Synthesis and silver ion complexation behavior of fluoroionophores containing a benzothiazolyl group linked to an *N*-phenylpolythiazaalkane moiety

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Cyclic and acyclic polythiazaalkane derivatives bearing a benzothiazolyl group as a fluorophore have been synthesized. The protonation and the metal ion complexation behavior were studied in a 1,4-dioxane–water (52/48 v/v) solution by spectrophotometry and/or spectrofluorometry. The changes in the absorption spectra (blue shift and hypochromic effect) and the fluorescence emission spectra (quenching) were observed by the addition of Ag^+ ion selectively. On complexation with the Ag^+ ion, the degree of the spectral changes of the benzothiazole derivatives is dependent on the extent of the interactions of the complexed Ag^+ ion with the nitrogen atom of the polythiazaalkane moiety and with the benzothiazolylphenyl moiety. The complexation and the protonation behavior of the benzothiazole derivatives were investigated using ^1H NMR spectroscopy.

Introduction

The detection of a particular metal ion by using an ion-selective ionophore has been given considerable attention in the fields of analytical and environmental chemistry.[1] Among the numerous methods investigated for the application of the ionophores in cation selective determination so far, a fluoroionophore has a distinct advantage in terms of its sensitivity.[2–5] Moreover, the fluoroionophores are useful for remote sensing as cation receptors for optical fibers. Some fluoroionophores containing a crown ether moiety have been designed for alkali or alkaline earth metal ions[6–14] although those for transition metal ions have not been investigated so much.[15–19]

We studied previously the syntheses of cyclic and acyclic polythiazaalkane derivatives bearing a hydrazono group as a chromogenic group and their complexation properties for some heavy metal ions.[20] Those compounds exhibited high Ag^+-selectivity in the liquid–liquid extraction system.[21] And excellent Ag^+ ion selectivity was observed in the transport of some heavy metal ions through a liquid membrane containing an acyclic polythiazaalkane derivative.[22] These results persuaded us to investigate the fluoroionophores based on the polythiazaalkane derivatives.

In this study, we synthesized cyclic and acyclic *N*-phenylpolythiazaalkane derivatives bearing a benzothiazolyl group as a fluorophore as shown in Fig. 1. When these benzothiazolyl polythiazaalkane derivatives formed complexes with an Ag^+ ion, their absorption and fluorescence spectra were perturbed by the interaction of the bound Ag^+ ion with a nitrogen atom, which is linked to a *p*-(benzothiazolyl)phenyl group, in the polythiazaalkane moiety.

We report here the complexation behavior of the benzothiazole derivatives for some heavy metal ions and especially for Ag^+ ion in 1,4-dioxane–water solution. Ag^+ ion complexation and protonation behaviors of the benzothiazole derivatives were, furthermore, examined using ^1H NMR spectroscopy and the relationship between the chemical shifts and the spectral changes was also studied.

Results and discussion

Synthesis

Syntheses of fluoroionophores were accomplished by the condensation reaction of *N*-(*p*-formylphenyl)polythiazaalkane derivatives with 2-aminobenzenethiol. *N*-Phenylpolythiazaalkane derivatives were synthesized according to the procedure reported elsewhere.[20,23] In the syntheses of the benzothiazole derivatives, the formylation reaction of the phenyl group was done by the Vilsmeier reaction using $POCl_3$ in DMF, followed by the condensation reaction of the resulting formyl group with 2-aminobenzenethiol in the presence of a small amount of acetic acid in ethanol. The formylation reaction of the *N*-phenyl derivatives of polythiazaalkane analogs and the subsequent condensation reaction with 2-aminobenzenethiol were done continuously *in situ* to easily give the desired compounds with yields of 29–43%.

Protonation behavior

The protonation behavior was examined in 1,4-dioxane–water (52/48 v/v) solution by spectrophotometry and spectrofluorometry, because all compounds used in this study were insoluble in pure water. The absorption and the fluorescence spectral changes with pH of the solution for acyclic compound **6** are shown in Fig. 2. The red shift and the bathochromic effect of the absorption spectra and the quenching of the emission spectra were observed with a decrease in pH. Maximum absorption wavelengths of the neutral and the protonated species are 362 and 429 nm, respectively. There is a clear isosbestic point at 387 nm, demonstrating that one acid–base equilibrium between HL^+ and L exists in this pH range. Similar pH-dependent spectral changes were also observed for the other analogs. The protonation constants (K_H) and the molar absorptivities (ε) of the benzothiazole derivatives were determined from the pH-dependent absorption changes at their maximum absorption wavelengths as follows. The protonation constant, K_H, is defined in eqn. (1), and the total concentration of the ligand

