Natural Phosphate As Solid Catalyst To Synthesis Of 1- Acetal diethyl-1H-indole-3-carbaldehyde Assisted Microwave Irradiation

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Abstract: - An efficient method for synthesis of 1- Acetal diethyl-1H-indole-3-carbaldehyde by combinaison of 1H-indole-3-carbaldehyde and bromoacetal diethyl using Natural phosphate doped with K2CO3 (NP/K2CO3) is described .The reactions promoted by microwave irradiation are advantageous in many ways because of short reaction time, and solvent free reaction conditions . Several reactions of synthetic importance such as alkylation. have been satisfactorily done under microwave irradiation.

Index Terms: -Natural phosphate doped wit K2CO3, 1-methyl-1H-indole-3-carbaldehyde, Mw.

INTRODUCTION

The application of microwave irradiation to expedite solid-phase organic reactions could be the tool that allows combinatorial chemistry to deliver on its promise—providing rapid access to large collections of diverse small molecules. Herein, several different approaches to microwave (MW)-assisted solid-phase reactions and library synthesis are introduced, including the use of solid-supported reagents, multicomponent coupling reactions, solvent free parallel library synthesis, and spatially addressable library synthesis on planar solid supports. The future impact of MW-assisted organic reactions on solid-phase and combinatoria chemistry could prove to be immense, and methods for further improvement of this strategic combination of technologies are highlighted. Numerous reactions in organic synthesis can be achieved under microwave irradiation in the absence of solvent, generally under normal pressure in open vessels. Increased amounts of reactants can be concerned in order to ensure a better compatibility between the in-depth penetrability of materials and the radiation wavelength. Since microwave activation is a rather recent technique, the number of examples can appear limited at the present time, but is rapidly expanding.(i) O-Alkylations [1] (ii) N-Alkylations [2] (iii) C-alkylation of Active Methylenes [3].N-Alkylation is an important reaction organic synthesis, and provides access to valuable building blocks that are used as intermediates or additives in the preparation ofdyes [4], fluorescenceprobes[5], agrochemicals[6], andpharmaceuticals[7].

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Theacyclonucleosides can be gotten according to three different strategies "A method so-called" total synthesis ".From a nucléoside preformed by rupture of one or several links of the cycle osidique." By condensation of a hétérocycle appropriately protected with a chain alkyle or alkoxyle. This last is the more used, it is about a reaction of N-alkylation of the bases heterocycliques. The C-N link of the acyclonucléoside is formed after condensation of the basis hétérocyclique, activated or no, and of an acyclic chain appropriately substituted according to a mechanism of substitution nucléophile. Although some methods for the direct N-monoalkylation are available, alternative routes are always of interest. Generally, when alkyl bromides or alkyl chlorides are used as alkylating agents, the reactionsproceed slowly and several polyalkylation/halogenated by-products are observed.
Surface–mediated solid phase reactions are of growing interest because of (i) environmentally friendly processes they offer, when compared to conventional reaction conditions (ii) advantages as ease of set up , mild conditions, rapid reactions , selectivity, increased yields of the products and low cost. In an effort to develop new practical and economic catalysts, we and others recently investigated the use of natural phosphate (NP) alone or doped in various chemical transformations [8-11]. These types of catalysts represent an important environmentally friendly alternative to reactions otherwise toxic and expensive. Since his/her/its creation, the Bio-Organic chemistry laboratory had for objectives the conception and the synthesis of molecules to therapeutic aim (antiviraux, anticancéreux,… etc.). most these molecules are of nature nucleoside (cyclic or acyclic). This work appears in the continuity of the research developed at the Bio-Organic chemistry laboratory. it has for objective the synthesis of new acyclonucléosides derivative of the nucleobase. Here, we report an easy one pot synthesis of acyclic nucleosides using natural phosphate coated with K2CO3 (NP/ K2CO3) as catalyst by N-alkylation reaction of a mixture of 1H-indole-3-carbaldehyde and bromoacetal diethyl (scheme 1).

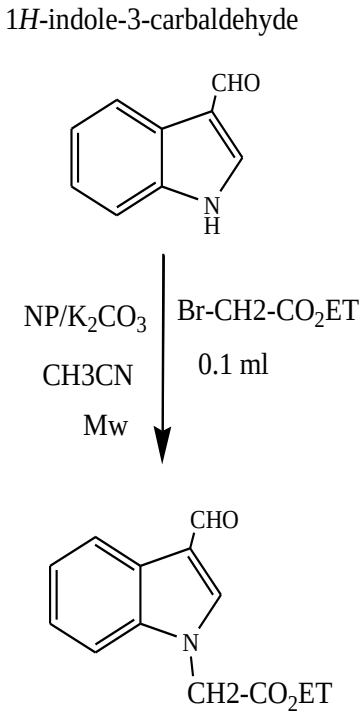


Fig. 1. Magnetization as a function of applied field. Note that "Fig." is abbreviated. There is a period after the figure number, followed by one space. It is good practice to briefly explain the significance of the figure in the caption.

