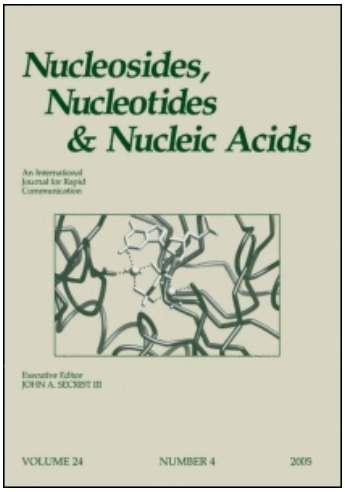

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Nucleic Acid Analog Peptide Containing β-Aminoalanine Modified with Nucleobases

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To cite this Article Fujii, Masayuki and Hidaka, Jinsai(1999) 'Nucleic Acid Analog Peptide Containing β-Aminoalanine Modified with Nucleobases', Nucleosides, Nucleotides and Nucleic Acids, 18: 6, 1421 — 1422
To link to this Article: DOI: 10.1080/07328319908044739
URL: http://dx.doi.org/10.1080/07328319908044739

NUCLEOSIDES & NUCLEOTIDES, 18(6&7), 1421–1422 (1999)

NUCLEIC ACID ANALOG PEPTIDE CONTAINING β-AMINOALANINE MODIFIED WITH NUCLEOBASES

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ABSTRACT

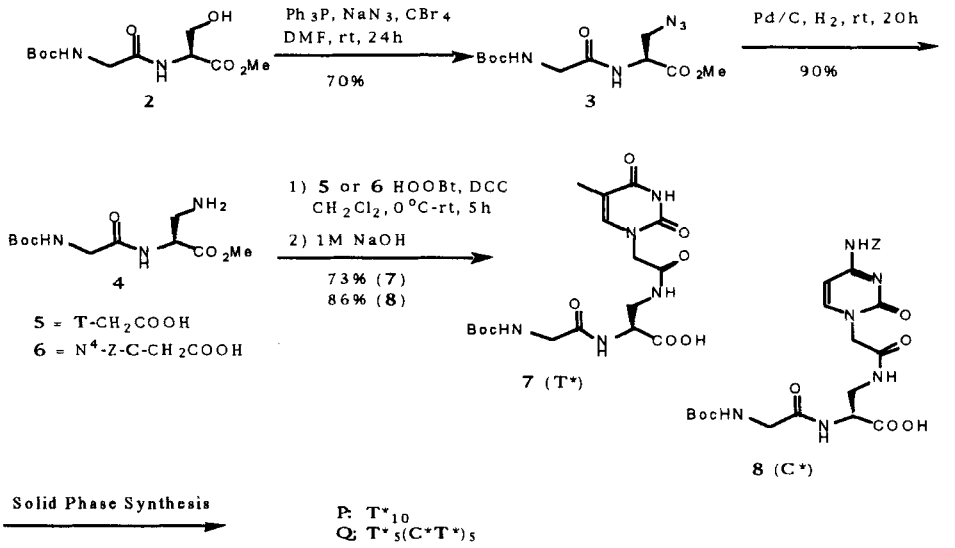
Oligopeptides containing N^{β}-(thymin-1-ylacetyl) β-aminoalanine and N^{β}-(cytosin-1-ylacetyl) β-aminoalanine moieties synthesized on solid phase using standard boc-chemistry showed hybridization properties with single stranded DNA and RNA, and also with double stranded DNA at pH 7.0.

In this study, oligopeptides (**1**) containing β-aminoalanine bearing a nucleobase were synthesized and hybridization properties of them with ssDNA, ssRNA, and dsDNA were examined by T_m measurement.

Syntheses of *N-t*-butoxycarbonylglycyl-N^{β}-(thymin-1-ylacetyl)-L-β-aminoalanine (**7**, T*) and *N-t*-butoxycarbonylglycyl-N^{β}-(cytosin-1-ylacetyl)-L-β-amino-alanine (**8**, ^{Z}C*) were achieved as shown in Scheme 1.

These protected amino acids **7** and **8** were readily applicable to solid phase peptide synthesis using standard boc chemistry on MBHA resin. The obtained 20mer peptide T^*_{10} (**P**) and 30mer peptide $T^*_5(C^*T^*)_5$ (**Q**) were purified by RP HPLC and confirmed by FAB mass spectrometry; mass for **P** $C_{122}H_{154}N_{52}O_{51}$ m/z calcd 3164.9, found 3165.9 [$(M+H)^+$], and for **Q** $C_{177}H_{224}N_{82}O_{71}$ m/z calcd 4636.2, found 4637.2 [$(M+H)^+$]

Formation of hybrid double strand by **P** and dA_{10} was confirmed by observing hypochromic effect at pH 7.0. It is to be noted that the melting temperature (T_m) was higher than that for natural DNA double strand by +13.5 °C (+1.35 °C/base).[1] The stability of the hybrid was not affected by salt concentration. The peptide **P** also



Scheme 1. Synthesis of DNA Analogs Containing β-Aminoalanine Modified with Nucleobases

formed double strand with rA_{10} and the T_m was 21 °C. Moreover, it was shown that **P** could bind to double stranded DNA by triple helix formation with comparable affinity (T_m = 19.3 °C, ΔT_m = - 0.7 °C). Oligopeptide **Q** containing mixed pyrimidine bases was also shown to form triple helix with double stranded DNA (T_m = 22.8 °C, ΔT_m = +1.5 °C).[2)]

It can be postulated that Watson-Crick base pairing in duplex and Hoogsteen base pairing in triplex by **P** and **Q** is made possible because of the favorable orientation of the base moieties caused by intramolecular hydrogen bond.

ACKNOWLEDGEMENTS

The authors are grateful for the financial support from Takeda Chemical Industries Award in Synthetic Organic Chemistry, Japan, and also from Mitsubishi Chemicals Research Foundation.

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