Diaza-18-crown-6 appended dual 7-hydroxyquinolines; mercury ion recognition in aqueous solution†

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8,8′-(1,4,10,13-Tetraoxa-7,16-diazacyclooctadecane-7,16-diyl)-bis(methylene)diquinolin-7-ol (TDBQ) was synthesized and proved to recognize Hg^{2+} *via* reducing Hg^{2+} to Hg^+, forming a unique Hg_2^{2+}–TDBQ complex.

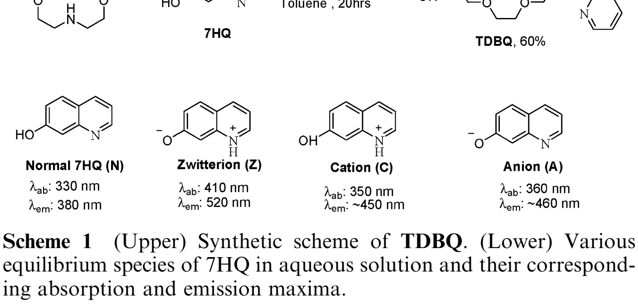
Mercury is considered to be one of the most serious environmental and health threats. The long atmosphere residence span of Hg^0 vapour and its oxidized inorganic Hg^{2+} form provide facile pathways to contaminate vast amounts of water and soil.[1] To date, intensive efforts have been made to develop molecular sensing systems for the mercury ion.[2] Most of the detection methods have one or more limitations in terms of actual applicability,[3] including interference from other metal ions, slow response to Hg^{2+}, incompatibility with aqueous solution, low selectivity and fluorescence quenching upon Hg^{2+} coordination *via* enhanced spin–orbit coupling, energy or electron transfer. To date, the fluorescence technique offers a promising approach for simple and rapid tracking of mercury ions.

Herein, we present the facile synthesis of a novel mercury ion chemosensor based on diaza-18-crown-6 appended with dual 7-hydroxyquinoline (7HQ) groups, forming 8,8′-(1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7,16-diyl)bis(methylene)diquinolin-7-ol (**TDBQ**) *via* a Mannich type of condensation (see Scheme 1 and ESI). In this approach, diaza-crown ethers are especially focused on.[4] Upon binding, the positive charge density of the metal ion leads to a reduction in electron density on the coordinating aza nitrogen atom and thereby may cause changes in the optical properties.[5] Moreover, metal ion complexation abilities and selectivities of the diaza-crown can be greatly improved when ligating, proton-ionizable groups are attached to the crown ethers.[6] As a strategic design, the phenolic groups and/or the pyridyl nitrogen in 7HQ may act as a sidearm to enhance the complexing ability for selected f metal ions. Also, the double armed diaza-crowns in **TDBQ** may serve as a pseudo-cryptand,[4,7] which renders additional binding capability. This viewpoint has been supported by elegant work recently published by Farruggia *et al.*,[8] in which they applied two 8-hydroxyquinolines bearing a diaza-18-crown-6 derivative binding site as a fluorescent sensor for Mg^{2+}.

As for the signal transduction, 7HQ[9] is selected mainly based on two characteristics. First, 7HQ is water soluble and is a bifunctional probe with derivatives comparable to those in many biological molecules, including DNA base units.[9a] Second, due to the unique proton tautomerization, 7HQ in aqueous solutions, depending on pH, consists of four protropic equilibrium species: a normal molecule (**N**), a cation (**C**), an anion (**A**), and a zwitterion (**Z**).[9d] (See Scheme 1). Upon metal ion binding, we then expect significant spectral variation suited for signal differentiation.

As depicted in Fig. 1 (line (a)), **TDBQ** in H_2O (pH = 7) revealed lower lying absorption bands at ~330 and ~410 nm, the results of which are reminiscent of normal (**N**) and zwitterion (**Z**) species of 7HQ, respectively, assigned in neutral water.[9a–c] Based on the spectral convolution, Mason *et al.*[9d] deduced the equilibrium molar percentages of **N** and **Z** species in 7HQ to be ~67% and 30%, while the sum of cation (**C**) and anion (**A**) species was estimated to be as small as ~3% in neutral water. Upon adding Hg^{2+}, the absorbance of both **N** (330 nm) and **Z** (410 nm) tends to decrease, accompanied by a gradual increase of the anion species (**A**) at 358 nm. Throughout the titration, the appearance of isosbestic points at 383, 327, 315 nm was observed.

