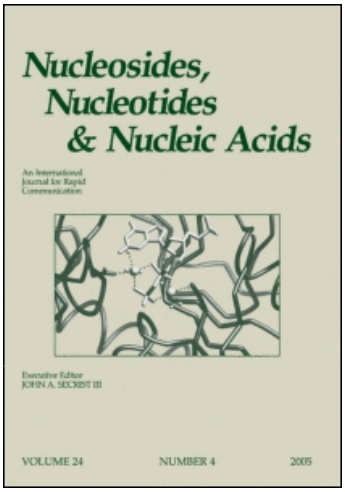

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Comparison of FAB and FD Mass Spectrometry in the Analysis of Unusually Linked Nucleotides

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COMPARISON OF FAB AND FD MASS SPECTROMETRY IN THE ANALYSIS OF UNUSUALLY LINKED NUCLEOTIDES

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In the study of phosphorothioate analogs of 2-5 A core, protected dinucleoside and trinucleoside monothiophosphates were synthesized in order to obtain dimer and trimer adenilates with 2'-5' phosphorothioate linkages.

The analysis of compounds was carried out by using FAB (positive and negative ions) and FD techniques. Here are reported and compared the results obtained on the following substances [1,2,3]:

1 N^6-Benzoyl-3',5'-O-TIPDSi-(Rp)-P-methoxy-P-thioadenylyl-(2'-5')-N^6,N^6,$O^{2'}$,$O^{3'}$-tetrabenzoyladenosine ($C_{68}H_{73}N_{10}O_{15}PSSi_2$ MW = 1388)

2 N^6-Benzoyl-3',5'-O-TIPDSi-(Sp)-P-methoxy-P-thioadenylyl-(2'-5')-N^6,N^6,$O^{2'}$,$O^{3'}$-tetrabenzoyladenosine

3 (Rp)-P-thioadenylyl-(2'-5')-adenosine, sodium salt ($C_{20}H_{24}N_{10}O_9NaPS$ MW = 634)

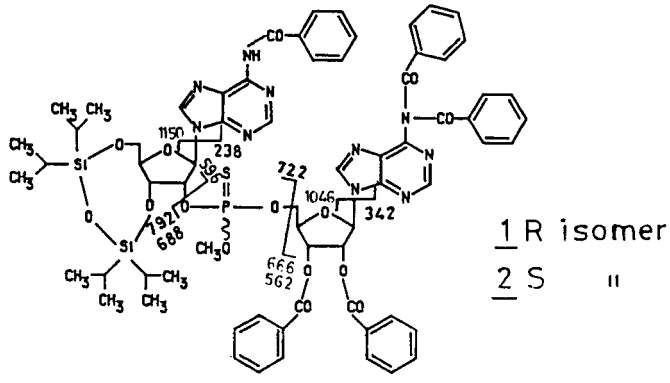
4 (Sp)-P-thioadenylyl-(2'-5')-adenosine, sodium salt

5 (Rp)-P-thioadenylyl-(2'-5')-(Sp)-P-thioadenylyl-(2'-5')-adenosine, disodium salt ($C_{30}H_{35}N_{15}O_{14}Na_2P_2S_2$ MW = 1001)

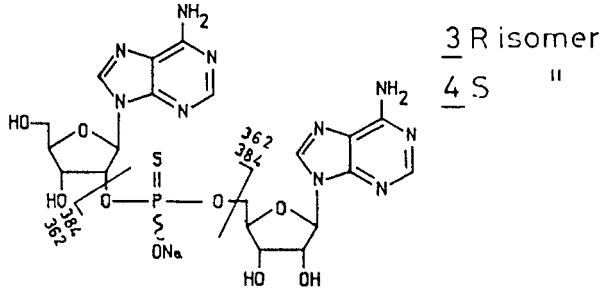
6 (Sp)-P-thioadenylyl-(2'-5')-(Sp)-P-thioadenylyl-(2'-5')-adenosine, disodium salt

Negative ions FAB mass spectra are the most interesting and informative among those examined. They show for the three couples of substances 1-2, 3-4, and 5-6 very intense $[M - H]^-$ ions at m/z 1387, 633, and 1000 respectively.

