

The Synthesis of Bis(benzo-15-crown-5) Derivatives and Their Use in Potassium–PVC Membrane Electrodes

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Abstract. Five new bis(benzo-15-crown-5) derivatives with different connecting groups were synthesized. Potassium ion-selective PVC membrane electrodes based on these bis(crown ether)s were prepared and their selective properties were measured. The results showed that most of these electrodes are stable over a wide pH range and their selectivity coefficients were better than those of an electrode based on natural valinomycin.

Key words: Bis(benzo-crown ether)s, PVC membrane, potassium ion-selective electrodes, neutral carriers.

1. Introduction

Extensive studies of ion-selective electrodes based on the crown ethers [1] have been carried out since the special metal ion complexing properties of the crown ethers were reported [2,3]. Research interest was initially concentrated on electrodes based on monomeric crown ethers with different ring sizes and different substituents [4–8]. Research showed that electrodes based on these monomeric systems were not satisfactory for practical use because the selectivity coefficients of the electrode based on simple crowns were much lower than those of electrodes based on valinomycin [9,10]. In recent years, potassium selective electrodes based on bis(crown ether)s have been studied because these electrodes have much higher selectivities for K^+ over Na^+ than do electrodes based on the monomeric crown ethers [11–15]. The working life of electrodes based on the bis(crown ether)s containing ether connecting groups is much longer than where ester or amide connecting groups are used, since the ester and amide linkages can be hydrolyzed easily [15]. It was also suggested that the properties of the electrodes are closely related to the length, structure and flexibility of the connecting groups in the bis(crown ether)s

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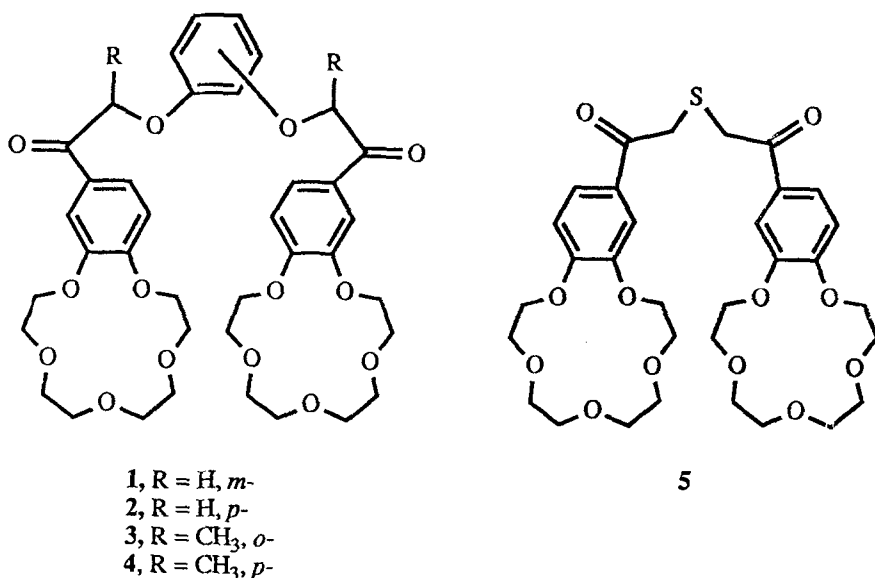
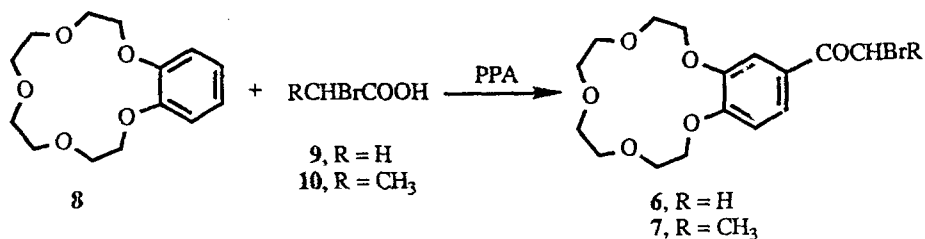


Fig. 1. Bis(benzo-15-crown-5) ethers 1-5

Scheme I. Preparation of 4'-(α -bromoacyl)benzo-15-crown-5 (6 and 7).

