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Research article

Redox-responsive probes for selective chelation of bivalent cations

Noureddine Raouafi*, Janet Bahri, Rihab Sahli, Khaled Boujlel

University of Tunis El-Manar, Faculty of Sciences of Tunis, Department of Chemistry, Tunis, Tunisia

*Email: noureddine.raouafi@gmail.com

ABSTRACT

N,N-disubstituted bis(furanyl-2-methyl)aminoanilines are new electrochemically-active probes for cations relying on the phenylenediamine moiety as an electroactive transducer and the difuranylamino group as an ionophore site. The electrochemical investigations, by means of cyclic and Osteryoung square wave voltammetries (CV and SWV, respectively), showed that these compounds are able to bind Mg^{2+}, Ca^{2+}, Ni^{2+} and Zn^{2+} cations with strong affinities. The addition of catalytic amounts of trifluoromethanesulfonic acid (TfOH) was found necessary to achieve rapid cation complexation. The electroactive redox features of the probes were drastically modified when the ionophore site was bonded to the cations. The anodic potential shifts of the oxidation peaks were between 905 and 1030 mV depending on the cations. The electrochemical investigations suggested the formation of a 1:2 stoichiometric complex: $[M(L)_2]^{2+}$, M = Mg, Ca, Ni and Zn. These probes were found to be selective of Ca^{2+} and chelates, with strong preference for Ca^{2+} even in presence of others cations ($Ca^{2+} > Mg^{2+}$, $Ca^{2+} > Ni^{2+}$ and $Ni^{2+} > Zn^{2+}$). UV-visible spectrophotometric studies also showed blue shifts of the absorption bands comprising between 5 and 29 nm ligands when the metal ions were added to the solution, which confirmed the complexes formation.

Keywords: Bivalent cations, tetraalkylated p-phenylenediamine (TAPD), electroactive probes, UV-visible spectrophotometry, cyclic and square wave voltammetries, selectivity

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INTRODUCTION

Metal ions play pivotal roles in biological systems. Magnesium, calcium and zinc are undoubtedly the most abundant cations in the human body. Other cations like nickel are less abundant but also have great importance [1–4]. For instance, magnesium, calcium and zinc triad are the major actors in the central nervous system's signal transmission reactions. Moreover, these cations act as enzyme co-factors to trigger the enzymes action as they take part in cell exocytosis and in immune system response [1–4]. The amounts of these ions necessary for functionality varies, e.g., it has been proven that small amounts of nickel are necessary for living organisms and large amounts are found to be toxic [5]. Therefore, it is imperative to be able to detect and evaluate the concentrations of such cations and eventually to monitor their fluxes in biological medium [6,7]. A plethora of chromogenic probes exist, which are used to determine concentration and to monitor the flux of ionic species in solution or biological medium. Reversible electrochemical probes are less known [8–10]. Many redox reversible groups such as ruthenium complex and ferrocene [10–12], and organic groups like phenylenediamine and phenazine [13,14], have been used recently as transducers to build electrochemically responsive probes. The guest detection or release can be monitored through the modification of the electrochemical features of the redox center [15–17]. Pearson et al. [13,18] and Sibert et al. [19,20] popularized electroactive phenylenediamine-based probes containing various-sized crown or thiocrown ethers to chelate metals ions.

Herein, we report the use of redox-responsive probes based on furanyl receptors for magnesium, calcium, nickel and zinc sensing in acetonitrile. Electrochemical methods have been used to investigate the chelation of the metal through the changes induced in the electrochemical features of the probes. UV-visible spectrophotometry was also used to detect the formation of complexes in acetonitrile solution. Moreover, the selectivity of these probes toward cations was examined. All compounds were prepared according to a previously published procedure (Fig. 1) [9].

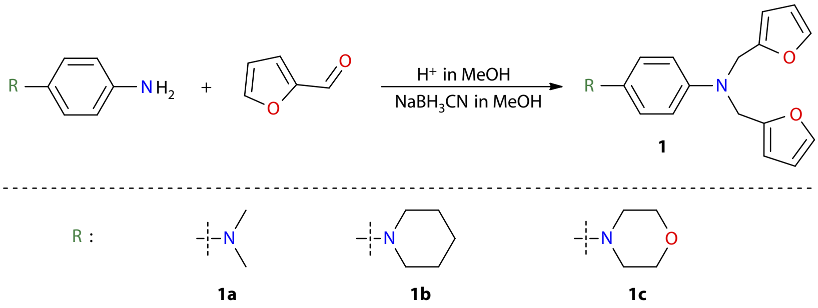

Figure 1. General route to tetraalkylated phenylenediamines 1a-c preparation *via* reductive alkylation reaction.

