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PAPER

Electrochemically active phenylenediamine probes for transition metal cation detection†

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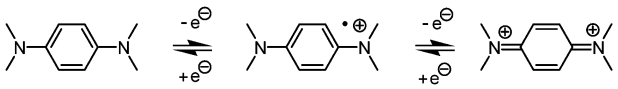
A novel family of tetraalkyl-*p*-phenylenediamine (TAPD)-based ligands has been efficiently prepared by reductive amination of heterocyclic aldehydes. The redox properties of these electrochemical active ligands change dramatically upon complexation of the transition metal cations Zn^{2+}, Ni^{2+} and Cd^{2+} leading to large oxidation potential shifts of up to 950 mV depending on the nature of the ligand. Complexes with a metal to ligand ratio of 1 : 2 were formed and ^{113}Cd NMR revealed an octahedral coordination sphere of the metal. All pyridyl derivatives show a distinct chemoselectivity (Zn^{2+} > Cd^{2+} > Ni^{2+}). The thiophenyl containing derivatives display a particularly high selectivity for zinc cations (Zn^{2+} ≫ Ni^{2+}, Cd^{2+}).

Introduction

Metal ion sensing is regaining interest because of the pivotal role of such species in many biological processes where the presence of specific metal cations is essential for the good functioning of several organs.[1] Particularly, the importance of transition metals is under focus.[2] Zinc, for instance, is the second most abundant d-block metal ion in human brain. High levels of nickel ions are lethal to animals and human beings, although small amounts of it are conversely vital. In the biology of living organisms nickel plays numerous roles. Effectively many enzymes such as urease, methyl-coenzyme M reductase, acetyl coenzyme A ligase *etc*. rely on the nickel ions in their corresponding actions.[3] On the other hand, cadmium toxicity is well established and is known to provoke severe pollution.[4] In fact, contamination of food and water[5] by cadmium derivatives is now known to induce several types of cancer and to be highly neurotoxic.[6]

The monitoring of cationic exchanges remains an important challenge. Since Cram, Lehn and Pedersen have been awarded the Nobel Prize "for their development and use of molecules with structure-specific interactions of high selectivity", many types of chemosensors have been reported in the literature.[7] Among the various ligands for electrochemical ion sensing, in particular crown ethers have been frequently used because of their capacity to bind metal cations due to the hard oxygen donor atoms supporting their coordination.[8] More recently, it was reported that tetraalkylated *p*-phenylenediamines (TAPD) attached to suitable ligands are useful probes for the detection of a variety of alkali, alkaline earth[9,10] and transition metal ions.[11] Their physicochemical properties are modified upon coordination of a guest which gives the possibility to control the ionic effectors. These compounds have been a subject for spectroscopic studies as typical fluorophores[12] and chromophores.[13] The redox-active phenylenediamine centres can also be reversibly oxidized in two single electron processes to the radical cation and the dication, respectively, as shown in Scheme 1.[14,15]

In this work, we report the synthesis of a series of new electroactive transition metal ligands based on TAPD bearing pyridyl and thiophenyl binding sites, potentially interesting for the development of new selective chemosensors. The spectroscopic and electrochemical properties of these compounds have been evaluated in the presence of the transition metals Zn(II), Ni(II) and Cd(II).



Scheme 1 Reversible oxidation of *N*,*N*′-tetramethyl-*p*-phenylenediamine (TMPD).

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Experimental

General

All reactions were performed with previously dried solvents under argon atmosphere. The chemicals were purchased from Sigma/Aldrich and Acros (France) and used as received. Anhydrous acetonitrile was purchased from LabScan. Thin layer chromatography (TLC) was performed on Fluka or Merck aluminium sheets pre-coated with F_{254} silica gel. Preparative column chromatography was performed on Fluka silica gel 60 (0.040–0.063). ^{1}H, ^{13}C, ^{113}Cd NMR spectra were recorded on a Bruker Advance 300 MHz apparatus in deuterated solvents. Chemical shifts for ^{1}H, ^{13}C NMR were reported using TMS signals as internal references and a solution of cadmium perchlorate as external reference for ^{113}Cd NMR spectra. IR (ATR) spectra were measured on a Perkin Elmer Alpha spectrophotometer and UV-visible spectra were measured in 1 cm quartz cells using a Perkin Elmer Lambda 2 spectrophotometer.