[11,15]. The effects of some of the connecting groups on electrode properties were studied [11,14,15].

In order to more fully understand the influences of the structure and flexibility of the connecting groups of the bis(crown ether)s on electrode properties, and to search for new bis(crown ether)s with better electrode properties, we have synthesized five new bis(benzo-15-crown-5) ethers 1-5 each containing different connecting units (Figure 1). Two intermediate bromoacylbenzo-15-crown-5 derivatives (6 and 7) (Scheme I) were also prepared. The potassium-selective electrode properties of the new bis(benzo-15-crown-5) ethers are also reported.

2. Experimental

Benzo-15-crown-5 (B15C5) (**8**) was prepared according to a literature method [16]. Polyphosphoric acid (PPA) was prepared via a published procedure [17]. All other starting materials and reagents used were analytical or chemical grades.

2.1. PREPARATION OF 4'-(α -BROMOACETYL)BENZO-15-CROWN-5 (**6**)

A mixture of 2.7 g (10 mmole) of B15C5 (**8**), 4.2 g (30 mmole) of bromoacetic acid (**9**) and 27 g of PPA was stirred for 45 min at 55 °C. The mixture was hydrolyzed with water. The obtained solution was extracted with chloroform. The chloroform layer was washed with 5% aqueous sodium hydroxide and then with water, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure. The residue was chromatographed on neutral alumina using chloroform/petroleum ether (60–90 °C) (1 : 2) as the eluent (an aqueous 2,4-dinitrophenylhydrazine solution was used to detect the eluate). The solvent was removed and the yellow solid was recrystallized from chloroform/*n*-heptane to give 3.2 g (82%) of **6** as white flakes; m.p. 87.5–88.5 °C (lit. [18] m.p. 80–81 °C); ¹H NMR: (δ) 3.65–4.15 (*m*, 16H), 4.28 (*s*, 2H), 6.28 (*d*, 1H), 7.50 (*s*, 1H), 7.62 (*d*, 1H); IR (cm⁻¹): 1670 (*s*, C=O), 1595, 1520 (*s*, aromatic C=C), 1275, 1050 (*s*, Ar-O-C); MS : *m/z* 390 (M⁺ + 1), 388 (M⁺ - 1).

2.2. PREPARATION OF 4'-(α -BROMOPROPIONYL)BENZO-15-CROWN-5 (**7**)

A mixture of 2.7 g (10 mmole) of B15C5 (**8**), 4.6 g (30 mmole) of α -bromopropionic acid (**10**) and 27 g of PPA was stirred for 45 min at 55 °C. The mixture was treated as above for **6** to give 3.1 g (77%) of **7** as white needles, m.p. 105.5–106.5 °C; ¹H NMR: (δ) 1.86 (*d*, 3H), 3.73–4.22 (*m*, 16H), 5.20 (*q*, 1H), 6.28 (*d*, 1H), 7.50 (*s*, 1H), 7.62 (*d*, 1H); IR (cm⁻¹): 1673 (*s*, C=O); MS: *m/z* 404 (M⁺ + 1), 402 (M⁺ - 1).

Anal. Calcd. for C₁₇H₂₃O₆Br: C, 50.63; H, 5.57; mol. wt. 403.3. *Found:* C, 50.28; H, 5.65.