EXPERIMENTAL SECTION

Reagents

4-Dimethylaminoaniline, 4-piperidinylaniline, 4-morpholinoaniline, sodium cyanoborohydride, acetic acid, perchlorate salts, tetraethylammonium hexafluorophosphate, trifluoromethanesulfonic acid (TfOH) and methanol were available from Sigma-Aldrich and were used without further purification. Furfuryl-2-carboxaldehyde was freshly distilled before use. AnhydroScan® acetonitrile was purchased from LabScan and used as received.

Preparation of the probes

The reaction was performed under argon atmosphere at room temperature and shielded from the light by an aluminium foil. To a solution of 2.0 mmol of the primary aromatic amine dissolved in methanol (50 mL), 8.0 mmol of furfural and 10.0 mmol of acetic acid were added and the mixture was stirred for 12 h. Sodium cyanoborohydride (2.0 mmol) was added and stirring was continued for a further 4 h. The mixture was neutralized with 50 mL of saturated sodium bicarbonate solution and extracted twice with 20 mL of dichloromethane. The organic phase was washed twice with 10 mL of distilled water, dried over magnesium sulfate and evaporated to dryness.The oily brownish residue was chromatographed on silica gel and eluted with 30:70 ethyl acetate–cyclohexane binary system to afford the desired products.

Instrumentation

^{1}H, ^{13}C NMR spectra were recorded on a Bruker Advance 300 MHz apparatus in deuterated solvents. Chemical shift values are given in ppm relative to tetramethylsilane as an internal reference. Infrared spectra were measured on a Perkin-Elmer spectrophotometer as KBr pellets. The electrochemical experiments were conducted at ambient temperatures and at potential sweep rates equal to 0.1 Vs^{-1}; in 0.1 M tetraethylammonium hexafluorophosphate acetonitrile solution. A three-electrode glass cell was controlled by a Radiometer Analytical POL 150 with a MED 150 stand. The cell was fitted with a carbon glassy disk as a working electrode (3 mm in diameter), with a platinum wire as a counter electrode and an Ag/AgCl (3M KCl) electrode used as reference electrode. Data acquisition and treatment were respectively performed with TraceMaster 5 Software for cyclic voltammetry (CV) and square wave voltammetries (SWV) experiments. The working electrode was polished at the beginning of each experiment.

Synthesis and characterization

The spectroscopic data for physical characterization of compounds **1a-c** are given in the Supplementary Material File (SMF file).

RESULTS AND DISCUSSION

UV-visible spectrophotometric study

The UV-visible spectrum of the free probe **1a** showed two major bands located at 267 and 326 nm corresponding to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ of the aromatic moieties (Fig. 2).

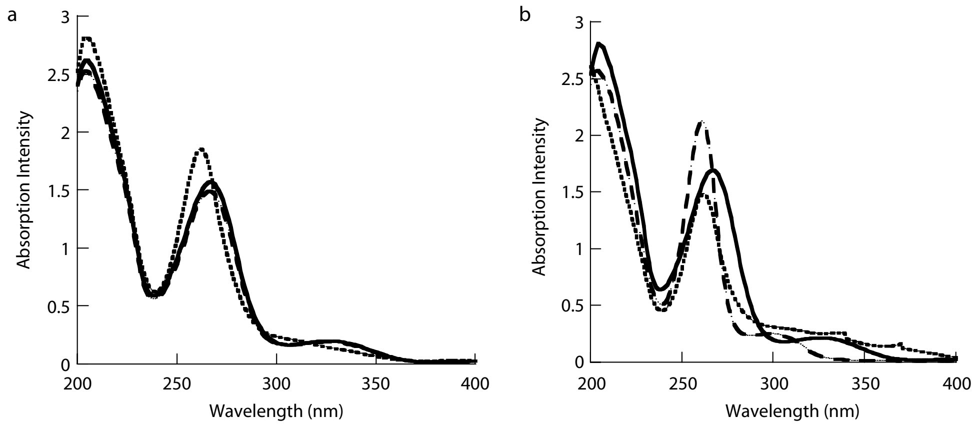

Figure 2. UV-visible absorption spectra before (—) and after the addition of: a- 0.5 equivalent of Mg^{2+} (●●●), 0.5 equivalent of Ca^{2+}(- - -), b- 0.5 equivalent of Zn^{2+}(- - -), 0.5 equivalent of Ni^{2+}(●●●) to an acetonitrile solution of 1a compound.

TfOH speeds up the chelation of the metal ions (*vide infra*), and the probes **1a-c** contain two aromatic nitrogen atoms. The addition of catalytic amounts did not influence the positions of the absorption bands or their intensities. As shown in Fig. 2(a), the addition of a 0.5 equivalent of Mg^{2+} to a solution of free probe **1a** induced simultaneously a 5 nm blue and an hyperchromic effect of the band at 267 nm. The other weak band underwent a hypsochromic shift of 13 nm. No change was observed when 0.5 equivalent of Ca^{2+} was added. In addition, a 27 nm blue shift of the band at 326 nm and an increasing of the absorption intensity of the band at 267 nm with a hypsochromic shift of about 6 nm were observed when Zn^{2+} was added. Ni^{2+} provoked similar effects, but the band at 267 nm underwent a blue shift by 5 nm and saw its intensity reduced.

