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Spectroscopic and Thermodynamic Studies of Interaction Between Dopamine and Cobalt(III) Schiff-Base Complexes

S. Baniyaghoob[1] **and D.M. Boghaei**[1,*]

Abstract. *In this paper, the interactions of cobalt(III) tetradentate Schiff-base complexes, [Co(3-MeO-salophen)]ClO*$_4$*, (1), [Co(5-NO*$_2$*-salophen)]ClO*$_4$*, (2), and [Co(5-Br-salophen)]ClO*$_4$*, (3), with dopamine, an important neurotransmitter, have been investigated. The formation and kinetic constants for complex formation of [Co(3-MeO-salophen)]ClO*$_4$*, (1), with dopamine were determined spectrophotometrically in H*$_2$*O/EtOH solution (4:1) at 30 °C by using the Benesi-Hildbrand and Guggenheim equations, respectively. The stoichiometry has been found to be 1:1. The rate and equilibrium constants for the coordination of dopamine to [Co(3-MeO-salophen)]ClO*$_4$ *were found to be 0.0053 min*$^{-1}$ *and 1600 dm*^{3} *mol*$^{-1}$*, respectively.*

Keywords: *Cobalt(III) Schiff-base complexes; Dopamine; Benesi-Hildbrand equation; Guggenheim's method; Neurotransmitter.*

INTRODUCTION

Cobalt(III) Schiff-base complexes have been extensively used to mimic biologically important centers in nature. The discovery of certain cobalt(III) Schiff-base complexes that have antiviral properties prompted scientists to initiate an investigation of Co(III) interactions with proteins and nucleic acids [1]. Since complexes with relatively labile axial ligands exhibit higher activity, it is suspected that the axial binding of Co(III) to biological targets is somehow involved in the mechanism of action [2].

Neurotransmitters are frequently organic bases that form adducts with electron acceptor systems such as metal ions, proteins and components of proteins by direct or indirect interaction [3]. Dopamine is a catecholeamine neurotransmitter that is synthesized in the hypothalamus and plays an important role in cardiovascular, renal, hormonal and central nervous system regulation through stimulation of the alpha and beta adnerengic and dopaminergic receptors. The nigrostriatal pathway degenerates in Parkinson's disease, producing a loss of dopamine in the neostriatum; an area involved in the coordination of motor function [4-9].

The study of molecular complex formation between the neurotransmitter dopamine and a series of cobalt(III) Schiff-base complexes is, therefore, expected to have some importance in the context of biochemical processes. In continuation of our work on the thermodynamic studies of the interaction of some water soluble cobalt(II) Schiff-base complexes with some biologically important molecules [10,11], the thermodynamic and kinetic properties of the interaction between some other cobalt Schiff-base complexes and dopamine have been examined.

EXPERIMENTAL

Dopamine (4-(2-aminoethyl)benzene-1,2-diol) hydrochloride was purchased from Merck. Cobalt(III) Schiff-base complexes:

(i) [{bis(3-methoxy-salicylaldehyde)-*o*-phenylenediiminato} cobalt(III)] perchlorate, [Co (3-MeO-salophen)]ClO$_4$ (**1**),

(ii) [{bis(5-nitro-salicylaldehyde)-*o*-phenylenediimi nato} cobalt(III)] perchlorate, [Co(5-NO$_2$-salophen)] ClO$_4$ (**2**),

(iii) [{bis (5-bromo-salicylaldehyde)-*o*-phenylenedii minato} cobalt(III)] perchlorate, [Co(5-Br-

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1. *Department of Chemitry, Sharif University of Technology, Tehran, P.O. Box 11155-3516, Iran.*
*. *Corresponding author. E-mail: dboghaei@sharif.edu*

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salophen)]ClO_4 (**3**)], were synthesized according to [12].

The complexes were characterized by IR, NMR and UV-vis spectroscopy.

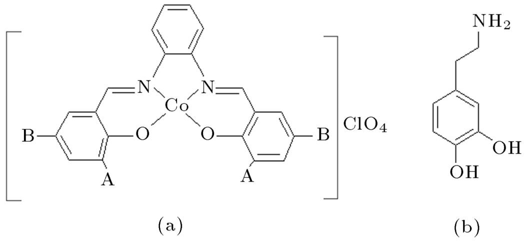
UV-vis spectra were recorded by a CARY 100 Bio VARIAN UV-vis spectrophotometer, equipped with a PCB-150 water circulator and thermostated multicell holder. A matched pair of quartz cells of 1cm optical path length were used for the measurements.

