Redox-switched Crown Ethers. Part 2.† Redox-mediated Monocrown–Biscrown Interconversion and its Application to Membrane Transport

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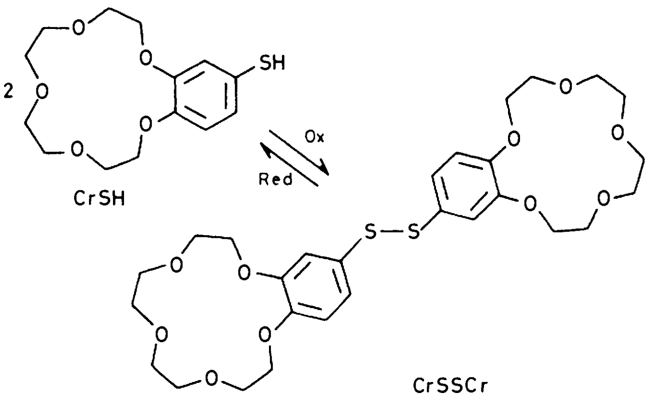
To give a redox-switch function to crown ethers, 4′-mercaptomonobenzo-15-crown-5 (CrSH), 4′-mercaptomethylmonobenzo-15-crown-5 ($CrCH_2SH$), and the corresponding oxidised forms (CrSSCr and $CrCH_2SSCH_2Cr$, respectively) were synthesized. The affinity of these crown ethers for metal, together with that of monobenzo-15-crown-5 (Cr), was evaluated by the solvent-extraction method. The results proved that (i) the affinity of CrSSCr for alkali-metal cations is almost equal to that of Cr, whereas CrSH has an affinity greater than CrSSCr probably because of the electron-donating effect of the 4′-mercapto group toward the metal-binding crown centre, and (ii) $CrCH_2SSCH_2Cr$ has an affinity for large alkali-metal cations greater than $CrCH_2SH$ because of the co-operative action of the two crown rings to form 1:2 cation–crown sandwich-type complexes. The formation of 1:2 complexes in $CrCH_2SSCH_2Cr$ was also supported by the concentration dependence of the extraction equilibrium and spectral analysis of alkali picrates in tetrahydrofuran. The difference between CrSSCr and $CrCH_2SSCH_2Cr$ was accounted for by a difference in conformational preference, *i.e.*, the *cis*-conformation of diphenyl disulphide is very unfavourable and the distance between the two crown rings is too short to sandwich a metal ion even though it adopts the *cis*-conformation, whereas the *cis*-conformer of $CrCH_2SSCH_2Cr$ can provide a moderate cavity consisting of the two crown rings due to the methylene groups. The redox function between $CrCH_2SH$ and $CrCH_2SSCH_2Cr$ was applied to ion transport across a liquid membrane. It was shown that in K^+ transport, (i) $CrCH_2SSCH_2Cr$ is a more efficient carrier than $CrCH_2SH$, and (ii) when $CrCH_2SH$ is oxidised to $CrCH_2SSCH_2Cr$ by iodine added to the membrane phase, the rate of the K^+ transport is efficiently accelerated.

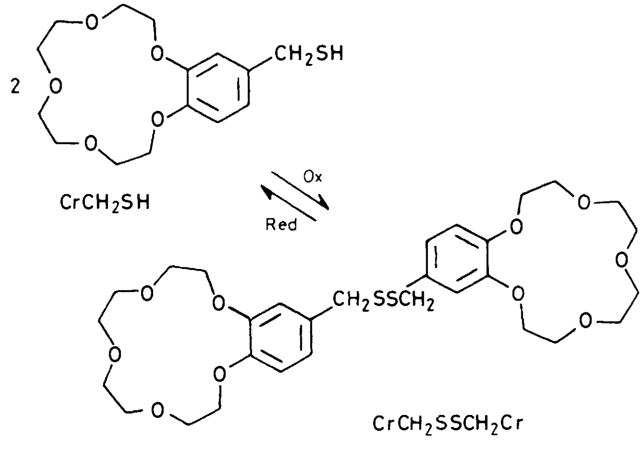
Cations are known to be transported through lipid membranes with the aid of synthetic macrocyclic polyethers as well as by antibiotics. Model studies with liquid membranes and macrocyclic polyethers have demonstrated that the best carrier for ion transport is a ligand that gives a moderately stable rather than a very stable complex.[1–3] This is a serious limitation on rapid ion transport through membranes. It is well known that natural ionophores such as monensin and nigericin skilfully overcome this limitation by utilising the interconversion between the cyclic and acyclic forms.[4,5] The phenomenon in nature suggests the idea that, if the binding ability of crown ethers is changed in response to some appropriate input, they could function as efficient ion-transport carriers. Thus, we and others have reported 'photoresponsive crown ethers' which change binding ability in response to light irradiation.[6–13] Photoresponsive surfactants and spiropyran derivatives are also useful to photocontrol the permeability of lipid membranes.[14,15] Similarly, Rebek *et al.*[16] reported a crown ether, the binding ability of which was controlled through the interaction between heavy metals and the incorporated 2,2′-bipyridyl unit.