Electrochemistry

The electrochemical experiments were conducted in 0.1 M tetrabutylammonium tetrafluoroborate acetonitrile solution in a three-electrode glass cell controlled by a Radiometer Analytical potentiostat consisting of a Voltalab PST050 equipped with a HBV 100 booster (for cyclic voltammetry) and a POL 150 with a MED 150 stand (for differential pulse voltammetry). VoltaMaster 4 (CV) and TraceMaster 5 (DPV) software was used for data acquisition. A platinum wire was used as the counter electrode. $Ag|Ag^{+}$ 0.01 M and Ag|AgCl (3 M KCl) electrodes were used as reference electrodes in CV and DPV experiments respectively. A 3 mm-diameter glassy carbon disk electrode was used as the working electrode. It was polished prior to each experiment. Tetrabutylammonium tetrafluoroborate has been recrystallized from methanol and dried at 60 °C for 12 h. Acetonitrile was stored over an activated 3 Å molecular sieve. Cyclo and differential pulse voltammograms were recorded at ambient temperature and at a potential sweep rate of 100 mV s^{-1}. Metal transition ions were added as a solution of the corresponding perchlorate salts in acetonitrile. The solutions were dried over activated 3 Å molecular sieves.

Synthesis

The reductive amination reaction was performed under argon atmosphere at room temperature in the dark (shielded from the light by an aluminium foil). The primary aromatic amine (2.0 mmol) was dissolved in 50 mL of methanol. Aldehyde (8.0 mmol) and acetic acid (10.0 mmol) were added and the mixture was stirred for 12 h. Sodium cyanoborohydride (2.0 mmol) was added and the mixture was stirred for 4 h. The reaction progress was followed by thin layer chromatography. After completion the reaction mixture was neutralized by 50 mL of saturated ammonium chloride solution and extracted twice with 20 mL of dichloromethane. The organic layer was washed twice with 10 mL of distilled water, and then dried over magnesium sulfate. The filtrate was concentrated under vacuum and the residue was purified by column chromatography on silica (20% ethyl acetate in petroleum ether).

Compound 1a ($C_{20}H_{22}N_4$). Yield 61%; mp 84–86 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm 2.9 (s, 6H, CH_3), 4.75 (s, 4H, CH_2), 6.67 (m, 4H, CHarom.), 7.15 (t, 2H, $^{3}J_{H-H}$ = 7.8 Hz, CHarom.), 7.26 (d, 2H, $^{3}J_{H-H}$ = 7.5 Hz, CHarom.), 7.61 (t, 2H, $^{3}J_{H-H}$ = 7.8 Hz, CHarom.), 8.56 (d, 2H, $^{3}J_{H-H}$ = 7.5 Hz, CHarom.); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ/ppm 41.9, 57.9, 114.4, 115.6, 121.2, 122.23, 136.8, 149.3, 149.3, 149.7, 159.5. MS (CI^{+}, CH_4): m/z(%): 319 (100) $[M + H]^{+}$; 318 (51) $[M^{+}]$; 227 (49) $(M - C_6H_6N + H)$. IR ν_{max}/cm^{-1} 3048 (CH), 2916 (CH), 1522 (C=N), 1224, 1432.

Compound 2a ($C_{18}H_{20}N_2S_2$). Yield 74%; mp 62–64 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm 2.84 (s, 6H, CH_3), 4.53 (s, 4H, CH_2), 6.74 (d, 2H, $^{3}J_{H-H}$ = 7.5 Hz, CHarom.), 6.87 (d, 2H, $^{3}J_{H-H}$ = 7.5 Hz, CHarom.), 6.90 (mu, 4H, thiophene), 7.18 (mu, 2H, thiophene); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ/ppm 41.6, 50.6, 114.7, 118.2, 125.2, 126.2, 127.5, 140.8, 142.4. MS (EI^{+}): m/z(%): 328 (76) $[M^{+}]$; 231 (100) $[M - C_5H_5S]^{+}$. IR ν_{max}/cm^{-1} 3066 (CH), 2884 (CH), 1514 (C=N), 1243, 705.

Compound 1b ($C_{23}H_{26}N_4$). Yield 76%; mp 144–146 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm 1.69 (m, 4H, CH_2), 1.92 (m, 2H, CH_2), 2.98 (t, 4H, $^{3}J_{H-H}$ = 7.6 Hz, CH_2), 4.76 (s, 4H, CH_2), 6.63–6.81 (d, 4H, $^{3}J_{H-H}$ = 7.6 Hz, CHarom.), 7.13 (t, 2H, $^{3}J_{H-H}$ = 7.6 Hz, CHarom.), 7.31 (d, 2H, $^{3}J_{H-H}$ = 7.9 Hz, CHarom.), 7.58 (t, 2H, $^{3}J_{H-H}$ = 7.9 Hz, CHarom.), 8.56 (d, 2H, $^{3}J_{H-H}$ = 7.9 Hz, CHarom.); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ/ppm 24.0, 25.9, 52.6, 57.7, 113.6, 119.1, 121.9, 136.7, 149.5, 159.2. MS (EI^{+}): m/z(%): 358 (3) $[M^{+}]$; 266 (43) $[M - C_6H_6N]^{+}$. IR ν_{max}/cm^{-1} 3070 (CH), 2900 (CH), 1501 (C=N), 1200, 1110.