The absorption spectral changes suggest that equilibrium greatly shifts from **N** and **Z** species to **A** in the presence of Hg^{2+}. Moreover, the sigmoid plot for *e.g.* 358 nm absorbance *versus* Hg^{2+} concentration (see inset of Fig. 1) leads to a proposal of **TDBQ** complexation requiring a cooperative addition of two Hg^{2+}.[10a] Firm support of this was provided by the Job's plot analysis,[10b] in which increases of absorbance



Scheme 1 (Upper) Synthetic scheme of **TDBQ**. (Lower) Various equilibrium species of 7HQ in aqueous solution and their corresponding absorption and emission maxima.

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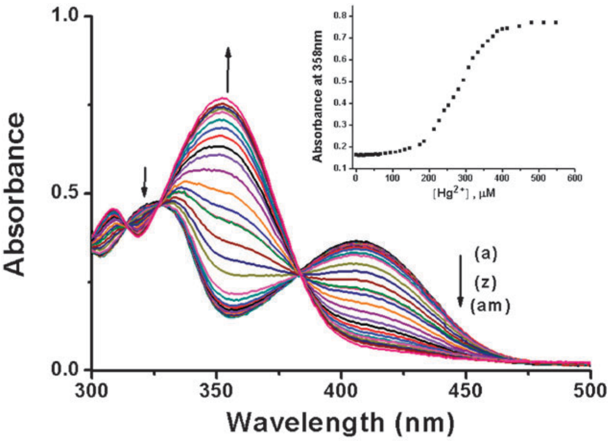

Fig. 1 Absorption spectra of **TDBQ** (7.8 μM) in H_2O (a, pH = 7) upon addition of Hg^{2+} in an increment of 6.7 μM (b–k), followed by 13.3 μM (l–z), 33.4 μM (ai–am). Inset: Absorbance at 358 nm against $[Hg^{2+}]$.

at *e.g.* 358 nm were plotted against molar fractions of **TDBQ** and Hg^{2+} under the condition of a constant total concentration. As such, the concentration of **TDBQ**–Hg^{2+} reached a turning point when the molar fraction of $[Hg^{2+}]/([Hg^{2+}] + [\mathbf{TDBQ}])$ was about 0.6 (Fig. 2A), indicating a stoichiometry of $2(Hg^{2+})$: 1(**TDBQ**) for the association.

A direct, firm evidence of the stoichiometry of complexation perhaps relies on the structural identification. In this approach, a single crystal was successfully obtained from a slow diffusion of MeOH into a water solution of either Hg^{2+} free **TDBQ** or a 1 : 2 mixture of **TDBQ** and $Hg(ClO_4)_2{\cdot}xH_2O$. As shown in Fig. S5(a) (ESI), the molecular structure of **TDBQ** reveals a pocket-like geometric conformation due to the hydrogen bond interaction between the hydroxyl group (O(11)–H(11) of 7HQ and nitrogen atom (N(1)) of the macrocycle with an O(11)–N(1) distance of 2.683 Å. Upon addition of Hg^{2+}, **TDBQ** also forms a pocket-like geometric conformation (Fig. S5(b)), in which two mercury cations are trapped by the macrocycle, mainly due to the coordination of mercury ions (Hg(1) and Hg(2)) with two nitrogen atoms (N(1) and N(2)), two oxygen atoms (O(1) and O(3)) of the macrocycle and nitrogen atoms (N(3), N(4)) of 7HQ. In a qualitative manner, the motion of **TDBQ** to recognize mercury ion resembles the Sensitive Plant. In other words, **TDBQ** is able to pinch and form a cavity suitable for accommodating dual mercury ions.

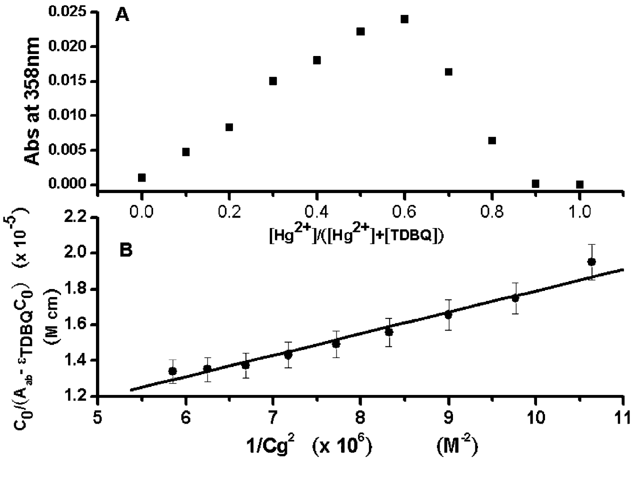

Fig. 2 (A) The increase of absorption at 358 nm was plotted against the mole fraction of Hg^{2+} (Job's plot). $[\mathbf{TDBQ}] + [Hg^{2+}] = 7.0$ μM. (B) The plot of $C_0/(A_{ab} - \varepsilon_{\mathbf{TDBQ}}C_0)$ against $1/C_g{}^2$ at 358 nm (see text).

