Lipophilic Crown-4 Derivatives as Lithium Ionophores for Lithium Ion Selective Liquid Membrane Electrodes

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New lipophilic Crown-4 compounds of 16-membered rings containing furan (neutral carrier, I), tetrahydrofuran (neutral carrier, II) and lithium complex of the latter (neutral carrier, III) have been synthesized and tested as the active sensors for lithium ion in poly (vinyl chloride) (PVC) membrane electrode, in the presence and absence of an anion excluder, tetrakis (4-chloro-phenyl) borate (KTClPB). 2-nitrophenyl phenyl ether (NPPE), tris (2-ethylhexyl) phosphate (TEHP), *o*-nitrophenyl octyl ether (NPOE), dioctyl adipate (DOA), bis (2-ethylhexyl) adipate (BEHA), di-*n*-octyl phenyl phosphonate (DOPP) were used as plasticizing solvent mediators. The electrode response function had a nearly Nernstian slope of 54-61 mV per decade (25℃) within the concentration range of 10^{-1}-10^{-4} M LiCl and the detection limits for all electrodes were *ca.* 5×10^{-4} M. The response time of the electrode was faster at the higher lithium concentration and the response of the electrode was stable for longer than 6 months. The sensor membranes exhibit improved response times and increased lifetimes as compared to the system described earlier.

Introduction

Considerable efforts have been invested in the design of the lithium ion selective electrodes with improved selectivity and detection limits.

Several neutral carriers for Li^+- selective electrodes have been reported so far, such as crown ethers, noncyclic polyethers, and so on.[1,2]

Li^+-selective electrodes are of great interest for the direct potentiometric determination of Li^+ ion concentration in whole blood during the lithium theraphy of patients suffering from manic-depressive psychosis, where Li^+ concentration of 0.8 to 1.0 mM in blood is required.[3,4] The main problem of the Li^+-ionophores published until now is their unsatisfying selectivity especially against Na^+ which is present in a relatively high concentration of 86 mM in blood.[5]

During the search for more appropriate carriers, an interesting class of lipophilic compounds derived from THF-containing fragments was designed (Figure 1).[1] The ubiquity of THF unit in the naturally occurring antibiotic ionophores (*e.g.*, monactin, nigerisin, and monensin contain tetrahydrofuran) encourage this purpose. The THF unit is expected to have a potential utility as a macrocyclic chain component because of its greater donor ability as well as its hydrophilic and lipophilic balance.

We have investigated the complexing ability between Li^+ and the 2,2,7,7,12,12,17,17-octamethyl-21,22,23,24-tetraoxaperhydroquaterene (neutral caier II, Figure 1) by ^{1}H, ^{13}C and ^{7}Li-NMR spectroscopy.[6]

In this paper we report that PVC membrane electrodes based on lipophilic crown-4 derivatives exhibit good selectivity for Li^+ over other alkali and alkaline earth metal ions.

Experimental

Reagents. Materials and reagents were obtained as follows: Poly (vinyl Chloride) (PVC, secondary standard), bis (2-ethylhexyl) adipate (BEHA) and Tris (2-ethylhexyl) phosphate (TEHP) from Aldrich. Dioctyladipate (DOA) from Pflatz and Bauer, *o*-nitrophenyl octyl ether (*o*-NPOE) and potassium tetrakis (*p*-chlophenyl) borate (KTClPB, purum p.a.) from Fluka AG, 2-nitrophenyl ether (NPPE) from Eastman Kodak and di-*n*-octyl phenyl phosphate (DOPP) from Lancaster.

The electrolyte solutions for the potentiometric measurements were prepared with doubly distilled water and chloride salts of high purity (E. Merck, pro analysis). Tetrahydrofuran were dried and purified by refluxing over sodium metal, followed by distillation under a N_2 atomosphere.

