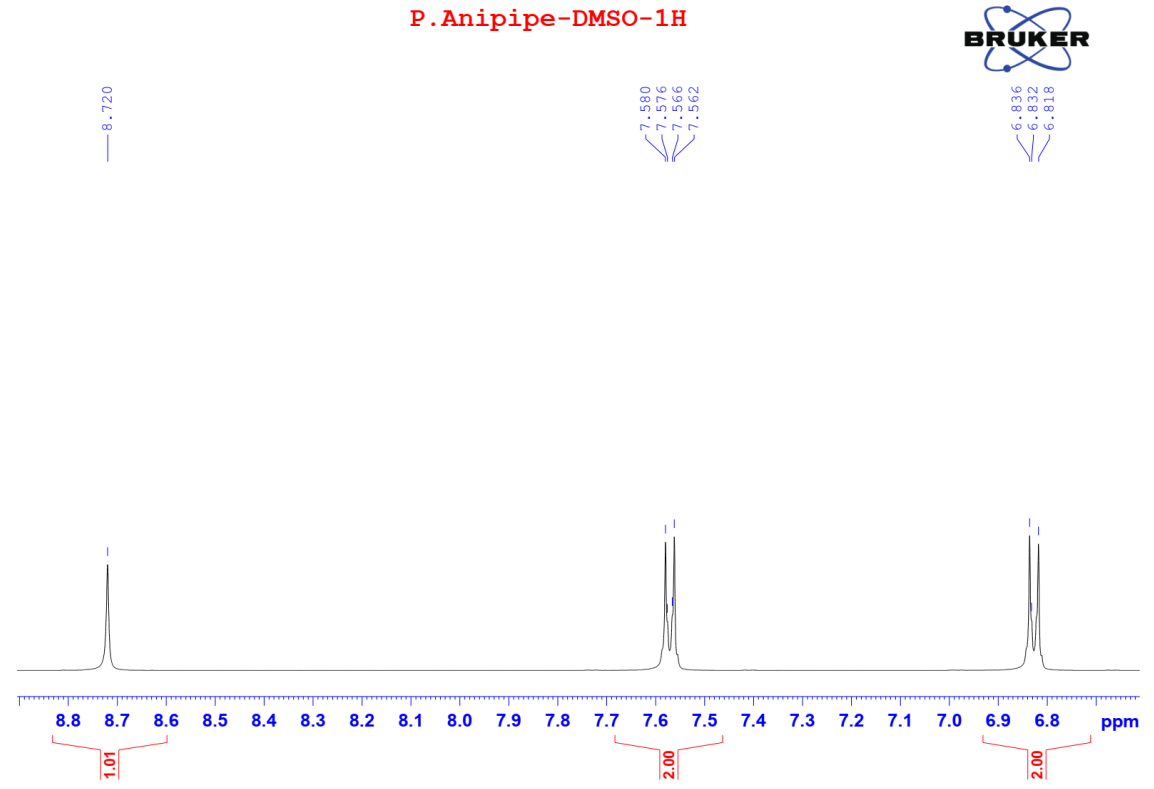



```
Current Data Parameters
NAME      113T_P.Anipipe
EXPNO                 10
PROCNO                 1

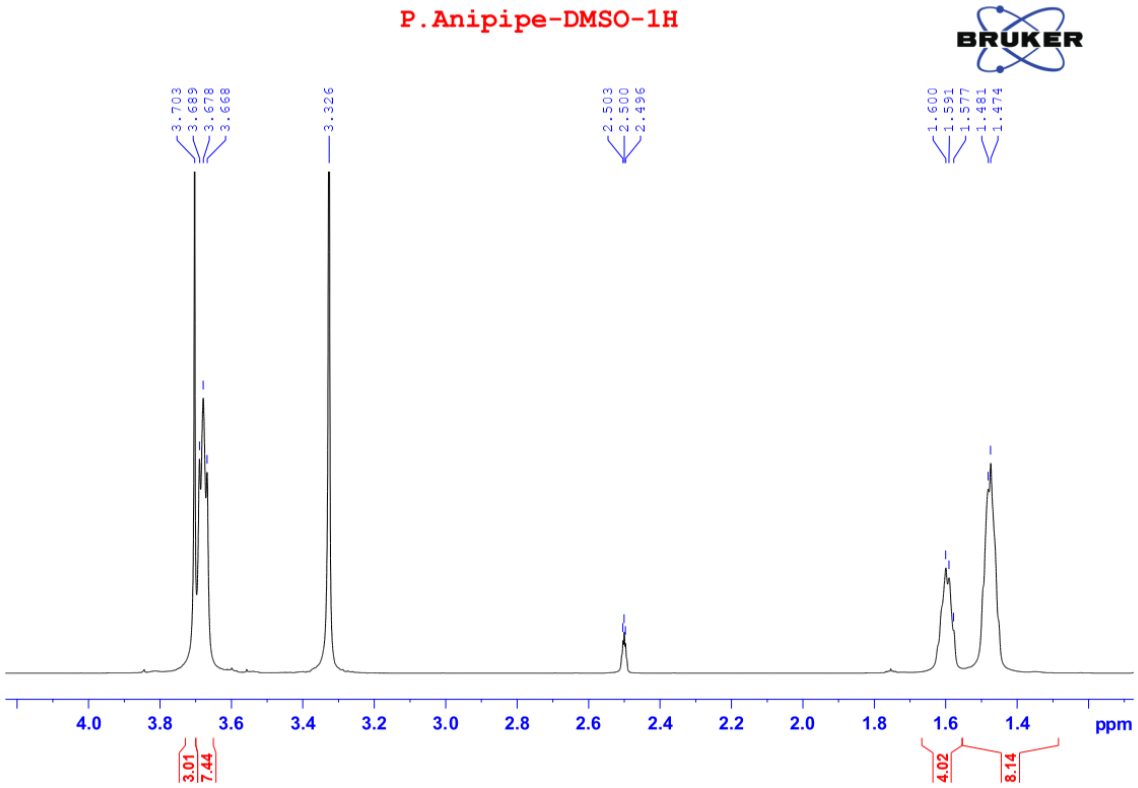
F2 - Acquisition Parameters
Date_           20200907
Time              11.12
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                   16
DS                    2
SWH           10000.000 Hz
FIDRES            0.152588 Hz
AQ             3.2767999 sec
RG                57.21
DW                50.000 usec
DE                 6.50 usec
TE                304.3 K
D1             1.00000000 sec
TD0                   1

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

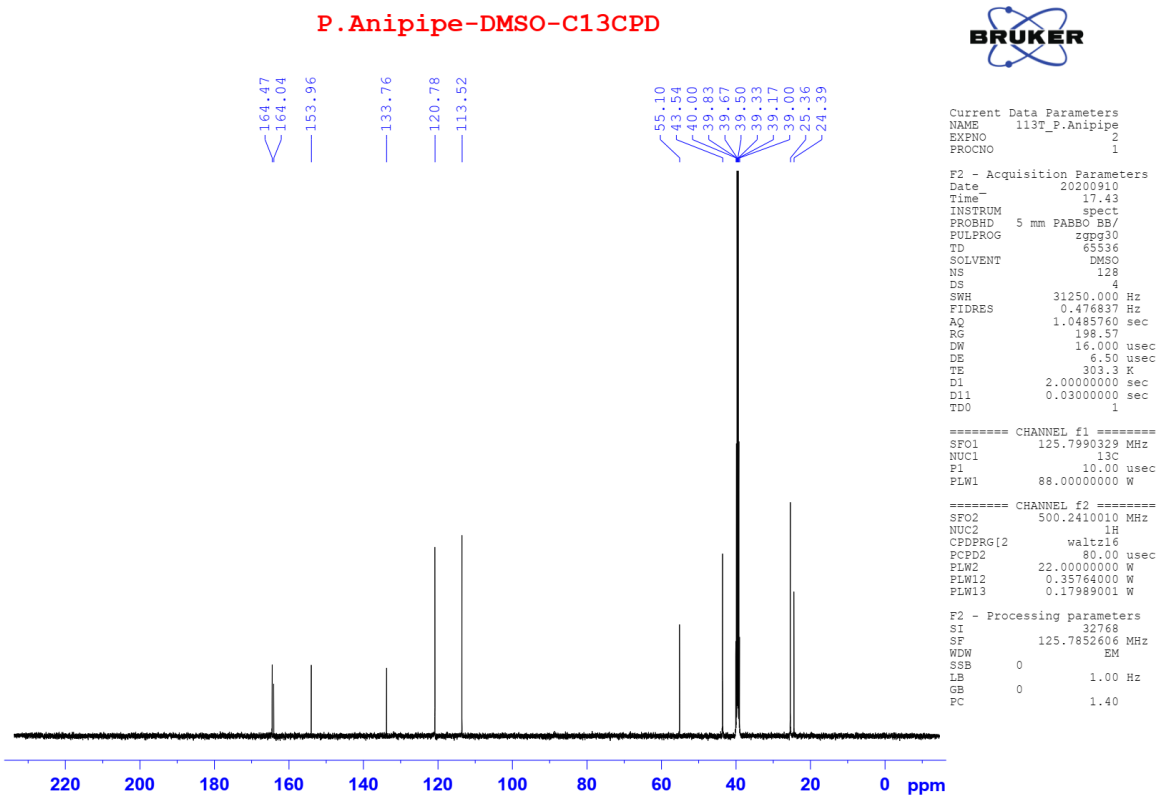
F2 - Processing parameters
SI                65536
SF           500.2390051 MHz
WDW                  EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



P.Anipipe-DMSO-1H



^{13}C NMR (2c)

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Current Data Parameters
NAME      113T_P.Anipipe
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200910
Time              17.43
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                 128
DS                   4
SWH          31250.000 Hz
FIDRES        0.476837 Hz
AQ           1.0485760 sec
RG              198.57
DW              16.000 usec
DE               6.50 usec
TE              303.3 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1        125.7990329 MHz
NUC1               13C
P1               10.00 usec
PLW1        88.00000000 W

======== CHANNEL f2 ========
SFO2        500.2410010 MHz
NUC2               1H
CPDPRG[2        waltz16
PCPD2            80.00 usec
PLW2        22.00000000 W
PLW12        0.35764000 W
PLW13        0.17989001 W

F2 - Processing parameters
SI                32768
SF          125.7852606 MHz
WDW                EM
SSB       0
LB               1.00 Hz
GB        0
PC               1.40
```
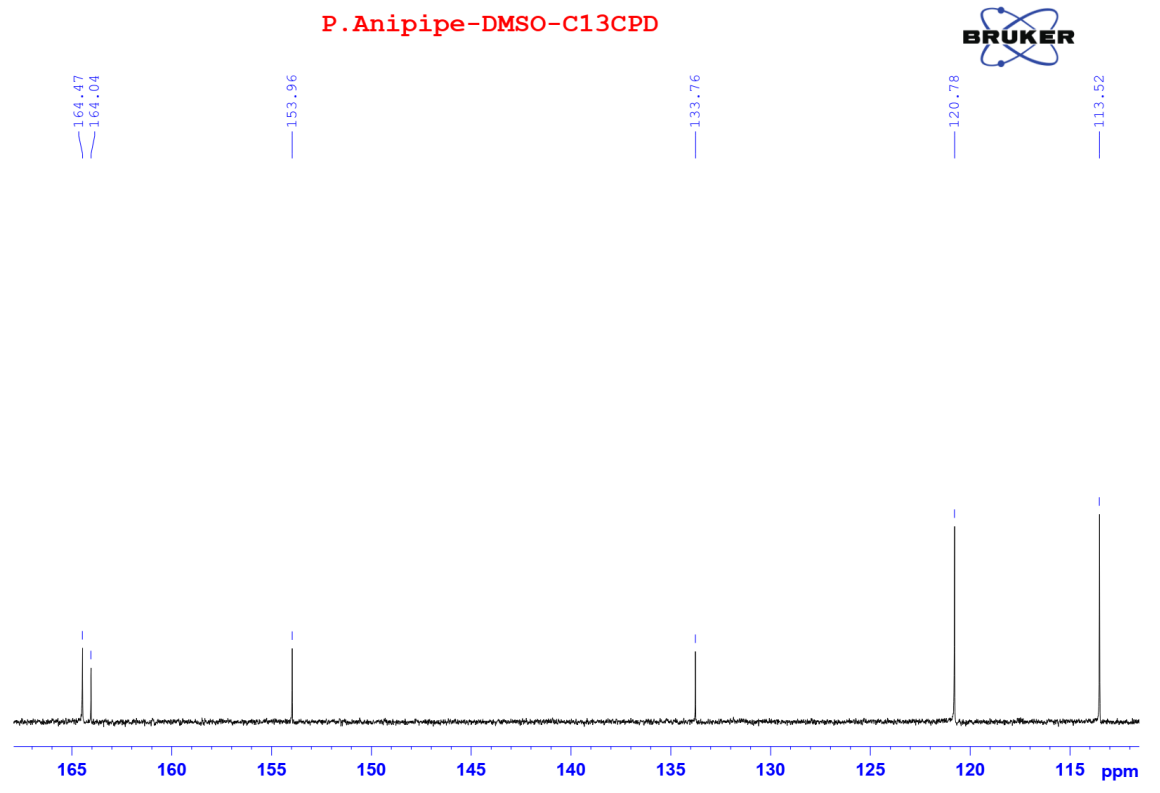
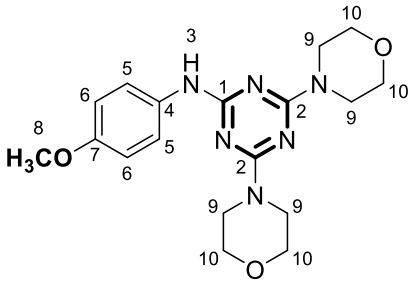



COMPOUND 3c



Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	8.90 (1H, s)	-NH-
5	7.55 (2H, d, *J* = 9.0 Hz)	H_{Ar}
6	6.84 (2H, d, *J* = 9.0 Hz)	H_{Ar}
8	3.70 (3H, s)	-OCH_3
9	3.68 (8H, t, *J* = 5.0 Hz)	-CH_2-
10	3.61 (8H, t, *J* = 4.5 Hz)	-CH_2-

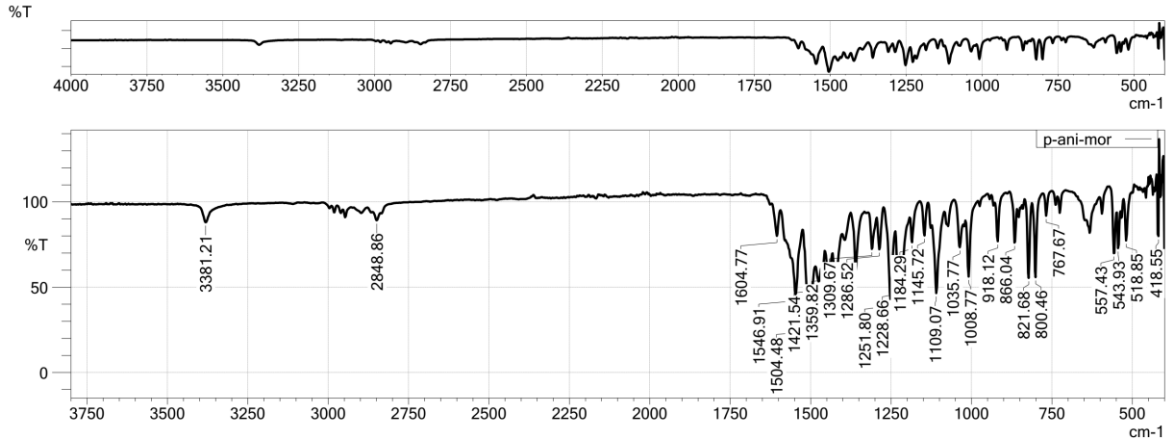
^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 164.7 (>C=, C_2), 163.9 (>C=, C_1), 154.2 (>C=, C_7), 133.3 (>C=, C_4), 121.1 (>C=, C_5), 113.6 (>C=, C_6), 66.0 (-CH_2-, C_{10}), 55.1 (-OCH_3, C_8), 43.3 (-CH_2-, C_9).

LC-MS (*m/z*)

Expected formula: $C_{18}H_{24}N_6O_3$ Exact mass: 372.1910

$[M+H]^+$ calcd: 373.1983 $[M+H]^+$ found: 373.1981

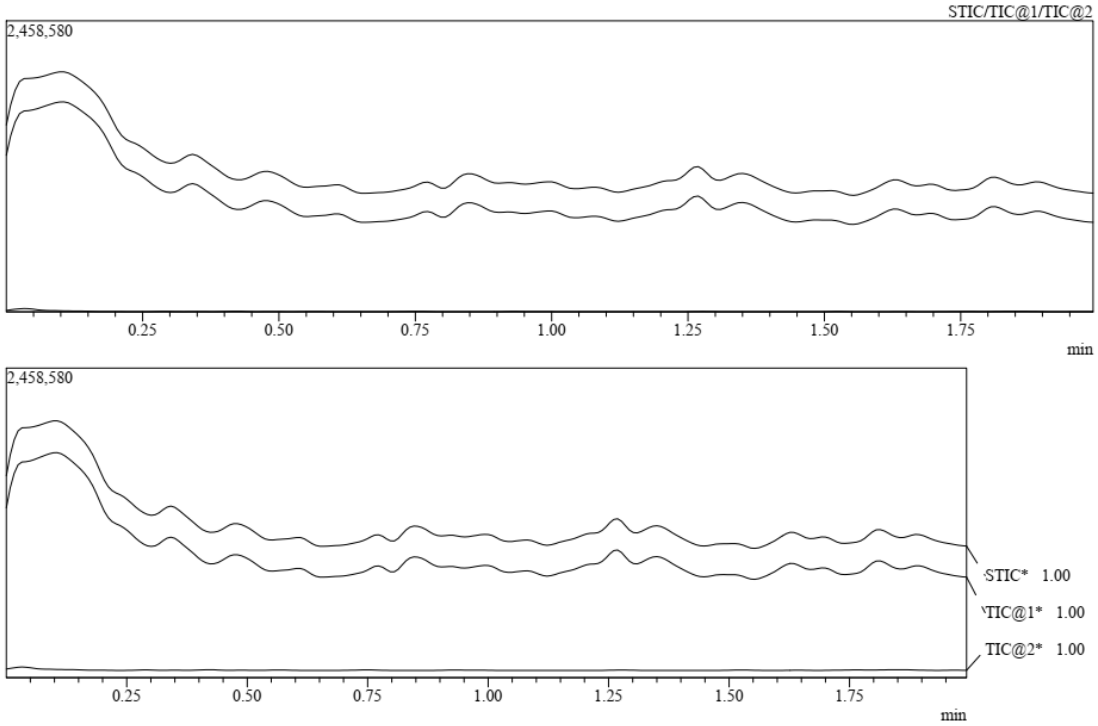
IR (3c)


%T
4000 3750 3500 3250 3000 2750 2500 2250 2000 1750 1500 1250 1000 750 500
cm-1
p-ani-mor
100
%T
50
0
3381.21
2848.86
1604.77
1546.91
1504.48
1421.54
1359.82
1309.67
1286.52
1251.80
1228.66
1184.29
1145.72
1109.07
1035.77
1008.77
918.12
866.04
821.68
800.46
767.67
557.43
543.93
518.85
418.55
3750 3500 3250 3000 2750 2500 2250 2000 1750 1500 1250 1000 750 500
cm-1

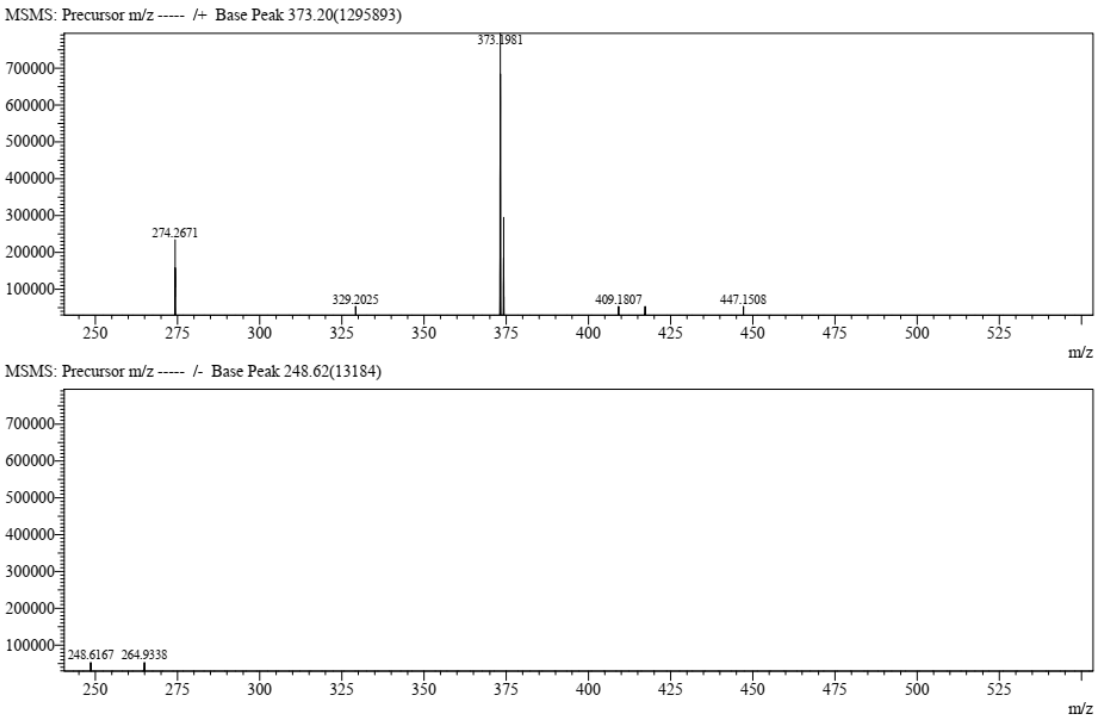
MS (3c)

==== Shimadzu LCMSsolution Data Report ====

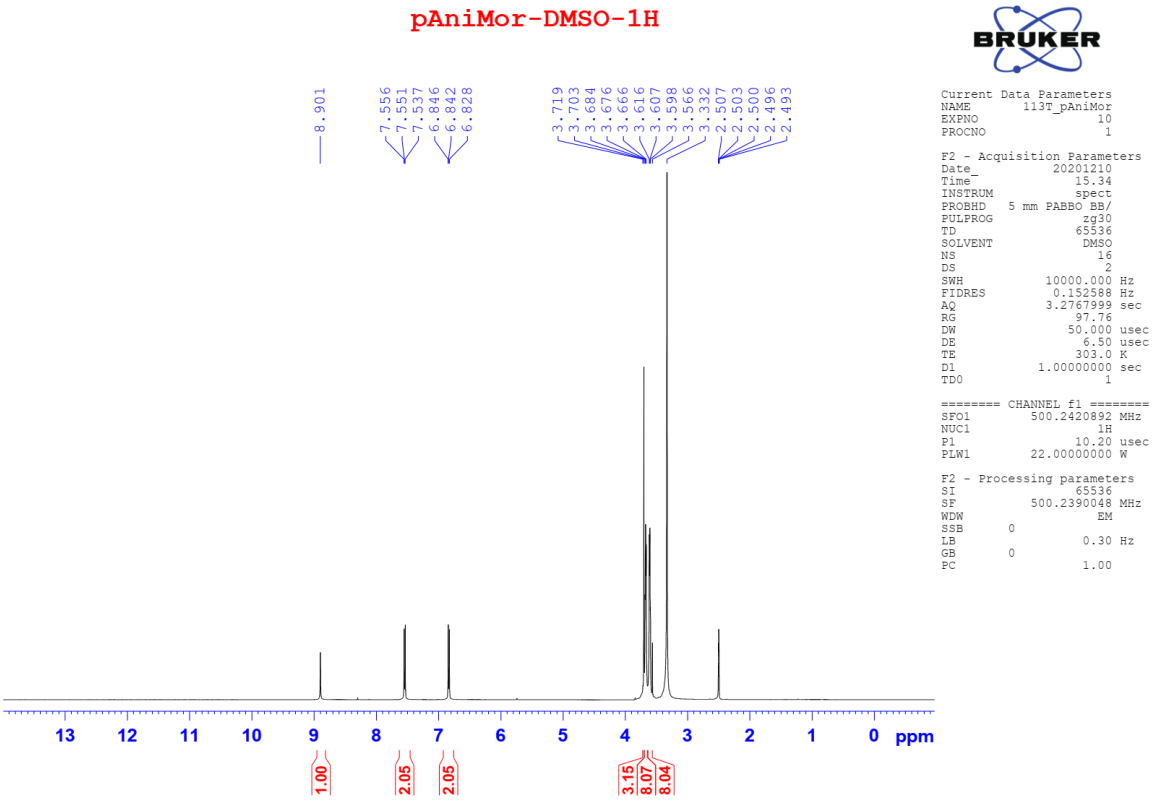
<Chromatogram>



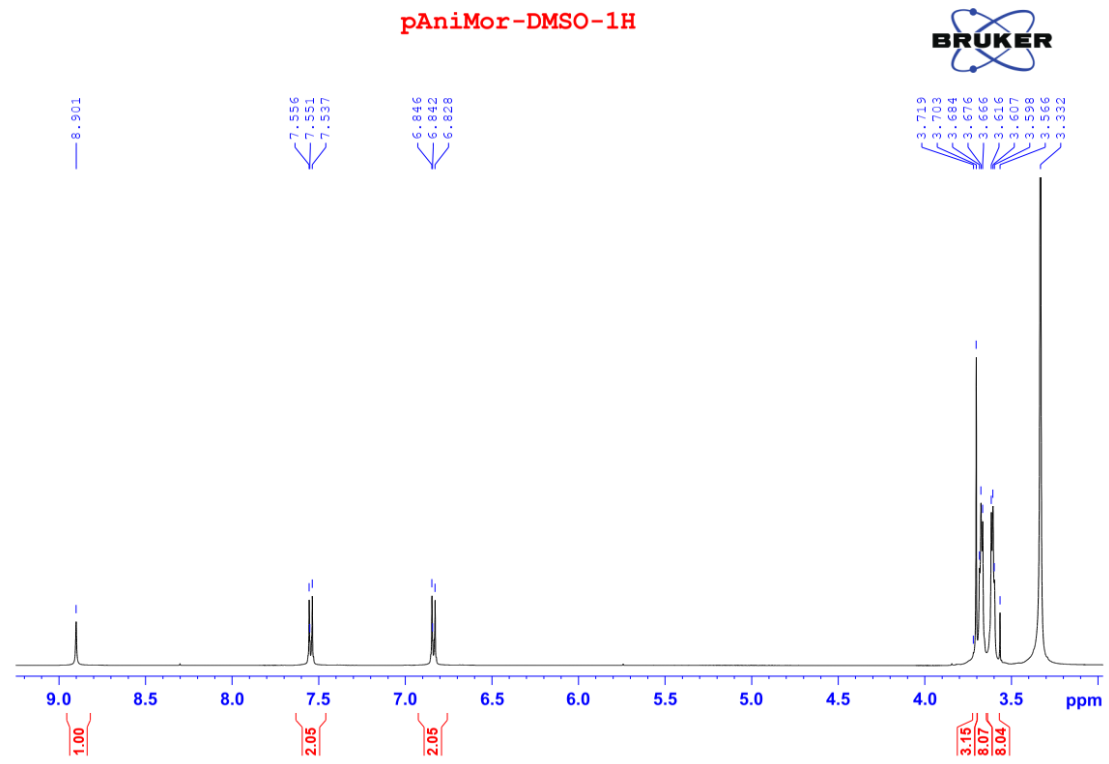
<Spectrum>

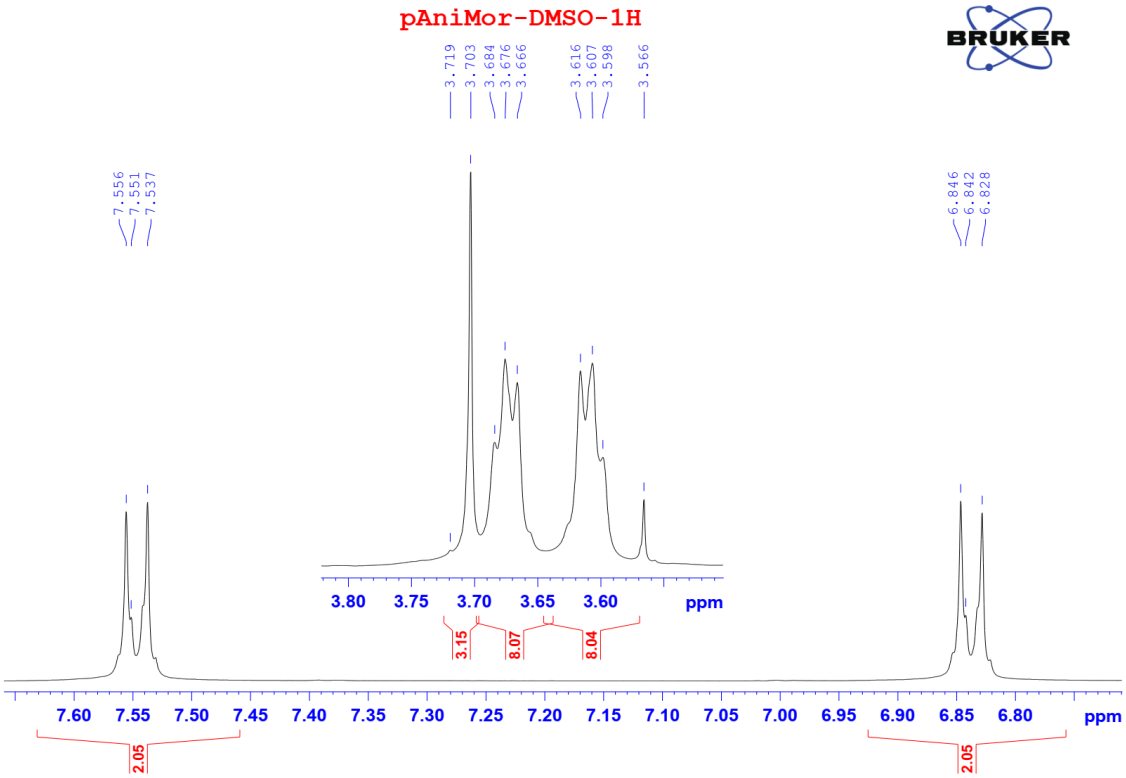


^{1}H NMR (3c)

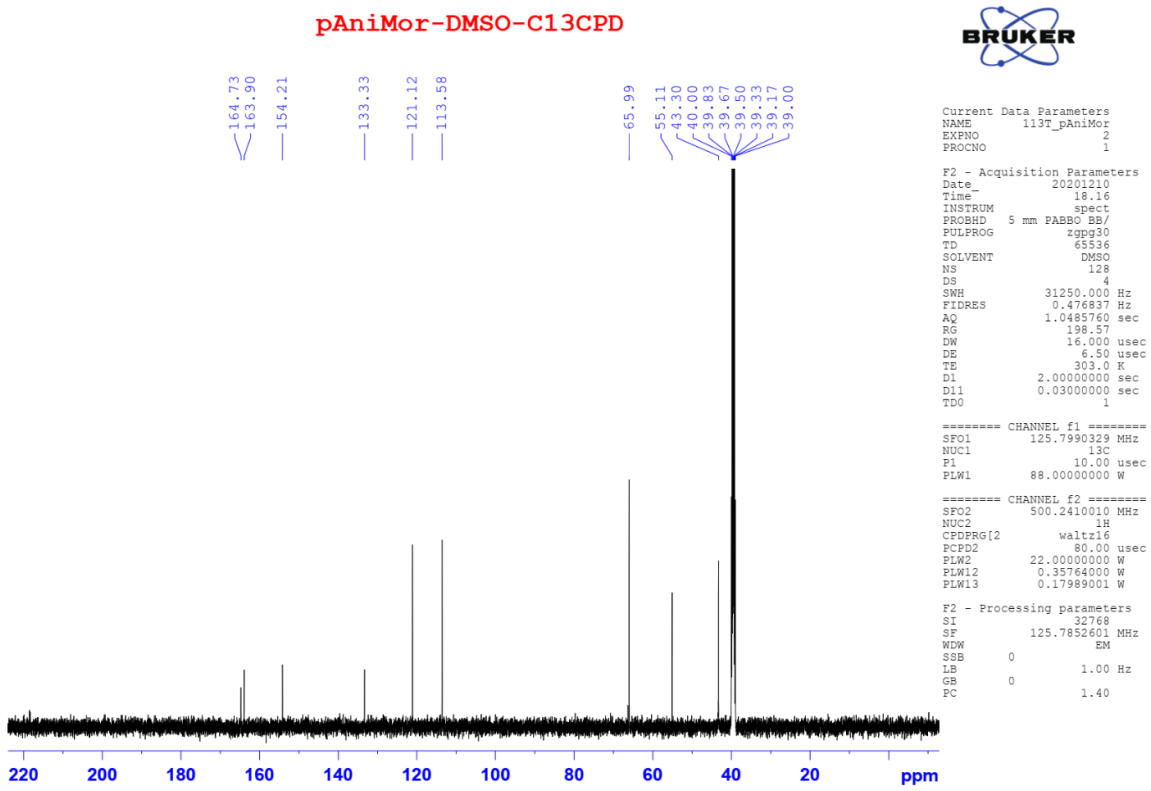


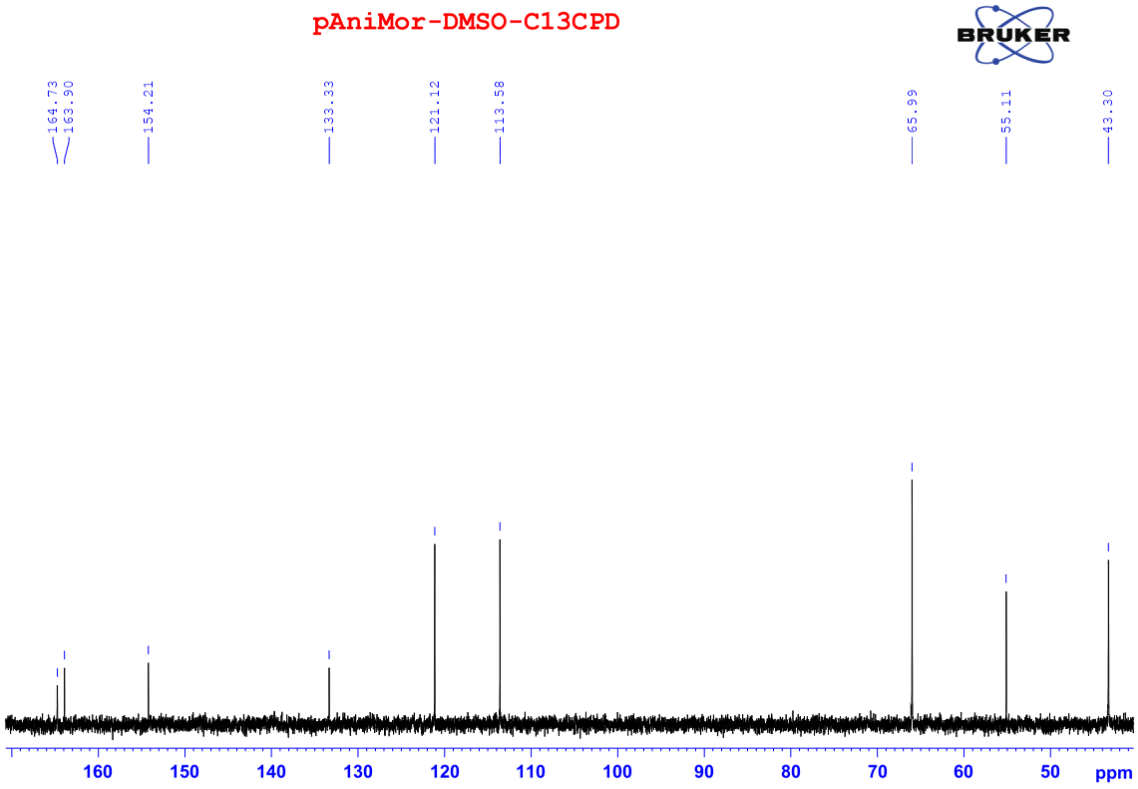

```
Current Data Parameters
NAME          113T_pAniMor
EXPNO                   10
PROCNO                   1

F2 - Acquisition Parameters
Date_              20201210
Time                 15.34
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                   97.76
DW                  50.000 usec
DE                   6.50 usec
TE                  303.0 K
D1              1.00000000 sec
TD0                     1

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

F2 - Processing parameters
SI                  65536
SF             500.2390048 MHz
WDW                    EM
SSB          0
LB                   0.30 Hz
GB           0
PC                   1.00
```



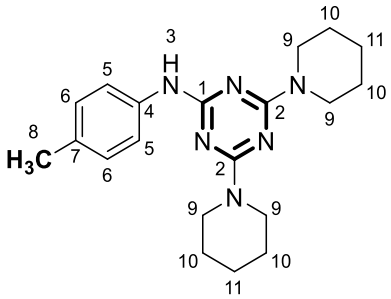

pAniMor-DMSO-1H
BRUKER
3.719
3.703
3.684
3.676
3.666
3.616
3.607
3.598
3.566
7.556
7.551
7.537
6.846
6.842
6.828
3.80
3.75
3.70
3.65
3.60
ppm
3.15
8.07
8.04
7.60
7.55
7.50
7.45
7.40
7.35
7.30
7.25
7.20
7.15
7.10
7.05
7.00
6.95
6.90
6.85
6.80
ppm
2.05
2.05

^{13}C NMR (3c)


pAniMor-DMSO-C13CPD
BRUKER
164.73
163.90
154.21
133.33
121.12
113.58
65.99
55.11
43.30
40.00
39.83
39.67
39.50
39.33
39.17
39.00
Current Data Parameters
NAME 113T_pAniMor
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201210
Time 18.16
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 128
DS 4
SWH 31250.000 Hz
FIDRES 0.476837 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
TD0 1
======== CHANNEL f1 ========
SFO1 125.7990329 MHz
NUC1 13C
P1 10.00 usec
PLW1 88.00000000 W
======== CHANNEL f2 ========
SFO2 500.2410010 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 22.00000000 W
PLW12 0.35764000 W
PLW13 0.17989001 W
F2 - Processing parameters
SI 32768
SF 125.7852601 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
220
200
180
160
140
120
100
80
60
40
20
ppm


pAniMor-DMSO-C13CPD
BRUKER
164.73
163.90
154.21
133.33
121.12
113.58
65.99
55.11
43.30
160
150
140
130
120
110
100
90
80
70
60
50
ppm

COMPOUND 2d



Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	8.48 (1H, s)	-NH-
5	7.55 (2H, d, *J* = 8.5 Hz)	H_{Ar}
6	7.04 (2H, d, *J* = 8.0 Hz)	H_{Ar}
8	2.24 (3H, s)	-CH_3
9	3.70 (8H, t, *J* = 5.5 Hz)	-CH_2-
10	1.52 (8H, t, *J* = 5.5 Hz)	-CH_2-
11	1.63 (4H, t, *J* = 5.5 Hz)	-CH_2-

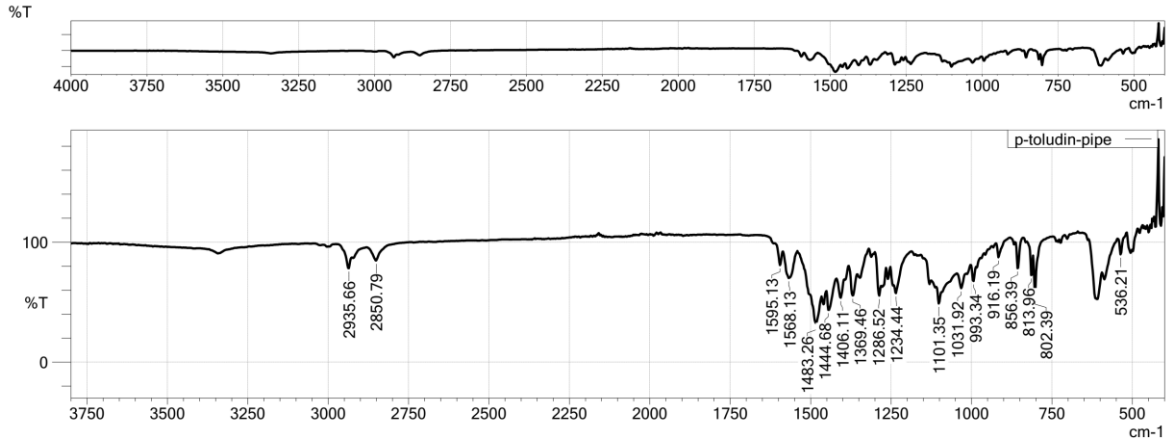
^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 164.4 (>C=, C_2), 163.9 (>C=, C_1), 137.7 (>C=, C_4), 129.6 (>C=, C_7), 128.2 (>C=, C_6), 119.3 (>C=, C_5), 43.3 (-CH_2-, C_9), 24.9 (-CH_2-, C_{10}), 24.0 (-CH_2-, C_{11}), 19.8 (-CH_3, C_8).

