

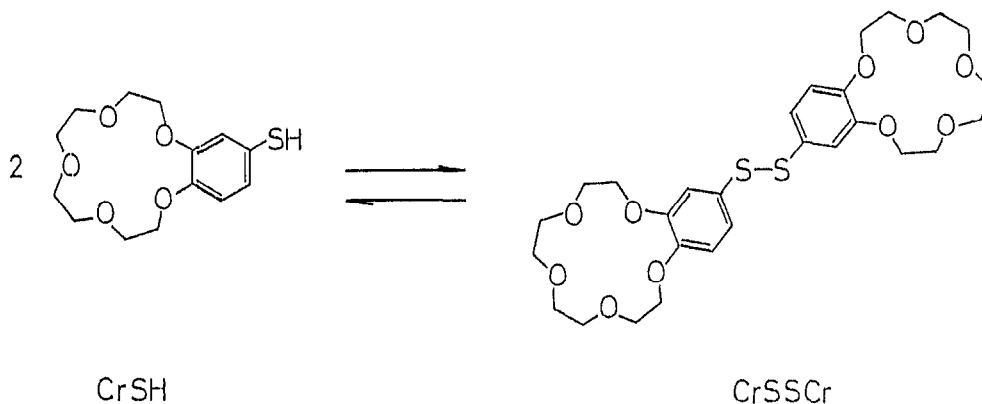
REDOX-SWITCHED CROWN ETHERS
MONOCROWN-BISCROWN INTERCONVERSION COUPLED
WITH REDOX OF A THIOL-DISULFIDE COUPLE

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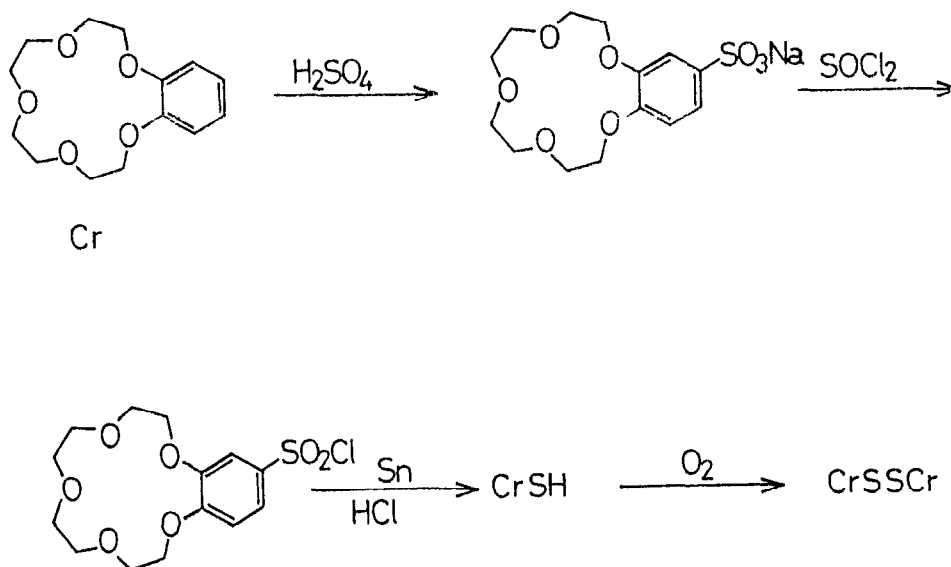
To give a redox-switch function to crown ethers, 4'-mercaptomono-benzo-15-crown-5(CrSH) and its oxidized disulfide form (CrSSCr) were synthesized. The solvent extraction proved that the ion affinity of CrSH is generally greater than that of CrSSCr.

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 membrane systems have demonstrated that the best carrier for the ion-transport is a ligand that gives a moderately stable rather than a very stable complex.¹⁻³⁾ This is a serious limitation on the rapid ion-transport through membranes. It is well-known that natural ionophores such as monensin and nigericin skillfully break the limitation by utilizing the interconversion between the cyclic and the acyclic form.⁴⁾ The phenomenon in nature suggests an idea that, if the binding ability of crown ethers is changed in response to some appropriate input, they would function as efficient ion-transport carriers. Thus, we and others have reported "photoresponsive crown ethers" which change the binding ability in response to light irradiation.⁵⁻⁹⁾ Similarly, Rebek et al.¹⁰⁾ 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 wish to report a new "switched-on crown ether" which exhibits a monocrown-biscrown interconversion coupled with redox of a thiol-disulfide couple. The reduced form (CrSH) is oxidized by molecular oxygen or hydrogen peroxide while the oxidized form (CrSSCr) is reduced by sodium dithionite back to CrSH, the interconversion being completely reversible. Hence, if CrSH and CrSSCr have different binding constants, this would become a potential candidate for the rapid ion-transport through membranes.



