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Synthesis of Novel Photochromic Calix[4]arene Ligand Bearing a Spirobenzopyran and Three Ethyl-Ester Moieties and Photocontrol of Its Alkali Metal Ion Extractability

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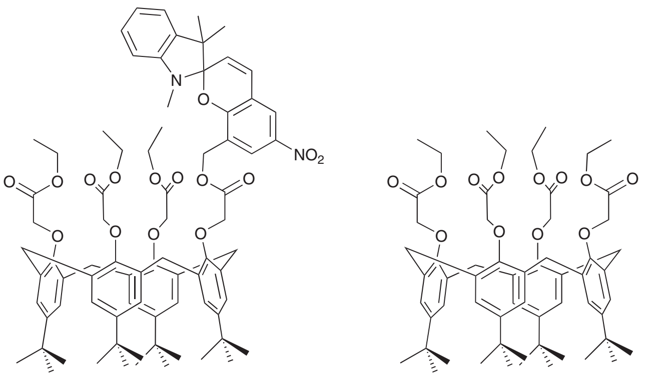
A novel photochromic calix[4]arene ligand bearing a spirobenzopyran and three ethyl-ester moieties (compound **1**) was synthesized, and photocontrol of its alkali metal ion extractability was studied. In the dark, compound **1** showed the largest changes of absorption spectra for Na^+ among alkali metal ions. When Na^+ was gradually added to the solution of compound **1**, its complexation behavior was evaluated by ^{1}H NMR, which suggests that Na^+ was taken into the cavity formed by four carbonyl oxygens and four ether oxygens, and that compound **1** formed a 1:1 complex with Na^+. The proton signals originating from the spirobenzopyran moiety were slightly changed by metal-ion complexation. This means that the spirobenzopyran moiety was not very close to Na^+ under dark conditions. Liquid–liquid extraction experiments with alkali metal ion using compound **1** made it clear that the extractability of Na^+ was enhanced under UV-light irradiation, compared with that under visible-light irradiation. This suggests that the electrostatic interaction between a phenolate anion of the merocyanine moiety generated by UV-light irradiation and Na^+ promotes the extractability to some extent.

Spirobenzopyran is known as a typical photochromic compound, which isomerizes from an electrically-neutral colorless spiropyran (SP) to the corresponding zwitterionic merocyanine (MC) with an absorption spectrum in the visible region by UV-light irradiation and vice versa by visible light irradiation.[1–3] Spirobenzopyran derivatives bearing a crown ether moiety, which we call crowned spirobenzopyrans, have some interesting characteristics, and they have been used as colorimetric reagents for liquid–liquid extraction of metal ions.[4,5] Crowned spirobenzopyrans isomerize from their SP form to the corresponding MC form by metal-ion complexation even in the dark. The metal-ion complexing ability of crowned spirobenzopyrans is drastically increased compared to that of the parent crown ether moiety due to the interaction between the phenolate anion of the MC moiety and the metal ion. Therefore, there has been a lot of interest in the control of the metal-ion complexing ability based on the isomerization of the spirobenzopyran.[5–12]

Calixarene, which is called the third host compound, is a cyclic oligomer formed by the condensation of phenol derivatives, and has a hydrophobic cavity that can accommodate small organic molecules. Moreover, the introduction of substituents into the hydroxy groups of the lower rim is easy. Various functionalized calixarenes have been synthesized, and their applications to metal-ion sensors and extractants have been studied.[13–16] For example, calix[4]arenes bearing two spirobenzopyran moieties have been developed, and it was shown that they are excellent colorimetric probes for lanthanide ions.[17,18] Also, the tetraethyl-ester derivatives of calix[4]arene have a very high Na^+ selectivity among alkali metal ions.[15,19] Nowadays, they are used in commercial applications as Na^+-selective electrodes for the measurement of Na^+ levels in blood. In consideration of these backgrounds, in this study, a novel photochromic calix[4]arene derivative (compound **1**) bearing a spirobenzopyran moiety as the photochemically functional group and three ethyl-ester moieties as the selective complexation moiety with Na^+ was synthesized, and the calix[4]arene derivative (compound **2**)[19] bearing four ethyl-ester moieties was used for comparison (Figure 1). Their alkali metal-ion complexation behaviors and photocontrol of liquid–liquid extraction abilities were examined.



1 **2**

Figure 1. Calix[4]arene derivatives (compounds **1** and **2**) used in this study.

