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Differential Sensing of Zn(II) and Cu(II) via Two Independent Mechanisms

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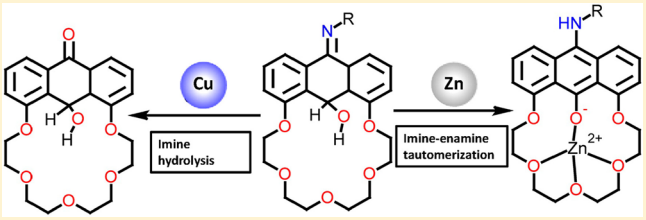
Supporting Information

ABSTRACT: Selective reduction of an anthracenone−quinoline imine derivative, **2**, using 1.0 equiv of $NaBH_4$ in 95% ethanol affords the corresponding anthracen-9-ol derivative, **3**, as confirmed by ^1H NMR, ^{13}C NMR, ESI-MS, FTIR, and elemental analysis results. UV−vis and fluorescence data reveal dramatic spectroscopic changes in the presence of Zn(II) and Cu(II). Zinc(II) coordination induces a 1,5-prototropic shift resulting in anthracene fluorophore formation via an imine−enamine tautomerization pathway. Copper(II) induces a colorimetric change from pale yellow to orange-red and results in imine hydrolysis in the presence of water. Spectroscopic investigations of metal ion response, selectivity, stoichiometry, and competition studies all suggest the proposed mechanisms. ESI-MS analysis, FTIR, and single-crystal XRD further support the hydrolysis phenomenon. This is a rare case of a single sensor that can be used either as a chemosensor (reversibly in the case of Zn(II)) or as a chemodosimeter (irreversibly in the case of Cu(II)); however, the imine must contain a coordinating Lewis base, such as quinoline, to be active for Cu(II).



INTRODUCTION

Chemosensors[1] and chemodosimeters[2] of single-ion responsive systems are common in the literature, but multi-ion responsive, unimolecular systems are still rare.[3] Such systems are of great interest in stimuli-responsive supramolecular systems because they can differentiate and detect analytes of interest in the presence of interfering ions. Multi-ion systems are also of fundamental importance when it comes to designing and developing complex molecular logic gates,[4] molecular keypad lock devices,[5] and "lab on molecule" type devices.[5c,6] However, challenges exist in developing such complex molecular systems, especially in detecting ions of biological interest.

Zinc(II) and copper(II) are prime cations of interest in biochemistry and neurobiology not only because they play key roles in enzymatic transformation reactions, but also because they are also known to contribute to serious pathological disorders such as Alzheimer's and Parkinson's diseases.[7] Copper is a serious environmental pollutant, and fluorimetric detection of this cation is often difficult because of its paramagnetic nature. Individual reports for either Zn(II) or Cu(II) are common;[8] however, reports on differential sensing of Zn(II)/Cu(II) are still rare.[9]

Because of their excellent selectivity and sensitivity, imine-based chemosensors and their metal complexes as chemodosimeters have proven attractive in this regard.[10] Aldimines and their metal complexes are well-known to undergo hydrolysis.[11] However, ketimines and their hydrolytic cleavage phenomena are less explored, although there is a growing number of ketimine derivatives as chemosensors,[12] macrocycles,[13] polymers,[14] and fluorescent dyes.[15]

Tautomerization is becoming an increasingly utilized mechanism for the fluorescent detection of cations, where cations can cause geometric changes in the sensor, which induces dramatic spectroscopic changes.[16] Recently, we reported the Zn(II)-mediated imine−enamine tautomerization of anthracenone−imine compounds, where a reduced 1,8-anthracenone−imine crown ether derivative undergoes a 1,5-prototopic shift upon Zn(II) coordination to yield an anthracene emission manifold and results in a 50−100-fold fluorescence enhancement upon Zn(II) binding.[17] This report follows this mechanism whereby Zn(II) induces a similar tautomeric shift in a quinolinyl-substituted anthracenone−imine molecular sensor; however, Cu(II) induces a different colorimetric change due to a hydrolysis mechanism of the imine group, as a new sensing paradigm for the multimode detection of Zn(II) and Cu(II) through disparate structural changes of the parent ligand. To the best of our knowledge, incorporating both a chemosensor and a chemodosimeter onto a single molecular system has never been reported.

