Lithium Ion Selective Electrode Based on a Synthetic Neutural Carrier

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중성운반체를 이용한 리튬이온 선택 전극

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요 약. 리튬·이온의 새로운 중성운반체로서 tetrahydrofuran 단위의 16고리형 crown-4를 퓨란과 아세톤으로부터 산 촉매하에서 합성하여 수소화시킨 후 리튬·이온과의 착물형성반응을 Li-7 NMR과 전기전도도법으로 조사했다. 합성한 리간드를 PVC-액체막 전극에 사용하여 분리용액법에 의한 리튬· 이온의 선택성을 결정하였다. 막용매, tris(2-ethylhexyl) phosphate에서 리튬이온의 선택계수는 알칼 리금속이온 및 알칼리토금속이온에 대해 2.4×10^{-1}에서 2.3×10^{-4} 범위의 값을 가졌으며, 산성용액 (pH=2 이하, 0.1M LiCl)에서 액체막은 H· 이온의 방해로 불안정하였다.

ABSTRACT. THF-based crown-4 of 16-membered rings having tetrahydrofuran unit was synthesized by an acid-catalyzed condensation of furan and acetone followed by hydrogenation in an effort to obtain highly selective ionophores for lithium ions. The new ionophore was compared with previously reported ionophores under similar measurement conditions with the same plasticizer, tris (2-ethylhexyl) phosphate in poly(vinyl chloride)(PVC) membrane electrodes. Separate solution method was used to determine relative selectivity coefficients for the electrode. The selectivity coefficients(K_{LiM}^{POT}) of lithium over ammonium, alkali and alkaline earth metal ions go from about 2.4×10^{-1} to 2.3×10^{-4} to working range and pH dependence have also been studied.

Key Word : ionophores, membrane electrode, separate solution method.

I. Introduction

Much attention has been paid to the lithium ion-selective electrodes for environmental and biological applications. Several neutral carriers for Li+-selective electrodes have been reported so far, such as crown ethers, noncyclic polyethers, and so on.[1,2]

Lithium selective electrodes are of great interest for the direct potentiometric determination of Li+ ion in whole blood during the lithium therapy of patients suffering from manic-depressive psychosis, where a Li+-concentration in blood of 0.8 to 1.0 mM 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). The ubiquity of THF unit in the naturally occuring antibiotic ionophores(e.g.,monactin, nigerisin, and monesin contain tetrahydrofuran) encourage this purpose. Tetrahydrofuran unit is expected to have a poten-

tial 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(THF-based Crown-4, *Figure* 1)by ¹H, ¹³C and ⁷Li NMR spectroscopy.[6]

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

II. Experimental

Chemicals. Solvents were dried and purified by refluxing over a suitable drying agent, followed by distillation under a N_2 atmosphere. Ethyl acetate, THF and pyridine were distilled over CaH_2, Na and KOH respectively. Water was deionized and distilled over $KMnO_4$. Alkali and alkaline-earth metal chlorides were analytical grade. PVC(secondary standard) and tris(2-ethylhexyl) phosphate were purchased from Aldrich chemicals and used without prior purification.

Aparatus. Infrared spectra were recorded on a Perkin-Elmer 457 grating spectrophotometer. Melting points were determined on a MP melting point appratus. Mass spectra were measured at AEI MS 902 mass spectrometer. ¹H NMR spectra was recorded on a Bruker WH-300 spectrometer. Chemical shifts(δ/ppm) are measured relative to SiMe₄.

Conductivity measurements were performed on a PTI-18 conductivity meter. TLC and column chromatography were performed utilizing aluminium sheets silica gel 60 F₂₅₄(E. Merck) and 70-230 mesh silica gel 60(E. Merck). Elemental analyses were performed by Oxford microanalytical service.