Table 1. Shifts of the UV-visible spectrophotometric absorption bands upon complexation of probes 1a-c by metallic ions in acetonitrile.

	1a (λ_{max}/nm)		**1b** (λ_{max}/nm)		**1c** (λ_{max}/nm)	
Without	267	326	265	319	265	319
Mg^{2+}	262	313	262	310	265	319
Ca^{2+}	266	326	263	310	265	318
Ni^{2+}	262	326	261	299	265	319
Zn^{2+}	261	299	261	299	262	295

The spectrophotometric behaviors of **1b** and **1c** in the presence of metal ions were similar to that of **1a** (Figs. 1S-a and 1S-b see the SMF file). The absorption bands shifts for compounds **1a-c** were summarized in Table 1.

Electrochemistry of free probes

The cyclic voltammetry of compounds **1a-c** shows two mono-electronic reversible oxidation peaks similar to those observable in tetramethylated *para*-phenylenediamine (TMPD) [21], corresponding respectively to the formation of a radical-cation and a dication. The electrochemical features of **1a-c** did not change much comparatively to TMPD, although the probes became less easy to oxidize likely due to an increase of inductive effects (Fig. 3). SWV curves are given in (Fig. 2S).

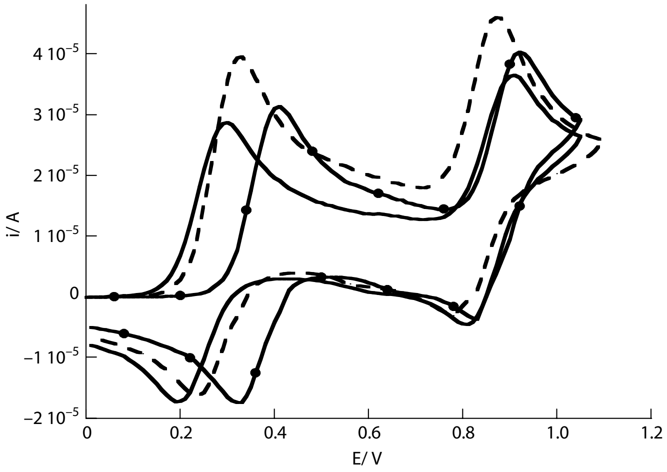

Figure 3. Cyclic voltammograms free probes 1a (—), 1b (- - -) and 1c (– ● –) (2.0 mM) in 0.1 M TEAPF$_6$ acetonitrile solution. Glassy carbon as working electrode (diameter: 3 mm), Pt wire as counter-electrode and Ag/AgCl (3M) as a reference electrode.

Moreover, the addition of catalytic quantities of TfOH did not alter the electrochemical features of the redox system, but a 20 to 30 percent decrease in the peaks' currents was observed due to the protonation of the nitrogen compounds (Fig. 4). Preliminary investigations showed that after several CV scans, a purple coloration developed slowly, probably due to electro-generated protons occurring at the electrode. These protons accelerated tremendously the cations' chelation. The same coloration was observed and was related solely to protons since the same results were obtained by adding TfOH in presence and absence of the cations. Furthermore, the acid did not influence the oxidation potentials of the probes.

The CV for a 2.0 mM solution of **1a** in acetonitrile showed two anodic peaks during the sweep potential scan associated with two cathodic peaks in the reverse scan indicating that the two oxidation processes remained, as expected, reversible. Similar conclusions were also observed for compounds **1b** and **1c** [22,23], and these results are in agreement with our previous reported works [8,9,29].

