Hydrazones Derived from Dithiamonoaza and Tetrathiamonoaza Analogs of Polyethers as Silver Ion Selective Ionophores: Syntheses, Proton-Dissociation Behaviors, and Metal Ion Complexing Properties in 1,4-Dioxane–Water Acidic Solution

Junichi Ishikawa, Hidefumi Sakamoto,* Tamao Mizuno, and Makoto Otomo

Department of Applied Chemistry, Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya 466

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Cyclic and acyclic dithiamonoaza, tetrathiamonoaza, and tetrathiadiaza analogs of polyethers bearing a hydrazone moiety on nitrogen atom(s) were synthesized. Their acidity constants in 1,4-dioxane–water solution and stability constants of hydrazones derived from dithiamonoaza and tetrathiamonoaza analogs of polyethers for some heavy metal ions in same acidic media were measured spectrophotometrically. Hydrazones of cyclic and acyclic tetrathiamonoaza series had highly Ag^+-selective complexability.

Some chromogenic crown compounds with complexabilities for a particular metal ion have been reported so far. The chromogenic crown ethers used in most of these investigations had selectivity for alkali metal, alkaline earth metal, and ammonium ions.[1—4)]

On the other hand, complexation behavior for heavy metal ions has been studied using acyclic and cyclic polythioethers, such as thiacrown ethers, because of high affinity of the sulfur atom for some soft metal ions.[5—8)] Several chromogenic thiacrown ethers and a chromogenic acyclic polythioether, which have complexability for particular heavy metal ions, have also been synthesized in a similar way to that used in the preparation of the analogous chromogenic crown ethers.[9—11)]

To obtain highly Ag^+-selective reagents that are analogs of polythioethers, we have attempted to synthesize novel acyclic and cyclic thiazaalkanes, incorporating nitrogen and sulfur atoms as heteroatoms in the molecule. The obtained thiazacrown ethers had Ag^+ selectivity in the solvent extraction.[12)] Therefore, dithiamonoaza- and tetrathiamonoazaalkanes bearing a hydrazone unit, which is a proton-dissociable chromogenic moiety, were synthesized and used as chromogenic extractants of Ag^+. We previously reported on Ag^+-selective extraction behaviors of these chromogenic monoaza analogs of polythioethers.[13)] In this paper, we will describe the syntheses of dithiamonoaza- and tetrathiamonoazaalkane monohydrazones, **1b**—**4b**, tetrathiadiazaalkane dihydrazones, **5b** and **6b**, and analogous azacrown ether hydrazones, **7b** and **8b**, and their proton dissociation properties in 1,4-dioxane–water solution. Complexation behaviors of dithiamonoaza- and tetrathiamonoazaalkane monohydrazones, **1b**—**4b**, for some heavy metal ions in 1,4-dioxane–water acidic solution will also be reported.

Results and Discussion

Syntheses. All of the thiaza analogs of crown ether derivatives, **1a**, **2a**, and **5a**, were synthesized according to the procedure reported elsewhere (Fig. 1).[13)] Acyclic *N*-phenyl derivatives of tetrathiamonoazaalkane, **3a** and **4a**, and the *N*,*N*′-diphenyl derivative of tetrathiadiazaalkane **6a** were obtained by the reactions of appropriate thiols with a corresponding tosylate or iodide of corresponding *N*-phenyl-substituted azaalkanes in the presence of sodium ethanolate using ethanol as a solvent. In these reactions, little difference in the yields between **3a** (73%) and **4a** (62%) which were synthesized using tosylate and iodide of *N*-phenyl-substituted azaalkanes as reactants, respectively, was observed. *N*,*N*′-Diphenyltetrathiadiazaeicosane **6a** was also given in a good yield (72%) in a similar manner. The much higher yield of **6a** compared with the yield of cyclic analog **5a** (11%) would result from the high flexibility of the acyclic structure of the former.

In the syntheses of the hydrazono derivatives, formylation of the phenyl group was done by the Vilsmeier reaction using $POCl_3$ in DMF in fairly good yield,[14,15)] followed by a condensation reaction of the resulting formyl group with 2,4-dinitro-6-(trifluoromethyl)phenylhydrazine in the presence of a small amount of acetic

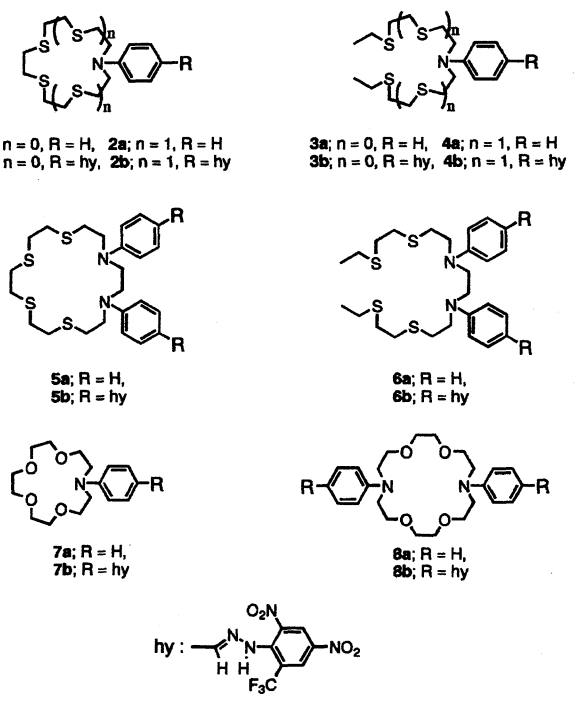

Fig. 1. Structural formulas of cyclic and acyclic thiaza analogs of polyethers, along with corresponding hydrazone derivatives.

