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Novel Stereocontrolled Glycosidations of Olivoses Using Montmorillonite K-10 as an Environmentally Benign Catalyst

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Abstract: Novel stereocontrolled glycosidations of 3,4-di-*O*-protected olivoses and alcohols using a heterogeneous and environmentally benign solid acid, montmorillonite K-10, have been developed. The glycosidations of the 3-*O*-Ac-4-*O*-TBS-olivose (**4**) and various alcohols using montmorillonite K-10 in CH_2Cl_2 at 25 °C exclusively gave the corresponding α-olivosides in high yields. On the other hand, the corresponding β-olivosides were predominately obtained by the glycosidations of the 3-*O*-TBS-4-*O*-Ac-olivose (**5**) and various alcohols under similar conditions. © 1999 Elsevier Science Ltd. All rights reserved.

***Keywords*:** glycosidation; olivose; olivoside; montmorillonite K-10; environmentally benign synthesis.

Highly effective and environmentally friendly glycosidation methods have attracted considerable attention in current synthetic organic chemistry related to both biomolecules and functional materials.[1] In this context, the direct and stereoselective formation of a glycosidic bond from a 1-hydroxy sugar has undoubtedly high efficiency.[1,2] On the other hand, deoxyglycosides frequently appear in the sugar components of bioactive substances. Among them, olivoside, a typical 2,6-dideoxy glycoside, is one of the most common and important, and found in many biologically attractive natural products such as aureolic acids, angucyclines, avilamycins, concanamycins, venturicidins, *etc.*[3] However, the stereoselective glycosidation of a 2-deoxy sugar, especially β-selective glycosidation, is generally difficult due to the lack of stereodirecting anchimeric assistance from the C-2 position, and the stereoselective glycosidation of olivose (1-hydroxy form) has never been reported. Therefore, the development of stereocontrolled glycosidations of olivose in an environmentally acceptable manner is of particular interest. In this letter, we now report the novel stereocontrolled glycosidations of 3,4-di-*O*-protected olivose and alcohols using a heterogeneous and environmentally benign solid acid, montmorillonite K-10, for the selective syntheses of both the α- and β-olivosides (Figure 1).

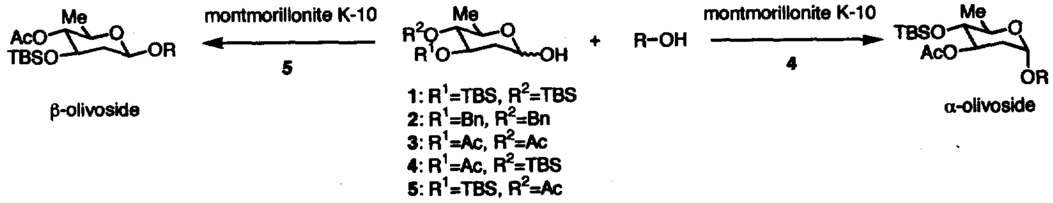

Figure 1

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During our initial attempts of searching for a new activator, we examined the glycosidations of the 3,4-di-*O*-*t*-butyldimethylsilyl (TBS)-olivose (**1**)[4] and cyclohexylmethanol (**6**) using several heterogeneous solid acids such as montmorillonite K-10,[5] Nafion-H®[6] and SO_4/ZrO_2[7], all of which could be recovered from the reaction mixture by only filtration and then reused.[8] It was found that only montmorillonite K-10 showed a sharp contrast to the other solid acids and worked efficiently. As shown by the entry 1 result in Table 1, the 3,4-di-*O*-TBS-olivose (**1**) was smoothly coupled with the alcohol **6** using montmorillonite K-10 in CH_2Cl_2 at 25 °C for 2 h to give the corresponding *O*-olivosides in 94% yield with α-stereoselectivity. This result clearly indicated that montmorillonite K-10 worked well as both the activating reagent for the 1-hydroxy group of olivose and the dehydrating agent of water generated during the reaction. Our attention next turned to the effect of the protecting group of olivose on the stereocontrol in this novel glycosidation. Therefore, we tested several 3,4-di-*O*-protected olivoses **2**~**5**[4] and **6** under similar conditions. From the results summarized in Table 1, the 3-*O*-acetyl (Ac)-4-*O*-TBS-olivose (**4**) was found to be the best glycosyl donor to selectively obtain the α-olivoside. In contrast, it was found that the stereoselectivity of the glycosidation was dramatically changed by the C-3 and C-4 protecting groups of olivose, and the β-olivoside was predominately produced when the 3-*O*-TBS-4-*O*-Ac-olivose (**5**) was used as the glycosyl donor probably due to the participating effect of the C-4 carbonyl group.[9]

To enhance the synthetic utility of this novel and simple reaction, the glycosidations using other primary and secondary alcohols **7**~**11** were next examined. Based on the results shown in Table 2, all glycosidations of **4** and **7**~**11** using 150 wt% of montmorillonite K-10 in CH_2Cl_2 at 25 °C, as well as that of **6**, effectively proceeded to give the corresponding α-olivosides in high to excellent yields with high stereoselectivities. On the other hand, the stereoselective syntheses of the corresponding β-olivosides are outlined in Table 3. Although the stereoselectivity was relatively lower compared to that of the glycosidation of **4**, the corresponding β-glycosides were obtained with moderate to good stereoselectivities by the glycosidations of **5** and **7**~**11** using 150 wt% of montmorillonite K-10 in CH_2Cl_2 at 25 °C. Furthermore, it was found that no epimerization at the anomeric center occurred during the reaction.

