Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Synthesis of PS/PO-Chimeric Oligonucleotides Using Mixed Oxathiaphospholane and Phosphoramidite Chemistry

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Supporting

The nuclear magnetic resonance spectra were recorded on a Brüker AC-200 instrument (200 MHz, TMS internal standard for 1H and 85% H_3PO_4 as the external standard for ^{31}P) unless stated otherwise. The FAB-MS spectra (13 keV, Cs+) were recorded on a Finnigan MAT 95 spectrometer, negative ion MALDI mass spectra were recorded on a Voyager-Elite instrument (PerSeptive Biosystems Inc., Framingham, USA) and on SHIMADZU Axima Performance MALDI-TOF mass spectrometer; while electrospray mass spectrometry analyses were done at Brüker amaZon speed ETD instrument. Mixture of 0.05M solution of 2,4,6-trihydroxyacetophenone (THA) or 3-hydroxypicolinic acid (HPA) in 50% acetonitryle and 0.2 M solution of diammonium hydrogen citrate in water (8:1, vv) was used as a matrix.

Oligonucleotide purification procedure:

The sample was concentrated under reduced pressure in a Speed-Vac concentrator and the remaining residue was dissolved in distilled water. Then two-step RP-HPLC (DMT-on and DMT-off) was used to isolate the product [Grace LC-18 column (2.1x250 mm), 1 mL/min flow rate;

buffer A, 0.05 M TEAB pH 7.5; buffer B, 40% CH_3CN in 0.05 M TEAB; gradient from 0 to 100% B over 40 min]. Retention times in the range 22-30 or 12-15 min were recorded for DMT-on or DMT-off analyses, respectively. DMT group was removed under treatment of acetic acid 50% aqueous solution (200µl; 2h).

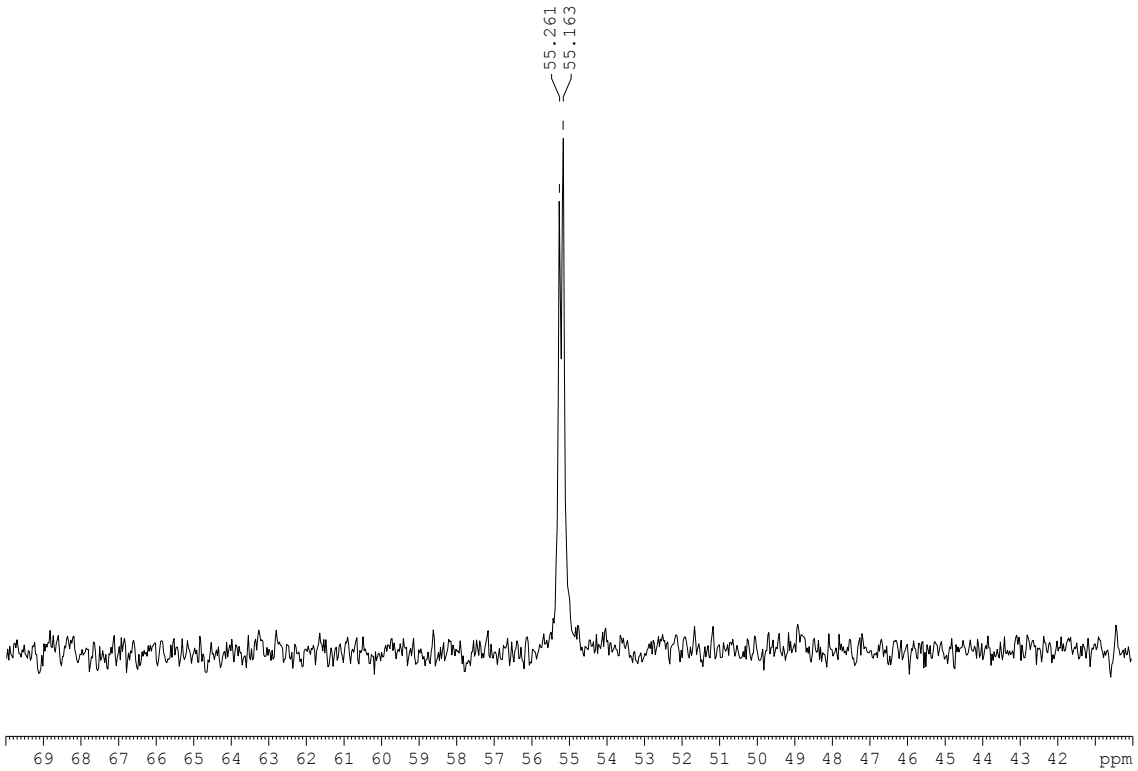

Fig. S1. 202 MHz ^{31}P NMR spectrum of the model phosphorothioate dinucleotide 2

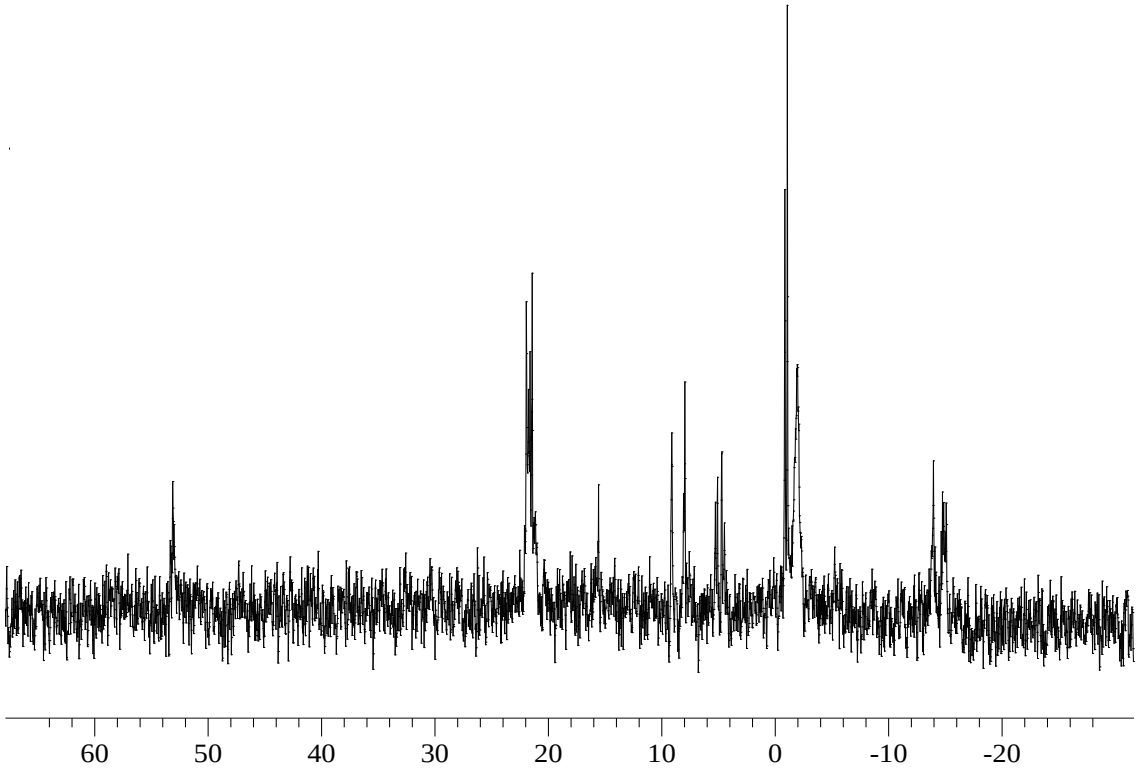

Fig. S2. 202 MHz ^{31}P NMR spectrum of the model phosphorothioate dinucleotide 2 after treatment with 50 equiv. of TBHP

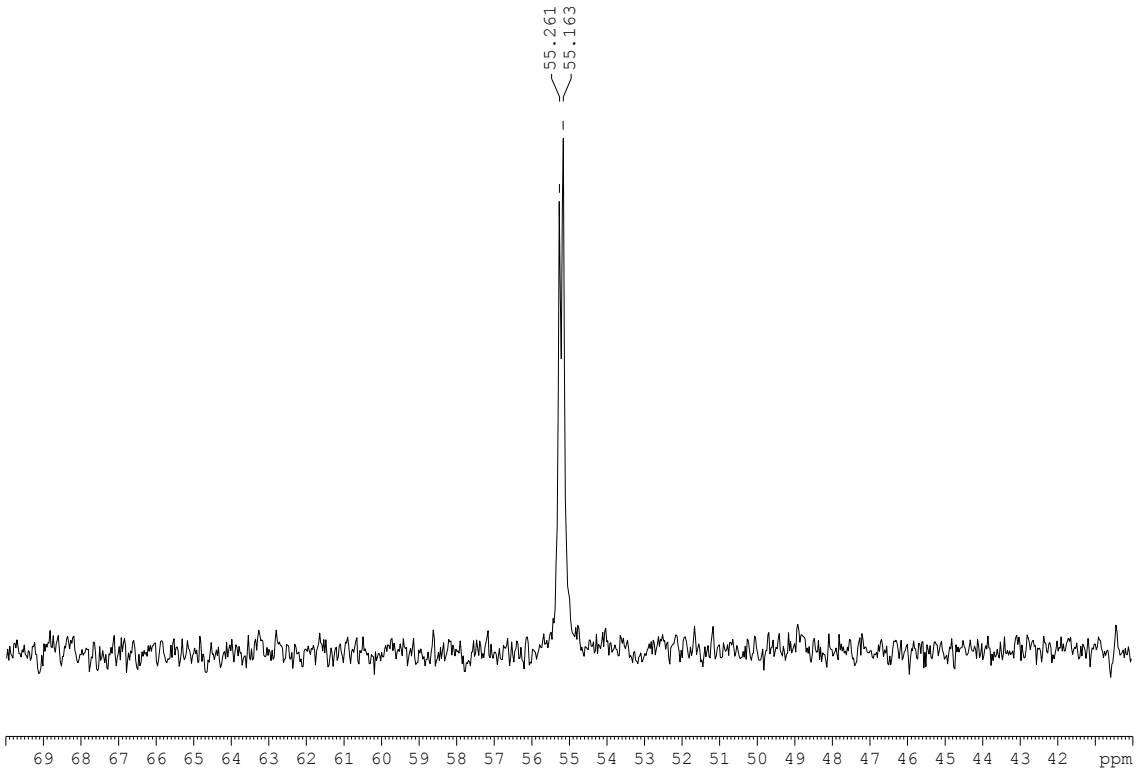

Fig. S3. 202 MHz ^{31}P NMR spectrum of the model phosphorothioate dinucleotide 2 recorded 30 minutes after treatment with 50 equiv. of *tert*-$BuOOSiMe_3$

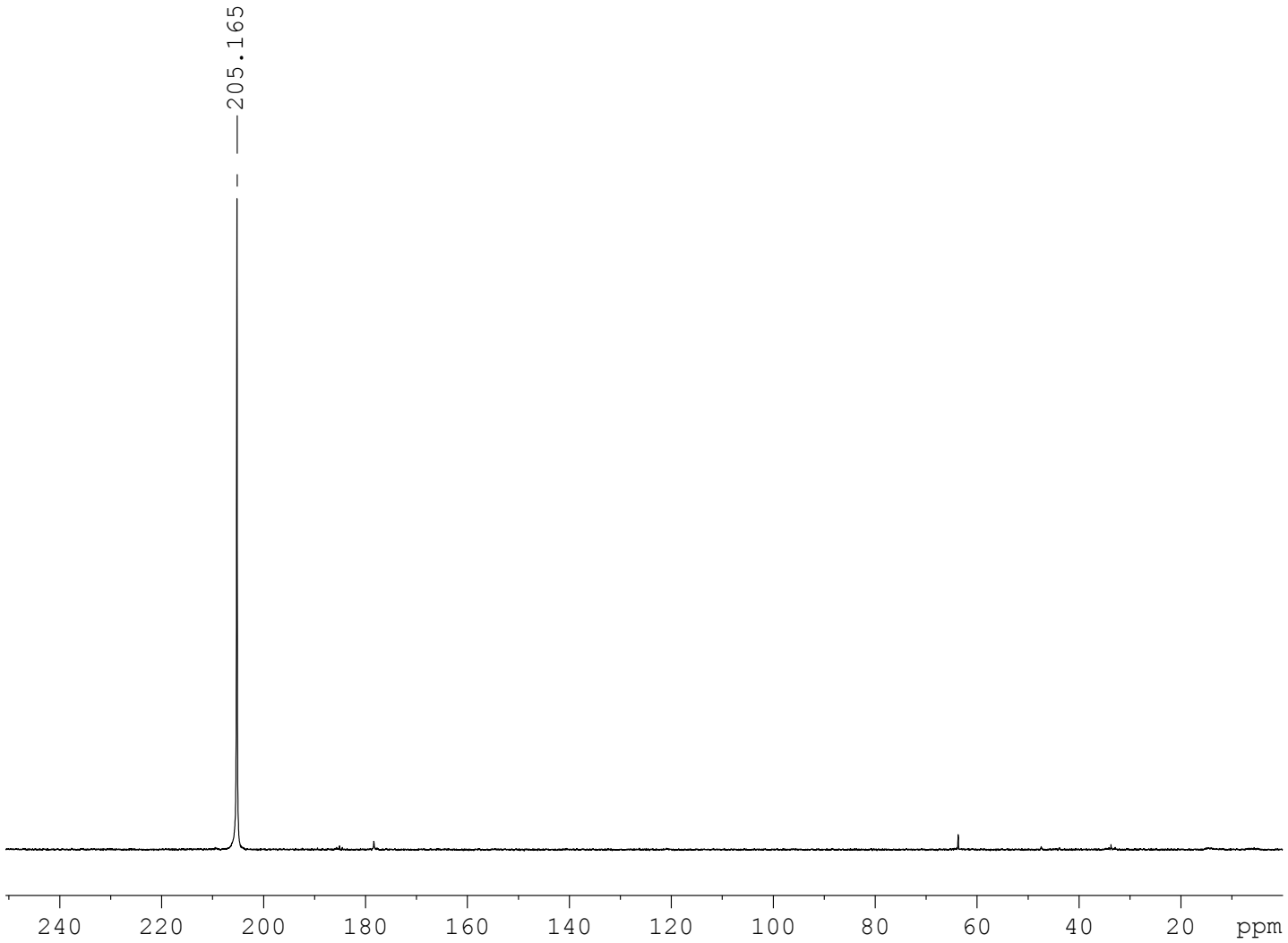

Fig.S4. ^{31}P NMR spectrum of 2-chloro-1,3,2-oxathiaphospholane (**14**)

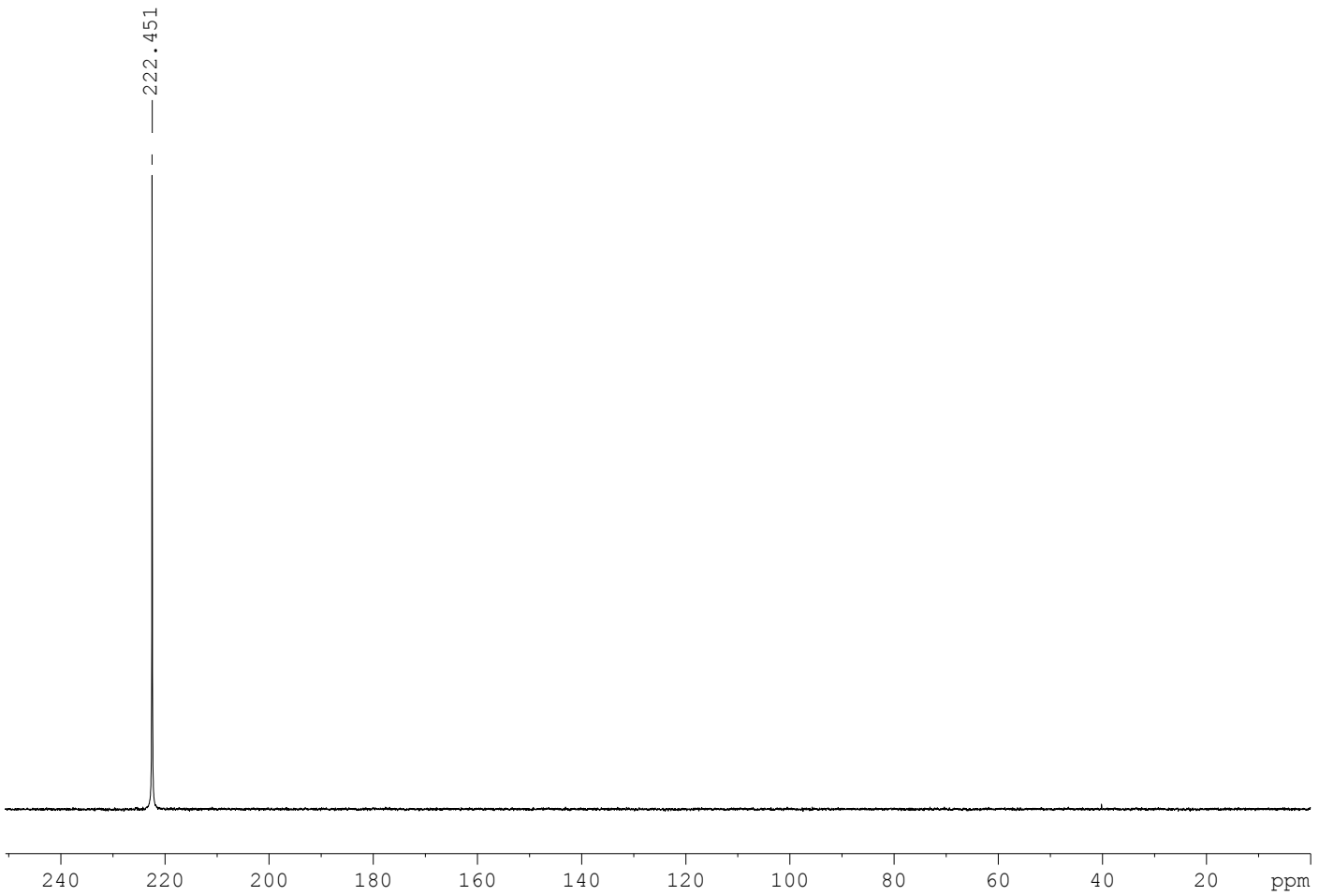

Fig.S5. ^{31}P NMR spectrum of 2-chloro-4,4-dimethyl-1,3,2-oxathiaphospholane (**15**)

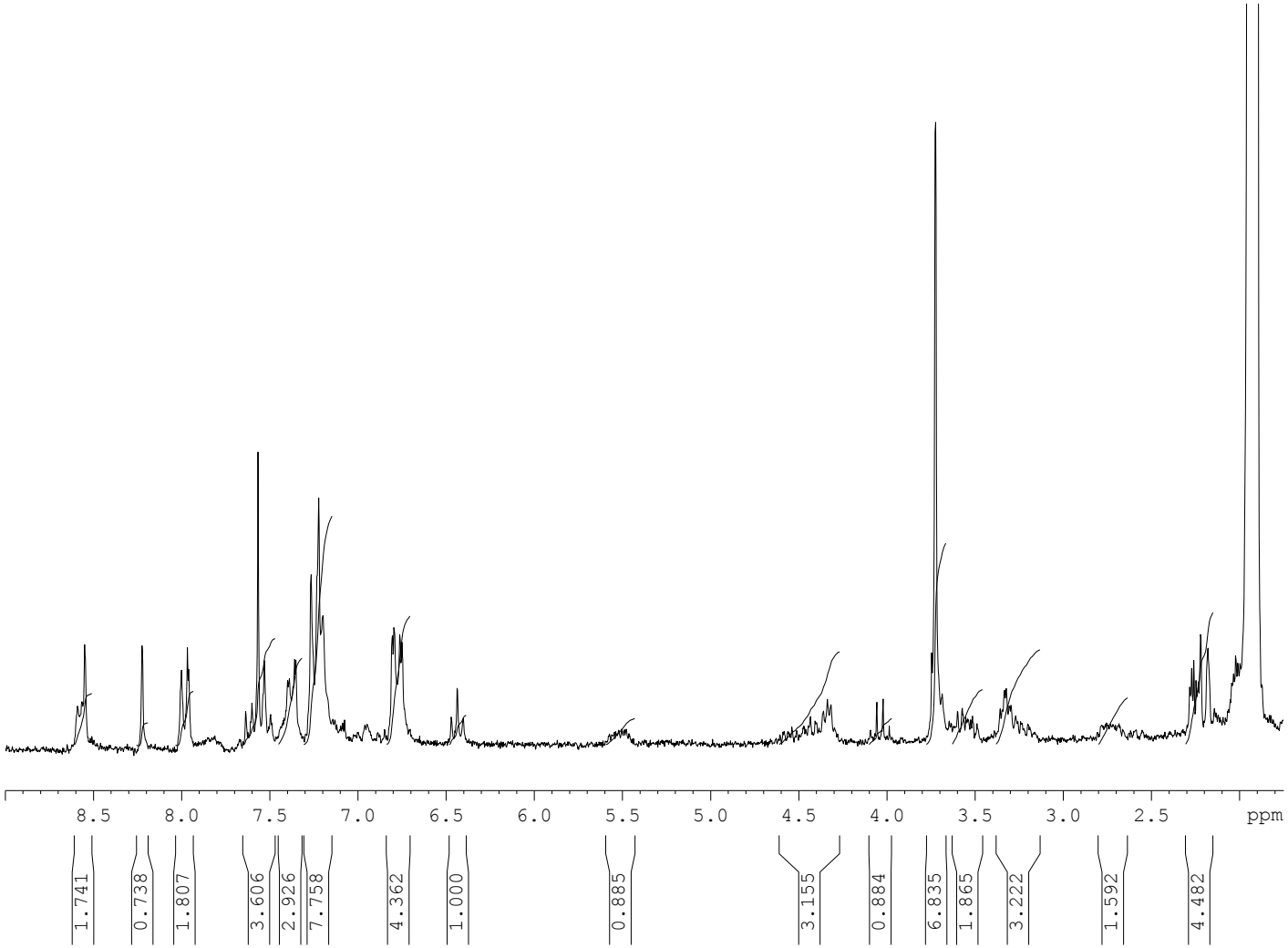

Fig.S6. ^{1}H NMR spectrum of 5'-*O*-(4,4'-dimethoxytrityl)-N^{6}-benzoyl-2'-deoxyadenosine-3'-*O*-(2-thio-1,3,2-oxathiaphospholane) **(3a)**

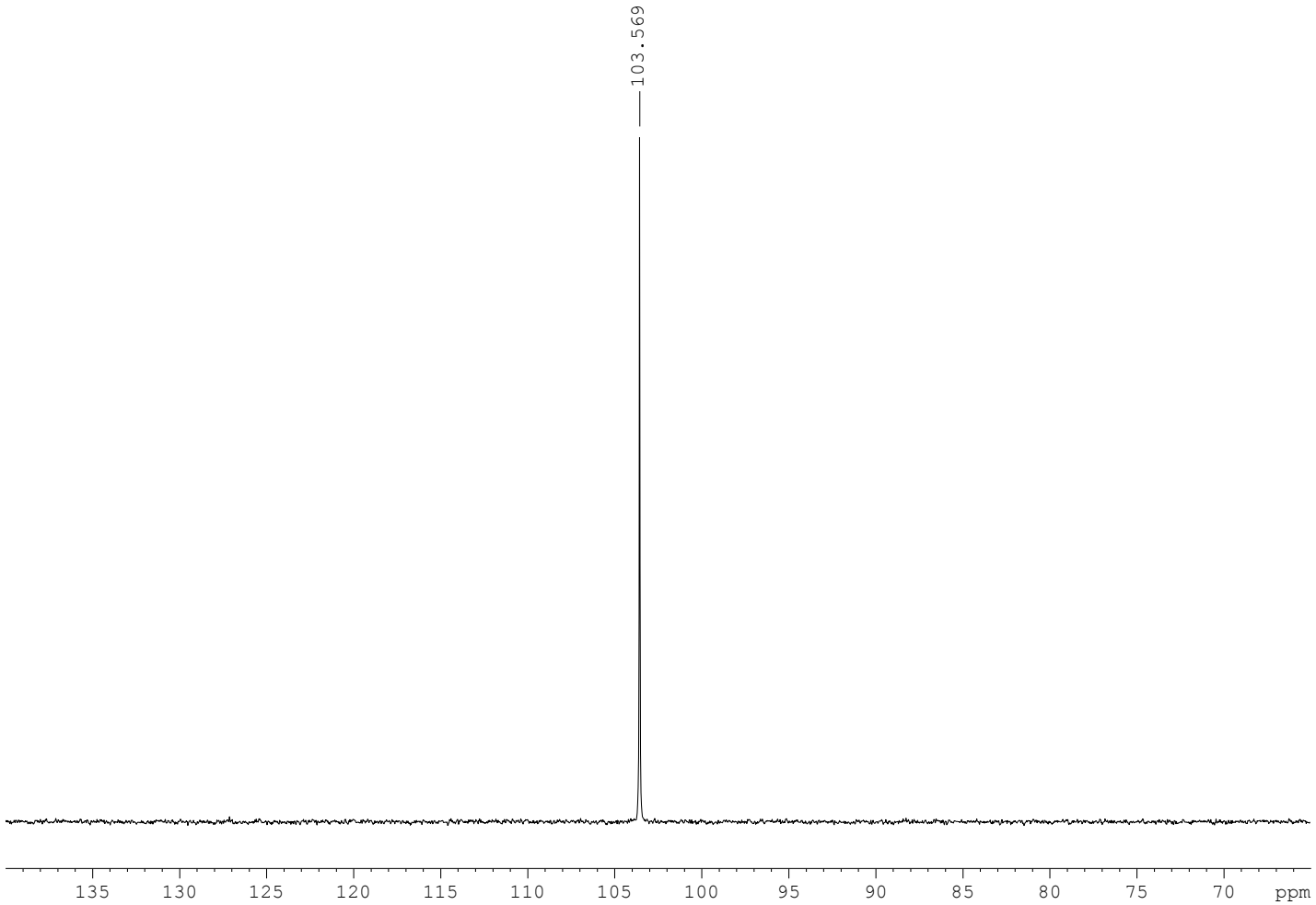

Fig.S7. ^{31}P NMR spectrum of 5'-*O*-(4,4'-dimethoxytrityl)-N^6-benzoyl-2'-deoxyadenosine-3'-*O*-(2-thio-1,3,2-oxathiaphospholane) **(S_P-3a)**

