Lewis Acid-Catalyzed Allylation Reactions of Acylhydrazones with Tetraallyltin in Aqueous Media

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Abstract: Allylation reactions of various benzoylhydrazones with tetraallyltin were found to proceed smoothly in the presence of scandium triflate as a Lewis acid catalyst at ambient temperature in aqueous media, to afford the corresponding homoallylic amine derivatives in high yields. Three-component reactions of aldehydes, benzoylhydrazine, and tetraallyltin were also catalyzed by scandium triflate in the same media. Furthermore, a simple procedure to prepare oxazolidinone derivatives utilizing these reactions was developed.

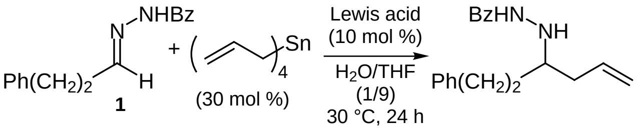
Key words: hydrazone, Lewis acid, allylation, aqueous media, scandium triflate

In recent years, organic reactions in aqueous media have attracted a great deal of attention, not only because these reactions eliminate the necessity of vigorous drying of solvents and substrates, but also because unique reactivity and selectivity are often observed in the aqueous reactions.[1] Along this line, we have developed several reactions catalyzed by water-compatible Lewis acids such as rare earth metal triflates in aqueous solvents.[2]

Lewis acid-mediated addition of allyltins or allylsilanes to carbon−nitrogen double bonds provides one of the most important methods to obtain homoallylic amines, which constitute versatile intermediates for the synthesis of nitrogen-containing compounds.[3] We[4] and others[5] have reported the allylation reactions of imines in the presence of catalytic amounts of Lewis acids in organic solvents. Recently, we have also reported the reactions of acylhydrazones with tetraallyltin using scandium triflate ($Sc(OTf)_3$) as a Lewis acid catalyst in acetonitrile.[6] Acylhydrazones are useful imine surrogates and are easily prepared from acylhydrazines and carbonyl compounds. In addition, most acylhydrazones, including the ones derived from aliphatic aldehydes, can be purified by recrystallization and are easy to handle under air, while the corresponding imine derivatives are generally unstable. Furthermore, the hydrazines produced by the reactions of hydrazones with nucleophiles can be converted not only to amines by facile cleavage of the nitrogen−nitrogen single bonds[7] but also to various compounds retaining the nitrogen−nitrogen bonds.[8] In spite of these attractive features for the use of acylhydrazones as substrates, there has been no report on Lewis acid-catalyzed allylation reaction of acylhydrazones in aqueous media. In this paper, we describe the first example of such reaction.

First, the reaction of benzoylhydrazone **1**, which is derived from an aliphatic aldehyde, with tetraallyltin in aqueous solvents was carried out in the presence of various Lewis acids. After several trials, we were pleased to find that the reaction proceeded smoothly in water/THF. As shown in Table 1, $Sc(OTf)_3$[9] was found to be the best catalyst among the Lewis acids tested.[10]

Table 1 Allylation of **1** in the Presence of Various Lewis Acids in Aqueous Media



Lewis acid	Yield (%)
$Sc(OTf)_3$	77
$Cu(OTf)_2$	56
$Zn(OTf)_2$	40
AgOTf	69
$Yb(OTf)_3$	40

This reaction system was applied to various benzoylhydrazones (Table 2). Not only aliphatic hydrazones (entries 1, 2) but also aromatic (entries 3−5) and α,β-unsaturated hydrazones (entry 6) reacted under these conditions to give the desired hydrazines in good yields. It is noted that a hydrazone with α-ester functionality also worked well (entry 7). In addition, the hydrazone trimer derived from formaldehyde afforded the 3-butenylhydrazine in good yield (entry 8).

A typical experimental procedure is described for the reaction of **1**. A solution of tetraallyltin (0.24 mmol) in water/THF (1/9, 0.77 mL) was added to a mixture of **1** (0.48 mmol) and $Sc(OTf)_3$ (0.024 mmol) in water/THF (1/9, 1.18 mL) at 30 °C. After stirring for 20 h, the reaction was quenched with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with dichloromethane. The organic extract was dried over Na_2SO_4, concentrated, and purified with silica gel chromatography (hexane/ethyl acetate = 2/1) to give the desired product in 85% yield.

Multi-component reactions are one of the most efficient methods to construct complex molecules from simple

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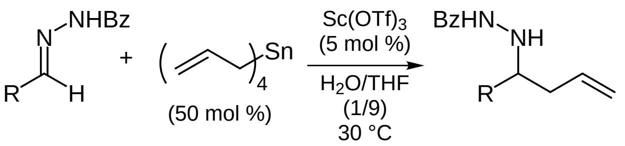
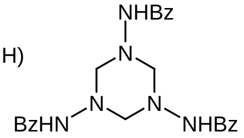
Table 2 $Sc(OTf)_3$-Catalyzed Allylation of Benzoylhydrazones in Aqueous Media[a]



