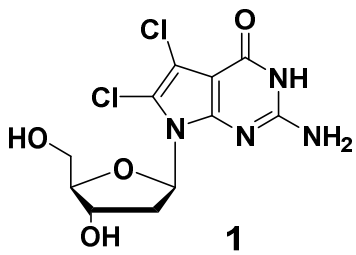
Supplementary Materials

Development of MTH1-binding nucleotide analogs based on 7,8-dihalogenated 7-deaza-dG derivatives

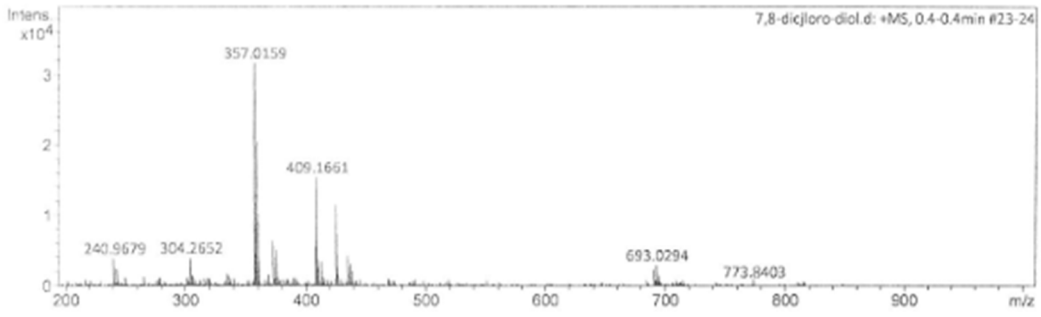
Hui Shi, Ren Ishikawa, Choon Han Heh, Shigeki Sasaki, and Yosuke Taniguchi

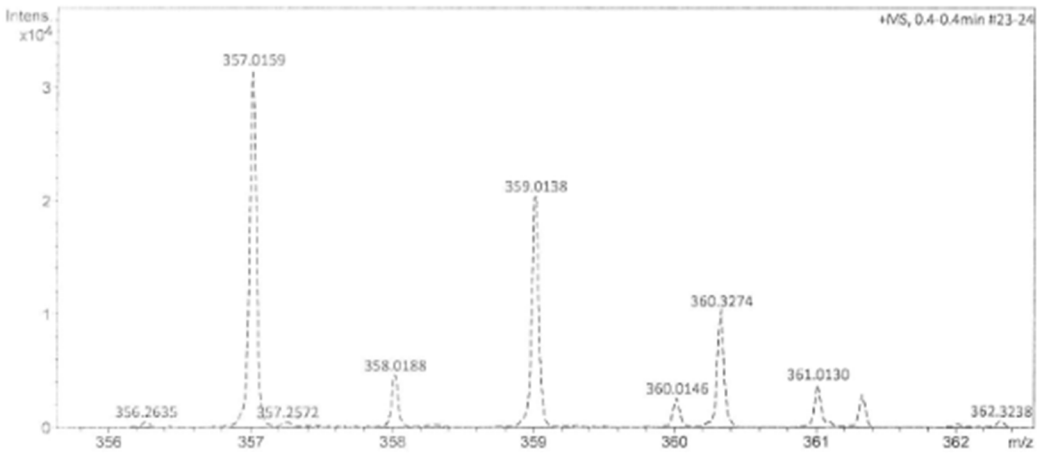
Contents:


Cl
O
Cl
NH
HO
N
N
NH2
O
OH

1

9
8
7
6
5
4
3
2
1
ppm


Intens.
x10^4
7,8-dicjloro-diol.d: +MS, 0.4-0.4min #23-24
357.0159
409.1661
240.9679
304.2652
693.0294
773.8403
200
300
400
500
600
700
800
900
m/z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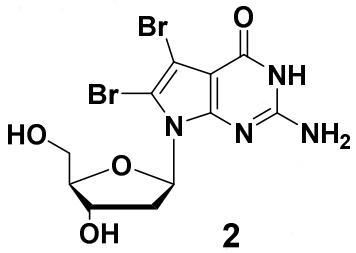
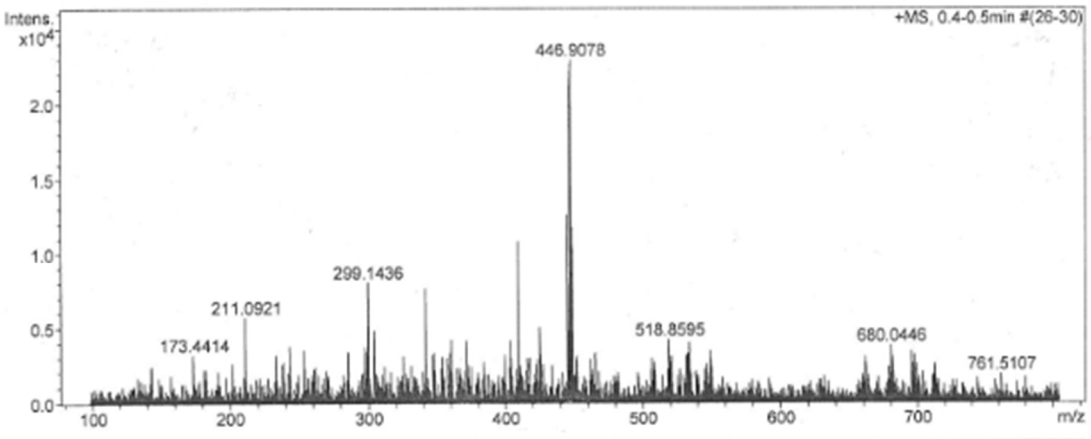
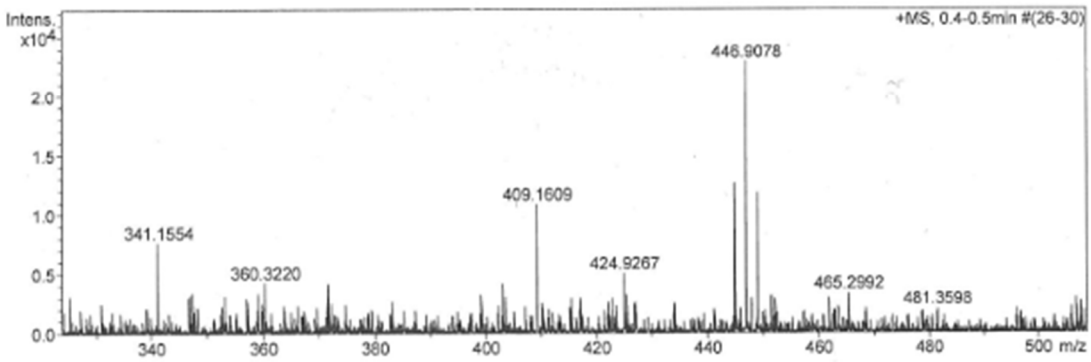
x10^4
+MS, 0.4-0.4min #23-24
357.0159
359.0138
360.3274
358.0188
361.0130
360.0146
356.2635
357.2572
362.3238
356
357
358
359
360
361
362
m/z

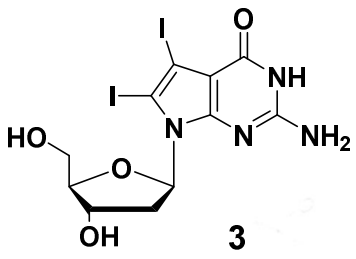

Br
O
Br
NH
HO
N
N
NH2
O
OH

2

11
10
9
8
7
6
5
4
3
2
1
0
ppm

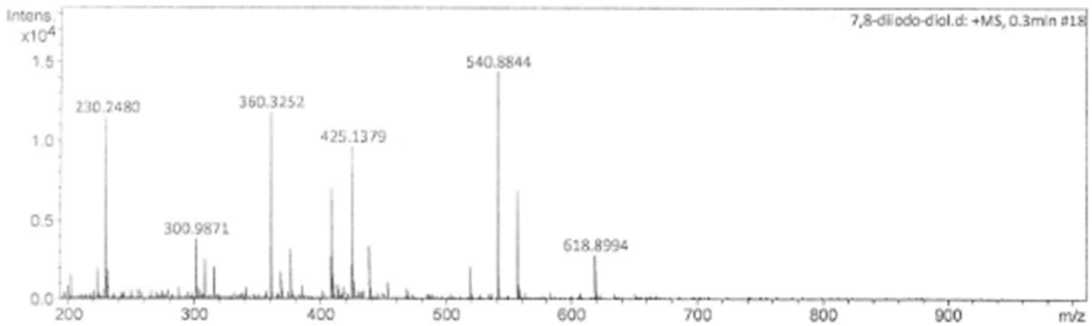

Intens.
x10^4
+MS, 0.4-0.5min #(26-30)
446.9078
299.1436
211.0921
173.4414
518.8595
680.0446
761.5107
m/z