RESULTS AND DISCUSSION

Compound **2**, containing a quinolinyl group, was synthesized by a previously reported procedure via selective imination of the external carbonyl of compound **1** (Scheme 1).[12] Selective reduction of the internal carbonyl was achieved using 1.0 equiv of $NaBH_4$ in aqueous ethanolic solution. Only the more electronegative carbonyl group is reduced leaving the imine group unreacted, even when reduced over a lengthy period of

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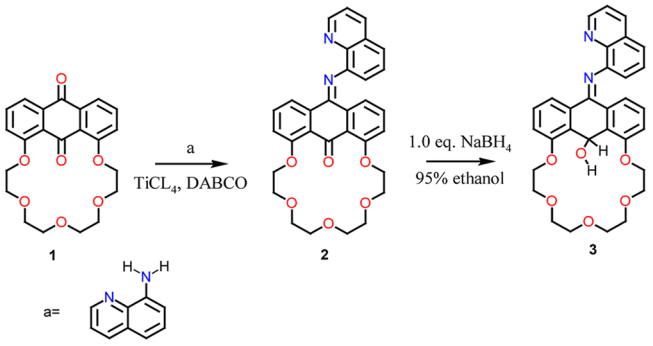
Scheme 1. Synthesis of Reduced Imines and Selective Reduction of Carbonyl Group



time (15 h). Solid-state crystallographic evidence contained in our previous report also indicates the preferential reduction of the carbonyl group.[17] FTIR analysis shows a C=N stretching band at 1629 cm^{-1} for **3**, no carbonyl stretch, and ESI-MS shows the sodiated parent ion peak at 549 *m/z*, as well. ^1H NMR analysis reveals formation of a hydroxyl proton at 5.7 ppm and a methine proton at 6.7 ppm for **3**, which is also indicative of reduction (Figures S1–S4, Supporting Information). Elemental analyses data are in good agreement with the expected product.

Photophysical properties that describe the optical changes upon metal ion addition were carried out using metal perchlorate salts of NH_4^+, Ba^{2+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, Li^+, Mg^{2+}, Mn^{2+}, Na^+, Ni^{2+}, Pb^{2+}, Sr^{2+}, and Zn^{2+} in acetonitrile. In the absence of any metal ion, compound **3** has a very weak emission due to nonradiative quenching processes that occur via a standard C=N isomerization deactivation pathway. Compound **2** shows neither selectivity nor enhancement in fluorescence upon the addition of any metal ion (Figures S5 and S6, Supporting Information). However, compound **3** shows nice selectivity and fluorescence enhancement for Zn(II) only (Figure 1a,b). A 42-fold fluorescence enhancement with a bright blue emission is evidenced upon the addition of 5.0 equiv of Zn(II). Pb(II) is the only other cation that showed slight interference with Zn(II). Paramagnetic cations such as Fe(III) and Cu(II) completely quench the fluorescence emission of **3** in acetonitrile. The UV–vis absorbance spectrum of **3** shows peak maxima at 325 and 386 nm. Upon the successive addition of Zn(II), a red shift in the absorbance spectrum is observed (Figure 2).

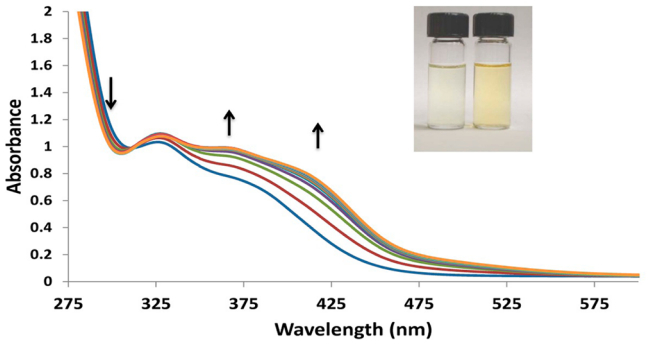


Figure 2. UV–vis titration of 5.0×10^{-5} M of compound **3** in acetonitrile with increasing amounts of the Zn(II) addition, from 0.0 to 3.0 equiv. Inset: photograph showing the color change, before (left) and after (right) Zn(II) addition.

