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An Efficient Synthesis of 3-Chlorohomoallyl Alcohols. Zinc-Promoted 2-Chloroallylation of Carbonyl Compounds with 2,3-Dichloropropene in an Aqueous Solvent System

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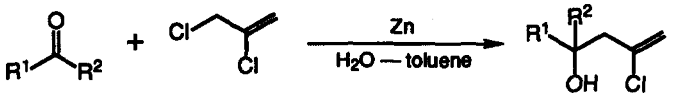
Key Words: 2-chloroallylation of carbonyl compounds; 3-chlorohomoallyl alcohols; zinc; 2,3-dichloropropene; aqueous solvent

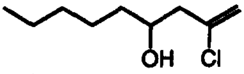
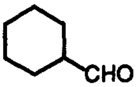
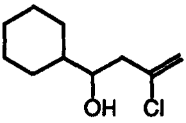
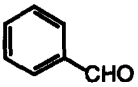
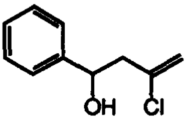
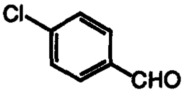
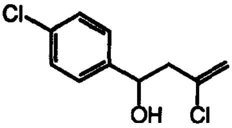
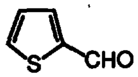
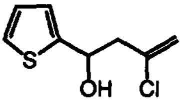
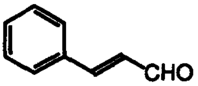
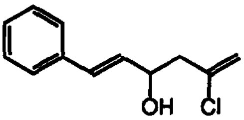
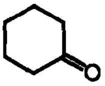
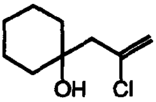
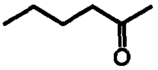
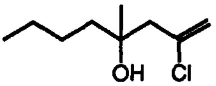
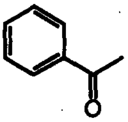
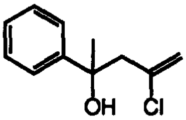
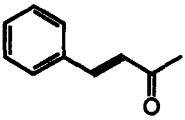
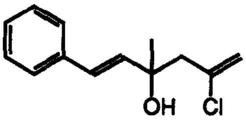
Abstract: *In the presence of metallic zinc, 2,3-dichloropropene has been found to react smoothly with a variety of carbonyl compounds in an aqueous solvent system to give the corresponding 3-chlorohomoallyl alcohols in excellent yields.*

3-Halohomoallyl alcohols, which are useful synthetic intermediates for α-methylene-γ-lactones[1] and homopropargyl alcohols,[2] have been prepared by various methods[3-5] such as ring opening reaction of epoxides with [1-(trimethylsilyl)vinyl]magnesium bromide and Lewis acid catalyzed addition of 2-bromo-3-(trimethylsilyl)propene to carbonyl groups. Among those, 2-haloallylation of carbonyl compounds with 2,3-dihalopropene provides a straightforward entry to the alcohols. However, this method so far reported has been achieved only by using 2,3-dibromopropene with metallic tin as a promoter.[5] From an industrial viewpoint, the use of 2,3-dichloropropene is more desirable than that of the bromide because of the low cost as well as its easy availability.[6] With metallic tin, however, no effective 2-chloroallylation of carbonyl groups by the chloride takes place. We now wish to report the first example of zinc-promoted 2-chloroallylation of aldehydes and ketones with 2,3-dichloropropene in a two-phase system of water and toluene containing a small amount of acetic acid (eq 1).[7] This process, which is operationally simple and gives excellent yields of 3-chlorohomoallyl alcohols, is readily applicable to an industrial scale synthesis.



(1)

Table 1. Synthesis of 3-Chlorohomoallyl Alcohols[a]

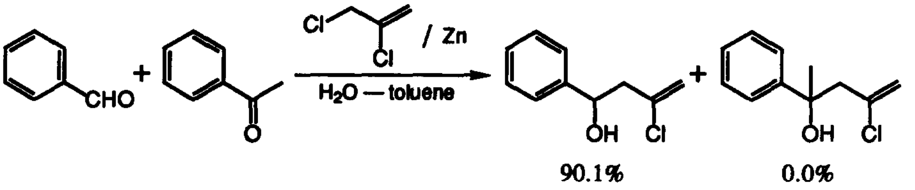
entry	substrate	product	yield[b],%
1			99
2			96
3		 1	95
4			95
5			92
6			91
7			99
8	 2		94[c]
9	 3		94[d]
10	 4		81[d]

[a] All reactions were carried out according to the standard procedure (substrate : 2,3-dichloropropene : zinc = 1 : 2 : 2) described in the text. [b] Isolated yield based on the starting substrate. [c] 3 Equiv. of 2,3-dichloropropene were used with the same amount of zinc. [d] 6 Equiv. of 2,3-dichloropropene were used with the same amount of zinc.

