

Computational and electrochemical studies on the redox reaction of 2-(2,3-dihydroxy phenyl)-1,3-dithiane in aqueous solution

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ABSTRACT

Electrode potential of 2-(2,3-dihydroxy phenyl)-1,3-dithiane (DPD) was investigated by means of cyclic voltammetry (CV) at various potential scan rates. The calculated value was compared with the experimental value obtained by cyclic voltammetry (CV). All experiments were done in aqueous phosphate buffer solutions at different pHs. The experimental redox potential of DPD was obtained to be 0.753 V versus SHE (Standard Hydrogen Electrode). DFT-B3LYP calculations using 6-311++G** basis set were performed to calculate the absolute redox potential of DPD. The calculated value of the redox potential relative to SHE is 0.766 V which is in good agreement with the experimental value (0.753).

Keywords: Redox reaction, density functional theory, computational chemistry, cyclic Voltammetry.

1. INTRODUCTION

Recently, Electrochemical methods are widely used for the study of electroactive compounds in pharmaceutical forms and physiological fluids due to their simple, rapid, and economical properties [1]. Catechol derivatives can be easily oxidized to the corresponding reactive o-benzoquinones mainly due to their low oxidation potentials. Catechol derivatives play an important role in mammalian metabolism, and many compounds of this type are known to be secondary metabolites of higher plants. Also, many drugs such as doxorubicin, daunorubicin and mitomycin C which are used in cancer chemotherapy contain quinones [2].

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Computational chemistry has evolved to the point that it is sometimes competitive to experiment to obtain precise values for certain molecular properties. Density functional theory (DFT) [3] has played a predominant role in this evolution in the last decade [4, 5]. The ability to calculate redox potentials accurately using the theoretical methods would be advantageous in a number of different areas, particularly where the experimental measurements are difficult, due to the complex chemical equilibrium and the reactions of the involved chemical species. Recently, *ab initio* methods have been employed for the calculation of redox potential of different species in aqueous solutions [6]. In this paper, the redox potential of DPD was calculated with the employment of the density functional theory (DFT) molecular orbital calculations at the B3LYP/6-311++G** level of theory. The Polarizable Continuum Model (PCM) [7] was used to calculate the free energy solvation of species involved in the reaction. The details of calculation will be explained in the theoretical section of the present paper.

2. EXPERIMENTAL

2.1. Apparatus and chemicals

Electrochemical experiments were carried out using a computerized potentiostat/galvanostat (Autolab model 302N, Eco Chemie B.V.A). The experimental conditions were controlled with General Purpose Electrochemical System (GPES) software. A conventional three electrode cell was used at $25 \pm 1^\circ\text{C}$. An Ag / AgCl / KCl 3.0 M electrode, a platinum wire, and a glassy carbon (GC) electrode (Metrohm, 2 mm diameter) were used as reference, auxiliary and working electrodes, respectively. A Metrohm 691 pH / ion meter was used for pH measurements. All solutions were freshly prepared with twice distilled water. The buffer solutions were prepared from orthophosphoric acid and its salts in the pH range 2.0-11.0. The GCE surface was polished mechanically with 0.05 μm alumina powders, using a polishing cloth until the electrode surfaces had a mirror-finish and then rinsed thoroughly with double distilled water, successively.

2.2. Synthesis of 2-(2,3-dihydroxy phenyl)-1,3-dithiane

A mixture of 2,3-dihydroxy benzaldehyde (1 mmol), 1,3-propanedithiol (1.2 mmol) and 37% $\text{BF}_3 \cdot \text{SiO}_2$ (0.3 g) was ground in a pestle at ambient temperature. The progress of reaction was monitored by thin layer chromatography. After the completion of the reaction, the products were dissolved in ethanol, filtered, and the solvent was evaporated. The

obtained solid was recrystallized in chloroform (yield= 92%). Characteristics of product as described previously [8].

