A novel fluorescent sensor for Fe^{3+} and Cr^{3+} based on a calix[4]arene bearing two coumarin units

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A novel turn-on fluorescent sensor based on a calix[4]arene with two coumarin units as fluorophores and imino-groups as ionophores on the upper rim has been synthesised. Its recognition properties towards heavy and transition metal ions have been studied by UV-Vis and fluorescence spectrometry. The compound showed an enhanced fluorescent intensity in the presence of Fe^{3+} or Cr^{3+} ion, a high selectivity to Fe^{3+} or Cr^{3+} ions and a complexation ratio towards Fe^{3+} or Cr^{3+} of 1:1. The association constant for Fe^{3+} was 5.37×10^5 M^{-1} and for Cr^{3+} was 9.18×10^5 M^{-1}.

Keywords: calixarene, coumarin, fluorescent sensor, recognition of metal ions

The design and synthesis of selective fluorescent sensors for cation detection, especially for heavy metal and transition metal cations, is of great interest.[1] Compared with divalent transition metal cations, few studies have been devoted to developing organic probes that are sensitive to triple-charged metal cations, such as Fe^{3+} ion[2–4] and Cr^{3+} ion.[5–7] The trivalent forms of iron and chromium play important roles in environmental and biological systems and therefore it is worthwhile to develop fluorescent sensors for the detection of Fe^{3+} and Cr^{3+}.

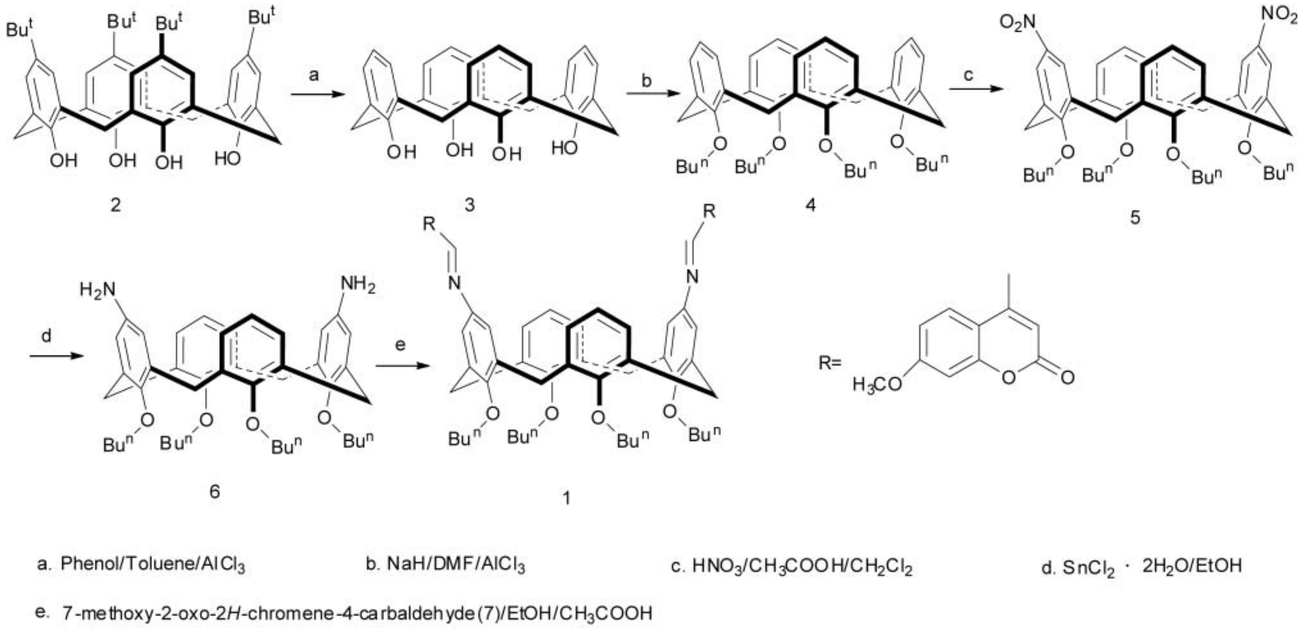
Calixarene, a basic molecular scaffold for construction of selective ionophores, has been incorporated into fluorescent ion sensors. Calixarene-based fluorescent sensors show great sensitivity and selectivity for alkali metal ions,[8] alkaline earth metal ions[9] and several transition metal ions.[10] However, only a few fluorescent calixarene derivatives for Fe^{3+} and Cr^{3+} have been reported.[11,12] Due to the paramagnetic nature of iron and chromium ions, their presence is mostly signaled by fluorescence quenching. In terms of sensitivity, fluoroionophores showing fluorescence enhancement as a result of metal-ion binding are superior to those exhibiting fluorescence quenching. As a continuation of our work[13,14] on the design and synthesis of fluorogenic chemosensors, we report a novel turn-on fluorescent sensor for selective recognition of $Fe^{3+}$and Cr^{3+} ion, based on a calix[4]arene having, on its upper rim, imine groups as ionophores and coumarin units as fluorophores (**1**, see Scheme 1).

