Inorganic Chemistry
Communication
pubs.acs.org/IC

Iridium-Based Lab-on-a-Molecule for Hg^{2+} and ClO^- with Two Distinct Light-Up Emissions

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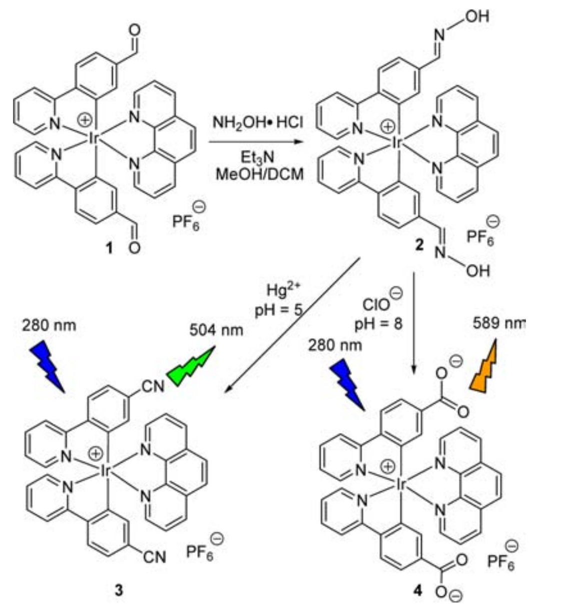
Supporting Information

ABSTRACT: The nonemissive iridium complex **2** is a lab-on-a-molecule for the highly selective detection of Hg^{2+} and ClO^- among 33 analytes using its oxime residues as reactive units. At pH 5, chemodosimeter **2** responds to Hg^{2+} by dehydration, whereas at pH 8, it is oxidized by ClO^-, resulting in 450- and 235-fold emission increases, respectively, at two distinct wavelengths.

Ever since de Silva proposed the concept of the lab-on-a-molecule[1] for multiplex recognition, research on molecular probes has been seeking to overcome the boundary of single-analyte detection and to initiate highly selective orthogonal signaling protocols for multianalyte mixtures. Nowadays, chemists are searching for the most advanced lab-on-a-molecule, i.e., a molecular probe that detects and quantifies as many analytes in a mixture as possible without interference (at present, the record is three analytes[2]). The three favored strategies for lab-on-a-molecule probes are (1) incorporation of several binding/reaction sites using one site per analyte;[1,3] (2) interrogation utilizing various channels to detect one analyte per channel;[2,4] (3) merging of several interactions and/or photophysical properties in one molecule to evaluate the analytes by combinatorial analysis.[5] In contrast to approaches (1)−(3), it is rather challenging to establish multianalyte detection using one-channel probes with only one binding/reaction site. At present, such probes[6] exhibiting differential responses (e.g., wavelength) for distinct analytes have rarely been built on rational design.

Ruthenium and iridium complexes are famous for their luminescence properties.[7] On the basis of their unique electrogenerated chemiluminescence, we and others have developed a small series of lab-on-a-molecule probes for cations[2] and anions[4] using an approach based on different interrogation channels. On the other hand, even photoluminescence (PL) alone may be instructed for multianalyte detection when emissions shift between ligand-centered (LC) and metal-to-ligand charge-transfer (MLCT) transitions:[7,8] one has to instruct the analytes to manipulate the relevant energy levels through alteration of the electronic character of the substituents.[9] In particular, precise control over the LC excited state of iridium will affect both the intensity and fine structure of PL. Consequently, iridium complexes are good candidates for lab-on-a-molecule probes with a single binding/reaction site if one is able to set up distinct chemical transformations for different analytes. For the present work, we selected the aldoxime group because of its facile conversion under mild conditions into aldehyde,[10] nitrile, amide,[11] and acid[12] groups. The character of an acid functionality can, furthermore, be adjusted easily by the pH. As a result, dioxime iridium(III) complex **2** was conceived as a lab-on-a-molecule, allowing detection of Hg^{2+} and/or hypochlorite (ClO^-) by light-up PL at different wavelengths (Scheme 1).

Scheme 1. Synthesis and Mode of Operation of Probe 2



Quantification of Hg^{2+} by **2** is achieved using a dehydration reaction in an acidic aqueous solution, while that of ClO^- is achieved using oxidative hydrolysis in an alkaline aqueous solution.

