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Catalytic Electrosynthesis in Ionic Liquid: Performance of Nickel–(2,2′-Bipyridine) Complexes for Production of Aryl Propan-2-ones

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The nickel-catalyzed electroreductive coupling of a benzylic chloride with an acyl donor reagent in the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate has been studied in the preparative scale to obtain aryl propan-2-ones in galvanostatic mode. Poor solubility of metallic salts prevents the use of the sacrificial anode process in an undivided cell. Moderate chemical yields are obtained within a divided cell configuration using an anionic membrane as a separator, which shows the compatibility of ionic liquids with this kind of electrochemical device. Aryl propan-2-ones were prepared with chemical yield up to 65%. Cyclic voltammetry and UV–vis spectroscopy confirm that the mechanism is the same in the ionic liquid and in a classical molecular solvent such as DMF. Nevertheless, degradation of the imidazolium cation induced by redox catalysis involving the bipyridine ligand has been observed, which explains the low faradaic yields.

Ionic liquids (ILs) are organic salts that are liquid at, or near, room temperature.[1] These materials have been extensively mentioned as "green" reaction media for numerous chemical reactions.[1–3] Compared with conventional molecular organic solvents, ILs have a number of unique advantages including their non-volatility/non-flammability which render them less hazardous, and their ability to dissolve a wide range of dissimilar substances.[1,2] Also, because ILs are inherently conducting and are electrochemically stable, they are considered to be appropriate reaction media for organic electrosynthesis. To this end, several studies have shown that ILs media are compatible with organic electrochemistry and preparative-scale organic electrosynthesis.[4–8]

One class of indirect electrochemical transformations is the use of transition-metal complexes as efficient catalysts for a large variety of homo or cross coupling reactions. Particularly, low-valent nickel–(2,2′-bipyridine) (Ni–bpy) complexes have been extensively used to achieve numerous electroreductive coupling involving organic halides.[9] More recently, one example proved that Ni–bpy-catalyzed electrosynthesis of biaryls from aromatic halides can be successfully achieved in ionic liquid.[4] This is particularly advantageous so far as it represents the association of homogeneous catalysis with a "green" process, since electron does not give any by-product, and in also "green" reaction media.

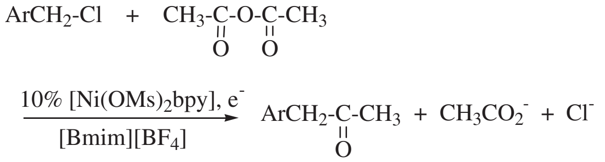
As an example of a Ni–bpy-catalyzed electrosynthesis we have chosen in this paper the reductive cross coupling between benzylic halides and either acetic anhydride or acetyl chloride yielding aryl propan-2-ones which are interesting intermediates in the preparation of amphetamines and methamphetamines.

We report here the results of electrolyses achieved in 1-butyl-3-methylimidazolium tetrafluoroborate $[\mathrm{Bmim}][\mathrm{BF_4}]$ and the electrochemical behavior of Ni–bpy complexes in this solvent.

Results and Discussion

Electrosynthesis. Undivided Cell: Our first experiments were achieved in an undivided cell fitted with a sacrificial metallic anode according to the procedure described in the experimental section.

The overall reaction can be written according to eq 1:



$$\mathrm{ArCH_2\text{-}Cl} + \mathrm{CH_3\text{-}\underset{\underset{O}{\|}}{C}\text{-}O\text{-}\underset{\underset{O}{\|}}{C}\text{-}CH_3} \xrightarrow[{[\mathrm{Bmim}][\mathrm{BF_4}]}]{10\%\ [\mathrm{Ni(OMs)_2bpy}],\ e^-} \mathrm{ArCH_2\text{-}\underset{\underset{O}{\|}}{C}\text{-}CH_3} + \mathrm{CH_3CO_2^-} + \mathrm{Cl^-} \quad (1)$$

If the anode metal is magnesium (or aluminum), coating of the electrode by an insulating salt induces rapidly a high cell voltage which prevents continuing electrolysis. This result was rather disappointing since similar electrolyses achieved in pure DMF afforded the desired product in good chemical yield (ca. 80%) and without any passivation of the anode.[10]

When zinc or stainless steel is used as anode, electrolyses can be conducted until full consumption of benzyl chloride but only poor yields (20–30%) of benzyl methyl ketone are obtained.

