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Electrochemically Driven Catalytic Pd(0)/Cr(II) Mediated Coupling of Organic Halides with Aldehydes. The Nozaki-Hiyama-Kishi Reaction.

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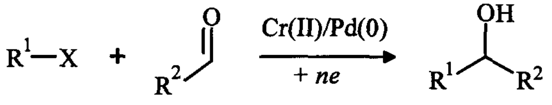
Abstract. An electrochemically driven, catalytic, Pd(0)/Cr(II) mediated coupling of organic halides with aldehydes is described. The reaction proceedes under mild conditions and the influence of reaction conditions and the mechanism are briefly discussed. © 1997 Elsevier Science Ltd.

The Cr(II)/Ni(0) mediated coupling of vinyl and aryl halides with aldehydes (the *Nozaki-Hiyama-Kishi reaction*) has been widely applied in organic synthesis.[1] The reactivity of organochromium(III) intermediates under the mild reaction conditions and the chemoselectivity for aldehydes in the presence of all other functional groups offers attractive advantages over other conventional organometallic carbonyl addition reagents. However, the reaction has suffered from the requirement for greater than stoichiometric amounts of divalent chromium salts although it is catalytic in nickel. We now report an electrochemically driven Nozaki-Hiyama-Kishi reaction which permits the use of catalytic amounts of Cr(II) salts in combination with catalytic amounts of Pd(0) (**Scheme 1**).[2,3]

The broad outline of the mechanism involves oxidative addition of a vinyl- or aryl-halide (**1**) to a zerovalent palladium complex followed by transmetallation with a chromium salt and addition of the resulting organochromate to an aldehyde (**2**).[4] In the presence of an oxophile[2] [Li(I) salts or TMSCl] the O-Cr(III) bond is cleaved and the liberated Cr(III) is reduced to Cr(II) on the electrode surface. Detailed mechanistic investigations (*e.g.* the nature of organic ligand exchange reaction and reactivation of palladium) are underway in our laboratory.

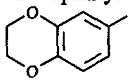


(1) (2) (3)

Scheme 1

As it can be seen from **Table 1**, both vinyl and aryl halides (**1**) react with aldehydes (**2**) in the presence of the Cr(II)/Pd(0) catalyst combination under constant current conditions.[5]

Table 1

Entry	X	R¹	R²	Yield (%)
1	Br	2-propenyl	Ph	69
2	Br	2-propenyl	2-Naphthyl	55
3	Br	2-propenyl		62
4	I	Ph	Ph	66
5	I	Ph	2-Naphthyl	54
6	Br	Ph	Ph	57
7	Br	Ph	2-Naphthyl	51

Preliminary optimisation of the process showed that the current density must be precisely controlled to avoid side reactions (biaryl formation or inactivation of mediator), that further increasing the molarity of $LiClO_4$ (oxophile and supporting electrolyte) does not influence the yields and that the best results were obtained when four ligand equivalents *per* palladium precatalyst were employed.

The advantages of this electrochemical protocol are mild reaction conditions, ease of scale-up, and reduction in waste. We thank Leeds University and Zeneca for support.

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5. *General procedure*: Electrolysis of the organic halide (1eq), aldehyde (1.2eq), $CrCl_2$ (10mol%) and 0.1mol% $Pd(OAc)_2$/0.4mol% PPh_3 was performed in 0.1M $LiClO_4$ in dry DMF, in a thermostatted divided H-type glass cell under constant current conditions (40mAcm^{-2}). A carbon working electrode and a platinum auxiliary electrode were employed under a N_2 atmosphere and reactions were run until t.l.c. monitoring showed the absence of starting material. Usual workup of the catholyte afforded the products (**Table 1**).

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