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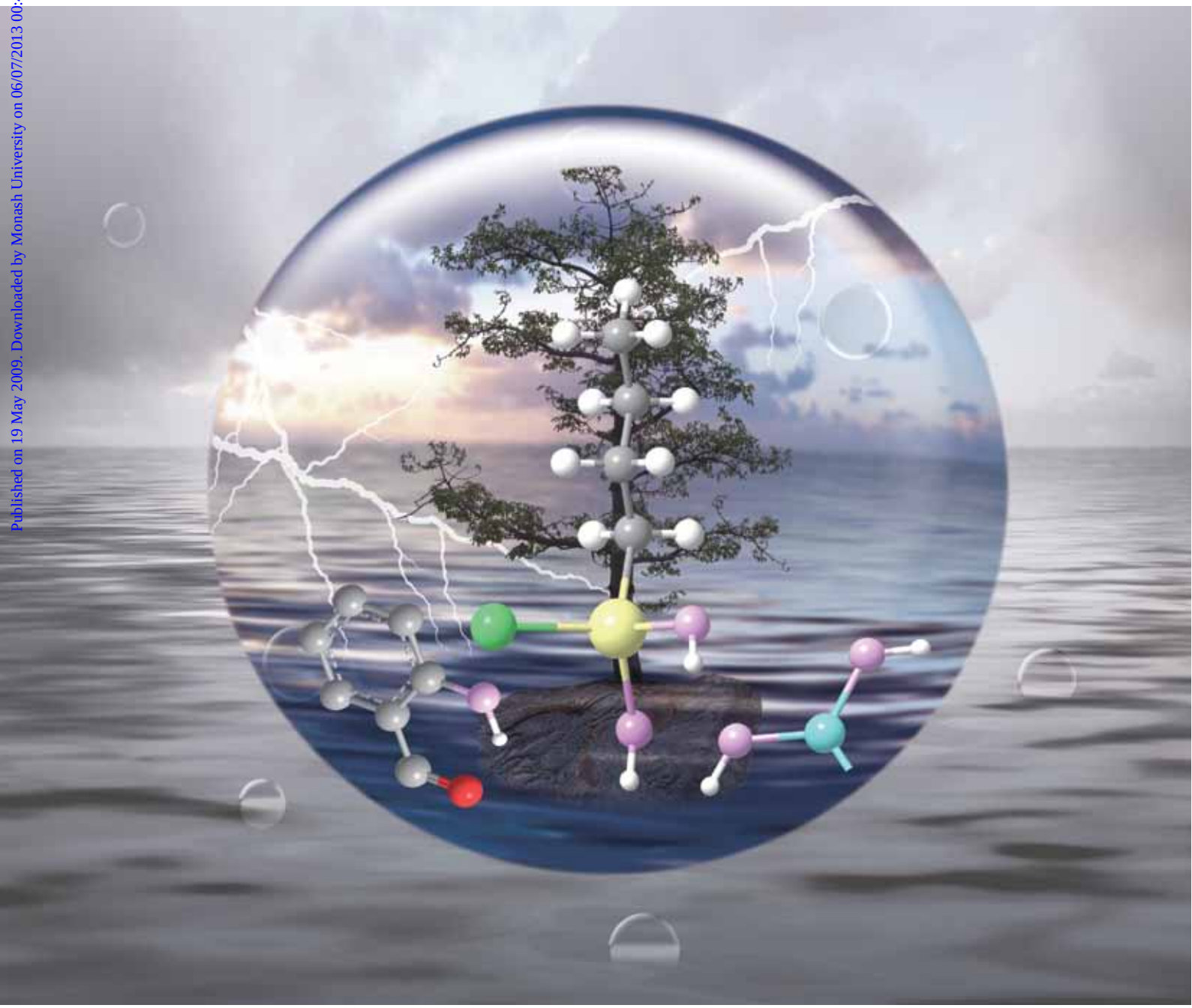

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Enhanced fluorescence sensing of hydroxylated organotins by a boronic acid-linked Schiff base†

