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Kinetic and thermodynamic study of the transfer of anionic polyamidoamine dendrimers across two immiscible liquids

Miguel A. González-Fuentes, J. Manríquez, R. Antaño-López, Luis A. Godínez*

Centro de Investigación y Desarrollo Tecnológico en Electroquímica S.C., Parque Tecnológico Querétaro Sanfandila, P.O. Box 064, Pedro Escobedo 76703, Querétaro, Mexico

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ABSTRACT

The kinetics and thermodynamics for the phase transfer of carboxyl-terminated polyamidoamine (PAMAM) dendrimers across the water/dichloroethane interface were analyzed by cyclic voltammetry and electrochemical impedance spectroscopy. A three phase junction was employed by inserting a cylindrical gold electrode through the liquid–liquid interface. The reversible redox species decamethylferrocene (DMFc) was used in the organic phase in order to promote dendrimer transfer. It was found that the electrochemical behaviour of DMFc at the gold/dichloroethane interface depends on the generation and concentration of the dendrimer species in the aqueous phase. In addition, it was observed that the electrochemically driven transfer of these macromolecules corresponds to a quasi-reversible process. The data obtained from thermodynamic studies indicate that dendrimers are transferred between the two phases under study by an entropy controlled process.

1. Introduction

The possibility of analyzing the hydrophobicity and the interfacial behaviour of molecules by means of electrochemical techniques has attracted the attention of researchers towards the characterization of drugs and other biologically important compounds [1,2]. In this regard, dendrimers constitute a class of organic molecules to which it has been conferred an increasing interest due to their possible application as drug carriers for medical applications [3], since their number and variety of functional groups provide different interactions with molecules and solvents, leading to a control of mass transport and complexation selectivity to specific molecules or ions [4]. Since the application of dendrimers to drug delivery implies the transport of these species through a biological membrane, it is important to understand their behaviour while transferring between two different media and this can be approached by examination of the related phenomena at a liquid–liquid interface.

In this context, Berduque and co-workers have reported electrochemical studies on the transfer of amine terminated poly(amidoamine) and poly(propylenimine) dendrimers across the Interface Between Two Immiscilbe Liquids (ITIES) with the use of a four electrode arrangement. They suggested that dendrimer transfer is accompanied by adsorption at the interface and found that this process is more complex for higher generations of the macromolecules [5]. In addition, Nagatani and co-workers reported a spectroelectrochemical study of the transfer and adsorption of an amine terminated G4 PAMAM dendrimer at the ITIES and concluded that dendrimer transfer is influenced by both, pH of the aqueous medium and concentration of macromolecules [6].

On the other hand, Calderon and co-workers analyzed the electrochemistry of dendrons at the water/dichloroethane (w/DCE) interface possessing only one ionizable site that corresponds to the amine group in their focal point [7]. In this study, they distinguished two mechanisms of dendron transfer that depend on the functionality of the transferring surface.

Other few works corresponding to the study of dendrimers at the liquid–liquid interface can be identified, where the equilibrium partition of polylysine [8] and PAMAM dendrimers [9], and PAMAM-terfenadine conjugates [10], were analyzed by non-electrochemical methods.

Recently, we published a communication on preliminary studies of the transfer of carboxyl-terminated PAMAM dendrimers from water to DCE by means of the three phase junction (TPJ) system formed at a water/gold/dichloroethane interface [11]. This kind of set-up was recently reported by Bak and co-workers and consists on a gold wire electrode that crosses vertically the boundary of two immiscible liquids [12]. In this way, the transfer of anions is driven from the aqueous phase to the organic solvent to compensate the positive charge generated by the oxidation of a hydrophobic redox molecule (DMFc) at the electrode–organic solvent interface. It has been proven that the potential at which the redox probe is oxi-

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* Corresponding author. Tel.: +52 442 211 6006; fax: +52 442 211 6007.
E-mail address: lgodinez@cideteq.mx (L.A. Godínez).

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dized in this type of experiments depends on the nature of the transferred ion, thus constituting an indirect measurement of the energy required for ion transfer [13].

In the present work, we report the complete study of kinetic and thermodynamic properties for the phase transfer of this kind of dendrimers from water to DCE, obtained by means of cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS).

2. Experimental

The electrochemical system employed consisted in a three electrode cell that allows setting the two immiscible phases in contact. A Ag/AgCl reference electrode and a Pt coil counter electrode were placed in the aqueous phase, while a gold wire working electrode (d = 0.5 mm) was located vertically crossing the interface between the two solvents. The length of the working electrode immersed in each phase was 0.5 cm.

While a BAS-Epsilon Potentiostat/Galvanostat was used for cyclic voltammetry (CV) and square wave voltammetry (SWV) experiments, a BAS-Zhaner Potentiostat/Galvanostat was utilized for electrochemical impedance spectroscopy (EIS) analysis. CV experiments were carried out using ohmic drop compensation. The parameters for SWV were frequency (f_{sw}) = 10 Hz, amplitude (E_{sw}) = 10 mV, and scan increment (dE) = 1 mV. For kinetic measurements, the scan rate was varied from 0.1 to 1 V s^{-1}. EIS experiments were carried out by applying a potential perturbation of 10 mV of amplitude in the range of frequencies from 0.1 Hz to 1 MHz. Square wave voltammetry (SWV) was carried out with a potential amplitude of 50 mV, potential step of 1 mV and 10 Hz of amplitude.