Experimental

Reagents and Chemicals. $Ba(ClO_4)_2 \cdot 3H_2O$ was purchased

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from Kishida Chemical Co., Ltd. (Osaka, Japan). $LiClO_4$, $NaClO_4$, KI, K_2CO_3, *N*,*N*-dimethylformamide (DMF), and acetonitrile were purchased from Sigma-Aldrich Japan Co., Ltd. (Osaka, Japan). Tetramethylammonium hydroxide (TMAOH) (10% in water) was purchased from Tokyo Kasei Kogyo Co., Inc. (Tokyo, Japan). Tetrahydrofuran (THF) was obtained from Wako Pure Chemical Industries (Osaka, Japan). $KClO_4$ was purchased from Katayama Chemical Industries Co., Ltd. (Osaka, Japan). $Mg(ClO_4)_2$ was purchased from Kanto Chemical Co., Inc. (Tokyo, Japan). Metal salts were of analytical grade and used without further purification. All other reagents were of analytical grade and used as received. DMF for organic synthesis was purified by distillation under reduced pressure.

Synthesis of Calix[4]arene Derivative: 5,11,17,23-Tetra-*tert*-butyl-25-{1′,3′,3′-trimethyl-8″-methoxycarbonylmethoxy-6″-nitrospiro([2*H*-1]benzopyran-2′,2″-indoline)}-26,27,28-tris(ethoxycarbonylmethoxy)calix[4]arene (Compound 1). The precursor, which is a calix[4]arene derivative bearing a carboxylic group and three ethyl-ester groups, was synthesized according to previous papers.[19,20] Under N_2 atmosphere, a mixture of the precursor (2.74 g, 2.84 mmol), K_2CO_3 (0.39 g, 2.84 mmol), and KI (0.47 g, 2.84 mmol) in 40 mL DMF was stirred at 90 °C. A solution of 8′-chloromethyl-1,3,3-trimethyl-6′-nitrospiro([2*H*-1]benzopyran-2,2′-indoline) (1.05 g, 2.84 mmol) in 10 mL DMF was added to the mixed solution. The reaction mixture was stirred for 5 h. The reaction solution was cooled to room temperature, and the solvent was removed in vacuo. The residue was purified by gel permeation chromatography using chloroform as an eluent ($R_t = 30$ min). Compound **1** was obtained as a purple powder. Yield: 0.42 g, 32.0%. Mp: 103–104 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15 (1H, d, $J =$ 2.7 Hz, 7″-*H* of benzopyran), 7.98 (1H, d, $J =$ 2.7 Hz, 5″-*H* of benzopyran), 7.14 (1H, t, $J =$ 7.5 Hz, 6′-*H* of indoline), 7.06 (1H, d, $J =$ 14.7 Hz, 4′-*H* of indoline), 6.98 (1H, d, $J =$ 19.5 Hz, 4″-*H* of benzopyran), 6.82 (1H, t, $J =$ 7.5 Hz, 5′-*H* of indoline), 6.79 (4H, s, Ar–*H*), 6.73 (4H, s, Ar–*H*), 6.50 (1H, d, $J =$ 7.5 Hz, 7′-*H* of indoline), 5.88 (1H, d, $J =$ 10.5 Hz, 3″-*H* of benzopyran), 4.96–4.66 (14H, m, 8″-CH_2– of benzopyran, Ar–CH_2–Ar, O–CH_2–COO), 4.21–4.09 (6H, m, –CH_2CH$_3$), 3.19 (2H, d, $J =$ 16.8 Hz, Ar–CH_2–Ar), 3.17 (2H, d, $J =$ 16.4 Hz, Ar–CH_2–Ar), 2.67 (3H, s, 1′-CH_3 of indoline), 1.26–1.14 (15H, m, 3′-CH_3 of indoline, –CH$_2$CH_3), 1.09–1.03 (36H, m, –C(CH_3)$_3$). m/z (ESI): 1322.2 (100% $[M + Na]^+$).

