

This article was downloaded by:

On: 27 January 2011

Access details: *Access Details: Free Access*

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, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

Substituent Influence on the Reaction Rate of Deoxyribonucleoside Phosphoramidites with Deoxyribonucleosides Catalysed by Tetrazole

Bjarne H. Dahl^a; John Nielsen^a; Otto Dahl^a

^a Department of General and Organic Chemistry, University of Copenhagen, The H. C. Ørsted Institute, Universitetsparken 5, Copenhagen, Denmark

To cite this Article Dahl, Bjarne H. , Nielsen, John and Dahl, Otto(1987) 'Substituent Influence on the Reaction Rate of Deoxyribonucleoside Phosphoramidites with Deoxyribonucleosides Catalysed by Tetrazole', *Nucleosides, Nucleotides and Nucleic Acids*, 6: 1, 457 – 460

To link to this Article: DOI: 10.1080/07328318708056255

URL: <http://dx.doi.org/10.1080/07328318708056255>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

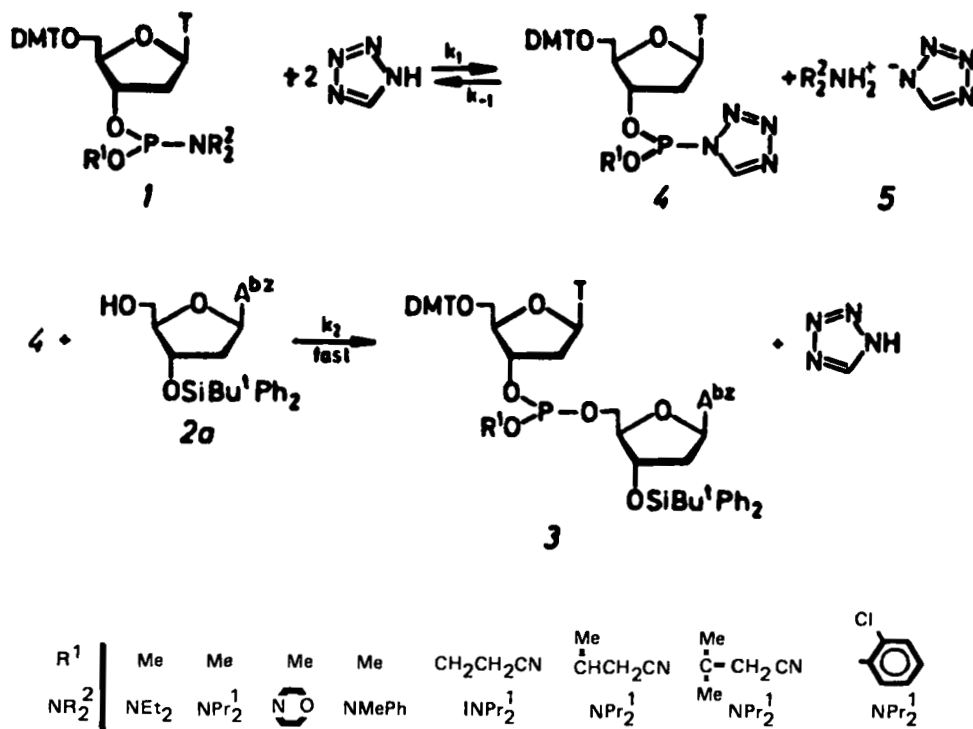
This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

SUBSTITUENT INFLUENCE ON THE REACTION RATE OF
DEOXYRIBONUCLEOSIDE PHOSPHORAMIDITES WITH
DEOXYRIBONUCLEOSIDES CATALYSED BY TETRAZOLE

Bjarne H. Dahl, John Nielsen, and Otto Dahl^{*}
Department of General and Organic Chemistry, University of
Copenhagen, The H. C. Ørsted Institute, Universitetsparken 5,
DK-2100 Copenhagen, Denmark.

The rates of formation of some dinucleoside phosphites **3** from different deoxyribonucleoside phosphoramidites **1** and a common nucleoside **2a** (Scheme) have been compared.



