Synthesis of Crown Ether Dyes[1)]

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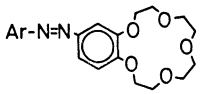
Crown ether dyes were synthesized in order to develop photometric reagents which are highly selective to alkali and alkaline earth metals. They contain dissociable protons attached to the chromophores of crown ether molecule. Their extraction behavior for alkali and alkaline earth metal ions as neutral complex was examined. The dyes extract potassium and alkaline earth metals, respectively. Dyes with picrylamino chromophore are effective for extractive photometric determination of potassium. A molecular design of colorimetric reagents is discussed on the basis of crown ethers.

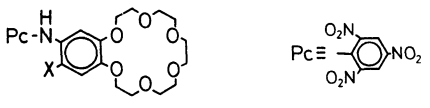
In view of the recent success in extraction photometric determination of alkali metals by crown ether-based chromogenic reagents,[2,3)] a series of crown ethers dyes with dissociable protons attached to the chromophores were synthesized, and their extraction behavior for alkali and alkaline earth metal ions was examined. Since only a very few chromogenic crown ethers are known,[4)] development of this type of compound is highly desirable for its use as a crown ether reagent in analysis.

Results and Discussion

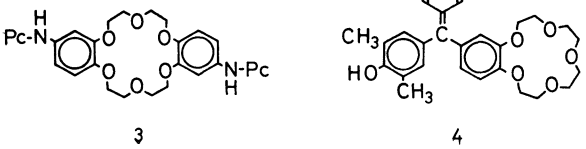
Synthesis. The dyes synthesized are summarized in structural formulae **1**—**6**, and the synthetic routes are illustrated in (1)—(6). Since the reactions involved are the chemical transformations, no details are given except for the method of purification. Most of the dyes were isolated and purified by column chromatography followed by recrystallization. Readily crystallizable compounds, *e.g.*, **1a**, **1b**, **1d**, **5a**, or **5b**, were isolated by recrystallization, the yields being often very low, due to loss by repeated recrystallization (**1b** and **1d**). It is preferable to carry out a rough separation of the reaction product first by column procedure either on silica gel or alumina. The recrystallization of the main product then becomes easier. Preparation of crown ether dyes was difficult due to the difficulty in isolation. For example, the synthesis of benzein dye from 4′-formylbenzo-15-crown-5 and phenol by reactions similar to (4) could not be achieved, since the isolation of triarylmethane precursor of the dye was unsuccessful. The compound is difficult to handle, being both hydrophilic and lipophilic as regards solubility.



1, Ar= 2-hydroxy-1-naphthyl (a)
4-hydroxyphenyl (b)
3-*t*-butyl-4-hyroxyphenyl (d)
3-chloro-4-hydroxyphenyl (e)



2, X = H (a)
NO_2 (b)



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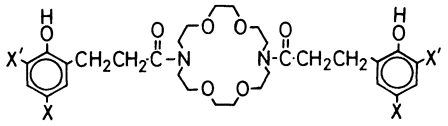
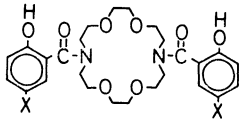


5, X = H H, X′ = H (a)
NO_2 H (b)
-N=N- H (c)
-N=N-NO_2 H (d)
-N=N-NO_2 -N=N-NO_2 (e)



6, X = H (a)
NO_2 (b)

Acid Dissociation and Metal Extraction. The acid dissociation constants (K_{HA}) of crown ether dyes were determined photometrically in water containing 20% dioxane by volume. The results, together with the λ_{max}

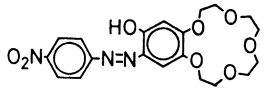
Table 1. Physical properties of crown ether dyes

Dyes	pK_{HA}[a)]	λ_{max}, nm[b)]	$\varepsilon(\lambda_{max})\times 10^{-3}$ [b)]
1a	11.6	473	13.2
1b	8.6	363	22.9
1c	9.7	368	22.4
1d	7.3	370	17.2
2a	10.6[c)]	400	11.5
2b	8.8[c)]	425	14.6
4	7.9	465[d)]	4.6[d)]

a) 20% Dioxane, μ=0.10 (LiCl), 25 °C. b) Chloroform. c) 10% Dioxane, μ=0.10 (LiCl), 25 °C. d) Dioxane.

and ε values for the undissociated dyes in chloroform solution, are summarized in Table 1. The dissociation constants reflect the structural characteristics of the dyes.

