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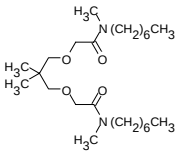
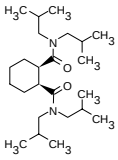
Lithium



Lithium ionophore I

(ETH 149; *N,N'*-Diheptyl-*N,N'*,5,5-tetramethyl-3,7-dioxanonanediamide)
$C_{25}H_{50}N_2O_4$ M_r = 442.67 [58821-96-8]

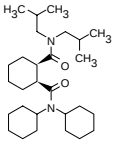
62557 **Selectophore®, function tested** 50 mg



Lithium ionophore II

(ETH 1644; *N,N,N',N'*-Tetraisobutyl-*cis*-cyclohexane-1,2-dicarboxamide)
$C_{24}H_{46}N_2O_2$ M_r = 394.64 [80547-18-8]

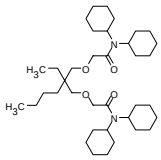
62559 **Selectophore®, function tested** 50 mg



Lithium ionophore III

(ETH 1810; *N,N*-Dicyclohexyl-*N',N'*-diisobutyl-*cis*-cyclohexane-1,2-dicarboxamide)
$C_{28}H_{50}N_2O_2$ M_r = 602.95 [99281-50-2]

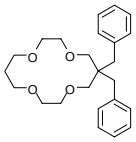
62558 **Selectophore®, function tested** 50 mg



Lithium ionophore IV

(ETH 2137; 5-Butyl-5-ethyl-*N,N,N',N'*-tetracyclohexyl-3,7-dioxaazelaic diamide)
$C_{37}H_{66}N_2O_4$ M_r = 602.95 [108083-23-4]

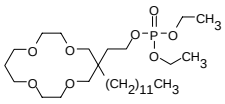
62561 **Selectophore®, function tested** 50 mg (solution in 0.5 mL heptane)



Lithium ionophore VI

(6,6-Dibenzyl-14-crown-4; 6,6-Dibenzyl-1,4,8-11-tetraoxacyclotetradecane)
$C_{24}H_{32}O_4$ M_r = 384.52 [106868-21-7]

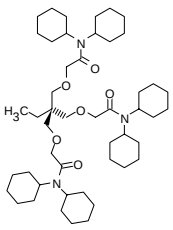
62567 **Selectophore®, function tested** 10 mg, 100 mg



Lithium ionophore VII

(6-[2-(Diethylphosphonooxy)ethyl]-6-dodecyl-14-crown-4; 6-Dodecyl(14-crown-4)-6-ethanol diethyl phosphate)
$C_{28}H_{57}O_8P$ M_r = 552.73 [106868-29-5]

62569 **Selectophore®, function tested** 10 mg (solution in 0.1 mL heptane)



Lithium ionophore VIII

(*N,N,N',N',N'',N''*-Hexacyclohexyl-4,4',4''-propylidynetris(3-oxabutyramide))
$C_{48}H_{83}N_3O_6$ M_r = 798.16 [133338-85-9]

62571 **Selectophore®, function tested** 50 mg

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Electrochemical Transduction

Ion-Selective Electrodes

Application 1 and Sensor Type [1]

Assay of Li^+ activity in biological systems with solvent polymeric membrane electrode based on Lithium ionophore I.

Recommended Membrane Composition

1.00	wt%	Lithium ionophore I (62557)
62.80	wt%	Tris(2-ethylhexyl) phosphate (TEHP) (93299)
33.00	wt%	Poly(vinyl chloride) high molecular weight (81392)

Recommended Cell Assembly

Reference | | sample solution | | liquid membrane | 0.001 M LiCl | AgCl,Ag

Electrode Characteristics and Function

Selectivity Coefficients $\log K^{Pot}_{Li,M}$ as obtained by the separate solution method (0.1 M solutions of the chlorides)

$\log K^{Pot}_{Li,H}$	-0.1	$\log K^{Pot}_{Li,NH_4}$	-1.3
$\log K^{Pot}_{Li,Na}$	-1.3	$\log K^{Pot}_{Li,Mg}$	-3.7
$\log K^{Pot}_{Li,K}$	-2.1	$\log K^{Pot}_{Li,Ca}$	-3.3

Detection limit: ~ $6 \cdot 10^{-6}$ M LiCl

Application 2 and Sensor Type [2,3]

Assay of Li^+ activity in serum (therapeutical Li^+ range) with solvent polymeric membrane electrode based on Lithium ionophore II.

