

## Supporting Information

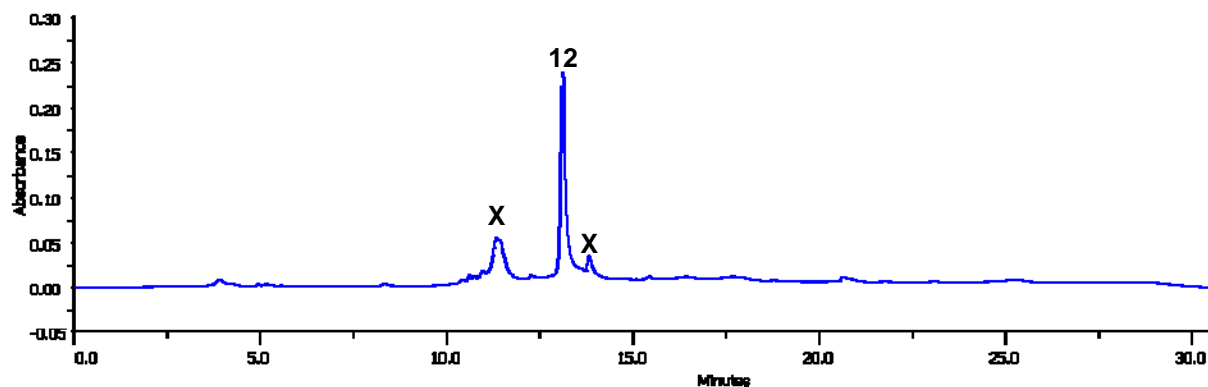
### **Fast RNA Conjugations on Solid Phase by Strain-Promoted Cycloadditions**

**Ishwar Singh,\* Colin Freeman, Annemieke Madder, Joseph S. Vyle and Frances Heaney\***

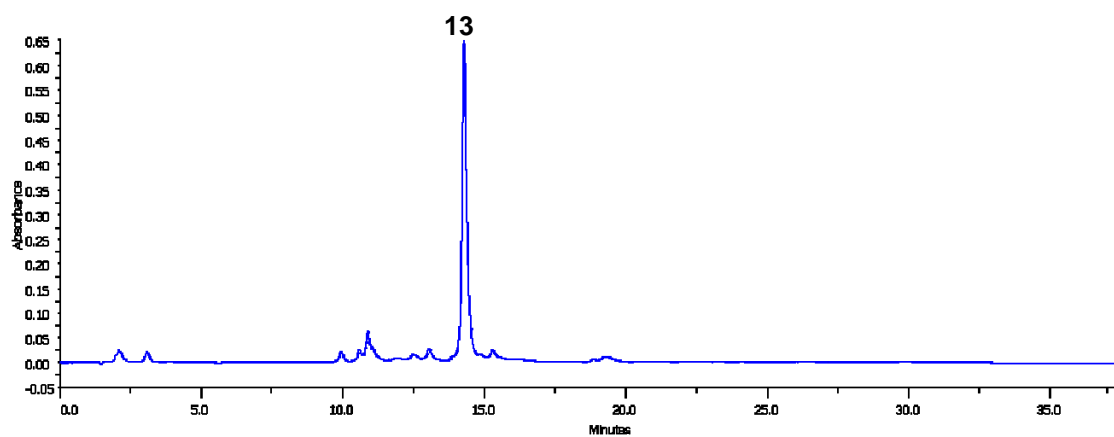
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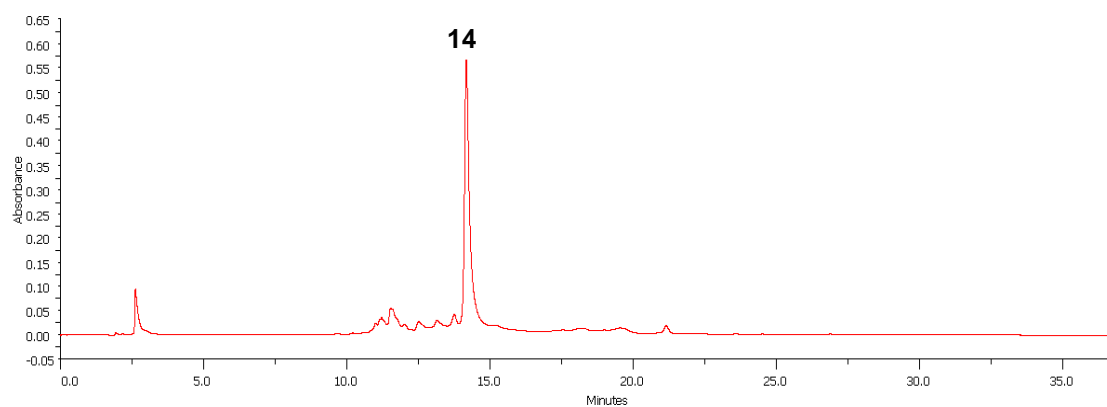
### HPLC Traces



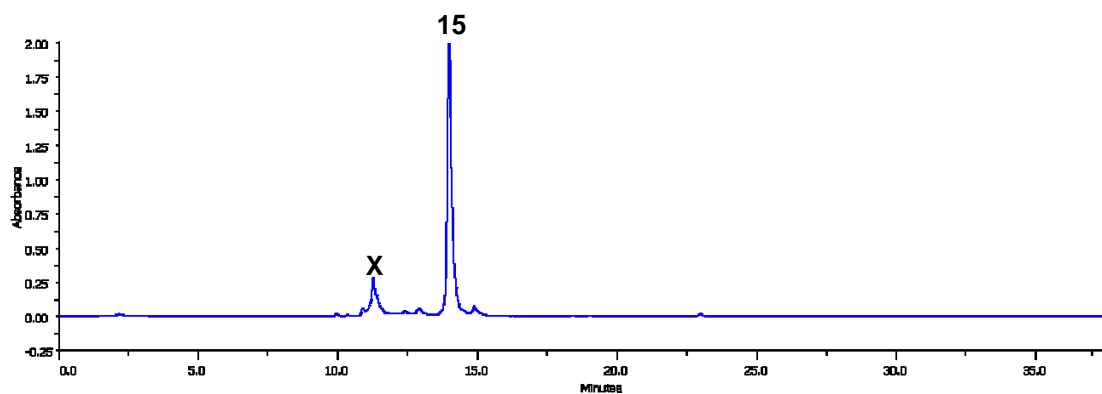
**Figure 1** Reversed-phase HPLC trace of crude **12** (19-mer RNA-cyclooctyne)



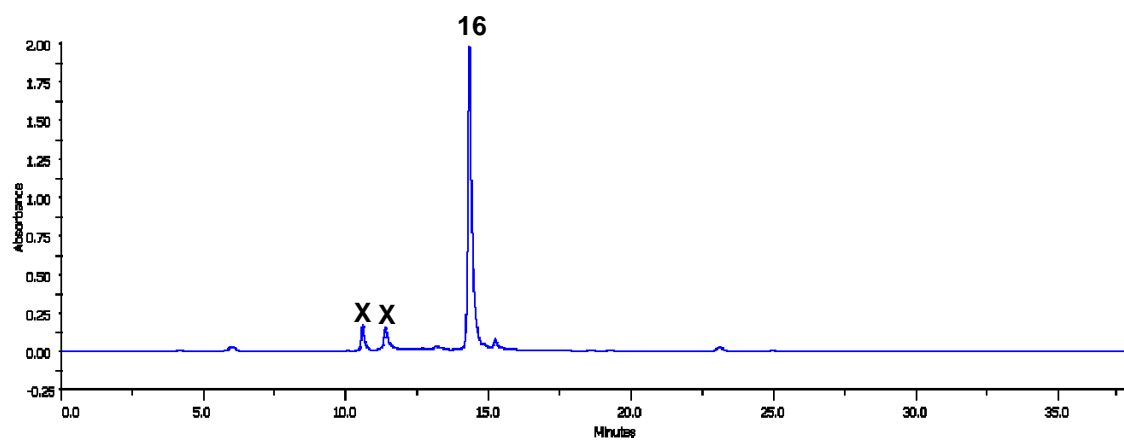
**Figure 2** Reversed-phase HPLC trace of crude **13** (U<sub>4</sub>-cyclooctyne)



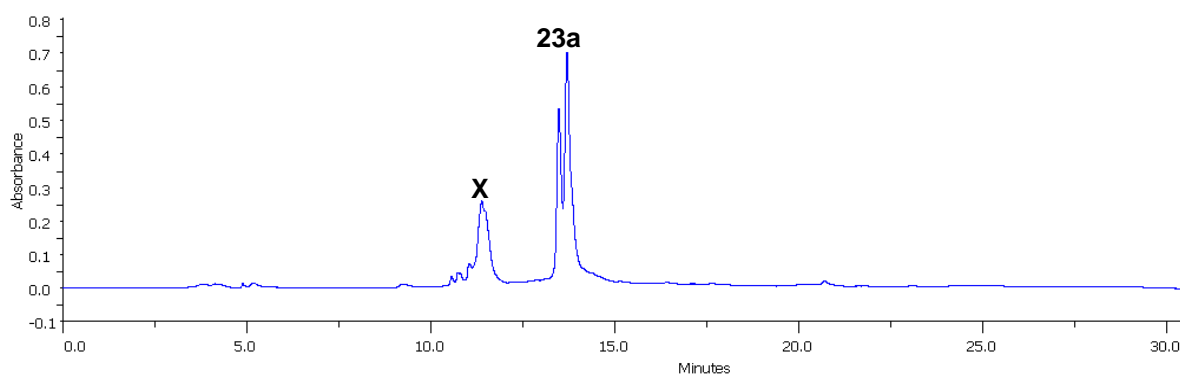
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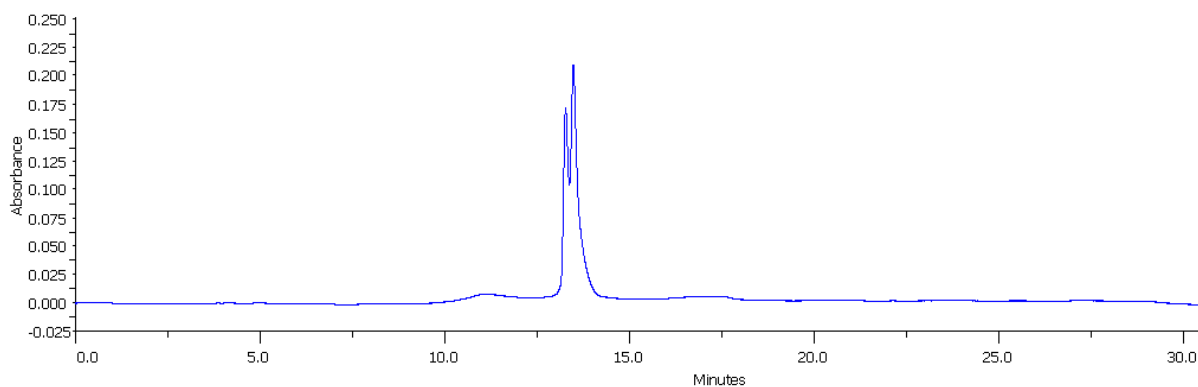
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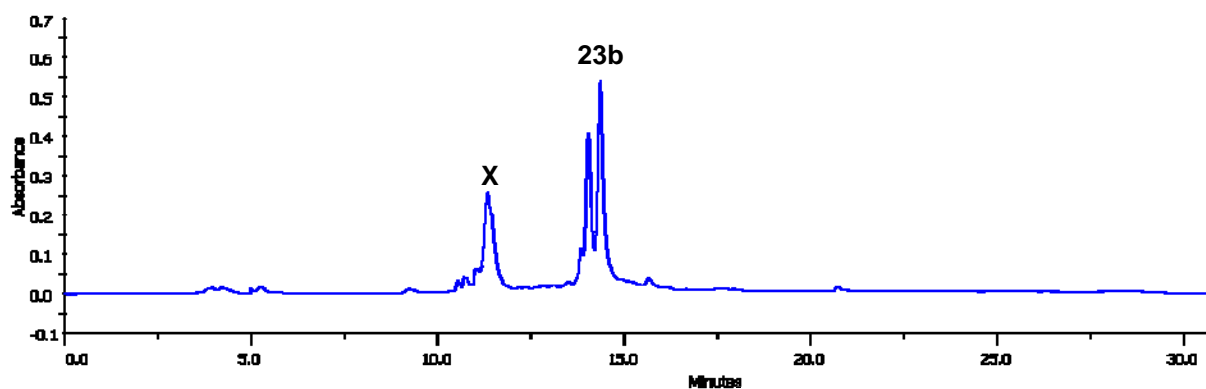
**Figure 5** Reversed-phase HPLC trace of crude **16** (gapmer RNA-cyclooctyne)



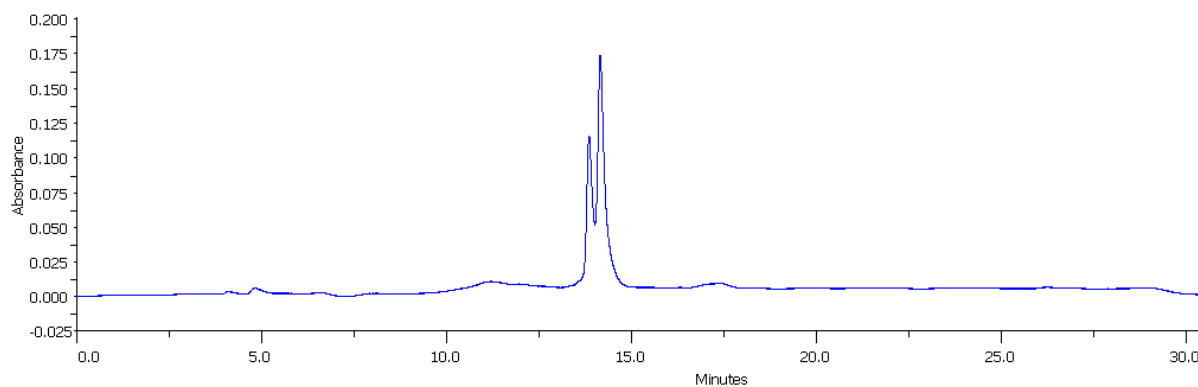
**Figure 6** Reversed-phase HPLC trace of crude **23a** (19-mer RNA benzyl triazole conjugate)



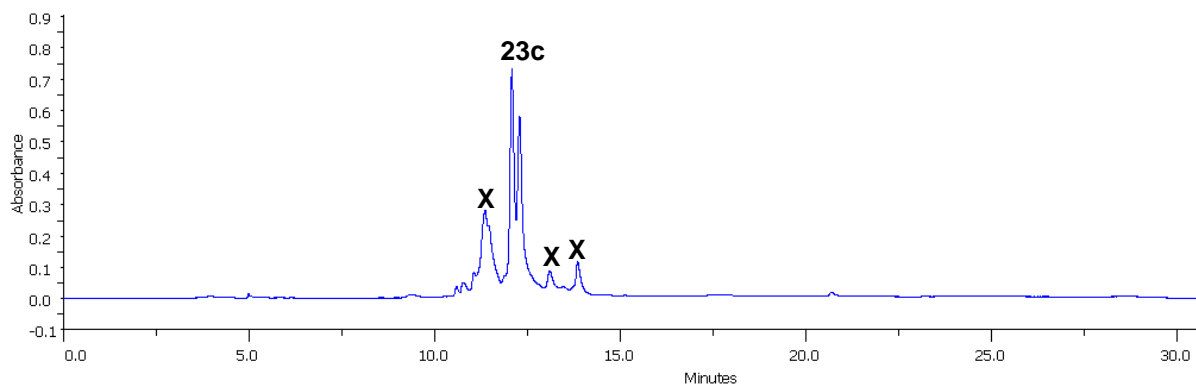
**Figure 7** Reversed-phase HPLC trace of pure **23a** (19-mer RNA benzyl triazole conjugate)