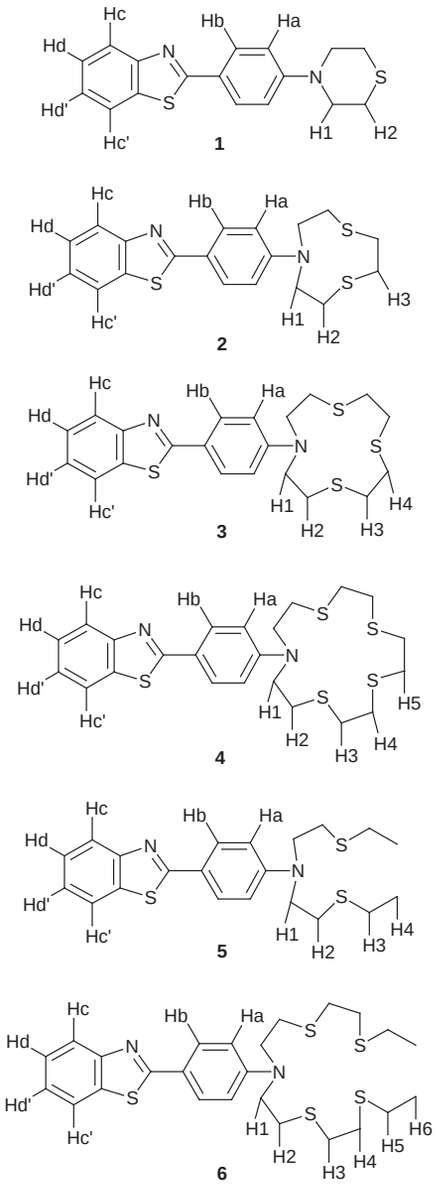


Fig. 1 Structural formulas of benzothiazole derivatives based on *N*-phenylpolythiazaalkanes.

$$K_H = [HL^+]/[H^+][L] \quad (1)$$

(C_L) is given in eqn. (2), where L and HL^+ denote the free benzothiazole derivative and the protonated one, respectively.

$$C_L = [L] + [HL^+] \quad (2)$$

The absorbance (A) of the solution at a given wavelength is given by eqn. (3), where ε_L and ε_{HL} are molar absorptivities of

$$A = \varepsilon_L[L] + \varepsilon_{HL}[HL^+] \quad (3)$$

L and HL^+, respectively. Because the value of ε_L was determined by the preliminary work, the values of ε_{HL} and K_H can be obtained simultaneously by minimizing the error square sum (U) defined by $U = \Sigma(A_{obs,i} - A_{cal,i})^2$, where $A_{obs,i}$ and $A_{cal,i}$ are the observed and the calculated absorbances, respectively. The protonation constants and the molar absorptivities of the benzothiazole derivatives are summarized in Table 1. Each of the analogs has similar properties for the protonation and the absorption and fluorescence spectra. The protonation mechanism of the *N*-(benzothiazolyl)phenylpolythiazaalkane derivatives is described in detail in the section concerning ^{1}H NMR spectroscopy studies.

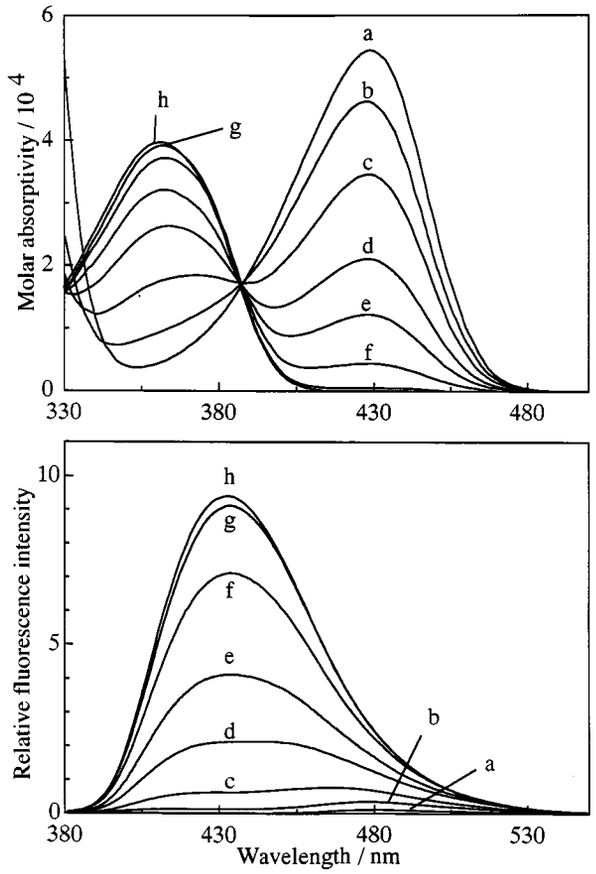


Fig. 2 pH-Dependent absorbance (top) and emission (bottom) spectral changes of 1,4-dioxane–water (52/48 v/v) solution containing **6**. [**6**] = 1.5×10^{-5} mol dm^{-3}, pH = a, 0.0; b, 0.5; c, 0.8; d, 1.2; e, 1.5; f, 1.9; g, 2.7; h, 5.6.

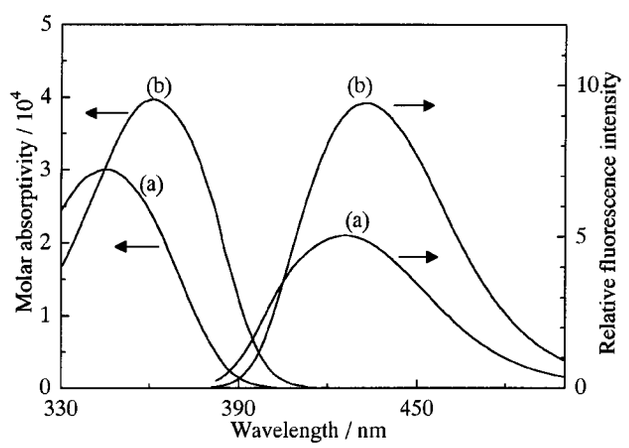


Fig. 3 Absorption and emission spectra of 1,4-dioxane–water (52/48 v/v) solution containing **6**. [**6**] = 1.5×10^{-5} mol dm^{-3} at pH 4.0, (a) [Ag^+] = 1.5×10^{-5} mol dm^{-3}, (b) [M^{n+}] = 1.5×10^{-5} mol dm^{-3} (M^{n+}: Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+}, Tl^+) and without metal ion.