A typical experimental procedure is illustrated by the synthesis of 3-chloro-1-phenyl-3-buten-1-ol (**1**): To a mixture of benzaldehyde (31.8 g, 0.300 mol) and zinc powder[8] (39.2 g, 0.600 mol) in water (124 mL), toluene (110 mL), and acetic acid (6 mL) was added dropwise 2,3-dichloropropene (66.6 g, 0.600 mol) with vigorous stirring at 45 °C over a period of 1 h. After stirring for furher 2 h, the suspension was filtered through Celite, and the precipitate was washed with toluene. The combined filtrates were washed with 7% aqueous Na_2CO_3 solution, dried over Na_2SO_4, filtered, and evaporated. Distillation (bp 103-104 °C / 2.5 mmHg) gave **1**[9] (52.2 g, 0.286 mmol, 95.3%) as a colorless oil.

The reaction proceeds well without using acetic acid as an additive, but it takes a longer reaction time (18 h). In order to promote the reaction efficiently an aqueous solvent system is essential. Without using water no reaction occurs.[10] Metallic zinc has proved to be the most effective promoter. Other promoters in an aqueous solvent system such as Sn-Al,[11] $SnCl_2$-Al,[12] and $BiCl_3$-Al[13] which have been utilized in other allylations of carbonyl compounds are ineffective. For zinc-promoted allylations of carbonyl compounds so far reported, activation of zinc[14] by ammonium chloride or ultrasound has been applied. Compared to this, it is notable that the present reaction proceeds with metallic zinc alone. Under the reaction conditions, 2,3-dichloropropene undergoes competitive dechlorination leading to allene.[15] This requires to use excess amounts of the chloride. Nevertheless, the desired products are cleanly isolated by simple distillation.

The zinc-promoted 2-chloroallylation can be successfully applied to a wide variety of carbonyl compounds as shown in Table 1. Aldehydes can be readily converted into the corresponding 3-chlorohomoallyl alcohols in excellent yields (entries 1-6), whereas ketones except cyclohexanone (entry 7) are less reactive. For instance, when a 1 : 1 mixture of benzaldehyde and acetophenone was subjected to 2-chloroallylation under the standard conditions, no addition product from acetophenone was formed (eq 2). This result reflects that the 2-chloroallylation is highly chemoselective. The efficient preparation of 3-chlorohomoallyl alcohols from ketones is attained simply by increasing the amounts of 2,3-dichloropropene and zinc (3-6 equiv. each) (entries 8-10).[16] α,β-Unsaturated carbonyl compounds (entries 6 and 10) produce the 1,2-addition products exclusively.



(2)

The process developed here is now designed to make an industrial application, and further work is in progress to provide mechanistic information and to apply the present method to other systems.

Acknowledgment. We are grateful to Dr. Takahiro Hosokawa, Osaka University, for helpful discussion. We are also indebted to Mr. Kiyoshi Nakatsuji, Sumitomo Chemical Co., Ltd., for his skillful assistance.

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6. 2,3-Dichloropropene is readily prepared by dehydrochlorination of commercially available 1,2,3-trichloropropane with NaOH in the presence of various phase transfer catalysts (e.g., *N*-cetylpyridinium bromide and benzyltriethylammonium chloride): (a) Chin-Hsien, W. *Synthesis* **1982**, 494-496. (b) Treger, Yu. A.; Sirovskii, F. S.; Berlin, E. R.; Velichko, S. M.; Zanaveskin, L. N. *Khim. Prom-st. (Moscow)* **1987**, 393-397.
7. Presented in part at 60th Annu. Meet. Jpn. Chem. Soc. (Hiroshima), 1990, Abstr. I, 7.
8. Zinc powder (Hakusui Chemical Industries, Limited, 7 µm) was used as recieved.
9. IR (neat) 3390, 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 2.22 (br s, 1 H), 2.60-2.80 (m, 2 H), 5.00 (dd, *J* = 8.9 and 4.3 Hz, 1 H), 5.20 (d, *J* = 1.0 Hz, 1 H), 5.26 (d, *J* = 1.3 Hz, 1H), 7.23-7.38 (m, 5 H). Anal. Calcd for $C_{10}H_{11}OCl$: C, 65.76; H, 6.07; Cl, 19.41. Found: C, 65.71; H, 6.19; Cl, 19.47.
10. In aqueous solvent systems toluene was found to be the best organic solvent. The yields of **1** in other aqueous solvents are as follows: ethyl acetate (79%), tetrahydrofuran (66%), methanol (55%), and *N,N*-dimethylformamide (47%).
11. (a) Nokami, J.; Otera, J.; Sudo, T.; Okawara, R. *Organometallics* **1983**, *2*, 191-193. (b) Nokami, J.; Wakabayashi, S.; Okawara, R. *Chem. Lett.* **1984**, 869-870.
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15. Dechlorination of 2,3-dichloropropene with zinc powder in aqueous ethanol has been known to give allene: Cripps, H. N.; Kiefer, E. F. *Org. Synthesis* **1962**, *42*, 12-14.
16. Under the standard conditions (substrate : 2,3-dichloropropene : zinc = 1 : 2 : 2) ketones **2**, **3**, and **4** gave the corresponding 3-chlorohomoallyl alcohols only in 52, 42, and 27% yields, respectively.

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