Nitroxyl Radical Self-Assembled Monolayers on Gold: Versatile Electroactive Centers in Aqueous and Organic Media

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Dedicated to Professor E. Laviron

Since the pioneering work by Nuzzo and Allara in 1983,[1] self-assembled monolayers (SAMs) of alkanethiols have gained much attention in the interfacial electrochemistry and other research fields.[2,3] During the last decade,[4,5] increasing attention has been dedicated to the design and elaboration of redox-responsive SAMs. Employing redox SAM-modified electrodes for catalysis, recognition and sensing has resulted in some elegant examples that incorporate sophisticated receptors on the electrode surfaces.[6] However, to the best of our knowledge, no redox-responsive SAM was designed to be active and stable in both aqueous (on wide range of pH) and organic media.

TEMPO (2,2,6,6-Tetramethylpiperidine-1-oxyl) and its derivatives (under their oxoammonium form) have been extensively studied in the search for organic synthesis as a redox mediator, mostly, for the oxidation of primary alcohols.[6–8] The electrochemical oxidation of TEMPO is known to be a stable and reversible one-electron process in both aqueous[9–11] and non-aqueous electrolytes.[12,13] Despite the wide electrochemical applications of nitroxyl radical, rare works have been devoted to design and elaborate of redox-responsive TEMPO SAMs.[14–16] In 1997, Fuchigami et al.[14] reported the first preparation of stable self-assembled TEMPO-modified electrodes in acetonitrile: the electrochemical stability was only reached with highly diluted mixed SAMs of nitroxyl radical derivative and hexadecanethiol. In 1999, Kashiwagi et al.[15] reported electrocatalysis attempts of amines with a mixed SAM of chiral nitroxyl radical derivative and hexadecanethiol: as mentioned by authors, results could be applied to the determination of optical purity of chiral amines. After a ten-years pause, Finklea et al.[15] worked on Au-S(CH2)16CO(O)NH(TMP)-TEMPO SAM to the first estimation of the standard rate constant and the reorganization energies of TEMPO/TEMPO+ in 1 M H2SO4.

Herein, we raised the challenge of a design of redox-responsive TEMPO SAMs to be active, stable and providing electrocatalytic activities in both aqueous and non-aqueous solvents. To reach this goal, we synthesized the three nitroxyl radical derivatives 1a, 1b and 1c shown in Scheme 1. The synthesis of 1a, 1b and 1c were carried out as outlined in Scheme 1. α-thiocarbonyl carboxylic acids with different carbon chains length 2a–c were synthesized from the corresponding α-bromocarboxylic acids by nucleophilic displacement with potassium thiocyanate in DMF.[17] 4-aminoTEMPO was coupled to α-thiocarbonyl carboxylic acids 2a–c via the active ester method, using dicyclohexylcarbodiimide (DCC) and 1-hydroxybenzotriazole (HOBT) in methylene chloride (CH2Cl2), to give the TEMPO derivatives 3a–c in good yields (77 to 84%). The thiocarboxylic acids 3a–c were subsequently deprotected to thiols 1a–c, under basic conditions, using CsOH.H2O in a mixture of THF and MeOH (yields: 50 to 91%).

Cyclic voltammograms (CVs)[18] of 3a, 3b or 3c exhibit a reversible one-electron process in CH2Cl2 and CH3CN, close to 0.56 V and 0.41 V (vs Ag/AgNO3 in 0.1 M Bu4NPF6) respectively.

The kinetics for the formation of SAMs, prepared on Au substrate[19] from 1 mM solution of 1a, 1b or 1c in CH2Cl2 or CH3CN, were followed by using quartz crystal microbalance (QCM) measurements. By employing, the Langmuir adsorption isotherm model,[20] it is possible to establish that deposition ki...
netics are chain-length ($n$) dependent: $k$, increase with $n$ and are smaller than 0.1 s$^{-1}$ (see Supporting Information Figure SI-1). A maximum coverage, close to $-4.5 \times 10^{-10}$ mol cm$^{-2}$ in both solvents, is reached within a few minutes ($\tau_{\text{onset}} < 3$ min for 1a).

