Environmentally compatible *C*-glycosidation of glycals using montmorillonite K-10

Kazunobu Toshima,* Naoki Miyamoto, Goh Matsuo, Masaya Nakata and Shuichi Matsumura

Department of Applied Chemistry, Faculty of Science and Technology, Keio University, 3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223, Japan

The *C*-glycosidations of glycal acetates 1–4 with allyltrimethylsilane 5, vinyloxytrimethylsilane 6 or isopropenyl acetate 7 using montmorillonite K-10 as an environmentally acceptable and inexpensive industrial catalyst under mild conditions proceed effectively to give the corresponding 2,3-unsaturated *C*-glycosides in high yields.

A simple, practical and environmentally compatible chemical glycosidation protocol, which is important synthetically in the preparation of both natural and unnatural glycosides, is urgently needed both in the laboratory and in industry.[1] Several types of *C*-glycosides are versatile synthetic intermediates for optically active compounds,[2] and carbon-linked glycosides, stable analogues of naturally occurring *O*- and *N*-glycosides, have become the subject of considerable interest in bioorganic and medicinal chemistry.[3] Although several *C*-glycosidations using glycals as the glycosyl donors have been reported,[4] a Lewis acid such as boron trifluoride etherate or tin(IV) chloride, which was not resuable and made the reaction solvent dirty, was generally required as an activator. Here we report that an easily available, inexpensive and reusable acidic clay,[5] montmorillonite K-10,† serves as an efficient catalyst for the novel *C*-glycosidations of glycals. Thus, the *C*-glycosidations of glycal acetates **1–4** with allyltrimethylsilane **5**, vinyloxytrimethylsilane **6** or isopropenyl acetate **7** using montmorillonite K-10 under mild conditions proceeded smoothly to give the corresponding 2,3-unsaturated *C*-glycosides in high yields with good α-stereoselectivity (Fig. 1). To the best of our knowledge, this is the first example of *C*-glycosidation methods employing a solid acid.

We first examined the *C*-glycosidations of a representative glycal acetate, 3,4-di-*O*-acetyl-L-rhamnal **1**, with allyltrimethylsilane **5** (1.5 equiv.) using various amounts of montmorillonite K-10 in CH_2Cl_2 at 25 °C for 1 h. The results summarized in Table 1 show that the use of 10% (*m*/*m* for **1**) montmorillonite K-10 was most effective for performing the glycosidation. The 2,3-unsaturated allyl *C*-glycoside **8**[6] was obtained *via* Ferrier rearrangement[7] in 97% yield (entry 4). It was found that CH_2Cl_2 was shown to be superior to other solvents, $CHCl_3$, PhH, PhMe, Et_2O, THF and MeCN.[8] Our attention then turned to the effect of the allyl species in this reaction. The glycosidation of **1** with another typical allyl species, allyltributyltin **9** (1.5 equiv.), was investigated. Although the reaction using 10% montmorillonite K-10 proceeded under similar conditions, as above, the glycosidation was clearly less effective than that of allyltrimethylsilane **5**, and the 2,3-unsaturated allyl *C*-glycoside **8** was obtained in 42% yield after 1 h at 25 °C. With the optimum reaction conditions determined, we next examined the glycosidations of other typical glycal acetates, tri-*O*-acetyl-D-glucal **2**, tri-*O*-acetyl-D-galactal **3** and di-*O*-acetyle-D-fucal **4** with allyltrimethylsilane **5** mediated by a catalytic amount of montmorillonite K-10 noting both the yields and the stereoselectivity. The results are shown in Table 2 and demonstrate that these glycals were also glycosidated with **5** under similar conditions to afford the

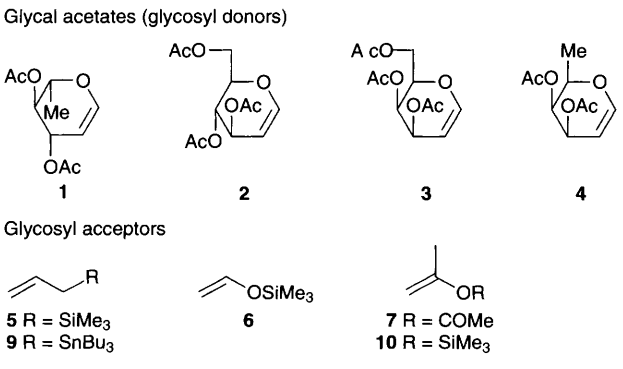
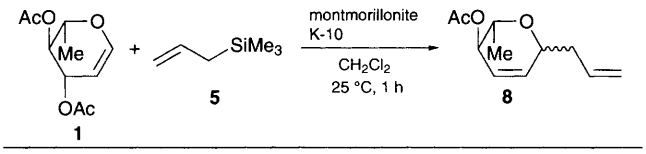


Fig. 1

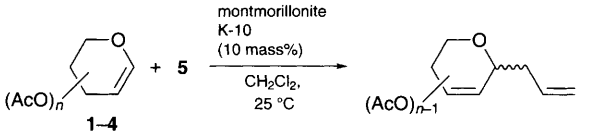
Table 1 *C*-Glycosidations of **1** and **5** by montmorillonite K-10[a]



Entry	Mass% of catalyst for **1**	Yield (%)[b]
1	100	79
2	50	82
3	30	89
4	10	97
5	5	93
6	3	82
7	1	49

[a] All reactions were carried out by use of 1.5 equiv. of **5** to **1**. [b] Isolated yields after purification by column chromatography.

