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A highly selective ratiometric chemosensor for Hg^{2+} based on the anthraquinone derivative with urea groups

Hong Yang, Zhi-Guo Zhou, Jia Xu, Fu-You Li,* Tao Yi and Chun-Hui Huang*

Department of Chemistry and Laboratory of Advanced Materials, Fudan University, 200433 Shanghai, PR China

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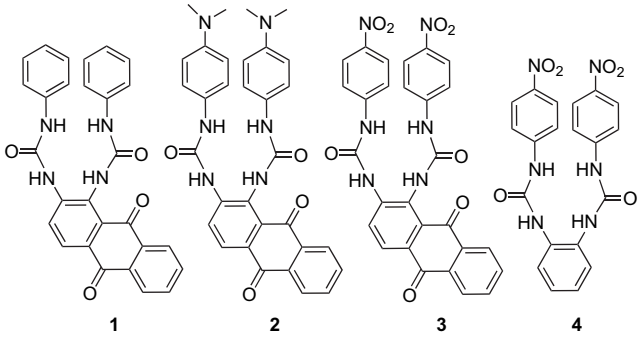
Abstract—Anthraquinone derivatives with different substituents **1**–**3** were synthesized by introducing the urea group. Their cations' binding properties were investigated by UV–vis absorption spectroscopy. Compared with **1** and **2**, **3** with electron-withdrawing group ($-NO_2$) showed a remarkable absorption change for Hg^{2+} over the other metal ions. The anthraquinone moiety and the N–H fragment of the urea moiety played key roles in sensing Hg^{2+}. The different acidity of N–H fragments of the urea moiety, caused by electron push–pull properties of the substituents on the phenyl *para* position, is the main reason for recognition.

1. Introduction

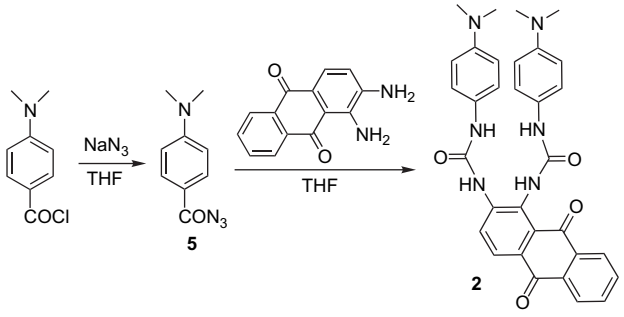
Design and synthesis of new chemosensors for transition and heavy metal ions have been of interest to chemists for many years because these ions play important roles in the areas of biological, environmental, and chemical systems.[1] As one of the most important environmental pollutants and an essential trace element in various biological systems, the Hg^{2+} recognition in particular has received more attention by using the colorimetric,[2] fluorogenic,[3] redox-active method,[4] and chemodosimeter.[5] According to the hard–soft acid–base theory, [6] nitrogen and sulfur binding sites may be the best choice for the selective recognition of soft heavy metal ion Hg^{2+}. Up to now, most receptors were still limited to be polyaza or thia-based chromophore. As one type of important receptors, urea groups have been widely adapted as fluoregenic and colorimetric receptors of anion sensors based on hydrogen bond mechanism.[7–8] However, urea receptors have rarely attracted interest in recognizing heavy metal ions.[9] Recently, we have succeeded in detecting Cu^{2+} bearing two urea groups as the receptor.[9b] In the present study, using the anthraquinone as chromophore, compounds **1**–**3** (see Scheme 1) with the urea group were synthesized to detect Hg^{2+}. The recognition–structure relationship was studied by introducing the electron-donating and electron-withdrawing groups. Interestingly, **3** showed a colorimetric recognition for Hg^{2+} with a high selectivity.



Scheme 1. Chemical structures of **1**–**3** with different substituents and the control compound **4**.

