Two-Stage Sensing Property via a Conjugated Donor–Acceptor–Donor Constitution: Application to the Visual Detection of Mercuric Ion

Ju-Hui Huang,† Wen-Hsien Wen,† Yueh-Yang Sun,† Pi-Tai Chou,† and Jim-Min Fang*,†,‡
Department of Chemistry, National Taiwan University, Taipei 106, Taiwan, and Genomics Research Center, Academia Sinica, Taipei 115, Taiwan

Received March 2, 2005

A conjugated donor–acceptor–donor molecule incorporating a central moiety of naphthyridine and two terminal moieties of di(hydroxyethyl)aniline connected by ethynyl bridges shows two-stage color changes on binding with mercury(II) ion in Me2SO/H2O (1:1) solution with a bathochromic shift from 450 to 498 nm, and then an extraordinarily large hypsochromic shift to 378 nm. In comparison, the corresponding donor–acceptor molecule weakly binds mercury(II) ion with a hypsochromic shift from 408 to 375 nm. Our designed sensor of the donor–acceptor–donor system shows high selectivity toward mercury(II) ion over other competing metal ions.

Introduction

A molecule bearing conjugated electron acceptor (A) and electron donor (D) usually undergoes an intramolecular charge transfer (ICT) upon electronic excitation.1 The ICT and hence an elongation of the π electron conjugation occurring upon Franck Condon excitation contributes considerably to the absorption profile. If the A–D molecule binds a metal ion at the acceptor site, a bathochromic shift occurs to account for the enhanced ICT.1,2 However, in most cases, a metal ion tends to bind at the electron-rich donor site to cause a hypsochromic shift, often making visual detection difficult.1,2 To extend the A–D recognition concept, the optical properties and binding behavior of D–A–D assembly, in comparison with molecule I of A–D constitution, as a simple model to demonstrate the concept of the two-stage sensing with enhanced signal transduction.4 As shown by the schematic drawing (Scheme 1), the naphthyridine moiety acts as the acceptor site, whereas the di(hydroxyethyl)amino moiety functions as the donor site, whereas the di(hydroxyethyl)amino moiety functions as the donor site.

We have previously explored that 2,7-bis(1H-pyrro-2-yl)ethyl-1,8-naphthyridine (BPN), a push–pull conjugated molecule, exhibits a very large Stokes shift of fluorescence upon complexation with glucopyranoside.3 Along this line, we herein designed the molecule 2 of D–A–D assembly, in comparison with molecule 1 of A–D constitution, as a simple model to demonstrate the concept of the two-stage sensing with enhanced signal transduction.4 As shown by the schematic drawing (Scheme 1), the naphthyridine moiety acts as the acceptor site, whereas the di(hydroxyethyl)amino moiety functions as the donor site.

1 National Taiwan University.
2 Academia Sinica.

10.1021/jo050389e CCC: $30.25 © 2005 American Chemical Society
Published on Web 06/24/2005
SCHEME 1. Design of Metal Ion Sensor with Conjugated A–D and D–A–D Assemblies

(a) Sensor of A–D assembly

(b) Sensor of D–A–D assembly

A : acceptor
D : donor
metal ion (M)

Enhanced blue shift by the prohibition of ICT

Enhanced red shift by facilitating ICT

as the donor site. The acceptor and donor moieties are connected by ethynyl bridges to form a conjugated scaffold.

In general, several binding states may exist in equilibrium. The degree of π electron conjugation induced by ICT, in a qualitative sense, can be designated by the dipolar vector depicted in Scheme 1. For example, the binding of the A–D molecule with a metal ion at the acceptor site, forming MA–D, would enhance the acceptor strength to facilitate ICT, whereas the binding at the donor site, forming A–DM, would reduce ICT. When both the acceptor and donor sites are bound to metal ions, the original donor group D is changed to an electron-withdrawing group DM, and the dipole would diminish. According to the preference of binding states in equilibrium, a bathochromic shift might be attributed to the ICT increase, and a hypsochromic shift might be attributable to the ICT diminution.

