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## Nucleosides, Nucleotides and Nucleic Acids

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**NUCLEIC ACID ANALOG PEPTIDE CONTAINING  $\beta$ -AMINOALANINE  
MODIFIED WITH NUCLEOBASES**

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**ABSTRACT**

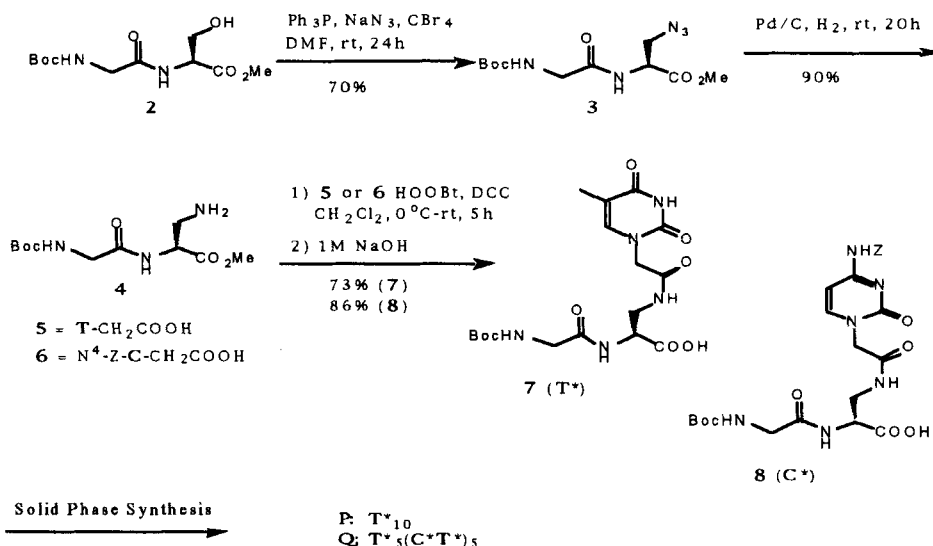
Oligopeptides containing  $N^{\beta}$ -(thymine-1-ylacetyl)  $\beta$ -aminoalanine and  $N^{\beta}$ -(cytosine-1-ylacetyl)  $\beta$ -aminoalanine moieties synthesized on solid phase using standard boc-chemistry showed hybridization properties with single stranded DNA and RNA, and also with double stranded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

In this study, oligopeptides (**1**) containing  $\beta$ -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- $N^{\beta}$ -(thymine-1-ylacetyl)-L- $\beta$ -aminoalanine (**7**, **T\***) and *N*-*t*-butoxycarbonylglycyl- $N^{\beta}$ -(cytosine-1-ylacetyl)-L- $\beta$ -aminoalanine (**8**, **<sup>z</sup>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\***<sub>10</sub> (**P**) and 30mer peptide **T\***<sub>5</sub>(**C\*T\***)<sub>5</sub> (**Q**) were purified by RP HPLC and confirmed by FAB mass spectrometry; mass for **P** C<sub>122</sub>H<sub>154</sub>N<sub>52</sub>O<sub>51</sub> m/z calcd 3164.9, found 3165.9 [(M+H)<sup>+</sup>], and for **Q** C<sub>177</sub>H<sub>224</sub>N<sub>82</sub>O<sub>71</sub> m/z calcd 4636.2, found 4637.2 [(M+H)<sup>+</sup>]

Formation of hybrid double strand by **P** and dA<sub>10</sub> 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).<sup>1)</sup> The stability of the hybrid was not affected by salt concentration. The peptide **P** also



Scheme 1. Synthesis of DNA Analogs Containing  $\beta$ -Aminoalanine Modified with Nucleobases

formed double strand with  $\text{rA}_{10}$  and the  $T_m$  was  $21^\circ\text{C}$ . Moreover, it was shown that **P** could bind to double stranded DNA by triple helix formation with comparable affinity ( $T_m = 19.3^\circ\text{C}$ ,  $\Delta T_m = -0.7^\circ\text{C}$ ). Oligopeptide **Q** containing mixed pyrimidine bases was also shown to form triple helix with double stranded DNA ( $T_m = 22.8^\circ\text{C}$ ,  $\Delta T_m = +1.5^\circ\text{C}$ ).<sup>2)</sup>

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.

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