General Procedure for Ultraviolet/Visible Spectrophotometry. The absorption spectra were measured with a V-550 UV/VIS Spectrophotometer (Jasco) at 25 °C and with quartz cells of 1-cm optical path length. Temperature control was carried out using an EHC-477T Temp. Controller (Jasco). The visible and UV lights were irradiated to a quartz cell containing a sample solution through a color filter (VY-49 and UV-D36B, respectively) with a Xe lamp. For the measurement of photoisomerization of compound **1**, the concentration of compound **1** was 2×10^{-5} mol dm^{-3}, and the absorption spectra of sample solution were recorded after UV-light irradiation at different times. To evaluate the metal-ion selectivity of compound **1** under dark conditions, the absorption spectra of acetonitrile solutions including compound **1** were measured in the absence and presence of alkali metal perchlorate. The concentrations of compound **1** and metal ion were 2.0×10^{-5} mol dm^{-3} each. After the sample solutions were prepared, they were allowed to stand for 24 h in the dark. All the experiments were carried out at 25 °C protected from light. The thermal decoloration constants of 2.0×10^{-5} mol dm^{-3} for compound **1** in the absence and presence of equimolar of alkali metal perchlorate were determined in the absence of light after UV-light irradiation for 10 min at 25 °C.

^{1}H NMR Titration of Compound 1 with Na$^+$. ^{1}H NMR titration measurements were performed on a JEOL JNM-ECA 400 FT NMR (400 MHz) at 25 °C. The concentration of compound **1** was fixed at 1.0×10^{-2} mol dm^{-3} in acetone-d_6. The sample solutions containing various concentrations of Na$^+$ (0–1.6×10^{-2} mol dm^{-3}) were measured. Thiocyanate was chosen as a counter anion of Na$^+$. Before the measurements, all the sample solutions were allowed to stand for 48 h at 25 °C in the dark for complete metal-ion complexation.

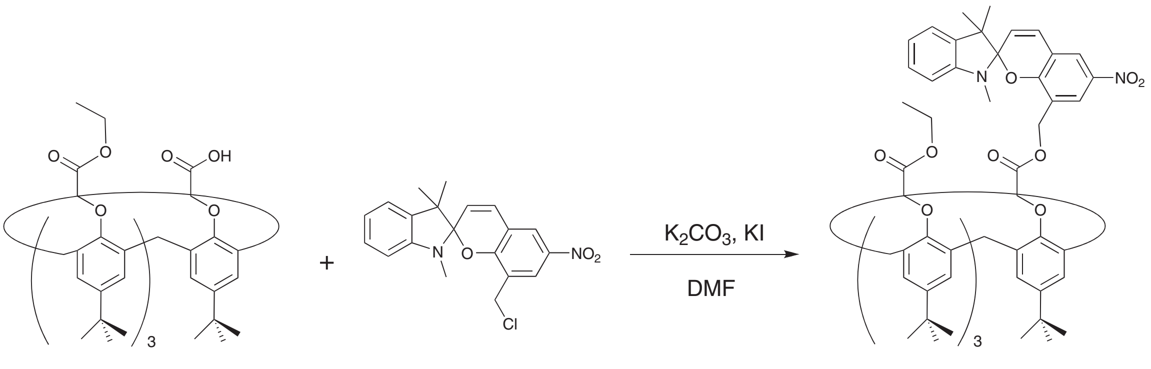
Liquid–Liquid Extraction Study of Alkali Metal Ion. The extractability of calix[4]arene derivatives toward alkali metal ions under different photoirradiation conditions was examined by liquid–liquid extraction (batch system). Compound **2**, which is a calix[4]arene derivative bearing four ethyl-ester groups, was used for comparison. A Tris-HCl buffer solution (pH 9) of 10 mL containing metal chloride (Li$^+$, Na$^+$, and K$^+$, 5.0×10^{-5} mol dm^{-3}) and tetramethylammonium perchlorate (1.0×10^{-2} mol dm^{-3}) for supplying an easily-extractable counter anion, and a 1,2-dichloroethane solution of 10 mL containing compound **1** or **2** (5.0×10^{-5} mol dm^{-3}), were mixed and then shaken for 10 min under UV- or visible-light irradiation. After phase separation, the organic phase was removed. The aqueous solution was then centrifuged at 15000 rpm for 10 min. The aqueous phase was subjected to determination of metal ion concentration by using atomic absorption spectrometry.

Results and Discussion

Synthesis of Compound 1. In this study, the calix[4]arene derivative bearing a spirobenzopyran as photochemically functional moiety and three ethyl-ester groups as metal-ion complexation moiety was synthesized. The precursor, which is a calix[4]arene derivative bearing a carboxylic group and three ethyl-ester groups, was synthesized according to previous papers.[19,20] As shown in Scheme 1, the novel photochromic calix[4]arene derivative was synthesized by the nucleophilic substitution of the precursor with chloromethyl-substituted spirobenzopyran in the presence of K_2CO_3.[21] The target compound **1** was obtained in a yield of 32.0%.

