Synthesis and Properties of Novel Macrocyclic Compounds Bearing Thiourea Moieties by Use of Chemical Feature of Hypervalent Sulfur

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Macrocyclic compounds **5a-i** bearing two tetraazathiapentalene frameworks were synthesized by the reaction of 10-S-3 tetraazathiapentalene derivatives **3a-f** with compounds having various diisothiocyanate functions **4a-e**. The reduction of the macrocyclic compounds with $NaBH_4$ afforded the ring-opened macrocyclic compounds **11a-b** and **11e-h** by elimination of the hypervalent sulfur. The structures of these compounds were established by their spectral data and also by the X-ray crystallographic analysis of **11a**. The other ring-opened macrocyclic compounds **14a** and **14e-h** that bear four thiourea groups were synthesized by alkaline hydrolysis of **5a** and **5e-h** in that elimination of the $C=S^{IV}$ moiety in the tetraazathiapentalene rings occurred.

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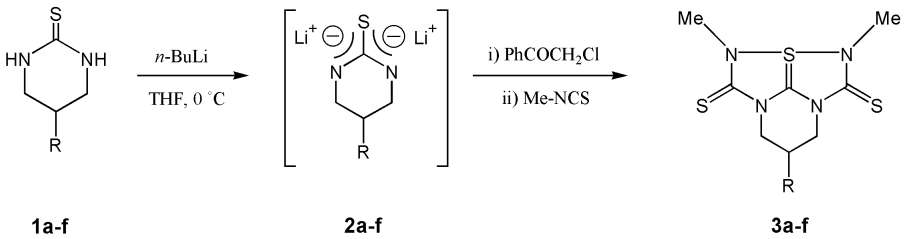
Introduction.

Since the discovery of an unusual structure of trithiapentalene [1], which is sometimes referred to as no bond resonance, the chemistry of π-hypervalent heterocyclic systems has been a subject of considerable interest. A number of π-electron systems containing a 10-S-3 framework have been synthesized [2], and their structures and reactivities have also been investigated [2-3]. However, the characteristic chemical properties of the apical and equatorial bonds on the π-hypervalent atom have little been applied to organic synthesis. Previously, we have reported the synthesis and reactivities of 10-S-3 tetraazathiapentalene derivatives, namely 2,3-disubstituted 6,7-dihydro-5*H*-2a-thia(2a-S^{IV})-2,3,4a,7a-tetraazacyclopent[*cd*]indene-1,4(2*H*,3*H*)-dithiones [4-5]. These compounds underwent unique reactions that were attributable to the chemical nature of the hypervalent sulfur. For example, the reaction of **3** (R = H) with $NaBH_4$ gave the ring-opened compound, 1,3-bis(methylthiocarbamoyl)-perhydropyrimidine, in good yield with release of the hypervalent sulfur [6], and the reaction of **3** (R = H) with an excess of isothiocyanates and isocyanates afforded tetraazathiapentalene derivatives having thiocarbonyl and carbonyl groups [7], respectively. We have applied these reactions to the synthesis of macrocyclic azacrown and azathiacrown ethers [8]. We have also found that alkaline hydrolysis of **3a** gives the ring-opened compound **12** which bears two thiourea groups by elimination of the $C=S^{IV}$ moiety (see Scheme 7). On these backgrounds, we planned to synthesize new macrocyclic compounds that contain thiourea functions in the ring and also are soluble in organic solvents. The anion binding abilities of thiourea derivatives are much stronger than those of urea derivatives, because of higher acidity of the former compounds [9-10]. Very recently, Umezawa *et al*. reported that receptors with a rigid xanthene moiety show a strong complexation ability toward dihydrogen phosphate anion through the thiourea function in the xanthene moiety [11]. Therefore, macrocyclic compounds having thiourea function are expected to serve as a receptor of inorganic anions in molecular recognition events [12]. In this paper, we report a new methodology for preparing macrocyclic compounds bearing a π-hypervalent sulfur in the ring and also the conversion of these macrocyclic compounds to compounds bearing thiourea functions by ring-opening reaction [13].

Scheme 1



1a-f **2a-f** **3a-f**

a: R = $(CH_2)_7CH_3$; **b:** R = $(CH_2)_{11}CH_3$; **c**: R = $(CH_2)_{17}CH_3$
d: R = $(CH_2)_4OCH_2Ph$; **e:** R = $(CH_2)_4OPh$; **f:** R = 9-anthrylmethyl

Table 1
Preparation of Tetraazathiapentalene Derivatives **3a-f** [a]

entry	R	product	yield /% [b]
1	$(CH_2)_7CH_3$	**3a**	66
2	$(CH_2)_{11}CH_3$	**3b**	66
3	$(CH_2)_{17}CH_3$	**3c**	46
4	$(CH_2)_4OCH_2Ph$	**3d**	46
5	$(CH_2)_4OPh$	**3e**	80
6	9-anthrylmethyl	**3f**	45

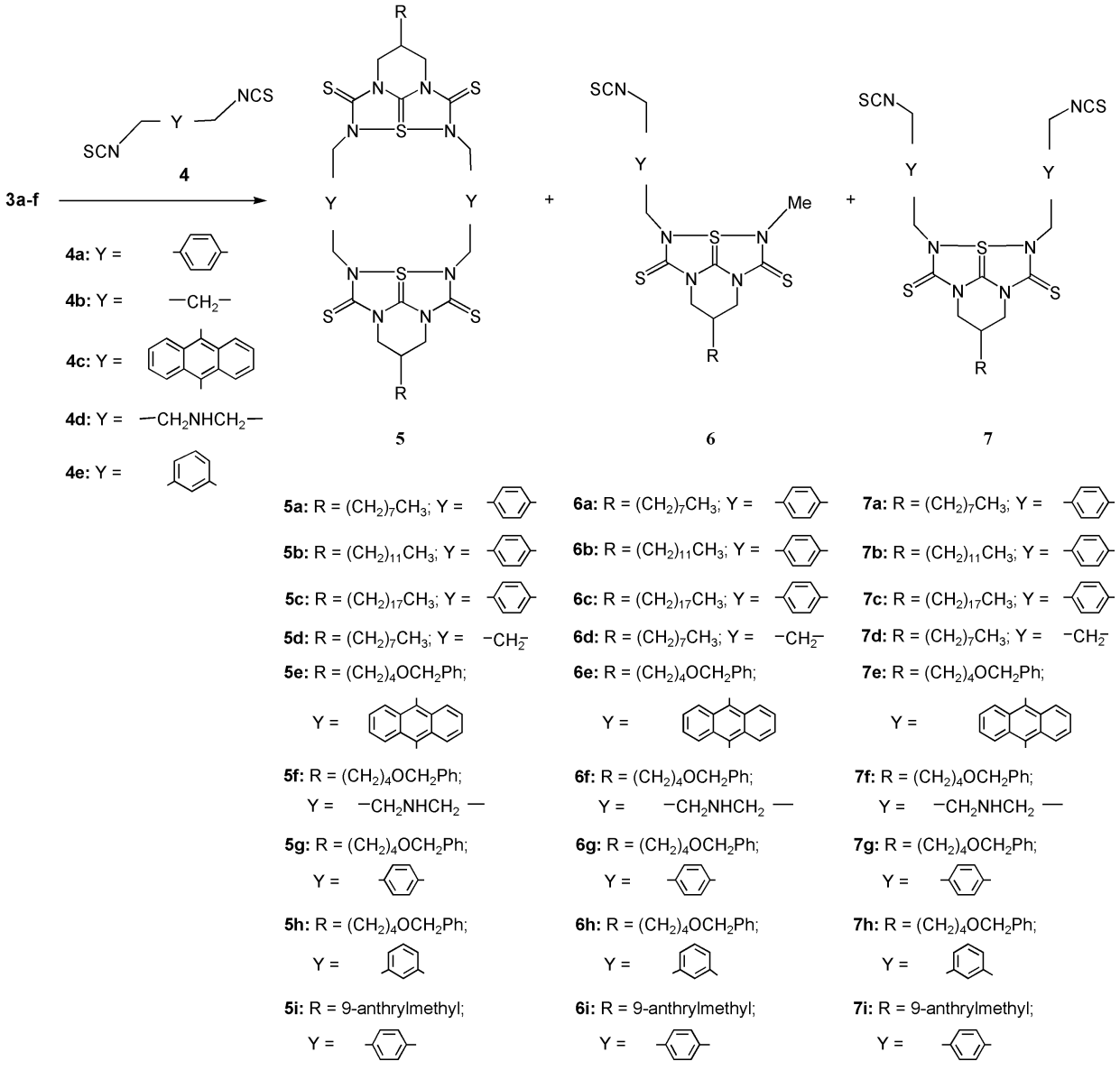
[a] The reaction was carried out in THF at room temperature for 24 h under argon. [b] Isolated yields.

Results and Discussion.

Synthesis of Macrocyclic Compounds.

5-Alkyl-3,4,5,6-tetrahydropyrimidine-2-thiols **1a-f**, which were prepared from 2-alkyl-1,3-diaminopropanes and carbon disulfide under acidic conditions, were converted into dianions **2a-f** by treating with two equivalents of butyllithium in THF at 0 °C under argon. The reaction of **2a-f** with one equivalent of phenacyl chloride, followed by addition of three equivalents of methylisothiocyanate, gave tetraazathiapentalene derivatives **3a-f** in moderate yields (Scheme 1). The yields of **3a-f** are shown in Table 1. The structures of **3a-f** were determined by their IR, ^{1}H-NMR, mass spectra, and elemental analyses. The compounds were colorless solids, stable in air, and highly soluble in organic solvents.

Scheme 2



Treatment of **3a** with 1 equivalent of *p*-xylylenediisothiocyanate (**4a**) in refluxing benzene for 24 hours gave the 18 membered macrocyclic compound **5a** in 50% yield, along with the monosubstituted tetraazathiapentalene derivative **6a** in 17% yield and the disubstituted tetraazathiapentalene derivative **7a** in 3% yield (Scheme 2). This method is referred to as Method A in this paper. The reaction of **3a-c** with diisothiocyanates **4a-b** was carried out under similar conditions. The results are summarized in Table 2.

Table 2
Reactions of **3a-c** with Diisothiocyanates **4a-b** [a]

entry	compound	diisothiocyanate	product(yield / %) [b]		
	3	**4**			
1	**3a**	**4a**	**5a**(50)	**6a**(17)	**7a**(3)
2	**3b**	**4a**	**5b**(46)	**6b**(17)	**7b**(4)
3	**3c**	**4a**	**5c**(39)	**6c**(16)	**7c**(3)
4	**3a**	**4b**	**5d**(17)	**6d**(32)	**7d**(22)

[a] The reaction was carried out under reflux in benzene for 24 h. [b] Isolated yields based on **3a-c** used.

The reaction of **3a-c** with **4a** gave the macrocyclic compounds **5a-c** in moderate yields (entries 1-3), but the reaction of **3a** with **4b** afforded **5d** in a low yield (entry 4). The structures of **5a-d** were determined by their IR, ^{1}H NMR, FAB mass spectra, and elemental analyses. The ^{1}H NMR spectrum of **5a** in $CDCl_3$ showed a singlet at δ 5.00 due to benzylic protons and a singlet at δ 7.29 due to phenyl protons. The FAB mass spectrum of **5a** showed a parent peak (M^++H) at 893.

Both of **6a** and **7a** changed to **5a** upon refluxing in benzene for 24 hours in 77% and 91% yields, respectively (Scheme 3). These results suggest that **5a** is derived *via* **6a** and/or **7a**.