acid in ethanol.[16,17)] Tetrathia-13-aza-15-crown-5 hydrazone **2b** and 1,10-diaza-18-crown-6 hydrazone **8b** were synthesized by the reaction of the purified *N*-(4-formylphenyl)-substituted crown ether with a hydrazine derivative. The formylation of the other *N*-phenyl derivatives of polyether analogs and the subsequent condensation reaction with the hydrazine derivative was done continuously in situ to easily give the hydrazones in the yield of 39—71%.

Proton Dissociation Behaviors of Hydrazono Derivatives. Proton dissociation on the hydrazono groups was measured spectrophotometrically in 1,4-dioxane–water (60/40 vol% except for **3b** and **4b** (48/52 vol%)) solution. For controlling pH, tetramethylammonium hydroxide (TMAOH) was used because TMA$^+$ ion has too low ability of complexation with thiazaalkane and azacrown ether moieties to affect the proton dissociation.

The spectral changes in acyclic tetrathiamonoazaalkane hydrazone **4b** at various pH are shown in Fig. 2. Maximum absorptions based on the undissociated species (HL) and the proton-dissociated one (L^-) of **4b** were observed at 441 and 519 nm, respectively. Similar pH-dependent spectral changes were also found for the other hydrazono derivatives used here. The acidity constants (K_a) and the molar absorptivities (ε) of hydrazones were calculated from the absorbance changes at their maximum absorption wavelengths in a similar manner as described before[18)] and are summarized in Table 1. Each of the monohydrazones, **1b**—**4b**, and **7b**, has a close value of acidity constant and similar spectral properties to each other. These results demonstrate that the proton dissociation property of the hydrazone moiety is independent of the kinds of polythiamonoazaalkane and azacrown ether units.

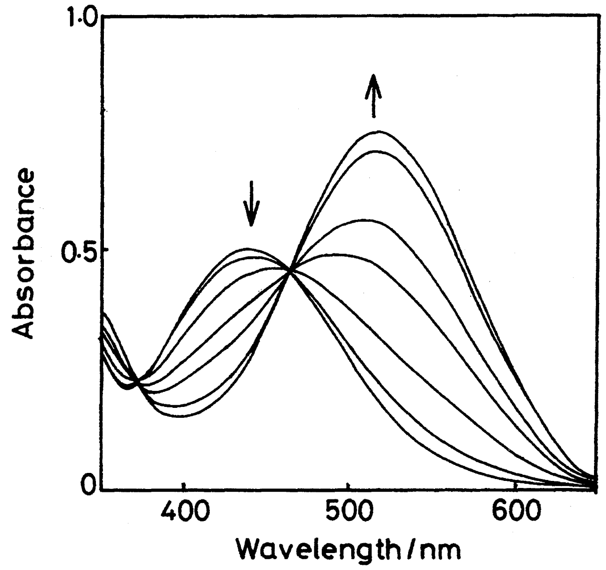

Fig. 2. pH-dependent spectral change of tetrathiamonoazaheptadecane hydrazone **4b** in 1,4-dioxane–water (48/52 vol%). pH=6.1, 7.0, 7.7, 8.2, 8.6, 9.0, 9.7.

In the cases of dihydrazones, the values of ε_{H_2L} of **5b** and **6b**, which have two hydrazone moieties in the adjusting places on the polythiadiazaalkane units, are much less than that of **8b**, having two hydrazones on the detached places and a symmetrical structure. The separation between both hydrazone moieties of the proton-undissociated tetrathiadiazaalkane dihydrazone gives the greater absorption cross section of the light. On the other hand, differences among the dihydrazones, **5b**, **6b**, and **8b**, were also observed in proton dissociation and spectral properties. Especially, **5b**, with an asymmetrical cyclic structure, had a much lower molar absorptivity of L^{2-} than those of **6b** and **8b**. For the proton-dissociation of the dihydrazones, such a low molar absorptivity of **5b** with a cyclic structure would be attributable to the narrow absorption cross section caused by the proximity of two hydrazono groups because of the steric rigidity. The molar absorptivity of **6b** is comparable to that of **8b**, probably because the distance between the two hydrazono groups of **6b** is separated by the repulsion of negative charges.