As depicted in Fig. S5(b), the nitrogen of 7HQ also donates a lone-pair electron to the mercury ion, facilitating the complex formation. The selected bond lengths around the Hg(1) and Hg(2) atoms are given in Table S1 (see ESI). Surprisingly, the Hg(1)–Hg(2) distance of 2.5207(3) Å is significantly shorter than Hg–Hg distances of 2.7362(6), 2.6881(4), and 2.5469(8) Å reported in $[Pt_2Hg_2(P_2phen)_3](PF_6)_2$, $[Pd_2Hg_2(P_2phen)_3](PF_6)_2$, and $[Hg_2(TLA)_2](ClO_4)_2$, respectively;[11a,b] however, it is comparable with that of 2.5358(8) Å in $[Hg_2(C_{36}H_{46}N_6Se_2)](PF_6)_2$.[11c] It is also noteworthy that the bond length for $Hg_2{}^{2+}$ is 2.524(2) Å in water.[11d] The result indicates the sum of charges for two mercury ions to be +2 in the crystal.

To provide another evidence of the charge of mercury ion in the solid crystal, XANES measurement was performed at Hg L_{III}-edge of the corresponding crystal. For comparison, spectra of $HgCl_2$ and Hg_2Cl_2 are also shown in Fig. S6 (see ESI). According to the electric-dipole selection rules, the spectral region from 12 280–12 295 eV is assigned to the transition of $2p_{3/2} \rightarrow 6s$,[12] while those of > 12295 eV are attributed to the transitions of $2p_{3/2} \rightarrow 6d$. Hg^{2+} exhibits an obvious peak at 12 285 eV, which apparently is lacking at the same energy for Hg^+. This is due to the fact that Hg^{2+} has a higher density of the empty 6s electronic state than that of Hg^+. The XANES spectrum of the prepared **TDBQ**–mercury crystal resembles that of the reference Hg^+, indicating that the oxidation state of the crystal is best described as Hg^+.

The reduction of Hg^{2+} has been observed in the structural characterization of a $Hg_2{}^{2+}$ complex containing a tripodal nitrogen ligand.[11b,13] It is plausible that Hg^{2+} would be reduced to Hg^+ under the tripodal nitrogen ligands, *i.e.* diazacyclooctadecane in **TDBQ**, containing solution. The reduction of Hg^{2+} may be facilitated by Hg(I)–Hg(I) bonding formation in combination with further stabilization by diazacyclooctadecane complexation, forming a stable $Hg_2{}^{2+}$–**TDBQ** complex. This may lead to a positive reduction potential, which is large enough to have overall negative changes of ΔG upon coupling with *e.g.* oxidation of water. Nevertheless, full decipherment of the actual redox mechanism is still pending resolution.

On the above basis, thermodynamic parameters such as the association constant of the complexation can be deduced *via* the, relationship of absorbance, A_{ab}, *versus* added Hg^{2+} concentration (C_g) expressed in eqn (1) (also see ESI for detailed derivation)

$$\frac{C_0}{A_{ab} - \varepsilon_{\mathbf{TDBQ}}C_0} = \left[\frac{1}{K_a(\varepsilon_{\mathbf{TDBQ}\text{-}Hg^+} - \varepsilon_{\mathbf{TDBQ}})}\right]\frac{1}{C_g^2} + \frac{1}{\varepsilon_{\mathbf{TDBQ}\text{-}Hg^+} - \varepsilon_{\mathbf{TDBQ}}} \qquad (1)$$

where C_0 denotes the initially prepared concentration of **TDBQ**, $\varepsilon_{\mathbf{TDBQ}}$ ($\sim 2.1 \times 10^4\ M^{-1}\ cm^{-1}$) is the molar extinction coefficient of **TDBQ** (**A**) at peak wavelength of 358 nm. As a result, a straight line plot of $C_0/(A_{ab} - \varepsilon_{\mathbf{TDBQ}}C_0)$ *versus* $\mathbf{TDBQ}/[Hg^{2+}]^2$ (see Fig. 2B) supports the proposal of

