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Organic synthesis in solid media. Silica gel as an effective and reusable medium for the selective allylation of aldehydes with tetraallyltin

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Abstract—Wet silica gel promotes the chemoselective and almost complete allylation of aldehydes with 0.25–0.30 molar equivalents of tetraallyltin without an organic solvent, leaving no organotin compounds, requiring neither extraction nor chromatographic separation after the reaction, and enabling the repeated use of the silica gel.

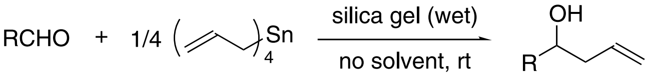
Solvent-free reactions using organic or inorganic solid media have been known for some time, and the environmentally friendly goal of making organic compounds without using solvents has come several steps closer in recent years.[1] Especially, silica gel has been effectively utilized in organic synthesis not only as a simple medium but also as a mild acid catalyst or an accelerator, which is easily separable from the reaction products.[2] We now report that silica gel can be an excellent and practical medium for the solvent-free allylation of aldehydes with tetraallyltin.[3–6]

The allylation of carbonyl compounds, especially aldehydes, is an extremely useful transformation in synthetic organic chemistry. Allylic stannanes have received considerable attention in this respect and their addition to aldehydes has been achieved by employing heat, high pressure, or a Lewis acid promoter.[7] More recently, the allylation of carbonyl compounds with tetraallyltin without a Lewis acid catalyst in acidic aqueous media[5,8] or even in neutral polar solvents like aqueous methanol[9,10] and ionic liquids[11] has been reported. However, there is no example using solid media in the absence of organic solvents for such transformations.

We found that the use of wet silica gel without a solvent is exceptionally effective for this transformation. Simply mixing and stirring aldehydes and 0.25 molar equivalents of tetraallyltin with wet silica gel at room temperature for 1 h produced the corresponding homoallylic alcohols in almost quantitative yields (Scheme 1).

The use of 300–400 mg of silica gel[12] was found to be sufficient to realize highly effective allylation of benzaldehyde in a 1 mmol scale experiment as shown in Table 1. When the reaction was performed under neat conditions without silica gel as the control experiment, a significant amount of by-products such as benzyl alcohol and 1-phenyl-3-butenone was produced (entry 1) via the Meerwein–Ponndorf–Verley–Oppenauer process (Scheme 2). The reaction in the presence of water completely suppressed the side reaction but the yield of the desired product was low (entry 2) and the use of silica gel in an organic solvent such as dichloromethane or tetrahydrofuran hardly afforded the allylated product (entry 8).

Other inorganic and organic solids examined as a medium for the allylation of benzaldehyde under solvent-free conditions were found to be less effective than silica gel as the results show in Table 2. The notable low yields obtained by using organic polymers might be



Scheme 1. Solvent-free allylation of aldehydes with tetraallyltin in silica gel.

Keywords: solvent-free reaction; solid media; allylation; homoallylic alcohol; environmentally-benign method; green chemistry.

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Table 1. Allylation of benzaldehyde (1 mmol) with tetraallyltin (0.25 mmol)

Entry	Silica gel (mg)[a]	Solvent	Yield (%)[b]
1	None	None	43[c]
2[d]	None	None	33
3	100	None	63[e]
4	200	None	87[e]
5	300	None	94[e]
6	400	None	95 (99)[f]
7	400[g]	None	55[e]
8	400	THF	3

The reaction was carried out at room temperature for 1 h.

[a] Commercial silica gel was directly used as 'wet silica gel' unless otherwise noted.

[b] Isolated yield of the allylated product.

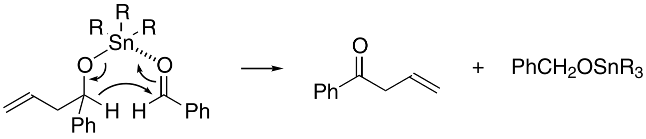
[c] Benzyl alcohol (10%) and 1-phenyl-3-butenone (12%) were also isolated.

[d] H_2O (1 mmol) was added.

[e] The by-products were also detected.

[f] GC yield.

