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Structural investigation on ion-selective ionophoric properties of armed 12-oxacrown-3 derivatives

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Abstract

We designed and synthesized new armed 12-oxacrown-3s bearing oxygen donor arms and forming encapsulated complexes with metal ions. The ISEs based on the single armed 12-oxacrown-3s exhibited Na^+ ion selectivity, while the ISE based on the double armed 12-oxacrown-3 exhibited Li^+ ion selectivity. The conformational analysis was performed on the free armed 12-oxaciown-3s and the non-encapsulated and the encapsulated armed 12-oxacrown-3 complexes using a semi-empirical method. The conformational analysis indicated that all armed 12-oxacrown-3s structurally prefer the Na^+ ion rather than the Li^+ ion. Further, it became apparent that the single armed 12-oxacrown-3s without a guest cation have the C_{3v} 12-oxaciown-3 ring and the double armed 12-oxacrown-3 without a guest cation has the bent 12-oxacrown-3 ring. The oxygens except carbonyl oxygens were directed toward the cation center in the structures of the complexes. It was clear that the ether and ester oxygens participate in the sidearm coordination.

Keywords: Computational chemistry; Conformational analysis; 12-Oxacrown-3; Sidearm; Armed crown ethers; Ion selectivity; Ion-selective electrode

1. Introduction

The computational study of crown ethers is of interest because of its ion selectivities for specific cations [1–17]. This characteristic has led to the widespread use of crown ethers. In analytical chemistry, crown ethers have been used in solvent extractions, sorptions in chromatography, ion-selective electrodes, and separations [18]. The interaction between the host molecule and the metal ion can be estimated from the calculation data on the conformation of the free host and the complex with the metal ion [3–8], the binding [9–15], and the solvation [16,17]. A thorough understanding of the interaction between crown ethers and cations would provide a basis for the rational design of new crown ethers. However, computational study for this purpose is too time-consuming to employ them in analytical chemistry. Still, conformational analysis of crown ethers or its complexes would give simple and fundamental information on the ion-selective properties. We previously have demonstrated by the conformational analysis of a 12-oxacrown-3 ring with the ab initio theory that a 12-oxacrown-3 ring has the exodentate C_{3v} conformation optimal for the complexation with a cation and its oxygen to center-of-mass distance is 1.68 Å and that bis(12-oxacrown-3) is apparently suitable for the sandwich-type complexation with the Na^+ ion [19].

The ion-selective electrode (ISE) is related to the activity (concentration) of a sensed ion in the tested solution [20,21]. The potentiometric liquid membrane for the ISE includes an ionophore, which captures the specific ion more tightly than other ions. The development of the ionophore directly results in an increase of the ion selectivity. Oxacrown ethers as ionophores of ISEs have attracted great attention because of the facile design of novel materials for analytical agents [18,22,23]. Hence, a great number of ion-selective electrodes based on oxacrown ethers have been reported [24,25].

The Li^+ and Na^+ ions are of particular interest for clinical and technological analysis. On the basis of the hole-size concept for oxacrown ethers, the diameter suitable for the Li^+ or Na^+ ions is that of 12-membered or 15-membered $3n$-oxacrown-n ethers in calculation [26]. The 12-oxacrown-4s as ionophores generally prefer the Na^+ ion to the Li^+ ion [24,25]. Most computational

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work using semi-empirical and ab initio methods in this area has focused on 18-oxacrown-6, 15-oxacrown-5, and 12-oxacrown-4 [1,3,5–7,9,11,13–17]. There is no structural investigation of 12-oxacrown-3s by using computer. From our conformational analysis, 12-oxacrown-3 derivatives should be good candidates for the Li$^+$ and Na$^+$ ion-selective ionophores. The number of reports of armed 12-oxacrown-3s as ionophores is, however, rather limited [27].

The experimental results have not always accorded with the hole-size concept, because the prime parameter for the ion selectivity is not only the cavity size but also the number of available donor atoms that can effectively participate, the binding energy and the solvation [28,29]. Therefore, various combinations of the crown ring and sidearm have been attempted to attain enhancement of the ion selectivity [30–32]. The ionophoric properties of armed crown ethers should be also influenced by the topology and the electrostatic effect of the cation-ligating sidearms [33,34]. In this study, we designed and synthesized new armed 12-oxacrown-3s forming encapsulated complexes with metal ions to investigate the conformations and the effects of the sidearms on the ionophoric properties. The ionophoric properties of the armed 12-oxacrown-3s were evaluated by the potentiometry with the polymeric liquid membrane-based ISEs.

In the potentiometric liquid membrane for the ISE, if the structural change of a ionophore by the complexation would be comparatively (or remarkably) restricted, the conformation of the free (uncomplexed) ionophore is considered to be an important factor for the ionophoric properties. We also attempted to obtain simple and fundamental information on the relationship between the structure and the ion selectivities by conformational analysis.