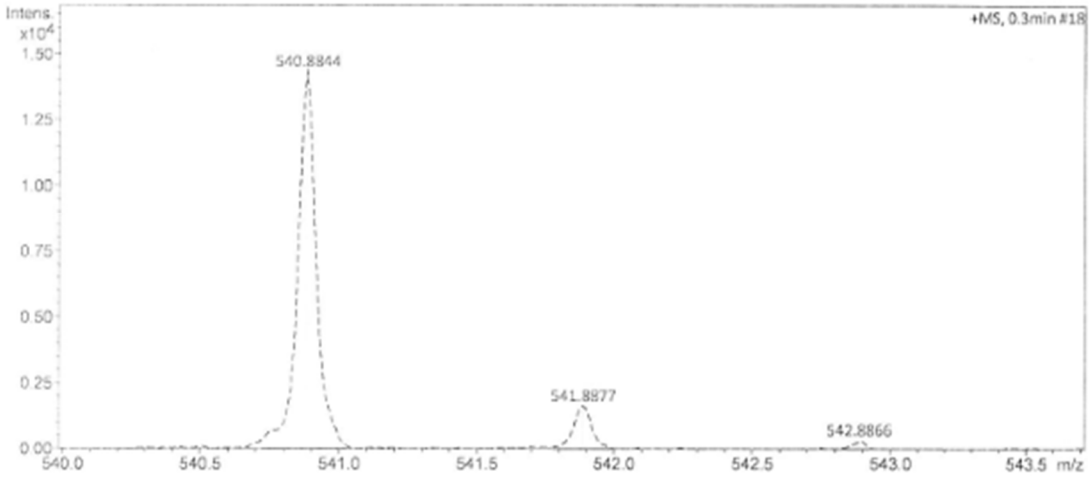

Intens.
x10^4
+MS, 0.4-0.5min #(26-30)
446.9078
409.1609
341.1554
360.3220
424.9267
465.2992
481.3598
m/z

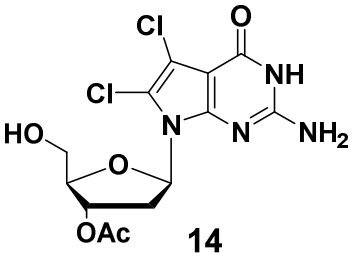

I
O
NH
I
N
N
NH2
HO
O
OH

3

11
10
9
8
7
6
5
4
3
2
1
ppm

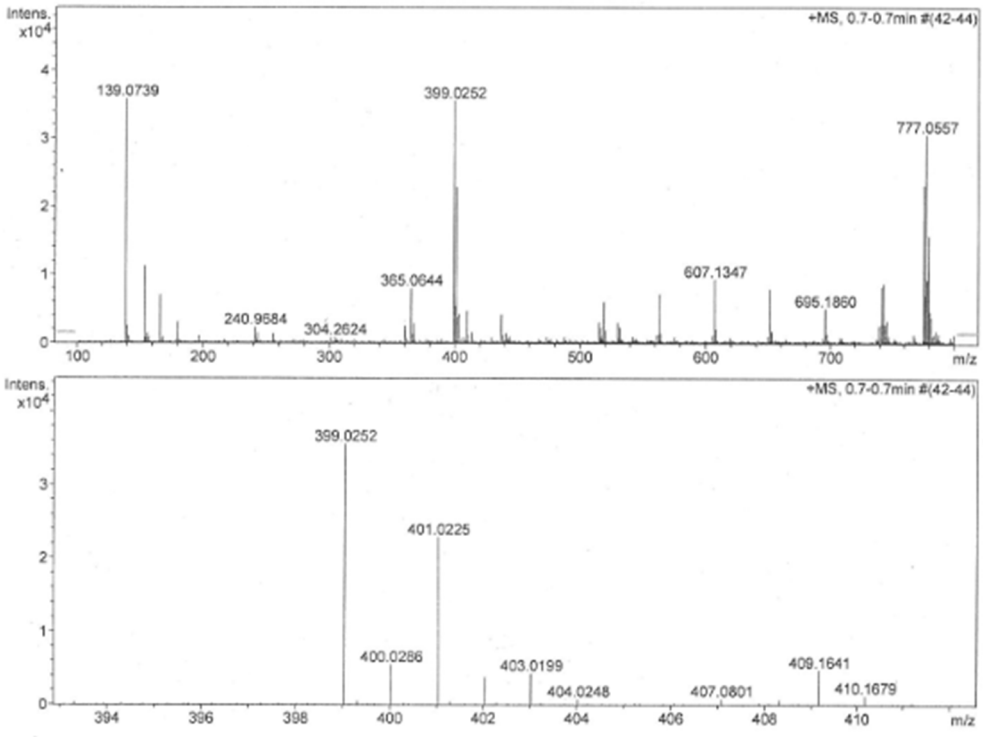

Intens.
x10^4
7,8-diiodo-diol.d: +MS, 0.3min #18
540.8844
230.2480
360.3252
425.1379
300.9871
618.8994
m/z

