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The Synthesis of Bis(benzo-crown ether)s and Their Incorporation into Potassium-Selective PVC Membrane Electrodes

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Abstract. Five bis(benzo-15-crown-5) derivatives connected with different bridge chains were synthesized as neutral carriers in K^+-selective electrodes. Potassium ion-selective PVC membrane electrodes based on these bis(crown ether)s were prepared using dibutyl phthalate (DBP) and dioctyl phthalate (DOP) as plasticizers of the PVC membrane. The selectivity coefficients ($K_{M^{n+}}:K_{K^+}$) for various alkali and alkaline-earth metal ions were measured. The electrodes based on the bis(crown ether)s are more selective for K^+ than those based on monomeric crown ethers. The selectivity of one of the prepared potassium selective electrodes was higher than that of the electrode based on valinomycin and three of them were stable over a wide pH range.

Key words. Bis(crown ethers), PVC membrane, potassium ion-selective electrodes, neutral carriers.

1. Introduction

The discovery of the high affinity of crown ethers for alkali metal ions [1] provided a new approach to the choice of the neutral carrier in preparing potassium- or other metal cation-selective electrodes. Monomeric crown ethers with different ring sizes and different numbers and types of substituents have been used to prepare cation selective electrodes [2, 3, 4]. However, the selectivity coefficients of these systems were found to be much lower than that of the electrode based on the natural antibiotic valinomycin [5]. This result suggests that superior selectivity is not likely to be achieved by simply changing the molecular size and substituents of the monomeric crown ethers. High selectivity potassium-selective electrodes based on bis- and poly(crown ether)s have been prepared [6–9]. Potassium ion can form a sandwich-type complex with both of the moieties of these poly crown ethers, while Na^+ can form a complex with only one of the moieties. Therefore, the bis(crown ether)s are more selective than the monomeric crown ethers for K^+ over Na^+. However, the bis(crown ether)s containing the ester or amide linkages [6] can be hydrolyzed easily. As a result, the working life of the electrodes is relatively short. The properties of these electrodes are closely related to the length, structure and flexibility of the linkage in the bis(crown ether)s [6, 7]. Fung *et al.* [7] found that the

