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Environmentally Benign Aryl *C*-Glycosidations of Unprotected Sugars Using Montmorillonite K-10 as a Solid Acid

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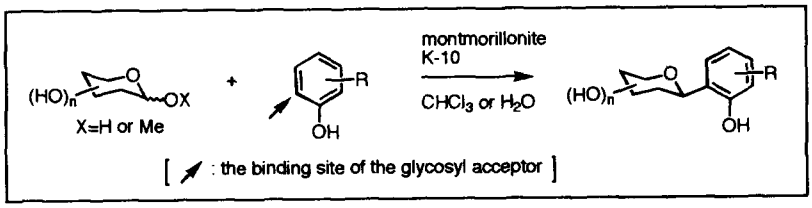
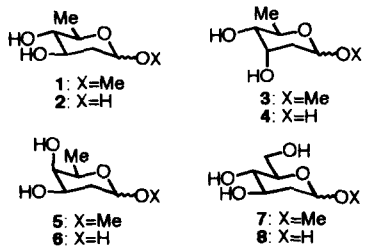
Abstract: *Highly practical aryl C-glycosidations of unprotected 1-OMe and 1-OH sugars with phenol and naphthol derivatives were effectively realized using montmorillonite K-10 as an environmentally compatible solid acid in $CHCl_3$ or H_2O.* © 1997 Elsevier Science Ltd.

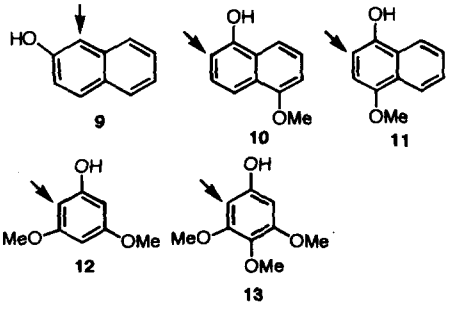
An efficient aryl *C*-glycosidation is of considerable importance in synthetic organic chemistry due to the synthesis of biologically and architecturally attractive aryl *C*-glycoside antibiotics such as angucyclins and pluramycins.[1,2] Although several effective methods in this area have been developed so far,[3] a practical and environmentally benign protocol is now urgently needed both in the laboratory and in industry. On the other hand, montmorillonite K-10 is well known to be a readily available, easy to use, inexpensive, non-corrosive, and reusable acidic clay.[4,5] In this letter, we report that the solid acid, montmorillonite K-10, serves as a new and efficient activator for the aryl *C*-glycosidations of unprotected sugars with phenol and naphthol derivatives. To the best of our knowledge, this is the first protocol for aryl *C*-glycosidation employing such an environmentally friendly catalyst.



Glycosyl donors



Glycosyl acceptors



In our first experiments, we examined the aryl *C*-glycosidations of unprotected methyl olivoside (**1**) and olivose (**2**) with 2-naphthol (**9**) to assay the ability of montmorillonite K-10 for the titled glycosidation. Olivose is a most representative sugar which exists as a glycosidic component in many aryl *C*-glycoside antibiotics.[1] The results summarized in Table 1 as entries 1 and 6 showed that these glycosidations proceeded smoothly in dry $CHCl_3$ at 50 °C for 24 h to afford the unprotected *o*-hydroxyaryl β-*C*-glycoside **14** with high stereoselectivity in high yields. Although an excess amount of montmorillonite K-10 was needed to obtain the aryl *C*-glycoside in high yield, it was confirmed that the work-up involved only filtration before evaporation of the solvent, and both the catalyst and the solvent could be easily recovered after the reaction was complete. These results clearly indicated that the montmorillonite K-10 was very useful for environmentally acceptable and practical aryl *C*-glycosidations using unprotected sugars.[6] Our next attempts were the aryl *C*-glycosidations of **1** and **2** with other phenol and naphthol derivatives **10**~**13**. It was found that these glycosidations also proceeded effectively under similar conditions to give the corresponding unprotected aryl β-*C*-glycosides **15**~**18** with high stereoselectivity in high yields.

To enhance the synthetic utility of this reaction using montmorillonite K-10, we next examined the aryl *C*-glycosidations of other unprotected 1-OMe sugars, **3**, **5** and **7**, which mainly occurred in aryl *C*-glycoside antibiotics, with 2-naphthol (**9**). The results shown in Table 2 clearly demonstrated that all unprotected 1-OMe sugars were effectively coupled with 2-naphthol to afford the corresponding β-*C*-glycosides **19**~**21** in high to excellent yields. These results indicated that the high yield and stereoselectivity were highly independent of the stereochemistry of the hydroxy groups in the sugar.

Table 1. Aryl *C*-Glycosidations of **1** and **2** with **9**~**13** by montmorillonite K-10.

