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## Nucleosides, Nucleotides and Nucleic Acids

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### Synthesis and MS Analysis of Thiazolium and Pyridinium Derivatives of Peptide Nucleic Acids (PNAs) and Peptides

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## Synthesis and MS Analysis of Thiazolium and Pyridinium Derivatives of Peptide Nucleic Acids (PNAs) and Peptides

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### ABSTRACT

Sensitivity of ESI-MS analysis of crude PNAs is enhanced using their pyridinium or thiazolium derivatives. Identification of the molecular ion of the product is easier when the label contains bromine, based on the isotope distribution. Study of side reactions, occurred upon the synthesis and/or cleavage, is simple with labelling. Sequencing of non-polar peptides is clear as only a<sub>n</sub> type ions can be observed during their MS/MS analysis.

### RESULTS AND DISCUSSION

Mass spectra of the crude products in PNA oligomer synthesis are usually not interpretable. Cheap and reactive labels, 5-bromo-*N*-ethyl-pyridinium (BEP) and 5-bromo-*N*-ethyl-thiazolium (BET) tetrafluoroborate synthesized by us and

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Mukaiyama reagent (CMP) were studied to solve these problems. Molecular ion ( $[M_{\text{lab}}]^+$  and even  $([M_{\text{lab}} + H]^{2+})$  of the product occurs in ESI-MS spectra of crude labelled PNAs.  $[M_{\text{lab}}]^+$  peak can be easily identified when the label contains bromine atom in MALDI-MS spectra where higher resolution can be achieved (Fig. 1).

Many types of side reaction can occur during the synthesis and/or cleavage that affects both product and capped sequences. Identification of the side products is simple by using labelling as only those peaks change that belongs to the whole sequence. In our case incomplete protecting group removal (2,2,4,6,7-pentamethyldihydrobenzofuran-5-sulfonyl (Pbf)  $[M_{\text{lab}} + 252]^+$ ), oxidation of methionine ( $[M_{\text{lab}} + 16]^+$ ) and cleavage of the linker of the resin ( $[M_{\text{lab}} + 106]^+$ ) took place.

Peptides not containing amino acids with nucleophilic functional groups in their side chain (test pentamer: GPVYF) can be labelled in solution followed by a zip-tip purification. MS/MS analysis of the pentamer gave a clear spectrum that contained only  $a_n$  peaks (Fig. 2). ( $M_{\text{lab}} = M - H + 93$  ( $M = 581$ );  $a_2 - a_1 = 98$  (Pro);  $a_3 - a_2 = 99$  (Val);  $a_4 - a_3 = 163$  (Tyr);  $a_5 - a_4 = 147$  (Phe))

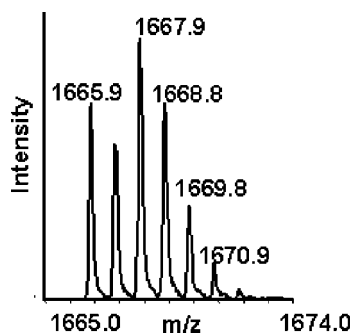


Figure 1.

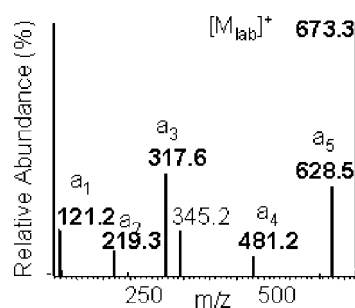


Figure 2.

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