Apparatus. Infrared spectra were recorded on a Perkin-Elmer 457 grating spectrophotometer. Melting points were determined on a MP melting point apparatus. Mass spectra were measured at AEI MS 902 mass spectrometer. ^{1}H-NMR spectra were recorded on a Bruker WH-300 (300 MHz) spectrometer. TLC and column chromatography were performed utilizing aluminium sheets silica gel 60 F_{254} (E. Merck) and 70-230 mesh silica gel 60 (E. Merck). Elemental analyses were performed by Oxford microanalytical service.

Syntheses of Ionophores. 2,2,7,7,12,12,17,17-octamethyl-21,22,23,24-tetraoxaquaterene (carrier I). $LiClO_4$ (0.2 mol) was placed in a 500 m*l* flask fitted with a mechanical stirrer and reflux condenser. Absolute ethanol (36 m*l*) was added, and the mixture was stirred until homogeneous. Concentrated HCl (24 m*l*) and 70.2 g (1.2 mol) of acetone were added, then 40.8 g (0.6 m*l*) of furan was added in one portion. After stirring at room temperature 30 min, the mixture was immersed in a water-bath and maintained at 60℃ for 3 h. The mixture was then stirred overnight at room temperature, 30 m*l* of H_2O was added. The mixture was extracted with benzene, and the organic layer was washed with water and dried with anhydrous $MgSO_4$. Evaporation of benzene afforded an off-white oily substance which, on washing with ethanol gave a white powder. The product was recrystallized from a 60 : 40 mixture of hexane/toluene; mp. 235-237℃ (lit.[7] 240-243℃). Anal. Calcd. for $C_{28}H_{32}O_4$: C, 77.8; H, 7.5. Found: C, 77.6: H, 7.7; IR (KBr) 1600, 1262, 1208,

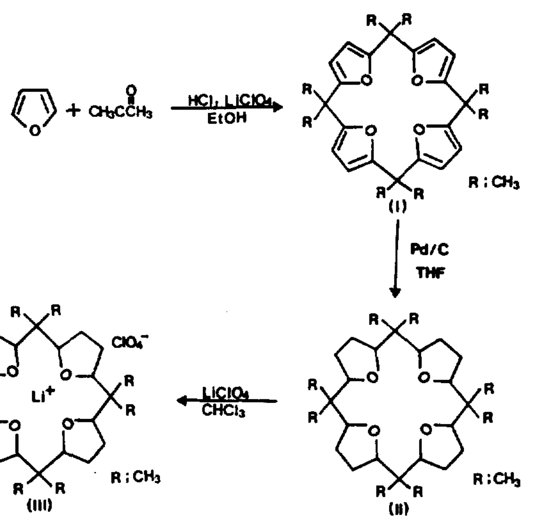

Figure 1. Synthetic scheme and structures of the neutral carrier I, II and Li^+ complex (carrier III).

1112, 1030, 995, and 775 cm^{-1}; mass spectrum (m/e) 432.7 (M+1 ion); ^{1}H-NMR 1.45 (2, 24H), 5.88 ppm (s, 8H).

2,2,7,7,12,12,17,17-octamethyl-21,22,23,24-tetraoxaperhydroquaterene(carrier II). This product was hydrogenated over 1 g of 10% Pd/C in tetrahydrofuran at 140℃ and 120 atm of H_2 for 20 h shown as Figure 1. After removal of catalyst by filteration and evaporation of solvent, the crude product was chromatographed (70% hexane-toluene) to gave a white solid product.: mp. 207-209℃ (lit.[7] 207-210℃). Anal. Calcd. for $C_{28}H_{48}O_4$: C, 74.95; H, 6.43. Found: C, 74.65; H, 10.80; mass spectrum(m/e) 449.1 (M+1 ion); IR (KBr) 3096, 1558, 1210 and 1084 (C-O-C), 957 and 779 cm^{-1}; ^{1}H-NMR 0.85-0.95 (m, 24H), 1.3-1.5 (m, 16H) 3.4-3.9 ppm (m, 8H).