Kinetic and equilibria studies were run at 30 ± 0.5°C and monitored with the CARY 100 Bio VARIAN UV-vis spectrophotometer. We monitored the appearance of the spectra due to the product formed following the addition of dopamine to solutions of the complex in water and ethanol (unbuffered pH = 6). Typically, a known volume of the aqueous solution of [Co(3-MeO-salophen)]ClO_4 was added to a 1cm path length spectrophotometric cell and deaerated using nitrogen. Then, a known volume of an aqueous solution of dopamine was added to the cell and the changes in absorbance were monitored with time. For thermodynamic studies, concentrations of the cobalt(III) Schiff-base complex were kept constant at 5.00×10^{-5} mol.dm^{-3}, while dopamine concentrations were varied from 2.50×10^{-3} to 12.5×10^{-3} mol.dm^{-3}. Since the concentration of dopamine was larger than that of the cobalt(III) Schiff-base complex, pseudo-first order conditions were assumed for kinetic studies.

RESULTS AND DISCUSSION

Electronic Spectra

The electronic absorption spectra of cobalt(III) Schiff-base complexes (Figure 1) in H_2O/EtOH (4:1) were obtained at 30°C (Figures 2 to 4a).



(a) (b)

Compound	A	B
1	OMe	H
2	H	NO_2
3	H	Br

Figure 1. The structure of the (a) cobalt(III) Schiff-base complexes **1**, **2** and **3** and (b) dopamine.

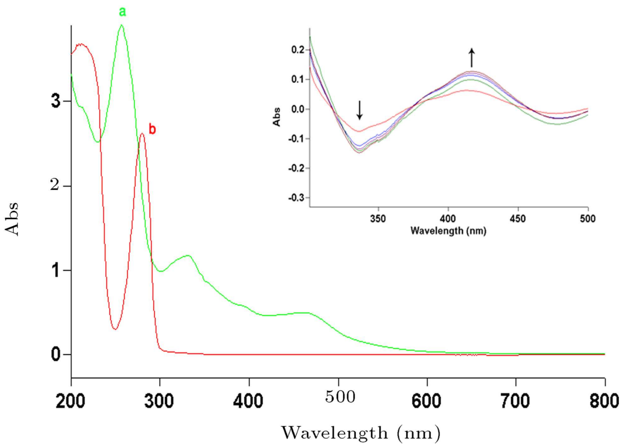


Figure 2. Absorption spectra of (a) dopamine (1.5×10^{-4} mol dm^{-3}) and (b) [Co(5-Br-salophen)]ClO_4 (5.0×10^{-5}) against the solvent as a reference. Inset: absorption spectra of the complex between dopamine (2.5×10^{-3} mol dm^{-3}) and [Co(5-Br-salophen)]ClO_4 (5.0×10^{-5}) obtained by a difference method during the time.

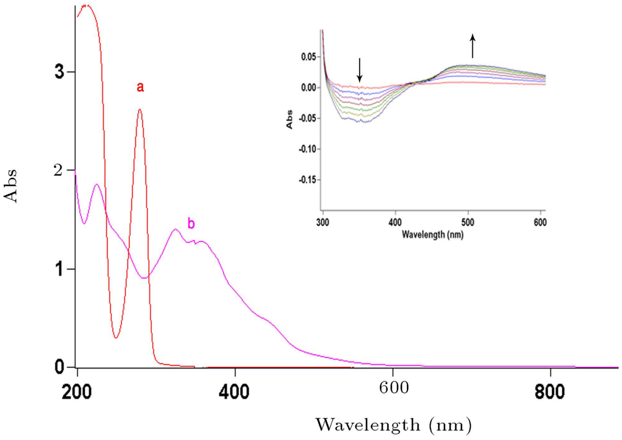
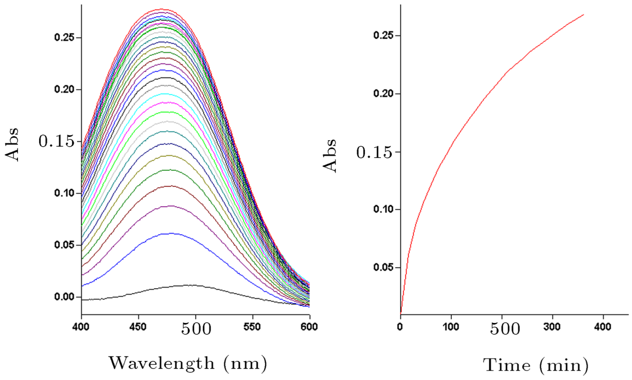


Figure 3. Absorption spectra of (a) dopamine (1.5×10^{-4} mol dm^{-3}) and (b) [Co(5-NO_2-salophen)]ClO_4 (5.0×10^{-5}) against the solvent as reference. Inset: absorption spectra of the complex between dopamine (2.5×10^{-3} mol dm^{-3}) and [Co(5-NO_2-salophen)]ClO_4 (5.0×10^{-5}) obtained by a difference method during the time (every 10 minutes).

