Highly Efficient Deprotection of Acetals by Titanium Cation-exchanged Montmorillonite as a Strong Solid Acid Catalyst

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Deprotection of various kinds of acetals sufficiently occured in the presence of Ti^{4+}-exchanged montmorillonite as a recyclable strong solid acid catalyst.

In organic synthesis, carbonyl functionalities are commonly protected as acetals, which are typically converted back to the parent carbonyl moieties using acids or metal complexes.[1,2] However, these homogeneous deprotections suffer from several drawbacks, including difficult product isolation and production of unrecoverable salt wastes. To overcome these problems, much effort has been devoted toward the development of heterogeneous deprotection systems that can be performed under neutral conditions.[3] Unfortunately, these heterogeneous systems often demonstrate limited applicability for the substrate due to low activities.

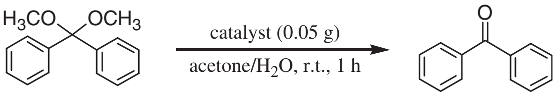
Montmorillonites (monts) are structurally defined as layers of two-dimensional silicate sheets separated by interlayer cationic species. The cationic species can be readily replaced by various metal cations, giving metal cation-exchanged monts (M^{n+}-monts) that can act as heterogeneous catalysts for a variety of organic reactions.[4]

Recently, we have succeeded in creating a chain-like titanium species within the interlayers of montmorillonite (Ti^{4+}-mont), which acts as an efficient solid acid catalyst for aromatic alkylation[5a] and acetalization of carbonyl compounds.[5b] Notably, the catalytic activities of the Ti^{4+}-mont toward bulky substrates exceeded those of conventional solid acids. Herein, we report that the Ti^{4+}-mont can efficiently catalyze the deprotection of various acetal compounds in aqueous acetone solution.

Treatment of Na^+-mont (Kunipia F, Kunimine Industry Co. Ltd.) with an aqueous solution of $TiCl_4$ afforded the Ti^{4+}-mont with an interlayer space of 2.7 Å (Ti content: 0.68 mmol/g).[5] The chain-like structure of titanium oxides along the silicate sheets was determined by Ti K-edge XAFS spectroscopy.

Deprotections of 1,1′-(dimethoxymethylene)bisbenzene were carried out using various M^{n+}-monts, as summarized in Table 1.[6] The M^{n+}-monts that contain metal cations with high valency, such as Ti^{4+}, Fe^{3+}, and Zr^{4+}, served as effective catalysts (Entries 1, 5, and 6). Among these catalysts, the Ti^{4+}-mont afforded benzophenone with the highest yield, which increased in relation to the amount of strongly adsorbed NH_3. In contrast, the catalytic activities of Sc^{3+}- and Cu^{2+}-mont under similar conditions were insubstantial, irrespective of the moderate amounts of adsorbed NH_3 (Entries 8 and 9). It is noteworthy that the Ti^{4+}-mont exhibited significantly higher catalytic activities than that of commercial mont K10 (Entry 11),[7] and those of conventional solid acids, such as H^+-beta,[8] H^+-mordenite, H^+-ZSM-5, and sulfate ion-treated zirconium oxide (SO_4^{2-}-ZrO_2)[9] (Entry 1 vs Entries 12–15).

Table 1. Deprotection of 1,1′-(dimethoxymethylene)bisbenzene catalyzed by M^{n+}-montmorillonites and typical solid acids[a]

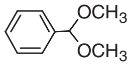
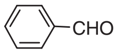
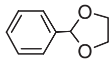
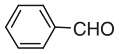
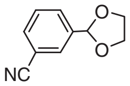
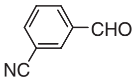
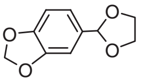
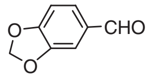
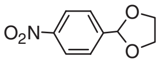
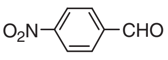
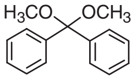
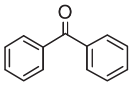
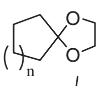
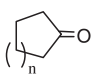
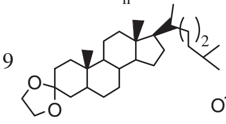
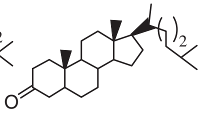
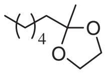
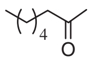
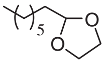
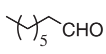
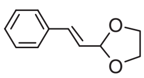
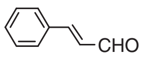
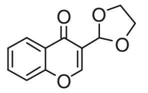
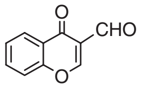


Entry	Catalyst	Yield /%[b,c]	Amount of adsorbed NH_3/mmol/g[d]
1	Ti^{4+}-mont[e]	>99	1.89
2	Reuse-1[f]	>99	1.89
3	Reuse-2	>99	1.89
4[g]	Ti^{4+}-mont	92	1.89
5	Fe^{3+}-mont	86	0.95
6	Zr^{4+}-mont	59	0.81
7	Al^{3+}-mont	20	0.75
8	Sc^{3+}-mont	1	0.89
9	Cu^{2+}-mont	1	0.74
10	Na^+-mont	10	0.17
11	mont K10[h]	16	n.m.[i]
12	H^+-beta[j]	7	0.95
13	H^+-mordenite[k,l]	3	0.24
14	H^+-ZSM-5[k,m]	1	n.m.[i]
15	SO_4^{2-}-ZrO_2[n]	7	0.44
16	—	trace	—

