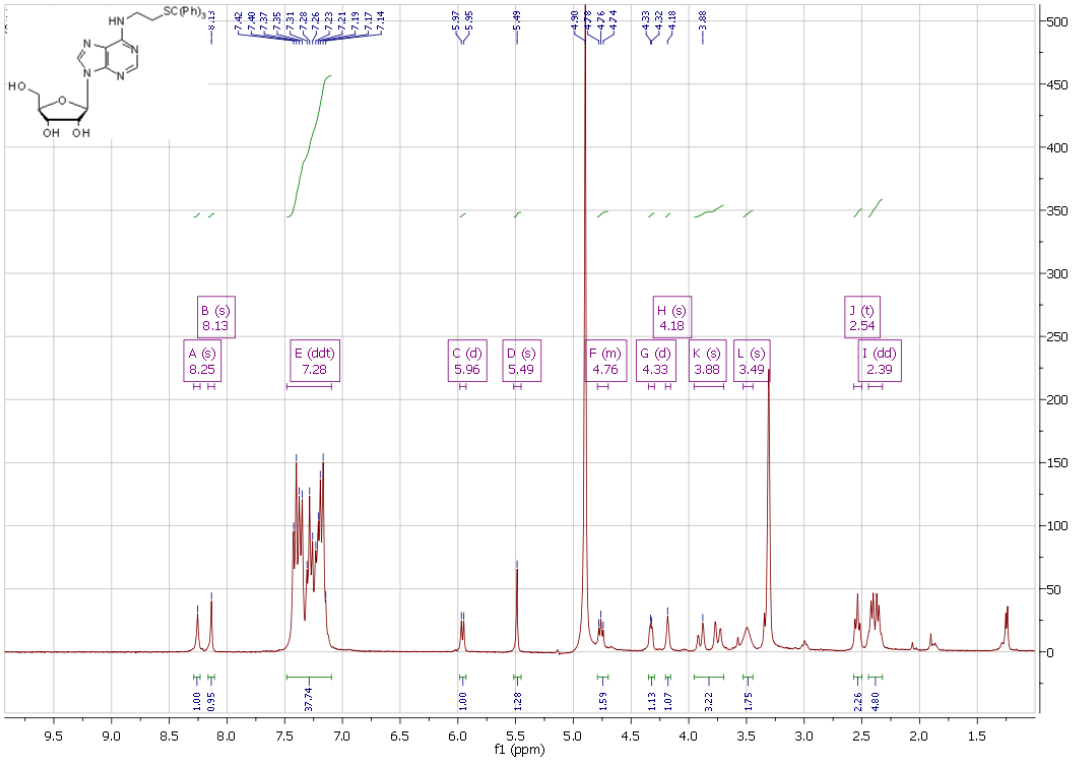
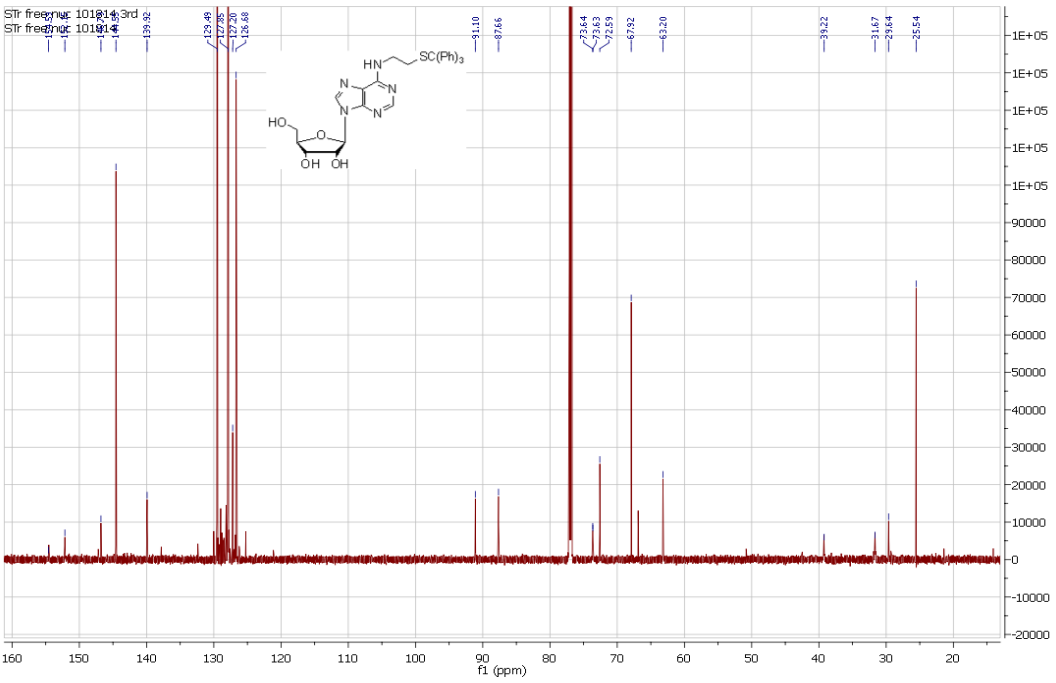
Supporting Information

Table of Contents

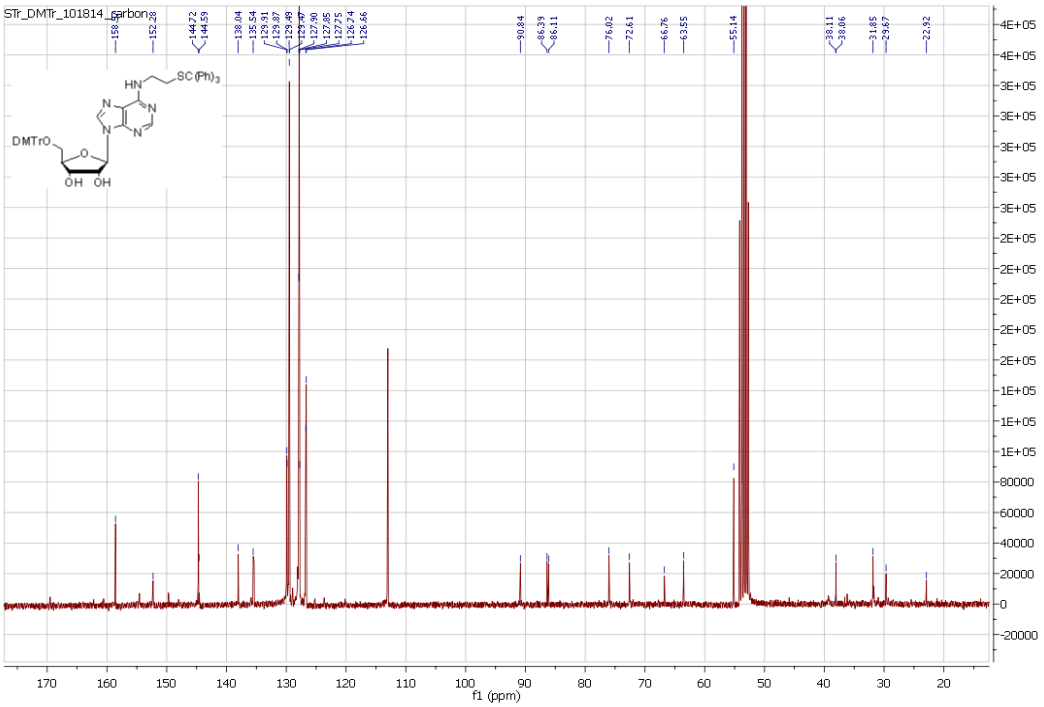
1. ^{1}H &^{13}C-NMR Spectra of Compounds 1–4



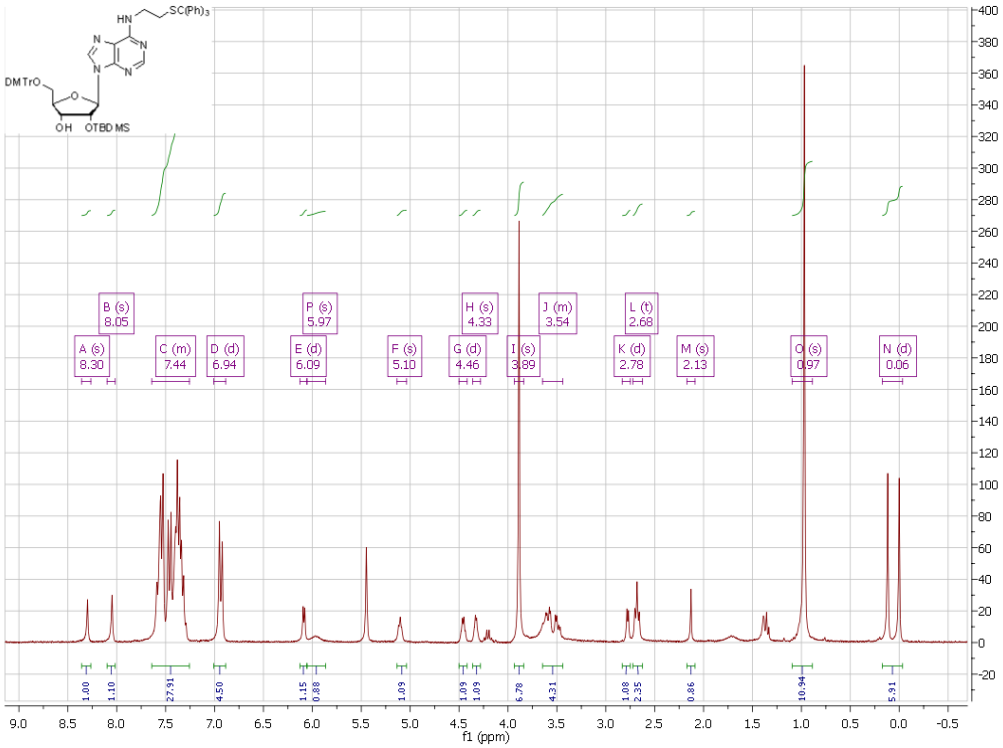


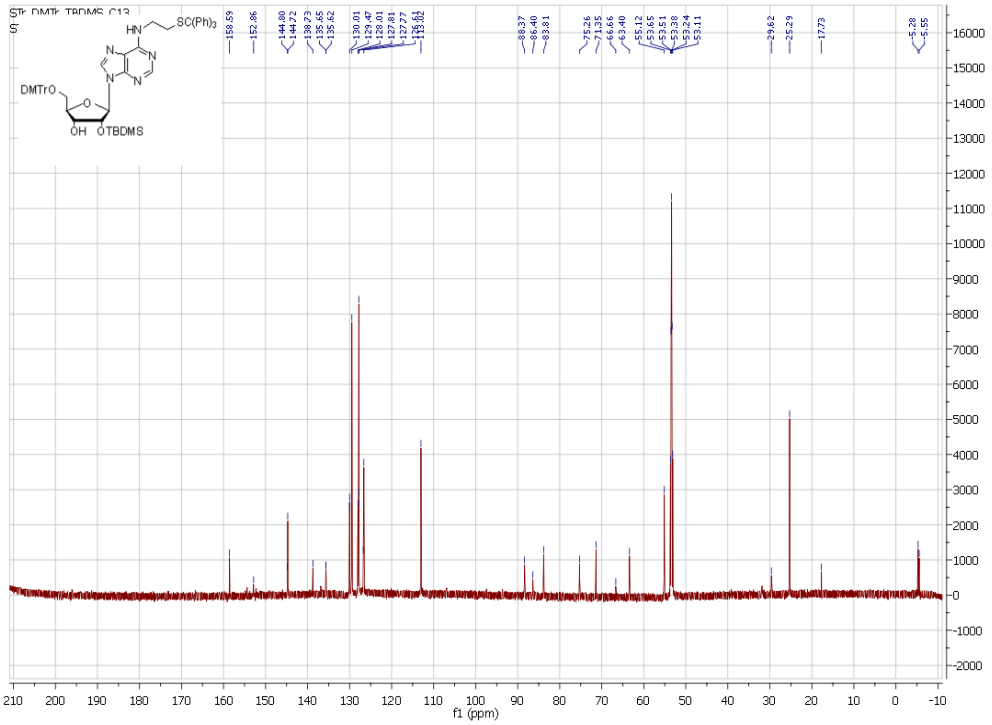
Compound 1


B (s) 8.03
E (m) 7.26
G (d) 5.99
M (t) 2.31
A (s) 8.22
D (d) 7.44
C (m) 6.79
F (s) 6.26
H (t) 4.73
I (d) 4.40
J (s) 3.75
K (m) 3.36
L (m) 2.57
f1 (ppm)

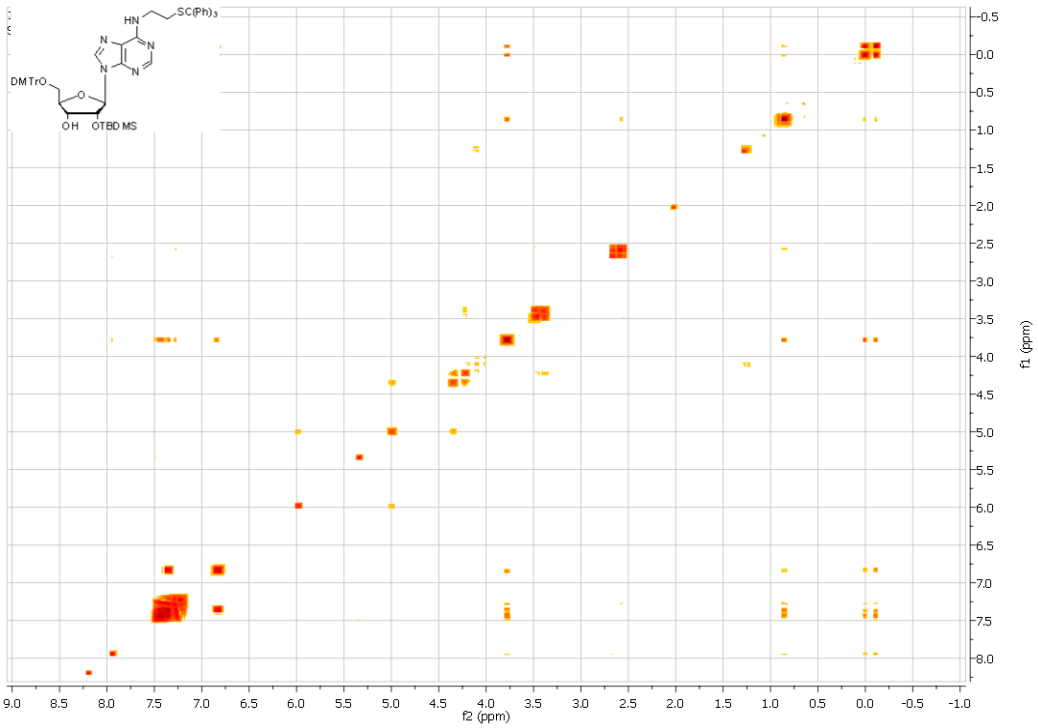

STr_DMTr_101814_Carbon
f1 (ppm)

Compound 2


HN
SC(Ph)3
DMTrO
OH
OTBDMS
B (s) 8.05
A (s) 8.30
C (m) 7.44
D (d) 6.94
P (s) 5.97
E (d) 6.09
F (s) 5.10
H (s) 4.33
G (d) 4.46
I (s) 3.89
J (m) 3.54
L (t) 2.68
K (d) 2.78
M (s) 2.13
O (s) 0.97
N (d) 0.06
f1 (ppm)

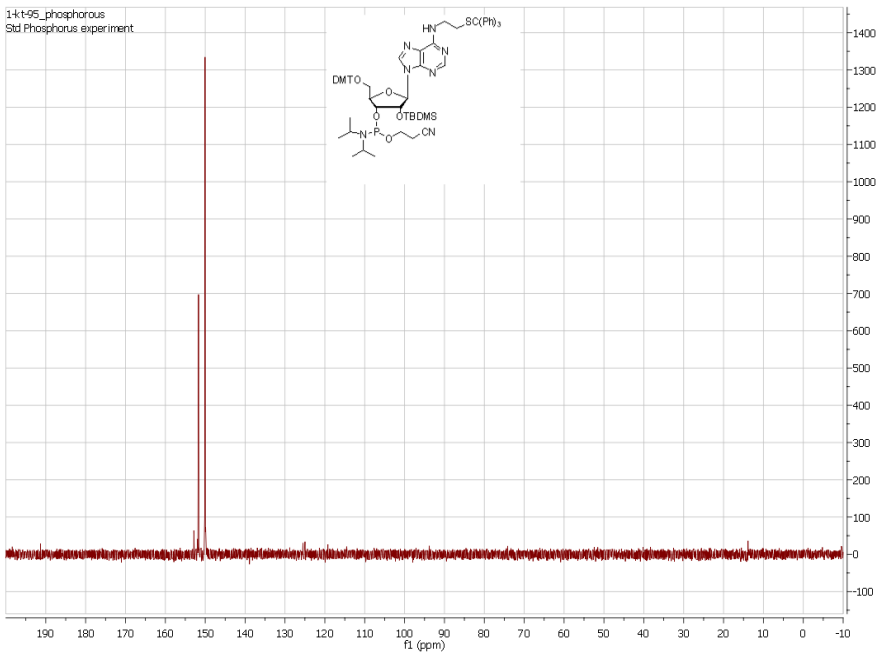

HN
SC(Ph)3
DMTrO
OH
OTBDMS
f1 (ppm)

Compound 3



Compound 3

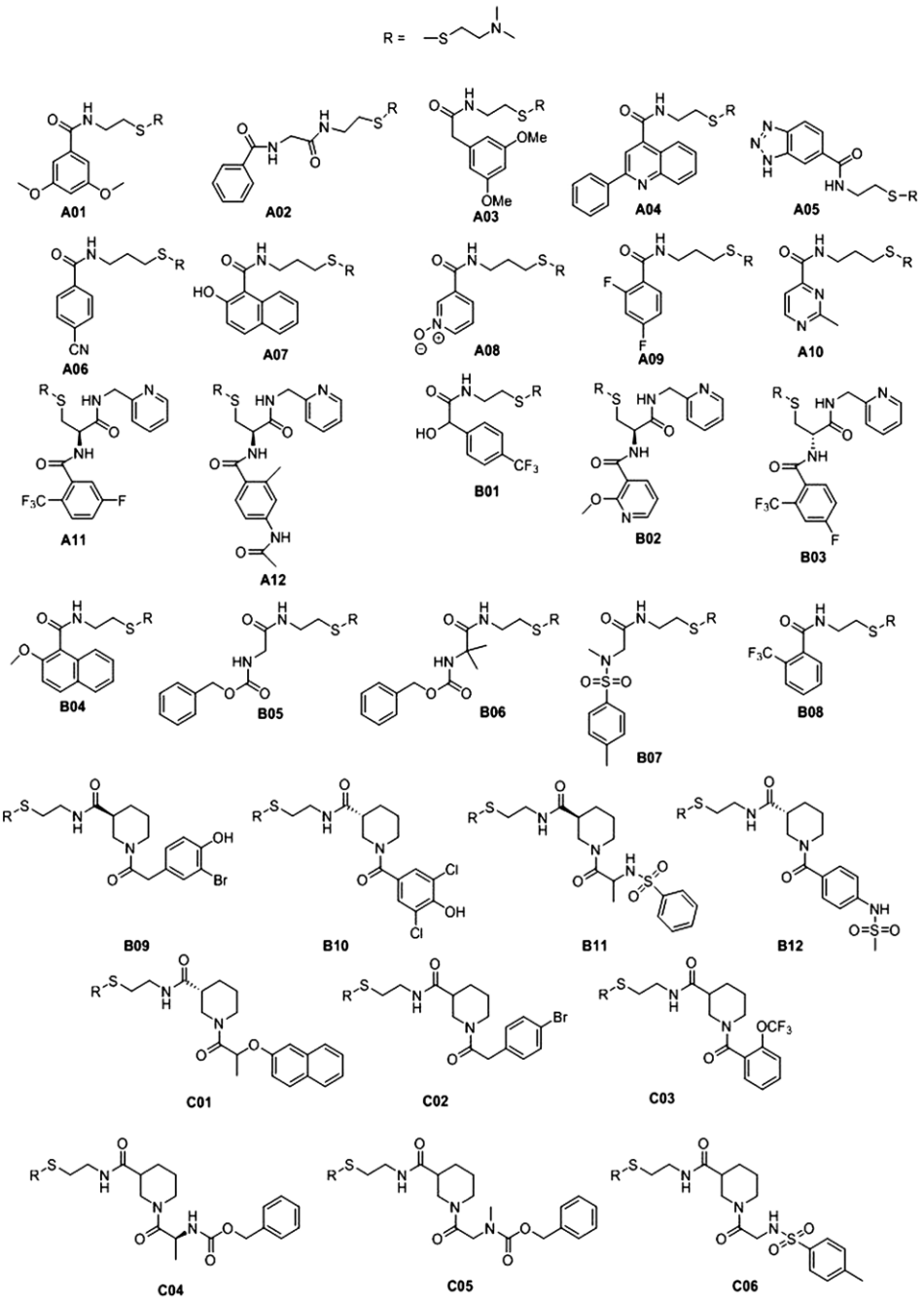
2. ^{31}P-NMR of Compound 4



Compound 4

3. Small Molecule Library Structures

Structures for all 30 disulfide-containing small molecules used in this study.



