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New and mild allyl carbamate deprotection method catalyzed by electrogenerated nickel complexes

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Abstract

A Ni(II)-catalyzed electrochemical procedure for the simple and mild deprotection of allyl carbamates to the corresponding amines is described. The amines are obtained in yields of 40–99% and the method is compatible with several functional groups. Electrolyses are carried out in DMF or in THF in single-compartment cells in the presence of a consumable zinc anode. © 2000 Elsevier Science Ltd. All rights reserved.

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The development of mild and selective methods for the deprotection of functional groups constitutes a significant aspect in the synthesis of polyfunctional molecules. Carbamates are widely used as protecting groups for amines in amino-acid, peptide and oligonucleotide chemistry.[1]

Among the various amine protecting groups, the Boc group (*t*-butoxycarbonyl) has been frequently used in organic synthesis for its easy removal under acidic conditions.[2] Allyl carbamates have also been widely used, due to the fact that allyloxycarbamoyl groups are stable under mild acidic or basic conditions. Their selective deprotection is generally carried out in the presence of a Pd(0) catalyst and a reducing agent.[3–6]

Allyl groups constitute useful protecting units for carboxylic acids or alcohols, and several methods, including double-bond isomerization[7] and organometallic catalysis[6,8–10] are available for their deprotection.

Electrochemistry has also been reported for the selective deprotection of several functional groups.[11] To our knowledge, the electrochemical methodology has not yet been reported for allyl carbamate deprotection to the corresponding amines. However, electrochemistry, associated with catalysis by metal complexes has been reported as an efficient methodology for the related

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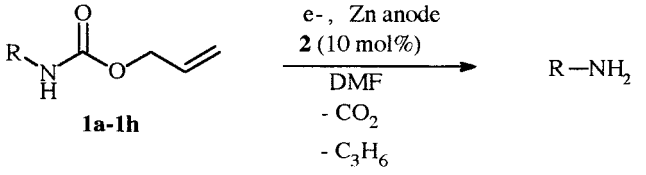
deprotection of allyl and propargyl ethers and esters in Sm(III),[12] Ni(II),[13] and Pd(II)-catalyzed reactions.[14,15]

We present here our results on the electrochemical reductive deprotection of allyl carbamates such as **1** in the presence of a catalytic amount of $[Ni(bipy)_3](BF_4)_2$ complex, **2** (bipy = 2,2′-bipyridine), in a reductive decarboxylative-type process as shown in Eq. (1).



(1)

The reactions were carried out in DMF under mild and neutral conditions, at room temperature, in a single-compartment cell fitted with a consumable Zn rod anode. The use of consumable anodes in selective electrosynthesis has already been reported.[16,17] The electrolyses were run at constant current with 10 mol% of Ni(II) complex, **2** with respect to substrates **1**. The results of the electrolyses of **1a**–**h** are presented in Table 1.

Allyl aryl carbamates **1a**–**d** were selectively deprotected in yields of 70–99%. The reaction generally consumed 2–3 F/mol of **1**. Esters and nitrile groups were compatible with the reaction conditions (entries 2, 3). Interestingly, the acetophenone group of **1d** (entry 4) remained unreacted and was not reduced during electrolysis, although aryl ketones are known to be electrochemically reduced to their pinacol adducts.[18]

Allylamines were found as by-products in other reported examples of allyl carbamate deprotection,[19] thus lowering the efficiency of the deprotection method. It is interesting to note that in the electrochemical procedure, no competitive allylamine formation could be observed.

Benzyl and cyclohexyl amines could be obtained in good to excellent yields from the corresponding allyl carbamates **1e** and **1f** (entries 5, 6). In the case of the acetal-carbamate **1g** (entry 7), the reaction afforded better isolated yields in THF than in DMF, due to the easier work-up procedure in THF. In the case of THF electrolyses, bis(trifluoromethylsulfonimide) lithium salt was used as supporting electrolyte (10^{-2} M) instead of tetrabutylammonium tetrafluorobarate (used in 10^{-2} M in DMF reactions), for its better solubility in THF. The dimethyl acetal of 2-aminoacetaldehyde was obtained in 60% yield.