1 or **2** + **9**~**13** (2.0 equiv.) —montmorillonite K-10, dry $CHCl_3$, 50 °C, 24 h→ unprotected *o*-hydroxyaryl *C*-glycosides **14**~**18**

entry	glycosyl donor	glycosyl acceptor	weight % of catalyst	product	yield (%)	α / β
1	**1**	**9**	500	**14**	98	1 / >99
2	**1**	**10**	500	**15**	66	1 / >99
3	**1**	**11**	500	**16**	71	1 / >99
4	**1**	**12**	300	**17**	80	1 / >99
5	**1**	**13**	400	**18**	85	1 / >99
6	**2**	**9**	500	**14**	85	1 / >99
7	**2**	**10**	500	**15**	65	1 / >99
8	**2**	**11**	500	**16**	70	1 / >99
9	**2**	**12**	500	**17**	73	1 / >99
10	**2**	**13**	400	**18**	82	1 / >99

Table 2. Aryl *C*-Glycosidations of **1**, **3**, **5** and **7** with **9** by montmorillonite K-10.

1,**3**, **5** or **7** + **9** (2.0 equiv.) —montmorillonite K-10, dry $CHCl_3$, 50 °C, 24 h→ **14**, **19**, **20** or **21**

entry	glycosyl donor	weight % of catalyst	product	yield (%)	α / β
1	**1**	500	**14**	98	1 / >99
2	**3**	300	**19**	91	1 / >99
3	**5**	300	**20**	92	1 / >99
4	**7**	500	**21**	68	1 / >99

Table 3. Aryl *C*-Glycosidations of **2**, **4**, **6** and **8** with **12** by montmorillonite K-10.

2, **4**, **6** or **8** + **12** (2.0 equiv.) —montmorillonite K-10→ **17**, **22**, **23** or **24**

entry	glycosyl donor	solvent	weight % of catalyst	T / °C	t / h	product	yield (%)	α / β
1	**2**	dry $CHCl_3$	500	50	24	**17**	73	1 / >99
2	**2**	$CHCl_3$	500	50	24	**17**	72	1 / >99
3	**2**	H_2O	500	70	48	**17**	70	1 / >99
4	**4**	dry $CHCl_3$	300	50	24	**22**	78	1 / >99
5	**4**	$CHCl_3$	300	50	24	**22**	77	1 / >99
6	**4**	H_2O	300	70	48	**22**	72	1 / >99
7	**6**	dry $CHCl_3$	300	50	24	**23**	79	1 / >99
8	**6**	$CHCl_3$	300	50	24	**23**	79	1 / >99
9	**6**	H_2O	400	60	48	**23**	75	1 / >99
10	**8**	H_2O	500	80	24	**24**	61	1 / >99

Finally, we examined the aryl *C*-glycosidations of unprotected 1-OH sugars, **2**, **4**, **6** and **8** with 3,5-dimethoxyphenol (**12**) under several conditions. The results are summarized in Table 3. The aryl *C*-glycosidations of **2**, **4** and **6** under similar conditions in dry $CHCl_3$ proceeded smoothly to give the corresponding aryl β-*C*-glycosides in high yields. Furthermore, remarkably, it was found that the aryl *C*-

glycosidations of **2**, **4** and **6** with **12**, all of which exhibited considerable solubility both in $CHCl_3$ and in H_2O, were effectively realized both in $CHCl_3$, which was not dried by a drying reagent,[7] and in H_2O to furnish the corresponding unprotected aryl β-*C*-glycosides in high yields. In addition, **8**, which showed high solubility in H_2O, was also coupled with **12** by montmorillonite K-10 in H_2O. Notably, both the yield and stereoselectivity of the glycosidation in $CHCl_3$ and H_2O were very similar to those of the glycosidation using dry $CHCl_3$ as the solvent. These results interestingly indicated that anhydrous conditions were not necessary for the aryl *C*-glycosidations of unprotected 1-OH sugars using montmorillonite K-10.

A typical experimental procedure is described for the reaction of **2** and **12** in $CHCl_3$ and H_2O.[8,9,10] To a mixture of **2** (33.3 mg, 0.225 mmol) and **12** (69.3 mg, 0.450 mmol) in $CHCl_3$ (2.25 ml) was added montmorillonite K-10 (167 mg). After stirring for 24 h at 50 °C, the mixture was filtered and the filtrate was concentrated *in vacuo*. Purification of the residue by flash column chromatography with 2:1 hexane-acetone gave **17** (46.0 mg, 72%, α:β = 1:>99) as a colorless oil. In the case of H_2O as the solvent, H_2O (0.86 ml) was used, and **2** (38.1 mg, 0.257 mmol) and **12** (79.3 mg, 0.514 mmol) gave **17** (51.2 mg, 70%, α:β = 1:>99) after 48 h at 70 °C.

In summary, the use of montmorillonite K-10 provides a significant new and effective method for the environmentally compatible and practical aryl *C*-glycosidations of unprotected sugars and should find wide application in the synthesis of aryl *C*-glycosides.

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7. Dry $CHCl_3$ was prepared by drying with P_2O_5 and distillation.
8. Isolated yields after purification by column chromatography.
9. α:β Ratios were determined by ^1H NMR spectroscopy (270 MHz).
10. All aryl *C*-glycosides were purified by silica-gel column chromatography and were fully characterized by spectroscopic means.

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