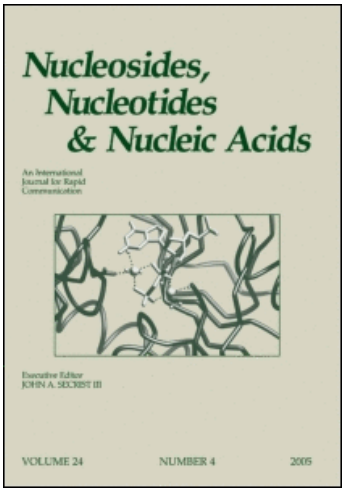


**Nucleosides, Nucleotides and Nucleic Acids**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

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Online publication date: 09 August 2003

**To cite this Article** Kumamoto, Hiroki , Onuma, Sayoko and Tanaka, Hiromichi(2003) 'Stannylation Approach to the Synthesis of 2'- and 3'-Substituted Analogues of 2',3'-Didehydro-2',3'-dideoxynucleosides', Nucleosides, Nucleotides and Nucleic Acids, 22: 5, 767 — 769
**To link to this Article: DOI:** 10.1081/NCN-120022630
**URL:** http://dx.doi.org/10.1081/NCN-120022630

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
Vol. 22, Nos. 5–8, pp. 767–769, 2003

# Stannylation Approach to the Synthesis of 2′- and 3′-Substituted Analogues of 2′,3′-Didehydro-2′,3′-dideoxynucleosides

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## ABSTRACT

Three methods are described for the introduction of a tributylstannyl group to the $sp^2$-carbon of 2′,3′-didehydro-2′,3′-dideoxy nucleosides (d44Ns). The resulting stannylated products serve as versatile intermediates for the synthesis of d4Ns having various types of carbon-substituent.

*Key Words:* 2′,3′-Didehydro-2′,3′-dideoxy nucleoside; Stannylation; Anionic migration; Desulfonylative-stannylation; Sulfoxide-metal exchange.

Although the discovery of potent anti-HIV activity of d4T has stimulated the synthesis and evaluation of 2′,3′-didehydro-2′,3′-dideoxynucleosides (d4Ns), there have been known only a narrow range of their analogues bearing a carbon-substituent at the 3′- or 2′-position.[1] Since transformation of vinylstannanes to various

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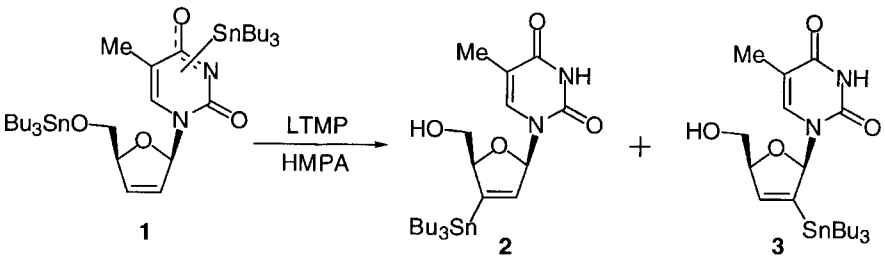
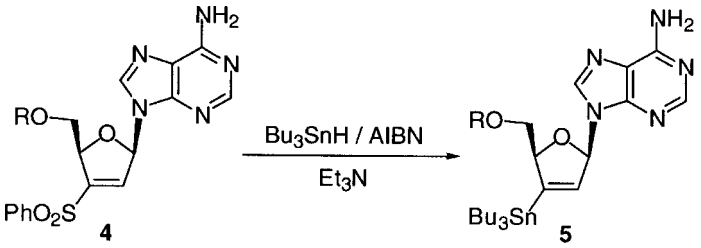
DOI: 10.1081/NCN-120022630
1525-7770 (Print); 1532-2335 (Online)

carbon-substituents is well appreciated, we investigated three different methods to introduce $SnBu_3$ group to the 3′- or 2′-position of d4Ns.

**Anionic O → C Stannyl Migration.**[2] Transalkoxylation between $Bu_3SnOMe$ and d4T gave the 5′-*O*-stannylated derivative **1** as evidenced by $^{119}Sn$ and $^{1}H$ NMR spectra in benzene-$d_6$. When **1** was treated with LTMP in the presence of HMPA, the 5′-*O*-$SnBu_3$ group underwent migration to the 3′-position, as a result of C3′-lithiation, to give **2** in 60% yield along with a small amount of **3** (9%). The observed highly unusual vinylic deprotonation in the presence of allylic protons (H-1′ and H-4′) could be due to the base moiety which acts as a Lewis base and thus directs the regiochemistry of lithiation.




**Radical-mediated Desulfonylative Stannylation.**[3] The 3′-*C*-benzenesulfonyl d4A (**4**) was prepared from 9-(2,3-anhydro-β-D-ribofuranosyl)adenine[4] in good overall yield. Radical-mediated *ipso*-substitution of the $SO_2Ph$ group proceeded efficiently by reacting $Bu_3SnH$/AIBN in refluxing benzene containing $Et_3N$ to yield **5** (76%). The presence of $Et_3N$ in this reaction is crucial for the subsequent successful chromatographic isolation of **5**.




**Sulfoxide-metal Exchange Reaction.**[5] For the introduction of $SnBu_3$ group to the 2′-position of d4U, sulfoxide-metal exchange was examined. Preparation of the substrate **6** was carried out by the reported $O^2$,2′-anhydro-bond cleavage with PhSH,[6] which was followed by oxidation. When **6** was reacted with EtMgBr, the





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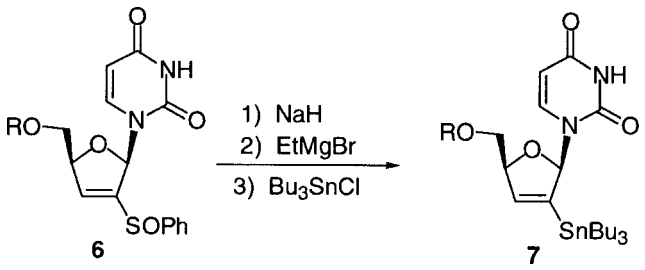


6 7

generated 2′-vinylmagnesium was found to undergo partial protonation with $N^3$-H. By treating **6** initially with NaH, the desired **7** was isolated in 62% yield.

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