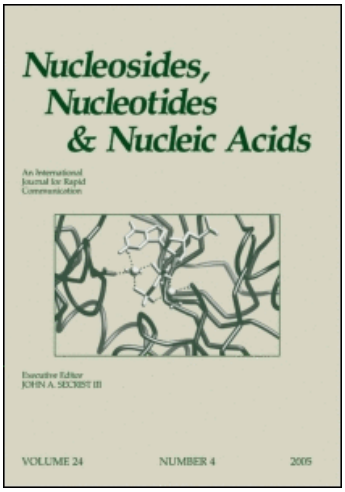


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# A New Synthesis of 3'-Fluoro-3'-deoxyadenosine

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

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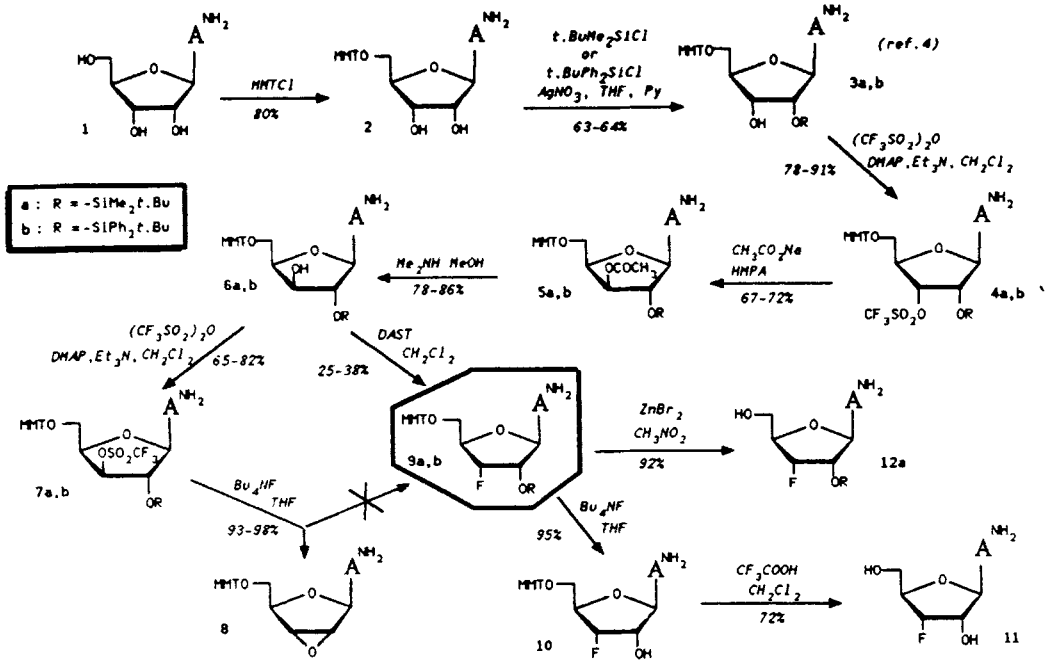
Abstract: 3'-Fluoro-3'-deoxyadenosine is synthesized starting from adenosine via double inversion and by using DAST. Intermediates are also obtained where 2' and 5'-position can be independently deprotected for further synthetic elaboration.

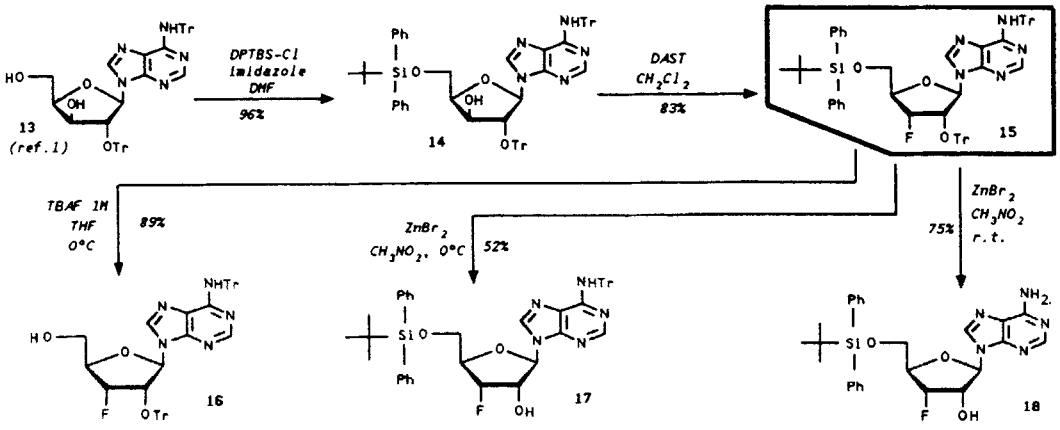
3'-Fluoro-3'-deoxy adenosine, a compound endowed with antiviral properties, has been recently synthesized[1,2], but our interest in its introduction into more complex biologically active structures addressed us to a different and shorter synthesis.

Starting from adenosine our synthetic route[3] 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 $ZnBr_2$ in nitrometane (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




SCHEME 1




SCHEME 2

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 $ZnBr_2$ detritylation under controlled conditions (low temperature) affords the $N^6$-5'-O-diprotected derivative **17**.

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