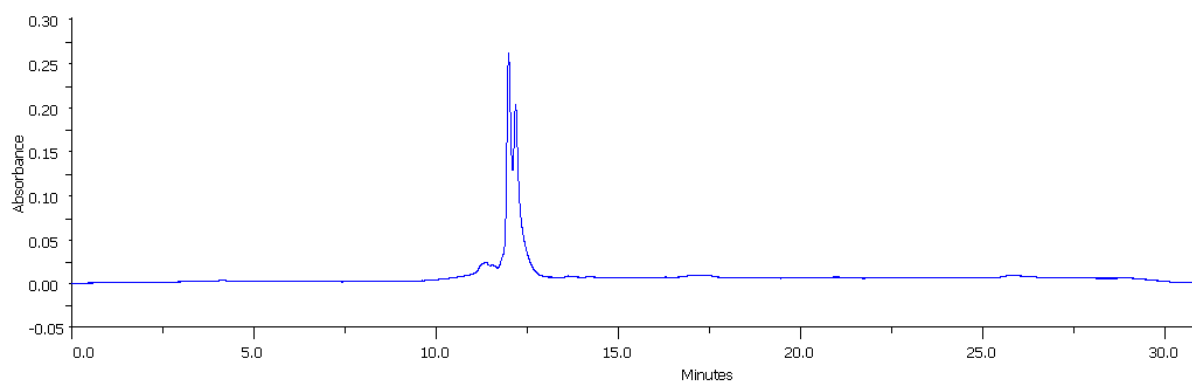
**Figure 8** Reversed-phase HPLC trace of crude **23b** (19-mer RNA cinamoyl triazole conjugate)



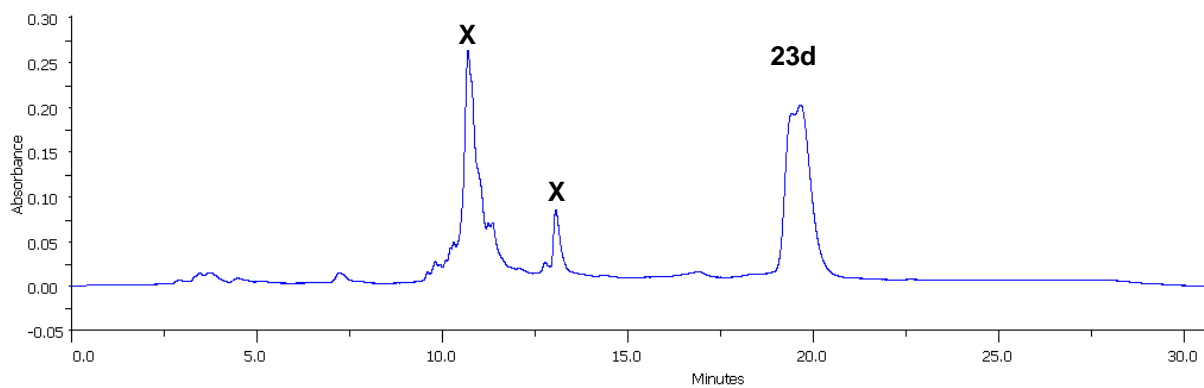
**Figure 9** Reversed-phase HPLC trace of pure **23b** (19-mer RNA cinamoyl triazole conjugate)



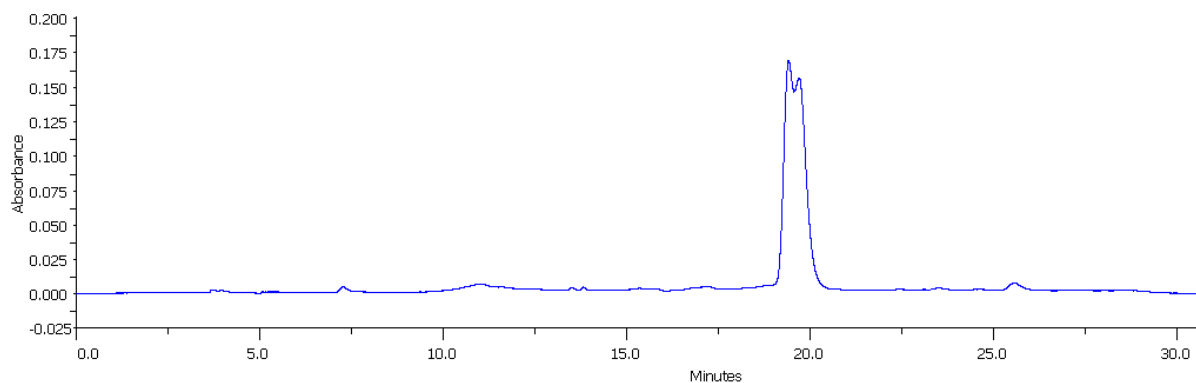
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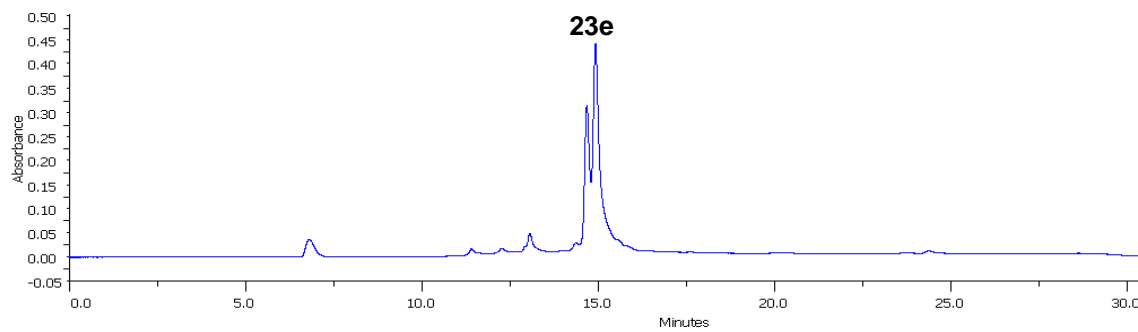
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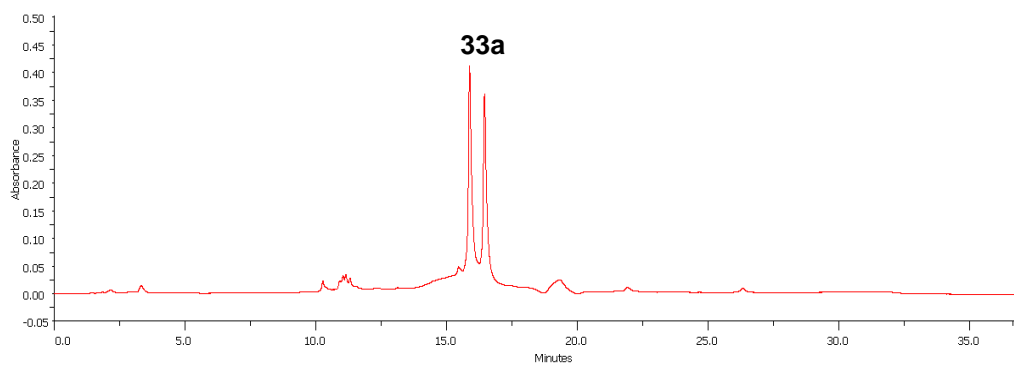
**Figure 12** Reversed-phase HPLC trace of crude **23d** (19-mer RNA cholesteryl triazole conjugate)



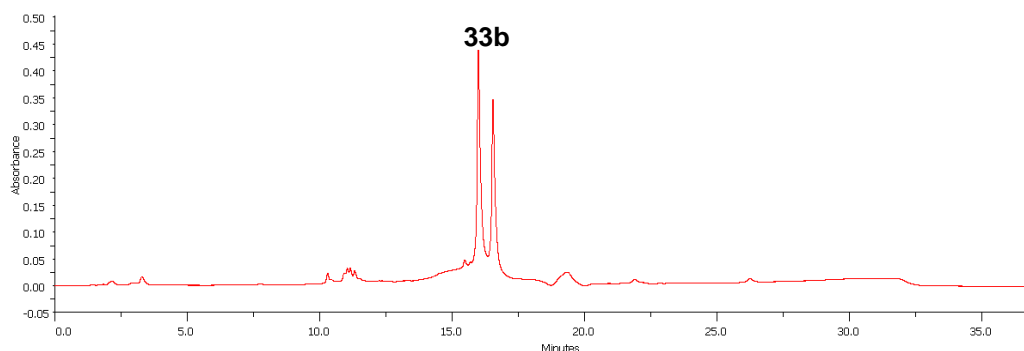
**Figure 13** Reversed-phase HPLC trace of pure **23d** (19-mer RNA cholesteryl triazole conjugate)



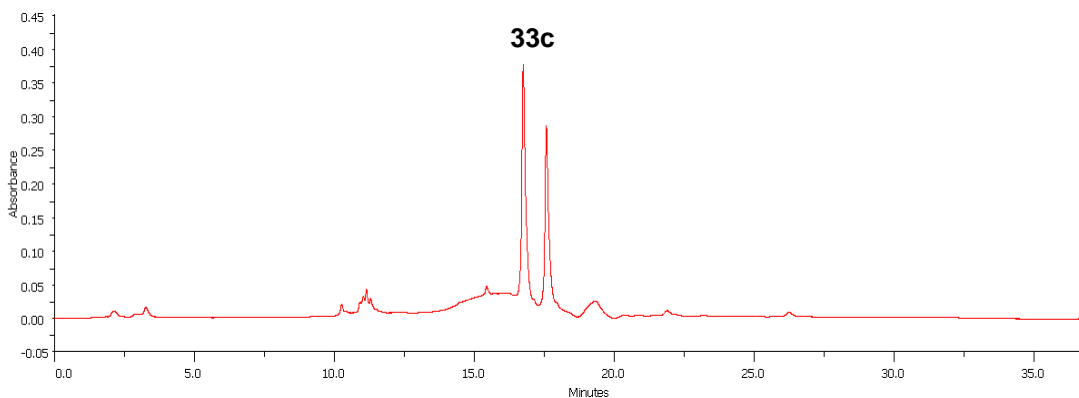
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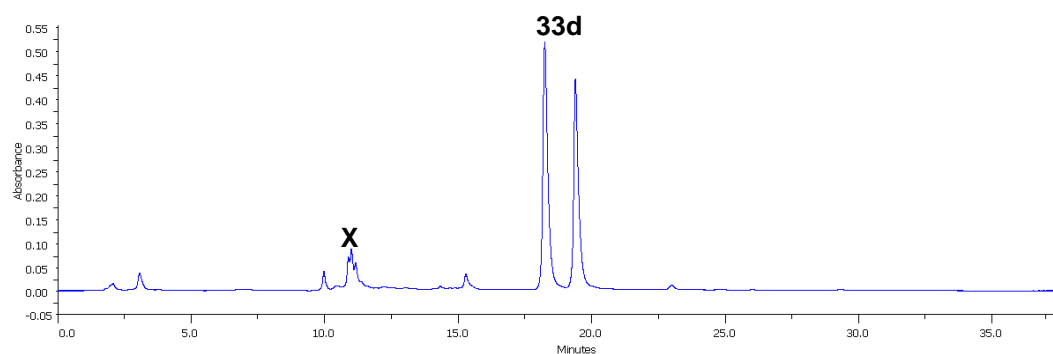
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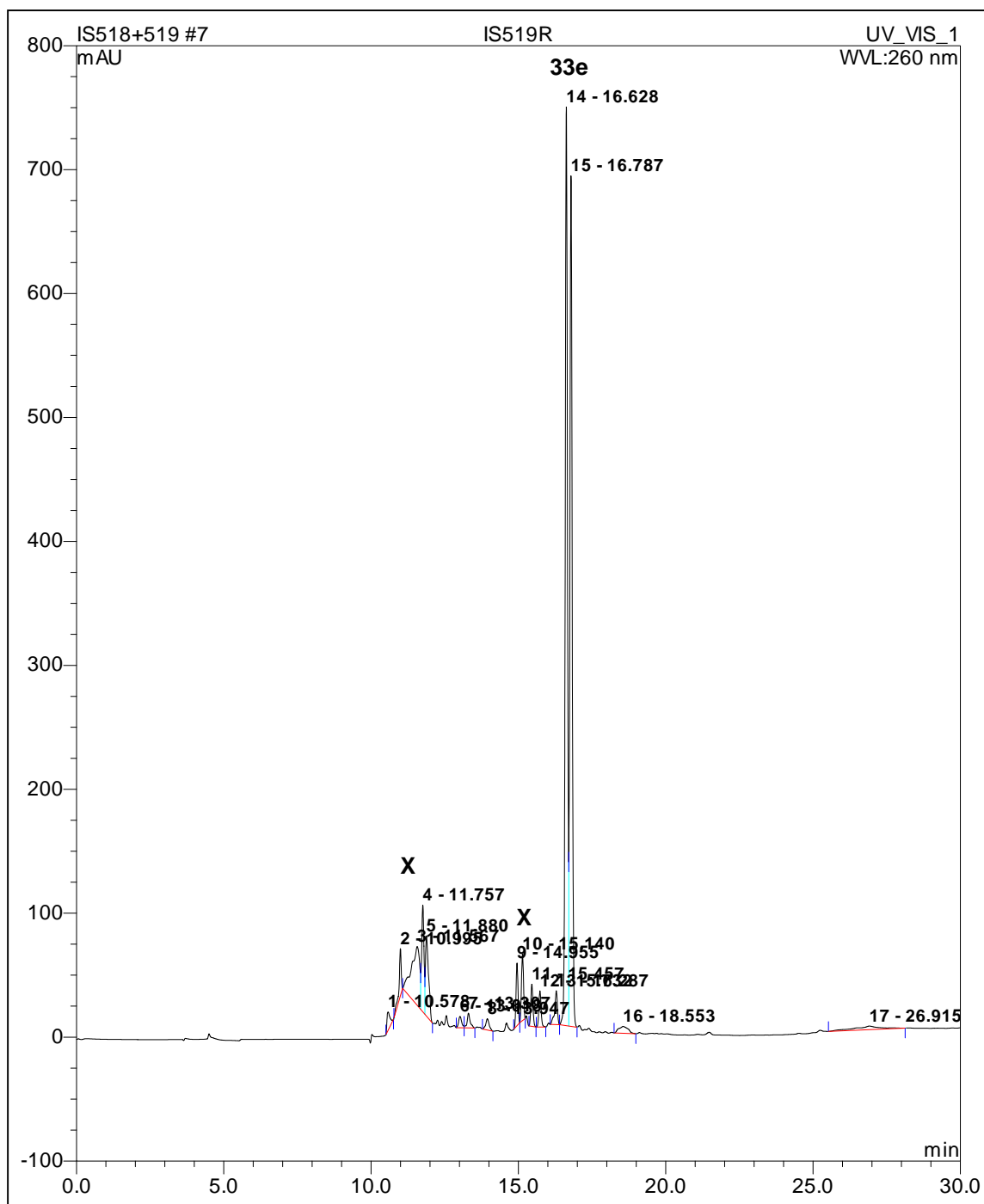
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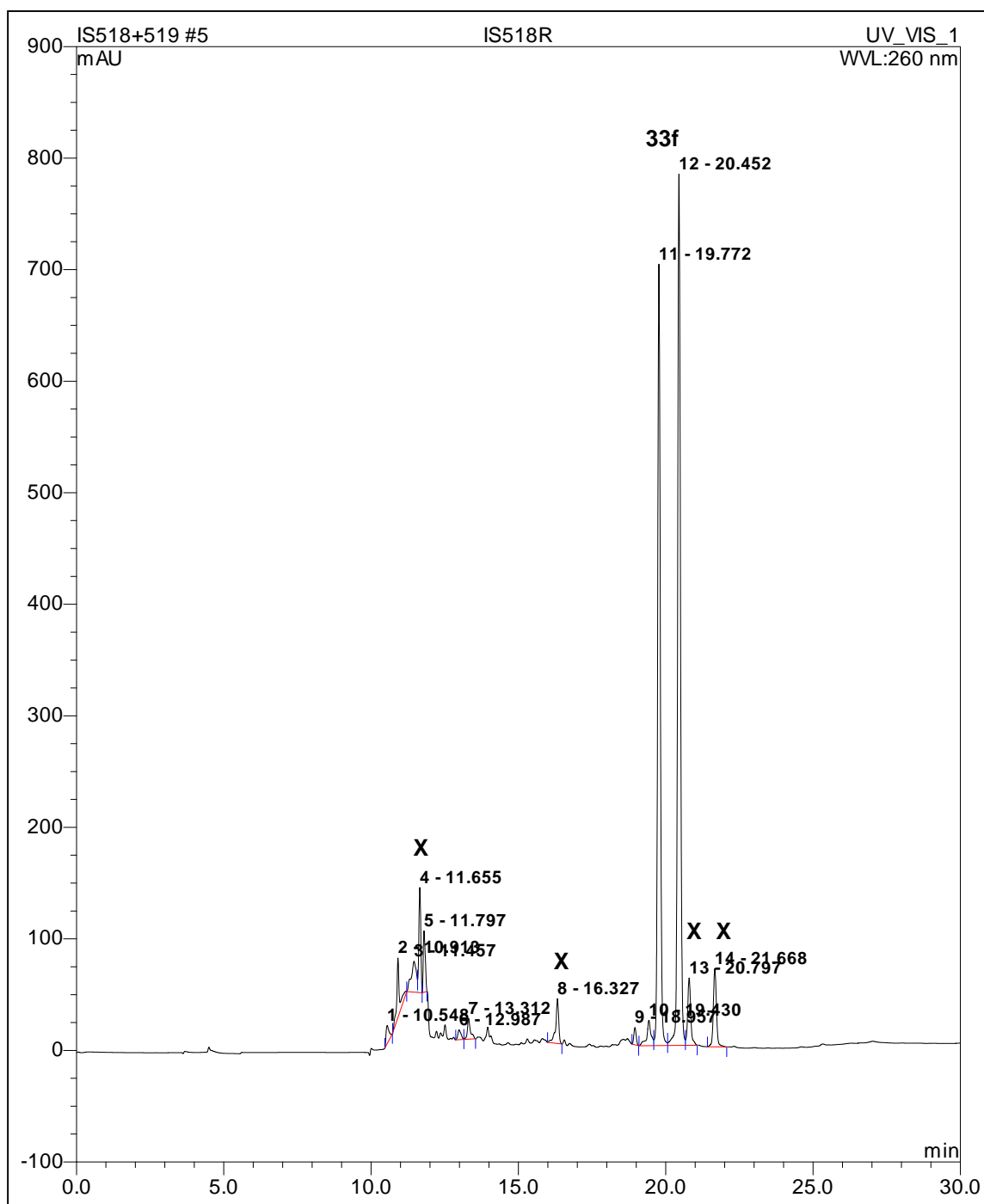


