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On the Mechanism of Unexpected Potentiometric Response to Neutral Phenols by Liquid Membranes Based on Quaternary Ammonium Salts−Systematic Experimental and Theoretical Approaches

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Abstract: Changes in membrane potentials (potentiometric responses) induced by undissociated, neutral phenols (ArOH), though unexpected in terms of the conventional response mechanism for charged species, were systematically investigated using poly(vinyl chloride) (PVC) matrix liquid membranes containing quaternary ammonium and phosphonium salts (Q^+X^-) as the sensory elements. The observed anionic responses were characteristic in that they accompanied large response slopes (-65 to -200 mV decade^{-1}) and selectivities reflecting the acidity and lipophilicity of phenolic compounds. In two phase systems, the extracted and complexed ArOH ($Q^+X^- + \mathrm{ArOH} \rightarrow Q^+X^-\cdot\mathrm{ArOH}$) further underwent proton dissociation ($Q^+X^-\cdot\mathrm{ArOH} \rightarrow Q^+\mathrm{ArO}^- + \mathrm{HX}$) with concomitant ejection of HX to the aqueous phase. Based on these experimental results, a model for potentiometric responses to *neutral* phenols, which explains the anionic responses on the basis of a decrease in the amount of the cationic and anionic species that are charge-separated across the membrane interface, was proposed. A theoretical treatment based on the above model reproduced the potentiometric response behaviors for undissociated phenols. This model was further supported by optical second harmonic generation (SHG), which enabled direct observation of the processes occurring at the interface of a liquid membrane and an aqueous solution.

Introduction

Changes in membrane potentials (potentiometric responses) induced by ionic species contribute as the principle of ion-selective electrodes (ISEs), which provide an important sensing method for a variety of chemical analyses. A number of ISEs having high sensitivities and selectivities for target analyte ions are now commercially available.[1] Theoretical studies on liquid and bilayer membrane systems[2] as well as experimental studies based on the techniques of electrodialysis[3,4c] and radiotracer[3b,d,4] have demonstrated the general mechanism of potentiometric response to charged species to be preferential permeation of primary ions from the aqueous sample solution to the phase boundary region of an organic membrane, essentially leaving the counterions on the aqueous side of the interface (permselectivity). This view is supported by experimental confirmation of a theoretical response model based on surface charge density[5] and by direct observation of permselectivity at membrane surfaces, achieved recently by FTIR-ATR[6a−d] and optical second harmonic generation (SHG)[6e−g] techniques.

Although the prerequisite for this mechanism is the occurrence of a charge on an analyte, there have been some instances in which membrane potentials are affected by uncharged molecules. Such systems include poly(vinyl chloride) (PVC) matrix liquid membranes,[7,8] Langmuir-Blodgett type monolayers,[9] and lipid bilayer vesicles.[10] Although no explicit explanation is available in most cases, there are a few examples of liquid

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membrane systems for which the response mechanism can be reasonably interpreted on the basis of changes in the amount of charge separation across the membrane interface. For example, cationic responses to polyether surfactants,[7a–d,f] some of which show response curves with a theoretical slope,[7a–d] were explained by partitioning of the surfactant–metal cation complexes into the membrane. A theoretical treatment was recently made for a related system by Meyerhoff *et al.*[7f]

Based on the previous findings of Kimura et al.[11] that a macrocyclic polyamine forms stable complexes with neutral catecholic compounds in aqueous solutions, we have examined potentiometric responses to various phenolic compounds by PVC matrix liquid membranes based on lipophilic macrocyclic polyamines (*e.g.,* **1** in Figure 1).[12] A number of phenols examined induced potentiometric responses under the pH conditions in which they occur almost exclusively as their undissociated, neutral forms. The prerequisite for the responses to phenols seemed to be the existence of a phenolic OH. Interestingly, such unexpected "potentiometric" responses to neutral species were observed for several types of nitrogen-containing sensory elements, including intrinsically cationic ones (*e.g.,* lipophilic quaternary ammonium or phosphonium salts) as well as such ones that acquire a cationic property by protonation (*e.g.,* lipophilic aliphatic or heteroaromatic amines).[13] Compared to the polyether surfactant system described above, the onium and protonated amine systems are characteristic in that the membranes intrinsically contain as the sensory elements charged species, which contribute to control the membrane potential. The recent report by Mokrov *et al.*[8] also demonstrates anionic responses to neutral phenols by PVC matrix liquid membranes based on tetra(decyl)ammonium salts.

In this paper, we report comprehensive investigations on the mechanism of anionic potentiometric responses to neutral phenols, based on experimental and theoretical approaches. The present approaches are featured by the following points: (1) As the charged sensory elements of PVC matrix liquid membranes, quaternary ammonium and phosphonium salts (Q^+X^-; **2**–**6** and **7**, respectively, in Figure 1) were used throughout the study because they bear an invariable charge

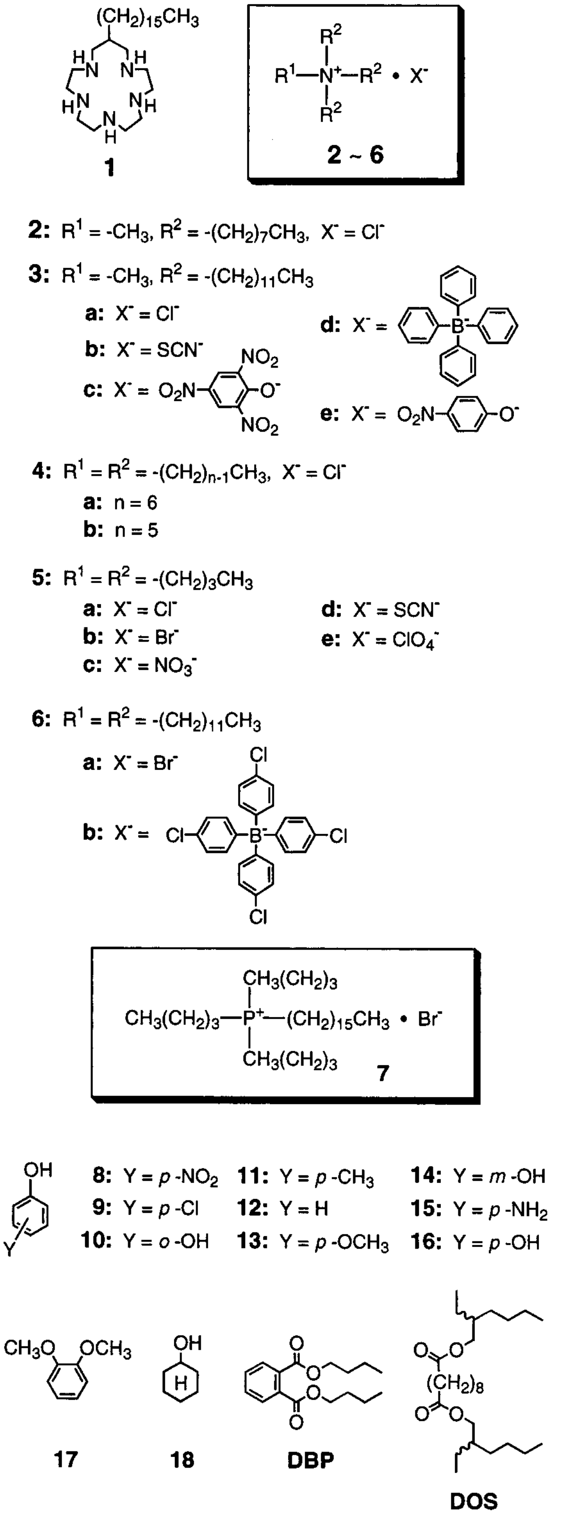

Figure 1. Chemical structures of the compounds used in the present study. Quaternary ammonium salts **2**–**6** and quaternary phosphonium salt **7** were used for the potentiometry and/or extraction experiments. Phenol and related compounds (**8**–**18**) were used as analytes. Dibutyl phthalate (DBP) and bis(2-ethylhexyl) decanedioate [dioctyl sebacate (DOS)] were used as membrane solvents. The structure of lipophilic macrocyclic pentaamine **1** is also shown.

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regardless of pH and hence are suited for the purpose as compared to the amine sensory elements.[12,13] (2) Potentiometric responses of these membranes to a series of phenols (ArOH; Figure 1) and some reference compounds were systematically examined at varying pH conditions to disclose the structural requirement of the phenols for potentiometric responses in their undissociated, neutral forms. (3) The interactions between Q^+X^- and ArOH were discussed on the basis of the results of not only complexation studies in homogeneous solutions[14] but also solvent extraction experiments in two phase systems. (4) On the basis of these results, a model for anionic potentiometric responses to neutral phenols is proposed. This model explains the anionic responses on the basis of an analyte-induced decrease in the amount of the cationic and anionic species that are charge-separated across the membrane interface. (5) The observed potential vs concentration curves could be reproduced by a theoretical treatment of this model. Direct observation of the processes occurring at the membrane interface by optical SHG measurements further supported the present potentiometric response model for *neutral* phenols.

