8-Hydroxyquinoline Benzoates as Highly Sensitive Fluorescent Chemosensors for Transition Metal Ions
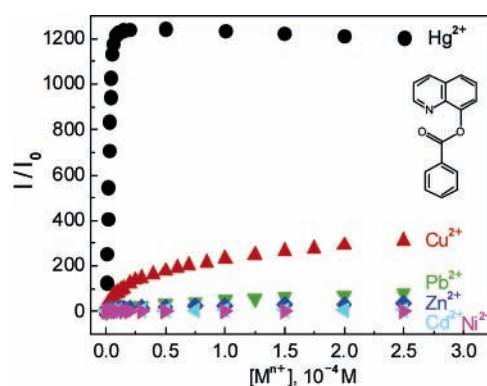
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ABSTRACT

8-Hydroxyquinoline benzoates were developed as a new set of 8-HQ derivatives for highly sensitive fluorescent chemosensors for transition metal ions. A prominent fluorescence enhancement was found in the presence of transition metal ions such as Hg^{2+} and Cu^{2+}, and this was suggested to result from the suppression of radiationless transitions from the $n\pi^*$ state in the chemosensors.

8-Hydroxyquinoline (8-HQ, **1**, Figure 1) is one of the most important chelators for metal ions and has found significant applications in a variety of investigations involving metal complexes.[1] An important property that makes 8-HQ even more attractive as a chelator is the appreciable change in its fluorescence upon metal binding.[2] Therefore, 8-HQ has been used extensively to construct highly sensitive fluorescent chemosensors for sensing and imaging of metal ions of important biological and/or environmental significance,[3−6]

and its chelates, in particular those with Al^{3+}, are major components for organic light-emitting diodes (OLEDs).[7] It is known that the excited-state intramolecular proton transfer (ESIPT), from 8-OH to the quinolino N atom, makes 8-HQ
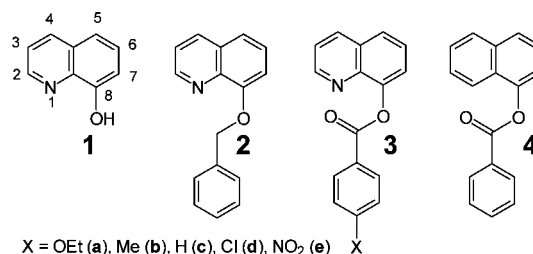

Figure 1. Chemical structure of 8-HQ **1** and its derivatives **2−4**.

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Table 1. Absorption and Fluorescence Spectral Data of **3a−e** and Their Hg^{2+}, Cu^{2+} and Pb^{2+} Chelates in ACN

	λ_{abs}, nm	ϵ, $10^4\,M^{-1}\,cm^{-1}$	λ_{flu}, nm	FEF[b]	K_a, $10^4\,M^{-1c}$	Φ[d]	τ, ns[e]	k_r, s^{-1}	k_{rl}, s^{-1}
3a	226/260	3.43/2.17	385[a]			0.00051	f		
3a + Hg^{2+}	239/265	3.78/2.08	450	2.7	4.49 ± 0.69	0.00092	f		
3a + Cu^{2+}	226/260	3.43/1.04	450	1.3					
3a + Pb^{2+}	226/260	3.43/2.17	450	1.2					
3b	228/276	4.17/0.68	385[a]			0.00078	0.178	0.44×10^7	5.61×10^9
3b + Hg^{2+}	238/313	4.76/0.58	462	647	$>10^3$	0.60	29.38	2.04×10^7	1.36×10^7
3b + Cu^{2+}	228/313	4.17/0.19	462	243	4.96 ± 0.84	0.14			
3b + Pb^{2+}	228/276	4.17/0.68	462	37	1.88 ± 0.33	0.045			
3c	226/276	4.70/0.58	385[a]			0.00076	0.204	0.37×10^7	4.90×10^9
3c + Hg^{2+}	237/312	4.58/0.58	460	1204	$>10^3$	0.57	31.23	1.83×10^7	1.38×10^7
3c + Cu^{2+}	226/312	4.70/0.32	460	312	3.63 ± 0.47	0.13			
3c + Pb^{2+}	226/276	4.70/0.58	460	79	1.15 ± 0.17	0.038			
3d	228/276	4.17/0.68	385[a]			0.00074	0.115	0.64×10^7	8.69×10^9
3d + Hg^{2+}	238/313	4.63/0.55	457	855	$>10^3$	0.63	31.73	1.99×10^7	1.17×10^7
3d + Cu^{2+}	228/276	4.17/0.68	457	341	4.94 ± 0.92	0.13			
3d + Pb^{2+}	228/276	4.17/0.68	457	50	1.70 ± 0.26	0.035			
3e	225/262	3.53/1.61	385[a]			0.00040	0.148	0.27×10^7	6.75×10^9
3e + Hg^{2+}	238/259	3.60/1.62	450	53	$>10^3$	0.0096	0.964	1.00×10^7	1.03×10^9
3e + Cu^{2+}	225/262	3.53/1.61	450	8.0	2.20 ± 0.32	0.0038			
3e + Pb^{2+}	225/262	3.53/1.61	450	2.5		0.00074			

