

Alkali Metal Ion Sensing in Aqueous Media by a Dibenzo-16-crown-5 Chromoionophore

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Abstract: A new chromoionophore *sym*-(decyl)(2-hydroxy-5-nitrobenzyloxy)-dibenzo-16-crown-5 (**1**) has been synthesized for Na⁺ photometry in aqueous media. Apparent pK_a values of **1** in the presence of 0.10 M LiCl, NaCl, and KCl were measured by spectrophotometry in 50% 1,4-dioxane-50% water (v/v) and compared with the pK_a of 8.68 in the presence of 0.10 M TMACl. A significant pK_a shift to a lower pH was only observed for Na⁺ ($\Delta\text{pH} = 1.31$) due to selective binding of **1** with Na⁺. Based upon this pK_a shift, chromoionophore **1** was found to selectively respond to Na⁺ with a detection limit of 10⁻³ M and no interference from K⁺ up to 0.05 M for detection of 10.0 mM Na⁺ in 50% 1,4-dioxane-50% water (v/v).

Keywords: Crown ether, Chromoionophore, Photometry, Alkali metal ion sensing, Stability constant.

1. Introduction

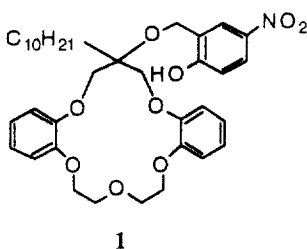
Several chromogenic crown ether dyes (chromoionophores) have been developed for extraction photometry of alkali metal cations in aqueous solution[1]. However this method requires

toxic and volatile organic solvents and an inconvenient phase separation step for the analysis. If alkali metal cation photometry could be performed in homogeneous aqueous media, a wide variety of applications would be possible[2].

Cram and coworkers have demonstrated that

rigid macrocycles such as spherands and hemispherands with three-dimensional preorganization of the metal-binding heteroatoms may exhibit strong binding ability and selectivity toward alkali metal cations in solution[3]. Introduction of a protonic chromophore into the skeleton at a proper site was shown to provide a new class of chromoionophore which responds selectively to desired alkali metal cation species in essentially aqueous solution[4]. However lengthy multistep syntheses are required for the preparation of these highly preorganized chromoionophores.

In contrast, alkali metal cation photometry by synthetically more accessible crown ether chromoionophores in aqueous media has been unsuccessful until now[2]. This was attributed to weak interaction of metal cations with the crown ether binding site in aqueous media. However, it should be noted that most of the crown ether chromoionophores investigated were derived from an azacrown ether skeleton with pendent phenolic chromophore units. In aqueous media, such a chromoionophore will form a zwitterionic structure in which the phenolic proton of the chromophore is dissociated and the amine group in the azacrown moiety is protonated[5]. In such a system, it would be difficult to obtain an effective color change from deprotonation of the phenolic chromophore.



In this study, the new chromoionophore, *sym*-(decyl)(2-hydroxy-5-nitrobenzyloxy)dibenzo-16-crown-5 chromoionophore **1** which is not based upon an azacrown ether moiety site has been

synthesized. Based upon the results of earlier studies, attachment of a decyl group to the same polyether ring carbon that bears the chromophore side arm was anticipated to orient the phenolic group of the chromophore over the crown ether cavity[6]. Such preorganization should enhance selective interaction of the dibenzo-16-crown-5 binding site with Na⁺ over other alkali metal cations in solution[7]. To develop an effective sensing method for alkali metal cations, photometric response of chromoionophore **1** for Na⁺ in homogenous aqueous 1,4-dioxane solution was examined[8].

2. Experimental

Apparatus. UV-Vis spectra were taken with a Shimadzu UV-2100 spectrophotometer. pH measurements were made with an Orion Model 720A pH meter. Titration was made with an APB-410 auto piston buret (Kyoto Electronic Ltd.). To prevent metal contamination, all glassware was soaked in 5% HNO₃ solution for 24 h and rinsed with distilled, deionized water before use.

Reagents. Sources of reagents include Wako Pure Chemical Co. [tetramethylammonium hydroxide (TMAOH, 15 wt%), tetramethylammonium chloride (TMAC)], Dojindo Co. [3-morpholino-propanesulfonic acid (MOPS)], Aldrich Co. [sodium hydroxide (99.9% semiconductor grade)]. Other inorganic and organic compounds were reagent grade and were used as received from commercial suppliers. Reagent grade 1,4-dioxane was purified by distillation from LiAlH₄. Distilled and deionized water was purified with a Milli-Q SP TOC (Nihon Millipore Ltd.). The resistivity value of pure water was more than 17 MΩ cm.

