

*Dedicated to prof. dr. I. C. Popescu
on the occasion of his 70th anniversary*

ELECTROCHEMICAL BEHAVIOUR OF THE NEW HETEROCYCLIC PYRIDINIUM LIGANDS

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ABSTRACT. New heterocyclic pyridinium compounds as N,N' di-(p-bromophenacyl)-4,4'-bipyridinium dibromide (Lr) and N,N' di-(p-bromophenacyl)-1,2-bis(4-pyridinium)-ethane dibromide (Lm) were investigated applying cyclic voltammetry to evaluate the electrochemical behaviour. The stability of new heterocyclic pyridinium compounds in aq. media depends on pH and the dependence was correlated with spectrophotometric data. Ethylenic group from Lm induces changes on the stability and on the electrochemical performances of the ligand. The quasireversible process on electron transfer between functional groups depends on pH and also on the scan rates of the potential applied. The alkaline pH of a media is more favorable than acidic pH for the ligands stability and the electron transfer process on platinum electrode. The study of the redox potential on the two ligands indicates the role as mediator candidate in the reduction mechanism. We believe that the present work will stimulate the investigations of the chemical features of ligands and their role in biological and medicinal chemistry.

Keywords: *pyridinium compounds, electrochemical, aq. media, cyclic voltammetry*

INTRODUCTION

The concept of molecules with biologic properties is very interesting and opens an important field on research in molecular biology and

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pharmacology. Quaternary ammonium salts and their variously substituted derivatives are important biological agents and have found applications in different fields [1-3]. An increasing attention is given to the synthesis and characterization of the new pyridinium derivatives based on their wide range of interesting properties such as their ability to easily functionalise at the nitrogen heterocyclic atom in order to obtain useful compounds for biological and industrial applications [4-9]. Furthermore, their application in gene delivery, pharmaceuticals, polymerization stand on their ability to be employed as electron carriers, model system in photosynthesis, neuromuscular agents, enzyme inhibitors, antimicrobial agents, initiators of cationic polymerization and phase transfer agents was reported [5, 7-9]. Pyridinium derivatives were found to be ionic liquids whereas others compounds, named viologens (4,4'-bipyridinium salts) demonstrated electrochromic properties [10].

We previously reported the synthesis of a novel series of heterocyclic compounds with nitrogen using an efficient synthesis through N-alkylation of pyridinium substituted nucleus with reactive halides. The structures of the compounds were fully characterized using IR, ¹H-NMR, MS and elemental analysis. In addition, their thermal stability was determined using the thermogravimetric analysis [3, 11-12]. The elucidation of the electro-changes of the synthesized compounds is useful for the electrochemical investigation [13]. Compounds can be used as biological redox indicators, electrochemical sensors, electronic transporters and precursors for compounds such as indolizines, biologically active compounds which can serve as potential markers and fluorescent ligands for estrogen receptors [14-20]. This research also helps us to understand the mechanism of cycloaddition of these ligands with dipolarophiles for obtaining indolizine compounds [21]. The behaviour of the compounds bearing aryl substituents on the quaternarized nitrogen atoms has been examined showing that the spectroscopic and electrochemical properties are fine tuned by the nature of the nitrogen ring [22]. These quaternisation reactions will be done in aq. media. The redox potentials of the compounds are interesting for determining the donor - acceptor properties of the radicals [23]. Another aspect that we will study in the future would be understanding reactions of cycloaddition and substitutions, realized in aq. media [24-25]. Viologens compounds present a significant interest due to their changing properties and colour connected to the reaction medium [11-12]. In this work, the electrochemical behaviour of two pyridinium heterocyclic compounds has been recorded for the first time by cyclic voltammetry in aq. media.

