

Preparation of Polystyrene-Bound Dichlorotitanium Dialkoxide and Its Application as a Polymer-Supported Lewis Acid Catalyst in Organic Syntheses

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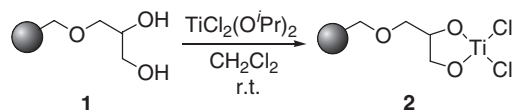
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Polymer-supported dichlorotitanium dialkoxide was readily prepared from polystyrene-bound α -glycol and dichlorotitanium diisopropoxide. When we employed it as an immobilized Lewis acid catalyst, several fundamental and important Lewis acid-catalyzed reactions proceeded smoothly with fair chemical yields.

The utility of titanium compounds as Lewis acid catalysts has been widely accepted in organic synthesis.¹ In various titanium catalysts, titanium(IV) chloride and its alkoxide derivatives have been widely used in Lewis acid-mediated synthetic transformations.² Insoluble polymer-supported catalysts offer advantages of easy separation of the supported catalyst from the reaction mixture, possible recycling and, in many cases, enhanced stability of the polymer-bound catalyst as compared to the soluble analogue.³

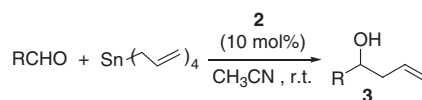
Although several polymer-supported titanium catalysts have been reported,^{4,5} most of them are monodentate-immobilized catalysts,⁴ except for those catalysts for asymmetric syntheses.⁵ Herein, we wish to report the very simple preparation of polystyrene-bound dichlorotitanium dialkoxide, which is embedded by stable bidentate immobilization, and its application as a polymer-supported Lewis acid catalyst in carbon-carbon bond-forming reactions.

Polystyrene-bound dichlorotitanium dialkoxide **2** was synthesized according to the method outlined in Scheme 1. Commercially available polystyrene-bound α -glycol **1** (i.e., polystyrene-bound glycerol, crosslinked with 1% divinylbenzene) was treated with dichlorotitanium diisopropoxide in dry dichloromethane at room temperature under a nitrogen atmo-



Scheme 1.

Table 1. Allylation Reactions of Aldehydes Using **2** as Lewis Acid Catalyst



Entry	RCHO	Yield/% ^{a)}
1		89
2	PhCHO	87 ^{b)}
3	Ph-CH ₂ -CHO	85
4	Ph-CH=CH-CHO	82 ^{b)}
5	Ph-CH=CH-CHO	86
6		70
7		72
8		68

a) Isolated yield. b) Recovered catalyst was used.

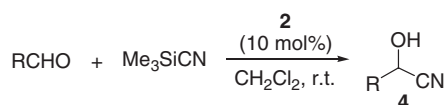
sphere. Elemental analyses of chlorine and oxygen showed that polystyrene-bound dichlorotitanium dialkoxide **2** was obtained in nearly quantitative yield. It was found by chlorine elemental analyses that **2** was hardly decomposed, even by the air moisture, even though **2** was exposed to the air for 24 h.⁶ The stability of **2** in the presence of air moisture, which was different from the cases of titanium(IV) chloride and its alkoxide derivatives, was probably due to the polymer-immobilization of titanium, especially in this case, which was a case of bidentate immobilization.

We then used **2** as an immobilized Lewis acid catalyst in several fundamental and important carbon-carbon bond-forming reactions. First, allylation reactions of aldehydes⁷ were carried out (Table 1). A mixture of **2** (10 mol%), aldehyde, and tetraallylstin in acetonitrile was agitated with shaking at room temperature under a nitrogen atmosphere. Allylation reactions proceeded smoothly to provide the corresponding homoallyl alcohol **3** in fair chemical yields in all cases. In the case of benzaldehyde, **3** was obtained in the highest chemical yield (89% yield; Entry 1). Furthermore, the polymer catalyst **2** could be recovered by simple filtration after the reaction, and could be reused to provide **3** in fair chemical yields (Entries 2 and 4), which were comparable to the yields obtained in Entries 1 and 3.

Encouraged by these results, we next carried out cyanation reactions of aldehydes using trimethylsilyl cyanide⁸ (Table 2). However, in this case, only aliphatic aldehydes provided the corresponding cyanohydrin **4**, contrary to our expectation, because of a low catalytic activity of **2** due to polymer-immobilization of the titanium catalyst.

