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Subtle Structural Changes in $(Cu^{II}L)_2Mn^{II}$ Complexes To Induce Heterometallic Cooperative Catalytic Oxidase Activities on Phenolic Substrates (H₂L = Salen Type Unsymmetrical Schiff Base)

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Supporting Information

ABSTRACT: A new Cu(II) complex of an asymmetrically dicondensed Schiff base ($H_2L = N$ -(2-hydroxyacetophenylidene)-N'-salicylidene-1,3-propanediamine) derived from 1,3-propanediamine, salicylaldehyde, and *o*-hydroxyacetophenone has been synthesized. Using this complex, [CuL] (1), as a metalloligand, two new trinuclear Cu-Mn complexes, [(CuL)₂Mn(N₃)(H₂O)]-(ClO₄)·H₂O (2) and [(CuL)₂Mn(NCS)₂] (3), have been prepared. Single-crystal structural analyses reveal that complexes 2 and 3 both have the same bent trinuclear {(CuL)₂Mn²⁺ structural unit in which two terminal bidentate square-planar (CuL) units are chelated to the central octahedral Mn(II) ion. This structural similarity is also evident from the variable-temperature



magnetic susceptibility measurements, which suggest that compounds 2 and 3 are both antiferromagnetically coupled with comparable exchange coupling constants (-21.8 and -22.3 cm⁻¹, respectively). The only difference between 2 and 3 lies in the coordination around the central Mn(II) ion; in 3, two SCN⁻ groups are coordinated to the Mn(II), leaving a neutral complex, but in 2, one N₃⁻ group and one H₂O molecule are coordinated to give a positively charged species. The presence of such a labile H₂O coligand makes 2 catalytically active in mimicking two well-known polynuclear copper proteins, catecholase and phenoxazinone synthase. The turnover numbers (k_{cat}) for the aerial oxidation of 3,5-di-*tert*-butylcatechol and *o*-aminophenol are 1118 and 6581 h⁻¹, respectively, values which reflect the facility of the heterometallic catalyst in terms of both efficiency and catalytic promiscuity for aerial dioxygen activation. The mechanisms of these biomimetic oxidase reactions are proposed for the first time involving any heterometallic catalyst on the basis of mass spectral analysis, EPR spectroscopy, and cyclic voltammetry. The evidence of the intermediates indicates possible heterometallic cooperative activity where the substrates bind to a Mn(II) center and Cu(II) plays the role of an electron carrier for transformation of the phenolic substrates to their respective products with the reduction of aerial dioxygen.

INTRODUCTION

The large range of N,O-donor ligands has already become one of the most essential tools in present-day research for the syntheses of metal-containing molecular materials due to their ability to assemble multiple metal ions in a predetermined stereochemical environment.¹ Among them, a small group of ligands termed as Salen type N₂O₂-donor symmetrical tetradentate Schiff bases has taken a significant share of the library of coordination compounds, presumably due to their synthetic simplicity.² In contrast, their asymmetrically dicondensed analogues are rarely reported due to the inherent synthetic challenges of the asymmetric condensation of the aliphatic diamine precursor.³ Costes et al. reported an efficient high-dilution method, but this is effective only when one of the carbonyl compounds is acetylacetone or its derivatives.⁴ Recently, Öz et al. synthesized an unsymmetrical ligand by condensation of 1,3-propanediamine with salicyladehyde and *o*-hydroxycaetophenone at low temperature.⁵ However, the method needs rigorous separation of the unsymmetrical Schiff base from the two symmetrical bases and the yield of the former is rather low and is highly susceptible to experimental conditions. As a result, only a handful of monouclear complexes of such asymmetric ligands are known and, barring only three trinuclear Ni(II) complex and one trinuclear Ni(II)-Cu(II) complex, no other polynuclear complexes of such ligands have been reported.^{3–5} On the other hand, very recently we have developed a modified Elder's method for the synthesis of unsymmetrical Schiff bases exclusively in a very quick and simple manner.⁶ Here, we wish to synthesize the

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mononuclear Cu(II) complex of this unsymmetrical ligand H_2L , which has not yet been reported, and use it as a metalloligand for the synthesis of heterometallic polynuclear complexes.

In relation to bioinspired and biomimetic catalysts, the polynuclear complexes are very useful, as the closely assembled metal centers with specific stereochemical arrangement can recognize typical molecules, such as natural metalloproteins.^{1a,d} A few of these metalloproteins utilize their active sites for the activation, storage, and transport of aerial dioxygen molecules in enzymatic pathways: e.g., catechol oxidase (COx), phenoxazinone synthase (PHS), cytochrome c oxidase, etc. Catechol oxidase is a dicopper-containing type III active-site protein that catalyzes the oxidation reaction of a wide range of o-diphenols (catechols) to the corresponding o-quinones, a process known as catecholase activity.7 Similarly, activity of PHS (in which the active site contains five Cu ions) is also important to understand the relevance of the copper oxidase model in a biological system where o-aminophenol (OAP) is oxidized to produce aminophenoxazinone (APX).8 These two enzymatic activities have also been modeled in vitro with several biomimetic copper complexes using aerial oxygen as a naturally viable oxidant, which is of immense importance in economic and environmental issues.^{9,10} The catalytic action of a large number of mono-/polynuclear Mn(II/III), Fe(II/III), and Co(II/III) as well as polynuclear Ni(II), Cu(II), and Zn(II) complexes in terms of catecholase and phenoxazinone synthase activity has already been explored extensively.^{11,12} However, until now the COx activity of heterometallic polynuclear complexes has been rarely examined and to our knowledge there has been no report on the PHS activity of any such complex.¹³ In fact, except for the mimicking of cytochrome c oxidase,^{14a,b} heterometallic systems still remain largely unexplored for dioxygen activation in catalytic oxidase reactions and are limited to only a few β -diketiminate ligand based high-valent heterometallic dinuclear complexes.¹⁴ However, exploration of heterometallic complexes as multimetallic cooperative catalysts is one of the foremost areas in current research trends on catalysis, yet their potential for catalytic promiscuity in multiple catalytic transformations has been rarely evaluated.^{8c,15}

Herein, we prepare a tetradentate N2O2 donor unsymmetrical Schiff base ligand ($H_2L = N$ -(2-hydroxyacetophenylidene)-N'-salicylidene-1,3-propanediamine) using 1,3-propanediamine, salicylaldehyde, and o-hydroxyacetophenone. The ligand H_2L is used to produce the mononuclear copper(II) complex [CuL] (1) by reacting with $Cu(ClO_4)_2 \cdot 6H_2O$ in methanol. Using this [CuL] chelate (1) as a bidentate asymmetric metalloligand, we have synthesized two new trinuclear complexes $[(CuL)_2Mn(N_3)(H_2O)](ClO_4) \cdot H_2O$ (2) and $[(CuL)_2Mn(NCS)_2] \cdot H_2O$ (3). All three complexes have been characterized by X-ray crystal structure determinations. Among the three complexes, only complex 2 exhibits a novel catalytic promiscuity in model biomimetic catecholase like activity and phenoxazinone synthase like activity under an aerial atmosphere. Cyclic voltammograms, ESI-mass spectra analysis, and EPR studies have also been performed to investigate the possible intermediates of the catalytic reactions and consequently to devise a probable mechanism.

EXPERIMENTAL SECTION

Starting Materials. Salicylaldehyde, *o*-hydroxoacetophenone, and 1,3-propanediamine were purchased from Spectrochem India and were of reagent grade. They were used without further purification. The

other reagents and solvents were of commercially available reagent quality, unless otherwise stated.

Caution! Although not encountered during experiment, perchlorate and azide salts of metal complexes with organic ligands are potentially explosive. Only a small amount of material should be prepared, and it should be handled with care.

Synthesis of the Unsymmetrical Schiff Base Ligand N-(2-Hydroxyacetophenylidene)-N'-salicylidene-1,3-propanediamine (H_2L). The unsymmetrical di-Schiff base ligand H_2L was synthesized in our laboratory by the method developed recently by us.⁶ First, the complex $[Ni(L_1)_2] \cdot 2H_2O$ (HL₁ = 2-((E)-(3aminopropylimino)methyl)phenol) was prepared by the reaction of bis(salicylaldehyde)nickel(II) dihydrate (3.09 g, 10 mmol) and 1,3propanediamine (2.10 mL, 25 mmol). Then, this complex (4.11 g, 10 mmol) was dissolved in 50 mL of methanol and solid bis(ohydroxoacetophenone)nickel(II) dihydrate (3.37 g, 10 mmol) was added to it and the mixture was refluxed for 2 h. The complex $[Ni_2(L_1)_2(o-Hap)_2]$ (o-Hap = o-hydroxyacetophenone), which separated out during this reaction, was filtered and air-dried. A 5 mmol portion (3.85 g) of this complex was dissolved in 25 mL of methanol, and solid dimethylglyoxime (DMG; 2.32 g, 20 mmol) was added to it. The mixture was refluxed on a water bath for 2 h, cooled, and filtered. The yellow filtrate was subjected to ESI mass spectroscopy (Figure \$30 in the Supporting Information), and the product was found to be exclusively the unsymmetrical Schiff base (H₂L: m/z 297.18, calcd 297.16); no signals corresponding to any of the possible symmetrical Schiff bases were detected (calcd m/z 283.14 and 311.18). The methanolic solution of the ligand [H₂L] was used directly for the complex preparation. The ¹H NMR spectrum of the ligand was also recorded (Figure S29 in the Supporting Information).

