HETEROCYCLES, Vol. 75, No. 6, 2008, pp. 1457 - 1466. © The Japan Institute of Heterocyclic Chemistry
Received, 14th December, 2007, Accepted, 8th February, 2008, Published online, 15th February, 2008. COM-07-11305

METALLORECEPTORS COMPOSED OF ORGANOPALLADIUM COMPLEXES CONTAINING 5-MERCAPTO-3*H*-1,3,4-THIADIAZOLIN-2-ONES

Nam Sook Cho,* Sang Beom Kim, Min Hye Kim, Seong Gyun Park, Sung Kown Kang, Se Jin Lee, and Yeong-Joon Kim

Department of Chemistry, Chungnam National University, Daejeon, 305-764, Korea *E-mail: nsmcho@cnu.ac.kr

Abstract – Macrocyclic ligands containing two 5-mercapto-3*H*-1,3,4-thiadiazoline-2-one groups and one 1,3-benzenedimethanethiol group, which served to link the 2- and 5-positions of the heterocycle unit and chelate palladium ion, respectively, were synthesized by regiospecific *S*-alkylation of 5-ethoxy-3*H*-1,3,4-thiadiazoline-2-thione. The structures of the resulting metalloreceptors were established using ^{1}H and ^{13}C NMR, FTIR spectroscopy, MS spectrometry, and elemental analysis. The molecular recognition ability of the metalloreceptors was examined against DNA/RNA nucleobases and acetanilide. The complexation strength of both compounds increased in the order acetanilide/uracil/thymine < adenine < cytosine.

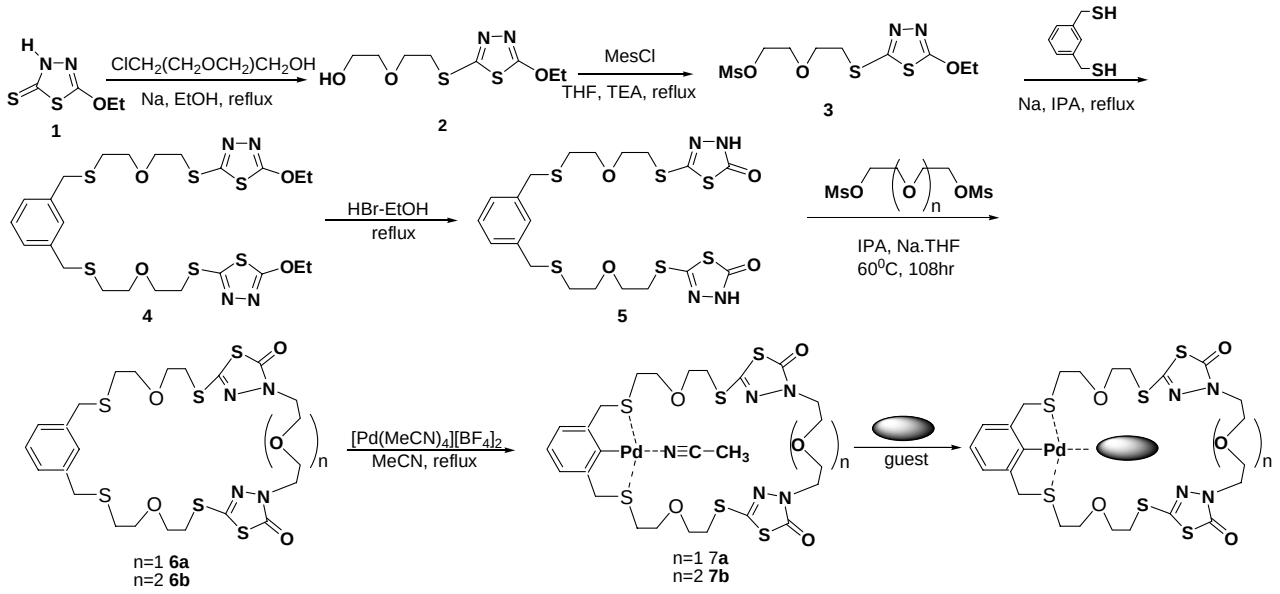
INTRODUCTION

Metalloreceptors are transition metal complexes containing peripheral sites capable of hydrogen-bonding or π -stacking interactions and serve as hosts for neutral guests. Organopalladium metalloreceptors use δ-donation to a transition metal (Pd) and non-covalent second-sphere interaction, such as hydrogen bonding and π-stacking, to produce molecular recognition. Organopalladium complexes containing heterocyclic moieties such as 5-amino-3*H*-1,3,4-thiadiazolin-2-one[1] and 5-amino-3*H*-1,3,4-thiadiazolin-2-thione[2] have been studied previously as metalloreceptors for DNA/RNA nucleobases. As a continuation of these studies[1,2] and to improve specific molecular recognition of nucleobases, we have turned our attention to the synthesis of compounds composed of two 5-mercapto-3*H*-1,3,4-bithiadiazolin-2-one functional groups and one 1,3-benzenedimethane-thiol group. Heterocyclic moieties such as 5-mercapto-3*H*-1,3,4-thiadiazolin-2-one, 5-amino-3*H*-1,3,4-thiadiazolin-2-one[1] and 5-amino-3*H*- 1,3,4-

thiadiazolin-2-thione[2] differently serve to form hydrogen bonding. Thus the complexation constants were measured to examine the effect of heterocyclic moieties on the molecular recognition.