RESULTS AND DISCUSSION

Stability of ligands

The synthesized compounds were N,N' di-(p-bromophenacyl)-4,4'-bipyridinium dibromide (named rigid Ligand-Lr) and N,N' di-(p-bromophenacyl)-1,2-bis(4-pyridinium)-ethane dibromide (named mobil Ligand-Lm) [3]. The stability of ligands derived from 4,4'-bipyridil (Lr) and 1,2-bis(4-pyridil)-ethane (Lm) respectively was performed by spectrophotometric analysis and open circuit potential (OCP) measurements. The aq. compounds (0.1 mM) were prepared and the analysis was conducted by adjusting the pH between the range of 3 and 11. Solutions shown variable colours depending on pH, beginning from light yellow to violet (N,N' di-(p-bromofenacyl)-4,4'-bipyridinium dibromide (Lr) and orange (N,N' di-(p-bromofenacyl)-1,2-bis(4-pyridinium)-ethane dibromide (Lm). A discoloration of the solution was observed when the ligand concentration was lower than 10^{-5} M.

The UV/VIS spectra of aq. solutions were analyzed at 264 nm (λ_{\max}) [3, 25] with the purpose to study the initial stability and after 24 hours (Figure 1). The highest absorbance are registered for Lr on pH 3 (weak yellow colour) and pH around 7 (weak violet colour) when protonated species are formed. Fresh aq. Lr solution presents most stable form in lower alkaline medium (pH around 8). On the other hand, Lm is more stable in lower acidic medium (pH around 6) and the dication form is unstable in alkaline media. This behaviour suggests the presence of the anionic species AH^- at the addition of base excess and transition from AH_2 to AH^- .

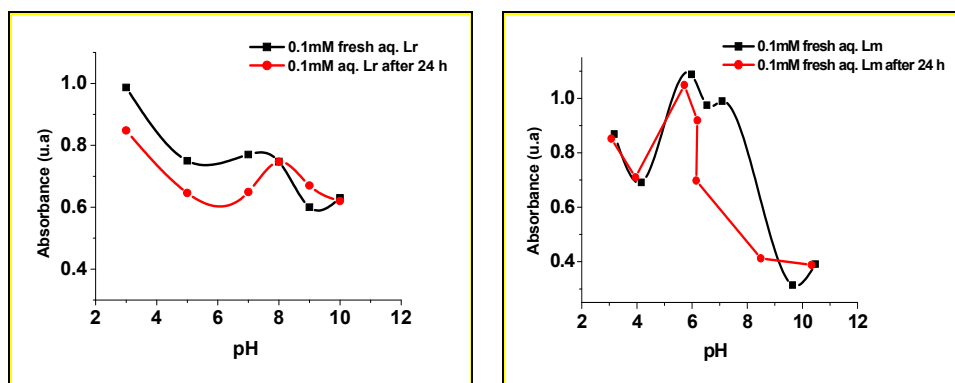


Figure 1. Overview of absorbance vs. pH of aq. Lr and Lm.

The ligands solutions kept at room temperature shown after 24 hours a slightly absorbance change; for Lr decreases with about 2 units. The electro-oxidation process is more active due to favourable dynamic

acid-basic equilibrium of the electrons transfer reaction from the dication to produce radical cation ($AH^{\cdot+}$), and then neutral specie. At the same time Lm indicates stability in acidic medium (till pH 6), but an evident decrease of absorbance values in neutral and alkaline medium. This behaviour could be explained by the ethylenic group from Lm, that is more favourable for some cycloarrangement additions in alkaline than in acidic media.

The absorbance from UV/VIS spectra are well correlated with OCP measurements. Bispyridinium compounds are organic oxidants and electrochemical techniques are useful to allow the characterization of the electro-oxidation behaviour of electroactive species, to establish the redox potential and to predict the reaction mechanism. The electrochemical investigations of each aq. ligand (0.1 mM) began with monitoring of OCP from fresh solutions (pH acid). Measurements at neutral and alkaline pH were also performed by adjusting pH using buffer solutions. OCP measurements were performed again after 24 hours, 120 hours and respectively 168 hours (7 days) in order to evaluate the electrochemical stability of the acidic - basic equilibrium and electro-oxidation process of compounds kept in closed bottles in the refrigerator ($4^{\circ}C$).

