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Bis(crown ether) Dyes Incorporating Azophenol Structure

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Three types of bis(crown ether) dyes bearing one or two azophenol units were synthesized, which may be expected to show different cation-complexing properties from the corresponding monocyclic crown ether dyes. The extraction of alkali and alkaline-earth metal salts with the crown ether dyes suggested that some cooperative action of the two adjacent crown ether moieties of the bis(crown ether)s occurs on complexing metal cations, although the bis(crown ether) effect is not very remarkable.

Considerable attention has been focussed on crown ether dyes(or chromogenic crown ethers), where a chromophore such as picrylamine,[1,2] azo dye,[3–5] and other dye stuff,[6,7] is incorporated into a crown ether moiety. Some of the crown ether dyes possess a potential anionic site attached to their chromophore either inside or outside the crown ether cavity, which results in formation of intramolecular ion-pair complexes with alkali and alkaline-earth metal cations under basic conditions. The complex formation leads to marked color changes of dye solutions. In the other crown ether dyes which do not contain any dissociable group in the vicinity of the chromophore, crown ether amines are incorporated into dye molecules in such a manner that the chromophore directly affects the complexation with metal cations, thus showing characteristic coloration in the presence of various metal cations. The coloration of both types of crown ether dyes is influenced considerably by the relative size of crown ether cavity and complexed metal cations, and the charge density of cations, so they are often called ion-selective dyes. Thus, the crown ether derivatives bearing chromophore are promising analytical reagents for colorimetry and metal-ion indicators.

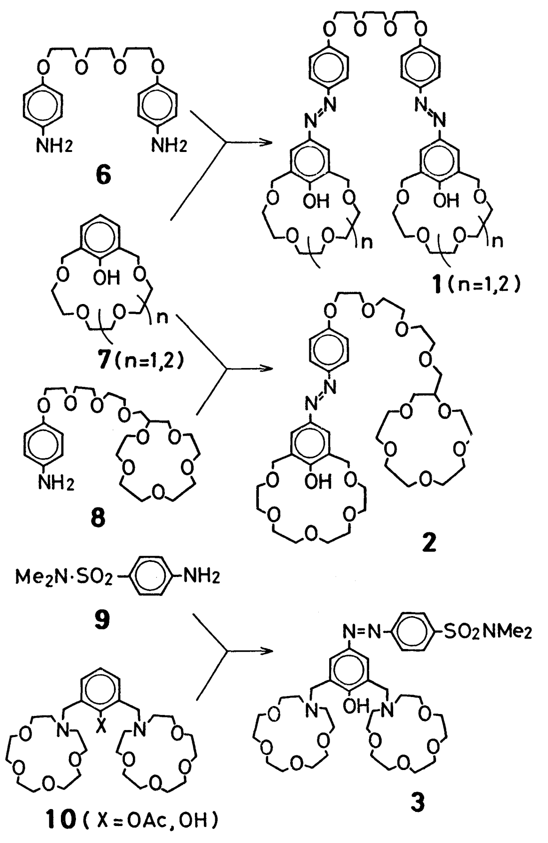
Bis(crown ether) derivatives, macrobicyclic polyethers containing two crown ether moieties at the end of a short aliphatic chain, are known to have attractive cation-complexing properties different from the corresponding monocyclic crown ethers.[8–10] They can form intramolecular sandwich-type metal complexes easily by cooperative action of two adjacent crown ether rings. The complexing behavior of the bis(crown ether)s is typical of certain alkali metal cations which are slightly larger in size than the cavity of the crown ether ring. It seems likely that this type of complex formation provides the bis(crown ether) derivatives with excellent cation-complexing abilities and/or selectivities.

These observations induced us to incorporate chromophore into bis(crown ether)s and to see what the difference in the ion-selectivity is between the bis(crown ether) dyes and the corresponding monocyclic ones. This paper concerns with the syntheses of various bis(crown ether) dyes containing azophenol skeleton and their coloration behavior on extraction of alkali and alkaline-earth metal salts.

