Piperidine-Catalyzed Synthesis of (*E*)-2-Cyanoacrylamides: Crystallographic, Antiproliferative, and Docking Studies

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[b] Departamento de Química Orgánica y Química Inorgánica, Ctra. Madrid-Barcelona, Universidad de Alcalá, Km. 33, 6, 28871 Madrid, Spain
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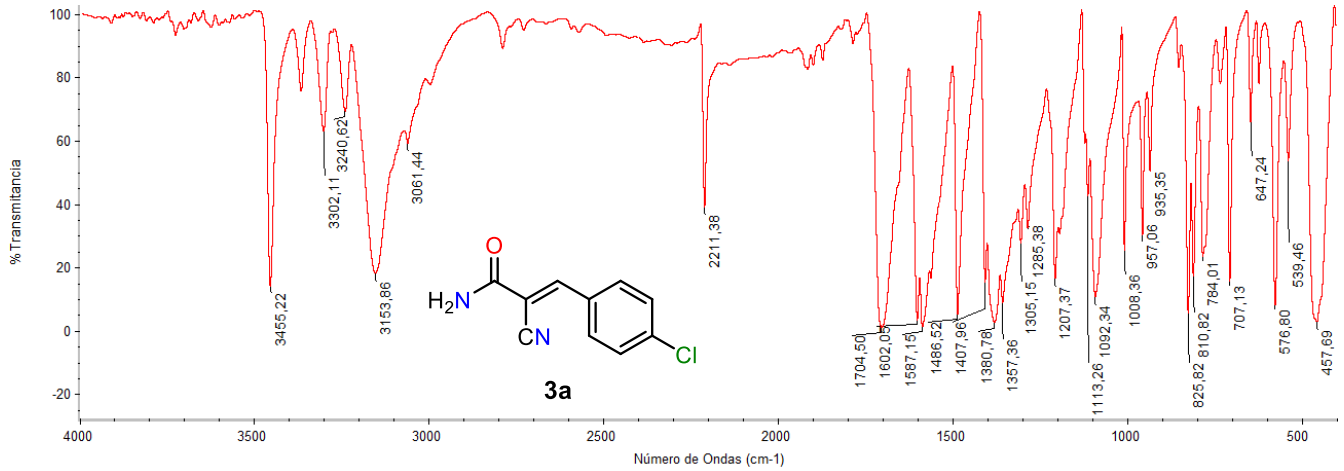
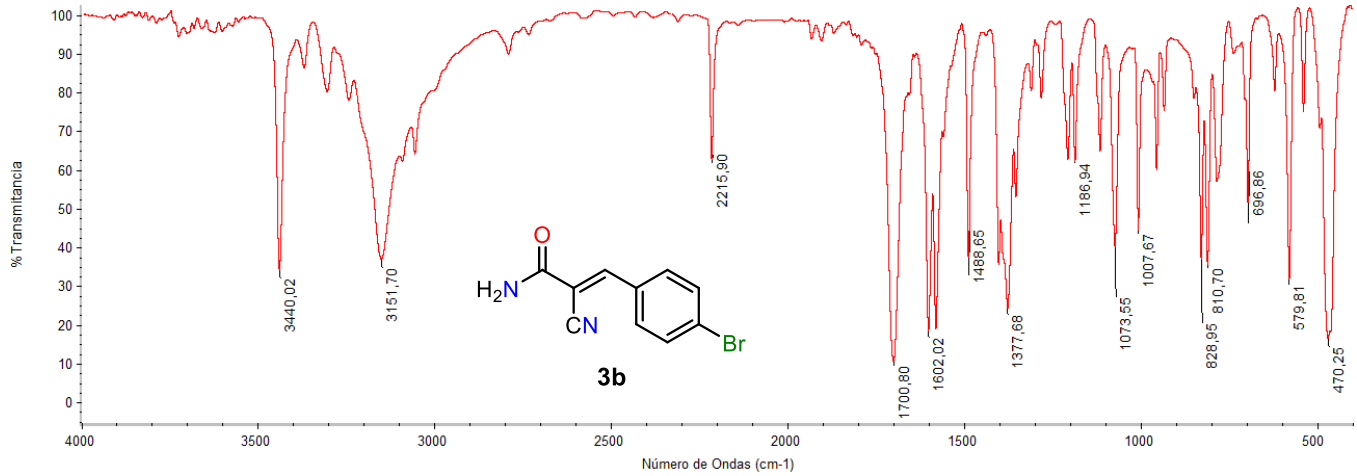
[d] Cristalografía y Química de Materiales, Departamento de Química, Universidad de los Andes, Carrera 1 No. 18A–10, Bogotá 111711, Colombia

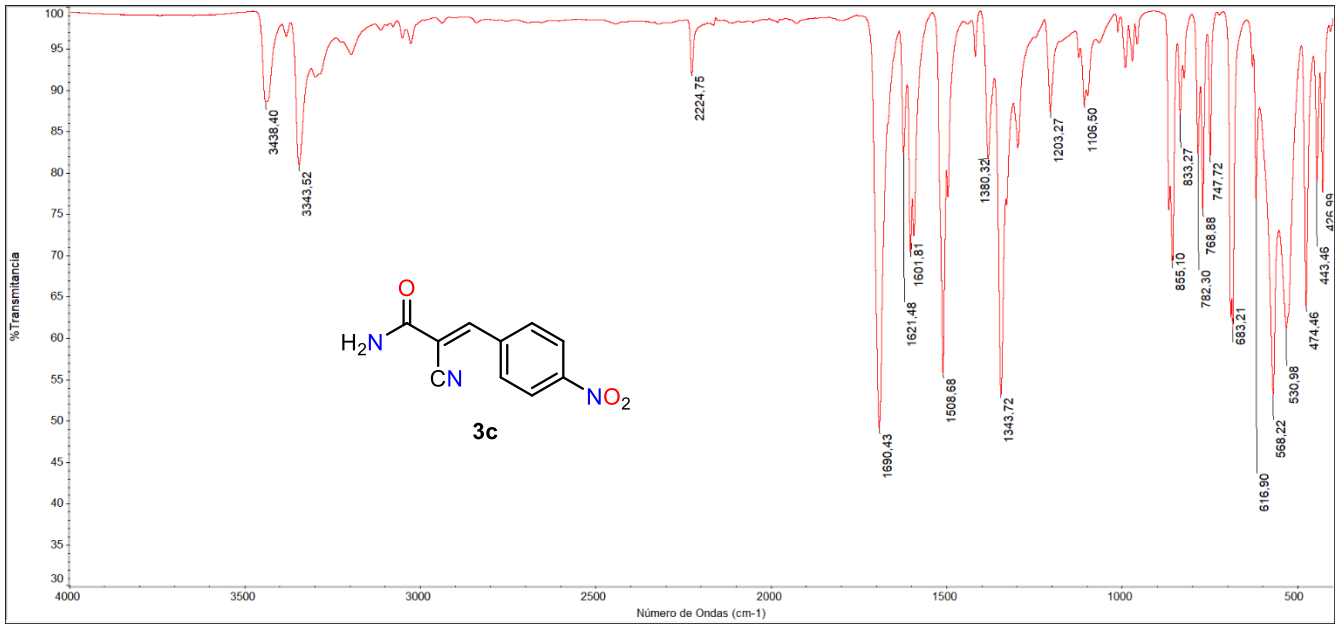
* Correspondence E-mails: juan.castillo06@uptc.edu.co, diana.becerra08@uptc.edu.co

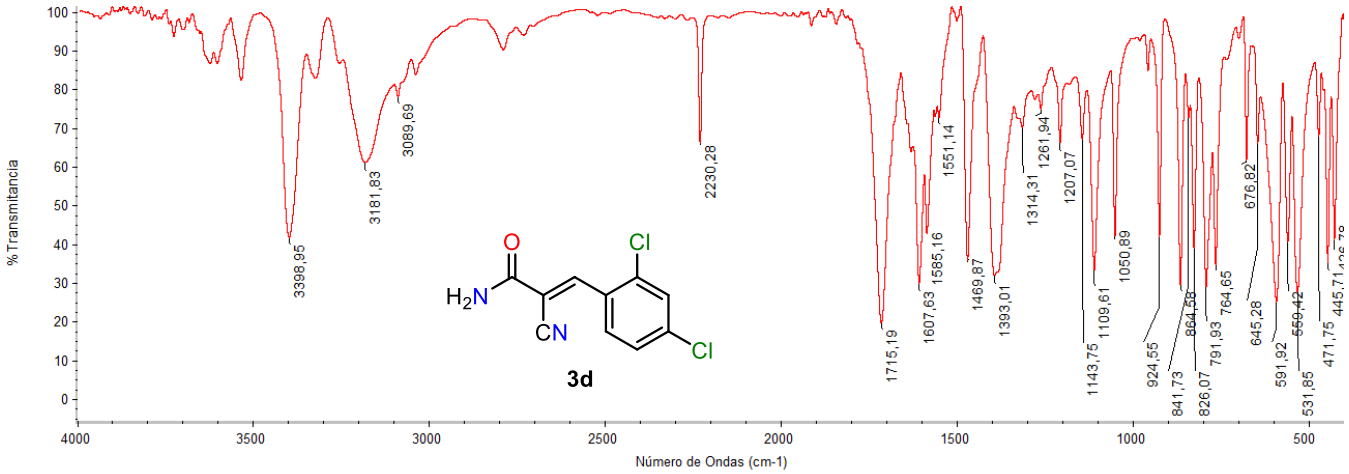
SUPPORTING INFORMATION

1. Copies of FT-IR spectra for compounds 3a–o, 5, and 6





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1314,31
1261,94
1207,07
1143,75
1109,61
1050,89
924,55
841,73
826,07
791,93
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591,92
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471,75
445,71
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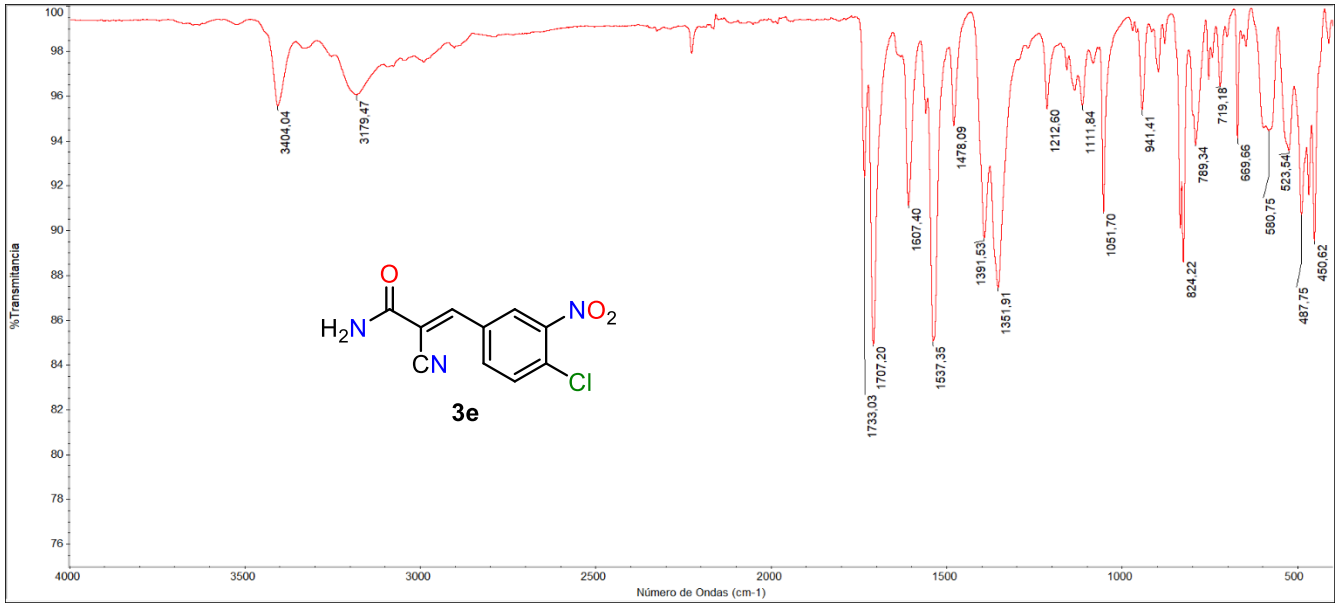
H2N
CN
Cl
Cl
3d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1351,91
1212,60
1111,84
1051,70
941,41
824,22
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O
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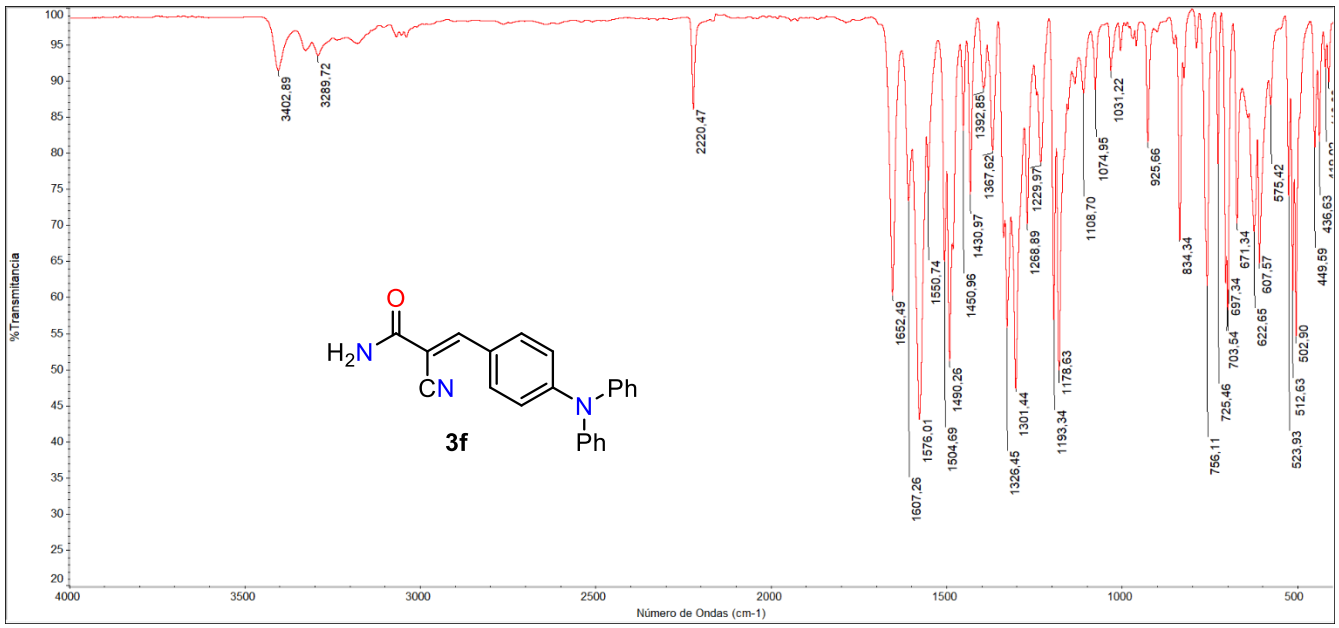
CN
NO2
Cl
3e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1430,97
1392,85
1367,62
1326,45
1301,44
1268,89
1229,97
1193,34
1178,63
1108,70
1074,96
1031,22
925,66
834,34
756,11
725,46
703,54
697,34
671,34
622,65
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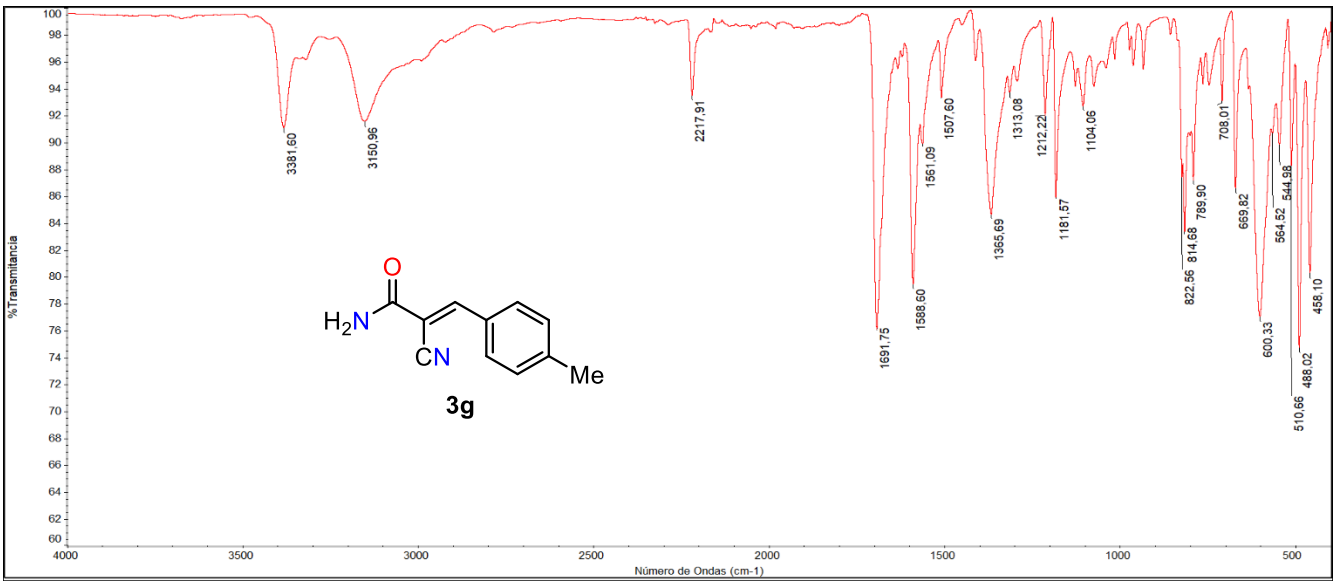
CN
N
Ph
Ph
3f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1104.06
822.56
814.68
789.90
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CN
Me
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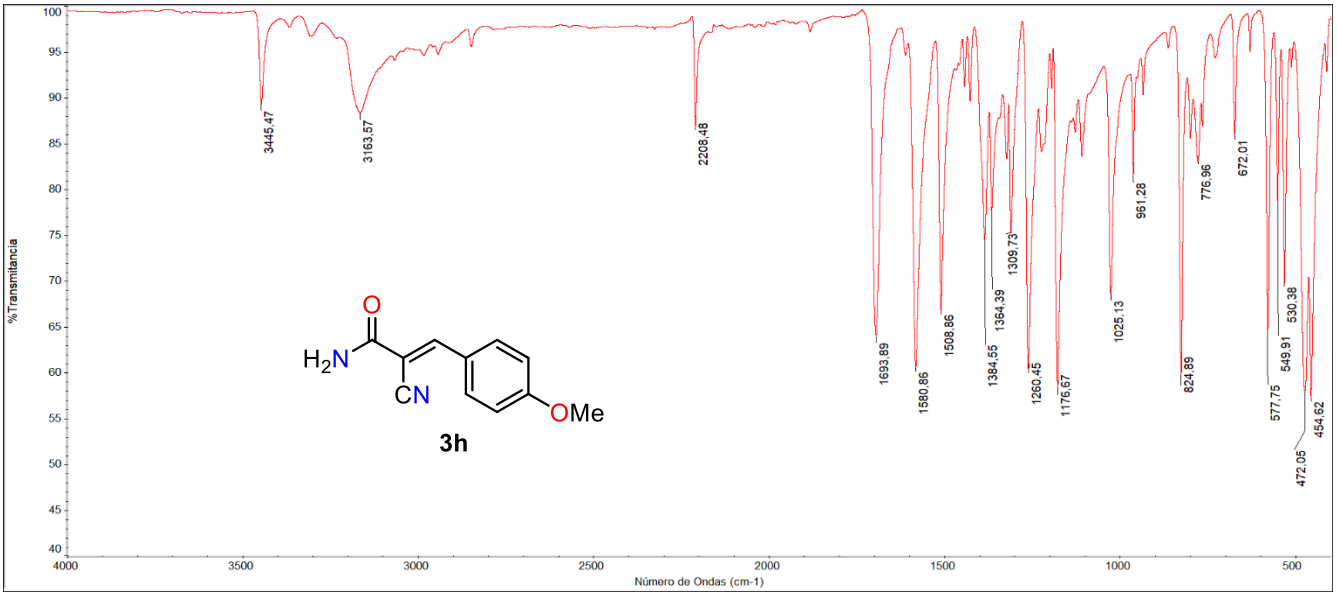
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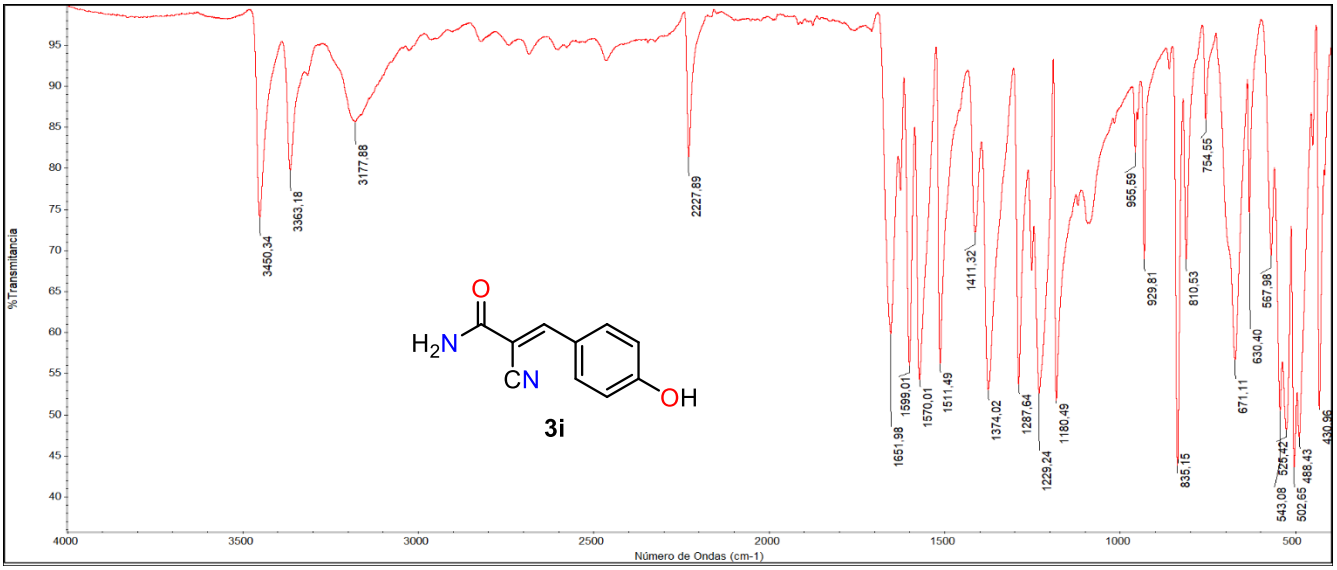
H2N
CN
OMe
3h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1229.24
1180.49
965.59
929.81
835.15
810.53
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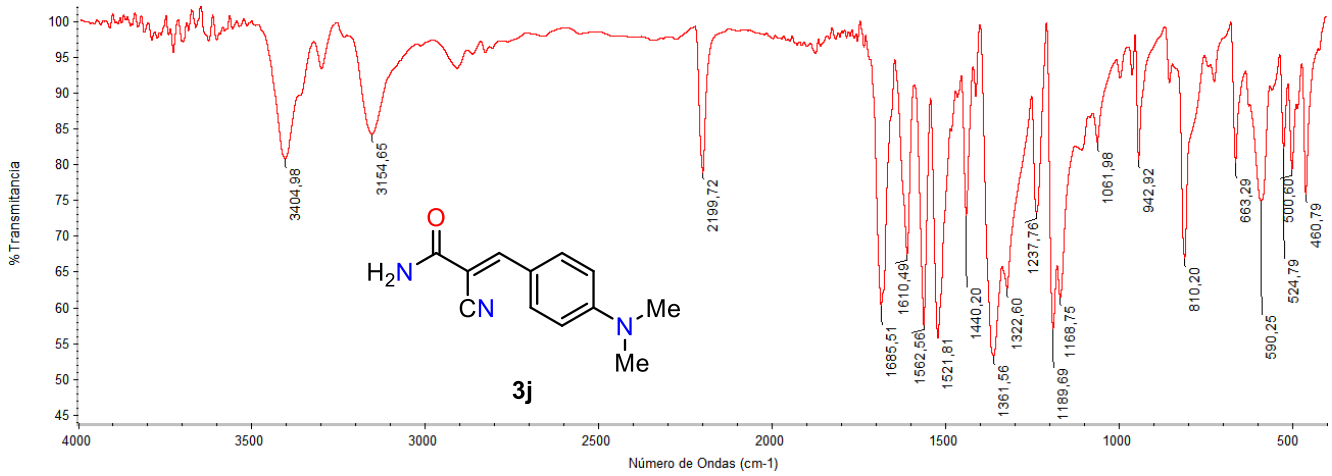
O
H2N
CN
OH
3i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1237,76
1189,69
1168,75
1061,98
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CN
N
Me
Me
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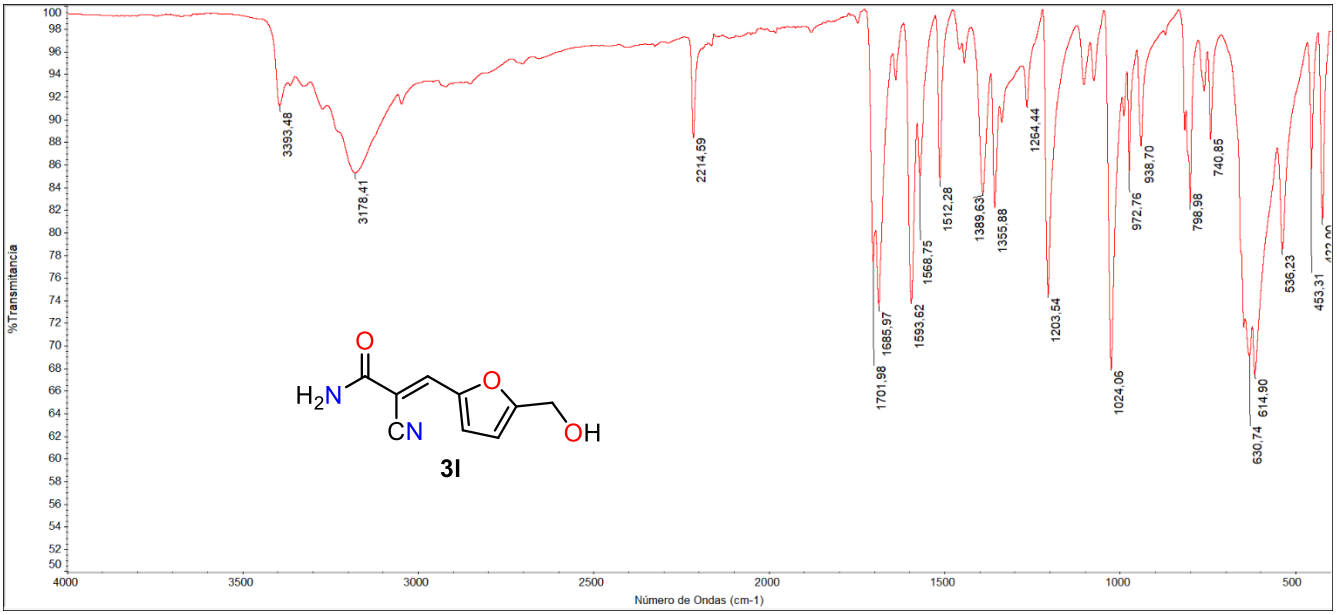
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CN
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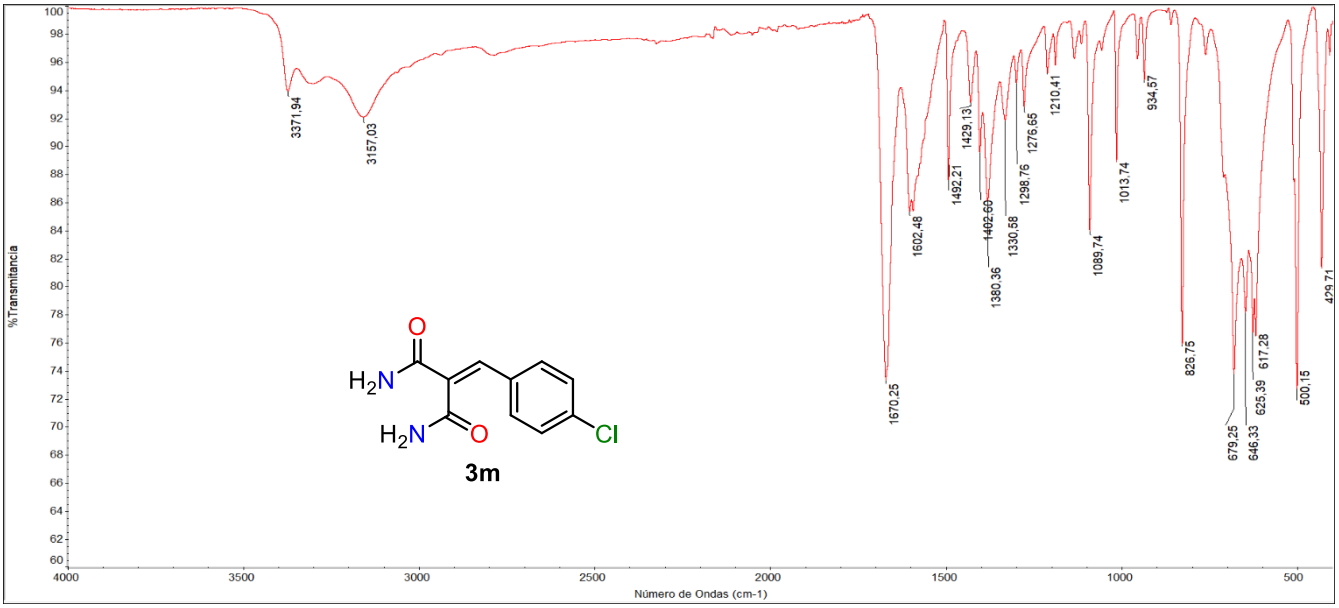
OH
3l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1210,41
1089,74
1013,74
934,57
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646,33
625,39
617,28
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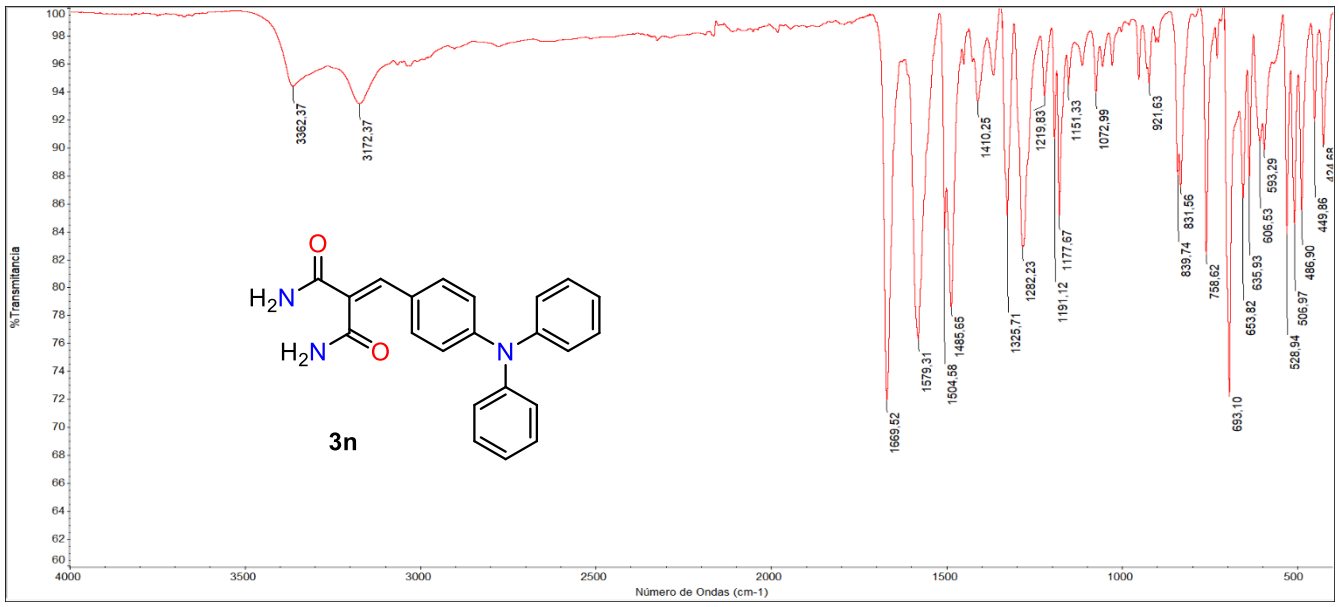
O
H2N
H2N
O
Cl
3m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1191.12
1177.67
1151.33
1072.99
921.63
839.74
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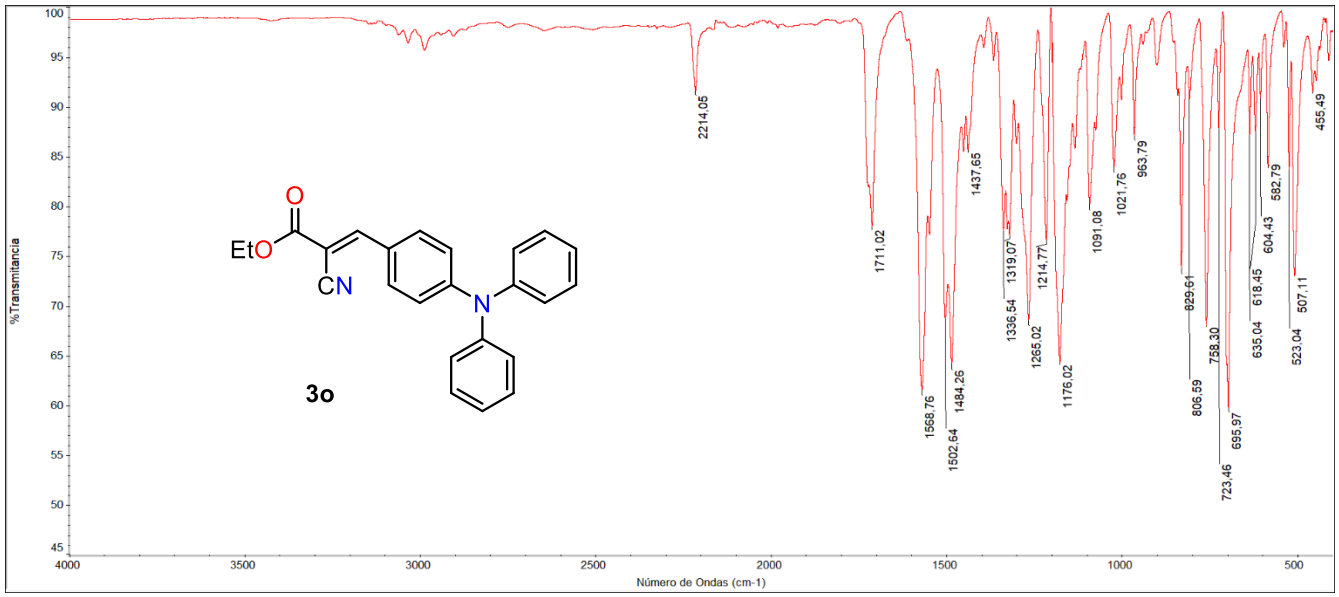
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507.11
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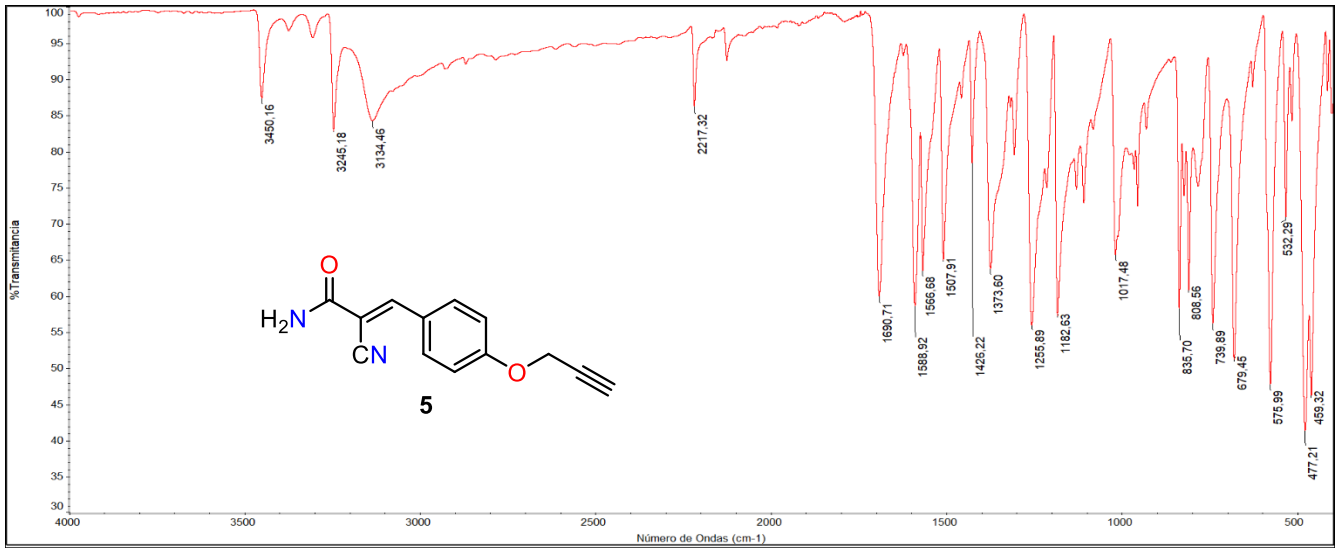
3o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575.99
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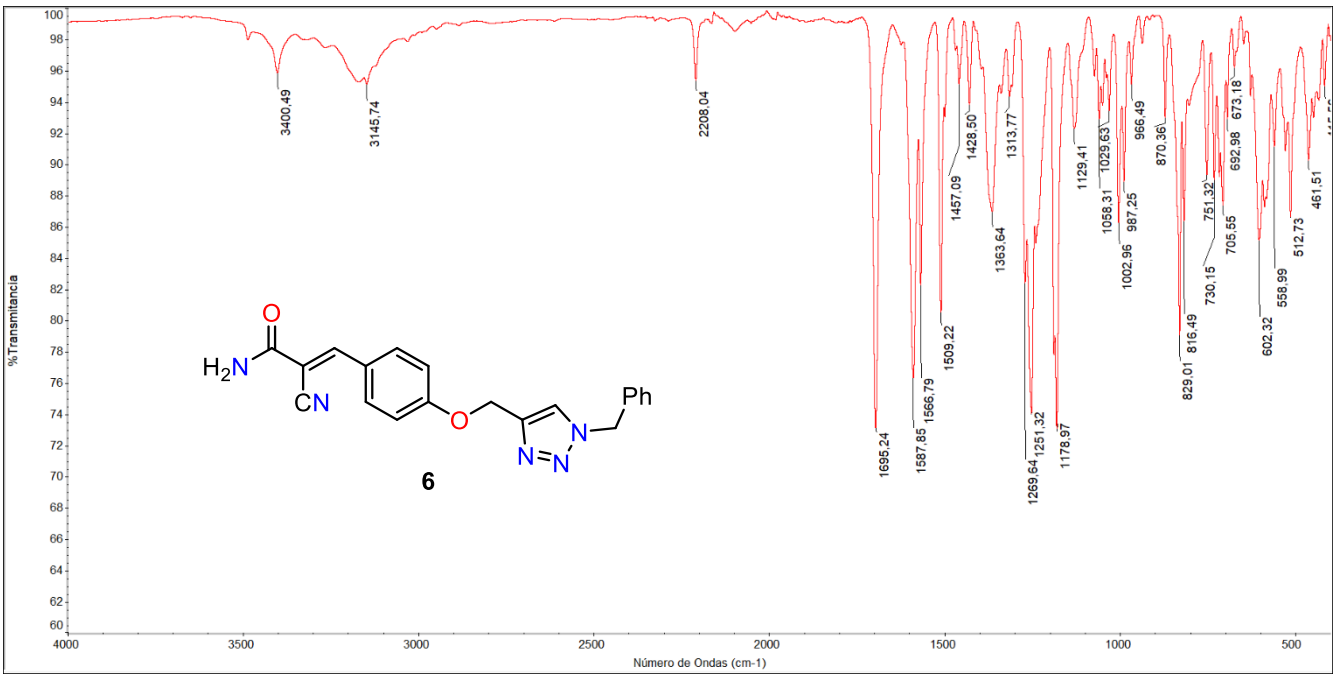
5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1269.64
1251.32
1178.97
1129.41
1058.31
1029.63
1002.96
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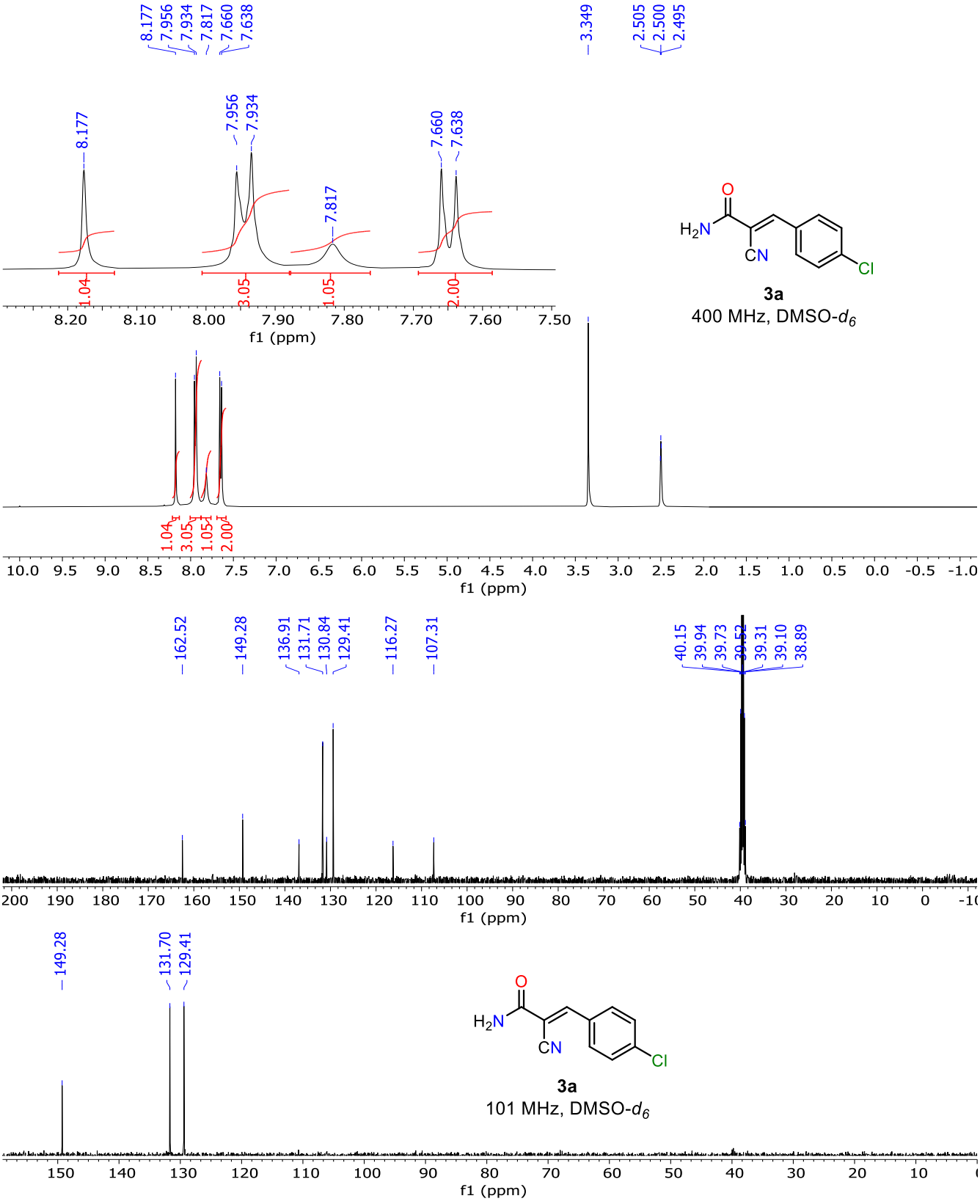
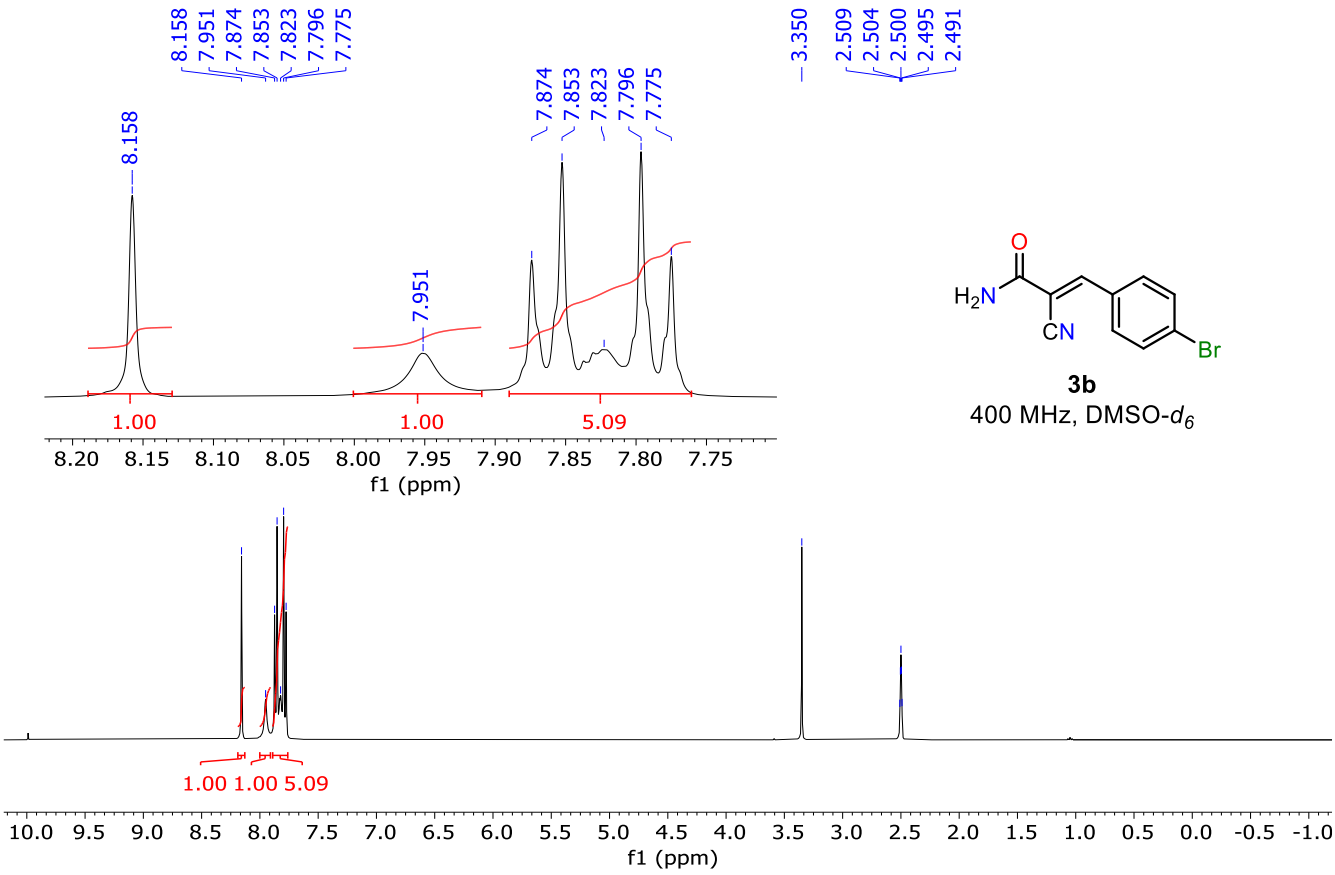
966.49
870.36
829.01
816.49
751.32
730.15
705.55
692.98
673.18
602.32
558.99
512.73
461.51
O
H2N
CN
O
N
N=N
Ph
6

