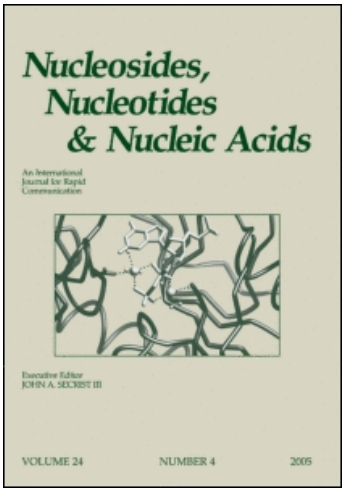

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Synthesis and Properties of Symmetrically Linked Diribonucleotides

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SYNTHESIS AND PROPERTIES OF SYMMETRICALLY LINKED DIRIBONUCLEOTIDES

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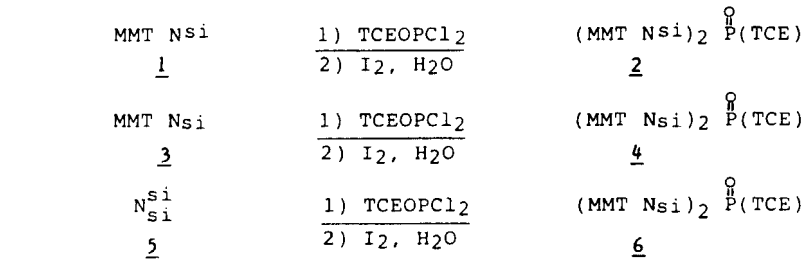
Summary. Several symmetrically linked (3'-3', 2'-2' and 5'-5') diribonucleoside monophosphates were prepared using the phosphodichloridite procedure. The 3'-3' and 2'-2' dimers showed unusual lability towards both acid and base due to the two hydroxyls adjacent to the phosphate moiety.

Ribonucleotides possessing 3'-5' or 2'-5' phosphate linkages have been widely synthesized and their properties are well documented. Little is known about symmetrically linked oligoribonucleotides especially 3'-3' and 2'-2' dimers. We present here a complete investigation of the synthesis and properties of symmetrically linked ribonucleotides.

Symmetrically linked dinucleotides were prepared by a simple two step reaction that involved adding a one fold excess of the suitably protected nucleoside to the trichloroethylphosphodichloridite followed by iodine-water oxidation as illustrated below:



a; N = uridine
b; N = adenosine
c; N = N benzoyl cytosine

The fully protected dimers 2, 4 and 6 were purified on silica gel chromatography. Their physical properties were very different from those of their 2'-5' and 3'-5' counterparts. Their ^{31}P nmr spectra showed only one peak as a result of the loss of chirality at the phosphorus atom.

The deprotection of the 5'-5' linked dimers proceeded smoothly to give the expected products which were good substrates for snake venom phosphodiesterase but were resistant to ribonuclease (Rnase) and spleen phosphodiesterase. On the other hand some problems were encountered in the deprotection of the 3'-3' and 2'-2' dimers which are readily degraded in slightly alkaline conditions presumably because of the two hydroxyls adjacent to the phosphate linkage. Neither 3'-3' nor 2-2' linked dimers

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were substrates for Rnase A_1 Rnase T_2 and snake phosphodiesterase ; they were at best poor substrates for spleen phosphodiesterase.

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