A Polymer-Supported Scandium Catalyst

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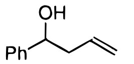
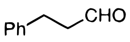
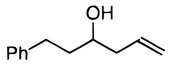
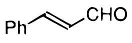
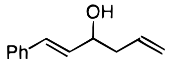
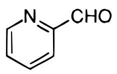
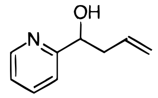
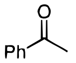
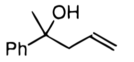
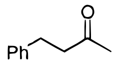
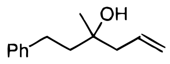
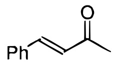
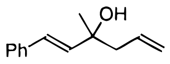
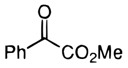
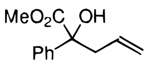
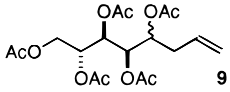
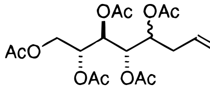
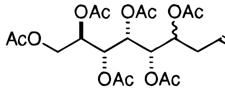
Use of polymer-supported catalysts offers several advantages in preparative procedures. Simplification of product workup, separation, and isolation as well as reuse of the catalyst including use of flow reactions could lead to an economical automation system. Although the use of immobilized homogeneous catalysts is of continuing interest,[1] few examples are known for polymer-supported Lewis acids.[2,3] Our purpose is to combine the advantages of immobilized catalysis and Lewis acid-mediated reactions and to develop polymer-supported Lewis acids for the efficient synthesis of diverse lower molecular weight compounds. In this paper, we describe a polymer-supported scandium catalyst, which is effective in several useful synthetic reactions and can be used in both organic and aqueous solvents.

Recently, scandium triflate ($Sc(OTf)_3$) was found to be stable in water and could successfully carry out Lewis acid catalysis in both water and organic solvents.[4] $Sc(OTf)_3$ coordinates to Lewis bases under equilibrium conditions, and thus, activation of carbonyl compounds using a catalytic amount of the acid has been realized. In addition, effective activation of nitrogen-containing compounds such as imines, amino aldehydes, etc. has been performed successfully.[5] Encouraged by the characteristics and the usefulness of $Sc(OTf)_3$ as a Lewis acid catalyst, we intended to prepare a polymer-supported scandium catalyst.

Table 1. Sc−Nafion-Catalyzed Allylation Reactions of Carbonyl Compounds with Tetraallyltin[a]

Carbonyl Compound	Product		Solvent[b]	Yield(%)
PhCHO		**1**	A B C	91 90 91
		**2**	A C	83 83
		**3**	A C	93 98
		**4**	A	78
		**5**	A	57[c]
		**6**	A C	64[c] 87[c]
		**7**	A C	95[c] 85[c]
		**8**	A C	81[c] 84[c]
D-arabinose		**9**	A	76[c,d,e]
D-ribose		**10**	A	91[c,d,f]
D-glucose		**11**	A	64[c,d,g]

[a] The reaction was carried out at rt unless otherwise noted. [b] A: H_2O/THF (1:9). B: H_2O/MeOH/toluene (1:7:4). C: CH_3CN. [c] The reaction was carried out at 60 °C. [d] The products were isolated after acetylation. [e] *Syn*/*anti* = 59:41. [f] *Syn*/*anti* = 65:35. [g] Diastereomer ratio = 68:32. Relative configuration assignment was not made.

We chose Nafion (NR-50)[6] as the supporting framework.[7] Three equivalents of Nafion was treated with $ScCl_3\cdot6H_2O$ in acetonitrile under reflux conditions.[8] After 40 h, 96% of the $ScCl_3\cdot6H_2O$ was consumed, and the polymer thus prepared (Nafion−Sc) contained 1.3% Sc, according to ICP analysis. Choice of solvents is important at this stage; only 27% of the $ScCl_3\cdot6H_2O$ was consumed when 1,2-dichloroethane was used as a solvent.

We then tested this Nafion−Sc catalyst in several synthetic reactions. First, allylation reactions of carbonyl compounds were investigated. Allylation reactions of carbonyl compounds are among the most important carbon−carbon bond-forming reactions, and the products, homoallylic alcohols having hydroxyl and double bond groups, are synthetically useful intermediates.[9] Moreover, in our previous report on $Sc(OTf)_3$-catalyzed ally-

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[1] Reviews: (a) Bailey, D. C.; Langer, S. H. *Chem. Rev.* **1981**, *81*, 109. (b) Akelah, A.; Sherrington, D. C. *Ibid.* **1981**, *81*, 557. (c) Frechet, J. M. J. *Tetrahedron* **1981**, *37*, 663.

[2] Recently, Lewis acid-mediated reactions have been especially focused upon because of their unique reactivities, selectivities, and mild conditions. Schinzer, D., Ed. *Selectivities in Lewis Acid Promoted Reactions*; Kluwer Academic Publishers: Dordrecht, 1989.