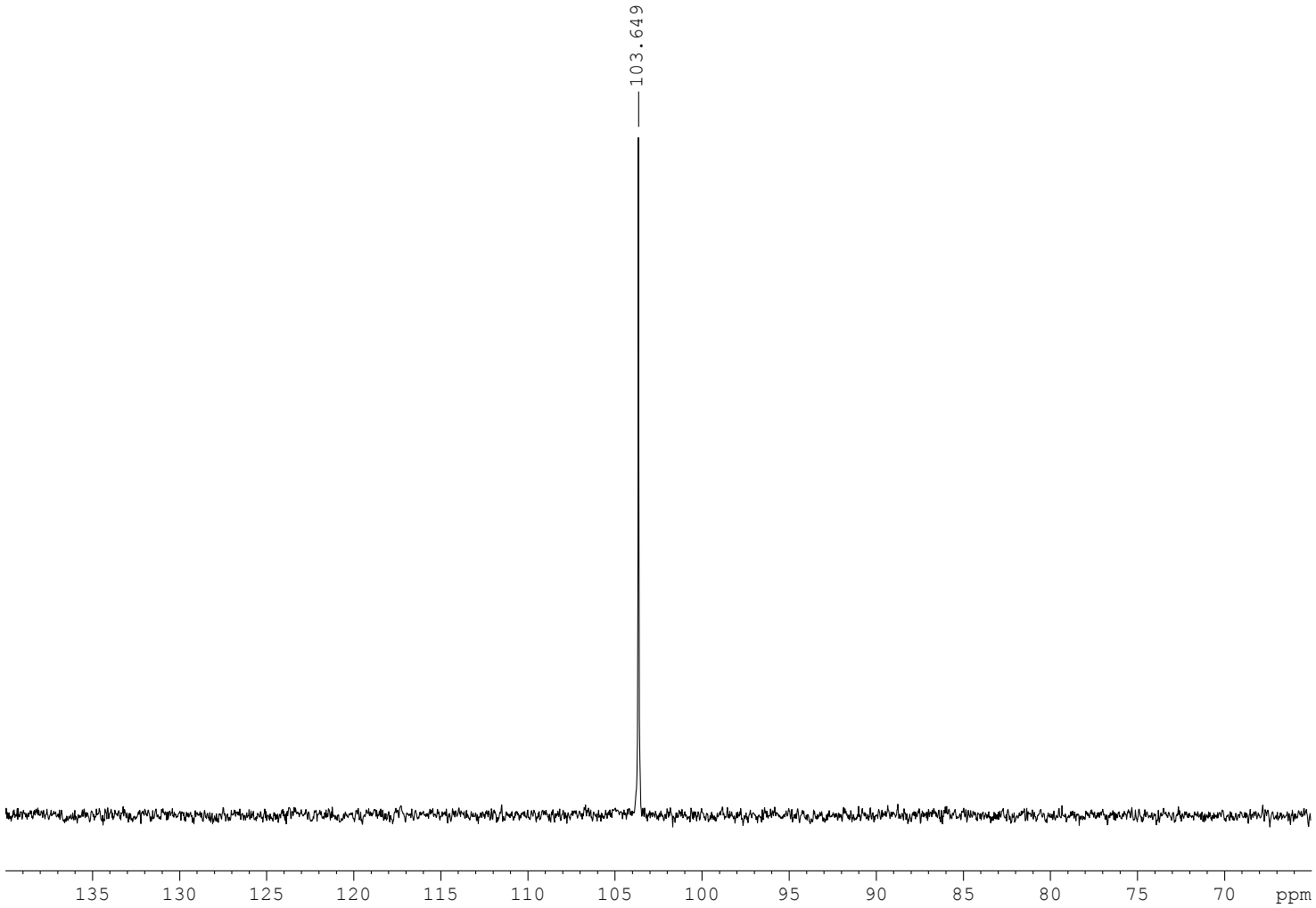

Fig.S8. ^{31}P NMR spectrum of 5'-*O*-(4,4'-dimethoxytrityl)-N^6-benzoyl-2'-deoxyadenosine-3'-*O*-(2-thio-1,3,2-oxathiaphospholane) **(R_P-3a)**

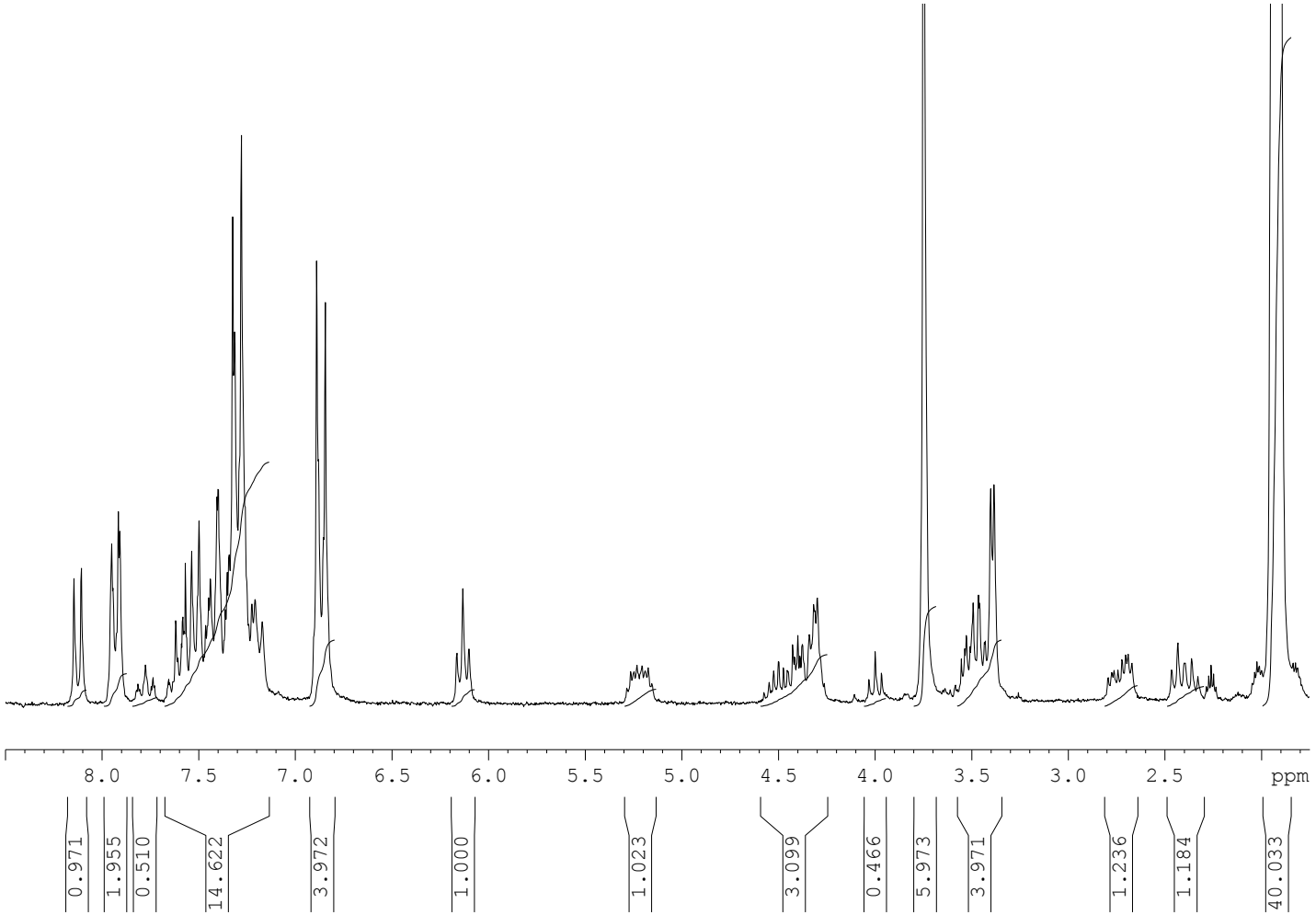

Fig.S9. ^{1}H NMR spectrum of 5'-*O*-(4,4'-dimethoxytrityl)-N^{4}-benzoyl-2'-deoxycitidine-3'-*O*-(2-thio-1,3,2-oxathiaphospholane) **(3b)**

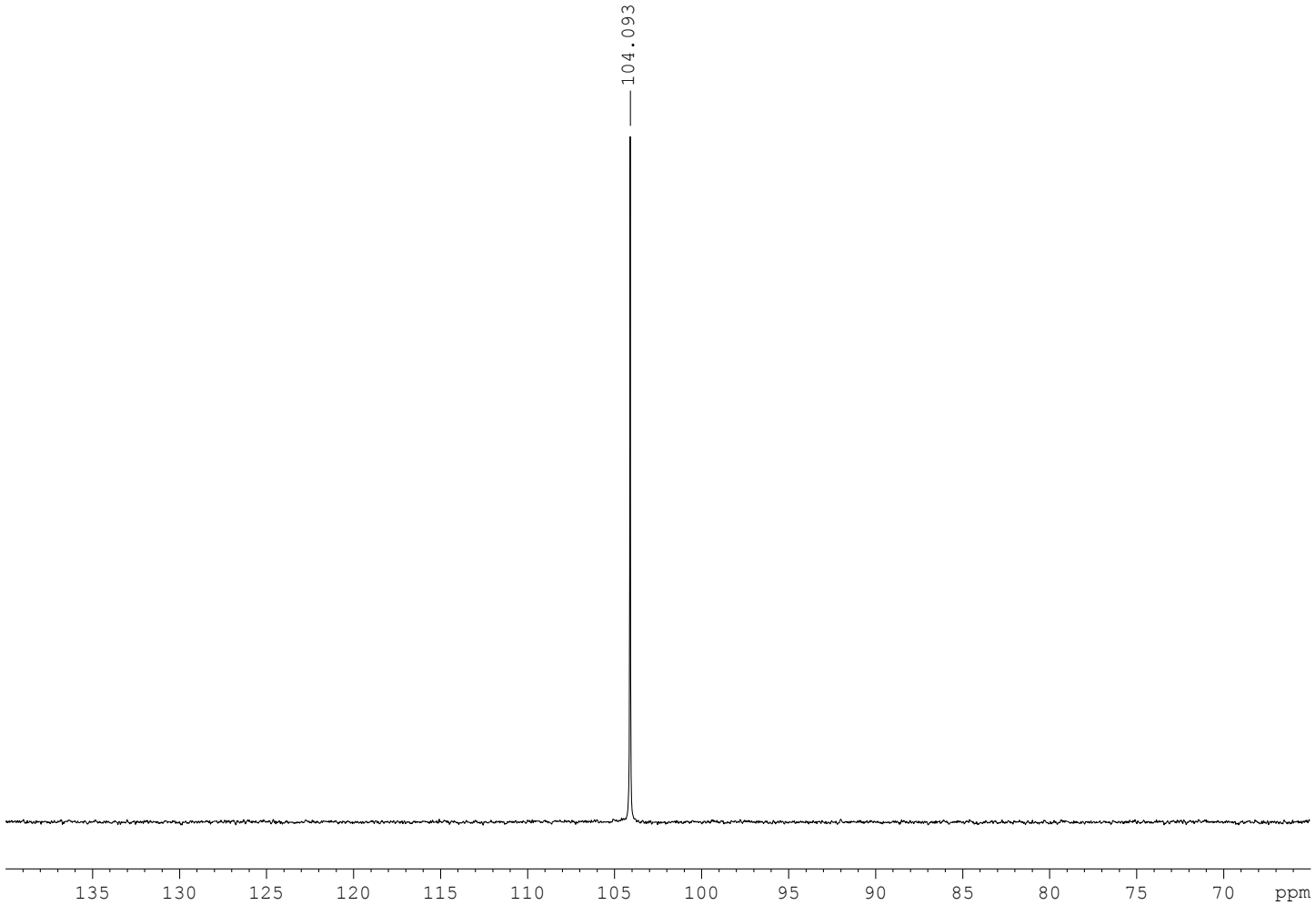

Fig.S10. ^{31}P NMR spectrum of 5'-*O*-(4,4'-dimethoxytrityl)-N^4-benzoyl-2'-deoxycitidine-3'-*O*-(2-thio-1,3,2-oxathiaphospholane) **(S_P-3b)**

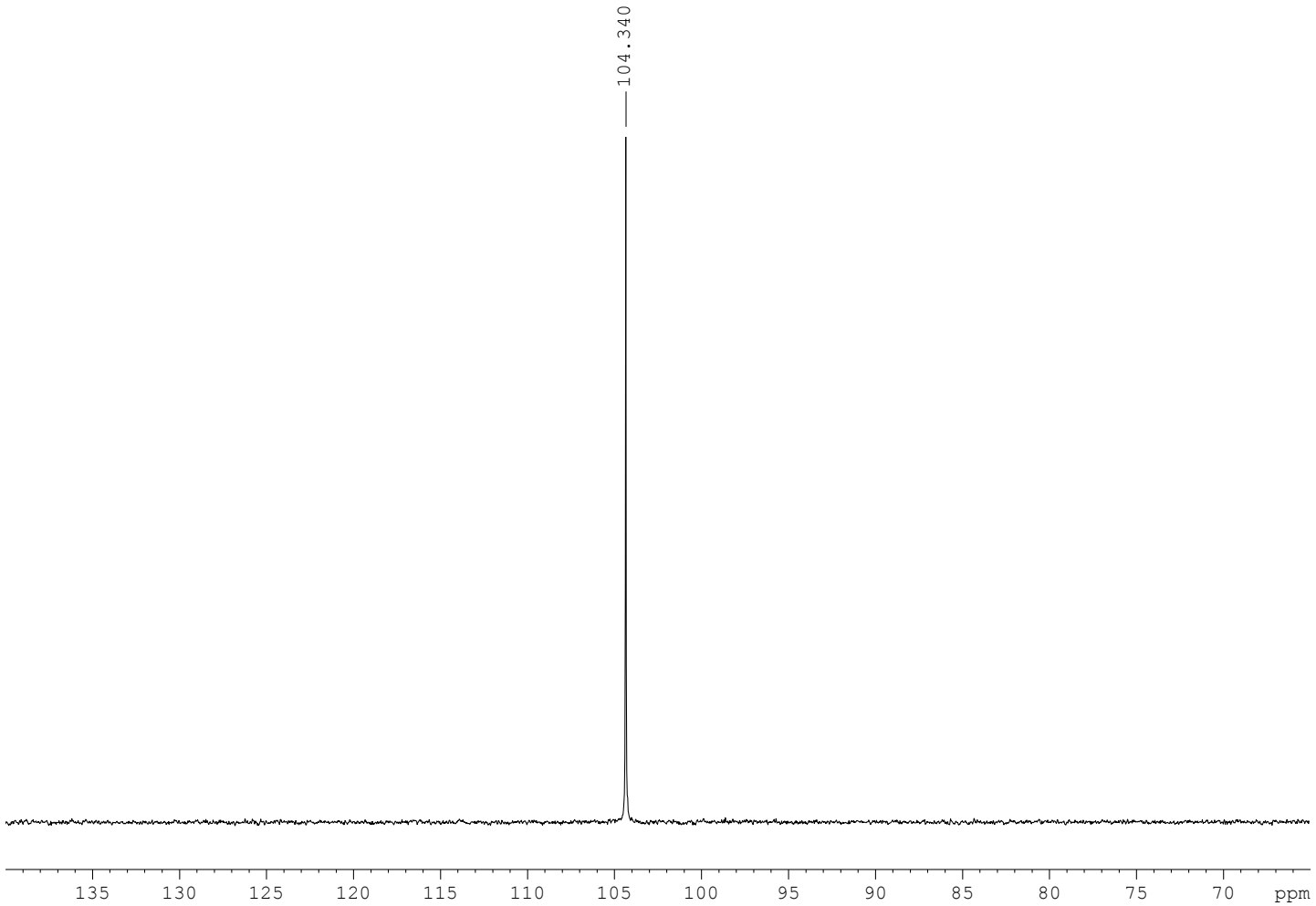

Fig.S11. ^{31}P NMR spectrum of 5'-*O*-(4,4'-dimethoxytrityl)-N^4-benzoyl-2'-deoxycitidine-3'-*O*-(2-thio-1,3,2-oxathiaphospholane) **(R_P-3b)**

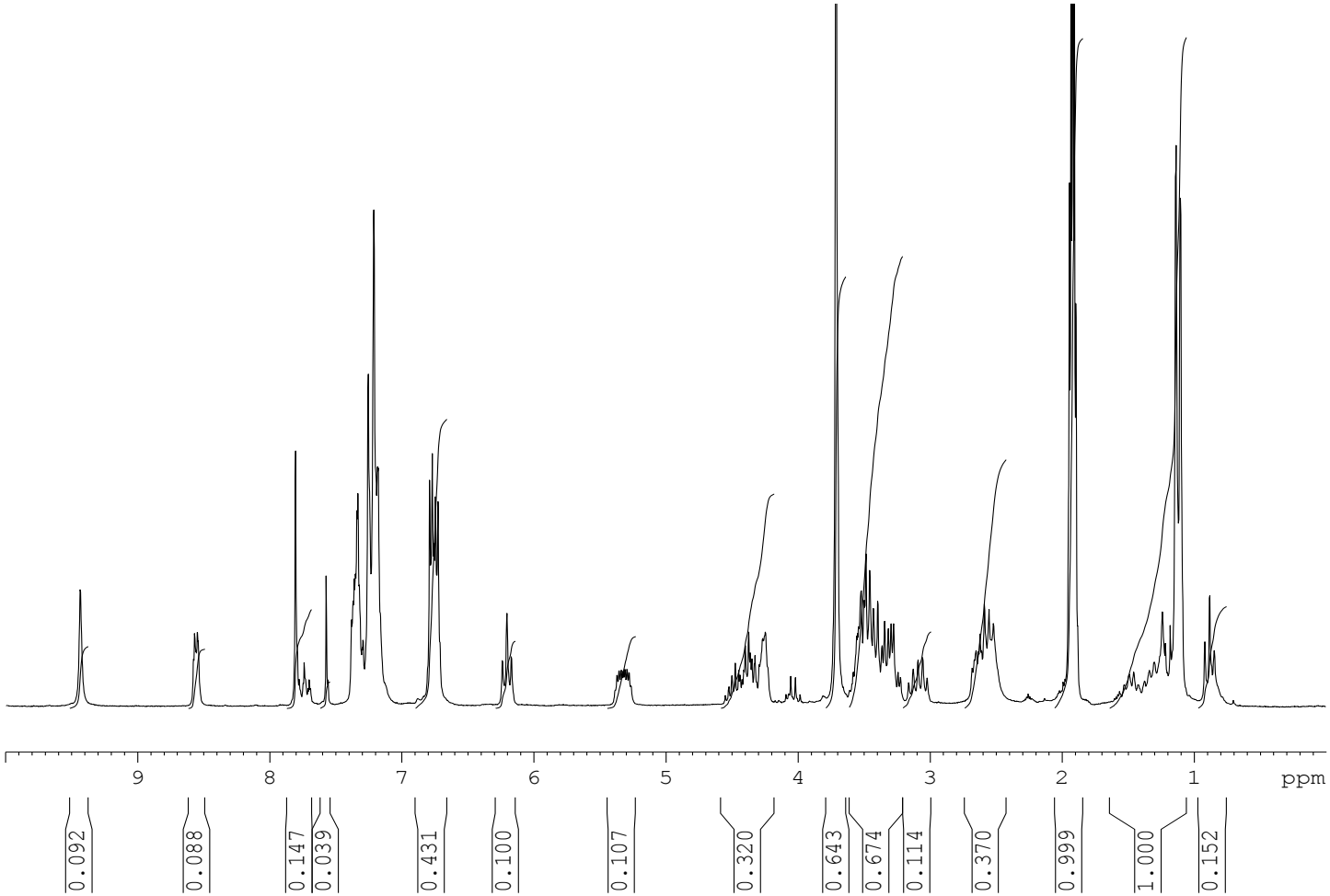

Fig.S12. ^{1}H NMR spectrum of 5'-*O*-(4,4'-dimethoxytrityl)-N^{2}-isobutyryl-2'-deoxyguanosine-3'-*O*-(2-thio-1,3,2-oxathiaphospholane) **(3c)**

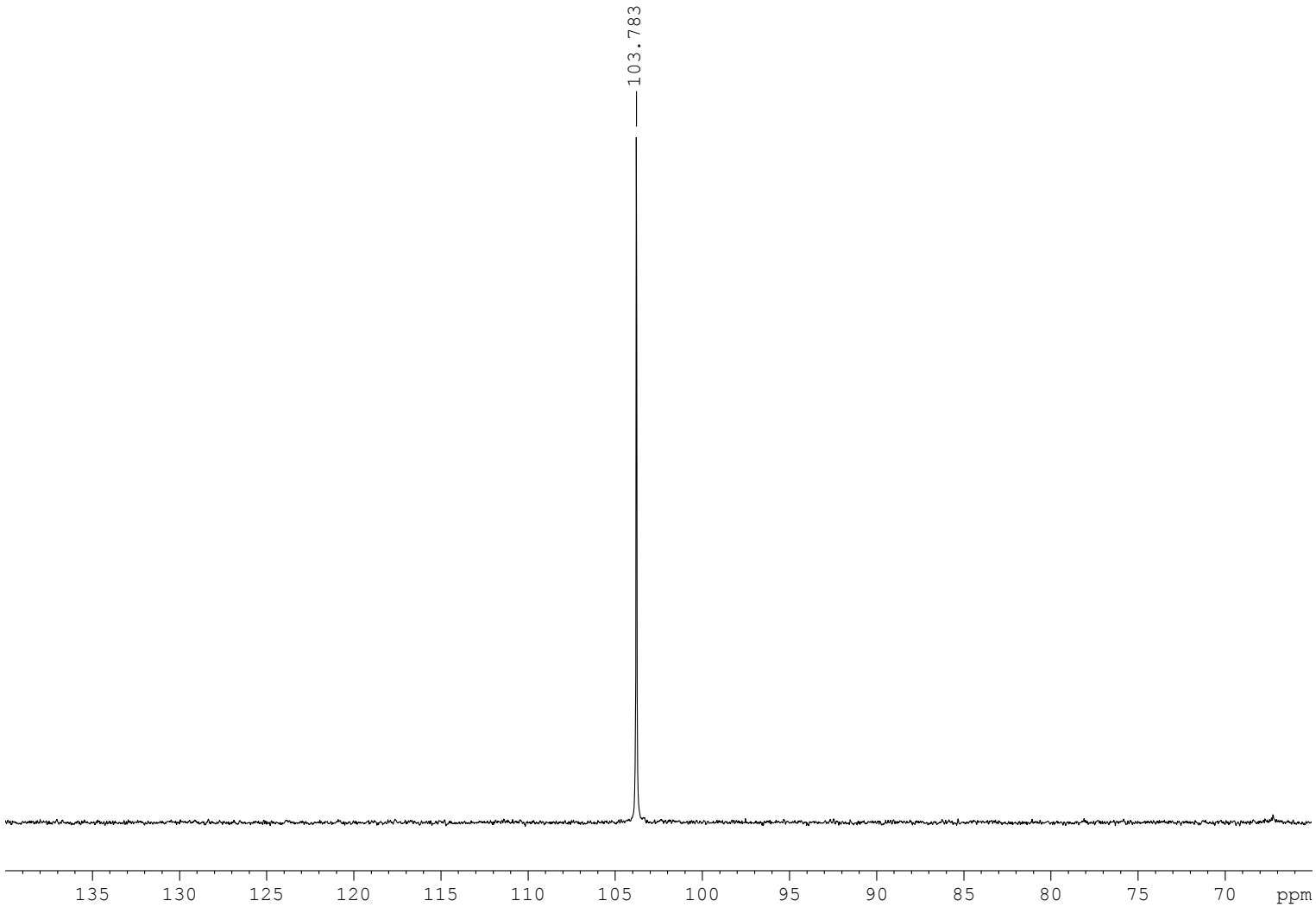

Fig.S13. ^{31}P NMR spectrum of 5'-*O*-(4,4'-dimethoxytrityl)-*N*^{2}-isobutyryl-2'-deoxyguanosine-3'-*O*-(2-thio-1,3,2-oxathiaphospholane) **(S_P-3c)**

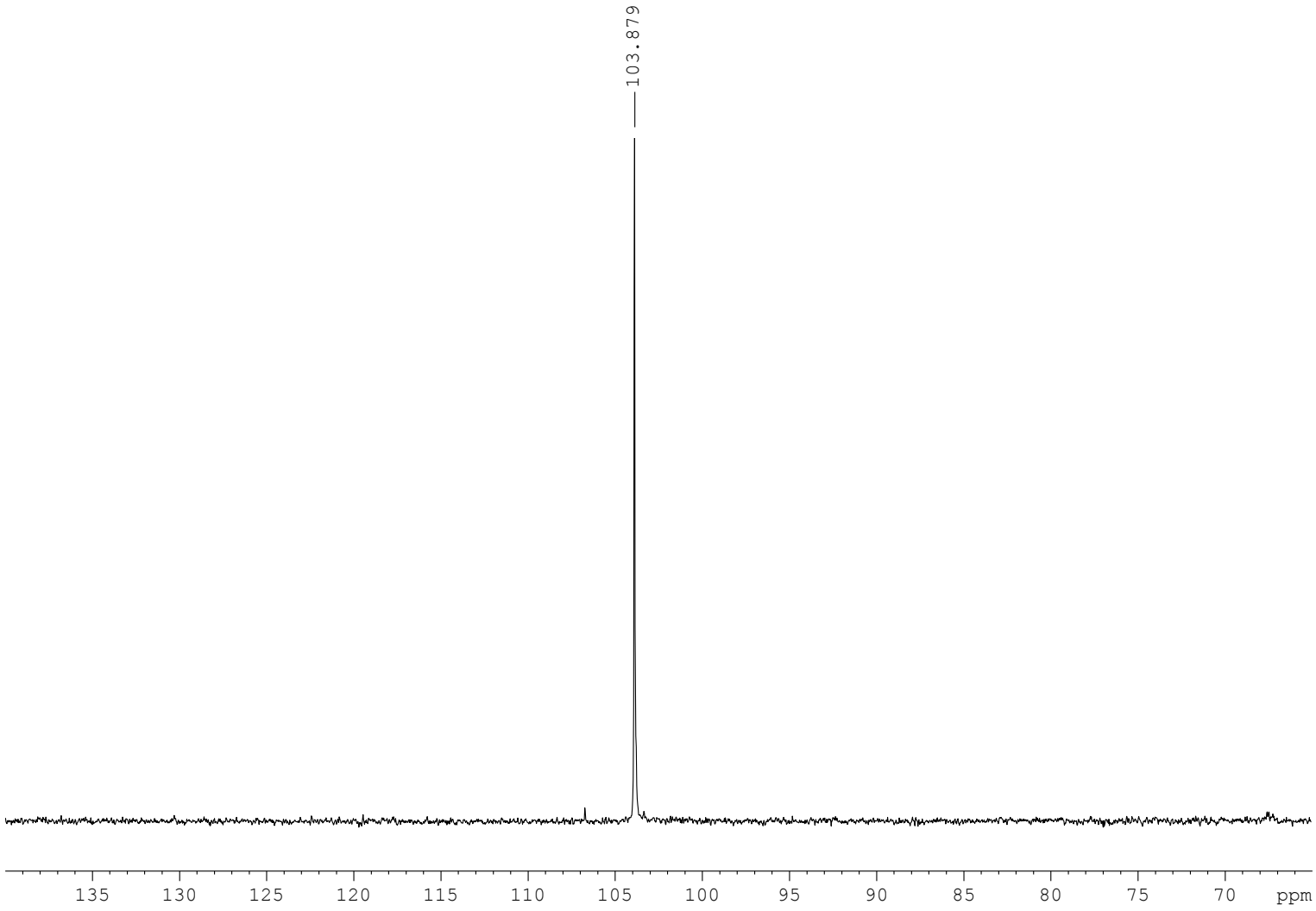

Fig.S14. ^{31}P NMR spectrum of 5'-*O*-(4,4'-dimethoxytrityl)-*N*^{2}-isobutyryl-2'-deoxyguanosine-3'-*O*-(2-thio-1,3,2-oxathiaphospholane) **(R_P-3c)**

