Synthesis, Spectroscopic Characterization, pH Dependent Electrochemistry and Computational Studies of Piperazinic Compounds

Nazia Parveen, a Afzal Shah, a,b,z Shahan Zeb Khan, a Salah Ud-Din Khan, c Usman Ali Rana, c Farkhondeh Fathi, a Aamir Hassan Shah, a Muhammad Naem Ashiq, a Abdur Rauf, a Rumana Qureshi, a Zia-ur Rehman, a and Heinz-Bernhard Kraatz b

a Department of Chemistry, Quaid-i-Azam University, 45320 Islamabad, Pakistan
b Department of Physical and Environmental Sciences, University of Toronto Scarborough, Toronto M1C 1A4, Canada
c Sustainable Energy Technologies Center, College of Engineering, King Saud University, Riyadh 11421, Saudi Arabia

This work presents the synthesis, redox behavior and spectroscopic characterization of two novel compounds Sodium 4-(3-methoxyphenyl) piperazincarbodithioate and sodium 4-(4-nitrophenyl) piperazincarbodithioate. Pulse voltammetric techniques were utilized to determine the number of electrons involved in the oxidation and/or the reduction step and to ensure the nature of the redox processes. The pH dependent redox mechanistic pathways of the compounds were proposed on the basis of electrochemical and computational results. Different thermodynamic parameters like ΔG° and AH° revealed that electrode processes are non-spontaneous and endergonic in nature. Increase in ΔS° values at higher temperature indicated the randomness of the electrode reactions at higher temperatures. Limits of detection and quantification were determined by square wave voltammetry due to its high sensitivity and fast speed. Ionization energy, electron affinity, dipole moment and charge distribution on atoms were computationally determined. Acid-base dissociation constant (pKa) values of the compounds evaluated by voltammetry and electronic spectroscopy were found comparable.

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Molecular architectures bearing piperazine group have gained the utmost attention due to their vast applications in medical and industrial fields. Piperazines have special importance among nitrogen containing heterocyclic compounds due to their hydrogen bonding ability that make such compounds very specific for the generation of supramolecular structures.1 Piperazine can exhibit chair or boat conformation with chair form being more stable by 17.2 kJ/mol.2 Compounds containing piperazine ring are used as raw materials for the synthesis of epoxy resins, antioxidants, urethane catalysts, insecticides and accelerators for rubber.3 Such compounds possess versatile binding properties and act as potent and selective ligands for different biological activities. The attachment of piperazine to porphrin ring has been reported to enhance the anticancer activity and play the role of sensitizer in photodynamic therapy.4–8 Piperazine derivatives show good activities against chloroquine resistant strain of Plasmodium falciparum in vitro with low toxicity against murine monocyte/macrophage cells.9 Such compounds are also used as chelating agents due to their ability of forming complex with metal ions. Free radicals formation in many bioorganic redox processes may result in oxidation of lipids, proteins, or DNA and thus initiate cancer, cardiovascular, autoimmune, inflammatory and age-related degenerative brain diseases. So, piperazine as reducing agent is gaining mounting attention due to free radicals scavenging ability.10–12 Dithio ligands have been documented to play vital roles in numerous biological and non-biological processes.11–13 Dithiocarbamate (DTC) derivatives are used as organic intermediates, vulcanizing agents, rubber additives and fungicides.14 DTC a putative immunomodulator plays pivotal roles in agriculture and enhances immune response in AIDS treatment.15 Complexes of dithiocarbamates with different metal ions are preferred candidates for the development of anticancer agents.15 Recently diethyl dithiocarbamates have been found to act as chemoprotective agent against cisplatin toxicity. The Sn (IV) dithiocarbamate complexes are reported to have biocidal, antitumor and antimalarial activities.16 Some reports on their cytotoxicity against different types of tumor cells like colon, lung, melanoma, ovarian and breast cancer are available in literature.17–18

