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Synthesis, structure and DNA binding studies of mononuclear copper(II) complexes with mixed donor macroacyclic ligands, 2,6-bis({*N*-[2&3-(phenylselenato)alkyl]}benzimidoyl)-4-methylphenol

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ABSTRACT

Two new phenol based macroacyclic Schiff base ligands, 2,6-bis({*N*-[2-(phenylselenato)ethyl]}-benzimidoyl)-4-methylphenol (bpebmpH, **1**) and 2,6-bis({*N*-[3-(phenylselenato)propyl]}benzimidoyl)-4-methylphenol (bppbmpH, **2**) of the Se_2N_2O type have been prepared by the condensation of 4-methyl-2,6-dibenzoylphenol (mdbpH) with the appropriate (for specific reactions) phenylselenato(alkyl)amine. These ligands with Cu(II) acetate monohydrate in a 2:1 molar ratio in methanol form complexes of the composition $[(C_6H_2(O)(CH_3)\{(C_6H_5)C{=}N(CH_2)_nSe(C_6H_5)\}\{(C_6H_5)C{=}O\}_2Cu]$ (**3** ($n = 2$), **4** ($n = 3$)) with the loss of phenylselenato(alkyl)amine and acetic acid. In both these complexes, one arm of the ligand molecule undergoes hydrolysis, and links with Cu(II) in a bidentate (NO) fashion, as confirmed by single crystal X-ray crystallography of complex **3**. The selenium atoms do not form part of the copper(II) distorted square planar coordination sphere which has a *trans*-CuN_2O_2 core. The average Cu–N and Cu–O distances are, respectively, 1.973(3) and 1.898(2) Å. The N–Cu–N and O–Cu–O angles are, respectively, 167.4(11)° and 164.5(12)°. The compounds **1–4** have been characterized by elemental analysis, conductivity measurements, mass spectrometry, IR, electronic, ^1H and $^{77}Se\{^1H\}$ NMR spectroscopy and cyclic voltammetry. The interaction of complex **3** with calf thymus DNA has been investigated by a spectrophotometric method and cyclic voltammetry.

1. Introduction

Ligands bearing variable donor functionalities such as O, S, N and P in their structural framework have been studied for several years and continue to be an area of active research for understanding the properties of donors that offer the opportunity to design metal complexes for specific purposes and applications [1–27]. The coordination chemistry of organochalcogen ligands containing 'hard' donor atoms (such as N and O) along with a 'soft' donor (Se or Te) is interesting because such a ligand framework can provide insight into competitive coordination behaviour between the 'hard' and 'soft' donors towards the metal center [28,29] and also stabilize low as well as high oxidation states of a metal atom. Such molecular systems may be important in transition metal catalyzed asymmetric synthesis [30,31] and as single source precursors in MOCVD processes [32–34]. Recently Khandelwal et al. have reported some pyridine based acyclic [35,36] and phenol based cyclic [37] Schiff bases. In fact, a number of polydentate ligands bearing N_3N_2, N_3O_2, N_3S_2 and NS_2P_2 are well documented and among them, a few of the systems have shown promising catalytic, biological, environmental and material properties [38–41]. We report herein the design and synthesis of a new (Se_2N_2O) molecular system (bpebmpH, **1** and bppbmpH, **2**), having both 'hard' and 'soft' donors in the ligand framework, and its reactivity towards Cu(II) ions. We also report our findings on a DNA binding study with one of the synthesized Cu(II) complexes.

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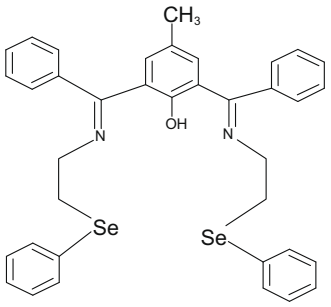
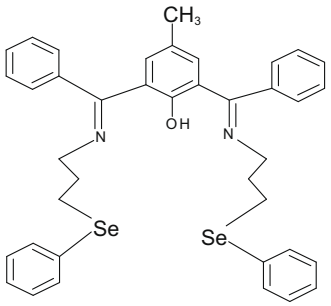


bpebmpH, 1



bppbmpH, 2

2. Experimental

All the chemicals used were of reagent grade. Solvents were purified by standard methods [42] and freshly distilled prior to use. The precursors 4-methyl-2,6-dibenzoylphenol (mdbpH) [43,44] and phenylselenato(alkyl) amine [45] were synthesized following the reported methods. Calf thymus DNA was obtained from Sigma and used as received. The sodium salt of CT-DNA was stored at 4 °C.

2.1. Physical measurements

Melting points of the compounds in the capillary tubes were recorded and are uncorrected. Elemental analyses were carried out on a Carlo-Erba Model DP 200 analyzer. The electrospray ion mass spectra (ESIMS) were recorded on a MICROMASS QUATTRO II triple quadrupole mass spectrometer. The solution was introduced into the ESI source through a syringe pump at the rate of 5 μL/min. The ESI capillary was set at 3.5 kV and the cone voltage was 40 V. The spectral print outs are the average of 6–8 scans. The ^{1}H NMR spectra were recorded on a Brucker AMX-400 FT NMR spectrophotometer in $CDCl_3$; the chemical shifts are recorded, relative to $SiMe_4$. The $^{77}Se\{^1H\}$ NMR spectra were recorded on the same instrument using Ph_2Se_2 as an external reference. Infrared spectra were recorded in the range 4000–400 cm^{-1} on a Nicolet Megna 750 FTIR spectrophotometer on a KBr disc. Electronic spectra were obtained with a Shimadzu UV-160A recording spectrophotometer.

2.1.1. Electrochemical measurements

Cyclic voltammetric measurements were carried out with an advanced electrochemical system, PARSTAT 2253 instrument equipped with a three-electrode system. The micro-cell model KO264 consisted of a glassy carbon working electrode, Pt wire as auxiliary electrode and a non-aqueous Ag/Ag^+ reference electrode with 0.1 M $AgNO_3$ in acetonitrile as the filling solution. Tetrabutylammonium perchlorate (0.1 M solution in CH_3CN) was used as the supporting electrolyte. Cyclic voltammograms with scan speeds of 50–350 mV/s were run in 10^{-4} M CH_3CN solution in a nitrogen atmosphere. Under these conditions the ferrocenium/ferrocene (fc^+/fc) couple shows a peak separation of 84 mV.

