Metal Ion-Exchanged Montmorillonites as Practical and Useful Solid Catalysts for the Synthesis of α-Tocopherol

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Metal ion-exchanged montmorillonites were found to be efficient catalysts for the condensation reaction of trimethylhydroquinone with isophytol to afford α-tocopherol in high yield. The condensation reaction proceeded smoothly using 50 w/w% of catalyst in various solvents. The catalyst was easily recovered by filtration of the reaction mixture after the reaction was completed, and could be reused.

There has been a considerable growth in our knowledge of the chemistry of the catalysis of organic reactions by inorganic reagents supported in inorganic materials of high surface area.[1] A solid catalyst has great advantages: (1) it is inexpensive; (2) it is robust enough for a particular separation and/or the separation is easy; (3) catalyst contamination in products can be minimized. Acidic clay montmorillonite is a useful solid catalyst in liquid-phase organic reactions.[2] Metal ion-exchanged montmorillonites are also known to be strongly acidic and efficient for several acid-catalyzed organic reactions.[3]

The condensation reaction of hydroquinone with allylic alcohols is an important process in the synthesis of chroman ring structure. It is carried out using one molar amount of $ZnCl_2$, BF_3, and $AlCl_3$, as a Lewis acid catalyst (Scheme 1).[4] The catalysts are deactivated by water generated during the reaction, making it difficult to recover them. If the catalyst can be recovered easily and reused, the system would be of great value in an industrial process. In the course of our investigations on the synthesis of α-tocopherol, we became interested in the use of metal ion-exchanged montmorillonites as a catalyst for the condensation reaction of hydroquinone with allylic alcohol. Here, we report that metal ion-exchanged montmorillonites are quite efficient for the Friedel–Crafts alkylation–cyclization reaction of trimethylhydroquinone (**1**) with isophytol (**2**) (Scheme 2).

Metal ion-exchanged montmorillonites were easily prepared from sodium ion-exchanged montmorillonite[5] (Na–Mont) by cation-exchange using aqueous solutions of corresponding salts, metal nitrate or metal chloride.[3] The activity of metal ion-exchanged montmorillonites was evaluated in the condensation reaction of trimethylhydroquinone (**1**) with isophytol (**2**) (Table 1). Most metal ion-exchange montmorillonites advanced the condensation reaction to give α-tocopherol in high yield, while lanthanide ion-exchange montmorillonite, La–Mont and Sm–Mont were found to be relatively slow in the rate of the reaction. When Na–Mont was used as the catalyst, the reaction proceeded hardly at all (Entry 15).

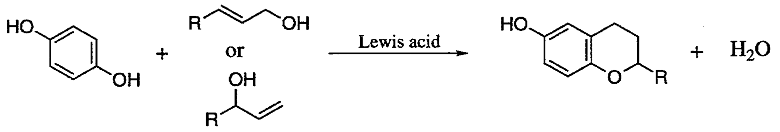
Table 1. Reaction of Trimethylhydroquinone (**1**) and Isophytol (**2**) Using Metal Ion-Exchanged Montmorillonites[a)]

Entry	Catalyst	Time/h	Yield/%[b)]
1	Al–Mont	3	95
2	Sc–Mont	2	91
3	Ti–Mont	2	94
4	Fe–Mont	2	95
5	Ni–Mont[c)]	2	96
6	Ni–Mont	2	96
7	Ni–Mont[d)]	3	94
8	Cu–Mont	3	94
9	Zn–Mont	2	95
10	Ga–Mont	2	93
11	Zr–Mont	2	92
12	Sn–Mont	2	94
13	La–Mont	3	N.D.[e)]
14	Sm–Mont	2	N.D.[e)]
15	Na–Mont[f)]	3	N.D.[e)]

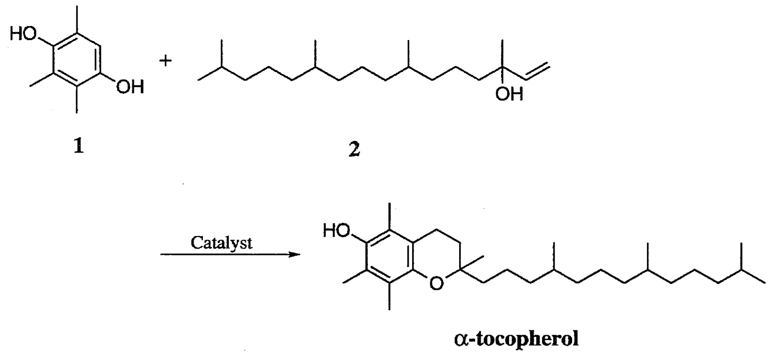
a) Unless otherwise specified, the reaction was carried out in octane under reflux using trimethylhydroquinone, catalyst (50 w/w%) and isophytol that was added dropwise. b) Determined by GLC analysis. c) 100 w/w% of catalyst was used. d) 25 w/w% of catalyst was used. e) Not determined because the reaction did not proceed satisfactorily. f) Toluene was used as solvent.

