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A Chromo- and Fluoroionophoric Thiaoxaaza-Macrocycle Functionalized with Nitrobenzofurazan Exhibiting Mercury(II) Selectivity

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A chromo/fluorogenic NO_2S_2-macrocycle **L** functionalized with nitrobenzofurazan unit as a dual-signaling probe was synthesized and structurally characterized by single crystal X-ray analysis. In a cation-induced color change experiment, **L** exhibited excellent Hg^{2+} ion selectivity by showing the color change from orange-red to yellow. However, this hypochromic shift by Hg^{2+} was observed for the weaker coordinating anion system such as NO_3^- and ClO_4^- ions. The observed anion effect is due to the strong coordination of anions inhibits the bond formation between Hg^{2+} and the macrocyclic *tert*-N atom, which is sensitive to induce the color change. In the fluorometric experiment, **L** showed chelate-enhanced fluorescence change effect only with Hg^{2+} ion, together with a change from yellow to green emission. The sensing ability for Hg^{2+} with the proposed chemosensor **L** is due to the stable complexation with 1:1 stoichiometry (metal-to-ligand).

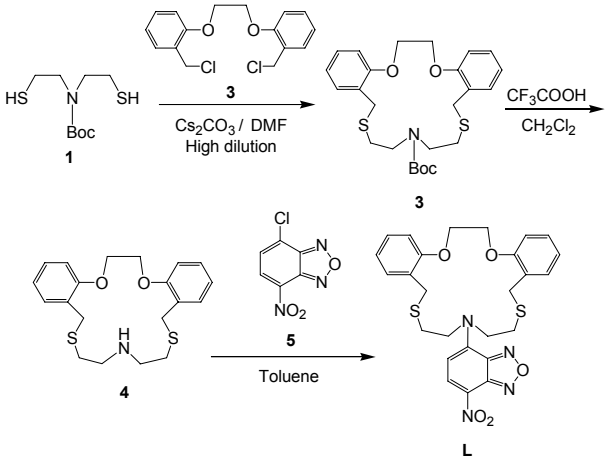
Key Words: NO_2S_2-Macrocycle, Dual-signaling probe, Chromoionophore, Fluoroionophore, Hg^{2+}-selectivity

Introduction

Due to the extreme toxicity of mercury in clinical and environmental areas, many efforts have been devoted to design and prepare various types of mercury(II) sensors.[1-3] A wide range of chemosensors for Hg^{2+} have been progressively improved using redox, chromogenic, or fluorogenic changes.[4-11] Previously, we also reported the pyridine-based N_2S_2 macrocycles functionalized with *p*-nitrobenzene and phenyltricynovinyl moieties, which display attractive color changes by selective Hg^{2+} sensing.[12] Despite the development of individual chromogenic and fluorogenic receptor molecules, there are few examples of receptors capable of displaying two or more signals upon guest (mercury) binding.[13-15] Some organic dye molecules exhibit not only color but also fluorescence. The 7-nitrobenzo-2-oxa-1,3-diazolyl (NBD) unit is a chromo/fluorophore and seemed ideal probe for incorporation in new type of dual-signaling receptors.[16-19] As an extension of our previously results for the Hg^{2+} sensing host system with mono-channel (color) probe,[12] we have worked on the functional macrocycle in terms of the construction of dual-channel (color/fluorescence) probe sensing system. We herein report the synthesis of NBD-attached NO_2S_2 macrocycle **L** (Scheme 1) and its photophysical behaviors as a mercury(II) sensor.

Results and Discussion

As a key precursor, NO_2S_2 macrocycle **4** was synthesized by mercaptan-dihalide coupling reaction of *N*-Boc-dithiol (**1**) with dibenzo-dichloride (**2**) in high dilution condition and then Boc-deprotection as reported previously (Scheme 1).[22] Reaction of the macrocycle **4** with 1.1 equiv of NBD chloride **5** in toluene afforded the target compound 9-(7-nitrobenzo[c][1,2,5]oxadiazol-4-yl)-7,8,9,10,11,13,19,20-octahydro-5H-dibenzo[e,p][1,4,8,14,11]dioxadithiaazacycloheptadecine (**L**) as an orange-colored solid.



