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Communication

Synthesis of 5-Dialkyl(aryl)aminomethyl-8-hydroxyquinoline Dansylates as Selective Fluorescent Sensors for Fe^{3+}

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Abstract: A series of 5-dialkyl(aryl)aminomethyl-8-hydroxyquinoline dansylates were synthesized and their fluoroionophoric properties toward representative alkali ions, alkaline earth ions and transition metal ions were investigated. Among the selected ions, Fe^{3+} caused considerable quenching of the fluorescence, while Cr^{3+} caused quenching to some extent. The absence of any significant fluorescence quenching effects of the other ions examined, especially Fe^{2+}, renders these compounds highly useful Fe^{3+}-selective fluorescent sensors.

Keywords: Fluorescent sensor, Fe^{3+}, fluorescence quenching.

Introduction

A variety of metal ions are known to play vital roles in the structural, catalytic and regulatory aspects of biological systems [1a], therefore, sensitive and selective detection of these metal ions is of great importance. A large number of fluorescent sensors have been reported in recent years [1b-f].

Iron is one of the most important trace elements in the human body [2a]. Increased iron availability in serum or tissues is associated with an increased risk of several tumors and may promote carcinogenesis [2b]. Moreover, hereditary hemochromatosis is characterized by excess iron that causes tissue damage and fibrosis with irreversible damage to various organs [2c]. Iron homeostasis is an important factor involved in neuroinflammation and progression of Alzheimer's disease [2d].

Compared to the number of fluorescent sensors for other transition metal ions, such as Hg^{2+} [3] and Zn^{2+} [4], Fe^{3+}-specific fluorescent sensors are comparatively rare.

Regarding the Fe^{3+} sensors reported up to date (Figure 1), their detection of Fe^{3+} is always accompanied by interference from Cu^{2+} and Cr^{3+}, which affects their selectivity. For example, 4-amino-1,8-dicyanonaphthalene derivatives exhibit considerable fluorescence enhancement by both Fe^{3+} and Cr^{3+}, with a $Fe^{3+}:Cr^{3+}$ amplification ratio of 1:0.84 [5a]. Another naphthalene-derived fluorescent sensor showed a $Fe^{3+}:Cr^{3+}$ fluorescence-quenching ratio of 1:0.83 [2a]. A calix[4]arene-derived fluorescent sensor could selectively detect Fe^{3+} and Cu^{2+} [5b] with a $Fe^{3+}:Cu^{2+}$ fluorescence-quenching ratio of 1:1.17, depending on the pH. The best sensor reported so far is a derivative of 1-oxa-4,10-dithia-7-aza-cyclododecane, which displayed significant Fe^{3+}-amplified fluorescence with slight interference from Cu^{2+} [5c]. However, the test for its interaction with Cr^{3+} was not undertaken.

Figure 1. Reference Fe^{3+} sensors.
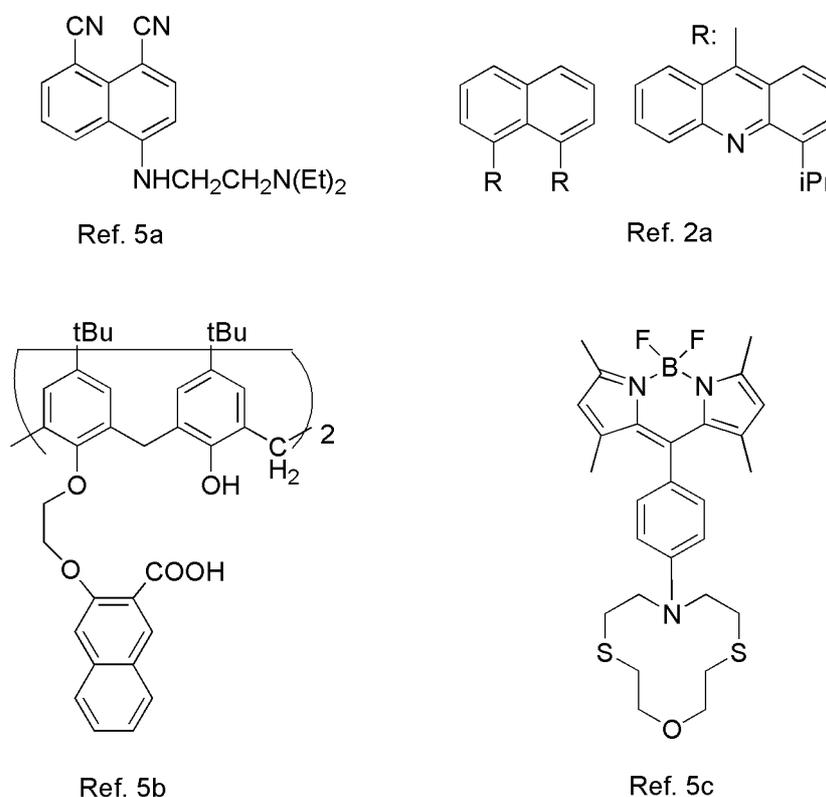
With an aim of developing more selective fluorescent sensors for Fe^{3+}, we noticed that most fluorescent sensors are composed of metal-binding sites and a proximal fluorophore, and function via a photo-induced electron transfer (PET) mechanism [2a,3a,3j]. Herein, we report the investigation of the 8-hydroxyquinoline dansylate structure as a fluorescent sensor. The dansyl group is a commonly used fluorophore that emits strong fluorescence [6], while 8-hydroxyquinoline is an excellent chelator of metal ions and has many significant applications [7]. The sulfonic group in the dansylate group and the nitrogen in the quinoline could cooperatively chelate metal ions. In the predicted chelation process, concerted changes in the distances and angles between the two ligands are required. The structural limitations of such conformational changes could lead to ion selection. Therefore, a series of

8-hydroxyquinoline dansylate derivatives were synthesized and found to be highly sensitive and more selective for Fe^{3+}.