Scheme 1: Conditions: BNP/ K2CO3/CH3CN, Mw

RESULTS AND DISCUSSION

As shown in Table 1 , when NP and microwave (5 min and 10 min) were used , the reaction of 1H-indole-3-carbaldehyde and bromoacetal diethyl gave the acyclonucleoside 5% yields Entry (1-2) . When NP doped with KF and microwave was used. The desired acyclonucleoside was obtained in only 37 and 38% yields respectively (Entry 3 and Entry 4). The good yield (44%, Entry 6) is obtained when using NP doped with K2CO3 and microwave in 10 min at 350W was used.

Table 1: Synthesis of 1-methyl-1H-indole-3-carbaldehyde

Entry	Catalyst	Time	Yield %
1	NP	350W, 5min	5
2	NP	350W,10min	5
3	NP /KF (0.35 eq)	350W, 5min	37
4	NP /KF (0.35 eq)	350W,10min	38
5	NP /K2CO3 (0.6eq)	350W,5min	38
6	NP /K2CO3 (0.6 eq)	350W, 10min	44

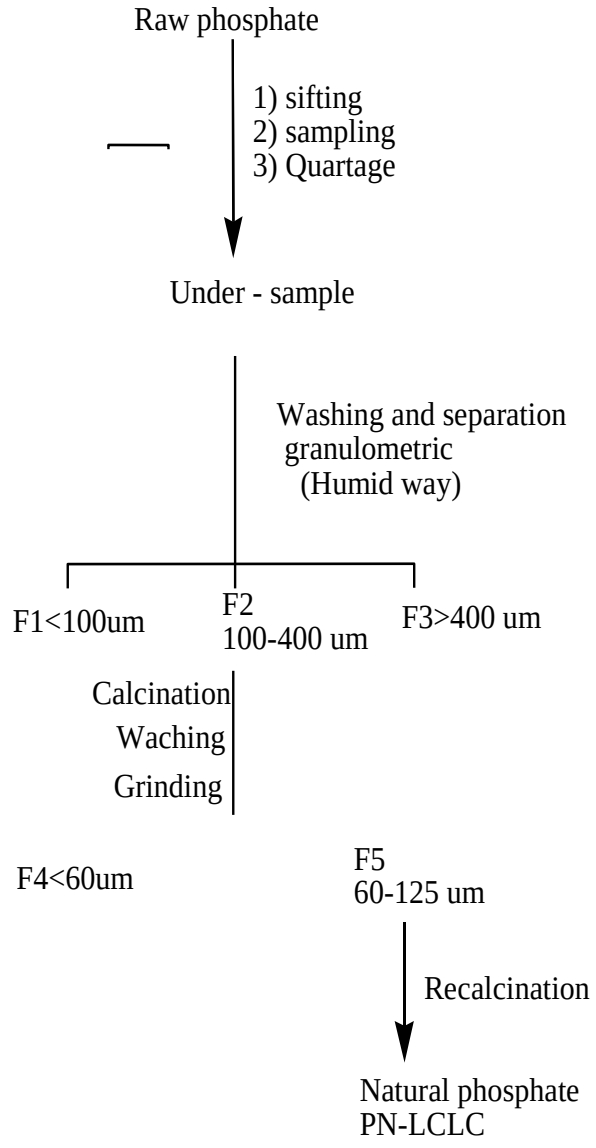
CONCLUSION

In summary, we describe a simpl, and efficient methods for the synthesis of acyclonucleosides at microwave using cheap and readily available catalyst (NP/ K2CO3). This new method has advantages such as: The soft, low cost, is part of green chemistry and ease of treatment.

EXPERIMENTAL

A-Treatment of natural phosphate

The phosphate is the first Moroccan wealth. He/it represents 94% of the production of the mining sector, his/her/its transformation in manure and in phosphoric acid represents the most important outletsof this ore.The raw phosphate has been treated like indicated below (schem 2).



After relavage and recalcination the gotten phosphate is called the natural phosphate. The characterization of the natural phosphate has been achieved to show his composition, by diffraction of the X-rays (RX). His majority composition driven to the family of the formula apatites phosphocalcic in the state pure C10(PO4)6F2 fluoroapatite (figuire 1)