Metal Ion Selectivity of Compound 1. Compound **1** showed very interesting absorption-spectral changes, depending on the kind of metal ions. The plots of absorbance at maximum absorption wavelength (λ_{max}) vs. λ_{max} of the solutions containing ligand and metal ions are shown in Figure 2. As for the absorption-spectral change in the presence of an alkali metal ion, the absorbance attributable to the MC moiety was increased most significantly for Na$^+$. This result corresponds to the fact that the tetraethyl-ester derivatives of calix[4]arene show a high Na$^+$ selectivity.[15,19]

Evaluation of Metal-Ion Complexation Behavior of Compound 1 by ^{1}H NMR Titration. The metal-ion complexation behavior of compound **1** in the presence of Na$^+$ was



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Scheme 1. Synthesis of photochromic calix[4]arene derivative (compound **1**).

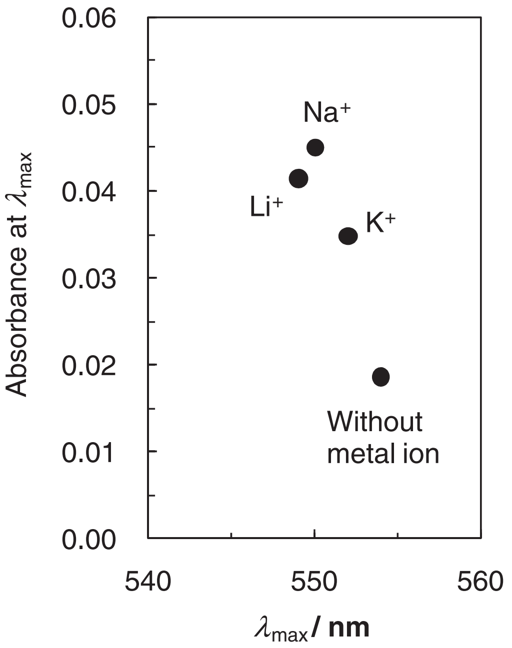

Figure 2. Plots of absorbance at maximum absorption wavelength ($\lambda_{\max}$) vs. $\lambda_{\max}$ of compound **1** in the presence of an alkali metal ion in acetonitrile. The concentrations of ligand and metal perchlorate were 2.0×10^{-5} mol dm^{-3} each.

evaluated by ^{1}H NMR titration experiments in acetone-d_6 at 25 °C in the dark. The ^{1}H NMR spectra are shown in Figure 3. The signals from the calix[4]arene framework were broaden and shifted when sodium thiocyanate was added to the solution containing compound **1**. In the absence of Na$^+$, the proton signals (H$_a$ and H$_e$) at the axial and equatorial positions of the methylene bridge were observed at 3.2 and 4.6–4.9 ppm, respectively. By addition of Na$^+$, the two signals shifted downfield and upfield, respectively. This suggests that the lower rim of the calix[4]arene frame was extended and that the upper rim was narrowed by the complexation with Na$^+$. Moreover, the proton signals originating from phenyl groups (H$_{Ar}$) of calix[4]arene frames and carbonylmethoxy moieties (H$_3$) were drastically changed by addition of Na$^+$. From the chemical shift changes, it became clear that four carbonyl oxygens and four ether oxygens interact strongly with Na$^+$. These spectral changes continued until the Na$^+$ concentration reached 1.0 equivalent of compound **1**, and no more change was observed by addition of more than 1.0 equivalent of Na$^+$. This shows that compound **1** formed a 1:1 complex with Na$^+$. On the other hand, the proton signals originating from the spirobenzopyran moiety were slightly changed by addition of Na$^+$. From the above-mentioned results, it is thought that the isomerization behavior from the SP form to its MC form was hardly induced by complexation with Na$^+$ in the absence of light.

