when the photoirradiation is performed with a glass filter plus a visible-cut filter (Toshiba UV-D35) which cuts light >400 nm. As an alkali ion source, we used alkali metal salts of dodecanoic acid for the sake of experimental convenience. Further details of the kinetic method were described previously.[12c] The method of solvent extraction was also described previously.[12c]

Acknowledgment. The authors thank Professors T. Kunitake and M. Takagi (Kyushu University) for helpful discussions. Acknowledgment is also made to Professor T. C. Bruice for encouragement and advice. This research was supported in part by a grant from the Ministry of Education of Japan (No. 56850214).

Registry No. *cis*-**1**(4,4), 80764-64-3; *trans*-**1**(4,4), 80764-65-4; *cis*-**1**-(5,5), 73491-38-0; *trans*-**1**(5,5), 73491-37-9; *cis*-**1**(6,6), 80764-66-5; *trans*-**1**(6,6), 80764-67-6; *cis*-**2**(5,5), 80764-68-7; *trans*-**2**(5,5), 80764-69-8; *cis*-**2**(6,6), 80764-70-1; *trans*-**2**(6,6), 80764-71-2; **6** (*n* = 2), 80764-72-3; **6** (*n* = 3), 80764-73-4; **7** (*n* = 2), 80764-74-5; **7** (*n* = 3), 80764-75-6; Li^+, 17341-24-1; Na^+, 17341-25-2; K^+, 24203-36-9; Kb^+, 22537-38-8; Cs^+, 18459-37-5.

Photoresponsive Crown Ethers. 5. Light-Driven Ion Transport by Crown Ethers with a Photoresponsive Anionic Cap

Seiji Shinkai,* Takahide Minami, Yumiko Kusano, and Osamu Manabe*

Contribution from the Department of Industrial Chemistry, Faculty of Engineering, Nagasaki University, Nagasaki 852, Japan. *Received August 13, 1981*

Abstract: Three photoresponsive ionophores (Cr-*o*, Cr-*m*, and Cr-*p*) in which benzo-18-crown-6 and a phenol group are linked with a photoisomerizable azo linkage were synthesized. On the irradiation of UV light, the azo linkage isomerized to the cis forms (46–73%) in which the crown ring wears an anionic phenoxide cap. The cis forms isomerized back to the trans forms slowly in the dark and rapidly by the irradiation of visible light. In solvent extraction, the extractability of alkali and alkaline earth metal cations with Cr-*o*, Cr-*m*, and Cr-*p*, which have the cap of 2-hydroxy-5-nitrophenyl, 3-hydroxyphenyl, and 4-hydroxyphenyl, respectively, was in most cases enhanced by UV light irradiation. In particular, cis-formed Cr-*o* exhibited markedly improved extractabilities for Na^+ and Ca^{2+}. The result suggests that the enhanced extractability is due to the formation of an intramolecular sandwich-type complex like $PhO^-\cdots M^{+(+)}\cdots$crown. In ion transport across a liquid membrane (90 vol % *o*-dichlorobenzene + 10 vol % *n*-butyl alcohol) in a U-tube, the rates of Na^+ and Ca^{2+} transport were enhanced by 4.0- and 276-fold, respectively, by adding 0.01 N HCl into the second OUT aqueous phase. The rates were further enhanced by irradiating the liquid membrane phase by UV light (1.7- and 2.8-fold, respectively), and the rate of Ca^{2+} transport was greater than that of Na^+ transport in spite of the lower concentration in the first IN aqueous phase ($[Na^+] = 0.10$ M, $[Ca^{2+}] = 0.0225$ M). The finding implies that transport of the Ca^{2+} ion is efficiently mediated with an anionic, photoresponsive ionophore Cr-*o* under a countercurrent of proton flux and UV light irradiation. This is the first example of the light-driven Ca^{2+} transport across a liquid membrane.

A substantial part of the ion transport phenomena across cell and organelle membranes is well mimicked by a liquid membrane which is an organic liquid phase separating two other aqueous phases with which it is immiscible. Cations are transported from one water phase (IN aqueous phase) to the other water phase (OUT aqueous phase) through membranes with the aid of synthetic macrocyclic polyethers such as crown ethers as well as with the aid of naturally occurring antibiotic macrocycles.[1-7] In contrast to numerous studies on the transport of alkali metal cations, the study on the transport of alkaline earth metal cations has been very limited[1-3] and the transport rate mediated by simple crown ethers is usually much slower than that of alkali metal cations.[2,3] In a biochemical field, the more often employed ionophores for alkaline earth metal cations are the polyether antibiotics which represent the class of monobasic, carrier-type ionophores.[1,8] Similarly, crown ethers which have within a molecule a carboxylate anionic cap can extract and transport alkaline earth metal cations efficiently.[1,9-11] These results imply that an ionophore which has a crown ring and an anionic cap in a suitable geometrical position would act as an efficient carrier for alkaline earth metal cations.