Preparation of Li^+-carrier II complex (carrier III). 0.5 g (0.001 mol) of the purified free ligand (prepared as above) was dissolved in diethyl ehter. An equivalent of dried LiSCN was added (0.07 g, assuming zero water content)-this dissolved gradually with stirring after 1-2 hours. The solution was left to stirr at room temperature for 24 hours. The crude product was isolated from diethyl ether and recrystallized from chloroform: mp. 154-158℃; Anal. Calcd. for $C_{28}H_{48}O_4 \cdot$ LiSCN: C, 67.8; H, 9.4; N, 2.7; Li, 1.4 Found: C, 68.4; H, 9.3; N, 2.7; Li, 1.4; IR (KBr) 1043 (C-O-C); ^{1}H-NMR 0.78 (s, 24H), 1.49-1.75 (m, 16H), 3.89-3.93 ppm (t, 8H).

Electrode System. Measurements were performed by the use of the following cell: Hg; Hg_2Cl_2, KCl (sat'd) | | sample solution | PVC membrane | 0.1 M LiCl, AgCl; Ag. EMF measurements were made at 25℃, using a pH/mV meter of high input impedance in combination with a recorder. Sample solutions were magnetically stirred and kept in a double-wall glass container connected with a circulating bath. The EMF readings are not corrected for changes in the liquid juction potential. The uncertainties in the EMF readings should be comparable to those estimated by orthers using the same kind of experimental set up.[8]

Membrane Preparation. Membrane preparation have been performed according to the procedure of Moody and Thomas.[9] The membrane components (~28 wt% PVC, ~70 wt% plasticizer, 0-100 wt% KT*p*ClPB (with respect to the sensor), and neutral carrier 3-7 wt% ionophore) totaling 540 mg were dissolved in 10 m*l* of THF. This solution was then poured into a flat petri-dish of 40 mm inner diameter. Gradual evaporation of the solvent at room temperature gave a transparent, flexible membrane of about 0.2 mm in thickness. A disk of 8 mm diameter was cut with a cork-borer and soaked in 0.1 M LiCl solution for 24 hours. The disk was then inserted into the electrode assembly.

Table 1. Properties of Li^+-Selective PVC Membrane Electrodes

Carrier	Plasticizer Lipophilic salt	Maximal slope mV $decade^{-1}$	Linear range *p*Li
I	TEHP	60	1-4
	TEHP/KTClPB	60	1-4
	DOPP/KTClPB	61	1-4
	DOA/KTClPB	58	1-3
	BEHA/KTClPB	54	1-3
II	TEHP	61	1-4
	TEHP/KTClPB	60	1-5
	DOPP/KTClPB	58	1-4
III	TEHP	61	1-4
	TEHP/KTClPB	60	1-4
	DOPP/KTClPB	55	1-4

Potentiometric Selectivity Coefficients. Selectivity coefficients were determined by the separate solution technique on 10^{-1} M aqueous solutions of the chlorides using the Nicolsky-Eisenman equation[10]:

$$\log k^{pot}_{LiM} = \frac{(E_1 - E_2)F}{2.303RT} - \log a^{1/z}_{M+Z} + \log a_{Li+}$$

where R=gas constant, a=ion activities, T=absolute temperature, z=charge of the interfering ion, F=Faraday constant, E_1=EMF of the cell assembly, the sample being a LiCl solution of analytical concentration 10^{-1} M, E_2=EMF of the cell assembly, the sample being a 10^{-1} M solution of the chloride of the interfering cation. The activity coefficient γ were calculated by using the following equation based on the Debye-Hückel theory:

$$\log \gamma = -0.509(I)^{1/2}/(1+I^{1/2})$$

where I denotes the ionic strength. Some of the experimental values of activity coefficients in the literature were also employed.[11]

Results and Discussion

The lithium selectivities of the carriers I, II and III (Figure 1) were evaluated as potentiometric selectivity coefficients of polymeric membranes based on them. The potentiometric selectivity coefficients were determined by a separate solution method.[11] The selectivity coefficient given as k^{pot}_{LiM} represents the preference of the PVC membranes containing the neutral carrier for Li^+ over other metal ion (M). It should be kept in mind that smaller the k^{pot}_{LiM} value, the higher the Li selectivity of the neutral carrier based PVC membrane.

