Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supplementary Information

Synthesis of new triazole linked carbohybrids with ROS-mediated toxicity in breast cancer

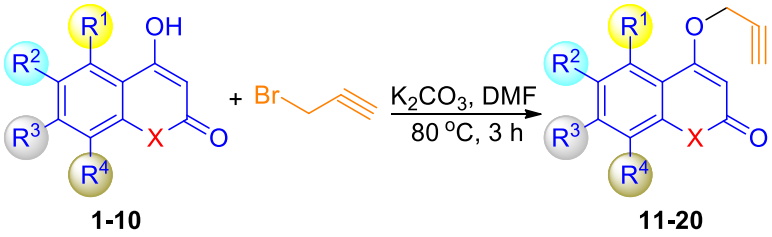
Priti Kumari,[a†] Shraddha Dubey,[b†] Sneha Venkatachalapathy,[a†] Chintam Narayana,[a] Ashish Gupta*[b] and Ram Sagar*[a,c]

[a]Department of Chemistry, School of Natural Sciences, Shiv Nadar University (SNU), NH91, Tehsil-Dadri, Gautam Buddha Nagar, Uttar Pradesh, 201314, India.
[b]Department of Life Sciences, School of Natural Sciences, Shiv Nadar University (SNU), NH91, Tehsil-Dadri, Gautam Buddha Nagar, Uttar Pradesh, 201314, India.
[c]Department of Chemistry, Institute of Science, Banaras Hindu University, Varanasi, Uttar Pradesh, 221005, India.

*E-mail (Corresponding author): ram.sagar@bhu.ac.in; ashish.gupta@snu.edu.in,

†equal contribution

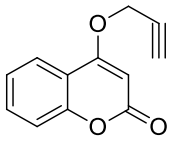
Table S1. Synthesis of 4-*O*-propargyl coumarins and quinolones **11-20**



Entry	R^1	R^2	R^3	R^4	X	Product [a]	Yield (%)
1	H	H	H	H	O	**11**	70
2	H	OCH_3	H	H	O	**12**	71
3	H	Cl	H	H	O	**13**	72
4	H	CH_3	H	H	O	**14**	72
5	H	Br	H	H	O	**15**	73
6	H	H	F	H	O	**16**	77
7[b]	H	H	H	H	NH	**17**	40
8[b]	H	H	H	F	NH	**18**	37
9[b]	H	H	H	NO_2	NH	**19**	59
10[b]	H	H	H	OCF_3	NH	**20**	41

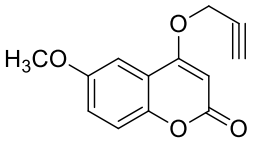
[a]Isolated yield, [b] in these cases di and trisubstituted propargyl products were also formed but yield is reported here for required one.

Typical method for the synthesis of 4-*O*-propargylated Coumarins and Quinolones 11-20. In a 100 ml round, bottom flask taken 500 mg (3.08 mmol) of 4-hydroxycoumarin in dry DMF then added K_2CO_3 (1.062 gm, 7.7 mmol) and stirred for half an hour. Then added propargyl bromide (0.231 ml, 363 mg, 3.08 mmol) and reaction mixture refluxed for 2 h. The progress of reaction was monitored bt TLC. Completion of reaction was confirmed by TLC. Then reaction mixture was quenched by aq. solution of $NaHCO_3$ and extracted with ethyl acetate (3 × 20 ml). The, organic layer dried over anhydrous Na_2SO_4, Crude mixture was purified by flash column chromatography. Same reaction protocol followed for **12-20**.



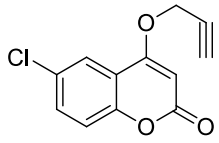
11

4-(prop-2-yn-1-yloxy)-2H-chromen-2-one (11): Light pink amorphous solid, R_f = 0.64 (4:6, Ethyl acetate:hexave, v/v), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (dd, *J* = 1.2 Hz,8.0 Hz,1H), 7.58-7.54 (m, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.30-7.28 (m, 1H), 5.83 (s, 1H, H-3), 4.87 (d, *J* = 2.4 Hz, 2H), 2.68 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 153.3, 132.6, 124.0, 123.0, 116.8, 91.7, 56.8. HRMS (ESI) m/z calcd for $C_{12}H_8O_3$ $[M+H]^+$ 201.0546; Found: 201.0557.



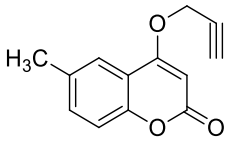
12

6-methoxy-4-(prop-2-yn-1-yloxy)-2H-chromen-2-one (12): Brown amorphous solid, R_f = 0.54 (4:6, Ethyl acetate:Hexane, v/v) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, *J* = 2.0 Hz, 1H), 7.25 (d, *J* = 2.8 Hz, 1H), 7.15 (dd, *J* = 2.8 Hz, *J* = 8.8 Hz, 1H), 5.85 (s, 1H, H-3), 4.89 (d, *J* = 2.0 Hz, 2H), 3.87 (s, 3H, OCH_3), 2.69 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9, 155.9, 147.8, 120.7, 117.9, 104.8, 91.9, 56.8, 55.8, 53.3; HRMS (ESI): *m/z* calcd for $C_{13}H_{10}O_4$ $[M+H]^+$ 231.0652; Found: 231.0664.



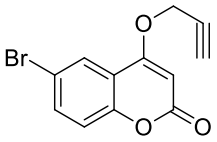
13

6-chloro-4-(prop-2-yn-1-yloxy)-2H-chromen-2-one (13): Off white amorphous solid, R_f = 0.67 (4:6, Ethyl acetate:Hexane, v/v) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 2.0 Hz, 1H), 7.48 (dd, *J* = 2.4 Hz, *J* = 8.8 Hz,1H), 7.24 (d, *J* = 1.6 Hz, 1H), 5.83 (s,1H, H-3), 4.85 (d, *J* = 2.0 Hz, 2H), 2.67 (t, *J* = 2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 161.7, 151.7, 132.5, 129.6, 122.7, 118.2, 116.5, 92.4, 78.2, 75.3, 57.0; HRMS (ESI): *m/z* calcd for $C_{12}H_7ClO_3$ $[M+H]^+$ 235.0156; Found: 235.0164.



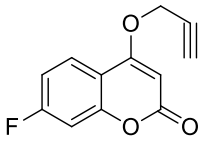
14

6-methyl-4-(prop-2-yn-1-yloxy)-2H-chromen-2-one (14): Light pink amorphous solid, R_f = 0.66 (4:6, Ethylacetate : Hexane, v/v), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 5.80 (s, 1H, H-3), 4.85 (d, *J* = 2.0 Hz, 2H), 2,66 (brs, 1H), 2.40 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 162.6, 151.5, 133.7, 133.5, 122.7, 116.5, 91.6, 56.7, 20.8; HRMS (ESI): *m/z* calcd for $C_{13}H_{10}O_3$ $[M+H]^+$ 215.0703; Found: 215.0711.



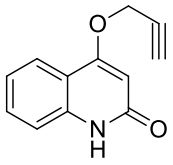
15

6-bromo-4-(prop-2-yn-1-yloxy)-2H-chromen-2-one (15): Yellow colour amorphous solid**,** R_f = 0.64 (4:6, Ethyl acetate: Hexane, v/v) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.64 (d, *J* = 6.8 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 5.84 (s, 1H, H-3), 4.87 (brs, 2H), 2.69 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 152.2, 135.3, 125.7, 118.5, 116.9, 116.8, 92.4, 78.2, 75.3, 57.0, 53.4; HRMS (ESI): *m/z* calcd for $C_{12}H_7BrO_3$ $[M+H]^+$ 280.9632; Found: 280.9631.



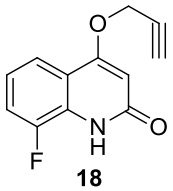
16

7-fluoro-4-(prop-2-yn-1-yloxy)-2H-chromen-2-one (16): Light brown amorphous solid, R_f = 0.59 (4:6, Ethylacetate:Hexane, v/v) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83(dd, *J* = 6.0 Hz, *J* = 8.4 Hz, 1H), 7.06-7.03 (m, 1H), 7.01 (dd, *J* = 2.8 Hz, *J* = 8.4 Hz, 1H), 5.78 (s, 1H, H-3), 4.87 (d, *J* = 2.4 Hz, 2H), 2.68 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 164.1, 163.9, 162.2, 154.7, 154.6, 125.1, 125.0, 112.3, 112.1, 104.4, 104.2, 90.8, 90.80, 78.1, 75.6, 57.0; HRMS (ESI): *m/z* calcd for $C_{12}H_7FO_3$ $[M+H]^+$ 219.0452; Found: 219.0457.



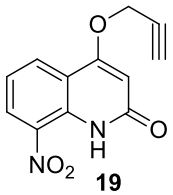
17

4-(prop-2-yn-1-yloxy)quinolin-2(1H)-one (17): Light Brown amorphous solid, R_f = 0.07 (4 : 6, Ethyl acetate : Hexane, v/v), ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.43 (brs, 1H, NH), 7.76 (d, *J* = 8.0 Hz, 1H), 7.54-7.50 (m, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.19-7.15 (m, 1H), 5.96 (s, 1H, H-3), 5.00 (d, *J* = 2.0 Hz, 2H), 3.75 (t, *J* = 3.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.3, 161.1, 139.1, 131.5, 122.6, 121.9, 115.7, 114.7, 98.6, 79.8, 78.3, 56.84 HRMS (ESI): *m/z* calcd for $C_{12}H_9NO_2$ $[M+H]^+$ 200.0706; Found: 200.0528.



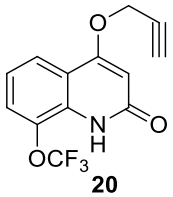
18

8-fluoro-4-(prop-2-yn-1-yloxy)quinolin-2(1H)-one (18): Off white amorphos solid, R_f = 0.14 (4:6, Ethylacetate:Hexane, v/v), ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.47 (brs,1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.45 (m, 1H), 7.17(brs, 1H), 6.03 (s, 1H, H-3), 5.02 (brs, 2H), 3.75 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.6, 161.3, 127.7, 122.1, 118.5, 117.1, 117.0, 116.9, 116.7, 99.2, 79.7, 79.4, 79.1, 78.9 57.0; HRMS (ESI): *m/z* calcd for $C_{12}H_8FNO_2$ $[M+H]^+$ 218.0612; Found: 218.0614.



19

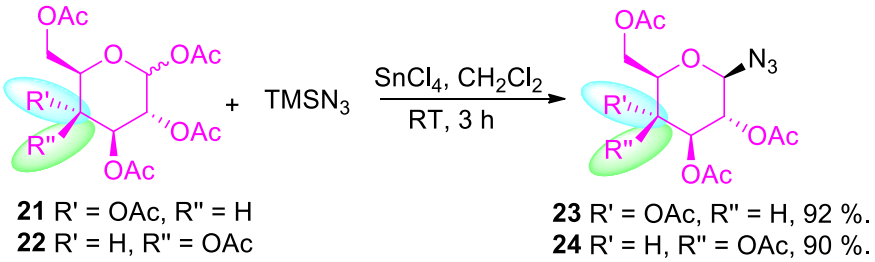
8-nitro-4-(prop-2-yn-1-yloxy)quinolin-2(1H)-one (19): Yellow amorphous solid, R_f = 0.25 (4:6, Ethylacetate:Hexane, v/v) ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (dd, *J* = 1.5 Hz, *J* = 8.5 Hz, 1H), 8.30 (dd, *J* = 1.5 Hz, *J* = 8.0 Hz, 1H), 7.30 (t, *J* = 8.5 Hz, 1H), 5.29 (s, 1H, H-3), 4.88 (d, *J* = 3.0 Hz, 2H), 2.67 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.8, 161.1, 133.7, 131.2, 128.8, 120.9, 118.1, 99.1, 77.9, 75.8, 56.9; HRMS (ESI): *m/z* calcd for $C_{12}H_8N_2O_4$ $[M+H]^+$ 245.0557; Found: 245.0566.



20

4-(prop-2-yn-1-yloxy)-8-(trifluoromethoxy)quinolin-2(1H)-one (20): Off white amorphous solid, R_f = 0.26 (4:6, Ethylacetate:Hexane, v/v) ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.65 (s, 1H), 7.79 (dd, *J* = 0.8 Hz, *J* = 8.4 Hz,1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 6.07 (s, 1H, H-3), 5.04 (d, *J* = 2.0 Hz, 2H), 3.78 (t, *J* = 2.4 Hz, 1H) ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.2, 160.7, 132.2, 123.9, 121.9, 121.8, 117.0, 99.7, 80.1, 78.1, 57.1, 49.04; HRMS (ESI): *m/z* calcd for $C_{13}H_8F_3NO_3$ $[M+H]^+$ 284.0529; Found: 284.0548.

General Synthesis of Glucose and Galactose derived azido glycosides 23-24. To a 250 ml round bottom flask taken 10 gm (25.64 mmol) of 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose **21** in anhydrous dichloromethane under nitrogen atmosphere. Then added $SnCl_4$ 2.57 ml (22.05 mmol) dropwise at ice bath and stirred for half an hour followed by addition of $TMSN_3$ 3.80 ml (28.97mmol) at room temperature and stirred reaction mixture for 3-4 h. Completion of reaction was confirmed by TLC. After completion of reaction it was quenched with cold water and aq. solution of $NaHCO_3$ and extracted using dichloromethane (3 × 100 ml). The, organic layer washed by brine solution (3 × 50 ml), and dried over anhydrous Na_2SO_4 and evaporated on rotary evaporator to get crude product. Crude residue was purified by column chromatography and azido glucoside **23** was obtained as an off white solid in 92% isolated yield. Using similar reaction protocol azido galactoside **24** was prepared starting with 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose **22** (Scheme S1).

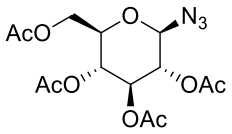


21 R' = OAc, R'' = H
22 R' = H, R'' = OAc

23 R' = OAc, R'' = H, 92 %.
24 R' = H, R'' = OAc, 90 %.

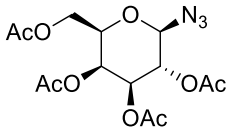
Scheme S1. Synthesis of Azido glycosides **23-24**.

Spectroscopic data of azido glycosides 23-24.



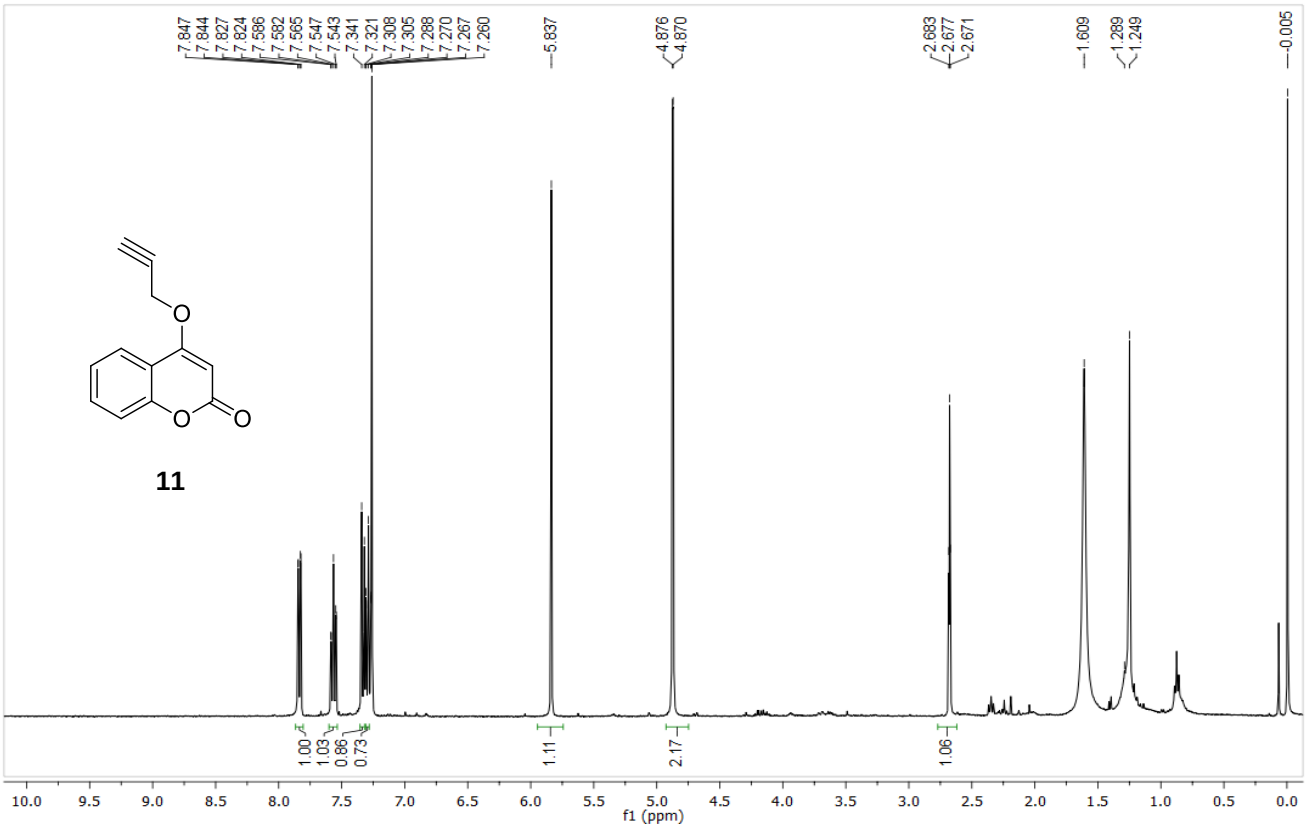
23

1-azido-2,3,4.6-tetra-O-acetyl β-D-glucose (23): Off white amorphous solid, R_f = 0.8 (3:7, Ethylacetate Hexane, v/v), ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.23 (t, *J* = 9.2 Hz, 1H), 5.12 (t, *J* = 9.6 Hz, 1H), 4.97 (t, *J* = 9.2 Hz, 1H), 4.66 (d, *J* = 8.8 Hz, 1H), 4.29 (dd, *J* = 4.8 Hz, *J* = 12.4 Hz, 1H), 4.18 (dd, *J* = 2.4 Hz, *J* =12.4 Hz, 1H), 3.81 (ddd, *J* = 2.0 Hz, *J* = 6.8 Hz, *J* = 12.0 Hz, 1H), 2.11 (s, 3H, CH_3 of $COCH_3$), 2.09 (s, 3H, CH_3 of $COCH_3$), 2.04 (s, 3H, CH_3 of $COCH_3$), 2.02 (s, 3H, CH_3 of $COCH_3$); ^{13} C NMR (100 MHz, $CDCl_3$): δ 170.5, 170.0, 169.2, 169.1, 87.9, 74.0, 72.6, 70.6, 67.9, 61.6, 20.6, 20.52, 20.5; HRMS (ESI): *m/z* calcd for $C_{14}H_{19}N_3O_9$ $[M+Na]^+$ 396.1014; Found: 396.1038.



24

1-azido-2,3,4.6-tetra-O-acetyl β-D-galactose (24): Off white amorphous solid, R_f = 0.78 (3:7, Ethylacetate:Hexane, v/v), ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.42 (d, *J* = 2.8 Hz, 1H), 5.18-5.13 (m, 1H), 5.03 (dd, *J* = 3.2 Hz, *J* = 10.4 Hz, 1H), 4.59 (d, *J* = 8.8 Hz, 1H), 4.16 (dd, *J* = 4.4 Hz, *J* = 6.0 Hz, 1H), 4.10 (m, 1H), 4.01 (t, *J* = 6.4 Hz, 1H), 2.16 (s, 3H, CH_3 of $COCH_3$), 2.08 (s, 3H, CH_3 of $COCH_3$), 2.05 (s, 3H, CH_3 of $COCH_3$), 1.98 (s, 3H, CH_3 of $COCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 170.1, 170.0, 169.4, 88.3, 72.8, 70.7, 68.0, 66.8, 61.2, 53.4, 20.69, 20.67, 20.6, 20.5; HRMS (ESI): *m/z* calcd for $C_{14}H_{19}N_3O_9$ $[M+K]^+$ 412.0753; Found: 412.0778.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7.586
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7.341
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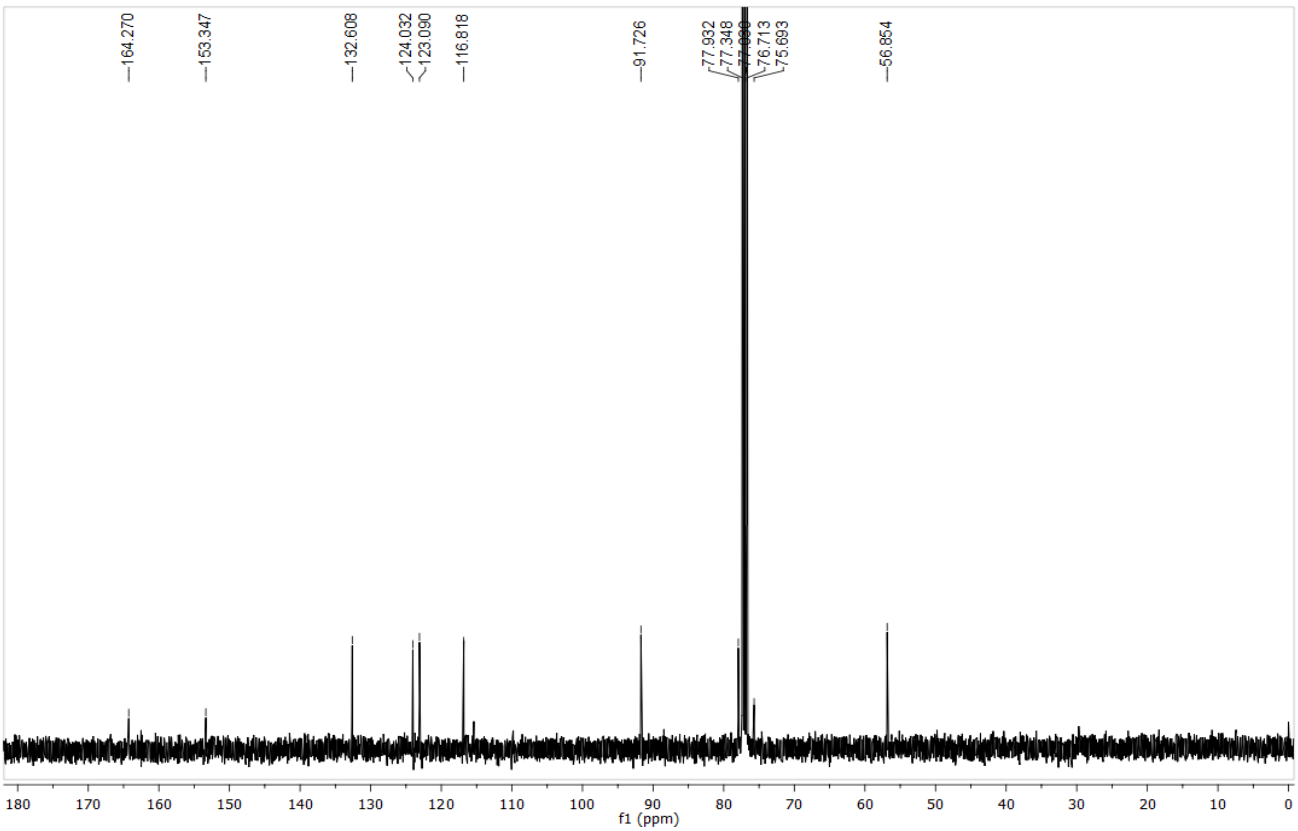
7.305
7.288
7.270
7.267
7.260
5.837
4.876
4.870
2.683
2.677
2.671
1.609
1.289
1.249
0.005
1.00
1.03
0.86
0.73
1.11
2.17
1.06
f1 (ppm)

11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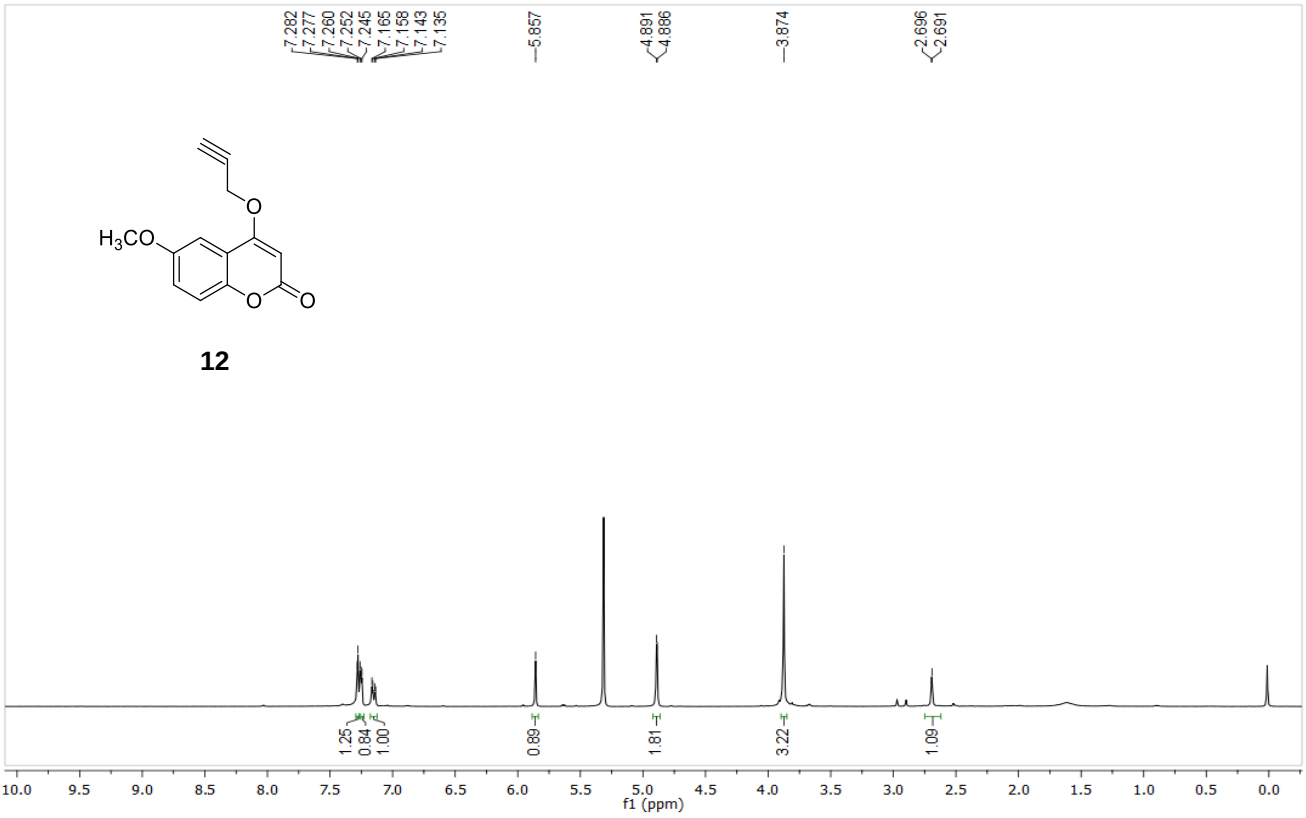
56.854
f1 (ppm)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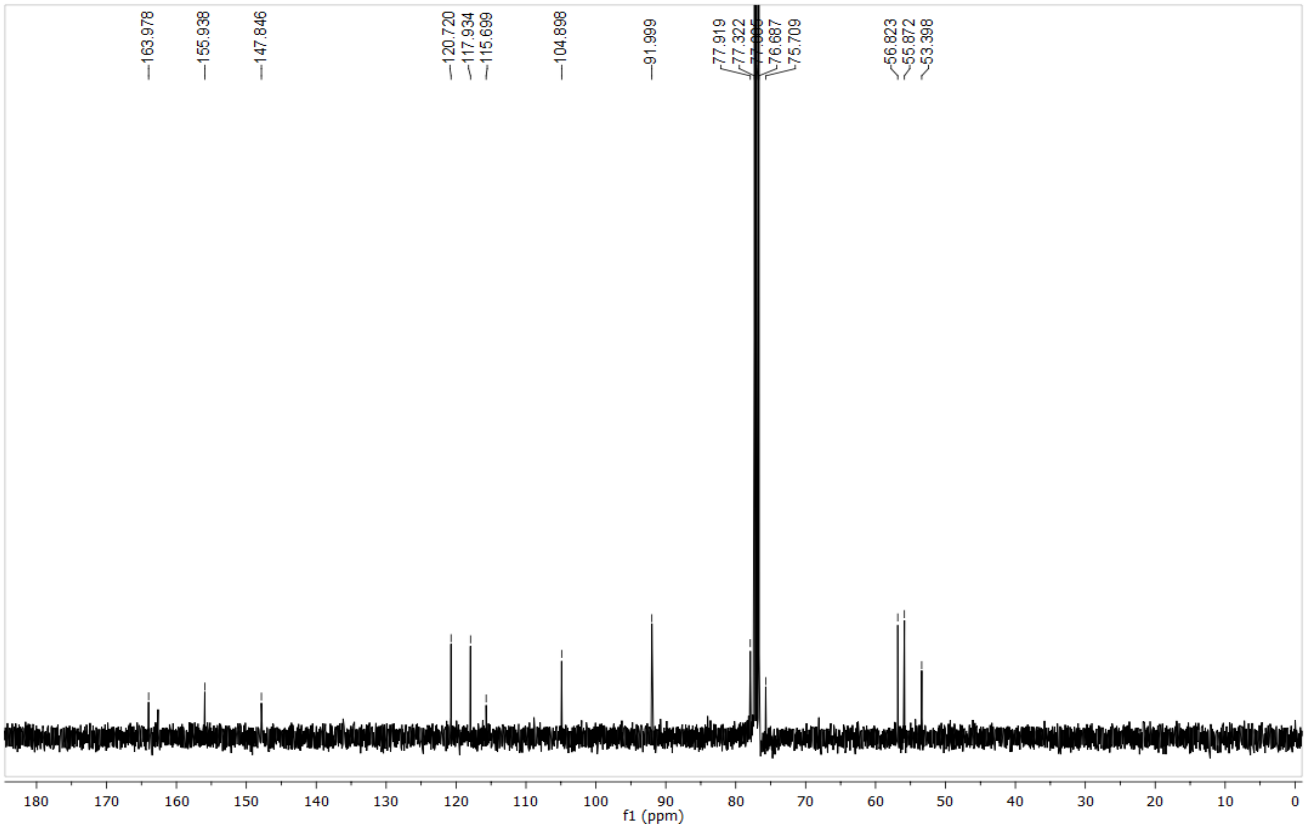
3.874
2.696
2.691
H3CO
O
O
O
1.25
0.84
1.00
0.89
1.81
3.22
1.09
f1 (ppm)

12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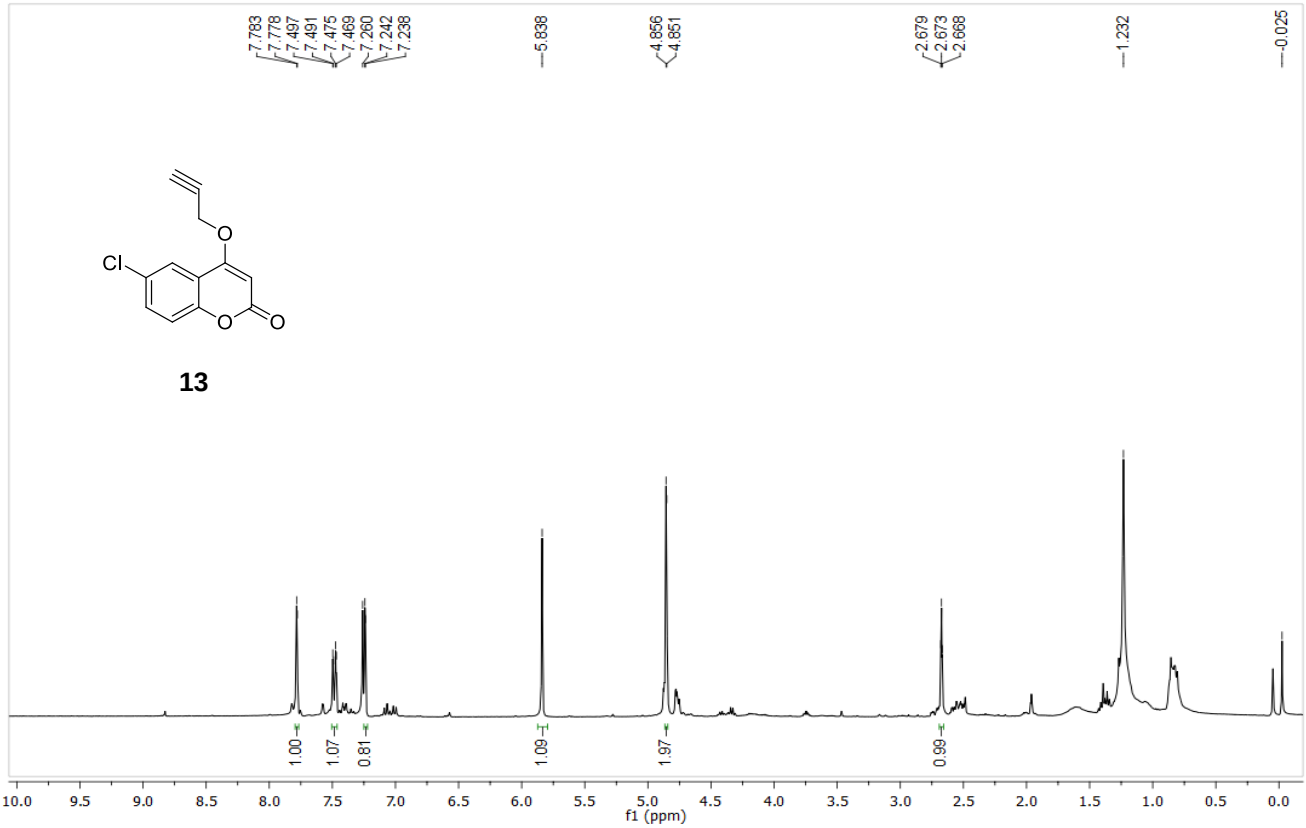
75.709
56.823
55.872
53.398
f1 (ppm)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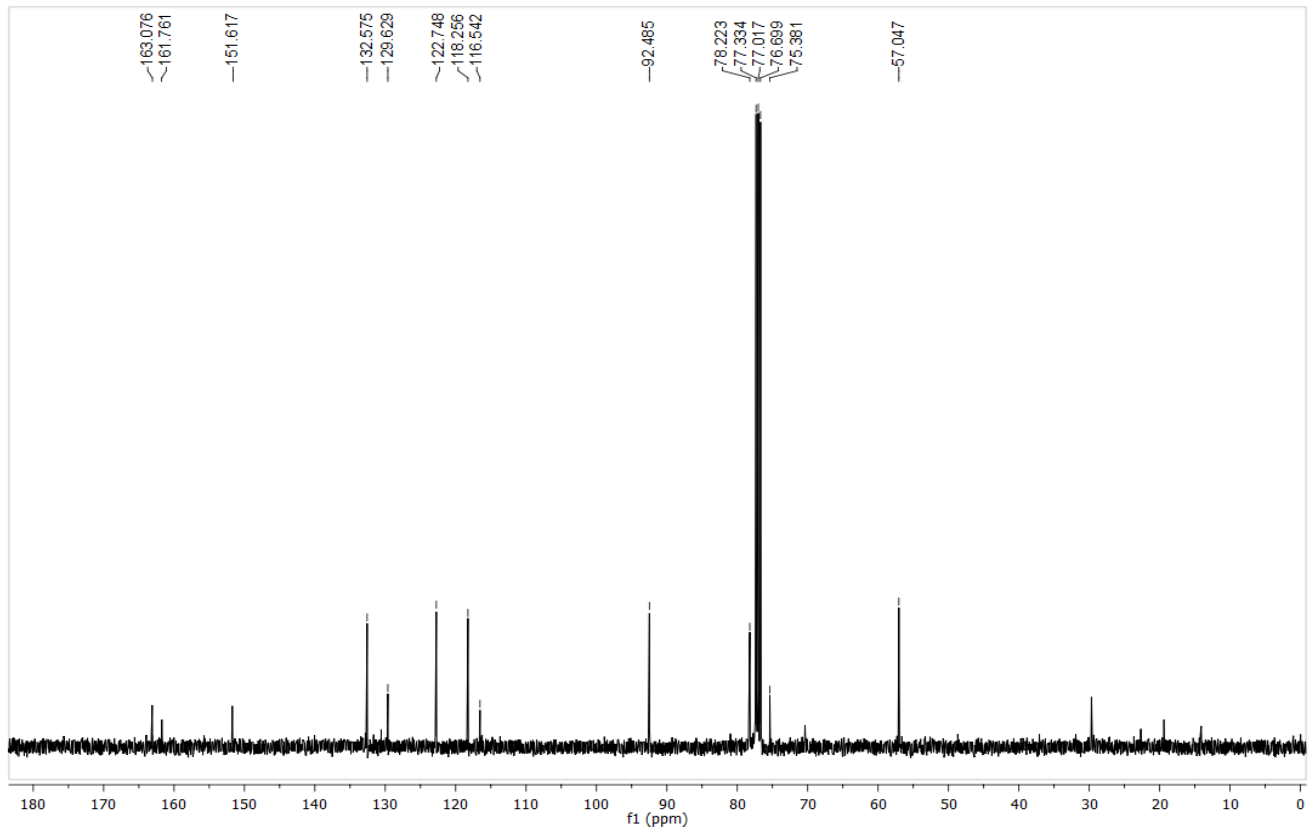
7.778
7.497
7.491
7.475
7.469
7.260
7.242
7.238
5.838
4.856
4.851
2.679
2.673
2.668
1.232
0.025
Cl
O
O
O
1.00
1.07
0.81
1.09
1.97
0.99
f1 (ppm)