2. Results and discussion

According to the literature, compounds **1** and **3** were synthesized by the reaction of anthraquinone diamine with the corresponding urea.[10] As shown in Scheme 2, **2** was synthesized by the condensation of 1,2-diaminoanthraquinone and the intermediate **5**.



Scheme 2. Synthetic routine of **2**.

* Corresponding authors. Tel.: +86 21 55664185; e-mail addresses: fyli@fudan.edu.cn; chhuang@pku.edu.cn

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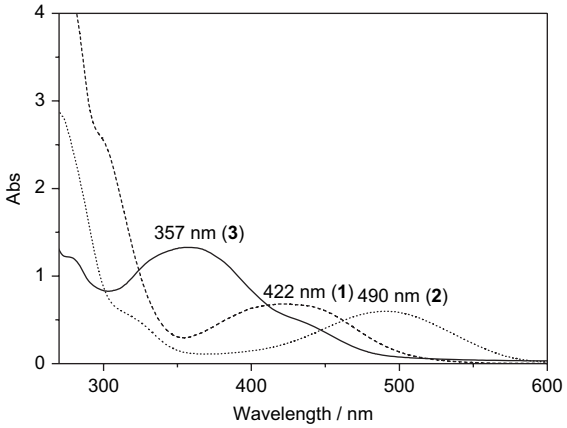

Figure 1. Absorption spectra of **1** (---), **2** (···), and **3** (—) in solution (5×10^{-5} mol L^{-1}) at room temperature.

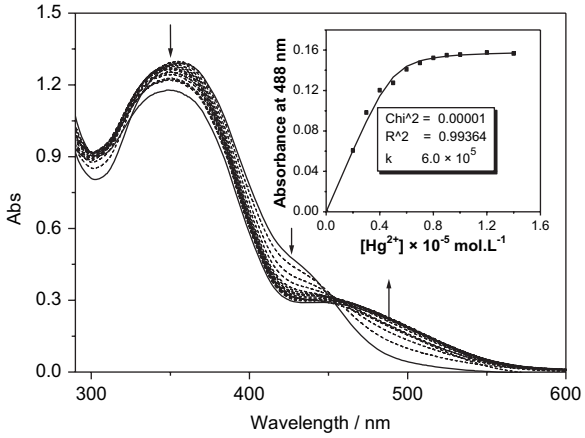

Figure 2. Changes in absorption spectra of **3** (50 μM) in CH_3CN/DMSO (9:1, v/v) upon addition of Hg^{2+} (0–6 equiv).

The absorption spectra of **1**–**3** in the mixed solution of DMSO/CH_3CN (v/v=1:9) are shown in Figure 1. Compounds **1** and **2** exhibited strong absorbance at 422 and 490 nm with the molar extinction coefficients (ε) of ~10^5, respectively, which were ascribed to the charge-transfer interaction (CT1) between the electron-rich urea moiety and the electron-deficient anthraquinone moiety. Compound **3** had a strong absorbance maximum around 357 nm and a weaker absorbance at 420 nm. The former was assigned to the intramolecular charge-transfer transition (CT2) between the strong electron-withdrawing ability of nitro group and the electron-rich urea groups and the later was consistent with the CT1 band. Obviously, **2** with electron-donating group (–$N(CH_3)_2$) and **3** with electron-withdrawing group (–NO_2) showed red-shifted and blue-shifted CT1 band in comparison with **1**, respectively. Therefore, the introduction of push–pull substituents affected obviously the photo-physical properties of compounds **1**–**3**. The shift evidently was arisen from the different push–pull substituent. Especially, the stronger electron-donating ability of *N*,*N*-dimethylamino group in compound **2** induced a large red shift of 68 nm compared with **1**.

