Novel Neutral Anion Ionophores Based on Fluorinated (Poly)Ether Compounds as a Sensory Molecule for an Ion-Selective Electrode

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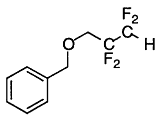
Novel neutral anion ionophores based on fluorinated (poly)ether compounds have been synthesized which were first obtained and applied as anion sensory molecules for an ion-selective electrode (ISE).

The design and synthesis of anion sensory molecules for an ion-selective electrode application is a challenging subject, because the designing strategy for obtaining highly selective anion ionophores is not as simple as the case of cation ionophores that were succesfully designed based on polyamides, polyethers and crown ethers, which are electrically neutral ionophores. The useful anion selective electrodes reported to date were based on quaternary ammonium salts,[1] guanidine,[2] metal complexes,[3] and organometallic compounds,[4] but none were based on a truly electrically neutral ionophore. In this communication, we report the design and synthesis of electrically neutral fluorinated (poly)ether ionophores as a novel anion sensory molecule for an ion-selective electrode.

We investigated anion binding sites which contain electron-deficient hydrogen atom(s) functioning as a Lewis acid, taking advantage of the highly electronegative fluorine atoms positioned at the same carbon atom or an adjacent carbon atom ($-CF_2-H$ or $-O-CH_2-CF_2$). McMahon et al.[5] and Farnham et al.[6] have reported the interaction between halogen anions and fluorinated compounds in the gas phase and in the complex structural studies, repectively, that gave us an important hint for the present investigation. Employing these anion binding sites, ionophores **1** - **4** were designed and synthesized. Ionophores **1** - **4** were prepared using the corresponding fluorinated alcohols or diols with NaH and benzyl bromide or o-xylylene bromide in 58.3, 40.3, 85.0 and 10.8% yield, respectively.[7]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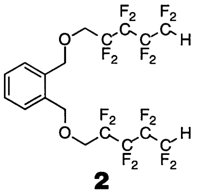
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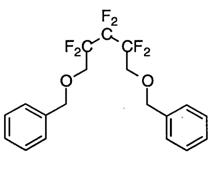
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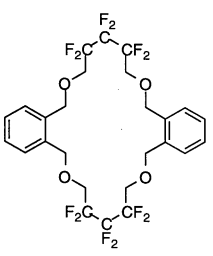
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The obtained ionophores were incorporated in PVC matrix electrode membranes and examined for their potentiometric responses to Cl^- and ClO_4^-, which have large different lipophilicity in the Hofmeister anion series. The polymeric membrane compositions were 3% (by weight) ionophore, 70% membrane solvent NPOE and 27% PVC. The electrode response potential (e.m.f.) measurements were performed according to the reported procedure at 25 ± 0.5 °C using the following cell assembly;[8]

Ag|AgCl|KCl(satd.)||0.3 M NH_4NO_3|| test solution| membrane| 0.1 M NaCl| AgCl|Ag

All test solutions were made from sodium salts and adjusted to pH 7.0 using 0.1 M Tris-H_2SO_4 buffer reagent. The selectivity coefficients were calculated from the response potentials using the separate solution method, based on the IUPAC recommendation.[9]

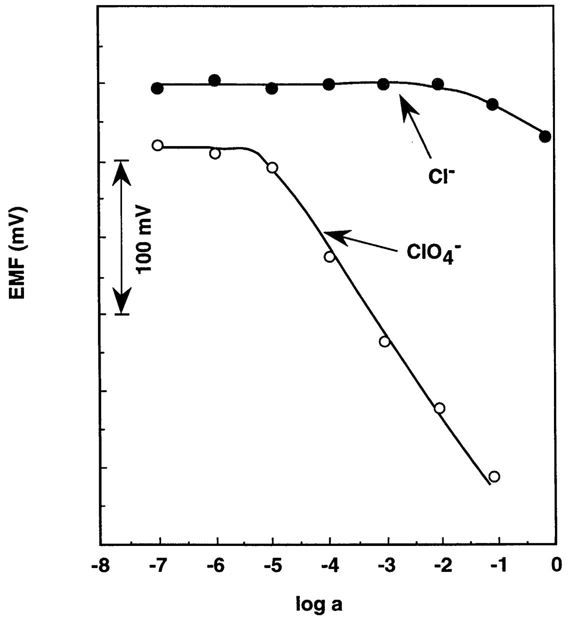

Figure 1. Response curves of the ISE based on ionophore **4**.

