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Indium-catalyzed allylation of imines with electrochemically assisted catalyst regeneration

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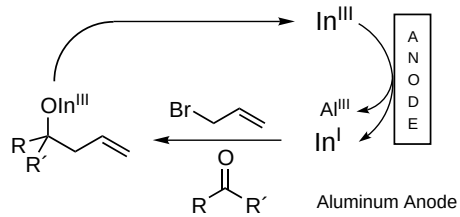
Abstract—The chemo-electrochemical regeneration of low valent indium(I) reagents for Barbier-type carbon–carbon bond formation processes is described for several C=N double bond systems. The homoallylic amines are obtained in good yields from aniline-derived aldimines. However, with ketimines and electron-poor aldimines, direct electrochemical or chemical reduction becomes a competing side reaction. Thus, hydrazones and sulfonimines gave almost exclusively the reduced products with only minor amounts of the allylated products being formed. © 2002 Elsevier Science Ltd. All rights reserved.

The allylation of imines, enamines and nitriles to afford homoallylic amines under Barbier-type conditions is a reaction of great interest in organic synthesis.[1] Many (transition) metal assisted protocols have been developed using stoichiometric amounts of the (transition) metal[2] or catalytic amounts of the (transition) metal in combination with another stoichiometric reducing agent.[3] Our attempt to establish an electrochemical version of the process, with regeneration of the spent low valent metal, in order to minimize the amount of salt-like by-products, generally the spent reducing agents, led to a chemo-electrochemical regeneration process for low valent indium(I) species.[4] Unusual in this regeneration process was the overall reduction of indium(III) at the anode, since the combination of an aluminum surface which acts as a reducing agent and the anodic polarization of the aluminum led to the overall production of reactive indium(I) species. This process could then be used for the indium-catalyzed allylation of aldehydes, ketones and esters as shown in Scheme 1.

We then focused our attention upon imines as starting materials for such an electrochemical allylation process. The results for several functionalized aldimines and ketimines are summarized in Table 1. The corresponding homoallylic secondary amines were isolated in good yields, while the current yield was in the range 80–95% (for runs 1, 2, 3 and 5).[5]



Scheme 1. Chemo-electrochemical regeneration of low valent indium(I)-species.

However, the cyano group (Table 1, entry 4) did not seem to be inert under the reaction conditions.[1k,l] Besides the desired product, which could be isolated in acceptable yield, other allylation products as well as unidentified side products were also formed, which could not be separated from each other and characterized with certainty. While the reactions with aniline-derived aldimines gave the allylated products, ketimines (entries 6 and 7) gave a mixture of the desired allylated product and a reduced product, which is derived from direct cathodic reduction of the ketimine. The reaction rate for the allylation is apparently quite low for such substrates, so that the direct electrochemical reduction at the cathode or the chemical reduction at the freshly generated aluminum surface of the anode become alternative reaction pathways.[6] Consequently this protocol is currently of somewhat limited use for aniline-derived ketimines.

Thereafter, other C=N double bond systems were examined, with nitrogen substituents that are more easily removed than the phenyl substituents of the aniline-

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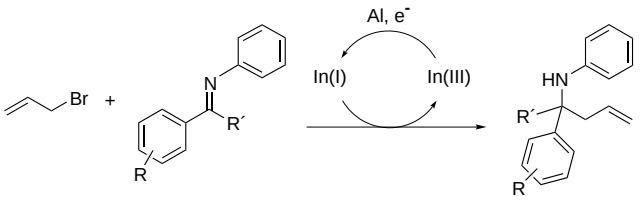
Table 1. Indium-catalyzed allylations of aldimines and ketimines under chemo-electrochemical regeneration of the catalyst[5,7]



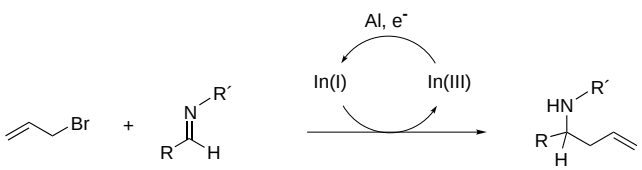
Run	R	R′	Yield (%)
1	H	H	86
2	4-Cl	H	95
3	4-MeO	H	76
4	4-CN	H	42[a]
5	3,5-$(MeO)_2$	H	93
6	H	CH_3	58[b]
7	4-MeO	CH_3	25[b]
8	*N*-Cyclopentyliden-*N*-phenylamin		55