This work aims at developing a new class of ionophores which have within a molecule both a crown ring and a photoresponsive anionic cap and carry alkaline earth metal cations in response to photoirradiation. We previously designed a photoresponsive crown ether which combines monobenzo-15-crown-5 and a carboxylate function through a photoisomerizable azo linkage, expecting that the photoisomerized cis form would bind alkaline earth metal cations in a cavity between the crown and the carboxylate group.[12] However, the extractability of this ionophore was rather inferior owing to its relatively low lipophilicity. Here, we newly synthesized three ionophores, Cr-*m*, Cr-*p*, and Cr-*o*, with a phenoxide anion cap. To strengthen the lipophilicity, we chose a phenoxide function instead of a carboxylate function and introduced an *n*-butyl group. A 5-nitro group in Cr-*o* was introduced to lower the pK_a of the phenol group so that Cr-*o* may extract the Ca^{2+} ion at almost

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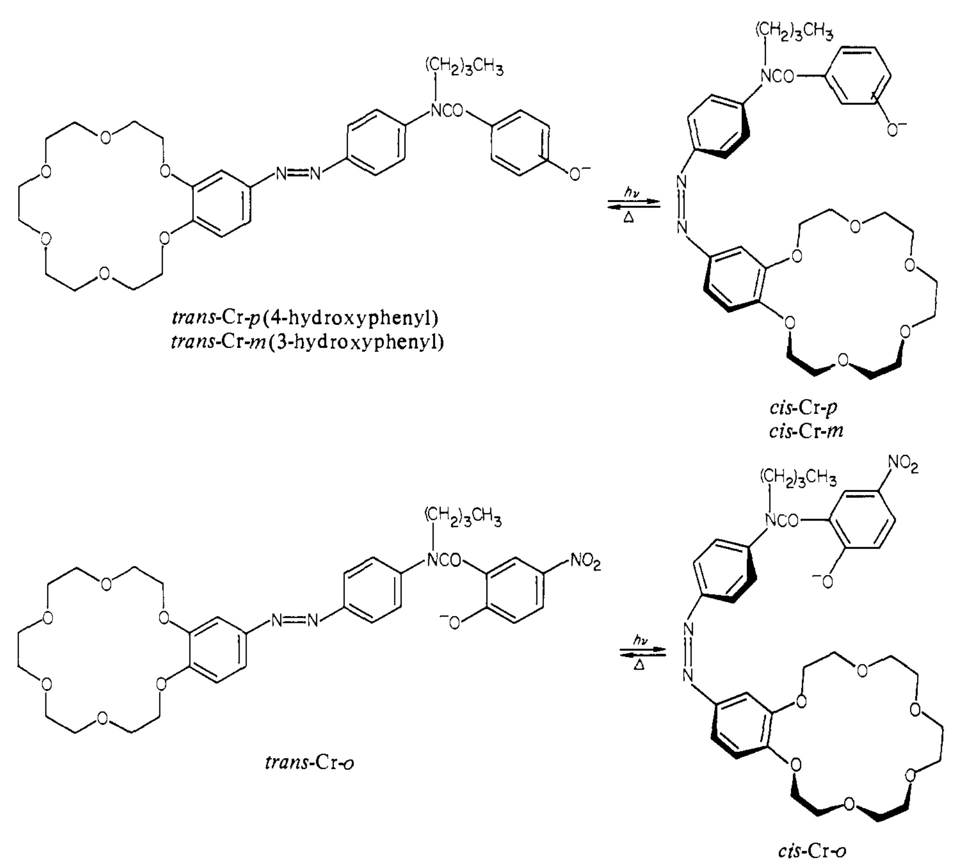
Scheme I



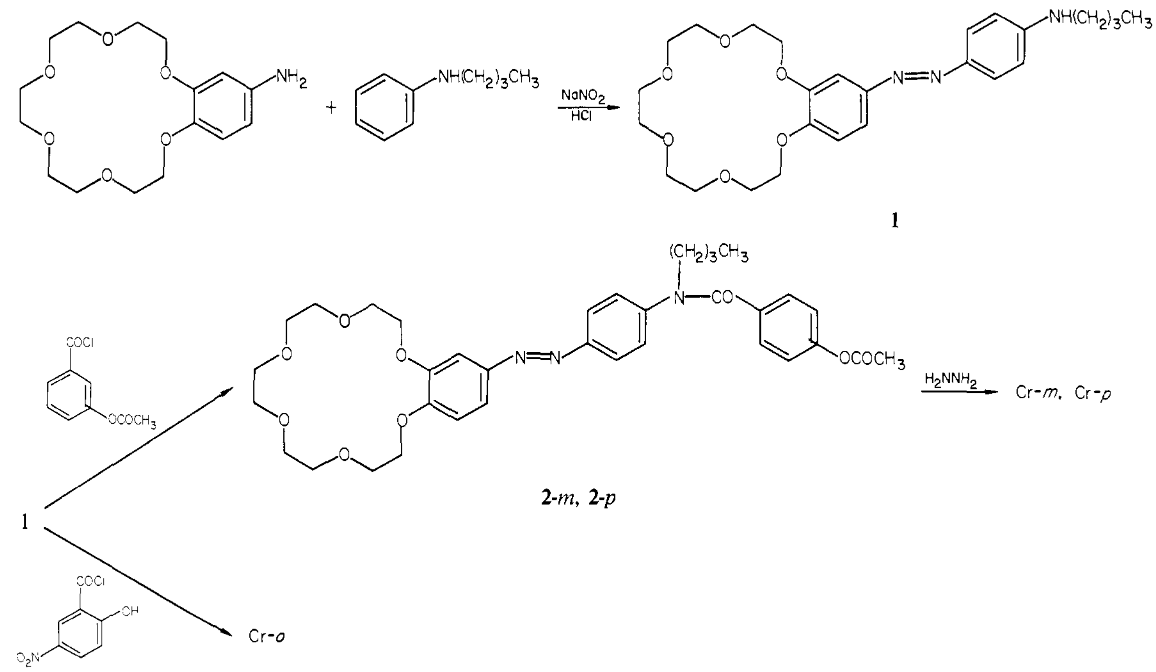
trans-Cr-*p*(4-hydroxyphenyl)
trans-Cr-*m*(3-hydroxyphenyl)