As previously reported, emission enhancement is the result of zinc-mediated imine–enamine tautomerization (Scheme 2) that produces an anthracene lumophore and the readily recognizable anthracene emission manifold (Figures 1 and 3).[17] The proton undergoes a 1,5-prototropic shift to the imine nitrogen, resulting in formation of the extended π-conjugated anthracene lumophore. Upon Zn(II) addition, the UV–vis spectra (Figure 2) also suggest the growth of the concomitant anthracene absorbance manifold under the broad absorption band of the starting material.

A fluorescence titration was carried out using **3** in acetonitrile and, upon increasing amounts of Zn(II) ion addition, a gradual enhancement in fluorescence occurs as shown in Figure 3. Stoichiometric analysis indicated a 1:1 ligand–metal formation as is evidenced by the saturation of fluorescence at the addition of 1 equiv of Zn(II) (Figure 2, inset). Fitting the data to a L +

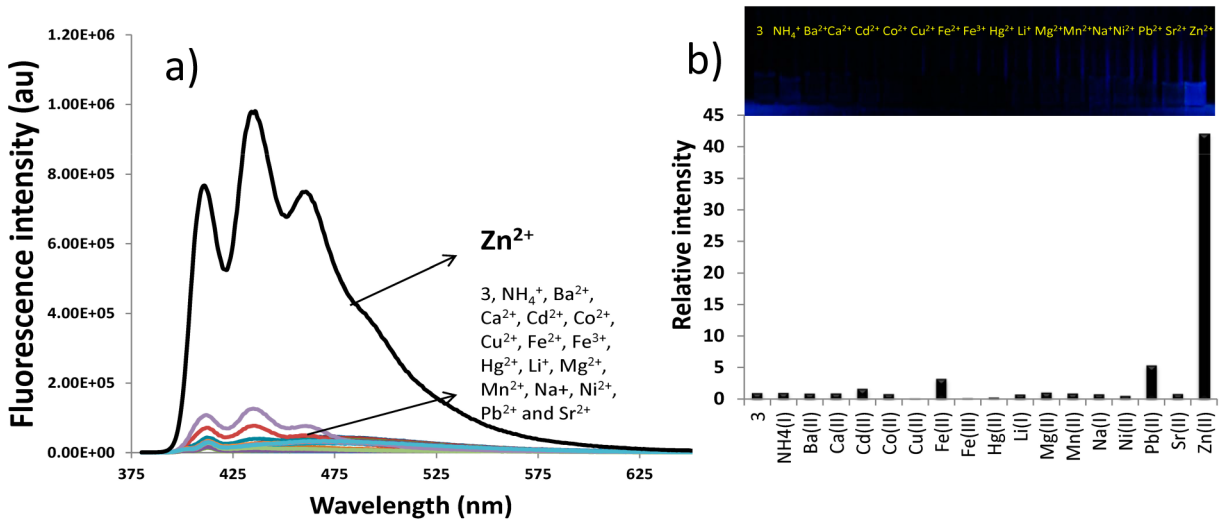


Figure 1. (a) Fluorescence emission profile of compound **3** (4.0×10^{-5} M) in the presence of various metal perchlorate salts of NH_4^+, Ba^{2+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, Li^+, Mg^{2+}, Mn^{2+}, Na^+, Ni^{2+}, Pb^{2+}, Sr^{2+}, and Zn^{2+} (5.0 equiv) in acetonitrile. λ_{ext} = 367 nm. (b) Fluorescence enhancement bar graph and optical photograph under UV-light excitation in presence of various metal ions.

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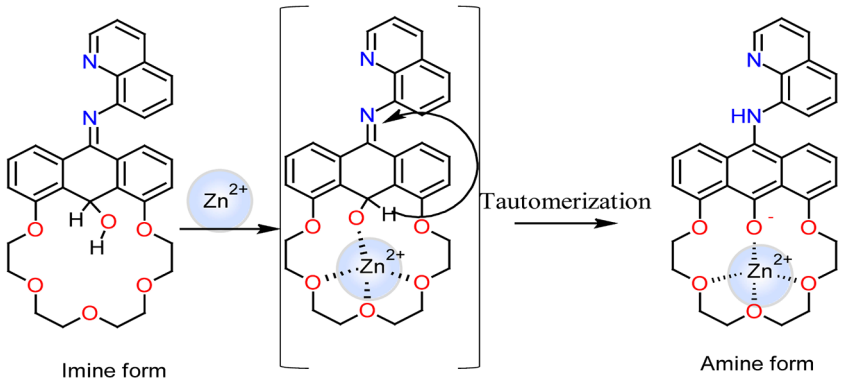
Scheme 2. Zn(II)-Induced Tautomerization of Compound 3