LC-MS (*m/z*)

Expected formula: $C_{20}H_{28}N_6$ Exact mass: 352.2375

$[M+H]^+$ calcd: 353.2448 $[M+H]^+$ found: 353.2369

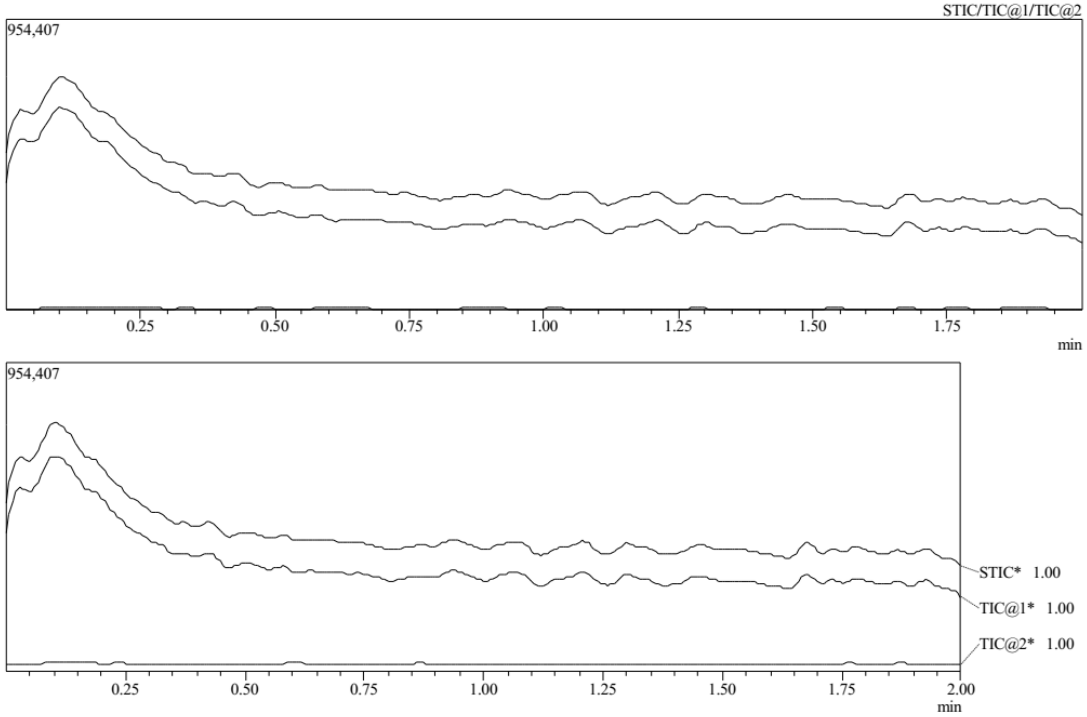
IR (2d)


%T
4000 3750 3500 3250 3000 2750 2500 2250 2000 1750 1500 1250 1000 750 500
cm-1
p-toludin-pipe
100
%T
0
2935.66
2850.79
1595.13
1568.13
1483.26
1444.68
1406.11
1369.46
1286.52
1234.44
1101.35
1031.92
993.34
916.19
856.39
813.96
802.39
536.21
3750 3500 3250 3000 2750 2500 2250 2000 1750 1500 1250 1000 750 500
cm-1

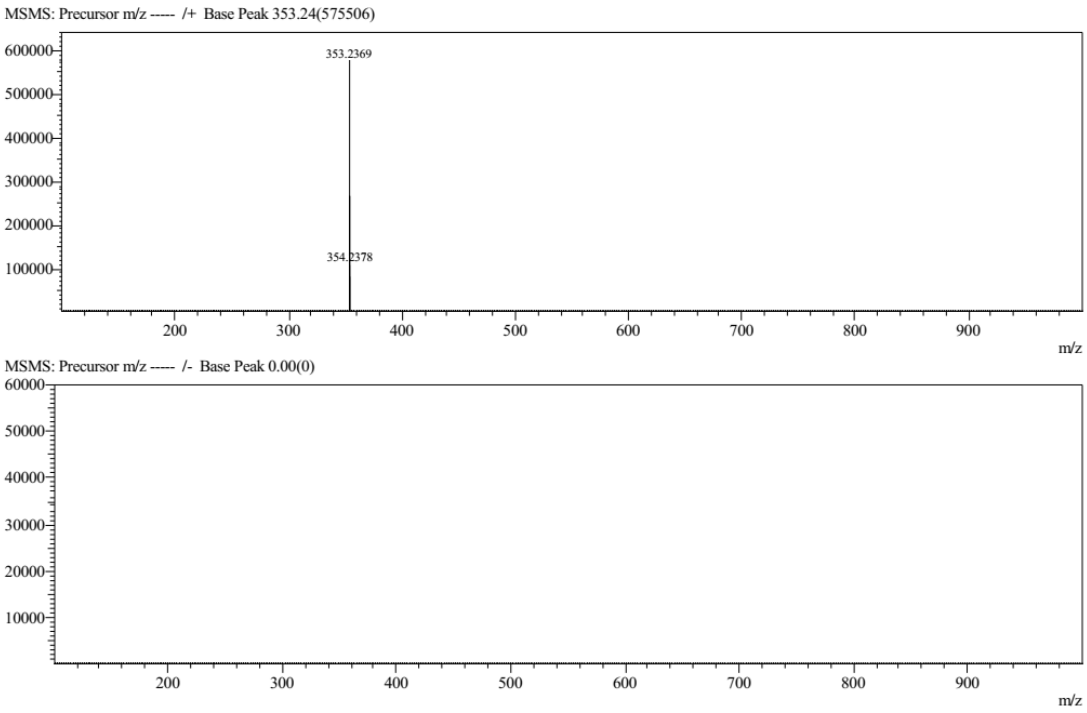
MS (2d)

==== Shimadzu LCMSsolution Data Report ====

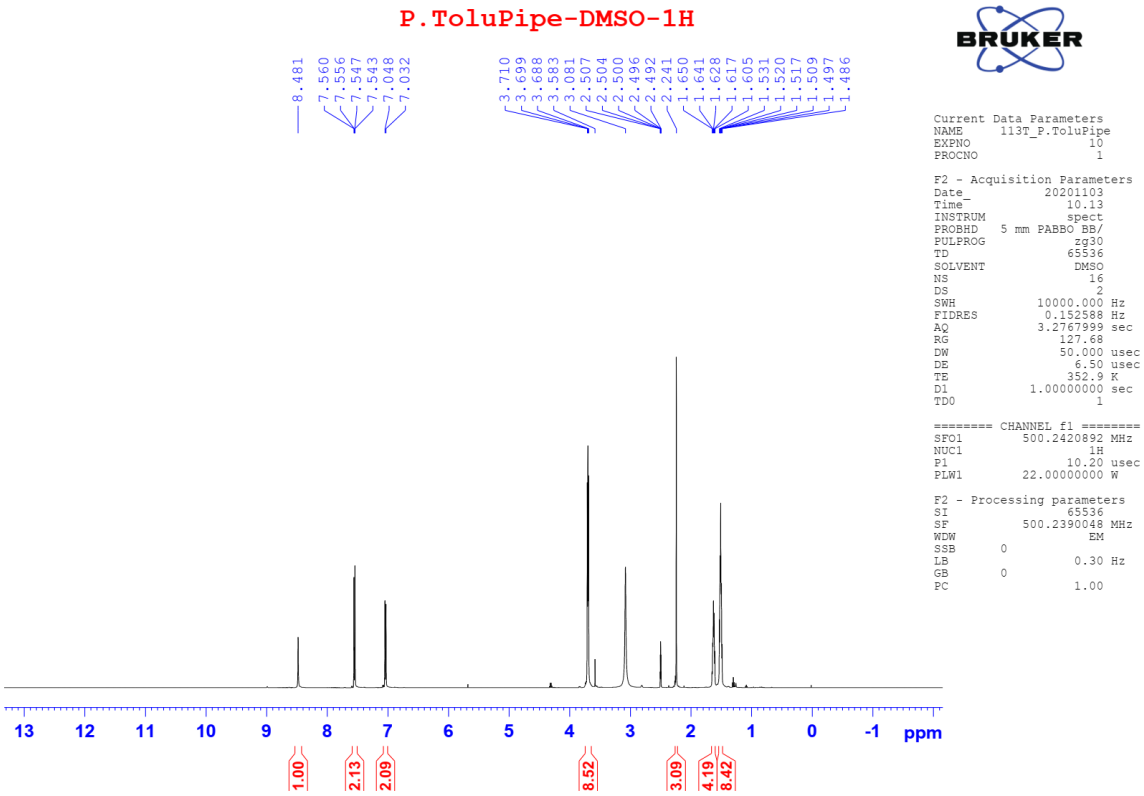
<Chromatogram>

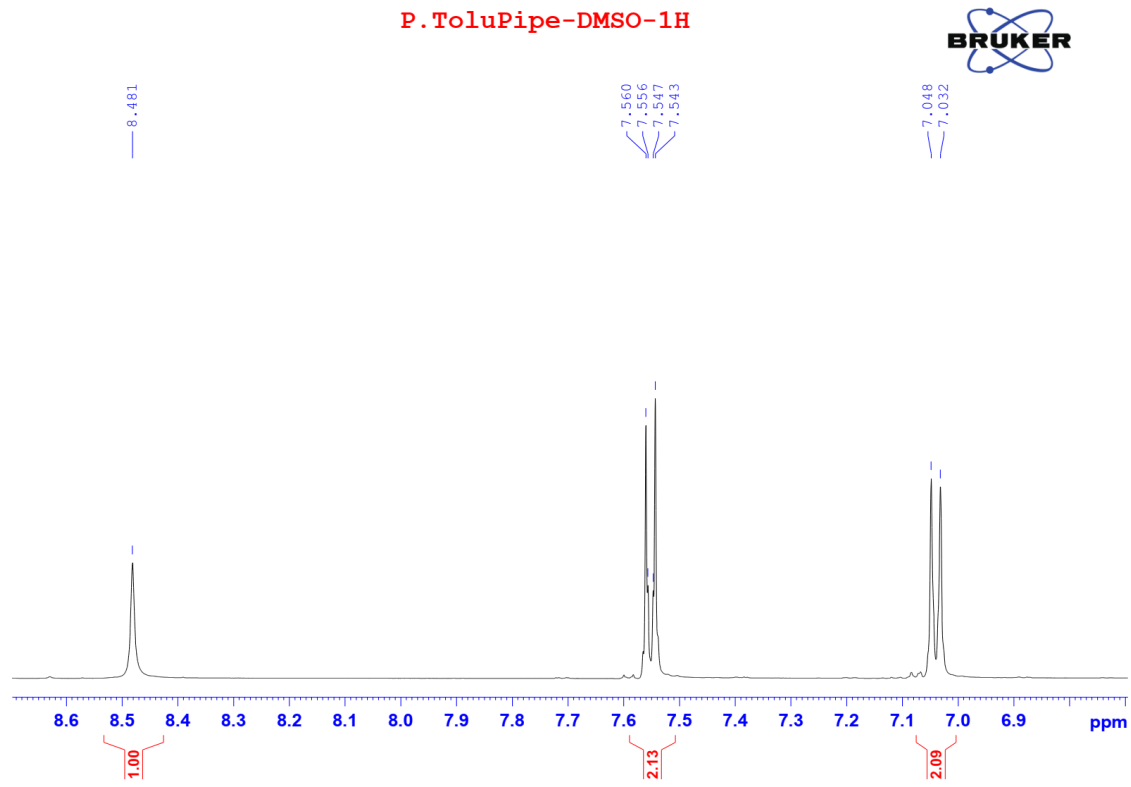


<Spectrum>

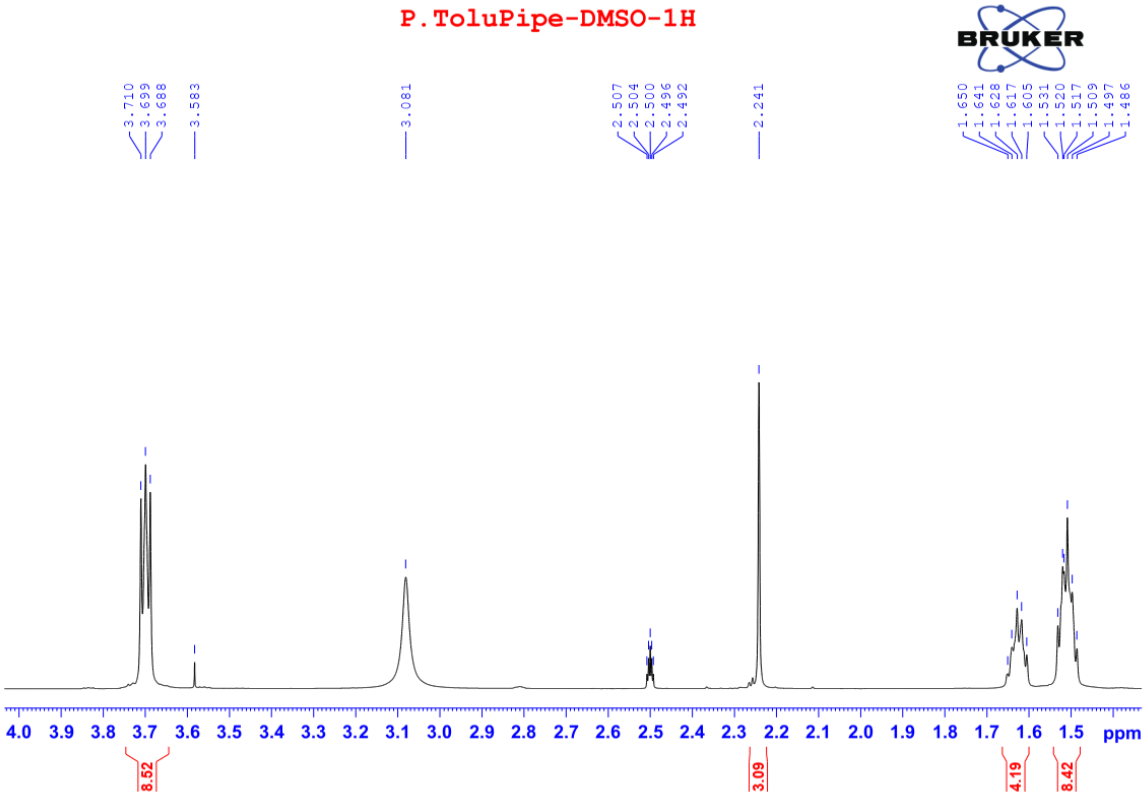


^{1}H NMR (2d)

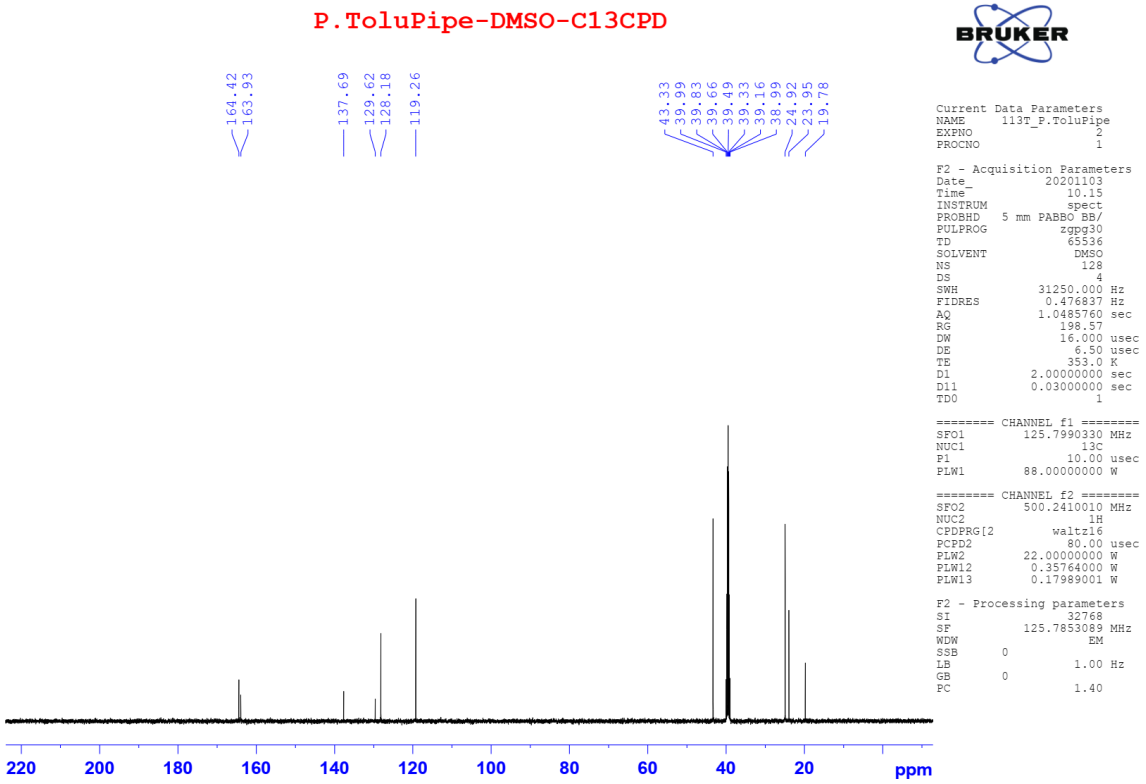

P.ToluPipe-DMSO-1H
BRUKER
8.481
7.560
7.556
7.547
7.543
7.048
7.032
3.710
3.699
3.688
3.583
3.081
2.507
2.504
2.500
2.496
2.492
2.241
1.650
1.641
1.628
1.617
1.605
1.531
1.520
1.517
1.509
1.497
1.486
Current Data Parameters
NAME 113T_P.ToluPipe
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201103
Time 10.13
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 127.68
DW 50.000 usec
DE 6.50 usec
TE 352.9 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.2420892 MHz
NUC1 1H
P1 10.20 usec
PLW1 22.00000000 W
F2 - Processing parameters
SI 65536
SF 500.2390048 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 ppm
1.00
2.13
2.09
8.52
3.09
4.19
8.42


P.ToluPipe-DMSO-1H
BRUKER
8.481
7.560
7.556
7.547
7.543
7.048
7.032
8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 ppm
1.00
2.13
2.09

P.ToluPipe-DMSO-1H



^{13}C NMR (2d)

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Current Data Parameters
NAME      113T_P.ToluPipe
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_           20201103
Time               10.15
INSTRUM             spect
PROBHD   5 mm PABBO BB/
PULPROG          zgpg30
TD                65536
SOLVENT             DMSO
NS                    128
DS                      4
SWH           31250.000 Hz
FIDRES         0.476837 Hz
AQ             1.0485760 sec
RG               198.57
DW               16.000 usec
DE                6.50 usec
TE               353.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                     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
CPDPRG[2          waltz16
PCPD2               80.00 usec
PLW2         22.00000000 W
PLW12         0.35764000 W
PLW13         0.17989001 W

F2 - Processing parameters
SI                  32768
SF           125.7853089 MHz
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
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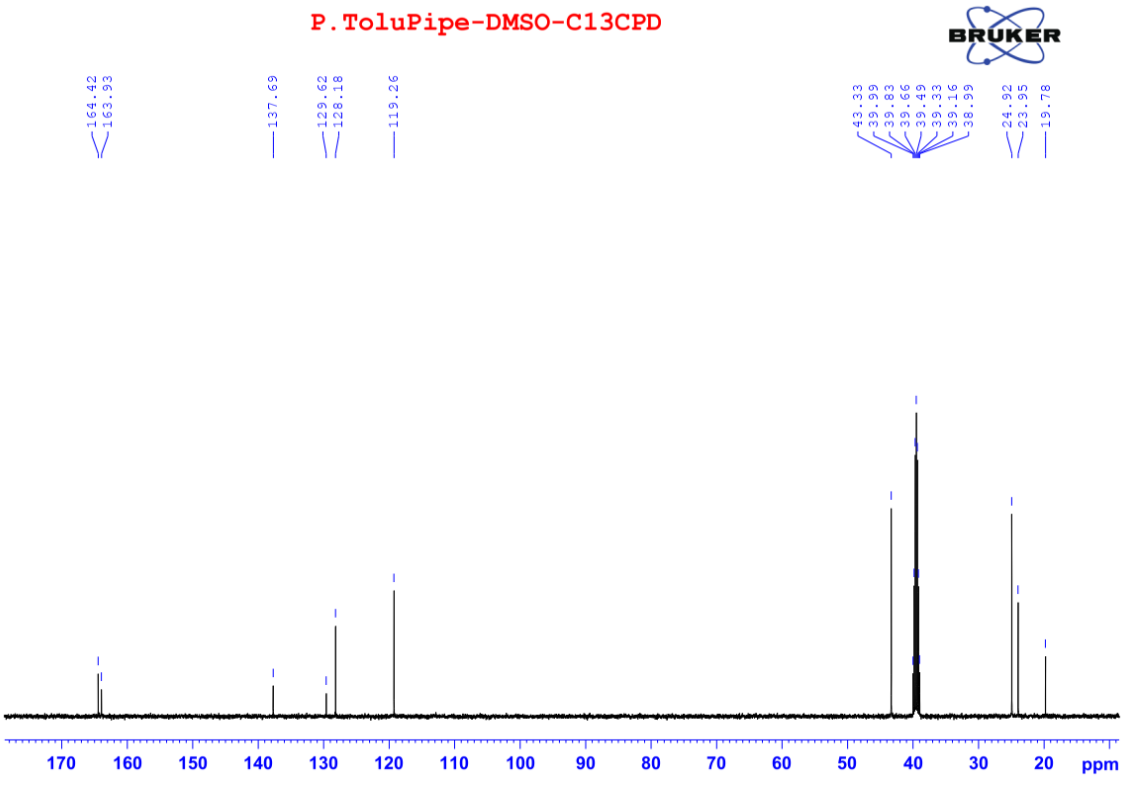
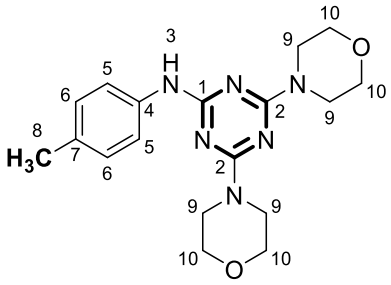


COMPOUND 3d



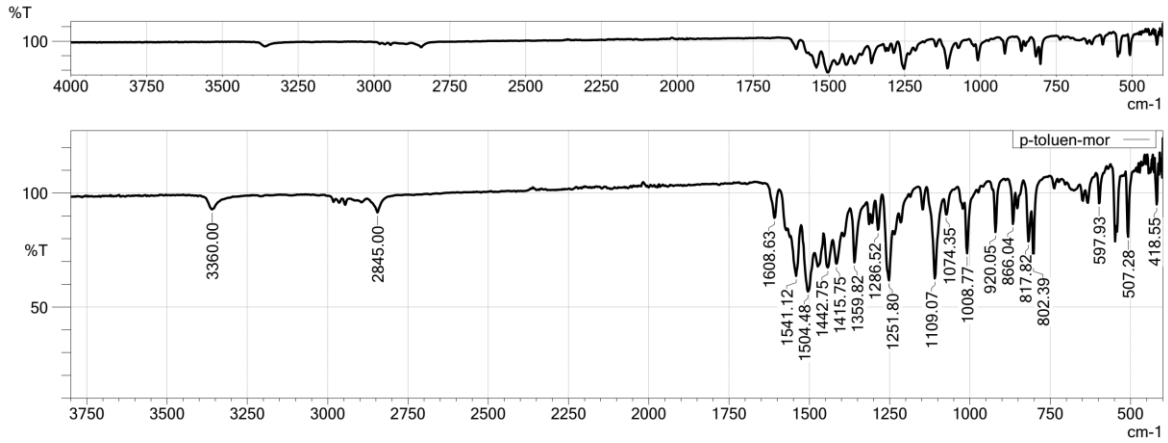
Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	8.95 (1H, s)	-NH-
5	7.53 (2H, d, *J* = 8.5 Hz)	H_{Ar}
6	7.05 (2H, d, *J* = 8.0 Hz)	H_{Ar}
8	2.23 (3H, s)	-CH_3
9	3.69 (8H, t, *J* = 5.0 Hz)	-CH_2-
10	3.61 (8H, t, *J* = 4.5 Hz)	-CH_2-

^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 164.7 (>C=, C_2), 163.9 (>C=, C_1), 137.6 (>C=, C_4), 130.2 (>C=, C_7), 128.7 (>C=, C_6), 119.7 (>C=, C_5), 66.0 (-CH_2-, C_{10}), 43.3 (-CH_2-, C_9), 20.3 (-CH_3, C_8).

LC-MS (*m/z*)

Expected formula: $C_{18}H_{24}N_6O_2$	Exact mass: 356.1961
$[M+H]^+$ calcd: 357.2304	$[M+H]^+$ found: 357.2304

IR (3d)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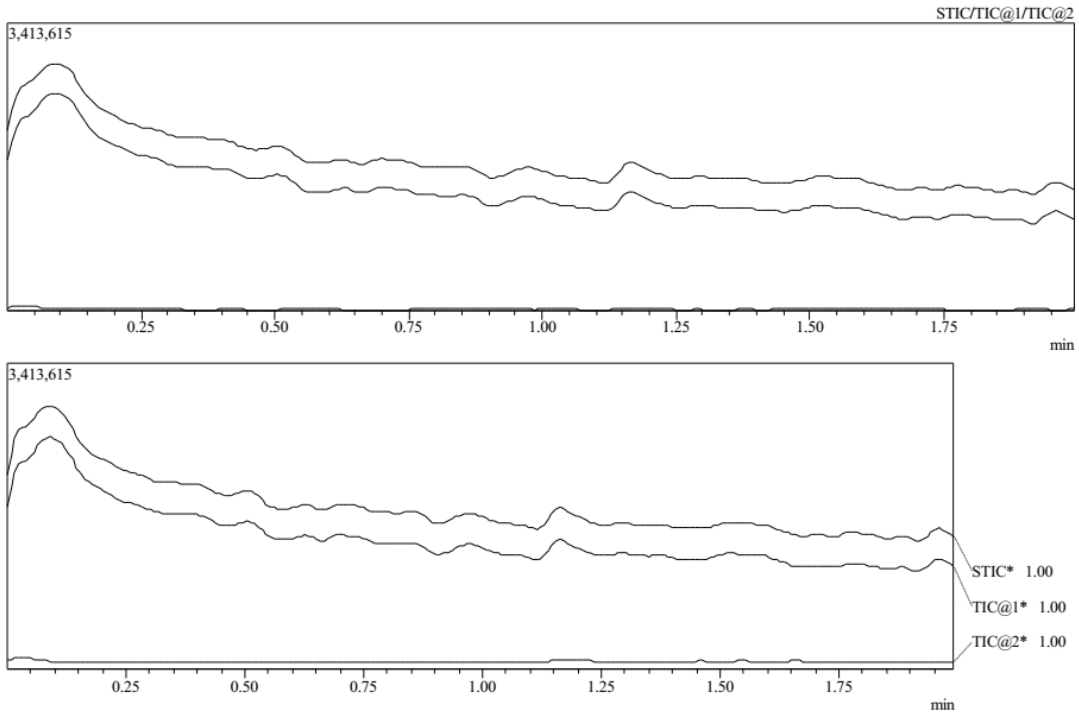
3500
3250
3000
2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1
p-toluen-mor
100
%T
50
3360.00
2845.00
1608.63
1541.12
1504.48
1442.75
1415.75
1359.82
1286.52
1251.80
1109.07
1074.35
1008.77
920.05
866.04
817.82
802.39
597.93
507.28
418.55
3750
3500
3250
3000
2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1

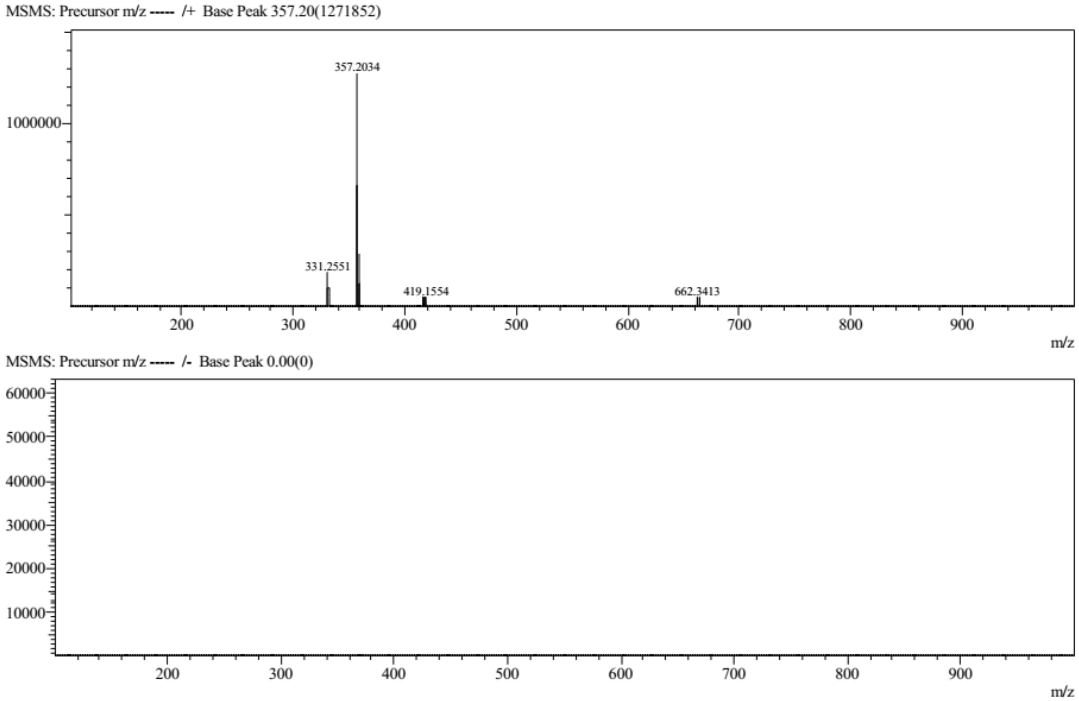
MS (3d)

==== Shimadzu LCMSsolution Data Report ====

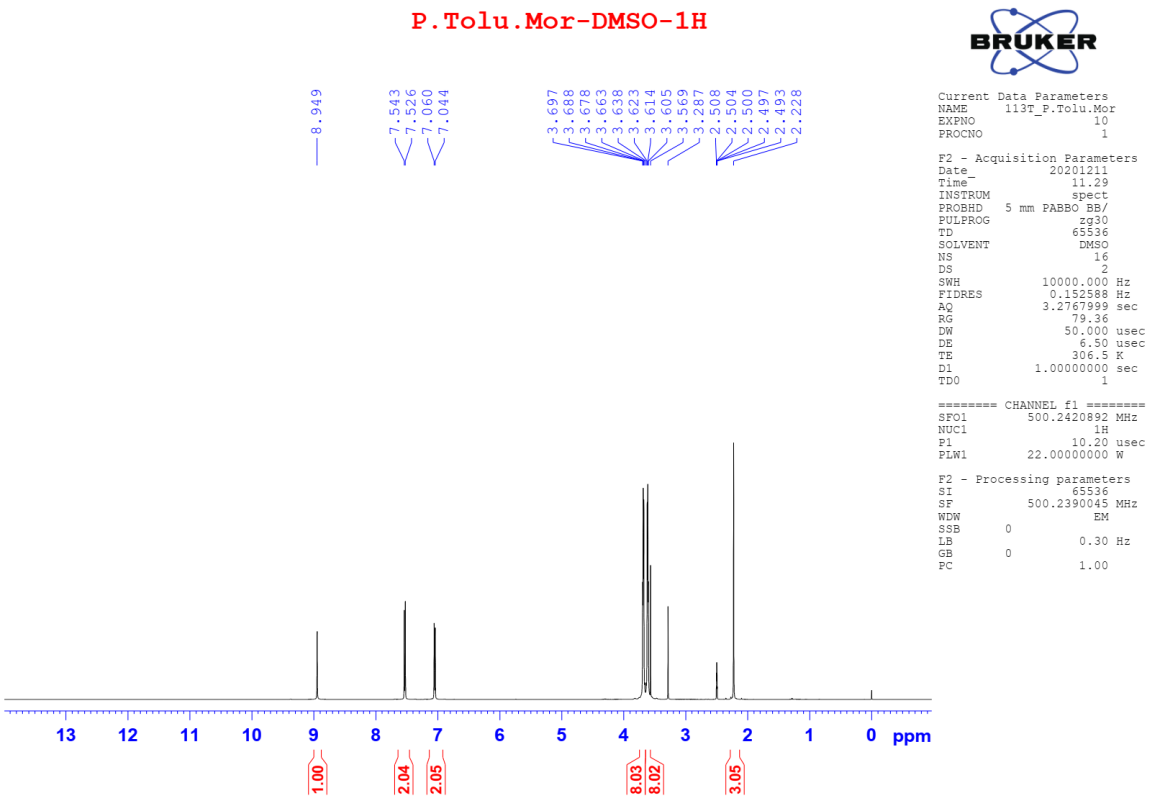
<Chromatogram>



<Spectrum>



^{1}H NMR (3d)