2.2. Synthesis of Schiff bases **1** and **2**

A solution of 4-methyl-2,6-dibenzoylphenol (mdbpH) (1.58 g, 5.0 mM) in dry acetonitrile (200 mL) was added drop-wise to a solution of the appropriate phenylselenato(ethyl)amine (2.0 g, 10.0 mM)/phenylselenato(propyl)amine (2.14 g, 10.0 mM) in acetonitrile (800 mL) in a 1:2 molar ratio respectively with stirring over a period of 7–8 h. The progress of the reaction was monitored by TLC. It took about 60 h for completion of the reaction. The organic solvent was removed under reduced pressure to obtain a viscous oily crude product. The product was purified by column chromatography (silica gel, 60–120 mesh, second fraction) using a solvent mixture of hexane:ethylacetate in 85:15 or 70:30 ratio. The characteristics of these compounds are given below.

2.2.1. 2,6-Bis({N-[2-(phenylselenato)ethyl]}benzimidoyl)-4-methylphenol(bpebmpH, **1**) [2,6-{$PhSe(CH_2)_2N{=}CPh\}_2C_6H_2$ (4-CH_3)(OH)]

Colour and state: yellow viscous liquid; yield: 2.48 g (73%). *Anal.* Calc. for $C_{37}H_{34}N_2OSe_2$: C, 65.29; H, 5.03; N, 4.11. Found: C, 65.23; H, 4.38; N, 4.08%. Positive ES–MS: *m/z* 683 [MH^+], 523, 500, 399, 158. FT IR (selected, cm^{-1}): *ν*(OH) 3450, *ν*(C=N) 1597, *ν*(C–O) 1252. UV–Vis λ_{max}/nm ($\varepsilon/M^{-1}\,cm^{-1}$) ($CH_3CN$): 391 ($PhO^- \rightarrow Ph$). ^{1}H NMR ($CDCl_3$, δ ppm): 15.90 (s, 1H, OH), 7.90–7.20 (m, 22H, C_6H_5 and C_6H_2), 3.47 (t, 4H, N–CH_2), 2.99 (t, 4H, Se–CH_2), 2.03 (s, 3H, CH_3). $^{77}Se\{^1H\}$ NMR ($CDCl_3$, δ ppm): 288.

2.2.2. 2,6-Bis({N-[3-(phenylselenato)propyl]}benzimidoyl)-4-methylphenol(bppbmpH, **2**) [2,6-{$PhSe(CH_2)_3N{=}CPh\}_2C_6H_2$ (4-CH_3)(OH)]

Colour and state: yellow viscous liquid; yield: 3.29 g (93%). *Anal.* Calc. for $C_{39}H_{38}N_2OSe_2$: C, 65.74; H, 5.37; N, 3.93. Found: C, 65.63; H, 5.31; N, 3.96%. Positive ES–MS: *m/z* 711 [MH^+], 553, 539, 514, 353, 158. FTIR (selected, cm^{-1}): *ν*(OH) 3416, *ν*(C=N) 1582, *ν*(C–O) 1253. UV–Vis λ_{max}/nm ($\varepsilon/M^{-1}\,cm^{-1}$) ($CH_3CN$): 390 ($PhO^- \rightarrow Ph$). ^{1}H NMR ($CDCl_3$, δ ppm): 15.90 (s, 1H, OH), 7.90–7.20 (m, 22H, C_6H_5 and C_6H_2), 3.40 (t, 4H, N–CH_2), 2.85 (t, 4H, Se–CH_2), 2.19 (q, 4 H, mid CH_2 (CH_2 between N–CH_2 and Se–CH_2)), 2.15 (s, 3H, CH_3). $^{77}Se\{^1H\}$ NMR ($CDCl_3$, δ ppm): 288.

2.3. Reactions of Schiff bases (**1**) and (**2**) with Cu(II)

A degassed solution of $Cu(OCOCH_3)_2.H_2O$ (0.10 g, 0.5 mM) in freshly distilled methanol (5 mL) was added to the degassed solution of the ligand *bpebmpH* (0.68 g, 1.0 mL)/*bppbmpH* (0.71 g, 1.0 mM) in dry methanol (15 mL) under an argon atmosphere. The reaction was carried out at room temperature with vigorous stirring. Precipitation of a green solid started almost immediately after mixing the reactants. After stirring the reaction mixture for 12 h, the precipitate thus obtained was filtered, washed with cold methanol and diethylether, and dried under vacuum. The characteristics of these complexes are given below.

2.3.1. Bis (2-[N-{2-(phenylselenato)ethyl}benzimidoyl]-6-benzoyl-4-methylphenolato)copper(II) (**3**) [(C_6H_2(O) (4-CH_3){PhC=N(CH_2)$_2$SePh}PhCO)$_2$.Cu]

Colour and state: dark green crystalline solid; yield: 0.42 g (79%). M.p.165 °C. *Anal.* Calc. for $C_{58}H_{48}N_2O_4Se_2Cu$: C, 65.81; H, 4.57; N, 2.64. Found: C, 65.12; H, 4.68; N, 2.51%. Positive ES–MS: *m/z* 1060 [MH^+]. FTIR (selected, cm^{-1}): *ν*(C=O) 1656, *ν*(C=N) 1531, *ν*(C–O) 1244, *ν*(Cu–N) 578, *ν*(Cu–O) 445. UV–Vis (nm) ($\varepsilon/M^{-1}cm^{-1}$)($CH_3CN$): 610 (167), 380 (10,080). ^{1}H NMR ($CDCl_3$, δ ppm): 7.90–7.20 (m, 34H, C_6H_5 and C_6H_2), 3.56 (t, 4H, N–CH_2), 3.05 (t, 4H, Se–CH_2), 2.07 (s, 3H, CH_3). Λ_M (10^{-3} M, CH_3CN, 298 K): 15 *S* cm^2 mol^{-1}.