Results and Discussion

The synthesis of the title compounds is shown in Scheme 1. First, 8-hydroxyquinoline (**1**) was chloromethylated to give crude 5-chloromethyl-8-hydroxyquinoline (**2**). High purity products were obtained by washing with concentrated hydrochloric acid (37%) instead of acetone [8]. The residual 8-hydroxyquinoline was not removed completely by washing with acetone and a substitution reaction occurred during the crystallization in ethanol. Next, **2** was reacted with different secondary amines in dichloromethane at room temperature to give **3a-3d** in high yields. Triethylamine was used as the base. The use of inorganic bases, such as sodium carbonate, sodium hydrogen carbonate and sodium hydroxide, led to either a very slow reaction rates or many unexpected byproducts. The final products, **4a-4d**, were prepared by reaction of **3a-3d** with dansyl chloride in tetrahydrofuran in good yield. **4e** was prepared by direct dansylation of **1**. The structures were identified by ^{1}H-NMR, ^{13}C-NMR, elemental analysis and ESI-MS.

Scheme 1.

4a: 75%; **4b**: 79%; **4c**: 83%; **4d**:88%

a: R=Me; **b**:R=Et; **c**:R=n-Bu; **d**:R=Ph
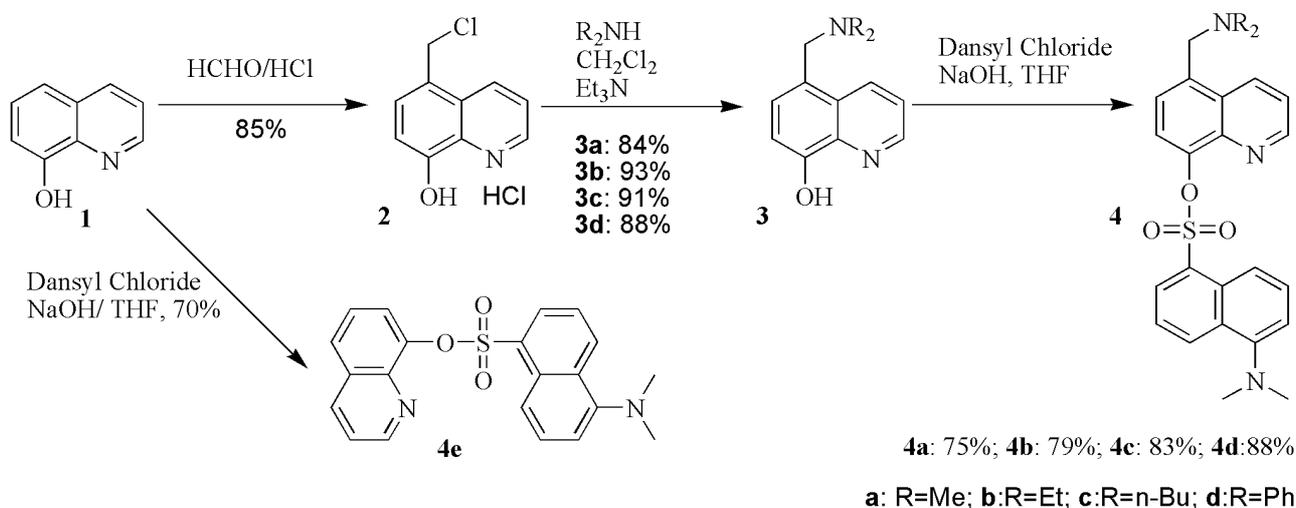
The absorption spectra of representative compounds **4c** and **4e** are shown in Figure 2. When excited at 360 nm, **4a-4e** showed similar emission patterns. The maximum emission wavelengths were 466, 468, 465, 466 and 463 nm, respectively, for **4a-4e**. Their fluoroionophoric properties toward representative alkali ions (K^+), alkaline earth ions (Mg^{2+}, Ca^{2+}, Ba^{2+}) and transition metal ions (Fe^{3+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Ag^+, Zn^{2+}, Cd^{2+} Pb^{2+}, Mn^{2+}, Cr^{3+}) were investigated in methanol solutions. The results (Table 1) revealed that only Fe^{3+} and Cr^{3+} caused considerable fluorescence quenching, similar to levels previously described in the literature [2a,5b]. However, there were differences in the sensitivities of **4a-4e**. The best result was obtained with **4e**, which showed a quenching percentage (calculated by [(I_0-I)/I_0] × 100%) of 91.2% for Fe^{3+}. Compound **4d** behaved in the same way as **4e**, while **4a-4c** behaved similarly, but showed slightly poorer selectivity.