Scheme

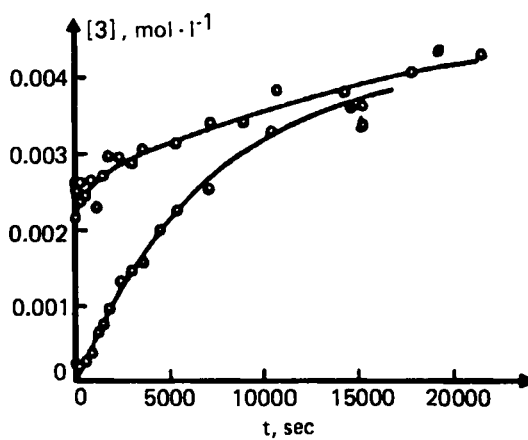


Fig. 1

a, 2a last added

b, tetrazole added last

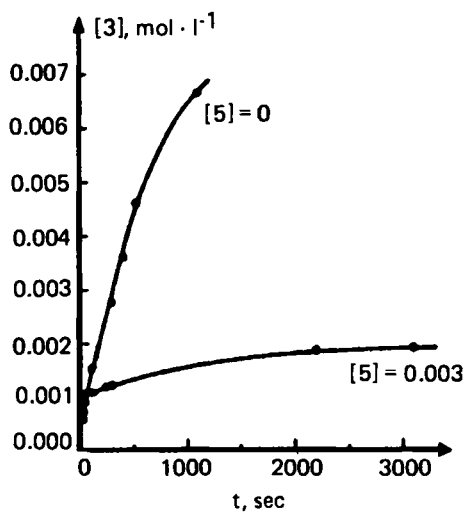
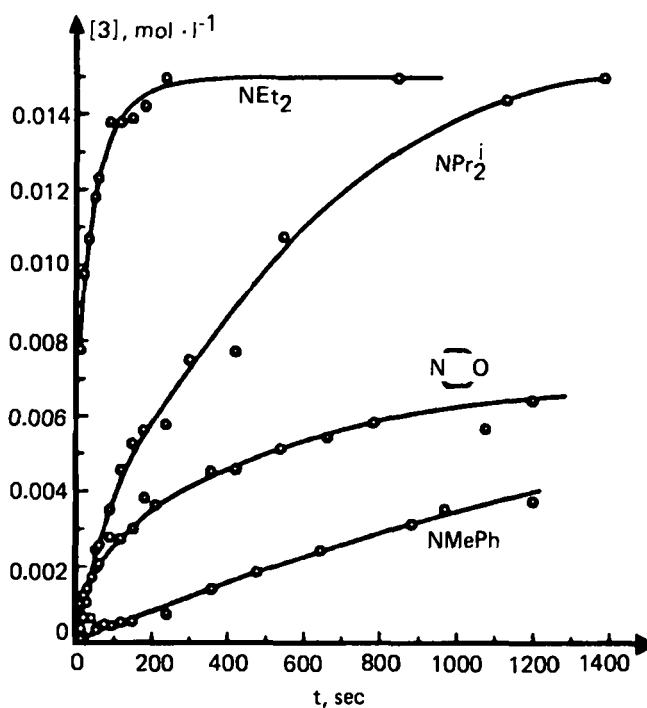


Fig. 2

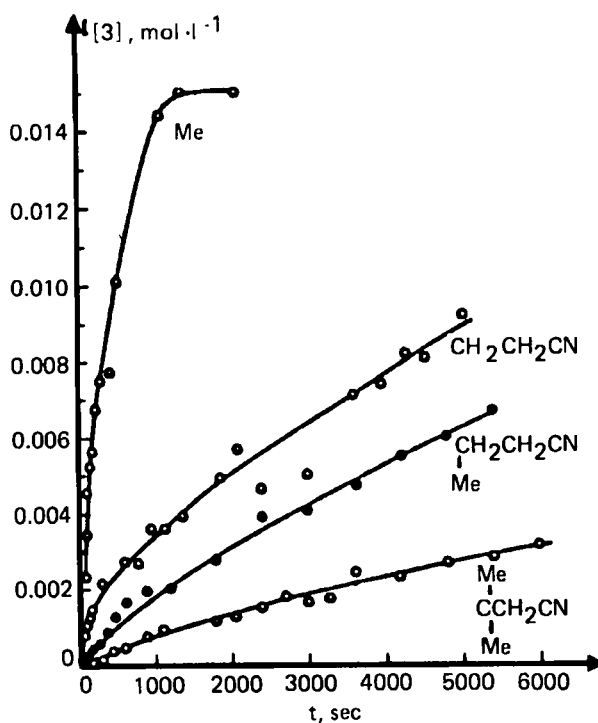
Effect of added salt 5.

 $c_1^0 = 0.030 \text{ M}$, $c_{\text{tet}}^0 = 0.015 \text{ M}$

Fig. 3, $R^1 = \text{Me}$

Nucleophilic catalysis via intermediate 4, when substantial amounts of the catalyst tetrazole are used, is inferred from experiments illustrated in Fig. 1 and Fig. 2. The rate variations with the amino substituents are shown in Fig. 3, and those with the alkoxy substituents in Fig. 4. Under the conditions used to obtain the curves (premixing 1 with 2a and adding tetrazole at time zero) the formation of 4 is probably rate-limiting; accordingly it is the rate of formation of this intermediate which is illustrated.

Fig. 3 shows that the more basic the $R^2_2\text{NH}$, the higher is the rate. The opposite order is found for model systems catalysed by small amounts of $R_2\text{NH}_2^+\text{Cl}^{-,1}$, where probably only acid catalysis occur (the stereochemistry was inversion²), and where the leaving group ability is important. With large amounts of tetrazole the formation of

Fig. 4, $R^2 = \text{Pr}^1$

5 apparently drives the reaction. Fig. 4 shows that a 2-cyanoethyl amidite is less reactive than a methyl amidite, and that the reaction is subject to some steric hindrance.

REFERENCES

1. Dahl, O.; *Phosphorus Sulfur*, 1983, 18, 201.
2. Nielsen, J.; Dahl, O.; *J. Chem. Soc. Perkin Trans II*, 1984, 553.