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**α -DNA. SYNTHESIS, CHARACTERIZATION AND BASE-PAIRING
PROPERTIES OF UNNATURAL α -OLIGODEOXYRIBONUCLEOTIDES.**

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Abstract : The novel hexadeoxyribonucleotides α -d(CpCpTpTpCpC) and α -d(CpApTpGpCpG), in which each glycosidic linkage exhibit the anomeric α -configuration, were synthesized by the phosphotriester method. ¹H-NMR and thermal denaturation studies provided evidence for these α -oligonucleotides to exhibit a secondary structure similar to that of the natural nucleic acids.

The aim of this work was to synthesize unnatural oligodeoxyribonucleotides consisting exclusively of α -nucleotide units, to test their substrate activities towards nucleases and to study their structure and conformation, as well as their ability to form duplexes with complementary β - or α -strands.

Starting from N-protected α -deoxy-2'-ribonucleosides, the corresponding fully-protected α -nucleotides were prepared by selective 5'-O-tritylation and 3'-O-phosphorylation. The α -hexadeoxyribonucleotides α -d(CpCpTpTpCpC) and α -d(CpApTpGpCpG) were synthesized¹ by the classical phosphotriester method, using MSNT as coupling agent.

Enzymatic studies indicated that both α -hexamers were completely resistant to calf spleen phosphodiesterase while they were degraded by *crotalus durissus terrificus* snake venom phosphodiesterase and alkaline phosphatase, yielding the expected α -nucleoside ratio. However the rate of hydrolysis of these α -strands is considerably smaller than that of the analogous β -strands. The higher hypochromicity as determined for α -d(CpApTpGpCpG) (19.5%) compared to that of the analogous

β - strand (14.2%) may reflect a higher degree of base stacking in the former strand.

^1H -NMR NOE examination of α -d(CpCpTpTpCpC) strand indicate that all the bases adopt the *anti* conformation ; the furanose ring of thymidine moieties probably adopt a C_3' -*endo* conformation and the cytidine furanose groups are close to C_2' -*endo* conformations. Both hyperchromicity in thermal melting and detection of base paired imino protons in ^1H -NMR studies provided evidence for annealing of α -d(CpCpTpTpCpC) and β -d(GpGpApApGpG).

In conclusion, unnatural oligodeoxyribonucleotides consisting exclusively of α -nucleotide units have been synthesized by the phosphotriester approach. Thermal denaturation, enzymatic and ^1H -NMR studies provided evidence for α -oligodeoxynucleotides to exhibit a secondary structure similar to that of the natural nucleic acids, featuring base stacking, base pairing and duplex formation with β -strands.

Work is in progress in order to determine the polarity of the strands in α,β - and α,α -duplexes as well as the thermal stability of these duplexes.

REFERENCES

1. F. Morvan, B. Rayner, J.-L. Imbach, D.-K. Chang and J.W. Lown, *Nucl. Acid Res.*, **14**, 5019 (1986).