Figure 2. Absorption spectra of **4c** and **4e** (100 μM) upon adding 1.0 equiv of Fe^{3+} in methanol.
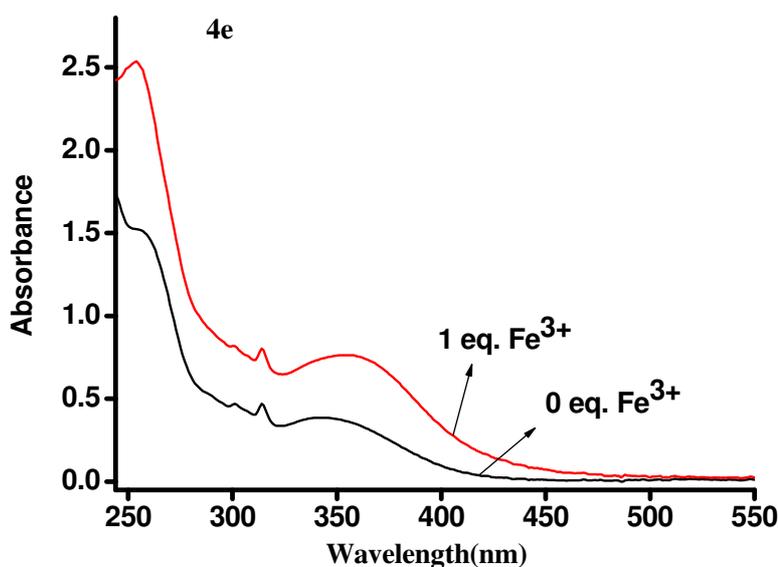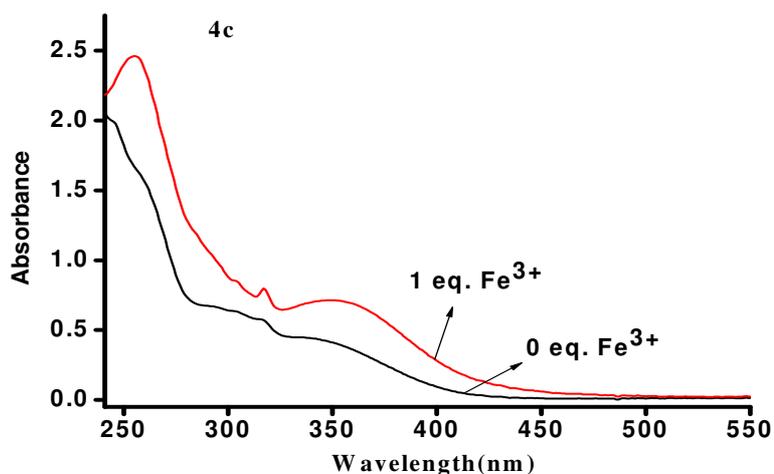
Table 1. Fluorescence quenching of **4a**-**4e** by 1.0 equiv of Fe^{3+}.

Compd.	λ_{max}(nm)	Relevant intensity	Quenching percent. of Fe^{3+}(%)	Quenching percent. of Cr^{3+}(%)	Quenching ratio(Fe^{3+}:Cr^{3+})
4a	466	57.8	72.2	59.2	1:0.82
4b	468	58.7	74.8	62.8	1:0.84
4c	465	59.7	70.5	58.5	1:0.83
4d	466	26.5	87.4	60.6	1:0.69
4e	463	38.5	91.2	52.9	1:0.58

The fluorescence quenching data for sensors **4c** and **4e** are shown in Figure 3. Fe^{3+} caused the highest level of fluorescence quenching, while Cr^{3+} caused quenching to some extent. The other ions

showed little fluorescence quenching. However, the selectivity between Fe^{3+} and Cr^{3+} was improved comparative with previously reported Fe^{3+} sensors. For example, the best quenching ratio was 1:0.58 (Fe^{3+}:Cr^{3+}) for **4e**, which is better than the previously reported ratio of 1:0.83 for a naphthalene-derived fluorescent sensor [5b]. Furthermore, the absence of any significant fluorescence quenching effects by Cu^{2+}, Mn^{2+}, Co^{2+}, Ni^{2+} and especially Fe^{2+} renders these derivatives highly useful Fe^{3+}-selective sensors.

Figure 3. Quenching percentages [(I_0-I)/ I_0]×100% of the fluorescence intensities of **4c** and **4e** (100 μM) upon the addition of 1.0 equiv of metal ions in methanol.
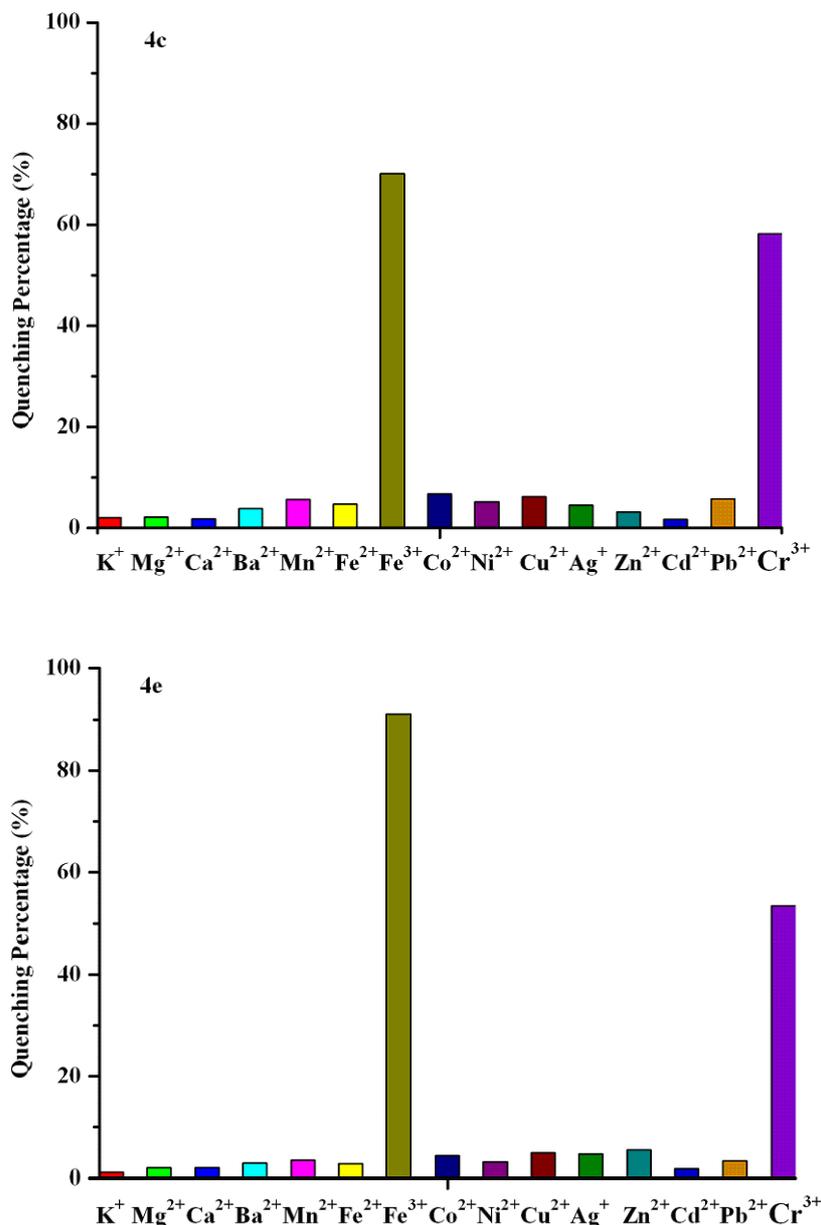
In order to gain further insights into the analytical possibilities, fluorescence titration of **4e** by Fe^{3+} was performed and the obtained curves are shown in Figure 4. The quenching was very effective and a quenching efficiency of 91.2% was obtained at a ratio of 1:1. The break around 1.0 equiv of Fe^{3+} suggested a 1:1 stoichiometry for the **4e**-Fe^{3+} complex system [3j]. By working on the Stern-Volmer equation [9,3a], the association constant was calculated to be about $1.1×10^5$ M^{-1}.

