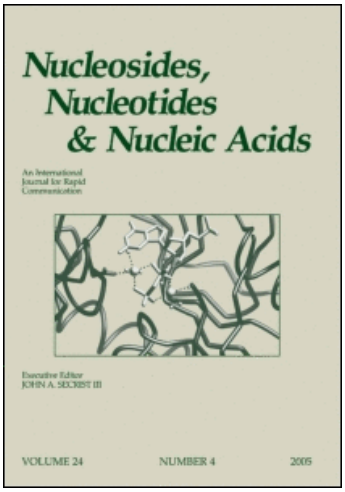

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

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

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Online publication date: 09 August 2003

To cite this Article Kovács, G. , Pádár, P. , Kupihár, Z. , Kele, Z. , Forgó, P. and Kovács, L.(2003) 'Synthesis and MS Analysis of Thiazolium and Pyridinium Derivatives of Peptide Nucleic Acids (PNAs) and Peptides', Nucleosides, Nucleotides and Nucleic Acids, 22: 5, 1301 — 1303
To link to this Article: DOI: 10.1081/NCN-120022951
URL: http://dx.doi.org/10.1081/NCN-120022951

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
Vol. 22, Nos. 5–8, pp. 1301–1303, 2003

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_n 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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DOI: 10.1081/NCN-120022951
1525-7770 (Print); 1532-2335 (Online)

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Mukaiyama reagent (CMP) were studied to solve these problems. Molecular ion ($[M_{lab}]^+$ and even ($[M_{lab}+H]^{2+}$) of the product occurs in ESI-MS spectra of crude labelled PNAs. $[M_{lab}]^+$ 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) $[M_{lab}+252]^+$), oxidation of methionine ($[M_{lab}+16]^+$) and cleavage of the linker of the resin ($[M_{lab}+106]^+$) 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). ($M_{lab} = M - H + 93$ ($M = 581$); $a_2 - a_1 = 98$ (Pro); $a_3 - a_2 = 99$ (Val); $a_4 - a_3 = 163$ (Tyr); $a_5 - a_4 = 147$ (Phe))

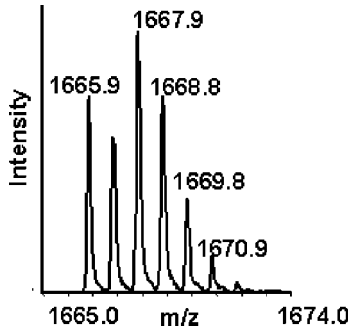

Figure 1.

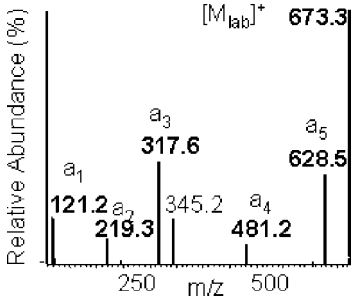

Figure 2.

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ACKNOWLEDGMENTS

OTKA T30 135, FKFP 0597/1999, Foundation for Hungarian Peptide and Protein Research, G. RICHTER Centennial Foundation, OM MECENATURA, OTKA Travel Grant.

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