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ARTICLE TYPE

# Binding sites-driving sensing properties of a quinazoline derivative with metal cations

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A compound, 6-furyl-5,6-dihydrobenzoimidazo[1,2-c]quinazoline (L) was synthesized and characterized. L showed weak fluorescence emission at 416 nm in CH<sub>3</sub>OH when excited by 383 nm. Upon addition of Al<sup>3+</sup>, Cr<sup>3+</sup> or Fe<sup>3+</sup> ions, enhanced fluorescence emission and spectral shift (55 nm) could be observed. Job's plot, fluorescence titration, <sup>1</sup>H NMR and ESI-MS data for binding of L with Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> ions showed 1:1 metal to L complexation with the transformation of the quinazoline compound (L) to the Schiff base ligand [2-(1H-benzimidazol-2-yl)-phenyl]-furan-2-ylmethyleneamine (L<sup>1</sup>). Cr<sup>3+</sup> can be differentiated from Al<sup>3+</sup> and Fe<sup>3+</sup> by time-dependent fluorescence spectra, while Al<sup>3+</sup> can be distinguished from Fe<sup>3+</sup> by the emission at 430 nm when excited by 300 nm in the aqueous media CH<sub>3</sub>OH-H<sub>2</sub>O (1/9, v/v). The detection limits were in the order of 10<sup>-6</sup> M for Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> ions. L is insensitive to Cd(II) ion. The crystal structures of Cd(II) complexes, [CdL<sub>2</sub>(OAc)<sub>2</sub>](**1**) and [CdL<sub>2</sub>Cl<sub>2</sub>](**2**) indicate the binding site of L with Cd(II) is one imidazole nitrogen atom. UV-vis spectra and fluorescence spectra of L, **1** and **2** in CH<sub>3</sub>OH showed no significant difference. Also <sup>1</sup>H NMR signals of **1** were almost the same as that of L. These observations indicated that the coordination of L with Cd(II) has little effect on spectroscopic properties of L. The response mechanism of L to Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> ions was discussed.

## 20 Introduction

Aluminum is the most abundant metal in earth's crust (approximately 8%) and is extensively used in modern life.<sup>[1]</sup> The general population is exposed to aluminum from its wide spread use in water treatment, food additives, aluminum-based pharmaceuticals and cooking utensils. The WHO recommended tolerable weekly aluminum dietary intake in the human body to be 7mg/kg body weight.<sup>[2]</sup> But it is neurotoxic to humans and induces many health problems, such as Alzheimer's disease and Parkinson's disease.<sup>[3]</sup> Chromium(III) is an essential trace component in human nutrition and has great impacts on the metabolism of carbohydrates, fats, proteins and nucleic acids. The deficiency of chromium would cause disturbances in the glucose levels and lipid metabolism, and lead to a variety of diseases including diabetes and cardiovascular disease.<sup>[4]</sup> In addition, high levels of chromium(III) can bind to DNA, negatively affecting cellular structures and damaging the cellular components.<sup>[5]</sup> Among the biologically important metals, iron(III) is an essential element in human body and plays an important role in the transport and storage of oxygen.<sup>[6]</sup> A deficiency or excess of iron can cause various pathological disorders in humans.<sup>[7]</sup> Thus, detection of Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> is important to control the concentration level in the biosphere and minimize direct effect on human health. In recent decades, fluorescent chemosensors have attracted significant interest because of their potential applications in medical and environmental sciences. The

development of chemosensors for the facile detection of Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> is of great importance in environmental monitoring and biological assays. However, compared to divalent metal ions, such as Zn<sup>2+</sup>, Cd<sup>2+</sup>, Hg<sup>2+</sup>, Pb<sup>2+</sup> and Cu<sup>2+</sup>, limited chemosensors for Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> based on a single molecule have been reported.<sup>[8]</sup>

It has been shown that the quinazoline derivatives as fluorescent chemosensors are available for detection of M<sup>3+</sup> ions.<sup>[9]</sup> We have confirmed with a combination of experiments and theoretical calculations that in sensing process, the appropriate metal ion can assist the C-N bond breakage of the quinazoline ring, forming a metal Schiff-base complex with metal-containing six-membered ring.<sup>[10]</sup> At the same time a large spectral shift as well as great fluorescence-enhancement were observed.<sup>[11]</sup> The chelation-enhanced fluorescence(CHEF) effect makes the quinazoline-based compounds to be excellent probes for metal ions. As is known, Schiff-base compounds are good platform for detection of Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> ions.<sup>[12]</sup> Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> possess smaller radius and larger positive charge, they as strong Lewis acids have high affinity for oxygen atom and tend to form M-O bond, resulting in the metal(III) complexes when combined with oxygen-containing ligands like metal-furyl complexes.<sup>[13]</sup> Herein, we report a quinazoline-based compound as chemosensor for Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> ions obtained by coupling 2-(2-aminophenyl)-1H-benzimidazole with furfural. And the response mechanism was discussed.