Scheme 3

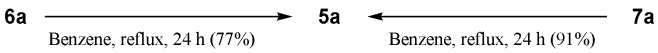


Table 3
Reaction of **3a** with **4a** [a]

entry	solvent	concen [b] (x 10^2mol/dm^3)	product(yield / %) [c] **5a**	**6a**	**7a**
1	benzene	2.68	50	17	3
2	benzene	6.70	53	14	3
3	benzene	13.40	55	11	3
4	toluene	2.68	43	13	5
5	benzene/hexane [d]	10.00	77	6	1

[a] The reaction of **3a** with **4a** was carried out under reflux in benzene or toluene for 24 h. [b] The concentration of **3a** and **4a** employed in the reaction. [c] Isolated yields based on **3a** used. [d] Benzene/Hexane = 3 : 2.

We then studied the concentration dependence of **3a** and **4a** on the formation of **5a**. The results are shown in Table 3. The change in the concentration of **3a** did not affect the yield of **5a** (entries 1-3), but the yield of **5a** slightly decreased with increasing the reaction temperature (entry 4). On the other hand, when a 3:2 mixture of benzene and hexane was used as solvent, the yield of **5a** increased markedly (entry 5).

Solubility.

In general, macrocyclic compounds bearing a π-hypervalent sulfur show a poor solubility in organic solvents. In fact, **5** (R = H in **5a**) is almost insoluble in any organic solvent. However, introduction of longer alkyl chains on the ring increases the solubility. Macrocyclic compounds **5a-c** are slightly soluble in ethanol, ether, acetone, and ethyl acetate, but fairly soluble in $CHCl_3$, CH_2Cl_2 and benzene.

Table 4
Solubility of **5a-c** and **5** in Dichloromethane [a]

Compound	R	Y	solubility x 10^3 (mol/l)
5a	$(CH_2)_7CH_3$		2.41
5b	$(CH_2)_{11}CH_3$		3.18
5c	$(CH_2)_{17}CH_3$		0.41
5 [b]	H		0.13

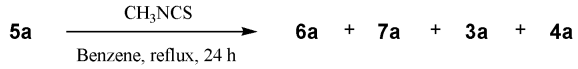
[a] The solubility was measured at 21.0-21.4 °C; [b] Compound **5** is the compound having the substituent R = H in **5a**.

The solubility of the macrocyclic compounds in CH_2Cl_2 decreased in the order of **5b** > **5a** > **5c** > **5** (R = H in **5a**) (Table 4).

Exchange Reaction in Tetraazathiapentalene Rings of Macrocyclic Compounds.

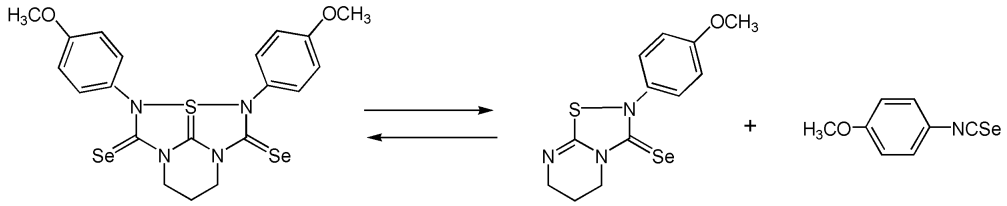
The reaction of **5a** with excess of methylisothiocyanate in refluxing benzene gave **6a**, **7a**, **3a**, and **4a** in 15, 4, 35, and 32% yields, respectively, accompanying with the recovery of **5a** (Scheme 4).

Scheme 4



This result indicates that the exchange reaction of the NCS moiety in the tetraazathiapentalene ring of **5a** is occurring, and this is due to the weakness of the apical bond of the hypervalent sulfur in the tetraazathiapentalene ring. The tetraazathiapentalene derivative **8** in solid state is stable in air, but decomposes slowly in solution. In fact, the ^{1}H NMR spectrum revealed that **8** decompose in ben-

Scheme 5



8 **9** **10**

zene to give the thiadiazole derivative **9** and the isoselenocyanate **10** (Scheme 5).

Furthermore, **9** undergoes a 1,3-dipolar cycloaddition with **10** to give **8** in good yield. These results suggest that in the reaction shown in Scheme 2, the removal of methylisothiocyanate produced during the reactions serves as a procedure for improving the yields of the macrocyclic compounds. Based on this result, compound **5d** was quantitatively obtained by the following procedure (Method B): A mixture of **3a** and 2 equivalents of trimethyleneisothiocyanate **4b** was refluxed in benzene for 24 hours, followed by removal of benzene under reduced pressure. After addition of benzene and *n*-hexane to the residue, the mixture was refluxed for 2 hours. The solvent mixture was again removed under reduced pressure. These operations were repeated three times to give **5d**. This method (Method B) was applied to the reaction of tetraazathiapentalene derivatives **3a, 3d,** and **3f** with a variety of diisothiocyanates. As diisothiocyanates, we used *p*-xylylenediisothiocyanate (**4a**), 9,10-bis(isothiocyanatomethyl)anthracene (**4c**), *N*,*N*-bis(2-isothiocyanatomethyl)amine (**4d**), and *m*-xylylenediisothiocyanate (**4e**). The reactions of **3a**, **3d**, and **3f** with **4a-e** was carried out by both of Method A and Method B. The results are summarized in Table 5.

Table 5
The Reactions of **3a**, **3d**, and **3f** with Diisothiocyanates **4a-e**

entry	3	4	method [a]	macrocyclic compound (yield / %) [b]
1	**3a**	**4b**	A	**5d**(50)
	3a	**4b**	B	**5d**(quant.)
2	**3d**	**4a**	A	**5g**(80)
	3d	**4a**	B	**5g**(quant.)
3	**3d**	**4e**	A	**5h**(67)
	3d	**4e**	B	**5h**(quant.)
4	**3d**	**4d**	A	**5f**(30)
	3d	**4d**	B	**5f**(quant.)
5	**3d**	**4c**	A	**5e**(43)
	3d	**4c**	B	**5e**(45)
6	**3f**	**4a**	A	**5i**(13)
	3f	**4a**	B	**5i**(15)

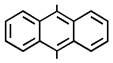
[a] Mehod A: The reactions were carried out under reflux in benzene for 24 h. Method B: After the reactions were carried out under reflux in benzene for 24 h, benzene was removed. Mixed solvent of benzene-n-hexane was added to the residue and refluxed for 2 h. The solvent was then removed again under reduced pressure. These operations were repeated three times. [b] Isolated yields.

When Method B was employed, the yields of the macrocyclic compounds were remarkably improved (entries 1-4). However, for **3f** and **4c** that have bulky group, the yields of the macrocyclic compounds **5i** and **5e** were not improved even by employing Method B. The structures of the macrocyclic compounds **5d-i** were determind by their IR, ^{1}H NMR spectra, and elemental analyses.

Reduction of Macrocyclic Compounds.

Previously, we have reported that **3** (R = H) is converted into the ring-opened compound, 1,3-bis(methylthiocarbamoyl)perhydropyrimidine, by elimination of the hypervalent sulfur upon treating with $NaBH_4$ [6]. We applied this reaction to the ring-opening reaction of the macrocyclic compounds **5a-5b**, and **5e-h**. For example, the reaction of **5a** with $NaBH_4$ in DMSO at room temperature for 24 hours afforded the 26–membered macrocyclic compound **11a** that contains four thiourea moieties in the ring in 66% yield. The other macrocyclic compounds **5b** and **5e-h** reacted similarly with $NaBH_4$ to give the macrocyclic compounds **11b** and **11e-h** in moderate yields (Scheme 6). The results are summarized in Table 6.

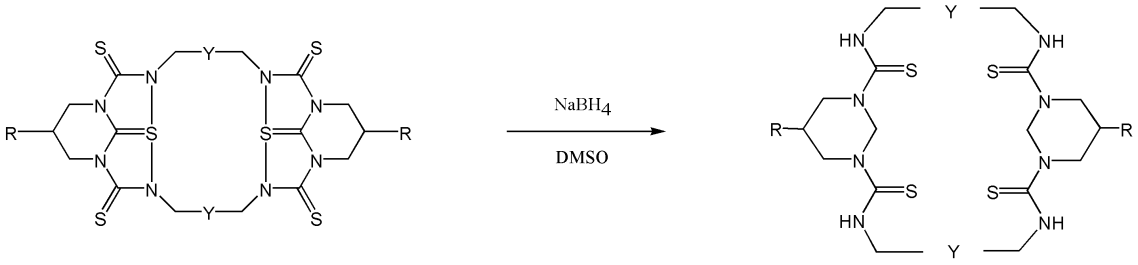
Table 6
Reaction of Macrocyclic Compounds **5a-b, and 5e-h** with $NaBH_4$ [a]

entry	compound	macrocyclic compound R	macrocyclic compound Y	product (yield / %) [b]
1	**5a**	$(CH_2)_7CH_3$		**11a**(66)
2	**5b**	$(CH_2)_{11}CH_3$		**11b**(46)
3	**5e**	$(CH_2)_4OCH_2Ph$		**11e**(53)
4	**5f**	$(CH_2)_4OCH_2Ph$	$-CH_2NHCH_2-$	**11f**(35)
5	**5g**	$(CH_2)_4OCH_2Ph$		**11g**(37)
6	**5h**	$(CH_2)_4OCH_2Ph$		**11h**(64)

[a] The reaction was carried out in DMSO at room tempareture for 24 h. [b] Isolated yields.

The structures of **11a-b** and **11e-h** were determined by their IR, ^{1}H NMR and MS spectra, and elemental analyses.

Scheme 6



5

5a: R = $(CH_2)_7CH_3$; Y =

5b: R = $(CH_2)_{11}CH_3$; Y =

5e: R = $(CH_2)_4OCH_2Ph$; Y =

5f: R = $(CH_2)_4OCH_2Ph$; Y = $-CH_2NHCH_2-$

5g: R = $(CH_2)_4OCH_2Ph$; Y =

5h: R = $(CH_2)_4OCH_2Ph$; Y =

11

11a: R = $(CH_2)_7CH_3$; Y =

11b: R = $(CH_2)_{11}CH_3$; Y =

11e: R = $(CH_2)_4OCH_2Ph$; Y =

11f: R = $(CH_2)_4OCH_2Ph$; Y = $-CH_2NHCH_2-$

11g: R = $(CH_2)_4OCH_2Ph$; Y =

11h: R = $(CH_2)_4OCH_2Ph$; Y =

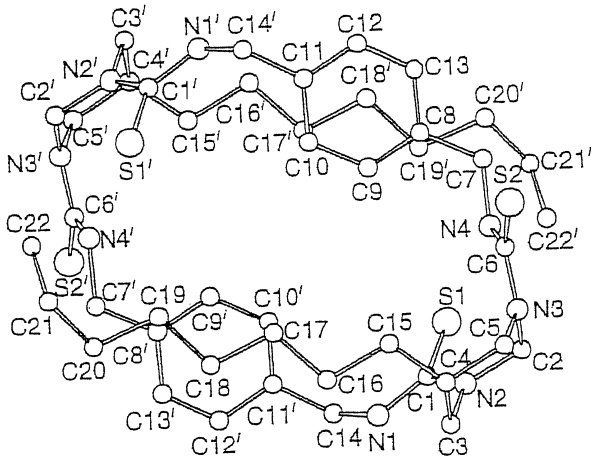


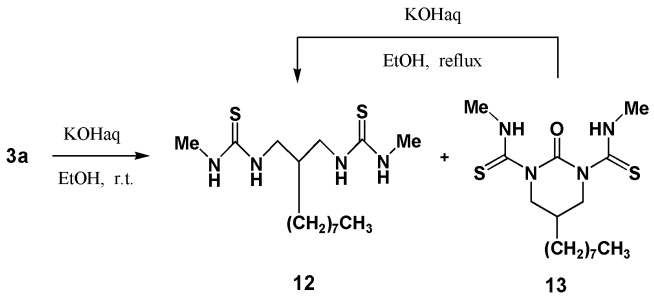
Figure 1. ORTEP drawing of **11a** [15]. 10 H atoms and solvent molecules are omitted. The molecule has a crystallographic center of symmetry at the center of the macrocycle. Symmetry code: i (1-x, -y, 2-z). Selected bond lengths (A) and angles (degrees): S1-C1=1.70(2), N1-C1=1.36(2), N1-C14=1.43(2), N2-C1=1.38(2), N2-C2=1.43(2), N2-C3=1.49(2), C1-N1-C14=124(2), C1-N2-C2=125(2), N1-C1-N2=117.4(14), C2-N2-C3= 110(2).

