Comparative Study of Neutral Carriers in Polymeric Lithium Ion Selective Electrodes

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New lipophilic diamide compounds have been synthesized and tested as ionophores for lithium in poly(vinyl chloride) (PVC) membrane electrodes, including compounds with pyridine, furan, dioxanonane, and polyether backbones with different lipophilic diamide groups. The new ionophores were compared with previously reported ionophores under similar measurement conditions with the same plasticizer, tris(2-ethylhexyl) phosphate, in all membranes. Fixed interference and matched potential methods were used to determine relative selectivity coefficients for all the electrodes. The highest selectivity for lithium relative to sodium was obtained with *N*,*N*-dicyclohexyl-*N'*,*N'*-diisobutyl-*cis*-cyclohexane-1,2-dicarboxamide (140:1) and the 14-crown-4 ether, 3-dodecyl-3-methyl-1,5,8,12-tetraoxacyclotetradecane (125:1) when using NPOE plasticizer. The latter exhibited faster response at low lithium concentrations. It exhibited consistently high selectivity using different measurement methods and was stable for 5 months.

Electrically neutral, lipophilic ion-complexing agents of rather small relative molar mass are known to behave as ionophores or ion carriers (*1*). These neutral carriers have the capability to selectively extract ions from aqueous solutions into a hydrophobic membrane phase and to transport these ions across barriers by carrier translocation. The neutral carriers, when incorporated into a water-immiscible membrane, an appropriate organic solvent, or an inert matrix, function as cation-selective electrodes and often exhibit a nearly Nernstian response to the primary ions. The potentiometric selectivity of these sensors among different ions is dictated largely by the complexation specificity of the carrier molecules involved, but it may also be influenced by the membrane solvent and by other parameters (*2*). Selectivities are influenced by the plasticizer employed as well as the relative concentrations of ions to which the sensor is exposed.

Several neutral carriers have been reported for lithium ion in a lithium ion selective electrode. While providing Nernstian or near-Nernstian response to lithium ion, the electrodes have often exhibited only moderate selectivity for lithium with respect to sodium. Zhukov et al. (*3*) described a diamide neutral carrier with a measured selectivity of about 100 for lithium relative to sodium, and Metzger et al. (*4*) have recently described a derivative with about a 3-fold improvement in this selectivity.

We have prepared several variations of lipophilic diamides, with pyridine or furan groups as the backbone, as neutral carriers in lithium ion selective electrodes. The relative lithium response and selectivities with respect to sodium of these neutral carriers in PVC membranes have been determined and compared with previous ionophores under different measurement conditions using the same plasticizer in all membranes. In addition, comparison is made with a 14-crown-4 ether neutral carrier as reported by Kitazawa et al. (*5*).

Cation complexing properties of a large number of macrocyclic polyether–diester compounds have also been reported (*6–19*). These compounds generally form weaker complexes than the cyclic polyethers. They have been reported to show significant affinities for alkali, alkaline-earth, and primary alkylammonium cations (*12, 13, 15, 16, 19*). Gadzekpo et al. have reviewed the literature of lithium sensors (*20*).

EXPERIMENTAL SECTION

Reagents and Chemicals. High molecular weight poly(vinyl chloride) (PVC) was obtained from Fluka AG. Tris(2-ethylhexyl) phosphate was obtained by U. C. C. Flexoh. All solutions were prepared from salts of reagent grade using deionized water. The chlorides of the metals were used in all cases. Neutral carriers were prepared in our laboratory as described below.

Electrode System. Measurements were performed by the use of the following cell:

Hg, Hg_2Cl_2, KCl (satd)||sample solution|membrane|AgCl, Ag

A Beckman digital pH meter (Model 4500) was used in monitoring the voltage.

PVC-Plasticizer Stock Solution. Poly(vinyl chloride) (0.6 g) was mixed with 1.36 g of tris(2-ethylhexyl) phosphate plasticizer (unless otherwise stated) as outlined in an earlier publication (*21*). Cyclohexanone (7.5 mL) was next added to the mixture and the mixture shaken until all the PVC dissolved. Individual neutral carriers were added to 250 μL of this as follows (mg): **1** (2.7), **2** (5.7), **3** (5.6), **4** (3.0), **5** (4.8), **6** (3.0), **7** (3.0), **8** (3.3), **9** (3.5), **10** (3.7), **11** (3.1), **12** (4.2), **13** (5.3), **14** (4.8), **15** (1.1), **16** (1.1), **17** (4.0). This corresponds to a minimum of 4% (w/w) of neutral carrier in the membrane for all but **15** and **16**.

Electrode Fabrication. Two aliquots of 25 μL of PVC–plasticizer–lithium carrier solution were carefully deposited on a compact silver–silver chloride plug of a Beckman threaded ion-selective electrode tip. The second aliquot was deposited after the first aliquot had almost dried. The tip was left to stand for 24 h and then it was soaked in 0.1 M LiCl solution for 24 h before use.