The binding event of the D–A–D molecule with a metal ion at the early stage will cause a bathochromic spectral shift, whereas the binding at the acceptor site, forming D–AM–D, due to the enhanced acceptor strength. When a metal ion binds at one of the donor sites, the resulting A–DM unit may also function as an enhanced electron-withdrawing group to facilitate ICT, a consequence differing from the binding of the A–D molecule at the donor site. Therefore, one can predict that the binding of the D–A–D molecule with a metal ion at the early stage will cause a bathochromic spectral shift, regardless of the binding at the acceptor or donor site. When the D–A–D molecule is saturated with metal ions at the late stage, all the acceptor and donor sites are bound to metal ions to form a 1:3 complex (MD–AM–DM). A hypsochromic spectral shift thus occurs to account for the great decrease of dipole at this stage.

Results and Discussion

Two consecutive Sonogashira coupling reactions were applied to synthesize sensor molecules 1 and 2 (Scheme 2). The coupling reaction of N,N-di(2-hydroxyethyl)-4-idoaniline with (trimethylsilyl)acetylene was promoted by 10 mol % of PdCl2(PPh3)2 and CuI in the presence of Et3N to give 3, after a subsequent removal of the trimethylsilyl group by K2CO3. Under similar conditions, coupling of 3 with 1 equiv of 2-chloro-1,8-naphthyridine gave sensor 1, whereas that with 0.5 equiv of 2,7-dichloro-1,8-naphthyridine afforded sensor 2.

The solution of molecule 1 in Me2SO/H2O (1:1) solution showed the absorption maximum at 408 nm (ε = 45 000 M⁻¹ cm⁻¹) (Figure 1), whereas the dual-armed molecule 2 exhibited the absorption maximum at a much longer wavelength, λmax = 450 nm (ε = 54 000 M⁻¹ cm⁻¹) (Figure 2). The large red-shift (42 nm) from 1 to 2 of the A–D constitution to 2 of the D–A–D constitution may be tentatively rationalized by the ethynyl substituent effect in one of the arms of 2, which, in part, elongates the π conjugation upon exciting the other A–D chromophore. However, the possibility of exciton coupling due to the crosstalk of two chromophores cannot be excluded at this stage.

Both the naphthyridine5 and di(hydroxyethyl)anilines6 moieties are known to have affinity toward metal ions. During our preliminary screening, molecules 1 and 2 were found to bind Hg²⁺ ions in aqueous media (e.g. Me2SO/H2O = 1:1). The pollution of mercury and its derivatives has posed severe problems for human health and the environment.7 Many methods have been developed to detect Hg²⁺ ion.2,8 In our study, the stock solutions of 1 and 2 (1 × 10⁻⁵ M) in Me2SO/H2O (1:1) were prepared.

References


This hypsochromic shift is ascribed to the preferable complexation at both the acceptor and donor sites, as the MA–DM species with diminution of ICT. When ≤1 equiv of Hg\textsuperscript{2+} ions was added to 1, a very weak absorption occurring at ~500 nm might be attributable to a transient binding of Hg\textsuperscript{2+} ion at the acceptor (naphthyridine) site, as the enhanced ICT species of AM–D in Scheme 1a.

The \textsuperscript{1}H NMR titration study of 1 in Me\textsubscript{2}SO-\textsubscript{d\textsubscript{6}} solution (see Figure S1 in the Supporting Information) indicated that the initial addition of Hg\textsuperscript{2+} ions (<0.5 equiv in CD\textsubscript{3}CN) caused the disappearance of the hydroxyl protons and significant downfield shifts of the protons on the naphthyridine ring, but no apparent change of the protons on the di(hydroxyethyl)aniline moiety. The \textsuperscript{1}H NMR spectra became complicated on further addition of Hg\textsuperscript{2+} ions (1–4 equiv in this study), presumably due to existence of several complexation species. According to the chemical-shift changes of H-7, from δ 9.08 to 9.20 during the titration, the association constant (K\textsubscript{as}) of 1490 ± 31 for 1–Hg\textsuperscript{2+} (1:1 complex) at 298 K in Me\textsubscript{2}SO-\textsubscript{d\textsubscript{6}} solution was deduced by the nonlinear regression method.\textsuperscript{9}

and the binding event was monitored by the UV–vis spectroscopic method. The titrations were carried out by using various amounts of Hg\textsuperscript{2+} ion (1 × 10\textsuperscript{-2} M in distilled water).

