

Simple and Clean Synthesis: Tin-mediated Allylation of Carbonyl Compounds in Water

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Tin-mediated allylation of aldehydes or ketones in distilled water gives rise to the corresponding homoallyl alcohols in high yield without assistance such as heat, supersonic and acidic media.

Keywords carbonyl compounds, tin-catalyzed allylation, water

Introduction

In new millennium, organic chemists confront with a great challenge, that is, to find novel methodologies in organic synthesis in order to reduce and finally eliminate the impacts of hazardous organic solvents and flotsam on the environment. As a result, the chemists have been pursuing the simple and efficient synthetic method and searching for safe and harmless reaction solvent for a long time. In this area, organic reactions in aqueous media have attracted considerable interests because water is considered to be a safe and environmentally benign solvent.¹ Allylations of aldehydes and ketones to give homoallylic alcohols have extensively been studied among these reactions.² The reaction can be achieved by the use of metals such as copper, manganese,³ aluminum,⁴ lead, tin,⁵ magnesium,⁶ zinc, indium,⁷ or organometallics compounds such as diallylmercury, allylmercury bromide,⁸ allyltributylstannanes⁹ and tetraallylgermane.¹⁰ Also, all of these reactions occurred on unprotected carbohydrates in protic media under mild condition. Nevertheless in most cases it is necessary to carry out the reaction in acidic co-reagents such as ammonium chloride, hydrobromic acid

and co-solvent such as mixture of THF and water. Herein, we wish to report tin-mediated allylations of aldehydes and ketones in distilled water.

Experimental

Chemicals

Zinc, aluminum, magnesium and iron were all purchased from the second Chemical Reagent Factory of Shanghai. Other chemicals were purchased from the first Chemical Reagent Factory of Shanghai. The crude product was purified by column chromatography with silica gel and then characterized by IR (Perkin-Elmer, 2000FTIR), ¹H NMR (Bruker DMX 500) and MS-GC (HP 5890(II)/HP5972, EI) spectroscopies.

Procedure

To a mixture of carbonyl compound (1 mmol) and allyl bromide (2 mmol) in distilled water (5 mL) was added tin powder (1 mmol). The mixture was stirred at room temperature for 13 h. The reaction was quenched by aqueous 1 mol/L HCl and extracted with ethyl ether. The extract was dried over anhydrous magnesium sulfate and the organic solvent was removed by rotor-vapor under vacuum. The residue was purified by column chromatography to afford pure product, which was characterized by ¹H NMR spectra.

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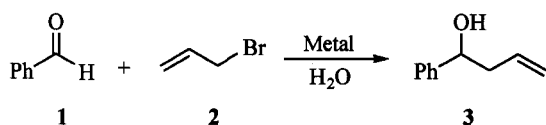
Received February 28, 2002; revised April 29, 2002; accepted June 5, 2002.

Project supported by the National Natural Science Foundation of China (No. 50073021) and the Natural Science Foundation of Anhui Province (No. 01046301).

Results and discussion

Here we report a useful synthetic procedure with great ease and efficiency in distilled water, without the help of either acidic co-reagent (*e. g.* HBr, AcOH), organic co-solvent (*e. g.* THF, Et₂O) or heat and sonication, which are necessary in the case of several other methods.^{3,10} To start this experiment, a mixture of benzaldehyde, allyl bromide, and zinc powder in 5 mL of distilled water was stirred at room temperature for 24 h. TLC measurement of the ether extract clearly showed that there was a new spot corresponding to the desired allylation product. Subsequently, ¹H NMR measurement of the crude reaction mixture showed that there was about 20% of allylation product (Entry 5, Table 1). The corresponding reactions with other metals were studied and the results are shown in Table 1.

Table 1 Allylation of benzaldehyde mediated by various metals



Entry	Metal ^a (1 mmol)	Yield (%) ^b /Time (h)
1	Fe	polymerization
2	Mg	0
3	Al	0
4	Bi	35/15
5	Zn	20/24
6	Sn	94/13

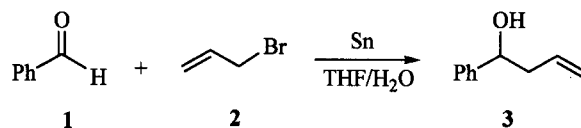
^a All metals are powder. ^b Determined by ¹H NMR spectra.

The result showed that polymerization occurred when reaction was mediated by iron (Entry 1, Table 1). When mediated by either magnesium or aluminum, the allylations failed. (Entries 2, 3, Table 1). In comparison with other metals, tin-mediated allylation proceeded smoothly to afford the allylation product in a higher yield (Entry 6, Table 1).

