# Photoresponsive Crown Ethers. Part 18.† Photochemically 'Switched-on' Crown Ethers Containing an Intra-annular Azo Substituent and their Application to Membrane Transport

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Photoresponsive crown ethers (3) having an intra-annular azo substituent have been synthesized. These crown ethers have been designed so that the crown-metal interaction can only occur upon photoisomerisation of the intra-annular azo substituent from *trans* to *cis*. In thermal *cis*-to-*trans* isomerisation, the first-order rate constants (k) were suppressed to 14—66% by the addition of Na$^+$ or K$^+$, indicating that an additional free energy of activation (1.0—5.0 kJ mol^{-1}) is required to disrupt the favourable crown-metal interactions. From the plots of k *vs.* [M$^+$] the association constants (K_c) for the *cis*-forms were estimated to be $10^{4.07} - 10^{4.81}$ l mol^{-1}, which are comparable with the K_c for regular crown ethers. The spectral study established that the high metal affinity of the *cis*-forms is due to the co-ordination of one of the azo nitrogens to the metal ion. In two-phase extraction of alkali-metal cations the Ex% values for *cis*-(3) were always higher than those for *trans*-(3). In particular, the dramatic photoirradiation effect was observed for Na$^+$: *cis*-(3) extracts Na$^+$ (8.1—14.1%), whereas *trans*-(3) extracts no Na$^+$. This system was applied to ion transport across a liquid membrane. As expected, Na$^+$ transport occurred only when the membrane phase was irradiated by u.v. light. The marked difference can be used to control the ion permeability by an on-off light switch.

Macrocyclic polyethers contain intramolecular cavities in which metal cations may be bound. The metal selectivity of crown ethers (*i.e.* spherical recognition pattern) is based primarily on the goodness of fit between the cavity size and the cation radius.‡ Crown ethers of type (1), bearing an intra-annular substituent X, bind metal cations in two different ways. When X has no metal-co-ordination ability (X = methyl, phenyl, halides, *etc.*), X acts as a simple steric spacer and the association constant decreases.[1-5] In contrast, when it has a metal-co-ordination ability (X = OH, CO$_2$H, NH$_2$, *etc.*), X acts as a ligand group and the association constant increases.[1-7]
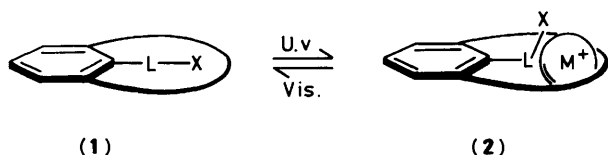
The purpose of our investigation has been to control the functions of a crown ether family by an on-off light switch, which would lead to photoregulation of ion-extraction and carrier-mediated membrane transport.[8] Through this study, we have noticed that as with some polyether antibiotics such as nigericin and monensin,[9] rapid, reversible interconversion between two states can lead to highly efficient artificial carrier molecules.[10-13] From this point of view, crown ethers whose intra-annular substituent can change the position [(1) ⇌ (2)], *e.g.*, upon photolysis, are of particular interest since this allows specific modification of the cavity shape controlling the ion-binding properties of the crown ether. We report here the synthesis and properties of the crown ethers (3a), (3b), and (3c), which contain a photochemically 'switched-on' intra-annular azo substituent. In these photoresponsive crown ethers,
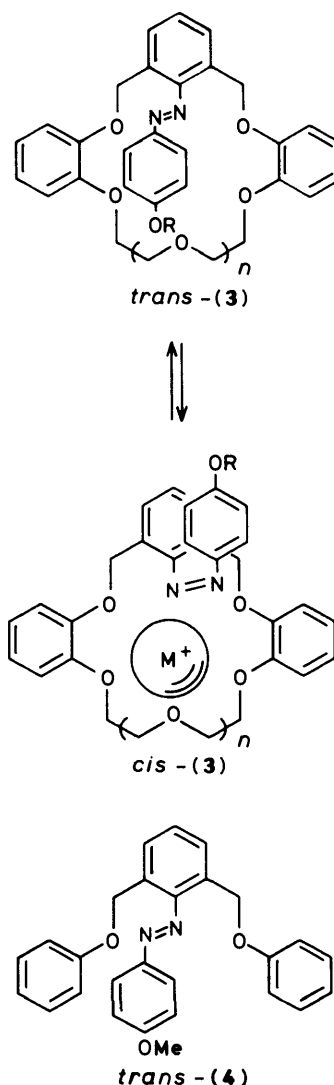
trans -(3)

cis -(3)

OMe

trans -(4)

(1)   (2)

‡ Gokel *et al.* suggested that the concept of 'hole-size' selectivity does not explain cation binding selectivities in flexible macrocycles: G. W. Gokel, D. M. Goli, C. Minganti, and L. Ehœgoyen, *J. Am. Chem. Soc.*, 1983, **105**, 6786.

the intra-annular substituent is taken out by photochemically induced *trans–cis* isomerisation of the azo group. Furthermore, one of the two nitrogens in the *cis*-forms may contribute to the binding of metal cations. Thus, one might expect a large photo-induced change in the binding constant. Compound (4) was used as a noncyclic reference compound.

Experimental

Materials.—The three crown ethers used in this study were synthesized according to Scheme 1. Two *ortho*-benzeno groups were introduced for the ease of preparation. Since the preparative methods are similar for each other, the synthesis of *trans*-(3a) is described in detail; results for the other two crown ethers are described only briefly.

21-*Nitro*-1,4,7,14,23-*pentaoxa*[7.2.2]*orthometaorthobenzeno-phane* (5; n = 1).—Compound (5; *n* = 1) was prepared from 2,6-bis(bromomethyl)nitrobenzene and 1,5-bis(*o*-hydroxy-phenoxy)-3-oxapentane according to the method of Weber and Vögtle;[2] yield 55%, m.p. 174—176 °C (lit.[2] 179—180 °C); *m/z* 437.

24-*Nitro*-1,4,7,10,17,26-*hexaoxa*[10.2.2]*orthometaortho-benzenophane* (5; n = 2).—Compound (5; *n* = 2) was prepared from 2,6-bis(bromomethyl)nitrobenzene and 1,8-bis(*o*-hydroxy-phenoxy)-3,6-dioxaoctane in a manner similar to the synthesis of (5; *n* = 1); yield 26%, m.p. 145—147 °C; $v_{max.}$(KBr) 1 330 and 1 530 (NO₂) and 1 130 and 1 240 cm⁻¹ (C–O–C); δ(CDCl₃) 3.52, 3.81, 4.12, and 5.42 (4 H, each, OCH₂) and 7.08 and 7.87 (8 H, and 3 H, ArH) (Found: C, 65.0; H, 5.7; N, 2.9. Calc. for C₂₆H₂₇NO₈: 65.0; H, 5.7; N, 2.9%).