Complexation behavior for some heavy metal ions

The complexation behavior of the benzothiazole derivatives with heavy metal ions was examined in 1,4-dioxane–water solution. Fig. 3 illustrates the changes in the absorption and the fluorescence spectra for **6** on the addition of metal ions. The addition of Ag^+ ion to the solution of **6** at pH = 4 caused a blue shift and a hypochromic effect in the absorption spectrum and a decrease in the fluorescence intensity, while no spectral change was observed for the addition of the other metal ions. Fig. 4 shows the changes in the molar absorptivity and the relative fluorescence intensity of solutions containing **6** with the concentrations of various metal ions. It is noted that the absorptiv-

Table 1 Acidity constants (K_H) and spectral properties for benzothiazole derivatives[a]

	L		HL		
Compound	λ_{abs}/nm ($\varepsilon_L/10^4$ mol^{-1} dm^3 cm^{-1})	λ_{em}/nm	λ_{abs}/nm ($\varepsilon_{HL}/10^4$ mol^{-1} dm^3 cm^{-1})	λ_{em}/nm	log K_H[b]
1	356 (3.39)	437	429 (3.16)	—[c]	1.27
2	361 (3.89)	432	428 (5.76)	—[c]	1.11
3	361 (3.87)	431	429 (5.70)	—[c]	1.15
4	361 (3.80)	431	429 (5.85)	—[c]	1.14
5	362 (4.13)	432	429 (5.95)	—[c]	1.14
6	362 (4.07)	434	429 (6.03)	—[c]	1.11

[a] [Ligand] = 1.5×10^{-5} mol dm^{-3} in 1,4-dioxane–water (52/48 v/v). [b] $K_H = [HL^+]/[H^+][L]$. [c] Quenching.

Table 2 Stability constants (K_{ML})[a] of metal ion–benzothiazole complexes

	log K_{ML}								
Compound	Mn^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}	Tl^+	Ag^+
1	<0	<0	<0	<0	<0	<0	<0	<0	3.29
2	<0	<0	<0	<0	<0	<0	<0	<0	5.05
3	<0	<0	<0	0.44	<0	<0	<0	<0	>7[b]
4	<0	<0	<0	0.91	<0	<0	<0	<0	>7[b]
5	<0	<0	<0	<0	<0	<0	<0	<0	4.75
6	<0	<0	<0	<0	<0	<0	<0	<0	>7[b]

[a] [Ligand] = 1.5×10^{-5} mol dm^{-3} in 1,4-dioxane–water (52/48 v/v) solution. [b] The value of K_{ML} is larger than that of the determination limit.

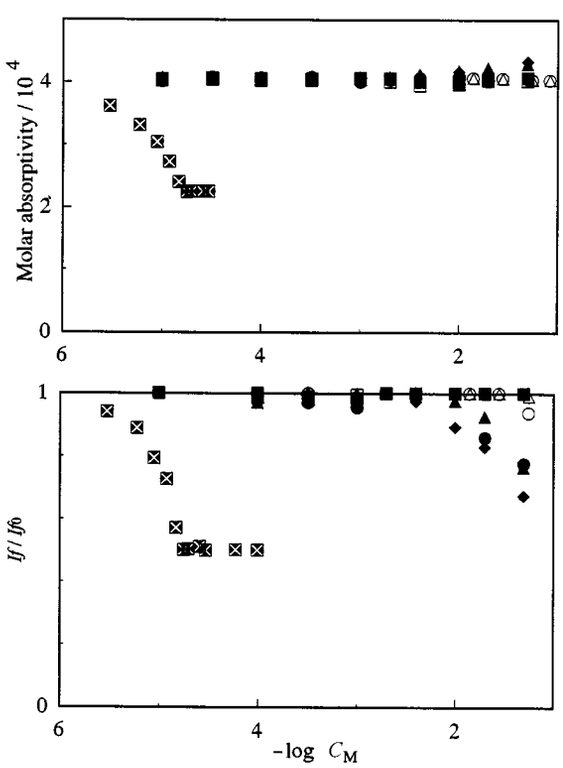


Fig. 4 Plots of molar absorptivity and relative fluorescence intensity of 1,4-dioxane–water (52/48 v/v) solution containing **6** *vs.* $-\log C_M$. [**6**] = 1.5×10^{-5} mol dm^{-3} at pH = 4.0. (■); Mn^{2+}, (●); Co^{2+}, (▲); Ni^{2+}, (◆); Cu^{2+}, (□); Zn^{2+}, (◇); Cd^{2+}, (○); Pb^{2+}, (△); Tl^+, (⊠); Ag^+.

ity and the fluorescence intensity were changed by the addition of Ag^+ ion selectively up to 1.5×10^{-5} mol dm^{-3} and then remained constant. This is attributable to the quantitative formation of the 1 : 1 complex. This indicates that the *N*-phenylpolythiazaalkane moiety acts as an Ag^+-selective ionophore. For the other metal ions, the spectral changes which occur according to the absorption of the added metal ion itself are observed in the high metal ion concentration. The other benzothiazole derivatives also exhibited similar Ag^+ ion-induced spectral changes. This kind of spectral change is also known for the donor–acceptor type chromoionophores.[24–26]

The stability constants of the complexes with some heavy metal ions in 1,4-dioxane–water solution were determined by spectrophotometry.

