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SYNTHESIS OF NOVEL BISCROWN ETHERS WITH INTERCONVERTIBLE REDOX STRUCTURES

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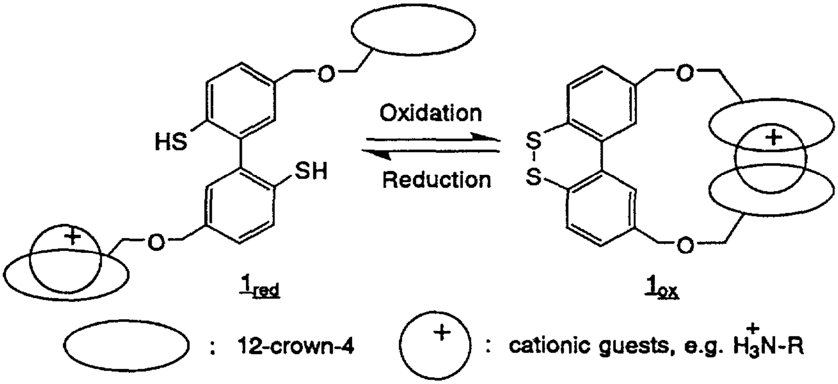
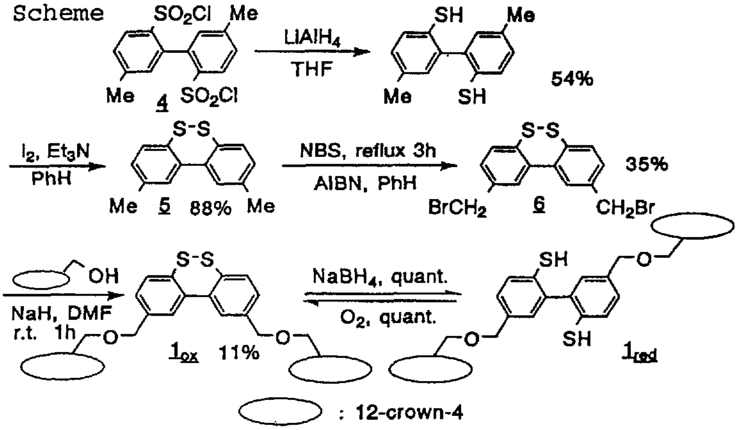
Abstract: Sulfur containing biscrown ethers 1_{red} and 1_{ox} have been synthesized, which are interconverted quantitatively by redox reactions between thiol and disulfide. Recognition ability for ammonium salt was found to be dependent upon the redox structures.

Interconversion between molecules having different structures is one of the most useful methods to control binding affinity to cations in biological[2] as well as artificial ionophores,[3] where stimuli, such as electron, photon, metal ion, etc., cause different spacial arrangement and configurational or conformational change of the original recognition sites for cations. We intended to construct an artificial ionophore, whose affinity to cations can be regulated by an external stimulus to change the specific recognition field. Now we wish to report synthesis and cation-binding properties of novel ionophores 1_{ox} and 1_{red}, which are interconvertible by redox reactions.

Synthetic route is shown in the Scheme. The bromination of 5 seems to be very curious, in view of general tendency that disulfide linkages are cleaved readily by the reaction with NBS or bromine to afford the corresponding oxidized products after hydrolysis.[5] This unusual inertness of the disulfide bond should have come from the proximity effect of the two sulfur atoms in 5 with cyclic structure:[6] even if the -SS- bond in 5 is



Scheme



cleaved, intramolecular regeneration of the bond takes place very easily because of the proximate location. The desired ionophore $\underline{1}_{ox}$ was obtained in 11% yield by the reaction of $\underline{6}$ with hydroxylmethyl-12-crown-4 and NaH. The $NaBH_4$ reduction of $\underline{1}_{ox}$ yielded $\underline{1}_{red}$, which was easily reverted to $\underline{1}_{ox}$ by molecular oxygen. The structures of these artificial ionophores were ascertained unambiguously by the 500 MHz ^1H NMR spectra. Due to the proximity effect, the interconversion between $\underline{1}_{ox}$ and $\underline{1}_{red}$ was achieved almost quantitatively, judging from the ^1H NMR spectra and TLC.

In order to evaluate the affinity of $\underline{1}$ to ammonium salt as a cationic guest, a solution of $\underline{1}$ in 1,2-dichloroethane (1.0×10^{-4} M, 5ml) was mixed vigorously with an aqueous solution of p-bromobenzylammonium picrate (1.36×10^{-5} M, 5ml) at room temperature. After reaching equilibrium, the extractability[7] was determined spectrophotometrically.[3] Compared to $\underline{1}_{red}$ (3%), higher extractability (15%) in $\underline{1}_{ox}$ implies that the two 12-crown-4 rings of $\underline{1}_{ox}$ capture the two ammonium protons of the one guest molecule more strongly in a face-to-face fashion than those of $\underline{1}_{red}$. Detailed study of the affinity of $\underline{1}_{red}$ and $\underline{1}_{ox}$ is now in progress.

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7. Extractability(%) = $[\text{ammonium}]_{org}/[\text{ammonium}]_{aq,0} \times 100$
$[\text{ammonium}]_{org}$ = conc. of ammonium picrate in organic phase
$[\text{ammonium}]_{aq,0}$ = initial conc. of ammonium picrate in aqueous phase

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