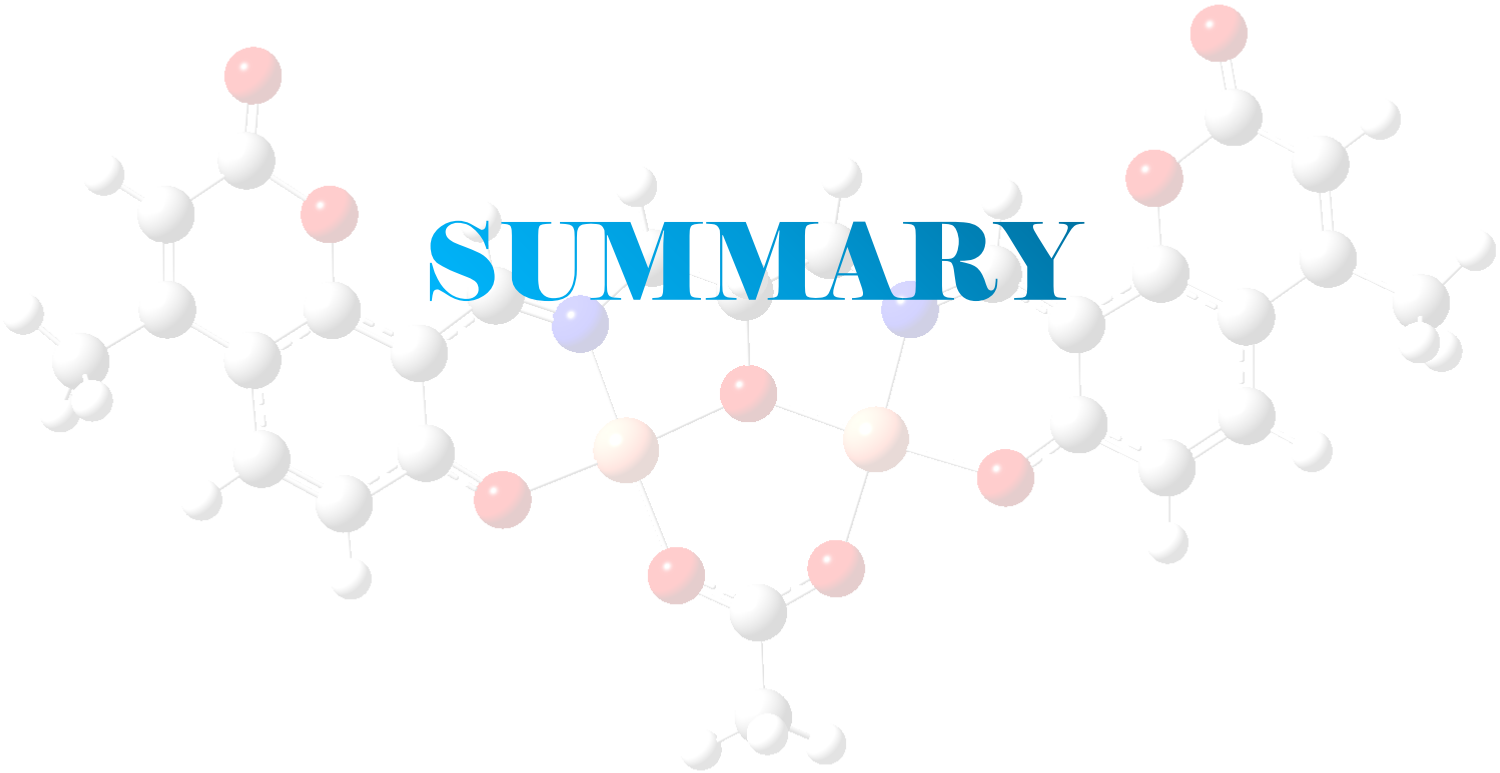


SUMMARY

The aim of this work was to develop new synthetic models for the type 3 active sites in copper proteins and get insight into the effect of auxiliary groups on the ligands on the activity of the complexes.