Complexation of Polythiamonoazaalkane Hydrazones with Heavy Metal Ions in Acidic Solution. The undissociated polythiamonoazaalkane hydrazones (HL) used here and heavy metal ions (M^{n+}) formed complexes (MHL^{n+}) in 1,4-dioxane–water solution under acidic conditions. The complexation properties of HL were analyzed in the pH 4.0 to 4.3 region, except for the cases of Hg^{2+} and Cu^{2+}, those of which were established in the pH 2.0 to 2.3 region,

Table 1. Acidity Constants (K_a) and Molar Absorptivities (ε)$^{a)}$ of Hydrazones in 1,4-Dioxane–Water (60/40 vol%) Solution

Compound	p$K_a^{b)}$ or p$K_{a1}^{b)}$	p$K_{a2}^{b)}$	ε_{HL} or $\varepsilon_{H2L}/10^4$ (at λ_{max}/nm)	$\varepsilon_L/10^4$ (at λ_{max}/nm)
			Monohydrazones	
1b	8.07		2.63 (441)	3.98 (516)
2b	8.04		2.64 (444)	3.97 (517)
3b$^{c)}$	8.03		2.66 (446)	4.03 (519)
4b$^{c)}$	8.05		2.52 (441)	3.80 (519)
7b	8.10		2.24 (427)	3.14 (516)
			Dihydrazones	
5b	7.81	8.15	3.09 (437)	5.87 (516)
6b	7.68	8.26	3.43 (445)	7.72 (522)
8b	7.84	8.46	4.58 (440)	7.17 (520)

a) Errors for values of ε were less than ±300 $\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$. b) p$K_a = -\log K_a$; errors for values of p$K_a$ were within ±0.02. c) In 1,4-dioxane–water (48/52 vol%).

where no protonation of a nitrogen atom of polythiamonoazaalkane moiety was observed in separate experiments. The complexation induced a considerable hypsochromic shift of absorption spectra in the visible region in the solution containing the polythiamonoazaalkane hydrazones (Fig. 3). Such a hypsochromic shift is caused by the reduction of electron density of the 2,4-dinitro-6-(trifluoromethyl)phenylhydrazone moiety owing to interaction between the metal ion and nitrogen atom in polythiamonoazaalkane moiety. These spectral changes of undissociated polythiamonoazaalkane hydrazones are similar to those of donor-acceptor type chromoionophores, e.g., *N*-[4-(4-nitrophenylazo)phenyl]aza-18-crown-6.[1,14] On the other hand, the formation of the proton dissociated hydrazone–metal ion complexes (ML) was hardly observed under the conditions used here.

The stability constant, K_{MHL}, is defined as Eq. 1.

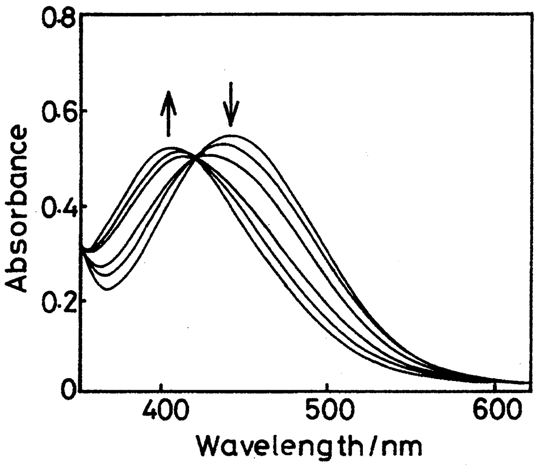

Fig. 3. Ag^+-concentration dependent spectral change of dithiamonoazaundecane hydrazone **3b** in 1,4-dioxane–water (48/52 vol%). $[Ag^+]=0$, 4.0×10^{-6}, 1.6×10^{-5}, 4.0×10^{-5}, 1.0×10^{-4}, 1.0×10^{-3} $\mathrm{mol\,dm^{-3}}$.

$$K_{MHL} = [MHL^{n+}]/[M^{n+}][HL] \,. \tag{1}$$

The total concentrations of the metal ion (C_M) and ligand (C_L) in acidic solution are respectively represented as Eqs. 2 and 3.

$$C_M = [M^{n+}] + [MHL^{n+}] \,, \tag{2}$$

$$C_L = [HL] + [MHL^{n+}] \,. \tag{3}$$

When the concentration of the metal ion, $[M^{n+}]$, except for Ag^+ is much greater than [HL], Eq. 2 can be simplified as $C_M = [M^{n+}]$. The absorbance (A) of the solution at an appropriate wavelength is given by Eq. 4, where ε_M, ε_{HL}, and ε_{MHL} are molar absorptivities of metal ion, HL and MHL^{n+}, respectively.

$$A = \varepsilon_M[M^{n+}] + \varepsilon_{HL}[HL] + \varepsilon_{MHL}[MHL^{n+}] \,. \tag{4}$$

Because the values of ε_M and ε_{HL} are preliminarily measured, the values of ε_{MHL} and K_{MHL} can be obtained simultaneously by minimizing the error square sum (U) defined by $U = \sum(A_{obs,i} - A_{cal,i})^2$, where $A_{obs,i}$ and $A_{cal,i}$ are the experimentally observed and the calculated absorbances, respectively.

