



Three component synthesis of homoallylic amines. Efficient catalysis by lanthanum triflate/benzoic acid

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Abstract—Lanthanum triflate–benzoic acid catalyses the in situ formation and allylation of various imines from aldehydes and an aromatic amine. © 2002 Elsevier Science Ltd. All rights reserved.

In the preceding paper, we reported the lanthanum triflate–benzoic acid catalyst system for the allylation of aldehydes with allyltributyltin to give homoallylic alcohols.¹ We wish to report an extension of the methodology to the in situ formation and allylation of imines.

One of the first examples was reported by Keck using TiCl₄ and BF₃·OEt₂ as catalysts.² Other developments in this field have seen the use of palladium catalysts with allyltributyltin,³ allyltrimethylsilane⁴ and an enantioselective version.⁴ Itsuno has developed a chiral boron catalyst with triallylborane and a chiral modifier derived from (–)-norephedrine.⁵ The formation of the imine in situ is very desirable given the inherent problems associated with handling them. In response to this, one-pot reactions have been reported by Kobayashi and Akiyama both with scandium triflate as the catalyst.^{6,7} Whilst these procedures are novel and afford the desired products, there are still improvements to be made as some of these methods require up to 10 mol%, or more, catalyst and sometimes anhydrous conditions. In addition, some of the reactions can be quite sluggish.

We carried out our first studies into this reaction using benzaldehyde and *m*-toluidine as our two components with *activated* (heated to 160°C under high vacuum for 2 h immediately before use) lanthanum triflate at 5 mol% loading. In this initial study, we pre-formed the imine before reaction. Satisfied that the imine was

allylated under our conditions, we attempted a one-pot formation and allylation of the imine again with 5 mol% activated lanthanum triflate. Gratifyingly no alcohol was seen in the reaction and the amine was formed exclusively. At this stage the catalyst was still activated by drying and we were keen to apply our unactivated catalyst procedure that had been successful for aldehyde allylations.¹ Table 1 shows the results using unactivated lanthanum triflate catalyst; note the reduced catalyst loading.

Good yields were obtained for aromatic aldehydes. Enolisable aldehydes, however, failed to give the desired product. A 19% yield of the octaldehyde derived product was obtained but could not be repeated. It is known, however, that imines with α -protons undergo side reactions with allyltributylstannane⁸ and Kobayashi reported that his procedure allowed the allylation of imines derived from octaldehyde and hydrocinnamaldehyde.⁷ The imine derived from octaldehyde gave 19% of the allylated product at best and the imine derived from hydrocinnamaldehyde failed to give any identifiable products.

The problem with our choice of amine was that the final products were not synthetically useful. A far better strategy would be to employ a removable group that could be cleaved to reveal the homoallylic amine, which would be far more useful synthetically. Such a group would be a *para*-methoxyphenyl group derived from *p*-anisidine, that could be cleaved in three steps to reveal the primary amine.⁹ Table 2 shows the results of the allylation of the *p*-anisidine derived imines.

Keywords: lanthanum triflate; allylation; Brønsted acidity; Lewis acidity; imines.

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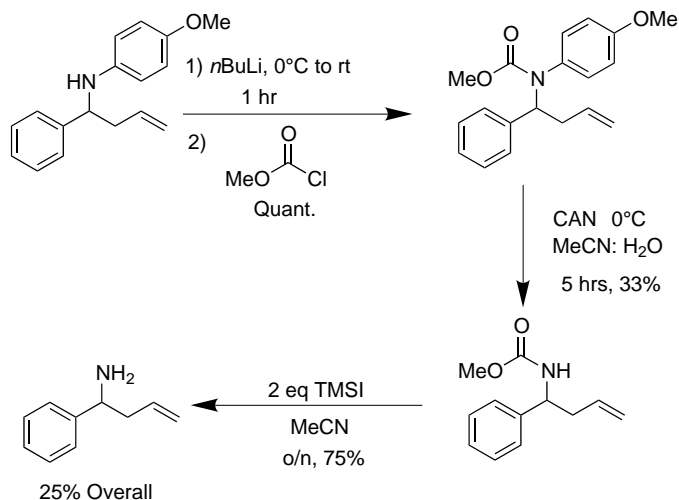
Table 1. Unactivated catalyst for in situ imine allylation

Aldehyde	Time/ mins	Yield/ %	Aldehyde	Time/ mins	Yield/ %
	o/n	67		160	19 [†]
	100	89		100	77
	100	64		160	88 [‡]
				100	80

[†] Activated 5 mol% catalyst, no reaction with 2mol% [‡] Activated 2 mol% catalyst

Table 2. *p*-Anisidine derived imine allylations

Aldehyde	Time/ mins	Yield/ %	Aldehyde	Time/ mins	Yield/ %
	135	87		150	54
	180	76		210	57
	150	66		420	50
	220	88			
	145	96			



Scheme 1. Cleavage of *p*-methoxyphenyl group.

Moderate to excellent yields were obtained at low catalyst loading. Cyclohexanecarboxaldehyde, which is enolisable, albeit slowly, gave a moderate yield of the allylated product. A range of aldehydes are tolerated including electron rich/depleted aldehydes and tertiary aldehydes.

The final step was to cleave the *p*-methoxyphenyl group and this was carried out on the benzaldehyde derived amine product. Conversion to the carbamate proceeded in quantitative yield but the cleavage of the *p*-methoxyphenyl group proceeded in low (33%) yield. The final step proceeded in good (75%) yield to yield the primary amine in overall 28% yield⁹ (Scheme 1).

So, in summary we have demonstrated that the unactivated lanthanum triflate–benzoic acid catalyst system can be applied to the one-pot allylation of imines. This occurs at low catalyst loading, under mild conditions and with two aromatic amines. The *p*-methoxyphenyl group was then cleaved in three steps to yield the primary amine in overall 25% yield.

Typical procedure: Lanthanum triflate (0.0141 g, 0.024 mmol, 2 mol%) and benzoic acid (0.149 g, 1.22 mmol)

were placed in a 25 mL round bottom flask with a stirrer bar. MeCN (2 mL) was added and the solution was stirred until the benzoic acid and the lanthanum triflate had both dissolved. Freshly distilled aldehyde (1.22 mmol, 1.0 equiv.) followed by amine (*m*-toluidine 131 μL , 1.22 mmol, 1.0 equiv. or *p*-anisidine 0.1501 g, 1.22 mmol, 1.0 equiv.) were added. Allyltributylstannane (454 μL , 1.46 mmol, 1.2 equiv.) was then added and the reaction left to stir, monitoring by TLC. The mixture was then quenched with 2 M NaOH (2 mL) and extracted into CH_2Cl_2 (3 \times 15 mL), the combined organic layers were dried (MgSO_4) and the solvent removed in vacuo to yield the crude homoallylic amine product. Purification by flash column chromatography (typical eluant; 10–30% diethyl ether:petroleum ether) yielded the product.

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