J Appl Electrochem (2007) 37:723–728
DOI 10.1007/s10800-007-9307-3

ORIGINAL PAPER

The electrochemistry of TEMPO-mediated oxidation of alcohols in ionic liquid

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Received: 18 October 2006 / Accepted: 31 January 2007 / Published online: 7 March 2007

Abstract The detailed electrochemistry of TEMPO-mediated oxidation of alcohols to carbonyl compounds in ionic liquid medium is presented. It is shown that TEMPO diffusion currents are suppressed in IL medium, relative to acetonitrile solvent, due to the high viscosity of the IL medium; however, the presence of substrate and base reagent significantly reduces IL viscosity, improving performances significantly. Cyclic voltametry shows that the kinetics of the reaction between electrooxidized TEMPO and the alcohol are similar in both media. It was also observed that in the case where the oxidation product is non-enolizable, electrolyses (diaphragm cell) with catalytic quantities of TEMPO, and in the presence of base (2,6-lutidine), results in close to 100% Faradaic and 100% chemical efficiencies. In contrast, prolonged electrolysis of alcohols yielding enolizable products results in catalyst deactivation due to the irreversible reaction between the active form of the catalyst and the product, which ultimately leads to low product yields and catalyst loss. Under these circumstances, reasonable Faradaic and chemical selectivities can only be obtained with partial electrolyses (to ≤1F/mol).

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Keywords Alcohol oxidation · Electrochemistry · Ionic liquids · Mediated · TEMPO

1 Introduction

Ionic liquids (ILs) are organic salts that are liquid at, or near, room temperature [1]. These materials have been extensively shown to act as ‘‘green’’ reaction media for various chemical reactions [1, 2]. Compared to conventional 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 very stable electrochemically, they are considered to be ideal reaction media for organic electrosynthesis. To this end, a number of studies have shown that ILs media are compatible with direct organic electrochemistry and preparative-scale organic electrosynthesis [3–7].

One class of indirect redox transformation reaction, which was firstly reported by Semmelhack et al. [8], is the highly selective TEMPO-mediated (TEMPO = 2,2′,6,6′-tetramethylpiperidin-N-oxyl, (Fig. 1a)) oxidation of alcohols (including carbohydrates) to their corresponding carbonyl (in organic solvent) or carboxylic species (in the presence of water) [9–12]. In this scenario, one-electron oxidation of TEMPO generates the active oxoammonium species (T^+, Fig. 1b) which oxidises alcohols. TEMPO/T^+ can be used either in catalytic amounts, or as a stoichiometric reagent, where T^+ generation is effected by either a chemical process (O_2 or H_2O_2 oxidants with metal or halide-based secondary mediators) or directly by an electrochemical process.

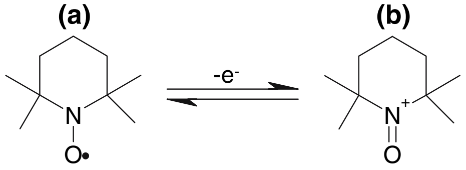


Fig. 1 Structure of TEMPO (2,2′,6,6′-tetramethylpiperidin-N-oxyl (Fig. 1a) and the oxoammonium species (Fig. 1b)

The electrochemical approach, which avoids use of chemical oxidant or mediators, offers an inherently cleaner process, and product recovery (not a feature of this work) can be much simpler. Therefore, coupling the green credentials of ILs with electrochemically-recyclable redox catalysts such as TEMPO presents the opportunity to perform very selective clean chemical transformations.

A number of reports have already appeared describing TEMPO-mediated (or TEMPO derivatives) oxidation of alcohols in ILs [13–17]. The chemical (re)generation of T^+ has been used in 1-butyl-3-methylimidazolium hexafluorophosphate ([Bmim][PF_6]) [13], N-butyl-N-methylpyrrolidinium hexafluorophosphate ([Bmpyrd][PF_6]) [14], and [Bmim][PF_6] [15] medium. In terms of electrochemical approach in ILs, only one study has been reported to date [17] which described oxidation of 1-(4-chlorophenyl) ethanol into the corresponding ketone. In this example, TEMPO was functionalised with imidazolium-type substituents in the form of a bistriflimide (NTf_2) salt. Electro-oxidations were performed in an undivided cell with yields of up to 80% reported, provided that 30 mol% of TEMPO was used.

