Direct dizinc displacement approach for efficient detection of Cu^{2+} in aqueous media: acetate *versus* phenolate bridging platforms†

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Two chiral and one racemic fluorescent dimeric zinc complex {$[Zn_2(slysH)_2Cl_2]\cdot(CH_3OH)_2\cdot(H_2O)_3$ (**1**), $[Zn_2(slysH)_2\ (NO_3)_2]\cdot(H_2O)_3$ (**2**), $[Zn_2(rslysH)_2(\mu\text{-}OAc)_2]$ (**3**)} are compared herein. Presently, **3** has been synthesized by a one-pot reaction in which the D-/L- lysine-based Schiff base ligand [*slys* = 6-amino-2-{(2-hydroxybenzylidene)amino}hexanoate] is generated *in situ*. These compounds have been characterized by single-crystal X-ray diffraction and by various spectroscopic techniques. The structures of previously reported compounds **1** and **2** are closely related in which two zinc centers possess two phenolate-bridges and an axial chloride or nitrate ligand. The novel compound **3** differs structurally through the presence and coordination mode of two bridging acetate groups spanning the dizinc core and formally releasing the phenolate bridging Schiff base ligands. These compounds (**1–3**) are highly blue fluorescent, either as solids or dissolved species. Under neutral and aqueous conditions (pH 7.4; 0.01 M HEPES buffer, H_2O–MeOH = 9 : 1), the quantum yields are Φ_F = 0.17 (**1**), 0.21 (**2**) (λ_{ex} = 352 nm, λ_{em} = 452 nm), Φ_F = 0.16 (**3**) (λ_{ex} = 354 nm, λ_{em} = 452 nm). Complex **3** metal ion detection capability (*i.e.*, Na^+, K^+, Ca^{2+}, Mg^{2+}, Co^{2+}, Ni^{2+}, Mn^{2+}, Cu^{2+}, Pb^{2+}, Ag^+, Hg^{2+}, and Cd^{2+}) was gauged in aqueous media at physiological pH facilitated by the similarity of its starting photophysical properties with those of **1** and **2**. These dizinc species were all found to act as a highly selective fluorescent ON–OFF probes for Cu^{2+} through the direct displacement of two zinc ions in aqueous media at physiological pH range. The phenolate-bridged compounds **1** and **2**, however, showed better selectivity towards Cu^{2+} over competitive ions, Ni^{2+} and Co^{2+} than the acetate-bridged compound **3**.

Introduction

The importance of the soluble free and complexed cupric ion, through its redox chemistry, has enormous natural consequences in the fields of biology and disease which cannot be understated. The homeostasis of biological copper involves a careful balance of a variety of natural transporters and biological processes.[1] When there is disruption to this homeostasis, pathology can manifest in ways that include neurodegeneration. Serious neurodegenerative diseases such as Wilson's disease, Alzheimer's disease and prion-induced diseases may emerge.[2] Thus, to understand the propensities of copper, especially in biological systems, there are continued efforts involved in inspecting copper transporters[3] and aqueous solution copper sensing (*vide infra*).

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† Electronic supplementary information (ESI) available: Reproductions of proton NMR spectra, ESI-MS data, related UV-vis and emission spectra, Job plot of compound **3** and ORTEP diagram of compounds **1** and **2**, all types of UV-vis data, emission spectra, and NMR spectra of zinc complex of L-lysine-based Schiff base ligands (**2**) and some digital photographs in PDF format. CCDC reference number 748438. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b9nj00770a

Metal ion sensing in chemistry and chemical biology is an enormously interesting and important area of ongoing research often involving creative exploits in organic chemistry and an understanding of detailed ligand-metal host/guest chemistry.[4] There are various important characteristics when trying to design an optical sensor (for, *e.g.*, Cu^{2+} ion). These criteria include selectivity, in terms of qualitatively determining the particular metal ion present in a mixture and quantitating the metal ion concentration; a ratiometric type response is often preferred. This ties in with detection sensitivity toward the specified solvated metal ion present at very low concentration. Additionally, high stability of the receptor is an important requirement that allows for intermediate host–guest speciation with eventual analyte release to afford reversibility. Next, various fluorescent "turn-on" species have been reported[5] as well as optical species exhibiting *on–off* behaviour[6] in aqueous media.[7]

In terms of receptor design, it should also be relatively easy to synthesize molecular sensing entities for the highest reproducibility.[8] While there are hundreds of thousands of "ligands" and metal complexes, one critical concern is that sensors should not interfere with the native workings of biology; there is extreme complexity when considering sensors for the central nervous system which entail the issue of traversing the blood brain barrier. Thus, the design of the sensor should be rational to account for selective metal binding and optimization

of optical properties. Accordingly, various related designs of Cu^{2+}-specific molecular probes is on-going in the realms of biological and analytical chemical sciences.[5–7,8b] Various zinc designs, including dimeric ones, have been reported recently for, *e.g.*, this journal.[8d,e] Further consideration of Zn···Zn spacings can lead to an understanding of controlling anion docking/recognition.