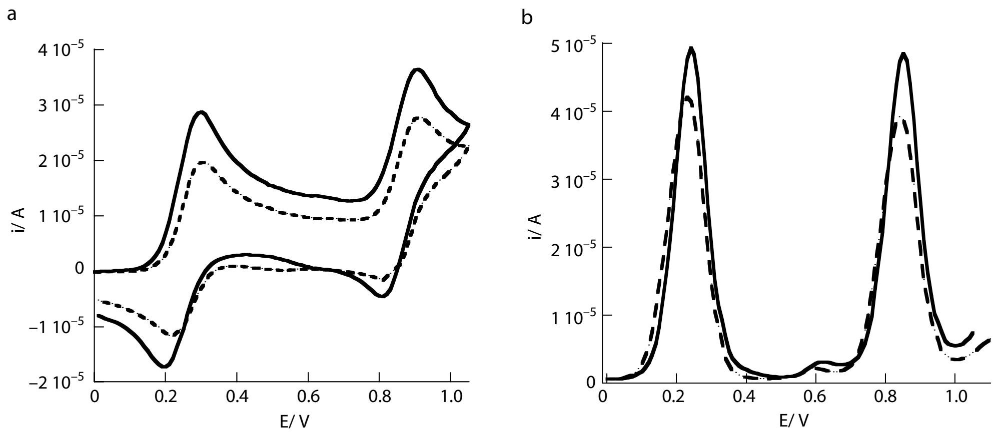

Figure 4. Cyclic (a) and square wave voltammograms (b) of 2.0 mM of free probe **1a** (—) and in 10 percent molar (0.2 mM) of TfOH (- - -) in 0.1 M TEAPF$_6$ acetonitrile solution. Scan rate: 0.1 Vs^{-1}; Glassy carbon as working electrode (diameter: 3 mm), Pt wire as counter-electrode and Ag/AgCl (3M) as a reference electrode.

Table 2. Thermodynamic data of probes **1a-c**[a].

	1st oxidation wave/mV					2nd oxidation wave/mV			
Compd.	E_{pa}	E_{pc}	ΔE_p[b]	$E_{1/2}$[c]	i_{pa}/i_{pc}	E_{pa}	E_{pc}	ΔE_p[b]	$E_{1/2}$[c]
1a	300	190	110	250	0,96	910	810	100	860
1b	320	230	90	280	0,98	880	780	100	830
1c	410	320	90	370	0,97	920	830	90	880

[a] 0.1 M TEAPF$_6$ in acetonitrile, scan rate: 0.1 Vs^{-1}; working electrode: glassy carbon (diameter: 3 mm); counter-electrode: Pt wire and reference electrode: Ag/AgCl;

[b] $\Delta E_p = E_{pa} - E_{pc}$;

[c] $E_{1/2} = (E_{pa} + E_{pc})/2$

The effect of the scan rate on the first oxidation peak current ($i_{pa}/\nu^{1/2}$) was studied in the range of 0.05–1.0 Vs^{-1} when the potential was poised approximately to 0.4–0.6 V (Fig. 3S). The linearity of the straight line of the logarithm of the first peak current as a function of logarithm of scan rate was close to 0.5 V (Fig. 4S) indicating a diffusion-controlled electrochemical process [22,23].

The electrochemical characteristics for the compounds **1a-c** are summarized in Table 2.

Sensing of calcium and magnesium

CV and SWV studies in the presence of calcium or magnesium ions revealed that compounds **1a-c** were able to bind these cations. As shown in Fig. 5, the chelation of Ca^{2+} or Mg^{2+} by the compound **1a** provoked very important anodic shifts in the CV curves when a 0.5 equivalent of ions is added. In fact, the two peaks of oxidation (O$_1$ and O$_2$) related to the free probe disappeared, and an irreversible peak (O$_3$) was observed at much higher anodic potentials attributed to oxidation of the complexes. On the reverse scan, two reduction peaks were observed: an R$_4$ peak occurred at the same potential as an R$_2$, indicating that the dication generated from the oxidation of the complex remained uncoordinated because of the electronic repulsion between the positive charges on the phenylenediamine moiety and the cations. Reduction into the neutral initial species took place at higher potentials (R$_5$) compared to those without calcium or magnesium (R$_1$), because the recomplexation reaction displaces the interfacial equilibrium, thus facilitating the electron transfer [24,25].

CV as well as SWV showed that the third peak O$_3$ is probably due to the oxidation of the furan and the chelated phenylenediamine rings [26,27]. The peak was more prominent in the case of calcium compared to magnesium.

For CV, the potentials shifts reported in Table 3 were between 780 and 990 mV. In SWV the increases of peaks potentials were slightly less important and were between 710 and 930 mV. The