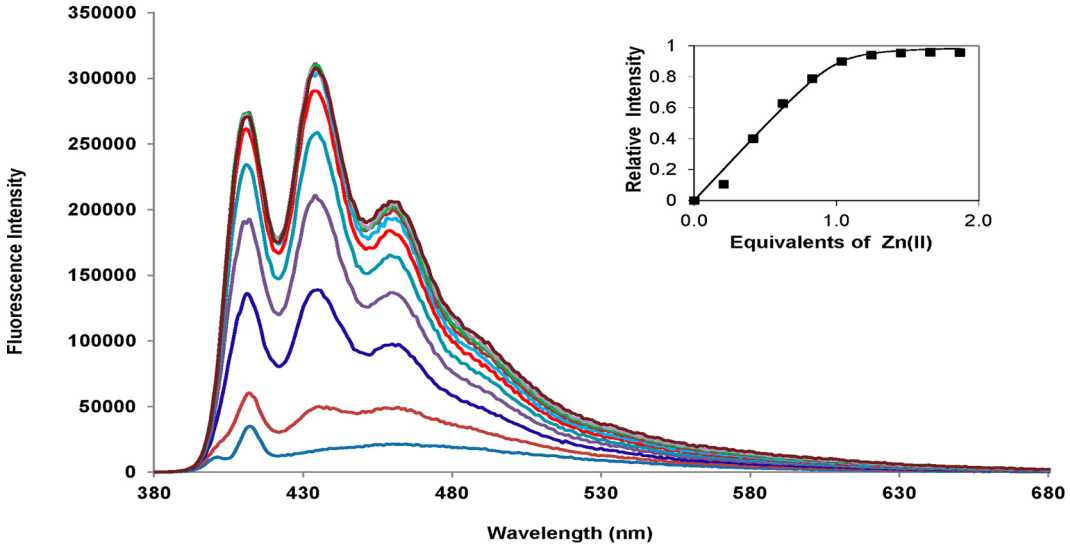


Figure 3. Fluorescence titration of 1.0×10^{-5} M of compound **3** in acetonitrile with increasing amounts of Zn(II), λ_{ext} = 367 nm. Inset: intensity vs equivalents of Zn(II), monitored at 430 nm.

Zn(II) → LZn(II) stoichiometry (solid line) results in an association constant equal to 8.0×10^6 M^{-1} (±15%).

The selectivity of **3** for Zn(II) in the presence of an excess of other metal ions was determined via a competition experiment, starting with 4.0×10^{-5} M of **3**, 6.0 equiv of Zn(II), and the addition of 10.0 equiv of other metal cations. Figure 4 indicates

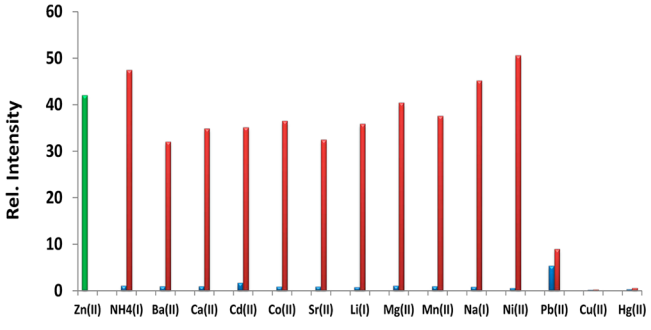


Figure 4. Ion selectivity–competition study of compound **3** with added M(II) perchlorate salts (10.0 equiv) followed by 6.0 equiv of added Zn(II). 4.0×10^{-5} M = [**3**], λ_{ext} = 367 nm. Fluorescence intensity monitored at 434 nm: blue = **3** + 5.0 equiv of M(II); red = **3** + 10.0 equiv of M(II) + 6.0 equiv of Zn(II); green = **3** + 6.0 equiv of Zn(II).

that the fluorescence of **3** remains stable in the presence of all alkali and alkaline earth cations. However, the transition-metal cations Pb(II), Fe(III)/Fe(II), and Hg(II) tend to quench the emission due to either a paramagnetic or a heavy atom effect. Aqueous solubility and pH effects on Zn(II) induced emission were also tested, by taking a 1:1 solution of CH_3CN/water (buffer), compound **3** and 6.0 equiv of Zn(II), and luminescence remained stable under a wide pH range and other competing metal ions (Figure S7, Supporting Information).