Selectivity Coefficients ($K^{Pot}_{Li,M}$). Selectivity coefficients were determined by the mixed solution (fixed interference) method and the matched potential method (*22*). In the former, a background concentration of the interference ion was employed that was approximately equal to that found in blood serum, i.e., 140 mM NaCl, 4 mM KCl, 2.5 mM $CaCl_2$, and 1 mM $MgCl_2$, respectively. In the latter, a comparison is made of the concentrations of primary ions and interference ions needed to give the same potential change when added to a fixed reference solution of either the primary ion or the secondary ion. The ratio of concentrations needed to give the same potential change represents the selectivity. A reference solution of 1 mM LiCl was employed. The potential change was recorded upon incrementing the lithium concentration by 1 mM and the concentration of sodium required to give the same potential change in the reference solution was determined, to provide the relative response for the two ions.

SYNTHESES

The neutral carriers synthesized are shown in Figure 1. Compound **1**, first described by Shanzer et al. (*23*), was synthesized by a new method as previously reported (*24*). Compound **5** was synthesized as described by Güggi et al. (*25*), compound **13** as

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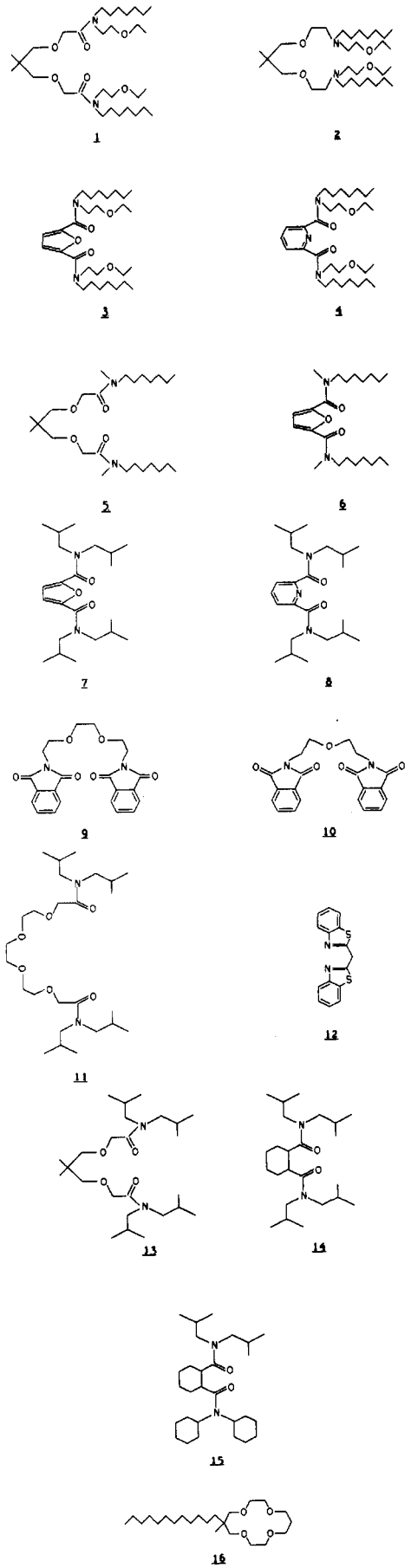
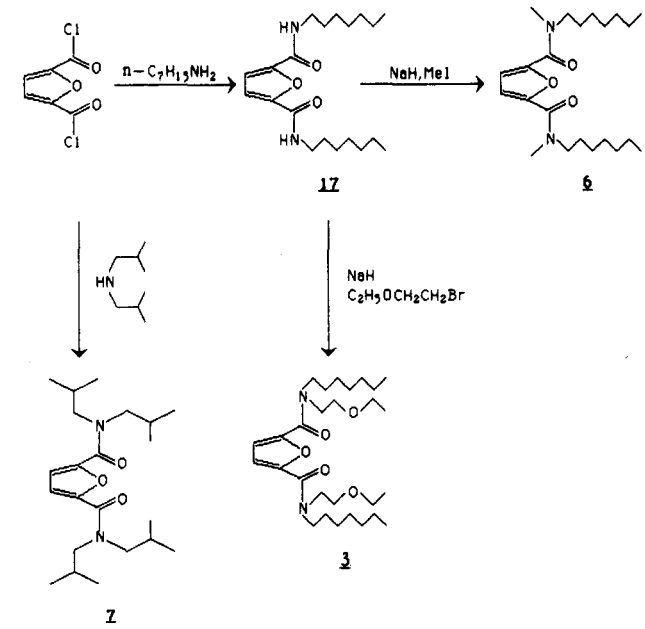