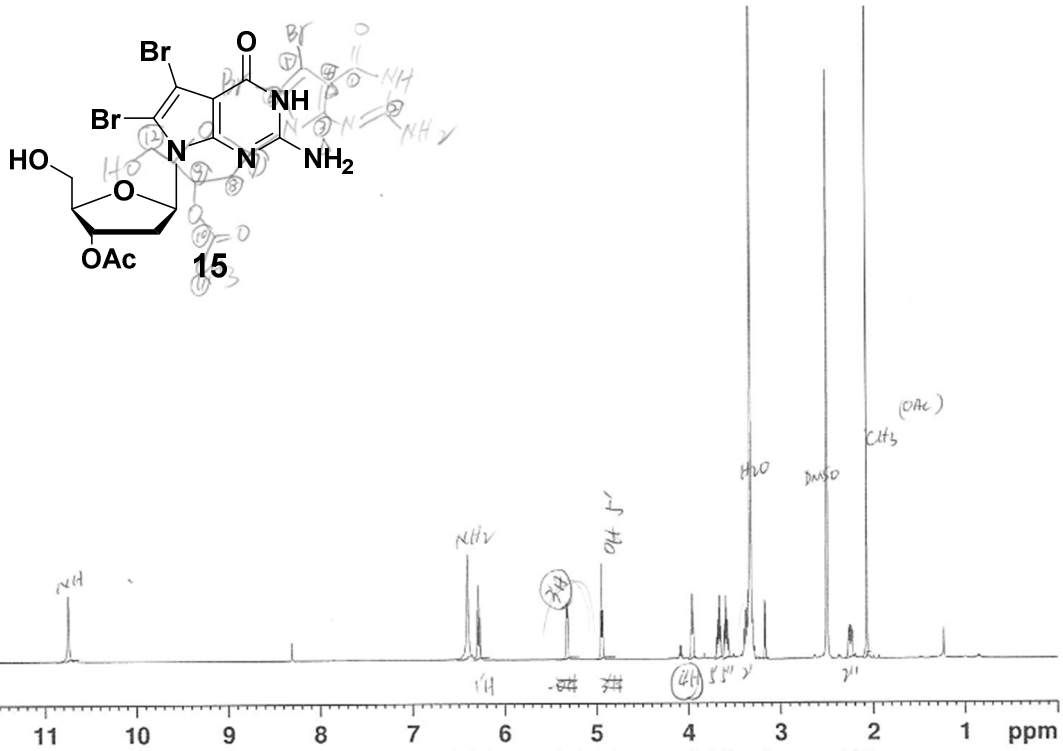

Intens.
x10^4
+MS, 0.3min #18
540.8844
541.8877
542.8866
m/z

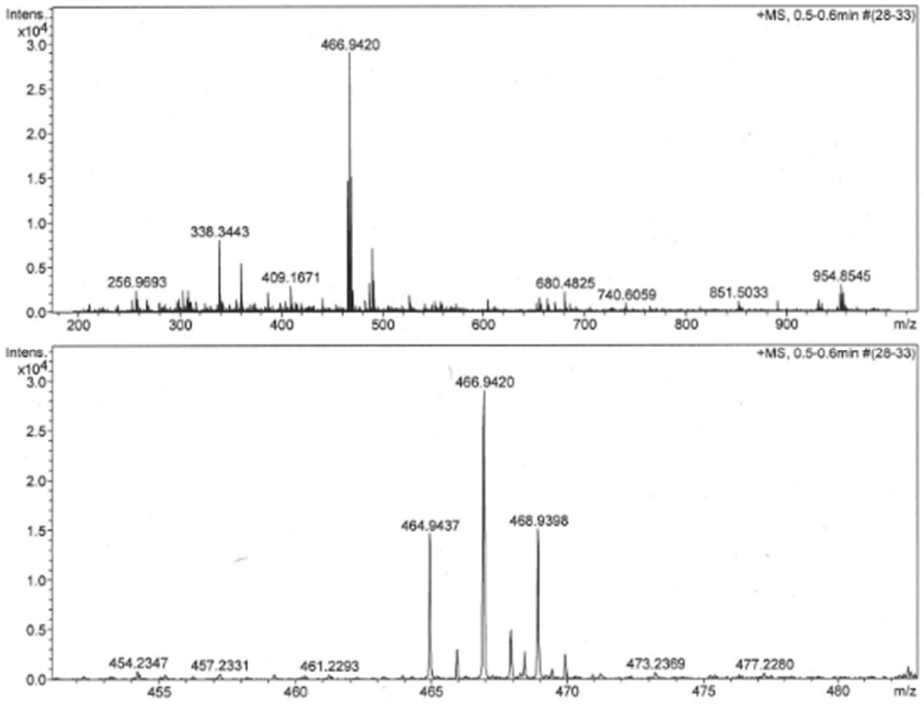

Cl
O
NH
Cl
N
N
NH2
HO
O
OAc

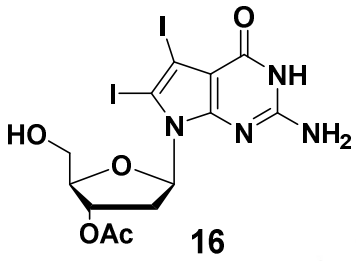
14

11
10
9
8
7
6
5
4
3
2
1
ppm


Intens.
x10^4
+MS, 0.7-0.7min #(42-44)
139.0739
399.0252
777.0557
365.0644
607.1347
695.1860
240.9584
304.2624
100
200
300
400
500
600
700
m/z
Intens.
x10^4
+MS, 0.7-0.7min #(42-44)
399.0252
401.0225
400.0286
403.0199
404.0248
407.0801
409.1641
410.1679
394
396
398
400
402
404
406
408
410
m/z

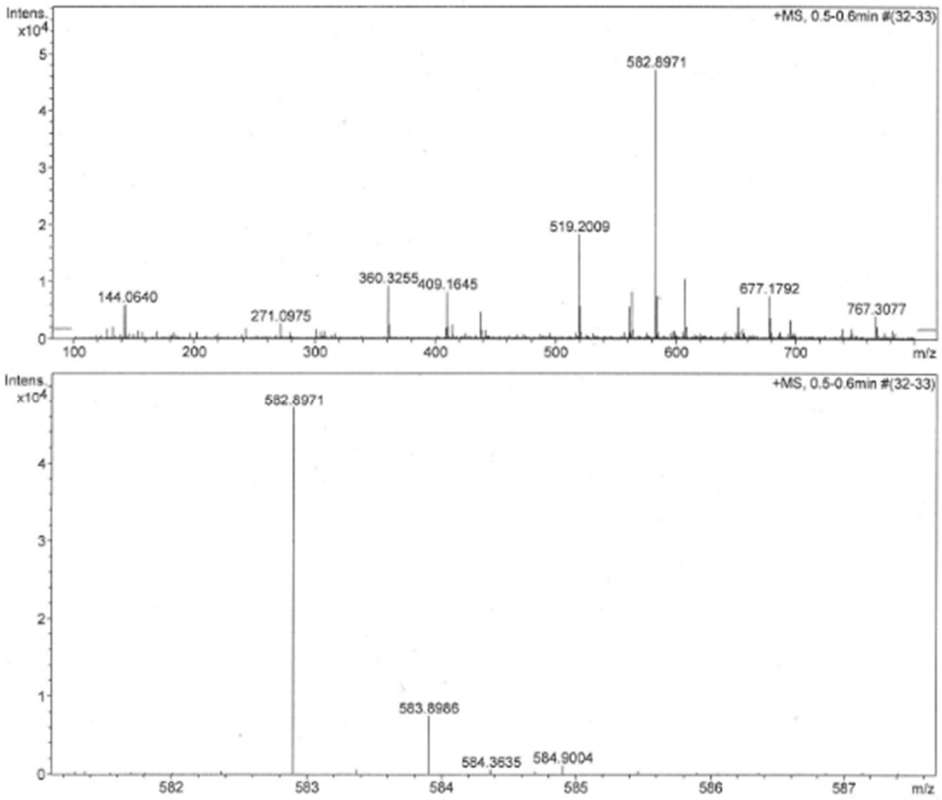

Br
O
Br
NH
HO
N
N
NH2
O
OAc
15
11
10
9
8
7
6
5
4
3
2
1
ppm

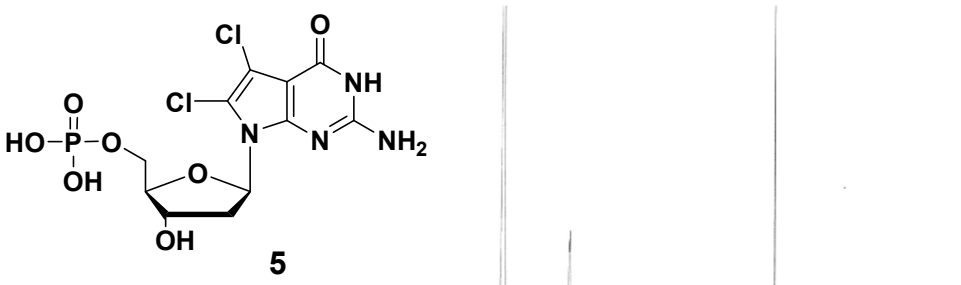

Intens.
x10^4
+MS, 0.5-0.6min #(28-33)
466.9420
338.3443
256.9693
409.1671
680.4825
740.6059
851.5033
954.8545
m/z
Intens.
x10^4
+MS, 0.5-0.6min #(28-33)
466.9420
464.9437
468.9398
454.2347
457.2331
461.2293
473.2369
477.2280
m/z


I
O
NH
I
N
N
NH2
HO
O
OAc

16

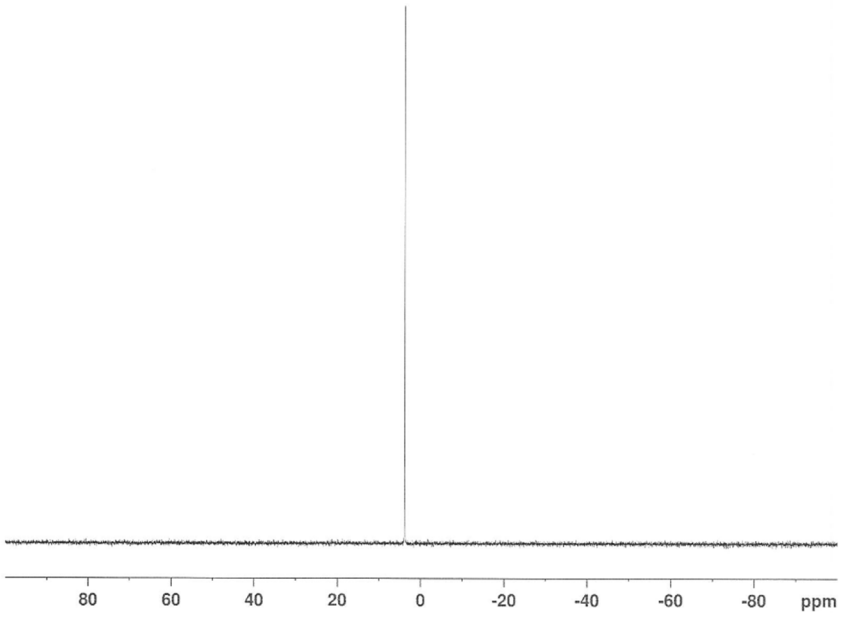
11
10
9
8
7
6
5
4
3
2
1
ppm

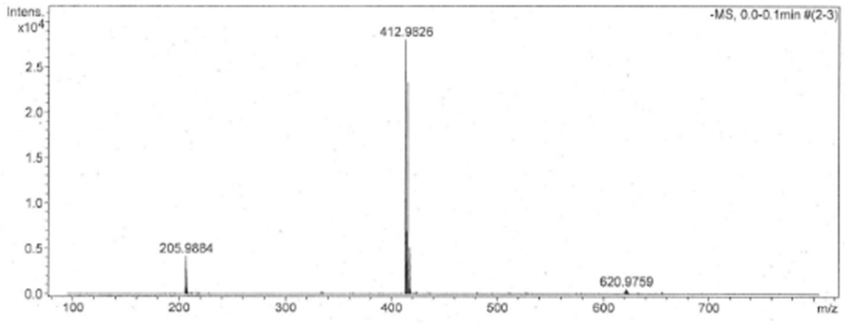

Intens.
x10^4
+MS, 0.5-0.6min #(32-33)
582.8971
519.2009
360.3255
409.1645
144.0640
271.0975
677.1792
767.3077
m/z
Intens.
x10^4
+MS, 0.5-0.6min #(32-33)
582.8971
583.8966
584.3635
584.9004
m/z