RESULTS AND DISCUSSION

The macrocyclic compounds **6a** and **6b** were synthesized from **1** in a similar method as previously reported, through regiospecific *S*-alkylation of 5-ethoxy-3*H*-1,3,4-thiadizoline-2-thione under basic conditions,[3,4] and N-alkylation of 5-substituted-3*H*-1,3,4-thiadiazolin-2-one[3,4] as shown in **Scheme 1**. According the regiospecific *S*-alkylation of **1**, the reaction of **1** with 5-chloro-3-oxa-pentanol, in the presence of NaOEt in EtOH, yielded product **2**,[3,4] confirmed by ^{1}H and ^{13}C NMR spectra. NMR peaks corresponding to the NH group in compound **1** were replaced by SCH_2 signals at 3.42 and 33.2 ppm in the ^{1}H and ^{13}C NMR spectra, respectively.[3,4] In the ^{13}C NMR, the peaks corresponding to the thione



Scheme 1. Synthesis of macrocycles and palladium metalloreceptors

component of **1** (184.2 ppm) were replaced by peaks more representative of a sulfide group (157.4 ppm).[3,4] The OH group in compound **2** was mesylated to increase lability, yielding **3**. To introduce a palladium chelation site, 1,3-benzenedimethanthiol was *S*-alkylated with **3** under basic conditions (N π aOCH$(CH_3)_2$/$(CH_3)_2$CHOH).[5] The formation of **4** was confirmed by the replacement of the SH signal of 1,3-benzenedimethanethiol by peaks corresponding to the presence of a SCH_2 group at 2.60 and 30.7 ppm in the ^{1}H and ^{13}C NMR spectra, respectively.[5] Compound **4** was cleanly dealkylated with HBr yielding compound **5**.[3,4] NMR spectra showed that the ethoxy group in **4** was replaced by a lactam NH (^{1}H chemical shift 10.33 ppm) and the chemical shifts of atoms C(2) and C(5) in the aromatic ring were shifted from 174.9 and 157.5 ppm to 172.6 and 150.5 ppm, respectively.[3,4] Furthermore, FTIR spectra showed a strong amide carbonyl band at 1692 cm^{-1}.[3,4] This suggests that **5** exists in a primarily lactam

form. The NH of **5** is sufficiently acidic to be alkylated in $NaOCH(CH_3)_2/(CH_3)_2CHOH$ with either 3-oxa-pentyl-1,5-dimethanesulfonate or 1,6-dioxa-octyl-1,8-dimethanesulfonate. To create the final macrocyclic compounds, an intermolecular Cs^+-mediated cyclization was employed through N,N-bisalkylation of **5** using the corresponding α,ω-dimethanesulfonate at high dilution.[3,4] The structures of the macrocycles were firmly established by ^1H NMR, ^{13}C NMR, FTIR, and FAB-HRMS. The successful macrocyclization of **5** to **6a** through *N*-alkylation was evident from the replacement of the NCH_2 group in **5** by the NH functional group in **6a**, represented by chemical shifts at 3.75 and 46.6 ppm in the ^1H and ^{13}C NMR spectra, respectively.[3,4] The chemical composition of **6a** was confirmed by FAB-HRMS data ($C_{24}H_{32}N_4O_5S_6$, 648.0775, Found 648.0773). Furthermore, X-ray crystallographic studies of **6a** indicate a macrocyclic structure (**Figure 1**).

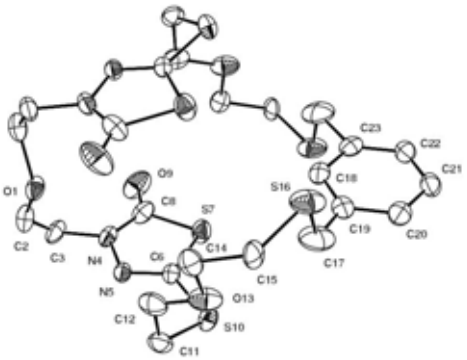


Figure 1. ORTEP rendering of **6a** showing the atomic numbering used in the crystallographic analysis