The structure of **11a** was further confirmed by an X-ray crystallographic analysis [14]. Figure 1 shows an ORTEP drawing of **11a** [15]. The distance between two benzene rings was about 4.0 Å.

Alkaline Hydrolysis of Macrocyclic Compounds.

We have found that treatment of **3a** with an aqueous EtOH- KOH solution gave the ring-opened product, 1-methyl-3-{2-[(3-methyl-thioureido)-methyl]-decyl}-thiourea **12** and 5-octyl-2-oxo-dihydro-pyrimidine-1,3-dicarbothioic acid bismethylamide **13** in 28% and 37% yields, respectively [13].

Scheme 7



We also found that treatment of **13** with an aqueous EtOH-KOH solution under the similar conditions gave **12** in 69% yield (Scheme 7). These results clearly show that the conversion of **3a** into **12** proceeds *via* cyclic urea intermediate such as **13**. We applied this alkaline hydrolysis reaction to **5a** and **5e-h**. For example, treatment of **5a** with an aqueous EtOH-KOH solution gave the 30-membered macrocyclic compound **14a** that has four thiourea moieties in the ring in 44% yield with elimination of the $C=S^{IV}$ function of the tetraazathiapentalene ring. The other macrocyclic compounds **5e-h** reacted similarly with an aqueous EtOH-KOH solution to give **14e-h** in moderate yields (Scheme 8). The structures of **14a** and **14e-h** were determined by comparison of their spectrtal data with those of **11a-b** and **11e-h**, and elemental analyses. The results are summarized in Table 7. The conversion of **5a** and **5e-h** into **14a** and **14e-h** is considered to proceed *via* carbonyl intermediate such as **13** shown in Scheme 7.

Scheme 8

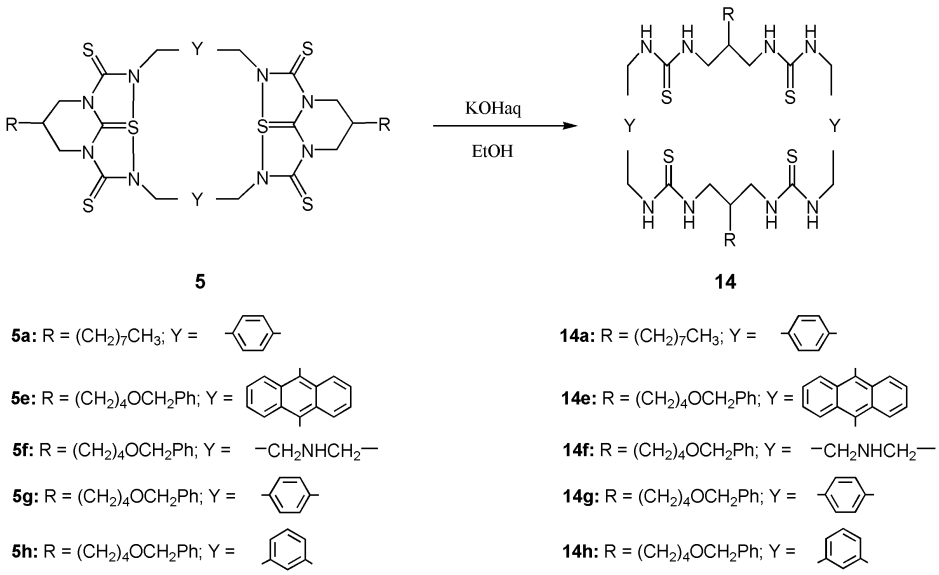
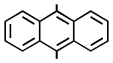


Table 7

Ring-Expansion of Macrocyclic Compounds **5a and 5e-h** by Use of Alkaline Hydrolysis [a]

entry	compound	macrocyclic compound R	macrocyclic compound Y	product (yield / %) [b]
1	**5a**	$(CH_2)_7CH_3$		**14a**(44)
2	**5e**	$(CH_2)_4OCH_2Ph$		**14e**(44)
3	**5f**	$(CH_2)_4OCH_2Ph$	$-CH_2NHCH_2-$	**14f**(83)
4	**5g**	$(CH_2)_4OCH_2Ph$		**14g**(52)
5	**5h**	$(CH_2)_4OCH_2Ph$		**14h**(26)

[a] The reaction was carried out in aqueous EtOH-KOH solution for 4 h. [b] Isolated yields.

Conclusions.

In summary, we synthesized successfully new tetraazathiapentalene derivatives having long alkyl-chains and a hypervalent sulfur. These hypervalent compounds were converted into macrocyclic compounds bearing two tetraazathiapentalene rings by utilizing the chemical nature of apical and equatorial bonds of the hypervalent sulfur. The reduction with $NaBH_4$ of the macrocyclic compounds having tetraazathiapentalene rings gave ring-opened rigid macrocyclic compounds bearing thiourea function by the reductive desulfurization of the hypervalent sulfur. Their structures were confirmed by their spectral data and X-ray crystallographic analysis. On the other hand, alkaline hydrolysis of the macrocyclic compounds having the hypervalent sulfur afforded flexible macrocyclic compounds containing four thiourea moieties by release of the $C=S^{IV}$ function. These macrocyclic compounds are supposed to have potential as an anion receptor in the host-guest chemistry. The methodology reported in this paper would provide a useful tool for the synthesis of macrocyclic compounds containing thiourea function.

EXPERIMENTAL

All the solvents used in this study were purified by usual procedures. TLC was performed on a Merck Art 25 DC-plastikfolien Kieselgel 60 F_{254}. Column chromatography was performed on silica gel (Merck, 70-230 mesh). NMR spectra were obtained with a Varian Murcury 300 NMR spectrometer. Chemical shifts are expressed in ppm with TMS as an internal standard. Melting points were determined with a Yanaco MP-500 and are uncorrected. Infrared spectra were recorded by a Jasco Herschel FT IR 230 or a PERKIN ERMER 1600. UV spectra were taken with a SHIMADU UV-160A. MS spectra were obtained on a JEOL-DX 303HF. Elemental analysis were done on a YANAGIMOTO CHN corder MT-3.

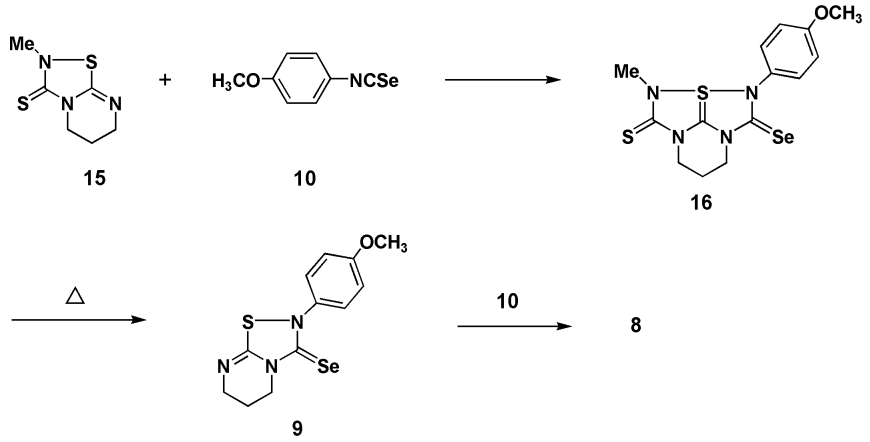
Materials.

p-Xylylenediisothiocianate (**4a**), *m*-xylylenediisothiocianate (**4e**), 2-octyldiethylmalonate, 2-dodecyldiethyl malonate, 2-octadecyldiethyl malonate, 2-octylmalone diamide, 2-dodecylmalonediamide, and 2-octadecylmalone diamide were prepared according to the procedures described in literatures [16-17].

Preparation of 5-Alkyl-3,4,5,6-tetrahydroprimidine-2-thiols **1a-f**.

5-Alkyl-3,4,5,6-tetrahydropyrimidine-2-thiols **1a-f** were prepared in a similar manner to that reported in literature [18-19]. They were prepared according to the following procedure: 1) Alkylation of dimethyl malonate, 2) conversion of dimethylmalonates to amides, 3) reduction of amides to amines, and 4) cyclization of diamines by use of CS_2.

Scheme 9



2-(4-Benzyloxybutyl)dimethyl malonate.

A solution of 4-bromobutyl benzyl ether (243 mg, 1 mmol) in DMF (8 mL) was added to a mixture of dimethyl malonate (132 mg,1 mmol) and K_2CO_3 276 mg, 2 mmol) in DMF (7 mL) at room temperature under argon. The mixture was stirred at the same temperature for 24 hours, and then extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with toluene-AcOEt (9:1 v/v). 2-(4-Benzyloxybutyl)dimethylmalonate was obtained in 82% yield (242 mg) as an oil, bp 110°/ 5 mmHg; ir (potassium bromide): 3036, 2960, 2859, 1735, 1448, 1360, 1249, 1153, 1031, 817, and 743 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 137-1.44 (m, 2H), 1.61-1.67 (m, 2H), 1.92 (q, 2H), 3.36 (t, 1H), 3.46 (t, 2H), 3.72 (s,6H), 4.48 (s, 2H), 7.27-7.35 (m,5H).

Anal. Calcd. for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.20; H, 7.57.

2-(4-Benzyloxybutyl)malone diamide.

A catalytic amount (500 mg) of Na was added to an NH_3 saturated cooled methanol, and 2-(4-benzyloxybutyl)dimethylmalonate (331 mg, 1.1 mmol) was added to this mixture. The mixture was stirred at room temperature for 3 days. The precipitates were isolated by filtration, washed with methanol, and dried *in vacuo*. 2-(4-Benzyloxybutyl)malone diamide was obtained in 98% yield (302 mg) as colorless solid, mp 183-184° (decomp); ir (potassium bromide): 3377, 3297, 3198, 2944, 2855, 1671, 1498, 1475, 1458, 1451, 1382, 1278, 1250, 1114, and 696 cm^{-1}; ^1H nmr (300 MHz, dimethylsulfoxide-d_6): δ 1.23-1.31 (m, 2H), 1.47-1.58 (m, 2H), 1.66 (q, 2H, J = 6.7 Hz), 3.39 (t, 2H, J = 6.7 Hz), 4.43 (s, 2H), 7.03 (br,2H), 7.29-7.37 (m, 7H).

Anal. Calcd. for $C_{14}H_{20}N_2O_3$: C, 63.62; H, 7.63; N, 10.60. Found: C, 63.90; H, 7.72; N, 10.30.

2-(4-Benzyloxybutyl)-1,3-diaminopropane.

