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Mechanism of the Nickel-Catalyzed Electrosynthesis of Ketones by Heterocoupling of Acyl and Benzyl Halides

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Summary. The mechanism of the nickel-catalyzed electrosynthesis of ketones by heterocoupling of phenacyl chloride and benzyl bromide has been investigated by fast scan rate cyclic voltammetry with $[Ni(bpy)_3^{2+}](BF_4^-)_2$ as the catalytic precursor ($bpy = 2,2'$-bipyridine). The key step is an oxidative addition of $Ni^0(bpy)$ (electrogenerated by reduction of the Ni(II) precursor) to $PhCH_2Br$ whose rate constant is found to be 10 times higher than that of $PhCH_2COCl$. The complex $PhCH_2Ni^{II}Br(bpy)$ formed in the oxidative addition is reduced at the potential of the Ni^{II}/Ni^0 reduction by a two-electron process which affords an anionic complex $PhCH_2Ni^0(bpy)^-$ able to react with $PhCH_2COCl$ to generate eventually the homocoupling product $PhCH_2COCH_2Ph$. The formation of the homocoupling product $PhCH_2COCOCH_2Ph$ is prevented because of the too slow oxidative addition of $Ni^0(bpy)$ to $PhCH_2COCl$ compared to $PhCH_2Br$. The formation of the homocoupling product $PhCH_2CH_2Ph$ is also prevented because $PhCH_2Ni^0(bpy)^-$ does not react with $PhCH_2Br$. This explains why the electrosynthesis of the ketone can be performed selectively in a one-pot procedure, starting from an equal mixture of $PhCH_2COCl$ and $PhCH_2Br$ and a nickel catalyst ligated by the *bpy* ligand.

Keywords. Electron transfer; Heterocoupling; Kinetics; Mechanism; Nickel.

Introduction

The synthesis of symmetrical biaryls by homocoupling of aryl halides [1] or triflates [2] requires a nickel or palladium catalyst and a reducing agent: a metallic powder or the electrons delivered by a cathode (Eq. (1)).

$$2ArX + 2e^- \ (\text{or Zn}) \xrightarrow{\text{Ni or Pd}} ArAr + 2X^- \ (\text{or Zn}X_2) \qquad (1)$$

The detailed mechanism of such reactions has been established under catalytic conditions [3] for a nickel catalyst ligated by a bidentate phosphine (*dppe* = 1,2-*bis*-(diphenylphophino)-ethane) in which monoelectronic transfers are involved (Scheme 1) [4a,b] and for a palladium catalyst ligated by a monodenate phosphine (PPh_3) in which the reaction proceeds *via* bielectronic transfers (Scheme 2) [5]. When the

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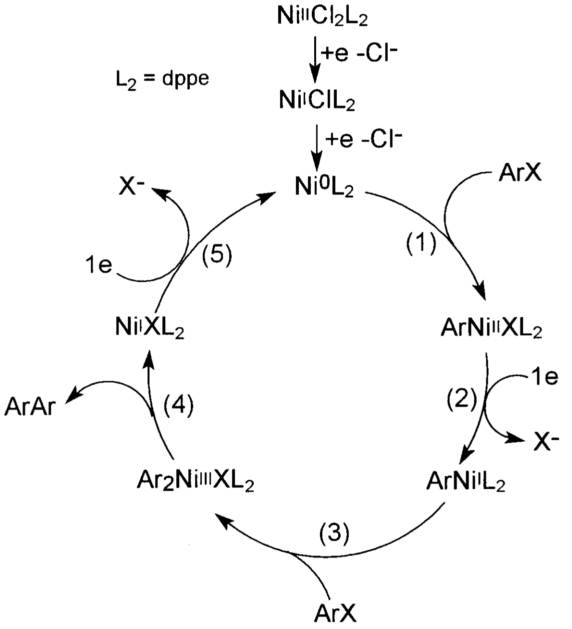
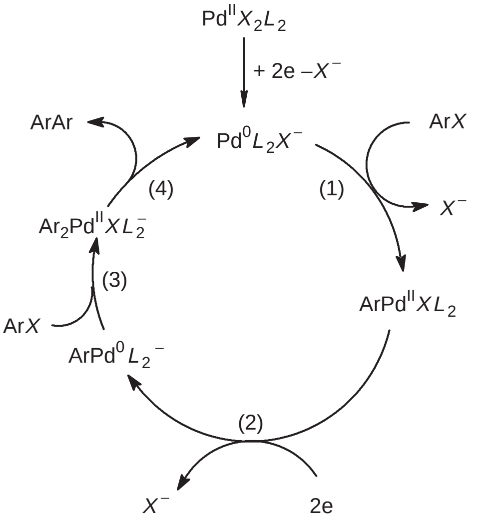


Scheme 1. Mechanism of the Ni-catalyzed homocoupling of aryl halides



Scheme 2. Mechanism of the Pd-catalyzed homocoupling of aryl halides

nickel catalyst is ligated by PPh_3 [4c] or by 2,2′-bipyridine (*bpy*) [4d], the mechanism is similar to that reported in Scheme 1.

In both mechanisms, two sequential oxidative additions are involved: between ArX and an M^0 complex (steps 1 in Schemes 1 and 2) and between ArX and an Ar-M^{I} complex (step 3 in Scheme 1) or an Ar-M^{0-} complex (step 3 in Scheme 2). Those oxidative additions are separated by either a monoelectronic transfer (step 2 in Scheme 1) or by a bielectronic transfer (step 2 in Scheme 2).