Herein, we report the synthesis and characterization of a highly fluorescent di-acetate-bridged D/L-lysine-based Schiff base dizinc complex **3** $[Zn_2(rslysH)_2(\mu\text{-}OAc)_2]$ and its Cu(II) ion detection in aqueous media through direct metal ion displacement. The structural and reactivity relationships and the comparison with previously reported phenolate-bridged two chiral complexes $[Zn_2(slysH)_2Cl_2]\cdot(CH_3OH)_2\cdot(H_2O)_3$ (**1**)[8a] and $[Zn_2(slysH)_2\ (NO_3)_2]\cdot(H_2O)_3$ (**2**)[8b] are also discussed herein. This study allows for an approximate comparison between dimetallic systems of phenolate *versus* acetate bridging in the context of "direct displacement" M^{n+} ion detection.

Results and discussion

Synthesis

Compounds **1–3** were synthesized by an extremely facile "one pot" procedure as illustrated in Scheme 1, and were isolated in high yield. The aqueous solution of zinc salts were added to salicylaldehyde in methanol, followed by the addition of an aqueous solution of L-lysine or D/L-lysine (for compounds **1–2**: L lysine; for **3**: D/L lysine). An aqueous NaOH solution was then added dropwise into the reaction mixture; finally, an aqueous solution of sodium acetate was added to the reaction mixture to maintain a pH value of 7–8 (for **1** and **2**, several drops of Et_3N were used to keep the pH ~7.0). The appearance of a light yellow solid after 12 h indicated the formation of the intended product. The solid was characterized by elemental analyses, IR, UV-visible, ESI-MS, CD spectroscopy (for **1** and **2**) and finally by single-crystal X-ray diffraction.

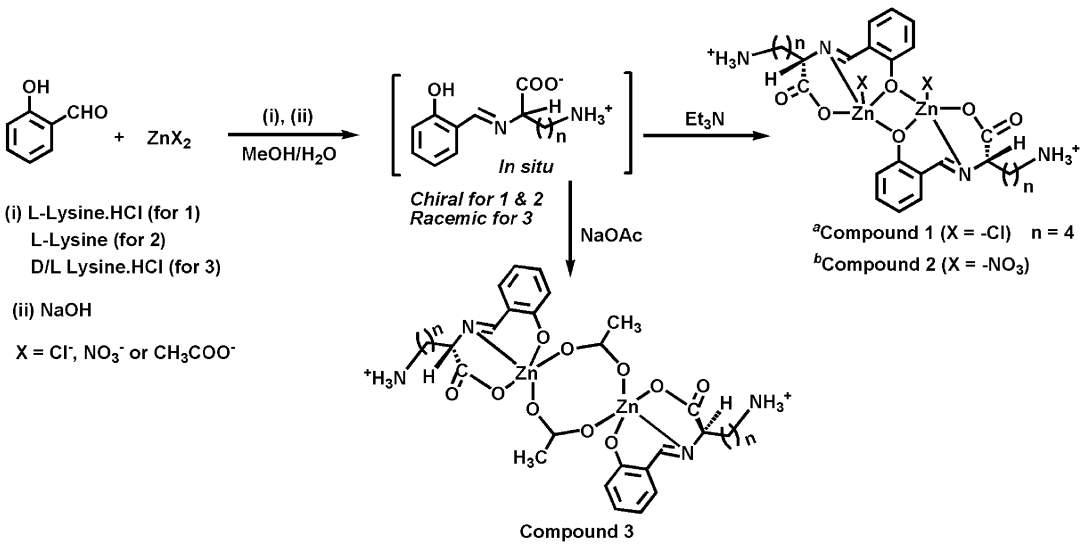
X-Ray crystallography

Suitable X-ray diffraction quality single crystals of compound **3** were obtained from a water–methanol mixture (3 : 1). The compound crystallized in the triclinic space group $P\bar{1}$. The molecular structure of the compound is shown in Fig. 1 and 2. The molecular structure of compounds **1** and **2** are shown, respectively, in Fig. S9 (a and b).†