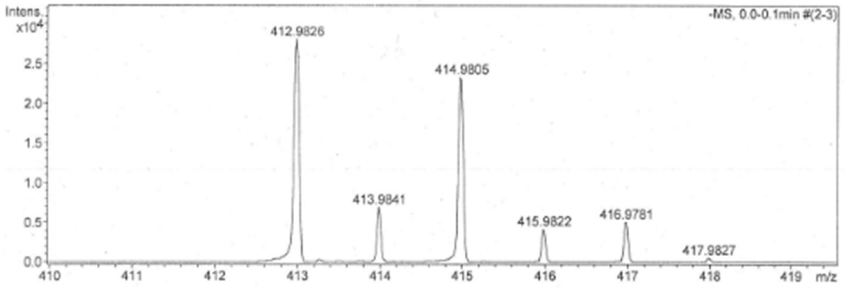

Cl
O
NH
Cl
O
P
O
HO
OH
N
N
NH2
O
OH

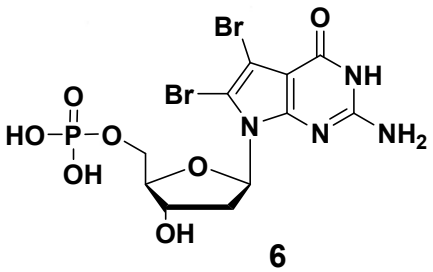
5

9
8
7
6
5
4
3
2
1
ppm


80
60
40
20
0
-20
-40
-60
-80
ppm

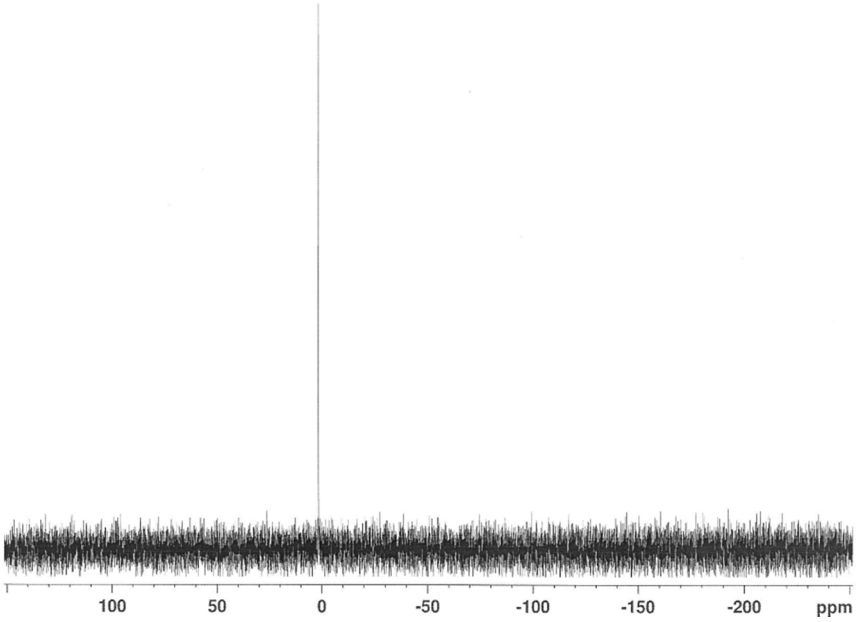

Intens.
x10^4
-MS, 0.0-0.1min #(2-3)
412.9826
205.9884
620.9759
m/z

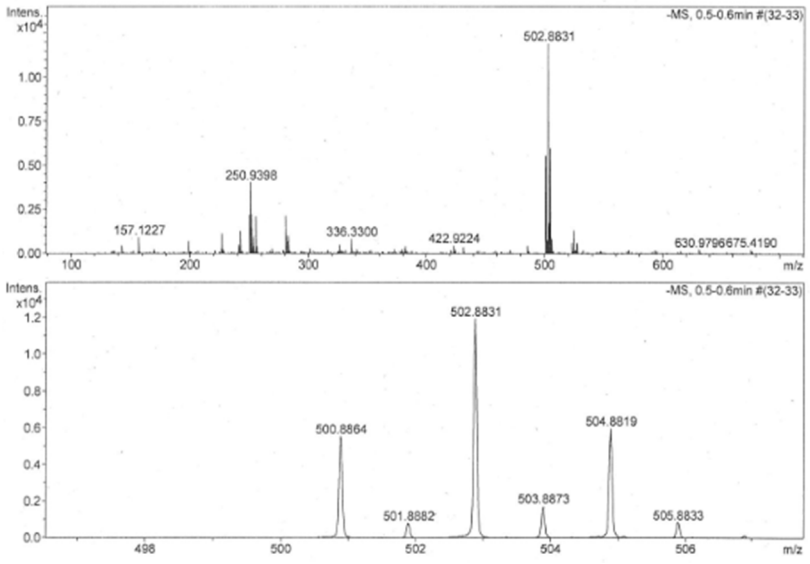

Intens.
x10^4
-MS, 0.0-0.1min #(2-3)
412.9826
414.9805
413.9841
415.9822
416.9781
417.9827
m/z