Although, initially the aq. ligands presented a difference about 0.5 pH units no significant differences between OCP values (± 2 mV) were found. OCP was around +72 mV vs. SCE for fresh aq. ligands. The open potential was also measured for the synthesized salts precursors (0.1 mM) by dissolving them in aq. media. The precursors 4,4-bipyridil (for Lr) presents a $E_{WE} = +69$ mV vs. SCE and 1,2 - bis (pyridil) ethane (for Lm) have a potential of $E_{WE} = +75$ mV vs. SCE which does not indicate essential modifications compared with the new ligands obtained.

After 24 hours a difference of about of 30 mV between the acid aq. ligands was measured for the OCP values; Lr indicates +45 mV vs. SCE and Lm indicate + 63 mV vs. SCE as a result of their structures. The fresh Lm solutions shown larger variations of OCP values for the entire pH range because it is more unstable due to the position of ethylenic group in base excess. Meanwhile Lr which does not have the ethylene group in its structure is more stable at the same conditions.

In time the OCP data for Lr showed lower variations. Aq. Lr indicates a more positive electro-oxidation potential for the fresh aqueous solutions of pH 6, similar with the solutions kept for 7 days having neutral or alkaline pH. Thus Lr is a more powerful oxidant with greater stability in time and its property is also kept at neutral and alkaline pH. A significant difference was observed for the fresh aq. Lm (pH 5.50) in time, a decrease with 10 mV. Anyway, at the neutral and alkaline pH OCP values for Lm indicated larger variations than those at acidic pH.

Thus, OCP values sustain the ligands structure shown in Scheme 1 and explain their stability as confirmed by the spectrophotometric measurements. The data results are helpful to provide an explanation for the proposed electro-oxidation mechanism of the ligands but are insufficient data for the reaction kinetics in aq. solutions.

Cyclic voltammograms measurements

The electrochemical measurements give information on the electrochemical state of the organic compounds on the working electrode in an active or passive state. CV provides information about the redox couples and this remains the most attractive gain of this technique [26]. CVs data are useful for the presence of the protonated/deprotonated structures and supply information about the kinetics of reactions. A series of CVs measurements were obtained in aq. media of the ligands at variable pH from acidic to alkaline range and different scan rates of the potential applied.

Effect of the pH

The pH has an important role for the organic compounds as a result of the proton concentration from aq. media. Changes in CVs are the result of the different ligand structures in aq. solutions with variable pH (Figure 2 and 3). The shapes can explain the influence of functional groups from the ligand molecule in aq. media correlated with their stability in time, depending on pH.

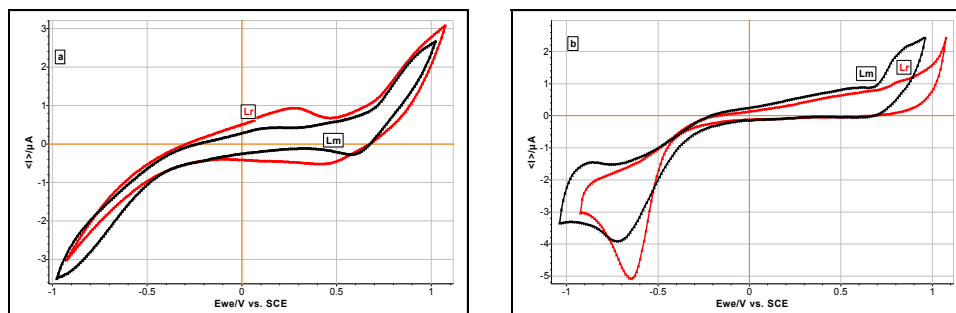


Figure 2. Cyclic voltammograms in aq. Lr and Lm from fresh solutions with initial pH (a) and at pH 9.0 (b); $E = \pm 1.0$ V vs. SCE, from a negative direction, scan rate 100 mVs^{-1} (a), scan rate 50 mVs^{-1} (b).