Piperazine and carbodithioates have broad range pharmacological properties. Therefore, tethering the two components in one structure can be more potent than either of the parent components. Based on these considerations, we have synthesized two novel piperazinic carbodithioates. In spite of numerous applications of this class of compounds, their pH dependent electrochemical and UV-Vis spectroscopic fate is an unexplored matter. So to bridge this gap in literature and to provide useful insights about their biological activities, the detailed electrochemical and spectroscopic investigations of the synthesized piperazinic carbodithioates were carried out in a wide pH range. Computational studies were also performed to further characterize the synthesized compounds and to support the experimental findings. The proposed redox mechanism is expected to unravel the hidden pathways by which piperazinic carbodithioates exert their biochemical actions. Moreover, the current investigations can give valuable information about the metabolic fate of piperazine derivatives.

Experimental

General methods.— Voltammetric measurements were carried out using Eco Chemie Autolab PGSTAT 12 running with GPES 4.9 (Utrecht, The Netherlands) software package. A three electrode system with an electrochemical cell of 10 mL capacity was used for voltammetric experiments. Glassy carbon electrode with geometric area of 0.071 cm² was used as working electrode. Glassy carbon electrode (GCE) was used because of its resistance to high temperature and chemical attack. Pt wire and Ag / AgCl (3 M KCl) were employed as counter and reference electrodes. Square wave voltammetry was performed at 100 mVs⁻¹ by setting a step potential of 50 mV and frequency of 20 Hz. Differential pulse voltammetry was carried out at 5 mVs⁻¹. Square wave and differential pulse voltammograms were baseline corrected by using the moving average with a step window of 3 mV included in GPES version 4.9 software. GCE electrode was cleaned by rubbing on nylon buffering pad using diamond powder of 1 μm particle size followed by thorough washing with distilled water. Electrochemical measurement cell was used to immerse in a water circulating bath (IRMECO I-2400 GmbH Germany) in order to hold a constant temperature. All electrochemical experiments were done in a high purity N₂ atmosphere. The pH measurements were

E-mail: afzals_qau@yahoo.com; afzal.shah@utoronto.ca

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carried out using INOLAB pH meter with Model no pH 720. Gaussian software 09 and Hartree Fock method with 621G basis set was used for computational studies. Absorption spectra were also obtained computationally and the results obtained on a Thermo Nicolet 6700 FT-IR spectrophotometer. 1H and 13C NMR were recorded on a Bruker-300 MHz FT-NMR spectrometer using DMSO as an internal reference.

Chemicals.— The compounds were synthesized by using sodium hydroxide, carbon disulfide, 1-(4-nitrophenyl) piperazine and 1-(3-methoxyphenyl) piperazine dihydrochloride. For voltammetric measurements stock solutions of the compounds were prepared in ethanol. Fresh working solutions were prepared in a 50:50 Britton-Robinson buffer-ethanol mixture. Britton-Robinson buffer (BRb) of pH 2–12 was used as supporting electrolytes.

Synthesis and structural confirmation of the compounds.— Sodium 4-(3-methoxyphenyl)piperazine-1-carbodithioate (SMPC).— Methanolic sodium hydroxide solution (0.3 M) was added to a methanolic solution of 1-(3-methoxyphenyl) piperazine dihydrochloride (7.5 mM) and stirred for half an hour. The precipitates formed were filtered and to the filtrate, methanolic solution of carbon disulfide (0.37 M) was added drop wise. The resulting mixture was stirred in ice bath for four hours and rotary evaporated to get a white colored product in 70% yield. The NMR and IR data of SMPC are given below:

1H NMR (300 MHz) δ - ppm: Piperazine: (3.07, 2H, t, J = 5.1 Hz); (4.44, 2H, t, J = 4.8 Hz); Methyl: (3.71, 3H, s); Phenyl: (6.54, 1H, s); (6.54, 1H, d, J = 1.8 Hz); (6.44, 1H, d, J = 2.1 Hz); (6.34, 1H, d, J = 2.1 Hz); 13CNMR (75.47 MHz) δ - ppm: 200 (C1), 49.1 (C2, C2′), 48.6 (C3, C3′), 152.8 (C4), 112.4 (C5-C5′), 130.1 (C8), 108.4 (C9), 55.31 (C10). IR (cm−1): 1417 (C-N), 1209 (C\(\equiv\)S), 955 (C-S).

