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# Allylation of aldimines promoted by $NbCl_5$

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**Abstract**—Niobium chloride promoted the addition of allylstannanes to aromatic aldimines. Excellent *syn* diastereoselectivity was obtained in the addition of crotylstannane to *N*-benzylideneaniline (46:1). © 2002 Elsevier Science Ltd. All rights reserved.

Although the Lewis acid-promoted addition of allylstannane to aldehydes is a well-established synthetic method,[1] the allylation of aldimines still needs further development. The homoallylic amines thus obtained are of great interest since the C=C double bond of the allyl moiety can be further functionalized.

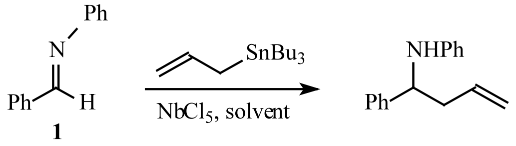
Due to the low reactivity of imines towards nucleophilic addition of allylstannanes, additives such as Lewis acids must be used. Thus, $BF_3\cdot OEt_2$, $TiCl_4$, $MgBr_2$, $Et_2AlCl$, among others, have been reported to accelerate the reaction rate.[2] Recent improvements in this reaction deal with imine activation by chlorotrimethylsilane,[3] catalytic lanthanide triflates[4] and catalytic Pd(II) or Pt(II) complexes.[5]

In our previous work in this area,[6] we studied the niobium(V) chloride-mediated allylation of aldehydes. $NbCl_5$ has proved to be a versatile Lewis acid[7] and is readily available in our country since Brazil accounts for about 60% of total niobium production.[8] Now we wish to report our results on the allylation of imines.

We initiated our study by searching for the best solvent system. Ethyl ether, acetonitrile and dichloromethane were investigated in the allylation of *N*-benzylideneaniline (**1**) at different temperatures. The results are shown in Table 1. Either $CH_3CN$ or $CH_2Cl_2$ gave satisfactory results at −15°C.[9] The yields were the same at lower temperatures using $CH_2Cl_2$ (entry 1) and decreased in all cases when the reaction was allowed to reach room temperature. A control experiment indicated that no reaction takes place in the absence of $NbCl_5$.

Next, the stoichiometry of the reaction was assessed (Table 2). We found that an excess of stannane improves the yields but is not critical to the success of the reaction, except when $Et_2O$ was used (entry 2). The lower yields obtained with 1 equiv. of allystannane may be due to its slight decomposition in the presence of $NbCl_5$.

**Table 1.** Experimental conditions and yields of the reactions between *N*-benzylideneaniline (**1**) and allyltri-*n*-butylstannane[a]



| Entry | Solvent | Yields (%)[b] | | |
|---|---|---|---|---|
| | | 0°C→rt | −15°C | −78°C |
| 1 | $CH_2Cl_2$ | 27 | 82 | 83 |
| 2 | $Et_2O$ | 18 | 41 | - |
| 3 | $CH_3CN$ | 62 | 80 | - |

[a] 1 equiv. of $NbCl_5$ and 2 equiv. of allylstannane were employed.
[b] Isolated yields of the chromatographically pure products.

**Table 2.** Influence of an excess of allylstannane on the allylation of *N*-benzylideneaniline (**1**), at −15°C

| Entry | Solvent | Yields (%)[a] | |
|---|---|---|---|
| | | −15°C[b] | −15°C[c] |
| 1 | $CH_2Cl_2$ | 72 | 82 |
| 2 | $Et_2O$ | 17 | 41 |
| 3 | $CH_3CN$ | 60 | 80 |

[a] Isolated yields of the chromatographically pure products.
[b] Imine:$NbCl_5$:stannane = 1:1:1
[c] Imine:$NbCl_5$:stannane = 1:1:2