Recommended Membrane Composition

1.00	wt%	Lithium ionophore II (ETH 1644) (62559)*
0.40	wt%	Potassium tetrakis(*p*-chlorophenyl)borate (KT*p*ClPB) (60591)
65.60	wt%	2-Nitrophenyl octyl ether (73732)
33.00	wt%	Poly(vinyl chloride) high molecular weight (81392)

* Membranes based on Lithium ionophore III exhibit improved selectivity for measurements in blood.

Recommended Cell Assembly

Reference | | sample solution | | liquid membrane | 0.1 M LiCl | AgCl,Ag

Electrode Characteristics and Function

Selectivity Coefficients $\log K^{Pot}_{Li,M}$.

	Required (blood[1)])	Found
$\log K^{Pot}_{Li,H}$	<2.1	1.0
$\log K^{Pot}_{Li,Na}$	<-4.3	-2.1
$\log K^{Pot}_{Li,K}$	<-2.8	-2.2
$\log K^{Pot}_{Li,Mg}$	<-3.5	-3.0
$\log K^{Pot}_{Li,Ca}$	<-3.6	-1.7

[1)] for therapeutical Li^+ concentrations (1% interference, worst case)[4,5]

[1] M. Güggi, U. Fiedler, E. Pretsch, W. Simon, A lithium ion-selective electrode based on a neutral carrier. **Anal. Let. *8***, 857 (1975).
[2] D. Erne, D. Ammann, A.F. Zhukov, F. Behm, E. Pretsch, W. Simon, Lipophilic diamides as ionophores for alkali and alkaline earth metal cations. **Helv. Chim. Acta *65***, 538 (1982).
[3] E. Metzger, D. Ammann, U. Schefer, E. Pretsch, W. Simon, Lipophilic neutral carriers for lithium selective liquid membrane electrodes. **Chimia *38***, 440 (1984).

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Application 3 and Sensor Type [3,6,7,8]
Assay of Li^+ activity in whole blood, plasma and serum (therapeutical Li^+ range) with solvent polymeric membrane electrode based on Lithium ionophore III.

Recommended Membrane Composition

1.20	wt%	Lithium ionophore III (ETH 1810) (62558)
0.40	wt	Potassium tetrakis(4-chlorophenyl)borate (60591)
65.60	wt%	2-Nitrophenyl octyl ether (73732)
32.80	wt%	Poly(vinyl chloride) high molecular weight (81392)

Recommended Cell Assembly
Reference | | sample solution | | liquid membrane | 0.001 M LiCl | AgCl,Ag

Electrode Characteristics and Function

Selectivity Coefficients $\log K^{Pot}_{Li,M}$.

	Required (blood[1])	Found
$\log K^{Pot}_{Li,H}$	<2.1	1.0
$\log K^{Pot}_{Li,Na}$	<-4.3	-2.3 (-2.45)[3]
$\log K^{Pot}_{Li,K}$	<-2.8	-2.6
$\log K^{Pot}_{Li,Mg}$	<-3.5	-4.0
$\log K^{Pot}_{Li,Ca}$	<-3.6	-2.7

Lifetime: log P_{TLC}[2] ionophore >8.4 8.3
log P_{TLC}[2] plasticizer >12.8 9.3

Stability: Drift [mV/h] 0.02

[1] for therapeutical Li+ concentrations (1% interference, worst case)[4,5]
[2] lipophilicity, determined by thin layer chromatography[9]
[3] fixed interference method