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Current Data Parameters
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EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_            20201211
Time                11.29
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                  79.36
DW                 50.000 usec
DE                  6.50 usec
TE                 306.5 K
D1            1.00000000 sec
TD0                     1

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

F2 - Processing parameters
SI                   65536
SF            500.2390045 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
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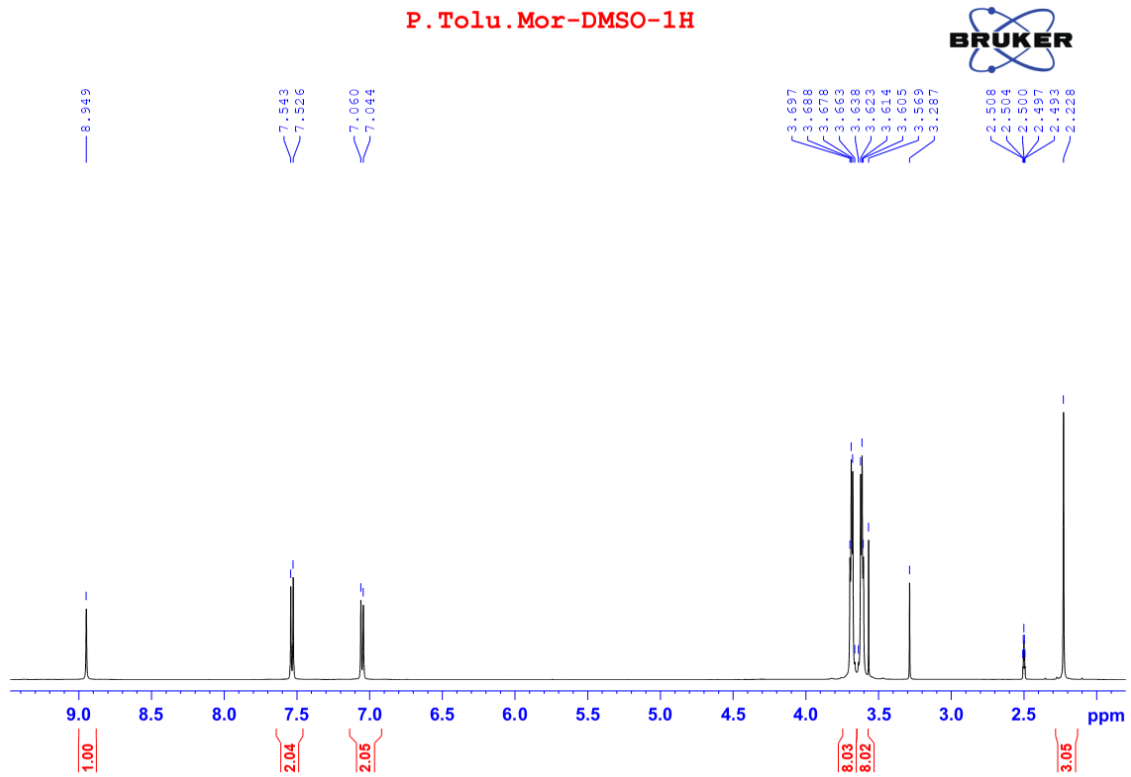
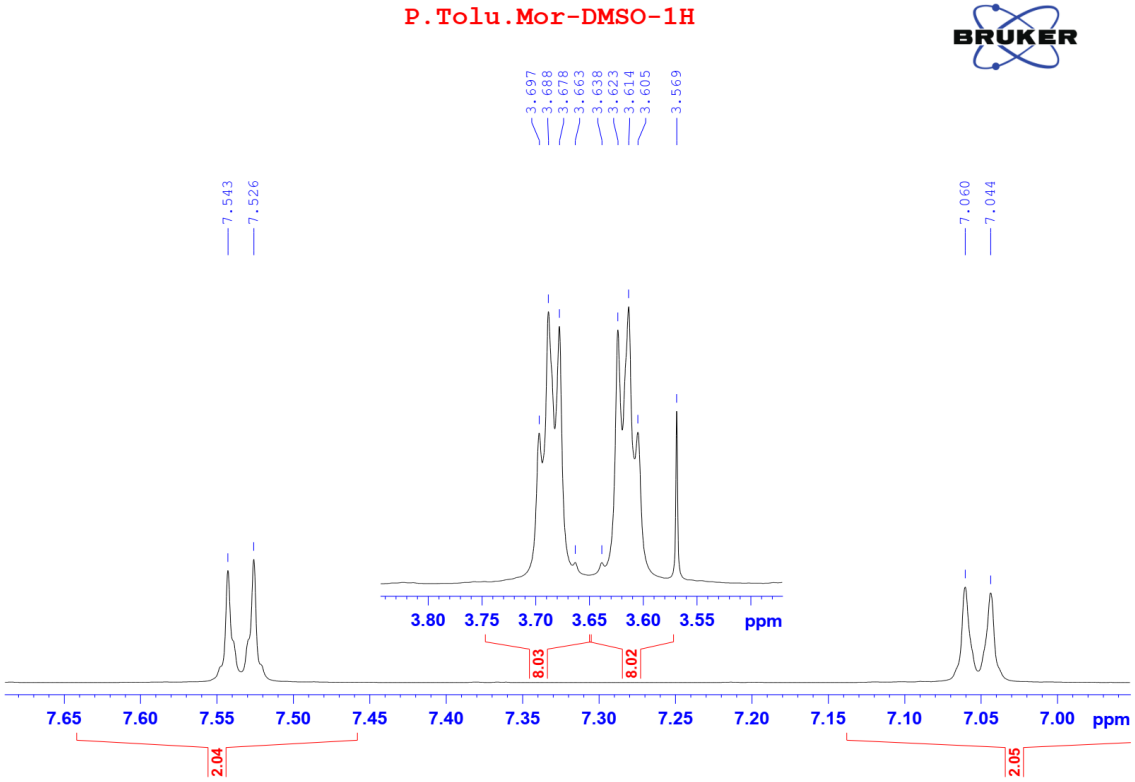
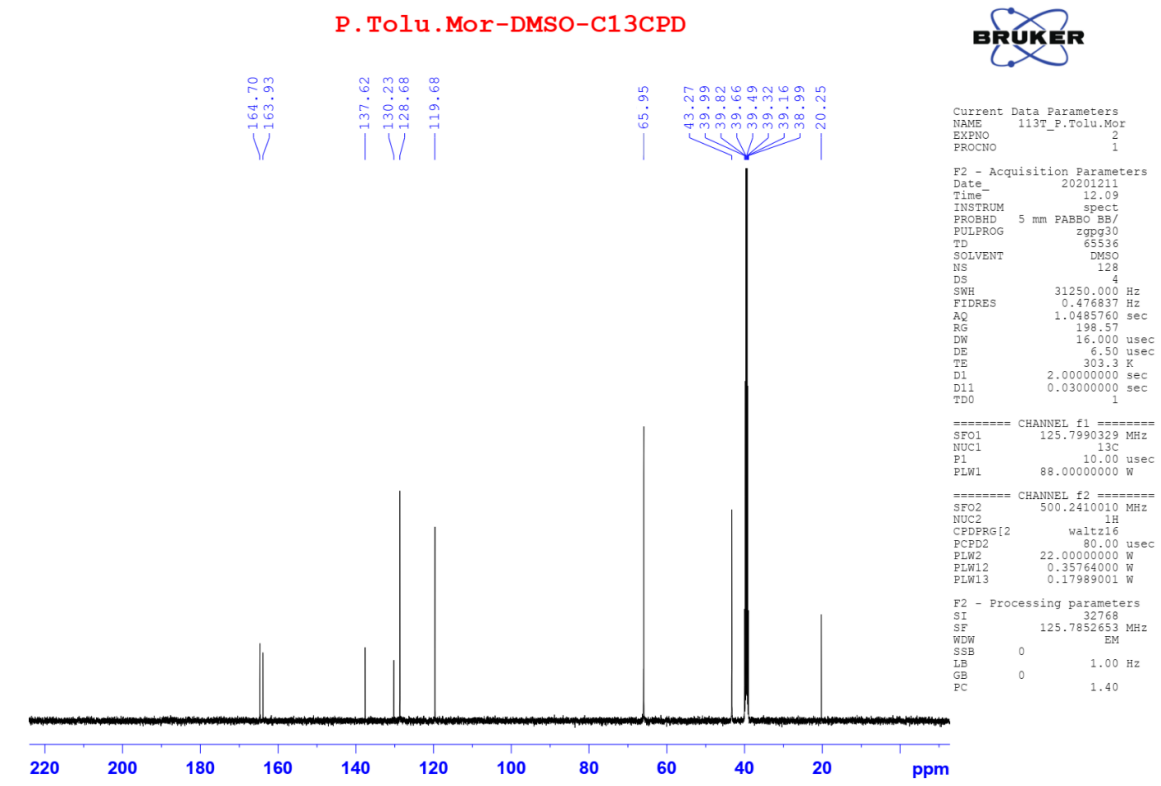
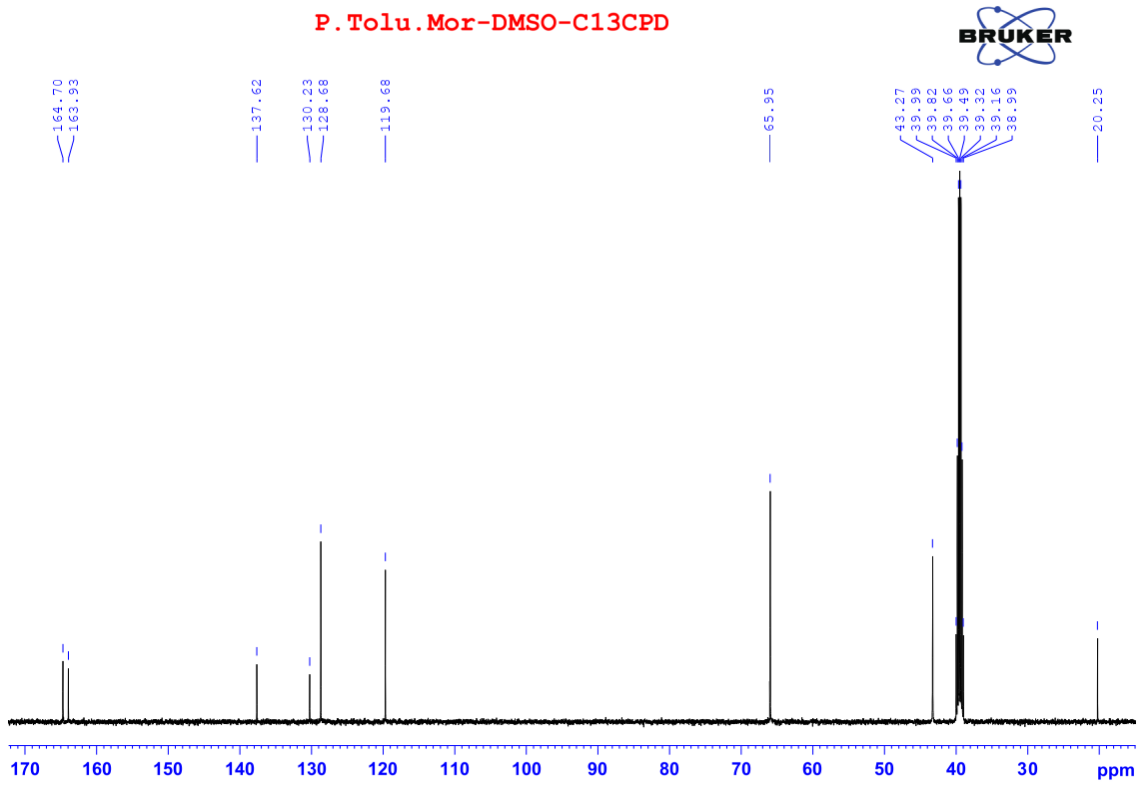


P.Tolu.Mor-DMSO-1H

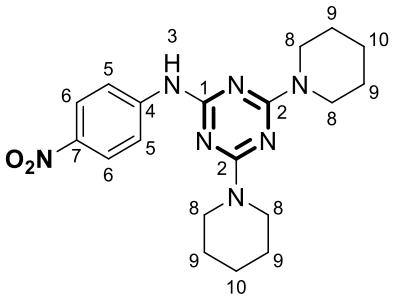


^{13}C NMR (3d)


P.Tolu.Mor-DMSO-C13CPD
BRUKER
164.70
163.93
137.62
130.23
128.68
119.68
65.95
43.27
39.99
39.82
39.66
39.49
39.32
39.16
38.99
20.25
220
200
180
160
140
120
100
80
60
40
20
ppm
Current Data Parameters
NAME 1137_P.Tolu.Mor
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201211
Time 12.09
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 128
DS 4
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0485760 sec
RG 198.57
DW 16.000 usec
DE 6.50 usec
TE 303.3 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7990329 MHz
NUC1 13C
P1 10.00 usec
PLW1 88.00000000 W
======== CHANNEL f2 ========
SFO2 500.2410010 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 22.00000000 W
PLW12 0.35764000 W
PLW13 0.17989001 W
F2 - Processing parameters
SI 32768
SF 125.7852653 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40


P.Tolu.Mor-DMSO-C13CPD
BRUKER
164.70
163.93
137.62
130.23
128.68
119.68
65.95
43.27
39.99
39.82
39.66
39.49
39.32
39.16
38.99
20.25
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm

COMPOUND 2e



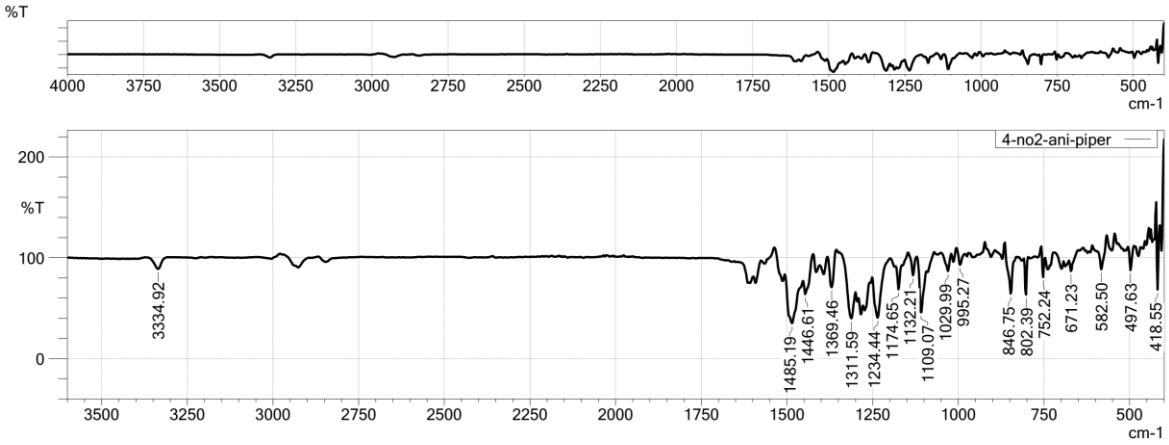
Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	9.46 (1H, s)	-NH-
5	7.95 (2H, d, *J* = 9.5 Hz)	H_{Ar}
6	8.13 (2H, d, *J* = 9.5 Hz)	H_{Ar}
8	3.73 (8H, t, *J* = 5.0 Hz)	-CH_2-
9	1.56-1.51 (8H, m)	-CH_2-
10	1.65 (4H, t, *J* = 5.0 Hz)	-CH_2-

^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 164.2 (>C=, C_2), 163.7 (>C=, C_1), 147.0 (>C=, C_4), 140.2 (>C=, C_7), 124.1 (>C=, C_6), 118.0 (>C=, C_5), 43.5 (-CH_2-, C_8), 24.9 (-CH_2-, C_9), 23.8 (-CH_2-, C_{10}).

LC-MS (*m/z*)

Expected formula: $C_{19}H_{25}N_7O_2$	Exact mass: 383.2070
$[M+H]^+$ calcd: 384.2142	$[M+H]^+$ found: 384.2064
$[M-H]^-$ calcd: 382.1997	$[M-H]^-$ found: 382.1951

IR (2e)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3250
3000
2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1
4-no2-ani-piper
200
%T
100
0
3334.92
1485.19
1446.61
1369.46
1311.59
1234.44
1174.65
1132.21
1109.07
1029.99
995.27
846.75
802.39
752.24
671.23
582.50
497.63
418.55
3500
3250
3000
2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1

MS (2e)

==== Shimadzu LCMSsolution Data Report ====

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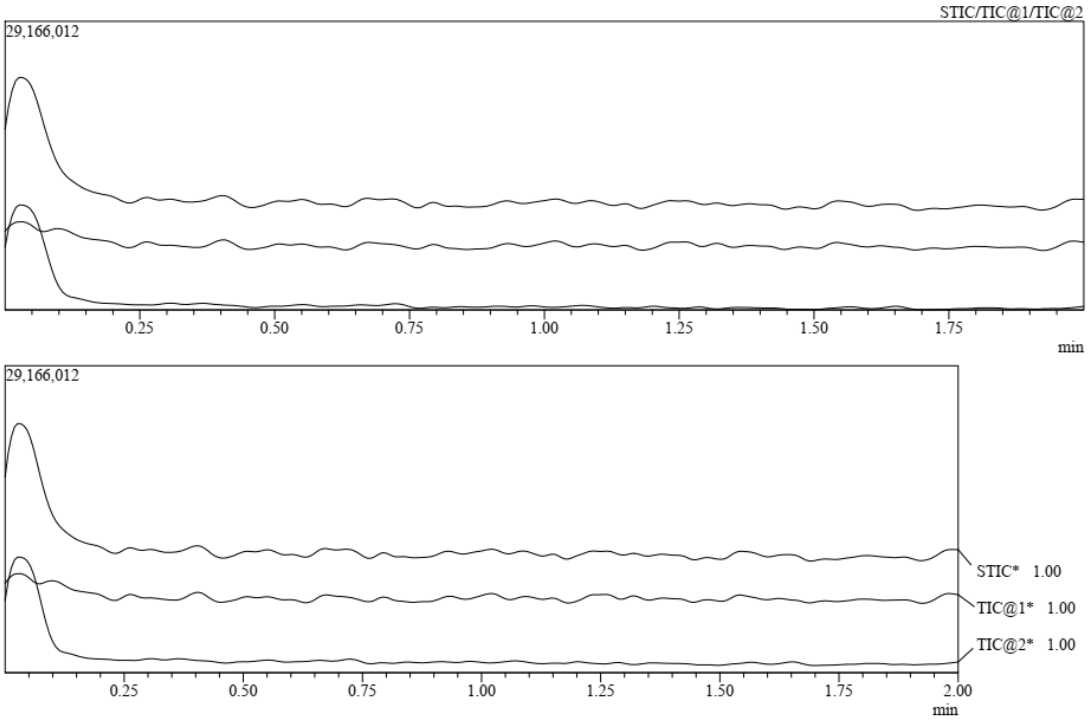

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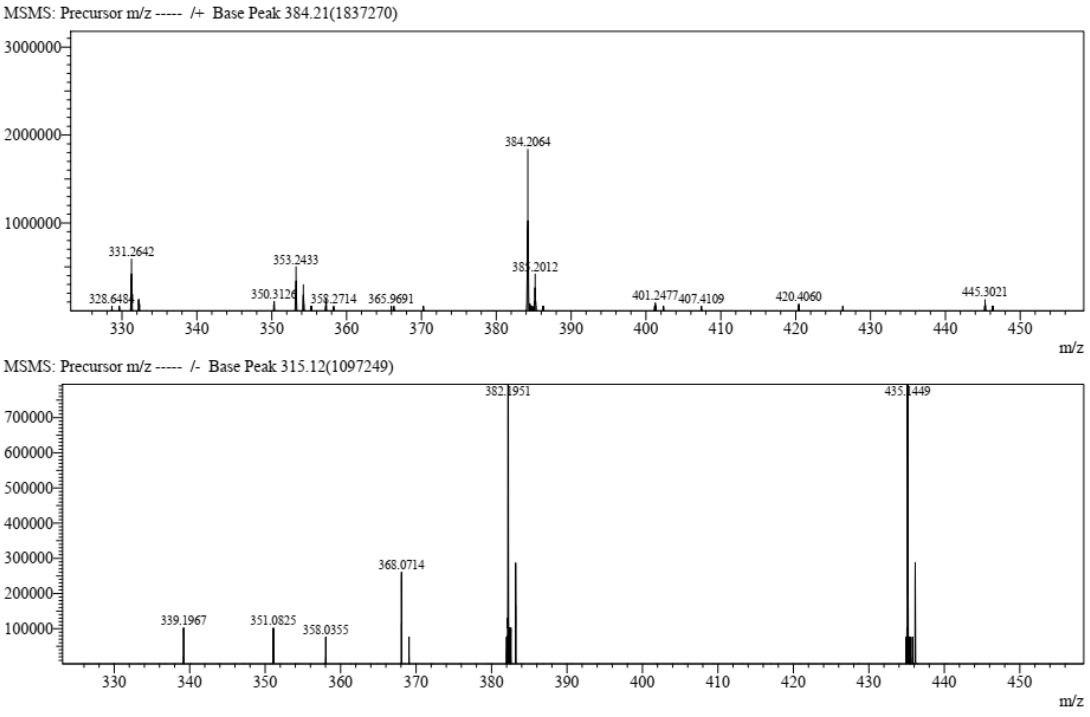
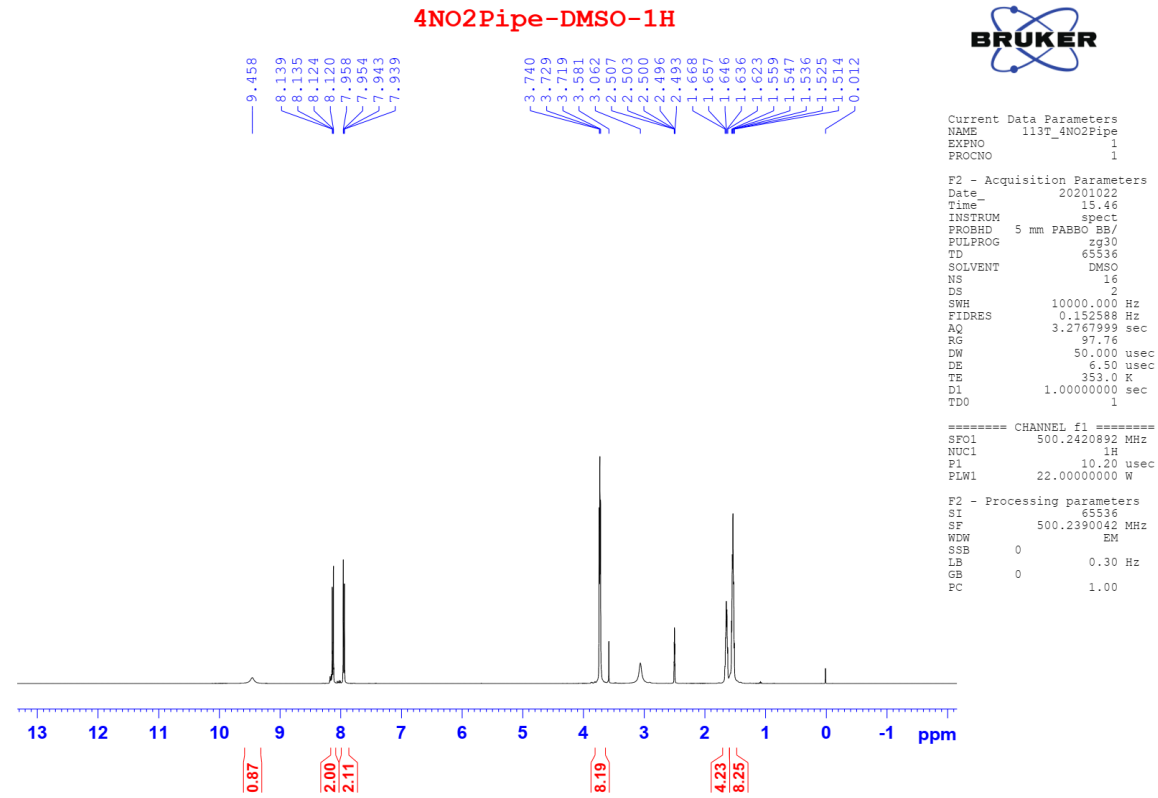


^{1}H NMR (2e)



Current Data Parameters
NAME 113T_4NO2Pipe
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20201022
Time 15.46
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 97.76
DW 50.000 usec
DE 6.50 usec
TE 353.0 K
D1 1.00000000 sec
TD0 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 0.30 Hz
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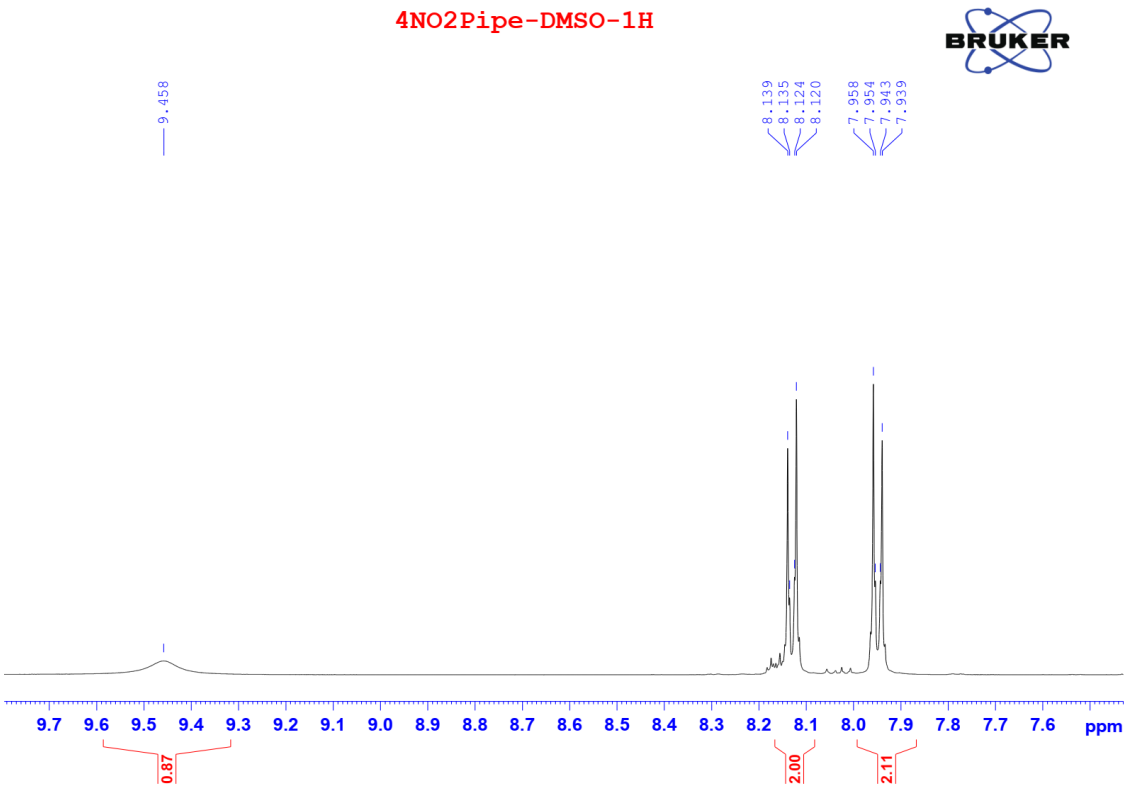
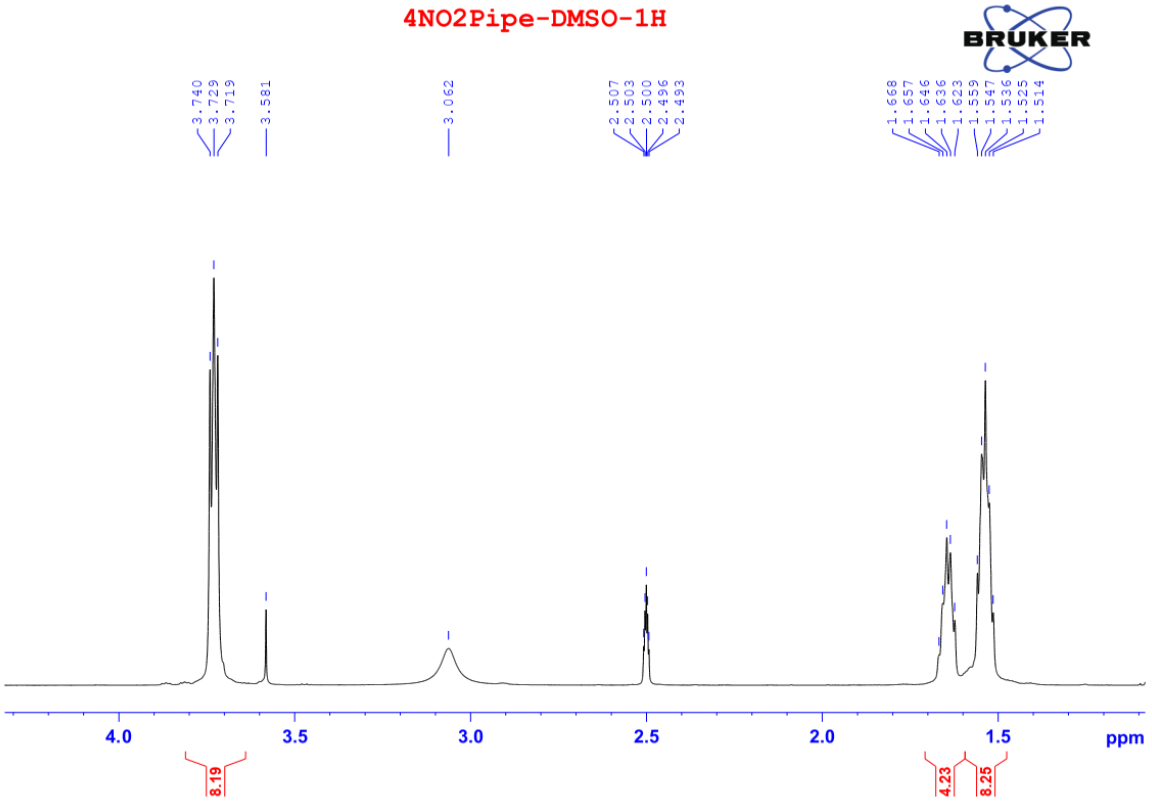
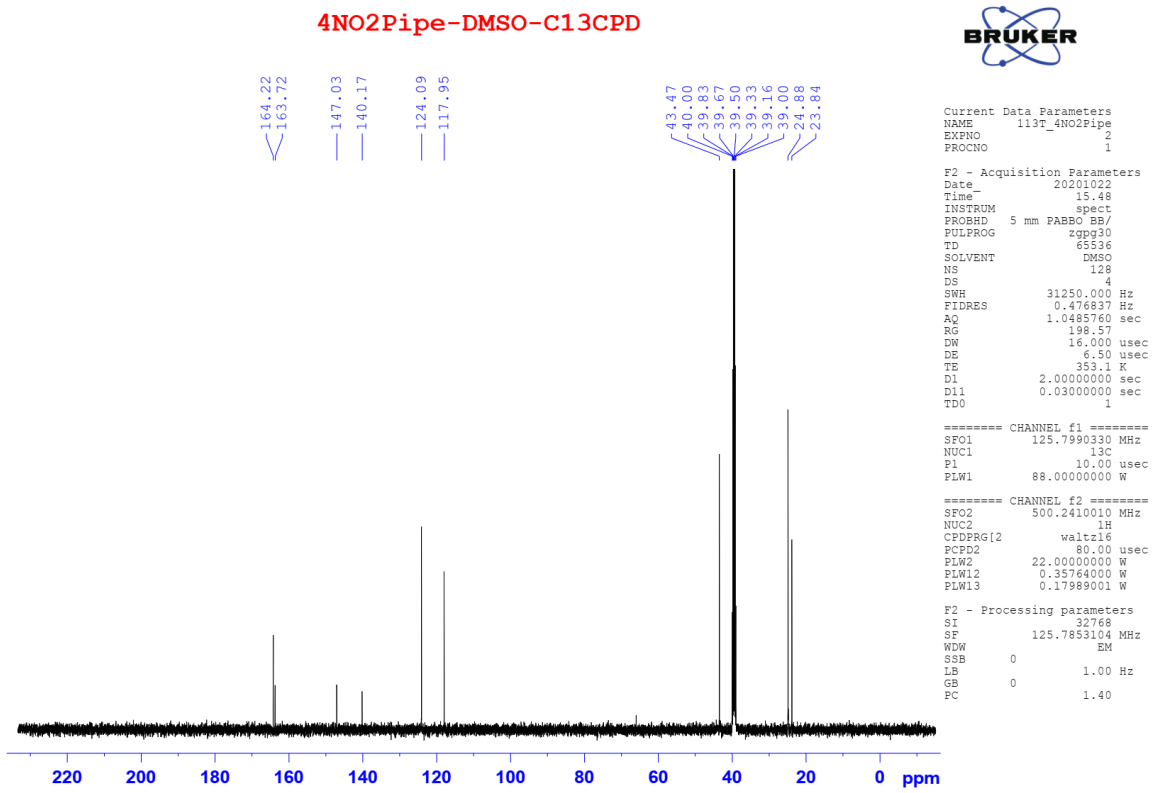
PC 1.00



4NO2Pipe-DMSO-1H



^{13}C NMR (2e)


4NO2Pipe-DMSO-C13CPD
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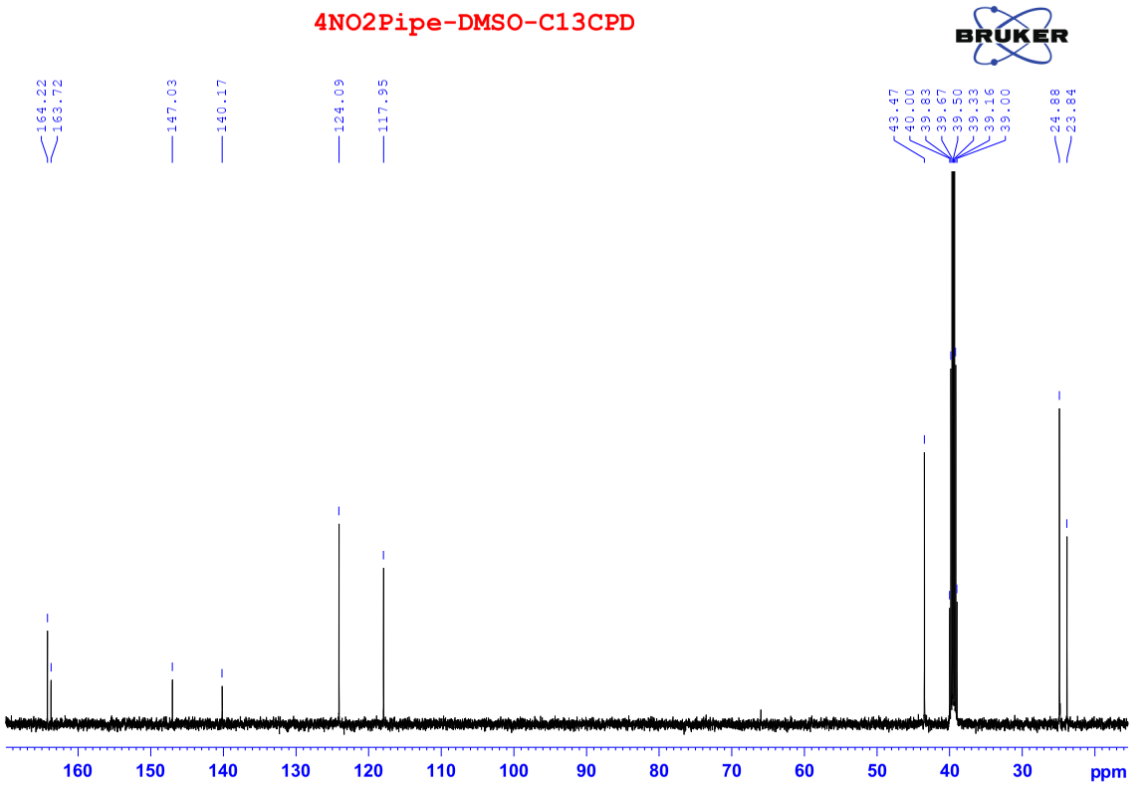
147.03
140.17
124.09
117.95
43.47
40.00
39.83
39.67
39.50
39.33
39.16
39.00
24.88
23.84
220
200
180
160
140
120
100
80
60
40
20
0
ppm
Current Data Parameters
NAME 113T_4NO2Pipe
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201022
Time 15.48
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 128
DS 4
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0485760 sec
RG 198.57
DW 16.000 usec
DE 6.50 usec
TE 353.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 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
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 22.00000000 W
PLW12 0.35764000 W
PLW13 0.17989001 W
F2 - Processing parameters
SI 32768
SF 125.7853104 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40


4NO2Pipe-DMSO-C13CPD
164.22
163.72
147.03
140.17
124.09
117.95
43.47
40.00
39.83
39.67
39.50
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39.16
39.00
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23.84
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90
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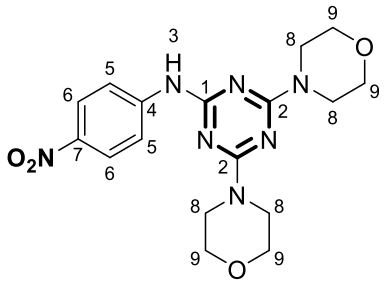
50
40
30
ppm

COMPOUND 3e



Position	^{1}H NMR δppm, 500 MHz, DMSO-d_6	Type
3	9.85 (1H, s)	-NH-
5	8.16 (2H, d, *J* = 9.5 Hz)	H_{Ar}
6	7.93 (2H, d, *J* = 9.5 Hz)	H_{Ar}
8	3.71 (8H, t, *J* = 4.5 Hz)	-CH_2-
9	3.64 (8H, t, *J* = 4.5 Hz)	-CH_2-

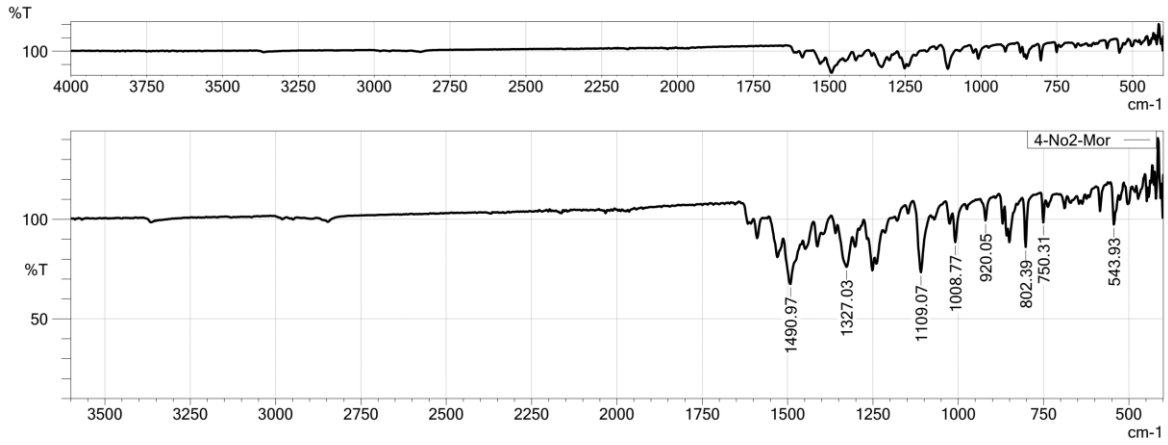
^{13}C NMR (125 MHz, DMSO-d_6, δ ppm): 164.6 (>C=, C_2), 163.9 (>C=, C_1), 147.1 (>C=, C_4), 140.4 (>C=, C_7), 124.8 (>C=, C_6), 118.5 (>C=, C_5), 65.9 (-CH_2-, C_9), 43.4 (-CH_2-, C_8).