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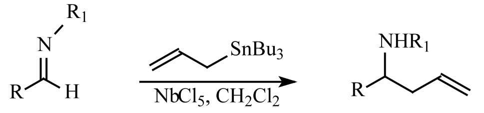
In this way, we defined the ideal conditions for the $NbCl_5$-mediated allylation of imines as being $CH_2Cl_2$ as the solvent,[10] at −15°C and using an excess of allylstannane. Under these conditions a variety of aromatics aldimines[11] were allylated in reasonable to good yields (Table 3).[12]

In some cases, bis-allylated[13] by-products were also obtained (ca. 10–15%) when 2 equiv. of allylstannane were used (Fig. 1). This can be circumvented using only a slight excess of this reagent.

The activation of the imines probably occurs via the formation of an iminium salt with $NbCl_5$ (Scheme 1). As an example, a dark-orange precipitate forms when imine **1** is added to a suspension of $NbCl_5$ in $CH_2Cl_2$.[14]

The stereo- and regioselectivity of these $NbCl_5$-promoted allylation reactions were assessed in the reaction between crotylstannane (3-methyl-allylstannane, 1:1 mixture of isomers) and imine **1** in the presence of $NbCl_5$ (Table 4).

**Table 3.** Results of the reactions between aldimines and allyltri-*n*-butylstannane



| Entry | Imine | R | $R_1$ | Yield[a] (%) |
|---|---|---|---|---|
| 1 | **1** | Ph | Ph | 82 |
| 2 | **2** | *p*-$NO_2$Ph | Ph | 80 |
| 3 | **3** | 2-Furyl | Ph | 59 |
| 4 | **4** | *p*-ClPh | *n*-Bu | 35 |
| 5 | **5** | *p*-ClPh | Ph | 51 |
| 6 | **6** | *p*-OMePh | Ph | 85 |

[a] Isolated yields of the chromatographically pure products.

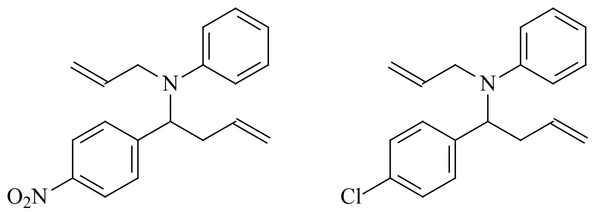


**Figure 1.** Bis-allylated by-products.

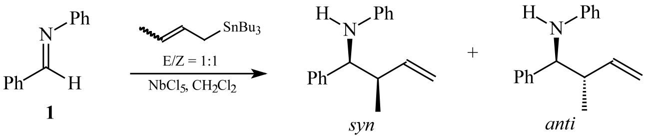
The reaction proved to be regiospecific in that no linear products were formed under any conditions. The allylated products were obtained in good yields and excellent diastereoselectivities (entries 1 and 2). The diastereomeric ratio was determined by GC analysis of the mixture of products and by $^1H$ NMR integration of the proton on the carbon attached to the nitrogen (*syn*: $\delta$ 4.33, $J=4.5$ Hz and *anti*: $\delta$ 4.07, $J=7.2$ Hz) and methyl groups (*syn*: $\delta$ 1.01, $J=6.9$ Hz and *anti*: $\delta$ 0.99, $J=6.9$ Hz). These data are in accordance with those reported.[2b]

At −78°C, the *syn* isomer is obtained almost exclusively, regardless of the stereochemistry of the stannane double bond.[15] These results are even superior to those obtained with other Lewis acids such as $BF_3 \cdot OEt_2$ and $TiCl_4$.[2]

Although the mechanism of these reactions is still controversial, the observed *syn* selectivity could be explained through an acyclic *antiperiplanar* transition state[16] (Fig. 2). Among the possible geometries, including the *synclinals*, the *antiperiplanar* (**ET1**) seems to be preferred since it has less steric crowding as compared to the others.