Photochromism of Compound 1. The photochromic calix[4]arene derivative bearing a spirobenzopyran moiety can isomerize by photoirradiation as shown in Figure 4. The photoisomerization behavior of compound **1** was investigated by UV-light irradiation. The absorption spectra were measured using a 2.0×10^{-5} mol dm^{-3} acetonitrile solution of compound **1** after UV-light irradiation of 10, 20, 30, 60, 90, 180, 300, 600, and 900 s. These results are shown in Figure 5a. Figure 5b shows the time-dependent change of the absorbance at 553 nm. Before UV-light irradiation, most of the spirobenzopyran moiety was SP form because the absorbance in the visible region, which originates from the absorption of MC form, was not observed. After UV-light irradiation, the absorption originating from the MC form began to emerge, and increased depending on the UV-light irradiation time. Furthermore, the maximum absorbance in the visible region slightly decreased after UV-light irradiation of longer than 600 s. This may show that the spirobenzopyran moiety begins to be degraded by UV-light irradiation of longer than 600 s. Therefore, the UV-light irradiation time in the following experiments was determined to be 600 s.

Thermal Decoloration of Compound 1 in Acetonitrile. In order to elucidate the thermal stability of colored MC forms of compound **1** in the absence and presence of an alkali metal ion, their thermal decoloration rate constants were determined. The absorbances at $\lambda_{\max}$ in 2.0×10^{-5} mol dm^{-3} acetonitrile solutions of compound **1** in the absence and presence of equimolar metal perchlorate were recorded in the absence of light after UV-light irradiation for 600 s at 25 °C. This result is shown in Figure 6. The thermal decoloration rate constants were calculated using the following expression (Table 1); $\log[(A_t - A_\infty)/(A_0 - A_\infty)] = -kt$. Here, A_0 is the initial absorbance; A_t is the given time; A_∞ is the final absorbance at

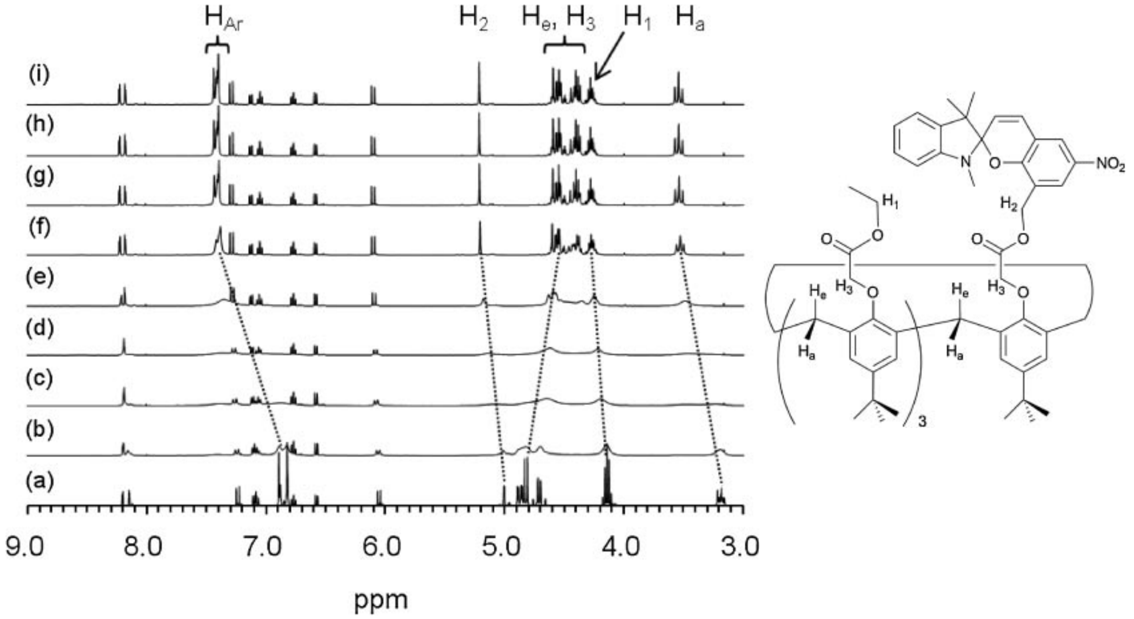

Figure 3. ^{1}H NMR spectral changes of compound **1** on addition of Na^+ (as its thiocyanate salt) in acetone-d_6 at 25 °C. The concentration of compound **1** was fixed at 1.0×10^{-2} mol dm^{-3}. The Na^+ concentrations were 0 (a), 0.2 (b), 0.4 (c), 0.6 (d), 0.8 (e), 1.0 (f), 1.2 (g), 1.4 (h), and 1.6 (i) equivalent to compound **1**.