Syntheses of Ionophore. 2,2,7,7,12,12,17,17-octamethyl-21,22,23,24-tetraoxaperhydroquaterene. The compound was prepared by condensation of furan with acetone in ethanol, as described by Healy and Rest.[7] Catalytic hydrogenation in THF over Pd/C(140℃, 120 atm, 20h) gave the crude product. The product was chromatographed(70% hexane-toluene) to give a white

solid product which is possibly mixtures of configurational isomers : m.p. 207~209℃(lit.[12]207~210℃). Anal. Calcd. for $C_{28}H_{32}O_4$: C,74. 95 ; H, 6.43. Found : C, 74.65 ; H, 10.80.; ir(KBr) 3096, 1558, 1210 and 1027(C−O−C), 957 and 779 Cm⁻².

Electrode system. Measurements were performed by the use of the following cell : Hg ; Hg₂Cl₂,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.

Membrane Preparation. The typical procedure for membrane preparation is as follows : PVC(180mg), tris-(2-ethylhexyl) phosphate(350mg) and neutral carrier (8.5mg) were dissolved in 10m*l* of THF. This solution was then poured into a flat petri-dish of 40mm inner diameter. Gradual evaporation of the solvent at room temperature gave a transparent, flexible membrane of about 0.2mm in thickness. A disk of 8mm diameter was cut with a cork-borer and soaked in 0.1M LiCl solution for 24 hours. The disk was then inserted into the electrode assembly.

Potentiometric Selectivity Coefficients. Selectivity coefficients were determined by the separate solution technique on 10⁻¹M aqueous solutions of the chlorides using the Niclosky-Eisenman equation[8]:

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

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 10⁻¹M, E_2 = EMF of the cell assembly, the sample being a 10⁻¹M solution of the chloride of the interfering cation.

The activity coefficient γ were calcurated by using the following equation based on the Debye-Huckel theory[9]:

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

where I denotes the ionic strength. Some of the experimental values of activity coefficients in the literature[10] were also employed.

Conductivity Measurements. The conductivity measurements were carried out at 17 ± 0.1 ℃ with use of a conductivity cell with a cell constant of 0.098 cm^{-1}. The procedure is as follow: An ethylacetate solutions of the LiClO$_4$(5.6×10^{-4}) and NaClO$_4$(4.8×10^{-4}) was placed in the cell and the specific conductivity of the solution was measured. A stepwise increment in the ligand concentration was obtained by addition of a ligand solution(3 × 10^{-3}M) to the cell with a microburette. In order to keep the salt concentration constant during the titration, the ligand solution contained the same concentration of salt as the initial salt solution.

Ⅲ. Results and Discussion

The lithium selectivities of the crown ether, 2,2,7,7,12, 12,,17.17-octamethyl-21,22,23,24-tetraoxaperhydroquaterene(Ⅰ)(THF-based Crown-4, *Figure* 1) were evaluated as potentiometric selectivity coefficients of polymeric membranes based on them. For comparison, 3,3, 7,7,11,11,15,15-octamethyl-1,5,9,13-tetraoxacyclohexadecane(Ⅱ)(OM-16-crown- 4, *Figure* 1)[11] and glass electrode[12] were also empolyed. The polymeric membrane consists of poly(vinulchloride)(PVC) as the support, tris-(2-ethylhexyl) phosphate(TEHP) as the membrane solvent, and a crown ether as the ionophore.
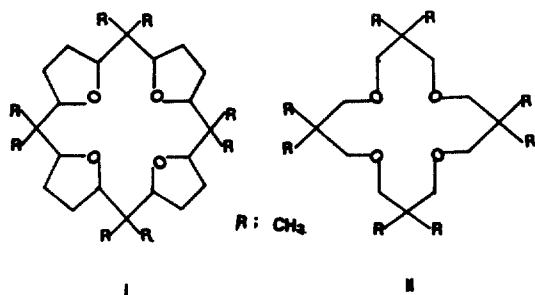

Figure 1. Structure of the THF-based Crown-4(Ⅰ) and OM-16-crown-4(Ⅱ)