The dyes sythesized are sparingly soluble in water but appreciably soluble in most organic solvents. Some of the dyes (**3**, **5b**, **5c**, **6a**, and **6b**) are not very soluble in the usual solvents and it is difficult to increase the concentration sufficient for spectrophotometry. The extraction behavior of the dyes **1**—**4** toward potassium, an element which seems to be the most easily extracted[2,3] was studied under various conditions. No spectral change was observed for azo dyes **1** dissolved in organic solvents such as chloroform, isobutyl methyl ketone, nitrobenzene or 1-pentanol, when the solution was brought in contact with 1 M K^+ aqueous solution buffered at pH 9.5—12.5 with carbonate (K_2CO_3) or borate ($Li_2B_4O_7$–LiOH). The spectra of the organic solution remained as those of HA (undissociated form), indicating that no extraction of K^+A^- type species took place. The azo crown ether dye **7** (pK_a, 9.2; 10% dioxane)[5] was found to behave similarly (no extraction).



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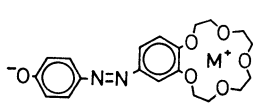
In the presence of potassium in aqueous solution the dye partially leaked out from organic into aqueous phase for **1b**. This suggests that with azo dyes **1a** and **1d**, complexation of potassium with the benzo-15-crown-5 function occurs, but the resulting complex of zwitter ion structure M^+A^- is hardly distributed in either organic or aqueous phase. At most, the complex partially goes into aqueous phase with relatively less lipophilic dye such as **1b**.

In contrast to azo dyes **1**, the picrylamino-substituted benzo-18-crown-6 (**2**) extracts potassium successfully. This is in line with the behavior of benzo-15-crown-5 homologues.[2,3] In fact, **2** is an extraction reagent for potassium, more effective than benzo-15-crown-5 homologues, and can be used for the determination of ppm level of potassium.[6] The dibasic ether dye **3** behaves similarly, but a detailed study could not be made because of the low solubility of the compound (in chloroform) and the precipitation of metal complex at high concentration of potassium. No alkaline earth metal ions were extracted by **3**.

The benzein dye **4** was studied in a similar way for the extraction of potassium. The absorbance of the organic phase at 600 nm was 0.02 (optical path, 1 cm) when 3.8×10^{-5} M solution of **4** in isobutyl methyl ketone was shaken with an equal volume of 0.1 M Li_3EDTA–OH (trilithium salt of *N'*-(2-hydroxyethyl)-ethylenediamine-*N*,*N*,*N'*-triacetic acid, pH 10.1). On addition of potassium chloride, the absorbance increased to 0.09 (0.01 M KCl) and 0.19 (0.1 M KCl), indicating the extraction of K^+A^-. However, the dye was unstable in alkaline solution, probably because of the irreversible oxidation of ionized species.

The difference in extraction behavior between hydroxyarylazo- and picrylamino-substituted benzo crown ethers should be mentioned. Both types of dyes would extract metals by forming complexes of the zwitter-ion structure, *e.g.*, **8** and **9**, as in the following.



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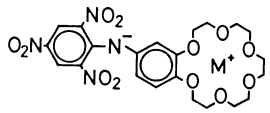

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8 and **9** each represent perhaps the most important of the many canonical formulae for the resonance stabilized zwitter-ion complexes from the corresponding azo and picrylamino crown ether dyes, respectively. In **9**, there is a steric congestion around anionic nitrogen, and the hydration would be considerably hindered. On the other hand, the phenolate oxygen in **8** may be easily hydrated and this canonical structure should be greatly stabilized in aqueous solution. In other words, negative charge of the dye would be more delocalized in **9** than in **8**. A negative-positive charge separation in the complex might be smaller with the picrylamino crown ether complexes than with azo crown ether complexes. This might increase the distribution of the picrylamino metal complexes in organic solution. That the benzein dye extracts potassium to some extent suggests the better charge delocalization than in azo dyes.

Compounds **5** and **6** were synthesized with the hope that chelate-type coordination by phenolate anion to the crown ether-encapsulated metal might help increase both stability and extractability of the alkali as well as alkaline earth metals.