A mixture of 2-(4-benzyloxybutyl)malone diamide (2.0 g, 9.3 mmol) and BH_3-THF complex (46.7 mL, 46.7 mmol) in THF (50 mL) was refluxed under argon for 3 hours, cooled to room temperature, and then 6 M HCl (7 mL) was added to the mixture. The THF solution was evaporated, and the residue was extracted under an alkaline condition (pH = 11) with diethyl ether. The ether extract was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The crude product of 2-(4-benzyloxybutyl)-1,3-diaminopropane was used for the next step without purification.

5-(4-Benzyloxybutyl)-3,4,5,6-tetrahydropyrimidine-2-thiol (**1d**).

Half of an ethanol solution containing CS_2 (1.142 g, 15 mmol) was added to a solution of crude 2-(4-benzyloxybutyl)-1,3-diaminopropane in EtOH-H_2O under ice-cooling. The mixture was warmed to 60 °C, and then the other half of the CS_2 ethanol solution was added at the same temperature. The reaction mixture was refluxed for 5 hours, concentrated HCl solution (1 mL) was added, and then further refluxed for 18 hours. The solvent was removed and the residue was extracted with CH_2Cl_2. The extract was washed with brine, dried (Na_2SO_4) and evaporated under reduced pressure. The product was purified by column chromatography on silica gel with CH_2Cl_2–AcOEt (9:1 v/v). Compound **1d** was obtaind in 58% yield (1.264 g) as colorless solid, mp 128-130°; ir (potassium bromide): 3229, 2930, 2857, 1553, 1497, 1454, 1366, 1203, 1116, and 751 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 1.17-1.40 (m, 4H), 1.52 (q, 2H), 1.86 (m, 1H), 2.87 (br t, 2H), 3.26 (br d, 2H), 3.39 (t, 2H, J = 6.7Hz), 4.41 (s, 2H), 6.94 (br, 2H), 7.26-7.29 (m, 5H).

Anal. Calcd. for $C_{15}H_{22}N_2OS$: C, 64.71; H, 7.96; N, 10.06. Found: C, 64.47; H, 8.22; N, 9.76.

2-(4-Phenoxybutyl)dimethyl malonate.

2-(4-Phenoxybutyl)dimethylmalonate was obtained in 70% yield (2.273 g) from 4-bromophenyl butyl ether and dimethylmalonate,: bp 240°/ 12mmHg; ir (potassium bromide): 2953, 2869, 1734, 1559, 1542, 1497, 1436, 1244, 1033, 884, and 693 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 1.47 (m, 2H), 1.67 (m, 2H), 1.96 (m, 2H), 3.73 (t, 1H), 3.75 (s, 6H), 3.95 (t, 2H), 6.88 (m, 3H), 7.22 (m, 5H).

Anal. Calcd. for $C_{15}H_{10}O_5$: C, 66.67; H, 3.73. Found: C, 66.37; H, 3.83.

2-(9-Anthrylmethyl)dimethyl malonate.

2-(9-Anthrylmethyl)dimethyl malonate was obtained in 40% yield (4.807g) from 9-bromomethylanthracene and dimethymalonate, mp 128-130°; ir (potassium bromide): 2152, 2909, 1734, 1654, 1560, 1437, 1284, 754, and 690 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 3.59 (s, 6H), 3.88 (t, 1H, J = 7.4Hz), 3.95 (d, 2H, J = 7.4Hz), 7.58 (m, 5H), 8.31 (m, 2H), 8.65 (m, 2H).

2-(4-Phenoxybutyl)malone diamide.

2-(4-Phenoxybutyl)malone diamide was obtained in 92% yield (3.299g) from2-(4-phenoxybutyl)dimethylmalonate and NH_3, mp 230° (decomp); ir (potassium bromide): 3368, 3191, 2938, 2858, 1670, 1468, 1382, 1246, 1177, 1035, 893, and 696 cm^{-1}; ^1H nmr (300 MHz, dimethylsulfoxide-d_6): δ 1.38 (m, 2H), 1.70 (m, 4H), 2.98 (t, 1H, J = 6.4Hz), 3.92 (t, 2H, J = 7.4Hz), 6.90 (m, 5H), 7.03 (br, 2H), 7.26 (m, 2H).

Anal. Calcd. for $C_{13}H_{18}N_2O_3$: C, 62.38; H, 7.25; N, 11.24. Found: C, 62.31; H, 7.25; N, 11.22.

2-(9-Anthrylmethyl)malone diamide.

2-(9-Anthrylmethyl)malone diamide was obtained in 87% yield (3.801 g) from 2-(9-anthrylmethyl)dimethylmalonate and NH_3, mp 247° (decomp); ir (potassium bromide): 3385, 3186, 2909, 2849, 1718, 1684, 1637, 901, 750, and 686 cm^{-1}; ^1H nmr (300 MHz, dimethylsulfoxide-d_6): δ 4.08 (d, 2H, J = 6.3Hz), 7.14 (br, 2H), 7.24 (br, 2H), 7.67 (m, 5H), 8.45 (d, 2H, J = 10.7Hz), 8.50 (d, 2H, J = 11.2Hz); FAB mass m/e 292 ($M+H^+$).

5-Octyl-3,4,5,6-tetrahydropyrimidine-2-thiol (**1a**).

5-Octyl-3,4,5,6-tetrahydropyrimidine-2-thiol (**1a**) was obtained in 70% yield (1.489 g) from 2-octyl-1,3-diaminopropane and CS_2 (1.421 g, 18 mmol) under an acidic condition, mp 139-140°; ir (potassium bromide): 3210, 3100, 2973, 2950, 2922, 2852, 1574, 1557, 1466, 1392, 1352, 1295, 1276, 1215, 722, 637, and 619 cm^{-1}; uv (CH_3CN) λmax 252 (logε 4.22) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 3H, J = 6.7 Hz), 1.27-1.31 (m, 14H), 1.96 (m, 1H), 2.95 (dd, 2H, J = 12.2 Hz and 10.4 Hz), 3.31-3.39 (m, 2H), 6.60 (br, 2H).

Anal. Calcd. for $C_{12}H_{24}N_2S$: C, 63.10; H, 10.59; N, 12.27. Found: C, 63.02; H, 10.47; N, 12.00.

5-Dodecyl-3,4,5,6-tetrahydropyrimidine-2-thiol (**1b**).

5-Dodecyl-3,4,5,6-tetrahydropyrimidine-2-thiol (**1b**) was obtained in 72% yield (3.062g), mp 137-138°; ir (potassium bromide): 3205, 3100, 2976, 2962, 2951, 2921, 2850, 1574, 1557, 1466, 1391, 1289, 1271, 1218, 721, 638, and 620 cm^{-1}; uv (CH_3CN) λmax 252 (logε 4.26) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 3H, J = 6.7Hz), 1.26-1.31 (m, 22H), 1.95 (m, 1H), 2.95 (dd, 2H, J = 12.2Hz and 10.4Hz), 3.31-3.39 (m, 2H), 6.61 (br, 2H).

Anal. Calcd. for $C_{16}H_{32}N_2S$: C, 67.55; H, 11.34; N, 9.85. Found: C, 67.59; H, 11.61; N, 9.73.

5-Octadecyl-3,4,5,6-tetrahydropyrimidine-2-thiol (**1c**).

5-Octadecyl-3,4,5,6-tetrahydropyrimidine-2-thiol (**1c**) was obtained in 13% yield (1.623 g) from 2-octadecyl-1,3-diaminopropane and CS_2, mp 132-133°; ir (potassium bromide): 3202, 3102, 2951, 2919, 2850, 1576, 1557, 1472, 1352, 1286, 1273, 1218, 721, and 637 cm^{-1}; uv (CH_2Cl_2) λmax 254 (logε 4.19) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 3H, J = 6.7Hz), 1.25-1.31 (m, 34H), 1.96 (m, 1H), 2.96 (dd, 2H, J = 12.2Hz and 10.4Hz), 3.32-3.39 (m, 2H), 6.34 (br, 2H).

Anal. Calcd. for $C_{22}H_{44}N_2S$: C, 71.67; H, 12.03; N, 7.60. Found: C, 71.92; H, 11.84; N, 7.47.

5-(4-Phenoxybutyl)-3,4,5,6-tetrahydropyrimidine-2-thiol (**1e**).

5-(4-Phenoxybutyl)-3,4,5,6-tetrahydropyrimidine-2-thiol (**1e**) was obtained in 27% yield (962 mg) from 2-(4-phenoxybutyl)-1,3-diaminopropane and CS_2, mp 168-169°; ir (potassium bromide): 3278, 2928, 2855, 1560, 1271, 1202, 1114, 985, 750, and 698 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 1.44 (m, 2H), 1.53 (m, 2H), 1.79 (m, 2H), 1.98 (m, 1H), 2.99 (br t, 2H), 3.40 (br d, 2H), 3.95 (t, 2H), 6.96 (m, 3H), 7.08 (br, 2H), 7.30 (m, 2H).

Anal. Calcd. for $C_{14}H_{20}N_2OS$: C, 63.60; H, 7.62; N, 10.59. Found: C, 63.72; H, 7.59; N, 10.60.

5-(9-Anthrylmethyl)-3,4,5,6-tetrahydropyrimidine-2-thiol (**1f**).

5-(9-Anthrylmethyl)-3,4,5,6-tetrahydropyrimidine-2-thiol (**1f**) was obtained in 8% yield (192 mg) from 2-(9-anthrylmethyl)-1,3-diaminopropane and CS_2, mp 275-277° (decomp); ir (potassium bromide): 3188, 3091, 2875, 2857, 1576, 1559, 1490, 1458, 1439, 1377, 1324, 1301, 1217, 1028, 900, 751, and 684 cm^{-1}; uv (CH_2Cl_2) λmax 402 (logε 3.88), 380 (logε 3.90), 361 (logε 3.68), 257 (logε 4.72) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 2.60 (m, 1H), 3.23 (br t, 2H), 3.32 (br d, 2H), 3.75 (d, 2H, J = 7.7 Hz), 6.27 (br, 2H), 7.62 (m, 5H), 8.21 (d, 2H, J = 7.1 Hz).

Anal. Calcd. for $C_{19}H_{18}N_2S$: C, 74.35; H, 5.91; N, 9.29. Found: C, 74.60; H, 5.65; N, 9.19.

2,3-Dimethyl-6-octyl-5*H*,7*H*-2a-thia(2a-S^{IV})-2,3,4a,7a-tetraazacyclopent[*c*,*d*]indene-1,4(2*H*,3*H*)–dithione (**3a**).

Typical procedure is as follows**:** A hexane solution of butyllithium (1.9 mmol) was added to a solution of cyclic thiourea **1a** (200 mg, 0.88 mmol) in THF (15 ml) with stirring at 0 °C under argon. The mixture was stirred for 1 hour at the same temperature. To the resulting dianion **2a** was added dropwise a THF solution (5 ml) of phenacyl chloride (135 mg, 0.88 mmol). The solution immediately became wine red. The reaction mixture was refluxed for 2 hours under argon and cooled to room temperature. A solution of methylisothiocyanate (192 mg, 2.7 mmol) in THF (5 mL) was added, and the mixture was stirred at room temperature for 20 hours under argon, and then evaporated. The residue was poured into an aqueous NH_4Cl solution. The solution was extracted with CH_2Cl_2, and the extract was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was chromatographed on a silica gel with CH_2Cl_2-*n*-hexane (20:1 v/v) to give **3a** (215mg, 66%) as a colorless solid, mp 156-158°; ir (potassium bromide): 2924, 2852, 1585, 1541, 1492, 1468, 1238, 1200, 1172, 1118, 1099, 724, and 646 cm^{-1}; uv (CH_3CN) λmax 260 (logε 4.52) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.89 (t, 3H, J = 6.7 Hz), 1.28-1.55 (m, 14H), 2.23 (m, 1H), 3.23 (s, 6H), 3.59 (dd, 2H, J = 13.9 Hz and 9.9 Hz), 4.87 (dd, 2H, J = 13.9 Hz and 4.5 Hz).

