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Intermolecular $FeCl_3$-Catalyzed Hydroamination of Styrenes

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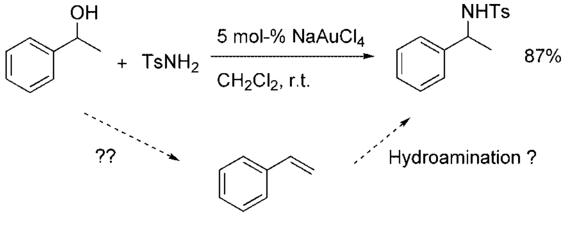
Hydroamination reactions of vinylarenes with nonnucleophilic nitrogen derivatives (*p*-toluenesulfonamide, *p*-nitroaniline, *p*-nitrobenzamide, ...) catalyzed by $FeCl_3$ are described. Interestingly, these reactions are catalyzed by an environmentally friendly and an inexpensive catalyst in the absence of any ligand or cocatalyst.

Introduction

The hydroamination reaction is a highly atom-economical process in which an amine N–H bond adds to an alkene (or an alkyne).[1,2] Intermolecular[3] hydroaminations have been traditionally carried out in the presence of alkali metals, lanthanides and group 4 complexes.[1] Acid-promoted hydroaminations are generally unsuccessful mainly due to the buffering effect of the amine substrate; thus, these reactions are scarcely reported.[4] However, Arnold and Bergman described the proton-catalyzed addition of amines to alkenes by using $PhNH_3B(C_6H_5)_4{\cdot}Et_2O$ as the promoter.[5] More recently, catalysis by late transition metals have been explored.[6] Hartwig first described the Markovnikov hydroamination reaction using a palladium catalyst, in the presence of a diphosphane and an acidic cocatalyst.[7,8] The same group then reported anti-Markovnikov reactions with the use of Rh^I and Ru^{II} complexes.[9] More recently, platinum(II)[10] and gold(I)[11,12] catalysis have been explored. Widenhoefer described a very efficient platinum-catalyzed Markovnikov hydroamination reaction of vinylarenes with amide derivatives. However, this reaction still requires the use of an expensive metal source and the presence of a ligand at high temperature.[10] Very recently, He and Che described a very interesting inter- and intramolecular gold(I) hydroamination reaction.[11,12] However, the high cost of such metals and ligands precludes their large-scale use. Therefore, the development of a general, efficient, cheap and readily available catalyst for hydroamination reactions is highly desirable. During the preparation of this manuscript, an efficient Fe^{III}-catalyzed *intramolecular* hydroamination reaction of tosylamides was described by Komeyama and Takaki.[3d] That paper prompted us to report our preliminary results on the Fe^{III}-catalyzed *intermolecular* hydroamination of vinylarenes.

As part of a program directed towards the preparation of new mono- and diamines and their use in the design of new transition-metal ligands,[13] we recently studied the direct Lewis acid catalyzed amination of benzylic alcohols (and diarylmethanols) and we found that gold(III) complexes are efficient catalysts in these reactions (Scheme 1).[14] An intriguing possibility is that this process could go through a vinylarene species followed by a hydroamination reaction.



Scheme 1.

Results and Discussion

Initial hydroamination reactions of styrene with $TsNH_2$ in the presence of gold(III) catalysts proved unsuccessful (Table 1, Entries 1 and 2).[15] Nevertheless, iron(III)[16] catalysts led to more promising results (Table 1, Entries 3–8). Several iron sources under different reaction conditions were explored. The best results were obtained in the presence of 10 mol-% of $FeCl_3$ in dioxane heated at 120 °C to afford the hydroaminated product in 73% yield (Table 1,

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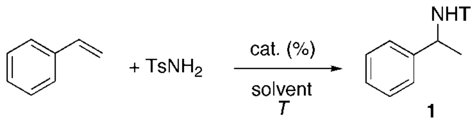
Table 1. Optimization of the catalyzed hydroamination of styrene with $TsNH_2$.

Entry	Catalyst	Equivalents [mol-%]	Conditions[b] Solvent	T [°C]	Isolated yield of **1** [%]
1	$NaAuCl_4$	10	DCM	room temp.	NR[c]
2	$NaAuCl_4$	10	dioxane	120	NR[c]
3	$FeCl_3$ anhydrous	10	dioxane	120	68
4	$FeCl_3$[a]	10	dioxane	120	73
5	$FeCl_3·6H_2O$	10	DCM	room temp	NR[c]
6	$FeCl_3·6H_2O$	10	THF	60	13
7	$FeCl_3·6H_2O$	10	DCE	80	27
8	$FeCl_3·6H_2O$	10	dioxane	120	71
9	$FeBr_3$	10	dioxane	120	<5
10	$FeCl_3·6H_2O/Bu_4NBr$	10/30	dioxane	120	NR[c]

[a] $FeCl_3$ 97% from Aldrich. [b] Reactions have been carried out with tosylamine (5 mmol), styrene (1 mmol) in solvent (2 mL). [c] NR = no reaction.

Entry 4). Although the different commercial sources of $FeCl_3$ [i.e. anhydrous $FeCl_3$, $FeCl_3$ (97% from Aldrich) and $FeCl_3·6H_2O$] gave similar results (compare Entries 3, 4 and 8), no reaction or low yields were obtained with $FeCl_2$, FeS, $Fe(NO_3)_3$, $Fe(acac)_3$, $FeBr_3$ and $FeCl_3$ on silica.

When the reaction was carried out in DCE at 80 °C, the product was obtained in low yield (27%). Careful examination of the TLC plates suggested that **1** might be unstable under these conditions. Indeed, complete decomposition occurred when compound **1** (Scheme 2) was heated to 80 °C in DCE overnight in the presence of 10 mol-% of $FeCl_3$ (in dioxane, such a decomposition could not be observed).