The binding of 1 with Hg\textsuperscript{2+} was rather weak; only after addition of more than 1 equiv of Hg\textsuperscript{2+} ions did a new blue-shifted absorption band at \(\lambda_{\text{max}} = 375\) nm appear and increase at the expense of the 408 nm band (Figure 1). This hypsochromic shift is ascribed to the preferable binding of Hg\textsuperscript{2+} ion at the donor site of di(hydroxyethyl)aniline, as the A–DM species in Scheme 1a,\textsuperscript{1,2,8} or complexation with the MA–DM species with diminution of ICT.
On the other hand, titration of 1 with methanesulfonic acid (MeSO\textsubscript{2}−H\textsubscript{2}) gave a red-shift absorption band at 489 nm with an isosbestic point occurring at 442 nm throughout the titration (see Figure S2 in the Supporting Information). This result indicated that the A–D molecule 1 was protonated at the naphthyridine site to form a 1:1 complex with prominent ICT, which prevented further protonation of the di(hydroxyethyl)aniline moiety. The association constant for protonated 1 (1:1 complex of 1−H\textsuperscript{+}) was determined to be 355 ± 70 in Me\textsubscript{2}SO/H\textsubscript{2}O (1:1) solution.

In sharp contrast, the D–A–D molecule 2 was much more responsive to the Hg\textsuperscript{2+} ion than the A–D molecule 1 in the UV−vis titration. The initial addition of Hg\textsuperscript{2+} ions to 2 caused a prominent new absorption band at \(\lambda_{\text{max}} = 498\) nm (Figure 2). The yellow solution of 2 immediately changed to magenta in accordance with this large red-shift (\(\Delta\lambda = 48\) nm). As predicted in Scheme 1b, the Hg\textsuperscript{2+} ion might either bind to the acceptor site at the early stage of titration to facilitate ICT or bind to one of the donor sites to form an enhanced A−D−Hg\textsuperscript{2+} electron-withdrawing unit that also facilitates the net ICT, resulting in an additive effect in the dipolar change.

The magenta color of the mixture solution faded when more than 10 equiv of Hg\textsuperscript{2+} ions were added. Accordingly, an extraordinarily large hypsochromic shift (\(\Delta\lambda = 120\) nm) from 498 to 378 nm was observed. By addition of more than 10 equiv of Hg\textsuperscript{2+} ions, all the acceptor and donor sites in molecule 2 were likely saturated to reach a late stage of complexation (as the MD−AM−DM species in Scheme 1b), in which the saturated complex would only possess the least ICT property. The prohibition of \(\pi\) conjugation thus results in a great hypsochromic shift of the absorption band.

Calculations with Specfit global analysis software (Specfit/32) supported our experimental results of complex formation, i.e., the primary formed 1:1 complex (2−Hg\textsuperscript{2+}) decreased after addition of 10 equiv of Hg\textsuperscript{2+} ions, along with the growth of the 1:3 complex, 2−(Hg\textsuperscript{2+})\textsubscript{3}. The association constants for 2−Hg\textsuperscript{2+} and 2−(Hg\textsuperscript{2+})\textsubscript{3} complexes at 298 K were estimated to be (2.82 ± 0.17) \(\times 10^5\) M\textsuperscript{−1} and (8.91 ± 0.24) \(\times 10^{11}\) M\textsuperscript{−3}, respectively. The binding strength of receptor 2 toward Hg\textsuperscript{2+} (1:1 complex) is comparable to that of azatetraethia-15-crown-5,

FIGURE 3. \(^1\)H NMR titration of 2 (2.5 × 10\textsuperscript{−3} M in Me\textsubscript{2}SO-d\textsubscript{6}) by incremental additions of MeSO\textsubscript{2}OH (1.25 M in Me\textsubscript{2}SO-d\textsubscript{6}).

