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Intramolecular Propargyl Transfer Reaction Catalyzed by Electrogenerated Nickel Complexes

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Abstract : The intramolecular transfer of the propargyl group of aryl propargyl ethers to a carbonyl group can be effected by a nickel-catalyzed electrochemical reaction. Homopropargyl alcohols with 2-hydroxyphenyl substituents can be obtained, using a magnesium anode in single compartment cells.

Key words: nickel; electrochemical; intramolecular; propargyl ether; aldehyde.

The use of organometallic catalysis associated with electrochemical reactions has already shown its potentiality in several coupling reactions involving organic compounds[1]. We report here our results on a novel electrochemical reactivity of bifunctional molecules derived from propargyl ethers and containing a carbonyl group, such as **1a-1f**, in the presence of nickel complexes.

We have recently reported that the selective reduction of aryl propargyl ethers to the parent phenols can be carried out in good yields, in a nickel-catalyzed electrochemical reaction[2]. This process, involving the cleavage of the propargyl-oxygen bond of the starting ether takes place under mild conditions and constitutes a new method of propargyl ether deprotection.

In order to get some insight on the reactivity of the propargyl moiety issued from the propargyl ether cleavage, we attempted to quench the unsaturated C-3 unit with carbonyl compounds. As an extension of the carbonyl propargylation by propargyl halides[3,4,5], the reaction of propargyl ether derivatives with carbonyl compounds has been recently described in the presence of diethyl zinc and Pd(0) catalysts[6]. Mixtures of allenic and propargylic alcohols were obtained, and the presence of diethyl zinc has been proposed as responsible for the umpolung of the propargyl palladium intermediates.

Propargylation of carbonyl compounds under electrochemical conditions has, to our

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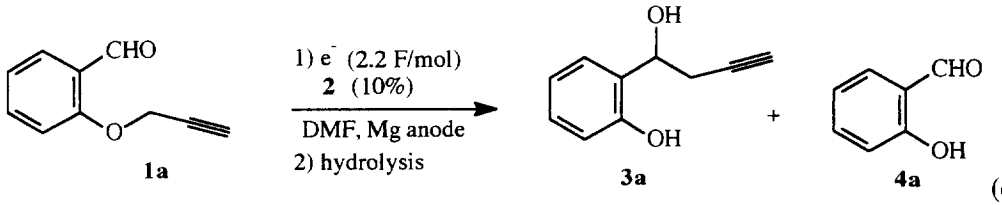
knowledge, not yet been reported. Related electrochemical allylation of carbonyl derivatives has been described, both in inter-[7,8,9] and intramolecular[10] versions, to afford homoallylic alcohols in good yields.

Our first attempts to react phenyl propargyl ether in the presence of aldehydes, such as pivaldehyde or benzaldehyde under electrochemical conditions, led mainly to the formation of pinacol products, issued from the reductive homocoupling of the carbonyl substrates.

The electrochemical intramolecular version of the carbonyl propargylation was then examined in the presence of *o*-substituted aryl aldehydes, such as **1**. Propargyloxy benzaldehyde **1a** was taken as the model compound for the study of the propargyl transfer reaction (eq. 1). The electrolyses were carried out at room temperature in DMF, in single compartment cells, and were catalyzed by the cationic Ni(II) complex, $Ni(bipy)_3^{2+}$, 2 BF_4^-, **2** (bipy = 2,2'-bipyridine)[11].



(eq. 1)

The Ni-catalyzed electroreduction of **1a** led to its complete conversion after the passage of 2.2 F/mol. Adduct **3a** was formed in 51% yield, together with 2-hydroxybenzaldehyde, **4a** (49% yield). The cleavage of the O-C bond of **1a** occurred quantitatively in this reductive process. The 2-(1-hydroxy-but-3-ynyl)-phenol, **3a** is issued from a first Ni-catalyzed O-C(propargyl) bond cleavage of **1a**, followed by the intramolecular propargyl transfer reaction to the carbonyl group. By-product **4a** is issued from the O-C(propargyl) cleavage, without C-3 transfer. The transfer of the propargyl unit to the carbonyl group occurred chemoselectively: only the homopropargyl alcohol was formed, without the allene isomer being present. It is also noteworthy that the aldehyde group was not reduced in this electrochemical process, and no alcohol or pinacol coupling products were formed.

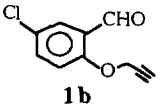
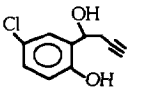
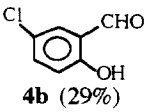
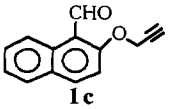
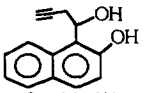
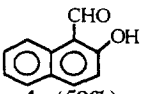
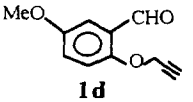
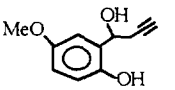
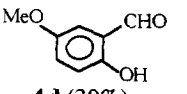
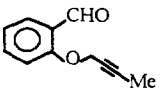
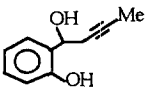
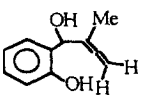
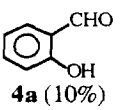
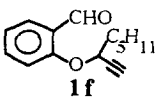
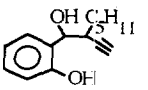
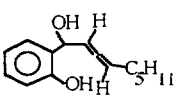
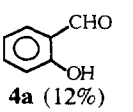
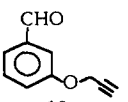
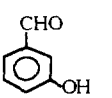
The presence of the nickel complex was essential for the coupling reaction. In the absence of **2**, the electrolysis of **1a** led to the recovery of 90% of the starting material without any propargyl transfer. In the electrochemical process, starting Ni(II) is reduced to Ni(0) at -1.2 V vs SCE; Ni(0) is presumably the active catalytic species effecting the O-C cleavage and the further carbonyl addition.