Figure 4. Fluorescence titration curves of **4e** with Fe^{3+} in methanol. [4e]=100 μM. The inset shows a plot of the fluorescence intensities against $[Fe^{3+}]/[4e]$.
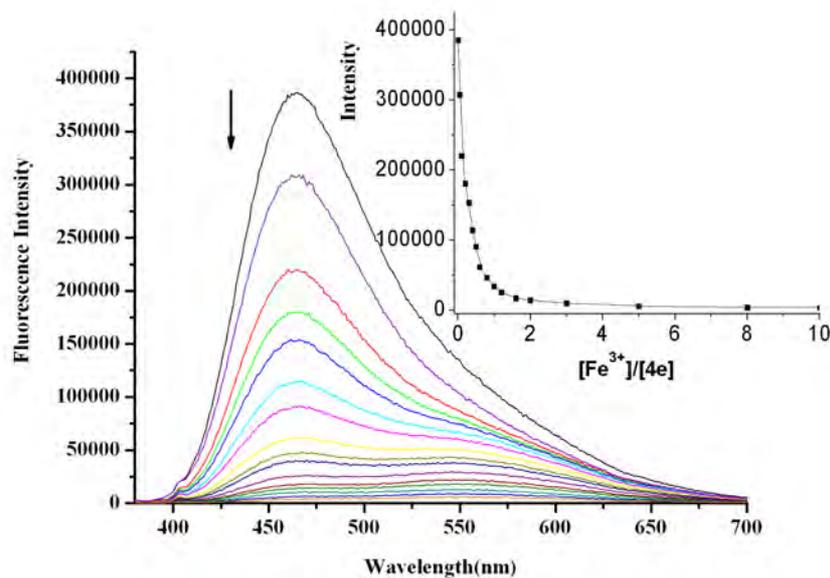
Next, a competition experiment was carried out in the presence of 4.0 equiv of background metal ions in order to confirm the practical applicability of **4e** as a Fe^{3+} sensor (Figure 5). Most of the metal ions, including Cr^{3+}, did not show any obvious interference with the detection of Fe^{3+}, while Cu^{2+}, Co^{2+}, Zn^{2+} and Mn^{2+} showed only moderate interference. Therefore, **4e** is a potential Fe^{3+}-selective fluorescent chemosensor.

Figure 5. Fluorescence quenching percentages $[(I_0-I)/I_0]\times100\%$ of **4e** (100 μM) upon the addition of 1.0 equiv of Fe^{3+} and 4.0 equiv of background metal ions in methanol.
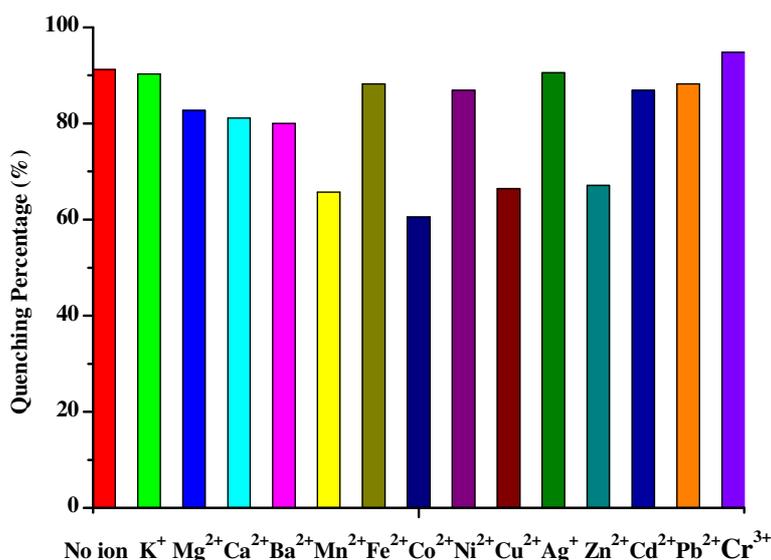
In order to gain further insights into the interaction between Fe^{3+} and designed sensors, related conformations were simulated using the MM2 method as implemented in Chem3D. The optimized conformation of **4e** is shown in Figure **4e** and the **4e**-Fe^{3+} complex in Figure 6. Among the changes, the most important would be the naphthyl conformation. It actually changed from a plane form to a

twisted one. Therefore the conjugation system of dansyl moiety has been severely damaged and this may be the actual cause of the observed fluorescence quenching.

