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Highly efficient heterogeneous acetalization of carbonyl compounds catalyzed by a titanium cation-exchanged montmorillonite

Tomonori Kawabata, Tomoo Mizugaki, Kohki Ebitani and Kiyotomi Kaneda*

Department of Chemical Science and Engineering, Graduate School of Engineering Science, Osaka University,
1-3 Machikaneyama, Toyonaka, Osaka 560-8531, Japan

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Abstract—The titanium cation-exchanged montmorillonite efficiently catalyzed the selective acetalization of various carbonyl compounds as a recyclable solid acid. This heterogeneous catalyst has an advantage of a strikingly simple workup procedure over conventional homogeneous acids. © 2001 Elsevier Science Ltd. All rights reserved.

Acetalization is commonly utilized as a protecting method for carbonyl functions because dimethyl acetals and 1,3-dioxolanes are stable under neutral and basic conditions.[1] It has been usually performed in the presence of *p*-toluenesulfonic acid (PTSA), BF_3–etherate, $FeCl_3$, or trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf).[2] These homogeneous acetalizations often suffer from drawbacks such as troublesome isolation of products and the production of large volumes of salt wastes during neutralization of the acids. From the standpoint of environmental demand for chemical processes,[3] much attention has been paid to development of solid catalysts for the acetal formations.[4,5] These heterogeneous systems are, however, not applicable to a wide range of carbonyl compounds. Recently, we have reported a simple and clean synthesis of a dialkyl

Table 1. Acetalization of benzophenone with diols using various solid catalysts[a]

Entry	Catalyst	Diol	Conv. of benzophenone (%)[b]	Amount of adsorbed NH_3 (mmol/g)[c]
1	Ti^{4+}-mont	*meso*-2,3-Butanediol	89	1.89
2	Ti^{4+}-mont	Propane-1,2-diol	53	1.89
3	Ti^{4+}-mont	Ethane-1,2-diol	14	1.89
4	Ti^{4+}-mont	Catechol	11	1.89
5	Fe^{3+}-mont	*meso*-2,3-Butanediol	69	0.95
6	Al^{3+}-mont	*meso*-2,3-Butanediol	25	0.75
7	Na^{+}-mont	*meso*-2,3-Butanediol	9	0.17
8	Mont K-10	*meso*-2,3-Butanediol	0	n.m.[d]
9	SO_4^{2-}/ZrO_2	*meso*-2,3-Butanediol	11	0.44
10	H^{+}-beta	*meso*-2,3-Butanediol	8	n.m.[d]
11	H^{+}-USY[e]	*meso*-2,3-Butanediol	0	0.36
12	H^{+}-mordenite[e]	*meso*-2,3-Butanediol	0	0.24

[a] All reactions were carried out under Dean–Stark conditions for 2 h: catalyst (0.15 g), benzophenone (3 mmol), diol (5 mmol), toluene (20 mL).

[b] Conversion of benzophenone was determined by GC using an internal standard method. In all cases, the corresponding acetals were exclusively obtained.

[c] Acid amount was volumetrically measured. The value corresponded to the number of strongly adsorbed NH_3. See Ref. 6.

[d] Not measured.

[e] Si/Al = 10.

Keywords: chemoselective acetalization; carbonyl compounds; montmorillonite catalyst.

* Corresponding author. Tel./fax: +81-6-6850-6260; e-mail: kaneda@cheng.es.osaka-u.ac.jp