The extraction of alkali and alkaline earth metal ions by dyes **5c**, **5d**, **5e**, **6a**, and **6b** was studied, only **5e** being found to extract the metals. Figure 1 shows the spectra of 9.4×10^{-6} M **5e** in chloroform in contact

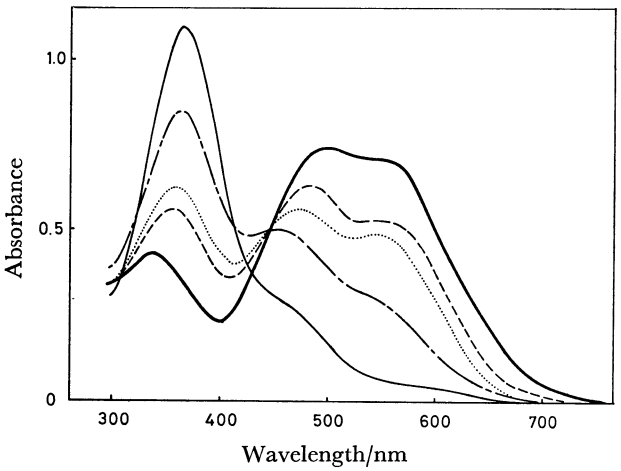
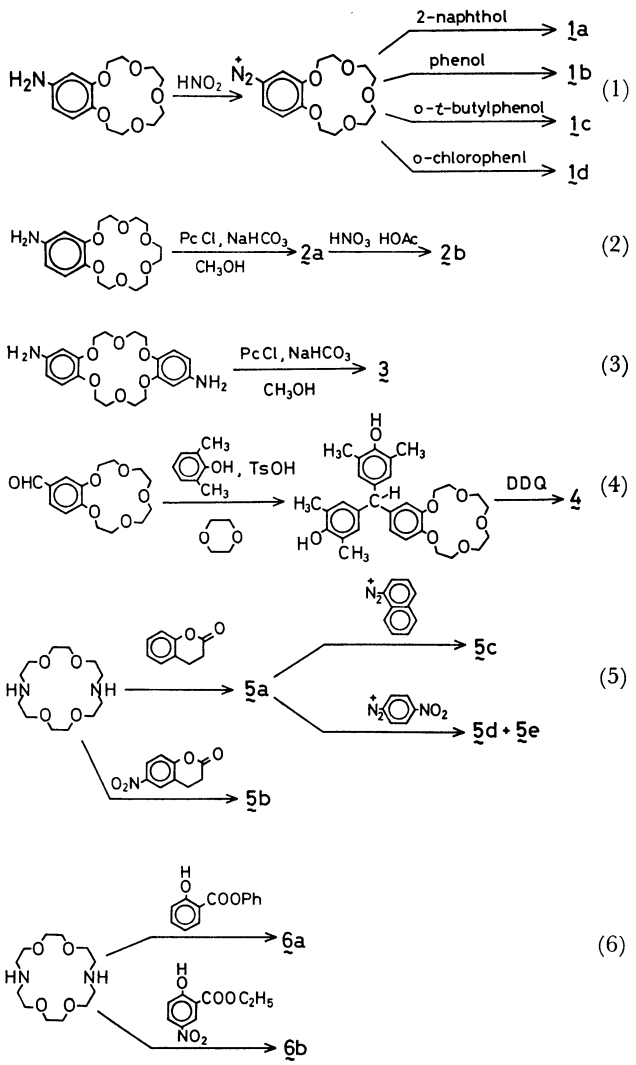
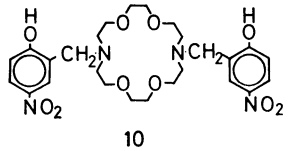


Fig. 1. Absorption spectra of 9.4×10^{-6} M **5e** in chloroform contacted with an equal volume of 1 M metal chloride solution buffered with 1 M triethanolamine at pH 10.9.
——, Without metal chloride (blank); -·-·-, LiCl; ·····, $CaCl_2$; ------, $BaCl_2$; ——, 9.4×10^{-6} M **5e** in 0.1 M LiOH (20% dioxane), 25 °C.