Scheme 1. Synthesis of **L**

In acetonitrile, **L** displays very sensitive orange color (λ_{max} = 486 nm, λ_{max} = 24,000 M cm^{-1}) which can be assigned to charge-transfer absorptions (Fig. 1a).[15-18] **L** also showed an intense yellow fluorescence around 536 nm, which is typical of the NBD moiety (λ_{ex} = 480 nm) (Fig. 1b).[16-19]

Colorless crystals of **L** suitable for X-ray crystallography were grown by vapor diffusion of diethyl ether into a dichloromethane solution of this ligand at room temperature. The molecular structure of **L** is shown in Fig. 2 The macrocyclic unit is folded over the NBD subunit. The intercentroid distance of the NBD and the closest benzo moiety is 3.466 Å, reflecting the presence of an offset-face-to-face π-π interaction. Two oxygen atoms are orientated endodentate and two sulfur donors are

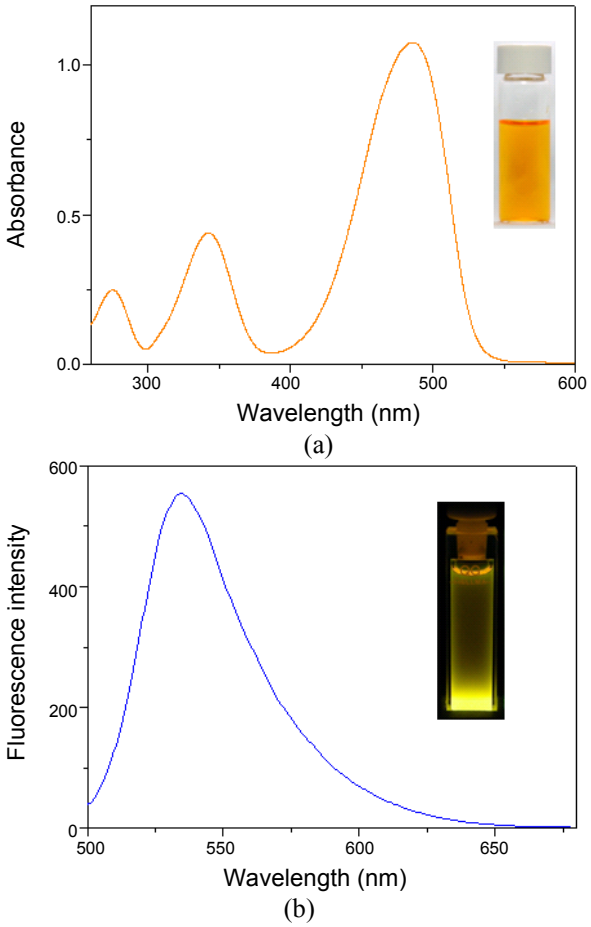


Figure 1. (a) UV-vis and (b) fluorescence spectra of **L** in acetonitrile.

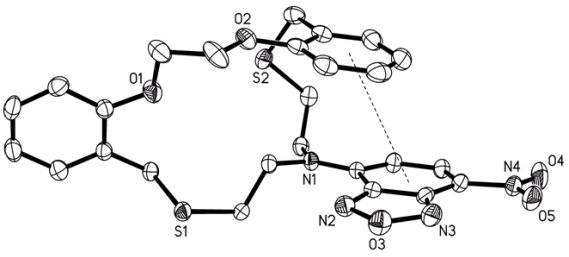


Figure 2. Molecular structure of **L**·0.5CH_2Cl_2 showing an offset-face-to-face π-π interaction (dashed line, centroid-to-centroid distance: 3.466 Å). Hydrogen atoms and solvent molecule are omitted.

exodentate with respect to the macrocyclic cavity. The S1···S2 distance is large at 5.490(2) Å, presumably due to the presence of a repulsive interaction between these donors. The ligand torsion angles between donor atoms are indicative of gauche arrangements [O1-C-C-O2 71.8(4)° and S2-C-C-N1 -76.2(3)°] except that for N1-C-C-S1 [-171.9(2)°].

We next investigated the metal-induced color changes of the ligand in acetonitrile by adding the group I and II (Li^+, Na^+, K^+, and Ba^{2+}), transition and heavy (Ni^{2+}, Cu^{2+}, Zn^{2+}, Al^{3+}, Ag^+, Hg^{2+}, Cd^{2+}, and Pb^{2+}) metal ions. Fig. 3a shows the spectral changes of **L** after adding 5.0 equiv of the metal perchlorates together with the corresponding color changes before and after adding Hg^{2+}. Notably, the large metal-induced hypochromic shift for Hg^{2+} ($\Delta\lambda$ = 86 nm) resulted color change from red-