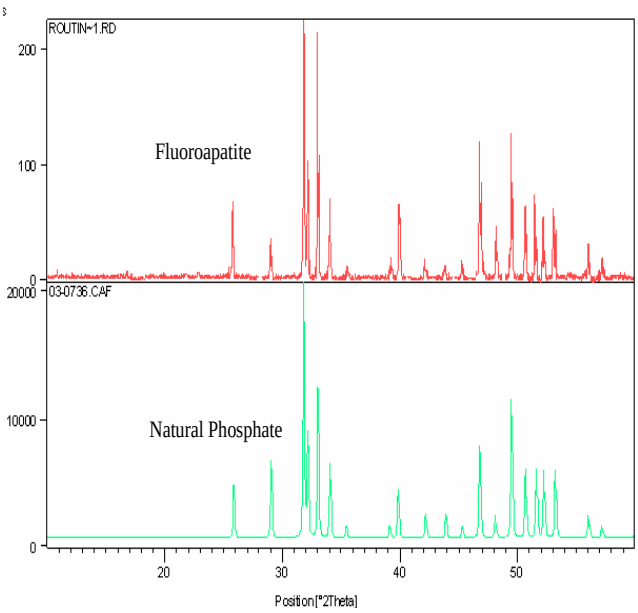


Figure 1: Specter of diffraction of the X-rays of the fluoroapatite and the Specter of diffraction of the X-rays of the natural phosphate

B-Catalyst Preparation Natural phosphate coated with K2CO3 To a solution of K2CO3 (759 mg) in water (5 ml) was added natural phosphate (3 g) and stirred for 15 min. The mixture was evaporated to dryness.

C-Experimental Procedures (Mw)
To a mixture of 1H-indole-3-carbaldehyde (0.69 mmol), bromoacetal diethyl (0. 1 ml), and NP/ K2CO3 (349 mg, 0.69 eq of K2CO3) were added acetonitrile (0.5 ml). The open flask was placed in a baker containing neutral alumina and mixture was heated in an unmodified microwave oven (150 C, 350W) for 10 min. The black resulting solid was suspended in CH2Cl2 and the precipitate was filtered. The filtrate was evaporated and residue was purified by column chromatography (CH2Cl2/MeOH (98/2 v/v)) to give the desired acyclonucleoside

REFERENCES

[1] Iurduc, N., Abdelylal~ D.; Buisine, J. M.; Decock, P.; Surpateann, G. Eur. Polym. J. 1997, 33, 187-190.

[2] Ding, J.; Gu, H.; Wen, J.; Lin, C. Synth. Commun. 1994, 24, 301-303.

[3] Jiang, Y.; Wang, Y.; Deng, R.; Mi, A. A. C S. Syrup. Ser. 1997, 659, 203-213.

[4] Suwanprasop, S.; Nhujak, T.; Roengsumran, S.; Petsom, A. Ind. Eng. Chem. Res. 2004, 43, 4973.

[5] (a) Stauffer, S. R.; Hartwig, J. F. J. Am. Chem. Soc. 2003,125, 6977; (b) Kim, J. S.; Shon, O. J.; Rim, J. A.; Kim, S.K.; Yoon, J. J. Org. Chem. 2002, 67, 2348.

[6] Montgomery, J. H. Agrochemicals Desk Reference: EnvironmentalData; Lewis: Chelsea, MI, 1993.

[7] Negwer, M. Organic-chemical drugs and their synonyms (An international survey), 7th ed.; Akademie VerlagGmbH: Berlin, 1994.

[8] Alahiane, A.; Rochdi, A.; Taourirte, M.; Redwane, N.; Sebti, S.; Engels, J. W. ; Lazrek, H. B. Nucleosides, Nucleotides, Nucleic Acids, 2003,22, 109-114.

[9] Zahouily, M.; Mezdar, A.; Elmakssoudi, A.; Mounir, B.; Rayadh, A.; Sebti, S.; Lazrek, H. B. ARKIVOC 2006, 31-40. (e) Zahouily, M.; Elmakssoudi, A.; Mezdar, A.; Bahlaouan, B.; Rayadha, A.; Sebti, S.; Lazrek, H. B. Lett. Org. Chem. 2005, 2, 136-138 (f) Zahouily, M; Mezdar, A.; Rakik, J.; Elmakssoudi, A.; Rayadh, A.; Sebti, S. J. Mol. Catal. A: Chemical 2005, 233, 43-47

[10] Lazrek, H.B. ; Rochdi, A. ; Redwane, N.; Ouzebla, D.; Vasseur, J.J. Letters in Organic Chemistry, 2006, 3, 313-314. 8

[11] (a)Lazrek, H.B.; Ouzebla, D.;Vasseur, J.J. Nucleosides, Nucleotides, Nucleic Acids, 2007,26,1095-109(b) Lazrek .H.B, Baddi .L, Ouzebla D., Smietana. M., Vasseur .J.J. Nucleic Acids Symposium Serie 2008 .52 ,549–550, (c) Sebti, S.; Zahouily, M.; Lazrek, H.B.; Mayoral, J.A.; Macquerrie, D.J. Current Organic Chemistry, 2008,12, 203-232 (d) Baddi, L.; Smietana, M.; Vasseur, J.J.; Lazrek, H.B. Lett. Org. Chem 2010,7,196–199; (e) Lazrek .H. B, .Ouzebla,D, Faraj. A Nucleosides, Nucleotides and Nucleic Acids 2011, 30,227–234