

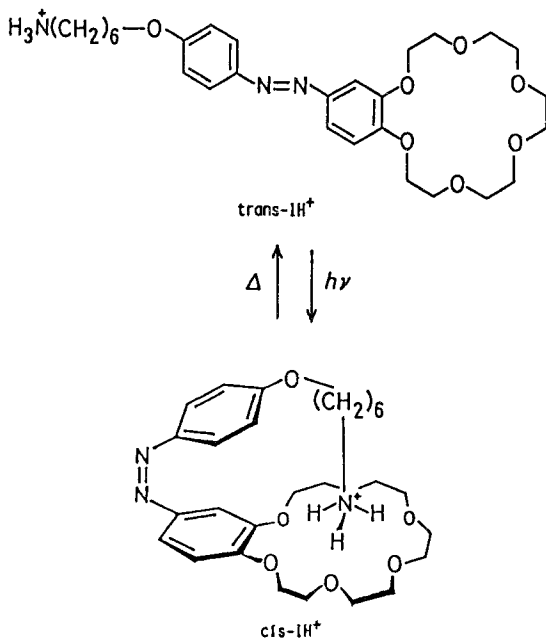
ON-OFF-SWITCHED CROWN-METAL COMPLEXATION BY PHOTOINDUCED  
INTRAMOLECULAR TAIL (AMMONIUM)-BITING

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ABSTRACT. New photoresponsive crown ethers ( $1\text{H}^+$ ) having a crown ring and an ammoniumalkyl ( $\text{H}_3\text{N}^+(\text{CH}_2)_n$ ,  $n=4,6,10$ ) group attached to the two sides of an azobenzene have been synthesized. Photoresponsive properties (thermal isomerization, metal extraction, membrane transport, etc.) were examined, and the results were compared with those of other photoresponsive crown ethers and complexons.

1. INTRODUCTION

Cations are known to be transported through membranes by synthetic macrocyclic polyethers as well as by antibiotics. In particular, some polyether antibiotics feature the interconversion between the cyclic and the acyclic form in the membrane phase, a feature which is believed to be the origin of rapid ion-transport through membranes. The phenomenon suggests that the reversible interconversion between two states can be responsible for the high efficiency of carrier molecules. As an attempt to mimic the natural photoresponsive systems, we have synthesized several photoresponsive crown ethers.<sup>1</sup> Here, we address a new photoresponsive crown ether ( $1\text{H}^+$ ) with an ammonium tail. This



"tail-biting" crown ether is designed so that the crown ring can bind the intramolecular ammonium group only when it is photoisomerized to the cis-isomer. Examination of Corey-Pauling-Koltun models suggests that hexamethylene spacer is required to optimize the interaction between the ammonium tail and the crown ring in cis-1H<sup>+</sup>. In this article, we describe photoresponsive behaviors of 1H<sup>+</sup> and 1 (free amino analogues) and compare them with those of other photoresponsive crown ethers and complexes 2-6 (for abbreviations see Table I) we synthesized previously.

## 2. SECONDARY VALENCE FORCES AFFECTING THE RATE OF THERMAL CIS-TO-TRANS ISOMERIZATION OF AZO COMPOUNDS.

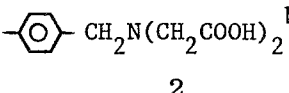
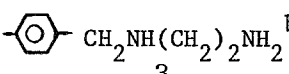
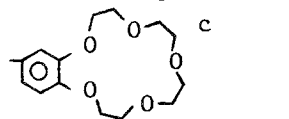
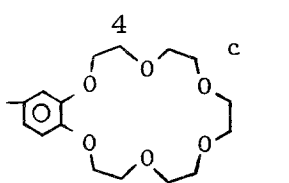
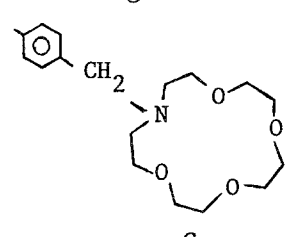
We have been investigating the effect of added metal ions on the thermal cis-to-trans isomerization of azo compounds. It has been found that when ligands substituted at the two sides of a cis-azobenzene coordinate intramolecularly to one metal cation, the rate of the thermal cis-to-trans isomerization is suppressed. This novel phenomenon is attributed to the "lock-in" effect of the metal ion flanked by two ligands. That is, an additional free energy of activation is required to disrupt favorable interactions between the metal ion and the ligands. The typical ligands are iminodiacetic acid, ethylenediamine, crown ethers, etc. (Table I).<sup>2-5</sup>