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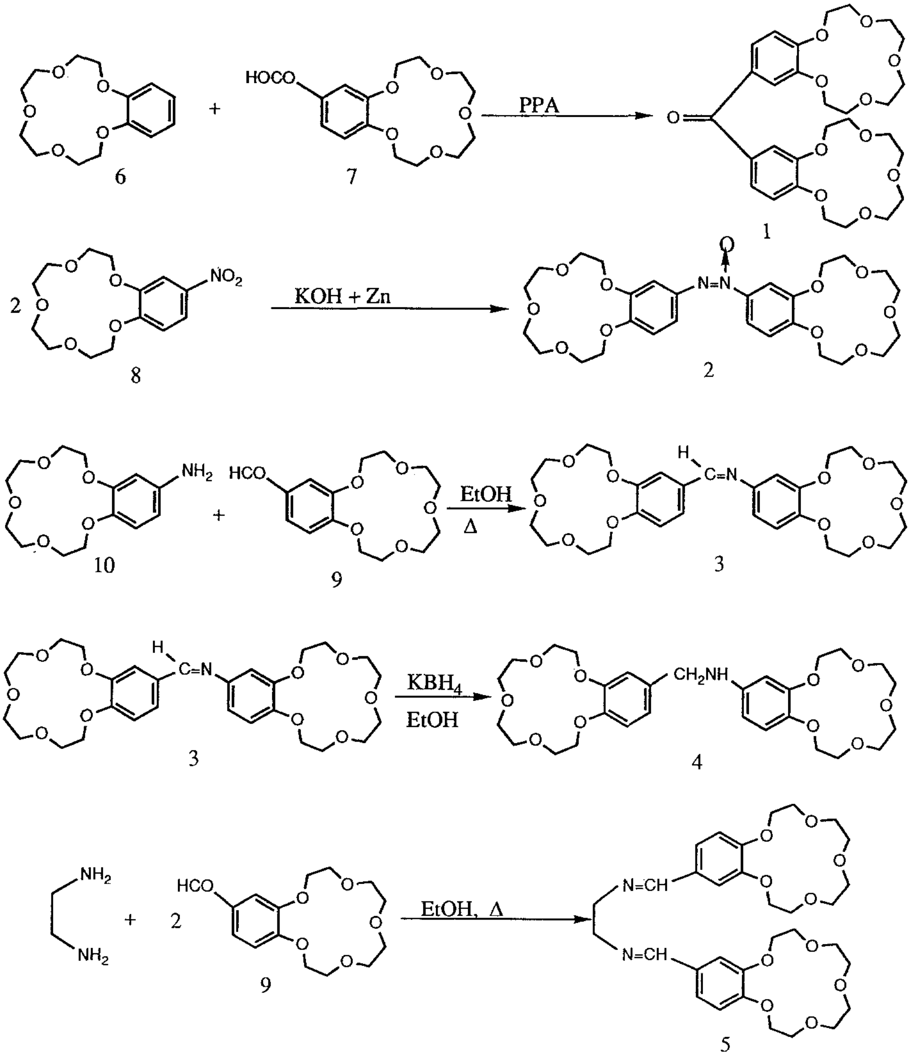
electrode based on the bis(crown ether) with the shortest linkage(—CH_2OCH_2—) had the best selectivity. This may be attributed to the fact that this bis(crown ether) exists as a distorted V shape and it is easy to form a sandwich complex with K^+. The bis(crown ether)s reported earlier have relatively long aliphatic linkages [6–10]. However, electrodes based on bis(crown ether)s with rigid linkages of fewer than three atoms have not been prepared. In order to more fully understand the influences of length and flexibility of linkages in bis(crown ether)s on electrode properties, and to search for bis(crown ether)s with better electrode properties, we have synthesized five bis(benzo-15-crown-5) ethers with different linkages (Scheme 1) and investigated their potassium-selective electrode properties.



Scheme 1. Synthesis of bis(benzo-15-crown-5) (**1**–**5**).

2. Experimental

Benzo-15-crown-5 (**6**) was prepared by an improved method [11, 12]. 4′-Carboxyl-(**7**) [13], 4′-nitro-(**8**) [14] and 4′-formyl-(**9**) [15] benzo-15-crown-5 were prepared as reported. Polyphosphoric acid (PPA) was prepared by a literature method [16]. Deionized water was used for all electrode measurements. All other reagents used were analytical or chemical grades.

PREPARATION OF BIS-(4′-BENZO-15-CROWN-5)KETONE(**1**)

4′-Carboxylbenzo-15-crown-5 (**7**) (1.25 g, 4 mmole) was added to a stirred mixture containing 30 g of PPA, 8 mL of phosphoric acid and 1.1 g (4 mmole) of benzo-15-crown-5 (**6**) at 70 °C. The mixture was stirred for an additional 7 h at 80 °C. The red solution was cooled and hydrolyzed with 100 mL of water. The aqueous mixture was extracted with 100 mL of chloroform and the chloroform extract was washed with 5% of aqueous sodium hydroxide and dried over anhydrous sodium sulfate. The solvent was then evaporated under reduced pressure and the residue was recrystallized from anhydrous ethanol to give 2.1 g (92%) of white, crystalline product (**1**), m.p. 143.5–144.5 °C. ^{1}HNMR: (δ) 3.70–4.24(*m*, 32H), 6.83(*d*, 2H), 7.28(*d*, 2H), 7.35(*s*, 2H). UV(3.857×10^{-5} M in methanol): λ_{max} 235 nm(ε, 25250) 283, nm(ε, 13280), 316.3 nm(ε, 17400).

Anal. Calcd. for $C_{29}H_{38}O_{11}$: C, 61.9; H, 6.81; mol. wt., 562.61 *Found*: C, 61.75; H, 6.79; mol. wt., 562.