Results and discussion

Synthesis of the compound **1** is depicted in Scheme 1. Compounds **2**[15], **3**[16], **4**[17], **5**[18], **6**[19] and **7**[20] were prepared according to the literature. The reaction of 5,17-diaminocalix[4]arene (**6**) with 5 equiv. of 7-methoxy-2-oxo-2H-chromene-4-carbaldehyde (**7**) in ethanol afforded calix[4]arene **1** in 67% yield. Compound **1** was fully characterised by ^1H NMR, ^{13}C NMR, IR, MS and elemental analysis.

Compound **1** adopts a cone conformation which is confirmed by the presence of an AB (J = 13.5 Hz) system characteristic of methylene bridges ($Ar–CH_2–Ar$) at 3.23 ppm and 4.50 ppm in its ^1H NMR spectrum and by the position of the carbon atoms of the methylene bridges at 31.4 ppm in its ^{13}C NMR spectrum. Only one signal of the imino-protons (CH=N at 7.70 ppm) shows that the C=N bonds adopt the E-configuration, in accord with the literature.[21]

The complexation behaviour of calix[4]arene **1** towards different heavy and transition metal cations (Ni^{2+}, Cr^{3+}, Pb^{2+}, Cd^{2+}, Cu^{2+}, Zn^{2+}, Ag^+, Hg^{2+}, Co^{2+}, Fe^{2+}, Fe^{3+}, Mn^{2+}, Ca^{2+} and



Scheme 1 Synthesis of compound **1**.

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La^{3+}) was investigated by UV-Vis absorption spectroscopy. As shown in Fig. 1, the absorption spectrum of **1** in dichloromethane-methanol solution(1:1, v/v) exhibits one absorption band at 360nm. Upon addition of Fe^{3+} or Cr^{3+} to the solution, the band at 360nm decreased and a new blue-shifted band at 329 nm for Fe^{3+} or 327 nm for Cr^{3+} appeared while the other metal ions gave no changes, which indicates that compound **1** can selectively recognise Fe^{3+} and Cr^{3+}.

Figure 2 shows the fluorescence spectra (λ_{ex}=360nm) of **1** (10^{-5} M) measured in dichloromethane–methanol solution (1:1, v/v) with Fe^{3+} and Cr^{3+}(10^{-5} M). Because of the photo-induced electron transfer (PET) from the lone-pair electron of the imine nitrogen atom to the coumarin units, the very weak fluorescent emissions of compound **1** were observed at 435 nm. When Fe^{3+} or Cr^{3+} were added, the nitrogen atom of an imino-group donates its lone pair of electrons to an empty orbital of Fe^{3+} or Cr^{3+} and inhibits the PET process, thus the fluorescent emission intensity was enhanced remarkably (about 28-fold for Fe^{3+}; 31-fold for Cr^{3+}). As shown in Fig. 3, under the same conditions, no obvious fluorescence changes were observed for other tested metal ions except for Cu^{2+} or Hg^{2+}, which induce a very weak emission enhancement (about 1.88-fold for Cu^{2+}; 1.85-fold for Hg^{2+}). The results suggest that the novel coumarin-calix[4]arene derivative can serve as a turn-on fluorescent sensor for Fe^{3+} and Cr^{3+}.