The response characteristics of the ISEs based on non-cyclic ionophores **1** and **2** containing two basic binding sites ($-CF_2-H$ and $O-CH_2-CF_2-$) and a lipophilic benzyl group were examined for their response slopes to ClO_4^- and Cl^- (the theoretical response slope for these ions is -59.2 mV/activity decade at 25 °C). The ISEs based on **1** and **2** exhibited weak cationic responses to Cl^- sample solutions (positive slopes, 21 and 11 mV/activity decade, respectively) and weak anionic responses to ClO_4^- (-10 and -16 mV/activity decade). The electrode based on another type of non-cyclic ionophore **3** also exhibited a weak anionic response to ClO_4^- (-18.8 mV/activity decade).

As in the case of a crown ether as an effective cation ionophore, one favorable chemical structural design for anion ionophore is that a cyclic molecule including four or more anion binding sites which effectively pre-organizes the binding sites to coordinate to an anion. Therefore, **4** was designed and synthesized as a 22-membered macrocyclic ionophore containing four units of binding sites in a cyclic system. As we expected, the electrode based on **4** exhibited a near-Nernstian response to ClO_4^- (slope = -55 mV/decade) and a weak anionic response to Cl^- (slope = -15 mV/decade) as shown in Figure 1. This obviously indicates that ionophore **4** interacts with anions stronger than the non-cyclic ionophores **1** - **3**, that is a significant evidence of the success of the pre-organization attempt. As shown in Figure 2, the structural model of **4** shows that the hydrogen atoms of four binding sites achieve a favorable inward direction to interact effectively with anion. Furthermore, the lone pairs of the ethereal oxygens are outward directed, so that the cationic binding is not in favor.

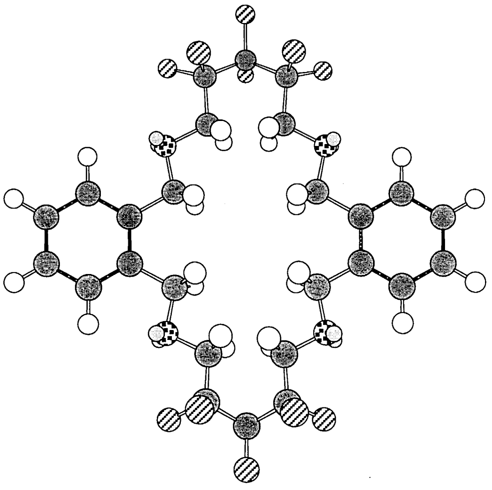

Figure 2. Model for ionophore **4**, that showed the inward-directed hidrogen atoms as the binding sites for anion.

The selectivity pattern of the electrode based on ionophore 4 was similar to the Hofmeister series, except for the reversal of the selectivity of F^- over Cl^- ($ClO_4^- >$ o-$C_6H_5(OH)COO^- > SCN^- > I^- > NO_3^- > Br^- > F^- > NO_2^- > Cl^- > SO_4^{2-}$). As this ionophore interacts with anions by hydrogen bonding interaction, it is reasonable that the binding of F^- will be stronger than that of Cl^-. Although further investigation on macrocyclic molecular design was required for obtaining a desirable anion ionophore with a high selectivity for an analyte ion, the present investigation opens the way to the design of truly neutral anion-selective ionophores for chemical ion sensors.

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7 Satisfactory elemental analyses and i.r. spectroscopic data were obtained for all new compounds. Selected analytical data for **1** are as follows: ^{1}H-NMR (90 MHz, $CDCl_3$) δ (ppm) 3.86 (t-t, 2H); 4.65 (s, 2H); 5.98 (t-t, 1H); 7.35 (m, 5H). **2**: ^{1}H-NMR (90 MHz, $CDCl_3$) δ (ppm) 3.97 (t-t, 4H); 4.75 (s, 4H); 6.03 (t-t, 2H); 7.38 (m, 4H). **3**: ^{1}H-NMR (90 MHz, $CDCl_3$) δ (ppm) 3.94 (t, 4H); 4.68 (s, 4H); 7.30-7.39 (m, 10H). **4**: ^{1}H-NMR (270 MHz, CDCl3) δ (ppm) 3.97 (t, 8H); 4.75 (s, 8H); 7.37 (m, 8H).

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