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A Variety of Lipophilic Amines Incorporated in Liquid Membranes Exhibit Potentiometric Responses to Neutral Phenols

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A variety of lipophilic amines incorporated in PVC matrix liquid membranes exhibited anionic potentiometric responses to phenolic compounds at the pH conditions under which the phenols exist mainly or exclusively in their undissociated, neutral forms. The examined lipophilic amines include a macrocyclic pentaamine, tri(decyl)amine, 4,7-diphenyl-1,10-phenanthroline (bathophenanthroline), 4-octadecylpyridine, and sapphyrin. The potentiometric selectivities of the membranes based on lipophilic aliphatic amines (B) reflected the acidity (hydrogen bond donor activity) and lipophilicity (extractability) of the phenols (ArOH), similarly as membranes based on lipophilic quaternary ammonium salts (Q^+X^-). The anionic responses were explained on the basis of a decrease in the charge separation of protonated amines (BH^+) and their counteranions (X^-) across the membrane interface. Possible processes leading to a decrease in the charge separation between BH^+ and X^- are (i) complexation between ArOH and BH^+X^-, followed by proton dissociation and ejection of HX into the aqueous phase, as well as (ii) complexation between ArOH and B. The membrane based on sapphyrin showed a high potentiometric selectivity to catechol, possibly due to geometrical discrimination of the *ortho* dihydroxy structure of catechol by the nitrogen(s) on the rigid macrocyclic structure of sapphyrin.

Keywords Liquid membrane electrode, lipophilic amine, potentiometric response, phenolic analyte,response mechanism

In a preceding paper[1] we reported on a systematic study of potentiometric responses to neutral phenols (ArOH) by poly(vinyl chloride) (PVC) matrix liquid membranes based on quaternary ammonium or phosphonium salts (Q^+X^-), and proposed a new model for the observed anionic responses. In this model, the decrease in the amount of Q^+ and X^- that are charge-separated across the membrane interface is explained on the basis of the following two processes: (i) Complexation of Q^+X^- and the extracted ArOH, leading to a net movement of anionic species (X^-) from the aqueous to the membrane phase. (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. 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 a direct observation of the processes occurring at the interface of a liquid membrane and an aqueous solution.

Based on the findings of Kimura *et al.*[2] that a macrocyclic polyamine forms complexes with neutral phenols in aqueous solutions, we previously examined potentiometric responses to phenols by a PVC matrix liquid membrane based on lipophilic macrocyclic pentaamine **1**, and found that the membrane exhibits anionic responses to undissociated, neutral phenols.[3,4] This response behavior is quite similar to that observed for PVC matrix liquid membranes based on quaternary ammonium or phosphonium salts.[1] In this paper we report on a comprehensive investigation showing that

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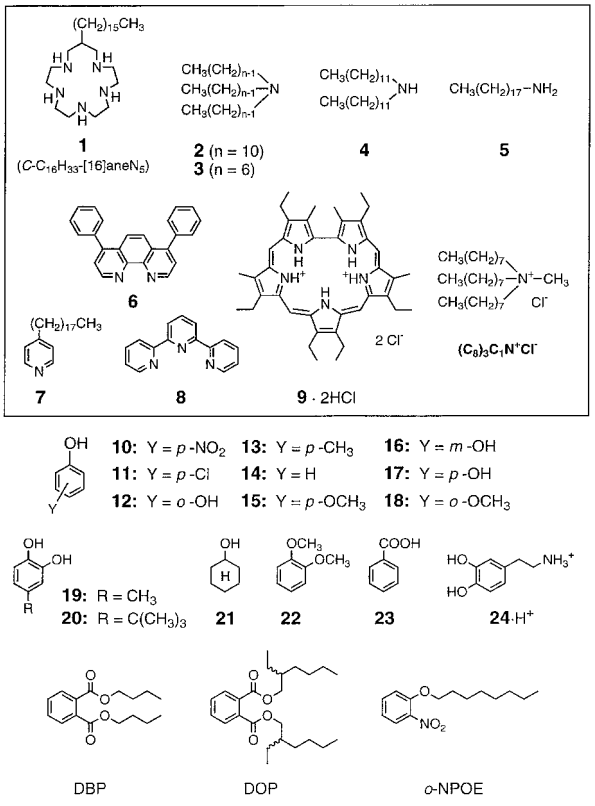