The cis-isomers of azobis(benzocrown ether)s, 4 and 5, can form intramolecular 1:2 metal/crown sandwich-type complexes with Rb<sup>+</sup> and Cs<sup>+</sup>.<sup>2,5</sup> Examination of Table I reveals that the cis-to-trans isomerization from these sandwich-type complexes requires extra free energies of activation by 0.6-1.7 kcal mol<sup>-1</sup>. The energies should be consumed to disrupt the interaction between the metal and the crown ethers. On the other hand, the rate inhibition was not observed for 6 which has methylene spacers between the benzenes and the crown rings.<sup>3</sup> Conceivably, the geometrical change induced by the isomerization of the N=N bond may be absorbed by the rotational freedom of these methylene groups. Thus, the effective inhibition occurs only in the rigid cis-isomers.

2 bears the iminodiacetic acid groups via methylene spacers, but the rate of cis-to-trans isomerization is strongly inhibited by Zn<sup>2+</sup> and Cu<sup>2+</sup>.<sup>4</sup> This implies that the interaction between the carboxylate groups and these metal ions is relatively strong. In fact, the first-order rate constant in the presence of Zn<sup>2+</sup> ( $8.3 \times 10^{-7} \text{ s}^{-1}$ ) is the smallest one we have ever observed. The isomerization rate of 3 bearing the ethylenediamine groups is also suppressed by Cu<sup>2+</sup> but not by Zn<sup>2+</sup>. Probably, coordination of "soft" ethylenediamine groups to "hard" Zn<sup>2+</sup> ion is not strong enough to suppress the isomerization rate.

The thermal cis-to-trans isomerization of cis-1 and cis-1H<sup>+</sup> is summarized in Table II. The rates for cis-1H<sup>+</sup> increased with increasing K<sup>+</sup> ion concentration and reached maximum values at [K<sup>+</sup>]=ca. 10<sup>-4</sup> M. The data in Table II reveal that the maximum k values are enhanced by 2.1-fold in cis-1H<sup>+</sup>(n=4) and cis-1H<sup>+</sup>(n=6) and by 1.5-fold in cis-1H<sup>+</sup>(n=10). These rate enhancements are ascribed to competitive complexation of K<sup>+</sup> to the crown ring which binds to the intramolecular

TABLE I. First-order rate constants(k) for thermal cis-to-trans isomerization of several azo compounds (30 °C)

| Azo compound<br>(X-N=N-X)<br>X   | $10^5 \cdot k/s^{-1}$ |  | $\Delta\Delta G^\ddagger$ a<br>kcal/mol |
|--|-----------------------|--|---|
|  | no metal              | with metal   |   |
| <br>2   | 0.137                 | 0.0083(Zn <sup>2+</sup> )<br>0.0367(Cu <sup>2+</sup> ) | 1.7<br>0.8                              |
| <br>3   | 0.300                 | 0.287(Zn <sup>2+</sup> )<br>0.147(Cu <sup>2+</sup> )   | ~0<br>0.4                               |
| <br>4   | 185                   | 24.1(Rb <sup>+</sup> )<br>33.3(Cs <sup>+</sup> )       | 1.2<br>1.0                              |
| <br>5   | 85.2                  | 30.8(Rb <sup>+</sup> )<br>5.3(Cs <sup>+</sup> )        | 0.6<br>1.7                              |
| <br>6 | 0.44                  | 1.10(Rb <sup>+</sup> )<br>0.91(Cs <sup>+</sup> )       | -0.6<br>-0.4                            |

$$^a \Delta\Delta G^\ddagger = \Delta G^\ddagger_{\text{metal}} - \Delta G^\ddagger_{\text{no metal}}$$

<sup>b</sup> Water

<sup>c</sup> o-DCB(86.8): n-BuOH(13.2).

ammonium-tail. In other words, the intramolecular interaction between the crown ring and the ammonium group is responsible for the extra free energies of activation (0.3-0.5 kcal mol<sup>-1</sup>). The smaller  $\Delta\Delta G^\ddagger$  in cis-1H<sup>+</sup>(n=10) may again reflect the greater conformational freedom of the decamethylene spacer. Interestingly, k for cis-1(n=6) also increased, although to a smaller extent, with increasing K<sup>+</sup> concentra-