**Figure 18** Reversed-phase HPLC trace of crude **33d** (U<sub>4</sub>-pyrenyl isoxazole conjugate)

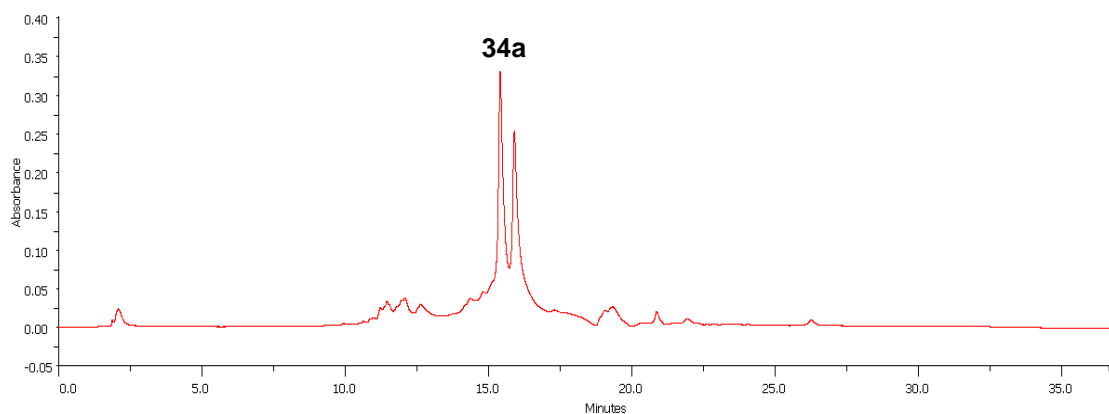


**Figure 19** Reversed-phase HPLC trace of crude **33e** ( $U_4$ -coumarinyl isoxazole conjugate)

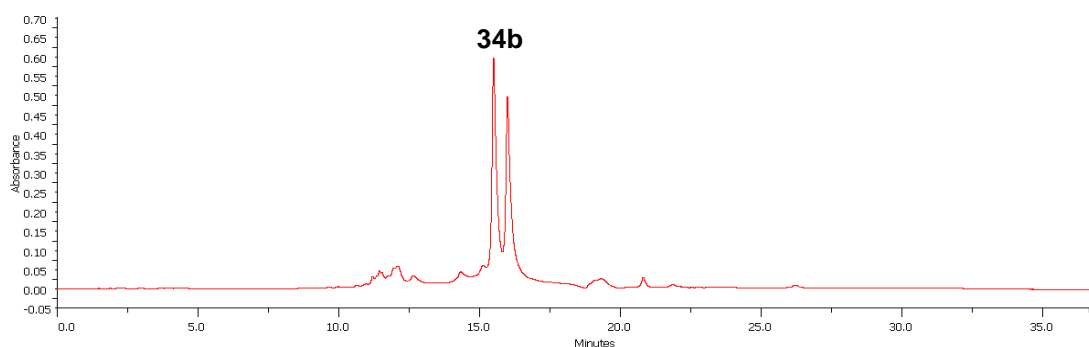




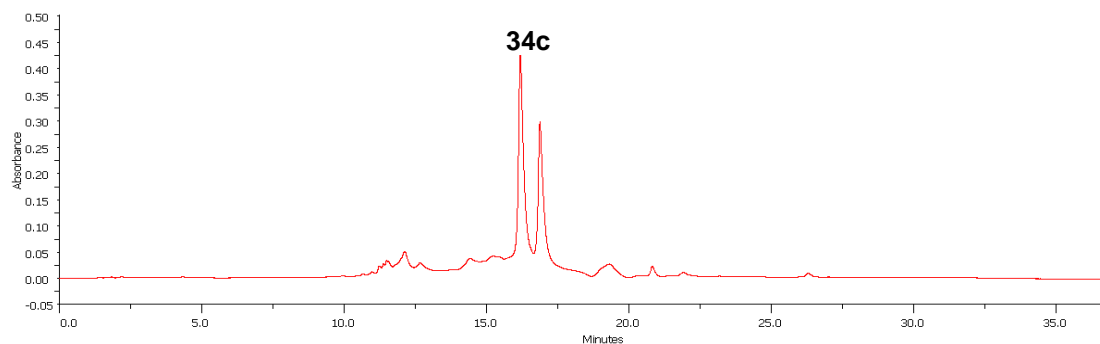
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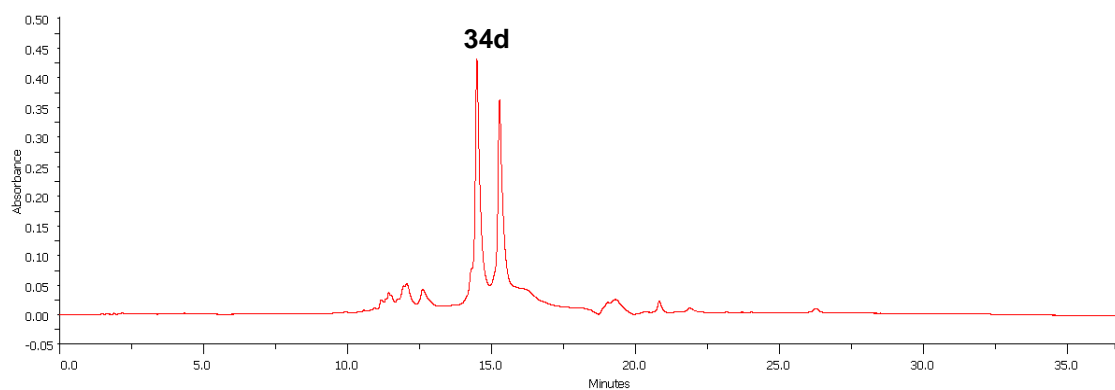
**Figure 21** Reversed-phase HPLC trace of crude **34a** (9-mer RNA phenyl isoxazole conjugate)



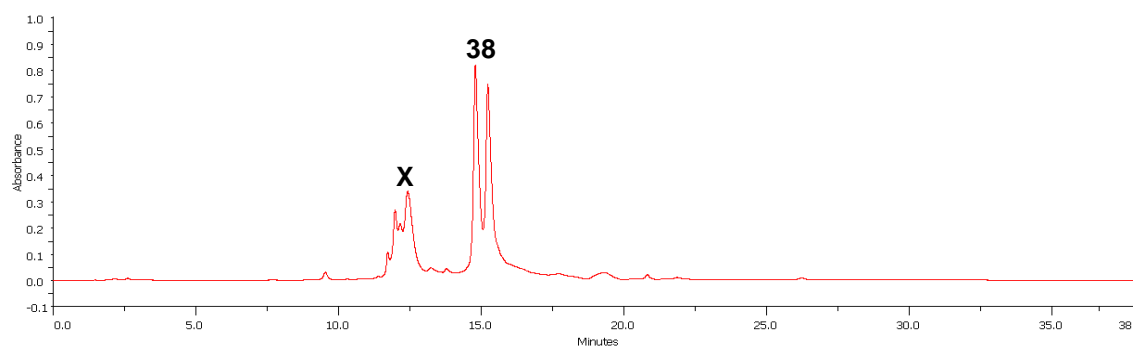
**Figure 22** Reversed-phase HPLC trace of crude **34b** (9-mer RNA 2-fluorophenyl isoxazole conjugate)



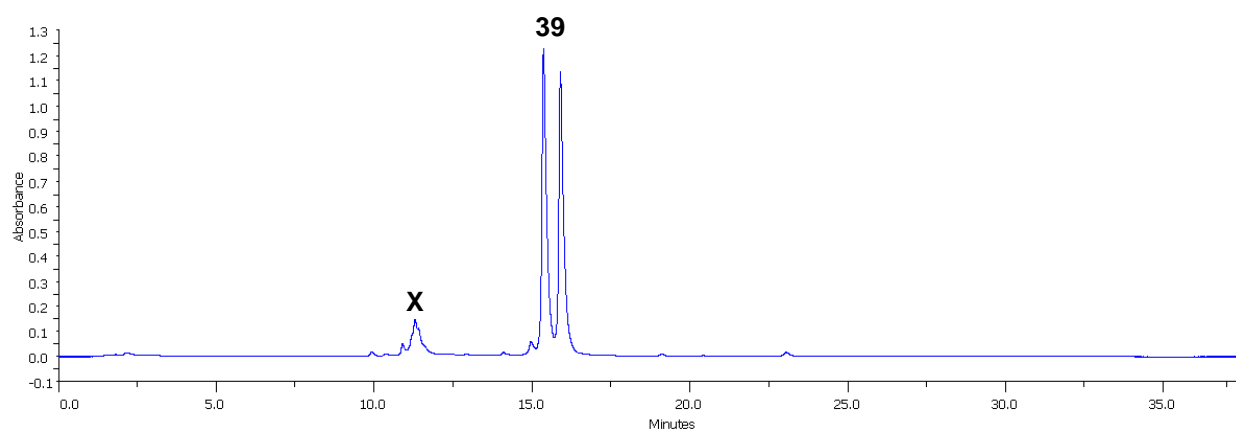
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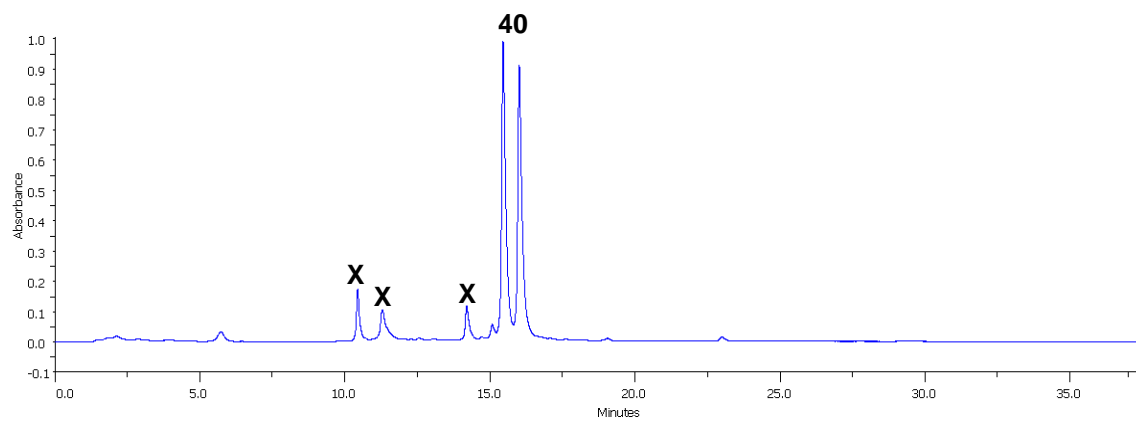
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**Figure 25** Reversed-phase HPLC trace of crude **38** (19-mer RNA phenyl isoxazole conjugate)



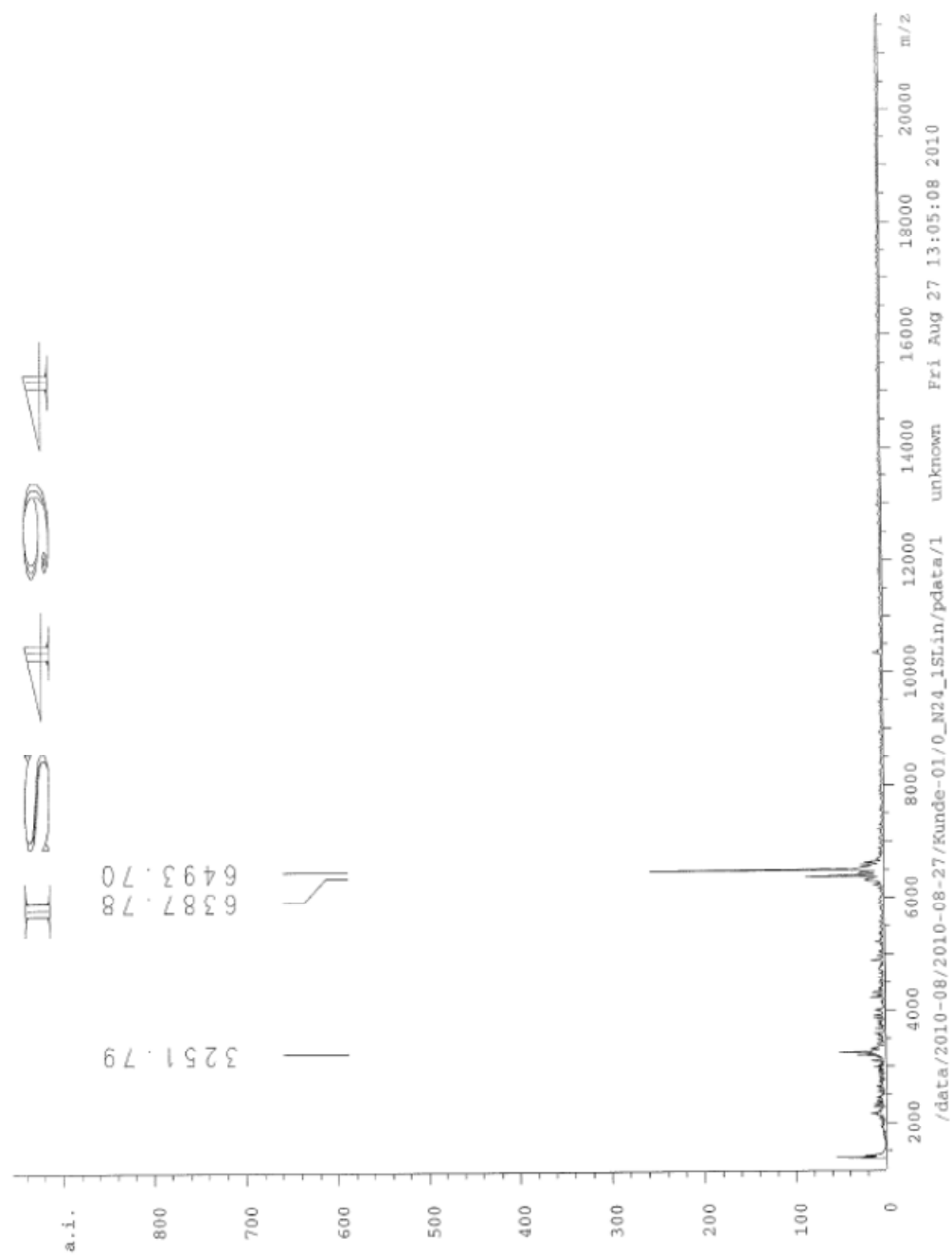
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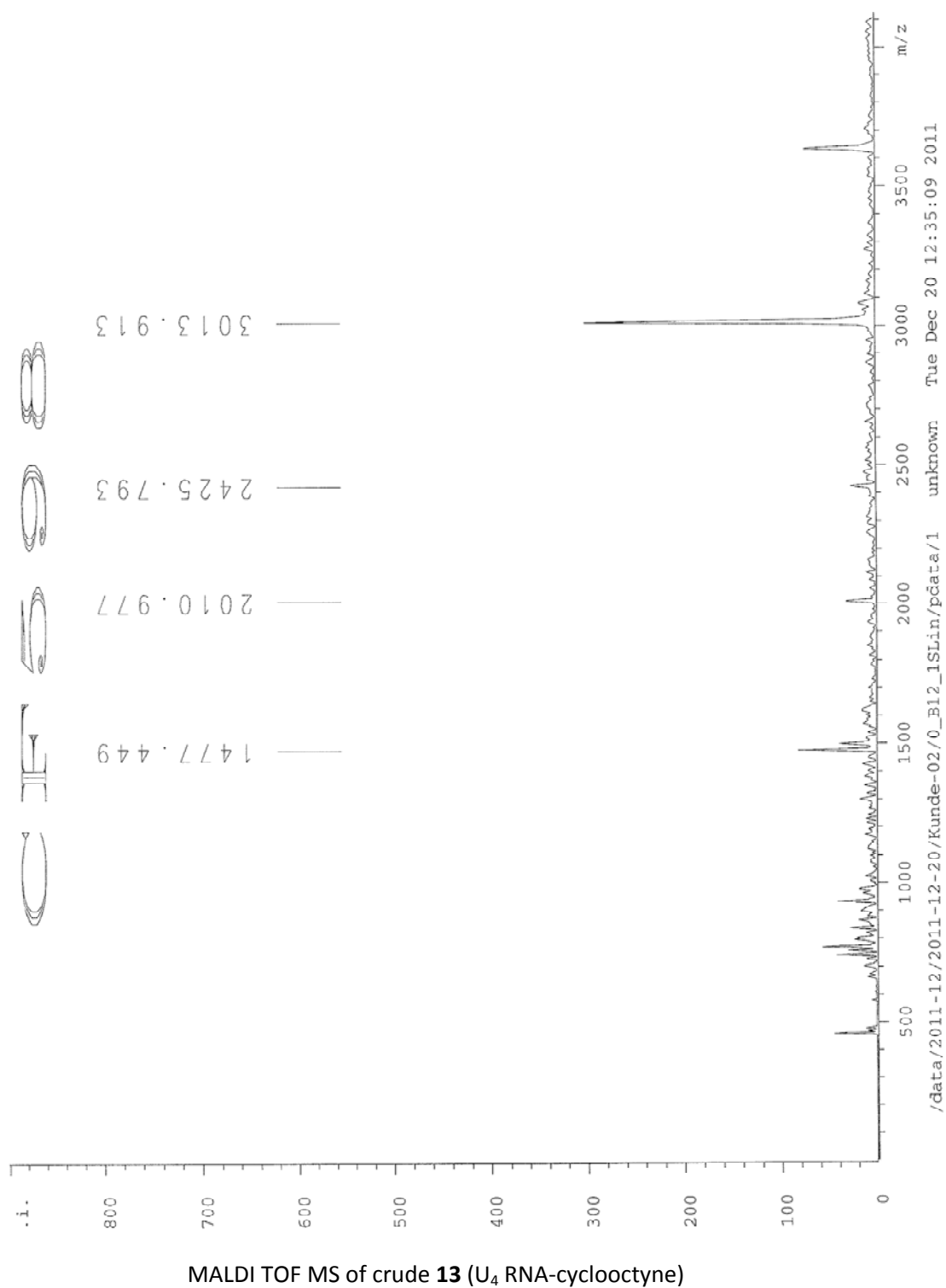
**Figure 27** Reversed-phase HPLC trace of crude **40** (gapmer phenyl isoxazole RNA-conjugate)

