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Stereoselective 5'-Monodeuterated Ribonucleoside Phosphoramidites as Tools for Conformational Studies of RNA by the NMR Approach

M. A. Lukin^a & V. N. Bushuev^a

^a Institute of Experimental Cardiology, Russian Cardiology Research and Development Center, 3-rd Cherepkovskaya St. 15a, 121552, Russia

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**STERESELECTIVE 5'-MONODEUTERATED RIBONUCLEOSIDE
PHOSPHORAMIDITES AS TOOLS FOR CONFORMATIONAL STUDIES OF
RNA BY THE NMR APPROACH**

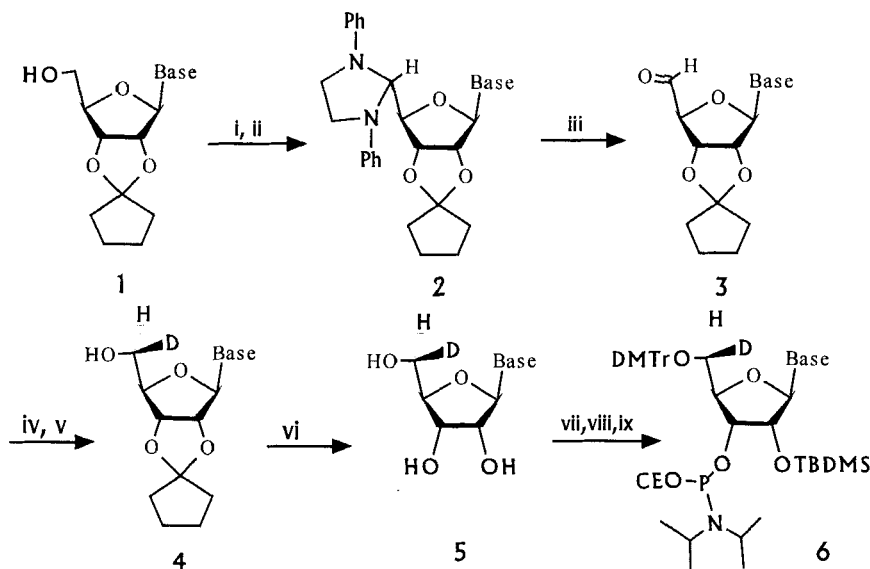
M.A.Lukin*, V.N.Bushuev.

Institute of Experimental Cardiology, Russian Cardiology Research
and Development Center, 3-rd Cherepkovskya St. 15a 121552 Russia

The analysis of NMR spectra of DNA and RNA, in particular, homo- and heteronuclear vicinal coupling constants of the nuclei of the sugar-phosphate backbone, can provide important information about the conformation of macromolecules¹. For example, 5'H - P coupling constant allows us to obtain a value of β torsional angle, 5'H-4'H - γ , whereas 3'H-P constant gives the angle ϵ . Unfortunately, due to the complex structure of H5', H4' and H3' multiplets in moderate and large RNA fragments (>15 nucleotides), it is very difficult to assign signals and extract accurate structural data.

To simplify NMR spectra we propose to mask one 5' sugar proton with deuterium. This procedure allows to transform a second order 5',4' ABC spin system to an AB system and remove one proton signal per a nucleoside residue from the crowded region at 4-5 ppm, and thus, to clarify a spectrum. From the other hand, since both 5' protons only slightly contributed to inter- and intranucleotide NOEs, the absence of one of the 5'-protons cannot cause missing of the informative signals at cross-relaxation spectra.

We elaborated a synthetic procedure for the stereoselective deuteration of the 5'-position of nucleosides (Scheme 1). A key step is the reduction of 5'-oxonucleoside (3) by deuterio AlpineBorane, an adduct of B-²H-BBN and α -(-)-pinene². As aldehydes



Base = a) Uracyl-1-yl; b) 6-N-Phenoxyacetyladen-9-yl

(i) DMSO/DCC; (ii) dianilinoethane; (iii) TsOH/acetone; (iv) deuterio-AlpineBorane; (v) H_2O_2 ; (vi) 80% HCOOH ; (vii) DMTCl/Py; (viii) TBDMSCl, Py, AgNO_3/THF ; (ix) 2-Cyanoethoxydiisopropylaminochlorophosphine.

(3) are unstable³ and have the chromatographic mobility close with that of the corresponding nucleosides, we convert them into imidazolidines (2) to remove traces of the starting nucleoside. Rapid acid treatment of imidazolines (2) gives free aldehydes, which are reduced without purification.

The comparison of NMR spectra of deuterated and nondeuterated nucleosides shows, that the reduction is highly stereoselective: S and R deuterated nucleoside ratio is approximately 20:1 and it is comparable with the enantiomeric purity of the starting α -pinene.

Phosphoramidites (6) of 5'-deuterated nucleosides were synthesized using the standard protocol. The synthesis and NMR investigation of deuterated RNA fragments are under progress.

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