2.3.2. Bis (2-[N-{3-(phenylselenato)propyl}benzimidoyl]-6-benzoyl-4-methylphenolato)copper(II) (**4**) [(C_6H_2(O)(4-CH_3) {PhC=N(CH_2)$_3$SePh}PhCO)$_2$.Cu)]

Colour and state: light green crystalline solid; yield: 0.29 g, (54%). M.p.176 °C. *Anal.* Calc. for $C_{60}H_{52}N_2O_4Se_2Cu$: C, 66.32; H, 4.82; N, 2.57. Found: C, 66.42; H, 4.61; N, 2.48%. Positive ES–MS: *m/z* 1088 [MH^+]. FTIR (selected, cm^{-1}): *ν*(C=O) 1657, *ν*(C=N)

1532, ν(C–O) 1244, ν(Cu–N) 569, ν(Cu–O) 445. UV–Vis (nm) (ε/M^{-1} cm^{-1}) (CH_3CN): 615 (170), 389 (10,100). ^1H NMR ($CDCl_3$, δ ppm): 7.90–7.20 (m, 34H, C_6H_5 and C_6H_2), 3.56 (t, 4H, N–CH_2), 2.85 (t, 4H, Se–CH_2), 2.19 (q, 4 H, mid-CH_2), 2.14 (s, 3H, CH_3). Λ_M (10^{-3} M, CH_3CN, 298 K): 70 S cm^2 mol^{-1}.

2.4. DNA binding studies

The experiments involving the interaction of the complex with CT-DNA were carried out in doubly distilled water buffer containing 5.0 mM Tris [Tris(hydroxymethyl)-aminomethane] and 50 mM NaCl and adjusted to pH 7.2 with hydrochloric acid. Solutions of CT-DNA gave ratios of absorbance at 260 and 280 nm of about 1.8–1.9, indicating that the DNA was free of protein contamination [46]. The DNA concentration per nucleotide was determined spectrophotometrically by employing a molar absorption coefficient of 6600 M^{-1} cm^{-1} at 260 nm after 1:100 dilution [47]. The complex was dissolved in 1% DMSO and 99% Tris–HCl buffer (5.0 mM Tris–HCl, 50 mM NaCl, pH 7.2) at a concentration of 3.0×10^{-5} M. An absorption titration was performed on 30 μmol L^{-1} compound by varying the concentration of nucleic acid. While measuring the absorption spectra, an equal amount of CT-DNA was added to both the compound solution and the reference solution to eliminate the absorbance of CT-DNA itself. Titration curves were constructed from the fractional change in absorption intensity as a function of DNA concentration. The intrinsic binding constant, K_b of the complex with CT-DNA was determined according to the following equation [48] through a plot of [DNA]/($\varepsilon_a - \varepsilon_f$) versus [DNA]/($\varepsilon_b - \varepsilon_f$)

$$[DNA]/(\varepsilon_a - \varepsilon_f) = [DNA]/(\varepsilon_b - \varepsilon_f) + 1/K_b(\varepsilon_b - \varepsilon_f), \quad (1)$$

where [DNA] is the concentration of DNA in base pairs, the apparent absorption coefficients ε_a, ε_f and ε_b correspond to A_{obsd}/[Cu], the extinction coefficient for the free copper complex and the extinction coefficient for the bound copper complex, respectively. In plots of [DNA]/($\varepsilon_a - \varepsilon_f$) versus [DNA]/($\varepsilon_b - \varepsilon_f$), K_b is given by the ratio of the slope to the intercept.

For the cyclic voltammetry, the supporting electrolyte was 50 mM NaCl, 5 mM Tris, pH 7.2 and an aqueous Ag/AgCl reference electrode with 3 M NaCl in saturated AgCl as the filling solution was used.

2.5. X-ray structure determination

Crystals of the complex 3 were grown as dark green needles by slow evaporation from the chloroform solution. Data were collected on a Nonius-Kappa CCD diffractometer and the structure solution and refinements were made by SHELXL-97 [49], as incorporated in the package WINGX [50]. Absorption corrections were made by MULTISCAN [51]. Non-hydrogen atoms were anisotropic and hydrogen atom positions were included in the riding mode. The ORTEP-3 program [52] was used to prepare the molecular drawings. Data collection parameters are given in Table 1. Selected bond lengths and angles are listed in Table 2.

Table 1
Crystal data and structure refinement for the copper complex **3**.

Empirical formula	$C_{58}H_{48}CuN_2O_4Se_2$
Formula weight	1058.44
T (K)	173(2)
Wavelength (Å)	0.71073
Crystal system	monoclinic
Space group	$P2_1/c$ (No. 14)
Unit cell dimensions	
a (Å)	9.4574(1)
b (Å)	32.4848(7)
c (Å)	15.7356(3)
α (°)	90
β (°)	5.842(1)
γ (°)	90
Volume (Å^3)	4809.21(15)
Z	4
Density (calculated) (Mg/m^3)	1.46
Absorption coefficient (mm^{-1})	2.02
F(0 0 0)	2156
Crystal size (mm^3)	0.25 × 0.20 × 0.05
θ Range for data collection (°)	3.45–26.02.
Index ranges	$-11 \leqslant h \leqslant 11$, $-36 \leqslant k \leqslant 40$, $-19 \leqslant l \leqslant 18$
Reflections collected	32 720
Independent reflections	9413 [R_{int} = 0.060]
Reflections with $I > 2\sigma(I)$	6496
Completeness to θ = 26.02°	99.0%
$T_{max.}$ and $T_{min.}$	0.7705 and 0.6207
Refinement method	full-matrix least-squares on F^2
Data/restraints/parameters	9413/0/606
Goodness-of-fit (GOF) on F^2	1.009
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.050, wR_2 = 0.098
R indices (all data)	R_1 = 0.088, wR_2 = 0.112
Largest difference peak and hole (e Å^{-3})	0.99 and −1.09

Table 2
Selected bond lengths (Å) and bond angles (°) for compound **3**.