Figure 6. Computer simulated conformation of **4e**(a) and **4e**-Fe^{3+} complex(b).
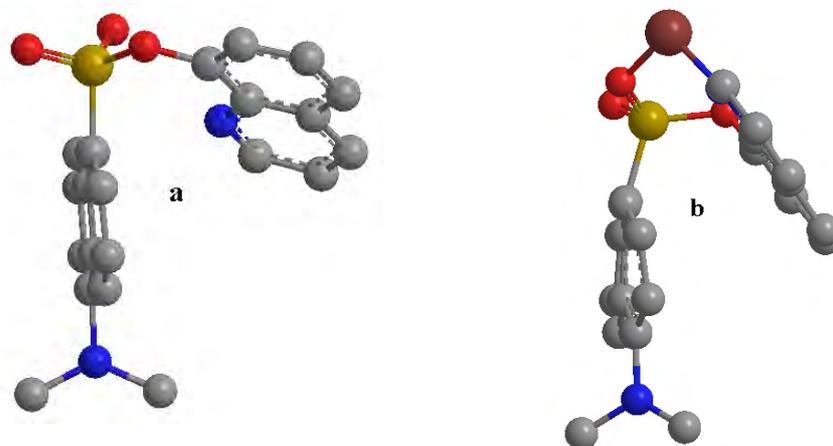
Conclusions

A series of novel Fe^{3+} fluorescent sensors based on 8-hydroxyquinoline and the dansyl group were synthesized and their fluoroionophoric properties toward K^+, Mg^{2+}, Ca^{2+}, Ba^{2+}, Fe^{3+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Ag^+, Zn^{2+}, Cd^{2+}, Pb^{2+}, Mn^{2+} and Cr^{3+} were investigated in methanol solutions. Only Fe^{3+} caused considerable quenching of the fluorescence emission, and the other metal ions showed little interference with the detection of Fe^{3+}. Among these potential metal ion fluorescent sensors, **4e** showed the best efficiency and selectivity toward Fe^{3+}.

Experimental

General

All solvents and reagents were purchased from Aldrich and used without further purification. ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75 MHz) spectra were recorded on a JOEL JNM-ECA300 spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane (TMS) as an internal standard, and coupling constants (*J*) are given in hertz (Hz). Elemental analyses were carried out on an Elementar Vario EL CHN element analysis instrument. All ESI-MS experiments were undertaken on a Bruker ESQUIRE-LC. Fluorescence intensity was measured using a HORABA Fluoromax 3.

General procedure for the preparation of 5-chloromethyl-8-hydroxyquinoline hydrogen chloride 2

A stream of hydrogen chloride gas was blown through a solution of 8-hydroxyquinoline **1** (0.1 mol) and formaldehyde (20 mL, 37%) in 37% hydrochloric acid (50 mL) for 8 hours at 50°C. After filtration, the product was washed with 37% hydrochloric acid and dried to afford **2** in 85% yield.

*General procedure for the preparation of 5-dialkyl(aryl)aminomethyl-8-hydroxyquinoline **3a-3d***

To a solution of **2** (10 mmol) and triethylamine (30 mmol) in dichloromethane (50 mL) was added dropwise a solution of the appropriate dialkyl(aryl)amine (10 mmol) in dichloromethane (50 mL) at room temperature over 30 minutes. After a further 15 minute of reaction, the solution was washed thoroughly with brine, dried over magnesium sulfate and concentrated to afford **3a-3d** without further purification (yields are listed in Scheme 1).

*General procedure for the preparation of 5-dialkylaminomethyl-8-hydroxyquinoline dansylate **4a-4e***

To a solution of **3a-3d** or **1** (1 mmol) in THF (10 mL) was added sodium hydroxide (5 mmol), followed by stirring for 5 minutes. Next, a solution of dansyl chloride (1 mmol) in THF (10 mL) was added dropwise at room temperature over 5 minutes. The reaction was kept at room temperature for a further 10 minutes and then filtered. The filtrate was evaporated under vacuum and the crude product was purified by silica gel column chromatography (EtOAc-Petroleum Ether).

5-Dimethylaminomethyl-8-hydroxyquinoline dansylate (**4a**). ^{1}H-NMR (CDCl$_3$) δ 8.68-8.71 (m, 2H), δ 8.53-8.60 (m, 2H), 8.17 (d, 1H, *J*=7.20), 7.58-7.63 (m, 1H), 7.44 (t, 1H, *J*=7.89), 7.31-7.35 (m, 2H), 7.17-7.25 (m, 2H), 3.70 (s, 2H), 2.87 (s, 6H), 2.21 (s, 6H); ^{13}C-NMR (CDCl$_3$) δ 151.7, 150.5, 145.6, 142.1, 134.6, 133.1, 132.5, 131.8, 130.7, 130.5, 129.9, 128.9, 128.8, 127.0, 123.0, 121.7, 121.0, 120.4, 115.6, 61.7, 45.6, 37.5; ESI-MS: calcd for (M+H)/*z*: 436.2. Found: (M+H)/*z*: 436.2. Anal. Calcd for C$_{24}$H$_{25}$N$_3$O$_3$S: C 66.18, H 5.19, N 9.65; found C 65.92, H 5.36, N 9.55.