Synthesis of [CuL] (1). A methanolic solution (10 mL) of $Cu(ClO_4)_2.6H_2O$ (1.85 g, 5 mmol) was added to a methanolic solution of H_2L (5 mmol, 25 mL). The mixed solution was stirred for 0.5 h and kept in a desiccator. X-ray-quality green single crystals started to grow in the beaker after 2–3 days on slow evaporation of methanol. Crystals were filtered from the solution after 5 days and dried in air.

Complex 1. Yield 1.431 g (80%). Anal. Calcd for $C_{18}H_{18}CuN_2O_2$ (357.89): C, 60.41; H, 5.07; N, 7.83. Found: C, 60.27; H, 5.11; N, 7.79. Anal. Calcd: Cu, 17.76. Found: 17.63 (determined by SEMEDS). IR: $\nu_{C=N}$ 1625 and 1595 cm⁻¹ for formylimine and acetylimine, respectively.

Synthesis of the Complex $[(CuL)_2Mn(N_3)(H_2O)](ClO_4) \cdot H_2O$ (2). Complex 1 [CuL] (0.716 g, 2 mmol) was dissolved in 20 mL of methanol, and Mn(ClO₄)₂·6H₂O (0.361 g, 1 mmol) was added to the solution. The solution was stirred for 10 min and then 2 mL of a 1/1 (v/v) H₂O/MeOH solution of NaN₃ (0.130 g, 2 mmol) was added to it dropwise at room temperature. Stirring of the mixture was continued for 0.5 h. The small amount of precipitate that appeared during this process was filtered, and the filtrate was kept in a beaker inside a desiccator. Brown single crystals of X-ray quality appeared inside the beaker, which were separated by filtration after 3 days and dried in air.

Complex 2. Yield 0.664 g (70%). Anal. Calcd for $C_{36}H_{40}ClCu_2MnN_7O_{10}$ (948.23): C, 45.60; H, 4.25; N, 10.34. Found: C, 45.52; H, 4.27; N, 10.38. Cu:Mn ratio 2.08:1.05 (determined by SEM-EDS). IR: $\nu_{C=N}$ 1633 and 1599, $\nu_{N=N=N}$ 2062 and 1599, $\nu_{C1=O}$ 1108 cm⁻¹.

Synthesis of the Complex $[(CuL)_2Mn(NCS)_2]$ (3). The compound was prepared following a procedure similar to that for the synthesis of 2. The only difference was that here NH₄SCN (0.152 g, 2 mmol) was used instead of NaN₃. In this case, yellowish-green single crystals of X-ray quality appeared in the beaker after 2–3 days on the slow evaporation of solvent. Crystals were filtered from the solution and air-dried.

Complex 3. Yield 0.603 g (68%). Anal. Calcd for $C_{38}H_{36}Cu_2MnN_6O_4S_2$ (886.89): C, 51.46; H, 4.09; N, 9.48. Found: C, 51.42; H, 4.05; N, 9.45. Cu:Mn ratio 7.01:3.56 (determined by SEM-EDS). IR: $\nu_{C=N}$ 1627 and 1597, $\nu_{N=C=S}$ 2068 and 2054 cm⁻¹.

Physical Measurements. Elemental analyses (C, H, and N) were performed using a PerkinElmer 2400 series II CHN analyzer. IR

Table 1. Crystal Data and Structure Refinement Details of Complexes 1-3

	1	2	3
formula	$C_{36}H_{36}Cu_2N_4O_4$	C ₃₆ H ₃₆ Cu ₂ MnN ₇ O ₅ , ClO ₄ ,O	$C_{38}H_{36}Cu_2MnN_6C$
mol wt	715.79	944.21	886.89
cryst yst	monoclinic	monoclinic	monoclinic
space group	$P2_1/c$	Cc	$P2_1/n$
a, Å	7.317(5)	25.260(5)	13.659(4)
b, Å	22.932(5)	10.146(2)	18.556(4)
c, Å	9.537(5)	15.128(2)	15.412(2)
α , deg	90	90	90
β , deg	105.390(5)	95.317(14)	96.028(15)
γ, deg	90	90	90
<i>V</i> , Å ³	1542.9(14)	3860.4(12)	3884.7(15)
Z	2	4	4
$D_{cr} \text{ g cm}^{-3}$	1.541	1.625	1.516
μ , mm ⁻¹	1.427	1.550	1.560
F(000)	740	1924	1812
R(int)	0.037	0.082	0.105
total no. of reflns	10647	9407	17748
no. of unique reflns	2767	4660	6802
no. of rflns with $I > 2\sigma(I)$	2242	3760	4248
$R1,^{a} wR2^{b}$	0.0332, 0.0859	0.1073, 0.2470	0.1128, 0.2208
GOF^{c} on F^{2}	1.03	1.13	1.18
R(all)	0.0441	0.1305	0.1919
temp, K	293	150	150
residual electron density, e Å ⁻³	-0.56, 0.23	-0.87, 1.60	-0.49, 0.96

spectra as KBr pellets (4000-500 cm⁻¹) were recorded using a PerkinElmer RXI FT-IR spectrophotometer. The electronic absorption spectra (1000-240 nm) in methanol solution were collected with a Hitachi U-3501 spectrophotometer. Temperature-dependent molar susceptibilities for powdered crystalline samples of compounds 2 and 3 were measured using a superconducting quantum interference device vibrating sample magnetometer (SQUID-VSM, Quantum Design) with an applied field of 500 Oe throughout the temperature range 2-300 K. The susceptibility data were corrected by Pascal's diamagnetic contributions. Isothermal magnetization measurements were performed at 2, 3, 5, 7, and 10 K up to 5 T magnetic field. ¹H NMR spectral analysis of the ligand (after purification by crystallization from methanol) in CDCl₃ was carried out on a 300 MHz instrument (Bruker), where tetramethylsilane (TMS) was used as an internal standard. The Cu and Mn contents and their ratios in complexes 2 and 3 were measured on a ZEISS EVO-MA 10 scanning electron microscope equipped with an EDS (INCA Energy 250 Microanalysis System). Powdered samples of all three compounds were placed on pieces of carbon tape before imaging. Powder X-ray diffractograms are recorded on a Bruker D-8 Advance diffractometer operated at 40 kV voltage and 40 mA current and calibrated with a standard silicon sample, under Ni-filtered Cu-K α (α = 0.15406 nm) radiation.

Electrochemical Measurements. The electrochemical measurements of all three complexes (1-3) were performed using an Epsilon Basi-C3 Cell instrument at a scan rate of $100-400 \text{ mV s}^{-1}$ within the potential range of 0 to -1.80 V vs Ag/AgCl. Cyclic voltammograms were carried out using 0.1 M tetrabutylamonium perchlorate (TBAP) as supporting electrolyte and 1.0×10^{-3} M of complexes in dichloromethane solution, which were deoxygenated by bubbling with argon. The working electrode was a glassy-carbon disk (0.32 cm²) that was polished with alumina solution, washed with absolute acetone and dichloromethane, and air-dried before each electrochemical run. The reference electrode was Ag/AgCl, with platinum as the counter electrode. All experiments were performed in standard electrochemical cells at 25 °C.

ESI-HRMS. Electrospray ionization mass spectrometry (ESI-MS positive) ion mass spectra were acquired using a Xevo G2-S QTof (Waters) mass spectrometer, equipped with a Z-spray interface, over a

mass range of 100–1200 Da, in a continuum mode. Aqueous sodium formate was used for Q-oa-ToF calibration. L-Leucine was used as the external mass calibrant lock with mass $[M + H]^+$ 556.2771 Da. Solutions of compounds were injected at a flow rate of 5 μ L/min. All solutions were made in mass spectrometric grade methanol. The concentrations of complexes 2 and 3 as well as complexes + substrates in solutions were the same (10⁻⁶ M) during acquisitions of mass spectra.

X-ray Crystallographic Data Collection and Refinement. The independent reflection data were collected with Mo K α radiation, for 1 at 293 K and for 2 and 3 at 150 K, with the Oxford Diffraction X-Calibur CCD System. The crystals were positioned at 50 mm from the CCD, and 321 frames were measured with counting times of 10 s. Data analysis was carried out with the CrysAlis program.¹⁶ The structures were solved using direct methods with the Shelxs97 program.¹⁷ The non-hydrogen atoms were refined with anisotropic thermal parameters. The hydrogen atoms bonded to carbon were included in geometric positions and given thermal parameters equivalent to 1.2 times those of the atom to which they were attached. Absorption corrections for 1-3 were carried out using the ABSPACK program.¹⁸ The hydrogen atoms bonded to the coordinated water molecule and solvent water molecule in 2 could not be located. The structures were refined on F^2 using Shelx197.¹⁷ Data collection, structure refinement parameters, and crystallographic data for complexes 1-3 are given in Table 1.