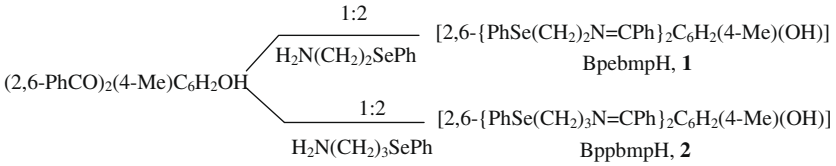
Bond lengths	
Cu–O(3)	1.884(2)
Cu–O(1)	1.913(2)
Cu–N(1)	1.973(3)
Cu–N(2)	1.974(3)
Se(1)–C(24)	1.925(4)
Se(1)–C(23)	1.938(4)
Se(2)–C(53)	1.913(4)
Se(2)–C(52)	1.949(4)
O(1)–C(1)	1.311(4)
O(2)–C(7)	1.217(4)
O(3)–C(30)	1.315(4)
O(4)–C(36)	1.220(4)
N(1)–C(15)	1.298(4)
N(1)–C(22)	1.479(4)
N(2)–C(44)	1.298(4)
N(2)–C(51)	1.485(4)
Bond angles	
O(3)–Cu–O(1)	167.38(11)
O(3)–Cu–N(1)	88.23(10)
O(1)–Cu–N(1)	89.35(11)
O(3)–Cu–N(2)	92.27(11)
O(1)–Cu–N(2)	93.35(11)
N(1)–Cu–N(2)	164.50(12)
C(22)–N(1)–Cu	116.8(2)
C(51)–N(2)–Cu	112.6(2)

3. Results and discussion

3.1. Ligand syntheses and characterization

The monoprotic hybrid macroacyclic ligands **1** and **2** were synthesized via a one step dipodal condensation of 4-methyl-2,6-dibenzoylphenol with the appropriate phenylselenato(alkyl)amine in a 1:2 molar ratio in acetonitrile (Scheme 1).

The condensation product is dependent on the reaction conditions. In a concentrated solution of reactants, only one carbonyl group of phenol condenses with the amine group of the phenylselenato(alkyl)amine to give rise to open-chain end-off unsymmetrical ($SeNO_2$) ligands, whereas in dilute solution both arms condense to yield symmetrical (Se_2N_2O) ligands in high yield along with some one arm condensed products. The open-chain end-off unsymmetrical ($SeNO_2$) type ligands are less soluble in the solvent, and therefore separate out first as a yellow solid powder. However following the experimental conditions, open-chain end-off



Scheme 1. Synthesis of ligands 1 and 2.

symmetrical (Se_2N_2O) macroacyclic ligands (**1**) and (**2**) were obtained in the pure form. Since the ligands (**1**) and (**2**) are obtained in good yield, after chromatographic workup, only these have been used for further characterization and complexation reactions.

The elemental analyses agreed well with their formulation. The ESI mass spectra of the ligands show the molecular ion peak along with typical isotopic patterns for selenium containing peaks. The molecular ion peak of these ligands corresponds to the condensation product of the precursors, 4-methyl-2,6-dibenzoylphenol with phenylselenato(ethyl)amine and phenylselenato(propyl)amine in a 1:2 molar ratio, respectively. The IR spectra of both ligands (**1**) and (**2**) show no N–H stretching frequency, suggesting that both the nitrogens are tertiary. The bands at 1597 cm^{-1} in **1** and 1581 cm^{-1} in **2** are attributable to ν(C=N). In addition, another band of low intensity appears in both the ligands at 1662 cm^{-1}, which may be due to ν(C=O). The appearance of this band may be due to presence of ethylacetate in traces, which was used as an eluent during the purification of the ligands by column chromatography. Further, a broad band appearing around 3450 in **1** and 3416 cm^{-1} in **2** due to ν(O–H) strongly suggests the presence of intramolecular hydrogen bonding between the phenolic hydrogen and azomethine nitrogen.

Intramolecular hydrogen bonding is also confirmed by significant deshielding of the phenolic (OH) proton signal by the order of 3.7 ppm as compared to 4-methyl-2,6-dibenzoylphenol (appears at δ 12.2 ppm) in their ^{1}H NMR spectra. The triplets due to N–CH_2 and Se–CH_2 protons in both ligands are appreciably shifted downfield as compared to the precursors 2- phenylselenato(ethyl)amine (δ 3.1 (t, 4H, N–CH_2), 2.9 (t, 4H, Se–CH_2)) and phenylselenato(propyl)amine (δ 2.9 (t, N–CH_2), 2.71 (t, Se–CH_2)). The appreciable deshielding in these proton signals along with the intensity ratios, as well as the disappearance of the –NH_2 signal [δ = 1.55 ppm {phenylselenato(ethyl)amine}, δ = 1.05 ppm {phenylselenato(propyl)amine}] suggest the condensation of the benzoyl oxygen of 4-methyl-2,6-dibenzoylphenol with the –NH_2 group of phenylselenato(alkyl)amine in a 1:2 molar ratio.

Structurally, this ligand framework is interesting as the presence of hetero (N, O, Se) donor sites could make it practical to design molecular complexes with a variety of coordination modes, depending on the nature of the central metal atom.

3.2. Synthesis and properties of complexes *3* and *4*

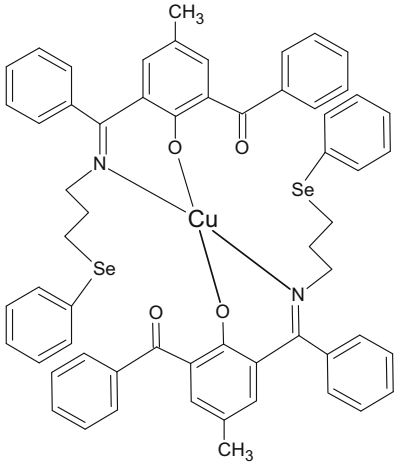
The reactivity of the selenium bearing ligands towards $Cu(OCOCH_3)_2H_2O$ has been studied by reacting them in a 2:1 molar ratio. The products obtained are found to have the composition $[(C_6H_2(O)(CH_3)\{(C_6H_5)C{=}N(CH_2)_nSe(C_6H_5)\}\{(C_6H_5)C{=}O\})_2Cu]$; n = 2, 3. The analytical data surprisingly suggests that one arm of the ligand is hydrolyzed at the C=N position, resulting in the release of the $PhSe(CH_2)_nNH_2$ moiety, whilst the other arm remains intact. The Cu(II) compounds are soluble in polar as well as non-polar solvents and are non-electrolytes.