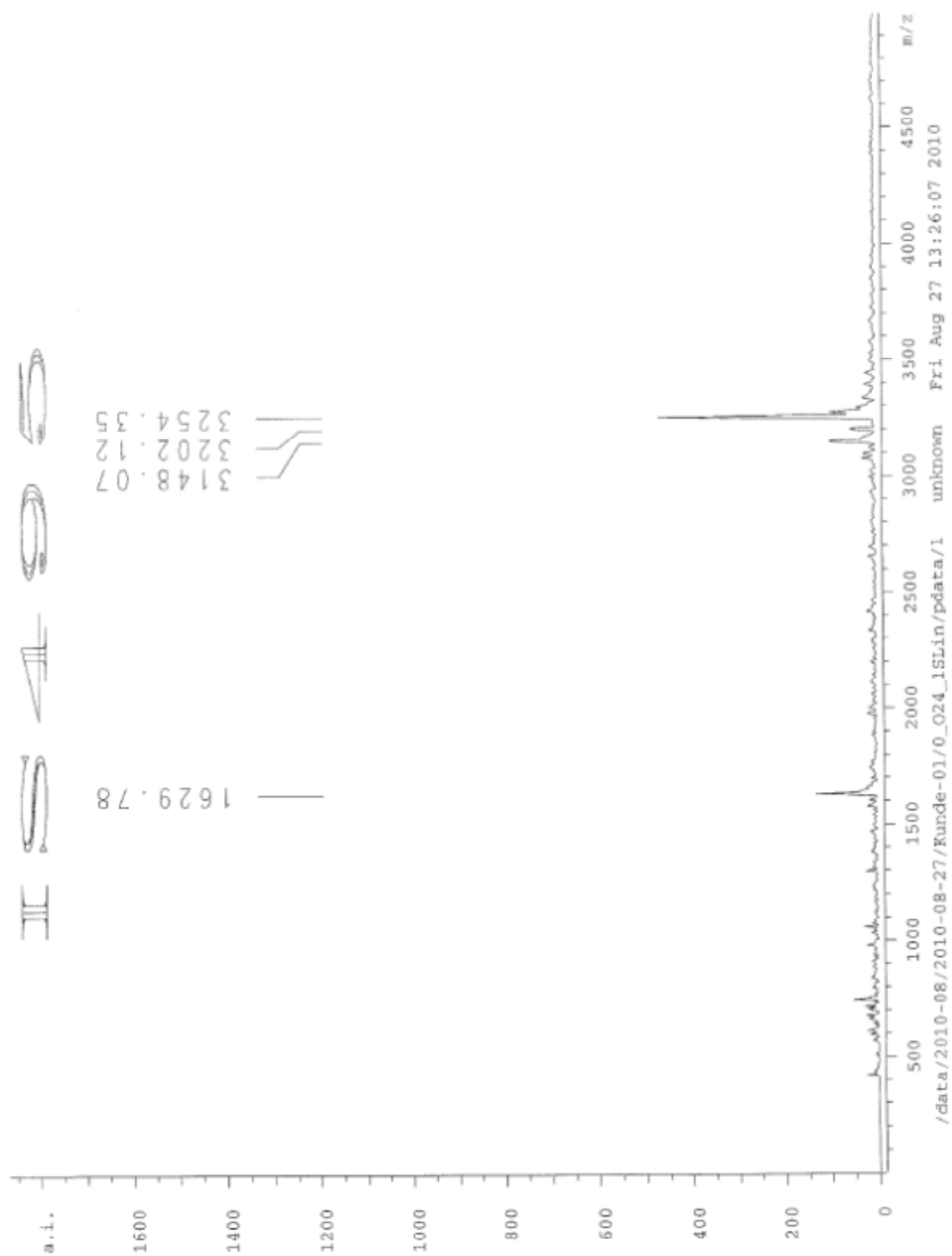
**Table 1: MALDI-TOF MS data**

<b>Compound no</b>	<b>RNA Mass calcd., found</b>	<b>Compound no</b>	<b>RNA Mass calcd., found</b>
<b>7</b>	6488, 6493	<b>33e</b>	1688, 1684
<b>8</b>	1476, 1477	<b>33f</b>	1744, 1746
<b>9</b>	3255, 3254	<b>34a</b>	3374, 3379
<b>10</b>	2115, 2118	<b>34b</b>	3392, 3393
<b>11</b>	1839, 1840	<b>34c</b>	3424, 3428
<b>23a</b>	6624, 6623	<b>34d</b>	3434, 3436
<b>23b</b>	6650, 6650	<b>38</b>	6607, 6611
<b>23c</b>	6831, 6833	<b>39</b>	2234, 2238
<b>23d</b>	7018, 7020	<b>40</b>	1958, 1960
<b>23e</b>	6931, 6934		
<b>33a</b>	1595, 1596		
<b>33b</b>	1613, 1614		
<b>33c</b>	1645, 1647		
<b>33d</b>	1719, 1721		

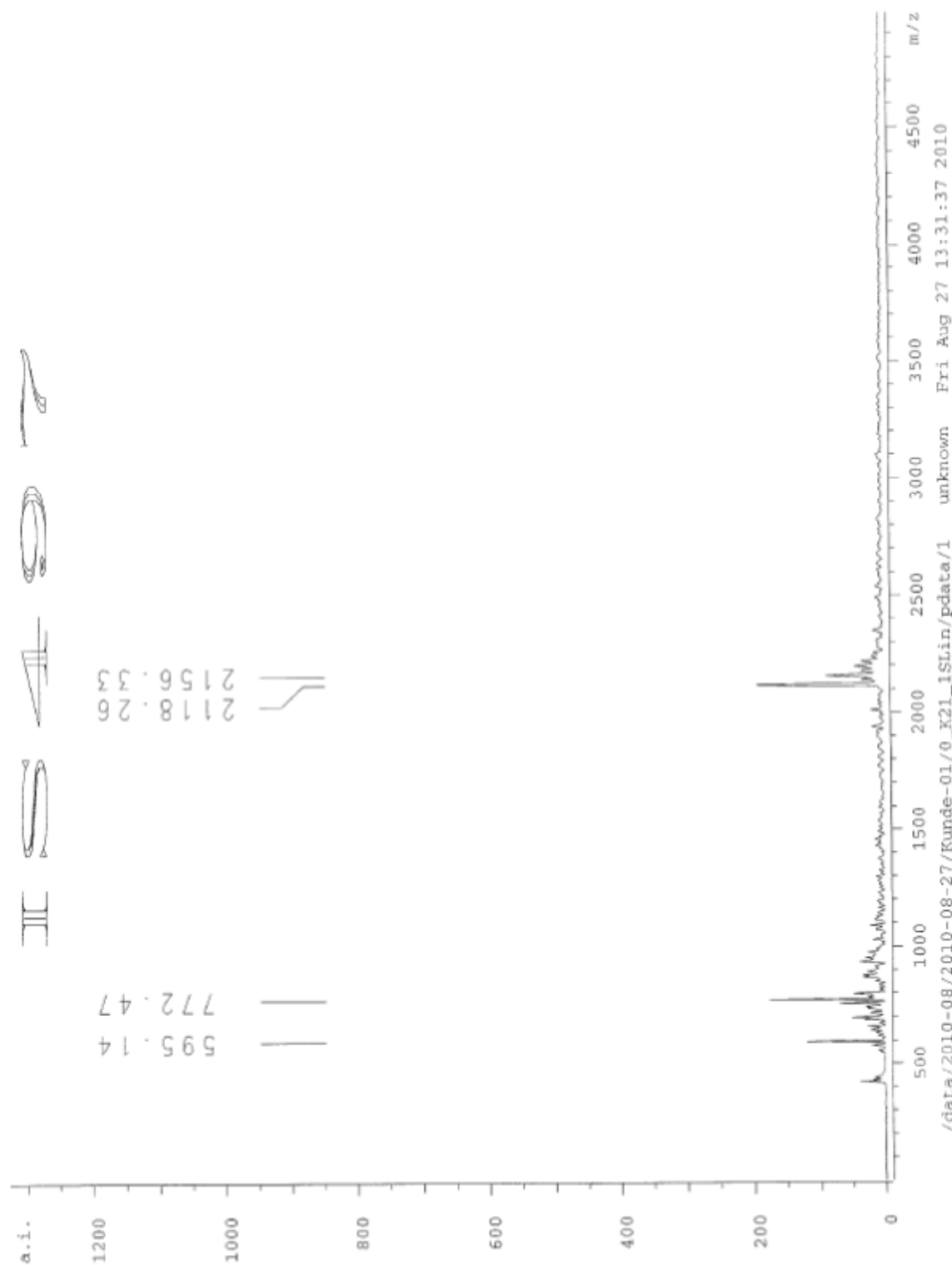


MALDI TOF MS of crude **12** (19-mer RNA-cyclooctyne)



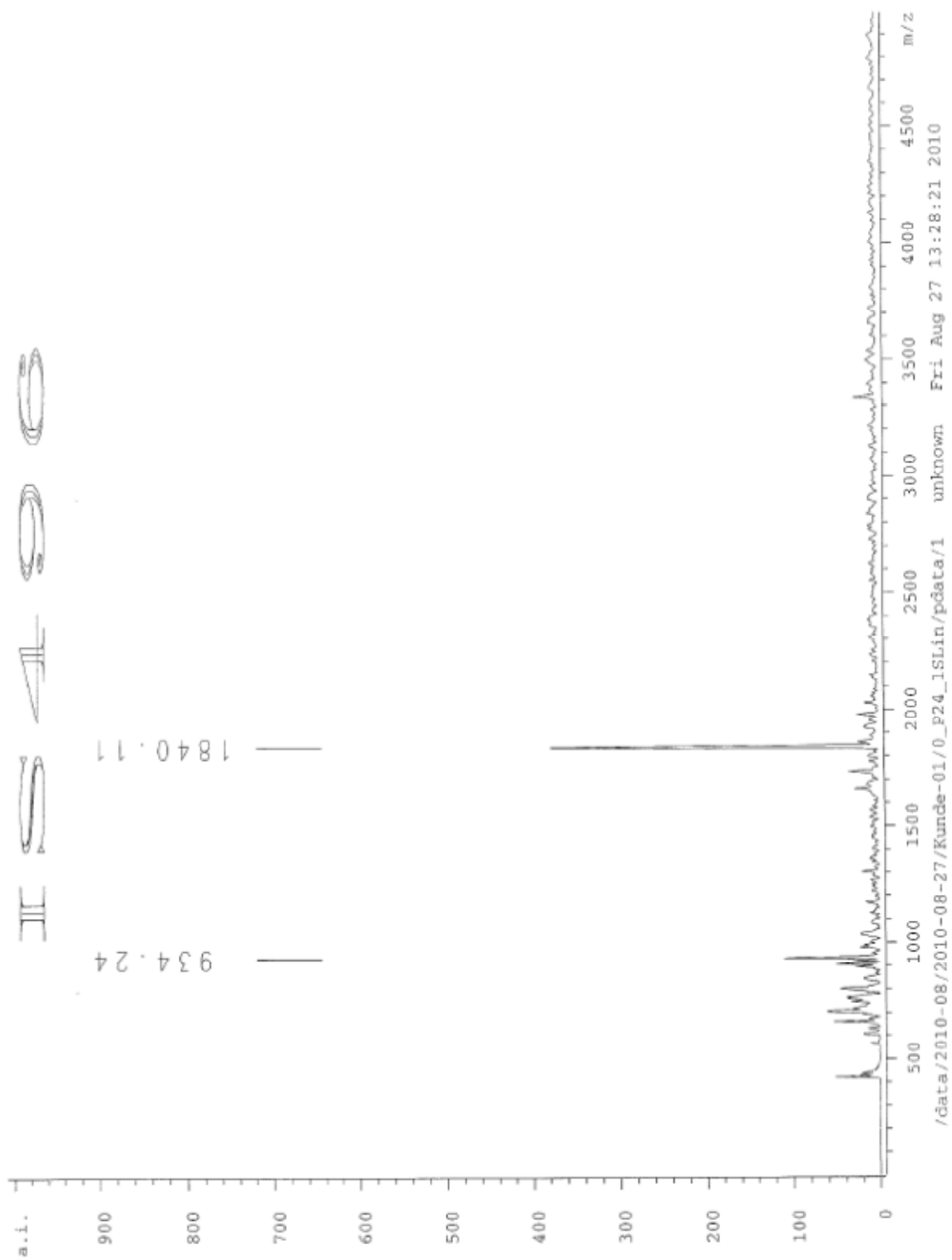


MALDI TOF MS of crude **14** (9-mer RNA-cyclooctyne)