2. Copies of NMR spectra for compounds 3a–o, 5, and 6

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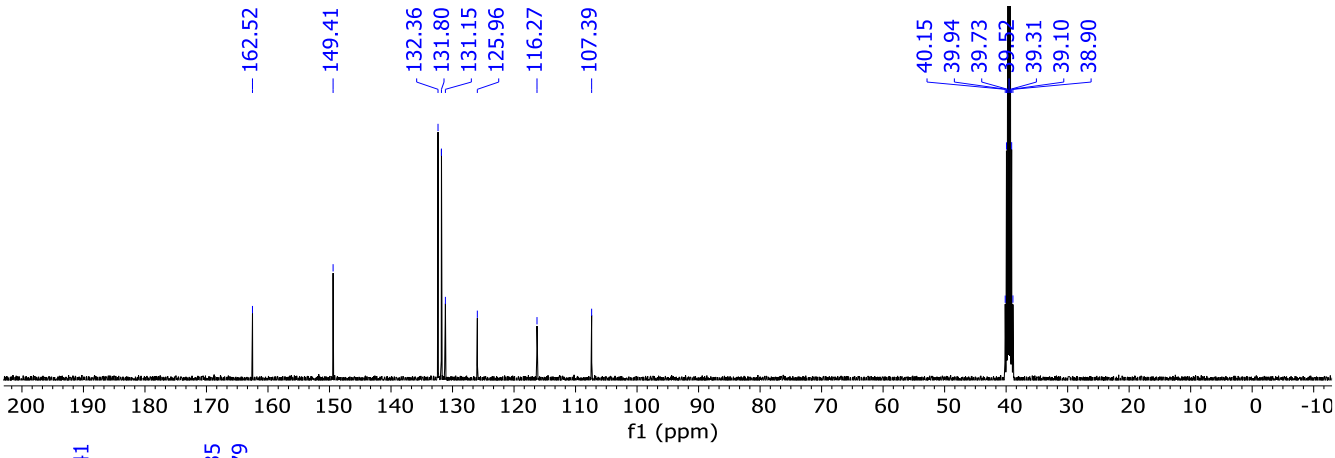
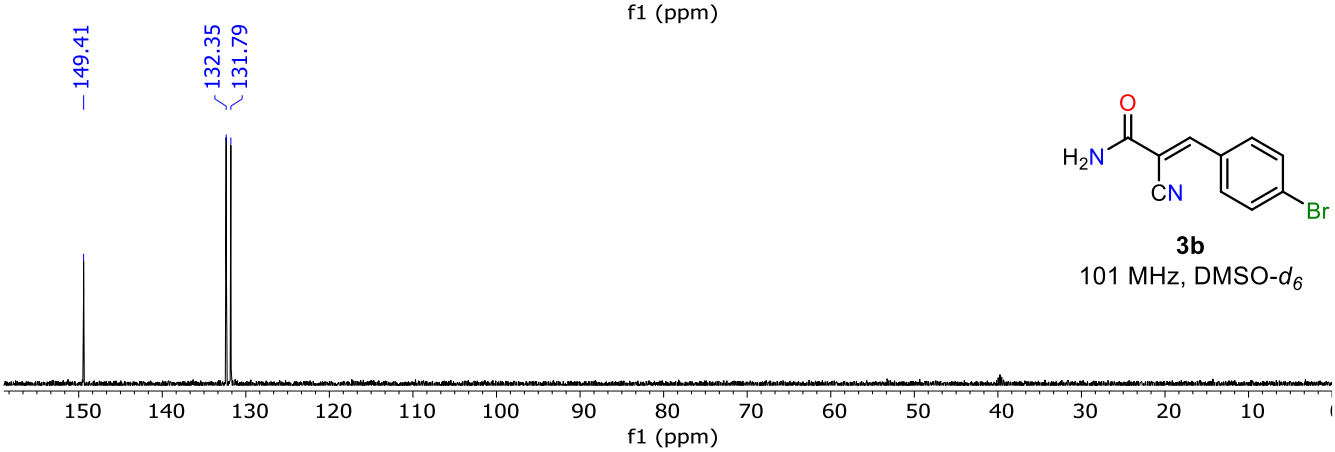
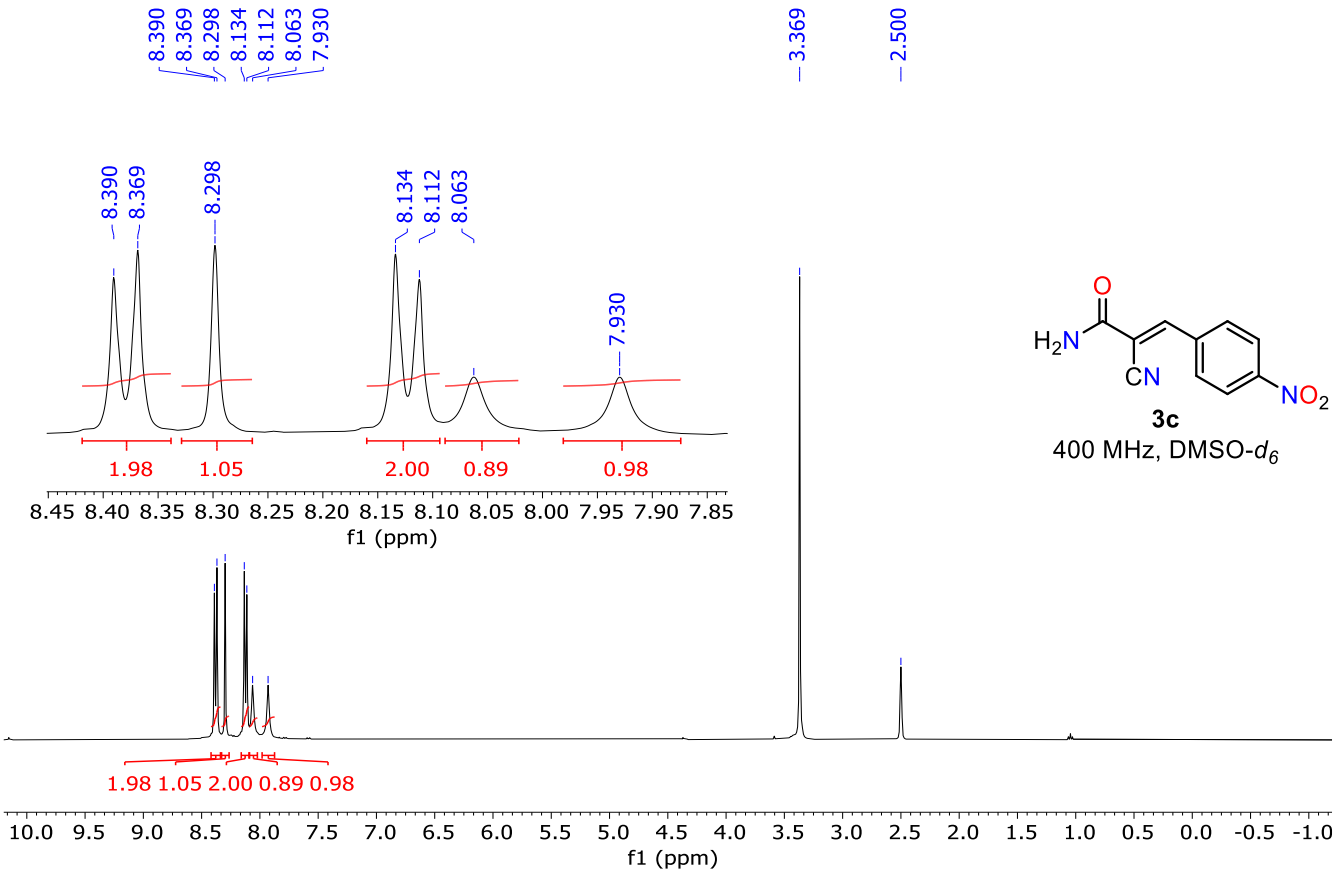
7.874
7.853
7.823
7.796
7.775
3.350
2.509
2.504
2.500
2.495
2.491
1.00
1.00
5.09
f1 (ppm)
O
H2N
CN
Br
3b
400 MHz, DMSO-d6

1.00 1.00 5.09
f1 (ppm)


162.52
149.41
132.36
131.80
131.15
125.96
116.27
107.39
40.15
39.94
39.73
39.52
39.31
39.10
38.90
f1 (ppm)


149.41
132.35
131.79
f1 (ppm)
O
H2N
CN
Br
3b
101 MHz, DMSO-d6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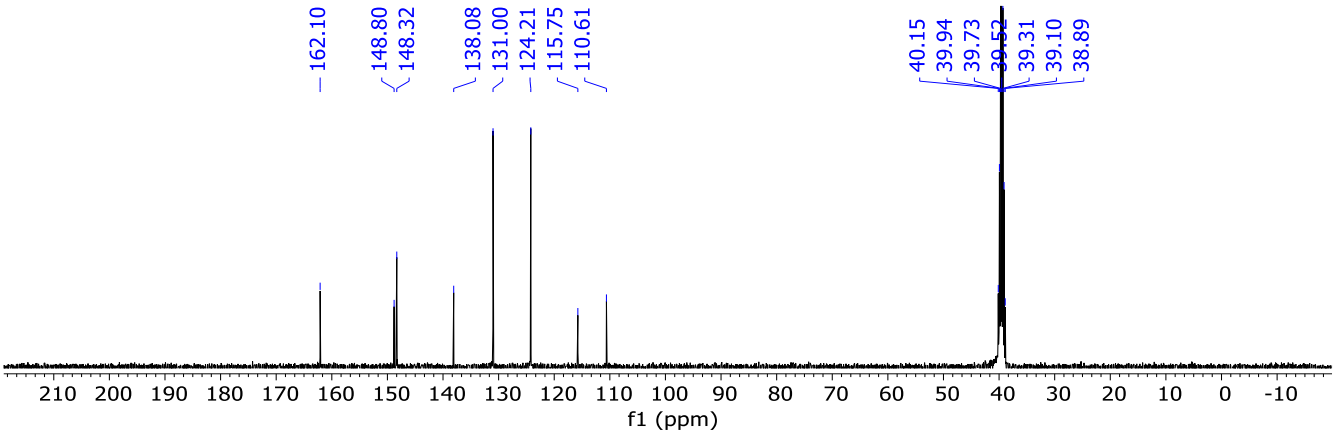
8.298
8.134
8.112
8.063
7.930
3.369
2.500
1.98
1.05
2.00
0.89
0.98
f1 (ppm)
O
H2N
CN
NO2
3c
400 MHz, DMSO-d6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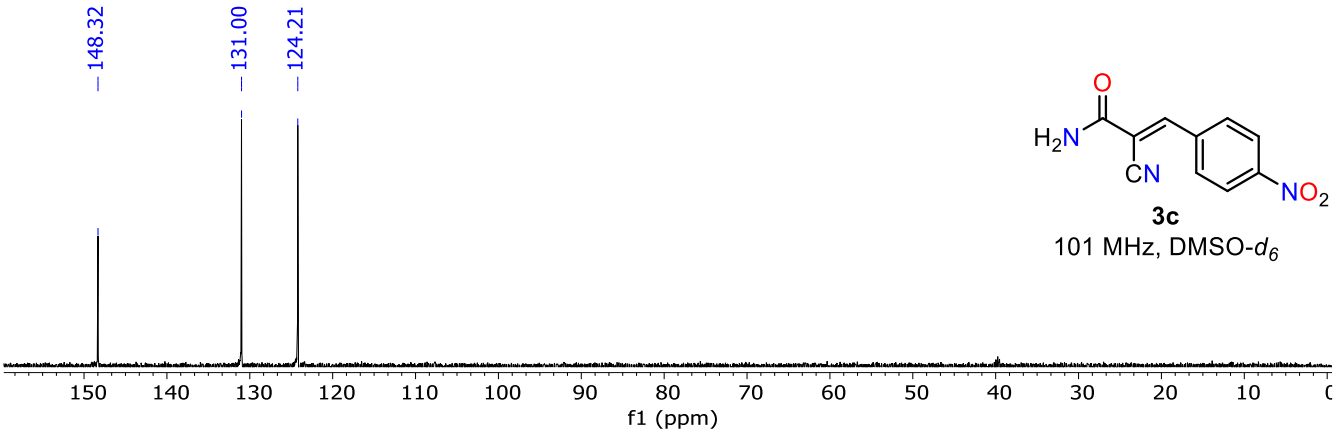
148.32
138.08
131.00
124.21
115.75
110.61
40.15
39.94
39.73
39.52
39.31
39.10
38.89
f1 (ppm)


