Synthesis of 1,4-Benzoquinone Derivatives Having Two Side-Armed Polyethers and Crown Ethers, and Their Electrochemical Study in the Presence of Alkali Metal Cations (Na^+ and K^+)

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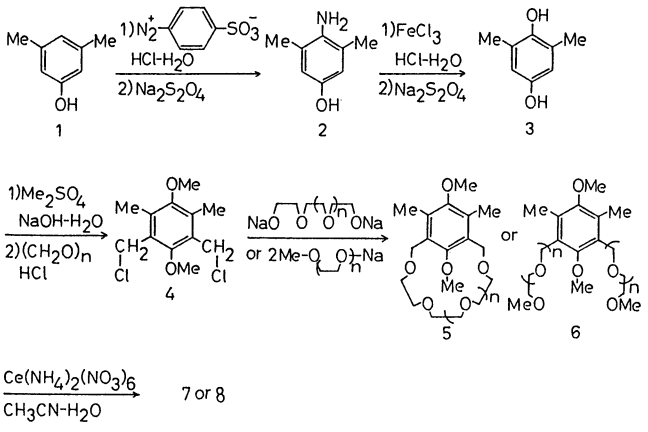
Synopsis. Several crown ethers and two side-armed polyethers which have reducible quinonoid groups were prepared. Some of them, **7a**, **7b**, and **7d**, showed highly enhanced cation-binding properties for the Na^+ cation upon electrochemical reduction.

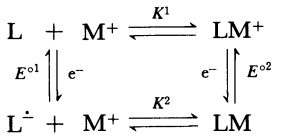
The design of redox-switched crown ethers and polyethers has been achieved by several researchers. The reducible functions involved in these compounds are disulfide,[1] quinone derivatives,[2] and nitrobenzene.[3] Their complexation abilities with metal cations are accelerated by the interaction of metal cations and polyether functions, and also by the ionic interaction of reduced functions with metal cations upon electrochemical reduction. In general, Li^+ has a large binding enhancement in most of the redox crowns or polyethers due to the strong affinity of Li^+ to heteroatoms, i.e. oxygen or nitrogen during electrochemical reduction.[2,3] In the case of Na^+ and K^+, the binding enhancements depend on the structures of the host compounds; it is a very interesting problem to determine the new redox-switched compounds which have large binding enhancements for Na^+ and K^+ cations. Here, we report on a series of crown ethers and two side-armed polyethers having quinonoid groups as well as their cyclic voltammetric studies, both in the presence and absence of metal cations (Na^+ and K^+).

Results and Discussion

We prepared the compounds **7a—d** and **8a—c**, which were obtained from 3,5-dimethylphenol by the following procedure.



Cyclic voltammetric studies of **7** and **8** in acetonitrile were carried out in the presence of metal cations, Na^+ and K^+, in order to examine the relative complexing abilities of the neutral ligand and the reduced one with metal cations; the binding enhancement, K^2/K^1, upon a one-electron reduction was obtained from the shift values ($E^{o1}-E^{o2}$) by Eq. 1.[3]



$$K^2/K^1 = \exp\left\{-\frac{F}{RT}(E^{o1}-E^{o2})\right\} \quad (1)$$

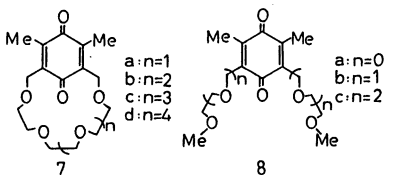
L : ligand, M^+: metal cation,
K^1 : binding constant for the neutral ligand,
K^2 : binding constant for the reduced ligand,
E^{o1} : redox potential for the free ligand,
E^{o2} : redox potential for the complex.

The binding enhancements and other electrochemical results are summarized in Table 1. In **7a**, the presence of Na^+ cation results in the observation of a new reduction peak, which corresponds to a one-electron reduction of the complex of crown **7a** and the Na^+ cation.