13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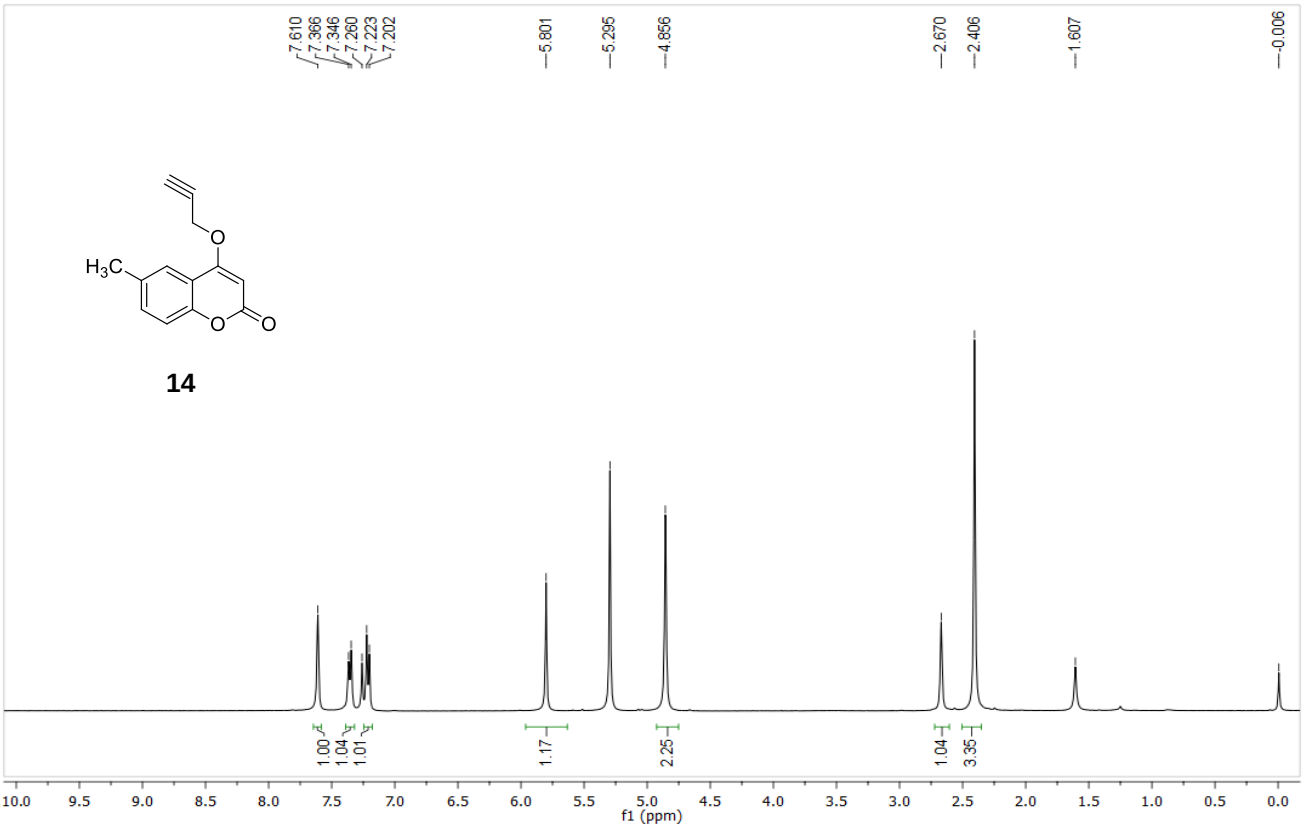
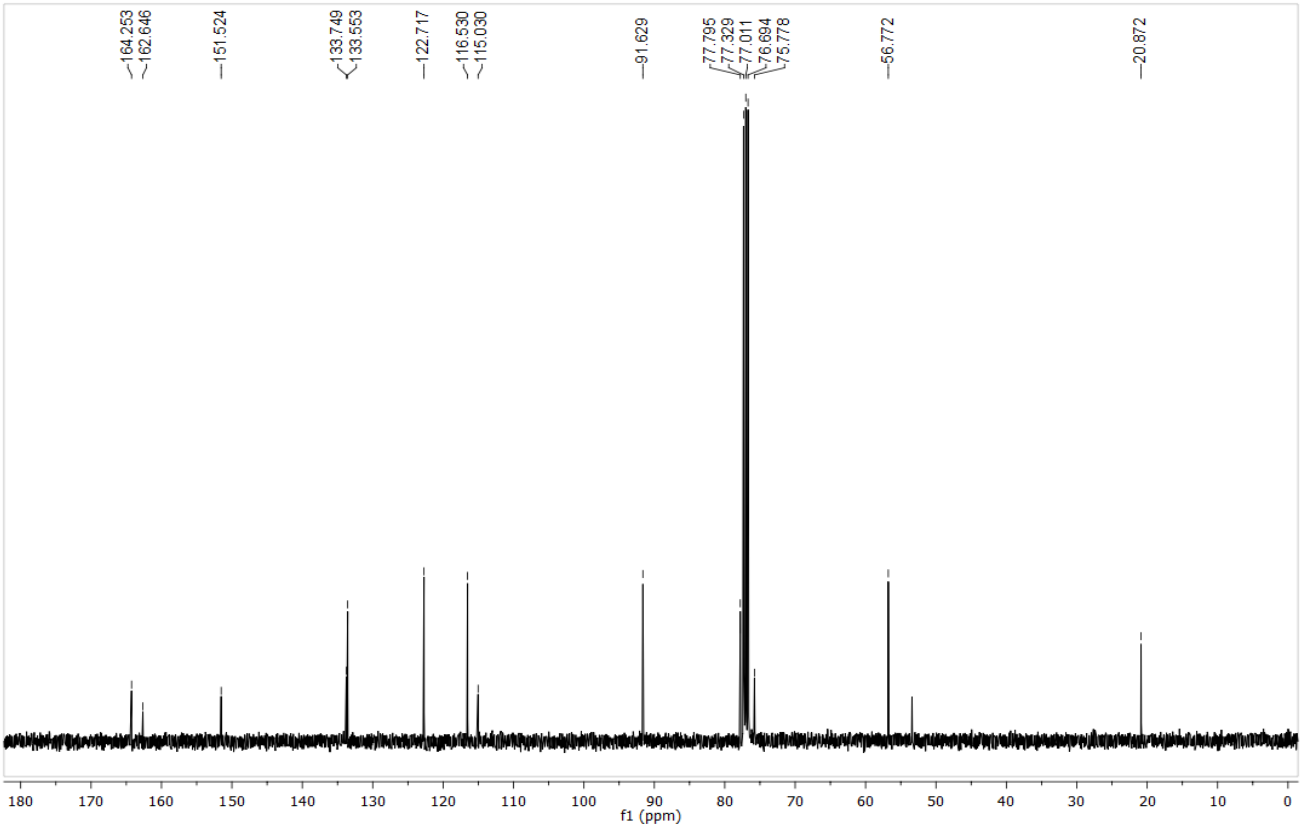
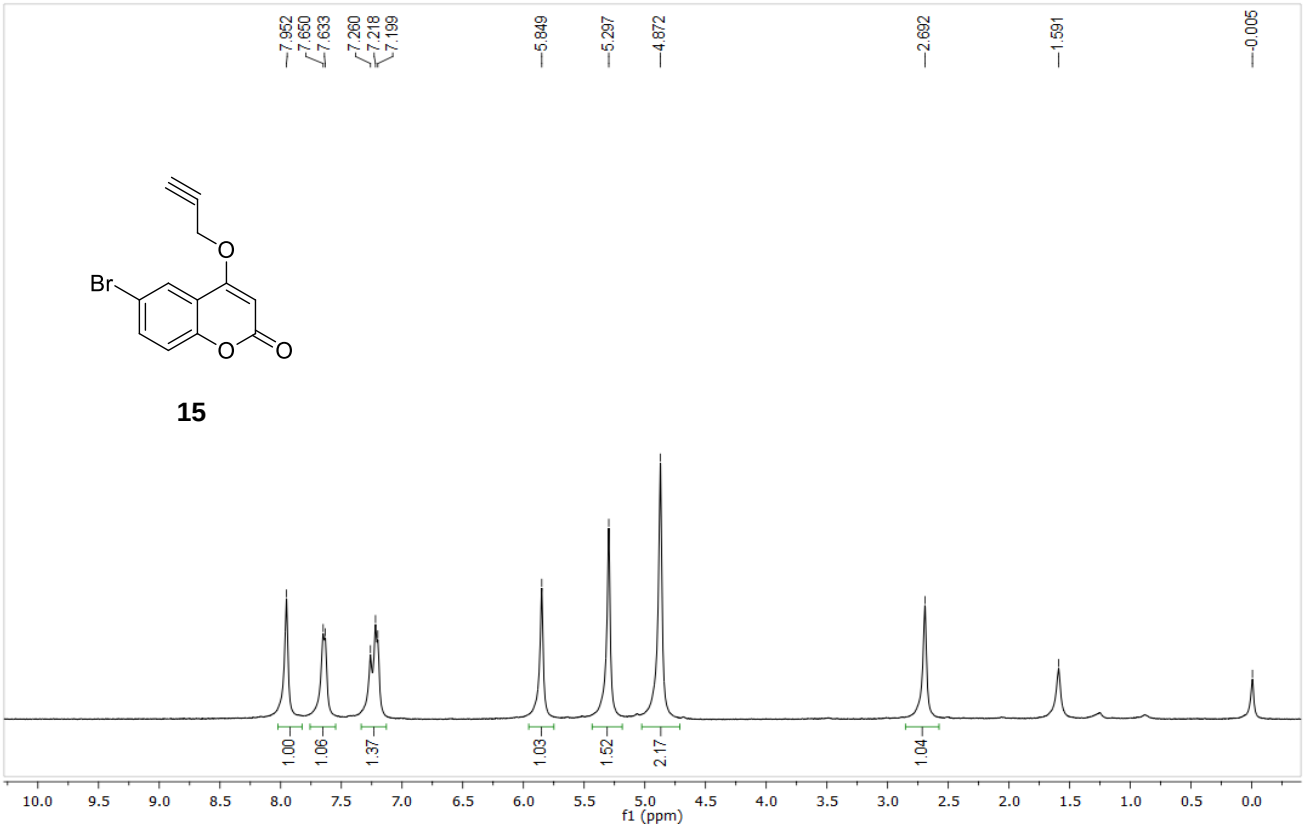
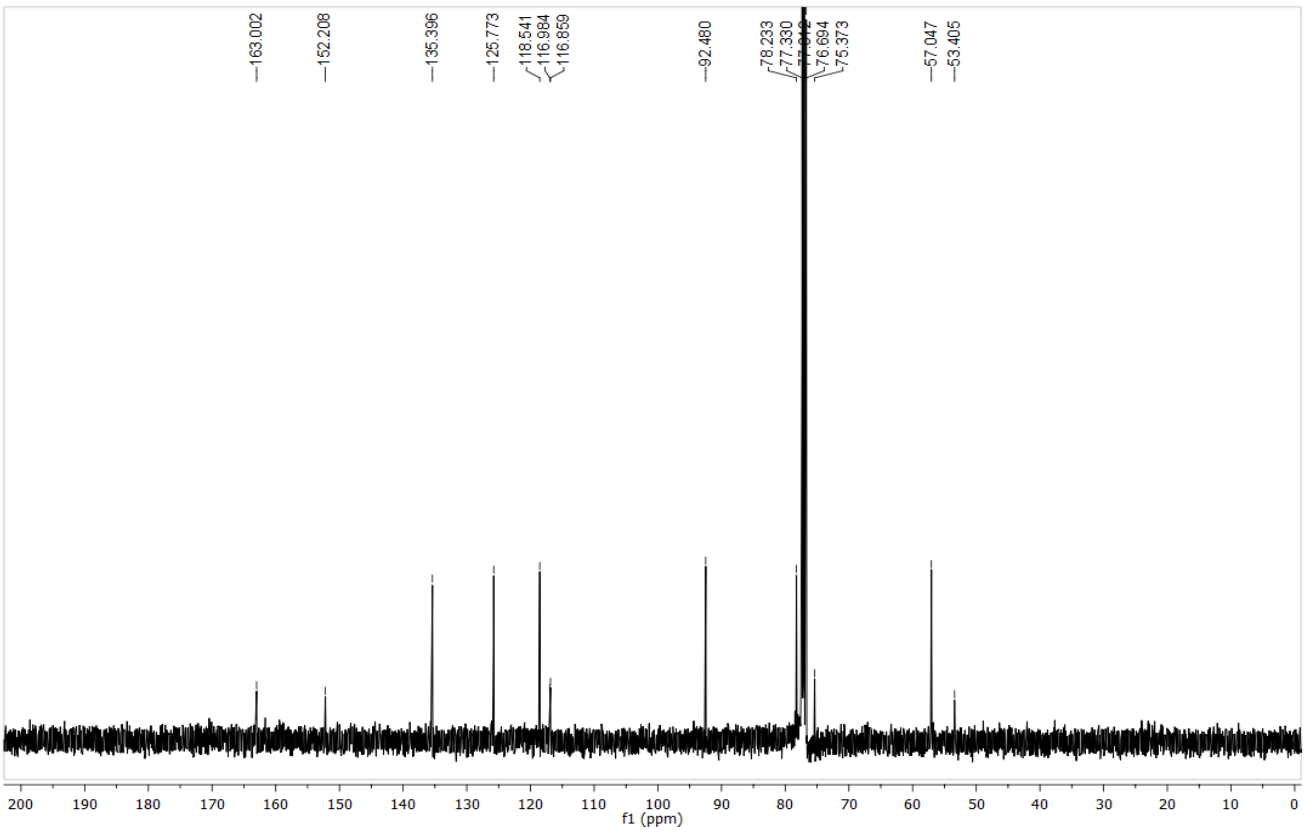
161.761
151.617
132.575
129.629
122.748
118.256
116.542
92.485
78.223
77.334
77.017
76.699
75.381
57.047
f1 (ppm)


7.610
7.366
7.346
7.260
7.223
7.202
5.801
5.295
4.856
2.670
2.406
1.607
0.006
O
H3C
O
O
1.00
1.04
1.01
1.17
2.25
1.04
3.35
f1 (ppm)

14


164.253
162.646
151.524
133.749
133.553
122.717
116.530
115.030
91.629
77.795
77.329
77.011
76.694
75.778
56.772
20.872
f1 (ppm)


7.952
7.650
7.633
7.260
7.218
7.199
5.849
5.297
4.872
2.692
1.591
0.005
Br
O
O
O
15
1.00
1.06
1.37
1.03
1.52
2.17
1.04
f1 (ppm)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152.208
135.396
125.773
118.541
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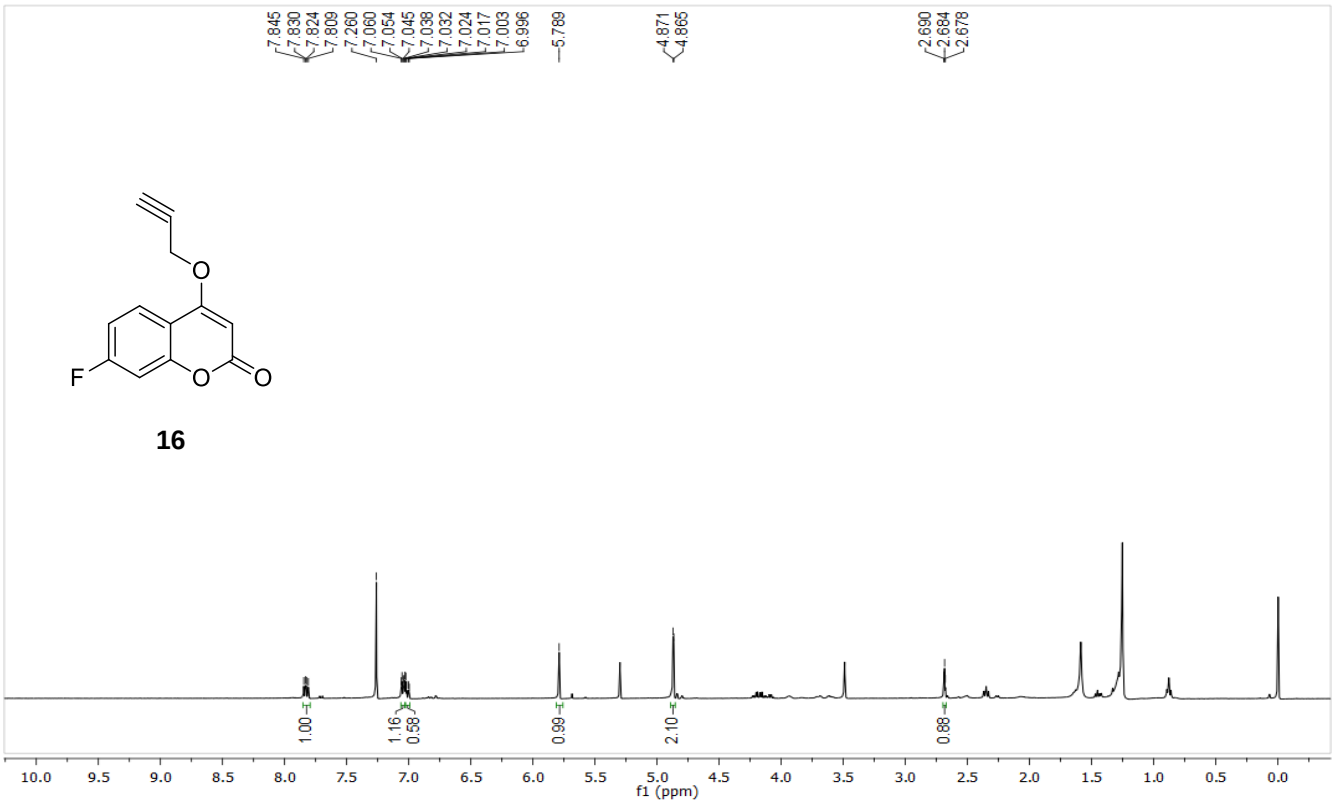
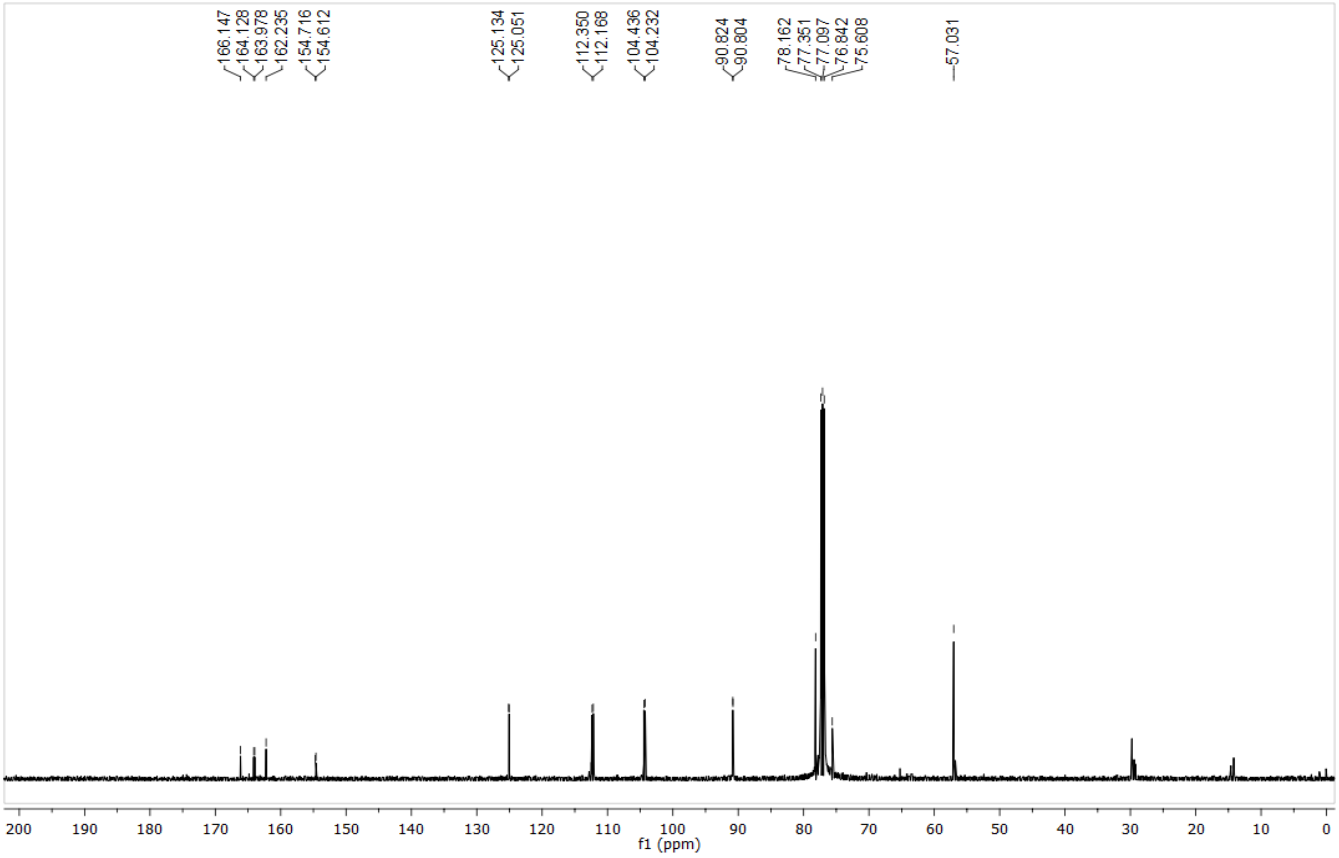
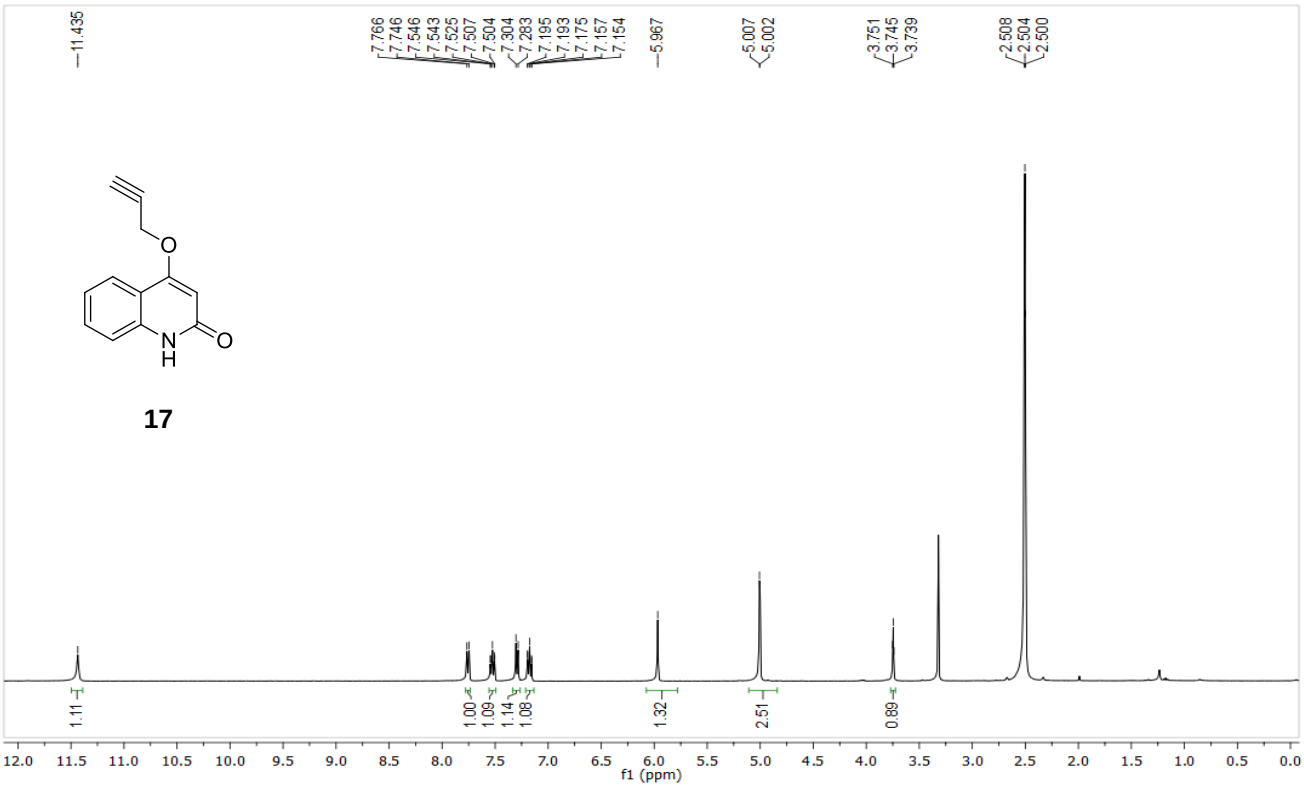
116.859
92.480
78.233
77.330
76.694
75.373
57.047
53.405
f1 (ppm)

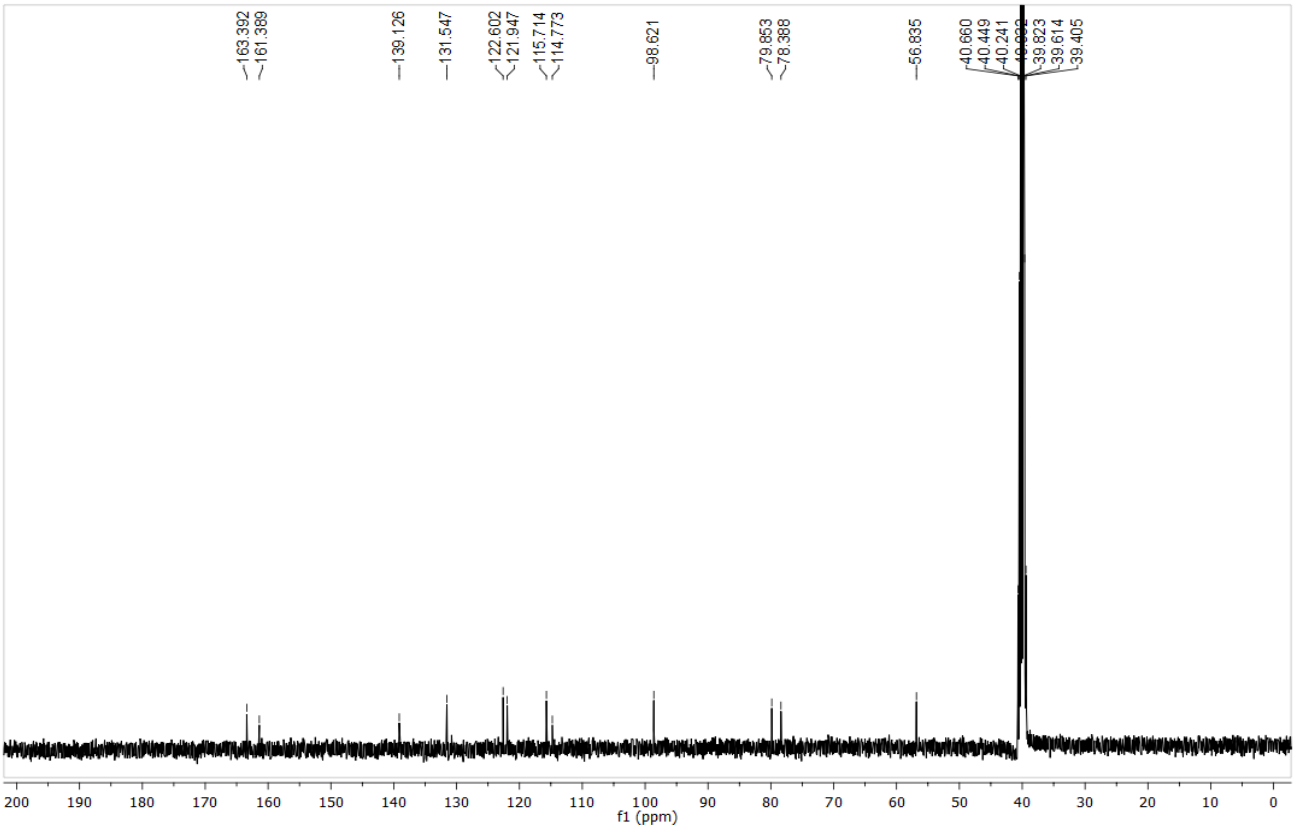

7.845
7.830
7.824
7.809
7.260
7.060
7.054
7.045
7.038
7.032
7.024
7.017
7.003
6.996
5.789
4.871
4.865
2.690
2.684
2.678
1.00
1.16
0.58
0.99
2.10
0.88
f1 (ppm)

O
F
O
O

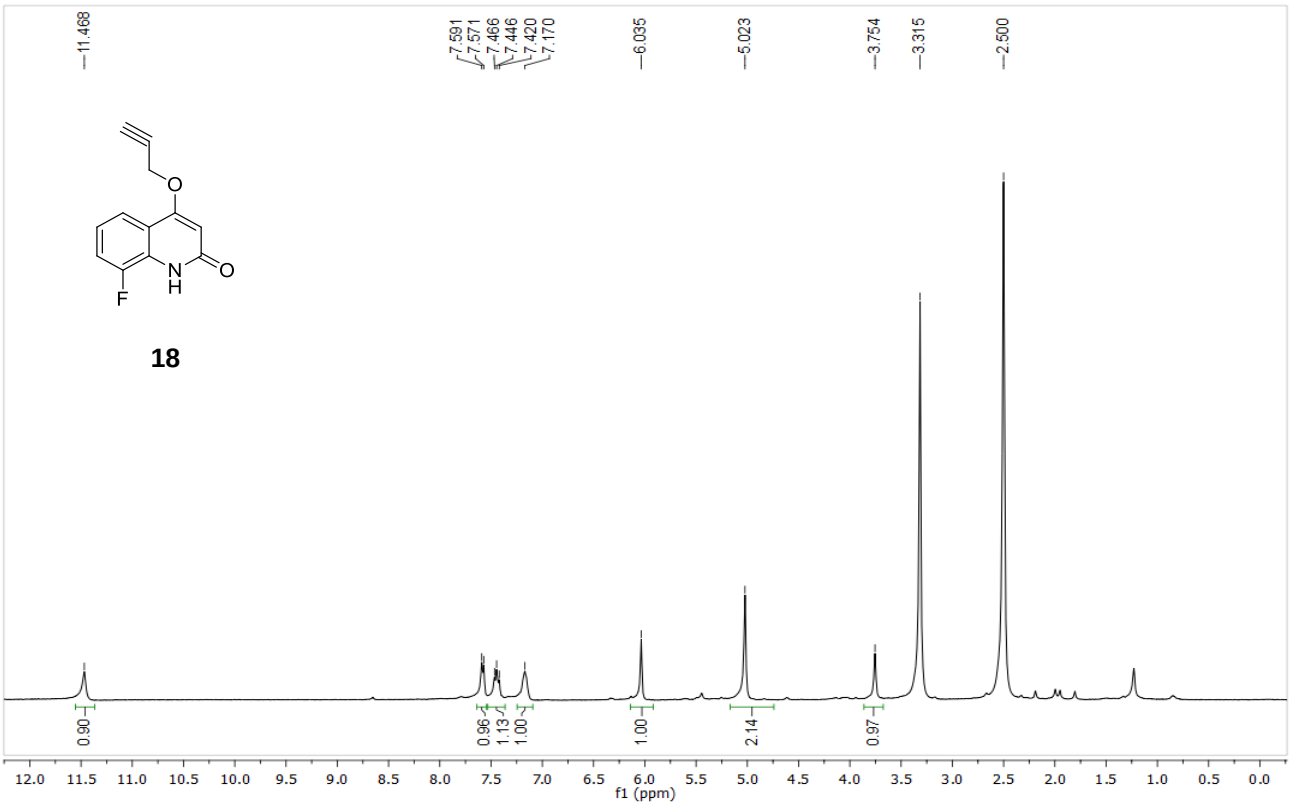
16


166.147
164.128
163.978
162.235
154.716
154.612
125.134
125.051
112.350
112.168
104.436
104.232
90.824
90.804
78.162
77.351
77.097
76.842
75.608
57.031
f1 (ppm)

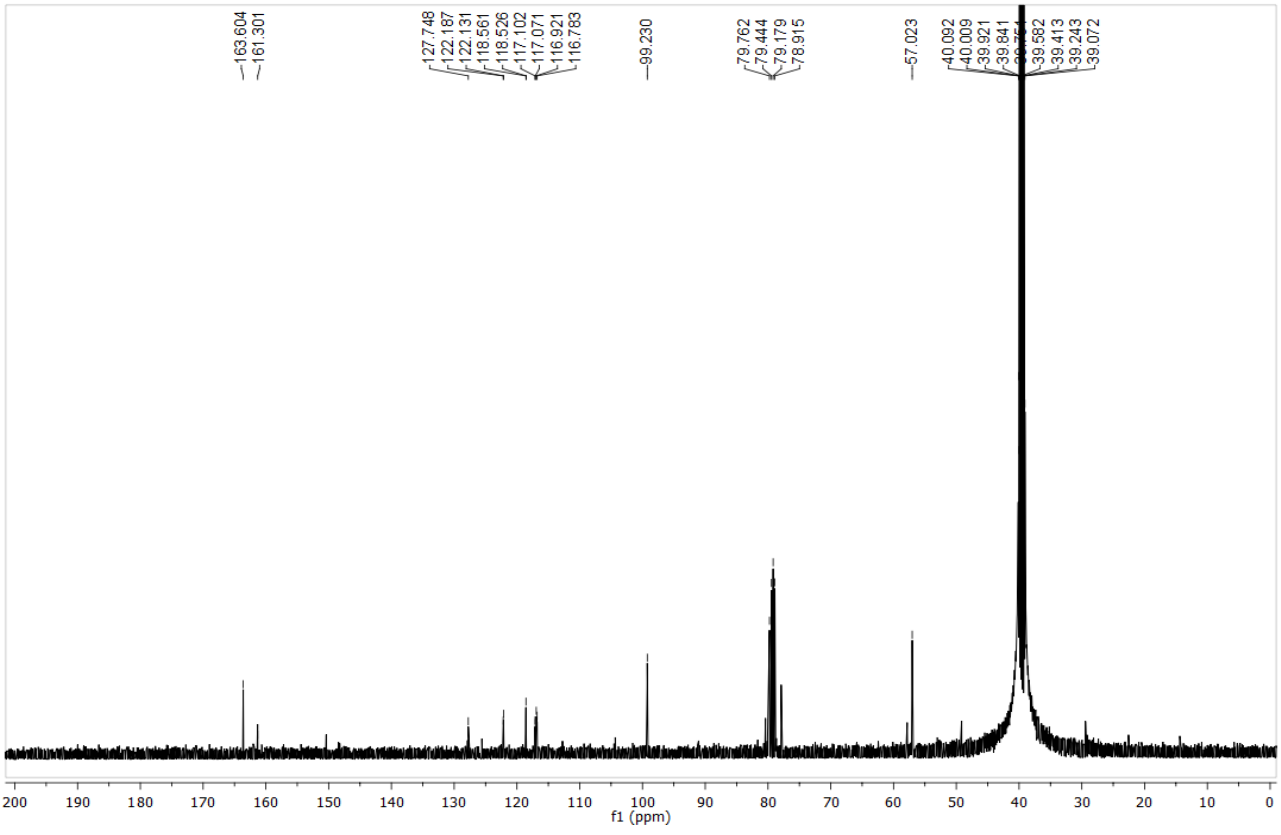

11.435
7.766
7.746
7.546
7.543
7.525
7.507
7.504
7.304
7.283
7.195
7.193
7.175
7.157
7.154
5.967
5.007
5.002
3.751
3.745
3.739
2.508
2.504
2.500
1.11
1.00
1.09
1.14
1.08
1.32
2.51
0.89
f1 (ppm)

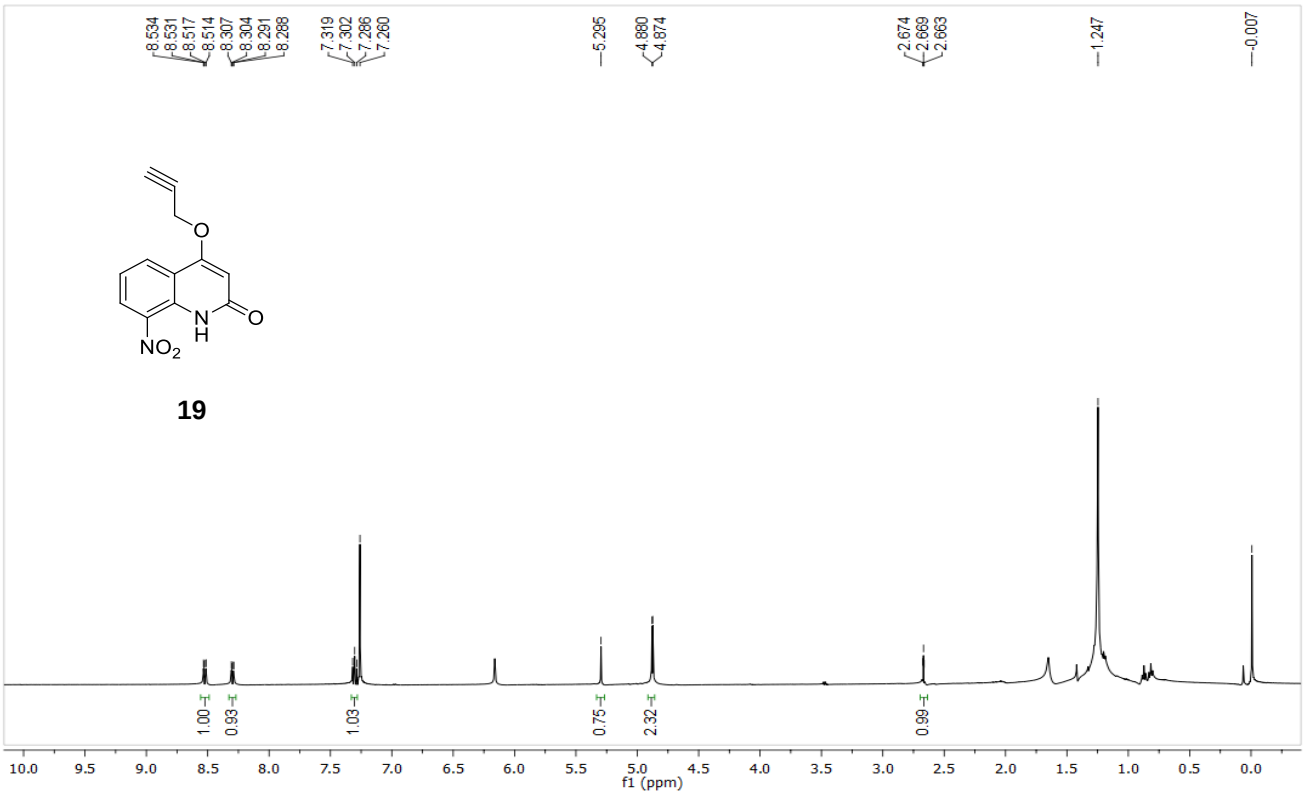

163.392
161.389
139.126
131.547
122.602
121.947
115.714
114.773
98.621
79.853
78.388
56.835
40.660
40.449
40.241
39.823
39.614
39.405
f1 (ppm)

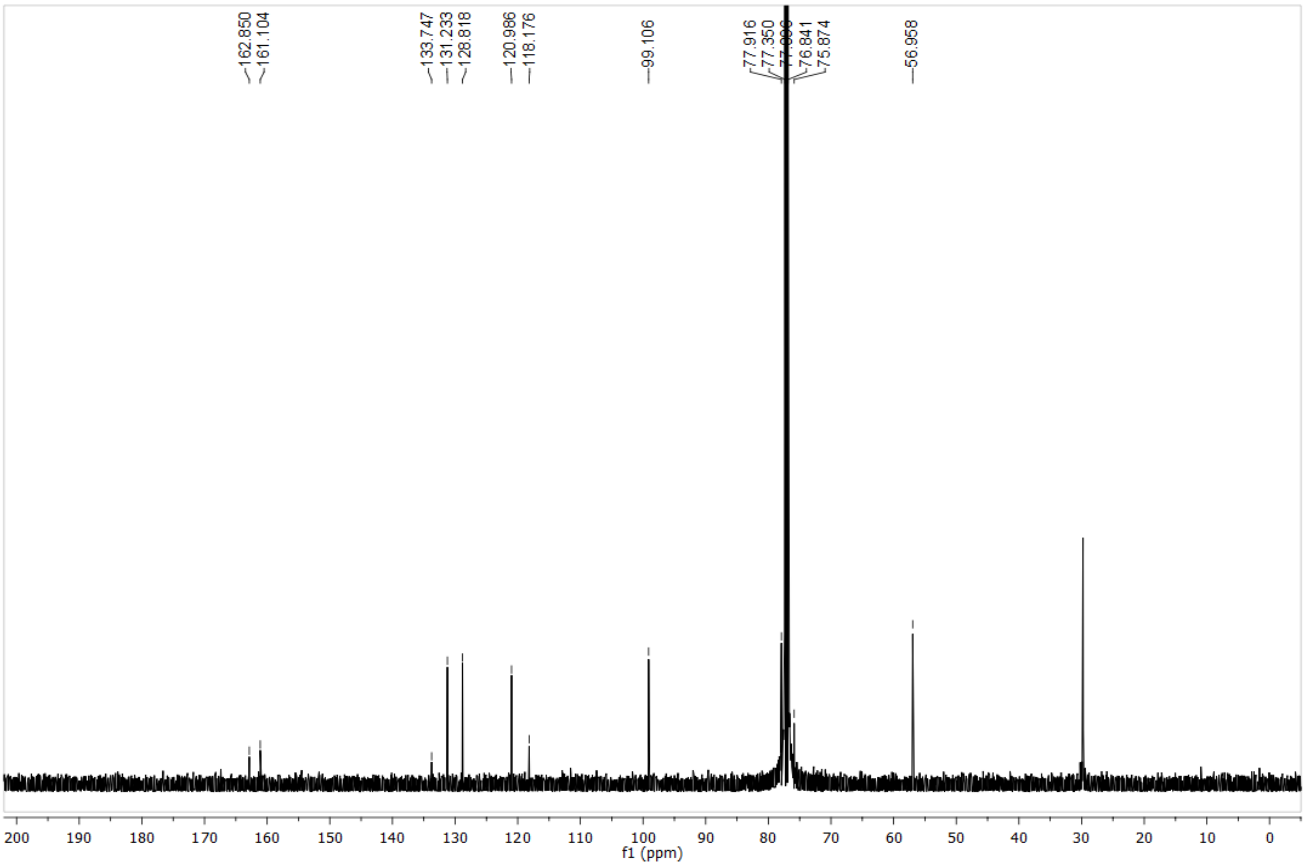
17

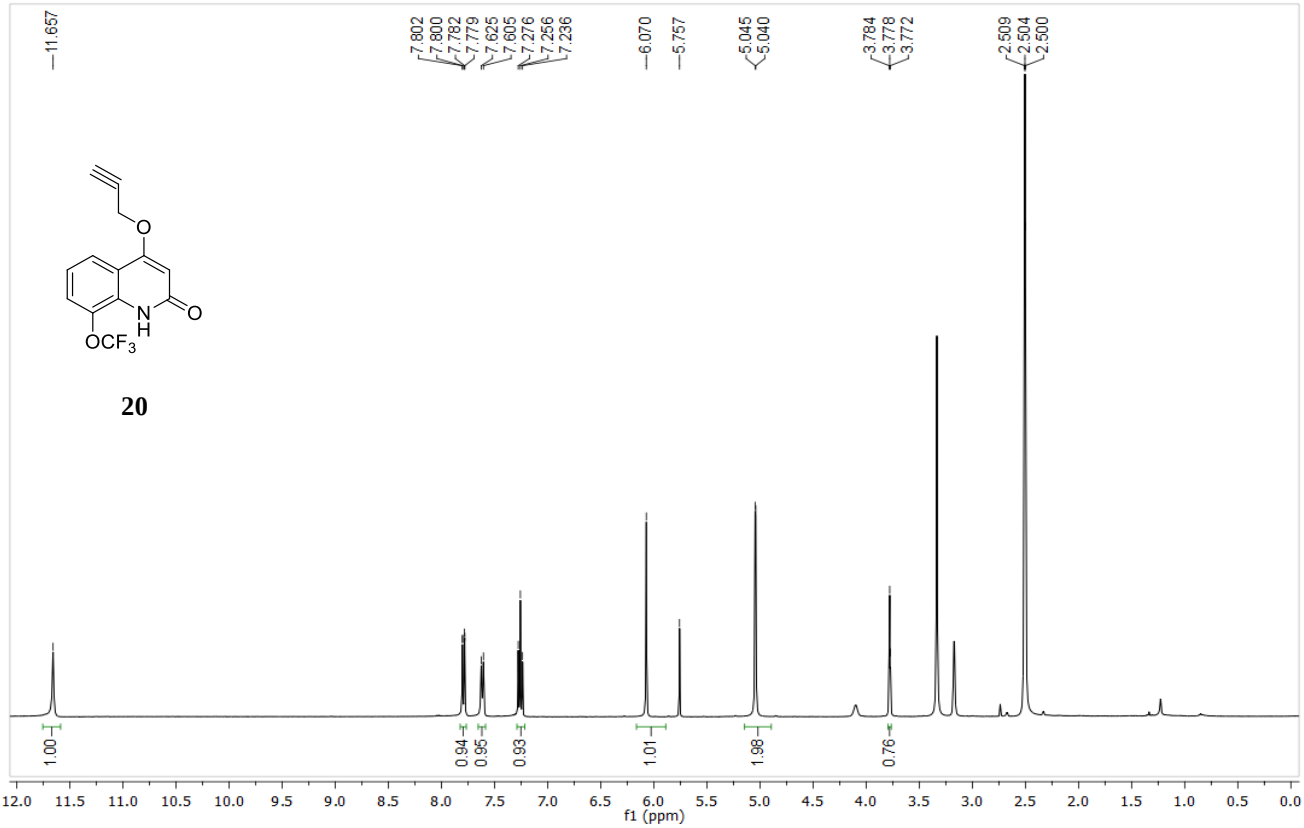

11.468
7.591
7.571
7.466
7.446
7.420
7.170
6.035
5.023
3.754
3.315
2.500
O
N
H
O
F
0.90
0.96
1.13
1.00
1.00
2.14
0.97
f1 (ppm)