The response of the membrane electrode to akali and akaline earth metal ions using THF-based Crown-4(Ⅰ) as the neutral carrier is shown in *Figure* 2. The EMF readings are not corrected for changes in the liquid junction potential. The uncertainties in the EMF readings should be comparable to those estimated by orthers using the same kind of experimental set up.[11]

As shown in *Figure* 2, the response is linear over the activity range nearly 10^{-4} to 10^{-1} M for Li$^+$, with nearly Nernstian slope of 59 mV per activity decade at 25℃. The membrane can also be used at lower concentrations. The electrodes also react in a near Nernstian fashion in different concentration regions for H$^+$, NH$_4$$^+$, Na$^+$ and K$^+$.
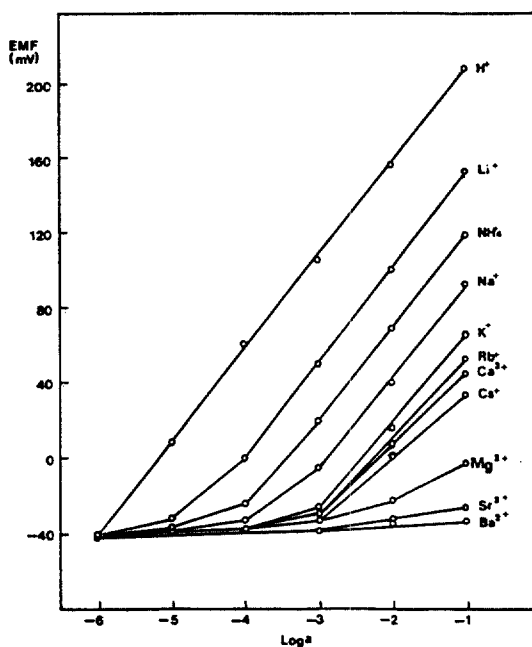

Figure 2. EMF response of cell to aqueous solutions of the chlorides of H$^+$, NH$_4$$^+$, alkali and alkaline earth metal ion using THF-based Crown-4 as a membrane component.

Selectivity coefficients obtained by the separate solution technique on 10^{-1} M solutions of the chlorides are indicated in *Figure* 3 together with results from a glass electrode[11] and investigations by J. Krane et al.[11] on their neutral carrier PVC membrane electrode. The
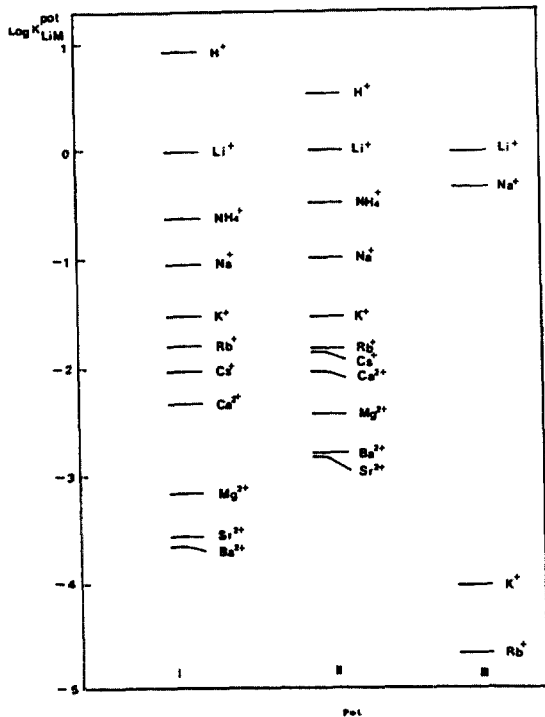
Figure 3. Selectivity coefficients, $\log K_{LiM}^{pot}$, for PVC-TEHP membrane of carrier I and II (ref. 11). Column III: glass electrode(ref. 12). The values in column I and II were obtained by the separate solution technique on 10^{-1} M solutions of the chlorides.

selectivity coefficients are listed in *Table* 1. The present electrodes based on the neutral carrier give better selectivity for lithium to sodium than can be obtained with the glass electrode, but the selectivities are similar to those found by J. Krane using the neutral carrier, OM-16-crown-4.