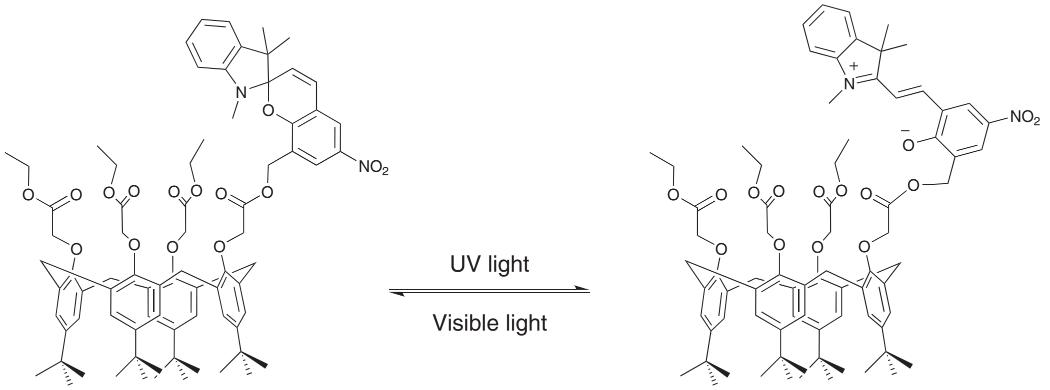

Figure 4. Photochromism of compound **1**.

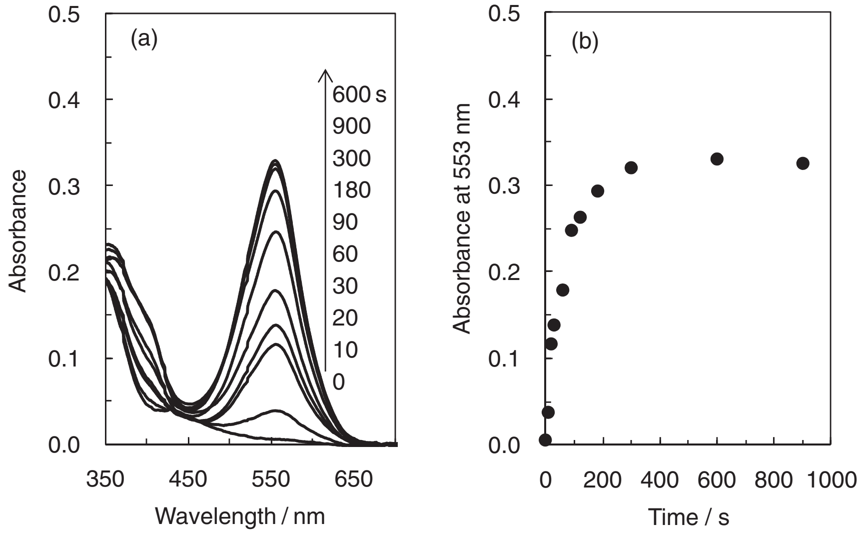

Figure 5. (a) UV–vis absorption spectra of acetonitrile solution containing 2.0×10^{-5} mol dm^{-3} of compound **1** upon UV-light irradiation. The UV-light irradiation time was 10–900 s. (b) Time-dependent change of absorbance at λ_{max}.

$t = \infty$. The k value is the thermal decoloration rate constant, and is calculated from the slope of the straight line obtained from the plot for $\log[(A_t - A_\infty)/(A_0 - A_\infty)]$ vs. time, respectively.[10] The smaller rate constant means that the colored MC form is more stable. The rate constant in the presence of Na^+ was much smaller than that in the absence of an alkali metal ion. This shows that the phenolate anion of the MC form generated by UV-light irradiation contributes to the stabilization of the complex of compound **1** with Na^+. The order of thermal decoloration rate constants among alkali metal ions corresponds to the tendency for the absorbance changes, as shown in Figure 2.

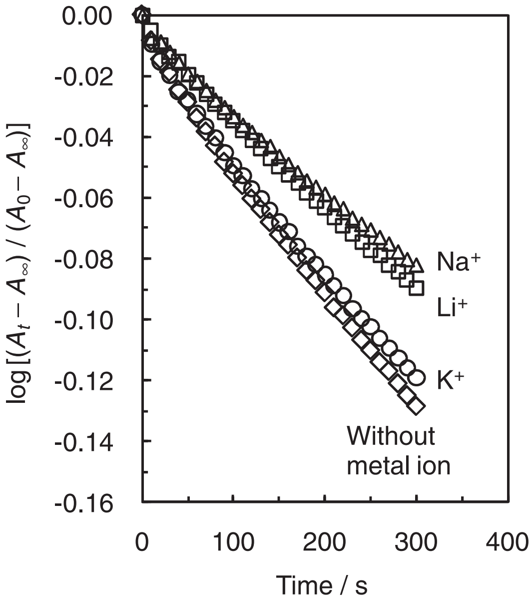

Figure 6. First-order plots of thermal decoloration of compound **1** in the dark after UV-light irradiation for 600 s.