18

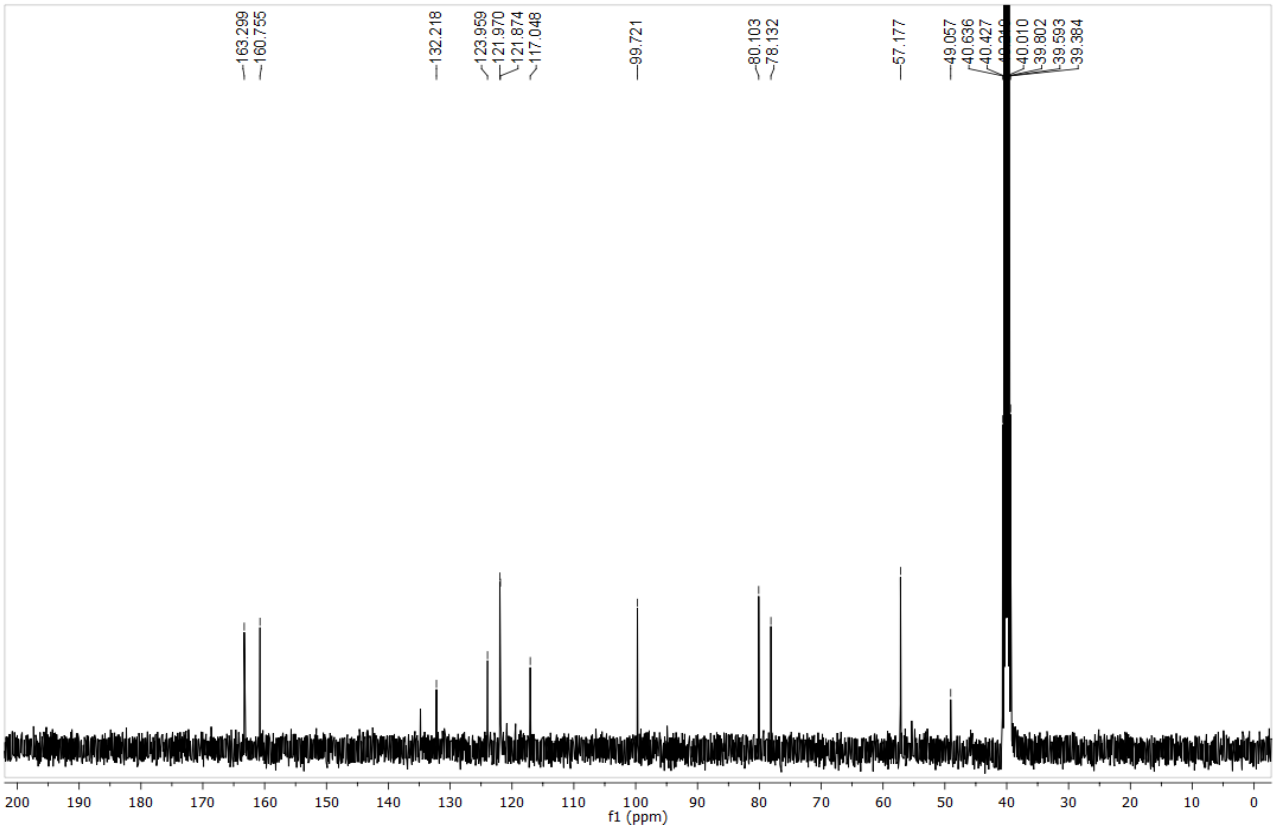

163.604
161.301
127.748
122.187
122.131
118.561
118.526
117.102
117.071
116.921
116.783
99.230
79.762
79.444
79.179
78.915
57.023
40.092
40.009
39.921
39.841
39.582
39.413
39.243
39.072
f1 (ppm)

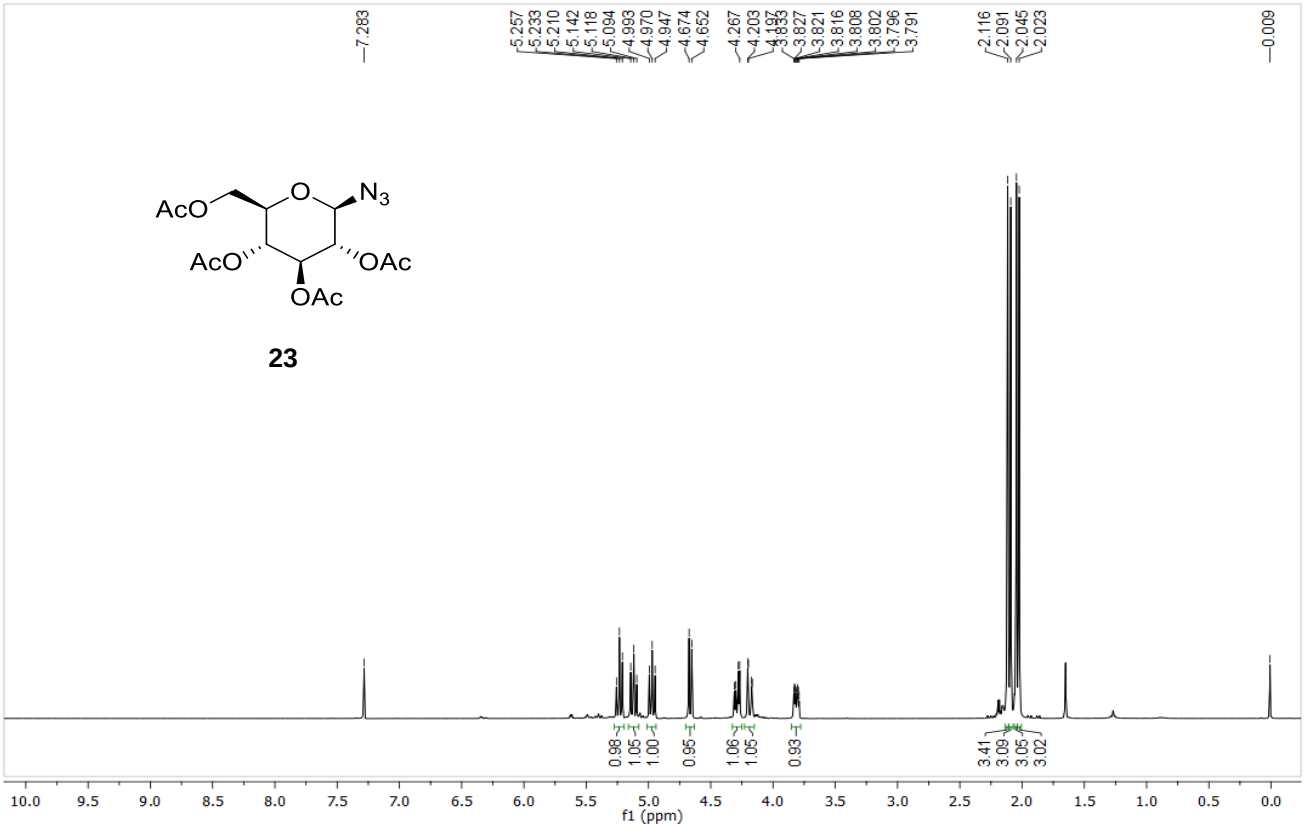

8.534
8.531
8.517
8.514
8.307
8.304
8.291
8.288
7.319
7.302
7.286
7.260
5.295
4.880
4.874
2.674
2.669
2.663
1.247
0.007
O
N
H
O
NO2
19
1.00
0.93
1.03
0.75
2.32
0.99
f1 (ppm)


162.850
161.104
133.747
131.233
128.818
120.986
118.176
99.106
77.916
77.350
76.841
75.874
56.958
f1 (ppm)

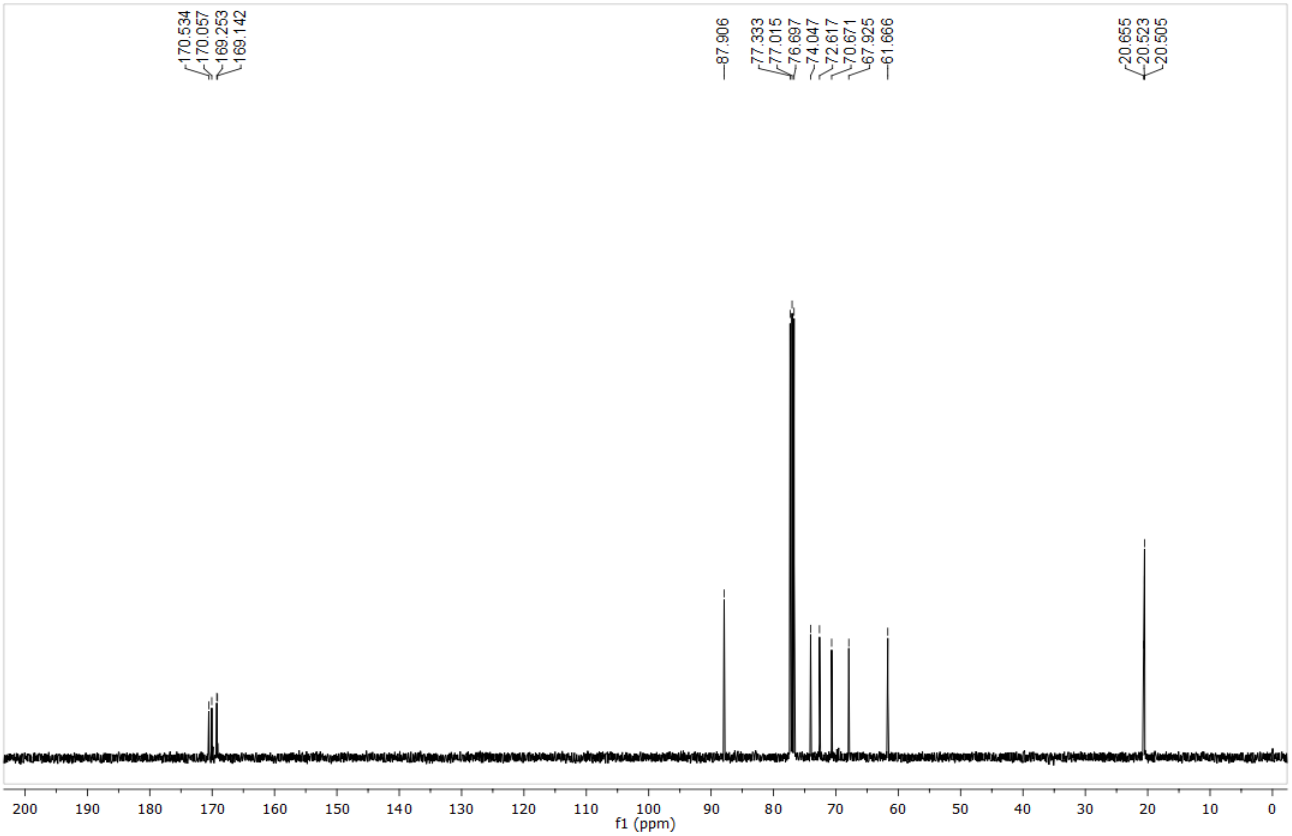

11.657
7.802
7.800
7.782
7.779
7.625
7.605
7.276
7.256
7.236
6.070
5.757
5.045
5.040
3.784
3.778
3.772
2.509
2.504
2.500
O
N
H
O
OCF3
1.00
0.94
0.95
0.93
1.01
1.98
0.76
f1 (ppm)

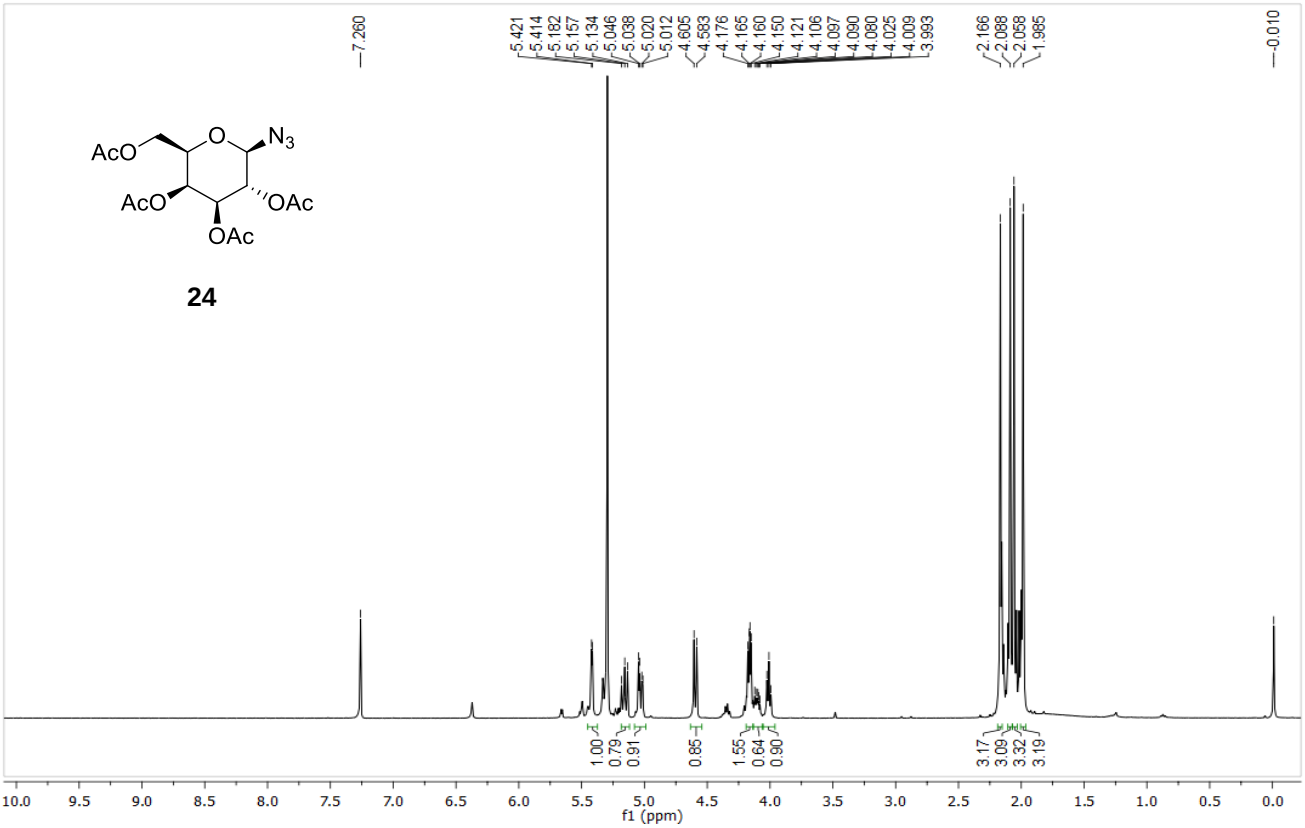
20

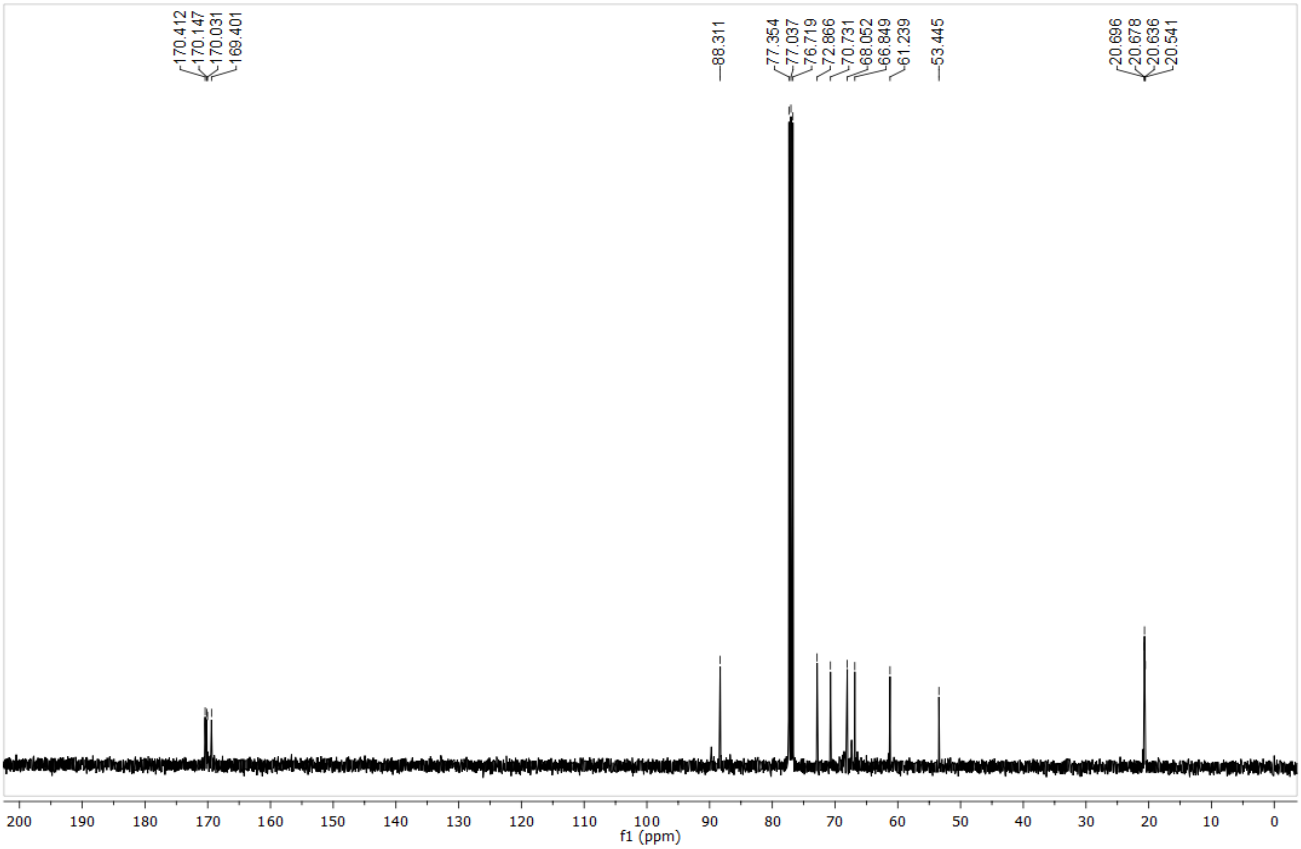

163.299
160.755
132.218
123.959
121.970
121.874
117.048
99.721
80.103
78.132
57.177
49.057
40.636
40.427
40.010
39.802
39.593
39.384
f1 (ppm)


7.283
5.257
5.233
5.210
5.142
5.118
5.094
4.993
4.970
4.947
4.674
4.652
4.267
4.203
4.197
3.833
3.827
3.821
3.816
3.808
3.802
3.796
3.791
2.116
2.091
2.045
2.023
0.009
AcO
O
N3
AcO
OAc
OAc
0.98
1.05
1.00
0.95
1.06
1.05
0.93
3.41
3.09
3.05
3.02
f1 (ppm)

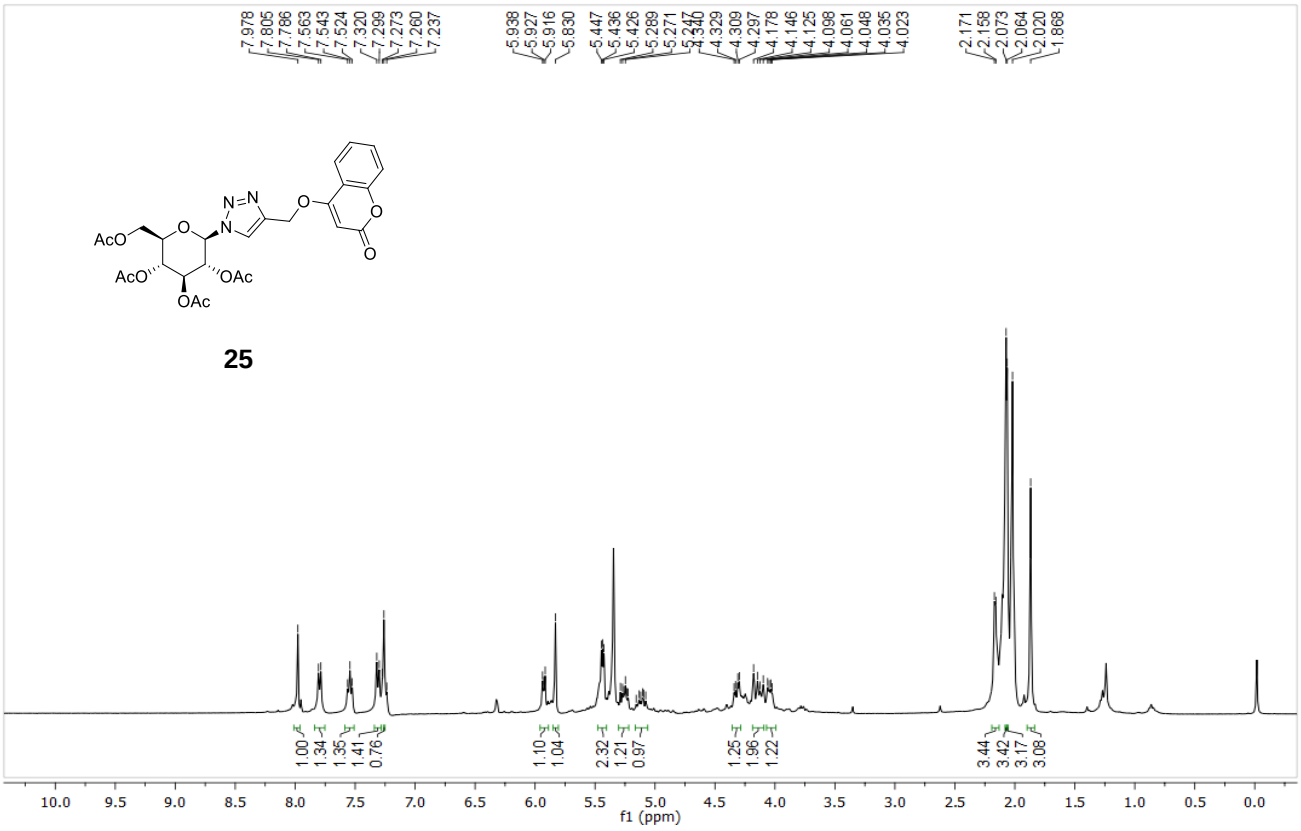
23


170.534
170.057
169.253
169.142
87.906
77.333
77.015
76.697
74.047
72.617
70.671
67.925
61.666
20.655
20.523
20.505
f1 (ppm)

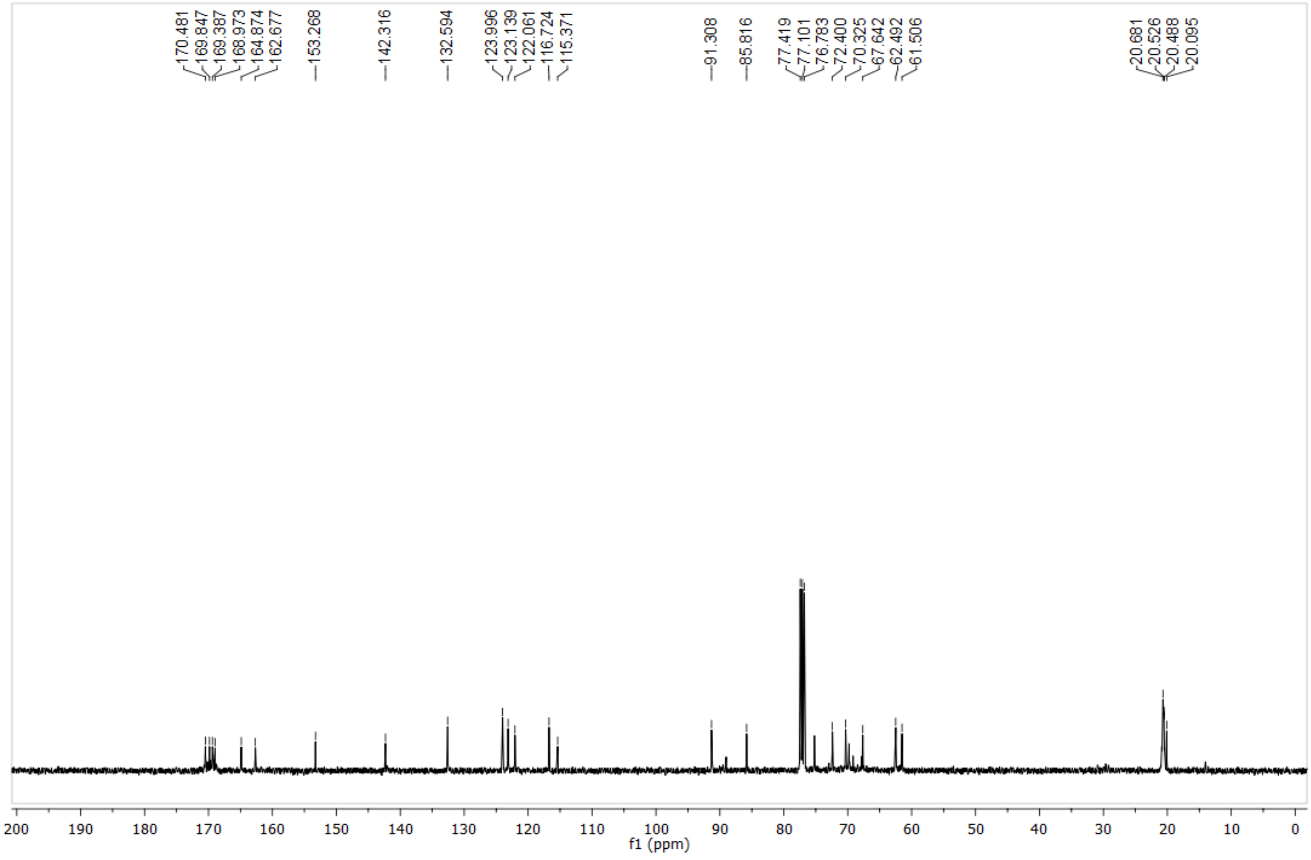

7.260
5.421
5.414
5.182
5.157
5.134
5.046
5.038
5.020
5.012
4.605
4.583
4.176
4.165
4.160
4.150
4.121
4.106
4.097
4.090
4.080
4.025
4.009
3.993
2.166
2.088
2.058
1.985
0.010
1.00
0.79
0.91
0.85
1.55
0.64
0.90
3.17
3.09
3.32
3.19
f1 (ppm)

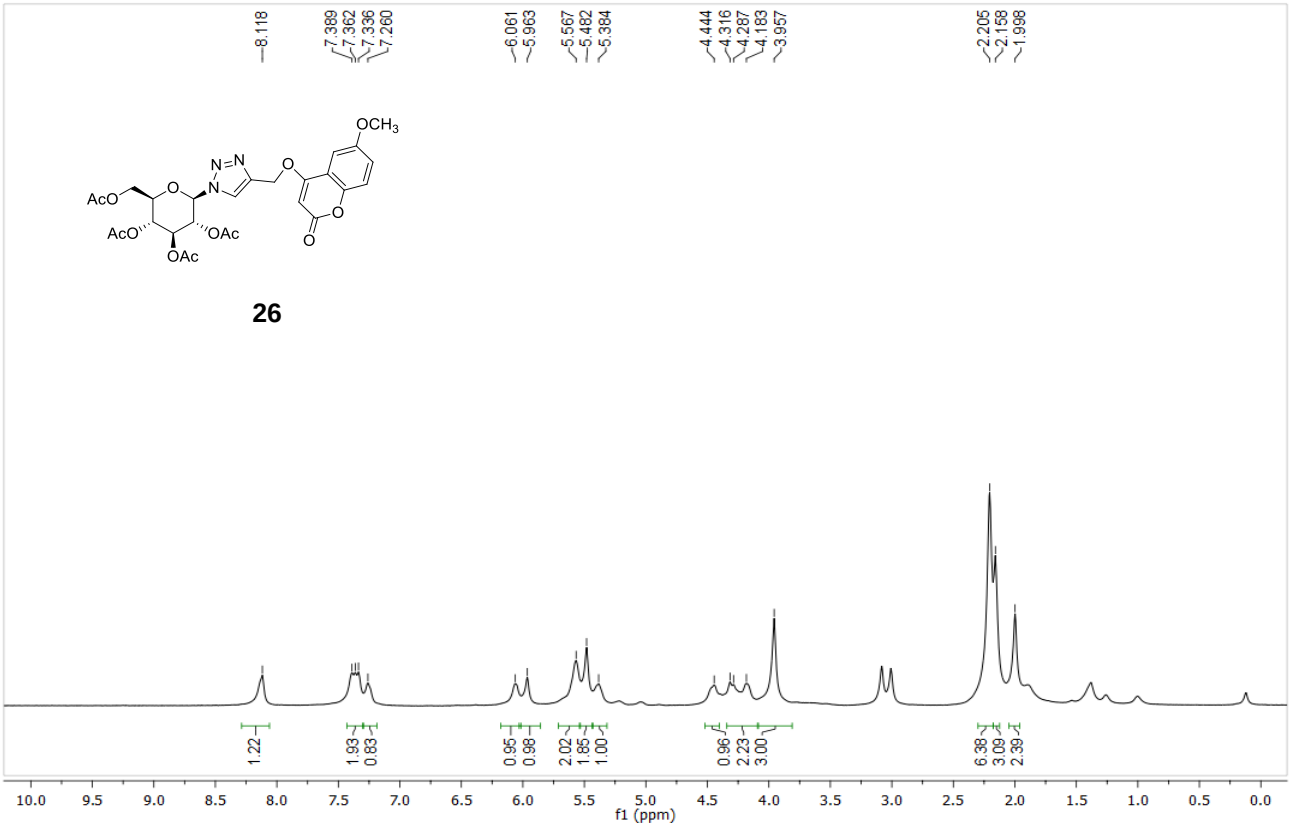

170.412
170.147
170.031
169.401
88.311
77.354
77.037
76.719
72.866
70.731
68.052
66.849
61.239
53.445
20.696
20.678
20.636
20.541
f1 (ppm)

24

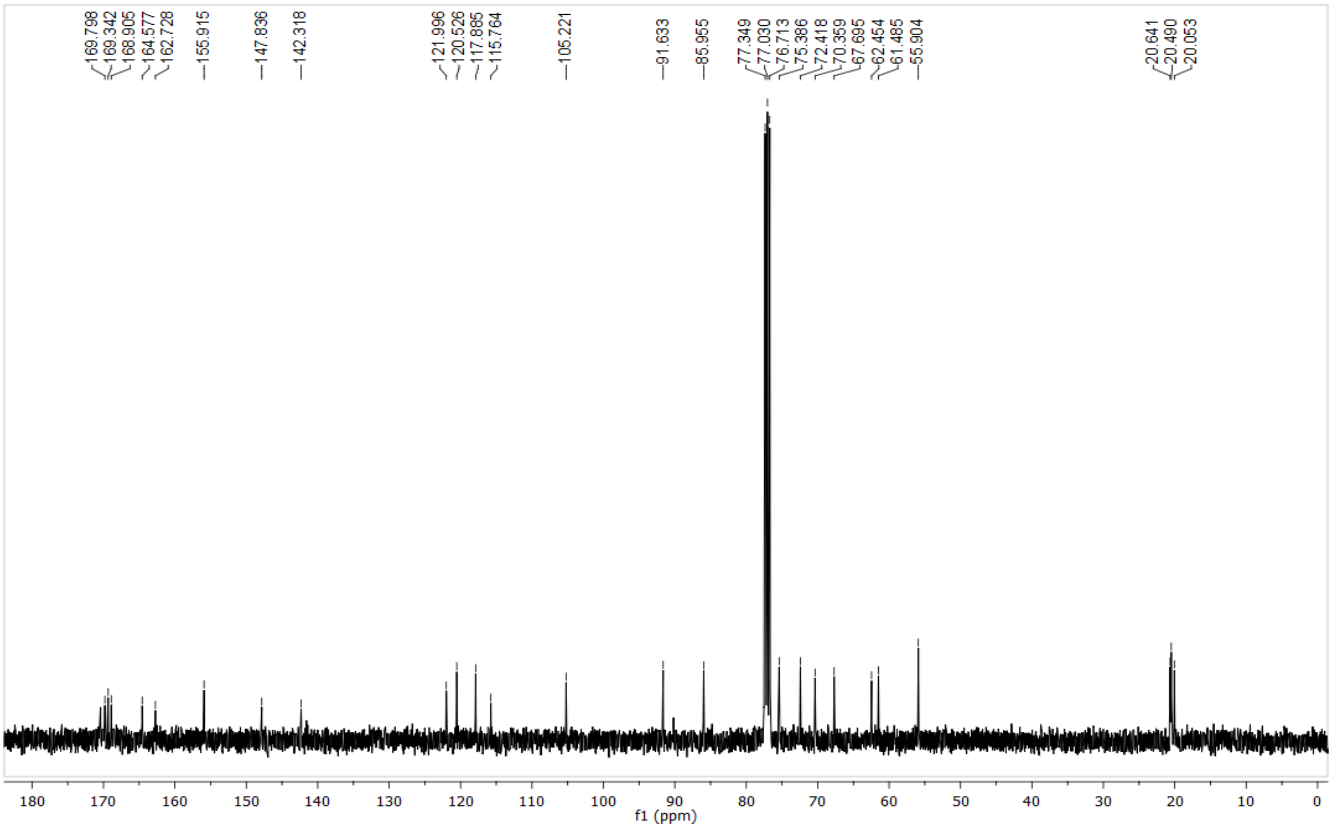

7.978
7.805
7.786
7.563
7.543
7.524
7.320
7.299
7.273
7.260
7.237
5.938
5.927
5.916
5.830
5.447
5.436
5.426
5.289
5.271
4.340
4.329
4.309
4.297
4.178
4.146
4.125
4.098
4.061
4.048
4.035
4.023
2.171
2.158
2.073
2.064
2.020
1.868
AcO
AcO
OAc
OAc
O
N
N
O
O
1.00
1.34
1.35
1.41
0.76
1.10
1.04
2.32
1.21
0.97
1.25
1.96
1.22
3.44
3.42
3.17
3.08
f1 (ppm)

25


170.481
169.847
169.387
168.973
164.874
162.677
153.268
142.316
132.594
123.996
123.139
122.061
116.724
115.371
91.308
85.816
77.419
77.101
76.783
72.400
70.325
67.642
62.492
61.506
20.681
20.526
20.488
20.095
f1 (ppm)


8.118
7.389
7.362
7.336
7.260
6.061
5.963
5.567
5.462
5.384
4.444
4.316
4.287
4.183
3.957
2.205
2.158
1.998
OCH3
AcO
AcO
OAc
OAc
O
O
O
N
N
N
1.22
1.93
0.83
0.95
0.98
2.02
1.85
1.00
0.96
2.23
3.00
6.38
3.09
2.39
f1 (ppm)