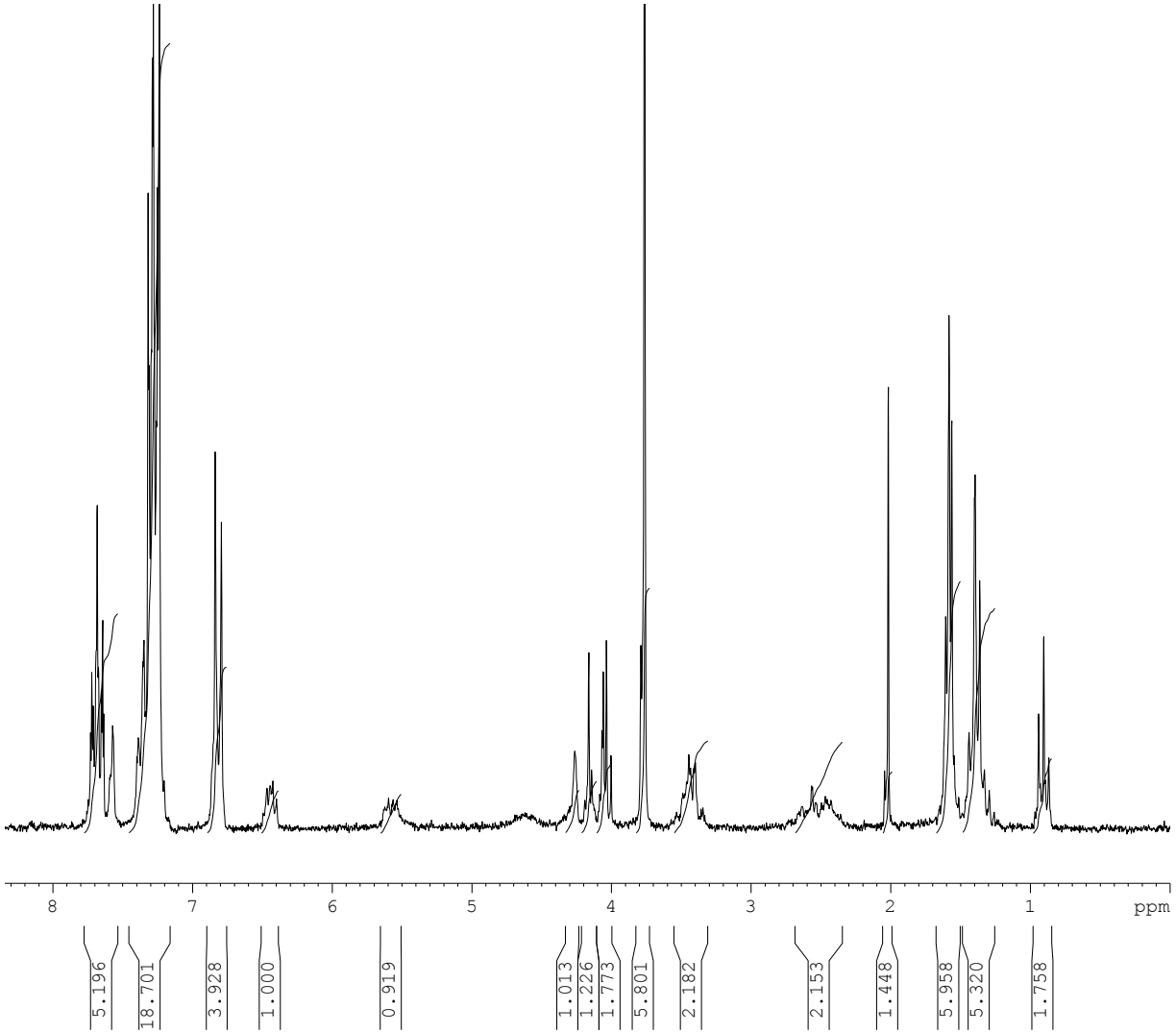

Fig.S15. ^{1}H NMR spectrum of 5'-*O*-(4,4'-dimethoxytrityl)thymidine-3'-*O*-(2-thio-4,4-dimethyl-1,3,2-oxathiaphospholane) **(3d)**

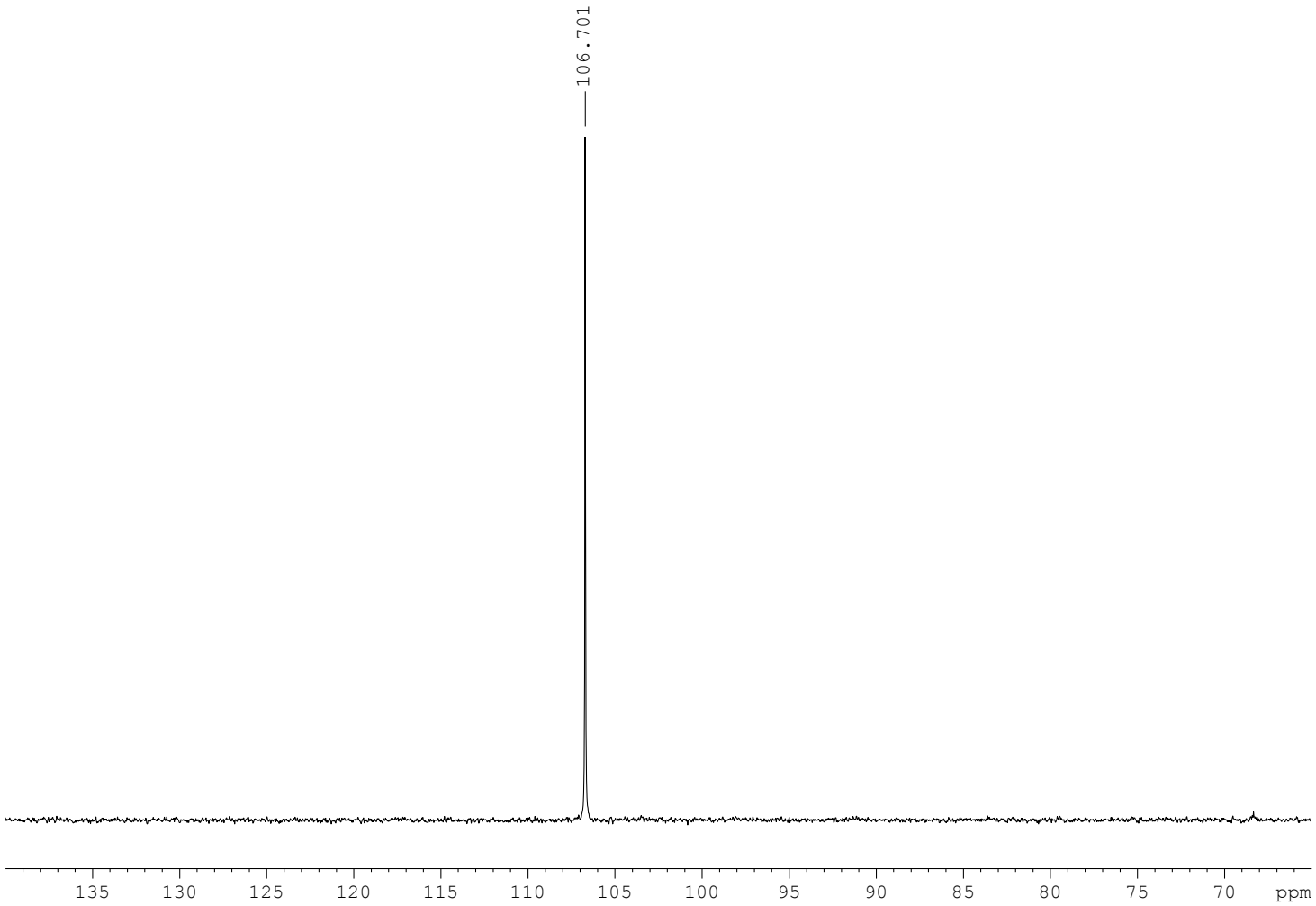

Fig.S16. ^{31}P NMR spectrum of 5'-*O*-(4,4'-dimethoxytrityl)thymidine-3'-*O*-(2-thio-4,4-dimethyl-1,3,2-oxathiaphospholane) **(R_P-3d)**

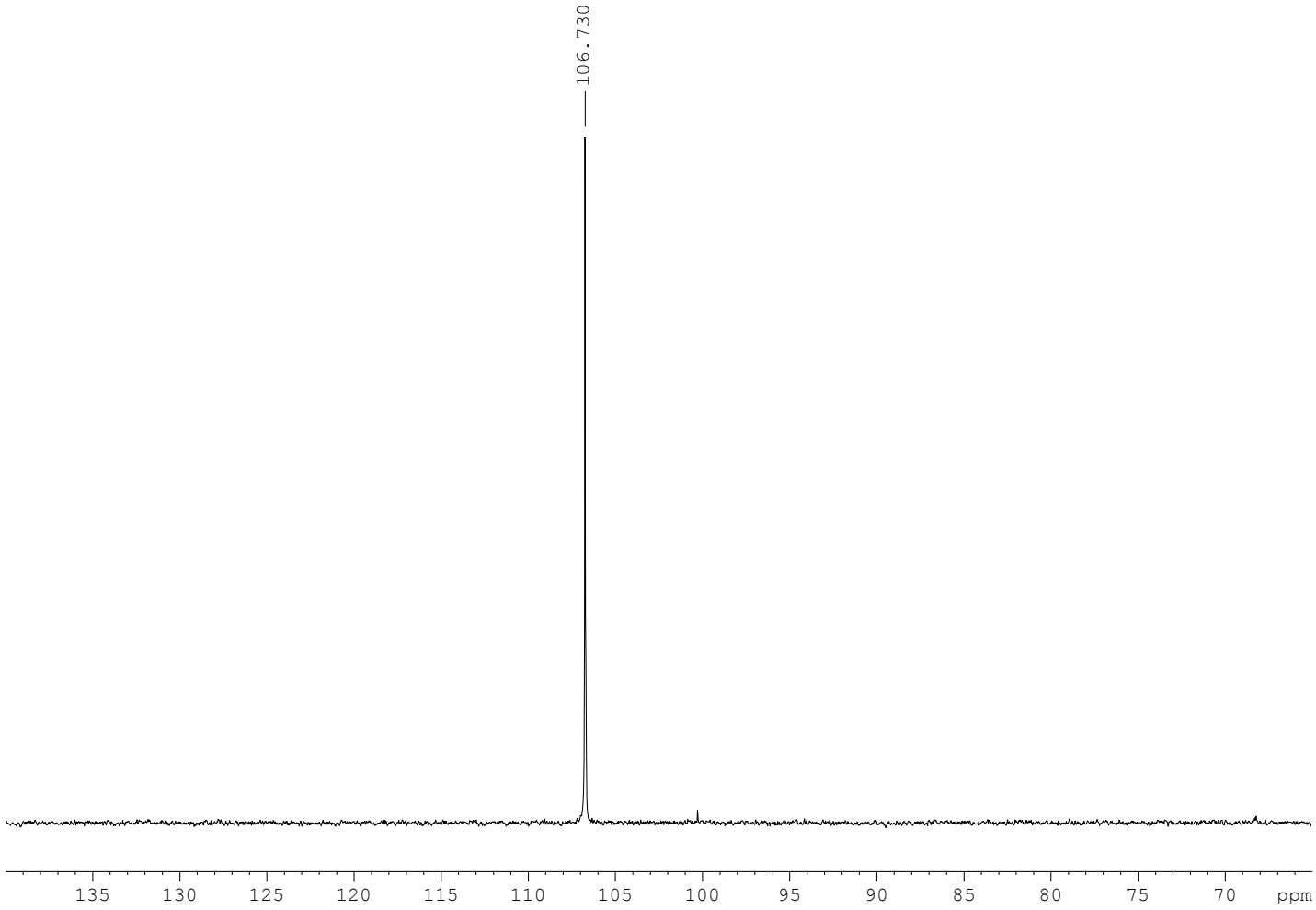

Fig.S17. ^{31}P NMR spectrum of 5'-*O*-(4,4'-dimethoxytrityl)thymidine-3'-*O*-(2-thio-4,4-dimethyl-1,3,2-oxathiaphospholane) **(S_P-3d)**

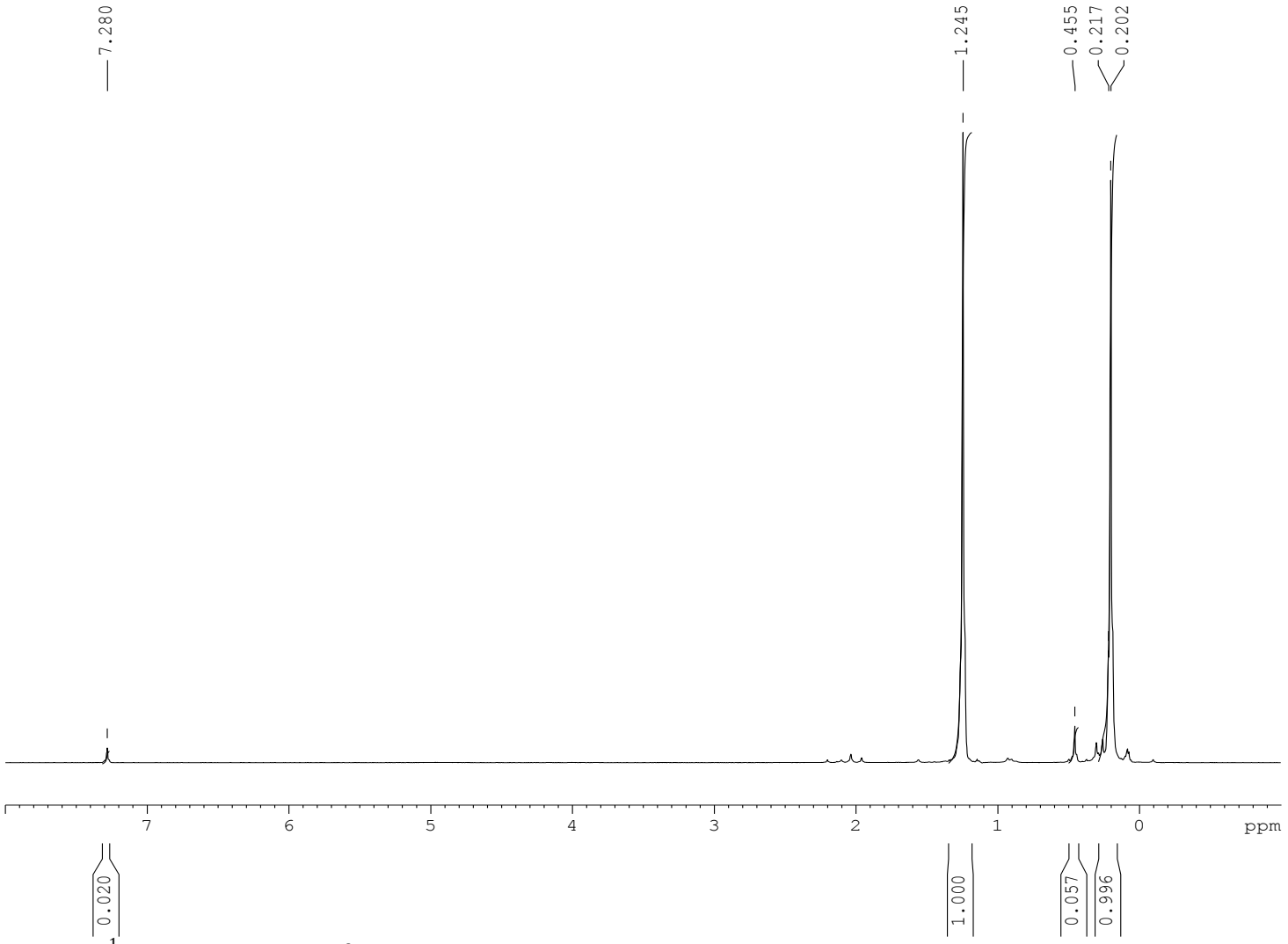

Fig.S18. ^{1}H NMR spectrum of trimethyl(*tert*-butylperoxy)silane **(6)**

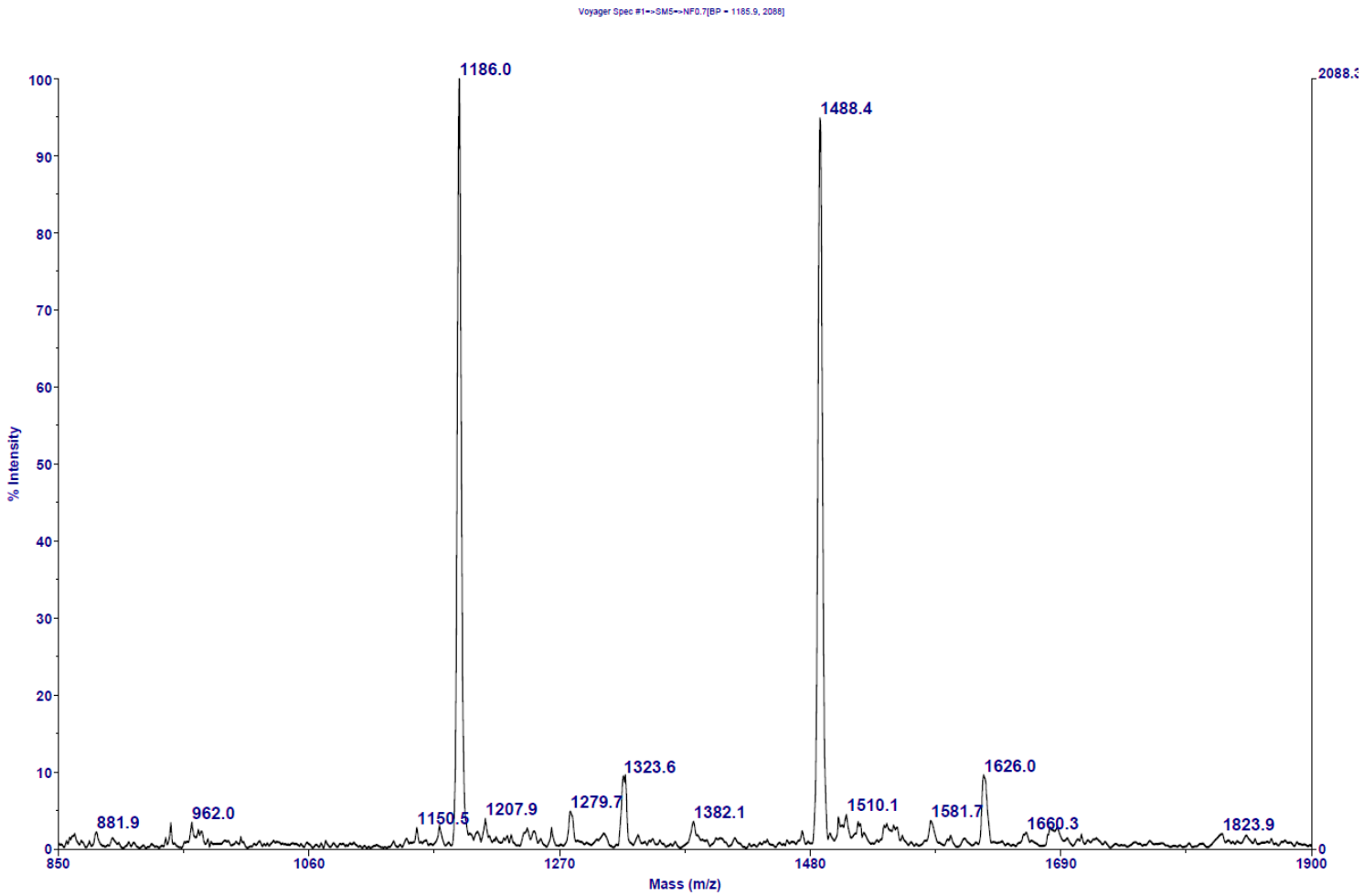

Fig.S19. MALDI-TOF MS spectrum of oligo **13a** (Voyager-Elite mass spectrometer; HPA matrix)

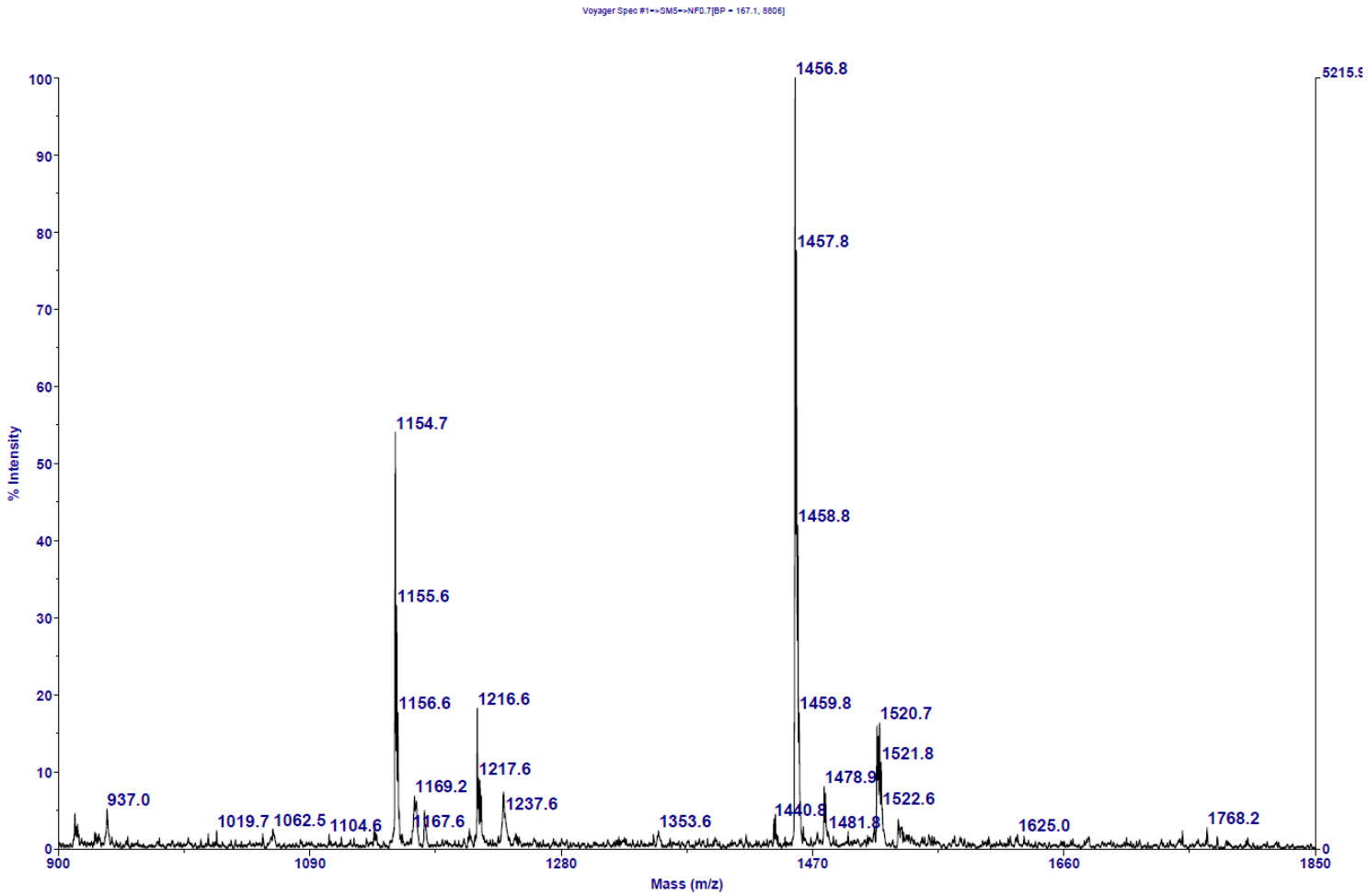

Fig.S20. MALDI-TOF MS spectrum of oligo **13b** (Voyager-Elite mass spectrometer; THA matrix)

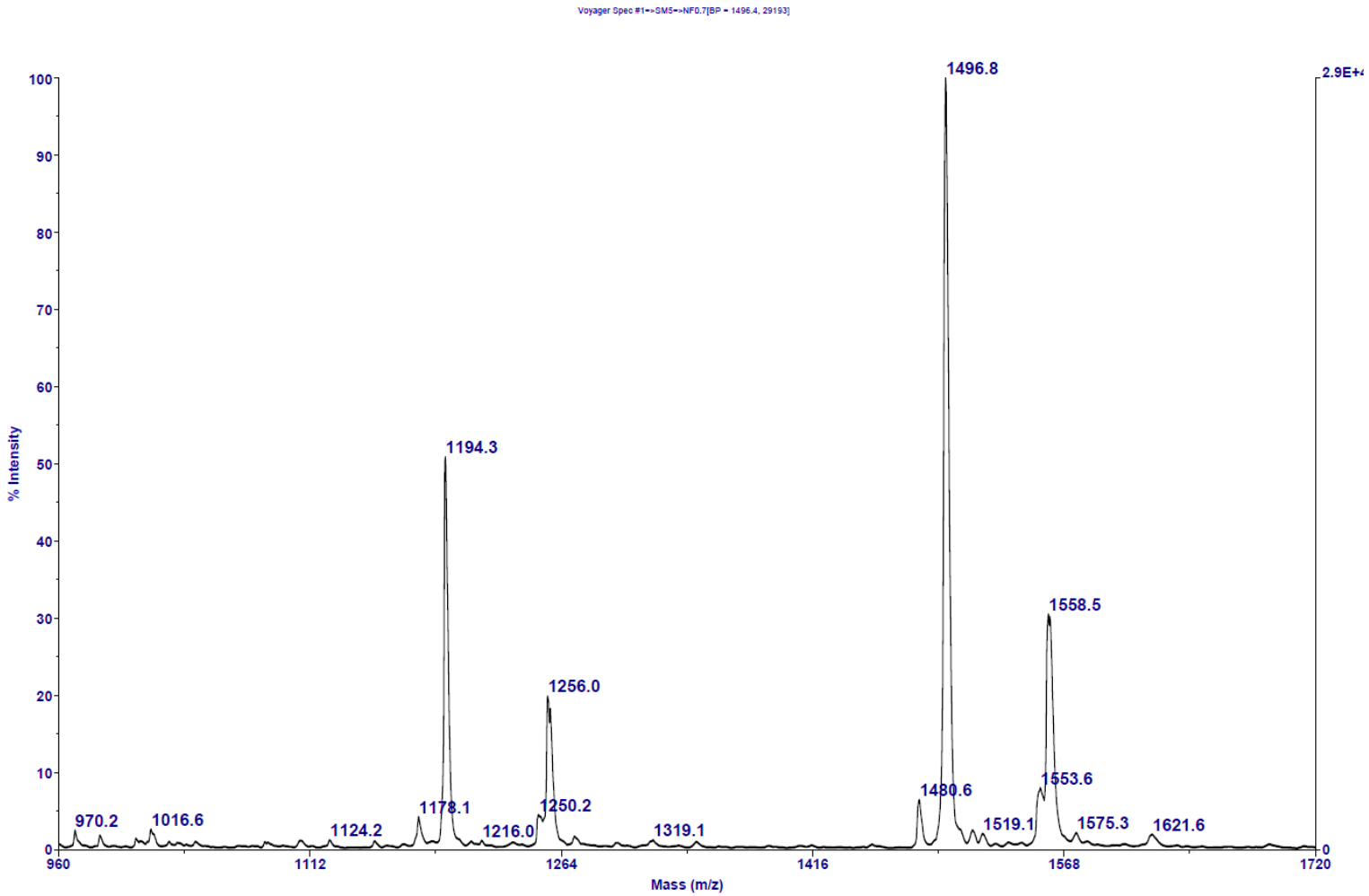

Fig.S21. MALDI-TOF MS spectrum of oligo **13c** (Voyager-Elite mass spectrometer; THA matrix)