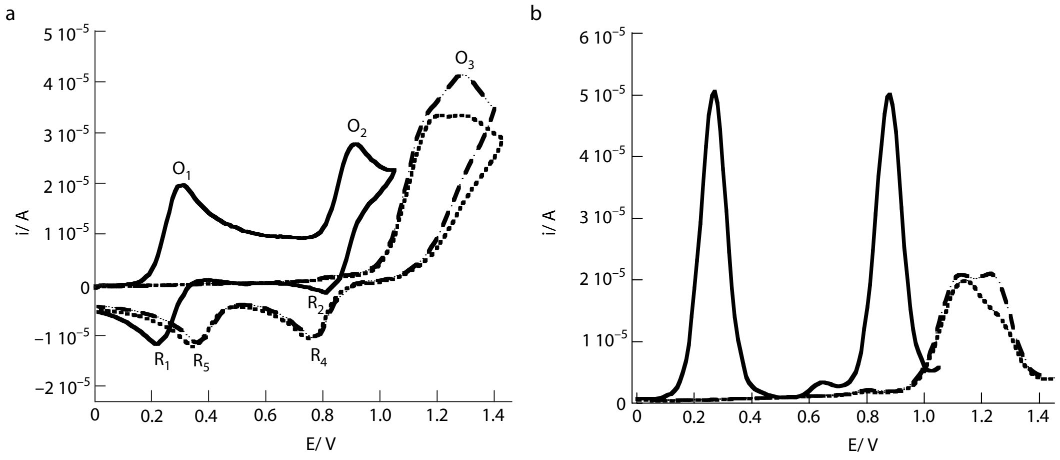

Figure 5. CV voltammograms of 2.0 mM solution of **1a** in acetonitrile 0.1M TEAPF$_6$ solution in the absence (—) and in presence of 0.5 equivalent of Ca^{2+} (● ● ●) of 0.5 equivalent of Mg^{2+} (- - -), b- SWV voltammograms of 2 mM solution **1a** in acetonitrile 0.1M TEAPF$_6$ solution in the absence (—) and in presence of 0.5 equivalents of Ca^{2+} (● ● ●) of 0.5 equivalents of Mg^{2+} (- - -).

Table 3. CV and SWV potentials of first oxidation peak and third oxidation peak (complex peaks) and their differences for compounds **1a-c** in the presence of 0.5 equivalent of Ca^{2+}, Mg^{2+}, Ni^{2+} and Zn^{2+} in acetonitrile/0.1M TEAPF$_6$.

		Ca^{2+}	Mg^{2+}	Ni^{2+}	Zn^{2+}
		CV Data			
1a	$E_{pa}(O_1)$/mV	300	300	300	300
	E_{pa} (O_3)/mV	1290	1230	1270	1240
	ΔE_p/mV	990	930	970	940
1b	$E_{pa}(O_1)$/mV	330	330	330	330
	E_{pa} (O_3) /mV	1280	1210	1230	1300
	ΔE_p/mV	950	880	900	970
1c	$E_{pa}(O_1)$/mV	430	430	430	430
	E_{pa} (O_3)/mV	1210	1220	1260	1230
	ΔE_p/mV	780	790	830	800
		SWV Data			
1a	$E_{pa}(O_1)$/mV	270	270	270	270
	E_{pa} (O_3) /mV	1120	1140	1200	1160
	ΔE_p/mV	850	870	930	890
1b	$E_{pa}(O_1)$/mV	290	290	290	290
	E_{pa} (O_3) /mV	1220	1150	1260	1180
	ΔE_p/mV	930	860	890	970
1c	$E_{pa}(O_1)$/mV	400	400	400	400
	E_{pa} (O_3) /mV	1150	1110	1200	1170
	ΔE_p/mV	750	710	800	770

* $\Delta E_p = E_{pa}(O_3) - E_{pa}(O_1)$.

substituent on the para position to the ionophore site affected the magnitude of the potential shifts. Beer et al. established that the stability of the complexes was proportional to the potential shifts [28].

Sensing of nickel and zinc

Electrochemical studies of the probe **1a** in the presence of Ni^{2+} and Zn^{2+} gave similar results to those observed with alkaline earth cations (Fig. 5S-a). The signals of the uncoordinated probe disappeared due to the cations' addition along with the appearance of more anodic signals related to the oxidation of the chelated forms. The potential peaks' shifts were in the range of 800 to 970 mV

(Table 3). For all compounds, the addition of TfOH accelerated the Zn^{2+} complexation; however, the reaction could occur without it. For Ni^{2+}, a 10 percent molar solution of TfOH was necessary to achieve the chelation. Effectively, if no acid was added and in presence of 0.5 equivalent of Ni^{2+}, the electrochemical features of the free probe did change even if the Ni^{2+}/ligand solution was kept under stirring overnight. Compounds **1b** and **1c** behaved similarly in presence of nickel. Probably, the complexation reaction needs a change in the conformation of the probes induced by the protonation followed by metal-proton exchange reaction.

In cases of Ni^{2+} and Zn^{2+}, no overlapping peaks were observed in the voltammograms due to the oxidation of the furan ring as noticeable with the alkaline earth ions, a phenomenon confirmed by single peaks observed in square wave voltammetry curves (Fig. 5S-b).

For all cations, a 1:2 metal-to-ligand ratio was observed which lead to the conclusion that the obtained complexes in solution were $[M(L)_2]^{2+}$.