LC-MS (*m/z*)

Expected formula: $C_{17}H_{21}N_7O_4$ Exact mass: 387.1655

$[M-H]^-$ calcd: 386.1582 $[M-H]^-$ found: 386.1509

IR (3e)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3000
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2500
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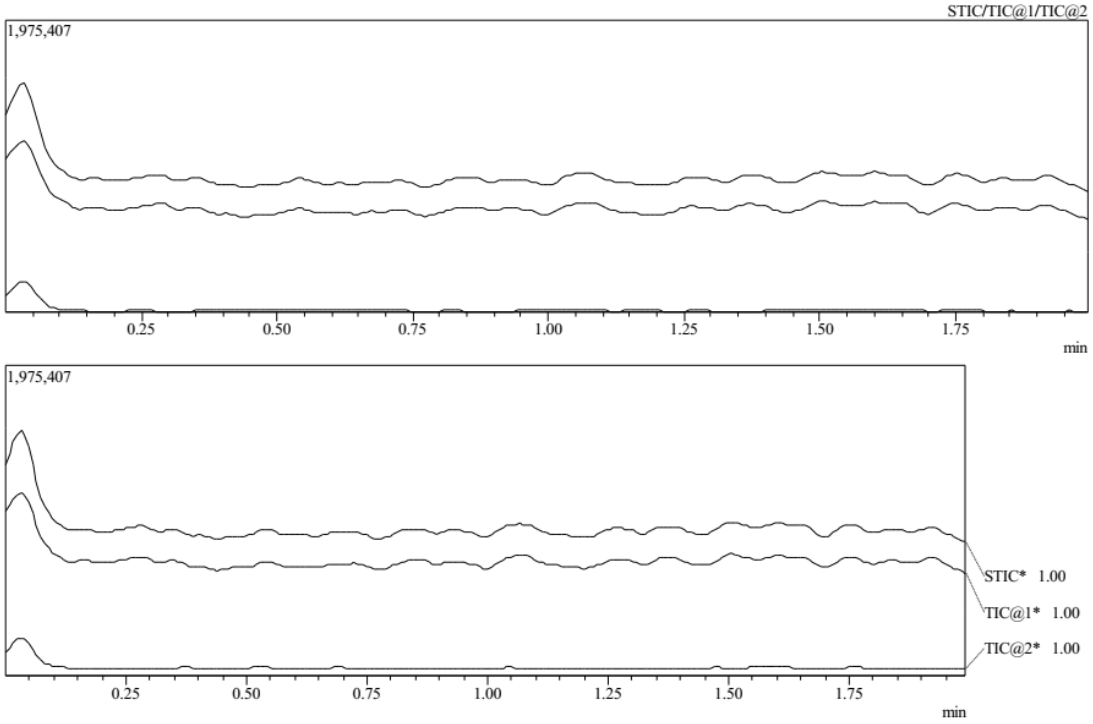
2000
1750
1500
1250
1000
750
500
cm-1
4-No2-Mor
100
%T
50
1490.97
1327.03
1109.07
1008.77
920.05
802.39
750.31
543.93
3500
3250
3000
2750
2500
2250
2000
1750
1500
1250
1000
750
500
cm-1

MS (3e)

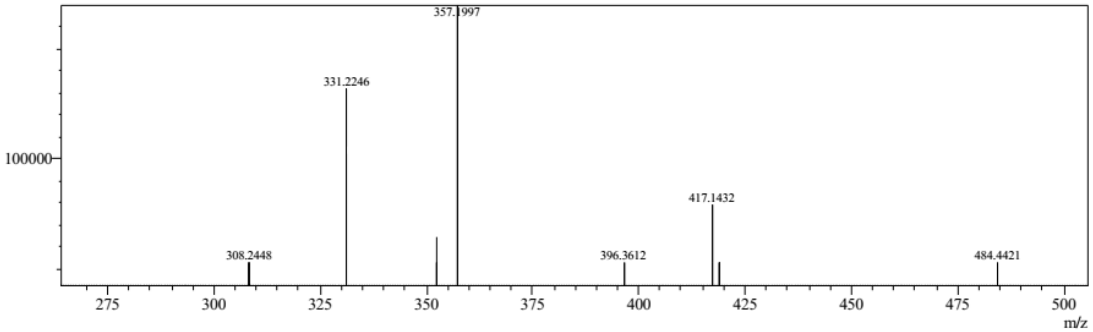
==== Shimadzu LCMSsolution Data Report ====

<Chromatogram>

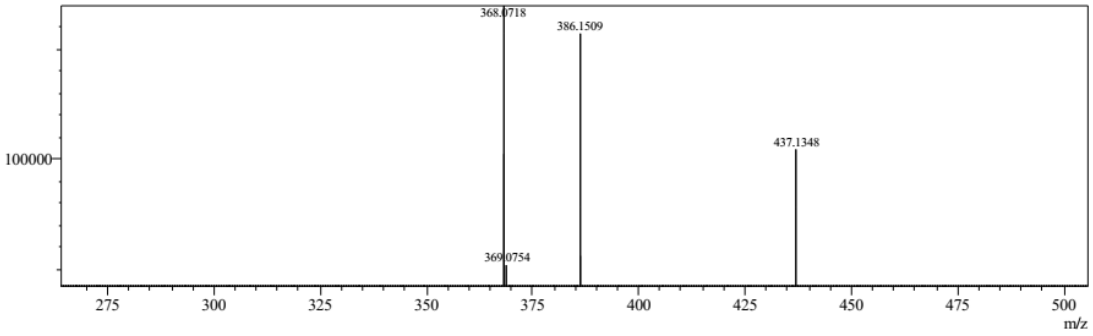


<Spectrum>

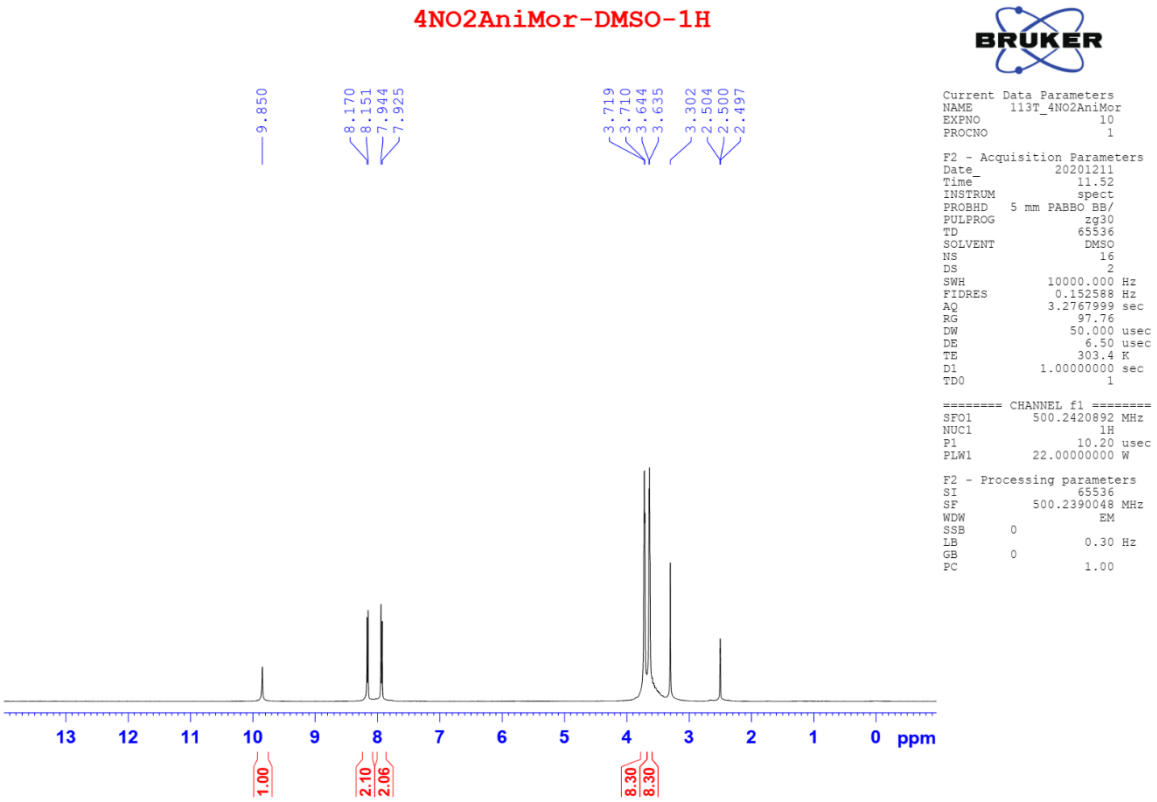
MSMS: Precursor m/z ----- /+ Base Peak 357.20(319925)



MSMS: Precursor m/z ----- /- Base Peak 368.07(102459)



^{1}H NMR (3e)

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EXPNO                  10
PROCNO                  1

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Time                 11.52
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                   97.76
DW                  50.000 usec
DE                   6.50 usec
TE                  303.4 K
D1               1.00000000 sec
TD0                     1

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

F2 - Processing parameters
SI                    65536
SF              500.2390048 MHz
WDW                     EM
SSB          0
LB                   0.30 Hz
GB           0
PC                   1.00
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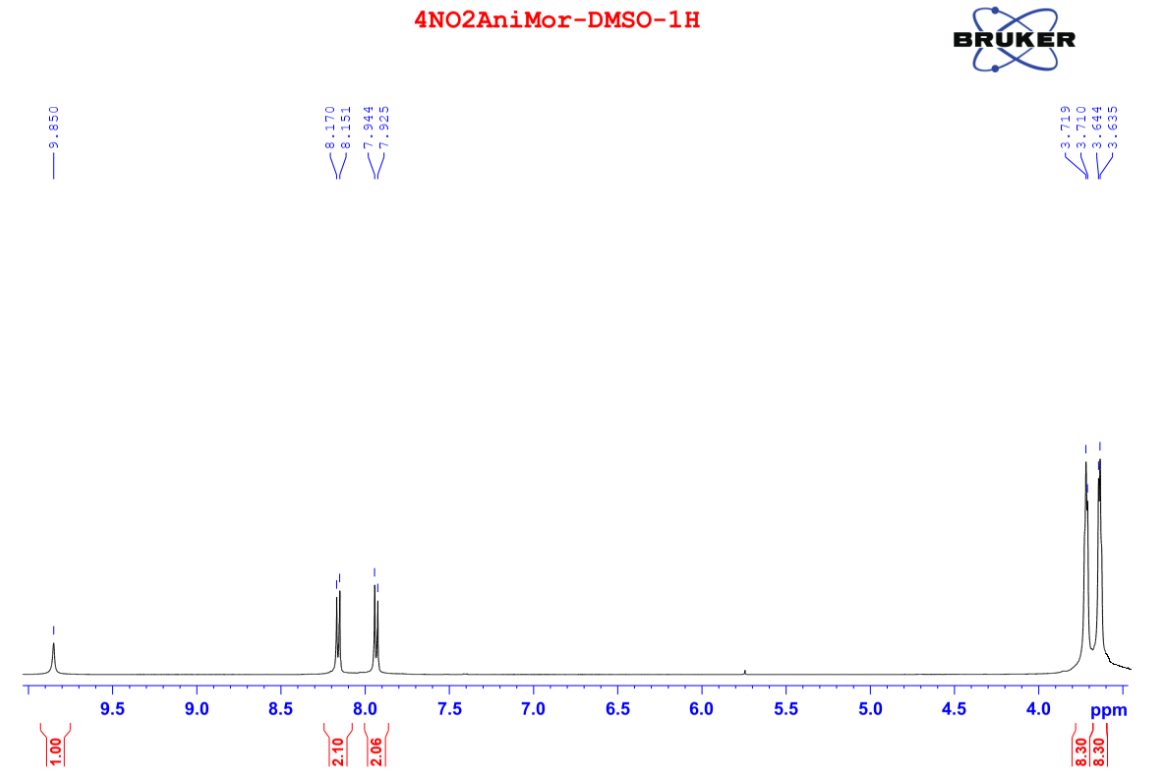
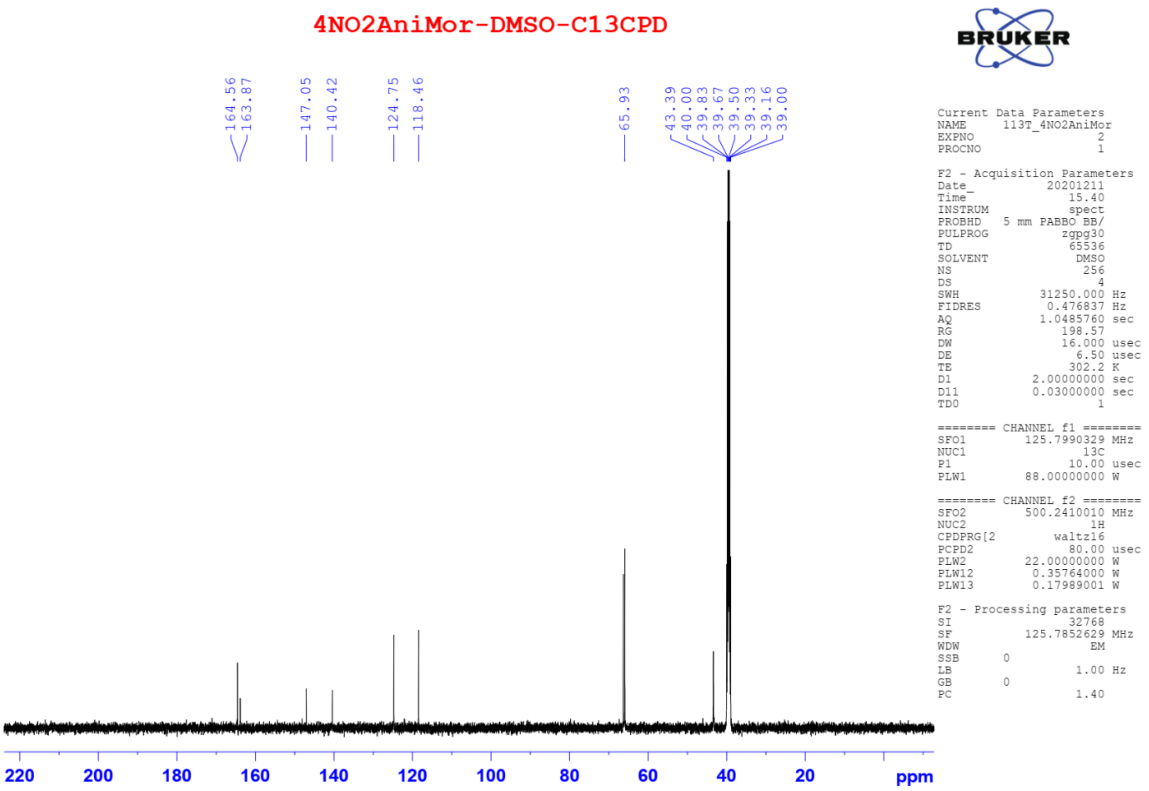
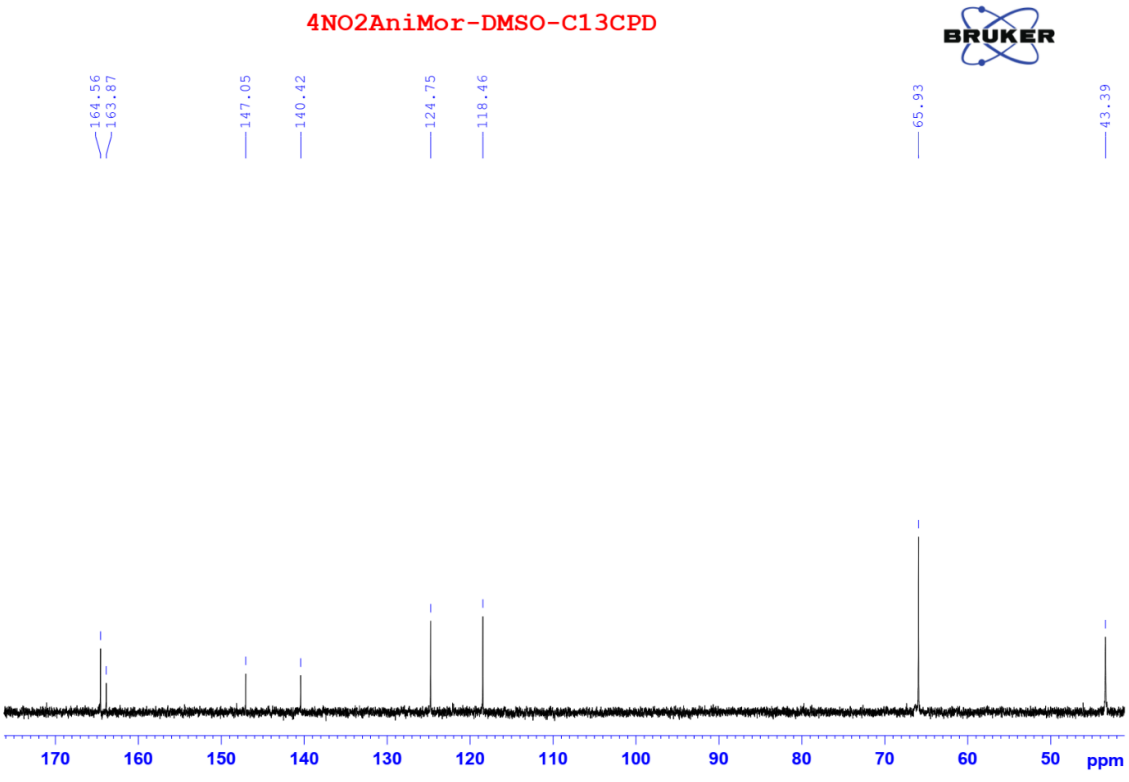


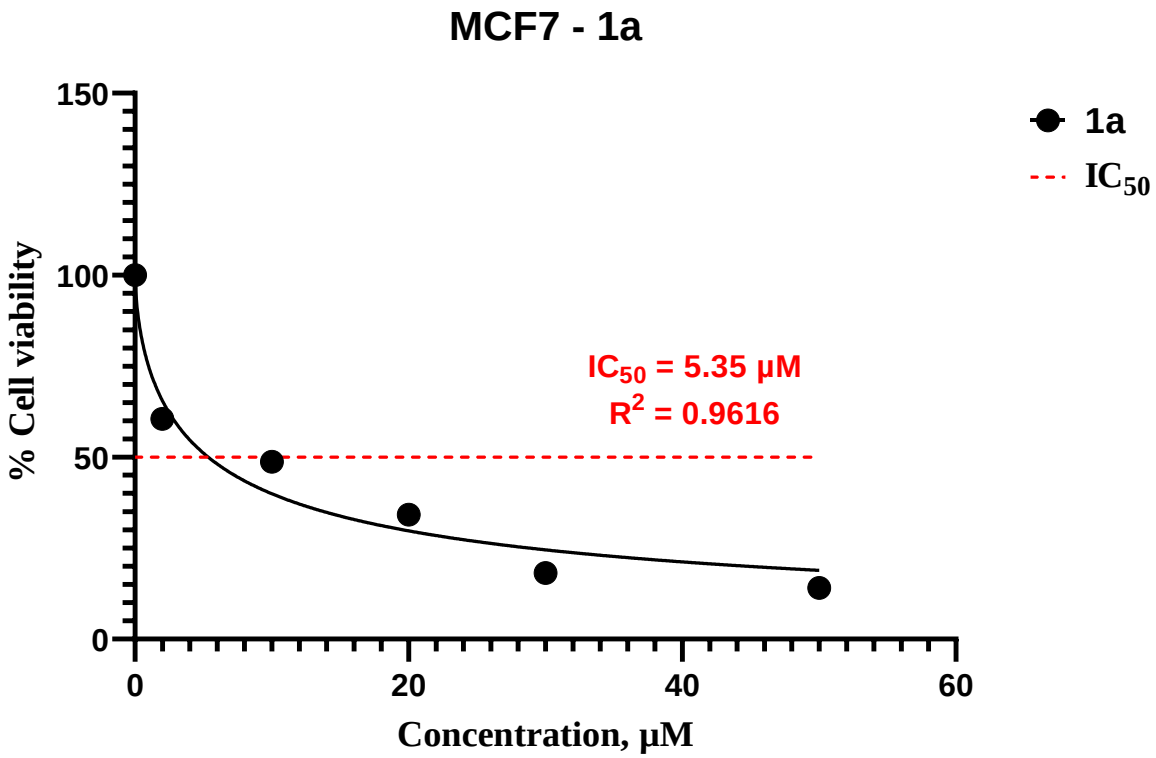
^{13}C NMR (3e)

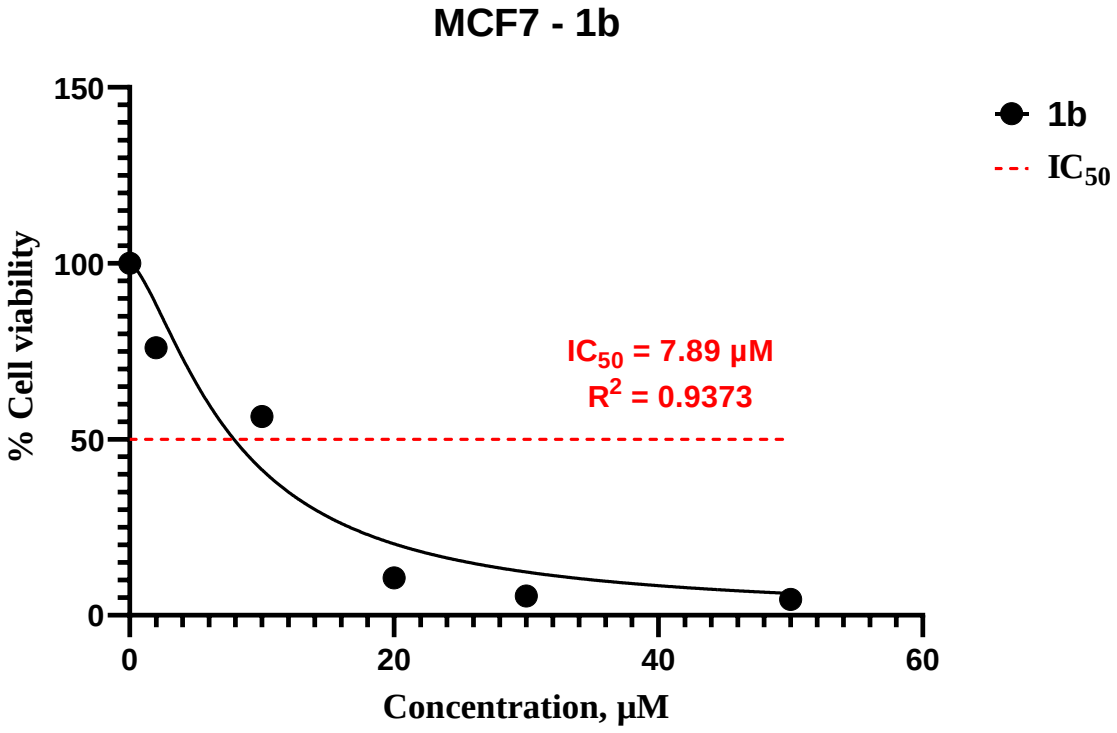

4NO2AniMor-DMSO-C13CPD
BRUKER
164.56
163.87
147.05
140.42
124.75
118.46
65.93
43.39
40.00
39.83
39.67
39.50
39.33
39.16
39.00
220
200
180
160
140
120
100
80
60
40
20
ppm
Current Data Parameters
NAME 113T_4NO2AniMor
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20201211
Time 15.40
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 256
DS 4
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0485760 sec
RG 198.57
DW 16.000 usec
DE 6.50 usec
TE 302.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7990329 MHz
NUC1 13C
P1 10.00 usec
PLW1 88.00000000 W
======== CHANNEL f2 ========
SFO2 500.2410010 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 22.00000000 W
PLW12 0.35764000 W
PLW13 0.17989001 W
F2 - Processing parameters
SI 32768
SF 125.7852629 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

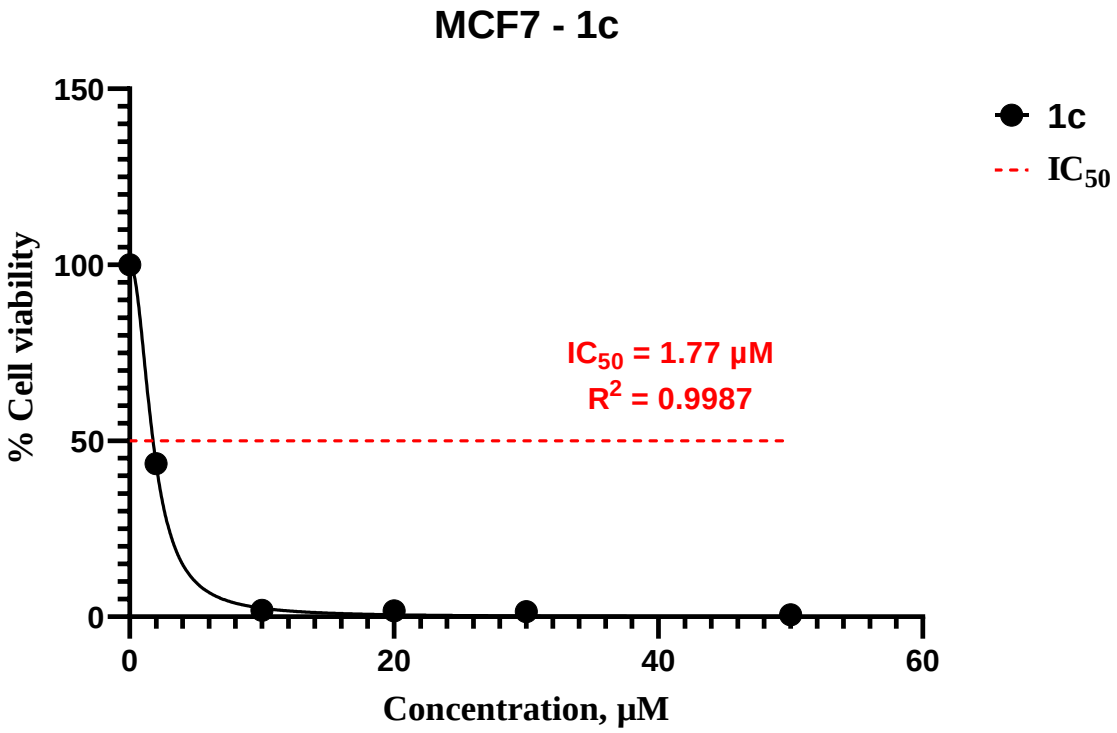

4NO2AniMor-DMSO-C13CPD
BRUKER
164.56
163.87
147.05
140.42
124.75
118.46
65.93
43.39
170
160
150
140
130
120
110
100
90
80
70
60
50
ppm