Catalytic Oxidation of 3,5-DTBC. The catecholase activity of complex **2** was studied using 3,5-di-*tert*-butylcatechol (3,5-DTBC) as the substrate in an methanolic solution under aerobic conditions at room temperature. The reactions were followed spectrophotometrically by monitoring the increase in the absorbance maxima of the quinone band at 400 nm as a function of time (time scan). To detect the formation of hydrogen peroxide during the catalytic reaction, we followed the iodometric method as reported earlier.¹⁹

Phenoxazinone Synthase of OAP. The phenoxazinone synthase activity of complex 2 was studied using *o*-aminophenol (OAP) as the substrate in a methanolic solution under aerobic conditions at room temperature. The reactions were followed spectrophotometrically by monitoring the increase in the absorbance maxima of the amino

Scheme 1. Syntheses of Complexes 1-3



phenoxazinone (APX) band at 425 nm as a function of time (time scan).

EPR Spectra. The EPR spectra were recorded with a Bruker EMX series spectrometer operating at X-band with 100 kHz modulation frequency. DPPH (g = 2.0036) was used as a g standard. To ensure good glass formation, 20-30% ethanol was added to the solutions of the studied compounds in methanol. Typical experimental parameters were as follows: modulation amplitude 2 G, microwave power 7 mW, time constant 20.48 ms, conversion time 40 ms.

RESULTS AND DISCUSSION

Syntheses of the Complexes. Recently we developed a rapid and facile method⁶ for the synthesis of tetradentate N_2O_2 donor unsymmetrical Schiff base ligands as exclusive products by modification of Elder's method. Following that method, we prepared here N-(2-hydroxyacetophenylidene)-N'-salicylidene-1,3-propanediamine $[H_2L]$ and reacted this N_2O_2 donor ligand with $Cu(ClO_4)_2 \cdot 6H_2O$ to synthesize its hitherto unknown mononuclear Cu(II) complex (1). This complex [CuL] on reaction with $Mn(ClO_4)_2 \cdot 6H_2O$ in the presence of N_3^- and SCN⁻ ions yielded the complexes $[(CuL)_2Mn(N_3)(H_2O)]$ - $(ClO_4) \cdot H_2O$ (2) and $[(CuL)_2Mn(NCS)_2]$ (3), respectively (Scheme 1). It is to be noted that, although the [CuL]:Mn- $(ClO_4)_2 \cdot 6H_2O:(NaN_3 \text{ or } NH_4SCN)$ ratios are the same (2:1:2), the compositions of the complexes 2 and 3 are different with respect to the coligands. In addition to elemental analyses of all three complexes, the weight percent of Cu in complex 1 and the ratio of the weight percent of Cu and Mn in complexes 2 and 3 were evaluated from SEM-EDS analyses (Figure S31 in the Supporting Information). The resemblance of the measured powdered diffractograms of complexes 1-3 to

their respective simulated (from Mercury 3.8) diffractograms (Figures S32–S34 in the Supporting Information) indicates the purity of the complexes.

It is worthwhile to mention that a large number of mononuclear/polynuclear complexes of symmetrically dicondensed salen type Schiff base ligands have been reported during the last five decades. Recently, we have shown that Cu(II) and Ni(II) complexes of such ligands can be conveniently used to prepare various heterometallic polynuclear complexes by the "complex as ligand" strategy. On the other hand, only recently Öz et al. synthesized three homometallic Ni(II) complexes and one heterometallic Ni(II)/Cu(II) polynuclear complex using asymmetrically dicondensed N2O2-donor salen type di-Schiff base ligands. However, no mononuclear complexes of such asymmetric ligands have yet been reported to be used as metalloligands. The reported heterometallic complex was synthesized by relying on serendipity as two metal ions were added simultaneously to the ligand solution. For the designed synthesis of heterometallic complexes, use of the mononuclear complex is the key component of the "complex as ligand" strategy. In the present study, we isolated the key Cu(II) metalloligand derived from an asymmetrically dicondensed salen type Schiff base ligand and used it to prepare two heterometallic trinuclear Cu-Mn complexes with azide and thiocyanate as coligands.

IR Spectra of Complexes 1–3. In the IR spectra of these complexes (1-3), strong peaks at 1625 and 1595 cm⁻¹ for compound 1 (Figure S1 in the Supporting Information), 1633 and 1599 cm⁻¹ for compound 2 (Figure S2 in the Supporting Information), and 1627 and 1597 cm⁻¹ for compound 3

(Figure S3 in the Supporting Information) are observed due to azomethine $\nu_{C=N}$ stretching.⁵ The appearance of two peaks for the azomethine groups in all of the complexes indicates the asymmetric nature of the Schiff base. In the spectrum of compound **2**, the strong bands at 2062 and 1108 cm⁻¹ are attributable to the stretching vibrations for N₃⁻ and ClO₄⁻, respectively. Compound **3** shows strong and sharp peaks at 2068 and 2054 cm⁻¹ for SCN⁻ stretching.²⁰ The appearance of two bands indicates that the two SCN⁻ ions are not identical in the compound, as was corroborated by a structural analysis.

Description of Structures. Complex 1 possesses a diphenoxido-bridged centrosymmetric dinuclear structure of formula $[Cu_2L_2]$, as shown in Figure 1. In the asymmetric unit,



Figure 1. Structure of the centrosymmetric dimeric complex 1 with thermal ellipsoids at 20% probability.

the central metal atom Cu(II) is bonded to four donor atoms of the ligand (L^{2-}) . Two phenoxido oxygen atoms (O(11) and O(31)) and two imine nitrogen atoms (N(19) and N(23)) of the unsymmetrical Schiff base ligand constitute the basal plane around Cu(II). The phenoxido oxygen $O(11)^a$ of the ohydroxyacetophenone moiety of the Schiff base of another symmetry-related unit coordinates to one of the axial sites of Cu(II) to make its geometry pentacoordinated. The Addison parameter $\tau_5 = 0.171$ ($\tau_5 = (\beta - \alpha)/60$) indicates a distorted-square-pyramidal geometry.²¹ In the basal plane, Cu–O distances are 1.910(2) and 1.935(2) Å and Cu-N distances are 1.965(2) and 2.030(2) Å, whereas the axial bond length $Cu(1)-O(11)^{a}$ (where the superscript "a" denotes the symmetry transformation 1 - x, -y, 2 - z) is 2.519(2) Å. The root mean squared (r.m.s.) deviation of the four basally coordinated atoms of Cu(1) from the mean plane is 0.217 Å, with the metal atom placed at 0.071(1) Å away from the plane, toward the $O(11)^a$ atom. It should be noted that between the two basal $Cu(1)-O_{phenoxo}$ bonds of the [CuL] in complex 1, the bond to the phenoxo oxygen atom of salicylaldehyde is slightly longer (0.025 Å) than that to the phenoxo oxygen of ohydroxyacetophenone. The relative elongation of the Cu-O_{phenoxo} bonds in salen type asymmetric ligands within a range of 0.02-0.03 Å has been discussed earlier in terms of "push-pull charge asymmetry".^{3c} Such differences in Cu-O_{phenoxo} bond distances indicate the induction of electronic asymmetry within the metalloligand, which results because the "-R" effect of the formylimine group on O(31) is greater than that of the acetylimine group on O(11) of ligand L²⁻. This also suggests that, as O(11) is more electron rich than O(31), the former atom bridges the two Cu centers in 1. The bond lengths and angles are shown in Table S1 in the Supporting Information.

The asymmetric unit of **2** consists of a discrete $[(CuL)_2Mn-(N_3)(OH_2)]^+$ cation, a perchlorate anion, and a water molecule. In the cation, shown in Figure 2, two molecules of the



Figure 2. Structure of the cation of **2** with thermal ellipsoids at 20% probability. The perchlorate anion and solvent water molecules are not shown. The hydrogen atoms on the coordinated water molecule were not located.

metalloligand [CuL] are bonded to a central Mn(3) atom through four oxygen bridges. The octahedral coordination of the Mn(3) atom is completed by an azide anion and a water molecule. Charge balance is then provided by a perchlorate anion. A noncoordinated water molecule is also present in the asymmetric unit. The copper atoms in the metalloligands retain their four-coordinate square-planar arrangement, being bonded to the four donor atoms of the asymmetric ligand L^{2-} , but the square plane is far less distorted with τ_5 values of 0.077 and 0.055. The bond lengths around Cu(1) and Mn(3) are shown in Table S1 in the Supporting Information. The equatorial planes show r.m.s. deviations for the donor atoms of 0.148 and 0.046 Å with the metal atoms deviating by 0.033(7) and 0.020(7) Å. The two planes intersect at $28.1(3)^{\circ}$. In 2 there are short contacts between the water molecule O(1W) and oxygen atoms, namely a perchlorate oxygen O(72) at 2.753(3) Å and the coordinated water molecule O(1) (symmetry transformation 1/2 + x, 1/2 + y, z) at 2.744(3) Å, and these are likely to be hydrogen bonds, although the hydrogen atoms on O(1W) and O(1) were not located.