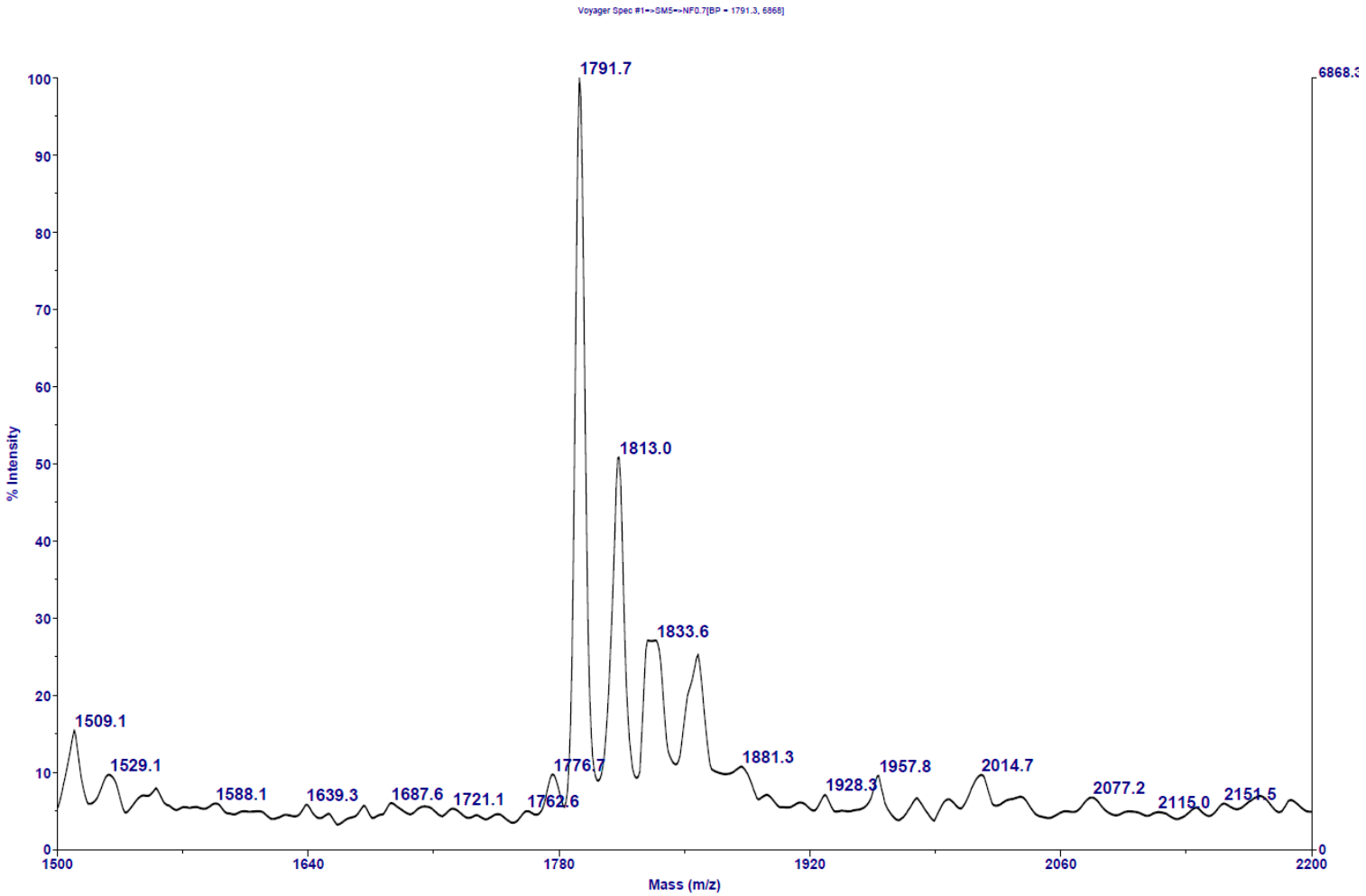

Fig.S22. MALDI-TOF MS spectrum of oligo **13d** (Voyager-Elite mass spectrometer; HPA matrix)

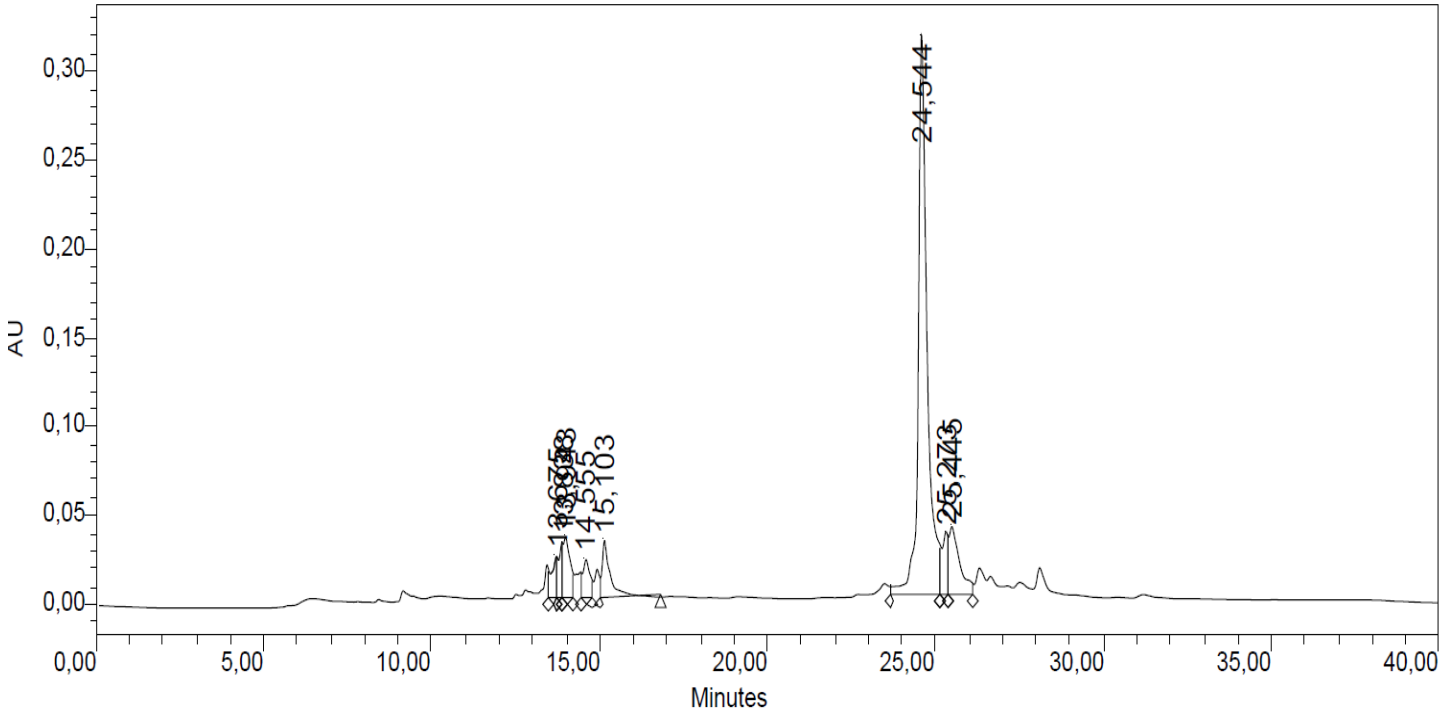

Fig.S23. HPLC profile of oligo **13d** (DMT-on stage)

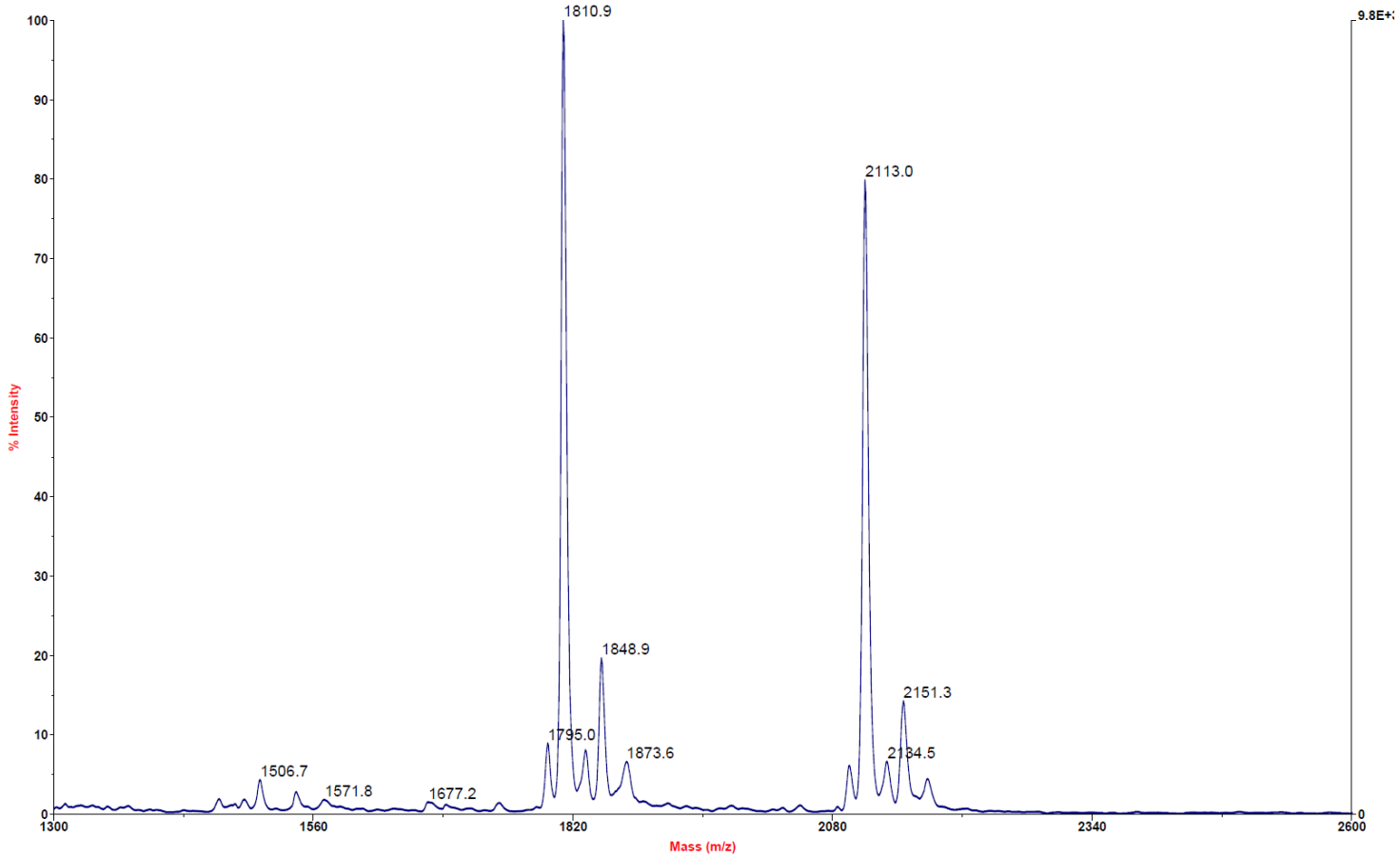

Fig.S24. MALDI-TOF MS spectrum of oligo **13e** (Voyager-Elite mass spectrometer; THA matrix)

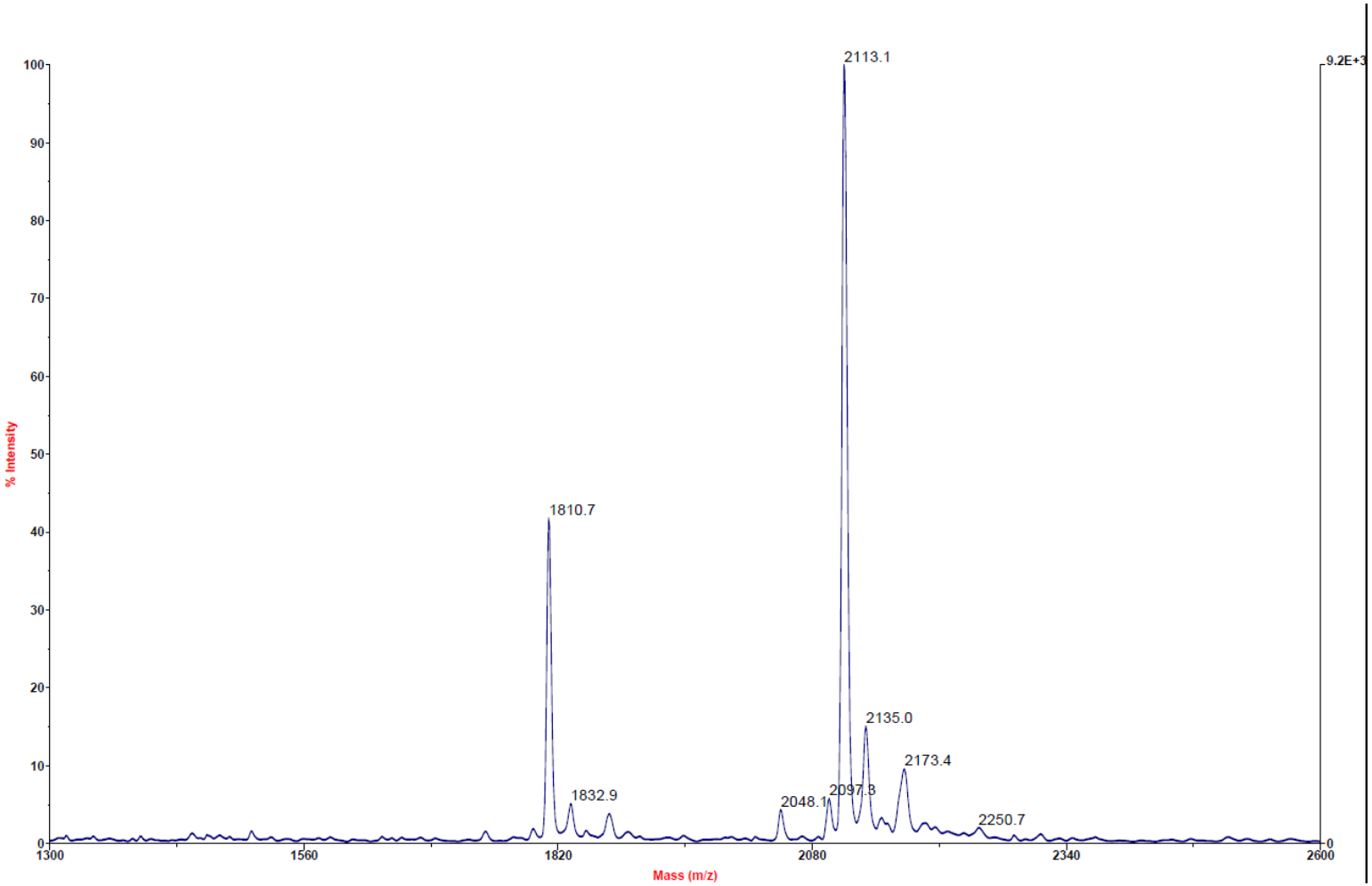

Fig.S25. MALDI-TOF MS spectrum of oligo **13e** (Voyager-Elite mass spectrometer; HPA matrix)

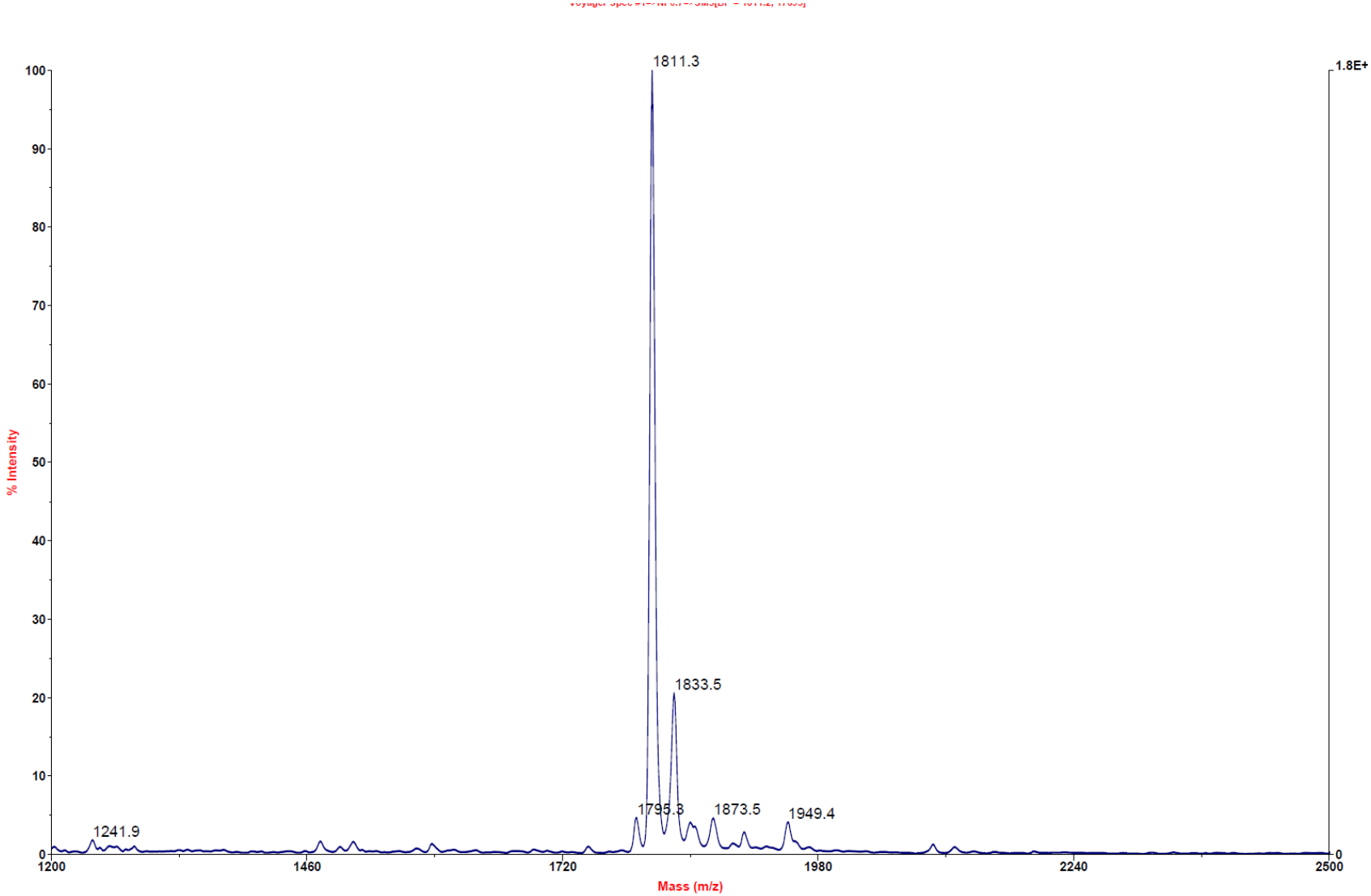

Fig.S26. MALDI-TOF MS spectrum of oligo **13f** (Voyager-Elite mass spectrometer; HPA matrix)

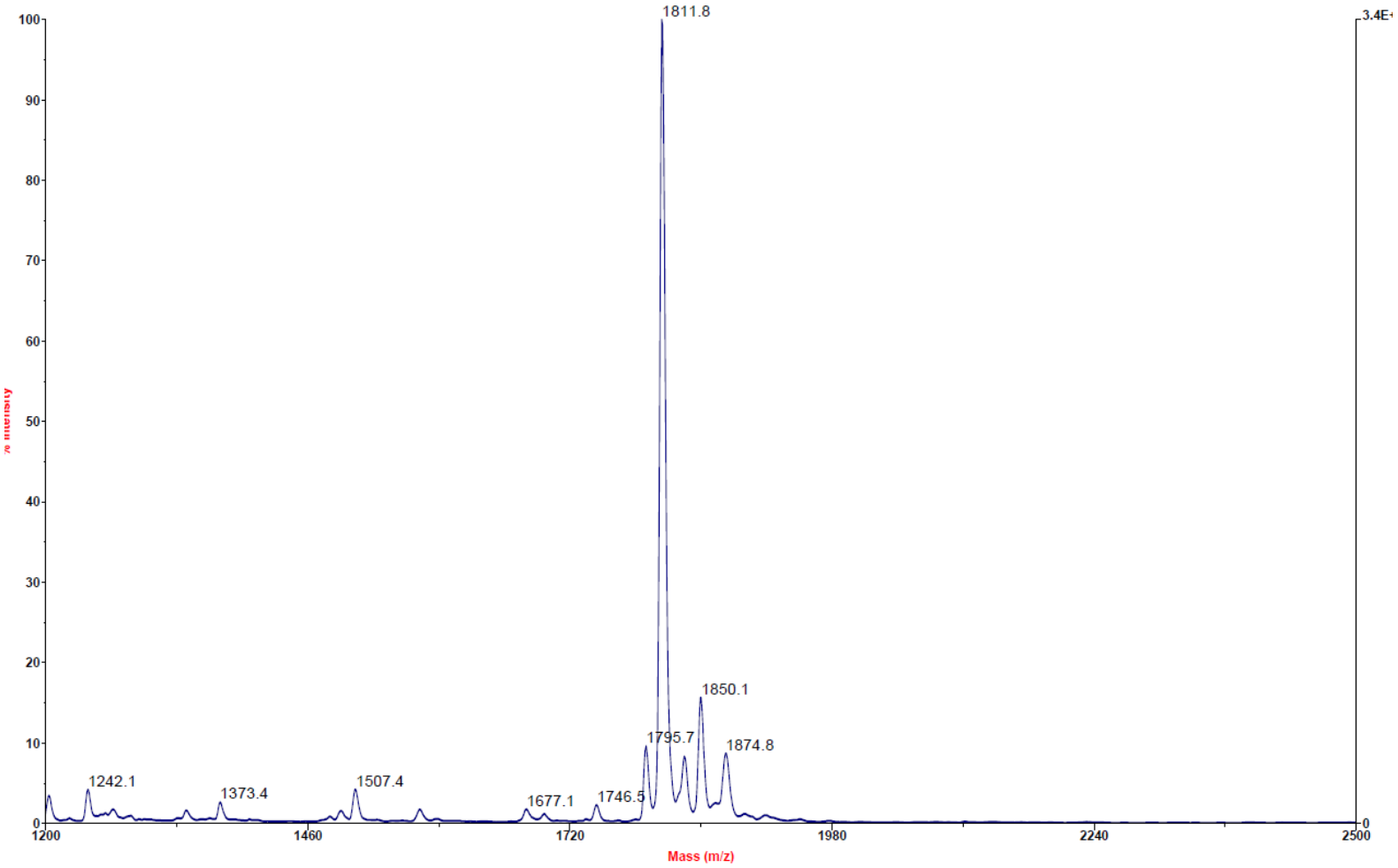

Fig.S27. MALDI-TOF MS spectrum of oligo **13f** (Voyager-Elite mass spectrometer; THA matrix)

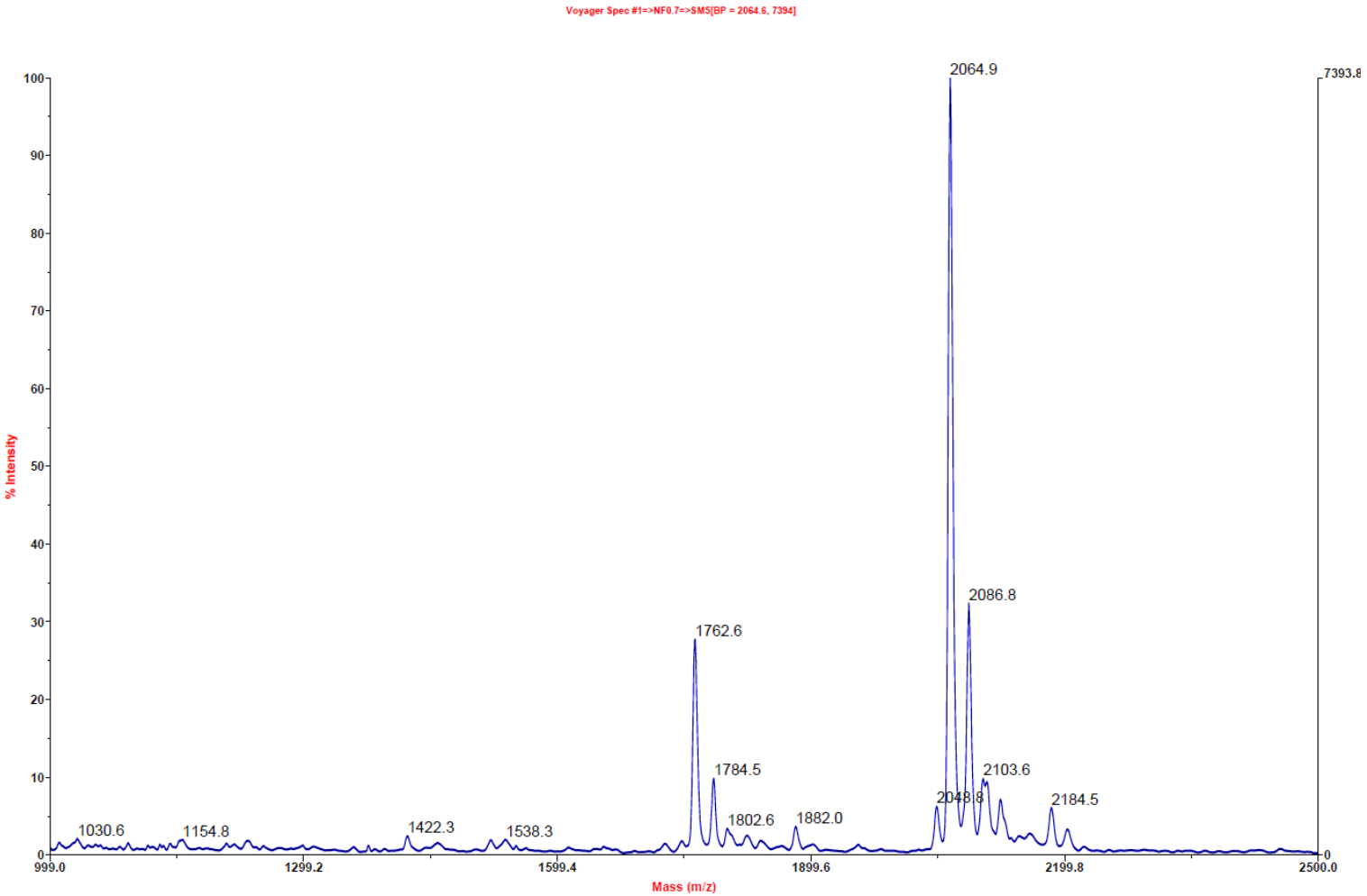

Fig.S28. MALDI-TOF MS spectrum of oligo **13g** (Voyager-Elite mass spectrometer; HPA matrix)

