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Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Published online: 19 Aug 2006.

To cite this article: Jun Wang & Gu Yuan (2006) Synthesis of Homoallylic Alcohols From Ketones in Water, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 36:3, 401-405, DOI: 10.1080/00397910500377560

To link to this article: http://dx.doi.org/10.1080/00397910500377560

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Synthetic Communications®, 36: 401–405, 2006
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ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910500377560

Synthesis of Homoallylic Alcohols From Ketones in Water

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Abstract: Homoallylic alcohols have been prepared in good yields by allylation of ketones with allyl bromide in the presence of stannous chloride dihydrate, zinc iodide, and ammonium chloride in water.

Keywords: Allylation, aqueous media, stannous chloride, zinc iodide

Homoallylic alcohols are very useful intermediates and are widely used in organic synthesis.[1] Numerous methods for the synthesis of homoallylic alcohols have been developed.[2] Recently, the synthesis of homoallylic alcohols in aqueous media has drawn much interest because the reactions offer the operational simplicity and the advantages of using an environmentally friendly solvent. Many metals have been used to mediate the carbonyl allylation in aqueous media, such as indium,[3] zinc,[4] and tin.[5] Some of the reactions give good yields; however, the use of these zero-valent metals unavoidably leads to problems because the metal-mediated allylation is a heterogeneous reaction in water. For instance, it is often difficult to stir the reaction mixture and metal oxide or hydroxide precipitation on the surface of metal may slow or stop the reaction.

Received in Japan July 21, 2005

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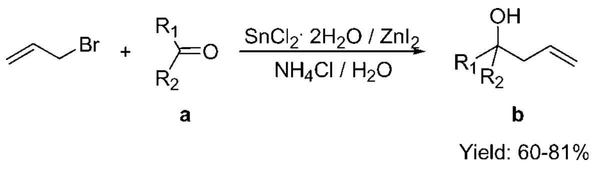
Water-soluble reductive metal salts, such as $SnCl_2$, can provide an alternative way to mediate the coupling between allyl halide and carbonyl compounds to produce the corresponding homoallylic alcohols in aqueous media, which can solve these problems when the salt is applied in the reaction. Nevertheless, $SnCl_2$ cannot efficiently mediate the coupling between allyl bromide and a carbonyl compound in water stirred at room temperature. Therefore, some water-soluble catalyst was introduced into the system to catalyze the reactions, for example $TiCl_3$,[6] Cu(II),[7] or Pd (II).[8] In addition, the formation of homoallylic alcohols mediated by $SnCl_2$ can also be activated by addition of potassium iodide in water.[9] But most of the carbonyl compounds used in these reactions to produce homoallylic alcohols are aldehydes. The allylation of ketones under the same condition does not successfully proceed because of the inactivity of ketones compared to aldehydes, so there are few publications describing the direct synthesis of homoallylic alcohols from ketones in water, except those where ultrasonication[10] or water-insoluble Cu powder catalyst[11] was applied. Consequently, it is essential that a new method should be developed to efficiently allylate ketones with water-soluble salts and catalysts without using other special appliances under mild conditions.

In this article, we report a mild and simple synthesis of homoallylic alcohols from ketones by treatment with allyl bromide, $SnCl_2$, ZnI_2 and NH_4Cl in water (Scheme 1). The system of zinc iodide and ammonium chloride has a good solubility in water and can smoothly catalyze the reaction.

The experimental results are summarized in Table 1.

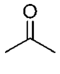
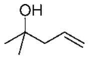
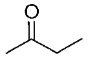
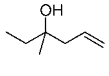
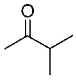
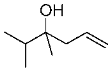
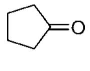
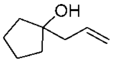
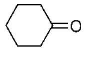
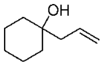
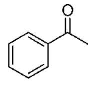
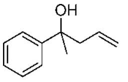
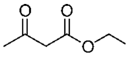
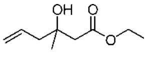
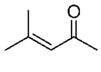
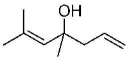
As shown in Table 1, both aliphatic and aromatic ketones can smoothly be allylated and offer good yields in the reaction. Aromatic ketone (entry 6) and α,β-unsaturated ketone (entry 8) need longer time to react with allyl bromide than aliphatic ketones under the condition. Owing to the different strain of the rings, cyclohexanone (entry 5) provides a higher yield than cyclopentanone (entry 4). It was noticed that an ester-containing substrate (entry 7) was successfully allylated without affecting the ester group. Also, α,β-unsaturated ketone (entry 8) was efficiently allylated, whereas carbon–carbon double bond was not changed.

In summary, we report here a simple and efficient method to synthesize homoallylic alcohols in good yields from ketones in water. The reaction extends the scope of substrates that were used to synthesize homoallylic alcohols in water. Ketones that often are inert to allylation mediated by



Scheme 1.

Table 1. Allylation of various ketones in water

Entry	Substrates	Products	Time (h)	Yield (%)[a]
1	 **1a**	 **1b**	15	65
2	 **2a**	 **2b**	15	73
3	 **3a**	 **3b**	17	68
4	 **4a**	 **4b**	20	60
5	 **5a**	 **5b**	16	81
6	 **6a**	 **6b**	22	62
7	 **7a**	 **7b**	17	72
8	 **8a**	 **8b**	20	66

[a] Isolated yield.

$SnCl_2$ in aqueous media were successfully allylated in the reaction. More kinds of homoallylic alcohols can be prepared by the method.

EXPERIMENTAL

Typical Procedures for the Allylation of Ketones

ZnI_2 (0.8 mmol) and NH_4Cl (0.8 mmol) were added to a mixture of ketone (1 mmol) and allyl bromide (1.4 mmol) in water (3 mL). After the mixture was stirred about 1 min, $SnCl_2 \cdot 2H_2O$ (1.5 mmol) was added. The mixture was vigorously stirred at room temperature (30°C) for several hours. Then, the mixture was extracted with diethyl ether directly (3 × 10 mL). The combined ether was washed with brine (2 × 10 mL). After the operation, the organic layer was dried over anhydrous sodium sulfate, filtered, and then evaporated. The residue was purified by flash chromatography (silica gel; ether–petroleum ether). The structure of products was identified by ^{1}H NMR, ^{13}C NMR, and IR spectra.

Representative Spectroscopic Data

Compound 2b: IR (KBr): ν 3390, 3077, 1640, 1149; ^{1}H 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 5b: IR (KBr): ν 3408, 3075, 2932, 2857, 1639, 1448, 1265, 1140; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.85–5.94 (m, 1H), 5.07–5.17 (m, 2H), 2.22 (d, $J = 7.2$ Hz, 2H), 1.42–1.63 (m, 10H), 1.29 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 133.7, 118.6, 70.9, 46.7, 37.4, 25.7, 22.1.

Compound 6b: IR (KBr): ν 3445, 3062, 2978, 1640, 1494, 1446, 1069; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42–7.46 (m, 2H), 7.32–7.37 (m, 2H), 7.21–7.27 (m, 1H), 5.54–5.68 (m, 1H), 5.09–5.17 (m, 1H), 2.65–2.73 (m, 1H), 2.46–2.54 (m, 1H), 2.07 (br, 1H), 1.55 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.6, 133.6, 128.1, 126.6, 124.7, 119.5, 73.6, 48.4, 29.9.

Compound 7b: IR (KBr): ν 3513, 3078, 2981, 1717, 1641, 1371, 1195; ^{1}H 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.

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