



Electro- and acid-catalysis in tetrafluoroborate-based ionic liquid: new alternative routes for the oxidation of sulfides with UHP

Laura Palombi ^{a,*}, Carmen Bocchino ^a, Tonino Caruso ^a, Rosaria Villano ^b, Arrigo Scettri ^a

^a Dipartimento di Chimica, Università di Salerno, Via Ponte don Melillo 84084 Fisciano (Salerno), Italy

^b Istituto di Chimica Biomolecolare-CNR, trav. La Crucca 3, Reg. Balduca, 07040 Li Punti (Sassari), Italy

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ABSTRACT

By means of anodic activation, BF₄-based ionic liquid was found to play the triple role of electrolysis/reaction medium, supporting electrolyte and pre-catalyst versus the oxidation of sulfides with UHP. Galvanostatic electrolysis in the presence of substrate and UHP molecules allowed the fast, efficient and selective achievement of sulfoxides. Comparable results have been attained by acid catalysis based on R-CSA.

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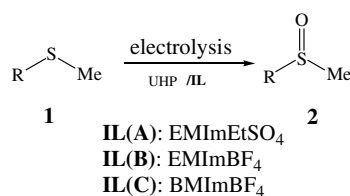
As evidenced by a number of literature reports, room temperature ionic liquids (RTILs) are recently finding large application in organic synthesis both as reaction media and as catalysts or co-catalysts.¹ The versatile use of this class of compounds arises from their unique and tunable properties such as high thermal stability, negligible vapour pressure and high polarity.

On the contrary, despite their recognized potential as conducting media, which avoid the employment of supporting electrolytes, the use of RTILs in electrosynthesis remains rare.² Furthermore, the few examples concerning electrosynthetic procedures in RTIL mainly refer to cathodic processes, and very little references have addressed attention to the anodic ones.

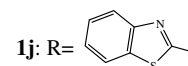
Here we describe the first electro-activation of urea hydrogen peroxide (UHP) adduct in tetrafluoroborate-based ionic liquid at a platinum anode, usefully exploited for the in situ oxidation of sulfides (Scheme 1). In parallel with the electrochemical procedure, we also report a purely chemical method, based on the (1*R*)-(–)-10-Camphor sulfonic acid (R-CSA) catalysis in 1-ethyl-3-methylimidazolium tetrafluoroborate (EMImBF₄).

The electrochemical experiments were carried out under galvanostatic conditions, using a U-two compartment cell equipped with a Pt anode and cathode and a G4-glass diaphragm as separator septum.

In a typical experiment, the anolyte was made up of a solution of sulfide **1** and UHP in ionic liquid, while the catholyte consisted in pure ionic liquid. The cell was put in a water bath to avoid the overheating during the electrolysis.



1a: R= p-MeC₆H₄
1b: R= p-MeOC₆H₄
1c: R= o-MeOC₆H₄
1d: R= p-BrC₆H₄
1e: R= o-BrC₆H₄
1f: R= p-NO₂C₆H₄
1g: R= 2-naphthyl
1h: R= n-C₈H₁₇
1i: R= C₆H₅CH₂



Scheme 1.

As summarized in Table 1, the preliminary investigations pertained to the choice of the suitable ionic liquid and the optimal setting of the electrochemical conditions, focusing on the oxidation of sulfide **1a** as a model substrate. Interestingly, all the RTILs explored ensured a good transport of current through the cell. Nevertheless, the presence of the BF₄[–] counteranion was strictly required to enable the efficient conversion of the starting material **1a**.

Concerning the set-up of the optimal operational conditions, we can highlight the following features of the electrochemical procedure:

- the reaction requires sub-stoichiometric amount of electricity to proceed ($Q = 0.3$ F/mol);
- the application of a higher current density and quantity (from 50 mA/cm² to 150 mA/cm²; from 0.1 F/mol to 0.3 F/mol) markedly reduces the reaction time without affecting the chemoselectivity of the process;

* Corresponding author.

E-mail address: lpalombi@unisa.it (L. Palombi).

Table 1
Electrochemically promoted oxidation of **1a** with UHP in ionic liquids

Entry	Electrolysis method ^a	Ionic liquid	Current density (mA/cm ²)	Current quantity (F/mol)	Reaction time (h)	2a Yield ^b (%)
1	1	IL(A)	50	0.1	18	Trace
2	1	IL(B)	50	0.1	3	58
3	1	IL(C)	50	0.1	2	65
4	2	IL(C)	150	0.1	2	67
5	2	IL(C)	150	0.3	n.d. ^c	>99

^a Method 1: catholyte: pure ionic liquid **1**; anolyte: UHP/**IL**. At the end of the electrolysis, substrate **1** was added to the anode compartment and the reaction prolonged for the time reported in the table. Method 2: catholyte: pure ionic liquid; anolyte: **1a**/UHP/**IL** (1 mmol/1.06 mmol/0.6 ml).

^b The yields refer to isolated, chromatographically pure products.

^c TLC analysis at the end of the electrolysis (time: 7 min) showed a complete consumption of the starting material **1a**.

– the electrolysis may be successfully performed in the presence of the substrate **1a**, showing the best result in term of efficiency, selectivity and reaction time.

Under a similar electrochemical set-up (Table 1, entry 5), we tested the general applicability of the one-pot procedure by performing the electrolysis of the UHP/BMImBF₄ in the presence of a series of sulfides (**1b–j**). At the end of the electrolysis, the reaction was monitored by TLC analysis and was prolonged until complete consumption of the starting material **1** (Table 2). After extraction with ethyl acetate, the crude mixtures were purified by filtration over silica gel providing pure sulfoxides **2** with fair to very good yields in almost all the cases.