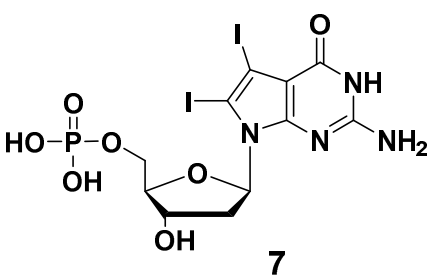

Br
O
NH
Br
O
HO
P
O
N
N
NH2
OH
O
OH

6

9
8
7
6
5
4
3
2
1
ppm

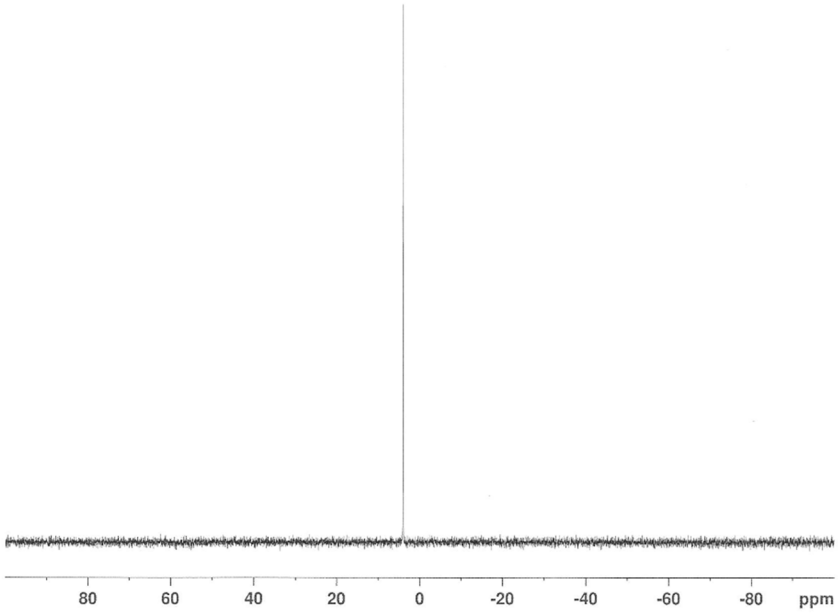

100
50
0
-50
-100
-150
-200
ppm

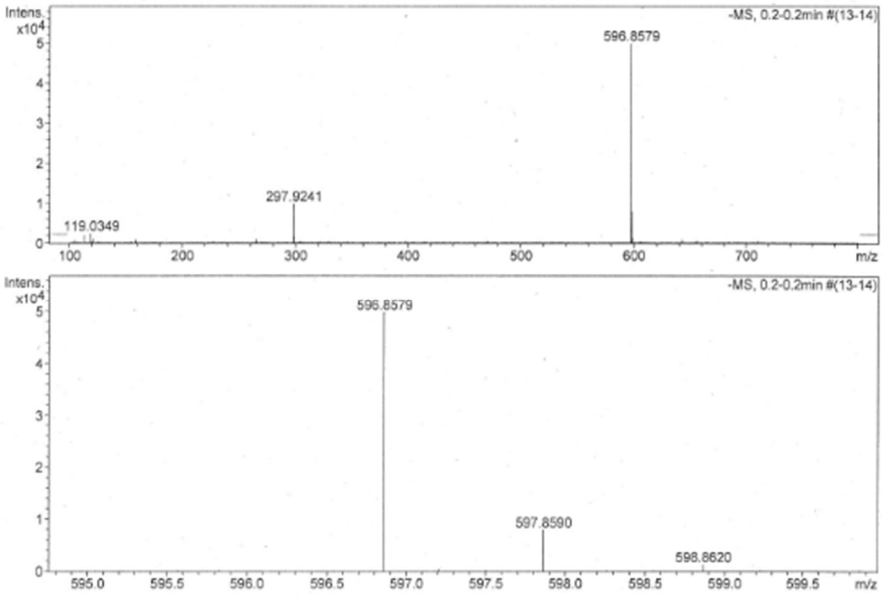

Intens.
x10^4
-MS, 0.5-0.6min #(32-33)
502.8831
250.9398
157.1227
336.3300
422.9224
630.9796675.4190
m/z
Intens.
x10^4
-MS, 0.5-0.6min #(32-33)
502.8831
500.8864
504.8819
503.8873
501.8882
505.8833
m/z

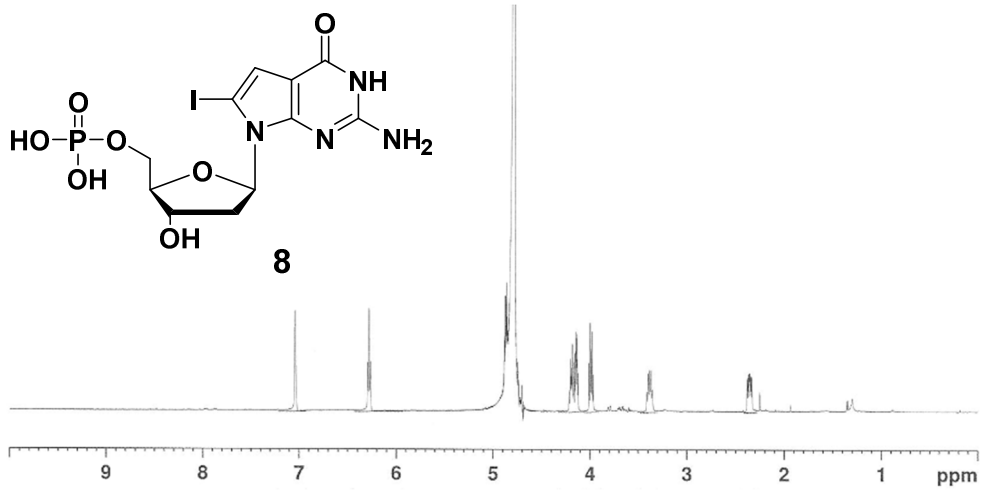

I
O
NH
I
N
N
NH2
HO
P
O
O
OH
O
OH

7

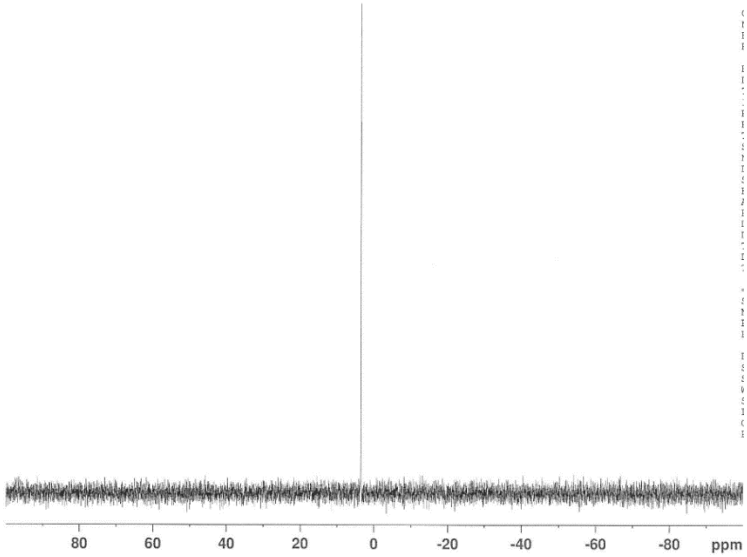
1'H
4'H
9
8
7
6
5
4
3
2
1
ppm

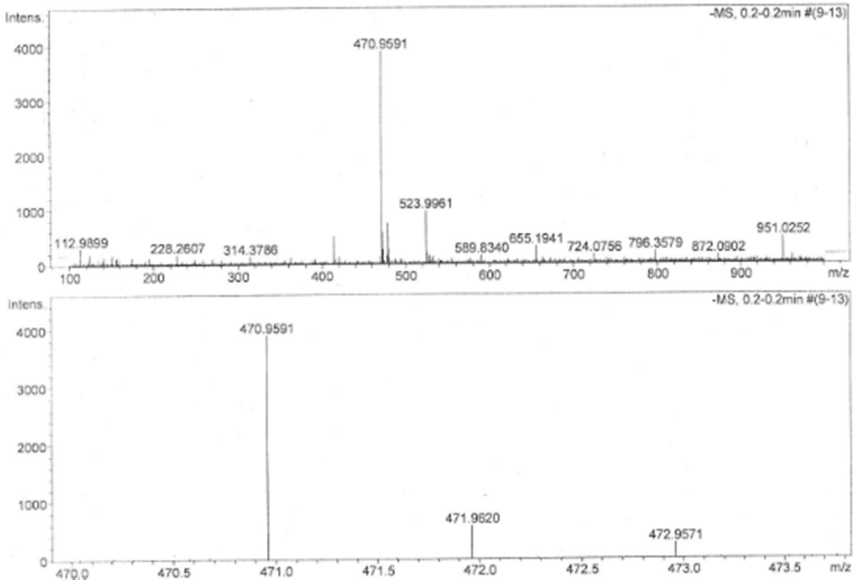

80
60
40
20
0
-20
-40
-60
-80
ppm

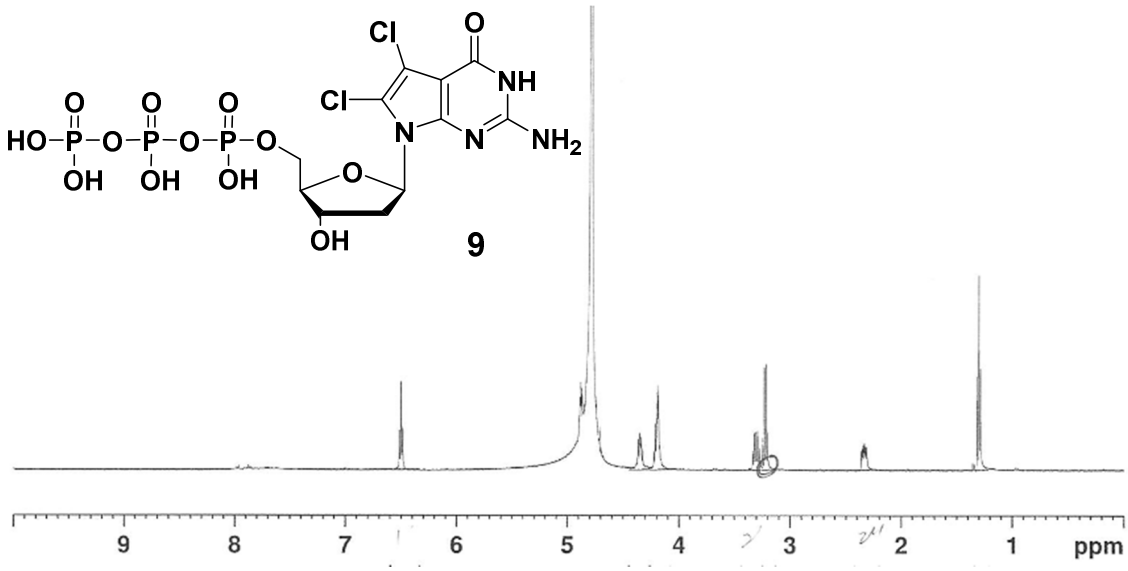

Intens.
x10^4
-MS, 0.2-0.2min #(13-14)
596.8579
297.9241
119.0349
100
200
300
400
500
600
700
m/z
Intens.
x10^4
-MS, 0.2-0.2min #(13-14)
596.8579
597.8590
598.8620
595.0
595.5
596.0
596.5
597.0
597.5
598.0
598.5
599.0
599.5
m/z