The stability constant, K_{ML}, is defined by eqn. (4). The total

$$K_{ML} = [ML^{n+}]/[M^{n+}][L] \quad (4)$$

concentrations of the metal ion (C_M) and ligand (C_L) are presented in eqns. (5) and (6) and the absorbance (A) of the solu-

$$C_M = [M^{n+}] + [ML^{n+}] \quad (5)$$

$$C_L = [L] + [ML^{n+}] \quad (6)$$

tion at a given wavelength is shown by eqn. (7), where ε_M, ε_L and

$$A = \varepsilon_M[M^{n+}] + \varepsilon_L[L] + \varepsilon_{ML}[ML^{n+}] \quad (7)$$

ε_{ML} are the molar absorptivities of the metal ion, L and ML^{n+}, respectively. Because the values of ε_M and ε_L were measured by the preliminary work, the values of ε_{ML} and K_{ML} can be obtained simultaneously by minimizing the error square sum (U) defined by $U = \Sigma(A_{obs,i} - A_{cal,i})^2$, where $A_{obs,i}$ and $A_{cal,i}$ are the observed and the calculated absorbances, respectively.

The stability constants of heavy metal ion complexes of benzothiazole derivatives in 1,4-dioxane–water solution are summarized in Table 2. This table shows that all compounds form their most stable complexes with Ag^+ ion among the heavy metal ions examined. Under the experimental conditions used, **3**, **4** and **6** formed the complexes with Ag^+ ion almost

quantitatively and the values of log K_{AgL} were estimated to be larger than 7 which is the determination limit of the method used here. The order of the stability of Ag(I) complexes decreased as **3**, **4**, **6** > **2** ≈ **5** > **1**, and the stabilities for the cyclic and the acyclic derivatives were **3**, **4** > **2** > **1** and **6** > **5**, respectively. These facts indicate that the complexability for Ag^+ ion is primarily dependent upon the number of the sulfur donor atom(s) of the *N*-phenylpolythiazaalkane moiety, and are compatible with the results reported by Craig and co-workers.[27]

Cu^{2+} ion complexabilities were slightly observed for **3** and **4**. Sulfur atoms of a thioether are well-known to interact with soft (or *class b*) metal ions. Cu^{2+} ion is a borderline, *i.e.*, *class ab*, metal ion and, in general, the stabilities of Cu^{2+} ion–thioether complexes are not very high compared with those of soft, *i.e.*, *class b*, metal ions. Cu^{2+} ion has a higher affinity for nitrogen atoms than for sulfur atoms. Therefore, Cu^{2+} ion should more strongly bind to the aniline nitrogen of the *N*-phenylpolythiazaalkane moiety than to sulfur atoms.

The benzothiazole derivatives used in this study exhibited no complexability for the other metal ions, *i.e.*, Mn^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+} and Tl^+.

^{1}H NMR spectroscopy studies on Ag^+ ion complexation and protonation

Protonation and Ag^+ ion binding behavior for fluoroionophores were examined by ^{1}H NMR spectroscopy. Acetonitrile-d_3 was chosen as a solvent because of the lack of solubility of the benzothiazole derivatives and because it does not overlap the proton peaks of acetonitrile and polythiazaalkane units.

Ag^+ ion complexation behavior. Ag^+ ion complexation behavior was examined by ^{1}H NMR titration. The extents of the changes in the ^{1}H NMR chemical shifts of the protons of the benzothiazole derivatives which were induced by the addition of equimolar CF_3SO_3Ag are illustrated in Fig. 5. The downfield shifts in the proton signals of the methylenes adjacent to the sulfur atoms of polythiazaalkane moieties could be caused by the strong interaction of Ag^+ ion with the sulfur atoms of the polythiazaalkane moiety. On the other hand, the decrease in π-electron density of the aromatic group caused by the interaction between the nitrogen atom and the complexed Ag^+ ion results in a downfield shift in the chemical shifts of the aromatic protons.

For the cyclic analogs, **1** and **2**, with a small crown ring, all of the changes in the chemical shifts are much smaller than those for the other analogs. The addition of CF_3SO_3Ag to a solution containing **1** caused slightly and continuously downfield shifts of the chemical shifts of all protons even $[Ag^+]/[\mathbf{1}] \geqslant 1$, because of the low complexability of **1** for Ag^+ ion. The downfield shifts of the aromatic proton signals for **1** and **2** are much smaller than those for the other analogs. It is likely that the interaction between the complexed Ag^+ ion and the nitrogen atom of the *N*-phenylpolythiazaalkane moiety is too weak to decrease the π-electron density of the aromatic ring system. It should be noted that the Ag^+ ion is far from the nitrogen atom of the *N*-phenylpolythiazaalkane moiety and forms complexes with **1** and **2** in an *exo* conformation. Thus, the environment of the protons in the molecule was hardly affected by the complexation with Ag^+ ion.