The influence of the nature of the electrodes in the reduction of **1a** was examined, and a magnesium anode associated with a nickel foam cathode afforded the best results.

The extension of this Ni-catalyzed reaction to other propargyl ethers, **1b-1h** was carried out, and some of these results are presented in Table 1.

The electrolysis of 5-chloro-2-propargyloxy benzaldehyde, **1b** led to the corresponding homopropargyl alcohol, **3b** in 71% yield (entry 2). A clean reaction occurred without any carbonyl reduction or homocoupling. It is interesting to note that the cleavage of the C-Cl

Table 1. Ni(bipy)$_3$(BF$_4$)$_2$-catalysed Electrochemical Propargyl Transfer from 1[a].

Entry	Substrate	F/mol	Products (% yield) Coupling Compounds		Cleavage Compounds
1	**1a**	2,2	**3a** (51%)		**4a** (49%)
2	 **1b**	2,0	 **3b** (71%)		 **4b** (29%)
3	 **1c**	3,2	 **3c** (41%)		 **4c** (59%)
4	 **1d**	2,5	 **3d** (65%)		 **4d** (30%)
5	 **1e**	2,6	 **3e** (47%)	 **5e** (33%)	 **4a** (10%)
6	 **1f**	2,0	 **3f** (33% of 2 diastereoisomers 10:1)	 **5f** (12 %)	 **4a** (12%)
7	 **1h**	2,0	—		 **4h** (83%)

a) General electrolysis procedure: The electrochemical single-compartment cell is a cylindrical glass vessel (capacity 30 ml), such as that described in ref. 12, equipped with a magnesium rod anode (immersed to 3 cm) and a nickel foam grid cathode. The electrolyses are carried out by using a stabilized constant current supply, Sodilec EDL 36.07. In the cell are introduced 20 ml of freshly distilled DMF, n-Bu$_4$NBF$_4$ (10^{-2}M), Ni(bipy)$_3$(BF$_4$)$_2$ (0.1 mmol) and the propargyl ether substrates **1** (1 mmol). The solution is stirred and electrolysed at constant current of 60 mA (3-10V between electrodes), up to the total consumption of the starting material (checked by GLC analysis of aliquots). The DMF solvent is then evaporated under vacuum and the solution hydrolysed with HCl 0.1M saturated with NaCl, up to pH 1-2 and extracted with Et$_2$O. The organic layers, dried over MgSO$_4$, are filtered and evaporated. The products are purified by column chromatography on silica-gel with hexane-ethylacetate (90/10) or pentane-diethyl ether (90:10) as the eluents. The products are analysed by NMR, IR, mass spectroscopy and GLC, and their spectra compared, when available, to those of authentic samples.

bond did not take place, although the aryl-chlorine bond is known to be reduced under similar electrochemical conditions[12]. In the presence of the nickel complex, the activation of the propargyloxy unit is selectively favoured.

The reduction of the naphthyl derivative, **1c** (entry 3), afforded **3c** in 41% yield, together with the cleavage compound, **4c**, in 59% yield. Electron-rich substrate **1d** (entry 4) gave 65% of **3d** in a selective reaction.

Substituted propargyl groups in substrates **1e** and **1f** could also be cleaved and intramolecularly transferred to the aldehyde group in 80 and 45% yield respectively (entries 5, 6). However, in these cases, a mixture of propargyl and allene alcohols was formed.

Propargyl transfer reactions with analogous methyl ketones was also tested. The electrosynthesis of the corresponding homopropargyl alcohol from 2-propargyloxy acetophenone, **1g**, was less efficient (≤ 10% yield), and the main reaction product was 2-hydroxy acetophenone. The low yield of propargyl transfer to ketones can be explained by their lower electrophilicity and is in agreement with the observations made in the electrochemical intramolecular transfer reactions of allyl groups[10].

The 3-propargyloxy benzaldehyde, **1h** was also prepared in order to examine the possibility of propargyl transfer from a *meta* position. No homopropargyl alcohol was formed and only 3-hydroxybenzaldehyde, the cleavage compound, was obtained in 83% yield. This result suggests that the transfer of the propargyl group to the carbonyl takes place intramolecularly.

In conclusion, a new nickel-catalyzed tandem electrochemical reaction has been developed. The process involves the propargyl transfer reaction from aryl propargyl ethers to aldehydes, with a first cleavage of the O-C bond of the propargyl ether, followed by the addition of the C-3 unit to the carbonyl group. In the case of non-substituted propargyl ethers, the reaction enables the chemoselective formation of 1-[2-hydroxyaryl]-3-butyn-1-ols without allene isomers.

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