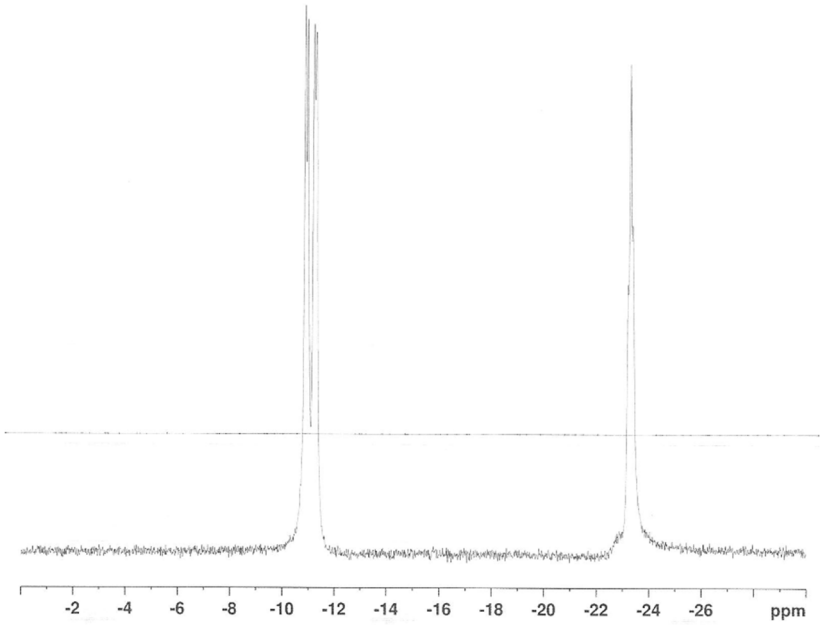

O
NH
I
N
N
NH2
HO
P
O
OH
O
OH
9
8
7
6
5
4
3
2
1
ppm

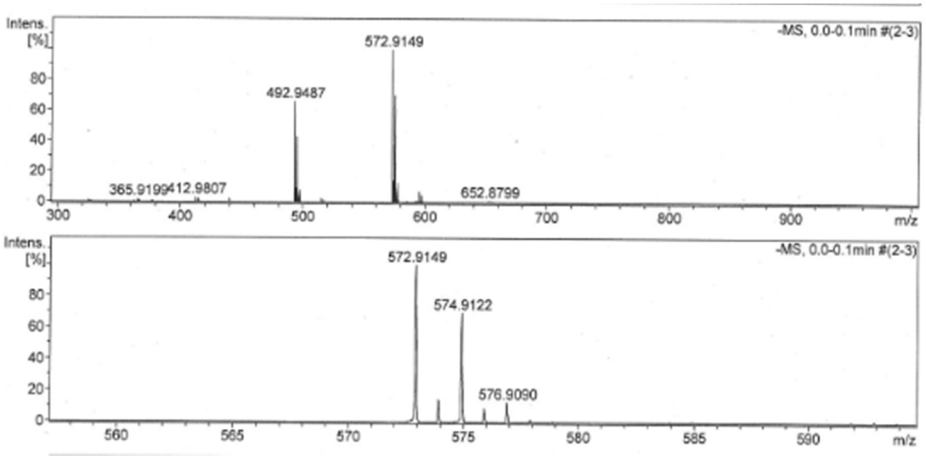
8

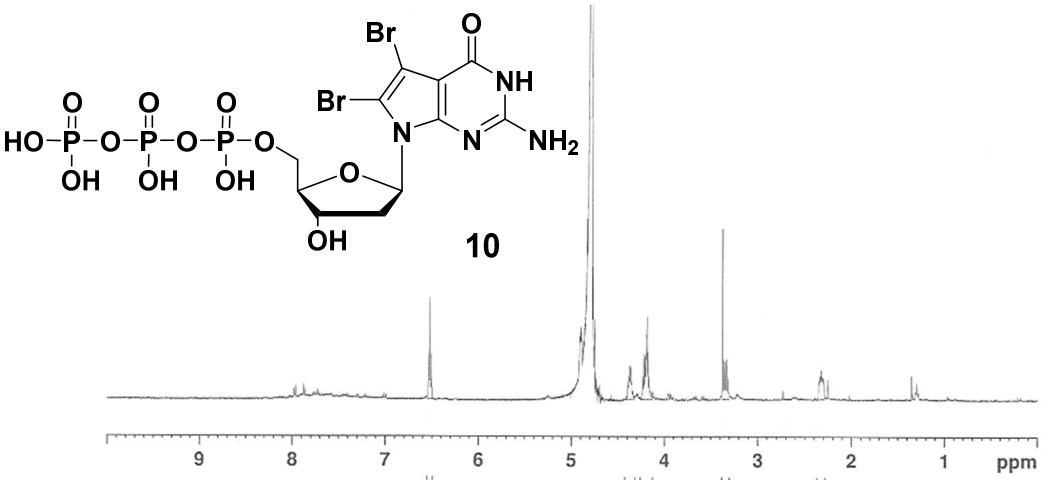

80
60
40
20
0
-20
-40
-60
-80
ppm

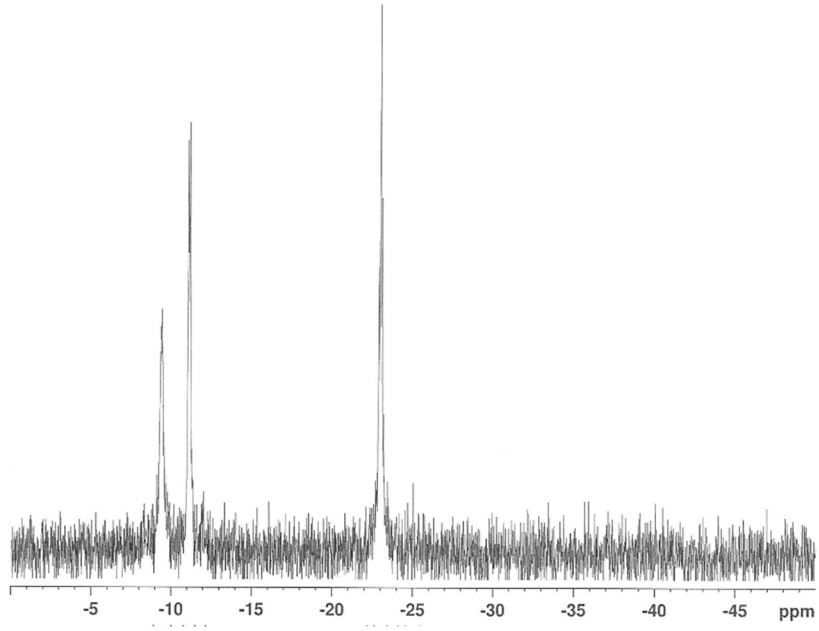

Intens.
-MS, 0.2-0.2min #(9-13)
4000
3000
2000
1000
0
470.9591
523.9961
951.0252
112.9899
228.2607
314.3786
589.8340
655.1941
724.0756
796.3579
872.0902
100
200
300
400
500
600
700
800
900
m/z
Intens.
-MS, 0.2-0.2min #(9-13)
4000
3000
2000
1000
0
470.9591
471.9620
472.9571
470.0
470.5
471.0
471.5
472.0
472.5
473.0
473.5
m/z