Sodium 4-(4-nitrophenyl)piperazine-1-carbodithioate (SNPC).— Methanolic solution of sodium hydroxide (0.19 M) was added to a solution of 1-(4-nitrophenyl) piperazine (4.8 mM) and stirred for half an hour. Methanolic solution of carbon disulfide (0.24 M) was added drop wise to the reaction mixture and stirred in ice bath for four hours. The solution was then filtered and rotary evaporated to get orange colored product in 88% yield. The NMR and IR data given below indicate the formation of SNPC.

1H NMR (300 MHz) δ - ppm: Piperazine: (3.49, 2H, t, J = 5.1 Hz); (4.44, 2H, t, J = 5.4 Hz); Phenyl: (6.97, 1H, d, J = 9.6); (8.05, 1H, d, J = 9.3). 13CNMR (75.47 MHz) δ - ppm: 214.6 (C1), 48.5 (C2, C2′), 46.3 (C3, C3′), 154.9 (C4), 112.4 (C5-C5′), 126.2 (C6-C6′), 136.8 (C7). IR (cm-1): 1393 (C-N), 1201 (C = S), 923 (C-S). NMR (1H, 13C) spectra were also obtained computationally and the results were found in good agreement with the experimental findings. The NMR and FTIR spectra can be seen in section 1 of the supporting information.

Results and Discussion

Differential pulse voltammetry.— The electrochemical behavior of SMPC and SNPC was investigated over a wide pH range 2–12 using differential pulse voltammetry. From the DPVs shown in Fig. 1, it is evident that electron removal from SMPC is facile as compared to SNPC. This finding is in good agreement with computationally obtained EHOMO of SMPC (−0.277) and SNPC (−0.360). Less negative value of EHOMO is a manifestation of easy electron abstraction from the electropore of the analyte.10–22 The presence of electron withdrawing NO2 group causes SNPC to oxidize at comparatively higher potential.

In acidic media, SMPC registered one anodic peak that resolved into two and three peaks in basic and neutral conditions (Fig. 2A). This behavior is in accordance with the reported voltammetric behavior of piperazine containing compound, vardenafil.23 An examination of Fig. 2A reveals that peak 2a shifts cathodically by increasing the pH of the medium. From the plot of \(E_p\) vs. pH (Fig. 2B), acid-base dissociation constant, pka, of SMPC was evaluated as 8 which is lower than the literature reported value of a closely related compound, 1-phenylpiperazine having pKa of 8.924 due to the presence of electron withdrawing carbodithioate moiety in SMPC. An examination of Fig. 3 reveals that SMPC gets reduced in a single step. Reduction peak shows cathodic shift in the pH range 2–7.4 and anodic shift at pH higher than 7.4. In acidic media reduction occurs by the gain of electron and protons. Reduction becomes facile by lowering pH owing to more concentration of H+.

The number of electrons (n) involved during redox processes was determined from the width at half peak heights of differential pulse voltammetric signals using equation.25

\[
W_{1/2} = \frac{3.52 \times RT}{aF}
\]  

Figure 2. (A) DPVs (oxidation region) of 1 mM solution of (a) SNPC and (b) SMPC obtained at 5 mV/s in a medium of pH 10.

Figure 1. Comparative differential pulse voltammograms of 1 mM solution of (a) SNPC and (b) SMPC obtained at 5 mV/s in a medium of pH 10.

\[
\text{Slope} = -0.054 \text{ V/pH}
\]  

\[
R^2 = 0.99
\]
Here α represents charge transfer coefficient. The value of α was determined from $E_p-E_{p2} = 47.7$ mV/αn. While the numbers of protons accompanying electron transfer during oxidation and reduction processes were determined from the slope of $E_p$ - pH plots using equation:

$$dE_p/d\text{pH} = 0.0599/\alpha_n$$  \[2\]