Compound 2b ($C_{21}H_{24}N_2S_2$). Yield 85%; mp 69–71 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm 1.52 (m, 4H, CH_2), 1.66 (m, 2H,CH_2), 3.03 (t, 4H, $^{3}J_{H-H}$ = 7.6 Hz, CH_2), 4.56 (s, 4H, CH_2), 6.86 (d, 2H, $^{3}J_{H-H}$ = 7.2 Hz, CHarom.), 6.90 (m, 4H, thiophene), 7.17 (m, 2H, thiophene), 7.25 (d, 2H, $^{3}J_{H-H}$ = 7.2 Hz, CHarom.); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ/ppm 24.3, 25.9, 50.6, 52.0, 117.3, 118.4, 124.8, 126.2, 127.0, 141.3, 142.3. MS (EI^{+}): m/z(%): 368 (93) $[M^{+}]$; 271 (85) $[M - C_5H_5S]^{+}$. IR ν_{max}/cm^{-1} 3000 (CH), 2950 (CH), 1500 (C=N), 1210, 1109, 701.

Compound 1c ($C_{22}H_{24}N_4O$). Yield 75%; mp 138–140 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm 3.33 (t, 4H, $^{3}J_{H-H}$ = 7.1 Hz, CH_2), 3.79 (t, 4H, $^{3}J_{H-H}$ = 7.1 Hz, CH_2), 4.78 (s, 4H, CH_2), 6.70–6.83 (d, 4H, $^{3}J_{H-H}$ = 7.5 Hz, CHarom.), 7.29 (t, 2H, $^{3}J_{H-H}$ = 7.6 Hz, CHarom.), 7.39 (d, 2H, $^{3}J_{H-H}$ = 7.5 Hz, CHarom.), 7.75 (t, 2H, $^{3}J_{H-H}$ = 7.6 Hz, CHarom.), 8.50 (d, 2H, $^{3}J_{H-H}$ = 3 Hz, CHarom.); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ/ppm 49.2, 56.5, 65.8, 112.5, 120.6, 121.1, 140.5, 148.6, 156.7. MS (EI^{+}): m/z(%): 360 (16) $[M^{+}]$; 268 (100) $[M - C_6H_6N]^{+}$. IR ν_{max}/cm^{-1} 3050 (CH), 2916 (CH), 1514 (C=N), 1232, 1434, 1182, 1112.

Compound 2c ($C_{20}H_{22}N_2S_2O$). Yield 52%; mp 98–99 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm 3.01 (t, 4H, $^{3}J_{H-H}$ = 7.1 Hz, CH_2), 3.81 (t, 4H, $^{3}J_{H-H}$ = 7.1 Hz, CH_2), 4.60 (s, 4H, CH_2), 6.81

(d, 4H, $^{3}J_{H-H}$ = 7.5 Hz, CHarom.), 6.91 (m, 4H, thiophene), 7.21 (m, 2H, thiophene); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ/ppm 52.6, 57.7, 76.5, 113.3, 121.1, 121.9, 136.7, 149.5. MS (CI^+, CH_4): m/z(%): 371 (41) $[M + H]^+$. IR ν_{max}/cm^{-1} 3066 (CH), 2843 (CH), 1511 (C=N), 1283, 1161, 1122, 694.

Preparation of the $[Cd\ (1a)_2]^{2+}$ complex. The complex was prepared by dissolving 1.0 mmol cadmium perchlorate $Cd(ClO_4)_2$ in 10 mL of anhydrous dichloromethane (caution: perchlorates are explosive in the solid state). After stirring the solution for 1 h at room temperature, 2.0 mmol of **1a** were added and stirring was maintained for 24 h. The solvent was evaporated to yield a brownish solid which was filtrated and washed with diethylether. Yield: 85%; ^{113}Cd NMR (CH_2Cl_2, 66 MHz, T = 298 K) δ/ppm 231 (s); ^{113}Cd NMR (CH_2Cl_2/CD_2Cl_2, 66 MHz, T = 208 K) δ/ppm 272 (s).