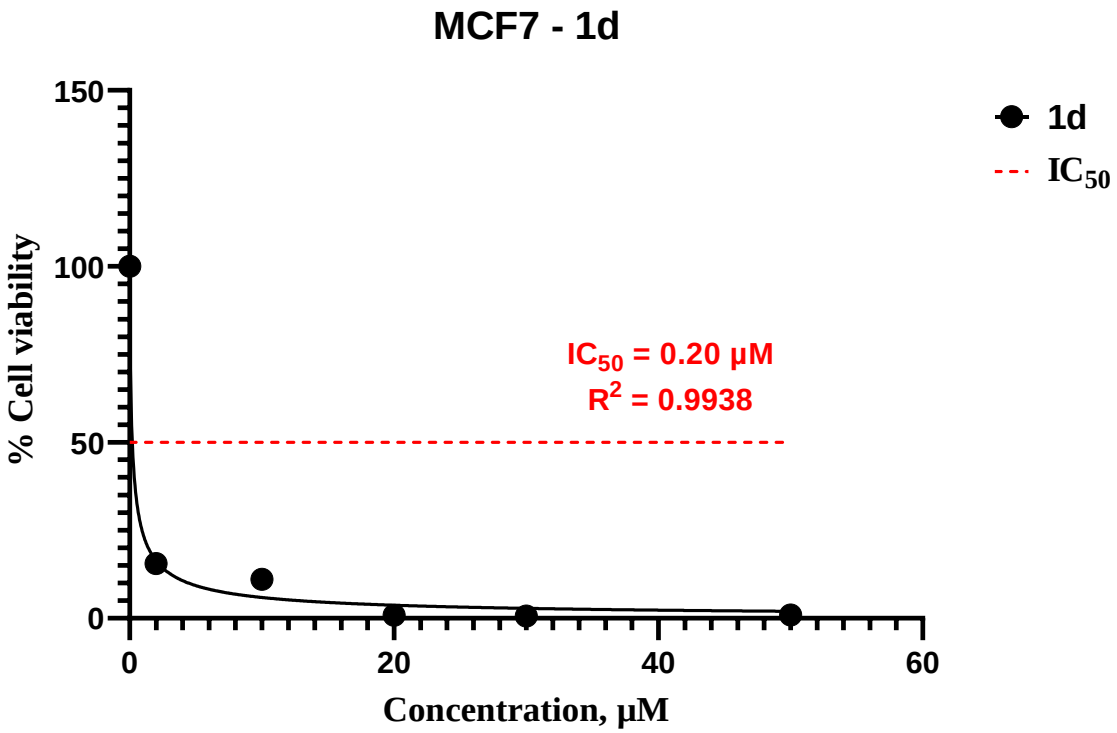
ANTICANCER ACTIVITY

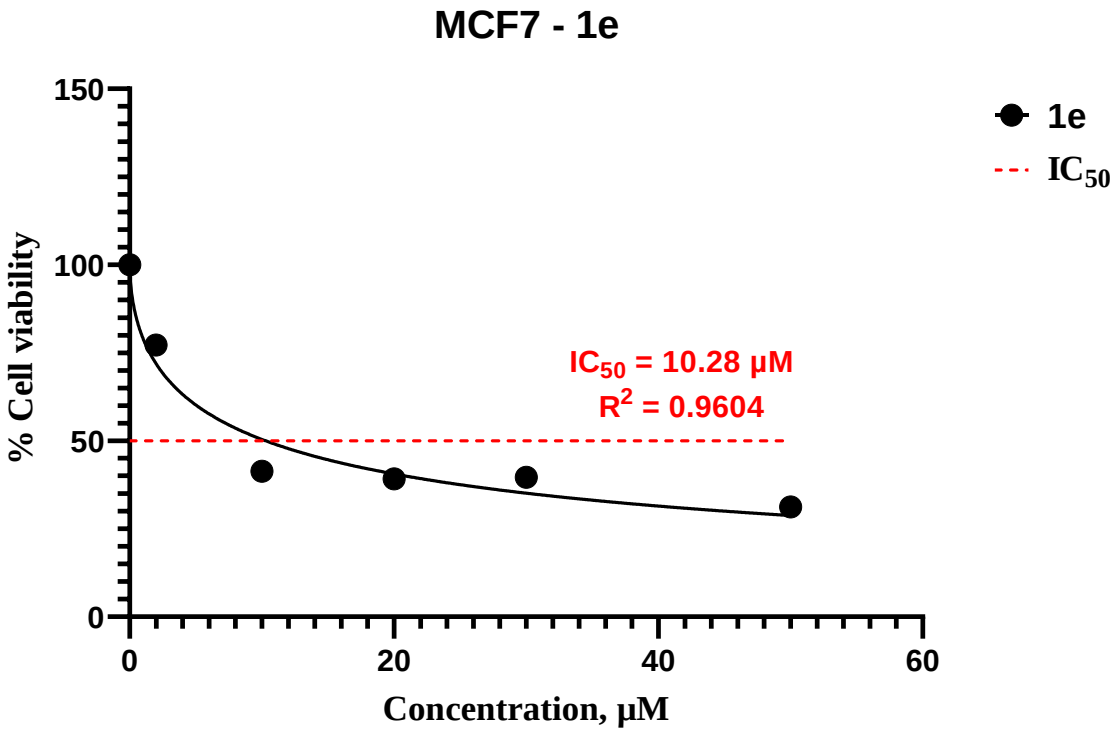
IC_{50} (1a-1e) MCF7



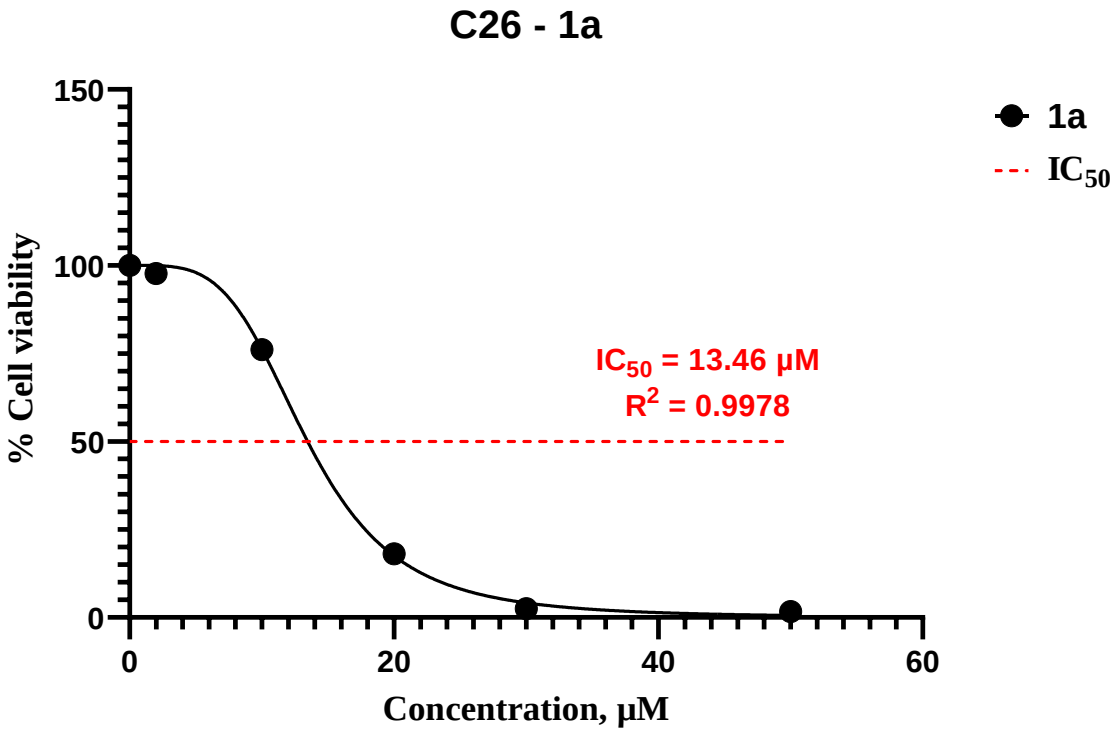


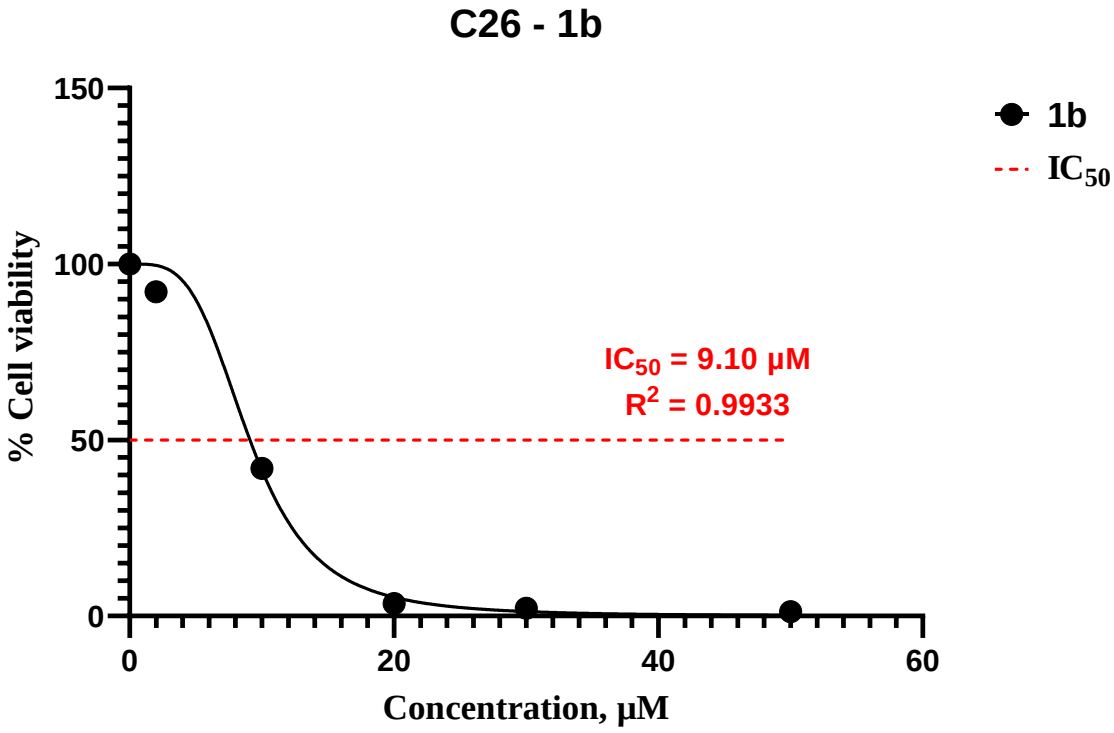

MCF7 - 1c
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 1.77 µM
R2 = 0.9987
1c
IC50

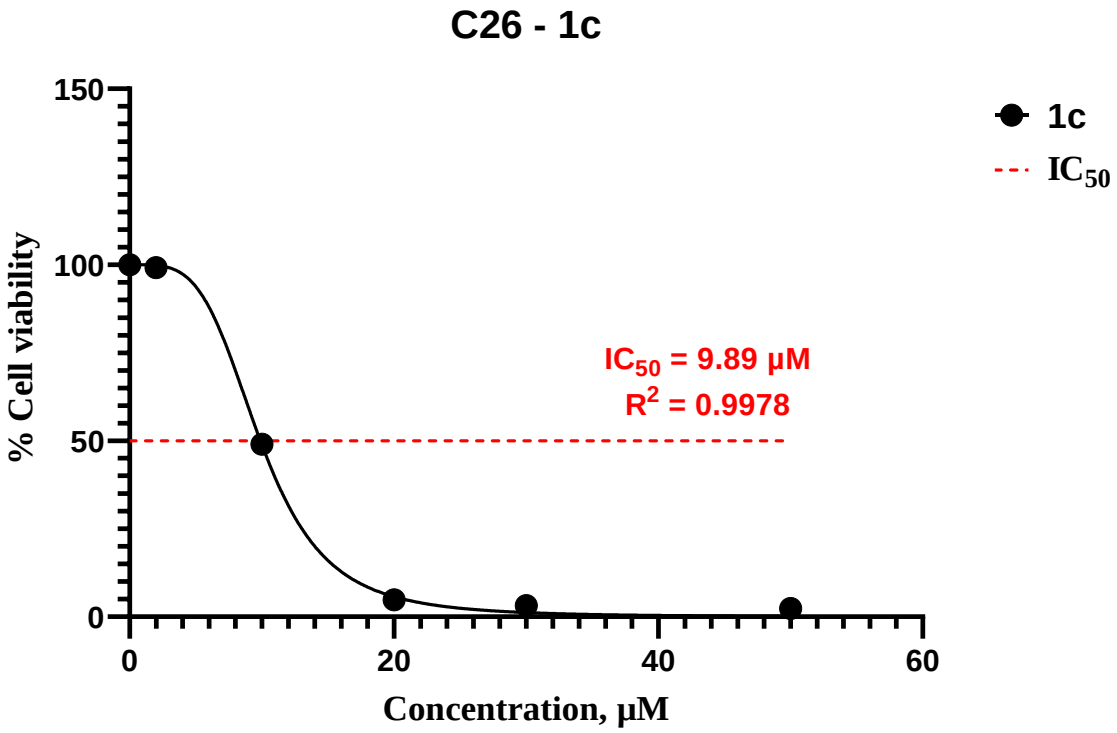

MCF7 - 1d
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 0.20 µM
R2 = 0.9938
1d
IC50

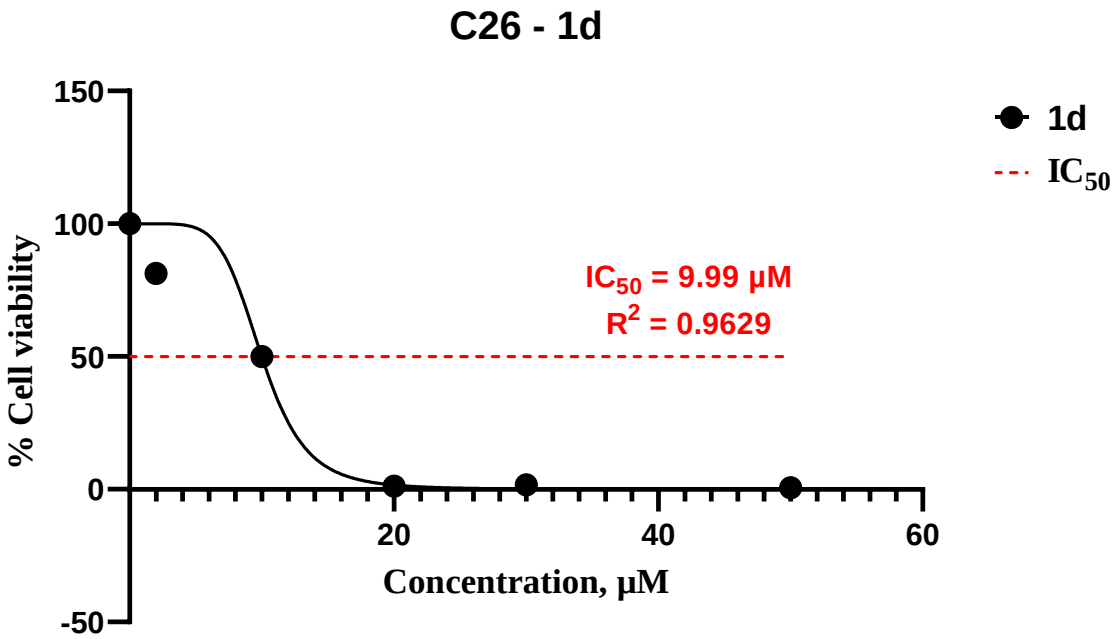

MCF7 - 1e
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 10.28 µM
R2 = 0.9604
1e
IC50

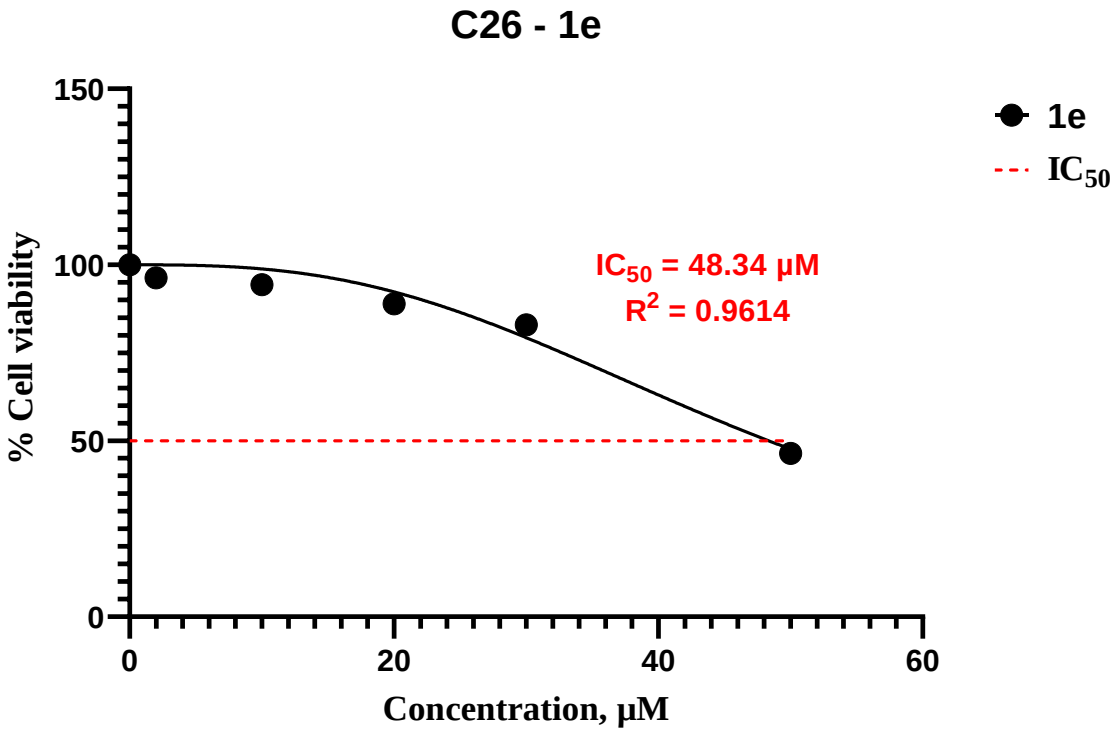
IC_{50} (1a-1e) C26



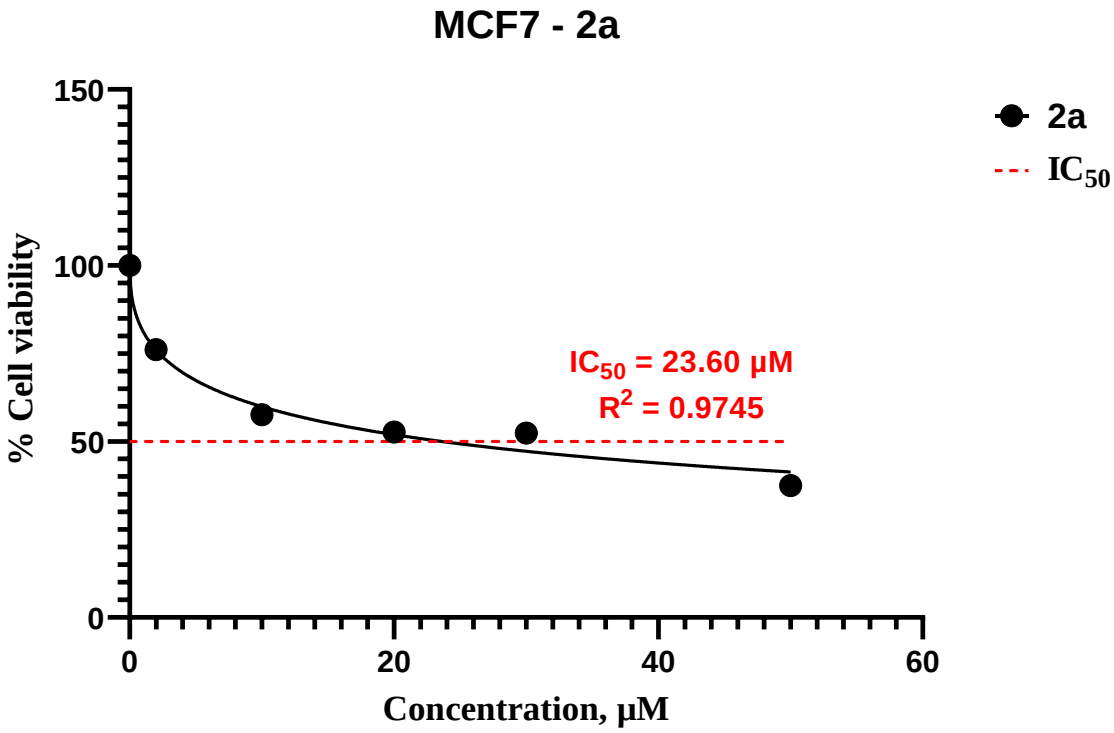


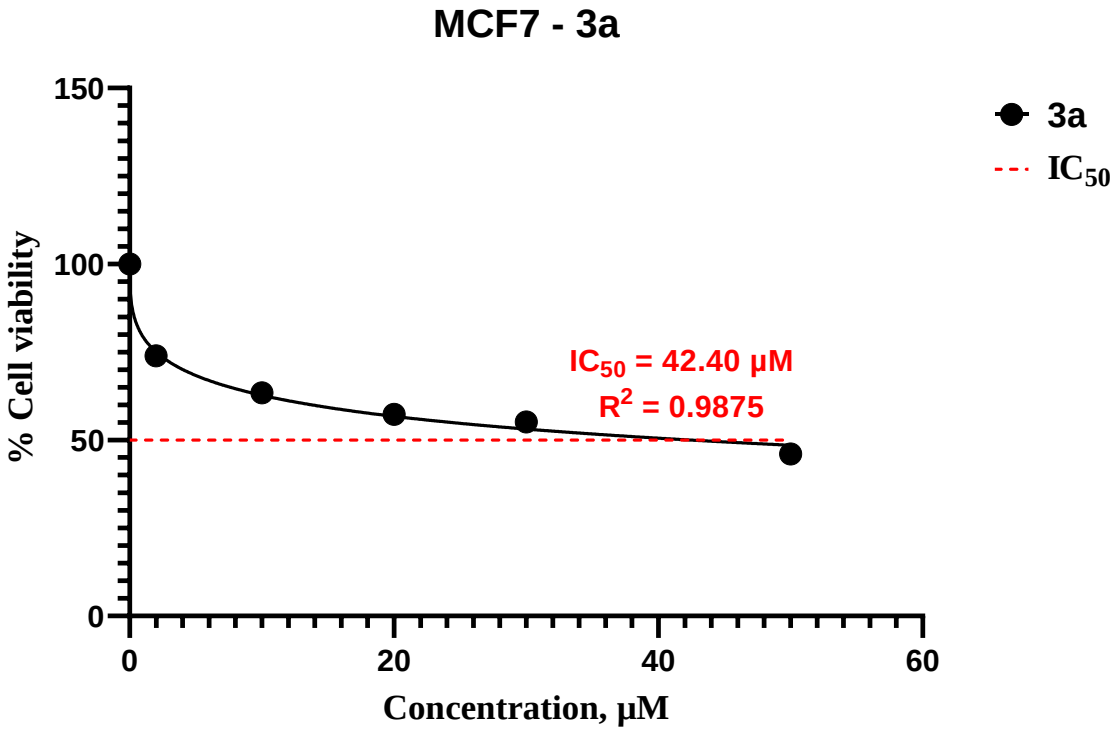

C26 - 1c
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 9.89 µM
R2 = 0.9978
1c
IC50

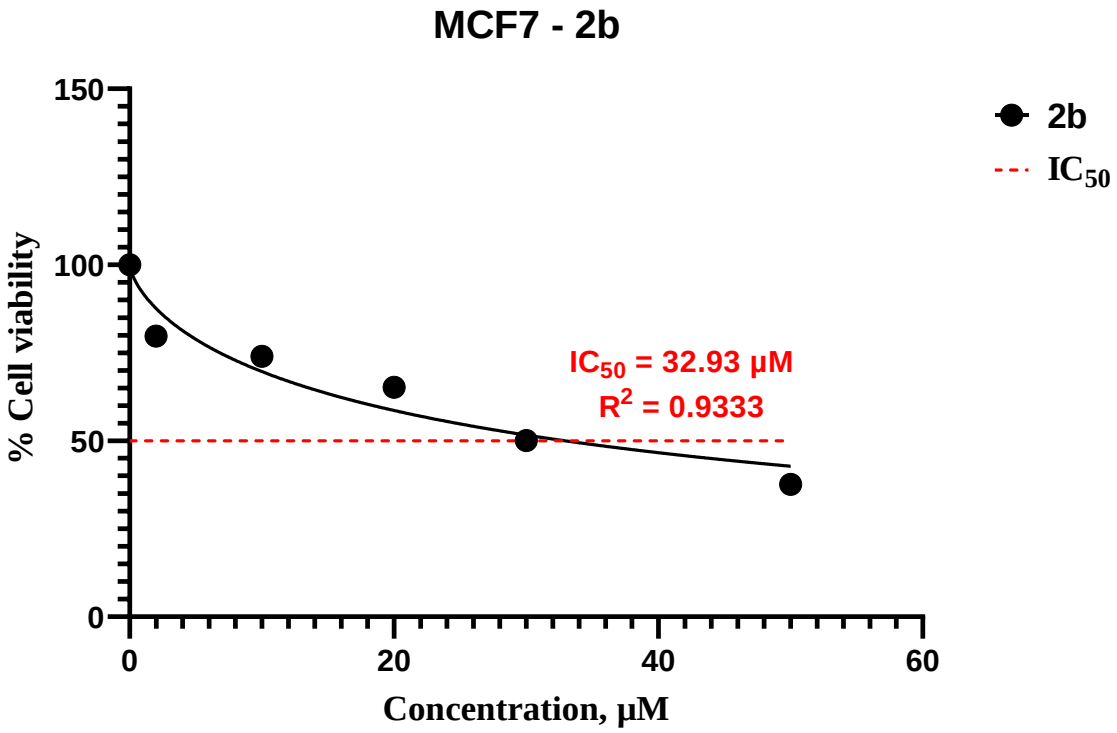

C26 - 1d
150
100
50
0
-50
% Cell viability
20
40
60
Concentration, µM
IC50 = 9.99 µM
R2 = 0.9629
1d
IC50

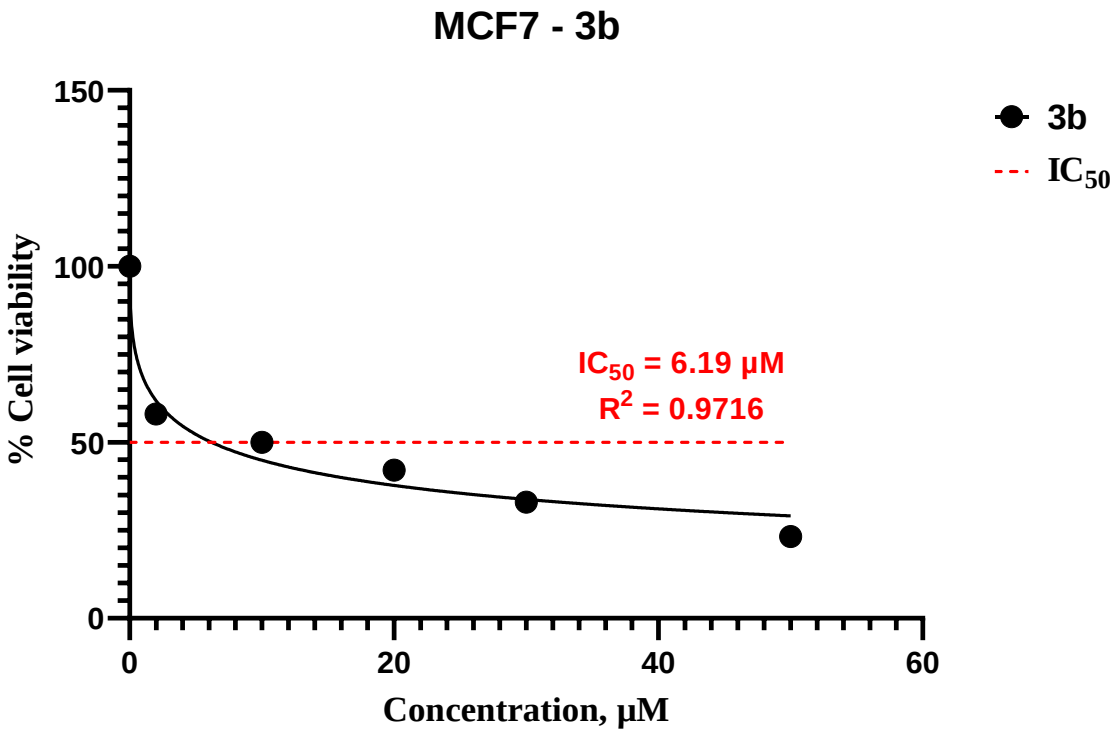

C26 - 1e
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 48.34 µM
R2 = 0.9614
1e
IC50

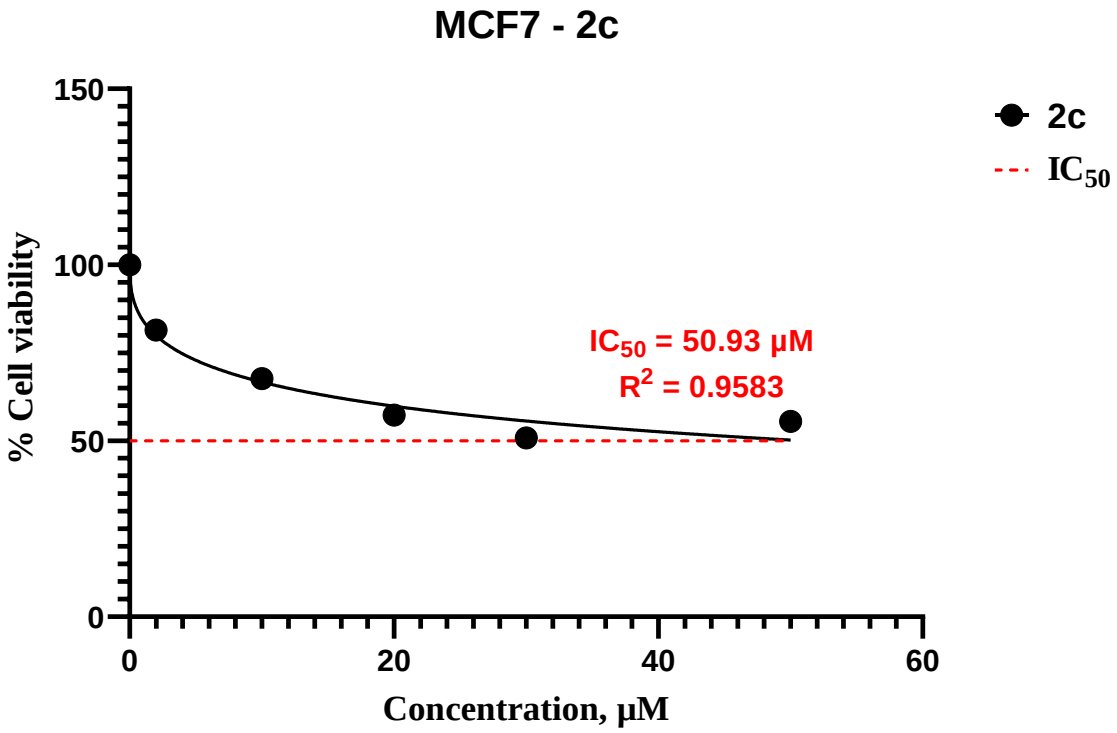
IC_{50} (2-3) MCF7

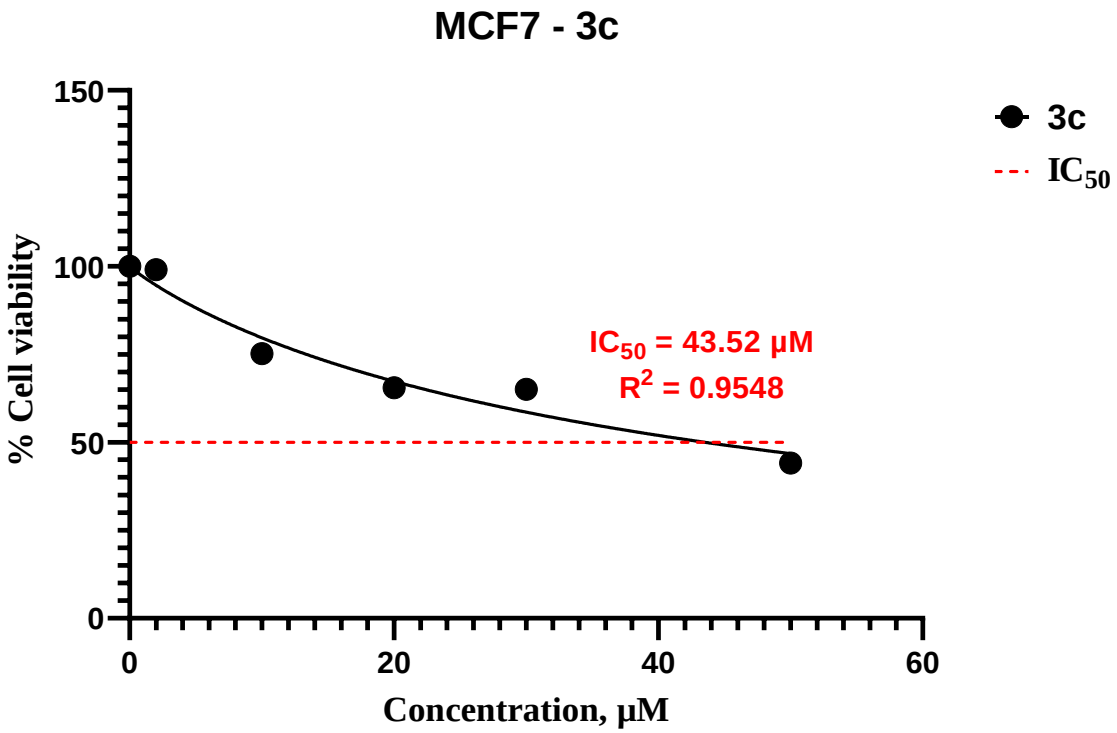

MCF7 - 2a
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 23.60 µM
R2 = 0.9745
2a
IC50

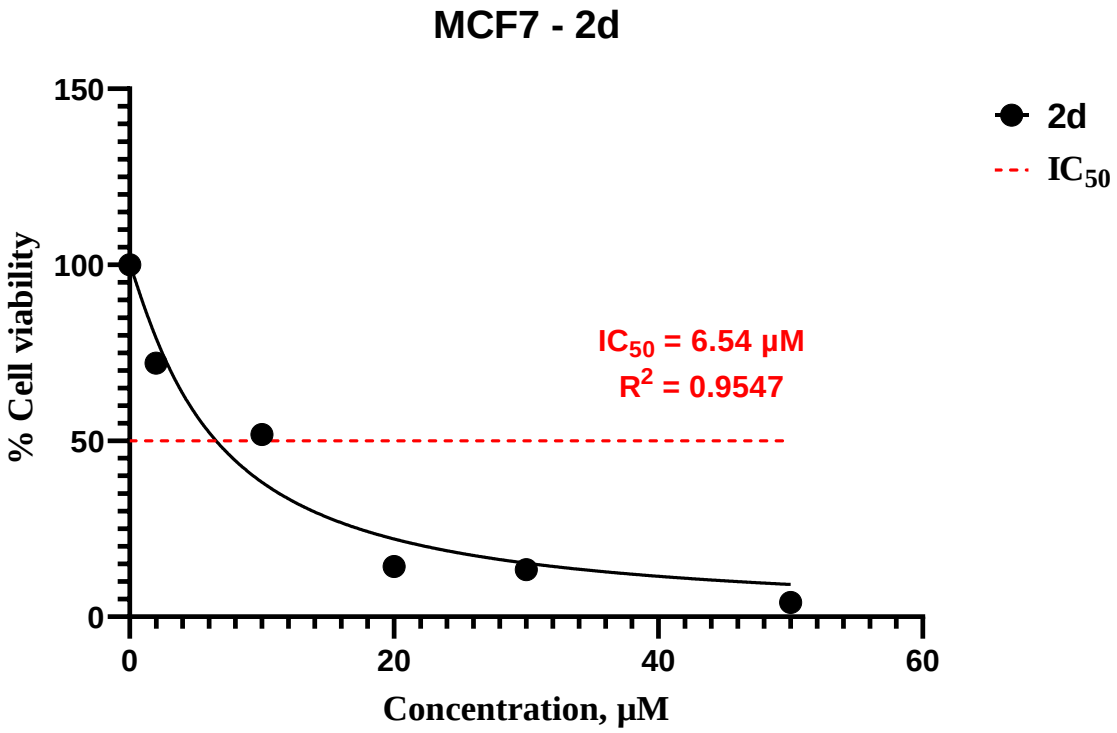

MCF7 - 3a
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 42.40 µM
R2 = 0.9875
3a
IC50

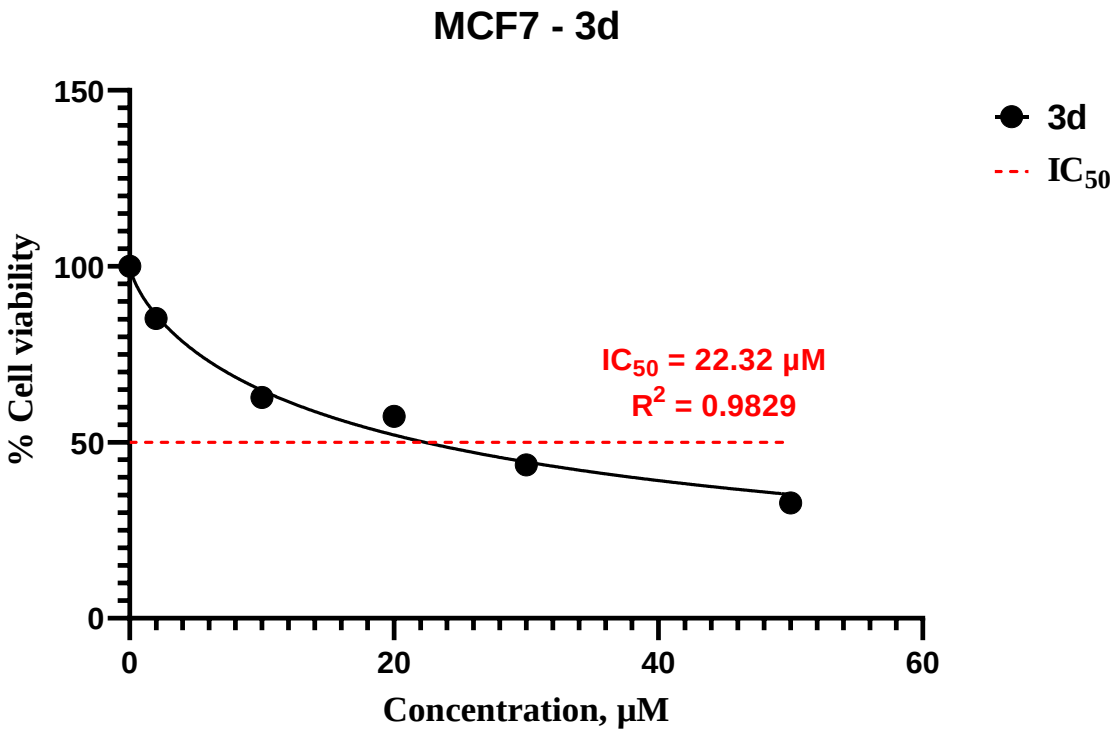

MCF7 - 2b
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 32.93 µM
R2 = 0.9333
2b
IC50