P denotes number of protons. The voltammetric response of SNPC was also investigated in various pH media by using differential pulse voltammetry. In acidic conditions, SNPC registered one anodic peak, while in neutral and alkaline conditions; its oxidation was evidenced by two anodic peaks (Fig. 4A). Peak 1a did not appear in highly acidic media because of the possible high concentration of H⁺ around the oxidizable moiety that may prevent its oxidation. The cathodic shift of peak 2a with rise in pH suggests comparatively facile oxidation of SNPC in basic conditions than acidic and neutral media. However, in basic media, redox process becomes pH independent because of protons scarcity. The pKa of SNPC is 7 as evident from Fig. 4B. The pka of SNPC is less than SMPC due to the presence of electron withdrawing nitro group at the aromatic ring. Figure 5 shows the effect of pH on the reduction behavior of SNPC. The reduction peak shifts cathodically till pH 9 indicating difficult reduction owing to lesser concentration of H⁺ in media of higher pH. But in highly basic conditions, without a pronounced shift in peak potential indicates the transfer of electron to occur without the involvement of proton. This behavior is in accordance with the pH dependent redox behavior of a structurally related compound to SNPC.33

Cyclic voltammetry (CV).— The effect of scan rate was monitored by cyclic voltammetry in order to evaluate the diffusion coefficient. The irreversibility of the oxidation processes of SMPC and SNPC was ensured from the shift in peak potential with changing scan rate.28 The diffusion coefficient for irreversible process was calculated by using Randles-Sevcik equation.29 The $D$ of SMPC and SNPC with values of $5.0 \times 10^{-6}$ and $1.14 \times 10^{-5}$ cm² s⁻¹ were evaluated from the measured slopes ($3.91 \times 10^{-5}$ and $1.8 \times 10^{-5}$ A(V/s)¹/²) of the plots of $I_p$ vs. $v^{1/2}$. The plots of logarithm of peak current of SMPC and SNPC versus logarithm of scan rate (V/s) gave straight lines with slopes of 0.45 and 0.65. The slope value of 0.45 indicates the redox process of SNPC to be diffusion controlled30,31 whereas, a value of 0.65 demonstrates the electrode process of SNPC to be limited by partial diffusion and partial adsorption.30

The influence of concentration on the peak current intensity was examined to determine rate constant. Peak current intensity was found to increase linearly with concentration as expected. Reinmuth expression was used for the determination of rate constant.32 From the slope values of the plots of $I_p$ vs. concentration, $k_c$ of SMPC and SNPC with values of $8 \times 10^{-4}$ and $5.5 \times 10^{-5}$ cm s⁻¹ evaluated. These heterogeneous electron transfer rate constant values are well within the range of irreversible electrode processes.33 Rate constant of SMPC is greater as compared to SNPC which may be due to the electron donating group of SMPC that could facilitate its electron transfer. This result is complemented by DPV results which show facile oxidation of SMPC as compared to SNPC.

Square wave voltammetry.— In order to check the reversible/irreversible or quasi-reversible nature of the electrode processes of the compounds SWV was performed. The SWV results were in good agreement with CV findings. The irreversibility of oxidation and reduction processes of SMPC was evidenced by the same direction of forward and backward components of the total current in square wave voltammetry.34,35 Whereas, anodic and cathodic peaks of SNPC showed irreversible and quasi-reversible electrode processes respectively.

The applicability of the sensitive square wave voltammetric technique for the quantification of SNPC and SMPC was examined by the evaluation of limit of detection (LOD) and limit of quantification (LOQ). The detection limits were determined by investigating the effect of concentration on peak intensity. The values of LOD and LOQ evaluated as 72 μM and 0.2 mM for SMPC (Fig. 6A), and 73 μM and 0.24 mM (Fig. 6B) for SNPC using the method reported in literature.36 The 2nd oxidation signal of SNPC showed saturation at 0.7 mM due to the possible adsorption of the oxidation product formed around 0.3 V. Therefore, the peak at 0.3 V was used for analytical determination.