Structure of $[Zn_2(rslysH)_2(\mu\text{-}OAc)_2]$ (3). X-Ray diffraction analysis reveals that the asymmetric unit for **3** contains only half of the molecule as it is positioned over an inversion center. The unit is composed of one D- or L-lysine-based ligand bonded to a zinc atomic center in a tridentate fashion. The acetate ligands span both zinc centers and are nearly perpendicular to the [O1, N1, O2, Zn1] mean plane as shown by the full crystallographic structure of the compound. This ligation allows for each of the zinc centers (Zn···Zn: 4.02 Å) to adopt a highly distorted square pyramidal environment. The observed Zn–O distances (1.982–2.109 Å) are comparable to those of previously reported dimeric zinc complexes.[8a,b] The complex is nominally neutral: the two bridging acetate groups are countered by the protonation of the ε-NH_2 groups ($-NH_3^+$). Since we started with D/L lysine in preparing the ligand, the dimeric complex is racemic, containing both ligand isomers (stemming from the D- and L-lysine-based Schiff base) (see Scheme 1 and Fig. 1). In the solid state, hydrogens of the terminal $-NH_3^+$ group are observed to point in the direction of the phenolate oxygen and carbonyl and carboxylate oxygens of Schiff base ligand. This assignment of hydrogen bonding [N2–H2B···O1$^{\#}$, 2.679(4) Å; N2–H2C···O3$^{\#\#}$, 2.748(4) Å; and N2–H2A···O2$^{\#\#\#}$, 2.812(4) Å. Symmetry code: # = x, 1 + y, z; ## = 1+ x, y, z; ### = $-x$, 1$-y$, 1 $-$ z.] allows for the consideration of formal 2-D networks (Fig. 2).

Solution properties and Cu^{2+} detection

The structure for **3** differs from the previously reported dinuclear zinc complexes **1** and **2**, in which the phenolate acts



Scheme 1 Synthesis of compounds **1–3** in which '*a*' and '*b*' stand for ref. 8*a* and 8*b*, respectively.

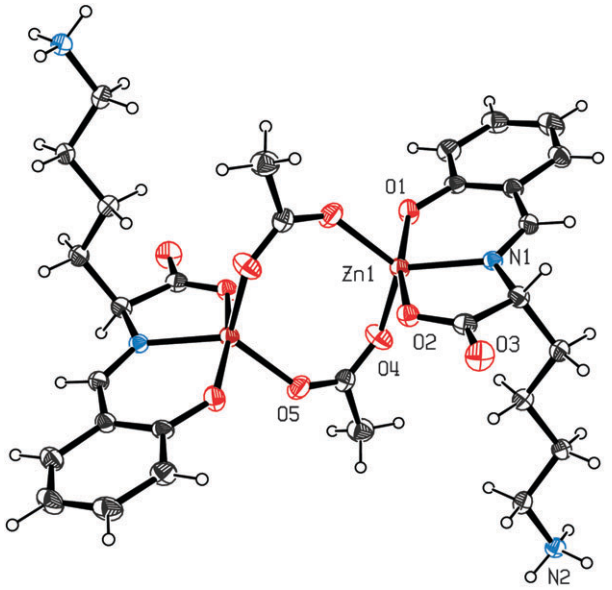


Fig. 1 Crystal structure of compound **3**. Thermal ellipsoids are drawn at a 30% probability level.

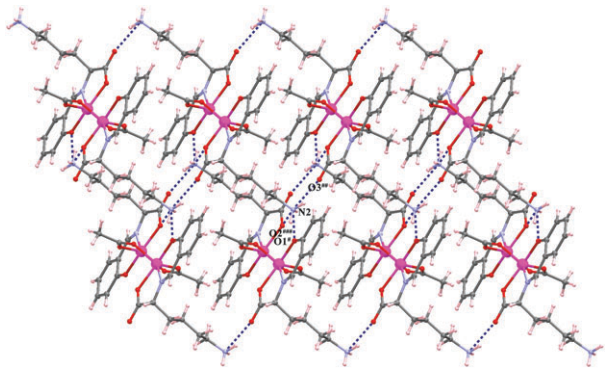
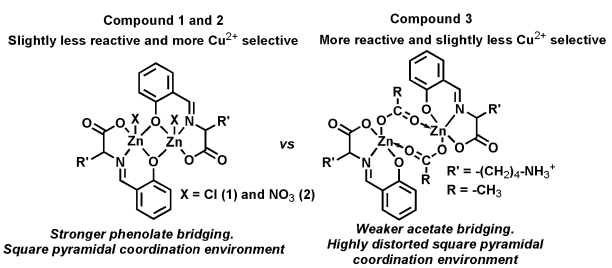


Fig. 2 2-D hydrogen bonded packing structure of compound **3** along the crystallographic *c*-axis. The dotted line represents the hydrogen bond.

as a bridge between two zinc centers (see Scheme 1 and ESI for structure of compound **1** and **2**†). Armed with this structural information, we are able to probe the relative stability of the diacetate-bridged dimeric zinc complex (**3**) with respect to their dissociation or displacement in solution. The possibility for the displacement of one, or both, acetate groups in **3** may easily allow for a different conformation, *e.g.*, that for the (phenolate-bridged) dinitrate in compound **2**. (Scheme 2).