## Experimental section

## Materials and method

All solvents and reagents were used as received (analytical grade and spectroscopic grade). The solutions of metal ions were prepared from LiCl, NaCl, CaCl<sub>2</sub>, KNO<sub>3</sub>, MgCl<sub>2</sub>·6H<sub>2</sub>O, CrCl<sub>3</sub>·6H<sub>2</sub>O, Mn(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O, Co(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, Ni(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, Cd(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, Zn(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, Al(ClO<sub>4</sub>)<sub>3</sub>·9H<sub>2</sub>O and Pb(ClO<sub>4</sub>)<sub>2</sub>·3H<sub>2</sub>O, respectively. Fluorescence spectra were recorded on a Cary Eclipse fluorescence spectrophotometer and UV-Vis absorption spectra were recorded by a spectrophotometer UV-2450, with a quartz cuvette (path length = 1 cm). <sup>1</sup>H NMR was obtained using a Bruker Avance III 400MHz spectrometer. Mass spectra (ESI-MS) were obtained on Quattro microtriple quadrupole mass spectrometer. PH was measured on PHS-3C PH meter.

## X-ray crystallography

Single-crystal data were collected on a Bruker APEX II CCD diffractometer with graphite monochromated Mo-K $\alpha$  radiation ( $\lambda$ ) at 293 K. The structure was solved by the direct method and refined by full matrix least squares based on  $F^2$  using the SHELX 97 program.<sup>[14]</sup> All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed in calculated positions. Crystallographic data for Cd(II) complexes (**1** and **2**) are summarized in Table 1. Selected bond distances and angles of two structures are summarized in Table S1. CCDC nos. 1041496-1041497 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [http://www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

**Table 1.** Crystal data and structure refinement parameters of **1** and **2**

Compounds	<b>1</b>	<b>2</b>
Empirical formula	C <sub>40</sub> H <sub>32</sub> Cd N <sub>6</sub> O <sub>6</sub>	C <sub>36</sub> H <sub>26</sub> CdCl <sub>2</sub> N <sub>6</sub> O <sub>2</sub>
Formula weight	805.11	757.94
Crystal system	Monoclinic	Monoclinic
space group	C2/c	C2/c
a(Å)	18.697(3)	18.732(7)
b(Å)	10.5490(18)	9.935(4)
c(Å)	18.017(3)	17.851(7)
$\alpha$ (°)	90	90
$\beta$ (°)	110.149(3)	103.003(7)
$\gamma$ (°)	90	90
V(Å <sup>3</sup> )	3336.2(10)	3237(2)
Z	4	4
D <sub>c</sub> (gcm <sup>-3</sup> )	1.603	1.555
$\mu$ (mm <sup>-1</sup> )	0.716	0.883
F(000)	1640	1528
$\theta$ range (°)	2.25 to 27.52	2.33 to 27.60
R <sub>int</sub>	0.0318	0.0617
R <sub>1</sub> , $\omega$ R <sub>2</sub> [I>2 $\sigma$ (I)]	0.0448, 0.1234	0.0465, 0.1098
R <sub>1</sub> , $\omega$ R <sub>2</sub> (all data)	0.0512, 0.1272	0.0805, 0.1399

$$R_1 = \sum(|F_o| - |F_c|) / \sum |F_o|; wR_2 = \{ \sum [ (w|F_o|^2 - |F_c|^2)^2 / \sum w(F_o^2) ] \}^{1/2}$$

## Preparation of L

A mixture of furfural (44  $\mu$ L, 0.4 mmol) and 2-(2-aminophenyl)benzimidazole (0.0837 g, 0.4 mmol) in 2 mL isopropanol was sealed in 25 mL Teflon-lined autoclave and heated at 80°C for 1 day and then the resulting solution was kept at room temperature for 4-5 days. The reddish brown block-shaped crystals were obtained and filtered, washed with isopropanol several times and dried at room temperature. Brown block-shaped crystals of L were collected in a yield of 43.7%.

C<sub>18</sub>H<sub>13</sub>N<sub>3</sub>O, Anal. Found (%): C, 75.40; H, 4.46; N, 14.72; calc.(%): C, 75.25; H, 4.56; N, 14.63; IR (KBr pellet, cm<sup>-1</sup>): 3261 (s), 1616(s), 1585(s), 1512(s), 1474(s), 1450(s), 1396(s), 1332(s), 1263(s), 1148(s), 758(s), 735(s).