A similar behaviour appears in the redox process on platinum electrode in both compounds mainly for the anodic current peak. The corresponding peak of the initiation of the anodic oxidation indicates that at least a prototropic couple ($\text{AH}_2^+/ \text{AH}^\cdot$) of the organic compounds is present. The anodic current peak (i_a) around of + 300 mV vs. SCE is more evident for Lr and it appears diminished for Lm, with a difference of $0.5 \mu\text{A}$ and shifted to a less positive potential.

The voltammograms sustain the electrons transfer between functional groups of ligands and the prototropic couple, depending on the pH of the solution. If the pH solutions are changed the typical voltammograms will be observed. Figure 2b shows the voltammograms of aq. ligands at pH of 9.0 indicate the electron transfer by characteristic cathodic peak on Pt electrode which is similar in both salts under the same potential conditions and scan rates applied ($E = 1 \text{ V}$; 50 mVs^{-1}). Lm indicates a slight modification to more negative potential as a result of a favourable rearrangement of ethylenic group present in the structure. An anodic peak can be observed related with the oxidation of Lr to Lr product (radical anion), as an irreversible process due to its higher reactivity. The compounds described by CVs measurements could be more complex and show more than a single redox transaction. Water as proton acceptor suggests that in this case, the proton charge is delocalized over the primary shell of water molecules firmly formed around the pyridinium ligand. Lr indicates an evident reduction process in the alkaline domain (around pH 9), having quite a different behaviour, compared to the acidic and neutral domains (Figure 3a). The scan rate also remains an important condition in these electron transfers (Figure 3b). In alkaline pH, the current peak is shifted to more positive potential around +800 mV while in cathodic reduction is an intensive active process. At the same time Lm does not indicate an obvious electro-oxidation transformation (Figure 4).

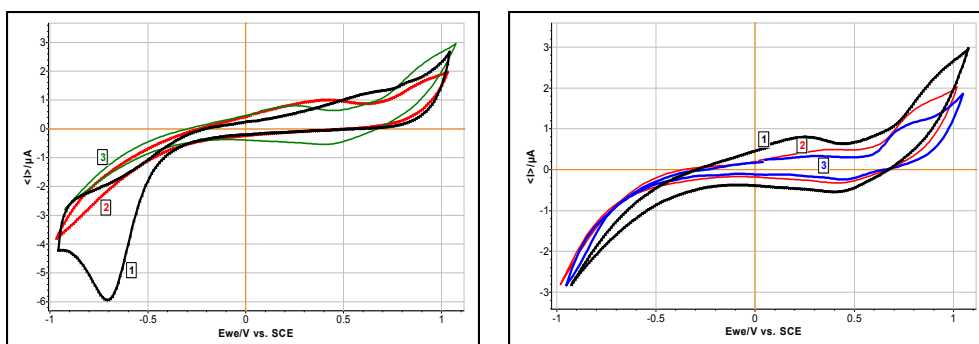


Figure 3 (a). Cyclic voltammograms measured in aq. Lr ranging pH: 9.0 (1); 7.0 (2) and 6.0 (3); $E = 1 \text{ V}$, scan rate 100 mVs^{-1} . **(b)** Cyclic voltammograms measured in aq. fresh Lr (pH 6.0) at different scan rate: 100 mVs^{-1} (1); 50 mVs^{-1} (2) and 20 mVs^{-1} (3), $E = 1 \text{ V}$.

It is evident that in the cathodic process on Pt electrode and at alkaline pH the deprotonic conjugate couple (from AH^- to AH) changes slower in comparison with acid and neutral pH. A blockage of the electron transfer by adsorption on Pt substrate of the reduced pyridinium ligands can suggest this behaviour.

Effect of the potential scan rate

There are registered CVs on platinum electrode for both aq. ligands (0.1 mM) at different scan rates (100 – 20 mVs⁻¹) for E = 1 V (Figures 3b and 4a). No significant shifts were observed in the redox potential when the scan rate was increased from 20 to 100 mVs⁻¹ in CVs of fresh aq. Lr at 6.00 pH (Figure 3b). Moreover, an increase of the anodic current was obtained when the scan rate was higher as an effect of faster prototropic conjugate in the form of AH₂/AH[·]-or AH⁻/AH₂ from ylides stage that immediately formed when a potential is applied [25].