The monomeric structure of $[(CuL)_2Mn(NCS)_2]$ (3) is shown in Figure 3. In this case, charge balance is obtained by two thiocyanate ligands bonded via nitrogen to the Mn atom. The overall dimensions in the three metal coordination spheres, shown in Table S1 in the Supporting Information, are very similar to those in 2 and also to values found in previous trinuclear structures of this type.^{13,22} The two independent copper atoms are both four-coordinate with square-planar environments, each being bonded to four donor atoms of the tetradentate asymmetric ligand L^{2–}. The τ_5 values are 0.053 and 0.075, respectively. In the two equatorial planes, the four donor atoms show a tetrahedral distortion with r.m.s. deviations of 0.173 and 0.119 Å with the metal atoms 0.021(3) and 0.041(4) Å from the plane. The two planes intersect at $38.1(2)^{\circ}$. The manganese atom is six-coordinate with a distorted-octahedral environment, being bonded to four oxygen atoms which bridge to one of the copper atoms together with two nitrogen atoms



Figure 3. Structure of 3 with thermal ellipsoids at 20% probability.

of monodentate thiocyanate ligands. The two oxygen atoms O(31) and O(61) that are trans to the thiocyanate ligands form longer bonds to the metal at 2.217(7) and 2.213(6) Å in comparison to O(11) and O(41), which are mutually trans, albeit with an angle of 149.3(3)°, at 2.074(7) and 2.086(7) Å. The two Mn–Cu distances are 3.209(3) and 3.128(3) Å in 3 in comparison to 3.209(3) and 3.135(3) Å in 2.

It is also to be noted that the "electronic push-pull charge asymmetry" effect on the elongation of Cu-O_{phenoxo} bonds in complexes 2 and 3 is prominent, where the more electron rich O(11) and O(41) form shorter Cu-O bonds and the less electron rich O(31) and O(61) form longer Cu-O bonds. This effect also has a considerable impact on Mn-O_{phenoxo} bond distances in complexes 2 and 3. The more electron rich O(11)and O(41) form shorter Mn-O_{phenoxo} bonds and the less electron rich O(31) and O(61) form longer Mn-O_{phenoxo} bonds. It is worthwhile to point out that all of the previously reported heterometallic trinuclear complexes derived from several salen type Schiff bases are structurally analogous to complex 3, where the divalent central metal ions (s, p, or d block) are usually octahedral (few are tetrahedral or squareplanar) and are coordinated to the two same coligands (e.g., water, azide, thiocyanate, cyanate, dicyanamide, chloride, nitrite, nitrate, perchlorate, carboxylates, etc.). On the other hand, complex 2 is the first of its kind where the central metal ion of such a complex possesses two different coligands (azide and water).

Magnetic Properties. Temperature variations of the product of molar magnetic susceptibility and temperature $(\gamma_{\rm M}T)$ for compounds 2 and 3 are shown in Figure 4. The compounds show room-temperature $\chi_M T$ values of ca. 4.13 cm³ K mol⁻¹ for **2** and 4.23 cm³ K mol⁻¹ for **3**, which are lower than the value of a magnetically noninteracting Cu₂Mn system of 5.1 cm³ K mol⁻¹ for $g_{Mn} = g_{Cu} = 2$ at 300 K.²² In both cases, the behaviors are very similar; a progressive decrease in $\chi_{\rm M}T$ value takes place upon cooling and reaches a plateau of ca. 1.90 cm³ K mol⁻¹ for 2 and 1.80 cm³ K mol⁻¹ for 3 around a temperature range of ca. 8-28 K. At very low temperatures (below ca. 5 K), the $\chi_M T$ value further decreases to reach a value of 1.85 cm³ K mol⁻¹ for 2 and 1.66 cm³ K mol⁻¹ for 3 at 2 K. The progressively decreasing nature of $\chi_{\rm M}T$ with a decrease in temperature is attributed to the presence of strong antiferromagnetic interactions. The saturated molar magnetization values at 2 K are 2.90 $\mu_{\rm B}$ for complex 2 (Figure S4 in the Supporting Information) and 2.84 $\mu_{\rm B}$ for complex 3 (Figure S5



Figure 4. Thermal variations of the $\chi_M T$ product for compounds 2 and 3. The solid yellow line represents the best fit to the appropriate model for 2, and the solid blue line represents the best fit to the appropriate model for 3.

in the Supporting Information), which represents to a nonzero spin ground state with $S_{\rm T} = |S_{\rm Mn} - 2S_{\rm Cu}| = 3/2$. This behavior also suggested the presence of dominant antiferromagnetic coupling. To evaluate the magnetic interaction parameters, we used the spin-only Hamiltonian $H = -2J[S_1S_2 + S_1S_3]$, where S_1 = S_{Mn} and $S_2 = S_3 = S_{Cu}$ on the basis of a linear trinuclear structure. It can be noted that the exchange coupling between the two terminal Cu^{II} ions was assumed to be 0 ($J_{Cu-Cu} = 0$ cm⁻¹) because of large Cu…Cu separation. Simulations were carried out using the PHI program with consideration of molecular field approximations.²³ The best fits lead to the following parameters: $J_{\text{Mn-Cu}} = -21.8 \text{ cm}^{-1}$, $g_{\text{cu}} = 2.08$, $g_{\text{Mn}} = 2.01$, $zJ' = 0.032 \text{ cm}^{-1}$, $R = 1.22 \times 10^{-5}$ for compound **2**; $J_{\text{Mn-Cu}}$ $= -22.3 \text{ cm}^{-1}$, $g_{cu} = 2.11$, $g_{Mn} = 2.00$, $zJ' = -0.008 \text{ cm}^{-1}$, R = 1.28×10^{-5} for compound 3. The nature and magnitude of the coupling constants are as expected, considering the Cu-O-Mn angles.

Electrochemistry. The cyclic voltammogram (CV) of complex 1 in dichloromethane (Figure S6 in the Supporting Information) shows one wave on a cathodic scan (0 to -1.8 V) for the quasi-reversible reduction process at the electrode surface. The peak is observed at $E_c = -1.05$ V on a forward cathodic scan with respect to an Ag/AgCl electrode, whereas on reverse scan the corresponding peak observed at $E_a = -0.86$ V with the peak separation value $\Delta E_{\rm pc} = E_{\rm cathodic} - E_{\rm anodic}^{24}$ is -0.19 V. The cyclic voltammograms of complex 1 suggest that the mononuclear Cu(II) complex reduced to the Cu(I) state through a one-electron process. Complex 2 shows two peaks at $E_1 = -0.54$ V and $E_2 = -1.05$ V on a forward cathodic scan and one peak at $E_1 = -0.83$ V on a reverse scan (Figure 5). Here the peak separation value (ΔE_{pc}) is -0.22 V and the potential difference $(\Delta E_{12} = E_1 - E_2)^{25}$ between two peaks on a forward scan is -0.51 V. On the other hand, complex 3 also shows two peaks at $E_1 = -0.74$ V and $E_2 = -1.00$ V on a forward cathodic scan and one peak at $E_1 = -0.78$ V on a reverse scan (Figure S7 in the Supporting Information). In this complex the peak separation value (ΔE_{pc}) of -0.22 V is observed, like that for 2. Both complexes 2 and 3 show similar CVs with one irreversible followed by one quasi-reversible wave for the reduction process. It is evident that complexes 2 and 3 dissociate in solution to form a mixture of free metalloligand [CuL] as well as polynuclear $\{(CuL)_2Mn\}^{2+}$ species. On comparison of the



Figure 5. Cyclic voltammograms (CVs) of 10^{-3} M solution of complex **2** in dichloromethane at room temperature and different scan rates, using TBAP as supporting electrolyte.

cyclic voltammograms (CV) of the three complexes 1–3, the quasi-reversible peak (observed at E = -1.05, -1.05. and -1.00 V for complexes 1–3, respectively) is common for all, which resembles the one-electron reduction of Cu(II) to Cu(I) for the free mononuclear metalloligand [CuL].²⁶ On the other hand, the additional wave for the forward cathodic scan appears only for complexes 2 and 3 (observed at E = -0.54 and -0.74 V for 2 and 3, respectively), which might come from the reduction of remaining polynuclear {(CuL)₂Mn}²⁺ species. After the reduction of Cu(II) to Cu(I) in the {(CuL)₂Mn}²⁺ species, Mn(II) with higher ionic potential possibly replaces the Cu(I) from the Schiff base core and makes the reduction process irreversible. This also suggests that the Cu center of complex 2 is reduced at lower potential in comparison to complex 3.