The rate of oxidative additions strongly depends on the aryl derivatives (reactivity order: ArI > ArO*Tf* > ArBr > ArCl [6]) as well as on the Ar structure, Aryl derivatives being more reactive when substituted by electron-withdrawing groups [6b,c, 7]. For these reasons, starting with a stoichiometric mixture of two differently reactive substrates ArX and Ar$'X'$ affords a mixture of symmetrical and unsymmetrical biaryls [5, 8] (Eq. (2)).

$$\mathrm{Ar}X + \mathrm{Ar}'X' + 2\mathrm{e}^- \xrightarrow{\text{Ni or Pd}} \mathrm{ArAr}' + \mathrm{ArAr} + \mathrm{Ar}'\mathrm{Ar}' + X^- + X'^- \qquad (2)$$

Therefore, the synthesis or electrosynthesis of unsymmetrical biaryls by heterocoupling of two different aryl derivatives is problematic. This difficulty may be bypassed by starting with the less reactive aryl halide in a batch process [5] or by a slow controlled introduction of the more reactive aryl halide during the course of the electrosynthesis using a syringe pump [8]. However, the Ni- or Pd-catalyzed cross-coupling of an aryl halide ArX and an organometallic derivative $\mathrm{Ar}'MX'$ (M = Mg, Zn) remains the most efficient process for the synthesis of unsymmetrical biaryls (Eq. (3)) [9]. Indeed, only the first oxidative addition step is required, the second one being replaced by a transmetallation step of the $\mathrm{Ar}M^{\mathrm{II}}XL_2$ complex by the organometallic derivative $\mathrm{Ar}'MX'$, which of course requires to be preliminary synthesized from $\mathrm{Ar}'X'$.

$$\mathrm{Ar}X + \mathrm{Ar}'MX' \xrightarrow{\text{Ni or Pd}} \mathrm{ArAr}' + MXX' \qquad (3)$$

On the contrary, the Ni-catalyzed heterocoupling of acyl and benzyl halides can be achieved in a one-pot procedure starting from an equal amount of the two organic reagents and a nickel catalyst ligated by the 2,2$'$-bipyridine ligand; the electrosyntheses afford selectively the corresponding ketones (Eq. (4)) [10].

$$R\mathrm{CO}X + R'X' + 2\mathrm{e}^- \xrightarrow{\text{Ni}} R\mathrm{CO}R' + X^- + X'^- \qquad (4)$$

This result necessarily requires that a different mechanism operates in which at least one step is not an oxidative addition. We report herein a mechanistic investigation of this reaction starting from an acyl chloride, a benzyl bromide, and a nickel catalyst ligated by the *bpy* ligand (Eq. (5)).

$$\mathrm{PhCH_2COCl} + \mathrm{PhCH_2Br} + 2\mathrm{e}^- \xrightarrow[-1.2\,\mathrm{V\ vs.\ SCE,\ CH_3CN}]{[\mathrm{Ni}(bpy)_3^{2+}](\mathrm{BF_4^-})_2} \mathrm{PhCH_2COCH_2Ph} + \mathrm{Cl}^- + \mathrm{Br}^- \qquad (5)$$

Results and Discussion

Rate and mechanism of the oxidative addition of $Ni^0(bpy)_2$ to $PhCH_2Br$

The mechanism of the electrochemical reduction of $\mathrm{Ni}X_2(bpy)$ (X = Cl, Br) in polar solvents such as *NMP* [11] or *DMF* [4d] has been reported. Depending on the halide ligated to the Ni(II) complex and the solvent, the electrochemical reduction may proceed in two one-electron steps (X = Cl in *DMF* or X = Br in *NMP* [4d, 11]) or in one two-electron step (X = Br in *DMF* [4d] or in *NMP* in the presence of excess *bpy* [11]). When the reduction is performed in the presence of excess *bpy*, the resulting Ni(0) complex is ligated by two *bpy* ligands ($Ni^0(bpy)_2$). However, the reactive complex in oxidative additions in the low-ligated complex $Ni^0(bpy)$, as evidenced by a negative (−1) reaction order in *bpy* (Eqs. (6, 7)) [11].

$$Ni^0(bpy)_2 \rightleftharpoons Ni^0(bpy) + bpy \tag{6}$$

$$Ni^0(bpy) + PhBr \longrightarrow PhNi^{II}Br(bpy) \tag{7}$$

The cyclic voltammogram of a solution of $[Ni(bpy)_3^{2+}](BF_4^-)_2$ (2 m*M* in acetonitrile containing $0.3\,mol \cdot dm^{-3}$ *n*-Bu_4NBF_4 as supporting electrolyte) at a steady gold disk electrode in the presence of excess *bpy* (40 m*M*) exhibited a single *quasi*-reversible reduction peak R_1 at −1.25 V *vs.* SCE (Fig. 1a, solid line), followed by a second *quasi*-reversible reduction peak R_2 at −1.94 V of half magnitude [12]. Determination of the absolute number of electron(s) involved in the first process revealed a two electron transfer at R_1 [13] (Eq. (8)) under the conditions of Fig. 1a. Consequently, R_2 involves a one-electron transfer, the electron being presumably transferred to the *bpy* ligand (Eq. (9)) as already observed for the reduction of $NiBr_2(bpy)$ [11].

$$Ni^{II}(bpy)_3^{2+} + 2e^- \longrightarrow Ni^0(bpy)_2 + bpy \quad \text{at } R_1 \tag{8}$$

$$Ni^0(bpy)_2 \rightleftharpoons Ni^0(bpy) + bpy \tag{6}$$

$$Ni^0(bpy) + 1e \longrightarrow Ni^0(bpy)^{\bullet -} \quad \text{at } R_2 \tag{9}$$

The Ni(0) complex formed in the electrochemical reduction at R_1 was characterized by its oxidation peak O_1 at −1.15 V (Fig. 1a, solid line). The mechanism of the reduction of $[Ni(bpy)_3^{2+}](BF_4^-)_2$ in acetonitrile is thus very similar to that of $NiBr_2(bpy)$ in the presence of excess *bpy* in *DMF* or *NMP* [4d, 11].