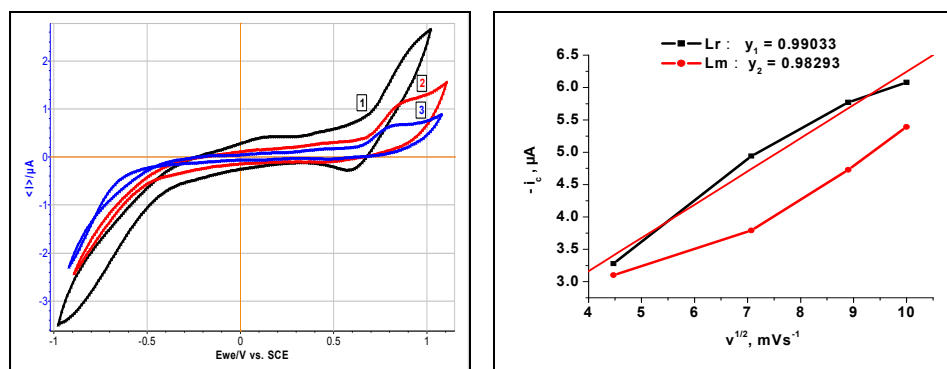


Figure 4 (a). Cyclic voltammograms in aq. fresh Lm (pH 5.50), at different scan rate: 100 mVs⁻¹ (1); 50 mVs⁻¹ (2) and 20 mVs⁻¹ (3), E = 1 V. **(b).** Plot of cathodic current vs. square root of scan rates.

The cathodic peak position obtained at 100 mVs⁻¹ corresponds to the redox changes from potential (E_{pc}) of + 350 mV for Lr to the potential of + 600 mV for Lm (Figure 4a). A comparative study of aq. alkaline pH shows the different behaviour between the pyridinium heterocyclic ligands. The electrochemical parameters are presented in Table 1.

Table 1. Electrochemical data vs. scan rate of the potential applied for aq. pyridinium ligands at pH 9.00.

scan rate (mV·s ⁻¹)	- E_{pc} (mV vs. SCE)		- i_c (μ A)		E_{pa} (mV vs. SCE)		i_a (μ A)	
	Lr	Lm	Lr	Lm	Lr	Lm	Lr	Lm
100	670	901	6.08	5.39	910	876	2.85	2.35
80	652	886	5.65	4.73	880	780	2.54	2.27
50	647	874	4.94	3.79	790	760	1.66	2.15
20	613	818	3.28	3.10	690	660	1.45	1.87

The reduction peak of ligands was significantly shifted towards a more negative potential, whereas a small shift in the oxidation peak was obtained at aq. Lr. Lm presents a different potential between the anodic peak and the cathodic peak that is considered an effect of quasireversible redox process of electrons transfer, due to presence of the ethylenic group. Both ligands show characteristic peaks as a result of electron transfer between the functional groups, more evident on cathodic range at alkaline solutions. The cathodic peak at very lower potentials cannot be clearly assigned to reduction (Figure 4b).

Assuming that the electron transfer rate is faster, the current i_a is measured while the potential decreases and it will be directly related to the diffusion rate of oxidized species on the Pt surface, by the flux governed by Fick law [26]. Thus, the oxido-reduction process involves a transfer of hydrogen proton and electron transfer of pyridinium ligands functioning as mediators in the aq. media. The peak is characterized by E_p , i_a and there is a shift peak while the pH increase.

The pyridinium ligands generate some current waves in cyclic voltammogram which are described as two typical one-electron transfer steps. The first step is reduction of AH_2 ($AH_2/AH^{\cdot-}$) and the second step is the role of electron carrier of pyridinium ligand ($AH^{\cdot-}/AH^-$). To explain this behaviour, a mechanism can be proposed when a catalytic reduction of the H^+ ion takes place via a neutral (alkaline) an intermediate of 1 H adsorbed on the Pt electrode in aq. media. The addition of proton donor produces changes, not only to the electroactive species, but also to the overall mechanism of reaction, making it simultaneous. Aq. alkaline ligands indicate an electron transfer irreversible, confirmed also by the cathodic peak on electrode, which is more evident on Lr than on Lm; it is a well correlation that ligands has different mechanism depending on aq. pH.