The stability constants of heavy metal complexes of **1b**—**4b** are summarized in Table 2. The solid line in Fig. 4, which is calculated from the obtained stability constant of the complex of Ag^+ with **1b**, demonstrates the validity of the constants measured. It is found from the table that cyclic and acyclic tetrathiamonoazaalkane hydrazones, **2b** and **4b**, form the most stable complexes with Ag^+ among the heavy metal ions examined. Under the experimental conditions used, **2b** and **4b** formed complexes with Ag^+ almost quantitatively. Consequently, the values of $\log K_{AgHL}$ of these hydrazones can be estimated to be larger than 7, which is a value of identification limit of spectrophotometric technique used here. The complexabilities of **2b** and **4b** for Ag^+ were much higher than those of dithiamonoazaalkanes **1b** and **3b**. On the comparison of cyclic dithia-

Table 2. Stability Constants (K_{MHL})[a] of Metal Complexes of Dithiamonoazaalkane and Tetrathiamonoazaalkane Hydrazones, **1b**—**4b**

	Stability constant ($\log K_{\mathrm{MHL}}$)			
Compound	Ni^{2+}	Cu^{2+}	Ag^+	Hg^{2+}
1b[b]		—[d]	4.8	4.5
2b[b]	0.5	3.3	>7[e]	
3b[c]		—[d]	5.3	4.5
4b[c]		3.2	>7[e]	4.5

a) Errors for values of $\log K_{\mathrm{MHL}}$ were within ±0.1. b) In 1,4-Dioxane–water (60/40 vol%) solution. c) In 1,4-Dioxane–water (48/52 vol%) solution. d) The value of $\log K_{\mathrm{MHL}}$ is less than 0.1. e) The value of K_{MHL} is larger than that of determination limit.

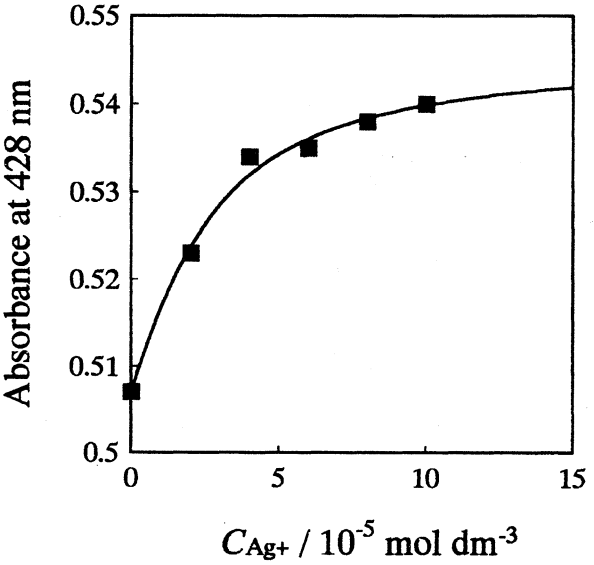

Fig. 4. Plot of absorbance at 428 nm using dithia-7-aza-9-crown-3 **1b** vs. $C_{\mathrm{Ag^+}}$. $C_{\mathrm{HL}}=1.99\times10^{-5}$ mol dm^{-3}.

monoazaalkane hydrazone **1b** and acyclic one **3b**, the latter had slightly higher complexability than the former, probably because the more flexible structure of **3b** is favorable for formation of the complex with Ag^+.

Among the other metal ions, similar complexabilities of **1b**, **3b**, and **4b** for Hg^{2+} and slight complexabilities of **2b** and **4b** for Cu^{2+} were observed, while these metal ions were hardly extracted by these polythiamonoazaalkane hydrazones in the solvent extraction reported before.[13] Sulfur atoms of a thioether are well-known to interact with soft (or *class b*) metal ions.[6,19,20] Therefore, the similar complexabilities of these polythiamonoazaalkane hydrazones for Hg^{2+} should be attributable to the affinity of the sulfur atom for Hg^{2+} rather than structural flexibilities of the polythiamonoazaalkane moieties and/or suitable crown ring sizes.[21—23] Such a difference in the complexabilities of the polythiamonoazaalkane hydrazones between for Ag^+ and for Hg^{2+} may be attributed to the different affinities of these metal ions for sulfur and nitrogen atoms with a hydrazono group which is an electron-drawing unit.[22]

Cu^{2+} is a borderline, i.e., *class ab*, metal ion and the stabilities of Cu^{2+}–thioether complexes are not so high as those of soft, i.e., *class b*, metal ions. Thus, Cu^{2+} has a higher affinity for nitrogen atoms than for sulfur atoms. Consequently, the complexabilities of these compounds for Cu^{2+} can be explained by the cooperative effect of the association of a nitrogen atom[24,25] and the low affinity of sulfur atoms.

The hydrazones used here hardly formed stable complexes with the other heavy metal ions, i.e., Zn^{2+}, Cd^{2+}, Tl^+, and Pb^{2+}.

