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Biphenylthioureas as organocatalysts for electrochemical reductions

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Dedicated to Professor Miguel Yus on the occasion of his 60th birthday

Abstract—Thioureas are able to act as organocatalysts in the electrochemical reduction of aromatic carboxylates.

Over the past years an increasing interest towards the so called organocatalysts has been developed.[1] Organocatalysts are organic molecules that can be used as efficient catalysts for different type of reactions. These catalysts do not contain any transition metals and for this reason they are very interesting from the environmental point of view. Among the different interactions that can be established between the catalyst and the substrate, hydrogen-bonding has demonstrated to be very useful[2] and the potential of *N*,*N*-disubstituted (thio)ureas to serve as active metal-free organocatalysts for a wide range of synthetically useful reactions susceptible to the influence of general acid catalysis has been recognized.[3] Although, urea and thiourea derivatives have been successfully used for a variety of diastereo- and enantioselective reactions, to the best of our knowledge no examples of catalysis in electrochemical reactions of organic compounds have been described. Only some examples related to cation oxidation have been reported.[4]

During several years we have been studying the complexing properties of ligands derived from biphenyl and their possible application in anion sensing.[5] Several of these ligands have been successfully used as photophysical sensors and we were interested in exploring their utility as electrochemical sensors. In the course of this study we have observed that ligands **1**–**3** (Chart 1) play a fundamental role in the electroreduction of some carboxylates.

The electrochemical properties of receptors **1**–**3** were studied by cyclic voltammetry (CV). As shown in Figure 1a, the CV response of a 0.50 mM solution of **1** at platinum electrode in 0.10 M Bu_4NPF_6/DMSO consists of a cathodic peak at −0.93 V (C_1) coupled with an anodic one at −0.86 V (A_1).[6]

The C_1/A_1 couple can be described in terms of an essentially reversible one-electron transfer process, as judged by the values of the cathodic-to-anodic peak potential separation. The formal electrode potential, $E^{0\prime}$, calculated as the half sum of the cathodic and anodic peak potentials, remains independent on the potential scan rate, with a value of −0.89 V. The CV response of **2** was similar, the reversible C_1/A_1 couple appearing at a formal potential of −0.85 V, whereas for **3** (Fig. 1b) the couple C_1/A_1 is accompanied by a second reversible couple (C_2/A_2) at −1.26 V. This couple can be attributed to the one-electron reduction of the

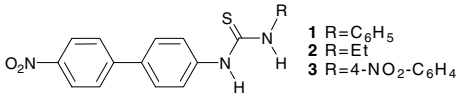

Chart 1.

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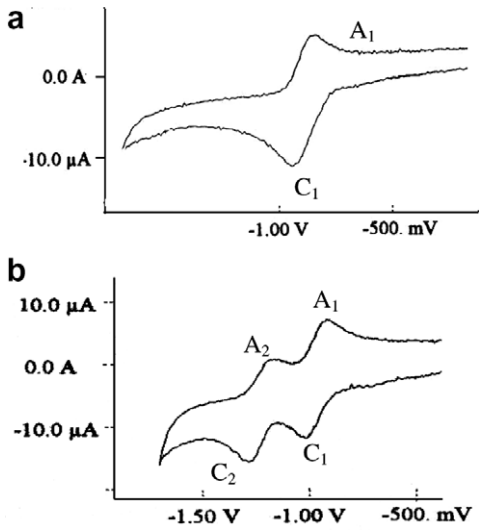


Figure 1. CVs at Pt electrode for 0.5 mM: (a) ligand **1**, and (b) ligand **3**, both in 0.10 M Bu_4NPF_6/DMSO. Potential scan rate 100 mV/s.

nitrophenyl pendant group existing in this receptor. The reductive voltammetry of the ligands can be interpreted on the basis of the well-known electrochemistry of nitro-substituted aromatic compounds in nonaqueous media.[7]

The effect of the addition of 4-methoxybenzoate anion as tetrabutylammonium (TBA) salts to DMSO solutions of the ligands is illustrated in Figure 2 for the case of **1** (for **2** and **3** see ESI). Here, a cathodic peak (C_3) near to −0.60 V precedes an apparently reversible couple (C_4/A_4) at potentials of −1.05 and −0.86 V. The peak C_3 cannot be described in terms of the electrochemical reduction of the free carboxylate nor the carboxylic acid (see ESI) but as an apparently irreversible carboxylate-centred reduction of an adduct formed between the receptor and the 4-methoxybenzoate anion. In turn, the C_4/A_4 couple can in principle be attributed to a reversible receptor-centred reduction/oxidation. Interestingly, on increasing the concentration of 4-methoxybenzoate at a fixed concentration of receptor, both peaks C_3 and C_4 monotonically increase.

