Bull. Chem. Soc. Jpn., 71, 657—660 (1998)

Calix[4]arene-Modified Oligosiloxane as a Quasi-Immobilized Neutral Carrier for Silicone-Rubber-Membrane Sodium Ion-Selective Electrodes

Keiichi Kimura,* Yutaka Tsujimura, Masaaki Yokoyama, and Takumi Maeda†

Chemical Process Engineering, Faculty of Engineering, Osaka University, Yamada-oka, Suita, Osaka 565

†General Planning Research and Development Management Department, Shimadzu Corporation, Nakagyou-ku, Kyoto 604

(Received October 20, 1997)

An oligo(dimethylsiloxane) carrying ionophorous calix[4]arene moieties at the side chain was synthesized as a Na$^+$ neutral carrier for highly durable silicone-rubber membranes of ion-selective electrodes by reacting calix[4]arene tetraallyl ester with an oligo(methylsiloxane). This medium-molecular-weight calix[4]arene ionophore alleviated the drawback of chemically-modified calixarene-based silicone-rubber membranes, such as a high membrane impedance and a slow electrode response.

Although solvent-polymeric membranes, such as plasticized poly(vinyl chloride) (PVC), are good membrane materials for neutral-carrier-type ion-selective electrodes, they still have some drawbacks concerning their practical use, i.e., comparatively easy extrusion of a plasticizer and neutral carrier, and therefore a poor durability of ion-sensing membranes. One of the best ways to solve this problem is the immobilization of neutral carriers onto the membrane support by covalent bonding[1—3] and a simultaneous employment of elastic polymers without any special plasticizer.[4—7] Therefore, we had already attempted a chemical modification of crosslinked poly(dimethylsiloxane) (silicone rubber) with a neutral carrier to obtain highly durable ion-sensing membranes.[8] The immobilization of a neutral carrier by chemical bonding may, however, cause a high membrane impedance and slow response for the resulting membrane electrodes due to the low mobility of the neutral carrier derived from the chemical modification. Neutral-carrier-modified silicone-rubber membranes often exhibit an anomalous electrode response, unless a lipophilic salt is not included in them to overcome their high membrane impedance. It occurred to us that the design of an oligomeric neutral carrier having medium molecular weight and its blending with a silicone rubber might alleviate the demerits of the silicone-rubber membranes modified chemically by a neutral carrier. The medium-molecular-weight neutral carrier is expected to improve the poor mobility of the covalently-immobilized neutral carriers and to be hard to outflow from the membrane, due to its relatively high molecular weight. This paper is concerned with the design of an oligo(dimethylsiloxane) derivative incorporating calix[4]arene ionophore and its application to Na$^+$-selective electrodes.

Experimental

Synthesis. 5,11,17,23-Tetra-*t*-butyl-25,26,27,28-tetrakis(allyloxycarbonylmethoxy)calix[4]arene (calix[4]arene tetraallyl ester) was synthesized by the following method. Allyl 1-bromoacetate was prepared by azeotropic condensation of bromoacetic acid (0.36 mol) and allyl alcohol (0.36 mol) benzene (100 cm^3) in the presence of H_2SO_4 (0.7 g) (reflux, 6 h). Under an argon atmosphere, to *t*-butylcalix[4]arene (4.62 mmol), was added a mixture of allyl 1-bromoacetate and K_2CO_3 (110 mmol), together with dry acetone (100 cm^3). The mixture was refluxed while stirring for 15 h. After the reaction, iced water (100 cm^3) and chloroform (100 cm^3) were added to the mixture. The mixture was neutralized by hydrochloric acid while cooling, and then stirred vigorously. The organic phase was separated, washed with water (50 cm^3×3), and then dried over $MgSO_4$. Evaporation of the chloroform afforded a crude product of calix[4]arene tetraallyl ester, which was purified by recrystallization with ethanol–water. Yield (56%); ^{1}H NMR (270 MHz, $CDCl_3$) $\delta_H = 1.07$ (36H, s, *t*-Bu), 3.19 (4H, d, $J = 12.9$ Hz, $ArCH_2$), 4.6—4.7 (8H, m, $CO_2C\mathit{H}_2CH$), 4.86 (4H, $J = 12.8$ Hz, $ArCH_2$), 5.2—5.4 (8H, m, $C{=}C\mathit{H}_2$), 5.8—6.0 (4H, m, $C\mathit{H}{=}CH_2$), 6.78 (8H, s, ArH); MS *m/z* (% rel intensity) 1040 (M$^+$; 12), 57 (100).

