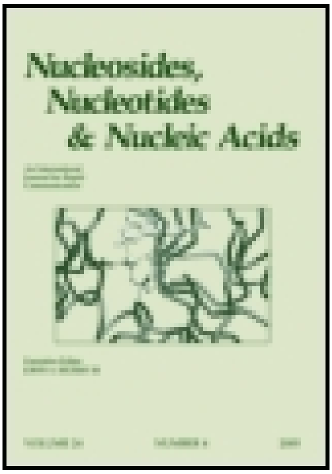
This article was downloaded by: [University of Bristol]
On: 29 January 2015, At: 14:49
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Nucleosides and Nucleotides
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lncn19

Radical Mediated Synthesis of 3′-α-C-Allenyl-2′,3′-dideoxythymidine as a Non-polar Analogue of AZT

S. Becouarn [a] , S. Czernecki [a] & J. M. Valéry [a]
[a] Université Pierre et Marie Curie, Laboratoire de Chimie des Glucides , 4 Place Jussieu, 75005, Paris, France

Published online: 16 Feb 2007.

To cite this article: S. Becouarn , S. Czernecki & J. M. Valéry (1995) Radical Mediated Synthesis of 3′-α-C-Allenyl-2′,3′-dideoxythymidine as a Non-polar Analogue of AZT, Nucleosides and Nucleotides, 14:3-5, 307-309

To link to this article: http://dx.doi.org/10.1080/15257779508012368

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the “Content”) contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions

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

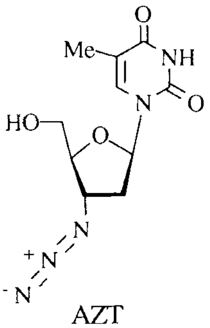
RADICAL MEDIATED SYNTHESIS OF 3'-α-C-ALLENYL-2',3'-DIDEOXYTHYMIDINE AS A NON-POLAR ANALOGUE OF AZT.

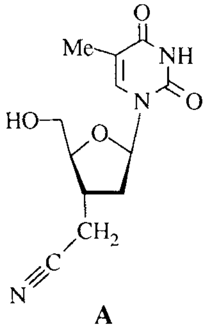
S. Becouarn, S. Czernecki* and J. M. Valéry
Université Pierre et Marie Curie. Laboratoire de Chimie des Glucides
4 Place Jussieu. 75005 Paris. France

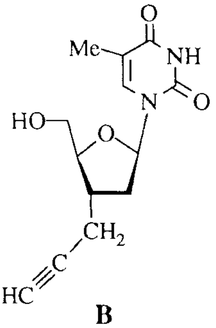
Abstract. The synthesis of the novel modified nucleoside (**1**) exhibiting the 1,2-propadienyl [allenyl] group at the 3'-α- position is described. The 3'-C-C bond was formed by radical reaction between triphenylprop-2-ynylstannane (**2**) and the 3'-bromo(iodo)-2',3'-dideoxynucleoside derivative (**3**).

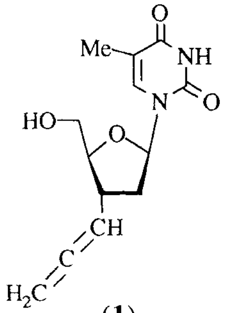
Since 3'-azido-2',3'-dideoxythymidine (AZT) was discovered as a selective anti-HIV agent and introduced in wide clinical use, a number of 2',3'-dideoxynucleoside analogues have been targeted at the reverse transcriptase step.[1]

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**)

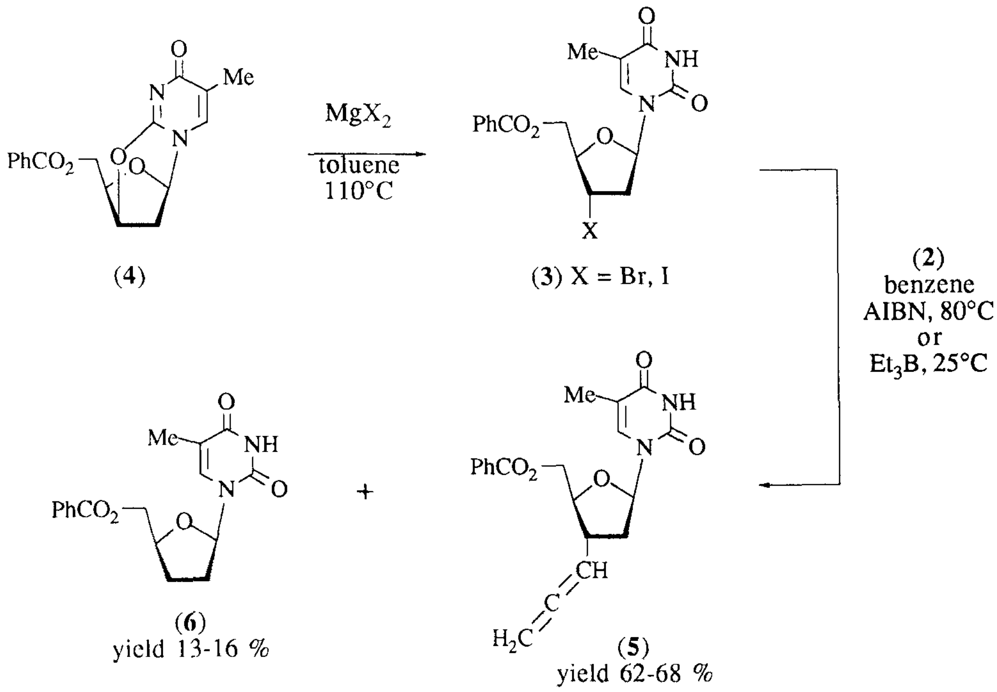
Free radical methodology was recently employed by two groups in the synthesis of 3'-α-C-allyl-2',3'-dideoxythymidine .[2,3] In the alicyclic series, the 1,2-propadienyl group can be introduced in this way, as shown by Baldwin *et al.*,[4] by reaction between triphenylprop-2-ynylstannane $Ph_3Sn-CH_2-C{\equiv}CH$ (**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.



REFERENCES

1. E. De Clercq *in* "Design of Anti-AIDS Drugs", E. De Clercq editor; Pharmacochemistry Library, Vol. 14, pp 1-24; Elsevier (Amsterdam) **1990**.
2. Fiandor J.; Tam S. *Tetrahedron Lett.* **1990**, *31*, 597.

3. Chu C. K.; Doboszewski B.; Schmidt W.; Ullas G. V. *J. Org. Chem.* **1989**, *54*, 2767.

4. BaldwinJ. E.; Adlington R. M.; Basak A. *J. Chem. Soc. Chem. Commun.* **1984**, 1284.

5. Czernecki S.; Valéry J. M. *J. Chem. Soc. Chem. Commun.* **1990**, 801.