148.32
131.00
124.21
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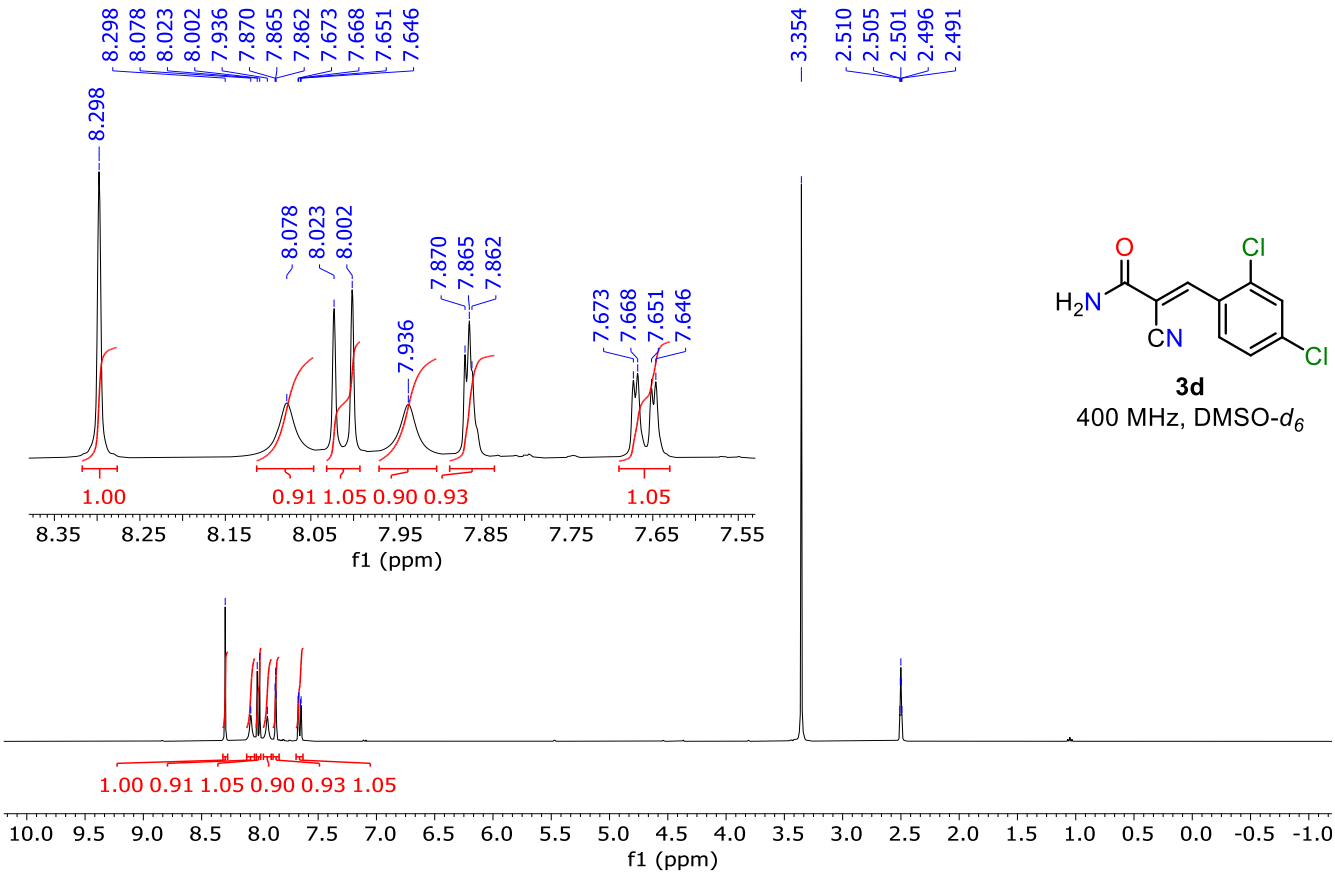
O
H2N
CN
NO2
3c
101 MHz, DMSO-d6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7.862
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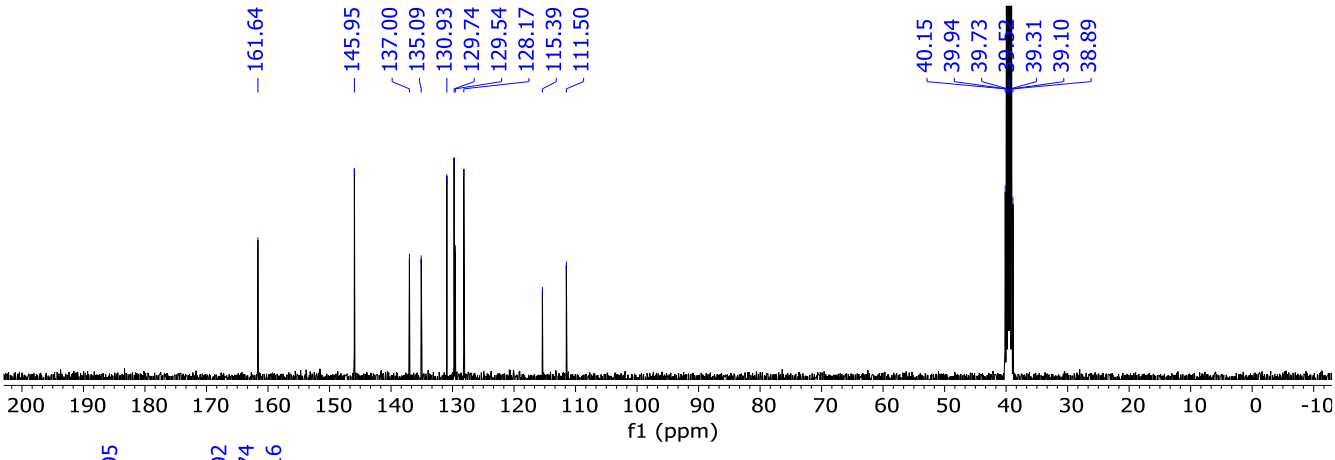
7.668
7.651
7.646
3.354
2.510
2.505
2.501
2.496
2.491
1.00
0.91 1.05 0.90 0.93
1.05
1.00 0.91 1.05 0.90 0.93 1.05
f1 (ppm)
O
Cl
H2N
CN
Cl
3d
400 MHz, DMSO-d6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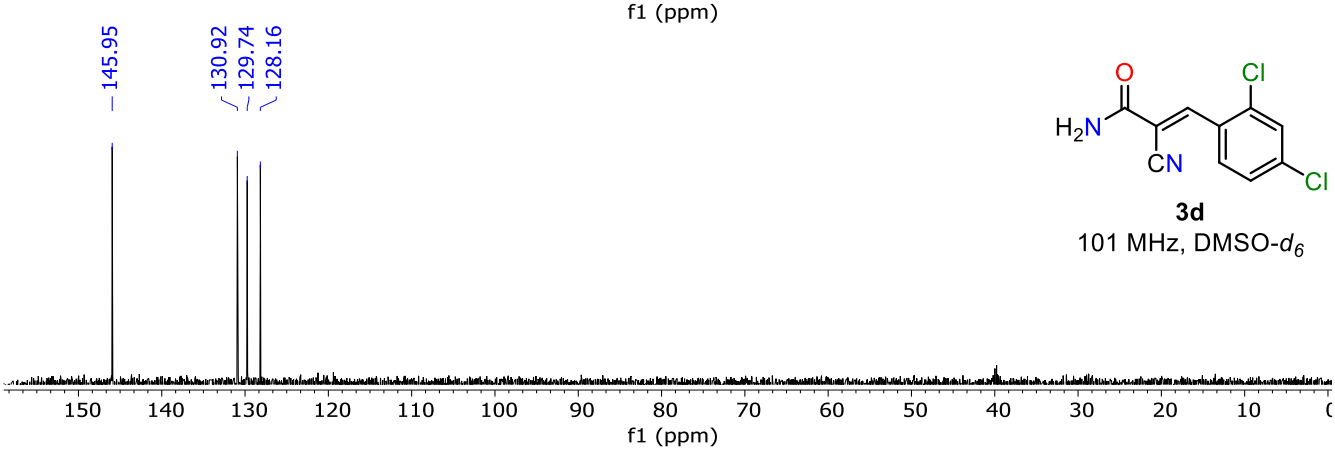
39.52
39.31
39.10
38.89
f1 (ppm)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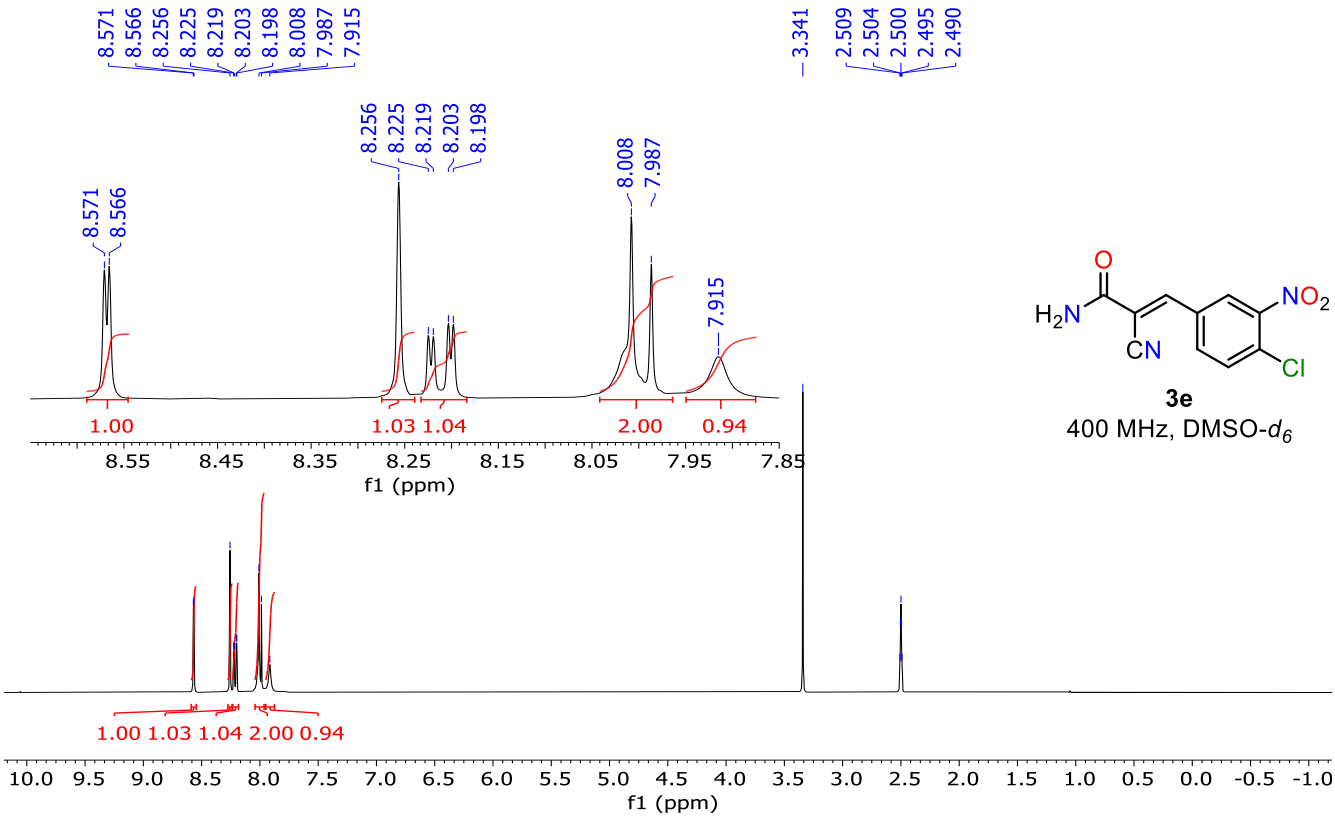
128.16
f1 (ppm)
O
Cl
H2N
CN
Cl
3d
101 MHz, DMSO-d6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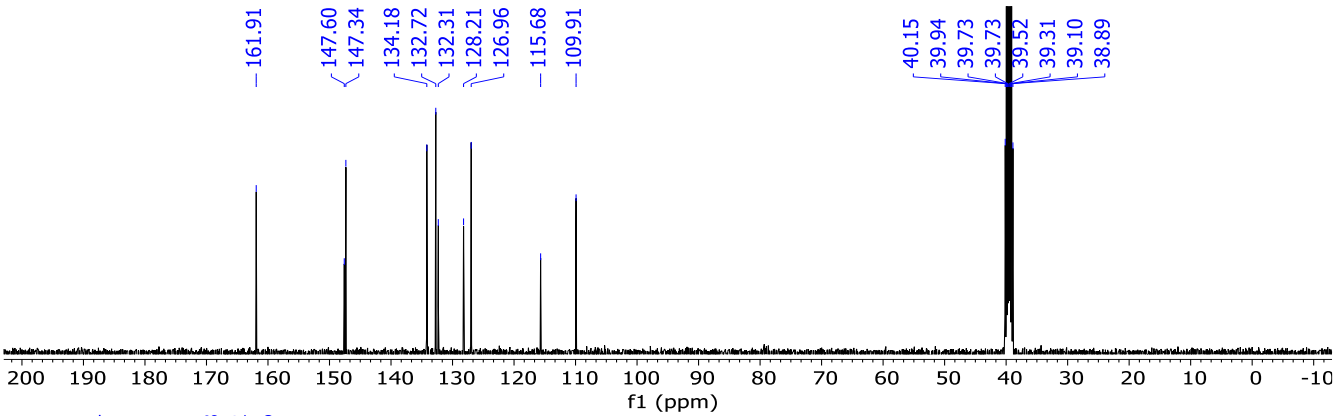
8.256
8.225
8.219
8.203
8.198
8.008
7.987
7.915
3.341
2.509
2.504
2.500
2.495
2.490
1.00
1.03 1.04
2.00
0.94
f1 (ppm)
1.00 1.03 1.04 2.00 0.94
f1 (ppm)
O
H2N
CN
NO2
Cl
3e
400 MHz, DMSO-d6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132.31
128.21
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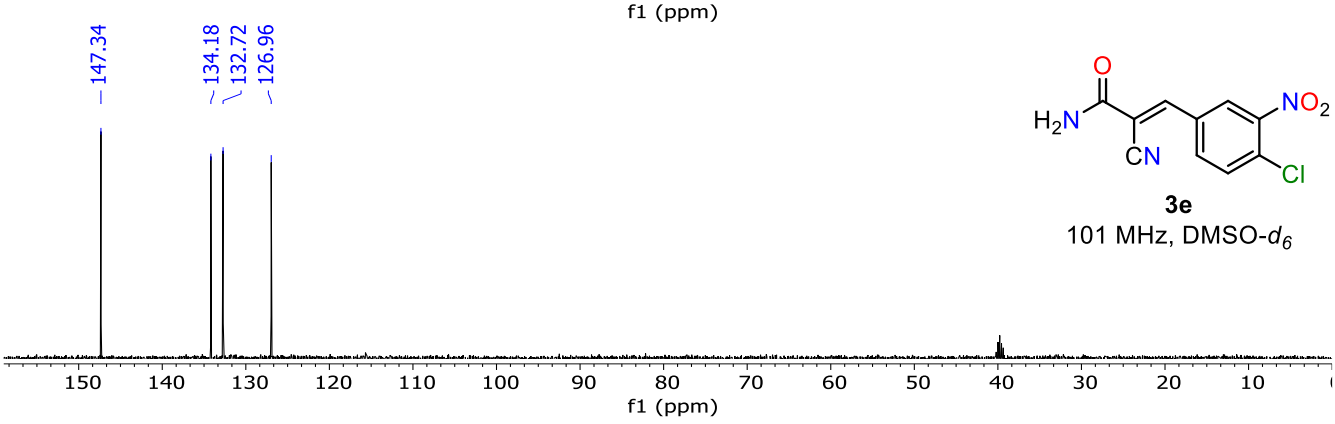
39.73
39.73
39.52
39.31
39.10
38.89
f1 (ppm)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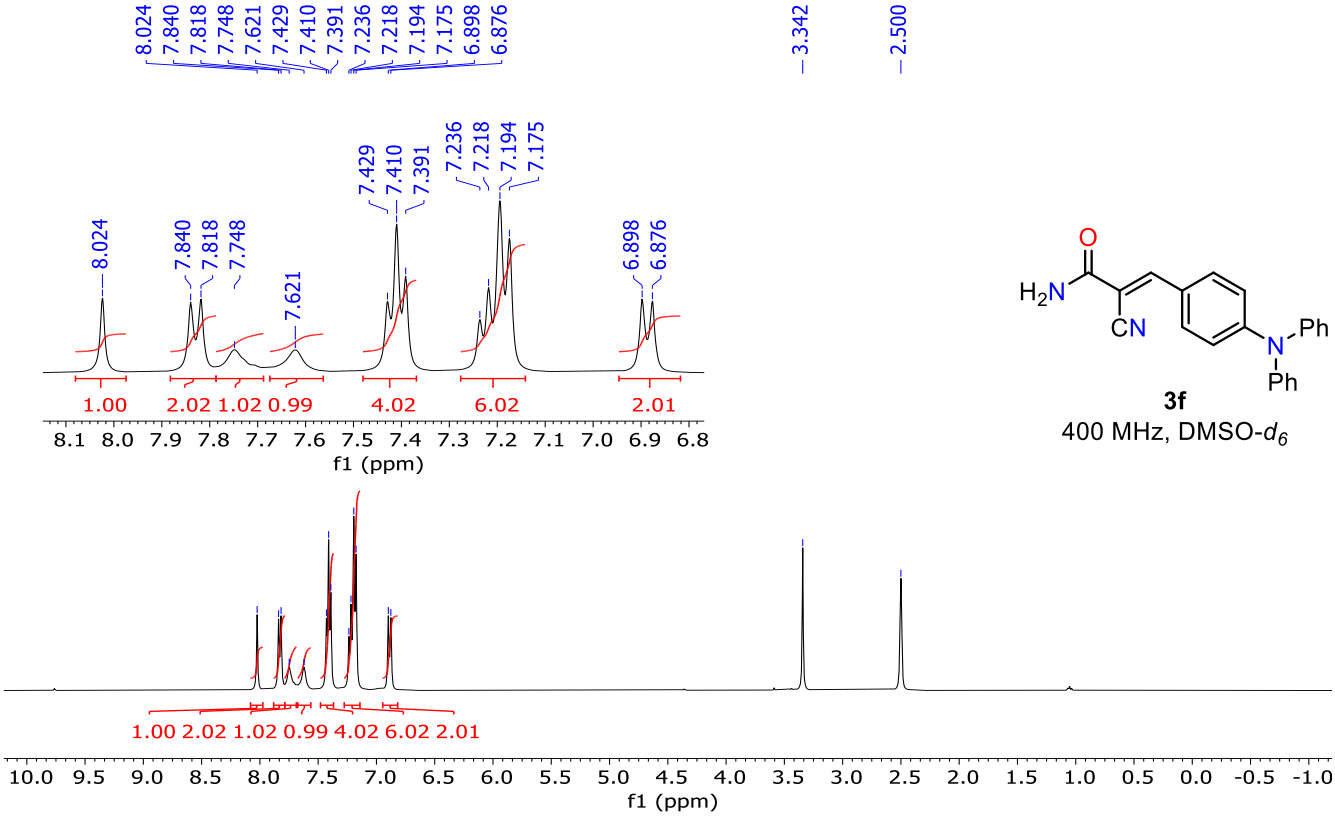
134.18
132.72
126.96
f1 (ppm)
O
H2N
CN
NO2
Cl
3e
101 MHz, DMSO-d6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7.748
7.621
7.429
7.410
7.391
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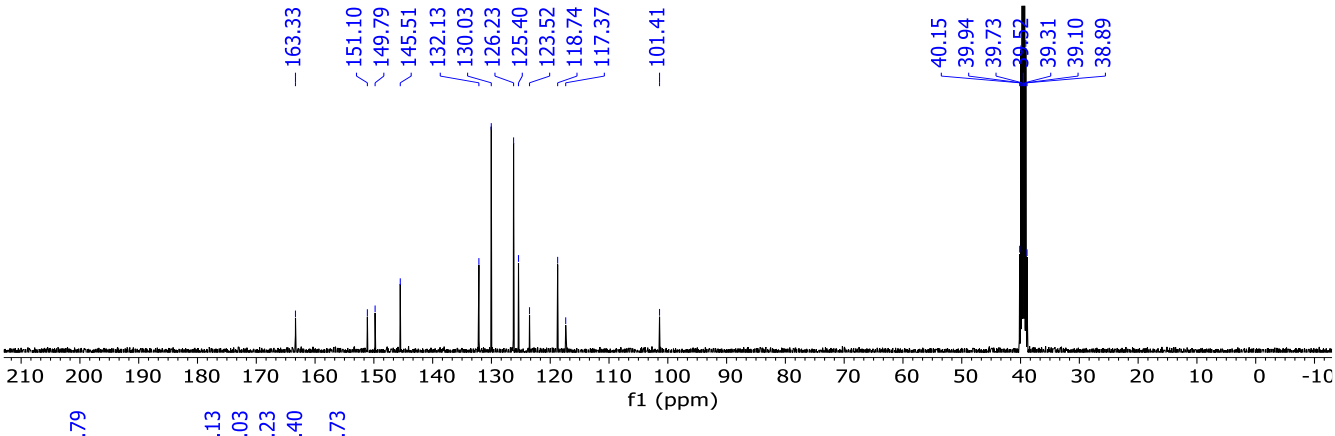
7.218
7.194
7.175
6.898
6.876
3.342
2.500
1.00 2.02 1.02 0.99 4.02 6.02 2.01
f1 (ppm)
O
H2N
CN
N
Ph
Ph
3f
400 MHz, DMSO-d6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117.37
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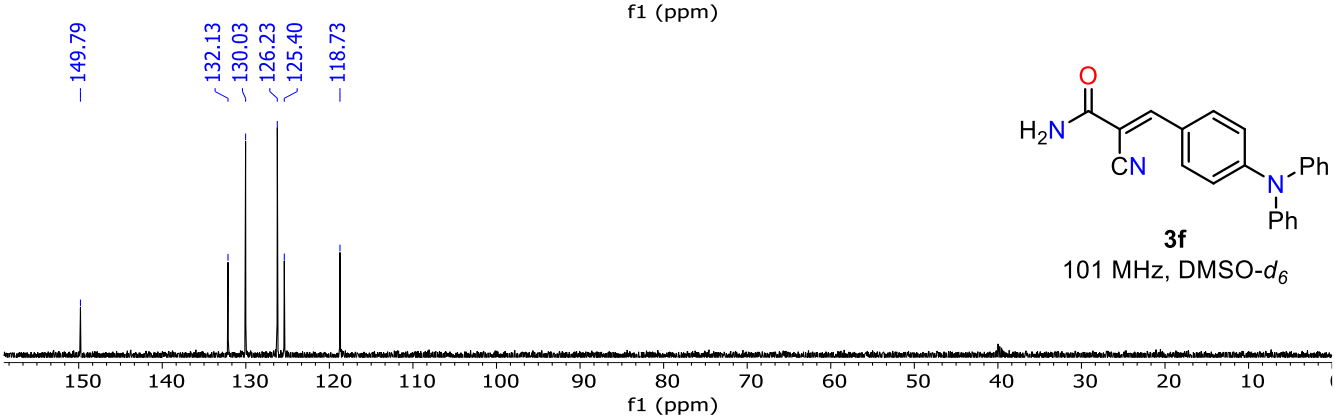
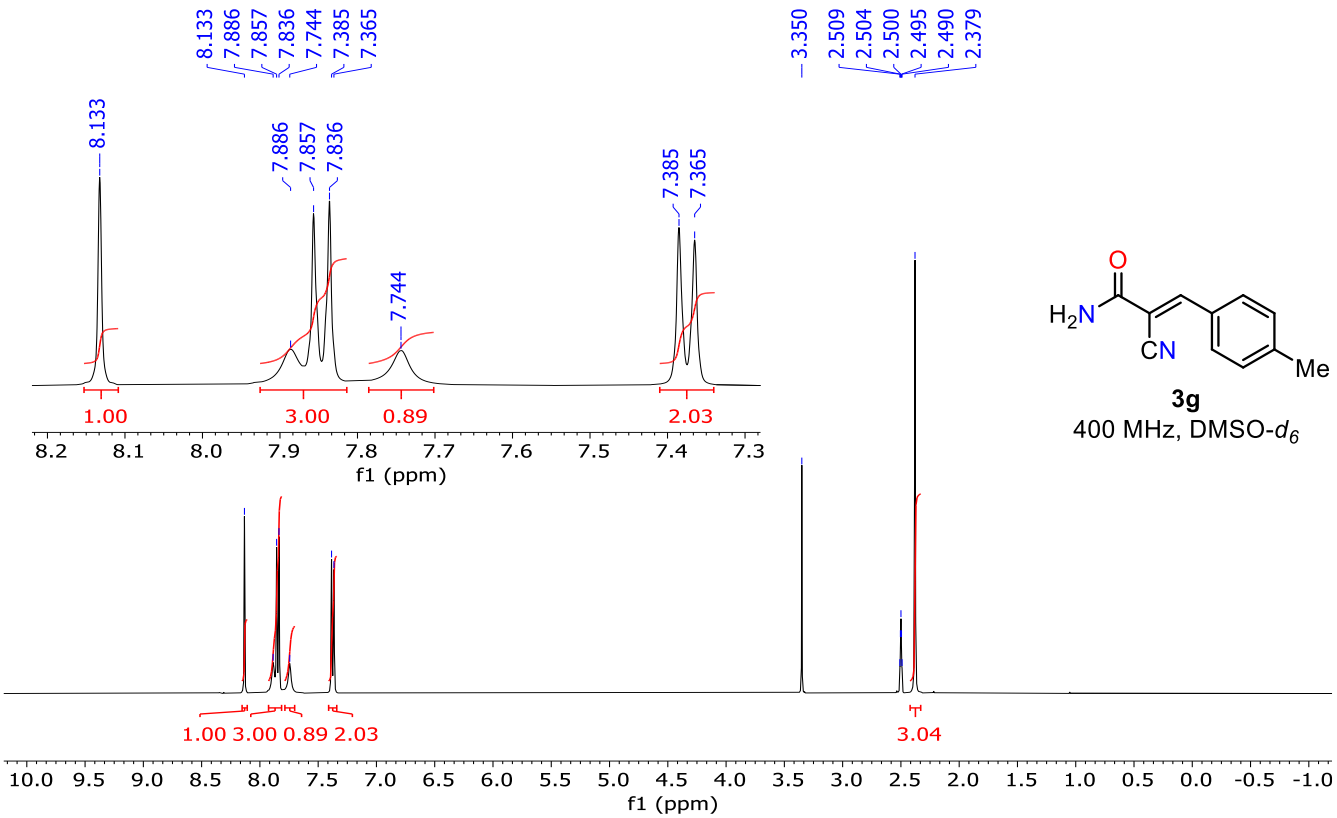
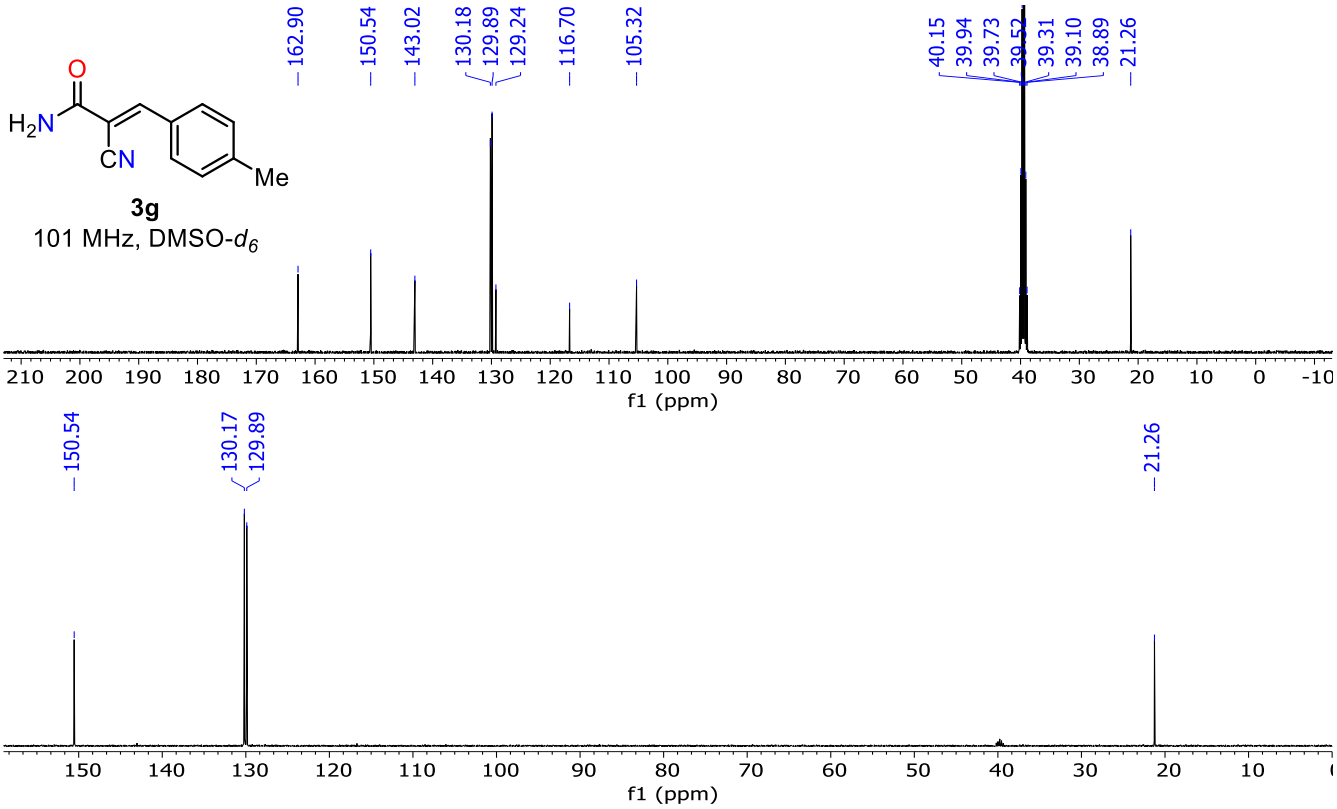
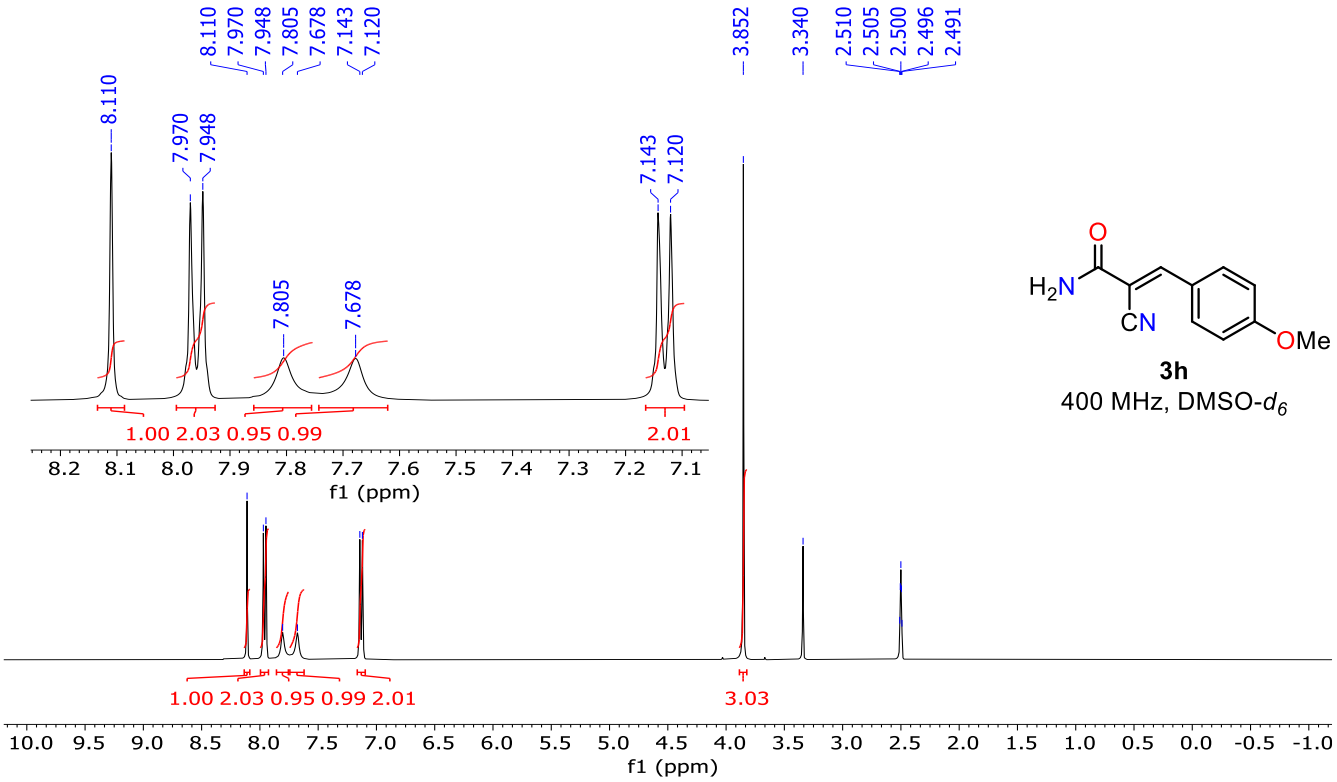
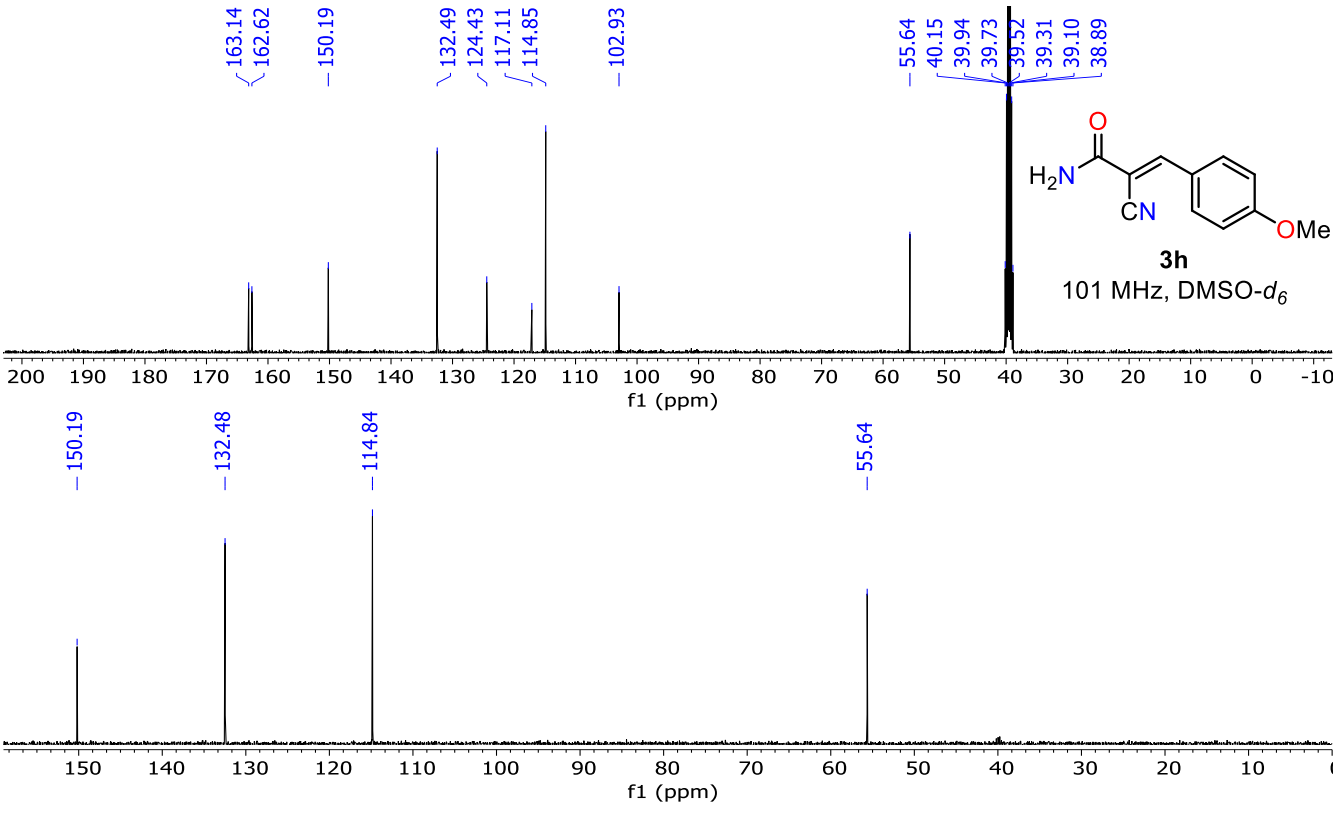
40.15
39.94
39.73
39.52
39.31
39.10
38.89
f1 (ppm)


149.79
132.13
130.03
126.23
125.40
118.73
f1 (ppm)
O
H2N
CN
N
Ph
Ph
3f
101 MHz, DMSO-d6

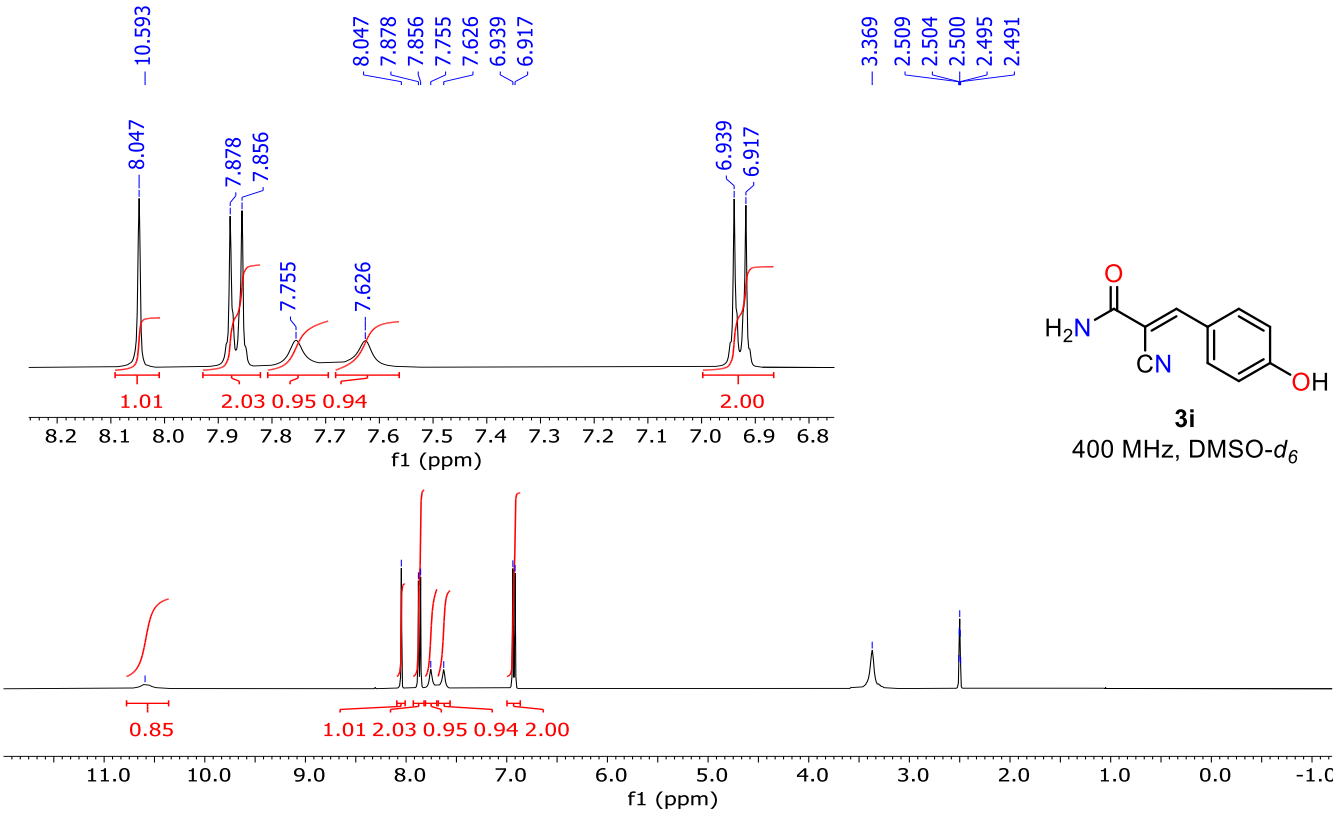

8.133
7.886
7.857
7.836
7.744
7.385
7.365
3.350
2.509
2.504
2.500
2.495
2.490
2.379
1.00
3.00
0.89
2.03
f1 (ppm)
1.00 3.00 0.89 2.03
3.04
f1 (ppm)
O
H2N
CN
Me
3g
400 MHz, DMSO-d6


162.90
150.54
143.02
130.18
129.89
129.24
116.70
105.32
40.15
39.94
39.73
39.52
39.31
39.10
38.89
21.26
f1 (ppm)
O
H2N
CN
Me
3g
101 MHz, DMSO-d6
150.54
130.17
129.89
21.26
f1 (ppm)

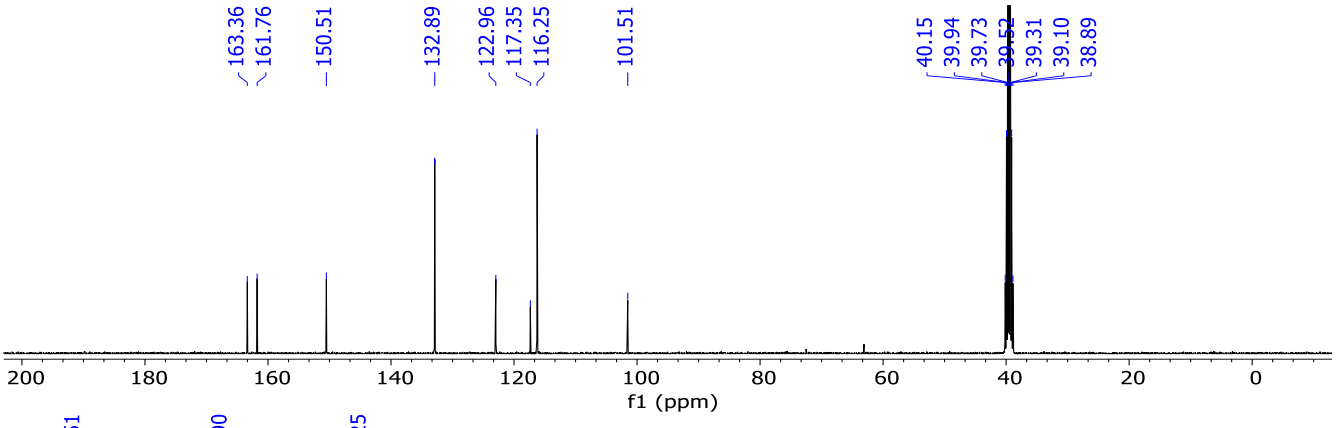

8.110
7.970
7.948
7.805
7.678
7.143
7.120
3.852
3.340
2.510
2.505
2.500
2.496
2.491
1.00 2.03 0.95 0.99
2.01
1.00 2.03 0.95 0.99 2.01
3.03
f1 (ppm)
O
H2N
CN
OMe
3h
400 MHz, DMSO-d6

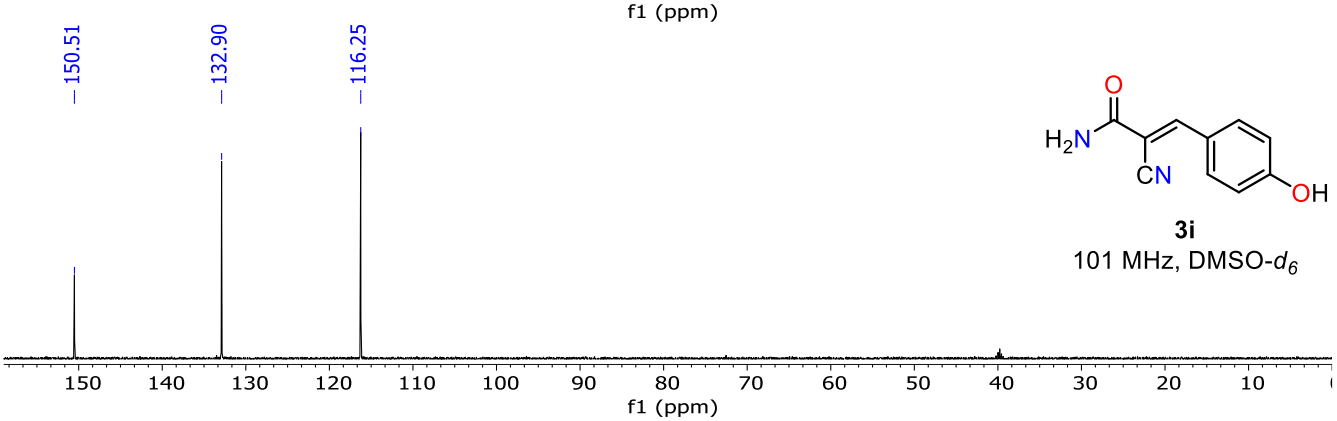

163.14
162.62
150.19
132.49
124.43
117.11
114.85
102.93
55.64
40.15
39.94
39.73
39.52
39.31
39.10
38.89
f1 (ppm)
O
H2N
CN
OMe
3h
101 MHz, DMSO-d6

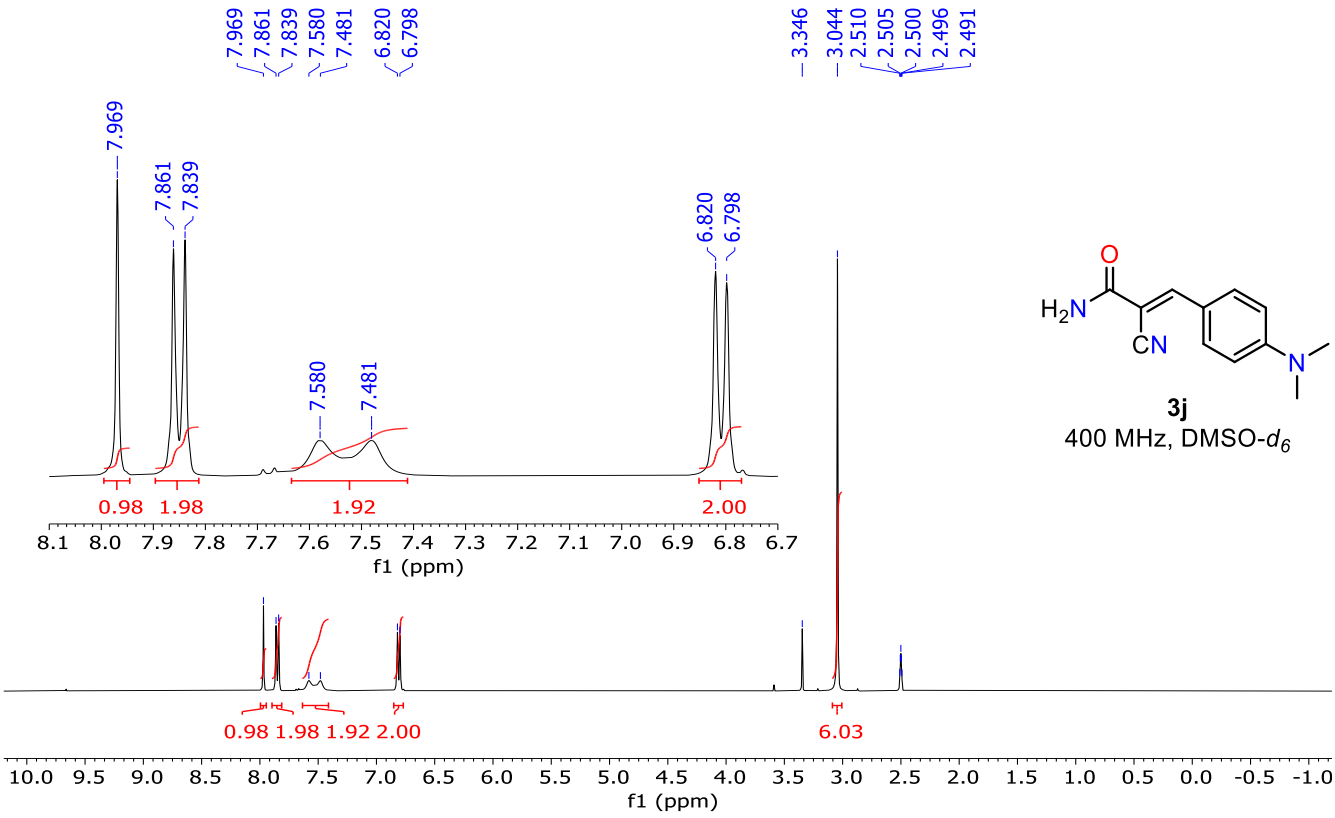
150.19
132.48
114.84
55.64
f1 (ppm)