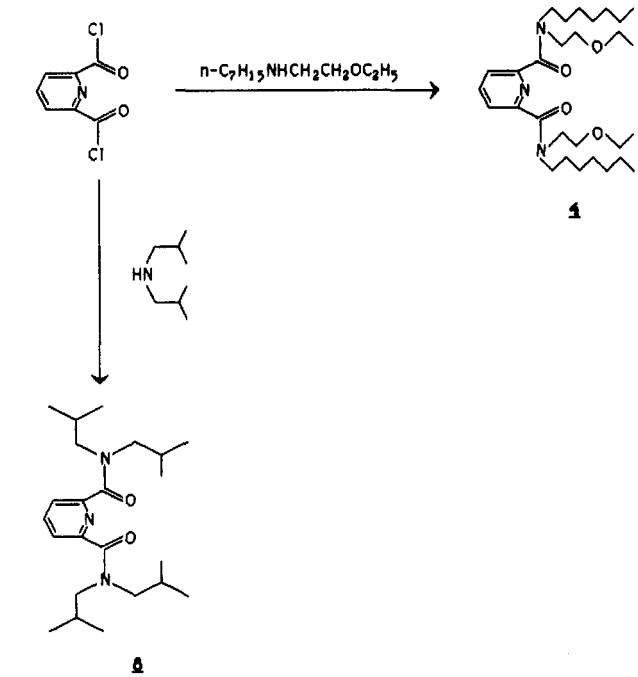
Figure 1. Neutral carriers.

described by Xie et al. (*26*), and compound **14** as described by Zhukov et al. (*3*). Compounds **9** and **10** were obtained from potassium phthalimide and the appropriate dichloro compounds

Scheme I



Scheme II



in dimethyl sulfoxide instead of dimethylformamide as reported (*27*). Compound **12** was also prepared as described (*28 29*).

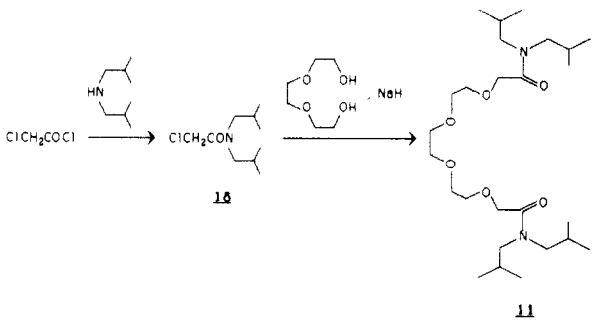
Compound **2** was prepared by reducing compound **1** with lithium aluminum hydride (LAH). Compounds **3** and **6** were prepared starting from furan-2,5-dicarboxylic acid, which was first converted to the diacid chloride (*30*) which was then reacted with *n*-heptylamine to give *N,N'*-diheptylfuran-2,5-dicarboxamide (**17**). The latter was then alkylated with methyl iodide or 2-ethoxyethyl bromide to give compounds **6** and **3**, respectively (Scheme I). The diamide **7** was obtained by reacting furan-2,5-dicarbonyl dichloride with disobutylamine. The diamides **4** and **8** were prepared by reacting pyridine-2,6-dicarbonyl dichloride with *N*-(2-oxapentyl)heptylamine or diisobutylamine, respectively (Scheme II).

The diamide **11** was synthesized as shown in Scheme III by first reacting chloroacetyl chloride with diisobutylamine to give *N,N*-diisobutylchloroacetamide (**18**), which was then reacted with triethylene glycol and sodium hydride to give compound **11**.

Compound **15** was the kind gift of W. Simon. Compound **16** was synthesized as described by Kitazawa et al. (*5*).

Experimental Methods. All oily products were purified by silica gel column chromatography using petroleum ether (bp 30–60

Scheme III



16 11

°C) and a mixture of petroleum ether (bp 30–60 °C) and chloroform (2:1).

General Procedure for the Reaction of Diacid Chlorides with Secondary Amines: Synthesis of Compounds 4, 7, and 8. A solution of the appropriate acid chloride (2 mmol) in 5 mL of methylene chloride was added portionwise with stirring and cooling over a period of $^1/_2$ h to the appropriate secondary amine (2.2 mmol) and triethylamine (3 mmol) in methylene chloride (10 mL). The reaction mixture was then stirred at room temperature overnight and then methylene chloride (20 mL) was added. The solution was washed twice with each of distilled water, hydrochloric acid (20 mL, 3 M), water, saturated sodium bicarbonate, and water. The organic layer was dried over anhydrous sodium sulfate and concentrated in vacuo to give the corresponding diamide **4**, **7**, or **8**.

N,N'-Diheptyl-*N,N'*-di(2-oxapentyl)pyridine-2,6-dicarboxamide (compound **4**) was obtained as a yellow oil (65%): IR (neat) 2920, 2895, 2820, 1620 (br), 1105 cm^{-1}; ^1H NMR δ 0.8–1.8 (m, 32 H, $(CH_2)_5CH_3$ and $CH_3(CH_2O)$), 3.2–3.8 (m, 16 H, $NCH_2CH_2OCH_2CH_3$ and $NCH_2(CH_2)_5CH_3$), 7.5–8.0 (m, 3 H, Py H's). Anal. Calcd for $C_{29}H_{51}N_3O_4$ (505.74): C, 68.87; H, 10.16; N, 8.30. Found: C, 68.60; H, 10.30; N, 8.50.