The electrode properties in optimal conditions were evaluated by maximal slope and linearity of calibration plots,

Table 2. Selectivity Coefficients $I(k^{pot}_{LiM})$ of Li$^+$-Selective PVC Membrane Electrodes Based on Neutral Carrier I, II and III

Carrier	Plastcizer	k^{pot}_{LiM}							
		Na$^+$	NH$_4$$^+$	K$^+$	Rb$^+$	Cs$^+$	Mg^{2+}	Ca^{2+}	Ba^{2+}
I	TEHP	1.0×10^{-1}	2.5×10^{-1}	1.7×10^{-2}	7.2×10^{-3}	8.5×10^{-3}	4.8×10^{-4}	1.2×10^{-3}	5.3×10^{-4}
	DOPP	5.5×10^{-1}	1.2×10^{-1}	1.1×10^{-2}	1.3×10^{-3}	1.3×10^{-2}	9.4×10^{-3}	9.8×10^{-3}	8.3×10^{-3}
II	TEHP	3.1×10^{-2}	2.9×10^{-1}	9.7×10^{-3}	1.4×10^{-2}	1.1×10^{-2}	5.4×10^{-4}	1.4×10^{-3}	5.3×10^{-4}
	DOPP	8.2×10^{-1}	2.1×10^{-1}	1.5×10^{-1}	1.4×10^{-2}	1.2×10^{-2}	1.5×10^{-2}	7.8×10^{-2}	2.1×10^{-2}
III	TEHP	6.7×10^{-2}	5.2×10^{-2}	1.3×10^{-2}	9.1×10^{-3}	8.2×10^{-3}	8.4×10^{-4}	1.3×10^{-3}	7.5×10^{-4}
	DOPP	5.4×10^{-2}	8.7×10^{-2}	6.0×10^{-3}	4.5×10^{-3}	4.9×10^{-3}	9.9×10^{-3}	2.3×10^{-3}	8.8×10^{-4}

which are summarized in Table 1.

The calibration curve obtained for the electrode based on carrier I, II and III was linear over the activity range 1.0 $\times10^{-4}$ to 0.1 M with a slope of 54-61 mV for Li$^+$ (Table 1). A comparison of the selectivities of membranes based on the Li$^+$ carrier I, II and III is given in Table 2.

The THF-based crown-4 (carrier II) and its lithium complex (carrier III), when utilized as neutral carriers of the Li$^+$ selective electrodes with the PVC-TEHP membrane system, certainly showed enhanced Li$^+$ selectivities against Na$^+$ and K$^+$ as compared to unsaturated furan-based crown-4 (carrier I). In carrier III system, high concentration of complexed species in the membrane exist. Boles and Buck have reported that at high concentrations of complexes species in membranes, and anion response can be observed that results in the reduction of the cation response.[12] Conversly, the weak complexation between the Li$^+$ ion and unsaturated crown-4 (carrier I) may lead weakly attracted to the membrane. As expected, the THF-based crown-4 (carrier II) is the best system for the neutral carrier of the Li$^+$ ion-selective electrode.

The selectivity coefficients of neutral carrier, I, II, and III decrease in the following orders; NH$_4$$^+$>Na$^+$>Rb$^+$>Cs$^+$>K$^+$>Ca^{2+}>Ba^{2+}>Mg^{2+} in TEHP plasticizer. These trends of response of the electrode are inherently similar to those in extractabilities[13], indicating that the selectivities of the PVC membrane electrodes are controlled by the complexing property of the crown ether.

The dependence of the selectivity coefficient on the neutral carrier concentration was also examined, and is shown in Figure 2. In the case of the neutral carrier type ion selective electrode, the mechanism of electrode response depends mainly on the extraction equilibrium at the vicinity of the interface between the membrane and aqueous layer,[14] and it can be attained rapidly and easily when a large amount of crown ether complex is contained in a PVC membrane. Selectivity coefficient also depends on the amount of complex in the PVC membrane for the same reason. In spite of these consideration, a neutral carrier content of 7 wt% was chosen as the optimal condition, because the surface condition of the PVC membrane deteriorated when increasing the neutral carrier content to 7 over wt%.