2. Experimental

2.1. Reagents

Organic reagents were commercially available. Aqueous solutions were prepared with doubly quartz-distilled water and salts of the highest purity available. Before the use, organic solvents were dehydrated by sodium (for benzene, diethyl ether (Et_2O), tetrahydrofuran (THF), and toluene) or molecular sieve 3 Å (for 1,4-dioxane, ethyl alcohol, and pyridine (Py)). For the potentiometric liquid membranes, THF was freshly distilled over sodium benzophenone ketyl, and high-molecular-weight poly(vinyl chloride) (PVC) was purified in MeOH.

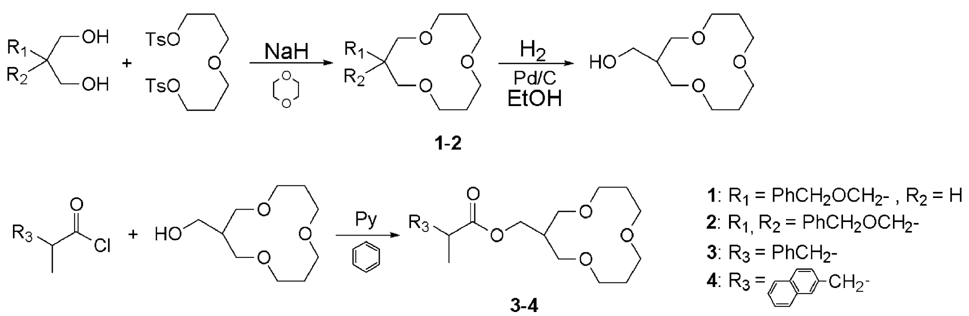
2.2. Syntheses of ionophores

12-Oxacrown-3 was mainly obtained by the cyclization reaction of 1,3-diol derivative with 4-oxa-heptane-l,7-diol [35] ditosylate in the presence of NaH as the base [35,36]. As a template of the cyclization [37], LiC1O$_4$ was added in excess to the reaction systems. The ether-armed 12-oxacrown-3s were prepared by the functionalization of 1,3-diol [19]. The ester-armed 12-oxacrown-3s were prepared by the reaction of 3-hydroxylmethyl-12-crown-3 with corresponding carboxylic acid chlorides [38]. The preparation of a series of armed 12-oxacrown-3s was illustrated in Scheme 1. All reactions were carried out under dry nitrogen. After the reactions, the reaction mixtures were distilled under reduced pressure, following the removal of solvents. If it was necessary, further purification were performed by HPLC on a ODS column (CHEMCOSORB 5-ODS-H, Chemco company), eluting with MeOH. All products were determined with ^{1}H and ^{13}C NMR (Varian XL-300), IR (Shimazu FTIR-8600), and mass spectra (JEOL JAM-DA5000).

3-Benzyloxymethyl-l,5,9-trioxa-cyclododecane **1**: ^{1}H NMR (CDC1$_3$) δ 1.74–1.85 (m, 4H), 2.21–2.34 (m, 1H), 3.44 (d, 1H, $J = 3.0$ Hz), 3.46 (d, 1H, $J = 3.0$ Hz), 3.48–3.74 (m, 12H), 4.50 (s, 2H), 7.26–7.34 (m, 5H); ^{13}C NMR (CDC1$_3$) δ 28.99, 39.53, 67.82, 68.35, 69.39, 69.80, 73.07, 127.47, 128.29, 129.53, 138.46; IR (neat) 1128, 737, 698 cm^{-1}; MS (FAB) *m/z* 295 ($M + H$).

3,3-Bis-benzyloxymethyl-l,5,9-trioxa-cyclododecane **2**: ^{1}H NMR (CDC1$_3$) δ 1.77 (tt, 4H, $J = 5.4$ and 5.4 Hz), 3.51 (s, 4H), 3.53 (s, 4H), 3.53–3.64 (m, 8H), 4.49 (s, 4H), 7.19–7.38 (m, 10H); ^{13}C NMR (CDC1$_3$) δ 69.86, 69.96, 70.30, 70.54, 71.40, 73.03, 78.30, 127.20, 127.24, 128.00, 137.92; IR (neat) 1101, 735, 698 cm^{-1}.

2-Methyl-3-phenyl-propionic acid l,5,9-trioxa-cyclododec-3-ylmethyl ester **3**: ^{1}H NMR (CDC1$_3$) δ 1.16 (d, 3H, $J = 6.3$ Hz), 1.78 (tt, 4H, $J = 5.4$ and 5.4 Hz), 2.08–2.21 (m, 1H), 2.64–2.80 (m, 2H), 2.96–3.03 (m, 1H), 3.40–3.70 (m, 12H), 4.02 (d, 2H, $J = 6.6$ Hz), 7.14–7.30 (m, 5H); ^{13}C NMR (CDC1$_3$) δ 16.80, 28.87, 38.69, 39.74, 41.44, 63.56, 67.82, 68.56, 68.63, 126.26, 128.30, 128.86, 139.25, 175.88; IR (neat) 1130, 1734 cm^{-1}; MS (EI) *m/z* 350 (M^+).



Scheme 1. Syntheses of armed 12-oxacrown-3s.