4. Supplementary Table S1. Pre21 RNA1 Conjugation Data

Table S1. Small molecule disulfide screening data for pre21 RNA1.

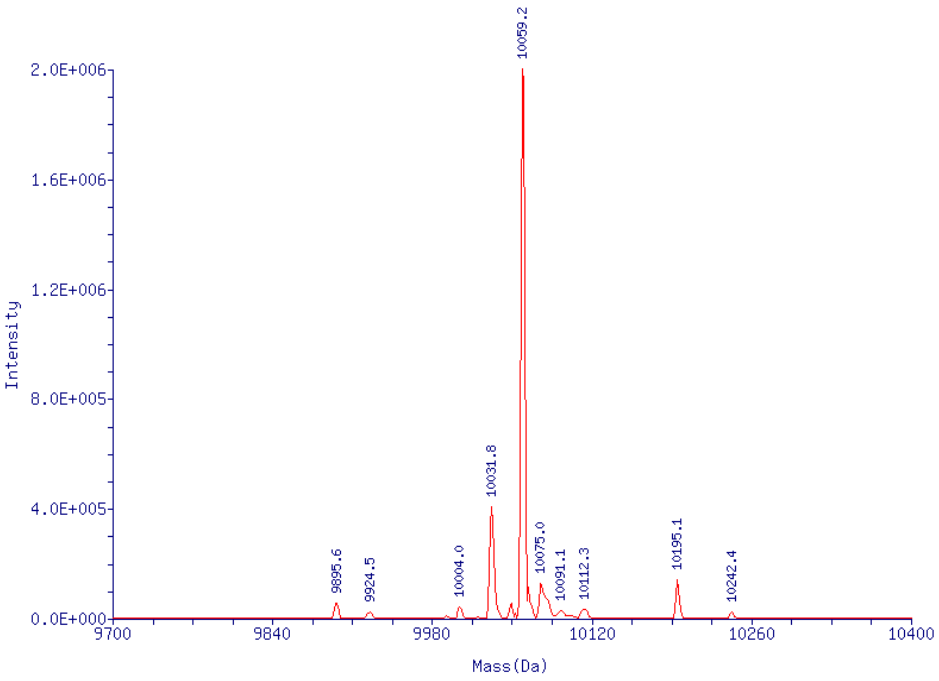
	% Relative Abundances		
Compound	**Thiol**	**N,N-DMA**	**Target**
A01	0	68.03	4.71
A02	29.34	46.34	3.17
A03	13.16	39.72	8.26
A04	10.23	38.87	36.41
A05	6.2	57.13	31.04
A06	3.23	49.22	5.04
A07	15.62	19.99	9.82
A08	8.82	51.06	0
A09	69.8	1.81	0
A10	78.07	1.94	1.52
A11	80.32	2.63	3.62
A12	59.8	17.41	0
B01	31.4	42.7	0:00
B02	71.79	10.63	4.76
B03	66.56	11.43	4.51
B04	83.94	3.31	1.53
B05	83.1	1.4	0
B06	82.2	0	0
B07	82.17	1.31	0
B08	84.8	1.92	0
B09	86.18	0	0
B10	88.3	1.33	0
B11	83.86	0	1.73
B12	87.32	1.31	0
C01	4.23	62.6	0
C02	62.96	3.00	2.58
C03	64.31	2.03	2.27
C04	66.39	2.65	2.44
C05	59.73	3.35	3.6
C06	60.27	1.36	2.45

5. Supplementary Table S2. Pre21 RNA2 Conjugation Data

Table S2. Small molecule disulfide screening data for pre21 RNA2.

	% Relative Abundances		
Compound	**Thiol**	**N,N-DMA**	**Target**
A01	6.72	68.03	1.94
A02	2.51	76.25	2.25
A03	8.57	69.06	0
A04	0	44.96	32.05
A05	0	74.56	13.63
A06	3.23	49.22	5.04
A07	15.24	74.14	0
A08	0	73.5	0
A09	35.1	5.32	0
A10	81.9	2.25	0
A11	72.58	5.04	2.3
A12	20.46	44.1	0
B01	7.65	63.77	0:00
B02	55.58	23.04	1.87
B03	29.9	28.09	0
B04	72.9	8.17	0
B05	76.5	4.02	0
B06	77.1	1.68	0
B07	76.8	1.48	0
B08	78	6.34	0
B09	80.2	2.02	0
B10	69.3	1.92	0
B11	71.87	2.7	1.75
B12	51.9	2.96	0
C01	30.66	39.92	3.24
C02	54.16	2.99	1.25
C03	40.11	3.11	0
C04	39.21	3.5	1.65
C05	31.88	6.33	1.59
C06	55.1	2.63	1.67

6. Pre21 RNA1 Conjugation Data Mass Spectra



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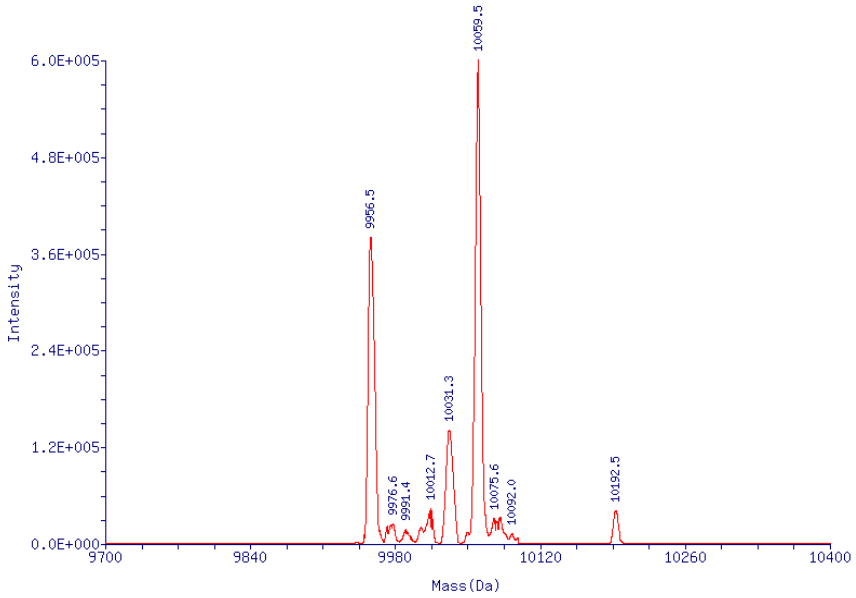

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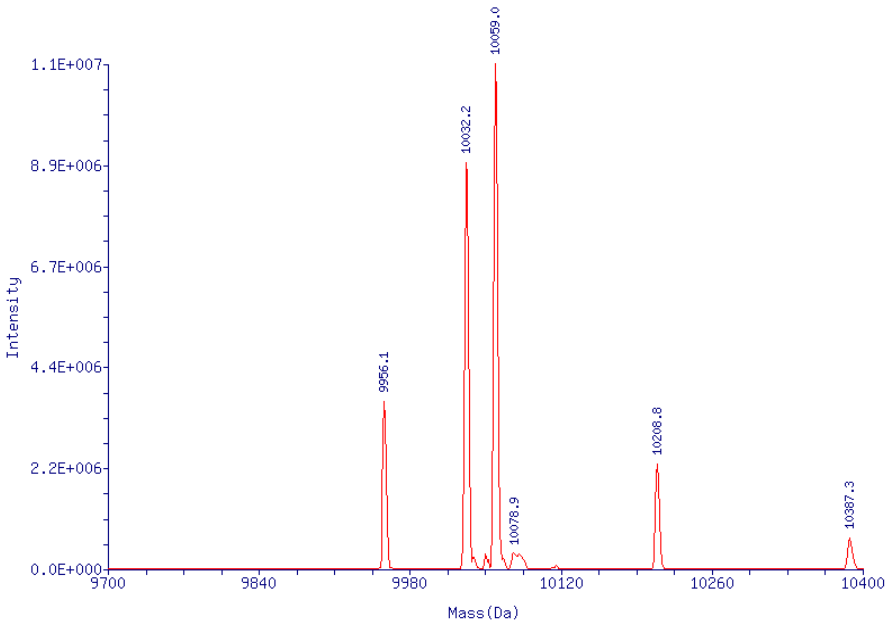

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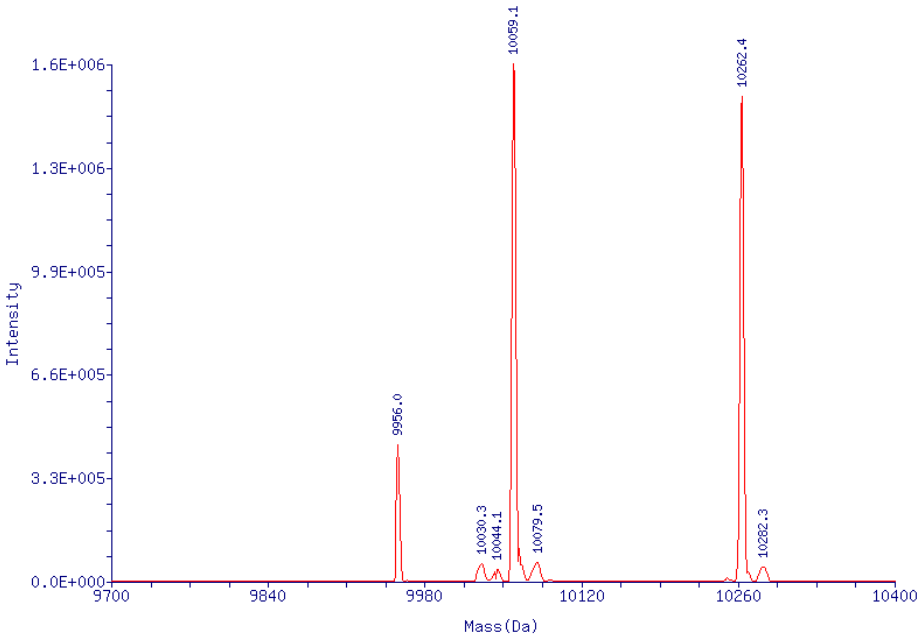

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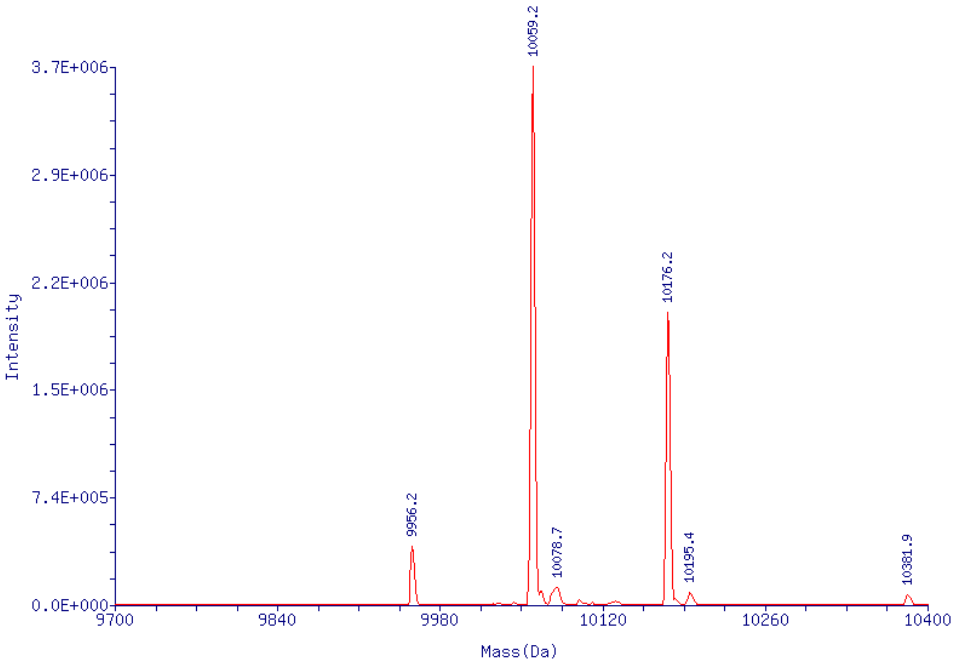

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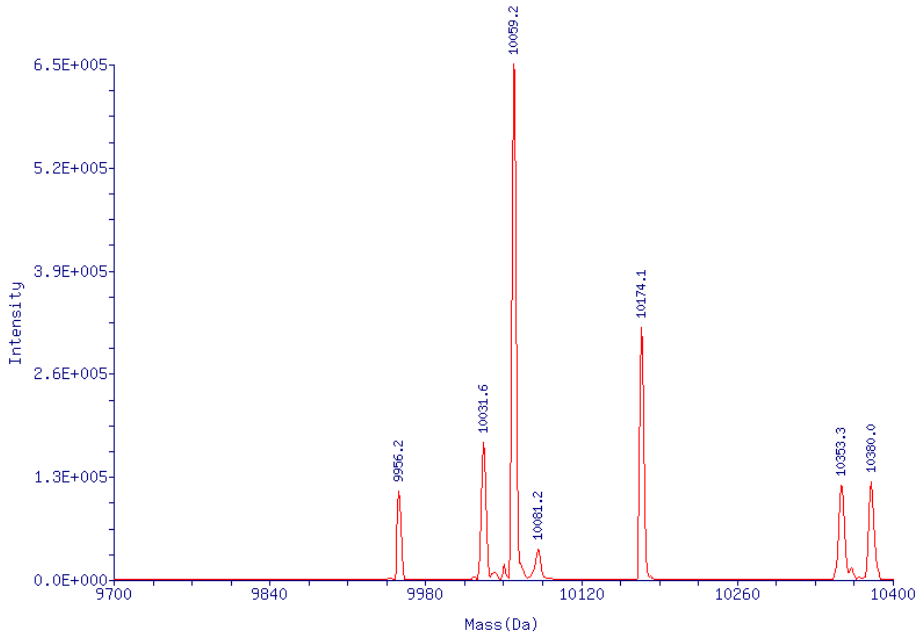
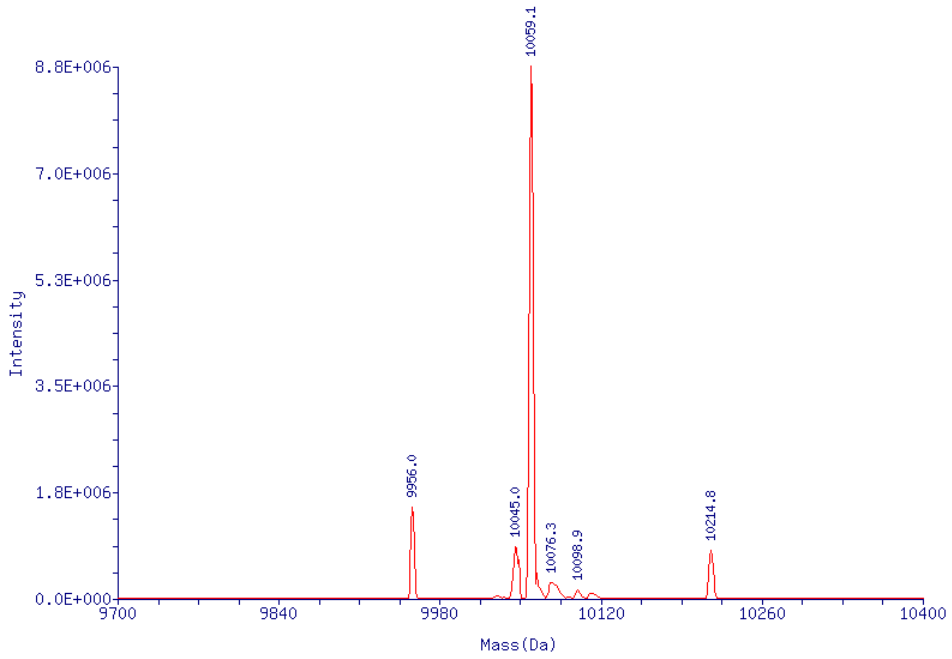


Compound A06.