Selectivity

As the studies showed, the probes can bind all the cations, and it was interesting to investigate the selectivity between them. First, alkaline earth ions were compared, then a comparison was made between Zn^{2+} and Ni^{2+} and finally alkaline earth were compared to transition metal ions. **1a** did not allow for distinguishing between the ions and **1c** was discarded because of the morpholine ring oxygen which could compete with the ionophore site, so **1b** was the most fitted for this study. CV (Fig. 6S) and SWV (Fig. 6) voltammograms showed that **1b** in the presence of a mixture of Ca^{2+} and Mg^{2+} gave curves which were close to those of Ca^{2+} alone, although the intensity of the peak current was less important. So it could be concluded that **1b** was more selective to calcium over magnesium [29].

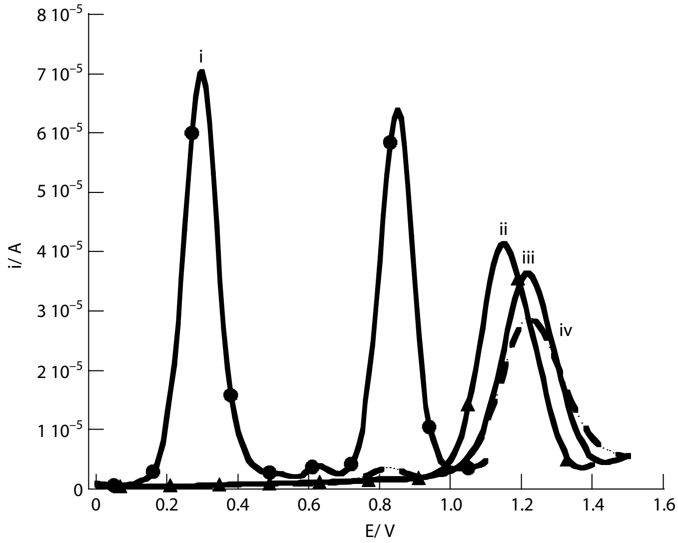

Figure 6. SWV voltammograms of (i) metal free 1b (2.0mM) (), (ii) 1b in the presence of 0.5 equivalent of Mg^{2+} (—), (iii) 1b in the presence of 0.5 equivalent of Ca^{2+} (– ▲ –) and (iv) solution in the presence of 0.5 equivalent of Mg^{2+} and of 0.5 equivalent of Ca^{2+} (- - -) in acetonitrile/0.1M $TEAPF_6$ solution.

In addition, analogous treatment showed that **1b** was more selective to Ni^{2+} over Zn^{2+} (Fig. 7). In fact, even in the presence of a large amount of Zn^{2+} (5 equivalent), the addition of a stoichiometric quantity of Ni^{2+} was enough to form the 1:2 complex, thus zinc was ejected from the receptor ionophore site and nickel replaced it indicating that the probe was very selective to nickel.

As shown in the Fig. 8, only one peak was observed after the addition of a equimolar mixture of the Ca^{2+} and Ni^{2+}. The peak is almost superimposable with that of the oxidation of the calcium complex, which lead to the conclusion that the **1b** compound was more selective to calcium over nickel. These results indicated that **1b** was more selective to $Ca^{2+} > Mg^{2+} > Ni^{2+} > Zn^{2+}$.

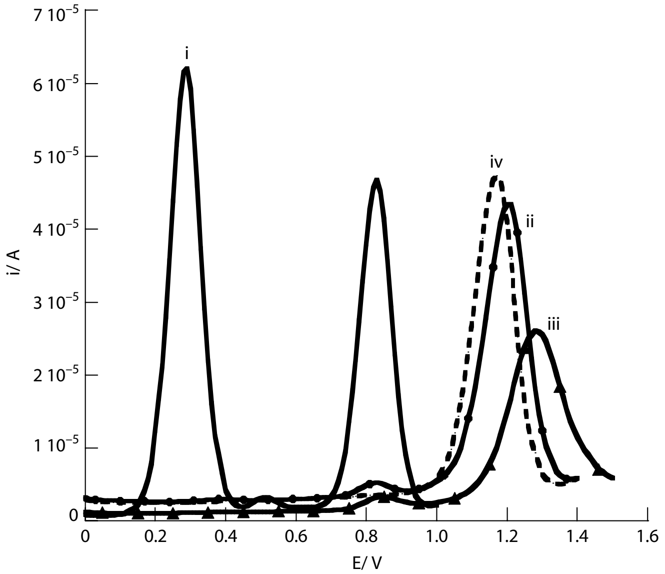

Figure 7. SWV voltammograms of (i) metal free **1b** (2.0 mM) (—), (ii) **1b** in the presence of 0.5 equivalent of Ni^{2+} (– ● –), (iii) **1b** in the presence of 0.5 equivalent of Zn^{2+} (– ▲ –) and (iv) solution in the presence of 0.5 equivalent of Ni^{2+} and of 5 equivalents of Zn^{2+} (- - -) in acetonitrile/0.1M $TEAPF_6$ solution.

