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Nickel- and chromium-catalysed electrochemical coupling of aryl halides with arenecarboxaldehydes

Muriel Durandetti,* Jacques Périchon and Jean-Yves Nédélec

Laboratoire d'Electrochimie, Catalyse et Synthèse Organique, CNRS et Université Paris XII, 2 rue Henri-Dunant, 94320 Thiais, France

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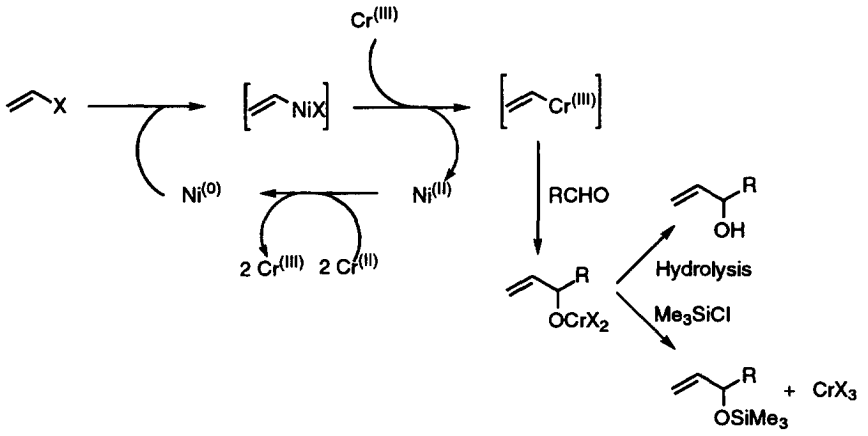
Abstract

Electrochemical arylation of arenecarboxaldehydes using a stainless steel sacrificial anode in the presence of Ni catalysts afforded the corresponding arylated secondary alcohols in good yields.

The Nozaki–Hiyama–Kishi reaction (coupling of vinyl or aryl halides with aldehydes) has been widely applied in organic synthesis.[1] The nucleophiles are readily available by oxidative insertion of $Cr^{(II)}$ or by transmetallation with $Cr^{(III)}$ from a wide range of functionalised substrates such as allyl, propargyl, aryl or alkenyl halides, alkenyl triflates or allyl phosphates.[2] Organonickel compounds are usually used as precursors of reactive vinylchromium reagents as illustrated in Scheme 1.



Scheme 1.

* Corresponding author. E-mail: durandetti@glvt-cnrs.fr

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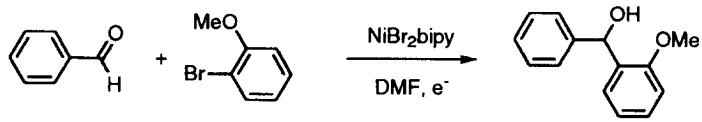
This reaction, however, has serious drawbacks in that a large amount of toxic $Cr^{(II)}$ reagent, sometimes up to 400 mol%, should be used. To minimise the amount of Cr reagent is a subject of keen studies, and regeneration of $Cr^{(II)}$ by reduction of $Cr^{(III)}$ with Mn,[3] Al,[4] or by electroreduction[5] was recently reported. However, although this reaction occurs with alkenyl halides, only few examples with aryl halides are reported and those only with aryl iodides. Also, best results are obtained with aromatic aldehydes bearing an electron-donating substituent, whereas electron-poor aromatic aldehydes give poor results, affording the corresponding pinacol derivatives predominantly. Herein, we address this shortcoming and report an electrochemical version of the Nozaki–Hiyama–Kishi reaction, which is catalytic in both chromium and nickel, and applies to aryl bromides and chlorides on the one hand and to aromatic aldehydes bearing electron-withdrawing groups on the other.

We have previously described electroreductive cross-coupling of aryl halides catalysed by nickel complexes in combination with the sacrificial anode process.[6] Therefore, we first tried to obtain arylated secondary alcohols by using the same procedure in the coupling between benzaldehyde and 2-bromoanisole taken as the model reaction (Eq. 1), but we only obtained quite a low yield for the addition product (less than 5%, Table 1, entry 1). We found, however, that the yield could be increased by use of larger amounts of the nickel catalyst, either introduced before starting the electrolysis (Table 1, entry 2), or generated continuously by oxidation of the anode made of a nickel rod (Table 1, entry 3). Stainless steel can alternatively be used as the anode to minimise the amount of nickel released, but care should be taken to keep the potential of the working electrode not less than −1.2 V/ECS (Table 1, entries 4–6), by adjusting the current intensity. Not surprisingly, a higher yield was obtained with the stainless steel anode containing some chromium (Fe:Cr:Ni, 72:18:10). This led us to find a convenient procedure, which is applicable to a large variety of arylations of benzaldehyde.