5-Diethylaminomethyl-8-hydroxyquinoline dansylate (**4b**). ^{1}H-NMR (CDCl$_3$) δ 8.70-8.73 (m, 2H), δ 8.57-8.66 (m, 2H), 8.18 (d, 1H, *J*=7.23), 7.58-7.63 (m, 1H), 7.44 (t, 1H, *J*=7.89), 7.31-7.36 (m, 2H), 7.17-7.21 (m, 2H), 3.87 (s, 2H), 2.87 (s, 6H), 2.51 (q, 4H, J=6.84), 1.00 (t, 6H, *J*=6.84); ^{13}C-NMR (CDCl$_3$) δ 151.7, 150.4, 145.3, 142.1, 133.1, 132.5, 131.8, 130.7, 130.5, 129.9, 128.9, 128.8, 126.8, 125.6, 123.0, 121.4, 121.0, 120.4, 115.6, 55.5, 46.8, 45.6, 11.4; ESI-MS: calcd for (M+H)/*z*: 464.2. Found: (M+H)/*z*: 464.1. Anal. Calcd for C$_{26}$H$_{29}$N$_3$O$_3$S: C 67.36, H 6.31, N 9.06; found C 67.13, H 6.44, N 9.31.

5-Di-n-butylaminomethyl-8-hydroxyquinoline dansylate (**4c**). ^{1}H-NMR (CDCl$_3$) δ 8.75 (d, 1H, J=8.58), 8.70 (d, 1H, *J*=3.78), 8.64 (d, 1H, *J*=8.58), 8.59 (d, 1H, *J*=8.58), 8.17 (d, 1H, *J*=7.56), 7.60-7.66 (m, 1H), 7.43 (t, 1H, *J*=7.92), 7.30-7.34 (m, 2H), 7.19-7.23 (m, 2H), 3.84 (s, 2H), 2.88 (s, 6H), 2.38 (d, 4H, *J*=7.20), 1.35-1.42 (m, 4H), 1.15-1.22 (m, 4H), 0.77 (t, 6H, *J*=7.23); ^{13}C-NMR (CDCl$_3$) δ 151.7, 150.4, 145.2, 142.1, 136.0, 133.3, 132.6, 131.8, 130.7, 130.6, 129.9, 128.9, 128.7, 126.6, 122.9, 121.2, 121.1, 120.5, 115.6, 57.1, 53.7, 45.6, 28.9, 20.7, 14.1; ESI-MS: calcd for (M+H)/*z*: 520.3. Found: (M+H)/*z*: 520.3. Anal. Calcd for C$_{30}$H$_{37}$N$_3$O$_3$S: C 69.33, H 7.18, N 8.09; found C 69.23, H 7.04, N 8.27.

5-Diphenylaminomethyl-8-hydroxyquinoline dansylate (**4d**). ^{1}H-NMR (CDCl$_3$) δ 8.62-8.83 (m, 3H), δ 8.20-8.31 (m, 2H), 7.61-7.66 (m, 1H), 7.39-7.50 (m, 3H), 7.22-7.26 (m, 6H), 6.95-7.17 (m, 6H), 5.34

(s, 2H), 2.91 (s, 6H); ^{13}C-NMR (CDCl$_3$) δ 151.7, 150.6, 147.8, 145.2, 142.3, 133.4, 132.6, 131.9, 130.9, 130.7, 130.5, 130.0, 129.5, 129.4, 128.9, 127.3, 123.1, 122.0, 121.8, 121.0, 120.8, 120.4, 115.7, 53.6, 45.6; ESI-MS: calcd for (M+H)/*z*: 560.2. Found: (M+H)/*z*: 560.3. Anal. Calcd for C$_{34}$H$_{29}$N$_3$O$_3$S: C 72.96, H 5.22, N 7.51; found C 72.70, H 5.05, N 7.68.

8-Hydroxyquinoline dansylate (**4e**). ^{1}H-NMR (CDCl$_3$) δ 8.71-8.75 (m, 2H), 8.60 (d, 1H, *J*=8.58), 8.18 (d, 1H, *J*=7.56), 8.06 (d, 1H, *J*=8.22), 7.60-7.67 (m, 2H), 7.45 (t, 1H, *J*=7.89), 7.31-7.40 (m, 2H), 7.20-7.25 (m, 2H), 2.88 (s, 6H); ^{13}C-NMR (CDCl$_3$) δ151.7, 150.9, 145.9, 141.9, 135.7, 132.4, 131.9, 130.7, 130.5, 129.9, 129.7, 128.8, 127.0, 125.9, 123.0, 122.0, 121.9, 120.4, 115.7, 45.6; ESI-MS: calcd for (M+H)/*z*: 379.1. Found: (M+H)/*z*: 379.0. Anal. Calcd for C$_{21}$H$_{18}$N$_2$O$_3$S: C 66.65, H 4.79, N 7.40; found C 66.88, H 5.26, N 7.38.

References

1. a) Ngwendson, J.N.; Amiot, C.L.; Srivastava, D.K.; Banerjee, A. Design of a zinc(II) ion specific fluorescence sensor. *Tetrahedron Lett*. **2006**, *47*, 2327–2330; b) Baruah, M.; Qin, W.W.; Valle´e, R.A.L.; Beljonne, D.; Rohand, T.; Dehaen, W.; Boens, N. Highly Potassium-Selective Ratiometric Fluorescent Indicator Based on BODIPY Azacrown Ether Excitable with Visible Light. *Org. Lett*, **2005**, *7*, 4377-4380; c) Kim, S.H.; Choi, J.K.; Kim, S.K.; Sim, W.; Kim, J.S. On/off fluorescence switch of a calix[4]arene by metal ion exchange. *Tetrahedron Lett*. **2006** *47* 3737-3741; d) Prodi, L.; Bolletta, F.; Montalti, M.; Zaccheroni, N.; Savage, P.B.; Bradshaw, J.S.; Izatt, R.M. A fluorescent sensor for magnesium ions. *Tetrahedron Lett*. **1998**, *39*, 5451–5454; e) Behannaa, H.A.; Stupp, S.I. Synthesis of stilbene carboxylic acids as scaffolds for calcium sensors. *Chem. Commun*. **2005**, 4845–4847; f) Kondo, S.I.; Kinjo, T.; Yano, Y. Barium ion sensing by a 2,2'-binaphthalene derivative bearing two monoaza-15-crown-5 ethers. *Tetrahedron Lett*. **2005**, *46*, 3183–3186.