We also examined in great detail the effect of the solvent system on this tin-mediated reaction by changing the ratio of water and THF. The results are listed in Table 2. It was found that the amount of THF had no remarkable effect on this reaction. Moreover, it means that tin-mediated allylations of various aldehydes and ketones can occur smoothly in water with help of either organic solvent

or sonication. Relatively, tin is considered to be a safe and available metal.¹¹ Actually, there were some reports about tin-mediated allylation previously.³ However, all of these reactions were carried out in acidic conditions such as hydrobromic acid, saturated ammonium chloride with the help of sonication or co-solvent such as a mixture of water and THF.

Table 2 Tin-mediated allylation of benzaldehyde in co-solvents with different ratios of water and THF

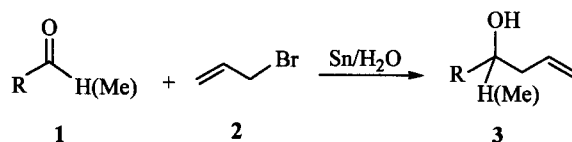


Entry	Solvent (THF %, V/V)	Yield (%) ^a
1	2	94
2	5	98
3	15	97
4	20	97

^a Determined by ¹H NMR spectra.

Subsequently, a variety of aldehydes and ketones were tested with this allylation method (Scheme 1). The summary of the reactions is listed in Table 3.

Scheme 1



In terms of Table 3, most of the reactions were carried out smoothly in high yield and the side reactions such as reduction and coupling were not observed (Entries 1—6, Table 3). Generally, reaction condition is mild enough not to affect the groups that attached in aromatic ring (Entries 4—6, 8, Table 3). Allylation of acetophenone also gave the corresponding product in about 40% yield despite its steric hindrance (Entry 7, Table 3). It is noted that allylation of *N,N*-dimethylaminobenzaldehyde also gave the corresponding production in about 33% yield under this condition (Entry 8, Table 3), whereas it did not occur at all in neutral aqueous media when Zn, Bi or Al was used as mediator respectively. Particularly, the allylations of aliphatic aldehydes or ketones that were deemed to be unreactive could be also al-

lylated under this condition to give the corresponding products in satisfactory yield (Entries 10–11, Table 3).

Table 3 Allylation reaction mediated by tin in water^a

Entry	Substrate	Time (h)	Product	Yield (%) ^b
1	PhCHO (1a)	13	3a	93 (89)
2	2-NaPhCHO (1b)	18	3b	95 (92)
3	Piperonal (1c)	17	3c	95 (91)
4	4-MeO-PhCHO (1d)	16	3d	95 (91)
5	4-ClPhCHO (1e)	13	3e	95 (90)
6	4-MePhCHO (1f)	15	3f	82 (79)
7	PhCOMe (1g)	18	3g	40 (35)
8	4-Me ₂ N-PhCHO (1h)	12	3h	33 (29)
9	Furaldehyde (1i)	13	3i	90 (85)
10	CH ₃ COC ₂ H ₅ (1j)	7	3j	40 (36)
11	HOC(CH ₂) ₃ CHO (1k)	8	3k	60 (56)

^a Reaction conditions: V [aldehyde(ketone)]: V (allyl bromide): V (tin) = 1:2:1, at room temperature in 5 mL of distilled water. The amount of tin powder effects the yield, some aldehydes (**1a**, **1b**, **1c**, **1d**, **1e**, **1f**) can be allylated quantitatively when 1.2 mmol of tin powder was used. ^b Yield were determined by ¹H NMR spectra, data in parentheses are isolated yield.

Conclusion

A high-yielding, efficient and clean synthetic method for homoallyl alcohols in distilled water was developed. The advantage of this methodology is that the allylation for the aldehydes and ketones, which are usually sensitive to acidic condition, also underwent smoothly. As a result, we have made an approach to carry out organic reactions in water avoiding the pollution from organic solvent.

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- IR (Perkin-Elmer, 2000FTIR), NMR (Bruker DMX500) and MS-GC (HP 5890(II)/HP5972, EI) spectral data are as follows:
1-Phenyl-3-buten-1-ol (**3a**)¹³ ¹H NMR (CDCl₃, 500 MHz) δ : 2.40 (t, $J = 7.13$, 6.59 Hz, 2H), 2.91–2.98 (br, 1H), 4.57 (t, $J = 6.59$ Hz, 1H), 5.02–5.04 (m, 1H), 5.03–5.06 (m, 1H), 5.66–5.74 (m, 1H), 7.29–7.70 (m, 5H); ¹³C NMR (CDCl₃, 125.7 MHz) δ : 43.64, 73.40, 117.94, 125.92, 127.41, 128.30, 134.55,

143.99; IR (film) ν : 3383, 3075, 1641 cm^{-1} ; MS m/z (%): 148 (M^+).