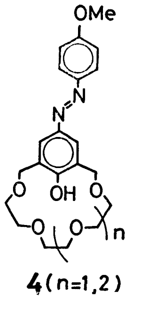
Results and Discussion

Syntheses of Bis(crown ether) Dyes. Azophenol structure was selected as a chromophore of bis(crown ether) dyes. Three types of bis(crown ether) dyes **1** through **3** were synthesized as shown in scheme 1. The general procedure consists of a conventional diazotization-coupling reaction of aromatic amines with phenols containing crown ether moieties.

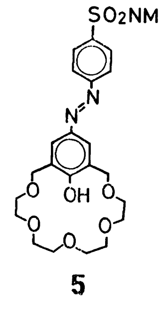
The first type of bis(crown ether) dyes **1** (*n*=1,2) are made up of two monocyclic crown ether bearing an intra-annular phenolic group in the azophenol structure. Diazotization of triethylene glycol bis(*p*-amino-



Scheme 1.



4(n=1,2)



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phenyl) ether (**6**), followed by coupling reaction with crown ether phenol **7** ($n=1,2$)[11] affords yellow-powdery bis(crown ether) dyes **1** ($n=1,2$).

In the second type of bis(crown ether) dye **2**, monocyclic crown ether dye **4** ($n=2$) is connected to 15-crown-5 using an oligo(oxyethylene) chain. The yellow oil of the unsymmetrical bis(crown ether) dye was obtained by the diazotization-coupling reaction of crown ether phenol **7** ($n=2$) with 15-crown-5 derivative carrying aminophenyl group, which can be prepared by the condensation of hydroxymethyl-15-crown-5 and triethylene glycol mono(*p*-nitrophenyl) ether, followed by hydrogenation over palladium-carbon.

In the third type of bis(crown ether) dye **3**, an azophenol dye is set up on the bridge containing two azacrown ether rings, the phenolic group being outside the crown ether cavity unlike the preceding ones. Bis(crown ether) **10** ($X=OCOCH_3$) was synthesized at first by condensation reaction of 2,6-bis(bromomethyl)phenyl acetate with two equivalents of monoaza-15-crown-5, and then hydrolyzed to bis(crown ether) phenol **10** ($X=OH$). The diazotization-coupling reaction of *N*,*N*-dimethyl-*p*-aminobenzenesulfonamide with the bis(crown ether) phenol gave orange oil of bis(crown ether) dye **3**.

Monocyclic crown ether dyes **4** ($n=1,2$) and **5** were also synthesized by the conventional diazotization-coupling reaction for comparison.

Complexation with Alkali and Alkaline-earth Metal Salts. For rapid screening of the complexing abilities of the bis(crown ether) dyes, **1** through **3**, extractions were carried out from aqueous solutions of alkali and alkaline-earth metal(Li^+, Na^+, K^+, Sr^{2+}, and Ba^{2+}) hydroxide with crown ether dye chloroform solutions. The corresponding monocyclic crown ether dyes, **4** and **5**, were also employed for comparison. Figures 1 and 2 depict the absorption spectra of the chloroform layer containing bis(crown ether) dyes **1** ($n=1,2$), which were obtained immediately after the extraction. The color of the chloroform layer changed from yellow to orange after the extraction of metal hydroxides, that is, a new peak appears at the higher wavelength, as the peak based on the uncomplexed crown ether dye diminishes at the lower wavelength. This indicates that when the crown ether dye complexes metal cations, the phenolic group interacts with the complexed cation appreciably. Since the molar absorptivity for the metal complexes does not change very much from one metal cation to the other, the complexing abilities of the crown ether dyes for metal cations can be discussed qualitatively from the absorbance of the new peaks. The complexing ability of bis(crown ether) dye **1**($n=1$) decreases in the order $Ba^{2+}>Sr^{2+}\gg Li^+>Na^+>K^+$, while that of bis(crown ether) dye **1**($n=2$) follows the order $Ba^{2+}>Sr^{2+}>K^+>Na^+>Li^+$. The corresponding monocyclic crown ether dyes **4** and **5** were essentially the same in the complexing tendency. However, it is worth noting that there is some difference in the absorption spectra between bis(crown ether) dye **1**($n=1$) and monocyclic one **4**($n=1$), as illustrated in Fig. 3. The complexing abilities of **4**($n=1$) for Ba^{2+}, Sr^{2+}, Na^+, and K^+ were improved by the introduction of bis(crown ether) structure.