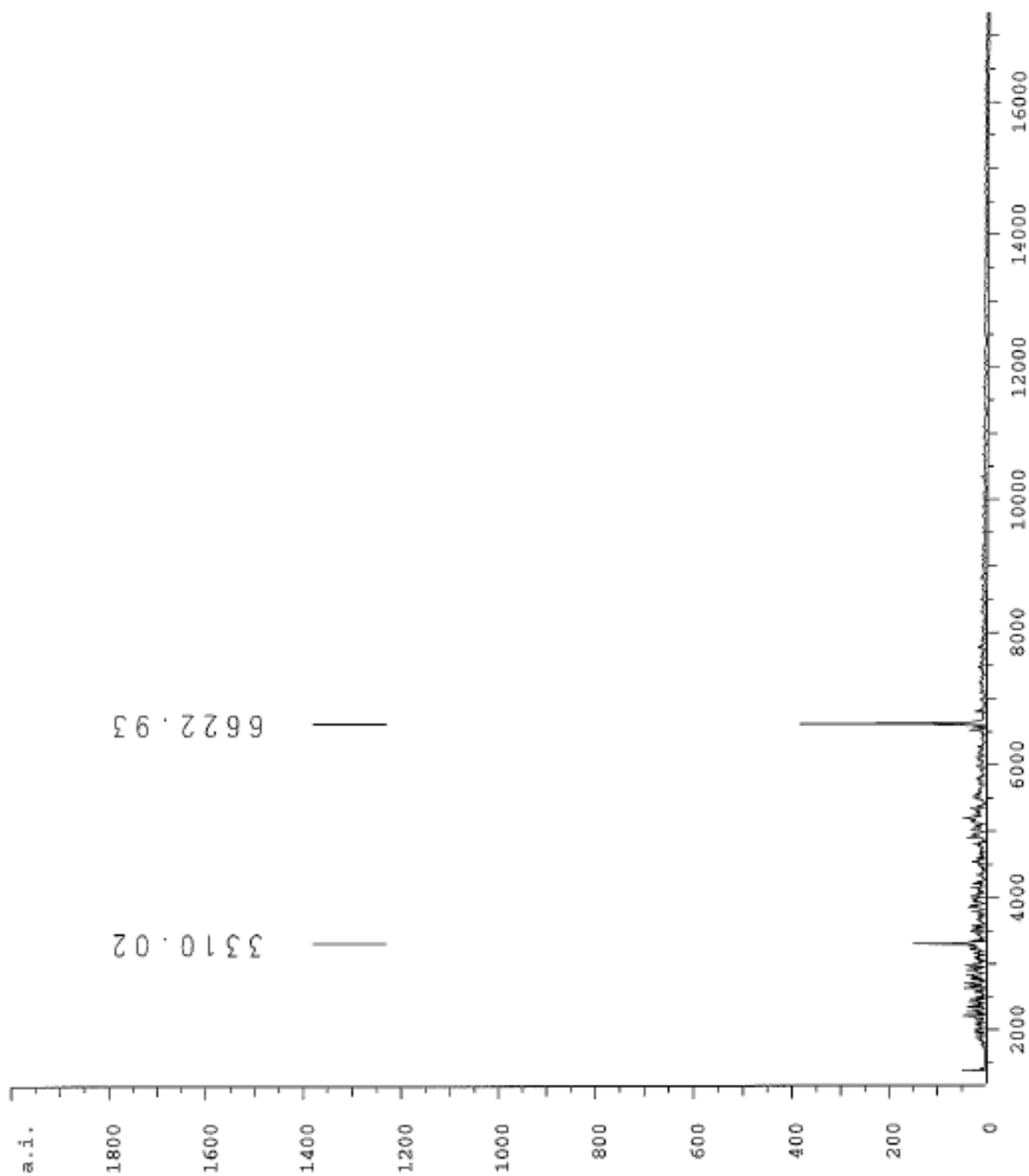


MALDI TOF MS of crude **15** (U<sub>6</sub>-alternate RNA-cyclooctyne)

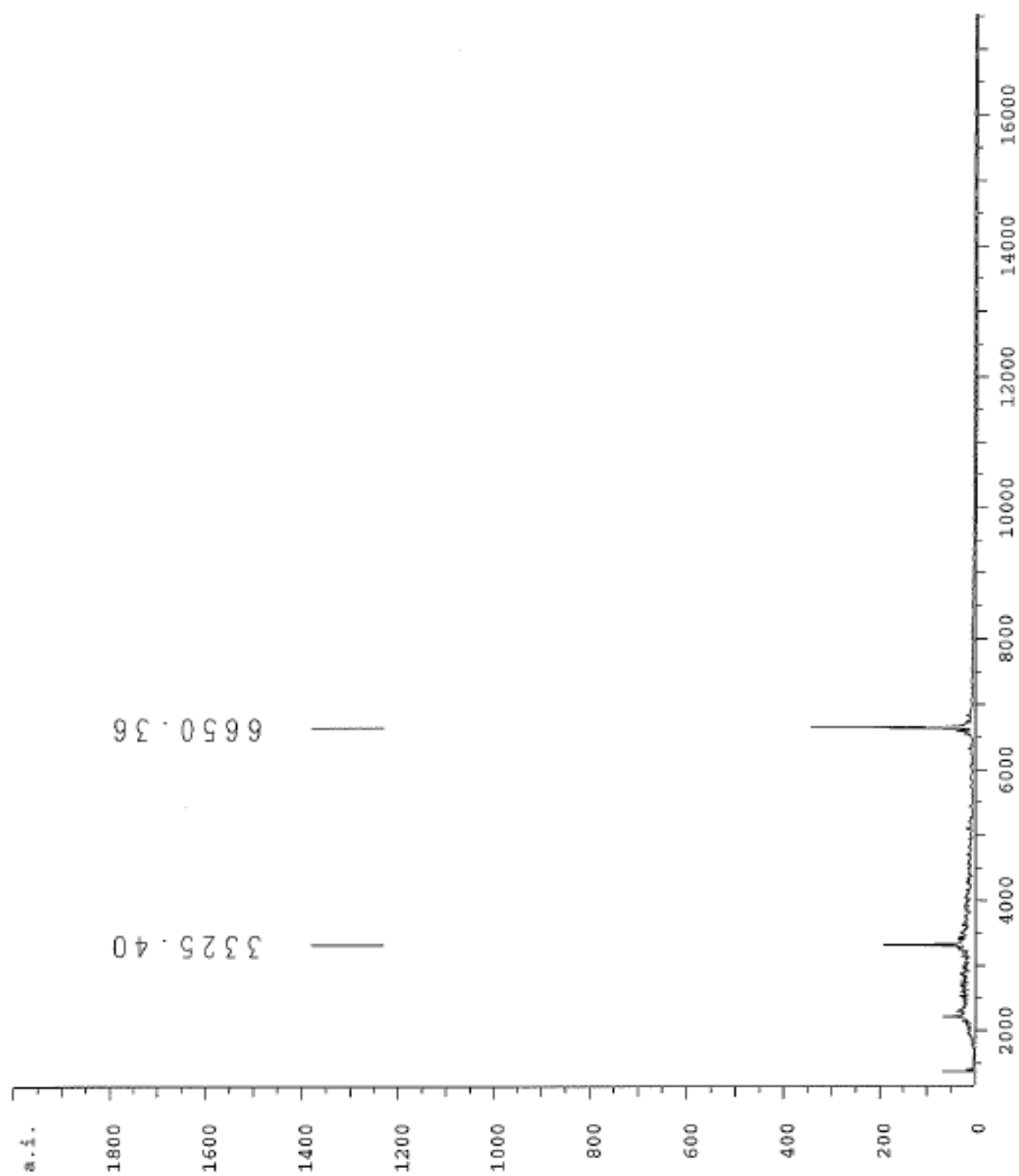




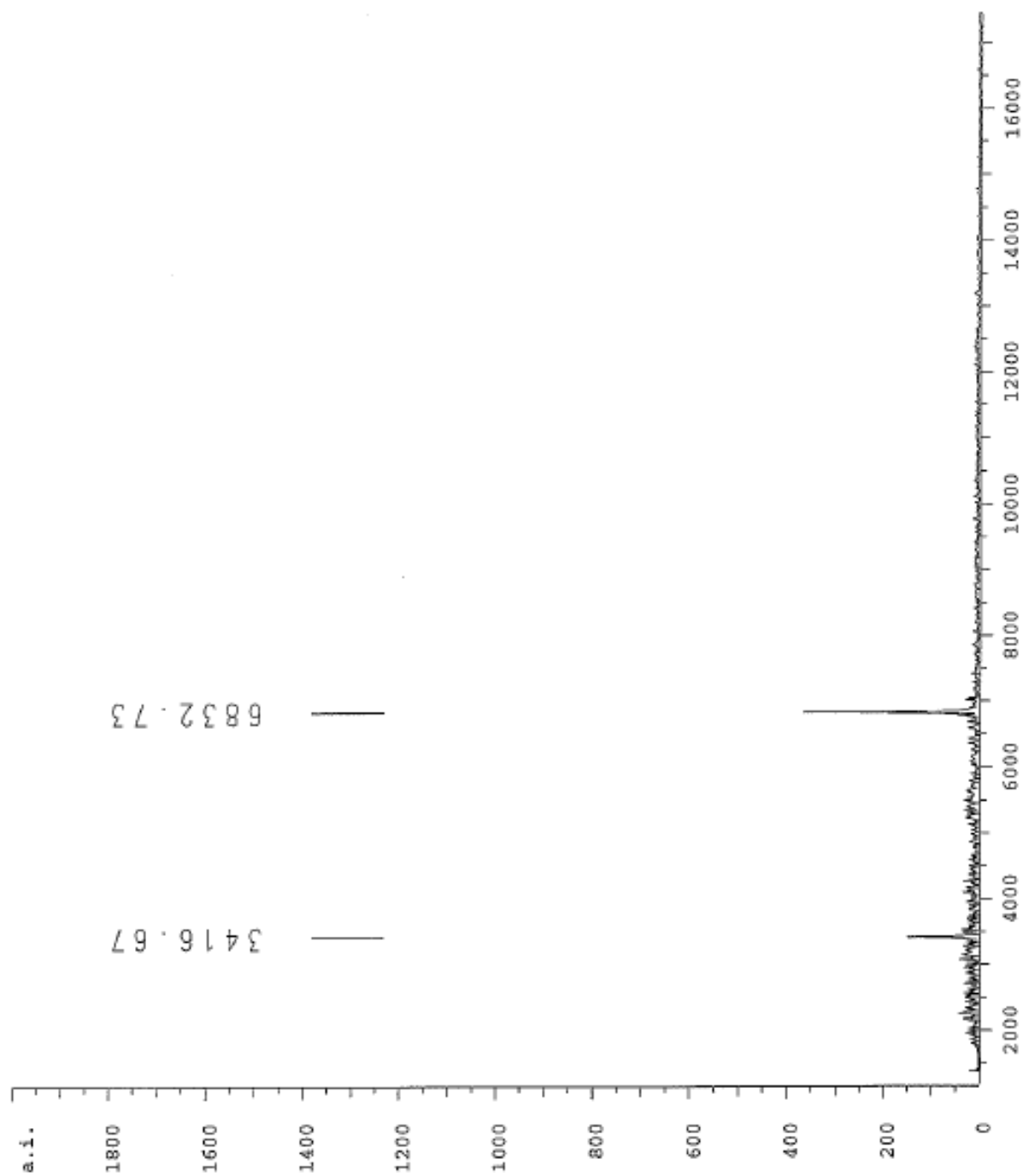
MALDI TOF MS of crude **16** (gapmer RNA-cyclooctyne)



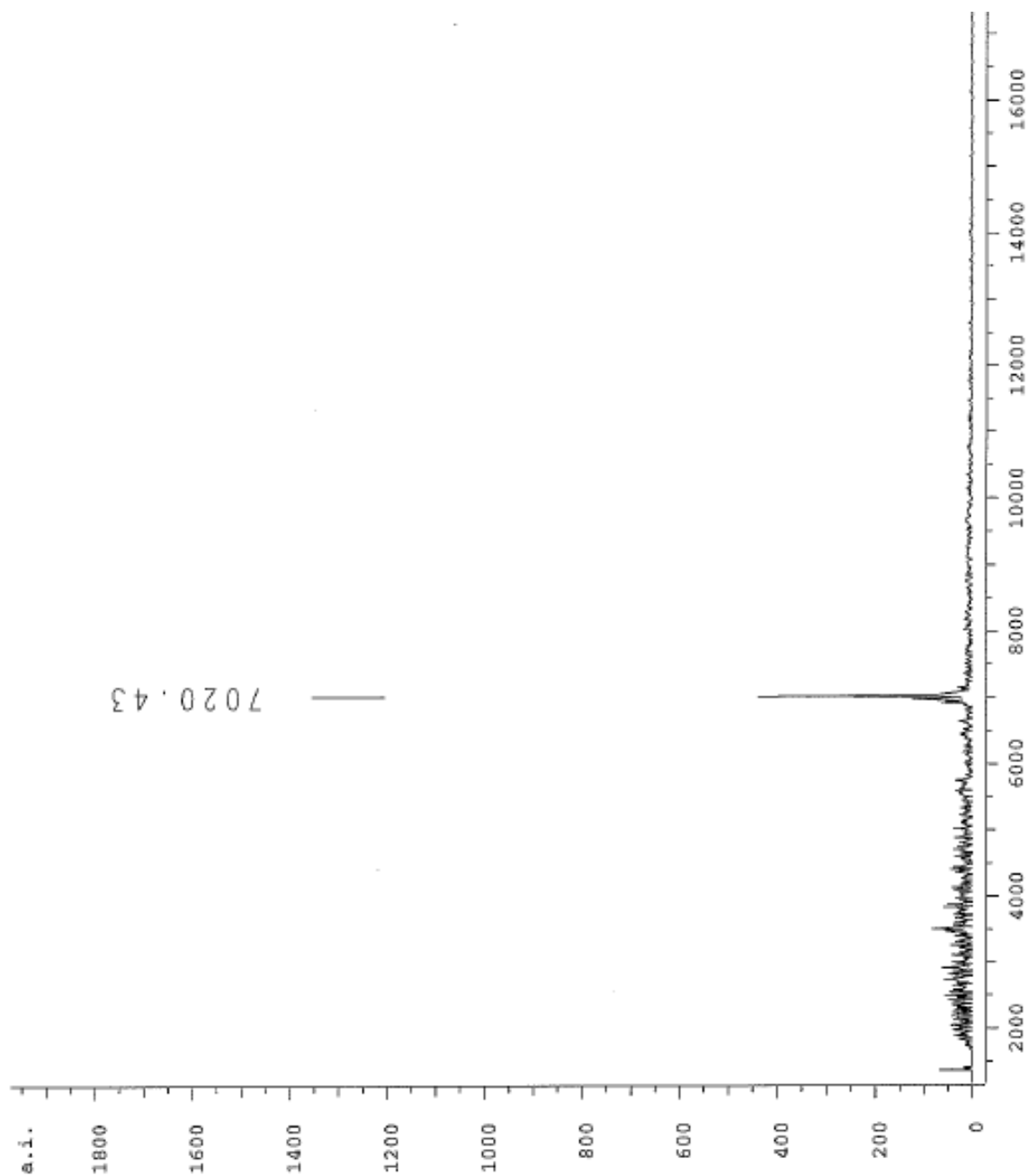
MALDI TOF MS of pure **23a** (19-mer RNA benzyl triazole conjugate)



MALDI TOF MS of pure **23b** (19-mer RNA cinamoyl triazole conjugate)



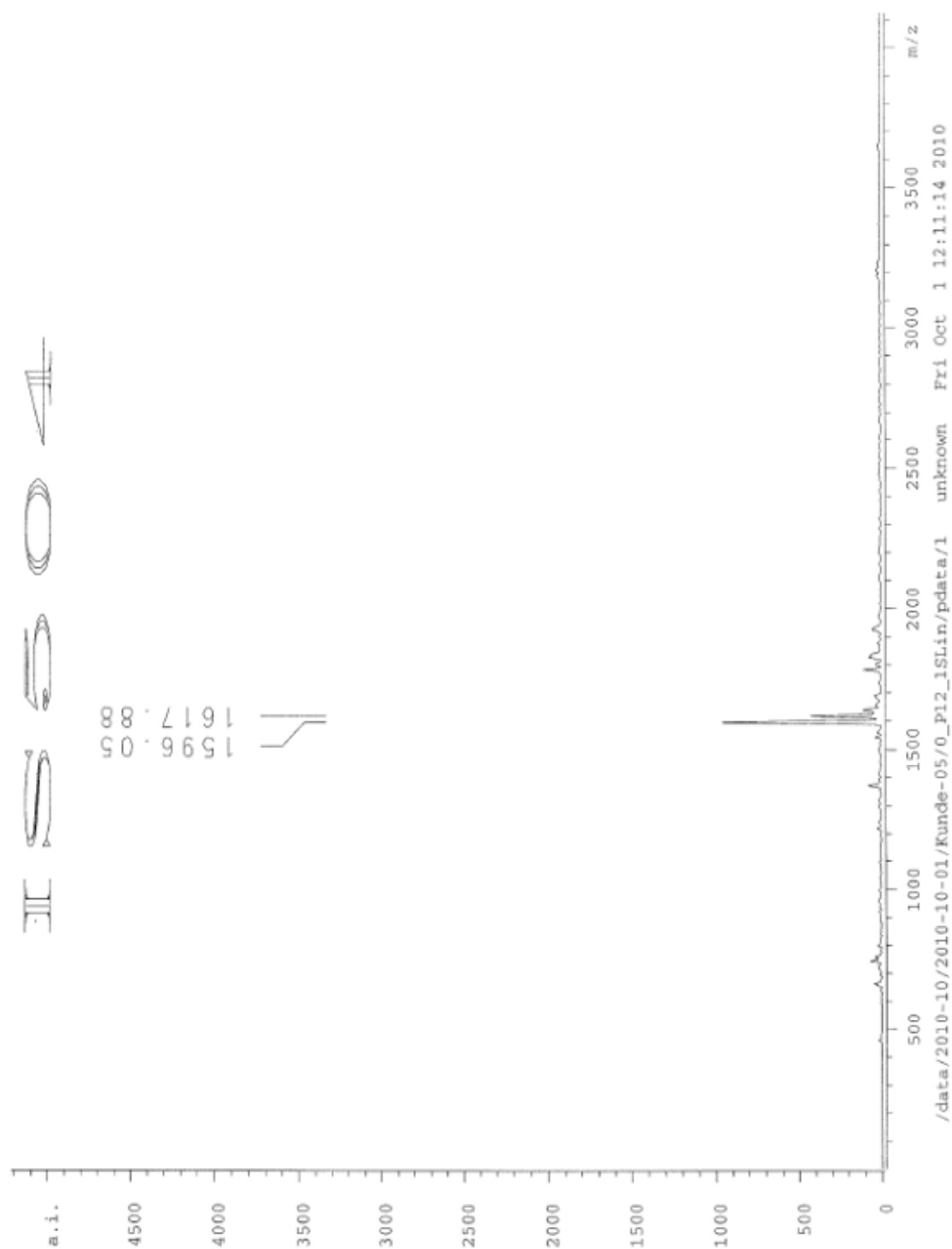
MALDI TOF MS of pure **23c** (19-mer RNA biotinyl triazole conjugate)