2.3. PREPARATION OF *m*-PHENYLENEDIOXYBIS[α -(4'-ACETYL)BENZO-15-CROWN-5)] (**1**)

A mixture of 0.30 g (2.7 mmole) of resorcinol (**12**), 0.76 g (5.8 mmole) of anhydrous potassium carbonate (dried at 180 °C before used), and 120 mL of acetone was stirred under nitrogen and heated to reflux. A solution of 2.13 g (5.5 mmole) of **6** in 100 mL of acetone was added dropwise with stirring over a period of 2 h. The mixture was stirred under nitrogen for 10 h. The mixture was cooled and filtered. The solvent was removed under reduced pressure. The residue was dissolved in a small amount of chloroform and added dropwise into 100 mL of ether with vigorous agitation. The resulting yellow solid was filtered and chromatographed on neutral

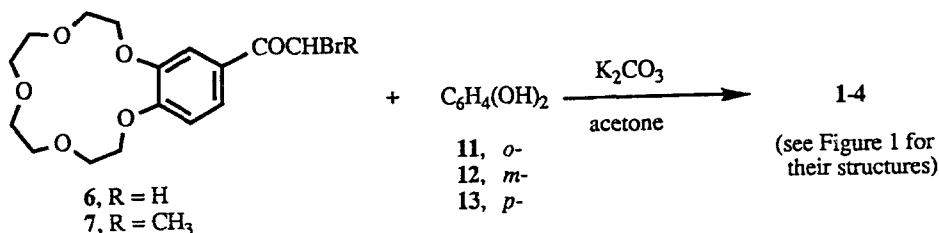
alumina using chloroform as the eluent. The solvent was removed under reduced pressure and the residue was recrystallized from chloroform/ethanol to give 0.89 g (45%) of **1** as a white powder, m.p. 142–143 °C; $^1\text{H NMR}$: (δ) 3.78–4.27 (*m*, 32H), 5.21 (*s*, 4H), 7.10–8.05 (*m*, 10H); $^{13}\text{C NMR}$: (δ) 68.6, 69.1, 70.3, 70.5, 70.7, 71.0, 88.9, 102.3, 107.7, 111.7, 112.7, 122.9, 127.7, 129.9, 148.9, 153.9, 159.1, 192.5. IR (cm^{-1}): 1680 (*s*, C=O); MS: m/z 726 (M^+).

Anal. Calcd. for $\text{C}_{38}\text{H}_{46}\text{O}_{14}$: C, 62.80; H, 6.38; mol. wt. 726.7. *Found*: C, 62.41; H, 6.24.

2.4. PREPARATION OF *p*-PHENYLENEDIOXYBIS[α -(4'-ACETYLBENZO-15-CROWN-5)] (**2**)

A solution of 2.13 g (5.5 mmole) of **6** in 100 mL of acetone was added dropwise to a mixture of 0.30 g (2.7 mmole) of hydroquinone (**13**), 0.76 g (5.5 mmole) of anhydrous potassium carbonate and 120 mL of acetone. The mixture was treated as above for **1** to give 0.89 g (45%) of **2** as a white powder, m.p. 162–163 °C; $^1\text{H NMR}$: (δ) 3.93–4.43 (*m*, 32H), 5.40 (*s*, 4H), 7.10–8.05 (*m*, 10H); IR (cm^{-1}): 1685 (*s*, C=O); MS; m/z 726 (M^+).

Anal. Calcd. for $\text{C}_{38}\text{H}_{46}\text{O}_{14}$: C, 62.80; H, 6.38; mol. wt. 726.7 *Found*: C, 62.49; H, 6.38.



Scheme II. Synthesis of bis(benzo-15-crown-5) ethers **1-4**.

2.5. PREPARATION OF *o*-PHENYLENEDIOXYBIS[α -(4'-PROPIONYLBENZO-15-CROWN-5)] (**3**)

A solution of 2.20 g (5.5 mmole) of **7** in 100 mL of acetone was added dropwise to a mixture of 0.30 g (2.7 mmole) of catechol (**11**), 0.76 g (5.5 mmole) of anhydrous potassium carbonate and 120 mL of acetone. The mixture was treated as above for **1** to give 1.00 g (49%) of **3** as a white powder, m.p. 144–145 °C; $^1\text{H NMR}$: (δ) 1.66–1.78 (*d*, 6H), 3.94–4.40 (*m*, 32H), 5.85 (*q*, 2H), 7.08–8.15 (*m*, 10H); IR (cm^{-1}): 1680 (*s*, C=O); MS: m/z 754 (M^+).