[g] Silica gel dried under vacuum at room temperature was used.



Scheme 2. Formation of the by-products.

Table 2. Allylation of benzaldehyde in various solid media

Entry	Medium	Yield (%)[a]
1	Zeolite Y	73
2	Molecular sieves 4A	79
3	See sand	72
4	Celite	78
5	Acidic alumina	62
6	Chitin	19
7	Cellulose	29
8	Poly(vinyl chloride)	11
9	Poly(vinyl alcohol)	14
10	Poly(ethylene oxide)	2
11	Poly(styrene-co-divinylbenzene)	13
12	Poly(acrylic acid)	35

The reaction was carried out using benzaldehyde (1 mmol) and tetraallyltin (0.25 mmol) in solid media (400 mg, containing ca. 1 equiv. of water) at room temperature for 1 h.

[a] GC yield.

ascribable to the difficulty in mechanically stirring the reaction mixture which became sticky (entries 6–12). Also, other allylating reagents such as allyltributyltin, allyltrimethylsilane, and tetraallylsilane turned out to be totally useless under the silica gel-mediated conditions.

A typical procedure for the allylation of aldehydes in wet silica gel follows. To commercial silica gel (Merck, Kieselgel 60, 70–230 mesh, 400 mg) were successively added benzaldehyde (106 mg, 1.0 mmol) and tetraallyltin (97%, 73 mg, 0.25 mmol) and the mixture was stirred or rotated for 1 h at room temperature. The product-containing silica gel was transferred to a short column and eluted with ether (10 ml). Evaporation of the eluate gave 1-phenyl-3-buten-1-ol (141 mg, 95%), the ^{1}H NMR and GC–MS spectra of which indicates a purity of >99%.

As can be seen from Table 3, a variety of aldehydes were cleanly reacted with 0.25 equiv. of tetraallyltin to give the corresponding homoallylic alcohols in good to excellent isolated yields. Practically, however, the use of a small excess of tetraallyltin is recommended so as not to leave unreacted aldehydes, which allows almost pure allylated products to be obtained simply by ether-elution, because any allylstannane derivatives may be hydrolyzed[13] during the reaction and work-up stage affording gaseous 1-propen and ether-insoluble inorganic tin compounds. Thus, a quantitative conversion was accomplished in a 100-mmol scale experiment using 30 mmol of tetraallyltin (entry 3). In the case of pivalaldehyde (entry 10), the primary product, tin alkoxide of the homoallylic alcohol, was found to be fairly stable to the hydrolysis probably because of the steric bulkiness. Simple elution with ether afforded the homoallylic alcohol only in 42% yield; therefore, a drop of acetic acid was added at the work-up stage to improve the yield via the complete acetolysis. The reaction of phenylglyoxal monohydrate required 0.5 equivalents of tetraallyltin to obtain a satisfactory yield, but it did not produce any trace amount of the corresponding keto-allylated compounds as by-products (entry 12). In most cases, commercial silica gel can be directly used as 'wet silica gel' affording almost comparable product yields.

Table 3. Silica gel-promoted allylation of aldehydes under solvent-free conditions

Entry	Aldehyde	Time (h)	Yield (%)[a]
1	PhCHO	1	95
2	4-MeO-C_6H_4CHO	1	95[b]
3[c]	4-MeO-C_6H_4CHO	1	99
4	4-Me-C_6H_4CHO	1	90
5	4-Cl-C_6H_4CHO	1	90
6	4-NC-C_6H_4CHO	1	93
7	4-NO_2-C_6H_4CHO	1	92
8	*n*-C_6H_{13}CHO	1	96
9	*c*-C_6H_{11}CHO	1	95
10	*t*-BuCHO	1	77[d,e]
11	PhCH(Me)CHO	1	95[f]
12	PhC(O)CHO·H_2O	5 (1)[g]	58 (84)[g]

The reaction was carried out using aldehyde (1 mmol) and tetraallyltin (0.25 mmol) in wet silica gel (400 mg) at room temperature unless otherwise noted.

[a] Isolated yield.

[b] NMR yield.

[c] The reaction was carried out in 100 mmol scale using tetraallyltin (30 mmol) and silica gel (40 g).