The complexation abilities of **1**–**3** with Hg^{2+} ion were investigated by the UV–vis absorption techniques. In our present experiments, $Hg(ClO_4)_2$ as a Hg^{2+} source was gradually added to the CH_3CN/DMSO (9:1, v/v) solution of **1**–**3**. The changes in the UV–vis spectra of **3** upon addition of Hg^{2+} are presented in Figure 2. Notably, the CT1 band at 420 nm decreased gradually, and the new band at 488 nm appeared and concomitantly grew with increasing Hg^{2+} concentration with a isosbestic point of 456 nm, indicating an interaction between Hg^{2+} and **3** in the ground state. Of course, the above results were not due to the presence of ClO_4^- (see the Supplementary data). The facts suggested that the presence of Hg^{2+} influenced the charge-transfer from the electron-rich urea groups to the electron-deficient anthraquinone moiety. A Job's plot (see Supplementary data) indicated that **3** formed a 1:1 complex with Hg^{2+} ion in CH_3CN/DMSO (9:1, v/v) solution. The association constant for **3**–Hg^{2+} complex at 298 K was estimated to be 6.0×10^5 M^{-1}, which could be comparable to those of the Hg^{2+}-sensor reported previously.[11]

To explore practical applicability of **3** as a Hg^{2+}-selective naked eye chemosensor, the titration experiments were also investigated in the mixed solvent of DMSO/H_2O=1:1. The similar spectral changes of **3** were observed upon addition of Hg^{2+}. The association constant for **3**–Hg^{2+} complex at 298 K was calculated to be 4.2×10^5 M^{-1}. This fact indicated that this system could be used in semi-aqueous system.

For an excellent chemosensor, high selectivity is a matter of necessity. To examine the selectivity of **3**, we investigated its affinity for other metal cations. The experimental results suggested that **3** showed a high selectivity in colorimetric sensing Hg^{2+}. As depicted in Figure 3, **3** showed scarcely any response with other metal ions, such as Cu^{2+}, Ag^+, Cd^{2+}, Cr^{3+}, Fe^{3+}, Ni^{2+}, and Zn^{2+}.

Furthermore, competition experiments were also performed for **3** in the presence of Hg^{2+} at 50 μM mixed with 200 μM background metal cations such as Fe^{3+}, Co^{2+}, Ni^{2+}, and Zn^{2+} (Fig. 3). In the presence of other metal ions, no obvious variation in the absorption was observed in sensing Hg^{2+}. Importantly, the presence of Ag^+ and Cd^{2+} did not affect the selectivity of **3** for Hg^{2+}. All these results implied that

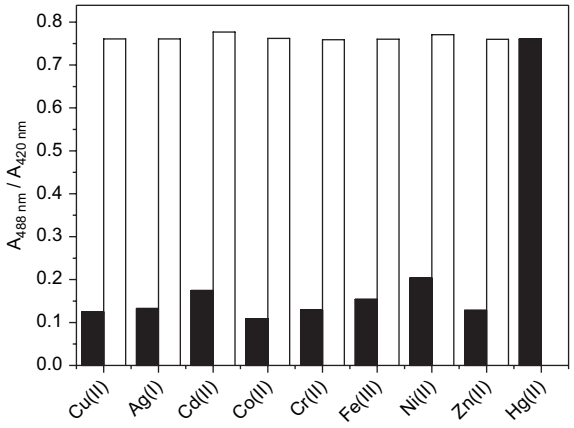

Figure 3. Absorption ratiometric responses of **3** (50 μM) to various metal ions (200 μM) in CH_3CN/DMSO (9:1, v/v). Bars represent the intensity ratios of absorption at 488 nm to that at 425 nm. Black bars represent response of **3** to different metal ions; blank bars responses of **3** containing 50 μM Hg^{2+} to different metal ions.