Results and discussion

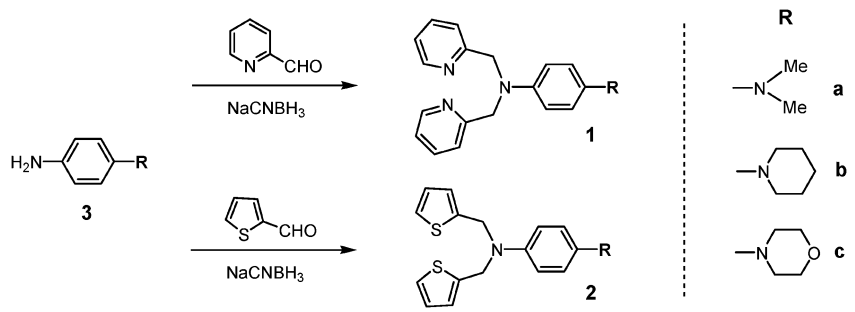
Synthesis

Several methods for the preparation of tetra-substituted phenylenediamine derivatives have been described in the literature.[16] Reductive amination[17] of aldehydes is a straightforward procedure that has been chosen to obtain in a one pot two-steps reaction of the compounds **1** and **2** (Scheme 2). 4-Dimethylaminoaniline (**3a**), 4-piperidinylaniline (**3b**) and 4-morpholinoaniline (**3c**) were used to react with pyridinyl-2-carboxaldehyde and thiophenyl-2-carboxaldehyde leading to two series of products **1a–c** and **2a–c**. The condensation of the *N*,*N*-dialkylated phenylenediamines **3a–c** with a heteroaromatic aldehyde in methanol/acetic acid provided the corresponding imine which was then reduced *in situ* by sodium cyanoborohydride to the respective secondary amine. This amine reacted with a second molecule of aldehyde giving, after final reduction, the corresponding TAPD derivatives **1** and **2** in yields of 52% to 85%. The aldehydes were used in excess in order to ensure complete transformation of the starting amine.

UV spectroscopy

Evolution of UV spectra is a common method for exploring the formation of metal complexes.[14,18] We examined the effect of gradual addition of Zn^{2+} to compounds **1a** and **2a** on the UV-visible absorption curves. The absorption spectrum of the free ligand **1a** shows two bands, the major one being located at 262 nm and the weaker band at 325 nm (Fig. 1a). The UV spectrum of compound **2a** revealed two intense absorption bands (λ_{max} = 235, 265 nm) and a weaker one at 323 nm (Fig. 1b).

The observation of a bathochromic shift upon the increase of solvent polarity (acetonitrile/ethanol) confirmed the assumption that the absorption bands are related to n → π* transitions of the aromatic phenylenediamine system. The addition of Zn^{2+} to a solution of the free ligands induced significant changes of the respective UV spectra. The addition of 0.5 equivalents of Zn^{2+} to a solution of ligand **1a** provoked an increase in the absorption intensity of the band at 262 nm and a blue shift of *ca.* 15 nm of the band at 325 nm. In the case of compound **2a** both strong bands increased in the presence of zinc cations. The bands at 265 and 323 nm display hypsochromic shifts of about 8 and 24 nm respectively. These results can be explained by the formation of zinc complexes with both



Scheme 2 General route to TAPD derivatives.

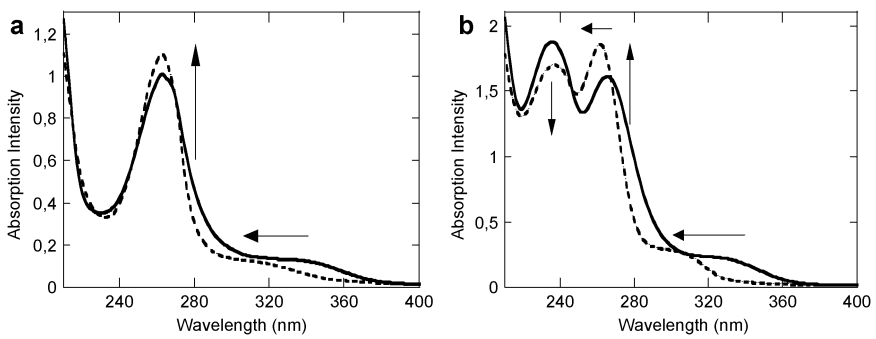


Fig. 1 UV absorption spectra before (solid line) and after (dashed line) the addition of $Zn(ClO_4)_2$ to an acetonitrile solution of (a) **1a** (0.5 equiv. of Zn^{2+}) and (b) **2a** (1 equiv. of Zn^{2+}).

representative ligands **1a** and **2a**. The participation of the phenylenediamine nitrogen lone pairs in the zinc coordination is very likely and probably affects the corresponding transition energy being responsible for the observed hypsochromic shifts.[19]