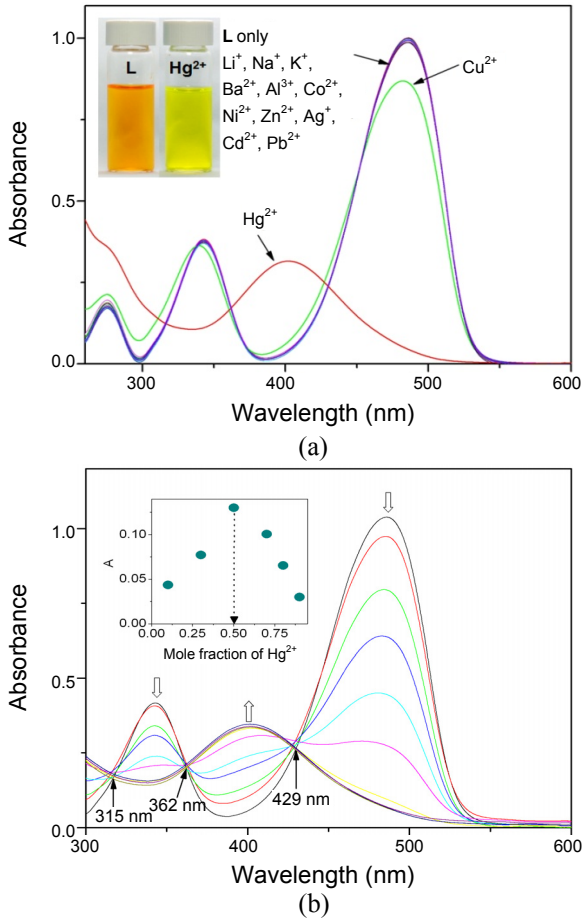


Figure 3. (a) UV-vis spectra of **L** on addition of metal perchlorates (ligand concentration: 0.05 mM in CH_3CN, added metal ion: 5.0 equiv) and (b) UV-vis titration of **L** (0.050 mM) with $Hg(ClO_4)_2$ (0 - 5.0 equiv) in acetonitrile; (inset) Job's plot.

orange to yellow. Whereas, no significant color changes were observed upon addition of selected other metal ions. The color change is attributed to the metal coordination with the bridgehead nitrogen donor (N1 in Fig. 3a) in **L**.

Obvious complex formation of **L** was clearly observed when it was titrated with Hg^{2+} in acetonitrile (Fig. 3b). The stepwise addition of Hg^{2+} causes the ligand absorption (486 nm) to gradually decrease, whereas the complex absorption (400 nm) increases to give isosbestic points at 315, 362 and 429 nm. The spectral features in Fig. 3b are consistent with a 1:1 binding ratio between ligand and Hg^{2+}. Further support for 1:1 binding was also demonstrated by means of a Job's plot experiment. The apparent weaker affinity of **L** towards metals may be explained by the effect of the strong electron-withdrawing NBD group, which may inhibit the coordination of the nitrogen donor to Hg^{2+}. From these results, it is noted that the unique behavior of the proposed ligand system can thus be attributed to its selective complexation affinity for Hg^{2+}.

We also found that the color change for **L** with Hg^{2+} can be affected by the anion employed. For instance, the addition of NO_3^- or ClO_4^- resulted in hypochromic shifts in the spectrum of the mercury complex to 440 nm (NO_3^-) and 400 nm (ClO_4^-) (pale-yellow), respectively (Fig. 4). However, no color changes were observed upon addition of Cl^-, Br^-, I^-, AcO^-, SCN^-, or SO_4^{2-}.

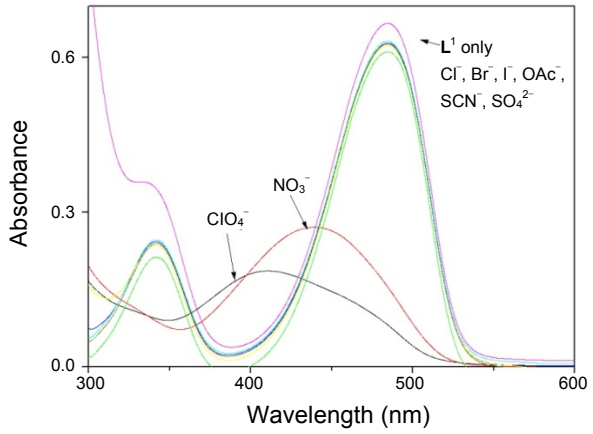


Figure 4. Anion-dependent UV-vis spectral changes of **L** for different Hg(II) salts in acetonitrile.