1-(2-Naphthaldehyde)-3-buten-ol (**3b**)¹³ ¹H NMR (CDCl_3 , 500 MHz) δ : 2.15—2.34 (br, 1H), 2.56 (q, $J = 5.13, 7.70$ Hz, 2H), 4.80 (t, $J = 7.70$ Hz, 1H), 5.11—5.12 (m, 1H), 5.13—5.17 (m, 1H), 5.75—5.83 (m, 1H), 7.47—7.42 (m, 3H), 7.76 (s, 1H), 7.79—7.80 (m, 3H); ¹³C NMR (CDCl_3 , 125.7 MHz) δ : 43.88, 73.55, 118.69, 124.17, 124.68, 125.98, 126.29, 127.85, 128.13, 128.37, 133.10, 133.40, 134.53, 141.40; IR (film) ν : 3386, 3057, 1640 cm^{-1} ; MS m/z (%): 198 (M^+).

1-(3,4-Methylenedioxyphenyl)-3-buten-1-ol (**3c**)¹³ ¹H NMR (CDCl_3 , 500 MHz) δ : 2.42 (t, $J = 6.36, 7.78$ Hz, 2H), 2.48—2.57 (br, 1H), 4.57 (t, $J = 6.36$ Hz, 1H), 5.07 (m, 1H), 5.09 (m, 1H), 5.70—5.78 (m, 1H), 5.89 (s, 2H), 6.70—6.76 (m, 2H), 6.81 (s, 1H); ¹³C NMR (CDCl_3 , 125.7 MHz) δ : 43.79, 73.35, 101.00, 106.51, 108.06, 118.14, 119.31, 134.59, 138.17, 146.89, 147.74; IR (film) ν : 3386, 3075, 1640 cm^{-1} ; MS m/z (%): 192 (M^+).

1-(4-Methoxyphenyl)-3-buten-1-ol (**3d**)¹³ ¹H NMR (CDCl_3 , 500 MHz) δ : 2.45 (q, $J = 6.58, 7.13$ Hz, 2H), 2.77—2.87 (br, 1H), 3.75 (s, 3H), 4.60 (t, $J = 6.58$ Hz, 1H), 5.06—5.08 (m, 1H), 5.08—5.11 (m, 1H), 5.71—5.80 (m, 1H), 6.84 (d, $J = 8.78$ Hz, 2H), 7.22 (d, $J = 8.78$ Hz, 2H); ¹³C NMR (CDCl_3 , 125.7 MHz) δ : 43.62, 76.03, 78.71, 113.69, 117.75, 127.14, 134.76, 136.26, 158.90; IR (film) ν : 3418, 3074, 1640 cm^{-1} ; MS m/z (%): 178 (M^+).

1-(4-Chlorophenyl)-3-buten-1-ol (**3e**)¹³ ¹H NMR (CDCl_3 , 500 MHz) δ : 2.40 (t, $J = 6.58, 12.75$ Hz, 2H), 3.05—3.15 (br, 1H), 4.58 (t, $J = 6.58$ Hz, 1H), 5.06—5.07 (m, 1H), 5.09 (m, 1H), 5.66—5.75 (m, 1H), 7.19 (d, $J = 8.23$ Hz, 2H), 7.26 (d, $J = 8.23$ Hz, 2H); ¹³C NMR (CDCl_3 , 125.7 MHz) δ : 43.61, 72.69, 118.41, 127.30, 128.43, 133.01, 134.01, 142.37; IR (film) ν : 3383, 3077, 1641 cm^{-1} ; MS m/z (%): 182 (M^+).

1-(4-Methylphenyl)-3-buten-1-ol (**3f**)¹³ ¹H NMR (CDCl_3 , 500 MHz) δ : 2.32 (s, 3H), 2.27—2.36 (br, 1H), 2.45 (q, $J = 6.41, 7.26$ Hz, 2H), 4.62 (t, $J = 6.41$ Hz, 1H), 5.07—5.08 (m, 1H), 5.09—5.12 (m, 1H), 5.71—5.79 (m, 1H), 7.12 (d, $J = 8.12$ Hz, 2H), 7.19 (d, $J = 8.12$ Hz, 2H); ¹³C NMR (CDCl_3 , 125.7 MHz) δ : 21.23, 43.80, 73.72, 118.17, 125.92, 129.15, 134.76, 137.18, 141.07; IR (film) ν : 3386, 3070, 1640 cm^{-1} ; MS m/z (%): 162 (M^+).