26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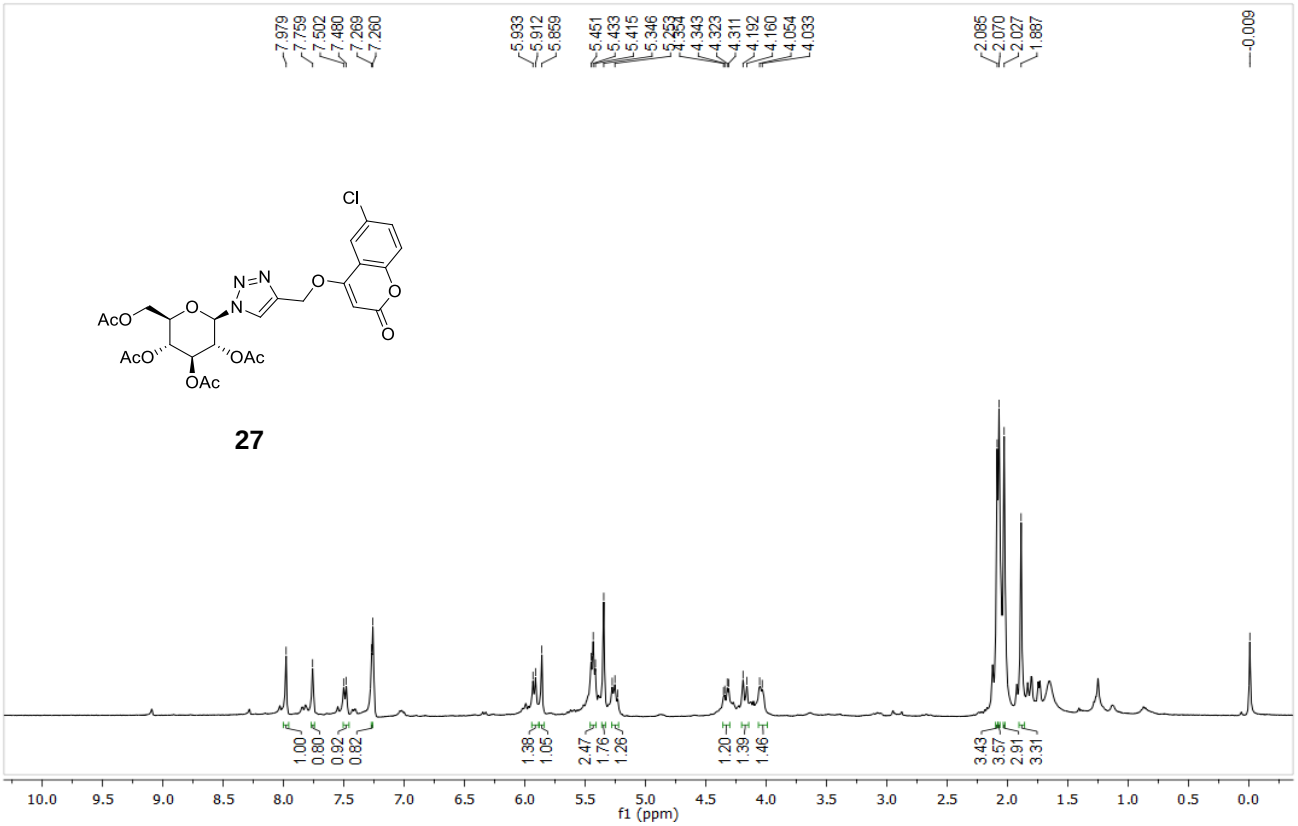
168.905
164.577
162.728
155.915
147.836
142.318
121.996
120.526
117.885
115.764
105.221
91.633
85.955
77.349
77.030
76.713
75.386
72.418
70.359
67.695
62.454
61.485
55.904
20.641
20.490
20.053
f1 (ppm)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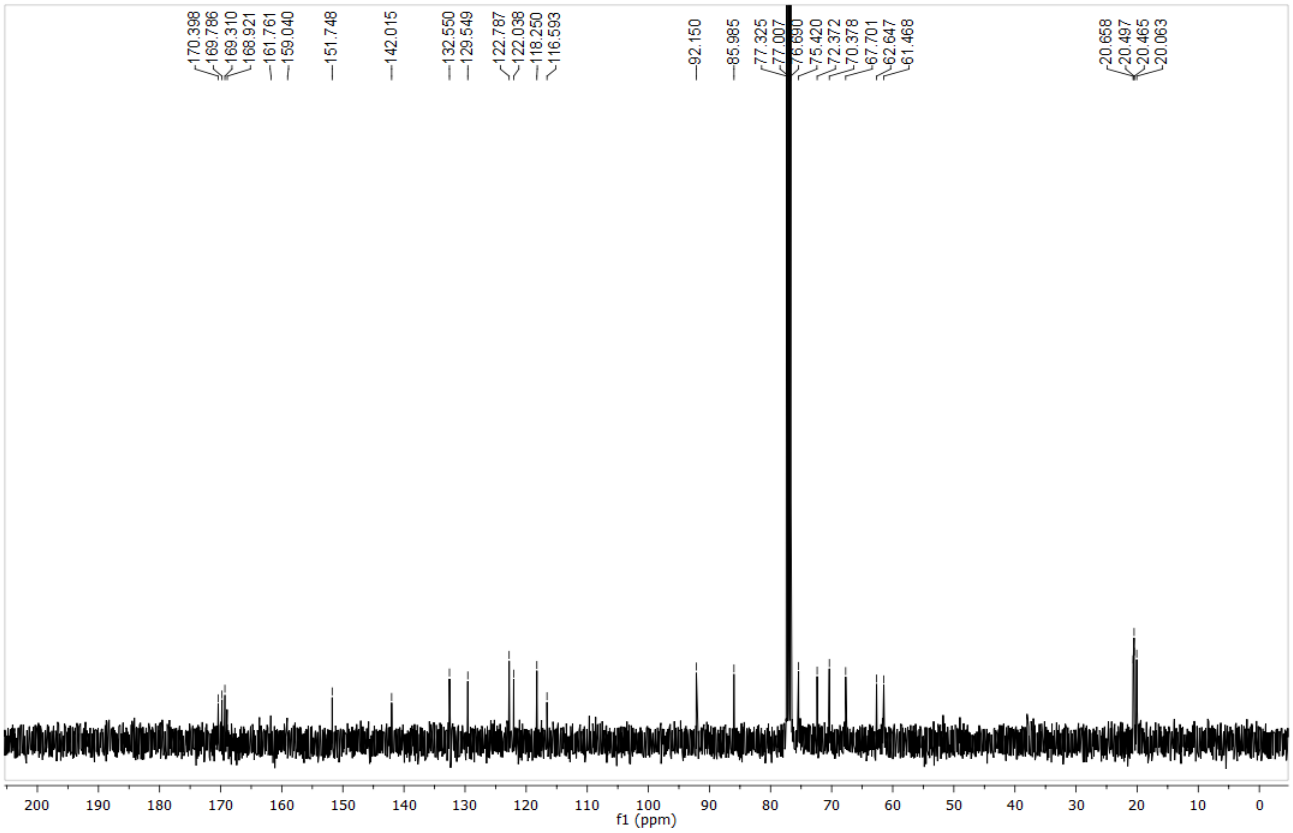
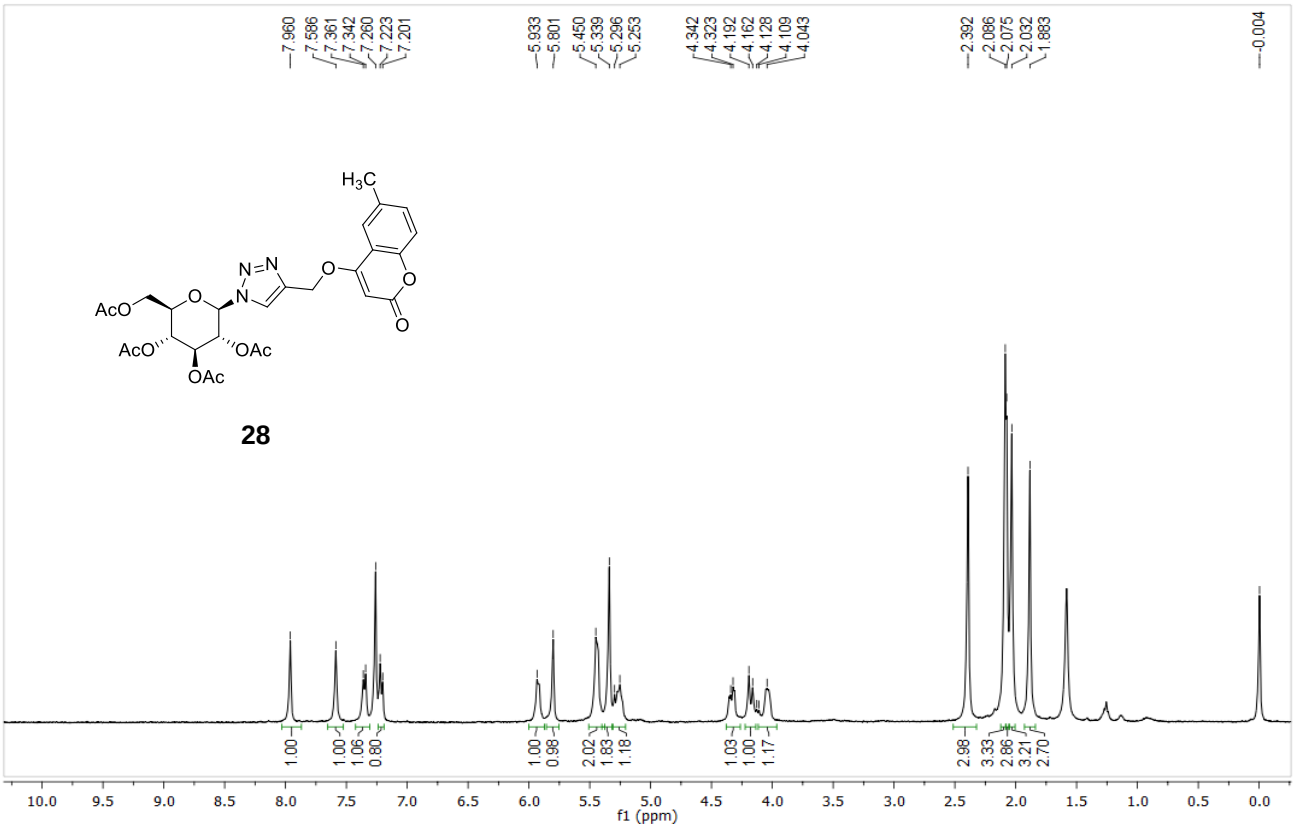
7.502
7.480
7.269
7.260
5.933
5.912
5.859
5.451
5.433
5.415
5.346
4.343
4.323
4.311
4.192
4.160
4.054
4.033
2.085
2.070
2.027
1.887
0.009
Cl
N=N
N
O
AcO
AcO
OAc
OAc
1.00
0.80
0.92
0.82
1.38
1.05
2.47
1.76
1.26
1.20
1.39
1.46
3.43
3.57
2.91
3.31
f1 (ppm)

27


170.398
169.786
169.310
168.921
161.761
159.040
151.748
142.015
132.550
129.549
122.787
122.038
118.250
116.593
92.150
85.985
77.325
77.007
76.690
75.420
72.372
70.378
67.701
62.647
61.468
20.658
20.497
20.465
20.063
f1 (ppm)


7.960
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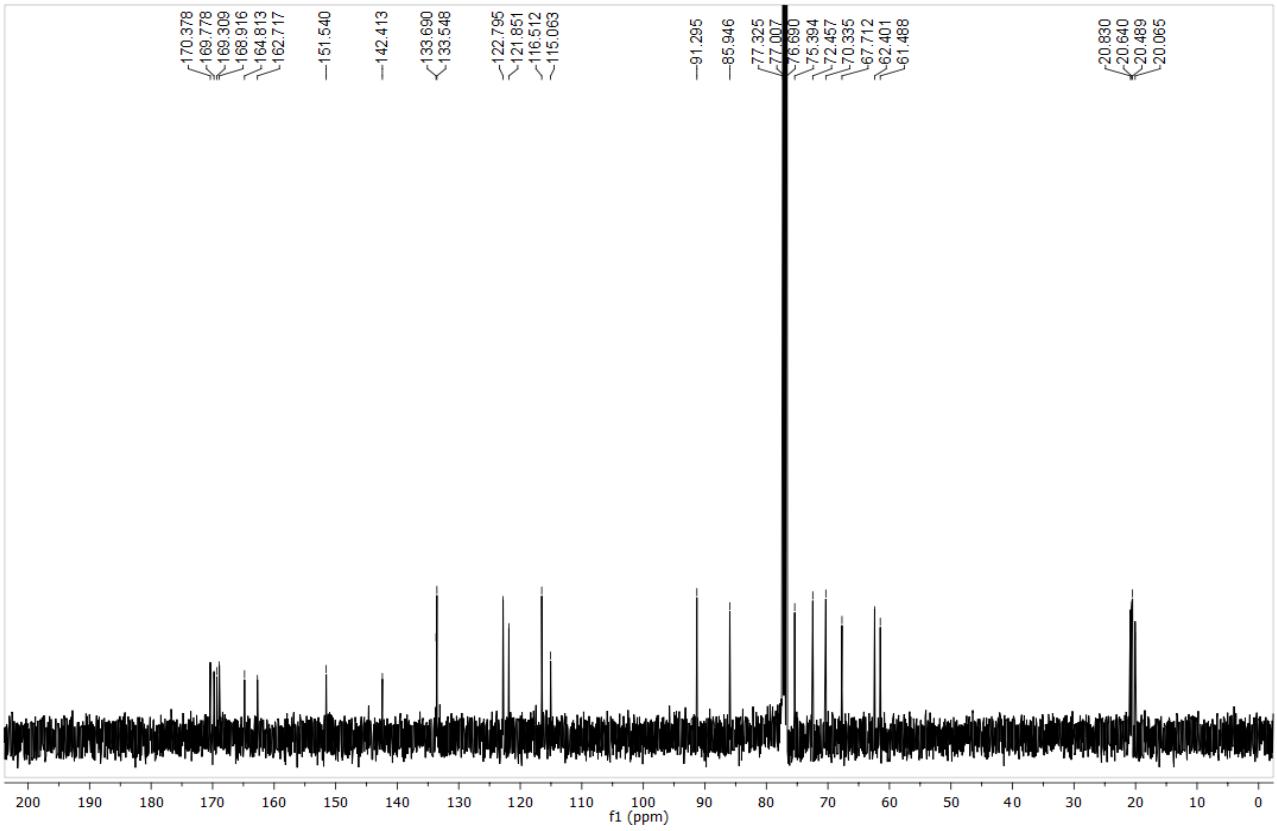
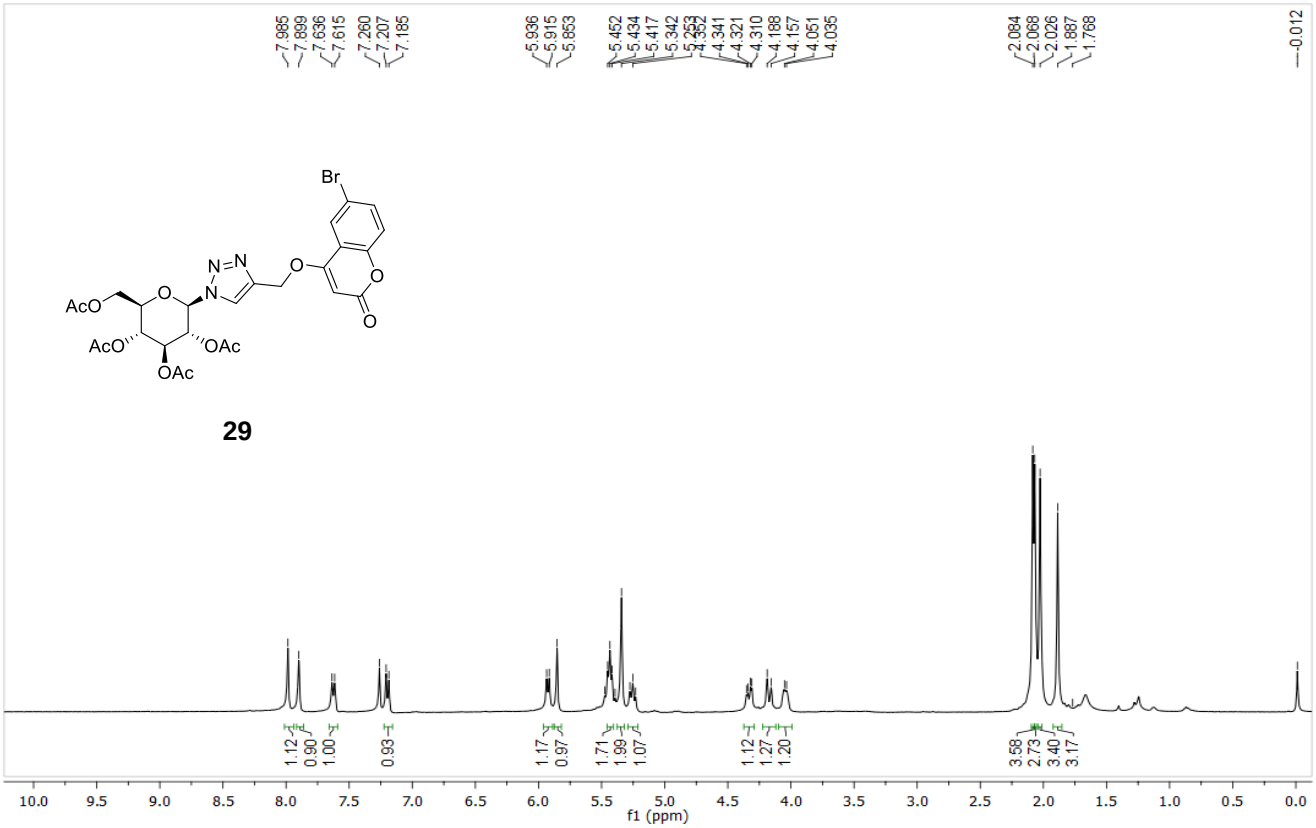
7.342
7.260
7.223
7.201
5.933
5.801
5.450
5.339
5.296
5.253
4.342
4.323
4.192
4.162
4.128
4.109
4.043
2.392
2.086
2.075
2.032
1.883
0.004
1.00
1.00
1.06
0.80
1.00
0.98
2.02
1.83
1.18
1.03
1.00
1.17
2.98
3.33
2.86
3.21
2.70
f1 (ppm)

H3C
N=N
N
O
O
O
AcO
AcO
OAc
OAc

28


170.378
169.778
169.309
168.916
164.813
162.717
151.540
142.413
133.690
133.548
122.795
121.851
116.512
115.063
91.295
85.946
77.325
77.007
76.690
75.394
72.457
70.335
67.712
62.401
61.488
20.830
20.640
20.489
20.065
f1 (ppm)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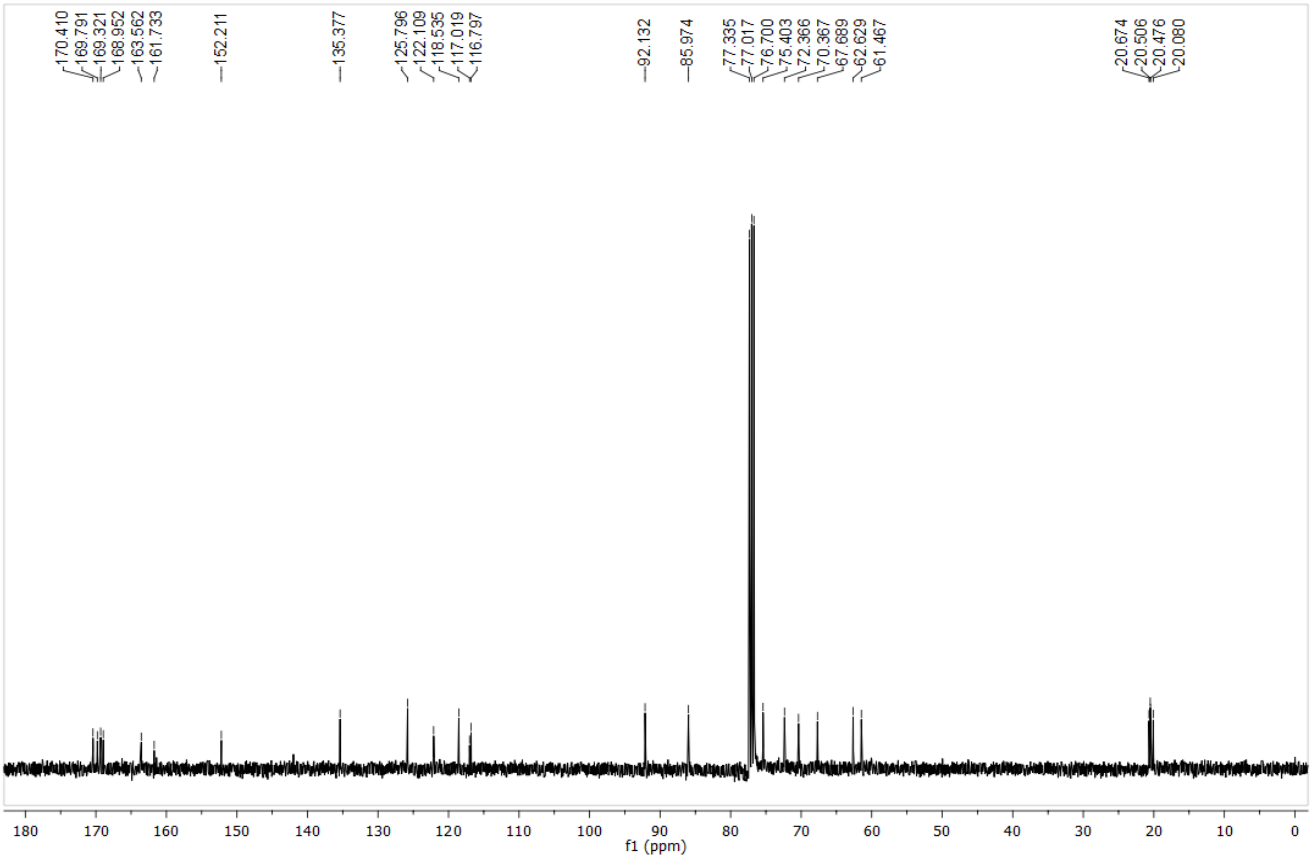
7.636
7.615
7.260
7.207
7.185
5.936
5.915
5.853
5.452
5.434
5.417
5.342
5.253
4.352
4.341
4.321
4.310
4.188
4.157
4.051
4.035
2.084
2.068
2.026
1.887
1.768
-0.012
Br
N=N
N
O
O
O
AcO
AcO
OAc
OAc
1.12
0.90
1.00
0.93
1.17
0.97
1.71
1.99
1.07
1.12
1.27
1.20
3.58
2.73
3.40
3.17
f1 (ppm)

29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169.321
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135.377
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122.109
118.535
117.019
116.797
92.132
85.974
77.335
77.017
76.700
75.403
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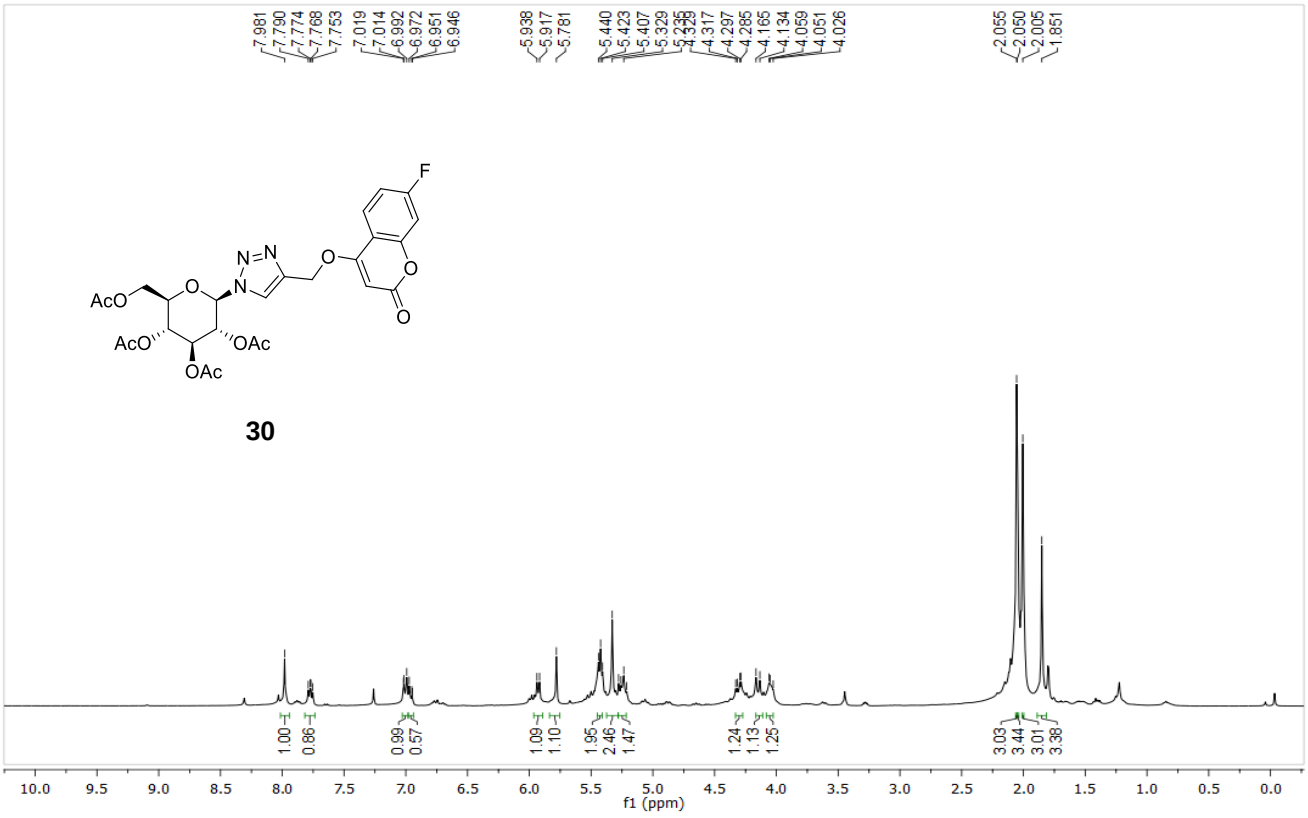
70.367
67.689
62.629
61.467
20.674
20.506
20.476
20.080
f1 (ppm)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7.790
7.774
7.768
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7.014
6.992
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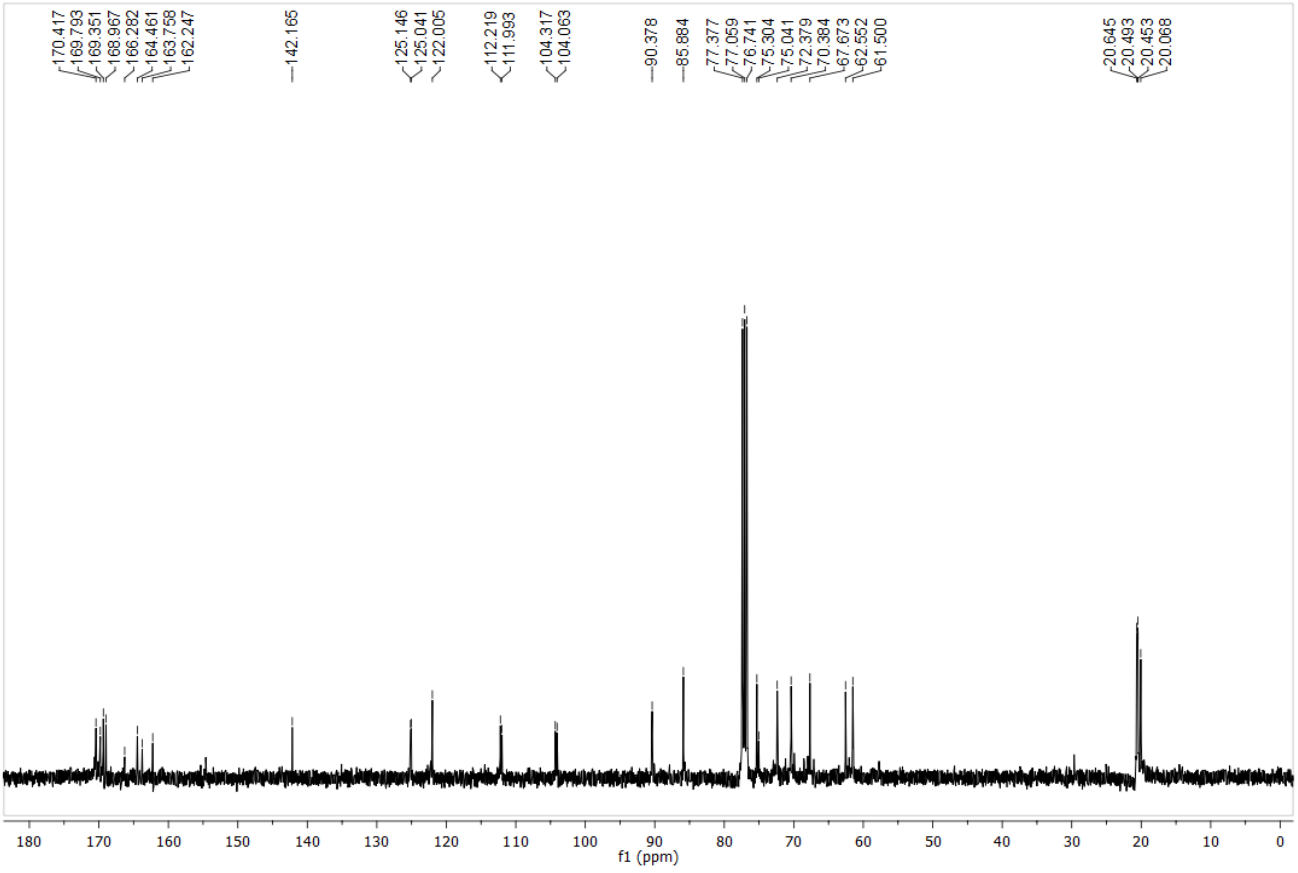
6.951
6.946
5.938
5.917
5.781
5.440
5.423
5.407
5.329
4.317
4.297
4.285
4.165
4.134
4.059
4.051
4.026
2.055
2.050
2.005
1.851
F
O
O
N
N
N
O
AcO
AcO
OAc
OAc
1.00
0.86
0.99
0.57
1.09
1.10
1.95
2.46
1.47
1.24
1.13
1.25
3.03
3.44
3.01
3.38
f1 (ppm)

30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112.219
111.993
104.317
104.063
90.378
85.884
77.377
77.059
76.741
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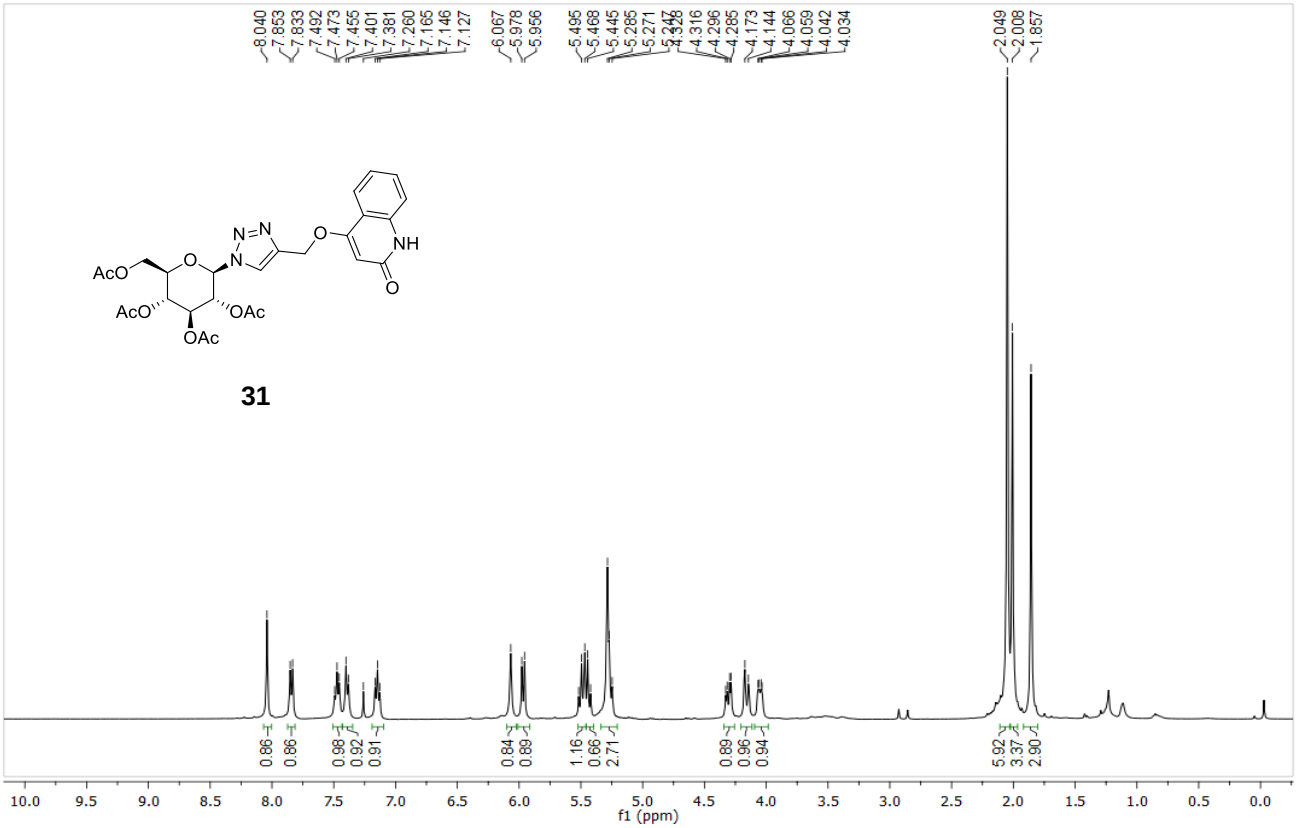
20.453
20.068
f1 (ppm)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7.833
7.492
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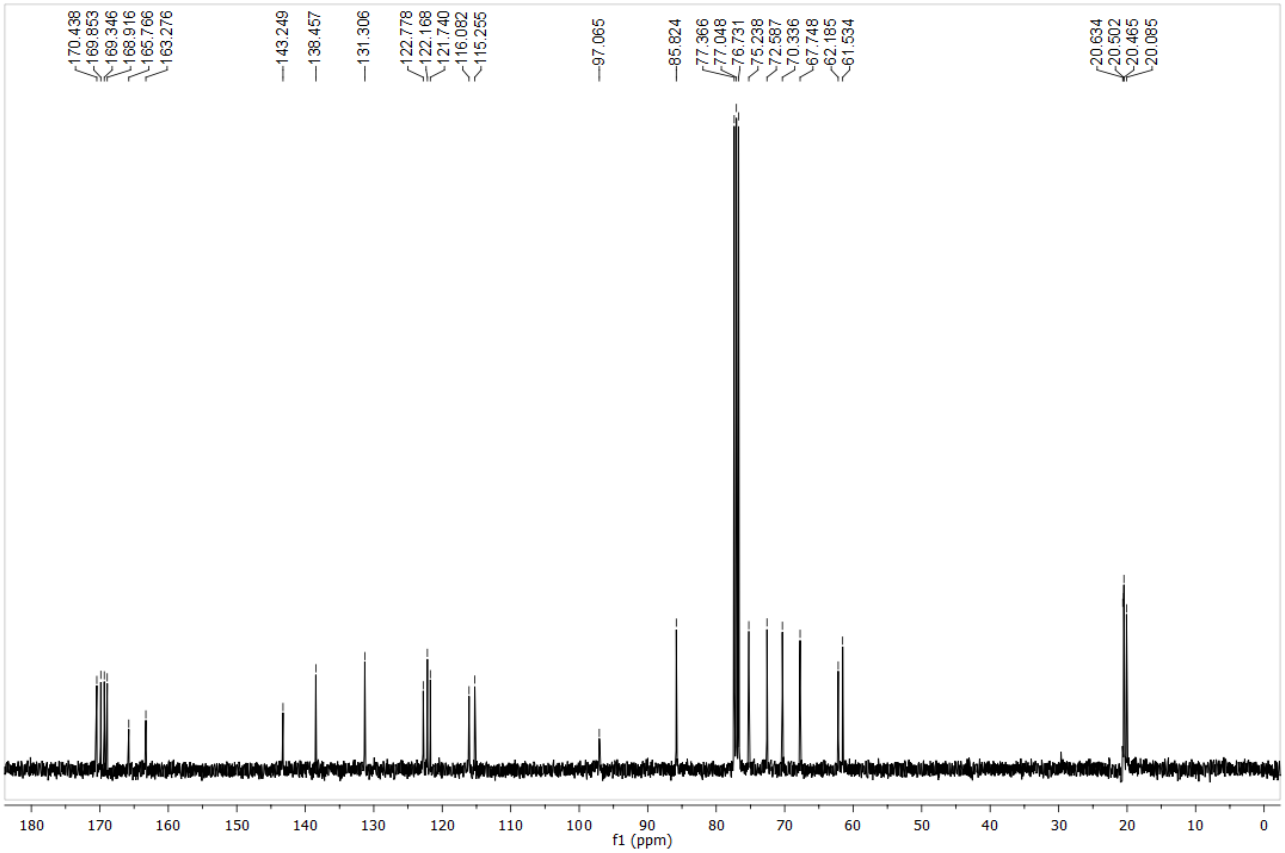
7.401
7.381
7.260
7.165
7.146
7.127
6.067
5.978
5.956
5.495
5.468
5.445
5.285
5.271
4.316
4.296
4.285
4.173
4.144
4.066
4.059
4.042
4.034
2.049
2.008
1.857
AcO
AcO
OAc
OAc
N=N
O
NH
O
0.86
0.86
0.98
0.92
0.91
0.84
0.89
1.16
0.66
2.71
0.89
0.96
0.94
5.92
3.37
2.90
f1 (ppm)

