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Polymer-supported formamides as reusable organocatalysts for allylation of aldehydes with allyltrichlorosilane

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New types of polymer-supported formamides have been synthesized from chloromethylated resins and formamides; it was found that the polymers worked well as organocatalysts in the allylation of aldehydes with allyltrichlorosilane to afford homoallylic alcohols in high yields; the polymers were easily recovered and reused several times without loss of activity.

Metal-free organocatalysts have been intensively studied from the viewpoint of their environmentally benign nature.[1] Compared with metal-catalyzed reactions, while there is no concern of contamination, waste and disposal of metals in reactions using organocatalysts, problems have been incurred in the separation of the catalysts from the products. Polymer-supported organocatalysts may address this issue; however, only a limited number of examples have been reported.[2] This is in remarkable contrast to versatile metal-containing polymer-supported catalysts reported, in the use of which, however, leaching of metals from polymer supports is still a serious problem in many cases.[3]

We have recently reported that aldehydes[4] or hydrazones[5] react with allyltrichlorosilanes in the presence of a Lewis base such as *N*,*N*-dimethylformamide (DMF) and hexamethylphosphoramide (HMPA) without any metal catalysts, to afford the corresponding homoallylic alcohols or homoallylic hydrazines in high yields with high diastereoselectivities.[6] In these reactions, the Lewis base acts as an organocatalyst, coordinating to the silicon atom of allyltrichlorosilanes to form reactive hypervalent silicates. Although it is easy to remove Lewis bases such as DMF and HMPA from the products by simple extraction, immobilization of these Lewis bases onto polymers would lead to more convenient and efficient reactions and processes. Herein, we report the first example of polymer-supported formamides[7] as recoverable and reusable organocatalysts.

To begin the study of polymer-supported organocatalysts, we prepared chloromethylated resins with several loadings from a cross-linked polystyrene and chloromethyl methyl ether in the presence of a catalytic amount of $SnCl_4$.[8] The loading levels of the resins ranged from 2.22 to 5.11 mmol g^{-1}. Commercially available Merrifield resins (0.63 and 1.20 mmol g^{-1}) were also used. Five resins were then reacted with *N*-methylformamide under basic conditions. It was revealed that the formamide function could not be introduced using K_2CO_3 as a base in THF, but that treatment of the chloromethylated resins with NaH in DMF gave the desired polymer-supported formamide (PS-Formamide **1**) in excellent yields (99% to quantitative). The precise structure of **1** was confirmed by ^{13}C Swollen Resin Magic Angle Spinning (SR-MAS) NMR[9,10] and IR analyses, and the loadings of **1** were determined by chlorine titrations. Polymer-supported *N*-formylpiperazine (PS-Formamide **2**) was also prepared according to a similar procedure.

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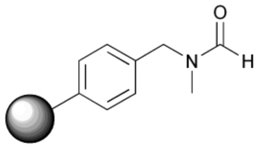
We then performed a model reaction of 3-phenylpropanal with allyltrichlorosilane using PS-Formamides **1** and **2**. Acetonitrile was chosen as an appropriate solvent, in which no reaction occurred in a control experiment. Several reaction conditions were examined, and the results are summarized in Table 1. In the initial experiments, PS-Formamide **1** was shown to be more reactive than **2** (entry 1 *vs.* 2). Next, we examined the effect of the loading levels of PS-Formamide **1**. It was found that the polymers with higher loadings showed higher activity, though the difference between 2.12 and 4.66 mmol g^{-1} loadings was not significant (entries 3–7). Moreover, the yield of the desired homoallylic alcohol was improved when the amounts of **1** and allyltrichlorosilane were increased (entries 8–10). Finally, it is noted that even a catalytic amount of **1** was shown to be effective at a longer reaction time or at a higher concentration (entries 11 and 12).


PS-Formamide **1**

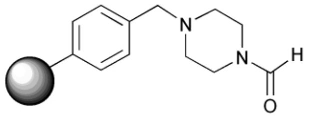
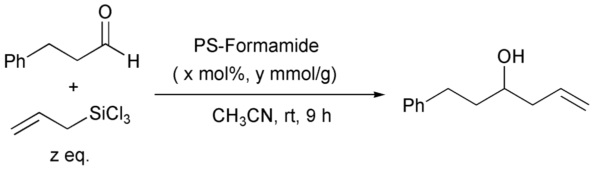

PS-Formamide **2**

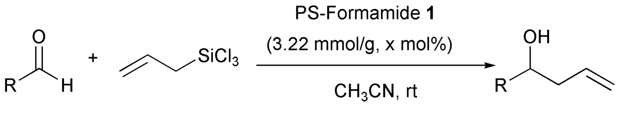
Table 1 Optimization of the reaction conditions



Entry	Polymer	*x*	*y*	*z*	Conc./M	Yield (%)
1	**1**	100	0.61	3	0.06	40
2	**2**	100	0.61	3	0.06	26
3	**1**	50	0.62	1.5	0.33	43
4	**1**	50	1.10	1.5	0.33	49
5	**1**	50	2.12	1.5	0.33	56
6	**1**	50	3.22	1.5	0.33	58
7	**1**	50	4.66	1.5	0.33	58
8	**1**	100	3.22	1.5	0.33	73
9	**1**	100	3.22	3	0.33	91
10	**1**	200	3.22	3	0.33	92
11[a]	**1**	10	3.22	3	0.33	54
12	**1**	10	3.22	3	0.66	79

[a] For 24 h.