[d] A drop of acetic acid was added at the work-up stage.

[e] GC yield.

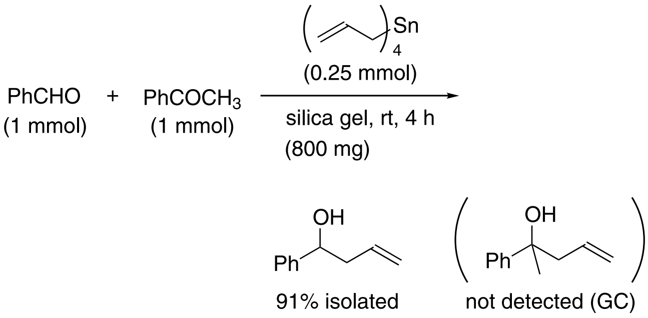
[f] A diastereomeric mixture (64:36).

[g] Tetraallyltin (0.5 mmol) was used.

The present allylation reaction was found to be highly chemoselective for aldehydes.[8] Ketones hardly reacted with tetraallyltin under these conditions.[10] For example, benzaldehyde was exclusively allylated in the presence of acetophenone as shown in Scheme 3.

A possible reaction pathway is shown in Figure 1. As can be expected from the reaction pathway, no trace of the tin ion (<10 ppm) was detected by ICP emission analysis of the residue of the eluate,[14] and the tin compound remains on the silica gel probably as tin hydroxide or siloxide. Silica gel used for the reaction was washed with ether, dried, treated with one equivalent of water, and successfully reused several times for the next round of reactions as shown in Table 4.

In conclusion, we have demonstrated the utility of silica gel as a reaction medium for the allylation of aldehydes. The protocol is quite convenient and environmentally friendly as (1) neither extraction nor chromatographic separation is necessary, (2) no organotin compounds remain after the reaction, and (3) the silica gel can be recovered and reused several times without serious loss of its activity.



Scheme 3. Chemoselectivity of the allylation.

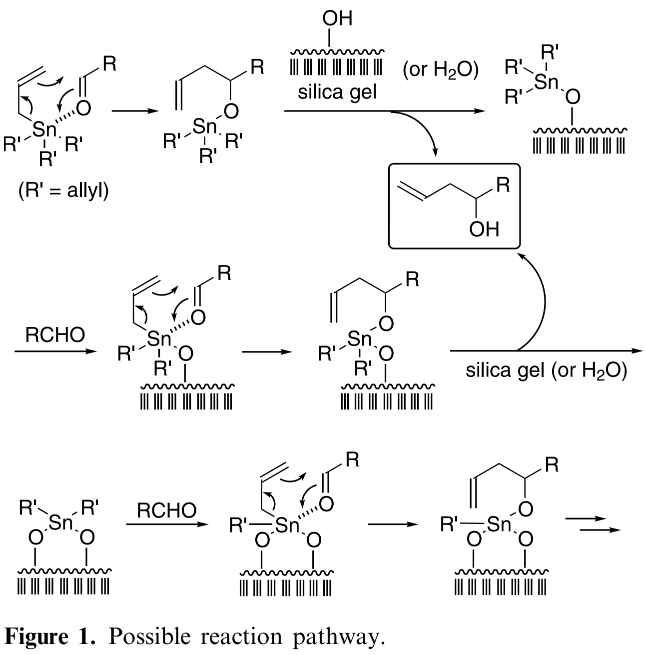


Figure 1. Possible reaction pathway.

Table 4. Reuse of silica gel

Run	Yield (%)[a]	Run	Yield (%)[a]
1	96	4	95
2	99	5	91
3	99	6	89

The reaction was carried out using benzaldehyde (1 mmol) and tetraallyltin (0.25 mmol) in silica gel (400 mg in the first run) at room temperature for 1 h.

[a] GC yield.

Acknowledgements

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13. The half-life of tetraallyltin in commercial silica gel in the absence of aldehydes was checked by GC–MS to be ca. 2.5 h.
14. We are grateful to Tosoh Analysis and Research Center, Japan for the ICP emission analysis.