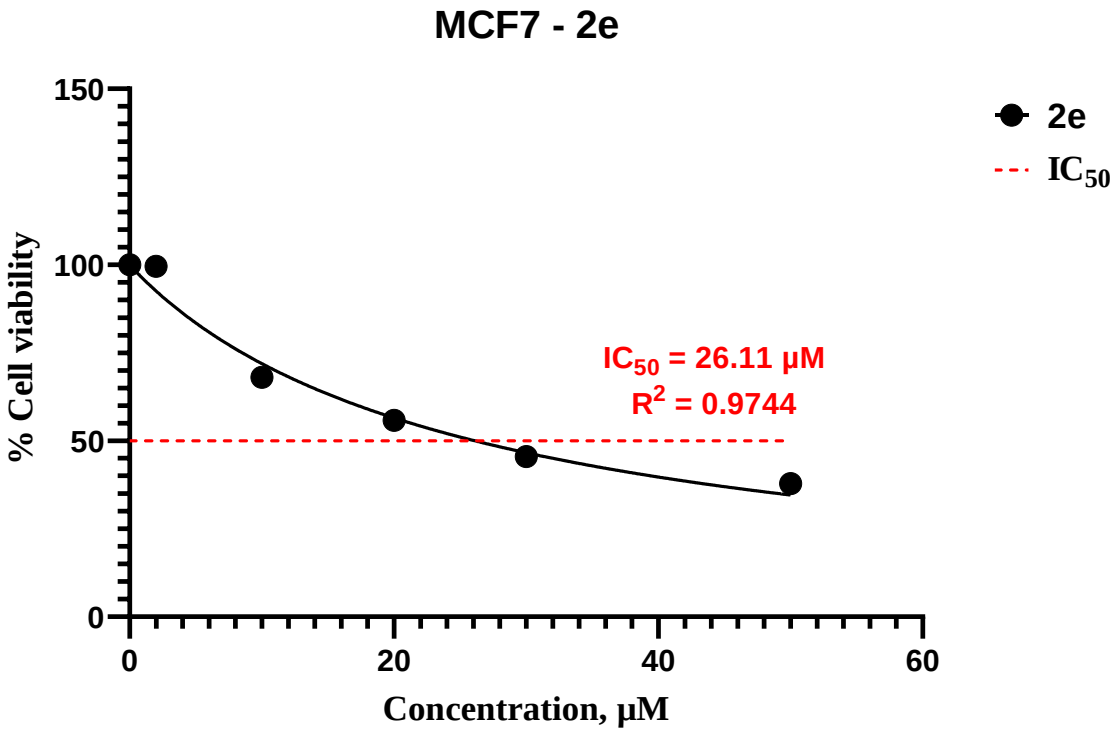

MCF7 - 3b
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 6.19 µM
R2 = 0.9716
3b
IC50

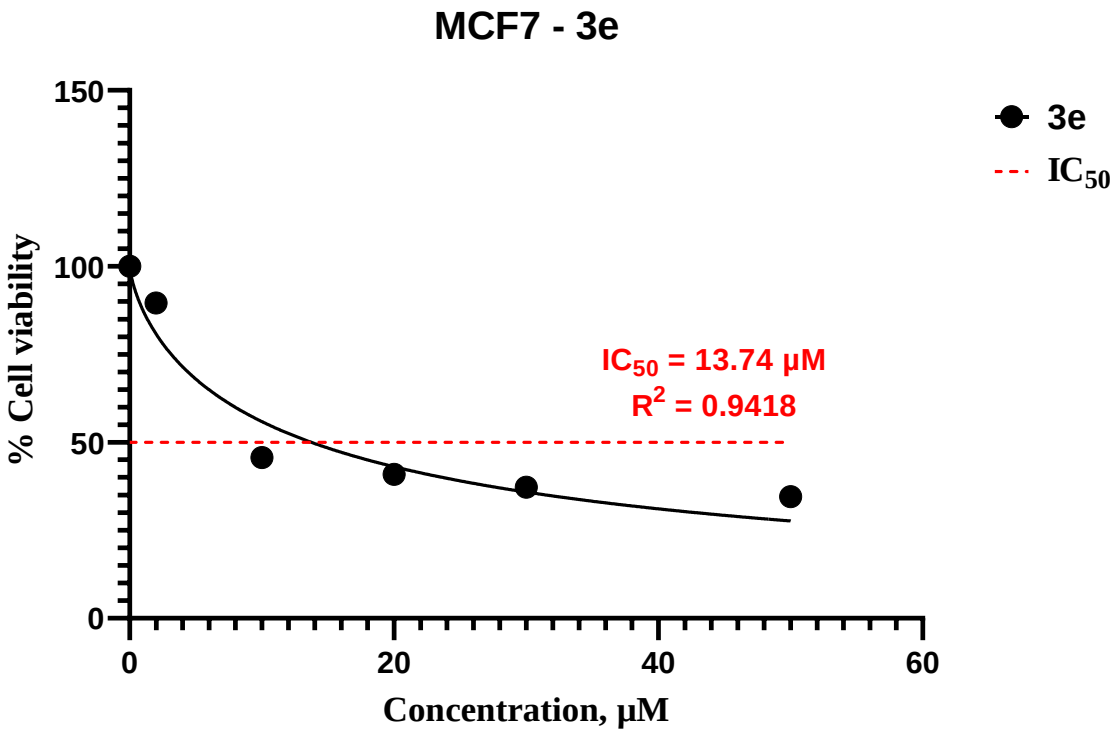

MCF7 - 2c
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 50.93 µM
R2 = 0.9583
2c
IC50


MCF7 - 3c
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 43.52 µM
R2 = 0.9548
3c
IC50

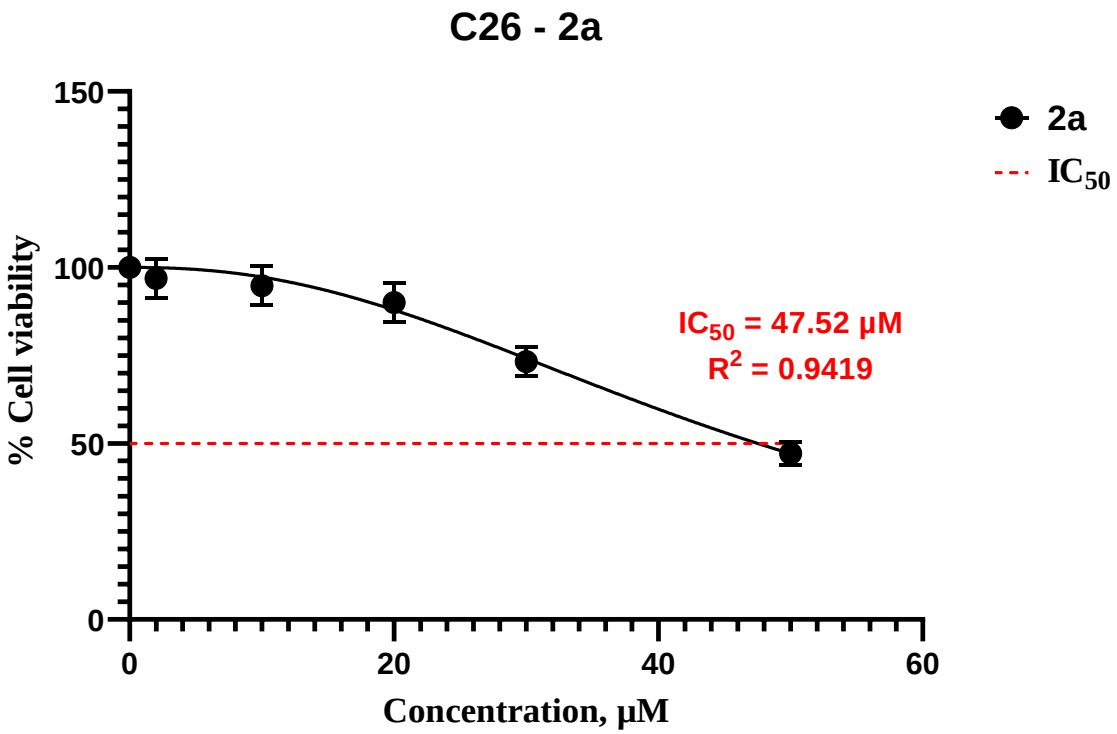

MCF7 - 2d
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 6.54 µM
R2 = 0.9547
2d
IC50

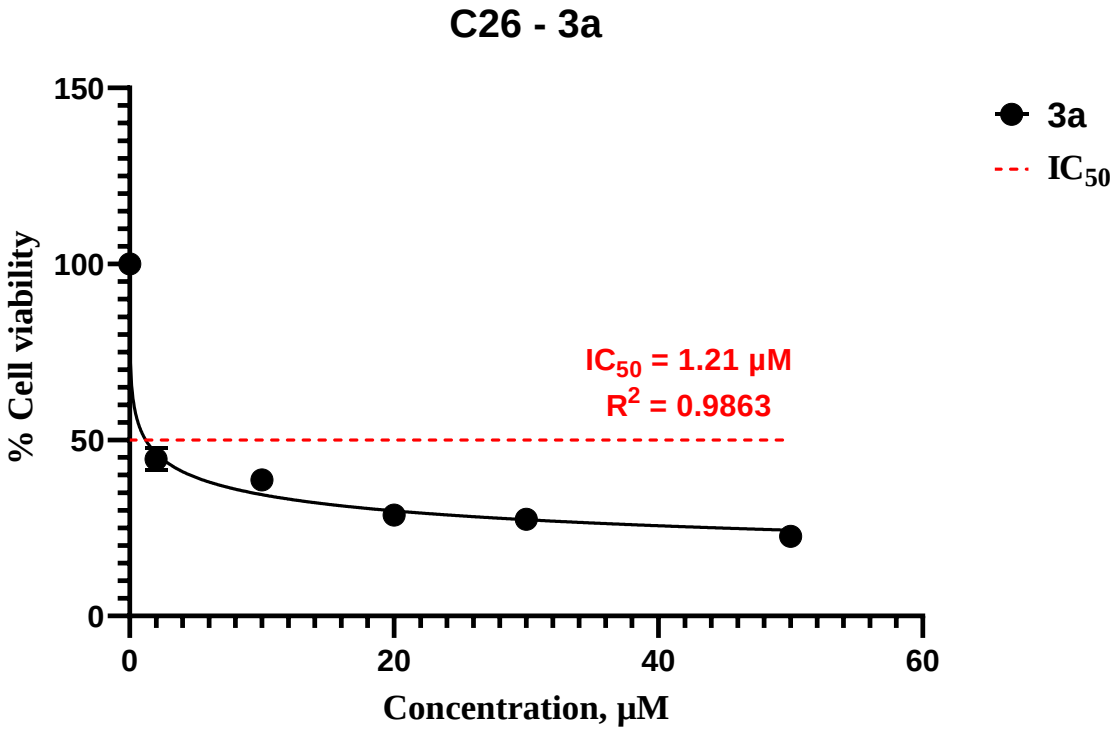

MCF7 - 3d
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 22.32 µM
R2 = 0.9829
3d
IC50

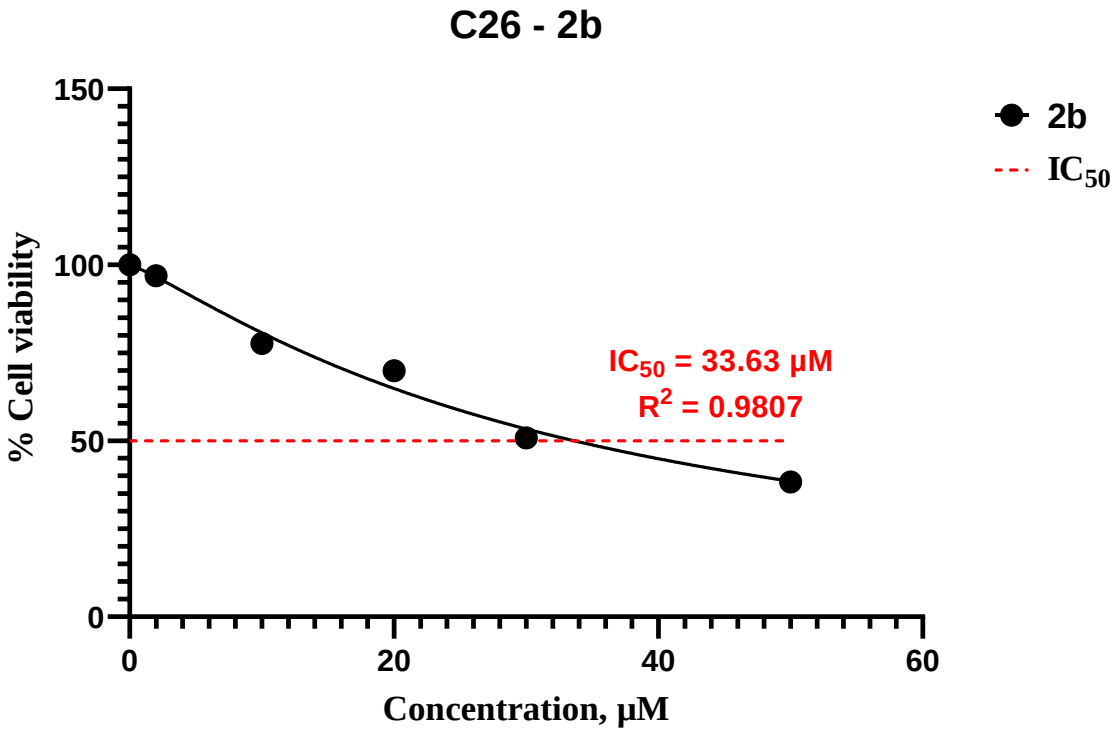

MCF7 - 2e
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 26.11 µM
R2 = 0.9744
2e
IC50

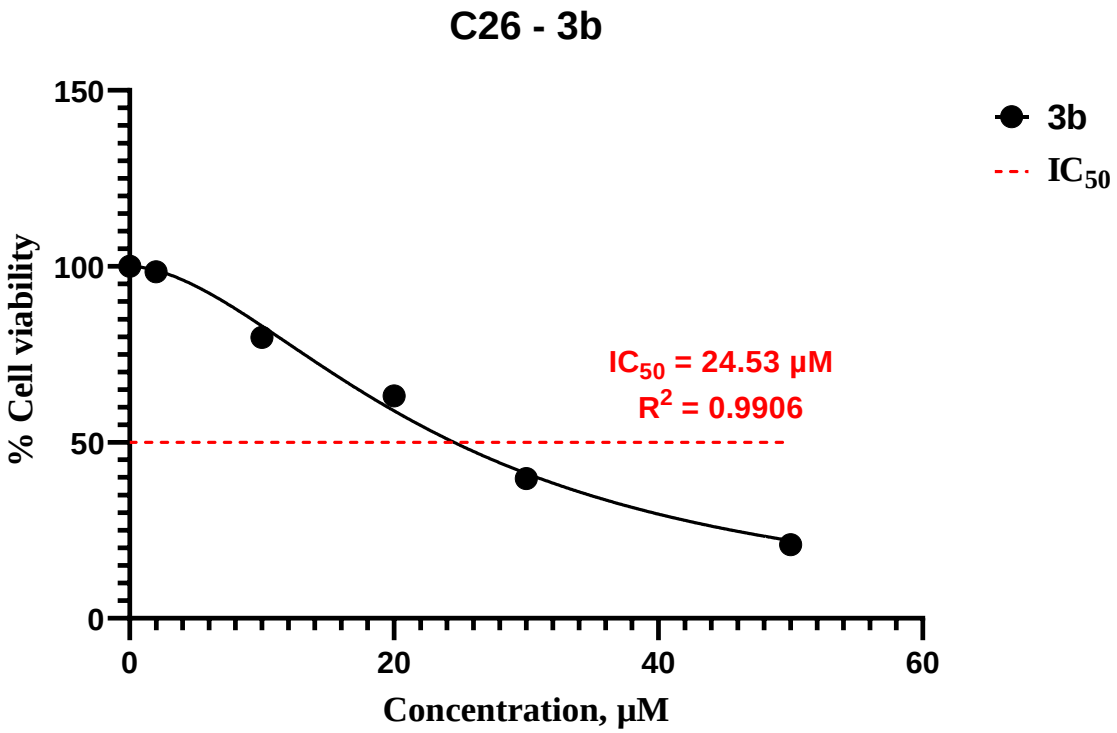

MCF7 - 3e
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 13.74 µM
R2 = 0.9418
3e
IC50

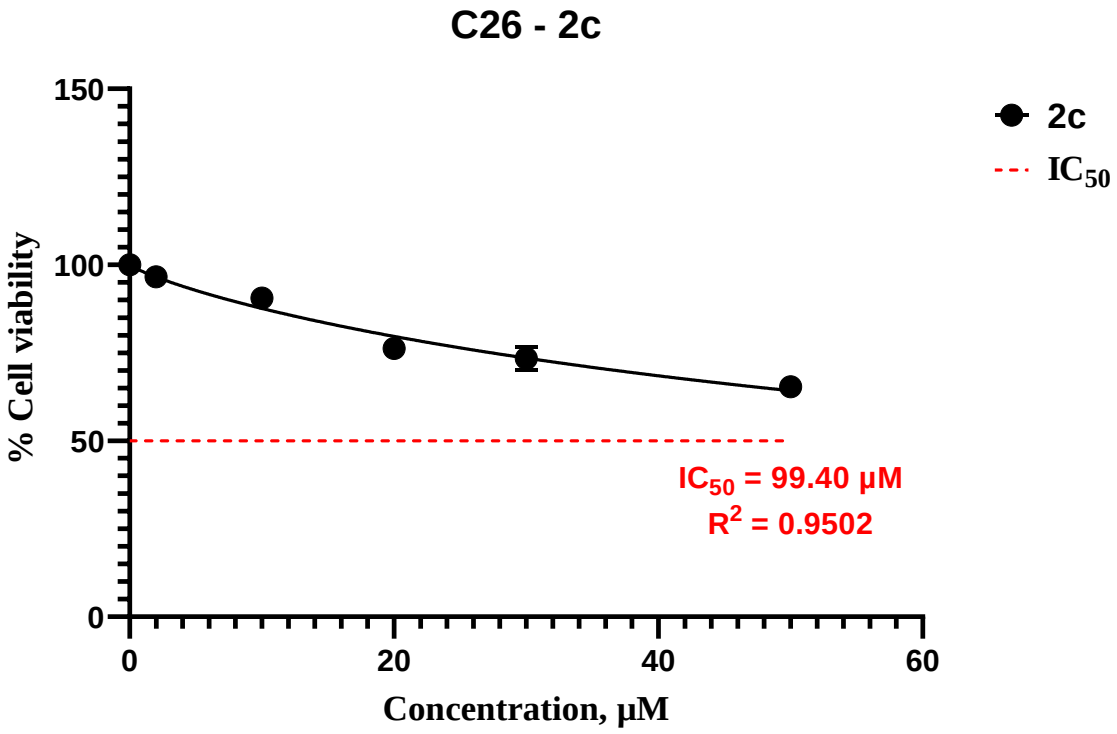
IC_{50} (2-3) C26

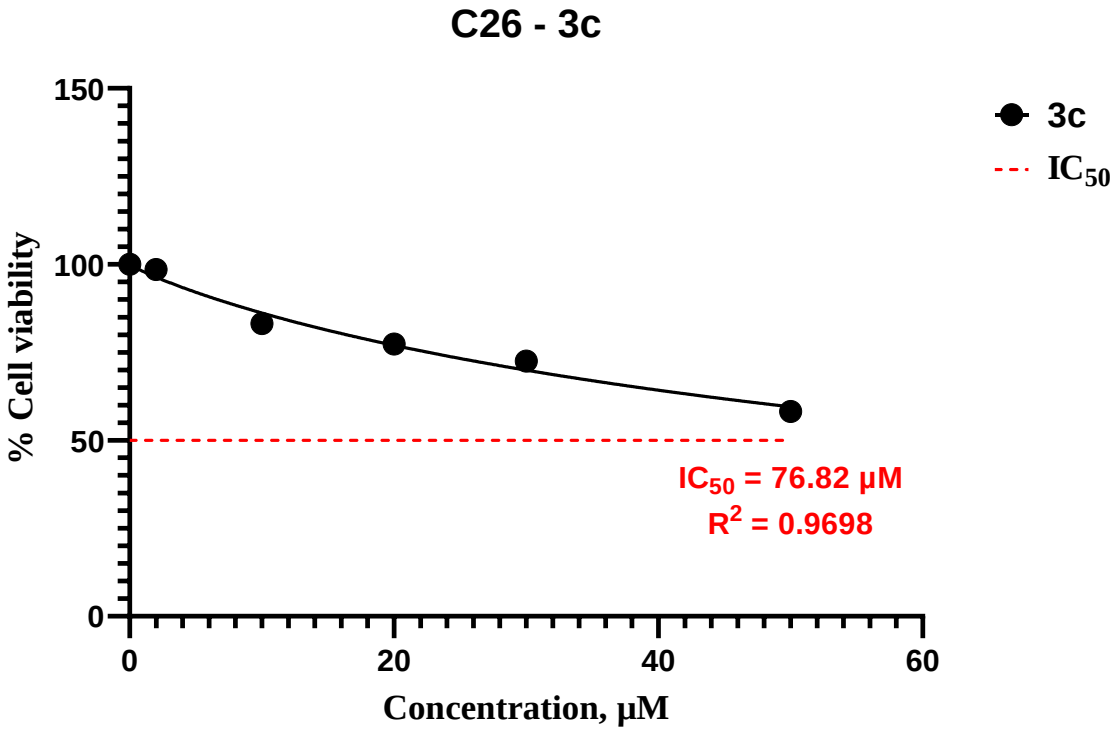

C26 - 2a
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 47.52 µM
R2 = 0.9419
2a
IC50

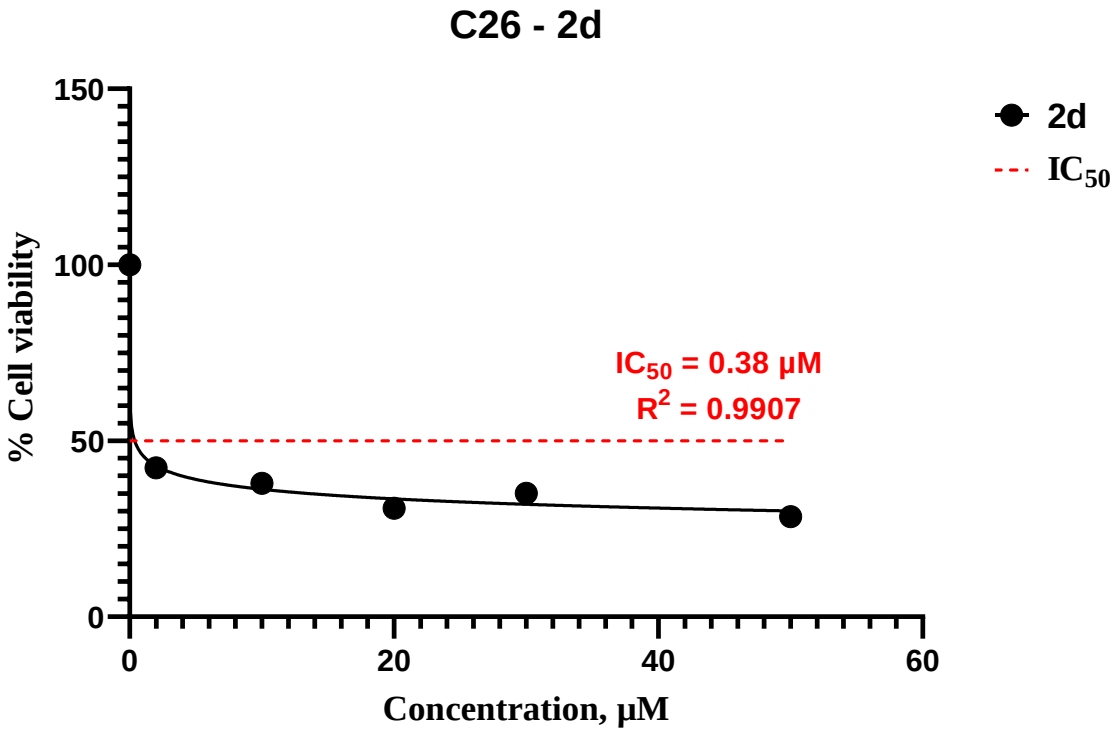

C26 - 3a
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 1.21 µM
R2 = 0.9863
3a
IC50

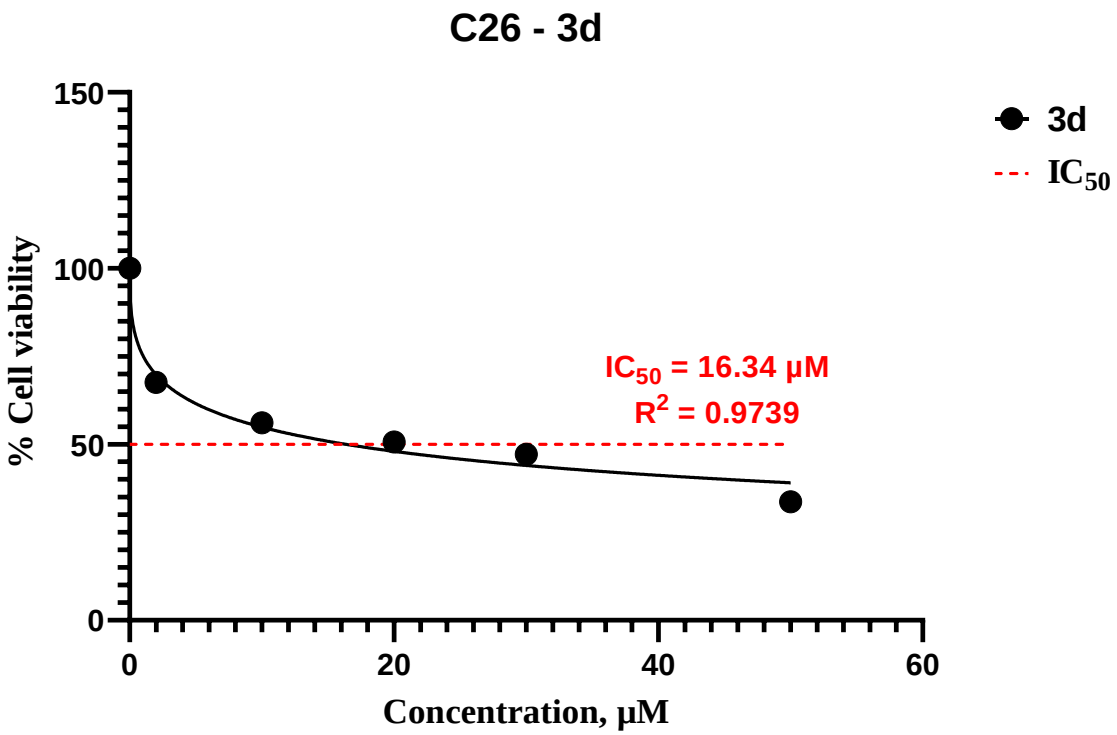

C26 - 2b
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 33.63 µM
R2 = 0.9807
2b
IC50

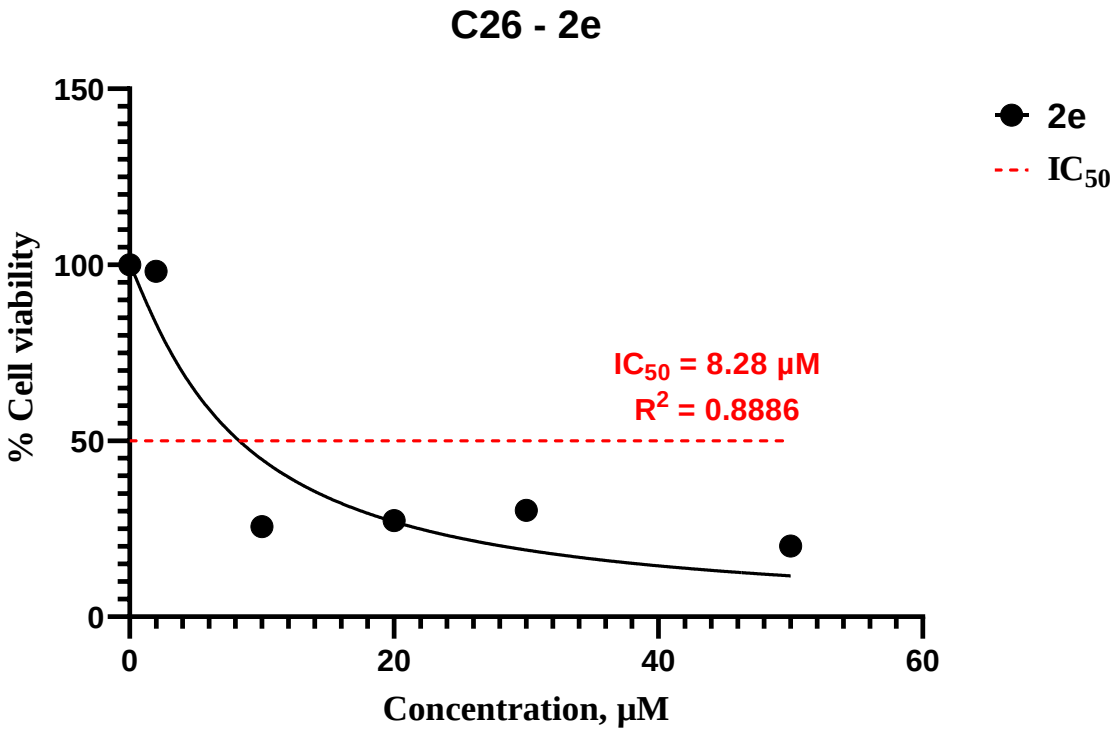

C26 - 3b
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 24.53 µM
R2 = 0.9906
3b
IC50

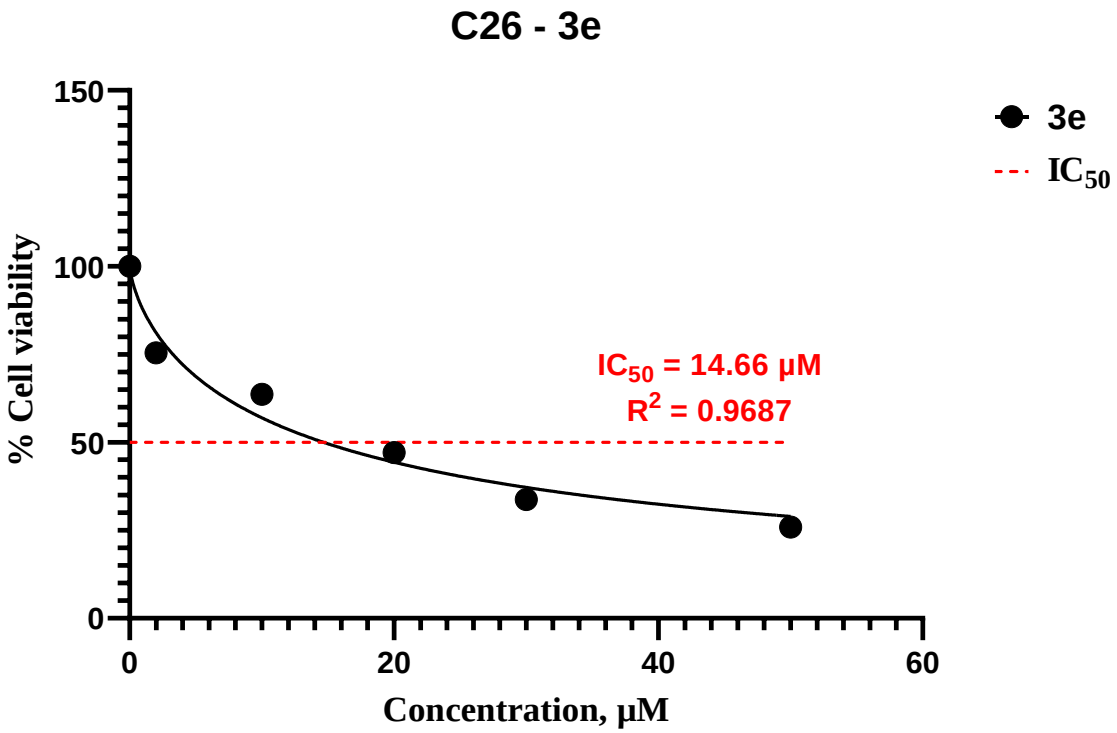

C26 - 2c
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
2c
IC50
IC50 = 99.40 µM
R2 = 0.9502


C26 - 3c
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
3c
IC50
IC50 = 76.82 µM
R2 = 0.9698


C26 - 2d
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 0.38 µM
R2 = 0.9907
2d
IC50


C26 - 3d
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 16.34 µM
R2 = 0.9739
3d
IC50


C26 - 2e
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 8.28 µM
R2 = 0.8886
2e
IC50


C26 - 3e
150
100
50
0
% Cell viability
0
20
40
60
Concentration, µM
IC50 = 14.66 µM
R2 = 0.9687
3e
IC50

IN SILICO ADMET

2d

ADMETlab 3.0

Cc1ccc(Nc2nc(N3CCCCC3)nc(N3CCCCC3)n2)cc1

1. Physicochemical Property

Property	Value	Comment
Molecular Weight	352.24	Contain hydrogen atoms. Optimal:100~600
Volume	370.412	Van der Waals volume
Density	0.951	Density = MW / Volume
nHA	6.0	Number of hydrogen bond acceptors. Optimal:0~12
nHD	1.0	Number of hydrogen bond donors. Optimal:0~7
nRot	4.0	Number of rotatable bonds. Optimal:0~11
nRing	4.0	Number of rings. Optimal:0~6
MaxRing	6.0	Number of atoms in the biggest ring. Optimal:0~18
nHet	6.0	Number of heteroatoms. Optimal:1~15
fChar	0.0	Formal charge. Optimal:-4 ~4
nRig	24.0	Number of rigid bonds. Optimal:0~30
Flexibility	0.167	Flexibility = nRot /nRig
Stereo Centers	0.0	Stereo Centers. Optimal: ≤ 2
TPSA	57.18	Topological Polar Surface Area. Optimal:0~140
logS	-6.53	The logarithm of aqueous solubility value.
logP	5.922	The logarithm of the n-octanol/water distribution coefficients at pH=7.4.
logD	4.163	The logarithm of the n-octanol/water distribution coefficient.
pka (Acid)	10.737	Acid-base dissociation constant (pKa) value represents the strength of a drug molecule's acidity or basicity.
pka (Base)	3.319	Acid-base dissociation constant (pKa) value represents the strength of a drug molecule's acidity or basicity.
Melting point	160.039	The predicted melting point of a compound is expressed in degrees Celsius (°C). Melting points below 25°C are classified as liquids, while melting points above 25°C are classified as solids.
Boiling point	403.858	The predicted melting point of a compound is expressed in degrees Celsius (°C). A normal boiling point below 25°C is categorized as a gas.

2. Medicinal Chemistry

Property	Value	Decision	Comment

QED	0.9	●	■ A measure of drug-likeness based on the concept of desirability; ■ Attractive: > 0.67; ■ unattractive: 0.49~0.67; ■ too complex: < 0.34
GASA	0.0	●	■ ES: Easy to synthesize; HS: Hard to synthesize; ■ The output value represents the probability of being difficult to synthesize, ranging from 0 to 1.
Synth	2.0	●	■ Synthetic accessibility score is designed to estimate ease of synthesis of drug-like molecules. ■ SAscore ≥ 6, difficult to synthesize; SAscore <6, easy to synthesize
Fsp3	0.55	●	■ The number of sp3 hybridized carbons / total carbon count, correlating with melting point and solubility. ■ Fsp^3 ≥0.42 is considered a suitable value.
MCE-18	50.258	●	■ MCE-18 stands for medicinal chemistry evolution. ■ MCE-18≥45 is considered a suitable value.
NPscore	-1.287	-	■ Natural product-likeness score. ■ This score is typically in the range from -5 to 5. ■ The higher the score is, the higher the probability is that the molecule is a NP.
Lipinski Rule	0.0	●	■ MW ≤ 500; logP ≤ 5; Hacc ≤ 10; Hdon ≤ 5 ■ If two properties are out of range, a poor absorption or permeability is possible, one is acceptable.
Pfizer Rule	1.0	●	■ logP > 3; TPSA < 75 ■ Compounds with a high log P (>3) and low TPSA (<75) are likely to be toxic.
GSK Rule	1.0	●	■ MW ≤ 400; logP ≤ 4 ■ Compounds satisfying the GSK rule may have a more favorable ADMET profile
Golden Triangle	0.0	●	■ 200 ≤ MW ≤ 500; -2 ≤ logD ≤ 5 ■ Compounds satisfying the Golden Triangle rule may have a more favorable ADMET profile.
PAINS	0 alerts	-	frequent hitters, Alpha-screen artifacts and reactive compound 480 substructures (J Med Chem 201053:2719-40)
ALARM NMR	1 alerts	-	Thiol reactive compounds.
BMS	0 alerts	-	undesirable, reactive compounds 176 substructures (J Chem Inf Model 200646:1060-8)
Chelator Rule	0 alerts	-	Chelating compounds.
Colloidal aggregators	0.415	-	■ Category 0: non-colloidal aggregators; ■ Category 1: colloidal aggregators. ■ The output value is the probability of being colloidal aggregators, within the range of 0 to 1.