The organic phase contained tetrabutylammonium-hexafluorophosphate (TBAHFP) 0.1 M as supporting electrolyte and decamethylferrocene as the redox reversible probe. The gold electrode was electrochemically cleaned in a 0.5 M H_2SO_4 solution before each experiment. TBAHFP, DMFc, PAMAM dendrimers and DCE were obtained from Sigma–Aldrich and used without further purification. Dendrimers of generations 0.5, 1.5, 2.5 and 3.5 were studied. The macromolecule concentrations were such that the concentration of carboxylic groups, [$-COO^-$] was varied as follows: 2.5, 5.0, 10.0 and 20.0 mM for each dendrimer. The aqueous phase was prepared using deionized water ($\rho \approx 18$ MΩ cm) with no supporting electrolyte. When dendrimers were dissolved in the aqueous phase, the solutions attained a pH value of about 10. Experiments were carried out at 298 K, unless otherwise stated.

3. Results and discussion

3.1. Kinetics of dendrimer transfer measured by cyclic voltammetry

Cyclic voltammetry experiments were conducted with the three phase system in order to study the transfer of dendrimers between the aqueous and the organic phase, as shown in Fig. 1. The dotted line corresponds to the response obtained in the absence of dendrimers in the aqueous phase. Here, the oxidation of DMFc does not occur in the potential window surveyed since neither ions are transferred from water to DCE nor the supporting electrolyte ions in the organic phase are transferred into the aqueous phase.

In contrast, if dendrimer is dissolved in the aqueous phase, the oxidation of DMFc in the forward and its subsequent reduction in the reverse scan can be detected (Fig. 1, continuous line). This indicates that dendrimer transfer from water to DCE occurs within the potential window studied in order to compensate the positive charge generated by de oxidation of DMFc. Thus, this approach gives the possibility to inspect the ion transfer features of dendrimers between the two immiscible liquids under study.

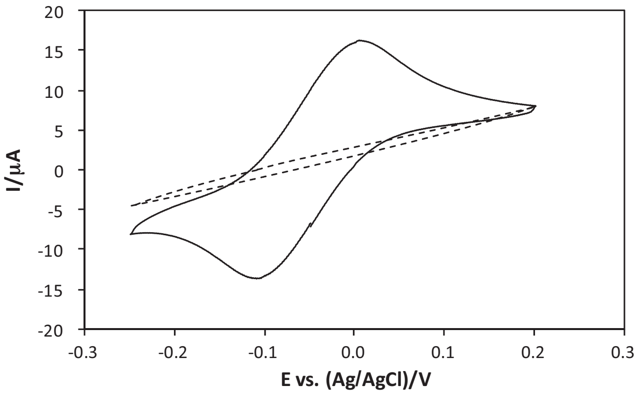

Fig. 1. Cyclic voltammetry response for the TPJ in the absence (—) and in the presence (—) of PAMAM G 3.5 dendrimer in the aqueous phase. [$-COO^-$] = 2.5 mM. Scan rate: 100 mV s^{-1}.

In order to assess the influence of dendrimers on the electrochemical reaction of DMFc, experiments with different concentrations and sizes of dendrimers were carried out. The peak potential difference (ΔE_p) for all dendrimers was larger than 100 mV, and its dependence with scan rate was linear, indicating kinetic limitations [14,15].

Similar to the findings of Berduque et al. [5] and Nagatani et al. [6], who studied the transfer of amine terminated dendrimers across the water/DCE interface using the four electrode system, it is likely that carboxyl terminated dendrimers also adsorb at the liquid–liquid interface, thus being a factor that affects the ion transfer.

In any case, since the system shows a dependence of ΔE_p with scan rate, kinetic information about the redox process of DMFc under these conditions and thus, of the transfer of dendrimers between water and DCE can be obtained. In this regard, it is also important to point out that since the number of functional groups in each macromolecule increases with generation, not only the size of the dendrimer molecule, but also the charge density is varying. This parameter determines the hydrophilicity of the dendrimer species and it is the reason for the differences in voltammetric behaviour.

Fig. 2 shows the variation of ΔE_p with the concentration of carboxylic groups and dendrimer size. Inspection of this figure shows that the charge transfer of DMFc in the organic phase depends on the concentration of charge carriers (anions present in dendrimer functionalities) in the aqueous phase.

The inset in Fig. 2 shows a representative plot of the variation of oxidation peak current (I_{pa}) with concentration of carboxylic groups. The linear increase in I_{pa} as a function of [$-COO^-$] is related to the increase in the amount of DMFc that can be oxidized due to

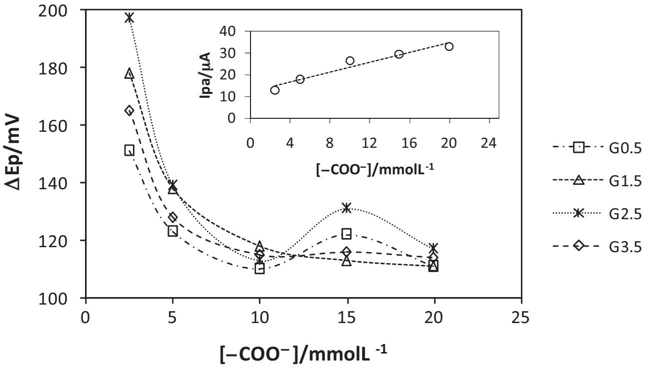

Fig. 2. Dependence of ΔE_p on the concentration of carboxylic groups at the dendrimer surface. Inset: Representative plot of the dependence of peak current with concentration of carboxylic groups.