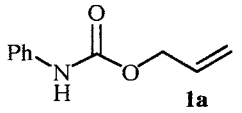
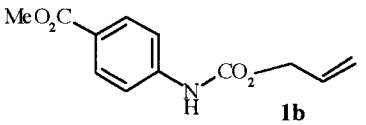
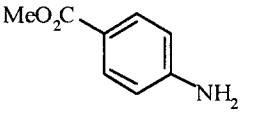
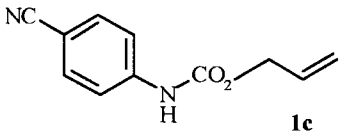
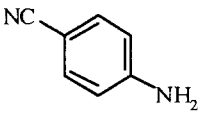
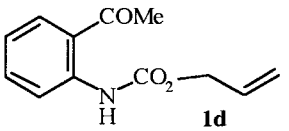
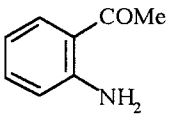
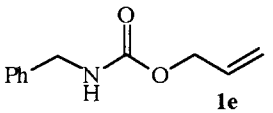
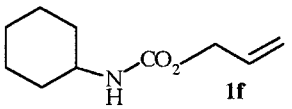
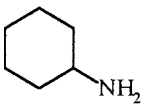
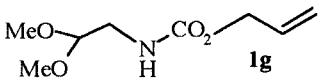
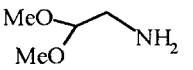
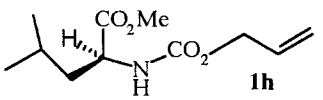
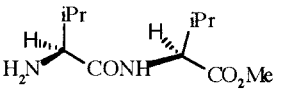
Protected *S*-(+)-amino acid **1h** afforded the corresponding deallylated dipeptide in 40% yield. No racemization occurred upon removal of the allyloxycarbonyl group and no formation of diketopiperazine was observed either.

In the one-compartment electrolysis, the reactions at the electrodes are, at the anode, the oxidation of the zinc metal rod into Zn^{2+} ions and at the cathode, we propose that Ni(0) species are generated and recycled from the reduction of the Ni(II) catalyst precursor, **2**.[20]

When compared to the Pd-catalyzed methodology,[3–6] the present method avoids the use of a stoichiometric amount of a reducing agent such as tin hydrides.

In conclusion, electrochemistry may provide an interesting and useful alternative method for allyl carbamate deprotection under mild and catalytic conditions, the reaction taking place at room temperature and under neutral conditions. The method is compatible with several functional groups such as ester, nitrile, ketone or acetal. It also presents the advantage of using a stable and easily available Ni(II) complex as the starting catalyst precursor.

Table 1
Electroreduction of allyl carbamates **1** catalyzed by complex **2**[a)]

Entry	Substrate	F/mol	Product	Isolated Yield
1	 **1a**	2.2	$PhNH_2$	78%
2	 **1b**	3.0		90%
3	 **1c**	3.0		70%
4	 **1d**	3.4		99%
5	 **1e**	3.0	$PhCH_2NH_2$	80%
6	 **1f**	2.0		99%
7	 **1g**	2.2		60%
8	 **1h**	5.0		40%

a) General electrolysis procedure. Electroreductions were carried out with 1 mmol of allyl carbamate in anhydrous DMF (entries 1-6, 8) or THF (entry 7) (20 mL) at constant current intensity of 60 mA using tetrabutylammonium tetrafluoroborate (entries 1-6), bis(trifluoromethyl sulfonimide) lithium (entry 7) or KBr (entry 8) as supporting electrolytes (10^{-2} M). The catalyst **2** was introduced in a 10% molar ratio with respect to the substrate. The electrolyses were performed with Zn/stainless steel couple electrodes at 20 °C and were followed by GC. A first acidic hydrolysis and diethyl ether extraction was followed by basification of the aqueous phase to pH 8-9 and diethyl ether extraction. The organic phase was dried over $MgSO_4$ and evaporated, affording the corresponding amine products. They were analyzed by GC and NMR and compared to authentic samples.

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