3. RESULTS AND DISCUSSION

3. 1. Electrochemical properties of DPD at GCE

The DPD is soluble in aqueous media; therefore we used GCE and studied its electrochemical properties in a buffer aqueous solution (pH 6.0) by cyclic voltammetry. Cyclic voltammograms of DPD in the buffer solution (pH 6.0) exhibited an anodic and corresponding cathodic peak. Experimental results show (Figure 1) well-defined and reproducible anodic and cathodic peaks related to the DPD redox system (with $E_{pa}= 0.293$ V, $E_{pc}= 0.227$ V vs. Ag/ AgCl (sat.), KCl (3 M). and $\Delta E = 0.066$ V). As can be seen, the peak separation potential, $\Delta E_p (=E_{pa}-E_{pc})$, is greater than the $(59/n)$ mV expected for a reversible system. This result suggests that the redox couple in DPD shows a quasireversible behavior in an aqueous medium at the GCE.

In addition, the effect of the scan rate of the potential on the electrochemical properties of the redox couple in DPD was studied in an aqueous solution by cyclic voltammetry. The plots of the anodic and cathodic peak currents were linearly dependent on square root of the sweep rate ($v^{1/2}$) at all scan rates ($v= 10-400$ mV s⁻¹) (Figure 1A). This behavior indicates that the nature of redox process is diffusion controlled. Also, as shown in Figure 1B, the peak current ratio (I_{pc}/I_{pa}), increases gradually with the increase of the potential scan rate until it reaches a fixed value.

One of the methods to calculate the heterogeneous electron transfer rate constant was given by Nicholson [9]. This method is based on cyclic voltammetry procedure and potential difference between peaks (ΔE_p). They presented a working curve that $n\Delta E_p$ vs. ψ was defined. Also ψ was as follow:

$$\psi = k_s (RT)^{1/2} / (nFD \pi v)^{1/2} \quad (1)$$

From this working curve for the scan rate of 200 mV s⁻¹, the values of ψ is obtained 0.1188. By diffusion coefficient of DPD in solution, determined by chronoamperometry ($D = 1.017 \times 10^{-6}$ cm² s⁻¹) and related equation, the k_s value was calculated as 1.33×10^{-3} cm s⁻¹. Figure 2 shows Tafel plots obtained from the data of the rising part of the current voltage curves recorded at scan rate of 10 mV s⁻¹. This part of voltammogram, known as Tafel region, is affected by the electron transfer kinetics between the substrate (DPD) and the electrode surface. In this condition, the transfer coefficient (α) can be estimated from the slope of Tafel plot [10]:

$$\eta = b \log i + \text{constant} \quad (2)$$

where $b = 2.3RT/(1 - \alpha)nF$

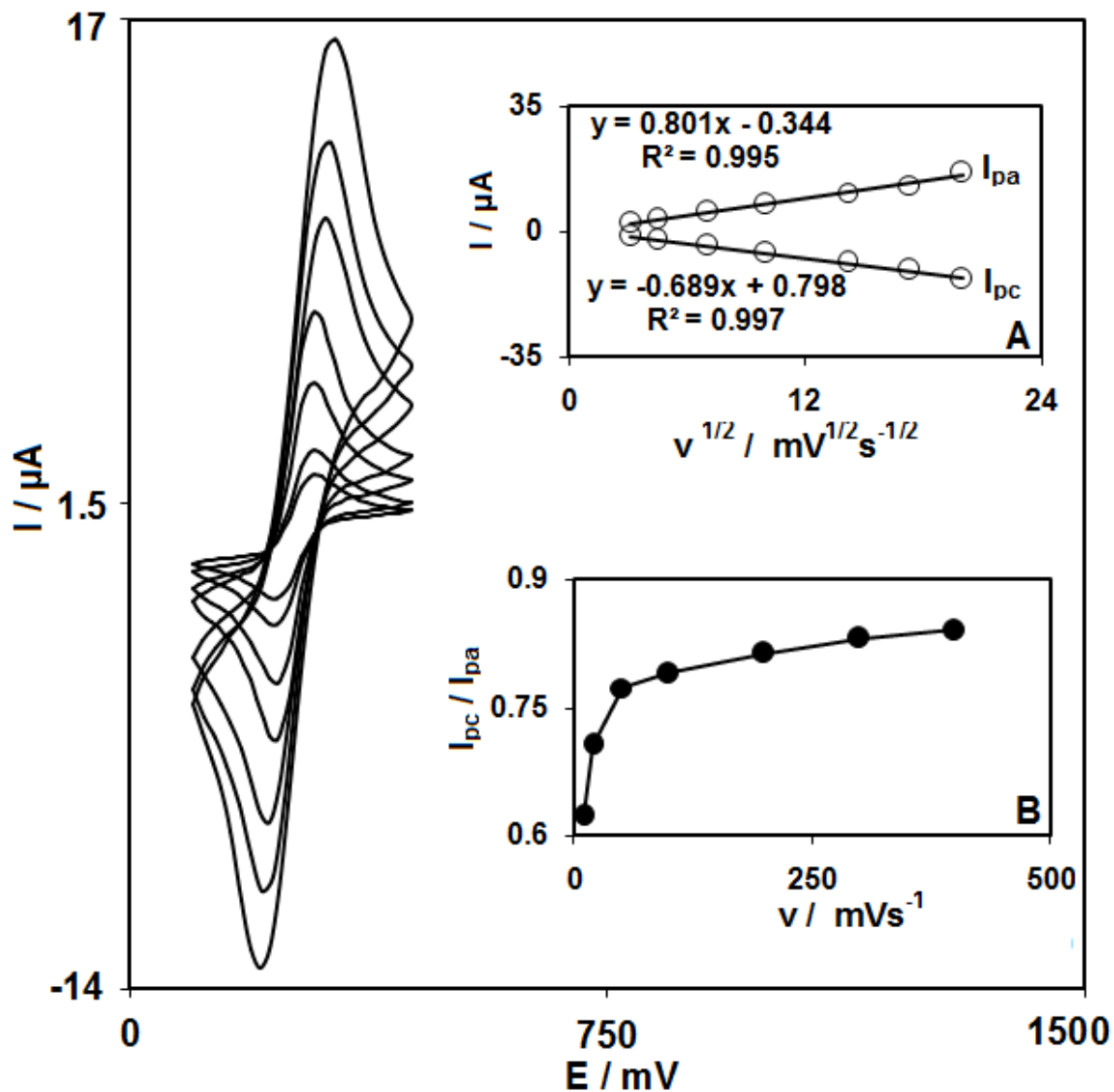


Figure 1. Cyclic voltammograms of 0.833 mM DPD in 0.1 M phosphate buffer solution (pH 6.0) at the surface of GC electrode at various scan rates: from inner to outer 10, 20, 50, 100, 200, 300 and 400 mV s^{-1} scan rates, respectively. Insets: (A) Variations of I_p versus square root of scan rates (B) Variation of the peak currents ratio (I_{pc}/I_{pa}) versus scan rate.

A slope of $0.0408 \text{ V decade}^{-1}$ is obtained, indicating a one-electron transfer for a rate-limiting step assuming a transfer coefficient of $\alpha=0.446$.