Figure 4 shows that Cu(II) prevents Zn(II)-induced fluorescence as well, which we do not attribute to the paramagnetic characteristic of this important cation. Interestingly, the UV–vis absorbance spectrum of compound **3** produced a color change from pale yellow to orange-brown only in the presence of Cu(II). A visual photograph of compound **3** (4.0×10^{-5} M) in the presence of 5.0 equiv of various metal ions, NH_4^+, Ba^{2+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, Li^+, Mg^{2+}, Mn^{2+}, Na^+, Ni^{2+}, Pb^{2+}, Sr^{2+}, and Zn^{2+} in acetonitrile, show the colorimetric and spectroscopic changes associated with addition of Cu(II) (Figure 5a,b). Compound **2**, the unreduced analogue, does not show such a color change, *nor does any other reduced imine compound* which do not contain a potential chelating ligand such as the quinolyl group. Thus, the hydroxyl group as well as the chelating quinolyl group both

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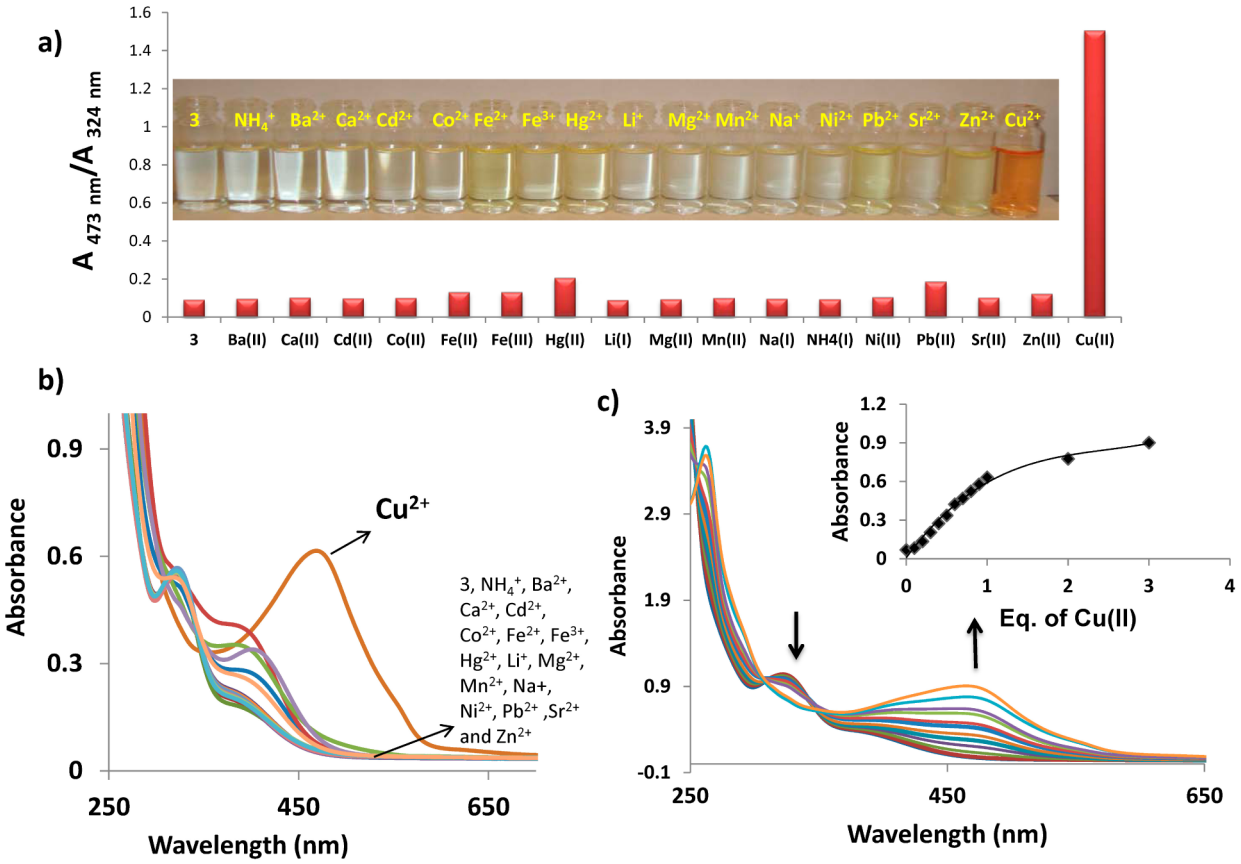
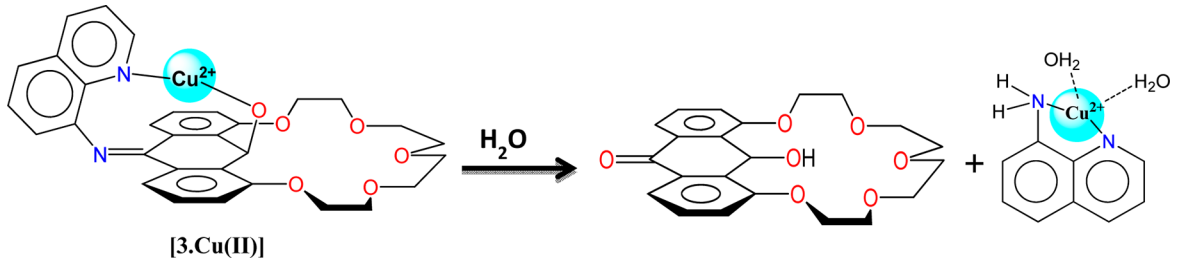