FLuc inhibitors	0.338	●	■ Category 0: non-fLuc inhibitors; ■ Category 1: fLuc inhibitors. ■ The output value is the probability of being fLuc inhibitors, within the range of 0 to 1.
Blue fluorescence	0.013	●	■ Category 0: non-blue fluorescence; ■ Category 1: blue fluorescence. ■ The output value is the probability of being blue fluorescence, within the range of 0 to 1.
Green fluorescence	0.528	●	■ Category 0: non-green fluorescence; ■ Category 1: green fluorescence. ■ The output value is the probability of being green fluorescence, within the range of 0 to 1.
Reactive compounds	0.002	●	■ Category 0: non-reactive compound; ■ Category 1: reactive compound. ■ The output value is the probability of being reactive compound, within the range of 0 to 1.
Promiscuous compounds	0.047	●	■ Category 0: non-promiscuous compound; ■ Category 1: promiscuous compound. ■ The output value is the probability of being promiscuous compound, within the range of 0 to 1.

3. Absorption

Property	Value	Decision	Comment
Caco-2 Permeability	-4.745	●	Optimal: higher than -5.15 Log unit
MDCK Permeability	-4.711	●	■ low permeability: < 2 × 10-6 cm/s ■ medium permeability: 2-20 × 10^{-6} cm/s ■ high passive permeability: > 20 × 10^{-6} cm/s
PAMPA	0.0	●	■ The experimental data for Peff was logarithmically transformed (logPeff). ■ Molecules with log Peff values below 2.0 were classified as low-permeability (Category 0), while those with log Peff values exceeding 2.5 were classified as high-permeability (Category 1).
Pgp-inhibitor	1.0	●	■ Category 1: Inhibitor; ■ Category 0: Non-inhibitor; ■ The output value is the probability of being Pgp-inhibitor
Pgp-substrate	0.0	●	■ Category 1: substrate; ■ Category 0: Non-substrate; ■ The output value is the probability of being Pgp-substrate
HIA	0.0	●	■ Human Intestinal Absorption ■ Category 1: HIA+(HIA < 30%); ■ Category 0: HIA-(HIA >= 30%); ■ The output value is the probability of being HIA+

$F_{20\%}$	0.0	●	■ 20% Bioavailability ■ Category 1: F 20% + (bioavailability < 20%); ■ Category 0: F 20% - (bioavailability ≥ 20%); ■ The output value is the probability of being F 20% +
$F_{30\%}$	0.0	●	■ 30% Bioavailability ■ Category 1: F 30% + (bioavailability < 30%); ■ Category 0: F 30% - (bioavailability ≥ 30%); ■ The output value is the probability of being F 30% +
$F_{50\%}$	0.362	●	■ 50% Bioavailability ■ Category 1: F 50% + (bioavailability < 50%); ■ Category 0: F 50% - (bioavailability ≥ 50%); ■ The output value is the probability of being F 50% +

4. Distribution

Property	Value	Decision	Comment
PPB	99.171	●	■ Plasma Protein Binding Optimal: < 90%. ■ Drugs with high protein-bound may have a low therapeutic index.
VDss	0.646	●	■ Volume Distribution ■ Optimal: 0.04-20L/kg
BBB	0.161	●	■ Blood-Brain Barrier Penetration ■ Category 1: BBB+; Category 0: BBB-; ■ The output value is the probability of being BBB+
Fu	0.449	●	■ The fraction unbound in plasms ■ Low: <5%; Middle: 5~20%; High: > 20%
OATP1B1 inhibitor	0.999	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
OATP1B3 inhibitor	0.999	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
BCRP inhibitor	0.178	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
MRP1 inhibitor	0.932	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.

5. Metabolism

Property	Value	Decision	Comment
CYP1A2 inhibitor	1.0	●	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.

CYP1A2 substrate	1.0	🔴	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C19 inhibitor	0.997	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2C19 substrate	0.998	🔴	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C9 inhibitor	0.864	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2C9 substrate	0.002	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2D6 inhibitor	0.097	🟢	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2D6 substrate	0.785	🔴	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP3A4 inhibitor	0.077	🟢	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP3A4 substrate	0.992	🔴	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2B6 inhibitor	0.992	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2B6 substrate	0.029	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C8 inhibitor	0.965	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
HLM Stability	0.999	🔴	■ human liver microsomal (HLM) stability ■ Category 0: stable+ (HLM > 30 min); Category 1: unstable- (HLM ≤ 30 min). The output value is the probability of human liver microsomal instability, where a value closer to 1 indicates a higher likelihood of instability. The range is between 0 and 1.

6. Excretion

Property	Value	Decision	Comment

CL_{plasma}	4.995	●	■ The unit of predicted CLplasma penetration is ml/min/kg. >15 ml/min/kg: high clearance; 5-15 ml/min/kg: moderate clearance; < 5 ml/min/kg: low clearance.
$T_{1/2}$	0.226	●	■ The unit of predicted T1/2 is hours. ■ ultra-short half-life drugs: 1/2 < 1 hour; short half-life drugs: T1/2 between 1-4 hours; intermediate short half-life drugs: T1/2 between 4-8 hours; long half-life drugs: T1/2 > 8 hours.

7. Toxicity

Property	Value	Decision	Comment
hERG Blockers	0.555	●	■ Molecules with IC50 ≤10μM or ≥50% inhibition at 10 μM were classified as hERG+ (Category 1), ■ while molecules with IC50 >10μM or < 50% inhibition at 10μM were classified as hERG - (Category 0). ■ The output value is the probability of being hERG+, within the range of 0 to 1.
hERG Blockers (10um)	0.801	●	■ Molecules with IC50 ≤10 μM are classified as hERG+ (Category 1), ■ and molecules with IC50 > 10μM are classified as hERG- (Category 0). ■ The output value is the probability of being hERG+, within the range of 0 to 1.
DILI	0.647	●	■ Drug Induced Liver Injury. ■ Category 1: drugs with a high risk of DILI; ■ Category 0: drugs with no risk of DILI. ■ The output value is the probability of being toxic.
AMES Muta genicity	0.19	●	■ AMES Toxicity ■ Category 1: Ames positive(+); ■ Category 0: Ames negative(-); ■ The output value is the probability of being toxic.
Rat Oral Acute Toxicity	0.119	●	■ Rat Oral Acute Toxicity. ■ Category 0: low-toxicity, > 500 mg/kg; ■ Category 1: high-toxicity; < 500 mg/kg. ■ The output value is the probability of being toxic, within the range of 0 to 1.
FDAMDD	0.525	●	■ FDA Maximum (Recommended) Daily Dose. ■ Category 1: FDAMDD (+); ■ Category 0: FDAMDD (-); The output value is the probability of being positive.
Skin Sensiti zation	0.359	●	■ Category 1: Sensitizer; ■ Category 0: Non-sensitizer. ■ The output value is the probability of being toxic, within the range of 0 to 1.
Carcinogeni city	0.658	●	■ Category 1: carcinogens; ■ Category 0: non-carcinogens; ■ The output value is the probability of being toxic.

Eye Corrosion	0.001	●	■ Eye Corrosion ■ Category 1: corrosives; Category 0: noncorrosives; ■ The output value is the probability of being corrosives.
Eye Irritation	0.771	●	■ Eye Irritation ■ Category 1: irritants; Category 0: nonirritants; ■ The output value is the probability of being irritants.
Respiratory	0.538	●	■ Category 1: respiratory toxicants; ■ Category 0: non-respiratory toxicants. ■ The output value is the probability of being toxic, within the range of 0 to 1.
Human Hepatotoxicity	0.773	●	■ Human Hepatotoxicity ■ Category 1: H-HT positive(+); ■ Category 0: H-HT negative(-); ■ The output value is the probability of being toxic.
Drug-induced Nephrotoxicity	0.615	●	■ Category 0: non-nephrotoxic (-); ■ Category 1: nephrotoxic (+). ■ The output value is the probability of being nephrotoxic (+), within the range of 0 to 1.
Ototoxicity	0.354	●	■ Category 0: non-ototoxicity (-); ■ Category 1: ototoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Hematotoxicity	0.227	●	■ Category 0: non-hematotoxicity (-); ■ Category 1: hematotoxicity (+). ■ The output value is the probability of being hematotoxicity (+), within the range of 0 to 1.
Genotoxicity	0.672	●	■ Category 0: non-Genotoxicity (-); ■ Category 1: Genotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
RPMI-8226 Immunitoxicity	0.072	●	■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
A549 Cytotoxicity	0.451	●	■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Hek293 Cytotoxicity	0.75	●	■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Drug-induced Neurotoxicity	0.781	●	■ Category 0: non-neurotoxic (-); ■ Category 1: neurotoxic (+). ■ The output value is the probability of being neurotoxic (+), within the range of 0 to 1.

8. Environmental toxicity

Property	Value	Comment
Bioconcentration Factors	1.679	■ Bioconcentration factors are used for considering secondary poisoning potential and assessing risks to human health via the food chain. ■ The unit is –log10[(mg/L)/(1000*MW)]
IGC_{50}	3.759	■ Tetrahymena pyriformis 50 percent growth inhibition concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]
$LC_{50}FM$	4.432	■ 96-hour fathead minnow 50 percent lethal concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]
$LC_{50}DM$	4.558	■ 48-hour daphnia magna 50 percent lethal concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]

9. Tox21 pathway

Property	Value	Decision	Comment
NR-AhR	0.89	🔴	■ Aryl hydrocarbon receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-AR	0.332	🟠	■ Androgen receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-AR-LBD	0.003	🟢	■ Androgen receptor ligand-binding domain ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-Aromatase	0.085	🟢	■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-ER	0.555	🟠	■ Estrogen receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-ER-LBD	0.003	🟢	■ Estrogen receptor ligand-binding domain ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-PPAR-gamma	0.069	🟢	■ Peroxisome proliferator-activated receptor gamma ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-ARE	0.826	🔴	■ Antioxidant response element ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.

SR-ATAD5	0.332	●	■ ATPase family AAA domain-containing protein 5 ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-HSE	0.061	●	■ Heat shock factor response element ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-MMP	0.147	●	■ Mitochondrial membrane potential ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-p53	0.887	●	■ p53, a tumor suppressor protein ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.

10. Toxicophore Rules

Property	Value	Comment
Acute Toxicity Rule	0	■ 20 substructures; ■ acute toxicity during oral administration
Genotoxic Carcinogenicity Rule	1 alerts	■ 117 substructures; ■ carcinogenicity or mutagenicity
NonGenotoxic Carcinogenicity Rule	0	■ 23 substructures; ■ carcinogenicity through nongenotoxic mechanisms
Skin Sensitization Rule	2 alerts	■ 155 substructures; ■ skin irritation
Aquatic Toxicity Rule	0	■ 99 substructures; ■ toxicity to liquid(water)
NonBiodegradable Rule	1 alerts	■ 19 substructures; ■ non-biodegradable
SureChEMBL Rule	0	■ 164 substructures; ■ MedChem unfriendly status
FAF-Drugs4 Rule	1 alerts	154 toxic substructures from FAF-Drug4

2e

ADMETlab 3.0

O=[N+]([O-])c1ccc(Nc2nc(N3CCCCC3)nc(N3CCCCC3)n2)cc1

1. Physicochemical Property

Property	Value	Comment
Molecular Weight	383.21	Contain hydrogen atoms. Optimal:100~600
Volume	379.057	Van der Waals volume
Density	1.011	Density = MW / Volume
nHA	9.0	Number of hydrogen bond acceptors. Optimal:0~12
nHD	1.0	Number of hydrogen bond donors. Optimal:0~7
nRot	5.0	Number of rotatable bonds. Optimal:0~11
nRing	4.0	Number of rings. Optimal:0~6
MaxRing	6.0	Number of atoms in the biggest ring. Optimal:0~18
nHet	9.0	Number of heteroatoms. Optimal:1~15
fChar	0.0	Formal charge. Optimal:-4 ~4
nRig	25.0	Number of rigid bonds. Optimal:0~30
Flexibility	0.2	Flexibility = nRot /nRig
Stereo Centers	0.0	Stereo Centers. Optimal: ≤ 2
TPSA	100.32	Topological Polar Surface Area. Optimal:0~140
logS	-5.461	The logarithm of aqueous solubility value.
logP	4.587	The logarithm of the n-octanol/water distribution coefficients at pH=7.4.
logD	3.457	The logarithm of the n-octanol/water distribution coefficient.
pka (Acid)	9.794	Acid-base dissociation constant (pKa) value represents the strength of a drug molecule's acidity or basicity.
pka (Base)	2.611	Acid-base dissociation constant (pKa) value represents the strength of a drug molecule's acidity or basicity.
Melting point	165.565	The predicted melting point of a compound is expressed in degrees Celsius (°C). Melting points below 25°C are classified as liquids, while melting points above 25°C are classified as solids.
Boiling point	384.728	The predicted melting point of a compound is expressed in degrees Celsius (°C). A normal boiling point below 25°C is categorized as a gas.

2. Medicinal Chemistry

Property	Value	Decision	Comment

QED	0.618	🔴	■ A measure of drug-likeness based on the concept of desirability; ■ Attractive: > 0.67; ■ unattractive: 0.49~0.67; ■ too complex: < 0.34
GASA	0.0	🟢	■ ES: Easy to synthesize; HS: Hard to synthesize; ■ The output value represents the probability of being difficult to synthesize, ranging from 0 to 1.
Synth	2.0	🟢	■ Synthetic accessibility score is designed to estimate ease of synthesis of drug-like molecules. ■ SAscore ≥ 6, difficult to synthesize; SAscore <6, easy to synthesize
Fsp3	0.526	🟢	■ The number of sp3 hybridized carbons / total carbon count, correlating with melting point and solubility. ■ Fsp^3 ≥0.42 is considered a suitable value.
MCE-18	53.793	🟢	■ MCE-18 stands for medicinal chemistry evolution. ■ MCE-18≥45 is considered a suitable value.
NPscore	-1.463	-	■ Natural product-likeness score. ■ This score is typically in the range from -5 to 5. ■ The higher the score is, the higher the probability is that the molecule is a NP.
Lipinski Rule	0.0	🟢	■ MW ≤ 500; logP ≤ 5; Hacc ≤ 10; Hdon ≤ 5 ■ If two properties are out of range, a poor absorption or permeability is possible, one is acceptable.
Pfizer Rule	0.0	🟢	■ logP > 3; TPSA < 75 ■ Compounds with a high log P (>3) and low TPSA (<75) are likely to be toxic.
GSK Rule	1.0	🔴	■ MW ≤ 400; logP ≤ 4 ■ Compounds satisfying the GSK rule may have a more favorable ADMET profile
Golden Triangle	0.0	🟢	■ 200 ≤ MW ≤ 500; -2 ≤ logD ≤ 5 ■ Compounds satisfying the Golden Triangle rule may have a more favorable ADMET profile.
PAINS	0 alerts	-	frequent hitters, Alpha-screen artifacts and reactive compound 480 substructures (J Med Chem 201053:2719-40)
ALARM NMR	3 alerts	-	Thiol reactive compounds.
BMS	0 alerts	-	undesirable, reactive compounds 176 substructures (J Chem Inf Model 200646:1060-8)
Chelator Rule	0 alerts	-	Chelating compounds.
Colloidal aggregators	0.996	-	■ Category 0: non-colloidal aggregators; ■ Category 1: colloidal aggregators. ■ The output value is the probability of being colloidal aggregators, within the range of 0 to 1.

FLuc inhibitors	0.052	●	■ Category 0: non-fLuc inhibitors; ■ Category 1: fLuc inhibitors. ■ The output value is the probability of being fLuc inhibitors, within the range of 0 to 1.
Blue fluorescence	0.01	●	■ Category 0: non-blue fluorescence; ■ Category 1: blue fluorescence. ■ The output value is the probability of being blue fluorescence, within the range of 0 to 1.
Green fluorescence	0.924	●	■ Category 0: non-green fluorescence; ■ Category 1: green fluorescence. ■ The output value is the probability of being green fluorescence, within the range of 0 to 1.
Reactive compounds	0.009	●	■ Category 0: non-reactive compound; ■ Category 1: reactive compound. ■ The output value is the probability of being reactive compound, within the range of 0 to 1.
Promiscuous compounds	0.013	●	■ Category 0: non-promiscuous compound; ■ Category 1: promiscuous compound. ■ The output value is the probability of being promiscuous compound, within the range of 0 to 1.

3. Absorption

Property	Value	Decision	Comment
Caco-2 Permeability	-4.713	●	Optimal: higher than -5.15 Log unit
MDCK Permeability	-4.706	●	■ low permeability: < 2 × 10-6 cm/s ■ medium permeability: 2-20 × 10^{-6} cm/s ■ high passive permeability: > 20 × 10^{-6} cm/s
PAMPA	0.0	●	■ The experimental data for Peff was logarithmically transformed (logPeff). ■ Molecules with log Peff values below 2.0 were classified as low-permeability (Category 0), while those with log Peff values exceeding 2.5 were classified as high-permeability (Category 1).
Pgp-inhibitor	1.0	●	■ Category 1: Inhibitor; ■ Category 0: Non-inhibitor; ■ The output value is the probability of being Pgp-inhibitor
Pgp-substrate	0.0	●	■ Category 1: substrate; ■ Category 0: Non-substrate; ■ The output value is the probability of being Pgp-substrate
HIA	0.0	●	■ Human Intestinal Absorption ■ Category 1: HIA+(HIA < 30%); ■ Category 0: HIA-(HIA >= 30%); ■ The output value is the probability of being HIA+

$F_{20\%}$	0.0	●	■ 20% Bioavailability ■ Category 1: F 20% + (bioavailability < 20%); ■ Category 0: F 20% - (bioavailability ≥ 20%); ■ The output value is the probability of being F 20% +
$F_{30\%}$	0.0	●	■ 30% Bioavailability ■ Category 1: F 30% + (bioavailability < 30%); ■ Category 0: F 30% - (bioavailability ≥ 30%); ■ The output value is the probability of being F 30% +
$F_{50\%}$	0.224	●	■ 50% Bioavailability ■ Category 1: F 50% + (bioavailability < 50%); ■ Category 0: F 50% - (bioavailability ≥ 50%); ■ The output value is the probability of being F 50% +

4. Distribution

Property	Value	Decision	Comment
PPB	99.2	●	■ Plasma Protein Binding Optimal: < 90%. ■ Drugs with high protein-bound may have a low therapeutic index.
VDss	0.498	●	■ Volume Distribution ■ Optimal: 0.04-20L/kg
BBB	0.011	●	■ Blood-Brain Barrier Penetration ■ Category 1: BBB+; Category 0: BBB-; ■ The output value is the probability of being BBB+
Fu	0.407	●	■ The fraction unbound in plasms ■ Low: <5%; Middle: 5~20%; High: > 20%
OATP1B1 inhibitor	0.964	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
OATP1B3 inhibitor	0.992	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
BCRP inhibitor	0.2	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
MRP1 inhibitor	0.999	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.

5. Metabolism

Property	Value	Decision	Comment
CYP1A2 inhibitor	1.0	●	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.

CYP1A2 substrate	1.0	🔴	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C19 inhibitor	0.998	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2C19 substrate	0.927	🔴	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C9 inhibitor	0.082	🟢	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2C9 substrate	0.053	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2D6 inhibitor	0.91	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2D6 substrate	0.574	🟡	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP3A4 inhibitor	0.025	🟢	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP3A4 substrate	0.999	🔴	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2B6 inhibitor	0.996	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2B6 substrate	0.001	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C8 inhibitor	0.558	🟡	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
HLM Stability	0.993	🔴	■ human liver microsomal (HLM) stability ■ Category 0: stable+ (HLM > 30 min); Category 1: unstable- (HLM ≤ 30 min). The output value is the probability of human liver microsomal instability, where a value closer to 1 indicates a higher likelihood of instability. The range is between 0 and 1.

6. Excretion

Property	Value	Decision	Comment

CL_{plasma}	4.479	●	■ The unit of predicted CLplasma penetration is ml/min/kg. >15 ml/min/kg: high clearance; 5-15 ml/min/kg: moderate clearance; < 5 ml/min/kg: low clearance.
$T_{1/2}$	0.464	●	■ The unit of predicted T1/2 is hours. ■ ultra-short half-life drugs: 1/2 < 1 hour; short half-life drugs: T1/2 between 1-4 hours; intermediate short half-life drugs: T1/2 between 4-8 hours; long half-life drugs: T1/2 > 8 hours.

7. Toxicity

Property	Value	Decision	Comment
hERG Blockers	0.569	●	■ Molecules with IC50 ≤10μM or ≥50% inhibition at 10 μM were classified as hERG+ (Category 1), ■ while molecules with IC50 >10μM or < 50% inhibition at 10μM were classified as hERG - (Category 0). ■ The output value is the probability of being hERG+, within the range of 0 to 1.
hERG Blockers (10um)	0.795	●	■ Molecules with IC50 ≤10 μM are classified as hERG+ (Category 1), ■ and molecules with IC50 > 10μM are classified as hERG- (Category 0). ■ The output value is the probability of being hERG+, within the range of 0 to 1.
DILI	0.974	●	■ Drug Induced Liver Injury. ■ Category 1: drugs with a high risk of DILI; ■ Category 0: drugs with no risk of DILI. ■ The output value is the probability of being toxic.
AMES Muta genicity	0.697	●	■ AMES Toxicity ■ Category 1: Ames positive(+); ■ Category 0: Ames negative(-); ■ The output value is the probability of being toxic.
Rat Oral Acute Toxicity	0.242	●	■ Rat Oral Acute Toxicity. ■ Category 0: low-toxicity, > 500 mg/kg; ■ Category 1: high-toxicity; < 500 mg/kg. ■ The output value is the probability of being toxic, within the range of 0 to 1.
FDAMDD	0.624	●	■ FDA Maximum (Recommended) Daily Dose. ■ Category 1: FDAMDD (+); ■ Category 0: FDAMDD (-); The output value is the probability of being positive.
Skin Sensiti zation	0.72	●	■ Category 1: Sensitizer; ■ Category 0: Non-sensitizer. ■ The output value is the probability of being toxic, within the range of 0 to 1.
Carcinogeni city	0.71	●	■ Category 1: carcinogens; ■ Category 0: non-carcinogens; ■ The output value is the probability of being toxic.

Eye Corrosion	0.001	🟢	■ Eye Corrosion ■ Category 1: corrosives; Category 0: noncorrosives; ■ The output value is the probability of being corrosives.
Eye Irritation	0.873	🔴	■ Eye Irritation ■ Category 1: irritants; Category 0: nonirritants; ■ The output value is the probability of being irritants.
Respiratory	0.748	🔴	■ Category 1: respiratory toxicants; ■ Category 0: non-respiratory toxicants. ■ The output value is the probability of being toxic, within the range of 0 to 1.
Human Hepatotoxicity	0.829	🔴	■ Human Hepatotoxicity ■ Category 1: H-HT positive(+); ■ Category 0: H-HT negative(-); ■ The output value is the probability of being toxic.
Drug-induced Nephrotoxicity	0.5	🟠	■ Category 0: non-nephrotoxic (-); ■ Category 1: nephrotoxic (+). ■ The output value is the probability of being nephrotoxic (+), within the range of 0 to 1.
Ototoxicity	0.314	🟠	■ Category 0: non-ototoxicity (-); ■ Category 1: ototoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Hematotoxicity	0.364	🟠	■ Category 0: non-hematotoxicity (-); ■ Category 1: hematotoxicity (+). ■ The output value is the probability of being hematotoxicity (+), within the range of 0 to 1.
Genotoxicity	1.0	🔴	■ Category 0: non-Genotoxicity (-); ■ Category 1: Genotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
RPMI-8226 Immunitoxicity	0.078	🟢	■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
A549 Cytotoxicity	0.57	🟠	■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Hek293 Cytotoxicity	0.822	🔴	■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Drug-induced Neurotoxicity	0.178	🟢	■ Category 0: non-neurotoxic (-); ■ Category 1: neurotoxic (+). ■ The output value is the probability of being neurotoxic (+), within the range of 0 to 1.

8. Environmental toxicity

Property	Value	Comment
Bioconcentration Factors	1.168	■ Bioconcentration factors are used for considering secondary poisoning potential and assessing risks to human health via the food chain. ■ The unit is –log10[(mg/L)/(1000*MW)]
IGC_{50}	3.772	■ Tetrahymena pyriformis 50 percent growth inhibition concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]
$LC_{50}FM$	4.479	■ 96-hour fathead minnow 50 percent lethal concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]
$LC_{50}DM$	4.802	■ 48-hour daphnia magna 50 percent lethal concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]

9. Tox21 pathway

Property	Value	Decision	Comment
NR-AhR	0.4	🟠	■ Aryl hydrocarbon receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-AR	0.088	🟢	■ Androgen receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-AR-LBD	0.028	🟢	■ Androgen receptor ligand-binding domain ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-Aromatase	0.404	🟠	■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-ER	0.487	🟠	■ Estrogen receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-ER-LBD	0.019	🟢	■ Estrogen receptor ligand-binding domain ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-PPAR-gamma	0.143	🟢	■ Peroxisome proliferator-activated receptor gamma ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-ARE	0.854	🔴	■ Antioxidant response element ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.

SR-ATAD5	0.151	●	■ ATPase family AAA domain-containing protein 5 ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-HSE	0.02	●	■ Heat shock factor response element ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-MMP	0.417	●	■ Mitochondrial membrane potential ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-p53	0.967	●	■ p53, a tumor suppressor protein ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.

10. Toxicophore Rules

Property	Value	Comment
Acute Toxicity Rule	0	■ 20 substructures; ■ acute toxicity during oral administration
Genotoxic Carcinogenicity Rule	6 alerts	■ 117 substructures; ■ carcinogenicity or mutagenicity
NonGenotoxic Carcinogenicity Rule	0	■ 23 substructures; ■ carcinogenicity through nongenotoxic mechanisms
Skin Sensitization Rule	2 alerts	■ 155 substructures; ■ skin irritation
Aquatic Toxicity Rule	0	■ 99 substructures; ■ toxicity to liquid(water)
NonBiodegradable Rule	3 alerts	■ 19 substructures; ■ non-biodegradable
SureChEMBL Rule	0	■ 164 substructures; ■ MedChem unfriendly status
FAF-Drugs4 Rule	3 alerts	154 toxic substructures from FAF-Drug4

3a

ADMETlab 3.0

Clc1ccc(Nc2nc(N3CCOCC3)nc(N3CCOCC3)n2)cc1

1. Physicochemical Property

Property	Value	Comment
Molecular Weight	376.14	Contain hydrogen atoms. Optimal:100~600
Volume	351.316	Van der Waals volume
Density	1.071	Density = MW / Volume
nHA	8.0	Number of hydrogen bond acceptors. Optimal:0~12
nHD	1.0	Number of hydrogen bond donors. Optimal:0~7
nRot	4.0	Number of rotatable bonds. Optimal:0~11
nRing	4.0	Number of rings. Optimal:0~6
MaxRing	6.0	Number of atoms in the biggest ring. Optimal:0~18
nHet	9.0	Number of heteroatoms. Optimal:1~15
fChar	0.0	Formal charge. Optimal:-4 ~4
nRig	24.0	Number of rigid bonds. Optimal:0~30
Flexibility	0.167	Flexibility = nRot /nRig
Stereo Centers	0.0	Stereo Centers. Optimal: ≤ 2
TPSA	75.64	Topological Polar Surface Area. Optimal:0~140
logS	-4.738	The logarithm of aqueous solubility value.
logP	4.058	The logarithm of the n-octanol/water distribution coefficients at pH=7.4.
logD	3.22	The logarithm of the n-octanol/water distribution coefficient.
pka (Acid)	8.576	Acid-base dissociation constant (pKa) value represents the strength of a drug molecule's acidity or basicity.
pka (Base)	5.361	Acid-base dissociation constant (pKa) value represents the strength of a drug molecule's acidity or basicity.
Melting point	137.33	The predicted melting point of a compound is expressed in degrees Celsius (°C). Melting points below 25°C are classified as liquids, while melting points above 25°C are classified as solids.
Boiling point	331.769	The predicted melting point of a compound is expressed in degrees Celsius (°C). A normal boiling point below 25°C is categorized as a gas.

2. Medicinal Chemistry

Property	Value	Decision	Comment

QED	0.867	●	■ A measure of drug-likeness based on the concept of desirability; ■ Attractive: > 0.67; ■ unattractive: 0.49~0.67; ■ too complex: < 0.34
GASA	0.0	●	■ ES: Easy to synthesize; HS: Hard to synthesize; ■ The output value represents the probability of being difficult to synthesize, ranging from 0 to 1.
Synth	2.0	●	■ Synthetic accessibility score is designed to estimate ease of synthesis of drug-like molecules. ■ SAscore ≥ 6, difficult to synthesize; SAscore <6, easy to synthesize
Fsp3	0.471	●	■ The number of sp3 hybridized carbons / total carbon count, correlating with melting point and solubility. ■ Fsp^3 ≥0.42 is considered a suitable value.
MCE-18	50.16	●	■ MCE-18 stands for medicinal chemistry evolution. ■ MCE-18≥45 is considered a suitable value.
NPscore	-1.574	-	■ Natural product-likeness score. ■ This score is typically in the range from -5 to 5. ■ The higher the score is, the higher the probability is that the molecule is a NP.
Lipinski Rule	0.0	●	■ MW ≤ 500; logP ≤ 5; Hacc ≤ 10; Hdon ≤ 5 ■ If two properties are out of range, a poor absorption or permeability is possible, one is acceptable.
Pfizer Rule	0.0	●	■ logP > 3; TPSA < 75 ■ Compounds with a high log P (>3) and low TPSA (<75) are likely to be toxic.
GSK Rule	1.0	●	■ MW ≤ 400; logP ≤ 4 ■ Compounds satisfying the GSK rule may have a more favorable ADMET profile
Golden Triangle	0.0	●	■ 200 ≤ MW ≤ 500; -2 ≤ logD ≤ 5 ■ Compounds satisfying the Golden Triangle rule may have a more favorable ADMET profile.
PAINS	0 alerts	-	frequent hitters, Alpha-screen artifacts and reactive compound 480 substructures (J Med Chem 201053:2719-40)
ALARM NMR	1 alerts	-	Thiol reactive compounds.
BMS	0 alerts	-	undesirable, reactive compounds 176 substructures (J Chem Inf Model 200646:1060-8)
Chelator Rule	0 alerts	-	Chelating compounds.
Colloidal aggregators	0.073	-	■ Category 0: non-colloidal aggregators; ■ Category 1: colloidal aggregators. ■ The output value is the probability of being colloidal aggregators, within the range of 0 to 1.

FLuc inhibitors	0.038	●	■ Category 0: non-fLuc inhibitors; ■ Category 1: fLuc inhibitors. ■ The output value is the probability of being fLuc inhibitors, within the range of 0 to 1.
Blue fluorescence	0.012	●	■ Category 0: non-blue fluorescence; ■ Category 1: blue fluorescence. ■ The output value is the probability of being blue fluorescence, within the range of 0 to 1.
Green fluorescence	0.459	●	■ Category 0: non-green fluorescence; ■ Category 1: green fluorescence. ■ The output value is the probability of being green fluorescence, within the range of 0 to 1.
Reactive compounds	0.008	●	■ Category 0: non-reactive compound; ■ Category 1: reactive compound. ■ The output value is the probability of being reactive compound, within the range of 0 to 1.
Promiscuous compounds	0.078	●	■ Category 0: non-promiscuous compound; ■ Category 1: promiscuous compound. ■ The output value is the probability of being promiscuous compound, within the range of 0 to 1.

3. Absorption

Property	Value	Decision	Comment
Caco-2 Permeability	-4.769	●	Optimal: higher than -5.15 Log unit
MDCK Permeability	-4.801	●	■ low permeability: < 2 × 10-6 cm/s ■ medium permeability: 2-20 × 10^{-6} cm/s ■ high passive permeability: > 20 × 10^{-6} cm/s
PAMPA	0.0	●	■ The experimental data for Peff was logarithmically transformed (logPeff). ■ Molecules with log Peff values below 2.0 were classified as low-permeability (Category 0), while those with log Peff values exceeding 2.5 were classified as high-permeability (Category 1).
Pgp-inhibitor	0.984	●	■ Category 1: Inhibitor; ■ Category 0: Non-inhibitor; ■ The output value is the probability of being Pgp-inhibitor
Pgp-substrate	0.0	●	■ Category 1: substrate; ■ Category 0: Non-substrate; ■ The output value is the probability of being Pgp-substrate
HIA	0.001	●	■ Human Intestinal Absorption ■ Category 1: HIA+(HIA < 30%); ■ Category 0: HIA-(HIA >= 30%); ■ The output value is the probability of being HIA+

$F_{20\%}$	0.0	●	■ 20% Bioavailability ■ Category 1: F 20% + (bioavailability < 20%); ■ Category 0: F 20% - (bioavailability ≥ 20%); ■ The output value is the probability of being F 20% +
$F_{30\%}$	0.013	●	■ 30% Bioavailability ■ Category 1: F 30% + (bioavailability < 30%); ■ Category 0: F 30% - (bioavailability ≥ 30%); ■ The output value is the probability of being F 30% +
$F_{50\%}$	0.8	●	■ 50% Bioavailability ■ Category 1: F 50% + (bioavailability < 50%); ■ Category 0: F 50% - (bioavailability ≥ 50%); ■ The output value is the probability of being F 50% +

4. Distribution

Property	Value	Decision	Comment
PPB	97.058	●	■ Plasma Protein Binding Optimal: < 90%. ■ Drugs with high protein-bound may have a low therapeutic index.
VDss	0.128	●	■ Volume Distribution ■ Optimal: 0.04-20L/kg
BBB	0.004	●	■ Blood-Brain Barrier Penetration ■ Category 1: BBB+; Category 0: BBB-; ■ The output value is the probability of being BBB+
Fu	3.019	●	■ The fraction unbound in plasms ■ Low: <5%; Middle: 5~20%; High: > 20%
OATP1B1 inhibitor	1.0	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
OATP1B3 inhibitor	1.0	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
BCRP inhibitor	0.002	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
MRP1 inhibitor	0.525	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.

5. Metabolism

Property	Value	Decision	Comment
CYP1A2 inhibitor	1.0	●	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.

CYP1A2 substrate	0.966	🔴	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C19 inhibitor	0.83	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2C19 substrate	0.001	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C9 inhibitor	0.882	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2C9 substrate	0.001	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2D6 inhibitor	0.003	🟢	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2D6 substrate	0.005	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP3A4 inhibitor	0.869	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP3A4 substrate	0.038	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2B6 inhibitor	0.107	🟢	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2B6 substrate	0.0	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C8 inhibitor	0.984	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
HLM Stability	0.0	🟢	■ human liver microsomal (HLM) stability ■ Category 0: stable+ (HLM > 30 min); Category 1: unstable- (HLM ≤ 30 min). The output value is the probability of human liver microsomal instability, where a value closer to 1 indicates a higher likelihood of instability. The range is between 0 and 1.

6. Excretion

Property	Value	Decision	Comment

CL_{plasma}	5.307	🟡	■ The unit of predicted CLplasma penetration is ml/min/kg. >15 ml/min/kg: high clearance; 5-15 ml/min/kg: moderate clearance; < 5 ml/min/kg: low clearance.
$T_{1/2}$	0.229	🔴	■ The unit of predicted T1/2 is hours. ■ ultra-short half-life drugs: 1/2 < 1 hour; short half-life drugs: T1/2 between 1-4 hours; intermediate short half-life drugs: T1/2 between 4-8 hours; long half-life drugs: T1/2 > 8 hours.