PREPARATION OF AZOXYBIS(4′-BENZO-15-CROWN-5) (**2**)

The mixture containing 1.6 g (5 mmole) of 4′-nitrobenzo-15-crown-5 (**8**), 20 mL of distilled water, 20 mL of methanol and 2 g of potassium hydroxide was stirred under reflux for 10 min. Powdered zinc (2 g) was added in batches to the stirred mixture without heating. The reaction mixture was then stirred under reflux for an additional 2 h. The hot mixture was filtered and the filtrate was extracted with chloroform. The chloroform extract was dried over anhydrous sodium sulfate and then evaporated under reduced pressure to give a yellow solid, m.p. 160–161 °C. The crude product was purified by chromatography (Chromatotron) on silica gel G using benzene/carbon tetrachloride/methanol (1 : 3 : 4) as the eluent. Most of the solvent in the central section (one band) was evaporated and cooled to give yellow needles, m.p. 166–167 °C. Recrystallization from ethyl acetate gave 0.65 g (45%) of bright yellow needles (**2**), m.p. 171.5–172.5 °C (lit. [17], yield 24.2%, m.p. 159–160 °C). UV(1.460×10^{-5} M in methanol): λ_{max} 373 nm(ε, 16705). IR(cm^{-1}): 1570(*m*, N=N), 1272(*s*, N—O) (other peaks are similar to those of other bis-crown ethers).

Anal. Calcd. for $C_{28}H_{38}N_2O_{11}$: C, 58.13; H, 6.62; N, 4.85; mol. wt., 578.62. *Found*: C, 58.21; H, 6.61; N, 5.28; mol. wt., 578.

PREPARATION OF 4′-FORMYL(BENZO-15-CROWN-5)-4′-AMINO(BENZO-15-CROWN-5) SCHIFF BASE (**3**)

4′-Nitrobenzo-15-crown-5 (**8**) (2.5 g, 8 mmole) was first reduced to 4′-aminobenzo-15-crown-5 (**10**) [18]. The resulting solution of **10** in ethanol was added immediately to the stirred mixture containing 2.37 g (8 mmole) of 4′-formylbenzo-15-crown-5 (**9**) and 10 mL of anhydrous ethanol at room temperature under an atmosphere of nitrogen. The resulting mixture was heated to 40 °C and a large amount of precipitate formed. The mixture stirred under reflux for 10 min to dissolve the precipitate and then stirred under reflux for an additional 10 min. The reaction mixture was cooled to give a pale yellow precipitate. The crude product was recrystallized from anhydrous ethanol to give 4.3 g (overall 96%) of white needles which were dried by infrared lamp, m.p. 152.5–153.5 °C. ^{1}HNMR: (δ) 3.76–4.15(*m*, 32H), 6.82(*d*, 2H), 6.96(*d*, 1H), 7.25(*s*, 1H), 7.37(*d*, 1H), 7.58(*s*, 1H), 8.36(*s*, 1H CH=N). UV(2.998×10^{-5} M in methanol): λ_{max} 230.5 nm(ε, 21178), 279 nm(ε, 12874), 338 nm(ε,12473).

Anal. Calcd. for $C_{29}H_{39}NO_{10}$: C, 62.02; H, 7.00; N, 2.49; mol. wt., 561.64. *Found*: C, 61.54; H, 6.85; N, 2.12; mol. wt., 561.

PREPARATION OF N,C-BIS(4′-BENZO-15-CROWN-5)METHYL AMINE (4)

The mixture containing 1.1 g (1.96 mmole) of bis(crown ether) (**3**), 30 mL of anhydrous ethanol, and 0.7 g (13 mmole) of potassium borohydride was stirred for 20 min at 40 °C and then stirred under reflux for 2 h. Distilled water (30 mL) was added to the cooled reaction mixture which was then extracted with chloroform. The chloroform extract was dried over anhydrous sodium sulfate and evaporated under reduced pressure to give a pale yellow solid. Recrystallization from anhydrous ethanol gave 1.0 g (91%) of white transparent needles, m.p. 124–125 °C. ^{1}HNMR: (δ) 3.80–4.10(*m*, 32H), 3.25(*b*, 1H, NH), 4.21(*d*, 2H, CH_2N), 6.16–6.30(*m*, 4H), 6.80(*s*, 1H), 6.94(*s*, 1H). UV(4.134×10^{-5} M in methanol): λ_{max} 193.5 nm(ε, 58153), 282.5 nm(ε, 5225), 300 nm(ε, 3725).