21-*Amino*-1,4,7,14,23-*pentaoxa*[7.2.2]*orthometaortho-benzenophane* (6; n = 1).—Compound (5; *n* = 1) (1.00 g, 2.29 mmol) was dissolved in ethylene glycol monomethyl ether (30 ml) containing active charcoal (0.30 g) and FeCl₃·6H₂O (0.030 g, 1.11 mmol). Hydrazine monohydrate (0.60 ml, 12.3 mmol) in ethylene glycol monomethyl ether (3 ml) was added dropwise and the reaction was followed by t.l.c. Active charcoal was filtered off and washed with hot ethylene glycol monomethyl ether. The combined solutions were evaporated to dryness under reduced pressure and the residual white solid was recrystallised from ethyl acetate; yield 74%, m.p. 193—195 °C; $v_{max.}$(KBr) 3 390 and 3 460 (NH₂) and 1 110 and 1 240 cm⁻¹ (C–O–C); δ(CDCl₃) 3.98, 4.20, and 5.06 (4 H each, OCH₂), 6.00 (2 H, br, NH₂), and 6.98 and 7.16 (8 H, and 3 H, ArH) (Found: C, 70.5; H, 6.2; N, 3.2. Calc. for C₂₄H₂₅NO₅: C, 70.8; H, 6.2; N, 3.4%).

24-*Amino*-1,4,7,10,17,26-*hexaoxa*[10.2.2]*orthometaortho-benzenophane* (6; n = 2).—This compound was formed in 70% yield from (5; *n* = 2), m.p. 110—112 °C; $v_{max.}$(KBr) 3 380 and 3 440 (NH₂) and 1 140 and 1 260 cm⁻¹ (C–O–C); δ(CDCl₃) 3.81, 3.93, 4.25, and 5.16 (4 H each OCH₂), 5.45 (2 H, br, NH₂), and 7.01 and 7.34 (8 H, and 3 H, ArH) (Found: C, 69.2; H, 6.5; N, 2.7. Calc. for C₂₆H₂₉NO₆: C, 69.2; H, 6.5; N, 3.1%).

21-(4′-*Hydroxyphenylazo*)-1,4,7,14,23-*pentaoxa*[7.2.2]*ortho-metaorthobenzenophane* (8; n = 1).—Compound (6; *n* = 1) (0.20 g, 0.49 mmol) was dissolved in a mixture of acetic acid (10 ml), water (10 ml), and concentrated HCl (2 ml) and sodium nitrite [1.0 mmol in water (2 ml)] was added in small portions to the stirred solution; potassium iodide starch paper showed that sodium nitrite was in excess over (6; *n* = 1). The excess of nitrous acid was treated with sulphamic acid after which phenol (0.50 g, 5.31 mmol) was added and the solution was adjusted to pH 11 with 1.0M-NaOH. Completion of the reaction was confirmed when the reaction mixture was no longer coloured on the addition of 8-amino-1-naphthol 3,6-disulphonate. The solution was neutralised by acetic acid and extracted with chloroform. The chloroform solution was evaporated to dryness at room temperature under reduced pressure and the evaporation was further continued at 60 °C to remove unchanged phenol. The reddish residue was washed with methanol to give the yellow crystals of (8; *n* = 1); yield 76%, m.p. 175—177 °C; $v_{max.}$(KBr)
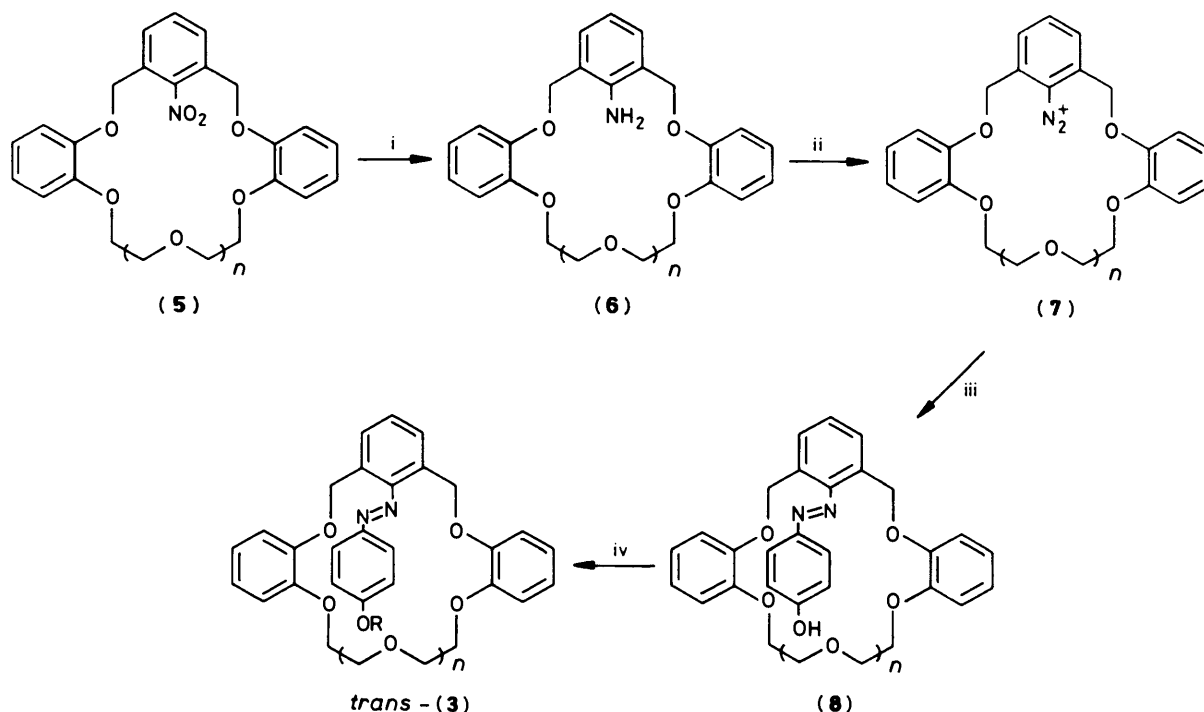
Scheme 1. *Reagents:* i, H₂NNH₂–FeCl₃; ii, NaNO₂–HCl; iii, phenol; iv, methyl iodide or octyl bromide

3 440 (OH), 1 590 (N=N) and 1 110 and 1 240 cm^{-1} (C–O–C) (Found: C, 69.1; H, 5.5; N, 4.8. Calc. for $C_{30}H_{28}N_2O_6$: C, 70.3; H, 5.5; N, 5.5%). Although the elemental analysis data were not satisfactory, this compound was used for the synthesis of *trans*-(3a) without further purification.