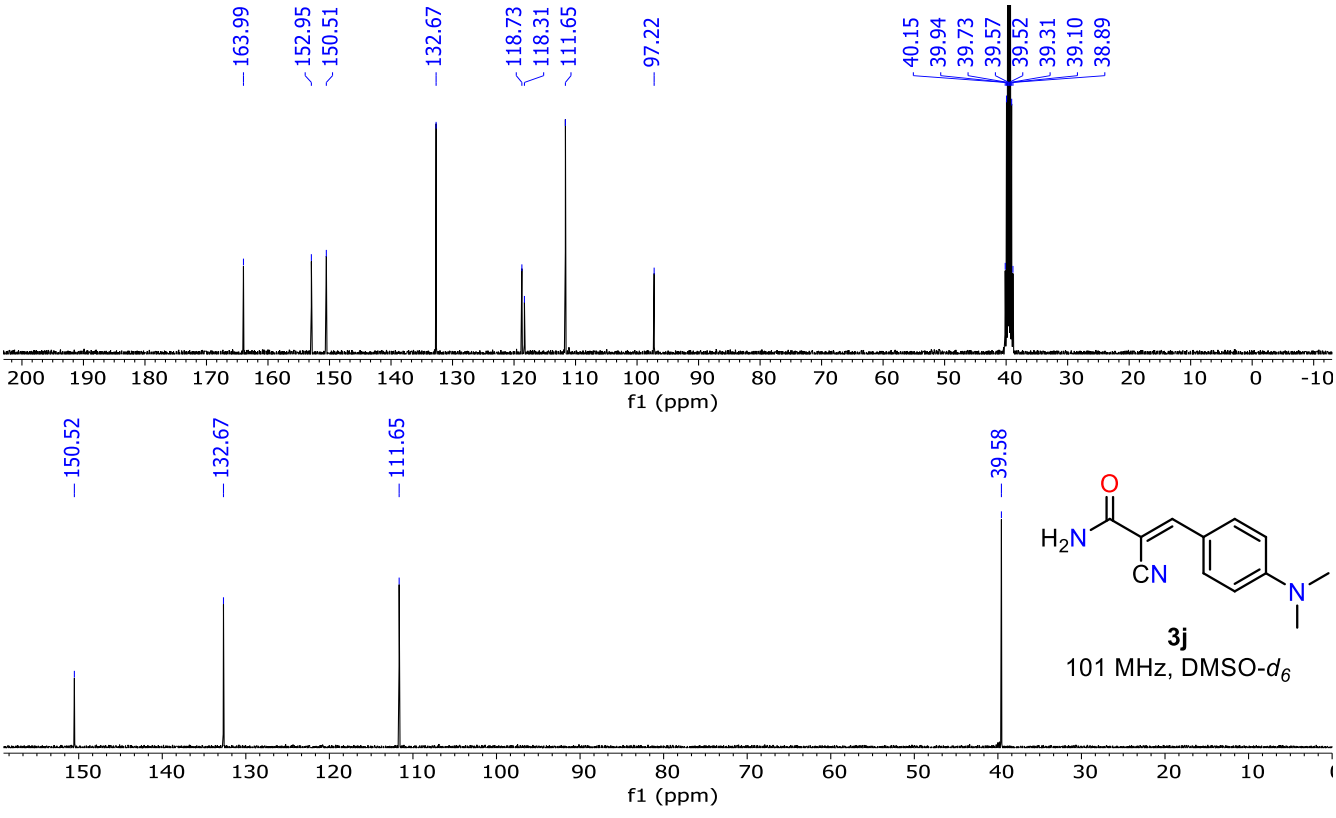

10.593
8.047
7.878
7.856
7.755
7.626
6.939
6.917
3.369
2.509
2.504
2.500
2.495
2.491
1.01
2.03 0.95 0.94
2.00
f1 (ppm)
O
H2N
CN
OH
3i
400 MHz, DMSO-d6

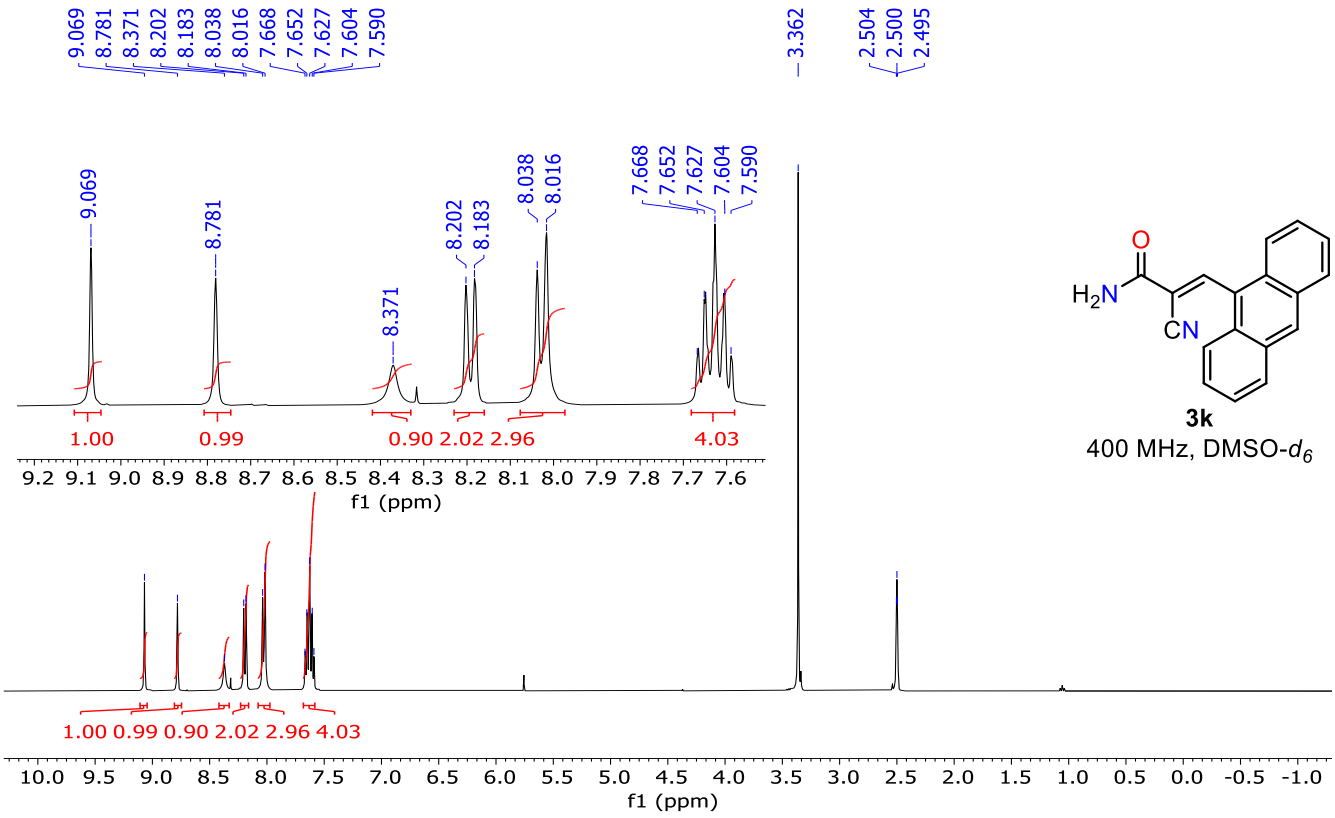
0.85
1.01 2.03 0.95 0.94 2.00
f1 (ppm)

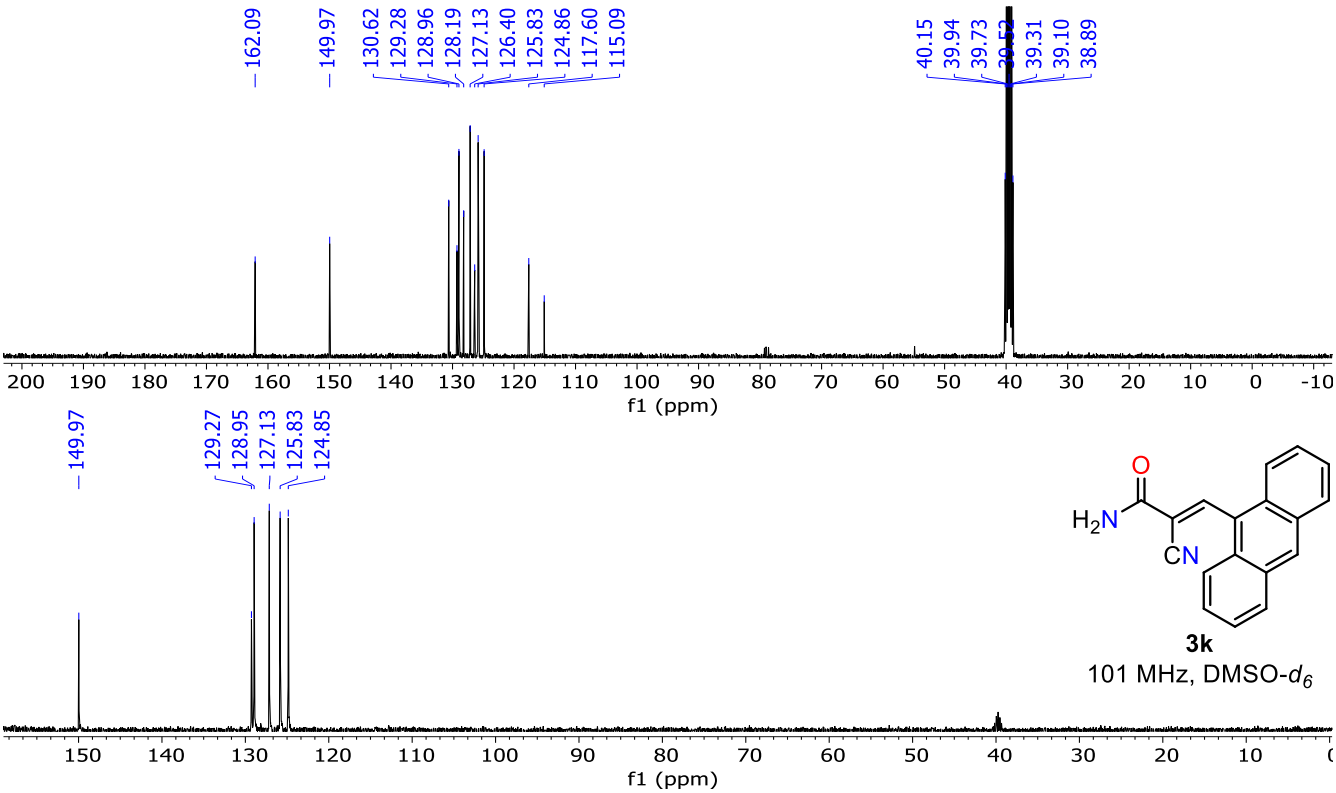

163.36
161.76
150.51
132.89
122.96
117.35
116.25
101.51
40.15
39.94
39.73
39.52
39.31
39.10
38.89
f1 (ppm)


150.51
132.90
116.25
f1 (ppm)
O
H2N
CN
OH
3i
101 MHz, DMSO-d6

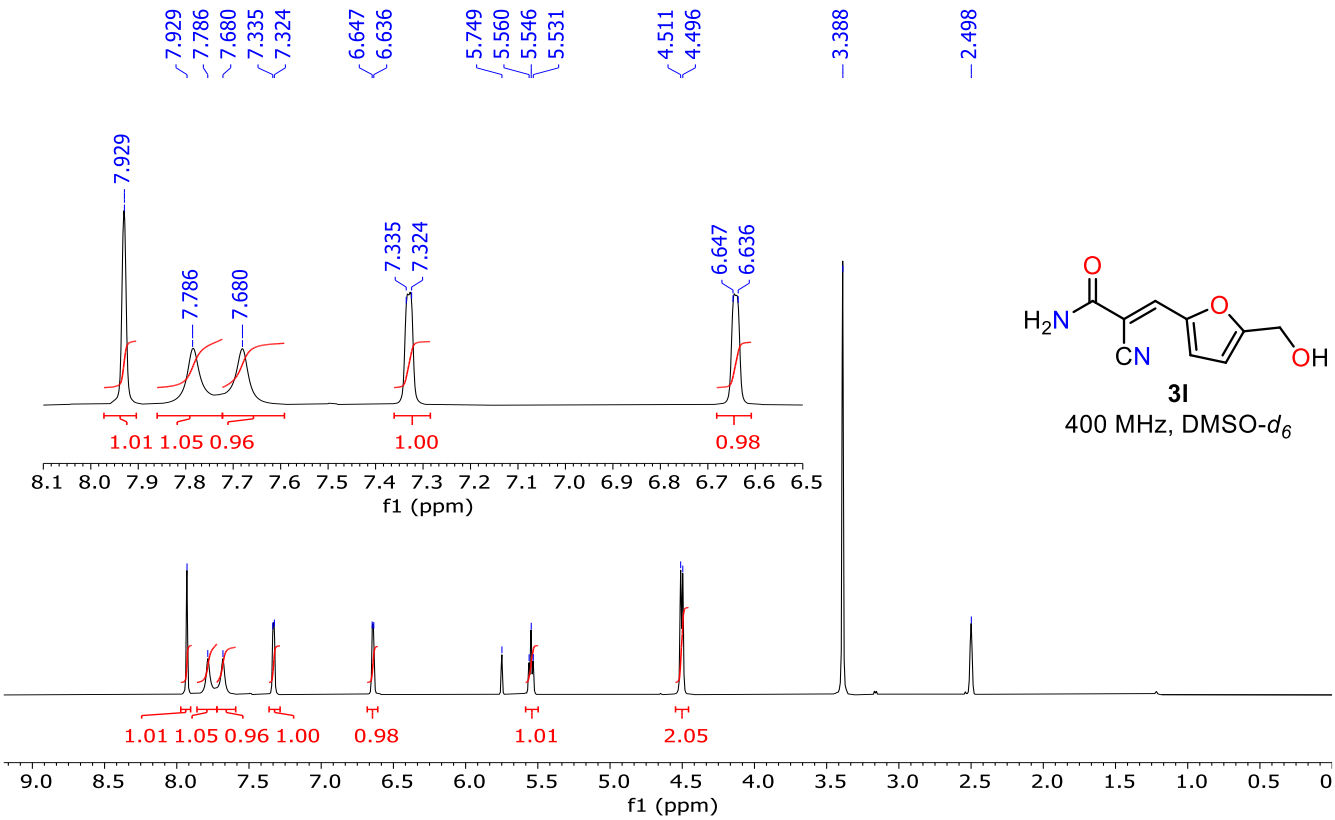

7.969
7.861
7.839
7.580
7.481
6.820
6.798
3.346
3.044
2.510
2.505
2.500
2.496
2.491
0.98 1.98 1.92 2.00
6.03
f1 (ppm)
O
H2N
CN
N
3j
400 MHz, DMSO-d6

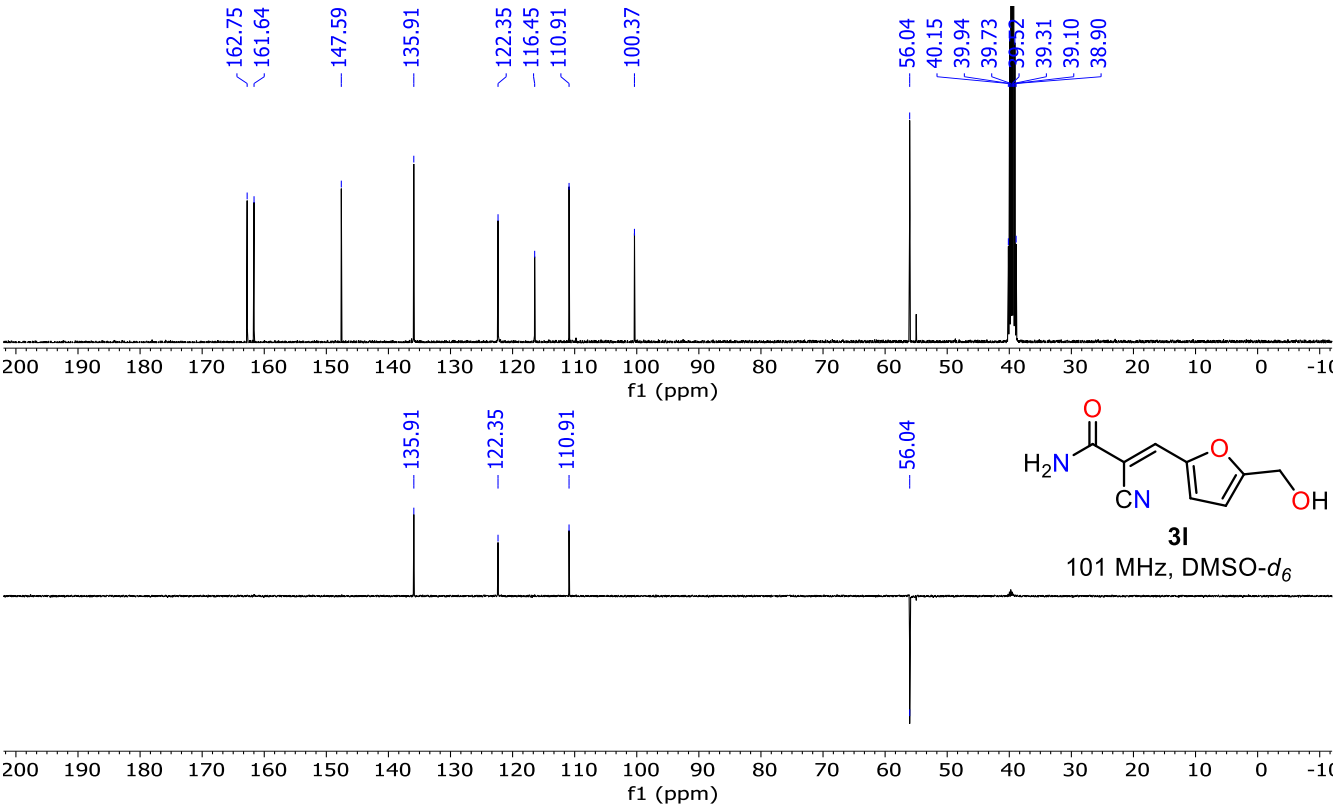

163.99
152.95
150.51
132.67
118.73
118.31
111.65
97.22
40.15
39.94
39.73
39.57
39.52
39.31
39.10
38.89
f1 (ppm)
150.52
132.67
111.65
39.58
O
H2N
CN
N
3j
101 MHz, DMSO-d6

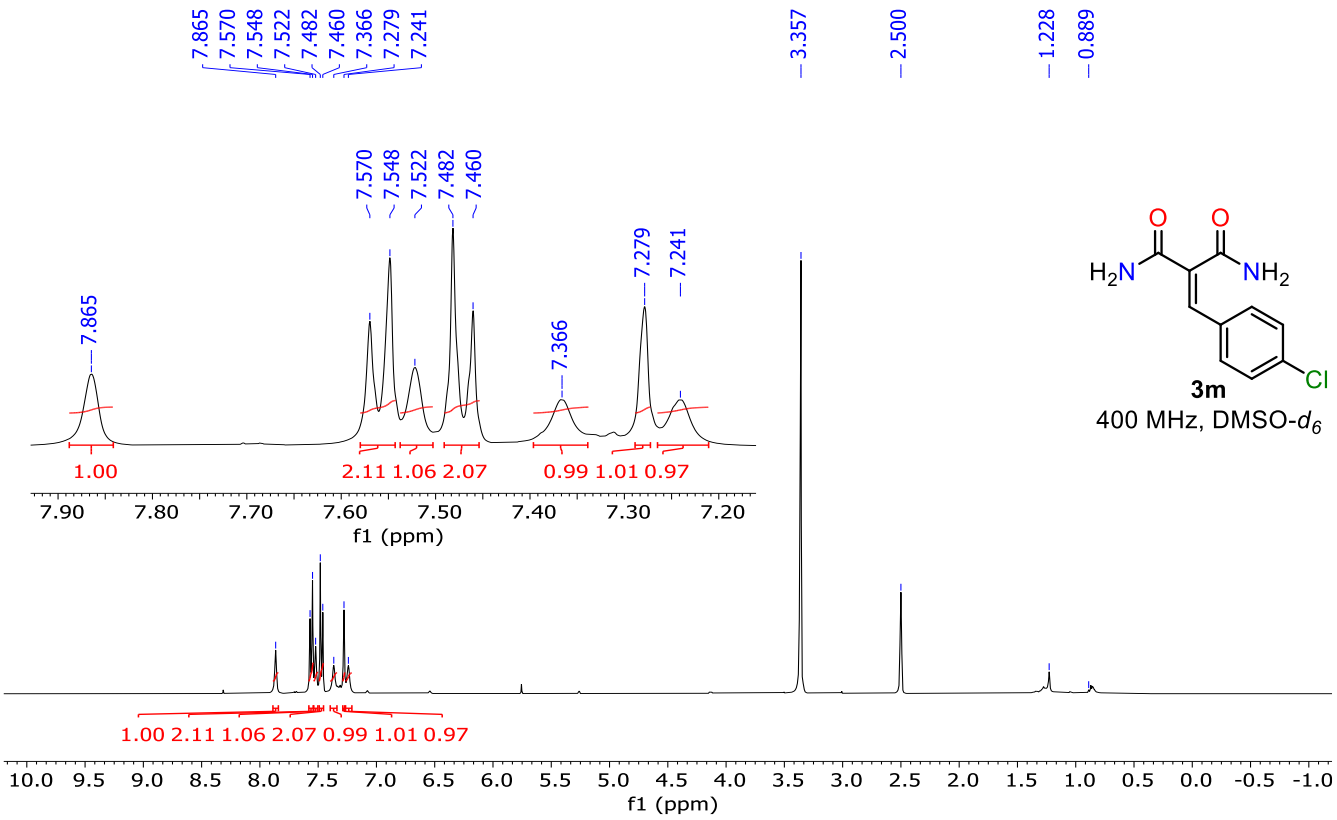

9.069
8.781
8.371
8.202
8.183
8.038
8.016
7.668
7.652
7.627
7.604
7.590
3.362
2.504
2.500
2.495
1.00 0.99 0.90 2.02 2.96 4.03
f1 (ppm)
O
H2N
CN
3k
400 MHz, DMSO-d6

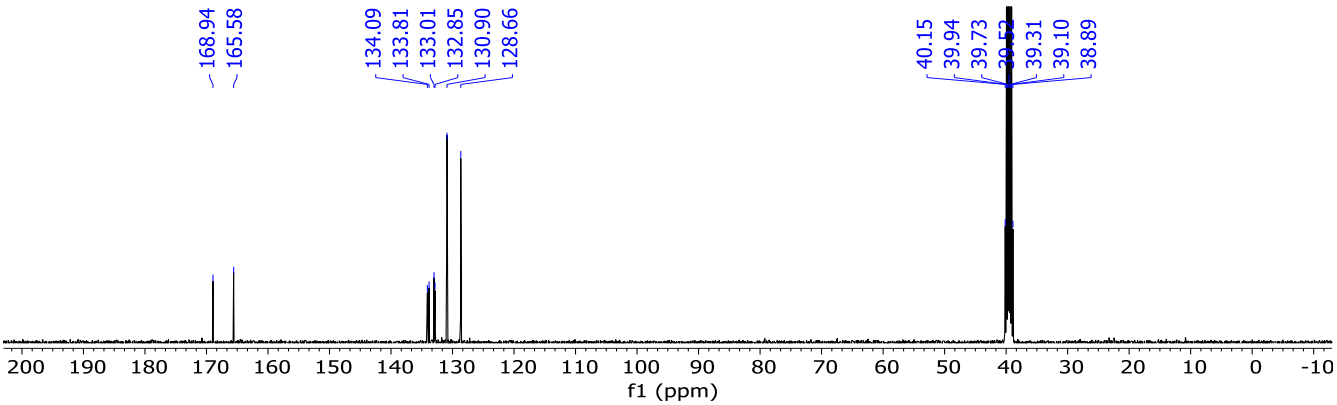

162.09
149.97
130.62
129.28
128.96
128.19
127.13
126.40
125.83
124.86
117.60
115.09
40.15
39.94
39.73
39.52
39.31
39.10
38.89
f1 (ppm)

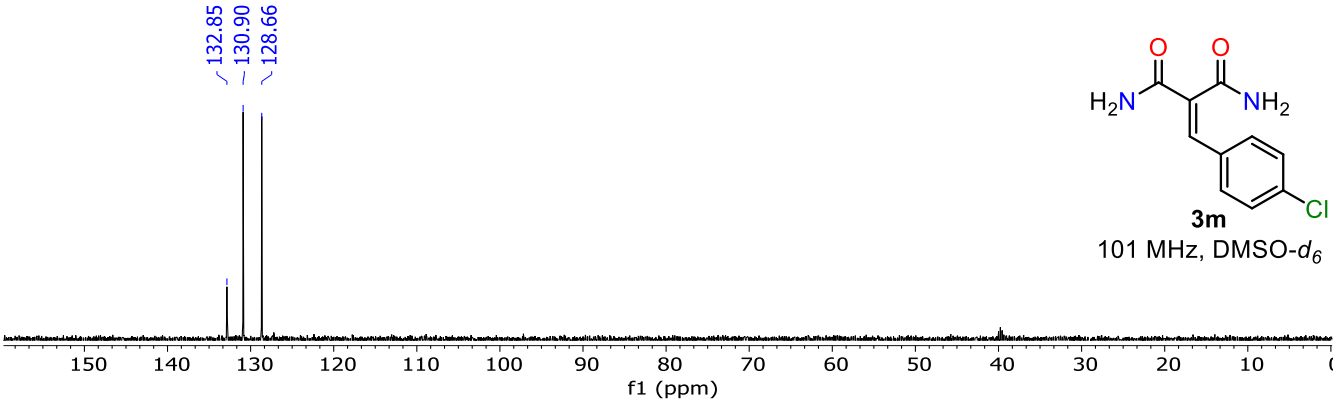
149.97
129.27
128.95
127.13
125.83
124.85
f1 (ppm)
O
H2N
CN
3k
101 MHz, DMSO-d6

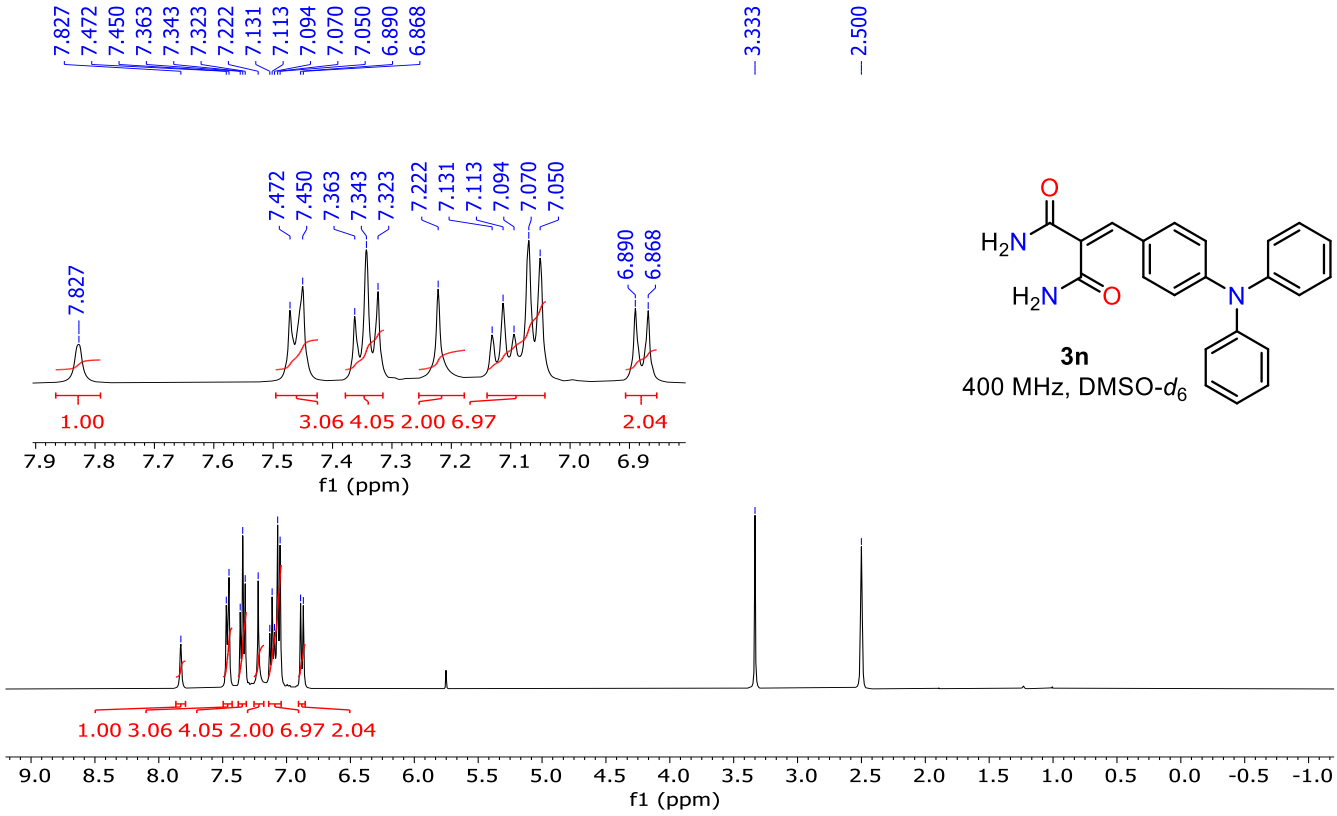

7.929
7.786
7.680
7.335
7.324
6.647
6.636
5.749
5.560
5.546
5.531
4.511
4.496
3.388
2.498
1.01 1.05 0.96
1.00
0.98
f1 (ppm)
1.01 1.05 0.96 1.00
0.98
1.01
2.05
f1 (ppm)
O
H2N
CN
O
OH
3l
400 MHz, DMSO-d6


162.75
161.64
147.59
135.91
122.35
116.45
110.91
100.37
56.04
40.15
39.94
39.73
39.52
39.31
39.10
38.90
f1 (ppm)
135.91
122.35
110.91
56.04
f1 (ppm)
O
H2N
CN
O
OH
3l
101 MHz, DMSO-d6

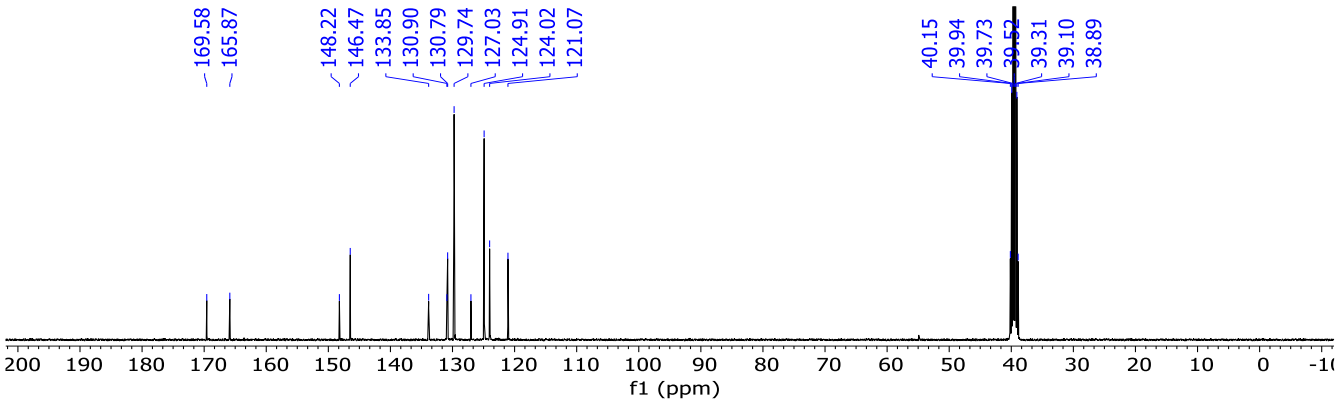

7.865
7.570
7.548
7.522
7.482
7.460
7.366
7.279
7.241
3.357
2.500
1.228
0.889
1.00
2.11 1.06 2.07
0.99 1.01 0.97
f1 (ppm)
3m
400 MHz, DMSO-d6

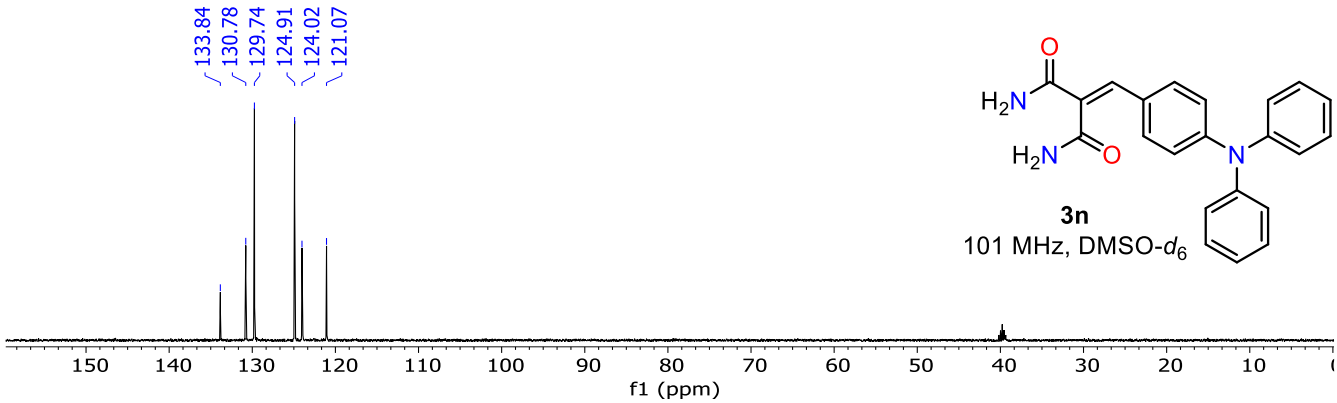

168.94
165.58
134.09
133.81
133.01
132.85
130.90
128.66
40.15
39.94
39.73
39.52
39.31
39.10
38.89
f1 (ppm)

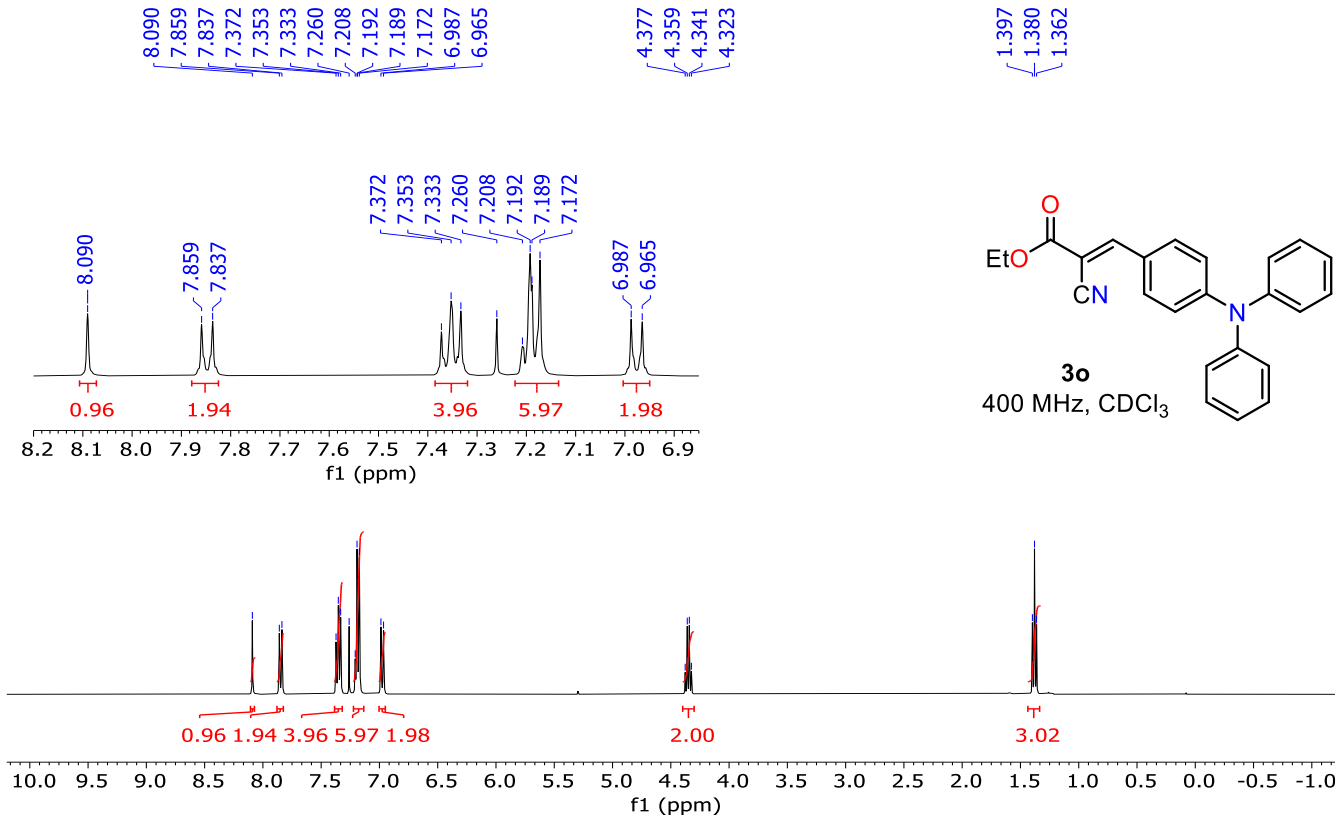

132.85
130.90
128.66
f1 (ppm)
3m
101 MHz, DMSO-d6

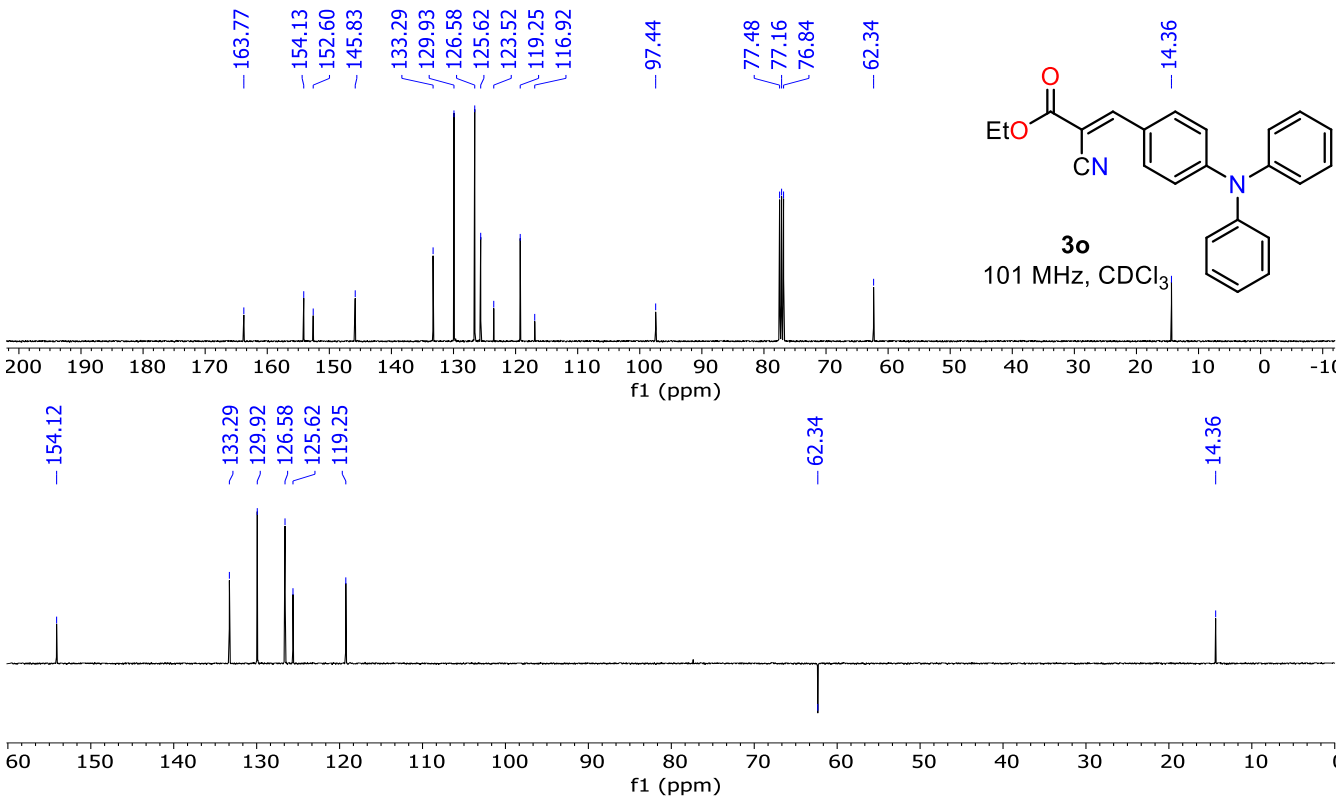

7.827
7.472
7.450
7.363
7.343
7.323
7.222
7.131
7.113
7.094
7.070
7.050
6.890
6.868
3.333
2.500
1.00
3.06 4.05 2.00 6.97
2.04
f1 (ppm)
3n
400 MHz, DMSO-d6

