3068 © 1987 The Chemical Society of Japan NOTES Bull. Chem. Soc. Jpn., 60, 3068—3070 (1987) [Vol. 60, No. 8

Ion Selectivity of 14-Crown-4 Derivative Possessing Two Potential Anionic Sites on Extraction of Alkali and Alkaline-Earth Metal Ions

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(Received March 18, 1987)

Synopsis. A lipophilic 14-crown-4 derivative bearing two dinitrophenol moieties was synthesized and its ion selectivity was elucidated on cation extraction from a basic aqueous phase into an organic phase. The crown ether derivative was found to possess preferences for Ca^{2+} and Sr^{2+} as well as Li^+.

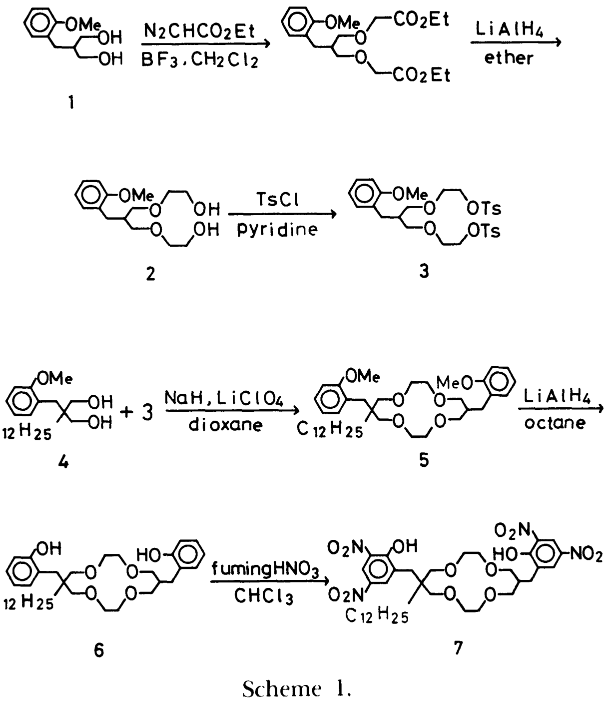
One of the highly selective ligands for Li^+ is 14-crown-4 (1,4,8,11-tetraoxacyclotetradecane) derivatives.[1,2] Such high Li^+ selectivity has also been realized in 14-crown-4 derivatives carrying an proton-dissociable moiety in the side chain, which extract Li^+ selectively from basic aqueous solutions containing alkali and alkaline-earth metal ions by the proton-cation exchange mechanism.[3-6] If a chromogen is included in the proton-dissociable moiety,[6] the ionizable 14-crown-4 derivatives also serve as spectrophotometric reagents after the selective cation extraction.[3,5] In addition, the ionizable 14-crown-4 derivatives carry out proton-driven membrane transport of Li^+ with excellent selectivities.[7] In the Li^+ complexes of 14-crown-4 derivatives bearing a proton-dissociated moiety, the positive charge of the cation is counterbalanced intramolecularly by the monovalent anion. The electroneutrality of the resulted complexes, combined with the fitness of Li^+ into the 14-crown-4 ring, contributes remarkably to the Li^+ selectivity of the crown ethers bearing a potential monovalent anion, especially against multivalent cations like alkaline-earth metal ions. It occurred to us that 14-crown-4 derivatives incorporating two proton-dissociable substituents might exhibit some selectivities for divalent small cations like Mg^{2+} and Ca^{2+} on the cation extraction and the membrane cation transport. This paper reports synthesis of a 14-crown-4 bearing two dinitrophenol moieties and its ion selectivity on the cation extraction.