[a] **3a−e** are extremely weakly fluorescent, and their emission maxima were therefore located at ca. 385 nm with uncertainty. [b] Fluorescence enhancement factor, ratio of the intensity of **3** in the presence of 50 equiv of metal ion to that in the absence of metal ion. [c] Metal binding constant was obtained via nonlinear fitting of the fluorescence titration data assuming a 1:1 binding stoichiometry; see: Bourson, J.; Pouget, J.; Valeur, B. *J. Phys. Chem.* **1993**, *97*, 4552−4557. Nice fitting supported the assumed 1:1 stioichiometry, which was also confirmed by Job plots (Figure S4). [d] The uncertainties in the fluorescence quantum yields were within 10% for **3**-metal chelates and within 30% for **3a−e**. [e] Lifetimes were measured on a nanosecond TCSPC setup with a pulsed N_2 lamp; for details, see: Leinhos, U.; Kühnle, W.; Zachariasse, K. A. *J. Phys. Chem.* **1991**, *95*, 2013−2021. [f] The lifetimes are too short to be measured on this nanosecond setup.

weakly fluorescent and metal binding to 8-HQ blocks the ESIPT channel, thereby restoring the fluorescence.[2,5a] 8-HQ could hence be employed to build fluorescent chemosensors for metal ions via ESIPT suppression, with increased fluorescence signal upon metal binding. To enhance metal binding selectivity of 8-HQ, introduction of additional binding sites at the C-2 and/or C-7 positions, adjacent to the original binding sites in 8-HQ (Figure 1), has been extensively examined.[3−6] In the case where 8-HQ was substituted with methyleneamine at the C-2 or C-7 position, a photoinduced electron transfer (PET) process leading to fluorescence quenching was recently identified,[4a] and metal binding resulting in PET suppression was also demonstrated, which mechanism is currently intensively employed in constructing fluorescent chemosensors for transition metal ions operating under fluorescence enhancement mode.[8] It is noted, however, that these investigations hitherto reported are limited mainly to 8-HQ derivatives with substituents on the aryl ring. Derivation at the 8-OH group has not been explored in detail. A possible reason could be that the intensively investigated ether derivatives of 8-HQ, such as **2** (Figure 1), are highly fluorescent,[9] as the ESIPT channel is blocked, and hence not much room remains for further fluorescence enhancement resulting from metal binding. We report here on a new set of 8-HQ derivatives modified at the 8-OH group, the readily synthesized benzoates of 8-HQ