Anal. Calcd. for $C_{16}H_{28}N_4S_3$: C, 51.57; H, 7.57; N, 15.04. Found: C, 51.51; H, 7.73; N, 14.58.

2,3-Dimethyl-6-dodecyl-5*H*,7*H*-2a-thia(2a-S^{IV})-2,3,4a,7a-tetraazacyclopent[*c*,*d*]indene-1,4(2*H*,3*H*)–dithione (**3b**).

Tetraazathiapentalene **3b** was obtained in 66% yield (283 mg) by use of the **2b**/$PhCOCH_2Cl$/MeNCS system, mp 148-152°; ir (potassium bromide): 2923, 2852, 1586, 1542, 1492, 1469, 1240, 1201, 1173, 1123, 1107, and 646 cm^{-1}; uv (CH_2Cl_2) λmax 263(logε 4.56) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 3H, J = 6.7 Hz), 1.28-1.53 (m, 22H), 2.23 (m, 1H), 3.23 (s, 6H), 3.59 (dd, 2H, J = 13.9 Hz and 9.9 Hz), 4.88 (dd, 2H, J = 13.9 Hz and 4.5 Hz).

Anal. Calcd. for $C_{20}H_{36}N_4S_3$: C, 56.03; H, 8.46; N, 13.07. Found: C, 56.13; H, 8.67; N, 12.95.

2,3-Dimethyl-6-octadecyl-5*H*,7*H*-2a-thia(2a-S^{IV})-2,3,4a,7a-tetraazacyclopent[*c*,*d*]indene-1,4(2*H*,3*H*)–dithione (**3c**).

Tetraazathiapentalene **3c** was obtained in 46% yield (238 mg) by use of the

2c/PhCOCH$_2$Cl/MeNCS system, mp 148-152°; ir (potassium bromide): 2921, 2851, 1586, 1541, 1490, 1238, 1201, 1172, 1111, 1094, and 646 cm^{-1}; uv (CH$_2$Cl$_2$) λmax 264 (logε 4.58) nm; ^{1}H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 3H, J = 6.7Hz), 1.26-1.53 (m, 34H), 2.22 (m, 1H), 3.23 (s, 6H), 3.58 (dd, 2H), 4.88 (dd, 2H).

Anal. Calcd. for $C_{26}H_{48}N_4S_3$: C, 60.89; H, 9.43; N, 10.92. Found: C, 61.09; H, 9.12; N, 10.68.

2,3-Dimethyl-6-(4-benzyloxybutane)-5*H*,7*H*-2a-thia(2a-S^{IV})-2,3,4a,7a-tetraazacyclopent[*cd*]indene-1,4(2*H*,3*H*)–dithione (**3d**).

Tetraazathiapentalene **3d** was obtained in 46% yield (196 mg) by use of the **2d**/PhCOCH$_2$Cl/MeNCS system, mp 101-103°; ir (potassium bromide): 2921, 2849, 1578, 1541, 1490, 1458, 1388, 1239, 1200, 1113, 750, 693, and 675 cm^{-1}; uv (CH$_2$Cl$_2$) λmax 263 (logε 4.90) nm; ^{1}H nmr (300 MHz, deuteriochloroform): δ 1.55 (m, 6H), 2.22 (m, 1H), 3.23 (s, 6H), 3.49 (t, 2H, J = 5.8 Hz), 3.58 (t, 2H, J = 13.1 Hz), 4.51(s, 2H), 4.87(d, 2H, J = 13.1 Hz), 7.36(m, 5H).

Anal. Calcd. for $C_{19}H_{26}N_4OS_3$: C, 54.04; H, 6.21; N, 13.27. Found: C, 54.21; H, 6.19; N, 13.53.

2,3-Dimethyl-6-(4-phenoxybutane)-5*H*,7*H*-2a-thia(2a-S^{IV})-2,3,4a,7a-tetraazacyclopent[*cd*]indene-1,4(2*H*,3*H*)–dithione (**3e**).

Tetraazathiapentalene **3e** was obtained in 80% yield (322 mg) by use of the **2e**/PhCOCH$_2$Cl/MeNCS system, mp 165-167°; ir (potassium bromide): 2940, 2857, 1581, 1540, 1498, 1466, 1389, 1276, 1243, 1198, 1173, 1121, 1032, 933, 814, 754, and 689 cm^{-1}; ^{1}H nmr (300 MHz, deuteriochloroform): δ 1.67 (m, 4H), 1.85 (m, 2H), 2.27 (m, 1H), 3.23 (s, 6H), 3.49 (dd, 2H, J = 9.9 Hz and 3.8 Hz), 4.00 (t, 2H, J = 6.0 Hz), 4.89 (dd, 2H, J = 4.4 Hz and 9.3 Hz), 6.94 (m, 3H), 7.29 (m, 2H).

Anal. Calcd for $C_{18}H_{24}N_4OS_3$: C, 52.95; H, 5.92; N, 13.72. Found: C, 53.23; H, 6.03; N, 13.42.

2,3-Dimethyl-6-(9-anthrylmethyl)-5*H*,7*H*-2a-thia(2a-S^{IV})-2,3,4a,7a-tetraazacyclopent[*cd*]indene-1,4(2*H*,3*H*)–dithione (**3f**).

Tetraazathiapentalene **3f** was obtained in 45% yield (81 mg) by use of the **2f** / PhCOCH$_2$Cl/MeNCS system; Yellow solid, mp 145-146°; ir (potassium bromide): 3039, 2922, 2849, 1676, 1578, 1541, 1490, 1444, 1401, 1280, 1199, 1055, 1011, 887, 756, and 679 cm^{-1}; uv (CH$_2$Cl$_2$) λmax 389 (logε 4.06), 378 (logε 3.88), 360 (logε 3.96), 256 (logε 5.11) nm; ^{1}H nmr (300 MHz, deuteriochloroform): δ 2.80 (m, 1H), 3.18 (s, 6H), 3.86 (d, 2H, J = 6.0 Hz), 3.91 (d, 2H, J = 11.4 Hz), 4.64 (t, 2H, J = 12.9 Hz), 7.62 (m, 5H), 8.01 (t, 2H, J = 8.8 Hz).

Anal. Calcd for $C_{23}H_{22}N_4S_3$: C, 61.30; H, 4.92; N, 12.43. Found: C, 61.00; H, 5.22; N, 12.17.

Synthesis of Macrocyclic Compound (**5a**).

1) Method A.

A solution of **3a** (373 mg, 1 mmol) and **4a** (220 mg, 1 mmol) in benzene (10 mL) was refluxed for 24 hours, and cooled to room temperature. The precipitate was isolated by filtration, washed with *n*-hexane, and dried *in vacuo*. Compound **5a** was obtained in 50% yield (224 mg) as colorless solid. On the other hand, the filtrate was evaporated, and the residue was purified by column chromatography on silica gel with CH$_2$Cl$_2$-*n*-hexane (3:1 v/v) to give **6a** (82 mg, 17%) and **7a** (21 mg, 3%).

The same reaction was conducted by employing benzene-*n*-hexane as solvent system: A solution of **3a** (373 mg, 1 mmol) and **4a** (220 mg, 1 mmol) in a 3:2 mixture (10 mL) benzene and *n*-hexane was refluxed for 24 hours, and cooled to room temperature. The precipitate was isolated by filtration, washed with *n*-hexane, and dried under reduced pressure. Compound **5a** was obtained in a 77% yield (745 mg) as colorless solid. On the other hand, the filtrate was removed under reduced pressure and the residue was purified by column chromatography on silica gel with CH$_2$Cl$_2$:*n*-hexane = 3: 1 (v/v) to give **6a** (29 mg, 6%) and **7a** (7 mg, 1%).

2) Method B.

A mixture of **3a** (373 mg, 1 mmol) and **4a** (220 mg, 1 mmol) in benzene was refluxed for 24 hours, and benzene was removed *in vacuo*. A 3:2 (v/v) mixture (10 mL) of benzene and *n*-hexane was added to the residue, and refluxed for 2 hours. The solvent was removed under reduced pressure. These operations were repeated three times. Products were purified by the same method as those used for Method A. Compound **5a** was obtained in a quantitative yield.

Macrocyclic Compound (**5a**).

Compound **5a** has mp 223-225° (decomp); ir (potassium bromide): 2922, 2853, 1575, 1528, 1477, 1417, 1235, 1198, 1163, 1144, 1132, and 1106 cm^{-1}; uv (CH$_2$Cl$_2$) λmax 266 (logε 4.74) nm; ^{1}H nmr (300 MHz, deuteriochloroform): δ 0.89 (t, 6H, J = 6.7 Hz), 1.27-1.55 (m, 28H), 2.16 (m, 2H), 3.47 (dd, 4H, J = 13.4 Hz and 10.4 Hz), 4.89 (dd, 4H, J = 13.4 Hz and 10.4 Hz), 5.00 (s, 8H), 7.29 (s, 8H); FAB-mass m/z 893(M+H$^+$).

Anal. Calcd. for $C_{44}H_{60}N_8S_6$: C, 59.15; H, 6.77; N, 12.54. Found: C, 58.98; H, 6.82; N, 12.65.

2-(4-Isothiocyanatomethyl-benzyl)-3-methyl-6-octyl-*5H,7H*-2a-thia(2a-S^{IV})-2,3,4a,7a-tetraazacyclopenta[*cd*]-indene-1,4(2*H*,3*H*)-dithione (**6a**).

Compound **6a** has mp 215-217° (decomp); ir (potassium bromide): 2926, 2854, 2189, 2097, 1579, 1531, 1484, 1466, 1427, 1406, 1342, 1236, 1189, 1173, 1130, 1101, and 720 cm^{-x1}; uv (CH$_2$Cl$_2$) λmax 264 (logε 4.50) nm; ^{1}H nmr (300 MHz, deuteriochloroform): δ 0.89 (t, 3H, J = 6.7 Hz), 1.28-1.54 (m, 14H), 2.23 (m, 1H), 3.18 (s, 6H), 3.51-3.62 (m, 2H), 4.69 (s, 2H), 4.85-4.96 (m, 4H), 7.27-7.41 (m, 4H).

Anal. Calcd for $C_{24}H_{33}N_5S_4$: C, 55.45; H, 6.40; N, 13.47. Found: C, 55.29; H, 6.25; N, 13.32.

2,3-Bis-(4-isothiocyanatomethyl-benzyl)-6-octyl-*5H,7H*-2a-thia(2a-S^{IV})-2,3,4a,7a-tetraazacyclopenta[*cd*]-indene-1,4(2*H*,3*H*)-dithione (**7a**).

Compound **7a** has mp 209-211° (decomp); ir (potassium bromide: 2925, 2854, 2090, 1579, 1532, 1474, 1420, 1406, 1334, 1236, 1198, 1163, 752, 724, and 671 cm^{-1}; uv (CH$_2$Cl$_2$) λmax 265 (logε 4.54) nm; ^{1}H nmr (300 MHz, deuteriochloroform): δ 0.89 (t, 3H, J = 6.7Hz), 1.28-1.53 (m, 14H), 2.22 (m, 1H), 3.52 (m, 2H), 4.71 (s, 2H), 4.87-4.95 (m, 4H), 7.25-7.35 (m, 4H).