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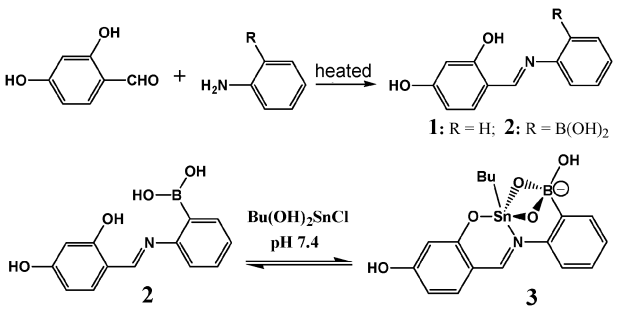
A simple Schiff base, 2-(2′,4′-dihydroxybenzylidene)aminobenzeneboronic acid, was found to show a fluorescence enhancement in the presence of hydroxylated organotins in aqueous solution.

Fluorescent chemosensors offer an essential strategy for real-time and real-space monitoring or imaging. Many fluorescent chemosensors have been reported for transition metal species of biological or environmental interest.[1] While organotin compounds (OTCs) are known for their high toxicity yet wide use,[2] selective and sensitive fluorescent chemosensors for OTCs remain largely unexplored. Hydroxylated organotins (HOTs) of high biological activities[3] are important OTC metabolites, which result mainly from the dealkylation and hydrolysis processes in OTC biodegradation.[4] Sensitive optical sensors for HOTs should therefore be of great use for studying the absorption, accumulation, degradation and delayed toxicity of the related OTCs in aquatic organisms. Herein, we report a simple fluorescent chemosensor for HOTs, operative in aqueous solutions of physiological pH.

The sensory molecule, **2**, was designed to combine an *o*-hydroxyl Schiff base moiety with a boronic acid group as a cooperative HOT binding site (Scheme 1). Many Schiff bases, especially those containing an *o*-hydroxyl group,[5] have proven to be efficient ligands for the tin centre in OTCs. On the other hand, boronic acid is known to have a high affinity for the vicinal diol group.[6] It has recently been reported that boronic acid was also able to bind to transition metal ions.[7] This enlightened us to examine boronic acid as a binding group for hydroxylated transition metals. Rational conjugation of boronic acid group with *o*-hydroxyl Schiff bases was assumed to achieve highly selective HOT receptors. Because transition metal cations are usually known to be efficient fluorescence quenchers, an operating mode with fluorescence enhancement is preferable in sensing transition metal species, due to selectivity reasons. In this design, the binding of a HOT substance would lead to conformational restriction of the receptor and that might result in fluorescence enhancement due to the strong increase of molecular rigidity.

2 was synthesized by direct treatment of 2,4-dihydroxybenzaldehyde with 2-aminobenzeneboronic acid, while Schiff base analogue **1** as a control complex was similarly derived from aniline. A variety of metal species were tested in aqueous solutions of **2** at physiological pH. Fig. 1 shows a distinct fluorescence response of **2** toward $BuSn(OH)_2Cl$, a model complex for HOTs in relation to the widely-concerned toxicity of tributyltins (TBTs).[4b] Emission of **2** (λ_{em} = 474 nm) is dramatically enhanced upon addition of $BuSn(OH)_2Cl$, whereas no obvious change is observed upon addition of other metal species, including K^+, Na^+, Mg^{2+}, Ca^{2+}, Ba^{2+}, Al^{3+}, Cd^{2+}, Ag^+, Mn^{2+}, Ni^{2+}, Zn^{2+}, Pb^{2+}, Co^{2+}, Fe^{3+}, Cr^{3+}, Cu^{2+}, Bu_3SnCl, Bu_2SnCl_2, $BuSnCl_3$, $SnCl_4$, $SnCl_2$, Me_2SnCl_2 and Ph_2SnCl_2, despite the Hg^{2+}-induced little quenching. Fluorescence quenching of **2** induced by Hg^{2+} binding might result from the heavy-atom effect. Under the test conditions, an approximately 13-fold increase in the relative fluorescence quantum yield of **2** (Φ_0 = 0.017) was induced by addition of excess $BuSn(OH)_2Cl$, using quinine sulfate as a reference standard for the determination. Obviously noted in Fig. 1, highly selective and sensitive fluorescence enhancement was obtained in HOT sensing.