Experimental

Synthesis of 14-Crown-4 Bis(dinitrophenol) 7 or 6,13-Bis(2-hydroxy-3,5-dinitrobenzyl)-6-dodecyl-1,4,8,11-tetraoxacyclotetradecane The synthetic route is given in Scheme 1. The synthesis of 1,3-propanediol derivatives **1** and **4** has been described elsewhere.[5] The reaction of **1** (77 mmol) with ethyl diazoacetate (230 mmol) in dry dichloromethane (700 cm^3) in the presence of $BF_3 \cdot OEt_2$ (1 cm^3, dropwise addition under a nitrogen atmosphere while cooling in an ice bath) for 1 h at room temperature and then for 2 h at the refluxing temperature gave diethyl 5-(2-methoxybenzyl)-3,7-dioxanonane-1,9-dioate (72%), which (55 mmol) was reduced with $LiAlH_4$ (84 mmol) in diethyl ether (150 cm^3) to yield 5-(2-methoxybenzyl)-3,7-dioxanonane-1,9-diol (**2**, ≈100%). The diol was then converted to corresponding ditosylate **3** in a usual fashion.

The procedures for the cyclization to **5**, demethylation, and nitration are as follows. In a dioxane solution (125 cm^3) of **4** (1.9 mmol), NaH (20 mmol), and $LiClO_4$ (2.5 mmol) were suspended and the mixture refluxed for 0.5 h. To the refluxing suspension was added a dioxane (25 cm^3) solution of **3** (1.9 mmol) dropwise in 1 h. The reflux was continued for 3 d. Preparative reversed-phase liquid chromatography (octadecylsilanized silica(ODS), MeOH-$CHCl_3$(10/1)) afforded colorless liquid of **5** (17%). The demethylation was performed by treating **5** (0.82 mmol) with $LiAlH_4$ (16 mmol) in refluxing octane (100 cm^3) for 8 h to yield colorless liquid of crown bisphenol **6** (50%). The crown bisphenol was nitrated by fuming HNO_3. To a chloroform (200 cm^3) solution of **6** (0.34 mmol) was added fuming HNO_3 (50 cm^3). The mixture was then stirred for 5 min at room temperature. After the reaction, water (200 cm^3) was added to the mixture. The chloroform phase was separated and washed with water. Evaporation of the chloroform gave crude product of **7**, which was purified by the reversed-phase chromatography (MeOH) to yield yellow liquid of **7** (50%): UV-VIS ($ClCH_2CH_2Cl$) 268 (ε 2.64×10^4) and ca. 350 nm (sh, ε 6.14×10^3); IR (neat) 3180 and 1260 (O-H), 1540 (N=O), and 1120 and 1100 cm^{-1} (C-O); ^{1}H NMR (CCl_4) δ=0.88 (3H, t, J=6 Hz, CH_3), 1.1—1.5 (22H, m, $(C\underline{H}_2)_{11}CH_3$), 1.9—2.1 (1H, m, $(OCH_2)_2C\underline{H}$), 2.7—2.9 (4H, m, CH_2Ph), 3.2—3.7 (16H, m, OCH_2), 8.2—9.0 (4H, m, aromatic H), 11.4—11.6 (2H, m, OH). Found: C, 56.83; H, 6.87; N, 7.03%; M^+ 764. Calcd for $C_{36}H_{52}O_{14}N_4$: C, 56.53; H, 6.85; N, 7.33%; M, 764.

Cation Extraction. The metal salts employed here were



Scheme 1.

of analytical grade. Water and 1,2-dichloroethane were purified by distillation and deionization. The extraction was undertaken at room temperature for the qualitative comparison of cation extractability. Equal volumes (5 cm^3) of a 1,2-dichloroethane solution of 3.5×10^{-5} mol dm^{-3} crown ether and a buffered aqueous solution of 1 mol dm^{-3} metal chloride were placed in a stoppered centrifuge tube (10 cm height×1.5 cm diameter). The pH in the aqueous phase was adjusted to pH 7.23 by using 3-morpholino-1-propanesulfonic acid (MOPS)-tetramethylammonium hydroxide (TMAOH) buffer. The tube was shaken vigorously for 30 s. After the centrifugation, 4 cm^3 of the organic phase solution was taken up for the spectrophotometry.