Anal. Calcd. for $C_{29}H_{41}NO_{10}$: C, 61.80; H, 7.33; N, 2.49; mol. wt. 563.65. *Found*: C, 61.80; H, 7.36; N, 2.31; mol. wt., 563.

PREPARATION OF ETHYLENEDIAMINE BIS(4′-FORMYLBENZO-15-CROWN-5)SCHIFF BASE (5)

A solution of 0.1 g (1.53 mmole) of ethylenediamine in 5 mL of anhydrous ethanol was added dropwise to the stirred mixture containing 0.9 g (3.04 mmole) of 4′-formylbenzo-15-crown-5 (**9**) and 25 mL of anhydrous ethanol under reflux. The resulting mixture was stirred under reflux for 3 h. The cooled reaction mixture was extracted with chloroform. The chloroform extract was dried over anhydrous sodium sulfate and then evaporated to give a white solid which was recrystallized from anhydrous ethanol to give 0.6 g (64%) of white plates, m.p. 131–132 °C (lit. [9] m.p. 128 °C). ^{1}HNMR: (δ) 3.81–4.17(*m*, 36H), 6.84–8.04(*m*, 6H), 8.27(*s*, 2H, 2 CH=N).

Anal. Calcd. for $G_{32}H_{44}N_2O_{10}$: C, 62.32; H, 7.19; N, 4.54; mol. wt., 616.72. *Found*: C, 62.30; H, 7.24; N, 4.40; mol. wt., 616.

PREPARATION OF PVC MEMBRANE ELECTRODES

In order to choose the best membrane composition, multiple factor analyses were performed on three major components of the membrane by using benzo-15-crown-5

Table I. E_{pot} of the PVC membrane electrodes.

Electrode*	1	2	3	4	5
E_{pot}(mV)	−70	−100	−56	−125	unstable

*The electrode number corresponds to the number of the bis(benzo-15-crown-5) derivative in Scheme 1.

as neutral carrier and dibutyl-phthalate (DBP) as plasticizer. The result indicates that the superior membrane composition is: 2.5–3.0 mg of neutral carrier, 0.5–0.6 g of plasticizer and 3 mL of 5% PVC solution in tetrahydrofuran (THF). The membrane obtained from bis(crown ether) **3** and plasticizer DBP changed to a yellow color; therefore, dioctyl phthalate (DOP) was used as plasticizer for bis(crown ether) **3**.

Bis(crown ether) (2–3 mg) and 0.50 g plasticizer (DBP for membranes 1, 2, 4, and 5; DOP for membrane 3) were dissolved in 2.3 mL of 5% PVC solution in THF. The uniform and transparent solution was poured into a glass ring with 32 mm diameter. THF was evaporated slowly at room temperature to give a film of 0.15 mm thickness. Discs were cut and sealed onto the commercial Ag/AgCl electrode bodies with 5% PVC–THF solution. The internal filling solution was 10^{-2} M KCl saturated with AgCl. The external reference electrode was a double junction saturated calomel electrode with 0.1 M LiCl in the salt bridge.

The PVC membrane electrodes loaded with carriers were conditioned in 10^{-2} M KCl for over 3 h and then washed with deionized water until the measured E_{pot} was constant (Table I).

MEASUREMENTS

All measurements of the potentials were made using a PXJ-1B type digital potentiometer which allowed readings to be made to ± 0.1 mV. Selectivity coefficients were determined via the separate solution method [19]. The pH values were measured using a PHS-2 type pH-meter.

