Supporting information for

Design and Synthesis of Thiazoline-Thiazole Hybrid Macrocycles Possessing Strong Binding Affinity to Pb^{2+} and Cd^{2+}

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1. Procedure for the synthesis of macrocycles 7 and 8 via cyclooligomerization

To an anhydrous CH_2Cl_2 (82 mL) solution of thiol carboxylic acid **4** (105 mg, 0.33 mmol, 4 mmol/L) was added BOP-Cl (251 mg, 3.0 eq.) and Et_3N (275 μL, 6.0 eq.), the mixture was stirred at ambient temperature for 18 to 20 h. The solution was then washed with 5% aq. $NaHCO_3$ and brine. The separated organic layer was dried over $MgSO_4$, concentrated, and purified by flash column chromatography on silica gel (Hexane/EtOAc, 2:1) to give a mixture of cyclooligomerization product, tetramer **5** and pentamer **6** (67 mg, 68% total, molar ratio = ca. 1.9:1). The mixture was then treated with neat TFA at room temperature for 20 min and the evaporated to dryness. The residue was dissolved in benzene and the solution was refluxed for 4 h, and the solution was evaporated to leave a crude mixture. The crude mixture were purified by PTLC (MeOH/EtOAc, 1:6) to give pure **7** (17.7 mg, 68%) and **8** (10.3 mg, 64%).

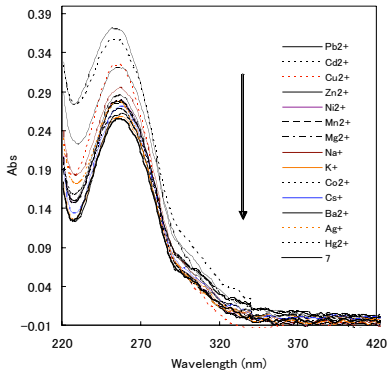
1.1 Physical and spectra data of macrocycles 7 and 8

Macrocycle 7: $[\alpha]_D^{25}$ –147.6 (*c* 0.26 in $CHCl_3$); IR (neat, cm^{-1}) 3112, 2961, 2923, 2853, 1592, 1036; ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.90 (s, 1H), 4.58 (d, *J* = 11.2 Hz, 1H), 3.28 (d, *J* = 11.2 Hz, 1H), 1.98 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 172.1, 164.4, 147.2, 121.5, 83.6, 40.8, 29.6; FABMS: [M^+]: 729; HRMS Calcd. for $C_{28}H_{25}N_8S_8$: 728.9968; Found: 728.9967.

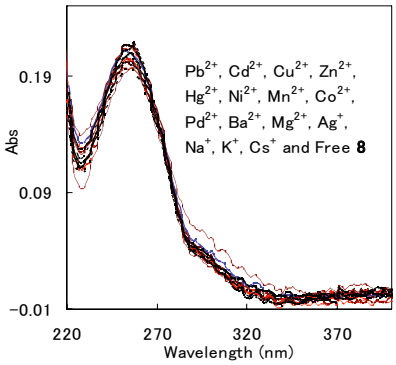
Macrocycle 8: $[\alpha]_D^{25}$ –157.9 (*c* 0.13 in $CHCl_3$); IR (neat, cm^{-1}) 3112, 2962, 2923, 2853, 1593, 1036; ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.83 (s, 1H), 4.43 (d, *J* = 11.2 Hz, 1H), 3.28 (d, *J* = 11.2 Hz, 1H), 1.85 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 174.6, 164.5, 147.6, 121.2, 83.8, 41.9, 29.3; FABMS: [M^+]: 911; HRMS Calcd. for $C_{35}H_{30}N_{10}S_{10}$: 909.9862; Found: 909.9822.

2. **Binding studies of macrocyclic receptors with various metal ions using UV/Vis titrations (representative example using compound 7).**

Stock solutions of compound **7** (1 mM) and metal chlorides (5 mM, nitrate salt for Ag^{+}) of Na^{+}, K^{+}, Cs^{+}, Mg^{2+}, Ba^{2+}, Co^{2+}, Mn^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Pd^{2+}, Cd^{2+}, Hg^{2+}, and Pb^{2+} were prepared by using a mixture of spectroscopic grade MeOH and de-ionized H_2O (95:5, v:v). To a solution of **7** (50 μL) was added 10 μL of each metal-ion solution, and the resulting solution was diluted to 500 μL with a mixture of MeOH and de-ionized H_2O (95:5, v:v). The solution was then stood at room temperature for 30 min. UV/Vis absorption was measured, and each measurement was at least duplicated. Titrations of **8** with various metal ions were carried out by executing the same procedure. Titration studies using the acetate form of metal ions showed similar results to those using the corresponding chloride forms.