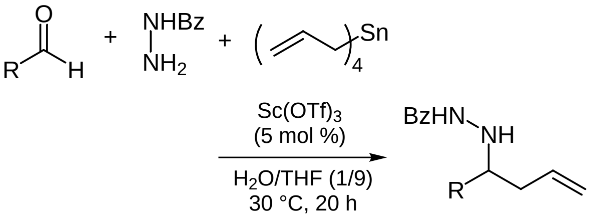
Entry	R	Yield (%)
1	$PhCH_2CH_2$	85
2	Me_2CHCH_2	84
3	Ph	58[b]
4	$4\text{-}MeOC_6H_4$	84
5	$4\text{-}ClC_6H_4$	77
6	PhCH=CH (*trans*)	86
7	EtO_2C	81
8	(R = H) 	79

[a] 20-68 h. [b] $Sc(OTf)_3$ (10 mol%).

starting materials in one pot.[11] Therefore, we next studied three-component reactions[6a] of aldehydes, benzoylhydrazine, and tetraallyltin in an aqueous solvent (Table 3). An advantage of these reactions is that the reactions could be carried out without a separate step for hydrazone preparation prior to the allylation. In the presence of 5 mol% $Sc(OTf)_3$, aldehydes reacted with benzoylhydrazine and tetraallyltin successively at 30 °C in aqueous media to afford the desired homoallylic amine derivatives in high yields. The by-products produced by allylation of the aldehydes instead of the hydrazones were generated only in very low yields. For example, in the case of entry 1, 1-phenyl-5-hexen-3-ol was obtained only in 4% yield along with the desired hydrazine. It should be also mentioned that the aldehydes were successfully used as commercial aqueous solutions (entries 2 and 3). These direct uses of water-containing aldehydes clearly demonstrate an advantageous point in reactions catalyzed by water-compatible Lewis acids in aqueous media.

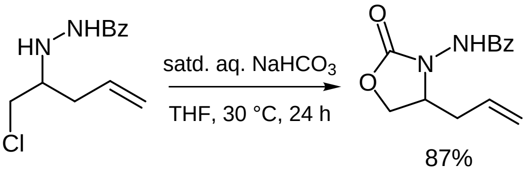
As an example for transformation of the allylation products to various compounds, we have developed a facile method to produce oxazolidinones. By simply treating with a saturated aqueous solution of $NaHCO_3$, the product derived from chloroacetaldehyde, benzoylhydrazine, and tetraallyltin was easily transformed to the corresponding oxazolidinone derivative as shown in Eq. 1.[12] This reaction is useful to synthesize *N*-amido-4-allyl-oxazolidin-2-one derivatives, and one-pot reactions could also be performed for various benzoylhydrazines as shown in Table 4.

Table 3 Three-Component Allylation Reactions in Aqueous Media[a]



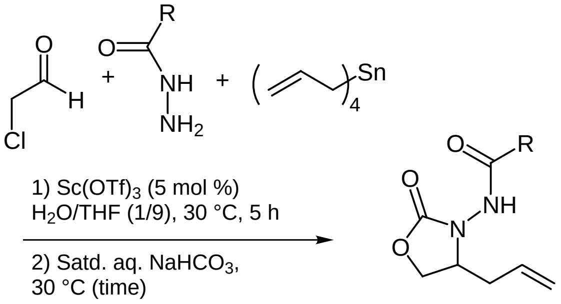
Entry	R	Yield (%)
1	$PhCH_2CH_2$	85
2	H [b]	72
3	$ClCH_2$ [b]	68

[a] The molar ratio of aldehyde:benzoylhydrazine:tetraallyltin is 1:1:0.5 for entry 1, and 1.2:1:0.5 for entries 2 and 3. [b] A commercial aqueous solution of the aldehyde was directly used.



Equation 1

Table 4 Synthesis of Oxazolidinone Derivatives[a]



Entry	R	Time	Yield (%)
1	Ph	23 h	75
2	$4\text{-}MeOC_6H_4$	43 h	69
3	$4\text{-}ClC_6H_4$	8 d	69
4[b]	$4\text{-}ClC_6H_4$	24 h	69
5	$4\text{-}CF_3C_6H_4$	10 d	63

[a] The molar ratio of aldehyde:acylhydrazine:tetraallyltin is 1.2:1:0.5. A commercial aqueous solution of the aldehyde was directly used. [b] The reaction temperature for the oxazolidinone formation is 60 °C.

In summary, the allylation reactions of various benzoylhydrazones with tetraallyltin were smoothly catalyzed by $Sc(OTf)_3$ in aqueous media to afford the corresponding homoallylic amine derivatives in high yields. In addition, three-component reactions of aldehydes, benzoylhydrazine, and tetraallyltin also proceeded under the same conditions. Furthermore, a simple procedure to synthesize oxazolidinone derivatives was developed. It is noted that the reactions proceeded smoothly at ambient temperature in aqueous media, and that water-soluble materials were successfully used in these systems. Since the nitrogen−nitrogen bonds of acylhydrazines are known to be easily cleaved, the present allylation will provide a useful method for the synthesis of homoallylic amines as well as nitrogen−nitrogen bond-containing compounds.

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