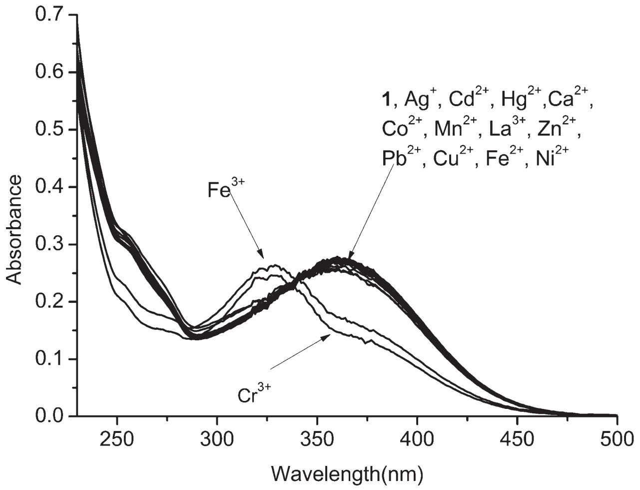

Fig. 1 UV-Vis spectra of compound 1 (10μM) upon addition of various ions (10μM) in CH_2Cl_2 and CH_3OH (v/v=1/1).

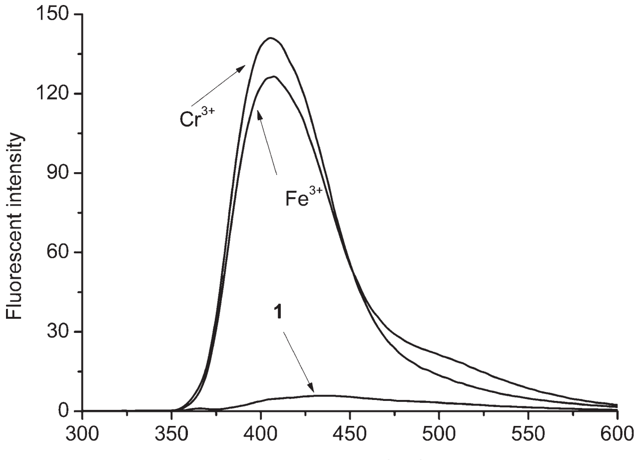

Fig. 2 Fluorescence emission spectra of compound **1** (10μM) upon addition of Fe^{3+} and Cr^{3+} (10μM) in CH_2Cl_2 and CH_3OH (v/v=1/1) (λex= 360 nm).

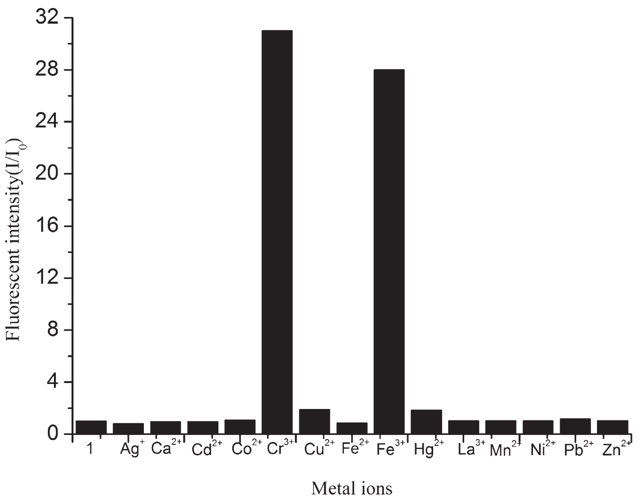

Fig. 3 Change in the fluorescence intensity at 435 nm of compound **1** (10μM) upon addition of different metal ions (10μM) in CH_2Cl_2 and CH_3OH (v/v=1/1) (λex= 360 nm).