Here, we report new 'redox-switched crown ethers', which change the binding ability in response to the level of redox potentials and thus serve as carriers in the redox-driven ion-transport system. In the past decade, various kinds of chemical potentials have been utilised to increase the rate of ion transport through membranes: pH difference,[17–24] difference in the ion concentration,[25] light energy,[7–11,14,15,26] energy of the thermal and photochemical redox systems,[27–29] *etc.* To the best of our knowledge, however, no precedent exists for the utilisation of redox-switched carriers in membrane transport. It occurred to us that the redox couple between thiol and disulphide, which is widely utilised in nature to maintain protein structure or to



CrSH

CrSSCr



$CrCH_2SH$

$CrCH_2SSCH_2Cr$

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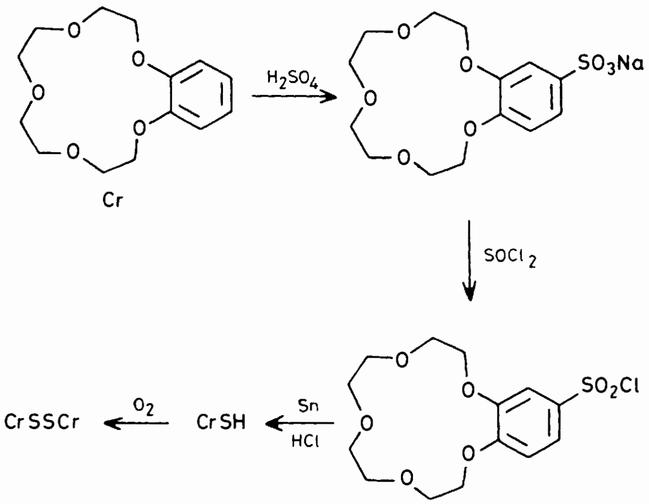
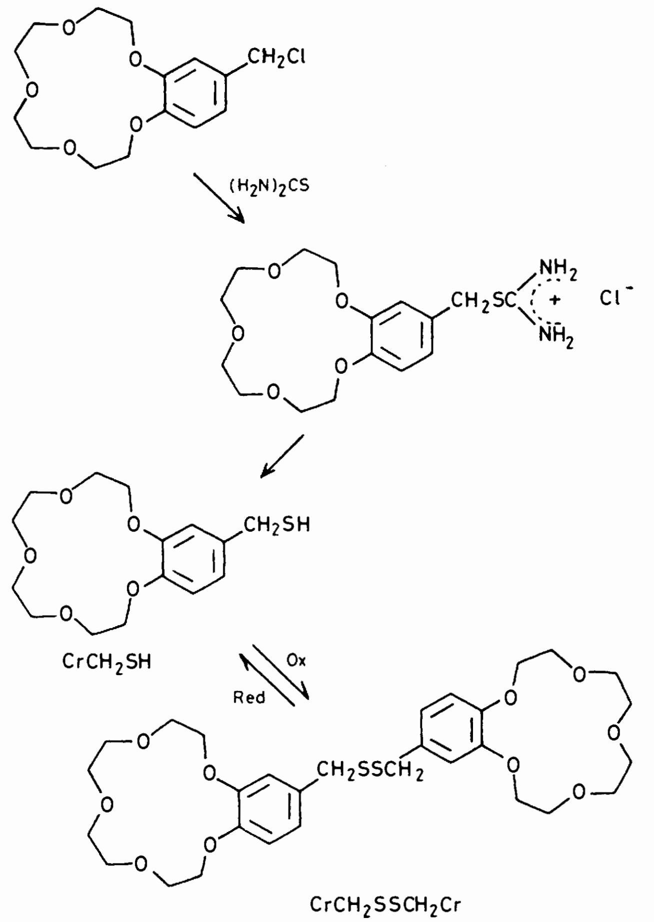
† Preliminary communication, T. Minami, S. Shinkai, and O. Manabe, *Tetrahedron Lett.*, 1982, **23**, 5167.



Scheme 1.



Scheme 2.

transfer electrons to and from mercapto coenzymes, would be most suitable for our requirements. We thus synthesized 4′-mercaptomonobenzo-15-crown-5 (CrSH), 4′-mercaptomethylmonobenzo-15-crown-5 (CrCH$_2$SH), and their oxidised forms (CrSSCr and CrCH$_2$SSCH$_2$Cr, respectively). We have found that both the ion-binding ability and the ion-selectivity change in response to the redox state of the crown ethers and that the redox-mediated interconversion between CrCH$_2$SH and CrCH$_2$SSCH$_2$Cr is applicable to the control of the rate of K$^+$ transport across a liquid membrane.

Experimental

Materials.—CrSH and CrSSCr were synthesized from monobenzo-15-crown-5 (Cr) according to Scheme 1. Cr (30 g, 0.114 mol) was added in several portions to concentrated H$_2$SO$_4$ (60 ml). Since the reaction was exothermic, the mixture was cooled in an ice-bath. After 30 min, the mixture was poured into ice–water and the solution was neutralised by CaCO$_3$. The hot solution was filtered to remove CaSO$_4$, and NaCO$_3$ was added to the filtrate until the solution pH was shifted to *ca.* 9. After cooling, the solution was filtered to remove CaCO$_3$, the filtrate being evaporated *in vacuo* to dryness. The residue [sodium (monobenzo-15-crown-5)-4′-sulphonate] was recrystallised from water, m.p. >280 °C, yield 78.7%; ν(KBr) 1 420 and 1 350 (SO$_3$) and 1 140—1 070 (C-O-C) cm^{-1} (Found: C, 44.9; H, 5.3. Calc. for C$_{14}$H$_{19}$O$_8$NaS: C, 45.4; H, 5.2%).