## Preparation of [CdL<sub>2</sub>(OAc)<sub>2</sub>] (**1**)

A mixture of cadmium acetate dihydrate (0.0533 g, 0.2 mmol), furfural (44  $\mu$ L, 0.4 mmol) and 2-(2-aminophenyl)benzimidazole (0.0837 g, 0.4 mmol) in 5 mL methanol and isopropanol (V(methanol):V(isopropanol)=4:1) solution, was sealed in 25 mL Teflon-lined autoclave and heated at 80°C for 1 day and then the resulting solution was evaporated at room temperature for 4-5 days. The brown block-shaped crystals were obtained and filtered, washed with methanol several times and dried at room temperature in a yield of 26.1%. C<sub>40</sub>H<sub>32</sub>CdN<sub>6</sub>O<sub>6</sub>, Anal. Found (%): C, 59.52; H, 4.18; N, 10.43; calc.(%): C, 59.67; H, 4.00; N, 10.44; IR (KBr pellet, cm<sup>-1</sup>): 3264 (s), 1622 (s), 1551 (s), 1514 (s), 1458 (s), 1412 (s), 1383 (w), 1267 (s), 1152 (s), 1013 (s), 735 (s), 669 (s).

## Preparation of **1'**

A mixture of cadmium acetate dihydrate (0.0533 g, 0.2 mmol) and L (0.1148 g, 0.4 mmol) in 5 mL methanol and isopropanol (V(methanol):V(isopropanol)=4:1) solution, was sealed in 25 mL Teflon-lined autoclave and heated at 80°C for 1 day and then the resulting solution was evaporated at room temperature for 4-5 days. The brown block-shaped crystals were obtained and filtered, washed with methanol several times and dried at room temperature in a yield of 28.7%. C<sub>40</sub>H<sub>32</sub>CdN<sub>6</sub>O<sub>6</sub>, Anal. Found (%): C, 59.31; H, 4.08; N, 10.43; calc.(%): C, 59.67; H, 4.00; N, 10.44; IR (KBr pellet, cm<sup>-1</sup>): 3264 (s), 1622 (s), 1553 (s), 1516 (s), 1456 (s), 1414 (s), 1383 (s), 1267 (s), 1152 (s), 1013 (s), 735 (s), 669 (s).

## Preparation of [CdL<sub>2</sub>Cl<sub>2</sub>] (**2**)

A mixture of cadmium chloride hemipentahydrate (0.0456 g, 0.2 mmol), furfural (44  $\mu$ L, 0.4 mmol) and 2-(2-aminophenyl)benzimidazole (0.0837 g, 0.4 mmol) in 5 mL methanol and isopropanol (V(methanol):V(isopropanol)=4:1) solution, was sealed in 25 mL Teflon-lined autoclave and heated at 80°C for 1 day and then the resulting solution was evaporated at room temperature for 4-5 days. The brown block-shaped crystals were obtained and filtered, washed with methanol several times and dried at room temperature in a yield of 38.8%. C<sub>36</sub>H<sub>26</sub>CdCl<sub>2</sub>N<sub>6</sub>O<sub>2</sub>, Anal. Found (%): C, 57.07; H, 3.48; N, 11.08; calc.(%): C, 57.05; H, 3.46; N, 11.09; IR (KBr pellet, cm<sup>-1</sup>): 3325 (s), 1618 (s), 1585 (s), 1530 (s), 1504 (s), 1479 (s), 1456 (s), 1412 (s), 1315 (s), 1263 (s), 1229 (s), 1146 (s), 1013 (s), 762 (s), 748 (s), 733 (s).

## Results and Discussion

### Crystal structure of L

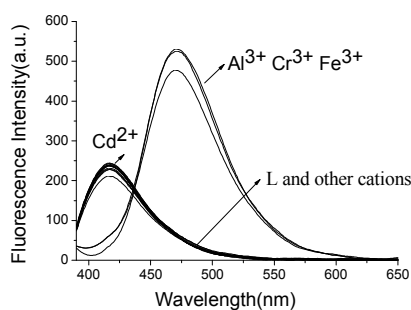
The quinazoline derivative, L was prepared by condensation of furfural and 2-(2-aminophenyl)-1H-benzimidazole under solvothermal condition. The crystal structure (Fig. S1) is the same as reported.<sup>[15]</sup> The selected bond distances and angles were tabulated in Table S1.

### Photophysical property of L

Since L is insoluble in H<sub>2</sub>O while soluble in CH<sub>3</sub>OH, its fluorescence property in CH<sub>3</sub>OH was observed. An emission band at 416 nm for L in CH<sub>3</sub>OH could be seen (Fig. S2). It is attributed to  $\pi$  -  $\pi^*$  transition of L. Fig. S2 also showed emission changes of L upon addition of HCl in CH<sub>3</sub>OH. A double band at 416 nm and 462 nm appeared when  $c_{\text{HCl}} : c_{\text{L}} = 2 : 1$ . Further addition of HCl to CH<sub>3</sub>OH solution of L made the emission band at 416 nm for L completely disappear. This could be ascribed to formation of a new compound. But the emission band of L remained unchanged when NaOH was added to L in CH<sub>3</sub>OH.