When the electrochemical reduction of $[Ni(bpy)_3^{2+}](BF_4^-)_2$ was performed at low scan rate ($0.5\,V\,s^{-1}$) in the presence of $PhCH_2Br$ (from 1 to 12 equivalents), the oxidation peak O_1 of the electrogenerated $Ni^0(bpy)_2$ was no longer observed (Fig. 1a, dashed line) as well as the reduction peak at R_2, evidencing a reaction of $Ni^0(bpy)_2$ with $PhCH_2Br$. Under these conditions, the reduction peak current intensity of $[Ni(bpy)_3^{2+}](BF_4^-)_2$ at R_1 exactly doubled (Fig. 1a, dashed line; note the twofold increased scaling) independent of the excess of $PhCH_2Br$. These experiments show that the electrogenerated $Ni^0(bpy)_2$ complex undergoes an oxidative addition to $PhCH_2Br$ affording a 16-electron complex $PhCH_2Ni^{II}Br(bpy)$ whose electrochemical reduction occurs at the same reduction potential as that of $[Ni(bpy)_3^{2+}](BF_4^-)_2$ (or at less negative potential) and also involves two electrons, resulting in an overall four-electron process at R_1 (Eqs. (10, 11)).

$$Ni^0(bpy)_2 + PhCH_2Br \xrightarrow{k_1^{app}} PhCH_2Ni^{II}Br(bpy) + bpy \tag{10}$$

$$PhCH_2Ni^{II}Br(bpy) + 2e^- \longrightarrow PhCH_2Ni^0(bpy)^- + Br^- \quad \text{at } R_1 \tag{11}$$

This four-electron reduction ends up with the formation of an anionic 16-electron complex $PhCH_2Ni^0(bpy)^-$, formally a Ni^0 complex ligated by the anion $PhCH_2^-$. Similar anionic $ArPd^0(PPh_3)_2^-$ complexes have been characterized during the bielectronic reduction of $ArPd^{II}Br(PPh_3)_2$ [14]. Although $ArPd^0(PPh_3)_2^-$ complexes are involved in an equilibrium with the anion Ar^- and $Pd^0(PPh_3)_2$ this is not the

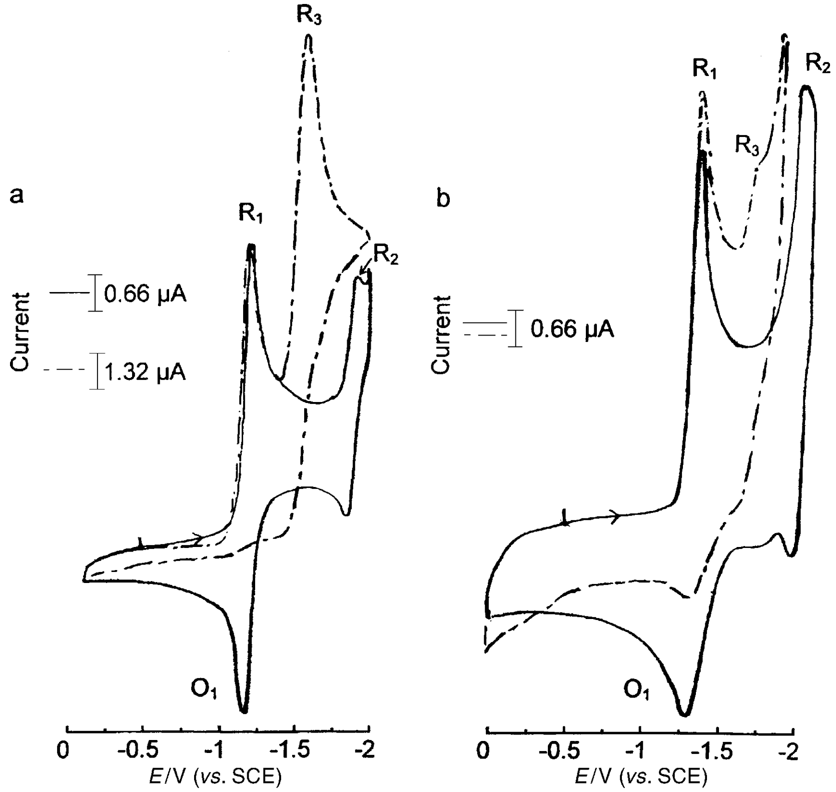


Fig. 1. Cyclic voltammetry performed in acetonitrile (containing $0.3\,M$ n-$Bu_4NBF_4)^{2+}$ at a steady gold disk electrode (i.d.: 0.5 mm) at a scan rate of $0.5\,V \cdot s^{-1}$ at 25°C; a) (—): $[Ni(bpy)_3^{2+}](BF_4^-)_2$ (2 m*M*) and 2,2′-bipyridine (40 m*M*); (·—·—·): $[Ni(bpy)_3^{2+}](BF_4^-)_2$ (2 m*M*), 2,2′-bipyridine (40 m*M*), and $PhCH_2Br$ (8 m*M*); b) same experimental conditions as in Fig. 1a except that both voltammograms were performed at a faster scan rate ($500\,V \cdot s^{-1}$), at a smaller gold disk electrode (*i.d.*: 0.125 mm), and recorded at the same current scaling

case for $PhCH_2Ni^0(bpy)^-$ since the anion $PhCH_2^-$, if present, would easily react with $PhCH_2Br$ producing $PhCH_2CH_2Ph$ in a catalytic process. This reaction can be excluded since (*i*) the reduction peak R_1 is not a catalytic peak (*i.e.* its current intensity does not increase with $PhCH_2Br$ concentration provided it is over-stoichiometric) and (*ii*) no $PhCH_2CH_2Ph$ was formed during an electrosynthesis performed at the potential of R_1 ($-1.2\,V$).