Figure 4 shows the EMF response for different lithium cholride solutions as a function of pH. The response are constant in a wide range of the pH scale,

Table 1. Comparison of Selectivity Coefficients, K_{Lij}^{pot} (j: interferring ions) of Li^+-Selective Electrodes Based on PVC-TEHP[a] Membrane of I and II[b]

interferring ion	carrier I		carrier II	
	K_{LiM}	$1/K_{LiM}$	K_{LiM}	$1/K_{LiM}$
Li^+	1.0	1.0	1.0	1.0
H^+	8.9	0.1	3.5	0.3
NH_4^+	2.4×10^{-1}	4	3.2×10^{-1}	3
Na^+	8.9×10^{-2}	11	9.9×10^{-1}	10
K^+	3.0×10^{-2}	33	2.9×10^{-2}	35
Rb^+	1.6×10^{-2}	63	1.5×10^{-2}	67
Cs^{2+}	9.4×10^{-3}	106	1.4×10^{-2}	72
Mg^{2+}	7.1×10^{-4}	1386	3.5×10^{-3}	286
Ca^{2+}	4.5×10^{-3}	223	9.5×10^{-3}	105
Sr^{2+}	2.9×10^{-4}	3417	9.5×10^{-4}	105
Ba^{2+}	2.3×10^{-4}	4437	1.6×10^{-3}	625

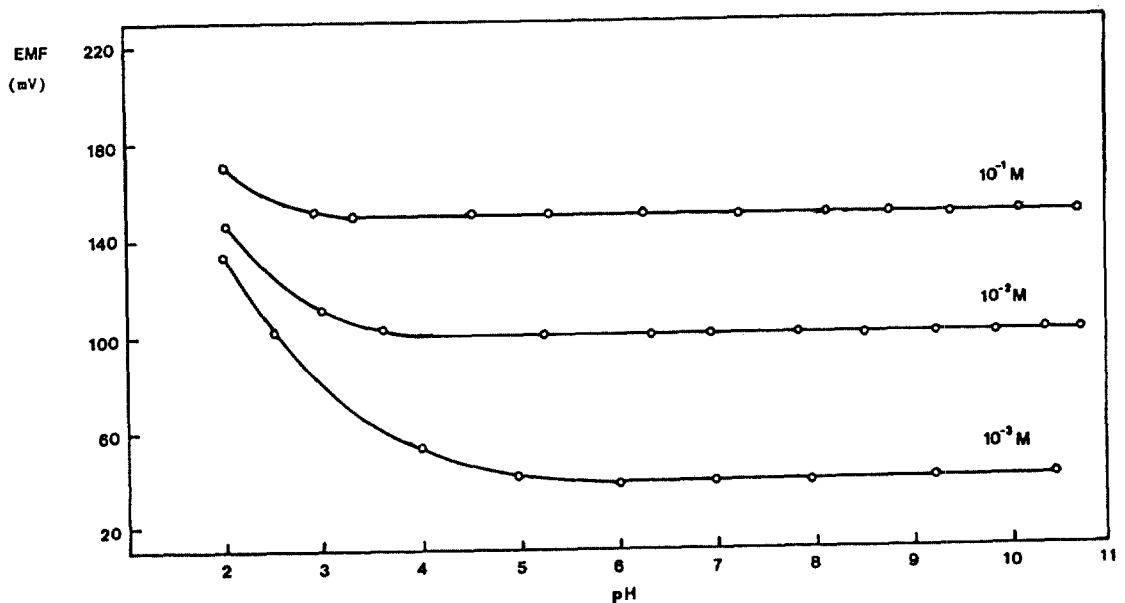a) TEHP;tris-(2-ethylhexyl)-phosphate, b) reference 11

Figure 4. EMF response of cell for different LiCl concentrations as a function of pH. THF-based Crown-4 used as membrane component, HCl and KOH used to change the pH value.

but at low pH values there is serious interference with H+ ions. This is to be expected according to the selectivity coefficients measured in 10^{-1}M solutions(*Figure* 3 and *Table* 1).