Determination of thermodynamic parameters by square wave voltammetry.— Thermodynamic parameters such as Gibbs free energy ($\Delta G^\circ$), enthalpy ($\Delta H^\circ$) and entropy changes ($\Delta S^\circ$) were determined by studying the effect of temperature on square wave voltammograms (Figs. 7A and 7B of SMPC and SNPC. Electron transfer rate...
Figure 5. DPVs demonstrating reduction behavior of 1 mM solution of SNPC recorded in pH 2–12 at a scan rate of 5 mVs\(^{-1}\).

Figure 6. (A) Square wave voltammograms of different concentrations of SMPC obtained at a scan rate 100 mV/s in pH 4 using Britton-Robinson buffer (BRb), inset shows \(I_p\) as a function of concentration. (B) Square wave voltammograms of different concentrations of SNPC obtained at a scan rate 100 mV/s in pH 11, inset is a plot of \(I_p\) vs concentration.

Figure 7. (A) Influence of temperature on the redox behavior of 1mM solution of SMPC determined by SWV at a scan rate of 100 mV s\(^{-1}\). Inset is a plot of log \(k_{sh}\) vs.1/T. (B) Square wave voltammograms of 1mM solution of SNPC recorded under different temperature conditions at a scan rate of 100 mV s\(^{-1}\). Inset is a plot of log \(k_{sh}\) vs.1/T.
constant was determined at different temperatures for the calculation of $\Delta G^\circ$ was then calculated.\textsuperscript{27} Kinetic and thermodynamic parameters of SMPC and SNPC are listed in Tables I and II. Positive value of $\Delta G^\circ$ indicates non-spontaneous nature of the redox processes. The decrease in $\Delta G^\circ$ value with increase in temperature indicates that the electrode process becomes easier and degree of irreversibility gets decreased at higher temperature.\textsuperscript{37} Positive value of $\Delta H^\circ$ shows endergonic nature of the electrode process. Negative value of entropy for both compounds explains the fact that reaction at electrode is in more ordered form than in solution. Less negative value of $\Delta S^\circ$ at higher temperature indicates the electrode reaction to become less ordered at higher temperatures. The values of $\Delta H^\circ$ and $\Delta S^\circ$ at different temperatures signify the process to be both enthalpy and entropy driven.

The peak currents intensify considerably with rise in temperature because at higher temperature solvation sphere around the electrode and electroactive moiety of the analyte gets thinner and thus, expected to result in greater sensitivity of the electrode and closer approach of the analyte to the electrode surface. Cathodic shift of peak potential with escalation of temperature indicates comparatively easier redox process at higher temperature. This behavior can be attributed to the decrease in viscosity (thus more diffusion) at higher temperature.

Computational study.— DFT calculations were carried out using 3–21G basis set for optimization and energy calculations. Computational calculations of sodium 4-(3-methoxyphenyl)piperazine-1-carbodithioate and sodium 4-(4-nitrophenyl)piperazine-1-carbodithioate were carried out to obtain charge distribution on atoms and energies of HOMO and LUMO orbitals. These calculations enabled to determine the charge distribution of the molecular structures and predict the possible oxidizable or reducible electrophore of the compounds. Charge distribution of SMPC and SNPC has been shown in Figs. 8A and 8B. Nitrogen that have methoxy phenyl group has more –ve charge, thus, susceptible to oxidation. An examination of Table III reveals that ionization energy of SNPC is greater than SMPC thus indicating its easier oxidation than SNPC. This is complemented with the experimental results because SMPC oxidizes at 0.21 V, while the oxidation potential of SNPC is 0.40 V. Electron affinity of SMPC is negative while that of SNPC is positive. Negative value of electron affinity is a manifestation of difficult reduction. So SNPC should reduce easily as compared to SMPC. This finding is in accordance with the experimental results because reduction potentials of SNPC and SMPC are –0.68 V and –0.84 V respectively. Dipole moment values show SNPC to have more polarity than SMPC.

SNPC has higher electronegativity because of the presence of electron withdrawing group.