Anal. Calcd for $C_{32}H_{38}N_6S_5$: C, 57.62; H, 5.74; N, 12.60. Found: C, 57.86; H, 5.76; N, 12.38.

Conversion of **6a** to **5a**.

Compound **6a** (166 mg, 0.32 mmol) was refluxed in benzene (25 mL) for 24 hours. The precipitate was isolated by filtration, washed with *n*-hexane, and dried *in vacuo*. Compound **5a** was obtained in 77% yield (110 mg). After the filtrate was removed

in vacuo, the crude product was purified by column chromatography (silica gel, CH_2Cl_2:*n*-hexane = 9 : 1 v/v) to give **4a** (5 mg, 7%), **7a** (trace), and **3a** (20 mg, 17%).

Conversion of **7a** to **5a**.

Compound **7a** (77 mg, 0.12 mmol) was refluxed in benzene (9 mL) for 24 hours. The precipitate was isolated by filtration, washed with *n*-hexane and dried *in vacuo*. Compound **5a** was obtained in 91% yield (47 mg). After the filtrate was evaporated under reduced pressure, the residue was purified by column chromatography (silica gel, CH_2Cl_2:*n*-hexane = 9:1 v/v) to give **4a** (23 mg, 91%).

The Reaction of **5a** with Methylisothiocyanate.

A solution of **5a** (134 mg, 0.15 mmol) and methylisothicyanate (78 mg, 1.05 mmol) in benzene (15 mL) was refluxed for 24 hours. After the solvent was removed *in vacuo*,

CH_2Cl_2-*n*-hexane was added to the residue. The precipitate was isolated by filtration, washed with *n*-hexane and dried *in vacuo*. Compound **5a** was recovered in 43% yield. On the other hand, the filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography (silica gel, benzene:ethyl acetate = 3:1 v/v) to give **3a** (39mg, 35%), **6a** (23mg, 15%), **7a** (7mg, 4%), and **4a** (21mg, 32%).

Preparation of **8**.

Compound **8** was prepared by a similar method to that described previously [4] (Scheme 9). Treatment of 6,7-dihydro-2-methyl-5*H*-pyrimido[1,2-*d*][1,2,4]thiadiazole-3(2*H*)-thione (**15**) (0.187 g, 1 mmol), which was prepared by thermolysis of 3,4-dimethyl-1,6-propano-1*H*,6*H*-3a-thia(S^{IV})-1,3,4,6-tetraaza-thiapentalene-2,5(3*H*,4*H*)-dithione (**3**: R = H), with *p*-methoxyphenyl-isoselenocyanate (**10**) [20] (0.212 g, 1 mmol) in $CHCl_3$ (20 mL) gave unsymmetrical tetraazathiapentalene derivative **16** in 95% yield (0.38 g). Thermolysis of **16** at 170 °C under reduced pressure (2mmHg) gave selectively the thiadiazole derivative **9** in 91% yield (0.273 g). The reaction of **9** with 1.5 equivalents of **10** in refluxing $CHCl_3$ for 3 hours gave **8** in a 59% yield (0.295 g).

2-Methyl-3-*p*-methoxyphenyl-6,7-dihydro-5*H*-2a-thia(2a-S^{IV})-2,3,4a,7a-tetraazacyclopent[*cd*]inden-1(2*H*)-thione-4(3*H*)-selenone (**16**).

Compound **16** has mp 124-126°(decomp); ir (potassium bromide): 3454, 2924, 2832, 2362, 1606, 1568, 1522, 1476, 1372, 1309, 1242, 1210, 1173, 1155, 1121, 1064, 1033, 942, 906, 828, 769, 697, and 516 cm^{-1}; uv (CH_2Cl_2) λmax 254 (logε 4.60), 290 (logε 4.44), 352 (logε 3.79) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 2.44 (m, 2H), 3.24 (s, 3H), 3.85 (s, 3H), 4.45 (t, 2H, J = 5.8Hz), 4.66 (t, 2H, J = 5.8Hz), 7.01-7.31 (AA?XX?type, 4H); ms m/z 401 ($M+H^+$).

Anal. Calcd. for $C_{14}H_{16}N_4S_2$ Se: C, 42.10; H, 4.04; N, 14.03. Found: C, 42.00; H, 4.01; N, 13.89.

2-*p*-Methoxyphenyl-6,7-dihydro-5*H*-1,2,4-thiadiazolo[4,5-*a*]-pyrimidine-3(2*H*)-selenone (**9**).

Compound **9** has mp 94-96°(decomp); ir (potassium bromide): 3480, 1697, 1584, 16519, 1502, 1314, 1252, 1213, 1153, 1062, 1028, 984, 833, 766, and 744 cm^{-1}; uv (CH_2Cl_2) λmax 265 (logε 4.01) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 1.89 (m, 2H), 3.61 (t, 2H, J = 5.5Hz), 3.81 (s, 3H), 4.03 (t, 2H, J = 5.8Hz), 6.90 (s, 4H).

Anal. Calcd. for $C_{12}H_{13}N_3$ OSSe: C, 44.17; H, 4.02; N, 12.88 Found: C, 44.00; H, 4.01; N, 13.00.

2,3-Bis(*p*-methoxyphenyl)-6,7-dihydro-5*H*-2a-thia(2a-S^{IV})-2,3,4a,7a-tetraazacyclopent[*cd*]inden-1,4(2*H*,3*H*)-diselenone (**8**).

Compound **8** has mp 146-148°(decomp); ir (potassium bromide): 2930, 2833, 2130, 1606, 1563, 1514, 1447, 1311, 1251, 1210, 1148, 1084, 1033, 979, 884, 834, 779, 731, 684, 563, 521, and 500 cm^{-1}; uv (CH_2Cl_2) λmax 288 (logε 4.38), 352 (logε 3.84) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 2.51 (m, 2H), 4.69 (t, 4H, J = 5.8 Hz), 6.90-7.30 (m, 8H).

Anal. Calcd. for $C_{12}H_{13}N_3$ OSSe: C, 44.17; H, 4.02; N, 12.88 Found: C, 44.00; H, 4.01; N, 13.00.

Thermolysis of **8**.

Compound **8** in solid state was stable to air, but decomposed slowly in benzene or $CHCl_3$ solution (see Scheme 5). When the ^1H NMR spectrum of **8** was measured immediately after dissolving in benzene-d_6, characteristic signals due to **8** appeared at 3.86 ppm (s, 6H) and at 4.69 ppm (t, 4H, J = 5.8 Hz). However, after standing for 2 hours, new signals due to the methoxy group of **9** and **10** was observed at 3.81 ppm (s, 3H) and 3.78 ppm (s, 3H), respectively. These two new singlet signals were identified by comparison with the signals of authentic samples.

Macrocyclic Compound **5d**.

Macrocyclic compound **5d** was obtained in 17% yield (64 mg) from **3a** and **4b** by the same procedure as that described in Method A for **5a**. In this reaction, compounds **6d** and **7d** were also obtained in 32% (146 mg) and 22% (115 mg) yields, respectively.

Compound **5d** has mp 220-221°(decomp); ir (potassium bromide): 2924, 2853, 1579, 1519, 1480, 1432, 1420, 1342, 1235, 1186, 1156, 1090, 1049, 914, and 720 cm^{-1}; uv(CH_2Cl_2) λmax 266 (logε 4.75) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.89 (t, 6H, J = 6.7Hz), 1.29-1.58 (m, 28H), 2.28 (br, 2H), 2.59 (br, 4H), 3.48-3.63 (m, 12H), and 4.89-5.00 (m, 4H); FAB-mass m/z 769 ($M+H^+$).

Anal. Calcd. for $C_{34}H_{56}N_4S_3$: C, 53.09; H, 7.38; N, 14.57. Found: C, 53.23; H, 7.33; N, 14.46.

Compound **6d** has mp 119.5-120.5°; ir (potassium bromide): 2957, 2924, 2850, 2185, 2122, 2082, 1582, 1535, 1487, 1341, 1237, 1192, 1171, 1148, 1135, and 1103 cm^{-1}; uv (CH_2Cl_2) λmax 264 (logε 4.54) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.89 (t, 3H, J = 6.7Hz), 1.28-1.55 (m, 14H), 2.12-2.36 (m, 3H), 3.28 (s, 3H), 3.52-3.61 (m, 4H), 3.86 (t, 2H, J = 6.1Hz), 4.88-4.93 (m, 2H).

Anal. Calcd. for $C_{19}H_{31}N_6S_4$: C, 49.85; H, 6.83; N, 15.30. Found: C, 50.15; H, 6.95; N, 15.15.

Compound **7d** has mp 104 -106°; ir (potassium bromide): 2923, 2853, 2189, 2129, 2078, 1584, 1532, 1480, 1420, 1238, 1235, 1184, 1166, 1146, 1135, and 1080cm^{-1}; uv (CH_2Cl_2) λmax 265 (logε 4.54) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.89 (t, 3H, J = 6.7Hz), 1.28-1.55 (m, 14H), 2.17-2.35 (m, 5H), 3.53 (dd, 2H), 3.66 (t, 4H, J = 6.1Hz), 3.92 (t, 4H, J = 6.1Hz), 6.41 (dd, 2H).

Anal. Calcd. for $C_{22}H_{34}N_6S_5$: C, 48.67; H, 6.31; N, 15.48 Found: C, 48.93; H, 6.30; N, 15.18.

Macrocyclic Compound **5b**.

Macrocyclic compound **5b** was obtained in 46% yield (115 mg) from **3b** and **4a** by the same procedure as that described in Method A for **5a.** In this reaction, compounds **6b** and **7b** were

obtained in 17 % (48 mg) and 4 % (14 mg) yields, respectively.

Compound **5b** has mp 233-235° (decomp); ir (potassium bromide): 2919, 2851, 1575, 1531, 1478, 1416, 1236, 1198, 1162, 1143, 1111, and 753 cm^{-1}; uv(CH_2Cl_2) λmax 266 (logε 4.76) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 6H, J = 6.7Hz), 1.27-1.51 (m, 44H), 2.15 (m, 2H), 3.47 (dd, 4H), 4.90 (dd, 4H), 5.00 (s, 8H), 7.29 (s, 8H).

Anal. Calcd for $C_{52}H_{76}N_8S_6$: C, 59.15; H, 6.77; N, 12.54. Found: C, 59.32; H, 6.52; N, 12.55.

Compound **6b** has mp 224 – 225.5°(decomp); ir (potassium bromide): 2919, 2849, 2150, 2076, 1583, 1531, 1482, 1470, 1416, 1400, 1332, 1239, 1204, 1189, 1149, 1107, and 718 cm^{-1}; uv (CH_2Cl_2) λmax 264 (logε 4.54) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 3H, J = 6.7Hz), 1.27-1.54 (m, 22H), 2.23 (m, 1H), 3.19 (s, 3H), 3.51-3.61 (m, 2H), 4.69 (s, 2H), 4.85-4.96 (m, 4H), and 7.27-7.42 (m, 4H).

Anal. Calcd for $C_{28}H_{41}N_5S_4$: C, 58.39; H, 7.18; N, 12.16. Found: C, 58.69; H, 7.11; N, 11.87.

Compound **7b** has mp 204 – 207°(decomp); ir (potassium bromide): 2922, 2852, 2174, 2088, 1582, 1531, 1469, 1421, 1337, 1236, 1165, 1144, 753, and 668 cm^{-1}; uv (CH_2Cl_2) λmax 265 (logε 4.53) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 3H, J = 6.7Hz), 1.26-1.53 (m, 22H), 2.22 (m, 1H), 3.52 (dd, 2H), 4.71 (s, 4H), 4.88 (s, 4H), 4.93 (dd, 2H), and 7.26-7.36 (m, 8H).