When the scan rate ν was progressively increased (from 0.2 to $2000\,V \cdot s^{-1}$), the reduction peak at R_1 became more and more reversible (Fig. 1b, dashed line), and its reduction peak current relatively decreased, going from 4 to 2 electrons, as evidenced by the plot of $i^{red}(R_1)/i^{red}(R_1)_0$ *vs.* $\log([PhCH_2Br]/\nu)$ (Fig. 2a); $i^{red}(R_1)$ is the reduction peak current at R_1 in the presence of $PhCh_2Br$, $i^{red}(R_1)_0$ is the reduction peak current at R_1 in the absence of $PhCH_2Br$; both currents were determined at the same scan rate) [15]. This behavior is characteristic of the progressive suppression of a subsequent chemical step involving $PhCH_2Br$ with a reaction order of unity when the time scale of the experiment is decreased (*i.e.* when the scan rate ν is increased). The curves shown in Fig. 2a are thus representative of the kinetics of the oxidative addition of $PhCH_2Br$ to the electrogenerated $Ni^0(bpy)_2$ (Eq. (10)). The higher the

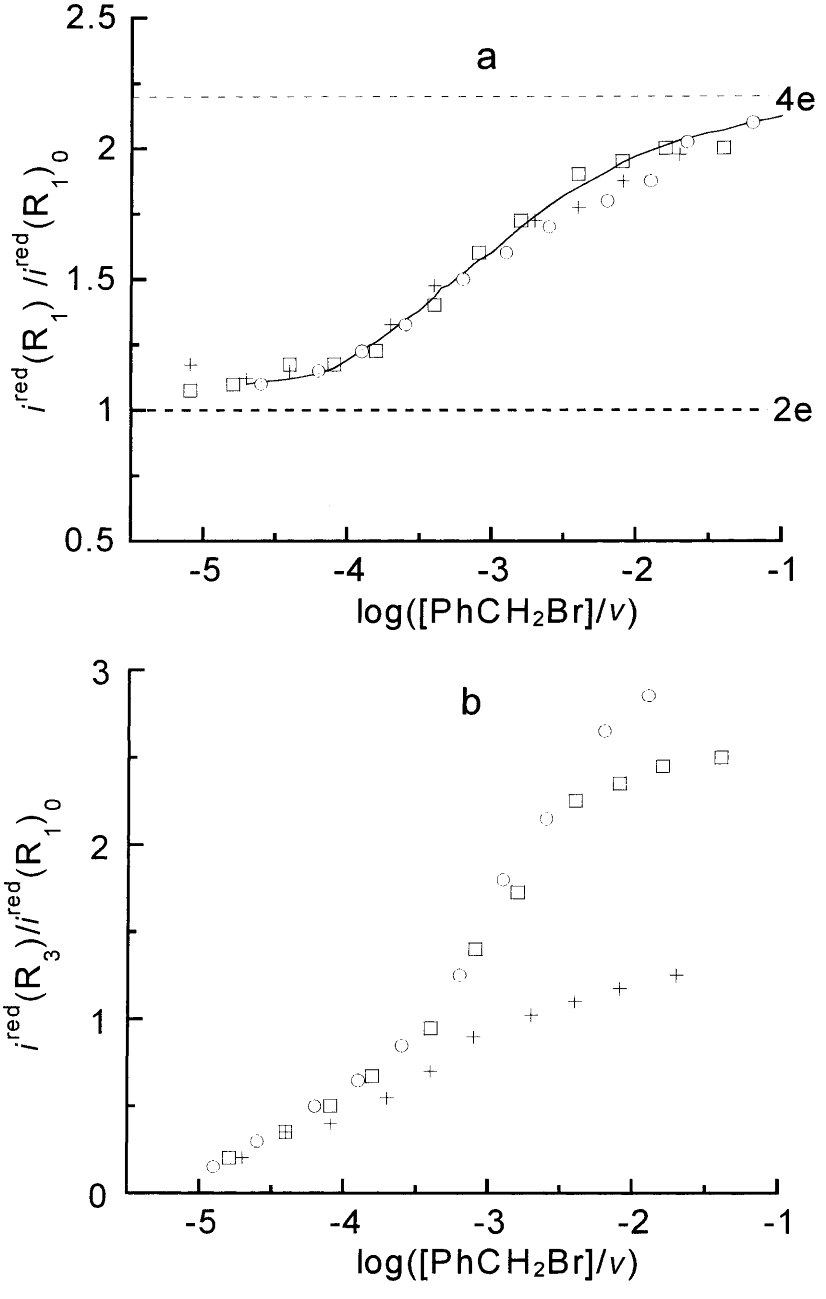


Fig. 2. a) Kinetics of the oxidative addition of $PhCH_2Br$ to the $Ni^0(bpy)_2$ complex generated by the reduction of $[Ni(bpy)_3^{2+}](BF_4^-)_2$ (2 m*M*) in the presence of 2,2-bipyridine (40 m*M*) in acetonitrile (containing 0.3 *M*, n-Bu_4NBF_4) at 25°C: variation of $i^{red}(R_1)/i^{red}(R_1)_0$ *vs.* $\log([PhCH_2Br]/\nu)$. $i^{red}(R_1)$ is the reduction peak current at R_1 (see Fig. 1) in the presence of $PhCH_2Br$ ($[PhCH_2Br] = 4$ m*M* (+), 8 m*M* (□), 12 m*M* (o)), $i^{red}(R_1)_0$ is the reduction peak current at R_1 in the absence of $PhCH_2Br$. Both currents were determined at the same scan rate in the range $0.2 < \nu < 2000\,V \cdot s^{-1}$. The solid line is the theoretical kinetic curve [15] with $k_1^{app} = 6 \times 10^4\,M^{-1}s^{-1}$ [15a]. b) Kinetics of the catalysis of the homocoupling of $PhCH_2Br$ by the $Ni^0(bpy)_2$ complex generated by the reduction of $[Ni(bpy)_3^{2+}](BF_4^-)_2$ (2 m*M*) in the presence of 2,2′-bipyridine (40 m*M*) in acetonitrile (containing 0.3 *M*, n-Bu_4NBF_4) at 25°C: variation of $i^{red}(R_3)/i^{red}(R_1)_0$ *vs.* $\log([PhCH_2Br]/\nu)$. $i^{red}(R_3)$ is the reduction peak current at R_3 (see Fig. 1) in the presence of $PhCH_2Br$ ($[PhCH_2Br] = 4$ m*M* (+), 8 m*M* (□), 12 m*M* (o)), $i^{red}(R_1)_0$ is the reduction peak current at R_1 in the absence of $PhCH_2Br$. Both currents were determined at the same scan rate in the range $0.2 < \nu < 1000\,V \cdot s^{-1}$.

scan rate, the smaller the time scale for the oxidative addition, and consequetly the smaller the amount of $PhCH_2Ni^{II}Br(bpy)$ formed during the voltammetric scan. The rate constant of the overall oxidative addition (Eq. (10)) was determined after a simulation of the theoretical kinetic curve [15b] to $k_1^{app} = 8 \times 10^5\,M^{-1}s^{-1}$. In the presence of added *bpy* (20 equivalents), the rate of the oxidative addition was smaller ($k_1^{app} = 6 \times 10^4\,M^{-1}s^{-1}$).