24-(4′-*Hydroxyphenylazo*)-1,4,7,10,17,26-*hexaoxa*[10.2.2]-*orthometaorthobenzenophane* (**8**; n = 2).—This compound was formed in 65% yield from (**6**; n = 2); single spot on t.l.c., m.p. 175—176 °C; $v_{max.}$(KBr) 3 400 (OH), 1 620 (N=N), and 1 120 and 1 260 cm^{-1} (C–O–C) (Found: C, 69.0; H, 5.8; N, 4.7. Calc. for $C_{32}H_{34}N_2O_7$: C, 69.1, H, 5.8; N, 5.0%).

21-(4′-*Methoxyphenylazo*)-1,4,7,14,23-*pentaoxa*[7.2.2]*orthometaorthobenzenophane* *trans*-(3a).—Compound (**8**; n = 1) (0.10 g, 0.19 mmol) was treated with methyl iodide (0.28 g, 1.99 mmol) in *N,N*-dimethylformamide (DMF; 5.10 ml) at 80 °C in the presence of an excess of K_2CO_3 (0.28 g). The progress of the reaction was followed by a t.l.c. After 4 h the reaction mixture was cooled and diluted with water. The precipitate was filtered off and recrystallised from ethanol; yield 87%, m.p. 127—130 °C; m/z 526; $v_{max.}$(KBr) 1 580 (N=N) and 1 130 and 1 250 (C–O–C) (no v_{OH}); δ(CDCl$_3$) 3.64, 3.82, 4.97, and 5.49 (4 H, 4 H, 2 H, and 2 H, respectively, OCH$_2$), 3.74 (3 H, OCH$_3$), 6.78, 7.18, and 7.52 (8 H, 4 H, and 3 H, respectively, ArH) (Found: C, 69.9; H, 5.8; N, 4.9. Calc. for $C_{31}H_{30}N_2O_6$: C, 70.7; H, 5.7; N, 5.3%).

21-(4′-*Octyloxyphenylazo*)-1,4,7,14,23-*pentaoxa*[7.2.2]*orthometaorthobenzenophane* *trans*-(3b).—This compound formed in 30% yield from (**8**; n = 1) and octyl bromide, had m.p. 99—101 °C; δ(CDCl$_3$) 0.87 (3 H, CH$_3$), 1.3—1.6 [12 H, (CH$_2$)$_6$], 3.56, 3.81, 3.86, 4.94, and 5.50 (2 H, 4 H, 4 H, 2 H, and 2 H, respectively, OCH$_2$), and 6.77, 7.21, and 7.35 (8 H, 4 H, and 3 H, respectively, ArH) (Found: C, 73.0; H, 7.1; N, 4.4. Calc. for $C_{38}H_{44}N_2O_6$: C, 73.1; H, 7.1; N, 4.5%).

24-(4′-*Methoxyphenylazo*)-1,4,7,10,17,26-*hexaoxa*[10.2.2]-*orthometaorthobenzenophane* *trans*-(3c).—This compound was formed in 88% yield from (**8**; n = 2) and methyl iodide; single spot on t.l.c., m.p. < room temperature; $v_{max.}$(KBr) 1 590 (N=N) 1 120 and 1 250 cm^{-1} (C–O–C) (no v_{NOH}); δ(CDCl$_3$) 3.35, 3.64, 3.82, and 5.47 (4 H each, OCH$_2$), 3.76 (3 H, OCH$_3$), and 6.83, 7.46, and 7.72 (8 H, 4 H, and 3 H, respectively, ArH) (Found: C, 69.1; H, 6.1; N, 4.6. Calc. for $C_{33}H_{34}N_2O_7$: C, 69.5; H, 6.0; N, 4.9%).

4′-Methoxy-2,6-bis(phenoxymethyl)azobenzene [*trans*-(**4**)], a noncyclic analogue of *trans*-(**3**) was prepared in a manner similar to that shown in Scheme 1.

2,6-*Bis(phenoxymethyl)nitrobenzene*.—2,6-Bis(bromomethyl)nitrobenzene (3.09 g, 10 mmol) and phenol (2.26 g, 24 mmol) were dissolved in butan-1-ol (100 ml) and NaOH (1.0 g) in water (10 ml) was added in small portions to the stirred solution at 40—55 °C under a stream of nitrogen. The reaction was continued for 21 h at 90 °C. The solution was concentrated to 50 ml under reduced. After cooling, the precipitate was filtered off and recrystallised from ethanol; yield 54%, m.p. 109—110 °C; δ(CDCl$_3$) 5.15 (4 H, OCH$_2$), 6.94, 7.25, and 7.57 (6 H, 4 H, 3 H, respectively, ArH) (Found: C, 71.6; H, 5.1; N, 4.3. Calc. for $C_{20}H_{17}NO_4$: C, 71.6; H, 5.1; N, 4.2%).

2,6-*Bis(phenoxymethyl)aniline*.—This compound was formed in 58% yield from 2,6-bis(phenoxymethyl)nitrobenzene in a manner similar to that described for the reduction of (**5**; n = 1), m.p. 89—91 °C; $v_{max.}$(KBr) 3 390 and 3 460 (NH$_2$) cm^{-1} (Found: C, 78.7; H, 6.2; N, 4.4. Calc. for $C_{20}H_{19}NO_2$: C, 78.7; H, 6.3; N, 4.6%).

4′-*Hydroxy*-2,6-*bis(phenoxymethyl)azobenzene*.—2,6-Bis-(phenoxymethyl)aniline was diazotised and coupled to phenol. The operation was similar to that described for the synthesis of (**8**; n = 1). The product (reddish oil) was subjected to a preparative t.l.c. method (silica gel–chloroform); yield 100%, m.p. 90—93 °C (Found: C, 77.1; H, 5.6; N, 5.5. Calc. for $C_{26}H_{22}N_2O_3$: C, 76.1; H, 5.4; N, 6.8%). Although the elemental analysis data were not satisfactory, the compound was used for the synthesis of *trans*-(**4**) without further purification.

4′-*Methoxy*-2,6-*bis(phenoxymethyl)azobenzene* *trans*-(**4**).—This compound was formed in 52% yield from 4′-hydroxy-2,6-bis(phenoxymethyl)azobenzene and methyl iodide. The operation was similar to that described for the synthesis of *trans*-(3a) except solvent (acetonitrile instead of DMF). The product was recrystallised from methanol, m.p. 102—104 °C; $v_{max.}$(KBr) 1 580 (N=N) and 1 240 (C–O–C) cm^{-1} (no v_{OH}); δ(CDCl$_3$) 3.87 (3 H, OCH$_3$), 5.40 (4 H, OCH$_2$), 6.96, 7.16, 7.62, 7.73, and 7.80 (8 H, 2 H, 4 H, 2 H, and 1 H, respectively, ArH) (Found: C, 76.6; H, 5.7; N, 6.4. Calc. for $C_{27}H_{24}N_2O_3$: C, 76.4; H, 5.7; N, 6.6%).