CONCLUSIONS

Pyridinium heterocycle ring of dibromide ligands having as difference an ethylenic group in their structure have been synthesized and the electrochemical properties have been explored. The stability of the acidic - basic activity of solutions depends on pH.

Spectrophotometric absorbance registered in different solutions, fresh and kept at constant temperature indicates that pH 6-7 is better for stability of aq. ligands. The open circuit potential is a useful tool to characterize the ligands stability in aqueous media on Pt electrode. CV has been applied to characterize the electron transfer of aq. pyridinium ligands and the possibility to become a useful mediator. Electrochemical measurements offer

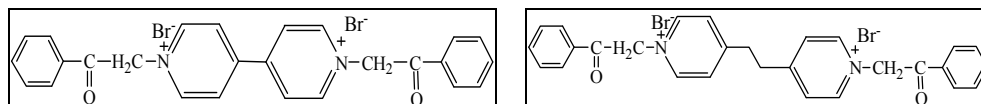
the possibility to study the redox potential and the influence of pH and scan rates applied.

A good correlation was found between the electro-oxidation potential and the stability in aq. media of the ligands at acidic and neutral pH. Moreover, at alkaline pH, the pyridinium ligands indicate a difference taking into account the acidic-basic and electrochemical properties which might result from the most favourable arrangement.

The presence of the ethylenic group diminishes this effect as a result of more cyclofavourable addition in alkaline pH. We believe that the present work will stimulate the investigations; CV can be used to characterize the reduction ability and electrochemical behaviour of the compounds as pyridinium ligands and their role in biological chemistry. This study helps us better understand the ligands mechanism in aq. media and our purpose is to use them in cycloaddition to obtain indolizines in catalytic systems and for the synthesis of new Ln complexes.

EXPERIMENTAL SECTION

The pyridinium salts were prepared starting from 4,4 bipyridil (for Lr) and 1,2 - bis (pyridil) ethane (for Lm) and phenacyl bromide by substitution reactions as it was mentioned in reference 3 Scheme 1. All chemical reagents were commercially available of analytical grade with maxim purity (Merck) and were used without further purification.



Scheme 1. Structure of bipyridinium salts Lr and Lm.

Both dibromide ligands solutions (0.1 mM) were prepared using deionized water ($1.6 \mu\text{S cm}^{-2}$ - measured with Milli-Q Millipore Losheim France). The Lr solution presents initially a pH of 6.0 and Lm a pH of 5.50. The pH adjustment of solutions for a neutral and alkaline media was made using different buffer solutions, according with [20, 27].

The electrochemical behaviour of ligands (0.1 mM) as deaerated aq. solutions, using KCl 0.1 M as support electrolyte was examined by cyclic voltammetry (CV) at 20°C (Biologic SP-150, with EC-Lab® Express v 9.46 software): three-electrode cell (20 mL capacity): WE -platinum (1.6 mm^2) with a platinum auxiliary electrode, and an saturated calomel reference electrode RE ($E_{\text{SCE}} = 0.241 \text{ V vs. SHE}$). The potential range of $E = 1 \text{ V vs. SCE}$ from a negative direction. Scan rates were: 100 mVs^{-1} , 80 mVs^{-1} , 50 mVs^{-1} and 20 mVs^{-1} .

The measurements were repeated for five times to mark the significant changes that might appear. Three types of solutions were analyzed: fresh-made solutions (lower acidic pH), neutral and alkaline solutions by controlling their pH using buffering solution. The measurements were registered and after 24 hours, 120 and respectively 168 hours (7 days) to relive the electrochemical behaviour of the ligands in time. The aq. solutions were kept in closed bottle refrigerator at 4°C.

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