Experimental

Infrared spectra were recorded on a Shimadzu IR-408 grating spectrophotometer. Mass spectra were measured with a Hitachi M-2000S (for FAB) and JEOL JMS-DX303 (for EI) instruments. Melting points were determined with Yanaco melting point apparatus and were uncorrected. ^{1}H NMR spectra were recorded on Hitachi R-90 and Varian XL-200 spectrometers as $CDCl_3$ solutions containing tetramethylsilane as an internal standard. Electronic spectra were obtained on a Hitachi 150-20 spectrophotometer with 1-cm quartz cells. pH measurements were made using a Toa pH Meter HM-30S equipped with a Toa GST-5311C glass electrode. Elemental analyses were achieved on a Yanaco MT-2 CHN Corder. Unless otherwise specified, all reagents were the best grade and were used as received. The syntheses of *N*-phenyldithia-7-aza-9-crown-3 (**1a**), *N*-phenyltetrathia-13-aza-15-crown-5 (**2a**), *N*,*N'*-diphenyltetrathia-13,16-diaza-18-crown-6 (**5a**), and *N*,*N'*-diphenyl-1,10-diaza-18-crown-6 (**8a**) have been described elsewhere.[12] *N*-Phenylaza-15-crown-5 (**7a**) was purchased from Merck & Co., Inc. and was used without further purification. THF and 1,4-dioxane were distilled over NaH. Ethanol was dried over magnesium ethanolate. 1,2-Dichloroethane, chloroform, and acetone were purified by distillation in the usual way. DMF was purified by vacuum distillation after drying over $MgSO_4$. Water was doubly distilled. Metal salts were analytical grade.

Synthesis. 6-Phenyl-3,9-dithia-6-azaundecane 3a: The tosylation of 3-phenyl-3-azapentane-1,5-diol with *p*-toluenesulfonyl chloride in the presence of NaOH in water/THF solution gave 1,5-bis(*p*-tolylsulfonyloxy)-3-phenyl-3-azapentane (62%).[26] Na (1.27 g, 55 mmol) was dissolved in dry ethanol under nitrogen atmosphere. To the solution was added an ethanethiol (3.36 g, 55 mmol) and then the mixture was stirred at r.t. for 1 h. The mixed solution was heated to the refluxing temperature. To the refluxing solution was added 1,5-bis(*p*-tolysulfonyloxy)-3-phenyl-3-azapentane (12.24 g, 25 mmol) and then the mixture was stirred for 12 h. After the reaction was completed, the solvent of the mixture was evaporated in vacuo and then to the residue was added 100 cm^3 of water. The aqueous solution was extracted with $CHCl_3$ (100 cm^3×3). The extract was dried over Na_2SO_4. After removal of the solvent the vacuum distillation of the residue yielded **3a** (73%) as a pale yellow oil. **3a**: Bp 100—105 °C/0.1 Torr (1 Torr=133.322 Pa); ^{1}H NMR ($CDCl_3$) $\delta=1.12$—1.34 (m, 6H, CH_3), 2.45—2.79 (m, 8H, CH_2SCH_2), 3.43—3.61 (m, 4H, CH_2NCH_2), 6.59—

7.36 (m, 5H, ArH).

9-Phenyl-3,6,12,15-tetrathia-9-azaheptadecane 4a: The reaction of 1,5-diiodo-3-phenyl-3-azapentane (4.01 g, 10 mmol), which was obtained by the reaction of NaI and 1,5-bis(*p*-tolylsulfonyloxy)-3-phenyl-3-azapentane in acetone, with 3-thiapentane-1-thiol (2.69 g, 10 mmol) afforded **4a** (62%) in a similar way to **3a** except for purification using Kugelrohr distillation. **4a**: Pale yellow viscous oil; bp ca. 200 °C/0.1 Torr (by Kugelrohr distillation); ^{1}H NMR ($CDCl_3$) δ=1.12—1.37 (m, 6H, CH_3), 2.40—2.81 (m, 16H, SCH_2), 3.42—3.61 (m, 4H, CH_2NCH_2), 6.59—7.34 (m, 5H, ArH).

9, 12- Diphenyl- 3, 6, 15, 18- tetrathia- 9, 12- diazaeicosane 6a: The tosylation of 3,6-diphenyl-3,6-diazaoctane-1,8-diol, which was prepared according to the procedure previously reported,[12] with *p*-toluenesulfonyl chloride gave 1,8-bis(*p*-tolysulfonyloxy)-3,6-diphenyl-3,6-diazaoctane. Compound **6a** was prepared by the reaction of this ditosylate (3.04 g, 5 mmol) with 3-thiapentane-1-thiol (1.22 g, 10 mmol) in ethanol solution (20 cm^3) containing sodium ethanolate (12 mmol) in a similar way to **3a**. The pure product was isolated by recrystallization from hexane. **6a**: White needles (72%); ^{1}H NMR ($CDCl_3$) δ=1.10—1.38 (m, 6H, CH_3), 2.38 —2.80 (m, 16H, CH_2SCH_2), 3.38—3.58 (m, 8H, CH_2NCH_2), 6.63—7.34 (m, 10H, ArH).