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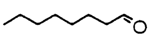
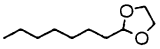
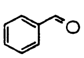
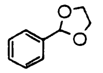
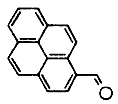
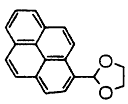
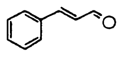
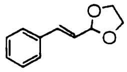
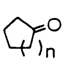
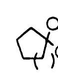
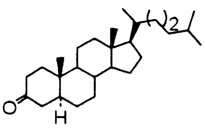
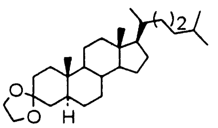
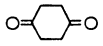
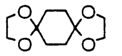
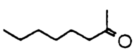
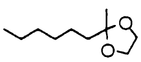
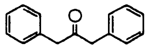
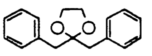
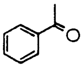
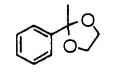
fluorene derivative from the aromatic alkylation of phenoxyethanol with fluoren-9-one using a titanium cation-exchanged montmorillonite (Ti^{4+}-mont) as a strong solid acid catalyst.[6] In the course of our studies on its catalysis, we found that this Ti^{4+}-mont catalyst was also effective for the selective acetalization of a variety of carbonyl compounds to the corresponding 1,3-dioxolanes. This montmorillonite catalyst system does not require tedious neutralization during workup procedures.

The Ti^{4+}-mont catalyst was prepared as follows: 3.0 g of Na^{+}-montmorillonite (Kunipia F, Kunimine Industry Co. Ltd.) was stirred in 100 mL of 1.8 M aqueous $TiCl_4$ solution at 50°C for 24 h. The obtained slurry was filtered and washed with distilled water, then dried at 110°C to afford 2.5 g of whitish gray powder (Ti content: 3.25 wt%). Analyses using XRD, XPS and Ti K-edge XAFS showed that the Ti^{4+}-mont had a chain-like structure of titanium oxides along anionic sheets of the montmorillonite.[6]

Acetalizations of benzophenone with diols using various types of heterogeneous catalysts were summarized in Table 1.[7] Among diols used, *meso*-2,3-butanediol was the most suitable reagent for the acetalization of benzophenone (entries 1–4).[†] It should be noted that the metal cation-exchanged montmorillonites (M^{n+}-monts) exhibited higher catalytic activity than conventional solid acids such as sulfate ion-treated zirconium oxide (SO_4^{2-}/ZrO_2), H^{+}-beta, H^{+}-USY and H^{+}-mordenite. In the case of the M^{n+}-monts (entries 1 and 5–7), the catalytic activities were increased with increasing their acid amounts. It can be said that the preeminent

Table 2. Acetalization of various carbonyl compounds catalyzed by Ti^{4+}-montmorillonite[a]

Entry	Substrate	Product[b]	Time (h)	yield[c] (%)
1			1	>99 (93)
2			1	>99
3[d]			1	>99
4[e]			1	>99
5[f]			1	>99 (95)
6			1	97
7 n = 1			1	>99
8 n = 2			1	>99
9 n = 4			4	95
10[f]			1	>99 (96)
11			1	98 (94)
12			1	>99
13			3	>99 (94)
14			1	93 (90)

[a] All reactions were carried out under Dean-Stark conditions: catalyst (0.15 g), substrate (3 mmol), ethane-1,2-diol (5 mmol), toluene (20 mL).

[b] All products were characterized by ^{1}H NMR and Mass spectra.

[c] Yields of products were determined by GC or LC using an internal standard method. Values in parentheses are isolated yields.

[d] Reuse-1.

[e] Reuse-2.

[f] Substrate (1 mmol).

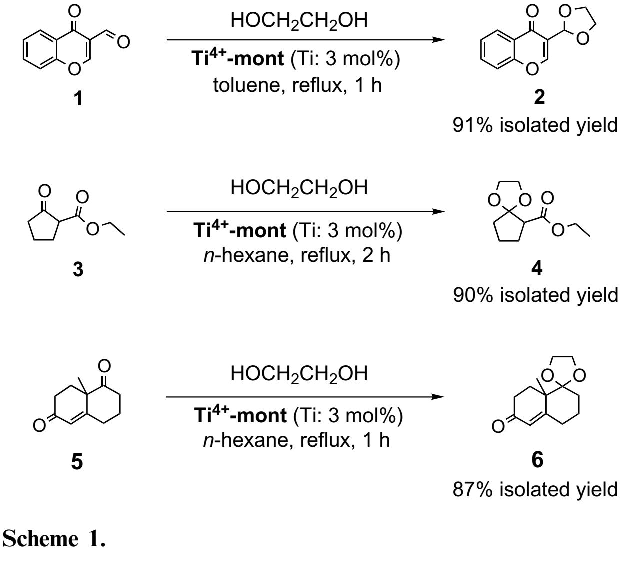
[†] Concerning a leaching of Ti^{4+} into the reaction mixture, we carried out the following experiment. To a reaction vessel with a Dean–Stark trap and a reflux condenser were successively added the Ti^{4+}-mont (0.15 g), toluene (30 mL), benzophenone (5 mmol) and *meso*-2,3-butanediol (15 mmol). After the resulting mixture was stirred under reflux for 2 h, the Ti^{4+}-mont was removed by filtration (acetal yield: 54%). No acetalization occurred while the colorless filtrate was further refluxed for 4 h. This result clearly shows that active titanium species did not leach from the Ti^{4+}-mont during the acetalization.