Scheme 2 Stability, reactivity and selectivity in phenolate *versus* acetate bridging platforms.

Compound **3** has also been characterized by ^{1}H NMR spectroscopy and ESI mass spectrometry. All signals in the ^{1}H NMR spectrum have been assigned with the help of ^{1}H–^{1}H COSY NMR for the related dizinc species compound **2**.[8a] The spectrum reveals one singlet at 1.83 ppm for the methyl group of the bridged acetate group; this is overlapped with the δ-CH_2 group of the lysine (1.79–1.89 ppm). The ESI mass spectra show the base peak at *m*/*z* 685.1, corresponding to the dizinc compound **3** formulated with only one (bridging) acetate group [$C_{28}H_{35}N_4O_8Zn_2$ {**3**–($CH_3COO^- + 2H^+$)}$^+$]. This implies that compound **3** is slightly unstable in dilute aqueous solution because the bridging acetate group can easily dissociate in the presence of competitive anions and solvent water. It should be noted, however, that in concentrated solution ([**3**] $\geq$ 0.001 M) the compound is stable over 3 weeks underscored by the observation that the material that provided the single crystal for X-ray diffraction (confirming the diacetate-bridged dizinc structure) was obtained cleanly from a concentrated solution.

As for compounds **1** and **2**, compound **3** is also moderate-to-highly blue fluorescent in solution (Φ_F = 0.16, reference: fluorescein), as well as in the solid state. It is already mentioned that the impure metal-free Schiff base ligand (H_2*rslys*) has weak green fluorescence; it did not show any fluorescence enhancement in the presence of heavy metal ions Hg^{2+} and Pb^{2+} and d-block metals such as Cu^{2+} known generally as fluorescence quenching species. The nitrogen of the imine group (C=N) is one of the principal binding atoms; this binding affects the phenyl-group conjugation inhibited in the strong chelate with Zn^{2+}; this generates the observed intense OFF–ON blue fluorescence. The Schiff base ligand (H_2*rslys*) itself is weakly fluorescent, it is a less effective *turn-off* sensor for the aforementioned heavy metal ions. But, compound **3** is highly fluorescent; so, like compound **1** and **2**, significant quenching effects would be expected from the aforementioned metal ions *via* direct displacement. Due to structural dissimilarity, different ion selectivity and sensitivity is also expected.

Compound **3** was tested by UV-vis and fluorescence spectroscopy with various metal cations (*e.g.* Na^+, K^+, Ca^{2+}, Co^{2+}, Ni^{2+}, Mn^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Ag^+, Hg^{2+}, and Pb^{2+}) in neutral an aqueous media (pH 7.4; 0.01 M HEPES buffer, H_2O : MeOH = 9 : 1). The UV-vis spectrum of compound **3** (50 μM) in aqueous solution reveals two bands at 267 and 354 nm due to intra-ligand charge transfer transition. When 2.0 equiv. of Cu^{2+} ions (100 μM) were added the absorbance decreased slightly while the λ_{max} is red-shifted to 358 nm. Under these same conditions, other metal ions, such as Ca^{2+}, Mn^{2+}, Co^{2+}, Ni^{2+}, Hg^{2+}, Cd^{2+}, Na^+, K^+, Ca^{2+}, and Mg^{2+} showed very minor, unremarkable changes in the UV–vis spectrum (Fig. 3a). The addition of 2 equiv. of Pb^{2+} to a solution of **3** unexpectedly increases the absorbance and blue-shifts the λ_{max} of **3** by ~12 nm. Pb^{2+}, however, had no effect on the UV-vis spectra of compounds **1** and **2** (see ESI†). Here Pb^{2+} may react with, and thus disrupt, the diacetate-bridged compound **3**; but, an exact reason behind this optical behaviour is still unclear. Even though the Pb^{2+} ion may react with **3** and change the absorbance, compound **3** is not a "probe" for Pb^{2+} because this heavy metal ion did not give

a response in aqueous solution (pH 7.4, 0.01 M HEPES buffer, H_2O) in the emission spectrum (*vide infra*). During the absorbance titration of **3** (50 μM) with increasing amounts of Cu^{2+} (100 μM), the band at 354 nm slowly red-shifted to 358 nm; no more signal shifting was observed after the addition of more than 2.0 equiv. of Cu^{2+} ion (Fig. 3b).