The cyclic voltammogram for the K^+ cation is reversible and the potential shift is small (0.10 V). Obviously, **7a** forms a 1-to-1 complex with Na^+ and K^+ cations during a one-electron reduction. Compounds **7b** and **7c** also form 1-to-1 complexes, both with Na^+ and K^+ cations, as shown in Table 1; compound **7b**, which has been reported by Cooper,[2a] exhibits large binding enhancements in both Na^+ and K^+ cations in acetonitrile, although Cooper used *N,N*-dimethylformamide as a solvent. Compound **7c** exhibits a small binding enhancement with both Na^+ and K^+ cations. Compound **7d** forms a 1-to-2 complex with the Na^+ cation, and its binding enhancement was the largest in the present ligands. On the other hand, **7d** forms a 1-to-1 complex with the K^+ cation and the binding enhancement was small. The binding enhancements of **8a—c** were found to be very small, though single-armed anthraquinone derivatives have large binding enhancements (ca. 10^2).[2c] We believe that one of the reasons is the result of a steric hindrance between two arms of **8** in the formation of a complex with metal cations during electrochemical reduction.

Experimental

Apparatus. ^1H NMR spectra were obtained on a JEOL FX-100 spectrometer. The chemical shifts are in ppm using TMS as an internal standard. IR spectra were measured on a



7 8

Table 1. Cation Dependance of Quinone Electrochemistry[a)]

Compound	M^+	Equiv	E^{c1}	E^{a1}	E^{o1}	E^{c2}	E^{a2}	E^{o2}	ΔE^{1-2}	Binding Enhancement (K^2/K^1)
7a[d)]	None	—	−0.67	−0.53	−0.60	—	—	—		
	Na^+	0.5	−0.64	−0.55	−0.60	−0.46	—	—	0.18[g)]	12×10^2
		1.0	—	—	—	−0.46	—	—		
	K^+	0.5	−0.63	−0.55	−0.59	−0.53	−0.45	−0.49	0.10	51
		1.0	—	—	—	−0.55	−0.43	−0.49		
7b[d)]	None	—	−-0.66	−0.56	−0.61	—	—	—		
	Na^+	0.5	−0.64	−0.56	−0.60	−0.46	−0.37	−0.42	0.18	12×10^2
		1.0	—	—	—	−0.46	−0.35	−0.41		
									0.12[c)]	
	K^+	0.5	−0.63	−0.57	−0.60	−0.46	−0.36	−0.41	0.19	18×10^2
		1.0	—	—	—	−0.46	−0.36	−0.41		
									0.13[c)]	
7c[d)]	None	—	−0.67	−0.55	−0.61	—	—	—		
	Na^+	0.5	−0.65	−0.57	−0.61	−0.52	−0.44	−0.48	0.13	166
		1.0	—	—	—	−0.54	−0.41	−0.48		
	K^+	0.5				−0.58[b)]	−0.45[b)]	−0.52		
		1.0	—	—	—	−0.55	−0.45	−0.50	0.11	76
7d[e)]	None	—	−0.65	−0.55	−0.60	—	—	—		
	Na^+	0.5	−0.65	−0.54	−0.60	−0.43	−0.35	−0.39	0.21	38×10^2
		1.0	−0.62	−0.55	−0.59	−0.43	−0.32	−0.38	0.21	
		1.5	−0.61	−0.55	−0.58	−0.43	−0.31	−0.37	0.21	
		2.0	—	—	—	−0.43	−0.30	−0.37		
	K^+	0.5				−0.63[b)]	−0.48[b)]	−0.56		
		1.0	—	—	—	−0.58	−0.46	−0.52	0.08	23
8a[f)]	None	—	−0.71	−0.61	−0.66	—	—	—		
	Na^+	1.0				−0.71	−0.58	−0.65	0.01[h)]	2
	K^+	1.0				−0.71	−0.61	−0.66	0.00[h)]	1
8b[f)]	None	—	−0.71	−0.61	−0.66	—	—	—		
	Na^+	1.0				−0.67	−0.53	−0.60	0.06[h)]	10
	K^+	1.0				−0.70	−0.60	−0.65	0.01[h)]	2
8c[f)]	None	—	−0.70	−0.60	−0.65	—	—	—		
	Na^+	1.0				−0.66	−0.50	−0.58	0.07[h)]	15
	K^+	1.0				−0.68	−0.57	−0.63	0.02[h)]	2

