

Novel Ultrasonication-assisted Carbonyl Allylation Mediated by SnCl_2 in Water

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(Received December 10, 2003; CL-031210)

Under ultrasonication, it was found that SnCl_2 could efficiently mediate the aqueous Barbier reactions between carbonyl compounds and allyl bromide to give the corresponding homoallylic alcohols in high yields without using any Lewis acid catalyst.

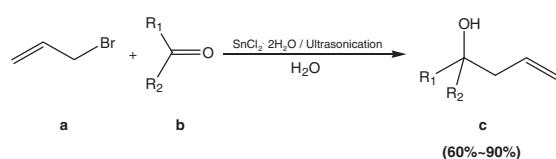
Allylation of carbonyl compounds to produce homoallylic alcohols plays a very important role in synthetic organic and pharmaceutical chemistry. Therefore numerous reagents and methods have been developed to prepare synthetically useful homoallylic alcohols.¹

Organometallic reactions in aqueous media have recently found considerable application in organic synthesis because they offer simple operation and avoid using dry organic solvents. The discovery in the past decade that the allylation of carbonyl compounds could be achieved in aqueous media through a Barbier-type reaction² has drawn much interest. So far numerous metals have been reported to be effective in mediating the aqueous Barbier reaction to prepare the corresponding homoallylic alcohols. The metals include antimony,³ aluminium,⁴ indium,⁵ bismuth,⁶ lead,⁷ magnesium,⁸ zinc,⁹ and tin.¹⁰ Although good yields can often be obtained in a part of these reactions, the use of zero-valent metals always causes some operational problems because the metal-mediated allylation is a heterogeneous reaction in water. For instance, it is often difficult to stir the reaction mixture when a large amount of metal is used. Furthermore, metal oxide or hydroxide precipitation on the surface of metal may slow or stop the reaction.¹¹

Water-soluble reductive metal salts such as SnCl_2 can solve the above operational problem when the salt applied to the aqueous Barbier reaction. However, it was reported that SnCl_2 can not efficiently mediate the coupling between allyl halide and a carbonyl compound in water stirred at room temperature,¹² unless some TiCl_3 ,¹¹ Cu(I) ,^{12,13} or Pd(II) ¹⁴ catalyst was added to the reaction. So, it is inevitable that some substrates sensitive to acid can rearrange or decompose when the Lewis acid catalysts are used in the reactions. Therefore, a new method needs to be developed to overcome the problem.

In the present study, we find that SnCl_2 can efficiently mediate carbonyl allylation in water without using any catalyst under ultrasonication (Scheme 1).¹⁵

Typical procedures for the allylation are as follows: To a



Scheme 1.

mixture of carbonyl compound (10 mmol) and allyl bromide (15 mmol) in water (10 mL), $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (20 mmol) was added. The mixture was vigorously stirred at room temperature for 2 min, and the mixture was radiated by ultrasonication for several hours. Ultrasonication was carried out at room temperature in an ultrasonic cleaner bath, which delivered a 40 kHz wave, with a fixed electrical power of 100 W. Then, the mixture was extracted with ether (3 × 20 mL). The combined ether extract was washed with brine (2 × 10 mL). Then, the organic layer was dried over anhydrous sodium sulfate and was filtered, and evaporated. The residue was purified by flash chromatography over silica gel. The structure of products was identified by IR, ¹H NMR, and ¹³C NMR spectra.

The experimental results are summarized in Table 1.