Experimental Section

Reagents. The chemical structures of quaternary ammonium and phosphonium salts, phenols and related compounds, and membrane solvents used in the present study are shown in Figure 1. The sources and/or the details of preparation and purification of these reagents are described in the Supporting Information. Stock buffer solutions of pH 8−12 and pH 6−7 were prepared with 1.0×10^{-2} M boric acid and 1.0×10^{-2} M MES (2-morpholinoethanesulfonic acid), respectively. The pH was adjusted by adding an NaOH solution of appropriate concentration. The pH of all solutions was measured at room temperature (*ca.* 20 °C), using an ion meter Model IOL-40 or 50 [Denki Kagaku Keiki (DKK), Tokyo, Japan] with a pH glass electrode (Type 6157, DKK). All of the sample and buffer solutions were prepared with Milli-Q water with a specific resistance greater than 17.5 MΩ cm and bubbled with nitrogen for 20 min just before potentiometric measurements in order to prevent the phenolic compounds from oxidation by dissolved oxygen.

Electrode Preparation and Potential Measurements. PVC matrix liquid membranes 2, 3a, 3b, 3c, 3d, 4a, 5a, and 7, based on lipophilic quaternary ammonium and phosphonium salts **2**, **3a**, **3b**, **3c**, **3d**, **4a**, **5a**, and **7**, respectively, and the corresponding blank membrane with no particular sensory element were prepared according to the procedure reported previously.[5,15] The composition of the membranes containing sensory elements was 2.5 wt % quaternary onium salts, 70 wt % DBP, and 27.5 wt % PVC, and that of the blank membrane was 72 wt % DBP and 28 wt % PVC. From the membrane thus prepared (*ca.* 0.2-mm thickness), a circle of *ca.* 7-mm diameter was cut out and mounted on a liquid membrane type ISE body (DKK). A reference electrode used was a double-junction type based on an Ag/AgCl electrode (Type 4083, DKK). The electrode cell for the potential measurements was as follows:

Ag/AgCl | 3 M KCl ¦ buffer solution used in each measurement ¦
sample solution | membrane | 1.00 M KCl | Ag/AgCl

For the membranes based on quaternary ammonium salts with highly lipophilic anions (**3b**, **3c**, **3d**), 0.1 M KCl + 0.1 M KSCN, 10 mM KCl + 1 mM sodium picrate, and 0.1 M NaCl + 0.1 M sodium tetraphenylborate solutions were used, respectively, as the inner reference solution.

Membrane potentials were measured at room temperature (*ca.* 20 °C) with an ion meter Model IOL-40 or IOL-50 (DKK). Before each set of measurements, electrodes were conditioned overnight in an appropriate buffer solution without an analyte. Membrane potentials with varying concentrations of phenol and related compounds were recorded when the differential quotient ($\Delta E/\Delta t$) of the potential-time curve became smaller than a prechosen value ($\Delta E/\Delta t < 0.4$ or $\Delta E < 0.4$ mV within $\Delta t = 1$ min); this point was taken as the response time t (Δt, ΔE), as defined in the previous articles.[16a−c] For the electrodes examined in the present study, the response time was generally short and within 5 min.[16d]

For membrane 2, potentiometric selectivity coefficients ($K^{\mathrm{pot}}_{\mathrm{A,B}}$) were determined by the matched potential method in mixed solutions according to Gadzekpo and Christian[17] for each group of analytes in 1.0×10^{-2} M MES buffer of pH 6.0. In the present study with neutral species as analytes, the selectivity coefficient was defined as the ratio of the concentrations of the primary and interfering analytes which gave the same potential change under the same condition; a fixed concentration of 1.00×10^{-4} M **12** was used as a background because potential drift was negligible at this concentration. The $K^{\mathrm{pot}}_{\mathrm{A,B}}$ values were calculated from the concentration of the interfering analyte which induced the same potential change as that induced by increasing the concentration of **12** to 1.23×10^{-3} M.

As for the potential vs time curves, membrane 3a was conditioned with a buffer solution of pH 8.0, and the time profile for 1.00×10^{-2} M **12** was monitored first at pH 8.0 and then at pH 12.0. The time profiles at both pH 8.0 and 12.0 were repeatable.

Solvent Extraction. Changes of pH in the aqueous phase as a result of extraction of a phenolic compound into the organic phase containing a quaternary ammonium salt were measured at room temperature (*ca.* 25 °C) as follows. A 1.00×10^{-2} M aqueous solution of phenolic compound **8**, **10**, or **16** (3.0 mL; pH 4.0, preadjusted with HCl; 1.0×10^{-2} M NaCl; purged with nitrogen for 20 min) was shaken for 20 s by a vortex mixer with a solution of quaternary ammonium salt **2** (1 wt %) in benzene or DBP (3.0 mL; presaturated with water). The organic and aqueous phases were separated by centrifugation at 4000 rpm for *ca.* 20 min because, without centrifugation, an emulsified phase between the organic and aqueous phases still remained after 3 h. The pH of the aqueous phase was measured with a pH glass electrode. The extractability (percent extracted) of each phenolic compound was calculated from the concentration of the undissociated phenol in the aqueous solution before and after extraction, determined by the absorbance at 317 nm (**8**), 275 nm (**10**), or 288 nm (**16**), which correspond, respectively, to the $\lambda_{\max}$ of each substituted phenol in water. UV−visible spectra were recorded on a UV-240 spectrophotometer (Shimadzu, Kyoto, Japan).

The experiments to support the extraction/dissociation process were made as follows by the UV−visible spectra of **8** extracted to benzene and the change in the concentration of Cl^- in the aqueous phase: A 1.17×10^{-4} M solution of **8** in water (3.0 mL; preadjusted to pH 4.0 with H_2SO_4; prebubbled with nitrogen for 20 min) and a 1.05×10^{-4} M solution of **3a** in benzene (3.0 mL; presaturated with water) were shaken for 20 s by a vortex mixer. The organic and aqueous phases were separated by centrifugation at 4000 rpm for *ca.* 20 min, because, without centrifugation, an emulsified phase still remained after 6 h. The concentration of dissociated **8** in the organic phase was determined from the absorbance at 400 nm after extraction. The ratio of dissociated and undissociated **8** extracted in the organic phase was calculated from the concentration of dissociated **8** in the organic phase and the percent extracted of **8** determined as above (84% extracted, corresponding to a concentration of 9.81×10^{-5} M in the organic phase).

Changes in the concentration of Cl^- in the aqueous phase as a result of extraction of **8** into the organic phase containing **3a** were measured after similar extraction experiments as above. As the aqueous phase

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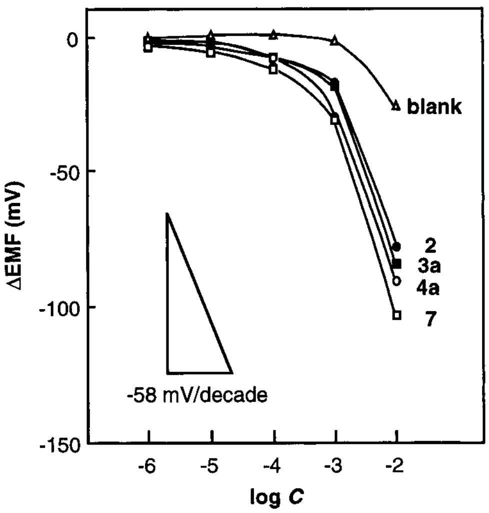

Figure 2. Potential (ΔEMF) vs concentration curves for phenol (**12**), obtained at pH 6.0 by membranes 2, 3a, 4a, and 7, based on lipophilic quaternary ammonium or phosphonium salts, and by a blank membrane containing no particular sensory element. Measured in 1.0×10^{-2} M MES-NaOH buffer (pH 6.0) at room temperature (*ca.* 20 °C).

(3.0 mL, pH 4.0; without NaCl), solution (a), containing 1.17×10^{-4} M **8**, or (b), containing no phenolic compound, was shaken with an equal volume of a 1.05×10^{-4} M solution of **3a** in benzene. After separation, the concentration of Cl^- in each aqueous phase was measured with an ion chromatograph (HIC-6A, Shimadzu; column: Shimpack IC-A1; eluent: 1.2 mM potassium hydrogen phthalate-phthalic acid buffer of pH 4.5; flow rate: 1.5 mL min^{-1}; temperature: 40 °C) connected to a conductivity detector (CDD-6A, Shimadzu). The retention time of Cl^- in this system was 4.5 min. The difference in the concentration of Cl^- between aqueous solutions (a) and (b) was $(1.26 \pm 0.95) \times 10^{-5}$ M.