Electrochemistry of the free ligands 1 and 2

The redox potentials of the described electroactive ligands were determined by cyclic voltammetry in anhydrous acetonitrile using a glassy carbon disc electrode (Tables 1–2). The electrochemical behaviour of compound **2a–c** is similar to TMPD, displaying two reversible oxidation waves (*cf.* Fig. 2a). Accordingly, these waves are assigned to the formation of the radical-cation (Ox_1/Red_1) and the corresponding dication (Ox_2/Red_2). The respective peak current ratios I_{pa}/I_{pc} are close to unity (Table 1). Furthermore the linear dependence of the anodic peak current I_{pa} on the square root indicates a diffusion limited signal. Accordingly the peak to peak separation is close to 60 mV as expected for a Nernstian behaviour.

In the case of the pyridyl derivatives **1a–c** the second wave is irreversible (see Fig. 2b) because the second electron oxidation is coupled to a chemical reaction, probably due to the enhanced C–H acidity of the CH_2 groups linked to the pyridyl moieties. The influence of the substituents **a**, **b** and **c** (Scheme 2) on the values of the oxidation potentials in each series **1** and **2** is relatively small but significant, with peak potential differences up to 130 mV (Table 1). The oxidation potentials of each ligand can thus be tuned within the range of over 100 mV without changing the inherent chemical behaviour of the free ligands (compare Table 2).

Electrochemistry of metal complexes of compound 1

The CV studies showed that all studied compounds are sensitive to the presence of Zn^{2+} ions. Upon the progressive addition of Zn^{2+} to a solution of the dipicolylamine derivative **1c** (Fig. 3) both oxidation peaks (Ox_1, Ox_2) disappeared progressively and an irreversible peak (Ox_3) was observed at a much higher potential at 516 mV (Fig. 3 and Table 2). The

Table 1 Characteristics of the cyclic voltammetric curves of compounds **1** and **2**[a]

	Ist oxidation wave					IInd oxidation wave			
Compound	E_{pa}/mV	E_{pc}/mV	ΔE_p[b]/mV	$E_{1/2}$[c]/mV	I_{pa}/I_{pc}	E_{pa}/mV	E_{pc}/mV	ΔE_p[b]/mV	$E_{1/2}$[c]/mV
1a	−63	−127	64	−95	0.91	302	—	—	—
1b	−23	−99	76	−61	0.97	321	—	—	—
1c	72	−01	73	35.5	0.97	401	—	—	—
2a	33	−52	85	−09.5	0.97	628	551	77	589.5
2b	67	−21	88	23	0.99	576	515	61	545.5
2c	108	40	68	74	0.96	581	492	89	536.5

[a] 0.1 M $TBABF_4$ in acetonitrile, scan rate: 0.1 mV s^{-1}; glassy carbon working electrode (diameter: 3 mm); Pt counter electrode and non-aqueous $Ag|Ag^+$ (0.01 M) reference electrode. [b] $\Delta E_p = E_{pa} - E_{pc}$. [c] $E_{1/2} = (E_{pa} + E_{pc})/2$.

Table 2 Cyclic voltammetry data of **1** and **2** in the presence of $Zn(ClO_4)_2$ and $Ni(ClO_4)_2$

		Zn^{2+}		Ni^{2+}	
Compounds	E_{pa} (Ox_1)/mV	E_{pa} (Ox_3)/mV	ΔE_{pa}/mV	E_{pa} (Ox_3)/mV	ΔE_{pa}/mV
1a	−63	385	448	500	563
1b	−23	489	512	503	526
1c	72	516	444	626	554
2a	33	950	917	33	0
2b	67	1016	949	67	0
2c	108	634	526	108	0

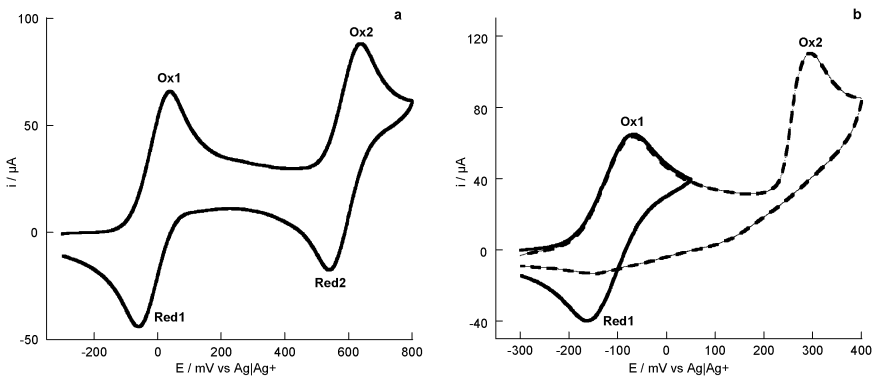


Fig. 2 Cyclic voltammograms of compounds (a) 4 mM **2a** and of (b) 6 mM **1a** (first wave: solid line) in 0.1 M $TBABF_4$ acetonitrile solution. Scan rate: 0.1 V s^{-1}; glassy carbon working electrode (diameter: 3 mm), Pt counter electrode and non-aqueous Ag|Ag+ (0.01 M) reference electrode.