Figure 5. (a) Photograph and UV−vis absorbance data plot ($A_{473\ nm}/A_{324\ nm}$) of compound **3**. (b) UV−vis data of compound **3** (4.0×10^{-5} M) vs 5.0 equiv of Ba^{2+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, Li^+, Mg^{2+}, Mn^{2+}, Na^+, NH_4^+, Ni^{2+}, Pb^{2+}, Sr^{2+}, Zn^{2+}, and Cu^{2+} in acetonitrile. (c) UV−vis titration of 8×10^{-5} M compound **3** with 0.0−3.0 equiv of Cu(II). Inset: absorbance plotted vs equiv of Cu(II) at 450 nm.

Scheme 3. Proposed Scheme for Water-Promoted Hydrolysis of Copper Complex of Compound 3 to Compound 4



play a key role in Cu(II) coordination and the resulting color change. As seen in Figure 5c, a UV−vis titration shows the corresponding increase in peak intensity at 473 nm and decrease at 324 nm upon increasing amounts of added Cu(II) to **3** in acetonitrile. ESI-MS analyses of solutions of a 1:1 copper complex solution of compound **3** in acetonitrile reveal a peak at 589 *m/z*, corresponding to the initial MCu^+ parent ion complex and a 509 *m/z* peak suggesting the possible loss of Cu(II) and the −OH group from the parent copper complex (Figure S8, Supporting Information).

To the copper complex solution in acetonitrile, addition of microliters of water produced a parent ion peak at 383 *m/z*, which is attributed to the hydrolyzed product with no quinolinyl or −OH group present, indicating the aminoquinolyl imine group has been hydrolyzed by Cu(II) in the presence of water (Scheme 3). Slow evaporation of a 1:1 mixture of compound **3** and Cu(II) perchlorate in acetonitrile/methanol (3:1) resulted in isolation of compound **4**.H_2O as confirmed by X-ray crystallography (Figure 6 and Table S1, Supporting Information). Addition of water to the proposed carbocation intermediate reforms the 2° alcohol, which is stabilized in the solid-state by intermolecular hydrogen bonding with an encapsulated water molecule. The imine has been converted back to the carbonyl group. FTIR analysis of the solid obtained by the complexation reaction of compound **3** and Cu(II) perchlorate, suggests the formation of a carbonyl group by the appearance of a C=O stretching frequency at 1660 cm^{-1} and loss of the imine peak at 1638 cm^{-1} (Figure S9, Supporting Information). A solution of compound **3** plus 1.0 equiv of Zn(II), after addition of 0.1 equiv of Cu(II) also undergoes complete loss of fluorescence which suggests the superiority of Cu(II) to interact with compound **3**. Thus, compound **3** can act as a multimode sensor; undergoing fluorescence turn-on in the presence of Zn(II) via imine−enamine tautomerization, and acting as a colorimetric chemodosimeter upon addition of Cu(II).