Optical Second Harmonic Generation (SHG) Experiments. The intensity of optical SHG from **8** was measured for a two phase system of an aqueous solution of **8** (1.0×10^{-2} M boric acid−NaOH buffer of pH 10.0 or 1.0×10^{-2} M MES-NaOH buffer of pH 6.0) and a PVC matrix liquid membrane containing **3a** or a blank membrane. The compositions of the membrane containing **3a** and of the blank membrane were the same as those for the potentiometric measurements except that DOS was used as a membrane solvent in place of DBP, because the former showed much weaker SHG signal (due to the lack of aromatic π electrons) and hence much smaller noise. When the signals stabilized after 10−20 min of irradiation, the SHG intensities at varying concentrations of **8** were measured by the same procedure as described in ref 6e, except for using a Q-switched Nd:YAG laser Quanta-Ray Model DCR130 (Spectra-Physics, Mountain View, CA) with a photomultiplier Model H1161 (Hamamatsu Photonics, Hamamatsu, Japan). A pulse radiation was made with the s-polarized 1064 nm output (intensity, 50 mJ cm^{-2}; pulse width, 10 nm; repetition rate, 10 Hz).

Results and Discussion

I. Potentiometric Response Behaviors. Potentiometric Responses and Selectivities at pH 6.0. Figure 2 shows the potential vs concentration curves for phenol (**12**) at pH 6.0, observed by PVC matrix liquid membranes 2, 3a, 4a, and 7, based on a series of lipophilic quaternary onium salts [$(C_8)_3C_1N^+\cdot Cl^-$ (**2**), $(C_{12})_3C_1N^+\cdot Cl^-$ (**3a**), $(C_6)_4N^+\cdot Cl^-$ (**4a**), $(C_4)_3C_{16}P^+\cdot Br^-$ (**7**)]. The response of the corresponding blank membrane containing no particular sensory element is also shown. Dibutyl phthalate (DBP) was used as a membrane solvent for all membranes unless noted otherwise. In contrast to a weak response by the blank membrane, all of membranes 2, 3a, 4a, and 7 showed strong anionic responses, which are similar to those reported previously by Mokrov *et al.*[8] for PVC matrix liquid membranes based on tetra(decyl)ammonium salts. These strong anionic responses are quite unexpected in terms of the conventional response mechanism for charged species, because, in an aqueous solution at pH 6.0, **12** (pK_a = 9.99)[18] occurs almost exclusively in its undissociated, neutral form. The magnitude of potentiometric response to **12** was similar for all of these membranes. The slopes of the response curves in the concentration range of 10^{-3}−10^{-2} M were −65 to −75 mV decade^{-1}. These slopes are larger than the theoretical value for a monoanion according to the Nernst equation (−58.2 mV decade^{-1} at 20 °C; Nernstian response), which is observed under alkaline conditions (*vide infra*). On the other hand, no appreciable response to **12** was observed for membrane 3a, based on $(C_4)_4N^+\cdot Cl^-$ (**5a**) with shorter alkyl chains. The lack of response can be reasonably explained by insufficient lipophilicity of **5a** to be retained in the membrane phase.

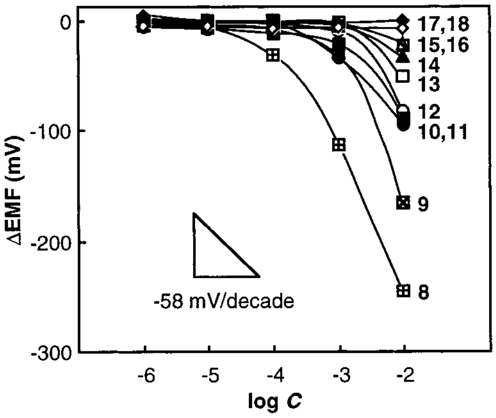

Figure 3. Potential (ΔEMF) vs concentration curves for phenols (**8**−**16**) and related compounds (**17** and **18**), obtained at pH 6.0 by membrane 2. Measured in 1.0×10^{-2} M MES-NaOH buffer (pH 6.0) at room temperature (*ca.* 20 °C).

Figure 3 shows potentiometric responses of membrane 2 to phenol and related compounds (**8**−**18**) at pH 6.0. The observed potentiometric selectivities can be summarized as follows.

(a) Phenolic vs Nonphenolic Compounds. Comparison of the potentiometric response to phenol (**12**) with that to catechol (**10**), its di-*O*-methyl derivative (**17**), and cyclohexanol (**18**) reveals that, whereas the magnitude of response was similar for the phenolic compounds **10** and **12**, no appreciable response was observed for the nonphenolic compounds **17** and **18**. These results clearly demonstrate the essential role of a phenolic OH for the responses by a membrane based on a lipophilic quaternary ammonium salt. An alcoholic OH seems to be ineffective for a potentiometric response by this membrane. This response behavior is quite similar to those observed for the same compounds by membrane 1 based on lipophilic macrocyclic pentaamine **1**.[12b,13]

(b) Substituted Phenols. All of the phenol derivatives **8**−**16**, the pK_a's of which range from 7 to 11, occur mainly or almost exclusively in their undissociated forms at pH 6.0. The strongest response was observed for **8**. On the other hand, the responses to **15** and **16** were negligible as compared with those by a blank membrane (figure not shown). Potentiometric selectivity coefficients ($K^{\mathrm{pot}}_{\mathrm{A,B}}$) for these substituted phenols ($Y\text{-}C_6H_4\text{-}OH$), determined at pH 6.0 by the matched potential method in mixed solutions, are listed in Table 1. Acid dissociation constants (pK_a)[18] and partition coefficients (1-octanol/water system; log

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Table 1. Potentiometric Selectivity Coefficients (log $K^{\mathrm{pot}}_{12,\mathrm{B}}$), Acid Dissociation Constants (pK_a), and Partition Coefficients (log P_{oct}) for a Series of Phenolic Analytes

compound (Y-C_6H_4-OH)	log $K^{\mathrm{pot}}_{12,\mathrm{B}}$ [a]	pK_a [b]	log P_{oct} [c]
8 (Y = *p*-NO_2)	1.85 (2.0)[d]	7.15	1.91
9 (Y = *p*-Cl)	1.07	9.43	2.43
10 (Y = *o*-OH)	0.65 (1.0)	9.36	0.95
11 (Y = *p*-CH_3)	0.30 (0.3)	10.26	1.93
12 (Y = H, phenol)	0 (0)	9.99	1.47
13 (Y = *p*-OCH_3)	−0.13	10.20	1.34
14 (Y = *m*-OH)	−0.27	9.44	0.79
15 (Y = *p*-NH_2)	<−0.72	10.30	0.04
16 (Y = *p*-OH)	<−1.1	9.91	0.55

[a] The potentiometric selectivity coefficients (log $K^{\mathrm{pot}}_{12,\mathrm{B}}$) were determined for membrane 2, based on $(C_8)_3C_1N^+\cdot Cl^-$ (**2**), in 1.0 × 10^{-2} M MES-NaOH buffer (pH 6.0) at room temperature (*ca.* 20 °C) by the matched potential method in mixed solutions with 1.00 × 10^{-4} M phenol as a background. [b] Acid dissociation constants (pK_a) at 25 °C, taken from ref 18. [c] Partition coefficients (1-octanol/water system; log P_{oct}) at room temperature, taken from ref 19. [d] The values in the parentheses are those reported by Mokrov *et al.*[8] for a PVC matrix liquid membrane based on a tetra(decyl)ammonium salt. Matched potential method in mixed solutions (unbuffered).

P_{oct})[19] are also listed. The magnitude of the potentiometric response by membrane 2 was in the order of **8** (Y = *p*-NO_2) > **9** (Y = *p*-Cl) > **10** (Y = *o*-OH) > **11** (Y = *p*-CH_3) > **12** (Y = H) > **13** (Y = *p*-OCH_3) > **14** (Y = *m*-OH) > **15** (Y = *p*-NH_2), **16** (Y = *p*-OH). This selectivity seems to reflect both acidity (pK_a) and lipophilicity (log P_{oct}) of each phenolic compound. The general trend is that a phenol derivative with a stronger acidity and higher lipophilicity induces a stronger anionic response. The effect of acidity is indicated by the response order **8** ≫ **11** as well as **12** ≥ **13**, whereas the effect of lipophilicity is manifested by the response order **9** ≫ **10** > **14** as well as **11** > **13**. A similar potentiometric selectivity (**8** > **9** > **11** > **12**) was also reported by Mokrov *et al.*[8] (Table 1).

Effect of pH on the Potentiometric Responses to Phenol and *p*-Nitrophenol. The effect of pH on the potentiometric responses was examined for two representative phenols, *p*-nitrophenol and phenol, and comparisons were made for (a) the responses to the monoanionic (dissociated) and neutral (undissociated) forms at the pH's above and below the pK_a, respectively, and (b) the responses to the neutral form at different pH's below the pK_a.