Compound **3** is blue-emissive like compounds **1** and **2** with an emission at 452 nm when excited at 354 nm. The treatment of compound **3** with 2.0 equiv. of various metal ions support the specific behaviour of this complex for Cu^{2+} (Fig. 4a). All metal ions except Cu^{2+} quenched the emission partially (Fig. 4a), whereas Cu^{2+} quenched the fluorescence of **3** fully, giving an emission intensity decrease of ~2660-fold after addition of 2.0 equiv. (Φ_F = ~0.00, Fig. 4b). The Job plot analysis supports a **3**:Cu^{2+} stoichiometry of 1 : 2 upon direct displacement (see ESI†). Although here the value is ~0.40, for ideal 1 : 2 stoichiometry the value should be 0.33. Thus, it is proposed in solution that an equilibrium may exist between 1 : 1 and 1 : 2 coordination.[9] During the emission titration of **3** (50 μM) with increasing amounts of Cu^{2+} (100 μM), the intensity of the emission band at 452 nm gradually decreased to almost zero; no more change was observed after the addition of more than 2.0 equiv. of Cu^{2+} ion (Fig. 4b). The apparent association constant (K_a) ~ $1.14 \pm 0.012 \times 10^8$ M^{-1} ($1.8 \pm 0.19 \times 10^8$ M^{-1} for compound **1** and $1.5 \pm 0.14 \times 10^8$ M^{-1} for **2**) was determined from emission titration data signifying the strong binding affinity of Cu^{2+} ion for the ligand.[10] Among other metal ions, Ni^{2+} and Co^{2+} also quenched the fluorescence but only ~1.4-fold and ~1.9-fold decrease of emission intensity when 2 equiv. of each metal ions were added. Association constants therefore were not calculated for these cases. As Cu^{2+} sensing occurs through zinc displacement, we sought the possible reverse reaction by treating the formed analogous copper complex (**3**: $2Cu^{2+}$ mixture) with excess Zn^{2+} ion in aqueous buffer solution. Fluorescence was not restored, even after the addition of ~40 equivalents of Zn^{2+} ion. This result implies that Cu^{2+} has a very strong binding affinity to the H_2*rslys* ligand compared to that of Zn^{2+} (Fig. S4†).

Compound **3** is highly selective towards Cu^{2+} over other competitive metal ions (Fig. 5). The emission intensity of compound **3** in the presence of 10.0 equiv. of other metal ions decreased little. Upon the addition of only 2.0 equiv. of Cu^{2+} to the 1 : 10 mixture of **3** and other metal ions, the fluorescence is instantly, and entirely, quenched. In contrast to **1** and **2**, for compound **3** the addition of 10 equivalents of transition metal ions Ni^{2+} and Co^{2+} quench the fluorescence of compound **3** distinctly (~2 and ~4.9 fold, respectively) whereas for **2**, this response was very minor (see Fig. S15 in the ESI†). So the selectivity of compound **3** toward Cu^{2+} in presence of other competitive ion is slightly less than that for compounds **1** and **2**.

In contrast to **1** and **2**, complex **3** is inactive when pursuing CD spectroscopy because it is racemic; a solution of **3** consists of both D- and L-lysine-derived Schiff base ligands. The absorbance titration of **3** (100 μM) with increasing amount of Cu^{2+} solution (200 μM) clearly shows the formation of a characteristic *d*–*d* transition band (500–800 nm) of a Cu^{2+} complex and confirms Zn^{2+} displacement by Cu^{2+} (Fig. 6).

A reaction was performed by mixing compound **3** and $Cu(OAc)_2 \cdot H_2O$ in a water–methanol (1 : 1) solution. After several attempts, single crystals were not obtained from this reaction mixture, but rather a bluish powder was isolated. This material is insoluble in common organic solvents as well as in water, and occurred together with other side products (displaced zinc salts). So we were unable to adequately characterize this product by mass spectrometry or elemental analysis. It should be noted that copper Schiff base complexes were synthesized directly by using $Cu(OAc)_2 \cdot H_2O$, salicylaldehyde and D/L-lysine by a one pot method: both the mono- (purple coloured) and di-nuclear (blue coloured) monoacetate bridged complex were isolated and structurally characterized.[11] This dinuclear blue crystalline compound formed a bluish precipitate after dissolution in water. This powder is suspected to be the neutral copper(II) Schiff base complex, free of acetate ion, based only on elemental analysis, however. So we assume that after direct displacement, similar monoacetate-bridged dinuclear copper species might be formed.

