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Electroreductive Coupling of Organic Halides in Alcoholic Solvents. An Example : The Electrosynthesis of Biaryls Catalysed by Nickel-2,2' Bipyridine Complexes.

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Abstract : Alcohols like methanol or ethanol are suitable solvents for achieving the electrosynthesis of biaryls from aryl halides according to a procedure which involves a catalysis by nickel-2,2'-bipyridine complexes. All electrolyses were carried out at constant current in an undivided cell fitted with an iron or duralumin sacrificial anode. © 1997 Elsevier Science Ltd.

Introduction :

Economic as well as environmental considerations constrain modern chemistry to integrate the control of costs and risks into their procedures. In this context a growing effort is made in the search for alternative solutions avoiding the use of expensive and / or hazardous solvents.

Except when a protic medium is proscribed, low molecular weight alcohols or alcohol-water mixtures are solvents of choice since they have a good dissolving power for both organic substrates and inorganic salts and are compatible with chemical and electrochemical requirements.

A wide variety of reactions yielding carbon-carbon bond formation by either a direct electroreduction or indirect electrolyses employing mediators in such solvents have been reported[1,2]. However these electroreductive couplings are limited to easily reducible substrates and reactions involving radical intermediates. Actually, the medium proton activity of alcohols and water reduces the usable cathodic potential range and consequently electrodes with high hydrogen overvoltage, for instance lead or mercury, should often be employed. Besides, the ability to donate protons rules out the use of basic intermediates which will be rapidly neutralized[1].

[1] FAX. 01 49 78 11 48

For these reasons, the cathodic cleavage of carbon-halogen bonds is usually performed in polar aprotic solvents (DMF, NMP, HMPA, DMSO,...) especially when reductive couplings involving anionic intermediates are required [1].

In the field of electrochemical coupling reactions employing halogenated compounds, homogeneous catalysis has been used increasingly over the last twenty years. Indeed, low-valent electrogenerated complexes of transition metals like nickel, palladium or cobalt with phosphorous or nitrogen ligands have proved to be efficient catalysts [3]. In addition, the sacrificial anode process which has been developed during the last decade has increased the efficiency of various reactions while using more simple electrolytic devices [4].

We thus decided to attempt similar coupling reactions in an alcoholic medium. For our first example, we chose the electrosynthesis of biaryls catalysed by 2,2'-bipyridine (bpy)-nickel complexes and our results are reported here in.

Results and discussion :

The device and procedure are the same as those previously used for the Ni-bpy catalysed electrochemical couplings of aryl halides in the solvent NMP [5]. The electrolyses were then conducted in an undivided cell fitted with a sacrificial metallic anode. The electrolytic solution contained the aryl halide (ArX), the catalytic precursor $NiBr_2bpy$ and the supporting electrolyte in the selected solvent. A constant current was supplied between the consumable anode and a nickel grid cathode. The overall cathodic reaction (eq.1) is :

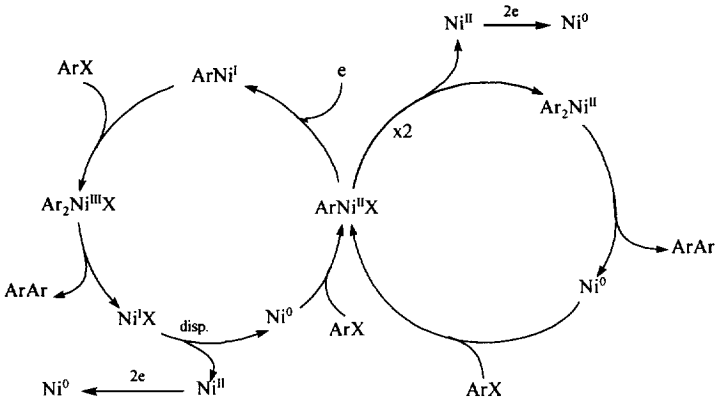
$$2\ ArX + 2\ e \xrightarrow[NiBr_2bpy\ catalyst]{Alcoholic\ solvent} Ar\text{-}Ar + 2\ X^- \qquad \text{eq. 1}$$

Previous works were devoted to the study of the catalytic mechanism of this reaction [6,7].The first step of the catalytic cycle is an oxidative addition (eq.3) of ArX to the zerovalent nickel complex generated at the cathode (eq.2).