On the other hand, the cyclic analogs, **3** and **4**, having larger crown rings and the acyclic derivatives, **5** and **6**, exhibited drastic downfield shifts of the aromatic proton signals. It is expected that the Ag^+ ion will approach more closely and interact electrostatically with the nitrogen atom of the *N*-phenylpolythiazaalkane moieties of the analogs **3**–**6**. The downfield shifts of aromatic proton signals, especially for Ha and Hb, of the *p*-(benzothiazolyl)phenyl moieties were observed by the complexation with Ag^+ ion. This change indicates that Ag^+ ion should interact not only with the sulfur atom but also with the nitrogen atom of the *N*-phenylpolythiazaalkane moiety, and should coordinate to the sulfur atoms of the cyclic and the acyclic polythiazaalkane moieties of the benzothiazole derivatives, **3** and **4**, and **5** and **6**, in the *endo* conformation. So the larger changes in the electron density in the molecules were produced by the much stronger interaction between the nitrogen atom of the *N*-phenylpolythiazaalkane moiety and the complexed Ag^+ ion.

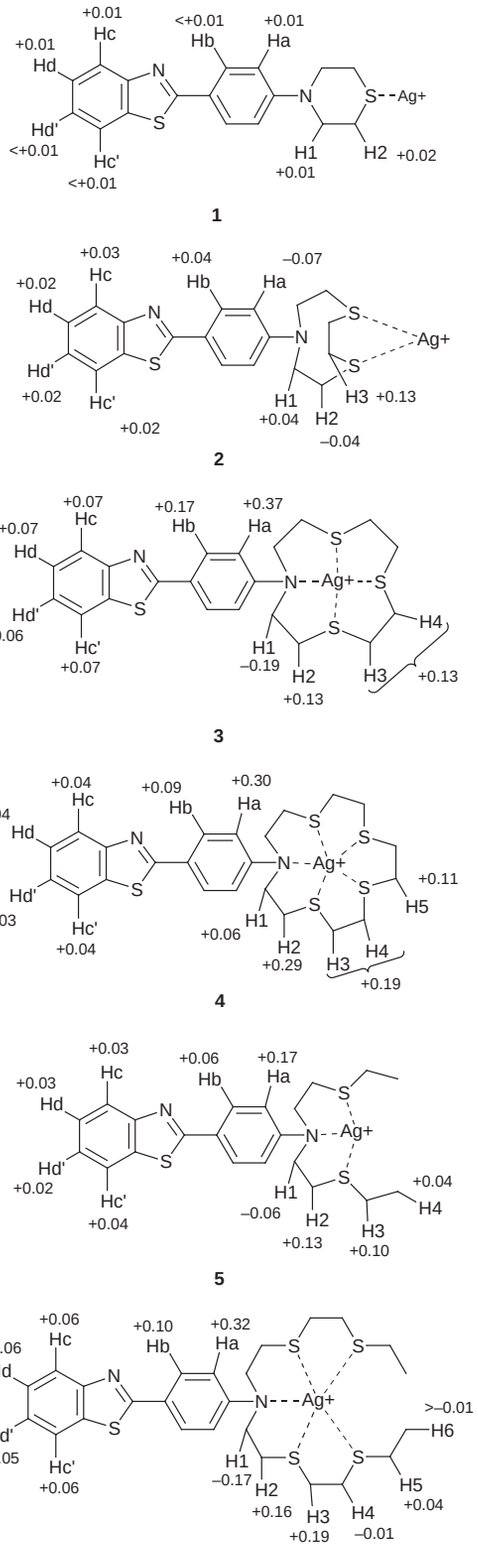


Fig. 5 Ag^+ induced changes in ^{1}H NMR chemical shifts and assumed structures of Ag^+ complexes of benzothiazole derivatives. A plus sign (+) and a minus sign (−) denote the shifts of the proton signals to lower and higher magnetic fields, respectively.

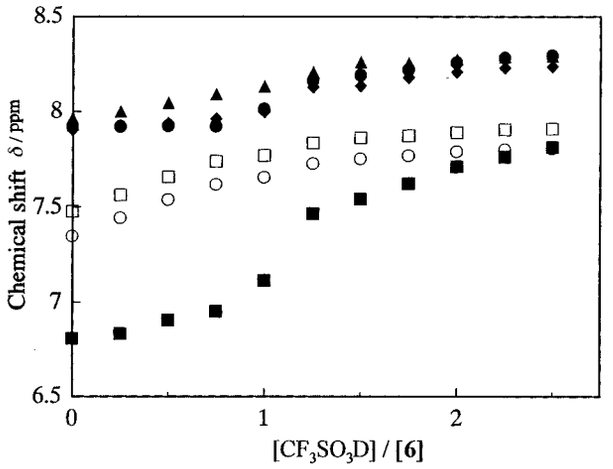
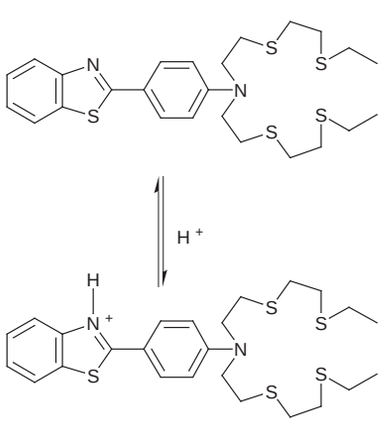


Fig. 6 Plots of $[CF_3SO_3D]/[\mathbf{6}]$ *vs.* chemical shift of proton signal of **6**. (■); Ha, (●); Hb, (▲); Hc, (◆); Hc′, (□); Hd, (○); Hd′.

