## Highly Efficient Allylation of Aldehydes and Three-Component Synthesis of Homoallylamines Using Bismuth Triflate Catalyst

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**Abstract:** Bismuth triflate catalyzed allylation of a variety of aldehydes and aldimines using allyltributylstannane has been presented. The reaction proceeds rapidly and yields corresponding homoallylic alcohols and homoallylic amines in good yields. The bismuth triflate displays manifold activity over the La, Yb, and Sc triflates. The catalyst is reused for allylation of aldehydes and aldimines without significant loss of catalytic activity for four cycles.

**Key words:** allylation, aldehydes and aldimines, bismuth triflate, Bronsted acids, turnover frequency

Over the past two decades, the Lewis acid (LA) catalyzed allylation of aldehydes<sup>1</sup> and aldimines<sup>2</sup> has become an important carbon-carbon bond forming reaction in organic synthesis. This is mainly because this reaction adds a new functionality into the substrate that can be extended to further organic transformations. Furthermore, allylation of aldimines provides a useful synthetic methodology for homoallylic amines, which are useful building blocks for natural products.

There are several different metal-based LA catalysts available for this reaction.<sup>3</sup> Lately, synthetic methodology involving lanthanide triflates in combination with rate accelerating agents<sup>4</sup> such as benzoic acid and sodium dodecyl sulfate (SDS)<sup>5</sup> as catalysts for allylation of aldehydes and aldimines has received considerable attention. High catalytic activity, low toxicity, moisture and air tolerance and their recyclability make use of lanthanide triflates attractive alternatives to LA's such as InCl<sub>3</sub> or AlCl<sub>3</sub>. However, unfortunately, lanthanide triflates are rather expensive and thus, their use in large-scale synthetic methodology is very limited. Thus, more cheaper and efficient LA catalysts are desirable for allylation reactions. In this direction, bismuth triflate is the center of focus to organic chemists.<sup>6–10</sup>

In view of this, we have examined bismuth triflate as a LA catalyst for the allylation of aldehydes and aldimines (as an one-pot synthesis) in our laboratory. We are particularly interested in bismuth triflate, because it is inexpensive<sup>11</sup> and can be easily prepared in laboratory from commercially available bismuth (III) oxide and triflic acid.<sup>12</sup> The results from our study are presented herein.

Synlett 2002, No. 10, Print: 01 10 2002. Art Id.1437-2096,E;2002,0,10,1694,1696,ftx,en;D12402ST.pdf. © Georg Thieme Verlag Stuttgart · New York ISSN 0936-5214 Initially, we studied the allylation of *p*-chlorobenzaldehyde with allyltributylstannane using 2 mol% of bismuth triflate and acetonitrile as a solvent at room temperature.<sup>14</sup> The reaction is very sluggish and a conversion of 20% was observed after 12 hours. However, when 1 equivalent of benzoic acid as an additive was employed, *p*-chlorobenzaldehyde reacted with allyltributylstannane rapidly and gave the corresponding homoallyl alcohol in good yields (90%). Encouraged by this result, we have carried out the allylation of a variety of aldehydes in order to understand the scope and reactivity. The results are summarized in Table 1. It is clear from Table 1 that the reaction was completed in 5–30 minutes. Interestingly, when *p*-nitrobenzaldehyde or 3,4,5-trimethoxy benzaldehyde was used, the reaction was completed in about 5 minutes.

It is very amazing to note that the allylation of all the aldehydes catalyzed by bismuth triflate proceeded with very high turnover frequency (TOF), 5–22 times over lanthanum triflate<sup>13</sup> under identical conditions as can be seen in Table 1. These results strongly suggest that bismuth triflate is a more efficient LA catalyst than lanthanum triflates for the allylation of aldehydes. The catalyst, which was precipitated at the end of the reaction, was filtered and reused for allylation reaction without significant loss of activity for four cycles (Table 1, entry 1).

The present catalytic system exhibited high chemoselectivity towards aldehydes in the presence of ketones when the allylation was conducted in a binary substrate system, *p*-chlorobenzaldehyde and acetophenone; aldehyde was allylated to the extent of 90%, whereas 5-10% of ketone was allylated at the same time.

