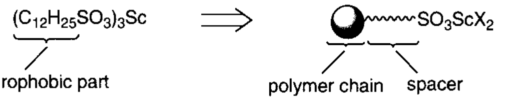
A Novel Polymer-Supported Scandium Catalyst Which Shows High Activity in Water**

Satoshi Nagayama and Shū Kobayashi*

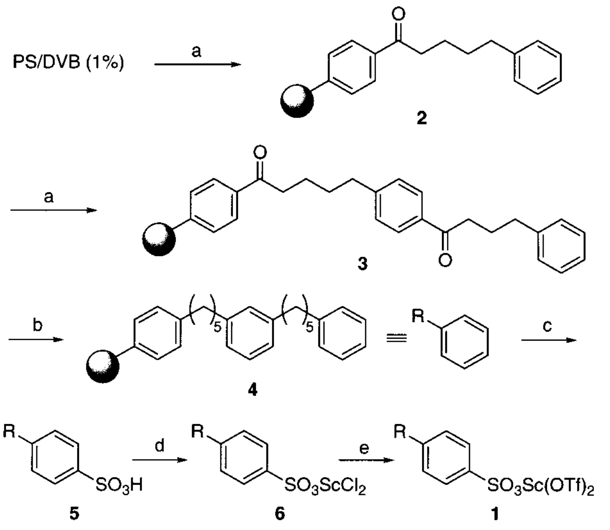
Organic reactions in water without the use of any harmful organic solvents are now of great interest in organic synthesis.[1] While several useful synthetic reactions in an aqueous media containing an amount of organic co-solvent have been reported,[1, 2] many of these reactions proceed sluggishly in pure water, probably because most of the organic reagents are not completely dissolved.[3] To address this issue, we have recently developed Lewis acid–surfactant combined catalysts (LASCs) such as scandium tris(dodecyl sulfate) and scandium tris(dodecanesulfonate).[4, 5] In the presence of a catalytic amount of a LASC, organic materials rapidly formed a dispersed colloidal system in water, and aldol reactions of silyl enol ethers with aldehydes proceeded smoothly without the use of organic solvents. While this is the first example of Lewis acid catalysis in pure water, a disadvantage is that rather tedious procedures are needed to recover the catalyst. In this paper, we report a solution of this problem: a novel polymer-supported scandium-based Lewis acid which shows high activity in water and can be easily recovered and reused.

The utility of polymer-supported catalysts in preparative procedures, such as simplification of product work-up, and the easy separation, isolation, and reuse of the catalysts is well-recognized.[6] Our idea was to change the hydrophobic part of a LASC to polymer chains having "spacers" composed of alkylaromatic moieties and to develop a novel polymer-supported catalyst that can be used in water (Scheme 1).



Scheme 1. Abstract representation of the Lewis acid catalysts reported here. Left: example LASC. Right: the scandium-based active site is separated by an alkylaromatic "spacer" moiety from polymeric support.

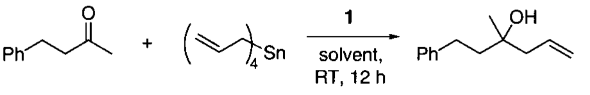
Preparation of the polymer-supported scandium catalyst **1** was performed according to Scheme 2.[7, 8] Polystyrene (PS), cross-linked with divinybenzene (DVB, 1%), was treated with 5-phenylvaleryl chloride in carbon disulfide in the presence of aluminum trichloride at room temperature for 24 h.[9] After quenching and washing with aqueous and organic solvents, the resulting resin **2** was treated with 5-phenylvaleryl chloride once again to afford ketone resin **3**. The carbonyl groups of **3** were reduced using aluminum trichloride–lithium aluminum hydride[10] in diethylether to afford "double spacer" resin **4**. After sulfonation (chlorosulfonic acid/acetic acid), resin **5** was treated with scandium(III) chloride in acetonitrile at room temperature for 24 h to give the polymer-supported scandium chloride **6**. Finally, **6** was treated with trifluoromethanesulfonic acid (TfOH) to afford **1**.[11]



Scheme 2. Preparation of **1**. a) $AlCl_3$, $Ph(CH_2)_4COCl/CS_2$; b) $AlCl_3$, $LiAlH_4/Et_2O$; c) $ClSO_3H/CH_2Cl_2$, CH_3CO_2H; d) $ScCl_3/CH_3CN$; e) TfOH/CH_2Cl_2.