cis-Cr-*p*
cis-Cr-*m*

trans-Cr-*o*

cis-Cr-*o*

Scheme II



1

2-*m*, **2**-*p*

1

neutral pH. We found that under UV light irradiation, Cr-*o* efficiently carries the Ca^{2+} ion across a liquid membrane with the aid of a countercurrent of proton flux.

Experimental Section

Materials. Cr-*m*, Cr-*p*, and Cr-*o* were synthesized according to a following reaction scheme via a key intermediate **1**.

4′-Aminobenzo-18-crown-6 was prepared by catalytic hydrogenation of 4′-nitrobenzo-18-crown-6 on Pd–C and used without further purification. 4′-Aminobenzo-18-crown-6 (9.17 g, 0.028 mol) was dissolved in 14 mL of a 7.5 N HCl solution in an ice bath, and 2.0 g (0.029 mol) of sodium nitrite were added in small portions to the stirred solution. It was corroborated by potassium iodide starch paper that sodium nitrite was in excess over 4′-aminobenzo-18-crown-6, and the excess amount was treated with sulfamic acid. Then, 25 g (0.167 mol) of *N*-*n*-butylaniline were added, and the reaction mixture was kept at room temperature for 1 day. The completion of the reaction was confirmed by the fact that the reaction mixture is not colored on the addition of H acid. The purple precipitate was recovered by adding sodium chloride to the solution. The crystal was dissolved in water, the mixt. was neutralized by sodium acetate, and the precipitated yellow solid (**1**) was collected by suction. Since we could not purify **1** by recrystallization, we used preparative TLC for the isolation (silica gel, 1:10 ethanol–chloroform): mp 93–97 °C; yield 9.9%; IR (KBr disk) ν_{NH} 3400, ν_{C-O-C} 1120–1150, $\nu_{N=N}$ 1500 cm^{-1}; mass spectrum, *m/e* 487 (M$^+$); NMR ($CDCl_3$) δ 0.95 (3 H, t, CH_3), 1.55 (6 H, m, CH_2 in the butyl group), 3.90 (20 H, m, CH_2 in the crown ring), 6.60, 6.90, 7.46, and 7.78 (7 H, aromatic ring protons). Anal. ($C_{26}H_{37}N_3O_6$) C, H, N.

Cr-*m* was prepared from **1** and *m*-acetoxybenzoyl chloride[13] via its ester derivative (**2**-*m*). One gram (2.05 mmol) of **1** and 0.40 g (3.95 mmol) of triethylamine were dissolved in 30 mL of anhydrous tetrahydrofuran, and *m*-acetoxybenzoyl chloride (0.80 g: 4.30 mmol) was added dropwise to the vigorously stirred solution at room temperature. After 3 h, precipitated triethylamine hydrochloride was removed by suction, the filtrate being concentrated in vacuo. The oily product (**2**-*m*) was dissolved in 60 mL of methanol and treated with 1.3 mL of hydrazine hydrate for 30 min at room temperature to remove the ester group. The methanol solution was poured into 200 mL of water. The solution was adjusted to pH 3 with dilute HCl and extracted with chloroform. The chloroform layer was concentrated to dryness in vacuo. The oily residue (Cr-*m*) was subjected to preparative TLC for the isolation (silica gel, 1:10 ethanol–chloroform): mp 150–152 °C; yield 32%; IR (KBr disk) ν_{OH} 3500, $\nu_{C=O}$ 1650, $\nu_{N=N}$ 1500, ν_{C-O-C} 1120–1150 cm^{-1}; mass spectrum, *m/e* 607 (M$^+$). Anal. ($C_{33}H_{41}N_3O_8$) C, H, N.

Similarly, Cr-*p* was prepared from **1** and *p*-acetoxybenzoyl chloride[14] via its ester derivative (**2**-*p*): mp 120–123 °C; yield 77%; IR (KBr disk), ν_{OH} 3500, $\nu_{C=O}$ 1640, $\nu_{N=N}$ 1500, ν_{C-O-C} 1120–1150 cm^{-1}; mass spectrum, *m/e* 607 (M$^+$). Anal. ($C_{33}H_{41}N_3O_8$) C, H, N.