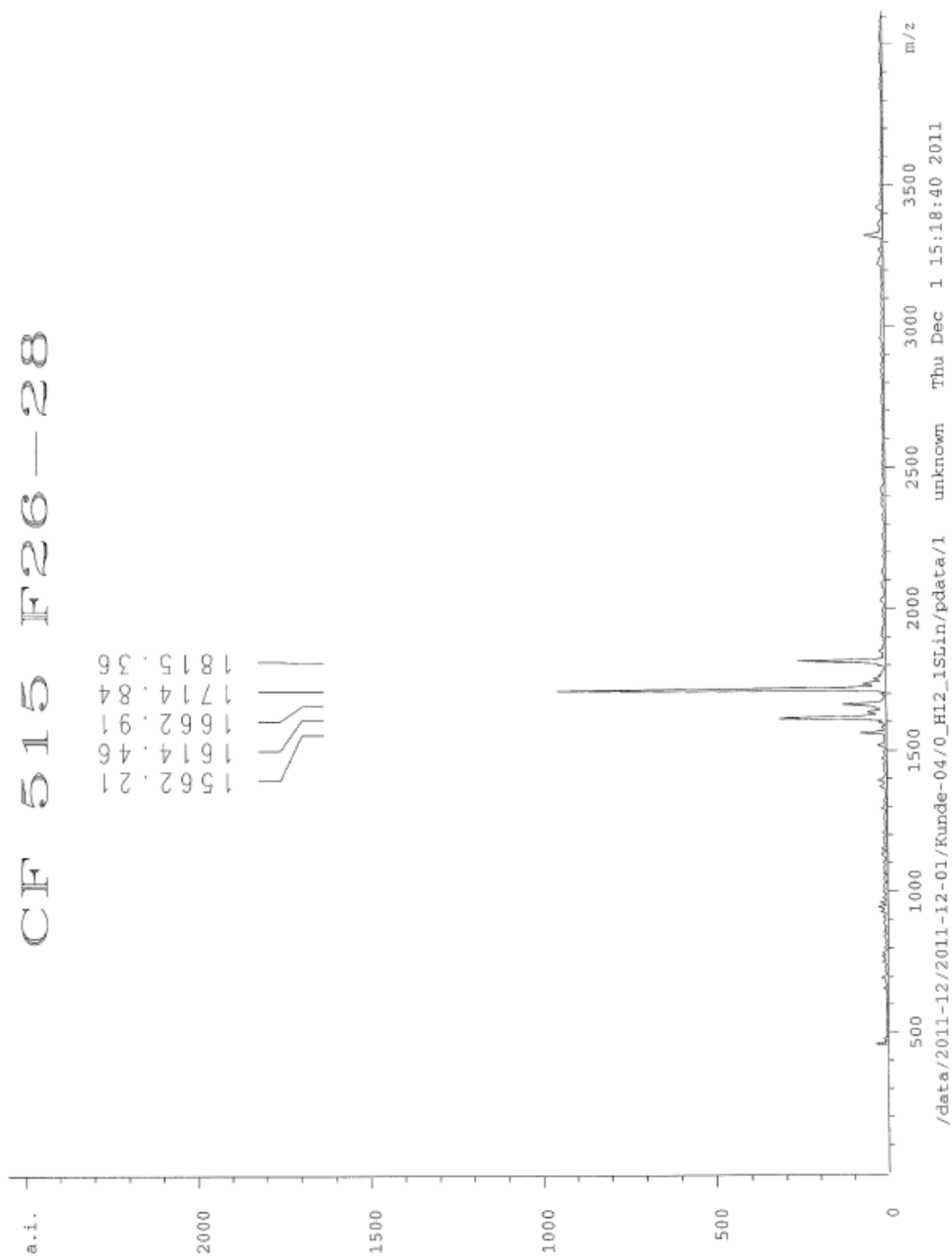
MALDI TOF MS of **23d** (19-mer RNA cholesteryl triazole conjugate)



MALDI TOF MS of pure **23e** (19-mer RNA fluoresceinyl triazole conjugate)

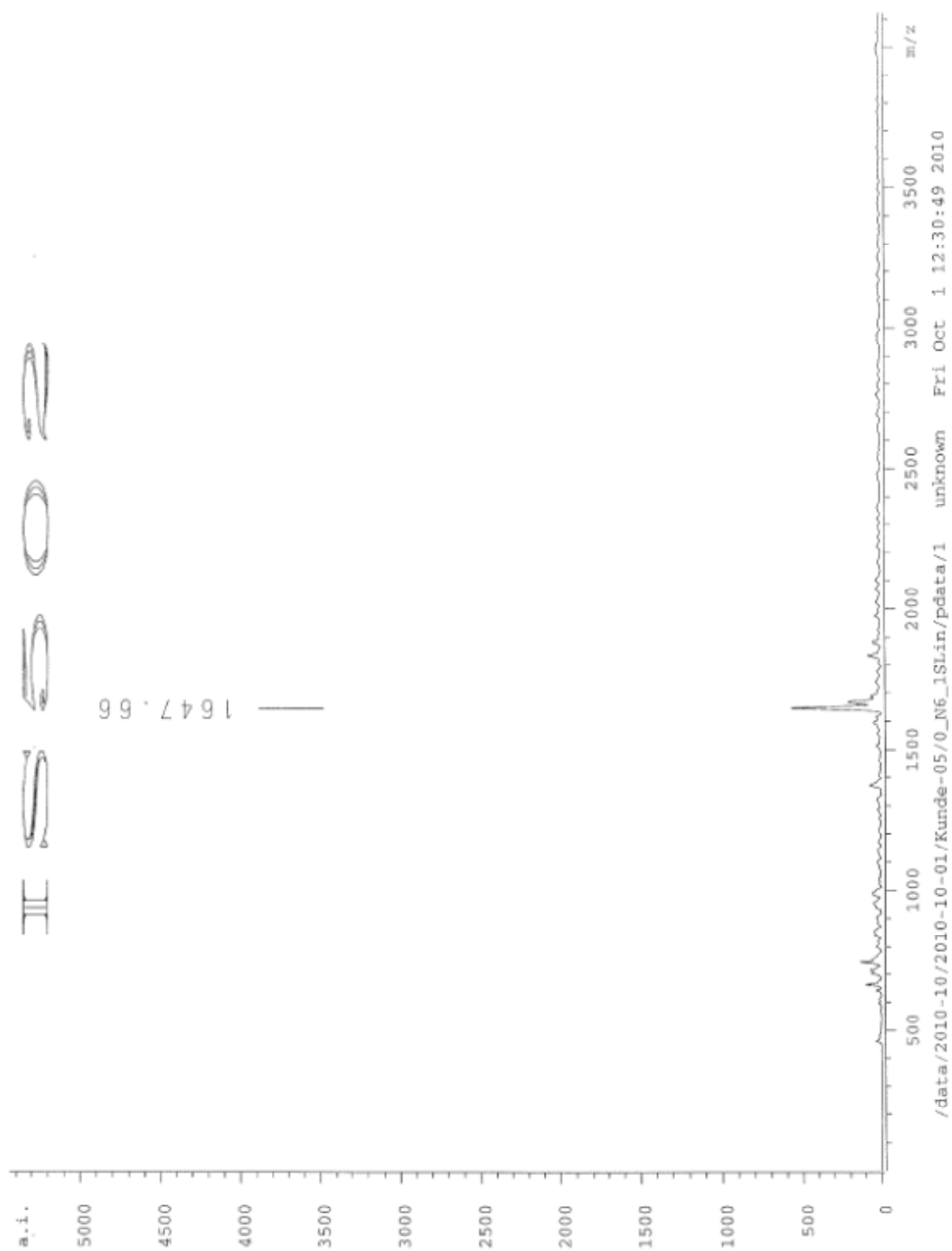


MALDI TOF MS of crude **33a** (U<sub>4</sub>-phenyl isoxazole RNA-conjugate)

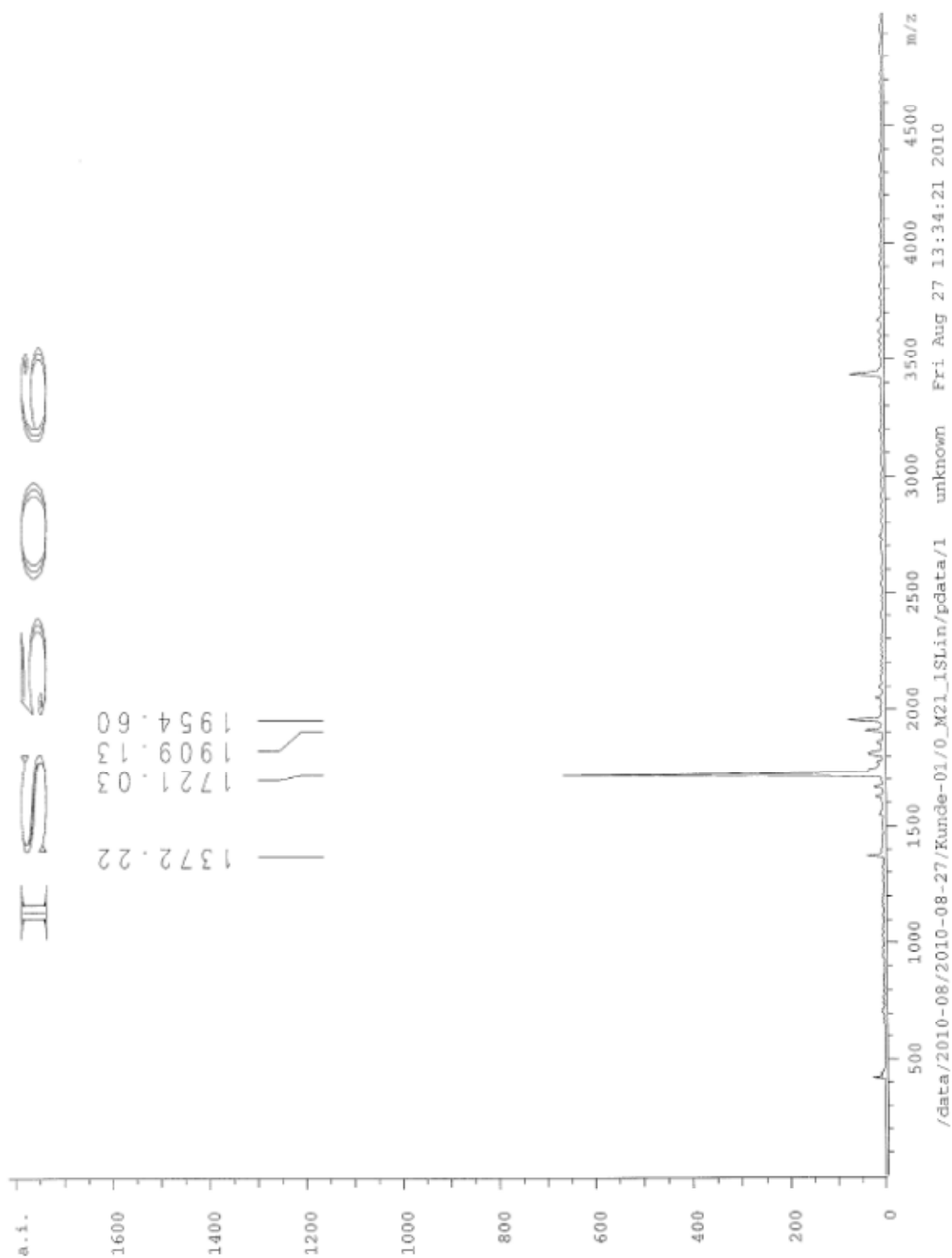


MALDI TOF MS of crude **33b** (U<sub>4</sub>-2-fluorophenyl isoxazole RNA-conjugate)

