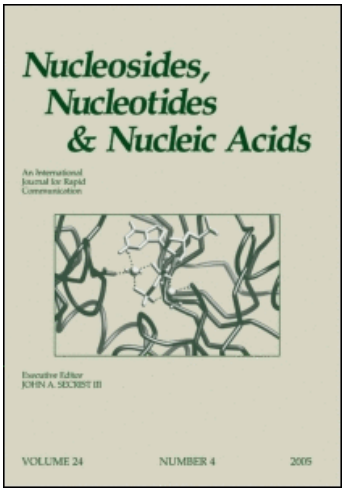

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

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To cite this Article Becouarn, S. , Czernecki, S. and Valéry, J. M.(1995) 'Radical Mediated Synthesis of 3'-α-C-Allenyl-2',3'-dideoxythymidine as a Non-polar Analogue of AZT', Nucleosides, Nucleotides and Nucleic Acids, 14: 3, 307 — 309
To link to this Article: DOI: 10.1080/15257779508012368
URL: http://dx.doi.org/10.1080/15257779508012368

NUCLEOSIDES & NUCLEOTIDES, 14(3-5), 307-309 (1995)

RADICAL MEDIATED SYNTHESIS OF 3'-α-C-ALLENYL-2',3'-DIDEOXYTHYMIDINE AS A NON-POLAR ANALOGUE OF AZT.

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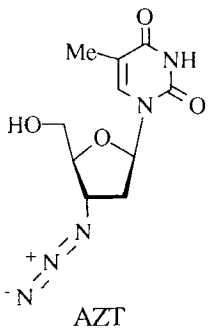
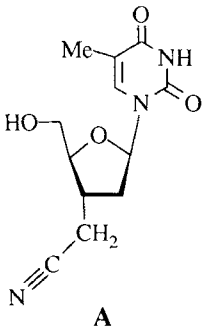
Abstract. The synthesis of the novel modified nucleoside (**1**) exhibiting the 1,2-propadienyl [allenyl] group at the 3'-α- position is described. The 3'-C-C bond was formed by radical reaction between triphenylprop-2-ynylstannane (**2**) and the 3'-bromo(iodo)-2',3'-dideoxynucleoside derivative (**3**).

Since 3'-azido-2',3'-dideoxythymidine (AZT) was discovered as a selective anti-HIV agent and introduced in wide clinical use, a number of 2',3'-dideoxynucleoside analogues have been targeted at the reverse transcriptase step.[1]

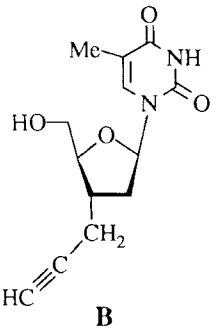
Among them, 3'-cyanomethyl-2',3'-dideoxythymidine (**A**) and 2',3'-dideoxy-3'-(2-propynyl)thymidine (**B**) were designed because of the claimed isosteric relationship of their carbon side chain with an azido group.[2] We found that the 1,2-propadienyl (allenyl) group would better fit this criterion and we decided to prepare the 3'-α-C-allenyl-2',3'-dideoxythymidine (**1**) as a novel nonpolar analogue of AZT.



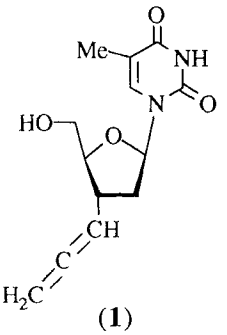
AZT



A



B



(1)

Free radical methodology was recently employed by two groups in the synthesis of 3'-α-C-allyl-2',3'-dideoxythymidine .[2,3] In the alicyclic series, the 1,2-propadienyl

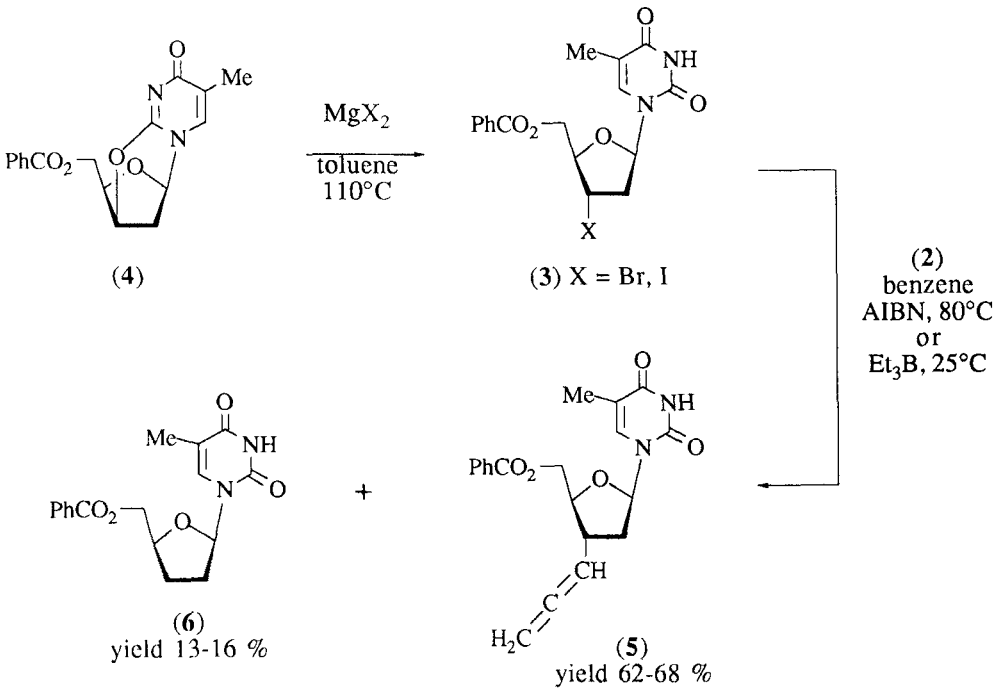
group can be introduced in this way,as shown by Baldwin *et al.*,[4] by reaction between triphenylprop-2-ynylstannane $Ph_3Sn-CH_2-C\equiv CH$ (**2**) and an alkyl halide which is more reactive than the thiocarbonate function.

The suitably halogenated nucleoside derivative (**3**) was obtained - under mild conditions and more than 70% yield - by reacting the readily available 2,3'-anhydroderivative (**4**)[5] with magnesium iodide or bromide.

Free radical reaction was then performed in the presence of different initiators and yielded 3'-α-C-allenyl-5'-*O*-benzoyl-2',3'-dideoxythymidine (**5**). The configuration at C-3' was established by X-ray spectroscopy.

Usual debenzoylation of (**5**) afforded the target compound (**1**).

As previously noticed in the free radical allylation procedure,[2] the 2',3'-dideoxy derivative (**6**) was isolated as a minor by-product.



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