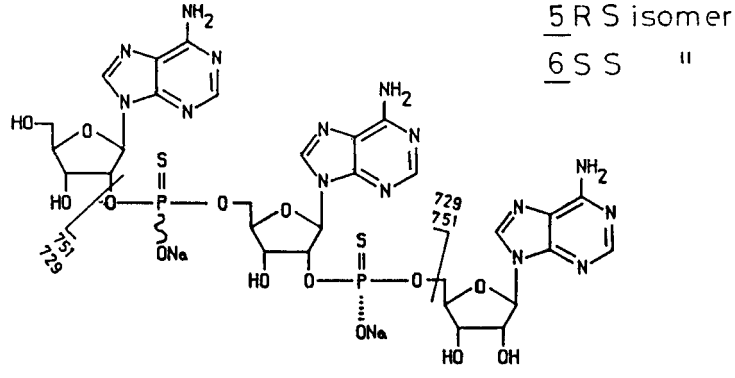
The spectra of compounds 3-4, and 5-6 have $[M - Na]^-$ ions at m/z 611 and 978 as the base peak, while for the protected dinucleoside monothio-



1 N^6-Benzoyl-3',5'-O-TIPDSi-(Rp)-P-methoxy-P-thioadenylyl-(2'- 5')-N^6;N^6,$O^{2'}$,$O^{3'}$-tetrabenzoyladenosine
2 N^6-Benzoyl-3',5'-O-TIPDSi-(Sp)-P-methoxy-P-thioadenylyl-(2'- 5')-N^6;N^6,$O^{2'}$,$O^{3'}$-tetrabenzoyladenosine



3 (Rp)-P-thiodenylyl-(2'-5')-adenosine, sodium salt
4 (Sp)-P-thiodenylyl-(2'-5')-adenosine, sodium salt



5 (Rp)-P-thioadenylyl-(2'-5')-(Sp)-P-thioadenylyl-(2'-5')-adenosine, disodium salt
6 (Sp)-P-thioadenylyl-(2'-5')-(Sp)-P-thioadenylyl-(2'-5')-adenosine, disodium salt

phosphates 1-2 the monoaminobenzoylated adenine ion at m/z 238 is the base peak accompanied by intense dibenzoylated adenine ion at m/z 342.

The 5' phosphate and 2' phosphate residue ions, corresponding to 5'-P and 3'-P sequence ions in conventional nucleotides (4,5), are present in all substances at m/z 792 and 722 for 1-2, at m/z 384 for 3-4 (accompanied by the corresponding ion without sodium at m/z 362) and at m/z 751 and 729 for 5-6.

Positive ions FAB mass spectra are less informative than corresponding negative ones and the ion intensities are low (i.e. forty times less intense for compounds 1 and 2). Spectra show always the protonated molecular ion $[MH]^+$, generally accompanied by ions $[MNa]^+$ and $[MK]^+$. Positive ions FAB mass spectra of protected dinucleoside monothiophosphates 1 and 2 show an additional fragmentation pattern, complementary to that obtained with negative ion detection, at m/z 1150, 1046, 596 and 562 (this last fragment corresponds to 666 - $\cdot COC_6H_5$ + H^+).

FD mass spectra of 1 and 2 (positive ions) are similar to that obtained by FAB technique. The fragmentation pattern is the same but ions are much more intense. The molecular weight is confirmed by ions $[MH]^+$, $[MNa]^+$ and $[M - \cdot COC_6H_5 + 2H]^+$ at m/z 1389, 1411 and 1285 respectively. FD technique however cannot be utilized for molecules 3-4, and 5-6 owing to the presence of sodium which does'nt allow the desorption of it.

In conclusion the results reported show that negative ion FAB is the best technique for the structure determination of protected dinucleoside monothiophosphates and of sodium salt dimer and trimer adenilates with 2'-5' phosphorothioate linkages. Positive ion FAB mass spectra give complementary information, being however the technique less sensitive. FD gives good results but suffers the limitation that cannot be applied to sodium salt compounds.

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