31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138.457
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116.082
115.255
97.065
85.824
77.366
77.048
76.731
75.238
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70.336
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62.185
61.534
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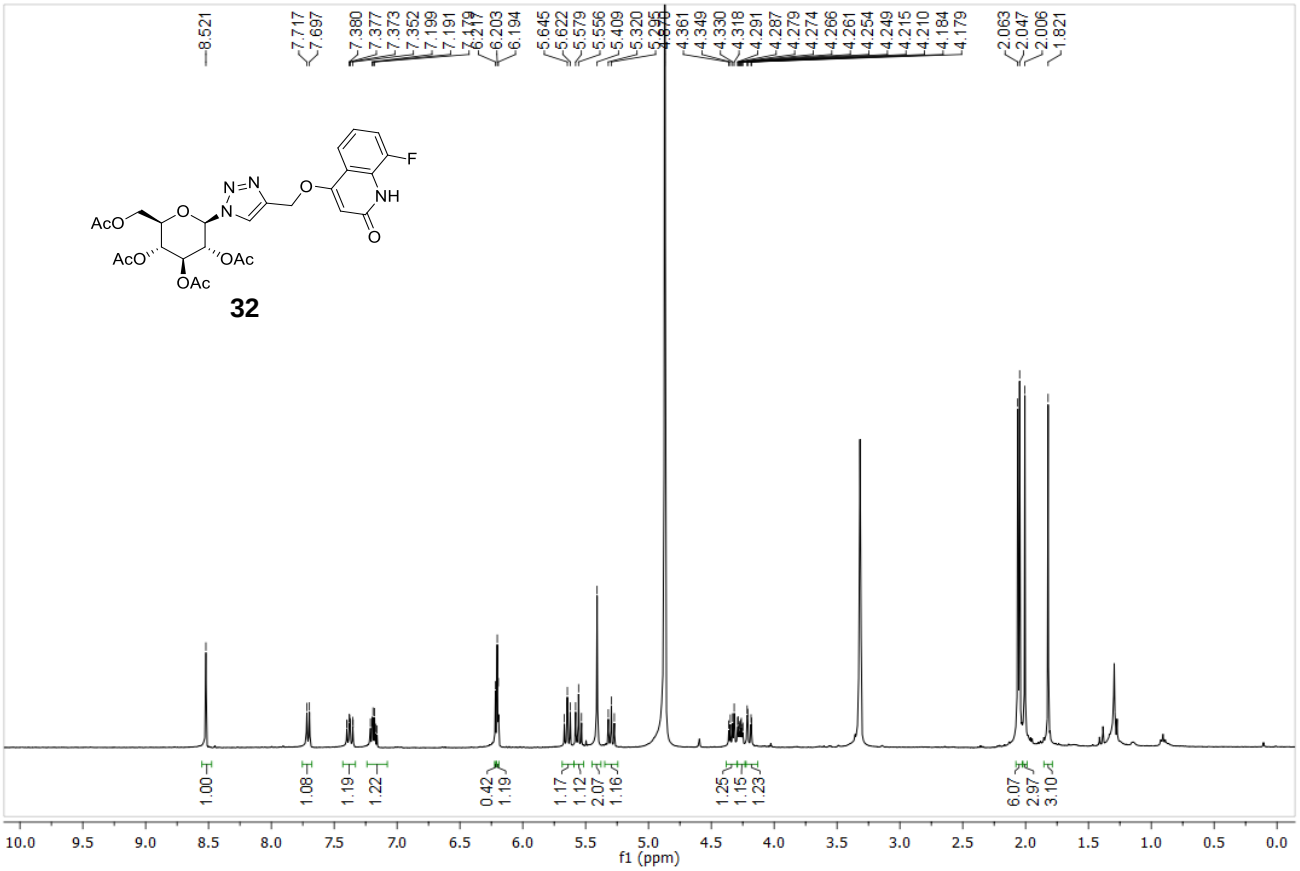
20.502
20.465
20.085
f1 (ppm)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7.697
7.380
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7.373
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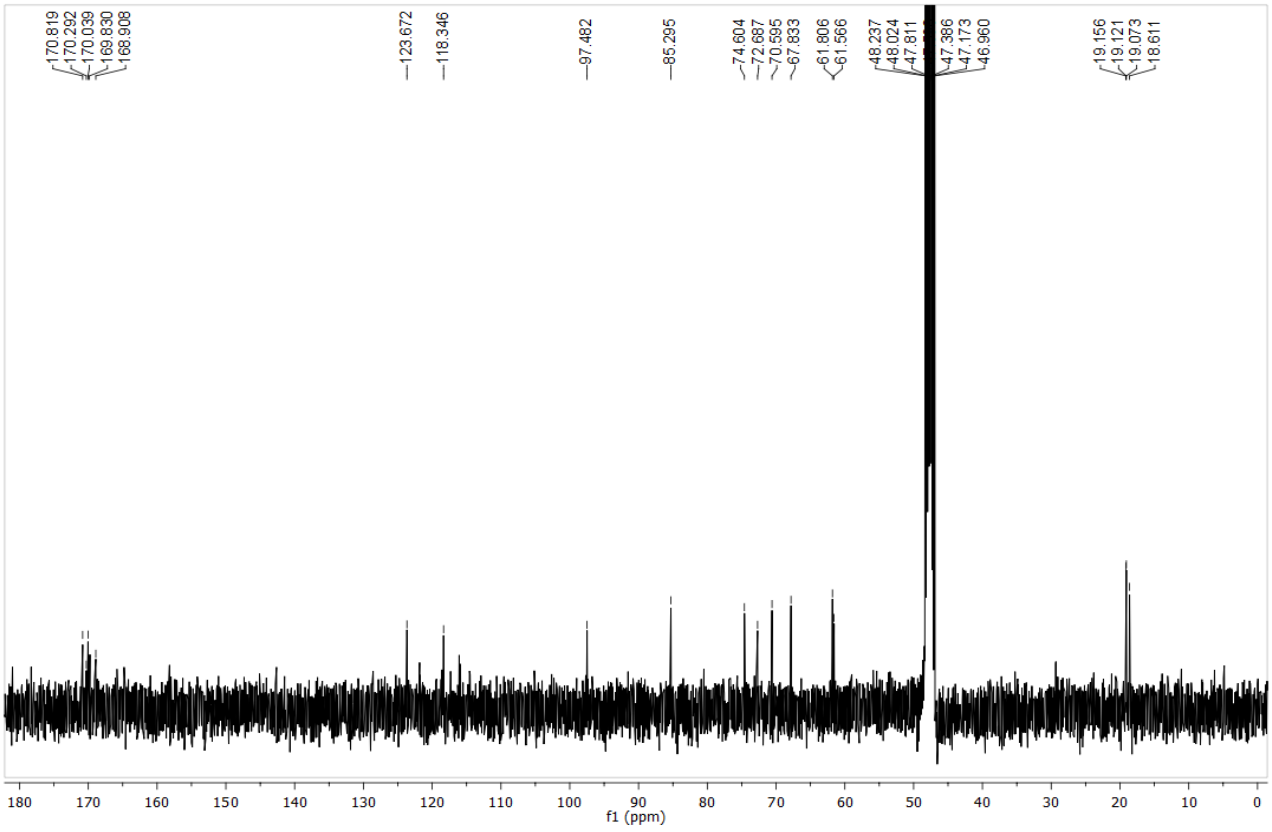
7.199
7.191
7.179
7.177
6.203
6.194
5.645
5.622
5.579
5.556
5.409
5.320
5.295
5.290
4.361
4.349
4.330
4.318
4.291
4.287
4.279
4.274
4.266
4.261
4.254
4.249
4.215
4.210
4.184
4.179
2.063
2.047
2.006
1.821
F
NH
O
N=N
N
O
AcO
AcO
OAc
OAc
32
1.00
1.08
1.19
1.22
0.42
1.19
1.17
1.12
2.07
1.16
1.25
1.15
1.23
6.07
2.97
3.10
f1 (ppm)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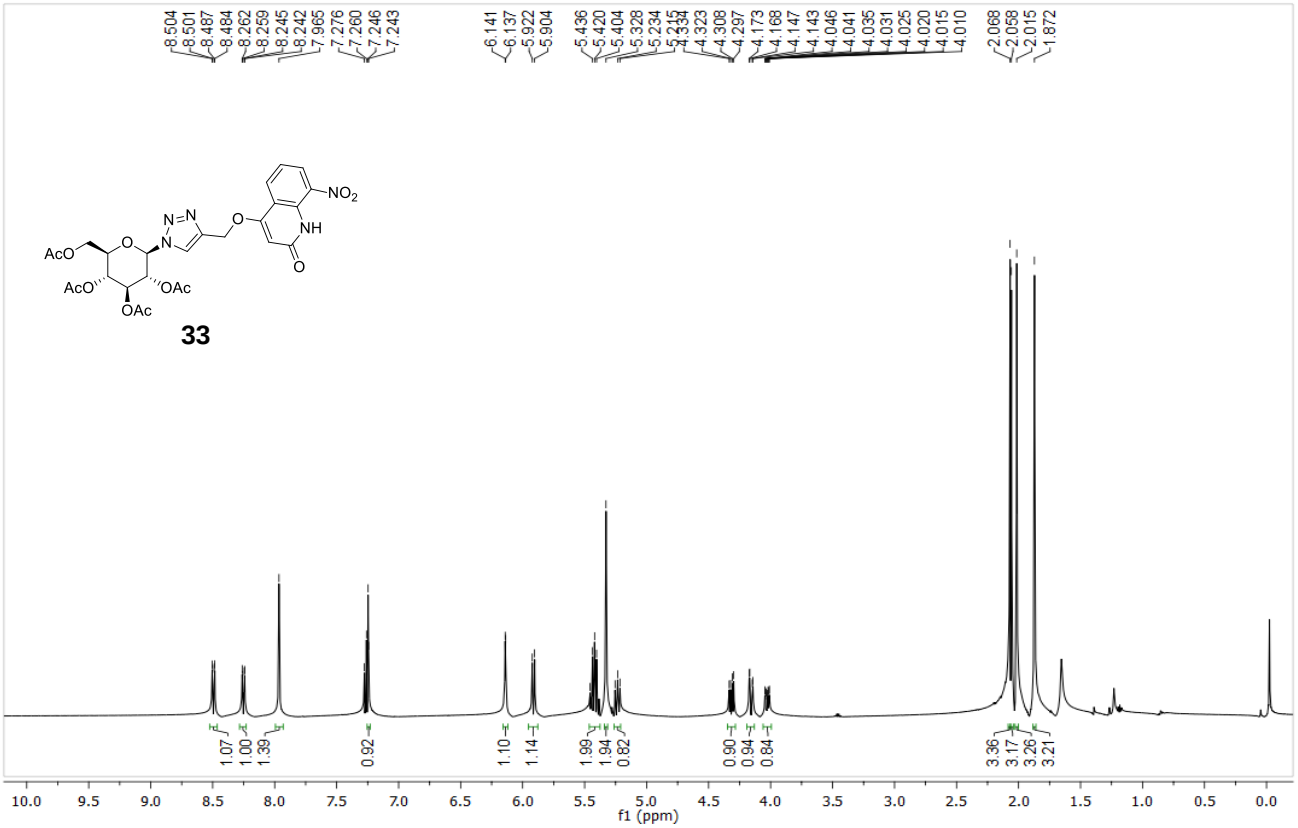
170.039
169.830
168.908
123.672
118.346
97.482
85.295
74.604
72.687
70.595
67.833
61.806
61.566
48.237
48.024
47.811
47.386
47.173
46.960
19.156
19.121
19.073
18.611
f1 (ppm)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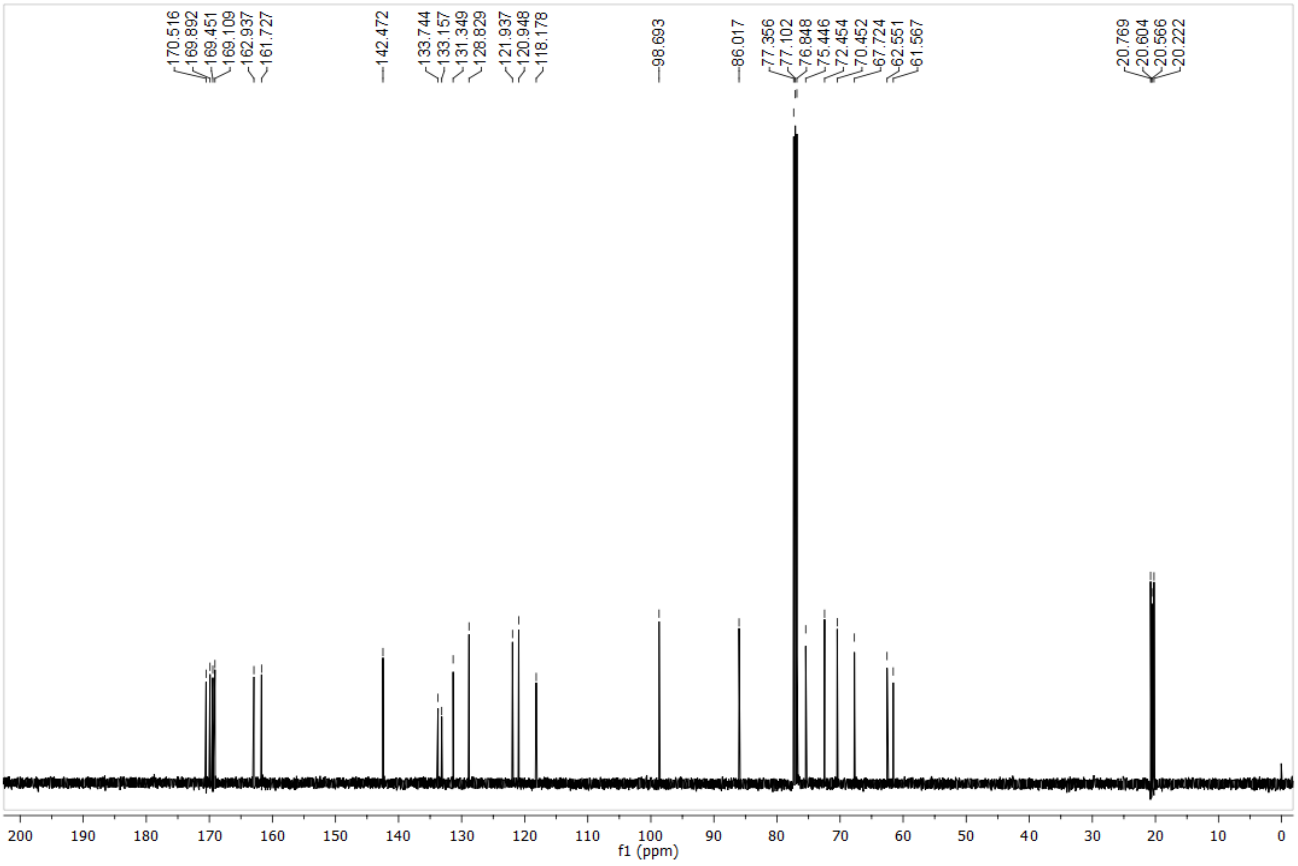
8.501
8.487
8.484
8.262
8.259
8.245
8.242
7.965
7.276
7.260
7.246
7.243
6.141
6.137
5.922
5.904
5.436
5.420
5.404
5.328
5.234
4.323
4.308
4.297
4.173
4.168
4.147
4.143
4.046
4.041
4.035
4.031
4.025
4.020
4.015
4.010
2.068
2.058
2.015
1.872
NO2
NH
O
N=N
AcO
AcO
OAc
OAc
1.07
1.00
1.39
0.92
1.10
1.14
1.99
1.94
0.82
0.90
0.94
0.84
3.36
3.17
3.26
3.21
f1 (ppm)

33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169.451
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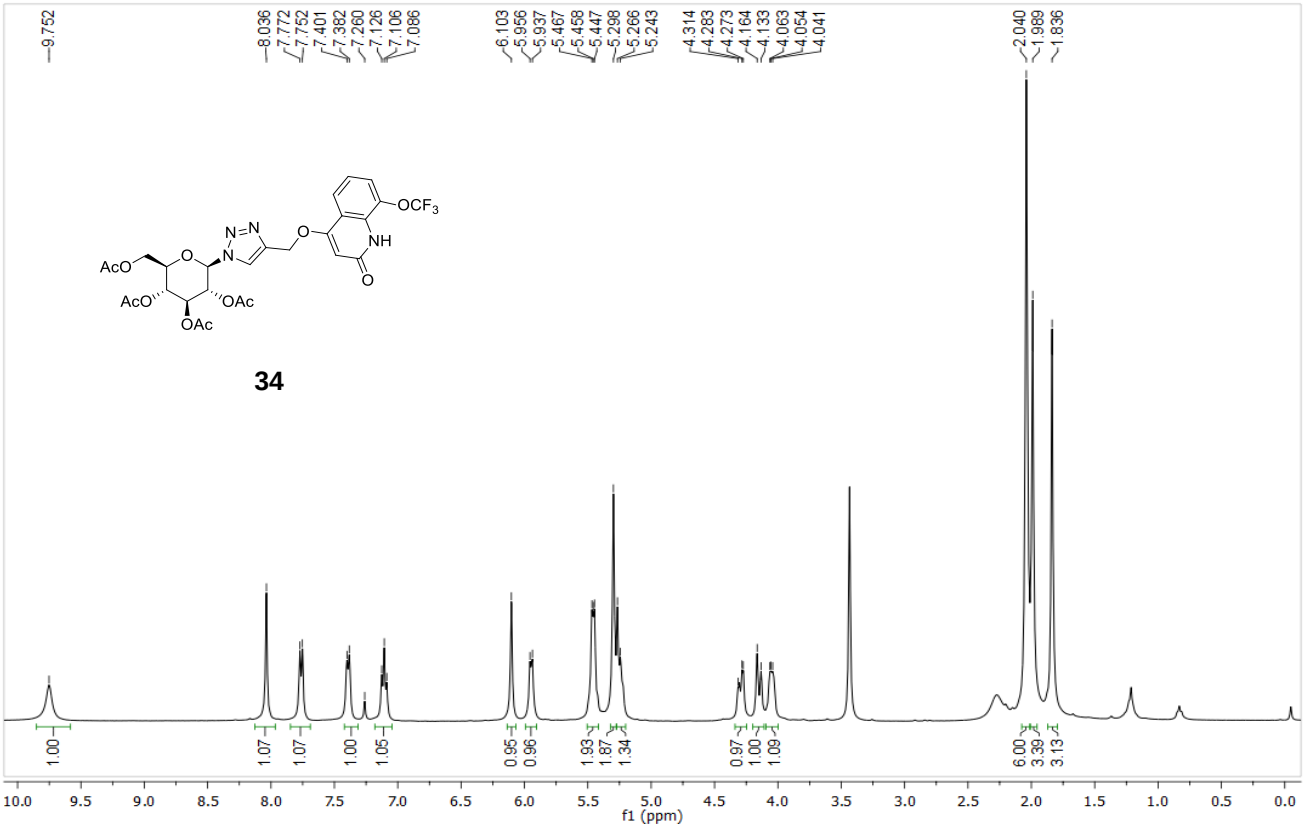
162.937
161.727
142.472
133.744
133.157
131.349
128.829
121.937
120.948
118.178
98.693
86.017
77.356
77.102
76.848
75.446
72.454
70.452
67.724
62.551
61.567
20.769
20.604
20.566
20.222
f1 (ppm)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7.401
7.382
7.260
7.126
7.106
7.086
6.103
5.956
5.937
5.467
5.458
5.447
5.298
5.266
5.243
4.314
4.283
4.273
4.164
4.133
4.063
4.054
4.041
2.040
1.989
1.836
OCF3
NH
O
AcO
AcO
OAc
OAc
1.00
1.07
1.07
1.00
1.05
0.95
0.96
1.93
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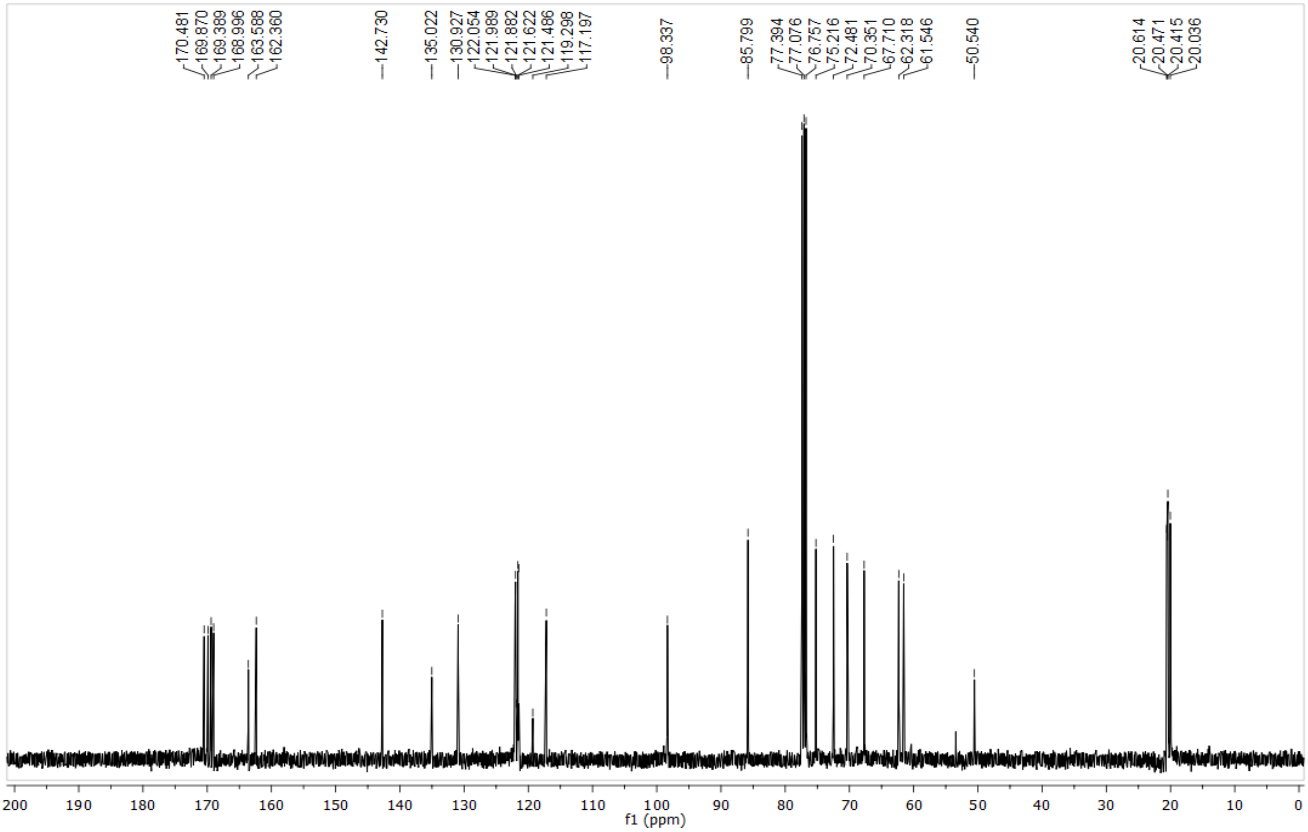
1.34
0.97
1.00
1.09
6.00
3.39
3.13
f1 (ppm)

34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135.022
130.927
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121.882
121.622
121.486
119.298
117.197
98.337
85.799
77.394
77.076
76.757
75.216
72.481
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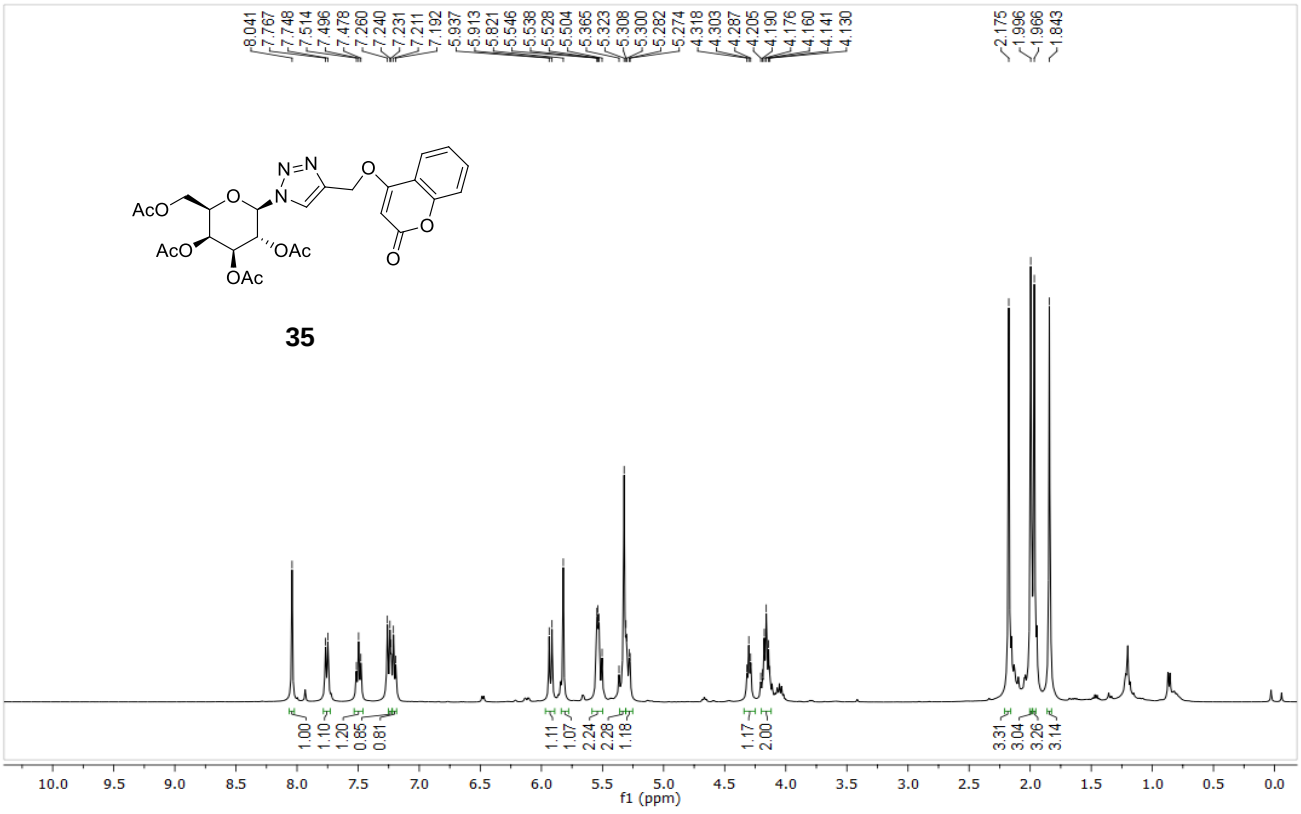
67.710
62.318
61.546
50.540
20.614
20.471
20.415
20.036
f1 (ppm)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7.767
7.748
7.514
7.496
7.478
7.260
7.240
7.231
7.211
7.192
5.937
5.913
5.821
5.546
5.538
5.528
5.504
5.365
5.323
5.308
5.300
5.282
5.274
4.318
4.303
4.287
4.205
4.190
4.176
4.160
4.141
4.130
2.175
1.996
1.966
1.843
AcO
AcO
OAc
OAc
N=N
N
O
O
O
O
1.00
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1.20
0.85
0.81
1.11
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1.18
1.17
2.00
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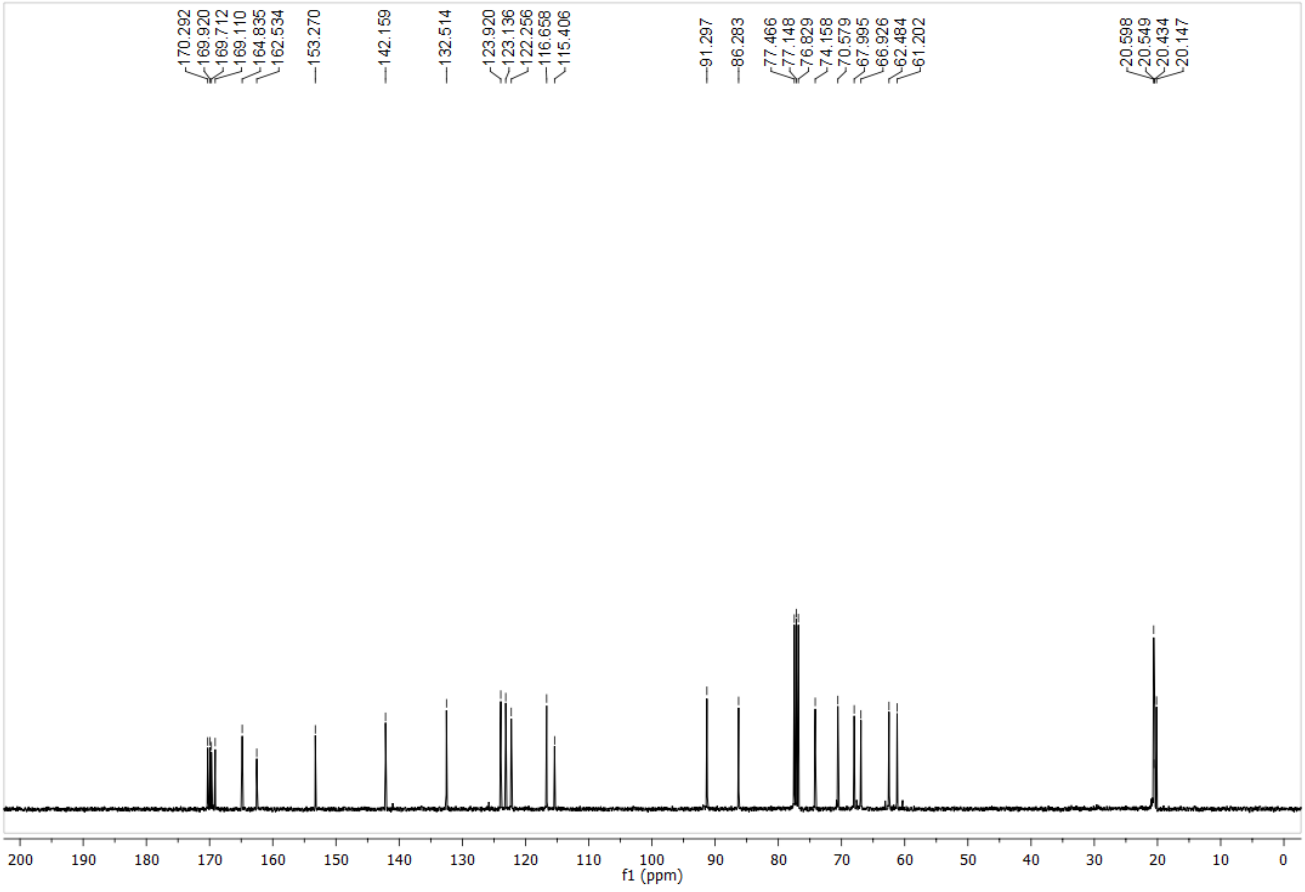
3.04
3.26
3.14
f1 (ppm)

35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142.159
132.514
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123.136
122.256
116.658
115.406
91.297
86.283
77.466
77.148
76.829
74.158
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67.995
66.926
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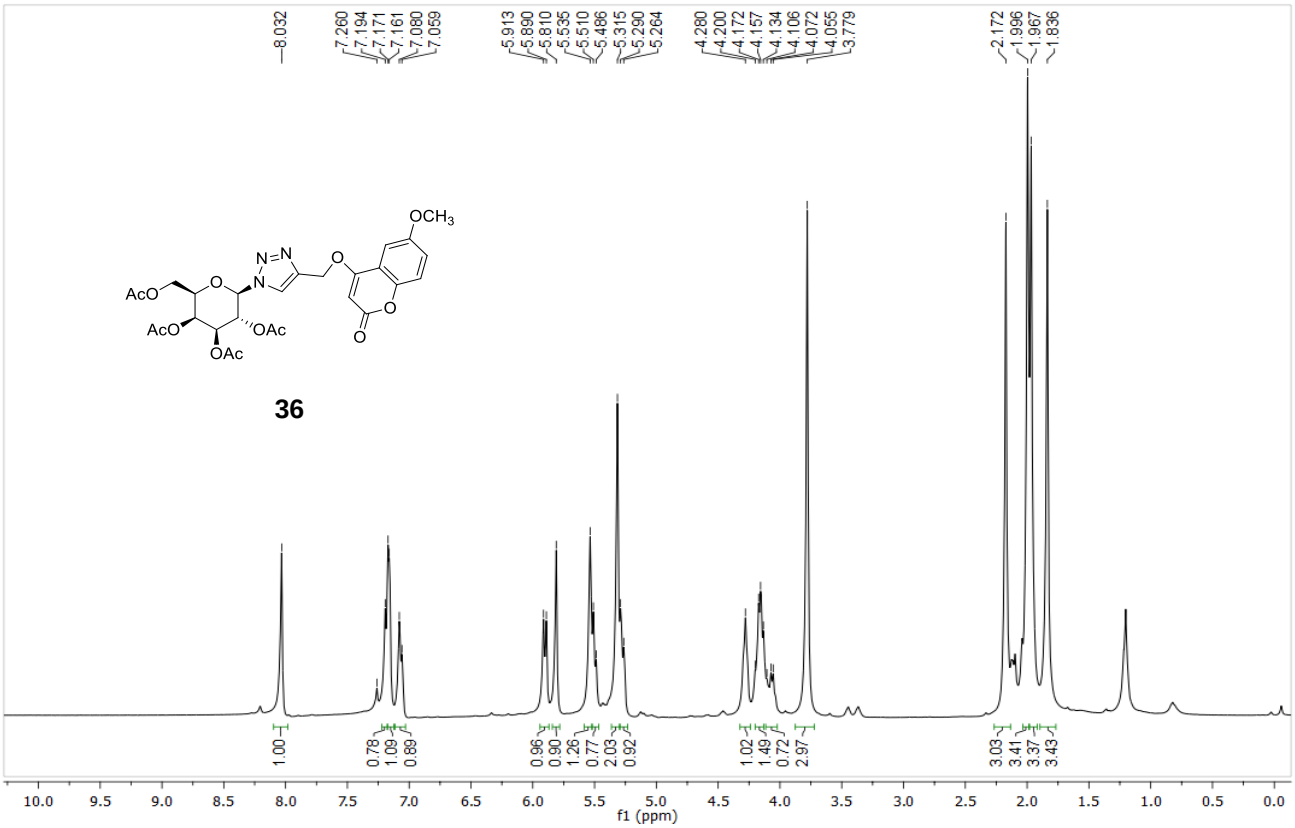
20.549
20.434
20.147
f1 (ppm)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5.810
5.535
5.510
5.486
5.315
5.290
5.264
4.280
4.200
4.172
4.157
4.134
4.106
4.072
4.055
3.779
2.172
1.996
1.967
1.836
OCH3
AcO
AcO
OAc
OAc
O
N=N
1.00
0.78
1.09
0.89
0.96
0.90
1.26
0.77
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1.49
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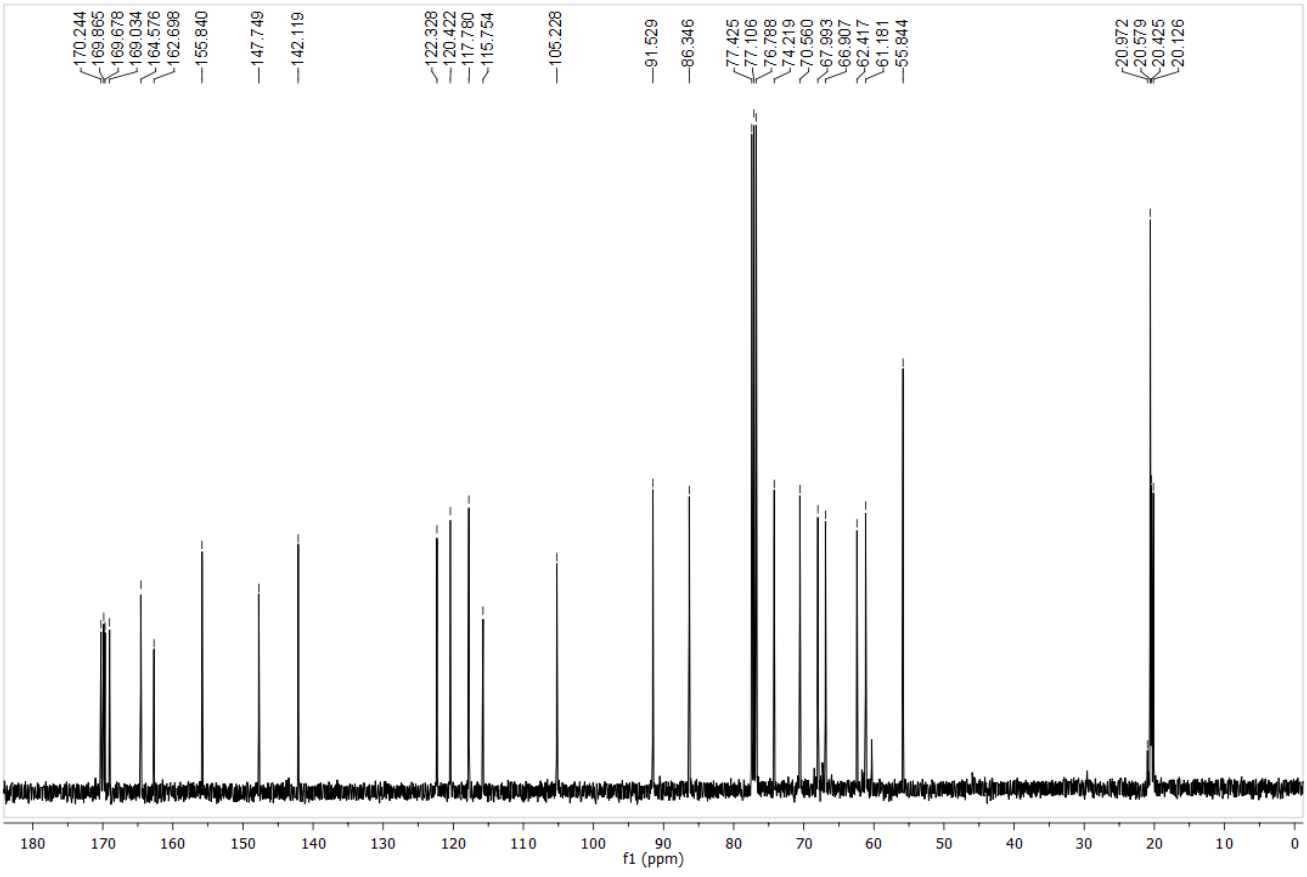
2.97
3.03
3.41
3.37
3.43
f1 (ppm)

36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117.780
115.754
105.228
91.529
86.346
77.425
77.106
76.788
74.219
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62.417
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55.844
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20.579
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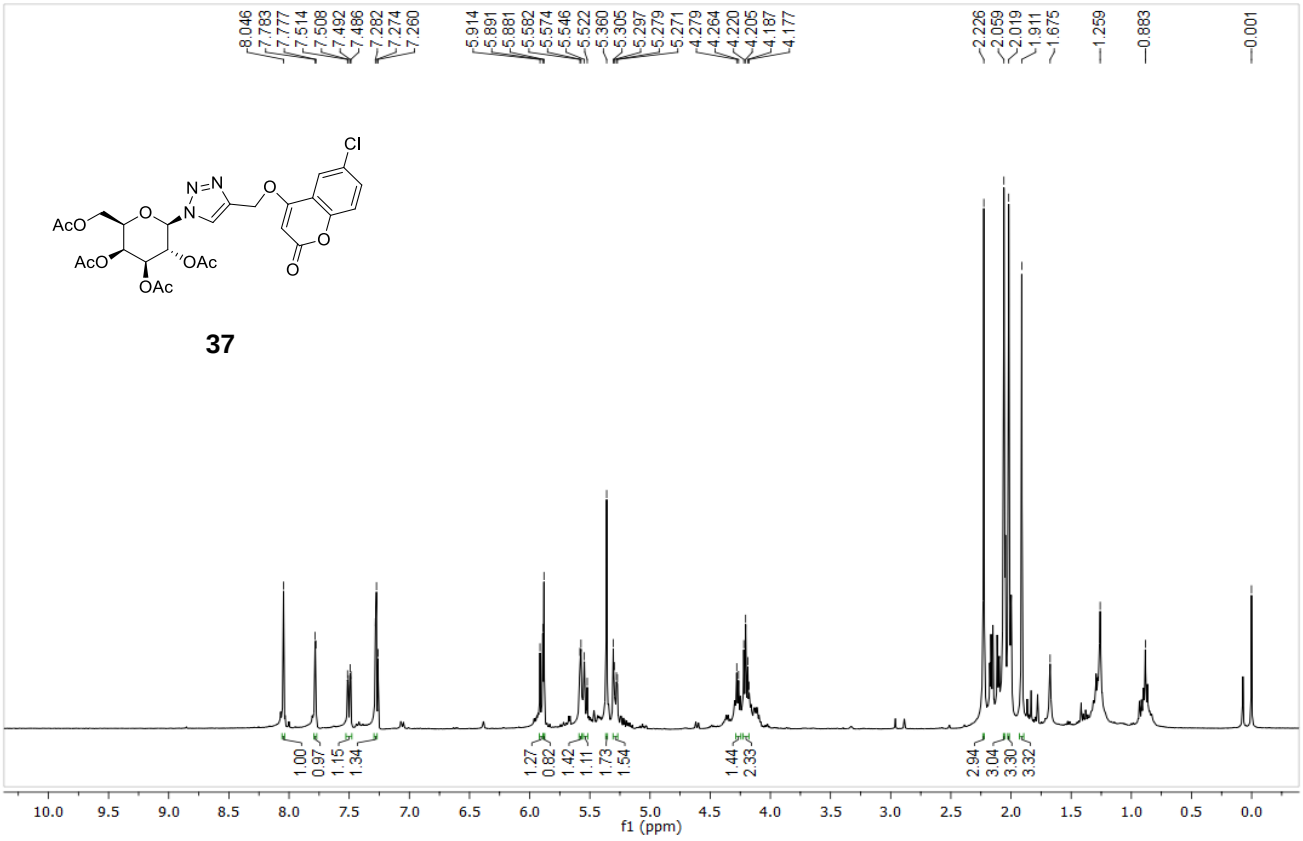
20.126
f1 (ppm)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5.881
5.582
5.574
5.546
5.522
5.360
5.305
5.297
5.279
5.271
4.279
4.264
4.220
4.205
4.187
4.177
2.226
2.059
2.019
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1.675
1.259
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0.001
Cl
N=N
O
AcO
AcO
OAc
OAc
O
O
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1.34
1.27
0.82
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1.54
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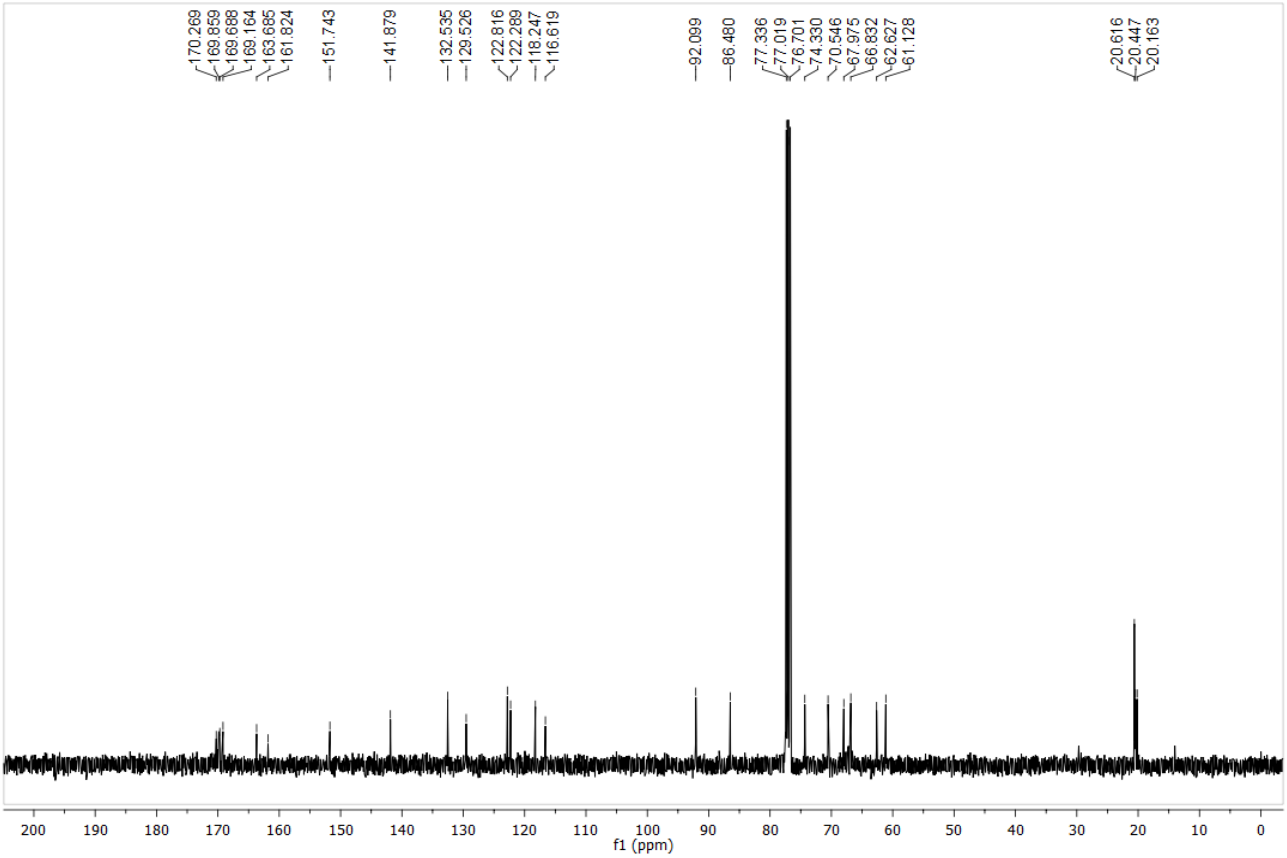
2.94
3.04
3.30
3.32
f1 (ppm)