catalysis of the Ti^{4+}-mont arises from the strong acid sites associated with TiO_2 domains within an interlayer space of the montmorillonite.[8]

Table 2 shows the acetalization of various carbonyl compounds using the Ti^{4+}-mont catalyst. Formyl functions were converted into 1,3-dioxolanes in excellent yields (entries 1–6). Moreover, this Ti^{4+}-mont could smoothly transform various kinds of cyclic, aliphatic and aromatic ketones into the cyclic acetals (entries 7–14).[‡] Remarkably, a bulky ketone of 1,3-diphenyl-2-propanone gave a quantitative yield of the corresponding acetal (entry 13), whereas some zeolite catalysts do not efficiently promote the acetalization of this ketone because small pores obstruct an access of the bulky compound to their acid sites.[5d,e] The above prominent catalysis of the Ti^{4+}-mont can be ascribed to its strong acidity and an expansion of the interlayer space under reaction conditions.[‡]

The spent Ti^{4+}-mont catalyst was readily separated from the reaction mixture by a simple filtration. The isolated Ti^{4+}-mont could be reused without an appreciable loss of its high catalytic activity and selectivity; the yield of 2-phenyl-1,3-dioxolane in the acetalization of benzaldehyde could be kept over 99% during recycling experiments (entries 3 and 4 in Table 2).[§] Additionally, hydrolysis of acetals to parent carbonyl compounds was easily attained by the Ti^{4+}-mont in the presence of water.[9]

Chemoselective acetalizations are exemplified in Scheme 1.[¶] In the presence of the Ti^{4+}-mont, the acetalization of 4-oxo-4*H*-1-benzopyran-3-carboxaldehyde **1** occurred exclusively at a formyl group to give 2-(4-oxo-4*H*-1-benzopyran-3-yl)-1,3-dioxolane **2**, and also ethyl 2-oxocyclopentanecarboxylate **3** afforded an acetal **4** leaving an ester function intact in a high yield. An unconjugated keto function of the Wieland–Miescher ketone **5** was selectively protected to 3′,4′,8′,8′a-tetrahydro-8′a-methylspiro[1,3-dioxolane-2,1′(2′*H*)-naphthalen]-6′(7′*H*)-one **6**.[10]



Scheme 1.

In conclusion, the acetalization of various kinds of carbonyl compounds sufficiently occurs in the presence of the Ti^{4+}-exchanged montmorillonite as a strong solid acid catalyst. This heterogeneous montmorillonite catalyst system has the following advantages: (1) high catalytic activity and chemoselectivity, (2) wide applicability even to bulky substrates, (3) simple workup procedures and (4) non-polluting and recyclable catalyst.