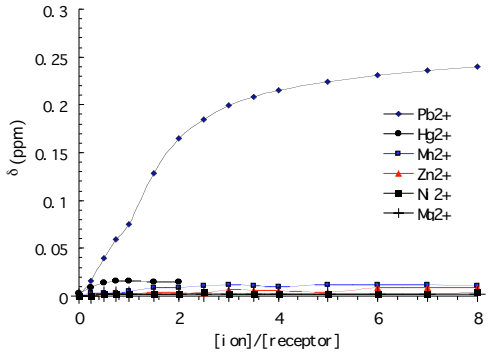
S-Figure 1. UV/Vis titrations of macrocycle **7** with various metal ions at a molar ratio of 1:1.



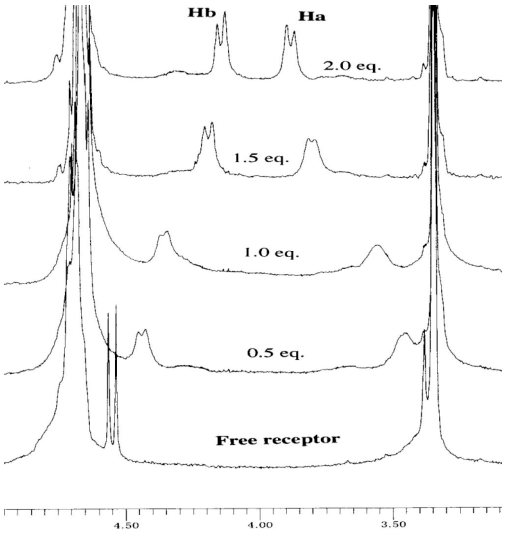
S-Figure 2. UV/Vis titrations of macrocycle **8** with various metal ions at a molar ratio of 1:1.

3. Binding studies of 7 with various metal ions using NMR titrations.

Seven samples of solution **7** (2 mM, 0.5 mL) in a mixture of $CD_3OD/CDCl_3$ (1:1, v:v) were prepared. Stock solutions of acetate salts of Pb^{2+}, Ni^{2+}, Mn^{2+}, Mg^{2+}, Zn^{2+}, Hg^{2+}, and Cd^{2+} (25 mM containing 2 mM of **7**) in a miture of $CD_3OD/CDCl_3$ (1:1, v:v) were prepared. After taking ^{1}H-NMR spectrum of free **7**, the stock solutions of metal ions were added to each solution of **7**, respectively, in an aliquot portions (10, 10, 10, 10, 20, 20, 20, 20, 40, 40, 40, 80, and 80 μL). ^{1}H-NMR spectra of the complexes were taken at room temperature after standing of the mixtures at room temperature for 30 min. The chemical shift changes were curved as a function of molar ratio between metal ions and free receptors. Time dependant titrations showed that further standing of the samples from 2 h to overnight resulted in no chemical shift change.



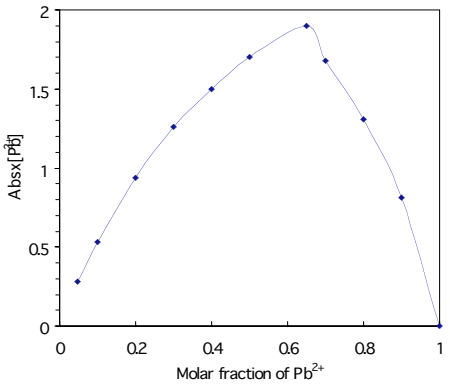
S-Figure 3. ^{1}H-NMR titration curves of macrocycle **7** with various metal ions



S-Figure 4. The thiazoline proton region of overlaid ^{1}H-NMR spectra of free **7** and the mixtures of **7** and Pb^{2+} at various molar ratio.

4. Determination stoichiometry by continuous variation methods using UV/Vis titrations

Stock solutions of Pb^{2+} (50 μM) and **7** (50 μM) were prepared, respectively, and were separated into 10 sample tubes with ion *vs.* receptor volume ratio as following: 20:1, 9:1, 4:1, 7:3, 3:2, 1:1, 2:3, 1:2, 1:4, 1:9. UV/Vis spectroscopies of all the samples were recorded and a Job's plot was curved.



S-Figure 5. Job's plot for the complexation of macrocycle **7** with Pb^{2+}