- Compartmental Schiff bases ligands were synthesized by condensation of dfc, dac, dap and bamnp with suitable biogenic amines, namely, tryptamine, histamine & pyridoxamine; N containing heterocyclic molecules such as N-aminoethyl piperazine, N-aminoethyl morpholine, N-aminoethyl pyrrolidine, 2-picoyl amine & tryptamine; and carbonyl compounds viz. 2-hydroxy-1-acetonaphthone, 1-hydroxy-2-acetonaphthone pyrrole-2-carboxaldehyde and 7-hydroxy-8-formyl-4-methyl coumarin. Homonuclear dicopper(II) complexes and heteronuclear copper(II)-zinc(II) complexes were synthesized using these ligands
- All ligands and complexes were characterized by various spectroscopic techniques such as UV-Vis and IR spectroscopies, mass spectrometry, elemental analysis and ESR spectroscopy.
- Crystal structures of representative complexes has been obtained.
- ESR spectra and magnetic properties of representative complexes suggest the presence of antiferromagnetic exchange between the copper(II) centers in the dicopper(II) complexes.
- SOD mimic activity of all synthesized ligands and complexes was studied by non-enzymatic (NADH-PMS-NBT) method to find their potential to dismutase superoxide.
- Ascorbic acid oxidase activity of all complexes was studied and the kinetic parameters determined.
- The catecholase activity of all complexes was studied for various o-diphenols as substrates, by varying parameters such as temperature, concentrations of substrate and catalysts. Michaelis-Menten approach was used to evaluate the potential of complexes as for functional models of catecholase.
- DNA and BSA binding studies of all synthesized compounds was carried out to find their efficacies to bind with the biomolecules using UV-Vis spectroscopy and fluorescence methods.
- Cytotoxic studies were carried out for selected copper(II) complexes on HepG2 cancer cell line.

The observations for all complexes are summarized in the tables given below:

SOD mimic activity

Cat.	IC_{50}	Dinuclear moiety	Endogenous bridge ligand	
C5	0.128	Cu-Cu	2,6-diacetyl-4-methylphenol	N-(aminoethyl) morpholine
C4	0.242	Cu-Cu	2,6-diacetyl-4-methylphenol	N-(aminoethyl) piperazine
C8	0.329	Cu-Cu	2,6-diacetyl-4-methylphenol	tryptamine
C1a	0.351	Cu-Cu	2,6-diformyl-4-methylphenol	Pyridoxamine
C13	0.385	Cu-Cu	2,6-diamiomethyl-4-nitrophenol	1-hyrdoxy-2-acetonaphthone
C2a	0.396	Cu-Cu	2,6-diformyl-4-methylphenol	tryptamine
C15	0.794	Cu-Cu	2,6-diamiomethyl-4-nitrophenol	2-formyl pyrrole
C14	0.925	Cu-Cu	2,6-diamiomethyl-4-nitrophenol	2-hyrdoxy-1-acetonaphthone
C6	1.157	Cu-Cu	2,6-diacetyl-4-methylphenol	N-(aminoethyl) pyrrolidine
C9	1.5582	Cu-Cu	1,3-diaminopropan-2-ol	1-hyrdoxy-2-acetonaphthone
C16	1.923	Cu-Cu	2,6-diamiomethyl-4-nitrophenol	8-formyl-7-hydroxy-4-Methylcoumarin
C10	2.4163	Cu-Cu	1,3-diaminopropan-2-ol	2-hyrdoxy-1-acetonaphthone
C2b	4.02	Cu-Zn	2,6-diformyl-4-methylphenol	tryptamine
C3a	7.45	Cu-Cu	2,6-diformyl-4-methylphenol	histamine
C1b	7.66	Cu-Zn	2,6-diformyl-4-methylphenol	pyridoxamine
C12	13.1729	Cu-Cu	1,3-diaminopropan-2-ol	8-formyl-7-hydroxy-4-Methylcoumarin
C3b	208.1	Cu-Zn	2,6-diformyl-4-methylphenol	histamine