Redox mechanism of sodium 4-(3-methoxyphenyl)piperazine-1-carbodithioate.— Voltammetric and computational results helped in suggesting the redox mechanism of SMPC and SNPC. Number of electrons and protons involved in the electrode processes were determined from potential at half peak width and slope of $E_p$ versus pH plot.\textsuperscript{30} Cyclic, square wave and differential pulse voltammetric results revealed that peak 1a is irreversible and involves the transfer of one electron as determined from half peak width values. Peak 1a appeared in neutral and alkaline conditions and did not change its position with rise in pH. It has been reported that when the aliphatic nitrogens of the piperazine rings are protonated, oxidation occurs on the proximal nitrogen.\textsuperscript{27} Computational studies showed that nitrogen of piperazine ring attached to methoxy phenyl group is more negatively charged and thus prone to facile oxidation as compared to the other nitrogen atom. Peak 1a demonstrated SNPC to oxidize by the loss of one electron and one proton to result in a cationic radical followed by the formation of a hydroxylated product as presented in Scheme 1.\textsuperscript{35}

In acidic media the reduction peak was found to involve the transfer of one electron and one proton per two molecules of SMPC. Computational results revealed the bond between nitrogen and benzene ring to have greater bond length so this weaker bond is suggested to be cleaved by the application of voltage thus resulting in the formation

| Temperature K | $E_a$ kJ/mol | $\Delta G^\circ$ kJ/mol | $\Delta H^\circ$ kJ/mol | $\Delta S^\circ$ J mol$^{-1}$ K$^{-1}$ |
|---------------|--------------|-------------------------|------------------------|---------------------------------|
| 278           | 8.58         | 49.9                    | 6.27                   | –157                            |
| 288           | 49.9         | 6.18                    | –150                   |
| 298           |              |                         |                        |
| 318           | 48.5         | 5.85                    | –135                   |
| 328           |              |                         |                        |

**Figure 8.** Mulliken charges on (A) SMPC and (B) SNPC.

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**Table I. Kinetic and thermodynamic parameters for oxidation process of SMPC.**

| Temperature K | $E_a$ kJ/mol | $\Delta G^\circ$ kJ/mol | $\Delta H^\circ$ kJ/mol | $\Delta S^\circ$ J mol$^{-1}$ K$^{-1}$ |
|---------------|--------------|-------------------------|------------------------|---------------------------------|
| 278           | 11.2         | 48.7                    | 8.90                   | –143                            |
| 288           | 48.4         | 8.82                    | –137                   |
| 298           | 48.3         | 8.78                    | –133                   |
| 308           | 47.4         | 8.69                    | –125                   |
| 318           | 46.5         | 8.61                    | –119                   |

**Table II. Kinetic and thermodynamic parameters for oxidation process of SNPC.**

**Table III. Different parameters obtained by HartreeFock method.**

| Parameters      | SMPC         | SNPC         |
|-----------------|--------------|--------------|
| Ionization energy | 174 (kcal/mol) | 193 (kcal/mol) |
| Electron affinity | –2.59 (kcal/mol) | 1.50 (kcal/mol) |
| Dipole moment   | 3.13D        | 11.5D        |
| Electronegativity | 0.148        | 0.154        |
of methoxy phenyl radical followed by either dimerization or attack on the 1st oxidation product of SMPC as shown in Scheme 2. Square wave, differential pulse voltammetry and computational results revealed that the oxidation mechanism of SNPC (Scheme 3) is quite similar to SMPC. The electrochemical reduction of nitro group of SNPC to aniline takes place according to the mechanism reported in literature.38,39

**UV-Vis spectroscopy.**—The UV-Vis spectra of SNPC shown in Fig. 9A indicate two electronic absorption bands in acidic media and three bands in basic conditions. The peak at 226 nm corresponding to $\pi \rightarrow \pi^*$ transition of benzene moiety appeared in acidic, neutral and basic media. The second signal at about 287 nm came to sight only in basic conditions. This peak is attributed to $n \rightarrow \pi^*$ transition of C=O group which can be due to the possible basic attack on C=S as shown
in Scheme 4. The signal at 378 nm is attributed to $n \rightarrow \pi^*$ transition of nitrogen of piperazine as the presence of nitro group is expected to make the benzene ring electron deficient hence, encourage the nitrogen of piperazine ring to donate more effectively. In acidic media, lone pair electrons bearing atoms are possible to be protonated so, larger energy will be required for their transition and that’s why signal appears at lower wavelength. This band shifts to higher wavelength in alkaline conditions due to less protonation possibility. The lack of this signal in the spectrum of SMPC is because of the presence of electron donating group attached to benzene ring that makes this ($n \rightarrow \pi^*$) transition less effective. The acid base dissociation constant, $pK_a$, of SNPC was determined from the plot of absorbance vs. pH as shown in Fig. 9B. The $pK_a$ with a value of 6.5 is close to the voltammetrically determined $pK_a = 7$.