Table 2 Allylation of aldehydes using PS-Formamide **1**



Entry	R	*x* (mol%)	Time/h	Yield (%)
1	$PhCH_2CH_2$	100	9	91
2	Ph	200	9	90
3	*p*-Tol	300	40	87
4	*p*-NO_2Ph	300	12	95
5	1-Naphtyl	300	34	92
6	PhCH=CH	300	12	66

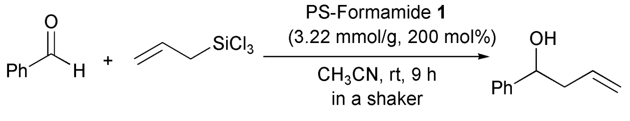
The allylation of other aldehydes was tested under the optimized conditions (Table 2). In all cases, the desired homoallylic alcohols were obtained in good to excellent yields, although 300 mol% of PS-Formamide **1** and longer reaction times were required to complete the reactions in some cases.

One advantage of polymer-supported catalysts is that the catalysts can be readily recovered and reused, even when excess amounts of catalysts are used as promoters in the reactions. For development of truly efficient polymer-supported catalysts, it is critical that recovery is simple and that the recovered catalysts retain their activity through multiple trials. We thus investigated the reusability of PS-Formamide **1**. In a preliminary attempt, the activity of the polymer-supported formamide decreased during multiple runs. It was observed that the shape of PS-Formamide **1** changed after repeated uses. At this stage, we suspected that physical destruction of the polymer matrix by magnetic stirring might occur to induce deactivation of the formamide. Thus, we used an automatic shaker instead of a magnetic stirrer to suppress the destruction of the polymer. It was interesting to find that shaking instead of stirring the reaction mixture was very effective, and that the activity of the polymer-supported formamide was retained even with multiple use to afford the desired homoallylic alcohols in high yields (Table 3). Recovery of the formamide was quantitative in all three runs, and no significant loss of activity of the formamide was observed. In addition, recovered samples of PS-Formamide **1** showed exactly the same ^{13}C NMR spectra as that of the freshly prepared **1**.

A typical experimental procedure is as follows: an aldehyde (0.3 mmol), allyltrichlorosilane (0.9 mmol) and PS-Formamide **1** (10–300 mol%) were combined in acetonitrile (1 cm^3). The mixture was stirred or shaken for 9–40 h at room temperature. For the reuse of **1**, shaking was recommended. After the reaction was complete, the mixture was quenched with water, and the catalyst **1** was recovered by filtration. A general work-up and purification by preparative TLC afforded the desired homoallylic alcohol.

In summary, we have synthesized new types of polymer-supported formamides as immobilized organocatalysts, which work well in allylation of aldehydes with allyltrichlorosilane. Easy and efficient recovery and reusability of the polymer-supported formamides have been demonstrated, and this may offset the use of the rather higher loadings of the formamides at this stage. It is noted that this report is the first example of successful usage of polymer-supported formamides as Lewis base-organocatalysts. Further investigations to survey the scope and limitations of the polymer-supported formamides as well as to develop other polymer-supported organocatalysts are in progress.

Table 3 Reuse of PS-Formamide **1**



Run	1st	2nd	3rd
Yield[a] (%)	90 (90)	86 (85)	86 (43)
Recovery (%)	Quant.	Quant.	Quant.

[a] Yields obtained using a magetic stirrer are given in parentheses.

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10 Polymer-supported formamide **1** was prepared by the following procedure: *N*-methylformamide (30 mmol) in DMF (30 cm^3) were added slowly to sodium hydride (30 mmol) in DMF (30 cm^3) and then chloromethylated resin (10 g, 11.0 mmol) was added. The reaction mixture was stirred for 12 h at room temperature and the reaction then stopped with water (15 cm^3). The polymer was filtered off and washed three times with methanol (15 cm^3), diethyl ether (15 cm^3), tetrahydrofuran (15 cm^3) and dichloromethane (15 cm^3) and then dried for 24 h under vacuum. ^{13}C SR-MAS NMR of **1** (100 MHz, CDCl$_3$, selected): δ 162.4 (C=O), 53.1 (CH$_2$), 33.9 (CH$_3$).