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Short Research Article

Synthesis of [5-^{3}H]uracil nucleoside analogue†

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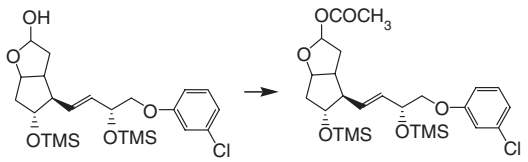
Introduction

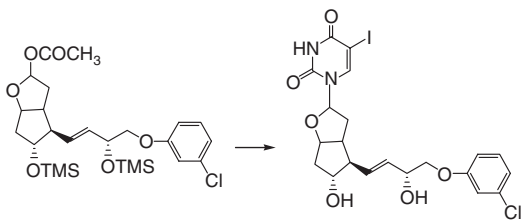
The development of new drugs with antitumoral and antiviral activity that exhibit greater efficacy, more favourable toxicity profile, and are less susceptible to cross-resistance is an important goal. We are exploring the synthesis of new biologically active nucleoside analogues, modified at the base or more frequently at the sugar moiety.

Uracil oxabicyclo3.3.0octanic derivative **3a**, was obtained using the Vorbruggen method (with trimethylsilyl trifluoromethanesulphonate as catalyst) starting from acetylated lactole **1** (easily obtained by acetylation of lactole **1**) (Scheme 1) and silylated uracil.[1,2] The new nucleoside was tested with good results for its biological activity (toxicity).



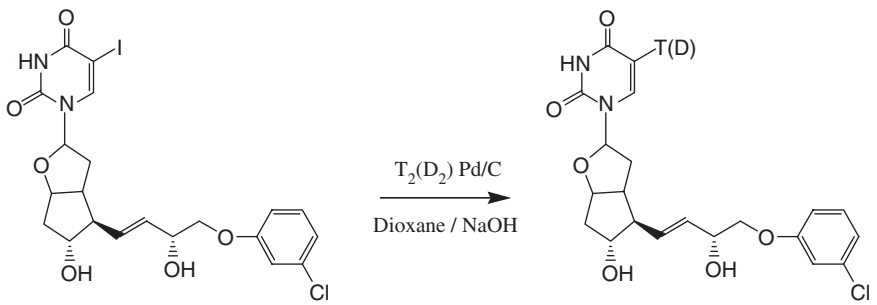
1 2

Scheme 1



2 3 a, X = H
b, X = I

Scheme 2



3b 4

Scheme 3

Results and discussion

5-Iodouracil oxabicyclo3.3.0octanic compound **3b**, was obtained similarly with 60.9% yield using the Vorbruggen method silylated 5-iodouracil (Scheme 2) as reagent.

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Table 1 Characteristics of [5-^{3}H] uracil nucleoside analogue

Radioactivity of crude labelled product (MBq)	4625
Radioactivity of purified labelled product (MBq)	4033
Purification yields (%)	87.2
Radiochemical purity detected by TLC (Silicagel GF254/dichloromethan–methanol, 9:1) (%)	98
Radioactive concentration (MBq/mL)	37
Chemical concentration determined at 288 nm in ethyl acetate solution (mg/mL)	0.018
Specific activity (GBq/mmol)	894

The structure of iodinated compound was determined by FT IR and 1H-NMR spectrometry.

Tritiated and deuterated compounds **4** in position 5 were synthesized by catalytic hydrogenations[3] of 5-iodouracil nucleoside analogue **3b** (Scheme 3).

The [5-^{2}H] and [5-^{3}H]uracil nucleoside analogue was purified by TLC. The labelled compound was characterized by determination of: radioactive concentration, chemical concentration; and radiochemical purity. Obtained results are presented in Table 1. Deuterated compound was characterized by FTIR ATR and ^{1}H NMR.

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