$$Nibpy^{2+} + 2\ e \longrightarrow Ni^0bpy \qquad \text{eq. 2}$$

$$Ni^0bpy + ArX \longrightarrow ArNi^{II}Xbpy \qquad \text{eq. 3}$$

Several catalytic cycles having the σ-aryl-nickel intermediate in common should be taken into account for the nickel-bpy system, as illustrated in scheme 1. In a first cycle (left hand side), the $ArNi^{II}X$ is first reduced into the corresponding $ArNi^{I}$ species then transformed into a diaryl-nickel(III) complex. The latter undergoes a reductive elimination leading to the biaryl and Ni^{I} followed by the regeneration of the Ni^0 system [8]. A similar pathway has been proposed for nickel based catalytic systems using ligands other than 2,2' bipyridine [9,10,11]. An alternative mechanism has also been proposed in which the product results from the metathesis of σ-aryl-nickel(II) complex associated with bpy [6,8] or tertiary phosphines [12] and regeneration of Ni^{II} (scheme 1, right hand side).



Scheme 1 : Electroreductive dimerisation of aryl halides catalysed by Ni-bpy complexes.

Whatever the pathway may be, this catalytic mechanism should be efficient in alcohols provided that the various intermediate nickel complexes are not too basic or too reducing towards the solvent.

The reduction of bromobenzene into biphenyl was chosen as a model in order to study the influence of various parameters, such as the nature of the solvent and the electrolyte, and the nature of the sacrificial anode. The results are given in Table 1.

When the synthesis of biphenyl is carried out in methanol (Table 1, entry 3), the chemical yield is the same as those obtained in NMP[5] or DMF (Table 1, entries 1-2). However, pure ethanol is not suitable because the catalytic precursor $NiBr_2bpy$, prepared in this solvent[13], is poorly soluble. The complex $NiBr_2bpy$ becomes soluble enough when DMF or MeOH is added to EtOH and the synthesis of biphenyl is efficient in these conditions (Table1, entries 4-6). The use of anhydrous alcohol is not indispensable since the yields are the same when these mixed solvents are prepared from absolute or 95-96% ethanol. Nevertheless the water content should not be too high, otherwise the yield in biphenyl is significantly lowered and benzene becomes the main product (Table1, entries 7-8). We suppose that benzene arises from the protonation by water of one or another arylnickel intermediate involved in the catalytic process (scheme 1).

Sacrificial magnesium or aluminium anodes which are usually employed in aprotic solvents are not suitable in alcoholic media. Indeed, as soon as the electrolysis starts, the electroscoured metal undergoes an oxidation by the solvent which induces abundant formation of hydrogen. This reaction is very attenuated when duralumin is used in EtOH-DMF mixtures. Iron or stainless steel anodes are compatible with all the solvents tested. Another advantage of iron is that Fe(II) ions released by the electrolysis are electroreducible in our conditions at about -1.2 V *vs.* SCE. Under intentiostatic conditions, this avoids a shift of the potential of the cathode from the value -1 V *vs.* SCE, where the catalytic cycle is induced by the reduction of $NiBr_2bpy$, to more negative values where EtOH or MeOH are reduced at a nickel cathode (-1.6 to -1.7 V *vs.* SCE). On the other hand, the reduction of divalent iron explains that faradaïc yields are only moderate. Actually a deposit of iron was observed on the cathode in the course of the electrolyses but this does not affect the chemical yield in biaryl.

Table 1 : Nickel catalysed electrosynthesis of biphenyl from bromobenzene in various solvents

Entry	Solvent (v/v %)	Faradaïc yield [(c)] (%)	Biphenyl isolated yield (%)
1	NMP [(a, b)]		75
2	DMF [(a,b)]	85	85
3	MeOH	64	75
4	EtOH / DMF (80 / 20)	79	80
5	EtOH / MeOH (50 / 50)	72	84
6	EtOH / MeOH (20 / 80)	70	80
7	EtOH / MeOH / H_2O (76 / 20 / 4)	45	40
8	EtOH / H_2O (92 / 8)	26	36

Experimental conditions : Solvent : 50 mL, PhBr 15 mmol., $NiBr_2bpy$ 1.5 mmol., supporting electrolyte : NaBr 4.10^{-2} mol.L^{-1} except [(b)], I = 0.3 A, nickel grid cathode, iron anode except [(a)], temperature = 45°C

[(a)] Magnesium anode [(b)] Supporting electrolyte Bu_4NBF_4

[(c)] faradaïc yield based on the quantity of electricity required for a complete conversion of PhBr into PhPh.