Acknowledgements

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2. Typical examples of homogeneous 1,3-dioxolane formation, see: PTSA: (a) Ciceri, P.; Demnitz, F. W. J. *Tetrahedron Lett*. **1997**, *38*, 389; (b) Crimmins, M. T.; DeLoach, J. A. *J. Am. Chem. Soc*. **1986**, *108*, 800; (c) Dauben, W. G.; Gerdes, J. M.; Look, G. C. *J. Org. Chem*. **1986**, *51*, 4964. BF_3–etherate: (d) Nagumo, S.; Matsukuma, A.; Suemune, H.; Sakai, K. *Tetrahedron* **1993**, *49*, 10501. $FeCl_3$: (e) Yang, H.; Li, B.; Cui, Y. *Synth. Commun*. **1998**, *28*, 1233. Me_3SiOTf: (f) Hwu, J. R.; Leu, L.-C.; Robl, J. A.; Anderson, D. A.; Wetzel, J. M. *J. Org. Chem*. **1987**, *52*, 188; (g) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett*. **1980**, *21*, 1357.
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[‡] Most of the heterogeneous catalysts are inactive for the protection of keto functions with diols because of their low acidities: Ref. 5.

[§] Interlayer distance of the Ti^{4+}-mont was expanded from 2.7 to 5.1 Å when soaked in toluene.

[¶] These reactions were carried out under the same conditions as shown in Table 2.

5. Examples of heterogeneous 1,3-dioxolane formation, see: clay: (a) Ponde, D. E.; Deshpande, V. H.; Bulbule, V. J.; Sudalai, A.; Gajare, A. S. *J. Org. Chem.* **1998**, *63*, 1058; (b) Li, T.-S.; Li, S.-H.; Li, J.-T.; Li, H.-Z. *J. Chem. Res. (S)* **1997**, 27; (c) Cramarossa, M. R.; Forti, L.; Ghelfi, F. *Tetrahedron* **1997**, *53*, 15889. Zeolite: (d) Ballini, R.; Bosica, G.; Frullanti, B.; Maggi, R.; Sartori, G.; Schroer, F. *Tetrahedron Lett.* **1998**, *39*, 1615; (e) Corma, A.; Climent, M. J.; Garcia, H.; Primo, J. *Appl. Catal.* **1990**, *59*, 333. Alumina: (f) Kamitori, Y.; Hojo, M.; Masuda, R.; Yoshida, T. *Tetrahedron Lett.* **1985**, *26*, 4767.
6. Ebitani, K.; Kawabata, T.; Nagashima, K.; Mizugaki, T.; Kaneda, K. *Green Chem.* **2000**, *2*, 157.
7. A typical procedure for the heterogeneous acetalization of carbonyl compounds is as follows. A mixture of acetophenone (3 mmol), ethane-1,2-diol (5 mmol), Ti^{4+}-mont (0.15 g) and toluene (20 mL) was refluxed under Dean–Stark conditions. After 1 h, the Ti^{4+}-mont was separated by filtration. The organic layer was concentrated and subjected to column chromatography on Florisil® with a mixture of *n*-hexane and ethyl acetate (10:1), which afforded 0.44 g of pure 2-methyl-2-phenyl-1,3-dioxolane (90%).
8. Presumably, the protonic acid sites of the Ti^{4+}-mont might be located on oxy anion species of Ti–O–Ti bonds, whose acidity could be strengthened by an efficient interaction through the oxy anions between Ti^{4+} and Si^{4+} of SiO_4 tetrahedra in the layer: Tanabe, K; Misono, M; Ono, Y; Hattori, H. *New Solid Acids and Bases*; Kodansha-Elsevier: Tokyo-Amsterdam, 1989.
9. In a typical deacetalization procedure, a mixture of 2-(4-oxo-4*H*-1-benzopyran-3-yl)-1,3-dioxolane **2** (1 mmol), Ti^{4+}-mont (0.15 g), acetone (5 mL) and water (0.2 mL) was stirred under reflux for 2 h. The GC analysis showed 99% yield of 4-oxo-4*H*-1-benzopyran-3-carboxaldehyde **1**.
10. In contrast, the use of a homogeneous distannoxane catalyst can protect a conjugated carbonyl group selectively to give 4′,4′a,7′,8′-tetrahydro-4′a-methylspiro[1,3-dioxolane-2,2′(3′*H*)-naphthalen]-5′(6′*H*)-one: Otera, J.; Dan-oh, N.; Nozaki, H. *Tetrahedron* **1992**, *48*, 1449.