The macrocyclic ligands (HL) **6a** and **6b** were easily palladated by refluxing an acetonitrile solution of HL with one equivalent of the Pd complex $[Pd(CH_3CN)_4][BF_4]_2$.[1,2] The three equivalent acetonitrile ligands on the Pd complex were effectively replaced with one equivalent of HL to yield a complete metalloreceptor. All spectroscopic and analytical data were consistent with palladation and the chemical formula $Pd(L)(CH_3CN)][BF_4]$. In accordance with previous results,[1,2] one hydrogen atom was lost from the aromatic ring, and the ^1H NMR chemical shifts of the benzylic CH_2S protons of **7a** were shifted downfield (3.88 ppm) and significantly broadened relative to those of the free ligand HL (3.77 ppm). The effect of palladation was also evident in the ^{13}C NMR spectrum, in which the resonance of benzylic carbon atoms was shifted downfield by 9.5 ppm (from 36.4 ppm to 45.9 ppm), and the resonance of the Pd-bound carbon atom shifted from 129.3 ppm to 151.7 ppm.[1,2] A strong peak in the FAB-HR mass spectrum corresponding to $[Pd(L)]^+$ (752.9651) provides further support for palladation. The resulting complexes were colorless, air-stable solids and soluble in most polar organic solvents.

A guest molecule can be coordinated within these organopalladium metalloreceptors by σ-donation to the Pd center with simultaneous hydrogen bond interactions with the peripheral oxygen and nitrogen atoms of

the thiadiazoline rings and the side chains. To examine the molecular recognition, that is, coordination, of the metalloreceptors synthesized herein, ^{1}H NMR spectra were recorded in the presence of the following guest molecules: cytosine, adenine, thymine, uracil, and acetanilide. The host molecule, a macrocyclic metalloreceptor, was dissolved in DMSO-d_6 (0.01–0.02 M). Guest stock solutions in DMSO-d_6 (0.04–0.08 M) were added in small increments until any changes to the ^{1}H NMR chemical shifts were complete.[1,2] The calculated complexation constants (K) are listed in **Table 1**.

No changes in the ^{1}H NMR chemical shifts were observed for **7a** and **7b** in response to up to ten equivalents of thymine, uracil, and acetanilide, indicating negligible coordination of the guest molecules. In contrast, **7b** exhibited major ^{1}H NMR chemical shifts upon addition of cytosine. One equivalent of guest molecule was sufficient to produce a complete change in chemical shift. We therefore assumed that $K > 10^4$ (K = [HG]/[H][G], where H = host, G = guest, and HG = host–guest complex). Complexation constants associated with **7a** increased in the following order: thymine/uracil/acetanilide < cytosine < adenine. The same trend was observed for **7b**, although the observed K values were a little larger. We therefore concluded that the larger macrocycle cavity of **7b** due to the increased chain length between thiadizoline rings showed similar the complexation ability of the metalloreceptor.

Table 1. Complexation constants (K)[a] of $ArCH_2S$ in metalloreceptor **7** upon addition of guest molecules

Guest		Cytosine	Adenine	Thymine	Uracil	Acetanilide
Host (**7a**)	**K**(M^{-1})	$9.00 \pm 0.14 \times 10^3$	$6.04 \pm 0.13 \times 10^3$	<1[b,d]	<1[b,d]	<1[b,d]
Host (**7b**)	**K**(M^{-1})	>1 × $10^{4c,d}$	$7.67 \pm 0.16 \times 10^3$	<1[b,d]	<1[b,d]	<1[b,d]

[a] K was obtained from the slope of the plot [HG]/[H] versus [G] measured by ^{1}H NMR titration.
[b] No chemical shift changes were observed upon the addition of up to ten equivalents of guest molecules.
[c] One equivalent of guest molecule was sufficient to produce a complete change in chemical shift.
[d] These values were estimated based on the approximation that peaks less than 1/10 of the major peak intensity usually cannot be recognized in a NMR experiment. Thus, K = (0.001 M)/(0.01 M × 0.1 M) = 1 M^{-1} and K = (0.01 M)/(0.001 M)(0.001 M) = 10000 M^{-1} under experimental conditions.

While a comprehensive explanation for the results in **Table 1** is not straightforward, it is clear that the basicity of the guest is an important factor in complex formation.[1,2] The trend in K is the same as that previously reported in similar systems, such as 5-amino-3*H*-1,3,4-thiadiazolin-2-one[1] and 5-amino-3*H*-1,3,4-thiadiazolin-2-thione.[2] While many possible binding sites exist on nucleobase molecules, metal ion binding predominantly occurs at N3 in pyrimidine bases and at N1 or N7 in purine bases.[6] The basicity at N3 in cytosine and N1 in adenine is much higher than that at any of the nitrogen sites in thymine, uracil, or acetanilide. If one solely considers the basicity of the guest binding site as the only factor contributing to complexation ability, then the difference between N3 in cytosine (pK_a = 4.5) and N1 in

adenine (pK_a = 4.1)[7] results in approximately 2.5 (= $10^{4.5-4.1}$) times greater binding ability for cytosine relative to adenine. The experimental values for the ratio of K(cytosine)/K(adenine) are 1.4 and 1.3 for **7a** and **7b**, respectively, which are smaller than the K_a(cytosine)/K_a(adenine) ratio. However, in a previous metalloreceptor system, 5-amino-3*H*-1,3,4-thiadiazoline-2-thione, the ratio of K(cytosine)/K(adenine) are 2.9 and 8 for small macrocycle and large macrocycle, respectively, which are larger than 2.5. In addition, K values observed in this study were larger than those in previous report with 5-amino-3*H*-1,3,4-thiadiazoline-2-thione[2] and similar constants obtained with 5-amino-3H-1,3,4-thiadazolin-2-one.[1] Therefore the observed differences in K cannot be explained only by the basicity of the guest molecule. Thus, other effects, such as hydrogen bonding, must play an important role in stabilizing the host–guest complex.