The HOT binding mechanism underlying the observed binding selectivity and fluorescence enhancement was studied. The characteristic bands of O–H bond stretching (3373 cm^{-1}) and Sn–Cl bond stretching (682, 612 and 511 cm^{-1}) in the IR spectrum of $BuSn(OH)_2Cl$ disappeared upon reaction with **2** (Fig. S3 in ESI†). This indicates that both the coordination substitution of Sn–Cl by the Schiff base and the boronic acid–diol interaction occur in the binding reaction. The combined binding mode described in Scheme 1 was also supported by characterising the **2**–$BuSn(OH)_2Cl$ adduct using mass spectrometry and NMR studies (Fig. S4 in ESI†). The cooperation of the *o*-hydroxyl Schiff base and boronic acid group of **2** was assumed to contribute to its higher binding constant for HOTs than for other OTCs, which explains the high selectivity in its sensing response. Cooperative participation of the *o*-hydroxyl Schiff base and boronic acid group in HOT binding induces a conformational restriction in **3**, leading to a



Scheme 1 Synthesis and sensing reactions of the investigated *o*-hydroxyl Schiff base.

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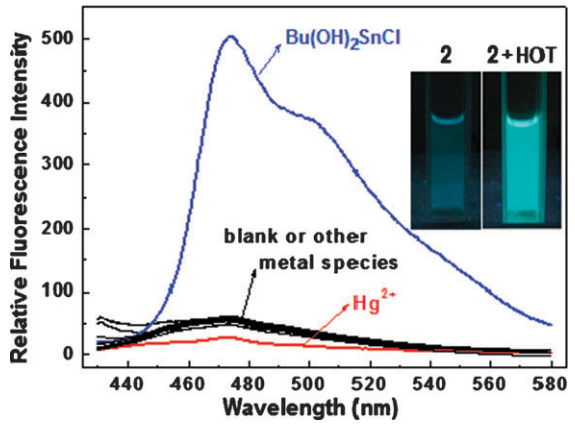

Fig. 1 The fluorescence response of **2** to a variety of metal species in H_2O–EtOH (90 : 10, v/v). **2**: 1.0×10^{-6} M; metal species: 5.0×10^{-5} M; pH: 7.4, buffered by 0.01 M Tris-HCl; excitation wavelength: 403 nm. Inset: photographs showing fluorescence of the sensory solution of **2** before and after addition of $BuSn(OH)_2Cl$.

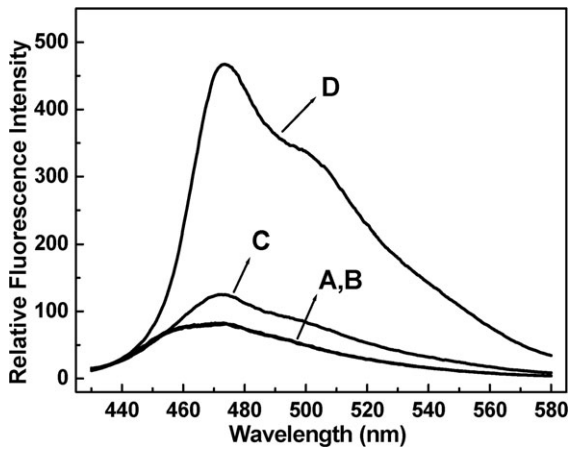

Fig. 2 The emission spectra of **2** in H_2O–EtOH (90 : 10, v/v). **2**: 1.0×10^{-6} M; pH: 7.4, buffered by 0.01 M Tris-HCl; excitation wavelength: 403 nm. A: **2** only; B: **2** + catechol (1 equiv.); C: **2** + catechol (1 equiv.) + $BuSn(OH)_2Cl$ (50 equiv.); D: **2** + $BuSn(OH)_2Cl$ (50 equiv.).

dramatic enhancement in the fluorescence. This is reflected by the observed vibrational structure in the fluorescence spectrum of **3** (Fig. 1). Fluorescence enhancement sensing based on the binding-induced rigidity increase of boronic acid-linked flexible fluorophores has been previously reported.[8] The increased rigidity of sensing product might be anticipated to significantly reduce non-radiative decay.[9] Wang *et al.*[10] recently reported a new fluorescence signaling mechanism based on C=N isomerization. It was similarly assumed that coordination of the unbridged C=N structure with transition metals would suppress C=N isomerization in the excited states and result in fluorescence enhancement. This is likely to be involved in the signaling mechanism of the binding-induced fluorescence enhancement in this design.