N,N,N',N'-Tetraisobutylfuran-2,5-dicarboxamide (compound **7**) was obtained as a semisolid (70%): IR (neat) 2920, 2895, 2840, 1620 (br), 1450, 1405, 1370, 1250, 1100 (br) cm^{-1}; ^1H NMR δ 0.9 (d, 24 H, CH_3), 1.7–2.3 (m, 4 H, $CH_2CH(CH_3)_2$), 3.35 (d, 8 H, $NCH_2CH(CH_3)_2$), 6.9 (s, 2 H, furane H's). Anal. Calcd for $C_{22}H_{38}N_2O_3$ (378.56): C, 69.80; H, 10.12; N, 7.40. Found: 69.60; H, 10.30; N, 7.30.

N,N,N',N'-Tetraisobutylpyridine-2,6-dicarboxamide (compound **8**) was obtained as a colorless solid (65%): mp 92 °C; IR (KBr) 2930–2910, 2900, 2835, 1610, 1450, 1425, 1115, 1105 cm^{-1}; ^1H NMR δ, 0.75 (d, 12 H, $CH(CH_3)_2$), 1.0 (d, 12 H, $CH(CH_3)_2$), 1.7–2.3 (m, 4 H, $CH_2CH(CH_3)_2$), 3.35 (two overlapped doublets, 8 H, $NCH_2CH(CH_3)_2$), 7.4–8 (m, 3 H pyridine H's). Anal. Calcd for $C_{23}H_{39}N_3O_2$(389.59): C, 70.91; H, 10.09; N, 10.78. Found: C, 71.20; H, 9.90; N, 10.60.

Synthesis of N,N'-Diheptyl-N,N'-di(2-oxapentyl)-5,5-dimethyl-3,7-dioxanondiamine (Compound 2). Compound **1** (0.5 g) was added to a suspension of lithium aluminum hydroxide (1 g) in dry ether (20 mL) and benzene (10 mL). The reaction mixture was then refluxed for 15 h. It was then cooled and decomposed by dropwise addition of water (2 mL). The organic solution was filtered and the precipitate was washed five times with 20 mL of ether. The combined organic filtrate was dried over anhydrous sodium sulfate and the solvent was removed in vacuo to give the diamine **2** as a yellow oil (0.2 g, 42%): IR(neat) 2920, 2895, 2825, 1440, 1360, 1335, 1100 cm^{-1}. Anal. Calcd for $C_{31}H_{66}N_2O_4$ (530.88): C, 70.13; H, 12.53; N, 5.28. Found: C, 69.80; H, 12.20; N, 5.30.

Synthesis of N,N'-Diheptylfuran-2,5-dicarboxamide (Compound 17). A solution of furan-2,5-dicarbonyl dichloride (**29**) (0.4 g) in methylene chloride (5 mL) was added dropwise with stirring and cooling to a solution of *n*-heptylamine (0.65 mL) and triethylamine (1.0 mL) in methylene chloride (5 mL). After half an hour the addition was complete and the mixture was stirred overnight at room temperature and then methylene chloride (20 mL) was added. The solution was washed twice with each of distilled water, hydrochloric acid (20 mL, 3 M), water, saturated sodium bicarbonate, and water. The organic layer was dried over anhydrous sodium sulfate and concentrated in vacuo to give a yellow oil of *N,N'*-diheptylfuran-2,5-dicarboxamide (0.6 g, 82%): ^1H NMR δ, 0.85 (t, 6 H, $(CH_2)_5CH_3$); 1–1.7 (m, 20 H, $CH_2(CH_2)_5CH_3$), 3.1–3.6 (br m, 4 H, $NCH_2(CH_2)_5CH_3$); 7.1 (br s, 2 H, furane H's); 8.25 (br s, 2 H, NH). Anal. Calcd for $C_{20}H_{34}N_2O_3$ (350.5): C, 68.53; H, 9.78. Found: C, 68.20; H, 9.60.

Synthesis of N,N'-Diheptyl-N,N'-dimethylfuran-2,5-dicarboxamide (Compound 6) and N,N'-Diheptyl-N,N'-di[3-(2-oxapentyl)furan]-2,5-dicarboxamide (Compound 3). A solution of *N,N'*-diheptylfuran-2,5-dicarboxamide (compound **15**) (1 mmol) in 25 mL of benzene was treated with 0.2 g of sodium hydride and heated under reflux for 15 min and then methyl iodide or 2-bromoethyl ethyl ether (3 mmol) was added and reflux was continued for 7 h. Excess sodium hydride was then decomposed with ethanol (95%). The precipitate was then filtered off and washed with ether. The organic solution filtrate was then dried and concentrated in vacuo to give the crude products **6** and **3**, respectively.