Ascorbic Acid Oxidase activity

Cat.	k_{cat} (h^{-1})	E_a (kJ/mole)	Dinuclear moiety	Endogenous bridge ligand	
C8	725	70.1	Cu-Cu	2,6-diacetyl-4-methylphenol	tryptamine
C5	595	71.5	Cu-Cu	2,6-diacetyl-4-methylphenol	N-(2-aminoethyl)morpholine
C13	367	60.9	Cu-Cu	2,6-diamiomethyl-4-nitrophenol	1-hydroxy-2-acetonaphthone
C14	363	68.3	Cu-Cu	2,6-diamiomethyl-4-nitrophenol	2-hydroxy-1-acetonaphthone
C15	360	63.1	Cu-Cu	2,6-diamiomethyl-4-nitrophenol	2-formyl pyrrole
C6	340	74.6	Cu-Cu	2,6-diacetyl-4-methylphenol	N-(2-aminoethyl)pyrrolidine
C2a	334.9	65.4	Cu-Cu	2,6-diformyl-4-methylphenol	tryptamine
C2b	332	71	Cu-Zn	2,6-diformyl-4-methylphenol	tryptamine
C1a	332	70.4	Cu-Cu	2,6-diformyl-4-methylphenol	pyridoxamine
C4	321	77.4	Cu-Cu	2,6-diacetyl-4-methylphenol	N-(2-aminoethyl)piperazine
C16	217	61.9	Cu-Cu	2,6-diamiomethyl-4-nitrophenol	8-formyl-7-hydroxy-4-methylcoumarin
C10	202	92.7	Cu-Cu	1,3-diaminopropan-2-ol	2-hydroxy-1-acetonaphthone
C7	202	79.0	Cu-Cu	2,6-diacetyl-4-methylphenol	2-picoylamine
C9	173	58.4	Cu-Cu	1,3-diaminopropan-2-ol	1-hydroxy-2-acetonaphthone
C12	80.9	27.0	Cu-Cu	1,3-diaminopropan-2-ol	8-formyl-7-hydroxy-4-methylcoumarin
C1b	75.5	71.8	Cu-Zn	2,6-diformyl-4-methylphenol	pyridoxamine
C3b	50.7	78.4	Cu-Zn	2,6-diformyl-4-methylphenol	histamine
C3a	37.3	77.6	Cu-Cu	2,6-diformyl-4-methylphenol	histamine

Catecholase activity

3,5-DTBC

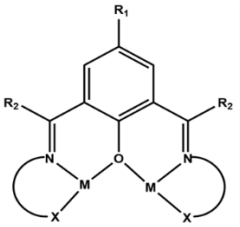
Cat.	k_{cat} (h^{-1})	E_a (kJ/mole)	Dinuclear moiety	Endogenous bridge ligand	
C6	832	16.3	Cu-Cu	2,6-diacetyl-4-methylphenol	N-(2-aminoethyl)pyrrolidine
C2a	624	24.26	Cu-Cu	2,6-diformyl-4-methylphenol	tryptamine
C8	133	19.7	Cu-Cu	2,6-diacetyl-4-methylphenol	tryptamine
C10	94.5	26.3	Cu-Cu	1,3-diaminopropan-2-ol	2-hydroxy-1-acetonaphthone
C13	45.9	12.9	Cu-Cu	2,6-bis(aminomethyl)-4-nitrophenol	1-hydroxy-2-acetonaphthone
C4	36.8	27.6	Cu-Cu	2,6-diacetyl-4-methylphenol	N-(2-aminoethyl)piperazine
C15	35.01	15.4	Cu-Cu	2,6-bis(aminomethyl)-4-nitrophenol	2-formyl pyrrole
C14	25.38	16.4	Cu-Cu	2,6-bis(aminomethyl)-4-nitrophenol	2-hydroxy-1-acetonaphthone
C5	18.9	30.0	Cu-Cu	2,6-diacetyl-4-methylphenol	N-(2-aminoethyl)morpholine
C3a	17.2	27.55	Cu-Cu	2,6-diformyl-4-methylphenol	histamine
C9	5.81	42.0	Cu-Cu	1,3-diaminopropan-2-ol	1-hydroxy-2-acetonaphthone
C7	3.19	38.0	Cu-Cu	2,6-diacetyl-4-methylphenol	2-picoylamine
C2b	0	0	Cu-Zn	2,6-diformyl-4-methylphenol	tryptamine
C1b	0	0	Cu-Zn	2,6-diformyl-4-methylphenol	pyridoxamine
C3b	0	0	Cu-Zn	2,6-diformyl-4-methylphenol	histamine
C1a	0	0	Cu-Cu	2,6-diformyl-4-methylphenol	pyridoxamine
C16	0	0	Cu-Cu	2,6-bis(aminomethyl)-4-nitrophenol	8-formyl-7-hydroxy-4-methylcoumarin
C12	0	0	Cu-Cu	1,3-diaminopropan-2-ol	8-formyl-7-hydroxy-4-methylcoumarin

