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Inorganic Chemistry
Note

Structural Model for the Cu$_\mathrm{B}$ Site of Dopamine β-Hydroxylase: Crystal Structure of a Copper(II) Complex Showing N$_3$OS Coordination with an Axial Sulfur Ligation

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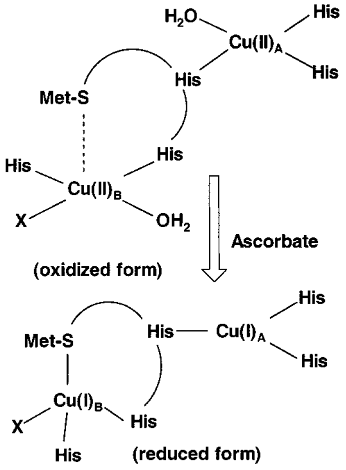
Introduction

Dopamine β-hydroxylase (DβH; E.C. 1.14.17.1) is a copper-containing glycoprotein which catalyzes the benzylic hydroxylation of dopamine to norepinephrine in the biosynthesis of the neurohormone epinephrine (adrenalin) in the sympathetic nervous system.[1−5] The enzyme has two essentially uncoupled copper centers per subunit. While the Cu$_\mathrm{A}$ site acts as an electron acceptor from the ascorbic acid, the Cu$_\mathrm{B}$ site is responsible for the functionalization of dopamine by dioxygen with the regeneration of the oxidized form of the enzyme. The structural and functional properties of DβH vary considerably with the other dicopper proteins, viz., tyrosinase which is involved in the conversion of L-tyrosine to L-dopa in the biosynthesis of catecholamines. Although the chemistry of complexes with a Cu$_2$O$_2$ core has been extensively studied for modeling the hemocyanin and tyrosinase activity,[4,6−8] the copper complexes modeling the structural and functional aspects of DβH are rare.

Scheme 1. Blackburn Model Showing the Active Site Coordination Geometry in the Oxidized and Reduced Forms of DβH[a]



[a] X could either be a His or an O-donor ligand.

The first report of a benzylic hydroxylation was made by Itoh and co-workers using a copper(II) complex having a pendant β-position of a tertiary amine group attached to a tridentate ligand system.[9] The product is a dialkoxo-bridged dicopper(II) complex. This model complex has a CuN$_3$O$_2$ coordination with a perchlorate anion occupying the axial site. Spectroscopic and biochemical studies on DβH have shown that the coordination geometries at the copper centers are significantly different from each other.[10−12] The Blackburn model[11] for the oxidized and reduced forms of the active sites in DβH is shown in Scheme 1. The ascorbate binding Cu$_\mathrm{A}$ site has a four-coordination geometry, Cu$_\mathrm{A}$(his)$_3$(H$_2$O). The Cu$_\mathrm{B}$ center which is located at a distance greater than 4 Å has a Cu$_\mathrm{B}$(his)$_2$X(H$_2$O) configuration, where X could be a histidine or an O-donor ligand. It has been proposed from EXAFS studies that one copper(I) center in reduced DβH is bonded to a Met-S ligand.[11,12] The EXAFS data also suggest that, in the oxidized form of DβH, the Met-S ligand may be present as a weakly bound axial ligand. A recent report[13] on the crystal structure analysis of peptidylglycine α-hydroxy-

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lating monooxygenase (E.C. 1.14.17.3) which has structural similarity to DβH shows the presence of a Met residue as a weakly bound ligand to the Cu_B site giving a distance of 2.68 Å. The present work stems from our interest in synthesizing a copper(II) complex having a CuN_3OS coordination geometry as a structural model for the Cu_B site of DβH.

The first attempt toward the synthesis of a structural model for the Cu_B site of DβH was made by Réglier and coworkers.[14,15] The complexes reported by them have a N_4S coordination and a square pyramidal geometry with the SMe group occupying the equatorial plane. Although several copper(II) complexes having a CuN_3OS coordination are known[16−22] in the literature, the sulfur ligation in these complexes is at the basal plane. Using 2,2′-bipyridine (bpy) and a NSO-donor Schiff base ligand (HL), we have been successful in preparing a copper(II) complex which shows a N_3OS coordination and an axial sulfur ligation. Herein we report the synthesis, structure, and properties of $[Cu^{II}(L)(bpy)](ClO_4)$ (**1**) and its reduced product $[Cu^{I}(HL)(bpy)](ClO_4)$ (**2**). Complex **1** has been characterized by X-ray crystallography.