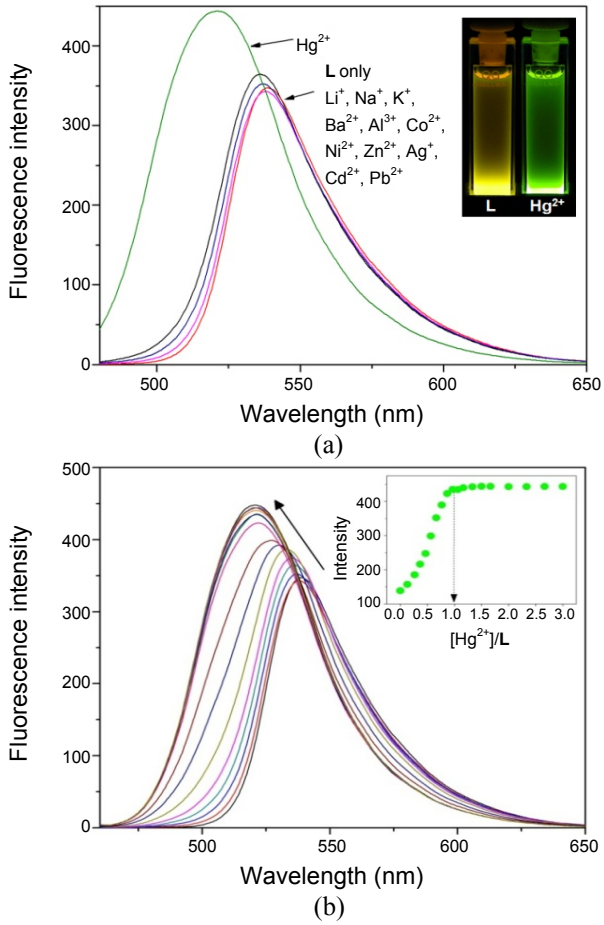


Figure 5. (a) Fluorescence spectra of **L** on addition of metal perchlorates (ligand concentration: 0.05 mM in CH_3CN, added metal ion: 5.0 equiv) and (b) Fluorescence titration spectra for **L** (0.050 mM) with $Hg(ClO_4)_2$ (0-5.0 equiv) in acetonitrile; (inset: fluorescence intensity at 520 nm *vs* the number of equivalents of Hg^{2+} added to **L**).

This is attributed to the stronger coordination ability of these latter anions to Hg^{2+} ion, because the strong coordination of anions inhibits the bond formation between Hg^{2+} and the macrocyclic *tert*-N atom, which is sensitive to induce the color change. The similar behaviors were reported in terms of the strong coordination of these latter anions acting to prevent $Hg\text{-}N_{bridgehead}$ bond formation, resulting in no color change.[23] In this case, the Hg^{2+} ion is expected to bind to two sulfur doners.[23]

The binding properties of **L** were also examined with respect to its fluorescence behavior. **L** shows a yellow fluorescence at 536 nm in acetonitrile. The fluoroionophoric behavior of **L** was investigated in acetonitrile on addition of metal ions. Fig. 5a shows the spectral changes for **L** after adding 5.0 equiv of the metal perchlorates shown together with the corresponding fluorescence emission changes. Interestingly, a cation-induced blue shift occurred for Hg^{2+} ($\Delta\lambda = 16$ nm), resulting in a change from yellow to green fluorescence; whereas, no significant color changes were observed upon addition of the other metal ions employed.

The fluorescence titration of **L** with $Hg(ClO_4)_2$ were also carried out. As shown in Fig. 5b, upon adding Hg^{2+} ion, the fluorescence intensity of **L** increases and is accompanied by a blue shift in the emission spectrum. The emission spectrum of free **L** displays a band with a maximum at 536 nm. When Hg^{2+} was added to the solution of **L**, an intensity increase at 520 nm was observed. Further support of the 1:1 binding ratio was demonstrated by means of a fluorescence titration experiment (see inset of Fig. 5b).

Conclusion

In summary, the chromo- and fluorogenic NBD-attached NO_2S_2-macrocycle **L** was synthesized and its structure was confirmed by NMR and X-ray crystallography. A cation-induced hypochromic shift for Hg^{2+} was observed resulting in a color change from orange to pale-yellow. Whereas, no significant color changes were observed upon addition of the selected other metal ions. In the fluorescence study for **L**, only Hg^{2+} induced fluorescence emission changes from yellow to green. These were monitored by both colorimetric and fluorescence techniques that showed fast 1:1 stoichiometric responses to the amount of Hg^{2+} present in solution.

Experimental Section

General methods. All commercial reagents including solvents were of analytical reagent grade. NMR spectra were recorded on a Bruker DRX-300 spectrometer (300 MHz). Infrared spectra were measured with a Mattson Genesis Series FT-IR spectrophotometer. The mass spectra were obtained on a JEOL JMS-700 spectrometer at the Central Instrument Facility of Gyeongsang National University. The melting points were determined on a Electrothermal IA-9200 laboratory device and were not corrected.