Mechanism of the Ni^0 (bpy)$_2$-catalyzed homocoupling of PhCH$_2$Br

When the electrochemical reduction of $[Ni(bpy)_3^{2+}](BF_4^-)_2$ was performed at low scan rate ($0.5\,V \cdot s^{-1}$) in the presence of an excess of $PhCH_2Br$, a new irreversible reduction peak R_3 was observed at -1.57 V (Fig. 1a, dashed line) whose peak current was found to increase when the $PhCH_2Br$ concentration was increased (Fig. 2b). Since peak R_3 does not pertain to the electrochemistry of $PhCH_2Br$ whose reduction potential is more negative than -1.6 V, it features a catalytic process. The reduction current of this catalytic peak relatively decreased when the scan rate was increased. The decrease of the reduction current of R_3 was concomitant with the decrease of the current R_1 from $4e^-$ to $2e^-$ (compare Fig. 1a, dashed line, with Fig. 1b, dashed line). This coincidence is better seen in Fig. 2b which shows the plot of $i^{red}(R_3)/i^{red}(R_1)_0$ *vs.* $\log([PhCH_2Br]/\nu)$ ($i^{red}(R_3)$ is the reduction peak current at R_3 in the presence of $PhCH_2Br$, $i^{red}(R_1)_0$ is the reduction peak current at R_1 in the absence of $PhCH_2Br$; both currents were determined at the same scan rate). Peak R_3 corresponds therefore to the second reduction step of the complex formed in the oxidative addition, presumably through injection of one electron to the *bpy* ligand (Eq. (12)).

$$PhCH_2Ni^0(bpy)^- + e^- \longrightarrow PhCH_2Ni^0(bpy)^{2-} \quad \text{at } R_3 \qquad (12)$$

As recalled above, an electrolysis performed at the reduction potential of R_1 (-1.2 V) did not afford any $PhCH_2CH_2Ph$, whereas the latter was formed when the electrolysis was performed at the reduction potential of R_3 (-1.6 V) according to the overall reaction given in Eq. (13).

$$2PhCH_2Br + 2e^- \xrightarrow{[Ni(bpy)_3^{2+}](BF_4^-)_2,\ -1.6\,V} PhCH_2CH_2Ph + 2Br^- \qquad (13)$$

To account for the catalytic current, the 17-electron complex $PhCH_2Ni^0(bpy)^{2-}$, electrogenerated at R_3, must then react with $PhCH_2Br$ (Eq. (14)) in a reaction which should ultimately regenerate $PhCH_2Ni^0(bpy)^{2-}$ (Eq. (15)).

$$PhCH_2Ni^0(bpy)^{2-} + PhCH_2Br \to\to PhCH_2CH_2Ph + Ni^0(bpy)^- + Br^- \qquad (14)$$

$$Ni^0(bpy)^- + PhCH_2Br \to PhCH_2Ni^{II}Br(bpy)^- \xrightarrow{2e^-} PhCH_2Ni^0(bpy)^{2-} + Br^- \qquad (15)$$

However, at the potential of -1.6 V, $Ni^0(bpy)^-$ should be oxidized (Fig. 1a, solid line). This suggests that either $Ni^0(bpy)^-$ undergoes a fast oxidative addition to $PhCH_2Br$ (Eq. (15)) before being oxidized or that the mechanism of the Ni(*bpy*)-catalyzed homocoupling of $PhCH_2Br$ (Eq. (13)) is more complex (formation of $Ni^0Br(bpy)^{2-}$).