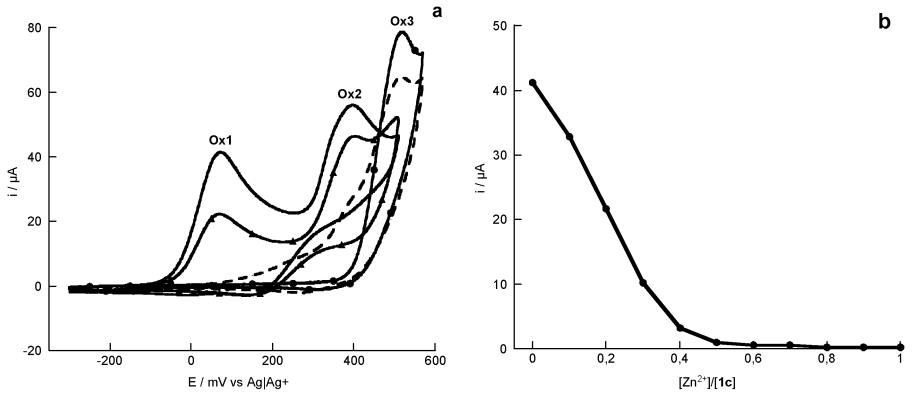


Fig. 3 (a) Cyclic voltammograms of **1c** (2 mM) showing the first oxidation wave in the absence of metal ions (—) and in the presence of 0.2 (–▲–), 0.5 (- - - -) and 1 equiv. (–●–) of $Zn(ClO_4)_2$. Scan rate: 0.1 V s^{-1}. (b) Variation of the peak current I_{pa} of the first oxidation wave of compound **1c** depending on the relative Zn^{2+} concentration.

conversion was complete when reaching 0.5 equivalents of zinc suggesting the formation of a 1 : 2 metal–ligand complex $[Zn(\mathbf{1c})_2]^{2+}$. The strong anodic potential shift of 444 mV (ΔE_{pa}) between the new (Ox_3) and the first (Ox_1) oxidation peak indicates a strong interaction between Zn^{2+} and the phenylenediamine nitrogen.[20,21] In fact, the decrease of the electronic density onto the redox center makes its oxidation more difficult.

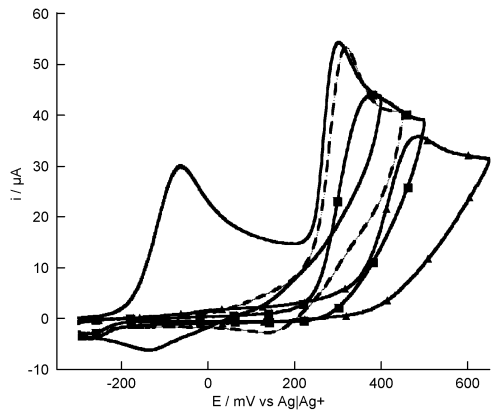


Fig. 4 Cyclic voltammograms of **1a** (2 mM) in the absence of metal ions (——) and in the presence of 0.5 eq. of Cd^{2+} (- - -), Zn^{2+} (–■–) and Ni^{2+} (–▲–) respectively. Scan rate: 0.1 V s^{-1}.

1a,b showed a similar behaviour with potential shifts of up to 512 mV indicating relatively strong metal complexes all with a M_1L_2 stoichiometry (see Table 2 and ESI†). These shifts depend strongly on the nature of the transition metal cation (Fig. 4) and increase in the following order: $Cd^{2+} < Zn^{2+} < Ni^{2+}$.

However, we observed a higher selectivity for zinc over nickel despite a smaller potential shift. Fig. 5 shows the cyclic voltammograms of the free ligand **1a** in the absence and in the presence of metal cations. The addition of nickel to a $[Zn(\mathbf{1a})_2]^{2+}$ solution did not affect the initial signal at all. Upon addition of Zn^{2+} (0.5 equiv.) to a $[Ni(\mathbf{1a})_2]^{2+}$ solution the oxidation peak shifted to the signal registered for $[Zn(\mathbf{1a})_2]^{2+}$ suggesting a complete and rapid metal exchange reaction towards the thermodynamically more stable complex. Zn^{2+} ions can be detected even in the presence of high nickel concentrations. These results are suggesting that the potential shift is certainly dominated by the sole electronic charge delocalisation from the redox center towards the metal, whereas the selectivity depends on the global interactions with 6 nitrogens forming the coordination sphere.