Unfortunately, none of these studies [13–17] examined the detailed (electro)chemistry of TEMPO-mediated oxidation within the IL media. In particular, the nature of the aldehyde product's influence on mediator stability and, in turn, process performance, are not considered.

Here, we report the detailed electrochemistry, and follow-up chemistry, of TEMPO-mediated alcohol oxidation in IL medium. We demonstrate that this electrosynthetic method is very efficient when the alcohol gives a non-enolizable aldehyde. We also give evidence for a gradual deactivation of the catalyst during prolonged electrolyses involving the formation of enolizable products.

2 Experimental

The ionic liquid used was [Bmpyrd][NTf_2], which was prepared via ion metathesis in deionized water according to a literature procedure [18]. The IL was characterised using ^1H and ^{13}C NMR (Bruker Advance 300 MHz) where spectra agreed with literature. Product analysis was carried out by gas chromatography (Varian 3400) and GC-MS (Finnigan MAT GCQ).

Electrochemical measurements were performed using a ParStat 2253 (Princeton Applied Research) potentiostat in the 3-electrode configuration. The working electrode was Au (area = 3.6×10^{-3} cm^2), while Pt gauze acted as the counter electrode and a Pt wire as a quasi-reference electrode. All potentials are quoted relative to the ferrocene/ferricinium ($E^0_{Fc/Fc+}$) redox couple recorded within the IL medium. The working electrode was polished with Emery 3/0 prior to use, and all measurements were performed at 293 K under an argon atmosphere.

Bulk electrolyses were performed in a divided cell [19] fitted with either a fritted glass or a Nafion® membrane in order to avoid parasitic reduction of either T^+ or carbonyl products. It was observed that the nature of the separator did not influence bulk electrolysis.

Typically, the anolyte volume was 10 cm^3 of the IL which contained 0.6 mol dm^{-3} of alcohol, 3–5 equivalents of 2,6-lutidine (relative to alcohol) as the base, 5–10 mol% of TEMPO (relative to alcohol), and 1.0×10^{-3} mol dm^{-3} of tert-butylbenzene (as internal standard for GC monitoring). Catholyte volumes were typically 10 cm^3 comprising of 4 cm^3 of IL, 5 cm^3 of acetonitrile and 1 cm^3 of water. H_2O participated in the counter-electrode reaction generating H_2.

For bulk electrolysis, both the anode and the cathode were platinum grids, while a Pt wire acted as a quasi-reference electrode. Electrolysis was performed at constant potential (0.45–0.55 V vs. $E^0_{Fc/Fc+}$, i.e. 0.2–0.3 V vs. $E^0_{T/T+}$) until either 2 F/mol (relative to alcohol) were passed or when the current decayed to zero (<5% of the initial value). The electrolysis was monitored by GC analysis using the following procedure. Periodically, a 50 μL sample was collected from the anolyte, whereupon the neutral species (alcohol, aldehyde, 2,6-lutidine and ter-butylbenzene) were extracted into a 5 cm^3 aliquot of pentane, which was then subjected to chromatographic analysis. The presence, or loss, of TEMPO was monitored by cyclic voltammetry.

3 Results and discussion

3.1 Electrochemistry of TEMPO in [Bmpyrd][NTf_2]

Figure 2a shows a cyclic voltammogram (CV) of TEMPO (4.2×10^{-2} mol dm^{-3}) in [Bmpyrd][NTf_2] at