Experimental Section

Materials and Measurements. Solvents and reagents used for the preparative procedures were obtained from commercial sources. The Schiff base ligand (2-(methylthio)phenyl)salicylaldimine (HL) was prepared by reacting salicylaldehyde and 2-(methylthio)aniline in a 1:1 molar ratio in methanol.[23] The solvents used for spectral and electrochemical measurements were purified. The elemental analyses were done using a Heraeus CHN-O rapid instrument. The ^{1}H NMR, electronic, infrared, and EPR spectral data were obtained from Bruker AMX 400, Hitachi U-3400, Bruker Equinox 55, and Varian E-109 X-band spectrometers, respectively. Electrochemical measurements were made with a three-electrode setup, consisting of a glassy carbon working, a saturated calomel (SCE) reference, and a platinum wire auxiliary electrode using a PAR model 253 Versa Stat potentiostat/galvanostat with EG&G electrochemical software. The measurements were made at 25 °C, and the data are uncorrected for junction potentials. Ferrocene was used as a standard showing the Fe(III)/Fe(II) couple at 0.38 V (vs SCE) under similar experimental conditions in MeCN containing 0.1 M tetrabutylammonium perchlorate (TBAP). Magnetic susceptibility data were obtained from a model 300 Lewis Coil force magnetometer (George Associates Inc.). $HgCo(NCS)_4$ was used as a standard.

Preparation of $[Cu(O\text{-}2\text{-}C_6H_4CH{=}NC_6H_4\text{-}2'\text{-}SMe)(bpy)](ClO_4)$ (1). A 0.2 g (0.5 mmol) quantity of $Cu_2(O_2CMe)_4(H_2O)_2$ in 5 mL of MeOH was reacted with 0.16 g (1.0 mmol) of 2,2′-bipyridine under stirring conditions for 0.5 h at 25 °C. The resulting solution was then reacted with 0.24 g (1.0 mmol) of (2-(methylthio)phenyl)salicylaldimine (HL) taken in 10 mL of MeOH. The mixture was stirred for 1.0 h, and the complex was precipitated as a green solid (~70% yield) on addition of a methanolic solution of $NaClO_4$ into the reaction mixture. The solid was isolated, washed with cold methanol, and dried under vacuum over P_4O_{10}. Anal. Calcd for $C_{24}H_{20}N_3O_5SClCu$: C, 51.34; H, 3.56; N, 7.49. Found: C, 51.32; H, 4.06; N, 7.35. λ_{max}, nm (ϵ, $M^{-1}cm^{-1}$): 638 (190), 388 (5980), 279 (25300) in MeCN. FT-IR, cm^{-1} (KBr phase): 3110m, 3061m, 1609s, 1576m, 1534s, 1495w, 1436s, 1374m, 1355w, 1320m, 1186m, 1150w, 1094vs, 1031m, 971w, 927w, 855w, 760s, 724m, 623s, 545w, 427w (vs, very strong; s, strong; m, medium; w, weak). μ_{eff}, μ_B: 1.8 at 300 K. EPR data: $g_{\|} = 2.21$ ($A_{\|} = 165 \times 10^{-4}$ cm^{-1}) and $g_{\perp} = 1.98$ in CH_2Cl_2 and MeCN−toluene (1:1 v/v) glasses at 77 K.