Iridium dioxime **2**, readily prepared from iridium dialdehyde **1**,[13] was characterized by spectroscopic techniques and its crystal structure (see a perspective view in Figure 1). Akin to **1**,[13] the iridium center in **2** adopts a distorted octahedral geometry, with

Received: July 31, 2013
Published: November 4, 2013

dx.doi.org/10.1021/ic401983h | *Inorg. Chem.* 2013, 52, 12863−12865

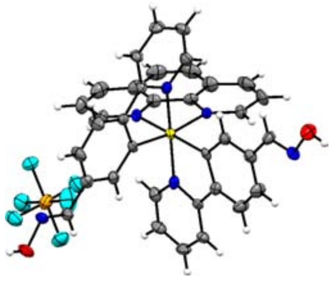


Figure 1. Perspective view of oxime **2** (X-ray structure) with thermal ellipsoids drawn at 50% probability. Color code: C, gray; H, white; N, blue; O, red; F, verdant; Ir, yellow; P, orange.

the angles ranging from 171.6(2)° to 173.4(3)°. The separation between both trans oxime groups is 12.0 Å (O−O distance).

In contrast to precursor **1**, complex **2** is nonemissive in acetonitrile (Φ_{PL} = 0.0001; λ_{ex}= 325 nm) because the excited iridium(III) unit is quenched by both photoinduced electron transfer and energy transfer (isomerization about C═NOH).[12] Moreover, **2** (10 μM) did not show any significant emission (Figure S1 in the Supporting Information, SI) in aqueous solution, i.e., *N*,*N*-dimethylformamide (DMF)/aqueous buffer (1:9, v/v), from pH 2 to 13. The oxime units in **2** are stable to hydrolysis, as judged by PL, because any tangible formation of dialdehyde **1** would lead to a strong increase in emission (Φ_{PL} = 0.079; λ_{ex}= 325 nm).

Upon screening of a large variety of cations and anions, such as K^+, Zn^{2+}, Cu^{2+}, Pb^{2+}, Ni^{2+}, Ba^{2+}, Cd^{2+}, Co^{2+}, Ca^{2+}, Ag^+, Hg^{2+}, Cu^+, PF_6^-, BF_4^-, ClO_4^-, NO_3^-, AcO^-, CN^-, Br^-, Cl^-, F^-, and ClO^-, at pH 5, probe **2** only exhibited increased emission (at 505, 541, and 578 nm; Figure 2a) in the presence of Hg^{2+}. While **2**

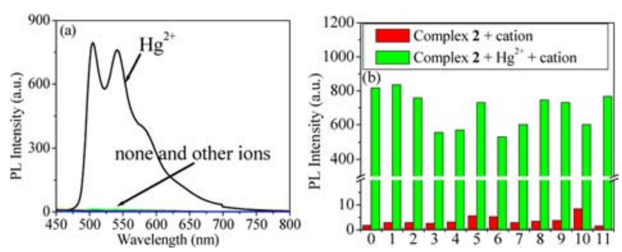


Figure 2. (a) PL spectra (λ_{ex} = 280 nm) of probe **2** (10 μM) in the presence of 400 equiv of various ions (Hg^{2+}, K^+, Zn^{2+}, Cu^{2+}, Pb^{2+}, Ni^{2+}, Ba^{2+}, Cd^{2+}, Co^{2+}, Ca^{2+}, Ag^+, Cu^+, PF_6^-, BF_4^-, ClO_4^-, NO_3^-, AcO^-, CN^-, Br^-, Cl^-, F^-, and ClO^-) in DMF/phthalate buffer (50 mM, pH 5) (1:9, v/v). (b) PL (λ_{em} = 505 nm) of **2** (10 μM) in the presence of various cations (0, none; 1, K^+; 2, Zn^{2+}; 3, Cu^{2+}; 4, Pb^{2+}; 5, Ni^{2+}; 6, Ba^{2+}; 7, Cd^{2+}; 8, Co^{2+}; 9, Ca^{2+}; 10, Ag^+; 11, Cu^+), with Hg^{2+} (400 equiv) being absent (red bars) or present (green bars). PL spectra and intensities were recorded after 120 ± 0.5 min.

responded toward Hg^{2+} by an emission increase from pH 5 to 7 (Figure S2 in the SI), detection worked best at pH 5 with an enhancement factor of 450 (at 400 equiv). Increasing pH led to a PL decrease with almost no more detectable response toward Hg^{2+} at pH 8. In neither more acidic nor more alkaline solution was the PL intensity enhanced. Other cations (Figure 2b) and anions (Figure S3 in the SI) did not trigger any significant enhancement or disturb the response toward Hg^{2+}.

A titration was performed in DMF/phthalate buffer (1:9, v/v) at pH 5. Because chemodosimeter **2** (10 μM) reacted only slowly (>4 h) even with 400 equiv of Hg^{2+}, as judged by a PL increase (Figure S4 in the SI), all spectra in the titration were recorded after a fixed reaction time of 120 ± 0.5 min. At first, we studied the titration by UV−vis spectroscopy. Upon the addition of Hg^{2+}, the absorption band at 325 nm decreased, while an isosbestic point emerged at 280 nm (Figure S5 in the SI). Using excitation at λ_{ex} = 280 nm, the pronounced PL changes (Figure 3a) allowed us to quantify Hg^{2+} from 0 to 5 mM (Figure 3b).