We have also evaluated the use of bismuth triflate-benzoic acid catalytic system for the one-pot synthesis of homoallylamines in acetonitrile as solvent.<sup>15</sup> As was the case with the allylation of *p*-chlorobenzaldehyde; the one-pot reaction of *p*-chlorobenzaldehyde, *o*-chloroaniline and allyltributylstannane also required 1 equivalent of the benzoic acid as an additive. This reaction was completed in 45 minutes and the corresponding homoallylamine product was isolated in 65% yield using flash chromatography (10% ethyl acetate-hexane). A variety of aldehydes and amines have been examined in an effort to understand the generality of this reaction, and the results from this study are shown in Table 2. It is clearly seen from Table 2 that moderate to good yields (60-90%) were obtained for all substrates, and the reactions were completed within 45 minutes. When p-nitrobenzaldehyde or p-nitroaniline was

	H + SnBu 3	Bi(OTf) <sub>3</sub> CH <sub>3</sub> CN, Ph	(2 mol%) CO <sub>2</sub> H,rt	RI OH
Entry	Aldehyde	Time (min)	Yield <sup>a</sup> (%)	$TOF^{b}(h^{-1})$
1	CHO	10 10	90 85	270 (26.66)
2	CHO	15	80	160 (18.20)
3	СНО	30	90	90 (18.75)
4	MeO MeO OMe	5	95	570 (24)
5	СНО	20	85	127 (20)
6	NO2 CHO	5	95	570 (31)
7	CHO	20	80	120 (8.85)
8	СНО	20	65	97.5 (9.7)

**Table 1**Scope of Improved Allylation of Aldehydes with BismuthTriflate

<sup>a</sup> Yields based on NMR

<sup>b</sup> The values in parentheses refer to the Ln(OTf)<sub>3</sub> catalyzed reaction conducted under identical conditions.

<sup>c</sup> Yield of the product after 4<sup>th</sup> cycle.

<sup>3</sup> Heid of the product after 4<sup>th</sup> cycl

used as the substrate, the reaction proceeded much faster than the other substrates and gave corresponding homoallylic amines in quantitative yields. Furthermore, in all these reactions, formation of homoallylic alcohol products was not detected even in small amounts. The allylation of aldimines was also effected with 2 mol% of bismuth triflate and 1 equivalent of sodium dodecyl sulfate (SDS) using water as a solvent to provide excellent yields of homoallylamines. The activity expressed in terms of turnover frequency using bismuth triflate-SDS system in water is 42-80 fold over the scandium triflate-SDS in water under identical conditions and 1.5-4 fold over the bismuth triflate-benzoic system described above. Under similar conditions, there is no reaction with aldehydes and allyltributylstannane using bismuth triflate-SDS in water, indicating that the aldimines are the intermediates in the three component reaction. Both the catalyst systems, bismuth triflate-SDS and bismuth triflatebenzoic acid conducted in the respective solvents, precipitated at the end of the reaction are recovered and reused (Table 3, entry 1; Table 2, entry 1) for four cycles.

In summary, the highly efficient allylation of aldehydes catalyzed by bismuth triflate-benzoic acid catalytic system and one pot synthesis of homoallylamines with allyltributylstannane with bismuth triflate-benzoic acid in acetonitrile or bismuth triflate-SDS in water in good to excellent yields under milder reaction conditions is described. We have not only improved the product yields but also shortened the reaction times. We have also demonstrated the recyclability of the catalytic system for the synthesis of homoallylic alcohols, and thus, bismuth triflate mediated allylation reaction is a simple, economical, high yielding, and time saving methodology for allylation of aldehydes and aldimines.

 Table 2
 Scope of Improved One-Pot Synthesis of Homoallylic Amines with Bismuth Triflate

		R <sup>i</sup>
0	$\sim NH_2$	Bi(OTf) 3 (2 mol%)
$R^{1}$ $H^{+}$	$SnBu_3 + \Theta$ C	H <sub>3</sub> CN, PhCO <sub>2</sub> H, rt
K	$\mathbf{R}^2$	$\mathbf{k}^2$

	K	K-			
Entry	Aldehyde and Amine	Time (min)	Yield <sup>a</sup> (%)	$\mathrm{TOF}^{\mathrm{b}}\left(\mathrm{h}^{-1} ight)$	
1	$R^1 = p$ -Cl-( $C_6H_4$ )-, $R^2 = o$ -Cl	45	65 (60)°	43.3 (18)	
2	$\mathbf{R}^1 = \mathbf{P}\mathbf{h},  \mathbf{R}^2 = o\mathbf{-C}\mathbf{l}$	60	60	30 (12.5)	
3	$R^1 = p-NO_2-(C_6H_4)-, R^2 = o-Cl$	35	70	60 (22.5)	
4	$R^1 = p$ -Cl-(C <sub>6</sub> H <sub>4</sub> )-, $R^2 = p$ -NO <sub>2</sub> -	20	70	106 (32.5)	
5	$\mathbf{R}^1 = \mathbf{Ph},  \mathbf{R}^2 = p \cdot \mathbf{NO}_2$	20	65	98.5 (24.3)	
6	$R2 = p-NO_2$	10	90	281.3 (46.6)	

<sup>a</sup> Yields based on NMR.

