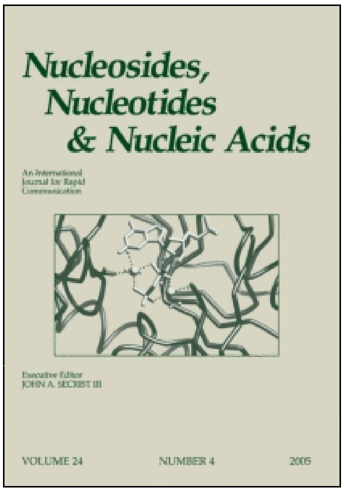

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# 3'/5'-Regioselectivity of Introduction of the 9-Fluorenyl-Methoxycarbonyl Group to 2'-O- Tetrahydropyran-2-Yl- and 2'-O-(4-methoxytetrahydropyran-4-Yl-)-nucleosides Useful Intermediates for Solid-Phase-RNA-Synthesis

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# 3'/5'-REGIOSELECTIVITY OF INTRODUCTION OF THE 9-FLUORENYL-METHOXYCARBONYL GROUP TO 2'-O-TETRAHYDROPYRAN-2-YL- AND 2'-O-(4-METHOXYTETRAHYDROPYRAN-4-YL-)-NUCLEOSIDES: USEFUL INTERMEDIATES FOR SOLID-PHASE-RNA-SYNTHESIS

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**ABSTRACT: X-ray structure analysis of the more laevorotatory isomers of 2'-O-tetrahydropyranyl-4N-benzoylcytidine (4b) and of 2'-O-tetrahydropyranyluridine (5b) confirmed their chirality at the satellite anomeric centre C2" to be S. The other diastereomers (4a resp. 5a) exhibited an unexpected reversal of 3'/5'-regio-selectivity when treated with 9-fluorenylmethoxycarbonyl chloride in pyridine. The X-ray crystallographic results form the basis for a mechanistic proposal.**

2'-O-Tetrahydropyran-2-yl-(thp)- and 2'-O-(4-methoxytetrahydropyran-4-yl-(mthp)-nucleosides are useful intermediates for solid-phase-RNA-synthesis (Lehmann, C., Xu, Y.-Z., Christodoulou, C., Tan, Z.-K., and Gait, M. J. (1989), *Nucleic Acids Res.* ***17***, 2379-2390, and references cited therein). The 3'/5'-regioselectivity of Fmoc acylation of 2'-O-thp-nucleosides (typically 1:5 in favour of the 5'-OH group) is reversed in the case of the 2'-O-thp-pyrimidine diastereomer with higher mobility (high $R_f$) on silicagel.

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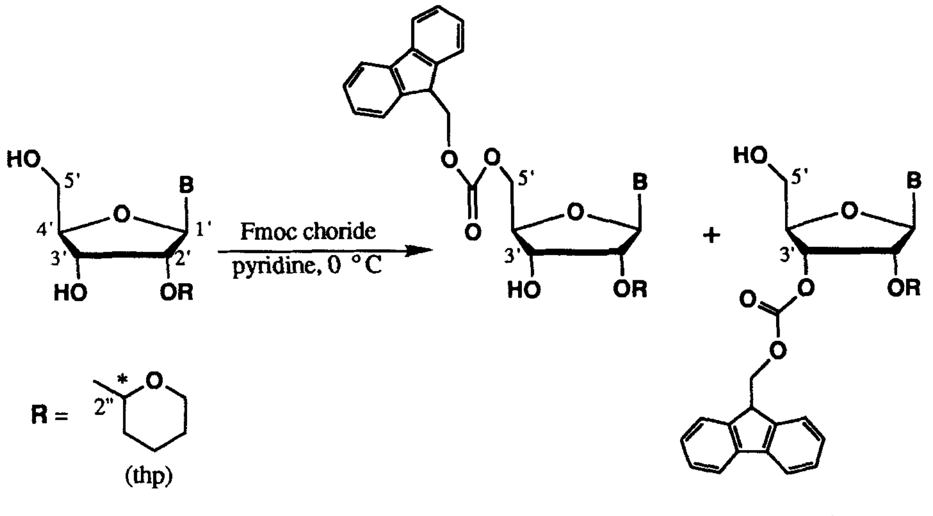
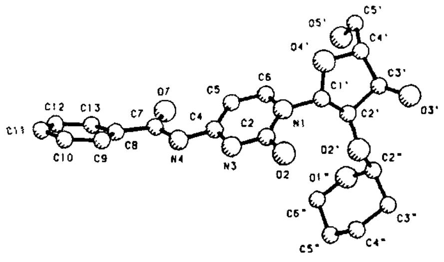
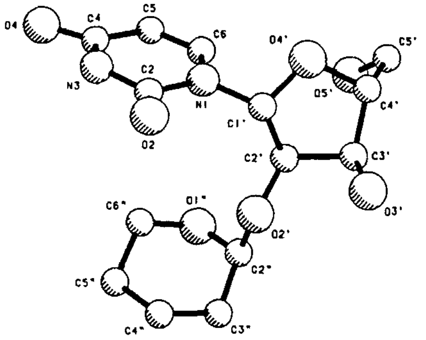


5'-O-Fmoc 3'-O-Fmoc

We have determined the crystal structures of 2'-O-(S)-thp-4N-benzoylcytidine (**4b**) and of 2'-O-(S)-thp-uridine (**5b**), giving complementary information to the previously determined structures of 2'-O-(S)-thp-adenosine (Kennard, O., Motherwell, W. D. S., Coppola, J. C., Griffin, B. E., Reese, C. B., Larson, A. C. (1971), *J. Chem. Soc. (B)*, 1940-1946) and 2'-O-(**R**)-thp-uridine (**5a**; Stothart, P. H., Brown, I. D., Neilson, T. (1973), *Acta Cryst.* ***B29***, 2237-2242). The structures confirm that the more laevorotatory, low $R_f$ isomer has the S configuration at the C2" satellite anomeric centre.

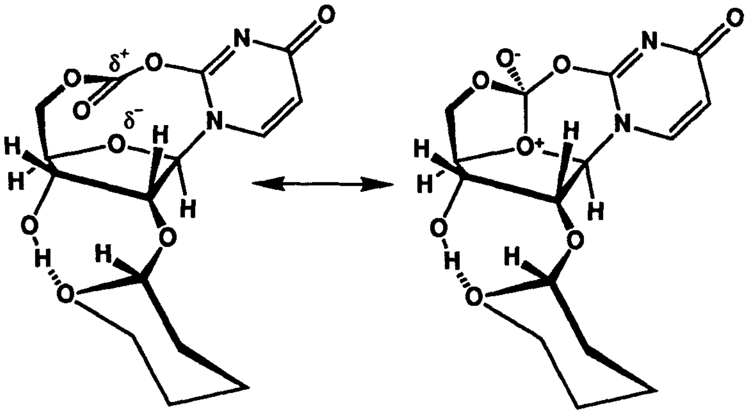


**4b**



**5b**

In order to explain the pyrimidine specific reversal of the 3'/5'-regioselectivity which is only observed for carbonate diester formation but not for ordinary acetylation, we propose the transient formation of an internal 5'-O-2O-carbonate diester. This intermediate can only be acylated at the free 3'-OH group, which exclusively for the **R** isomer is rendered more nucleophilic by internal hydrogen bonding.



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