Control experiments were carried out to identify the important role of the boronic acid group in the binding and signaling mechanisms. No optical response selectivity has been observed for $BuSn(OH)_2Cl$ against other investigated OTCs when **1**, bearing no boronic acid group, was employed as the receptor (Fig. S5 in ESI†). This confirms that the high selectivity of **2** in HOT recognition lies heavily on the covalent interaction of boronic acid with tin-centered diol. The HOT-induced fluorescence enhancement was suppressed to a high degree when **2** was pretreated with 1 equiv. of catechol (Fig. 2). In this test, the catechol protected boronic acid from reacting with the tin-centered diol. Consequently, the binding of tin can only lead to a restriction of the C=N conformation,[10] whereas it cannot conjugate the Schiff base moiety with the benzeneboronic acid group to form a highly rigid fluorophore. It is therefore concluded that the binding-induced increase in molecular rigidity, but not the suppression of C=N isomerization, is mainly responsible for the HOT-induced fluorescence enhancement of **2**.

The fluorescent receptor, **2**, was successfully applied to the determination of HOT in aqueous media. The solution fluorescence of **2** increases rapidly and substantially after addition of HOTs. Importantly, a stable fluorescence response can be achieved in 1 min at physiological pH (Fig. S6 in ESI†). Fig. 3 shows the spectral evolution of **2** upon titration with $BuSn(OH)_2Cl$ in H_2O–EtOH (90 : 10, v/v) at pH 7.4. The binding constant of **2** for $BuSn(OH)_2Cl$ was calculated to be 8.6×10^3 M^{-1}. A good linearity is observed between the relative fluorescence intensity and HOT concentration in the

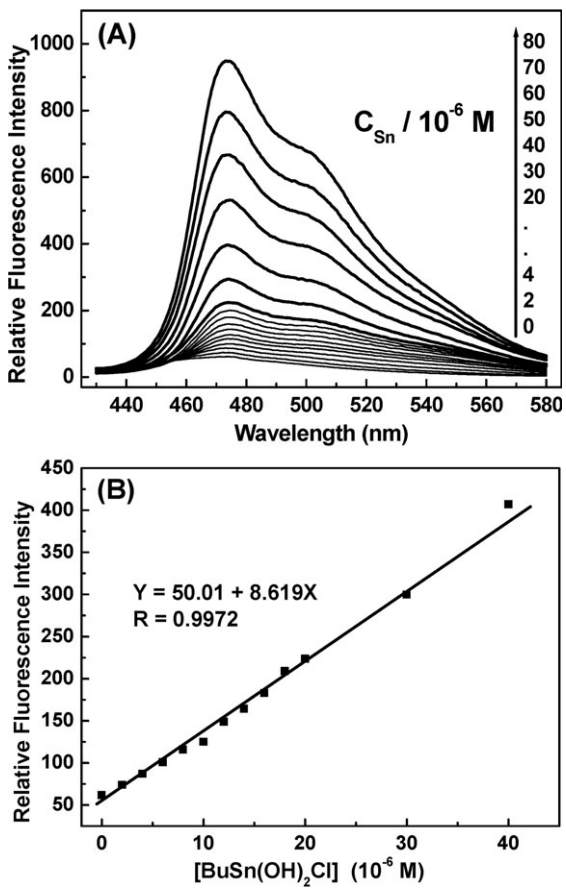

Fig. 3 The fluorescence evolution of **2** in H_2O–EtOH (90 : 10, v/v) upon titration with $BuSn(OH)_2Cl$ at increasing concentration. **2**: 1.0×10^{-6} M; pH: 7.4, buffered by 0.01 M Tris-HCl; excitation wavelength: 403 nm. The calibration curve was obtained by measuring the solution fluorescence at 474 nm.

range of 0–40 μM. It is therefore made clear that HOTs can be conveniently detected at low concentration levels, with a detection limit down to 4.9×10^{-7} M. It must be noted that pH greatly affects the HOT-sensing response of **2** (Fig. S7 in ESI†). Protonation of the *o*-hydroxyl Schiff base at low pH leads to sharp decreases of its fluorescence quantum yield and metal-binding affinity, while binding of hydroxide ions on the boronic acid group occurs at basic pH. In accordance with the binding and signaling mechanisms described above, the fluorescence response of **2** is dramatically weakened in acidic or basic solution. Therefore, high sensitivity in fluorometric determination of HOTs is conditioned at near neutral pH.