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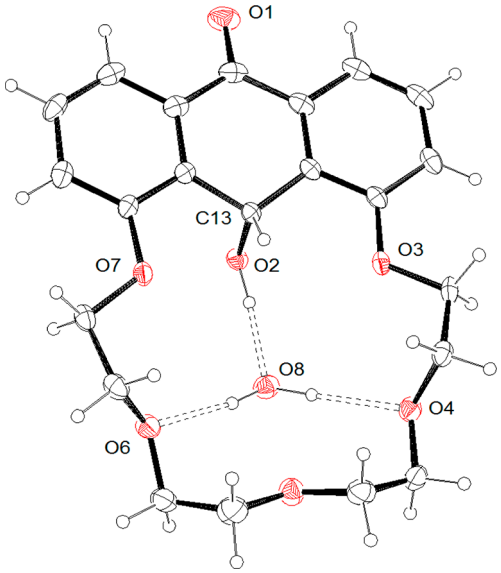

Figure 6. Thermal ellipsoidal diagram (30%) of compound **4** along with a hydrogen-bonded molecule of water: O2−O8 = 2.634(2) Å, 172(3)°; O4−O8 = 2.961(3) Å, 172(4)°; O6−O8 = 2.951(2) Å; 168(3)°; C13−O2 = 1.432(2) Å.

To test the possibility of interference from excess amounts of other cations on the Cu(II)-induced colorimetric response, metal ion competition experiments were carried. Starting from a 4.0 × 10^{-5} M of Compound **3** and 6.0 equiv of Cu(II) and 10.0 equiv of other salts, NH_4^+, Ba^{2+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, Li^+, Mg^{2+}, Mn^{2+}, Na^+, Ni^{2+}, Pb^{2+}, Sr^{2+}, and Zn^{2+}were added in acetonitrile/water (12/1) solvent system, and the response was recorded. Figure 7 suggests that Cu(II) complexation dominates in the presence of other metal cations.

We also explored the complexation ability of 8-aminoquinoline by itself. Aminoquinoline derivatives have previously been employed in the coordination chemistry of metal ions,[18] as fluorescent sensors for metal ions,[19] copper,[20] chromium,[21] mercury,[22] zinc,[23] and metal complexes as catalysts,[24] for transport and extraction of transition-metal cations,[25] as chelates and complexes of heavy transition metal ions,[26] and as analytical reagents for determination of Pd(II),[27] as drug candidates for malaria,[28] and Alzheimer's disease.[29] A solution of 8-aminoquinoline was tested with several metal perchlorate salts including; Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, and Mn^{2+} in acetonitrile. Unlike compound **3**, 8-aminoquinoline does not show the same colorimetric response toward Cu(II), although Fe(III) shows a distinct color change from pale yellow to red and Fe(II) from pale yellow to orange, even over a wide pH range (Figures S10 and S11, Supporting Information).

CONCLUSION

In summary, we describe a fluorescence sensor involving metal-induced imine−enamine tautomerization selective for Zn(II), combined with a Cu(II)-induced selective colorimetric change, involving irreversible imine hydrolysis in the presence of water. Hydrolysis does not take place for analogues of **3**, thus requiring the presence of a chelating receptor (as is the case with the quinolinyl derivative) in the imine. Here, a single molecular system acts as an OFF−ON sensor for Zn(II) fluorescence, and an OFF−ON colorimetric sensor for Cu(II), involving the integration of chemosensor and chemodosimeter principles.

EXPERIMENTAL SECTION

Materials and Methods. All chemicals and reagents were obtained and used without further purification. The glassware for the experiment was dried in an oven (100 °C) overnight. Metal perchlorate salts of NH_4^+, Ba^{2+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, Li^+, Mg^{2+}, Mn^{2+}, Na^+, Ni^{2+}, Pb^{2+}, Sr^{2+}, and Zn^{2+} were dried using an Abderhalden drying apparatus. Commercially available acetonitrile was dried over CaH_2 by distilling over a period of 5 h and used directly. ^{1}H NMR and ^{13}C NMR spectra were recorded at 200 and 50 MHz, respectively, at 298 K using $CDCl_3$ as solvent.

Note: Metal perchlorate salts are known be explosive, so care is to be taken while handling, especially while drying.