In an attempt to increase the selectivity of lithium over sodium, we incorporated into the PVC membrane lithium-carrier II complex (carrier III). Though we obtained some results for the complex crystals incorporated into the PVC, the selectivity was not improved.

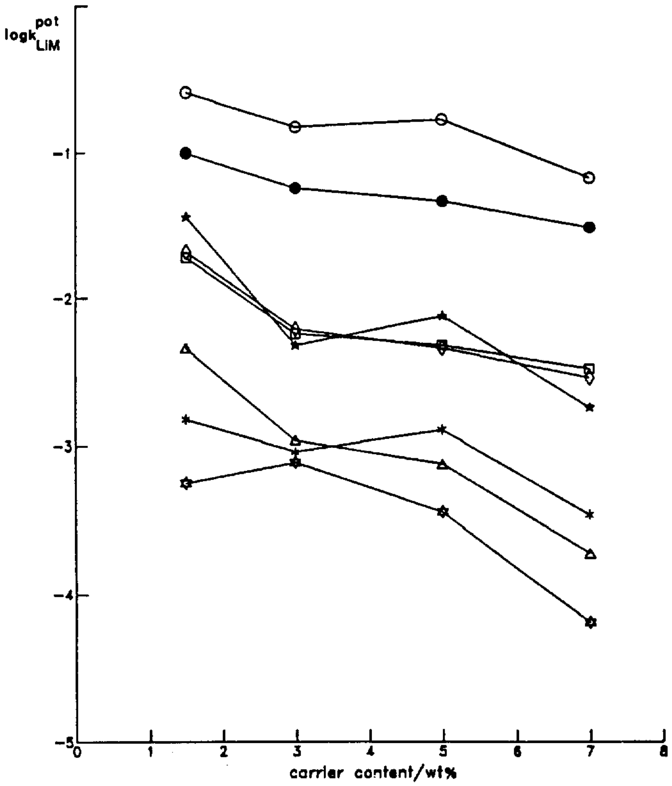

Figure 2. Dependence of log k^{pot}_{LiM} values on carrier II eoncentration in PVC-TEHP liquid membranes. NH$_4$$^+$(○), Na$^+$(●), Rb$^+$(★), Cs$^+$(◇), K$^+$(□), Ca^{2+}(△), Mg^{2+}(＊), Ba^{2+}(△).

Serveral plasticizers were tested as the membrane solvent for the PVC-carrier II membrane to further promote the Li$^+$ selectivity of the resulting electrodes, especially with respect to Na$^+$ (Table 1 and Figure 2). NPPE-based electrodes were noisy with poor response and were not, therefore, examined further. The electrodes based on TEHP, DOPP have similar linear range and detection limits, however the electrode based on BEHA, DOA, NPOE have shorter linear range and sub-Nernstian slopes. The membrane solvents used were TEHP, BEHA and which have low polarity (dielectric constant, $\varepsilon=4^{15}$), and NPOE and NPPE which have relatively high polarity (dielectric constant, $\varepsilon=24^{15}$). Large differences were not observed for k^{pot}_{LiM} of alkali metal ion on the five electrodes. However, electrodes with relatively low polarity solvent TEHP (dielectric constant, $\varepsilon=4$) give smaller k_{LiM} values for alkali metal ions compared with those of electrodes based on high polarity solvents NPOE (dielectric con-

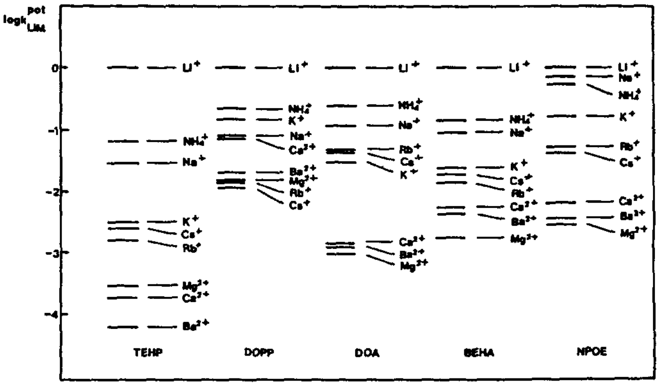

Figure 3. Selectivity coeffcient, log k_{LiM}^{pot} for alkali and alkaline earth metal ions based on neutral carrier II in PVC with TEHP, DOPP, DOA, BEHA and NPOE as plastcizer and with KTClPB.