As shown, the reaction was found to proceed with satisfactory efficiency and excellent chemoselectivity both with dialkyl (Table 2, entries 7 and 8) and with aryl-alkyl sulfides (Table 2, entries 1–6) bearing electron-donating and electro-withdrawing substituents in ortho- or para- position. Conversely, the ambident substrate **1j** showed a lower reactivity under a variety of experimental conditions. However, the reaction proceeded in a highly regio- and chemoselective way, with exclusively the exocyclic sulfur atom prone to oxidation. Finally, the use of stoichiometric amount of electricity as well as more prolonged reaction time or higher temperatures compromised the chemoselectivity affording a mixture of **2j** and the corresponding methyl-sulfone.

Examination of a recent study on the electrochemistry of BMImBF₄ reported by Xiao and Johnson³ suggested the involvement of the electrogenerated Lewis acid BF₃ as possible catalyst of the oxidation process.⁴ Thus, two experiments, without electrolysis, were carried out in the presence of 0.3 equiv of BF₃·OEt₂. As

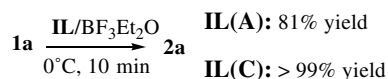
Table 2
Electrochemically promoted oxidation of **1b–j**

Entry	1	2	Reaction time (h)	Yield (%) ^a
1	1b	2b	n.d. ^b	>99
2	1c	2c	n.d. ^b	75
3	1d	2d	2	78
4	1e	2e	2	87
5	1f	2f	n.d. ^b	92 [8]
6	1g	2g	3	90
7	1h	2h	6	70
8	1i	2i	3	75
9	1j	2j	4	43 (57)
10 ^c	1j	2j	24	55 (16) [24]

^a Yields refer to isolated, chromatographically pure compounds. Yields in round parentheses refer to recovered starting material **1**. Yields in square brackets refer to isolated sulfones.

^b See footnote c, Table 1.

^c In this entry the electrolysis was performed using 1 F/mol of current.



Scheme 2.

shown in Scheme 2, an efficient conversion of the starting material **1a**, although with different yields, occurred both in **IL(A)** (which was ineffective towards the electrochemical activation) and in **IL(C)**, providing support to the hypothesized role of BF₃.

It must be pointed out, however, that the direct use of BF₃·Et₂O required the reaction to be performed at 0 °C, with careful slow addition of the catalyst to moderate the generation of HF gas. Conversely, the electrochemical induction facilitated the set-up and allowed the reaction to be performed at room temperature.

Despite the great number of procedures available, the preparation of sulfoxides from sulfides still represents a topical issue for organic chemists.⁵ In view of environmental reasons, particularly attractive are new, selective methodologies based on the use of benign oxidants, catalysts and solvents.⁶ On the other hand, the use of RTILs or metal-free catalysts, in combination with hydrogen peroxide or derivatives, is yet little explored.⁷

With this in mind, we decided to explore the UHP/EMImBF₄ system to establish an alternative sulfoxidation methodology, resorting to the 'purely chemical' acid catalysis.

As quoted by us as long ago as 1996,⁸ Brønsted acid CSA usefully promotes the chemoselective conversion of sulfides to sulfoxides by *t*-butyl hydroperoxide in CHCl₃. On the other hand, recently, Firouzabadi et al.⁹ have reported the highly selective oxidation of sulfides by H₂O₂ in aqueous medium promoted by the acid surfactant dodecyl hydrogen sulfate. According to what was proposed for the surfactant catalyst, we envisaged that *R*-CSA could activate the oxidant molecule by hydrogen bonding, favouring the oxygen transfer to the sulfide molecule.

So, we decided to investigate the catalytic ability of *R*-CSA versus the oxidation process of sulfides with UHP/EMImBF₄.

The data collected in Table 3 show a good reactivity of this system towards almost all the sulfides investigated, with reaction time in the order of about few hours and an excellent chemoselectivity towards sulfoxides. On the other hand, the system was not found to be effective from a stereochemical point of view, leading to sulfoxides with little enantioselectivity (3–4% ees).

As already noted for the electrochemical procedure, attempts to improve the chemical yield for the substrate **1j**, by increasing the temperature, the catalyst loading and the reaction time, gave unsatisfactory results. Finally, it is important to note that the background reactions (in the absence of electrolysis or *R*-CSA) were

Table 3
R-CSA-promoted oxidation of **1** with UHP in **IL(B)**

Entry	$\mathbf{1} \xrightarrow[\text{EMIMBF}_4 (0.3 \text{ ml/mmol}), \text{r.t.}]{\text{R-CSA}(0.1 \text{ eq})/\text{UHP} (1 \text{ eq.})} \mathbf{2}$		Reaction time (h)	Yield ^a (%)
	1	2		
1	1a	2a	4	>99
2	1b	2b	2	96
3	1c	2c	6	>99
4	1d	2d	3	92
5	1e	2e	24	>99
6	1f	2f	2	81
7	1g	2g	6	94
8	1h	2h	5	74
9	1j	2j	24	36 (64) ^b

^a Yields refer to isolated, chromatographically pure compounds. Yields in parentheses refer to recovered starting material **1**.

^b ¹H NMR yields.

generally negligible within the reaction time. Nevertheless, for oxidations requiring more than 6 h a significant contribution by the background reaction cannot be excluded.¹⁰

In summary, we have shown here the first electrochemical anodic activation of the UHP adduct in tetrafluoroborate-based ionic liquid for the chemoselective oxidation of sulfides. The proposed reaction pathway (i.e., via electrogenerated Lewis acid BF_3 from the pre-catalyst BMImBF_4) discloses a new approach to oxidation processes, combining the advantages of electrocatalysis and use of the benign oxidant and solvent. As a comparison, a purely chemical method, based on the use of the Brønsted acid *R*-CSA in an ionic liquid, has also been demonstrated.

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