Anal. Calcd. for $\text{C}_{40}\text{H}_{50}\text{O}_{14}$: C, 63.54; H, 6.68; mol. wt. 754.8. *Found*: C, 63.69; H, 6.68.

TABLE I. Blank potential E_{pot} of the PVC membrane electrodes.

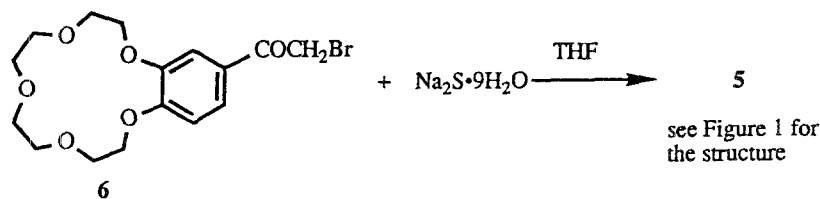
Electrode*	1	2	3	4	5
E_{pot} (mV)	-110	-120	-150	-90	-20

* The electrode numbers correspond to the number of the bis(crown ether)s in Figure 1.

2.6. PREPARATION OF *p*-PHENYLENEDIOXYBIS[α -(4'-PROPIONYLBENZO-15-CROWN-5)] (4)

A solution of 2.20 g (5.5 mmole) of **7** in 100 mL of acetone was added dropwise to a mixture of 0.30 g (2.7 mmole) of hydroquinone (**13**), 0.76 g (5.5 mmole) of anhydrous potassium carbonate and 120 mL of acetone. The mixture was treated as above for **1** to give 1.10 g (54%) of **4** as a white powder, m.p. 177–178 °C; $^1\text{H NMR}$: (δ) 1.63–1.75 (*d*, 6H), 3.94–4.40 (*m*, 32H), 5.85 (*q*, 2H), 6.98–8.15 (*m*, 10H); IR (cm^{-1}): 1680 (*s*, C=O); MS: m/z 754 (M^+).

Anal. Calcd. for $\text{C}_{40}\text{H}_{50}\text{O}_{14}$: C, 63.54; H, 6.68; mol. wt. 754.8. *Found*: C, 63.65; H, 6.97.

Scheme III. Synthesis of bis(benzo-15-crown-5) thioether **5**.

2.7. PREPARATION OF BIS[α -(4'-ACETYL BENZO-15-CROWN-5)] THIOETHER (5)

To a mixture of 1.52 g (3.9 mmole) of **6** and 35 mL of THF, a 5-mL aqueous solution of 0.48 g (2.0 mmol) of sodium sulfide monohydrate was added with stirring. The mixture was stirred for 10 min at room temperature to give a white precipitate. The mixture was refluxed for 5 h and the solid dissolved. The solvent was removed under reduced pressure and the residue was dissolved in chloroform. The chloroform was condensed and chromatographed on neutral alumina using chloroform as the eluent. The solvent was removed under reduced pressure and the yellow crude product was recrystallized from chloroform/ethanol to give 0.95 g (75%) of **5** as a white powder, m.p. 178–180 °C; $^1\text{H NMR}$: (δ) 3.77–4.27 (*m*, 32H), 3.95 (*s*, 4H), 6.77–7.68 (*m*, 6H); $^{13}\text{C NMR}$: (δ) 37.2, 68.6, 68.9, 69.1, 70.2, 70.3, 71.1, 111.6, 113.8, 123.7, 128.6, 148.9, 153.8, 192.9; IR (cm^{-1}): 1665 (*s*, C=O); MS: m/z 650 (M^+).

TABLE II. Properties of electrodes based on bis(crown ether)s 1–5.

Electrode*	1	2	3	4	5
Linear Response	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	5.0×10^{-6}	1.0×10^{-5}
Range	-3.2×10^{-2}	-1.0×10^{-1}	-1.0×10^{-1}	-3.2×10^{-2}	-1.0×10^{-1}
Detection Limit	4.0×10^{-6}	3.2×10^{-6}	4.0×10^{-6}	2.0×10^{-6}	3.2×10^{-6}
Slope	46 ± 1	38 ± 1	55 ± 1	38 ± 1	30 ± 1

Anal. Calcd. for $C_{32}H_{42}O_{12}S$: C, 59.06; H, 6.51; mol. wt. 650.7. *Found*: C, 58.92; H, 6.57.