The mass spectra of the Cu(II) complexes exhibit a molecular ion peak corresponding to a mass of double the partially hydrolyzed ligand plus one Cu(II) atom, suggesting the formation of complexes bearing a 2:1 ligand to metal stoichiometry. The ESIMS show a molecular ion peak with the typical isotopic patterns for selenium containing peaks.

In the infrared spectra of the Cu(II) complexes the absence of a ν(OH) absorption band suggests the combination of the phenolic proton with the CH_3COO^- ion of $Cu(OCOCH_3)_2H_2O$, and the linkage of the phenolic O with the Cu(II) ion. The combination of the phenolic proton of the ligand with the acetate group of $Cu(OCOCH_3)_2$-H_2O resulted in the release of water and the formation of CH_3COOH. The acid thus liberated probably catalyzes the hydrolysis of one arm of the ligand at the C=N position. Further, the ν(C=N) vibration is shifted to a lower frequency by ~50 cm^{-1}, suggesting the coordination of the azomethine N with Cu(II). However, the ν(C=O) band is found to be at almost the same position as in the precursor 4-methyl-2,6-dibenzoylphenol. This has been attributed to the non-involvement of the benzoyl O in coordination with the Cu(II) ion. Medium intensity bands, one in the 569–578 cm^{-1} region and one at 445 cm^{-1}, for both complexes can be assigned to ν(M–N) and ν(M–O), respectively [53,54].

The paramagnetic square planar Cu(II) complexes are expected to show three allowed absorption bands in the electronic spectra corresponding to the transitions: $e_g \rightarrow b_{1g}$ (d_{xz}, $d_{yz} \rightarrow d_{x2-y2}$), $a_{1g} \rightarrow b_{1g}$ ($d_{z2} \rightarrow d_{x2-y2}$), $b_{2g} \rightarrow b_{1g}$ ($d_{xy} \rightarrow d_{x2-y2}$) [55]. In the present investigation the Cu(II) complexes in CH_3CN show only one band in the 610–615 nm region before the charge transfer band takes over at higher energies. This band seems to have a major contribution from the $e_g \rightarrow b_{1g}$ transition, characteristic of a distorted square planar geometry [56].

The ^{1}H NMR spectra of the Cu(II) complexes do not show any phenolic proton signal, suggesting its displacement and coordination of the phenolic oxygen with Cu(II). Thus, based on the linkages in **3** and **4**, the partially hydrolyzed ligand molecules behave in a bidentate fashion and two molecules coordinate through the azomethine N and phenolic O atoms to one Cu(II) ion to give a N_2O_2 coordination sphere and forming two stable six membered rings around the Cu(II) ion. These binding modes are also confirmed by the X-ray crystal structure of complex **3**.



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3.3. Crystal structure of complex **3**

The molecular structure of complex **3** is shown in Fig. 1. The two monoanionic ligands are bidentate, coordinating through the imino nitrogen and phenolic oxygen atoms, with both the nitrogen donors and the phenolic oxygen donors being *trans*. The copper coordination sphere is almost square planar, slightly distorted towards tetrahedral [O–Cu–O 167(11)°, N–Cu–N 164(12)°]. The Se atoms are not coordinated to Cu [Cu–Se 4.05, 4.82 Å]; they are on one side of the molecule and the phenol fragments are on the other side. There is no symmetry in the molecule as a whole. Both *cis* and *trans* complexes with the CuO_2N_2 core are known. The configuration is probably determined mainly by intraligand constraints e.g. chains linking N atoms or by steric interactions between the ligands. The latter effect probably accounts for the *trans* configuration here. The phenolic C–O distances in the complex [1.311(4) and 1.315(4) Å] are significantly shorter than that in mdbpH [1.360(4) Å] [43]. The average Cu–O and Cu–N bond lengths [1.898(2) and 1.973(3) Å, respectively] are similar to those in other *trans*-Schiff base complexes [57,58]. It is possible that the bond lengths in the *cis*-complexes are slightly longer [54] [Cu–N 1.964(2)–1.974(2) Å, Cu–O 1.926(2)–1.938(2) Å]. The Cu–N bonds in imino complexes, or where the rings are saturated, are longer [59–62]. One chelate ring, containing NO, is almost planar, with Cu slightly above the mean plane; the other ring is in a distorted boat configuration. The benzoyl O does not coordinate to the copper because the large Cu–N–CH_2CH_2SePh angle directs the ligand away from it [Cu–N1–C22 116.8(2)° and Cu–N2–C51 112.6(2)°, both wider than tetrahedral angles].

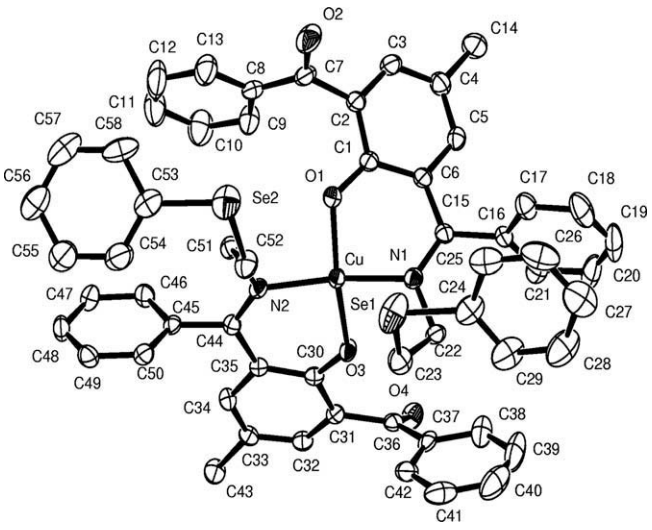

Fig. 1. Molecular structure of complex **3**.