Sodium (monobenzo-15-crown-5)-4′-sulphonate (5.10 g, 0.014 mol) was dissolved in hot, anhydrous *N,N*-dimethylformamide (DMF) (50 ml) (a part of the material remained undissolved). After cooling in an ice-bath, thionyl chloride (3 ml) was added dropwise. The reaction was allowed to continue for 2 h at room temperature, and the mixture was poured into ice–water. The precipitate [(monobenzo-15-crown-5)-4′-sulphonyl chloride] was recovered by suction and dried *in vacuo*, m.p. 78—82 °C; yield 79.2%; ν(KBr) 1 370 (SO$_2$Cl) and 1 140—1 070 (C-O-C) cm^{-1} (Found: C, 45.5; H, 5.3; S, 8.5. Calc. for C$_{14}$H$_{19}$ClO$_7$S: C, 45.8; H, 5.2; S, 8.7%).

(Monobenzo-15-crown-5)-4′-sulphonyl chloride (4.0 g, 0.010 mol) was mixed with tin (shot; 4.0 g, 0.030 g-atom) in concentrated HCl (20 ml), and the mixture was shaken vigorously. The reaction proceeded at 100—110 °C with evolution of HCl gas. After 5 h at 100 °C, the mixture was poured into ice–water followed by extraction with chloroform. Evaporation of the chloroform solution resulted in the oily product (CrSH). Oily CrSH (2.3 g, 7.66 mol) was dissolved in methanol (25 ml) containing triethylamine (3 ml) and an oxygen stream was introduced. The precipitate (CrSSCr) was recovered by suction, m.p. 83—85 °C; yield 48.4%; *M*$^+$, 598; ν(KBr) 1 150—1 070 (C-O-C) cm^{-1}; δ(CDCl$_3$) 3.7—3.8 (m, CH$_2$ at C-8, -9, -11, and -12 in the crown rings), 3.84—3.94 (m, CH$_2$ at C-6 and -14 in the crown rings), 4.05—4.14 (m, CH$_2$ at C-5 and -15 in the crown rings), 6.75 (m, 3′-ArH), and 6.95—7.03 (m, 5′- and 6′-ArH) (Found: C, 55.75; H, 6.4; S, 10.55. Calc. for C$_{28}$H$_{38}$O$_{10}$S$_2$: C, 56.2; H, 6.4; S, 10.7%).

CrSSCr (0.87 g, 1.45 mmol) was reduced to CrSH with tin (shot) and concentrated HCl. The reaction mixture was poured into ice–water followed by extraction with chloroform. Evaporation of chloroform gave the solid product, m.p. 48—53 °C; yield 99.7% (Found: C, 53.25; H, 6.55. Calc. for C$_{14}$H$_{20}$O$_5$S: C, 56.0; H, 6.7%).

CrCH$_2$SH and CrCH$_2$SSCH$_2$Cr were synthesized from 4′-chloromethylmonobenzo-15-crown-5 [30] according to Scheme 2.

4′-Chloromethylmonobenzo-15-crown-5 (1.0 g, 3.16 mmol), mixed with thiourea (0.25 g, 3.28 mmol) in ethanol, was refluxed for 2.5 h, and the solvent was removed. The resultant oily product (thiuronium salt) was used for the following reaction without further purification. The thiuronium salt (1.2 g, 3.05 mmol) was added to an aqueous solution (50 ml) containing NaOH (0.2 g) and Na$_2$S$_2$O$_4$ (0.05 g). The solution was refluxed under N$_2$ for 2 h. After cooling to room temperature, the solution, adjusted to pH 4, was extracted with benzene. Evaporation of the benzene solution resulted in the oily product

($CrCH_2SH$), which was at once oxidised to $CrCH_2SSCH_2Cr$ for purification.

To an ethanol solution (10 ml) containing $CrCH_2SH$ (0.90 g, 2.86 mmol) was added I_2 in methanol until the colour of I_2 did not disappear. The precipitate was collected and subjected to t.l.c. [silica gel, ethanol–chloroform (1:10 v/v)] and finally recrystallised from methanol, m.p. 120—122 °C; yield 59.1%; M^+, 626; ν(KBr) 1 150—1 080 (C-O-C) cm^{-1}; δ($CDCl_3$) 3.55 (s, SCH_2), 3.7—3.8 (m, CH_2 at C-8, -9, -11, and -12 in the crown rings), 3.84—3.88 (m, CH_2 at C-6 and -14 in the crown rings), 4.04—4.12 (m, CH_2 at C-5 and -15 in the crown rings), and 6.71 (s, ArH) (Found: C, 57.2; H, 6.8; S, 10.4%. Calc. for $C_{30}H_{42}O_{10}S_2$: C, 57.5; H, 6.75; S, 10.2%).