Purified compound **6** gave colorless crystals (petroleum ether 30/60 (75%)): mp 65 °C; IR (KBr) 2920, 2890, 2815, 1630–1600, 1550, 1450, 1390, 1295, 1110, 1080, 1050 cm^{-1}; ^1H NMR δ 0.85 (t, 6 H, CH_2CH_3), 1.1–1.9 (m, 20 H, $CH_2(CH_2)_5CH_3$), 3.15 (s, 6 H, NCH_3), 3.5 (t, 4 H, $NCH_2(CH_2)_5CH_3$), 7.0 (s, 2 H, furane H's). Anal. Calcd for $C_{22}H_{38}N_2O_3$ (378.56): C, 69.80; H, 10.12; N, 7.40. Found: C, 69.60; H, 10.30; N, 7.30.

Purified compound **3** was a yellow oil (62%): ^1H NMR δ 0.9 (t, 6 H $(CH_2)_5CH_3$), 1.15 (t, 6 H, OCH_2CH_3), 1.2–2 (m, 10 H, $NCH_2(CH_2)_5CH_3$), 3.35–3.8 (m, 16 H, $NCH_2CH_2OCH_2CH_3$ and $NCH_2(CH_2)_5CH_3$), 7 (s, 2 H, furane H's). Anal. Calcd for $C_{28}H_{50}N_2O_5$ (494.72): C, 67.98; H, 10.19. Found: C, 68.10; H, 9.90.

Synthesis of N,N,N',N'-Tetraisobutyl-2,5,8,11-tetraoxa-1,12-dodecanedicarboxamide (Compound 11). This compound was obtained in two steps, (a) and (b).

(a) *N,N*-Diisobutylchloroacetamide (compound **18**). A solution of chloroacetyl chloride (5.6 g, 0.05 mol) in 20 mL of methylene chloride was added dropwise with stirring and cooling to a solution of diisobutylamine (6.45 g, 0.05 mol) and triethylamine (6 g) in methylene chloride (50 mL) over a period of 1 h. The solution was then washed twice with each of water, hydrochloric acid (20 mL, 3 M), water, saturated sodium bicarbonate, and water and then dried over anhydrous sodium sulfate. The solvent was then removed with a rotary evaporator. The remaining brown oil (7 g, 78%) was used without further purification in the next step. ^1H NMR δ 0.9 (d, 12 H, $CH(CH_3)_2$), 1.7–2.3 (m, 2 H, $CH_2CH(CH_3)_2$), 3.15 (d, 4 H, $NCH_2CH(CH_3)_2$), 4.08 (s, 2 H, $ClCH_2CO$).

(b) Triethylene glycol (0.4 mL) and sodium hydride (0.4 g) in benzene (25 mL) were heated under reflux until the effervescence stopped and then *N,N*-diisobutylchloracetamide (compound **18**) (2.5 g) was added and the mixture was refluxed for 24 h. The excess sodium hydride was decomposed with ethanol (95%) and the precipitate was filtered off. The solution was washed with water several times and dried over anhydrous sodium sulfate and the solvent was removed in vacuo. The remaining oil was purified by column chromatography using silica gel with petroleum ether (30/60) as an eluent. The pure product, compound **11**, was obtained as a yellow oil (0.85 g, 65%): IR(neat) 2925, 2895, 2840, 1650–1615, 1450, 1370, 1355, 1130–1070 cm^{-1}. ^1H NMR δ 0.9 (d, 24 H, $CH(CH_3)_2$), 1.7–2.3 (m, 4 H, $CH_2CH(CH_3)_2$, 3.1 (two overlapped doublets, 8 H, N-CH_2-$CH(CH_3)_2$), 3.7 (s, 12 H, OCH_2), 4.2 (s, 4 H, OCH_2CO). Anal. Calcd for $C_{26}H_{52}N_2O_6$ (488.71): C, 63.90; H, 10.72; N, 5.73. Found: C, 64.10; H, 10.50; N, 5.50.

RESULTS AND DISCUSSION

Reported selectivities for a given ionophore vary depending on the exact membrane composition (and even the source of PVC), the composition of solutions to which the membrane is exposed, and consequently the method of measurement used for calculation of the selectivity coefficient. Xie et al. (*26*), for example, used flow injection analysis and stop flow techniques to demonstrate that $K^{Pot}_{Li,Na}$ for a new ionophore (**13**) varied from 0.57 to 0.045 depending on solution and measurement conditions; different electrode dynamic response and characteristics were also readily demonstrated by the FIA technique. The selectivity of one of the best ionophores for lithium with respect to sodium (*4*) was found to vary from 70 to 280 depending on the particular plasticizer used, whether