with an equal volume of 1 M LiCl, $CaCl_2$ or $BaCl_2$ solution buffered with 1 M triethanolamine at pH 10.9. Change in spectrum from the blank (1 M metal being absent) to that in the presence of 1 M metal chlorides is irregular (no apparent isosbestic point) due to the distribution of the dye to aqueous phase. However, a regular increase in absorbance at 500—550 nm region is observed from lithium to calcium and barium. From a comparison of the result with a limiting spectra taken in 0.1 M LiOH (20% dioxane), the metals seem to be extracted as $M^{II}A$ or M^{I}_2A (**5e**=H_2A) type complexes. With potassium salt a considerable fraction of the dye is distributed into aqueous phase. Dyes **5c**, **5d**, **6a**, and **6b** are distributed completely into aqueous solution under similar extraction conditions.



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While **6b** does not extract alkaline earth metals, the analogous crown ether dye **10** does.[7] The difference might be due to the lower donor property of the amide nitrogen combined with an unfavorable orientation of phenolic group in **6b** for coordination. The phenolic hydroxyl would be coplanar with the amide group because of conjugation and hydrogen bonding, prohibiting access of the phenolate group to the center of the diaza-18-crown-6 ring where the metal ions are to be captured. The introduction of the two methylene groups between the amide carbonyl and aromatic nucleus in **5e** releases the steric constraint enforced by the amide bonding, making it possible for phenolate anions to occupy the axial positions of the encapsulated metal. The increased acidity of phenolic hydroxyl groups assisted by two *p*-nitrophenylazo groups for each aromatic neucleus also helps increase the degree of formation of metal complex at a lower pH. That the phenolate anion in **10** can reach the encapsulated metal is readily envisaged by stereomodel inspection. The unusually high stability of alkaline earth metal complexes from *N,N'*-dipropionic acid derivative of the diaza-18-crown-6[8] supports this view.

In conclusion, the two factors seem to be most important in the molecular design of crown ether based extraction photometric reagents for alkali and alkaline earth metals: an extensive delocalization of anionic charge and a minimum distance of positive-negative charge separation in the resulting metal complex. Both factors are essential if the metal complexes are of zwitter-ion structure as with **2**. The charge delocalization factor would not be essential if the metal complexes can assume a chelate-type coordination structure (**5e** and **10**). In this case, however, a structural requirement which allows the coordination of the dye anion to the metal should be considered.

Experimental

Apparatus and Instruments. IR spectra were recorded on a JASCO DS-403G infra-red spectrophotometer, UV and visible absorption spectra on a Hitachi 200 double beam spectrophotometer and a Hitachi 556 dual wave-lengths double beam spectrophotometer. ^{1}H-NMR spectra were measured with either a Varian A-60 or a Bruker WH-90. The pH measurements were made on an Orion 801A ion-analyzer equipped with TOA GST-155C hybrid glass electrode.

Acid Dissociation Constant. Several miligrams of the dye sample was weighed and dissolved in 20 ml dioxane in a 100 ml measuring flask. Lithium chloride (0.42 g) was then added along with a small amount of aqueous acetic acid to make ionic strength and pH of the final solution 0.10 and $\leq$5, respectively, the mixture being diluted with water to 100 ml. One tenth molar lithium hydroxide was added, and the pH and the absorption spectra were measured. The effect of lithium salt and organic solvent (dioxane) on pH measurements was not corrected. The acid dissociation constant was obtained from the slope of the plot, $\Delta A[H^+]/[HA]_t$ *vs.* $\Delta A/[HL]_t$, by means of the equation

$$\frac{\Delta A[H^+]}{[HA]_t} = K_a\left(\Delta\varepsilon - \frac{\Delta A}{[HA]_t}\right).$$

Where $\Delta A(=A-A_0)$ is the increment of absorbance at any pH from the initial absorbance (A_0) where all the dye molecule (HA) exist in undissociated form. $[HA]_t$ is the total concentration of the dye and $\Delta\varepsilon$ is the difference between ε_A-

and ε_{HA}.

Synthesis of Dyes. The synthetic procedures are not optimized for the maximum yield of the product.