Considering that formation of large amounts of metallic salts from the anodic reaction is not an eco-friendly process, we did not attempt to improve these results.

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Table 1. Ni-Catalyzed Electrochemical Coupling between Benzyl Chloride and Acetic Anhydride in [Bmim][BF_4][a)]

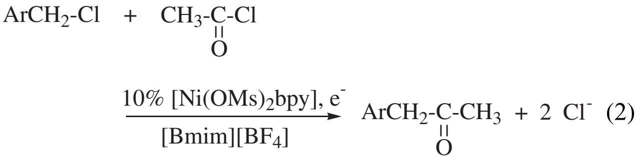
Entry	Separator	Electric charge vs. $PhCH_2Cl/F\,mol^{-1}$	$PhCH_2COCH_3$ GC yield/%	$PhCH_2OAc$ GC yield/%
1	Fritted glass	3	29	62
2	Anionic membrane	3	23	43
3	Fritted glass[b)]	4.5	47	0
4	Anionic membrane[b)]	3.5	51	0

a) Conditions: catholyte; 20 mL [Bmim][BF_4] + 2 mL DMF, 1 mmol [Ni(bpy)(CH_3SO_3)$_2$], 10 mmol $PhCH_2Cl$, 20 mmol acetic anhydride. Nickel grid cathode, $I = 0.1$ A, room temperature. b) $AlCl_3$ 10 mmol was added.

Divided Cell: Further electrosyntheses were conducted in a two-compartment cell fitted with either a fritted glass disk or an anionic membrane exchanger as separator. Details of the procedure are given in the experimental section.

Entries 1 and 2 of Table 1 show that when the acylating reagent is acetic anhydride, yield of benzyl methyl ketone is still low. Actually, acetate ions released by acetic anhydride consume a large portion of benzyl chloride giving mainly benzyl acetate. To avoid this side reaction, aluminum chloride was added to the catholyte to trap acetate ions (Table 1, Entries 3 and 4). Then, the by-product benzyl acetate was no more detected and benzyl methyl ketone was obtained with a better yield. In addition, it is noteworthy that separators, and particularly ionic membranes, can be easily used to perform electrolyses in ionic liquids.

Another way to obtain aryl propan-2-one, while avoiding side reaction induced by acetate anions, consists of the use of acetyl chloride instead of acetic anhydride (eq 2)



$$ArCH_2\text{-}Cl + CH_3\text{-}\underset{\underset{O}{\|}}{C}\text{-}Cl \xrightarrow[\text{[Bmim][BF}_4]]{10\%\ [Ni(OMs)_2bpy],\ e^-} ArCH_2\text{-}\underset{\underset{O}{\|}}{C}\text{-}CH_3 + 2\ Cl^- \quad (2)$$

Using experimental similar conditions, except for the acylating reagent, we then obtained better yields of benzyl methyl ketone either with a fritted glass or with an anionic membrane as separator. As presented in Table 2, the reaction was successfully extended to various benzylic chlorides.

Table 2. Ni-Catalyzed Electrosynthesis of Aryl Propan-2-one in [Bmim][BF_4][a)]

Entry	$ArCH_2Cl$	Electric charge vs. $ArCH_2Cl$ /F mol^{-1}	GC yield /%
1	$PhCH_2Cl$	5	63
2	4-$CH_3C_6H_4CH_2Cl$	5	54
3	3-$CF_3C_6H_4CH_2Cl$	5	65
4	3-$CH_3OC_6H_4CH_2Cl$	4.5	47

a) Conditions: divided cell with anionic membrane,[15] catholyte; 20 mL [Bmim][BF_4] + 2 mL DMF, 1 mmol [Ni(bpy)(CH_3SO_3)$_2$], 10 mmol $ArCH_2Cl$, 20 mmol of acetyl chloride. Nickel grid cathode, $I = 0.1$ A, room temperature.

These results prove that by using ionic liquids instead of conventional molecular solvents nickel-catalyzed electrochemical cross coupling can also be achieved under mild and simple conditions.

To complete this work, we have also investigated the electrochemical behavior of Ni–bpy complexes in [Bmim][BF_4] to obtain mechanistic information and particularly in order to explain the poor faradic yields (about 40%) of the electrolyses.