### Fluorescence responses of L to metal ions in CH<sub>3</sub>OH

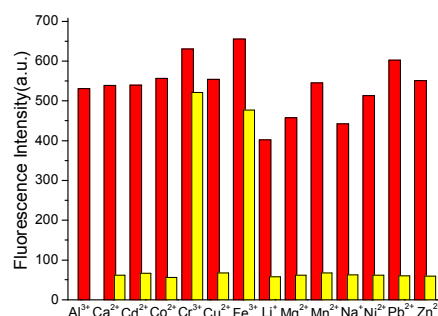
The fluorescence responses of L to metal cations were examined in CH<sub>3</sub>OH. The addition of 1.0 equiv. of Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup>, Ca<sup>2+</sup>, Mn<sup>2+</sup>, Fe<sup>3+</sup>, Co<sup>2+</sup>, Cr<sup>3+</sup>, Cd<sup>2+</sup>, Cu<sup>2+</sup>, Pb<sup>2+</sup>, Ni<sup>2+</sup>, Zn<sup>2+</sup> and Al<sup>3+</sup> ions to L in CH<sub>3</sub>OH was used to measure the selectivity of L for metal ions. As shown in Fig. 1, when excited by 383 nm, L showed weak fluorescence emission at 416 nm in CH<sub>3</sub>OH. While upon the addition of Al<sup>3+</sup>, Cr<sup>3+</sup> or Fe<sup>3+</sup> ions, an intensive fluorescence emission at 471 nm with a larger peak shift (55 nm) can be observed from the fluorescence spectra. For other metal ions except Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup>, no obvious fluorescence change could be observed upon their addition to the methanol solution of L. The shifting of emission peak for the response system makes L more sensitive to the metal ions.



**Figure 1.** Fluorescence spectra of L (30  $\mu\text{M}$ ) with 1.0 equiv. of Al<sup>3+</sup>, Ca<sup>2+</sup>, Cd<sup>2+</sup>, Co<sup>2+</sup>, Cr<sup>3+</sup>, Cu<sup>2+</sup>, Fe<sup>3+</sup>, Li<sup>+</sup>, Mg<sup>2+</sup>, Mn<sup>2+</sup>, Na<sup>+</sup>, Ni<sup>2+</sup>, Pb<sup>2+</sup> and Zn<sup>2+</sup> in CH<sub>3</sub>OH.

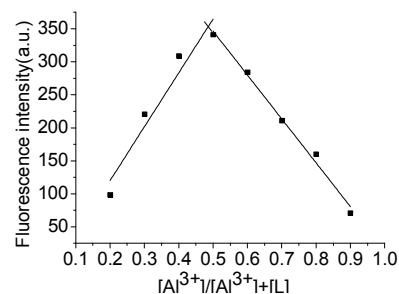
To further test the selectivity of L as a fluorescent chemosensor for Al<sup>3+</sup>, Cr<sup>3+</sup> or Fe<sup>3+</sup> ions, the competitive experiments to measure the fluorescence intensity of L at 471 nm with Al<sup>3+</sup> (Fig. 2), Cr<sup>3+</sup> (Fig. S4a) or Fe<sup>3+</sup> (Fig. S4b) ions in the presence of various metal ions in CH<sub>3</sub>OH were carried out. As a result, there is no or little interference for the fluorescence detection of Al<sup>3+</sup>, Cr<sup>3+</sup> or Fe<sup>3+</sup> ions in presence of other metal ions, so the binding of the sensor with Al<sup>3+</sup>, Cr<sup>3+</sup> or Fe<sup>3+</sup> ions is not affected by concomitant ions. Therefore, L was shown to be a promising selective fluorescent sensor for Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> ions in the presence of the competing metal ions stated.

The Job's plot for Al<sup>3+</sup> system was obtained as shown in Fig. 3 (Fig. S5 for Cr<sup>3+</sup> and Fe<sup>3+</sup>). 1:1 stoichiometric complexation of L with Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> in CH<sub>3</sub>OH was confirmed, respectively. In the fluorescence titration profiles (Fig. 4, Fig. S6), an increase of fluorescence intensity at 471 nm could be observed with increasing Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> concentration until 1.0 equiv. while the emission intensity tends to be the same with further increasing