Preparation of $[Cu(HO\text{-}2\text{-}C_6H_4CH{=}NC_6H_4\text{-}2'\text{-}SMe)(bpy)](ClO_4)$ (2). Complex **2** was prepared by reacting 0.2 g (0.36 mmol) of **1** in 15 mL of MeCN with 0.06 g (0.36 mmol) of ascorbic acid taken in 1.0 mL of deoxygenated water. The reaction was carried out under a dinitrogen atmosphere using a Schlenk line. The solvents were removed under vacuum after the solution was stirred for 5 min. The solid was washed with deoxygenated cold water and finally dried in a vacuum over P_4O_{10} (yield ~60%). Anal. Calcd for $C_{24}H_{21}N_3O_5SClCu$: C, 51.25; H, 3.74; N, 7.47. Found: C, 51.93; H, 4.32; N, 7.13. λ_{max}, nm (ϵ, $M^{-1}cm^{-1}$): 525sh, 348 (11150), 268 (30900) in MeCN (sh, shoulder). FT-IR, cm^{-1}(KBr phase): 3053w, 1602s, 1564w, 1528w, 1448m, 1436m, 1317w, 1275m, 1186w, 1082vs, 903w, 760s, 724w, 623s, 557w, 465w, 417w. ^{1}H NMR (δ, ppm) in CD_3CN: 2.55 (s, 3H, S-*Me*), 7.04−7.62 (16H, aromatic protons), 8.87 (s, N=C*H*), 13.15 (s, O*H*) (s, singlet).

Safety Note. *Perchlorate salts of metal complexes with organic ligands are potentially explosive! Only small quantities of material should be prepared, and these should be handled with great caution.*

Solubility and Stability. Complexes **1** and **2** are soluble in common organic solvents other than hydrocarbons. They show poor solubility in water. Complex **2** is susceptible to oxidation and disproportionation in the solution phase. The complex, when stored in the solid state under a dinitrogen atmosphere, is stable for 1 week at low temperature (−5 °C).

X-ray Crystallographic Procedures for $[Cu(L)(bpy)](ClO_4)\cdot 0.5MeOH$. Single crystals of **1** were obtained by slow evaporation of an aqueous methanolic solution of the complex. A crystal of approximate size 0.24 × 0.26 × 0.36 mm was mounted on a glass fiber with epoxy cement. All geometric and intensity data were collected using an automated Enraf-Nonius CAD4 diffractometer equipped with Mo Kα radiation. The intensity data, collected in the range $3.6° < 2\theta < 50°$ using an $\omega{-}2\theta$ scan technique for 4259 reflections, were corrected for Lorentz−polarization effects and for absorption.[24] Structure determination was done using 3430 data with $I > 2\sigma(I)$ and 407 parameters using the SHELX system of programs[25] by a combination of Patterson and Fourier techniques and refined by full-matrix least-squares on F^2. All non-hydrogen atoms were refined anisotropically except the carbon of the

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Table 1. Crystallographic Data for [Cu(L)(bpy)](ClO_4)·0.5MeOH (**1**)

molecular formula: $C_{24.5}H_{22}ClCuN_3O_{5.5}S$	fw: 577.5
	space group: $P2_1/c$ (No. 14)
a: 10.114(2) Å	temp: 293(2) K
b: 10.877(2) Å	radiation: Mo Kα
c: 22.720(8) Å	D_{calc}: 1.568 g cm^{-3}
β: 101.83(2)°	μ: 11.32 cm^{-1}
V: 2446(1) Å^3	R:^{a} 0.0326
Z: 4	R_w:^{b} 0.0904

^{a} $R = \sum||F_o| - |F_c||/\sum|F_o|$. ^{b} $R_w = [\sum_w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]^{0.5}$. $w = 1/[\sigma^2(F_o^2) + (0.0501P)^2 + 1.4555P]$ where $P = (\mathrm{Max}(F_o^2,0) + 2F_c^2)/3$.

Table 2. Selected Bond Distances (Å) and Angles (deg) for [Cu(L)(bpy)](ClO_4)·0.5MeOH (**1**) with Esd's in Parentheses

