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ON THE INTRODUCTION OF FLUORINE INTO NUCLEOTIDE PHOSPHOTRIESTERS

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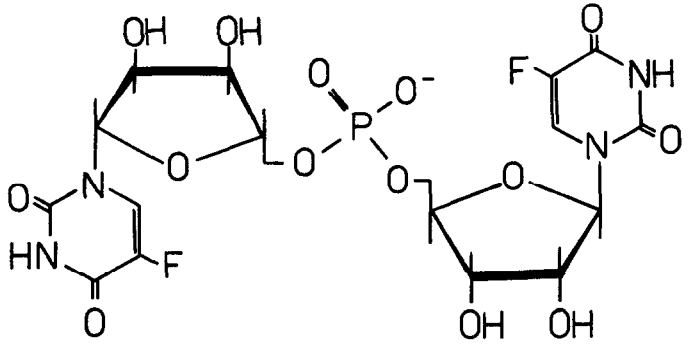
The synthesis of 5-fluorouridinyl-5-fluorouridine can be prepared in two different directions. According to well-known procedures uridine is firstly transformed by elemental fluorine to the corresponding 5-fluoroderivative, wich is condensed to the wished dinucleotide by a phosphotriester approach of oligonucleotide synthesis afterwards. For that purpose different protections and deprotections of the carbohydrate moiety are nessecary. On the other hand a direct fluorination of the unsubstituted uridine dinucleotide leads to the fluoro-product. In both directions the fluorination



follows the same manual procedure. The protected nucleotide or nucleoside is dissolved in dry acetic acid and 1,1 eq of fluorine solved in acetic acid is added at roomtemperature. After working up the intermediately formed 5,6-dihydro-5,6-difluorouracil derivative is dehydrofluorinated to the 5-fluorouracil derivative.

The selective fluorination of the sensitive nucleotide is much difficult than quantitative fluorination of nucleoside.