Use of the Complexes as Catalysts for Aerial Oxygen Activation. Literature reports reveal that complexes containing coordinated solvent molecules or vacant coordination sites in the metal ions show high catalytic activity, as these situations facilitate substrate-catalyst binding. In complexes 2 and 3 the axial sites of Cu(II) are vacant, but it should be noted that in complex 2 there is a coordinated water molecule on the central Mn(II). We checked the catecholase activities of all three complexes and found that only complex 2 is catalytically active. Moreover, from previous studies it is evident that active sites of different metalloenzymes are often very similar and complexes mimicking the active sites of one metalloenzyme can perform multiple catalytic transformations of similar reaction trajectories. For example, several catalysts that show catecholase like activity also often exhibit phenoxazinone synthase like activity.

Catechol Oxidase Studies and Kinetics. Detailed Description. The catecholase like activity of the complexes was determined by the catalytic oxidation of 3,5- DTBC. This substrate is most widely used for catecholase activity of biomimicking coordination compounds. The possible reasons for its suitability are the low redox potential of 3,5-DTBC, which facilitates its oxidation to quinone, and its bulky *tert*-butyl substituents, which prevent further oxidation reactions or ring opening.²⁷ The product of this oxidation reaction, 3,5-di-*tert*butylquinone (3,5-DTBQ), is highly stable and shows a characteristic absorption band maximum at around 401 nm ($\varepsilon = 1900 \text{ M}^{-1} \text{ cm}^{-1}$) in a pure methanol solvent.²⁸ Before the determination of detailed kinetics studies, we have examined the catalytic activity of complex **2** for the oxidation of 3,5-di*tert*-butylcatechol (3,5-DTBC) to the corresponding *o*-quinone (3,5-DTBQ) in methanol under an aerial atmosphere according to the reaction shown in Scheme 2.

Scheme 2. Catalytic Oxidation of 3,5-DTBC to 3,5-DTBQ in Methanol



For this purpose, a 4×10^{-5} M methanolic solution of complex 2 was treated with 250 equiv of 3,5-DTBC at room temperature under aerobic conditions. After mixing of 3,5-DTBC into the solution of complex 2, the progress of the reaction was followed by continuous recording of the UV-vis spectra of the mixtures at 5 min time intervals. The gradual increase of an absorption band at around 401 nm corresponding to the formation of 3,5-DTBQ^{10d,20a} for complex 2 is shown in Figure 6. The UV-vis spectra of the



Figure 6. Increase of the quinone band at around 400 nm after the addition of 250 equiv of 3,5-DTBC to a methanolic solution of complex **2**. The spectra were recorded at 5 min intervals.

solution of complex 2 in methanol showed a drastic change after the addition of 3,5-DTBC to the solution. The kinetics of this oxidation reaction of 3,5-DTBC to 3,5-DTBQ in the presence of complex 2 was determined by measuring the growth of the quinone band at 401 nm as a function of time. The rate constant for this complex-substrate mixture was calculated from a $\log[A_{\alpha}/(A_{\alpha} - A_{t})]$ vs time plot. The substrate-dependent oxidation rates and various kinetic parameters of the substrate concentration in this reaction were determined by using 4×10^{-5} M solutions of complex 2 mixed with different concentrations of 3,5-DTBC under aerobic conditions. In this case, first-order kinetics was followed at low concentrations of 3,5-DTBC, whereas at higher concentrations saturation kinetics was observed. The observed reaction rates versus the substrate concentration data were then analyzed on the basis of the Michaelis-Menten approach of enzymatic kinetics to obtain the Lineweaver-Burk (double reciprocal) plot and values of kinetic parameters V_{max} , K_{M} , and k_{cat} . The

curves of both the observed rate vs [substrate] and the Lineweaver–Burk plot for complex 2 are depicted in Figure 7.



Figure 7. Plot of the rate vs substrate concentration for complex **2**. The inset shows the corresponding Lineweaver–Burk plot.

For both cases the kinetic parameters are given in Table S3 in the Supporting Information. The calculation of the k_{cat} value was performed by dividing the V_{max} value by the concentration of the complex 2 (Table S3). The k_{cat} (in h⁻¹) value of this catalysis is 1118 for 2. The same procedure was applied to test the catecholase like activity using complexes 1 and 3 as catalysts, but they did not show such activity (Figure S8 in the Supporting Information). In the following sections we compare the ESI-MS and EPR spectra of the two heterometallic complexes 2 and 3 to gain an insight into the mechanisms of the reactions.

ESI-Mass Spectrometric Study. To get information about the complex-substrate intermediates and to draw the mechanistic inference of catecholase activity during the oxidation reaction of catechol, we have recorded ESI-MS spectra of complexes 1-3 and of 1/1 mixtures (v/v) of the complexes and 3,5-DTBC in methanol solution within 5 min of mixing (Figures S13-S15 in the Supporting Information). The mass spectrum of complex 2 shows a base peak at m/z 358.06 (calcd 358.07), which can be assigned to protonated metalloligand [(CuL) + H]⁺ (Figure S13). Another prominent peak at m/z 377.03 (calcd 377.08) is observed due to the water coordinated metalloligand species [(CuL·H₂O) + H]⁺. In addition, two low-intensity peaks at m/z 715.14 (calcd 715.14) and m/z 737.13 (calcd 737.12) are observed for the corresponding dinuclear protonated $[(CuL)_2 + H]^+$ and sodiated species $[(CuL)_2 + Na]^+$, respectively. In addition to these, there are several other signals; one of which at m/z384.52 (calcd 384.53) for the doubly charged trinuclear $[(CuL)_2Mn]^{2+}$ species is noteworthy.

After the addition of 3,5-DTBC to a solution of complex 2, a considerable change is observed in the overall mass spectrum (Figures S14 and S15 in the Supporting Information). It shows a base peak at m/z 380.04 (calcd 380.05), which can be assigned to the sodiated metalloligand species $[(CuL) + Na]^+$. The intensity of the peak at m/z 384.52 (calcd 384.53) for doubly charged trinuclear [(CuL)₂Mn]²⁺ species becomes considerably higher in this spectrum. The appearance of two new peaks at m/z 991.24 (calcd 991.23) and 769.08 (calcd 769.07) assignable to $[(Cu^{II}L)_2Mn(3,5-DTBC)]^+$ and $[(Cu^{I}L)_2Mn(3,5-DTBC)]^+$ Mn(Cu^{II}L)]⁺, respectively, is very important from a mechanistic point of view, as they clearly establish the complex-substrate bonding and subsequent reduction of one of the Cu(II) to Cu(I) in the trinuclear species (vide infra). Another important peak is observed at m/z 989.24 (calcd 989.21), which indicates the formation of the semiquinonate form of the intermediate $[(Cu(II)L)_2Mn(3,5-DTBSQ)]^+$. In addition, the spectrum shows a peak at m/z 243.12 (calcd 243.13), which can be assigned to the [3,5-DTBQ-Na]⁺ ion, the oxidized product of 3,5-DTBC.

The mass spectrum of complex **3** (Figure S18 in the Supporting Information) in methanolic solution shows a base peak at m/z 358.06 (calcd 358.07) for the protonated metalloligand [(CuL) + H]⁺ and at m/z 380.04 (calcd 380.05) and m/z 737.13 (calcd 737.12) for the species [(CuL) + Na]⁺ and [(CuL)₂ + Na]⁺, respectively, like those of complex **2**. In comparison with **2**, the presence of a very low intensity signal for [(CuL)₂Mn]²⁺ at m/z 384.52 (calcd 384.53) is noticeable, which is readily abolished after the addition of 3,5-DTBC.

The spectrum of the mixture of complex 3 and 3,5-DTBC in methanolic solution (Figure S19 in the Supporting Information) shows a base peak at m/z 380.04 (calcd 380.05) for the sodiated metalloligand species [(CuL) + Na]⁺. The relative intensities of the peaks at m/z 358.07 (calcd 358.07) for [(CuL) + H]⁺ and m/z 737.13 (calcd 737.12) for [(CuL)₂ + Na]⁺ are reduced significantly. It is noted that the peaks for species such as [(Cu^{II}L)₂Mn(3,5-DTBC)]⁺, [(Cu^{II}L)₂Mn(3,5-DTBSQ)]⁺, and 3,5-DTBQ are not present or are negligible in this spectrum.



Figure 8. EPR spectra of 0.1 mM solutions of 2 (left) and 3 (right) in methanol at 96 K.