Fig. 1 Chemical structures of the compounds used in the present study. Aliphatic (**1** – **5**) and heteroaromatic (**6** – **9**) amines were used as sensory elements. Phenol and related compounds (**10** – **24**) were used as analytes. Dibutyl phthalate (DBP), bis(2-ethylhexyl) phthalate ["dioctyl phthalate" (DOP)], and *o*-nitrophenyl octyl ether (*o*-NPOE) were used as membrane solvents. The structure of methyltrioctylammonium chloride [$(C_8)_3C_1N^+Cl^-$] is also shown.

such anionic potentiometric responses to neutral phenols are observed for a wide variety of aliphatic and heteroaromatic lipophilic amines. The chemical structures of the lipophilic amines (**1** – **9**), phenol and related compounds (**10** – **24**), and membrane solvents used in the present study are shown in Fig. 1. The examined amines include macrocyclic pentaamine **1**, tri(decyl)amine (**2**), 4,7-diphenyl-1,10-phenanthroline (bathophenanthroline, **6**), 4-octadecylpyridine (**7**), and sapphyrin (**9**). The membranes based on lipophilic aliphatic amines exhibited potentiometric selectivities that reflect the acidity and lipophilicity of phenols, similarly as membranes based on a quaternary ammonium salt.[1] The membrane based on sapphyrin showed a selectivity for catechol, reflecting geometrical discrimination.

Experimental

General

^{1}H NMR spectra were measured on a JEOL JMN-A500 Fourier-transform NMR spectrometer (500 MHz). The chemical shifts are reported in δ values in ppm downfield of tetramethylsilane (TMS, 0.03%) as the internal standard. UV-visible spectra were recorded on a Shimadzu UV-240 spectrophotometer. The pH of all solutions was measured at room temperature (ca. 20 °C) using an ion meter Model COM20, IOL-30, IOL-40 or IOL-50 [Denki Kagaku Keiki (DKK), Tokyo, Japan] with a pH glass electrode (Type 6157, DKK).

Reagents

The syntheses of lipophilic macrocyclic pentaamine **1**[5] and sapphyrin (3,8,12,13,17,22-hexaethyl-2,7,18,23-tetramethylsapphyrin) dihydrochloride (**9**·2HCl)[6] have been reported. The monohydrochloride of sapphyrin was prepared from the dihydrochloride as follows. After 10 mg of **9**·2HCl was dissolved in 200 ml $CHCl_3$ the solution was shaken repeatedly with water (1 l in total). The conversion to **9**·HCl was confirmed by the UV-visible spectra based on the absorption maxima of **9**·2HCl (λ_{max} 445.5 nm) and **9**·HCl (λ_{max} 450.5 nm) in $CHCl_3$. The other lipophilic amines used were purchased: Tri(decyl)amine (**2**; Tokyo Kasei Kogyo, Tokyo, Japan) and didodecylamine (**4**; Kanto Chemical, Tokyo, Japan) were purified by recrystallization as their hydrochlorides. Trihexylamine (**3**; Wako Pure Chemical, Osaka, Japan) was purified by distillation under reduced pressure (bp_4 137 °C). Octadecanamine (**5**; Aldrich Chemical, St. Louis, USA), 4,7-diphenyl-1,10-phenanthroline (bathophenanthroline, **6**; Wako Pure Chemical), 4-octadecylpyridine (**7**; Wako Pure Chemical), and 2,2':6',2"-terpyridine (**8**; Aldrich Chemical) were used without further purification after their purities were checked by ^{1}H NMR (500 MHz).

The following phenols and related compounds were of the highest grade commercially available, and used without further purification: *p*-Nitrophenol (**10**), *p*-chlorophenol (**11**), *p*-cresol (**13**), *o*-methoxyphenol (**18**), 2-hydroxy-4-methylphenol (**19**) and 4-*t*-butyl-2-hydroxyphenol (**20**) were purchased from Tokyo Kasei Kogyo. Catechol (**12**), phenol (**14**), *p*-methoxyphenol (**15**), resorcinol (**16**), hydroquinone (**17**), cyclohexanol (**21**) and 1,2-dimethoxybenzene (**22**) were purchased from Wako Pure Chemical. Benzoic acid (**23**) was purchased from Kanto Chemical. Dopamine (**24**) was purchased as its hydrochloride from Nacalai Tesque (Kyoto, Japan).