37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141.879
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122.816
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118.247
116.619
92.099
86.480
77.336
77.019
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67.975
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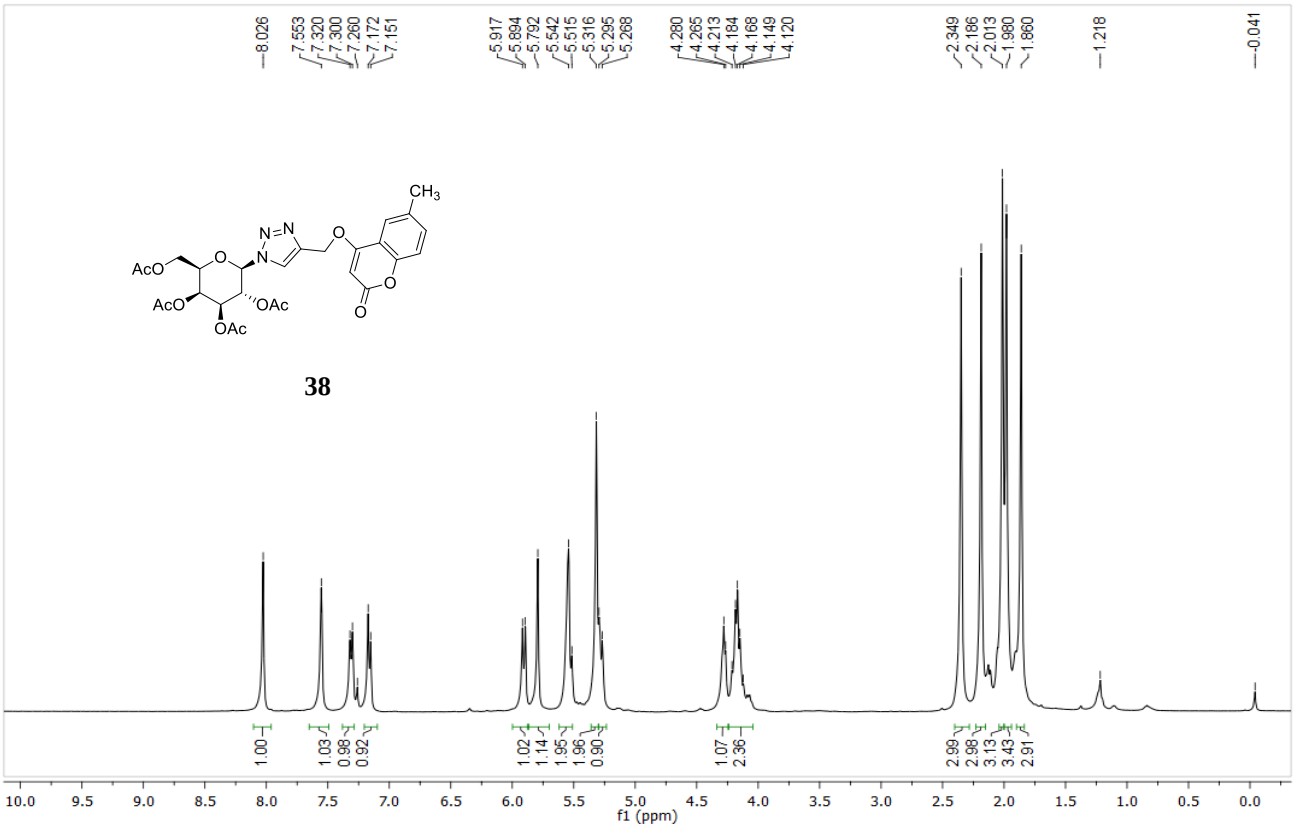
f1 (ppm)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5.316
5.295
5.268
4.280
4.265
4.213
4.184
4.168
4.149
4.120
2.349
2.186
2.013
1.980
1.860
1.218
0.041
AcO
AcO
OAc
OAc
N=N
O
O
O
CH3
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1.03
0.98
0.92
1.02
1.14
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2.99
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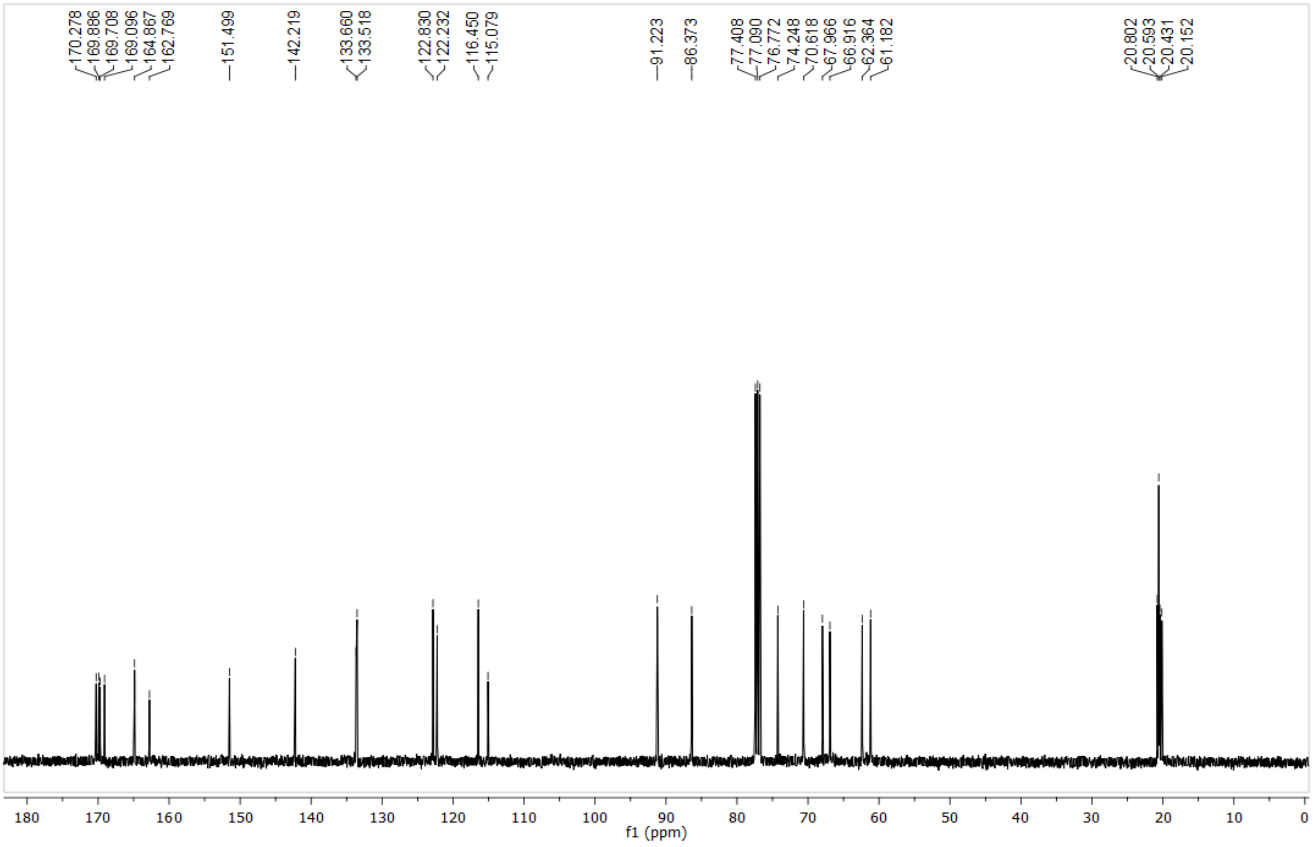
3.43
2.91
f1 (ppm)

38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142.219
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116.450
115.079
91.223
86.373
77.408
77.090
76.772
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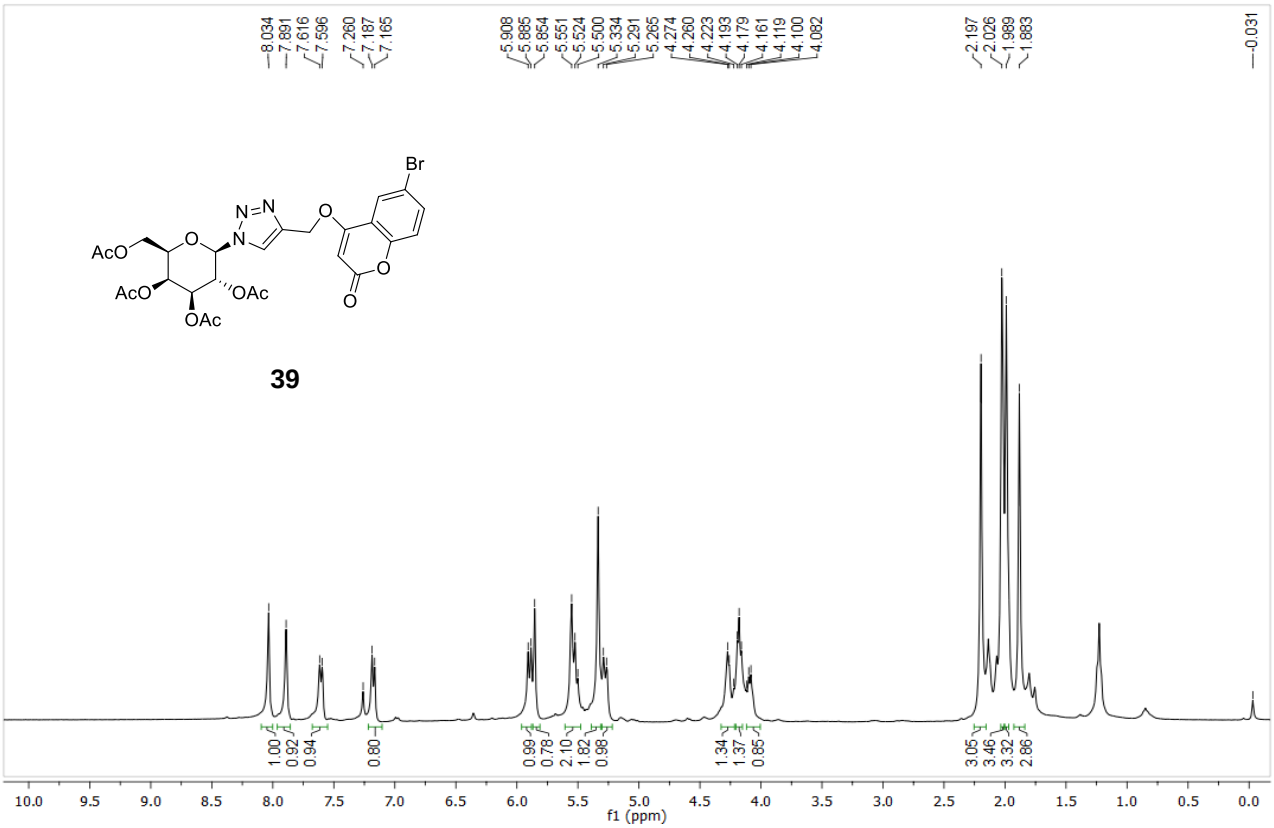
f1 (ppm)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5.551
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5.334
5.291
5.265
4.274
4.260
4.223
4.193
4.179
4.161
4.119
4.100
4.082
2.197
2.026
1.989
1.883
0.031
Br
AcO
AcO
OAc
OAc
O
N
N
O
O
O
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0.94
0.80
0.99
0.78
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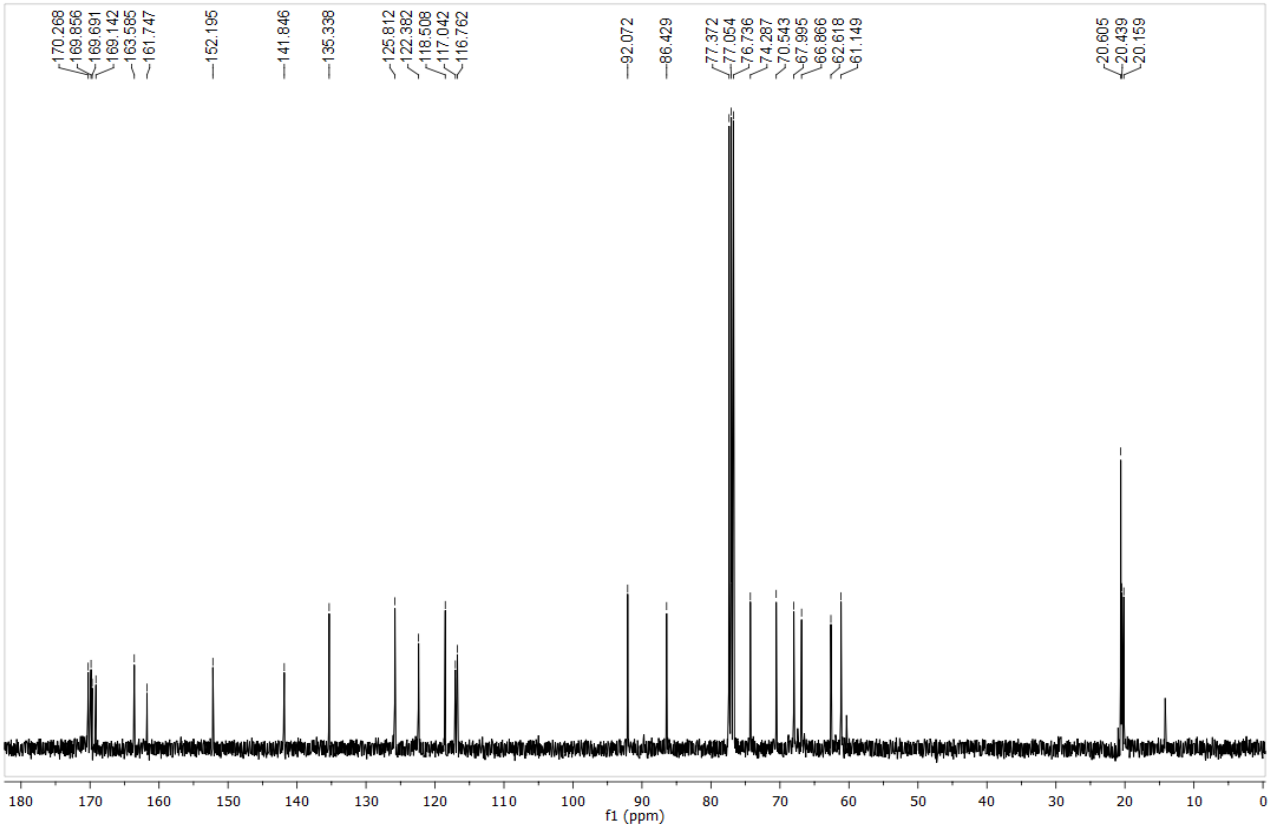
39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118.508
117.042
116.762
92.072
86.429
77.372
77.054
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70.543
67.995
66.866
62.618
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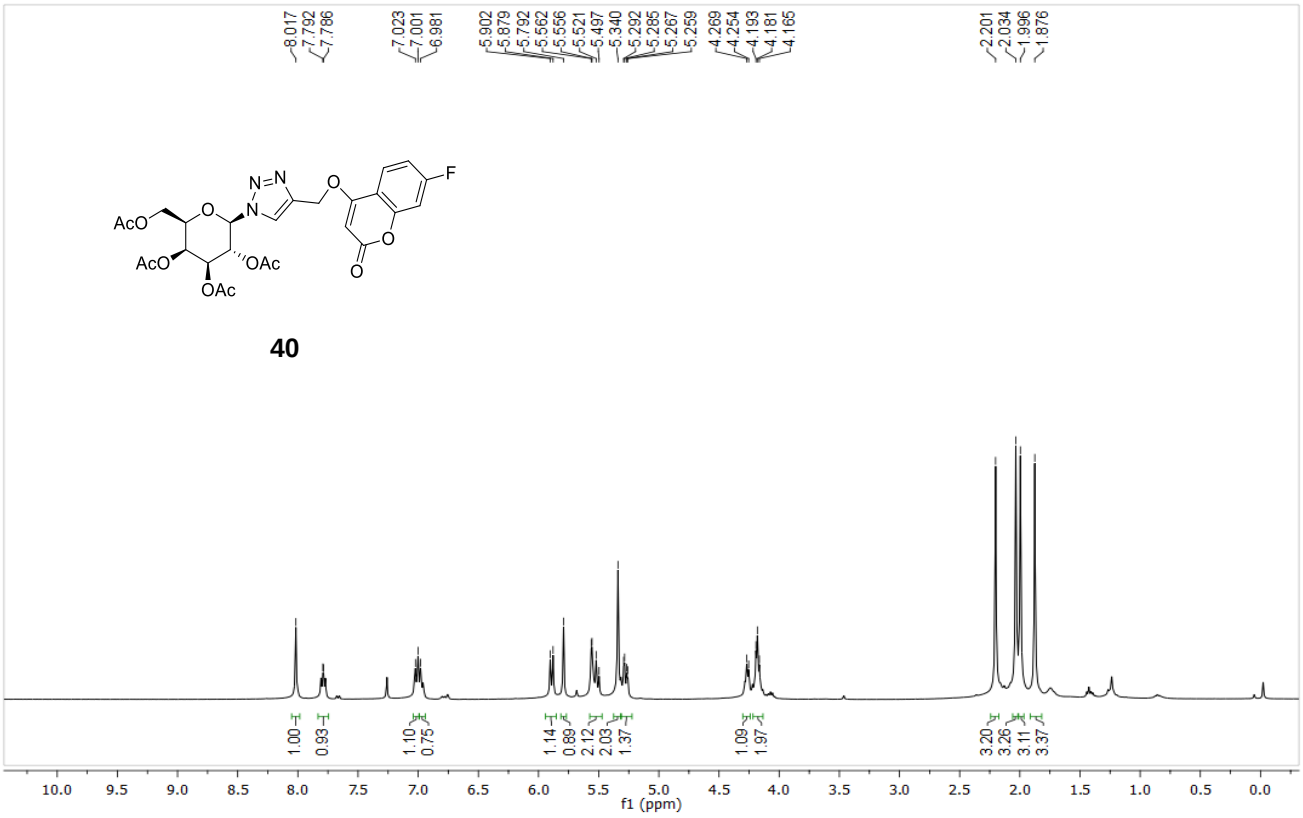
20.159
f1 (ppm)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5.556
5.521
5.497
5.340
5.292
5.285
5.267
5.259
4.269
4.254
4.193
4.181
4.165
2.201
2.034
1.996
1.876
AcO
AcO
OAc
OAc
N=N
N
O
O
O
F
O
1.00
0.93
1.10
0.75
1.14
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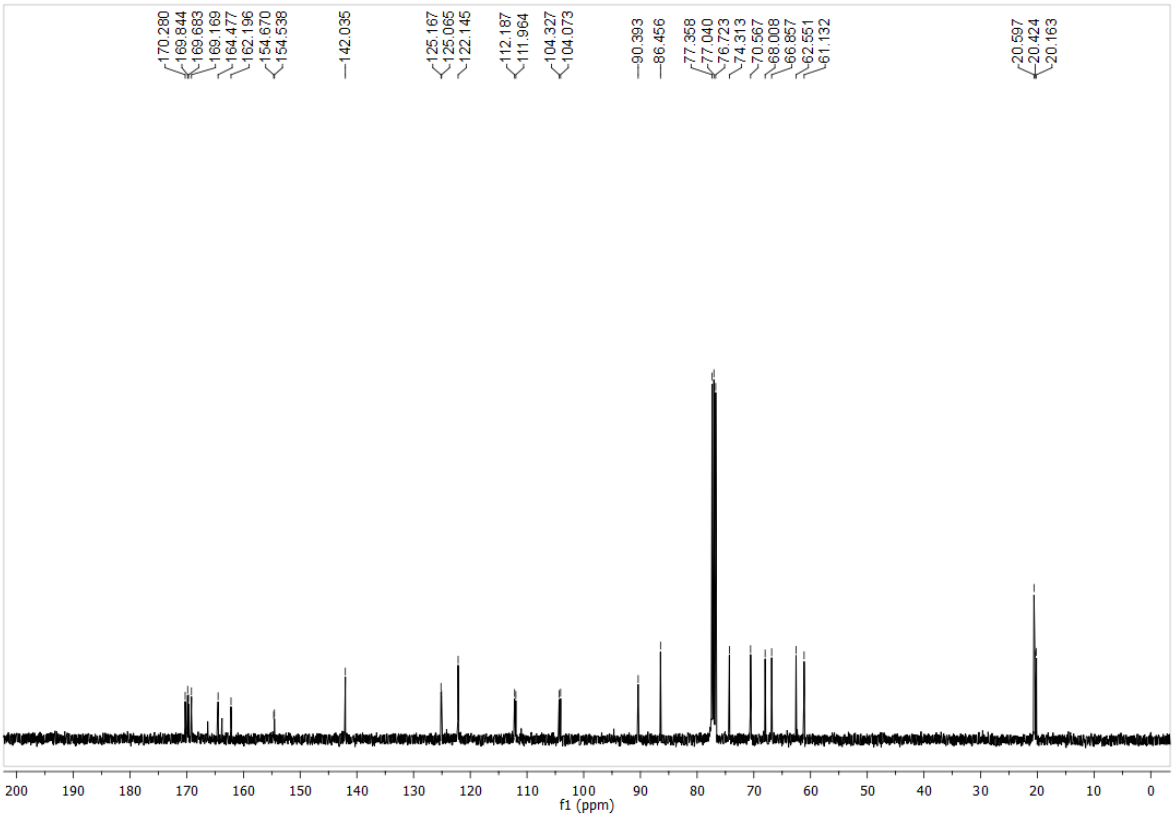
3.11
3.37
f1 (ppm)

40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162.196
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154.538
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125.065
122.145
112.187
111.964
104.327
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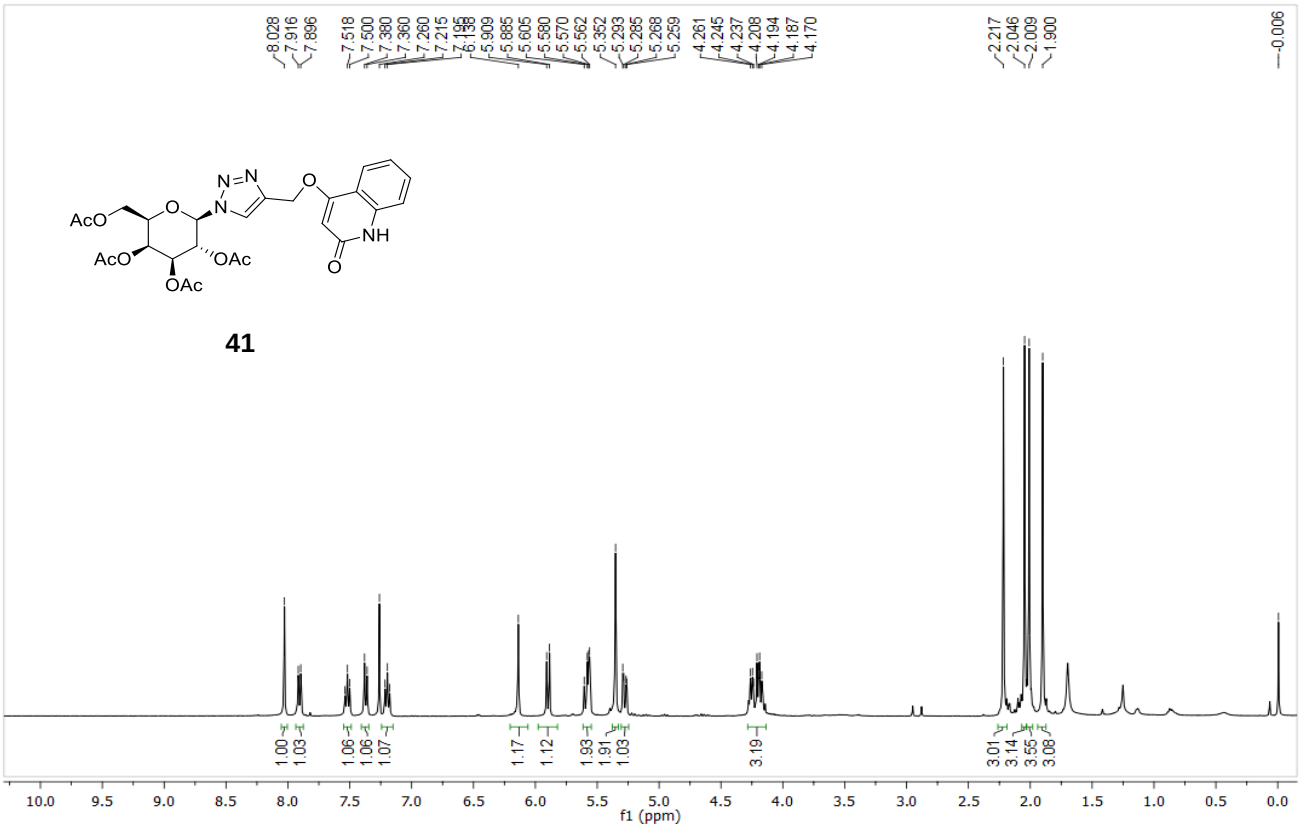
90.393
86.456
77.358
77.040
76.723
74.313
70.567
68.008
66.857
62.551
61.132
20.597
20.424
20.163
f1 (ppm)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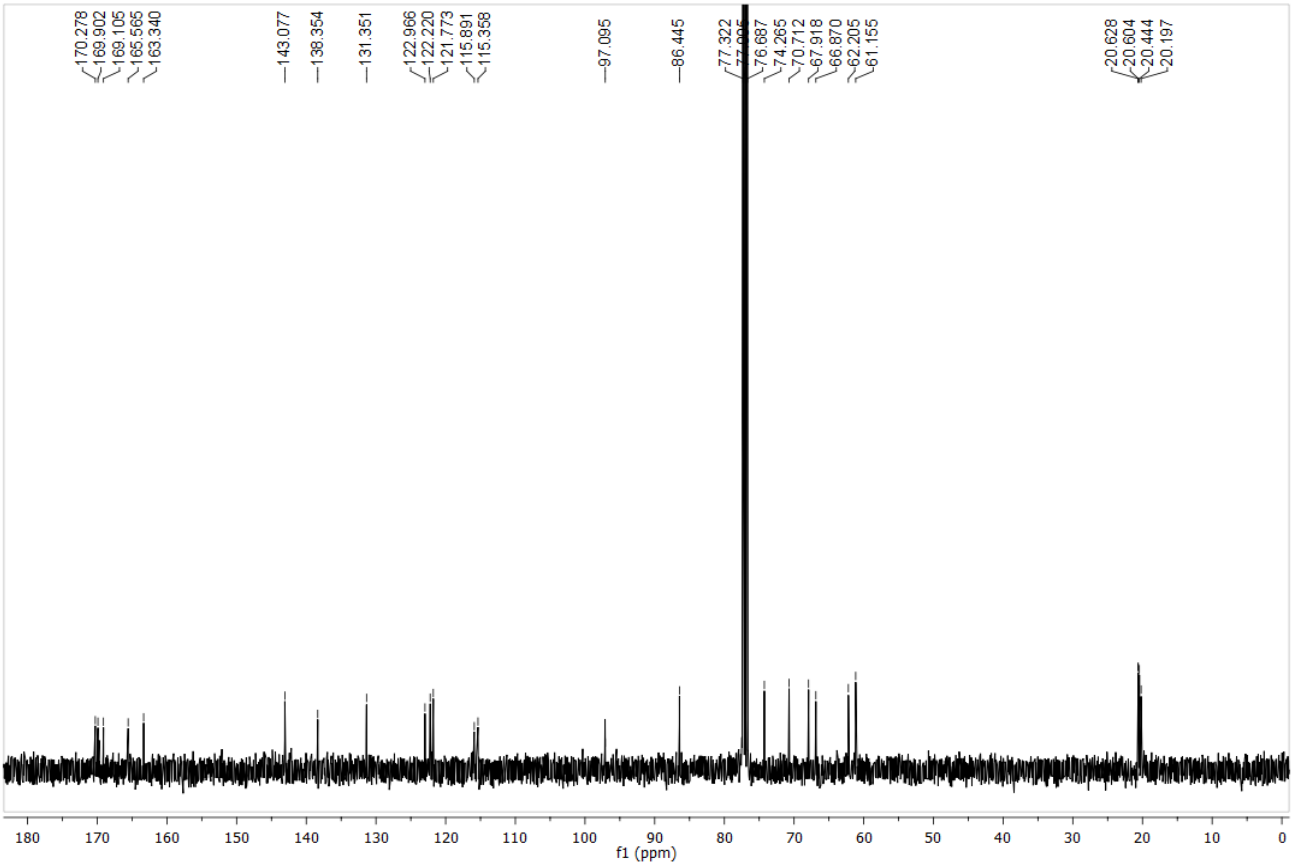
7.916
7.896
7.518
7.500
7.380
7.360
7.260
7.215
5.909
5.885
5.605
5.580
5.570
5.562
5.352
5.293
5.285
5.268
5.259
4.261
4.245
4.237
4.208
4.194
4.187
4.170
2.217
2.046
2.009
1.900
0.006
AcO
AcO
OAc
OAc
O
N=N
N
O
NH
O
1.00
1.03
1.06
1.06
1.07
1.17
1.12
1.93
1.91
1.03
3.19
3.01
3.14
3.55
3.08
f1 (ppm)

41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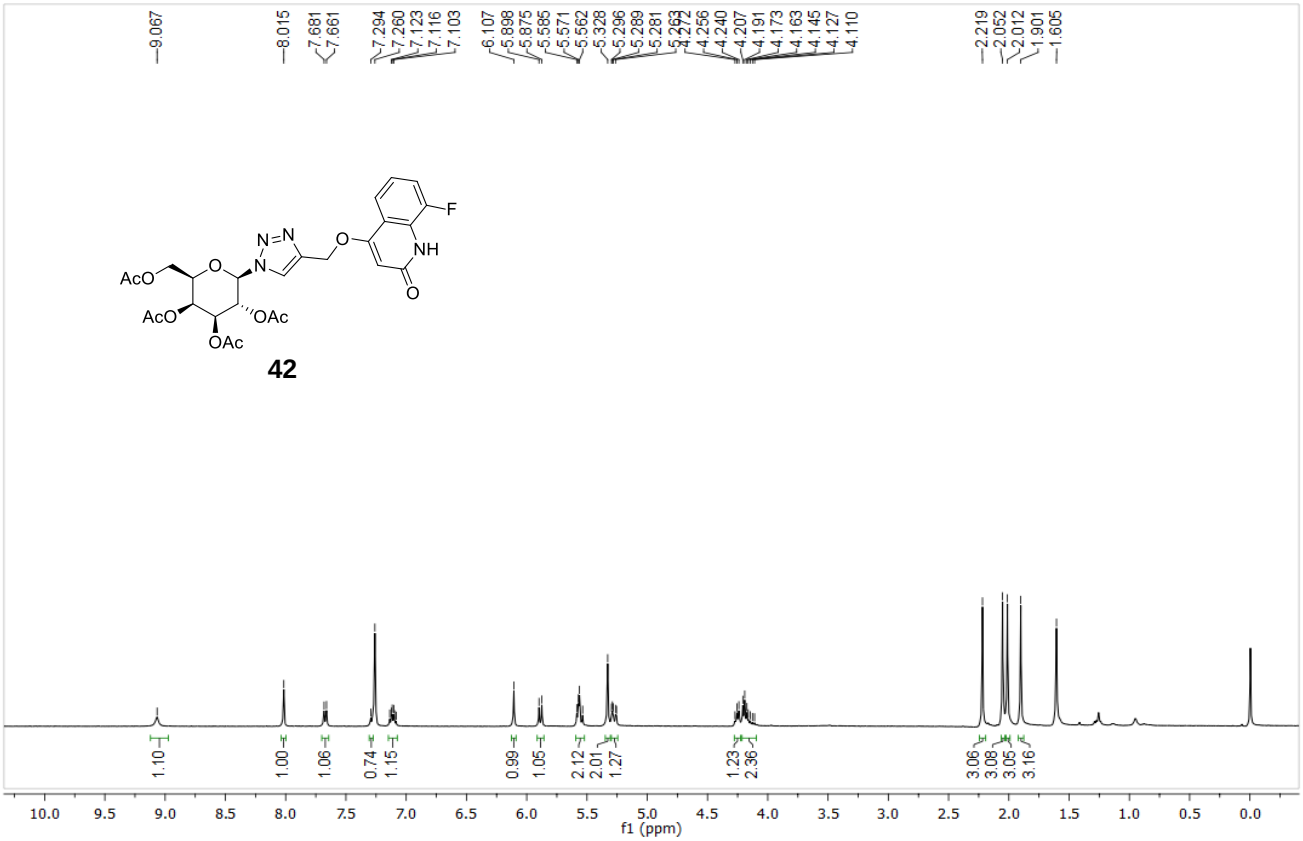
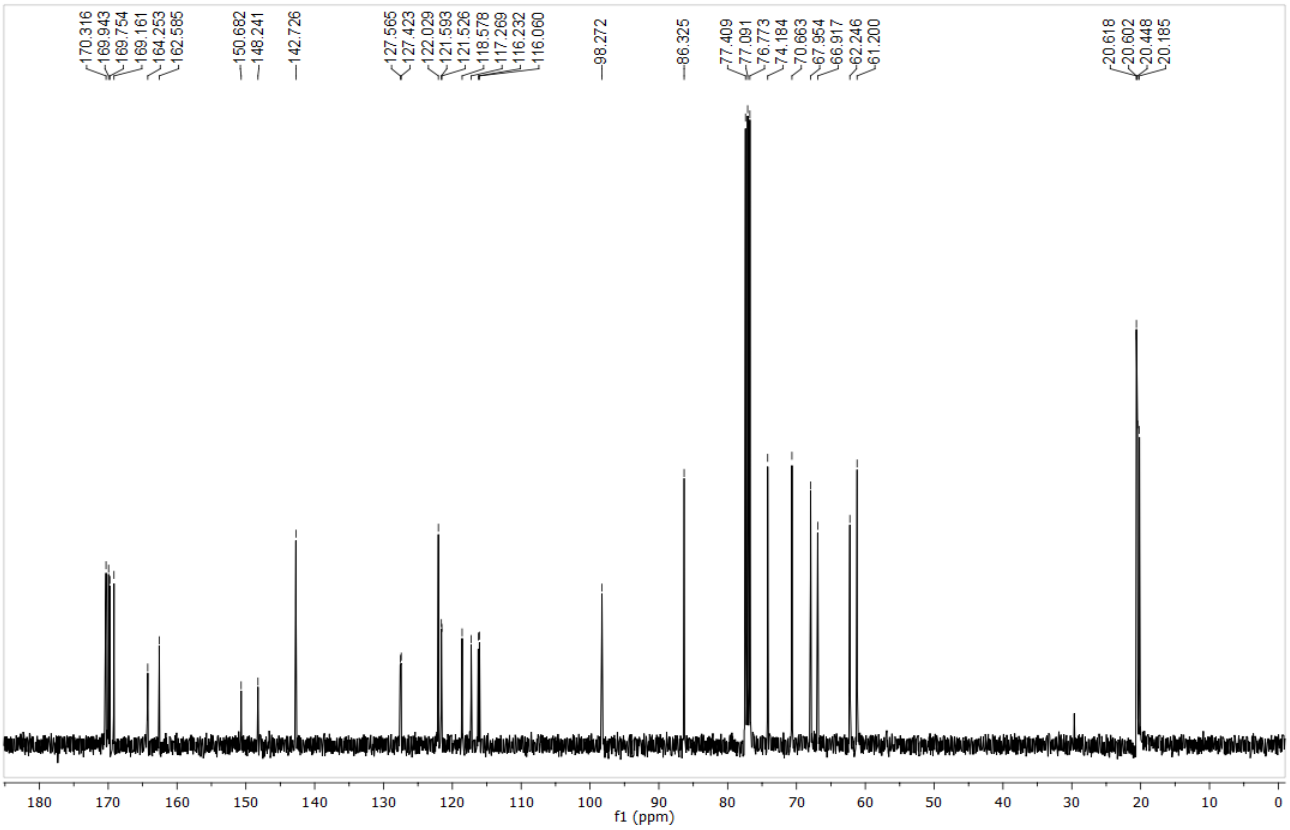
169.902
169.105
165.565
163.340
143.077
138.354
131.351
122.966
122.220
121.773
115.891
115.358
97.095
86.445
77.322
76.687
74.265
70.712
67.918
66.870
62.205
61.155
20.628
20.604
20.444
20.197
f1 (ppm)


9.067
8.015
7.681
7.661
7.294
7.260
7.123
7.116
7.103
6.107
5.898
5.875
5.585
5.571
5.562
5.328
5.296
5.289
5.281
5.263
4.272
4.256
4.240
4.207
4.191
4.173
4.163
4.145
4.127
4.110
2.219
2.052
2.012
1.901
1.605
F
NH
O
N=N
AcO
AcO
OAc
OAc
1.10
1.00
1.06
0.74
1.15
0.99
1.05
2.12
2.01
1.27
1.23
2.36
3.06
3.08
3.05
3.16
f1 (ppm)

42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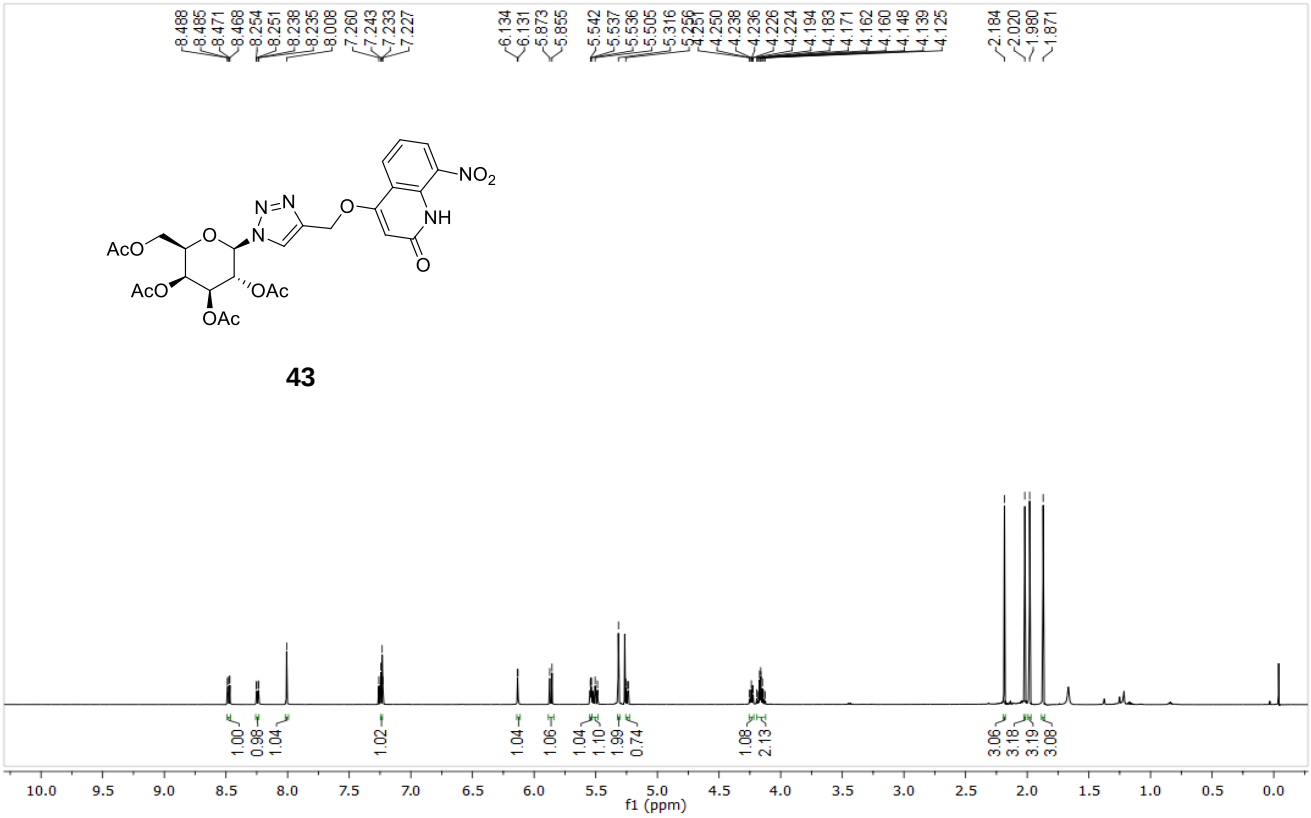
169.943
169.754
169.161
164.253
162.585
150.682
148.241
142.726
127.565
127.423
122.029
121.593
121.526
118.578
117.269
116.232
116.060
98.272
86.325
77.409
77.091
76.773
74.184
70.663
67.954
66.917
62.246
61.200
20.618
20.602
20.448
20.185
f1 (ppm)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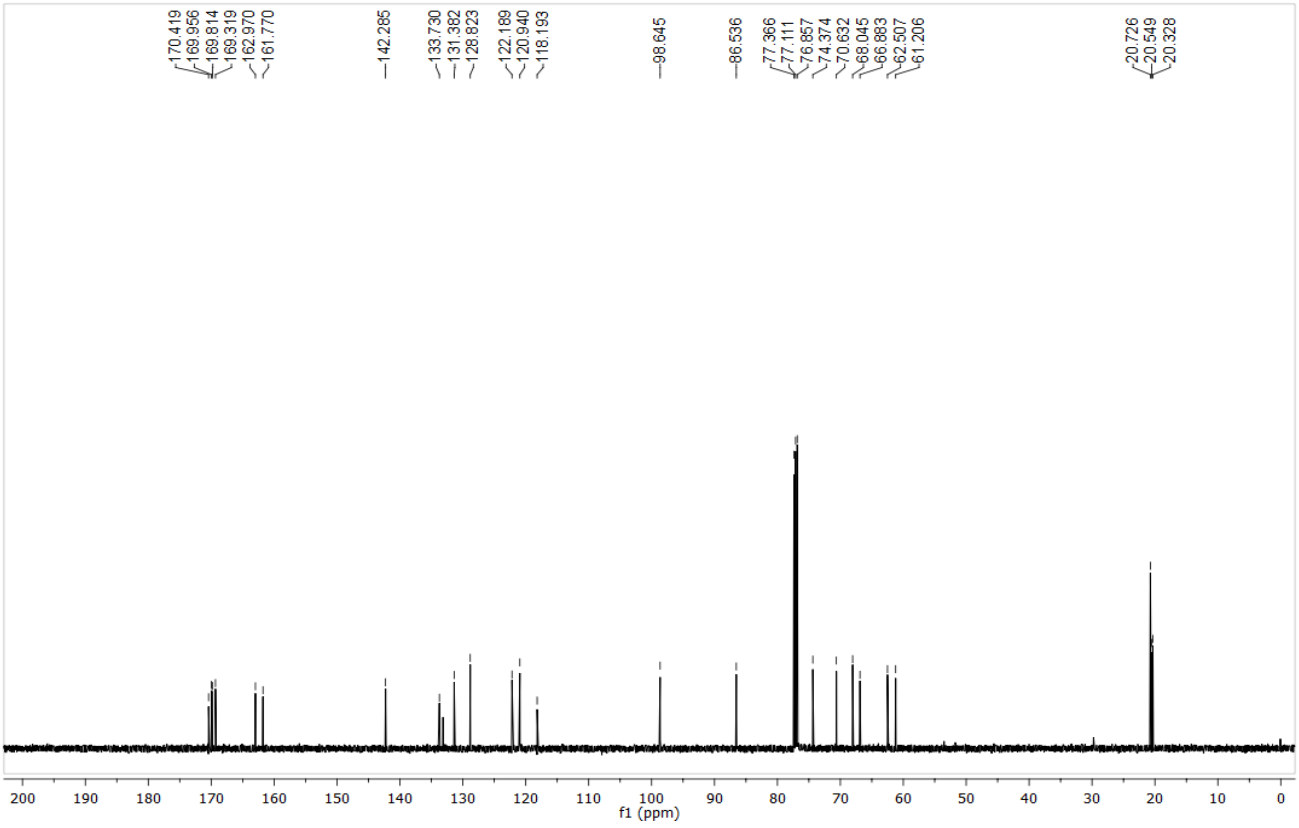
8.485
8.471
8.468
8.254
8.251
8.238
8.235
8.008
7.260
7.243
7.233
7.227
6.134
6.131
5.873
5.855
5.542
5.537
5.536
5.505
5.316
5.256
4.251
4.250
4.238
4.236
4.226
4.224
4.194
4.183
4.171
4.162
4.160
4.148
4.139
4.125
2.184
2.020
1.980
1.871
NO2
NH
O
N=N
N
O
AcO
AcO
OAc
OAc
1.00
0.98
1.04
1.02
1.04
1.06
1.04
1.10
1.99
0.74
1.08
2.13
3.06
3.18
3.19
3.08
f1 (ppm)

