

Highly efficient synthesis of homoallylic alcohols and amines via allylation of aldehydes and imines catalyzed by $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ in water

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Received 6 January 2008; revised 9 April 2008; accepted 11 April 2008

Available online 5 May 2008

Abstract

The allylation of aldehydes and imines has efficiently been carried out by treatment with allyltributylstannane in the presence of a catalytic amount of $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ in water to form the corresponding homoallylic alcohols and amines, respectively, in high yields.
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Keywords: Allylation; Allyltin; $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$; Water as solvent

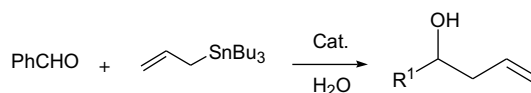
1. Introduction

Nucleophilic additions of allyltin reagents to carbonyl compounds¹ and imines² are important C–C bond forming reactions to afford homoallylic alcohols³ and amines,⁴ which are important building blocks for the construction of various biologically active compounds. Although a lot of important researches in this field have been reported, most of them use organic solvents and require strictly anhydrous conditions. On the other hand, development of organic reactions in aqueous media has attracted much attention⁵ because of its water-tolerance, easy handling, and the unique reactivity and selectivity attained. For the allylation reaction using allyltin reagent, water can be used not only as solvents, but also as necessary reagents involved in the process of intermediates hydrolysis.¹ⁱ Although several Lewis acid or Brønsted acid catalyzed allylation reactions in aqueous media with allyltributyltin have been reported, some of the catalysts are expensive,^{1a,d,g} some are strongly corrosive,^{1b,c} and others are toxic.^{1h,k} Moreover, solvents used in those reports are

usually the mixture of water and organic solvent. There has been increasing interest in the development of new catalysts, which are cheap, innocuous, and effective in pure water as solvent. Recently, $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ has emerged as a very effective catalyst for various organic transformations,⁶ and our group has been developing organic synthesis in water media.⁷ Herein, we would like to report a general and practical method for the synthesis of homoallylic alcohols and amines using $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ as a catalyst.

2. Results and discussion

Initially, several Lewis acids were screened for the allylation reaction of benzaldehyde (1 equiv) with allyltributyltin (1.2 equiv) in pure water (Scheme 1). It could be seen from Table 1 that even the most strong Lewis acids such as $\text{La}(\text{OTf})_3$ and $\text{Yb}(\text{OTf})_3$ provided no product in water, while $\text{Bi}(\text{OTf})_3$ gave moderate yields. When some perfluorooctanoates such as $\text{La}(\text{PFO})_3$ or $\text{Zn}(\text{PFO})_2$ which can



Scheme 1.

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Table 1
Synthesis of homoallylic alcohols from benzaldehyde in water^a

Entry	Lewis acid	Amount (mol %)	Conditions	Yield ^b (%)
1	None	—	30 °C, 16 h	Trace
2	La(OTf) ₃	10	30 °C, 16 h	Trace
3	Yb(OTf) ₃	10	30 °C, 16 h	Trace
4	Bi(OTf) ₃	10	30 °C, 16 h	57
5	La(PFO) ₃	10	30 °C, 16 h	28
6	Zn(PFO) ₂	10	30 °C, 16 h	43
7	Cd(ClO ₄) ₂	10	30 °C, 16 h	Trace
8	ZrOCl ₂ ·8H ₂ O	10	30 °C, 16 h	71
9	ZrOCl ₂ ·8H ₂ O	20	30 °C, 16 h	76
10	ZrOCl ₂ ·8H ₂ O	30	30 °C, 16 h	75
11	ZrOCl ₂ ·8H ₂ O	20	60 °C, 5 h	83
12	ZrOCl ₂ ·8H ₂ O	20	60 °C, 5 h	82, 80, 77 ^c

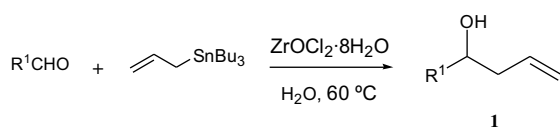
^a The reaction was conducted with 1 mmol of benzaldehyde and 1.2 mmol of allyltributylstannane in H₂O (2 mL).

^b Isolated yield after chromatographic purification.

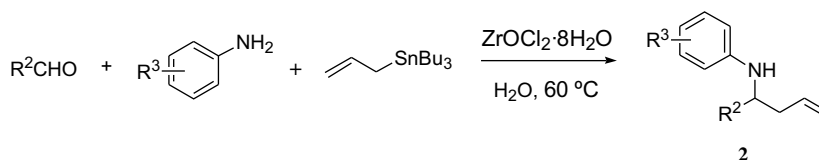
^c Catalyst was reused three times.

disperse substrates in water were used, the yield showed a limited increase. Moreover, cadmium perchlorate, the most effective catalyst in aqueous ethanol (H₂O/EtOH = 1/9),^{1h,k} seemed to lose catalytic activity in pure water and afforded no product. It was surprising to discover that reactivity was much better when adding 10 mol % ZrOCl₂·8H₂O as catalyst. Further study showed that the use of just 20 mol % of ZrOCl₂·8H₂O was sufficient to provide a satisfactory yield in 16 h. An increase in the amount of catalyst did not improve the result to any great extent. In order to complete the reaction in a shorter time, the temperature was increased to 60 °C with the reaction finishing in 5 h with yield as high as 83%. After the reaction, recovery of the zirconium oxychloride was realized by extraction with water (three times) after diluting the reaction mixture with isopropyl ether. Then the catalyst can be reused after concentrating the aqueous phase. Entry 12 describes the yields of three consecutive runs leading to the corresponding homoallylic alcohol, which showed little loss of catalytic activity of zirconium oxychloride.