A variety of solvents was used in the reaction under the influence of Al–Mont (50 w/w%); the results are shown in Table 2. Under reflux above 110 °C, the reaction proceeded smoothly and the condensation product was obtained in high yield regardless of the choice of solvent.

Features of these solid catalysts are as follows: (1) the work-up involves simple filtration before evaporation of the solvent, (2) the catalyst can be quite easily recovered by filtration of reaction mixture and can be reused. After the reaction was completed, the reaction mixture was filtered and the precipitate was washed with organic solvent, water



Scheme 1.



Scheme 2.

and then dried in vacuo at room temperature. The recovered Ni–Mont catalyst was also effective in the condensation reaction (Table 3). It should be noted that the yield of even the 5th use of the catalyst was almost as much as that of the first use.

In summary, metal ion-exchanged montmorillonites were efficient catalysts in the condensation reaction of trimethylhydroquinone with isophytol. The high activity in various solvents, and the possible recovery and reuse of catalyst suggest that system would be commercially viable.

Table 2. Reaction of Trimethylhydroquinone (**1**) and Isophytol (**2**) Using Aluminum Ion-Exchanged Montmorillonites in Various Solvents[a)]

Entry	Solvent	Time/h	Yield/%[b)]	Purity/%[c)]
1	Toluene	3	94	98
2	Heptane	3	88	98
3	Octane	3	98	98
4	1-Pentanol	7	94	94
5	3-Pentanone	3	94	99
6	Butyl acetate	3	93	93
7	Diisobutyl ether	3	98	99

a) Unless otherwise specified, the reaction was carried out in solvent under reflux for 3 h using trimethylhydroquinone, catalyst (50 w/w%) and isophytol that was added dropwise. b) Isolated yield. c) Determined by GLC analysis.

Table 3. Reaction of Trimethylhydroquinone (**1**) and Isophytol (**2**) Using Recovered Nickel Ion-Exchanged Montmorillonites[a)]

Entry	Ni–Mont	Yield/%[b)]
1	1st use	99
2	2nd use	98
3	3rd use	98
4	4th use	98
5	5th use	98

a) Unless otherwise specified, the reaction was carried out in toluene under reflux for 3 h using trimethylhydroquinone, catalyst (50 w/w%) and isophytol that was added dropwise. b) Determined by GLC analysis.

Experimental

General. Infrared (IR) spectra were recorded on a Shimadzu FTIR-8100 spectrometer. Analytical gas–liquid-phase chromatography (GLC) was performed on a Gaskuro Kogyo Model 370 instrument with a flame-ionization detector and a capillary column of HP-1(25 m) using nitrogen as the carrier gas. ^{1}H was measured on a Varian Gemini-300 (300 MHz) spectrometer. Chemical shifts of ^{1}H NMR were reported relative to tetramethylsilane ($\delta=0$) or chloroform ($\delta=7.26$). Splitting patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra were recorded with a Shimadzu QP-5000 mass spectrometer. All experiments were carried out under an atmosphere of dry argon. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF$_{254}$, 0.25 mm) were used. The products were purified by preparative column chromatography on silica gel E. Merck Art. 9385. Microanalyses were accomplished at the Faculty of Agriculture, Nagoya University.

In experiments requiring dry solvent, toluene was dried over sodium metal. Other simple chemicals were purchased and used without further purification.