Despite differences in the ring cavity size, similar K values were observed. This system would imply that the flexibility of the host molecule does not greatly influence its ability to form complexes with the guest molecule. However, in a previous metalloreceptor system, which contained two 5-amino-3*H*-1,3,4-thiadiazoline-2-thione groups, K values depended strongly on the cavity size.[2] The large metalloreceptor K(cytosine)/K(adenine) is 2.8 times larger than the small metalloreceptor.[2] Stabilizing factor of host-guest such as hydrogen bonding is particularly important in a flexible host 5-amino-3*H*-1,3,4-thiadiazoline-2-thione system,[2] in which conformational changes necessary to accommodate hydrogen bonding are much more feasible.[2] In these studies, differences in binding constants were indicative of large differences between metalloreceptors. However, the only structural difference could be found in carbonyl groups on the heterocycles and side chains. Since the larger binding constants were observed with the carbonyl-possessing compounds, we concluded that hydrogen bond formation played an important role in stabilizing the host-guest complex.

EXPERIMENTAL

All melting points were determined on an electrically heated Thomas-Hoover capillary melting point apparatus and were uncorrected. The IR spectra were recorded on a Jasco Report-100 spectrophotometer. The ^{1}H and ^{13}C NMR spectra were obtained using a Bruker ARX-400 spectrometer at 400 MHz and 100 MHz respectively with tetramethylsilane as the internal reference. NMR measurements were performed at the Central Research Facilities of Chungnam National University. Elemental analyses were carried out on an EA 1110 (CE Instrument). FAB-HRMS spectra were obtained on a JEOL-JMS HX-100/110A spectrometer at Korea Basic Science Institute, Taeduk, Taejeon.

Syntheses of (5-ethoxy-3*H*-1,3,4-thiadiazolin-2-thione) **(1)** followed the previous procedures.[8]

3-Oxo-5-(5-Ethoxy-1,3,4-thiadiazol-2-yl)thiopentanol (2)[3,4]

(5-Ethoxy-3*H*-1,3,4-thiadiazolin-2-thione **1** (12 g, 74.0 mmol) was dissolved in EtOH (200 mL)–Na (1.8 g, 77.7 mmol). The solution of 5-chloro-3-oxapentanol (9.2 g, 74.0 mmol) in EtOH (20 mL) was added to the above solution and the reaction mixture was at reflux for 31 hr. The mixture was cooled to room temperature and THF (100 mL) added to the reaction mixture. TEA salt was filtered off, the filtrate was washed with saturated aqueous NH_4Cl and dried with anhydrous $MgSO_4$. Solvent was removed under reduced pressure and then the residue was column chromatographed using *n*-hexane : EtOAc : EtOH = 5 : 3 : 1 as eluent affording colorless liquid product (4.6 g, 70%). R_f: 0.5 (*n*-hexane : EtOAc : EtOH = 5 : 3 : 1). IR (KBr pellet, cm^{-1}): 3398 (OH), 2932, 2867 (CH), 1697, 1512 (C=N).^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.55 (2H, q, *J* = 7.2 Hz, $OC\underline{H}_2CH_3$), 3.83 (2H, t, *J* = 6.4 Hz, $OC\underline{H}_2CH_2OH$), 3.73 (2H, t, *J* = 6.4 Hz, CH_2OH), 3.62 (2H, t, *J* = 6.4 Hz, OCH_2), 3.42 (2H, t, *J* = 6.4 Hz, SCH_2), 2.68 (1H, s, OH) 1.45 (3H, t, *J* = 7.2 Hz, CH_3).^{13}C NMR (100 MHz, $CDCl_3$, δ): 157.4 (S-C=N), 175.1 (0-C=N), 72.1 (CH_2OH), 69.2 ($O\underline{C}H_2CH_2OH$), 69.1 ($O\underline{C}H_2CH_3$), 61.5 ($O\underline{C}H_2CH_2S$), 33.2 (CH_2S), 14.3 (CH_3). Anal. Calcd for $C_8H_{14}N_2O_3S_2$: C 38.38; H 5.64; N 11.19; S 25.62. Found: C 38.39; H 5.63; N 11.19; S 25.64.