All three complexes have two intense bands in the UV region (197-331 nm), which can be assigned to $n \longrightarrow \pi^*$ and $\pi \longrightarrow \pi^*$ transitions of the ligand and another peak in the visible region (370-460 nm), which belongs to the $d-d$ transition of the metal ion [12]. After addition of an excess amount of dopamine to the Co(3-MeO-salophen)]ClO_4 (i.e. [dopamine]/[complex] = 50), one new absorption band, presumably due to the formation of the [dopamine-[Co(3-MeO-salophen)]ClO_4] complex, does apear at 475 nm (Figure 4). We have also one isosbestic point in the visible region, after the addition of dopamine to [Co(5-Br-salophen)]ClO_4 and [Co(5-NO_2-salophen)]ClO_4 (Figures 2 and 3).The



(a) (b)

Figure 4. (a) CT absorption spectra of admixture of [Co(3-MeOsalophen)]ClO_4 (5.0×10^{-5} M) and dopamine (2.5×10^{-3} M) in H_2O/EtOH solution at 30°C (time intervals of 15 minutes); (b) Absorbance-time plot of solution mentioned in (a).

bands in the UV region would stay intact in all three cases after addition of the donor.

The spectral and colour changes are similar to those observed on the oxidation of dopamine to semiquinone using oxidizing reagents such as $(NH_4)_2Ce(NO_3)_6$. Thus, the final spectra in Figures 2 to 4 may be due to the reduction of the cobalt(III) Schiff-base species as a result of the electron transfer from dopamine.

Axial ligation followed by electron transfer has also been suggested for the interaction of the neurotransmitter, NO, with iron porphyrins [13]. It has been also shown that the coordination of dopamine to iron(III) results in the formation of an [iron(III)(dopamine)] complex involving the use of both oxygen atoms in the dopamine, which is followed by internal electron transfer forming iron(II) and semiquinone, hence dissociation of the complex [14].

Oni et al. also suggested in their work that axial ligation of dopamine, DA, or serotonin, 5-HT, to iron(II) tetrasulfophthalocyanine, $[FeTSPc]^{4-}$, occurs prior to an internal electron transfer, resulting in the formation of $(DA^+)Fe^I$TSPc and $(5\text{-}HT^+)Fe^I$TSPc species, respectively [15]. The one electron oxidation product of dopamine is likely to be a semiquinone.

Determination of Kinetic Constant (k)

The spectra recorded for the complexes between dopamine and cobalt(III) Schiff-base complexes are time dependent. In order to obtain further information about the kinetics and mechanism of the reaction of dopamine with cobalt(III) Schiff-base complexes, the kinetics of the reaction, which was indicated by the change of the absorption band at 475 nm for [Co(3-MeO-salophen)] ClO_4, were studied. The absorbance of solutions containing reactants, the cobalt complex and dopamine, in a mole ratio of 1:50 in H_2O/EtOH (4:1) was monitored as a function of time at 475 nm. Absorbance-time plot is shown in Figure 4. The formation of the complex between dopamine and the Co(III) Schiff-base complex was found to follow pseudo-first order kinetic. The rate constant was calculated by using Guggenheim's method for first order reactions [16]. This method can be used in a case where the initial amount of reactant cannot be determined. The procedure is to take a series of readings of the absorbance of product (A) at time (t), which are spread over an interval that is two or three times the half life of the reaction. A second series of readings (A') is also made, each at time ($t + t'$) (t'= exactly constant intervals after the time of the corresponding reading, A). The period, t', must be at least two or three times the half life of the reaction. If A_0 is the (unknown) value of A at infinite time, it follows from the first-order rate equation that for a given reading;

$$A_0 - A_1 = A_0 \exp[-kt_1], \qquad (1)$$

and, for a reading after interval t';

$$A_0 - A'_1 = A_0 \exp[-k(t_1 - t')], \qquad (2)$$

similar equations are true at t_2 and $t_2 + t'$.

Substraction of Equation 2 from Equation 1 gives:

$$A'_1 - A_1 = A_0 e^{-kt_1}(1 - e^{-kt'}), \qquad (3)$$

whence;

$$kt_1 + Ln(A'_1 - A_1) = \ln[A_0 - (1 - e^{-kt'})], \qquad (4)$$

the right-hand side of this equation is constant, since t' has been chosen as constant; it, therefore, follows that for each of the corresponding readings (i.e. A'_1 and A_1, A'_2 and A_2 etc.),

$$kt + \ln(A' - A) = \text{const.}$$

A plot of $\ln(A' - A)$ against t will therefore give a straight line of slope equal to - k (Figure 5).