Protonation behavior. As mentioned above, it is seen that the red shifts of the absorption spectra and the decrease in the intensity of the emission spectra were induced by protonation on the nitrogen atom of the polythiazaalkane moiety. On the other hand, the blue shift of the absorption spectra and the decrease in the intensity and the slight blue shift of the fluorescence spectra were caused by the complexation with Ag^+ ion. The pattern of the spectral changes for the protonation on the nitrogen atom(s) and that for the complexation with Ag^+ ion were different from each other. Thus, ^1H NMR spectroscopy was used for the determination of the protonation behavior on the nitrogen atoms.

Fig. 6 shows the changes in ^1H NMR chemical shifts for the aromatic protons of **6** (see Fig. 1 for the assignment of protons) by titration with CF_3SO_3D in acetonitrile-d_3 solution. As the large changes of the chemical shifts were observed for the protons (Hc, Hc′, Hd and Hd′) of the benzothiazolyl moiety in the range of $[CF_3SO_3D]/[\mathbf{6}] \leqslant 1$, the changes should be caused by the first protonation. For the second protonation, the larger changes in the chemical shifts for Ha and Hb than for the other protons and the broadening of the proton signal for H1 were observed in the range of $[CF_3SO_3D]/[\mathbf{6}] \geqslant 1$.

These results demonstrate that the first and the second protonations would occur on the nitrogen atom in the benzothiazolyl moiety and one in the polythiazaalkane moiety, respectively, (Scheme 1). The first protonation behavior on the



Scheme 1

nitrogen atom is different from the Ag^+ ion–nitrogen atom interaction behavior on complexation. Therefore, the patterns of the spectral changes caused by the protonation and the complexation with Ag^+ ion are different from each other.

Table 3 Spectral properties of silver ion complexes[a] of benzothiazole derivatives

Compound	AgL		
	λ_{abs}/nm (ε_{AgL}/ 10^4 mol^{-1} dm^3 cm^{-1})	λ_{em}/nm	If/If_0[b]
1	350 (3.43)	424	0.95
2	350 (3.73)	423	0.81
3	339 (2.54)	427	0.04
4	338 (2.07)	427	0.32
5	346 (2.82)	427	0.57
6	346 (3.08)	427	0.50

[a] [Ligand] = 1.5×10^{-5} mol dm^{-3} in 1,4-dioxane–water (52/48 v/v). [b] If/If_0 means the fluorescence intensity ratio: If/If_0 = (relative fluorescence intensity of silver ion complex)/(relative fluorescence intensity of free ligand).

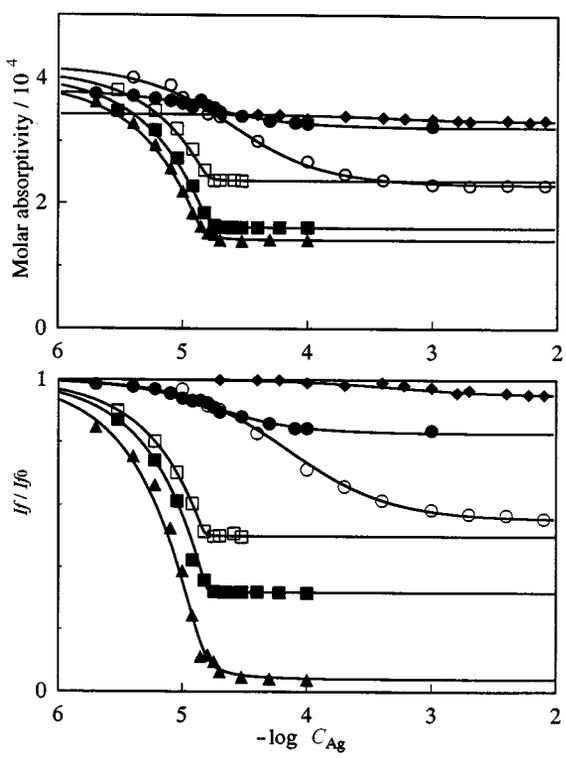


Fig. 7 Plots of molar absorptivity and relative fluorescence intensity of benzothiazole derivatives *vs.* $-\log C_{Ag}$. **1**; (◆): **2**; (●): **3**; (▲): **4**; (■): **5**; (○): **6**; (□). Initial concentration: [benzothiazole derivative] = 1.5×10^{-5} mol dm^{-3} at pH = 4.0.

Absorption and fluorescence spectral changes by complexation with Ag^+ ion

The molar absorptivity and the relative fluorescence intensity changes of the benzothiazole derivatives by the addition of Ag^+ ion are shown in Fig. 7. The solid curves in this figure show the calculated values from the obtained stability constant for the Ag^+ ion complex, demonstrating the validity of the calculated constants. It is apparent that the values of the molar absorptivity and the relative fluorescence intensity were decreased by the addition of Ag^+ ion. The spectral properties of the Ag^+ complexes of the fluoroionophores are summarized in Table 3.