[a] Substrate (1 mmol), catalyst (0.05 g), acetone (5 mL), H_2O (0.2 mL), room temp., 1 h. [b] Determined by GC analysis using an internal standard technique. [c] Yield of benzophenone. [d] Acid amount was volumetrically measured. The value corresponds to the number of strongly adsorbed NH_3. See Ref. 5(a). [e] Ti: 0.034 mmol. [f] The spent catalyst from entry 1. [g] Pure acetone (5.2 mL) was used as the solvent. [h] Purchased from Aldrich. [i] Not measured. [j] From Shokubai Kasei Kogyo. [k] From N. E. Chemcat. [l] Si/Al = 10. [m] Si/Al = 25. [n] From Wako Pure Chemicals.

In addition to 1,1′-(dimethoxymethylene)bisbenzene, the deprotection reaction was extended to other acetals, as shown in Table 2. Several aromatic acetals smoothly reacted to form the corresponding carbonyl compounds (Entries 1–6). Interestingly, less reactive 2-(4-nitrophenyl)-1,3-dioxolane[2c] gave 4-nitrobenzaldehyde in a high yield within 6 h (Entry 5). This catalyst system was also effective for the deprotection of 1,3-dioxolanes of aliphatic ketones (Entries 7–10), including that with a bulky steroid substrate (Entry 9). Although the deprotection of the acetals of acyclic aliphatic aldehydes using metal triflates was unsuccessful,[2a-c] the Ti^{4+}-mont was surprisingly effective in transforming such unreactive dioxolanes to the corresponding aldehydes within 4 h (Entry 11). In addition, fa-

Table 2. Ti^{4+}-mont-catalyzed deprotection of acetals[a]

Entry	Substrate	Product[b]	Time / h	Yield[c] / %
1[d]			1	99
2			1	>99
3			6	95
4			1	98
5			6	94
6[d]			1	>99 (98)
7 n = 1			1	99
8 n = 2			1	95 (92)
9			1	(99)
10			1	99
11			4	95
12			1	94
13			2	99

[a] Substrate (1 mmol), Ti^{4+}-mont (0.10 g, Ti: 0.067 mmol), acetone (5 mL), H_2O (0.2 mL), 60 °C. [b] All products were characterized by ^1H NMR and Mass spectra. [c] Yield was determined by GC using an internal standard, based on substrates. Values in parentheses are isolated yields. In the case of the product isolation expriments, the reaction scale was three times as much as that given in footnote (a). [d] Room temp.

vorable results were obtained for conjugated 1,3-dioxolanes (Entries 12 and 13).

As shown in Table 1 (Entries 2 and 3), the spent Ti^{4+}-mont catalysts could be reused with retention of its high activity and selectivity. In the case of 1,1′-(dimethoxymethylene)bisbenzene, the Ti^{4+}-mont was removed by filtration after ca. 50%-conversion of the substrate at the reaction temperature. Further treatment of the filtrate under similar reaction conditions did not afford any additional benzophenone. These phenomena showed that the deprotection occurred at the chain-like Ti species on the mont solid.

The present Ti^{4+}-mont showed higher catalytic activities than those of Lewis acids such as $Bi(OTf)_3$ and $Ce(OTf)_3$.[2b,c] Moreover, the presence of water improved the yields of benzophenone (Table 1, Entry 1 vs 4). These observations indicated that the Brønsted acid sites of the Ti^{4+}-mont play an important role in the above deprotection reactions. Presumably, the strong acid sites of the Ti^{4+}-mont are associated with the unique TiO_2 domains within the interlayers of mont.[5] One of the prominent characteristics of mont materials is an enlargement of the interlayer distance in solvents.[10] Indeed, the interlayer space of the Ti^{4+}-mont expanded from 2.7 Å to 17.5 Å when soaked in acetone/H_2O, as determined by XRD measurement, thus allowing access of the substrates to the acid sites within the interlayers.[11]

In conclusion, the Ti^{4+}-mont acted as a heterogeneous, recyclable acid catalyst for deprotection of various acetal compounds. In contrast to current catalytic systems for deprotection, our methodology has following advantages: (1) high catalytic activity, (2) strikingly simple workup procedure, (3) recyclable catalyst, and (4) use of a nontoxic solvent system (acetone/H_2O).

References and Notes

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11 With respect to the solvents, a mixture of acetone and water was the optimal solvent. A promotion effect of water might be attributable to the larger interlayer distance than that in pure acetone (12.3 Å). In relation to this, use of CH_3CN, THF, or toluene resulted in lower yields of benzophenone (26–29%); correspondingly, the interlayer spaces using these solvents were less than 10 Å.

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