TABLE II. First-order rate constants (k) for thermal cis-to-trans isomerization of cis-1 and cis-1H<sup>+</sup><sup>a</sup>

| Azo compound               | 10 <sup>5</sup> ·k/s <sup>-1</sup> |                                    | ΔΔG <sup>‡</sup><br>kcal/mol |
|----------------------------|------------------------------------|------------------------------------|------------------------------|
|                            | no metal                           | excess K <sup>+</sup> <sup>b</sup> |                              |
| cis-1(n=4)                 | 10.2                               | 10.5                               | ~0                           |
| cis-1(n=6)                 | 2.77                               | 3.4                                | -0.1                         |
| cis-1(n=10)                | 9.85                               | 9.6                                | ~0                           |
| cis-1H <sup>+</sup> (n=4)  | 4.68                               | 10.0                               | -0.5                         |
| cis-1H <sup>+</sup> (n=6)  | 1.59                               | 3.3                                | -0.4                         |
| cis-1H <sup>+</sup> (n=10) | 6.08                               | 9.3                                | -0.3                         |

<sup>a</sup> 30 °C, o-dichlorobenzene: n-BuOH = 80 : 20 v/v.

<sup>b</sup> [C<sub>11</sub>H<sub>23</sub>CO<sub>2</sub>K] = 1.2 × 10<sup>-4</sup> M.

tion. This result suggests that the amino group also interacts with the crown ring when it is placed at the optimized position.

### 3. EXTRACTION OF ALKALI METAL CATIONS WITH 1 AND 1H<sup>+</sup>

The photoresponsive ionophoric properties of 1 and 1H<sup>+</sup> were evaluated through two-phase extraction of alkali tosylates (M<sup>+</sup>Ts<sup>-</sup>) from water to o-dichlorobenzene(o-DCB): 1-butanol=45:55 (v/v). The results are summarized in Table III. Examination of Table III reveals the following facts: (i) trans-1(n=6) exhibits the highest affinity for K<sup>+</sup>, (ii) the ion concentrations extracted by n=6 series decrease, except for Li<sup>+</sup>, in the following sequence: trans-1(n=6) > cis-1(n=6) > trans-1H<sup>+</sup>(n=6) > cis-1H<sup>+</sup>(n=6), and (iii) most importantly, cis-1H<sup>+</sup>(n=6) shows very small K<sup>+</sup> ion affinity.

The extractabilities of trans-1H<sup>+</sup> are generally lower than those of trans-1 for three crown ethers having different spacer lengths. This lowering can be attributed to the intermolecular binding between the ammonium group and the crown ether ring. One may suppose, therefore, that the trans-1H<sup>+</sup>'s would exist (at least partially) as cyclic dimers or polymers. On the other hand, the further decrease observed for cis-1H<sup>+</sup>'s can be rationalized in terms of intramolecular complexation of the ammonium tail by the crown ether ring. Conceivably, the intramolecular complexation in the cis-configuration would displace K<sup>+</sup> ion from the crown ether ring.

### 4. PHOTOCONTROLLED ION-TRANSPORT ACROSS MEMBRANES

The cis-isomer of 4 forms relatively stable sandwich-type complexes with large alkali metal cations.<sup>2,5</sup> This phenomenon can be readily applicable to photocontrol of ion-transport across a liquid membrane

TABLE III. Extraction of alkali tosylates ( $M^+Ts^-$ ) with photoresponsive crown ethers<sup>a</sup>

| Crown ether | Metal           | $10^4 \cdot [M^+]$ in the organic phase |                                  |                      |                      |
|-------------|-----------------|---|----------------------------------|----------------------|----------------------|
|             |                 | trans-1H <sup>+</sup>                   | cis-1H <sup>+</sup> <sup>c</sup> | trans-1 <sup>b</sup> | cis-1 <sup>b,c</sup> |
| 1(n=4)      | K <sup>+</sup>  | 0.15                                    | 0.32                             | 0.45                 | 0.43                 |
| 1(n=6)      | Li <sup>+</sup> | 0.09                                    | 0.01                             | 0.12                 | 0.03                 |
|             | K <sup>+</sup>  | 0.22                                    | 0.04                             | 1.16                 | 0.39                 |
|             | Rb <sup>+</sup> | 0.30                                    | 0.17                             | 0.66                 | 0.43                 |
|             | Cs <sup>+</sup> | 0.38                                    | 0.24                             | 0.60                 | 0.63                 |
| 1(n=10)     | K <sup>+</sup>  | 0.29                                    | 0.02                             | 0.81                 | 0.49                 |