The modification of an oligosiloxane with calix[4]arene tetraallyl ester, that is, the synthesis of calix[4]arene-modified oligosiloxane **1** was performed in the following way. A benzene solution (30 cm^3) of calix[4]arene tetraallyl ester (0.4 g, 3.8×10^{-1} mmol) and oligo(methylsiloxane) [(poly(methylhydrosiloxane), $M_n = 2270$, average polymerization degree of ca. 30, Aldrich] (0.1 g, 4.4×10^{-2} mmol) was refluxed in the presence of $H_2PtCl_6\cdot6H_2O$ (2.5 mg×5) for 60 h. The reaction mixture was filtered by a membrane filter [poly(tetrafluoroethylene) film with a pore size of 0.5 mm]. Evaporation of the benzene afforded calix[4]arene-modified oligosiloxane **1**. The calixarene content of the calixarene-modified oligosiloxane was determined by ^{1}H NMR.

Other Chemicals. Sodium {4-[3-(triethoxysilyl)propyloxy]phenyl}triphenylborate for the chemical modification of the oligosiloxane with an anion excluder was obtained according to our previously-reported method.[9] The silicone-rubber precursor employed was an alcohol-evolving-type (Shin-Etsu Silicone KE47T). Alkali and alkaline-earth metal chlorides and ammonium chloride were of the best analytical grade. Control blood sera (Wako, Control Sera I) was purchased. The ion concentrations for the serum were 143 mmol dm^{-3} Na$^+$ and 4.1 mmol dm^{-3} K$^+$.

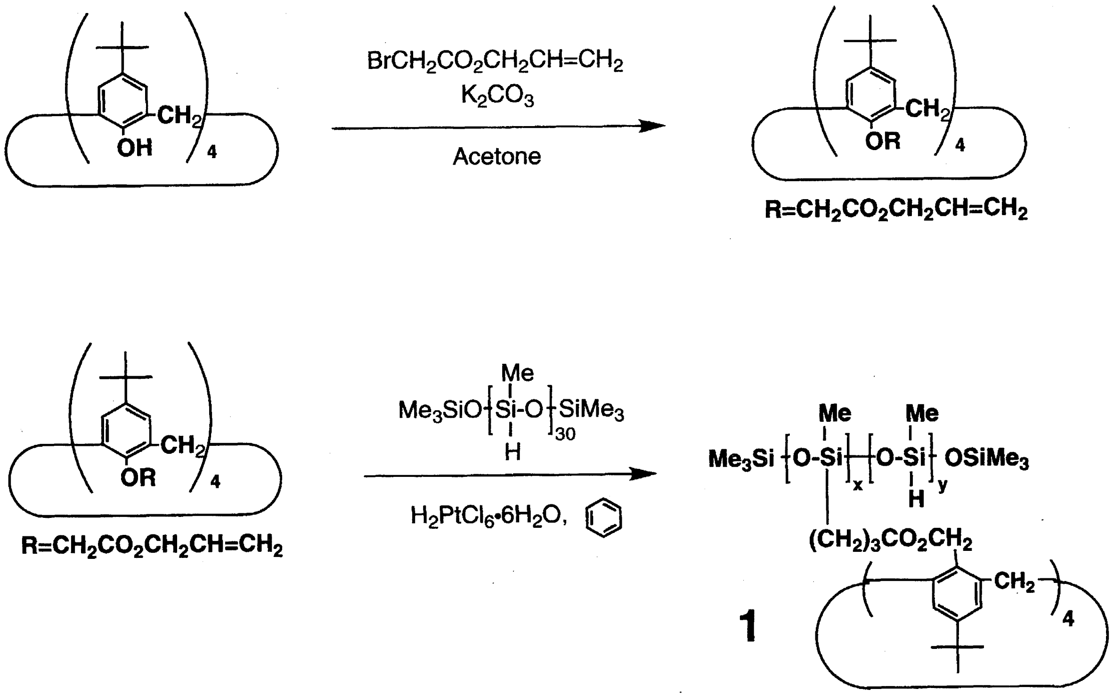
Fabrication of Membranes and Electrodes. The general procedure for casting ion-sensing membranes is as follows: A silicone-rubber precursor (90 mg) and a neutral carrier (10 mg) were dissolved in chloroform (0.6 cm^3). In some cases of the calixarene-bound silicone-rubber membranes employed for a comparison, the solution also contained a small quantity (25 mol% to the neutral carrier employed) of sodium {4-[3-(triethoxysilyl)propyloxy]phenyl}triphenylborate as an anionic site. The whole solution was poured into a Teflon®-made Petri dish having an inner diameter of 17 mm. Gradual evaporation of the chloroform and hardening at ambient temperature for 2 d afforded an elastic, semitransparent membrane with a thickness of 0.1—0.2 mm. A 7-mm diameter disk was cut from the membrane with a cork borer and then incorporated into an electrode body (Philips IS-561 type). The internal filling solution was 1×10^{-3} mol dm^{-3} NaCl aqueous solution. Conditioning of the electrodes was made by soaking in a NaCl solution overnight.