1a. 4′-Nitrobenzo-15-crown-5 was hydrogenated in ethanol over Pd/C catalyst.[9] After removal of the catalyst, 3—5 times molar excess of fluoroboric acid was gradually added and the mixture stored in a refrigerator overnight. The fluoroborate salt of 4′-aminobenzo-15-crown-5 was obtained as white needles. Yield, 90%. The salt (0.30 g, 0.82 mmol) and 1.6 ml of 1 M HCl were dissolved in 10 ml water and diazotized in the usual manner. 2-Naphthol (117 mg, 0.82 mmol) dissolved in 2.7 ml of 1M NaOH was chilled below 5° C. To this solution was added the diazotized solution under stirring. After being stirred for an hour, the mixture was acidified by addition of acetic acid, and the red precipitates formed were collected. The crude product was then digested in a small amount of hot methanol, turning into fine red crystals. Yield, 0.28 g, 66%; mp 162—163 °C; IR(KBr) 3440(OH), 1600(aromatic nuclei), and 1130 cm^{-1} (C–O–C); NMR($CDCl_3$) δ=3.76 (8H, s, OCH_2CH_2O), 3.85—4.10 (4H, m, OCH_2CH_2O), 4.10—4.30 (4H, m, OCH_2-CH_2O), 6.80—7.90 (9H, m, aromatic H). Found: C, 63.75; H, 5.93; N, 6.22%. Calcd for $C_{24}H_{26}N_2O_2$: C, 63.62; H, 5.94; N, 6.39%.

1b. Phenol and benzo-15-crown-5-4′-diazonium salt were allowed to react by a procedure similar to that for **1a**. Crystals with blackish-green sheen: yield 11%; mp 72—74 °C; IR(KBr) 3480(OH), 1590, 1502 (aromatic nuclei), 1261, and 1120 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=3.76 (8H, s, OCH_2CH_2O), 3.86—4.10 (4H, m, OCH_2CH_2O), 4.10—4.30 (4H, m, OCH_2-CH_2O), 6.82—7.87 (9H, m, aromatic H). Found: C, 54.62; H, 6.87; N, 6.38%. Calcd for $C_{20}H_{24}N_2O_6\cdot 3H_2O$: C, 54.29; H, 6.76; N, 6.31%.

1c. *o-t*-Butylphenol and benzo-15-crown-5-4′-diazonium salt were reacted by a procedure similar to that for **1a**. The crude product was passed through an alumina column with chloroform/ether (1/1, v/v), the main band being collected. The product was recrystallized from ethanol. Orange powder; yield 34%; mp 107—108 °C; IR(KBr) 3440(OH), 1590, 1502 (aromatic nuclei), 1265, and 1125 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=1.36 (9H, s, $C(CH_3)_3$), 3.80 (8H, s, OCH_2-CH_2O), 3.88—4.11 (4H, m, OCH_2CH_2O), 4.11—4.36 (4H, m, OCH_2CH_2O), 6.71—7.98 (6H, m, aromatic). Found: C, 62.15; H, 7.48; N, 5.90%. Calcd for $C_{24}H_{32}N_2O_6\cdot H_2O$: C, 62.33; H, 7.66; N, 6.01%.

1d. The compound was synthesized by reacting benzo-15-crown-5-4′-diazonium salt with *o*-chlorophenol. The product was purified by recrystallization from aqueous acetone. Needles with blackish-green sheen; yield 11%; mp 62—64 °C; IR(KBr) 3480 (OH), 1592, 1502 (aromatic nuclei), 1260, and 1120 cm^{-1} (C–O–C); NMR (acetone-d_6) δ=3.76 (8H, s, OCH_2CH_2O), 3.82—4.07 (4H, m, OCH_2CH_2O), 4.07—4.36 (4H, m, OCH_2CH_2O), 6.98—8.17 (6H, m, aromatic H). Found: C, 54.14; H, 5.31; N, 6.34%. Calcd for $C_{20}H_{23}N_2O_6Cl\cdot H_2O$: C, 54.45; H, 5.23; N, 6.36%.