2. a) Wolf, C.; Mei, X.F.; Rokadia, H.K. Selective detection of Fe(III) ions in aqueous solution with a 1,8-diacridylnaphthalene-derived fluorosensor. *Tetrahedron Lett*. **2004**, *45*, 7867–7871; b) Weiss, G.; Gordeuk, V.R. Benefits and risks of iron therapy for chronic anaemias. *Eur. J. Clin. Invest*. **2005**, *35*, 36-45; c) Franchini, M. Hereditary iron overload: update on pathophysiology, diagnosis, and treatment. *Am. J. Hematol*. **2006**, *81*, 202–209; d) Ong, W.Y.; Farooqui, A.A. Iron, neuroinflammation, and Alzheimer's disease. *J. Alzheimers Dis*. **2005**, *8*, 183-200.

3. a) Chen, Q.Y.; Chen, C.F. A new Hg^{2+}-selective fluorescent sensor based on a dansyl amide-armed calix[4]-aza-crown. *Tetrahedron Lett*. **2005**, *46*, 165–168; b) Hennrich, G.; Walther, W.; Resch-Genger, U.; Sonnenschein, H. Cu(II)- and Hg(II)-Induced Modulation of the Fluorescence Behavior of a Redox-Active Sensor Molecule. *Inorg. Chem*. **200**1, *40*, 641–644; c) Rurack, K.; Resch-Genger, U.; Bricks, J.L.; Spieles, M. Cation-triggered "switching on" of the red/near infra-red (NIR) fluorescence of rigid fluorophore-spacer-receptor ionophores. *Chem. Commun*. **2000**, *2*, 2103–2104; d) Yoon, J.Y.; Ohler, N.E.; Vance, D.H.; Aumiller, W.D.; Czarnik, A.W. A fluorescent chemosensor signaling only Hg(II) and Cu(II) in water. *Tetrahedron Lett*. **1997**, *38*, 3845–3848; e) Chan, W.H.; Yang, R.H.; Wang, K.M. Development of a mercury ion-selective optical sensor based on fluorescence quenching of 5,10,15,20-tetraphenylporphyrin.

Anal. Chim. Acta. **2001**, *444*, 261–269; f) Prodi, L.; Bargossi, C.; Montalti, M.; Zaccheroni, N.; Su, N.; Bradshaw, J.S.; Izatt, R.M.; Savage, P.B. An Effective Fluorescent Chemosensor for Mercury Ions. *J. Am. Chem. Soc*. **2000**, *122*, 6769–6770; g) Descalzo, A.B.; Martinez-Manez, R.; Radeglia, R.; Rurack K.; Soto J. Coupling Selectivity with Sensitivity in an Integrated Chemosensor Framework: Design of a Hg^{2+}-Responsive Probe, operating above 500 nm. *J. Am. Chem. Soc*. **2003**, *125*, 3418–3419; h) Moon S.Y.; Cha N.R.; Kim Y.H.; Chang S.K. New Hg^{2+}-selective chromo- and fluoroionophore based upon 8-hydroxyquinoline. *J. Org. Chem*. **2004**, *69*, 181–183; i) Rurack, K.; Kollmannsberger, M.; Resch-Genger, U.; Daub, J. A Selective and Sensitive Fluoroionophore for HgII, AgI, and CuII with Virtually Decoupled Fluorophore and Receptor Units. *J. Am. Chem. Soc*. **2000**, *122*, 968-969; j) Kim, S.H.; Song, K.C.; Ahn, S.; Kang, Y.S.; Chang, S.K. Hg^{2+}-selective fluoroionophoric behavior of pyrene appended diazatetrathia-crown ether. *Tetrahedron Lett*. **2006**, *47*, 497-500.

4. a) Meng, X.M.; Zhu, M.Z.; Liu, L.; Guo, Q.X.. Novel highly selective fluorescent chemosensors for Zn(II). *Tetrahedron Lett*. **2006**, *47*, 1559-1562; b) Dessingou, J.; Joseph, R.; Rao, C.P. A direct fluorescence-on chemo-sensor for selective recognition of Zn(II) by a lower rim 1,3-di-derivative of calix[4]arene possessing bis-{N-(2-hydroxynaphthyl-1-methylimine)} pendants. *Tetrahedron Lett*. **2005**, *46*, 7967-7971; c) Song, L.Q.; Hou, Y.J.; Wang, X.S.; Zhang, B.W.; Xie, P.H.; Ma, C.Q.; Cao, Y. Zn^{2+} recognition by two new bipyridine ligands. *Chin. J. Chem*. **2003**, *21*, 505–509; d) Henary, M.M.; Wu, Y.; Fahrni, C.J. Zinc(II)-selective ratiometric fluorescent sensors based on inhibition of excited-state intramolecular proton transfer. *Eur. J. Chem.* **2004**, *10*, 3015–3025; e) Woodroofe, C.C.; Won, A.C.; Lippard, S.J. Esterase-activated two-fluorophore system for ratiometric sensing of biological zinc(II). *Inorg. Chem*. **2005**, *44*, 3112– 3120; f) Komatsu, K.; Kukuchi, K.; Kojima, H.; Urano Y.; Nagano T. Selective Zinc Sensor Molecules with Various Affinities for Zn^{2+}, Revealing Dynamics and Regional Distribution of Synaptically Released Zn^{2+} in Hippocampal Slices. *J. Am. Chem. Soc*. **2005**, *127*, 10197–10204; g) Fan, J.L.; Wu, Y.K.; Peng, X.J. A naphthalimide fluorescent sensor for Zn^{2+} based on photo-induced electron transfer. *Chem. Lett*. **2004**, *33*, 1392– 1393; h) Wu Y.K.; Peng X.; Guo B.; Fan J.; Zhang Z.; Wang J.; Cui A.; Gao Y. Boron dipyrromethene fluorophore based fluorescence sensor for the selective imaging of Zn(II) in living cells. *Org. Biomol. Chem*. **2005**, *3*, 1387–1392; i) Jia, L.H.; Guo, X.F.; Liu, Y.; Qian, X.H. Anthracylmethyl benzoazacrown ether as selective fluorescence sensors for Zn^{2+}. *Chin. Chem. Lett*. **2004**, *15*, 118–120; j) Chen, Y.; Zeng, D.X. A selective, fluorescent sensor for Zn^{2+}. *Chem. Phys. Chem*. **2004**, *5*, 564–566.