[4] A. Lewenstam, Ion selective electrodes in clinical chemistry. **Anal. Proc. *28***, 106 (1991)
[5] U. Oesch, P. Anker, D. Ammann, W. Simon, in: Ion-Selective Electrodes, Eds. E. Pungor, I. Buzás, Akadémiai Kiadó, Budapest 81 (1985).
[6] E. Metzger, D. Ammann, R. Asper, W. Simon, Ion selective liquid membrane electrode for the assay of lithium in blood serum. **Anal. Chem. *58***, 132 (1986)
[7] E. Metzger, R. Dohner, W. Simon, D.J. Vonderschmitt, K. Gautschi, Lithium/sodium ion concentration ratio measurements in blood serum with lithium and sodium ion selective liquid membrane electrodes. **Anal. Chem. 59**, 1600 (1987).
[8] J.H. Sim, K.M. Lee, J.S. Lee, D.H. Cho, H. Nam, G.S. Cha, Lithium Ion-Selective Electrode with Improved Lifetime. Bull. **Korean Chem. Soc. *22***, 765 (2001)
[9] O. Dinten, U.E. Spichiger, N. Chaniotakis, P. Gehrig, B. Rusterholz, W.E. Morf, W. Simon, Lifetime of neutral-carrier-based liquid membranes in aqueous samples and blood and the lipophilicity of membrane components. **Anal. Chem. 63**, 596 (1991).

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Application 4 and Sensor Type [7,10]

Determination of Li+/Na+ concentration ratios in blood serum (therapeutical Li+ range) with solvent polymeric membrane electrodes based on Lithium ionophore IV, combined with a Na^+-selective polymeric membrane electrode.

Recommended Membrane Composition

2.00	wt%	Lithium ionophore IV (ETH 2137) (62561)
65.60	wt%	Bis(1-butylpentyl) adipate (02150)
32.40	wt%	Poly(vinyl chloride) high molecular weight (81392)

Recommended composition of the Na^+-selective solvent polymeric membrane

1.00	wt%	Sodium ionophore III (ETH 2120) (71734)
66.00	wt%	Bis(1-butylpentyl)decane-1,10-diyl diglutarate (ETH 469) (30585)
33.00	wt%	Poly(vinyl chloride) high molecular weight (81392)

Recommended Cell Assembly

AgCl,Ag | 0.001 M LiCl, 0.14 M NaCl in 0.5 % aqueous agar | Na^+-selective membrane | | sample solution | Li^+-selective membrane liquid membrane | 0.001 M LiCl, 0.14 M NaCl in 0.5% aqueous agar | AgCl,Ag

Electrode and System Characteristics

The electrode response function for Li^+/Na^+ concentration ratio is described by the following equation:

$$E_{ratio} = E^0_{ratio} + s \cdot \log\left(\frac{C_{Li}}{C_{Na}} + K^{Pot}_{LiNa}\right)$$

Selectivity coefficient $\log K^{Pot}_{Li,Na}$ -1.9

Response time: ~20 s

Residual standard deviation (EMF response function): <0.1 mV

Application 5 and Sensor Type [11,12,13]

Neutral carrier for Li^+ in ion-selective PVC membrane electrodes with high selectivity over potassium and sodium ions.

Recommended Membrane Composition

1.00	wt%	Lithium ionophore VI (62567)
0.70	wt%	Potassium tetrakis(4-chlorophenyl)borate (60591)
70.30	wt%	2-Nitrophenyl octyl ether (73732)
28.00	wt%	Poly(vinyl chloride) high molecular weight (81392)

Recommended Cell Assembly

Reference | | sample solution | | liquid membrane | 1 M LiCl | AgCl,Ag

Electrode Characteristics and Function

Selectivity Coefficients $\log K^{Pot}_{Li,M}$ determined by the fixed interference method (0.05 M solution for alkali metal ions and H^+, 0.5 M fro alkaline earth metal ions and NH_4^+).