Cr-*o* was prepared from **1** and 5-nitrosalicyloyl chloride.[15] Sodium bicarbonate (0.52 g, 6.15 mmol) was suspended in 30 mL of anhydrous tetrahydrofuran containing 2.0 g (2.1 mmol) of **1**, and 10 mL of an anhydrous tetrahydrofuran solution of 5-nitrosalicyloyl chloride (1.24 g; 6.15 mmol) was added dropwise to the stirred solution at room temperature. The progress of the reaction was followed by TLC method (silica gel, 1:10 ethanol–benzene). The reaction mixture was poured into 250 mL of water. The aqueous solution was adjusted to pH 1 with concentrated HCl and extracted with chloroform. The chloroform layer was washed with an aqueous solution of sodium acetate and then evaporated in vacuo to dryness. The oily residue was taken in benzene and the solution was poured into diethyl ether. The precipitate (mp 65–70 °C) was subjected to elemental analysis, but the result was not satisfactory. Thus, we again used the preparative TLC (silica gel, 1:10 ethanol–benzene) to isolate Cr-*o*: mp 75–78 °C; yield 17%; IR (KBr disk) ν_{OH} 3400–3600, $\nu_{C=O}$ 1650, ν_{NO_2} 1510, 1350, ν_{C-O-C} 1110 cm^{-1}; mass spectrum, *m/e* 652 (M$^+$). Anal. ($C_{33}H_{40}N_4O_{10}$) C, H, N.

Method of Solvent Extraction, Kinetic Measurements, and Ion Transport across a Liquid Membrane. The method of solvent extraction was described previously.[16,17] The details of the workup conditions are recorded in footnotes for Tables III and IV. A 500-W high-pressure Hg lamp with a 400-nm longer wavelength cutoff filter (Toshiba UV-D35) was used for the trans-to-cis photoisomerization, and the distance from the lamp to the sample was 8.0 cm. Since the thermal recovery of the trans forms in the dark was relatively slow ($t_{1/2}$ = 184–277 min at 30 °C) and the workup time of the solvent extraction was shorter than 5 min, the change in the cis/trans composition during the workup time was neglected.

The method of kinetic measurements was also described previously.[16,17] To enhance the reproducibility, we isolated alkali metal salts of three ionophores. A cuvette containing the salt of a trans isomer (5.0 × 10^{-5} M) was irradiated with UV light (500-W high-pressure Hg lamp with a 400-nm longer wavelength cutoff filter). The cuvette was transferred to a thermostated cell holder in a spectrophotometer (Hitachi 200), and the increase in the absorption band of the trans isomer (Table I) was monitored as a function of time.

The method of ion transport was explained in detail.[17] We used a U-tube which contained 100 mL of organic liquid membrane (90 vol % *o*-dichlorobenzene + 10 vol % *n*-butyl alcohol) and IN and OUT aqueous solutions (25 mL each). The U-tube was immersed in a water bath thermostated at 30 °C and the liquid membrane phase was stirred gently (180 rpm). The distance from the Hg lamp with a 400-nm longer wavelength cutoff filter (also immersed in the water bath) to the U-tube was 8.0 cm. Further details were recorded in footnotes for Table V. In order to find a light wavelength which accelerates the cis-to-trans photoisomerization of Cr-*o*, we inspected several color glass filters. The best filter was Toshiba Y-46 (460-nm longer wavelength cutoff filter). *cis*-Cr-*o* was isomerized quantitatively to *trans*-Cr-*o* within 10 min by the irradiation of a 500-W Hg lamp with this filter.

Table I. Properties of Photoresponsive Crown Ethers

crown ether	λ_{max},[a] nm	ϵ_{max},[a]	pK_a of the hydroxyl group[b]	cis/trans at the photostationary state[a]
trans-Cr-*m*	377	19800	9.57	73/27
trans-Cr-*p*	378	19200	9.06	72/28
trans-Cr-*o*	379	26300	6.33	46/54

[a] *o*-Dichlorobenzene at 30 °C. [b] Aqueous solution at 30 °C. The pK_a values were determined by photometric titration at 384 nm for *trans*-Cr-*o*, 290 nm for *trans*-Cr-*m*, and 296 nm for *trans*-Cr-*p*.

Table II. Influence of Alkali Metal Cations on the Rate of Thermal Cis-to-Trans Isomerization[a]

	$k \times 10^3$, min^{-1}		
metal cation	Cr-*m*	Cr-*p*	Cr-*o*
none (nondissociated form)	3.76	2.50	3.73
Na$^+$	2.50	2.05	2.82
K$^+$	2.62	1.92	3.04
Rb$^+$	2.73	2.30	3.99
Cs$^+$	2.80	2.58	3.92

[a] 30 °C, *o*-dichlorobenzene:*n*-butyl alcohol = 86.8:13.2 by volume. The relative experimental errors for the rate constants were less than 5%.

Results and Discussion

Photoisomerization and Thermal Isomerization of Ionophores. The *o*-dichlorobenzene solutions of three ionophores were photoirradiated with a 500-W high-pressure Hg lamp through a 400-nm longer wavelength cutoff filter. The photostationary state was attained within 2 min for Cr-*m* and Cr-*p* and 6 min for Cr-*o*. The cis/trans ratio at the photostationary state was calculated from the absorbance of each $\pi-\pi^*$ band (377–379 nm) assuming that the absorbance of the cis-isomer at this wavelength is negligible in comparison to that of the trans isomer. The result is recorded in Table I, together with other physicochemical properties. The cis % of Cr-*o*, which required longer photoirradiation time to reach the photostationary state, was lower that that of the other two ionophores.