[5-(5-Ethoxy-1,3,4-thiadiazol-2-yl)thio]-3-oxapentyl methanesulfonate (3)

Compound **2** (12.1 g, 48.5 mmol) was dissolved in THF (300 mL) and triethylamine (8.3 g, 72.7 mmol). The methanesulfonyl chloride (9.8 g, 96.9 mmol) in THF (30 mL) was added to the above solution dropwise and then the reaction mixture was stirred for 27 hr at rt. The completion of the reaction was followed with TLC by disappearance of compound **2**. After completion of reaction, the reaction mixture was washed with saturated aqueous NH_4Cl, organic layer was dried with $MgSO_4$. Solvent was removed under reduced pressure and then the residue was column chromatographed using *n*-hexane : EtOAc = 1 : 1 as eluent affording colorless liquid product (15 g, 95%). liquid. R_f: 0.25 (*n*-hexane : EtOAc = 1 : 1). IR (KBr pellet, cm^{-1}): 2984, 2937 (CH), 1696, 1512 (C=N), 1351, 1258 (S=O). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.55 (2H, q, *J* = 7.2 Hz, $OC\underline{H}_2CH_3$), 4.36 (2H, t, *J* = 6.4 Hz, CH_2OSO_2), 3.84 (2H, t, *J* = 6.4 Hz, $OC\underline{H}_2CH_2OSO_2$), 3.77 (2H, t, *J* = 6.4 Hz, OCH_2), 3.42 (2H, t, *J* = 6.4 Hz, SCH_2), 3.09 (3H, s, CH_3SO_2), 1.46 (3H, t, *J* = 7.2 Hz, CH_3).^{13}C NMR (100 MHz, $CDCl_3$, δ): 175.0 (O-C=N), 157.2 (S-C=N), 69.5, 69.4 ($O_2SOCH_2CH_2O$), 68.9 ($O\underline{C}H_2CH_3$), 68.7 ($O\underline{C}H_2CH_2S$), 37.7 (CH_3SO_2), 32.9 (CH_2S), 14.4 (CH_3). Anal. Calcd for $C_9H_{16}N_2O_5S_3$: C 32.91; H 4.91; N 8.53; S 29.29. Found: C 32.90; H 4.92; N 8.51; S 29.31.

***α,α′*-Bis[5-(5-ethoxy-1,3,4-thiadiazol-2-yl)thio]-3-oxa-1-pentythio-*m*- xylene (4)[5]**

1,3-Benzenedimethanthiol (2.4 g, 13.8 mmol) was dissolved in *i*-PrOH (300 mL)-Na (0.67 g, 29.1 mmol). The compound **3** (9.1 g, 27.7 mmol) in THF (20 mL) was added to the above solution and the reaction mixture was stirred at reflux for 32 hr. The mixture was cooled to rt and salt was filtered off. The filtrate was washed with saturated aqueous NH_4Cl and dried with anhydrous $MgSO_4$. Solvent was removed under reduced pressure and then the residue was column chromatographed using $CHCl_3$: EtOAc : *n*-hexane = 6 : 4 : 5 (4.4 g, 50%) as eluent affording colorless liquid product. R_f: 0.5 ($CHCl_3$:

n-hexane : EtOAc = 6 : 4 : 5). IR (KBr pellet, cm^{-1}): 2921 (CH), 1695, 1604 (C=N), 1587 (C=C). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.28-7.20 (4H, m, C_6H_4), 4.55 (4H, q, *J* = 7.2 Hz, $2OC\underline{H_2}CH_3$), 3.78 (s, $2C_6H_4C\underline{H_2}S$) 3.75 (4H, t, *J* = 6.4 Hz, $2C_6H_4CH_2SCH_2C\underline{H_2}O$), 3.60 (4H, t, *J* = 6.4 Hz, $2OCH_2$), 3.40 (4H, t, *J* = 6.4 Hz, $2CH_2S$), 2.60 (4H, t, *J* = 6.4 Hz, $2C_6H_4CH_2SC\underline{H_2}$), 1.45 (6H, t, *J* = 7.2 Hz, $2CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 174.9 (O-C=N), 157.5 (S-C=N), 138.5, 129.3, 128.5, 127.6 (C_6H_4), 70.7 ($O\underline{C}H_2CH_3$), 69.3, 69.1 (CH_2OCH_2), 36.6 ($C_6H_4\underline{C}H_2S$), 33.1 (CH_2S), 30.7 ($C_6H_4CH_2S\underline{C}H_2$), 14.4 ($CH_3$). Anal. Calcd for $C_{24}H_{34}N_4O_4S_6$: C 45.40; H 5.40; N 8.82; S 30.30. Found: C 45.41; H 5.42; N 8.80; S 30.32.

