Study on the glycosylation of cyclohexanol with different \(\alpha\)-glucosamine-derived glycosyl donors and catalysts

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Introduction

Peracetylated cyclohexyl N-acetylg glucosaminide 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\(^1\).

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\text{Figure 1. Structure of N-acetylg glucosaminide 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-acetylg glucosamine glycosides\(^2,3\). In the present work we selected four glycosyl donors (3-6, Figure 2) and silver trifluoromethanesulfonate, silver carbonate and mercuric bromide/mercuric oxide as catalysts to compare their efficiency in glycosylation of cyclohexanol.

\[
\text{Figure 2. Structures of halides 3-6.}
\]

The cyclohexyl glycosides from 4-6 can be converted into N-acetyl derivative 1 by known procedures\(^2,4\).

Results and Discussions

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.

\[
\text{Table 1. Results of studied reactions.}
\]

\[
\begin{array}{|c|c|c|c|c|}
\hline
\text{Donor} & \text{CF,SO}_{2}\text{Ag (A)*} & \text{Ag}_{2}\text{CO}_{3} (B) & \text{HgBr}_2\text{HgO (C)*} \\
\hline
\text{Yield} & \text{Time} & \text{Yield} & \text{Time} & \text{Yield} & \text{Time} \\
\hline
3 & - & 24h & - & 24h & - & 24h \\
\hline
4 & - & 24h & - & 24h & - & 24h \\
\hline
5 & 44\% & 5h & 58\% & 50 min & 33\% & 15h \\
\hline
6 & - & 24h & - & 24h & - & 24h \\
\hline
\end{array}
\]

* Temperature: A and B: room temperature\(^2,3\); C: 65\(^\circ\)C\(^4\)

The glycosyl donor 5 was the only halide derivative that allowed the glycosylation to occur. The Ag\(_2\)CO\(_3\) 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).

\[
\text{Figure 4 – Products of hydrolysis 7, 8 and 9.}
\]

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.

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\(^1\)Neel, M.D., et al. PLOS One, 2013, 8.e65779.