Cu(1)−O(1)	1.882(2)	O(1)−Cu(1)−N(1)	161.95(9)
Cu(1)−N(1)	2.009(3)	O(1)−Cu(1)−N(2)	92.30(9)
Cu(1)−N(2)	1.994(2)	O(1)−Cu(1)−N(3)	93.41(9)
Cu(1)−N(3)	1.981(2)	N(2)−Cu(1)−N(3)	160.53(10)
Cu(1)−S(1)	2.940(1)	N(2)−Cu(1)−N(1)	80.71(9)
S(1)−C(23)	1.773(3)	N(3)−Cu(1)−N(1)	98.67(9)
S(1)−C(24)	1.806(3)	S(1)−Cu(1)−O(1)	111.09(7)
O(1)−C(11)	1.315(3)	S(1)−Cu(1)−N(1)	85.75(6)
N(2)−C(10)	1.338(4)	S(1)−Cu(1)−N(2)	90.48(7)
N(2)−C(6)	1.355(3)	S(1)−Cu(1)−N(3)	70.10(7)
N(3)−C(17)	1.291(3)	Cu(1)−O(1)−C(11)	123.6(2)
N(3)−C(18)	1.429(3)	Cu(1)−N(2)−C(6)	114.3(2)
N(1)−C(1)	1.335(4)	Cu(1)−N(2)−C(10)	125.6(2)
N(1)−C(5)	1.354(3)	Cu(1)−S(1)−C(23)	85.1(1)
Cu(1)−N(3)−C(17)	121.7(2)	Cu(1)−S(1)−C(24)	118.2(1)
Cu(1)−N(3)−C(18)	119.0(2)	C(23)−S(1)−C(24)	103.1(2)
Cu(1)−N(1)−C(5)	113.3(2)	Cu(1)−N(1)−C(1)	126.9(2)

disordered solvent methanol. The crystallographic data are summarized in Table 1. Selected bond distances and bond angles are given in Table 2. A perspective view of the molecule was obtained using ORTEP.[26]

Results and Discussion

Synthesis and Structure. The mixed-ligand copper(II) complex **1** is prepared in high yield from a reaction of copper(II) acetate with the NSO-donor Schiff base and 2,2′-bpy in methanol. The copper(I) complex **2** is obtained by reducing **1** with ascorbic acid. The one-electron paramagnetic complex **1** shows a d−d spectral band at 638 nm and a charge transfer (CT) band at 388 nm in MeCN. The reduced complex displays a CT band at 348 nm. The complexes display very strong infrared bands for the perchlorate anion at 1094 and 1082 cm^{-1} for **1** and **2**, respectively. Complex **1** shows axial EPR spectra in CH_2Cl_2 and MeCN−toluene glasses at 77 K indicating the $d_{x^2-y^2}$ ground state. Complex **2** is diamagnetic. The ^{1}H NMR spectrum exhibits a singlet methyl peak for SMe at δ2.55 ppm. A singlet peak at δ13.15 which disappears on addition of D_2O is assignable to the phenolic OH. The imine proton of the Schiff base shows a singlet at δ8.87. The resonances for the aromatic protons belonging to bpy and the Schiff base appear in the range δ7.04−7.62. On the basis of the analytical and spectral data, complex **2** is formulated as [Cu(HO-2-C_6H_4CH═NC_6H_4-2′-SMe)(bpy)](ClO_4). The noninvolvement of the phenolic OH in metal coordination is evidenced from the negligible shift of this proton resonance in **2** and the free ligand [$\Delta\delta_2 - \Delta\delta_1 = 13.15(\text{complex}) - 13.16(\text{ligand}) = -0.01$ ppm]. The downfield shift of the S−methyl resonance from 2.48 ppm in the free ligand (HL) to 2.55 ppm indicates the presence of a copper−sulfur bond in **2**. Similar downfield shift of the S−Me resonance has earlier been reported in copper(I) complexes having a metal−sulfur bond.[14,27,28] The ^{1}H NMR data suggest a four coordinate structure of **2** with a CuN_3S chromophore.

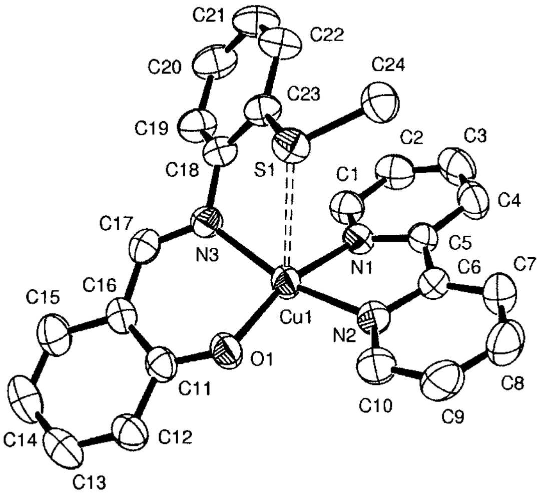

Figure 1. ORTEP view of the cationic copper(II) complex **1** showing the atom-numbering scheme and thermal ellipsoids at the 50% probability level.