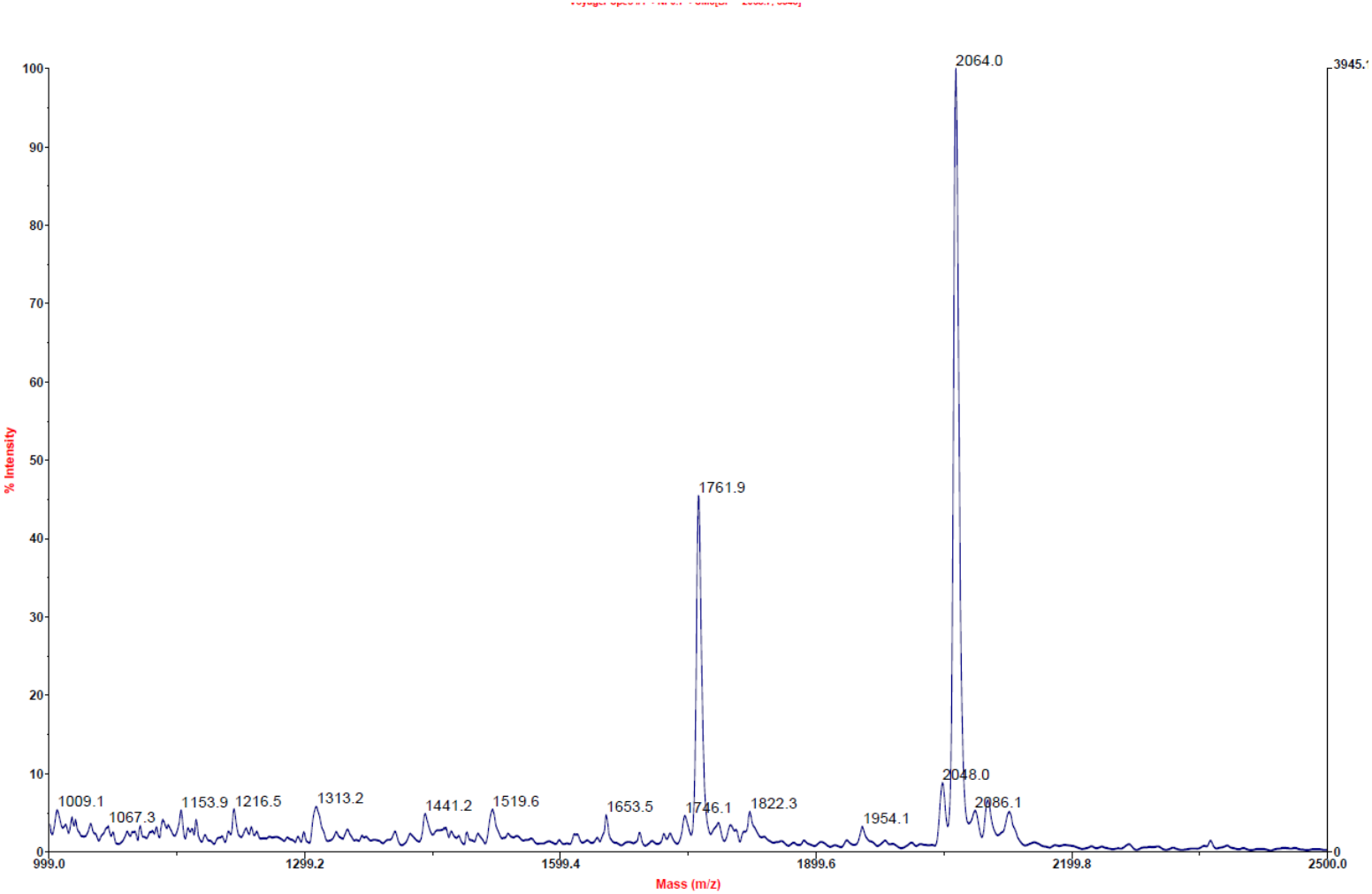

Fig.S29. MALDI-TOF MS spectrum of oligo **13g** (Voyager-Elite mass spectrometer; THA matrix)

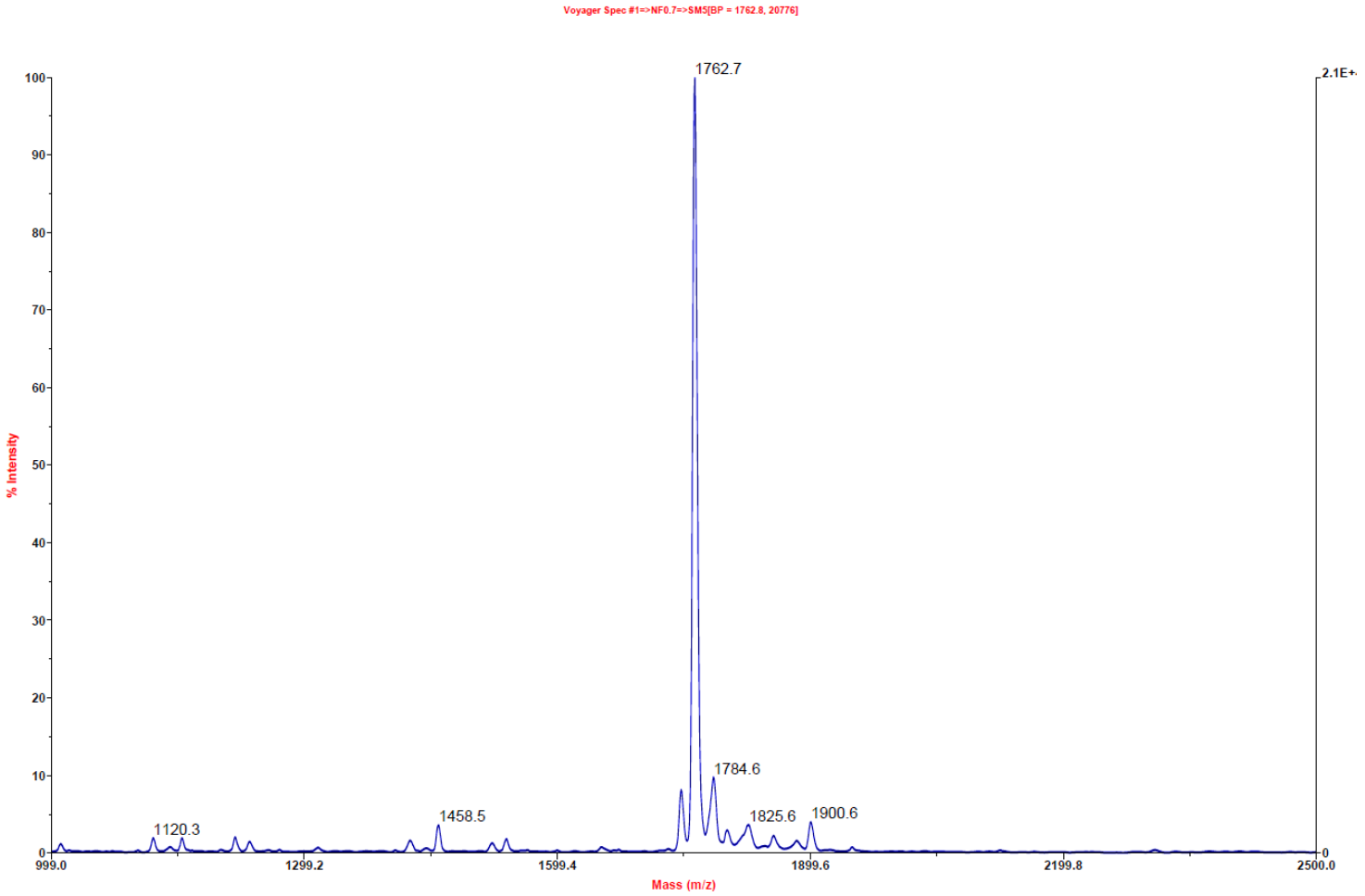

Fig.S30. MALDI-TOF MS spectrum of oligo **13h** (Voyager-Elite mass spectrometer; HPA matrix)

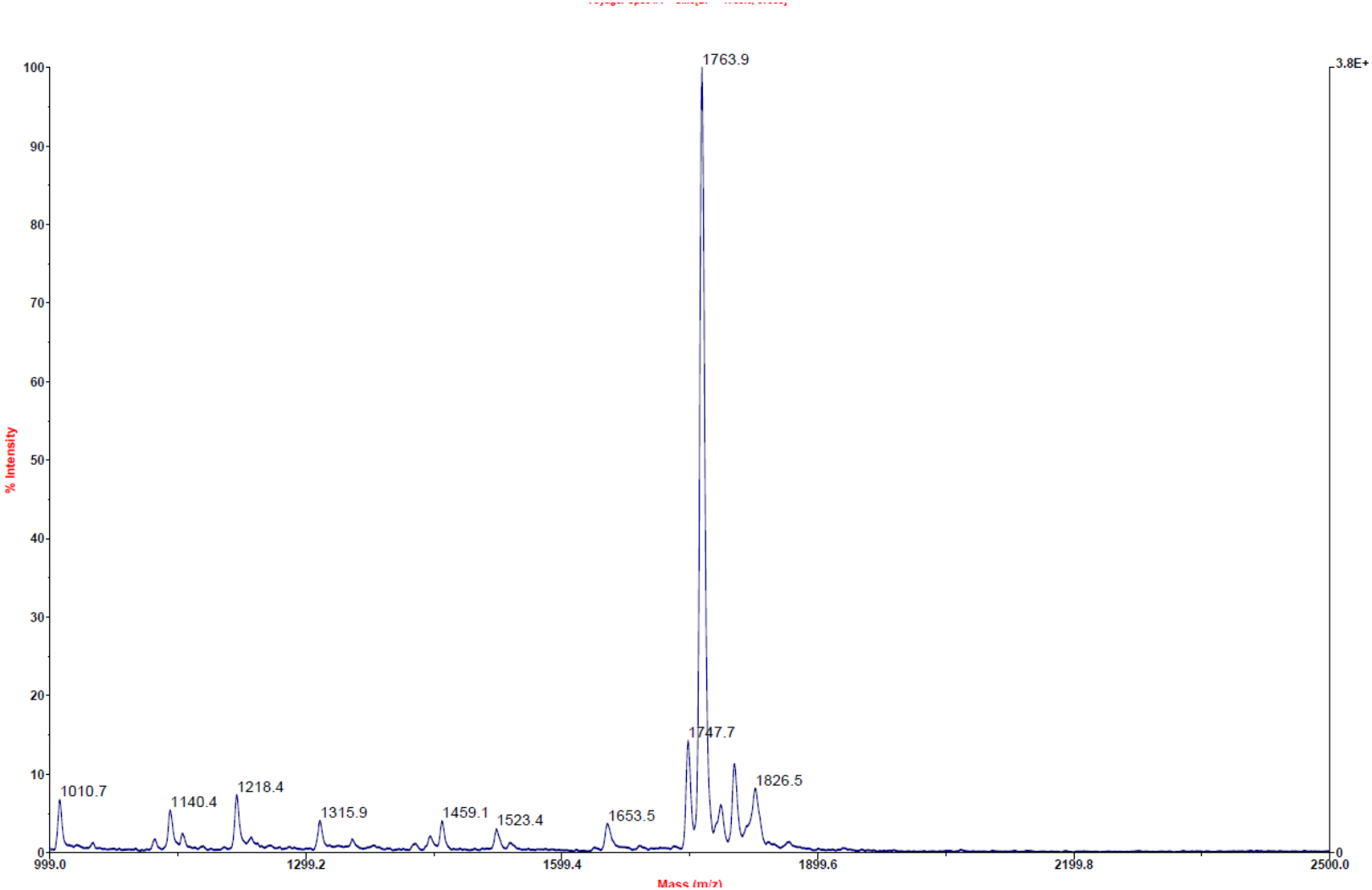

Fig.S31. MALDI-TOF MS spectrum of oligo **13h** (Voyager-Elite mass spectrometer; THA matrix)

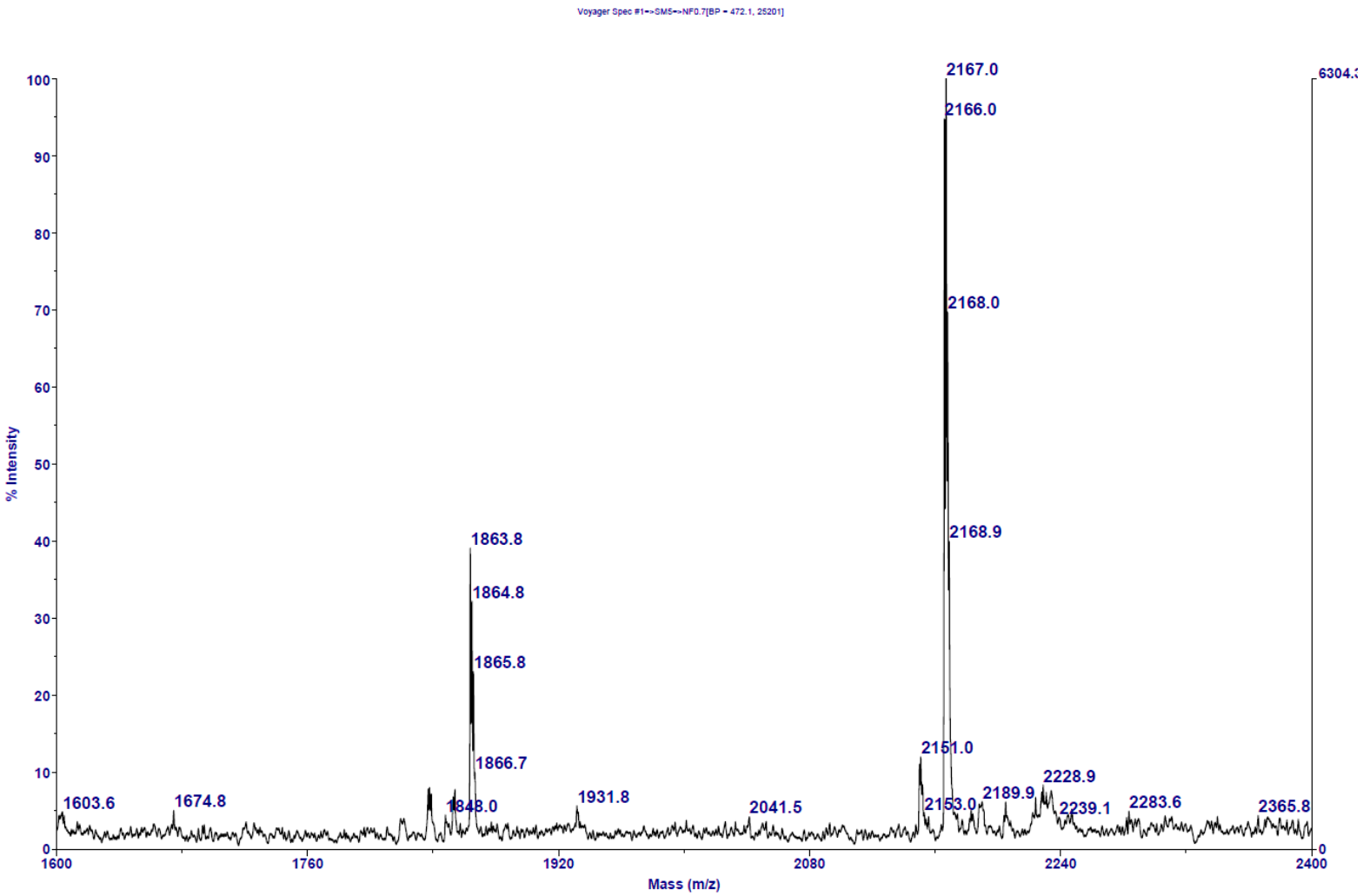

Fig.S32. MALDI-TOF MS spectrum of oligo **13i** (Voyager-Elite mass spectrometer; HPA matrix)

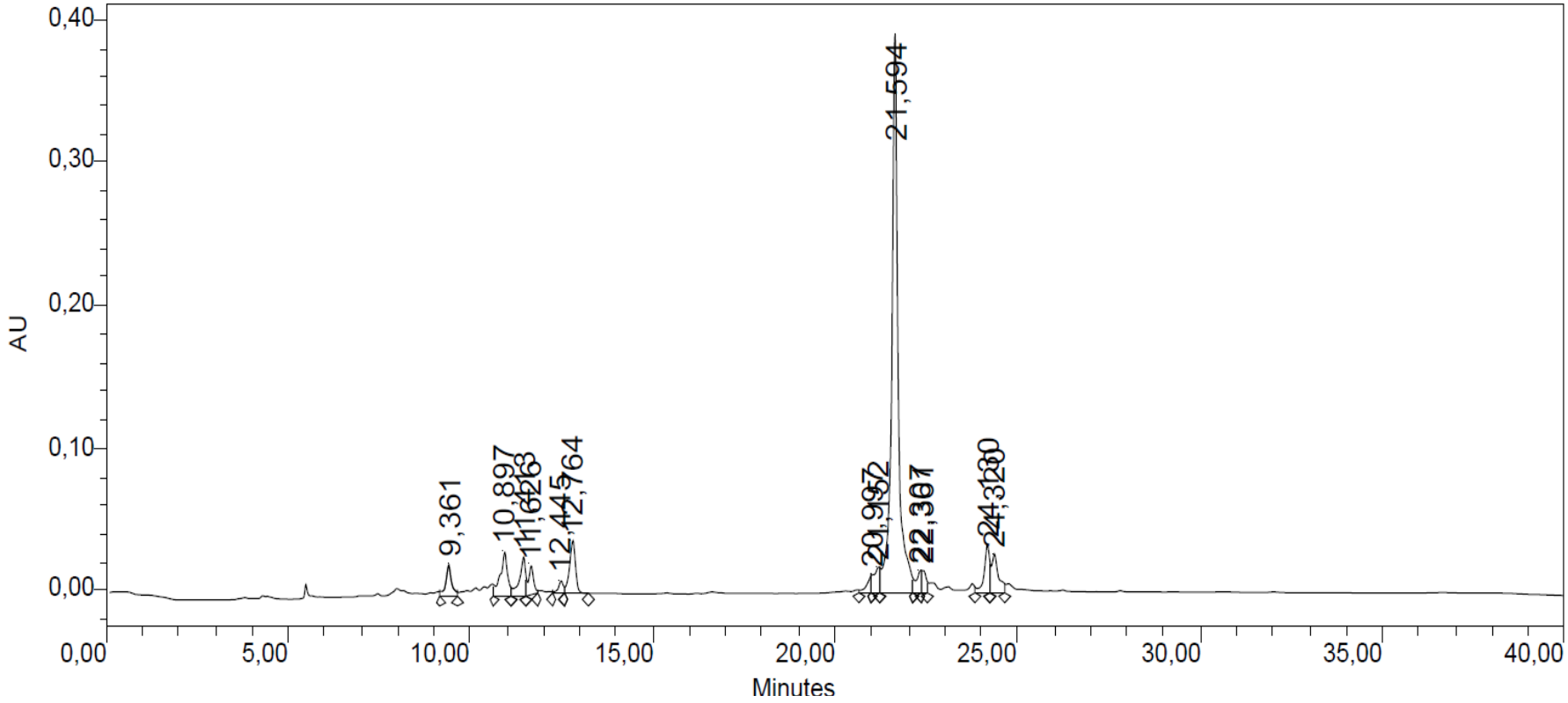

Fig.S33. HPLC profile of of oligo **13i** (DMT-on stage)

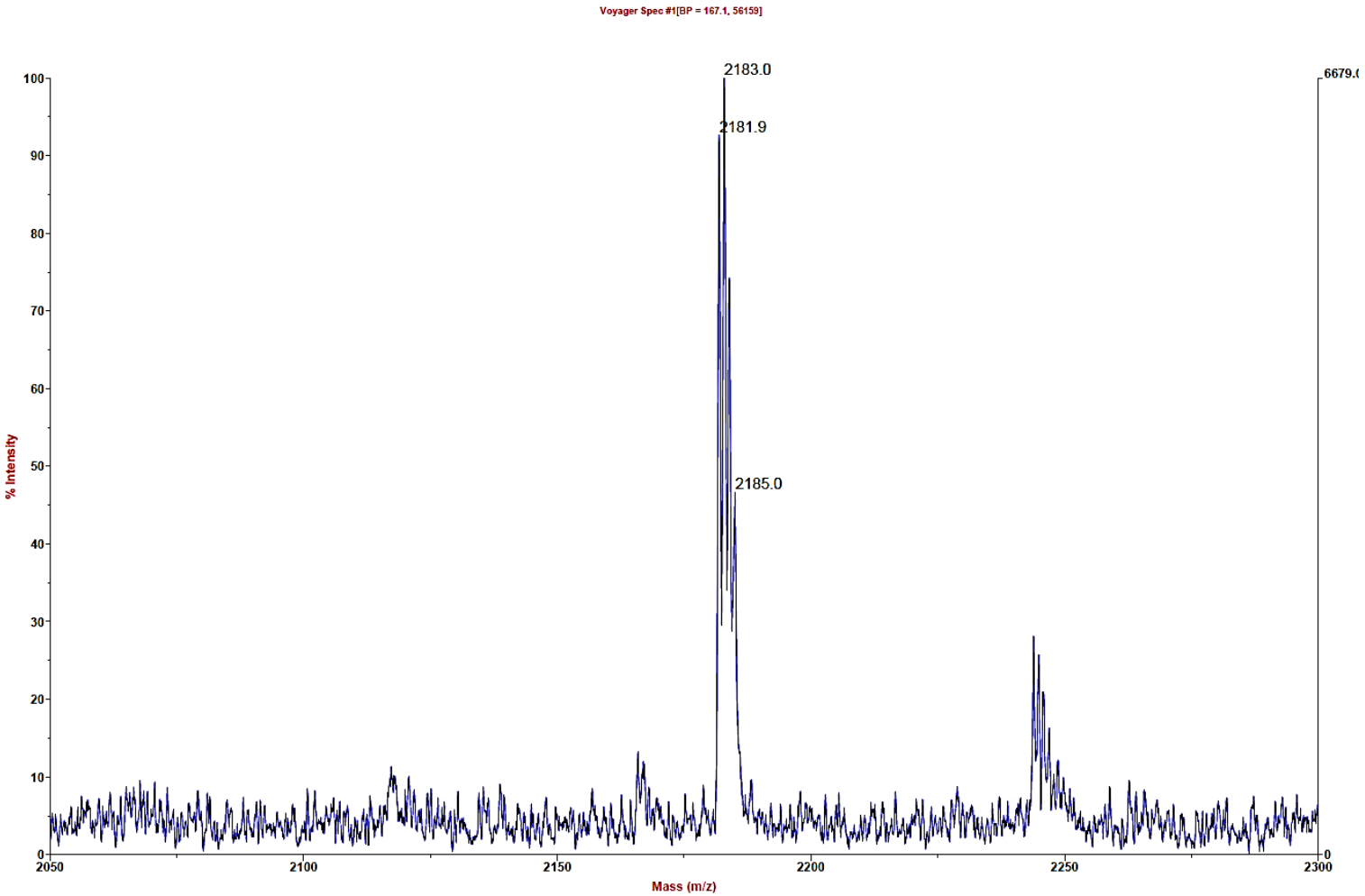

Fig.S34. MALDI-TOF MS spectrum of oligo **13j** (Voyager-Elite mass spectrometer; THA matrix)

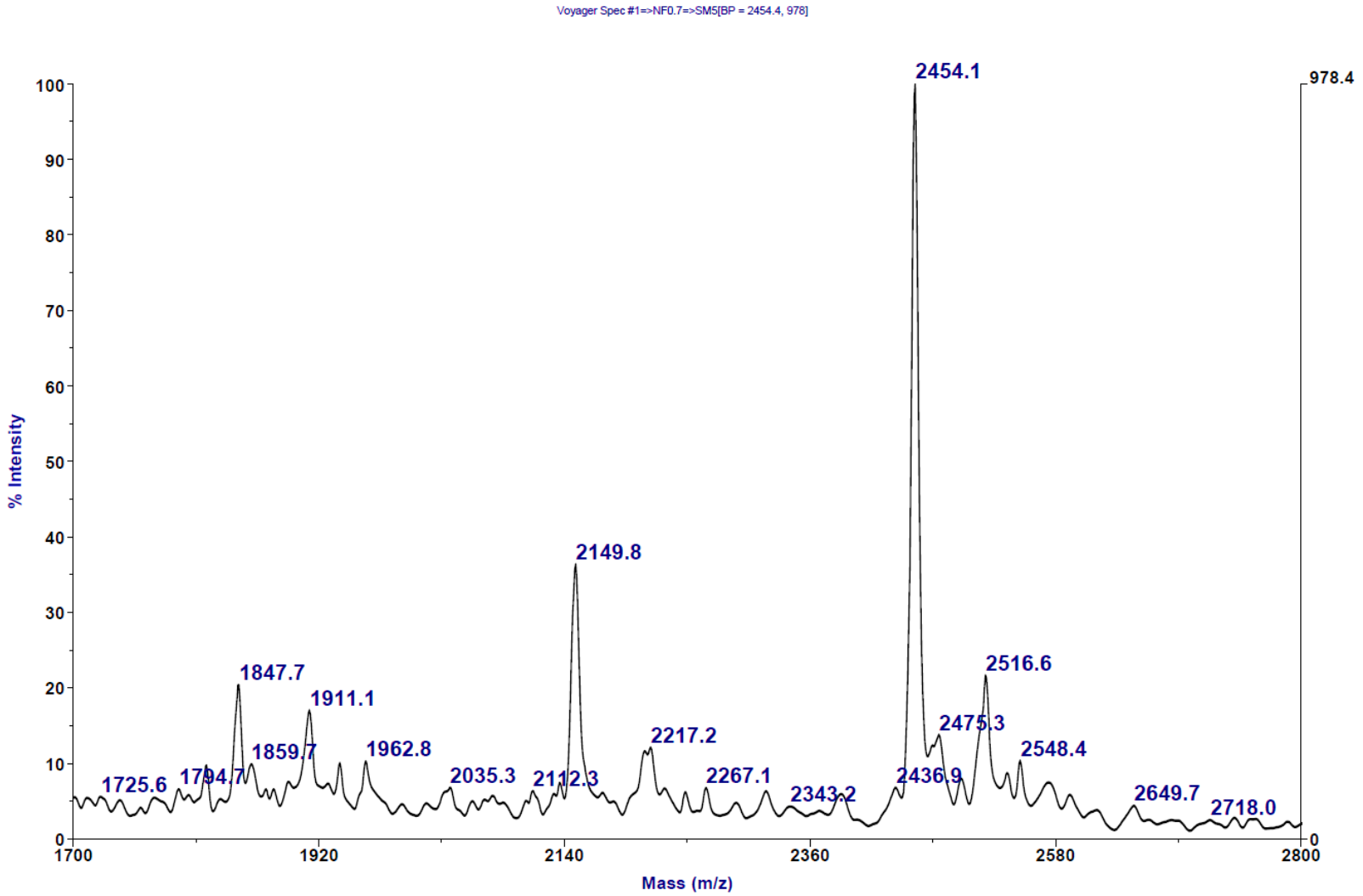

Fig.S35. MALDI-TOF MS spectrum of oligo **13k** (Voyager-Elite mass spectrometer; HPA matrix)

