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## Nucleosides, Nucleotides and Nucleic Acids

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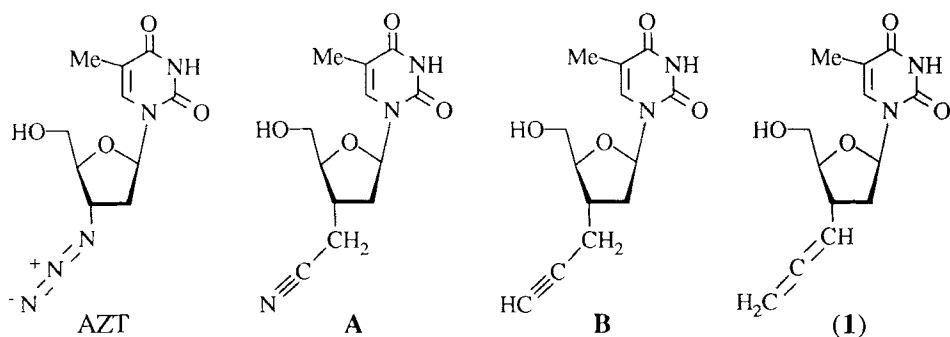
## RADICAL MEDIATED SYNTHESIS OF 3'- $\alpha$ -C-ALLENYL-2',3'-DIDEOXYTHYMIDINE AS A NON-POLAR ANALOGUE OF AZT.

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**Abstract.** The synthesis of the novel modified nucleoside (**1**) exhibiting the 1,2-propadienyl [allenyl] group at the 3'- $\alpha$ - 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.<sup>1</sup>

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.<sup>2</sup> We found that the 1,2-propadienyl (allenyl) group would better fit this criterion and we decided to prepare the 3'- $\alpha$ -C-allenyl-2',3'-dideoxythymidine (**1**) as a novel nonpolar analogue of AZT.



Free radical methodology was recently employed by two groups in the synthesis of 3'- $\alpha$ -C-allyl-2',3'-dideoxythymidine.<sup>2,3</sup> In the alicyclic series, the 1,2-propadienyl

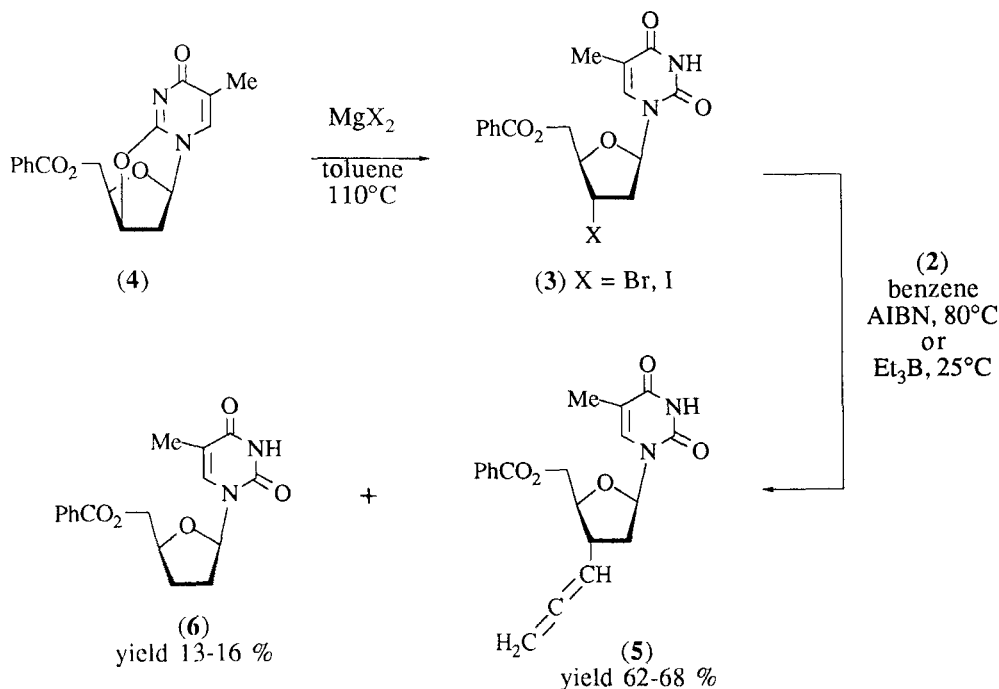
group can be introduced in this way, as shown by Baldwin *et al.*,<sup>4</sup> by reaction between triphenylprop-2-ynylstannane  $\text{Ph}_3\text{Sn}-\text{CH}_2-\text{C}\equiv\text{CH}$  (**2**) and an alkyl halide which is more reactive than the thiocarbonate function.

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**)<sup>5</sup> with magnesium iodide or bromide.

Free radical reaction was then performed in the presence of different initiators and yielded 3'- $\alpha$ -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,<sup>2</sup> the 2',3'-dideoxy derivative (**6**) was isolated as a minor by-product.



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