For the determination of the extraction equilibrium constant, the extraction was carried out at 25 °C by varying the metal ion concentration (0.1—1 mol dm^{-3}) and keeping the crown ether concentration constant (3.5×10^{-5} for Li^+ and Sr^{2+}, 7×10^{-5} for Ca^{2+}, and 1.4×10^{-4} mol dm^{-3} for Ba^{2+}). The pH in the aqueous phase was 7.60 with a MOPS-TMAOH buffer. A stoppered tube connected with 1-cm quartz cell containing the 1,2-dichloroethane and aqueous solutions (3 cm^3 each) was shaken vigorously and was then allowed to stand for 12 h in a thermostated bath of 25 °C. Visible spectra of the organic phase were in situ measured in a cell holder thermostated at the same temperature.

Extraction Equilibrium Constant.[5,6] On the assumption that the crown ether (H_2L) forms only 1 : 1 cation (M^+)-crown (HL^- or L^{2-}) complexes (MHL or ML), the constants (K_{ex}) are defined as Eq. 1 for monovalent cations and as Eq. 2 for divalent cations, where subscript "a" and "o" denote the aqueous and organic phases, respectively.

$$K_{ex}=([MHL]_o[H^+]_a)/([H_2L]_o[M^+]_a) \qquad (1)$$

$$K_{ex}=([ML]_o[H^+]_a^2)/([H_2L]_o[M^{2+}]_a) \qquad (2)$$

Since the crown ether is highly lipophilic, its undissociated, proton-dissociated, and complexed species are hardly partitioned to the aqueous phase, i.e., $[H_2L]_a\simeq0$, $[HL^-]_a$ (or $[L^{2-}]_a)\simeq0$, and $[MHL]_a$ (or $[ML]_a)\simeq0$. If the following assumptions are also made, i.e., $[H_2L]_t$ ("t" is "total".)$\simeq$ $[H_2L]_o+[MHL]_o$ (or $[ML]_o$) and $[M^+]_t$ (or $[M^{2+}]_t)\simeq[M^+]_a$ (or $[M^{2+}]_a$), Eqs. 1 and 2 can be transformed to Eqs. 3 and 4, respectively.

$$[H^+]_a/[M^+]_t=(K_{ex}\varepsilon_{MHL}[H_2L]_t/A_o)-K_{ex} \qquad (3)$$

$$[H^+]_a^2/[M^{2+}]_t=(K_{ex}\varepsilon_{ML}[H_2L]_t/A_o)-K_{ex} \qquad (4)$$

Here, ε_{MHL} (or ε_{ML}) and A_o stand for molar absorptivity and absorbance for MHL (or ML) in the organic phase at a wavelength where H_2L does not absorb at all. Thus the K_{ex} values were determined from the intercepts of the plots of $[H^+]_a/[M^+]_t$ (or $[H^+]_a^2/[M^{2+}]_t$) vs. $1/A_o$.