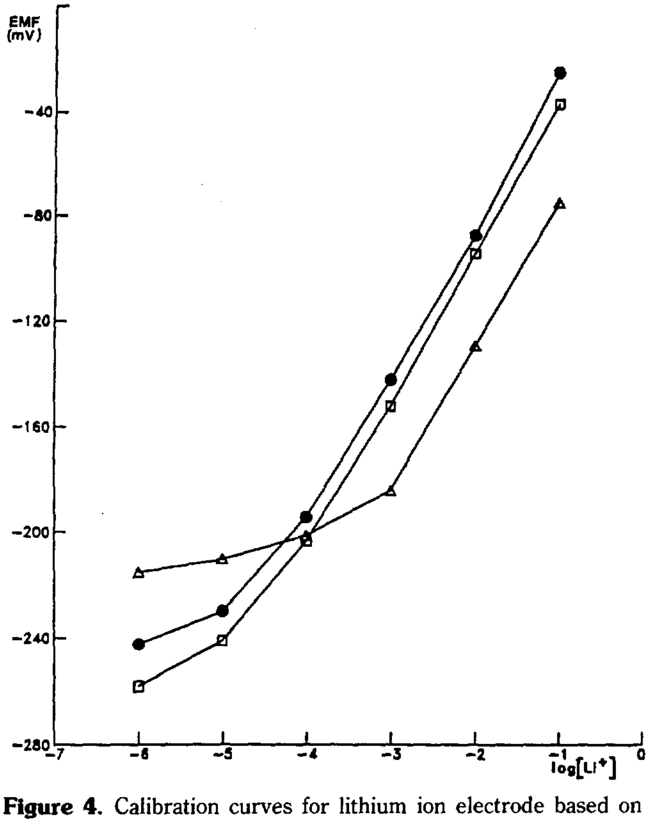

Figure 4. Calibration curves for lithium ion electrode based on neutral carrier II with TEHP as plasticizer after store in 0.1 M LiCl, first day (○), 6 months (□), one years (△).

stant, ε=24). Among all electrodes based on carrier II, the best selectivity was obtained with the one which used TEHP as membrane solvent.

The membranes also contain a small quantity of KTClPB for the purpose of reducing the membrane resistance and suppressing permeation of counter anions in aqueous phase into the membrane phase.[15] The addition of KTClPB (TBP is an anion excluder) ion-exchanger, as in carrier I, II and III based electrode, does not improve electrode selectivity. However the presence of lipophilic salt (KTClPB) produced a near-Nernstian slope and good sensitivity in the activity range 10^{-1}-10^{-6} M (Table 1). Membrane electrode prepared without a lipophilic salts showed poor response and slopes owing to either a high resistance or a anion in the test solution. The highest possible carrier-induced electrode for lithium ion is expected at concentrations of anionic sites of 30 mol% with respect to the total carrier concentration.