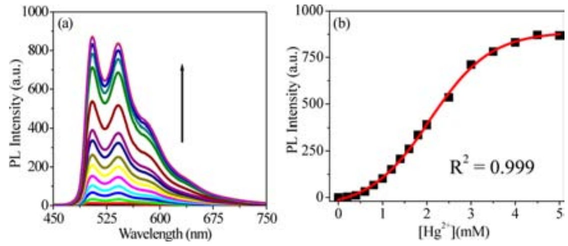


Figure 3. (a) PL spectra (λ_{ex} = 280 nm) from a titration of probe **2** (10 μM) with Hg^{2+} (0−5 mM) in DMF/phthalate buffer (50 mM, pH 5) (1:9, v/v). (b) Titration of **2** with Hg^{2+} (0−5 mM) following PL at 505 nm. PL spectra and intensities were recorded after 120 ± 0.5 min.

The PL spectrum of **2** after reaction with Hg^{2+} was different from that of the iridium complex **1** in terms of both the shape and wavelength (Figure S6 in the SI), which excluded simple hydrolysis. Rather, the structured emission in Figure 2a is indicative of dominant LC-based excited iridium states.[8] Such a finding suggests the formation of electron-withdrawing groups at the phenylpyridine periphery in the chemodosimeter reaction. Indeed, electrospray ionization mass spectrometry (ESI MS) spectra taken of a dilute solution after reaction of **2** with Hg^{2+} exhibited peaks at *m*/*z* 731.7 and 749.7 (Figure S7 in the SI), suggesting that the chemodosimeter had lost one or two H_2O molecules in the detection process. On the basis of these observations, it was reasonable to assume that the dioxime had dehydrated in the presence of Hg^{2+}. To probe this hypothesis, dinitrile **3** was prepared independently and characterized by NMR, ESI MS, and elemental analysis (see the SI). The PL spectrum of complex **3** proved to be congruent with that of **2** after reaction with Hg^{2+} at pH 5 (Figure S8 in the SI). These results convincingly suggest that in the presence of Hg^{2+} complex **2** experiences a 2-fold dehydration to afford the strongly emissive complex **3**. Although it is a common strategy to utilize Lewis-acid-induced reactions for light-up PL probes,[14] Hg^{2+} has been rarely reported as a catalyst for dehydration of oxime, and the present reaction scenario, to the best of our knowledge, has not been explored yet for sensing.

After a detection scheme was set up for Hg^{2+} at pH 5, which is nonoperative at higher pH, an alkaline buffered solution at pH 8 (50 mM NaH_2PO_4/Na_2HPO_4 and 150 mM NaCl) was adopted to screen for other analytes. Upon the addition of 400 equiv of ClO^-, a strong emission at λ_{em} = 589 nm (Figure 4a) was registered with an enhancement factor of 235. In contrast, other anions (Figure 4b) and cations (Figure S9 in the SI), such as PF_6^-, BF_4^-, ClO_4^-, NO_3^-, AcO^-, CN^-, Br^-, Cl^-, F^-, Hg^{2+}, K^+, Zn^{2+}, Cu^{2+}, Pb^{2+}, Ni^{2+}, Ba^{2+}, Cd^{2+}, Co^{2+}, and Ca^{2+}, neither led to any dramatic change nor disturbed the enhancement. While Hg^{2+} partly interferes, probe **2** still allows detection of ClO^- in the presence of Hg^{2+}. Further oxidative and reactive species (Fe^{3+}, ClO_3^-, ClO_2^-, NO_2^-, H_2O_2, $HO^\bullet$, $ONOO^-$, TBPH, $^1O_2$, NO, O_2^-, and ClO^-) were additionally investigated (Figure S10 in the SI), but only ClO^- generated significant PL enhancement.

Detection of ClO^- by **2** was strongly affected by the pH (Figure S11 in the SI), with the PL intensity notably enlarged