After optimizing the reaction conditions, the catalytic system was applied to the allylation of various aldehydes (Scheme 2). The results are summarized in Table 2, which showed that liquid aldehydes gave their allylated adducts



Scheme 2.



Scheme 3.

Table 2
Synthesis of different homoallylic alcohols using ZrOCl₂·8H₂O in water^a

Entry	R ¹	Time (h)	Product	Yield ^b (%)
1	C ₆ H ₅	5	1a	83
2	4-MeC ₆ H ₄	5	1b	84
3	4-MeOC ₆ H ₄	5	1c	79
4	2-HOC ₆ H ₄	5	1d	81
5	4-FC ₆ H ₄	5	1e	86
6	Me ₂ CH	5	1f	80
7	<i>n</i> -C ₇ H ₁₅	5	1g	83
8	CH ₃ CH=CH	5	1h	80
9	C ₆ H ₅ CH=CH	5	1i	76
10	4-ClC ₆ H ₄	16	1j	79
11	4-BrC ₆ H ₄	16	1k	84
12	3-NO ₂ C ₆ H ₄	16	1l	77
13	4-NO ₂ C ₆ H ₄	16	1m	71

^a All the reaction were carried out with 20 mol % ZrOCl₂·8H₂O in 2 mL H₂O at 60 °C.

^b Isolated yield after chromatographic purification.

in good yields, even sterically hindered aldehyde such as salicylaldehyde also underwent an easy conversion (entry 4), while solid aldehydes needed prolonged time to give satisfactory results. This is a consequence of the reaction taking place at the interface of organic substrates with water. Solid aldehydes are difficult to be dispersed in water due to their poor solubility in water. To ensure that the reaction proceeded successfully, vigorous stirring was required for solid aldehydes.

Inspired by the success of allylation to aldehydes, the synthesis of homoallylic amines by allylation to imines with the same catalytic system was explored (Scheme 3). The results are summarized in Table 3, which shows that both aromatic and aliphatic aldehydes afforded the desired products in satisfactory yields. The solid aldehydes also need prolonged time to give improved yields, while solid aromatic amines did not need any additives and can provide good yields.

Based on the proposed mechanism reported in the literatures,^{1g,n,o} a probable mechanistic pathway to explain the homoallylation process is depicted in Scheme 4. The reaction may proceed by initial coordination of ZrOCl₂ with the carbonyl group or imine group which facilitates X–Sn (X = O, NR') bond formation. Subsequent hydrolysis of –XSnBu₃ yielded the homoallylic alcohol or homoallylic amine. ZrOCl₂, used in catalytic amount, was recycled in the reaction and can be reused for subsequent reactions.

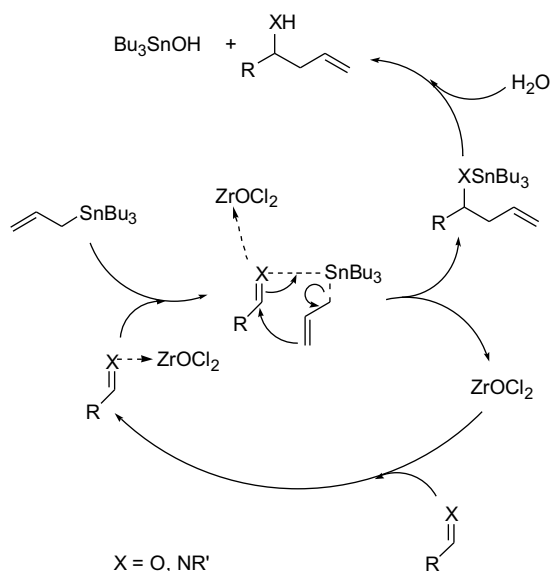
In conclusion, ZrOCl₂·8H₂O has efficiently been applied in sole water for the allylation of both aldehydes and imines with allyltributylstannane to prepare homoallylic alcohols and amines, respectively, in good yields. The

Table 3
Synthesis of different homoallylic amines using the $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ in water^a

Entry	R ²	R ³	Time (h)	Product	Yield ^b (%)
1	C ₆ H ₅	H	5	2a	87
2	4-MeC ₆ H ₄	H	5	2b	82
3	4-MeOC ₆ H ₄	H	5	2c	80
4	4-ClC ₆ H ₄	H	10	2d	81
5	4-NO ₂ C ₆ H ₄	H	10	2e	74
6	Me ₂ CH	H	5	2f	79
7	<i>n</i> -C ₇ H ₁₅	H	5	2g	83
8	C ₆ H ₅ CH=CH	H	5	2h	78
9	CH ₃ CH=CH	4-Cl	5	2i	81
10	C ₆ H ₅	4-Cl	5	2j	85
11	C ₆ H ₅	4-MeO	5	2k	83

^a Reaction conditions: Benzaldehyde (1 mmol); aromatic amine (1 mmol); allyltributylstannane (1.2 mmol); $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ (20 mol %); water (2 mL); 60 °C.

^b Isolated yield after chromatographic purification.



Scheme 4.

catalyst is cheap, innocuous, environmentally friendly, and may be reused several times without obvious loss of activity.

Acknowledgments

This project was financially supported by the National Nature Science Foundation of China (20672035) and Key

Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences.

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