The catalytic activity of **1** was first tested in the allylation reactions of carbonyl compounds with tetraallyltin, which are among the most fundamental and important carbon–carbon bond-forming reactions in organic synthesis.[12] We chose the reaction of 4-phenyl-2-butanone with tetraallyltin as a model [Eq. (1)]. It was found that the reaction proceeded smoothly in the presence of 3.2 mol% of **1** in water at room temperature for 12 h, to afford the corresponding homoallylic alcohol in 92% yield.[13] It is noted that even less reactive ketone reacted smoothly under these conditions. Moreover, **1** was easily recovered after the reaction was completed by simple filtration and reused (Table 1, entry 1). The recovery was quantitative in each case and no loss of activity was observed for the recovered catalyst. While 95% yield was attained

Table 1. Examination of reaction conditions [Eq. (1)].[a]



(1)

Entry	Solvent	Catalyst[b] [mol%]	Yield [%]
1	H_2O	3.2	92 (93,[c] 90[d])
2	H_2O	1.6	95 (90,[e] 92[f])
3	H_2O	0.8	84
4	CH_2Cl_2	3.2	38
5	CH_3CN	3.2	15
6	benzene	3.2	28
7	EtOH	3.2	20
8	DMF	3.2	trace

[a] 1.29 mmol g^{-1} of **5** was used unless otherwise noted. [b] Determined by elemental analysis of Sc in **1**. [c] 2nd use. [d] 3rd use. [e] 0.52 mmol g^{-1} of **5** was used. [f] 2.46 mmol g^{-1} of **5** was used.

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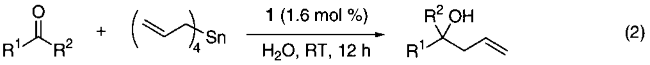
using 1.6 mol% of **1**, a slight decrease in the yield was observed when 0.8 mol% of **1** was employed under the same reaction conditions (RT, 12 h). As for the loading levels of **5**, similar results were obtained at the loading between 0.52–2.46 mmol g^{-1} (entry 2). We also examined the effect of solvents (entries 1, 4–8). While excellent yield was obtained in water, much lower yields were observed in the other solvents (dichloromethane, acetonitrile, benzene, ethanol, DMF). In all cases, the reaction mixture was clean as only the starting materials and the product were observed by thin-layer chromatography during the reaction. This meant that the reaction rate was much faster in water than in organic solvents and that use of water as the solvent was essential in this allylation reaction using **1** as a catalyst.

Several examples of the **1**-catalyzed allylation reactions in water [Eq. (2)] are shown in Table 2. Aromatic, aliphatic, as well as heterocyclic aldehydes worked well to give the corresponding homoallylic alcohols in high yields. In the reaction of an α,β-unsaturated aldehyde, only 1,2-addition occurred. When phenylglyoxal monohydrate was treated with tetraallyltin under the reaction conditions, the diallylated adduct was obtained in 90% yield. We also tested other ketones and the desired 1,2-addition adducts were obtained in high yields. No 1,4-addition took place when an α,β-unsaturated ketone was employed. It is noted that the catalyst was recovered quantitatively after the reactions and reused in all cases.

Table 2. Allylation reactions catalyzed by **1** as shown by Equation (2)



(2)

Entry	R^1	R^2	Yield [%]
1	Ph	H	82
2	Ph(CH$_2$)$_2$	H	quant.
3	*cyclo*-C$_6$H$_{11}$	H	72
4	(*E*)-PhCH=CH	H	99
5	2-pyridyl	H	83
6	PhCO	H[a]	90[b]
7	Ph(CH$_2$)$_2$	Me	quant.
8	(*E*)-PhCH=CH	Me	91
9	Ph	CO$_2$Et	90

[a] Monohydrate. [b] Diallylated adduct was obtained.