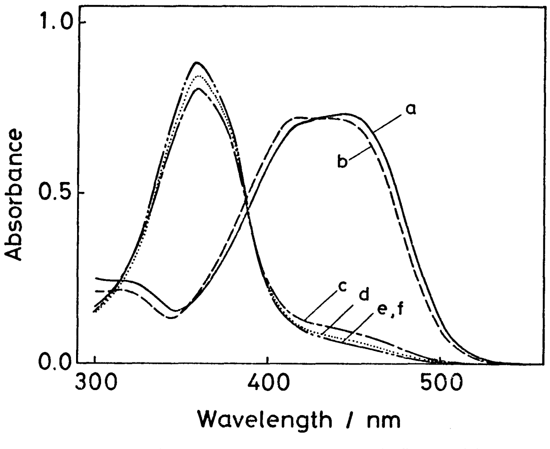


Fig. 1. Absorption spectra of 2×10^{-5} M **1**($n=1$) in chloroform equilibrated with 0.04 M aqueous metal hydroxide solution. (1 M = 1 mol dm^{-3})
a, $Ba(OH)_2$; b, $Sr(OH)_2$; c, LiOH; d, NaOH; e, KOH; f, without salt.

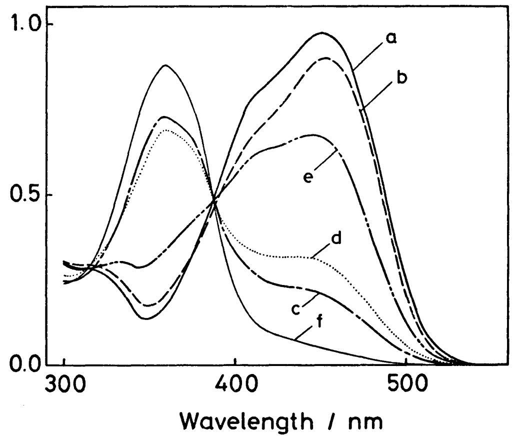


Fig. 2. Absorption spectra of 2×10^{-5} M **1**($n=2$) in chloroform equilibrated with 0.04 M aqueous metal hydroxide solution.
The symbols are the same as those in Fig. 1.

In the unsymmetrical bis(crown ether) dye **2**, the aliphatic crown ether moiety is expected to take an extra part in the complexation of the crown ether phenol moiety with metal cations. Unfortunately, the absorption spectra obtained in the **2**–metal hydroxide extraction system(Fig. 4) do not offer any distinct evidence about the cooperative complexation of two different crown ether moieties. Another possibility is that the aliphatic crown ether moiety complexes a metal cation by itself, then the crown ether phenol approaches the complex intramolecularly as the counter anion, but no further investigation was performed about this point.

In the third type of bis(crown ether) dye **3**, an azophenol unit exists on the bridge connecting two azacrown ethers, the phenolic group being outside the crown ether moieties unlike the preceding types of bis(crown ether) dyes, **1** and **2**. The absorption spectra obtained in the metal hydroxide extraction systems (Fig. 5) show that the complexing ability of bis(crown