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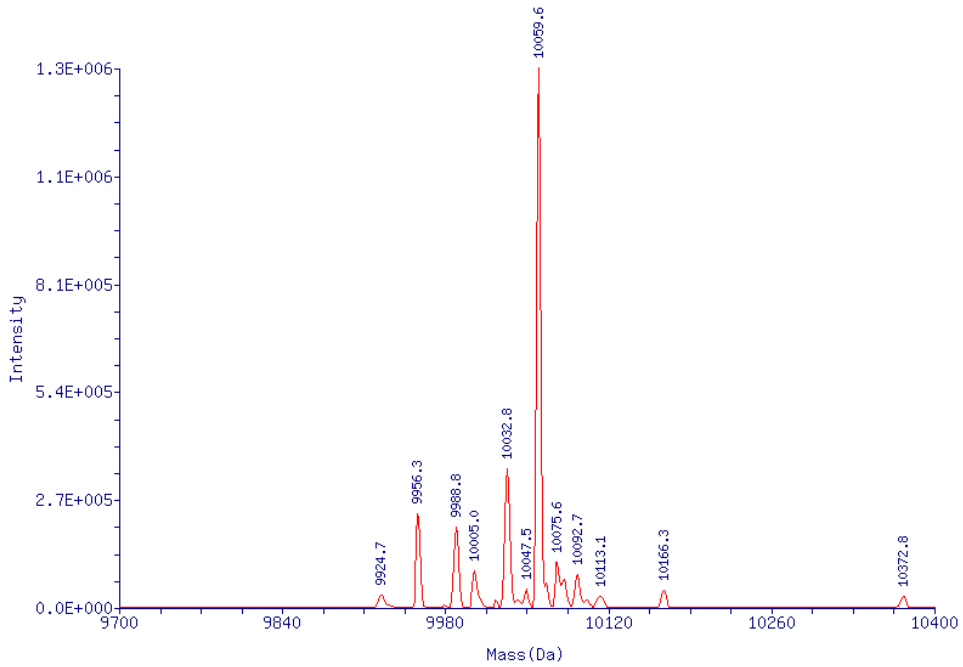

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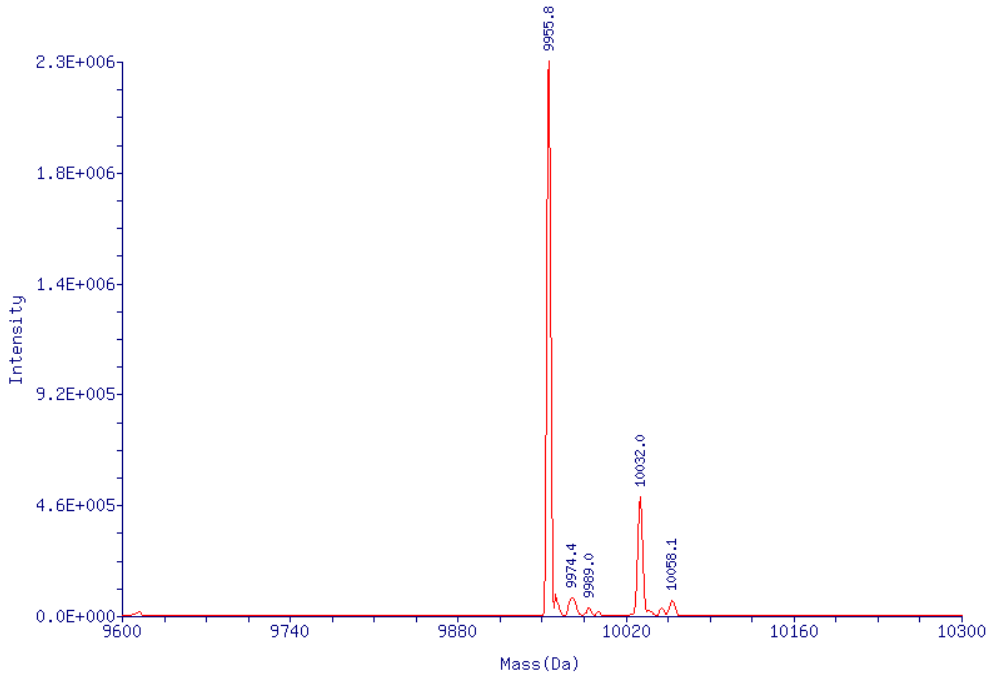

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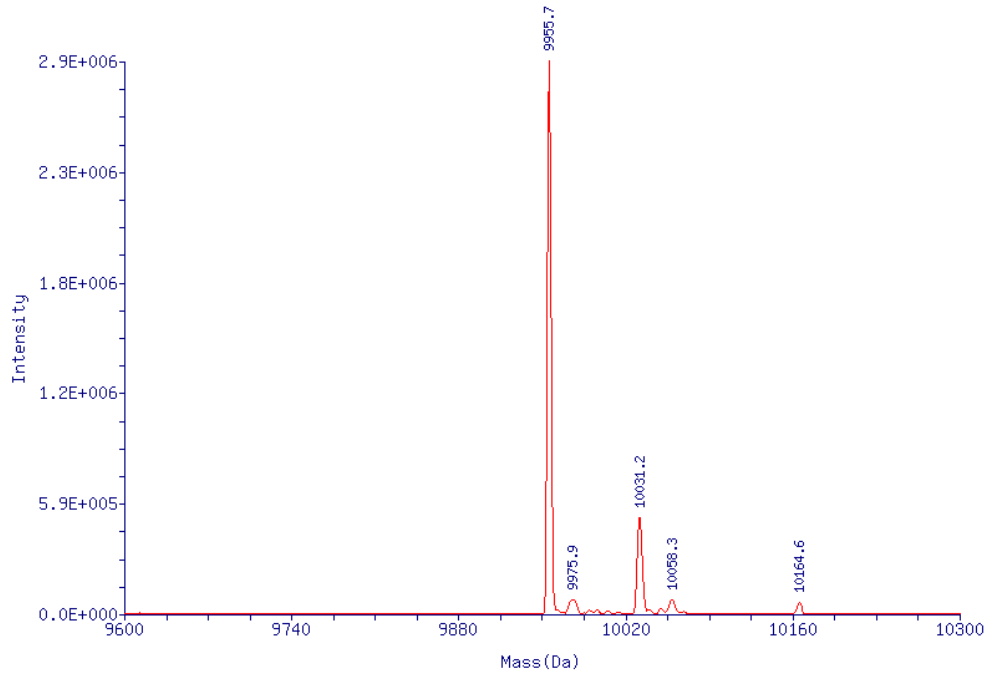

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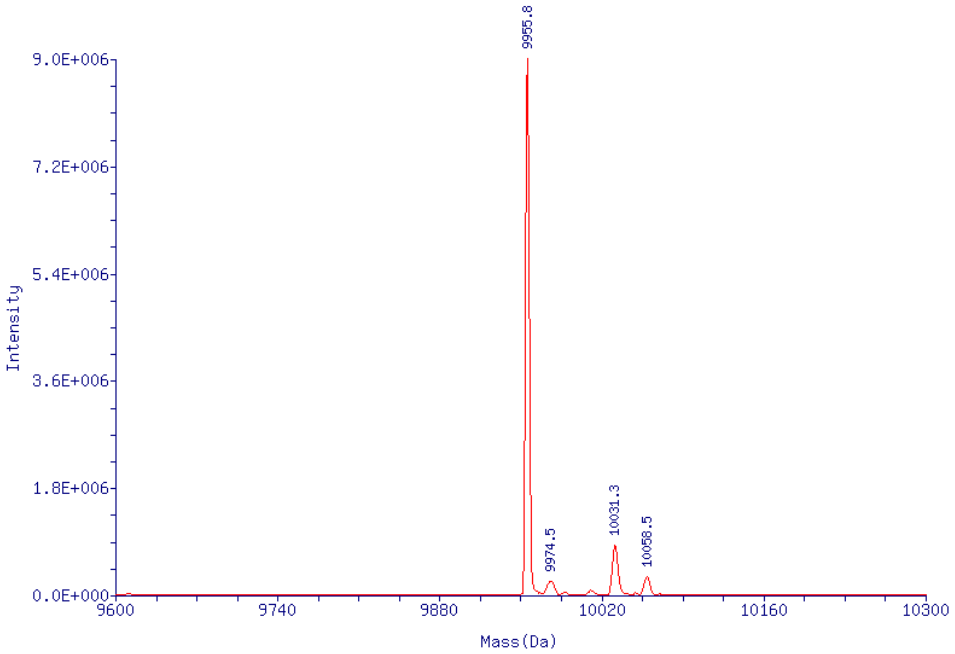

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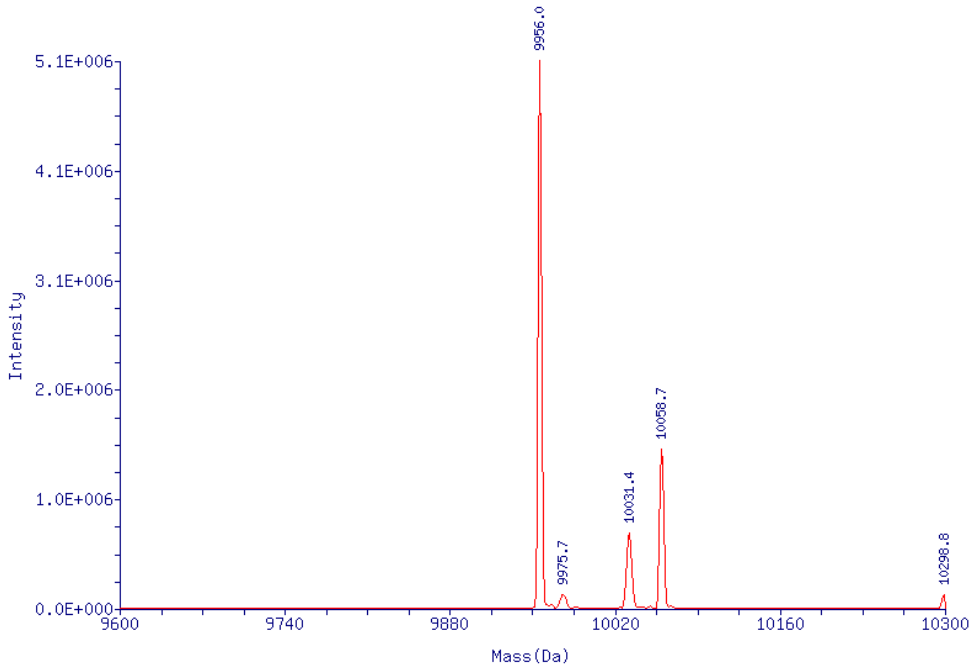

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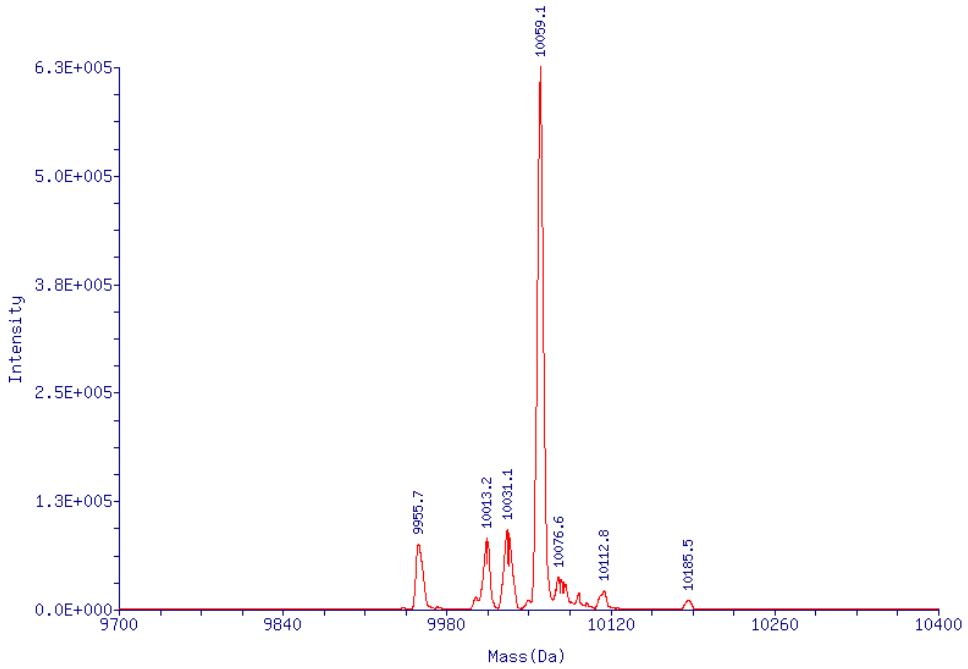

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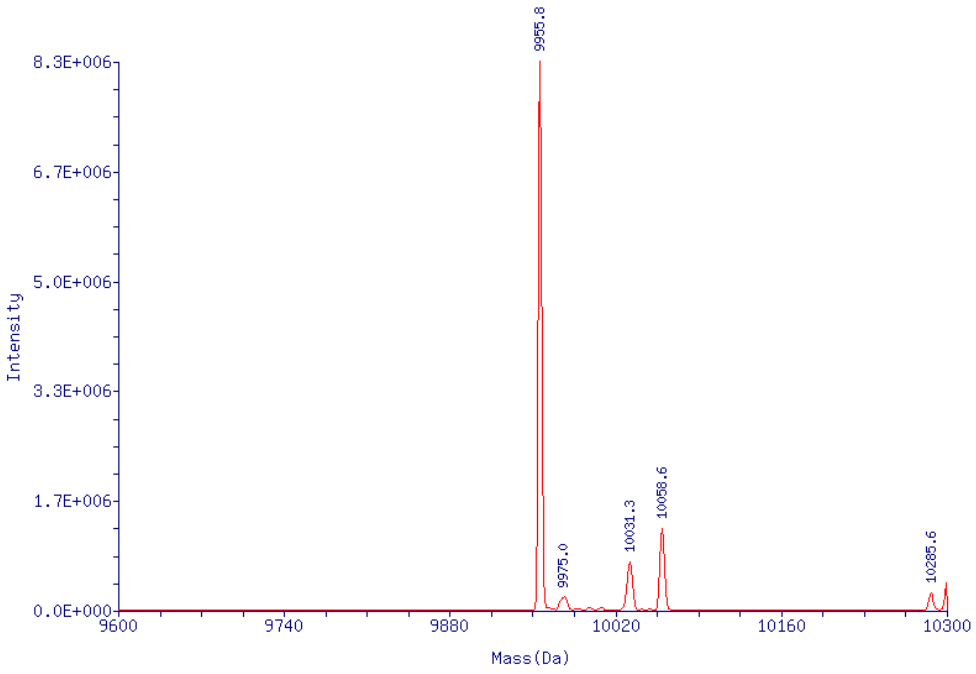

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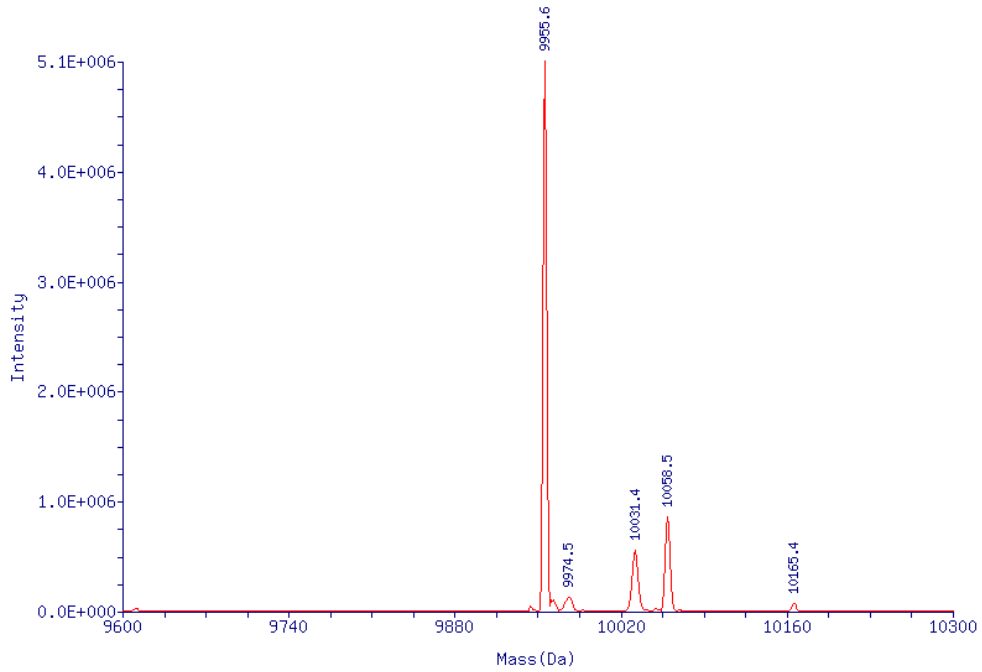

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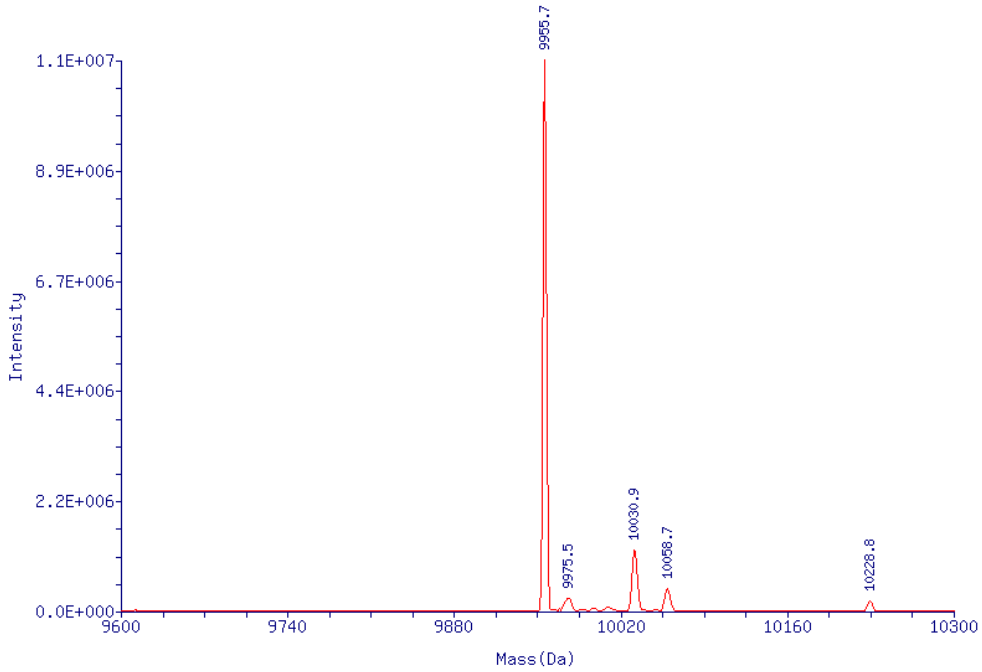

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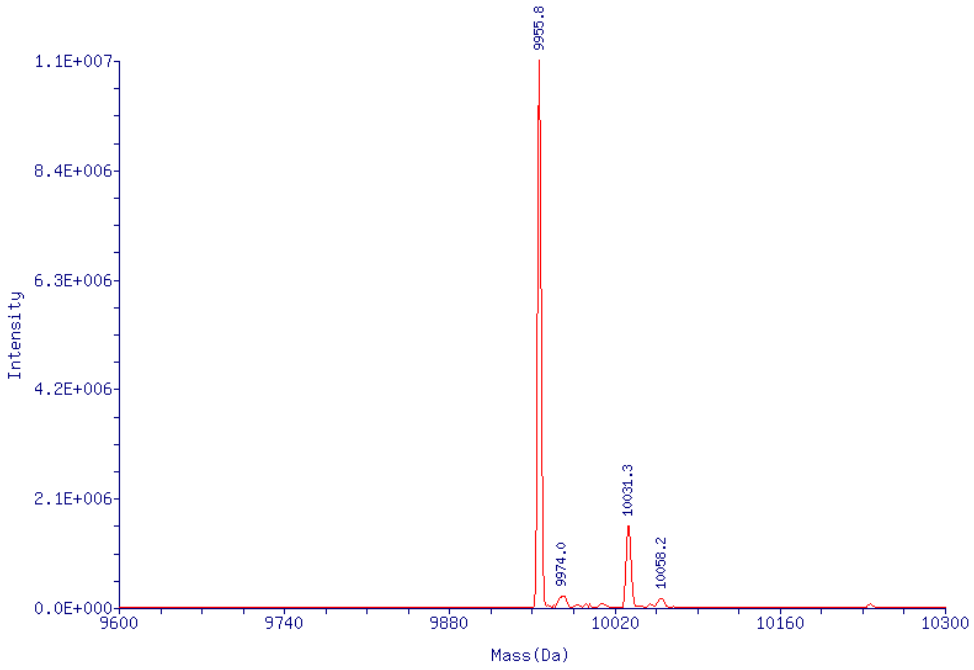

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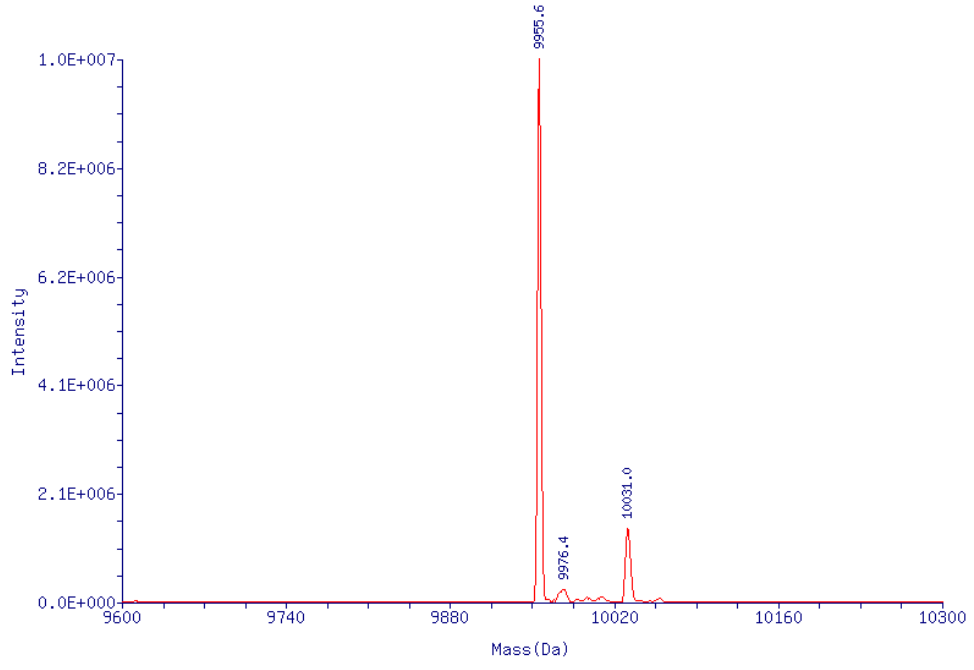