The kinetic constant for the interaction of [Co(3-MeO-salophen)]ClO_4 with dopamine in H_2O/EtOH (4:1) solution at 30°C is calculated to be 0.0052 min^{-1}.

Determination of Formation Constant (K)

The spectrophotometric data were employed to calculate the value of the equilibrium constants, K, of the complex. The Benesi-Hildbrand equation was used for this purpose. The changes in the absorbance upon addition of dopamine to a solution of a cobalt(III) Schiff-base complex of fixed concentration (Table 1) follow the Benesi-Hildbrand equation [17]:

$$\frac{[A]_0}{\text{Abs.}} = \frac{1}{K_{DA}\varepsilon_{DA}} \frac{1}{[D]_0} + \frac{1}{\varepsilon_{DA}}, \qquad (5)$$

Table 1. Absorbance data for spectrophotometric determination of stoichiometry, formation constant, K, and molar absorptivity, ε, of dopamine-Co(3-MeO-salophen)]ClO_4 complex in aqueous solution against pristine cobalt(III) Schiff-base solution as a reference.

Temperature (K)	10^2 Donor Concentration (mol dm^{-3})	$10^4[A]_0$ (mol dm^{-3})	Absorbance at λ_{CT}	K (dm^3 mol^{-1})	ε (dm^3 mol^{-1} cm^{-1})
303	0.25	0.5	0.529	1600	12500
	0.50		0.568		
	0.75		0.605		
	1.00		0.627		
	1.25		0.642		

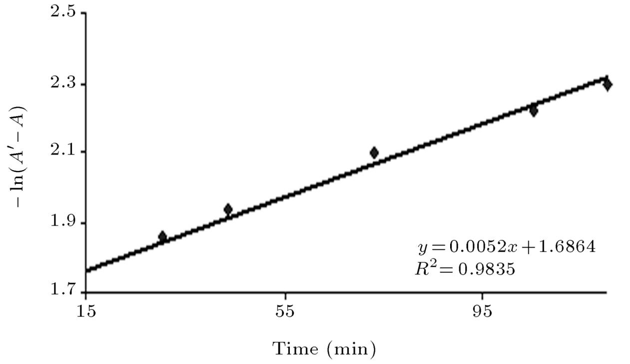


Figure 5. Guggenheim's plot for first-order reaction of dopamine (2.5×10^{-3} M) with [Co (3-MeO-salophen)]ClO_4 (5.0×10^{-5} M) in H_2O/EtOH (4:1) at 30 °C.

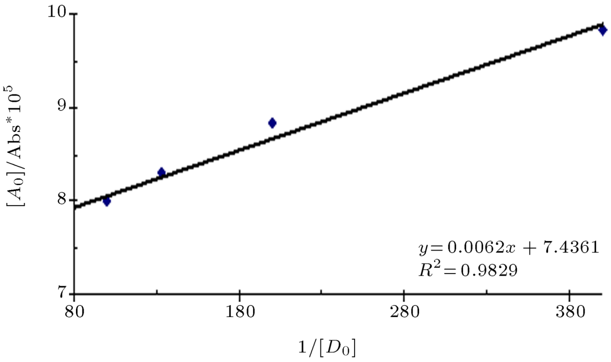


Figure 6. A plot for Benesi-Hildbrand equation for reaction of dopamine with [Co (3-MeO- salophen)]ClO_4 (5.0×10^{-5} M) in H_2O/EtOH at 30°C.

where $[D]_0$ and $[A]_0$ are the concentration of the dopamine, donor and cobalt(III) Schiff-base complex as acceptor molecules, respectively. K_{DA} is the association equilibrium constant and ε_{DA} is the molar extinction coefficient of the complex. Equation 5 is restricted to a condition where $[D]_0 >> [A]_0$, and data is collected in a spectral region, where only the complex with single 1:1 stoichiometry absorbs.

Plots of $[A]_0$/Abs against $1/[D]_0$ were found to be linear in all cases, showing a 1:1 complex [18] (Figure 6). From the slope and the intercept, the K_{DA} and ε_{DA} of the complex were calculated (Table 1).

CONCLUSIONS

We have investigated the complex formation of three cobalt(III) Schiff-base complexes with dopamine, spectroscopically. This interaction is probably through the axial position of Schiff-base complexes, which will be followed by an internal electron transfer. So, we can relate the peak growth in 475 nm to the ligand exchange of [Co (3-MeO-Salophen)]ClO_4, rather than just a simple charge transfer. This type of interaction can be used in modeling the interaction of biologically important Co(III) complexes with other natural molecules, such as neurotransmitters. The calculation of kinetic and thermodynamic constants suggests that they may be very slow reactions of the type and form moderately stable complexes.

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