On the other hand, addition of excess MeSO\textsubscript{2}OH (e.g., 1000 equiv) did not show blue-shifted absorption. It appeared that protonation at the naphthyridine site induced a prominent ICT, which prevented further protonation of the di(hydroxyethyl)aniline moieties. The \(^1\)H NMR titration with MeSO\textsubscript{2}OH (Figure 3) also clearly showed that the naphthyridine protons H-3/H-6 and H-4/H-5 shifted to lower fields,


5830 J. Org. Chem., Vol. 70, No. 15, 2005
Ca2⁺ detection, molecule free from the interference of other metal ions. The unique selectivity of metal ions and other possible analytes. Tentatively propose that Hg²⁺ causes the Hg²⁺ growth of 379-nm absorption, similar to the spectra shown in Figure 2. We also found that the sensing events are rationalized by a very specific orientation of electron (or charge) transfer on the logic gates based on its sensitivity and system, which may eventually lead to practical applications.

In conclusion, the dual-armed D-A-D molecule 2 exhibits absorptions at longer wavelengths than the A-D molecule 1, and hence provides a more convenient “naked-eye” colorimetric detection of the Hg²⁺ ion. Instead of the commonly used macromolecules for metal ion detection, molecule 2 with the acyclic di(hydroxyethyl)aniline components renders a straightforward preparation and good solubility in aqueous media. The D-A-D constitution demonstrated in this study can serve as a protocol for the future design of a multiple-stage sensing system, which may eventually lead to practical applications on the logic gates based on its sensitivity and selectivity of metal ions and other possible analytes.

Experimental Section

N,N-Di(2-hydroxyethyl)-4-ethynylaniline (3). Under an atmosphere of nitrogen, a mixture of 4-iodoaniline (1.3 g, 6 mmol), 2-chloroethanol (10 mL), and K₂CO₃ (4 g, 30 mmol) was heated at 55 °C for 10 h. The mixture was concentrated, brine was added (40 mL), and the solution was extracted with CH₂Cl₂. The combined organic phase was dried (Na₂SO₄), filtered, and concentrated under reduced pressure to give a crude product.

Visual Detection of Mercuric Ion

A mixture containing 1 equiv and metal ions (each 10 equiv) and MsOH (50 mol%) in MeOH (5 mL) was treated with 1,8-naphthyridine (1 equiv) and MeOH (5 mL) was heated at 55 °C for 14 h. The mixture was concentrated, taken by MeOH/CH₂Cl₂ (1:9), and passed through a short column of Celite by elution with MeOH/CH₂Cl₂. The organic phase was concentrated, and the crude product was purified by silica gel chromatography (MeOH/CH₂Cl₂ (1:9)) to give N,N-di(2-hydroxyethyl)-4-(trimethylsilyl)ethylnylaniline (303 mg, 91% yield) as yellow solids, mp 96–97 °C.

A solution of N,N-di(2-hydroxyethyl)-4-(trimethylsilyl)ethylnylaniline (300 mg, 1.08 mmol) in MeOH (5 mL) was heated at 55 °C for 10 h. The mixture was concentrated, brine was added (40 mL), and the solution was extracted with CH₂Cl₂. The combined organic phase was dried (Na₂SO₄), filtered, and concentrated under reduced pressure.

Under an atmosphere of nitrogen, a mixture of N,N-di(2-hydroxyethyl)-4-iodoaniline (370 mg, 1.2 mmol), (trimethylsilyl)acetylene (0.2 mL, 1.44 mmol), Et₃N (2 mL), PdCl₂(PPh₃)₂ (10 mg, 0.014 mmol), and CuI (3 mg, 0.016 mmol) in 1,4-dioxane (2 mL) was heated at 50–55 °C for 14 h. The mixture was concentrated, taken by MeOH/CH₂Cl₂ (1:9), and passed through a short column of Celite by elution with MeOH/CH₂Cl₂. The organic phase was concentrated, and the crude product was purified by silica gel chromatography (MeOH/CH₂Cl₂ (1:9)) to give N,N-di(2-hydroxyethyl)-4-(trimethylsilyl)ethylnylaniline (303 mg, 91% yield) as yellow solids, mp 96–97 °C.