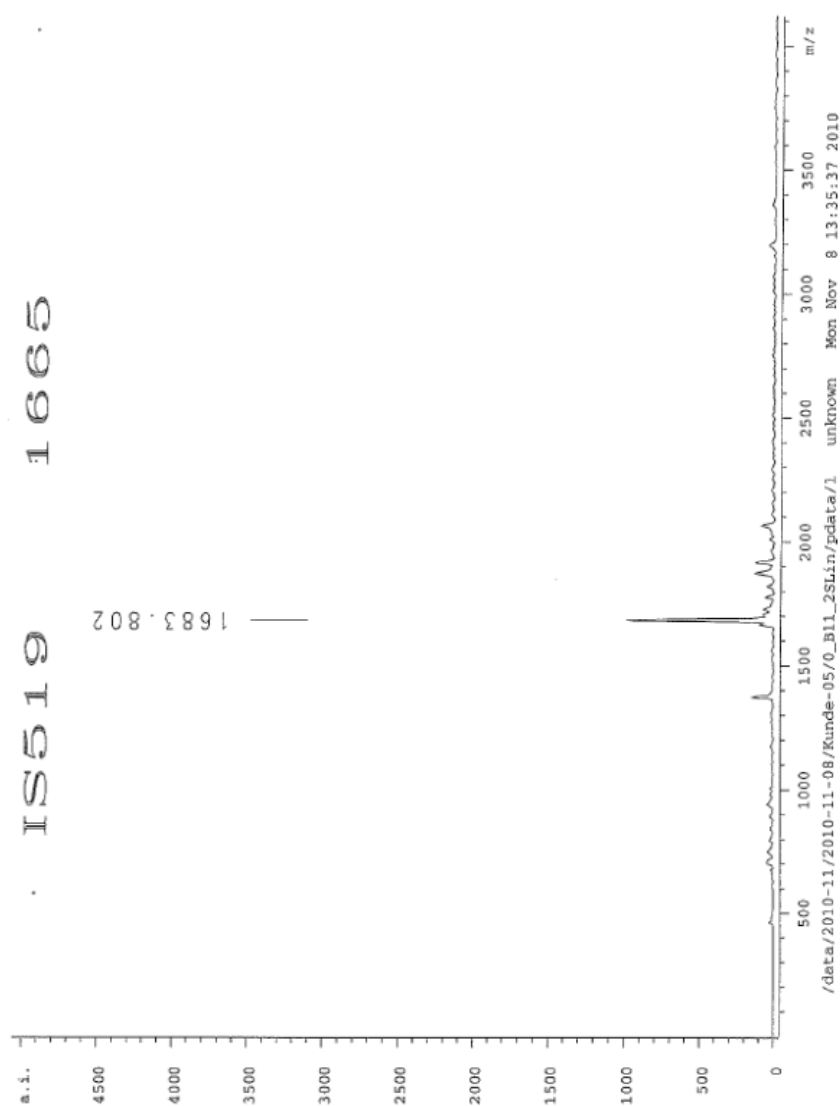




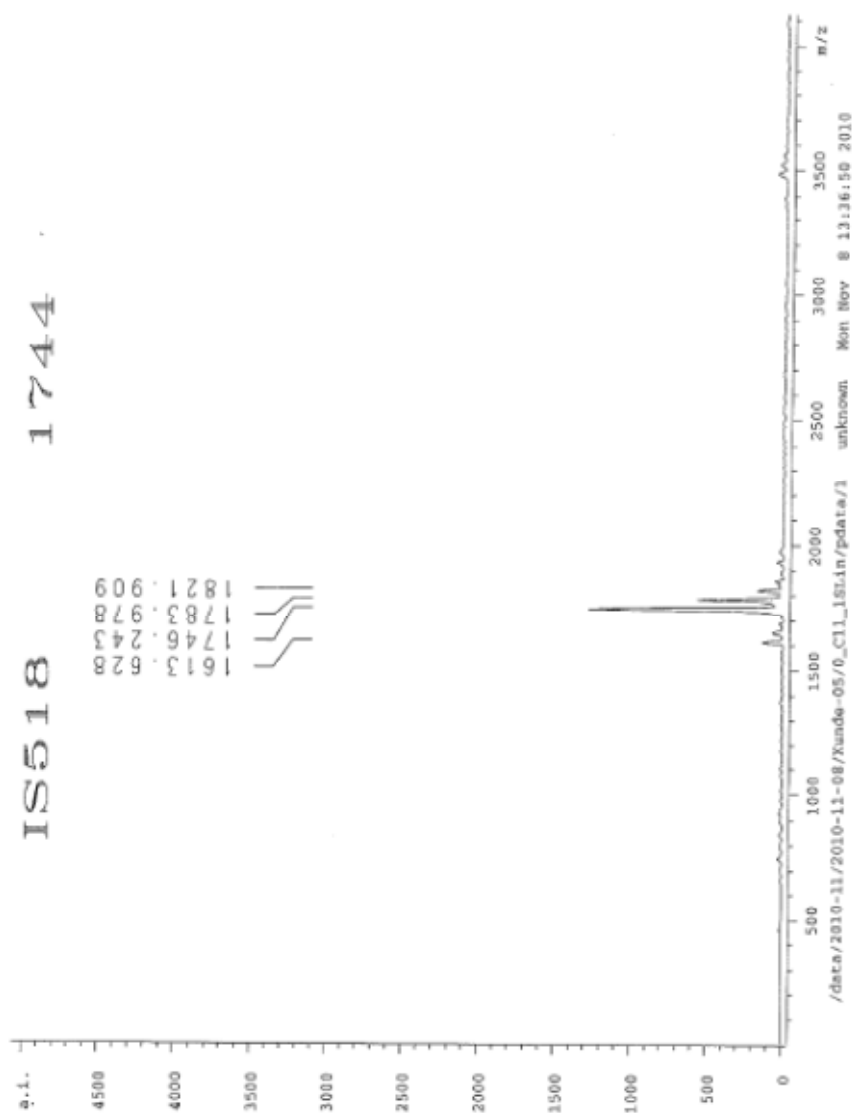
MALDI TOF MS of crude **33c** ( $U_4$ -naphthyl isoxazole RNA-conjugate)



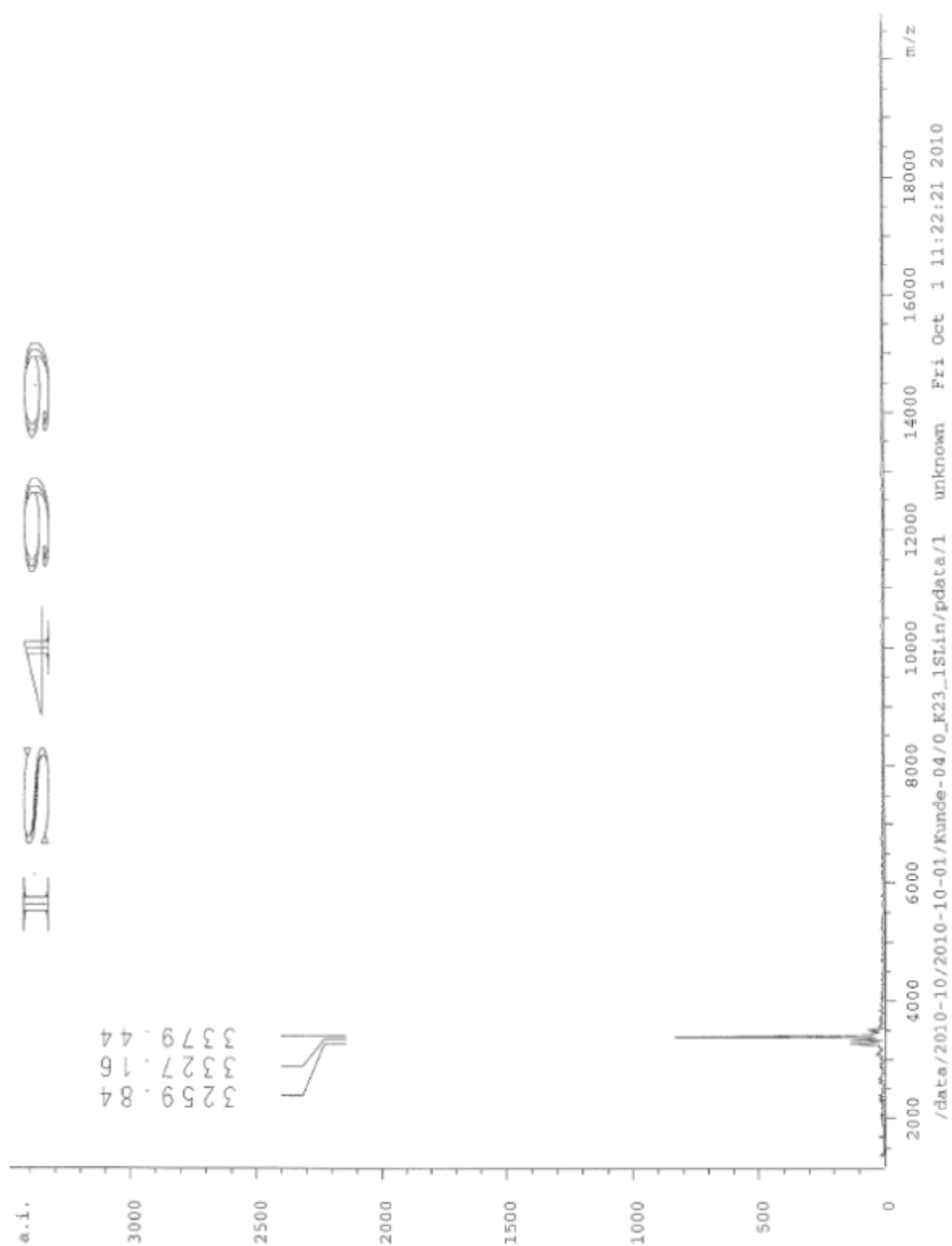
MALDI TOF MS of crude **33d** (U<sub>4</sub>-pyrene isoxazole RNA-conjugate)



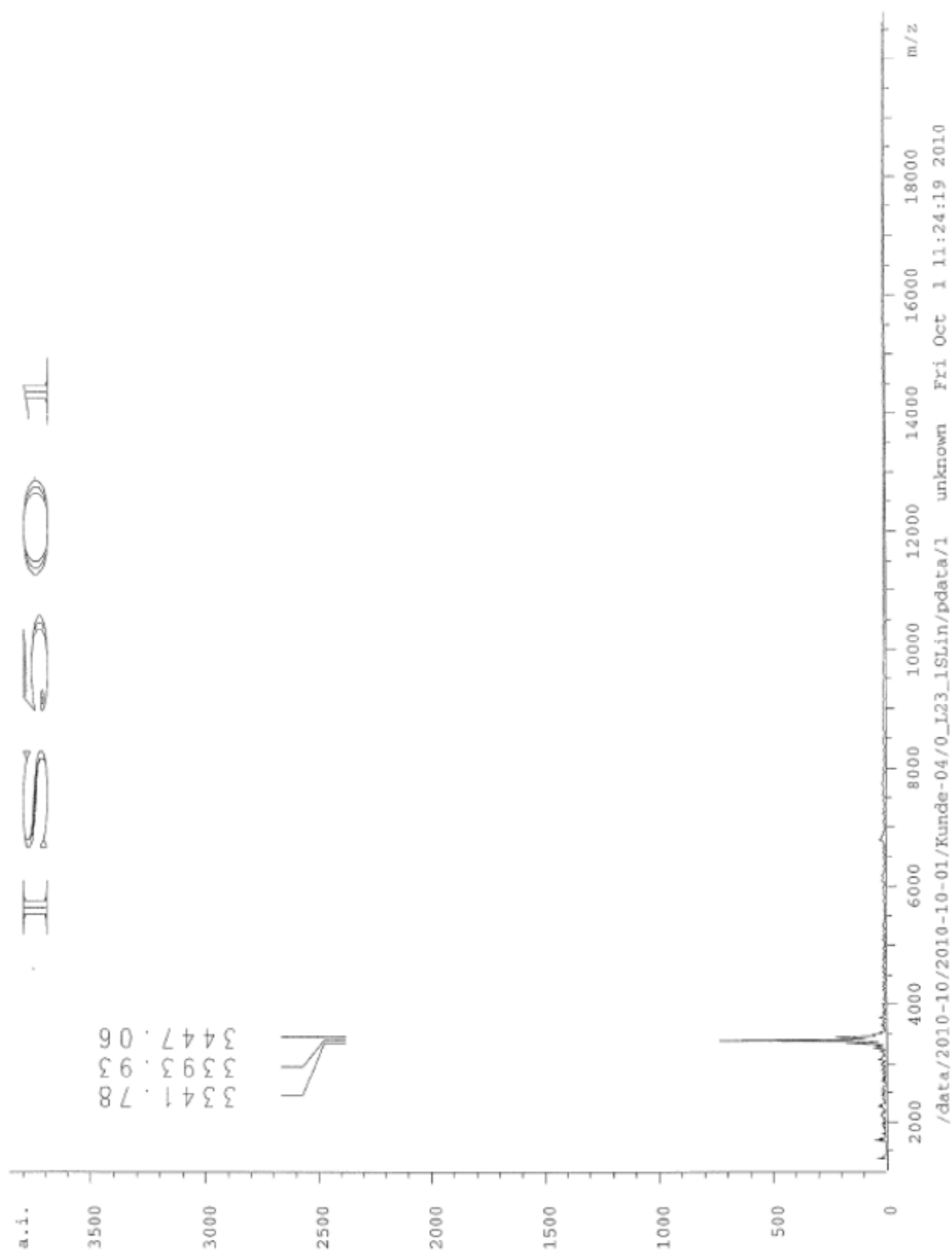
MALDI TOF MS of crude **33e** ( $U_4$ -coumarinyl isoxazole RNA-conjugate)



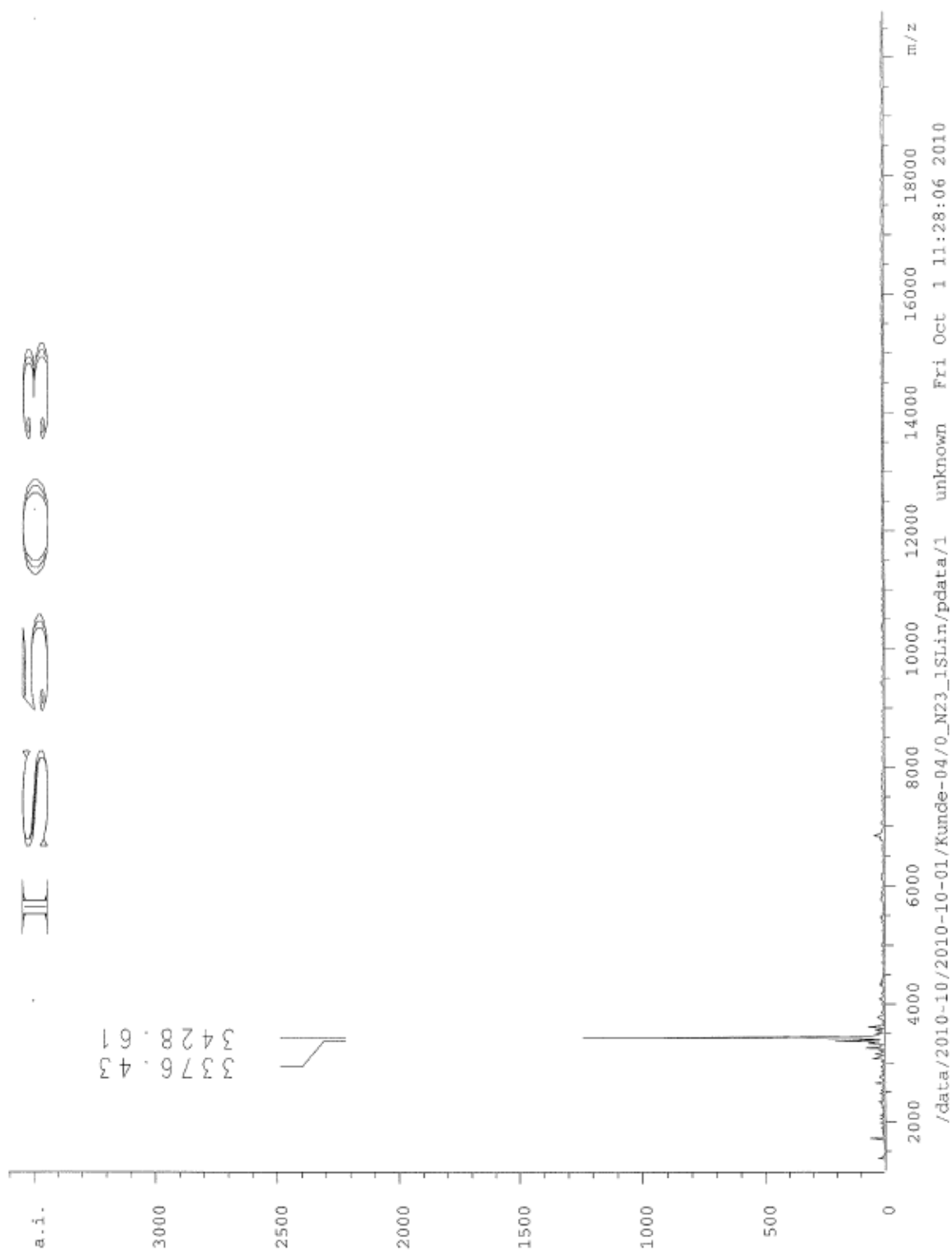
MALDI TOF MS of crude **33f** ( $U_4$ -dabcyI isoxazole RNA-conjugate)



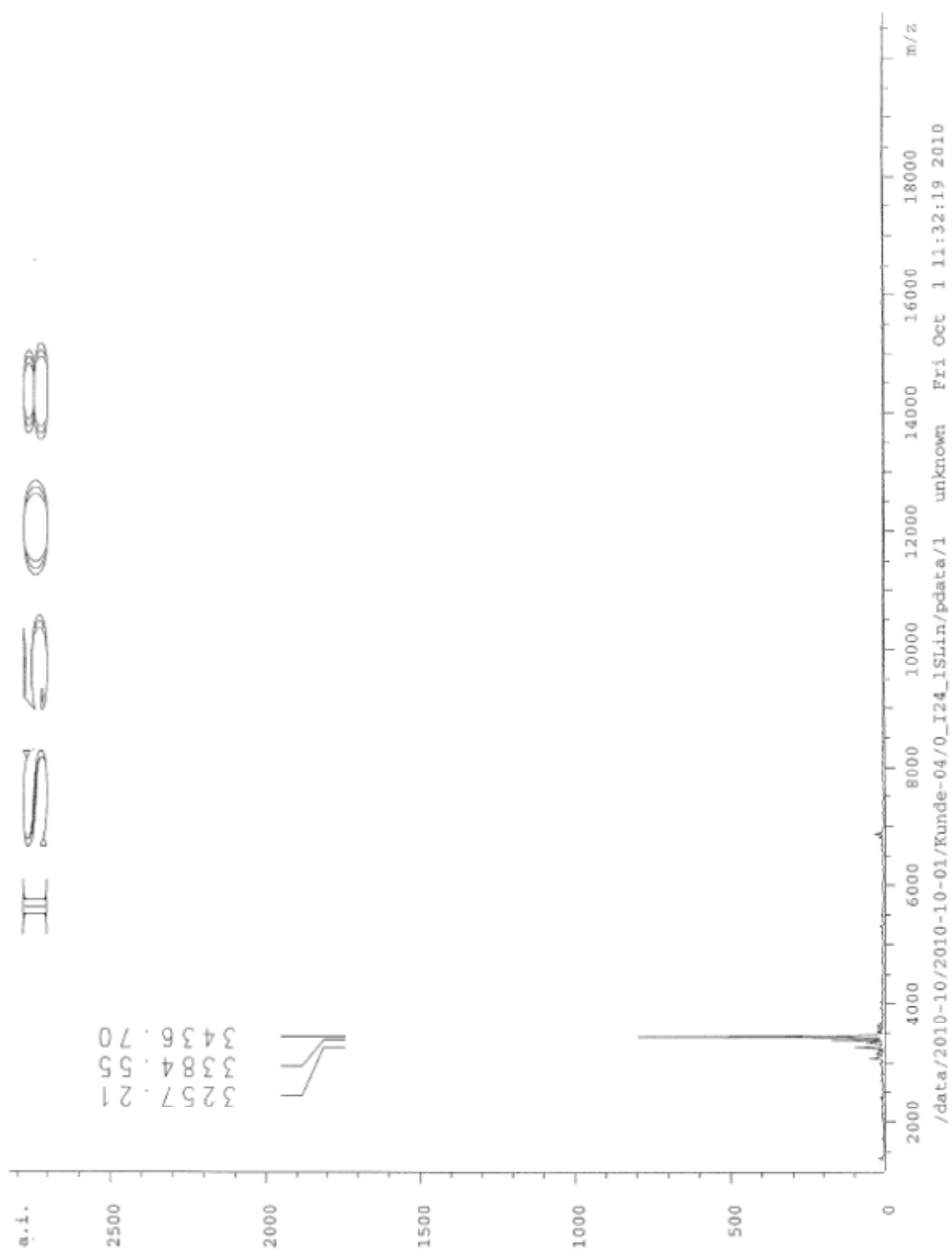
MALDI TOF MS of crude **34a** (9-mer RNA phenyl isoxazole conjugate)