Owing to its high resolution and sensitivity differential pulse voltammetry (DPV) can distinguish two electroactive species

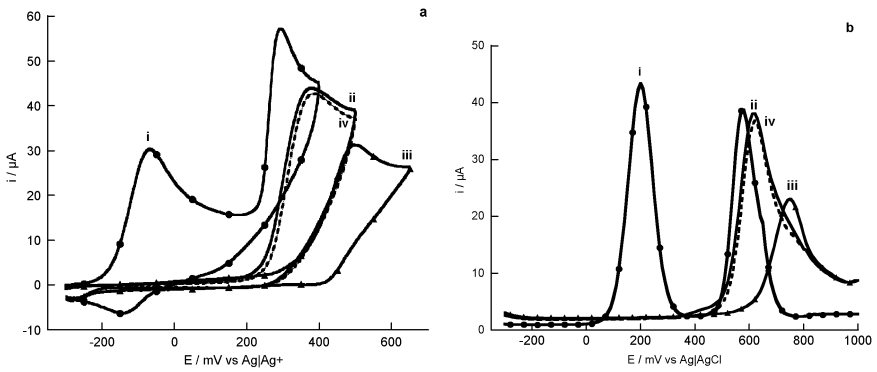


Fig. 5 Cyclic voltammograms (a) and differential pulse voltammograms (b) of (i) metal free **1a** (2 mM) (–●–), (ii) **1a** in the presence of 1 mM of Zn^{2+} (—), (iii) **1a** in the presence of 1 mM of Ni^{2+} (–▲–) and (iv) solution in the presence of 1 mM of Ni^{2+} and 1 mM of Zn^{2+} (– – –) in acetonitrile/0.1 M $TBABF_4$ solution. Scan rate: 0.1 V s^{-1}.

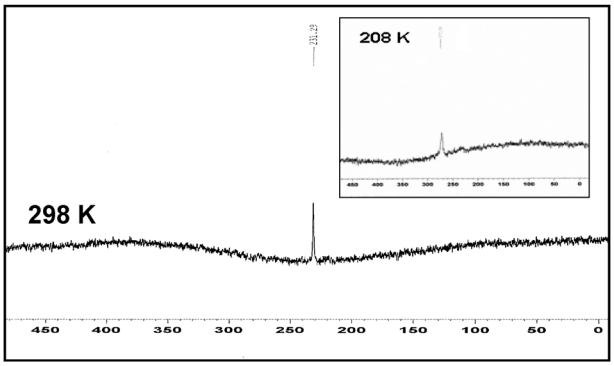


Fig. 6 ^{113}Cd spectra of the $[Cd(\mathbf{1a})_2]^{2+}$ complex at 298 K and at 208 K (inset) in CH_2Cl_2/CD_2Cl_2.

with peak potential separations of less than 50 mV.[22] The differential pulse voltammograms of compound **1a** (Fig. 5b) confirmed the CV experiments supporting the high selectivity for zinc cations. A series of similar competition experiments between Zn/Ni, Zn/Cd and Ni/Cd (see ESI†) clearly showed a selectivity for the studied metal cations in the following order: $Zn^{2+} > Cd^{2+} > Ni^{2+}$.

NMR study of the Cd complex

Among the three studied transition metals cadmium was the only one suitable to be used for NMR experiments because of the high natural abundance of the active ^{113}Cd isotope. Previous studies on ^{113}Cd NMR demonstrated that chemical shift and multiplicity of the signal strongly depend on the environment of the metal ion and consequently on the coordination number and geometry of the coordination sphere.[23] The ^{113}Cd NMR of the complex $[Cd(\mathbf{1a})_2]^{2+}$ was measured in dichloromethane at two different temperatures (Fig. 6). At 298 K and 208 K a singlet was observed at 231 ppm and at 272 ppm respectively. The absence of multiplets and the comparison of the obtained chemical shift to the literature values[24] are suggesting the presence of an octahedral complex. These results are further evidence for the formation of M_1L_2 complexes between the metal ions and ligand **1** in concordance with the electrochemical behavior.