(a) Comparison of the Responses to Monoanionic and Neutral Phenols. Figure 4a−c shows the potentiometric responses of membranes 2, 3a, and 7, respectively, to *p*-nitrophenol (**8**) at pH 6.0 and 10.0. In the aqueous solution bulk, **8** (pK_a = 7.15)[18] occurs mostly (*ca.* 90 %) as its undissociated form at pH 6.0 and almost exclusively as its dissociated form at pH 10.0. At pH 10.0, linear responses with a slope close to the theoretical value for a monoanion (−58.2 mV decade^{-1} at 20 °C) were observed, indicating that the potentiometric responses at pH 10.0 mainly reflect the responses to the dissociated form of **8**.

The response behavior of these membranes at pH 6.0 was quite different from that at pH 10.0. Although the direction of the responses was the same (anionic responses) at both pH's, the slope at pH 6.0 was in all cases much greater than the theoretical value for a monoanion observed for the dissociated form of **8** at pH 10.0 (*vide supra*). In the linear-response range (10^{-4}−10^{-2} M), the slopes were *ca.* −85, −200, and −100 mV decade^{-1} for membranes 2, 3a, and 7, respectively. Although these responses may partly be due to the monoanionic form of **8**, which occurs by *ca.* 10% at pH 6.0, the exceedingly greater response slopes cannot be explained unless "potentiometric responses" involving undissociated, neutral species are considered.

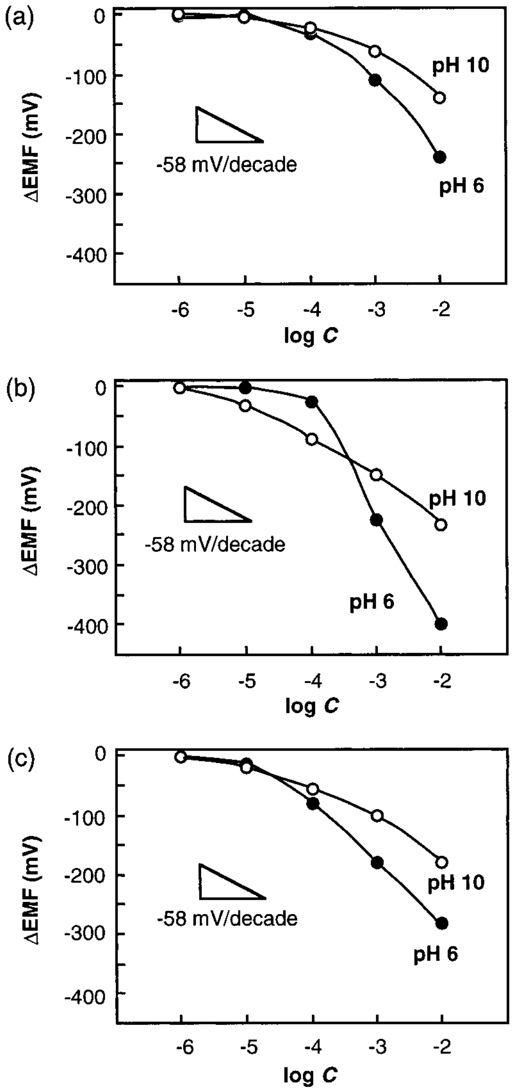

Figure 4. Potential (ΔEMF) vs concentration curves for *p*-nitrophenol (**8**), obtained at pH 6.0 and 10.0 by (a) membrane 2, (b) membrane 3a, and (c) membrane 7. Measured in 1.0 × 10^{-2} M MES-NaOH buffer (pH 6.0) or 1.0 × 10^{-2} M boric acid−NaOH buffer (pH 10.0) at room temperature (*ca.* 20 °C).

Figure 5a−c shows the potentiometric responses of membranes 2, 3a, and 7, respectively, to phenol (**12**) at pH 8.0, 9.0, 10.0, and 12.0. All of these pH's can be covered by a single combination of acid and base components, *i.e.*, boric acid−NaOH (1.0 × 10^{-2} M). In aqueous solutions of pH 8.0, 9.0, 10.0, and 12.0, *ca.* 99, 90, 50, and 1% of **12** (pK_a = 9.99)[18] occurs as its undissociated form. Here again, strong anionic responses were observed under the pH's at which undissociated **12** occurs at a substantial concentration (pH 8.0, 9.0, and 10.0). Strong responses (−100 to 210 mV decade^{-1}) were observed in the concentration range of 10^{-3}−10^{-2} M. The responses at pH 12.0 were much weaker than those at the more acidic pH's. For membrane 3a, a typical Nernstian response was observed (−58 mV decade^{-1} from 1.00 × 10^{-3} to 1.00 × 10^{-2} M; Figure 5b). These results indicate, again, major contribution of the neutral form to the anionic potentiometric responses below pH 10.[20]

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(19) Leo, A.; Hansch, C.; Elkins, D. *Chem. Rev.* **1971**, *71*, 525−616.

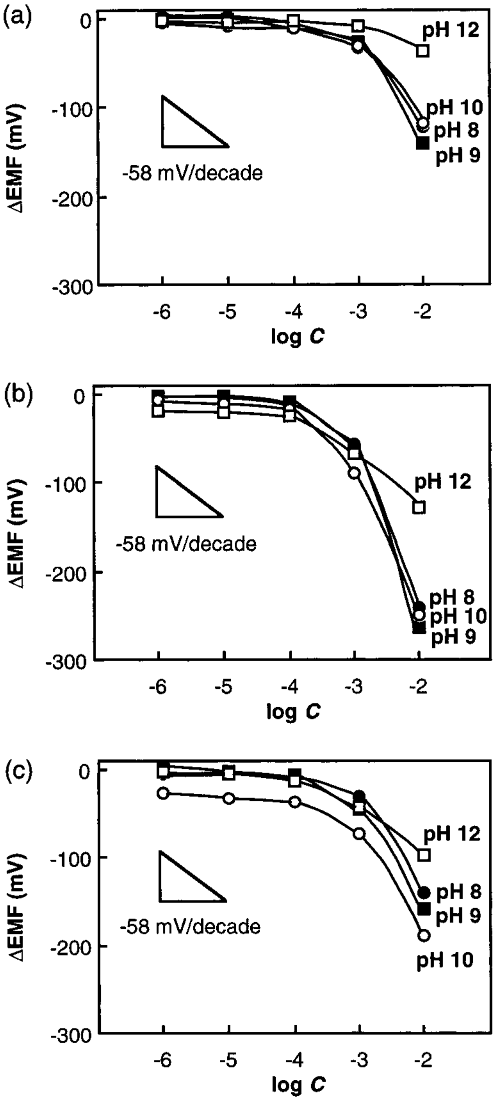

Figure 5. Potential (ΔEMF) vs concentration curves for phenol (**12**), obtained at pH 8.0, 9.0, 10.0, and 12.0 by (a) membrane 2, (b) membrane 3a, and (c) membrane 7. Measured in 1.0 × 10^{-2} M boric acid−NaOH buffer (pH 8.0, 9.0, and 10.0) or 1.0 × 10^{-2} M borate solution of pH 12.0 (adjusted with NaOH) at room temperature (*ca.* 20 °C).

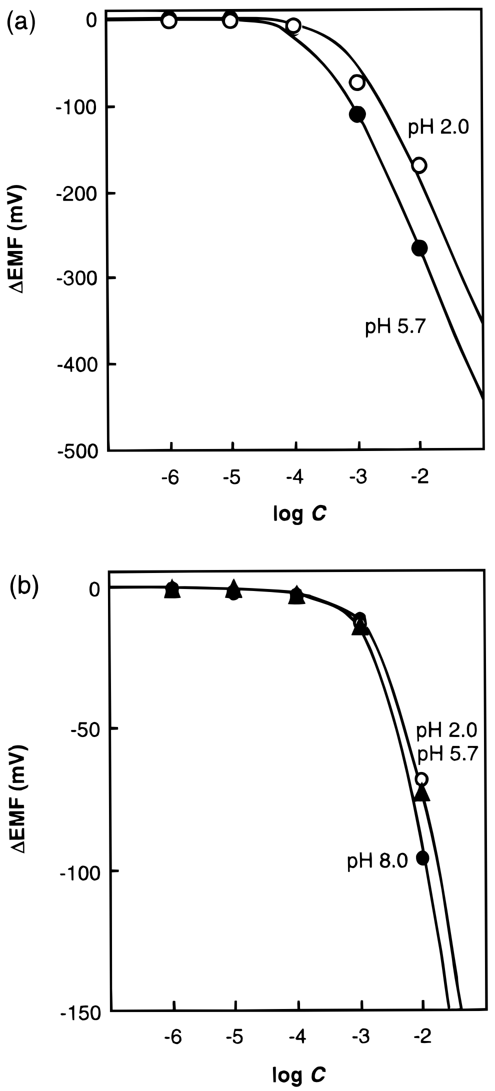

Figure 6. Potential vs concentration curves obtained by membrane 3a at room temperature (*ca.* 20 °C) under a constant concentration of Cl^- ion. (a) Curves for *p*-nitrophenol (**8**), obtained at pH 2.0 (○) and 5.7 (●). Measured in 1.00 × 10^{-2} M HCl (pH 2.0, unbuffered) or 1.00 × 10^{-2} M NaCl (pH 5.7, unbuffered). (b) Curves for phenol (**12**), obtained at pH 2.0 (▲), 5.7 (○) and 8.0 (●). Measured in 1.00 × 10^{-2} M HCl (pH 2.0, unbuffered), 1.00 × 10^{-2} M HCl−NaCl (pH 5.7, unbuffered), or 1.00 × 10^{-2} M Tris-HCl buffer (pH 8.0). The ordinate indicates relative potential (ΔEMF). Solid lines show theoretical curves (see the Appendix for calculation).