In summary, the scope of the $NbCl_5$-mediated allylation of imines has been studied. Homoallylic amines were obtained in good yields with excellent regio- and stereoselectivities. These results confirm the effective-

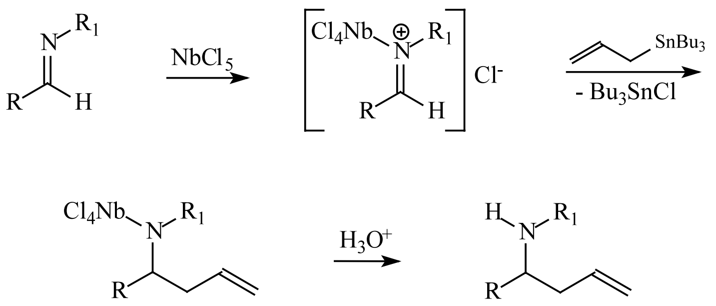
**Table 4.** Results of the reaction between crotylstannane[a] and *N*-benzylideneaniline (**1**) in $CH_2Cl_2$



| Entry | Temp (°C) | Mode of addition | *Syn*:*anti* | Yield[b] (%) |
|---|---|---|---|---|
| 1 | −15 | Normal | 9:1 | 60 |
| 2 | −78 | Normal | 46:1 | 62 |

[a] 2 equiv. of crotylstannane were used.

[b] Isolated yields of chromatographically pure products (*syn*/*anti* mixture).



**Scheme 1.** Activation of the imine by $NbCl_5$.

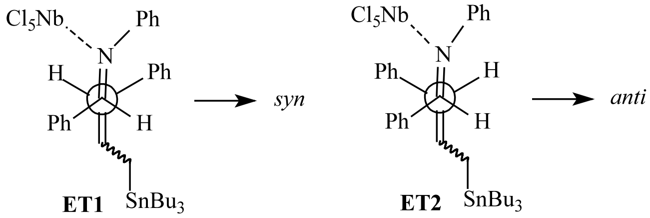


**Figure 2.** *Antiperiplanar* transition states proposed for the allylation of imines.

ness of $NbCl_5$ as a Lewis acid in these allylation reactions and make the procedure an attractive choice because of the simplicity and mildness of this methodology.

## Acknowledgements

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9. In contrast, $Et_2O$ was the best solvent in the allylation of aldehydes (see Ref. 6).
10. The choice for $CH_2Cl_2$ was based on the fact that the reaction in this solvent could be run at lower temperature (–78°C) as compared to $CH_3CN$.
11. Prepared from the corresponding aldehydes (1 equiv.) and primary amines (1 equiv.), in $Et_2O$, in the presence of $Na_2SO_4$.
12. Typical experimental procedure: To a fresh sublimed $NbCl_5$ (1 mmol) suspension in $CH_2Cl_2$ at –15°C, under an argon atmosphere, was added a solution of the imine in $CH_2Cl_2$ (1 mmol), followed by the addition of allylstannane (2 mmol), after 10 min. The reaction was monitored by TLC and after the consumption of the imine (1–2 h) it was quenched with sat. $NH_4Cl$, extracted with diethyl ether (3×15 mL) and stirred for 2 h with 10% KF in $H_2O$ (10 mL). The reaction mixture was then washed with brine, dried with $Na_2SO_4$ and concentrated at reduced pressure to furnish the crude product which was purified by silica gel chromatography (hexanes:EtOAc).
13. An example of palladium-catalyzed double allylation reaction has recently been reported: Nakamura, H.; Aoyagi, K.; Shim, J.-G.; Yamamoto, Y. *J. Am. Chem. Soc.* **2001**, *123*, 372.
14. A white precipitate attributed to the iminium salt formed when TMSCl was used as additive has been observed (see Ref. 3).
15. In contrast to the $NbCl_5$-mediated allylation of aldehydes (see Ref. 6)
16. For a complete discussion of the possible transition states geometries, see Ref. 2b.