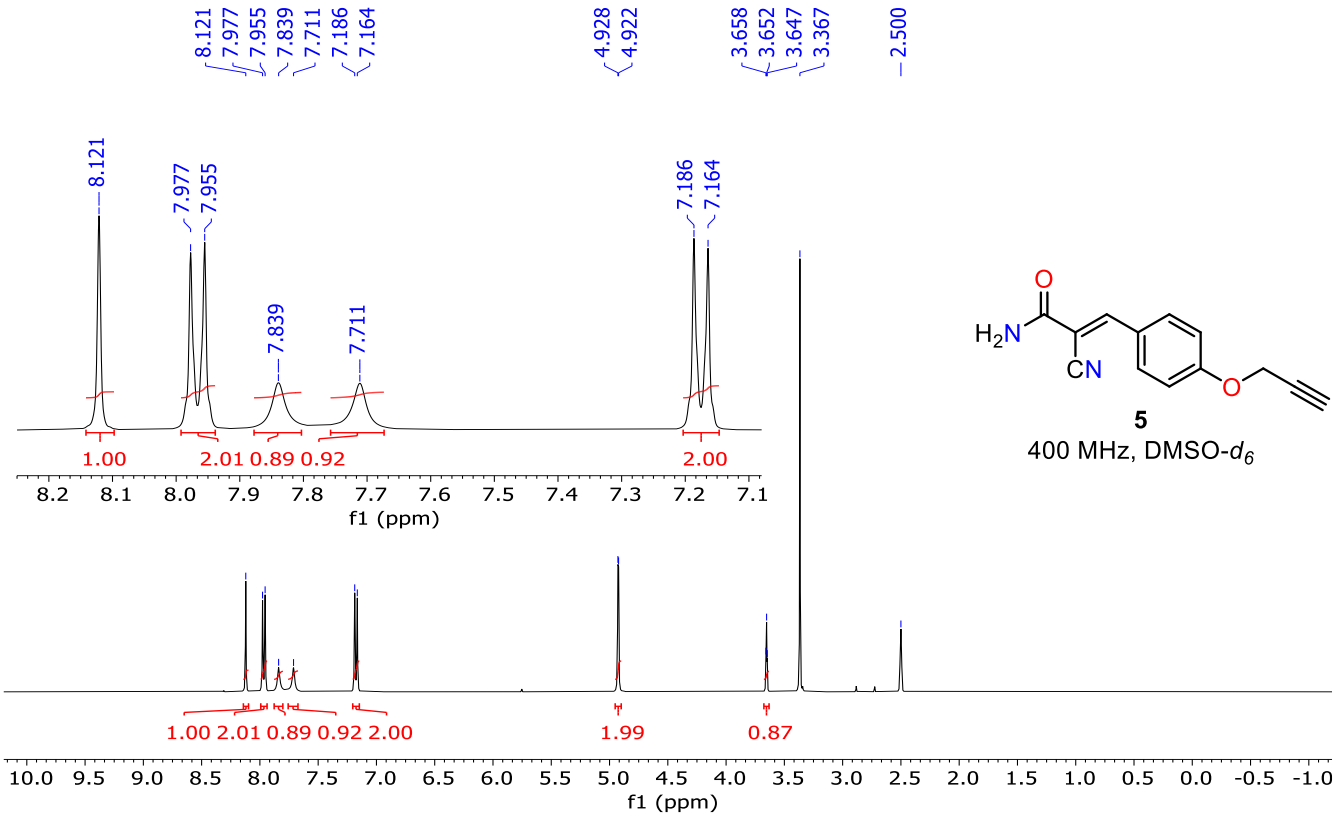
1.00 3.06 4.05 2.00 6.97 2.04
f1 (ppm)

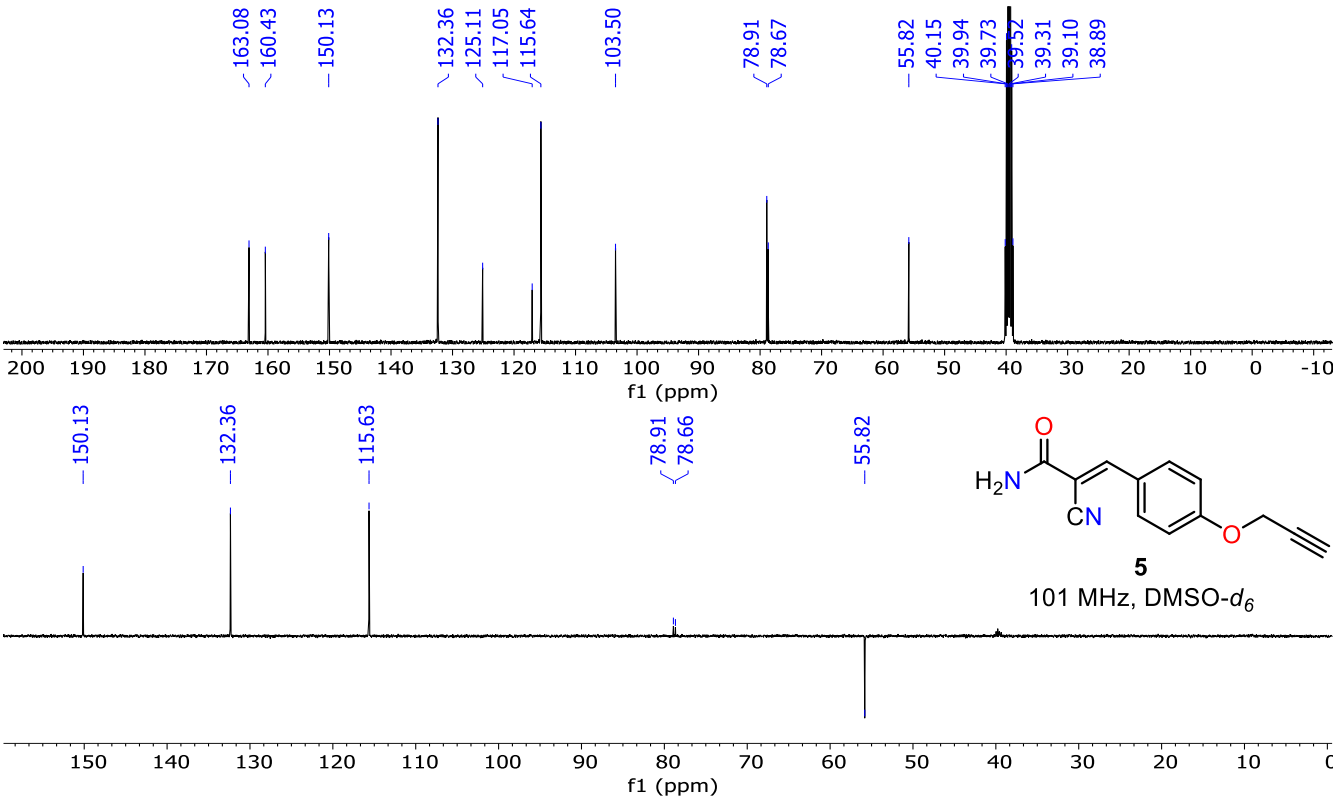

169.58
165.87
148.22
146.47
133.85
130.90
130.79
129.74
127.03
124.91
124.02
121.07
40.15
39.94
39.73
39.52
39.31
39.10
38.89
f1 (ppm)

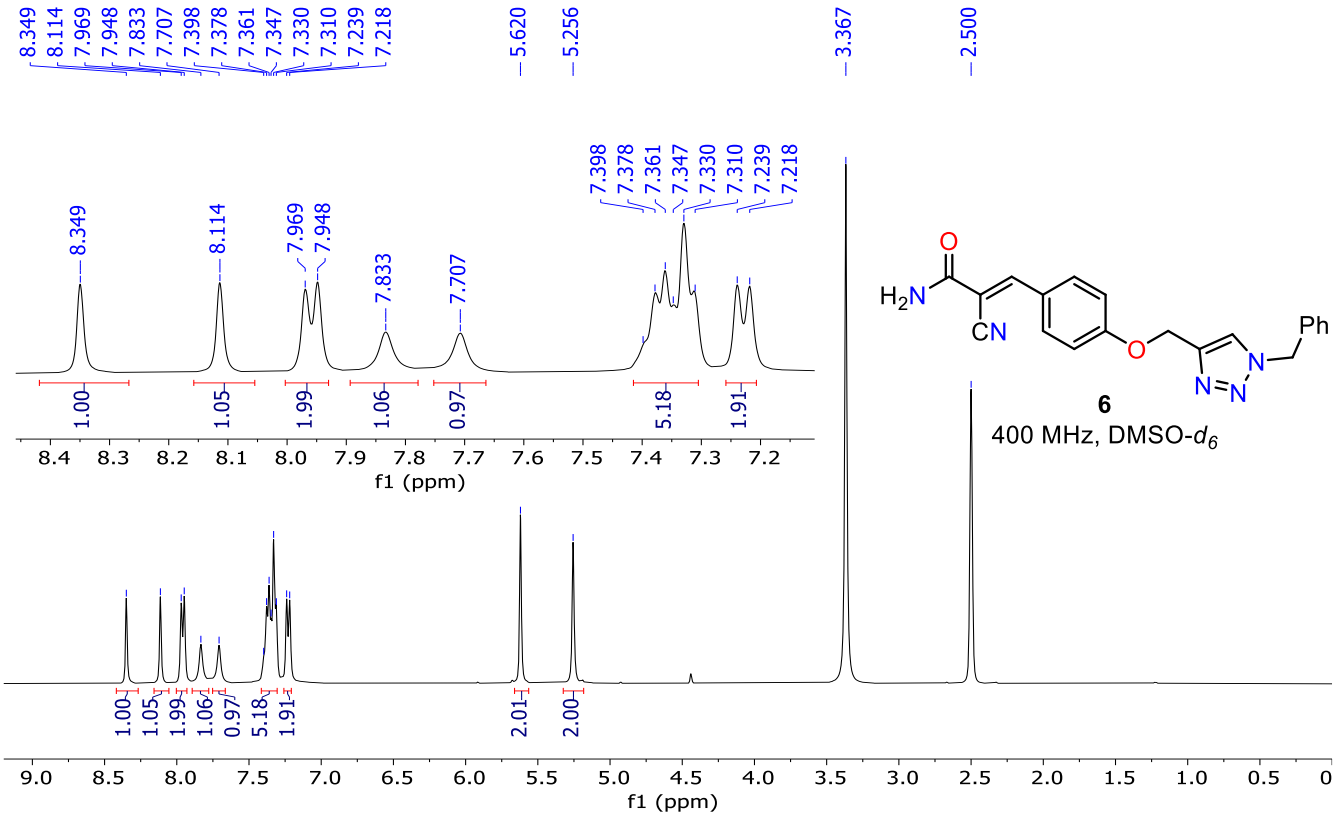

133.84
130.78
129.74
124.91
124.02
121.07
f1 (ppm)
3n
101 MHz, DMSO-d6

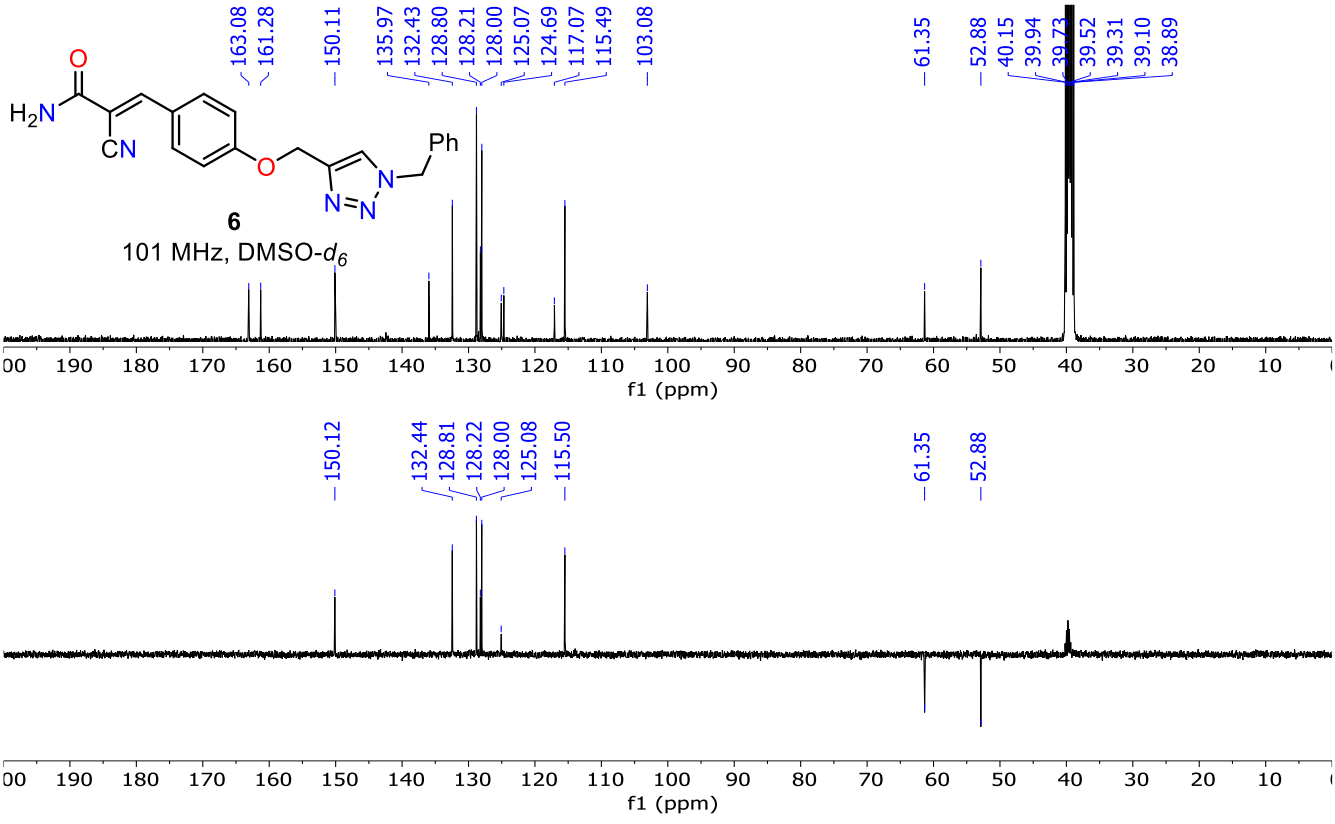

8.090
7.859
7.837
7.372
7.353
7.333
7.260
7.208
7.192
7.189
7.172
6.987
6.965
4.377
4.359
4.341
4.323
1.397
1.380
1.362
0.96
1.94
3.96
5.97
1.98
f1 (ppm)
EtO
CN
N
O
3o
400 MHz, CDCl3
0.96 1.94 3.96 5.97 1.98
2.00
3.02
f1 (ppm)


163.77
154.13
152.60
145.83
133.29
129.93
126.58
125.62
123.52
119.25
116.92
97.44
77.48
77.16
76.84
62.34
14.36
EtO
CN
N
O
3o
101 MHz, CDCl3
f1 (ppm)
154.12
133.29
129.92
126.58
125.62
119.25
62.34
14.36
f1 (ppm)


8.121
7.977
7.955
7.839
7.711
7.186
7.164
4.928
4.922
3.658
3.652
3.647
3.367
2.500
1.00 2.01 0.89 0.92 2.00
1.00 2.01 0.89 0.92 2.00 1.99 0.87
f1 (ppm)
O
H2N
CN
O
5
400 MHz, DMSO-d6


163.08
160.43
150.13
132.36
125.11
117.05
115.64
103.50
78.91
78.67
55.82
40.15
39.94
39.73
39.52
39.31
39.10
38.89
f1 (ppm)
150.13
132.36
115.63
78.91
78.66
55.82
f1 (ppm)
O
H2N
CN
O
5
101 MHz, DMSO-d6


8.349
8.114
7.969
7.948
7.833
7.707
7.398
7.378
7.361
7.347
7.330
7.310
7.239
7.218
5.620
5.256
3.367
2.500
1.00
1.05
1.99
1.06
0.97
5.18
1.91
2.01
2.00
f1 (ppm)
O
H2N
CN
O
N
N=N
Ph
6
400 MHz, DMSO-d6


163.08
161.28
150.11
135.97
132.43
128.80
128.21
128.00
125.07
124.69
117.07
115.49
103.08
61.35
52.88
40.15
39.94
39.73
39.52
39.31
39.10
38.89
f1 (ppm)
O
H2N
CN
O
N
N=N
Ph
6
101 MHz, DMSO-d6

150.12
132.44
128.81
128.22
128.00
125.08
115.50
61.35
52.88
f1 (ppm)

3. Mean %G, GI%, and lethality values for compounds 3a–o

Table S1. Mean growth, %GI, and lethality values displayed by the tested compound **3a** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program
One Dose Mean Graph

NSC: D-826729 / 1	Conc: 1.00E-5 Molar	Test Date: Nov 02, 2020
Experiment ID: 2011OS61		Report Date: Dec 07, 2020

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	107.62
HL-60(TB)	99.48
K-562	108.35
MOLT-4	101.50
RPMI-8226	115.04
SR	122.60
Non-Small Cell Lung Cancer	
A549/ATCC	107.10
EKVX	98.75
HOP-62	101.02
HOP-92	117.04
NCI-H226	110.72
NCI-H23	106.58
NCI-H322M	100.45
NCI-H460	104.48
NCI-H522	97.55
Colon Cancer	
COLO 205	117.48
HCC-2998	105.90
HCT-116	97.60
HCT-15	99.97
HT29	106.89
KM12	99.50
SW-620	101.72
CNS Cancer	
SF-268	99.38
SF-295	105.82
SF-539	99.83
SNB-19	99.20
SNB-75	82.85
U251	105.60
Melanoma	
LOX IMVI	99.21
MALME-3M	105.16
M14	104.13
MDA-MB-435	98.47
SK-MEL-2	104.09
SK-MEL-28	105.91
SK-MEL-5	100.54
UACC-257	103.49
UACC-62	99.59
Ovarian Cancer	
IGROV1	105.44
OVCAR-3	104.01
OVCAR-4	106.41
OVCAR-5	102.48
OVCAR-8	106.86
NCI/ADR-RES	109.10
SK-OV-3	106.84
Renal Cancer	
786-0	100.73
ACHN	100.92
CAKI-1	95.08
RXF 393	106.77
SN12C	102.75
TK-10	96.39
UO-31	94.93
Prostate Cancer	
PC-3	97.28
DU-145	111.58
Breast Cancer	
MCF7	95.01
MDA-MB-231/ATCC	102.96
HS 578T	104.58
BT-549	111.13
T-47D	97.14
MDA-MB-468	94.73
Mean	103.28
Delta	20.43
Range	39.75

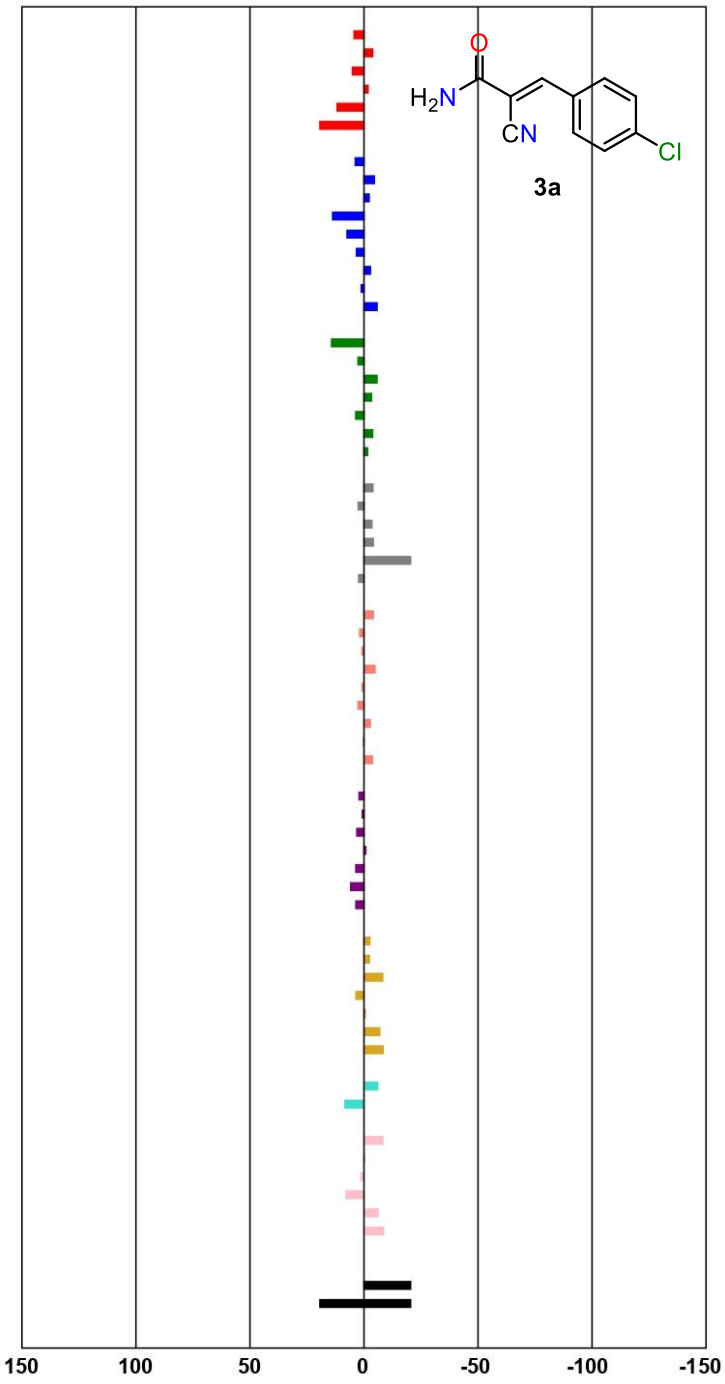


Table S2. Mean growth, %GI, and lethality values displayed by the tested compound **3b** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-826733 / 1	Conc: 1.00E-5 Molar	Test Date: Nov 02, 2020
Experiment ID: 2011OS61		Report Date: Nov 26, 2020

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	105.95
HL-60(TB)	105.57
K-562	105.60
MOLT-4	108.26
RPMI-8226	110.70
SR	112.89
Non-Small Cell Lung Cancer	
A549/ATCC	101.28
EKVX	103.18
HOP-62	103.78
HOP-92	114.23
NCI-H226	106.75
NCI-H23	100.30
NCI-H322M	104.59
NCI-H460	105.54
NCI-H522	94.93
Colon Cancer	
COLO 205	114.44
HCC-2998	108.60
HCT-116	101.65
HCT-15	101.37
HT29	106.02
KM12	102.74
SW-620	99.84
CNS Cancer	
SF-268	103.14
SF-295	105.15
SF-539	106.77
SNB-19	98.00
SNB-75	85.89
U251	104.57
Melanoma	
LOX IMVI	100.97
MALME-3M	106.30
M14	103.74
MDA-MB-435	104.06
SK-MEL-2	104.33
SK-MEL-28	106.26
SK-MEL-5	101.39
UACC-257	106.09
UACC-62	96.62
Ovarian Cancer	
IGROV1	104.12
OVCAR-3	108.65
OVCAR-4	103.21
OVCAR-5	105.39
OVCAR-8	105.50
NCI/ADR-RES	106.63
SK-OV-3	107.51
Renal Cancer	
786-0	99.04
ACHN	103.67
CAKI-1	100.50
RXF 393	108.98
SN12C	98.42
TK-10	98.19
UO-31	96.79
Prostate Cancer	
PC-3	99.29
DU-145	106.75
Breast Cancer	
MCF7	93.91
MDA-MB-231/ATCC	109.10
HS 578T	100.26
BT-549	110.80
T-47D	99.25
MDA-MB-468	103.14
Mean	103.74
Delta	17.85
Range	28.55

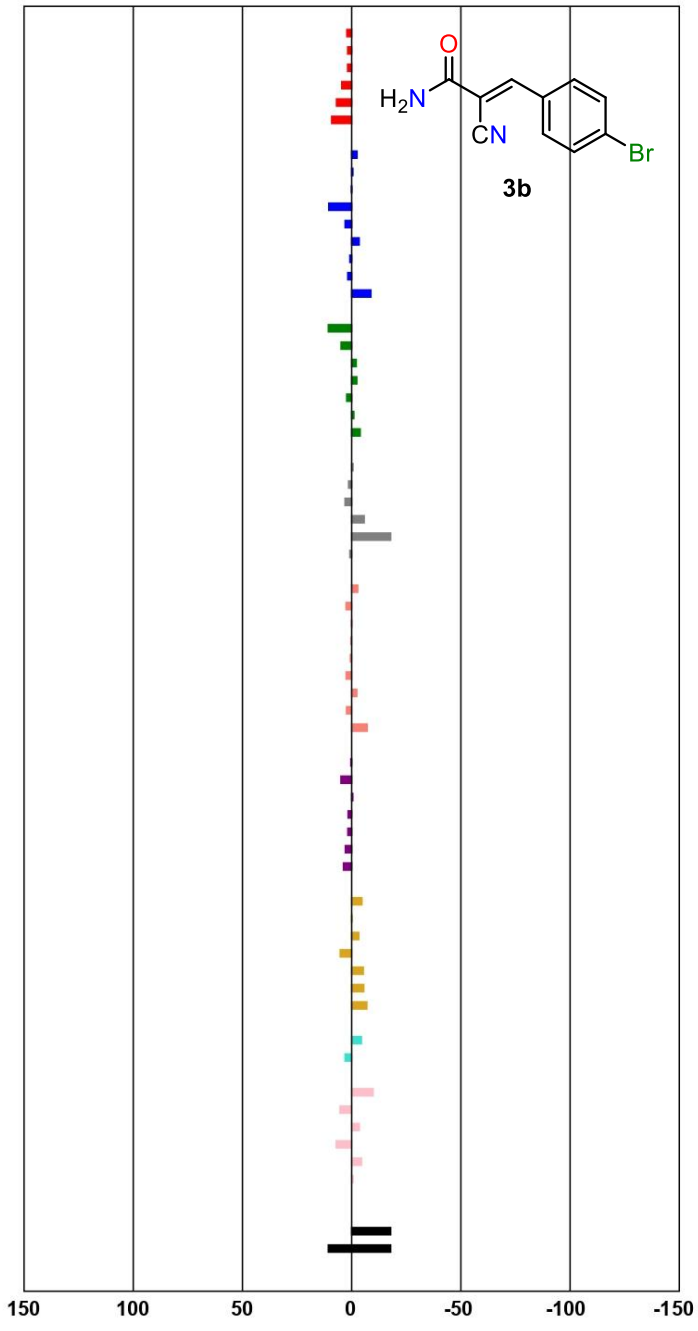


Table S3. Mean growth, %GI, and lethality values displayed by the tested compound **3c** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-835693 / 1	Conc: 1.00E-5 Molar	Test Date: Feb 28, 2022
Experiment ID: 2202OS75		Report Date: Mar 18, 2022

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	96.67
HL-60(TB)	107.33
K-562	102.41
MOLT-4	105.01
RPMI-8226	101.96
SR	104.21
Non-Small Cell Lung Cancer	
A549/ATCC	106.84
EKVX	106.72
HOP-62	98.12
HOP-92	115.30
NCI-H226	104.98
NCI-H23	105.08
NCI-H322M	116.29
NCI-H460	107.20
NCI-H522	88.42
Colon Cancer	
COLO 205	116.66
HCC-2998	115.80
HCT-116	94.81
HCT-15	101.46
HT29	106.01
KM12	99.51
SW-620	102.92
CNS Cancer	
SF-268	102.90
SF-295	99.61
SF-539	102.51
SNB-19	100.66
SNB-75	78.02
U251	106.82
Melanoma	
LOX IMVI	102.53
MALME-3M	107.41
M14	103.59
MDA-MB-435	103.23
SK-MEL-2	105.06
SK-MEL-28	114.08
SK-MEL-5	101.00
UACC-257	103.47
UACC-62	96.26
Ovarian Cancer	
IGROV1	111.24
OVCAR-3	103.08
OVCAR-4	104.91
OVCAR-5	115.23
OVCAR-8	112.65
NCI/ADR-RES	107.29
SK-OV-3	102.73
Renal Cancer	
786-0	101.67
A498	97.64
ACHN	105.01
CAKI-1	96.69
SN12C	125.46
TK-10	102.62
UO-31	85.75
Prostate Cancer	
PC-3	101.59
DU-145	106.84
Breast Cancer	
MCF7	101.87
MDA-MB-231/ATCC	102.80
HS 578T	96.80
BT-549	85.58
T-47D	93.31
MDA-MB-468	113.52
Mean	103.48
Delta	25.46
Range	47.44

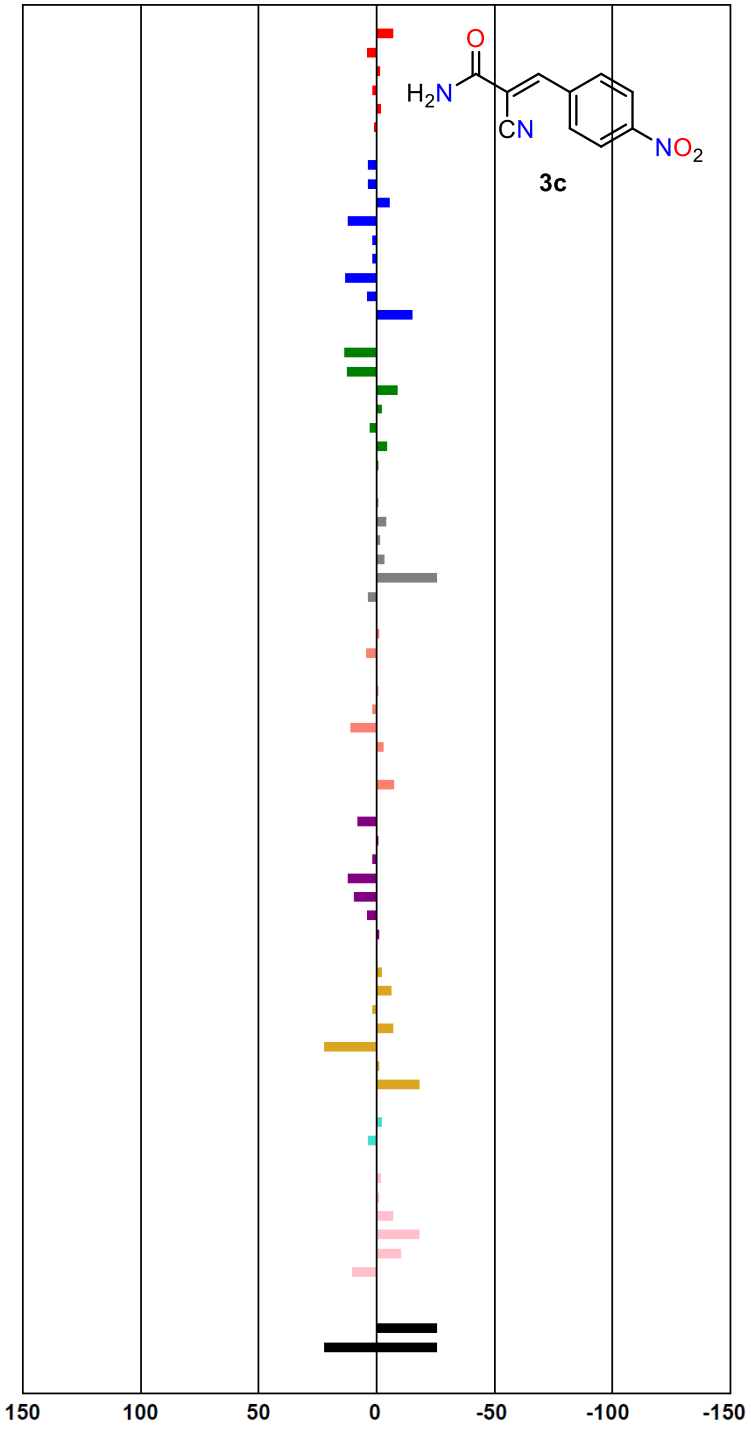


Table S4. Mean growth, %GI, and lethality values displayed by the tested compound **3d** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-826734 / 1	**Conc:** 1.00E-5 Molar	**Test Date:** Nov 02, 2020
Experiment ID: 2011OS61		**Report Date:** Nov 26, 2020

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	89.73
HL-60(TB)	90.88
K-562	80.30
MOLT-4	109.24
RPMI-8226	110.72
SR	80.48
Non-Small Cell Lung Cancer	
A549/ATCC	108.62
EKVX	105.37
HOP-62	100.65
HOP-92	121.57
NCI-H226	109.27
NCI-H23	103.55
NCI-H322M	100.47
NCI-H460	106.26
NCI-H522	93.88
Colon Cancer	
COLO 205	116.98
HCC-2998	102.82
HCT-116	74.01
HCT-15	87.65
HT29	106.16
KM12	102.96
SW-620	88.28
CNS Cancer	
SF-268	100.60
SF-295	107.35
SF-539	104.45
SNB-19	97.64
SNB-75	90.16
U251	95.47
Melanoma	
LOX IMVI	97.34
MALME-3M	105.13
M14	99.40
MDA-MB-435	98.51
SK-MEL-2	106.23
SK-MEL-28	112.43
SK-MEL-5	101.48
UACC-257	109.37
UACC-62	96.81
Ovarian Cancer	
IGROV1	102.09
OVCAR-3	109.02
OVCAR-4	106.78
OVCAR-5	99.68
OVCAR-8	106.08
NCI/ADR-RES	107.25
SK-OV-3	106.78
Renal Cancer	
786-0	100.77
ACHN	100.52
CAKI-1	90.76
RXF 393	101.62
SN12C	98.29
TK-10	102.41
UO-31	94.39
Prostate Cancer	
PC-3	92.54
DU-145	113.59
Breast Cancer	
MCF7	76.25
MDA-MB-231/ATCC	100.42
HS 578T	99.03
BT-549	102.02
T-47D	93.67
MDA-MB-468	96.27
Mean	100.21
Delta	26.20
Range	47.56