Under an atmosphere of argon, a mixture of N,N-di(2-hydroxyethyl)-4-iodoaniline (370 mg, 1.2 mmol), (trimethylsilyl)acetylene (0.2 mL, 1.44 mmol), Et₃N (2 mL), PdCl₂(PPh₃)₂ (10 mg, 0.014 mmol), and CuI (3 mg, 0.016 mmol) in 1,4-dioxane (2 mL) was heated at 50–55 °C for 14 h. The mixture was concentrated, taken by MeOH/CH₂Cl₂ (1:9), and passed through a short column of Celite by elution with MeOH/CH₂Cl₂. The organic phase was concentrated, and the crude product was purified by silica gel chromatography (MeOH/CH₂Cl₂ (1:9)) to give N,N-di(2-hydroxyethyl)-4-(trimethylsilyl)ethylnylaniline (303 mg, 91% yield) as yellow solids, mp 96–97 °C.

A mixture containing 1 equiv and metal ions (each 10 equiv) other than Hg²⁺ retained its yellow color (λmax = 450 nm), but changed instantly to magenta (λmax = 502 nm) upon addition of Hg²⁺ ion. When more than 10 equiv of Hg²⁺ ions were added, the color faded and the absorption band also shifted to 378 nm. Thus, the two-stage colorimetric property of 2 was unique in the detection of the Hg²⁺ ion in aqueous media, e.g., Me₂SO/H₂O (1:1), free from the interference of other metal ions. The unique selectivity of Hg²⁺ based on the current system is truly remarkable. At the current stage, although the actual cause of the Hg²⁺ selectivity is pending resolution, we tentatively propose that Hg²⁺ tends to bind molecule 2 or 1 with the naphthyridine chromophore at the first stage, whereas such a binding strength is rather weak for the other metal ions studied. This viewpoint may be rationalized by a very specific orientation of electron density for two pyridylin lone-pair electrons in the naphthyridine moiety. As a result, naphthyridine favors a complex formation with a soft metal ion of large radius such as Hg²⁺. Further firm support has been given in the NMR titration studies (vide supra), in which the major changes of proton signals occur at the naphthyridine sites in the early stage of the titration with Hg²⁺ ions.

In conclusion, the dual-armed D–A–D molecule 2 exhibits absorptions at longer wavelengths than the A–D molecule 1, and hence provides a more convenient “naked-eye” colorimetric detection of the Hg²⁺ ion. Instead of the commonly used macromolecules for metal ion detection, molecule 2 with the acyclic di(hydroxyethyl)aniline components renders a straightforward preparation and good solubility in aqueous media. The D–A–D constitution demonstrated in this study can serve as a protocol for the future design of a multiple-stage sensing system, which may eventually lead to practical applications on the logic gates based on its sensitivity and selectivity of metal ions and other possible analytes.
The stock solution of compound 1 (0.5 mL of 5 \times 10^{-4} M solution in MeSO-\text{d}_6) with Hg^{2+} ions was prepared by using spectroscopic grade MeSO and distilled water (v/v 1:1). The solution containing compound 2 (0.5 mL of stock solution) in a quartz cell (1 cm width) was placed in an NMR tube, and the \textsuperscript{1}H NMR spectrum was recorded at 298 K. The stock solution of Hg^{2+} ions was introduced in an incremental fashion (0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 4.0, 6.0, 10, and 16 \mu L; 5 \mu L corresponds to 1 equiv), and their corresponding \textsuperscript{1}H NMR spectra were recorded.

The \textsuperscript{1}H NMR titration of 2 (2.5 \times 10^{-3} M in MeSO-\text{d}_6) with MsOH was conducted similarly by incremental additions of MsOH (1.25 M in MeSO-\text{d}_6).

The binding constant was calculated according to the following equation.

\[
y = d/(2c)\left(K^{-1} + c + x - [(K^{-1} + c + x)^2 - 4cx]^{0.5}\right)
\]

where \(c\) is the receptor concentration, \(d\) the saturated chemical shift, \(K\) the association constant, \(x\) the substrate concentration, and \(y\) the chemical shift.

Acknowledgment. We thank the National Science Council for financial support.

Supporting Information Available: NMR spectra, UV–vis titration curves and figures. This material is available free of charge via the Internet at http://pubs.acs.org.

JO050389E