Table 3
CV data of a 0.1 mM solution of the Schiff bases, bpebmpH **1** and bppbmpH **2** in CH_3CN/0.1 M NBu_4ClO_4 at a platinum electrode vs. Ag/0.1 M $AgNO_3$ at different scan rates.

Compound	Scan Rate	E_{pa} (V)	i_{pa} (μA)
bpebmpH **1**	100	0.760	28.40
	200	0.769	40.61
	300	0.784	49.45
	400	0.787	56.81
	500	0.793	62.83
bppbmpH **2**	100	0.559	1.570
	200	0.454	5.344
	300	0.589	6.399
	400	0.601	7.681
	500	0.634	9.366

3.4. Cyclic voltammetry

The electrochemical properties of the ligands and complexes were investigated by cyclic voltammograms (CV) in 0.1 M [NBu_4][ClO_4] in CH_3CN solution with 100–500 mV/s scan rates. All CV data were collected under a nitrogen atmosphere and potentials are reported with reference to Ag/0.1 M Ag^+. The results are summarized in Tables 3 and 4. The cyclic voltammograms of the ligands bpebmpH **1** and bppbmpH **2** (Fig. 2) exhibit an oxidation peak at

Table 4
CV data of a 0.1 mM solution of the complexes **3** and **4** in CH_3CN/0.1 M NBu_4ClO_4 at a platinum electrode vs. Ag/0.1 M $AgNO_3$ at different scan rates.

Complex	Scan Rate	E_{pa}(V)	i_{pa} (μA)	E_{pc}(V)	i_{pc} (μA)
Complex **3**	100	−0.962	5.585	−1.382	−26.20
	200	−0.374	15.27	−1.382	−49.54
	300	−0.386	22.49	−1.412	−73.99
	400	−0.374	30.56	−1.466	−99.47
	500	−0.374	42.78	−1.466	−119.70
Complex **4**	100	−0.872	5.109	−1.400	−18.98
	200	−0.326	20.54	−1.562	−62.19
	300	−0.296	29.10	−1.574	−79.46
	400	−0.278	40.23	−1.598	−89.64
	500	−0.254	51.40	−1.616	−108.10

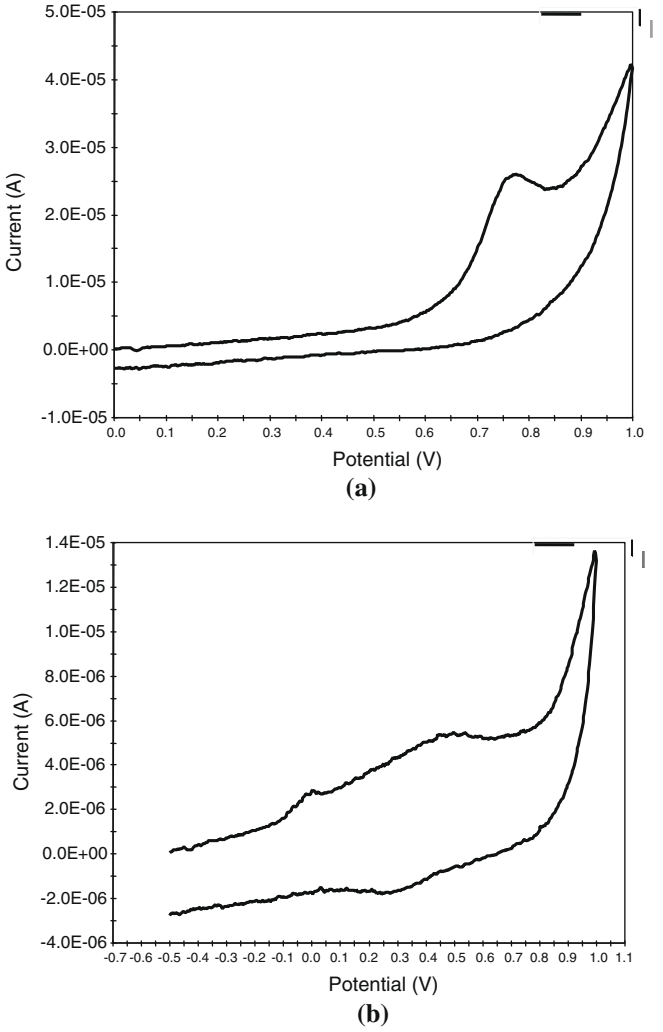

Fig. 2. Cyclic voltammograms of 0.1 mM solutions of the Schiff base bpebmpH **1** (a) and bppbmpH **2** (b) in CH_3CN/0.1 M NBu_4ClO_4 at a platinum electrode vs. Ag/0.1 M Ag^+ at 100 mV/s scan rate.