$CrCH_2SH$ was synthesized by reduction of $CrCH_2SSCH_2Cr$ with tin (shot) and concentrated HCl. Although the product immediately after reduction gave a single spot on t.l.c., it was reoxidised rapidly. We thus abandoned the identification of $CrCH_2SH$ and used the fresh sample after reduction under anaerobic conditions.

Solvent Extraction.—The method of solvent extraction has been described in detail previously.[6–9] In this study, *o*-dichlorobenzene (DCB) solution (5 ml) containing the crown ether was agitated with aqueous solution (5 ml; pH 3.6 with H_3PO_4) containing alkali-metal cation. The extractability (Ex %) was estimated from the partition of counteranion [picrate(Pic) or 8-anilinonaphthalene-1-sulphonate (ANS)] between the organic and the aqueous phase. In the extraction with CrSH, both the organic and aqueous solutions were prepared with N_2-saturated solvents and the extraction was conducted in an anaerobic flask. In the extraction with $CrCH_2SH$, $CrCH_2SH$ reduced from $CrCH_2SSCH_2Cr$ was used immediately. $CrCH_2SSCH_2Cr$ (6.00×10^{-3}M) was reduced with $Na_2S_2O_4$ (1.20×10^{-3} M), and M_2CO_3 (1.2×10^{-3}M) (M^+ alkali-metal cation) in hot water for 15 min. The solution (2.5 ml) was withdrawn and mixed with an anaerobic aqueous solution (2.5 ml) containing M^+ (0.060M) and ANS (1.00×10^{-4}M) adjusted to pH 3.0 with H_3PO_4. Thus, the concentrations of each species in the final aqueous phase (pH 3.6) were 0.0321M-M^+, 0.0012M-Na^+, and 5.00×10^{-5}M-ANS. We neglected the influence of the concomitant Na^+ ion. In separate studies, we confirmed by a spectroscopic method that $CrCH_2SH$ is almost completely extracted into the DCB phase during the extraction treatment and by a t.l.c. method that $CrCH_2SSCH_2Cr$ is completely reduced to $CrCH_2SH$.

In order to determine the extraction equilibrium constants, DCB solution (5 ml) containing $CrCH_2SSCH_2Cr$ {[crown ether unit] = (3—10) × 10^{-4}M)} was shaken with an aqueous solution (5 ml) containing alkali picrate {[PicM] = (0.1—1) × 10^{-3}M} for 20 min at 30 °C. After the complete phase separation, DCB solution (200 ml) was added to Bu^{n}OH (3 ml). The concentration of the picrate was determined spectrophotometrically [$\lambda_{max.}$ 361 nm, ε (Na^+) 1.67, (K^+) 1.63, (Rb^+) 1.64, (Cs^+) 1.66 (× 10^4) l mol^{-1} cm^{-1}].

Ion Transport.—Transport of K^+ across a liquid membrane was examined within a **U**-tube which consisted of two (IN and OUT) aqueous phases (5 ml each) and a membrane phase [40 ml, DCB–Bu^{n}OH (1:1 v/v)]. The tube was immersed in a water-bath thermostatted to 30 °C, and the membrane was stirred at a constant speed (400 r.p.m.). Experiments which involved $CrCH_2SH$ were carried out under N_2.

Results and Discussion

Absorption Spectra of Alkali Picrates in Tetrahydrofuran (THF).—According to Smid *et al.*,[31] bathochromic shifts observed in the optical spectra of alkali picrates in THF on addition of crown ethers can be rationalised in terms of tight and loose ion pair–crown ether complexes. For example, the absorption maximum of potassium picrate ($\lambda_{max.}$ 357 nm) shifts to 381 nm on addition of excess of 15-crown-5. Conductance measurements indicated that the shift is due to the formation of a 1:2 cation–crown sandwich-type complex. Furthermore, they and others found that the absorption maximum ascribable to the sandwich-type complex is readily observable in the presence of bis(crown ether)s and polymeric crown ethers.[31–35] We used this method to distinguish whether or not CrSSCr and $CrCH_2SSCH_2Cr$ are capable of forming the intramolecular 1:2 cation–crown sandwich-type complexes. In Figures 1 and 2, OD_{380}/OD_{357} (for K^+) and OD_{380}/OD_{358} (for Rb^+) are plotted against the crown concentrations. The absorption maximum (380 nm) of the 1:2 cation–crown complex gradually appeared on addition of monobenzo-15-crown-5 (Cr). The addition of CrSSCr resulted in the plots essentially identical to those of Cr, indicating that the two crown rings of CrSSCr act quite independently. In contrast, the addition of $CrCH_2SSCH_2Cr$ resulted in the absorption maximum of the 1:2 cation–crown complex at very low crown concentrations. Thus,

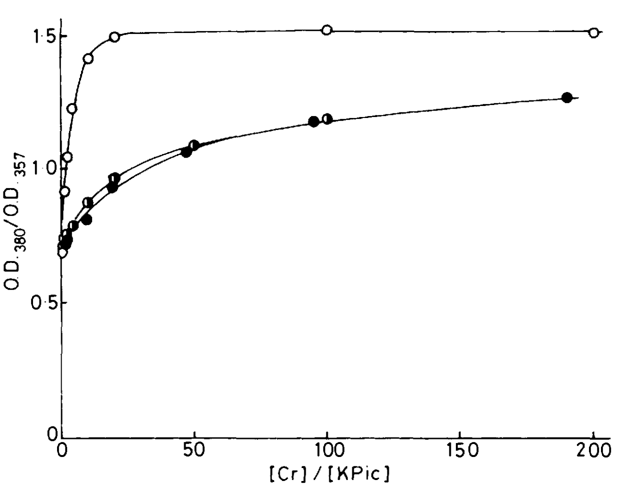


Figure 1. Influence of the added crown ethers on the absorption spectra of potassium picrate in THF. ● Cr; ◑ CrSSCr; ○ $CrCH_2SSCH_2Cr$. [KPic] 2.31×10^{-5}M