Preparation of *sym*-(decyl)(2-hydroxy-5-nitrobenzyloxy)dibenzo-16-crown-5 (1). To 1.15 g (35% dispersion in mineral oil, 10 mmol) of

potassium hydride under nitrogen was added 1.70 g (3.50 mmol) of *sym*-(hydroxy)(decyl)dibenzo-16-crown-5[9] in 50 mL of THF. After being stirred for 1 h, a solution of 0.89 g (3.85 mmol) of 2-hydroxy-5-nitrobenzyl bromide in 40 mL of THF was added dropwise. The reaction mixture was stirred for 15 h at room temperature. The excess KH was destroyed by careful addition of 10 mL of water. The THF was removed in vacuo and the remaining aqueous solution was extracted with dichloromethane (3x30 mL). The combined organic layers were washed with water (2x30 mL), dried over MgSO_4 and evaporated in vacuo. The residue was chromatographed on alumina with ethyl acetate-hexane (3:1) as eluent to give 0.65 g (29%) of chromoionophore 1 as a yellowish oil. IR (Deposit from CH_2Cl_2 solution on NaCl plate) 3336 (OH), 1588, 1123 (CO) cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 0.90 (t, 3H), 1.30-1.49 (m, 16H), 1.96 (t, 2H), 3.71-4.77 (m, 12H), 5.29 (s, 2H), 6.86-7.03 (m, 9H), 8.09 (d, 2H). Anal. Calcd for $\text{C}_{36}\text{H}_{47}\text{O}_9\text{N}$: C, 67.80%; H, 7.43%; N, 2.20%. Found: C, 67.91%; H, 7.48%; N, 2.19%.

Acidity Constant. The acidity constant of chromoionophore was evaluated spectrophotometrically at 30°C. The 50% 1,4-dioxane-50% water (v/v, 50 mL) contained $5.69 \times 10^{-5}\text{M}$ chromoionophore, $1 \times 10^{-3}\text{M}$ HCl, and 0.10M tetramethylammonium chloride (TMACl) or alkali metal chloride was stirred in 80-mL jacket cell at 30°C under N_2 atmosphere. Titration was made with 7.5wt% TMAOH aqueous solution using APB-410 auto piston buret (0.002-mL scale titration), and then electronic spectrum was measured at each pH. The pH of the aqueous 1,4-dioxane solution was calibrated from Gran's plot[10].

3. Results and Discussion

Spectral change of chromoionophore 1 in 50%

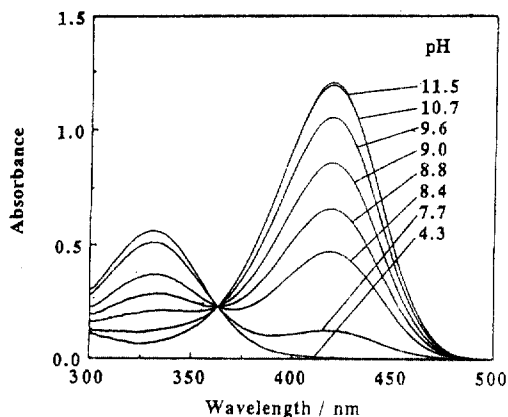


Figure 1. Spectral change of 1 as a function of pH in 50 % 1,4-dioxane-50 % water (v/v). Chromoionophore concn.: $5.69 \times 10^{-5}\text{M}$.

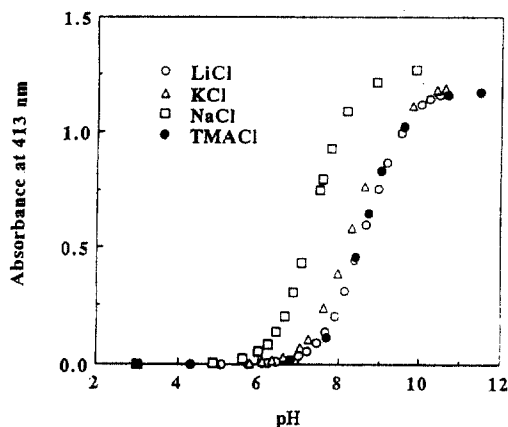
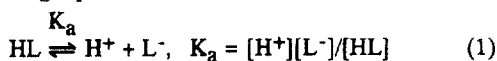


Figure 2. Increase in absorption intensity (413 nm) for 1 as a function of pH in 50 % 1,4-dioxane-50 % water (v/v) in the presence of 0.10 M LiCl (○), NaCl (□), KCl (△), and TMACl (●). Chromoionophore concn.: $5.69 \times 10^{-5}\text{M}$.