Preparation of Metal Ion-Exchanged Montmorillonites.[3b,3d)] Al–Mont, Sc–Mont, Ti–Mont, Fe–Mont, Ni–Mont, Cu–Mont, Zn–Mont, Ga–Mont, Zr–Mont, Sn–Mont, La–Mont, and Sm–Mont were prepared from Na–Mont (cation-exchange capacity = 1.19 mequiv g^{-1})[5)] by cation-exchange using aqueous solutions of corresponding salts, such as $Al(NO_3)_3\cdot9H_2O$, $Sc(NO_3)_3\cdot4H_2O$, $Ti(O\textit{i}\text{-}Pr)_4$ in aqueous hydrochloric acid, $Fe(NO_3)_3\cdot9H_2O$, $Ni(NO_3)_2\cdot6H_2O$, $Cu(NO_3)_2\cdot3H_2O$, $Zn(NO_3)_2\cdot6H_2O$, $Ga(NO_3)_3\cdot8H_2O$, $ZrCl_4$, $SnCl_4\cdot5H_2O$, $La(NO_3)_3\cdot6H_2O$, and $Sm(NO_3)_3\cdot6H_2O$. A typical procedure is described below: To a solution of $Ni(NO_3)_2\cdot6H_2O$ (232 g, 800 mmol) in deionized water (1600 ml) was added Na–Mont (200 g). The mixture was stirred vigorously at room temperature for 16 h. The resultant suspension was filtered on a Büchner funnel by suction. The clay was collected, suspended again in deionized water (800 ml) with stirring at room temperature for 15 h, filtered on a suction funnel, and washed with deionized water (400 ml). The precipitate was again suspended in deionized water (800 ml) with stirring at room temperature for 14 h, filtered on a suction funnel, and washed with deionized water (400 ml). The precipitate was suspended again in a mixture of deionized water (400 ml) and methanol (400 ml) with stirring at room temperature for 13 h and filtered. The collected clay was dried at 100 °C for 6 h and ground to pass through a 60 mesh screen. The powdery clay was dried in vacuo at 100 °C for 4 h to give Ni–Mont as a green solid (198 g).

General Procedure for Condensation Reaction of Trimethylhydroquinone (1) and Isophytol (2) Using Metal Ion-Exchanged Montmorillonites (Table 1): A mixture of trimethylhydroquinone (4.0 g, 26 mmol) and metal ion-exchanged montmorillonites (2.0 g, 50 w/w%) in octane (12 ml) was heated at reflux for 10 min. Isophytol (7.6 g, 25 mmol) was added dropwise to the suspension over 1 h with refluxing, and the mixture was heated at reflux for 2—3 h. After cooling, the resulting mixture was filtered and the filtrate was then washed with 1 M sodium hydroxide solution (20 ml) ($1\ \mathrm{M} = 1\ \mathrm{mol\,dm^{-3}}$). The organic layer was washed twice with deionized water (2×20 ml), dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was dried in vacuo to give α-tocopherol.

General Procedure for Condensation Reaction of Trimethylhydroquinone (1) and Isophytol (2) Using Aluminum Ion-Exchanged Montmorillonites in Various Solvents (Table 2): A mixture of trimethylhydroquinone (1.0 g, 6.6 mmol) and aluminum ion-exchanged montmorillonites (0.5 g, 50 w/w%) in solvent (2.0 ml) was heated at reflux for 10 min. A solution of isophytol (2.0 g, 6.8 mmol) in solvent (2.0 ml) was added dropwise to the suspension over 30 min with refluxing, and the mixture was heated at reflux for 3 h. After cooling, the resulting mixture was filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: hexane–diethyl ether) to give α-tocopherol as a brown oil.

General Procedure for Condensation Reaction of Trimethylhydroquinone (1) and Isophytol (2) Using Recovered Nickel Ion-Exchanged Montmorillonites (Table 3): A mixture of trimethylhydroquinone (1.0 g, 6.6 mmol) and nickel ion-exchanged montmorillonites (0.5 g, 50 w/w%) in toluene (2.0 ml) was heated at reflux for 10 min. A solution of isophytol (2.0 g, 6.8 mmol) in toluene (2.0 ml) was added dropwise to the suspension over 40 min with refluxing, and the mixture was heated at reflux for 3 h. After cooling, the resulting mixture was filtered and the filtrate was concentrated in vacuo. The residue was dried in vacuo to give α-tocopherol as a pale brown oil.

The precipitate, which is clay catalyst, was washed with hexane, ethyl acetate, methanol, and water in that order. The clay was suspended in deionized water and was stirred at room temperature for 1 h. The clay was collected, suspended again in methanol with stirring at room temperature for 1 h, filtered on a suction funnel, and washed with methanol, ethyl acetate and hexane in order. The clay was dried in vacuo at room temperature and reused.

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