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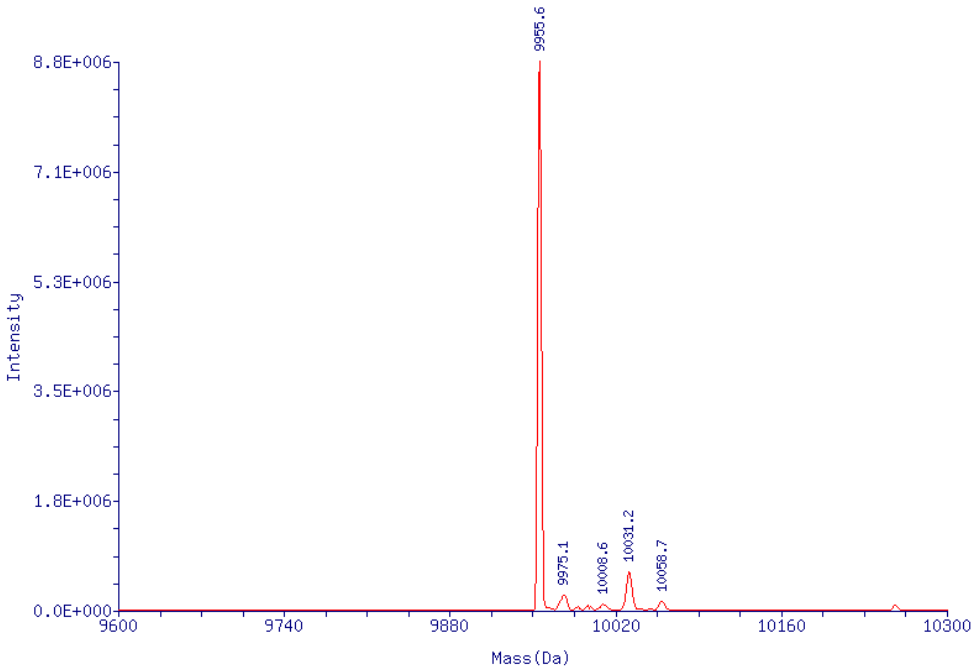

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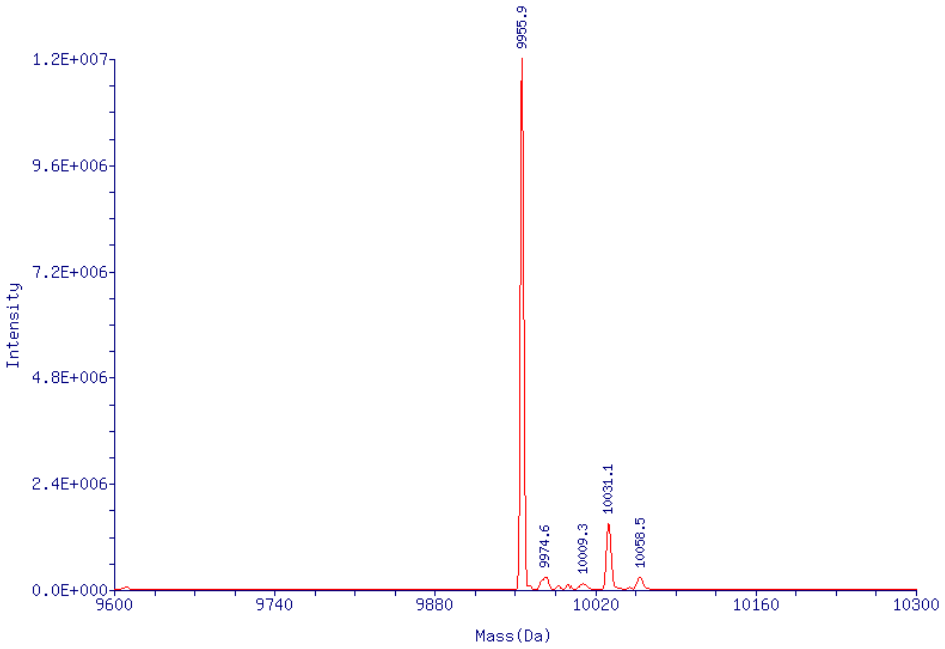

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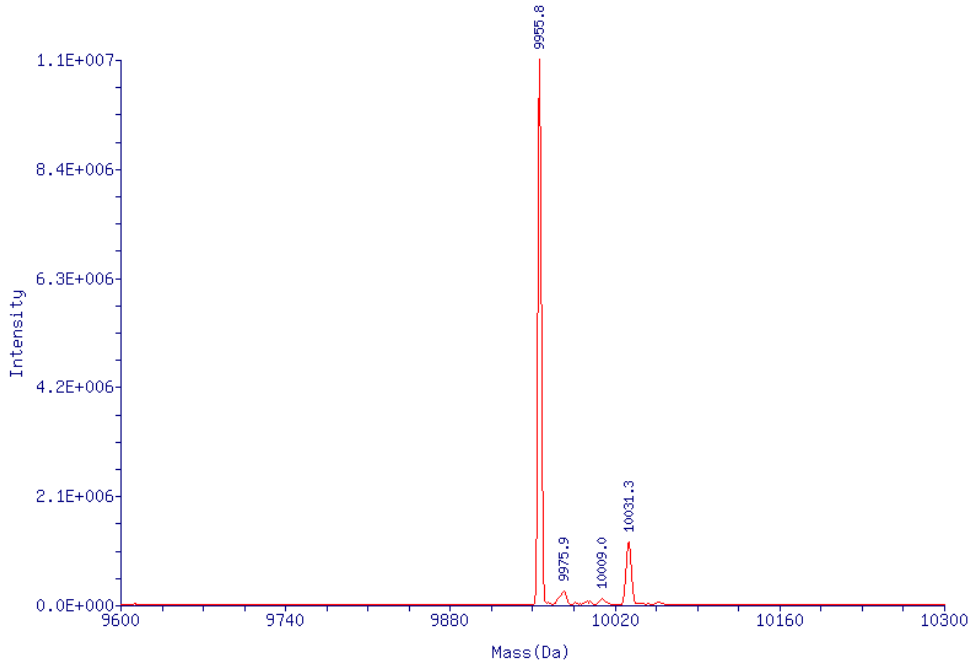

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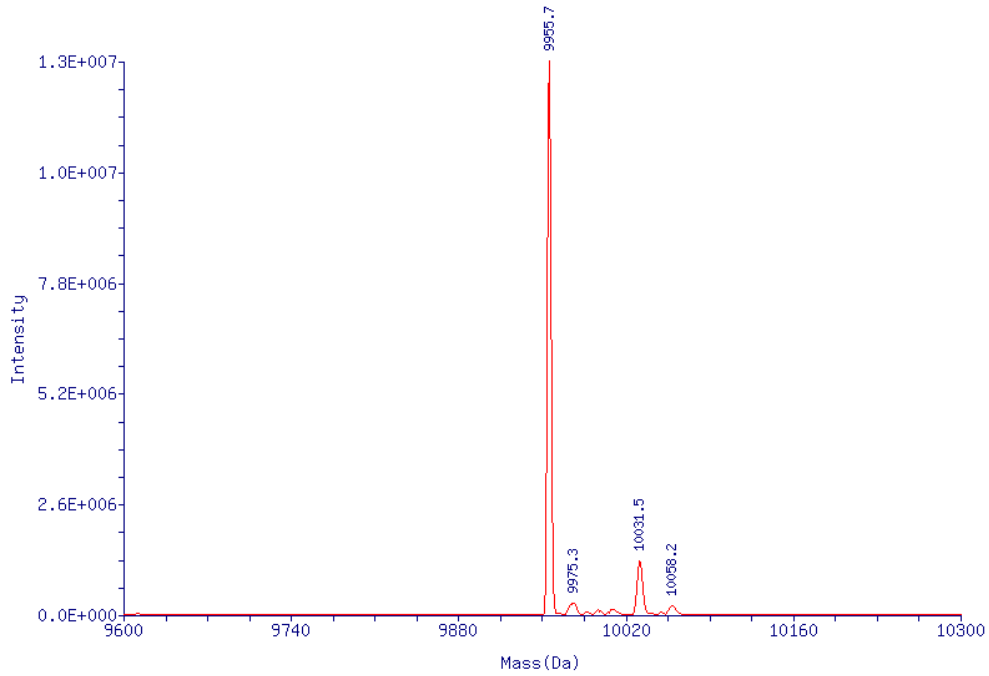

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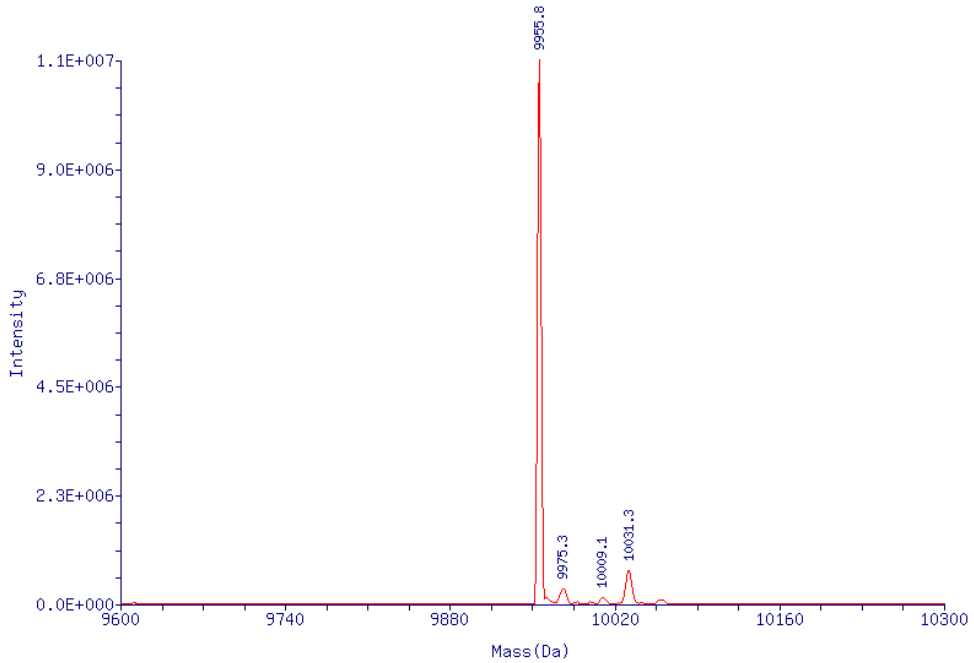

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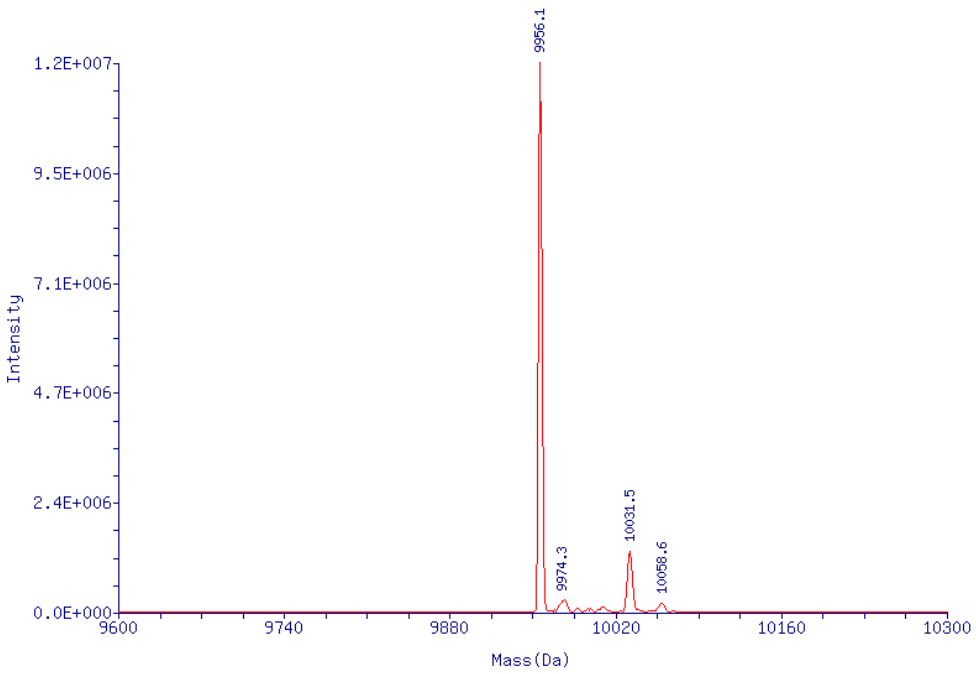

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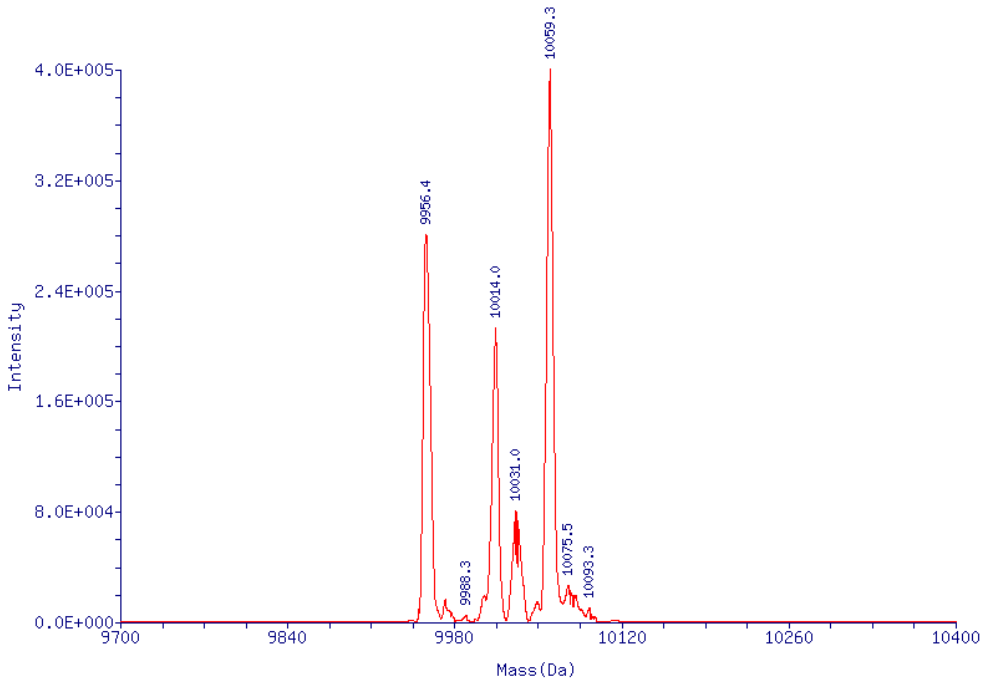

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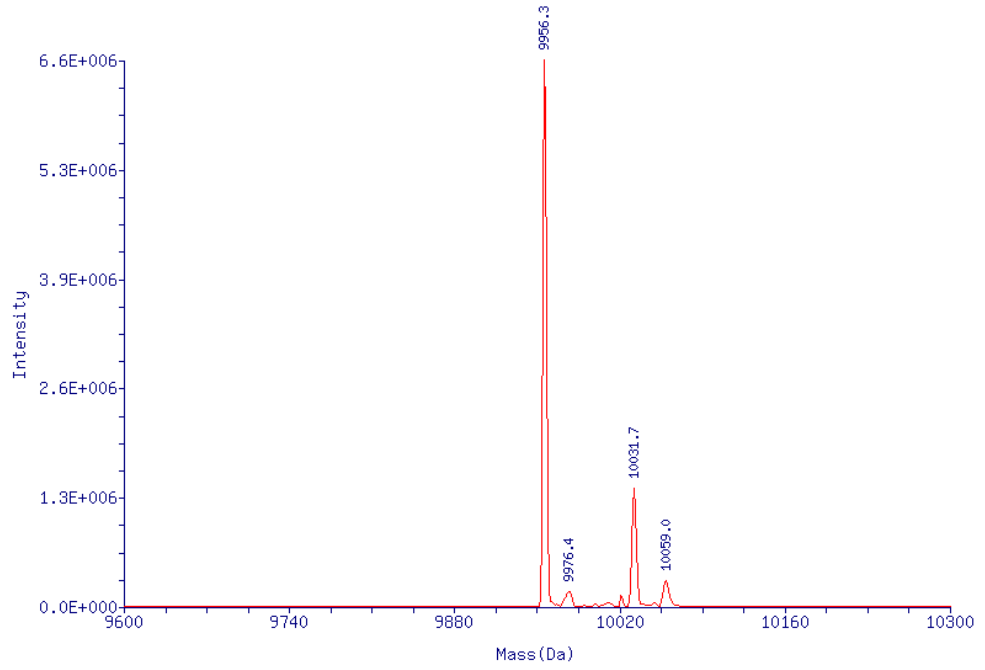

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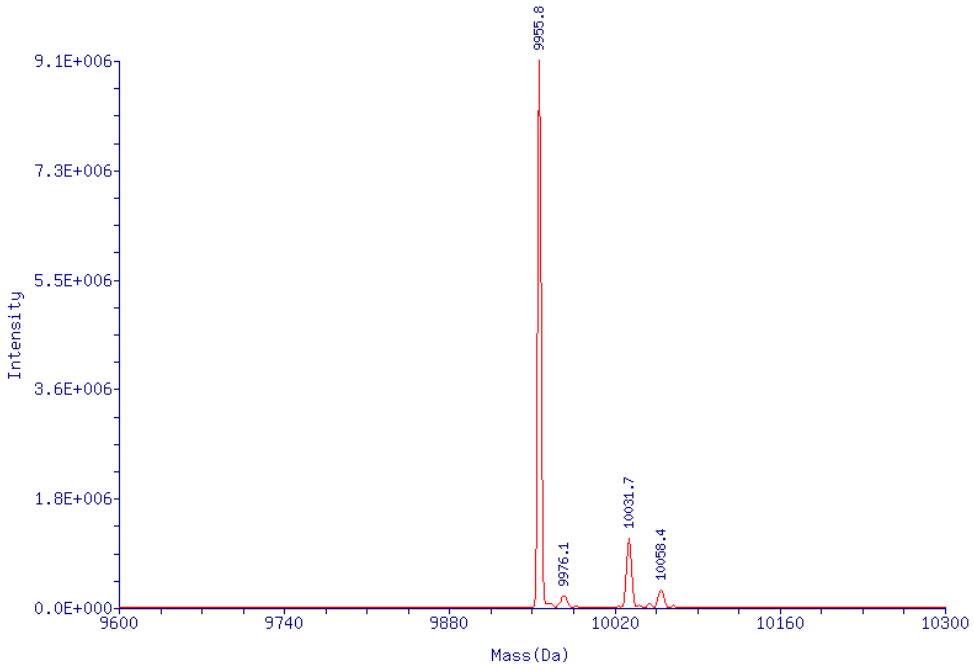