Since $PhCH_2CH_2Ph$ was not formed during the electrosynthesis of the ketone by the heterocoupling of $PhCH_2Br$ and $PhCH_2COCl$ (Eq. (5)) because the electrolysis potential was less negative (-1.2 V) than the reduction potential required for the formation of $PhCH_2CH_2Ph$ (-1.6 V), the mechanism of the Ni-catalyzed homocoupling of $PhCH_2Br$ (Eq. (13)) has not been investigated in much more details, focusing our attention on the mechanism of the heterocoupling. Nevertheless, it is worthwhile noting that the mechanism observed for the Ni(*bpy*)-catalyzed homocoupling of benzyl halides differs from the mechanism of the $NiCl_2$(*dppe*) or $PdCl_2(PPh_3)_2$-catalyzed homocoupling of aryl halides (Schemes 1 and 2). This is due to the aptitude of the *bpy* ligand to accept electrons, a feature which cannot not occur with *dppe* or PPh_3. This property enables the formation of the 17-electron complex $PhCH_2Ni^0(bpy)^{2-}$ which is a key intermediate at the origin of the catalytic cycle of the $PhCH_2Br$ homocoupling.

Rate and mechanism of the oxidative addition of $Ni^0(bpy)_2$ to $PhCH_2COCl$

When the electrochemical reduction of $[Ni(bpy)_3^{2+}](BF_4^-)_2$ (2 m*M* in acetonitrile) was performed at low scan rate ($0.5\,V \cdot s^{-1}$) in the presence of *bpy* (40 m*M*) and an excess of $PhCH_2COCl$ (in the range from 1 to 12 equivalents), the oxidation peak O_1 of the electrogenerated $Ni^0(bpy)_2$ was no longer observed (Fig. 3a, dashed line), evidencing a reaction of $Ni^0(bpy)_2$ with $PhCH_2COCl$. Concomitantly, the reduction peak current of $[Ni(bpy)_2^{2+}](BF_4^-)_2$ at R_1 increased (Fig. 3a, dashed line) to reach a value independent of the $PhCH_2COCl$ concentration and corresponding to an overall process involving three electrons [16]. These experiments show that the electrogenerated $Ni^0(bpy)_2$ complex undergoes an oxidative addition to $PhCH_2COCl$, affording a 16-electron complex $PhCH_2CONi^{II}Cl(bpy)$ whose electrochemical reduction occurs at the same reduction potential as that of $[Ni(bpy)_3^{2+}](BF_4^-)_2$ (or at less negative potential) and involves one electron, resulting in an overall three electron process at R_1 (Eq. (16, 17)). This ends up with the formation of an acyl-Ni^I complex.

$$Ni^0(bpy)_2 + PhCH_2COCl \xrightarrow{k_2^{app}} PhCH_2CONi^{II}Cl(bpy) + bpy \tag{16}$$

$$PhCH_2CONi^{II}Cl(bpy) + 1e^- \longrightarrow PhCH_2CONi^{I}(bpy) + Cl^- \text{ at } R_1 \tag{17}$$

A kinetic investigation of the oxidative addition of $Ni^0(bpy)_2$ to $PhCH_2COCl$ (Eq. (16)) by varying the scan rate as done with $PhCH_2Br$ (see above) allows the determination of the rate constant. It amounts to $k_2^{app} = 8 \times 10^4\,M^{-1}s^{-1}$, *i.e.* it is ten times smaller than the rate constant of the oxidative addition of $Ni^0(bpy)_2$ to $PhCH_2Br$ under the same conditions. This establishes that in the presence of identical concentrations of $PhCH_2Br$ and $PhCH_2COCl$ the electrogenerated $Ni^0(bpy)_2$ preferentially undergoes an oxidative addition to $PhCH_2Br$.

Mechanism of the $Ni^0(bpy)_2$-catalyzed heterocoupling of $PhCH_2COCl$ and $PhCH_2Br$ (Eq. (5))

From the kinetic investigations described above it ensures that the first step of the heterocoupling catalytic cycle is the oxidative addition of $Ni^0(bpy)_2$ to $PhCH_2Br$ affording $PhCH_2Ni^{II}Br(bpy)$. This complex is simultaneously reduced at R_1 by a two-electron process. As discussed above, the complex $PhCH_2Ni^0(bpy)^-$ electrogenerated at R_1 does not react with $PhCH_2Br$.

When $[Ni(bpy)_3^{2+}](BF_4^-)_2$ (2 m*M* in acetonitrile) was reduced at low scan rates in the presence of $PhCH_2Br$ (12 m*M*) but in the absence of $PhCH_2COCl$, the cyclic