CrSH(oil) and CrSSCr(mp 83-85°C) were synthesized from monobenzo-15-crown-5 (Cr) according to the following reaction sequence and identified by IR, NMR, mass spectrum, and elemental analysis.



The binding ability of CrSH and CrSSCr was estimated by preliminary solvent extraction of alkali picrates from water to *o*-dichlorobenzene and was compared with that of Cr. The extractability(Ex) was determined by the partition of picrate ion between the aqueous and the organic phase. The pH of the aqueous phase was buffered to 3.6 where picric acid is fully dissociated while CrSH is undissociated. To compare the extractability of the crown ether unit, the concentration of CrSSCr (3.00×10^{-4} M) was reduced to half of that of CrSH and Cr (6.00×10^{-4} M). The results are summarized in Table 1.

Table 1. Extraction of alkali metal salts of picrate ion with CrSH, CrSSCr, and monobenzo-15-crown-5(Cr) from water to o-dichlorobenzene.^{a)}

Metal	Ex (%)		
	CrSH	CrSSCr	Cr
Na ⁺	15.6 (13.3) ^{b)}	14.3	11.7
K ⁺	77.1 (54.9) ^{b)}	42.9	42.6
Rb ⁺	25.9 (13.3) ^{b)}	14.8	16.3
Cs ⁺	16.4 (13.9) ^{b)}	12.6	12.5

a) 30°C. Organic phase [CrSH] = [Cr] = 6.00×10^{-4} M or [CrSSCr] = 3.00×10^{-4} M in o-dichlorobenzene. Aqueous phase pH 3.6 with H₃PO₄ (0.0114 M)-MOH(0.0100 M), [picric acid] = 1.00×10^{-5} M.

b) [CrSH] = 3.00×10^{-4} M.

The examination of Table 1 reveals that Ex's of CrSSCr are almost in accord with those of Cr about all alkali metal cations. The finding suggests that two crown rings of CrSSCr behave independently and do not exhibit a cooperative action, for example, to form an intramolecular 1 2 metal/crown complex. On the other hand, CrSH had the ion-binding ability significantly higher than CrSSCr. In particular, the Ex for K⁺ was greatly improved.

The similar result was obtained when the concentration of extracted K⁺ was determined by atomic absorption spectrophotometer. That is, when equal volumes of a chloroform solution containing 6.00×10^{-4} M of crown and an aqueous solution containing 0.3 M of KCl and 1.00×10^{-3} M of picric acid (pH 4.0 with 0.013 M phosphate) were agitated thoroughly, the percentages of the ion-complexed crown in the organic phase were 7.7%, 3.6%, and 2.7% for CrSH, CrSSCr, and Cr, respectively.

The foregoing results consistently indicate that the ion-binding ability of CrSH is enhanced owing to the 4'-sulfhydryl group, whereas CrSSCr has no intramolecular cooperativity that some bis(crown ether)s exhibit. According to Ungaro et al.,¹¹⁾ the association constants of monobenzo-15-crown-5 series are enhanced by electron-donating 4'-substituents. It is known that Hammett's σ 's for thiols and thioethers are positive, whereas the σ^+ 's are considerably negative. Conceivably, the high ion-binding ability of CrSH is attributed to the electron-donating nature of 4'-SH toward the metal complexed "positive" crown ring.

Meanwhile, we previously reported that *cis*-azobis(benzo-15-crown-5) forms a 1 2 metal/crown sandwich-type complex with K^+ .⁶⁾ When comparing the structure of CrSSCr with *cis*-azobis(benzo-15-crown-5), we notice that diphenyl disulfide preferably adopts the *trans* conformation^{12,13)} and the disulfide bond angle is too small to sandwich a metal ion.¹³⁾

Although further improvement in the molecular design is necessitated, the present study demonstrates for the first time that the redox reaction between thiol and disulfide is useful to give a switch-function to a crown ether family.

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