dx.doi.org/10.1021/ic401983h | *Inorg. Chem.* 2013, 52, 12863−12865

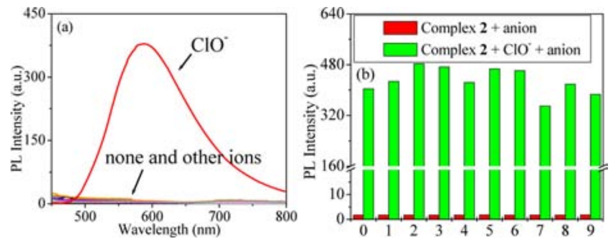


Figure 4. (a) PL spectra (λ_{ex} = 280 nm) of oxime **2** (10 μM) in the presence of 400 equiv of various ions (Hg^{2+}, K^+, Zn^{2+}, Cu^{2+}, Pb^{2+}, Ni^{2+}, Ba^{2+}, Cd^{2+}, Co^{2+}, Ca^{2+}, PF_6^-, BF_4^-, ClO_4^-, NO_3^-, AcO^-, CN^-, Br^-, Cl^-, F^-, and ClO^-) in DMF/aqueous phosphate buffer (50 mM NaH_2PO_4/Na_2HPO_4 and 150 mM NaCl; pH 8) (1:9, v/v). (b) PL (λ_{em} = 589 nm) of probe **2** (10 μM) in the presence of 400 equiv of anions (0, none; 1, PF_6^-; 2, BF_4^-; 3, ClO_4^-; 4, NO_3^-; 5, AcO^-; 6, CN^-; 7, Br^-; 8, Cl^-; 9, F^-) without (red bars) or with (green bars) 400 equiv of ClO^-. PL spectra and intensities were recorded after 120 ± 0.5 min.

upon an increase in the pH from 5 to 12. Reciprocally, the stability of **2** toward ClO^- in an acidic aqueous solution (pH 2–5) is very high, possibly because of a reduced oxidative activity and/or decomposition of hypochlorite acid.[10] Hypochlorite (ClO^-) plays an important role in living organisms, and its level is used as a diagnostic signal for various diseases.[15]

Similar to the dehydration process at pH 5, equally the kinetics of **2** with ClO^- was slow (Figure S12 in the SI). All spectra were thus recorded after 120 ± 0.5 min of reaction time. The UV–vis band at 325 nm exhibited a hypochromic effect upon the addition of ClO^- (Figure S13 in the SI). Different from **3**, the nonstructured emission at 589 nm (Figure 5a) suggests that

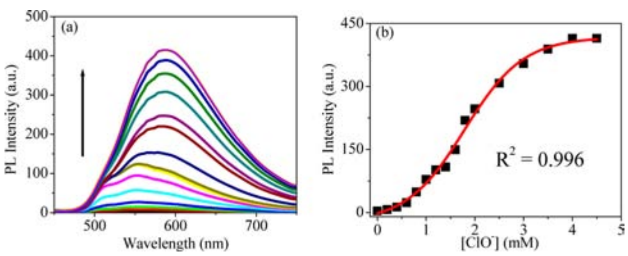


Figure 5. (a) PL spectra (λ_{ex} = 280 nm) of probe **2** (10 μM) after reaction with ClO^- (0–4 mM) in DMF/aqueous phosphate (50 mM NaH_2PO_4/Na_2HPO_4 and 150 mM NaCl; pH 8) (1:9, v/v). (b) Titration of probe **2** with ClO^- (0–4.5 mM). PL spectra and intensities were recorded after 120 ± 0.5 min.

PL arises dominantly from MLCT transitions. To probe for a possible product, dicarboxylic acid **4** was synthesized independently and characterized by NMR, ESI MS, and X-ray (Figure S14 in the SI) and elemental analysis. Its PL spectrum was consistent with that of oxime **2** after reaction with ClO^- (Figure S15 in the SI). The dicarboxylic acid **4** is readily deprotonated in an alkaline buffer solution, leading to a less vibrationally resolved PL spectrum.

Quantification of Hg^{2+} and ClO^- in a mixture using probe **2** was finally realized in a DMF/citric buffer solution (1:9, v/v; pH 6). As expected, PL spectra were less vibrationally resolved at an increased molar ratio of ClO^- (Figure S16 in the SI). From the PL intensity ratio I_{577}/I_{505} at two wavelengths, we extracted the ratio of both analytes (Figure S17 in the SI) and were able to determine their concentrations after assessing the content of Hg^{2+} in DMF/phthalate buffer at pH 5.

In conclusion, probe **2** acts as a light-up chemodosimeter for Hg^{2+} in acidic aqueous solution and ClO^- in alkaline aqueous solution and as a lab-on-a-molecule toward a solution containing both analytes. Thus, it is a selective two-analyte lab-on-a-molecule in the largest-ever-reported library of constituents (33 species). For proper manipulation of LC versus MLCT emission, mounting the oxime reaction sites onto the phenylpyridine ligands of probe **2** proved to be essential. Moreover, a new protocol for detecting Hg^{2+} by dehydration of the oxime group is reported. The use of two identical reaction sites in probe **2** does not hamper quantification (Figure S18 in the SI).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

X-ray crystallographic data of **2** (CCDC 945480) and **4** (CCDC 945481) in CIF format, experimental details. 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.

■ ACKNOWLEDGMENTS

We thank the DFG for continued support and the University of Siegen for allocation of a stipend to K.C.

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