a) Quinone crown concentration 2 mM in CH_3CN containing 0.1 M Bu_4NClO_4 under Ar atmosphere. b) These peaks were broad. c) Quinone crown concentration 1 mM in DMF containing 0.1 M Et_4NClO_4 in the presence of 0.1 M $NaClO_4$ or KBF_4 (see to Ref. 2a). d) At 22 °C. e) At 23 °C. f) At 24 °C. g) Obtained from the difference between E^{c1} and E^{c2}. h) Obtained from the difference between E^{o1} (in the absence of metal cation) and E^{o2} (in the presence of metal cation).

Hitachi 260-50 spectrometer. Mass spectra were obtained with a Hitachi High MS M-80B mass spectrometer. Cyclic voltammograms were obtained by using a Hokuto Denko HB-104 and an HA-303.

Preparation of 1,4-Dimethoxy-2,6-bis(chloromethyl)-3,5-dimethylbenzene (4). Compound **4** was obtained by a known method from 3,5-dimethylphenol. 3,5-Dimethyl-4-aminophenol; mp 185—186 °C (lit,[4)] mp 181.5—182.5 °C). 2,6-Dimethylhydroquinone; mp 153—154 °C (lit,[4)] mp 150—151 °C). 1,4-Dimethoxy-2,6-dimethylbenzene; bp 90—93 °C/4 mmHg (lit,[5)] bp 80—82 °C/2 mmHg, 1 mmHg=133.322 Pa). 1,4-Dimethoxy-2,6-dimethylbenzene was treated with paraformaldehyde in concd hydrochloric acid solution under a closed system at about 60 °C overnight to give the desired chloromethylated compound **4** in 39% yield. 1,4-Dimethoxy-2,6-bis(chloromethyl)-3,5-dimethylbenzene; mp 143.0—143.5 °C (lit,[6)] mp 141.5—142.0 °C).

Preparation of Compounds 7 and 8. To the THF (100 ml) solution of 4506 mg (95%, 28.5 mmol) of triethylene glycol was added 3420 mg (60%, 85.5 mmol) of sodium hydride under cooling with an ice bath and stirred for 20 min. Then, both the above THF solution of disodium salt of triethylene glycol and the THF (100 ml) solution of 7500 mg (28.5 mmol) of 1,4-dimethoxy-2,6-bis(chloromethyl)-3,5-dimethylbenzene were added slowly with dropping funnels, respectively, to the THF (100 ml) solution in a three-necked flask which was cooled with an ice bath under an Ar atmosphere. After the addition, the reaction mixture was stirred at room temperature overnight. The solvent was removed and the residue was poured into water; the solution was then extracted with dichloromethane twice and the organic layer was dried over $MgSO_4$. After removing the solvent, the residue was chromatographed on silica gel (eluent; ethyl acetate) to give 2035 mg of **5a**.

5a; 21%; oil; ^{1}H NMR ($CDCl_3$) δ=2.35 (s, 6H, CH_3), 3.10—3.80 (m, 12H, -CH_2CH_2-), 3.67 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 4.58 (d, 2H, J=11.4 Hz, CH-H), and 4.76 (d, 2H, J=11.4 Hz, CH-H); IR (NaCl) 1080 and 1250 cm^{-1}; Found: C, 63.18; H, 8.30%. Calcd for $C_{18}H_{28}O_6$: C, 63.50; H, 8.29%.

5b; 30%; mp 97—99 °C; ^{1}H NMR ($CDCl_3$) δ=2.32 (s, 6H, CH_3), 3.40—3.70 (m, 20H, -CH_2CH_2-), 3.66 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), and 4.60 (s, 4H, CH_2); IR (NaCl) 1115 cm^{-1}; Found: C, 62.21; H, 8.43%. Calcd for $C_{20}H_{32}O_7$: C, 62.48; H, 8.38%.

