Efficient and Selective Catalytic N-Glycosilation, by NP/ SnCl₄ in HMDS or BSA Under Eco-Friendly Conditions

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ABSTRACT

The 1-O-acetyl-2, 3,5-tri-O-benzoyl-β-D-ribofuranosides are synthesized by the coupling of sugar and silylated nucleobase. All these derivatives are synthesized using NP/SnCl₄ as catalyst.

Keywords: Natural Phosphate doped with SnCl₄ (NP/ SnCl₄), N-Glycosylation, D-ribonucleoside, hexamethyldisilazane (HMDS), Bis-silylacetamide (BSA).

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I. INTRODUCTION

Nucleosides are natural biological molecules of capital importance because they play an essential role in many biological activities [1]-[4]. Nucleosides represent a main class in chemotherapy. Their derivatives have been approved for the treatment of several viral diseases.

Ribonucleosides consist of the one hand of the base such as guanine, adenine, thymine, cytosine, and uracil and on the other hand of sugar such as D-ribose or D-deoxyribose [5] (Fig. 1).

D-ribonucleos play a fundamental role in the life and reproduction of animal cells, plant and microbial. The D-ribonucleoside is a blend of a monosaccharide (deoxy-ribose or ribose) and a nucleic base. Both units are connected by a covalent bond between the anomeric carbon C1 of monosaccharide and nitrogen atoms of the natural basis. In DNA and RNA structure of the base is always a deoxy-D-Ribose or D-ribose and configuration of this link is still β for almost all natural nucleosides. In terms of numbers, the base is seen as the main group and the ribose as a side chain. In a nucleoside, the anomeric carbon is numbered C1. Organic synthesis in a heterogeneous solid-liquid medium has been the subject of several studies. Thus, the large number of organic reactions carried out under these conditions and the variety of solid catalysts used, show the particular interest of these new synthesis methods. Several syntheses have been carried out using solid-liquid catalysis. The inorganic supports are very varied, among which one can quote for example, alumina, silica.

Fig. 1. Structure of D-Ribonucleoside derived from D- ribose and nucleic base.

Very recently, numerous studies have shown that natural phosphate [6] can be used in heterogeneous solid-liquid catalysis. This constitutes a new way of upgrading this ore. Natural phosphate [7]-[9] has advantages such as: its low cost, its modulable acid power, the simplicity and ease of handling, its compatibility ¹⁰with the environment and its. The object of this work is the valorisation of natural phosphate doped with SnCl₄ in the synthesis of D-ribonucleosides (Fig. 2).

Fig. 2. Synthesis of 2', 3,5-tri-O-benzoyl- β -D- Ribonucleosides.

II. RESEARCH METHOD

A. Experimental Procedures: N-Glycosylation using HMDS

To 1 mmol of uracil, the 4 ml of HMDS and 10 mg of ammonium sulfate are added, and then the mixture is heated under reflux for two hours. The 1-O-acetyl-2,3,5-tri-O-benzoyl- β -D-ribofuranose (0.9eq, 453mg), NP /SnCl₄ (526mg, 1eq of SnCl₄) and 5 ml of acetonitrile are added. Overnight at reflux, the mixture is filtered, and the solvent is evaporated off.

B. Experimental Procedures: N-Glycosylation using BSA

To 1 mmol of uracil, the Bis-silylacetamide (BSA) (1 ml), ammonium sulfate (catalytic amount) and acetonitrile (2.5 ml) are added, the mixture is heated to reflux for 30 minutes. Next, the 1-O-acetyl-2,3,5-tri-O-benzoyl- β -D-ribofuranose NP / SnCl₄ (526 mg, 1 eq of SnCl₄) are added. After overnight at reflux, the mixture was filtered, and the solvent was evaporated.

In order to assess the influence of natural phosphate (NP) doped with SnCl₄ as a catalyst on this reaction and to find the most effective conditions, a number of experiments were performed. The results of these studies are summarized in Table 1.

TABLE 1: SYNTHESIS OF 2',3,5'-TRI-O-BENZOYL-B-D RIBONUCLEOSIDES

Entry	Nucleobase	Silylated agent	Yield %	α/β
1	Uracil	HMDS	45	0/100
2	Uracil	BSA	30	0/100
3	Thymine	HMDS	30	0/100
4	Thymine	BSA	20	0/100
5	Cytosine	HMDS	26	0/100
6	Cytosine	BSA	20	0/100
7	Adenine	HMDS	20	0/100
8	Adenine	BSA	27	0/100

III. RESULTS AND ANALYSIS

In Table 1 when the NP/SnCl₄ (1 eq of SnCl₄) in HMDS is used only 45% of ribonucleoside was obtained (entry 1). However, the reaction with NP/SnCl₄ (1eq of SnCl₄) in BSA only leads to 30 % of the product (entry 2). The reaction of N-glycosylation has been applied to other pyrimidine nucleobases (thymine, cytosine) in the optimal conditions NP/SnCl₄ (1eq of SnCl₄), the yields are 30% (HMDS), 20% (BSA) (thymine, entry 3, 4) and 26% (HMDS), 20% (BSA) (cytosine, entry 5, 6), respectively. The reaction of N-glycosylation has been applied also to Adenine (purine nucleobase), the yield is 20% (HMDS) and 27% (BSA) (entry 7, 8). For pyrimidins nucleobase, the good yield is obtained when NP/SnCl₄ (1eq of SnCl₄) in HMDS is used,

and for purine nucleobase, the good yield is obtained when NP/SnCl₄ (1eq of SnCl₄) in BSA is used.

This reaction is stereoselective because we get β isomer alone as it is regioselective since we get only the N1 isomer for pyrimidines (uracil, thymine, and cytosine) and N9 for purine (adenine).

IV. CONCLUSION

This phosphate catalyst has shown catalytic efficiency by increasing results and reducing reaction time as it has also shown simplicity of handling compared to other catalysts.

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