$\log K^{Pot}_{Li,H}$	-3.0	$\log K^{Pot}_{Li,NH_4}$	-3.0
$\log K^{Pot}_{Li,Na}$	-2.4	$\log K^{Pot}_{Li,Mg}$	-4.3
$\log K^{Pot}_{Li,K}$	-2.3	$\log K^{Pot}_{Li,Ca}$	-4.7

Slope of linear regression: 59-60 mV/decade

[10] E. Metzger, R. Aeschimann, M. Egli, G. Suter, R. Dohner, D. Ammann, M. Dobler, W. Simon, 3,7-Dioxaazelaamides as Ionophores for Lithium Ion Selective Liquid Membrane Electrodes.. **Helv. Chim. Acta 69**, 1821 (1986).
[11] K. Kimura, H. Yano, S. Kitazawa, T. Shono, Synthesis and Selectivity for Lithium of Lipophilic 14-Crowm-4 Derivatives Bearing Bulky Substituents or an Additional Binding Site in the Side Arm, **J. Chem. Soc. Perkin Trans. II**, 1945 (1986).
[12] K. Kimura, O. Oishi, T. Miura, T. Shono, Lithium Ion Selective Electrodes Based on Crown Ethers for Serum Lithium Assay. **Anal. Chem. 59**, 2331 (1987).
[13] S. Sawada, T. Osakai, M. Senda,. Voltammetric Lithium Ion-Selective Electrodes Based on Ion Transfer at the Oil/Water Interface Facilitated by Neutral Ionophores. **Anal. Sci. *11***, 733 (1995).

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Application 6 and Sensor Type [14]

Neutral lithium ionophore in ion-selective polymer membrane electrodes with excellent selectivity over potassium and sodium ions.

Recommended Membrane Composition

1.00	wt%	Lithium ionophore VII (62569)
0.70	wt%	Potassium tetrakis(4-chlorophenyl)borate (60591)
70.20	wt%	2-Nitrophenyl octyl ether (73732)
28.10	wt%	Poly(vinyl chloride) high molecular weight (81392)

Recommended Cell Assembly

Reference | | sample solution | | liquid membrane | 1 M LiCl | AgCl,Ag

Electrode Characteristics and Function

Selectivity Coefficients $\log K^{Pot}_{Li,M}$ determined by the fixed interference method (0.05 M solution for alkali metal ions and H+, 0.5 M for alkaline earth metal ions and NH_4^+).

$\log K^{Pot}_{Li,H}$	-3.2	$\log K^{Pot}_{Li,NH_4}$	-3.0
$\log K^{Pot}_{Li,Na}$	-2.3	$\log K^{Pot}_{Li,Mg}$	-4.4
$\log K^{Pot}_{Li,K}$	-2.5	$\log K^{Pot}_{Li,Ca}$	-4.0

Slope of linear regression: 59-60 mV

Application 7 and Sensor Type [15]

Sensor with increased stability and lifetime for assay of Li^+ based on Lithium ionophore VIII.

Recommended Membrane Composition

2.50	wt%	Lithium ionophore VIII (62571)
0.23	wt%	Potassium tetrakis((4-chlorophenyl)borate (60591)
64.50	wt%	Bis(1-butylpentyl) adipate (02150)
32.80	wt%	Poly(vinyl chloride) high molecular weight (81392)

Recommended Cell Assembly

Reference | | sample solution | | liquid membrane | 0.01 M LiCl | AgCl,Ag

Electrode Characteristics and Function

Selectivity Coefficients $\log K^{Pot}_{Li,M}$ determined by the separate solution method (0.1 M solutions of the chlorides).

$\log K^{Pot}_{Li,Na}$	-2.4	$\log K^{Pot}_{Li,Mg}$	-4.3
$\log K^{Pot}_{Li,K}$	-2.3	$\log K^{Pot}_{Li,Ca}$	-4.7
$\log K^{Pot}_{Li,NH_4}$	-3.0		

Slope of linear regression: 59-60 mV

[14] K. Kimura, H. Yano. S. Kitazawa, T. Shono, Synthesis and selectivity for lithium of lipophilic 14-crown-4 derivatives bearing bulky substituents or an additional binding site in the side arm. **J. Chem. Soc. Perkin Trans. *2***, 1945 (1986).
[15] M. Bochenska, W. Simon, Performance of a highly lipophilic Li^+ ionophore in solvent polymeric membranes. **Microchim. Acta *III***, 277 (1990).