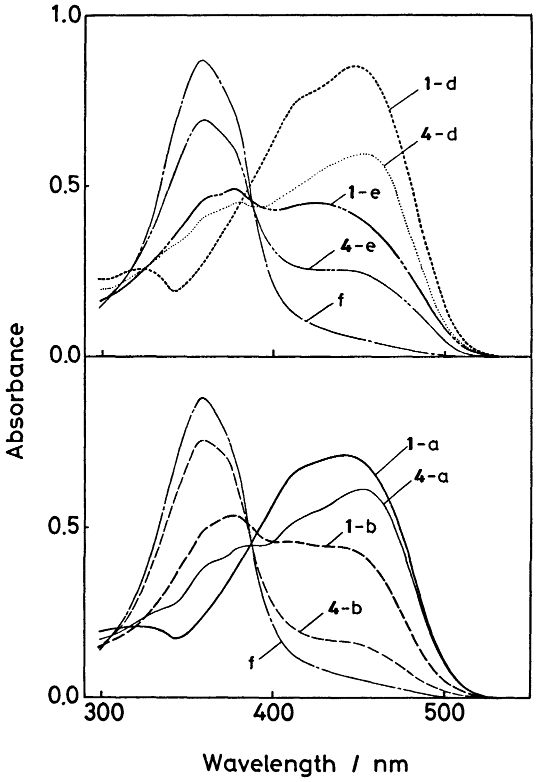


Fig. 3. Absorption spectra of $\mathbf{1}(n=1)$ and $\mathbf{4}(n=1)$ in chloroform equilibrated with aqueous metal hydroxide solution.
The symbols are the same as those in Fig. 1.
Crown ether unit concentration: 4×10^{-5} M, alkali metal concentration: 0.4 M, alkaline-earth metal concentration: 0.004 M.

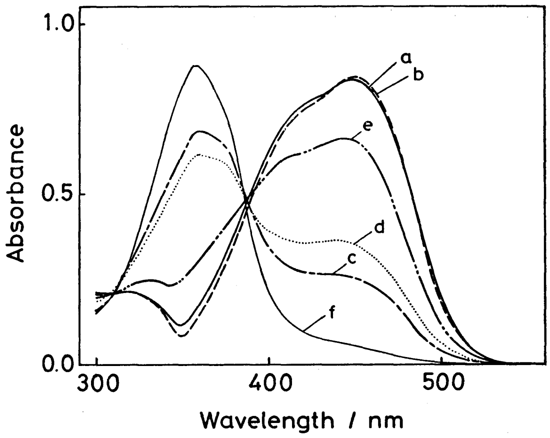


Fig. 4. Absorption spectra of 4×10^{-5} M **2** in chlorofrom equilibrated with 0.04 M aqueous metal hydroxide solution.
The symbols are the same as those in Fig. 1.

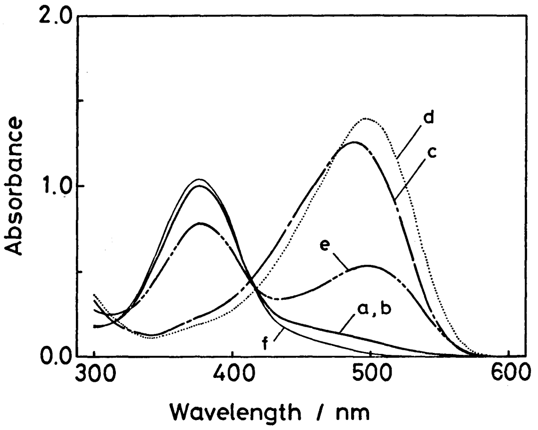
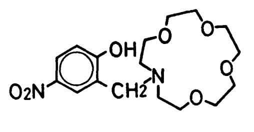


Fig. 5. Absorption spectra of 4×10^{-5} M **3** in chlorofrom equilibrated with 0.04 M aqueous metal hydroxide solution.
The symbols are the same as those in Fig. 1.

TABLE 1. EXTRACTION EQUILIBRIUM CONSTANT(K_e) AND ACID-DISSOCIATION CONSTANT(K_a) IN THE EXTRACTION OF ALKALI METAL SALTS

Crown ether dye	$-\log K_e$			$-\log K_a$
	Li^+	Na^+	K^+	
3	11.0	10.6	11.7	3.55[b)]
11[a)]	9.15	9.76	9.86	5.79

a) Taken from Ref. 12. b) Measured in H_2O containing about 0.1 M tetramethylammonium chloride.