Photoisomerisation and Kinetic Measurements of Thermal cis-to-trans *Isomerisation.*—*trans*-to-cis Photoisomerisation was carried out by using a 500 W high-pressure Hg lamp with a coloured glass filter (Toshiba UV-D35, 330 < λ < 380 nm). The photostationary state was attained in 30 s. The kinetic measurements were carried out spectrophotometrically at 30 °C in *o*-dichlorobenzene–methanol (5:1, v/v) by monitoring the increase in the absorption maxima of the *trans*-forms. Metal ions (as perchlorate salts) were added after photoisomerisation. Further details of the method have been described previously.[10-13]

Solvent Extraction.—The method of solvent extraction has been described previously.[10,12] In this study, the organic phase (3 ml; *o*-dichlorobenzene–butan-1-ol 4:1, v/v) containing 3.00 × 10^{-3}M of (**3**) was agitated thoroughly with the aqueous phase (3 ml) containing MCl (0.10M), MOH (1.00 × 10^{-4}M), and picric acid (1.00 × 10^{-4}M). The concentrations of alkali picrates extracted into the organic phase were determined by a spectrophotometric method.

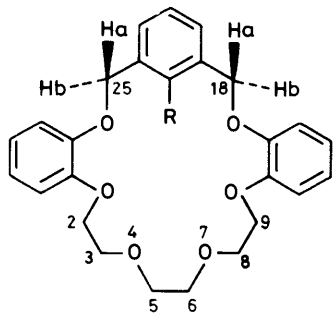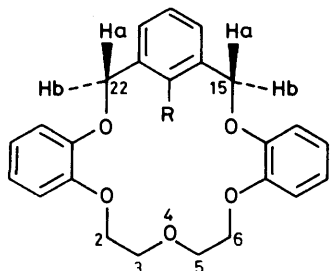*Ion Transport.*—Transport of Na$^+$ across a liquid membrane (*o*-dichlorobenzene–butan-1-ol 4:1, v/v) was carried out in a double glass-tube apparatus (*i.e.*, Shulman bridge illustrated in Figure 6: the inner diameters of the glass-tubes were 12 mm and 35 mm). The transport system consisted of the membrane phase (10 ml) and the first (IN) and the second (OUT) aqueous phase (25 ml and 5 ml, respectively), and the membrane phase was stirred (400 r.p.m.). The apparatus was immersed in a thermostatted water-bath (30 °C) and, when required, irraidated by a 100 W Hg lamp with a UV-D35 filter. We confirmed spectrophotometrically that in this apparatus, 50—60% of (**3**) in the membrane phase was isomerised to cis-(**3**) when the lamp was switched on for 15 min. The rates of ion transport were determined by monitoring the Na$^+$ concentration in the OUT aqueous phase by electric conductance. Further details of the transport conditions are recorded in the footnotes to Figure 7.

Results and Discussion

Comments on the Synthesis and Spectral Properties.—The diazonium group in (**7**) is an intra-annular substituent and therefore expected to be relatively deactivated because of steric hindrance. Also it is well-known that crown ethers can stabilise the diazonium ion through the O ··· N$_2$$^+$ interaction.[14,15] If this is the case in (**7**), the reactivity of the diazo group would be suppressed not only by steric hindrance but also by the electro-

static effect. In fact, the yield for the diazo coupling of non-cyclic 2,6-bis(phenoxymethyl)benzenediazonium ion was 100%, whereas those for (7; $n = 1$) and (7; $n = 2$) were much lower (76 and 65%, respectively). In a separate study, an attempt to induce diazo coupling between (7) and N,N-dimethylaniline failed. These data support the low reactivity of the intra-annular diazonium group.

In the ^{1}H n.m.r. measurements, we found that the chemical shift of methylene protons is affected specifically by the intra-annular 4'-methoxyphenylazo group (Figure 1 and 2). Compound (5; $n = 2$) has four different types of methylene protons at δ 3.52, 3.81, 4.12, and 5.24, which are assigned respectively to 5(and 6)-H, 3(and 8)-H, 2(and 9)-H, and 18(and 25)-H. The chemical shifts of these protons in *trans*-(3c) appear at δ 3.35, 3.64, 3.82, and 5.47, respectively. That is, the δ values for 5(and 6)-H, 3(and 8)-H, and 2(and 9)-H move to higher magnetic field by 0.17—0.30 p.p.m. whereas that for 18(and 25)-H moves to lower magnetic field by 0.23 p.p.m. Based on the shielding effect of the azobenzene,[16] it can be concluded that the crown strap of C(2)–C(3)–O(4)–C(5)–C(6)–O(7)–C(8)–C(9) exists on the phenyl ring of the azobenzene moiety whereas 18(and 25)-H lies on the same plane as the azobenzene. In other words, the crown rings in *trans*-(3) are considerably distorted. Examination of Corey-Pauling-Koltun models suggests that the crown rings cannot enjoy coplanarity with the azobenzene moiety. Conceivably, the steric crowding in *trans*-(3) is partly relaxed by such a distortion of the crown ether strap.

Also interesting is the fact that 18(and 25)-H in *trans*-(3c) and OCH$_2$ in *trans*-(4) give a sharp singlet while 15(and 22)-H in *trans*-(3a) gives a pair of doublets (Figure 2). The peak splitting is due to the geminal coupling between H$_a$ and H$_b$ ($J_{ab} = 11$ Hz). This implies that the crown ether ring in *trans*-(3a) is so rigid that the conformational fluctuation occurs slowly on the n.m.r. time scale. The sharp singlet in *trans*-(3c) implies, on the other hand, that the steric rigidity is considerably relaxed by insertion of one –OCH$_2$CH$_2$– unit into the crown ether ring.

Metal Effects on Photo and Thermal Isomerisation.—The spectroscopic properties of *trans*-(3) and *trans*-(5) are summarised in Table 1. Usually, *trans*-azobenzene derivatives show a π–π* absorption band at *ca.* 330 nm and an n–π* absorption band at *ca.* 440 nm. In *trans*-(3) and *trans*-(4), however, the

