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## CATALYTIC ALLYLATION OF IMINES PROMOTED BY LANTHANIDE TRIFLATES

Cristina Bellucci, Pier Giorgio Cozzi\* and Achille Umani-Ronchi\*

Dipartimento di Chimica "G. Ciamician ", Università di Bologna, via Selmi 2, 40126 Bologna, Italy

Abstract:Lanthanide triflates are effective catalysts for the allylation of imines with allyltributylstannane affording homoallylamines in moderate to good yields.

Lanthanide triflates are effective water-tolerant Lewis acids<sup>1</sup> and show a strong affinity towards carbonyl groups. They act as Lewis acid in several carbon-carbon bond forming reactions<sup>2</sup> which proceed in catalytic amounts under mild conditions. From the standpoint of catalytic use and reuse, lanthanide triflates can also solve important environmental and industrial problems.<sup>3</sup>

Recently reactions promoted by lanthanide triflates, which occur in the presence of strongly coordinating amine groups, were reported.<sup>4</sup> Moreover, addition reactions that involve imines promoted by catalytic amounts of Lewis acids are scarcely developed.<sup>5</sup>

Only a few examples of aldol-type reactions of ketene silyl acetals with aromatic or aliphatic imines using catalysts such as trimethylsilyltriflate<sup>6</sup>, iron iodide<sup>7</sup>, tritylhexafluoroantimonate<sup>7</sup>, and tris(pentafluorophenyl)boron<sup>8</sup> were described. Recently a catalytic methodology was reported that uses lanthanide triflates for promoting Mukaiyama and hetero-Diels Alder reactions<sup>9</sup> with imines. Although catalytic allylation<sup>10</sup> of aldehydes is a well established procedure and the enantioselective variants of this reaction were recently described<sup>11</sup>, to our knowledge, no carbon-carbon bond forming reactions have been reported using allylstannane and imines in the presence of catalytic amounts of Lewis acid. Indeed, the Lewis acids generally employed in these reactions are traditional ones, such as TiCl4 or BF<sub>3</sub>, and they are used in stoichiometric amounts.<sup>12</sup>

We report here the catalytic allylation of imines with allyltributylstannane in the presence of catalytic amounts of lanthanide triflates (Scheme 1)<sup>13</sup>. The results obtained with a variety of imines are presented in Table 1.

Scheme 1  $R = C_{6}H_{5}: C_{6}H_{5}CH=CH; C_{6}H_{11}: CH_{3}(CH_{2})_{4}: COOC_{2}H_{5}; \square$   $R' = C_{6}H_{5}: 4-CH_{3}OC_{6}H_{4}: (C_{6}H_{5})_{2}CH: C_{6}H_{5}CH_{2}$  In = Yb; Sc; Lai) *Reagents and conditions*: imine (1 mmol): Ln(OTf)\_{3} (0.15 mmol); allyltributylstannane (1.5 mmol) CH\_{2}Cl\_{2} (5 mL); R.T.

Homoallylic amines,<sup>14</sup> valuable precursors for a number of  $\alpha$ -substituted alkylamines, are accessible through this methodology.

Entry	R	R'	Catalyst <sup>b</sup> (%) <sup>c</sup>	Yield <sup>d,e</sup>
1	C6H5	C6H5	Yb(OTf)3 (15)	56
2	**	81	Yb(OTf)3 (5)	22
3	**	**	La(OTf)3 (15)	62
4	**		Sc(OTf)3 (15)	66
5	C6H5	4-CH3OC6H4	Yb(OTf)3 (20)	73
6	"		La(OTf)3 (20)	70
7	C6H5	C6H5CH2	Yb(OTf)3 (15)	8
8	11		Sc(OTf)3 (15)	29
9	C4H3O <sup>f</sup>	н	Yb(OTf)3 (15)	30
10	C6H5CH=CH	4-CH3OC6H4	Yb(OTf)3 (20)	32
11	C6H11	(C6H5)2CH	Yb(OTf)3 (15)	50
12	**	"	La(OTf)3 (15)	53
13	C6H5	C6H5CH2	Yb(OTf)3 (100)	49
14	COOC <sub>2</sub> H <sub>5</sub>	4-CH3OC6H4	Yb(OTf)3 (15)	46
15			La(OTf)3 (15)	70

Table 1. Allylation of imines with allyltributylstannane promoted by lanthanide triflates.<sup>a</sup>

a:see typical procedure reported as note; b:the lanthanide triflates were not dried or activated; c:% of the catalyst in mole to respect the imine; d: isolated yields; e: no other by-products except hydrolized or unreacted imine were isolated; f:see Scheme 1