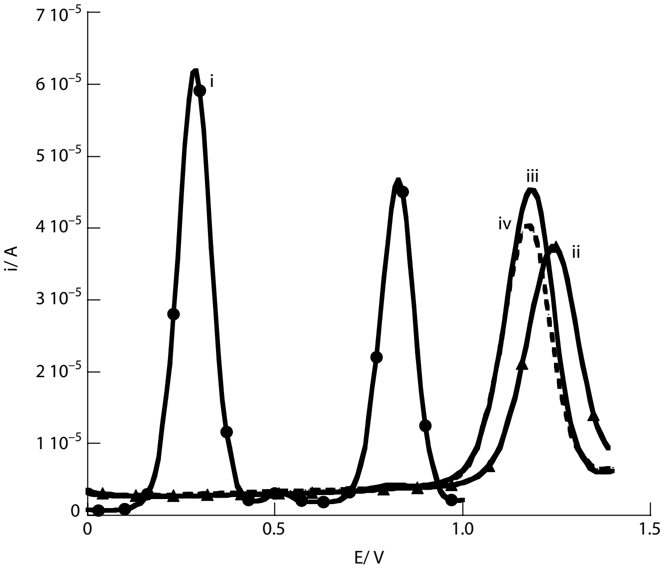

Figure 8. SWV voltammograms of (i) metal free **1b** (2.0mM) (– ● –), (iii) **1b** in the presence of 0.5 equivalent of Ca^{2+} (—), (ii) **1b** in the presence of 0.5 equivalent of Ni^{2+} (– ▲ –) and (iv) solution in the presence of 0.5 equivalent of Ni^{2+} and of 0.5 equivalent of Ca^{2+} (- - -) in acetonitrile/0.1M $TEAPF_6$ solution.

CONCLUSION

In summary, UV-visible spectrophotometric, cyclic, square wave and differential pulse voltammetry studies showed that a series of tetraalkylated pheneylenediamines containing a bis(furan-2-methyl)amino group as the ionophore site were found to be sensitive to the presence of calcium, magnesium, nickel and zinc ions in solution. All the complexes were formed in 1:2 stoichiometries. Comparative studies showed that **1b** was more selective to Ca^{2+} over Mg^{2+} and to Ni^{2+} over Zn^{2+}. Further investigation revealed that **1b** was more selective to Ca^{2+} over Ni^{2+}.

ACKNOWLEDGMENTS

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APPENDIX. SUPPLEMENTARY MATERIALS

Supplementary materials associated with this article can be found, in the online version doi:10.5339/connect.2012.8.