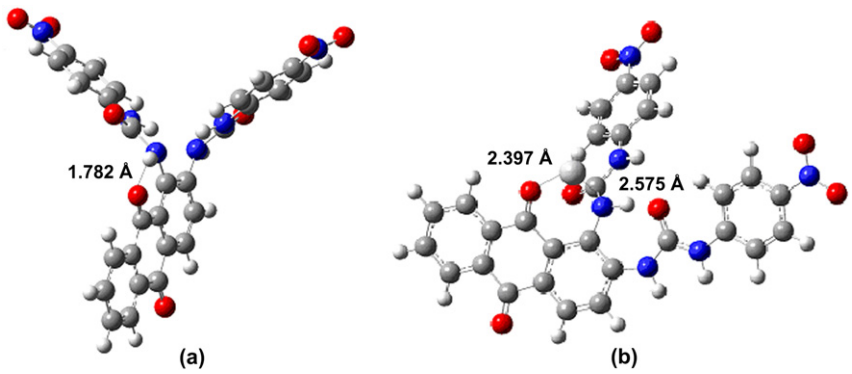

Figure 4. Optimized geometries for the free receptor **3** (a) and its complexes with Hg^{2+}(b).

3 could be used as a potential candidate of Hg^{2+} chemosensor with very high selectivity.

For comparison, the recognition of **1** and **2** to Hg^{2+} were also investigated. However, few changes were observed for **1** and **2** upon addition of Hg^{2+} (see Supplementary data), indicating weak complexation ability of **1** and **2** with Hg^{2+}. In the light of the observation of strong complexation of **3** with Hg^{2+}, we can conclude that the electron-withdrawing substituent ($–NO_2$) plays an important role in reorganization of **3** to Hg^{2+}.

Accordingly, on the basis of the evidence mentioned above, we can conclude that the bis-urea group attached electron-withdrawing group ($–NO_2$) plays a key role in sensing Hg^{2+}. To explore the complexation site, the structure of **3** and **3**–Hg^{2+} were optimized at the B3LYP density function theory and the results are shown in Figure 4. The SDD basis set was used to treat the Hg atom, whereas 3-21G** basis set was used to treat all other atoms for **3**–Hg^{2+}. The urea groups in **3** orient almost perpendicular to the anthraquinone ring. Upon complexation of **3** with Hg^{2+}, one of the amide units (no interaction with Hg^{2+}) lies in the plane of anthraquinone ring, but the other amide group (the interaction with Hg^{2+}) derived from planarity by ~49°. The intramolecular N–H···O hydrogen bond distance of **3** calculated at B3LYP/6-31G** is 1.782 Å between the anthraquinone oxygen and the amide carbonyl group (see Fig. 4a). After addition of Hg^{2+}, the N···Hg and O···Hg bond distances were calculated to be 2.575 and 2.397 Å, respectively (see Fig. 4b), and the N–H···O bond is much longer than that in the absence of Hg^{2+}, which are significantly deviated from the presence of the interaction between Hg^{2+} and anthraquinone oxygen. That is, Hg^{2+} breaks the intramolecular N–H···O hydrogen bond between the anthraquinone oxygen and the N–H group, and the carbonyl group of anthraquinone in **3** participates in the coordination of Hg^{2+}. As a similar urea derivative of **3**, **4** was synthesized, and the calculated results prompted us to investigate the complexation of **4** with Hg^{2+}. No change in UV–vis spectra was observed upon addition of Hg^{2+} and other metal ions (see Supplementary data). This fact indicated that the carbonyl group of anthraquinone in **3** played an important role in complexation of Hg^{2+}. Therefore, we can conclude that both the anthraquinone moiety and the urea moiety in conjugation with strong electron-withdrawing groups are necessary bonding-site for detecting Hg^{2+}.

The acidity of N–H fragments in urea moiety of **3** is enhanced for the existence of nitro-group and anthraquinone ring, and the deprotonation of **3** becomes easier in comparison with that of **1**. At this point, the coordinating ability of **3** can be improved between nitrogen of N–H fragments and Hg^{2+}. On the contrary, for **2**, the introduction of the electron-donating group can enhance the electron density of N–H fragments and consequently increases the basicity, and the deprotonation becomes more difficult. So no obvious new peak in the UV–vis absorption spectrum for **2** was observed.