Complex **1** has been characterized by single-crystal X-ray crystallographic studies. In this monomeric complex, the metal is bonded to a tridentate NSO-donor Schiff base and a bidentate NN-donor bpy ligand (Figure 1). The coordination geometry is distorted square pyramidal with three nitrogen and one oxygen donor atoms occupying the basal plane. The sulfur atom shows a weak axial contact at a distance of 2.940(1) Å. The Cu−N and Cu−O bond distances range between 1.981(2) and 2.009(2) Å. The Cu(1) and N(3) atoms are found to be 0.3 and 1.22 Å above the plane formed by N(1), N(2), and O(1) atoms.

The structural data on known copper(II) complexes having a N_3OS coordination are compared in Table 3. The coordination geometries in these complexes are distorted square pyramidal or trigonal bipyramidal with O and/or N-donor atoms occupying the axial site(s). Complex **1** with an axial sulfur contact models the Cu_B site of DβH in the oxidized form. The Cu−S bond in **1** is unusually long, and a similar weak axial sulfur ligation has been proposed for the Cu_B site from the EXAFS studies.[12]

Electrochemical and Catalytic Properties. The electron transfer properties of **1** and **2** were studied by cyclic voltammetric techniques using a glassy carbon working electrode in different solvents. Selected voltammetric data are given in Table 4, and representative voltammograms are shown in Figure 2.

Complex **1** in a mixture of DMF−Tris-HCl/0.1 M KCl buffer (1:4 v/v, pH 7.0) displays a quasi-reversible voltam-

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Table 3. A Comparison of the Structural Data among the Copper(II) Complexes Having a N_3OS Coordination

complex	geometry[a]	Cu−L_{ax}, Å	ref
1. $[Cu(L^1)(sacc)(H_2O)]$[b]	SQPY	Cu−O, 2.393(7)	16
2. $[Cu(STTP)(CO_3H)]$[c]	SQPY	Cu−O, 2.246(12)	17
3. $[Cu(SBPD)(phen)](ClO_4)$[d]	SQPY	Cu−N, 2.220(4)	18
4. $[Cu(bpy)(ATTH)(H_2O)](NO_3)_2$[e]	SQPY	Cu−O, 2.244(2)	19
5. $[Cu(bpy)(IMTHIM)(NO_3)](NO_3)\cdot H_2O$[f]	TBP	Cu−N, 1.921(3), 1.981(3)	19
6. $[Cu(Tp^{cum},Me)\{O(MeS)C_6H_4\}]$[g]	SQPY	Cu−N, 2.319(4)	20
7. $[Cu(PMDT)((methylthio)cresol)](ClO_4)$[h]	TBP	Cu−N,O[i]	21
8. $[Cu(PMDT)((methylthio)cresol)_2](ClO_4)$[h]	TBP	Cu−N,O[i]	21
9. $[Cu_2(BPCA)_2(1,2\text{-}DTSQ)(H_2O)\cdot 2H_2O$[j]	SQPY	Cu−O, 2.590(7)	22
10. $[Cu(L)(bpy)](ClO_4)\cdot 0.5MeOH$	SQPY	Cu−S, 2.940(1)	this work

[a] SQPY, square pyramidal; TBP, trigonal bipyramidal. [b] HL^1 = 2-formylpyridinethiosemicarbazone. Hsacc = saccharin. [c] STTPH = 21-thiatetra-*p*-tolylporphyrin. [d] SBPDH = *S*-benzyl-*β*-*N*-(pyridine *N*-oxide-2-ylmethylidene)dithiocarbazate. [e] ATTH = 4-amino-1,2,4-triazole-*S*-thione. [f] IMTHIM = imidazolidene-2-thione. [g] Tp^{cum},Me = cumenyl-functionalized hydrido-tris(pyrazolyl)borate. [h] PMDT = 1,1,4,7,7-pentamethyldiethylenetriamine. [i] Distances not reported. [j] BPCA = bis(2-pyridylcarbonyl)amide anion, 1,2-DTSQ = dianion of 3,4-dimercapto-3-cyclobutene.