General experimental protocols for the preparations of the α- and β-olivosides:[10] α-Olivosides: To a stirred solution of the 3-*O*-Ac-4-*O*-TBS-olivose (**4**) (0.5 mmol) and an alcohol (1.0 mmol) in dry CH_2Cl_2 (5.0 ml) was added montmorillonite K-10 (150 wt% to the glycosyl donor **4**). After stirring at 25 °C for the time indicated in Table 2, the mixture was filtered and the filtrate was concentrated *in vacuo*. Purification of the residue by flash column chromatography gave the corresponding olivosides which predominately contained the α-anomer. β-Olivosides: The similar protocol using the 3-*O*-TBS-4-*O*-Ac-olivose (**5**) instead of **4** gave the olivosides which included its β-anomer as the major product.

In conclusion, we have presented novel and stereocontrolled glycosidations of olivoses (1-hydroxy form) and alcohols using an environmentally acceptable solid acid, montmorillonite K-10. Moreover, the results including the simple protocol, high yield and stereoselectivity should find wide application in the synthesis of biologically important natural products which possess a olivose as a glycosidic component. Further studies in this area are currently underway.

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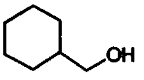
Table 1. Glycosidations of 1~5 and 6 by montmorillonite K-10.[a]

$$\mathbf{1}\sim\mathbf{5} + \mathbf{6} \xrightarrow[\text{dry } CH_2Cl_2,\ 25\ °C,\ 2\ h]{\text{montmorillonite K-10 (100 wt\%)}} \text{Olivosides}$$

entry	glycosyl donor	yield (%)[b]	α/β ratio[c]
1	**1**	94	84/16
2	**2**	89	73/17
3	**3**	21	67/33
4	**4**	82	92/ 8
5	**5**	77	18/82

[a] All reactions were carried out by use of 2.0 equiv. of **6** to the glycosyl donor. [b] Isolated yields after purification by column chromatography. [c] α/β Ratios were determined by ^{1}H-NMR (270 MHz) spectroscopy and / or isolation of pure isomers.



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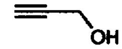

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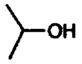

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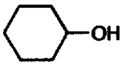

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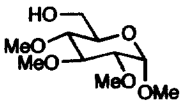

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Table 2. Glycosidations of 4 and 6~11 by montmorillonite K-10.[a]

$$\mathbf{4} + \mathbf{6}\sim\mathbf{11} \xrightarrow[\text{dry } CH_2Cl_2,\ 25\ °C]{\text{montmorillonite K-10 (150 wt\%)}} \text{Olivosides}$$

entry	alcohol	time (h)	yield (%)[b]	α/β ratio[c]
1	**6**	3	96	92/ 8
2	**7**	1	91	91/ 9
3	**8**	1	90	90/10
4	**9**	2	71	90/10
5	**10**	2	83	92/ 8
6	**11**	2	77	89/19

[a] All reactions were carried out by use of 2.0 equiv. of alcohol to **4**. [b] Isolated yields after purification by column chromatography. [c] α/β Ratios were determined by ^{1}H-NMR (270 MHz) spectroscopy and / or isolation of pure isomers.

Table 3. Glycosidations of 5 and 6~11 by montmorillonite K-10.[a]

$$\mathbf{5} + \mathbf{6}\sim\mathbf{11} \xrightarrow[\text{dry } CH_2Cl_2,\ 25\ °C]{\text{montmorillonite K-10 (150 wt\%)}} \text{Olivosides}$$

entry	alcohol	time (h)	yield (%)[b]	α/β ratio[c]
1	**6**	2	87	21/79
2	**7**	1	72	20/80
3	**8**	1	80	27/73
4	**9**	2	69	26/74
5	**10**	6	76	33/67
6	**11**	6	67	31/69

[a] All reactions were carried out by use of 2.0 equiv. of alcohol to **5**. [b] Isolated yields after purification by column chromatography. [c] α/β Ratios were determined by ^{1}H-NMR (270 MHz) spectroscopy and / or isolation of pure isomers.

References and Notes

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5. Montmorillonite K-10 was purchased from Aldrich Chemical Company, Inc. and dried at 25 °C/1 mmHg for 2 h before using.
6. Nafion-H$^{\circledR}$ was purchased from Wako Pure Chemical Industries, Ltd. as Nafion$^{\circledR}$ NR-50 and dried at 25 °C/1 mmHg for 2 h before using.
7. SO_4/ZrO_2 was purchased from Wako Pure Chemical Industries, Ltd and dried at 200 °C/1 mmHg for 12 h before using, see: ref. 8f.
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