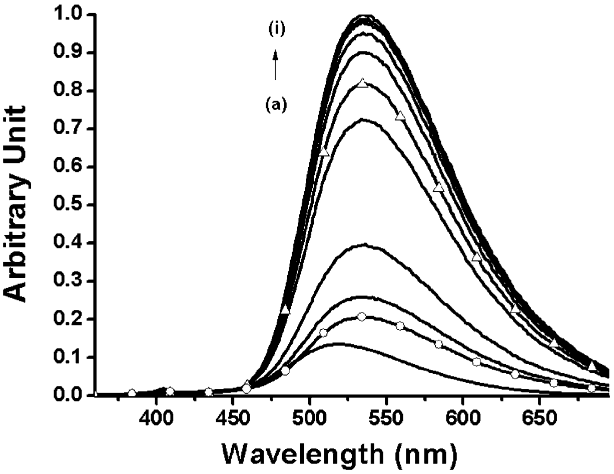

Fig. 3 Emission spectra of **TDBQ** (7.8 μM in H_2O, pH = 7) upon addition of Hg^{2+} in an increment of 133.3 μM (a–b), followed by 33.3 μM (c–i), λ_{ex} = 358 nm; (j) (-○-) The addition of 1 mM DMPS on (i). (k) (-△-) The addition of 1.5 mM [Hg^{2+}] on (j). λ_{ex} = 358 nm.

${Hg_2}^{2+}$ for the complexation. The association constant K_a was then deduced to be 4.47 × 10^6 M^{-2} from the quotient of intercept divided by the slope.

As for the fluorescence titration, the excitation of Hg^{2+} free **TDBQ** at *e.g.* 358 nm leads to a zwitterion-like (**Z**) emission maximized at ~517 nm. Upon addition of [Hg^{2+}], the 358 nm excitation, which is the peak wavelength of the **TDBQ** anion species incorporating ${Hg_2}^{2+}$, rendered an increase of the emission band with peak wavelength at 527 nm (see Fig. 3). The lack of 7HQ-anion-like 450 nm emission[9d] leads us to propose that the ${Hg_2}^{2+}$ incorporated **TDBQ** anion species undergo excited-state charge transfer from phenolic (HOMO) to the pyridyl (LUMO) moiety,[14] resulting in strengthening of the pyridyl–${Hg_2}^{2+}$ dative bond. The net result resembles a zwitterion-like structure (see Scheme 1) that gives rise to the 527 nm emission similar to that of the **Z** form of 7HQ.[14] Note the emission intensity increases by ~one order of magnitude during the titration (see Fig. 3). Based on emission spectra, the reversibility of the recognition process was performed by adding mercury chelating agents, sodium 2,3-dimercapto-1-propanesulfonate (DMPS). As shown in Fig. 3, after addition of 1 mM DMPS into the solution containing **TDBQ** and mercury ion, the zwitterion (**Z**) emission intensity decreased by ~5 fold. Subsequently, adding 1.5 mM $Hg(ClO_4)_2$ leads to the increase of the emission back to ~80% of the original intensity, revealing its good reversibility.

To probe the ${Hg_2}^{2+}$–**TDBQ** complex stability as a function of pH, the absorption spectrum of a solution containing **TDBQ** and Hg^{2+} in equimolar amounts (1.5 μM) at various pH values was constructed (see Fig. S7 in ESI). For comparison, acid–base absorption titration of **TDBQ** was also performed. The results of **TDBQ** showed that pK_a values for the deprotonation of the nitrogen atom and of the hydroxyl groups in H_2O were 5.5 and 9.2, respectively. For ${Hg_2}^{2+}$–**TDBQ**, the second deprotonation process (pK_a ~ 8.2) shifted to lower pH values than the first one. This change in pK_a was presumably caused by chelation of mercury ion with the phenolic oxygen. Deprotonation of both phenol groups on **TDBQ** associated with ${Hg_2}^{2+}$ yielded a neutral complex. This neutral complex with Hg^{2+} was formed at pH values higher than 7. Similar results have been reported in the structural characterization of diaza-18-crown-6 appended with two 5-chloro-8-hydroxyquinoline-7-yl groups, the effective chemosensors for Mg^{2+} or Hg^{2+}.[8,15]

Finally, competitive experiments have been performed and the results are depicted in Fig. S8 (ESI). In this experiment, 1 μM solution of **TDBQ** was tested in the presence of other metal cations, including alkali, alkaline earth metals and certain heavy metals. As shown by the enhancement of emission intensity after adding equal molar Hg^{2+} with respect to the competing metal ions (Fig. S8), **TDBQ** seems to retain moderate selectivity for Hg^{2+} in the presence of a range of competing ions found in environmental and biological settings.

In conclusion, **TDBQ** achieves Hg^{2+} recognition *via* the reduction of Hg^{2+}, forming a ${Hg_2}^{2+}$–**TDBQ** complex. In this approach, two 7HQ moieties not only act as dual sidearms attached to diaza-18-crown-6, forming pseudo-cryptand that greatly enhances the binding strength, but also serve as a signal transducer. Single crystals of **TDBQ**–mercury complex have unambiguously resolved a dinuclear (Hg) center with ${Hg_2}^{2+}$ formation that is unique among numerous approaches for sensing mercury ion.

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