

Synthesis of α -ribonucleoside (Majority) by the Coupling of NP/KI and NP/I₂

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ABSTRACT

In this work we will demonstrate a method of preparing α -D-ribonucleosides using the solid-phase approach using the combination between natural phosphate doped with potassium iodide (NP/KI) and natural phosphate doped with iodine (NP/I₂). All these derivatives ribonucleosides were prepared by N-glycosylation reaction between silylated bases and 1-O-acetyl-2,3,5-tri-O-benzoyl- β -D-ribofuranoside.

Keywords: α -ribonucleosides, NP/KI, NP/I₂, Reflux.

Published Online: December 3, 2020

ISSN: 2684-4478

DOI : 10.24018/ejchem.2020.1.6.30

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I. INTRODUCTION

In recent years, chemical researchers and biologists have been interested in nucleosides and their biological activities [1]-[3].

In this perspective, several synthetic methods have been described to synthesize nucleoside analogs by way of example: AZT, ddC and ddI [4] (Fig. 1).

For ribonucleosides the β configuration is almost major and the configuration remains minor [5]. Solid phase reactions play an important role in environmental friendliness, ease of handling, ease of product separation, as they are fast, selective, and cheaper.

With this in mind, we have used a solid catalyst which is less expensive; we are talking about natural phosphate NP alone or doped [6]-[8]. This catalyst is included in green chemistry.

At first and in our laboratory, several reactions were carried out using natural phosphate as a solid catalyst under optimal mild conditions and that the follow-up and the treatment are very easy and simple [9].

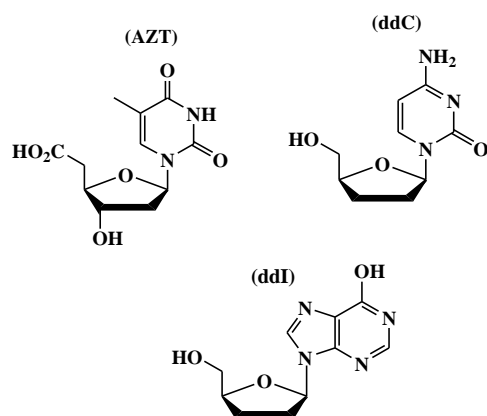
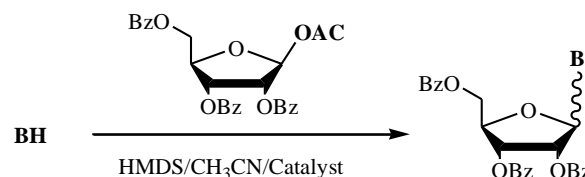


Fig. 1. AZT, ddC and ddI.

We describe a new method for the preparing of α -D-ribonucleosides using a coupling between natural phosphate doped with KI and natural phosphate doped with I₂ (Fig. 2).



BH= Uracile, azauracile, thymine

Fig. 2. Synthesis of 2,3,5-tri-O-benzoyl- α -D-Ribonucleosides (majority).

II. RESEARCH METHOD

A mixture of 112 mg of uracile (1 mmol), hexamethyldisilazane (4 ml) and ammonium sulfate (8 mg) is brought to reflux under reflux for two hours. Then 453 mg of 1-acetyl 2, 3,5-tri-O-benzoyl- β -D-ribofuranose (0.9 eq), 211 mg of NP/KI (0.4 eq), 111 mg of NP/I₂ (0.1 eq of I₂) and 5 ml of acetonitrile is added to the mixture obtained. After heating overnight at (80 °C.), the mixture is filtered and evaporated off. This reaction gave a good yield (56%) (α / β : 70/30) (Table 1, Entry 7).

III. RESULTS AND ANALYSIS

The analysis of this table shows that the uracile-derived ribonucleoside was obtained with a major configuration β in only (α / β : 13/87 entry 1) and (α / β : 22/78 entry 2). Also, we can draw from this table is that the stereo selectivity has changed to reach major configurations α when we used the coupling NP/KI and NP/I₂). For example, in entry 7 the ribonucleoside obtained give the majority isomer α (α / β :

70/30) using the coupling of (NP/KI (0.4 eq of KI) and NP/I₂ (0.1eq of I₂) in acetonitrile at 800 C overnight. We were able to generalize this method to other bases and always the N-1 isomer is obtained with major α configurations (entry 8, α/β : 65/35) and (entry 9, α/β : 64/36).

TABLE1: SYNTHESIS OF 2, 3,5-TRI-O-BENZOYL- α -D
RIBONUCLEOSIDES (MAJORITY)

Entry	Nucleic base	Catalyst	Yield %	α/β
1	Uracile	NP/KI (0.8 eq de KI)	30	13/87
2	Uracile	NP/I ₂ (0. 2eq de I ₂)	40	22/78
3	Uracile	NP/KI (1 eq of KI) +NP/I ₂ (0.1 eq of I ₂)	32	30/70
4	Uracile	NP/KI (0.8 eq of KI) + NP/I ₂ (0.1 eq of I ₂)	46	50/50
5	Uracile	NP/KI (0.4 eq of KI) +NP/I ₂ (0.2 eq of I ₂)	24	55/45
6	Uracile	NP/KI (0.2 eq of KI) +NP/I ₂ (0.1 eq of I ₂)	48	60/40
7	Uracile	NP/KI (0.4 eq of KI) +NP/I ₂ (0.1 eq of I ₂)	56	70/30
8	Azaauracile	NP/KI (0.4 eq of KI) +NP/I ₂ (0.1 eq of I ₂)	36	65/35
9	Thymine	NP/K I(0.4 eq of KI) +NP/I ₂ (0.1 eq of I ₂)	40	6 64/36

IV. CONCLUSION

Based on these results we have described a simple method, which falls within the scope of green chemistry by using catalysts that are cheaper than those in the literature. We also valued natural phosphate as a national wealth in the N-glycosylation reaction. Then to synthesize the major alphas isomers it was necessary to work by this coupling (NP / KI, NP / I₂).

ACKNOWLEDGMENT

This investigation was supported by the programme Action intégrée Franco-Marocaine AI n° MA/06/143.

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