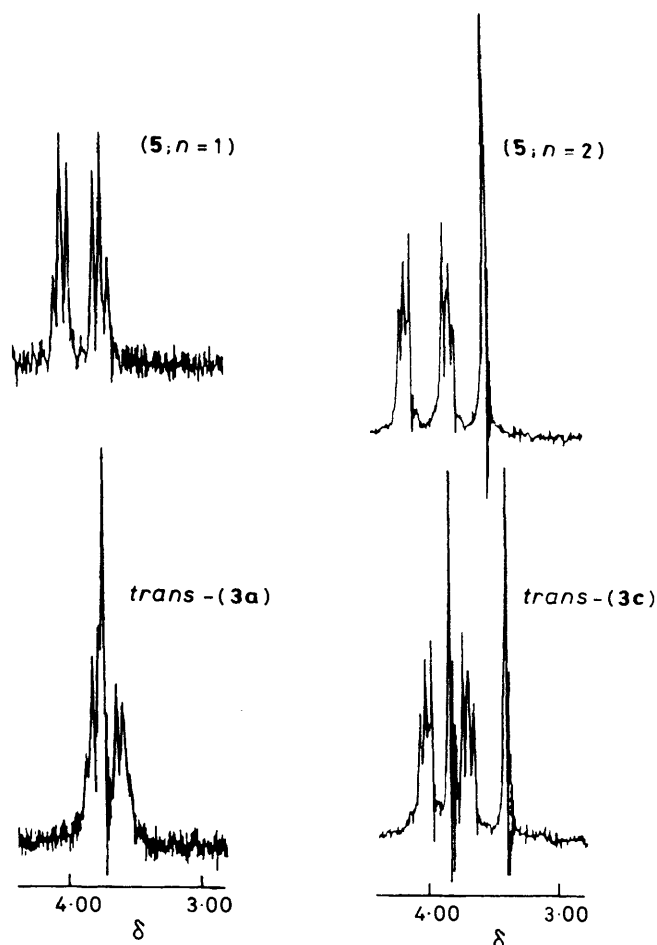

Figure 1. ^{1}H N.m.r. spectra for the ethylene protons (2-, 3-, 5-, and 6-H for $n = 1$ and 2-, 3-, 5-, 6-, 8-, and 9-H for $n = 2$) in CDCl$_3$ at 37 °C

n–π* absorption band could not be clearly detected probably because of a red shift of the π–π* absorption band. As shown in Table 1, the λ$_{max.}$ and ε$_{max.}$ for *trans*-(3a) which should be sterically crowded are similar to those for noncyclic *trans*-(4). This suggests that the steric distortion occurs only in the crown ether moiety but not in a chromophoric azobenzene moiety. The photoisomerisation was carried out using a 500 W high-pressure Hg-lamp equipped with a coloured glass filter (330 < λ < 380 nm). In *o*-dichlorobenzene–methanol (5:1, v/v) the photoisomerisation reached a photostationary state after 30 s, the *cis*:*trans* ratio being recorded in Table 1. The initial spectra of the *trans*-forms were quantitatively regenerated thermally or by irradiation of a tungsten lamp. The thermal *cis*-to-*trans* isomerisation obeyed a first-order equation, the first-order rate constants (k) being summarised in Table 2. Examination of these data reveals that in the absence of metal cations, the *cis*:*trans* ratio increases in the order (4) > (3c) > (3a) and k increases in the order (3a) > (3c) > (4). This implies that *cis*-(3a) is most destabilised and *cis*-(3c) is next: conceivably, *cis*-(3a) is particularly destabilised because of steric crowding compared with *cis*-(3c) and noncyclic *cis*-(4). The trend is in line with the n.m.r. data mentioned above.

Previously we studied the metal effect on the isomerisation behaviour of azobenzene-bridged bis(crown ethers).[10,17] In azobis(benzocrown ethers), the metal cations which can form intramolecular 1:2 metal/crown sandwich-type complexes with the *cis*-forms enhanced the *cis*-percentage at the photostationary state and suppressed the rate of the thermal *cis*-to-
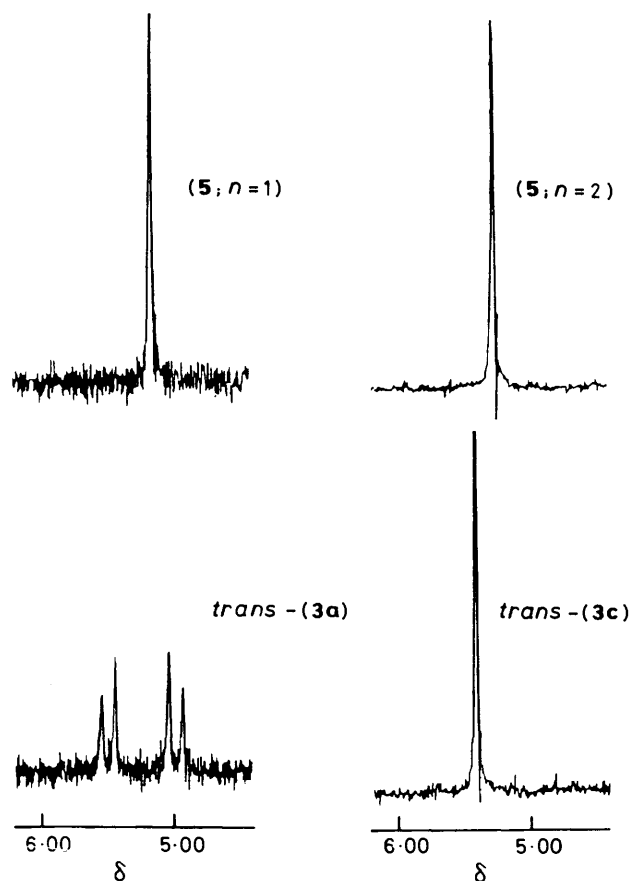
Figure 2. ^{1}H N.m.r. spectra for the methylene protons (15- and 22-H for $n = 1$ and 18- and 25-H for $n = 2$) in $CDCl_3$ at 37 °C
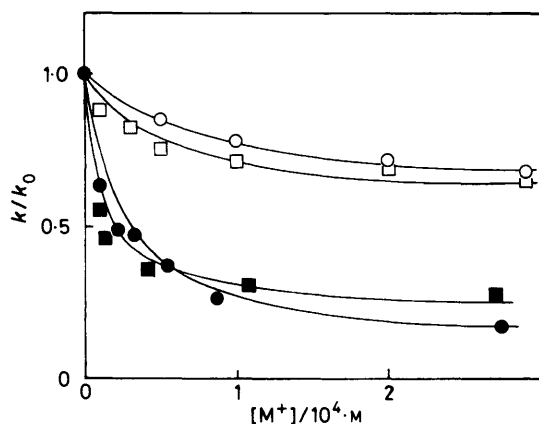

Figure 3. First-order rate constants for thermal *cis*-to-*trans* isomerisation plotted against metal concentrations. The k_o denotes the first-order rate constant in the absence of metals. 30 °C, *o*-dichlorobenzene–butan-1-ol (5:1, v/v), ● (3a) + Na$^+$; ■ (3a) + K$^+$; ○ (3c) + Na$^+$; □ (3c) + K$^+$.

trans isomerisation. This behaviour is rationalised in terms of the 'lock-in' effect of metal ions flanked by two crown rings. In other words, the *cis*-forms are considerably stabilised by metal complexation and an additional free energy of activation is required for the *cis-trans* isomerisation process, which reflects the need to disrupt favourable interactions between the metal cation and the crown ethers.[10,17,18] In the present system, the *cis*-percentage at the photostationary state was scarcely affected (less than 5%) by the addition of alkali-metal cations

Table 1. Spectroscopic properties[a]