<sup>b</sup> The values in parentheses refer to the Ln(OTf)<sub>3</sub> catalyzed reaction conducted under identical conditions.

<sup>c</sup> Yield of the product after 4<sup>th</sup> cycle.

Table 3 Scope of Improved One-Pot Synthesis of Homoallylic Amines with Bismuth Triflate

$R^{1} \xrightarrow{H} + SnBu_{3} + Q \xrightarrow{R^{2}} \xrightarrow{H_{2}O, SDS, \pi} R^{2} \xrightarrow{R^{1}} R^{2}$						
Entry	Aldehyde and Amine	Time (min)	Yield <sup>a</sup> (%)	$\mathrm{TOF}^{\mathrm{b}}\left(\mathrm{h}^{-1}\right)$		
1	$R^1 = p$ -Cl-(C <sub>6</sub> H <sub>4</sub> )-, $R^2 = o$ -Cl	15	80 (75)°	160 (0.20) <sup>b</sup>		
2	$R^1 = Ph, R^2 = o-Cl$	20	70	105 (0.25) <sup>b</sup>		
3	$R^1 = p-NO_2-(C_6H_4)-R^2 = o-Cl$	10	80	240		
4	$R^1 = p$ -Cl-(C <sub>6</sub> H <sub>4</sub> )-, $R^2 = p$ -NO <sub>2</sub> -	15	75	150		
5	$R^1 = Ph-, R^2 = p-NO_2$	15	70	140		
6	$R^1 = p-NO_2-(C_6H_4)-, R^2 = p-NO_2$	5	85	510		

<sup>a</sup> Yields based on NMR.

<sup>b</sup> The values in parentheses refer to the Sc(OTf)<sub>3</sub> catalyzed reaction conducted under identical conditions.

<sup>c</sup> Yield of the product after 4<sup>th</sup> cycle.

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- (14) Typical Experimental Procedure for the Allylation of Aldehydes: To a stirred solution of *p*-chlorobenzaldehyde (1 mmol), benzoic acid (1 mmol) and allyltributylstannane (1.2 mmol) in acetonitrile (5 mL) at r.t. was added bismuth triflate (2 mol%). The mixture was stirred at r.t. until reaction was completed as indicated by TLC. The catalyst, which was precipitated at the end of the reaction, was filtered off. The filtrate was concentrated under vacuum to obtain a crude product and was purified by column chromatography (10% ethyl acetate–hexane) (164 mg, 90%).
  <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 2.01(d, 1 H, OH), 2.52 (m, 2 H, CH<sub>2</sub>), 4.75 (t, 1 H,CH), 5.14–5.20 (m, 2 H, 2 vinyls), 5.82 (m, 1 H, vinyl), 7.20–7.30 (m, 4 H, aromatic) [Lit<sup>10a</sup>].
- (15) Typical Experimental Procedure for the One-Pot Allylation of Aldimines: To a stirred solution of *p*-chlorobenzaldehyde (1 mmol), benzoic acid (1 mmol), allyltributylstannane (1.2 mmol) and *o*-chloroaniline (1 mmol) in acetonitrile (5 mL) at r.t. was added bismuth triflate (2 mol%). The mixture was stirred at r.t. until reaction was completed as indicated by TLC. The catalyst, which was precipitated at the end of the reaction, was filtered off. The filtrate was concentrated under vacuum to obtain a crude product and was purified by column chromatography (10% ethyl acetate–hexane) (189 mg, 65%).

<sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 2.52 (m, 2 H, CH<sub>2</sub>), 4.40 (t, 1 H, CH), 5.14–5.20 (m, 2 H, 2 vinyls), 5.80 (m, 1 H, vinyl), 6.20 (d, 1 H, aromatic), 6.6 (m, 2 H, aromatic), 6.80–7.00 (m, 1 H, aromatic), 7.20–7.30 (m, 4 H, aromatic) [Lit <sup>16</sup>].

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