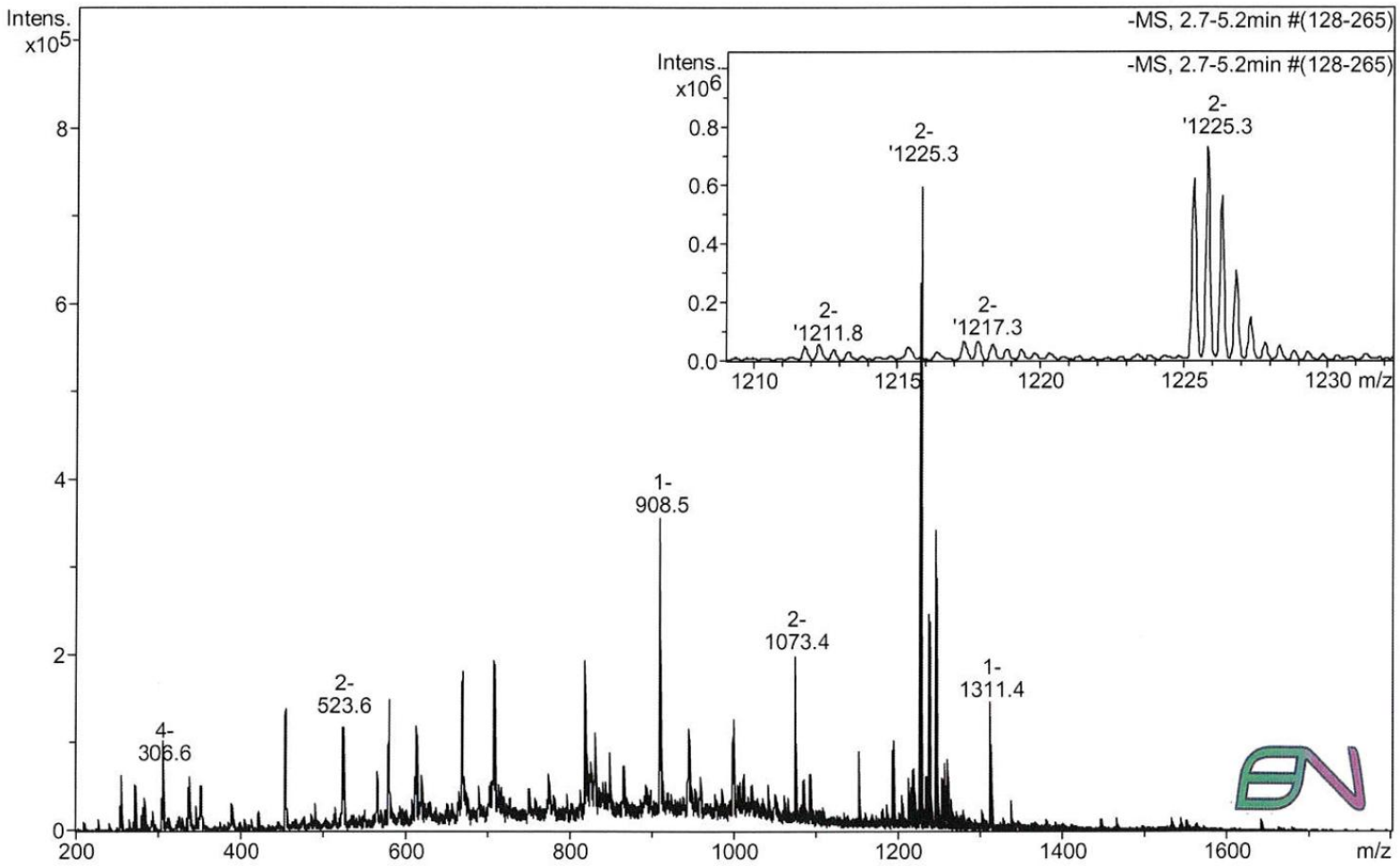

Fig.S36. ESI-MS spectrum of oligo **13k (**Brüker amaZon speed ETD instrument)

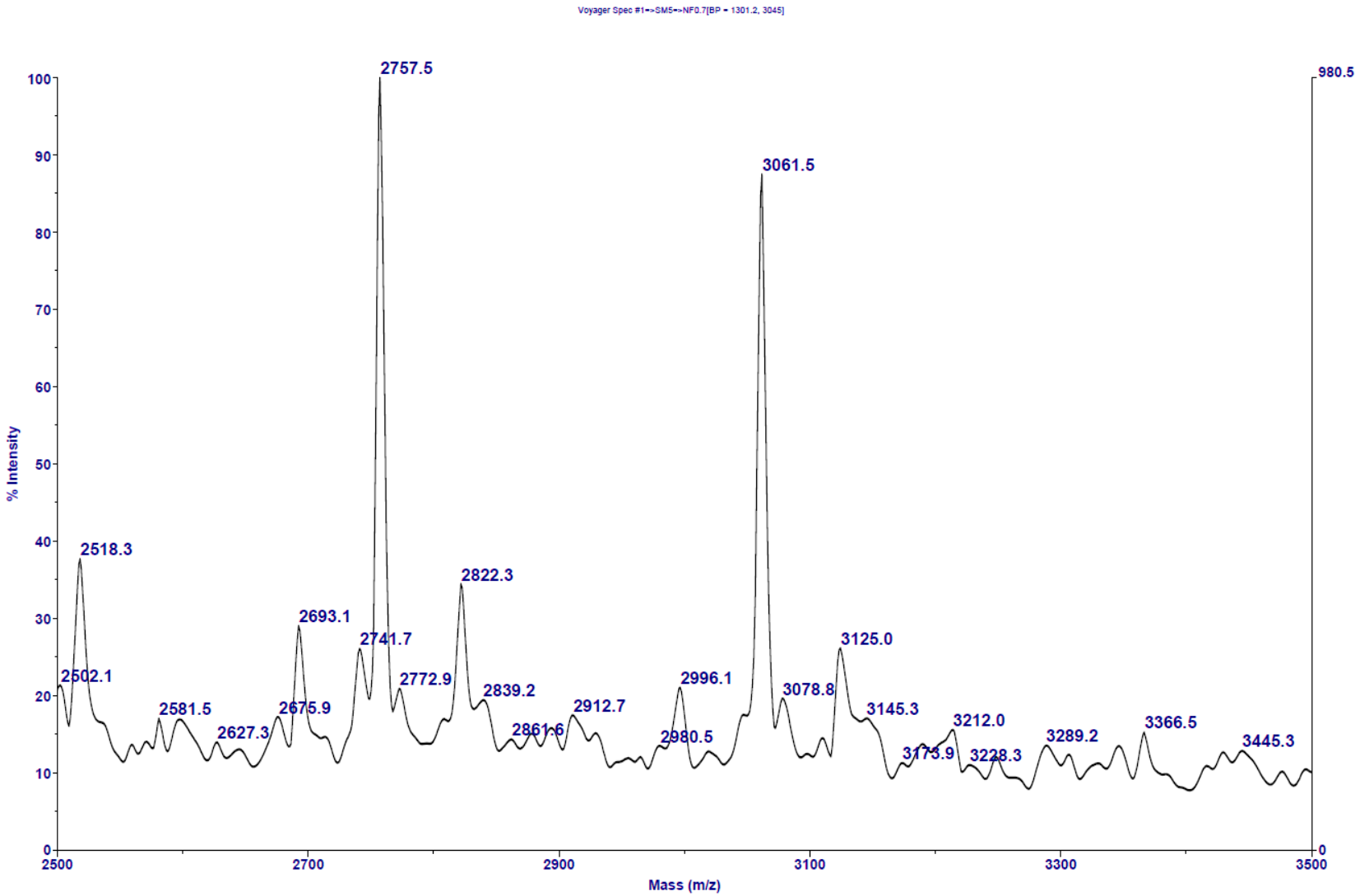

Fig.S37. MALDI-TOF MS spectrum of oligo **13l** (Voyager-Elite mass spectrometer; HPA matrix)

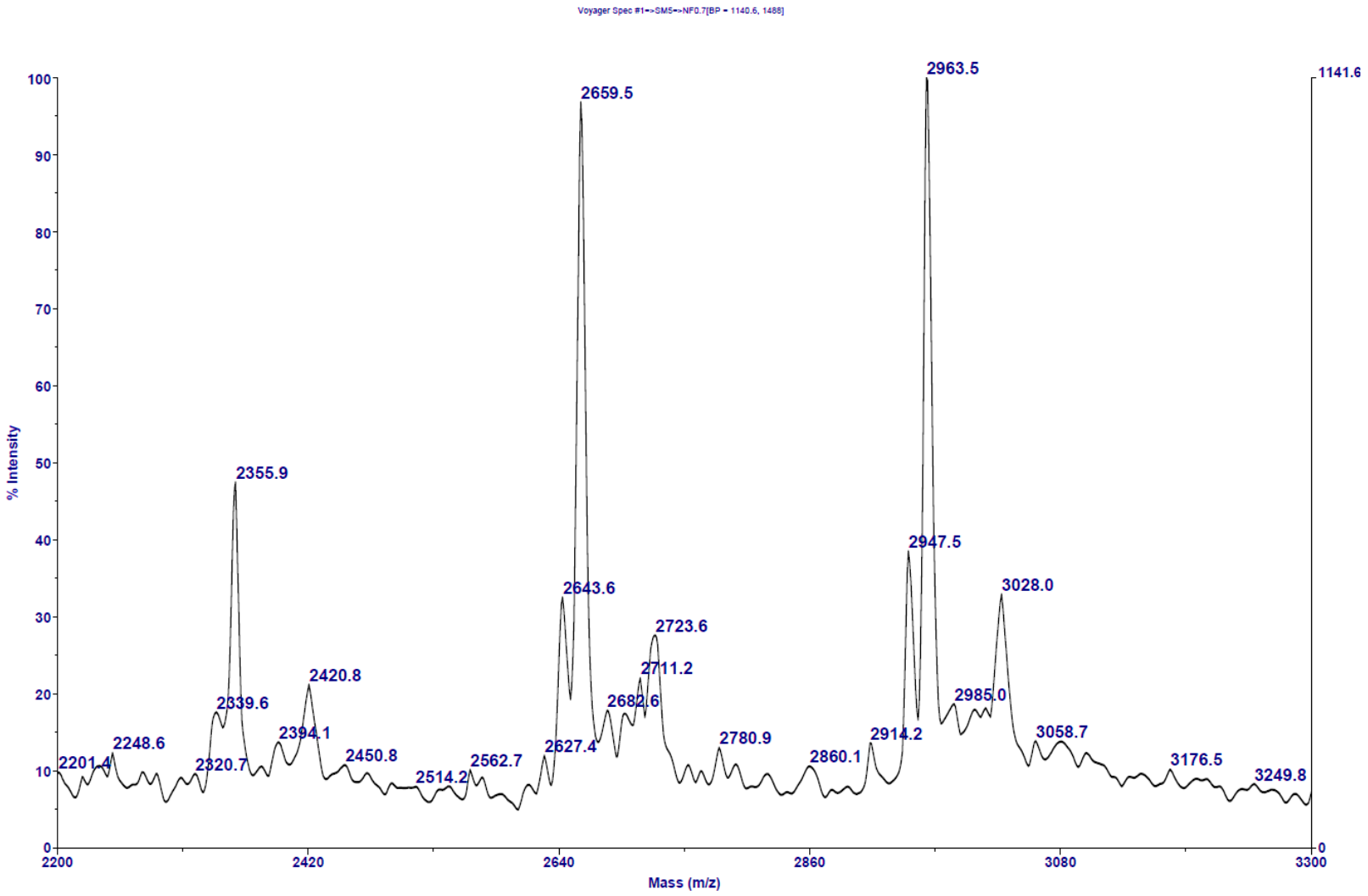

Fig.S38. MALDI-TOF MS spectrum of oligo **13m** (Voyager-Elite mass spectrometer; HPA matrix)

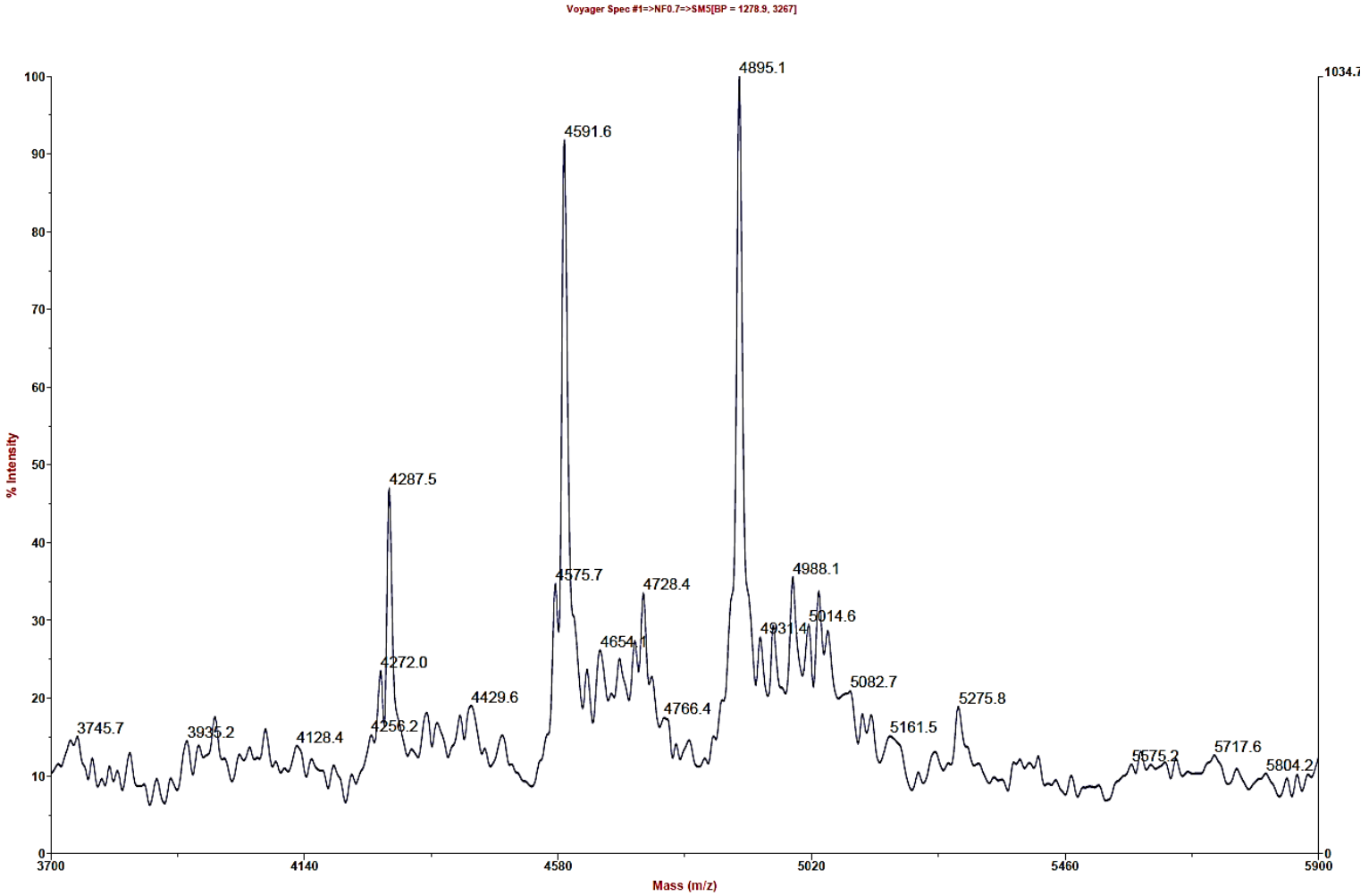

Fig.S39. MALDI-TOF MS spectrum of oligo **13n** (Voyager-Elite mass spectrometer; HPA matrix)

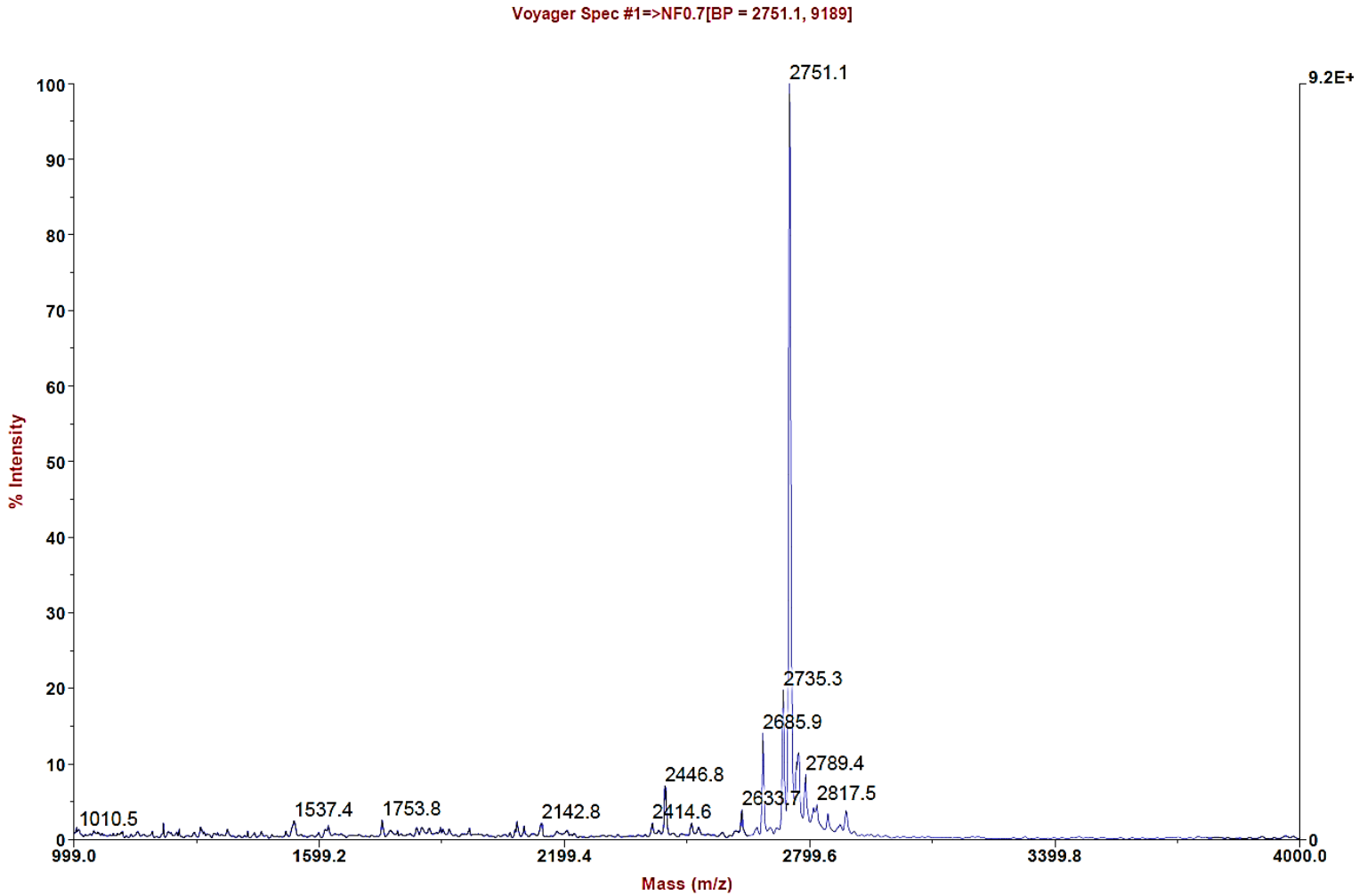

Fig.S40. MALDI-TOF MS spectrum of oligo **13o** (Voyager-Elite mass spectrometer; HPA matrix)

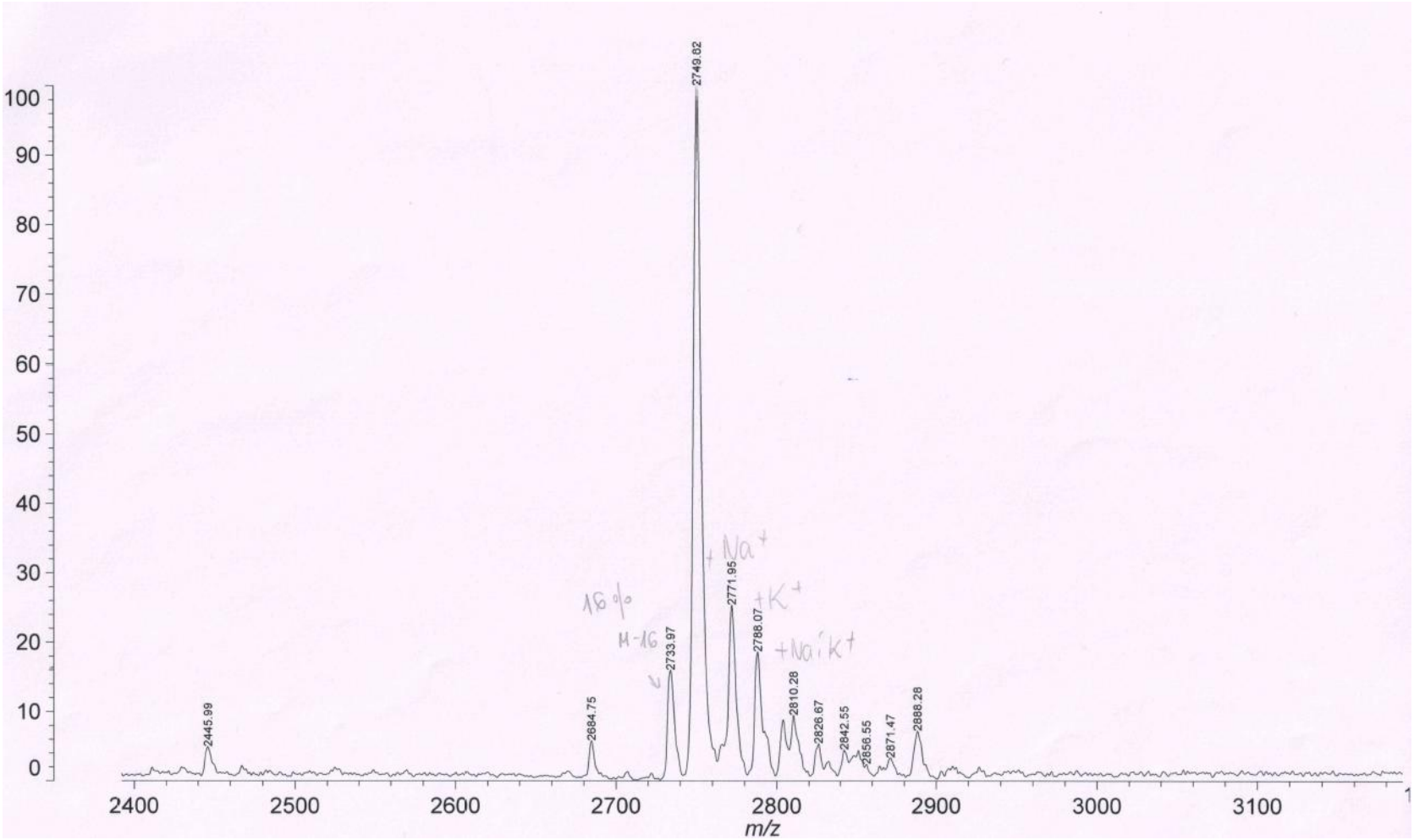

Fig.S41. MALDI-TOF MS spectrum of oligo **13o** (SHIMADZU Axima Performance mass spectrometer; HPA matrix)

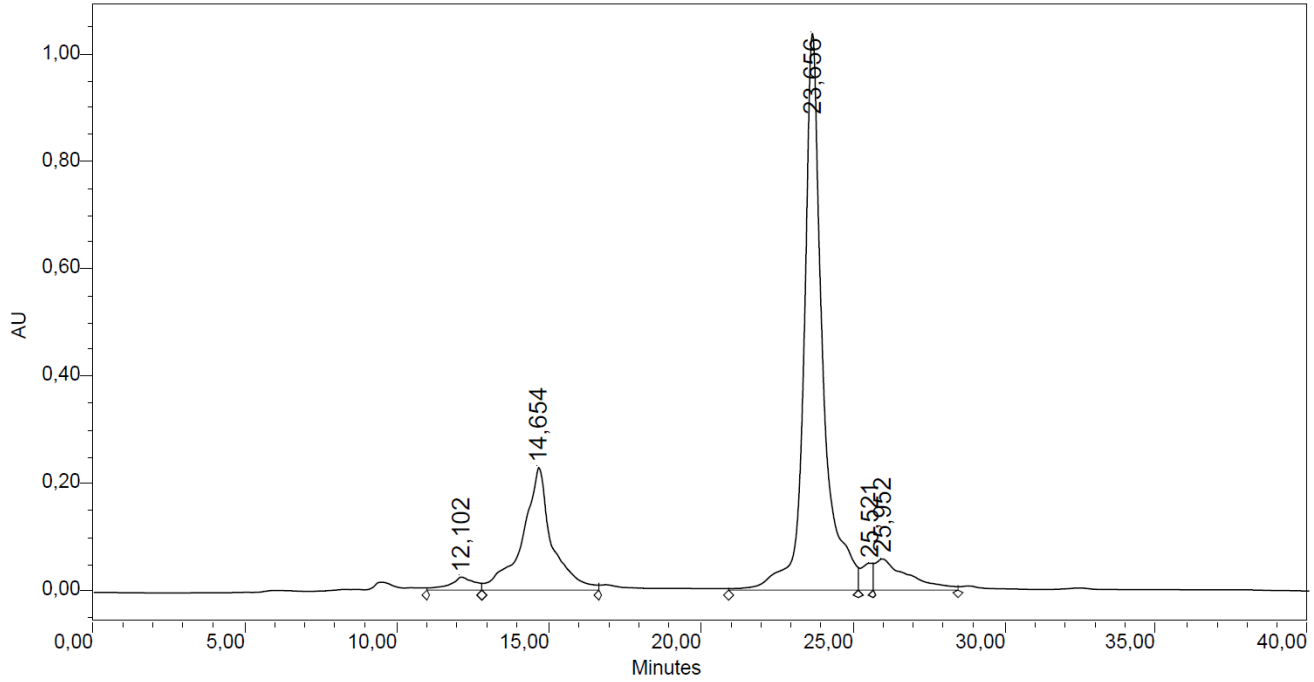

Fig.S42. HPLC profile of oligo **13o** (DMT-on stage)