Anal. Calcd for $C_{36}H_{46}N_6S_6$: C, 59.79; H, 6.41; N, 11.62. Found: C, 59.78; H, 6.44; N, 11.32.

Macrocyclic Compound **5c**.

Macrocyclic compound **5c** was obtained in 39% yield (114 mg) from **3c** and **4a** by the same procedure as that described in Method A for **5a**. In this reaction, compounds **6c** and **7c** were obtained in 16% (52 mg) and 3% (13 mg) yields, respectively; mp 218-219°(decomp); ir (potassium bromide): 2921, 2851, 1576, 1532, 1478, 1417, 1236, 1198, 1165, 1144, and 753 cm^{-1}; uv (CH_2Cl_2) λmax 266 (logε 4.66) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 6H, J = 6.7Hz), 1.26-1.52 (m, 68H), 2.17 (m, 2H), 3.47 (dd, 4H), 4.90 (dd, 4H), 5.00 (s, 8H), and 7.29 (s, 8H).

Anal. Calcd for $C_{64}H_{100}N_8S_6$: C, 65.48; H, 8.59; N, 9.55. Found: C, 65.22; H, 8.88; N, 9.25.

Compound **6c** has mp 123-124°; ir (potassium bromide): 2918, 2849, 2151, 2077, 1583, 1531, 1482, 1471, 1416, 1400, 1342, 1234, 1203, 1189, 1149, 1111, and 718 cm^{-1}; uv (CH_2Cl_2) λmax 264 (logε 4.54) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 3H, J = 6.7Hz), 1.26-1.54 (m, 34H), 2.23 (m, 1H), 3.18(s, 3H), 3.51-3.61 (m, 2H), 4.69 (s, 2H), 4.85-4.96 (m, 4H), and 7.27-7.41 (m, 4H).

Anal. Calcd for $C_{34}H_{53}N_5S_4$: C, 61.87; H, 8.09; N, 10.61. Found: C, 62.01; H, 8.01; N, 10.40.

Compound **7c** has mp 205-210° (decomp) ; ir (potassium bromide): 2928, 2854, 2175, 2100, 1586, 1524, 1472, 1421, 1334, 1236, 1169, 1144, 755, 721, and 669 cm^{-1}; uv (CH_2Cl_2) λmax 266 (logε 4.55) nm ; ^1H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 3H, J = 6.7Hz), 1.27-1.53 (m, 34H), 2.22 (m, 1H),3.52(dd, 2H), 4.71 (s, 4H), 4.87-4.96 (m, 6H), and 7.26-7.35 (m, 8H).

Anal. Calcd. for $C_{42}H_{58}N_6S_5$: C, 62.49; H, 7.24; N, 10.41. Found: C, 62.61; H, 7.40; N, 10.24.

Macrocyclic Compound **5e**.

Macrocyclic compound **5e** was obtained in 43% yield (51 mg) from **3d** and **4c** by the same procedure as that described in Method B for **5a**. Compound **5e** was obtained as a yellow solid, mp 195-197°; ir (potassium bromide): 3065, 3030, 2934, 2856, 1578, 1527, 1475, 1458, 1403, 1364, 1320, 1273, 1235, 1188, 1111, 932, 823, 756, and 696 cm^{-1}; uv (CH_2Cl_2) λmax 401 (logε 4.72), 380 (logε 4.72), 360 (logε 4.56), 258 (logε 5.60) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 1.27 (m, 4H), 1.54-1.72 (m, 8H), 2.20 (m, 2H), 3.48 (m, 4H+4H), 4.51 (s, 4H), 4.73 (d, 2H, J = 14.5Hz), 4.99 (d, 2H, 18.1Hz), 5.96 (d, 8H), 7.29 (m, 10H), 7.64 (m, 8H), 8.45 (m, 8H).

Anal. Calcd. for $C_{66}H_{64}O_2N_8S_6$: C, 66.41; H, 5.40; N, 9.39. Found: C, 66.37; H, 5.53; N, 9.53.

Macrocyclic Compound **5f**.

Macrocyclic compound **5f** was obtained in 30% yield (56 mg) from **3d** and **4d** by the same procedure as that described in Method B for **5a**. Compound **5f** has mp 195-197° (decomp); ir (potassium bromide): 2913, 2853, 1577, 1526, 1473, 1400, 1355, 1307, 1283, 1234, 1157, 1094, 996, 952, 737, 698, and 670 cm^{-1}; ^1H nmr (300MHz, deuteriochloroform): δ 1.52 (m, 12H), 2.22 (m, 2H), 3.49 (m, 4H+4H), 4.01 (m, 8H), 4.19 (m, 8H), 4.50 (s, 4H), 4.79 (br, 2H), 7.36 (m, 18H).

Anal. Calcd. for $C_{42}H_{58}O_2N_{10}S_6$: C, 54.39; H, 6.30; N, 15.10. Found: C, 54.41; H, 6.42; N, 14.95.

Macrocyclic Compound **5g**.

Macrocyclic compound **5g** was obtained in 90% yield (197 mg) from **3d** and **4a** by the same procedure as that described in Method B for **5a**. Compound **5g** has mp 215-216° (decomp); ir (potassium bromide): 2916, 2857, 1572, 1524, 1474, 1419, 1235, 1163, 1140, 814, 751, and 683 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 1.27 (m, 4H), 1.54-1.72 (m, 8H), 2.16 (m, 2H), 3.47 (m, 4H+4H), 4.49 (s, 4H), 4.99 (d, 4H, J = 2.4Hz), 5.14 (s, 8H), 7.29 (m, 18H); FAB-mass m/z 993($M+H^+$).

Anal. Calcd. for $C_{50}H_{56}O_2N_8S_6$: C, 60.45; H, 5.68; N, 11.28. Found: C, 60.75; H, 5.70; N, 10.98.

Macrocyclic Compound **5h**.

Macrocyclic compound **5h** was obtained in a 67% yield (133 mg) from **3d** and **4e** by the same procedure as that described in Method B for **5a**. Compound **5h** has mp 228-230° (decomp); ir (potassium bromide): 2929, 2854, 1576, 1515, 1457, 1340, 1231, 1184, 1162, 1129, 809, 776, 745, 697, and 670 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 1.25 (m, 4H), 1.61 (m, 8H), 2.22 (m, 2H), 3.48 (m, 4H+4H), 4.50 (s, 4H), 4.96 (d, 4H, J = 13.4Hz), 5.29 (s, 8H), 7.34 (m, 18H).

Anal. Calcd. for $C_{50}H_{56}O_2N_8S_6$: C, 60.45; H, 5.68; N, 11.28. Found: C, 60.71; H, 5.77; N, 11.31.

Macrocyclic Compound **5i**.

Macrocyclic compound **5i** was obtained in 13% yield (5 mg) from **3f** and **4a** by the same procedure to that described by Method B for **5a**. Compound **5i** was obtained as a Yellow solid, mp 253-255° (decomp); ir (potassium bromide): 2909, 2856, 1685, 1654, 1637, 1577, 1542, 1523, 1458, 1420, 1343, 1154, 1117, 901, 736, and 675 cm^{-1}; uv (CH_2Cl_2) λmax 389 (logε 4.35), 368 (logε 4.56), 358 (logε 4.25), 257 (logε 5.52) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 2.10 (m, 2H), 3.42 (m, 4H), 3.57 (m, 4H), 4.66 (m, 4H), 4.87 (s, 8H), 7.19 (m, 8H), 7.62 (m, 10H), 8.01 (br, 8H).

Anal. Calcd. for $C_{58}H_{48}N_8S_6$: C, 66.38; H, 4.61; N, 10.68. Found: C, 66.21; H, 4.51; N, 10.89.

Macrocyclic Compound **11a**.

A mixture of **5a** (179mg, 0.2mmol) and $NaBH_4$ (152mg, 4.0mmol) in DMSO (20 mL) was stirred at room tempareture for 24 hours, quenched with an aqueous NH_4Cl solution, and then extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography (silica gel, CH_2Cl_2:ethylacetate = 19:1) to give **11a** (111mg, 66%) as white solid, mp 210-211° (decomp); ir (potassium bromide): 3216, 3049, 2924, 2854, 1560, 1537, 1488, 1418, 1382, 1337, 1308, 1259, 1171, 1140, 1094, 961, 933, 901, 878, 827, and 754 cm^{-1}; uv (CH_2Cl_2) λmax 257 (logε 4.70) nm; ^1H nmr (300 MHz, acetone-d_6): δ 0.86 (t, 6H, J = 6.7Hz), 1.22-1.28 (m, 28H), 1.73 (m, 2H), 3.40-3.81 (br, 4H), 4.26-4.65 (br, 4H), 4.93 (br, 4H+8H), 7.26 (s, 8H), 8.64 (br, 4H); FAB-mass m/z 838 ($M+H^+$).

Anal. Calcd. for $C_{44}H_{68}N_8S_4$: C, 63.11; H, 8.19; N, 13.38. Found: C, 63.25; H, 8.19; N, 13.15.

Macrocyclic Compound **11b**.

Macrocyclic compound **11b** was obtained in 46% yield (44 mg) from **5b** by the same procedure as that described for **11a**. Compound **11b** has mp 134-135° (decomp); ir (potassium bromide): 3210, 3046, 2924, 2853, 1561, 1535, 1488, 1466, 1407, 1381, 1336, 1282, 1240, 1172, and 1092 cm^{-1}; uv (CH_2Cl_2) λmax 258 (logε 4.66) nm; ^1H nmr (300 MHz, acetone-d_6): δ 0.88 (t, 6H, J = 6.4Hz), 1.22-1.27 (m, 44H), 1.73 (m, 2H), 3.40-3.82 (br, 4H), 4.26-4.62 (br, 4H), 4.93 (br, 4H+8H), 7.26 (s, 8H), 8.64 (br, 4H).

Anal. Calcd. for $C_{52}H_{84}N_8S_4$: C, 65.77; H, 11.80; N, 8.92. Found: C, 65.48; H, 12.08; N, 9.16.

Macrocyclic Compound **11e**.

Macrocyclic compound **11e** was obtained in 53% yield (9 mg) as yellow solid from **5e** by the same procedure as that described for **11a**. Compound **11e** has mp 188-190° (decomp); ir (potassium bromide): 2925, 2857, 1654, 1542, 1458, 1284, and 695 cm^{-1}; uv (CH_2Cl_2) λmax 255 (logε 4.65) nm; ^1H nmr (300 MHz, acetone-d_6): δ 1.29 (m, 4H), 1.43 (br, 4H), 1.60 (br, 4H), 2.25 (m, 2H), 3.45 (m, 8H), 4.48 (m, 8H), 5.69 (m, 4H+8H), 7.35 (br, 10H), 7.51 (br, 4H), 7.93 (m, 8H), 8.30 (m, 8H).

Anal. Calcd. for $C_{66}H_{72}N_8O_2S_4$: C, 69.68; H, 6.38; N, 9.85. Found: C, 69.39; H, 6.68; N, 10.11.

Macrocyclic Compound **11f**.