In non-aqueous solvents (i.e. DCM or CH$_3$CN; Bu$_4$NPF$_6$ 0.1 m), the electrochemical properties of SAM prepared from 1a, 1b or 1c were very similar to those reported above for 3a, 3b or 3c in solution (vide supra), but the shape of voltammetric waves and the linear dependency between peak intensities and scan rates were characteristic of surface-confined redox species (Figure 1). CVs parameters are quasi chain-length ($n$) independent (Table 1) and surface coverages, deduced by integration of the voltammetric signal, are in agreement with QCM experiments in both solvents. Interestingly, shapes of voltammetric waves and the linear dependency between peak intensities and the experimental CVs. Based on diagnostic criteria reviewed in ref. [31], strong attractive interactions between immobilized oxidized centers lead to a sharp shape (i.e. in CH$_3$Cl$_2$) and, medium or weak repulsive interactions to a broad shape (i.e. in CH$_3$CN) (Figure 1 and Figure 2). Taken in concert, these results suggest that the local ionic environment (coulombic repulsion and solvation) of charged redox centers plays a significant role in the electrochemical behaviour of the electroactive SAMs.

![Figure 1](image1.png)

**Figure 1.** Left: (-----) CVs of SAM prepared from 1b in 0.1 m Bu$_4$NPF$_6$/CH$_2$Cl$_2$ and in Bu$_4$NPF$_6$/CH$_3$CN; Right: (----) CVs of SAM prepared from 1b in HClO$_4$/NaClO$_4$/H$_2$O; It is noteworthy that CVs are superimposable upon one another from pH 2 to pH 6.6. (-----): CVs calculated from theoretical models based on a Frumkin type isotherm. All CVs were performed at 0.1 V s$^{-1}$.

<table>
<thead>
<tr>
<th>Medium</th>
<th>CH$_2$Cl$_2$</th>
<th>MeCN</th>
<th>H$_2$O</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1 m Bu$_4$NPF$_6$</td>
<td>$\Gamma$ (mol cm$^{-2}$)</td>
<td>$4.7 \times 10^{-10}$</td>
<td>$4.5 \times 10^{-10}$</td>
</tr>
<tr>
<td></td>
<td>$E_p$ [V]</td>
<td>0.52$^{14}$</td>
<td>0.49$^{14}$</td>
</tr>
<tr>
<td>0.1 m NaClO$_4$</td>
<td>$\Gamma$ (mol cm$^{-2}$)</td>
<td>$4.6 \times 10^{-10}$</td>
<td>$5.0 \times 10^{-10}$</td>
</tr>
<tr>
<td></td>
<td>$E_p$ [V]</td>
<td>87</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>$E_{\text{app}}$ [V]</td>
<td>0.43$^{14}$</td>
<td>0.71$^{14}$</td>
</tr>
</tbody>
</table>

[a] vs Ag/AgNO$_3$ (0.01 m), [b] vs Ag/AgCl/KCl sat.

![Figure 2](image2.png)

**Figure 2.** CVs of SAM prepared from different 1:decanethiol ratios, leading to 4.6, 3.8, 2.9, 2.1, 1.5 and 0.9 $10^{-10}$ mol cm$^{-2}$; Right: CVs calculated from theoretical models based on a Frumkin type isotherm. In addition to the usual electrochemical parameters, calculations were performed with $r_i = 1.0$ (corresponding to a strong interaction between oxidized centers) and only one variable changes at a time, the surface coverage ($\theta = 1.00, 0.74, 0.62, 0.52$ and 0.38$)$. All CVs were performed in 0.1 m Bu$_4$NPF$_6$/CH$_2$Cl$_2$ at 0.1 V s$^{-1}$.

