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### A New Synthesis of 3'-Fluoro-3'-deoxyadenosine

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**A NEW SYNTHESIS OF 3'-FLUORO-3'-DEOXYADENOSINE**

A. Giordani, A. Ermoli and C. Battistini\*

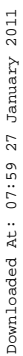
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**Abstract:** 3'-Fluoro-3'-deoxyadenosine is synthesized starting from adenosine via double inversion and by using DAST. Intermediates are also obtained where 2' and 5'-position can be independently deprotected for further synthetic elaboration.

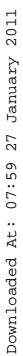
3'-Fluoro-3'-deoxy adenosine, a compound endowed with antiviral properties, has been recently synthesized<sup>1,2</sup>, but our interest in its introduction into more complex biologically active structures addressed us to a different and shorter synthesis.

Starting from adenosine our synthetic route<sup>3</sup> allows to obtain a suitable protected derivative of 3'-fluoro-3'-deoxyadenosine in six steps involving a double inversion to ensure the correct stereochemistry of 3'-position. The inversion of configuration at C-3' is provided by triflate activation of the hydroxyl group followed by nucleophilic displacement by sodium acetate (3 → 5). Aminolysis of the ester affords the properly protected xyloderivative 6. The introduction of the fluorine atom, with the correct stereochemistry is achieved by the use of diethylaminosulphur trifluoride (DAST) giving rise to the fluoroderivative 9 with yields from 25% (R= TBDMS) to 40% (R= TBDPS).

The protected fluorocompound 9 can be selectively deprotected at the 5'-position with ZnBr<sub>2</sub> in nitromethane (to give 12) or alternatively can be only deprotected at the 2'-position by reaction with TBAF to afford 10. A considerable improvement of the fluorination is obtained by reacting the protected xylofuranose 14 with DAST to give



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the fluoroderivative 15 in 83% yield. Also in this case a precious intermediate is obtained that can undergo selective deprotection to partially protected fluoro nucleosides 16 and 18. Moreover  $\text{ZnBr}_2$  detritylation under controlled conditions (low temperature) affords the N<sup>6</sup>-5'-O-diprotected derivative 17.

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