In order to get some information about Li+ selectivity over Na+ of THF-based crown-4 in a bulk phase, attempts were made to determine the stoichiometry of the THF-based crown-4 for perchlorates of Li+ and Na+ in ethylacetate(*Figure* 5). Inspection of *Figure* 5 showed that for THF-based crown-4 the equivalent conductance of LiClO₄ was increased as the concentration of crown ether increased. This is in marked contrast with the results for the addition of the crown ethers to ethylacetate solutions with sodium percholrate, where a little change is seen in *Figure* 5. Since in nonpolar solvent as ethylacetate lithium perchlorate either can by solubilized as Li+-ionophore (THF-based Crown-4) complex, or if in solution, exists as nonconducting ion pair, the addition of a crown to a solution of lithium perchlorate in ethylacetate results in an increase in the conductance until the stoichiometric

mole ratio is followed by a plateau. The stoichiometry for the Li+- ionophore complex was 1:1.

On the contrary, the conductivity changes were so small on stepwise addition of ligand to a sodium perchlorate ethylacetate solution that an accurate value could not be obtained. Thus , this result regarding complex formation in the bulk phase has again confirmed to us the excellent Li+ selectivity of the THF-based Crown-4 ionophore.

The interaction of the ion with the ligand can be observed by the NMR spectroscopy (*Figure* 6). *Figure* 6 shows the 300 MHz ¹H spectra of the THF-based Crown-4 and its Li+ complex in chloroform solution. A broad peak at $\delta=3.2\sim3.8$ ppm is due to the 8 oxymethine protons and at $\delta=1.3\sim2.4$ppm is due to the 16 methylene protons on the THF rings(*Figure* 6 (a)). Several sharp resonances around 1 ppm are due to the 24 methyl protons. The four subunits are magnetically not equivalent and several geometric isomers are possible. Corsini and Panoyan[13] have ovserved coalescence of the methyl signals above 66℃. This observation
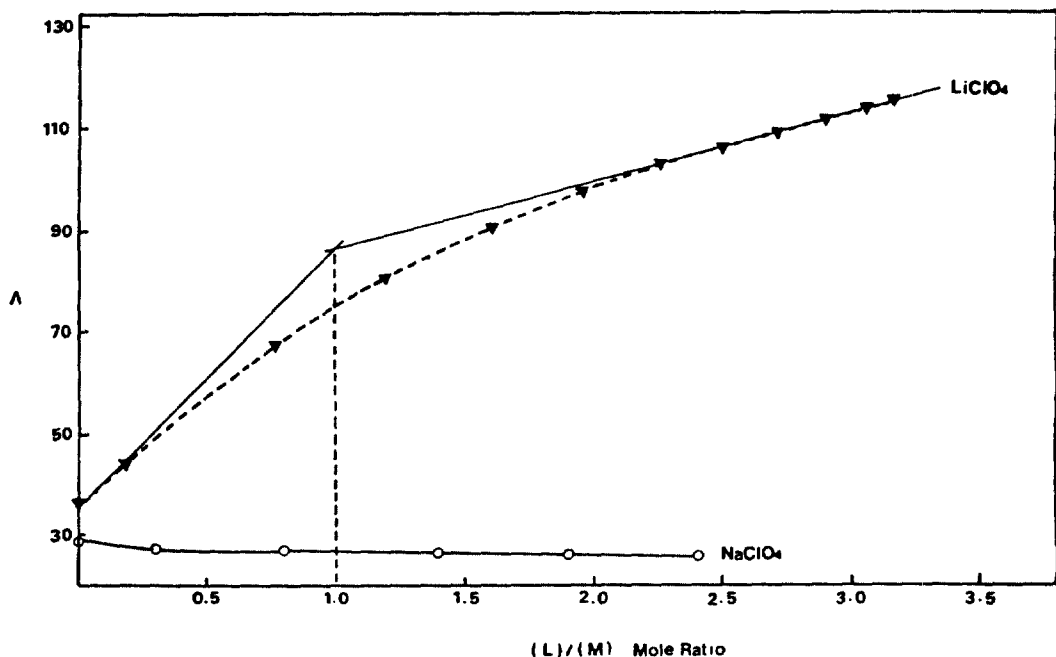