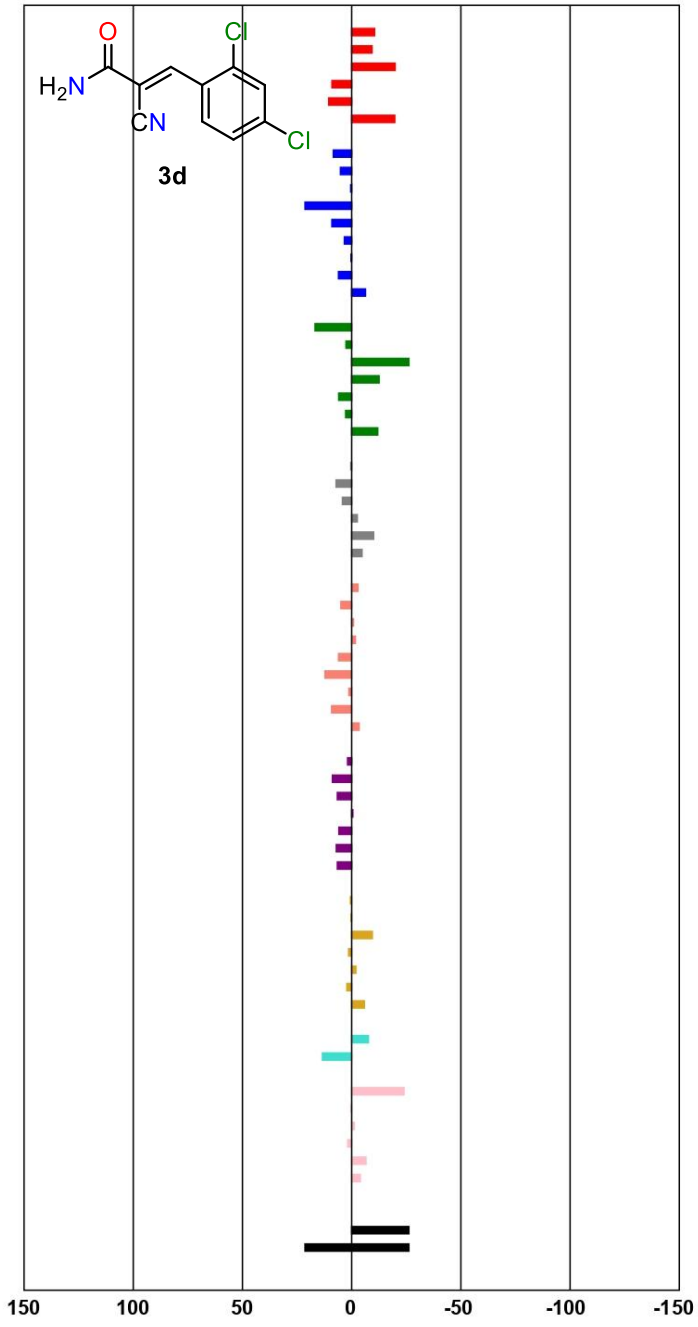


Table S5. Mean growth, %GI, and lethality values displayed by the tested compound **3e** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-835698 / 1	Conc: 1.00E-5 Molar	Test Date: Feb 28, 2022
Experiment ID: 2202OS75		Report Date: Mar 18, 2022

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	94.76
HL-60(TB)	99.14
K-562	46.88
MOLT-4	93.12
RPMI-8226	106.80
SR	43.37
Non-Small Cell Lung Cancer	
A549/ATCC	97.52
EKVX	102.02
HOP-62	95.29
HOP-92	139.36
NCI-H226	100.63
NCI-H23	86.22
NCI-H322M	89.56
NCI-H460	106.56
NCI-H522	84.28
Colon Cancer	
COLO 205	135.25
HCC-2998	101.70
HCT-116	60.63
HCT-15	88.49
HT29	80.25
KM12	96.38
SW-620	84.32
CNS Cancer	
SF-268	99.80
SF-295	96.69
SF-539	101.70
SNB-19	95.69
SNB-75	94.70
U251	73.32
Melanoma	
LOX IMVI	59.77
MALME-3M	101.77
M14	93.61
MDA-MB-435	103.08
SK-MEL-2	106.22
SK-MEL-28	94.91
SK-MEL-5	100.09
UACC-257	94.27
UACC-62	90.60
Ovarian Cancer	
IGROV1	100.69
OVCAR-3	106.36
OVCAR-4	103.04
OVCAR-5	101.12
OVCAR-8	90.79
NCI/ADR-RES	105.99
SK-OV-3	96.53
Renal Cancer	
786-0	100.82
A498	121.18
ACHN	105.82
CAKI-1	97.25
SN12C	95.21
TK-10	109.36
UO-31	102.52
Prostate Cancer	
PC-3	100.11
DU-145	88.32
Breast Cancer	
MCF7	33.15
MDA-MB-231/ATCC	99.26
HS 578T	96.87
BT-549	106.43
T-47D	86.35
MDA-MB-468	92.02
Mean	94.54
Delta	61.39
Range	106.21

Mean Growth Percent - Growth Percent

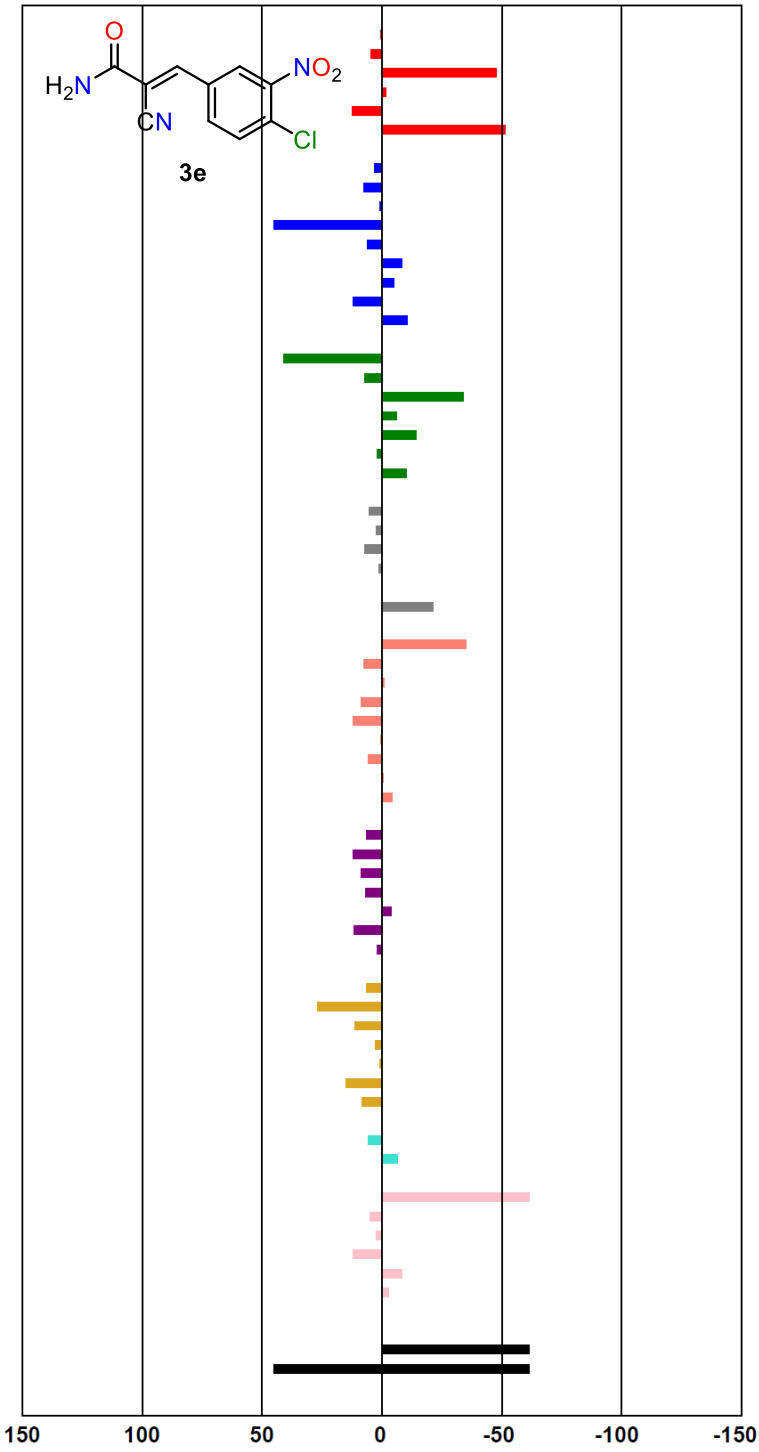


Table S6. Mean growth, %GI, and lethality values displayed by the tested compound **3f** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program
One Dose Mean Graph

NSC: D-835694 / 1	Conc: 1.00E-5 Molar	Test Date: Feb 28, 2022
Experiment ID: 2202OS75		Report Date: Mar 18, 2022

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	59.86
HL-60(TB)	68.67
K-562	35.36
MOLT-4	55.99
RPMI-8226	19.81
SR	69.09
Non-Small Cell Lung Cancer	
A549/ATCC	36.26
EKVX	90.22
HOP-62	48.93
HOP-92	75.47
NCI-H226	-82.62
NCI-H23	55.86
NCI-H322M	92.94
NCI-H460	5.51
NCI-H522	74.49
Colon Cancer	
COLO 205	19.70
HCC-2998	73.69
HCT-116	14.94
HCT-15	65.13
HT29	30.51
KM12	78.57
SW-620	45.60
CNS Cancer	
SF-268	101.86
SF-295	23.47
SF-539	96.98
SNB-19	77.01
SNB-75	95.36
U251	32.53
Melanoma	
LOX IMVI	79.04
MALME-3M	109.90
M14	90.68
MDA-MB-435	92.73
SK-MEL-2	23.46
SK-MEL-28	103.76
SK-MEL-5	31.19
UACC-257	-55.86
UACC-62	-47.34
Ovarian Cancer	
IGROV1	-21.16
OVCAR-3	3.69
OVCAR-4	4.67
OVCAR-5	-60.62
OVCAR-8	75.13
NCI/ADR-RES	57.41
SK-OV-3	55.99
Renal Cancer	
786-0	53.86
A498	-99.81
ACHN	87.98
CAKI-1	-24.02
SN12C	90.51
TK-10	-37.66
UO-31	49.87
Prostate Cancer	
PC-3	61.02
DU-145	84.77
Breast Cancer	
MCF7	6.51
MDA-MB-231/ATCC	89.29
HS 578T	99.19
BT-549	69.55
T-47D	-26.74
MDA-MB-468	-91.22
Mean	40.97
Delta	140.78
Range	209.71

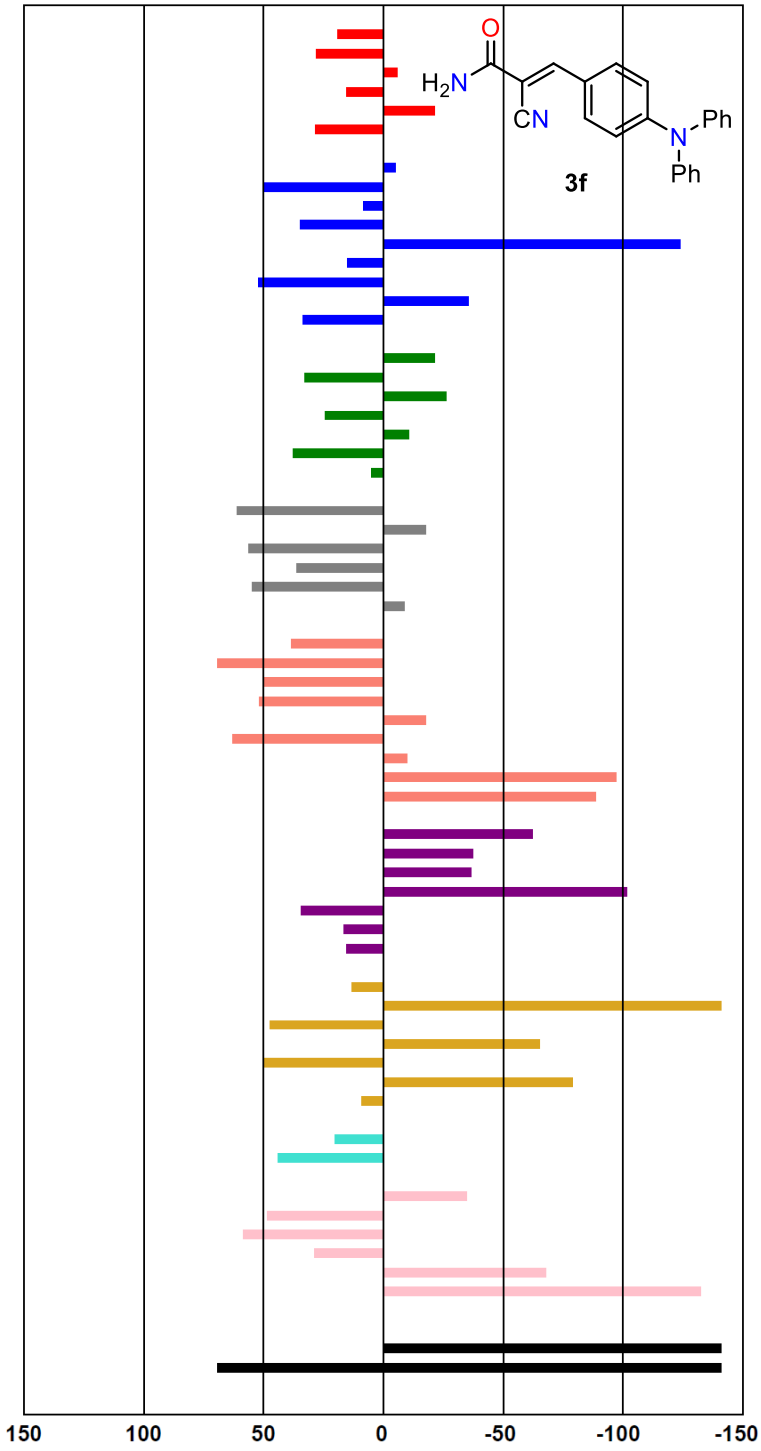


Table S7. Mean growth, %GI, and lethality values displayed by the tested compound **3g** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-826735 / 1	**Conc:** 1.00E-5 Molar	**Test Date:** Nov 02, 2020
Experiment ID: 2011OS61		**Report Date:** Nov 26, 2020

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	104.03
HL-60(TB)	93.56
K-562	99.28
MOLT-4	111.03
RPMI-8226	119.24
SR	97.61
Non-Small Cell Lung Cancer	
A549/ATCC	107.08
EKVX	106.40
HOP-62	101.27
HOP-92	120.86
NCI-H226	107.62
NCI-H23	104.79
NCI-H322M	103.53
NCI-H460	104.17
NCI-H522	79.28
Colon Cancer	
COLO 205	114.40
HCC-2998	105.56
HCT-116	104.19
HCT-15	104.21
HT29	103.45
KM12	105.51
SW-620	96.16
CNS Cancer	
SF-268	101.87
SF-295	108.11
SF-539	108.30
SNB-19	99.69
SNB-75	93.61
U251	100.95
Melanoma	
LOX IMVI	103.20
MALME-3M	106.37
M14	105.33
MDA-MB-435	105.04
SK-MEL-2	106.47
SK-MEL-28	109.20
SK-MEL-5	100.42
UACC-257	103.07
UACC-62	97.47
Ovarian Cancer	
IGROV1	104.40
OVCAR-3	114.06
OVCAR-4	105.13
OVCAR-5	105.23
OVCAR-8	105.70
NCI/ADR-RES	106.60
SK-OV-3	104.23
Renal Cancer	
786-0	99.53
ACHN	103.59
CAKI-1	101.65
RXF 393	108.18
SN12C	99.41
TK-10	98.21
UO-31	101.18
Prostate Cancer	
PC-3	101.39
DU-145	107.10
Breast Cancer	
MCF7	100.02
MDA-MB-231/ATCC	107.22
HS 578T	96.76
BT-549	104.04
T-47D	101.32
MDA-MB-468	97.80
Mean	103.65
Delta	24.37
Range	41.58

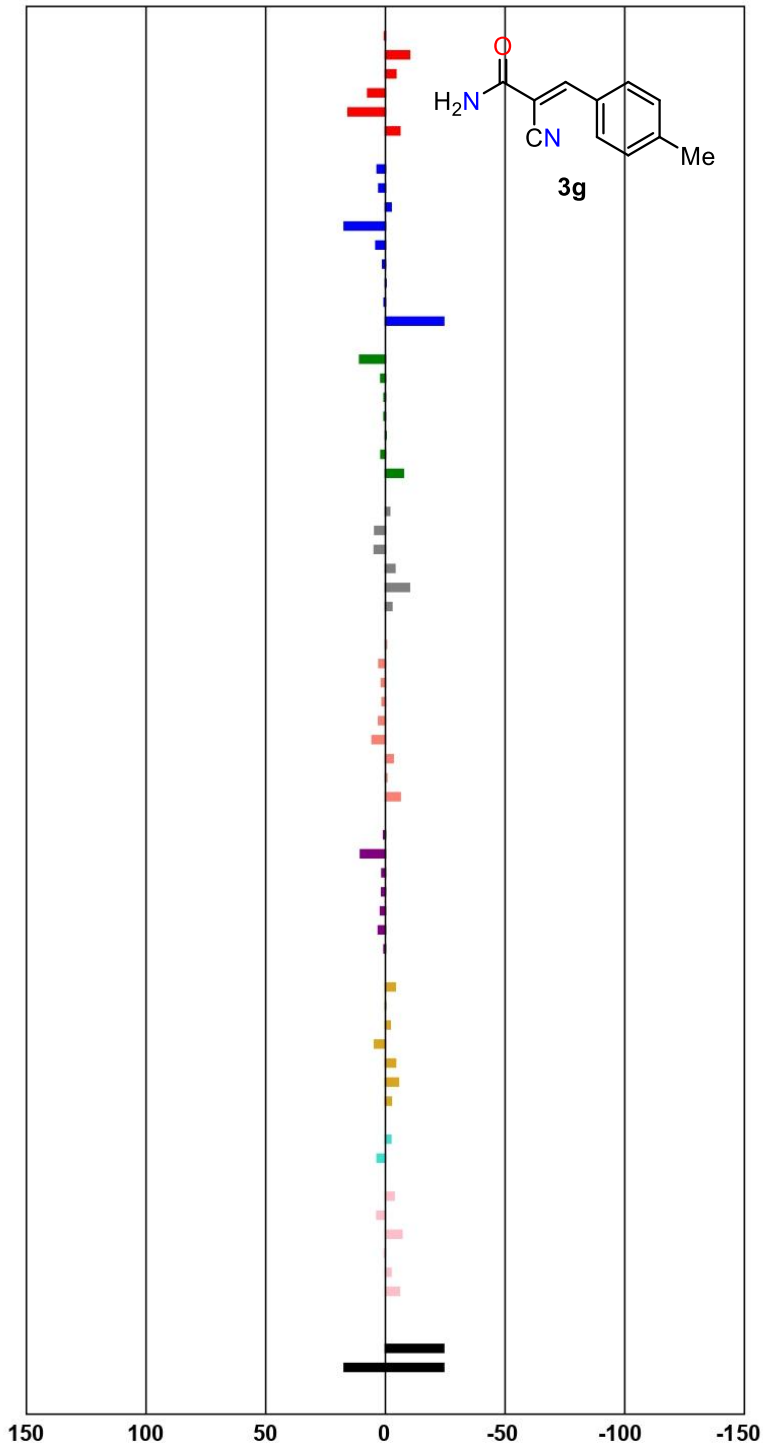


Table S8. Mean growth, %GI, and lethality values displayed by the tested compound **3h** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-826732 / 1	**Conc:** 1.00E-5 Molar	**Test Date:** Nov 02, 2020
Experiment ID: 2011OS61		**Report Date:** Nov 26, 2020

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	104.45
HL-60(TB)	104.24
K-562	97.31
MOLT-4	107.40
RPMI-8226	106.43
SR	111.96
Non-Small Cell Lung Cancer	
A549/ATCC	100.49
EKVX	104.57
HOP-62	105.55
HOP-92	104.71
NCI-H226	108.45
NCI-H23	103.05
NCI-H322M	103.35
NCI-H460	104.80
NCI-H522	97.36
Colon Cancer	
COLO 205	114.69
HCC-2998	109.96
HCT-116	106.82
HCT-15	100.64
HT29	107.46
KM12	103.94
SW-620	102.10
CNS Cancer	
SF-268	97.95
SF-295	110.40
SF-539	111.34
SNB-19	101.16
SNB-75	79.40
U251	101.75
Melanoma	
LOX IMVI	109.00
MALME-3M	104.79
M14	109.41
MDA-MB-435	102.09
SK-MEL-2	104.31
SK-MEL-28	108.41
SK-MEL-5	100.69
UACC-257	96.88
UACC-62	99.43
Ovarian Cancer	
IGROV1	107.30
OVCAR-3	117.73
OVCAR-4	109.35
OVCAR-5	100.99
OVCAR-8	107.81
NCI/ADR-RES	109.23
SK-OV-3	105.16
Renal Cancer	
786-0	101.84
ACHN	102.04
CAKI-1	99.76
RXF 393	105.72
SN12C	101.92
TK-10	95.77
UO-31	98.75
Prostate Cancer	
PC-3	100.64
DU-145	106.76
Breast Cancer	
MCF7	92.89
MDA-MB-231/ATCC	104.63
HS 578T	104.20
BT-549	108.81
T-47D	99.84
MDA-MB-468	98.44
Mean	103.84
Delta	24.44
Range	38.33

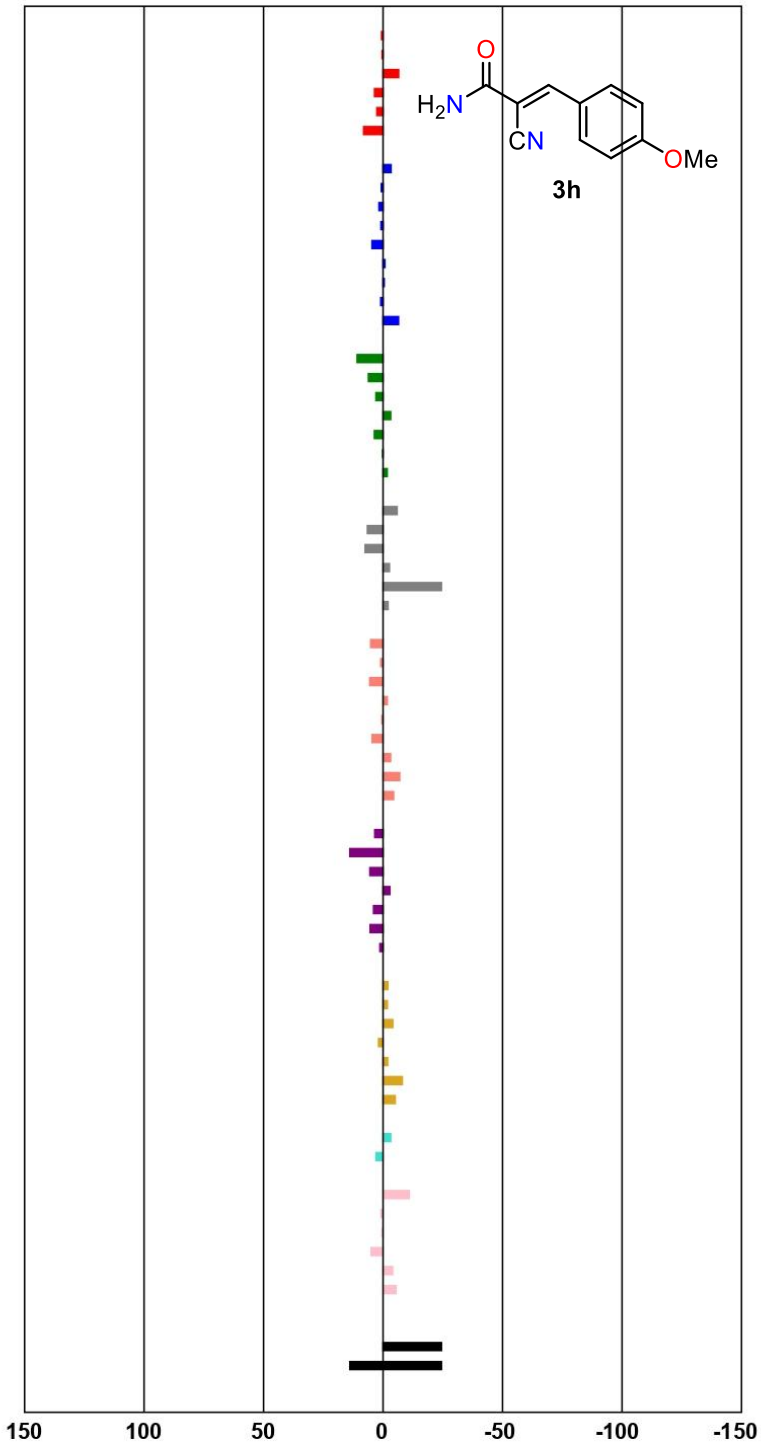


Table S9. Mean growth, %GI, and lethality values displayed by the tested compound **3i** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-826731 / 1	**Conc:** 1.00E-5 Molar	**Test Date:** Nov 02, 2020
Experiment ID: 2011OS61		**Report Date:** Nov 26, 2020

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	107.02
HL-60(TB)	99.02
K-562	98.17
MOLT-4	105.31
RPMI-8226	111.67
SR	114.83
Non-Small Cell Lung Cancer	
A549/ATCC	103.79
EKVX	107.00
HOP-62	104.60
HOP-92	114.03
NCI-H226	99.35
NCI-H23	98.72
NCI-H322M	102.43
NCI-H460	105.62
NCI-H522	97.82
Colon Cancer	
COLO 205	115.20
HCC-2998	104.86
HCT-116	100.49
HCT-15	102.59
HT29	107.27
KM12	99.28
SW-620	102.27
CNS Cancer	
SF-268	101.14
SF-295	107.61
SF-539	103.51
SNB-19	101.28
SNB-75	75.22
U251	102.77
Melanoma	
LOX IMVI	102.51
MALME-3M	98.62
M14	99.17
MDA-MB-435	102.83
SK-MEL-2	106.21
SK-MEL-28	105.76
SK-MEL-5	100.46
UACC-257	103.17
UACC-62	99.55
Ovarian Cancer	
IGROV1	109.93
OVCAR-3	108.35
OVCAR-4	103.28
OVCAR-5	103.97
OVCAR-8	108.07
NCI/ADR-RES	104.38
SK-OV-3	105.96
Renal Cancer	
786-0	102.53
ACHN	105.25
CAKI-1	99.63
RXF 393	98.25
SN12C	100.10
TK-10	94.74
UO-31	97.09
Prostate Cancer	
PC-3	102.33
DU-145	113.55
Breast Cancer	
MCF7	97.01
MDA-MB-231/ATCC	108.84
HS 578T	104.27
BT-549	109.86
T-47D	96.37
MDA-MB-468	94.17
Mean	103.04
Delta	27.82
Range	39.98

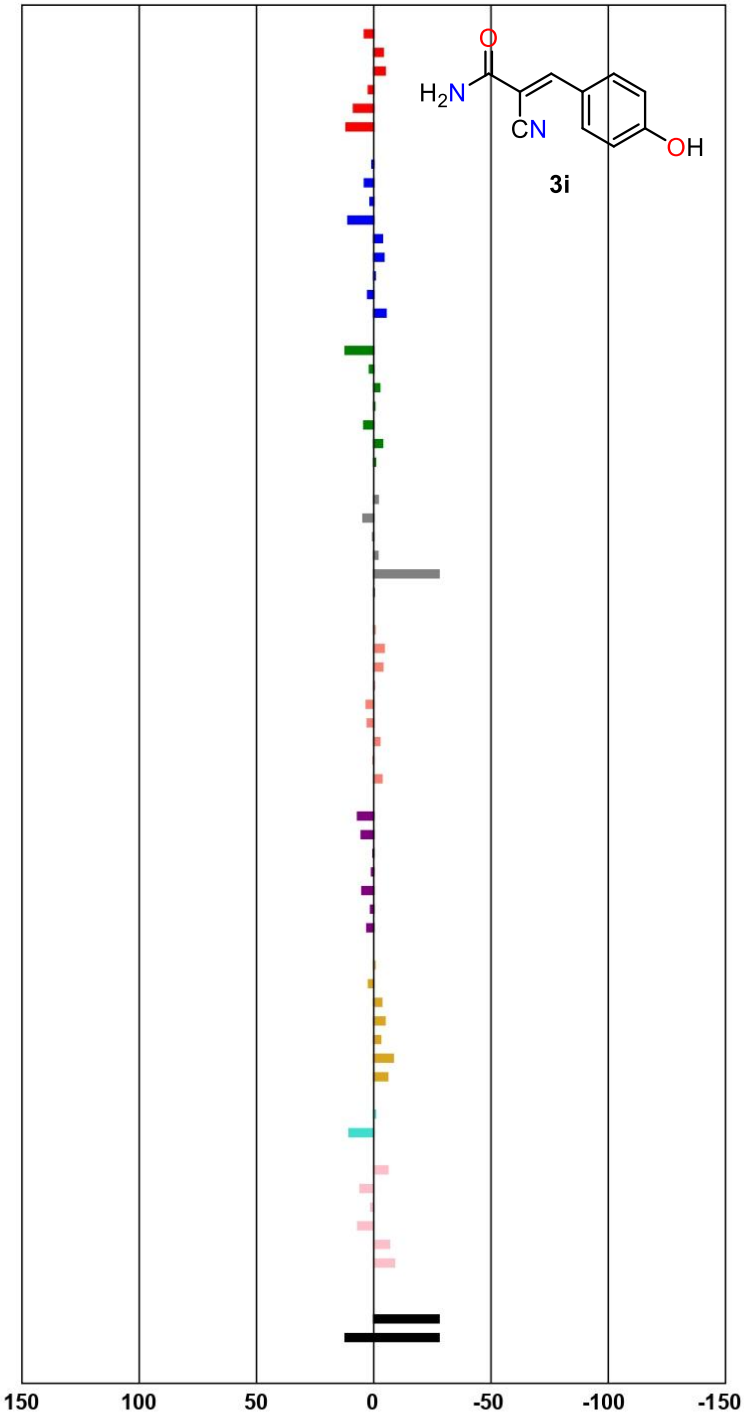


Table S10. Mean growth, %GI, and lethality values displayed by the tested compound **3j** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program
One Dose Mean Graph

NSC: D-835695 / 1	Conc: 1.00E-5 Molar	Test Date: Feb 28, 2022
Experiment ID: 2202OS75		Report Date: Mar 18, 2022

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	90.86
HL-60(TB)	97.22
K-562	93.30
MOLT-4	97.96
RPMI-8226	95.95
SR	91.42
Non-Small Cell Lung Cancer	
A549/ATCC	104.17
EKVX	96.08
HOP-62	96.91
HOP-92	113.08
NCI-H226	97.99
NCI-H23	97.48
NCI-H322M	100.96
NCI-H460	105.43
NCI-H522	85.01
Colon Cancer	
COLO 205	107.35
HCC-2998	109.83
HCT-116	97.23
HCT-15	96.89
HT29	102.75
KM12	98.42
SW-620	103.16
CNS Cancer	
SF-268	104.18
SF-295	100.10
SF-539	101.99
SNB-19	94.41
SNB-75	78.09
U251	101.71
Melanoma	
LOX IMVI	96.56
MALME-3M	103.75
M14	96.29
MDA-MB-435	99.11
SK-MEL-2	100.47
SK-MEL-28	107.77
SK-MEL-5	100.80
UACC-257	107.43
UACC-62	88.91
Ovarian Cancer	
IGROV1	109.93
OVCAR-3	107.78
OVCAR-4	100.59
OVCAR-5	102.51
OVCAR-8	102.96
NCI/ADR-RES	104.10
SK-OV-3	111.31
Renal Cancer	
786-0	91.63
A498	92.45
ACHN	104.19
CAKI-1	97.11
SN12C	106.06
TK-10	97.31
UO-31	85.63
Prostate Cancer	
PC-3	94.59
DU-145	107.16
Breast Cancer	
MCF7	95.74
MDA-MB-231/ATCC	101.58
HS 578T	103.27
BT-549	92.83
T-47D	95.12
MDA-MB-468	100.86
Mean	99.42
Delta	21.33
Range	34.99

Mean Growth Percent - Growth Percent

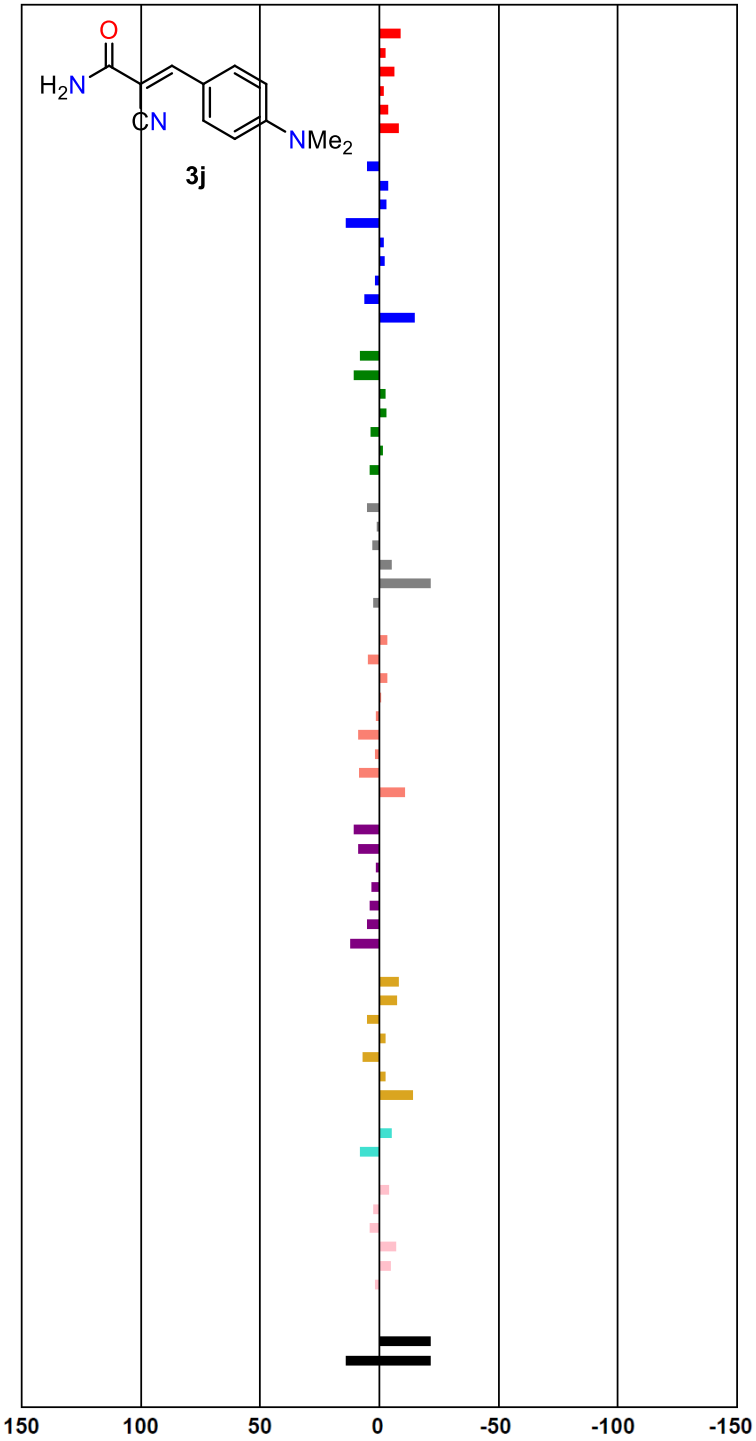


Table S11. Mean growth, %GI, and lethality values displayed by the tested compound **3k** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program
One Dose Mean Graph

NSC: D-835696 / 1 | **Conc:** 1.00E-5 Molar | **Test Date:** Feb 28, 2022
Experiment ID: 2202OS75 | **Report Date:** Mar 18, 2022

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	96.20
HL-60(TB)	95.05
K-562	85.80
MOLT-4	99.45
RPMI-8226	98.28
SR	88.77
Non-Small Cell Lung Cancer	
A549/ATCC	92.79
EKVX	85.98
HOP-62	94.42
HOP-92	89.07
NCI-H226	82.64
NCI-H23	95.83
NCI-H322M	86.81
NCI-H460	98.46
NCI-H522	78.35
Colon Cancer	
COLO 205	108.72
HCC-2998	102.90
HCT-116	94.08
HCT-15	88.29
HT29	98.27
KM12	93.77
SW-620	100.59
CNS Cancer	
SF-268	94.93
SF-295	89.25
SF-539	87.45
SNB-19	87.99
SNB-75	65.48
U251	95.83
Melanoma	
LOX IMVI	84.87
MALME-3M	92.26
M14	102.72
MDA-MB-435	98.15
SK-MEL-2	102.04
SK-MEL-28	95.75
SK-MEL-5	97.61
UACC-257	107.49
UACC-62	80.83
Ovarian Cancer	
IGROV1	89.22
OVCAR-3	91.51
OVCAR-4	83.50
OVCAR-5	97.39
OVCAR-8	93.90
NCI/ADR-RES	96.94
SK-OV-3	92.27
Renal Cancer	
786-0	90.29
A498	80.85
ACHN	89.32
CAKI-1	89.62
SN12C	85.63
TK-10	92.31
UO-31	55.80
Prostate Cancer	
PC-3	100.77
DU-145	104.95
Breast Cancer	
MCF7	80.31
MDA-MB-231/ATCC	91.95
HS 578T	76.86
BT-549	86.81
T-47D	51.06
MDA-MB-468	83.26
Mean	90.54
Delta	39.48
Range	57.66