MALDI TOF MS of crude **34b** (9-mer RNA 2-fluorophenyl isoxazole conjugate)

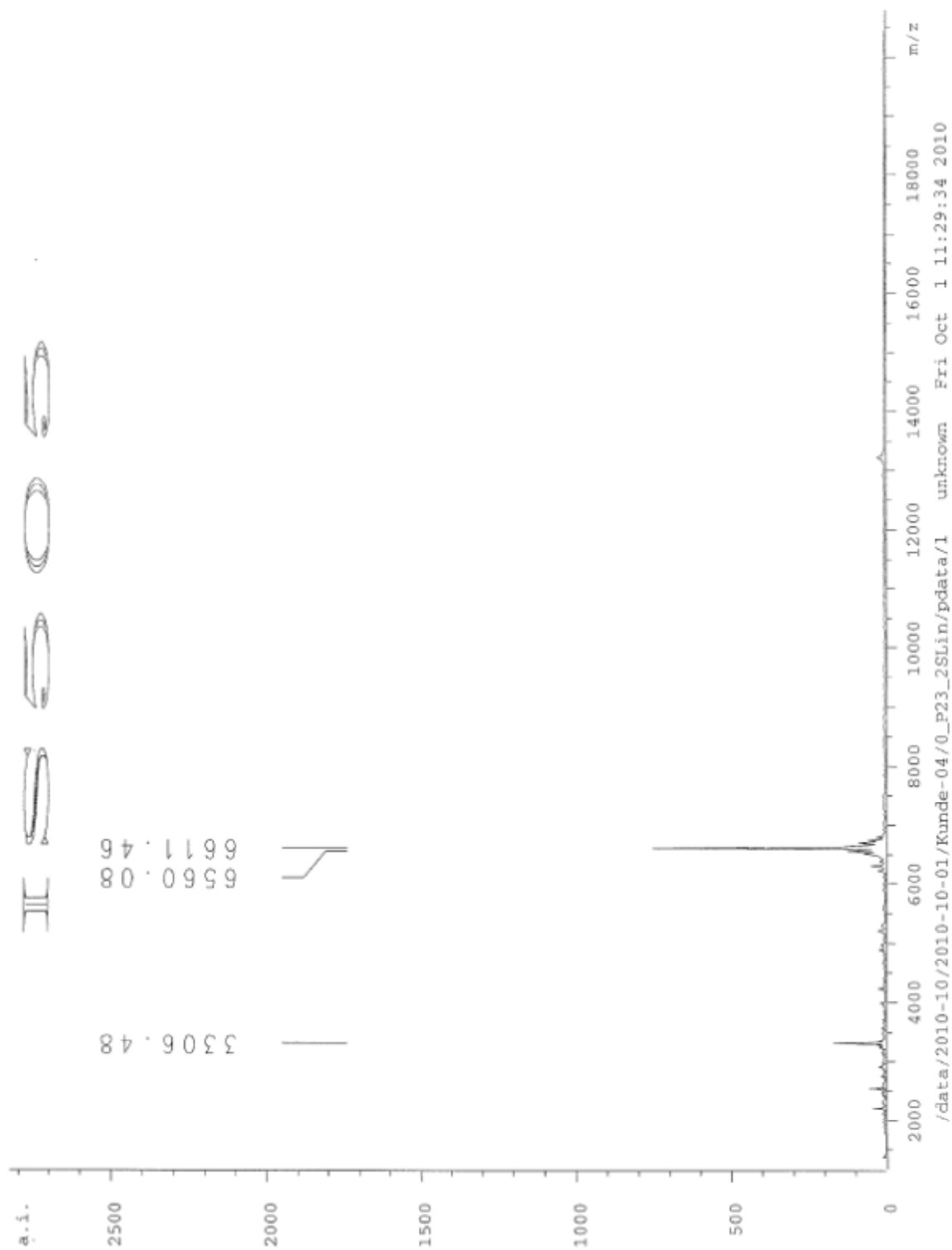


MALDI TOF MS of crude **34c** (9-mer RNA naphthyl isoxazole conjugate)

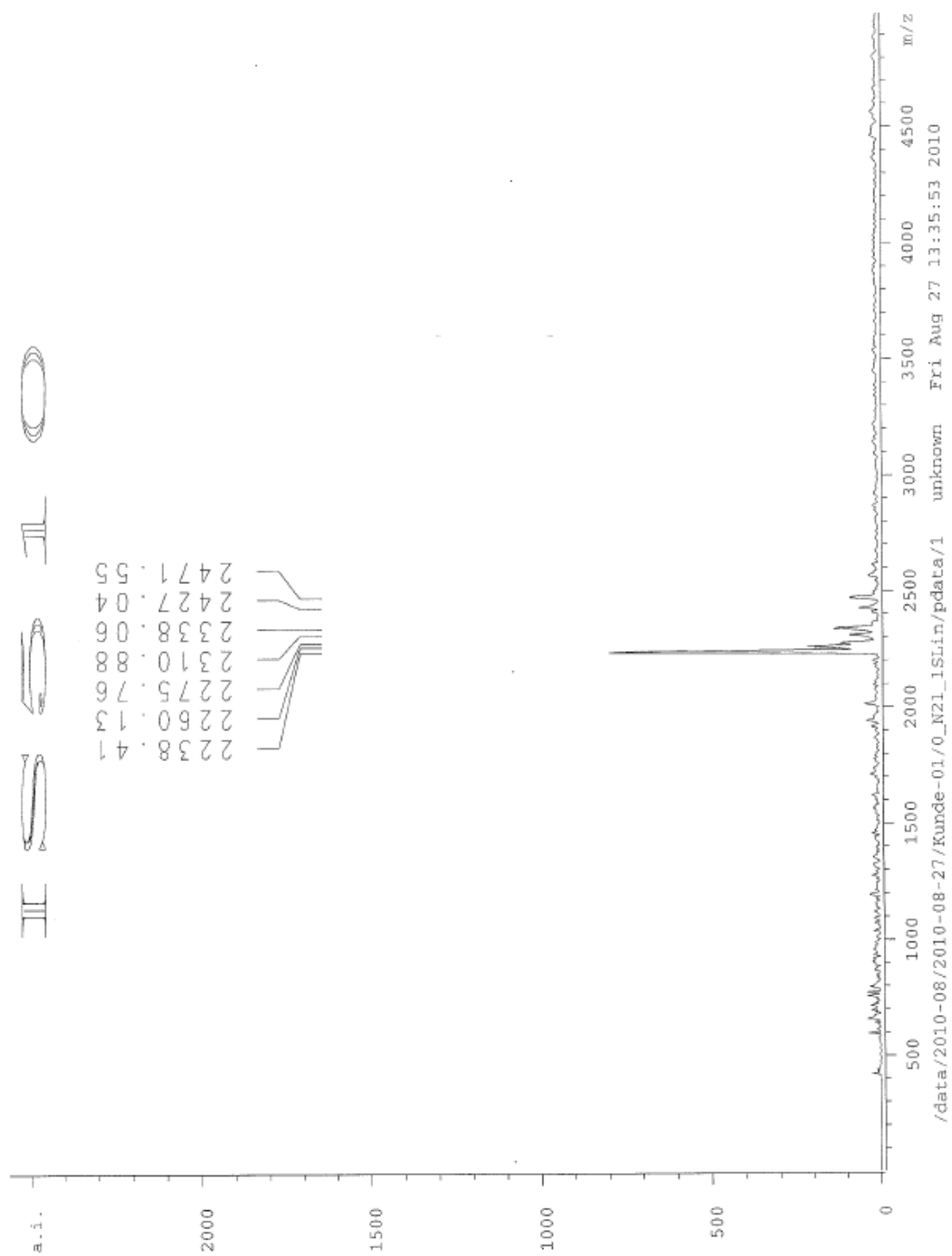


MALDI TOF MS of crude **34d** (9-mer RNA 2-(2-hydroxyethoxy)phenyl isoxazole conjugate)

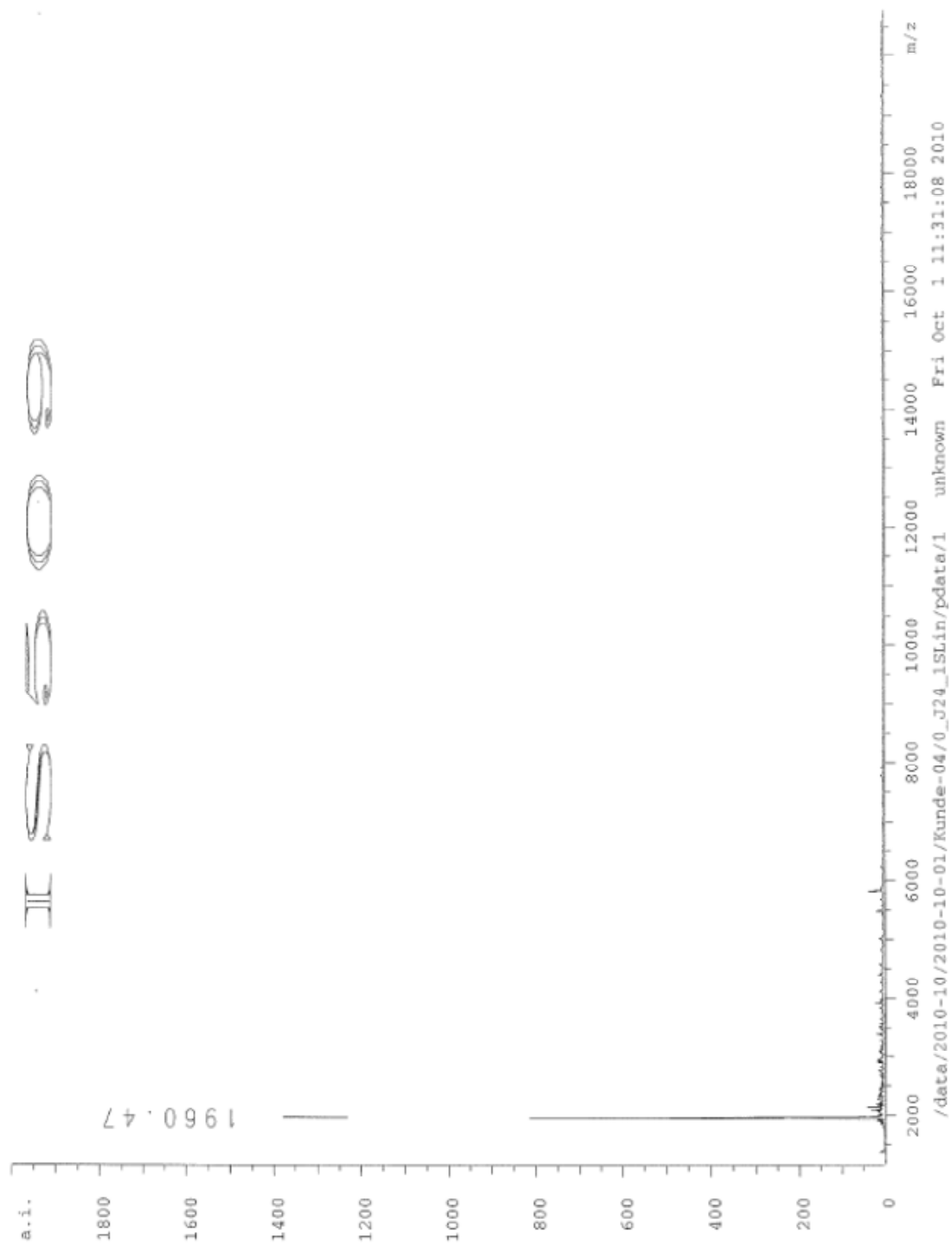




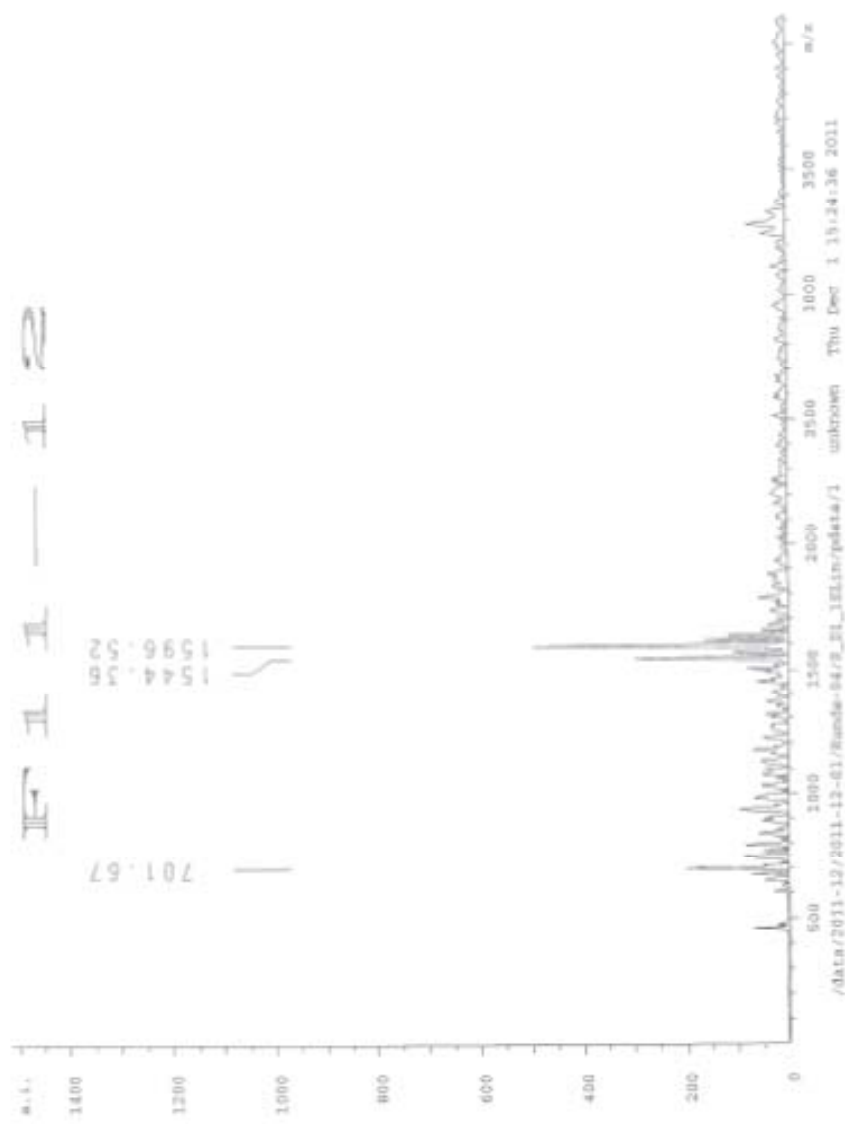
MALDI TOF MS of crude **38** (19-mer RNA phenyl isoxazole conjugate)



MALDI TOF MS of crude **39** (U<sub>4</sub>-alternate phenyl isoxazole RNA-conjugate)



MALDI TOF MS of crude **40** (gapmer phenyl isoxazole RNA-conjugate)



MALDI TOF MS of crude **23f** (U<sub>4</sub>-phenyl triazole RNA-conjugate)