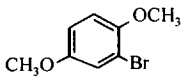
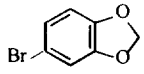
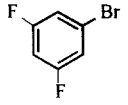
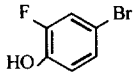
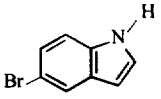
We have also shown that in the mixture EtOH-MeOH, the choice of the supporting electrolyte (BF_4NBu_4, NaBr or CH_3CO_2Na) has no significant influence on the faradaïc and chemical yields.

Then we have applied the method to the electroreductive coupling of various aryl halides. We chose to carry out the reactions either in the 1/1 (v/v) EtOH-MeOH mixture with an iron anode or in the 4/1 (v/v) EtOH-DMF mixture with an iron or duralumin anode. Results given in Table 2 show that the procedure is suitable to a wide range of aryl halides. In most cases, the yields are almost the same regardless of the solvent and the anode. As already observed in NMP[5,14], ortho-substituted aryl halides give only poor yields of dimer (Table 2, entries 15,16).

This synthesis of biaryls is as efficient in alcohols as in aprotic solvents, except for the case of poorly reactive aromatic chlorides. For instance, chlorobenzene does not react in alcoholic media whereas excellent yields in biphenyl were obtained in NMP[5] or pure DMF. This can be explained by a competition between two reactions involving zerovalent nickel : the oxidative addition leading to the σ-arylnickel complex (see eq. 3) or the oxidation by the alcohol (eq. 4).

$$Ni^0bpy + 2\ ROH \longrightarrow H_2 + Nibpy^{2+} + 2\ RO^- \qquad \text{eq. 4}$$

Table 2 : $NiBr_2$bpy catalysed electrosyntheses of biaryls from aryl halides

Entry	ArX	Solvent [a] / anode	Biaryl isolated yield (%)
1	PhBr	A / iron or duralumin	80
2	"	B / iron	84
3	PhI	B / iron	85
4	4 CH_3-C_6H_4Br	B / iron	90
5	4 CF_3-C_6H_4Cl	A / iron	80
6	3 F-C_6H_4Br	A / iron or duralumin	53
7	"	B / iron	46
8	4 F-C_6H_4Br	A / iron or duralumin	63
9	"	B / iron	82
10	4 HO-C_6H_4Br	A / iron or duralumin	84
11	"	B / iron	86
12	4 CH_3O-C_6H_4Br	A / iron	80
13	"	B / iron	46
14	4 CH_3O-C_6H_4I	A / duralumin	58
15	2 CH_3O-C_6H_4Br	B / iron	28
16		B / iron	29
17		A / iron or duralumin	48
18		B / iron	36
19		A / iron	54
20		B / iron	75
21		B / iron	86

[a] A = 4/1 (v/v) EtOH-DMF + Bu_4NBF_4 2.10^{-2} $mol.L^{-1}$

B = 1/1 (v/v) EtOH-MeOH + NaBr 4.10^{-2} $mol.L^{-1}$

Indeed, contrary to what is observed in NMP or DMF, even if the ligand bpy is added in excess, the zerovalent nickel-bpy complex is not stable in the mixed solvent EtOH-MeOH. The electrolysis of $NiBr_2$bpy in EtOH-MeOH at -1V vs S.C.E. can engage much more than two electrons and we had evidence for the formation of alkoxide ions in the electrolytic solution. This side reaction is negligible when the starting molecule is a iodo-, a bromo-, or an activated chloro-compound (e.g. 4 CF_3-C_6H_4Cl) which all react with zerovalent nickel much faster than chlorobenzene.

Di- or trichlorinated benzenes are also catalytically reduced under these conditions (4/1 (v/v) EtOH-DMF, iron anode, $NiBr_2$bpy 5%). The electrolyses afforded mixtures of polyaromatic products and chlorobenzene. The reaction is not selective but can offer an interesting method for disposing of polychlorinated compounds, as previously proposed by direct electroreduction in alcohol or other solvents [15]. For the di- or trichlorobenzenes tested, we have found that the dechlorination was obtained with a 80-90 % yield.

Conclusion :

The results presented in this paper show clearly that the nickel-bpy catalysed reductive coupling of aryl halides is efficient in more attractive experimental conditions than those which were previously used. Thus, aprotic solvents like DMF or NMP can be virtually or fully replaced by low molecular weight alcohols containing a cheap electrolyte like NaBr. The electrolytic technique using an undivided cell and a sacrificial iron or duralumin anode is very simple. The dehalogenation of polychlorinated compounds can also been carried out under these conditions.