7.5 mmol 1.5 - 2 eq (1)

Table 1
Electroreductive coupling between benzaldehyde and 2-bromoanisole[a]

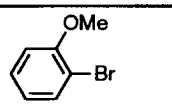
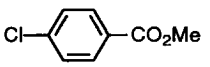
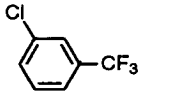
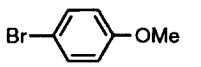
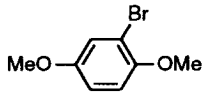
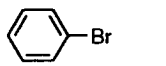
Entry	$NiBr_2$bipy (mol%)	Anode	Isolated yields[b] (%) of coupling product	PhCHO recovered (%)	nF/mol
1	13	Al	<5	–	2
2	100	Al	45	–	4.5
3	13	Ni	50	–	6.5
4	13	Fe/Ni 64/36[c]	30	15	4.5
5	13	Fe/Ni 64/36[d]	60	30	5
6	7	Fe/Cr/Ni 72/18/10[d]	71	20	5

a) For experimental conditions, see text. b) Based on initial benzaldehyde. c) During the electrolysis, the potential of the working electrode remains at *ca* -1.5 V/ECS affording pinacol. d) The current intensity was set between 0.1 and 0.25 A so that the potential of the working electrode remained ≥ -1.2 V/ECS. In addition, to minimise its dimerisation 2-bromoanisole was added constantly to the solution via a syringe pump at a rate of 2 mmol/h.

A typical procedure was as follows: DMF (40 mL), Bu_4NBF_4 (0.6 mmol), $NiBr_2$bipy (0.5 mmol), PhCHO (7.5 mmol), and a portion of ArX (ca. 0.3 mmol) were introduced into a one compartment cell fitted with a stainless steel rod (Fe:Cr:Ni, 72:18:10) as the anode, and a nickel sponge as the cathode (cathode area: ca. 20 cm^2). ArX was added constantly to the solution via a syringe pump at a rate of 2 mmol/h until the disappearance of PhCHO, as monitored by GC, and the electricity was supplied between 0.1 and 0.25 Å so that the potential of the working electrode remained ≥ -1.2 V/ECS. The reactions were conducted at room temperature.

A charge of 4–5 F/mol was necessary to consume benzaldehyde. A 5 F/mol charge corresponded to the release of 50% of chromium and 25% of nickel versus PhCHO. It was, however, possible to reduce the amount of chromium released to 20% by replacing an iron rod for the stainless steel rod after passing 2 F/mol, and then pursuing the electrolysis until 4–5 F/mol was passed. Results for the electrochemical coupling reaction between benzaldehyde and aryl bromides or chlorides under these standard reaction conditions are given in Table 2, where method A or method B refer to, respectively, the use of the stainless steel anode over the entire electrolysis, or its replacement by an iron anode after passing 2 F/mol.

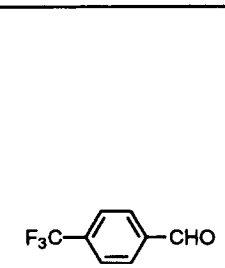
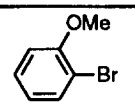
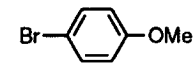
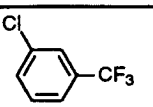
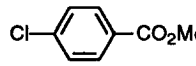
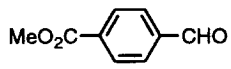
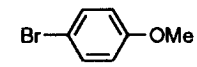
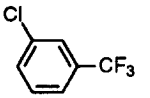
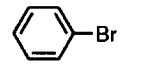
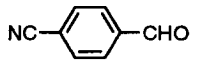
Table 2
Electroreductive cross-coupling between aryl halides and benzaldehyde

Entry	ArX	n eq.	Method[a]	Yield[b] (%) of alcohol	Yield (%) of ketone
1		1.5	A	71	8
2		1.4	B	60	3
3		1.7	A	66	3
4		1.4	B	64	< 1
5		1.3	A	45	5
6		1.3	B	52	2
7		1.6	A	51	4
8		1.7	B	48	6
9		1.3	A	64	6
10		1.2	B	64	6
11		1.6	A	50	6
12		1.6	B	52	5

a) Method A: the electrolysis was totally conducted with the stainless steel anode (Fe/Cr/Ni 72/18/10). Method B: the electrolysis was run with the stainless steel anode (Fe/Cr/Ni 72/18/10) during 1500 C, and then with an iron anode. b) Isolated yields, based on initial benzaldehyde; spectroscopic data for all products are in agreement with the given structures.