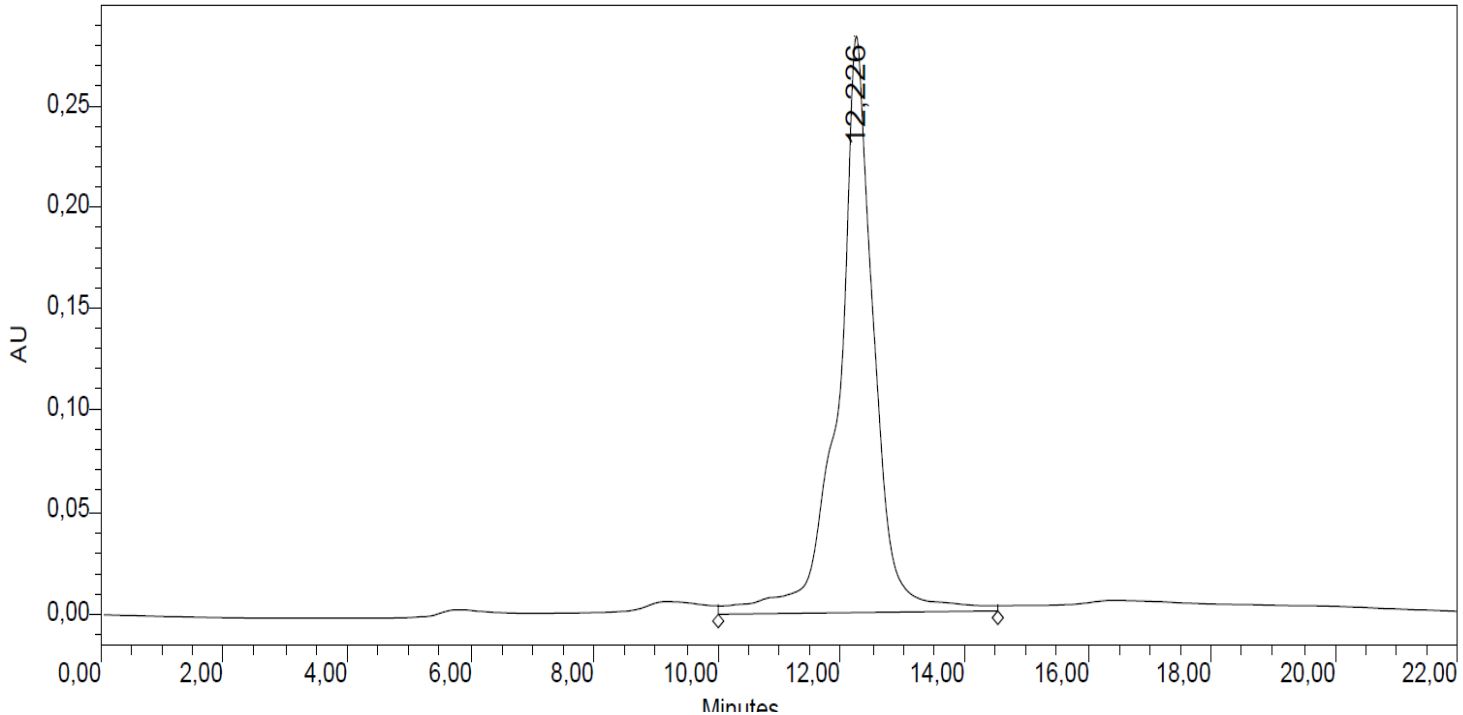

Fig.S43. HPLC profile of oligo **13o** (DMT-off stage)

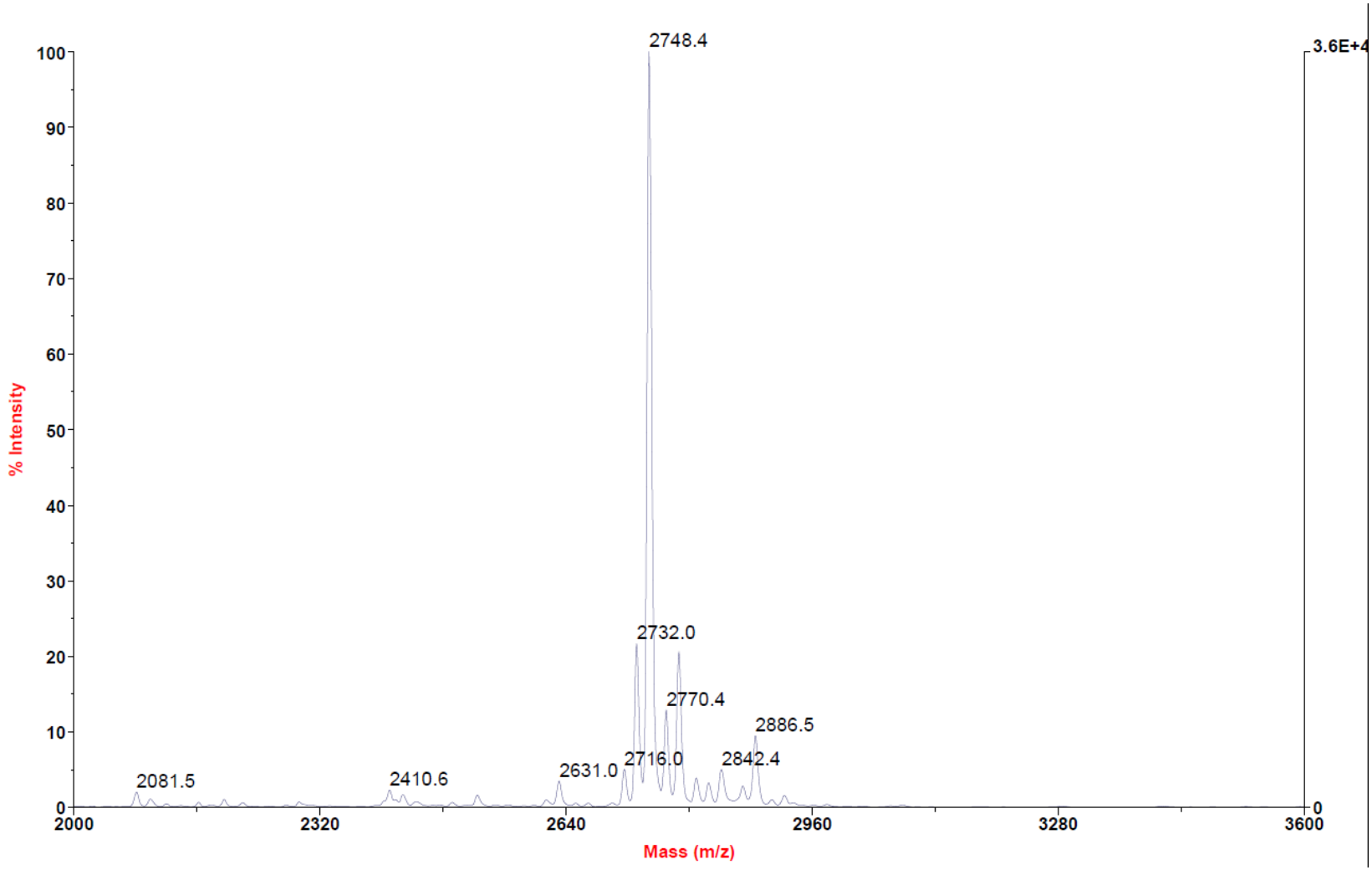

Fig.S44. MALDI-TOF MS spectrum of oligo **13o** synthesized by using only commercially available deoxyribonucleoside phosphoramidites **7** (B^1=Thy, Ade^{Bz}) (Voyager-Elite mass spectrometer; HPA matrix)

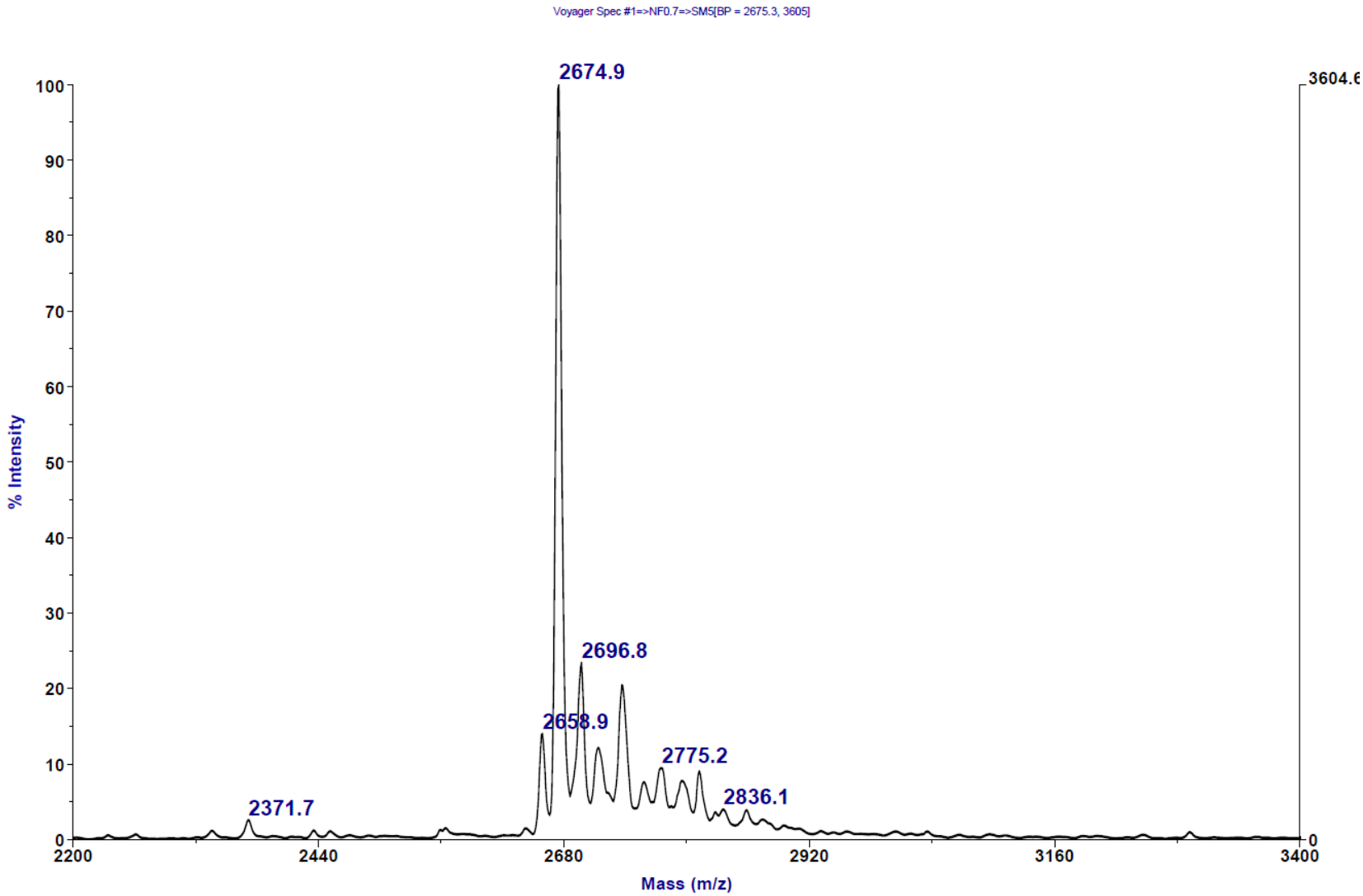

Fig.S45. MALDI-TOF MS spectrum of oligo **13p** (Voyager-Elite mass spectrometer; HPA matrix)

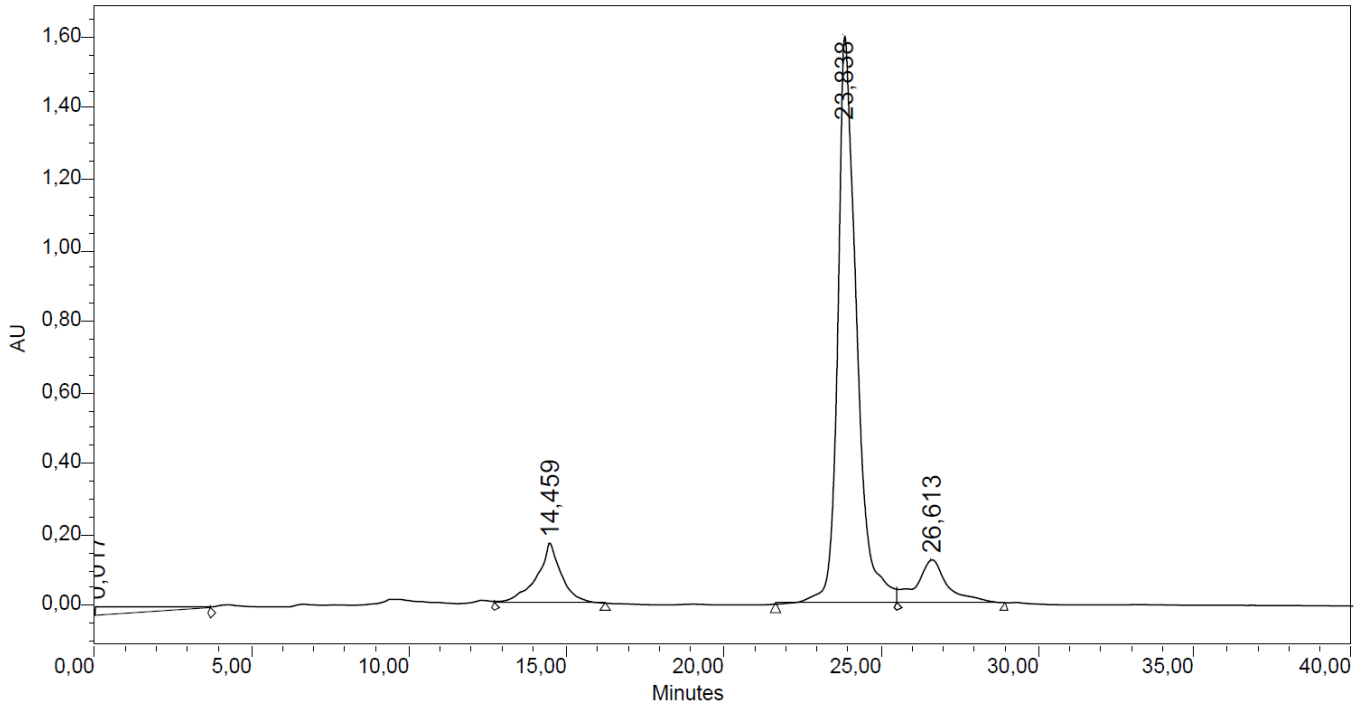

Fig.S46. HPLC profile of oligo **13p** (DMT-on stage)

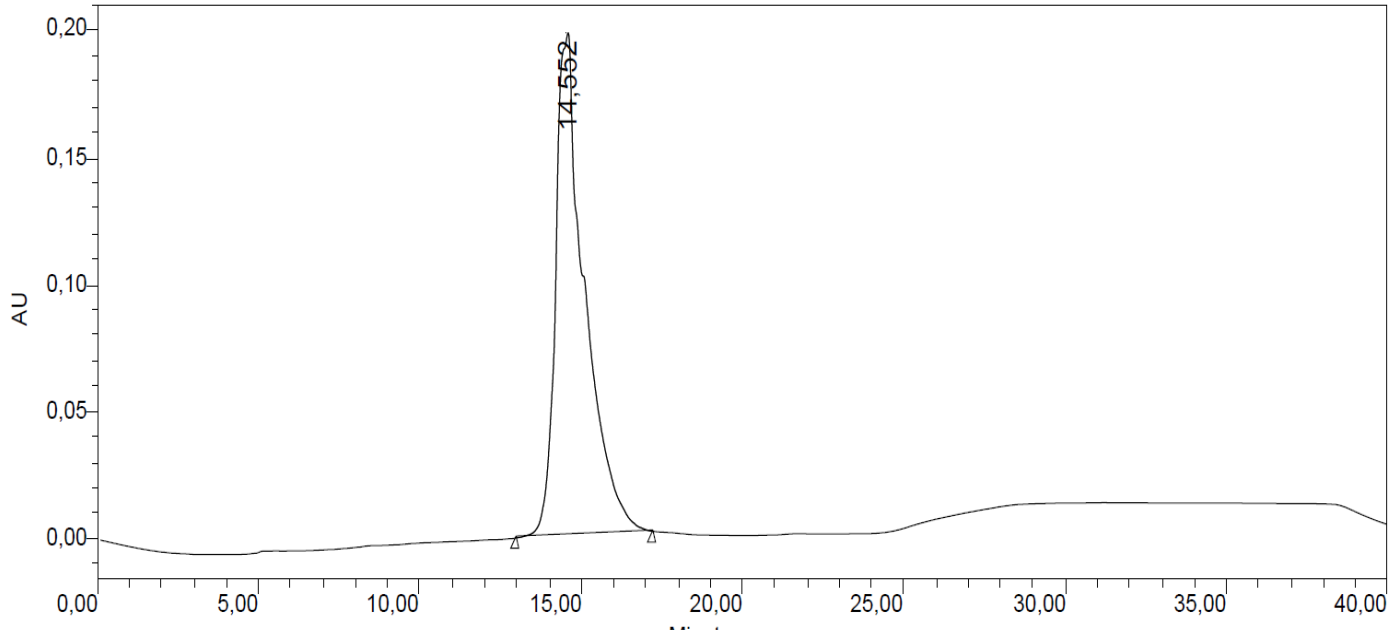

Fig.S47. HPLC profile of oligo **13p** (DMT-off stage)

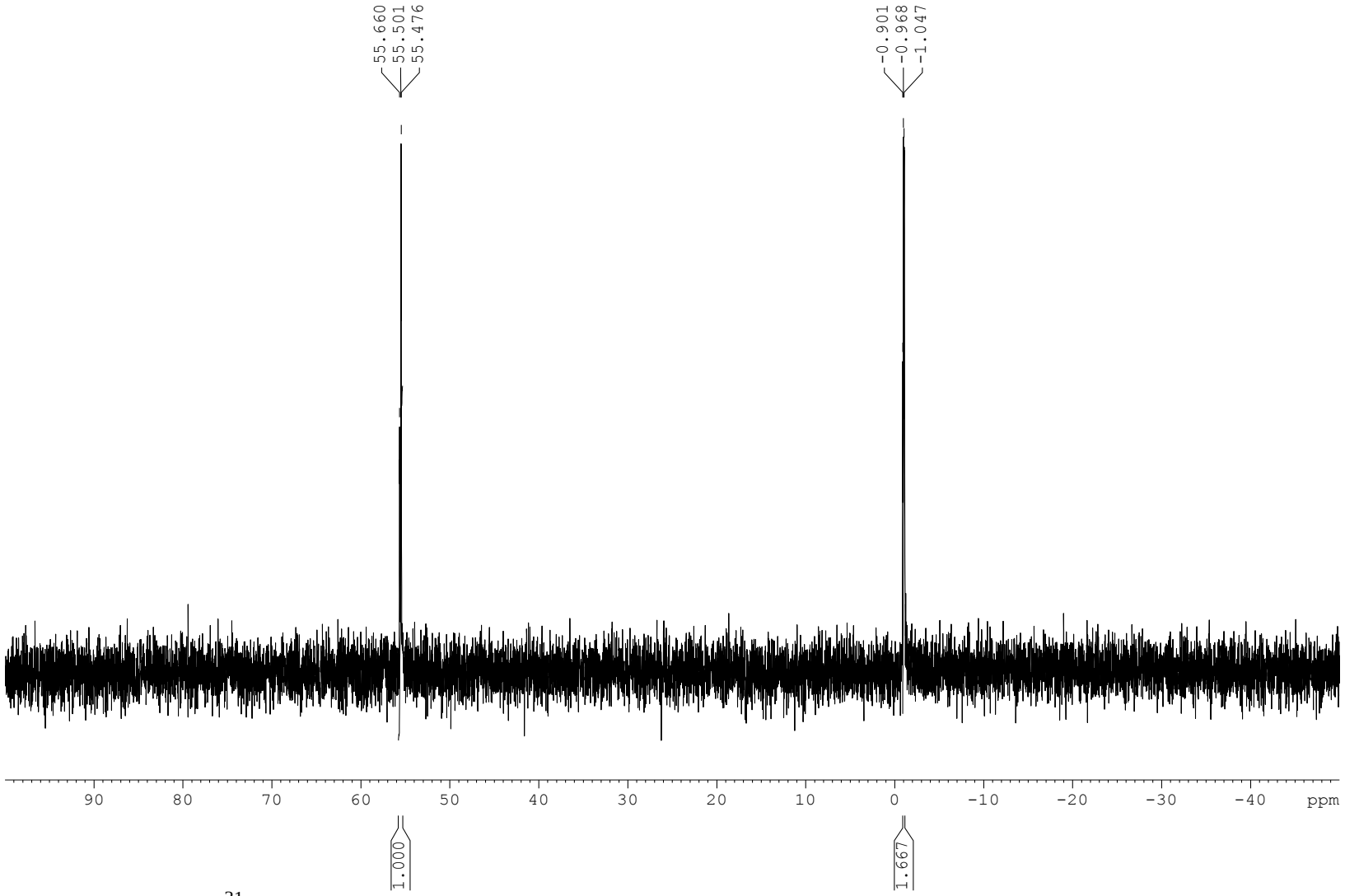

Fig.S48. 202 MHz ^{31}P NMR spectrum of crude **13r**

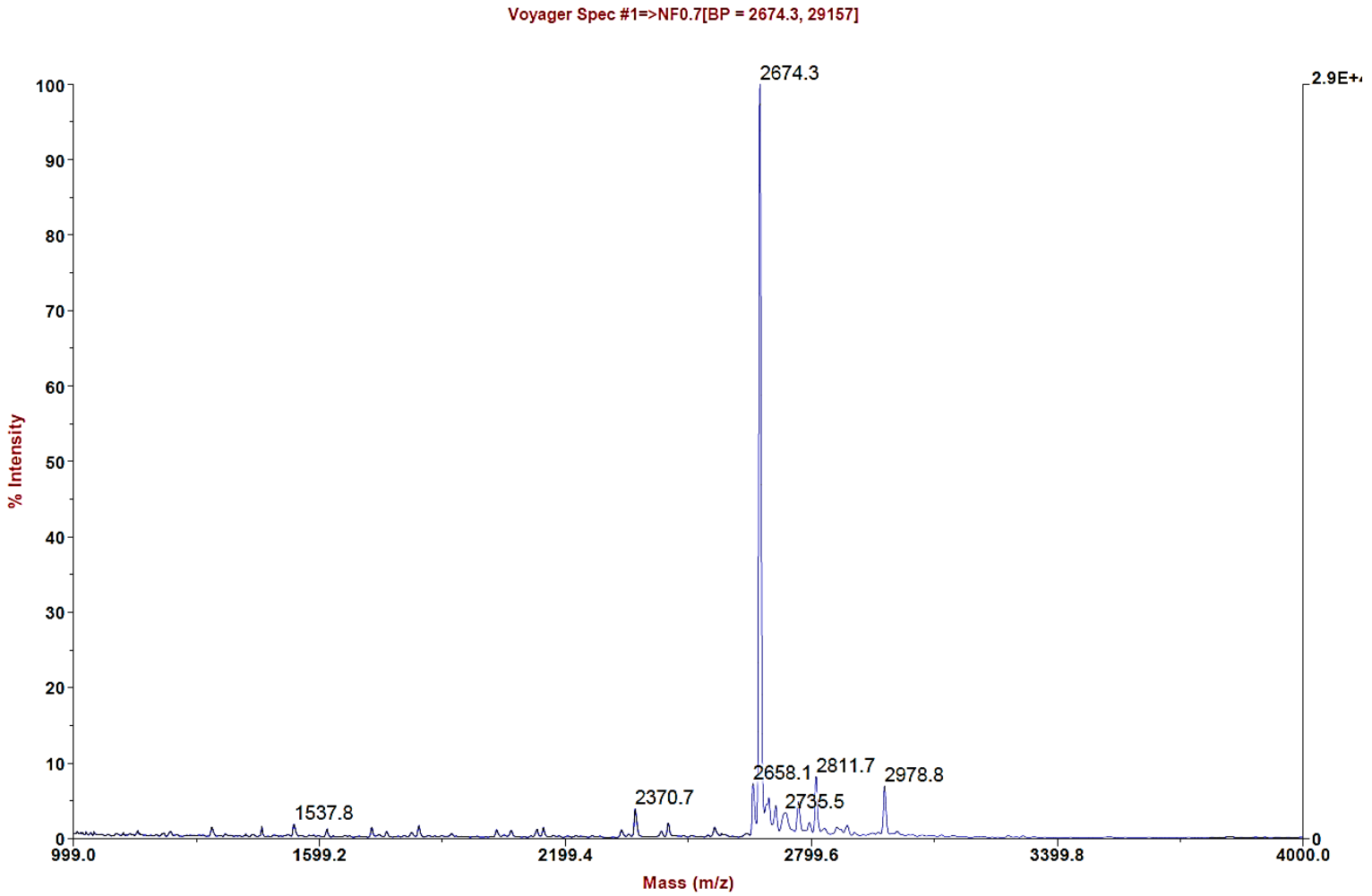

Fig.S49. MALDI-TOF MS spectrum of oligo **13r** (Voyager-Elite mass spectrometer; HPA matrix)