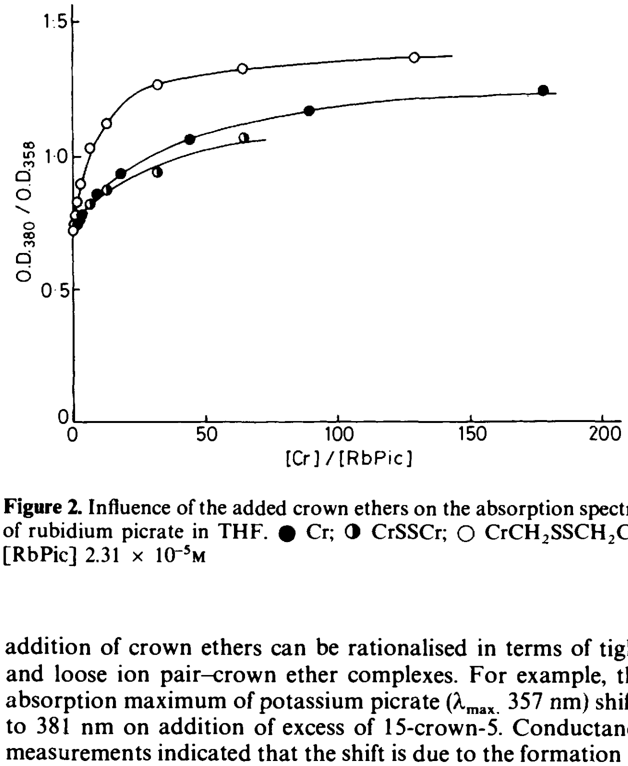
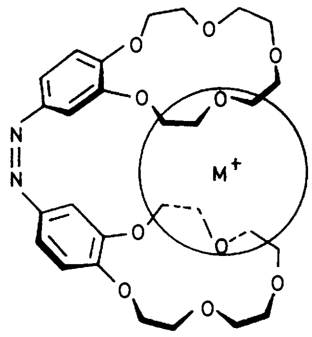
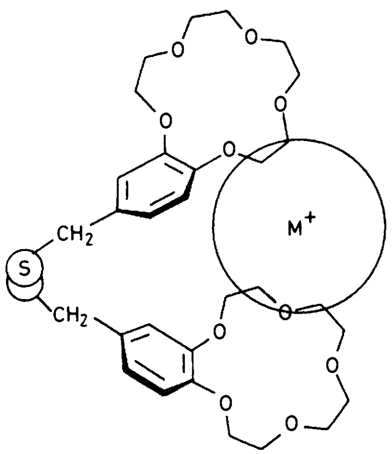


Figure 2. Influence of the added crown ethers on the absorption spectra of rubidium picrate in THF. ● Cr; ◑ CrSSCr; ○ $CrCH_2SSCH_2Cr$. [RbPic] 2.31×10^{-5}M



Sandwich-type complex with *cis*-azobis (monobenzo-15-crown-5)



Sandwich-type complex with $CrCH_2SSCH_2Cr$

the two crown rings of $CrCH_2SSCH_2Cr$ can act co-operatively on the binding of large alkali-metal cations such as K^+ and Rb^+.

We previously reported that *cis*-azobis(monobenzo-15-crown-5) forms a 1:2 cation–crown sandwich-type complex with K^+ and Rb^+.[7] The inability of CrSSCr to form the sandwich-type complex suggests that the *cis*-conformation of the disulphide linkage is energetically unfavourable. In fact, the azimuthal angle in the lowest-energy conformation of diethyl disulphide is considered to be 90°, and the bulky substituents further enlarge the angle.[36,37] Furthermore, the S–S–C valence angle is usually 105—107° which is significantly smaller than that of N=N–C in *cis*-azobis(monobenzo-15-crown-5).[38] As expected, the CPK model of CrSSCr in the *cis*-conformation showed that the distance between the two crown rings is too narrow to bind one alkali-metal cation. As a result, the two crown rings of CrSSCr cannot act co-operatively. In contrast, the CPK model of $CrCH_2SSCH_2Cr$ predicts that despite the unfavourable conformation of the disulphide linkage, the two crown rings are relatively flexible and can overlap each other owing to the two methylene groups. The foregoing spectral results are consistent with the following extraction results.

Solvent Extraction of Alkali-metal Cations.—The binding ability of four crown ethers was estimated by solvent extraction of alkali-metal salts from water to DCB and compared with that of Cr. We first tried to use picrate as counteranion for all crown ethers. We noticed, however, that in the extraction with $CrCH_2SH$ it is partially reduced either by $CrCH_2SH$ or by $Na_2S_2O_4$ remaining in the aqueous phase. We thus employed ANS to compare the extractabilities (Ex%) among Cr, $CrCH_2SH$, and $CrCH_2SSCH_2Cr$. The results are recorded in Tables 1 and 2.