Results and Discussion

Since 14-crown-4 bearing two dinitrophenol moieties **7** are easily proton-dissociable (the average pK_a: 5.20 in dioxane-water(1/1)), extractions of metal ions that have affinity to the crown ring, based on the H^+-M^+ exchange mechanism, should occur even under mild pH conditions of the aqueous phase, being accompanied by significant spectral changes of the chromogen in the organic phase. Figure 1 depicts typical spectral changes on the cation extraction of alkali and alkaline-earth metal ions. Definitely, increasing absorption in the visible region on the cation extraction is derived from the complex formation between the metal ions and the proton-dissociated species of **7** in the organic phase, inasmuch as any spectral change was not attained without metal ions in the initial aqueous phase under the identical pH conditions. The monovalent metal ion is different from the divalent ones in the wavelength of the visible absorption for the complexes (Table 1). Also, the monovalent cation complex possesses about one half the molar absorptivity for the divalent ones, which in turn is close to that for the ion pair between the dianionic species of **7** and two tetramethylammonium ions (ε 2.68×10^4 at 376 nm). The spectral data suggest that the monovalent and divalent ions (M^+ and M^{2+}) interact with mono- and dianionic species of **7** (HL^- and L^{2-}), respectively, to form electrically-neutral complexes (MHL and ML). In the group of alkali metal ions, Li^+ is extracted most effectively by the crown ether. Slight and practically no extractions were found with Na^+ and the other alkali metal ions, respectively. The high Li^+ selectivity of **7** against other alkali metal ions is quite similar to that of a corresponding 14-crown-4 derivative with only one dinitrophenol moiety, 6-dodecyl-6-(2-hydroxy-3,5-dinitrobenzyl)-1,4,8,11-tetraoxacyclotetradecane.[5] As anticipated from the easy charge compensation for divalent cations, **7** is able to extract alkaline-earth metal ions. This was not the case with the derivative possessing only one dinitrophenol moiety, which hardly extracted any alkaline-earth metal ions under the identical pH conditions.

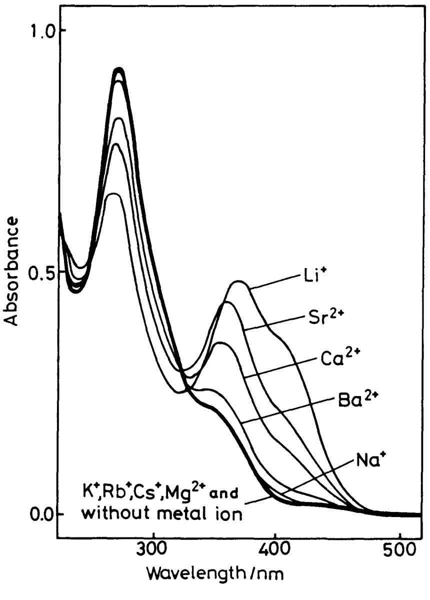


Fig. 1. Spectral change in organic phase on cation extraction with 14-crown-4 bis(dinitrophenol) **7**.

Table 1. Extraction Equilibrium Constants and Spectral Data for Cation Complexes of **7**

Complexed cation	pK_{ex} [a]	ε_{MHL} or ε_{ML} [b] (λ_{max}) [c]
Li^+	7.36	1.62×10^4 (368)
Ca^{2+}	15.61	2.75×10^4 (359)
Sr^{2+}	15.56	2.78×10^4 (359)
Ba^{2+}	16.43	2.92×10^4 (359)

a) In $ClCH_2CH_2Cl$-H_2O system, at 25°C. pK_{ex}= $-\log K_{ex}$. b) In dm^3 mol^{-1} cm^{-1}. c) In nm.

Interestingly, **7** exhibited good extractabilities for the medium-size alkaline-earth metal ions, but hardly did any extractability for Mg^{2+} that resembles Li^+ in size. The poor extractability for Ba^{2+} may be ascribable to the fact that the 14-crown-4 ring is too small to form stable complexes with the large cation.

An attempt was made to determine the extraction equilibrium constants of **7** for the electrically-neutral 1 : 1 cation–crown ether complexes. The plots of $[H^+]_a/[M^+]_t$ (for monovalent cations) or $[H^+]_a^2/[M^{2+}]_t$ (for divalent ones) vs. $1/A_o$ gave straight lines with coefficients of correlation of better than 0.999 for Li^+, Ca^{2+}, Sr^{2+}, and Ba^{2+}, thus affording their K_{ex} values (Table 1). The K_{ex} values for the other metal ions could not be obtained because of the poor extractabilities towards them.

In conclusion, the 14-crown-4 derivative bearing two dinitrophenol moieties **7** is still highly Li^+-selective against other alkali metal ions on the cation extraction. In addition, good affinity for some alkaline-earth metal ions, although not very drastic, was attained with the crown ether.

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