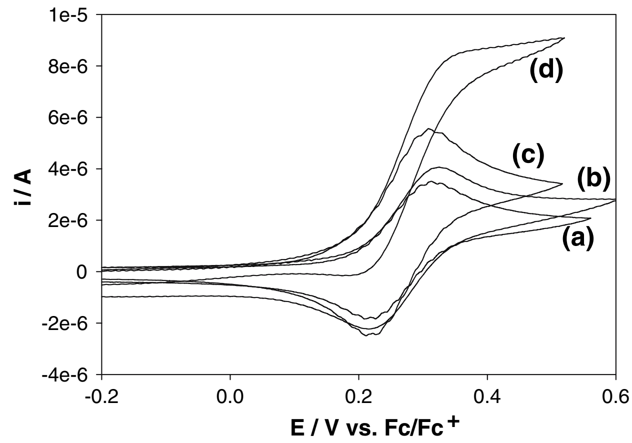


Fig. 2 CVs recorded at 0.1 V s^{-1} for; (**a**) [TEMPO] 0.042 mol dm^{-3}, (**b**) [TEMPO] 0.042 mol dm^{-3} + [3-phenylpropanol] 0.56 mol dm^{-3}, (**c**) [TEMPO] 0.042 mol dm^{-3} + [2,6-lutidine] 1.27 mol dm^{-3} and (**d**) [TEMPO] 0.042 mol dm^{-3} + [3-phenylpropanol] 0.56 mol dm^{-3} + [2,6-lutidine] 1.27 mol dm^{-3}

the Au working electrode, recorded at 0.10 V s^{-1} potential sweep-rate. The CV is characteristic of the well-known one-electron electrochemically reversible generation of the catalytically-active oxoammonium species (T^+) from TEMPO. The higher that theoretical (0.058V) peak-to-peak separation of ≈ 0.1 V is due to uncompensated iR. The anodic peak currents (i_{pa}) are a linear function of the square-root of potential sweep-rate, which is indicative of a diffusion controlled process. From these experiments, and rotating disk electrode experiments, the diffusion coefficient (D) for TEMPO and T^+ have been estimated to be 1.3×10^{-7} cm^2 s^{-1} and 1.0×10^{-7} cm^2 s^{-1}, respectively; which is in good agreement with the literature [20]. These values are *ca.* two orders of magnitude lower than in molecular solvent, which is due to the viscous nature of the IL.

The effects of alcohol addition ($Ph(CH_2)_3OH$, 0.56 mol dm^{-3}) or lutidine addition (1.27 mol dm^{-3}) to the TEMPO solution are shown in Fig. 2b and c respectively, where it can be seen that no significant alteration of the reversible voltammetry is evident. The observed increases of anodic/cathodic peak currents is due to the decreased viscosity of the medium, and consequently, the increase of the diffusion coefficients of solute species [21]. It is therefore evident that TEMPO and T^+ are stable (or react very slowly) in the presence of either alcohol alone, or lutidine alone.

Figure 2d shows a CV after the addition of both alcohol and base ($Ph(CH_2)_3OH$, 0.56 mol dm^{-3} + 2,6-lutidine, 1.27 mol dm^{-3}) to the TEMPO solution. It is clear that the anodic current is enhanced and exhibits steady-state catalytic (i_{cat} current) character [22], while the reverse cathodic current is absent. Such behaviour is indicative of a redox-catalytic reaction occurring between the electro-generated T^+ and alcohol under basic conditions [23, 24]. Also, steady-state catalytic currents were observed at potential sweep-rates up to 0.2 V s^{-1}, which suggests that the mediated oxidation reaction occurs at appreciable rates [22]. Similar behaviour was obtained for all the alcohols studied, and also when 2,6-lutidine was replaced with 2,4,6-collidine.

It was mentioned above that diffusion coefficients are typically two orders of magnitude lower in IL than in molecular solvents. Since catalytic currents are dependent on mediator mass transport ($i_{cat} \propto D^{1/2}$) [22], it is therefore informative to compare the relative catalytic performances between organic solvent and IL media. Fig. 3a and b show TEMPO-concentration-normalised CVs for TEMPO redox in acetonitrile (Fig. 3a, 0.043 mol dm^{-3}) and in IL medium (Fig. 3b, 0.048 mol dm^{-3}). The normalised peak current in acetonitrile is 13.3 times greater than in the IL, which is a reflection of the relative transport rates in either medium. As expected, this proportion is essentially equivalent to the square root of acetonitrile/IL viscosity ratio, which is ca. 14. However, Fig. 3c and d correspond to TEMPO-concentration-normalised TEMPO CVs recorded in the presence of base in acetonitrile (Fig. 3c, [lutidine] = 1.23 mol dm^{-3}) and IL (Fig. 3d, [lutidine] = 1.27 mol dm^{-3}). Addition of base dilutes TEMPO and results in lower peak currents (34.1 μA vs. 42.6 μA) in acetonitrile. Obviously, the dilution effect will be the same in IL, but the effect of