Figure 5. Plot of equivalent conductance $\wedge$ vs. the ratio of THF-based Crown-4(I) to LiClO₄(5.6×10^{-4}) and NaClO₄(4.8×10^{-4}) in ethylacetate at 17 ± 0.1℃.

suggests that the methyl groups are in different conformation, at a rate which produces a single time-averaged signal in the NMR spectrum.

On formation of the lithium complex(*Figure* 6(b)), the oxymethine protons give rise to only one resonace at δ = 3.8, indicating that they have become magnetically equivalent and the shifts due to complexation. This observation indicate that only one geometrical isomer(all cis-isomer) complexes with lithium. THF-based Crown- 4 has a cavity radius nearly equal to that of the unsolvated lithium ion. It is expected, therefore, that very stable lithium complexes are formed.

The Li-7 NMR studies for lithium complexation with THF-based Crown-4 has been carried out in the preceeding article.[6] In cases for Li-7 NMR resonance of the complexation with THF- based Crown- 4(I), in contrast to the OM-16-crown-4(II)[14], the exchange between the free and complexed lithium ion was slow on the NMR time scale, and two NMR signals were observed at 291 K. On the contrary, Na-23 NMR resonance for sodium ion complex with THF-based Crown-4 produced no measurable chemical shift changes.

The formation constant(Ks) for 1:1 complex in chloroform which obtained by Li-7 NMR method was around $> 10^4$ for Li[+6].

Althougth 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 the THF-based 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 of redox-active crown ethers in sensor

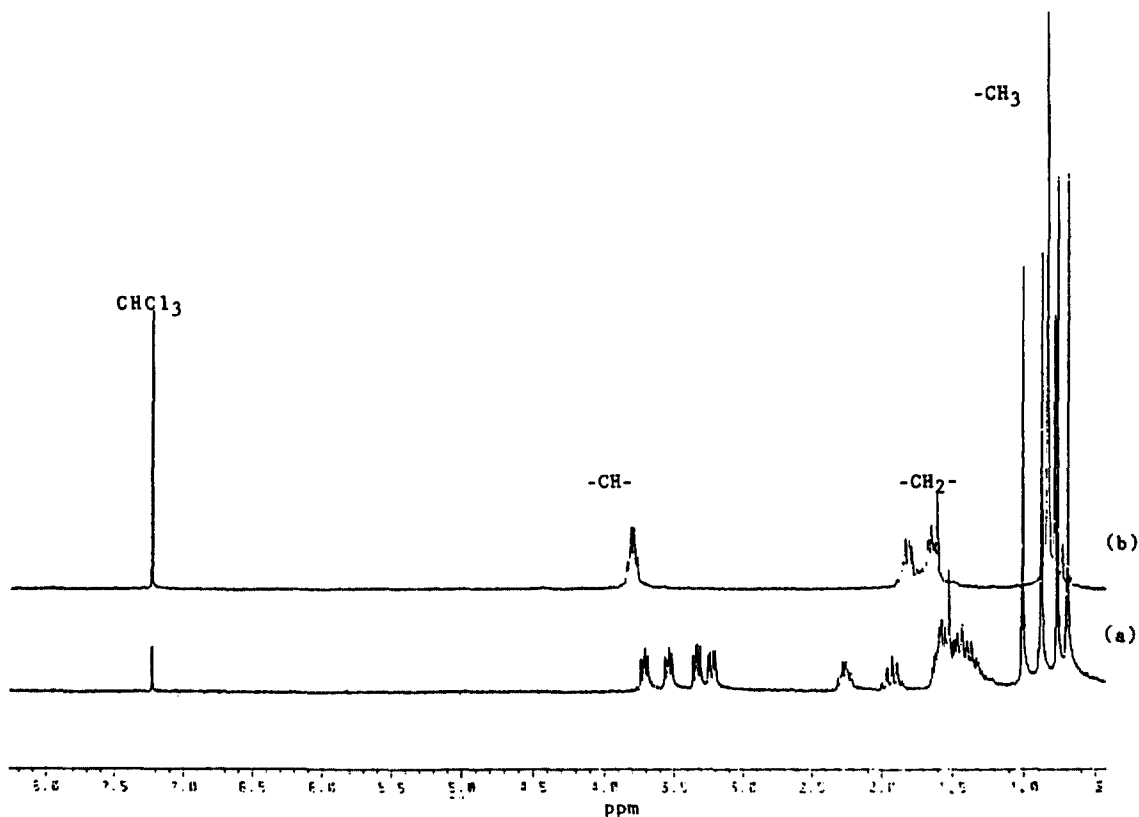*Figure* 6. ^{1}H Nmr spectra (300 MHz) of THF based Crown- 4(a), and in the presence of the LiClO$_4$(b) in CDCl$_3$.