Previously, we synthesized a series of bis(crown ether)s with an azo linkage.[17,18] In these photoresponsive bis(crown ether)s, the cis % under the photostationary state was markedly enhanced and the rate of the thermal cis-to-trans isomerization was suppressed by relatively large alkali metal cations. The results were consistently rationalized in terms of the "tying" of two crown ethers by sandwiched one alkali metal cations. A similar effect may be expected for the complexes of the cis forms of the ionophores with a phenoxide cap if a bound metal cation interacts strongly with both the crown ring and the phenoxide anion. To test the possibility, alkali phenoxide salts of three ionophores were isolated and photoisomerized to the cis isomers in an *o*-dichlorobenzene–*n*-butyl alcohol mixed solvent (86.8:13.2 by volume). The rate of the thermal cis-to-trans isomerization was determined by monitoring the appearance of the absorbance of the trans isomers periodically. It is seen from Table II that the first-order rate constants for the alkali phenoxide salts are scarcely different from those of the corresponding nondissociated forms, although the rate constants for Na$^+$ and K$^+$ are somewhat smaller than those for Rb$^+$ and Cs$^+$. Similarly, the cis % under the photostationary state was almost constant (within 6% relative

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(13) 3-Acetoxybenzoic acid was treated with thionyl chloride: bp 130–131 (°C 10 mmHg).

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(15) 5-Nitrosalicylic acid was treated with thionyl chloride and the reaction mixture was concentrated in vacuo. The residue was used without further purification.

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Table III. Extraction of Alkali Metal Cations with Cr-*m* and Cr-*p* (30 °C)[a]

	Ex: crown (%) remaining in organic phase					
	Cr-*m*			Cr-*p*		
M^+	Ex_{trans}	Ex_{photo}	Ex_{cis}[c]	Ex_{trans}	Ex_{photo}	Ex_{cis}[d]
none[b]	94.8			88.9		
Na^+	76.2	50.1	40.4	53.6	72.0	79.0
K^+	80.6	82.2	82.8	66.2	86.7	94.5
K^+[b]	3.0	6.6	7.9	2.4	4.0	4.6
Rb^+	82.1	83.2	83.6	85.6	95.0	98.6
Cs^+	87.6	79.8	76.9	81.9	90.3	93.5

[a] Organic phase (90 vol % *o*-dichlorobenzene + 10 vol % *n*-butyl alcohol), [Cr-*m*] = [Cr-*p*] = 3.00×10^{-4} M. Aqueous phase, [MOH] = 0.50 M. [b] Organic phase (100% *o*-dichlorobenzene). [c] Calculated by the equation $Ex_{cis} = (Ex_{photo} - 0.27Ex_{trans})/0.73$. [d] Calculated by the equation $Ex_{cis} = (Ex_{photo} - 0.28Ex_{trans})/0.72$.

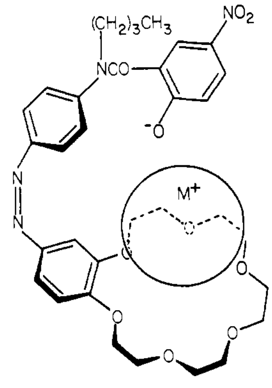
Table IV. Extraction of Alkali and Alkaline Earth Metal Cations with Cr-*o* (30 °C)[a]

	Ex: partition (%) to *o*-dichlorobenzene phase of					
	Cr-*o*			DCPI[d]		
M^+	Ex_{trans}	Ex_{photo}	Ex_{cis}[c]	Ex_{trans}	Ex_{photo}	Ex_{cis}[c]
none[b]	81.9					
Na^+[b]	3.6	17.0	32.7			
K^+[b]	85.6	92.8	~100			
Rb^+[b]	74.4	94.0	~100			
Cs^+[b]	75.1	93.3	~100			
Ca^{2+}	95.7	96.3	97.0	11.6	44.4	82.9
Sr^{2+}	90.7	69.7	45.0	4.5	5.6	6.9
Ba^{2+}	95.0	85.3	73.9	2.0	7.4	13.7

[a] Organic phase (90 vol % *o*-dichlorobenzene + 10 vol % *n*-butyl alcohol), [Cr-*o*] = 3.00×10^{-4} M; aqueous phase, [MOH] = 0.50 M or $[M(OH)_2] + [MCl_2] = 1.00 \times 10^{-2}$ M. [b] Organic phase (100% *o*-dichlorobenzene). [c] Calculated by the equation $Ex_{cis} = (Ex_{photo} - 0.54Ex_{trans})/0.46$. [d] [DCPI] = 1.00×10^{-4} M added in aqueous phase.

experimental error). These results suggest that the interaction $PhO^-\cdots M^+\cdots$crown is not so strong as that of crown$\cdots M^+\cdots$crown which suppresses the thermal cis-to-trans isomerization of azo linkage by factors of 10–10^2 fold.[17,18]