Measurements. Potential measurements were made at room temperature using a pH/mV meter (Toko, TP-1000). The external reference electrode was the double-junction-type Ag/AgCl electrode with a 3 mol dm^{-3} KCl internal solution and a 1 mol dm^{-3} CH_3CO_2Li external solution. The electrochemical cell was Ag-AgCl/1×10^{-3} mol dm^{-3} NaCl//silicone-rubber membrane//sample solution/1 mol dm^{-3} CH_3CO_2Li/3 mol dm^{-3} KCl/AgCl-Ag. The measuring metal-ion activities were changed by injection of high-concentration solutions to the testing solutions, while stirring with a magnetic stir bar. The emf readings were made after the potential reached a constant value. The selectivity coefficients for Na$^+$ with respect to other cations were determined by a mixed-solution method (FIM). The background metal-ion concentrations were 1×10^{-1} mol dm^{-3} for K$^+$ and H$^+$, 5×10^{-1} mol dm^{-3} for Li$^+$, Ca^{2+}, and Mg^{2+}, and 1 mol dm^{-3} for NH$_4^+$. The response time (t_{95}) was determined on changing the Na$^+$ activity of the sample solution from 1×10^{-3} to 3×10^{-3} mol dm^{-3}. A sodium assay in serum samples was carried out five times for each sample by Gran's plot method. For the standard addition method, the volumes for the sample and adding solution (1 mol dm^{-3} Na$^+$) were 5 (for serum) or 10 (for urine) and 0.1 cm^3, respectively.

Results and Discussion

Design of Calixarene-Modified Oligosiloxane. A calix[4]arene tetraester, which is a highly Na$^+$-selective ionophore, was chosen as the neutral carrier.[10—12] For obtaining a medium-molecular-weight calixarene neutral carrier, we decided to incorporate calix[4]arene tetraallyl ester into oligo(methylsiloxane) by a hydrosilylation reaction (Scheme 1). The oligo(dimethylsiloxane) backbone is expected to enhance the solubility or dispersibility of the resulting calixarene neutral carrier in silicone-rubber membranes, which also contain dimethylsiloxane repeating units. Each molecule of the resulting calixarene oligomer, **1**, was found to carry two or three calixarene units and to possess a molecular weight ranging from 4000 and 5000.

Potential Response of Silicone-Rubber Membrane. The oligomeric calix[4]arene neutral carrier, **1**, was blended with a silicone-rubber precursor in 10 wt%, which corresponds to 4—6 wt% for the calix[4]arene unit. The thus-obtained membranes were applied to Na$^+$-selective electrodes. A typical potential response is shown in Fig. 1, together with that for the electrodes based on silicone-rubber membranes modified chemically with a similar calixarene neutral carrier. The Na$^+$-selective electrodes based on silicone-rubber membranes containing the oligomeric calixarene neutral carrier **1** exhibited a Nernstian response to ten-time Na$^+$ activity changes over a wide activity range, while the electrode based on the calixarene-bound silicone-rubber membranes showed such curious potential response as demonstrated in the fig-



Scheme 1. Synthesis of oligomeric calix[4]arene neutral carrier **1**.