A preliminary kinetic study was performed in the allylation reaction of 4-phenyl-2-butanone with tetraallyltin (Figure 1). We have already reported that scandium triflate (Sc(OTf)$_3$) catalyzed allylation reactions of carbonyl compounds with tetraallyltin in aqueous media (H_2O/THF, H_2O/CH_3CN, H_2O/EtOH/toluene) and organic solvents.[14] It was found that the Sc(OTf)$_3$-catalyzed reaction in H_2O/THF (1/9, (e)) or H_2O/EtOH/toluene (1/7/4, (d)) proceeded much slower than the **1**-catalyzed reaction in water (a). Although the initial rate of the Sc(OTf)$_3$-catalyzed reaction in dichloromethane (c) was comparable to the **1**-catalyzed reaction in water, the former stopped after 2 h when the yield reached around 50%. It should be noted that the **1**-catalyzed reaction was faster than the example LASC-catalysed reaction (catalyst: scandium tris(dodecanesulfonate), STDS) in water (b).[15]

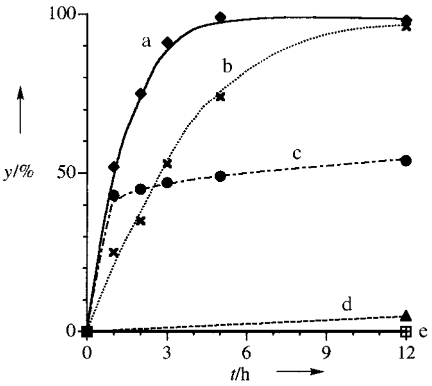
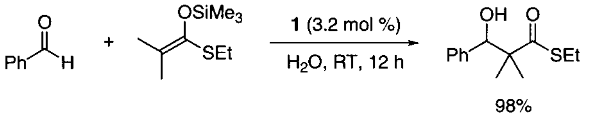
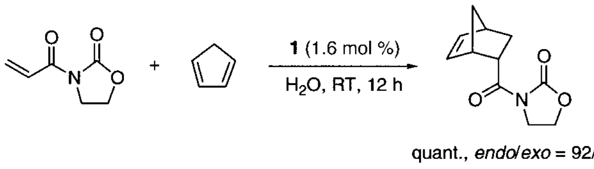


Figure 1. Kinetic studies in the reaction of 4-phenyl-2-butanone with tetraallyltin. a) **1** in water; b) STDS in water; c) Sc(OTf)$_3$ in CH_2Cl_2; d) Sc(OTf)$_3$ in H_2O/EtOH/toluene; e) Sc(OTf)$_3$ in H_2O/THF. All reactions were carried out using 3.2 mol% of the catalysts.

Finally, use of **1** in other synthetic reactions was briefly surveyed. In the presence of 3.2 mol% of **1**, benzaldehyde reacted with 1-ethylthio-1-trimethylsiloxy-2-methyl-1-propene at room temperature for 12 h in water [Eq. (3)] to afford the corresponding aldol-type product in 98% yield (77% yield using 1.6 mol% of **1**). The Diels–Alder reaction of 3-acryloyl-1,3-oxazolidin-2-one with cyclopentadiene also proceeded smoothly in the presence of 1.6 mol% of **1** in water [Eq. (4)] to afford the corresponding adduct quantitatively (RT, 12 h, *endo*/*exo* = 92/8). Moreover, the Strecker-type reaction of benzaldehyde, aniline, and tributyltin cyanide was performed.[16] The reaction proceeded cleanly in the presence of 1.6 mol% of **1** in water [Eq. (5)] to afford the corresponding α-amino nitrile derivative in 77% yield (RT, 12 h). These results indicated that **1** was an excellent Lewis acid catalyst for several useful carbon–carbon bond-forming reactions in water.