43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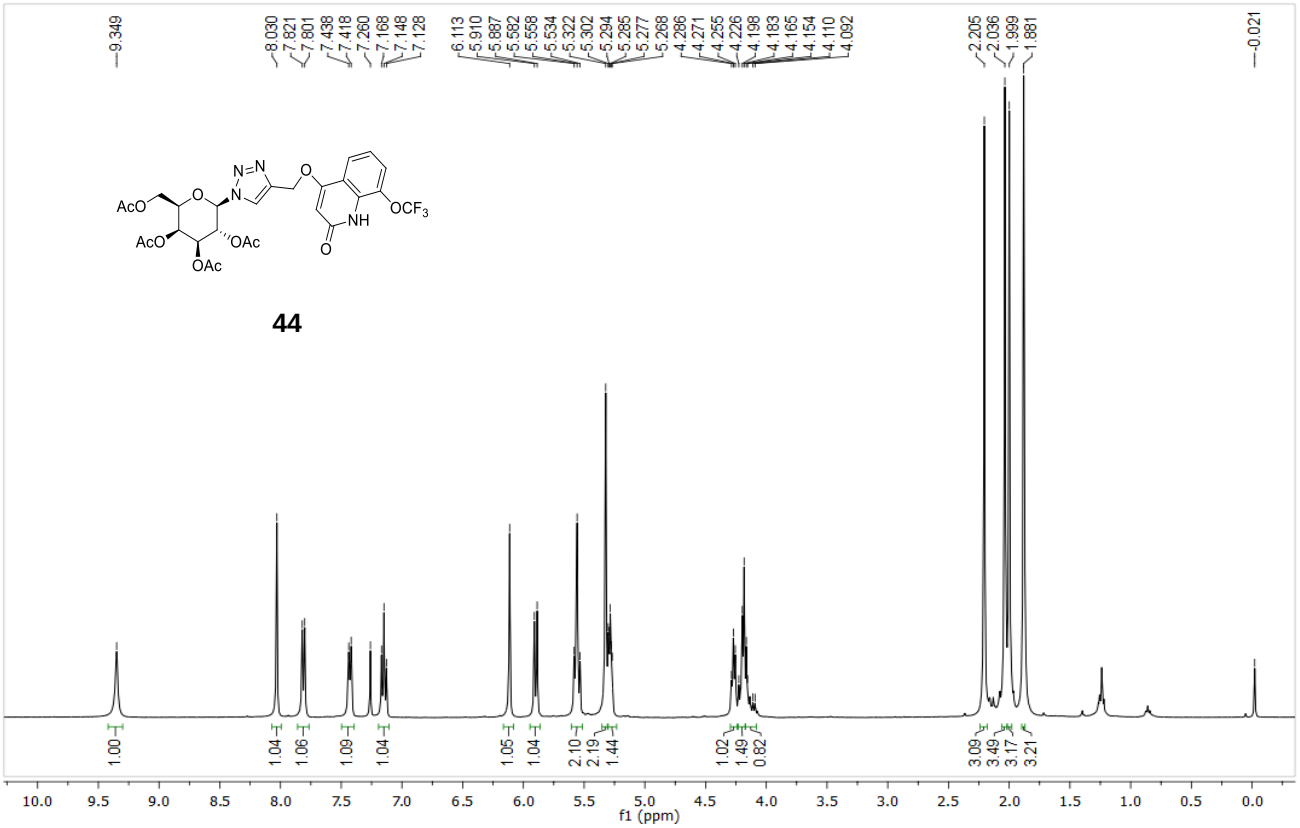
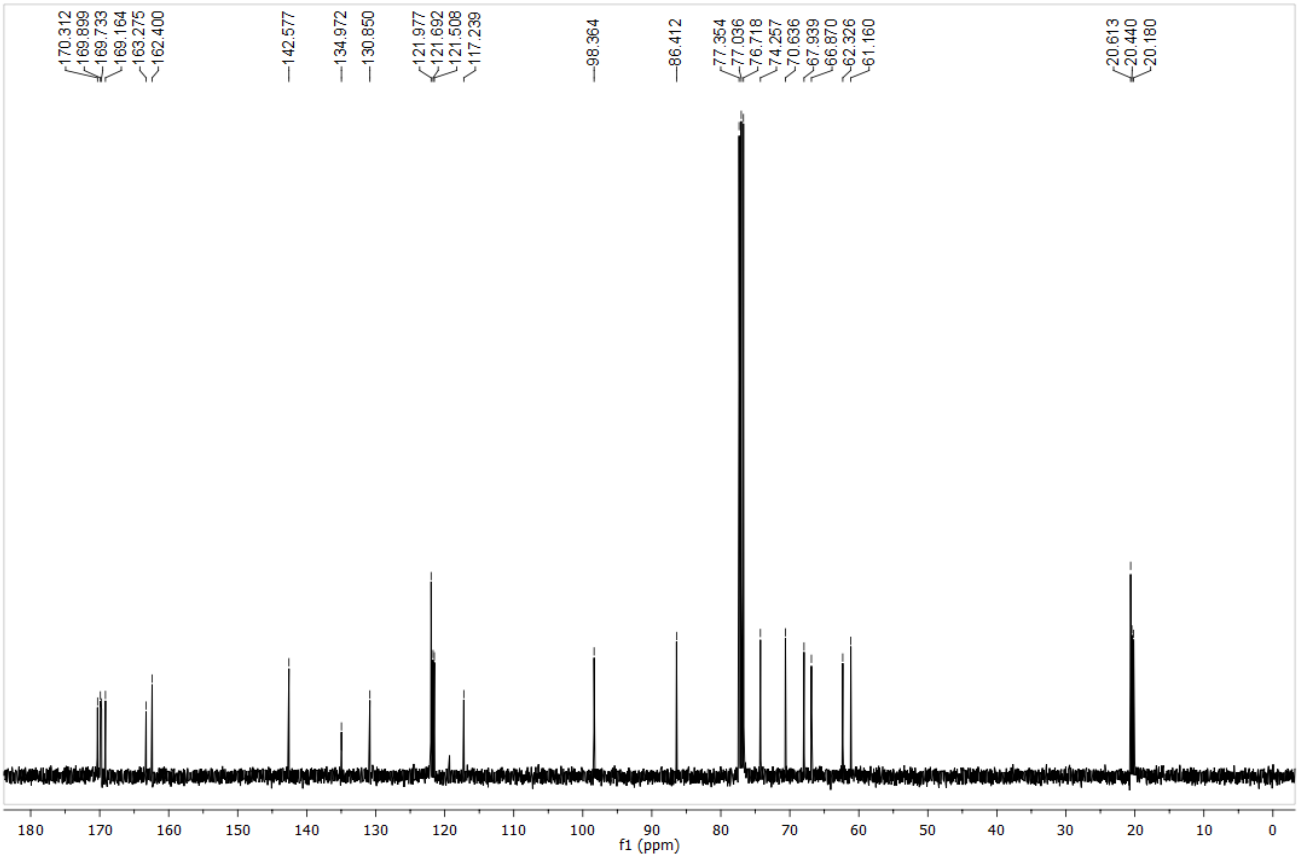
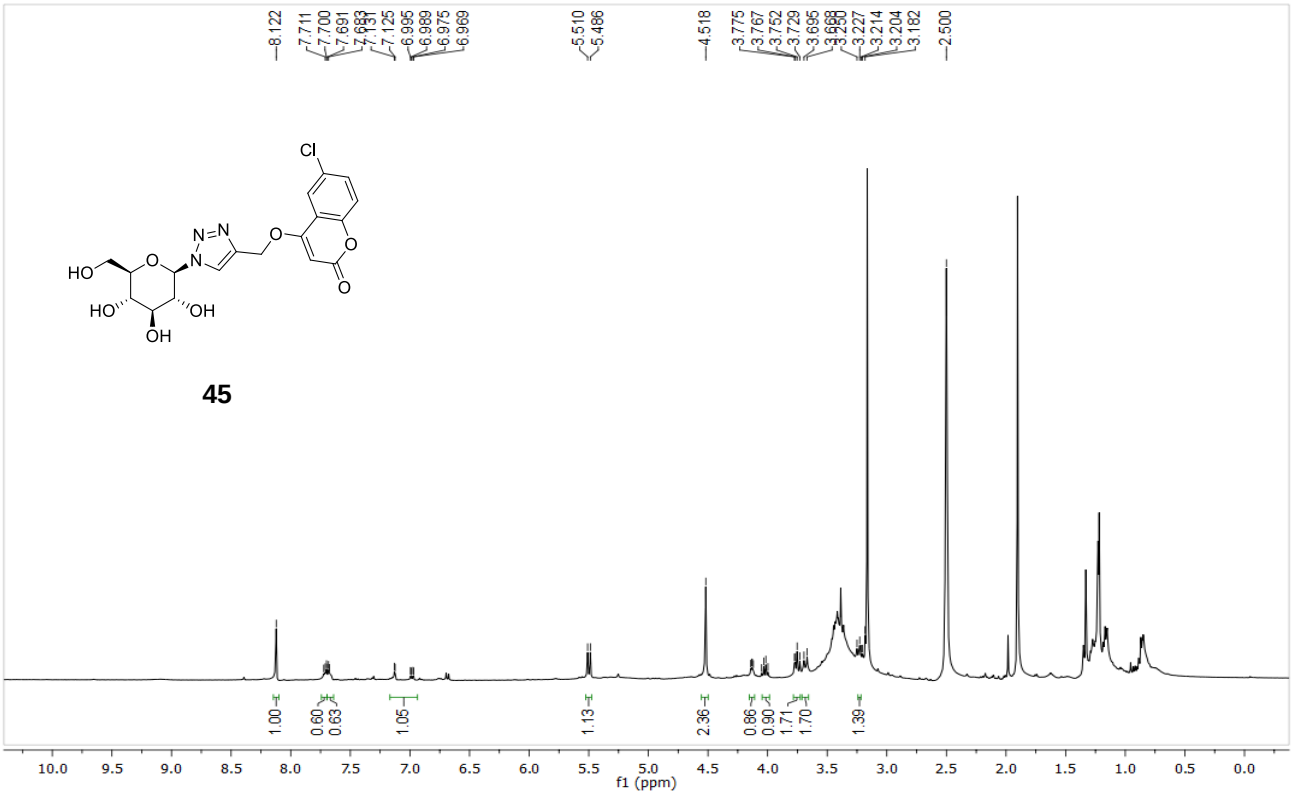
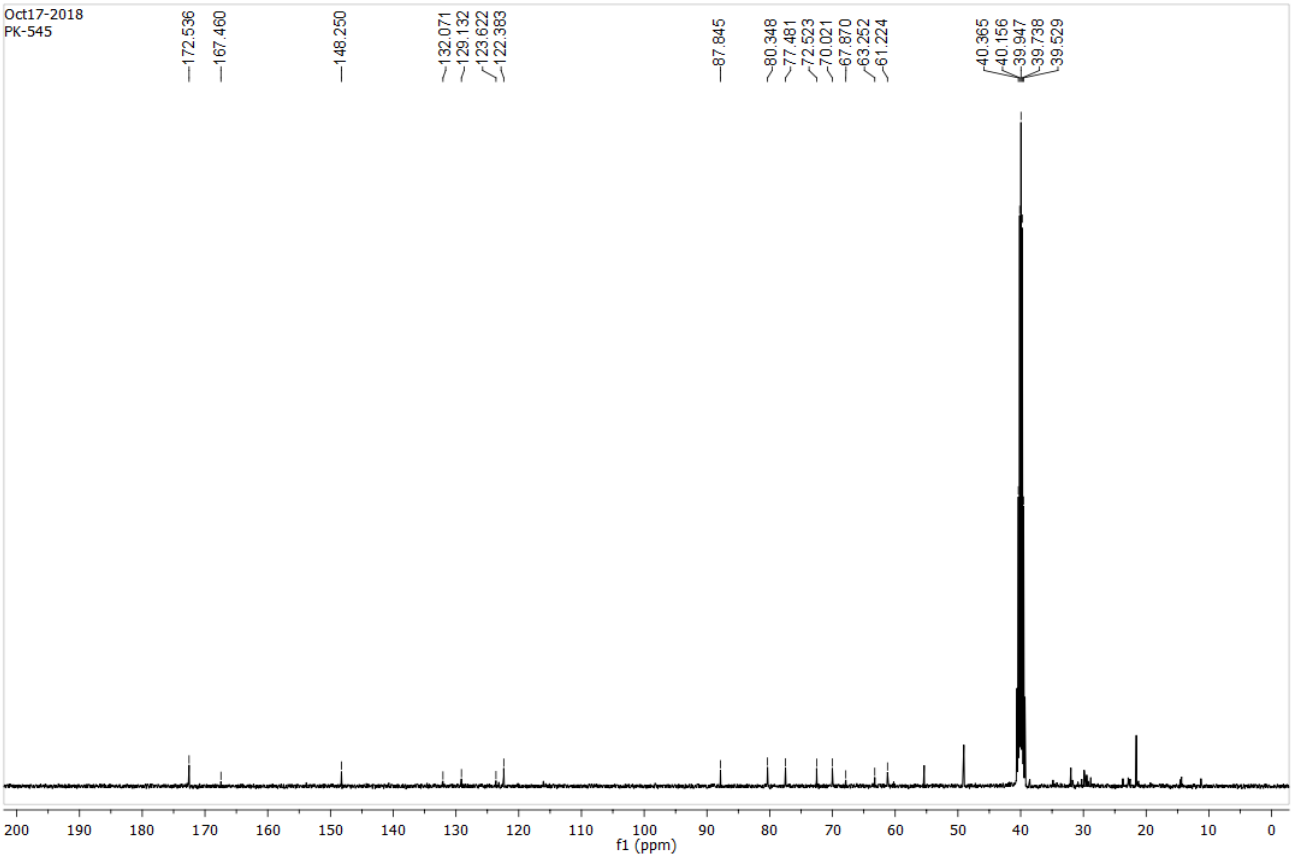
169.956
169.814
169.319
162.970
161.770
142.285
133.730
131.382
128.823
122.189
120.940
118.193
98.645
86.536
77.366
77.111
76.857
74.374
70.632
68.045
66.883
62.507
61.206
20.726
20.549
20.328
f1 (ppm)


9.349
8.030
7.821
7.801
7.438
7.418
7.260
7.168
7.148
7.128
6.113
5.910
5.887
5.582
5.558
5.534
5.322
5.302
5.294
5.285
5.277
5.268
4.286
4.271
4.255
4.226
4.198
4.183
4.165
4.154
4.110
4.092
2.205
2.036
1.999
1.881
0.021
AcO
AcO
OAc
OAc
O
N=N
N
O
NH
O
OCF3
44
1.00
1.04
1.06
1.09
1.04
1.05
1.04
2.10
2.19
1.44
1.02
1.49
0.82
3.09
3.49
3.17
3.21
f1 (ppm)


170.312
169.899
169.733
169.164
163.275
162.400
142.577
134.972
130.850
121.977
121.692
121.508
117.239
98.364
86.412
77.354
77.036
76.718
74.257
70.636
67.939
66.870
62.326
61.160
20.613
20.440
20.180
f1 (ppm)


8.122
7.711
7.700
7.691
7.683
7.125
6.995
6.989
6.975
6.969
5.510
5.486
4.518
3.775
3.767
3.752
3.729
3.695
3.688
3.680
3.227
3.214
3.204
3.182
2.500
Cl
N=N
N
O
O
O
HO
HO
OH
OH
1.00
0.60
0.63
1.05
1.13
2.36
0.86
0.90
1.71
1.70
1.39
f1 (ppm)

45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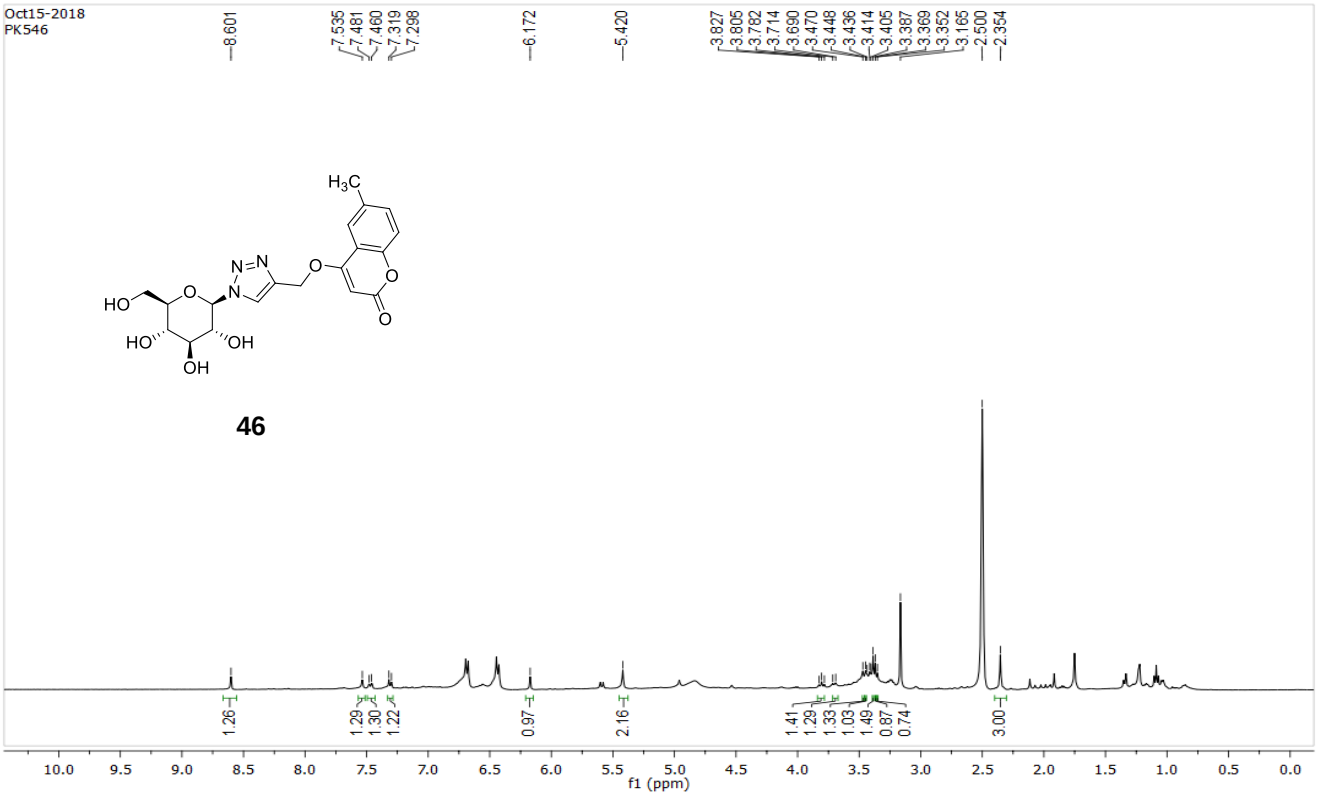
PK-545
172.536
167.460
148.250
132.071
129.132
123.622
122.383
87.845
80.348
77.481
72.523
70.021
67.870
63.252
61.224
40.365
40.156
39.947
39.738
39.529
f1 (ppm)


Oct15-2018
PK546
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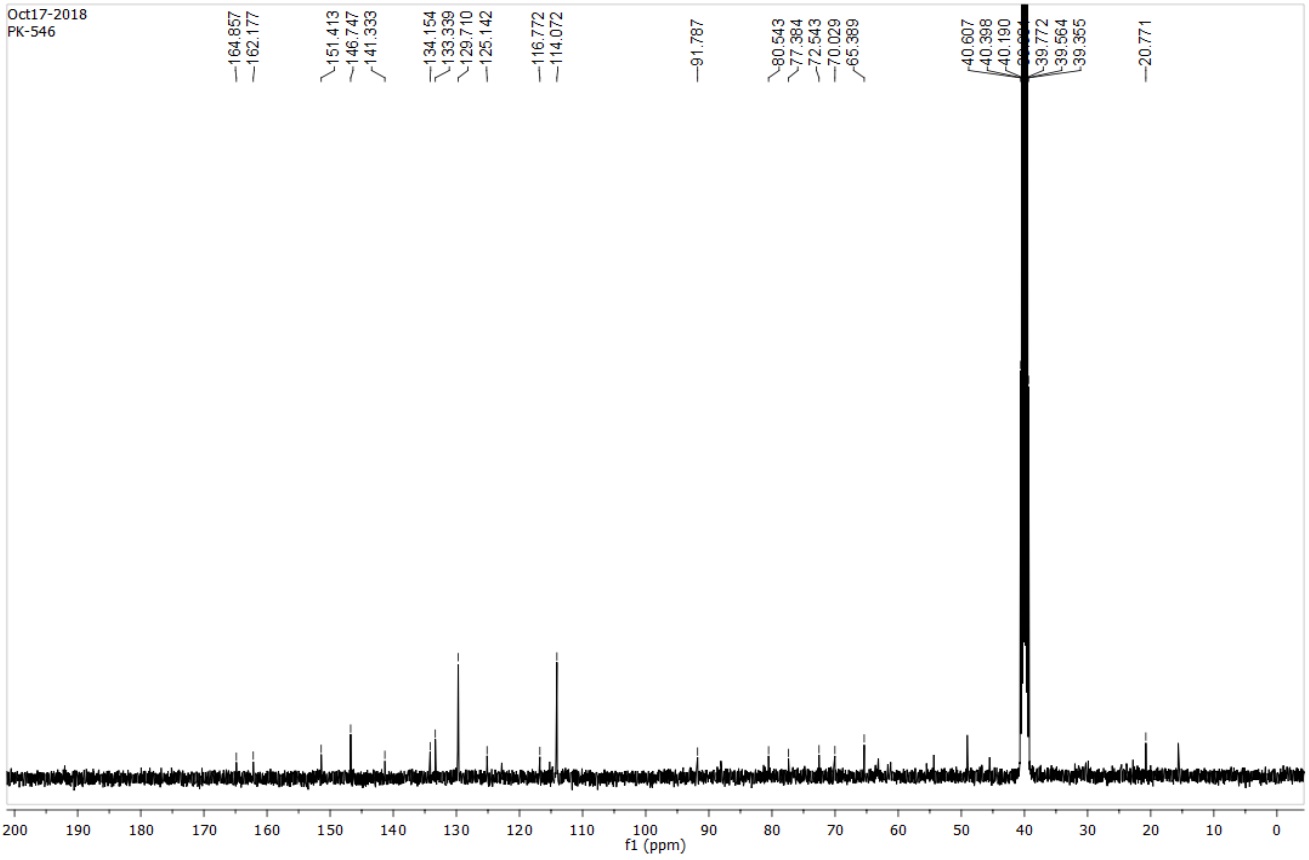
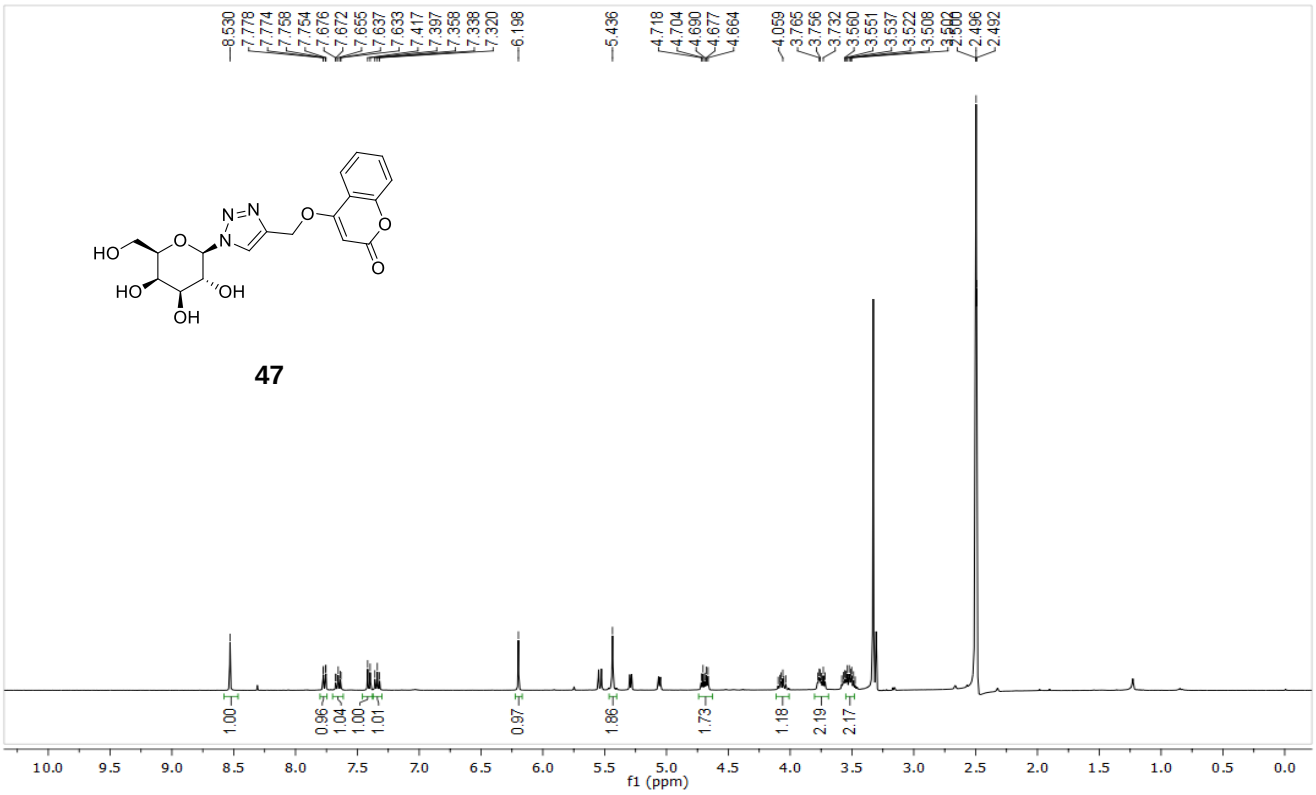
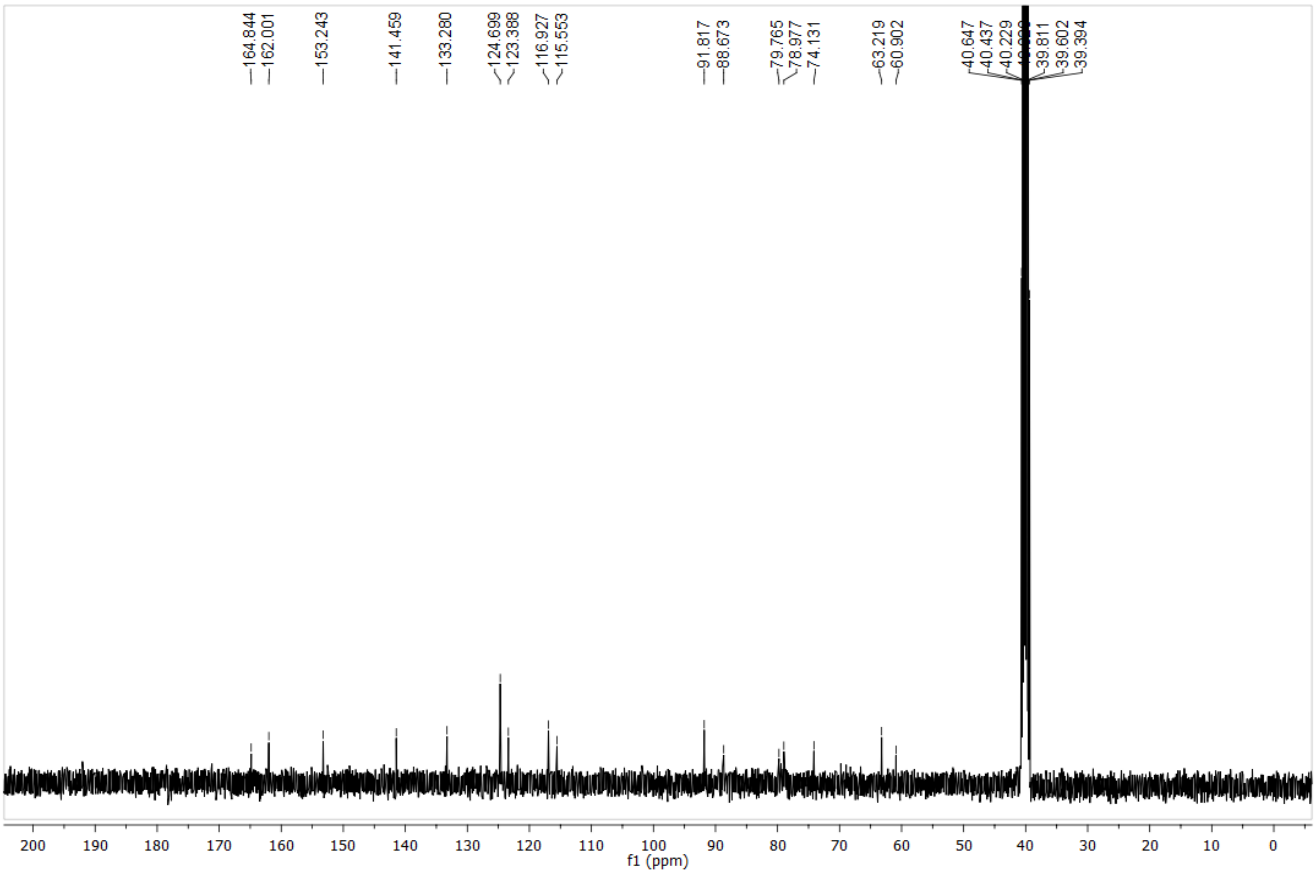
7.535
7.481
7.460
7.319
7.298
6.172
5.420
3.827
3.805
3.782
3.714
3.690
3.470
3.448
3.436
3.414
3.405
3.387
3.369
3.352
3.165
2.500
2.354
1.26
1.29
1.30
1.22
0.97
2.16
1.41
1.29
1.33
1.03
1.49
0.87
0.74
3.00
f1 (ppm)

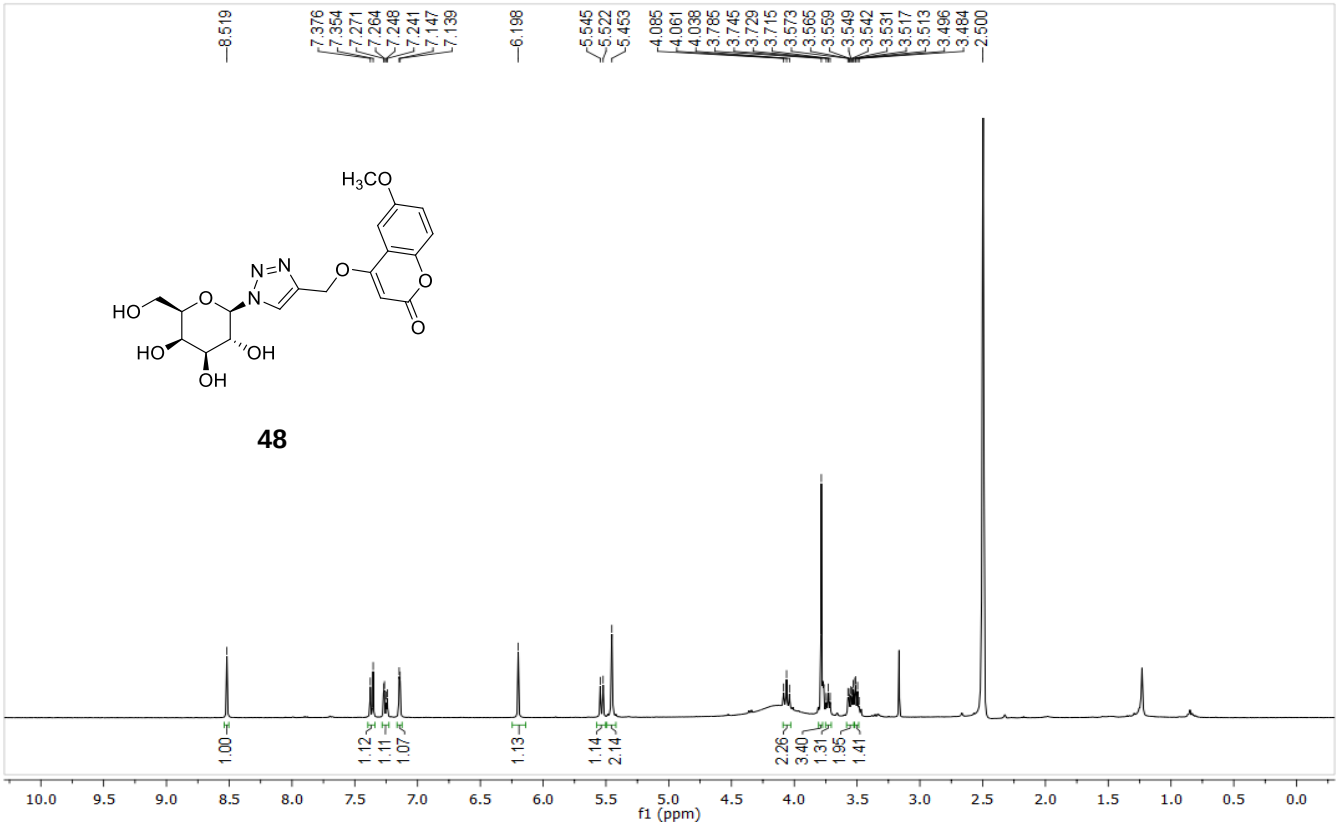

Oct17-2018
PK-546
164.857
162.177
151.413
146.747
141.333
134.154
133.339
129.710
125.142
116.772
114.072
91.787
80.543
77.384
72.543
70.029
65.389
40.607
40.398
40.190
39.772
39.564
39.355
20.771
f1 (ppm)

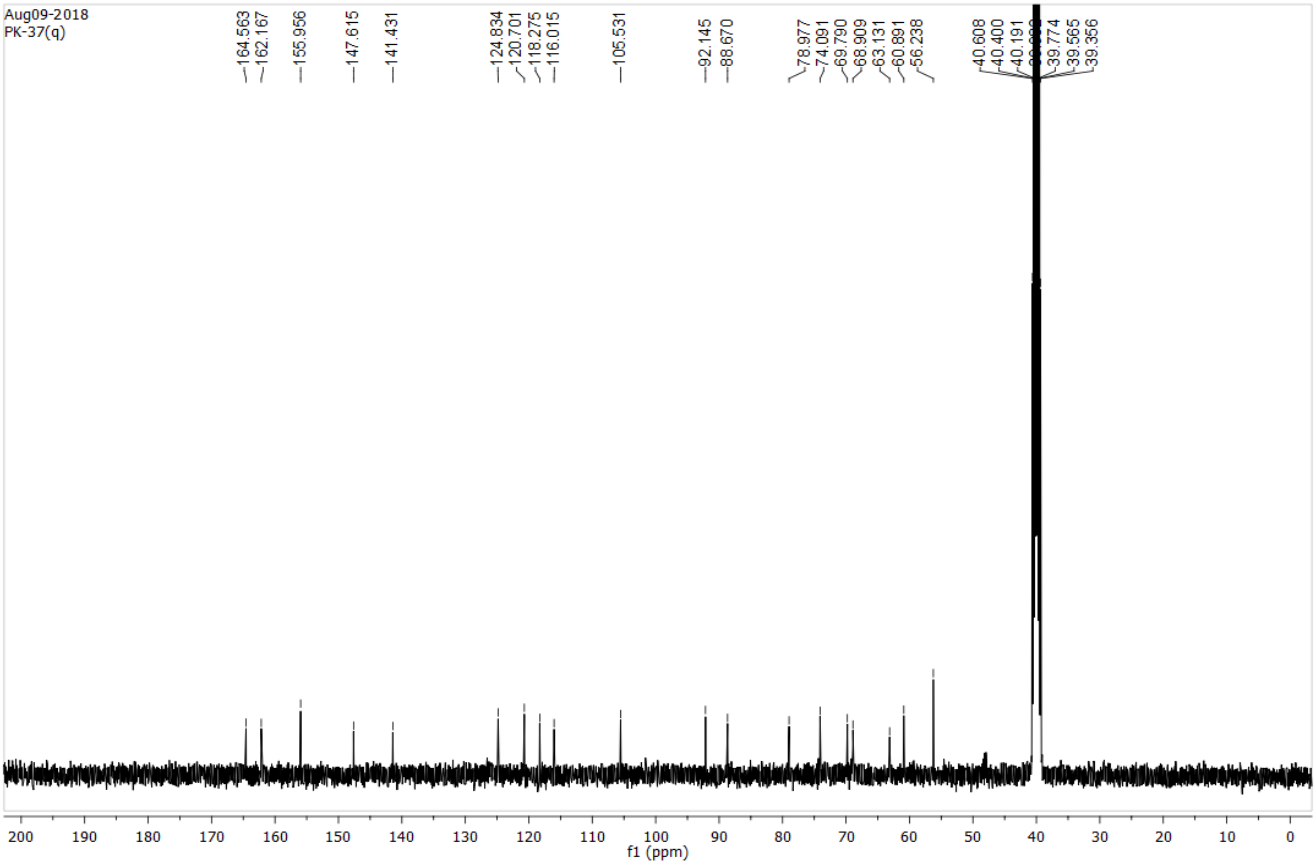
46


8.530
7.778
7.774
7.758
7.754
7.676
7.672
7.655
7.637
7.633
7.417
7.397
7.358
7.338
7.320
6.198
5.436
4.718
4.704
4.690
4.677
4.664
4.059
3.765
3.756
3.732
3.560
3.551
3.537
3.522
3.508
2.496
2.492
HO
O
N=N
N
O
O
O
HO
OH
OH
1.00
0.96
1.04
1.00
1.01
0.97
1.86
1.73
1.18
2.19
2.17
f1 (ppm)

47


164.844
162.001
153.243
141.459
133.280
124.699
123.388
116.927
115.553
91.817
88.673
79.765
78.977
74.131
63.219
60.902
40.647
40.437
40.229
39.811
39.602
39.394
f1 (ppm)


8.519
7.376
7.354
7.271
7.264
7.248
7.241
7.147
7.139
6.198
5.545
5.522
5.453
4.086
4.061
4.038
3.785
3.745
3.729
3.715
3.573
3.565
3.559
3.549
3.542
3.531
3.517
3.513
3.496
3.484
2.500
1.00
1.12
1.11
1.07
1.13
1.14
2.14
2.26
3.40
1.31
1.95
1.41
f1 (ppm)