Mean Growth Percent - Growth Percent

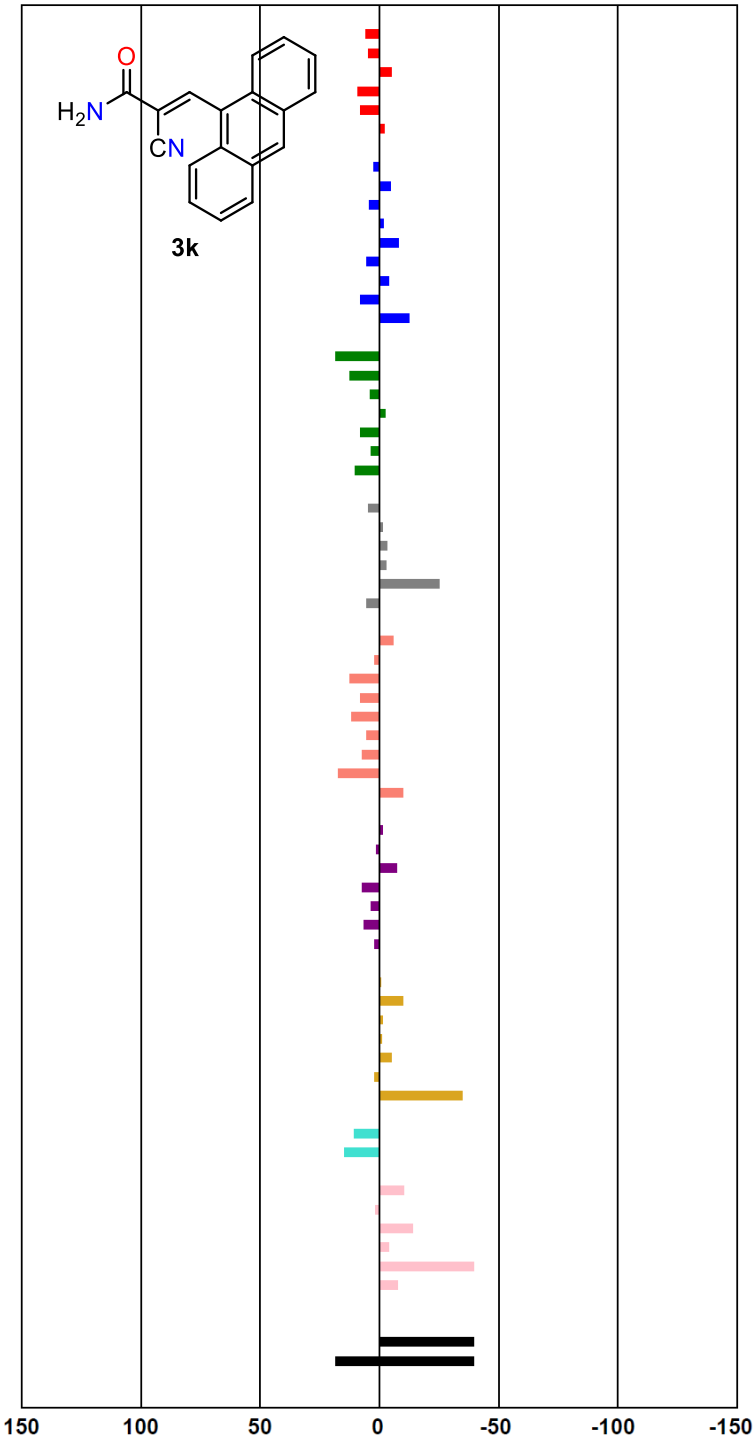


Table S12. Mean growth, %GI, and lethality values displayed by the tested compound **3l** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-835699 / 1	Conc: 1.00E-5 Molar	Test Date: Feb 28, 2022
Experiment ID: 2202OS75		Report Date: Mar 18, 2022

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	98.97
HL-60(TB)	103.02
K-562	103.76
MOLT-4	109.57
RPMI-8226	103.16
SR	97.17
Non-Small Cell Lung Cancer	
A549/ATCC	108.52
EKVX	101.32
HOP-62	96.80
HOP-92	129.97
NCI-H226	101.02
NCI-H23	105.49
NCI-H322M	101.31
NCI-H460	113.17
NCI-H522	91.18
Colon Cancer	
COLO 205	121.73
HCC-2998	120.51
HCT-116	104.30
HCT-15	101.93
HT29	108.68
KM12	101.19
SW-620	106.53
CNS Cancer	
SF-268	107.33
SF-295	102.97
SF-539	101.61
SNB-19	99.70
SNB-75	96.66
U251	108.46
Melanoma	
LOX IMVI	102.19
MALME-3M	108.65
M14	107.81
MDA-MB-435	107.83
SK-MEL-2	108.18
SK-MEL-28	104.98
SK-MEL-5	100.30
UACC-257	106.84
UACC-62	96.98
Ovarian Cancer	
IGROV1	113.67
OVCAR-3	114.77
OVCAR-4	100.10
OVCAR-5	109.79
OVCAR-8	109.03
NCI/ADR-RES	109.07
SK-OV-3	100.07
Renal Cancer	
786-0	96.11
A498	112.71
ACHN	107.07
CAKI-1	98.94
SN12C	104.84
TK-10	106.55
UO-31	88.18
Prostate Cancer	
PC-3	115.90
DU-145	107.66
Breast Cancer	
MCF7	97.29
MDA-MB-231/ATCC	101.12
HS 578T	108.17
BT-549	110.58
T-47D	95.89
MDA-MB-468	109.68
Mean	105.20
Delta	17.02
Range	41.79

Mean Growth Percent - Growth Percent

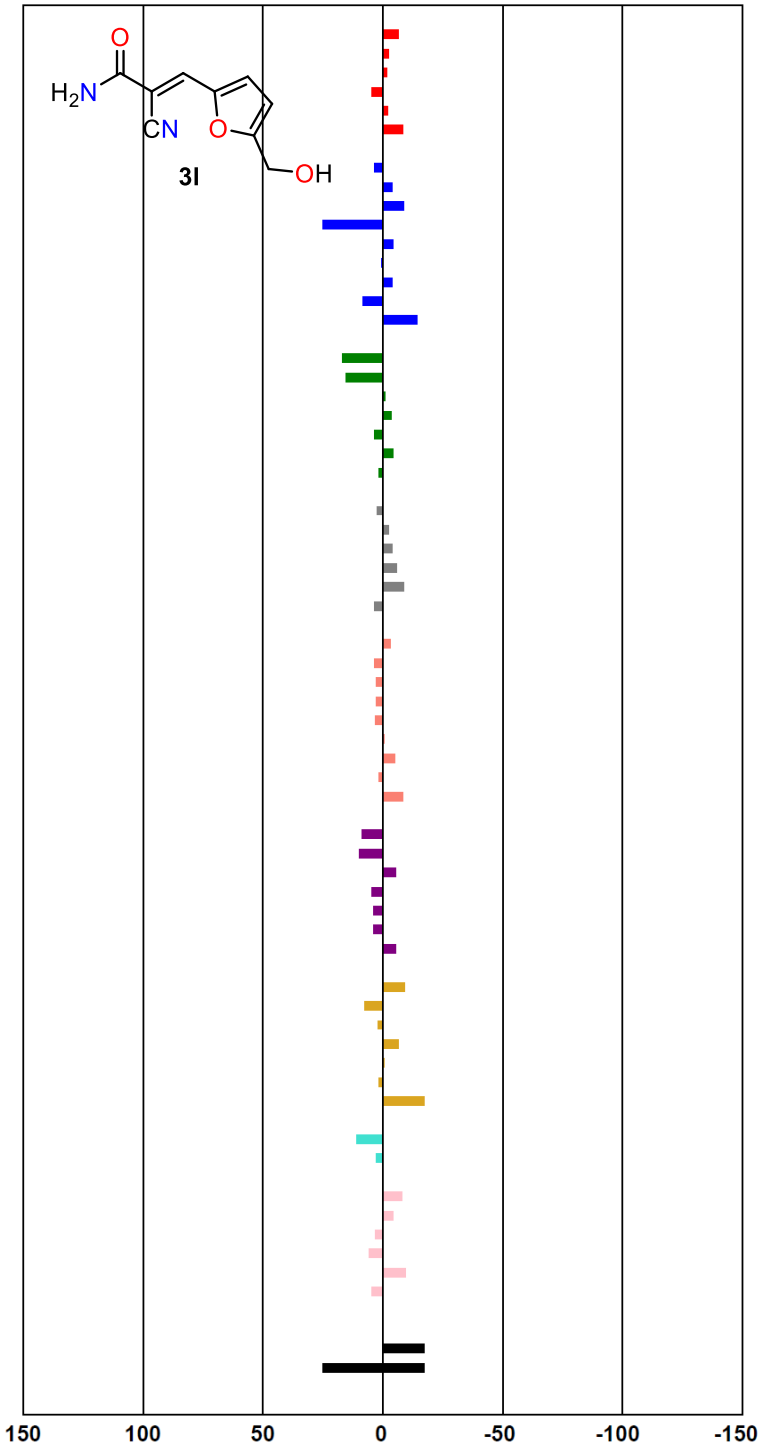


Table S13. Mean growth, %GI, and lethality values displayed by the tested compound **3m** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-826737 / 1	Conc: 1.00E-5 Molar	Test Date: Nov 02, 2020
Experiment ID: 2011OS61		Report Date: Nov 26, 2020

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	57.04
HL-60(TB)	26.60
K-562	31.85
MOLT-4	74.59
RPMI-8226	41.91
SR	53.29
Non-Small Cell Lung Cancer	
A549/ATCC	74.54
EKVX	59.81
HOP-62	95.88
HOP-92	34.81
NCI-H226	65.32
NCI-H23	74.48
NCI-H322M	79.60
NCI-H460	89.00
NCI-H522	46.54
Colon Cancer	
COLO 205	81.32
HCC-2998	85.66
HCT-116	52.25
HCT-15	36.65
HT29	77.39
KM12	85.21
SW-620	52.23
CNS Cancer	
SF-268	84.85
SF-295	71.87
SF-539	55.59
SNB-19	77.92
SNB-75	62.41
U251	68.71
Melanoma	
LOX IMVI	57.36
MALME-3M	82.01
M14	70.35
MDA-MB-435	69.58
SK-MEL-2	87.35
SK-MEL-28	70.04
SK-MEL-5	95.43
UACC-257	68.31
UACC-62	85.29
Ovarian Cancer	
IGROV1	59.08
OVCAR-3	52.03
OVCAR-4	62.32
OVCAR-5	78.24
OVCAR-8	65.57
NCI/ADR-RES	57.10
SK-OV-3	116.51
Renal Cancer	
786-0	70.68
ACHN	59.41
CAKI-1	49.23
RXF 393	62.91
SN12C	45.31
TK-10	67.91
UO-31	57.56
Prostate Cancer	
PC-3	70.41
DU-145	39.73
Breast Cancer	
MCF7	34.43
MDA-MB-231/ATCC	80.32
HS 578T	89.68
BT-549	58.08
T-47D	45.17
MDA-MB-468	3.10
Mean	64.54
Delta	61.44
Range	113.41

Mean Growth Percent - Growth Percent

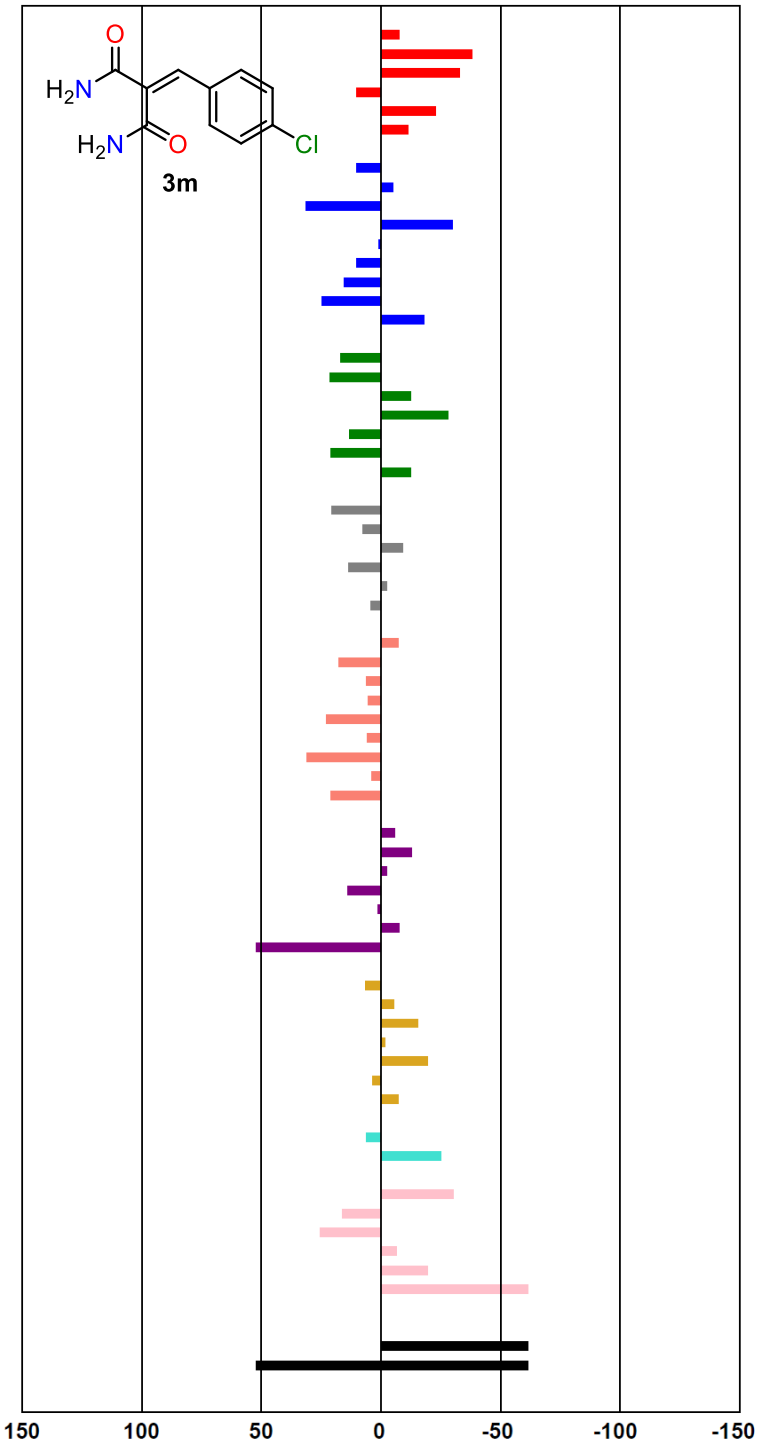


Table S14. Mean growth, %GI, and lethality values displayed by the tested compound **3n** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-843051 / 1	Conc: 1.00E-5 Molar	Test Date: Mar 20, 2023
Experiment ID: 2303OS10		Report Date: May 05, 2023

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	1.33
HL-60(TB)	-7.34
K-562	9.42
MOLT-4	5.40
RPMI-8226	-29.27
SR	0.10
Non-Small Cell Lung Cancer	
A549/ATCC	-40.26
EKVX	-68.27
HOP-62	-63.95
HOP-92	-47.62
NCI-H226	-82.44
NCI-H23	-80.93
NCI-H460	-31.40
NCI-H522	-83.07
Colon Cancer	
COLO 205	-55.51
HCC-2998	-95.34
HCT-116	-77.96
HCT-15	-80.15
HT29	-51.12
KM12	-87.50
SW-620	-63.43
CNS Cancer	
SF-268	-35.42
SF-295	-85.31
SF-539	-96.05
SNB-19	-96.36
SNB-75	-71.83
U251	-85.67
Melanoma	
LOX IMVI	-92.59
MALME-3M	-13.49
M14	-77.68
MDA-MB-435	-45.06
SK-MEL-2	-72.39
SK-MEL-28	-93.79
SK-MEL-5	-97.96
UACC-257	-78.18
UACC-62	-77.77
Ovarian Cancer	
IGROV1	-72.53
OVCAR-3	-71.57
OVCAR-4	-25.36
OVCAR-5	-83.09
OVCAR-8	-69.43
NCI/ADR-RES	-60.84
SK-OV-3	37.15
Renal Cancer	
786-0	-83.25
A498	-93.71
ACHN	-97.69
CAKI-1	-94.89
RXF 393	-90.46
SN12C	-89.48
TK-10	-93.14
UO-31	-93.05
Prostate Cancer	
PC-3	-31.57
DU-145	-90.11
Breast Cancer	
MCF7	-84.45
MDA-MB-231/ATCC	-79.69
HS 578T	-8.40
BT-549	-68.02
T-47D	-63.24
MDA-MB-468	-86.57
Mean	-63.43
Delta	34.53
Range	135.11

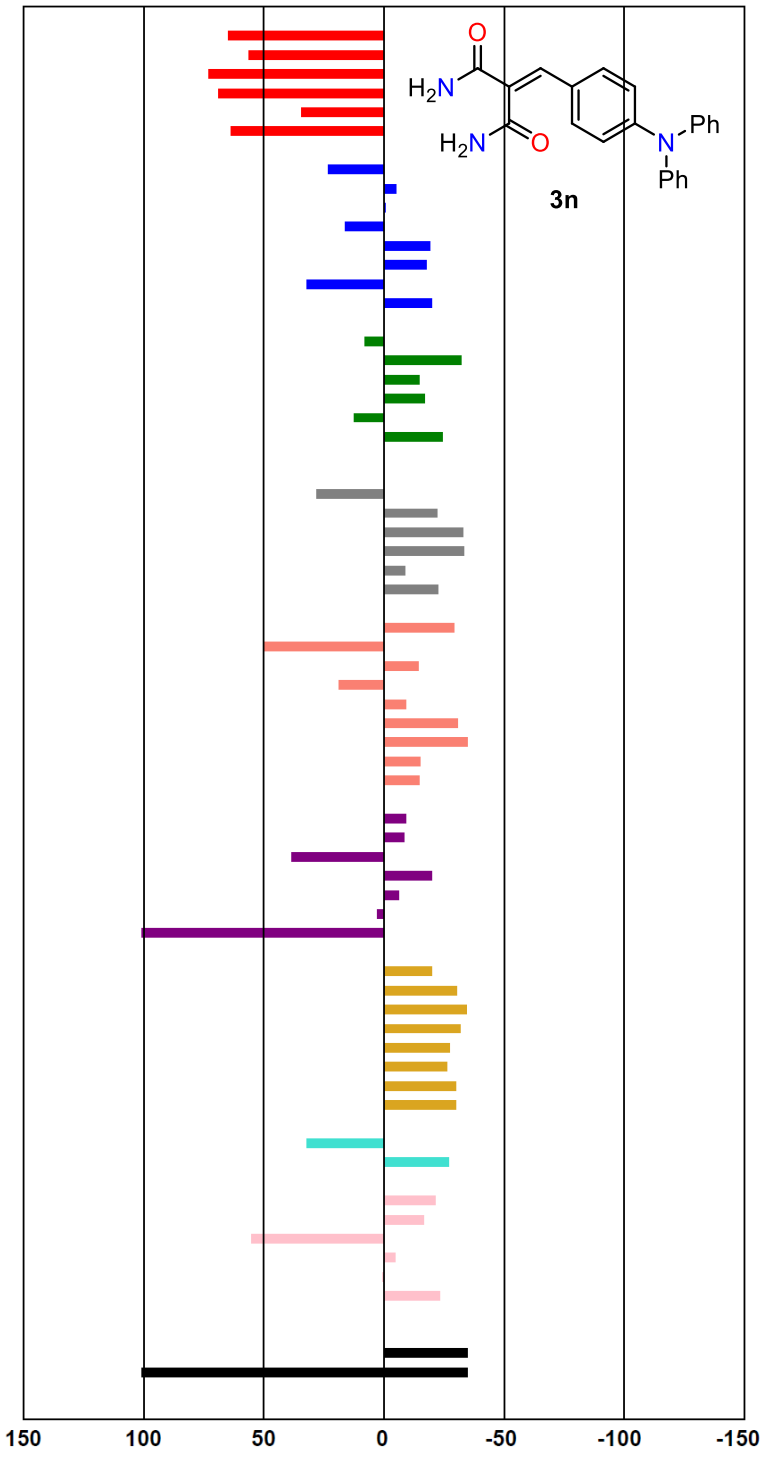


Table S15. GI_{50}, TGI, and LC_{50} values displayed by the tested compound **3n** against 60 NCI human cancer cell lines.

National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

NSC : D - 843051 / 1	Experiment ID : 2308NS66	Test Type : 08	Units : Molar
Report Date : November 16, 2023	Test Date : August 28, 2023	QNS :	MC :
COMI : JCC-L12	Stain Reagent : SRB Dual-Pass Related	SSPL : 1C0F	

			Log10 Concentration												
	Time		Mean Optical Densities					Percent Growth							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.489	2.464	2.415	2.379	1.597	0.464	0.284	98	96	56	-5	-42	1.26E-6	8.25E-6	> 1.00E-4
HL-60(TB)	0.609	2.194	2.028	1.834	1.240	0.364	0.279	90	77	40	-40	-54	5.34E-7	3.14E-6	4.99E-5
K-562	0.255	1.967	1.920	1.844	1.509	0.213	0.186	97	93	73	-16	-27	1.81E-6	6.55E-6	> 1.00E-4
MOLT-4	0.491	1.913	2.078	2.117	1.443	0.438	0.260	112	114	67	-11	-47	1.65E-6	7.26E-6	> 1.00E-4
RPMI-8226	0.768	2.318	2.336	2.092	1.121	0.559	0.535	101	85	23	-27	-30	3.67E-7	2.85E-6	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.294	1.894	1.843	1.840	1.438	0.150	0.024	97	97	72	-49	-92	1.51E-6	3.92E-6	1.06E-5
EKVX	0.960	2.525	2.398	2.415	2.425	1.885	0.005	92	93	94	59	-99	1.14E-5	2.36E-5	4.87E-5
HOP-62	0.633	2.575	2.275	2.204	2.019	0.556	0.198	85	81	71	-12	-69	1.80E-6	7.15E-6	4.66E-5
HOP-92	1.139	1.693	1.596	1.550	1.392	0.497	0.058	82	74	46	-56	-95	7.01E-7	2.80E-6	8.66E-6
NCI-H226	1.037	1.837	1.682	1.766	0.928	0.063	0.289	81	91	-11	-94	-72	2.54E-7	7.88E-7	2.97E-6
NCI-H23	0.591	1.939	1.859	1.892	1.745	0.283	0.057	94	97	86	-52	-90	1.81E-6	4.18E-6	9.65E-6
NCI-H322M	0.811	2.097	1.962	2.015	1.763	0.287	0.009	89	94	74	-65	-99	1.49E-6	3.42E-6	7.85E-6
NCI-H460	0.259	2.666	2.644	2.579	1.407	0.045	0.062	99	96	48	-83	-76	8.97E-7	2.32E-6	5.60E-6
NCI-H522	1.295	3.072	2.915	2.946	2.656	0.219	0.073	91	93	77	-83	-94	1.47E-6	3.02E-6	6.20E-6
Colon Cancer															
COLO 205	0.551	2.416	2.545	2.706	2.404	0.403	0.205	107	116	99	-27	-63	2.46E-6	6.12E-6	4.40E-5
HCC-2998	0.668	2.609	2.388	2.410	2.314	0.017	0.017	89	90	85	-98	-97	1.55E-6	2.92E-6	5.49E-6
HCT-116	0.301	2.604	2.703	2.802	2.078	0.201	0.311	104	109	77	-33	0	1.76E-6	.	> 1.00E-4
HCT-15	0.311	2.374	2.211	2.317	1.802	0.103	0.023	92	97	72	-67	-93	1.45E-6	3.30E-6	7.55E-6
HT29	0.217	1.653	1.534	1.636	1.400	0.075	0.051	92	99	82	-65	-77	1.66E-6	3.61E-6	7.86E-6
KM12	0.494	2.644	2.420	2.447	1.684	0.052	0.038	90	91	55	-89	-92	1.09E-6	2.41E-6	5.34E-6
SW-620	0.268	2.034	1.937	1.906	1.754	0.064	0.052	94	93	84	-76	-81	1.63E-6	3.35E-6	6.86E-6
CNS Cancer															
SF-268	1.072	2.818	2.679	2.701	2.516	0.594	0.207	92	93	83	-45	-81	1.81E-6	4.46E-6	1.41E-5
SF-295	1.309	3.224	3.081	3.111	2.987	1.022	0.005	92	94	88	-22	-100	2.20E-6	6.31E-6	2.30E-5
SF-539	0.818	2.411	2.403	2.396	1.628	0.007	.	100	99	51	-99	-100	1.01E-6	2.18E-6	4.70E-6
SNB-19	0.564	1.957	1.844	1.875	1.548	0.017	0.002	92	94	71	-97	-100	1.33E-6	2.64E-6	5.24E-6
SNB-75	1.773	2.738	2.429	2.454	2.232	0.241	0.016	68	71	48	-86	-99	7.85E-7	2.27E-6	5.35E-6
U251	0.353	1.788	1.666	1.679	1.295	0.011	0.004	92	92	66	-97	-99	1.25E-6	2.53E-6	5.15E-6
Melanoma															
LOX IMVI	0.406	2.747	2.581	2.611	1.938	0.023	0.022	93	94	65	-94	-95	1.25E-6	2.57E-6	5.27E-6
MALME-3M	0.616	1.583	1.451	1.501	1.352	0.055	0.015	86	92	76	-91	-98	1.43E-6	2.85E-6	5.67E-6
M14	0.601	2.440	2.422	2.332	2.206	0.358	0.095	99	94	87	-41	-84	1.96E-6	4.82E-6	1.65E-5
MDA-MB-435	0.676	2.937	2.847	2.861	2.490	0.193	0.011	96	97	80	-71	-98	1.58E-6	3.38E-6	7.22E-6
SK-MEL-2	0.850	1.983	1.957	1.936	1.666	0.169	0.031	98	96	72	-80	-96	1.40E-6	2.97E-6	6.34E-6
SK-MEL-28	0.751	2.018	1.998	2.074	1.931	0.078	0.008	98	104	93	-90	-99	1.72E-6	3.23E-6	6.07E-6
SK-MEL-5	0.904	3.189	2.935	3.027	2.828	0.229	0.007	89	93	84	-75	-99	1.64E-6	3.39E-6	6.99E-6
UACC-257	0.919	2.286	2.176	2.197	1.872	0.182	0.015	92	93	70	-80	-98	1.35E-6	2.92E-6	6.28E-6
UACC-62	0.974	2.777	2.632	2.574	2.153	0.124	0.004	92	89	65	-87	-100	1.26E-6	2.68E-6	5.70E-6
Ovarian Cancer															
IGROV1	0.436	1.889	1.882	1.844	1.475	0.075	0.032	100	97	71	-83	-93	1.38E-6	2.91E-6	6.13E-6
OVCAR-3	0.626	2.010	1.950	1.959	1.606	0.079	0.022	96	96	71	-87	-97	1.35E-6	2.80E-6	5.80E-6
OVCAR-4	0.715	1.832	1.763	1.846	1.663	0.596	0.055	94	101	85	-17	-92	2.20E-6	6.85E-6	2.76E-5
OVCAR-5	0.447	1.574	1.596	1.590	1.457	0.224	0.027	102	101	90	-50	-94	1.92E-6	4.38E-6	1.00E-5
OVCAR-8	0.337	1.777	1.778	1.762	1.486	0.133	0.010	100	99	80	-61	-97	1.63E-6	3.70E-6	8.41E-6
NCI/ADR-RES	0.357	1.343	1.324	1.342	1.126	0.117	0.070	98	100	78	-67	-81	1.56E-6	3.44E-6	7.59E-6
SK-OV-3	0.838	1.838	1.789	1.864	1.835	1.490	0.127	95	103	100	65	-85	1.26E-5	2.72E-5	5.85E-5
Renal Cancer															
786-0	0.777	2.966	2.936	2.910	3.021	0.310	0.352	99	97	103	-60	-55	2.10E-6	4.27E-6	8.66E-6
A498	1.209	2.195	2.056	2.125	2.087	0.012	0.153	86	93	89	-99	-87	1.61E-6	2.98E-6	5.49E-6
ACHN	0.374	1.690	1.630	1.737	1.507	0.006	-0.003	95	104	86	-98	-100	1.57E-6	2.93E-6	5.47E-6
CAKI-1	0.495	1.702	1.530	1.469	1.053	0.015	0.011	86	81	46	-97	-98	7.76E-7	2.10E-6	4.70E-6
RXF 393	0.750	1.520	1.430	1.497	1.347	0.031	0.043	88	97	78	-96	-94	1.44E-6	2.80E-6	5.44E-6
SN12C	0.631	2.211	2.180	2.024	1.712	0.146	0.017	98	88	68	-77	-97	1.34E-6	2.96E-6	6.53E-6
TK-10	1.084	2.111	1.995	2.067	2.307	0.056	0.016	89	96	119	-95	-99	2.10E-6	3.60E-6	6.17E-6
UO-31	0.664	2.019	1.774	1.720	1.478	0.002	0.005	82	78	60	-100	-99	1.16E-6	2.38E-6	4.88E-6
Prostate Cancer															
PC-3	0.562	2.237	2.108	2.161	1.698	0.381	0.078	92	95	68	-32	-86	1.51E-6	4.76E-6	2.14E-5
DU-145	0.375	1.687	1.683	1.682	1.147	0.003	0.005	100	100	59	-99	-99	1.14E-6	2.36E-6	4.88E-6
Breast Cancer															
MCF7	0.450	2.333	2.121	2.023	0.957	0.150	0.162	89	84	27	-67	-64	3.91E-7	1.94E-6	6.64E-6
MDA-MB-231/ATCC	0.566	1.140	1.116	1.129	1.028	0.130	0.002	96	98	80	-77	-100	1.56E-6	3.24E-6	6.73E-6
HS 578T	1.374	2.576	2.368	2.431	2.279	1.346	1.088	83	88	75	-2	-21	2.12E-6	9.41E-6	> 1.00E-4
BT-549	1.398	2.732	2.734	2.655	2.489	0.687	0.328	100	94	82	-51	-77	1.74E-6	4.14E-6	9.85E-6
T-47D	0.747	2.001	1.800	1.581	1.116	0.329	0.264	84	67	29	-56	-65	2.79E-7	2.21E-6	8.50E-6
MDA-MB-468	0.773	1.552	1.463	1.484	0.789	0.075	0.057	89	91	2	-90	-93	2.90E-7	1.05E-6	3.66E-6

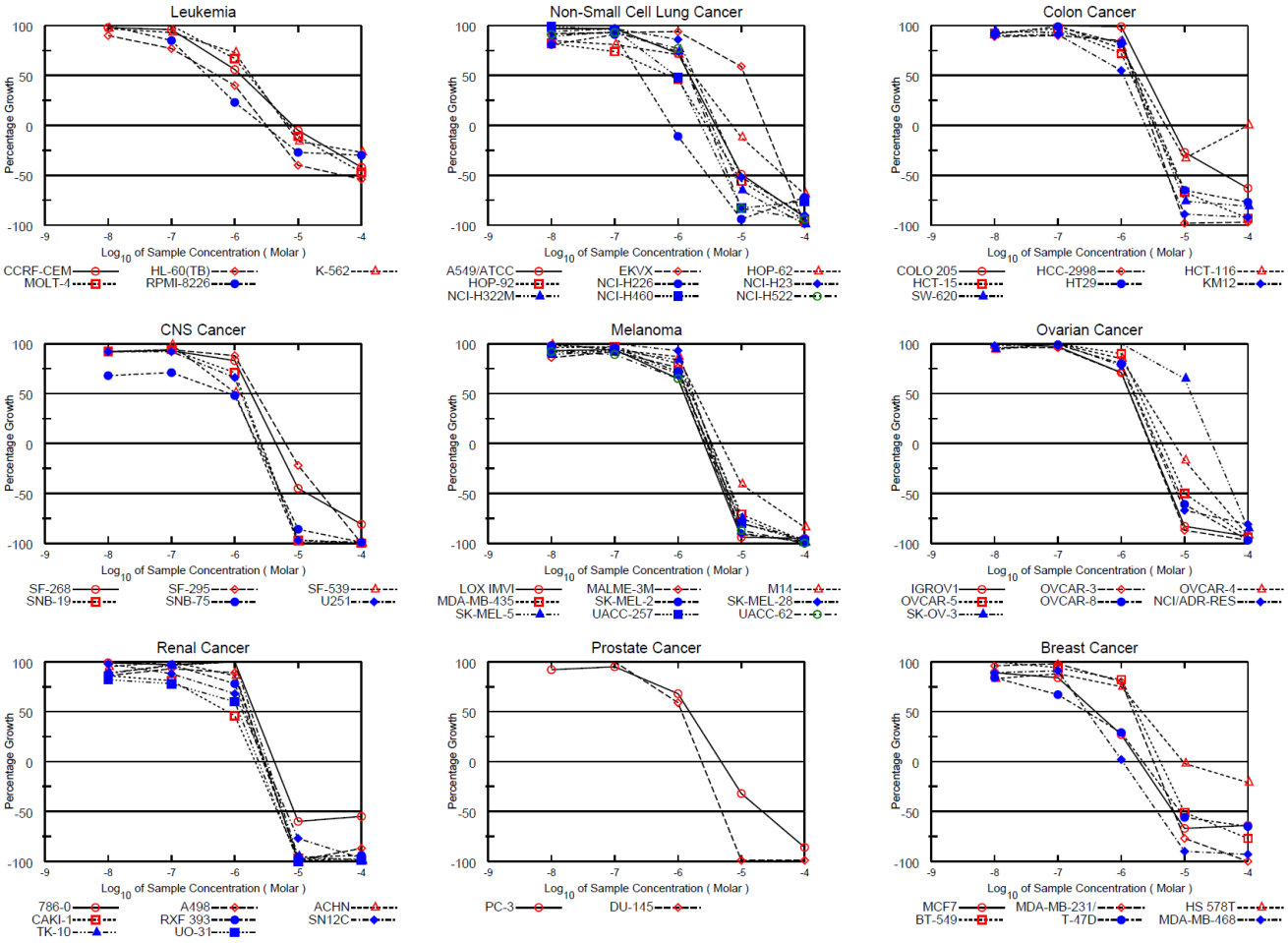

Leukemia
Percentage Growth
Log10 of Sample Concentration (Molar)
CCRF-CEM
HL-60(TB)
K-562
MOLT-4
RPMI-8226
Non-Small Cell Lung Cancer
A549/ATCC
EKVX
HOP-62
HOP-92
NCI-H226
NCI-H23
NCI-H322M
NCI-H460
NCI-H522
Colon Cancer
COLO 205
HCC-2998
HCT-116
HCT-15
HT29
KM12
SW-620
CNS Cancer
SF-268
SF-295
SF-539
SNB-19
SNB-75
U251
Melanoma
LOX IMVI
MALME-3M
M14
MDA-MB-435
SK-MEL-2
SK-MEL-28
SK-MEL-5
UACC-257
UACC-62
Ovarian Cancer
IGROV1
OVCAR-3
OVCAR-4
OVCAR-5
OVCAR-8
NCI/ADR-RES
SK-OV-3
Renal Cancer
786-0
A498
ACHN
CAKI-1
RXF 393
SN12C
TK-10
UO-31
Prostate Cancer
PC-3
DU-145
Breast Cancer
MCF7
MDA-MB-231/
HS 578T
BT-549
T-47D
MDA-MB-468

Table S16. Mean growth, %GI, and lethality values displayed by the tested compound **3o** against 60 NCI human cancer cell lines at 10 μM.