(b) Comparison of the Responses to Neutral Phenols at Different pH's. The effect of pH on the potentiometric responses to the neutral form of phenols was examined under a constant concentration of Cl^- ion. Under such a condition, the hydrophilic anionic component involved in the charge separation across the membrane interface can be essentially fixed to the Cl^- ion. The effect of pH can then be unambiguously evaluated without being affected by involvement of different anions in charge separation at different pH's.[21a]

Figure 6 (parts a and b) shows the potentiometric responses to **8** and **12**, respectively, under the pH conditions in which the phenols exist predominantly or almost exclusively in their neutral form. When the responses at two pH's that are relatively near the pK_a of the phenol are compared, a greater anionic response was observed at the higher pH (pH 2.0 vs 5.7 for **8** and pH 5.7 vs 8.0 for **12**). On the other hand, when the responses at two pH's that are relatively far from the pK_a of the phenol are compared, no appreciable pH effect was observed (pH 2.0 vs 5.7 for **12**). It is thus clearly shown that, only in the pH region near the pK_a of the phenol, the anionic response to a neutral phenol is facilitated by a decrease in the concentra-

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(20) Recently, potential changes induced by a series of catecholic compounds were reported for a platinum disk electrode coated with a polymerized binaphthyl-20-crown-6 (Ma, Y.; Galal, A.; Lunsford, S. K.; Zimmer, H.; Mark, H. B., Jr. *Biosens. Bioelectron.* **1995**, *10*, 705−715). In this case, anionic responses were observed at pH 9.4, at which the anionic and neutral forms of catecholic compounds coexist in the aqueous solution bulk. However, the response mechanism of this membrane may be quite different from that of the quaternary ammonium salt-based liquid membranes examined in the present study. The former showed much higher sensitivities but non-Nernstian responses with concentration-dependent potential changes at low concentrations (10^{-7}−10^{-5} M) and saturation at higher concentrations (>10^{-4} M).

(21) (a) Actually, the magnitude of negative potentiometric response varied with the buffer used. Thus, the ΔEMF value of −220 mV (from Figure 5b), observed for 1.00 × 10^{-2} M **12** in 1.0 × 10^{-2} M borate buffer, was much greater than the corresponding ΔEMF value of −85 mV (from Figure 2), observed in 1.0 × 10^{-2} M MES buffer. (b) Seemingly very small pH effect observed in Figures 4 and 5 does not contradict the pH dependence demonstrated by Figure 6 (parts a and b), because, in the former cases, the contribution of each anion to the charge separation could be different at different pH's.

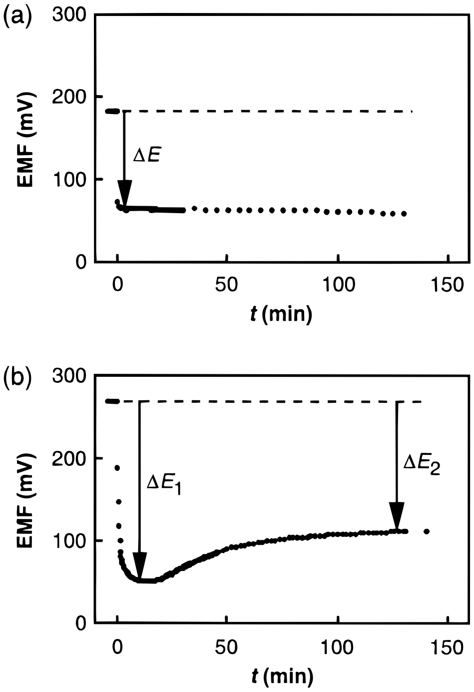

Figure 7. Time course of the potential (EMF) of membrane 3a in the presence of 1.00×10^{-2} M phenol (**12**) in 1.0×10^{-2} M borate buffer of (a) pH 12.0 and (b) pH 8.0. At $t = 0$, a conditioning buffer solution was changed to a 1.00×10^{-2} M solution of **12** with the corresponding pH. ΔE_1 and ΔE_2 in Figure 7b denote the difference in the starting potential and the initial or final stabilization potential, respectively.

tion of H$^+$ in the aqueous phase.[21b] Theoretical curves (solid lines in Figure 6 (parts a and b)), derived on the basis of a new response model, will be described later.

Time Profiles of Potentiometric Responses to Phenol. The potentiometric responses to **12** at pH 12.0 and 8.0 were monitored over an extended time period to compare the time profiles for the monoanionic and neutral forms of **12**. Figure 7 shows the potential vs time profiles of membrane 3a for 1.00×10^{-2} M **12**, monitored at room temperature (*ca.* 20 °C) at pH 12.0 and 8.0 (1.0×10^{-2} M boric acid−NaOH buffer). At pH 12.0, a rapid anionic response started and stabilized immediately (<2 min) with $\Delta E \approx -120$ mV (Figure 7a), showing a typical response behavior for charged species. In contrast, at pH 8.0, a relatively slow anionic response started, which temporarily stabilized after *ca.* 5−10 min with $\Delta E_1 \approx -220$ mV (Figure 7b). Additional difference between the response behaviors at pH 12.0 and 8.0 is that the latter involved, after the initial stabilization, a gradual increase in the potential for several hours,[22] which leveled off at $\Delta E_2 \approx -145$ mV and remained unchanged for more than 2 days (Figure 7b). In contrast, at pH 12.0, the potential did not change after the initial stabilization (Figure 7a). Potential drift as in Figure 7b was observed at neutral pH for a number of other phenolic compounds tested.

The above results show that the response behavior of a membrane based on a quaternary ammonium salt for an undissociated phenol at pH 8.0 is characteristic in (i) greater response magnitude, (ii) longer response time, and (iii) gradual potential drift (increase).

Table 2. Stability Constants (K_s) in Benzene for the 1:1 Complexes of *p*-Nitrophenol (**8**) and a Series of Quaternary Ammonium Salts (Q$^+$X$^-$), Together with Ionic Radii of X$^-$

Q$^+$X$^-$	$K_s{}^a$ (M^{-1})	$r^*{}_x{}^b$ (Å)
$(C_4)_4N^+ \cdot Cl^-$ (**5a**)	1.9×10^5	1.80
$(C_4)_4N^+ \cdot Br^-$ (**5b**)	5.2×10^4	1.95
$(C_4)_4N^+ \cdot NO_3^-$ (**5c**)	2.0×10^4	2.03
$(C_4)_4N^+ \cdot SCN^-$ (**5d**)	1.5×10^4	2.08
$(C_4)_4N^+ \cdot ClO_4^-$ (**5e**)	NC^d	2.28
$(C_{12})_4N^+ \cdot Br^-$ (**6a**)	5.7×10^4	1.95
$(C_{12})_4N^+ \cdot$T*p*ClPB$^-$ (**6b**)^c	NC^d	
$(C_{12})_3C_1N^+ \cdot Cl^-$ (**3a**)	1.3×10^5	1.80
$(C_6)_4N^+ \cdot Cl^-$ (**4a**)	2.1×10^5	1.80
$(C_5)_4N^+ \cdot Cl^-$ (**4b**)	2.1×10^5	1.80
$(C_4)_4N^+ \cdot Cl^-$ (**5a**)	1.9×10^5	1.80

^{a} Stability constants (K_s) of the 1:1 complexes of *p*-nitrophenol (**8**) and quaternary ammonium salts (Q$^+$X$^-$), determined by UV titration in benzene at room temperature (*ca.* 20 °C). Taken from ref 14. ^{b} Ionic radius of X$^-$,[24a] calculated from the molal volume of ion from the partial volume at infinite dilution.[24b] ^{c} T*p*ClPB = tetrakis(*p*-chlorophenyl)borate. ^{d} Negligible complexation.

II. Interactions between Phenols and Quaternary Ammonium Salts in Homogenous Solutions and in Two Phase Systems. Efforts were made to understand the interactions of phenols and quaternary ammonium salts in homogeneous solutions by complexation studies and in two phase systems by solvent extraction experiments.