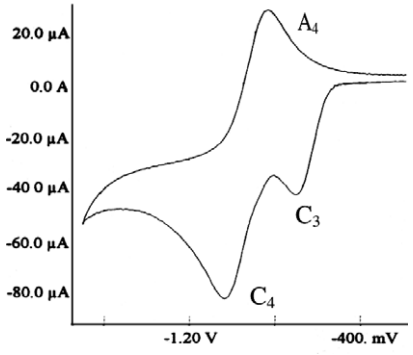


Figure 2. CV at Pt electrode for **1** (1.0 mM) plus 5.0 mM *p*-methoxybenzoate in 0.10 M Bu_4NPF_6/DMSO. Potential scan rate 100 mV/s (for 0.2 mM and 1 mM *p*-methoxybenzoate see ESI).

The voltammetry of the ligand plus anion could be interpreted on assuming that the anion coordinates to the ligand via hydrogen bond formation between the thiourea groups of the ligand and the carboxylate oxygens of the anion. However, the increment in the current as the concentration of anion increases only can be rationalized on considering the electrochemistry of the anion.

In order to have information about the species present in solution, UV spectra of the electrochemical solutions were registered during different times along controlled potential coulometric experiments performed at a reduction potential of −0.85 V under different conditions. First, the UV spectra of both free ligand **1** and a mixture of the ligand and 5 equiv of 4-methoxybenzoate samples were registered using as solvent a 0.10 M solution of Bu_4NPF_6 in DMSO (Fig. 3) to be used as reference sample. After reduction of the ligand concentration to 1% from the initial a consumption of 1.04 ± 0.04 Faraday/mol of ligand was obtained. Then, the UV spectrum shows a significant decrease of the absorption band at 285 nm corresponding to the anion and a concomitant increase of a new band near 300 nm overlapped with the band corresponding to the free ligand. This new band should be due to the new species generated under the electrochemical conditions. To have more information about the generated compound, the solution obtained after the coulometric experiment was treated with water and then extracted to dichloromethane. The main isolated product (57% yield) was studied by IR and ^1H NMR and it was identified as 4,4′-dimethoxybenzyl (see Supplementary data).

The generation of this compound agrees with the monotonical increment in the peak C_1 because the reversible pair in the CV of 4,4′-dimethoxybenzyl appears overlapped with the C_1/A_1 pair of ligand **1**, as can be seen in Figure 4. Figure 4 shows the CV for a 0.50 mM solution of 4,4′-dimethoxybenzyl 0.10 M Bu_4NPF_6/DMSO. Here, a one-electron reversible couple at an equilibrium potential of −1.00 V appears. Accordingly, CV in Fig-

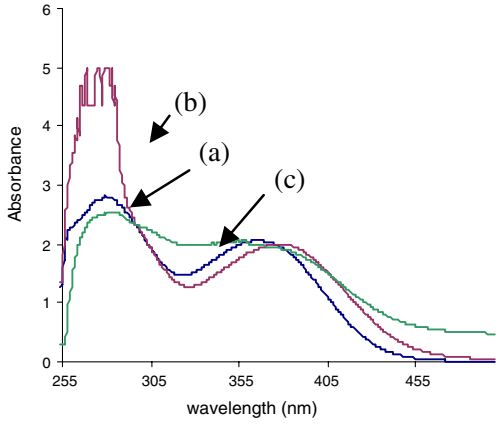


Figure 3. UV spectra of: (a) ligand 1 in 0.10 M Bu_4NPF_6/DMSO; (b) **1** + 5 equiv of TBA 4-methoxybenzoate in 0.10 M Bu_4NPF_6/DMSO; (c) **1** + 5 equiv of TBA 4-methoxybenzoate in 0.10 M Bu_4NPF_6/DMSO after reduction of the ligand concentration to 1% from the initial.