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ether) dye **3** for alkaline-earth metal cations is rather low compared to that of **1** and **2**. Crown ether dye **11**, the complexing ability of which has been studied by Nakamura *et al.*,[12)] can be chosen as the corresponding monocyclic one of **3**, although the dye component is not azophenol but *p*-nitrophenol unit. Therefore, in order to compare the complexing ability of **3** with that of **11**, extractions were also made under the identical conditions in the **11** system, that is, from a metal chloride aqueous solution with a crown ether dye chloroform solution containing triethylamine. The extraction equilibrium constant(K_e) and the acid-dissociation constant(K_a) are listed in Table 1, together with the values for **11**. In the monocyclic crown ether dye **11**, the extractability(the complexing ability) decreases in the order $Li^+>Na^+>K^+$. This moderate lithium selectivity of **11** was explained in terms of the coordination interaction of the phenolate anion with the crown-complexed cation.[12)] On the other hand, the extractability of bis(crown ether) dye **3** follows the order $Na^+>Li^+>K^+$, where the extractability for Na^+ is slightly higher than that for Li^+. It has been discussed in detail by Nakamura *et al.*,[5)] how the basicity(or acidity) of an anionic site can contribute to ion-selectivity of various crown ethers carrying a phenolic group in the periphery. It is likely that the anionic site possessing a localized charge(high basicity) coordinates to the crown-complexed metal cation, thus resulting in the preference for the smaller alkali metal cations. In contrast with the above site, the anionic site with a delocalized charge(low basicity) favors an ion-pair interaction with the complexed metal cations. As the acid-dissociation constant of bis(crown ether) dye **3** is larger than monocyclic one **11** by about two orders of magnitude, the azophenol unit itself tends to enhance the Li^+-extractability of the crown ether dye compared with the *p*-nitrophenol unit. Nevertheless, bis(crown ether) dye **3** prefers Na^+ to Li^+ in the extraction of alkali metal salts. This finding indicates the possibility of such specific complex formation of the bis(crown ether) dye as often observed in the conventional bis(crown ether) derivatives.

Experimental

Syntheses of Crown Ether Dyes. *General Procedure of Diazotization-coupling Reaction*: An aniline derivative (10 mmol) in 1 M† HCl (30 cm^3) was diazotized by treating with $NaNO_2$ (12 mmol) at 0°C. The resulting diazonium salt solution was added dropwise to a phenol derivative dissolved in 0.25 M NaOH (50 cm^3) with vigorous stirring at room temperature. In the meantime the color of the solution changed to orange and then to yellow. To this mixture was added 1 M NaOH until the color turned again to orange, and then the mixture was allowed to stand overnight. Acidification of this solution by 1 M HCl gave yellow or orange precipitates, which were recovered by filtration and washed with water. The purification steps depended on the nature of the product, and most of the solid product were purified by recrystallization from ethanol-water(2:1).

Bis(crown ether) Dyes ***1****(n=1,2)*: The aniline component, 1,8-bis(*p*-aminophenoxy)-3,6-dioxaoctane, was obtained by the reaction of *p*-nitrophenol with 1,8-dibromo-3,6-dioxaoctane in acetone in the presence of K_2CO_3, followed by hydrogenation on palladium-carbon in dioxane. **1**(*n*=1): yellow crystals; mp 150 °C(decomp); UV($CHCl_3$) 358 nm (ε 5.3×10^4); IR(KBr) 3300(O-H), 1600(aromatic nuclei), 1590(N=N), and 1120 cm^{-1}(C-O-C); ^{1}H-NMR($CDCl_3$) δ= 3.55—3.98(36H, m, OCH_2CH_2O), 4.10(4H, t, CH_2OPh), 4.71(8H, s, CH_2Ph), 6.98(4H, d, aromatic H), 7.68—7.96 (8H, m, aromatic H), and 8.12(2H, s, OH); Found: C, 61.72; H, 6.64; N, 6.17%. Calcd for $C_{46}H_{58}N_4O_{14}$: C, 62.01; H, 6.56; N, 6.29%. **1**(*n*=2): yellow crystals; mp 123 °C(decomp); UV($CHCl_3$) 358 nm(ε 5.4×10^4); IR(KBr) 3250(O-H), 1590(aromatic nuclei), 1575(N=N), and 1100 cm^{-1}(C-O-C); ^{1}H-NMR($CDCl_3$) δ=3.60—3.98(44H, m, OCH_2CH_2O), 4.11(4H, t, CH_2OPh), 4.76(8H, s, CH_2PH), 7.02(4H, d, aromatic H), 7.75—7.99(8H, m, aromatic H), and 8.57(2H, s, OH). Found: C, 60.88; H, 6.75; N, 5.68%. Calcd for $C_{50}H_{66}N_4O_{16}$; C, 61.34; H, 6.79; N, 5.72%.