1-Methyl-1-phenyl-3-buten-1-ol (**3g**)¹⁴ ¹H NMR (CDCl_3 , 500 MHz) δ : 1.58 (s, 3H), 2.14—2.24 (br,

1H), 2.53 (q, $J = 8.23, 13.72$ Hz, 1H), 2.71 (q, $J = 6.59, 13.72$ Hz, 1H), 5.13—5.14 (m, 1H), 5.15—5.17 (m, 1H), 5.66 (m, 1H), 7.27 (t, $J = 7.13$ Hz, 1H), 7.37 (t, $J = 7.13, 7.68$ Hz, 2H), 7.47 (d, $J = 7.68$ Hz, 2H); ¹³C NMR (CDCl_3 , 125.7 MHz) δ : 30.30, 48.65, 73.82, 119.56, 124.96, 126.79, 128.34, 133.89, 147.83; IR (film) ν : 3439, 3075, 1639 cm^{-1} ; MS m/z (%): 162 (M^+).

1-(4-N,N-Dimethylaminophenyl)-3-buten-1-ol (**3h**)¹⁵ ¹H NMR (CDCl_3 , 500 MHz) δ : 1.78—2.11 (br, 1H), 2.37 (t, $J = 6.58, 7.96$ Hz, 2H), 2.81 (s, 6H), 4.50 (t, $J = 6.58$ Hz, 1H), 4.96—4.97 (m, 1H), 4.99—5.03 (m, 1H), 5.63—5.71 (m, 1H), 6.62 (d, $J = 8.23$ Hz, 2H), 7.10 (d, $J = 8.23$ Hz, 2H); ¹³C NMR (CDCl_3 , 125.7 MHz) δ : 41.09, 43.69, 73.42, 113.03, 117.99, 127.09, 132.64, 135.19, 150.20; IR (film) ν : 3383, 3074, 1639 cm^{-1} ; MS m/z (%): 191 (M^+).

1-(2-Furaldehyde)-3-buten-1-ol (**3i**)¹⁶ ¹H NMR (CDCl_3 , 500 MHz) δ : 1.91—2.17 (br, 1H), 2.65 (q, $J = 7.13, 5.94$ Hz, 2H), 4.76 (t, $J = 7.13$ Hz, 1H), 5.14—5.16 (m, 1H), 5.17—5.21 (m, 1H), 5.77—5.85 (m, 1H), 6.26 (d, $J = 3.30$ Hz, 1H), 6.34 (q, $J = 3.30, 1.65$ Hz, 1H), 7.38 (d, $J = 1.65$ Hz, 1H); ¹³C NMR (CDCl_3 , 125.7 MHz) δ : 40.32, 67.18, 106.34, 110.38, 118.82, 133.93, 142.23, 156.27; IR (film) ν : 3382, 3078, 1643 cm^{-1} ; MS m/z (%): 138 (M^+).

3-Methyl-5-hexen-3-ol (**3j**)¹⁶ ¹H NMR (CDCl_3 , 500 MHz) δ : 0.92 (t, $J = 7.41$ Hz, 3H), 1.16 (s, 3H), 1.50 (q, $J = 7.41$ Hz, 2H), 2.22 (d, $J = 7.41$ Hz, 2H), 2.23—2.71 (br, 1H), 5.10—5.13 (m, 1H), 5.13—5.15 (m, 1H), 5.82—5.90 (m, 1H); ¹³C NMR (CDCl_3 , 125.7 MHz) δ : 8.93, 26.90, 34.99, 46.52, 73.26, 119.36, 134.84; IR (film) ν : 3417, 3077, 1640 cm^{-1} ; MS m/z (%): 114 (M^+).

4,8-Dihydroxy-1,10-undecadiene (**3k**) ¹H NMR (CDCl_3 , 500 MHz) δ : 1.43—1.55 (m, 6H), 2.18 (q, $J = 7.14, 7.68$ Hz, 4H), 2.63—2.68 (br, 2H), 3.63—3.67 (m, 2H), 5.08—5.10 (m, 2H), 5.11—5.12 (m, 2H), 5.78—5.87 (m, 2H); ¹³C NMR (CDCl_3 , 125.7 MHz) δ : 22.35, 37.21, 42.69, 71.32, 118.34, 135.69; IR (film) ν : 3355, 3076, 1641 cm^{-1} ; GC-HRMS calcd 166.1358 (M - H_2O), found 166.1346.

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