Synthesis of Compound 3. 1,8-Oxybis(ethylenoxyethylenoxy)-10-(quinolinylimino)anthracen-9-one, **2**, was synthesized according to the previously published procedure.[12] A reduction reaction was carried out using 0.45 mmol of compound **2** suspended in 5 mL of methylene chloride and 75 mL of 95% ethanol, followed by addition of 0.45 mmol of sodium borohydride. The mixture was stirred for 15 h at room temperature. Extraction was carried out with methylene chloride after adding distilled water. The organic layer was dried over anhydrous sodium sulfate, filtered, and the clear solution evaporated using a rotary evaporator to afford **3**.

1,8-Oxybis(ethylenoxyethylenoxy)-10-(quinolinylimino)-9,10-dihydroanthracen-9-ol (3). Yield = 0.090 g (~38%). Mp = 205−207 °C. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ 3.70−4.27 (*m*, 16H, CH_2−O, polyether), 5.77−5.81 (d, 1H), 6.61−6.86 (m, 4H), 7.06−7.19 (m, 1H), 7.30−7.34 (m, 2H), 7.41−7.51 (m, 2H), 7.62 (s, 1H), 7.75−7.91 (m, 1H), 7.99−8.16 (d, 1H), 8.47 (s, 1H), 9.00 (s,

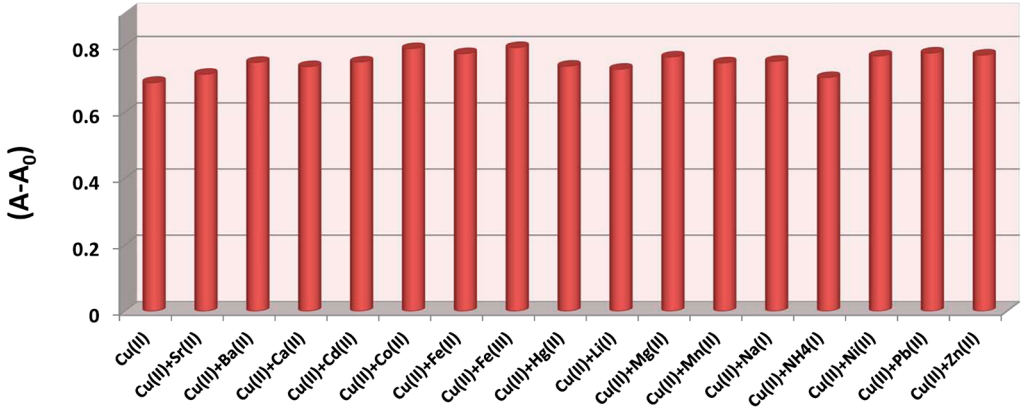

Figure 7. UV−vis selectivity−competition study of compound **3** with added M(II) perchlorate salts (10.0 equiv) followed by 4.0 equiv of added Cu(II). 4.0 × 10^{-5} M = [**3**], absorbance changes monitored at 473 nm.

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1H). ^{13}C NMR (50 MHz $CDCl_3$, 25 °C): 56.5, 67.0, 68.1, 69.2, 70.1, 70.7, 71.7, 110.7, 112.9, 116.3, 118.1, 119.5, 120.3, 122.3, 127.1, 128.6, 129.1, 130.8, 136.1, 142.4, 149.0, 150.0, 156.0, 156.3, 156.7. Anal. Calcd for $C_{31}H_{30}N_2O_6$: C, 70.71; H, 5.74; N, 5.32. Found: C, 70.52; H, 5.65; N, 5.44.

Crystallography. X-ray quality crystals were grown from samples dissolved in acetonitrile and diffused with diethyl ether. Crystallographic data were collected at 100 K using Mo Kα radiation. Cell constants were determined after integration from typically more than 9000 reflections.[30] Structures were solved by direct methods using SIR97[31] and refined using SHELXL-97.[32] Data reduction and refinement were completed using the WinGX suite of crystallographic software.[33] All non-hydrogen atoms were refined with anisotropic displacement parameters and all hydrogen atoms were placed in ideal positions and refined as riding atoms with relative isotropic displacement parameters, with the exception of hydrogen-bonded protons which were found from the difference map. Table S1 lists additional crystallographic and refinement information (Supporting Information).

■ ASSOCIATED CONTENT

Supporting Information

NMR, IR, MS characterization data, absorbance and fluorescence spectra, and crystallographic information. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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