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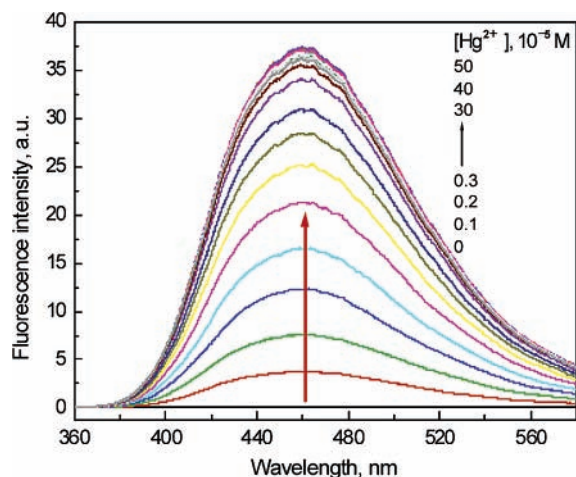(9) Hiratani, K. *J. Chem. Soc., Chem. Commun.* **1987**, 960−961.

Figure 2. Fluorescence spectra of **3c** in ACN in the presence of increasing concentration of Hg(ClO$_4$)$_2$. Excitation wavelength was 300 nm. [**3c**] $= 1.0 \times 10^{-5}$ M.

Figure 3. Plots against metal concentration of the fluorescence enhancement factors of **3a**−**e** in ACN. [**3a**−**e**] $= 1.0 \times 10^{-5}$ M. The curves through the data points are nonlinearly fitted ones assuming a 1:1 binding stoichiometry following a reported procedure: Bourson, J.; Pouget, J.; Valeur, B. *J. Phys. Chem.* **1993**, *97*, 4552−4557.

(**3**, Figure 1), as sensitive fluorescent chemsensors for transition metal ions that emit enhanced fluorescence upon metal binding.

Benzoates **3a**−**e** were synthesized via a simple one-step reaction of 8-HQ with benzoyl chlorides. They were designed on the basis of the consideration that in the esters the carbonyl oxygen lone pair is brought into immediate proximity to the 8-HQ fluorophore, making them weakly fluorescent as a result of a radiationless process via the nπ^* state.[10] This interpretation is supported by the fact that **3a**−**e** in acetonitrile (ACN) are extremely weakly fluorescent, with quantum yields (Φ) around 10^{-4} and lifetimes (τ) of 0.1−0.2 ns, irrespective of the substituent X, ranging from electron donating to highly withdrawing (Table 1). Further, the observation that Φ of **3c** in the protic solvent MeOH is 1.5 times that in ACN also supports this assumption. These parameters of **3a**−**e** clearly differ from those of their highly fluorescent ether derivatives, for example, $\Phi = 0.5$ and $\tau = 9.7$ ns for **2** in ACN. Therefore, **3a**−**e** appear to be promising candidates for fluorescent chemosensors for metal ions that show enhanced fluorescence emission upon binding metal ions, if their radiationless channel could be blocked by metal binding.