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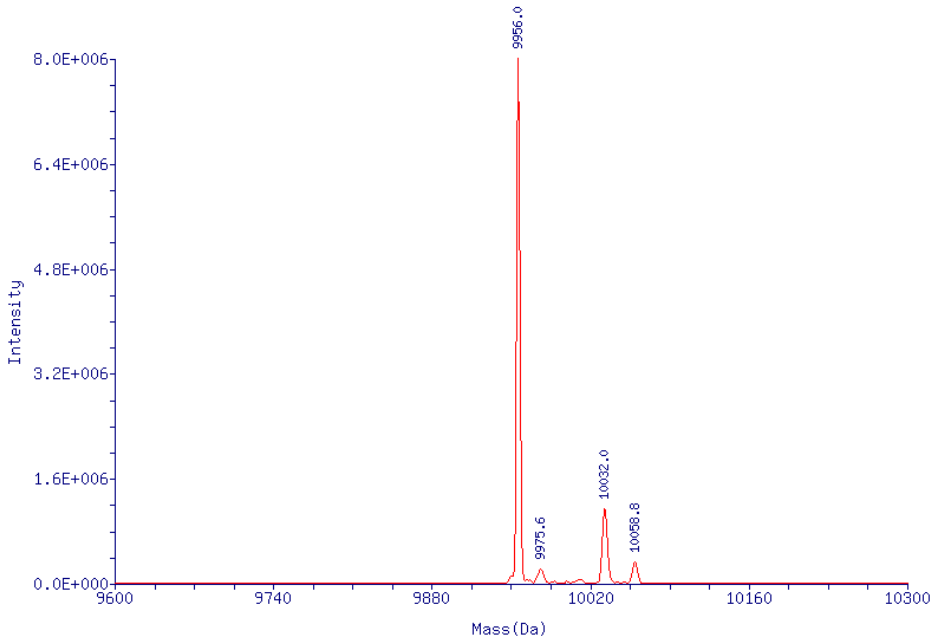

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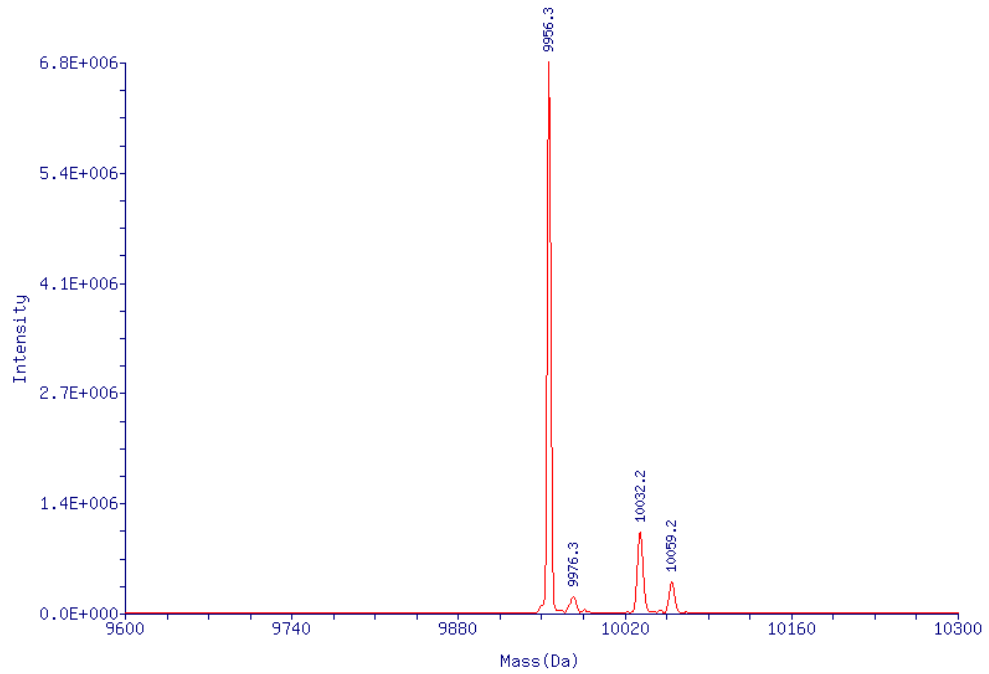

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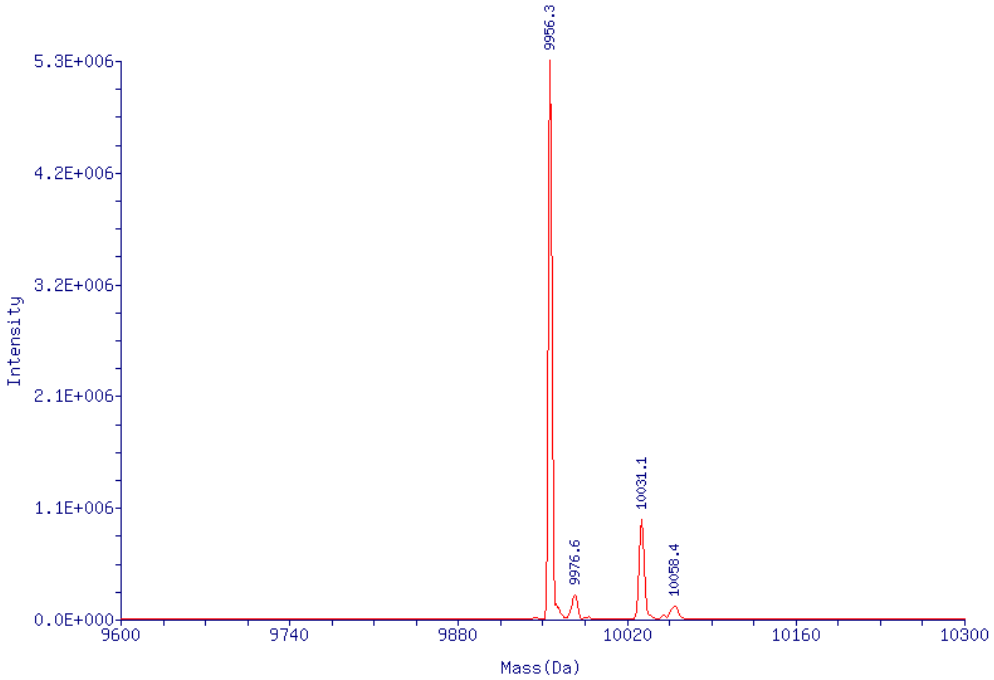
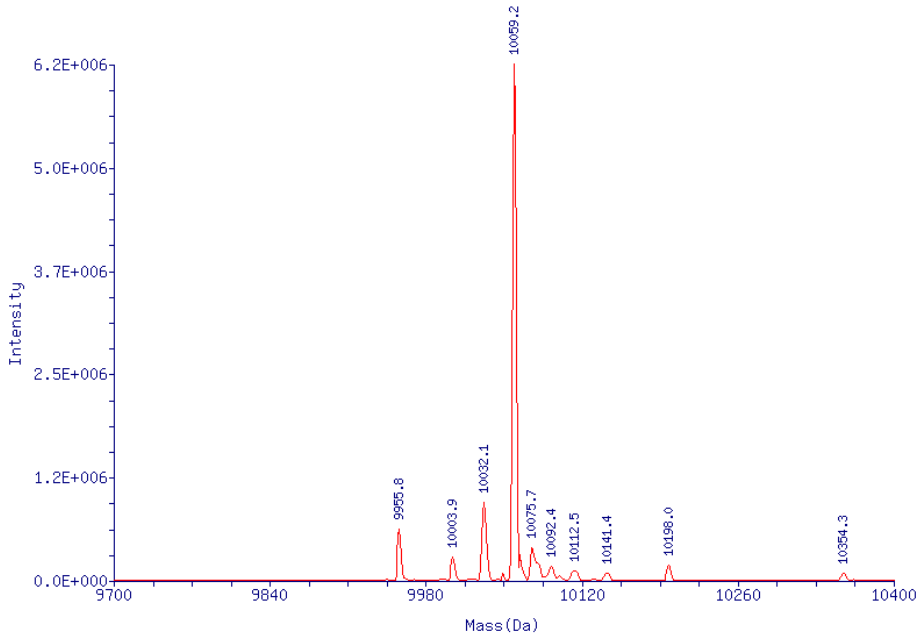


Compound C06.

7. Pre21 RNA2 Conjugation Data Mass Spectra.



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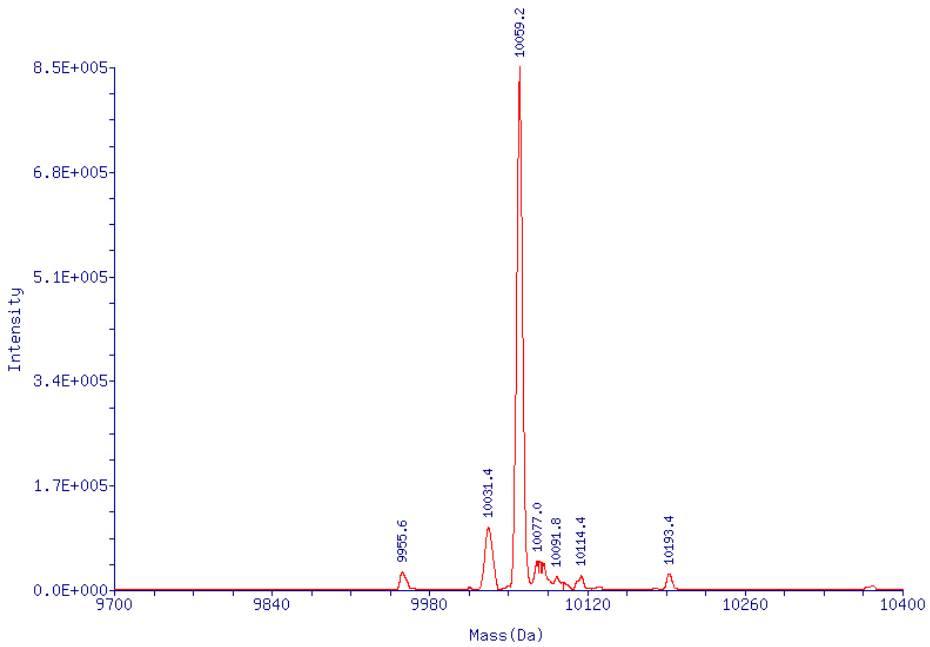

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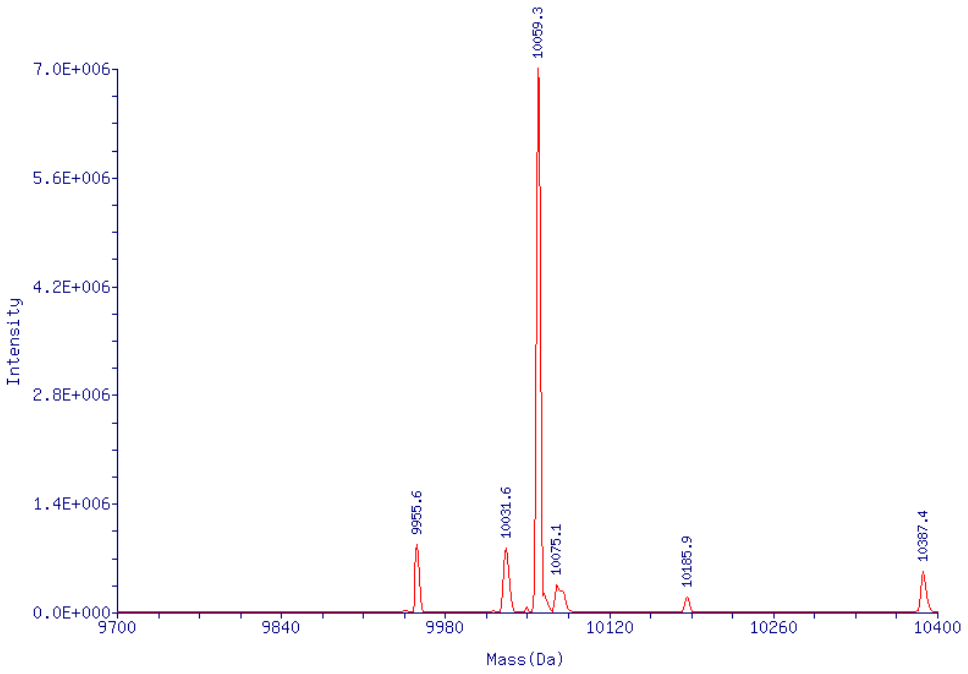

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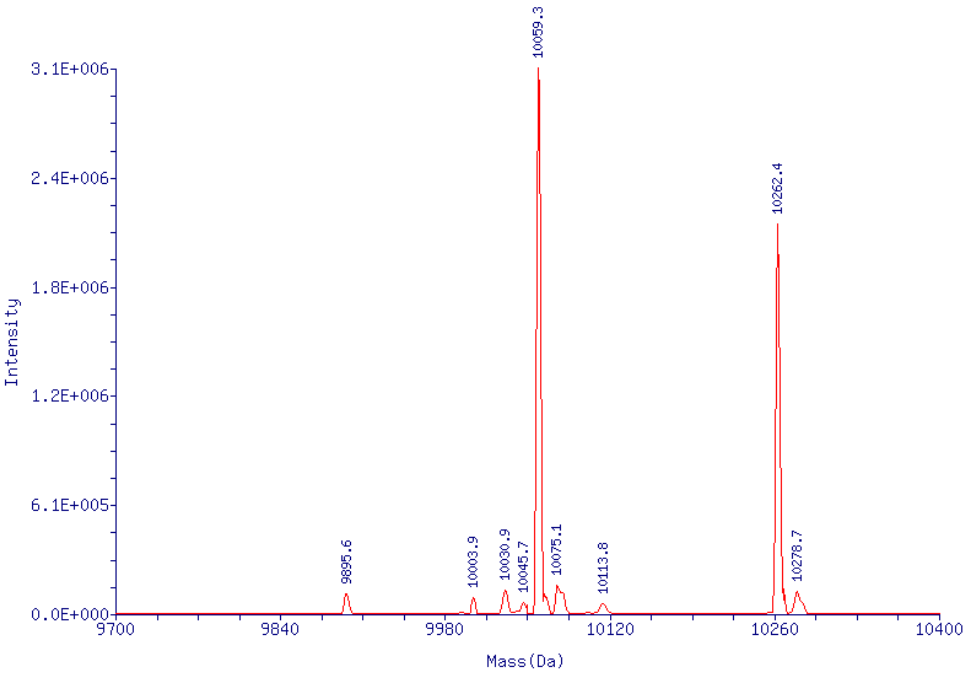

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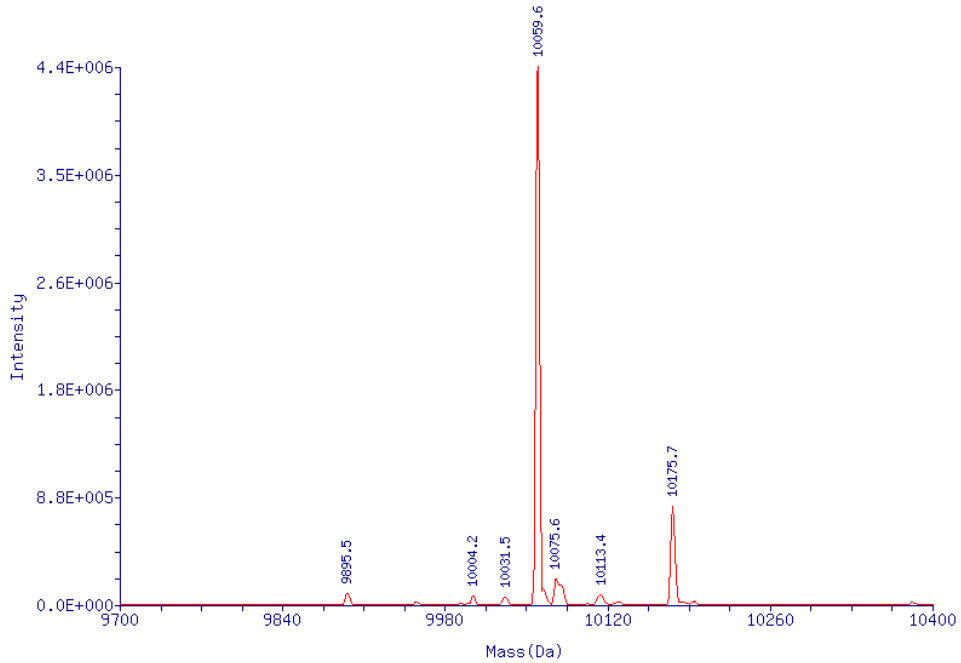

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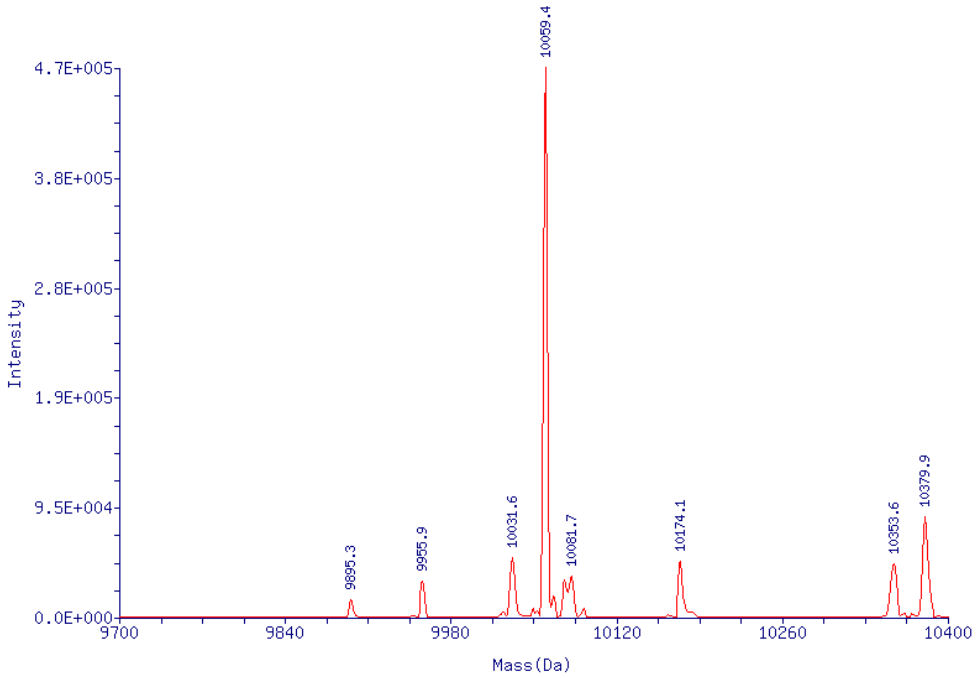

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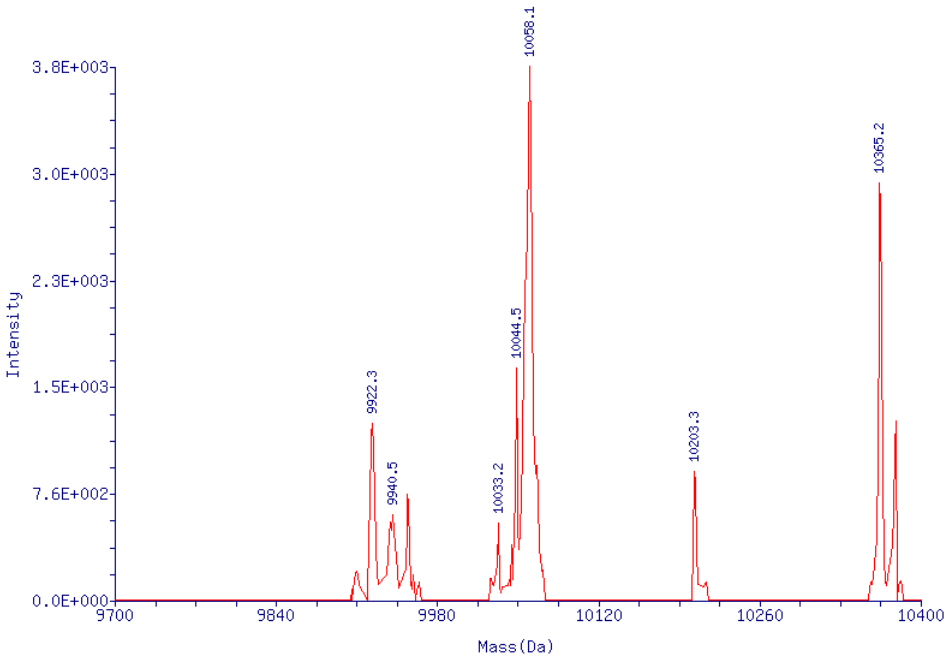