General Procedure for Preparation of Hydrazono Derivatives. A dry DMF (10 cm^3) solution containing an appropriate *N*-phenyl derivative of thiazaalkane (6 mmol for phenyl unit) was cooled in an ice bath. To the solution was dropwise added $POCl_3$ (1.16 g, 6.6 mmol) for 5 min. After the addition was completed, the mixture was stirred in an ice bath for 10 min, at r.t. for 1.5 h, and then at 100 °C for 3 h. After the reaction was completed, the reaction mixture was poured into the ice water (20 cm^3) and the mixed solution was stirred for 30 min, neutralized with sodium acetate, and extracted with $CHCl_3$ (20 $cm^3 \times 3$). The combined extract was concentrated to afford the crude corresponding *N*-(4-formylphenyl) derivative. A dry ethanol solution (50 cm^3) of hydrazine monohydrate (0.43 g, 85 mmol) was refluxed with stirring, and to the solution a solution of 1-chloro-2,4-dinitro-6-(trifluoromethyl)benzene (1.89 g, 7 mmol) in 50 cm^3 of ethanol was added dropwise for 15 min. After the addition, the reaction mixture was stirred for 2 h at the refluxing temperature. To the solution were added a small amount (ca. 0.1 cm^3) of acetic acid and the ethanol solution (20 cm^3) of the crude *N*-(4-formylphenyl) derivative of the thiazaalkane obtained previously. The mixed solution was refluxed with stirring for 2 h. After the reaction was completed, the precipitate obtained was filtered and was recrystallized from ethanol to yield the appropriate hydrazone.

1b: Deep red solid (39%); mp 245—246 °C; IR (KBr) 3300, 2900, 1670, 1600, 1560, 1540, 1390, 1320, 1260, 1240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.74—3.22 (m, 8H, CH_2SCH_2), 3.71—3.88 (m, 4H, CH_2NCH_2), 6.80—7.70 (m, 4H, ArH), 7.95 (s, 1H, CH), 8.69—9.20 (m, 2H, ArH), 11.13 (s, 1H, NH); MS (EI) *m/z* 515 (M^+). Anal. Calcd for $C_{20}H_{20}N_5O_4S_2F_3$: C, 46.60; H, 3.91; N, 13.59%. Found: C, 46.20; H, 3.90; N, 13.48%.

3b: Deep red solid (52%); mp 141—142 °C; IR (KBr) 3300, 2900, 1670, 1600, 1560, 1540, 1390, 1320, 1260, 1240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.15—1.40 (m, 6H, CH_3), 2.44—2.81 (m, 8H, CH_2SCH_2), 3.48—3.70 (m, 4H, CH_2NCH_2), 6.58—7.70 (m, 4H, ArH), 7.88 (s, 1H, CH), 8.69—9.17 (m, 2H, ArH), 11.13 (s, 1H, NH); MS (EI) *m/z* 545 (M^+). Anal. Calcd for $C_{22}H_{26}N_5O_4S_2F_3$: C, 48.43; H, 4.80; N, 12.84%. Found: C, 48.28; H, 4.65; N, 13.05%.

4b: Deep red solid (51%); mp 100—101 °C; IR (KBr) 3300, 2900, 1670, 1600, 1560, 1550, 1390, 1330, 1270, 1240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.15—1.40 (m, 6H, CH_3), 2.40—2.87 (m, 16H, CH_2SCH_2), 3.50—3.72 (m, 4H, CH_2NCH_2), 6.58—7.70 (m, 4H, ArH), 7.88 (s, 1H, CH), 8.69—9.17 (m, 2H, ArH), 11.13 (s, 1H, NH); MS (EI) *m/z* 665 (M^+). Anal. Calcd for $C_{26}H_{34}N_5O_4S_4F_3$: C, 46.90; H, 5.15; N, 10.52%. Found: C, 46.94; H, 5.12; N, 10.35%.

5b: Deep red solid (52%); mp>300 °C; IR (KBr) 3300, 2900, 1670, 1600, 1560, 1550, 1390, 1330, 1270 cm^{-1}; MS (FAB) *m/z* 1030 (M^+). Anal. Calcd for $C_{40}H_{40}N_{10}O_8S_4F_6$: C, 46.59; H, 3.91; N, 13.58%. Found: C, 46.81; H, 3.94; N, 13.67%.

6b: Deep red solid (71%); mp 184—185 °C; IR (KBr) 3300, 2900, 1670, 1600, 1560, 1550, 1390, 1330, 1270 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.10—1.40 (m, 6H, CH_3), 2.38—2.80 (m, 16H, CH_2SCH_2), 3.48—3.88 (m, 8H, CH_2NCH_2), 6.60—7.75 (m, 8H, ArH), 7.98 (s, 2H, CH), 8.70—9.20 (m, 4H, ArH), 11.13 (s, 2H, NH); MS (FAB) *m/z* 1061 (M^+). Anal. Calcd for $C_{42}H_{46}N_{10}O_8S_4F_6$: C, 47.54; H, 4.37; N, 13.19%. Found: C, 47.74; H, 4.31; N, 12.89%.