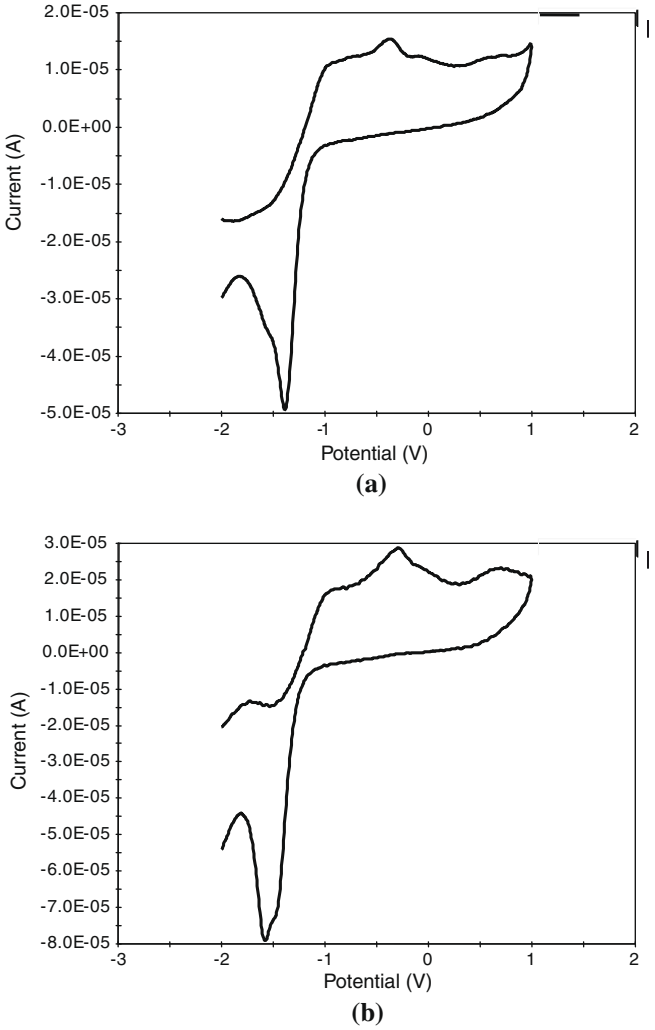

Fig. 3. Cyclic voltammograms of a 0.1 mM solution of complex **3** (a) and complex **4** (b) in CH_3CN/0.1 M NBu_4ClO_4 at a platinum electrode vs. Ag/0.1 M $AgNO_3$ at 200 mV/s scan rate.

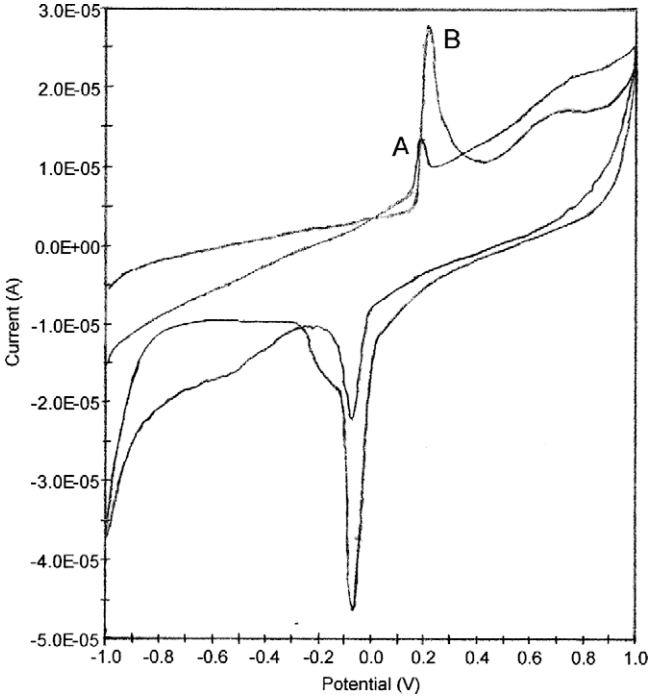

Fig. 5. Cyclic voltammograms of complex **3** (30 μM) in the absence (A) and the presence (B) of CT-DNA (30 μM) in 50 mM NaCl, 5 mM Tris, pH 7.2. Scan rate, 100 mV/s.

E_{pa} 0.778 and 0.567 V, respectively. The oxidation of **1** and **2** is electrochemically irreversible in spite of the strong intramolecular O–H···N hydrogen bond involving the phenol O and the imine N atoms. In the cyclic voltammograms of complexes **3** and **4** (Fig. 3), there is one oxidation peak (E_{pa} −0.494 (**3**), −0.405 V (**4**)) and one reduction peak (E_{pc} −1.422 (**3**), −1.550 V (**4**)). The reduction peaks for the complexes are due to Cu^{II} changing to Cu^{I}. The peak separation and current ratio between the related cathodic and anodic waves change with scan rate, indicating a quasi-reversible process. Free $Cu(CH_3COO)_2{\cdot}H_2O$ shows a different reduction

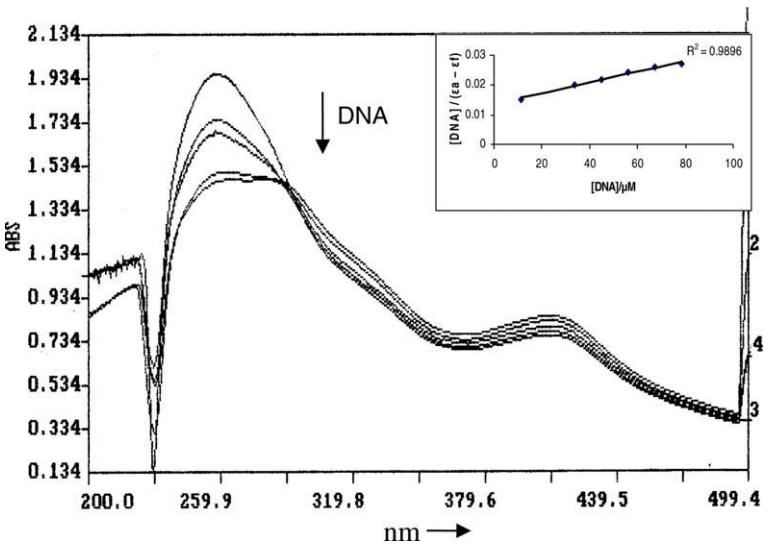

Fig. 4. Absorption spectra of complex **3** (30 μM) at 7.2 pH in the presence of increasing amounts of CT-DNA (0–80 μM). Inset: plot of [DNA]/($\varepsilon_a - \varepsilon_f$) vs. [DNA] for the titration of DNA with the Cu(II) complex **3**.

Table 5
Cyclic voltammetric behaviour of complex **3** in the presence of CT-DNA.