Table I. Selectivity Coefficient $K^{Pot}_{Li,M}$ for Various Neutral Carriers (Mixed Solution Method)

neutral carrier	slope, mV/decade	$K^{Pot}_{Li,Na}$	$K^{Pot}_{Li,K}$	$K^{Pot}_{Li,Ca}$	$K^{Pot}_{Li,Mg}$
1	53	0.063	0.01	7.1×10^{-3}	2.5×10^{-4}
2	14.6				
3	57.7	0.94	0.14	0.036	4.2×10^{-3}
4	54.7	0.094	0.15	0.017	
5	55.0	0.038	0.12	5.3×10^{-3}	3.3×10^{-3}
6	47.0	0.055	0.047	5.7×10^{-3}	6.0×10^{-4}
7	62.6	0.15	0.21	0.014	8.8×10^{-3}
8	53.8	0.13	0.17	7.3×10^{-3}	7.0×10^{-3}
9	53	0.070	0.02	2.2×10^{-3}	2.7×10^{-3}
10	56	0.082	0.20	0.043	
11	57	0.12	0.14	0.011	0.13
12	54	0.077	0.20	0.043	
13	51	0.052	0.026	3.9×10^{-3}	3.1×10^{-4}
14	57	0.15	3.9×10^{-3}	0.040	
15	59	0.042[a] (7.1×10^{3})[b]			
16	59	8.0×10^{-3} [a,b]			
17	55	0.17			

[a] Potassium tetrakis(*p*-chlorophenyl)borate (KT_pClPB), 0.4%. [b] *o*-Nitrophenyl octyl ether (NPOE) plasticizer, 65%.

potassium tetrakis(*p*-chlorophenyl)borate was added to the membrane, and whether the fixed interference method or the separate solution method was used for determination (*31*); these factors may influence the selectivity toward other ions differently.

Because of the above factors, we prepared all ionophores in the same PVC membrane and used the same plasticizer in order to obtain relative responses due to the ionophores. We employed two different methods for determining $K^{Pot}_{Li,Na}$. One was the standard fixed interference method, to allow some comparison with previously reported results (although the previous membrane compositions were not replicated). The other was the matched potential method (*22*), an empirical method that does not depend on Nernstian response nor equal slope for monovalent ions and in which solution conditions can more closely resemble analytical measurement conditions.

A sequential series of modifications was made to the previously reported diamide carriers to determine the effects of different arrangements on relative selectivities. New compounds were also prepared and studied. All neutral carrier electrodes investigated exhibited preferred selectivity for lithium ion compared to sodium, except that carrier **2** did not give a useful response. The selectivities in the following discussions are the relative selectivities with respect to sodium using the mixed solution method, unless otherwise specified. We have recently reported on the properties of electrodes containing neutral carrier **1** (*24*). Electrodes containing carrier **13** have also been characterized by using flow injection analysis measurements (*26*).

When the dioxanonane backbone of neutral carrier **1** was replaced with a furan group to obtain neutral carrier **3**, a selectivity of about 1.1 was obtained for lithium over sodium, compared with 16 for the original compound (Table I). When the backbone was replaced with a pyridine group (neutral carrier **4**), a selectivity of 11 was obtained for lithium over sodium. When the dioxanonane backbone of neutral carrier **5** was replaced with a furan group (neutral carrier **6**), the selectivity changed from 26 to 18 (although by the matched potential method, the value was 170—Table II). Güggi et al. (*25*) found a selectivity of 20 for neutral carrier **5** using the separate solution method. Replacing the dioxanonane group in neutral carrier **13** with a furan group in neutral carrier **7** or a pyridine group as in neutral carrier **8** changed the selectivity from 19 to 6.7 and 7.7, respectively.

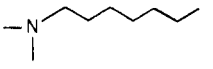
Different side chains on the furan backbone resulted in selectivites of 1.1 (carrier **3**), 18 (carrier **6**), and 6.7 (carrier **7**). Changing the chain on the pyridine backbone from compound **4** to compound **8** changed the selectivity from 11 to 7.7.

Table II. Selectivity Coefficient for Various Neutral Carriers (Matched Potential Method)

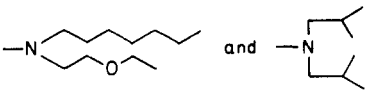
neutral carrier	$K^{Pot}_{Li,Na}$	$K^{Pot}_{Li,K}$	$K^{Pot}_{Li,Ca}$	$K^{Pot}_{Li,Mg}$
1	0.047			
2				
3	0.037	0.024	0.010	3.3×10^{-3}
4	0.10	0.056	0.19	0.049
5				
6	6.0×10^{-3}	2.5×10^{-3}	2.7×10^{-3}	1.1×10^{-3}
7	0.17	0.038	0.13	0.014
8	0.10	0.026	5.0×10^{-3}	2.8×10^{-3}
9	0.07	0.010	5.1×10^{-3}	1.5×10^{-3}
10	0.13	0.047	0.10	0.098
11	0.12	0.027	6.9×10^{-3}	3.1×10^{-3}
12	0.21	0.074	0.13	0.084
13	0.019	1.7×10^{-3}	1.9×10^{-3}	
14	0.082	0.022	0.027	6.8×10^{-3}
15	0.076[a] (0.012)[a,b]			
16	0.020[a] (0.012)[a,b]			

[a] Potassium tetrakis(*p*-chlorophenyl)borate (KT_pClPB), 0.4%. [b] *o*-Nitrophenyl octyl ether (NPOE) plasticizer, 65%.