EPR Spectroscopy. The complexes under study contain Cu²⁺ and Mn²⁺ ions, which are both paramagnetic. Hence, electron paramagnetic resonance can be very useful in understanding the role of these ions in catecholase activity. However, the distances between these ions in the complexes are such that they are expected to be exchange-coupled, and this is indeed established by the susceptibility measurements. Exchange coupling between the two Cu^{2+} (S = 1/2) and Mn^{2+} will lead to S = 3/2, 5/2, and 7/2 spin states, whose separation will depend on the strength of exchange interaction.²⁹ Susceptibility measurements reveals antiferromagnetic coupling and an exchange interaction of less than 30 cm^{-1} , implying that at room temperature the excited spin states would also be populated along with the ground states. Thus, we have employed low-temperature EPR experiments with the aim of reducing the contributions of excited spin states.

Figure 8 shows the EPR spectra of complexes 2 and 3 in methanol recorded at 96 K. The spectra show typical features of Mn²⁺ and Cu²⁺ isolated ions. Moreover, the relative amount of Cu lines is greater in the spectrum of complex 3. Now an exchange-coupled spectrum (ground state S = 3/2) would possibly not show these features, as the exchange interaction changes the hyperfine interaction of isolated ions. For example, studies by Krost et al. on a copper manganese bimetallic system³⁰ show that the hyperfine coupling of copper (\sim 23 G) decreases to about one-sixth of its value in typical monometallic copper complexes (150-190 G). This is understandable, since Cu-Mn is a six-electron system where each electron now spends one-sixth of the time around copper nuclei. In the current scenario we have a trimetallic system where this effect would again be present if there were significant exchange interaction. However, the observed copper parallel hyperfine couplings are 184 G, which are close to that of monometallic Cu^{2+} complexes. In addition, the spectrum of Mn^{2+} (including the forbidden transitions and the different line width of Mn lines) can be simulated (simulation not shown) by assuming a 5/2 spin state.

To further understand the EPR spectra, we synthesized the following analogues of 2, where the exchange coupling between Cu^{2+} and Mn^{2+} is absent: namely, (i) Zn-Mn-Zn (4) and (ii) Cu–Zn–Cu (5). In complex 4, the EPR of isolated Mn^{2+} can be obtained, while in complex 5 the spectrum of Cu^{2+} can be obtained (the terminal copper can be considered to be isolated; Figures S21 and S22 in the Supporting Information show the EPR spectra of complexes 2/4 and 3/5). It is clear that complexes 4 and 5 can explain almost all of the spectral features of complexes 2 and 3. Thus, the spectra of complexes 2/3 can be ascribed to isolated (exchange-free) Cu^{2+} and Mn^{2+} ions. One possibility to explain this behavior is that the complex is not completely stable and breaks partially into constituent ions. This is supported from the mass spectroscopy data, which shows the presence of species such as $(CuL)_{2}$, $(CuL)_{2}$, $(CuL)_{2}Mn$, etc.

The EPR spectra of such exchange-coupled systems have been studied only in the solid state by employing single crystals. To the best of our knowledge, we are not aware of such studies in solution. Colacio et al.³¹ have attempted to study the EPR of an exchange-coupled Cu–Mn–Cu system in frozen methanol at 100 K. However, they too observed features of isolated ions. The absence of a signal which can be ascribed to the intact complex may be because the signal is very broad and, coupled with its small concentration (limited by the solubility), escapes detection.

On addition of DTBC, the copper lines showed a strong decrease in both complexes 2 and 3. Figures S23 and S24 in the Supporting Information show the EPR spectra of complexes 2/ 3 in methanol containing an excess (>100-fold) of DTBC at different times after its addition. It is clear that both behave similarly after DTBC addition. In fact, the EPR spectra of both complexes overlap significantly after DTBC addition. This seems to contradict the optical behavior, in which catecholase activity was seen only with complex 2 and not with 3, and the mass spectrometric results of the mixture of DTBC + complex 2, in which the $[(CuL)_2Mn]^{2+}$ species is the base peak (unlike 3) along with an intense signal for (CuL), indicating that the trinuclear cluster is sufficiently present in the mixture for 2. However, it is important to note that the signals seen in EPR are predominantly from the broken complexes (as discussed earlier). Hence, a change in their intensity does not relate to the catalytic efficiency of the intact complex. Since we could not identify the EPR of the intact complex separately, we directed our attention toward the search for a new signal which could be assigned to a new intermediate species (possibly semiquinone radical).

Figure 9 shows the EPR spectra of complexes 2 and 3 after addition of DTBC recorded under comparable conditions. One



Figure 9. EPR spectra of 2 and 3 in methanol at 96 K immediately after addition of DTBC.

can observe a new signal close to $g \approx 2$ only in the case of complex 2, and not in 3. This signal could possibly be due to the semiquinone intermediate radical or a ligand-centered radical (in case the reduction involves transfer of an electron to the ligand instead of copper). The reason for the small intensity of the extra signal might be that the DTBSQ radical is an intermediate and is continuously decaying to its final diamagnetic product, thereby resulting in a small steady state concentration.

Mechanistic Insight. Mechanistic studies with copper-based model complexes have already established that there are two possible mechanisms for the oxidation of 3,5-di-*tert*-butyl-catechol to its respective quinone. One occurs through the formation of a dicopper(II) catecholate intermediate where the dicopper(II) species oxidizes the catecholic substrate to its respective quinone and itself reduces to a dicopper(I) species. This dicopper(I) species further reacts with an oxygen molecule to generate a peroxidodicopper(II) adduct, which then oxidizes a second molecule of the catechol substrate to quinone; water is formed as a byproduct through this four-electron-reduction process.³² The second mechanism involves the formation of an

organic radical intermediate such as copper(I) semiquinone.³³ Its subsequent reaction with an oxygen molecule may result in the two-electron reduction of two oxygens, leading to the further oxidation of the copper(I) ion and release of the quinone molecule, with hydrogen peroxide as a byproduct.³⁴ On the other hand, a number of studies of the possible mechanisms of the catechol oxidation reaction catalyzed by nickel(II), cobalt(II/III), manganese(II/III), and zinc(II) complexes with the formation of hydrogen peroxide have been reported. However, it is important to note that the participation of the metal center in the catechol to quinone oxidation reaction catalyzed by Ni(II), Co(III), Mn(III), or Zn(II) complexes proceeds through the formation of semiquinonate intermediate species similar to the case for Cu(II) complexes.

To understand the mechanism of this catalytic reaction for the present heterometallic Cu(II)-Mn(II) complexes, we estimated the amount (if any) of H_2O_2 formed (Figures S10 and S11 in the Supporting Information). It was observed that H_2O_2 is produced only when complex **2** is mixed with 3,5-DTBC. The quantitative estimation reveals that about 95.4% H_2O_2 is generated after 30 min of oxidation with respect to the conversion of 3,5-DTBQ from 3,5-DTBC (Table 2). Thus, it is evident that nearly an equimolecular amount of H_2O_2 is formed with respect to the formation of 3,5-DTBQ.

Table 2. Quantitative Estimation of H_2O_2 Formation (%) with Time (min) during the Catecholase Reaction

	time (min)						
	2	5	10	20	30		
H_2O_2 (%)	11.5	30.8	43.0	81.3	95.4		

On the basis of ESI-mass and EPR spectra, we propose here a possible mechanism for catechol oxidation. The doubly charged species [(CuL)₂Mn]²⁺ which is produced in solution (please see ESI-Mass Spectrometric Study) from the trinuclear complex 2 reacts with 3,5-DTBC to generate the intermediate species $[(CuL)_2Mn(3,5-DTBC)]^+$, in which one of the hydroxyl groups of 3,5-DTBC is deprotonated and coordinated to the Mn(II) center. This species then reacts with dissolved O_2 and is converted into its radical form (semiquinonate), [(Cu^{II}L)₂Mn-(3,5-DTBSQ)⁺, as is evident from mass spectra. O₂ is reduced to H_2O_2 . The EPR signal of an organic radical (Figure 9), which was found in the mixture of 2 and 3,5-DTBC, is presumably due to this semiquinone radical (3,5-DTBSQ), whereas the six-line EPR spectrum indicates that the oxidation state of Mn(II) remains unaltered during the catalysis (evident from the EPR spectrum of the Zn-Mn-Zn plus catechol system shown in Figure S25 in the Supporting Information). The semiguinone itself is converted to guinone and is eliminated from the metal center, leaving a singly charged trinuclear species, $[(Cu^{I}L)Mn^{II}(Cu^{II}L)]^{+}$, the existence of which is evident from mass spectra. Finally, Cu(I) of this species is oxidized to Cu(II) by O₂, regenerating the catalytically active species $[(CuL)_2Mn]^{2+}$ and producing H_2O_2 as the byproduct. The regenerated trinuclear species $[(CuL)_2Mn]^{2+}$ then coordinates to another 3,5-DTBC and converts it to 3,5-DTBQ following the same procedure.