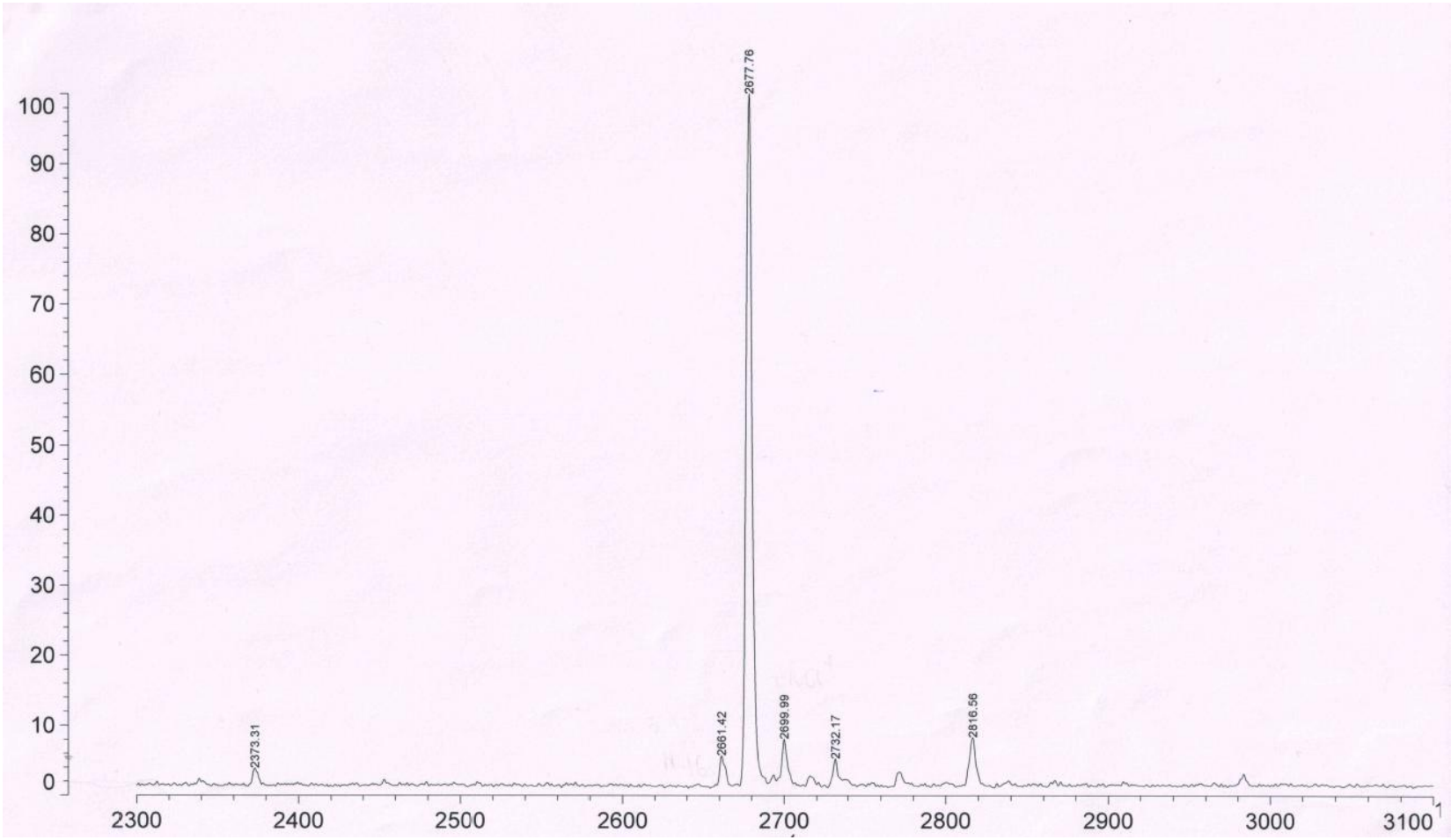

Fig.S50. MALDI-TOF MS spectrum of oligo **13r** (SHIMADZU Axima Performance mass spectrometer; HPA matrix)

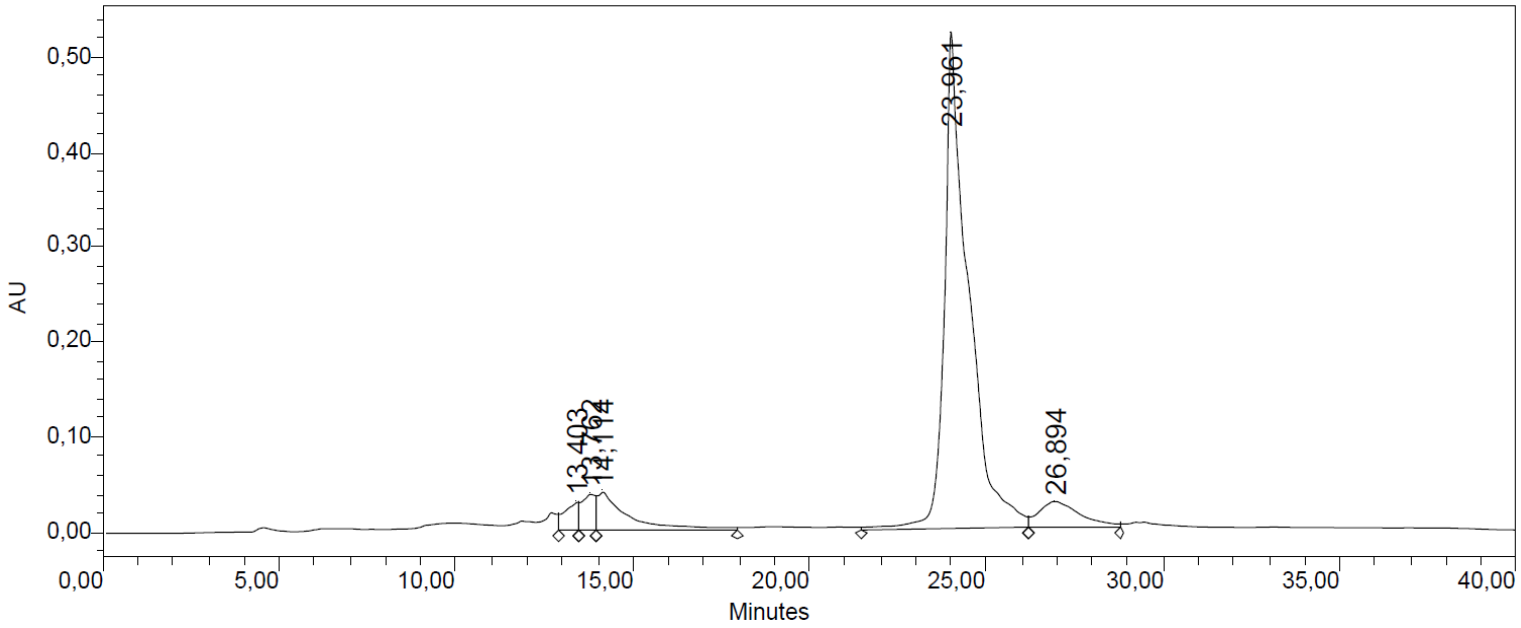

Fig.S51. HPLC profile of oligo **13r** (DMT-on stage)

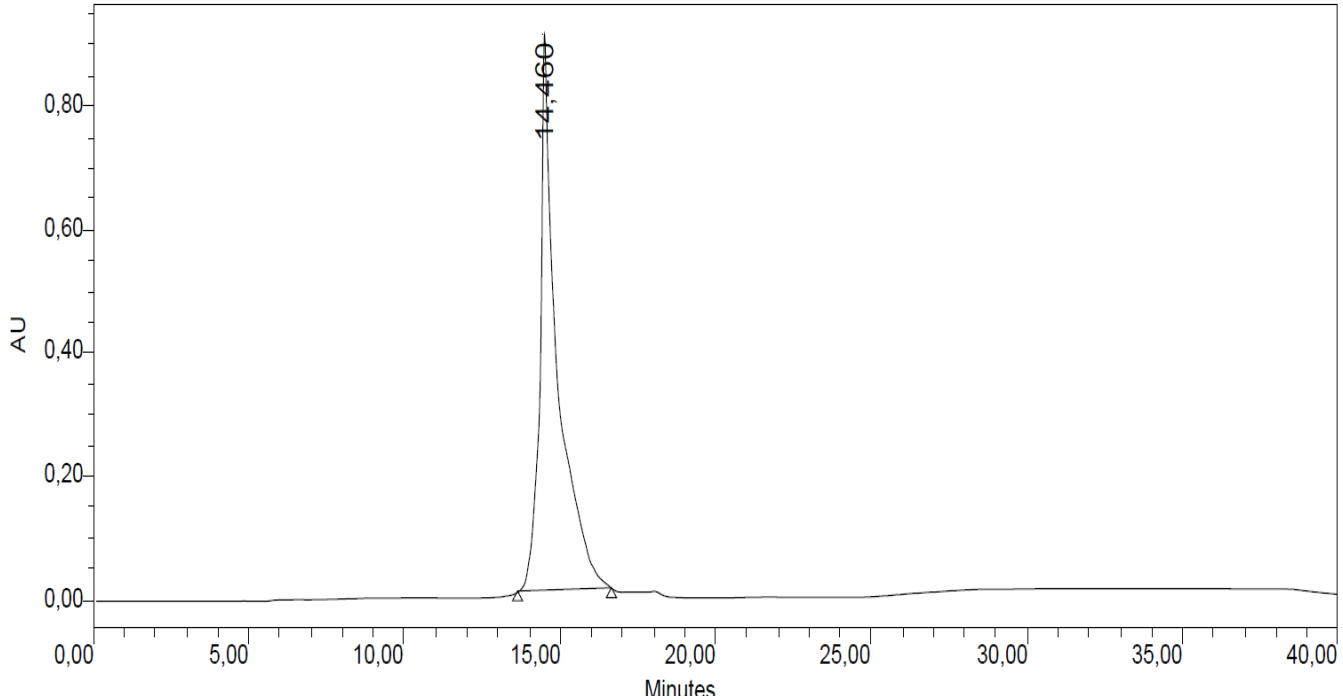

Fig.S52. HPLC profile of oligo **13r** (DMT-off stage)

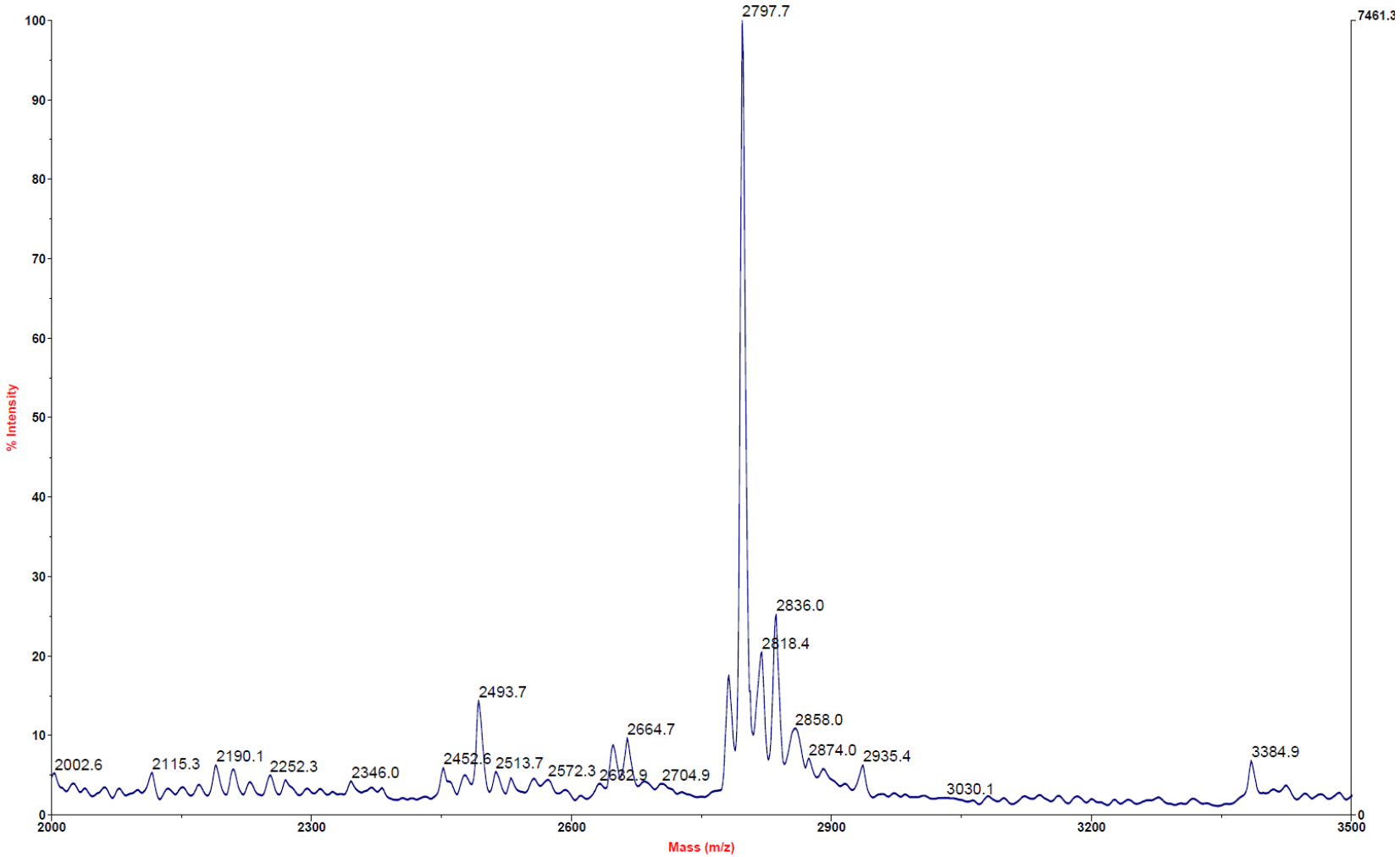

Fig.S53. MALDI-TOF MS spectrum of oligo **13s** (Voyager-Elite mass spectrometer; HPA matrix)

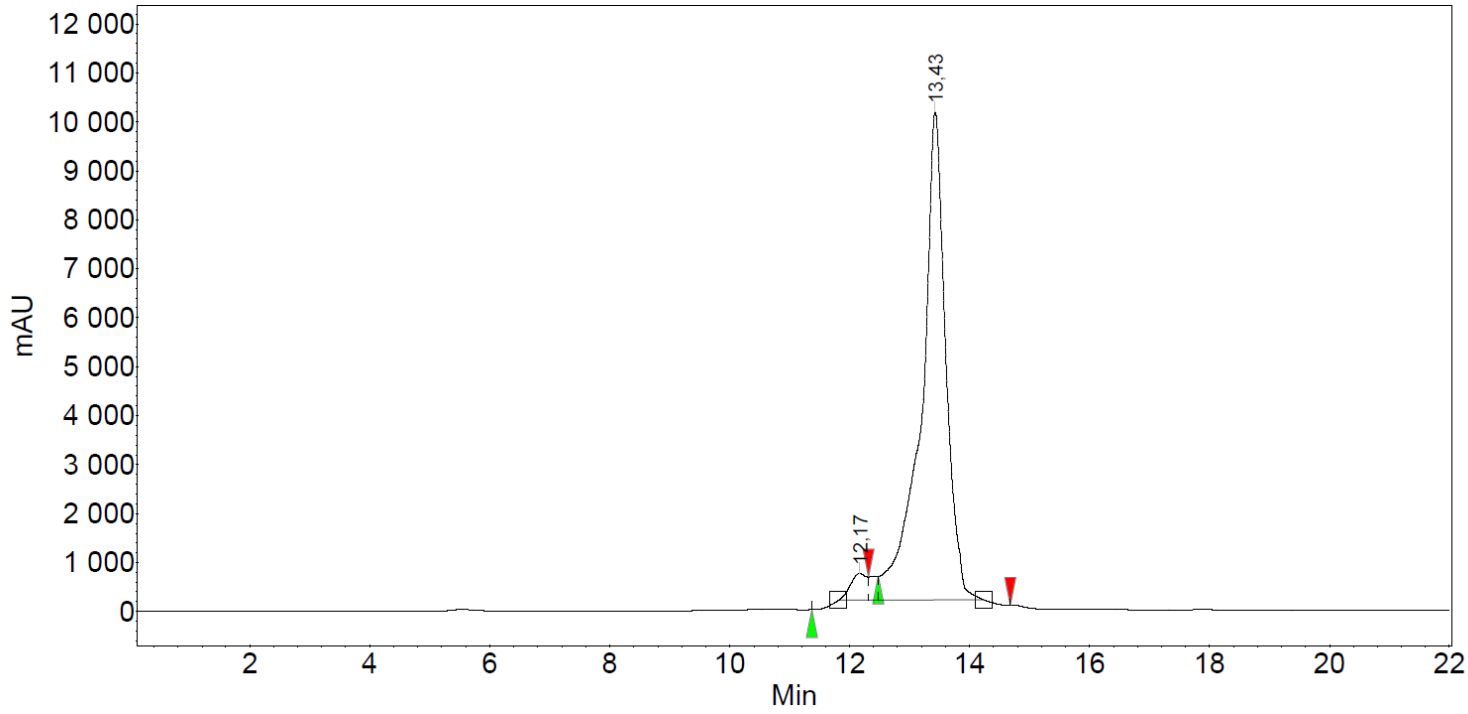

Fig.S54. HPLC profile of oligo **13s** (DMT-off stage)

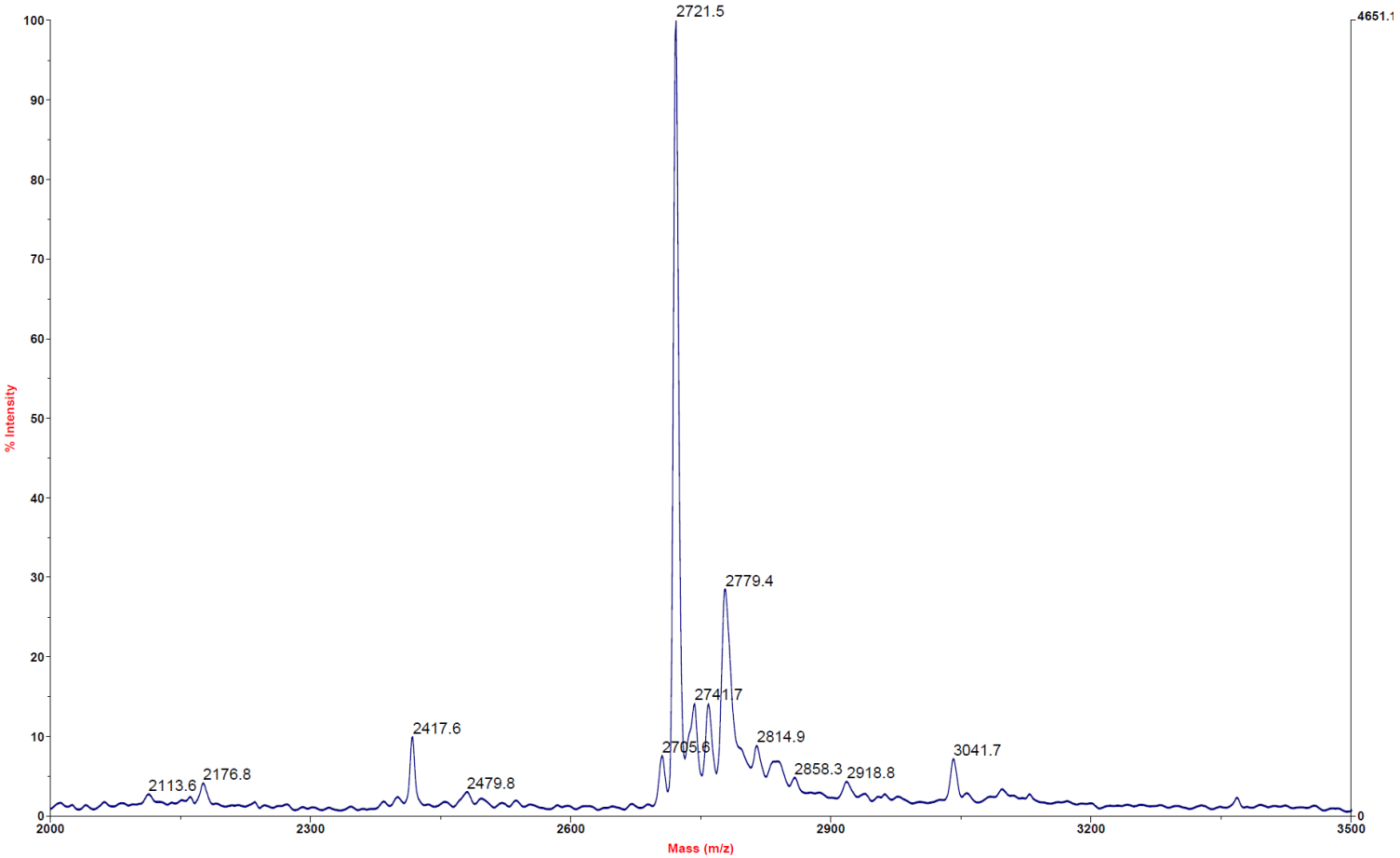

Fig.S55. MALDI-TOF MS spectrum of oligo **13t** (Voyager-Elite mass spectrometer; HPA matrix)

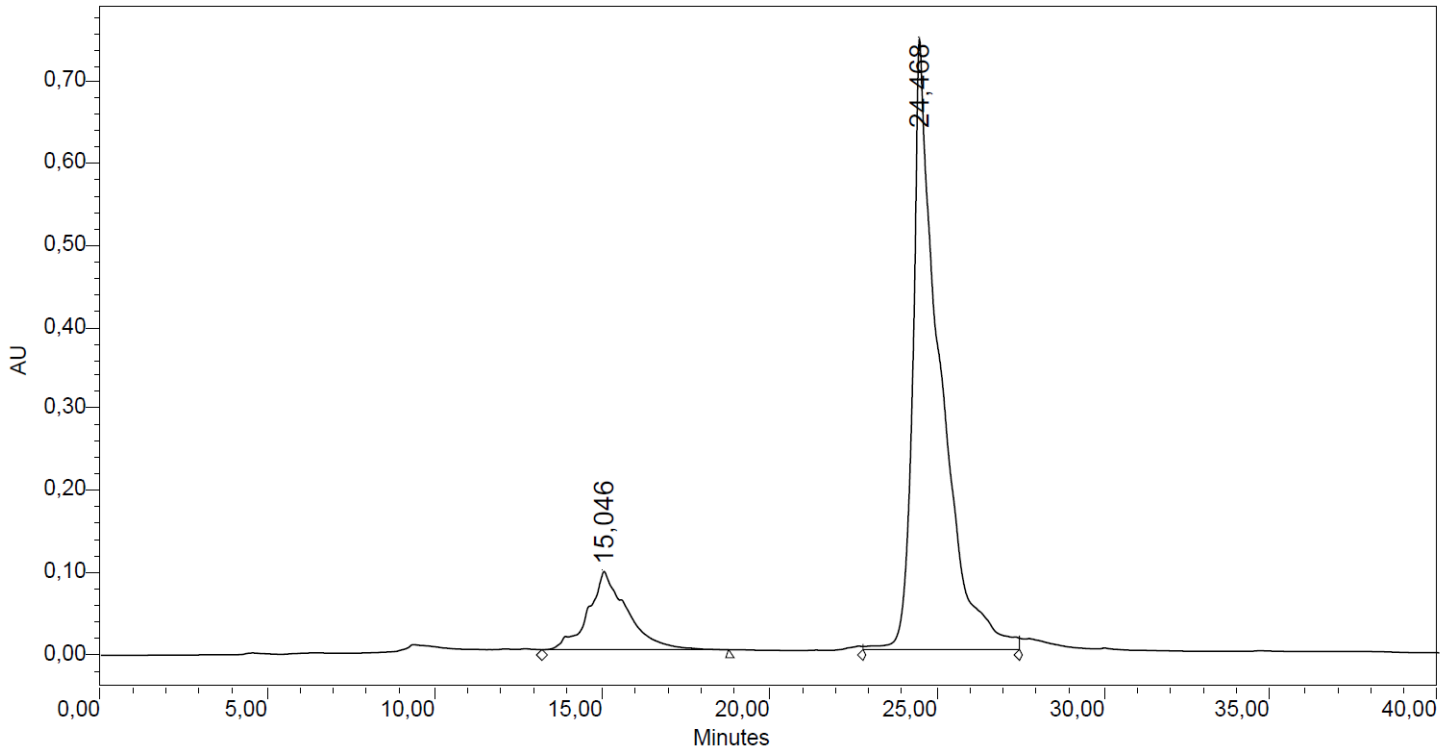

Fig.S56. HPLC profile of oligo **13t** (DMT-on stage)

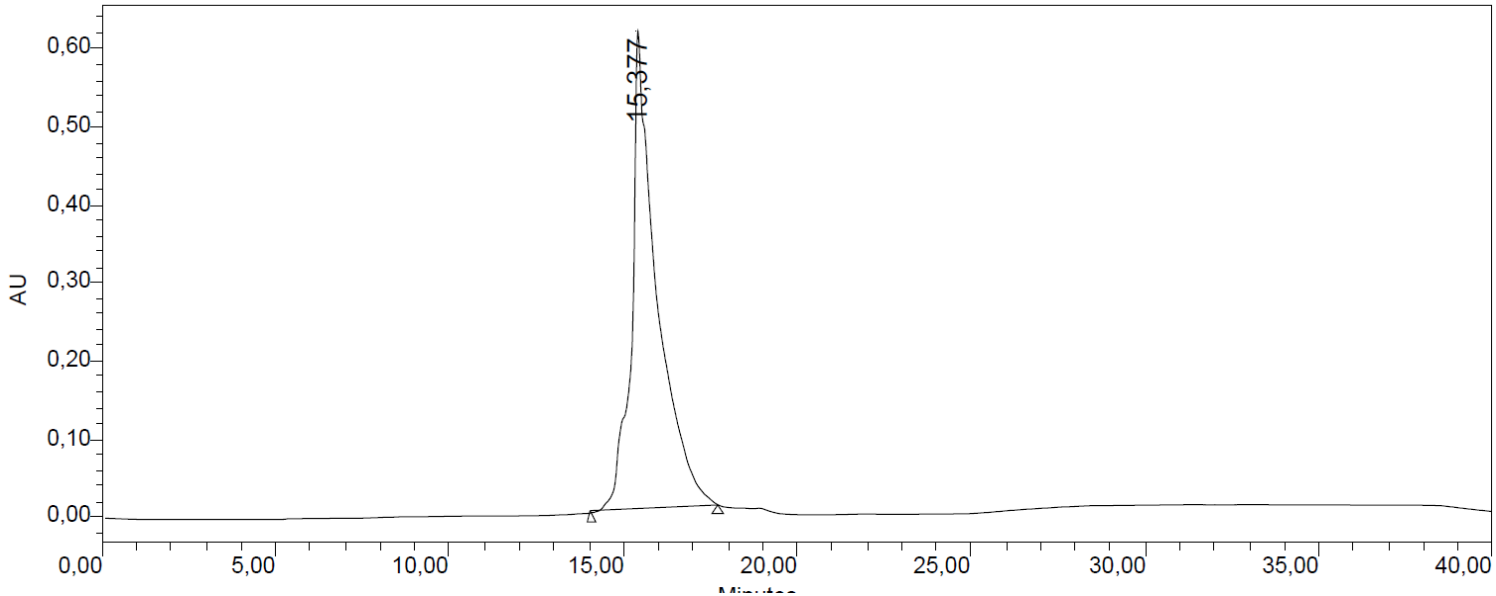

Fig.S57. HPLC profile of oligo **13t** (DMT-off stage)