Scheme 2.

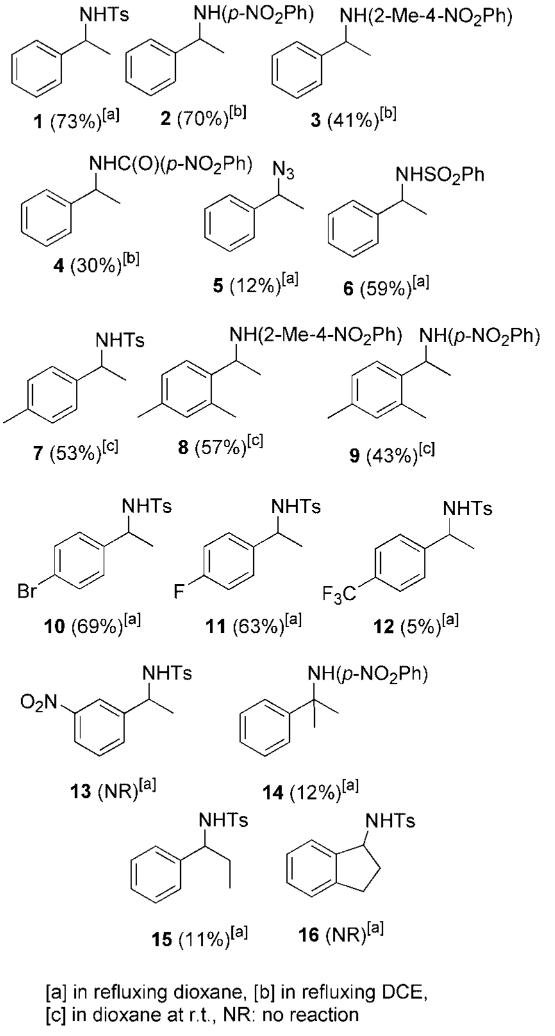
Next, other nitrogen sources were checked in the hydroamination reaction of styrene (Table 2). Interesting results were obtained with *p*-nitroaniline (Entry 3), 2-nitro-4-toluidine (Entry 4) and *p*-nitrobenzamide (Entry 5), whereas no reaction could be observed with substrates that contained more basic nitrogen atoms, such as phthalimide (Entries 6 and 7).

Table 2. Nitrogen sources in the $FeCl_3$-catalyzed hydroamination of styrene.

Entry	Nitrogen source	Conditions Solvent	T [°C]	Compound	Yield [%]
1	$TsNH_2$	dioxane	120	**1**	73
2	*p*-NO_2-aniline	dioxane	120	**2**	12[a]
3	*p*-NO_2-aniline	DCE	80	**2**	70
4	2-NO_2-4-toluidine	DCE	80	**3**	41
5	*p*-NO_2-benzamide	DCE	80	**4**	30
6	phthalimide	dioxane	120	–	NR[b]
7	phthalimide	DCE	80	–	NR[b]
8	$TMSN_3$	dioxane	120	**5**	12[c]

[a] Conversion completed with several unidentified byproducts. [b] NR = No reaction. [c] 60% conversion to product.

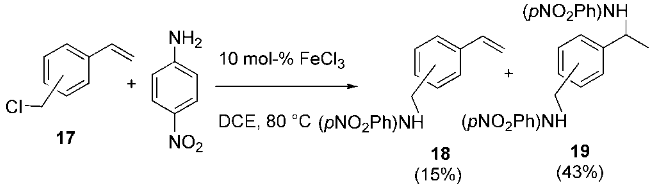
In addition, $TMSN_3$ was also used as a pronucleophile in these reactions (Table 1, Entry 8). Under similar conditions, the formation of a benzylic carbon–azide bond was clearly evidenced in the crude material through ^1H and ^{13}C NMR spectroscopic analysis in 60% conversion (Entry 8).



Scheme 3. Scope and limitations of the $FeCl_3$-catalyzed hydroamination of styrenes.

However, owing to product instability (degradation upon purification by column chromatography) a very low yield (12%) was obtained. Despite considerable experiments and careful purification attempts, this result could not be improved. Scope and limitations were next tested by varying the nature of the vinylarene residue (Scheme 3). Electron-donating groups ($+I$ and $+M$) are well tolerated in these reactions (compounds **6–11**) whereas electron-withdrawing groups ($–I$ and $–I$, $–M$) completely inhibit the hydroamination reaction (see compounds **12** and **13**). Interestingly, in the presence of electron-donating groups such as *p*-Me or 2,4-diMe, the reactions could be carried out at room temperature in moderate-to-good yields (see compounds **7–9**). As exemplified by compounds **14–16**, the hydroamination reaction is also sensitive to steric hindrance: reactions of either α- or β-substituted styrenes were slow and provided the hydroaminated products in rather low yields. It is also worth noting that styrene polymerization and/or hydroarylation byproducts could be observed in the crude NMR spectra when hydroamination-reluctant substrates were used.

Finally, the hydroamination of 1-(chloromethyl)-4-vinylbenzene[17] (**17**) was carried out and led to a mixture of monoaminated **18** (at the benzylic position) and diaminated **19** in 15 and 43% yields, respectively (Scheme 4).



Scheme 4.

Conclusions

We have developed a hydroamination reaction of vinylarenes with deactivated nitrogen nucleophiles. Interestingly, these reactions are catalyzed by environmentally friendly and inexpensive FeCl$_3$ in the absence of any ligand or cocatalyst. Further extension and optimization of this methodology is currently under investigation.

Supporting Information (see footnote on the first page of this article): General procedures for the hydroamination of styrenes and spectroscopic data.

Acknowledgments

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