Table 1. Solvent extraction of alkali-metal salts of picrate ion (Pic) into the organic phase (*o*-dichlorobenzene) at 30 °C[a]

	Extracted Pic(%)			
Metal	Cr	CrSH	CrSSCr	$CrCH_2SSCH_2Cr$
Na^+	11.7	15.6	14.3	23.6
K^+	42.6	77.1	42.9	98.9
Rb^+	16.3	25.9	14.8	84.1
Cs^+	12.5	16.4	12.9	39.3

[a] Organic phase: [crown ether unit] 6.00 × 10^{-4}M. Aqueous phase: 0.010M-MOH–0.0114M-H_3PO_4 (pH 3.6), [Pic] 1.00 × 10^{-5}M.

Table 2. Solvent extraction of alkali-metal salts of 8-anilinonaphthalene-1-sulphonate (ANS) into the organic phase (*o*-dichlorobenzene) at 30 °C[a]

	Extracted ANS(%)		
Metal	Cr	$CrCH_2SH$	$CrCH_2SSCH_2Cr$
Na^+	5.9	15.8	22.0
K^+	25.1	71.8	92.5
Rb^+	20.3	31.4	56.1
Cs^+	15.3	9.4	25.7

[a] Organic phase: [crown ether unit] 6.00 × 10^{-4}M. Aqueous phase: 0.030M-MOH–0.034M-H_3PO_4 (pH 3.6), [ANS] 5.00 × 10^{-5}M.

A number of points in these Tables are worthy of mention. First, Ex% values of CrSSCr are almost equal to those of Cr for all alkali-metal cations. The result suggests again that the two crown rings of CrSSCr behave independently and do not exhibit a co-operative action, for example, to form a 1:2 cation–crown complex. Second, Ex% values of CrSH are significantly higher than those of Cr. In particular, the Ex% value for K^+ was greatly enhanced. The difference can be explained in two ways. One possible explanation is that the change in lipophilicity is responsible for the improved extractability. The performance of crown ethers in solvent extraction is effectively improved by lipophilic substituents.[39–42] Hence, if CrSH is more lipophilic than Cr, CrSH should give higher extractability than Cr. We consider, however, that this is probably not the case in the present system, because CrSSCr, which is undoubtedly more lipophilic than Cr, results in an extractability similar to Cr. Another possible explanation is that the improved binding ability of CrSH is attributed to the electronic nature of the 4'-mercapto group. It is known that the association constants of monobenzo-15-crown-5 series are enhanced by electron-donating substituents at the 4'-position: for example, a good Hammett correlation with a negative slope is found by plotting log K (association constant) against σ for nine 4'-derivatives.[43] The Hammett σ values for SH and SCH_3 are usually positive or slightly negative (*e.g.*, σ_p for SH, −0.01), whereas SCH_3 has a large negative σ^+ value (−0.640).[38,44] We consider, therefore, that the improved binding ability of CrSH relative to Cr is mainly due to the σ^+-type electron-donating nature of the 4'-mercapto group toward the metal-binding 'cationic' crown centre.

Thirdly and most importantly, Ex% values of $CrCH_2SH$ are somewhat greater, except that for Cs^+, than those of Cr, and Ex% values of $CrCH_2SSCH_2Cr$ are further enhanced. In particular, the distinct difference between $CrCH_2SH$ and $CrCH_2SSCH_2Cr$ is seen for large alkali-metal cations. The improved extractability of $CrCH_2SH$ relative to Cr may be again rationalised in terms of the electron-donating nature of the mercaptomethyl group to the 'cationic' crown ring. On the other hand, the foregoing spectral data support the idea that the further increase in extractability of $CrCH_2SSCH_2Cr$ is accounted for by the formation of a 1:2 cation–crown complex.

The extraction equilibrium constants (K_e) and complexation constants (K_c) of $CrCH_2SSCH_2Cr$ with K^+ and Rb^+ were estimated on the basis of the extraction method. In the solvent extraction relations (1)—(3) have been derived,[33,34,45–47] where

$$D = K_e(M_0 - A)(Cr_0 - A) \qquad (1)$$

$$D = K_e(M_0 - A)(Cr_0 - 2A)^2 \qquad (2)$$

$$D = K_e(M_0 - A)(Cr_0 - 2A) \qquad (3)$$

D is the distribution ratio of the metal between two phases, and M_0, Cr_0, and A denote the initial concentrations of the metal cations and the crown ether unit, and the concentrations of the picrates extracted into the organic phase as the counteranions, respectively. Equations (1) and (2) are applied when 1:1 cation–crown complexes and 1:2 cation–crown complexes are formed by monomeric crown ethers, respectively. On the other hand, when intramolecular 1:2 cation–crown complexes are formed by poly- and bis-(crown ether)s, equation (3) should be applied.