Analytical Study. As shown in Figure 1a (curve 1) the cyclic voltammogram (CV) of a solution of [Ni(bpy)(CH_3SO_3)$_2$] in [Bmim][BF_4] at a gold microelectrode exhibits two poorly reversible reduction steps which can be explained by means of eqs 3 and 4.

$$[Ni^{II}(bpy)]^{2+} + e \leftrightarrows [Ni^{I}(bpy)]^{+} \quad (3)$$

$$[Ni^{I}(bpy)]^{+} + e \leftrightarrows [Ni^{0}(bpy)] \quad (4)$$

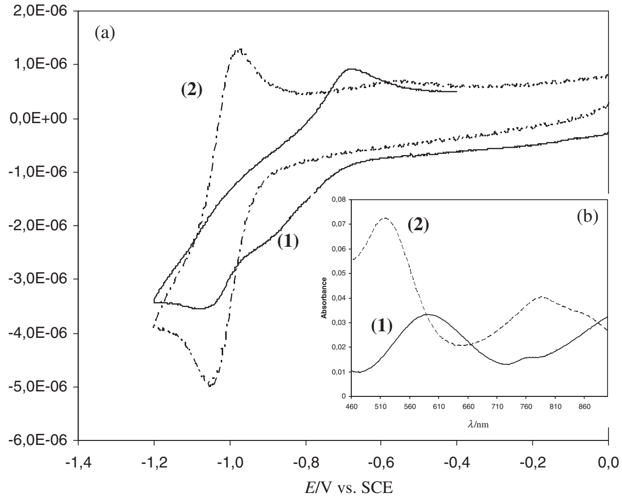


Figure 1. (a) CVs recorded at 0.1 V s^{-1} in [Bmim][BF_4] + DMF (10%) for: (1) [Ni(bpy)(CH_3SO_3)$_2$] (3×10^{-2} mol dm^{-3}), (2) [Ni(bpy)(CH_3SO_3)$_2$] (3×10^{-2} mol dm^{-3}) + bpy (6×10^{-2} mol dm^{-3}). (b) UV–vis spectra of Ni(II)–bpy complexes in [Bmim][BF_4] + DMF (10%): (1) [Ni(bpy)(CH_3SO_3)$_2$] (10^{-2} mol dm^{-3}) ($\lambda_{max} = 585$ nm), (2) [Ni(bpy)(CH_3SO_3)$_2$] (10^{-2} mol dm^{-3}) + bpy (2×10^{-2} mol dm^{-3}) ($\lambda_{max} = 515$ nm).

By adding an excess of bpy (bpy/Ni(II) $\geq$ 3 mol mol^{-1}) the dark green solution of [Ni(bpy)(CH_3SO_3)$_2$] turns to pink and a single reduction process occurs (Figure 1a, curve 2). This behavior, similar to the one reported in molecular solvents (NMP[11] and DMF[12]), corresponds to the quasi reversible two-electron transition (eq 5):

$$[Ni^{II}(bpy)_3]^{2+} + 2e \leftrightarrows [Ni^{0}(bpy)_3]\ (\text{or } [Ni^{0}(bpy)_2] + bpy) \quad (5)$$

As observed usually in various molecular solvents, the UV–vis spectra (Figure 1b) confirm the existence also in the