[a] A complex mixture of products was obtained.
[b] Together with the reduced secondary amine as by-product.

derived substrates. The reaction with the benzyl-protected imine (Table 2, entry 1) proceeded with quantitative conversion of the starting material and the product was isolated in good yields after recrystallization of the corresponding hydrochloride from water. However, for C=N double bond systems such as tosylimines, phenylhydrazones and sulfonylhydrazones, the direct reduction of the C=N double bond to the corresponding hydrazine derivatives was observed along with only minor amounts of the desired allylated reaction products.

Besides steric effects, in these cases the relatively electron poor nature of the C=N double bond systems favors the formation of the reduced products rather than formation of the allylation products. In this respect the electrochemical version has disadvantages

Table 2. Indium-catalyzed allylations of C=N double bond systems under chemo-electrochemical regeneration of the catalyst[5,6]



Entry	R′	Yield (%)
1	Bn	64
2	Tos	Traces
3	NHPh	10[a]
4	NHPh-2,4-$(NO_2)_2$	Traces[a]
5	$NHSO_2Ph$	Traces[a]

[a] Detected by GC/GCMS along with reduced secondary hydrazines as by-products.

over classical chemical processes using stoichiometric amounts of indium. Although the process was designed to reduce the amounts of salt by-products, the chemo-electrochemical version presented here generates stoichiometric amounts of aluminum salts. In order to eliminate the sacrificial anode and circumvent the overpotential of the cathodic indium reduction, investigations are underway towards the generation of a purely electrochemical version of the indium-catalyzed allylation process for imines and carbonyl compounds.

Acknowledgements

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5. General procedure for the chemo-electrochemical allylation of imines:
   In a 50 mL beaker cell the imine derivative (2.0 mmol), allyl bromide (605 mg, 5.0 mmol, 2.5 equiv.), indium trichloride (22 mg, 0.1 mmol, 5.0 mol%) and tetra-*n*-butylammonium bromide (0.1 M) were dissolved in dry THF (20 mL) under a nitrogen atmosphere. The solution was electrolyzed at constant current (100 mA) until 1.0 F mol^{-1} was consumed on an aluminum foil anode (6 cm^2) and a platinum foil cathode (6 cm^2) and then stirred for another

10 min. After the removal of the solvents and extraction with ether, the products were either isolated by column chromatography or as the corresponding hydrochloride salt by treatment with gaseous HCl and recrystallization from water.

6. All products were characterized by ^{1}H, ^{13}C and MS. Analytical data for: *N*-[1-(3,5-dimethoxyphenyl)-3-butenyl]-*N*-phenylamine (Table 1, entry 5): ^{1}H NMR ($CDCl_3$, 300 MHz) $\delta = 7.14$ (2H, dd, $J = 7.5$, 8.4 Hz,). 6.70 (1H, tt, $J = 7.5$, 0.9 Hz), 6.60 (2H, d, $J = 2.2$ Hz), 6.59 (1H, d, $J = 1.3$ Hz), 6.56–6.35 (2H, m), 5.75–5.91 (1H, m), 5.15–5.30 (2H, m), 4.35 (1H, dd, $J = 8.0$, 4.8 Hz), 4.17 (1H, s_{br}), 3.80 (6H, s), 2,45–2.71 (2H, m). ^{13}C NMR ($CDCl_3$, 75 MHz) $\delta = 43.0$, 55.1, 57.3, 98.5, 104.2, 112.4, 113.4, 117.3, 118.1, 128.9, 134.6, 146.4, 147.3, 160.9.
7. For the successful allylation reactions (Table 1, entries 1, 2, 3 and 5; Table 2, entry 1), the cathodic reaction is the reduction of allyl bromide, leading to 1,5-hexadiene as by-product.