Solvent Extraction of Alkali and Alkaline Earth Metal Cations. As a preliminary step to ion transport, we estimated the binding ability of three ionophores by solvent extraction of alkali and alkaline earth metal cations. In the extraction with the trans isomers, alkali metal ions are extracted simply as countercations of the phenoxide ion. On the other hand, one may expect an intramolecular, sandwich-type extraction species for the cis isomers provided that the size of alkali metal cations exactly fits the cavity constructed by the crown ring and the phenoxide cap. The examination of the CPK model reveals that the formation of such sandwich-type complexes is possible in *cis*-Cr-*m* and *cis*-Cr-*o* but not in *cis*-Cr-*p*, because in *cis*-Cr-*m* and *cis*-Cr-*o* the phenoxide cap exists exactly on the top of the crown ring, while that of *cis*-Cr-*p* is located in a parallel direction to the crown ether plane.



sandwich-type complex with *cis*-Cr-*o*

Extractability (Ex) of alkali metal cations was estimated by measuring a partitioning ratio of the ionophores between 0.5 M MOH aqueous solution and *o*-dichlorobenzene (in some cases, containing 10 vol % *n*-butyl alcohol). The results are summarized in Tables III and IV. In the extraction with *trans*-Cr-*m* and *trans*-Cr-*p* (Table III) Ex increases with increasing ion radius (except for Cs^+ with *trans*-Cr-*p*), and the orders differ from the stability orders of these ions with 18-crown-6.[2,3] The result suggests that alkali metal ions are extracted as a counterion of the phenoxide group and the crown ether plays almost no significant role. On the other hand, the extraction with *cis*-Cr-*m* and *cis*-Cr-*p* gives a maximum selectivity for Rb^+. *trans*-Cr-*o* extracted K^+ most efficiently, and Ex for alkali metal cations increases under UV light irradiation. The most distinct improvement by UV light irradiation is observed for the extraction of Na^+ with *cis*-Cr-*o* (3.6% → 32.7%). These findings indicate that the extraction species under photoirradiation is a sandwich-type 1:2 cation/crown complex.[17,18] The complicated extraction data suggest, however, that several species, in addition to a sandwich-type complex, contribute to the solvent extraction.

The estimation of Ex for alkaline earth metal ions is complicated.[9] The measurement of the metal concentration in the organic phase by an atomic absorption spectrophotometer lacked in reproducibility. We thus added alkaline earth metal salts of DCPI (2,4-dichlorophenolindophenol) to the aqueous phase. Since the absorption maximum (606 nm) does not overlap with that of Cr-*o*, the partitioning coefficients of Cr-*o* and DCPI were determined independently. When the aqueous solution of DCPI salts (1.00×10^{-4} M) was agitated with an equal volume of *o*-dichlorobenzene (containing 10 vol % *n*-butyl alcohol), the DCPI salts were not transferred to the organic phase at all. When agitated with the organic solution containing 3.00×10^{-4} M Cr-*o*, appreciable amounts of DCPI salts were transferred to the organic phase and the most of the Cr-*o* remained in the organic phase (Table IV). The Ex of the DCPI was again improved by UV light irradiation. In particular, the Ex of the Ca^{2+} salt of DCPI increased from 11.6% (in the dark) to 82.9% (UV light). Hence, the results of preliminary solvent extraction reveal that the most distinct improvement by photoirradiation is seen for Na^+ and Ca^{2+}. We thus carried out transport of these metal cations across a liquid membrane.

Ion Transport across a Liquid Membrane. It has been shown that various kinds of chemical and physical phenomena are uti-

Table V. Rate of Ion Transport across a Liquid (90 vol % *o*-Dichlorobenzene + 10 vol % *n*-Butyl Alcohol) Membrane with Cr-*o* (30 °C)[a]

metal cation	aqueous phase		rate, μmol h^{-1}		
	IN	OUT	dark	UV light[b]	UV + visible light[c]
Na^+	[NaOH] = 0.10 M	water	2.3	4.2	
Na^+	[NaOH] = 0.10 M	0.01 N HCl	9.3	16.1	
K^+	[KOH] = 0.10 M	0.01 N HCl	10.6	12.2	
Ca^{2+}	[Ca^{2+}] = 0.0125 M at pH 11.0	water	0.025	0.35	
Ca^{2+}	[Ca^{2+}] = 0.0225 M at pH 11.0	0.01 N HCl	6.9	19.0	17.3

[a] IN aqueous phase contains 5.0 mM picrate. The membrane phase contains 0.30 mM Cr-*o*. [b] The membrane phase was photoirradiated for 5 min at intervals of 2 h. [c] The membrane phase was photoirradiated alternatively by UV and visible light: 5 min (UV) → 55 min (dark) → 20 min (visible) → 40 min (dark) → repeated.

lizable to increase the rate of ion transport through membranes: redox energies,[19,20] countercurrent of different metal cations,[5] pH difference,[6,21,22] remote control by heavy metals,[23] etc. Here, we wish to add a new class of ion transport acceleration by both light energy and countercurrent of proton flux. In a U-tube transport apparatus, the IN aqueous phase contains metal cation and picrate (5.0 mM) and the OUT aqueous phase is either water or 0.01 N HCl aqueous solution. The liquid membrane phase (90 vol % *o*-dichlorobenzene + 10 vol % *n*-butyl alcohol) contains Cr-*o* (0.30 mM). These three phases were set up in the U-tube immersed in a thermostated water bath (30 °C), and the increase in the metal concentration in the OUT aqueous phase was followed by using an atomic absorption spectrophotometer. The rates of the ion transport are summarized in Table V.