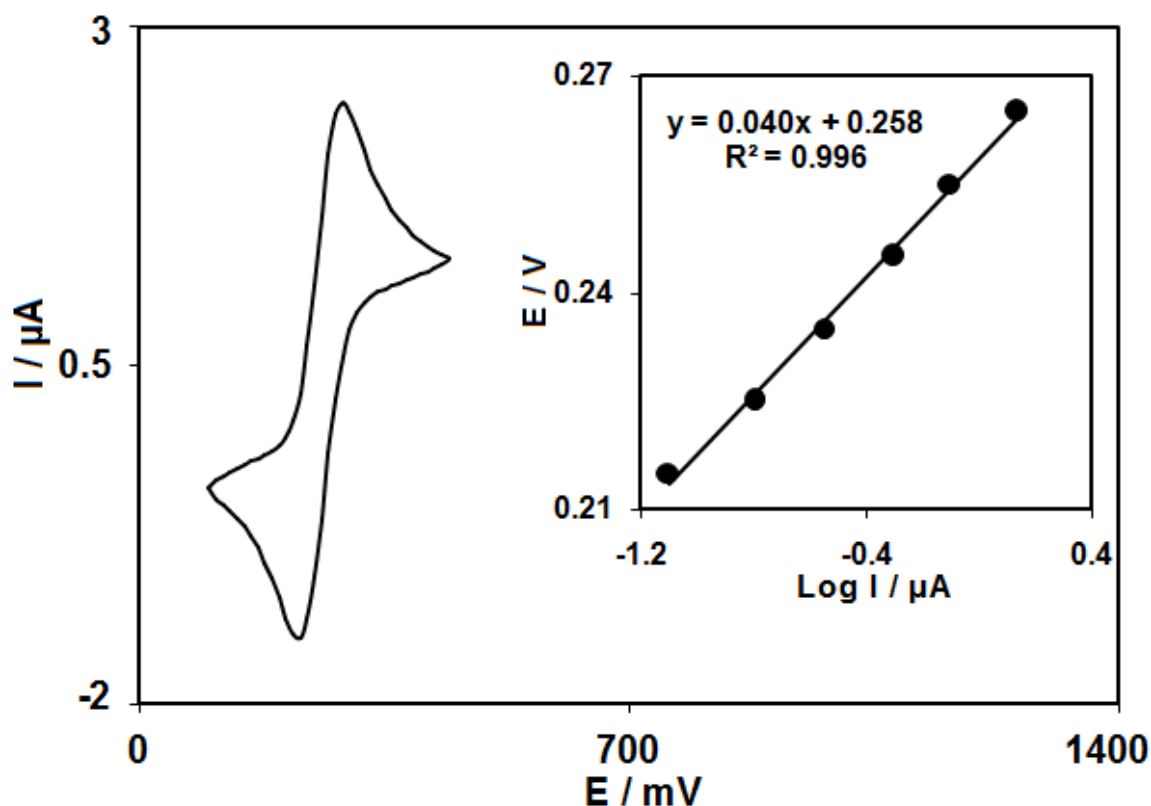


Figure 2. Cyclic voltammograms of 0.833 mM DPD in 0.1 M phosphate buffer solution (pH 6.0) at the surface of GC electrode at 10 mVs^{-1} . The inset shows the Tafel plot derived from the Cyclic voltammogram.

3.2. Effect of pH on the DPD at GCE

The electrochemical response of the DPD molecule is generally dependent on the pH. Thus, the electrochemical behavior of the DPD at GCE was studied at different pHs using cyclic voltammetry. Anodic and cathodic peak potentials of the DPD were shifted to less positive values with the increase of pH. The conditional formal potential $E^{\circ'}$, which will be used for determining of the standard redox potential, E° , can then be obtained from the equation $E^{\circ'} = E_{p.a} - \alpha(E_{p.a} - E_{p.c})$ and considering $\alpha = 0.446$ [10].

Figure 3 shows the measured values of $E^{\circ'}$, of the DPD redox couple as a function of pH. Based on the relation between $E^{\circ'}$ and pH, Eq. (3) [10], the standard redox potential of DPD, E° , was obtained from the intercept of Figure 3 and is equal to 0.5538 V versus Ag/AgCl (sat.), KCl (3 M).

$$E^{\circ'} = E^{\circ} - 2.303(mRT/nF)pH \quad (3)$$

In Eq. (3) m and n are the number of protons, H^+ , and electrons in the redox reaction, respectively and all the other symbols have their conventional meaning. In the studied range of pH, both m and n are two. Considering the standard electrode potential of the Ag/AgCl reference electrode as 0.20V [11]. relative to the Standard Hydrogen Electrode (SHE), the standard reduction potential of DPD is 0.7538 V versus SHE.