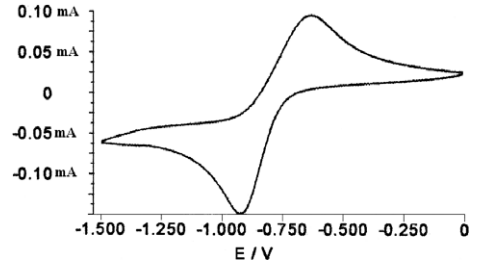
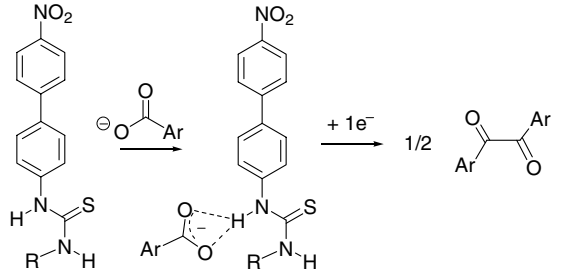


Figure 4. CV at Pt electrode for 4,4′-dimethoxybenzyl (1.0 mM) in 0.10 M Bu_4NPF_6/DMSO. Potential scan rate 100 mV/s.



Scheme 1.

ure 2 can be interpreted in terms of a two step process in which the irreversible reduction of the receptor-4-methoxybenzoate adduct (process C_3) first occurs. This process yields 4,4-dimethoxybenzyl which experiences a subsequent reversible reduction (C_4) strongly overlapped with the process C_1 for the reduction of the receptor.

The voltammetry of the ligand plus anion solutions could be interpreted on assuming that the anion coordinates to the ligand via hydrogen bond formation between the thiourea groups of the ligand and the carboxylate oxygens of the anion, as depicted in Scheme 1.[5] The overall reduction process C_3 can be represented as:

$$RCOO^- + H^+ + e^- \rightarrow 1/2\ RCOCOR + OH^- \quad (1)$$

This can formally be obtained as a combination of the following series of processes involving the ligand, represented here as LH_2:

$$RCOO^- + LH_2 \rightarrow \{LH \cdots RCOOH\}^- \quad (2)$$

$$\{LH \cdots RCOOH\}^- + e^- \rightarrow 1/2\ RCOCOR + LH^- + OH^- \quad (3)$$

$$LH^- + H^+ \rightarrow LH_2 \quad (4)$$

Benzyl generation through cathodic reduction has been reported in the literature for acid chlorides, esters and other related compounds.[8] In these reactions a C-centred radical gives rise to benzyl derivative through a dimerization reaction. The described mechanism involves the releasing of the corresponding leaving group (chloride, alcoxy, etc.). This type of reaction has never been observed with carboxylates due to the absence of an appropriate leaving group. However, the thiourea present in the solution firstly allows the electron transfer to the carbonyl carbon and secondly generates a good leaving group.

The reaction has been extended to different aromatic carboxylates (2-nitro-, 4-nitro-, 2-methoxy benzoates) with the same results. Until now the reactions have been carried out under substoichiometric conditions but as the ligand seems to be recovered unchanged after the reduction reaction, studies directed to know the lowest amount of thiourea needed are being carried out.

In conclusion it is possible to affirm that ligands **1**–**3** catalyze the cathodic reduction of aromatic carboxylates to give the corresponding dicarbonyl compounds.

Acknowledgements

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Supplementary data

CV's of TBA 4-methoxybenzoate and 4-methoxybenzoic acid. UV spectra (before and after coulometry) of 4-methoxybenzoate, 4-methoxybenzoic acid and ligand **1**. ^1H NMR and IR spectra of 4,4′-dimethoxybenzyl. CV's of **2** and **2** + 5 equiv TBA 4-methoxybenzoate in 0.1 M Bu_4NP_6/DMSO. CV of **3** + 5 equiv of TMA 4-methoxybenzoate in 0.1 M Bu_4NP_6/DMSO. CV's in 0.1 M Bu_4NP_6/DMSO of **1**, **1** + 0.2 equiv TBA 4-methoxybenzoate, **1** + 1 equiv TBA 4-methoxybenzoate and **1** + 5 equiv TBA 4-methoxybenzoate. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.07.149.

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