Crown ether	$\lambda_{max.}$/nm	$\varepsilon_{max.}$	*cis*:*trans* Ratio
trans-(3a)	347	14 700	58:42
trans-(3b)	352	19 800	64:36
trans-(3c)	350	18 000	63:37
trans-(4)	353	17 300	72:28

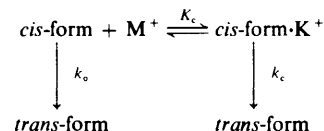[a] 30 °C, *o*-dichlorobenzene–methanol (5:1, v/v)

Table 2. First-order rate constants (k) for thermal *cis*-to-*trans* isomerisation and association constants (K_c) for the *cis*-forms[a]

Crown ether	Metal (conc. mM)[b]	$10^5 \cdot k/s^{-1}$	$10^5 \cdot k_c/s^{-1}$	$\log K_c$
cis-(3a)	None	15.1		
	Li$^+$ (0.271)	18.3	c	c
	Na$^+$ (0.274)	2.57	2.10	4.81
	K$^+$ (0.271)	4.25	3.63	4.65
	Cs$^+$ (0.287)	11.9	d	d
cis-(3c)	None	2.68		
	Li$^+$ (0.300)	2.58	c	c
	Na$^+$ (0.311)	1.83	1.60	4.07
	K$^+$ (0.300)	1.75	1.77	4.69
	Rb$^+$ (0.300)	2.28	d	d
	Cs$^+$ (0.300)	2.37	d	d
cis-(4)	None	0.57		

[a] 30 °C, *o*-dichlorobenzene–methanol (5:1, v/v). [b] Perchlorate salts were used. [c] The rate retardation was too small to estimate the k_c and the K_c accurately. [d] The plots did not satisfy equation (1) which holds for the formation of a 1:1 complex.

([$MClO_4$] = 1.0 mM). The absence of the rate retardation effect suggests that the metal-crown interaction in *cis*-(3a) and *cis*-(3c) is not strong enough to suppress the light-mediated isomerisation.

In contrast, the thermal *cis*-to-*trans* isomerisation process was significantly suppressed by certain metal cations. The k values were scarcely affected by the addition of Li$^+$ but decreased with increasing concentration of other metal cations. In particular, the isomerisation rate was strongly inhibited by Na$^+$ and K$^+$ (Figure 3 and Table 2). This trend suggests that as expected from the ring size, the crown cavities of *cis*-(3a) and *cis*-(3c) do not interact with Li$^+$ at all but can bind weakly to Rb$^+$ and Cs$^+$ and strongly to Na$^+$ and K$^+$. From the curvatures of the k *vs.* [M$^+$] plots one can estimate the association constants (K_c) for the *cis*-form·metal complexes.[19] In Scheme 2, k_o and k_c are the first-order rate constants in the absence of metal cation and in complex with metal cation, respectively.
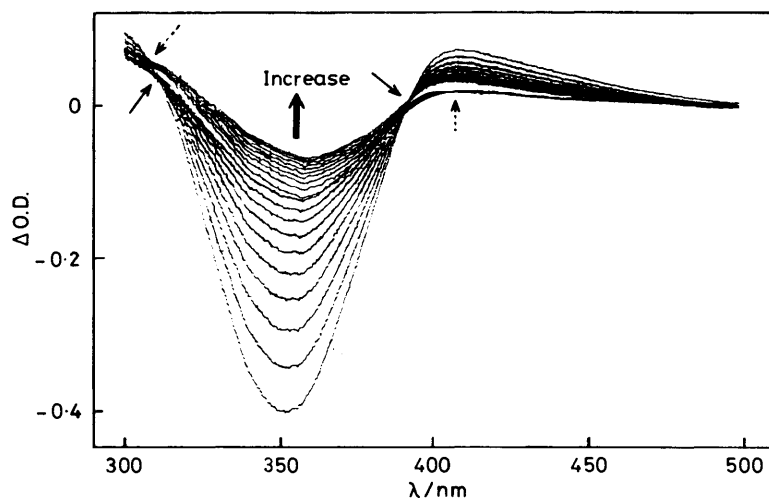
$$cis\text{-form} + M^+ \underset{}{\overset{K_c}{\rightleftharpoons}} cis\text{-form·}K^+$$

$$\downarrow k_o \qquad\qquad \downarrow k_c$$

$$trans\text{-form} \qquad\qquad trans\text{-form}$$

Scheme 2.

In the presence of an excess of M$^+$ over the *cis*-form, the relation in Scheme 2 is expressed by the kinetic Equation (1)

$$\frac{k_o}{k_o - k} = \frac{1}{qK_c[M^+]} + \frac{1}{q} \qquad (1)$$

which holds for the formation of a 1:1 complex, where $q = 1 - (k_c/k_o)$.[19] Plots of $k_o/(k_o - k)$ *vs.* [M$^+$]$^{-1}$ for Na$^+$ and

Figure 4. Difference spectra for thermal *cis*-to-*trans* isomerisation of (**3a**) (1.71 × 10⁻⁵M) in the absence and the presence of Ca(SCN)₂ (1.72 × 10⁻⁴M) in *o*-dichlorobenzene–methanol (5:1, v/v) at 30 °C. The solid arrows and the dotted arrows indicate the isosbestic points for the absence and the presence of Ca(SCN)₂, respectively. The spectra were scanned at 30 min time intervals. After 4.5 h Ca(SCN)₂ was added and the scan was further continued in the presence of Ca(SCN)₂

K⁺ according to Equation (1) gave good straight lines with a correlative coefficient better than 0.98. We estimated the slope (= $1/qK_c$) and the intercept (= $1/q$) from least-squares computation and determined k_c and K_c (Table 2). On the other hand, the plots for Rb⁺ and Cs⁺ did not give satisfactory straight lines. This is probably due to the formation of 1:2 metal/crown sandwich-type complexes.

Examination of Table 2 reveals that the k_c values for *cis*-(**3a**) are suppressed to 14—24% by the addition of Na⁺ or K⁺. This rate retardation corresponds to the energy difference of 3.5—5.0 kJ mol⁻¹. When the azobenzene moiety isomerises from *cis* to *trans*, it partly penetrates into the crown ether ring. Therefore, the metal cation nesting in the crown ether ring must be removed prior to, or simutaneously with, the thermal isomerisation. This requires an additional free energy of activation leading to the rate retardation. On the other hand, the rate retardation observed for *cis*-(**3c**) was only 60—66% (1.0—1.3 kJ mol⁻¹). The small inhibition effect can be rationalised again in terms of steric crowding: that is, the metal cations bound to more flexible *cis*-(**3c**) do not prevent the geometrical change of the azobenzene moiety as do the metal cations bound to *cis*-(**3a**). In azobis(benzocrown ethers) we obtained 4—7 kJ mol⁻¹ as an additional free energy of activation required for thermal isomerisation in the presence of the metal cations.[18] Therefore, the rate inhibition effect in the present system is relatively weak.