The complexation stoichiometric ratio between compound **1** and Fe^{3+} or Cr^{3+} ions was measured by a Job's plot experiment. As shown in Fig. 4, the Job's plot for compound **1** and Cr^{3+} shows the maximum point at the mole fraction of 0.5, indicating a typical 1:1 complexation. Similarly, the complexation ratio of compound **1** and Fe^{3+} is also 1:1.

The association constants between compound **1** and Fe^{3+} or Cr^{3+} ions were determined by fluorescent titration. Upon titration of **1** with Cr^{3+} exciting at 360 nm, (given in Fig. 5 as an example), the fluorescence intensity is enhanced remarkably. From linear fitting of the titration curve of the **1**-Cr^{3+} complex, the association constant was determined to be 9.18×10^5. Similarly, from the titration of **1** with Fe^{3+}, the association constant was calculated to be 5.37×10^5. The results indicate a high affinity of **1** with Fe^{3+} and Cr^{3+} ions.

In conclusion, we have synthesised a novel turn-on fluorescent chemosensor **1** based on calix[4]arene, which shows sensitive and selective recognition to Fe^{3+} and Cr^{3+}.

Experimental

All reagents are commercially available and purified by standard methods prior to use. The solvents for absorption and fluorescence measure were of spectrometric grade. Melting points were measured on an X4 apparatus (uncorrected). The FT-IR spectra (KBr pellets) were measured on a BIO-RAD FTS3000 IR spectrometer. The ^1H

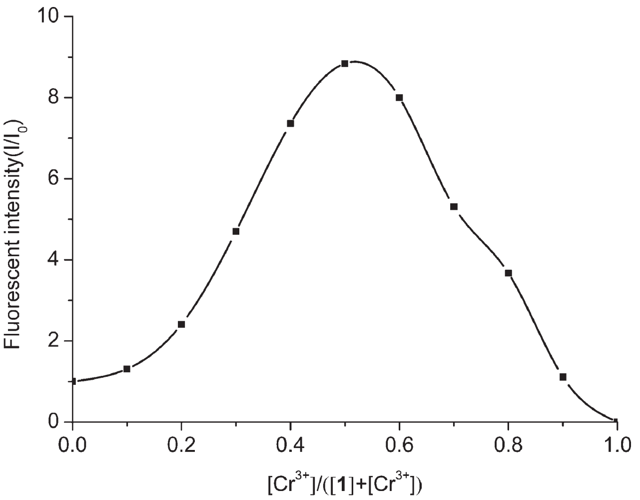

Fig. 4 Job's plot for compound **1** and Cr^{3+} (λex= 360 nm).

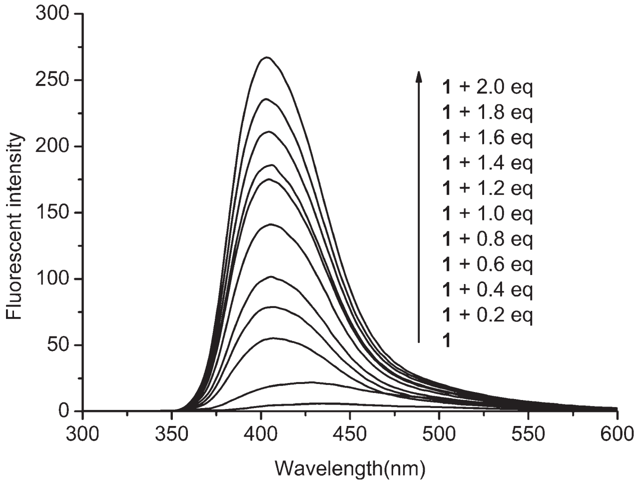

Fig. 5 Fluoresence emission spectra of **1** (10μM) for Cr^{3+} ion titration in CH_2Cl_2 and CH_3OH (v/v=1/1) (λex= 360 nm).

NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal standard on a Varian INOVA-500MHz at 298K. Chemical shifts (δ) are given in parts per million downfield from TMS and coupling constant (*J*) values are in hertz. Mass spectra were carried out on a LCQ Advantage MAX Spectrometer. Absorption spectra were recorded with a PerkinElmer Lambda 900 UV/Vis/NIR spectrophotometer. Fluorescence spectra were obtained with a PerkinElmer LS55 spectrofluorometer. Elemental analysis was performed on a Model 2400 II Perkin–Elmer elemental analyser.

Synthesis of compound **1**

5,17-Diaminocalix[4]arene (**6**) (0.5 mmol) and 7-methoxy-2-oxo-2H-chromene-4-carbaldehyde (**7**) (2.5mmol) were added to absolute anhydrous ethanol (30 mL) under N_2. The reaction mixture was refluxed until complete disappearance of **6** (monitored by TLC). The resulting solution was cooled to room temperature and the solvent evaporated under vacuum, giving the crude product, which was further purified by recrystallisation from dichloromethane and methanol.

5,17-Di-(7-methoxy-2-oxo-2H-chromene-4-methylimino)-25,26,27,28-tetrabutyloxycalix[4]arene **1**: Yellow solid; yield 67%; m.p. 244–245 °C (dec.); IR (KBr, cm^{-1}): 1728, 1616; ^1H NMR ($CDCl_3$): 8.44 (d, 2H, *J* = 9 Hz, cumarin-**H**), 7.70 (s, 2H, C**H**=N), 7.01 (d, 4H, *J* = 7.5 Hz, calixarene-Ar**H**), 6.87 (t, 2H, *J* = 7.5 Hz, calixarene-Ar**H**), 6.76–6.73 (m, 2H, cumarin-**H**), 6.65 (d, 2H, *J* = 2.5 Hz, cumarin-**H**), 6.35 (s, 4H, calixarene-Ar**H**), 6.13 (s, 2H, cumarin-**H**), 4.50(d, 4H, *J* = 13.5 Hz, Ar$\mathbf{CH_2}$Ar), 4.05 (t, 4H, *J* = 8 Hz, O$\mathbf{CH_2}CH_2CH_2CH_3$), 3.89 (s, 6H, cumarin-O$\mathbf{CH_3}$), 3.83 (t, 4H, *J* = 7 Hz, O$\mathbf{CH_2}CH_2CH_2CH_3$), 3.23 (d, 4H, *J* = 13.5 Hz, Ar$\mathbf{CH_2}$Ar), 2.00–1.93 (m, 4H, $\mathbf{CH_2}CH_2CH_3$), 1.93-1.87 (m, 4H, $\mathbf{CH_2}CH_2CH_3$), 1.61–1.53 (m, 4H, $\mathbf{CH_2}CH_3$), 1.43–1.36 (m, 4H, $\mathbf{CH_2}CH_3$), 1.04–1.01 (m, 12H, $\mathbf{CH_3}$); ^{13}C NMR ($CDCl_3$): 162.86, 161.06, 157.43, 156.50, 156.03, 155.38, 145.03, 136.20, 135.56, 129.08, 127.94, 122.48, 120.78, 116.43, 112.21, 110.22, 101.24, 75.52, 75.20, 55.95, 32.67, 32.34, 31.35, 19.75, 19.43, 14.38, 14.24; MS (*m/z*): 1051.4 ($M+H^+$) (Calcd for $C_{66}H_{70}N_2O_{10}$ 1050). Anal. Calcd for $C_{66}H_{70}N_2O_{10}$: C, 75.42; H, 6.73; N, 2.68. Found: C, 75.40; H, 6.71; N 2.66%.

Job plot experiment

Stock solutions of **1** (10μM) in CH_2Cl_2 and CH_3OH (v/v=1/1), $Fe(NO_3)_3{\cdot}9H_2O$ (10μM) and $Cr(NO_3)_3{\cdot}9H_2O$ (10μM) in CH_2Cl_2 and CH_3OH (v/v=1/1) were prepared. The concentrations of each CH_2Cl_2 and CH_3OH solution were varied, but the total volume was fixed to be 5.0 mL.

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