Table 1. Decoloration Rate Constants of Compound **1** in the Absence and Presence of an Alkali Metal Ion

Metal ion	Rate constant/$10^{-4}\,s^{-1}$
Without metal ion	4.50 ± 0.33
Li^+	2.88 ± 0.06
Na^+	2.62 ± 0.06
K^+	3.69 ± 0.06

Photocontrol of Alkali Metal Ion Extractability. Metal-ion extraction experiments using calix[4]arene derivatives as the extractant were carried out by a batch system under different photoirradiation conditions. Compound **2**, which has no spirobenzopyran moiety, was used for comparison of compound **1**. A buffer solution containing excess perchlorate was used as the aqueous phase, and 1,2-dichloroethane was used as the organic phase. The percentages of alkali metal ion extracted from aqueous to organic phases were determined in the manner described above (Figure 7). Here, the extraction percentage of K^+ could not be determined because the extraction amount was too small. In the case of compound **2**, the metal-ion extraction percentages were hardly changed by photoirradiation. This is reasonable because compound **2** has no photoresponsive moiety. On the other hand, in the case of compound **1**, although the extraction percentage of Li^+ was hardly changed by photoirradiation, the extraction percentage (10%) of Na^+ under UV-light irradiation was slightly larger than that (8%) under visible-light irradiation. This suggests that the photoisomerization from the SP form to its MC form induced by UV-light irradiation promotes the extraction of metal ion from the aqueous phase to the organic phase. Therefore, it seems that the phenolate anion of the MC form participates in the complexation of compound **1** with Na^+ to some extent.

Conclusion

In this study, photocontol of metal ion extractability could be realized by the photochromic calix[4]arene to some extent. To attain remarkable photo-induced effects, the spacer structure between the calix[4]arene frame and spirobenzopyran moiety should be optimized so that the spirobenzopyran moiety can

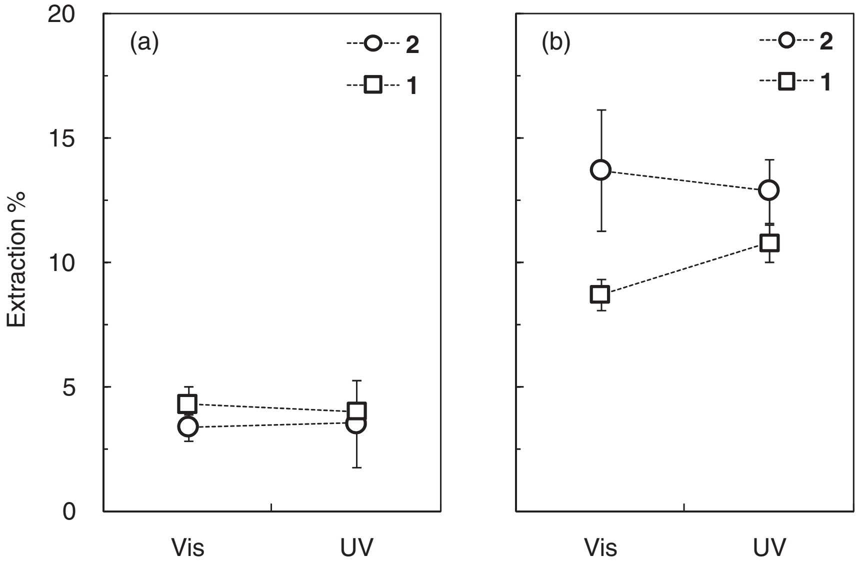

Figure 7. Extraction percentages of Li^+ (a) and Na^+ (b) with compound **1** or **2** under UV- and visible-light irradiation.

participate effectively in the complexation, because NMR studies show that the spirobenzopyran moiety of compound **1** was not close to Na^+. A novel type of photochromic calix[4]arene is being developed in order to obtain a more effective photo-induced effect in our laboratory now.

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