Table 4. Cyclic Voltammetric Data[a] on $[Cu^{II}(L)(bpy)](ClO_4)$ (**1**) and $[Cu^I(HL)(bpy)](ClO_4)$ (**2**) for the Copper(II)/Copper(I) Couple at 50 mV s^{-1}

complex	solvent[b]	E_{pc} (V)	E_{pa} (V)	$E_{1/2}$ (V) [ΔE_p (mV)]	i_{pc}/i_{pa}
1	DMF−Tris buffer[c]	−0.20	−0.06	−0.13 [140]	1.1
	MeOH−Tris buffer[d]	−0.18	−0.03	−0.11 [150]	1.0
	DMF[e]	0.0	0.13	0.07 [125]	1.0
	MeOH[e]	−0.01	0.10	0.05 [110]	1.1
	MeCN	−0.27	0.14	−0.07 [410]	3.3
	CH_2Cl_2	−0.23	0.22	−0.01 [450]	21
2	DMF−Tris buffer[c]	−0.18	−0.02	−0.10 [160]	1.0
	DMF[f]	−0.08, −0.18	0.06		
	MeOH[f]	0.01, −0.09	0.17		
	MeCN[g]	0.06	0.23	0.15 [170]	1.0
	CH_2Cl_2[g]	0.27	0.38	0.32 [110]	1.0

[a] Cathodic scan for **1** and anodic scan for **2**. E_{pa} = anodic peak potential, E_{pc} = cathodic peak potential, i_{pc} = cathodic peak current, i_{pa} = anodic peak current, $\Delta E_p = E_{pa} - E_{pc}$, $E_{1/2} = (E_{pa} + E_{pc})/2$. [b] Supporting electrolyte: 50 mM Tris-HCl containing 0.1 M KCl for buffer and 0.1 M TBAP for nonaqueous solvents. [c] Ratio 1:4 v/v, pH 7.0. [d] Ratio 1:1 v/v, pH 7.0. [e] Additional cathodic peak at −0.29 V in DMF and at −0.28 V in MeOH with a large anodic response at 0.08 V for DMF and at 0.16 V vs SCE for MeOH. [f] Large anodic response with two small cathodic counterparts. [g] Additional weak cathodic peak at −0.28 V in MeCN and at −0.26 V in CH_2Cl_2.

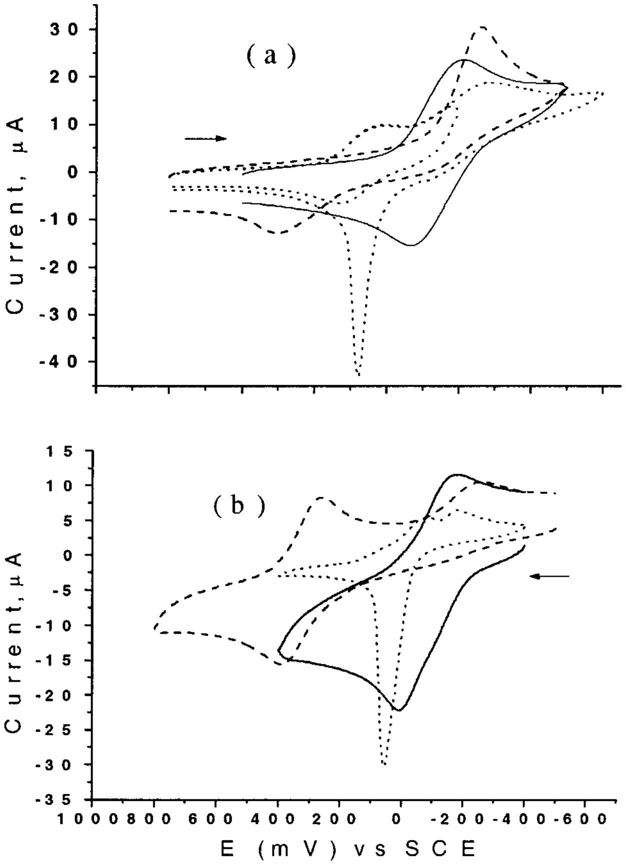


Figure 2. Cyclic voltammograms of $[Cu^{II}(L)(bpy)](ClO_4)$ (**1**) (a) and $[Cu^I(HL)(bpy)](ClO_4)$ (**2**) (b) in DMF−Tris-HCl/0.1 M KCl buffer (1:4 v/v, pH 7.0) (—), CH_2Cl_2−0.1 M TBAP (- - -), and DMF−0.1 M TBAP (···).