5. a) Qian, X.H.; Xiao, Y. 4-Amino-1,8-dicyanonaphthalene derivatives as novel fluorophore and fluorescence switches: efficient synthesis and fluorescence enhancement induced by transition metal ions and protons. *Tetrahedron Lett*. **2002**, *43*, 2991-2994; b) Liu, J.M.; Zheng, Q.Y.; Yang, J.L.; Chen, C.F.; Huang, Z.T. A new fluorescent chemosensor for Fe^{3+} and Cu^{2+} based on calix[4]arene. *Tetrahedron Lett*. **2002**, *43*, 9209-9212; c) Bricks, J.L.; Kovalchuk, A.; Trieflinger, C.; Nofz, M.; Büschel, M.; Tolmachev, A.I.; Daub, J.; Rurack, K. On the Development of Sensor Molecules that Display FeIII-amplified Fluorescence. *J. Am. Chem. Soc*. **2005**, *127*, 13522-13529.

6. a) Kavallieratos, K.; Rosenberg, J.M.; Chen, W.Z.; Ren, T. Fluorescent Sensing and Selective Pb(II) Extraction by a Dansylamide Ion-Exchanger. *J. Am. Chem. Soc*. **2005**, *127*, 6514-6515; b)

Chen, C.F.; Chen, Q.Y. A tetra-sulfonamide derivative bearing two dansyl groups designed as a new fluoride selective fluorescent chemosensor. *Tetrahedron Lett*. **2004,** *45*, 3957–3960; c) Prodi, L.; Bolletta, F.; Montalti, M.; Zaccheroni, N. Searching for new luminescent sensors. Synthesis and photophysical properties of a tripodal ligand incorporating the dansyl chromophore and of its metal complexes. *Eur. J. Inorg. Chem.* **1999**, 455-460. d) Walkup, G. K.; Imperiali, B. Exploiting Polypeptide Motifs for the Design of Selective Cu(II) Ion Chemosensors. *J. Am. Chem. Soc.* **1998**, *120*, 609-610. e) Zheng, Y.; Orbulescu, J.; Ji, X.; Andreopoulos F.M.; Pham S.M.; Leblanc R.M. Development of Fluorescent Film Sensors for the Detection of Divalent Copper. *J. Am. Chem. Soc.* **2003**, *125*, 2680-2686.

7. a) Zhang, H.; Han, L.F.; Zachariasse, K.A.; Jiang, Y.B. 8-Hydroxyquinoline benzoates as highly sensitive fluorescent chemosensors for transition metal ions. *Org. Lett*, **2005**, *7*, 4217-4220; b) Shen, L.; Li, F.Y.; Sha, Y.W.; Hong, X.; Huang, C. Synthesis of fluorescent dendritic 8-hydroxyquinoline ligands and investigation on their coordinated Zn(II) complexes. *Tetrahedron Lett*. **2004**, *45*, 3961-3964; c) Sha, Y.W.; Shen, L.; Hong, X.Y. A divergent synthesis of new aliphatic poly(ester-amine) dendrimers bearing peripheral hydroxyl or acrylate groups. *Tetrahedron Lett.* **2002**, *43*, 9417-9419; d) Prodi, L.; Montalti, M.; Zaccheroni, N.; Bradshaw, J.S.; Izatt, R.M.; Savage, P.B. Characterization of 5-chloro-8-methoxyquinoline appended diaza-18-crown-6 as a chemosensor for cadmium. *Tetrahedron Lett*. **2001**, *42*, 2941-2944. e) Bronson, R. T.; Montalti, M.; Prodi, L.; Zaccheroni, N.; Lamb, R.D.; Dalley, N.K.; Izatt, R.M.; Bradshaw, J.S.; Savage, P.B. Origins of on-off fluorescent behavior of 8-hydroxyquinoline containing chemosensors. *Tetrahedron*, **2004**, *60*, 11139-11144. f) Bronson, R.T.; Bradshaw, J.S.; Savage, P.B.; Fuangswasdi, S.; Lee, S.C.; Krakowiak, K.E.; Izatt, R.M. Bis-8-hydroxyquinoline-Armed Diazatrithia-15-crown-5 and Diazatrithia-16-crown-5 Ligands: Possible Fluorophoric Metal Ion Sensors. *J. Org. Chem.* **2001**, *66*, 4752-4758.

8. Mei, Q.B.; Du, N.Y.; Lv, M.G. Synthesis and Characterization of High Molecular Weight Polymer Containing Tris(8-hydroxyquinoline) Aluminum(III) Complexes. *Acta. Chimica. Sinica*. **2004**, *62*, 2113-2117

9. Andrade, S.M.; Costa, S.M.B. Spectroscopic studies on the interaction of a water soluble porphyrin and two drug carrier proteins. *Biophys. J*. **2002**, *82*, 1607-1619.

Sample Availability: Compound **4e** is available from the authors.