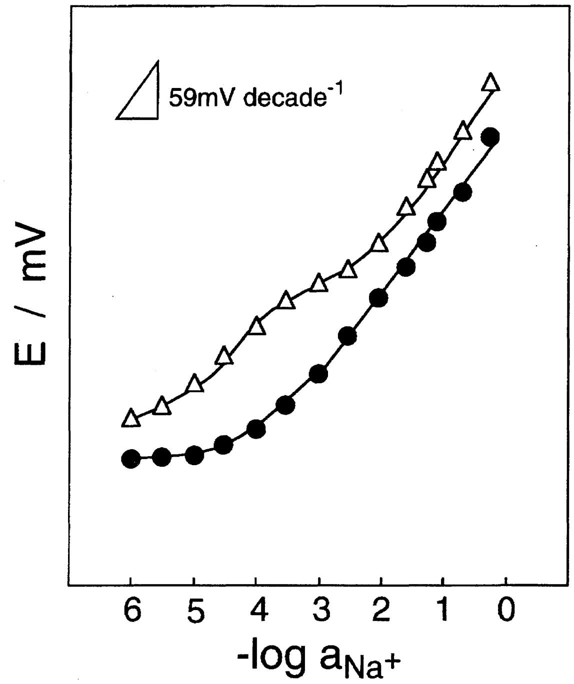


Fig. 1. Potential response to Na^+ activity changes for silicone-rubber-membranes Na^+-selective electrodes based on calix[4]arene neutral carrier.
(●) silicone-rubber membrane encapsulating oligomeric calixarene neutral carrier **1**, (△) silicone-rubber membrane modified chemically with calix[4]arene tetraester.[8]

ure. The poor response for the latter electrodes was probably due to a high membrane impedance, since the incorporation of an anionic site, such as tetraphenylborate salts, to the calixarene-bound silicone-rubber membranes, can alleviate the anomalous response behavior, as reported previously.[8] This means that the calixarene moiety itself is more mobile and easier to exchange Na^+ in the silicone-rubber membranes of oligomeric calixarene neutral carrier **1** than in those modified chemically with a calixarene moiety. Another significant difference between the membranes containing oligomeric calixarene neutral carrier **1** and incorporating a calixarene moiety by chemical bonding was also found in the response time. The response time (t_{95}) is no shorter than 3 min in the system of the calixarene-chemically-bound membranes without any anionic site. The incorporation of the tetraphenylborate anion to the membrane deceased the response time to about 1 min, as demonstrated in Fig. 2b. In the present membrane system containing an oligomeric calixarene neutral carrier **1**, on the other hand, the response time was already below 1 min without an addition of any anionic site (Fig. 2a). Thus, the employment of silicone-rubber membranes containing an oligomeric calixarene neutral carrier **1** instead of the calixarene-chemically-bound membranes has improved the electrode potential response and the response time, thanks to the enhanced mobility of the calixarene moiety in system **1**. Furthermore, the oligomeric calixarene neutral carrier **1** is much more insoluble in water than monomeric calix[4]arene neutral carriers, such as calix[4]arene tetraethyl ester, and is therefore still hard to outflow from the membrane to aqueous phases. The electrode property for the Na^+-selective electrodes based on a silicone-rubber membrane containing **1** has lasted for at least 5 months. Of course, the durability is much better than that of a PVC-membrane Na^+ sensor based on monomeric calix[4]arene ionophore, such as calix[4]arene tetraethyl ester (about 1 month).[5]

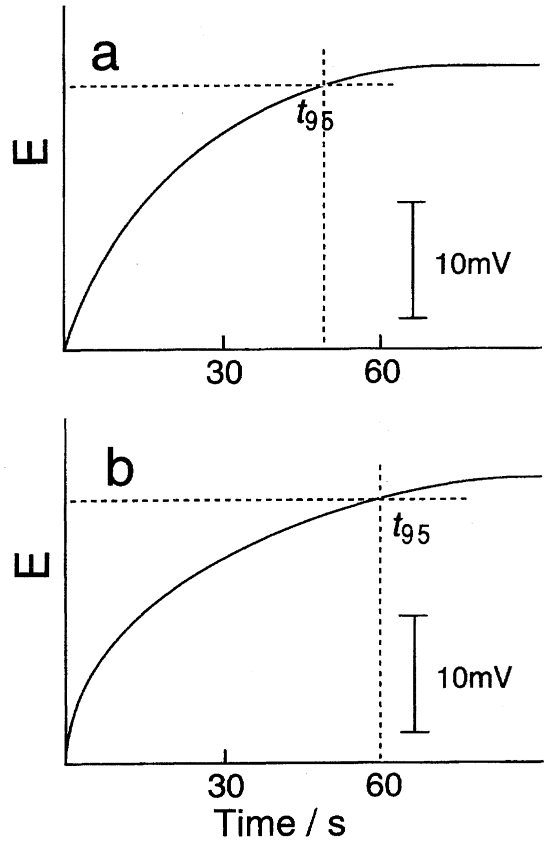


Fig. 2. Time-course changes of potential response for silicone-rubber membranes Na^+-selective electrodes based on calix[4]arene neutral carrier on changing Na^+ concentrations from 1×10^{-3} to 3×10^{-3} mol dm^{-3}.
(a) silicone-rubber membrane encapsulating oligomeric calixarene neutral carrier **1**, (b) silicone-rubber membrane modified chemically with calix[4]arene tetraester and tetraphenylborate anion.[8]