The K_c denotes the association constants between *cis*-forms and metal cations. As shown in Table 2, the K_c values for Na⁺ and K⁺ (log K_c = 4.07—4.81) are relatively large and comparable with those for 'regular' crown ethers (log K_c = 4—6 at 25 °C in methanol.)[1,20—22] If the *cis*-azobenzene group does not contribute to metal binding, such large K_c values would not be attained.[1–7] This suggests that one of the azo nitrogens in the *cis*-forms should contribute to metal binding. In order to obtain positive proof for the metal-nitrogen interaction, we carefully examined the absorption spectra in the absence of metal cations

Table 3. Extraction of alkali picrates (M⁺Pic⁻) with photoresponsive crown ethers[a]

Crown ether	Ex%					
	Li⁺	Na⁺	K⁺	Rb⁺	Cs⁺	NH₄⁺
trans-(**3a**)	0	0	17.9	10.3	10.9	7.46
Photoirradiated (**3a**)[b]	0	14.1	21.1	14.6	13.3	10.9
trans-(**3c**)	0	0	5.0	18.2	29.3	
Photoirradiated (**3c**)[b]	0	8.1	19.4	29.7	38.2	
trans-(**4**)	0	0	0	0	0	
Photoirradiated (**4**)[b]	0	0	0	0	0	

[a] Aqueous phase (3 ml):[M⁺Pic⁻] = 1.00 × 10⁻⁴M, [MCl] = 0.10M. Organic phase [*o*-dichlorobenzene–butan-1-ol (4:1, v/v)]: [crown ether] = 3.00 × 10⁻³M. 30 °C. [b] Contents of the *cis*-forms are recorded in Table 1.

and in their presence.† We have found that the n–π* absorption band of *cis*-(**3a**) changes significantly on the addition of metal cations. In the difference spectra for the thermal *cis*-to-*trans* isomerisation process, the maximum change (409 nm) shifted to 414 nm on the addition of NaClO₄ (0.50 mM). Ca²⁺ Which has a high cationic charge density induced a larger shift to 414 nm (Figure 4). Correspondingly, the different isosbestic points appeared in the presence of the metal cations. On the other hand, no spectral change was observed for *cis*-(**4**) under identical conditions. These spectral data offer support for one of the azo nitrogens contributing to metal binding. This metal-nitrogen interaction may be partly responsible for the retardation of thermal isomerisation.

Solvent Extraction of Alkali-metal Cations.—The photoresponsive ionophoric properties were evaluated through two-phase extraction of alkali picrates from water to *o*-dichlorobenzene–butan-1-ol (4:1, v/v). The extractability (Ex%) was determined from the picrate concentration decrease in the aqueous phase. The results are summarised in Table 3. Examination of Table 3 reveals the following facts: (i) neither *trans*-(**3**) nor *cis*-(**3**) could extract Li⁺; (ii) the dramatic 'all-or-nothing' photoirradiation effect is observed for Na⁺: for example *trans*-(**3a**) extracts no Na⁺ whereas *cis*-(**3a**) (mixture of *cis* and *trans*:

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† Gokel *et al.* reported that the metal-azo interaction can be detected by a cyclic voltammetric (c.v.) technique: A. Kaifer, D. A. Gustowski, L. Echegoyen, V. J. Gatto, R. A. Schultz, T. P. Cleary, C. R. Morgan, D. M. Goli, A. M. Rios, and G. W. Gokel, *J. Am. Chem. Soc.,* 1985, **107**, 1958. We carried out the c.v. measurements of (**3a**) in acetonitrile but could find no significant shift of the redox peaks in the presence of metal cations.
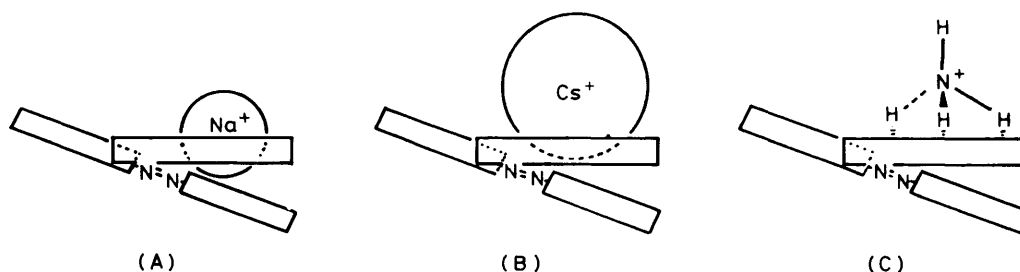
Figure 5. Schematic representation of (A) 'nest-in' complexation with Na$^+$. (B) 'perch-on' complexation with Cs$^+$, and (C) NH$_4^+$-crown complexation

see Table 1) extracts Na$^+$ in 14.1 Ex%; (iii) not only the *cis*-forms but also the *trans*-forms show the metal affinity with K$^+$, Rb$^+$, and Cs$^+$; (iv) the Ex% for *cis*-(**3a**) is in the order K$^+$ > Na$^+$, Rb$^+$ > Cs$^+$ while that for *cis*-(**3c**) is in the order Cs$^+$ > Rb$^+$ > K$^+$ > Na$^+$; and (v) the non cyclic compound (**4**) shows no metal affinity. The absence of the Li$^+$ affinity is in line with the absence of the inhibition effect on thermal isomerisation. Fact (iv) implies that the spheric recognition patterns, typical of crown ethers in solution, are reproduced in the present crown ethers with an intra-annular substituent: that is, the crown ether cavity of *cis*-(**3a**) best fits the ion radius of K$^+$ while that of *cis*-(**3c**) is somewhat greater than this, showing selectivity towards Cs$^+$.

Through the molecular design of (**3**) we expected that a dramatic Ex% change would take place in response to photo-irradiation because the *trans*-azo substituent could seriously interfere with the metal-crown interaction: such a phenomenon occurs in the extraction of Na$^+$. Unexpectedly, *trans*-(**3**) can extract alkali-metal cations larger than Na$^+$ although the Ex% values are always lower than those for *cis*-(**3**). It is difficult to envisage how *trans*-(**3**) interacts with metal cations, although one possible explanation makes use of the 'shallow floor' concept associated with cyclodextrin chemistry.[23] Since Na$^+$ is smaller than other metal cations under consideration, it should be deeply bound into the crown ring ('nest-in' complexation: Figure 5A) whereas other metal cations should be shallowly bound onto the crown ring ('perch-on' complexation: Figure 5B).[24] Thus, the shallow floor of the *trans*-azo substituent seriously affects the deep complexation with Na$^+$ but not the shallow complexation with other metal cations. In order to test this hypothesis we carried out solvent extraction of NH$_4^+$. It is known that the NH$_4^+$-crown complex is formed as a result of hydrogen-bonding between NH$_4^+$ and crown oxygens.[1,25–27] This is an example of the most shallow form of binding onto the crown ether ring and would, therefore, be less affected by the presence (*trans*-form) or the absence (*cis*-form) of the shallow floor (Figure 5C). The extraction data (Table 3) indicate, however, that the Ex% for *cis*-(**3a**) is significantly higher than *trans*-(**3a**). If the floor effect is absent in extraction of NH$_4^+$, the Ex% increase may be attributed either to a structural change in the crown ring or to favourable hydrogen bonding between NH$_4^+$ and one of the azo nitrogens. In summarizing these results, we consider that Ex% is governed not only by the direct 'floor effect' but also by the indirect conformational change of the crown ring induced by the configurational change in the intra-annular azo substituent.