Scan rate (mV/s)	R	E_{pa}/V (i_{pa})/μA	E_{pc}/V (i_{pc})/μA	ΔE_p (mV)	$E^{\circ\prime}$ (V)	i_{pa}/i_{pc}
100	0	0.192 (13.75)	−0.068 (−22.34)	260	0.062	0.61
	30	0.224 (27.95)	−0.060 (−46.10)	284	0.082	0.61
	60	0.192 (27.66)	−0.032 (−42.63)	224	0.080	0.64
	90	0.196 (32.21)	−0.028 (−44.81)	224	0.084	0.71
	120	0.196 (32.31)	−0.032 (−45.03)	228	0.082	0.71
200	0	0.200 (24.52)	−0.076 (−33.31)	276	0.062	0.73
	30	0.240 (71.87)	−0.056 (−56.65)	296	0.092	1.26
	60	0.236 (62.85)	−0.064 (−67.44)	300	0.086	0.93
	90	0.228 (56.41)	−0.056 (−67.50)	284	0.086	0.84
	120	0.256 (88.62)	−0.052 (−65.38)	308	0.102	1.35

$\Delta E_p = (E_{pa} - E_{pc})$; $E^{\circ\prime} = 1/2(E_{pa} + E_{pc})$; complex 30 μM; R = [DNA]/[complex].
Supporting electrolyte: 50 mM NaCl + 5 mM Tris, pH 7.2; working electrode: Pt; reference electrode: Ag/AgCl.

peak at −0.707 V under similar conditions. The anodic peak potentials of the complexes are shifted to more negative values than that observed in the case of the ligand, which is in further conformity with the formation of a complex between the ligand and the Cu metal ion [63].

3.5. DNA binding properties of compound **3**

3.5.1. Absorption spectral studies

The application of electronic absorption spectroscopy is one of the most useful techniques for DNA binding studies [64]. Complex binding with DNA through intercalation usually results in hypochromism and bathochromism, due to the intercalative mode involving a strong stacking interaction between an aromatic chromophore and the DNA base pairs. The extent of the hypochromism commonly parallels the intercalative binding strength. The electronic absorption spectrum of complex **3** in 5 mM Tris–HCl/50 mM NaCl buffer exhibits bands around 408 and 264 nm. The band at 408 nm, arising from ligand-based transition, was used for the absorption spectral titration with CT-DNA. On incremental addition of DNA, the band shows only a small (6.0%) decrease in absorption accompanied by a small blue shift of 4 nm (Fig. 4). The binding constant K_b for the complex is found to be $1.46 \times 10^4\ M^{-1}$. These features are equivalent to those observed for the square planar Cu(II) complex Cu(*o*-VANAHE)$_2$ (*o*-VANAHE = 2(*o*-vanillinamine)-1-hydroxy-ethane; a bidentate Schiff base with a *trans*-CuN_2O_2 core) ($K_b = 7.3 \times 10^4\ M^{-1}$) [65]. The results suggest an association of the compound with DNA and it is also likely that this complex binds to the helix by intercalation [66].

3.5.2. Electrochemical studies

The cyclic voltammetric technique has been employed to study the interaction of the redox active Cu(II) complex with DNA in order to confirm the DNA bonding modes, suggested by the spectral studies. Typical CV behaviour of the copper complex in the absence (curve A) and presence (curve B) of CT-DNA is shown in Fig. 5. Summaries of the voltammetric results are given in Table 5. The cyclic voltammogram of complex **3** (v = 100 mV/s) in the absence of DNA featured the copper reduction of +2 to +1 at a cathodic peak potential, E_{pc}, of −0.068 V versus Ag/AgCl. Reoxidation of the +1 state occurred upon scan reversal at 0.192 V. The separation of the anodic and the cathodic peak potentials, ΔE_p, 260 mV (Table 5), indicates a quasi-reversible $1-e^-$ redox process. The formal potential, $E^{\circ\prime}$ (or voltammetric $E1/2$), taken as the average of E_{pc} and E_{pa}, was 0.062 V, in the absence of DNA. In presence of 30 μM DNA, at the same concentration of the complex, E_{pc} = −0.060 V and E_{pa} = 0.224 V. Thus, both the anodic and cathodic peak potentials shifted to more positive values versus a solution without DNA ($E^{\circ\prime}$ = 0.082 V). The value of ΔE_p in the presence of DNA was ca. 240 mV, showing that reversibility of the electron transfer process was maintained or even improved under these conditions. The apparent $E^{\circ\prime}$ shifted to more positive potentials by 20 mV in the presence of DNA. The peak current for reduction of the Cu(II) species, i_{pc}, decreased to 51% of that in the absence of DNA, for a solution with R = 30 (100 mV/s). The peak current for oxidation did not decrease under similar conditions. The ratio i_{pa}/i_{pc} was 0.61–0.71 with increasing R. Among the three kinds of binding modes for small molecules to DNA, Bard and coworkers [67] reported that if $E^{\circ\prime}$ shifted to a more negative value when small molecules interacted with DNA, the interaction mode was electrostatic binding. On the contrary, if $E^{\circ\prime}$ shifted to a more positive value, the interaction mode was intercalative binding. Thus, the observed results suggest that complex **3** interacts with DNA through an intercalative mode that involves a stacking interaction between the aromatic chromophore of the complex and the base pair of DNA.

4. Conclusions

In summary, two phenol based ligands **1** and **2** have been synthesized by dipodal condensation of 4-methyl-2,6-dibenzoylphenol with phenylselenato(alkyl)amine in acetonitrile in a 1:2 molar ratio respectively. The reaction of these ligands with Cu(II) metal ion revealed the cleavage of one arm of these ligands due to hydrolysis at the C=N position, leading to the release of the $PhSe(CH_2)_nNH_2$ (where n = 2, 3) moiety and the formation of a benzoyl group at one end. The partially hydrolyzed moiety of the ligands then forms complexes **3** and **4**, bearing a 2:1 ligand to metal stoichiometry in which two monoanionic ligands are bidentate coordinating through the azomethine N and phenolic O to one Cu(II) to give a N_2O_2 coordination sphere. Thus the phenolic proton of the ligand molecules is found to combine with the CH_3COO^- group of $Cu(OCOCH_3)H_2O$, liberating CH_3COOH. The structure of complex **3** revealed that the N_2O_2-donor sets of the two ligand fragments form a *trans*-distorted square planar configuration. Complex **3** shows binding with the helix of CT-DNA by intercalation.

5. Supplementary data

CCDC 706265 contains the supplementary crystallographic data for complex **3**. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

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