Electrochemistry of metal complexes of compound 2

The thiophenyl derivatives **2** also form zinc complexes in solution. Upon the addition of Zn^{2+} to a solution of compound **2a** the oxidation peaks Ox_1 (33 mV) and Ox_2 (628 mV) disappeared in favour of a new peak Ox_3 at higher potential (950 mV) (Fig. 7, Table 2). The strikingly large peak potential difference of 917 mV ($\Delta E_{pa} = E_{pa}(Ox_3) - E_{pc}(Ox_1)$) indicated the formation of a relatively strong complex. On the reverse scan Red_4 (551 mV) was observed at the same potential as Red_2 which proves that a complete decomplexation took place when the phenylenediamine dication was formed due to electronic repulsion with the Zn^{2+} cation. The Red_5 (113 mV) peak appeared at a more anodic potential than Red_1 (−52 mV) meaning that when the radical-cations were reduced to their neutral species, fast recomplexation of the zinc occurred. This EC mechanism explains the facilitated reduction of the radical cation.[21,25] The zinc complexes of the other thiophenyl derivatives showed also high potential shifts of almost 950 mV for compound **2b** and 526 mV for **2c**.

In contrast to the pyridyl derivatives **1**, the oxidation of thiophenyl containing ligands **2** and their metal complexes to the corresponding dications are fully reversible and thus particularly interesting for Zn^{2+} sensing. The lower detection limit of zinc was observed at 10^{-5} M for a concentration of 1 mM of ligand **2a**. As detailed above the mechanism involves ejection and recomplexation of the zinc cation as we have recently shown for calcium crown ether complexes.[10] Unlike the pyridyl derivatives, compounds **2a–c** were found to be insensitive to Ni^{2+}, even at high nickel concentrations (Table 2 and Fig. 7b). Consequently these ligands selectively bind Zn^{2+} without being influenced by the presence of Ni^{2+}. The same observations were made for cadmium ions (see ESI†).

Conclusions

A novel family of electroactive tetraalkyl-*p*-phenylenediamine ligands has been prepared. Reductive amination of heterocyclic aldehydes afforded the desired target molecules in a clean one pot reaction. The oxidation potentials of the free ligands can easily be tuned within the range of 100 mV

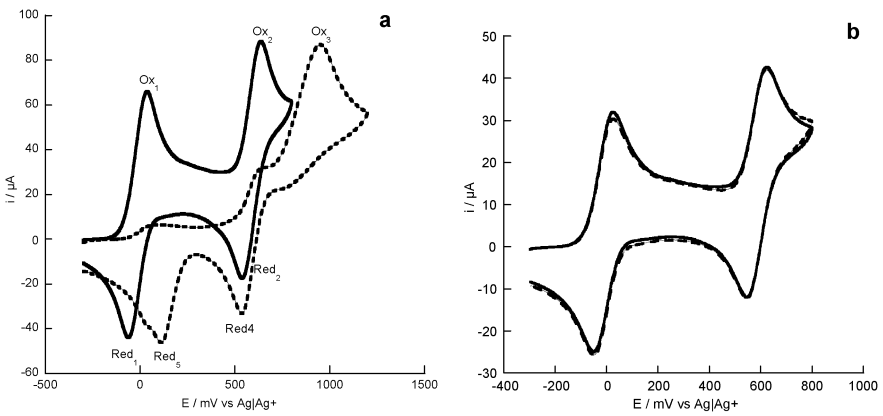


Fig. 7 Cyclic voltammograms of **2a** in the absence (solid line) and presence (dashed line) of 1 equiv. of metal cations in 0.1 M $TBABF_4$ acetonitrile with a scan rate of 0.1 V s^{-1}. Concentrations: (a) **2a** (4 mM) and $Zn(ClO_4)_2$ (4 mM); (b) **2a** (2 mM) and $Ni(ClO_4)_2$ (2 mM).

depending on the alkyl groups linked to the phenylenediamine nitrogens. M_1L_2 complexes were formed with zinc, nickel and cadmium ions. ^{113}Cd NMR revealed an octahedral coordination sphere of the metal. Extremely high oxidation potential shifts of up to 950 mV were observed upon complexation of the transition metal cations depending on the nature of the ligand. All ligands show a distinct chemoselectivity (for **1a–c**: Zn^{2+} > Cd^{2+} > Ni^{2+}; and for **2a–c**: $Zn^{2+} \gg Ni^{2+}$,Cd^{2+}). Contrary to the pyridyl derivatives **1** the oxidation of the thiophenyl containing ligands **2** and their metal complexes display a fully reversible oxidation to the corresponding dications. The mechanism involves ejection and recomplexation of the zinc cation. These compounds are thus predestined for the development of selective Zn^{2+} sensors as well as for potential applications as zinc release probes.

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