1,4-dioxane-50% water (v/v) as a function of pH are recorded in Figure 1. Below pH 6, only absorption of the undissociated species (HL) was observed at 323 nm. Increasing the pH promotes the proton dissociation of the phenolic chromophore and an absorption based on the dissociated species (L^-) appeared at around 413 nm. A good isosbestic point was observed at 358 nm.

Plots of the absorbance at 413 nm vs. pH of the aqueous 1,4-dioxane solution are shown in Figure 2.

The acid dissociation constant (K_a) is defined by the following equation,

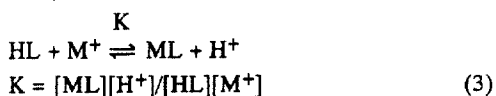


The $\text{p}K_a$ value is numerically equal to the pH at which the molar fraction of L^- is 0.5. It is seen that the apparent $\text{p}K_a$ value ($\text{p}K_a'$) shifts significantly to lower pH in the presence of Na^+ . A small $\text{p}K_a$ shift was also observed for K^+ . This indicates that the increase in absorption intensity at 413 nm due to Na^+ binding can be detected in the pH region of the $\text{p}K_a'$ observed for Na^+ .

The K_a value was determined graphically by the following equation[11],

$$[\text{H}^+]A_{\text{L}^-} = -K_a A_{\text{L}^-} + \epsilon_{\text{L}^-} K_a [(\text{HL})_{\text{t}}] \quad (2)$$

where A_{L^-} and ϵ_{L^-} denote the absorbance and molar absorptivity, respectively, for the proton-dissociated chromoionophore at 413 nm. $[(\text{HL})_{\text{t}}]$ represents the total concentration of the chromoionophore in the aqueous 1,4-dioxane solution. In the presence of a metal cation species (M^+), complex formation between HL and M^+ enhances the proton dissociation as follows,



When A_{ML} and ϵ_{ML} denote the absorbance and molar absorptivity of ML, eq. 3 may be rewritten as,

$$\begin{aligned} [\text{H}^+]A_{\text{ML}} &= -KA_{\text{ML}}[(\text{M}^+)_{\text{t}}] + \epsilon_{\text{ML}}K[(\text{M}^+)_{\text{t}}][(\text{HL})_{\text{t}}] \\ &= -K_a'A_{\text{ML}} + \epsilon_{\text{ML}}K_a'[(\text{HL})_{\text{t}}] \end{aligned} \quad (4)$$

$$K_a' = K[(\text{M}^+)_{\text{t}}] = \frac{[\text{ML}][\text{H}^+]}{[\text{HL}]} \quad (5)$$

where $[(\text{M}^+)_{\text{t}}]$ and K_a' represent total metal concentration and apparent acid dissociation constant in the presence of a large excess of metal cations. Thus the K_a' value can be determined graphically from eq. 4. The stability constant, K_s , for complexation of the metal cation and the chromoionophore is defined by the equation,

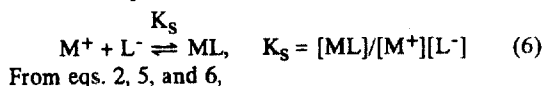


Table I. Spectral Characteristics, Acidity Constants, and Stability Constants of Chromoionophore 1 in 50 % 1,4-Dioxane-50 % Water (v/v).

Salt ^a	λ_{max} , nm (ϵ , $\text{M}^{-1}\text{cm}^{-1}$)		$\text{p}K_a$ ^b	K_s (M^{-1})
	HL	L^-		
TMACl	323 (9500)	416 (20600)	8.68	-
LiCl	323 (9700)	415 (20600)	8.68	$<0.10 \times 10^2$
NaCl	323 (9500)	412 (22300)	7.37	2.00×10^2
KCl	323 (9700)	411 (20700)	8.36	0.21×10^2

^aSalt concn.: 0.10 M. ^b $\text{p}K_a = -\log K_a$.

$$K_s = K_a'/K_a[(\text{M}^+)_{\text{t}}] \quad (7)$$

$$\Delta\text{p}K_a = \log K_a'/K_a = \log K_s[(\text{M}^+)_{\text{t}}] \quad (8)$$

Eqs. 7 and 8 indicate that $\Delta\text{p}K_a$ is a function of $[(\text{M}^+)_{\text{t}}]$ and the K_s value can be determined by the ratio of K_a' and K_a . It is noted from eq. 8 that a K_s value of $>10^3$ (M^{-1}) is theoretically required to obtain spectral change for a 10^{-3} M level of metal cations (M^+) to be detected.