α,α′-Bis[5-(5-oxo-4*H*-1,3,4-thiadiazol-2-yl)thio]-3-oxa-1-pentythio-*m*-xylene (5)[3,4]

Compound **4** (2.4 g, 3.8 mmol) was dissolved in EtOH (60 mL) and hydrobromic acid (48%, 1.3 mL, 11.5 mmol). The reaction mixture was stirred at reflux for 24 h. The completion of the reaction was followed with TLC by disappearance of compound **4**. After completion of reaction, the reaction mixture was washed with saturated aqueos NH_4Cl, organic layer was dried with $MgSO_4$. Solvent was removed under reduced pressure and then the residue was column chromatographed using *n*-hexane : EtOAc = 1 : 1 as eluent affording colorless liquid product (1.2 g, 53%). R_f: 0.18 (*n*-hexane : EtOAc = 1 : 1). IR (KBr pellet, cm^{-1}): 3191 (NH), 2915, 2858 (CH), 1692 (C=O), 1504 (C=C). ^1H NMR (400 MHz, $CDCl_3$, δ): 10.33 (2H, br, 2NH), 7.28-7.18 (4H, m, C_6H_4), 3.75 (4H, s, $2C_6H_4C\underline{H_2}S$), 3.69 (4H, t, *J* = 6.4 Hz, $2C_6H_4CH_2SCH_2C\underline{H_2}$), 3.59 (4H, t, *J* = 6.4 Hz, $2OCH_2$), 3.25 (4H, t, *J* = 6.4 Hz, $2CH_2S$), 2.60 (4H, t, *J* = 6.4 Hz, $2C_6H_4CH_2SC\underline{H_2}$). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.6 (S-C=O), 150.5 (N-C=N), 138.5, 129.4, 128.6, 127.6 (C_6H_4), 70.6, 69.0 (CH_2OCH_2), 36.6 ($C_6H_4\underline{C}H_2S$), 32.2 (CH_2S), 30.7 ($C_6H_4CH_2S\ \underline{C}H_2$). Anal. Calcd for $C_{20}H_{26}N_4O_4S_6$: C 41.50; H 4.43; N 9.68; S 33.24. Found: C 41.51; H 4.45; N 9.70; S 33.22.

13,19,36,37,-Tetraaza-6,16,26-trioxa-3,9,11,21,23,29-hexathiotetracyclo-[29,3,1,$1^{10.13}$,$1^{19.22}$]-hepta-triaconta-1(35), 10(36),22(37),31(32),33(34)-pentaene-12,20-dione (6a)[3,4]

Compound **5** (5.0 g, 8.7 mmol) was dissolved in *i*-PrOH (500 mL)-Na (0.4 g, 18.2 mmol) and cesium chloride (1.0 g, 6.2 mmol) was added to the *i*-PrOH solution. 3-Oxopentyl-1,5-dimethnesulfonate (1.8 g, 6.8 mmol) in THF (500 mL) was added very slowly during 96 hr to the above solution at 60 °C after addition the reaction mixture was stirred more for 12 hr at 60 °C. The completion of the reaction was followed with TLC by disappearance of compound **5**. After completion of reaction, solid was filtered off. The filtrate was washed with saturated aqueous NH_4Cl, organic layer was dried with $MgSO_4$. Solvent was removed under reduced pressure and then the residue was column chromatographed using n-hexane : EtOAc : EtOH = 5 : 3 : 1 as eluent affording colorless solid product (0.6 g, 11%). Yield 11 %, Solid. mp: 74~76 °C. Rf: 0.7 (*n*-hexane : EtOAc : EtOH = 5 : 3 : 1). IR (cm^{-1}): 1683 (C=O), 1505 (C=C). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.29-7.20 (4H, m, C_6H_4), 4.01 (4H, t, *J* = 5.6 Hz $2NCH_2C\underline{H_2}O$), 3.77 (4H, s, $2C_6H_4CH_2S$), 3.75 (4H, t, *J* = 5.6 Hz, $2NC\underline{H_2}CH_2O$), 3.69 (4H, t, *J* = 6.4 Hz, $2C_6H_4CH_2SCH_2C\underline{H_2}$

O), 3.57 (4H, t, *J* = 6.4 Hz, $2C_6H_4CH_2SCH_2CH_2OC\underline{H_2}$), 3.23 (4H, t, *J* = 6.4 Hz, $2CH_2$S-thiadiazole) 2.60 (4H, t, *J* = 6.4 Hz, $2C_6H_4CH_2SC\underline{H_2}$). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 169.4 (S-C=S), 147.2 (N-C=N), 138.4, 129.3, 128.7, 127.5 (C_6H_4), 70.6 ($NCH_2\underline{C}H_2O$), 68.8 ($C_6H_4CH_2SCH_2\underline{C}H_2OCH_2$), 67.5 ($C_6H_4CH_2S$ CH_2CH_2O $\underline{C}H_2$), 46.6 (NCH_2), 36.4 ($C_6H_4\underline{C}H_2S$), 32.1 (CH_2S), 30.5 ($C_6H_4CH_2S\underline{C}H_2$). FABHRMS calcd for $C_{24}H_{32}N_4O_5S_6$: 648.0775, found: 648.0773.