[3] Immobilization of $AlCl_3$ onto polymers or inorganic support materials has been reported, but the successful applications have been limited. (a) Neckers, D. C.; Kooistra, D. A.; Green, G. W. *J. Am. Chem. Soc.* **1972**, *94*, 9284. (b) Krzywicki, A.; Marczewski, M. *J. Chem. Soc., Faraday Trans. 1* **1980**, 1311. (c) Drago, R. S.; Getty, E. E. *J. Am. Chem. Soc.* **1988**, *110*, 3311. (d) Clark, J. H.; Martin, K.; Teasdale, A. J.; Barlow, S. J. *J. Chem. Soc., Chem. Commun.* **1995**, 2037. Montmorillonite-supported zinc chloride: (e) Clark, J. H.; Cullen, S. R.; Barlow, S. J.; Bastock, T. W. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1117. Immobilized trityl salts: (f) Mukaiyama, T.; Iwakiri, H. *Chem. Lett.* **1985**, 1363.

[4] Kobayashi, S. *Synlett* **1994**, 689.

[5] (a) Kobayashi, S.; Araki, M.; Ishitani, H.; Nagayama, S.; Hachiya, I. *Synlett* **1995**, 233. (b) Kobayashi, S.; Ishitani, H.; Nagayama, S. *Chem. Lett.* **1995**, 423. (c) Kobayashi, S.; Ishitani, H.; Nagayama, S. *Synthesis* **1995**, 1190.

[6] Purchased from Du Pont.

[7] As for metal Nafions, Hg: (a) Olah, G. A. Meidar, D. *Synthesis* **1978**, 671. (b) Saimoto, H.; Hiyama, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1985**, *56*, 3078. Si: (c) Murata, S.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 767. Cr, Ce: (d) Kanemoto, S.; Saimoto, H.; Oshima, K.; Nozaki, H. *Ibid.* **1984**, *25*, 3317. Al: (e) Waller, F. J. *Br. Polym. J.* **1984**, *16*, 239. Ta: (f) Olah, G. A.; Gupta, B.; Farina, M.; Felberg, J. D.; Ip, W. M.; Husain, A.; Karpeles, R.; Lammertsma, K.; Melhotra, A. K.; Trivedi, N. J. *J. Am. Chem. Soc.* **1985**, *107*, 7097. See also: (g) Waller, F. J. *Catal. Rev. Sci. Eng.* **1986**, *28*, 1.

[8] $ScCl_3\cdot6H_2O$ (519 mg, 2.0 mmol) and Nafion (5 g, 1.2 mequiv/g) were combined in acetonitrile (10 mL) under reflux for 40 h. After the mixture was cooled to rt, the polymer was filtered, washed with acetonitrile (20 mL × 3), and then dried under reduced pressure for 24 h. A trial to prepare Nafion−Sc from Sc_2O_3 and Nafion failed (only 0.1% Sc was included in the polymer (ICP analysis)).

[9] Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.

0022-3263/96/1961-2256$12.00/0

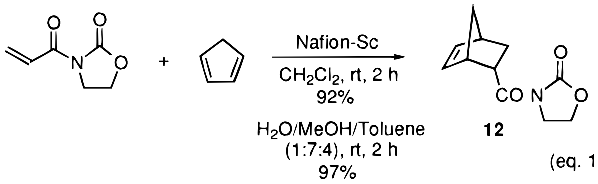
lation reactions using tetraallyltin,[10] it was shown that nonprotected sugars react directly to give the adducts, which are intermediates for the synthesis of higher sugars, in high yields. Nafion−Sc was also found to be effective in the allylation reactions of carbonyl compounds with tetraallyltin, and selected examples are listed in Table 1.[11] In every case, the reactions proceeded smoothly in both organic and aqueous solvents to afford the desired homoallylic alcohols in high yields. Not only aldehydes but also ketones worked well. Moreover, use of aqueous solvents enabled the reactions of nonprotected carbohydrates.[12] Salicylaldehyde and 2-pyridinecarboxaldehyde reacted with tetraallyltin to afford the corresponding homoallylic alcohols in good yields. These compounds react with the Lewis acids rather than the nucleophile under general Lewis acidic conditions.

Following is a typical experimental procedure for the Nafion−Sc-catalyzed allylation reaction in a batch system. To a mixture of Nafion−Sc (250 mg) and benzaldehyde (0.5 mmol) in H_2O/THF (1:9, 1.5 mL) was added tetraallyltin (0.5 mmol) in H_2O/THF (1:9, 1.5 mL) at rt. The mixture was stirred for 2 h at this temperature and then filtrated. The Nafion−Sc was washed with Et_2O, and the filtrates were combined. The solvent was removed under reduced pressure, and the crude product was chromatographed on silica gel to afford the corresponding homoallylic alcohol (91%).