Synthesis of L. A solution of 4-chloro-7-nitro-benzofurazan in toluene (11 mmol in 40 mL) was added dropwise to a boiling solution of precursor macrocycle **4** in toluene (10 mmol in 150 mL). The reaction mixture was then maintained at reflux for 3 h with rapid stirring, allowed to cool to room temperature, then filtered. The filtrate was evaporated and the residue was partitioned between water and dichloromethane. The aqueous phase was separated and extracted with two further portions of dichloromethane. The combined organic phases were dried with anhydrous sodium sulfate and then evaporated to dryness. Column chromatography on silica gel (30% ethyl acetate/*n*-hex-

Table 1. Crystal data and structural refinement

	L·0.5CH_2Cl_2
Formula	$C_{26.5}H_{26}ClN_4O_5S_2$
M	580.08
T/*K*	173(2)
Crystal system	Monoclinic
Space group	*C*2/*c*
a/Å	16.998(2)
b/Å	8.861(1)
c/Å	36.424(5)
β/°	99.648(2)
V/Å^3	5409 (1)
Z	8
μ(MoKα)/mm^{-1}	0.341
Reflections collected	12701
Independent reflections	5176
Goodness-of-fit on F^2	1.055
Final R_1, wR_2 [$I > 2\sigma(I)$]	0.0595, 0.1430
All data	0.0935, 0.1630

Table 2. Selected bond lengths (Å), bond angles (°) and torsion angles (°) for **L**·0.5CH_2Cl_2

S(1)-C(9)	1.801(3)	Hg(1)-Cl(2)	2.364(3)
S(1)-C(8)	1.820(3)	Hg(1)-S(2)	2.657(3)
S(2)-C(12)	1.814(4)	Hg(1)···O(1)	5.418(9)
S(2)-C(13)	1.818(4)		
C(9)-S(1)-C(8)	99.56(15)	C(21)-N(1)-C(11)	120.1(3)
C(12)-S(2)-C(13)	103.53(18)	C(21)-N(1)-C(10)	124.2(3)
C(2)-O(1)-C(1)	119.4(3)	C(11)-N(1)-C(10)	115.7(2)
C(19)-O(2)-C(20)	117.9(3)		
O(1)-C(1)-C(20)-O(3)	78.8(4)	S(1)-C(9)-C(10)-N(1)	−76.2(3)
S(2)-C(12)-C(11)-N(1)	−171.9(2)		

ane) gave **L** as an orange-colored solid. Yield: 52%. mp 120 - 122 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.78 (t, 4H, S$CH_2$$CH_2$), δ 3.88 (s, 4H, Ar$CH_2$), δ 4.16 (m, 4H, N$CH_2$$CH_2$), δ 4.41 (s, 4H, O$CH_2$), δ 5.87 (d, 1H, NBD), 6.09-7.37 (m, 8H, Ar), δ 8.30 (d, 1H, NBD). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3, 144.1, 135.1, 131.1, 128.7, 121.7, 111.9, 101.3, 67.5, 47.2, 31.4, 29.4. IR (KBr, cm^{-1}): 3383, 2923, 1678, 1494, 1451, 1241, 763. HRMS (*m*/*z*) calcd. For $C_{26}H_{26}N_4O_5S_2$: 538.1345; found: 538.1344.

Crystallography. A crystal suitable for X-ray diffraction was mounted on a Bruker SMART diffractometer equipped with a graphite monochromated Mo Kα (λ = 0.71073 Å) radiation source and a CCD detector and 45 frames of two-dimensional diffraction images were collected and processed to deduce the cell parameters and orientation matrix. A total of 1271 frames of two-dimensional diffraction images were collected, each of which was measured for 30 s. The frame data were processed to give structure factors by the program SAINT.[20] The intensity data were corrected for Lorentz and polarization effects. The structures were solved by a combination of the direct method and the difference Fourier methods provided by the program package SHELXTL,[21] and refined using a full matrix least square against F^2 for all data. All the non-H atoms were refined anisotropically. All hydrogen atoms were included in calculated positions with isotropic thermal parameters 1.2 times those of attached atoms. Crystallographic data are summarized in Table 1. Selected geometric parameters for the respective complexes are presented in Table 2.

Supplementary Material. Supplementary crystallographic data associated to **L** has been deposited at the Cambridge Crystallographic Data Centre, CCDC No. 746974. Copies of the data can be obtained free of charge on application to CCDC, 12 Union road, Cambridge CB2 1EZ, UK (fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk), or electronically *via* www.ccdc.cam.ac.uk/data_request/cif.

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