Aug09-2018
PK-37(q)
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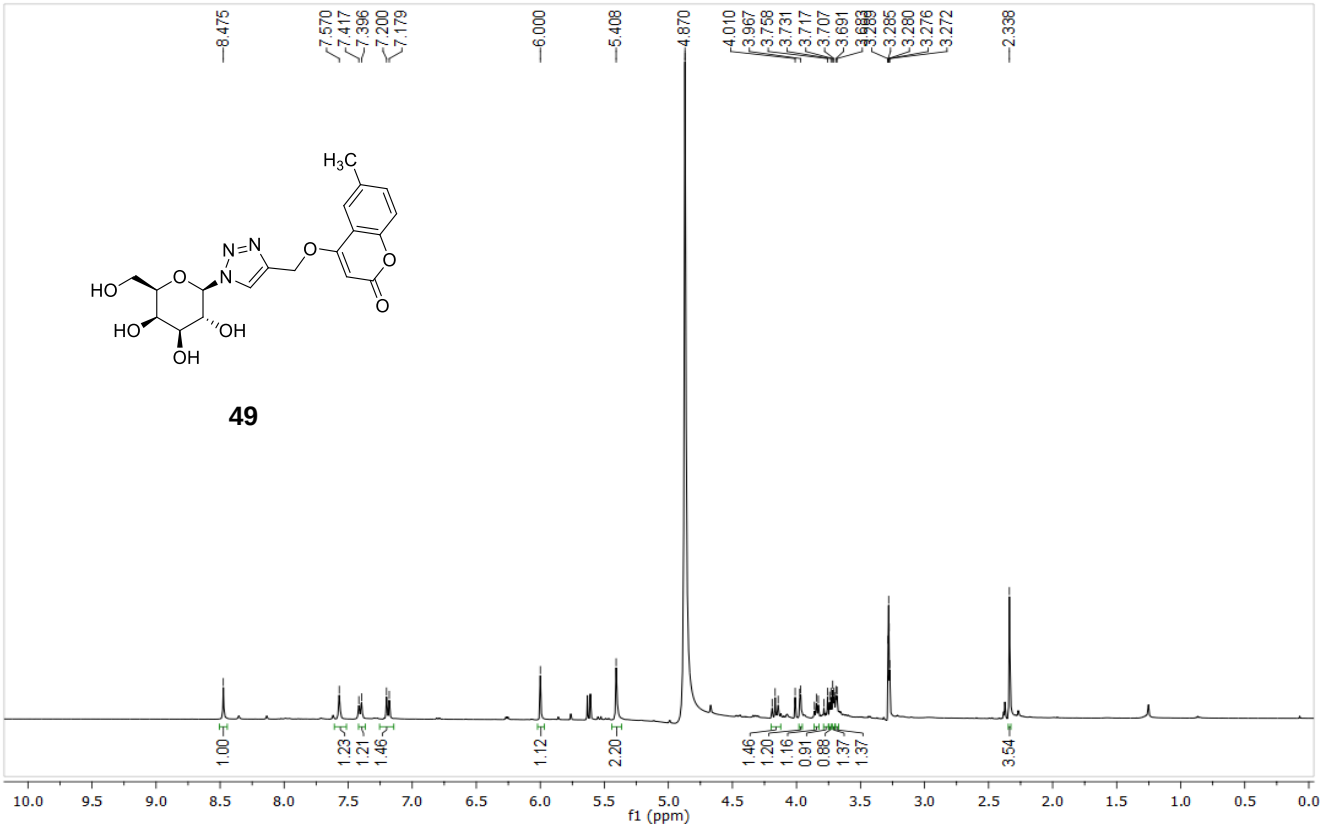
155.956
147.615
141.431
124.834
120.701
118.275
116.015
105.531
92.145
88.670
78.977
74.091
69.790
68.909
63.131
60.891
56.238
40.608
40.400
40.191
39.774
39.565
39.356
f1 (ppm)

48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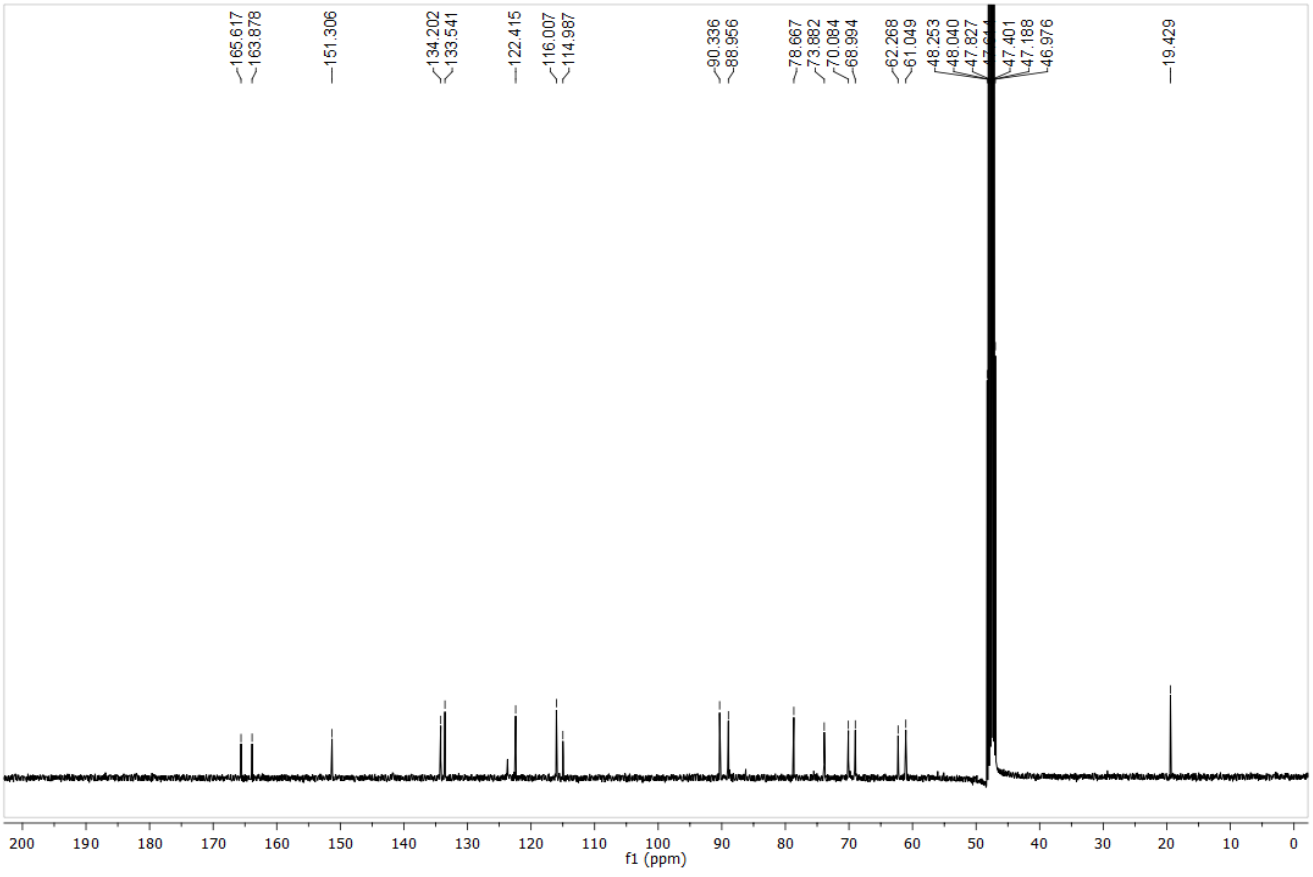
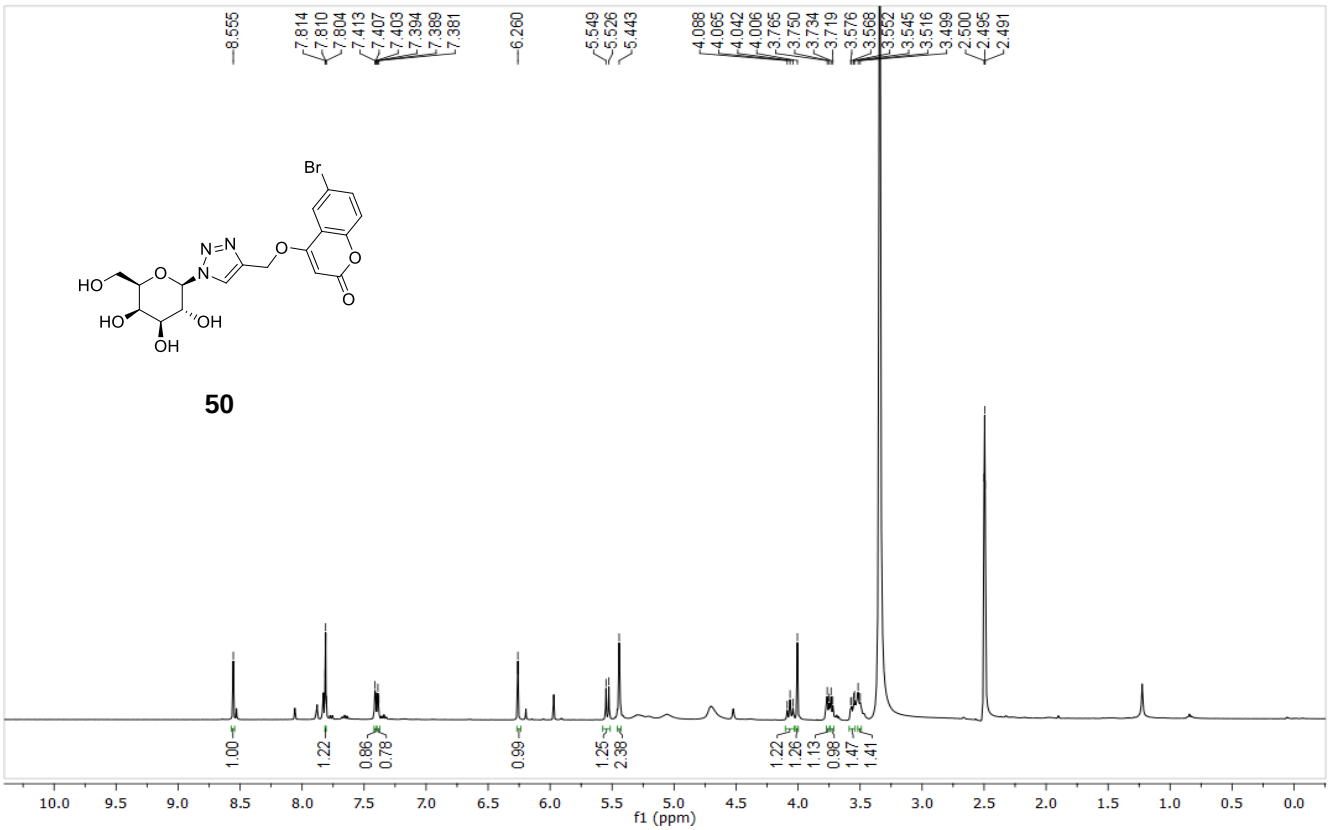
7.396
7.200
7.179
6.000
5.408
4.870
4.010
3.967
3.758
3.731
3.717
3.707
3.691
3.285
3.280
3.276
3.272
2.338
1.00
1.23
1.21
1.46
1.12
2.20
1.46
1.20
1.16
0.91
0.88
1.37
1.37
3.54
f1 (ppm)

H3C
HO
HO
OH
OH
N
N
N
O
O
O
O

49


165.617
163.878
151.306
134.202
133.541
122.415
116.007
114.987
90.336
88.956
78.667
73.882
70.084
68.994
62.268
61.049
48.253
48.040
47.827
47.401
47.188
46.976
19.429
f1 (ppm)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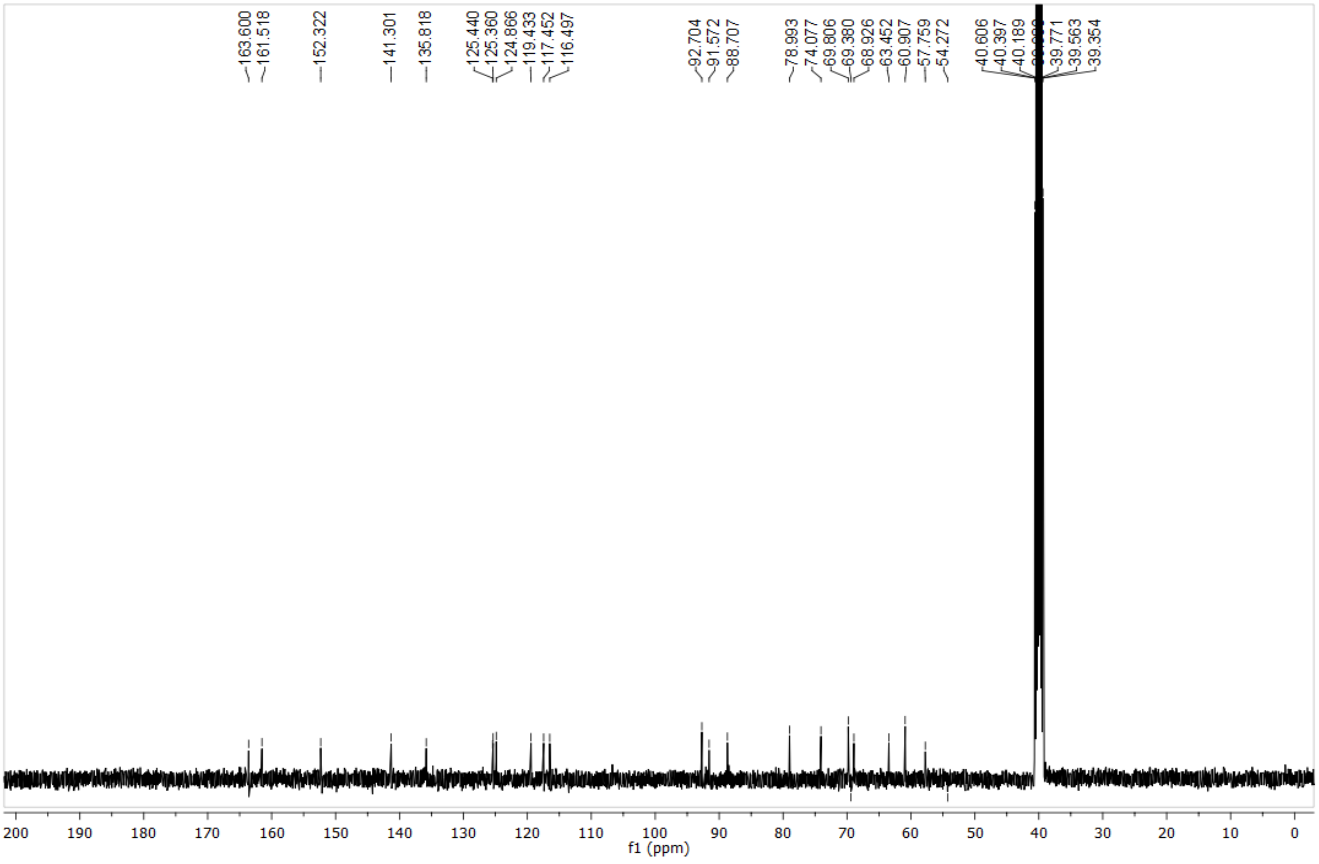
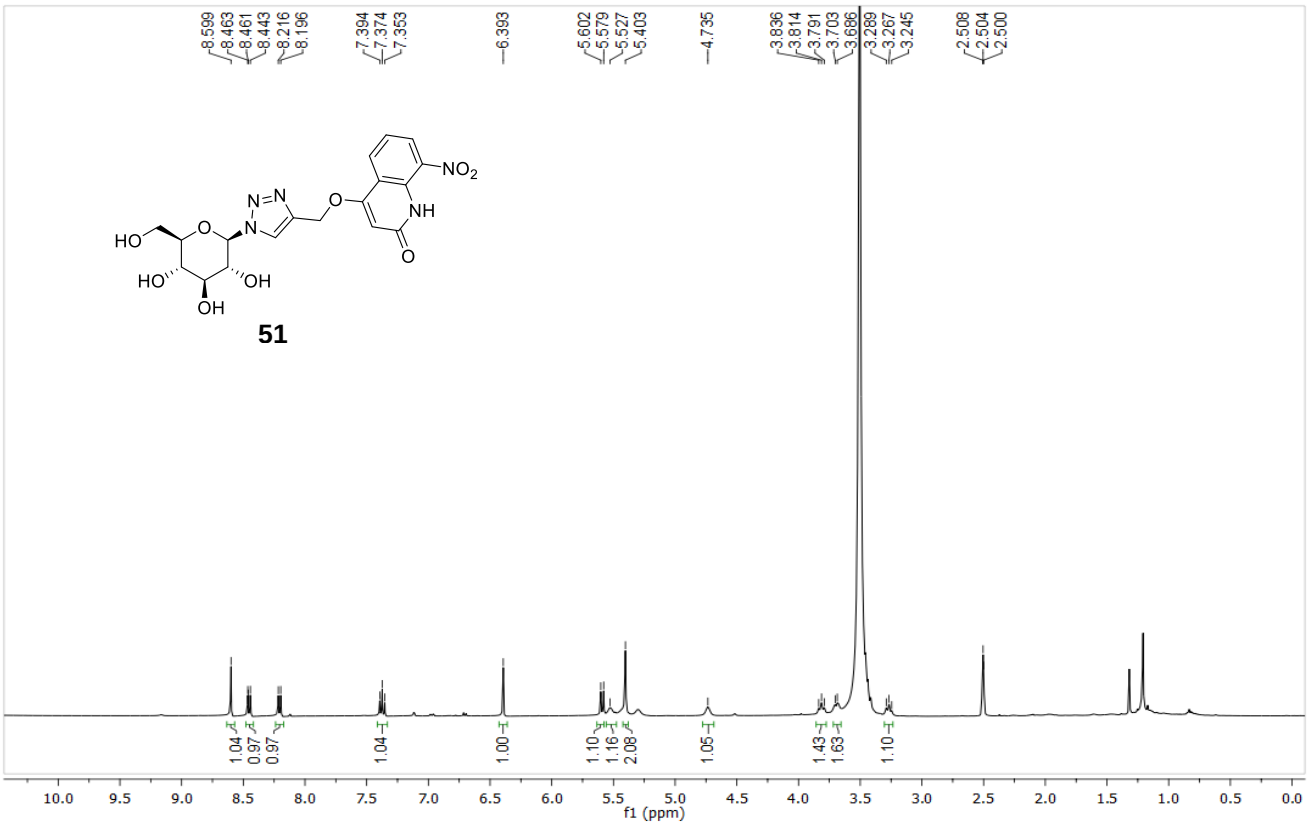
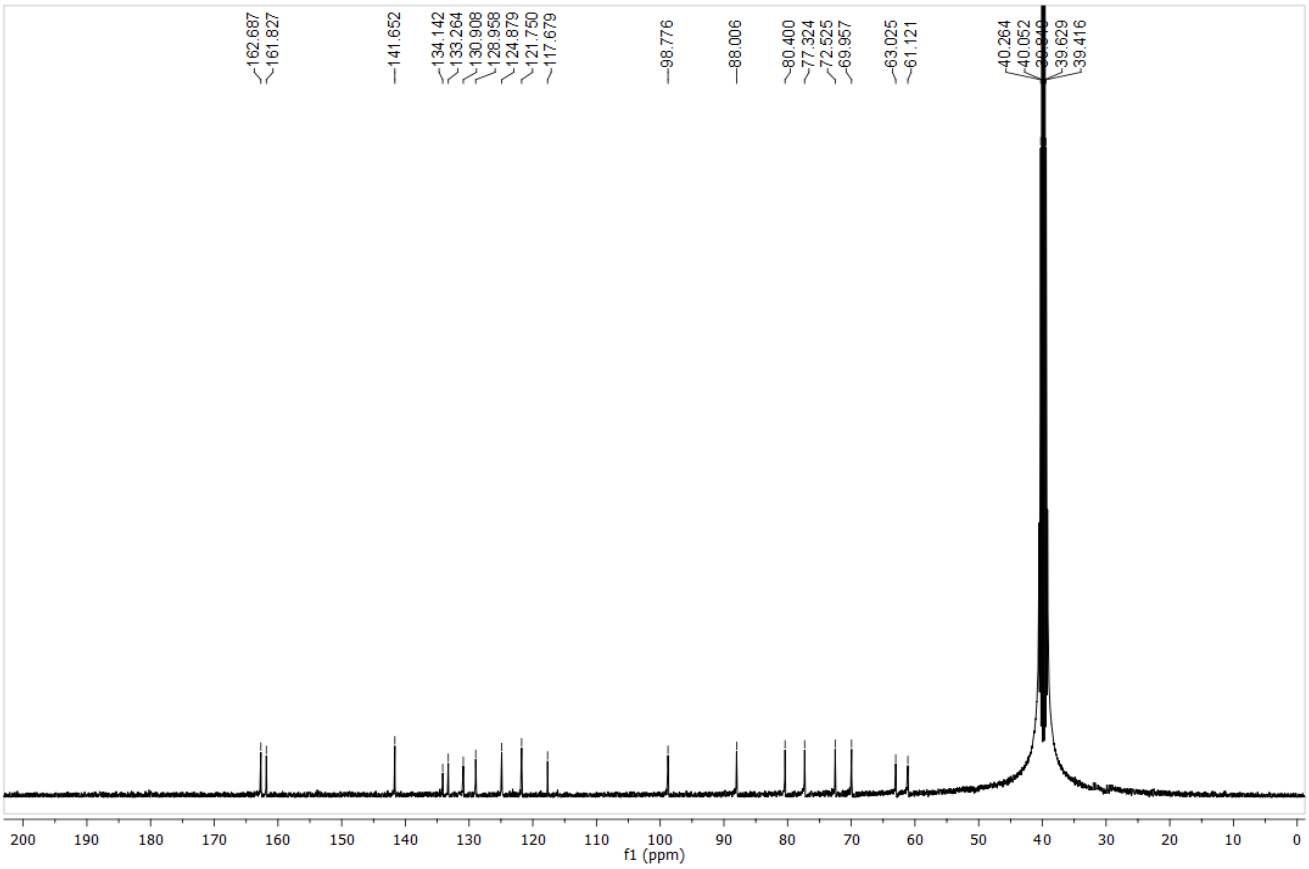
7.814
7.810
7.804
7.413
7.407
7.403
7.394
7.389
7.381
6.260
5.549
5.526
5.443
4.088
4.065
4.042
4.006
3.765
3.750
3.734
3.719
3.576
3.568
3.552
3.545
3.516
3.499
2.500
2.495
2.491
Br
HO
HO
OH
OH
N=N
O
O
O
1.00
1.22
0.86
0.78
0.99
1.25
2.38
1.22
1.26
1.13
0.98
1.47
1.41
f1 (ppm)

50

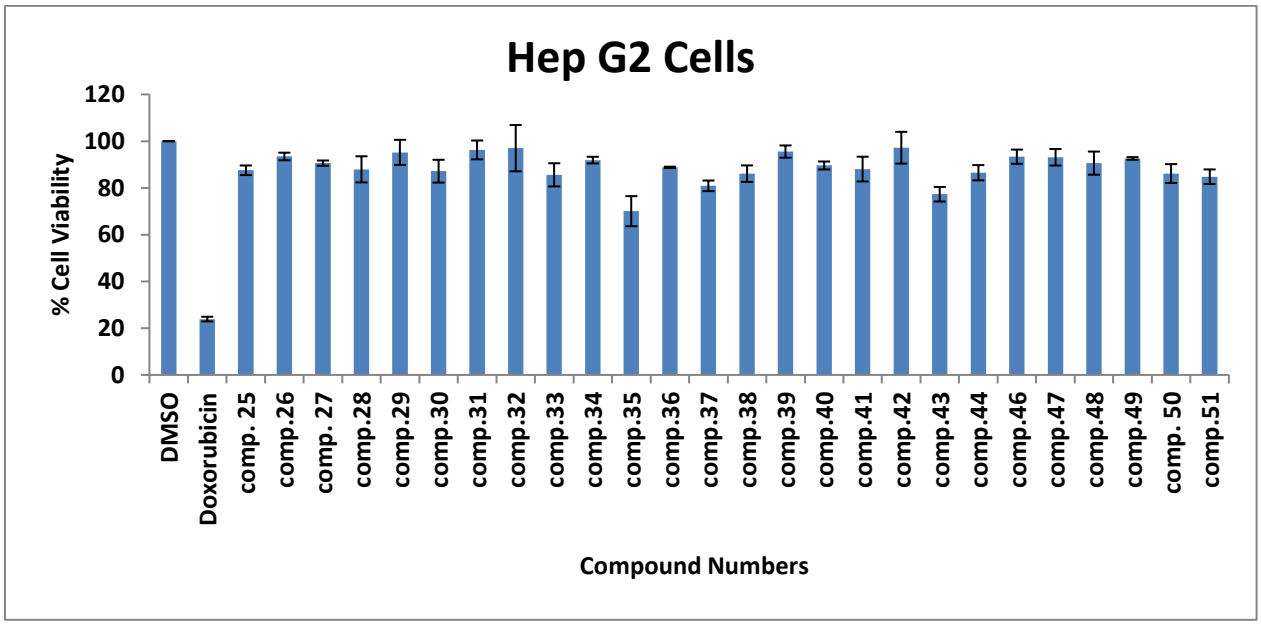

163.600
161.518
152.322
141.301
135.818
125.440
125.360
124.866
119.433
117.452
116.497
92.704
91.572
88.707
78.993
74.077
69.806
69.380
68.926
63.452
60.907
57.759
54.272
40.606
40.397
40.189
39.771
39.563
39.354
f1 (ppm)


8.599
8.463
8.461
8.443
8.216
8.196
7.394
7.374
7.353
6.393
5.602
5.579
5.527
5.403
4.735
3.836
3.814
3.791
3.703
3.686
3.289
3.267
3.245
2.508
2.504
2.500
NO2
NH
O
N=N
N
O
HO
HO
OH
OH
1.04
0.97
0.97
1.04
1.00
1.10
1.16
2.08
1.05
1.43
1.63
1.10
f1 (ppm)

51


162.687
161.827
141.652
134.142
133.264
130.908
128.958
124.879
121.750
117.679
98.776
88.006
80.400
77.324
72.525
69.957
63.025
61.121
40.264
40.052
39.629
39.416
f1 (ppm)

Results of Cell Viability Assays



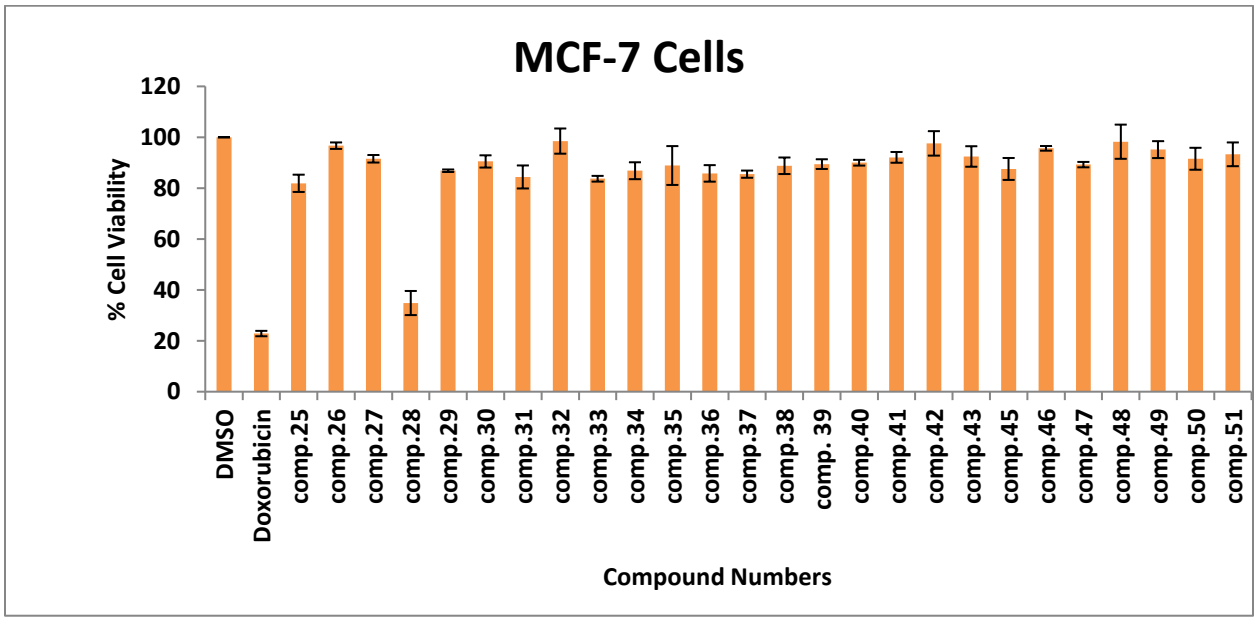


Figure S1. Results of cell viability assays with all the compounds (**25-51**) in HepG2 and MCF-7 cancer cell lines (20 µM concentration).

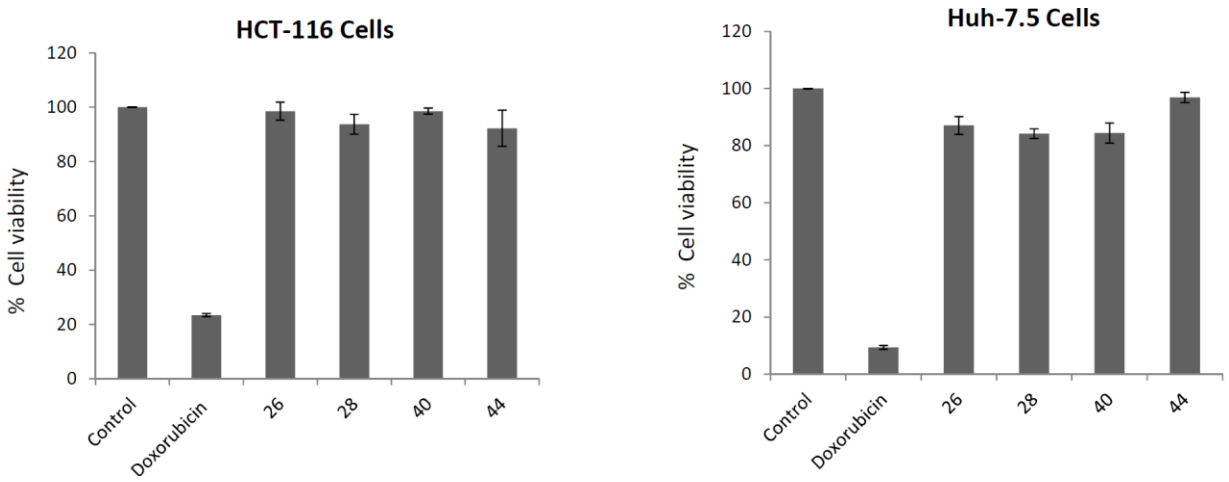


Figure S2. Cell viability assay of compounds **26, 28, 40** and **44** in HCT-116 and Huh-7.5 cell line (20 µM concentration).

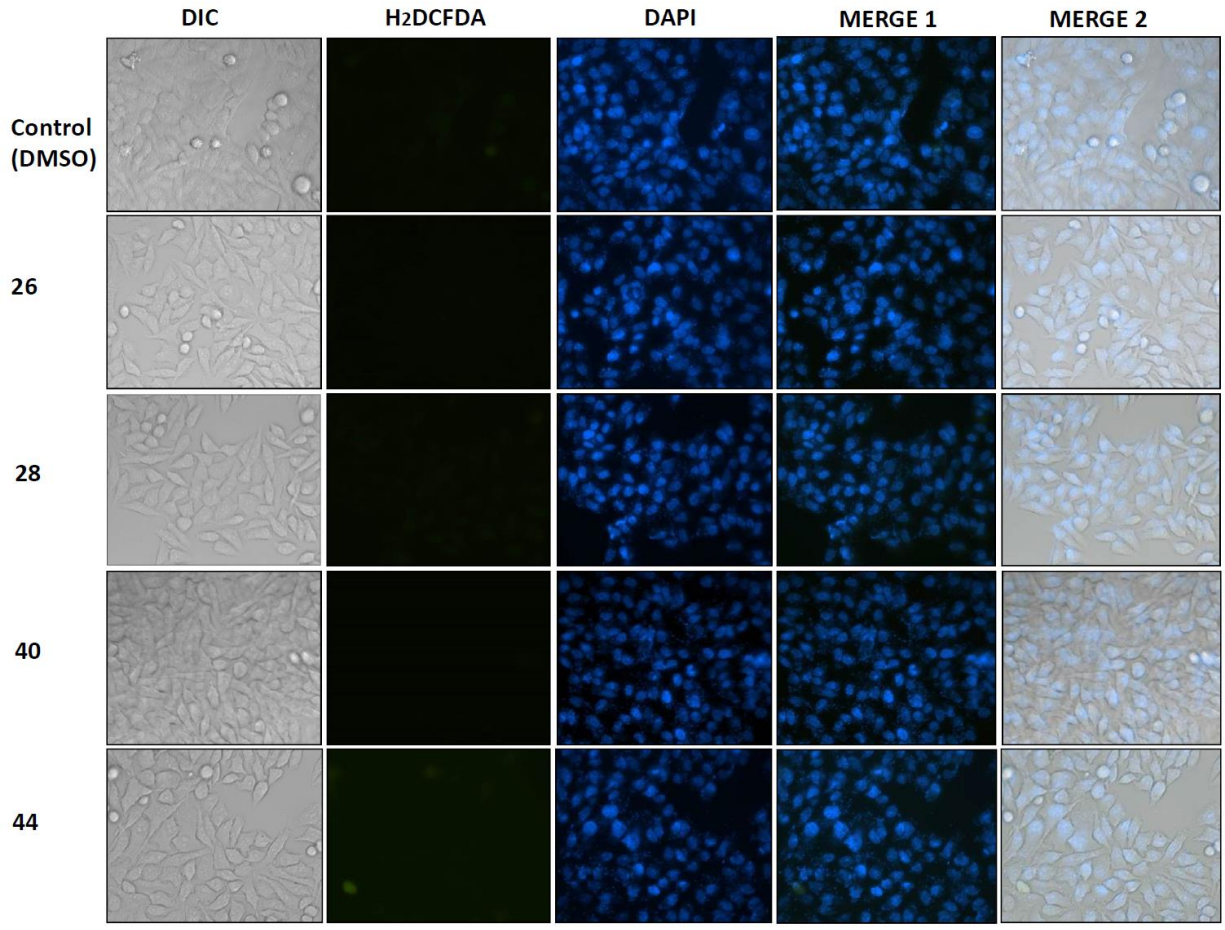


Figure S3. H2DCFDA Assay performed in HepG2 cells.

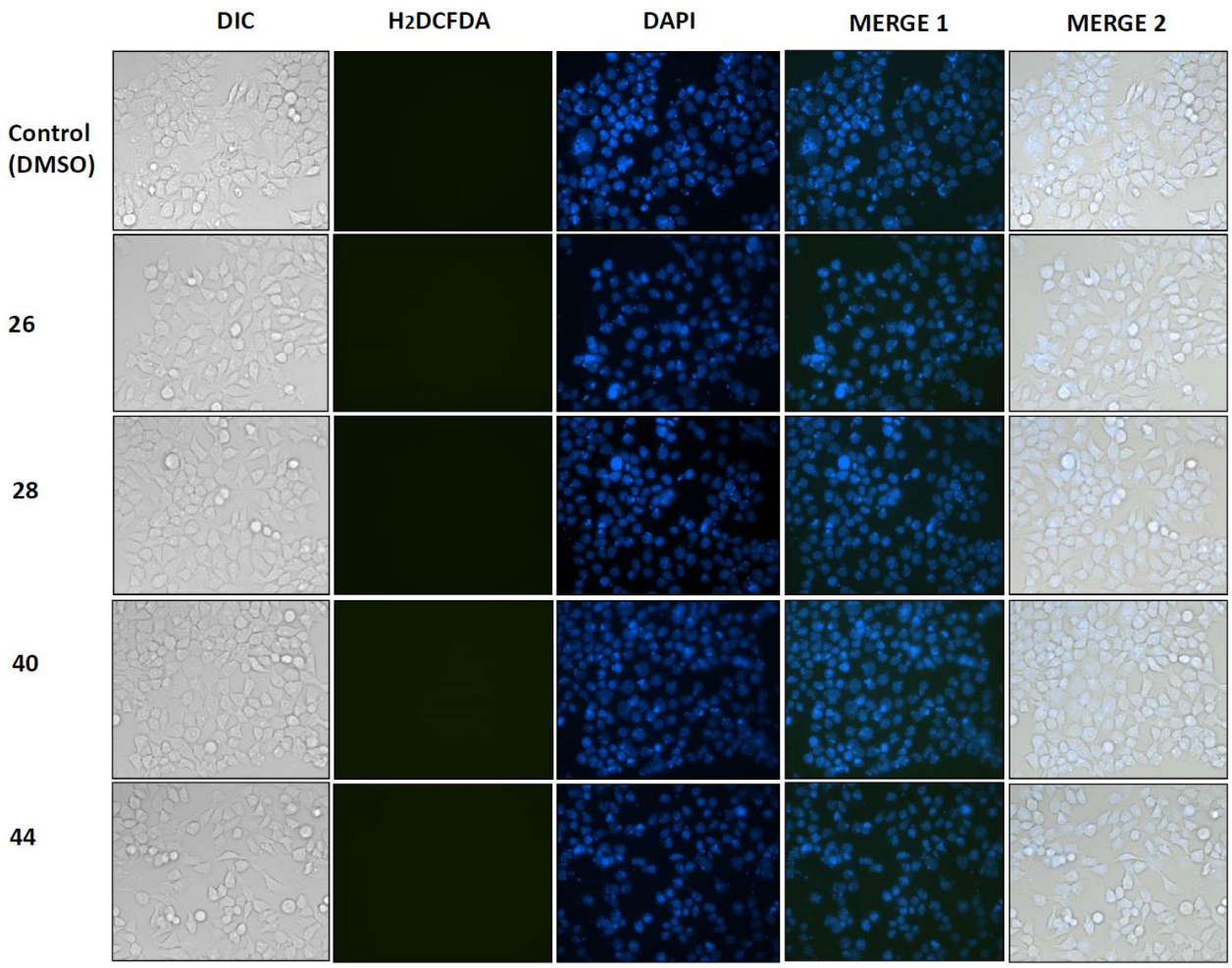


Figure S4. H2DCFDA Assay performed in HCT-116 cells.

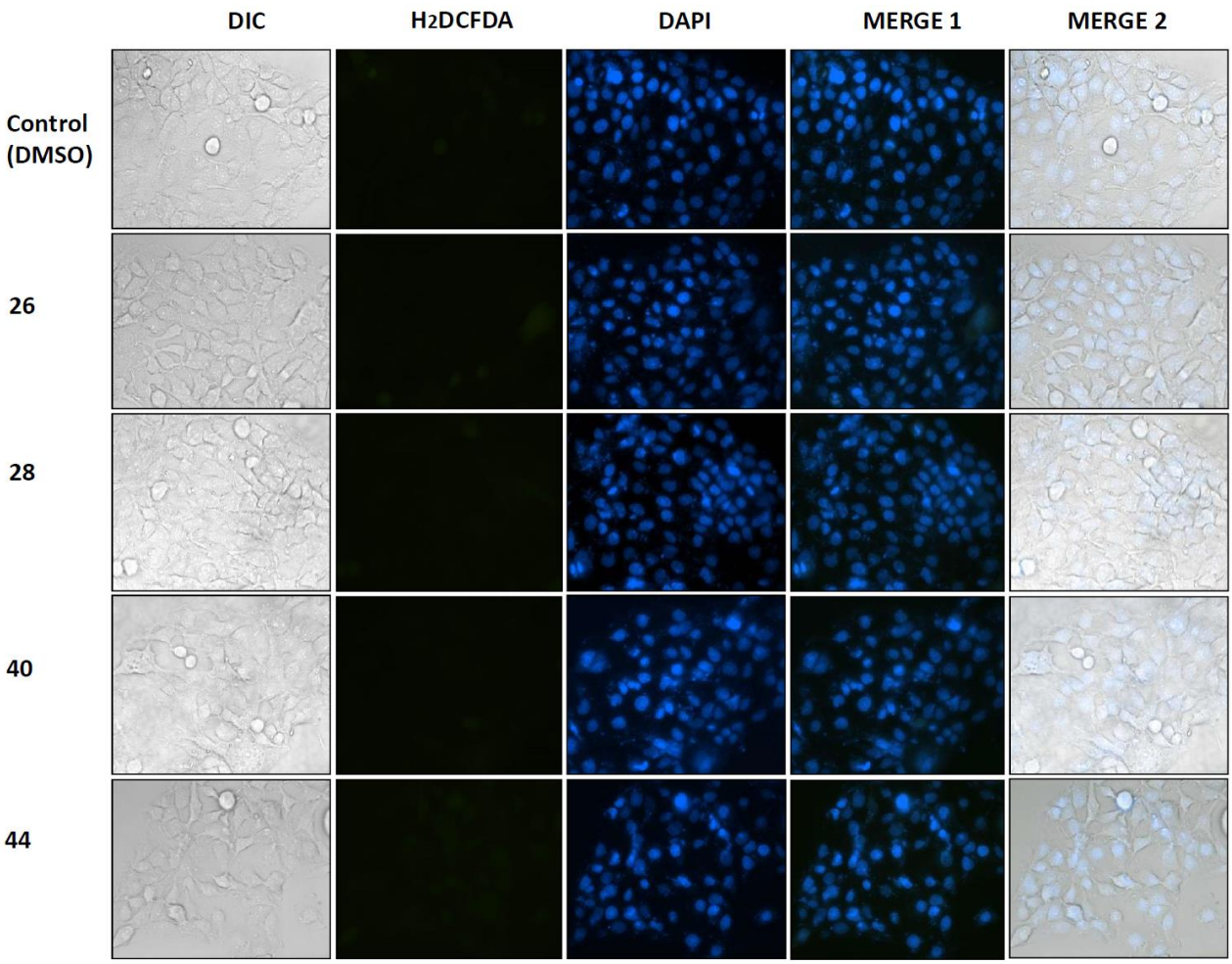


Figure S5. H2DCFDA Assay performed in Huh-7.5 cells.