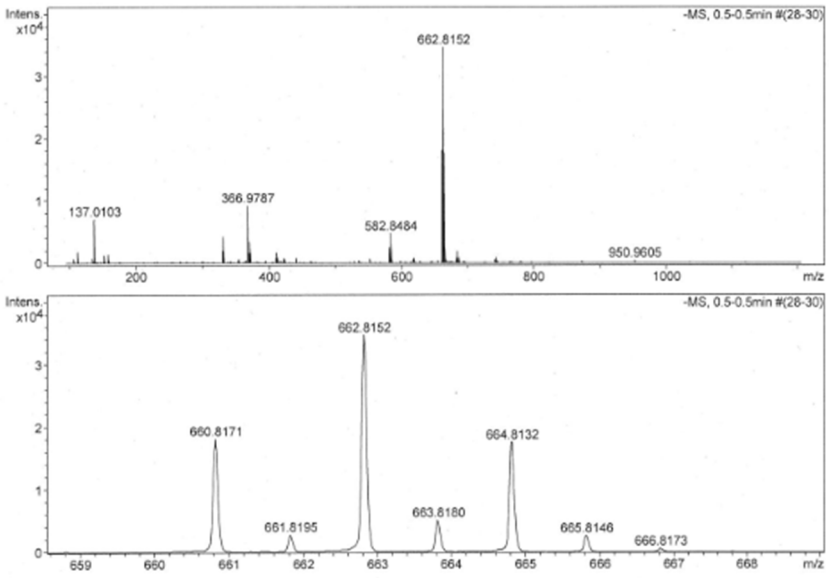

Cl
O
NH
Cl
N
N
NH2
HO–P–O–P–O–P–O
OH OH OH
O
OH
9
9 8 7 6 5 4 3 2 1 ppm

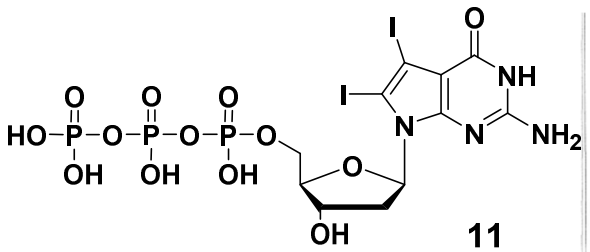

-2 -4 -6 -8 -10 -12 -14 -16 -18 -20 -22 -24 -26 ppm


Intens. [%]
-MS, 0.0-0.1min #(2-3)
572.9149
492.9487
365.9199
412.9807
652.8799
300 400 500 600 700 800 900 m/z
Intens. [%]
-MS, 0.0-0.1min #(2-3)
572.9149
574.9122
576.9090
560 565 570 575 580 585 590 m/z


Br
O
NH
Br
N
N
NH2
HO
P
O
OH
O
OH
O
OH
O
OH
10
9
8
7
6
5
4
3
2
1
ppm

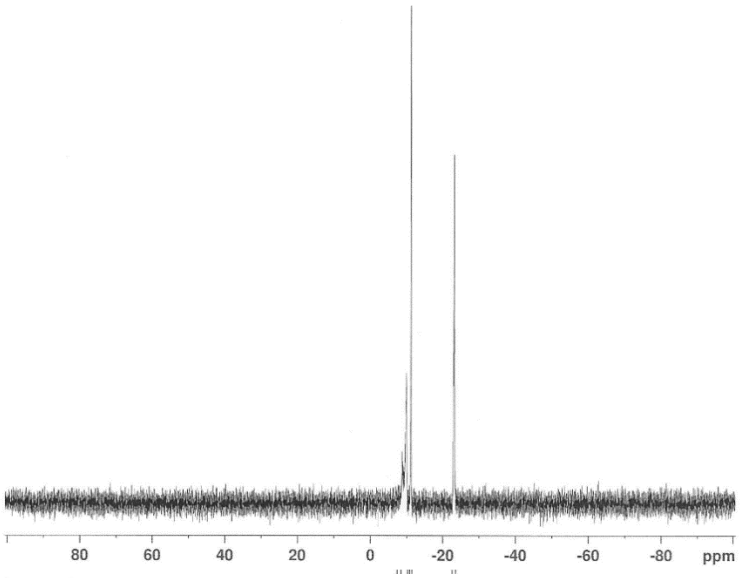

-5
-10
-15
-20
-25
-30
-35
-40
-45
ppm

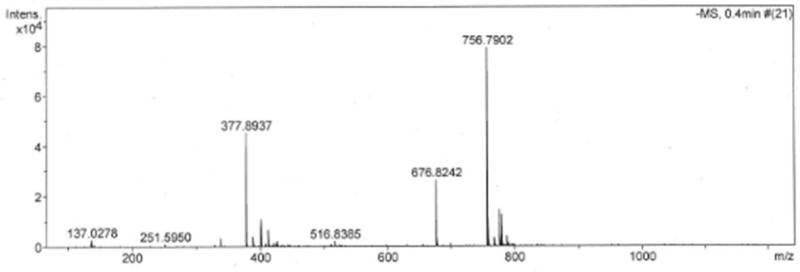

Intens.
x10^4
-MS, 0.5-0.5min #(28-30)
662.8152
366.9787
137.0103
582.8484
950.9605
200
400
600
800
1000
m/z
Intens.
x10^4
-MS, 0.5-0.5min #(28-30)
662.8152
660.8171
664.8132
661.8195
663.8180
665.8146
666.8173
659
660
661
662
663
664
665
666
667
668
m/z

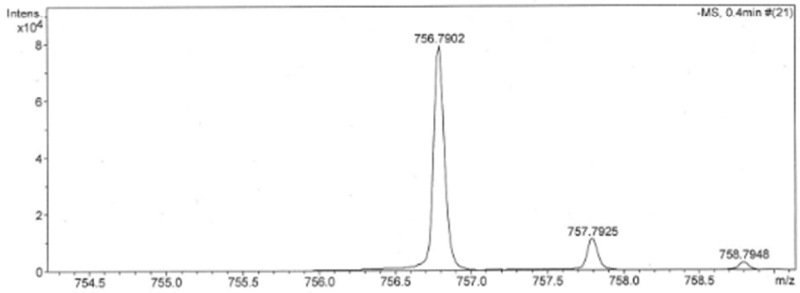

HO
P
O
OH
I
I
O
NH
N
N
NH2
OH

11

9
8
7
6
5
4
3
2
1
ppm


80
60
40
20
0
-20
-40
-60
-80
ppm


Intens.
x10^4
-MS, 0.4min #(21)
756.7902
377.8937
676.8242
137.0278
251.5950
516.8385
200
400
600
800
1000
m/z


Intens.
x10^4
-MS, 0.4min #(21)
756.7902
757.7925
758.7948
754.5
755.0
755.5
756.0
756.5
757.0
757.5
758.0
758.5
m/z

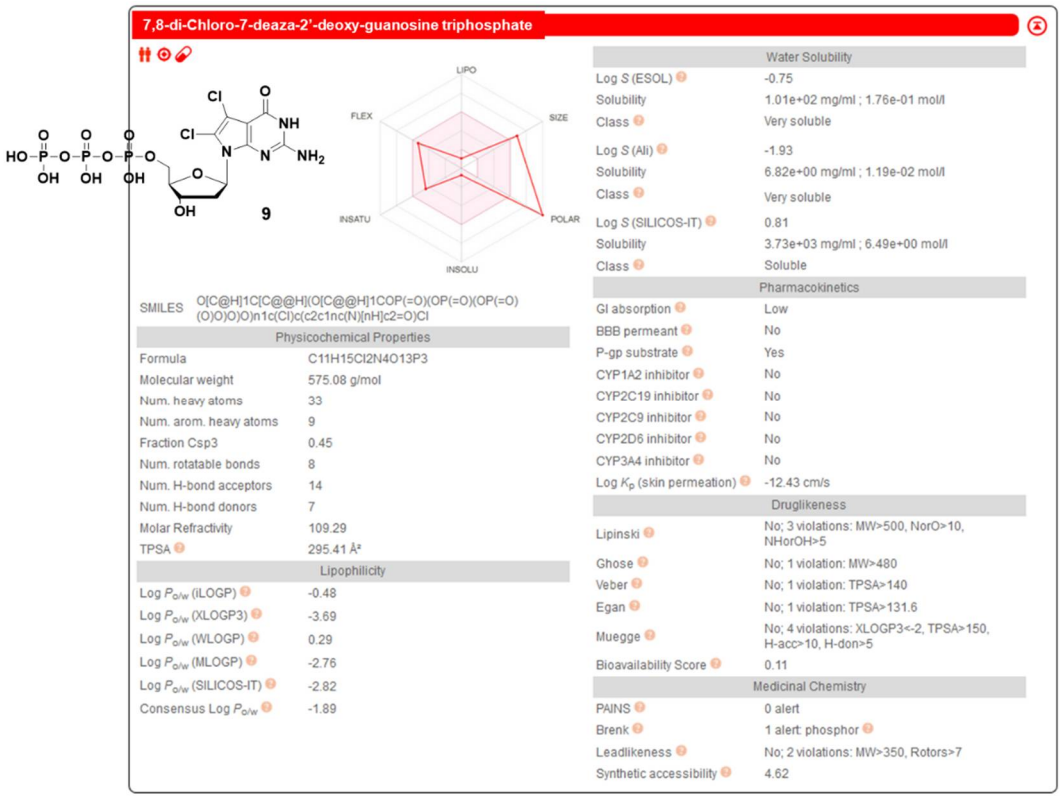


Figure S1. Predicted ADME parameter of compound **9**.