The observed spectral characteristics of 1, $\text{p}K_a$ values, and stability constants (K_s) are recorded in Table I. Selective recognition of Na^+ by 1 is demonstrated by the large $\Delta\text{p}K_a$ value (1.31) observed for Na^+ . Although the chromoionophore 1 formed a rather weak 1:1 complex with Na^+ ($K_s = 2.00 \times 10^2$ M^{-1}), the molar absorptivity was found to increase from 20600 $\text{M}^{-1}\text{cm}^{-1}$ for TMA^+ and Li^+ to 20700 $\text{M}^{-1}\text{cm}^{-1}$ for K^+ and to 22300 $\text{M}^{-1}\text{cm}^{-1}$ for Na^+ . Thus the detection limit for Na^+ predicted from eq. 8 must be enhanced.

To determine the detection limit, the response of 1 to Na^+ at pH 7.3 in 50 % 1,4-dioxane-50 % water (v/v) under various Na^+ concentrations was examined (Figure 3). It is apparent that 10^{-3} M level of Na^+ was effectively detected under the present condition (Figure 3a). The response of 1 to Na^+ was perfectly linear over a 10^{-3} variation in the Na^+ concentration (Figure 3b). For detection of 10.0 mM Na^+ , no interference was observed by the presence of K^+ up to 0.05 M. This photometry was performed in

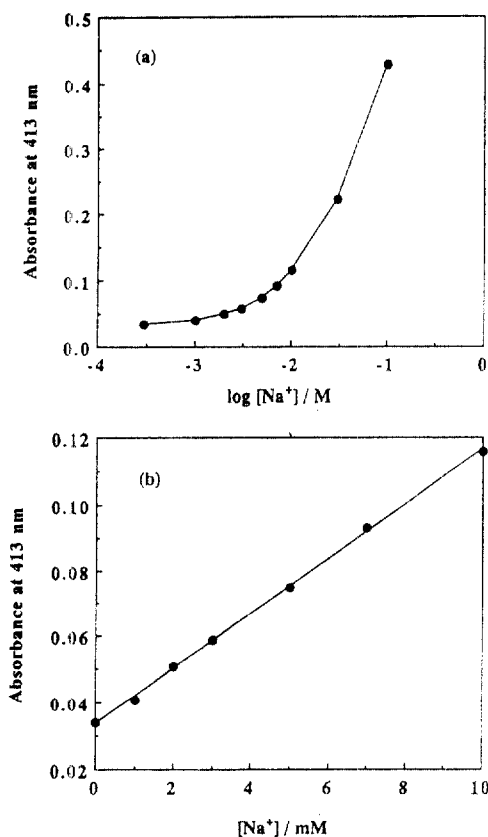


Figure 3. Relationship between the absorbance (413 nm) of **1** and the concentration of sodium ions at pH 7.3 in 50 % 1,4-dioxane-50 % water (v/v). The solution pH was adjusted by MOPS-TMAOH buffer.

homogeneous aqueous 1,4-dioxane solution which eliminates the phase separation step required for extraction photometry. Thus the present system would be suitable for use in an automatic analyzer for the determination of Na⁺ in practical aqueous samples such as blood serum and urine[12].

In conclusion, we have prepared chromoionophore **1** and found that it selectively responds to Na⁺ in the detection limit of 10⁻³ M level in 50 % dioxane-50 % water (v/v). When 80% 1,4-dioxane-20% water (v/v) was used as a medium, the apparent pK_a was found to shift from 10.15 in the presence of 0.1 M TMACl to 7.90 in the presence of 0.1 M NaCl ($\Delta pK_a = 2.25$). Thus it is evident that the

detection limit and the selectivity can be easily enhanced by lowering the dielectric constant of the medium. These results demonstrate that effective photometry of alkali metal cations in aqueous media may be feasible through the proper combination of a crown ether chromoionophore developed for extraction photometry and vesicle or microemulsion systems which can provide a hydrophobic microenvironment in an aqueous media[13] without requiring the use of highly sophisticated chromoionophores.

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