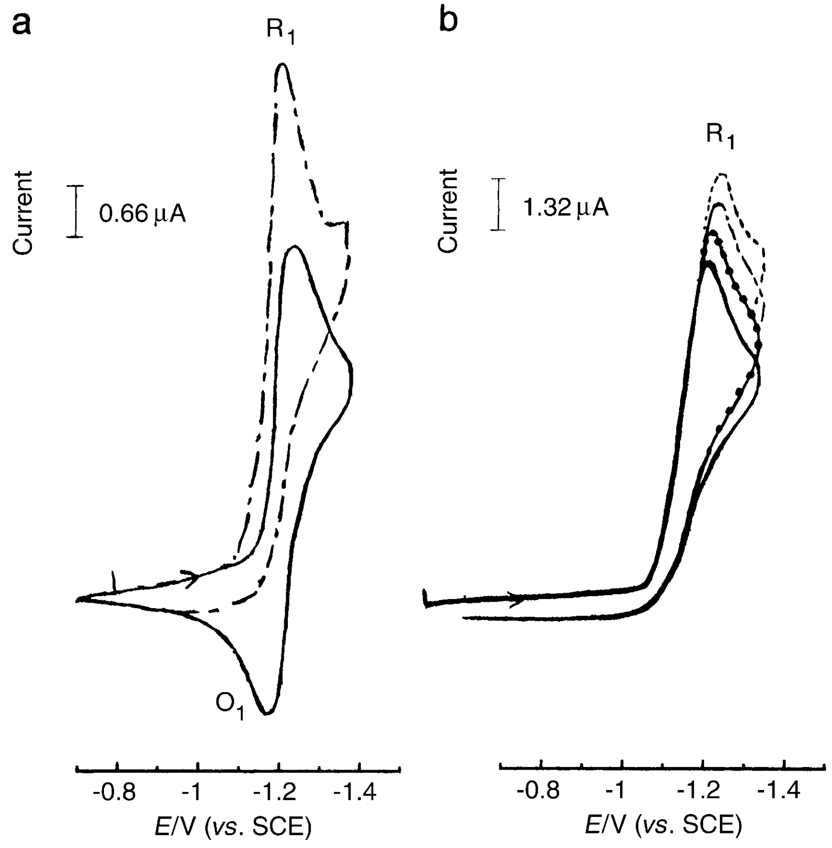
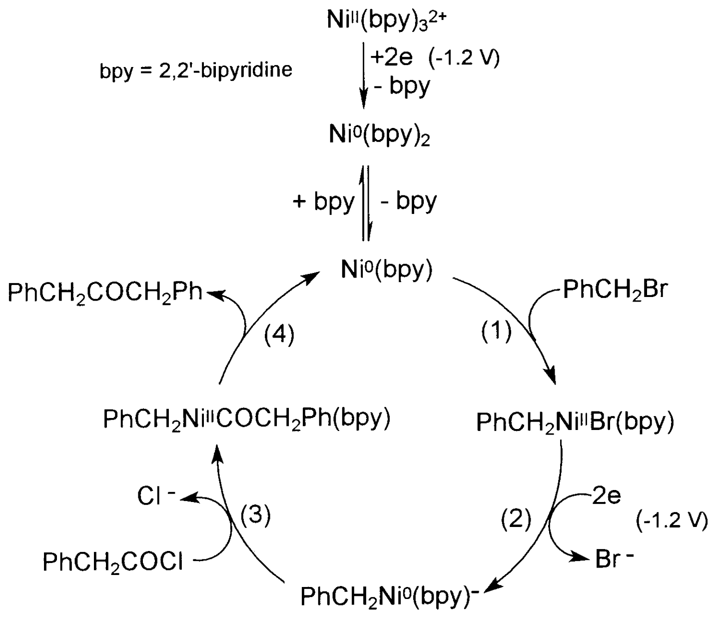


Fig. 3. Cyclic voltammetry performed in acetonitrile (containing 0.3 *M*, n-Bu_4NBF_4) at a steady gold disk electrode (i.d.: 0.5 mm) at a scan rate of $0.5\,V\cdot s^{-1}$ at 25°C. a) $[Ni(bpy)_3^{2+}](BF_4^-)_2$ (2 m*M*), 2,2′-bipyridine (40 m*M*), and $PhCH_2COCl$ (8 m*M*); b) $[Ni(bpy)_3^{2+}](BF_4^-)_2$ (2 m*M*), 2,2′-bipyridine (40 m*M*), $PhCH_2Br$ (8 m*M*), and $PhCH_2COCl$ (0 m*M* (—), 6 m*M* (-●●●-), 12 m*M* (·—·—·), 24 m*M* (- - - -))

voltammogram exhibited the four-electron reduction peak R_1 (Fig. 3b, solid line), featuring the formation of $PhCH_2Ni^0(bpy)^-$. The reduction peak current of R_1 increased in the presence of increasing amounts of $PhCH_2COCl$ (in the range of 6 to 24 m*M*) (Fig. 3b, dotted and dashed lines), although $Ni^0(bpy)_2$ was no longer available for a reaction with $PhCH_2COCl$ [17]. Therefore, in the presence of both $PhCH_2Br$ and $PhCH_2COCl$, a catalytic process was initiated at R_1. This agrees with the fact that the electrosynthesis of $PhCH_2COCH_2Ph$ by the $Ni(bpy)$-catalyzed heterocoupling of $PhCH_2Br$ and $PhCH_2COCl$ was indeed performed at −1.2 V, *i.e.* at the reduction potential of R_1 (Eq. (5)) [10], thus giving clear evidence that the second step of the catalytic cycle is a reaction of $PhCH_2Ni^0(bpy)^-$ (*i.e.* the species electrogenerated at R_1 in the presence of $PhCH_2Br$) with $PhCH_2COCl$. This reaction must eventually yield the heterocoupling product $PhCH_2COCH_2Ph$, together with a Ni^0 complex able to initiate a second catalytic cycle at the potential of R_1 (Eq. (18)).

$$PhCH_2Ni^0(bpy)^- + PhCH_2COCl \longrightarrow\!\!\!\longrightarrow PhCH_2COCH_2Ph + Ni^0(bpy) + Cl^- \quad (18)$$