Ion Selectivity and Serum Sodium Assay. The ion selectivities for Na^+-selective electrodes based on silicone-rubber membranes encapsulating an oligomeric calixarene neutral carrier **1** are as shown in Fig. 3. The Na^+ selectivity with respect to K^+ is almost comparable to an ion-selective electrode based on conventional calix[4]arene neutral carriers.[11] In order to check the applicability of Na^+-selective electrodes based on **1**, an attempt was made to assay Na^+ in a control serum sample with an actual Na^+ concentration of 135.0 mmol dm^{-3}. The assay by using the present Na^+ electrodes afforded a Na^+ concentration of 135.4 mmol dm^{-3} with a relative standard deviation of 0.72. This suggests that the Na^+-selective electrodes are reliable in a serum sodium assay.

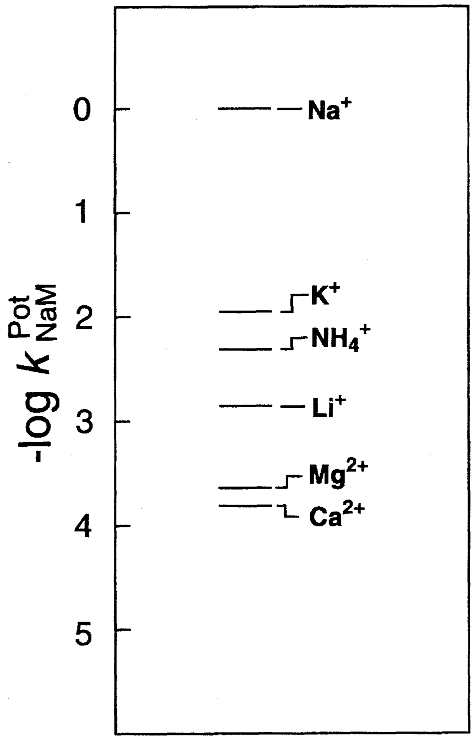


Fig. 3. Ion selectivities for Na$^+$-selective electrodes based on silicone-rubber membrane encapsulating oligomeric calixarene neutral carrier **1**.

The present work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture. Financial support from the Suzuken Memorial Foundation is also acknowledged.

References

1) S. Daunert and L. G. Bachas, *Anal. Chem.*, **62**, 1428 (1990).

2) J. Tietje-Girault, I. MacInnes, M. Schroder, G. Tennant, and H. H. Girault, *Electrochim. Acta*, **35**, 777 (1990).

3) G. G. Cross, T. M. Fyles, and V. V. Suresh, *Talanta*, **41**, 1589 (1994).

4) H.-B. Jenny, C. Riess, D. Ammann, B. Magyar, R. Asper, and W. Simon, *Mikrochim. Acta*, **II**, 309 (1980).

5) K. Kimura, T. Matsuba, Y. Tsujimura, and M. Yokoyama, *Anal. Chem.*, **64**, 2508 (1992).

6) Y. Tsujimura, M. Yokoyama, and K. Kimura, *Sens. Actuators B*, **22**, 195 (1994).

7) D. N. Reinhoudt, J. F. J. Engbersen, Z. Brzozka, H. H. v. d. Vlekkert, G. W. N. Honig, H. A. J. Holterman, and U. H. Verkerk, *Anal. Chem.*, **66**, 3618 (1994).

8) Y. Tsujimura, T. Sunagawa, M. Yokoyama, and K. Kimura, *Analyst (London)*, **121**, 1705 (1996).

9) K. Kimura, T. Sunagawa, and M. Yokoyama, *Chem. Commun.*, **1996**, 745.

10) D. Diamond, G. Svehla, E. M. Seward, and M. A. McKervey, *Anal. Chim. Acta*, **204**, 223 (1988).

11) K. Kimura, T. Miura, M. Matsuo, and T. Shono, *Anal. Chem.*, **62**, 1510 (1990).

12) T. Sasaki, T. Harada, G. Deng, H. Kawabata, Y. Kawahara, and S. Shinkai, *J. Inclusion Phenom.*, **14**, 285 (1992).