13,22,39,40,-Tetraaza-6,16,19,29-trioxa-3,9,11,21,24,26,32-hexathiotetracyclo-[32,3,1,1$^{10.13}$,1$^{22.25}$]-heptatriaconta-1(38),10(39),25(40),34(35),36(37)-pentaene-12,23-dione (6b)[3,4]

The synthesis of **6b** followed the same procedure of preparation of **6a**. Yield 9.6% liquid. R_f: 0.25 (*n*-hexane : EtOAc = 1 : 1). IR (cm^{-1}): 1685 (C=O), 1510 (C=C). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7. 17 - 7.26 (4H, m, C_6H_4), 4.02 (4H, t, *J* = 5.6 Hz $2NCH_2\underline{CH_2}O$), 3.76 (8H, s + t, *J* = 5.6 Hz, $2C_6H_4$ $C\underline{H_2}SCH_2CH_2O$, $2N\underline{CH_2}CH_2OCH_2$), 3.68 (4H, t, *J* = 6.4 Hz, $2SCH_2C\underline{H_2}O$), 3.57 (8H, s + t, *J* = 6.4 Hz, $2NCH_2CH_2OC\underline{H_2}CH_2O$ + $OC\underline{H_2}CH_2S$-thiadiazole), 3.23 (4H, t, *J* = 6.4 Hz, $2\underline{CH_2}S$- thiadiazole), 2.59 (4H, t, *J* = 6.4 Hz, $2C_6H_4CH_2S\underline{CH_2}$). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 169.4 (S-C=S), 147.0 (N-C=N), 138.4, 129.3, 128.6, 127.4 (C_6H_4), 70.8 ($2NCH_2\underline{C}H_2OCH_2$), 70.2 ($2NCH_2$ $CH_2O\underline{C}H_2$), 68.8 (C_6H_4 $CH_2SCH_2\underline{C}H_2OCH_2$), 67.9 ($C_6H_4CH_2SCH_2CH_2O\underline{C}H_2$), 46.6 ($2NCH_2$), 36.5 ($C_6H_4\underline{C}H_2S$), 32.1($CH_2S$), 30.5 ($C_6H_4CH_2S$ $\underline{C}H_2$). FABHRMS calcd for $C_{26}H_{36}N_4O_6S_6$: 692.1037, found: 692.1033

X-Ray crystal structure of macrocycle (6a)

Macrocycle (**6a**) was crystallized from slow evaporation of a solution acetone. $C_{24}H_{32}N_4O_5S_6$: 648.90 g/mol, 0.45 X 0.30 X 0.25 mm, monoclinic, space group (C2/c), a = 11.7399(19) Å, b = 14.979(2) Å, c = 17.436(3) Å, α= 90°, β= 90.440(14)°, γ = 90°, V =3066.1(8) Å^3, Z = 4, density = 1.406 mg/m^3, μ = 0.486 mm^{-1}, F(000) =1360, T = 293(2) K. The data were collected CAD-4 diffractometer (Enraf-Nonous, 1994) using graphite-mono-chromated Mo-Kα radiation (0.71037 Å). Structures were obtained by a combination of the direct methods and difference Fourier syntheses and refined by full-matix least-squares on F^2, using the SHELXTL[9] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were added in calculated positions. All non–hydrogen atoms were anisotropically refined, leading to a final R_1 and wR_2, 0.0576 and 0.1471 respectively, for 3816 unique reflections and 205 refined parameters. S[F^2] 1.045 and $(\Delta/\sigma)_{max}$ was 0.000. Maximum and minimum features in ΔF synthesis are 0.416 and -0.457 eÅ^{-3}, respectively.

Crystallographic data for the structures reported here have been deposited with the Cambridge Crystallographic Data Centre (Deposition No. CCDC-663488). The data can be obtained free of charge via www.ccdc.cam.ac.uk/deposit (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44-01223 336033; E-mail: deposit@ccdc.cam.ac.uk).

Palladium metalloreceptor (Pd[L(MeCN)]) (7a)[1,2]

Compound **6a** (0.2 g, 0.3 mmole) was dissolved in MeCN (10 mL) and $[Pd(MeCN)_4][BF_4]_2$ (137mg, 3.08 X 10^{-4} mol) in MeCN (5 mL) was added to the solution. The reaction mixture was stirred at reflux for 36 hrs. The completion of the reaction was followed with TLC by disappearance of compound **6a**. After completion of reaction, solvent distilled off under reduced pressure to afford oily product (262 mg, 96%). Liquid R_f: 0.75 ($CHCl_3$: MEOH = 9 : 1). IR (neat, cm^{-1}): 1683 (C=O), 1505 (C=C). ^{1}H NMR (400 MHz, CD_3CN, δ): 6.94-6.96(3H, m, C_6H_3), 4.41 (4H, br, $2C_6H_3CH_2SCH_2C\underline{H_2}O$), 3.88 (8H, s + t, *J* = 5.2 Hz, $2C_6H_3C\underline{H_2}S$ + $2OC\underline{H_2}CH_2$ S-thiadiazole) 3.70 (4H, t, *J* = 5.6 Hz, $2NCH_2C\underline{H_2}O$), 3.66 (4H, t, *J* = 5.6 Hz, $2NC\underline{H_2}CH_2O$), 3.25 (4H, t, *J* = 5.2 Hz, $2OCH_2C\underline{H_2}$ S-thiadiazole), 3.18 (4H, t, *J* = 6.4 Hz, $2C_6H_3CH_2SC\underline{H_2}$) ^{13}C NMR (100 MHz, CD_3CN, δ): 170.4 (S-C=S), 156.3 (N-C=N), 151.7, 147.8, 126.5, 123.8 (C_6H_3), 70.1, 68.2 (CH_2OCH_2), 67.2 ($CH_2\underline{C}H_2O$), 47.5 (NCH_2), 45.9 ($C_6H_3\underline{C}H_2S$), 38.8 ($\underline{C}H_2$S-thiadiazole), 33.7 ($C_6H_4CH_2S\underline{C}H_2$), FABHRMS calcd for $C_{24}H_{31}N_4O_5Pd\ S_6^+$: 752.9654, found: 752.9651.