Dibutyl phthalate (DBP; Wako Pure Chemical), bis(2-ethylhexyl) phthalate ["dioctyl phthalate" (DOP); Wako Pure Chemical] and *o*-nitrophenyl octyl ether (*o*-NPOE; Dojindo Laboratories, Kumamoto, Japan), used as membrane solvents (Fig. 1), were purified by distillation under reduced pressure. Poly(vinyl chloride) (PVC; n_{av}≈1100) as a polymer matrix was purchased from Wako Pure Chemical. 2-(*N*-Morpholino)ethanesulfonic acid (MES, pK_a=6.15) was purchased from Dojindo Laboratories. Boric acid, citric acid and acetic acid were purchased from Wako Pure Chemical. The pH was adjusted by adding a NaOH solution of appro-

priate concentration.

All sample and buffer solutions were prepared with Milli-Q water with a specific resistance of >17.5 MΩ cm, and bubbled with nitrogen for 20 min just before potentiometric measurements in order to prevent phenolic analytes from oxidation by dissolved oxygen.

Electrode preparation and potential measurements

PVC matrix liquid membrane 1, based on macrocyclic pentaamine **1**, was prepared according to the procedure described in our previous paper.[5] The composition of the membrane was 1.2 wt% **1**, 79 wt% DOP or *o*-NPOE, and 19.8 wt% PVC. A poly(tetrafluoroethylene) (PTFE) membrane filter (5 mm diameter, 0.2 μm pore size) was dipped in a THF solution of the above components and placed on the top of a reversed liquid membrane type ISE body supplied from DKK. Then, 10 μl of the THF solution was dropped onto the filter every 10 min; this process was repeated 10 times. This tip was allowed to stand for 24 h for evaporation of THF. The electrode cell for the potential measurements was as follows:

Ag/AgCl | 1.0×10^{-2} M KCl+1.0×10^{-1} M AcONa–AcOH buffer (pH 6.1) | membrane | sample solution || 1.0 M AcOLi || 3 M KCl | Ag/AgCl

PVC matrix liquid membranes 2 – 8, based on aliphatic or heteroaromatic amines **2** – **8**, respectively, and a blank membrane with no particular sensory element were prepared according to a previously described procedure.[7] The composition of membranes 2 – 8 was 2.5 wt% amine, 70.0 wt% DBP, and 27.5 wt% PVC, and that of the blank membrane was 72.0 wt% membrane solvent and 28.0 wt% PVC. A circle of *ca*. 7-mm diameter was cut out from the membrane thus prepared (*ca*. 0.2-mm thickness) and mounted on a liquid membrane type ISE body supplied from DKK. The electrode cell for the potential measurements was as follows:

Ag/AgCl | 1.0 M KCl | membrane | sample solution || buffer solution used in each measurement || 3 M KCl | Ag/AgCl

PVC matrix liquid membrane 9, based on sapphyrin (**9**), was prepared with **9**·HCl, because a spectroscopic examination indicates that sapphyrin, incorporated as **9**·HCl, exists mainly as **9**·H^+ in a membrane in equilibrium with water (pH 5.7) after being shaken with a large amount of water. This behavior may be expected from the pK_a of **9** [3.5 (**9**·$2H^+$/**9**·H^+) and 9.5 (**9**·H^+/**9**)], determined in a two phase system (CH_2Cl_2/water).[8] The composition of membrane 9 was 3 wt% **9**·HCl, 75 wt% DOP, and 22 wt% PVC. The membrane tips were prepared by the same procedure as described for membrane 1. The electrode cell for the potential measurements was as follows:

Ag/AgCl | 0.10 M KCl | membrane | sample solution || 0.10 M KCl || 3 M KCl | Ag/AgCl

The membrane potentials were measured at room temperature (*ca*. 20°C) with an ion meter Model COM20, IOL-30, IOL-40 or IOL-50 (DKK). The reference electrode used was a double-junction type based on an Ag/AgCl electrode (Type 4083, DKK). Before each set of measurements, the electrodes were conditioned overnight in an appropriate buffer solution without an analyte. In this work, the response time t (Δt, ΔE), defined in previous papers[9–11] as the time at which the differential quotient ($\Delta E/\Delta t$) of the potential–time curve becomes smaller than a prechosen value ($\Delta E/\Delta t <$ 0.4 or $\Delta E < 0.4$ mV within $\Delta t = 1$ min in the present study), was generally short and within 5 min. However, a substantial drift of the potential was sometimes observed, particularly at high analyte concentrations (*ca*. 10^{-2} M), similarly as for the membranes based on lipophilic quaternary onium salts.[1] The effect of the pH on the membrane potential was measured by the addition of a solution of NaOH containing Na_2SO_4, NaCl or trisodium citrate (for membrane 1, membranes 2 – 8 or membrane 9, respectively) to a solution, the pH of which was preadjusted by H_2SO_4, HCl or citric acid (for membranes 1, 2 – 8 and 9, respectively).