2a. 4′-Nitrobenzo-18-crown-6[9] (0.50 g, 1.5 mmol) was hydrogenated on Pd/C in ethanol. The reaction mixture after removal of the catalyst was concentrated under reduced pressure, the residue being redissolved in a small amount of methanol. Picryl chloride (0.4 g, 1.7 mmol) and sodium hydrogencarbonate (0.15 g) were added in succession. After being stirred for 30 min, the mixture was acidified by hydrochloric acid and then concentrated to dryness under reduced pressure. The residue was taken into chloroform, washed with water, dried, concentrated, and applied to a silica-gel column. Elution with chloroform/ether (1/1, v/v) gave the main band, from which a dark reddish mass was obtained by concentration. A careful recrystallization (several days) from aqueous acetone or aqueous methanol gave dark-red needles. Yield, 0.52 g, 45%; mp 55—56 °C; IR(KBr) 3300 (NH), 1620 (aromatic nuclei), 1510, 1330 (NO_2), and 1128 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=3.70 (4H, s, OCH_2-CH_2O), 3.76 (8H, s, OCH_2CH_2O), 3.85—4.35 (8H, m, OCH_2CH_2O), 6.35—6.9 (3H, m, aromatic H) and 9.05 (2H, s, aromatic H). Found: C, 48.81; H, 4.91; N, 10.58%. Calcd for $C_{22}H_{26}N_4O_{12}$: C, 49.07; H, 4.87; N, 10.41%.

2b. To a chloroform solution (25 ml) of **2a** (0.85 g) was added dropwise a mixture of 1.5 ml each of glacial acetic acid, chloroform, and fuming nitric acid (*d*, 1.42) at room temperature. The reaction mixture was then washed four times with 20 ml water, and the chloroform solution was evaporated to dryness. The residue was recrystallized from aqueous acetone. Orange crystals; yield, 0.30 g, 32%; mp 160—161 °C; IR (KBr) 1620 (aromatic nuclei), 1520, 1330 (NO_2) and 1130 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ= 3.69 (4H, s, OCH_2CH_2O), 3.73 (8H, s, OCH_2CH_2O), 3.85—4.35 (8H, m, OCH_2CH_2O), 6.38 (1H, s, aromatic H), 7.76 (1H, s, aromatic H), 9.19 (2H, s, aromatic H), 11.76 (1H, s, NH). Found: C, 45.24; H, 4.29; N, 11.80%. Calcd for $C_{22}H_{25}N_5O_{14}$: C, 45.29; H, 4.30; N, 12.00%.

3. *trans*-Dinitrodibenzo-18-crown-6[10,11] (1.0 g, 2.2 mmol) was suspended in acetic acid (10 ml) and hydrogenated over Pd/C catalyst. The catalyst was removed by filtration, and the acetic acid solution was concentrated under reduced pressure to a thick oil, which was redissolved in a small amount of methanol and neutralized with excess sodium hydrogen carbonate (0.85 g). Picryl chloride (1.5 g 6 mmol) was added and stirred at room temperature for a half hour. The reaction mixture was worked up in a similar manner to that for **2**. The compound becomes less soluble in chloroform with increase in purity. Recrystallization from aqueous *N,N*-dimethylformamide gave reddish brown crystalline powder. Yield, 1.2 g, 67%; mp 222—226 °C; IR(KBr) 1620 (aromatic nuclei), and 1130 cm^{-1} (C–O–C); NMR (DMSO-d_6) δ= 3.76, 4.25 (16H, broad, OCH_2CH_2O), 6.67, 6.89 (6H, s, aromatic H), 8.79 (4H, s, aromatic H), 10.21 (2H, s, NH). Found: C, 47.03; H, 3.54; N, 13.33%. Calcd for $C_{32}H_{28}$-$N_8O_{18}\cdot 1/4H_2O$: C, 47.03; H, 3.49; N, 13.72%.

