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Heterogeneous Solid-Liquid Catalysis Of N-glycosylation By Natural Phosphate Doped With Potassium Iodide

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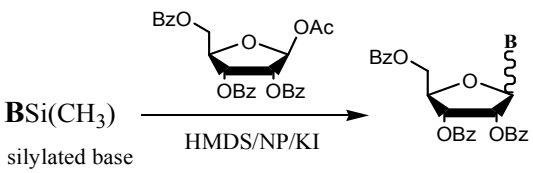
Abstract
Theone-step synthesis of several β-D-ribonucleosides was performed in good yields under reflux in HMDS.
Keywords: N-Glycosylation D-ribonucleosides,Natural phosphate doped with Potassium iodide KI (NP/KI), heterogeneous solid-liquid catalysis

Introduction

The heterogeneous solid-liquid catalysis is a relatively new field, most of the work has been to realize over the past 20 years. This technique is characterized by its simplicity and ease of implementation.Several syntheses were carried out using the solid-liquid catalysis. Inorganic supports are varied, among which may be mentioned by way of example, alumina, (Bergbereiter and al 1987) silica, (Nishiguchi and al 1989) the alkali metal fluorides and the most recent of these media is the natural phosphate NP ((a)Lazrek and al 2007 (b) Lazrek and al 2008(c) Baddi and al 2010(d) Lazrek and al 2011).This is an effective catalyst in organic chemistry, because it has many advantages such as:Non-toxic, recyclable and more environmentally friendly.Several studies have been reported in this direction, they have shown interest of NP in the condensation of Claisen-Schmidt, heterocyclization, Knoevenagel, alkylations of Fridel-Craftsreaction and Michael.“Condensation of Claisen-Schmidt”:some chalcones are used as anti-oxidant (Mukherjee and al 2001) anti-inflammatory(Hsieh and al 2000) anti-malarias (Ram and al 2000).These products are obtained by Claisen Schmidt reaction.The preparation of chalcones from acetophenone and derivatives of benzaldehyde with NP as a catalyst and the mixture (ethanol/water) as solvent at room temperature is with good yield “heterocyclization halogénocarboxyamides by NP/KF (or NP/$NaNO_3$)”: The doped NP /KFthe heterocyclization reaction in the presence of a phase transfer agent and the THF at reflux (Saber and al 1995).“Condensation of Knoevenagel “:The NP is an excellent catalyst in this reaction, it can condense((a) Sebti and al 2000 (b) Sebti and al 2001(c)Bennazha and al 2001)derivatives of aromatic aldehydes with active methylene in MeOH at room temperature (Saber and al 1995).“cycloaddition reaction***”:***In our laboratory, Lazrek (Lazrek and al 1999) showed that phosphate is a good catalyst for the 1,3-dipolar cycloaddition of N-9-propargyladénine with alkylazide. The products of these reactions are of great importance in chemistry antiviral therapy.“ N-Alkylation reaction”: The NP has a reactivity similar to those of $ZnCl_2$ or $ZnBr_2$ (Lazrek and al 1999) (Lazrek and al 1998).The NP-doped $ZnCl_2$ was used successfully as a Lewis acid to the N-alkylation to different nucleobases(G,T,C),The combination NP/KF was alsoused as a catalyst.It allowed the synthesis of several acyclonucleosides with satisfactory yields and high regeoselectivty(Lazrek and al 1999). Nucleosides have an important role in the antiviral and anticancer. Several studies have been developed to achieve this goal,but there are problems,such as:(i)The starting materials are not available, (ii)How complicated synthesis (several steps) (iii) Catalysts expensive and toxic.Our research aims at the synthesis of α, β-D-Ribonucleosides in one step and using NP doped with KI as catalyst (Scheme 1) .



Scheme

In order to assess the influence of natural phosphate (NP) doped with KI 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-α/β-D-ribonucleosides

Entry	Nucleobase	NP/KI	Yield* %	α/β
1	Uracil	325/0 mg	5	-
2	Uracil	0/129 mg(0.8 eq of KI)	28	37/63
3	Uracil	581 mg(1 eq of KI)	48	34/66
4	Uracil	473 mg(0.8 eq of KI)	55	13/87
5	Thymine	473 mg(0.8 eq of KI)	52	28/72
6	Cytosine	473 mg(0.8 eq of KI)	45	50/50
7	Adenine	473 mg(0.8 eq of KI)	51	50/50
8	N-acetyl-guanine	236mg(0.8 eq of KI)	54	50/50

Result and discussion

As shown in Table 1, when either NP and KI were used alone, the reaction of 1-O-acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranoside with bis-(trimethylsilyl)uracil gave the ribonucleoside in only 5 and 28 % yields respectively. As can be seen in the subsequent examples, the yield increased when NP doped with KI was used. For example, in entry 4 the desired ribonucleoside was obtained as a major isomer and in good yield by using NP/KI corresponding to 0.8 eq of KI.in acetonitrile at 1050 C overnight. This procedure appears to be regioselective and gives only the N-1 isomer. Other nucleobases (entries 6-8) were then also subjected to N-glycosylation and found to afford the corresponding nucleosides .this raction is stereoselective because the isomère N1 is obteined for pyrimidines (Uracil, Thymine,Cytosine) and N9 for purines(Adenine,R-Guanine)(Table1)