Table 2 *C*-Glycosidations of glycals **1–4** and **5** by montmorillonite K-10[a]



Entry	Glycal	*t*/h	Yield (%)[b]	α:β[c]
1	**1**	1	97	4.2/1
2	**2**	1	95	3.6/1
3	**3**	3	84	18/1
4	**4**	3	80	67/1

[a] All reactions were carried out by use of 1.5 equiv. of **5** to glycals. [b] Isolated yields after purification by column chromatography. [c] α:β Ratios were determined by ^{1}H NMR spectroscopy (270 MHz) and/or isolation of pure isomers.

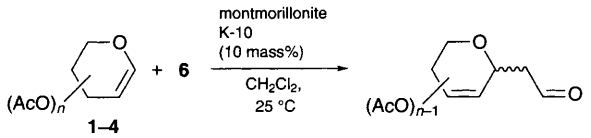
corresponding 2,3-unsaturated allyl *C*-glycosides[6c] in high yields with good α-stereoselectivity.

To enhance the synthetic utility of this reaction using montmorillonite K-10, the *C*-glycosidations of glycal acetates **1–4** with other nucleophilic species, vinyloxytrimethylsilane **6** (1.5 equiv.) and isopropenyl acetate **7** (2.0 equiv.), were examined. It was found that these glycosidations also proceeded effectively under similar conditions to give the corresponding 2,3-unsaturated *C*-glycosides[9] with satisfactory chemical yields and moderate to high α-stereoselectivity as shown in Tables 3 and 4. Interestingly, the glycosidations of the glycals **1–4** with 2-silyloxypropene **10** under similar conditions were found to be much less effective than those with isopropenyl acetate **7** with respect to the chemical yields.

Since the configuration of the anomeric position was not isomerized by exposure of the isolated single α-anomer of the *C*-glycoside to all reaction conditions, the predominate α-stereoselectivity‡ observed in these glycosidations must arise from a kinetic anomeric effect.[10] Furthermore, it is noted that the work-up involves only filtration before evaporation of the solvent, and both the catalyst and the solvent could be easily recovered after the reaction was complete.

A typical experimental procedure for the reaction of **1** and **5** is as follows: to a mixture of **1** (37.8 mg, 0.176 mmol) and **5** (0.0420 ml, 0.264 mmol) in CH_2Cl_2 (0.90 ml) was added montmorillonite K-10 (3.8 mg) with ice-cooling. After stirring for 1 h at 25 °C, the mixture was filtered and the filtrate concentrated *in vacuo*. Purification of the residue by flash column chromatography with 4 : 1 hexane–ethyl acetate gave **8** (33.4 mg, 97%, α : β = 4.2 : 1) as a colourless oil.

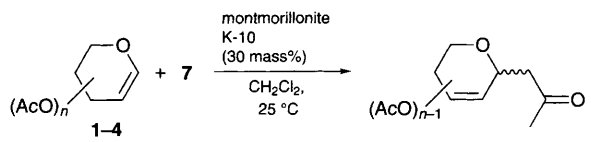
Table 3 *C*-Glycosidations of glycals **1–4** and **6** by montmorillonite K-10[a]



Entry	Glycal	*t*/h	Yield (%)[b]	α : β[c]
1	**1**	0.5	78	1/1
2	**2**	1	72	1.6/1
3	**3**	1	53	6.5/1
4	**4**	0.5	66	19/1

[a] All reactions were carried out by use of 1.5 equiv. of **6** to glycals. [b] Isolated yields after purification by column chromatography. [c] α : β Ratios were determined by ^{1}H NMR spectroscopy (270 MHz) and/or isolation of pure isomers.

Table 4 *C*-Glycosidations of glycals **1–4** and **7** by montmorillonite K-10[a]



Entry	Glycal	*t*/h	Yield (%)[b]	α : β[c]
1	**1**	0.5	96	5.5/1
2	**2**	0.5	97	4.5/1
3	**3**	0.5	85	>99/1
4	**4**	0.5	85	>99/1

[a] All reactions were carried out by use of 2.0 equiv. of **7** to glycals. [b] Isolated yields after purification by column chromatography. [c] α : β Ratios were determined by ^{1}H NMR spectroscopy (270 MHz) and/or isolation of pure isomers.

Footnotes

† Montmorillonite K-10 was purchased from Aldrich Chemical Company, Inc.

‡ The configuration of the anomeric centre was determined by ^{1}H NOE experiments; see ref. 6 and refs. cited therein.

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