In aqueous media, a drastic preparation$^{13}$ of SAMs is required to reach a stable and reproducible redox activity (Figure SI-2). As in solution$^{12,13}$ apparent redox potentials ($E_{\text{app}}$ at pH 7) $\sim 0.71$ V vs Ag/AgCl/KCl sat and shape of SAMs prepared from 1a, 1b and 1c are not pH dependent (Figure 1). Between pH 0 and pH 10.5, voltammetric waves (Figure SI-3) are quasi chain-length ($n$) independent and close to an “ideal system” (i.e. based on a Langmuir isotherm). Surface coverages, deduced by integration of the voltammetric signal, are comparable to the ones assessed in non-aqueous solvents (Table 1). Beyond pH 10.5, the electrochemical behaviour of SAMs is unstable due to the proximity of the water oxidation.

Because the structure of monolayer limits the accessibility of interfacial reactive sites,$^{13}$ the control of the structure-electroactivity relationship is decisive for enhancing interfacial reac-

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tions. An approach to improve the problems arising from intermolecular interactions is to dilute the electroactive species in the monolayer by mixing alkanethiols. Indeed, electrochemical behaviours of mixed SAMs, prepared from 1a, 1b or 1c alkanethiol mixtures, fit with the interaction model developed by Laviron: the full width at half maximum and the apparent redox potential are linearly dependent on the surface coverage by Laviron: the full width at half maximum and the apparent redox potential are linearly dependent on the surface coverage between theory and experiments provides evidence of a random distribution of electroactive centers on gold.

This outlook is established by electrocatalytic activities of SAMs towards benzyl-alcohol oxidation in CH2Cl2 and in H2O (pH 10). First, SAMs prepared from 1a, 1b or 1c are stable under electrocatalytic conditions because catalytic currents are persistent under repetitive potential scans in aqueous and non aqueous media (Figure 3 and Figure SI-5). Second, mixed SAMs (Figure 2). The excellent and rare agreement observed between theory and experiments provides evidence of a random distribution of electroactive centers on gold.

In summary, nitroxyl radical SAMs present a noteworthy electrochemical stability in both aqueous (from pH 0 to pH 10.5) and organic media. The control of the surface coverage associated with the catalytic properties of oxoammonium cation provide a clear and convincing illustration of potentialities of nitroxyl radical SAMs. Further work is aimed at developing mixed SAMs designed to a redox-responsive material.

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Keywords: cyclic voltammetry · electrocatalysis · monolayers · quartz crystal microbalance · self-assembly

[18] Electrochemical experiments were carried out with a Biologic SP-150 potentiostat in a glove box containing dry, oxygen-free (<1 ppm) argon, at 293 K. Cyclic voltammetry (CV) was performed in a three-electrode cell equipped with a platinum-plate counter electrode. Reference electrodes were Ag/AgNO3 (0.1 M CH3CN) or Ag/AgCl/KCl~0.1 M. CVs were recorded in dry HPLC-grade methylene chloride, HPLC-grade acetonitrile or H2O. Supporting electrolytes were tetraethylammonium hexafluorophosphate (Bu4NPF6) or sodium perchlorate (NaClO4). Based on repetitive measurements, absolute errors on potentials were found to be approximately ±5 mV.
[19] The substrates were prepared by deposition of ca. 5 nm of chrome followed by ca. 50 nm of gold onto a glass substrate using physical vapor deposition techniques and were made immediately before use. See: a) L. Sanguinetti, O. Alévêque, P. Blanchard, M. Dias, E. Levillain, D. Rondeau, J. Mass Spectrom. 2006, 41, 830–833; b) M. Bounichou, L. Sangui-


[32] To reach a stable and reproducible redox activity in aqueous media, SAMs, elaborated from CH₂Cl₂, must be immersed in pure CH₃CN and then in pure H₂O.


[33] Mixed SAMs were prepared from a mixture TEMPO derivative/Alkane-thiol solution. This procedure led to stable and reproducible SAMs.

[35] Rare because, as mentioned by G. M. Whitesides (Ref. [3]), "There are not enough experimental data to establish detailed structure-reactivity relationships for interfacial reactions on SAMs, especially on mixed SAMs."

[36] To the best of our knowledge, SEM or AFM microscopies are not suitable to confirm this conclusion because subnanometer spatial resolution is required to characterize the organization of mixed SAMs.


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