5c; 35%; mp 61—62 °C; ^{1}H NMR ($CDCl_3$) δ=2.32 (s, 6H, CH_3), 3.54 (s, 3H, OCH_3), 3.50—3.70 (m, 20H, -CH_2CH_2-), 3.93 (s, 3H, OCH_3), and 4.55 (s, 4H, CH_2); Found: C, 61.27; H, 8.49%. Calcd for $C_{22}H_{36}O_8$: C, 61.66; H, 8.46%; IR (NaCl) 1110 cm^{-1}.

5d; 10%; oil; ^{1}H NMR ($CDCl_3$) δ=2.32 (s, 6H, CH_3), 3.50—3.70 (m, 24H, -CH_2CH_2-), 3.66 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), and 4.58 (s, 4H, CH_2); IR (NaCl) 1115 cm^{-1}; Found: C, 60.67; H, 8.65%. Calcd for $C_{24}H_{40}O_9$: C, 60.99; H, 8.53%.

Two side-armed polyethers were obtained by the same procedure.

6a; 100%; mp 142—143 °C: ^{1}H NMR ($CDCl_3$) δ=2.31 (s, 6H, CH_3), 3.41 (s, 6H, OCH_3), 3.66 (s, 3H, aromatic OCH_3), 3.77 (s, 3H, aromatic OCH_3), and 4.47 (s, 4H, CH_2); IR (NaCl) 1255 and 1080 cm^{-1}; Found: C, 66.14; H, 8.82%. Calcd for $C_{14}H_{22}O_4$: C, 66.11; H, 8.71%.

6b; 100%; oil; ^{1}H NMR ($CDCl_3$) δ=2.32 (s, 6H, CH_3), 3.37 (s, 6H, OCH_3), 3.50—3.70 (m, 8H, -CH_2CH_2-), 3.66 (s, 3H, aromatic OCH_3), 3.77 (s, 3H, aromatic OCH_3), and 4.58 (s, 4H, CH_2); IR (NaCl) 1090 cm^{-1}; Found: C, 63.07; H, 8.90%. Calcd for $C_{18}H_{30}O_6$: C, 63.13; H, 8.83%.

6c; 100%; oil; ^{1}H NMR ($CDCl_3$) δ=2.32 (s, 6H, CH_3), 3.37 (s, 6H, OCH_3), 3.77 (s, 3H, aromatic OCH_3), 3.66 (s, 3H, aromatic OCH_3), 3.50—3.70 (m, 16H, -CH_2CH_2-), and 4.57 (s, 4H, CH_2); IR (NaCl) 1110 cm^{-1}; Found: C, 61.32; H, 8.97%. Calcd for $C_{22}H_{38}O_8$: C, 61.37; H, 8.89%.

Dimethyl crown compound **5a**, 1.31 g (3.85 mmol), which was obtained above, was dissolved in 12 ml of acetonitrile; then, 12 ml of water solution of 5.30 g (9.63 mmol) of cerium (IV) diammonium nitrate was added to the solution and stirred for 45 min at room temperature. After the reaction, the reaction mixture was poured into dichloromethane and washed twice with water. The organic layer was dried over $MgSO_4$. After removing the solvent, the residue was chromatographed on silica gel (eluent: ethyl acetate) to give 0.94 g of **7a**. Compounds **7b—d** and **8a—c** were obtained by the same procedure.

7a; 79%; mp 56—59 °C; ^{1}H NMR ($CDCl_3$) δ=2.12 (s, 6H, CH_3), 3.50—3.70 (m, 12H, -CH_2CH_2-), and 4.53 (s, 4H, CH_2); IR (NaCl) 1655, 1135, and 1080 cm^{-1}; Found: C, 61.96; H, 7.13; MS (70 eV) m/z 310 (M^+). Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.14; M, 310.