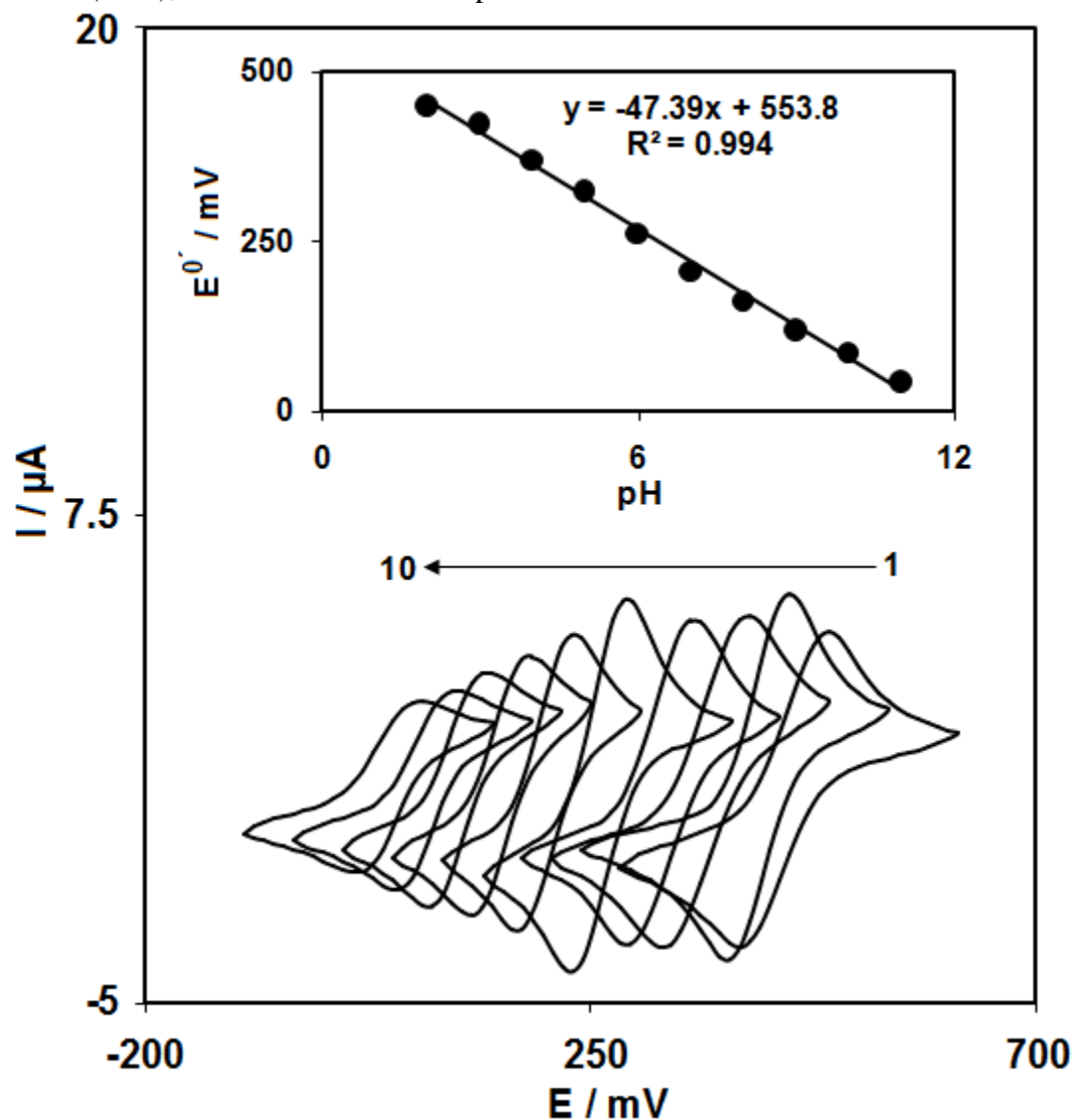


Figure 3. Cyclic voltammograms (at 100 mV s^{-1}) of 0.5 mM DPD in 0.1 M phosphate buffer solution at the surface of GC electrode at various buffered pHs. The numbers 1–10 correspond to 2, 3, 4, 5, 6, 7, 8, 9, 10, and 11 pHs, respectively. Inset: Plot of $E^{\circ'}$ vs. pH.