4-MC

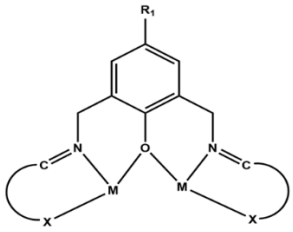
Cat.	k_{cat} (h^{-1})	E_a (kJ/mole)	Dinuclear moiety	Endogenous bridge ligand	
C10	24.3	37.7	Cu-Cu	1,3-diaminopropan-2-ol	2-hydroxy-1-acetonaphthone
C9	18.7	17.2	Cu-Cu	1,3-diaminopropan-2-ol	1-hydroxy-2-acetonaphthone
C4	16.4	26.7	Cu-Cu	2,6-diacetyl-4-methylphenol	N-(2-aminoethyl)piperazine
C8	14.0	60.1	Cu-Cu	2,6-diacetyl-4-methylphenol	tryptamine
C3a	10.7	31.41	Cu-Cu	2,6-diformyl-4-methylphenol	histamine
C5	8.91	17.7	Cu-Cu	2,6-diacetyl-4-methylphenol	N-(2-aminoethyl)morpholine
C6	6.61	39.1	Cu-Cu	2,6-diacetyl-4-methylphenol	N-(2-aminoethyl)pyrrolidine
C13	4.365	41.9	Cu-Cu	2,6-bis(aminomethyl)-4-nitrophenol	1-hydroxy-2-acetonaphthone
C2a	3.86	30.77	Cu-Cu	2,6-diformyl-4-methylphenol	tryptamine
C7	2.44	18.3	Cu-Cu	2,6-diacetyl-4-methylphenol	2-picoylamine
C2b	0	0	Cu-Zn	2,6-diformyl-4-methylphenol	tryptamine
C1b	0	0	Cu-Zn	2,6-diformyl-4-methylphenol	pyridoxamine
C3b	0	0	Cu-Zn	2,6-diformyl-4-methylphenol	histamine
C1a	0	0	Cu-Cu	2,6-diformyl-4-methylphenol	pyridoxamine
C15	0	0	Cu-Cu	2,6-bis(aminomethyl)-4-nitrophenol	2-formyl pyrrole
C14	0	0	Cu-Cu	2,6-bis(aminomethyl)-4-nitrophenol	2-hydroxy-1-acetonaphthone
C16	0	0	Cu-Cu	2,6-bis(aminomethyl)-4-nitrophenol	8-formyl-7-hydroxy-4-methylcoumarin
C12	0		Cu-Cu	1,3-diaminopropan-2-ol	8-formyl-7-hydroxy-4-methylcoumarin

The following general observations have been made :

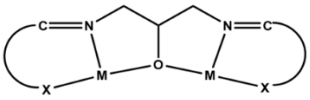
- Homometallic Cu(II)Cu(II) complexes are more active than heterometallic Cu(II)Zn(II)
- The complexes having imine groups conjugate to phenoxides are more active than those having imine in other part of molecules



C1-C3 and C4-C8



C13-C16



C9, C10 and C12

- Complexes having nitrogen donors are more active than those having oxygen donor groups. This variation in the activity must be because the conjugation in the phenoxide part of ligands can facilitate the delocalization of electron density over the metal centers through π-bonding. Thus, making Cu(I) to Cu(II) redox easier.
- The nitrogen donors used in the present study are all having heterocyclic nitrogen, which is a soft ligand, hence facilitating the delocalization of electron density better than the oxygen containing ligands which are relative hard binding sites.
- The complexes of ligands derived from isomeric acetonaphthones, and various other complexes are selective towards substrates underlining the fact that the auxiliary groups can play an important role in deciding the selectivity of active sites.

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