Interactions in Homogeneous Solutions. The stability constants (K_s) for the 1:1 complexes of undissociated phenols (ArOH) with different acidity and quaternary ammonium salts (Q$^+$X$^-$) with different cation (Q$^+$) and anion (X$^-$) components have been determined in benzene.[14] As indicated from the K_s values in benzene for the 1:1 complexes of **8** and a series of Q$^+$X$^-$ with different Q$^+$ or X$^-$ components (Table 2), the stability of the complex was greatly affected by X$^-$ (markedly different K_s values for **5a**−**e** and **6a**,**b**) but not by Q$^+$ (similar K_s values for **3a**, **4a**, **4b**, and **5a**). These results confirmed the interaction between an *undissociated* phenolic OH and the *anionic* component X$^-$ of Q$^+$X$^-$ to be essential for the complexation of Q$^+$X$^-$ and ArOH, as demonstrated previously by other groups on the basis of IR[23a−d] and NMR[23a,b,e] studies.

Table 3 lists the K_s values of the 1:1 complexes of **3a** and phenols (**8**, **11**, **13**) or related nonphenolic compounds (**17** and **18**), together with the pK_a and log P_{oct} values for the latters. The potentiometric selectivity coefficients ($K^{pot}_{A,B}$) for the responses by membrane 2, based on a related quaternary ammonium salt **2**, are also listed. Table 3 indicates that both acidity (pK_a) and lipophilicity (log P_{oct}) of ArOH are reflected to the stability of the complex Q$^+$X$^-\cdot$ArOH (K_s)[14] and that these parameters also reflect to the magnitude of potentiometric response ($K^{pot}_{A,B}$). Consistent with this relationship is the fact that the compounds with no phenolic OH group, the complexation of which with **3a** is very weak (**18**; $K_s = 74$ M^{-1} in benzene) or negligible (**17**)[14] showed very weak or negligible potentiometric response.

With regard to the anionic component X$^-$, the stability of the complex Q$^+$X$^-\cdot$ArOH was in the order of Cl$^-$ > Br$^-$ > NO$_3^-$ ≥ SCN$^-$ ≫ ClO$_4^-$, T*p*ClPB$^-$ (no interaction).[14] This

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[22] The gradual potential drift observed in Figure 7b is most likely due to the diffusion of the extracted ArOH to the interface of the membrane and the inner filling solution and the resulting changes in the overall membrane potential to the more positive direction. This view is supported by the fact that the response time of membrane 3a with 200 μm thickness was shorter than that of the corresponding membrane with 400 μm thickness (*ca.* 4 and 10 min, respectively, under a 1.00×10^{-2} M concentration of **12**). Similar discussions have also been given by Meyerhoff *et al.*[7f]

[23] (a) Relles, H. M. *J. Org. Chem.* **1970**, *35*, 4280−4282. (b) Taylor, R. P.; Kuntz, I. D., Jr. *J. Phys. Chem.* **1970**, *74*, 4573−4577. (c) Bacelon, P.; Corset, J.; De Loze, C. *Chem. Phys. Lett.* **1975**, *32*, 458−461. (d) Rulinda, J. B.; Zeegers-Huyskens, T. *Spectroscopy Lett.* **1979**, *12*, 33−43. (e) Bunton, C. A.; Cowell, C. P. *J. Colloid Interface Sci.* **1988**, *122*, 154−161.

Table 3. Complexation Constants (K_s), Acid Dissociation Constants (pK_a), Partition Coefficients (log P_{oct}), and Potentiometric Selectivity Coefficients (log $K^{pot}_{12,B}$) for Phenols and Related Compounds

ArOH	K_s[a] (M^{-1})	pK_a[b]	log P_{oct}[c]	log $K^{pot}_{12,B}$[d]
p-nitrophenol (**8**)	1.3 × 10^5	7.15	1.91	1.85
p-cresol (**11**)	1.5 × 10^4	10.26	1.93	0.30
p-methoxyphenol (**13**)	7.9 × 10^3	10.20	1.34	-0.13
cyclohexanol (**18**)	7.4 × 10^1	~16	1.23	negligible
1,2-dimethoxybenzene (**17**)	NC			negligible

[a] The stability constants of the 1:1 complexes with $(C_{12})_3C_1N^+{\cdot}Cl^-$ (**3a**) were determined at room temperature (*ca.* 25 °C) by either UV (**8**; *ca.* 20 °C), ^{1}H-NMR (**11**, **13**; *ca.* 25 °C), or ^{13}C-NMR (**18**; *ca.* 25 °C). Taken from ref 14. [b] Acid dissociation constant (pK_a) at 25 °C, taken from ref 18. [c] Partition coefficients for 1-octanol/water system (log P_{oct}) at room temperature, taken from ref 19. [d] The potentiometric selectivity coefficients (log $K^{pot}_{12,B}$) for membrane 2 based on $(C_8)_3C_1N^+{\cdot}Cl^-$ (**2**). Taken from Table 1.

Table 4. Effect of the Counteranions of Tridodecylmethylammonium Salts on the Potentiometric Responses to Phenol (**12**) at pH 8.0[a,b]

membrane [$(C_{12})_3C_1N^+{\cdot}X^-$]	ΔE_1 (mV)	ΔE_2 (mV)
3a [$(C_{12})_3C_1N^+{\cdot}Cl^-$ (**3a**)]	−244.0	−170.6
3b [$(C_{12})_3C_1N^+{\cdot}SCN^-$ (**3b**)]	−89.6	−49.2
3c [$(C_{12})_3C_1N^+{\cdot}Pic^-$ (**3c**)]	−74.9	−20.7
3d [$(C_{12})_3C_1N^+{\cdot}TPB^-$ (**3d**)]	~0	~0

[a] For each membrane, a conditioning buffer solution was changed to a 1.00 × 10^{-2} M solution of phenol (**12**), and the ΔE_1 and ΔE_2 values were measured. ΔE_1 = (initial stabilization potential) − (starting potential). ΔE_2 = (final stabilization potential) − (starting potential). Measured in 1.0 × 10^{-2} M boric acid−NaOH buffer (pH 8.0) at room temperature (*ca.* 20 °C). [b] The ΔE_1 and ΔE_2 values were measured for two (**3a**, **3d**) or three (**3b**, **3c**) different preparations of membrane.

order is parallel to that of the charge-dipole and/or hydrogen bonding interactions between X^- and ArOH as expected from the ionic radius of X^- calculated[24a] from its molal volume[24b] (r^*_x; see Table 2). This complexation tendency is also reflected to the order of the magnitude of potentiometric response to **12** by liquid membranes based on **3a**−**d**. As shown in Table 4, the order of the response was membrane 3a ($X^- = Cl^-$) > 3b ($X^- = SCN^-$) > 3c (X^- = picrate$^-$) > 3d ($X^- = BPh_4^-$; no response). These results suggest, again, that the hydrogen bonding through the phenolic OH group is reflected not only to the complexation between Q^+X^- and ArOH in a homogeneous solution but also for a potentiometric response, which involves chemical processes occurring at a membrane/aqueous solution interface.

Interactions in Two Phase Systems. To further examine the outcome of the complexation of neutral phenols (ArOH) and quaternary ammonium salts (Q^+X^-), extraction experiments in two phase systems were carried out with aqueous solutions containing ArOH and organic solutions containing Q^+Cl^-.

Upon vigorous shaking of a 1.00 × 10^{-2} M solution of **8** in water (preadjusted to pH 4.0) and a 1 wt % solution of **2** in DBP or benzene, extraction of **8** to the organic phase occurred and, in addition, a decrease in the pH of the aqueous phase was observed.[25] The extractability of **8**, calculated from the concentrations of its undissociated form in the aqueous solution before and after extraction, increased from 61 to 98% (benzene) or from 99 to 100% (DBP), respectively, by addition of **2** in the organic phase. Furthermore, the pH of the aqueous phase was significantly lower when shaken with an organic solution containing **2** [pH 3.63 (benzene) or 3.73 (DBP)] than after shaking with the corresponding solvents without **2** [pH 4.17 (benzene) or 4.19 (DBP)]. Enhanced extraction by addition of **2** was also observed for phenolic compounds **10** and **16** (82 → 93% and 52 → 70%, respectively, for benzene) with somewhat smaller net decrease in the aqueous pH [pH 4.04 vs 4.19 (**10**) and 4.08 vs 4.20 (**16**), respectively, for benzene containing or without **2**]. In the absence of **2** in the organic phase or a phenolic compound in the aqueous phase, no change in pH was observed.