(3)



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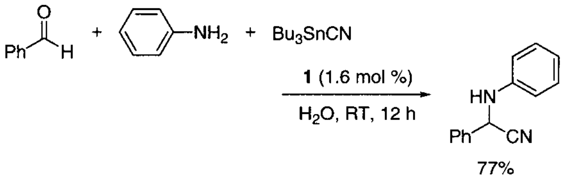

(5)

In summary, we have developed a novel polymer-supported scandium catalyst. The catalyst has polymer chains and spacers which would help to form hydrophobic reaction fields in water. Several useful carbon–carbon bond-forming reac-

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tions proceeded smoothly in the presence of a catalytic amount of **1** in water without using any organic co-solvents. To the best of our knowledge, this is the first example of the polymer-supported Lewis acid catalyst that can be used in this manner. It is noted that the reactions proceeded much faster in water than in other media including organic solvents. The simple procedures, easy recovery, reusable catalyst, and the use of water as a solvent are expected to contribute to development of benign chemical processes.

Experimental Section

A typical experimental procedure is described for the allylation reaction of 4-phenyl-2-butanone with tetraallyltin. 4-Phenyl-2-butanone (0.4 mmol), tetraallyltin (0.2 mmol), and **1** (0.0064 mmol, 1.6 mol%) were combined in water (3 mL). The mixture was stirred for 12 h at RT. Catalyst **1** was filtered and washed with ethyl acetate. The filtrate was extracted with ethyl acetate, and the combined organic layers were dried (Na_2SO_4). After filtration and concentration, the residue passed through a column packed with silica gel to afford the allylated adduct in 95% yield. The recovered **1** was reused several times without loss of activity.

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[8] While we have previously developed polymer-supported scandium catalysts, most of them work well in organic solvents but reactions proceed sluggishly in water without organic co-solvents. a) S. Kobayashi, S. Nagayama, *J. Org. Chem.* **1996**, *61*, 2256–2257; b) S. Kobayashi, S. Nagayama, *J. Am. Chem. Soc.* **1996**, *118*, 8977–8978; c) S. Kobayashi, S. Nagayama, *J. Am. Chem. Soc.* **1998**, *120*, 2985–2986.

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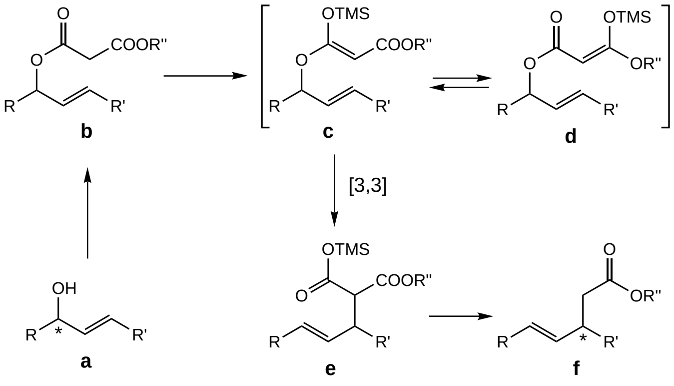
A New Variant of the Claisen Rearrangement from Malonate-Derived Allylic Trimethylsilyl Ketene Acetals: Efficient, Highly Enantio- and Diastereoselective Syntheses of (+)-Methyl Dihydroepijasmonate and (+)-Methyl Epijasmonate[**]

Charles Fehr[*] and José Galindo

Among the large variety of [3,3] sigmatropic rearrangements,[1] the Johnson ortho ester Claisen rearrangement[2] has proven to be particularly useful, owing to its facile and broad applicability. Nonetheless, it also suffers from some limitations: trimethyl orthoacetate is impractical, because the reaction temperature is limited by its low boiling point (105–110°C) and therefore, triethyl orthoacetate (b.p. 142–145°C) is commonly used. As the Johnson Claisen rearrangement requires excess ortho ester, its industrial application is unattractive in those cases that require ulterior transesterification (e.g. for the synthesis of methyl esters).

We now report an alternative methodology, which is based on the Claisen rearrangement of trimethylsilyl(TMS)-ketene acetals of type **c** (presumably in equilibrium with **d**) derived from malonates **b**, followed by desilylation/decarboxylation of malonates **e** to esters **f** (Scheme 1). The synthetic concept



Scheme 1. Claisen rearrangement from malonate-derived TMS ketene acetals.

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