The proposed mechanism may also be extended to explain the inactivity of the analogous Cu-Mn complex 3. Unlike 2, in the mass spectra of 3 there is no evidence for species such as $[(CuL)_2Mn]^{2+}$ or bonding of 3,5-DTBC to the metal complex, indicating their absence or negligible presence to sustain the catalytic process. The EPR spectrum also does not show any signal for a radical after addition of 3,5-DTBC to the solution of complex 3. On the other hand, the analogous Zn-Mn-Zn complex 4 does not show any catecholase like activity (Figure S9 in the Supporting Information) but shows a strong signal due to the formation of an organic radical, presumably the semiquinone (3,5-DTBSQ) (Figure S25 in the Supporting Information). Unlike Cu(II), Zn(II) cannot be reduced to Zn(I) by the semiqunone and hence is unable to catalyze the oxidation reaction; therefore, the radical concentration increased and is responsible for the strong signal.

From the present study it is apparent that a slight change in the structure of the heterometallic complexes can be very crucial for the catecholase like activity. The substrate-complex binding is essentially the important step in the process. At first sight, one may assume that catechol may simply coordinate to a vacant site of the metal ion or can easily replace a coordinated solvent molecule bonded with the metal ion. However, the process seems not to be that simple, as in the case of 2 no peak assignable to $[(Cu^{II}L)_2Mn(3,5-DTBSQ)]^+$ in which a solvent water molecule is replaced by catechol was detected. Instead, here generation of the dipositive species $[(CuL)_2Mn]^{2+}$ is vital for the catalyst-substrate binding. The vacant axial site of Cu(II), which is a common feature of complexes 2 and 3, seems to be of no use for coordination of catechol. Another unique feature of the catalytic activity of 2 is that, although the change in oxidation states of copper between 2+ and 1+ is the key for oxidation of catechol to quinone, the catechol does not bind to it but to Mn(II), which remains redox innocent throughout the process.

The explanation of the catalytic behavior of complex 2 over the catalytically nonresponsive complex 3 can be found in their structural difference. While both 2 and 3 contain vacant axial coordination sites of the square-planar Cu centers, only complex 2 contains a labile coordinated H_2O molecule, although it is bonded to the central Mn(II). It would seem that the presence of this coordinated H₂O molecule makes all the difference and induces catalytic activity of the heterometallic complex. Water is more easily removed than SCNfrom the complex in solution; this is why 3,5-DTBC can coordinate more readily to Mn(II) in complex 2 than in complex 3. The strong relative difference in the intensities of the mass spectral signals for the doubly charged trinuclear $[(CuL)_2Mn]^{2+}$ species obtained before and after adding catechol also suggests that the formation of this species in solution after adding catechol is highly favored (base peak) in 2 but practically vanishes in 3. A signal for the mass of the singly charged $[(CuL)_2Mn]^+$ species is also observed in the spectra of a mixture of 3,5-DTBC and complex 2 (Figure S14 in the Supporting Information), and this provides direct evidence for the further continuation of this reaction through a Cu(II)/ Cu(I) redox process and the presence of Cu(I) in the trinuclear Cu₂Mn unit. Mass spectra of the mixture of 3,5-DTBC and complex 3 show peaks only for protonated and sodiated metalloligand [CuL], indicating the almost complete dissociation of the basic [(CuL)₂Mn]²⁺ trinuclear unit (Figures S18 and S19 in the Supporting Information). Therefore, the reduction of Cu(II) to Cu(I) by the semiquinonate radical is important for this catalytic oxidative conversion of 3,5-DTBC to 3,5-DTBQ. The probable mechanism of this catalytic reaction is given in Scheme 3.

Scheme 3. Proposed Mechanism for Catalytic Oxidation of 3,5-DTBC to 3,5-DTBQ by Complex 2



Phenoxazinone Synthase Studies and Kinetics. *Detailed Description.* To establish the catalytic activity of these heterometallic complexes, toward another oxidase type reaction, we have studied phenoxazinone synthase like activity. This catalytic activity for several complexes was determined by the catalytic oxidation of o-aminophenol (OAP) to aminophenoxazinone (APX). OAP easily oxidizes and dimerizes to form APX according to the reaction shown in Scheme 4. APX

Scheme 4. Catalytic Oxidation of *o*-Aminophenol (OAP) to Phenoxazinone (APX) in Methanol



shows a broad absorption peak at 410-425 nm in pure methanol solvent; this is why OAP is used commonly for this study. The conversion of *o*-aminophenol to phenoxazinone is an oxidative dimerization reaction. Before the determination of detailed kinetics studies, we examined the catalytic activity of complexes 1-3 for the oxidation of *o*-aminophenol (OAP) to the corresponding amino phenoxazinone (APX) in methanol solvent under an aerial atmosphere and found that only complex 2 is catalytically active (Figure S12 in the Supporting Information).

A detailed kinetic study of this reaction was performed by following the aforementioned procedure of the catechol oxidase study. A 1×10^{-4} M methanolic solution of complex 2 is used as a catalyst, and 100 equiv of a 1×10^{-2} M solution of *o*-aminophenol in methanol is used as a substrate solution. The change in the spectral behavior of complex 2 in the presence of OAP is shown in Figure 10. The rate of this catalytic reaction



Figure 10. Increase of the APX band at around 425 nm after the addition of 100 equiv of OAP to a methanolic solution of complex **2**. The spectra were recorded at 4 min intervals.

has a linear dependence on catalyst concentration and shows first-order kinetics with respect to *o*-aminophenol (OAP). The curves of the observed rate vs [substrate] and Lineweaver–Burk plots for complex **2** are depicted in Figure 11. The k_{cat} (in



Figure 11. Plot of the rate vs substrate concentration for complex **2**. The inset shows the corresponding Lineweaver–Burk plot.

 $\rm h^{-1})$ value of this catalysis is 6581. This value is significantly greater than the $k_{\rm cat}$ values of the reported Co(II)/(III),

Mn(II)/Mn(III), Cu(II), and Ni(II) systems performing as functional models of phenoxazinone synthase.

ESI-Mass Spectrometric Study. To investigate the mechanism of phenoxazinone synthase activity and complexsubstrate intermediate during the oxidative dimerization reaction of o-aminophenol, we have recorded ESI-MS spectra of **2** in a 1/1 mixture (v/v) of the complex and *o*-aminophenol within 4 min of mixing in methanol (Figures S16 and S17 in the Supporting Information). A spectrum of a mixture of complex 2 and *o*-aminophenol shows a base peak at m/z 380.04 (calcd 380.05) (Figure S16), which can be assigned to the sodiated metalloligand species $[(CuL) + Na]^+$. The spectrum also shows two peaks at m/z 358.06 (calcd 358.07) for the protonated metalloligand species $[(CuL) + H]^+$ and m/z737.13 (calcd 737.12) for the sodiated dinuclear species $[(CuL)_2Na]^+$ (Figure S16). All of these species have previously appeared in the mass spectra of complex 2. In addition, two low-intensity peaks are observed at m/z 1026.43 (calcd 1026.14) and m/z 1052.45 (calcd 1052.11) (Figure S17), which indicate the presence of the two trinuclear species $[(Cu^{II}L)_2Mn(OAP)_2 + K]^+$ and $[(Cu^{I}L)_2Mn(OAP)_2 + 3Na]^+$, respectively. The peaks of intermediates $[(CuL)_2Mn(OAP)_2 +$ $K]^+$ and $[(CuL)_2Mn(OAP)_2 + 3Na]^+$ also indicate the oxidative conversion of o-aminophenol to phenoxazinone catalyzed by complex 2. We have also checked that no H₂O₂ was formed during this catalytic conversion reaction.

EPR Spectroscopy. The phenoxazinone synthase like activity of complexes 2 and 3 with OAP was also followed with EPR in a manner similar to that for DTBC. Figures S26 and S27 in the Supporting Information show the EPR spectra of complexes 2 and 3 in the presence of OAP at different times after addition of OAP. One can see that a new signal is formed in both complexes 2 and 3 after addition of OAP (Figure 12). It is present in the same region as that in the DTBC reaction. Thus, one could say that both complexes 2 and 3 show phenoxazinone synthase like activity with OAP. To see if they both are equally efficient, we compared the intensity of this new signal at different times. To get this information, the EPR spectra of the complexes before addition of OAP were subtracted from those obtained after OAP addition. This gives us the spectrum of the new radical, which is shown in Figure 12 for both complexes 2 and 3. The spectra show that the intensity of this new signal is less in complex 3 in comparison to that in



Figure 12. Difference EPR spectra of **2** (left) and **3** (right) in methanol at 96 K. The spectra have been generated by subtracting the EPR spectra of the complexes after addition of OAP from those obtained before addition of OAP. The magnetic field range is reduced so as to make the comparison clear.