3. Results and Discussion

Three new bis (benzo-crown ether)s (**1**, **3**, and **4** in Scheme 1) with short linkages were synthesized in high yields (91–96%) by simple and convenient methods. The synthesis of bis(crown ether) **2** was reported in low yield (24.2%) by using a very complicated catalyst (cross-linked polystyrene methylene phenyl pyridinium chloride) as an electron transfer reagent [17]. A large portion of by-product, 4′-aminobenzo-15-crown-5, was formed but not isolated. The bis(crown ether) product reported in Reference 17 was obtained as a yellow solid by washing with acetone and the melting point (159–160 °C) was much lower than that of our product (171.5–172.5 °C). We synthesized bis(crown ether) **2** as needle crystals in higher yield (45%) within a short reaction time period (2 h) by an inexpensive and convenient procedure. The product was shown to be the *cis*-isomer by its UV data, $\lambda_{\max}$ 373 nm, $\varepsilon = 16705$ [$\lambda_{\max}$(chloroform) 378 nm, $\varepsilon_{\mathrm{cis}} = 17000$, $\varepsilon_{\mathrm{trans}} = 21000$] [17].

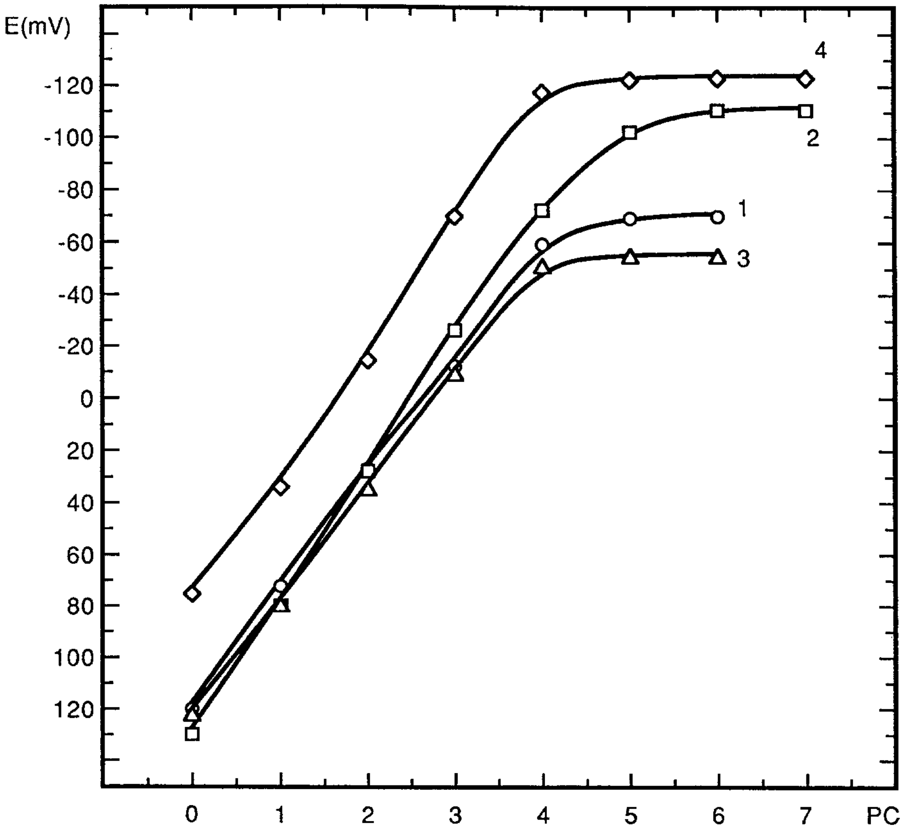


Fig. 1. Response curves of the potassium-selective electrodes vs potassium ion activity: The numbers (1–4) refer to the electrodes based on the corresponding bis(crown ether)s (Scheme 1).

Bis(crown ether) **5** with a long chain [9] was synthesized in order to compare its electrode properties with those of other bis(crown ether)s with short chains. It was found that bis(crown ether)s **3** and **5** containing Schiff base linkages have to be dried using an infrared lamp.