Macrocyclic compound **11f** was obtained in 35% yield (6 mg) from **5f** by the same procedure as that described for **11a**. Compound **11f** has mp 168-170° (decomp); ir (potassium bromide): 2935, 2857, 1654, 1560, 1542, 1262, 1117, and 803 cm^{-1}; uv (CH_2Cl_2) λmax 257 (logε 4.70) nm; ^1H nmr (300 MHz, acetone-d_6): δ 1.29 (m, 4H), 1.41 (br, 4H), 1.59 (br, 4H), 2.25 (m, 2H), 2.58 (br, 2H), 3.47 (m, 8H), 3.62 (m, 8H), 4.20 (m, 16H), 4.48 (s, 4H), 4.74 (br, 4H), 5.33 (m, 4H), 7.35 (m, 10H).

Anal. Calcd. for $C_{42}H_{66}N_{10}O_2S_4$: C, 57.90; H, 6.85; N, 16.07. Found: C, 58.15; H, 6.47; N, 15.98.

Macrocyclic Compound **11g**.

Macrocyclic compound **11g** was obtained in 37% yield (35 mg) from **5g** by the same procedure as that described for **11a**. Compound **11g** has mp 223-225° (decomp); ir (potassium bromide): 3056, 2926, 2857, 1637, 1542, 1284, 1102, 970, 740, and 699 cm^{-1}; uv (CH_2Cl_2) λmax 328 (logε 5.62), 275 (logε 5.08) nm; ^1H nmr (300 MHz, deuteriochloroform): δ 1.25 (m, 4H), 1.54-1.72 (m, 8H), 2.03 (m, 2H), 3.47 (m, 8H), 4.43 (s, 4H), 4.99 (m, 8H), 7.28 (m, 4H), 7.31 (m, 18H); FAB-mass m/z 937 ($M+H^+$).

Anal. Calcd. for $C_{50}H_{64}N_8O_2S_4$: C, 64.07; H, 6.88; N, 11.95. Found: C, 63.86; H, 7.03; N, 12.00.

Macrocyclic Compound **11h**.

Macrocyclic compound **11h** was obtained in 64% yield (31 mg) from **5h** by the same procedure as that described for **11a**. Compound **11h** has mp 214-215° (decomp); ir (potassium bromide): 3230, 3039, 2924, 2856, 1527, 1490, 1457, 1375, 1324, 1091, 873, 741, and 696 cm^{-1}; ^1H nmr (300 MHz, dimethylsulfoxide-d_6): δ 1.21 (m, 4H), 1.33-1.52 (m, 8H), 1.81 (m, 2H), 3.40 (m, 8H), 4.42 (s, 4H), 4.73 (m, 8H), 5.09 (s, 8H), 7.29 (m, 18H), 8.53 (br, 4H).

Anal. Calcd. for $C_{50}H_{64}N_8O_2S_4$: C, 64.07; H, 6.88; N, 11.95. Found: C, 64.26; H, 6.59; N, 11.68.

Alkaline Hydrolysis of **3a**.

An aqueous KOH solution (KOH 0.41 g/H_2O 5 mL) was added to an ethanol solution (45 mL) of **3a** (149 mg, 0.40 mmol). The mixture was stirred at room temperature for 40 minutes, and then neutralized with diluted HCl solution. The reaction mixture was concentrated and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and concentrated. The crude product was purified by column chromatography (silica gel, toluene : ethylacetate = 4 :1) to give **13** (37 mg, 28%) and **12** (53 mg, 37%).

1-Methyl-3-{2-[(3-methyl-thioureido)-methyl]-decyl}-thiourea(**12**).

Compound **12** was obtained as an oil; ir (potassium bromide): 3252, 2926, 2854, 1650, 1538, 1469, 1392, 1216, 1167, 1040, 741, 713, and 668 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 3H, J = 6.7Hz), 1.27-1.41 (m, 14H), 2.00 (m, 1H), 3.19 (d, 6H, J = 4.3Hz), 3.57-3.66 (m, 2H), 4.73-4.79 (m, 2H), 10.65 (br, 2H).

Anal. Calcd for $C_{15}H_{32}N_4OS_2$: C, 54.17; H, 9.25; N, 16.85. Found: C, 53.98; H, 9.34; N, 17.02.

5-Octyl-2-oxo-dihydro-pyrimidine-1, 3-dicarbothioic Acid bis-methylamide (**13**).

Compound **13** was obtained as an oil; ir (potassium bromide): 3263, 3071, 2923, 2857, 1556, 1462, 1347, 1291, 1211, 1056, and 666 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 0.88 (t, 3H, J = 6.7Hz), 1.27-1.39 (m, 14H), 1.97 (m, 1H), 2.98 (d, 6H, J = 3.1Hz), 3.36-3.45 (m, 2H), 3.84 (br, 2H), 6.40 (br, 2H), 6.91 (br, 2H).

Anal. Calcd for $C_{16}H_{30}N_4OS_2$: C, 53.59; H, 8.43; N, 15.62. Found: C, 53.29; H, 8.43; N, 15.32.

Alkaline Hydrolysis of **13**.

An aqueous KOH solution (KOH 0.41 g/H_2O 5 mL) was added to an ethanol solution (45 mL) of **13** (53 mg, 0.15 mmol). The reaction mixture was refluxed for 5 minutes, cooled to room temperature, and then neutralized with diluted HCl solution. The mixture was concentrated and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography (silica gel, toluene : ethylacetate = 1:3) to give **17** (34mg, 69%).

Macrocyclic Compound **14a**.

An aqueous KOH solution (KOH 2.0 g/H_2O 25 mL) was added to an ethanol solution (60 mL) of **5a** (125 mg, 0.14mmol).

The reaction mixture was refluxed for 4 hours, cooled to room tempareture, and then neutralized with diluted HCl solution. The mixture was concentrated and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography (silica gel, CH_2Cl_2:ethylacetate = 3:1) to give **14a** (50 mg, 44%) as a colorless solid, mp 199-200°(decomp); ir (potassium bromide): 3299, 3057, 2923, 2852, 1557, 1467, 1412, 1383, 1337, 1291, 1223, 970, 687, and 601 cm^{-1}; uv (methanol) λmax 244 (logε 4.77) nm; ^1H nmr (300 MHz, methanol-d_4): δ 0.89 (t, 6H, J = 6.7Hz), 1.25-1.30 (m, 28H), 1.90 (m, 2H), 3.56 (m, 4H), 4.59 (m, 8H), 7.24 (s, 8H), {4H signal was overlapped with methanol's one.}; FAB-mass m/z 814 ($M+H^+$).

Anal. Calcd. for $C_{42}H_{68}N_8S_4$: C, 62.02; H, 8.43; N, 13.78. Found: C, 61.75; H, 8.52; N, 13.59.

Macrocyclic Compound **14e**.

Macrocyclic compound **14e** was obtained in 44% yield (50 mg) from **5e** by the same procedure as that described for **14a**. Compound **14e** was obtained as a yellow solid; mp 180-182°(decomp); ir (potassium bromide): 2926, 2849, 1658, 1560, 1542, 1508, 1458, 1282, 1117, 1002, 745, and 701 cm^{-1}; uv (CH_2Cl_2) λmax 369 (logε 3.78), 252 (logε 5.33) nm; ^1H nmr (300 MHz, acetone-d_6): δ 1.29 (m, 4H), 1.43 (m, 4H), 1.59 (m, 4H), 2.25 (m, 2H), 3.48 (m, 8H), 4.38 (s, 4H), 4.48 (m, 12H), 7.33 (m, 10H), 7.65 (br, 2H), 7.87 (br, 2H), 7.94 (m, 8H), 8.28 (m, 8H).

Anal. Calcd. for $C_{64}H_{72}N_8O_2S_4$: C, 69.03; H, 6.52; N, 10.06. Found: C, 68.88; H, 6.35; N, 9.89.

Macrocyclic Compound **14f**.

Macrocyclic compound **14f** was obtained in 83% yield (14 mg) from **5f** by the same procedure as that described for **14a**. Compound **14f** was obtained as a yellow solid; mp 159-161°(decomp); ir (potassium bromide): 3238, 2929, 2849, 1685, 1654, 1560, 1457, 1369, 1273, 1205, 1117, 741, 698, and 658 cm^{-1}; ^1H nmr (300 MHz, acetone-d_6): δ 1.29 (m, 4H), 1.46 (m, 4H), 1.59 (m, 4H), 1.89 (m, 2H), 2.96 (br, 4H), 3.33 (m, 8H), 3.48 (m, 8H), 3.75 (m, 16H), 4.48 (s, 4H), 5.60 (m, 4H), 7.13 (br, 2H), 7.23 (br, 2H), 7.35 (m, 10H).

Anal. Calcd. for $C_{42}H_{66}N_{10}O_2S_4$: C, 57.89; H, 6.85; N, 16.07. Found: C, 57.59; H, 6.98; N, 15.79.

Macrocyclic Compound **14g**.

Macrocyclic compound **14g** was obtained in 52% yield (38 mg) from **5g** by the same procedure as that described for **14a**. Compound **14g** has mp 216-217° (decomp); ir (potassium bromide): 3258, 3033, 2924, 2849, 1560, 1283, 1100, and 698 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 1.22 (m, 4H), 1.46 (m, 8H), 1.97 (m, 2H), 3.36 (m, 8H), 4.41 (s, 4H), 4.89 (m, 8H), 5.14 (s, 8H), 7.19 (br, 4H), 7.24 (m, 10H); FAB-mass m/z 913 ($M+H^+$).

Anal. Calcd. for $C_{48}H_{64}N_8O_2S_4$: C, 63.12; H, 7.06; N, 12.27. Found: C, 62.88; H, 7.10; N, 12.42.

Macrocyclic Compound **14h**.

Macrocyclic compound **14h** was obtained in 26% yield (12 mg) from **5h** by the same procedure as that described for **14a**. Compound **14h** has mp 211-213° (decomp); ir (potassium bromide): 3362, 3299, 3057, 2923, 2852, 1557, 1467, 1412, 1383, 1337, 1291, 1223, 970, 687, and 601 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 1.23 (m, 4H), 1.36-1.52 (m, 8H), 1.84 (m, 2H), 2.74 (t, 4H), 3.15 (d, 4H, J = 12.4Hz), 3.41 (t, 4H), 4.41 (s, 4H), 4.59 (br, 8H), 7.15-7.37 (m, 18H), 7.46 (br, 4H), 7.83 (br, 4H); FAB-mass m/z 913 ($M+H^+$).

Anal. Calcd. for $C_{48}H_{64}N_8O_2S_4$: C, 63.12; H, 7.06; N, 12.27. Found: C, 62.88; H, 7.10; N, 12.42.

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[14] X-ray Crystallography. Crystallographic data of **11a**. $C_{44}H_{68}N_8S_4$+ 2.14$CHCl_3$, trigonal, space group R3(hexagonal setting), a = 30.380(8), c = 16.704(5) Å, V = 13351(5) $Å^3$, Z = 9, d_{calc} = 1.223g cm^{-3}. A colorless crystal with dimensions of 0.2x0.3x0.2 mm was sealed in a glass capillary immersed in a minimum amount of solvent soon after picked up from the $CHCl_3$/hexane solution, because the crystals were immediately deteriorated in the air. The specimen was cooled at 253 K during the data collection to reduce the deterioration. The intensity data were collected on a MAC Sceience DIP-3000 diffractometer using the imaging plate as a detector with Mo-Kα radiation. Whole data were collected within about 12 hours. 11828 reflections measured, 6715 unique, 1760 with $|Fo| > 2.5\sigma(F)$, R = 0.148, Rw_2 = 0.393 (315 variables). The terminal three atoms of alkyl chain and solvent molecules are disordered, so that R factors were not sufficiently reduced. The backbone structure, however, was obtained from the direct method followed by successive Fourier syntheses.

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