Study on the glycosylation of cyclohexanol with different D-glucosamine-derived glycosyl donors and catalysts

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Introduction

Peracetylated cyclohexyl *N*-acetylglycosaminide **1** presents anti-inflammatory activity due to inhibition of toll-like receptor 4 (TLR4)[1]. It is prepared by the glycosylation of cyclohexanol with oxazoline **2** in the presence of copper (II) chloride as catalyst[1].

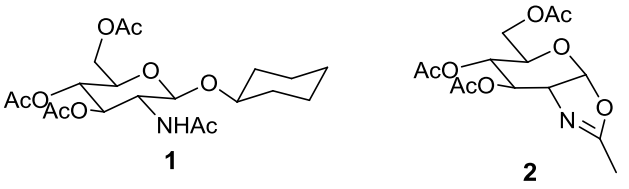

Figure 1. Structure of *N*-acetylglycosaminide **1** and oxazoline **2**.

Due to its interesting biological properties, the synthesis of **1** using other glycosyl donors and catalysts are of interest.

There are several glycosyl donors and catalysts described in the literature for the synthesis of *N*-acetyglucosamine glycosides[2,3]. In the present work we selected four glycosyl donors (**3-6**, **Figure 2**) and silver trifluormethanesulfonate, silver carbonate and mercuric bromide/mercuric oxide as catalysts to compare their efficiency in glycosylation of cyclohexanol.

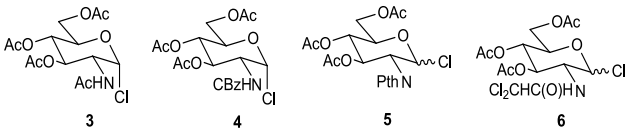

Figure 2. Structures of halides **3-6**.

The cyclohexyl glycosides from **4**-**6** can be converted into *N*-acetyl derivative **1** by known procedures[2,4].

Results and Discusions

The scheme for the glycosylation of cyclohexanol with glycosyl halides **3**-**6** using the three catalysts cited above is shown in **Figure 3** and the results are presented in **Table 1**.

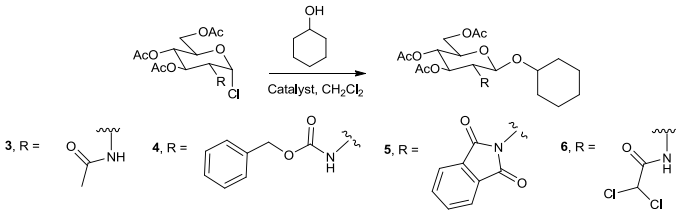

Figure 3. Synthetic scheme of glycosylation of cyclohexanol with **3**-**6**.

Table 1. Results of studied reactions.

Donor	CF_3SO_3Ag (A)*		Ag_2CO_3 (B)*		$HgBr_2/Hg_2O$ (C)*	
	Yield	Time	Yield	Time	Yield	Time
3	-	24h	-	24h	-	24h
4	-	24h	-	24h	-	24h
5	44%	5h	58%	50 min	39%	15h
6	-	24h	-	24h	-	24h

* Temperature: A and B: room temperature[2,3] ; C: 65°C[4]

The glycosyl donor **5** was the only halide derivative that allowed the glycosylation to occur. The Ag_2CO_3 catalyst was the most efficient.

The halides **3**, **4** and **6** did not act as glycosyl donors in any of the reaction conditions employed, up to 24 hours. In these cases, after work-up the products of hydrolysis **7**-**9** were obtained (**Figure 4**).

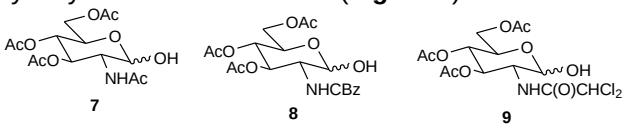

Figure 4 – Products of hydrolysis **7, 8** and **9.**

Conclusions

Compound **5** as glycosyl donor and silver carbonate as catalyst was the most efficient condition for the glycosylation of cyclohexanol and can be considered for the glycosylation of other alcohols.

Acknowlegdments

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