3.2. Theoretical Calculations

The *ab initio* calculation of the absolute redox potential of DPD in aqueous solution (water) is explained. The molecular orbital theory calculations were carried out using Gaussian 03 software [12]. To obtain the redox potential, it is necessary to calculate the standard free energy change (ΔG°) for reaction (4).

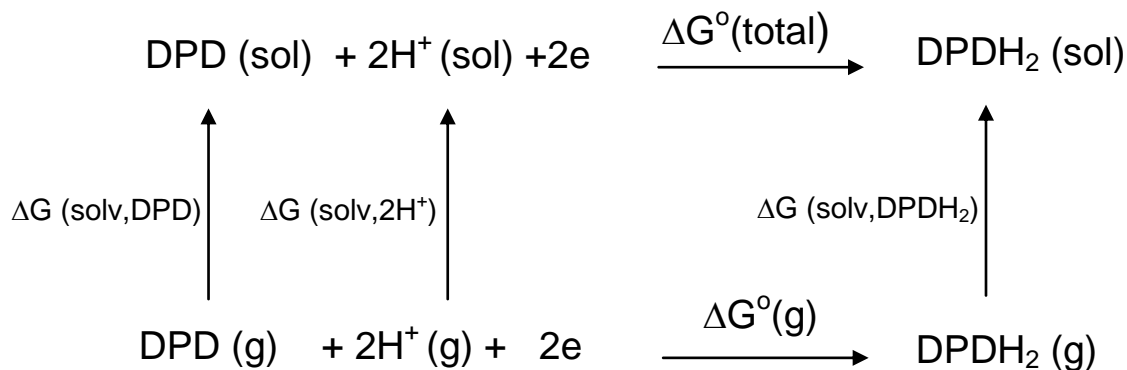


ΔG° is related to the absolute redox potential through the following thermodynamic relation:

$$E^\circ = - \Delta G^\circ/nF \quad (5)$$

where n is the number of transferred electrons in the reaction which is equal to 2 for reaction (4) and F is the Faraday constant (96485 C mol^{-1}). To calculate ΔG° , it is necessary to use the following thermodynamic cycle (Born-Haber) which is used for transferring all of the species involved in the reaction (4) from the gas to solution phase. Based on the above thermodynamic cycle, $\Delta G^\circ(\text{total})$ can be written as

$$\Delta G^\circ(\text{total}) = \Delta G^\circ(\text{g}) + \Delta G^\circ(\text{solv, DPDH}_2) - \Delta G^\circ(\text{solv, DPD}) - 2\Delta G^\circ(\text{solv, H}^+) \quad (6)$$



Scheme 1 . Thermodynamic cycle for obtaining the $\Delta G^\circ(\text{sol})$ of reaction in solution from the $\Delta G^\circ(\text{g})$ of reaction in gas phase.

where $\Delta G^\circ(\text{g})$ is the change of the standard free energy of reaction (4) in the gas phase. $\Delta G^\circ(\text{solv, DPDH}_2)$, $\Delta G^\circ(\text{solv, DPD})$ and $\Delta G^\circ(\text{solv, H}^+)$ are the standard free energy solvation of DPDH_2 , DPD and H^+ , respectively.

In order to calculate $\Delta G^\circ(\text{g})$, the standard free energy of DPD and DPDH_2 were calculated in the gas phase at the DFT-B3LYP level of theory using 6-311++G** basis set. To do this, the molecular structure of DPD and DPDH_2 were optimized at B3LYP/6-311++g** level of theory, separately and then, the vibrational frequencies calculation, at the same level of theory and basis set, were performed on the optimized structures to confirm that they are at the global minima and obtain the standard free energy of DPD and DPDH_2 in gas phase. To calculate $\Delta G^\circ(\text{g})$, we need to know the standard free energy of free electron and $\text{H}^+(\text{g})$. To obtain the standard free energy of electron, we used its energy ($3.720 \text{ kJ}\cdot\text{mol}^{-1}$) and entropy ($0.022734 \text{ J}\cdot\text{mol}^{-1}\text{K}^{-1}$) at 298 K [13]. The Gibbs free energy of $\text{H}^+(\text{g})$ has been reported to be $-26.3 \text{ kJ}\cdot\text{mol}^{-1}$ [14].