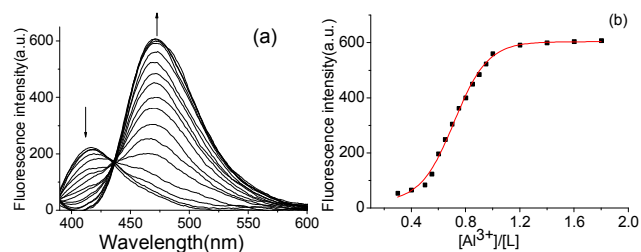


**Figure 2.** Fluorescence intensity of L with Al<sup>3+</sup> in the presence of various metal ions in CH<sub>3</sub>OH.  $\lambda_{\text{ex}} = 383$  nm and  $\lambda_{\text{em}} = 471$  nm. Red bars: L (30  $\mu\text{M}$ ) with 1.0 equiv. of Al<sup>3+</sup> and 1.0 equiv. of other metal ions stated. Yellow bars: L (30  $\mu\text{M}$ ) with 1.0 equiv. of other metal ions stated.

Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> concentration, respectively. The saturation behaviors of the fluorescence intensity after 1.0 equiv. of Al<sup>3+</sup>, Cr<sup>3+</sup> or Fe<sup>3+</sup> also reveal the 1:1 stoichiometry.



**Figure 3.** Job's plot for the determination of the stoichiometry of L and Al<sup>3+</sup> in the complexation.

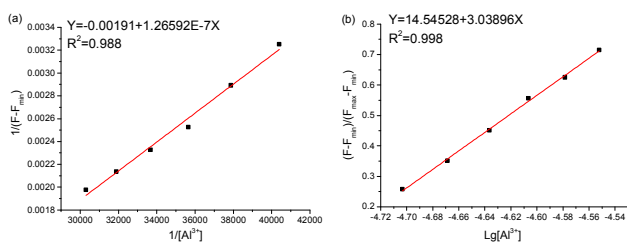


**Figure 4.** (a) Fluorescence emission spectra ( $\lambda_{\text{ex}}=383$ nm) of L (33  $\mu\text{M}$ ) in the presence of increasing amounts of Al<sup>3+</sup> (0.30, 0.40, 0.50, 0.55... 0.80, 0.85, 0.90, 0.95, 1.00, 1.20, 1.40, 1.60, 1.80 equiv.) in CH<sub>3</sub>OH. (b) Spectrofluorimetric titration curve at  $\lambda_{\text{em}}=471$ nm.

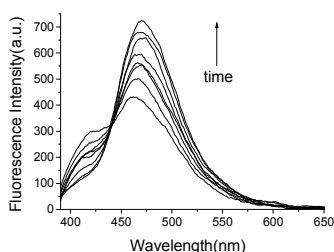
Based on the fluorescence titration data, the association constant K of L for Al<sup>3+</sup>, Cr<sup>3+</sup> or Fe<sup>3+</sup> was calculated by the Benesi-Hildebrand expression. The association constants were determined to be  $1.02 \times 10^4$ ,  $1.44 \times 10^4$  and  $3.04 \times 10^4$  for the complex of L with Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> in CH<sub>3</sub>OH, respectively as shown in Fig. 5(a), Fig. S7(a) and S7(c). The detection limits of L as a fluorescent chemosensor for the analysis of Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> were calculated and these were found to be 12, 15 and 11  $\mu\text{M}$ , respectively (Fig. 5(b), Fig. S7(b) and Fig. S7(d)).

Considering Al<sup>3+</sup>, Cr<sup>3+</sup> and Fe<sup>3+</sup> have the same fluorescence response to L in methanol when excited with 383 nm, some strategies were adopted to distinguish them by L. As shown in Fig. 6, the response of L to Cr<sup>3+</sup> is time-dependent in 20 minutes upon the addition of Cr<sup>3+</sup>. While the response of L to Al<sup>3+</sup> and



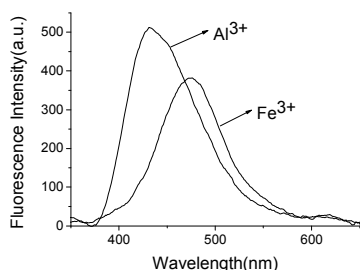


**Figure 5.** (a) Benesi-Hildebrand plot of L with  $\text{Al}^{3+}$  in  $\text{CH}_3\text{OH}$  ( $\lambda_{\text{em}}=471$  nm). (b) Normalized response of emission signal at 471 nm with changing  $\text{Al}^{3+}$  concentrations.



**Figure 6.** Fluorescence spectra variation of L (67  $\mu\text{M}$ ) upon addition of 1.0 equiv. of  $\text{Cr}^{3+}$  in  $\text{CH}_3\text{OH}$  after 1, 2, 3, 4, 5, 10, 15, and 20 min,  $\lambda_{\text{ex}}=383$  nm.