2.8. PREPARATION OF PVC MEMBRANE ELECTRODES

In order to choose the best membrane composition, multiple factor analyses were performed on the three major components of the membrane by using crown ether as the neutral carrier and dioctylphthalate (DOP) as the plasticizer. The result indicated that the superior membrane composition was: 3.0 mg of neutral carrier, 0.5–0.6 g of plasticizer and 3 mL of 5% PVC solution in THF. The prepared uniform and transparent solution was poured into a 32 mm diameter glass ring and the solvent was evaporated for 48 h at room temperature. A 10 mm diameter disc was cut from the obtained PVC membrane and sealed onto the commercial Ag/AgCl electrode bodies with a 5% PVC-THF solution. The internal filling solution was 0.01 M KCl saturated with AgCl. The external reference electrode was a double junction saturated calomel electrode with 0.1 M LiCl in the external salt bridge. The PVC membrane electrodes loaded with bis(crown ether)s 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).

2.9. MEASUREMENTS

Deionized water was used for all electrode measurements. All potential measurements were made using a PXJ-1B type digital potentiometer which allowed readings of ± 0.1 mV. Selectivity coefficients were determined via the separate solution method or the mixed solution method. A PHS-2 type pH-meter was used to measure pH values.

3. Results and Discussion

4'-(α -bromoacetyl)benzo-15-crown-5 (**6**) (Scheme I) was prepared by the acetylation of B15C5 (**8**) with bromoacetic acid (**9**) using PPA as catalyst. This method

is convenient and simple compared to the reported method [18]. Product **6** was obtained in the form of white flakes with a m.p. of 87.5–88.5 °C, while that reported [18] was in the form of yellow crystals with a m.p. of 80–81 °C. The new 4'-(α -bromopropionyl)benzo-15-crown-5 (**7**) (Scheme I) was also prepared in a good yield from **8** and α -bromopropionic acid.

Five new bis(crown ether)s (**1–5**) (Figure 1) with different connecting groups were synthesized by two methods (Schemes II and III). Bis(crown ether)s **1** and **2** were obtained by the reaction of bromoacetyl crown **6** with resorcinol (**12**) and hydroquinone (**13**) using potassium carbonate as the base. The crown ether reactant acted as a phase-transfer catalyst. Similarly, bis(crown ether)s **3** and **4** were obtained by the reaction of **7** with catechol (**11**) and hydroquinone (**13**), respectively. Bis(crown ether) **5** with the thioether bridge was synthesized in high yield by the coupling of bromocrown ether **6** using sodium sulfide as reported for the preparation of other thioethers [19].

The response curves of bis(crown ether) electrodes **1–5** towards various activities of K^+ are shown in Figure 2. The electrode properties are summarized in Tables II and III. The response times for bis(crown ether) electrodes **1–4** were fast. The equilibrium potential was reached in 30s at concentrations of 10^{-2} – 10^{-4} M. The electrode based on bis(crown ether) **5** responded slowly and the equilibrium potential was reached in 2 min.

From the selectivity coefficients in Table III, we can see that the electrodes do not respond to Ba^{2+} . Therefore, we adjusted the pH of a 10^{-2} M KCl solution with barium hydroxide and hydrochloric acid solutions. The changes of electrode potentials with solution pH were measured (Figure 3). The electrodes based on bis(crown ether)s **1**, **2**, **3**, and **4** were stable in the pH range of 4–10, and that based on **5** was stable only at pH 6–9, possibly because of the existence of a sulfide group in the linkage of **5**.