In order to calculate the solvation energy for DPD and DPDH_2 , the Polarized Continuum Model (PCM) which defines the cavity as the union of a series of interlocking atomic sphere [7], was used for ab initio calculations. Similar to gas phase calculations, the molecular structure of DPD and DPDH_2 were re-optimized in water solvent using PCM model at the same level of theory and basis set. Then, the vibrational frequency calculations were performed to obtain the Gibbs free energy of DPD and DPDH_2 in solution. $\Delta G^\circ(\text{solv},\text{DPDH}_2)$ and $\Delta G^\circ(\text{solv},\text{DPD})$ is obtained from the subtraction the standard Gibbs free energy of each compound in solution from the corresponding value in gas phase. We have used the literature value of $-1104.6 \text{ kJ}\cdot\text{mol}^{-1}$ for $\Delta G^\circ(\text{solv},\text{H}^+)$ [15]. Table 1 report the values of standard Gibbs free energy of DPD and DPDH_2 in gas phase and solution, their free energy of solvations and change in the free energy of the reaction (4) in gas phase and solution.

Table 1. The Gibbs free energy of DPD and DPDH_2 in gas phase and solution, together with salvation free energies of species calculated at B3LYP/6-311++G** level of theory.

| | <i>DPD</i> | <i>DPDH₂</i> | <i>Fig. 2</i> |
|---|-------------|-------------------------|---------------|
| B3LYP Free energy (g)/(a.u) | -1333.92771 | -1335.15931 | - |
| B3LYP free energy (sol)/(a.u) | -1333.95237 | -1335.19280 | - |
| $\Delta G^\circ(\text{solv}) / \text{kJ}\cdot\text{mol}^{-1}$ | -64.74483 | -87.92799 | - |
| $\Delta G^\circ(\text{g})/\text{KJ mol}^{-1}$ | - | - | -3174.85633 |
| $\Delta G^\circ (\text{total})/\text{KJ mol}^{-1}$ | - | - | -988.83949 |

It should be mentioned that this value is the change in the standard Gibbs free energy of reaction (4) in solution in the standard state of gas phase (1 atm). To obtain the change in the standard free energy of reaction (4) in solution, we need to add $\Delta n\Delta G^{\circ \rightarrow *}$ to $\Delta G^{\circ}(\text{total})$ where $\Delta G^{\circ \rightarrow *}$ is the correction for changing the standard state from gas phase (1 atm) to solution (1 mol.L⁻¹). Δn is the change of moles in reaction (4) which is equal to -2. The value of $\Delta G^{\circ \rightarrow *}$ is equal to 7.9 KJ.mol⁻¹. By considering this correction, the value of change in the standard Gibbs free energy of reaction (4) in solution $\Delta G^*(\text{total})$ is equal to -1004.63949 kJ.mol⁻¹. Using the value of $\Delta G^*(\text{total})$ and Eq. (5), the standard reduction potential of P is equal to 5.206 V. The standard reduction potential of DPD relative to Standard Hydrogen Electrode (SHE) (4.44 V) is about 0.766 Volt. The experimental value is 0.7538 V. As seen there is a difference about 12 mV between theory and experiment which can be attributed to the employed level of theory.

4. CONCLUSIONS

The results of this work show that the electrochemical behaviors of DPD strongly depend on the pH values of the solutions. The redox potential of DPD relative to SHE electrode were predicted using DFT method at B3LYP/6-311++G** level of theory. The experimental value of redox potential is in good agreement with the calculated value. The difference between the theory and experiment is about 12 meV which shows that the employed theoretical model in this work is suitable for DPD. This theoretical method is very effective for the prediction of an unknown formal electrode potential of any compound involved in biochemistry.

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