Nafion−Sc was found to be effective in some other reactions (eqs 1−3). In these cases also, both organic and aqueous solvents could be used. In typical Lewis acid-mediated reactions such as Diels−Alder,[13] Friedel−Crafts acylation,[14] and imino Diels−Alder reactions,[5b,c] Nafion−Sc worked efficiently to afford the corresponding adducts in high yields.

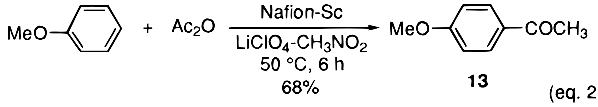
Nafion−Sc could be easily recovered and reused. The catalyst was recovered simply by filtration and washing with a suitable solvent, and the activity of the recovered Nafion−Sc was comparable to the fresh catalyst: in the reaction of benzaldehyde with tetraallyltin in H_2O−MeOH−toluene (1:7:4)[15] at rt, (1) 91% (15 h); (2) 81% (48 h); (3) 93% (40 h); in the reaction of 3-acryloyl-1,3-oxazolidin-2-one with cyclopentadiene at rt, (1) 92% (2 h); (2) 87% (2 h); (3) 91% (2 h).

Finally, Nafion−Sc was used in a flow system. Nafion−Sc was packed in a glass tube, and substrates were passed through the column using a motor pump.[16] Results of the reaction of benzaldehyde with tetraallyltin in aqueous solution are shown in Table 2. It is noted that even higher yields were obtained in the second, third, and fourth runs than in the first run.



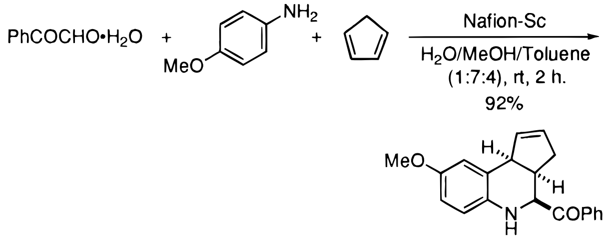
12

(eq. 1)



13

(eq. 2)

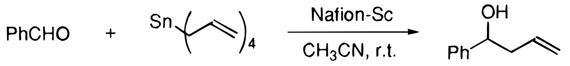


14

(eq. 3)

In summary, the first polymer-supported Sc catalyst has been prepared and the catalyst has been proved to be effective in several useful synthetic reactions. The polymer-supported Sc catalyst has all the advantages of $Sc(OTf)_3$ catalyst as far as we tested and has its own advantages originating from its polymer base; the simplification of product workup, separation, and isolation as well as reuse of the catalyst including reactions using flow reactors may provide an economical automation system.

Table 2. Nafion−Sc-Catalyzed Allylation Using a Flow System[a]



run	yield	run	yield
1	75	3	84
2	93	4	84

[a] See ref 16.

Acknowledgment. This work was partially supported by a Grant-in-Aid for Scientific Research from Ministry of Education, Science and Culture, Japan.

Supporting Information Available: Experimental procedures and characterization data (3 pages).

JO960003N

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[10] Hachiya, I.; Kobayashi, S. *J. Org. Chem.* **1993**, *58*, 6958.

[11] Nafion (NR-50) itself has much lower activity in this reaction. For example, only 19% yield of the adduct was obtained in the reaction of acetophenone with tetraallyltin.

[12] (a) Schmid, W.; Whitesides, G. M. *J. Am. Chem. Soc.* **1991**, *113*, 6674. (b) Kim, E.; Gordon, D. M.; Schmid, W.; Whitesides, G. M. *J. Org. Chem.* **1993**, *58*, 5500.

[13] (a) Yates, D.; Eaton, P. E. *J. Am. Chem. Soc.* **1960**, *82*, 4436. (b) Carruthers, W. *Cycloaddition Reactions in Organic Synthesis*; Pergamon Press: New York, 1990. (c) Kobayashi, S.; Hachiya, I.; Araki, M.; Ishitani, H. *Tetrahedron Lett.* **1993**, *34*, 3755.

[14] (a) Olah, G. A. *Friedel−Crafts Chemistry*; Wiley-Interscience: New York, 1973. (b) Heaney, H. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, p 733. (c) Kawada, A.; Mitamura, S.; Kobayashi, S. *Synlett* **1994**, 545. Cf. (d) Hachiya, I.; Moriwaki, M.; Kobayashi, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 2053.

[15] Kobayashi, S.; Hachiya, I.; Yamanoi, Y. *Bull Chem. Soc. Jpn.* **1994**, *67*, 2342.

[16] Nafion−Sc (2 g) and Sea Sand (2 g, 15−20 mesh) were combined, and the mixture was packed in a 6 mm glass tube. A carbonyl compound (0.5 mmol) and tetraallyltin (0.5 mmol) were dissolved in acetonitrile (4 mL) and passed through the column using a peristaltic pump (EYELA, MP-3).