SMPC registered one peak at 226 nm in acidic media and three signals at 226, 260 and 280 nm in alkaline conditions. The signal at 226 nm corresponds to $\pi \rightarrow \pi^*$ transition of benzene moiety. The other two bands at 260 and 280 nm appearing in basic media are because of $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transition of carbonyl group as shown in Scheme 4. Literature study shows $n \rightarrow \pi^*$ transition of $C=O$ to occur at 280 nm. The electronic spectrum of dipotassiumbis(2,2-dithiopiperazinato-2,2-diaminodiethylamine) exhibits two bands centered at 266 and 282 nm corresponding to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions of the thioureide group. The $pK_a = 7.75$ of SMPC was determined from the plot of absorbance vs. pH using UV-Vis spectroscopic data. The $pK_a$ obtained from electronic absorption spectroscopy is in good agreement with voltammetrically determined $pK_a$ of 7.98.

Figure 9. (A) UV spectra of 0.08 mM solution of SNPC rationalizing the consequence of pH on electronic transition (B) Absorbance vs. pH plot of SNPC.
Conclusions

Sodium 4-(3-methoxyphenyl)piperazine-1-carbodithioate and sodium 4-(4-nitrophenyl)piperazine-1-carbodithioate were synthesized and characterized by 1H-NMR, 13C-NMR, FTIR, voltammetry and UV–Vis spectroscopy. Their pH dependent redox mechanisms were proposed on the basis of results obtained from voltammetric results and computational calculations. $E_{\text{p}}$-pH plots demonstrated the participation of protons during electron transfer reactions. The greater electron transfer rate constant of SMPC than SNPC due to the participation of protons during electron transfer reactions. The results and computational calculations were proposed on the basis of results obtained from voltammetric and UV–Vis spectroscopy. Their pH dependent redox mechanisms in good agreement.

