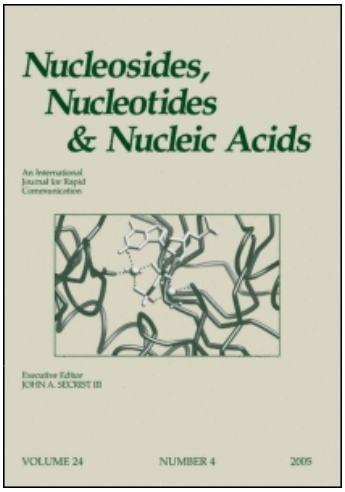

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Deuteration and Tritiation of 2'-Deoxyribonucleosides in the 5' and 4' Positions

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To cite this Article Berger, M. , Shaw, A. , Cadet, J. and Jones, J. R.(1987) 'Deuteration and Tritiation of 2'-Deoxyribonucleosides in the 5' and 4' Positions', Nucleosides, Nucleotides and Nucleic Acids, 6: 1, 395 — 396
To link to this Article: DOI: 10.1080/07328318708056234
URL: http://dx.doi.org/10.1080/07328318708056234

NUCLEOSIDES & NUCLEOTIDES, 6(1&2), 395-396 (1987)

DEUTERATION AND TRITIATION OF 2'-DEOXYRIBONUCLEOSIDES IN THE 5' AND 4' POSITIONS.

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The deuterations of 2'-deoxyguanosine in the 4' and 5' positions have been described elsewhere (1). The starting material is the 5'-aldehyde formed by mild oxidation with N,N-dicyclohexyl carbodiimide in dimethyl sulphoxide of the fully protected nucleoside with free 5'-alcoholic function. The 5'-deuteration was achieved by reduction with deuterated sodium borohydride. Incorporation of deuterium in the 4'-position was achieved via an enhanced keto-enol tautomerism by heating the aldehyde in 50/50 D_2O/pyridine, with subsequent reduction of the aldehyde with $NaBH_4$. The β-furanoid form was isolated from the α-lyxo by-product by reverse phase HPLC. Applied to pyrimidine 2'-deoxyribonucleosides, this method was shown to give deuterated 2'-deoxycytidine and thymidine in good yield.

The tritiation of 2'-deoxyguanosine and thymidine in both the 4' and 5' positions was attempted using a similar methodology. Thymidine was tritiated in the 5' position with good specific activity and was shown by ^3H n.m.r. to be substituted non-specifically in both 5' and 5" positions in equal yields. On the other hand, epimerisation at the 4' position after treatment with ^3H_2O and pyridine with subsequent RP-HPLC purification yielded a product of low specific activity despite $NaHCO_3$ catalysis. This method would appear to suffer from a severe isotope effect since although of high specific activity (55 Ci/ml), the tritiated water is only 0.2 % ^3H. The incorporated activity into 2'-deoxygua-

nosine was even lower. We envisage further experiments to test the effect of temperature and other catalysts in order to improve specific activities.

References

1. Table Ronde : Nucléosides Nucléotides, La Grande Motte, Octobre 1984.