7b; 31%; oil; ^{1}H NMR ($CDCl_3$) δ=2.13 (s, 6H, CH_3), 3.50—3.70 (m, 16H, -CH_2CH_2-), and 4.47 (s, 4H, CH_2); Found: C, 60.31; H, 7.43%; MS (70 eV) m/z 354 (M^+). Calcd for $C_{18}H_{26}O_7$: C, 61.00; H, 7.39%; M, 354; IR (NaCl) 1115 and 1650 cm^{-1}.

7c; 67%; oil; ^{1}H NMR ($CDCl_3$) δ=2.14 (s, 6H, CH_3), 3.60—3.70 (m, 20H, -CH_2CH_2-), and 4.48 (s, 4H, CH_2); IR (NaCl) 1650 and 1110 cm^{-1}; Found: C, 59.85; H, 7.64%; MS (70 eV) m/z 398 (M^+). Calcd for $C_{20}H_{30}O_8$: C, 60.28; H, 7.58%; M, 398.

7d; 60%; mp 48—51 °C; ^{1}H NMR ($CDCl_3$) δ=2.15 (s, 6H, CH_3), 3.50—3.70 (m, 24H, -CH_2CH_2-), and 4.49 (s, 4H, CH_2); IR (NaCl) 1650 and 1090 cm^{-1}; Found: C, 59.17; H, 7.69%; MS (70 eV) m/z 442 (M^+). Calcd for $C_{22}H_{34}O_9$: C, 59.71; H, 7.74%; M, 442.

8a; 94%; mp 47—48 °C; ^{1}H NMR ($CDCl_3$) δ=2.14 (s, 6H, CH_3), 3.38 (s, 6H, OCH_3), and 4.37 (s, 4H, CH_2); IR (NaCl) 1645 and 1095 cm^{-1}; Found: C, 64.11; H, 7.24%. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19%.

8b; 92%; oil; ^{1}H NMR ($CDCl_3$) δ=2.15 (s, 6H, CH_3), 3.36 (s, 6H, OCH_3), 3.50—3.70 (m, 8H, -CH_2CH_2-), and 4.47 (s, 4H, CH_2); IR (NaCl) 1640 and 1090 cm^{-1}; Found: C, 61.40; H, 7.77%. Calcd for $C_{16}H_{24}O_6$: C, 61.52; H, 7.74%.

8c; 84%; oil; ^{1}H NMR ($CDCl_3$) δ=2.15 (s, 6H, CH_3), 3.37 (s, 6H, OCH_3), 3.50—3.70 (m, 16H, -CH_2CH_2-), and 4.46 (s, 4H, CH_2); IR (NaCl) 1650 and 1110 cm^{-1}; Found: C, 59.82; H, 8.04%. Calcd for $C_{20}H_{32}O_8$: C, 59.98; H, 8.05%.

Reagents for Electrochemistry. Acetonitrile was distilled from CaH_2. Tetrabutylammonium perchlorate was twice recrystallized from ethyl acetate and alkali metal perchlorate salts were recrystallized from deionized water and dried over vacuum pumping at 100 °C. All these salts were stored in a desiccator, and samplings were carried out under an N_2 atmosphere in a dry box.

Cyclic Voltammetry Experiments. A 2 mM solution (1 M=1 mol dm^{-3}) of substrate was prepared by mixing of 0.1 mmol of quinone derivative, 1701 mg (5 mmol) of Bu_4NClO_4, and 50 ml of acetonitrile. Pt metallic working electrode (Beckman 39273) and Pt wire as the counter electrode were used. E° values were reported vs. saturated calomel electrode (SCE). A scan rate of 200 mV s^{-1} was used. 25 ml of the solution was added to a cell equipped with a magnetic stirrer and an inlet for an Ar atmosphere. After 30 min of Ar purging and stirring, cyclic voltammograms were recorded under unstirred conditions. Also, 0.5, 1.0, 1.5, and 2.0 equiv metal perchlorate solutions were prepared by the same procedure with 0.1 mmol of quinone derivative, 5 mmol of Bu_4NClO_4, and 50 ml of acetonitrile.

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