When the OUT aqueous phase was water, Na^+ ion was transported by Cr-*o* relatively efficiently (2.3 μmol h^{-1}) whereas Ca^{2+} ion was scarcely transported (0.025 μmol h^{-1}). The trend is in line with the rate of ion transport mediated by crown ethers.[2,3] In the Ca^{2+} transport, it was verified that the concentration of picrate (or DCPI used instead of picrate) in the membrane phase increased rapidly with time but the concentration of the Ca^{2+} ion in the OUT aqueous phase did not increase apperiably. The result indicates that the Ca^{2+} release to the OUT aqueous phase (water) is difficult and becomes a rate-determining step in the Ca^{2+} transport system.

When the OUT aqueous phase was substituted with 0.01 N HCl aqueous solution, the rates of Na^+ and Ca^{2+} were enhanced by 4.0-fold and 276-fold, respectively. The magnitude of the rate acceleration suggests that the dissociation equilibrium of the phenoxide group is important in the transport of Ca^{2+}. The rates of ion transport were further accelerated by photo(UV)irradiation by which about half of the Cr-*o* was isomerized to the cis form. Under the photo(UV)irradiation, the rate of Ca^{2+} transport (19.0 μmol h^{-1}) was greater than that of the Na^+ transport (16.1 μmol h^{-1}) in spite of the lower IN concentration ([Ca^{2+}] = 0.0225 M, [Na^+] = 0.10 M). It may be said, therefore, that light-driven ion transport with Cr-*o* shows the greatest transport selectivity toward Ca^{2+} ion.

Summarizing these observations, we may illustrate the Ca^{2+} transport phenomenon as Figure 1. A Ca^{2+} ion and a counteranion (A^-) are extracted by cis-formed Cr-*o* from the IN aqueous phase to the membrane phase, and after crossing the liquid membrane, the Ca^{2+} and the counteranion are released to the OUT aqueous phase in conjunction with protonation of the phenoxide group. Overall, a Ca^{2+} ion and a counteranion are carried from the IN to the OUT aqueous phase and a proton is carried back to the IN aqueous phase as countercurrent.

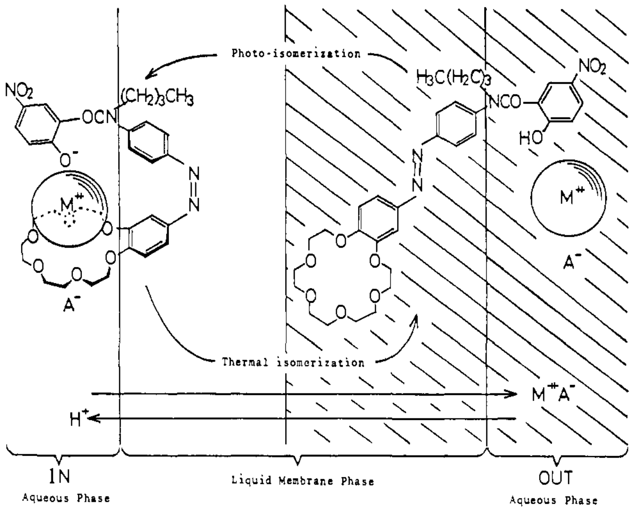


Figure 1. Schematic representation of light-driven M^{2+} transport across a liquid membrane.

It is not clear whether the thermal cis-to-trans isomerization occurring in the membrane phase has any significance in the Ca^{2+} transport. Since photo(UV)irradiation was conducted for 5 min at intervals of 2 h and the half-life of the thermal isomerization was 186 min, 36% of the cis form had isomerized to the trans form after 2 h at 30 °C. To test the possibility, we accelerated the cis-to-trans isomerization in the membrane phase by irradiation with visible light. The rate of the Ca^{2+} transport under alternative photoirradiation with UV and visible light (see footnote *c* for Table V) was a little retarded compared with that under UV light irradiation (19.0 → 17.3 μmol h^{-1}). Thus, when the OUT aqueous phase is the 0.01 N HCl solution, the rate-determining step in the Ca^{2+} transport under UV light irradiation is not the ion release from the *cis*-Cr-*o*-Ca^{2+} complex in the membrane phase to the OUT aqueous phase but the extraction of the Ca^{2+} ion from the IN aqueous phase into the membrane phase. In other words, light-driven ion transport in the Ca^{2+} transport is mainly due to the enhanced binding ability of *cis*-Cr-*o* toward the Ca^{2+} ion. It has been established that the best carrier for ion transport is a ligand that gives a moderately stable rather than a very stable complex, since the very stable complex cannot release the ion efficiently from the complex.[24,25] In bis(crown ether)s with an azo linkage, the alkali metal complexes with the cis isomers were fairly stable and the ion release was rate determining when hydrophobic counteranions were added in the IN aqueous phase.[17,18] In the Ca^{2+} transport by Cr-*o*, the *cis*-Cr-*o*-Ca^{2+} complex is not so stable as assigning the ion release to the rate-determining step. The fact that the cis % and the rate of the thermal isomerization

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are not affected by added alkali metal cations (Table II) also supports this presumption.