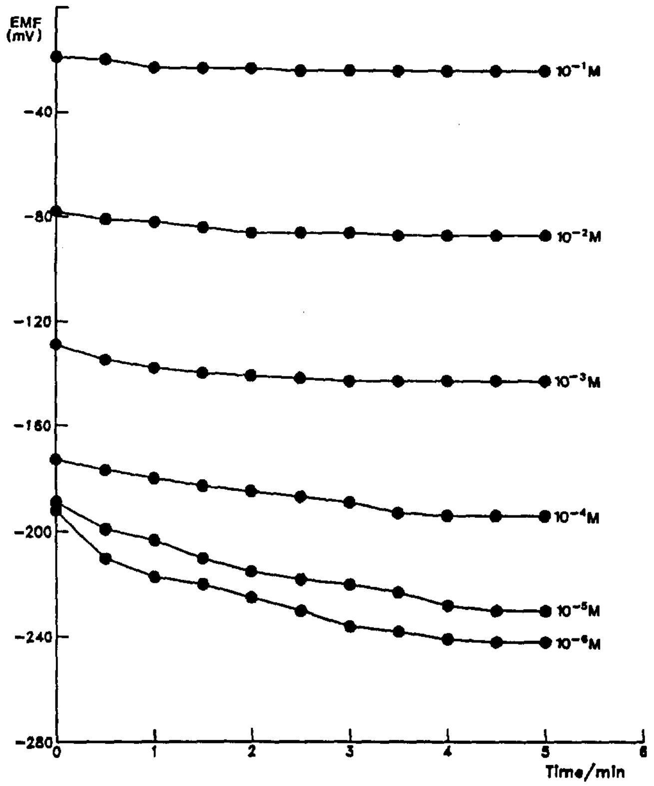

Figure 5. EMF-Time profile of Li$^+$-selective electrode based on neutral carier II.

All the electrodes have stored well in 10^{-1} M LiCl for 1 year. The crown ether electrode has a life time of at least 6 months with little change in response (Figure 4) and selectivity with respect to sodium. Therefore, the life time of the membrane was long enough for practical use, as was found for other PVC membranes (Figure 4).

Figure 5 shows the emf-time profile for the Li$^+$-selective electrode based on the carrier II and TEHP as membrane solvent with lipophilic salts, KTClPB. The electrode was observed to reach equilibrium potential faster at high lithium concentration. The response time of the electrode was less than 2 min.

The electrodes appear to be affected by an interference from H$^+$ in acidic solution, nonetheless the electrodes could be sufficiently utilized for Li$^+$ determination in solution above pH 2.

Although the theoretically required selectivities in respect to Na$^+$ are not reached, a practical application using adequate calibration solutions seems possible, because the blood concentrations of these ions can be expected within narrow limits. Future sensor applications of crown-4 derivatives require further optimization of their selectivity and affinity for Li$^+$ ion.

These results might be the first indication of the ultimate use redox-active crown ethers in sensor elements and the manufacture of ion selective electrodes and lithium batteries.

Other applications can be the extraction of lithium from sea water and waste brines.

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Gas Phase Optoacoustic Spectra and Raman Spectra of Some Chlorinated Pollutants

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Laser optoacoustic technique has been employed to obtain the gas phase absorption spectra of 1-chloronaphthalene, 3-chlorobiphenyl, and 2,5,2′-trichlorobiphenyl in conjunction with a gas chromatograph and a Helmholtz resonator at the various CO_2 laser wavelengths. Raman spectra of 1-chloronaphthalene, 4-chlorobiphenyl, and 4,4′-dichlorobiphenyl in condensed phase have been also obtained. The optoacoustic measurement of the infrared absorption in gas phase has been shown to be of value in monitoring the environmental pollutants.

Introduction

In recent years the development of ultra-high sensitivity detection techniques has taken on an increased importance as the environmental contamination from industrial and agricultural chemicals increases. One particular health and environmental concern is halogenated organic hydrocarbons, due to their ubiquity, stability, potential for biomagnification, and highly toxic nature. The most striking examples of such chemicals include halogenated dibenzo-*p*-dioxins (*e.g.,* TCDD), dibenzofurans, polychlorinated and polybrominated biphenyls (known as PCB and PBB), and chlorinated naphthalenes. These chemicals may be industrially useful (biphenyls and naphthalenes) or unwanted contaminants (dioxins and furans) of other useful compounds[1]. However, interest in their environmental effects has greatly increased as a result of their notorious toxicity; even in extremely small concentrations public health can be threatened.

Since almost all pollutants have their fundamental absorption bands in the infrared region, IR and Raman spectroscopic techniques have been found to be useful for these studies. However, from the fact that molecular vibrational absorption cross sections in this spectral region are not large in general, for extremely sensitive trace detection, the development of new techniques have been required. The combination of infrared detectors with gas chromatography (GC-