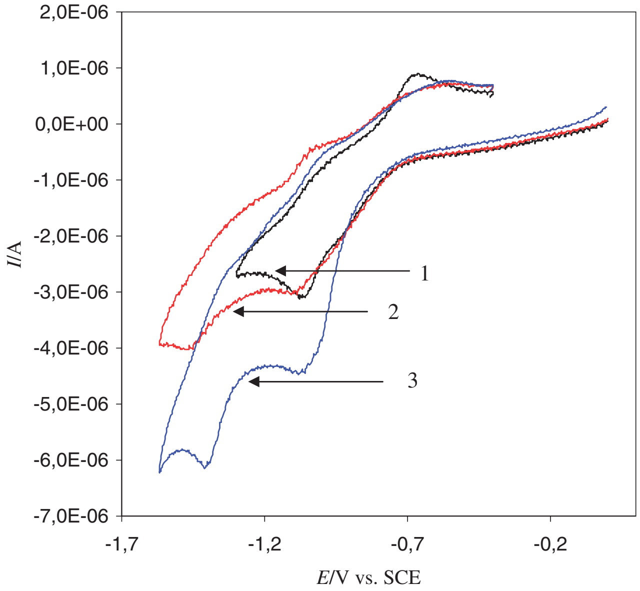


Figure 2. CVs recorded at $0.1\,\mathrm{V\,s^{-1}}$ in [Bmim][BF_4] + DMF (10%) for: (1) [Ni(bpy)(CH_3SO_3)$_2$] (3×10^{-2} mol dm^{-3}), (2) [Ni(bpy)(CH_3SO_3)$_2$] (3×10^{-2} mol dm^{-3}) + $PhCH_2Cl$ (6×10^{-2} mol dm^{-3}), (3) [Ni(bpy)(CH_3SO_3)$_2$] (3×10^{-2} mol dm^{-3}) + $PhCH_2Cl$ (15×10^{-2} mol dm^{-3}).

mixture [Bmim][BF_4] + DMF of different Ni–bpy complexes depending on the ratio between divalent nickel and ligand bpy.

The electroreduction of [Ni(bpy)(CH_3SO_3)$_2$] performed in the presence of $PhCH_2Cl$ is strongly dependent on the presence or absence of extra bpy. On the one hand, if bpy is in excess (bpy/Ni $\geq$ 3), the CV of $Ni^{II}(bpy)_3^{2+}$ is almost identical to the one shown by curve 2 of Figure 1a which means that under these conditions $Ni^0(bpy)_3$ does not react quickly with $PhCH_2Cl$. On the other hand, in the absence of extra bpy, the CV of [Ni(bpy)(CH_3SO_3)$_2$] is strongly modified (Figure 2, curves 2 and 3). A coalescence of the two reduction steps of $Ni^{II}(bpy)^{2+}$ occurs, the global intensity of the peak at -1.05 V increases, and the system becomes irreversible when the concentration of $PhCH_2Cl$ is increased. A new peak is observed at a more negative potential ($E_p = -1.4$ V). Considering a previous analytical study of the influence of $PhCH_2Br$ on the electroreduction of Ni–bpy complexes,[13] that can be presumably assigned to an oxidative addition of $PhCH_2Cl$ to the electrogenerated Ni^0bpy followed by electroreduction of the resulting complex $PhCH_2Ni^{II}Cl(bpy)$.

The CVs of solutions containing [Ni(bpy)(CH_3SO_3)$_2$] show also, especially if extra bpy is added, an additional reduction peak at a potential near of the one corresponding to the reduction of the solvent. Then we have considered the electrochemical behavior of solution of the sole bpy in the mixed solvent [Bmim][BF_4]/DMF (90/10 vol/vol).

Figure 3 shows that the electroreduction of bpy occurs at $E_p = -1.85$ V but does not correspond to the reversible one-electron system (bpy/bpy$^{\bullet-}$) usually observed in molecular solvents. Actually, the reduction of bpy is not reversible and, compared to the oxidation peak of ferrocene as reference, the reduction peak intensity of bpy is much more important.

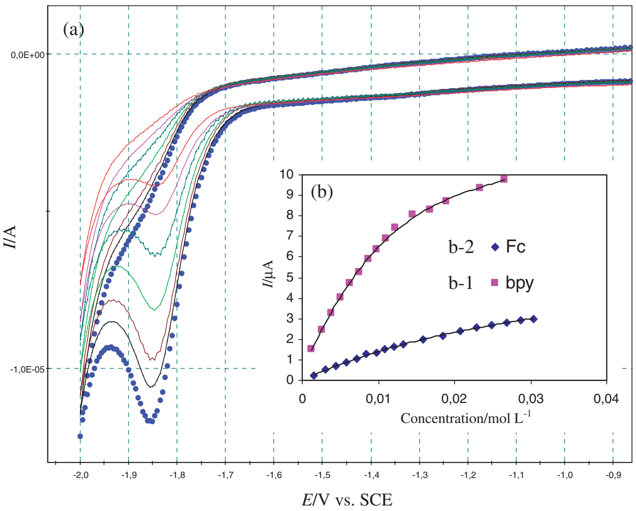
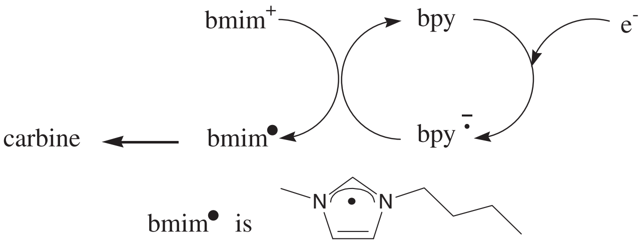


Figure 3. a) CVs recorded at $0.1\,\mathrm{V\,s^{-1}}$ in [Bmim][BF_4] + DMF (10%) + bpy from 10^{-3} to 2.6×10^{-2} mol dm^{-3}. b) Comparison of peak intensity obtained for: b-1 bpy reduction and b-2 ferrocene oxidation.