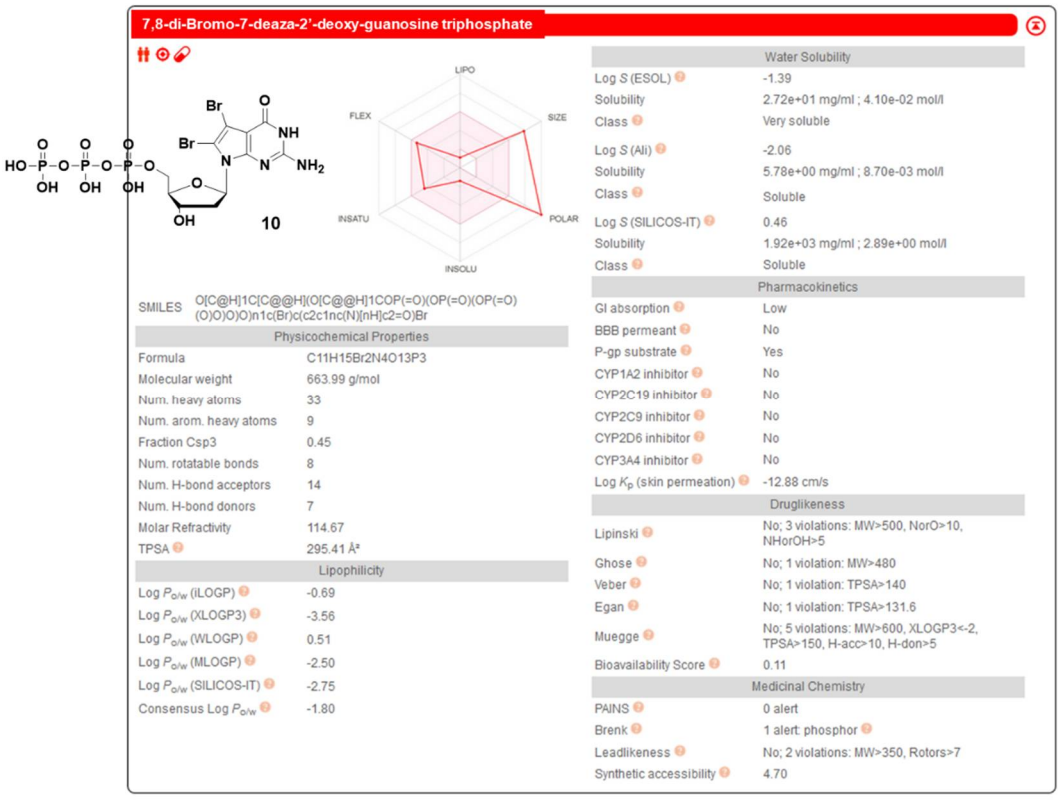


Figure S2. Predicted ADME parameter of compound **10**.

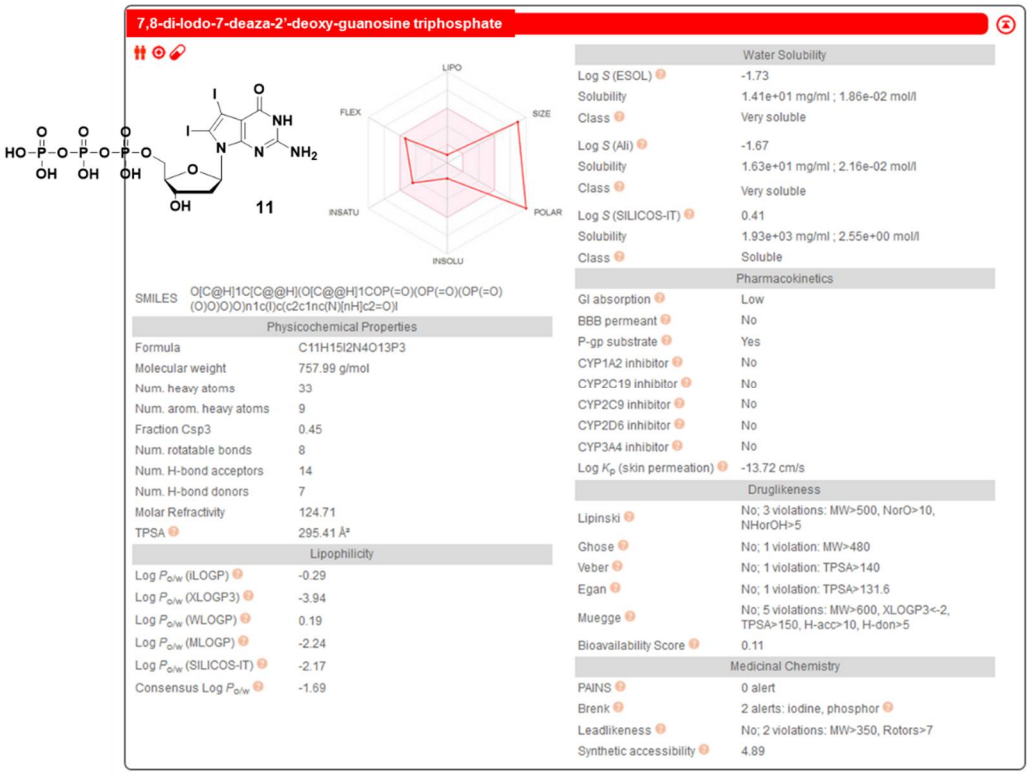


Figure S3. Predicted ADME parameter of compound **11**.

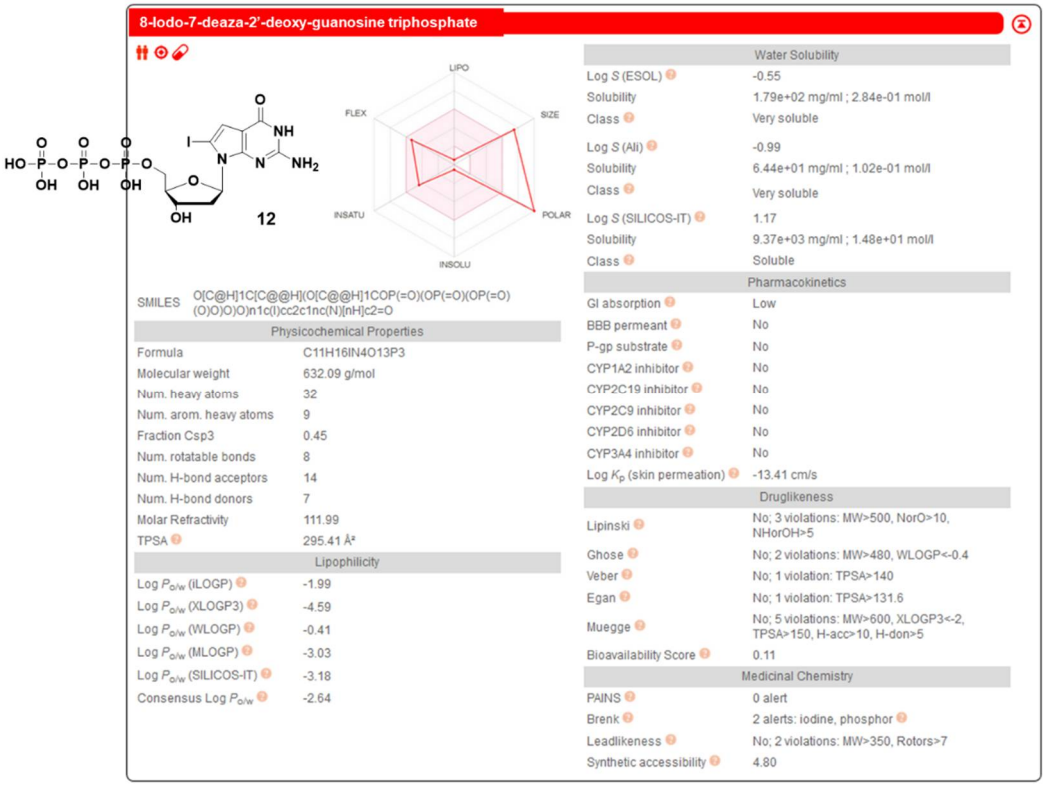


Figure S4. Predicted ADME parameter of compound **12**.