Concluding Remarks. The present system demonstrated that ion transport of alkali and alkaline earth metal cations can be controlled by light. The novel phenomenon is attained because the crown ether can put on and off a phenoxide anionic cap in response to photoirradiation. Also established is the fact that the countercurrent of proton flux is important (in particular, in the transport of the Ca^{2+} ion). We consider that the concept of "switched-on anionic cap" might lead to a more efficient and selective control of ion transport.

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Registry No. 1, 80764-58-5; *cis*-Cr-*m*, 80764-59-6; *trans*-Cr-*m*, 80764-60-9; *cis*-Cr-*p*, 80764-61-0; *trans*-Cr-*p*, 80764-62-1; *cis*-Cr-*o*, 80764-63-2; *trans*-Cr-*o*, 80780-59-2; Na^+, 17341-25-2; K^+, 24203-36-9; Rb^+, 22537-38-8; Cs^+, 18459-37-5; Ca^{2+}, 14127-61-8; Sr^{2+}, 22537-39-9; Ba^{2+}, 22541-12-4.

Conformational Effects in the Hydrolyses of Rigid Benzylic Epoxides: Implications for Diol Epoxides of Polycyclic Hydrocarbons[1]

J. M. Sayer,[†] H. Yagi,[†] J. V. Silverton,[†] S. L. Friedman,[‡] D. L. Whalen,[‡] and D. M. Jerina*[†]

Contribution from the Laboratory of Bioorganic Chemistry, National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases and Laboratory of Chemistry, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland 20205, and Laboratory for Chemical Dynamics, Department of Chemistry, University of Maryland Baltimore County, Baltimore, Maryland 21228. *Received July 20, 1981*

Abstract: The two conformationally rigid, diastereomeric 9,10-oxides derived from *trans*-1,2,3,4,4a,10a-hexahydrophenanthrene have been synthesized, and their relative stereochemistries have been verified by X-ray structure determination of the acetate of the bromohydrin precursor of one of these epoxides. Inspection of molecular models indicates that one of these epoxides has the benzylic C–O bond of the epoxide ring aligned nearly parallel to the π orbitals of the aromatic ring and has the epoxide oxygen cis to the adjacent ring juncture hydrogen, whereas the other epoxide has this C–O bond not aligned with the π orbitals and has the epoxide oxygen trans to the adjacent ring juncture hydrogen. Rates of solvolysis of these two epoxides in 1:9 dioxane–water, ionic strength 0.1 M ($NaClO_4$), at 25 °C, follow the rate law $k_{obsd} = k_{H^+}a_{H^+} + k_0$, with similar values of k_{H^+} for both diastereomers and a value of k_0 for the aligned isomer that is ~40 times larger than that for the nonaligned isomer. Upon solvolysis, the nonaligned isomer yields exclusively trans diol, whereas the aligned isomer yields predominantly cis diol (75%) under acidic conditions and ketone rearrangement product (~85%) under neutral conditions. The predominant diol from acid hydrolysis of both isomers is postulated to arise from attack of solvent on the carbonium ion derived from benzylic C–O cleavage of the epoxide, to yield a pseudoaxial substituent. The observed chemistry of these rigid epoxides is used to explain conformational effects on the rates and products of solvolysis of the conformationally flexible benzo-ring diol epoxides derived from metabolism of polycyclic aromatic hydrocarbons: (1) For the hydronium ion catalyzed process (k_{H^+}), rates are relatively insensitive to conformation, whereas product distribution is influenced (a) by the conformation of the carbonium ion that is *initially formed*, if this ion is relatively unstable, or (b) by the conformation of the carbonium ion that is *preferred at equilibrium*, if the ion is stable enough to undergo conformational equilibration prior to capture by solvent. (2) For the spontaneous process (k_0), the aligned conformation reacts considerably faster than the nonaligned conformation and also gives a carbonium ion with the required geometry for rearrangement to ketone. The observation that diol epoxides with the benzylic hydroxyl group cis to the epoxide ring ("isomer 1 series") ordinarily react via the k_0 process somewhat faster than their diastereomers with this hydroxyl group trans to the epoxide ring ("isomer 2 series") and also yield ketone products suggests that the isomer 1 diastereomers probably react predominantly via the conformer of the carbonium ion that is related to the aligned conformation of the reactant; reaction via this slightly less favored ground-state conformation may provide the lowest energy pathway for generation of the ion. For the isomer 2 series the absence of ketone formation at neutral pH is consistent with reaction only via the conformer of the carbonium ion that is related to the nonaligned ground-state conformation.

In accordance with predictions of the bay-region theory,[2] benzo-ring diol epoxides in which the epoxide group forms part of a bay region of the hydrocarbon are now widely accepted as ultimately carcinogenic metabolites of those polycyclic aromatic hydrocarbons that are biologically active.[3] Despite several investigations into the solvolytic reactivity of benzo-ring diol epoxides,[4] numerous aspects of the mechanisms by which these biologically important molecules react remain to be elucidated.

In particular, the influence of steric, stereoelectronic, and conformational factors on the rates and products of these reactions is difficult to assess for the conformationally mobile diol epoxides and tetrahydroepoxides of the polycyclic aromatic hydrocarbons.

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[‡] University of Maryland.

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