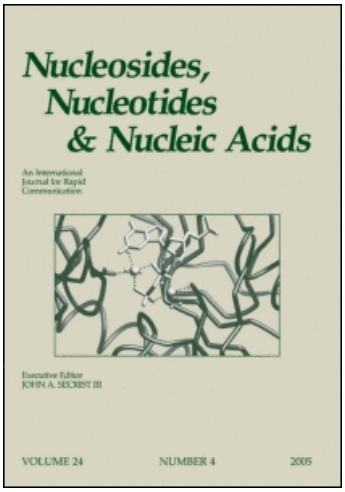

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

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Online publication date: 09 August 2003

To cite this Article Rochdi, A. , Taourirte, M. , Redwane, N. , Sebti, S. , Engels, J. W. and Lazrek, H. B.(2003) 'Doped Natural Phosphate: A New and Environmentally Friendly Catalyst in Nucleoside Synthesis', Nucleosides, Nucleotides and Nucleic Acids, 22: 5, 679 — 681
To link to this Article: DOI: 10.1081/NCN-120022699
URL: http://dx.doi.org/10.1081/NCN-120022699

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
Vol. 22, Nos. 5–8, pp. 679–681, 2003

Doped Natural Phosphate: A New and Environmentally Friendly Catalyst in Nucleoside Synthesis

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ABSTRACT

Doped natural phosphate is used as acidic or basic catalyst in nucleoside and acyclonucleoside synthesis. Some examples are given.

Since the discovery of modified acyclonucleosides as antiviral agents, substantial efforts have been devoted to the synthesis and biological evaluation of such compounds. Recently, various types of inorganic catalysts have been shown to function as effective heterogeneous catalyst for organic synthesis. The advantage of these heterogeneous catalysts over the homogeneous system include stability, ease of handling, lack of corrosion and other environmental hazard and ease of recovery and regeneration.

Natural phosphate (NP) is an important mining wealth of Morocco. Many investigations were performed in our laboratory to test the use of natural phosphate

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DOI: 10.1081/NCN-120022699
1525-7770 (Print); 1532-2335 (Online)

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Table 1.

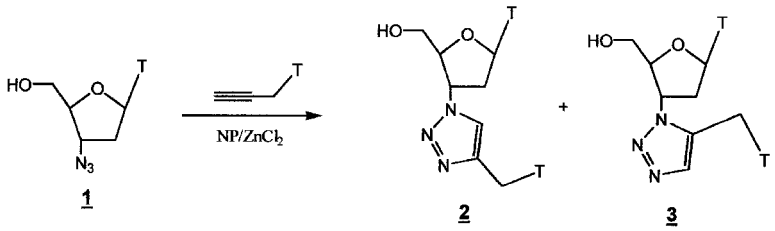
Entry	Catalyst	Isomers (2)(3)	Reaction time	Yield (%)
1	Without	4/1	46 h	67
2	$NP/ZnCl_2$	4/1	8 h	67

in heterogeneous catalysis. In this report, we describe some examples which show that natural phosphate can be used as catalyst in nucleoside and acyclonucleoside synthesis.

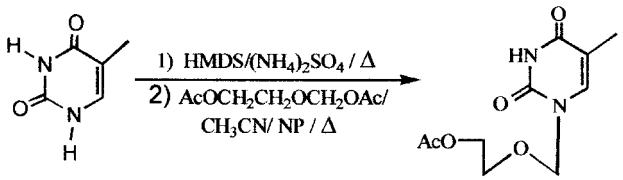
Substances containing 1,2,3-triazole heterocyclic ring are important targets in chemical synthesis because of their pronounced biological activities.[1] The use of 1,3-dipolar cycloaddition for preparing 1,2,3-triazole ring is well established, but suffers from some drawbacks (high temperature and long time of reaction). For these reasons we became interested in the use of zinc chloride doped natural phosphate as catalyst. For example: we reported the synthesis of 1,2,3-triazole acyclonucleoside derivative of AZT (Sch. 1). When NP supported $ZnCl_2$ is used as a catalyst all reactions worked smoothly. Furthermore, the ratio of 1,4-isomer/1,5-isomer was unchanged and the reaction time decreased.[2]

This example showed that $ZnCl_2$ doped natural phosphate can be used as Lewis acid catalyst for 1,3- dipolar cycloaddition.

In continuation of our program on the investigation of catalytic properties of natural phosphate and in the search of a new and easy way for acyclonucleoside synthesis, we have performed several N-alkylation reactions of nucleobases using natural phosphate alone (Sch. 2) or doped with KF or K_2CO_3 (Sch. 3). In order to assess the influence of natural phosphate as catalyst on these reactions, analogue



Scheme 1.



Scheme 2.

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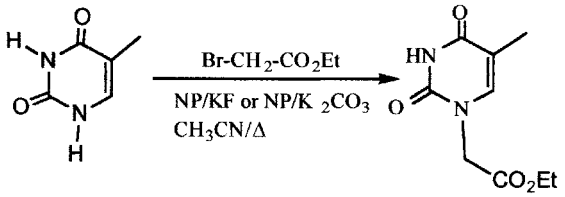

Scheme 3.

of Acyclovir[3] and the starting material for PNA were checked for the most effective conditions.

Both NP/KF (350 mg/50 mg) and NP/K_2CO_3 (350 mg/50 mg) showed a catalytic activity and the procedure is regioselective (N-1 isomer). After establishing the importance of NP in N-1-alkylation of thymine, we undertook the extension of this protocol to other natural heterocylic bases. The N-1(pyrimidine), N-9 (purine) acyclonucleoside isomers were obtained in 50–70% yield. All compounds were fully characterized by spectroscopic and elemental analysis. In conclusion we have shown that natural phosphate alone or doped with $ZnCl_2$, KF or K_2CO_3 can be used as catalyst in nucleoside and acyclonucleoside synthesis.

ACKNOWLEDGMENTS

This work was supported by the Ministry of National Education and Scientific Research (Morocco) (PARS : Chim 053/1998) and by CNR (Morocco)/DFG (Germany) program.

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