Chemical yields were moderate to good, using either method A or method B. Therefore, the substitution of the stainless steel rod by an iron rod does not significantly affect the chemical yield of the cross-coupling reaction, thus enabling the efficient cross-coupling between benzaldehyde and aryl halides using a catalytic amount of chromium (20% based on initial PhCHO). This method is efficient with aryl halides bearing electron-donating as well as electron-withdrawing substituents. However, with electron-donating substituents, aryl bromides must be used (no cross-coupling occurs with an aryl chloride), whereas with electron-withdrawing groups aryl chlorides are best used as aryl bromides preferentially give the biaryls.

Table 3
Electroreductive coupling between aromatic aldehydes bearing EWG and aromatic halides[a]

Entry	ArCHO	ArX	n eq.	Yield[b] (%) of alcohol	Yield (%) of ketone
1[c]			1.2	40	10
2			1.2	65	4
3			1.3	51	1
4[c]			1.1	72	1
5			1	58	1
6[c]			1.5	76	5
7[c]			1.2	62	1
8[c]			1.4	64	2
9[d]			1.2	40	4

a) For experimental conditions, see text. b) Isolated yields, based on initial ArCHO (7.5 mmol); spectroscopic data for all products are in agreement with the given structures. c) ArCHO was introduced in three portions to minimize its direct reduction. d) ArCHO and ArX were introduced constantly to the solution via a syringe pump at a rate of 1.7 mmol/h and 2 mmol/h respectively.

In all cases, two addition products were obtained: the alcohol Ph-CHOH-Ar as the major product, and a small amount of the ketone Ph-CO-Ar. The formation of benzyl alcohol in a same amount as the ketone indicates that a Meerwein–Pondorf–Verley reduction occurs between PhCHO and Ph-CHOH-Ar leading to $PhCH_2OH$ and Ph-CO-Ar.

We also applied the procedure to reactions involving arenecarboxaldehydes bearing electron-withdrawing groups. Results are reported in Table 3. These aldehydes are slightly more reactive than benzaldehyde. Therefore, the reactions can be conducted with both all the ArX initially in the solution, and a lower excess of ArX relative to the aromatic aldehyde. Yields are good and do not depend greatly on the nature of the substituent on the aromatic halide. The reduction of aromatic aldehydes bearing electron-withdrawing groups occurs before that of PhCHO (−1.55 V/ECS for *p*-CF_3-PhCHO, −1.45 V/ECS for *p*-CO_2Me-PhCHO, and −1.35 V/ECS for *p*-CN-PhCHO compared to −1.95 V/ECS for PhCHO). Therefore, the addition of the aromatic aldehyde in three portions to the reaction mixture was used to avoid the direct reductive coupling of the aldehyde into the corresponding pinacol. Thus, in the cross-coupling reaction between *p*-CF_3-PhCHO and *m*-CF_3-PhCl, yield of alcohol increased from 51% to 72% with the portionwise addition (Table 3, entries 3–4). Such an increase was also observed with *p*-MeOCO-PhCHO. In the case of *p*-CN-PhCHO, which is reduced at −1.35 V/ECS, i.e. near

the reduction potential of $Ni^{(II)}/Ni^{(0)}$ (−1.2 V/ECS), both reagents were added constantly via a syringe pump. For all reactions reported in Table 3 the electrolysis was stopped after passing 3 F/mol.

In conclusion, various substituted benzhydrols can be prepared in good yields in one step by a simple electrochemical method where chromium salts are released by oxidation of the anode, thus avoiding the use of $CrCl_2$, which is toxic, air and moisture sensitive, and expensive.

References

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2. For the use of substrates other than halides, see: (a) for alkenyl triflates: Takai, K.; Tagashira, M.; Kuroda, T.; Oshima, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 6048–6050; (b) for allylic phosphates: Nowotny, S.; Tucker, C. E.; Jubert, C.; Knochel, P. *J. Org. Chem.* **1995**, *60*, 2762–2772.
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6. Durandetti, M.; Nédélec, J.-Y.; Périchon, J. *J. Org. Chem.* **1996**, *61*, 1748–1755.