 $m/z(+3Na^+) = 1052.45$

2. Thus, one may conclude that complex 2 is more reactive toward OAP in comparison to 3.

Mechanistic Insight. After a thorough study of ESI-mass spectra and EPR spectra we have determined a possible mechanism. When o-aminophenol is added to a solution of complex 2, the trinuclear species $[(CuL)_2Mn(OAP)_2]$ is formed (Figure S17 in the Supporting Information). This is a neutral species in which two hydroxyl groups of two oaminophenols are deprotonated and coordinated to the Mn(II) center. Then the species releases a hydrogen from the amine $(-NH_2)$ group of one *o*-aminophenol and forms a radical. This is relatively very unstable and quickly turns into its iminophenolate form by releasing hydrogen from another oaminophenol. During this process one O₂ is reduced to H₂O. The existence and relative stability of this species can be assigned by mass spectra (Figure S16 in the Supporting Information). After that, one o-iminophenolate and one oaminophenolate combine to form phenoxazinone and eliminate the trinuclear complex where Cu(II) is reduced to Cu(I). During this total process 3/2 O2 is reduced and 3 H2O is formed as a byproduct. The probable mechanism of this catalytic reaction is given in Scheme 5.

Structure–Activity Correlation for the Observed Relative Performance of the Catalyst. There has been increased interest in synergistic catalysis, on the basis of heterometallic complexes and clusters with numerous combinations of metal ions.³⁵ For example, a Cu-Mn mixed-metal spinel has been reported to show increased efficiency as a heterogeneous oxidation catalyst, but no mechanistic insight was provided.³⁶ To pursue a mechanistic investigation into heterometallic complexes as homogeneous catalysts, the heterometallic core

should be stable enough in solution during the catalytic process, but no such report regarding a Cu(II)-Mn(II) complex has been found before.³⁵ Previous reports also indicate the use of stable heterometallic complexes as efficient synergistic catalysts which are often derived from multicompartmental ligands (e.g., N_2O_4 -donor di-Schiff bases, Robson-type macrocycles)³⁷ that increase the liberty of using the catalysts under different conditions.³⁸ In comparison to these complexes, $[(ML)_2M']$ type complexes (H_2L = salen type N_2O_2 donor di-Schiff bases, M, M' = different metal ions) are much less stable and they retain only partially their heterometallic core in solution, which lowers the effective concentration of the catalyst. Such trends are also observed for Shibasaki catalysts,³⁹ which possess a diphenoxido-bridged heterometallic core similar to that of $[(ML)_2M']$. In contrast, the inherent structural flexibility⁴⁰ associated with these trinuclear complexes might be advantageous^{15a,41} to be adaptable with different types of substrates in comparison to the rigid complexes. However, the use of $[(ML)_2M']$ type complexes as catalysts has been largely limited to only a very few occasions.¹³

Recently, we reported a few heterometallic Ni^{II}₂Mn^{II} complexes derived from symmetric salen type tetradentate Schiff base ligands which showed moderate to weak COx like activity. However, mechanistic insight into any such heterometallic complex as an oxidase model is not found in the literature.¹³ Interestingly, analogous Cu^{II}₂Mn^{II} (or other Cu^{II}₂M) heterometallic complexes derived from similar Schiff base ligands did not show COx or any other oxidase type catalytic activity.^{22a} Complex 3, derived from an asymmetric salen type Schiff base ligand, is also found to be ineffective toward oxidase type catalysis in the present study. Such

inactivity could be explained by the common structural feature of the central Mn(II) center of the basic Cu^{II}₂Mn^{II} unit. In all of these cases the coordination sites of the octahedral Mn(II) center are blocked by two anionic coligands (pseudohalides $(NCO^{-}, SCN^{-}, N_3^{-} \text{ or } C_2N_3^{-})$, nitrate, carboxylates) which do not leave easily to facilitate substrate binding with Mn(II) centers. On the other hand, as the Cu centers are buried within the large tetradentate Schiff base (usually in a square-planar environment), substrate coordination might cause increased steric crowding in intermediates, which hampers substratecatalyst binding. This could be one good reason for the inactive nature of complex 3 as a catalyst or for the weak to moderate catalytic activity of Ni^{II}₂Mn^{II} complexes in comparison to 2. Moreover, the mass signals of compound 3 or $[(CuL)_2Mn]$ are practically absent (signals appeared for only metalloligands) in the presence of catechol, suggesting that the substrate leads to almost complete rupture of the trinuclear cluster. On the other hand, unlike the case for complex 3, the presence of the labile water molecule at the Mn(II) center of complex 2 facilitates substrate-catalyst binding (catechol or OAP) through Mn and subsequent formation of the corresponding semiquinonate radical. The inhibitory role of SCN⁻ in both catalytic processes was also established by adding 2 equiv of SCN⁻ to the mixtures of compound 2 and the individual substrates, upon which complete quenching of the catalysis was observed (Figure S28 in the Supporting Information), whereas addition of the same amount of N_3^- had no effect on the processes.

In all the proposed mechanisms for biorelevant oxidase models, substrate coordination takes place directly to the redoxactive metal center. However, in the present study it is evident that the Cu center does the job of electron transfer while the Mn(II) center remains redox innocent during the course of the catalysis, acting only as a Lewis acid center for the binding of substrate. It is interesting to note that the k_{cat} value of complex 2 is more than 10-fold higher than those of the analogous Ni^{II}₂Mn^{II} complexes and for phenoxazinone synthase like activity it is more than 20-fold higher than the highest reported value for synthetic model coordination compounds^{7a,42} (Table S4 in the Supporting Information).^{44–48} This high biomimetic oxidase type catalytic activity of complex 2 might originate from the heterometallic cooperative effects of dioxygen activation-a field which remains rather unexplored with the use of heterometallic systems.43

It should also be noted that the previously reported highly efficient homometallic Cu(II) catalysts as functional models of catechol oxidase are often derived from multicompartmental ligands with dinuclear Cu₂ cores and are much more stable than complex 2 (as 2 only partially retains its trinuclear $[(CuL)_2Mn]$ unit in solution). Thus, the actual catalyst efficiency or the turnover number cannot be directly compared. The turnover number of 2 for the oxidation of DTBC is calculated from the amount of the catalyst dissolved and is close to that obtained from these highly efficient homometallic catalysts reported. Moreover, to the best of our knowledge only two homometallic Cu(II) complexes have been reported to show PHS-like activity.^{8c} Thus, complex **2** is only the third copper-based^{8t} and the first heterometallic catalyst showing phenoxazinone synthase like activity and its turnover number is the highest among all the model complexes reported so far. Thus, the present complex, derived from an asymmetric tetradentate Schiff base ligand, validates the heterometallic cooperative effects on apparently substrate independent dioxygen activation, where two different metal ions do different jobs to make the catalyst highly efficient for biomimetic oxidase reactions.

CONCLUSIONS

In the present work, an asymmetrically dicondensed Schiff base has been synthesized and its mononuclear copper complex [CuL] has been isolated in a quick and efficient manner. Using this copper complex as metalloligand, two trinuclear heterometallic complexes (2 and 3) have been synthesized. The magnetic properties of the solid compounds reveal antiferromagnetic coupling, as expected from bridging angles. An electrochemical investigation suggests that Cu(II) centers are reducible to Cu(I) in both complexes. The catalytic activities of the complexes in model biomimetic oxidase processes show that only complex 2 with a labile coordinated H_2O molecule at the Mn(II) center possess very high catalytic activity toward catecholase and the highest phenoxazinone synthase like activity among all of the reported synthetic complexes. The catalytic conversions take place with the formation of H₂O₂ and H₂O in catecholase and phenoxazinone synthase like activities, respectively. ESI-mass spectral analysis of complexes 2 and 3 and complex-substrate (3,5-DTBC and o-aminophenol) mixtures suggest the occurrence of a $[(CuL)_2Mn]^{2+}$ cluster as the active catalyst, complex-substrate binding, formation of a Cu(II) radical intermediate, and reduction of Cu(II) to Cu(I) in both catalytic processes using 2. On the other hand, EPR spectroscopic analysis suggests the formation of a radical intermediate. On the basis of ESI-mass and EPR spectral analyses, probable mechanisms for the catalytic reactions are proposed where the Mn(II) behaves as a Lewis acid center to bind the corresponding phenolic substrate, whereas Cu(II) behaves as a redox-active center that transports an electron from substrate to oxygen. The simultaneous action of these two processes on two metal centers leading to a heterometallic cooperativity of catalytic oxidase transformation of the two structurally analogous phenolic substrates seems to account for the very high catalytic activity of this complex. On the other hand, complex 3 does not show any discernible catalytic activity, presumably due to its inability to form a complexsubstrate intermediate in solution.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.7b00253. CCDC 1521947 (for 1), 1521948 (for 2), and 1521949 (for 3) contain supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www. ccdc.cam.ac.uk/data_request/cif.

UV, IR, mass, and EPR spectra, cyclic voltammograms, SEM micrographs, X-Ray powder diffractograms, and bond parameters of complexes 1–3, EPR and mass spectra of complexes 2 and 3 with 3,5-DTBC and OAP, and a list of complexes from the literature and their K_{cat} values for which catecholase-like activities have been analyzed (PDF)

Crystallographic data for 1-3 (CIF)

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