mogram at −0.13 V vs SCE with a ΔE_p value of 140 mV at 50 mV s^{-1}. The ΔE_p values range between 140 and 170 mV at 50−200 mV s^{-1} with an i_{pc}/i_{pa} ratio of 1.1. The voltammetric response is assignable to the Cu(II)/Cu(I) couple. The complex also shows a cathodic peak at −1.2 V with an anodic counterpart at −0.1 V, possibly due to the Cu(I)/Cu(0) couple, generating surface-adsorbed copper, as evidenced from the narrow width of the anodic response with a large peak current. The dependence of the $E_{1/2}$ value on the pH of the buffer medium is observed from a negative shift of 60 mV of the $E_{1/2}$ on increasing the pH value by one unit. The voltammetric response is similar in a MeOH−buffer medium.

The redox properties of **1** have also been studied in different nonaqueous solvents. The complex shows a cathodic peak near −0.2 V with an anodic counterpart at 0.2 V in CH_2Cl_2−0.1 M TBAP. The large separation of the peaks and an i_{pc}/i_{pa} ratio of 21 at 50 mV s^{-1} indicate poor reversibility of the electron transfer process. This is expected as the electroprotic process, $[Cu^{II}(L)(bpy)]^+ + H^+ + e^- \rightleftharpoons [Cu^I(HL)(bpy)]^+$, is unlikely to occur in an aprotic medium. A similar redox behavior is also observed in MeCN−0.1 M TBAP. In an aprotic medium like CH_2Cl_2 or MeCN, the one-electron-reduced species of **1**, $[Cu^I(L)(bpy)]^0$ is expected to be unstable in a square pyramidal geometry thus making the electron transfer process nearly irreversible in nature.

The redox process observed in MeOH or DMF medium is significantly different from those in the aprotic solvents. In MeOH−0.1 M TBAP, **1** shows a broad cathodic peak (E_{pc}) at −0.01 V with an anodic counterpart at 0.10 V. The i_{pc}/i_{pa} ratio of unity and the ΔE_p value of 110 mV at 50 mV s^{-1} indicate the quasi-reversible nature of the redox process. A similar redox behavior is also observed in DMF−0.1 M TBAP. The $E_{1/2}$ value of 0.07 V (ΔE_p = 125 mV at 50 mV s^{-1}) and an i_{pc}/i_{pa} ratio of unity at 20−200 mV s^{-1} suggest the quasi-reversible nature of the electron transfer process. In addition to the first cathodic response in DMF or MeOH medium, a second reduction peak appears near −0.3 V with a large anodic counterpart near 0.1 V possibly due to deposition of copper metal on the electrode surface. A similar voltammetric behavior is, however, not observed in CH_2Cl_2, MeCN, or the buffer medium.