All of the prepared electrodes show a Nernstian response towards the potassium ion activity with a detection limit down to 10^{-6} (Table II). The selectivity coefficients for sodium (K_{K^+,Na^+}) of the electrodes based on bis(crown ether)s **2**, **3** and **5** ranged from 1.0×10^{-4} to 2.5×10^{-4} , which were comparable to or a little better than that of the electrode based on natural valinomycin (2.6×10^{-4} [9] or 2.0×10^{-4} [10]). The selectivity coefficients of all prepared electrodes for Li^+ , NH_4^+ , Cs^+ , Mg^{2+} , Ca^{2+} , Sr^{2+} and Ba^{2+} were superior to those of the electrode based on valinomycin.

The selectivity of the electrodes based on bis(crown ether)s **3–5** for monovalent cations was found to be in the following order: $K^+ > NH_4^+ > Cs^+ > Na^+ > Li^+$, but that of the electrodes based on bis(crown ether)s **1** and **2** was different.

According to the literature [11,14] the electrode based on the bis(crown ether) with the shortest linkage has the best selectivity. The electrodes based on the bis(crown ether)s with long linkages containing phenylene bridges still have high selectivity in our work. This is probably because the aromatic ring in the linkage fixes the long linkage to a V shape so that two crown subunits form a sandwich

TABLE III
Selectivity coefficients ($K_{K^+, M^{n+}}$) of electrodes based on bis(crown ether)s 1-5.

Competing ion	1	2	3	4	5	B15C5[8]	Valinomycin [9]
Na ⁺	5.06×10^{-3} *	2.5×10^{-4} *	2.0×10^{-4} *	2.0×10^{-3} *	1.0×10^{-4} *	4.2×10^{-2}	2.6×10^{-4}
NH ₄ ⁺	1.0×10^{-3}	1.0×10^{-4}	6.3×10^{-3} *	2.0×10^{-2}	1.2×10^{-2}	7.0×10^{-2}	2.0×10^{-2}
Li ⁺	1.0×10^{-5}	1.0×10^{-4}	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	—	2.0×10^{-2}
CS ⁺	5.0×10^{-2}	1.0×10^{-4}	1.0×10^{-5}	4.0×10^{-5}	1.0×10^{-5}	2.8×10^{-2}	5.0×10^{-1}
Mg ²⁺	4.0×10^{-4}	5.0×10^{-3}	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	—	1.0×10^{-3}
Ca ²⁺	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	—	8.5×10^{-4}
Sr ²⁺	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	5.0×10^{-5}	1.0×10^{-5}	—	5.4×10^{-4}
Ba ²⁺	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	—	7.2×10^{-4}
Zn ²⁺	2.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	—	—

* Determined via the mixed solution method; all others were determined via the separate solution method.