Palladium metalloreceptor (Pd[L_2(MeCN)]) (7b)[1,2]

The synthesis of **7b** followed the same procedure of preparation of **7a**. Yield 97%. Liquid Rf: 0.75 ($CHCl_3$: MeOH = 9 : 1). IR (neat, cm^{-1}): 1684 (C=O), 1507 (C=C). ^{1}H NMR (400 MHz, CD_3CN, δ): 6.94-6.98 (3H, m, C_6H_3), 4.49 (4H, br, $2C_6H_3CH_2SCH_2C\underline{H_2}O$), 4.00 (8H, s + t, *J* = 5.2 Hz, $2C_6H_3C\underline{H_2}SCH_2$ + $2OC\underline{H_2}CH_2$S-thiadiazole), 3.80 (4H, t, *J* = 5.2 Hz, $2NCH_2C\underline{H_2}O$), 3.75 (4H, t, *J* = 5.2 Hz, $2NC\underline{H_2}CH_2O$), 3.57 (4H, s, *J* = 6.4 Hz, $2C_6H_4CH_2S$) 3.35, 3.29 (8H, m, *J* = 6.4 Hz, $2C_6H_3CH_2SCH_2$, $2CH_2S$) ^{13}C NMR (100 MHz, CD_3CN, δ): 169.1 (S-C=S), 154.9 (N-C=N), 150.2, 146.5, 125.1, 122.4 (C_6H_3), 69.4, 69.1 (CH_2OCH_2), 68.6, 67.1 ($NCH_2\underline{C}H_2O\underline{C}H_2$), 46.3, ($NCH_2$), 44.7 ($C_6H_3\underline{C}H_2S$), 37.8 ($\underline{C}H_2$S-thiadiazole), 32.2 $C_6H_3CH_2S\underline{C}H_2$). FABHRMS calcd for $C_{26}H_{35}N_4O_6PdS_6^+$: 796.9916, found: 796.9918.

Molecular recognition of 7

^{1}H NMR of the host molecules were measured in presence of the guest molecules. The solution of host molecule (0.01-0.02 M) was prepared in DMSO-d_6 and the guest stock solutions in DMSO-d_6 (0.04-0.08 M) were added several times small increments until ^{1}HNMR chemical shifts have been stopped. From the chemical shift changes, the concentration of H(host), G(guest), and HG(host-guest complex) were calculated. The complexation constants, K, in Table 1 were obtained from the slope of the plot [HG]/[H] versus [G].

ACKNOWLEDGEMENTS

This work was supported by a Grant from Chungnam National University. X-Ray data were collected at the Center for Research Facilities in Chungnam National University.

REFERENCES

1. N. S. Cho, C. H. Lee, Y.-J. Kim, J. S. Choi, and S. K. Kang, *Heterocycles*, 2004, **63**, 2827.

2. N. S. Cho, M. S. Park, Y. H. Kim, Y.-E. Yu, H. J. Kwon, and Y.-J. Kim, *Heterocycles*, 2006, **68**, 811.

3. N. S. Cho, C. K. Park, H. S. Kim, J. G. Oh, I.-H. Suh, and M. R. Oh, *Heterocycles*, 1999, **51**, 2739.

4. N. S. Cho, S. I. Hong, Y.-S. Park, and I.-H. Suh, *Bull. Korean Chem. Soc*., 2001, **22**, 1280.

5. N. S. Cho, Y. H. Kim, and C. H. Lee, *Bull. Korean Chem. Soc*., 2004, **25**, 1581.

6. (a) D. Amantia, C. Price, M. A. Shipman, M. R. J. Elsegood, W. Clegg, and A. Houlton, *Inorg. Chem.*, 2003, **42**, 3047. (b) R. B. Martin, *Acc. Chem. Res.*, 1985, **18**, 32.

7. J. Buter and R. M. Kellogg, *J. Org. Chem*., 1981, **46**, 4481.

8. N. S. Cho, C. K. Park, H. S. Kim, E. S. Choi, and S. K. Kang, *Bull. Korean Chem. Soc*., 1998, **19**, 103.

9. G. M. Sheldrick, SHELXTL, V6.1; Bruker Analytical X-ray Systems, Inc.: Madison, WI, 1997.