The spectral changes caused by the complexation of the benzothiazole derivatives were compared with each other. Although the tetrathiazaalkane derivatives, **4** and **6**, could react

quantitatively with equimolar Ag^+ ion, the degrees of the spectral changes are different from each other. For the fluorescence spectra, the relative intensity change for cyclic compound **4** ($If/If_0 = 0.32$) is larger than that for the acyclic one **6** ($If/If_0 = 0.50$). Cyclic trithiazaalkane derivative **3**, which also reacted quantitatively with the Ag^+ ion, exhibited the largest changes in the absorption and the fluorescence spectra ($If/If_0 = 0.04$) on complexation with Ag^+ ion. The dithiazaalkane derivatives, **2** and **5**, exhibited much weaker Ag^+ ion complexability. On the other hand, the fluorescence spectral change of acyclic derivative **5** ($If/If_0 = 0.57$) is larger than that for cyclic **2** ($If/If_0 = 0.81$). Cyclic monothiamonoazaalkane derivative **1** showed the least Ag^+ ion complexability among the benzothiazole derivatives used here, and the spectral changes were quite small ($If/If_0 = 0.95$).

These spectral changes should be caused by the perturbation owing to the interaction between the complexed Ag^+ ion and the nitrogen atom of the polythiazaalkane moiety, and by the interaction between the (benzothiazolyl)phenyl moiety and the complexed silver ion. Therefore, the extent of the spectral change would be highly dependent on the strength of the interaction similarly to the case of the chemical shift changes of ^1H NMR as shown above. In this study, **3**, **4** and **6** exhibited high Ag^+ ion complexability and **3** showed the largest spectral changes. Both of the dithiazaalkane derivatives, **2** and **5**, showed similar Ag^+ ion complexability, although the cyclic compound **2** exhibited smaller spectral changes compared with the acyclic one **5**. On the complexation of **1** and **2** with Ag^+ ion, the complexed Ag^+ ion would primarily interact with the sulfur atom and would not be associated so closely with the nitrogen atom of the polythiazaalkane moiety as described in ^1H NMR spectroscopy studies. Therefore, the electron density of the fluorophore was hardly affected by Ag^+-complex formation and there were less spectral changes. On the other hand, the larger cyclic analogs, **3** and **4**, and the acyclic ones, **5** and **6**, have much more flexible structures than the small cyclic compounds, **1** and **2**. It is likely that the complexed Ag^+ ion was placed more closely to and interacted more strongly with the lone pairs of the nitrogen atom of the polythiazaalkane moiety. So the resulting perturbation of the fluorophore by the interaction of the Ag^+ ion with the sulfur atom gave larger spectral changes. It is shown from examining the space filling model that, in the silver ion complex of **3**, the silver ion should lie on the plane made up of the three sulfur atoms of the tetrathiazapentadecane ring because the cavity size of the ring is slightly smaller than the diameter of silver ion. Thus, the complexed silver ion could approach and interact with the π-electron of the *p*-(benzothiazolyl)phenyl moiety to cause the larger decrease of the absorptivity and the fluorescence intensity. Such quenching phenomena were also reported for anthraceno-cryptands.[28–31]

Ag^+ ion complexability was influenced by the number of donor atoms of the polythiazaalkane moiety. The degrees of the changes in the absorption and the emission spectra by Ag^+ ion complexation, however, could not be related directly to the complexabilities of the analogs for the Ag^+ ion.

Experimental

General procedure for preparation of fluoroionophores

N-Phenylpolythiazaalkane derivatives were synthesized according to the procedure reported elsewhere.[20,23] A dry DMF (5 mL) solution containing an appropriate *N*-phenylpolythiazaalkane derivative (1 mmol) was cooled in an ice bath. To the solution was added dropwise $POCl_3$ (0.19 g, 1.2 mmol) for 5 min. After the addition, the mixture was stirred in an ice bath for 10 min, at rt for 1.5 h, and then at 100 °C for 3 h. After the reaction was completed, the reaction mixture was poured onto ice–water (20 mL) and the mixed solution was stirred for 30 min, neutralized with sodium acetate, and extracted with $CHCl_3$ (20 mL × 3). The combined extract was concentrated to afford the crude corresponding *N*-(4-formylphenyl) derivative. Then the mixed ethanol solution (20 mL) of the crude *N*-(4-formylphenyl) derivative, 2-aminobenzenethiol (0.15 g, 1.2 mmol) and a drop of acetic acid was refluxed with stirring for 2 h. After the reaction, the mixture was first concentrated, and then 20 mL of water was added. The solution was extracted with $CHCl_3$ (20 mL × 3). The combined extract was washed with water. The extract was dried over $MgSO_4$ and the solvent was evaporated *in vacuo*. The residue was purified with column chromatography (silica gel; eluent, $CHCl_3$) and recrystallized to yield the appropriate derivative.

4-[4′-(Benzothiazol-2″-yl)phenyl]-1-thia-4-azacyclohexane 1. Pale yellow solid (42%); mp 229–230 °C; ^1H NMR ($CDCl_3$) 2.62–2.79 (m, 4H, SCH_2), 3.68–3.80 (m, 4H, NCH_2), 6.85–8.05 (m, 8H, Ar); MS (EI) *m*/*z* 312 (M^+); Anal calc. for $C_{24}H_{28}N_5O_4S_4F_3$: C, 65.17; H, 5.19; N, 8.89%. Found: C, 65.35; H, 5.16; N, 8.97%.

7-[4′-(Benzothiazol-2″-yl)phenyl]-1,4-dithia-7-azacyclononane 2. Pale yellow solid (38%); mp 188–189 °C; ^1H NMR ($CDCl_3$) 2.85 (s, 4H, SCH_2), 3.05–3.23 (m, 4H, SCH_2), 3.78–3.89 (m, 4H, NCH_2), 6.85–8.03 (m, 8H, Ar); MS (EI) *m*/*z* 372 (M^+); Anal. calc. for $C_{19}H_{20}N_2S_3$: C, 60.58; H, 5.51; N, 7.44%. Found: C, 61.25; H, 5.41; N, 7.52%.

