Nickel-catalysed Electroreductive Coupling of α-Halogenoesters with Aryl or Vinyl Halides

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β, γ-Unsaturated esters are obtained in moderate to good yields by a one-step electrochemical procedure from α-chloroesters and aryl or vinyl halides; a sacrificial aluminium anode, dimethylformamide as solvent, and a catalytic amount of nickel bromide-2,2'-bipyridine complex are used.

Aryl acetic and aryl propionic esters are very useful compounds, known for their analgesic and anti-inflammatory properties. Although an efficient electrocarboxylation of benzylic halides has been proposed to access these products,[1] the instability of some benzyl derivatives makes their synthesis from aromatic halides and halogenoesters highly desirable. A number of processes have been described,[2—5] all of them involving an organometallic intermediate and a nickel or palladium catalyst. The coupling of the Reformatsky reagent[2] or lithium ester enolates[3] with aryl or vinyl halides has been reported. Alternatively aryl zinc[4] and aryl magnesium[5] have been coupled with bromoesters, using nickel catalysts. All these procedures are not entirely satisfactory because they involve the preparation of organometallic species in appropriate solvents.

Electrochemistry has been used for the preparation of aryl nickel species, by electroreduction of ArX–Ni^{II} mixtures, and coupling with α-halogenoesters has been realized.[6] However, the process is not catalytic in nickel, and the electroreduction of ArX–$RCHXCO_2R'$–Ni^{II} mixtures affords succinate and biaryl without the expected cross-coupling product.

In this communication we report a new electroreductive cross-coupling method based on the use of a nickel catalyst and a sacrificial aluminium anode in a one-compartment cell [see equations (1) and (2)].

$$\text{Anode:}\quad Al \rightarrow Al^{3+} + 3e \qquad (1)$$

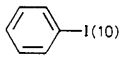
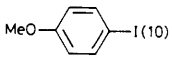
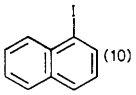
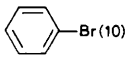
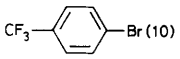
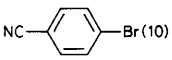
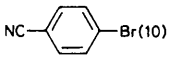
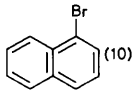
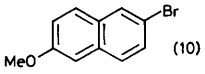
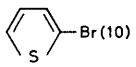
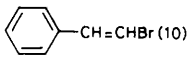
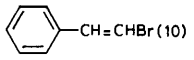
$$\text{Cathode:}\quad ArX + RCHClCO_2Me + 2e \xrightarrow{Ni} ArCHRCO_2Me + X^- + Cl^- \qquad (2)$$

A typical procedure is as follows: freshly distilled dimethylformamide (DMF; 35 ml), Bu_4NBr (1 mmol) as supporting electrolyte, $NiBR_2$, 2,2-bipyridine (0.5 mmol), iodobenzene (10 mmol), and methyl 2-chloropropionate (20 mmol) are introduced in the electrolysis cell fitted with an aluminium rod as the anode (1 cm diameter) and a carbon fibre cathode (20 cm^2 area). A constant intensity of 0.2 A is applied until 1.8 F/mol of chloropropionate have been passed (3500 C, 5 h). Hydrolysis with dilute HCl followed by diethyl ether extraction gives crude methyl phenyl-2-propionate contaminated by aluminium salts. Purification by column chromatography (silica gel, pentane: ether 85:15) gives 6.5 mmol of the product.

The procedure was successfully applied both to methyl chloroacetate and to methyl 2-chloropropionate, but α-chloro- and α-bromo-isobutyrates failed to give any coupling product. Iodobenzene could be replaced by aromatic, vinylic, or heterocyclic bromo-derivatives, with significantly lower but still interesting yields. Some typical results are collected in Table 1. By-products derived from methyl 2-chloropropionate are essentially $EtCO_2Me$ and $MeCH(CHO)CO_2Me$ resulting from solvent attack and $EtCOCH(Me)CO_2Me$ from Claisen condensation, no dimethyl succinate being found. The aromatic (vinylic) halide is reduced either to ArH or ArAr.

The whole cathodic process occurs at −1.2 V/SCE (SCE = standard calomel electrode), *i.e.* the reduction potential of Ni^{II} to Ni^0. Changing the aluminium anode for magnesium or zinc lowers drastically the yield of coupling product, as well as using a divided cell. In this later case, potentiostatic reduction at −1.2 V/SCE cannot be completed, implying that Ni^{II} is lost.

Table 1. Nickel-catalysed electroreductive coupling of α-chloroesters with aryl and vinyl halides.[a]

ArX(mmol)	Chloroester (mmol)	Isolated yield[b] of coupling product/%
	$ClCH_2CO_2Me$ (20)	70
	$MeCHClCO_2Me$ (20)	85
	$MeCHClCO_2Me$ (20)	80
	$MeCHClCO_2Me$ (50)	40
	$MeCHClCO_2Me$ (20)	66
	$ClCH_2CO_2Me$ (20)	60
	$MeCHClCO_2Me$ (20)	70
	$MeCHClCO_2Me$ (20)	40
	$MeCHClCO_2Me$ (20)	45
	$MeCHClCO_2Me$ (20)	40
	$ClCH_2CO_2Me$ (20)	55
	$MeCHClCO_2Me$ (20)	60

[a] For experimental conditions, see text. [b] Based on initial ArX. All products gave satisfactory ^1H NMR and mass spectra.

It may be inferred that the Al^{III} species produced by the anodic reaction are essential in the coupling process. Preliminary voltammetric investigations suggest the reaction sequence shown in equations (3)—(7).

$$Ni^{II} + 2e \rightarrow Ni^0 \quad \text{at } -1.2 \text{ V/SCE} \tag{3}$$

$$Ni^0 + RCHXCO_2Me \xrightarrow{fast} RCH(NiX)CO_2Me \tag{4}$$

$$Ni^0 + ArX \xrightarrow{slow} ArNiX \tag{5}$$

$$RCH(NiX)CO_2Me + AlX_3 \rightarrow RCH(AlX_2)CO_2Me + NiX_2 \tag{6}$$

$$RCH(AlX_2)CO_2Me + ArNiX \rightarrow RCH(Ar)CO_2Me + AlX_3 + Ni^0 \tag{7}$$

The key step appears to be the reaction in equation (6), which allows the cycling of the catalyst and accounts for the nature of the by-products. In conclusion, the use of sacrificial anodes in nickel-catalysed electrosyntheses not only allows simplification of the electrochemical procedure but also can alter the course of reactions involving different organometallic intermediates.

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