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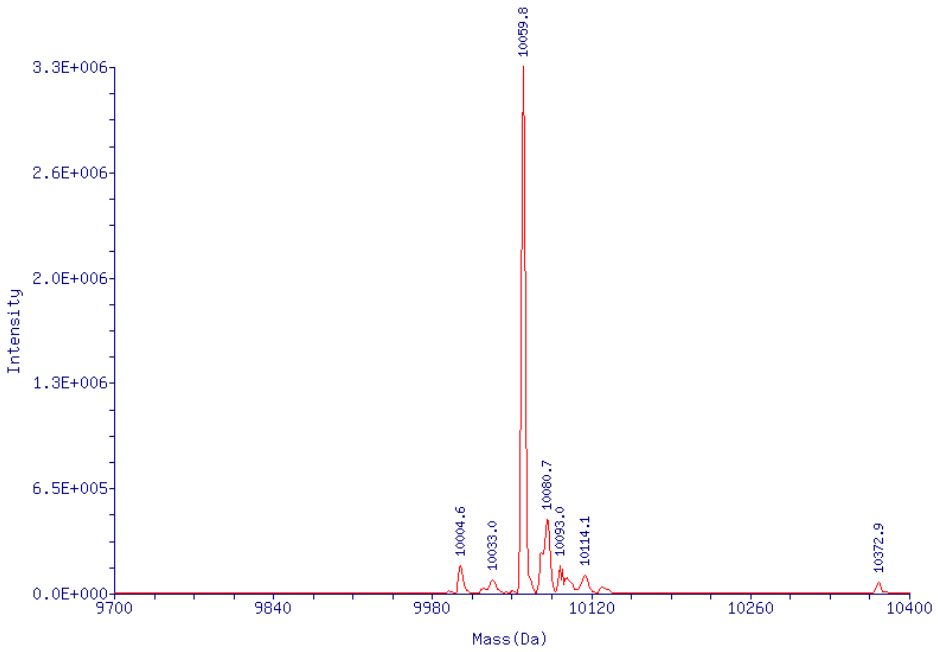

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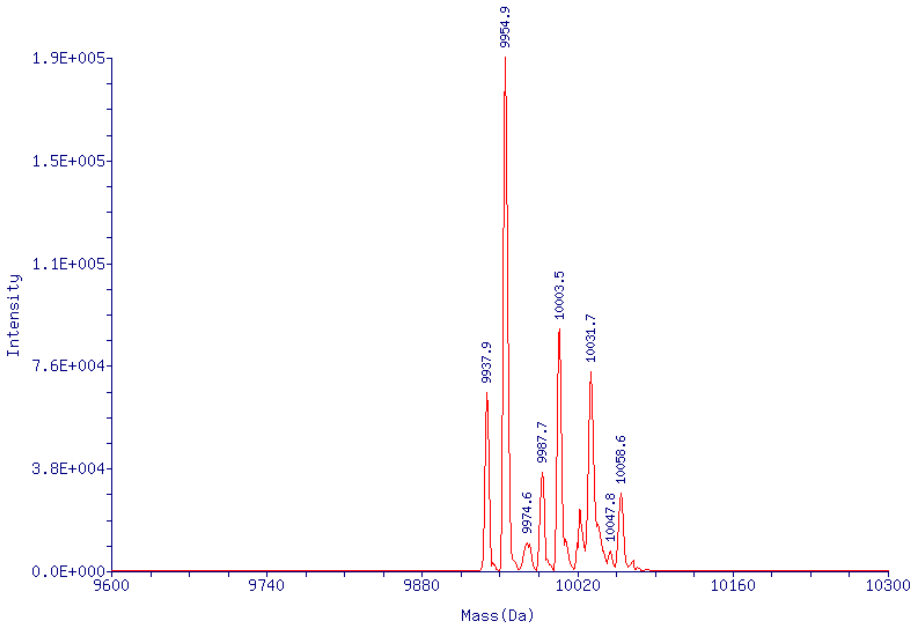

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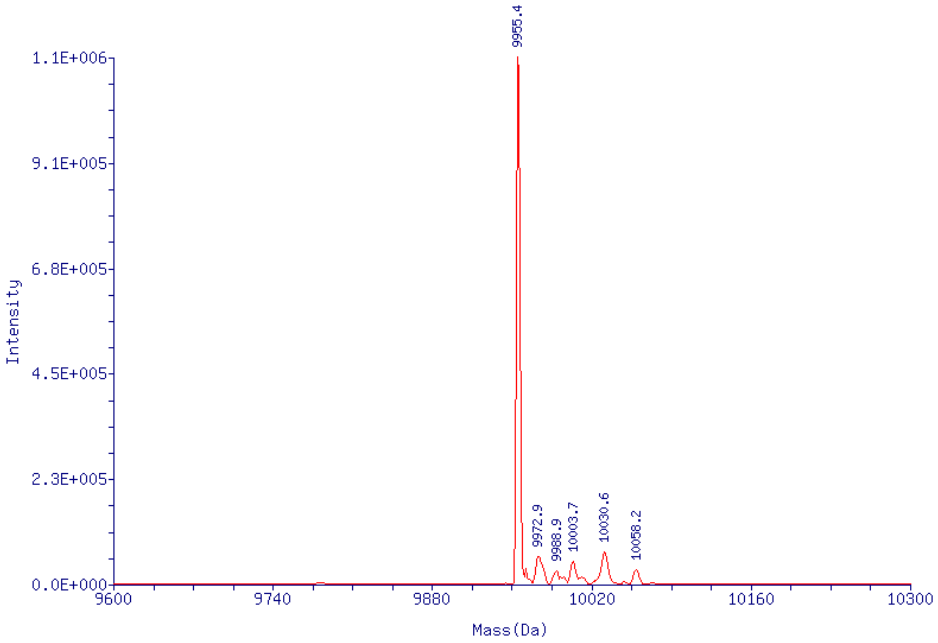

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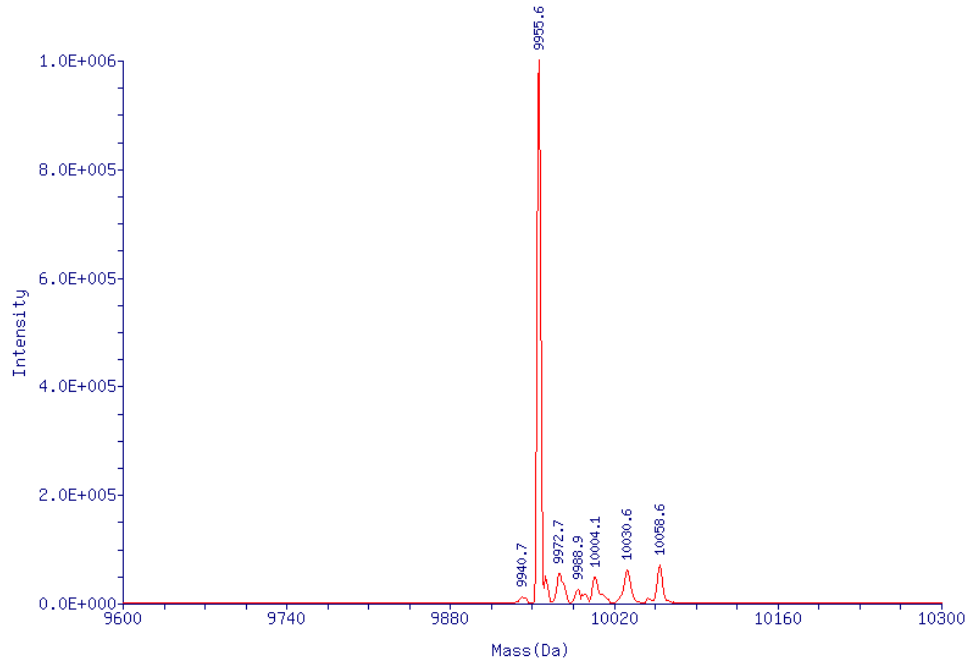
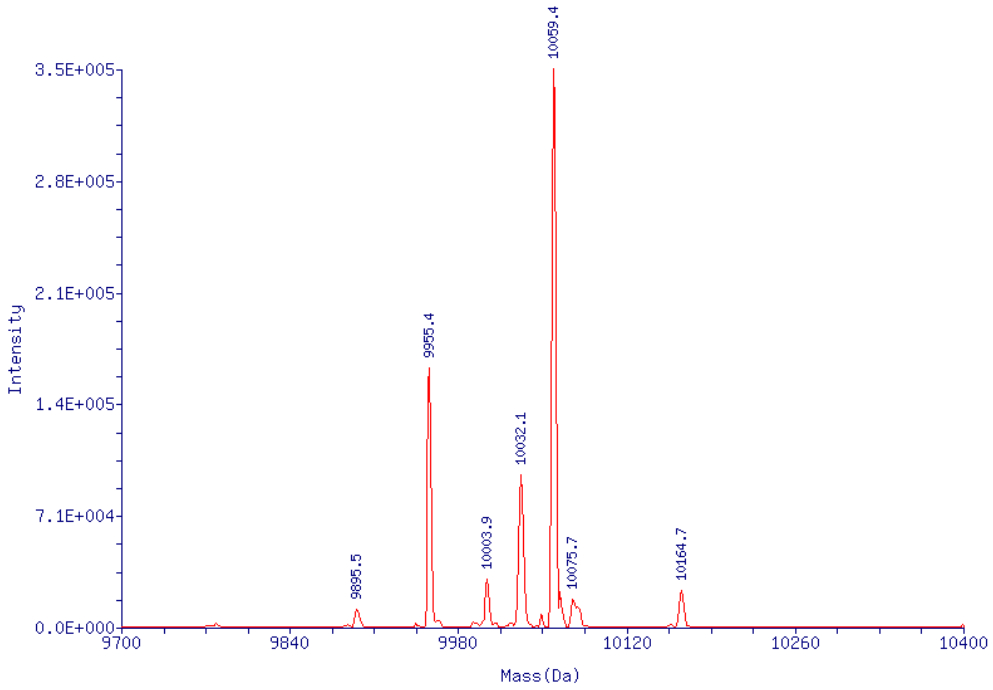
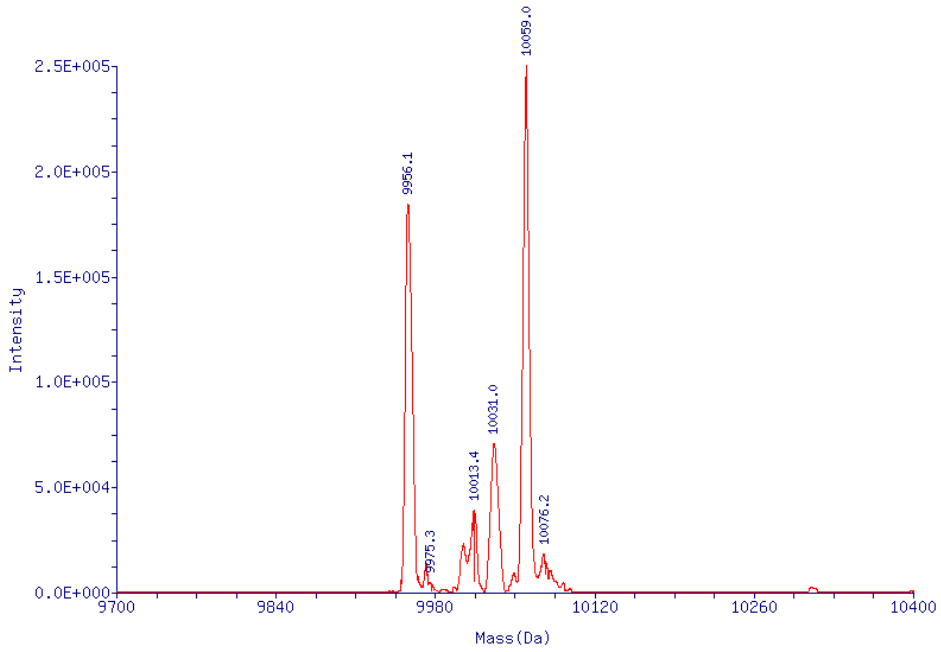


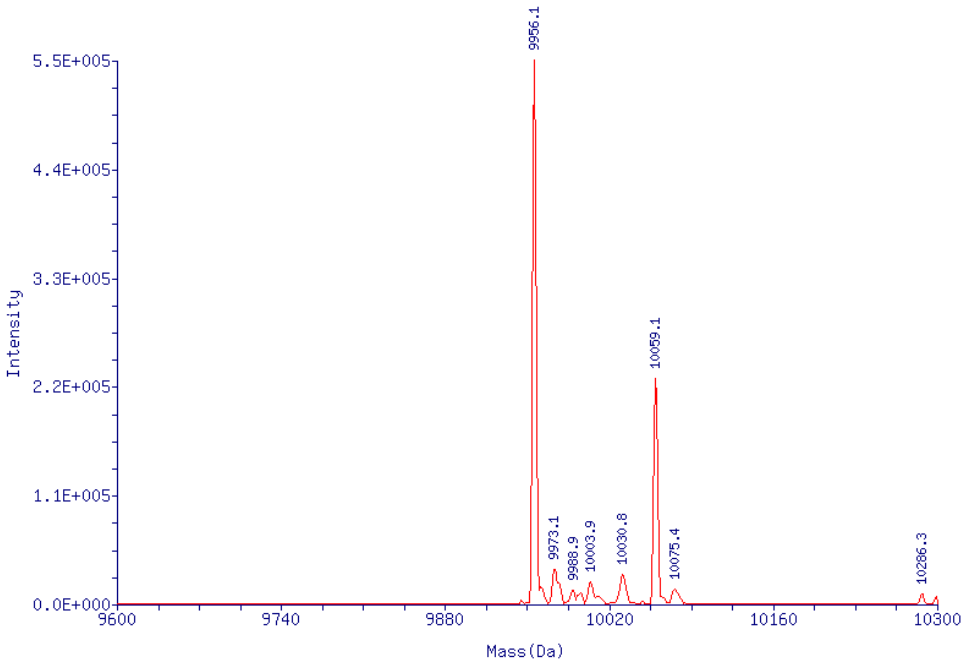
Compound A11.



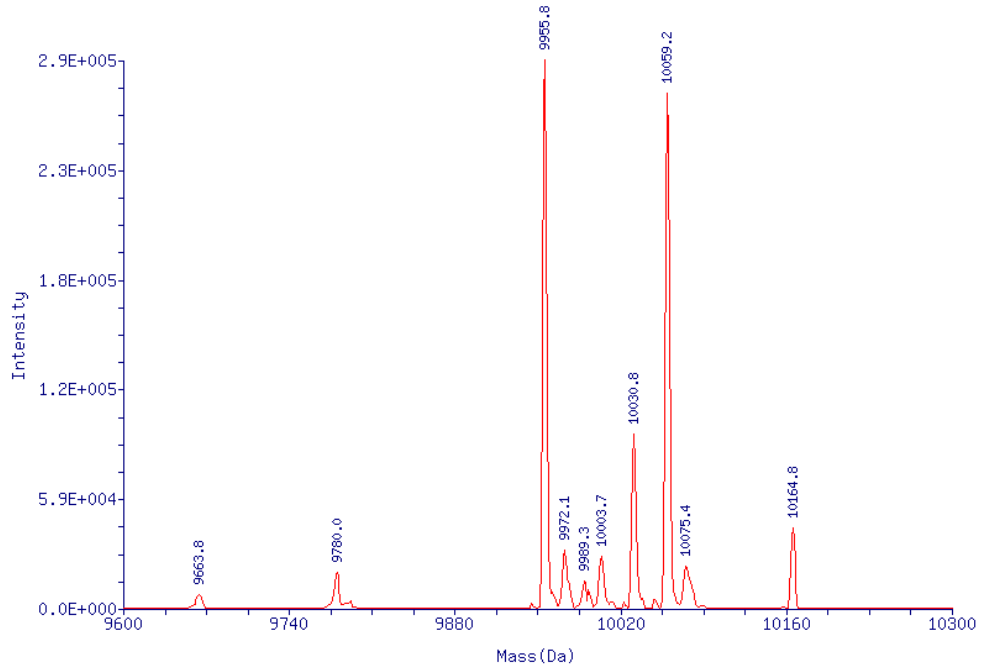
Compound A12.



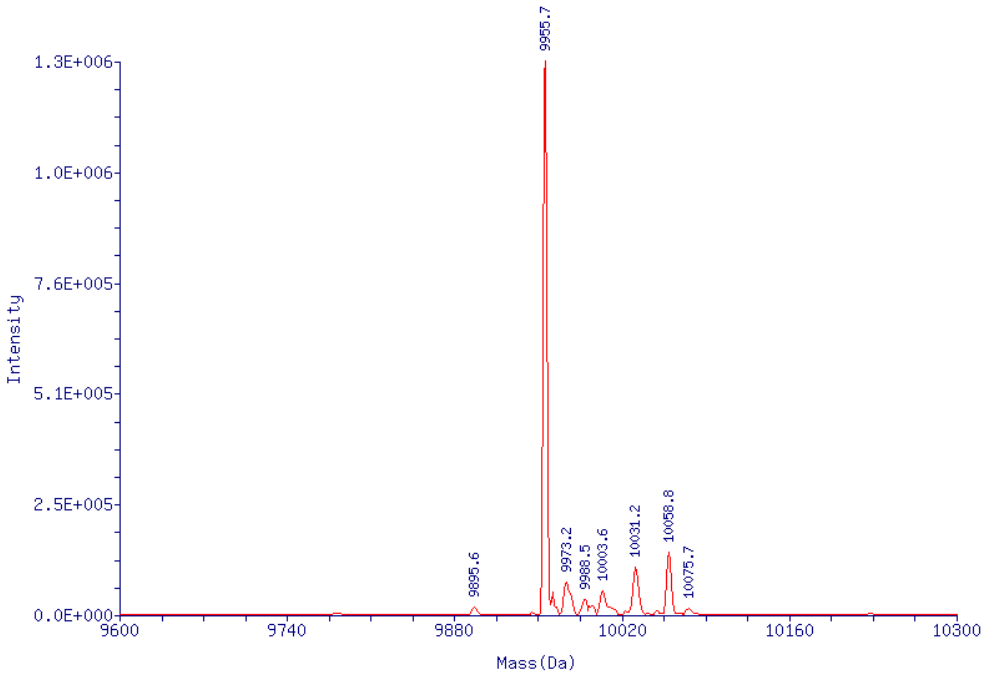
Compound B01.