The performance of HOT sensing was further evaluated in the coexistence of other metal species (Fig. 4). The presence of alkali or alkali-earth metal ions at high concentration (50 equiv. tin) caused no obvious interference. Absorption spectral studies indicated the binding affinity of the chromogenic *o*-hydroxyl Schiff base moiety towards transition metals such as Cr^{3+}, Fe^{3+}, Cu^{2+} and other organotins (Fig. S8 in ESI†), although this was not reported by fluorescence spectral changes in **2**. This explains the puny drifts of the HOT-sensing signal of **2** in the presence of these interfering species. It was observed that fluorescence responses resulting from the addition of these interfering species followed by the addition of $BuSn(OH)_2Cl$ to **2** were similar to those obtained in a reverse way. These results indicate that the binding affinity of HOT is higher than that of the investigated interfering species, ensuring the high selectivity of the designed HOT receptor. Standard addition methods confirmed that HOTs in synthetic samples could be determined with satisfactory recoveries (96–105%) at μM concentration level.

In summary, we have developed a highly selective fluorescent receptor for HOTs in aqueous solution. The new receptor nicely combines the binding character of an *o*-hydroxyl Schiff base for the transition metal and boronic acid for the vicinal diol. To the best of our knowledge, this is the first example of a fluorescent receptor for hydroxylated metal species. We also demonstrated that boronic acid acted as an efficient receptor group for metal-centered diols. This may lead to important applications of boronic acid in molecular recognition in further studies.

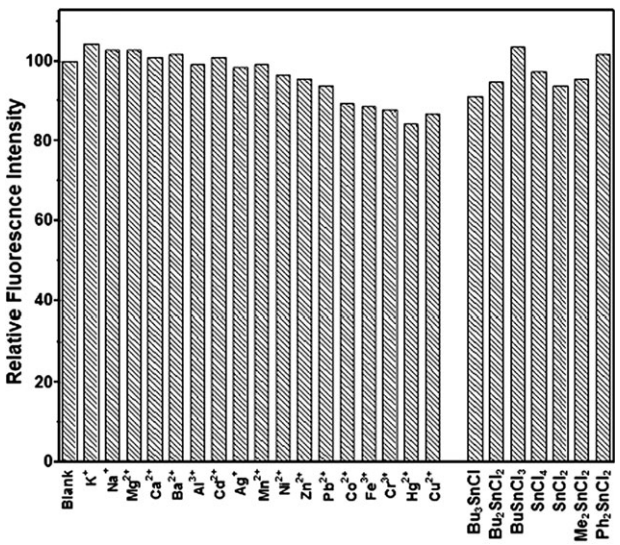

Fig. 4 The influence of coexistence of other metal species on the fluorescence response of **2** to 20 equiv. of $BuSn(OH)_2Cl$ in H_2O–EtOH (90 : 10, v/v). **2**: 1.0×10^{-6} M; pH: 7.4, buffered by 0.01 M Tris-HCl; $\lambda_{ex}/\lambda_{em}$: 403/474 nm. K^+, Na^+, Mg^{2+}, Ca^{2+}, Ba^{2+}, Al^{3+}: 1000 equiv.; Cd^{2+}, Ag^+, Mn^{2+}, Ni^{2+}, Zn^{2+}, Pb^{2+}, Co^{2+}, Fe^{3+}, Cr^{3+}: 100 equiv.; Hg^{2+}, Cu^{2+}, Bu_3SnCl, Bu_2SnCl_2 $BuSnCl_3$, $SnCl_4$, $SnCl_2$, Me_2SnCl_2, Ph_2SnCl_2: 20 equiv.

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