The synthesis of biaryls is the first example reported. We have already obtained preliminary results which prove that alcoholic solvents can also be used as an alternative medium to achieve cross-coupling reactions between aryl halides and activated alkyl halides such as α-chloroketones or α-chloroesters [16]. Work is in progress concerning the electrochemical behaviour and the reactivity of nickel-bpy complexes in alcohols. We would especially like to determine which is the real catalytic pathway involved in the reaction conditions.

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Experimental :

Electrolysis

The electrochemical cell which has been already described [4] was fitted with a cylindrical nickel foam cathode (20 cm^2) which surrounded a rod (diam. 1 cm) of iron or duralumin as the anode. The electrosyntheses were carried out according to the following procedure. In DMF (10 ml) + EtOH (40 ml) or in EtOH (25 ml) + MeOH (25ml) were added Bu_4NBF_4 (1 mmol.) or NaBr (2 mmol.), the aryl halide (15 mmol.) and $NiBr_2$bpy (1.5 mmol.). A constant current of 0.3 A was applied until the consumption of ArX was achieved. The progress of the reaction was checked by G.C analysis of samples.

Purification and analysis of the products

After electrolysis, most of the solvent was evaporated and the residue was acidified (except for entry 21 in Table 2) with 6 mol.L^{-1} aqueous hydrochloric acid (50ml). Most of the synthesised biaryls are solid products. They were isolated by filtration, washing and drying. When the biaryl is a liquid (entry 6 in Table 2), the aqueous solution was extracted twice with diethylether (2x40 ml.), the organic layer was dried over magnesium sulphate and evaporated.

The crude products were purified by chromatography on a silica gel column (elution by pentane) and characterised by ^1H NMR (δ ppm *vs.* TMS), ^{19}F NMR (δ ppm *vs.* $CFCl_3$), ^{13}C NMR (δ ppm *vs.* $CDCl_3$) with a Brücker 200 MHz and mass spectrometry. All the biaryls obtained gave satisfactory spectroscopic values which are given below.

4,4'-dimethylbiphenyl. R.N. [613-33-2]

Mass m/z (rel. intensity) : 182 (M^+, 100) ; 167 (M-CH_3, 34.8) ; ^1H NMR ($CDCl_3$) : 7.1-7.5 (m, 8H) ; 2.4 (s, 6H) ; m.p. = 119-121 °C (litt. : 118-120 °C).

4,4'-bis (trifluoromethyl) biphenyl. R.N. [581-80-6]

Mass m/z (rel. intensity) : 290 (M^+, 100) ; 271 (M-F, 19.5) ; 221 (M-CF_3, 7.4) ; ^1H NMR ($CDCl_3$) : 7.6-7.7 (m, 8H) ; ^{19}F NMR : -62.5 (s, 6F) ; m.p. = 90.6-92.7 °C (litt. : 91-92 °C).

3,3'-difluorobiphenyl. R.N. [396-64-5]

Mass m/z (rel. intensity) : 190 (M^+, 100) ; 171 (M-F, 6.6) ; 95 ($[C_6H_4F]^+$, 5.5) ; ^1H NMR ($CDCl_3$) : 7.2-7.6 (m, 8H) ; ^{19}F NMR : -112.0 to -112.1 (m, 2F).

4,4'-difluorobiphenyl. R.N. [398-23-2]

Mass m/z (rel. intensity) : 190 (M^+, 100) ; 171 (M-F, 7.2) ; 95 ($[C_6H_4F]^+$, 5.5) ; ^1H NMR ($CDCl_3$) : 7.2-7.4 (m, 8H) ; ^{19}F NMR : -115.7 to -115.8 (m, 2F) ; m.p. = 87-90 °C (litt : 88-91 °C).

4,4'-dihydroxybiphenyl. R.N. [92-88-6]

Mass m/z (rel. intensity) : 186 (M^+, 100) ; 93 ($[C_6H_4OH]^+$, 6.9) ; ^1H NMR ($CDCl_3$) : 9 (s, 2H) ; 7.3 (d, 4H, J = 8.66 Hz) ; 6.8 (d, 4H, J = 8.66 Hz) ; m.p. = 278-280 °C (litt. : 278 °C).