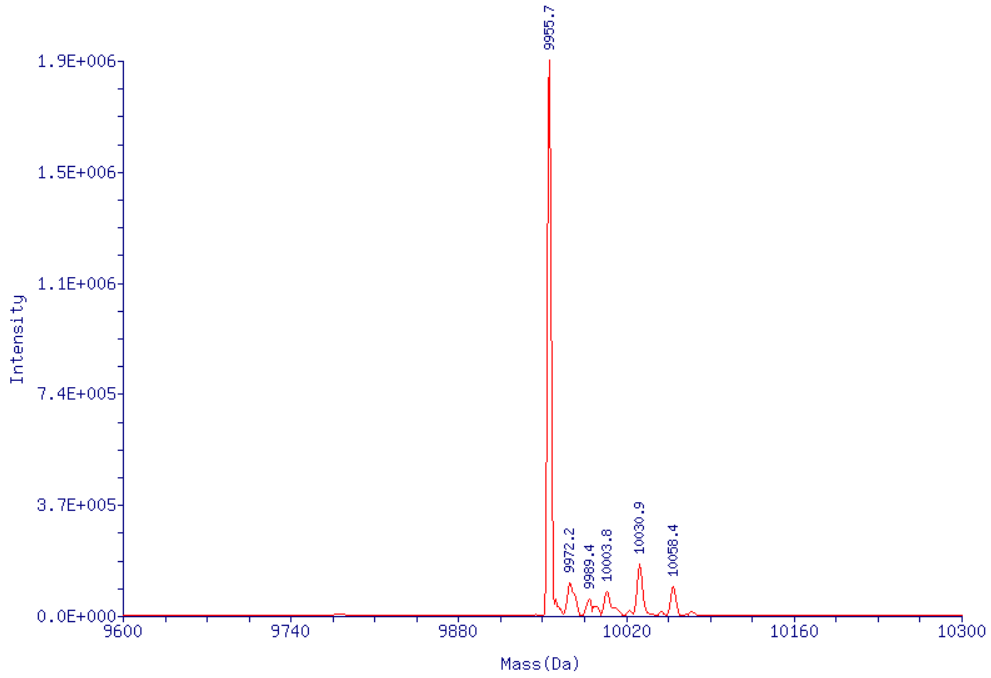
Compound B02.



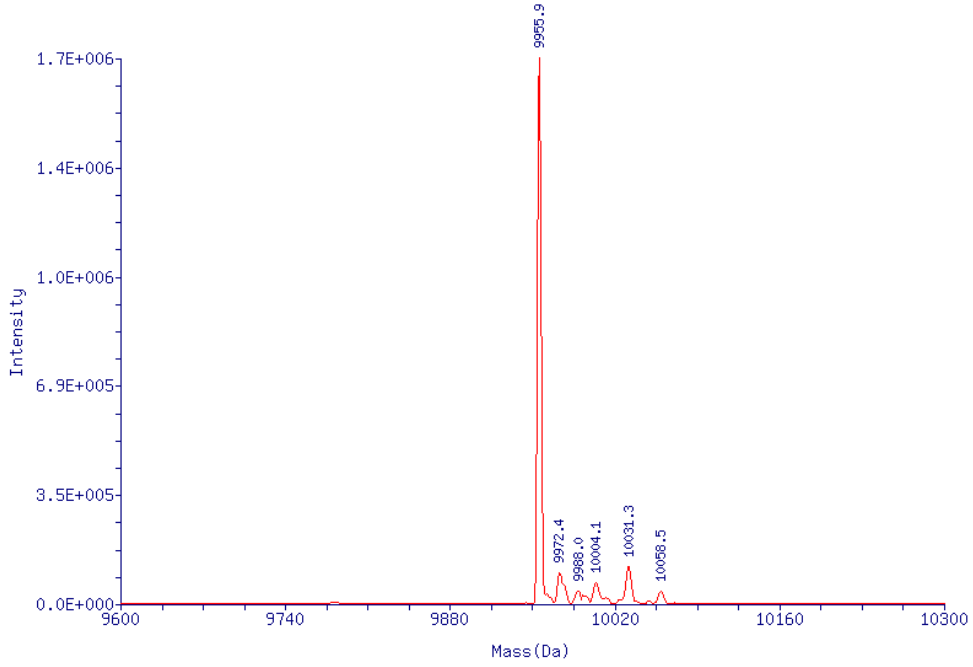
Compound B03.



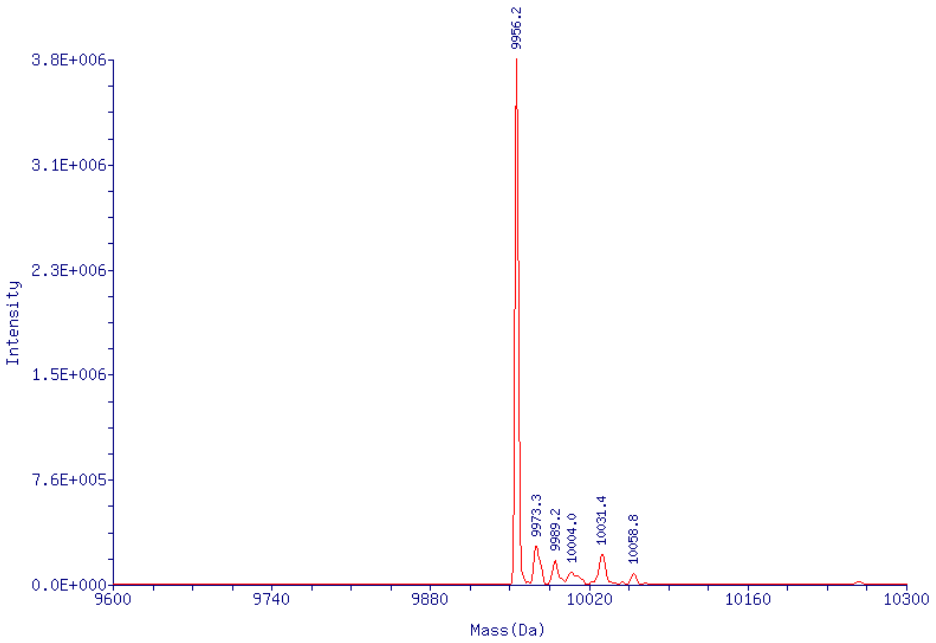
Compound B04.



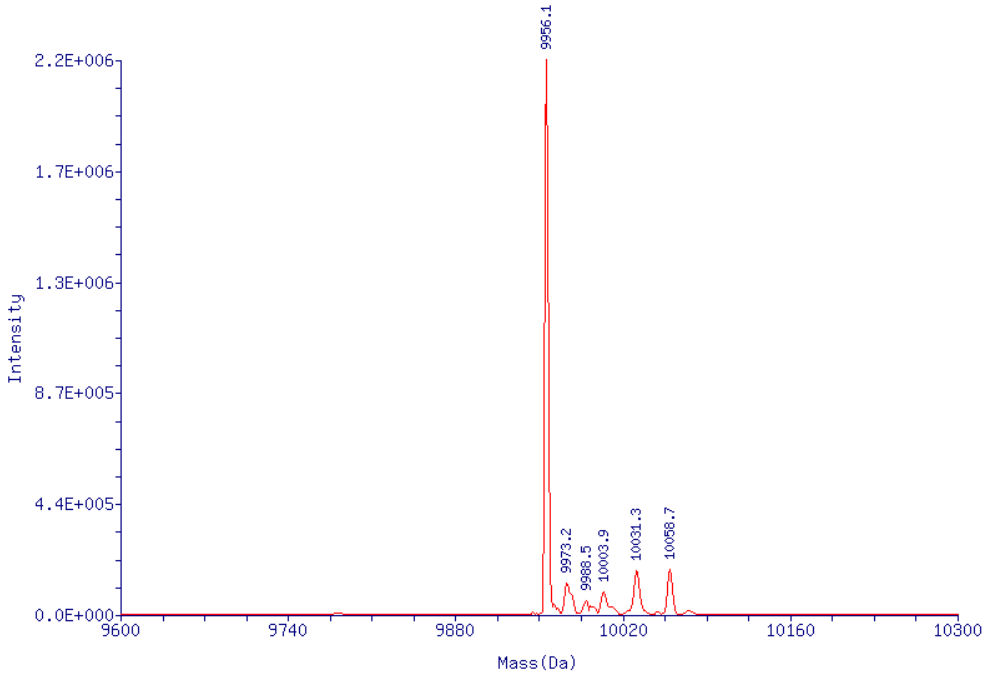
Compound B05.



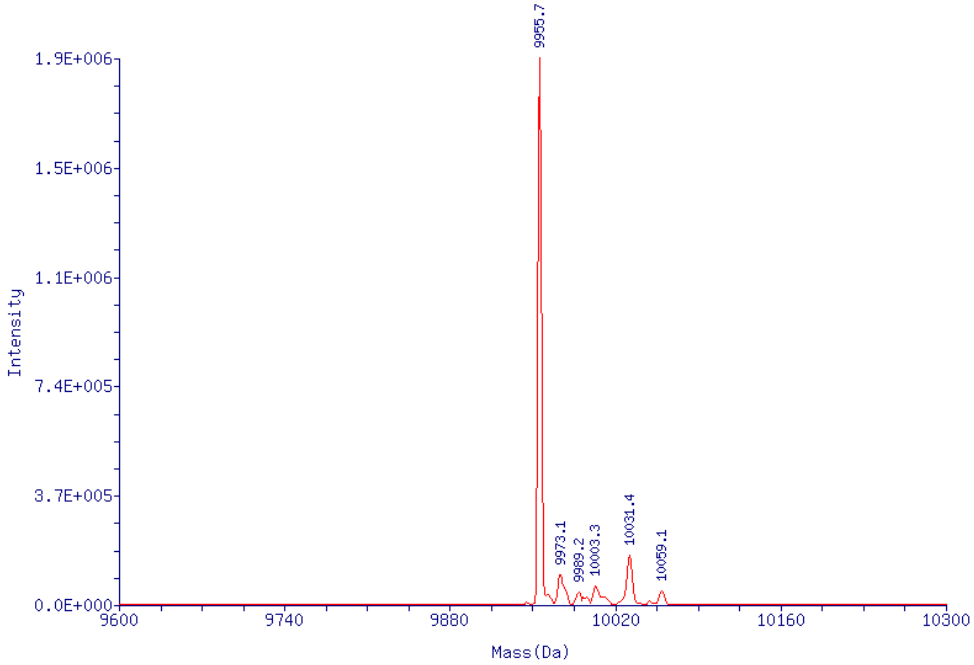
Compound B06.



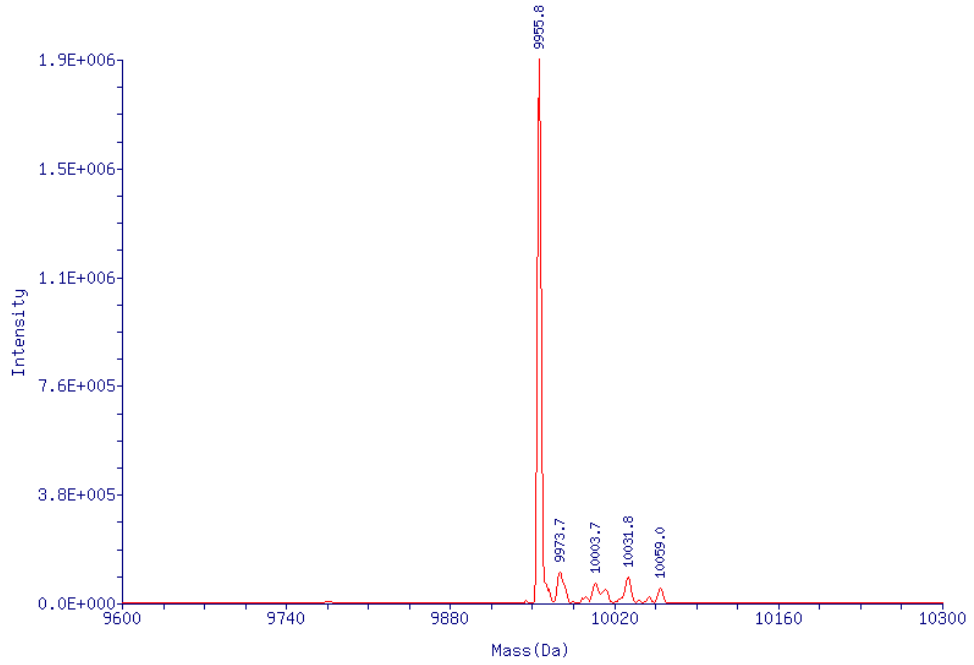
Compound B07.



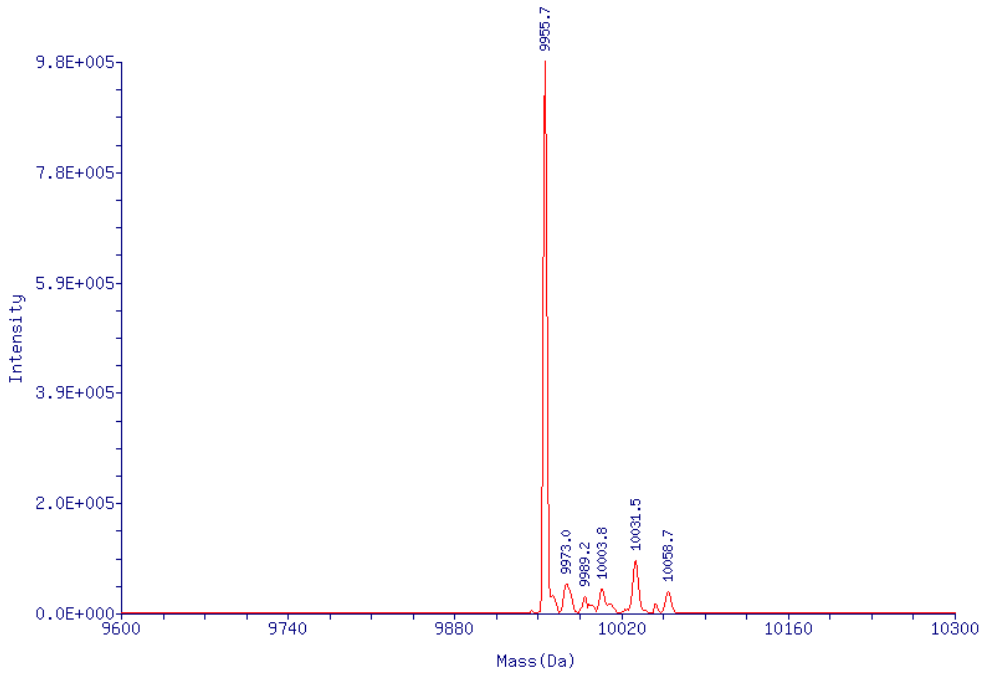
Compound B08.



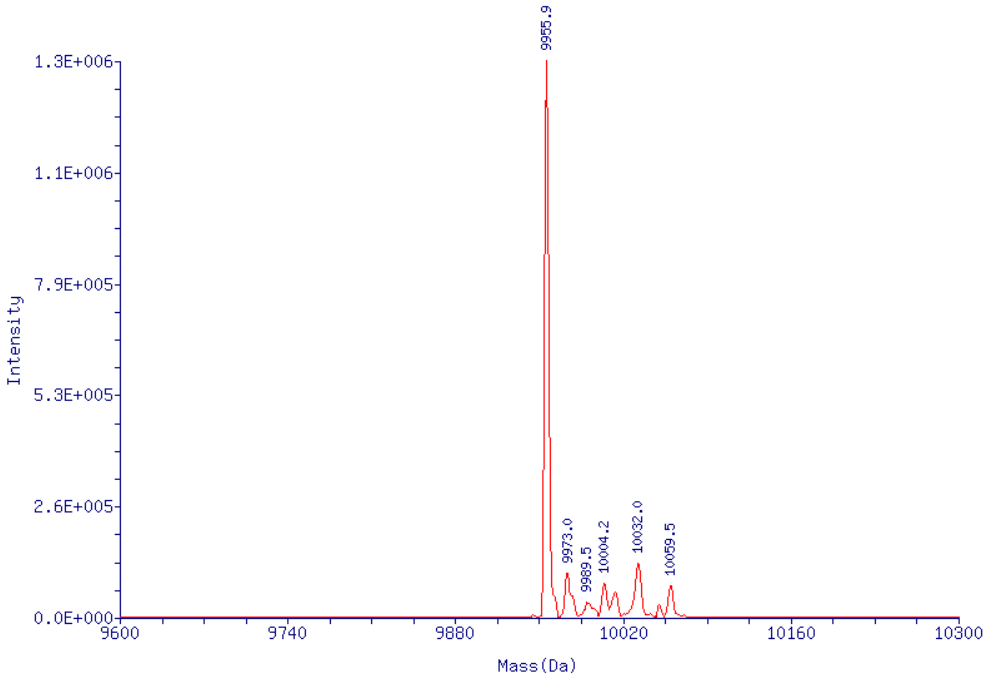
Compound B09.



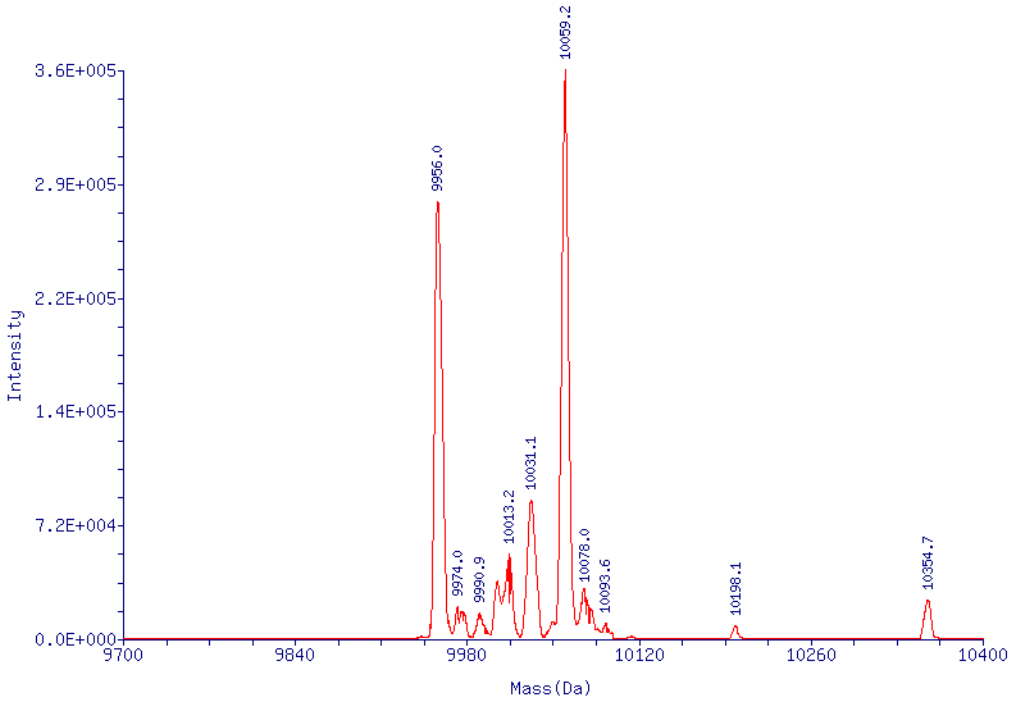
Compound B10.



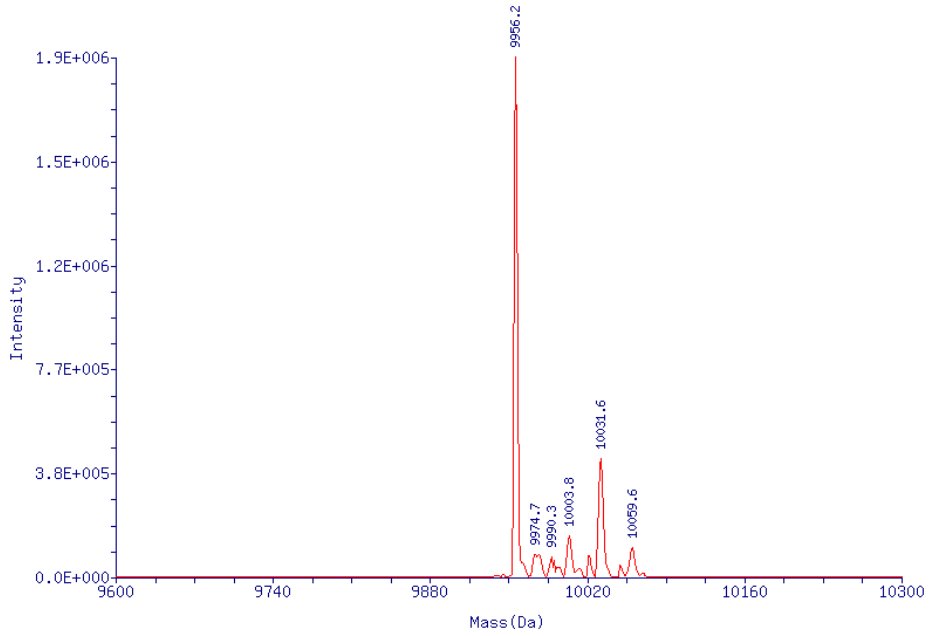
Compound B11.