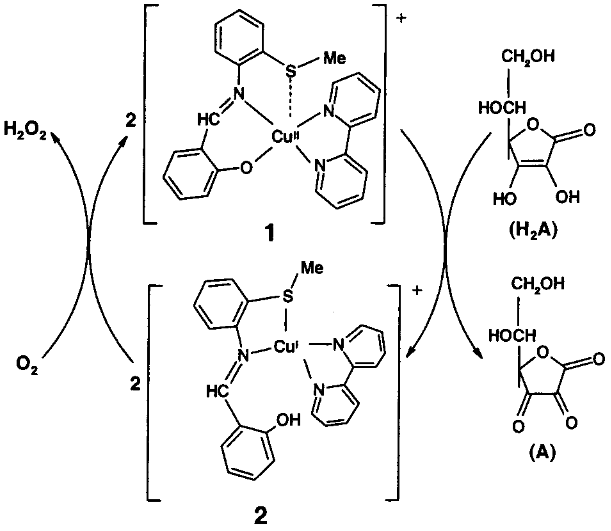
Complex **2** shows electrochemical behavior essentially similar to that of **1** in DMF−buffer (1:4 v/v, pH 7.0) mixture. In nonaqueous solvents like DMF−0.1 M TBAP or MeOH−0.1 M TBAP, the redox properties of **1** and **2** are similar. The redox properties of **2** differ considerably from those of **1** in aprotic solvents like CH_2Cl_2 or MeCN (Figure 2b). In CH_2Cl_2−0.1 M TBAP, complex **2** displays a quasi-reversible cyclic voltammetric response at 0.32 V with a ΔE_p value of 110 mV at 50 mV s^{-1}. The ΔE_p values range between 100 and 150 mV at 20−200 mV s^{-1} with an i_{pa}/i_{pc} ratio of unity. The redox process is assignable to the Cu(II)/Cu(I) couple involving the tetrahedral structure of **2** which does not seem to change in the cyclic voltammetric time scale in the aprotic medium. The high positive potential of the redox couple compared to that observed in the buffer medium indicates better stabilization of the copper(I) state in the aprotic solvent. This could only be feasible if we invoke a tetrahedral structure for complex **2** having a Cu−S bond and the noninvolvement of the OH group in the metal−ligand binding. Complex **2** also shows a quasi reversible redox process in MeCN−0.1 M TBAP at 0.15 V. In addition to this process, an irreversible weak cathodic response is observed near −0.25 V in CH_2Cl_2 or MeCN. The origin of this peak could be due to conversion of **2** to **1** in trace quantity during the electrochemical experiments.

Complex **2** was prepared by reacting **1** with ascorbic acid (H_2A) under dinitrogen atmosphere. It has been observed that **2** converts to **1** on exposure to air. The catalytic cycle is found to be effective for a turnover frequency of ca. 320 in MeOH−50 mM Tris-HCl buffer medium (1:1 v/v, pH 7.0) (Scheme 2). Similar catalytic processes involving a Cu(II)/Cu(I) redox couple, a reducing agent, and dioxygen in generating hydrogen peroxide are well-known in copper chemistry.[3,29,30] The significance of the present work lies in the observation of a catalytic cycle involving two copper species having $Cu^{II}N_3OS$ and $Cu^{I}N_3S$ coordination geometries thus modeling the structural changes involved in the enzymatic process at the Cu_B site in dopamine β-hydroxylase.

Conclusion

Our attempts to synthesize a copper(II) complex as a structural model for the oxidized form of the Cu_B site of dopamine β-hydroxylase has been successful. The copper(II) complex with a CuN_3OS coordination geometry exemplifies a structural model displaying a weakly bound axial sulfur ligand in a distorted square pyramidal geometry. The complex, on reduction with ascorbic acid, forms a copper(I) species with a CuN_3S coordination geometry which models the structure of the Cu_B site in the reduced state.

Scheme 2. Catalytic Cycle Showing the Oxidation of Ascorbic Acid by Dioxygen Mediated by **1** and **2** in MeOH−50 mM Tris-HCl Buffer Medium (pH 7.0)



Both the copper(I) and copper(II) complexes show similar redox behavior for the Cu(II)/Cu(I) couple in a buffer medium. The electroprotic reaction involving **1** and **2** in an aqueous medium is quasi-reversible in nature, giving voltammetric responses with an i_{pc}/i_{pa} ratio of unity at various scan rates. In a nonaqueous medium like methanol or DMF, the redox behavior is complicated. A different voltammetric response is obtained in aprotic solvents like MeCN or CH_2Cl_2−0.1 M TBAP. The ineffectiveness of the electroprotic reaction to be operative in an aprotic medium has caused a virtual trapping of the coordination geometry. While **1** shows a nearly irreversible electron transfer reduction process for the Cu(II)/Cu(I) couple, complex **2** displays a quasi-reversible Cu(II)/Cu(I) couple involving primarily the sulfur-bonded species. The electrochemical data are of significance toward understanding the effect of the structural changes associated with the oxidized and reduced forms of the Cu_B site in DβH under physiological reaction conditions.

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Supporting Information Available: ^1H NMR spectrum of complex **2** (Figure S1) and detailed crystallographic data, atomic positional parameters, and bond lengths and angles in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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