Scheme 1. bpy as redox mediator for electroreduction of imidazolium cation.

It is known that imidazolium ions can be chemically[14] or electrochemically reduced[15] and we think that bpy acts as a redox mediator toward the ionic liquid according to Scheme 1. This assumption is supported by a similar behavior obtained in the molecular solvent DMF. Actually, we have shown that in DMF the reversible one-electron bpy/bpy$^{\bullet-}$ system becomes irreversible with increasing reduction peak intensity when adding [Bmim][BF_4] (1–2 equivalent vs. bpy).

This side indirect electroreduction of the solvent [Bmim][BF_4] can explain the low faradaic yields obtained during electrosyntheses achieved at constant current without control of the potential of the cathode.

Conclusion

We have shown that the electroreductive coupling of a benzylic halide $ArCH_2Cl$ with an acyl donor reagent can afford a good method to obtain aryl propan-2-ones in an ionic liquid as the reaction medium. The use of acetyl chloride instead of acetic anhydride is more advantageous since it avoids the formation of the side product $ArCH_2OAc$.

We have also proved that the use of a membrane exchanger is compatible with ionic liquid to perform electrolyses in a divided cell, then allowing a very simple anodic auxiliary reaction.

The analytical study has shown that the oxidative addition of $ArCH_2Cl$ to an electrogenerated zerovalent nickel complex is rapid for [Ni^0(bpy)] but slow for [$Ni^0(bpy)_3$]. In other respects, evidence has been given for a redox catalytic process involving the reduction of the imidazolium cation via the electroreduction of the ligand bpy, a side reaction which explains the moderate faradaic yields of electrosyntheses. This drawback will be certainly avoided by use of ionic liquids which are not constituted with easily reducible cations.

Experimental

Undivided Cell. [Bmim][BF_4] was prepared according to a known procedure[16] and ^1H and ^{13}C NMR (Bruker AVANCE ^1H: 300 MHz, ^{13}C: 75 MHz) spectra agreed with literature. Products analyses were carried out by gas chromatography (Varian 3400) and GC-MS (Finnigan MAT GCQ).

Typical experiment: to [Bmim][BF_4] (30 mL) was added a small amount of *N,N*-dimethylformamide (DMF)[17] (3 mL), the catalytic precursor [Ni(bpy)$(CH_3SO_3)_2$] (1 mmol), benzyl chloride (10 mmol), and acetic anhydride (20 mmol). The undivided cell, described elsewhere,[18] was fitted with a metallic rod as anode surrounded by a cylindrical nickel grid (15 cm^2) as cathode. Constant current density (7 mA cm^{-2}) electrolyses were achieved at room temperature.

Divided Cell. The two-compartment cell[19] was fitted with either a fritted glass disk or an anionic membrane exchanger[20] as separator. The anolyte contained [Bmim][BF_4] (20 mL) and water (2 mL). The anodic reaction was obviously the oxidation of water into dioxygen since the used electrode was a platinum grid. In the catholyte was added [Bmim][BF_4] (20 mL), DMF (2 mL), [Ni(bpy)$(CH_3SO_3)_2$] (1 mmol), benzyl chloride (10 mmol), and acetic anhydride or acetyl chloride (20 mmol). Galvanostatic (7 mA cm^{-2}) electrolyses were achieved at a nickel grid electrode (15 cm^2).

Analytical Study. Electrochemical measurements were performed using a ParStat 2253 (Princeton Applied Research) potentiostat in the 3-electrodes configuration. The working electrode was Au (area: 3.6×10^{-3} cm^2), while Pt gauze acted as the counter electrode, and silver wire as a quasi-reference electrode. All potentials are referred to the saturated calomel electrode (SCE). The working electrode was polished with Emery 3/0 prior to use, and all measurements were performed at room temperature under an argon atmosphere.

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