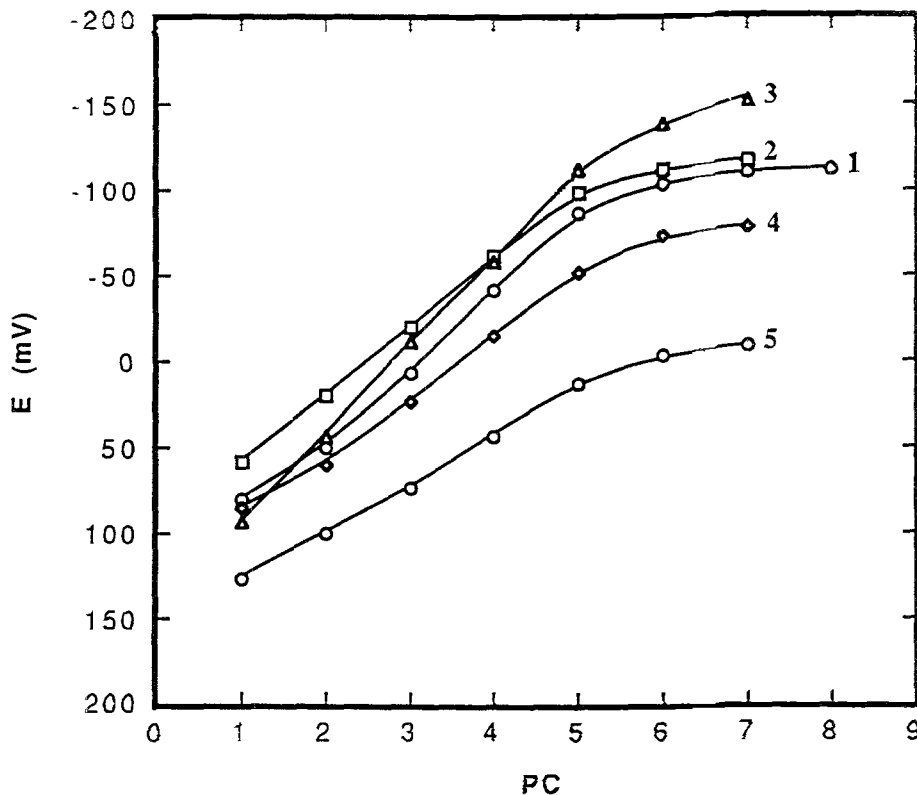


Fig. 2. Response curves of the potassium selective electrodes expressed as potential E (mV) vs potassium ion activity ($PC = -\log a_{K^+}$). The numbers (1-5) refer to the electrodes based on the corresponding bis(crown ether)s (Figure 1).

type complex with potassium ion. This was confirmed by the fact that the electrode based on *ortho*-carrier **3** has better electrode properties than the electrode based on the *para*-carrier **4**.

From all of the properties of the prepared electrodes (Tables I-III, Figures 2 and 3) we can draw a conclusion that the electrode based on **3** is the best one. Its selectivity coefficients for all determined ions ($K_{K^+,M^{n+}}$) are better than those of the electrode based on valinomycin and its other properties are very near to those of the valinomycin electrode.

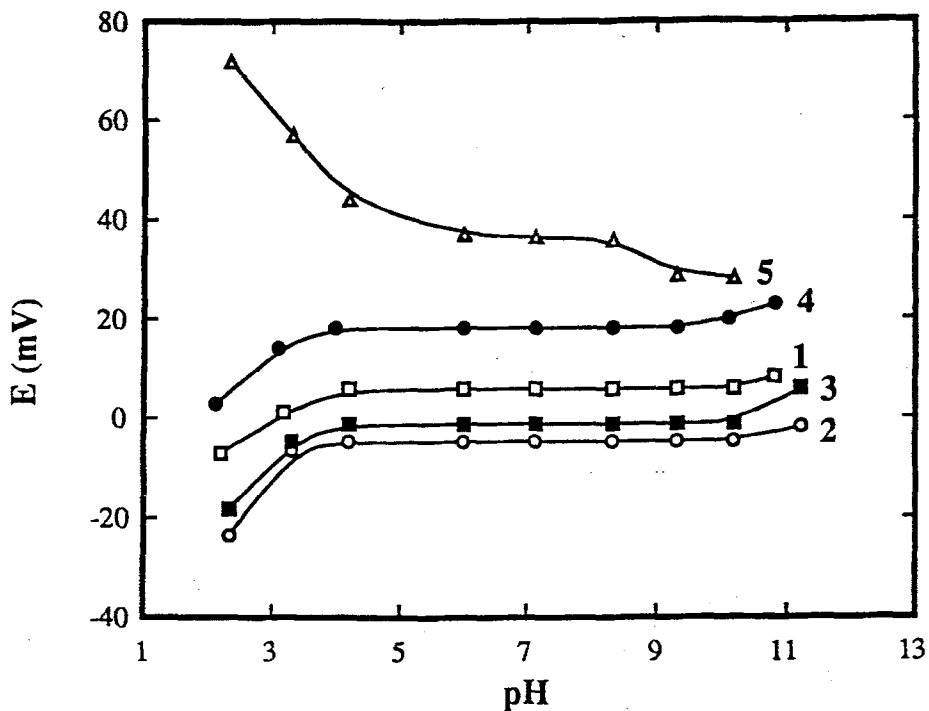


Fig. 3. Influence of pH on electrode response.

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