When the backbones of the compounds are kept constant with different side chains as illustrated in Table III, for the two measurement methods, it can be seen that lithium selectivity with the side chain



is best either on the furan backbone or on the dioxanonane backbone. This side chain was not studied on the pyridine backbone. The side chains



appear to provide similar selectivities for lithium over sodium regardless of the backbone, but depending on the method of measurement.

When the side chains are kept constant and the backbones are changed as illustrated in Table IV, it can be seen that the dioxanonane backbone appears to give best results regardless

Table III. Comparison of Selectivities for Lithium over Sodium ($1/K^{Pot}_{Li,Na}$) for Different Backbones

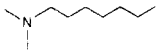
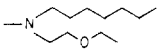
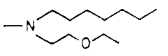
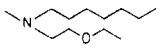
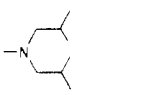
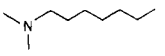
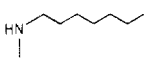
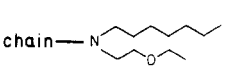
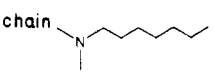
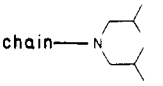
furan backbone				pyridine backbone				dioxanonane backbone			
no.	chain	mixed solution	matched potential	no.	chain	mixed solution	matched potential	no.	chain	mixed solution	matched potential
6		18	170	4		11	10	1		16	21
3		1.1	27	8		7.7	10	5		26	
7		6.7	5.9					13		19	53
17		6									

Table IV. Comparison of Selectivities for Lithium over Sodium ($1/K^{Pot}_{Li,Na}$) for Different Chains

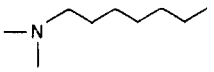






no.	backbone	mixed solution	matched potential	no.	backbone	mixed solution	matched potential	no.	backbone	mixed solution	matched potential
4	pyridine	11	10.0	6	furan	18	170	8	pyridine	7.7	10.0
3	furan	1.1	27	5	dioxanonane	26		7	furan	6.7	5.9
1	dioxanonane	16	21					13	dioxanonane	19	53
								11	crown	8.3	7.7

of the chain. The pyridine and furan backbones appear to give similar selectivities with the different chains, depending on the measurement method. The combination of the dioxanonane backbone and the



chains represents compound **5**, as reported by Güggi et al. (*25*). The selectivity found here is consistent with the results of Güggi et al., and the electrode is stable.

It is possible that electron-donating groups on the backbone of the various compounds could have an effect on the selectivities of these compounds and may be a worthwhile area of research.

Neutral carrier **12** was reported to flouresce with lithium (*32*). A selectivity value of 13 (Table I) to 4.8 (Table II) was obtained when this neutral carrier was embedded in a PVC membrane.

The number of donor atoms have an effect on the selectivity. Neutral carrier **9** gave a selectivity of 14, but when the number of oxygen atoms was decreased (neutral carrier **10**), a selectivity of 7.7 was obtained. It should be noted also that the cage size was decreased from 14 to 11 atoms. A 14-crown-4 compound gives high selectivity for lithium (see below). It is interesting that neutral carrier **11** showed a selectivity of 8.3 for lithium over sodium in spite of its relatively large cavity size.

Neutral carrier **14**, which was reported to have a lithium selectivity with respect to sodium of over 100 (*3*), was investigated. Selectivity values of 6.7 (Table I) to 12 (Table II) were obtained. Differences may be due in part to different methods of measurement (influenced also by type of solution exposure), different plasticizers, and so forth.

Diamide **15** and crown ether compound **16** are reported to exhibit lithium selectivities relative to sodium on the order of 280 (4) and 150 (5), respectively. Under our measurement conditions, a value of 24 was obtained for diamide **15** by use of the fixed interference method and with the reference plasticizer. However, when NPOE was used as plasticizer (as recommended by Metzger et al.), the selectivity increased to 140, and with crown ether **16** it was 125, very comparable. When the matched potential method and NPOE plasticizer were used, selectivities of 80 and 60 were obtained for the crown ether and diamide **15** electrodes, respectively. Both electrodes exhibited good stability and consistent high lithium selectivity. The crown ether electrode has a lifetime of at least 5 months with little change in response or selectivity with respect to sodium, when stored in 7 mM $Na_2B_4O_7$ solution. The diamide **15** electrode is similarly stable for several weeks. The former electrode was observed to reach equilibrium potential faster than the latter when measuring low millimolar concentrations of lithium in the presence of 140 mM sodium, but the latter was much faster at high lithium concentrations (Figure 2); note that the response time for the crown ether electrode appears to be fairly independent of the lithium concentration. Kitazawa et al. (*5*) have reported a selectivity of up to 500 for this compound when 1% trioctylphosphine oxide is added to the membrane, although the sensitivity is significantly reduced.