<sup>a</sup> Aqueous phase(3 ml):  $[M^+Ts^-] = 0.0102$  M, pH 4.7 with 10 mM phosphate. Organic phase(o-dichlorobenzene: 1-butanol = 45 : 55 v/v, 3 ml):  $[1 \text{ or } 1H^+] = 1.88 \times 10^{-4}$  M.

<sup>b</sup> Aqueous phase:  $[M^+Ts^-] = 0.0102$  M,  $[MOH] = 10$  mM.

<sup>c</sup> Contents of the cis-isomers are 63-80%.

(Figure 1).<sup>1,2</sup> We have found that the rate of K<sup>+</sup> transport is significantly enhanced by u.v. light irradiation or by alternate irradiation of u.v. and visible light.<sup>2,6</sup> Unfortunately, this system cannot be used to effect "light-driven active transport", because the reverse transport cannot be suppressed to zero. On the other hand, the photo- and pH-dependent interconversion between trans-1  $\rightleftharpoons$  cis-1H<sup>+</sup> may be useful to achieve "active K<sup>+</sup>-transport", because the extractabilities of cis-1H<sup>+</sup>(n=6) and cis-1H<sup>+</sup>(n=10) for K<sup>+</sup> are almost close to zero (Table III).

In passive ion-transport studies (entries 1-3 in Table IV), the K<sup>+</sup>-transport to the basic OUT aqueous phase was much faster than that to the acidic one. This means that trans-1(n=10) can transport K<sup>+</sup> more efficiently than interconvertible systems. Photoirradiation enhanced the rate by 2.1-fold: that is, the photoinduced ammonium-biting is useful as a tool to facilitate the ion-release from the membrane phase to the acidic OUT aqueous phase.

The results of the active ion-transport from the basic IN to the acidic OUT aqueous phase are recorded in entries 4-7. When 1(n=6) (1.00 mM) was used as a carrier, active K<sup>+</sup>-transport took place not only under photoirradiation but also in the dark. The finding suggests that active transport can be mediated not only by cis-1H<sup>+</sup>(n=6) in which intramolecular complexation is favored but also by trans-1H<sup>+</sup>(n=6) in which intermolecular complexation is occurring. In order to suppress the contribution from intermolecular complexation, we used a more lipophilic 1(n=10) and reduced the carrier concentration to 0.10 mM.

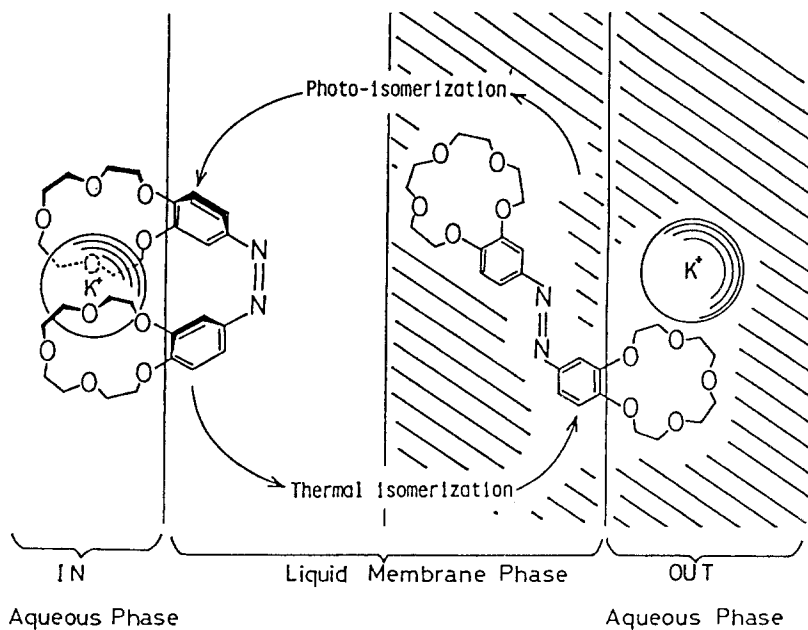


Figure 1. Schematic representation of light-driven  $K^+$  transport with 4.