$\text{Fe}^{3+}$  was quick (Fig. S8). This may be attributed to slow hydrolysis rate for Cr(III) ion, forming Cr(III) species containing  $\text{L}^1$  and  $\text{OH}^-$ . Therefore,  $\text{Cr}^{3+}$  could be differentiated from  $\text{Al}^{3+}$  and  $\text{Fe}^{3+}$  by time-dependent emission spectra. As to  $\text{Al}^{3+}$  and  $\text{Fe}^{3+}$ , it is found that their emission spectra are different when excited by 300 nm in the aqueous media  $\text{CH}_3\text{OH}-\text{H}_2\text{O}$  (1/9, v/v). As is shown in Fig. 7, the  $\text{Al}^{3+}$  system emits at 430 nm, while  $\text{Fe}^{3+}$  system emits at 471 nm. So they can be distinguished from each other. The blue-shifted fluorescence for  $\text{Al}^{3+}$  could be ascribed to formation of  $[\text{AlL}^1(\text{OH})_3]^+$ , which is confirmed by ESI-MS (Fig. S9). In a word, the results showed that our work is comparable with the reported (Table S2).

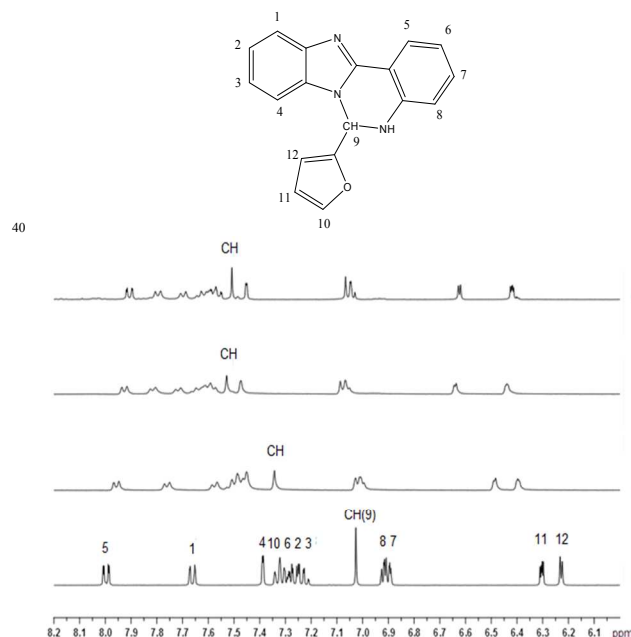


**Figure 7.** Fluorescence spectra of L (100  $\mu\text{M}$ ) upon addition of 1.0 equiv. of  $\text{Al}^{3+}$  and  $\text{Fe}^{3+}$  in the aqueous media  $\text{CH}_3\text{OH}-\text{H}_2\text{O}$  (1/9, v/v),  $\lambda_{\text{ex}}=300$  nm.

#### Binding modes of L with $\text{Al}^{3+}$ , $\text{Cr}^{3+}$ or $\text{Fe}^{3+}$ and possible fluorescent species formed in $\text{CH}_3\text{OH}$

As shown in Fig. 8 (a), proton signals of L were assigned similarly as the reported.<sup>[15]</sup> The binding modes of L with  $\text{Al}^{3+}$  was studied by  $^1\text{H}$  NMR titration, shown in Fig. 8 (a-d). Upon complexation of L with  $\text{Al}^{3+}$  (1:1), the proton signal ( $\text{H}_9$ ) of L downfield shifted from 7.03 to 7.51 ( $\Delta\delta=0.48$ ) due to HC(the quinazolin ring carbon)-N(the imidazole ring nitrogen) bond cleavage upon coordination of the two nitrogen atoms with  $\text{Al}^{3+}$  ion. Accordingly, benzimidazole protons and phenyl protons except  $\text{H}_5$  shifted to low magnetic field because of the reduction

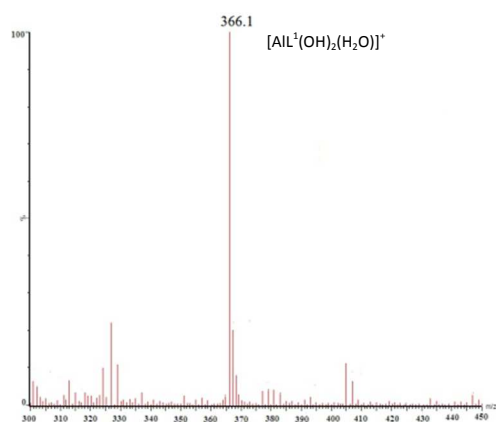
of electron density upon coordination to the  $\text{Al}^{3+}$ . Also, furyl proton signals ( $\text{H}_{10}-\text{H}_{12}$ ) shifted downfield after binding of furyl oxygen atom from L with  $\text{Al}^{3+}$ ,  $\Delta\delta=0.15-0.31$  ppm. Similarly, upon complexation of L with  $\text{Cr}^{3+}$  in  $\text{CH}_3\text{OH}-d_6$ , the proton peak ( $\text{H}_9$ ) downfield shifted from 7.03 to 7.46 ppm (Fig. S10). The  $^1\text{H}$