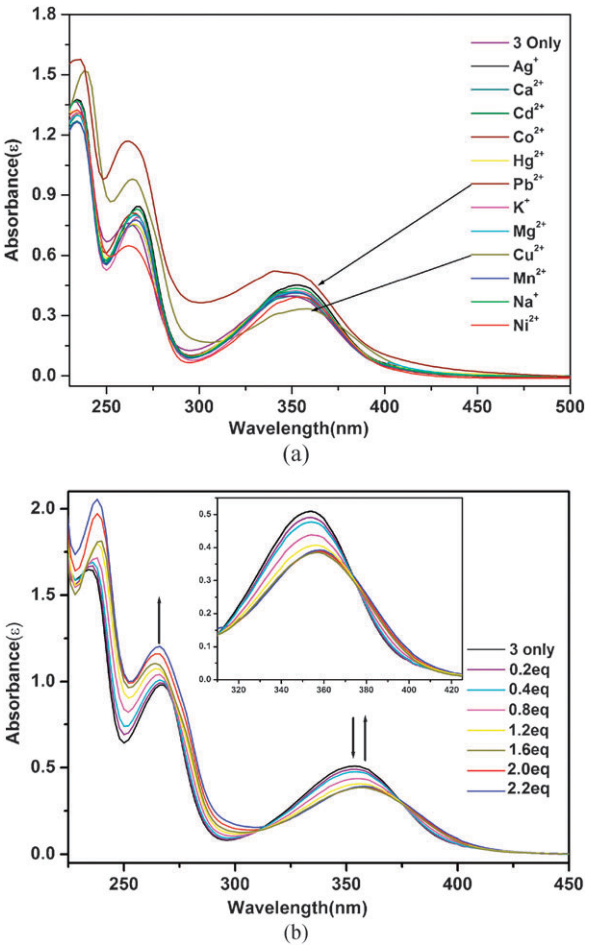


Fig. 3 (a) UV-vis spectra of **3** (50 μM) with different cations (100 μM). (b) Absorbance titration of **3** (50 μM) in aqueous buffer (pH 7.4, 0.01 M HEPES, H_2O: MeOH = 9 : 1) with increasing amounts of Cu^{2+} solution (100 μM). (*inset*) expanded 310–420 nm region of the spectrum.

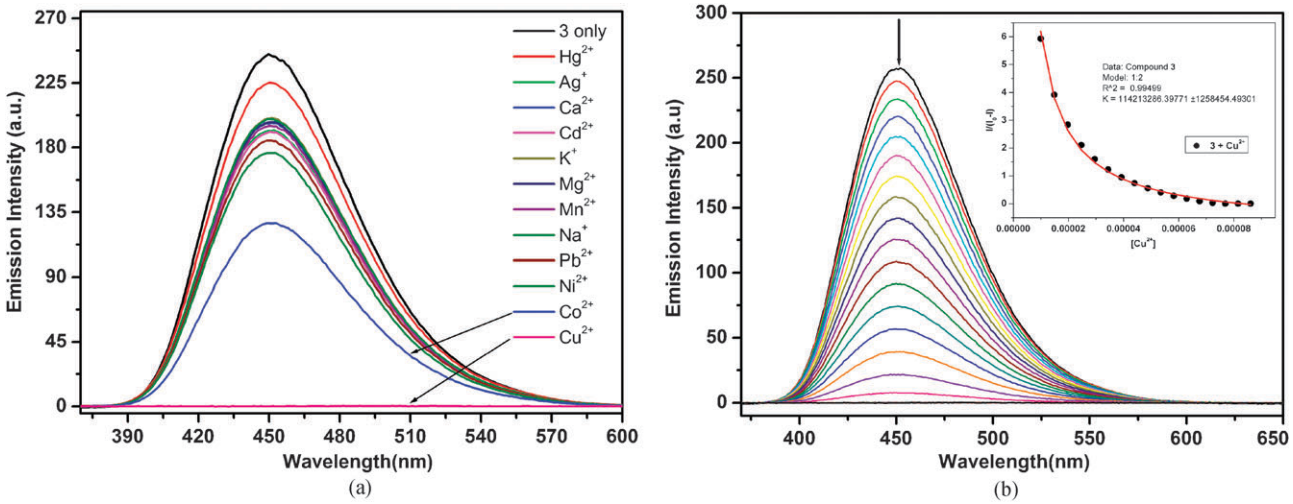


Fig. 4 (a) Emission spectra of **3** (50 μM, λ_{ex} = 354 nm, $\lambda_{em,max}$ = 452 nm) with different metal cations (100 μM). (b) Emission titration of **3** (50 μM) in aqueous buffer solution (pH 7.4, 0.01 M HEPES, H_2O–MeOH = 9 : 1) with increasing amount of Cu^{2+} solution (100 μM) (*inset*) the non-linear curve fitting from emission titration data.

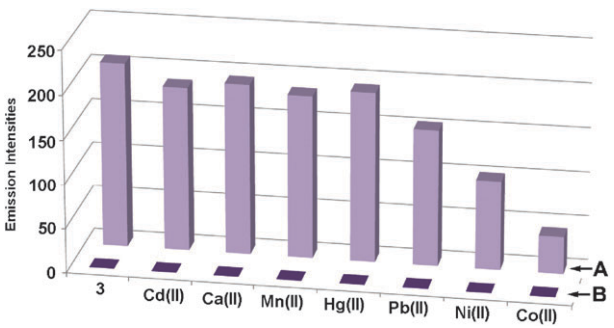


Fig. 5 (*Row A*) Emission spectra of **3** (50 μM) in aqueous buffer solution (pH 7.4, 0.01 M HEPES, H_2O–MeOH = 9 : 1) with different cations (500 μM), far left is only compound **3**. (*Row B*) Emission spectra of a mixture of **3** (50 μM) with other metal ions (500 μM) and with Cu^{2+} solution (100 μM).