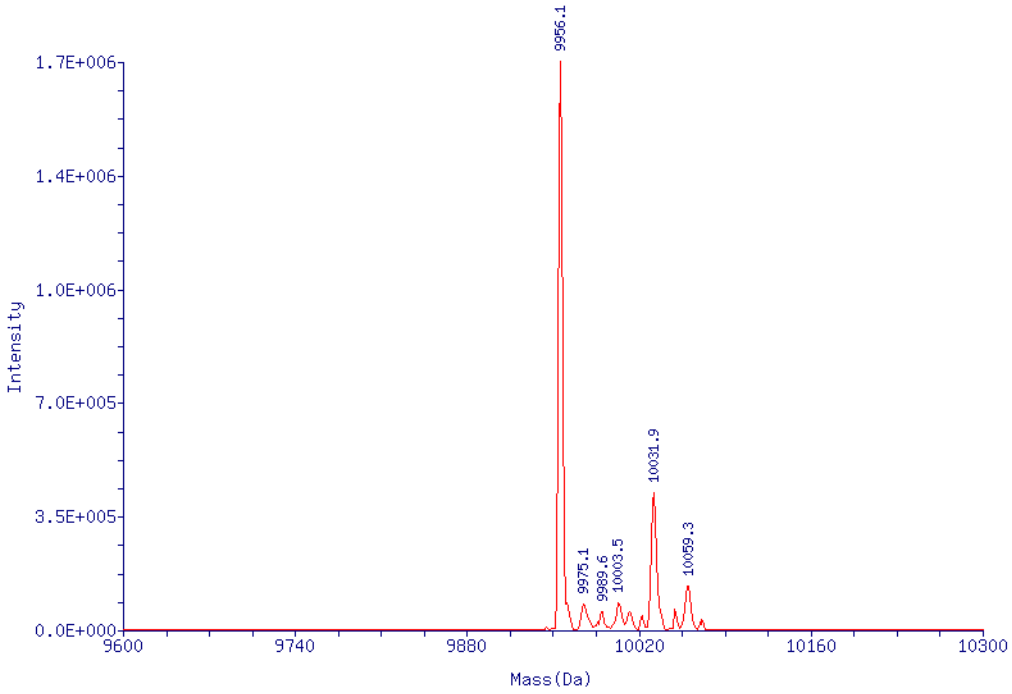
Compound B12.



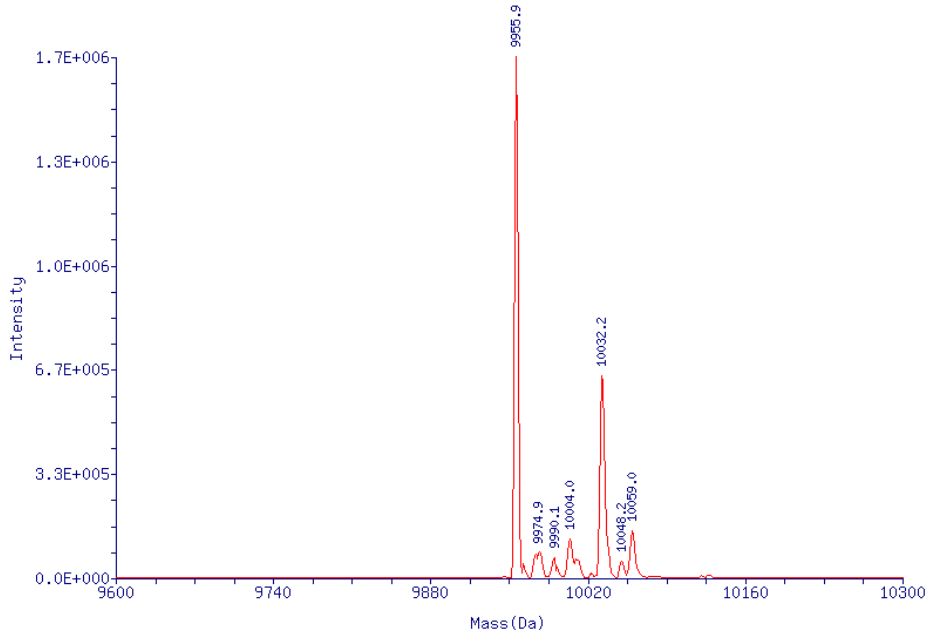
Compound C01.



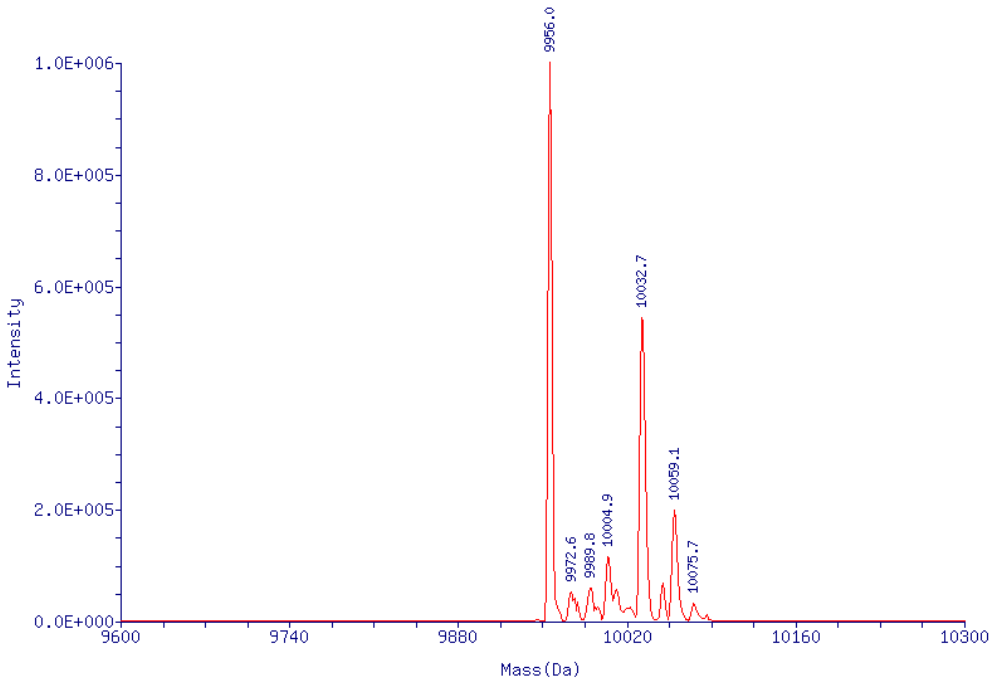
Compound C02.



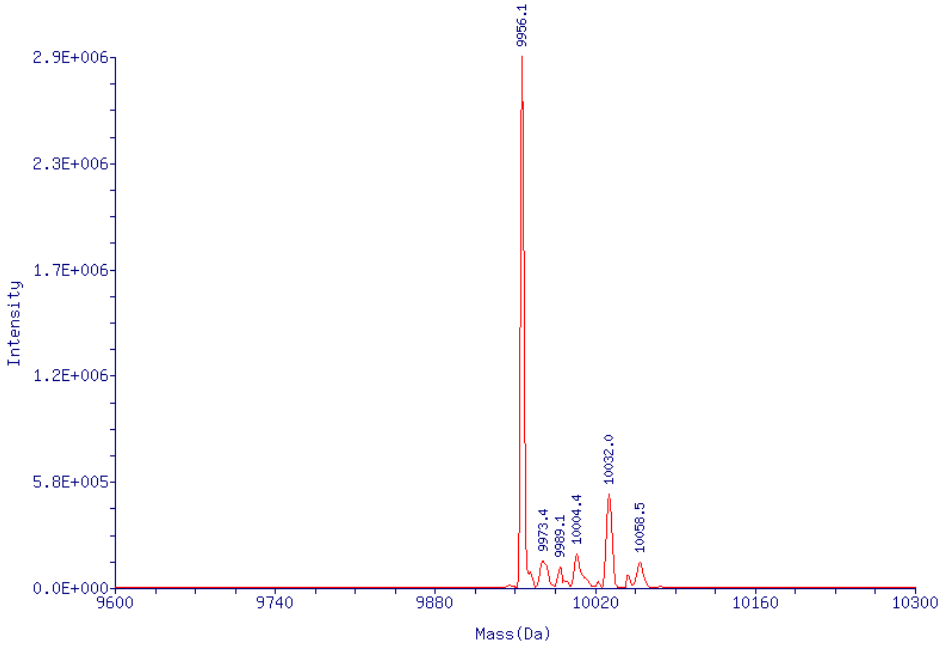
Compound C03.



Compound C04.



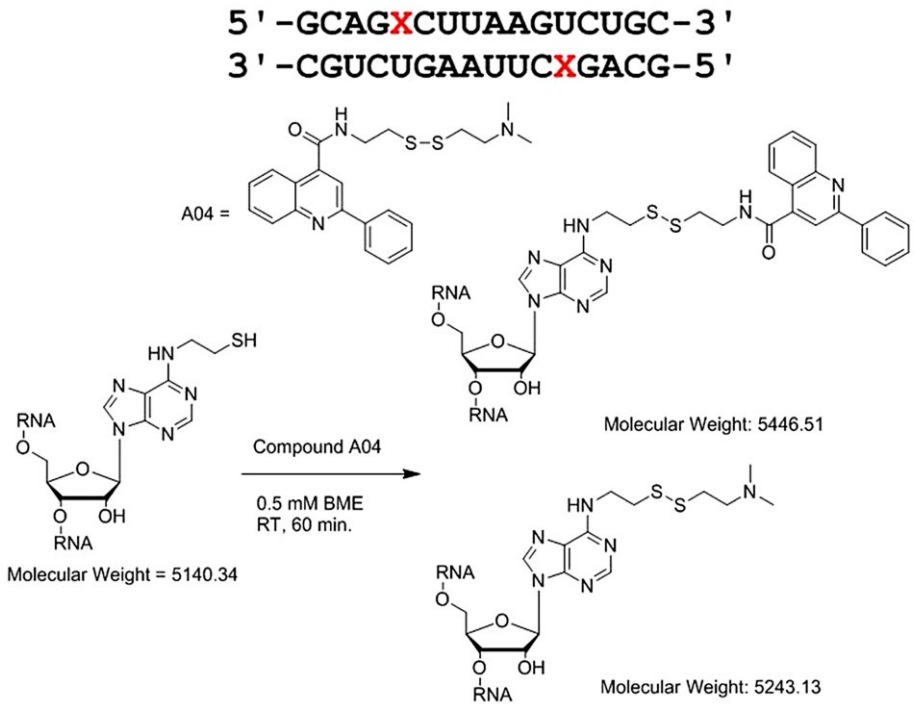
Compound C05.

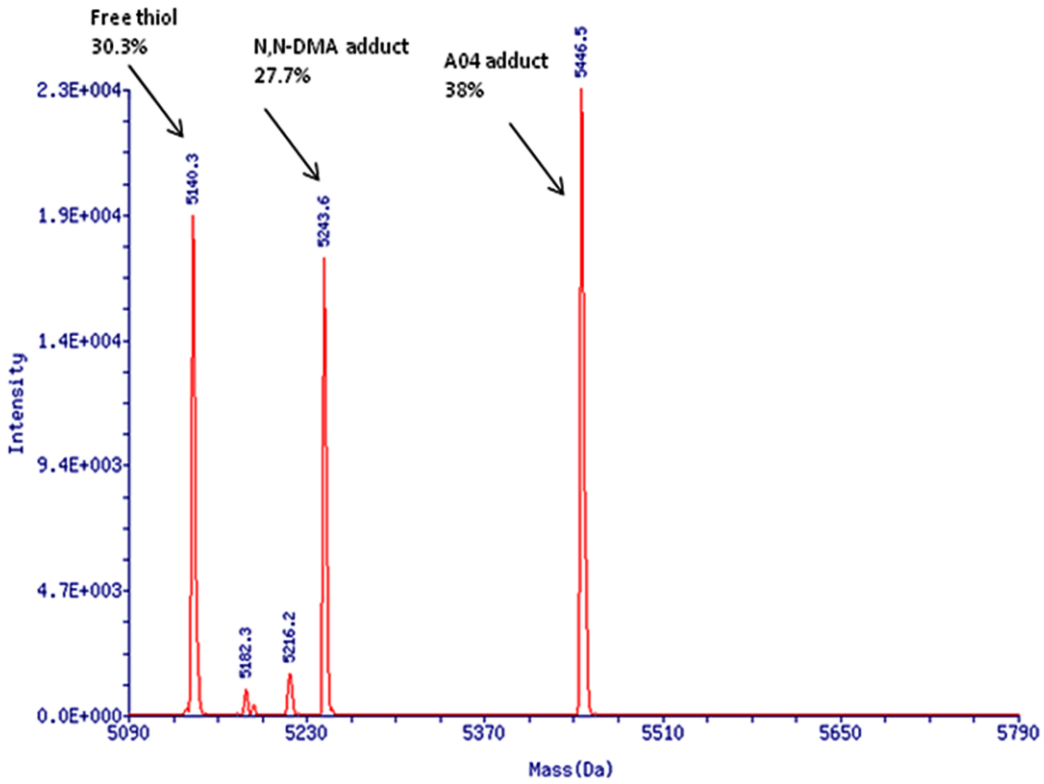


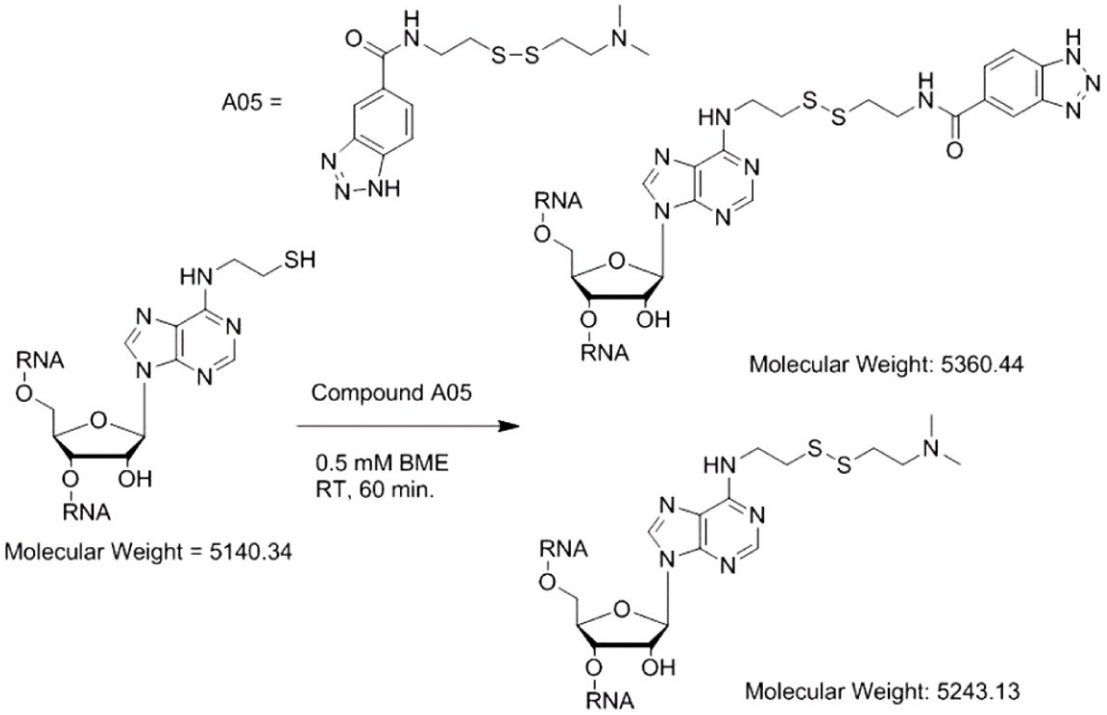
Compound C06.

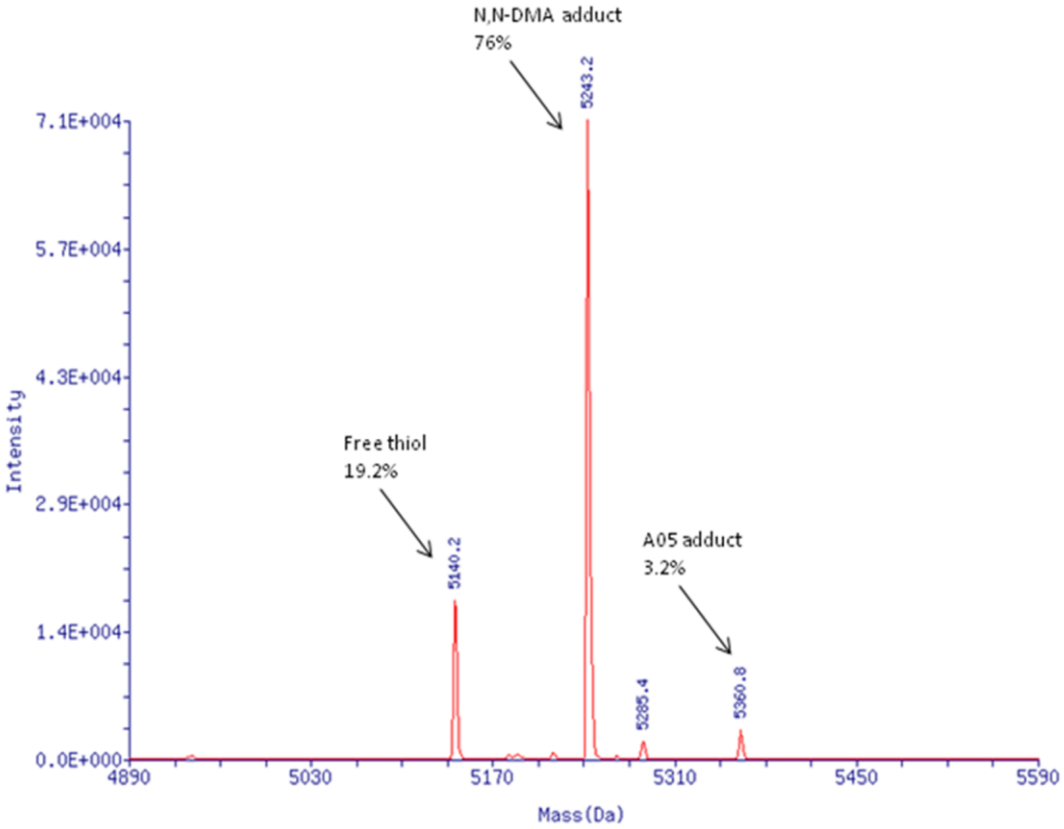
8. 16mer Conjugation Data with A04 & A05

Thiol-Modified 16-nt RNA






A05 =
Compound A05
0.5 mM BME
RT, 60 min.
Molecular Weight = 5140.34
Molecular Weight: 5360.44
Molecular Weight: 5243.13


N,N-DMA adduct
76%
5243.2
Free thiol
19.2%
5140.2
A05 adduct
3.2%
5285.4
5360.8
Intensity
7.1E+004
5.7E+004
4.3E+004
2.9E+004
1.4E+004
0.0E+000
4890
5030
5170
5310
5450
5590
Mass(Da)

9. Denaturing Gel Electrophoresis of RNA2 after Solid-phase Synthesis

The oxidation conditions used during the solid-phase synthesis of these oligonucleotides are:

- 0.02 M Iodine in pyridine/THF/water
- 15 s per cycle

A 19% polyacrylamide denaturing gel with a xylene cyanol blue standard was used to assess the solid phase RNA synthesis product. Approximately 12 nmol of sample was loaded into the lane and visualized by UV shadowing.