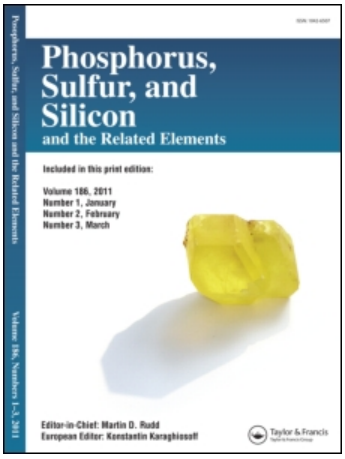

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Thio Nucleoside Derivatives as Intermediates or Target Compounds in the Attempt of Finding New Agents Against HIV

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To cite this Article Pedersen, Erik B. , Dueholm, Kim L. , El-emam, Ali , Kofoed, Thomas , El-Torgoman, Abdelmoneim A. -M. , Motawia, Mohammed S. , Aly, Youssef L. , Jørgensen, Per T. , El-barbary, Ahmed A. K. , Khodair, Ahmed and Larsen, Erik(1993) 'Thio Nucleoside Derivatives as Intermediates or Target Compounds in the Attempt of Finding New Agents Against HIV', Phosphorus, Sulfur, and Silicon and the Related Elements, 74: 1, 465 — 466
To link to this Article: DOI: 10.1080/10426509308038166
URL: http://dx.doi.org/10.1080/10426509308038166

Phosphorus, Sulfur, and Silicon, 1993, Vol. 74, pp. 465–466
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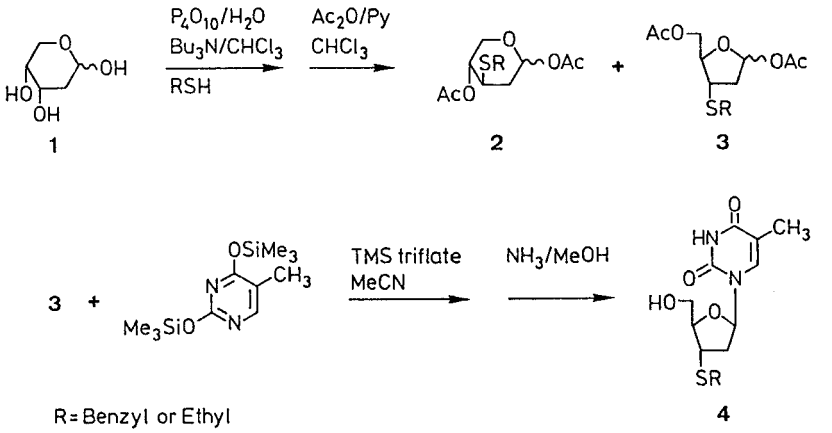
THIO NUCLEOSIDE DERIVATIVES AS INTERMEDIATES OR TARGET COMPOUNDS IN THE ATTEMPT OF FINDING NEW AGENTS AGAINST HIV

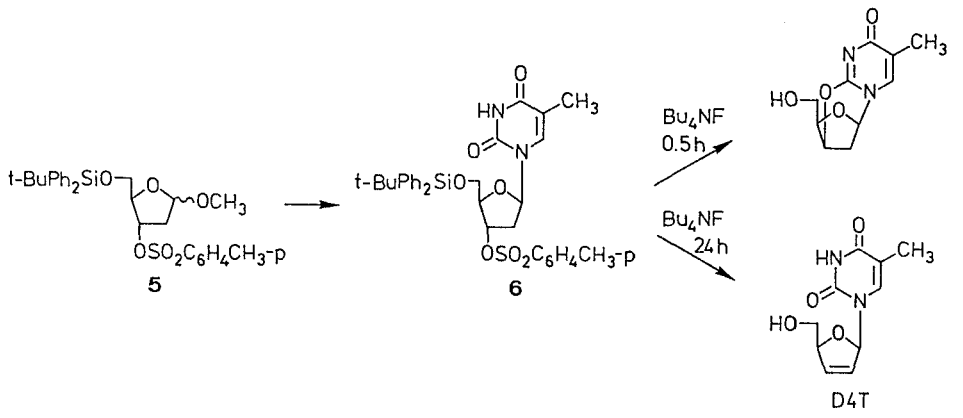
ERIK B. PEDERSEN, KIM L. DUEHOLM, ALI EL–EMAM, THOMAS KOFOED, ABDEL-MONEIM A.–M. EL–TORGOMAN, MOHAMMED S. MOTAWIA, YOUSSEF L. ALY, PER T. JØRGENSEN, AHMED A. K. EL–BARBARY, AHMED KHODAIR AND ERIK LARSEN.

Abstract 3'-Alkylthio-2',3'-dideoxy nucleosides and D4T are synthesized. An attempt of synthesizing a hybrid between AZT and HEPT is presented.

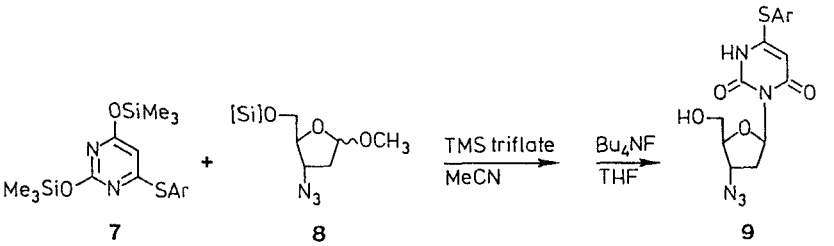
In our laboratory we have been very successful in using a convergent strategy for the synthesis of 2,3-dideoxy nucleosides by condensing appropriately substituted methyl glycosides with nucleobases.



Direct condensation of 2-deoxy-D-ribose **1** with mercaptans using the $P_4O_{10}/H_2O/Bu_3N$ reagent in chloroform resulted in coupling at C–3 to give the anomeric mixtures of the corresponding pentopyranoses **2** and pentofuranoses **3** after acetylation with acetic anhydride in dry pyridine. The latter was used in the synthesis of the nucleoside **4**.



The methyl glycoside **5** was synthesized from 2-deoxy-D-ribose by successive methyl glycosidation, silylation and tosylation and subsequently used for the synthesis of the nucleoside **6** which was isolated in 48% yield by precipitation. From this product D4T could be synthesized by refluxing with Bu_4NF in THF for 24 h in 20% overall yield from 2-deoxy-D-ribose. Using shorter reaction time and lower reaction temperature one can produce 2,3-anhydrothymidine which is an important intermediate in the synthesis of AZT.



It was attempted to synthesize a hybrid between AZT and HEPT by reaction the 6-arylthiopyrimidine derivative **7** with the sugar **8** using TMS triflate as the catalyst. Due to sterical hindrance from sulfur alkylation occurred at N–3 and not as expected at N–1.