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.

References

1. K. Kimura, H. Oishi, T. Miura, and T. Shono, *Anal. Chem.,* **59,** 2331(1987); V. P. Y. Godzekpo, J. M. Hungerford, A. M. Ibrahim, R. Y. Xie, and G. D. Christian, *Anal. Chem.,* **58,** 1948(1986); K. Hiratani, T. Okada, and H. Sugihara, *Anal. Chem.,* **58,** 766(1987);1. M. Güggi, U. Fiedler, E. Pretsch, and W. Simon, *Anal. Lett.,* **8,** 857(1975).

2. K. Hiratani, *Chem. Lett.,* 1021(1982).

3. A. Amidsen, *Dan Med. Bull.,* **22,** 277(1975).

4. John F. J. Cade, *Med. J. Aust.,* **2,** 349(1949).

5. H. J. M Bowen, *Environmental Chemistry of the Elements,* Academic Press, 1979; pp 105-106.

6. J. S. Kim and B. Y. Lee, The 5th Symposium on Biofunctional Chemistry, Hiroshima, Jappan, June 5-6, 1990, abstract P13;J. S. Kim and S. R. Cooper, submitted for publication.

7. M. de Sousa Healy and A. j. Rest, *J. Chem. Soc. Perkin I,* 973(1985).

8. J. Koryta, *"Ion-selective electrodes",* Cambridge University Press, Cambridge, 1975; pp 64-67.

9. J. N. Butler, *"Ionic Equilibrium", A Mathermatical Approach,* Addison-Wesley Reading, Palo Alto, London 1964; pp 432-434.

10. C. W. Davies, *J. Am. Chem. Soc.,* **60,** 2093(1938); J. Kielland, *J. Am. Chem. Soc,* **59,** 1675(1937).

11. K. M. Aalmo and J. Krane, *Acta Chem. Scand.* A **36,** 227(1982).

12. G. Eisenman. In C. N. Reilly, Ed., *"Advances in Analytical Chemistry and Instrumentation",* Wiley, New York 1965, Vol. 4, p 213.

13. A. Corsini, J. M. Panoyan, *J. Inorg. Nucl. Chem.,* **39,** 1449(1977).

14. K. M. Aalmo and J. Krane, *Acta Chem Scand.* A **36,** 219(1982).