4,4'-dimethoxybiphenyl. R.N. [2132-80-1]

Mass m/z (rel. intensity) : 214 (M^+, 100) ; 199 (M-CH_3, 29.7) ; ^1H NMR ($CDCl_3$) : 6.9-7.4 (m, 8H) ; 3.8 (s, 6H) ; m.p. = 176-178.3 °C (litt. : 177-180 °C).

2,2'-dimethoxybiphenyl. R.N. [4877-93-4]

Mass m/z (rel. intensity) : 214 (M^+, 100) ; 183 (M-OCH_3, 31.5) ; ^1H NMR ($CDCl_3$) : 6.9-7.2 (m, 8H) ; 3.7 (s, 6H) ; m.p. = 154-156 °C (litt. :154-156 °C).

2,2',5,5'-tetramethoxybiphenyl.

Mass m/z (rel. intensity) : 274 (M^+, 100) ; 259 (M-CH_3, 25.9) ; ^1H NMR ($CDCl_3$) : 6.8-7.0 (m, 6H) ; 3.70 (s, 6H) ; 3.66 (s, 6H) ; ^{13}C NMR ($CDCl_3$) : 55.4 ; 56.2 ; 112.3 ; 113.1 ; 116.9 ; 128.4 ; 151.1 ; 153.1 ; UV (solvent EtOH) : λ_{max} = 222 nm ; ε = 22273 ; m.p. = 105-106.3 °C. Calcd for $C_{16}H_{18}O_4$: C, 70.06 ; H, 6.61. Found C, 70.01 ; H, 6.69.

3,3',4,4'-Bis(methylenedioxy)biphenyl.

Mass m/z (rel. intensity) : 242 (M^+, 100) ; 212 (M-O=CH_2, 2.1) ; 121 ($[C_6H_3(CH_2O_2)]^+$, 3) ; ^{1}H NMR ($CDCl_3$) : 6.7-7 (m, 6H) ; 5.85 (s, 4H) ; ^{13}C NMR ($CDCl_3$) : 101 ; 107.2 ; 108.2 ; 120.0 ; 135.1 ; 146.5 ; 147.8 ; UV (solvent EtOH) : λ_{max} = 223 nm ; ε = 29443 ; m.p. = 146-148 °C. Calcd for $C_{14}H_{10}O_4$: C, 69.42 ; H, 4.16. Found C, 69.28 ; H, 4.23.

3,3',5,5'-tetrafluorobiphenyl.

Mass m/z (rel. intensity) : 226 (M^+, 100) ; 207 (M-F, 10.7) ; 113 ($[C_6H_3F_2]^+$, 2.4) ; ^{1}H NMR ($CDCl_3$) : 6.7-7.2 (m, 6H) ; ^{13}C NMR ($CDCl_3$) : 103.4 (t, J_2 = 25.2 Hz) ; 109.6 (d, J_2 = 25.7 Hz) ; 141 (t, J_3 = 12 Hz) ; 163.2 (dd, J_1 = 249.2 Hz, J_3 = 13 Hz) ; ^{19}F NMR : -108.6 (t, 4F, J_{F-H} = 7.85 Hz) ; UV (solvent EtOH) : λ_{max} = 246 nm ; ε = 22078 ; m.p. = 85.5-87 °C. Calcd for $C_{12}H_6F_4$: C, 63.73 ; H, 2.67 ; F, 33.60. Found C, 63.62 ; H, 2.81 ; F, 33.57.

3,3'-difluoro-4,4'-dihydroxybiphenyl. R.N. [396-86-1]

Mass m/z (rel. intensity) : 222 (M^+, 100) ; 111 ($[FC_6H_3(OH)]^+$, 6) ; ^{1}H NMR (CD_3COCD_3) : 8.6 (s, 2H) ; 7.0-7.2 (m, 6H) ; ^{19}F NMR : -132.7 to -132.9 (m, 2F) ; m.p. = 191-194°C (litt. : 189 °C).

5,5'-biindol. R.N. [66134-18-7]

Mass m/z (rel. intensity) : 232 (M^+, 100) ; 116 ($[C_6H_3(C_2H_2NH)]^+$, 6.7) ; ^{1}H NMR (CD_3COCD_3) : 10 (s, 2H) ; 7.7 (s, 2H) ; 7.4-7.2 (m, 6H) ; 6.4 (m, 2H) ; m.p. = 212-215 °C (litt. : 216-217 °C).

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