3. Conclusions

In conclusion, we developed a highly selective ratiometric Hg^{2+} chemosensor. The recognition of Hg^{2+} gave rise to the ratiometric change at the ratio of the absorption intensity of 420 and 488 nm for the complexation. Anthraquinone moiety is not only the signaling subunits but also plays a receptor role. For urea moiety as a receptor, the acidity of N–H fragments is a key point to detect Hg^{2+} selectively. Such a design strategy would be of great interest in the development of other chemosensors for heavy and transition metal cations.

4. Experimental

4.1. General

The ^{1}H NMR spectrum was recorded at 400 MHz on a Varian Gemin-400. UV–vis spectra were measured on UV–vis 2550 spectroscope (Shimadzu). The titration experiments were carried out in CH_3CN/DMSO mixture (9:1, v/v) by adding aliquots of metal ion solution.

4.1.1. Urea(*N*,*N*′-(9,10-dihydro-9,10-dioxo-1,2-anthracenediyl)bis[*N*′-phenyl]) (1). 1,2-Diaminoanthraquinone (238 mg, 1.0 mmol) was dissolved in a solvent mixture of dry DMF and THF (1:5 v/v) .To this solution was added phenylisocyanate (357 mg, 3.0 mmol) and stirred under inert atmosphere at 80 °C for 6 h. The reaction mixture was cooled to room temperature. Precipitate formed was filtered and washed thoroughly with THF and acetonitrile, respectively.[10a]

Compound **1**: ^{1}H NMR: (400 MHz, DMSO-d_6, ppm) δ 9.77 (s, 1H), 9.70 (s, 1H), 9.10 (s, 1H), 8.60 (s, 1H), 8.65 (d,

J=8.0, 1H), 8.15–8.17 (m, 3H), 7.90–7.91 (m, 2H), 7.54 (d, J=8.0, 2H), 7.47 (d, J=8.0, 2H), 7.28–7.30 (m, 4H), 6.98–7.00 (m, 2H). ^{13}C NMR: (100 MHz, DMSO-d_6, ppm) δ 207.8, 185.6, 182.1, 154.1, 152.7, 143.2, 140.3, 139.7, 135.1, 134.7, 133.0, 129.6, 129.5, 129.0, 128.1, 127.5, 127.3, 126.9, 126.3, 125.4, 123.1, 122.8, 119.0, 118.8. Anal. Calcd for $C_{28}H_{20}N_4O_4$: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.89; H, 4.21; N, 11.69.

4.1.2. Azido(4-(dimethylamino)phenyl)methanone (5). 4-(Dimethylamino)benzoyl chloride (1.84 g, 0.01 mol) was dissolved in 20 mL THF and dropped into 50 mL NaN_3 solution (6.5 g, 0.1 mol) under ice bath. The reaction mixture was stirred overnight, the precipitate was filtered and 4-(dimethylamino)benzoyl chloride was obtained as a yellow solid. The crude product was purified by column chromatography on silica gel with chloroform/petrol ether (1:1) as the eluent to obtain pure **5**. The product was obtained in 70% yield.[10b]

Compound **5**: ^{1}H NMR: ($CDCl_3$-d, ppm) δ 7.87 (d, J=8.0, 2H, ArH), 6.61 (d, J=8.0, 2H, ArH), 3.01 (s, 6H, –N(CH_3)$_2$).

4.1.3. Urea(*N*,*N*′-(9,10-dihydro-9,10-dioxo-1,2-anthracenediyl)bis[*N*′-4-dimethylamino-phenyl]) (2). The procedure followed was the same as that for receptor **1**. To a solution of 0.36 g (1.5 mmol) 1,2-diaminoanthraquinone in a 40 mL DMF solution was slowly added 1.14 g (6.0 mmol) **5** in 20 mL of THF over 30 min and refluxed for 6 h in a nitrogen atmosphere. The solid product was collected by filtration and washed with acetone. The product was obtained in a 65% yield.