7. Toxicity

Property	Value	Decision	Comment
hERG Blockers	0.564	🟠	■ Molecules with IC50 ≤10μM or ≥50% inhibition at 10 μM were classified as hERG+ (Category 1), ■ while molecules with IC50 >10μM or < 50% inhibition at 10μM were classified as hERG - (Category 0). ■ The output value is the probability of being hERG+, within the range of 0 to 1.
hERG Blockers (10um)	0.717	🔴	■ Molecules with IC50 ≤10 μM are classified as hERG+ (Category 1), ■ and molecules with IC50 > 10μM are classified as hERG- (Category 0). ■ The output value is the probability of being hERG+, within the range of 0 to 1.
DILI	0.991	🔴	■ Drug Induced Liver Injury. ■ Category 1: drugs with a high risk of DILI; ■ Category 0: drugs with no risk of DILI. ■ The output value is the probability of being toxic.
AMES Mutagenicity	0.3	🟢	■ AMES Toxicity ■ Category 1: Ames positive(+); ■ Category 0: Ames negative(-); ■ The output value is the probability of being toxic.
Rat Oral Acute Toxicity	0.117	🟢	■ Rat Oral Acute Toxicity. ■ Category 0: low-toxicity, > 500 mg/kg; ■ Category 1: high-toxicity; < 500 mg/kg. ■ The output value is the probability of being toxic, within the range of 0 to 1.
FDAMDD	0.067	🟢	■ FDA Maximum (Recommended) Daily Dose. ■ Category 1: FDAMDD (+); ■ Category 0: FDAMDD (-); The output value is the probability of being positive.
Skin Sensitization	0.775	🔴	■ Category 1: Sensitizer; ■ Category 0: Non-sensitizer. ■ The output value is the probability of being toxic, within the range of 0 to 1.
Carcinogenicity	0.966	🔴	■ Category 1: carcinogens; ■ Category 0: non-carcinogens; ■ The output value is the probability of being toxic.

Eye Corrosion	0.0		■ Eye Corrosion ■ Category 1: corrosives; Category 0: noncorrosives; ■ The output value is the probability of being corrosives.
Eye Irritation	0.625		■ Eye Irritation ■ Category 1: irritants; Category 0: nonirritants; ■ The output value is the probability of being irritants.
Respiratory	0.287		■ Category 1: respiratory toxicants; ■ Category 0: non-respiratory toxicants. ■ The output value is the probability of being toxic, within the range of 0 to 1.
Human Hepatotoxicity	0.906		■ Human Hepatotoxicity ■ Category 1: H-HT positive(+); ■ Category 0: H-HT negative(-); ■ The output value is the probability of being toxic.
Drug-induced Nephrotoxicity	0.977		■ Category 0: non-nephrotoxic (-); ■ Category 1: nephrotoxic (+). ■ The output value is the probability of being nephrotoxic (+), within the range of 0 to 1.
Ototoxicity	0.524		■ Category 0: non-ototoxicity (-); ■ Category 1: ototoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Hematotoxicity	0.169		■ Category 0: non-hematotoxicity (-); ■ Category 1: hematotoxicity (+). ■ The output value is the probability of being hematotoxicity (+), within the range of 0 to 1.
Genotoxicity	0.955		■ Category 0: non-Genotoxicity (-); ■ Category 1: Genotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
RPMI-8226 Immunitoxicity	0.138		■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
A549 Cytotoxicity	0.162		■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Hek293 Cytotoxicity	0.756		■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Drug-induced Neurotoxicity	0.937		■ Category 0: non-neurotoxic (-); ■ Category 1: neurotoxic (+). ■ The output value is the probability of being neurotoxic (+), within the range of 0 to 1.

8. Environmental toxicity

Property	Value	Comment
Bioconcentration Factors	1.387	■ Bioconcentration factors are used for considering secondary poisoning potential and assessing risks to human health via the food chain. ■ The unit is –log10[(mg/L)/(1000*MW)]
IGC_{50}	3.765	■ Tetrahymena pyriformis 50 percent growth inhibition concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]
$LC_{50}FM$	4.65	■ 96-hour fathead minnow 50 percent lethal concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]
$LC_{50}DM$	5.118	■ 48-hour daphnia magna 50 percent lethal concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]

9. Tox21 pathway

Property	Value	Decision	Comment
NR-AhR	0.974	🔴	■ Aryl hydrocarbon receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-AR	0.21	🟢	■ Androgen receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-AR-LBD	0.022	🟢	■ Androgen receptor ligand-binding domain ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-Aromatase	0.148	🟢	■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-ER	0.502	🟡	■ Estrogen receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-ER-LBD	0.007	🟢	■ Estrogen receptor ligand-binding domain ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-PPAR-gamma	0.034	🟢	■ Peroxisome proliferator-activated receptor gamma ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-ARE	0.816	🔴	■ Antioxidant response element ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.

SR-ATAD5	0.153	●	■ ATPase family AAA domain-containing protein 5 ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-HSE	0.031	●	■ Heat shock factor response element ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-MMP	0.39	●	■ Mitochondrial membrane potential ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-p53	0.774	●	■ p53, a tumor suppressor protein ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.

10. Toxicophore Rules

Property	Value	Comment
Acute Toxicity Rule	0	■ 20 substructures; ■ acute toxicity during oral administration
Genotoxic Carcinogenicity Rule	1 alerts	■ 117 substructures; ■ carcinogenicity or mutagenicity
NonGenotoxic Carcinogenicity Rule	1 alerts	■ 23 substructures; ■ carcinogenicity through nongenotoxic mechanisms
Skin Sensitization Rule	2 alerts	■ 155 substructures; ■ skin irritation
Aquatic Toxicity Rule	1 alerts	■ 99 substructures; ■ toxicity to liquid(water)
NonBiodegradable Rule	3 alerts	■ 19 substructures; ■ non-biodegradable
SureChEMBL Rule	0	■ 164 substructures; ■ MedChem unfriendly status
FAF-Drugs4 Rule	1 alerts	154 toxic substructures from FAF-Drug4

3b

ADMETlab 3.0

Fc1ccc(Nc2nc(N3CCOCC3)nc(N3CCOCC3)n2)cc1

1. Physicochemical Property

Property	Value	Comment
Molecular Weight	360.17	Contain hydrogen atoms. Optimal:100~600
Volume	342.172	Van der Waals volume
Density	1.053	Density = MW / Volume
nHA	8.0	Number of hydrogen bond acceptors. Optimal:0~12
nHD	1.0	Number of hydrogen bond donors. Optimal:0~7
nRot	4.0	Number of rotatable bonds. Optimal:0~11
nRing	4.0	Number of rings. Optimal:0~6
MaxRing	6.0	Number of atoms in the biggest ring. Optimal:0~18
nHet	9.0	Number of heteroatoms. Optimal:1~15
fChar	0.0	Formal charge. Optimal:-4 ~4
nRig	24.0	Number of rigid bonds. Optimal:0~30
Flexibility	0.167	Flexibility = nRot /nRig
Stereo Centers	0.0	Stereo Centers. Optimal: ≤ 2
TPSA	75.64	Topological Polar Surface Area. Optimal:0~140
logS	-4.306	The logarithm of aqueous solubility value.
logP	3.451	The logarithm of the n-octanol/water distribution coefficients at pH=7.4.
logD	3.174	The logarithm of the n-octanol/water distribution coefficient.
pka (Acid)	8.748	Acid-base dissociation constant (pKa) value represents the strength of a drug molecule's acidity or basicity.
pka (Base)	5.283	Acid-base dissociation constant (pKa) value represents the strength of a drug molecule's acidity or basicity.
Melting point	135.674	The predicted melting point of a compound is expressed in degrees Celsius (°C). Melting points below 25°C are classified as liquids, while melting points above 25°C are classified as solids.
Boiling point	306.135	The predicted melting point of a compound is expressed in degrees Celsius (°C). A normal boiling point below 25°C is categorized as a gas.

2. Medicinal Chemistry

Property	Value	Decision	Comment

QED	0.878	●	■ A measure of drug-likeness based on the concept of desirability; ■ Attractive: > 0.67; ■ unattractive: 0.49~0.67; ■ too complex: < 0.34
GASA	0.0	●	■ ES: Easy to synthesize; HS: Hard to synthesize; ■ The output value represents the probability of being difficult to synthesize, ranging from 0 to 1.
Synth	2.0	●	■ Synthetic accessibility score is designed to estimate ease of synthesis of drug-like molecules. ■ SAscore ≥ 6, difficult to synthesize; SAscore <6, easy to synthesize
Fsp3	0.471	●	■ The number of sp3 hybridized carbons / total carbon count, correlating with melting point and solubility. ■ Fsp^3 ≥0.42 is considered a suitable value.
MCE-18	50.16	●	■ MCE-18 stands for medicinal chemistry evolution. ■ MCE-18≥45 is considered a suitable value.
NPscore	-1.661	-	■ Natural product-likeness score. ■ This score is typically in the range from -5 to 5. ■ The higher the score is, the higher the probability is that the molecule is a NP.
Lipinski Rule	0.0	●	■ MW ≤ 500; logP ≤ 5; Hacc ≤ 10; Hdon ≤ 5 ■ If two properties are out of range, a poor absorption or permeability is possible, one is acceptable.
Pfizer Rule	0.0	●	■ logP > 3; TPSA < 75 ■ Compounds with a high log P (>3) and low TPSA (<75) are likely to be toxic.
GSK Rule	0.0	●	■ MW ≤ 400; logP ≤ 4 ■ Compounds satisfying the GSK rule may have a more favorable ADMET profile
Golden Triangle	0.0	●	■ 200 ≤ MW ≤ 500; -2 ≤ logD ≤ 5 ■ Compounds satisfying the Golden Triangle rule may have a more favorable ADMET profile.
PAINS	0 alerts	-	frequent hitters, Alpha-screen artifacts and reactive compound 480 substructures (J Med Chem 201053:2719-40)
ALARM NMR	1 alerts	-	Thiol reactive compounds.
BMS	0 alerts	-	undesirable, reactive compounds 176 substructures (J Chem Inf Model 200646:1060-8)
Chelator Rule	0 alerts	-	Chelating compounds.
Colloidal aggregators	0.064	-	■ Category 0: non-colloidal aggregators; ■ Category 1: colloidal aggregators. ■ The output value is the probability of being colloidal aggregators, within the range of 0 to 1.

FLuc inhibitors	0.012	●	■ Category 0: non-fLuc inhibitors; ■ Category 1: fLuc inhibitors. ■ The output value is the probability of being fLuc inhibitors, within the range of 0 to 1.
Blue fluorescence	0.008	●	■ Category 0: non-blue fluorescence; ■ Category 1: blue fluorescence. ■ The output value is the probability of being blue fluorescence, within the range of 0 to 1.
Green fluorescence	0.451	●	■ Category 0: non-green fluorescence; ■ Category 1: green fluorescence. ■ The output value is the probability of being green fluorescence, within the range of 0 to 1.
Reactive compounds	0.004	●	■ Category 0: non-reactive compound; ■ Category 1: reactive compound. ■ The output value is the probability of being reactive compound, within the range of 0 to 1.
Promiscuous compounds	0.03	●	■ Category 0: non-promiscuous compound; ■ Category 1: promiscuous compound. ■ The output value is the probability of being promiscuous compound, within the range of 0 to 1.

3. Absorption

Property	Value	Decision	Comment
Caco-2 Permeability	-4.756	●	Optimal: higher than -5.15 Log unit
MDCK Permeability	-4.758	●	■ low permeability: < 2 × 10-6 cm/s ■ medium permeability: 2-20 × 10^{-6} cm/s ■ high passive permeability: > 20 × 10^{-6} cm/s
PAMPA	0.0	●	■ The experimental data for Peff was logarithmically transformed (logPeff). ■ Molecules with log Peff values below 2.0 were classified as low-permeability (Category 0), while those with log Peff values exceeding 2.5 were classified as high-permeability (Category 1).
Pgp-inhibitor	0.993	●	■ Category 1: Inhibitor; ■ Category 0: Non-inhibitor; ■ The output value is the probability of being Pgp-inhibitor
Pgp-substrate	0.0	●	■ Category 1: substrate; ■ Category 0: Non-substrate; ■ The output value is the probability of being Pgp-substrate
HIA	0.002	●	■ Human Intestinal Absorption ■ Category 1: HIA+(HIA < 30%); ■ Category 0: HIA-(HIA >= 30%); ■ The output value is the probability of being HIA+

$F_{20\%}$	0.0	●	■ 20% Bioavailability ■ Category 1: F 20% + (bioavailability < 20%); ■ Category 0: F 20% - (bioavailability ≥ 20%); ■ The output value is the probability of being F 20% +
$F_{30\%}$	0.007	●	■ 30% Bioavailability ■ Category 1: F 30% + (bioavailability < 30%); ■ Category 0: F 30% - (bioavailability ≥ 30%); ■ The output value is the probability of being F 30% +
$F_{50\%}$	0.535	●	■ 50% Bioavailability ■ Category 1: F 50% + (bioavailability < 50%); ■ Category 0: F 50% - (bioavailability ≥ 50%); ■ The output value is the probability of being F 50% +

4. Distribution

Property	Value	Decision	Comment
PPB	94.609	●	■ Plasma Protein Binding Optimal: < 90%. ■ Drugs with high protein-bound may have a low therapeutic index.
VDss	0.308	●	■ Volume Distribution ■ Optimal: 0.04-20L/kg
BBB	0.002	●	■ Blood-Brain Barrier Penetration ■ Category 1: BBB+; Category 0: BBB-; ■ The output value is the probability of being BBB+
Fu	6.187	●	■ The fraction unbound in plasms ■ Low: <5%; Middle: 5~20%; High: > 20%
OATP1B1 inhibitor	1.0	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
OATP1B3 inhibitor	1.0	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
BCRP inhibitor	0.006	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
MRP1 inhibitor	0.546	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.

5. Metabolism

Property	Value	Decision	Comment
CYP1A2 inhibitor	1.0	●	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.

CYP1A2 substrate	0.892	🔴	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C19 inhibitor	0.377	🟠	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2C19 substrate	0.0	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C9 inhibitor	0.867	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2C9 substrate	0.0	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2D6 inhibitor	0.001	🟢	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2D6 substrate	0.068	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP3A4 inhibitor	0.575	🟠	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP3A4 substrate	0.003	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2B6 inhibitor	0.003	🟢	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2B6 substrate	0.0	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C8 inhibitor	0.998	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
HLM Stability	0.001	🟢	■ human liver microsomal (HLM) stability ■ Category 0: stable+ (HLM > 30 min); Category 1: unstable- (HLM ≤ 30 min). The output value is the probability of human liver microsomal instability, where a value closer to 1 indicates a higher likelihood of instability. The range is between 0 and 1.

6. Excretion

Property	Value	Decision	Comment

CL_{plasma}	5.254	🟡	■ The unit of predicted CLplasma penetration is ml/min/kg. >15 ml/min/kg: high clearance; 5-15 ml/min/kg: moderate clearance; < 5 ml/min/kg: low clearance.
$T_{1/2}$	0.254	🔴	■ The unit of predicted T1/2 is hours. ■ ultra-short half-life drugs: 1/2 < 1 hour; short half-life drugs: T1/2 between 1-4 hours; intermediate short half-life drugs: T1/2 between 4-8 hours; long half-life drugs: T1/2 > 8 hours.

7. Toxicity

Property	Value	Decision	Comment
hERG Blockers	0.411	🟠	■ Molecules with IC50 ≤10μM or ≥50% inhibition at 10 μM were classified as hERG+ (Category 1), ■ while molecules with IC50 >10μM or < 50% inhibition at 10μM were classified as hERG - (Category 0). ■ The output value is the probability of being hERG+, within the range of 0 to 1.
hERG Blockers (10um)	0.576	🟠	■ Molecules with IC50 ≤10 μM are classified as hERG+ (Category 1), ■ and molecules with IC50 > 10μM are classified as hERG- (Category 0). ■ The output value is the probability of being hERG+, within the range of 0 to 1.
DILI	0.958	🔴	■ Drug Induced Liver Injury. ■ Category 1: drugs with a high risk of DILI; ■ Category 0: drugs with no risk of DILI. ■ The output value is the probability of being toxic.
AMES Mutagenicity	0.517	🟠	■ AMES Toxicity ■ Category 1: Ames positive(+); ■ Category 0: Ames negative(-); ■ The output value is the probability of being toxic.
Rat Oral Acute Toxicity	0.189	🟢	■ Rat Oral Acute Toxicity. ■ Category 0: low-toxicity, > 500 mg/kg; ■ Category 1: high-toxicity; < 500 mg/kg. ■ The output value is the probability of being toxic, within the range of 0 to 1.
FDAMDD	0.128	🟢	■ FDA Maximum (Recommended) Daily Dose. ■ Category 1: FDAMDD (+); ■ Category 0: FDAMDD (-); The output value is the probability of being positive.
Skin Sensitization	0.467	🟠	■ Category 1: Sensitizer; ■ Category 0: Non-sensitizer. ■ The output value is the probability of being toxic, within the range of 0 to 1.
Carcinogenicity	0.978	🔴	■ Category 1: carcinogens; ■ Category 0: non-carcinogens; ■ The output value is the probability of being toxic.

Eye Corrosion	0.002	🟢	■ Eye Corrosion ■ Category 1: corrosives; Category 0: noncorrosives; ■ The output value is the probability of being corrosives.
Eye Irritation	0.763	🔴	■ Eye Irritation ■ Category 1: irritants; Category 0: nonirritants; ■ The output value is the probability of being irritants.
Respiratory	0.358	🟠	■ Category 1: respiratory toxicants; ■ Category 0: non-respiratory toxicants. ■ The output value is the probability of being toxic, within the range of 0 to 1.
Human Hepatotoxicity	0.916	🔴	■ Human Hepatotoxicity ■ Category 1: H-HT positive(+); ■ Category 0: H-HT negative(-); ■ The output value is the probability of being toxic.
Drug-induced Nephrotoxicity	0.988	🔴	■ Category 0: non-nephrotoxic (-); ■ Category 1: nephrotoxic (+). ■ The output value is the probability of being nephrotoxic (+), within the range of 0 to 1.
Ototoxicity	0.492	🟠	■ Category 0: non-ototoxicity (-); ■ Category 1: ototoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Hematotoxicity	0.183	🟢	■ Category 0: non-hematotoxicity (-); ■ Category 1: hematotoxicity (+). ■ The output value is the probability of being hematotoxicity (+), within the range of 0 to 1.
Genotoxicity	0.958	🔴	■ Category 0: non-Genotoxicity (-); ■ Category 1: Genotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
RPMI-8226 Immunitoxicity	0.159	🟢	■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
A549 Cytotoxicity	0.076	🟢	■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Hek293 Cytotoxicity	0.509	🟠	■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Drug-induced Neurotoxicity	0.968	🔴	■ Category 0: non-neurotoxic (-); ■ Category 1: neurotoxic (+). ■ The output value is the probability of being neurotoxic (+), within the range of 0 to 1.

8. Environmental toxicity

Property	Value	Comment
Bioconcentration Factors	0.532	■ Bioconcentration factors are used for considering secondary poisoning potential and assessing risks to human health via the food chain. ■ The unit is –log10[(mg/L)/(1000*MW)]
IGC_{50}	3.06	■ Tetrahymena pyriformis 50 percent growth inhibition concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]
$LC_{50}FM$	3.774	■ 96-hour fathead minnow 50 percent lethal concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]
$LC_{50}DM$	4.709	■ 48-hour daphnia magna 50 percent lethal concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]

9. Tox21 pathway

Property	Value	Decision	Comment
NR-AhR	0.961	🔴	■ Aryl hydrocarbon receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-AR	0.271	🟢	■ Androgen receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-AR-LBD	0.034	🟢	■ Androgen receptor ligand-binding domain ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-Aromatase	0.157	🟢	■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-ER	0.46	🟡	■ Estrogen receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-ER-LBD	0.007	🟢	■ Estrogen receptor ligand-binding domain ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-PPAR-gamma	0.04	🟢	■ Peroxisome proliferator-activated receptor gamma ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-ARE	0.798	🔴	■ Antioxidant response element ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.

SR-ATAD5	0.185	●	■ ATPase family AAA domain-containing protein 5 ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-HSE	0.027	●	■ Heat shock factor response element ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-MMP	0.302	●	■ Mitochondrial membrane potential ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-p53	0.741	●	■ p53, a tumor suppressor protein ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.

10. Toxicophore Rules

Property	Value	Comment
Acute Toxicity Rule	0	■ 20 substructures; ■ acute toxicity during oral administration
Genotoxic Carcinogenicity Rule	1 alerts	■ 117 substructures; ■ carcinogenicity or mutagenicity
NonGenotoxic Carcinogenicity Rule	1 alerts	■ 23 substructures; ■ carcinogenicity through nongenotoxic mechanisms
Skin Sensitization Rule	2 alerts	■ 155 substructures; ■ skin irritation
Aquatic Toxicity Rule	1 alerts	■ 99 substructures; ■ toxicity to liquid(water)
NonBiodegradable Rule	3 alerts	■ 19 substructures; ■ non-biodegradable
SureChEMBL Rule	0	■ 164 substructures; ■ MedChem unfriendly status
FAF-Drugs4 Rule	1 alerts	154 toxic substructures from FAF-Drug4

3e

ADMETlab 3.0

O=[N+]([O-])c1ccc(Nc2nc(N3CCOCC3)nc(N3CCOCC3)n2)cc1

1. Physicochemical Property

Property	Value	Comment
Molecular Weight	387.17	Contain hydrogen atoms. Optimal:100~600
Volume	362.045	Van der Waals volume
Density	1.069	Density = MW / Volume
nHA	11.0	Number of hydrogen bond acceptors. Optimal:0~12
nHD	1.0	Number of hydrogen bond donors. Optimal:0~7
nRot	5.0	Number of rotatable bonds. Optimal:0~11
nRing	4.0	Number of rings. Optimal:0~6
MaxRing	6.0	Number of atoms in the biggest ring. Optimal:0~18
nHet	11.0	Number of heteroatoms. Optimal:1~15
fChar	0.0	Formal charge. Optimal:-4 ~4
nRig	25.0	Number of rigid bonds. Optimal:0~30
Flexibility	0.2	Flexibility = nRot /nRig
Stereo Centers	0.0	Stereo Centers. Optimal: ≤ 2
TPSA	118.78	Topological Polar Surface Area. Optimal:0~140
logS	-4.216	The logarithm of aqueous solubility value.
logP	3.18	The logarithm of the n-octanol/water distribution coefficients at pH=7.4.
logD	3.164	The logarithm of the n-octanol/water distribution coefficient.
pka (Acid)	8.501	Acid-base dissociation constant (pKa) value represents the strength of a drug molecule's acidity or basicity.
pka (Base)	4.288	Acid-base dissociation constant (pKa) value represents the strength of a drug molecule's acidity or basicity.
Melting point	183.193	The predicted melting point of a compound is expressed in degrees Celsius (°C). Melting points below 25°C are classified as liquids, while melting points above 25°C are classified as solids.
Boiling point	344.872	The predicted melting point of a compound is expressed in degrees Celsius (°C). A normal boiling point below 25°C is categorized as a gas.

2. Medicinal Chemistry

Property	Value	Decision	Comment

QED	0.592	🔴	■ A measure of drug-likeness based on the concept of desirability; ■ Attractive: > 0.67; ■ unattractive: 0.49~0.67; ■ too complex: < 0.34
GASA	0.0	🟢	■ ES: Easy to synthesize; HS: Hard to synthesize; ■ The output value represents the probability of being difficult to synthesize, ranging from 0 to 1.
Synth	2.0	🟢	■ Synthetic accessibility score is designed to estimate ease of synthesis of drug-like molecules. ■ SAscore ≥ 6, difficult to synthesize; SAscore <6, easy to synthesize
Fsp3	0.471	🟢	■ The number of sp3 hybridized carbons / total carbon count, correlating with melting point and solubility. ■ Fsp^3 ≥0.42 is considered a suitable value.
MCE-18	52.8	🟢	■ MCE-18 stands for medicinal chemistry evolution. ■ MCE-18≥45 is considered a suitable value.
NPscore	-1.63	-	■ Natural product-likeness score. ■ This score is typically in the range from -5 to 5. ■ The higher the score is, the higher the probability is that the molecule is a NP.
Lipinski Rule	0.0	🟢	■ MW ≤ 500; logP ≤ 5; Hacc ≤ 10; Hdon ≤ 5 ■ If two properties are out of range, a poor absorption or permeability is possible, one is acceptable.
Pfizer Rule	0.0	🟢	■ logP > 3; TPSA < 75 ■ Compounds with a high log P (>3) and low TPSA (<75) are likely to be toxic.
GSK Rule	0.0	🟢	■ MW ≤ 400; logP ≤ 4 ■ Compounds satisfying the GSK rule may have a more favorable ADMET profile
Golden Triangle	0.0	🟢	■ 200 ≤ MW ≤ 500; -2 ≤ logD ≤ 5 ■ Compounds satisfying the Golden Triangle rule may have a more favorable ADMET profile.
PAINS	0 alerts	-	frequent hitters, Alpha-screen artifacts and reactive compound 480 substructures (J Med Chem 201053:2719-40)
ALARM NMR	3 alerts	-	Thiol reactive compounds.
BMS	0 alerts	-	undesirable, reactive compounds 176 substructures (J Chem Inf Model 200646:1060-8)
Chelator Rule	0 alerts	-	Chelating compounds.
Colloidal aggregators	0.789	-	■ Category 0: non-colloidal aggregators; ■ Category 1: colloidal aggregators. ■ The output value is the probability of being colloidal aggregators, within the range of 0 to 1.

FLuc inhibitors	0.006	●	■ Category 0: non-fLuc inhibitors; ■ Category 1: fLuc inhibitors. ■ The output value is the probability of being fLuc inhibitors, within the range of 0 to 1.
Blue fluorescence	0.006	●	■ Category 0: non-blue fluorescence; ■ Category 1: blue fluorescence. ■ The output value is the probability of being blue fluorescence, within the range of 0 to 1.
Green fluorescence	0.891	●	■ Category 0: non-green fluorescence; ■ Category 1: green fluorescence. ■ The output value is the probability of being green fluorescence, within the range of 0 to 1.
Reactive compounds	0.02	●	■ Category 0: non-reactive compound; ■ Category 1: reactive compound. ■ The output value is the probability of being reactive compound, within the range of 0 to 1.
Promiscuous compounds	0.01	●	■ Category 0: non-promiscuous compound; ■ Category 1: promiscuous compound. ■ The output value is the probability of being promiscuous compound, within the range of 0 to 1.

3. Absorption

Property	Value	Decision	Comment
Caco-2 Permeability	-4.801	●	Optimal: higher than -5.15 Log unit
MDCK Permeability	-4.819	●	■ low permeability: < 2 × 10-6 cm/s ■ medium permeability: 2-20 × 10^{-6} cm/s ■ high passive permeability: > 20 × 10^{-6} cm/s
PAMPA	0.001	●	■ The experimental data for Peff was logarithmically transformed (logPeff). ■ Molecules with log Peff values below 2.0 were classified as low-permeability (Category 0), while those with log Peff values exceeding 2.5 were classified as high-permeability (Category 1).
Pgp-inhibitor	0.871	●	■ Category 1: Inhibitor; ■ Category 0: Non-inhibitor; ■ The output value is the probability of being Pgp-inhibitor
Pgp-substrate	0.0	●	■ Category 1: substrate; ■ Category 0: Non-substrate; ■ The output value is the probability of being Pgp-substrate
HIA	0.001	●	■ Human Intestinal Absorption ■ Category 1: HIA+(HIA < 30%); ■ Category 0: HIA-(HIA >= 30%); ■ The output value is the probability of being HIA+

$F_{20\%}$	0.0	●	■ 20% Bioavailability ■ Category 1: F 20% + (bioavailability < 20%); ■ Category 0: F 20% - (bioavailability ≥ 20%); ■ The output value is the probability of being F 20% +
$F_{30\%}$	0.021	●	■ 30% Bioavailability ■ Category 1: F 30% + (bioavailability < 30%); ■ Category 0: F 30% - (bioavailability ≥ 30%); ■ The output value is the probability of being F 30% +
$F_{50\%}$	0.805	●	■ 50% Bioavailability ■ Category 1: F 50% + (bioavailability < 50%); ■ Category 0: F 50% - (bioavailability ≥ 50%); ■ The output value is the probability of being F 50% +

4. Distribution

Property	Value	Decision	Comment
PPB	94.675	●	■ Plasma Protein Binding Optimal: < 90%. ■ Drugs with high protein-bound may have a low therapeutic index.
VDss	0.214	●	■ Volume Distribution ■ Optimal: 0.04-20L/kg
BBB	0.0	●	■ Blood-Brain Barrier Penetration ■ Category 1: BBB+; Category 0: BBB-; ■ The output value is the probability of being BBB+
Fu	6.439	●	■ The fraction unbound in plasms ■ Low: <5%; Middle: 5~20%; High: > 20%
OATP1B1 inhibitor	0.992	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
OATP1B3 inhibitor	0.999	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
BCRP inhibitor	0.001	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.
MRP1 inhibitor	0.996	●	■ Category 0: Non-inhibitor; Category 1: inhibitor. ■ The output value is the probability of being inhibitor, within the range of 0 to 1.

5. Metabolism

Property	Value	Decision	Comment
CYP1A2 inhibitor	0.998	●	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.

CYP1A2 substrate	0.94	🔴	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C19 inhibitor	0.59	🟠	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2C19 substrate	0.0	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C9 inhibitor	0.653	🟠	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2C9 substrate	0.061	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2D6 inhibitor	0.0	🟢	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2D6 substrate	0.54	🟠	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP3A4 inhibitor	0.867	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP3A4 substrate	0.139	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2B6 inhibitor	0.091	🟢	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
CYP2B6 substrate	0.0	🟢	■ Category 1: Substrate; Category 0: Non-substrate; ■ The output value is the probability of being substrate.
CYP2C8 inhibitor	0.874	🔴	■ Category 1: Inhibitor; Category 0: Non-inhibitor; ■ The output value is the probability of being inhibitor.
HLM Stability	0.0	🟢	■ human liver microsomal (HLM) stability ■ Category 0: stable+ (HLM > 30 min); Category 1: unstable- (HLM ≤ 30 min). The output value is the probability of human liver microsomal instability, where a value closer to 1 indicates a higher likelihood of instability. The range is between 0 and 1.

6. Excretion

Property	Value	Decision	Comment

CL_{plasma}	4.902	🟢	■ The unit of predicted CLplasma penetration is ml/min/kg. >15 ml/min/kg: high clearance; 5-15 ml/min/kg: moderate clearance; < 5 ml/min/kg: low clearance.
$T_{1/2}$	0.54	🔴	■ The unit of predicted T1/2 is hours. ■ ultra-short half-life drugs: 1/2 < 1 hour; short half-life drugs: T1/2 between 1-4 hours; intermediate short half-life drugs: T1/2 between 4-8 hours; long half-life drugs: T1/2 > 8 hours.

7. Toxicity

Property	Value	Decision	Comment
hERG Blockers	0.43	🟡	■ Molecules with IC50 ≤10μM or ≥50% inhibition at 10 μM were classified as hERG+ (Category 1), ■ while molecules with IC50 >10μM or < 50% inhibition at 10μM were classified as hERG - (Category 0). ■ The output value is the probability of being hERG+, within the range of 0 to 1.
hERG Blockers (10um)	0.599	🟡	■ Molecules with IC50 ≤10 μM are classified as hERG+ (Category 1), ■ and molecules with IC50 > 10μM are classified as hERG- (Category 0). ■ The output value is the probability of being hERG+, within the range of 0 to 1.
DILI	0.999	🔴	■ Drug Induced Liver Injury. ■ Category 1: drugs with a high risk of DILI; ■ Category 0: drugs with no risk of DILI. ■ The output value is the probability of being toxic.
AMES Mutagenicity	0.883	🔴	■ AMES Toxicity ■ Category 1: Ames positive(+); ■ Category 0: Ames negative(-); ■ The output value is the probability of being toxic.
Rat Oral Acute Toxicity	0.179	🟢	■ Rat Oral Acute Toxicity. ■ Category 0: low-toxicity, > 500 mg/kg; ■ Category 1: high-toxicity; < 500 mg/kg. ■ The output value is the probability of being toxic, within the range of 0 to 1.
FDAMDD	0.09	🟢	■ FDA Maximum (Recommended) Daily Dose. ■ Category 1: FDAMDD (+); ■ Category 0: FDAMDD (-); The output value is the probability of being positive.
Skin Sensitization	0.926	🔴	■ Category 1: Sensitizer; ■ Category 0: Non-sensitizer. ■ The output value is the probability of being toxic, within the range of 0 to 1.
Carcinogenicity	0.98	🔴	■ Category 1: carcinogens; ■ Category 0: non-carcinogens; ■ The output value is the probability of being toxic.

Eye Corrosion	0.001	🟢	■ Eye Corrosion ■ Category 1: corrosives; Category 0: noncorrosives; ■ The output value is the probability of being corrosives.
Eye Irritation	0.915	🔴	■ Eye Irritation ■ Category 1: irritants; Category 0: nonirritants; ■ The output value is the probability of being irritants.
Respiratory	0.594	🟠	■ Category 1: respiratory toxicants; ■ Category 0: non-respiratory toxicants. ■ The output value is the probability of being toxic, within the range of 0 to 1.
Human Hepatotoxicity	0.936	🔴	■ Human Hepatotoxicity ■ Category 1: H-HT positive(+); ■ Category 0: H-HT negative(-); ■ The output value is the probability of being toxic.
Drug-induced Nephrotoxicity	0.917	🔴	■ Category 0: non-nephrotoxic (-); ■ Category 1: nephrotoxic (+). ■ The output value is the probability of being nephrotoxic (+), within the range of 0 to 1.
Ototoxicity	0.431	🟠	■ Category 0: non-ototoxicity (-); ■ Category 1: ototoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Hematotoxicity	0.267	🟢	■ Category 0: non-hematotoxicity (-); ■ Category 1: hematotoxicity (+). ■ The output value is the probability of being hematotoxicity (+), within the range of 0 to 1.
Genotoxicity	1.0	🔴	■ Category 0: non-Genotoxicity (-); ■ Category 1: Genotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
RPMI-8226 Immunitoxicity	0.162	🟢	■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
A549 Cytotoxicity	0.103	🟢	■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Hek293 Cytotoxicity	0.601	🟠	■ Category 0: non-cytotoxicity (-); ■ Category 1: cytotoxicity (+). ■ The output value is the probability of being ototoxicity (+), within the range of 0 to 1.
Drug-induced Neurotoxicity	0.439	🟠	■ Category 0: non-neurotoxic (-); ■ Category 1: neurotoxic (+). ■ The output value is the probability of being neurotoxic (+), within the range of 0 to 1.

8. Environmental toxicity

Property	Value	Comment
Bioconcentration Factors	0.482	■ Bioconcentration factors are used for considering secondary poisoning potential and assessing risks to human health via the food chain. ■ The unit is –log10[(mg/L)/(1000*MW)]
IGC_{50}	3.274	■ Tetrahymena pyriformis 50 percent growth inhibition concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]
$LC_{50}FM$	3.943	■ 96-hour fathead minnow 50 percent lethal concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]
$LC_{50}DM$	4.307	■ 48-hour daphnia magna 50 percent lethal concentration. ■ The unit is –log10[(mg/L)/(1000*MW)]

9. Tox21 pathway

Property	Value	Decision	Comment
NR-AhR	0.778	🔴	■ Aryl hydrocarbon receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-AR	0.066	🟢	■ Androgen receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-AR-LBD	0.105	🟢	■ Androgen receptor ligand-binding domain ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-Aromatase	0.311	🟡	■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-ER	0.497	🟡	■ Estrogen receptor ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-ER-LBD	0.023	🟢	■ Estrogen receptor ligand-binding domain ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
NR-PPAR-gamma	0.039	🟢	■ Peroxisome proliferator-activated receptor gamma ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-ARE	0.727	🔴	■ Antioxidant response element ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.

SR-ATAD5	0.075	●	■ ATPase family AAA domain-containing protein 5 ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-HSE	0.01	●	■ Heat shock factor response element ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-MMP	0.454	●	■ Mitochondrial membrane potential ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.
SR-p53	0.84	●	■ p53, a tumor suppressor protein ■ Category 1: actives ; ■ Category 0: inactives; ■ The output value is the probability of being active.

10. Toxicophore Rules

Property	Value	Comment
Acute Toxicity Rule	0	■ 20 substructures; ■ acute toxicity during oral administration
Genotoxic Carcinogenicity Rule	6 alerts	■ 117 substructures; ■ carcinogenicity or mutagenicity
NonGenotoxic Carcinogenicity Rule	0	■ 23 substructures; ■ carcinogenicity through nongenotoxic mechanisms
Skin Sensitization Rule	2 alerts	■ 155 substructures; ■ skin irritation
Aquatic Toxicity Rule	0	■ 99 substructures; ■ toxicity to liquid(water)
NonBiodegradable Rule	4 alerts	■ 19 substructures; ■ non-biodegradable
SureChEMBL Rule	0	■ 164 substructures; ■ MedChem unfriendly status
FAF-Drugs4 Rule	3 alerts	154 toxic substructures from FAF-Drug4