In order to obtain evidence that $CrCH_2SSCH_2Cr$ forms intramolecular 1:2 cation–crown complexes, we conducted the extraction experiments at various concentrations of K^+ and Rb^+. We found that the data obtained from $CrCH_2SSCH_2Cr$ well satisfy equation (3), *i.e.*, the plots of logarithms of both sides gave straight lines with slopes close to unity (1.07—1.08, Figure 3). The result clearly suggests that the stoicheiometry of the $CrCH_2SSCH_2Cr$ complexes with K^+ and Rb^+ is of an intramolecular 1:2 cation–crown-type. The K_e values were estimated by least-squares computation of the linear relationships in Figure 3. The K_c values were obtained by

$$K_c = K_e/K_d \qquad (4)$$

equation (4),[45–47] where K_d is the distribution constant of the picrates in the absence of crown ethers in water–DCB system (K^+ 0.639, Rb^+ 0.880 l mol^{-1}). We thus obtained K_e $10^{5.65}$ l^2 mol^{-2} and K_c $^{105.84}$ l mol^{-1} for K^+ and K_e $10^{4.92}$ l^2 mol^{-2} and K_c $10^{4.98}$ l mol^{-1} for Rb^+. The K_c values of $CrCH_2SSCH_2Cr$ in DCB are slightly greater than those of poly-(4′-vinylmonobenzo-15-crown-5) in dichloromethane (log K_c for K^+ 4.70)[48] but smaller than those of poly-(4′-acrylamidomonobenzo-15-crown-5) and its biscrown analogue in chloroform (log K_c for K^+ 10.3 and 9.20, respectively),[47] which are known to form intramolecular 1:2 cation–crown complexes.

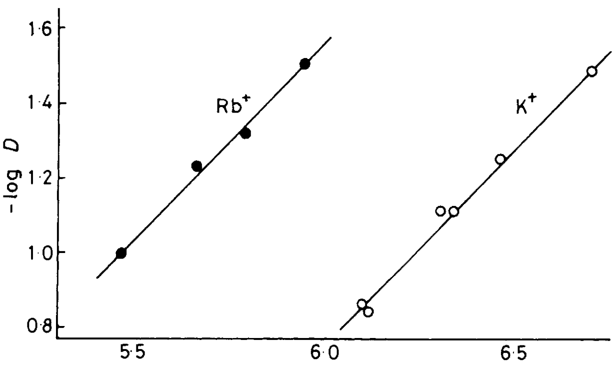


Figure 3. Plots of $-\log D$ *versus* $-\log(M_0 - A)(Cr_0 - 2A)$ for $CrCH_2SSCH_2Cr$ in water–DCB system at 30 °C. [PicM] (0.1—1) × 10^{-3}M, [crown ether unit] (3—10) × 10^{-4}M

According to Eisenman and Horn,[49] 'selectivity' can be classified into two sequences, Eisenman sequences and polarizability sequences. In the Eisenman sequences the plots of free energies of complex formation *versus* reciprocal cation radius give optima to intermediate sized ions, whereas the polarizability sequences would be described by upwardly concave curves having a single minimum. Thus, the selectivity observed in Tables 1 and 2 can be regarded as an example of the Eisenman sequences (case IV).

As described in the Introduction, the best carrier for ion transport across a liquid membrane is a ligand that gives a moderately stable rather than a very stable complex. This strange phenomenon occurs because the very stable complex cannot release the ion efficiently to the OUT aqueous phase. As a result, the maximum rate of ion transport arises with carriers having K_c *ca.* 10^6.[1–3] We thus expected that interconversion between $CrCH_2SH$ and $CrCH_2SSCH_2Cr$ may lead to the acceleration of K^+ transport.

K^+ *Transport controlled by Interconversion between* $CrCH_2SH$ *and* $CrCH_2SSCH_2Cr$.—We set up a **U**-type transport apparatus and evaluated the influence of redox interconversion on the rate of K^+ transport to the OUT aqueous phase under anaerobic conditions. We used 1-naphthoic acid instead of picrate ion as a counteranion, because the redox properties of picrate ion are unfavourable to the redox treatment of the membrane phase. The liquid membrane is DCB:Bu^{n}OH (1:1 v/v). The rate of K^+ transport was determined by monitoring the increase in the K^+ concentration in the OUT aqueous phase by atomic absorption spectroscopy. We also measured the time-dependence of 1-naphthoate in the OUT aqueous phase by absorption spectroscopy: the rates obtained by this method were in good accord with those determined by atomic absorption spectroscopy (within 4%). This means that K^+ ion permeates the liquid membrane in the form of $C_{10}H_7COO^- K^+$.

The concentration of $CrCH_2SH$ in the membrane phase was estimated qualitatively by a t.l.c. method and quantitatively by iodometry. In entry 4 where the ion transport was started with $CrCH_2SH$, the aliquot of the membrane phase was withdrawn after 10 h and subjected to iodometry. It showed that 90—96% $CrCH_2SH$ remains unoxidised. In entry 5, iodine ($[I_2]$ = 0.5$[CrCH_2SH]$) was added to the membrane phase after 6 h. We corroborated by t.l.c. that $CrCH_2SH$ has been oxidised to $CrCH_2SSCH_2Cr$ within 30 min in the membrane phase. Similarly, the reverse reaction ($CrCH_2SSCH_2Cr \longrightarrow 2CrCH_2SH$) could be effected by the addition of tri-n-butylphosphine ($[Bu\text{-}_3P]$ = 10 $[CrCH_2SSCH_2Cr]$) to the membrane phase. The reduction finished in 1.5 h. The typical time-dependences of K^+ transport are illustrated in Figure 4. Usually, the linear increase in K^+ concentration appeared after an induction period (*ca.* 1 h). From the linear portions we calculated the rates of K^+ transport. The results are recorded in Table 3.