7b: Deep red solid (49%); mp 185—186 °C; IR (KBr) 3480, 2820, 1630, 1560, 1130 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 3.52—3.82 (m, 20H, CH_2), 6.61—7.66 (m, 4H, ArH), 7.90 (s, 1H, CH), 8.71—9.18 (m, 2H, ArH), 11.14 (s, 1H, NH); MS (EI) *m/z* 571 (M^+). Anal. Calcd for $C_{24}H_{28}N_5O_8F_3$: C, 50.43; H, 4.90; N, 12.26%. Found: C, 50.27; H, 4.93; N, 12.62%.

2b: *N*-(4-Formylphenyl)tetrathia-13-aza-15-crown-5 was synthesized as described in general procedure and was isolated as follows: After the reaction of **2a** (0.47 g, 1.3 mmol), DMF (10 cm^3), and $POCl_3$ (0.23 g, 1.5 mmol) was completed, the reaction mixture was poured into the ice water (20 cm^3). The mixed solution was stirred for 30 min, neutralized with sodium acetate, and then was allowed to stand for ca. 12 h in a refrigerator to obtain a precipitate which was filtered to yield pale yellow crystals (95%); ^{1}H NMR ($CDCl_3$) δ=2.68—2.90 (m, 16H, CH_2SCH_2), 3.54—3.78 (m, 4H, CH_2NCH_2), 6.58—7.84 (m, 4H, ArH), 9.77 (s, 1H, CHO). The condensation reaction of the obtained *N*-(4-formylphenyl)tetrathia-13-aza-15-crown-5 (0.23 g, 0.6 mmol) with 2,4-dinitro-6-(trifluoromethyl)phenylhydrazine (0.18 g, 0.6 mmol) according to the general procedure was gave **2b** as a deep red solid (52%); mp 190—191 °C; IR (KBr) 3300, 2900, 1670, 1600, 1560, 1550, 1390, 1330, 1270, 1240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.67—2.88 (m, 16H, CH_2SCH_2), 3.50—3.78 (m, 4H, CH_2NCH_2), 6.60—7.68 (m, 4H, ArH), 7.88 (s, 1H, CH), 8.69—9.17 (m, 2H, ArH), 11.13 (s, 1H, NH); MS (EI) *m/z* 635 (M^+). Anal. Calcd for $C_{24}H_{28}N_5O_4S_4F_3$: C, 45.34; H, 4.44; N, 11.01%. Found: C, 45.10; H, 4.34; N, 10.79%.

8b: The synthetic procedure was similar to that for **2b**. The formylation reaction of **8a** with $POCl_3$ and DMF afforded *N,N′*-bis(4-formylphenyl)-1,10-diaza-18-crown-6 as a pale blue crystal (68%); mp 130—131 °C; IR (KBr) 2880, 1670, 1570, 1130 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.51—3.82 (m, 24H, CH_2), 6.97—7.80 (m, 8H, ArH), 9.72 (s, 2H, CHO); MS (EI) *m/z* 470 (M^+). Compounds **8b** was synthesized by the condensation reaction of *N*,*N*′-bis(4-formylphenyl)-1,10-diaza-18-crown-6 with 2,4-dinitro-6-(trifluoromethyl)phenylhydrazine in a similar manner as that for compound **2b** and was a deep red solid (68%); mp 228—229 °C; IR (KBr) 3480, 2820, 1630, 1560, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.51—3.79 (m, 24H, CH_2), 6.59—7.62 (m, 8H, ArH), 7.85 (s, 2H, CH), 8.64—9.18 (m, 4H, ArH), 11.10 (s, 2H, NH); MS (EI) *m*/*z* 966 (M^+). Anal. Calcd for $C_{40}H_{40}N_{10}O_{12}F_6$: C, 49.69; H, 4.14; N, 14.49%. Found: C, 50.27; H, 4.14; N, 14.46%.

Acidity Constants of Hydrazono Derivatives. The acidity constants of hydrazono derivatives were measured spectrophotometrically at 25.0±0.2 °C. Because the hydrazono derivatives used here are hardly soluble in water, 1,4-dioxane–water (60/40 vol% except for **3b** and **4b** (48/52 vol%)) solution was chosen as a solvent. The pH of the solution (25 cm^3), which contained 2.0×10^{-5} mol dm^{-3} hydrazono derivative of thiazaalkane and 0.2 mol dm^{-3} tetramethylammonium chloride (TMACl) for obtaining constant ionic strength, was controlled by tetramethylammonium hydroxide (TMAOH) and Good's buffers (0.01 M, 1 M=1 mol dm^{-3}) as follows: pH 4.0—6.5, 2-(morpholino)-1-ethanesulfonic acid (MES); pH 6.5—7.5, 3-(morpholino)-1-propanesulfonic acid (MOPS); pH 7.5—9.0, 3-[tris(hydroxymethyl)methylamino]-1-propanesulfonic acid (TAPS); 9.0—10.0, 2-(cyclohexylamino)-1-ethanesulfonic acid (CHES); 10.0—11.0, 3-(cyclohexylamino)-1-propanesulfonic acid (CAPS); above pH 11, only aqueous TMAOH solution. Electronic spectra were measured at each pH. The acidity constants (K_a) are defined as $K_a=[L^-][H^+]/[HL]$ for monohydrazono derivatives (HL) and $K_{a1}=[HL^-][H^+]/[H_2L]$ and $K_{a2}=[L^{2-}][H^+]/[HL^-]$ for dihydrazono ones (H_2L).