Developmental Therapeutics Program
One Dose Mean Graph

NSC: D-843050 / 1	Conc: 1.00E-5 Molar	Test Date: Mar 20, 2023
Experiment ID: 2303OS10		Report Date: May 05, 2023

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	58.05
HL-60(TB)	71.20
K-562	34.12
MOLT-4	64.38
RPMI-8226	35.59
SR	76.35
Non-Small Cell Lung Cancer	
A549/ATCC	45.05
EKVX	91.97
HOP-62	25.27
HOP-92	57.91
NCI-H226	-92.07
NCI-H23	42.38
NCI-H460	4.93
NCI-H522	69.12
Colon Cancer	
COLO 205	20.11
HCC-2998	71.00
HCT-116	8.52
HCT-15	63.81
HT29	32.57
KM12	97.10
SW-620	31.51
CNS Cancer	
SF-268	116.96
SF-295	8.51
SF-539	97.45
SNB-19	72.79
SNB-75	123.12
U251	50.18
Melanoma	
LOX IMVI	77.89
MALME-3M	59.59
M14	96.48
MDA-MB-435	93.66
SK-MEL-2	29.13
SK-MEL-28	93.36
SK-MEL-5	20.53
UACC-257	-71.20
UACC-62	-44.18
Ovarian Cancer	
IGROV1	-58.64
OVCAR-3	-20.85
OVCAR-4	-12.63
OVCAR-5	-76.11
OVCAR-8	89.47
NCI/ADR-RES	67.80
SK-OV-3	57.85
Renal Cancer	
786-0	36.45
A498	-95.45
ACHN	87.86
CAKI-1	-57.30
RXF 393	17.61
SN12C	75.48
TK-10	-67.37
UO-31	53.97
Prostate Cancer	
PC-3	73.77
DU-145	108.33
Breast Cancer	
MCF7	1.09
MDA-MB-231/ATCC	83.37
HS 578T	107.16
BT-549	91.18
T-47D	-42.19
MDA-MB-468	-82.94
Mean	36.80
Delta	132.25
Range	218.57

Mean Growth Percent - Growth Percent

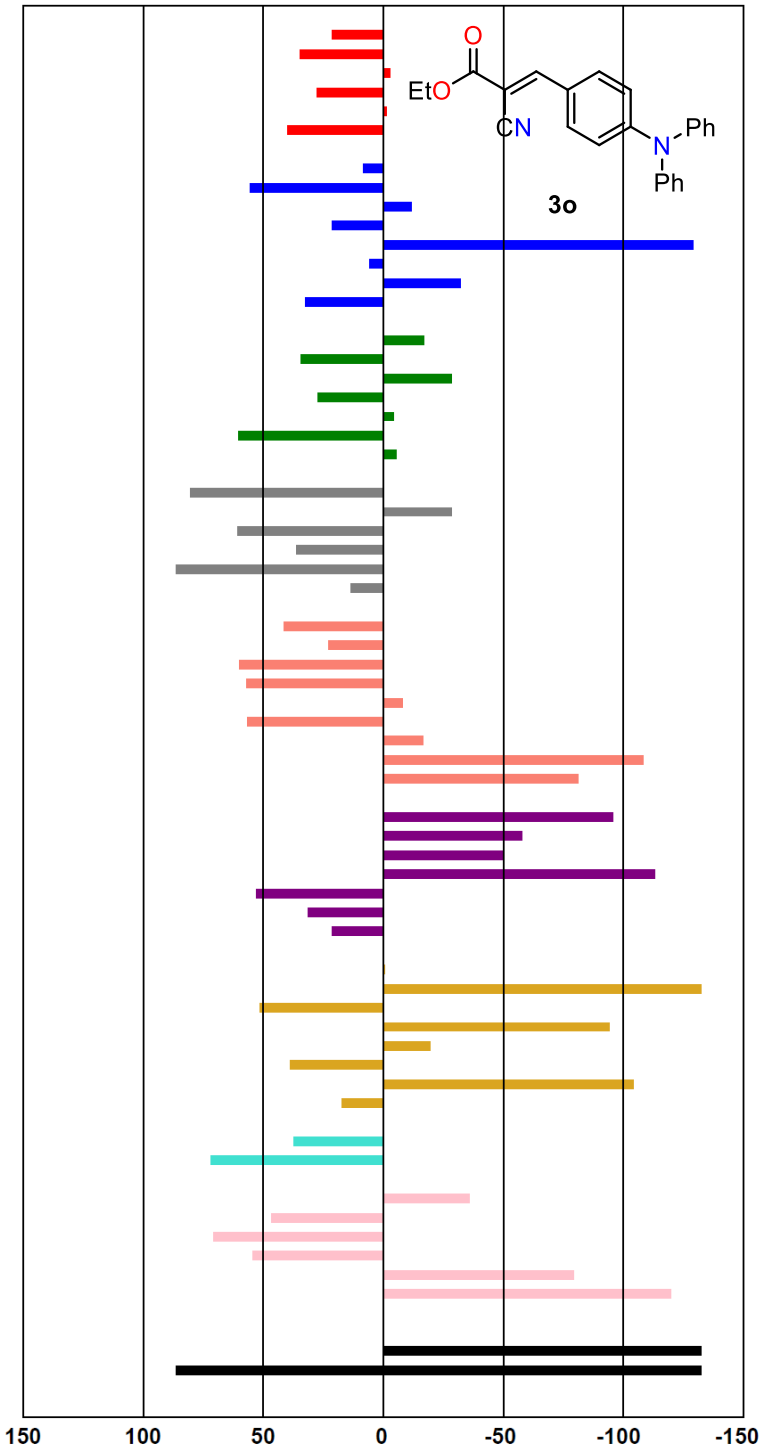
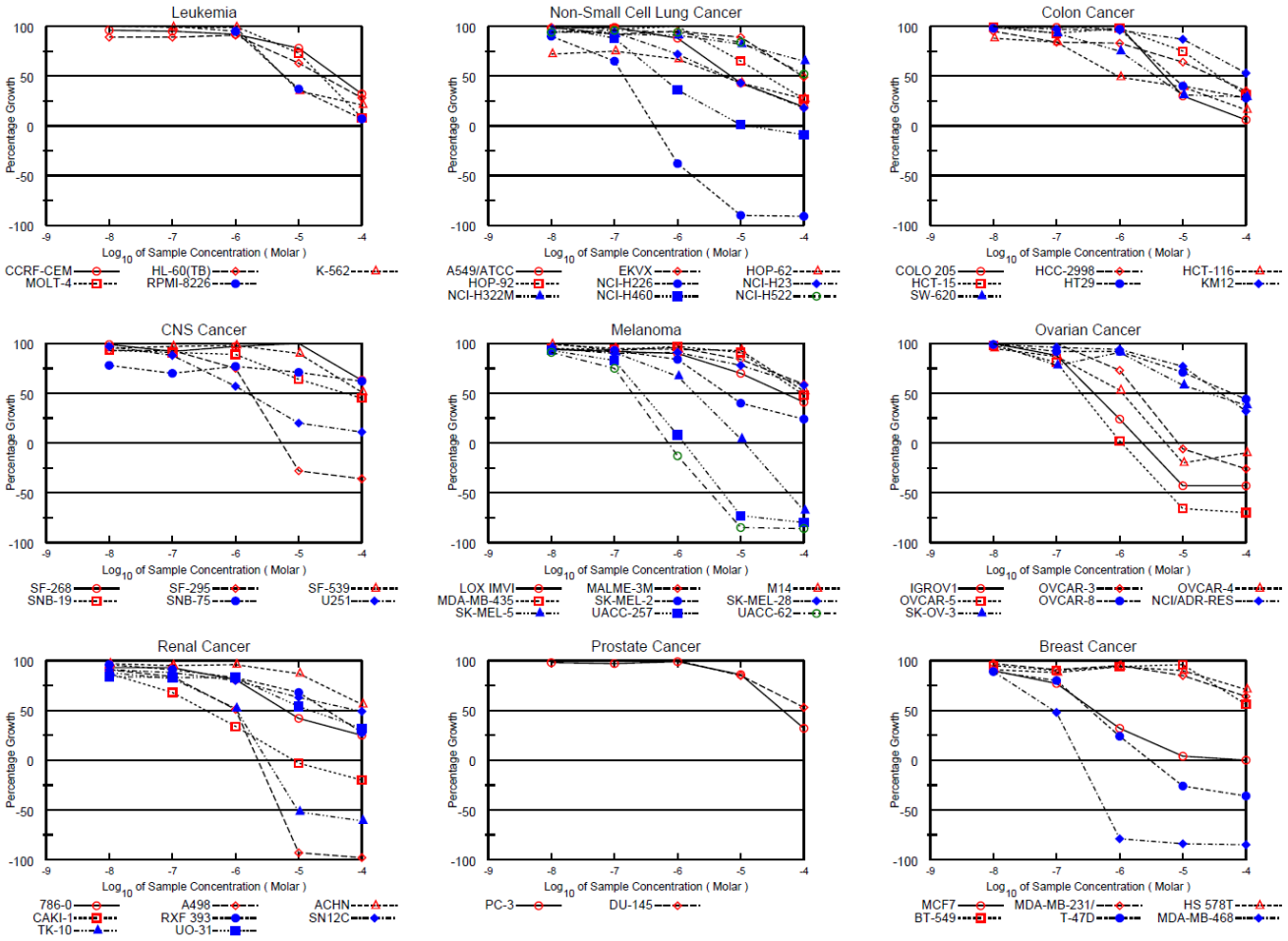


Table S17. GI_{50}, TGI, and LC_{50} values displayed by the tested compound **3o** against 60 NCI human cancer cell lines.

National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

NSC : D - 843050 / 1	Experiment ID : 2308NS66	Test Type : 08	Units : Molar
Report Date : November 16, 2023	Test Date : August 28, 2023	QNS :	MC :
COMI : JCC-K100	Stain Reagent : SRB Dual-Pass Related	SSPL : 1C0F	

			Log10 Concentration												
	Time		Mean Optical Densities					Percent Growth							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.489	2.464	2.378	2.358	2.300	2.023	1.123	96	95	92	78	32	4.04E-5	> 1.00E-4	> 1.00E-4
HL-60(TB)	0.609	2.194	2.018	2.023	2.044	1.609	1.060	89	89	91	63	28	2.39E-5	> 1.00E-4	> 1.00E-4
K-562	0.255	1.967	1.966	1.959	1.958	0.857	0.619	100	99	99	35	21	5.88E-6	> 1.00E-4	> 1.00E-4
MOLT-4	0.491	1.913	1.917	1.939	1.922	1.523	0.598	100	102	101	73	8	2.22E-5	> 1.00E-4	> 1.00E-4
RPMI-8226	0.768	2.318	2.314	2.322	2.244	1.337	0.871	100	100	95	37	7	5.93E-6	> 1.00E-4	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.294	1.894	1.870	1.876	1.703	0.982	0.604	98	99	88	43	19	6.99E-6	> 1.00E-4	> 1.00E-4
EKVX	0.960	2.525	2.507	2.402	2.440	2.357	1.726	99	92	95	89	49	9.41E-5	> 1.00E-4	> 1.00E-4
HOP-62	0.633	2.575	2.034	2.095	1.938	1.463	1.160	72	75	67	43	27	5.05E-6	> 1.00E-4	> 1.00E-4
HOP-92	1.139	1.693	1.693	1.676	1.707	1.498	1.291	100	97	103	65	27	2.48E-5	> 1.00E-4	> 1.00E-4
NCI-H226	1.037	1.837	1.755	1.555	0.647	0.104	0.089	90	65	-38	-90	-91	1.39E-7	4.29E-7	1.72E-6
NCI-H23	0.591	1.939	1.856	1.856	1.566	1.169	0.838	94	94	72	43	18	5.73E-6	> 1.00E-4	> 1.00E-4
NCI-H322M	0.811	2.097	2.051	1.998	1.978	1.860	1.652	96	92	91	82	65	> 1.00E-4	> 1.00E-4	> 1.00E-4
NCI-H460	0.259	2.666	2.809	2.373	1.137	0.284	0.236	106	88	36	1	-9	5.45E-7	1.27E-5	> 1.00E-4
NCI-H522	1.295	3.072	2.958	3.006	2.964	2.793	2.215	94	96	94	84	52	> 1.00E-4	> 1.00E-4	> 1.00E-4
Colon Cancer															
COLO 205	0.551	2.416	2.433	2.395	2.407	1.117	0.656	101	99	100	30	6	5.20E-6	> 1.00E-4	> 1.00E-4
HCC-2998	0.668	2.609	2.516	2.294	2.272	1.917	1.338	95	84	83	64	35	3.02E-5	> 1.00E-4	> 1.00E-4
HCT-116	0.301	2.604	2.337	2.247	1.428	1.203	0.670	88	84	49	39	16	9.33E-7	> 1.00E-4	> 1.00E-4
HCT-15	0.311	2.374	2.347	2.239	2.325	1.866	0.949	99	93	98	75	31	3.72E-5	> 1.00E-4	> 1.00E-4
HT29	0.217	1.653	1.622	1.652	1.616	0.787	0.618	98	100	97	40	28	6.62E-6	> 1.00E-4	> 1.00E-4
KM12	0.494	2.644	2.640	2.576	2.550	2.354	1.624	100	97	96	87	53	> 1.00E-4	> 1.00E-4	> 1.00E-4
SW-620	0.268	2.034	2.110	1.914	1.601	0.816	0.772	104	93	75	31	29	3.74E-6	> 1.00E-4	> 1.00E-4
CNS Cancer															
SF-268	1.072	2.818	2.797	2.679	2.768	2.909	2.179	99	92	97	105	63	> 1.00E-4	> 1.00E-4	> 1.00E-4
SF-295	1.309	3.224	3.091	3.095	2.739	0.946	0.843	93	93	75	-28	-36	1.74E-6	5.36E-6	> 1.00E-4
SF-539	0.818	2.411	2.327	2.366	2.377	2.251	1.635	95	97	98	90	51	> 1.00E-4	> 1.00E-4	> 1.00E-4
SNB-19	0.564	1.957	1.855	1.836	1.800	1.461	1.187	93	91	89	64	45	5.36E-5	> 1.00E-4	> 1.00E-4
SNB-75	1.773	2.738	2.522	2.450	2.517	2.458	2.371	78	70	77	71	62	> 1.00E-4	> 1.00E-4	> 1.00E-4
U251	0.353	1.788	1.748	1.622	1.175	0.646	0.516	97	88	57	20	11	1.58E-6	> 1.00E-4	> 1.00E-4
Melanoma															
LOX IMVI	0.406	2.747	2.605	2.570	2.522	2.041	1.375	94	92	90	70	41	4.98E-5	> 1.00E-4	> 1.00E-4
MALME-3M	0.616	1.583	1.529	1.512	1.549	1.432	1.191	94	93	96	84	59	> 1.00E-4	> 1.00E-4	> 1.00E-4
M14	0.601	2.440	2.417	2.352	2.324	2.304	1.560	99	95	94	93	52	> 1.00E-4	> 1.00E-4	> 1.00E-4
MDA-MB-435	0.676	2.937	2.835	2.805	2.872	2.734	1.772	95	94	97	91	48	9.21E-5	> 1.00E-4	> 1.00E-4
SK-MEL-2	0.850	1.983	1.998	1.909	1.807	1.307	1.118	101	93	84	40	24	6.03E-6	> 1.00E-4	> 1.00E-4
SK-MEL-28	0.751	2.018	1.955	1.891	1.903	1.742	1.482	95	90	91	78	58	> 1.00E-4	> 1.00E-4	> 1.00E-4
SK-MEL-5	0.904	3.189	3.079	2.988	2.444	0.991	0.294	95	91	67	4	-68	1.88E-6	1.13E-5	5.68E-5
UACC-257	0.919	2.286	2.192	2.057	1.023	0.251	0.182	93	83	8	-73	-80	2.75E-7	1.24E-6	5.21E-6
UACC-62	0.974	2.777	2.614	2.333	0.844	0.150	0.132	91	75	-13	-85	-86	1.93E-7	7.07E-7	3.27E-6
Ovarian Cancer															
IGROV1	0.436	1.889	1.882	1.709	0.784	0.250	0.247	100	88	24	-43	-43	3.90E-7	2.29E-6	> 1.00E-4
OVCAR-3	0.626	2.010	2.035	2.007	1.637	0.590	0.461	102	100	73	-6	-26	1.96E-6	8.43E-6	> 1.00E-4
OVCAR-4	0.715	1.832	1.773	1.686	1.306	0.575	0.646	95	87	53	-20	-10	1.09E-6	5.36E-6	> 1.00E-4
OVCAR-5	0.447	1.574	1.547	1.356	0.465	0.151	0.133	98	81	2	-66	-70	2.44E-7	1.05E-6	5.75E-6
OVCAR-8	0.337	1.777	1.770	1.660	1.666	1.363	0.972	99	92	92	71	44	6.06E-5	> 1.00E-4	> 1.00E-4
NCI/ADR-RES	0.357	1.343	1.331	1.302	1.279	1.115	0.673	99	96	94	77	32	3.98E-5	> 1.00E-4	> 1.00E-4
SK-OV-3	0.838	1.838	2.018	1.613	1.751	1.413	1.220	118	78	91	58	38	2.45E-5	> 1.00E-4	> 1.00E-4
Renal Cancer															
786-0	0.777	2.966	2.822	2.810	2.551	1.690	1.317	93	93	81	42	25	6.16E-6	> 1.00E-4	> 1.00E-4
A498	1.209	2.195	2.110	2.033	1.714	0.082	0.030	91	84	51	-93	-98	1.02E-6	2.26E-6	5.02E-6
ACHN	0.374	1.690	1.654	1.624	1.637	1.519	1.113	97	95	96	87	56	> 1.00E-4	> 1.00E-4	> 1.00E-4
CAKI-1	0.495	1.702	1.546	1.317	0.901	0.481	0.398	87	68	34	-3	-20	3.36E-7	8.37E-6	> 1.00E-4
RXF 393	0.750	1.520	1.492	1.450	1.390	1.277	0.967	96	91	83	68	28	2.87E-5	> 1.00E-4	> 1.00E-4
SN12C	0.631	2.211	2.075	2.027	1.900	1.626	1.403	91	88	80	63	49	8.31E-5	> 1.00E-4	> 1.00E-4
TK-10	1.084	2.111	1.986	1.925	1.619	0.516	0.420	88	82	52	-52	-61	1.05E-6	3.15E-6	9.48E-6
UO-31	0.664	2.019	1.796	1.784	1.794	1.391	1.098	84	83	83	54	32	1.47E-5	> 1.00E-4	> 1.00E-4
Prostate Cancer															
PC-3	0.562	2.237	2.200	2.188	2.220	2.009	1.091	98	97	99	86	32	4.61E-5	> 1.00E-4	> 1.00E-4
DU-145	0.375	1.687	1.715	1.683	1.686	1.496	1.076	102	100	100	85	53	> 1.00E-4	> 1.00E-4	> 1.00E-4
Breast Cancer															
MCF7	0.450	2.333	2.151	1.897	1.054	0.529	0.459	90	77	32	4	0	3.97E-7	> 1.00E-4	> 1.00E-4
MDA-MB-231/ATCC	0.566	1.140	1.121	1.087	1.113	1.056	0.936	97	91	95	85	64	> 1.00E-4	> 1.00E-4	> 1.00E-4
HS 578T	1.374	2.576	2.473	2.433	2.500	2.453	2.227	91	88	94	90	71	> 1.00E-4	> 1.00E-4	> 1.00E-4
BT-549	1.398	2.732	2.659	2.599	2.650	2.678	2.140	95	90	94	96	56	> 1.00E-4	> 1.00E-4	> 1.00E-4
T-47D	0.747	2.001	1.869	1.753	1.048	0.551	0.478	89	80	24	-26	-36	3.45E-7	3.01E-6	> 1.00E-4
MDA-MB-468	0.773	1.552	1.464	1.146	0.166	0.122	0.114	89	48	-79	-84	-85	8.87E-8	2.39E-7	5.95E-7


Leukemia
Non-Small Cell Lung Cancer
Colon Cancer
CNS Cancer
Melanoma
Ovarian Cancer
Renal Cancer
Prostate Cancer
Breast Cancer
Percentage Growth
Log10 of Sample Concentration (Molar)
CCRF-CEM
HL-60(TB)
K-562
MOLT-4
RPMI-8226
A549/ATCC
EKVX
HOP-62
HOP-92
NCI-H226
NCI-H23
NCI-H322M
NCI-H460
NCI-H522
COLO 205
HCC-2998
HCT-116
HCT-15
HT29
KM12
SW-620
SF-268
SF-295
SF-539
SNB-19
SNB-75
U251
LOX IMVI
MALME-3M
M14
MDA-MB-435
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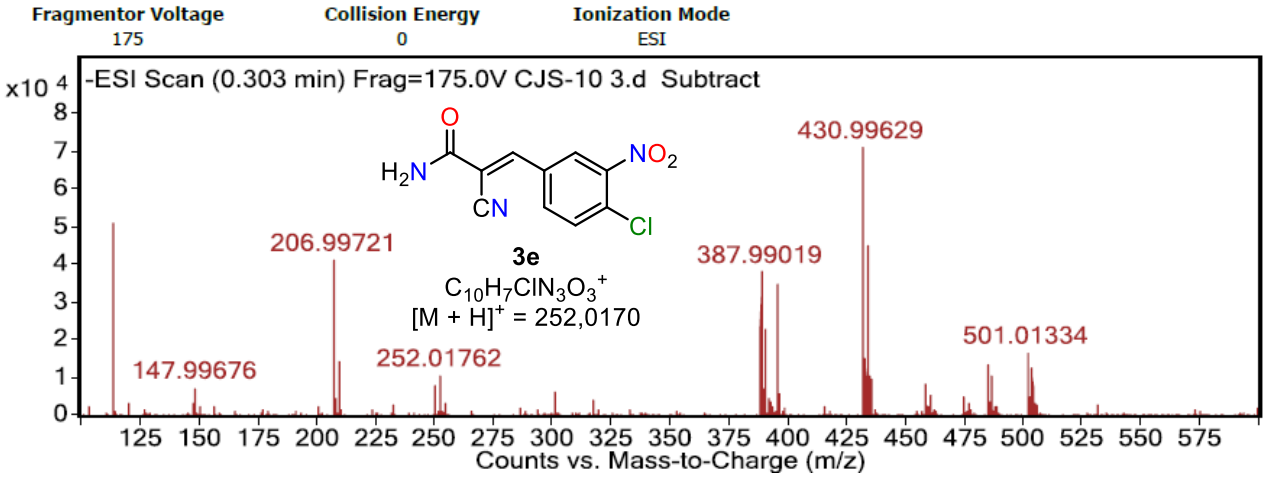
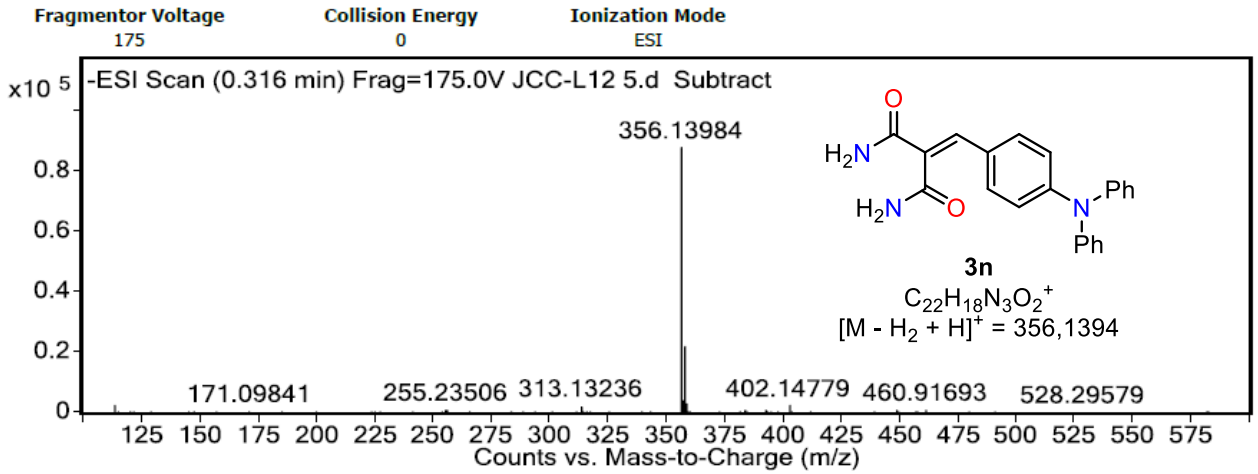
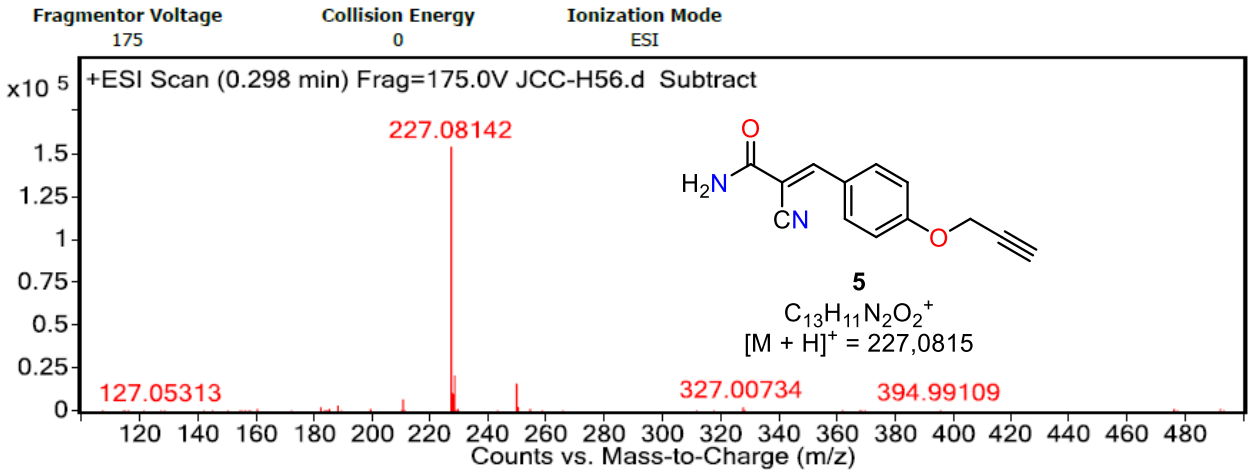
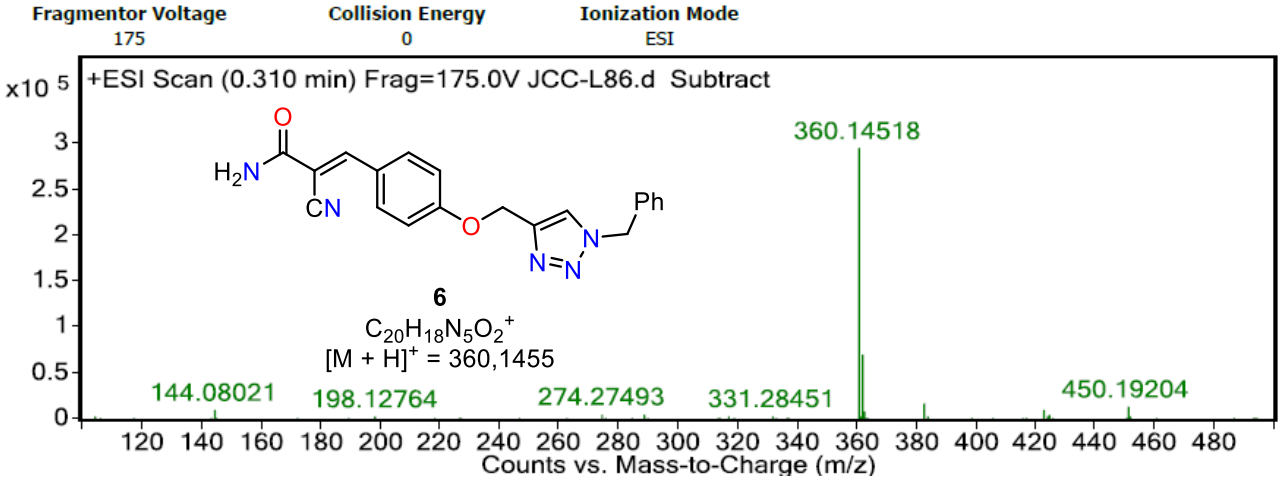
SK-MEL-28
SK-MEL-5
UACC-257
UACC-62
IGROV1
OVCAR-3
OVCAR-4
OVCAR-5
OVCAR-8
NCI/ADR-RES
SK-OV-3
786-0
A498
ACHN
CAKI-1
RXF 393
SN12C
TK-10
UO-31
PC-3
DU-145
MCF7
MDA-MB-231/
HS 578T
BT-549
T-47D
MDA-MB-468

4. Copies of HRMS spectra for compounds 3e, 3n, 5, and 6





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175
Collision Energy
0
Ionization Mode
ESI
+ESI Scan (0.310 min) Frag=175.0V JCC-L86.d Subtract
x10 5
3
2.5
2
1.5
1
0.5
0
O
H2N
CN
O
N
N=N
Ph
6
C20H18N5O2+
[M + H]+ = 360,1455
360.14518
144.08021
198.12764
274.27493
331.28451
450.19204
120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480
Counts vs. Mass-to-Charge (m/z)

5. X-ray crystallographic data for compounds 3i and 3n

Table S18. Crystallographic data for compound **3i**.

Crystal data	
Chemical formula	$C_{10}H_8N_2O_2$
M_r	188.18
Crystal system, space group	Triclinic, *P*-1
Temperature (K)	298
a, *b*, *c* (Å)	6.7404 (17), 7.146 (2), 10.511 (2)
α, β, γ (°)	105.94 (2), 97.682 (19), 111.43 (3)
V (Å^3)	437.4 (2)
Z	2
Radiation type	Cu *K*α
μ (mm^{-1})	0.85
Crystal size (mm)	0.15 × 0.12 × 0.11
Data collection	
Diffractometer	SuperNova, Dual, Cu at zero, Atlas
Absorption correction	Multi-scan *CrysAlis PRO* 1.171.41.119a (Rigaku Oxford Diffraction, 2021)
T_{min}, T_{max}	0.738, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	4333, 1791, 1336
R_{int}	0.048
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.632
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.061, 0.195, 1.05
No. of reflections	1791
No. of parameters	128
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.25, −0.28

Table S19. Hydrogen-bond geometry (Å, º) for compound **3i**.

D*—H···*A	***D*—H**	**H···*A***	***D*···*A***	***D*—H···*A***
O14—H14···O10^{i}	0.82	1.88	2.698 (2)	176
N11—H11*A*···O14^{ii}	0.86	2.24	2.964 (2)	142
N11—H11*B*···N13^{iii}	0.86	2.21	3.033 (3)	161
C3—H3···O10^{i}	0.93	2.60	3.262 (3)	129

Symmetry codes: (i) *x*+1, *y*+1, *z*+1; (ii) *x*, *y*−1, *z*−1; (iii) *x*+1, *y*, *z*.

Table S20. Crystallographic data for compound **3n**.

Crystal data	
Chemical formula	$C_{22}H_{19}N_3O_2$
M_r	357.4
Crystal system, space group	Triclinic, *P*-1
Temperature (K)	298
a, *b*, *c* (Å)	9.1161 (13), 11.3530 (12), 21.0258 (17)
α, β, γ (°)	99.481 (8), 95.989 (10), 102.881 (11)
V (Å^3)	2069.7 (4)
Z	2
Radiation type	Cu *K*α
μ (mm^{-1})	0.85
Crystal size (mm)	0.10 × 0.09 × 0.07
Data collection	
Diffractometer	SuperNova, Dual, Cu at zero, Atlas
Absorption correction	Multi-scan *CrysAlis PRO* 1.171.41.119a (Rigaku Oxford Diffraction, 2021)
T_{min}, T_{max}	0.13181, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	16069, 8420, 4649
R_{int}	0.193
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.632
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.289, 0.643, 2.17
No. of reflections	8420
No. of parameters	487
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	1.82, −0.97

Table S21. Hydrogen-bond geometry (Å, º) for compound **3n**.

D*—H···*A	***D*—H**	**H···*A***	***D*···*A***	***D*—H···*A***
N2—H2*A*···O3^{i}	0.86	2.21	3.034 (15)	161
N2—H2*B*···O4^{ii}	0.86	2.08	2.912 (18)	164
N2—H2*B*···N6^{iii}	0.86	2.65	3.135 (18)	117
N3—H3*A*···O2^{ii}	0.86	2.11	2.971 (11)	175
N5—H5*B*···O2	0.86	1.92	2.585 (19)	133
N6—H6*A*···O4^{iv}	0.86	2.25	3.043 (14)	153
N6—H6*B*···O3	0.86	2.14	2.792 (18)	133

Symmetry codes: (i) −*x*, −*y*, −*z*; (ii) −*x*+1, −*y*, −*z*; (iii) *x*, *y*+1, *z*; (iv) −*x*+1, −*y*−1, −*z*.

Table S22. Bond lengths (Å) – Compound 3i

O(10)	C(9)	1.225(3)	O(14)	C(4)	1.357(3)	N(11)	C(9)	1.323(3)	N(13)	C(12)	1.142(3)
C(1)	C(2)	1.405(3)	C(1)	C(6)	1.409(3)	C(1)	C(7)	1.451(3)	C(2)	C(3)	1.384(3)
C(3)	C(4)	1.392(3)	C(4)	C(5)	1.401(3)	C(5)	C(6)	1.377(3)	C(7)	C(8)	1.354(3)
C(8)	C(9)	1.505(3)	C(8)	C(12)	1.437(3)						
O(14)	H(14)	0.82	N(11)	H(11A)	0.86	N(11)	H(11B)	0.86	C(2)	H(2)	0.93
C(3)	H(3)	0.93	C(5)	H(5)	0.93	C(6)	H(6)	0.93	C(7)	H(7)	0.93

Table S23. Bond/Valence angles (°) – Compound 3i

C(2)	C(1)	C(6)	117.37(18)	C(2)	C(1)	C(7)	116.74(19)	C(6)	C(1)	C(7)	125.88(19)
C(1)	C(2)	C(3)	122.0(2)	C(2)	C(3)	C(4)	119.5(2)	O(14)	C(4)	C(3)	123.1(2)
O(14)	C(4)	C(5)	117.2(2)	C(3)	C(4)	C(5)	119.66(19)	C(4)	C(5)	C(6)	120.4(2)
C(1)	C(6)	C(5)	121.1(2)	C(1)	C(7)	C(8)	132.2(2)	C(7)	C(8)	C(9)	123.9(2)
C(7)	C(8)	C(12)	122.80(19)	C(9)	C(8)	C(12)	113.24(18)	O(10)	C(9)	N(11)	122.2(2)
O(10)	C(9)	C(8)	120.1(2)	N(11)	C(9)	C(8)	117.66(19)	N(13)	C(12)	C(8)	179.0(2)
C(4)	O(14)	H(14)	110	C(9)	N(11)	H(11A)	120	C(9)	N(11)	H(11B)	120
H(11A)	N(11)	H(11B)	120	C(1)	C(2)	H(2)	119	C(3)	C(2)	H(2)	119
C(2)	C(3)	H(3)	120	C(4)	C(3)	H(3)	120	C(4)	C(5)	H(5)	120
C(6)	C(5)	H(5)	120	C(1)	C(6)	H(6)	119	C(5)	C(6)	H(6)	119
C(1)	C(7)	H(7)	114	C(8)	C(7)	H(7)	114				

Table S24. Torsion/dihedral angles (Deg.) – Compound 3i

C(6)	C(1)	C(2)	C(3)	0.2(3)	C(7)	C(1)	C(2)	C(3)	179.7(2)	C(2)	C(1)	C(6)	C(5)	0.2(4)
C(7)	C(1)	C(6)	C(5)	-179.4(2)	C(2)	C(1)	C(7)	C(8)	-176.6(2)	C(6)	C(1)	C(7)	C(8)	3.0(4)
C(1)	C(2)	C(3)	C(4)	-0.5(3)	C(2)	C(3)	C(4)	O(14)	-178.7(2)	C(2)	C(3)	C(4)	C(5)	0.5(3)
O(14)	C(4)	C(5)	C(6)	179.0(2)	C(3)	C(4)	C(5)	C(6)	-0.2(4)	C(4)	C(5)	C(6)	C(1)	-0.1(4)
C(1)	C(7)	C(8)	C(9)	-177.0(2)	C(1)	C(7)	C(8)	C(12)	0.8(4)	C(7)	C(8)	C(9)	O(10)	163.3(2)
C(7)	C(8)	C(9)	N(11)	-14.5(4)	C(12)	C(8)	C(9)	O(10)	-14.7(3)	C(12)	C(8)	C(9)	N(11)	167.5(2)
H(14)	O(14)	C(4)	C(3)	2	H(14)	O(14)	C(4)	C(5)	-177	C(6)	C(1)	C(2)	H(2)	-180
C(7)	C(1)	C(2)	H(2)	0	C(2)	C(1)	C(6)	H(6)	-180	C(7)	C(1)	C(6)	H(6)	0
C(2)	C(1)	C(7)	H(7)	3	C(6)	C(1)	C(7)	H(7)	-177	C(1)	C(2)	C(3)	H(3)	180
H(2)	C(2)	C(3)	C(4)	180	H(2)	C(2)	C(3)	H(3)	0	H(3)	C(3)	C(4)	O(14)	1
H(3)	C(3)	C(4)	C(5)	-180	O(14)	C(4)	C(5)	H(5)	-1	C(3)	C(4)	C(5)	H(5)	180
C(4)	C(5)	C(6)	H(6)	180	H(5)	C(5)	C(6)	C(1)	180	H(5)	C(5)	C(6)	H(6)	0
H(7)	C(7)	C(8)	C(9)	3	H(7)	C(7)	C(8)	C(12)	-179	O(10)	C(9)	N(11)	H(11A)	0
O(10)	C(9)	N(11)	H(11B)	-180	C(8)	C(9)	N(11)	H(11A)	178	C(8)	C(9)	N(11)	H(11B)	-2

Figure S1. ORTEP representation and crystal packing for compound 3n.