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References

1. N. Jamai, M. Rzaigui, and S. A. Toumi, Acta Crystallogr. Sect. E., 70, m167 (2014).
2. A. Tarassoli and N. Jarrah, J. Iran. Chem. Soc., 10, 1013 (2013).
3. I. Nikolova and N. Danchev, Biotechnol. Biotechnol. Eq., 22, 652 (2008).
4. C. C. Guo, H.-P. Li, and X. B. Zhang, Bioorg. Med. Chem., 11, 1745 (2003).
5. S. Datta, R. Allman, C. Loh, M. Mason, and P. Matthews, Br. J. Cancer, 76, 312 (1997).
6. M. Yarim, M. Koskal, I. Durmaz, and Rengul Atalay, Int. J. Mol. Sci., 13, 8071 (2012).
7. C. Lottner, K. C. Bart, G. Bernhardt, and H. Brunner, J. Med. Chem., 45, 2064 (2002).
8. V. Sol, J. Blais, V. Carre, R. Granet, M. Guillotou, M. Spiro, and P. Krausz, J. Org. Chem., 64, 4431 (1999).
9. W. T. Vellasco Junior, G. P. Guedes, M. G. Vaz, M. V. de Souza, A. U. Kretti, L. G. Kretti, A. C. C. Aguiar, C. R. Gomes, and W. Cunico, Eur. J. Med. Chem., 46, 5688 (2011).
10. M. Prashanth, H. D. Revanasiddappa, V. Lokanatha Rai, and B. Veeresh, Bioorg. Med. Chem. Lett., 22, 7065 (2012).
11. M. T. H. Tarafder, N. Saravanam, and K. A. Crouse, Transition Met. Chem., 26, 613 (2001).
12. P. K. Bharadwaj and W. K. Musker, Inorg. Chem., 26, 1453 (1987).
13. H. K. Joshi, J. J. A. Cooney, F. E. Inscore, N. E. Gruhn, D. L. Lichtenberger, and J. H. Enemark, PNAS, 100, 5719 (2003).
14. D. Chatupruek and S. Ray, Tetrahedron Lett., 47, 1307 (2006).
15. M. Marta Nagy, L. Ronconi, C. Nardon, and D. Fregona, Mini Rev. Med. Chem., 12, 1216 (2012).
16. M. Eddaouati, D. B. Moler, H. Li, B. Chen, T. M. Reineke, M. O’keeffe, and O. M. Yaghi, Acc. Chem. Res., 34, 319 (2001).
17. R. Mital, N. Jain, and T. Srivastava, Inorg. Chem. Acta., 166, 135 (1989).
18. S. Khan, S. A. Nami, and K. Siddiqui, J. Organomet. Chem., 693, 1049 (2008).
19. M. Marindin, S. Minchev, N. Stoyanova, G. Ivanova, M. Spassova, and V. Enchev, Croat. Chem. Acta, 78, 9 (2005).
20. A. Rahman, R. Qureshi, M. Kiran, and F. L. Ansari, Turk. J. Chem., 31, 25 (2009).
21. B. W. D’Andrade, S. Datta, S. A. Toumi, P. Djurovich, E. Polikarpov, and M. E. Thompson, Org. Electro., 6, 11 (2005).
22. E. Nosheen, A. Shah, A. Badshah, H. Hussain, R. Qureshi, S. Ali, M. Siddiqui, and A. M. Khan, Electrochim. Acta., 90, 108 (2012).
23. B. Uslu and S. A. Ozkan, Anal. Lett., 40, 817 (2007).
24. J-F. H. Ploemen, J. Kelder, T. Harmans, H. van de Sandt, J. A. van Burgsteden, P. I. Salemink, and E. van Esch, Exp. Toxicol. Pathol., 55, 347 (2004).
25. A. H. Shah, A. Shah, U. A. Rana, S. U.-D. Khan, H. Hussain, S. B. Khan, R. Qureshi, and A. Badshah, Electroanal., 26, 2299 (2014).
26. A. H. Shah, A. Shah, S. U.-D. Khan, U. A. Rana, H. Hussain, S. B. Khan, R. Qureshi, A. Badshah, and A. Waseem, Electrochim. Acta., 147, 121 (2014).
27. S. A. Ozkan, B. Dogan, and B. Uslu, Microchem. Acta., 153, 27 (2006).
28. A. Khan, R. Ahmed, and M. L. Mirza, Port. Electrochim. Acta., 27, 429 (2009).
29. V. C. Diculescu, T. A. Enache, P. J. Oliveira, and A. M. Oliveira-Brett, Electroanal., 21, 1027 (2009).
30. A. Bard and L. Faulkner, Electrochemical Methods—Fundamentals and Applications, 1980, 218, in, Wiley, New York.
31. J. Wang, Anal. Electrochem., John Wiley & Sons (2006).
32. W. Reimnuth, Anal. Chem., 33, 1793 (1961).
33. J. G. Velasco, Electroanal., 9, 880 (1997).
34. M. Zelic, Croat. Chem. Acta., 79, 49 (2006).
35. A. Shah, V. C. Diculescu, R. Qureshi, and A. M. Oliveira-Brett, Bioelectrochem., 77, 145 (2010).
36. O. M. Pops and V. C. Diculescu, Electrochim. Acta., 112, 486 (2013).
37. S. A. Yasin, Port. Electrochim. Acta., 24, 23 (2006).
38. K. Stutz, C. Scorticini, and C. Repucci, J. Org. Chem., 54, 3740 (1989).
39. V. Lebrun, L. Mikhailchenko, M. V. Leonova, and V. Gulyay, Electrochim. Soc., 60 (2000).