Synthetic studies of multivalent-type inhibitors against human influenza virus (III): Verification of introduction of linker chain into sialyl α(2,6) lactose derivatives

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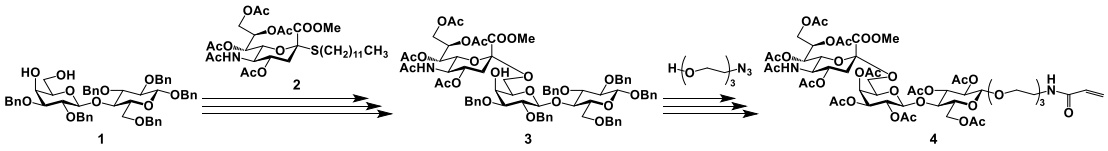
Keywords: Sialyllactose; Glycosides; Influenza; Inhibitors:

Human influenza virus causes infection by specifically recognizing and adhering sialyllacto-based sugar chains (Neu 5 Acα2-6 Galβ1-4 GlcNAc) on the cell membrane surface. Sialyl α (2, 6) lactose (Neu 5 Ac α 2-6 Gal β 1-4 Glc), which shows a similar structure to the sugar chain, is inexpensive and has been used for synthetic studies of influenza virus inhibitors [1)]. In order to expand the synthetic research widely, it is necessary to establish a large-scale preparation method for sialyl α (2, 6) lactose derivatives. In previous studies in the synthesis of lactose derivatives as intermediates, complicated column chromatography was needed to purify the 4', 6'-diol **1**. Therefore, in this study, we mainly focused on a work-up procedure of the 4', 6'-diol **1** from the reaction mixture. Since effective crystallization conditions were found, the detail for the crystallization will be presented. Glycosylation of the 4', 6'-diol **1** with a known sialyl donor **2** gave the corresponding sialyl α (2, 6) lactose derivative **3**. Then, linker synthesis was also performed, and compound 4 was obtained by glycosylation.



Scheme 1. Synthesis of sialyl α (2, 6) lactose derivatives

In the synthesis of the lactose derivative, the final target product, 4', 6'-diol **1** was successfully obtained by simple crystallization, and the total steps was 6 with 21% yield in 6 steps. The thioglycoside **2** was coupled with diol 1 to give **3** in 87% yield, which was converted into the imidate as a glycosyl donor. Finally, a linker alcohol was coupled with the imidate to afford the sialyl α (2, 6) lactose derivative **4** in good yield.

1） M. Nagao, *et. al*., *Biomacromolecules*, **2017**, *18*, 4385-4392.