In the presence of transition metal ions such as Cu^{2+}, Pb^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Ni^{2+}, an enhancement of **3a**−**e** fluorescence was observed to a different extent for the various substituent (X) in **3** and metal species (Table 1, Table S1 in Supporting Information). A prominent enhancement of the fluorescence of **3** bearing appropriate X (Me, H, Cl) was observed in the case of Hg^{2+} and Cu^{2+}, in particular Hg^{2+}, of otherwise highly efficient fluorescence quenchers, Figures 2 and 3. Under the same conditions, fluorescence
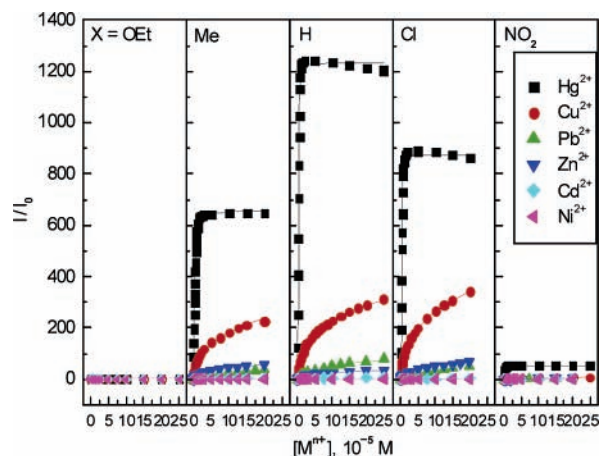
of **2**, an ether derivative of **1**, was found indeed to be highly efficiently quenched by the tested transition metal ions, especially Hg^{2+} and Cu^{2+} (Figure S1, Supporting Information). The fact that the emission band positions of the **3a**−**e** chelates at ca. 460 nm were almost independent of X suggests that metal ion binding blocks the radiationless decay channel in **3a**−**e**. The radiation (k_r) and radiationless (k_{rl}) rate constants of **3** and **3**-Hg^{2+} in ACN were calculated (Table 1). It was found that with **3b**−**d** the substantial increase in the quantum yield in the presence of Hg^{2+} is due to a dramatic decrease in k_{rl}, whereas k_r remains unchanged within experimental error. This means that the radiationless decay in **3** is indeed blocked upon metal binding and that the emission of Hg^{2+}-**3** and **3** too originates from a $\pi\pi^*$ state.[10a] Of particular significance is that the presence of 10 μM of Hg^{2+} results in an extraordinarily large enhancement (1204-fold) of the fluorescence of **3c** in ACN, whereas the other metal ions tested showed much smaller enhancements (Figure 3), **3c** being hence a highly sensitive and selective "turn-on" fluorescent chemosensor for Hg^{2+}.[11] In 5% H$_2$O−ACN solution, a highly selective, although less sensitive, response in the fluorescence of **3d** (for example) toward Hg^{2+} was also found (Figure S2, $K_a = 8.5 \times 10^4$ M^{-1}), indicating the potential of **3** as fluorescent chemsensors for practical applications.

The observed selectivity of the fluorescence response of **3** for metal ions was found to result from the differences both in the metal binding affinity, as seen from absorption titrations (Figure S3), and in the fluorescence quantum yields of the metal chelates (Tables 1 and S1). Job plots obtained for **3c**- and **3d**-Hg^{2+} systems in ACN suggest a 1:1 binding

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mode (Figure S4). This 1:1 binding stoichiometry was also supported by the nice nonlinear fitting of the fluorescence intensity against metal concentration assuming a 1:1 binding ratio (Figure 3). The fact that the fluorescence in ACN of **4** (Figure 1), a control molecule for **3c**, does not show a response toward Hg^{2+} indicates that the quinolino N atom in **3** is involved in the metal binding. It was also found that the emission of the **1**- and **2**-Hg^{2+} chelates in ACN was at 500 nm, whereas that of the **3**-Hg^{2+} chelates was at 460 nm (Figure S5). It is hence clear that, in **3**-Hg^{2+}, the carbonyl O atom together with the quinolino N atom is invloved in the binding of metal ion, thereby blocking radiationless decays via the nπ* state. The metal center is hence located further away from the fluorophore in the chelates of **3** than in those of **1** and **2**, making **3** more efficient fluorescent chemosensors.

In summary, we developed 8-HQ benzoates as a new set of fluorescent chemsensors for transition metal ions such as Hg^{2+} and Cu^{2+}. Especially **3c** shows a highly sensitive and selective response in its emission toward Hg^{2+}. We suggest that **3** operates under the mechanism that metal binding blocks the radiationless nπ* transition in **3**. Future work will be focused on tuning the selectivity for given metal ions, based on the known chemistry of 8-HQ and/or by modifying the benzoyl moiety (Figure 3) or replacing it with aliphatic counterparts. Metal chelates of **3** may also be a significant subject in OLED investigations, in view of their large fluorescence quantum yields (>0.5) and long lifetimes of ca. 30 ns (Table 1).

Supporting Information Available: Characterization data, absorption and fluorescence spectra, and reaction parameters of **3a**−**e** in the presence of metal ions. This material is available free of charge via the Internet at http://pubs.acs.org.

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