Bis(crown ether) Dye ***2***: The aniline component, [10-(*p*-nitrophenoxy)-2,5,8-trioxadecyl]-15-crown-5 (**8**) was prepared by the reaction of hydroxymethyl-15-crown-5 with 8-(*p*-nitrophenoxy)-3,6-dioxaoctyl tosylate in THF in the presence of NaH, followed by hydrogenation on palladium-carbon. After the coupling reaction and the acidification the product was extracted with chloroform(30 $cm^3\times5$). The combined extract was washed successively with 5% NaOH, water, 1 M HCl, and water and then dried. Bis(crown ether) dye **2** was purified by silica-gel column chromatography using chloroform-ethanol(5:2). **2**: orange oil: UV ($CHCl_3$) 358 nm(ε 2.2×10^4); IR(KBr) 3340(O-H), 1600 (aromatic nuclei), and 1110 cm^{-1}(C-O-C); ^{1}H-NMR($CDCl_3$) δ=3.50—3.90(47H, m, OCH_2CH_2O), 4.15(2H, m, CH_2OPh), 4.73(4H, s, CH_2Ph), 7.02(2H, d, aromatic H), 7.68—7.86 (4H, m, aromatic H), and 8.48(1H, s, OH).

Bis(croun ether) Dye ***3***: The precursor of the phenol component containing a bis(crown ether) moiety, **10**(X= $OCOCH_3$), was made up as follows. To an acetonitrile solution(50 cm^3) of monoaza-15-crown-5[13] (20 mmol) was added 2,6-bis(bromomethyl)phenyl acetate[14] (10 mmol) dissolved in acetonitrile(50 cm^3) under a nitrogen atmosphere at the refluxing temperature. After refluxing for 6 h, K_2CO_3 (20 mmol) was added to the reaction mixture, which was then continued to reflux with vigorous stirring for three more hours. The insoluble materials were filtered off and then washed with acetonitrile. Solvent evaporation of the filtrate gave a pale yellow oil of **10**(X=$OCOCH_3$); IR (neat) 1705(ester C=O), 1600(aromatic nucleus), and 1125 cm^{-1}(C-O-C); ^{1}H-NMR($CDCl_3$) δ=2.11(3H, s, CH_3CO), 2.70—3.00(8H, m, NCH_2), 3.50—3.90(32H, m, OCH_2), 3.83(4H, s, CH_2Ph), and 6.64—7.16(3H, m, aromatic H); MS(70 eV) *m/e*(rel intensity) 598(M^+, 4), 555(7), 379(32), 337(47), and 43(100). Bis(crown ether) phenol **10**(X= OH), which is accessible from **10**(X=$OCOCH_3$) by treating with 1 M NaOH, is labile to air oxidation, and subjected coupling reaction immediately after the hydrolysis. On the coupling reaction a small quantity of ethanol(10%) was required for solubilizing the aniline component **9**. After the reaction the crude product was extracted by chloroform (20 $cm^3\times5$) without the acidification process, and then back-extracted to 1 M HCl. The solution was adjusted to pH *ca.* 9 with concentrated aqueous ammonia and thereafter the product was again extracted with chloroform(20 $cm^3\times$ 5). The extract was washed with water, dried over Na_2SO_4, and concentrated to yield brown oil. Column chromatography[neutral alumina, ethanol-benzene(1:10)] affords pure bis(crown ether) dye **3**: reddish orange oil; UV($CHCl_3$) 378 nm(ε 2.6×10^4); IR(neat) 1600(aromatic nuclei), 1350 and 1165(SO_2), and 1125 cm^{-1}(C-O-C); ^{1}H-NMR($CDCl_3$) δ=2.74(6H, s, NCH_3), 2.86(8H, t, CH_2N), 3.50—3.90(32H, m, CH_2O), 3.86(4H, s, CH_2Ph), and 7.75—8.00(6H, m, aromatic H).