That the enhanced extraction accompanies dissociation of ArOH was confirmed by the UV−visible spectra of **8** extracted into benzene and, in addition, the change in the concentration of Cl^- ion in the aqueous phase. The extraction experiments were made with a 1.05 × 10^{-4} M solution of **3a** in benzene against a 1.17 × 10^{-4} M solution of **8** in water (preadjusted to pH 4.0). In the UV−visible spectra of the organic phase, the dissociated form of **8** (λ_{max} = 385 nm)[26] was observed in addition to the undissociated/complexed form (λ_{max} = 320 nm). The ratio of the dissociated and undissociated forms of **8** in the organic phase was estimated to be *ca.* 20:80 on the basis of the concentration of dissociated **8** in the organic phase and the extractability of **8** (see the Experimental Section). In contrast, the same treatment with benzene containing no quaternary ammonium salt lead to the corresponding spectrum showing only the undissociated/uncomplexed form of **8** at λ_{max} = 300 nm. With regard to the change in the concentration of Cl^- in the aqueous phase, the net increase in the concentration of Cl^- upon extraction of **8** with a solution of **3a** in benzene was (1.26 ± 0.95) × 10^{-5} M, as estimated by ion chromatography. This value is in the same order of magnitude as the concentration of dissociated **8** in the organic phase [(1.83 ± 0.46) × 10^{-5} M], as determined from the UV absorbance in the organic phase.

As a consequence, it is indicated that, in the enhanced extraction of ArOH by Q^+X^-, the formation of lipophilic ion pair Q^+ArO^- with concomitant ejection of HX into the aqueous phase is partly involved in addition to the simple extraction and complexation processes, whereas only the complexation process is involved in homogeneous organic solutions. It should be pointed out that the former process results in the formation of a stronger acid (HX) in an acid-base equilibrium.[27] The driving force for this otherwise unfavorable process is dissolution of HX, but not Q^+ArO^-, to the aqueous phase. It is therefore reasonable to assume that the proton dissociation of the complexed ArOH occurs at the membrane boundary region close to the aqueous phase.

III. A Model for the Anionic Potentiometric Responses to Neutral Phenols. Although anionic potentiometric responses are generated in this case by undissociated, neutral phenols, *i.e.*, uncharged species, a rational mechanistic interpretation must be based on a decrease in the amount of the species which is

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(24) (a) Sawada, K.; Sohara, T.; Kikuchi, Y. *J. Chem. Soc., Faraday Trans.* **1995**, *91*, 643−647. (b) Millero, F. J. *Chem. Rev.* **1971**, *71*, 147−176.

(25) Enhanced extraction of **12** in an aqueous solution (pH 4−5) by a solution of **2** in benzene or cyclohexane has been previously reported (Inoue, K.; Shishido, H. *Solvent Ext. Ion Exch.* **1986**, *4*, 199−216). However, no description is found for the change in the pH of the aqueous phase.

(26) The band at 385 nm can be assigned as the dissociated form of **8** in benzene containing a small amount of water, because the absorption maximum of 414 nm observed for a solution of **3e** in benzene shifted to 391 nm by shaking the benzene solution with an aqueous solution of H_2SO_4 (pH 4.0).

(27) Formation of a stronger acid by dissociation of a phenolic compound in acid−base equilibrium also occurs in a cationic micellar system[27a,b] and in a homogeneous solution under a strongly cationic environment generated by a multiply protonated macrocyclic polyamine.[27c] (a) Kohara, H. *Japan Analyst* **1968**, *17*, 1147−1148. (b) Mukerjee, P.; Banerjee, K. *J. Phys. Chem.* **1964**, *68*, 3567−3574. (c) Kimura, E.; Sakonaka, A.; Kodama, M. *J. Am. Chem. Soc.* **1982**, *104*, 4984−4985.

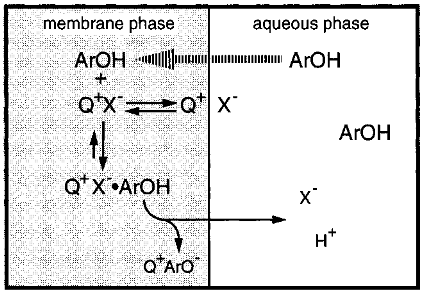

Figure 8. Schematic representation of a model for anionic potentiometric responses to undissociated phenols (ArOH) at acidic to neutral pH, displayed by liquid membranes based on quaternary ammonium salts (Q^+X^-) as the sensory elements. In this model, only X^- is involved as the anionic component in the charge separation across the membrane interface and hence in the membrane potential.

charge-separated across the membrane/aqueous solution interface. The experimental results showing the formation of 1:1 complex $Q^+X^-{\cdot}ArOH$[14] and proton dissociation of the complexed ArOH with concomitant ejection of acid HX into the aqueous phase (section II) afford a new model that can be described by considering eqs 1−3 as fundamental chemical processes (Figure 8; see the Supporting Information for the details).

$$\mathrm{ArOH(aq)} \rightleftharpoons \mathrm{ArOH(mem)} \qquad (1)$$

(extraction)

$$\mathrm{Q^+X^-(mem)} + \mathrm{ArOH(mem)} \rightleftharpoons \mathrm{Q^+X^-{\cdot}ArOH(mem)} \qquad (2)$$

(complexation)

$$\mathrm{Q^+X^-{\cdot}ArOH(mem)} \rightleftharpoons \mathrm{Q^+ArO^-(mem)} + \mathrm{HX(mem)}$$

$$\mathrm{HX(mem)} \rightleftharpoons \mathrm{HX(aq)} \qquad (3)$$

(proton dissociation and acid ejection)

In addition, the following equilibrium exists between the Q^+X^- that is charge-separated at the membrane interface and the Q^+X^- that is randomly oriented in the membrane bulk.

$$\mathrm{Q^+X^-(interface)} \rightleftharpoons \mathrm{Q^+X^-(mem)} \qquad (4)$$

This model explains the anionic responses to *neutral* phenols on the basis of a decrease in the amount of the cationic and anionic species that are charge-separated across the membrane interface. The decrease in the charge separation is caused by a shift of the equilibrium in eq 4 to the right, which may occur as (i) a direct result of complexation of Q^+X^- and the extracted ArOH (eq 2) and (ii) an indirect result *via* process (i) arising from proton dissociation of the complexed ArOH with concomitant ejection of the acid HX into the aqueous phase (eq 3). In terms of the movement of charge-separated species at the membrane interface into the bulk of either membrane or aqueous solution, the equilibrium shift by process (i) leads to a movement of the cationic species Q^+ (membrane side) and the anionic species X^- (aqueous side) into the membrane phase. This net movement of *anionic* species from the aqueous to the membrane phase results in a decrease in the charge separation of Q^+ and X^- across the membrane interface and hence leads to an anionic potentiometric response to ArOH. On the other hand, the equilibrium shift by process (ii) involves a movement of the charge-separated Q^+ and X^- into the membrane phase with concomitant ejection of H^+ (dissociated from extracted and complexed ArOH) and X^- into the aqueous solution bulk. Therefore, in this case, the anionic potentiometric response to ArOH is a result of a net movement of *cationic* species H^+ from the membrane to the aqueous phase.

Although complexation, proton dissociation, and HX ejection could occur *via* a direct interfacial process without involvement of extraction of ArOH (eq 1), the time profile of the response, showing a longer response time and a gradual drift,[22] suggests a process involving extraction of ArOH rather than a direct interfacial process. Whereas process (i) involving complexation of the extracted ArOH has also been mentioned by Mokrov *et al.*,[8] process (ii) involving proton dissociation of the complexed ArOH and concomitant ejection of HX into the aqueous phase affords a new mechanism for potentiometric responses to neutral phenols.

The experimental evidence that gives most straightforward support to the above response mechanism is the pH dependence that is unambiguously evaluated by the experiments with a constant concentration of Cl^- ion. When the responses at the two pH's that are relatively *near* the pK_a of the phenol are compared, a greater anionic response was observed at the higher pH [pH 2.0 vs 5.7 for **8** (pK_a = 7.15) in Figure 6a and pH 5.0 vs 8.0 for **12** (pK_a = 9.99) in Figure 6b]. This tendency can be reasonably explained by assuming that, at such pH regions, the involvement of process (ii), which will be facilitated with increasing pH, is significant. On the other hand, the lack of such a pH effect in the pH region *far* from the pK_a (pH 2.0 vs 5.0 for **12** in Figure 6b) can be explained by assuming significant involvement of process (i).

In the theoretical treatment of the model based on processes (i) and (ii), one should consider that the X^- existing as the counteranion of Q^+ or M^+ and the ArO^- generated by proton dissociation in process (ii) may both contribute to charge separation across the membrane interface. Therefore, three cases, in which (a) only X^- (Figure 8), (b) only ArO^-, and (c) both X^- and ArO^- contribute as the anionic component(s) in the charge separation, were assumed. For each case, theoretical curves were derived for the potentiometric responses to *p*-nitrophenol (**8**) and phenol (**12**) at a constant concentration of Cl^- ion (Figure 6 (parts a and b); $[Cl^-] = 1.00 \times 10^{-2}$ M).[28] The details of the theoretical treatment are described in the Supporting Information.