Compound **2**: ^{1}H NMR: (400 MHz, DMSO-d_6, ppm) 8.21 (s, 1H), 8.19 (s, 1H), 8.13 (s, 1H), 8.10 (s, 1H), 7.96 (d, J=8.0, 1H), 7.83–7.89 (m, 4H), 7.52 (d, J=8.0, 2H), 7.27 (d, J=8.0, 3H), 6.69 (d, J=8.0, 4H), 2.80 (s, 9H), 2.78 (s, 3H). ^{13}C NMR: (100 MHz, DMSO-d_6, ppm) δ 185.2, 182.6, 171.2, 153.2, 147.4, 144.4, 135.0, 134.9, 134.4, 133.4, 133.3, 129.5, 128.6, 127.2, 126.9, 126.0, 120.9, 117.8, 113.8, 60.5. Anal. Calcd for $C_{32}H_{30}N_6O_4$: C, 68.31; H, 5.37; N, 14.94. Found: C, 68.01; H, 5.69; N, 15.21.

4.1.4. Urea(*N*,*N*′-(9,10-dihydro-9,10-dioxo-1,2-anthracenediyl)bis[*N*′-4-nitrophenyl]) (3). The procedure followed was similar to that for receptor **1**. 4-Nitro-phenylisocyanate (492 mg, 3.0 mmol) was used instead of phenylisocyanate. Yield: 80%.

Compound **3**: ^{1}H NMR: (400 MHz, DMSO-d_6, ppm) δ 10.50 (s, 1H, NH), 10.28 (s, 1H, NH), 9.171 (s, 1H, NH), 8.76 (s, 1H, NH), 8.66 (d, J=7.2, 1H), 8.19–8.23 (t, J=8.0, 6H), 7.92–7.95 (m, 3H), 7.77 (d, J=8.0, 2H), 7.70 (d, J=8.0, 2H). ^{13}C NMR: (100 MHz, DMSO-d_6, ppm) δ 185.3, 182.1, 171.2, 163.2, 153.7, 152.2, 146.8, 146.2, 142.5, 142.1, 141.9, 135.2, 134.7, 133.0, 128.7, 128.3, 127.7, 127.5, 127.1, 127.0, 126.8, 125.9, 118.4, 118.2. Anal. Calcd for $C_{28}H_{18}N_6O_8$: C, 59.37; H, 3.20; N, 14.84. Found: C, 59.13; H, 3.22; N, 14.78.

4.1.5. *N*,*N*′-1,2-(Phenylenebis-[*N*′-*p*-nitrophenylurea]) (4). The procedure followed was similar to that for receptor **1**. 1,2-Diaminobenzene (108 mg, 1.0 mmol) was used instead of 1,2-diaminoanthraquinone. Yield: 85%.

^{1}H NMR: (400 MHz, DMSO-d_6, ppm) δ 9.82 (s, 2H), 8.83 (s, 2H), 8.18 (d, J=8.0, 4H), 7.69 (d, J=8.0, 4H), 7.61–7.59 (m, 2H), 7.16–7.13 (m, 2H). ^{13}C NMR: (100 MHz, DMSO-d_6, ppm) δ 153.2, 146.9, 141.7, 131.4, 125.8, 125.5, 125.1, 118.1.

Acknowledgements

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Supplementary data

UV–vis spectra of **1**, **2**, and **4** with different metal ions; UV–vis spectra of **3** with $[(Bu)_4N]ClO_4$; UV–vis spectra of **3** with different content of Hg^{2+} in H_2O/DMSO (1:1, v/v) solution; Job's plot of **3**; calculation methods and results of the energy minimized structure; NMR spectra of compound **1**–**4**. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.04.086.

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