The response curves of the electrodes based on bis(crown ether)s **1**–**4** towards various activities of K^+ are shown in Figure 1, and their performance is summarized in Table II. The electrode based on bis (crown ether) **5** had low transparency after it was immersed in 10^{-2} M KCl and its response was not stable; it was therefore discarded. The response time for the electrodes based on bis (crown ether)s **1**, **2**, and **3** was found to be fast and the equilibrium potential was reached in 30–60 s. The response of the electrodes based on bis(crown ether)s **4** and **5** was relatively slow.

From the selectivity coefficients in Table II, we can see that the electrodes do not respond to Ba^{2+}. Therefore, we adjusted the pH of 10^{-2} M KCl solution with barium hydroxide and hydrochloric acid solutions. The changes of electrode potential with solution pH were measured (Figure 2). These three potassium-selective PVC membrane electrodes were stable in the pH range of 5–10.5. The electrode based on bis(crown ether)**1** was stable over a relatively wide pH range because

Table II. Properties of electrodes containing bis(crown ether)s **1**–**4**.

Property	Competing ion	**1**	**2**	**3**	**4**	B15C5[20]	Valinomycin[5]
$K_{K^+, M^{n+}}$	Li^+	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	—	2.0×10^{-4}
	Na^+	2.5×10^{-3}	1.0×10^{-4}	5.0×10^{-4}	7.9×10^{-4}	4.2×10^{-2}	2.6×10^{-4}
	NH_4^+	5.0×10^{-3}	8.0×10^{-3}	3.0×10^{-2}	2.0×10^{-2}	7.0×10^{-2}	2.0×10^{-2}
	Cs^+	1.0×10^{-1}	1.0×10^{-2}	2.5×10^{-2}	2.5×10^{-2}	2.8×10^{-2}	5.0×10^{-1}
	Ca^{2+}	1.0×10^{-3}	1.2×10^{-3}	1.0×10^{-3}	1.0×10^{-4}	–	8.5×10^{-4}
	Sr^{2+}	2.5×10^{-3}	1.2×10^{-3}	2.5×10^{-2}	4.0×10^{-3}	–	5.4×10^{-4}
	Ba^{2+}	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	–	–	7.2×10^{-4}
	Mg^{2+}	1.8×10^{-4}	1.0×10^{-4}	2.5×10^{-3}	4.0×10^{-4}	–	1.0×10^{-3}
	Zn^{2+}	2.0×10^{-3}	1.0×10^{-5}	1.0×10^{-5}	4.2×10^{-3}	–	–
	Cu^{2+}	1.0×10^{-1}	3.2×10^{-3}	2.0×10^{-1}	3.2×10^{-2}	–	1.3×10^{-3}
Slope		44 ± 1	52 ± 1	43 ± 1	47 ± 1		
Detection Limit		5.6×10^{-5}	2.0×10^{-5}	7.9×10^{-5}	5.0×10^{-5}		
Linear Response Range		$10^0 - 10^{-4}$	$10^0 - 10^{-4}$	$10^0 - 10^{-4}$	$10^0 - 10^{-4}$		