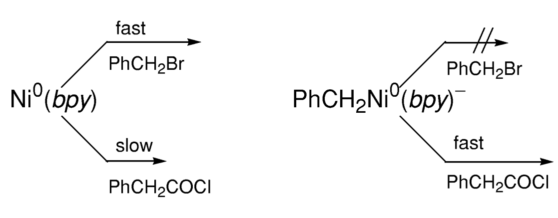


Scheme 3. Mechanism of the Ni-catalyzed heterocoupling of benzyl bromide and phenacyl chloride

Since $PhCH_2Ni^0(bpy)^-$ does not react with $PhCH_2Br$ and since the oxidative addition of Ni(0) is even slower with phenacyl chloride than with benzyl bromide, we propose that the reaction described by Eq. (18) is a nucleophilic substitution of $PhCH_2COCl$ by the anionic $PhCH_2Ni^0(bpy)^-$ (step 3 in Scheme 3), followed by the reductive elimination of $PhCH_2COCH_2Ph$ (step 4 in Scheme 3) to regenerate the $Ni^0(bpy)$ complex which closes the catalytic cycle.

Conclusions and final remarks

The success of the Ni(*bpy*)-catalyzed heterocoupling of benzyl bromide and phenacyl chloride comes from the fact that the oxidative addition of $Ni^0(bpy)_2$ to $PhCH_2Br$ is faster than that to $PhCH_2COCl$ and also that $PhCH_2Ni^0(bpy)^-$ cannot undergo a second oxidative addition to $PhCH_2Br$ to produce $PhCH_2CH_2Ph$ as it was observed for $ArPd^0(PPh_3)_2^-$ which is able to react with Ar*X* (Scheme 2). The mechanism established here for the Ni-catalyzed heterocoupling (Scheme 3) is, however, very reminiscent of the Pd-catalyzed homocoupling mechanism (Scheme 2) in the sense that only bielectronic transfers are involved.



The catalytic heterocoupling of benzyl bromide and acyl chlorides to form ketones $PhCH_2COR$ can therefore be selectively achieved in one pot, starting from an equal mixture of the two organic reagents and a catalytic amount of a nickel catalyst ligated by the *bpy* ligand [10]. These reactions afford selectively ketones because the electrolyses can be conducted at a low potential: the reduction potential of Ni(II) to Ni(0). This prevents the formation of the homocoupling product $PhCH_2CH_2Ph$ which requires a more negative potential. The homocoupling product *R*COCO*R* is not formed as well, due to the too slow oxidative addition of $Ni^0(bpy)_2$ to *R*COCl derivatives compared to $PhCH_2Br$.

Experimental

General

All experiments were performed under argon using *Schlenk* techniques. The chemicals were standard reagent grade. They were used without further purification except for $PhCH_2COCl$ which was distilled before use. $PhCH_2Br$ and acetonitrile were filtered over alumina under inert atmosphere. $[Ni(bpy)_3^{2+}](BF_4^-)_2$ was synthesized according to the literature [18].

Electrochemical set-up and electrochemical procedure for voltammetry

Cyclic voltammetry was performed with a wave-form generator PAR Model 175 and a home-made potentiostat equipped with an ohmic drop compensation. The cyclic voltammograms were recorded with a Nicolet 3091 digital oscilloscope. Experiments were carried out in a three-electrode cell connected to *Schlenk* line. The counter electrode was a platinum wire of ca. $1\,cm^2$ apparent surface area; the reference was a saturated calomel electrode (Radiometer Analytical Tacussel) separated from the solution by a bridge filled with $3\,cm^3$ of acetonitrile containing n-Bu_4NBF_4 ($0.3\,mol \cdot dm^{-3}$). $12\,cm^3$ of acetonitrile containing n-Bu_4NBF_4 ($0.3\,mol \cdot dm^{-3}$) were poured into the cell, followed by $[Ni(bpy)_3^{2+}](BF_4^-)_2$ (16.8 mg, 0.024 mmol), 2,2′-bipyridine (75 mg, 0.48 mmol), and suitable amounts of $PhCH_2Br$ (or/and $PhCH_2COCl$). Cyclic voltammetry was performed at a steady gold disk electrode (i.e.: 0.5 mm, scan rates: 0.2–$10\,V \cdot s^{-1}$, i.d.: 0.125 mm, scan rates: 20–$2000\,V \cdot s^{-1}$).

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[12] For a given electroactive species, at a given scan rate, the value of the peak current is proportional to the concentration of the species and to the number of electron(s) involved in the overall reaction initiated by the initial electron transfer at the scan rate of the measurement. Yet, the proportional constant depends on the mechanism at hand.

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[15] a) The ratio $i^{red}(R_1)/i^{red}(R_1)_0$ went from 2.2 to 1, corresponding to the passage of an irreversible peak involving four electrons to a reversible one involving two electrons [15b]; b) Nadjo L, Savéant JM (1973) J Electroanal Chem **48**: 113

[16] The reduction potential of $PhCH_2COCl$ alone under identical experimental conditions is -2.48 V *vs*. SCE. It is worthwhile to note that $PhCH_2COCl$ undergoes a slow reaction with 2,2-bipyridine to form a bipyridinium salt which was redued at -0.98 V. This is why the mechanistic investigation in the presence of the nickel catalyst was performed on freshly prepared solutions. The solutions were renewed as soon as the reduction peak of the bipyridinium salt appeared at -0.98 V.

[17] If a competitive reaction between $PhCH_2Br$ and $PhCH_2COCl$ would occur, a decrease of the peak current of R_1 should be observed since R_1 involves a three-electron process with $PhCH_2COCl$ *vs*. a four-electron process with $PhCH_2Br$.

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