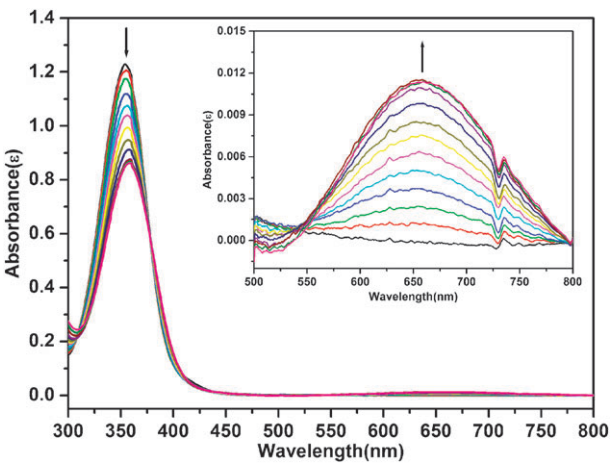


Fig. 6 Absorbance titration of compound **3** (100 μM) in aqueous buffer solution (pH 7.4, 0.01 M HEPES) with increasing amounts of Cu^{2+} titrant (200 μM) (*inset*). The *d*–*d* transition is clearly indicated in the 500–800 nm spectral regions due to Cu^{2+} complex formation as a result of Zn^{2+} displacement.

Conclusions

A diacetate-bridged dimeric zinc complex was synthesized by a facile "one-pot" method in which the Schiff base ligands were generated *in situ*. Other two dizinc species (**1** and **2**), which have also been synthesized by an analogous procedure, were compared herein. All compounds were characterized spectroscopically and structurally. Dimeric complexes **1–2** are highly soluble in water, whereas the solubility is lesser for **3**. The phenolate bridged compounds **1–2** are found to be more stable in solution than the fragile diacetate bridged compound **3** because in solution one bridging acetate is removed from the complex. All compounds detect copper ions (Cu^{2+}) over other competitive heavy transition metal ions in the useful physiological pH region by direct displacement of zinc metal. The sensitivity towards Cu^{2+} is very high in all cases, but due to structural dissimilarity and greater stability, the selectivity of compounds **1** and **2** towards Cu^{2+} is somewhat greater than that for compound **3**.

Experimental

Materials and physical measurements

All chemicals used herein were used as received from commercial suppliers (Aldrich and TCI companies). ^1H spectra were measured on either a Bruker Avance 300 MHz spectrometer, using TMS as the internal standard. Spectral signals were calibrated internally by the protio impurity of the D_2O solvent (δ 4.66). Absorption spectra were measured using a JASCO V-530 UV-Vis spectrophotometer. Fluorescence measurements were carried out with a Shimadzu RF-5301pc spectrofluorophotometer; all emission spectra were collected with the excitation and emission slits set at 3 nm and 1.5 nm (for compounds **1** and **2** set at 5 nm). Elemental analyses were performed using a EA1110-FISONS (Thermo Finnigan, Italia) CHNS–O elemental analyzer. ESI-MS was performed in Bruker micrOTOF II mass spectrometer. Digital photographs

Table 1 Crystal data collection and refinements data of compound **3**

Compound (CCDC #)	**3** (748438)
Empirical formula	$C_{30}H_{40}N_4O_{10}Zn_2$
FW	747.40
T/K	293(2)
Crystal system	Triclinic
Space group	$P\bar{1}$
a/Å	7.889(9)
b/Å	9.822(11)
c/Å	10.928(12)
α (°)	87.205(4)
β (°)	86.952(3)
γ (°)	69.015(3)
V/Å^3	789.08(15)
Z	1
ρ_c [Mg m^{-3}]	1.573
μ/mm^{-1}	1.583
F(000)	388
Crystal size/mm	0.15 × 0.10 × 0.10
Reflections collected	11000
Independent reflections	3757 [$R(int)$ = 0.0371]
Data/restraints/params.	3757/0/209
GOF on F^2	1.049
R_1,[a] w$R2$,[b] [$I > 2\sigma(I)$]	0.0444, 0.1219
R_1,[a] w$R2$,[b] [all data]	0.0689, 0.1525

[a] $R_1 = (\Sigma||F_o|-|F_c||)/\Sigma|F_o|$; [b] w$R2 = [(\Sigma(F_o^2-F_c^2)^2)/\Sigma w(F_o^2)^2]^{1/2}$.

of cuvettes for naked eye colourimetric and fluorometric detection of Cu^{2+} were taken using a Samsung VLUU NV4 digital camera.