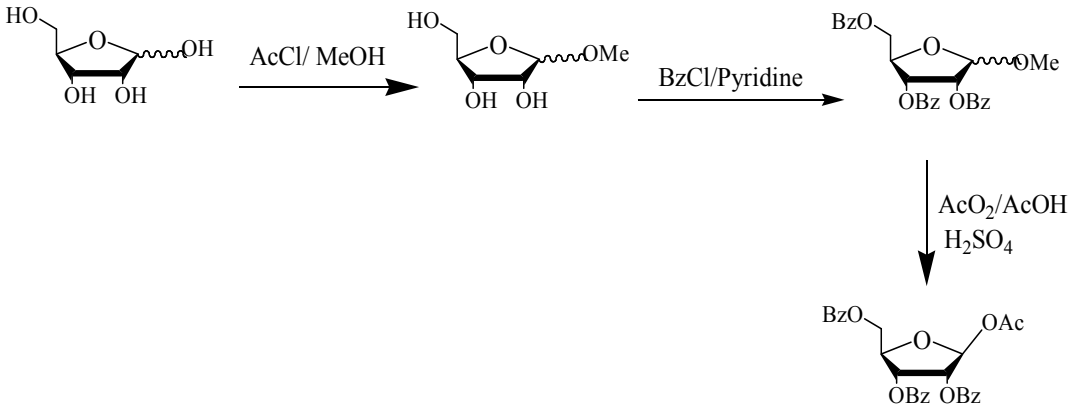
Conclusion

In conclusion, the mild conditions, low cost, and easy work-up of this new method offer some advantages over former procedures, and thus it should be of further interest in synthetic nucleoside chemistry. Other examples are under investigation and will be reported elsewhere.

Experimental Section

***Preparation of protected sugars (1-acetyl 2,3,5-tri-O-benzoyl-D-Ribofuranose)**

To achieve the pentofuranoses selectively acetylated in position C1, we first introduce a methoxy group in the anomeric C1 position that keeps the sugar furanose structure and protect other alcohol functions in position 2, 3, 5. The strategy for the pentofuranoses Peracylated requires three steps .



1g (D-ribose) are slurried with 24 ml of methanol containing 1% hydrochloric acid . The mixture is left about 4 h at room temperature and then treated immediately with 15 ml of anhydrous pyridine, the solvent is then evaporated to dryness and vacuum to remove traces of methanol. The resulting oil was diluted with 10 ml of anhydrous pyridine and treated with cold 2.8 ml of benzoyl chloride. The reaction is complete after one night, the resulting mixture was treated with ice and diluted with dichloromethane. The organic phase is then washed with water, respectively, a cold aqueous solution of sulfuric acid (3N) and then with a saturated aqueous solution of sodium hydrogenocarbonate NaHCO3.Oganique resultant phase is dried over sodium sulfate and the solvent was evaporated dry. 1-O-acetyl-2 ,3,5-tris-O-benzoyl-(D-ribose) is obtained by acetolisation of methyl 2,3,5tris-O-benzoyl-(D-ribose),the process is as follows:the oil obtained (4.7 g) was taken up in a mixture of

acetic anhydride (10 ml) and acetic acid (49.7 ml) is cooled to using ice then add H_2SO_4 (2.8 ml) dropwise with concentrated ice-cooling. After 5 hours of stirring at room temperature the mixture was left overnight in a refrigerator (4°C) then the reaction mixture was poured into ice and extracted with dichloromethane (CH_2Cl_2) and the organic phase is washed with water and then with aqueous solution of sodium hydrogen carbonate ($NaHCO_3$). The organic phase obtained was finally dried over sodium sulfate(Na_2SO_4) and evaporated under vacuum.Thedesired products are separated by chromatography on a column of silica gel eluted with a mixture of cyclohexane and ethyl acetate (91/9v/ v).

***Procedure for preparation of the catalyst (NP/KI , 3/1)**

The catalyst was prepared by making 400 mg of potassium iodide (KI) in 5 mL of water. The residu was stirred at room temperature for 5 minutes. After the slurry of activated natural phosphate (NP) (1,2g) was added , the slurry was stirred magnetically at room temperature for 10 minutes and the excess solvent was removed by evaporation under reduced pressure and at low temperature.When the slurry became dry and free falling it was ready for use .

***The typical experimental procedure is as follows:**

A suspension of uracil (0,892mmol) in HMDS (4 ml), ammonium sulfate (catalytic amount 3mg), and acetonitrile (2.5ml) was heated at reflux until a clear solution was obtained (30min). To this solution was added 1-acetyl 2,3,5-tri-O-benzoyl-D-Ribofuranose (453mg , 0.9eq) and NP/KI (422mg, 08eq of KI) and the mixture was heated (80°C) for one night. The resulting suspension was filtered and the precipitate was washed with dichloromethane. The filtrate was evaporated and the residue was purified by column chromatography to give the desired nucleoside with 55% yield.

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