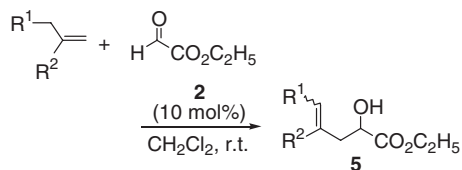
We subsequently examined glyoxylate-ene reactions⁹ using the polymer catalyst **2** (Table 3). A mixture of **2** (10 mol%), olefins, and an excess amount of ethyl glyoxylate provided the corresponding α -hydroxy ester **5** in dichloromethane. Even though the glyoxylate-ene reactions proceeded more slowly than did the above-mentioned addition reactions of aldehyde, the corresponding α -hydroxy ester **5** was obtained in decent chemical yields in all cases.

In conclusion, polystyrene-bound dichlorotitanium dialkoxide **2**, a bidentate-immobilized titanium compound, was read-

Table 2. Cyanation Reactions of Aldehydes Using **2**

Entry	RCHO	Yield/% ^{a)}
1		71
2		82
3		62

a) Isolated yield.

Table 3. Glyoxylate–Ene Reactions Using **2**

Entry	Olefin	Product	Yield/% ^{a)}
1			70
2			69
3			66
4			60 ^{b)}

a) Isolated yield. b) *E*:*Z* = 70:30 (determined by ¹H NMR).

ily prepared from commercially available polystyrene-bound α -glycol **1** and dichlorotitanium diisopropoxide under a nitrogen atmosphere. When we used it as an immobilized Lewis acid catalyst, several carbon–carbon bond-forming reactions proceeded.

Experimental

An agitation of the reaction mixture was performed on a solid-phase organic synthesizer (Tokyo Rikakikai Co. Ltd.). Polystyrene-bound glycerol **1**, dichlorotitanium diisopropoxide, and ethyl glyoxylate–toluene solution were purchased from Aldrich, Tokyo Kasei Kogyo Co. Ltd., and Fluka, respectively.

Preparation of **2.** A mixture of polystyrene-bound glycerol **1** (1.38 mmol/g, crosslinked with 1% divinylbenzene, 403.6 mg, 0.557 mmol) and dichlorotitanium diisopropoxide (262 mg, 1.11 mmol) in dry dichloromethane (4 mL) was agitated with shaking for 5 h at room temperature under a nitrogen atmosphere. After filtration of the reaction mixture, the resin was washed with dichloromethane and with acetonitrile, and then dried under reduced pressure (519 mg, pale yellow beads). IR (KBr): 3023.9, 2913.1, 1600.3, 1492.5, 1451.3, 1365.9, 1100.1, 747.9, 696.0 cm⁻¹; Anal. Found: Cl, 8.39; O, 5.63%. Calcd: Cl, 8.43; O, 5.71%.

General Procedure for Allylation Reaction. To polymer catalyst **2** (61.9 mg, 0.0700 mmol) was added a mixture of benzaldehyde (74.2 mg, 0.700 mmol) and tetraallyltin (98.8 mg, 0.349

mmol) in dry acetonitrile (3 mL) at room temperature under a nitrogen atmosphere, and the mixture was stirred for 30 min at the same temperature. After filtration of the reaction mixture and washing of **2** with dry acetonitrile under a nitrogen atmosphere, the filtrate was concentrated under reduced pressure, and the crude product was chromatographed on silica gel to give 1-phenyl-3-buten-1-ol (92.3 mg, 89% yield).

Polymer catalyst **2** was recovered nearly quantitatively (ca. 60 mg) after drying under reduced pressure, and was reused according to the above procedure.

General Procedure for Cyanation Reaction. To polymer catalyst **2** (61.9 mg, 0.0700 mmol) was added a mixture of cyclohexanecarboxaldehyde (75.8 mg, 0.676 mmol) and trimethylsilyl cyanide (279 mg, 2.81 mmol) in dry dichloromethane (3 mL) at room temperature, and the mixture was stirred for 20 h at the same temperature under a nitrogen atmosphere. After filtration and washing with dichloromethane, the filtrate was concentrated under reduced pressure. The crude material was treated with 1 M HCl–tetrahydrofuran (1:20 v/v) at 0 °C. After the usual workup, the crude product was chromatographed on silica gel to give 1-cyclohexyl cyanohydrin (76.7 mg, 82% yield).

General Procedure for Glyoxylate–Ene Reaction. To polymer catalyst **2** (63.3 mg, 0.0683 mmol) was added a mixture of α -methylstyrene (80.7 mg, 0.683 mmol) and ethyl glyoxylate–toluene solution (1.02 mmol/g, 3.60 g, 3.67 mmol) in dichloromethane (3 mL) at room temperature; the mixture was stirred for 30 h at the same temperature under a nitrogen atmosphere. After filtration and washing with dichloromethane, the filtrate was concentrated under reduced pressure, and the crude product was chromatographed on silica gel to give ethyl 2-hydroxy-4-phenyl-4-pentenoate (105 mg, 70% yield).

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