**Figure 8.**  $^1\text{H}$  NMR spectra in  $\text{CH}_3\text{OH}-d_6$ : (a) L only; (b) L and 0.5 equiv. of  $\text{Al}^{3+}$ ; (c) L and 1.0 equiv. of  $\text{Al}^{3+}$ ; (d) L and 1.5 equiv. of  $\text{Al}^{3+}$

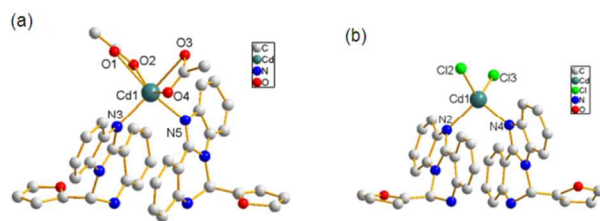
NMR signals of the quinazolin ring protons, benzimidazole ring protons and furyl ring protons of L showed changes for the both systems. The results suggest that  $\text{Al}^{3+}$  and  $\text{Cr}^{3+}$  are coordinated with the aldimine nitrogen atom, imidazole nitrogen atom and the furyl oxygen atom of L, resulting from C-N bond cleavage of the quinazolin ring to form a Schiff base [2-(1H-benzimidazol-2-yl)phenyl]-furan-2-ylmethyleamine ( $\text{L}^1$ ) and  $\text{M}^{3+}-\text{L}^1$  complexes were obtained.<sup>[10, 11(c)]</sup> In addition, there were no significant changes for the proton signals upon the addition of 1.5 equiv. of  $\text{Al}^{3+}$  (Fig. 8(c) and (d)) and  $\text{Cr}^{3+}$  (Fig. S10(c) and (d)) to L. This also confirmed the 1:1 stoichiometry for L to  $\text{Al}^{3+}$  and  $\text{Cr}^{3+}$ , respectively. We tried to observe  $^1\text{H}$  NMR spectrum of L with  $\text{Fe}^{3+}$ , we failed to get satisfactory result because of its paramagnetic nature.

To further study the coordination of L with  $\text{Al}^{3+}$ ,  $\text{Cr}^{3+}$  and  $\text{Fe}^{3+}$ , their ESI-MS spectra were recorded. As shown in Fig. 9, the mass spectrum of L upon addition of 1.0 equiv. of  $\text{Al}^{3+}$  exhibited an intense peak at  $m/z$  366.1, corresponding to the ion  $[\text{AlL}^1(\text{OH})_2(\text{H}_2\text{O})]^+$  (calcd  $m/z$  366.3). This could be attributed to the fact that  $-\text{OH}$  and  $\text{H}_2\text{O}$  can supply a hard-base environment for the hard-acid  $\text{Al}^{3+}$ , which makes it easier to form the  $\text{Al}^{3+}$  complex.<sup>[16]</sup> Also, in the literature  $[\text{Al}(\text{OH})_2(\text{H}_2\text{O})]^+$  could be found.<sup>[17]</sup> In Fig. S11a, the peak at  $m/z$  397.9 corresponds to the ion  $[\text{CrL}^1(\text{OH})_3] \text{Li}^+$  (calcd  $m/z$  397.3) and the peak at  $m/z$  416.8 corresponds to the ion  $[\text{FeL}^1(\text{OH})_3]\text{Na}^+$  (calcd  $m/z$  417.2) (Fig. S8b). From Job plot,  $^1\text{H}$  NMR data and ESI-MS results, it can be concluded that the  $\text{Al}^{3+}$ ,  $\text{Cr}^{3+}$  and  $\text{Fe}^{3+}$  may form  $[\text{AlL}^1(\text{OH})_2(\text{H}_2\text{O})]^+$ ,  $\text{CrL}^1(\text{OH})_3$  and  $\text{FeL}^1(\text{OH})_3$  in  $\text{CH}_3\text{OH}$ , respectively.



**Figure 9.** Positive-ion electrospray ionization mass spectra of L upon addition of 1.0 equiv.  $\text{Al}^{3+}$  in  $\text{CH}_3\text{OH}$ .