From Table 1, it can be seen that carbonyl allylation only

Table 1. Carbonyl allylation mediated by SnCl_2 in water under ultrasonication

Entry	Substrates	Products	Number	Time/h	Yield/% ^a
1	CH_3CHO		1c	2	82
2	$\text{i-C}_4\text{H}_9\text{CHO}$		2c	2	80
3	$\text{n-C}_6\text{H}_{13}\text{CHO}$		3c	2.5	78
4	$\text{C}_6\text{H}_5\text{CHO}$		4c	2	90
5	$\text{CH}_3\text{C}_6\text{H}_4\text{CHO}$		5c	3	75
6	$\text{C}_6\text{H}_5\text{Cl-CHO}$		6c	3	80
7	$\text{C}_3\text{H}_5\text{CO}$		7c	3	75
8	$\text{C}_3\text{H}_5\text{CH}_2\text{CO}$		8c	2.5	72
9	$\text{C}_5\text{H}_8\text{CO}$		9c	4	60
10	$\text{C}_7\text{H}_{12}\text{CO}$		10c	3	85
11	$\text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{CO}$		11c	3.5	60
12	$\text{C}_3\text{H}_5\text{CH}_2\text{CO}_2\text{CH}_3$		12c	3	70

a: Isolated yield.

mediated by SnCl_2 without Lewis acid catalyst (some substrates sensitive to it) in aqueous media usually in a high yield when ultrasonic radiation employed. Compared to the previously reported allylation mediated by zero-valent metals,³⁻¹⁰ there is no need to use any organic cosolvent and overcomes the difficult problem about stir (metal oxide or hydroxide precipitation on the surface of metal). Both aldehydes and ketones can be allylated under the condition. Also, both aliphatic and aromatic carbonyl compounds are reactive. Compared with ketones, aldehydes are easier to be allylated generally. Interestingly, ester-containing substrate (Entry 12) can be successfully allylated without making ester changed. Also, 2-chlorobenzaldehyde (Entry 6) can be smoothly allylated, but chloro group keeping stable.

In conclusion, the present research has succeeded in the novel carbonyl allylation reaction mediated by SnCl_2 without Lewis acid catalyst under ultrasonic radiation employed. The reaction which avoid affecting substrates sensitive to acid is very simple and efficient to be run, which provides a rapid and operationally simple method for the synthesis of homoallylic alcohols in high yields.

References and Notes

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- 15 Representative spectroscopic data for compound **3c**: IR: (cm^{-1}) 3358, 3077, 2930, 2858, 1641, 1466. ^1H NMR (300 MHz, CDCl_3): δ 5.76–5.90 (m, 1H), 5.10–5.17 (m, 2H), 3.60–3.68 (m, 1H), 2.26–2.34 (m, 1H), 2.10–2.20 (m, 1H), 1.89 (s, 1H), 1.30–1.46 (m, 10H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 134.9, 117.9, 70.7, 41.9, 36.8, 31.8, 29.3, 25.6, 22.5, 14.0. Compound **8c**: IR: (cm^{-1}) 3390, 3077, 1640, 1149. ^1H NMR (300 MHz, CDCl_3): δ 5.82–5.91 (m, 1H), 5.09–5.16 (m, 2H), 2.22 (d, J = 7.9 Hz, 2H), 1.65 (br, 1H), 1.51 (q, J = 7.5 Hz, 2H), 1.16 (s, 3H), 0.92 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 134.1, 118.4, 72.3, 45.7, 34.2, 26.1, 8.1. Compound **9c**: IR: (cm^{-1}) 3391, 3076, 2960, 2874, 1640, 1436, 1194. ^1H NMR (300 MHz, CDCl_3): δ 5.83–5.97 (m, 1H), 5.11–5.18 (m, 2H), 2.35 (d, J = 8.4 Hz, 2H), 1.82 (br, 1H), 1.61–1.76 (m, 8H); ^{13}C NMR (75 MHz, CDCl_3): δ 134.5, 118.6, 81.3, 45.8, 39.4, 23.8. Compound **12c**: IR: (cm^{-1}) 3513, 3078, 2981, 1717, 1641, 1371, 1195. ^1H NMR (300 MHz, CDCl_3): δ 5.80–5.90 (m, 1H), 5.05–5.14 (m, 2H), 4.18 (q, J = 7.2 Hz, 2H), 3.45 (s, 1H), 2.39–2.55 (q, J = 15.6 Hz, 2H), 2.29 (d, J = 7.5 Hz, 2H), 1.25–1.32 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 172.9, 133.6, 118.4, 70.6, 60.5, 46.4, 44.3, 26.7, 14.1.