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## Nucleosides, Nucleotides and Nucleic Acids

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

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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<sub>2</sub>O/pyridine, with subsequent reduction of the aldehyde with NaBH<sub>4</sub>. 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 <sup>3</sup>H 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 <sup>3</sup>H<sub>2</sub>O and pyridine with subsequent RP-HPLC purification yielded a product of low specific activity despite NaHCO<sub>3</sub> 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 % <sup>3</sup>H. 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.