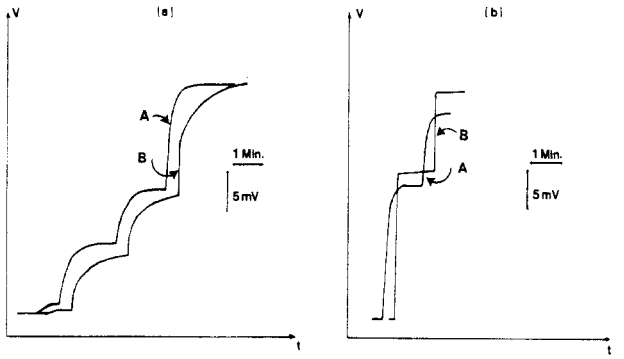


Figure 2. Response curves for 14-crown-4 electrode (A) and diamide **15** electrode (B): (a) base solution 140 mM NaCl, increments of 0.2, 0.8, 1.0, and 3.0 mM LiCl added (total LiCl 0.2, 1.0, 2.0, and 5.0 mM, respectively); (b) base solution 140 mM NaCl plus 50 mM LiCl, increments of 50 and 50 mM LiCl added (total LiCl 100 and 150 mM LiCl, respectively).

Two of the above ionophores in PVC electrodes have been demonstrated to perform successfully in blood serum. Metzger et al. (31) performed direct measurement of lithium added to blood serum using the diamide **15**. Xie and Christian (33) accurately measured lithium in serum samples from manic depressive patients using crown ether **16**.

ACKNOWLEDGMENT

The authors are indebted to W. Simon for supplying compound **15**.

Registry No. **1**, 80712-94-3; **2**, 102574-30-1; **3**, 102574-31-2; **4**, 102574-32-3; **5**, 58821-96-8; **6**, 102574-33-4; **7**, 102574-34-5; **8**, 102586-42-5; **9**, 31255-11-5; **10**, 43113-25-3; **11**, 102574-35-6; **12**, 1945-78-4; **13**, 102574-36-7; **14**, 102574-37-8; **15**, 102574-38-9; **16**, 91539-72-9; **17**, 102574-39-0; **18**, 5326-82-9; NPOE, 37682-29-4; Li, 7439-93-2; Na, 7440-23-5; furan-2,5-dicarbonyl dichloride, 10375-34-5; pyridine-2,6-dicarbonyl dichloride, 3739-94-4; diisobutylamine, 110-96-3; *N*-(2-oxapentyl)heptylamine, 93404-41-2; *N*-heptylamine, 111-68-2; 2-bromoethyl ethyl ether, 592-55-2; chloroacetyl chloride, 79-04-9; triethylene glycol, 112-27-6.

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RECEIVED for review February 10, 1986. Accepted April 14, 1986. Presented at the 1985 Pittsburgh Conference and Exposition on Analytical Chemistry and Applied Spectroscopy, New Orleans, LA, February 25-March 1. This work was supported in part by Beckman Instruments, Inc.

Oxygen Reduction at Electrochemically Treated Glassy Carbon Electrodes

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We studied dioxygen reduction at electrodes treated electrochemically and at ones on which quinone was adsorbed. Results were compared to see if the surface redox groups introduced on the electrochemically treated electrodes could serve as mediators. The electrodes behaved very differently for oxygen reduction, especially with respect to pH. For the quinone-adsorbed electrodes, oxygen reduction via quinone was not observed at a pH less than the semiquinone pK_a; for the other electrodes, reduction currents were unchanged in the pH range investigated. From these and other results, we concluded that quinones of the electrochemically treated electrodes cannot serve as mediators for oxygen reduction.

The activity of carbon electrodes increases after pretreatment (*1-8*) such as dipping a freshly polished electrode into chromic acid (*3*), exposure of an electrode to radio frequency plasma in an oxygen atmosphere (*4*), and anodization of an electrode at 1.3-1.8 V vs. SCE (*5-9*). By such treatment, the oxidation potentials of compounds such as NADH, hydroquinone, and ascorbic acid become less anodic, and the reduction potentials become less negative for systems such as Fe(III) in H_2SO_4 solution and dioxygen (*1-9*). However, the reason for the increased activity is not fully understood. Pretreatment introduces functional groups containing oxygen such as quinone on the carbon surface (*2*, *10-18*), and such groups may serve as mediators (*19*). Fagan, Hu, and Kuwana, reported that surface oxygen groups were unnecessary for the rapid electrooxidation of ascorbic acid (*20*). The purpose of this work is to see if quinone groups introduced on the surface by pretreatment can act as mediators. We studied dioxygen reduction mediated by quinone and compared the results with that for carbon treated beforehand.

EXPERIMENTAL SECTION

Voltammetric experiments were done with a laboratory-made potentiostat and a Toho Giken Model 2230 potential scanner at

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