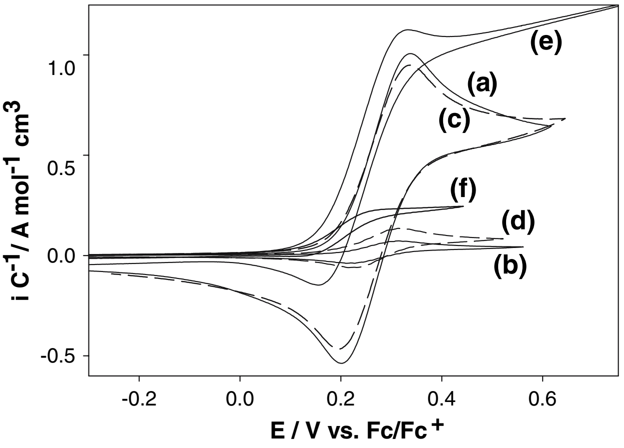
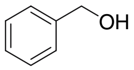
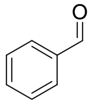
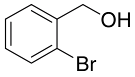
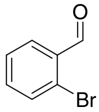
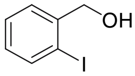
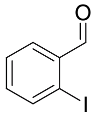
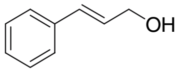
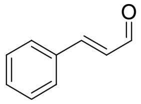
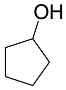
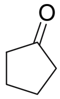
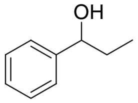
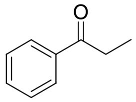
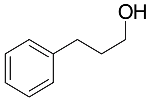
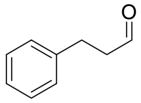


Fig. 3 TEMPO-concentration-normalised CVs of (**a**) TEMPO 0.043 M in acetonitrile, (**b**) TEMPO 0.048 M in IL, (**c**) TEMPO + base ([Tempo] = 0.037 M; [Lu] = 1.23 M) in acetonitrile, (**d**) TEMPO + base ([Tempo] = 0.041 M; [Lu] = 1.27 M) in IL, (**e**) TEMPO + base+ 3-phenylpropanol ([TEMPO] = 0.034 M, [Lu] = 1.14 M, [ROH] = 0.49 M) in acetonitrile and (**f**) TEMPO + base+ 3-phenylpropanol ([TEMPO] = 0.037 M, [Lu] = 1.20 M, [ROH] = 0.48 M in IL. Scan rate 100 mV/s; Au working electrode

Table 1 Bulk electrolysis experimental conditions, and corresponding performance data, where electrolysis proceed to 1 and 2 F/mol

Entry	Substrate ROH	Product	TEMPO/ROH /mol.%	[Lu]/[ROH] -	Charge/ F/mol	Conversion / %[a]	Chemical yield /%[a]	Selectivity /%[a]
1			4.8	2.9	1.0	50	50	100
					2.1	98	98	100
2			5.3	3.0	1.0	50	50	100
					2.0	100	97	97
3			5.1	2.9	1.0	50	46	92
					2.0	100	91	91
4			4.9	2.8	1.0	50	50	100
					2.0	100	95	95
5			10	5.0	1.0	50	43	86
					1.37 [b]	69	60	77
6			10	5.0	1.0	50	45	90
					1.39 [b]	70	54	77
7			12.2	3.0	1.0	36	35	97
					1.41 [b]	46	35	72