Photocontrol of Ion Transport across a Liquid Membrane.—In ion transport we used (**3b**) instead of (**3a**) because the extractability and the ion-transport ability of crown ethers are largely improved by introducing lipophilic substituents.[28–30] Since the Ex% for Na$^+$ showed an 'all-or-nothing' change in response to photoirradiation, we chose Na$^+$ as a transport
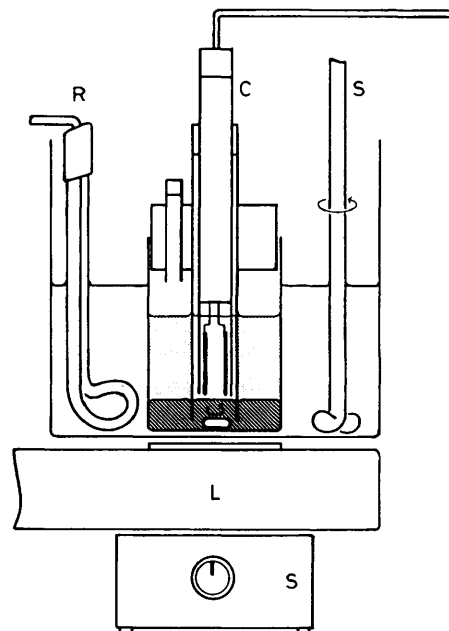

Figure 6. Membrane transport apparatus: R, temperature regulator; C, conductance cell; S, stirrer; L, Hg-lamp with a colour glass filter

metal cation. As a counteranion, on the other hand, we used tosylate ion instead of picrate ion, sodium picrate being partially soluble in the membrane phase [*o*-dichlorobenzene–butan-1-ol (4:1, v/v)] even in the absence of (**3b**). Firstly, we carried out two-phase extraction of sodium tosylate from the aqueous phase ([sodium tosylate] = 1.00 × 10^{-4}M, [NaCl] = 0.10M) to the membrane phase ([(**3b**)] = 3.00 × 10^{-3}M). Again, *trans*-(**3b**) could not extract Na$^+$ at all whereas *cis*-(**3b**) (mixture of *cis* and *trans*: see Table 1) extracted Na$^+$ in 10—12 Ex%.

Ion transport was carried out in a double-tube apparatus (*i.e.* Shulman bridge) as illustrated in Figure 6. In this apparatus the membrane phase becomes a thin layer, so that an efficient photoirradiation effect may be expected. This apparatus was immersed in a glass water-bath (30 °C) and the membrane phase was irradiated from the bottom of the water-bath through a colour glass filter for 15 min per 4 h. The concentration of *cis*-(**3b**) so photoirradiated was 50—60%. The progress of ion transport was monitored by the increase in electric conductance in the OUT aqueous phase and the Na$^+$ concentration transported was determined by using a calibration curve. Sodium tosylate permeated, although very slowly, through the liquid membrane even in the absence of (**3b**): this, we regarded as a background transport rate. We found that the rate of Na$^+$ transport across the liquid membrane containing *trans*-(**3b**)
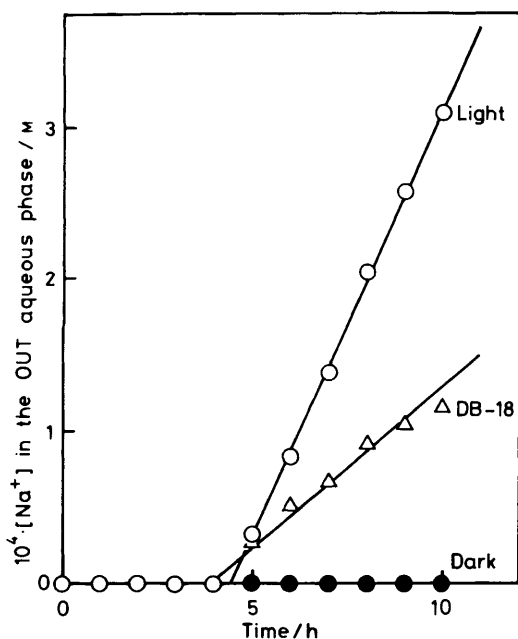
Figure 7. Transport of Na^+ across a liquid membrane [o-dichlorobenzene–butan-1-ol (4:1, v/v)] at 30 °C. IN aqueous phase (25 ml), [sodium tosylate] = 0.100M; OUT aqueous phase (5 ml); membrane phase (10 ml), [(3b) or DB-18(dibenzo-18-crown-6)] = 1.00 × 10^{-3}M

(1.00 × 10^{-3}M) is equal to the background rate, indicating that no Na^+ ion is carried by $trans$-(3b). Under u.v. light irradiation, on the other hand, the Na^+ concentration in the OUT aqueous phase increased linearly after an induction period ($ca.$ 4 h) (Figure 7): the net transport rate (v_{Na^+}) after reducing the background rate was 2.7 × 10^{-7} mol h^{-1}. This value is greater than the transport rate obtained for dibenzo-18-crown-6 (1.00 × 10^{-3}M) under identical conditions (v_{Na^+} = 1.4 × 10^{-7} mol h^{-1}). These results indicate that the $trans$-cis interconversion in (3b) creates a novel switch-functionalised membrane system in which the ion carrier acts as gate to control the transport rate in an 'all-or-nothing' manner.

$Conclusions$.—This study has demonstrated that photoregulation of metal binding to a crown ether ring can be achieved in an 'all-or nothing' manner by means of induced structural changes arising from the photoisomerisation of intraannular azobenzene. In extensions to membrane transport, it was found that the photoinduced 'all-or-nothing' change in the ion-binding ability could be used to transport Na^+ through the membrane only when u.v. light was irradiated. Therefore, further elaborations of the present system may lead to the eventual development of a series of photocontrollable membranes. Of particular interest is the light-driven active transport: that is, Na^+ may be transported against its concentration gradient from the photoirradiated phase to the dark phase since it cannot permeate the membrane in the dark. Further efforts are currently continued in this laboratory.

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$Received 3rd April$ 1986; $Paper$ 6/666