The solid lines in Figure 6 (parts a and b) show, respectively, the theoretical curves for **8** and **12**, derived under the assumption that only X^- is involved as the anionic component in the charge separation across the membrane interface (Figure 8). Comparison of these theoretical curves with the observed ones shows that the large slopes,[29] detection limits, and the pH dependence all can be reproduced under the above assumption. In contrast, the observed response curves could not be reproduced under the assumption that only ArO^- [case (b)] or both X^- and ArO^- [case (c)] are involved as the anionic component(s) in the charge separation (figure not shown). These results suggest that, as

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(28) With regard to a general concern to a competitive response behavior of quaternary ammonium salt-based liquid membranes toward phenol and Cl^- ion, potentiometric responses to phenol were measured under different concentrations of Cl^- ion. The anionic response to 1.00×10^{-2} M phenol was stronger under 1.0×10^{-4} M Cl^- in Tris-HCl buffer of pH 8.0 (EMF = +250 → +60 mV; ΔEMF = −190 mV) than 1.0×10^{-2} M Cl^- in Tris-HCl buffer of pH 8.0 (EMF = +132 → +22 mV; ΔEMF = −110 mV). The greater EMF value in the absence of phenol and the greater response (−ΔEMF) to phenol under the lower concentration of Cl^- ion clearly indicate competitive anionic responses to phenol and Cl^- ion.

(29) Based on a different model focused on kinetic processes, Meyerhoff *et al.* also explained the super-Nernstian anionic response to polyanion heparin by a PVC matrix liquid membrane based on quaternary ammonium salt **3a** (Fu, B.; Bakker, E.; Yang, J. H.; Meyerhoff, M. E. *Anal. Chem.* **1994**, *66*, 2250−2259).

the anionic component, the contribution of ArO^- to the charge separation and hence to the membrane potential is negligible as compared to that of X^-.

Experimental Support to the Response Model by Measurement of Optical Second Harmonic Generation (SHG). To obtain an experimental support to the above potentiometric response model, direct and specific observation of the membrane/aqueous solution interface was carried out by a measurement of optical SHG for a two phase system of an aqueous solution of **8** and a membrane based on **3a** (membrane 3a-DOS). Analyte **8** with a nitro group at the para position generates, upon orientating at the membrane interface, a strong SHG intensity due to its large second order nonlinear polarizability.

Figure 9a,b shows typical examples of the intensity (square root) vs concentration curves at pH 10.0 and 6.0, respectively, for membrane 3a-DOS and the corresponding blank membrane. The square root of the observed SHG intensity (ordinate of Figure 9) is theoretically proportional to the number, average orientation, and second order nonlinear electric polarizability of oriented species at the membrane surface.[30] At pH 10.0, concentration-dependent increase in the SHG intensity was observed above *ca.* 10^{-3} M **8** for membrane 3a-DOS (Figure 9a, curve A1). In contrast, no appreciable change was observed for the corresponding blank membrane (curve A2). These results indicate that curve A1 reflects a concentration-dependent increase in the enforced orientation of **8** at the membrane interface. Since **8** exists almost exclusively in its dissociated form at pH 10.0, the SHG-active species generated is most probably the dissociated form of **8** (ArO^-) that is involved in the charge separation across the membrane interface.[6g]

Figure 9b shows the intensity (square root) vs concentration curves at pH 6.0 for membrane 3a-DOS and the corresponding blank membrane. In this case, a distinct concentration-dependent *decrease* in the SHG intensity was observed for membrane 3a-DOS (curve B1) in contrast to the concentration-dependent increase at pH 10.0 (curve A1).[31,32] In addition, curve B1 agrees well with the relevant potential vs concentration curves (Figures 3 and 4); both SHG intensity and potential curves show a distinct decline at the concentration of 10^{-5}–10^{-4} M. The response by the blank membrane was negligible (curve B2) as in the case of pH 10.0.

The contrasting behaviors at pH 10.0 and 6.0 clearly indicate that, at the latter pH, the major SHG-active species is not the dissociated form of **8**. Since the dissociated or undissociated form of **8** is the only species capable of giving high SHG activity under the present experimental conditions, it is reasonable to consider that the undissociated form of **8** is the major SHG-active species at pH 6.0. Then, the concentration-dependent decrease in the SHG intensity can be ascribed to relaxation of undissociated **8** orientated at the membrane interface. For the reason of such relaxation, a concentration-dependent decrease in the charge separation of Q^+ and X^- across the membrane interface by complexation of Q^+X^- and extracted ArOH is most probable. In this sense, support for the above potentiometric response model was given from direct observation of the processes occurring at the membrane interface.

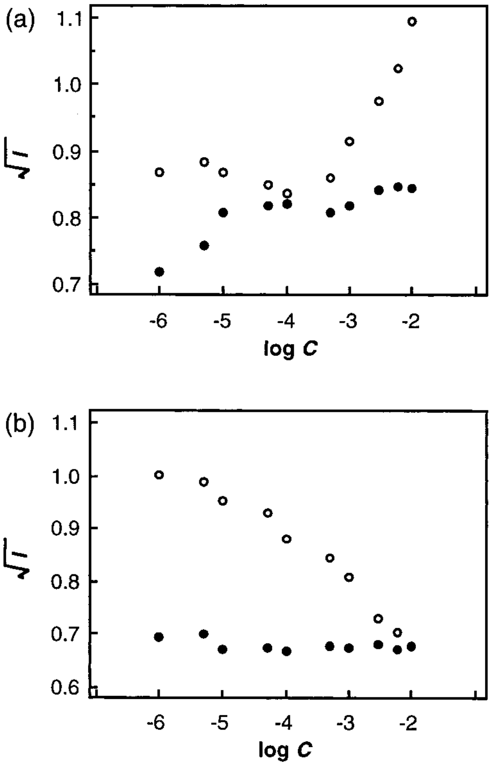

Figure 9. Intensity (square root) vs concentration curves obtained by the measurement of optical second harmonic generation (SHG) at (a) pH 10.0 and (b) pH 6.0 for a two phase system consisting of an aqueous solution of **8** in varying concentrations and membrane 3a-DOS (curves A1 and B1; ○) or the corresponding blank membrane (curves A2 and B2; ●). The ordinate indicates the square root of the observed SHG intensity. Representative curves out of two or more measurements are shown.

Conclusion

The development of "potentiometric" sensors for neutral molecules is intrinsically a puzzling problem but involves a significant question concerning how uncharged species can influence charge separation across the membrane interface and induce a potentiometric response. In the present study, systematic experimental and theoretical approaches were carried out on the anionic responses to undissociated, neutral phenols (ArOH) by PVC matrix liquid membranes based on quaternary ammonium or phosphonium salts (Q^+X^-). The experimental results on the potentiometric responses and on the complexation and extraction behaviors have led to a new potentiometric response model, which explains the ArOH-induced decrease in the membrane potential on the basis of the following two processes: (i) complexation of the extracted ArOH and Q^+X^-, leading to a net movement of anionic species (X^-) from the aqueous to the membrane phase; and (ii) proton dissociation of the complexed ArOH and concomitant ejection of HX into the aqueous phase, involving a net movement of cationic species (H^+) from the membrane to the aqueous phase. The observed response slopes, together with the detection limit and the pH dependence, could be reproduced by a theoretical treatment based on the model involving the above two processes. The present model was supported by optical second harmonic generation (SHG), which enabled direct observation of the processes occurring at the interface of a liquid membrane and an aqueous solution.

The process leading to a decrease in the membrane potential is thus quite different for the dissociated (ArO^-) and undisso-

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(30) Corn, R. M.; Higgins, D. A. *Chem. Rev.* **1994**, *94*, 107–125.

(31) The time profile of SHG, concerning with only the interface of the membrane and the sample solution, did not show a gradual increase after the initial decrease in contrast to the potential vs time curve shown in Figure 7a (see footnote 22).

(32) At the concentrations higher than 10^{-2} M, **8** is reported to show an appreciable SHG intensity at heptane/water[32a] or air/water[32a,b] interface. (a) Bell, A. J.; Frey, J. G.; VanderNoot, T. J. *J. Chem. Soc., Faraday Trans.* **1992**, *88*, 2027–2030. (b) Sarkar, N.; Das, K.; Das, S.; Nath, D.; Bhattacharyya, K. *J. Chem. Soc., Faraday Trans.* **1995**, *91*, 1769–1773.

ciated (ArOH) forms of phenols. The interpretation for the potentiometric responses to the latter neutral species cannot be made on the basis of the conventional response mechanism for charged species. The present investigations presented a new model capable of giving a reasonable interpretation for anionic potentiometric responses to undissociated, neutral phenols. The understanding of the response mechanism for neutral phenols may afford a starting point for developing a potentiometric sensing system for a variety of uncharged species.

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Supporting Information Available: The commercial sources and/or the details of preparation and purification of quaternary ammonium and phosphonium salts, phenols and related compounds, and membrane solvents and the details of theoretical treatments of the potentiometric responses to neutral phenols (9 pages, print/PDF). See any current masthead page for ordering and Web access instructions.

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