It is noteworthy that we do not use any activation procedure for the lanthanide triflates,<sup>10</sup> which are weighed in air without any particular precautions. The commercially available lanthanium, scandium and ytterbium triflates promote this allylation reaction, exhibiting a great variation of yield only for the case of entries 14 and 15. In this reaction a critical role is played by the  $R^{I}$  group of the imines, contrary to that which is observed for the reactions of enol sylanes with imines promoted by lanthanide triflates<sup>9</sup>. Only bulky and aromatic substituents are effective to achieve the desired amine. The origin of the difference in effects of the R<sup>1</sup> group (see Table1) will be addressed in further studies concerning the mechanism of the reaction. Lanthanide triflates are sparingly soluble in CH<sub>2</sub>Cl<sub>2</sub>, but complete dissolution was obtained when the imine was added at room temperature. We think that this indicates an effective complexation of the imino moiety to the lanthanide triflate. To examinate the role played by a possible transmetallation product resulting from mixing lanthanide triflates with allyltributyltin we prepared tributyltintriflate by an exchange reaction (from tributyltin chloride and silver triflate ) and we studied if this Lewis acid is an effective promoter for this reaction. The reaction of the pmethoxyimine of benzaldehyde with allyltributyltin in the presence of 15% of tributyltintriflate in methylene chloride, affords the corresponding homoallylamine in 14% yields. It is important to note that the imine derived from glyossylic acid can be used to access homoallylic aminoacids, precursor of non-proteogenic aminoacids. In these cases (entries 14 and 15 ), the yields are acceptable and this reaction does not suffer from the typical drawback of the attack of allylating species on the ester moiety.

Catalytic allylation of p-methoxy imine promoted by lanthanide triflates performed in other solvents like toluene or THF gives the desiderate product but in lower yields to respect the same reaction in CH<sub>2</sub>Cl<sub>2</sub>.

The reaction of allyltributyltin with chiral imines, promoted by lanthanide triflates, was also studied (Scheme 2).



In order to investigate the stereoselectivity of the allylation reaction, experiments were carried out with imines derived from S-1-phenyl-ethylamine or from S-valine methyl ester. The results with few examples of chiral imines are reported in Table 2.

Tab	le 2. Allylation of	chiral imine pro	moted by lanthanide t	riflatesa.	
Entry	R <sup>1</sup>	R <sup>2</sup>	Catalyst <sup>b</sup>	R,S:S,S <sup>c</sup>	Yield <sup>d</sup> %
1	Ph	Me	Yb(OTf)3	65:35	40
2	COOMe	iPr	Yb(OTf) <sub>3</sub>	18:82	41
3	COOMe	iPr	La(OTf)3	13:87	40
4	COOMe	iPr	Sc(OTf) <sub>3</sub>	9:91	36

a:see typical procedure. b:15% of catalyst was used. c: diastereoselection and configuration of the product was established with GC analysis: see ref. 14. d:isolated yields.

The reaction with chiral imines, although affording good stereoselection in some case, at this time only gives moderate yields. However the allylation of aldehydes promoted by lanthanide triflates<sup>10</sup> gives lower level of stereoselection. It is noteworthy that we obtained good levels of stereoselection using only catalyic amount of Lewis acids. This is almost unprecedent with imines, while in the case of chiral aldehydes LiClO4<sup>15</sup> can be used in catalytic amounts to obtain high levels of diastereoselection. It is interesting to note that the valine methyl ester auxiliary affords the prevalent formation of the S,S diastereoisomer, while the S-1-phenyl-ethylamine gives a slight prevalence for the R,S diastereoisomer. Our explanation is essentially based on the two different possible transition states showed in Fig 1.

Fig .1



In the case of the valine methyl ester the high diastereoselection can be derived from a chelate transition state. On the contrary, with the S-1-phenyl-ethylamine, to explain the different result a Felkin-Ahn transition state might be invoked. We are still working with other chiral imine to enhance the level of the diastereoselection. Addition of stereogenic and heterosubstituted stannanes and an enantioselective variant of this reaction will be our next efforts in this area.

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- 13 Typical procedure: To a stirred solution of imine (1 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) Ln(OTf)<sub>3</sub> (reagent grade) (Ln=Yb, Sc, La) (0.15 mmol) was added. After few minutes of stirring allyltributylstannane (1.5 mmol) was added and the resulting mixture was stirred under nitrogen for 24 hours at room temperature. The reaction was quenched by addition of water. The organic phase was separeted and the aqueous phase was extracted twice with CH<sub>2</sub>Cl<sub>2</sub>. The organic phases were combined, dried over sodium sulfate and the solvent was evaporated under low pressure to give an oil purified by flash cromatography (cyclohexane:ether from 95:5 to 70:30). Satisfactory analytical data, <sup>1</sup>H NMR, GC-MS and elemental analysis were obtained in all the cases.
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