General conditions: *Anolyte:* bmpyNTf$_2$ (10 mL) + Alcohol (6 mmol/0.5 mol L^{-1}) + 2,6-lutidine (Lu) + TEMPO; Nafion membrane; *Catholyte*: bmpyNTf$_2$ (4 mL) + MeCN (5 mL) + H$_2$0 (0.5 mL); room temperature; *Electrodes*: Platinum grids (A=7 cm^2); ref: Pt wire; Controlled potential electrolysis (E_{anode} = 0.55 V vs. Fc/Fc$^+$ i.e. +0.3V vs. T/T$^+$); [a] determined by GC analysis, [b] end of electrolysis due to current decayed to zero

reducing IL viscosity is pronounced (whilst negligible in acetonitrile) which explains the anodic current in IL (Fig. 3d) is higher in the presence of base (5.2 μA vs. 3.2 μA). In the presence of base, the ratio between the two anodic currents (5.2 μA in IL and 34.1 μA in acetonitrile) is 6.6 instead of 13.3. Collectively, this indicates under ‘‘worst case scenario’’ peak currents are ca. a factor of 14 smaller in IL medium relative to molecular solvent; whereas addition of small quantities of reagent (or solvent) dramatically improves mass transport.

Figures 3e and f show CVs following the addition of alcohol to acetonitrile/base and IL/base, respectively. It is evident that the i_{cat} is larger in acetonitrile by a factor of ca. 4.5, which is, again, a reflection of relative mass transport rates. However, comparing the kinetic peak current (i_{cat}) to anodic peak current (i_p^a) ratios (which corrects for diffusion and viscosity) for both media reveals a ratio of 1.2 in acetonitrile and 1.4 in IL, thus indicating slightly faster reaction kinetics in the IL medium.

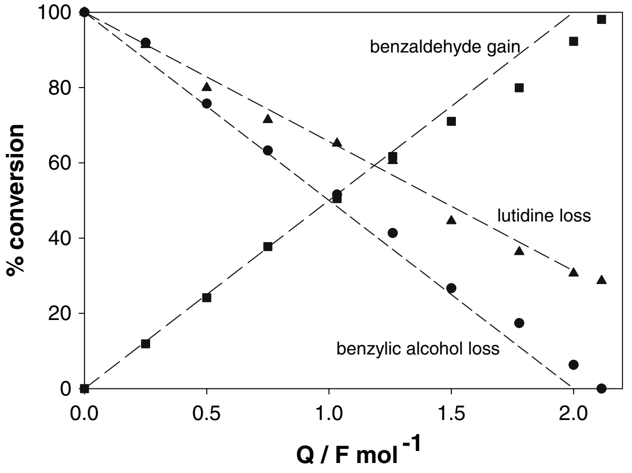


Fig. 4 Plots of percentage change in concentration of benzylic alcohol (●), benzaldehyde (■) and 2,6-lutidine (▲), as a function of charge passed during electrolysis. Dashed lines correspond to the theoretical change. Initial concentrations were, [TEMPO] = 2.4 × 10^{-2} mol dm^{-3}, [2,6-lutidine] = 1.45 mol dm^{-3} and [benzylic alcohol] = 0.5 mol dm^{-3}

3.2 Bulk electrolysis in [Bmpyrd][NTf$_2$]

Table 1 shows bulk electrolysis data for the various alcohols, along with the experimental conditions. It should be noted that electrolyses were performed under potentiostatic control; therefore, the electrolysis stopped when the current decayed to zero. Also, both substrate and product were quantified periodically during the electrolyses. A number of observations can be made from the data in Table 1, as detailed below.

Entries 1–4 in Table 1 involve benzylic or allylic alcohols which yield non-enolizable aldehyde products. It is noticeable that the electrolyses of these alcohols simply proceed to the theoretical 2F per mol of alcohol. As expected for these alcohols, close to 50–100% alcohol consumption is observed at 1 F/mol and 2 F/mol, respectively. Similarly, conversion and selectivities to the corresponding aldehyde are excellent. As an exemplar, a more detailed examination of the reaction corresponding to Entry 1 of Table 1 is illustrated by Fig. 4 which shows that consumption of benzyl alcohol and 2,6-lutidine, as well as formation of benzaldehyde are very close to theoretical curves. Similar trends were also observed for Entries 2–4. These observations demonstrate that the expected 2 F/mol oxidation occurs unaltered within the IL medium with excellent chemical and Faradaic yields.