Synthesis of [Zn_2(*rslys*H)$_2$(μ-OAc)$_2$] (3). An aqueous solution of $Zn(OAc)_2{\cdot}2H_2O$ (1.09 g, 5.00 mmol) was added to a methanolic solution of salicylaldehyde (0.52 mL, 5.00 mmol). After 30 min of stirring at room temperature, an aqueous solution of D/L-lysine monohydrochloride (0.913 g, 5.00 mmol) was added dropwise to the reaction mixture. This was followed by the successive slow addition of aqueous NaOH solution (0.20 g, 5.0 mmol). An aqueous solution of NaOAc (0.41 g, 5.0 mmol) was then added to the reaction mixture and the pH was maintained at 7–8; the stirring was maintained for a further 12 h. A light yellow precipitate was then filtered and washed thoroughly by methanol before being dried ambiently in air. Colourless single crystals suitable for X-ray diffraction study were obtained from a water: methanol (3 : 1) mixture. Yield: 42%. C, H, N analysis calc. (%) for $C_{30}H_{40}N_4O_{10}Zn_2$ (**3**) (M = 747.40 g mol^{-1}): C 48.21, H 5.39, N 7.50; found: C 48.34, H 5.22, N 7.51. FTIR in KBr disc (ν_{max}/cm^{-1} 2947, 1638, 1601, 1450, 1384, 1305, 1195, 1155. ^{1}H NMR (D_2O: δ 4.66) 1.27–1.39 (m, 2H$_\gamma$), 1.53–1.60 (m, 2H$_\delta$), 1.79–1.89 (m, 2H$_\beta$), 1.83 (s, 3H$_{O-C(=O)Me}$), 2.85–2.90 (t, $^3J_{H-H}$ = 7.6 Hz, 2H$_\varepsilon$), 3.84–3.88 (t, $^3J_{H-H}$ = 5.9 Hz, 1H$_\alpha$), 6.65–6.73 (m, 2H$_{11,13}$), 7.22–7.31 (m, 2H$_{10,12}$), 8.27 (s, 1H$_{imine}$). MS(ESI) calcd for $C_{28}H_{35}N_4O_8Zn_2$ [**3**-(CH_3COO^- + 2H^+)]$^-$ 685.1007, found 685.1043.

Compounds **1** and **2** were synthesized in an analogous, but slightly different, procedure in which the zinc and amino acid source (zinc chloride, L-lysine monohydrochloride for **1** and zinc nitrate, L-lysine for **2**) was different and aqueous NaOH solution and Et_3N was used to maintain the pH of the reaction medium. After 12 h of room temperature stirring, the volume of the reaction mixture was reduced under rotary evaporation and the light-yellow precipitate was isolated and washed and dried under vacuum.[8a,b]

Crystallographic studies. X-Ray diffraction measurements of compound **3** were performed with a Bruker-APEX II CCD diffractometer using graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å) at room temperature (293 K). Cell parameters were determined and refined by the SMART program.[12] Data reduction was performed using SAINT software.[12] The data were corrected for Lorentz and polarization effects. An empirical absorption correction was applied using the SADABS program.[13] All intensity data were corrected for Lorentz and polarization effects. The structures were solved by direct methods using the program SHELXS-97[14] and refined by full matrix least-squares calculations (F^2) by using the SHELXL-97 software.[15] For **3**, all non-H atoms were refined anisotropically against F^2 for all reflections. All H atoms, except those on the amine nitrogen atom (N2) were placed in calculated positions and refined isotropically. Hydrogen atoms attached to N2 were located in the difference Fourier maps and refined with isotropic displacement coefficients. Crystal data for compound **3** is given in Table 1. Selected bond lengths and angles are listed in Table 2.

Table 2 Selected bond lengths (Å) and angles (°)

N(1)–Zn(1)	2.051(3)	O(1)–Zn(1)	2.018(3)
O(2)–Zn(1)	2.109(3)	O(4)–Zn(1)	1.982(3)
O(5)–Zn(1)#1	1.998(3)	Zn(1)–O(5)#1	1.998(3)
O(4)–Zn(1)–O(5)#1	118.15(14)	O(4)–Zn(1)–O(1)	93.67(13)
O(5)#1–Zn(1)–O(1)	89.07(12)	O(4)–Zn(1)–O(2)	99.27(11)
O(4)–Zn(1)–N(1)	112.70(12)	O(5)#1–Zn(1)–O(2)	91.77(11)
O(5)#1–Zn(1)–N(1)	129.13(12)	O(1)–Zn(1)–O(2)	164.82(11)
O(1)–Zn(1)–N(1)	88.74(11)	N(1)–Zn(1)–O(2)	78.99(11)

Symmetry transformations used to generate equivalent atoms: #1 $-x,-y,-z$ + 1.

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