To investigate the structure of the species formed in the response system, we tried to cultivate the crystals of the  $\text{Al}^{3+}$ ,  $\text{Cr}^{3+}$  and  $\text{Fe}^{3+}$  complexes with L, but failed. However, two Cd complexes were obtained by one-pot reaction of furfural, 2-(2-aminophenyl)benzimidazole with cadmium acetate (**1**) and chloride (**2**), respectively. The crystal structures of the Cd(II) complexes **1** and **2** are shown in Fig. 10. In **1**, Cd(II) ion is six-coordinated by four acetate oxygen atoms and two imidazole nitrogen atoms from two L ligands. The polycrystals sample of **1** was obtained by the solvothermal reaction of cadmium acetate with L, which is confirmed to be the same phase as **1** by elemental analysis, IR and powder X-ray diffraction (Fig. S12). In **2**, Cd(II) ion is four-coordinated by two chloride anions and two imidazole nitrogen atoms from two L ligands. L in **1** and **2** is monodentate and the binding site of L with Cd(II) is not located at the quinazoline ring of L. The UV-Vis spectra, fluorescence spectra and  $^1\text{H}$  NMR of L and Cd(II)-species are shown in Figs. S13-15. No significant difference between L and its Cd(II) species in the corresponding spectra was found. This shows that the coordination of L with Cd(II) has a little effect on the intramolecular  $\pi$  to  $\pi^*$  transition and electric delocalization, and thus L for Cd(II) is insensitive.



**Figure 10.** The crystal structures of the Cd(II) complexes. (a)  $[\text{CdL}_2(\text{OAc})_2]$ ; (b)  $[\text{CdL}_2\text{Cl}_2]$ .

As is known, the ionic radii of  $\text{Al}^{3+}$ ,  $\text{Cr}^{3+}$ ,  $\text{Fe}^{3+}$  and  $\text{Cd}^{2+}$  are 67.5, 75, 78.5 and 109 pm, respectively with a coordination number of 6. For  $\text{Cd}^{2+}$  it is even 92 pm when coordination number falls to 4,<sup>[18]</sup> which is much larger than that of  $\text{Al}^{3+}$ ,  $\text{Cr}^{3+}$  and  $\text{Fe}^{3+}$ . According to the Hard-Soft Acid-Base theory,  $\text{Cd}^{2+}$  is soft acid, while  $\text{Al}^{3+}$ ,  $\text{Cr}^{3+}$ ,  $\text{Fe}^{3+}$  are hard acids. Thus  $\text{Cd}^{2+}$  as a soft acid has high affinity to nitrogen atom. Considering the steric effect and its large ionic radius,  $\text{Cd}^{2+}$  is apt to coordinate with the nitrogen atom at 3-position of imidazole section. While the  $\text{Al}^{3+}$ ,

$\text{Cr}^{3+}$ ,  $\text{Fe}^{3+}$  ions as hard acids have high affinity to oxygen atom. Their small radii make the furan oxygen atom and aldimine nitrogen atom available for them. Consequently the coordination of L with  $\text{Al}^{3+}$ ,  $\text{Cr}^{3+}$  and  $\text{Fe}^{3+}$  leads to the breakage of C-N bond, forming a Schiff base complex.

## Conclusions

We synthesized a quinazoline derivative (L) and two Cd(II) complexes (**1** and **2**). Their structures have been determined by single-crystal X-ray diffraction. The interaction site of L with Cd(II) is one imidazole nitrogen atom from L and thus L is monodentate in **1** and **2**. Spectroscopic determination showed that L for Cd(II) is insensitive. But L is employed as a highly sensitive and selective sensor for  $\text{Al}^{3+}$ ,  $\text{Cr}^{3+}$  and  $\text{Fe}^{3+}$  ions over a number of metal ions in  $\text{CH}_3\text{OH}$ . The  $\text{Al}^{3+}$ ,  $\text{Cr}^{3+}$  and  $\text{Fe}^{3+}$  detections have been demonstrated by absorption, fluorescence,  $^1\text{H}$  NMR and ESI-MS spectral studies. The 1:1 binding stoichiometry of  $\text{Al}^{3+}$ ,  $\text{Cr}^{3+}$  and  $\text{Fe}^{3+}$  with L was confirmed by Job's plot, fluorescence titration and ESI-MS data, respectively. The interaction sites of L for  $\text{Al}^{3+}$  and  $\text{Cr}^{3+}$  have been suggested by spectral changes and the transformation from L to  $\text{L}^1$  in the presence of  $\text{Al}^{3+}$ ,  $\text{Cr}^{3+}$  and  $\text{Fe}^{3+}$  ions was explored. The CHEF effect may be attributed to the formation of  $\text{M}^{3+}$ -containing five- and six-membered rings via two nitrogen atoms and one oxygen atom from  $\text{L}^1$  by increase of the donor-acceptor electric delocalization after complexation. It shows that nitrogen- and oxygen-containing quinazoline-base compounds can be served as a platform to explore chemosensors for multi-metal ions.

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## Notes and references

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† Electronic Supplementary Information (ESI) available: information on X-ray crystallographic data in CIF format, Fig. S1~S12, Tables S1. See DOI: 10.1039/b000000x/
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