4. 4′-Formylbenzo-15-crown-5[9] (0.50 g, 1.7 mmol), 2,6-dimethylphenol (0.60 g, 4.9 mmol), and *p*-toluenesulfonic acid (0.32 g, 1.7 mmol) were refluxed in 25 ml dioxane for 30 h. After removal of dioxane under reduced pressure, the residue was taken into chloroform and subjected to silica gel column chromatography with an eluting solvent starting from chloroform, chloroform/ether (1/1, v/v), ether to ether/ethanol (1/1, v/v). The main band appeared in ether fraction, giving light yellowish needles by recrystallization from aqueous acetone. The compound was found to be 4′-[bis(3,5-dimethyl-4-hydroxyphenyl)methyl]-benzo-15-crown-5, the precursor compound of **4**, from the analytical data. Yield, 0.37 g, 42%; mp 171—172.5 °C; IR(KBr) 3450 (OH), 1580 (aromatic nuclei), and 1150 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=2.05 (12H, s, CH_3), 3.5—4.1 (16H, m, OCH_2CH_2O), 4.48 (2H, s, OH), 5.05 (1H, –CH–), 6.51 (7H, s, aromatic H). Found: C, 70.61; H, 7.33%. Calcd for $C_{31}H_{38}O_7\cdot 1/4H_2O$: C, 70.65; H, 7.31%. The compound (λ_{max}, 410 nm; ε, 480; $CHCl_3$) is slightly contaminated with **4** due to the air-oxidation during the work-up. One tenth gram (0.19 mmol) of the dye precursor obtained above was dissolved in 10 ml anhydrous methanol, and 43 mg (0.19 mmol) of DDQ (dichlorodicyano-*p*-benzoquinone) was added under stirring. The color of the solution turned red, and red crystalline power precipitated after stirring for 10 min. Yield, 90 mg, 90%; mp 244—245 °C; IR(KBr) 3400 (OH), 1620, 1590 (aromatic nuclei), 1265, and

1140 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=2.15 (12H, s, CH_3), 3.75 (8H, s, OCH_2CH_2O), 3.85—4.05 (4H, m, OCH_2CH_2O), 4.05—4.30 (4H, m, OCH_2CH_2O), 6.65—7.35 (5H, m, aromatic H). Found: C, 70.83; H, 6.97%. Calcd for $C_{31}H_{36}O_7 \cdot 1/4H_2O$: C, 70.92; H, 6.96%.

5a. 3,4-Dihydrocoumarin (0.90 g, 6.1 mmol) and Kryptofix 22 (E. Merck, 7,16-diaza-1,4,10,13-tetraoxacyclooctadecane) (0.30 g, 1.1 mmol) were mixed and heated at 200 °C for 18 h under nitrogen. The excess dihydrocoumarin was then removed under reduced pressure, and the residue recrystallized from ethyl acetate to give white plates. Yield, 0.52 g, 80%; mp 131—131.5 °C; IR (KBr) 3400 (OH), 1620 (amide), 1590 (aromatic nuclei), 1285, and 1120 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=2.65—2.85 (8H, m, CH_2CH_2-CO), 3.15—3.65 (24H, m, OCH_2CH_2O), 6.80—7.25 (8H, m, aromatic H). Found: C, 64.22; H, 7.59; N, 4.91%. Calcd for $C_{30}H_{42}N_2O_8$: C, 64.52; H, 7.64; N, 5.02%.

5b. 6-Nitro-3,4-dihydrocoumarin (0.60 g, 3.0 mmol)[12] and Kryptofix 22 (0.20 g, 0.7 mmol) were mixed and heated at 140 °C for 15 h under nitrogen. After removal of excess 6-nitro-3,4-dihydrocoumarin by vacuum sublimation, the residue was recrystallized from a mixed solvent consisting of *N,N*-dimethylformamide, methanol and water. Yellow powder; Yield, 0.24 g, 48%; mp 124—125 °C; IR(KBr) 3400 (OH), 1620 (amide), 1510, 1345 (NO_2), 1285, and 1120 cm^{-1} (C–O–C); NMR (DMSO-d_6) δ=2.65, 2.85 (8H, m, CH_2CH_2CO), 3.15—3.65 (24H, m, OCH_2CH_2O), 6.85, 7.05 (2H, m, aromatic H), 7.90, 8.10 (4H, m, aromatic H).

5c. **5a** was reacted with 1-naphthalene diazonium salt in the usual manner at pH ≈9 for 1 h. The crude product was treated with a silica gel column with an eluting solvent starting from chloroform and ether to ethyl acetate. The main product appeared in ether fractions, from which brown powder was obtained by recrystallization. Yield, 0.20 g, 43%; mp 88—92 °C; IR(KBr) 3400 (OH), 1620 (amide), 1595 (aromatic nuclei), 1250, and 1130 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=2.65—2.85 (8H, m, CH_2CH_2CO), 3.15—3.65 (24H, m, OCH_2CH_2O), 6.90—8.0 (20H, m, aromatic H). Found: C, 68.99; H, 6.57; N, 9.10%. Calcd for $C_{30}H_{56}N_6O_8 \cdot 1/4H_2O$: C, 68.77; H, 6.48; N, 9.63%.