Table 3 shows that $CrCH_2SSCH_2Cr$ is 3.2 times as effective a carrier as $CrCH_2SH$ and that the rate with $CrCH_2SSCH_2Cr$ increases with increasing K^+ concentration in the IN aqueous phase. In entry 5, the rate of K^+ transport after I_2 addition was enhanced to 0.22 μmol h^{-1}, which is greater by a factor of 3.4 than the initial rate of K^+ transport with $CrCH_2SH$. The rate increase can be ascribed to the production of the capable ion-carrier in the membrane phase by treatment with the oxidising agent. The fact that $CrCH_2SSCH_2Cr$ with larger K^+ extractability always gives the larger transport rates suggests that ion-extraction from the IN aqueous phase to the membrane phase is rate-limiting. We also attempted the reverse control of K^+ transport by reducing $CrCH_2SSCH_2Cr$ to $CrCH_2SH$ (entries 6 and 7). As shown in Table 3, the rates did not increase on the reduction treatment. In entry 7, we increased the K^+

Table 3. Rate of K^+ transport across a liquid membrane (50 vol% DCB + 50 vol% Bu^nOH) at 30 °C[a]

Entry	Added crown	IN aqueous phase (mM) [KCl]	[KOH]	[1-NA][c]	Rate of K^+ transport (mol h^{-1})
1	$CrCH_2SSCH_2Cr$	1 000	20	5	1.24
2	$CrCH_2SSCH_2Cr$	500	20	5	0.86
3	$CrCH_2SSCH_2Cr$	100	16	1	0.20
4	$CrCH_2SH$	100	16	1	0.062
5[b]	$CrCH_2SH$	100	16	1	0.064
	$\longrightarrow CrCH_2SSCH_2Cr$				$\longrightarrow 0.22$
6[b]	$CrCH_2SSCH_2Cr$	100	16	1	0.22
	$\longrightarrow CrCH_2SH$				$\longrightarrow 0.16$
7[b]	$CrCH_2SSCH_2Cr$	1 000	20	5	1.26
	$\longrightarrow CrCH_2SH$				$\longrightarrow 1.04$

[a] [Crown ether unit] 2.0 × 10^{-4}M, pH(IN) 6.2—6.4 with 0.010M-phosphate, pH(OUT) 6.1 with 0.015M-phosphate. [b] The buffer concentrations are enhanced to 0.05M in order to suppress the pH change. [c] 1-Naphthoic acid.

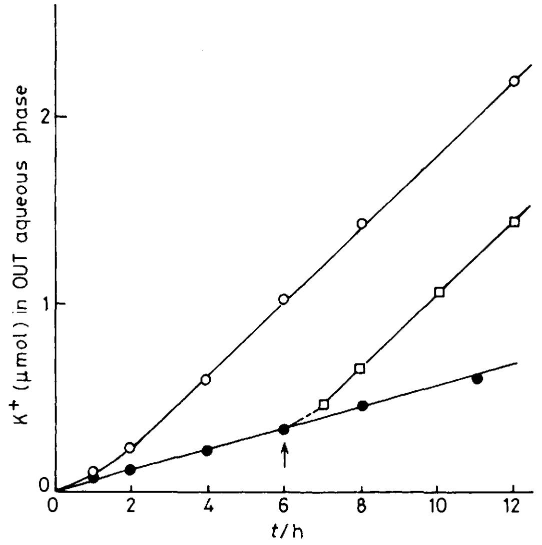


Figure 4. Transport of K^+ across a liquid membrane at 30 °C: ○ entry 3, ● entry 4, □ entry 5. The plots of entry 5 before I_2 addition are almost equal to those of entry 4. The arrow mark at 6 h indicates the time when I_2 was added

concentration in the IN aqueous phase to 1.0M expecting efficient ion-extraction into the membrane phase. However, the reduction to $CrCH_2SH$ did not lead to a significant rate increase. This indicates, probably, ion extraction still to be rate-limiting. Strangely, the rate after reduction (entry 6, 0.16 μmol h^{-1}) was much faster than the corresponding transport rate with $CrCH_2SH$ (0.062 μmol h^{-1}). Probably, K^+ ion extracted by $CrCH_2SSCH_2Cr$ before the reduction was released gradually to the OUT aqueous phase even after $CrCH_2SSCH_2Cr$ was reduced to $CrCH_2SH$.

Conclusions.—The present study demonstrated that with the aid of the redox-functionalised crown ethers, ion extraction and ion transport across a liquid membrane can be controlled by redox potentials. These novel phenomena are possible because these crown ethers have, within the molecule, a redox switch which accepts redox energy from the outside and a crown ether which acts as a functional group to recognise and carry metal ions. In other words, the redox-switched crown ethers mimic some natural antibiotics using redox energy as a trigger. Although the framework of redox-driven ion transport must be further improved, we expect that this concept might lead to a more generalised method to control the chemical and physical functions of the crown ether family by the redox energy source.

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