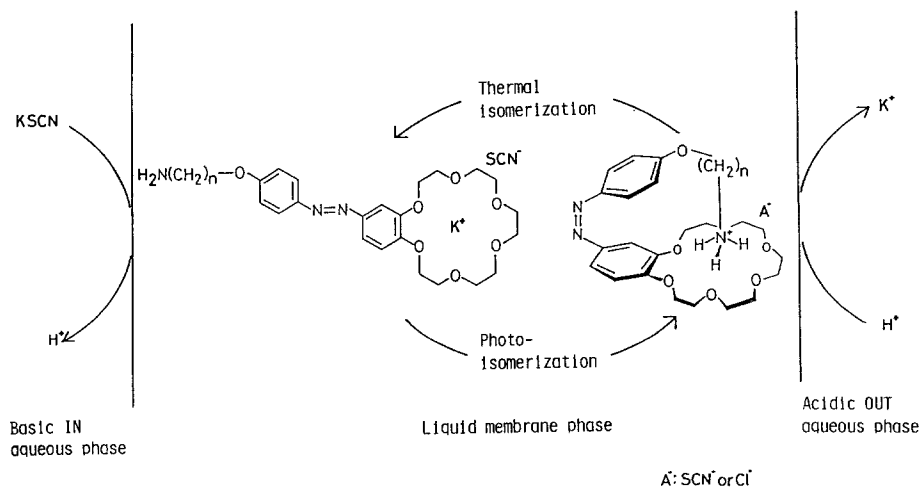


Figure 2. Schematic representation of  $K^+$  transport at the low 1 ( $n=10$ ) concentration.

TABLE IV Ion-transport across a liquid membrane (30 °C)<sup>a</sup>

| Entry | Membrane phase            | OUT aqueous phase            | $10^7 \cdot v / \text{mol h}^{-1}$ |
|-------|---------------------------|------------------------------|------------------------------------|
| 1     | 1(n=10) dark              | [Me <sub>4</sub> NOH]=0.10 M | 144                                |
| 2     | 1(n=10) dark              | [HCl]=0.50 M                 | 14.6                               |
| 3     | 1(n=10) photo             | [HCl]=0.50 M                 | 30.5                               |
| 4     | 1(n=6) <sup>b</sup> dark  | [KSCN]=[HCl]=30 mM           | 2.6                                |
| 5     | 1(n=6) <sup>b</sup> photo | [KSCN]=[HCl]=30 mM           | 2.7                                |
| 6     | 1(n=10) dark              | [KSCN]=[HCl]=30 mM           | 0.66                               |
| 7     | 1(n=10) photo             | [KSCN]=[HCl]=30 mM           | 1.4                                |

<sup>a</sup> Membrane phase : o-DCB(45) : n-BuOH (55), [1(n=10)]= $1.00 \times 10^{-4}$  M.  
IN aqueous phase: [KSCN]=0.50 M, [Me<sub>4</sub>NOH]=0.10 M for entries 1-3; [KSCN]=[Me<sub>4</sub>NOH]=30 mM for entries 4-7.

<sup>b</sup> [1(n=6)]= $1.00 \times 10^{-3}$  M.

In the dark, inefficient active transport ( $6.6 \times 10^{-8}$  mol h<sup>-1</sup>) was still observable due to intermolecular complexation. However, the rate was enhanced up to  $1.4 \times 10^{-7}$  mol h<sup>-1</sup> by photoirradiation. This significant rate increase can be rationalized in terms of a photoinduced intramolecular "tail-biting" which facilitates a competitive ion ejection into the acidic OUT aqueous phase (Figure 2). It appears, therefore, that the photoinduced "tail-biting" acts as an effective tool when the carrier concentration is lowered enough for the carrier to exist as a discrete monomeric unit.

## 5. CONCLUSION

As described in Introduction, the basic idea of the photoresponsive crown ethers originates from the responsive action of certain polyether antibiotics. In extensions to membrane transport studies, it was found that these photoinduced changes in affinity could be used to enhance the rate of ion-release from an artificial carrier, thereby increasing the overall rates of either passive or active transport across a membrane. We believe that further elaborations of this concept might lead to the eventual development of a series of photocontrollable membranes.

## 6. REFERENCES

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