5d and ***5e***. *p*-Nitroaniline (0.20 g, 1.5 mmol) was diazotized in the usual manner and added to an ice-cooled solution of **5a** (0.20 g, 0.36 mmol) in 1M LiOH (10 ml). The mixture was stirred at pH 8—9 for a half hour and acidified by acetic acid to give brownish powder. The precipitates were collected, washed with water and dried. The crude product (0.30 g) was dissolved in chloroform and chromatographed on a column of silica gel with an eluting solvent chloroform/ethyl acetate (1/1, v/v). The first fraction contained **5d** and the second fraction **5e**. **5d**. Yellowish brown crystalline powder; yield, 0.15 g, 49%; mp 196—203 °C (dec); IR (KBr) 1640 (amide), 1590 (aromatic nuclei), 1520, 1340 (NO_2), 1280, and 1095 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=2.65—2.85 (8H, m, CH_2CH_2CO), 3.15—3.65 (24H, m, OCH_2CH_2O), 6.75—7.15 (6H, aromatic H), 7.65—8.65 (8H, m, aromatic H). Found: C, 57.67; H, 5.50; N, 13.19%. Calcd for $C_{42}H_{48}N_8O_{12} \cdot H_2O$: C, 57.66; H, 5.72; N, 12.81%. ***5e***. Blackish brown powder; yield, 70 mg, 14%; mp 144 °C (dec); IR (KBr) 3400 (OH), 1640 (amide), 1520, 1340 (NO_2), 1280 and 1105 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=2.60—2.90 (4H, m, CH_2Ar), 2.92—3.14 (4H, m, CH_2CO), 3.40—3.76 (24H, m, OCH_2CH_2O), 7.80—8.10 (10H, m, aromatic H), 8.20—8.50 (10H, m, aromatic H). Found: C, 54.56; H, 4.80; N, 15.77%. Calcd for $C_{54}H_{54}N_{14}O_{16} \cdot 2H_2O$: C, 54.45; H, 4.87; N, 16.47%. A contamination from tris(*p*-nitrophenylazo) derivative could not be excluded.

6a. Phenyl salicylate (0.90 g, 6.9 mmol) and Kryptofix 22 (0.30 g, 1.1 mmol) were mixed and heated (melted) under nitrogen at 160 °C for 16 h. The excess phenyl salicylate was hydrolyzed by the addition of water followed by heating (3 h). Salicylic acid and phenol were removed by vacuum sublimation, and the residue was recrystallized from ethyl acetate/ether. White crystalline powder; yield, 0.21 g, 36%; mp 141—142 °C; IR(KBr) 3400 (OH), 1625 (amide), 1595 (aromatic nuclei), 1255, and 1140 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=3.05—3.75 (24H, m, OCH_2CH_2O), 6.65—7.30 (8H, m, aromatic H), 9.55 (2H, s, OH). Found: C, 61.61; H, 6.98; N, 5.32%. Calcd for $C_{26}H_{34}N_2O_8 \cdot 1/4H_2O$: C, 61.60; H, 6.72; N, 5.53%.

6b. Ethyl 5-nitrosalicylate (0.65 g, 3.0 mmol) was allowed to react with Kryptofix 22 (0.20 g, 0.8 mmol) at 140 °C for 15 h under nitrogen. The excess ethyl 5-nitrosalicylate was removed by vacuum sublimation, and the residue was recrystallized from ethanol to given yellowish powder. It was found by analysis that the preparation is contaminated by the mono *N*-salicyloyl-substituted product. Reactions under prolonged reaction time introduced decomposition products. Yield, 0.17 g, 38%; mp 114.5—117 °C; IR (KBr) 3400 (OH), 1620 (amide), 1590 (aromatic nuclei), 1315 (NO_2), and 1120 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=3.20—4.10 (24H, m, OCH_2CH_2O), 6.95 (1H, d, aromatic H), 8.25 (1H, q, aromatic H), 8.81 (1H, d, aromatic H). Found: C, 51.69; H, 6.42; N, 8.15%. Calcd for $C_{26}H_{32}N_4O_{12} \cdot 1/2H_2O$: C, 51.19; H, 5.36; N, 9.31%.

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