10-[4′-(Benzothiazol-2″-yl)phenyl]-1,4,7-trithia-10-azacyclododecane 3. Pale yellow solid (43%); mp 227–228 °C; ^1H NMR ($CDCl_3$) 2.79–2.96 (m, 12H, SCH_2), 3.65 (t, 4H, NCH_2), 6.73–8.00 (m, 8H, Ar); MS (EI) *m*/*z* 432 (M^+); Anal. calc. for $C_{21}H_{24}N_2S_4$: C, 58.22; H, 5.71; N, 6.31%. Found: C, 58.30; H, 5.59; N, 6.47%.

13-[4′-(Benzothiazol-2″-yl)phenyl]-1,4,7,10-tetrathia-13-azacyclopentadecane 4. Pale yellow solid (29%); mp 193–194 °C; ^1H NMR ($CDCl_3$) 2.74–2.95 (m, 16H, SCH_2), 3.66 (t, 4H, NCH_2), 6.65–8.05 (m, 8H, Ar); MS (EI) *m*/*z* 492 (M^+); Anal calc. for $C_{23}H_{28}N_2S_5$: C, 55.88; H, 5.85; N, 5.47%. Found: C, 56.06; H, 5.73; N, 5.68%.

6-[4′-(Benzothiazol-2″-yl)phenyl]-3,9-dithia-6-azaundecane 5. Pale yellow solid (38%); mp 188–189 °C; ^1H NMR ($CDCl_3$) 1.30 (t, 6H, CH_3), 2.49–2.85 (m, 8H, SCH_2), 3.63 (t, 4H, NCH_2), 6.66–8.01 (m, 8H, Ar); MS (EI) *m*/*z* 402 (M^+); Anal. calc. for $C_{21}H_{26}N_2S_3$: C, 62.76; H, 6.43; N, 7.09%. Found: C, 62.65; H, 6.51; N, 6.96%.

9-[4′-(Benzothiazol-2″-yl)phenyl]-3,6,12,15-tetrathia-9-azaheptadecane 6. Pale yellow solid (36%); mp 40–41 °C; ^1H NMR ($CDCl_3$) 1.26 (t, 6H, CH_3), 2.41–3.02 (m, 16H, SCH_2) 3.65 (t, 4H, NCH_2), 6.66–8.01 (m, 8H, Ar); MS (EI) *m*/*z* 522 (M^+); Anal calc. for $C_{25}H_{34}N_2S_5$: C, 57.19; H, 6.58; N, 5.30%. Found: C, 57.43; H, 6.55; N, 5.36%.

Apparatus

Mass spectra were measured with Jeol JMS-DX303 (for EI) instruments. Melting points were determined with Yanaco melting point apparatus and were uncorrected. The routine ^1H NMR measurements were carried out with a Hitachi R-90 spectrometer using $CDCl_3$ solutions containing tetramethylsilane as an internal standard. The specific ^1H NMR measurements, such as a titration measurement, were carried out with a Varian XL-200 spectrometer. Elemental analyses were achieved on a Yanaco MT-2 CHN Corder. UV–VIS absorption spectra and emission spectra were obtained on a Hitachi 150–20 spectrophotometer and a Shimadzu RF-5000 spectrofluorophotometer with 1 cm quartz cells, respectively. The pH measurements were made using a Toa pH meter HM-30S equipped with a Toa

GST-5311C glass electrode. Unless otherwise specified, all reagents were the best grade and were used as received. 1,4-Dioxane was distilled after drying over NaH. DMF was purified by vacuum distillation after drying over P_2O_5. Water was doubly distilled. Metal salts were analytical grade.

Spectrophotometry and spectrofluorometry

Measurement of protonation behavior. The protonation constants of fluoroionophores were measured by spectrophotometry and spectrofluorometry at 25.0 ± 0.2 °C. Because the benzothiazole derivatives used here were hardly soluble in water, 1,4-dioxane–water (52/48 v/v) solution was chosen as a solvent. The pH of the solution (25 mL), which contained 1.5×10^{-5} mol dm^{-3} benzothiazole derivative and 0.1 mol dm^{-3} potassium nitrate for adjusting the ionic strength, was controlled by aqueous HNO_3 solution. Absorption and emission spectra were measured at each pH.

Measurement of complexation behavior for some heavy metal ions. The metal ion complexation behavior of fluoroionophores was examined spectrophotometrically in a similar manner as described in the above protonation behavior. The stability constants were determined by keeping the solution at pH = 4 by HNO_3 solution and changing metal ion concentration in the solution. The medium used was 1,4-dioxane–water (52/48 v/v) solution. Concentration of the benzothiazole derivative was 1.5×10^{-5} mol dm^{-3}.

^{1}H NMR spectroscopy

The ^{1}H NMR titration experiments were performed in acetonitrile-d_3 and recorded on a Varian XL-200 spectrometer. The acetonitrile-d_3 solutions containing 2×10^{-3} mol dm^{-3} benzothiazole derivative and variable amounts of CF_3SO_3Ag or CF_3SO_3D were prepared and the chemical shifts were reported relative to the signal of tetramethylsilane at 0 ppm.

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