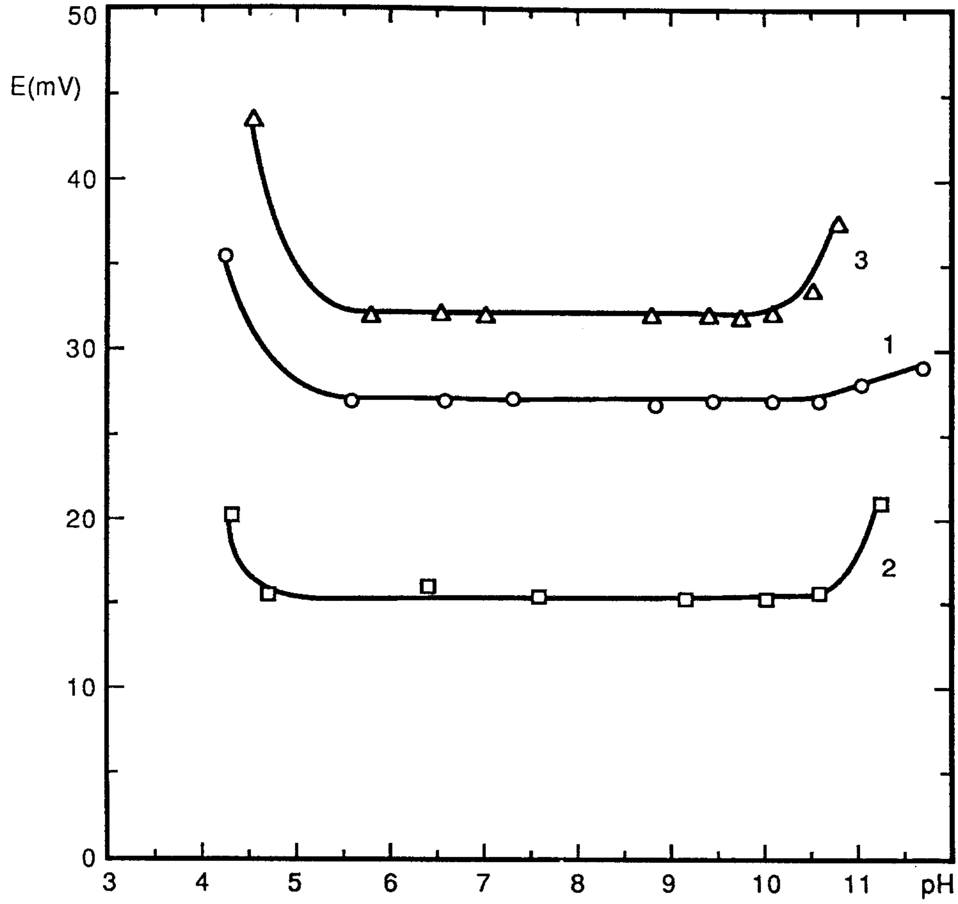


Fig. 2. Influence of pH on electrode response.

neither acid nor base has any influence on the neutral bis(crown ether) (see Scheme 1 for its structure).

All of the prepared electrodes show a Nernstian response towards the potassium ion activity with a detection limit down to 10^{-5}. The electrodes of these bis(crown ether)s exhibited a high preference for K^+ over Na^+. The selectivity coefficients for sodium ion (K_{K^+, Na^+}) of the electrodes based on bis(crown ether)s **2**, **3**, and **4** ranged from 1.0×10^{-4} to 7.9×10^{-4} which were comparable to that of the electrode based on valinomycin (2.6×10^{-4}). The selectivity coefficients for Li^+, NH_4^+, Cs^+, Ba^{2+}, and Mg^{2+} with all measured electrodes were superior to those of the electrode based on valinomycin. For Li^+ and Ba^{2+}, the selectivity coefficients of all electrodes reported here were below 1.0×10^{-5} and beyond the linear response range, therefore, the interference of these ions is negligible in practice.

The selectivity of these electrodes for monovalent cations was found to be: $K^+ > Cs^+ > NH_4^+ > Na^+ > Li^+$. Bis(crown ether)s **1**, **2**, and **3** with rigid linkages and **4** with a short linkage have high selectivity towards K^+. This suggests that they can exist in an appropriate V shape conformation so that they can easily form sandwich complexes with K^+. Bis(crown ether)s **2** and **3** have to exist as *cis*-isomers in order to have appropriate conformations to form sandwich complexes with K^+. However, bis(crown ether) **5** has very poor electrode properties, probably because the long connecting bridge (Scheme 1) does not allow effective complexation to occur with K^+. From all of the measured data, we can conclude that bis(crown ether) **2** is the best neutral carrier for K^+. Furthermore, the electrode based on **2** has somewhat higher selectivity than the commercially available potassium-selective electrode based on the antibiotic valinomycin. Therefore, the electrode may have commercial value. The bis(crown ether)s with rigid and shorter linkages would be better than those with longer linkages as a neutral carrier for use in the K^+ electrode.

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