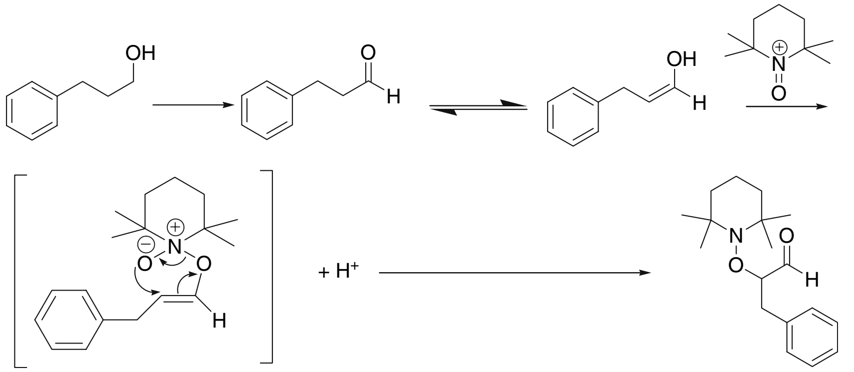
It was also observed, by cyclic voltammetry, that the TEMPO/T$^+$ mediator remained active within the reaction liquor at the end of these electrolyses such that electrolysis could be continued upon further addition of alcohol and 2,6-lutidine.

In contrast, when alcohols yield enolizable products, electrolytic efficiencies are low. For example, Entries 5 and 6 (which correspond to the formation of enolizable products) show that electrolyses proceeds as expected up to 1 F/mol of alcohol; whereas, thereafter, the electrolysis stops at significantly less than the theoretical value. The low F/mol values for these systems explicitly show that some of the alcohol must remain unreacted, although the electrolysis has stopped. This was confirmed by GC analysis. The situation for 3-phenylpropanol oxidation (yielding 3-phenylpropanal, entry 7 in Table 1) is more severe exhibiting both poor Faradaic and chemical yields, even at 1 F/mol electrolysis. Supplementary addition of TEMPO up to 25% vs. 3-phenylpropanol increased conversion to 78% but the selectivity of aldehyde product remained poor at 57%.

For these last three examples, the initial voltammetry indicated that both the expected reversible generation of T$^+$ (in absence of base) and the catalytic alcohol oxidation reaction (after addition of 2,6-lutidine) occurs as expected at the beginning of the experiment. However, after electrolysis proceeded until it stopped (i.e. current allowed to decay to zero), cyclic voltammetry clearly indicates that TEMPO/T$^+$ redox is no longer present. This observation demonstrates that the mediator is "trapped" and no longer participate electrochemically, thus giving rise to low performances. This result is in keeping with previous reports where T$^+$ was found to react with enolizable aldehydes [25, 26] in molecular solvents, as illustrated by Scheme 1. It should also be noted that the same enolizable product-dependent deactivation of TEMPO/T$^+$ appear in other works where either chemical [13, 14] or electrochemical [17] oxidations were used.

4 Conclusions

Cyclic voltammetry experiments have shown that TEMPO undergoes reversible redox in IL medium generating the catalytically-active oxoammonium species which oxidises alcohols to the corresponding aldehyde or ketone products. Although the relatively high viscosity of "pure" IL medium suppresses TEMPO mass transport rates, addition of base and alcohol substrate significantly reduces viscosity such that the relative difference between catalytic currents in molecular solvent and IL is only ca. 4.5 times smaller in IL. Under preparative-scale electrolysis conditions, much higher base/substrate concentrations are envisaged, such that catalytic performance would be improved further.



Scheme 1 Reaction of T$^+$ with enolized aldehyde product [25]

In terms of bulk electrolysis, where the products are non-enolizable, close to 100% Faradaic efficiencies and 100% chemical selectivities were observed. However, alcohols leading to enolisable aldehydes or ketones exhibit poor performance due to the irreversible reaction of the oxoammonium species with the products. Under these conditions, acceptable chemical yields, selectivities, and Faradaic efficiencies were obtained only with electrolyses proceeding to ≤1 F/mol.

Acknowledgments The Authors thank CORDIS for funding through the COST D29 Programme in Sustainable/Green Chemistry. S. O'Toole thanks Queen's University for an APG studentship.

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