References

[1] Sigel, H., & Siegel, A. (1984). Metal Ions in Biological System: Calcium and its Role in Biology. 17, M. Dekker, New York.
[2] Sigel, H., & Siegel, A. (1983). Metal Ions in Biological System: Zinc and its Role in Biology and Nutrition. 15, M. Dekker, New York.
[3] Sigel, H., & Siegel, A. (1990). Metal Ions in Biological System: Compendium on Magnesium and its Role in Biology, Nutrition, and Physiology. 26, M. Dekker, New York.
[4] Sigel, H., & Siegel, A. (1988). Metal Ions in Biological System: Nickel and its Role in Biology. 23, M. Dekker, New York.
[5] Denkhaus, E., & Salnikow, K. (2002). Nickel Essentiality, Toxicity, and Carcinogenicity. Crit Rev Oncol Hematol, 42, 35–56.
[6] Tang, Y.M., Travis, E.R., Wightman, R.M., & Schneider, A.S. (2000). Sodium–calcium exchange affects local calcium signal decay and the rate of exocytotic secretion in single chromaffin cells. J Neurochem, 74, 702–710.
[7] Haynes, C.L., Buhler, L.A., & Wightman, R.M. (2006). Vesicular Ca^{2+}-induced secretion promoted by intracellular pH-Gradient disruption. Biophys Chem, 123, 20–24.
[8] Amatore, C., Genovese, D., Maisonhaute, E., Raouafi, N., & Schöllhorn, B. (2008). Towards electrochemically-driven release of nanoscale quantities of cations with kinetic and spatial resolution. Angew Chem Int Ed, 47, 5811–5814.
[9] Sahli, R., Raouafi, N., Boujlel, K., Maisonhaute, E., Schöllhorn, B., & Amatore, C. (2011). Electrochemically active phenylenediamine probes for transition metal cation detection. New J Chem, 35, 709–715.
[10] Plenio, H, & Burth, D (1996). Indenyl-crown ethers: heterotopic ligands with a π- and a σ-face and the synthesis of cymantrene- and cobaltocene-crown ethers and their alkaline metal ion complexes. Organometallics, 15, 1151–1156.
[11] Lai, R.Y., Chiba, M., Kitamura, N., & Bard, A.J. (2002). Electrogenerated chemiluminescence. 68. Detection of sodium ion with a ruthenium(II) complex with crown ether moiety at the 3,3'-positions on the 2,2'-bipyridine ligand. Anal Chem, 74, 551–553.
[12] Chesney, A., Bryce, M.R., Batsanov, A.S., Howard, J.A.K., & Goldenberg, L.M. (1998). Selective electrochemical magnesium and calcium sensors based on non-macrocyclic nitrogen-containing ferrocene ligands. Chem Commun, 677–679.
[13] Pearson, A.J., & Hwang, J. (2001). Crown-annelated *p*-phenylenediamine derivatives as electrochemical and fluorescence-responsive chemosensors: cyclic voltammetry studies. Tetrahedron Lett, 42, 3541–3543.
[14] Fricke, T., Dickmans, A., Jana, U., Zabel, M., Jones, P.G.I., Dix König, B., & Herges, R. (2002). Synthesis and structure of bis-urea phenazines. Z Naturforsch B, 57, 937–945.
[15] Beer, P.D., Gale, P.A., & Chen, Z. (1999). Electrochemical recognition of charged and neutral guest species by redox-active receptor molecules. Adv Phys Org Chem, 31, 1–90.
[16] Bhattacharyya, K.X., Boubakeur-Lecaque, L., Tapsoba, I., Maisonhaute, E., Schollhorn, B., & Amatore, C. (2010). An organometallic derivative of a BAPTA ligand: towards electrochemically controlled cation release in biocompatible media. Chem Commun, 47, 5199–5201.
[17] Ferreira, D.C.M., Tapsoba, I., Arbault, S., Bouret, Y., Moreira, M.S.A., Pinto, A.V., Goulart, M.O., & Amatore, C. (2009). Ex Vivo Activities of beta-Lapachone and alpha-Lapachone on macrophages: a quantitative pharmacological analysis based on amperometric monitoring of oxidative bursts by single cells. ChemBioChem, 21, 528–538.
[18] Pearson, A.J., & Xiao, W. (2003). Fluorescent photoinduced electron transfer (PET) sensing molecules with *p*-phenylenediamine as electron donor. J Org Chem, 68, 5361–5368.
[19] Sibert, J.W., Forshee, P.B., & Lynch, V. (2005). Wurster's thiacrown ethers:? synthesis, properties, and Pt(II)-coordination chemistry. Inorg Chem, 44, 8602–8609.
[20] Sibert, J.W., Forshee, P.B., & Lynch, V. (2006). Electron transfer vs. coordination chemistry:? isomer-specific binding of Hg(II) by an *ortho*-Wurster's thiacrown ether. Inorg Chem, 45, 6108–6110.
[21] Long, J.S., Silvester, D.S., Barnes, A.S., Rees, N.V., Aldous, L., Hardacre, C., & Compton, R.G. (2008). Oxidation of several p-phenylenediamines in room temperature ionic liquids: estimation of transport and electrode kinetic parameters. J Phys Chem C, 112, 6993–7000.
[22] Nicholson, R.S., & Shain, I. (1964). Theory of stationary electrode polarography: single scan and cyclic methods applied to reversible, irreversible, and kinetic systems. Anal Chem, 36, 706–723.
[23] Polcyn, D., & Shain, I. (1966). Multistep charge transfers in stationary electrode polarography. Anal Chem, 38, 370–375.
[24] Nicholson, R.S., & Shain, I. (1965). Theory of stationary electrode polarography for a chemical reaction coupled between two charge transfers. Anal Chem, 37, 178–190.
[25] Savéant, J.M. (2006). Elements of Molecular and Biomolecular Electrochemistry: An Electrochemical Approach to Electron Transfer Chemistry. Wiley & Sons, New Jersey.
[26] Kabasakaloğlu, M., Talu, M., Yıldırım, F., & Sarı, B. (2003). The electrochemical homopolymerization of furan and thiophene and the structural elucidation of their bipolymer films. Appl Surf Sci, 28, 85–97.

[27] Moressi, M.B., Zon, M.A., & Fernandez, H. (2000). Solvent effects on the heterogeneous kinetics of N,N,N',N'-Tetramethyl p-Phenylendiamine (TMPD) in nonaqueous binary solvent mixtures. The role of the preferential solvation phenomenon. Electrochim Acta, 45, 1669–1682.
[28] Gale, P.A., Beer, P.D., & Chen, Z. (1999). Mechanisms of electrochemical recognition of cations, anions and neutral guest species by redox-active receptor molecules. Coord Chem Rev, 185–186, 3–36.
[29] Sahli, R., Raouafi, N., Maisonhaute, E., Boujlel, K., & Schöllhorn, B. (2012). Thiophene-based electrochemically active probes for selective calcium detection. Electrochim Acta, 63, 228–231.