Complexation of Polythiamonoazaalkane Hydrazones in Acidic Solution. The stability constants of metal complexes (MHL^{n+}) of monohydrazono derivatives (HL), **1b**—**4b**, were measured spectrophotometrically in a similar manner as described in the measurement method of the acidity constants, and KNO_3 was used for adjusting the ion strength at 0.2 mol dm^{-3}. The measurements of the stability constants were done by keeping the pH constant and changing metal ion concentration in the solution. The media used were 1,4-dioxane–water (60/40 vol% for **1b** and **2b** and 48/52 vol% for **3b** and **4b**) solution as mentioned above. Concentrations of hydrazones were 2.0×10^{-5} mol dm^{-3}.

References

1) H. Löhr and F. Vögtle, *Acc. Chem. Res.*, **18**, 65 (1985).

2) M. Takagi, "Cation Binding by Macrocycles," ed by Y. Inoue and G. W. Gokel, Marcel Dekker, New York (1991), p. 465.

3) M. Takagi and K. Ueno, *Top. Curr. Chem.*, **121**, 39 (1984).

4) S. Misumi and T. Kaneda, *J. Inclusion Phenom.*, *Mol. Recognit. Chem.*, **7**, 83 (1989).

5) F. Dietze, K. Gloe, R. Jacobi, P. Mühl, J. Beger, M. Petrich, L. Beyer, and E. Hoyer, *Solvent Extr. Ion Exch.*, **7**, 223 (1989).

6) K. Chayama and E. Sekido, *Anal. Sci.*, **3**, 535 (1987).

7) Z. Brzozka, *Analyst* (*London*), **114**, 1431 (1989).

8) M. Oue, K. Akama, K. Kimura, M. Tanaka, and T. Shono, *J. Chem. Soc.*, *Perkin Trans. 1*, **1989**, 1675.

9) E. Sekido, K. Chayama, and M. Muroi, *Talanta*, **32**, 797 (1985).

10) M. Muroi, T. Kamiki, and E. Sekido, *Bull. Chem. Soc. Jpn.*, **62**, 1797 (1989).

11) K. Chayama, Y. Tamari, H. Tsuji, Y. Kusaka, and E. Sekido, *Anal. Sci.*, **7** (**Supplement**), 57 (1991).

12) H. Sakamoto, J. Ishikawa, and M. Otomo, *Bull. Chem. Soc. Jpn.*, **68**, 2831 (1995).

13) H. Sakamoto, J. Ishikawa, T. Mizuno, K. Doi, and M. Otomo, *Chem. Lett.*, **1993**, 609.

14) J. P. Dix and F. Vögtle, *Chem. Ber.*, **113**, 457 (1980).

15) E. Campaigne and W. L. Archer, *Org. Synth.*, Coll. Vol. IV, 331 (1963).

16) H. Sakamoto, H. Goto, M. Yokoshima, M. Dobashi, J. Ishikawa, K. Doi, and M. Otomo, *Bull. Chem. Soc. Jpn.*, **66**, 2907 (1993).

17) T. Kanetake and M. Otomo, *Anal. Sci.*, **4**, 411 (1988).

18) T. Taya, T. Sakamoto, K. Doi, and M. Otomo, *Bull. Chem. Soc. Jpn.*, **66**, 3652 (1993).

19) E. Sekido, H. Kawahara, and K. Tsuji, *Bull. Chem. Soc. Jpn.*, **61**, 1587 (1988).

20) O. Heitzsch, K. Gloe, H. Stephan, and E. Weber, *Solvent Extr. Ion Exch.*, **12**, 475 (1994).

21) M. Oue, A. Ishigaki, K. Kimura, Y. Matsui, and T. Shono, *J. Polym. Sci.*, *Polym. Chem. Ed.*, **23**, 2033 (1985).

22) G. Wu, W. Jiang, J. D. Lamb, J. S. Bradshaw, and R. M. Izatt, *J. Am. Chem. Soc.*, **113**, 6538 (1991).

23) M. Lai and J. Shin, *Analyst* (*London*), **111**, 891 (1986).

24) B. C. Westerby, K. L. Juntunen, G. H. Leggett, V. B. Pett, M. J. Koenigbauer, M. D. Purgett, M. J. Taschner, L. A. Ochrymowycz, and D. B. Rorabacher, *Inorg. Chem.*, **30**, 2109 (1991).

25) L. F. Lindoy, *Pure Appl. Chem.*, **61**, 1575 (1989).

26) Y. Liu, Y. Inoue, and T. Hakushi, *Bull. Chem. Soc. Jpn.*, **63**, 3044 (1990).