Monocyclic Crown Ether Dyes ***4*** *and* ***5***: They can be synthesized according to the general procedure. **4**(*n*=1): yellow crystals; mp 136—137 °C; UV($CHCl_3$) 358 nm(ε 2.2×10^4); IR(KBr) 3260(O-H), 1600(aromatic nuclei), 1580(N=N), and 1130 cm^{-1}(C-O-C); ^{1}H-NMR($CDCl_3$) δ=3.60—3.80 (12H, m, OCH_2CH_2O), 3.87(3H, s, OCH_3), 4.71(4H, s, CH_2Ph), 6.98(2H, d, aromatic H), 7.69—7.89(4H, m, aromatic H), and 8.12(1H, s, OH). **4**(*n*=2): yellow crystals; mp 95.5—96.5 °C; UV($CHCl_3$) 358 nm(ε 2.2×10^4); IR (KBr) 3260(O-H), 1590(aromatic nuclei), and 1100 cm^{-1} (C-O-C); ^{1}H-NMR($CDCl_3$) δ=3.60—3.80(16H, m, OCH_2CH_2O), 3.87(3H, s, OCH_3), 4.75(4H, s, CH_2Ph), 6.98(2H, d, aromatic H), 7.73—7.79(4H, m, aromatic H), and 8.50 (1H, s, OH).

On the synthesis of **5**, the addition of ethanol was necessary because of the poor water-solubility, in a similar way to bis(crown ether) dye **3**. **5**: orange crystalline plates; mp 143.5—144.5 °C; UV($CHCl_3$) 364 nm(ε 2.9×10^4); IR (KBr) 3270(O-H), 1600(aromatic nuclei), 1350 and 1175 (SO_2), and 1120 cm^{-1}(C-O-C); ^{1}H-NMR($CDCl_3$) δ=2.74 (6H, s, NCH_3), 3.60—3.90(16H, m, OCH_2CH_2O), 4.77(4H, s, CH_2Ph), 7.79—8.04(6H, m, aromatic H), and 8.77(1H, s, OH).

Solvent Extraction. *Extraction of Metal Hydroxide*: In a stoppered 1-cm cell with about 10 cm^3 of volume was placed 4 cm^3 of a 0.04 M alkali or alkaline-earth metal hydroxide aqueous solution and 4 cm^3 of 4×10^{-5} M(for azophenol unit) crown ether dye chloroform solution, and

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† 1 M=1 mol dm^{-3}.

then shaken vigorously at ambient temperature. After the complete phase separation the absorption spectrum of the chloroform layer was taken using a Hitachi 340 recording spectrometer.

Extraction of Metal Chloride in the Presence of Triethylamine: The experiments were done in a similar way to that in the literature.[2] Equal volumes(10 cm^3) of 0.5 or 0.1 M alkali metal chloride solution and(0.5—2.5)$\times 10^{-5}$ M crown ether dye chloroform solution containing 0.2 M triethylamine were introduced into a stoppered flask and then shaken at 25.0 ±0.1 °C for 30 min. Then, the absorbance of the chloroform layer was measured at 378 nm(uncomplexed, ε 2.61$\times$10^4), and at 487 nm(Li$^+$ complex, ε 3.29$\times$10^4), 493 nm(Na$^+$ complex, ε 3.49$\times$10^4), or 500 nm(K$^+$ complex, ε 3.50$\times$10^4) using 1-cm standard cell. Thus, each of the species in the chloroform layer can be calculated using the ε values, which were determined in separate experiments. The values of K_e and K_a were determined according to the published method.[2]

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