Potentiometric selectivity coefficients ($K^{pot}_{A,B}$) for each group of guests were determined by the matched potential method in mixed solutions according to Gadzekpo and Christian[12,13] using the following buffers: 1.0×10^{-2} M AcONa–AcOH buffer of pH 6.2 (membrane 1), 1.0×10^{-2} M MES–NaOH buffer of pH 6.0 (membranes 2, 6, 7), and 5.0×10^{-2} M trisodium citrate–citric acid buffer of pH 6.0 (membrane 9). In the present study with neutral 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 conditions set as follows: Fixed concentrations of 1.00×10^{-3} M **12** (membrane 1), 1.00×10^{-4} M **14** (membranes 2, 6, 7) and 1.00×10^{-5} M **12** (membrane 9) were used as a background for respective membranes. The $K^{pot}_{A,B}$ 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 1.20×10^{-3} M (membrane 1) or 5.00×10^{-4} M (membrane 9), and the concentration of **14** to 2.70×10^{-4} M (membrane 2), 1.00×10^{-3} M (membrane 6) or 1.50×10^{-3} M (membrane 7).

Results and Discussion

Potential–pH profiles of membranes based on aliphatic and heteroaromatic amines

The intrinsic difference between the membranes based on amines and quaternary onium salts is the proton-uptake ability of the former membranes, resulting in charge separation of a protonated amine and its

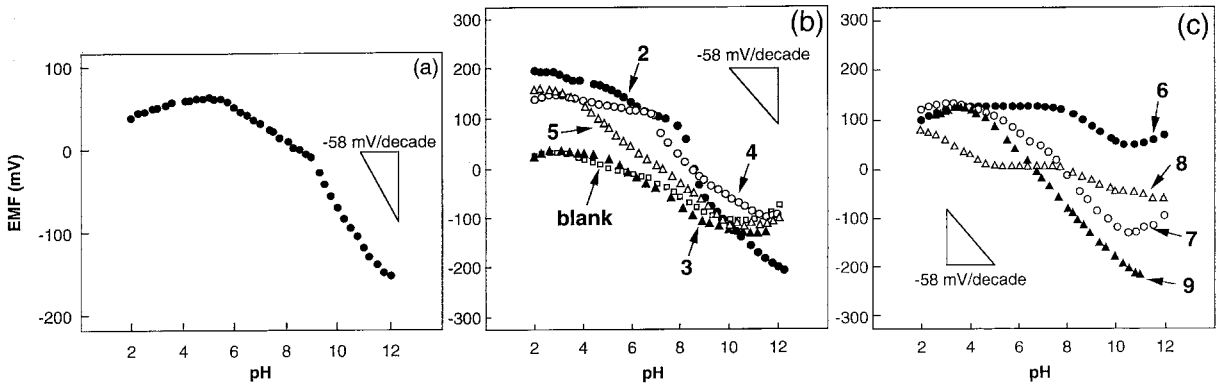

Fig. 2 Potential (EMF) *vs*. pH curves for (a) membrane 1 based on lipophilic macrocyclic pentaamine **1**, (b) membranes 2 – 5 based on aliphatic monoamines **2** – **5**, respectively, and the blank membrane without a particular sensory element, and (c) membranes 6 – 9 based on heteroaromatic amines **6** – **9**, respectively. DOP (membranes 1, 9) and DBP (membranes 2 – 8) were used as the membrane solvents. The pH of the sample solution was adjusted by adding a solution of NaOH containing 1.0×10^{-2} M Na_2SO_4 (a) or NaCl (b, c) to a 1.0×10^{-2} M solution of H_2SO_4 (a) or HCl (b, c) at room temperature. Figure 2a is taken from ref. 14.

counteranion across the interface of the membrane and the aqueous solution. Therefore, the pH profiles were first examined for the membranes based on different types of aliphatic and heteroaromatic amines.

Membranes 1 – 5 based on aliphatic amines. We have previously reported the potential–pH profile of a DOP/PVC membrane based on lipophilic macrocyclic pentaamine **1** (Fig. 2a).[5,14] As a characteristic pH profile, from pH 12 to 9, an increase in the membrane potential with decreasing pH was observed with a slope close to the theoretical value for a monovalent cation according to the Nernst equation (+58.2 mV decade^{-1} at 20°C; Nernstian slope). Such a pH-dependent potential increase was explained on the basis of a successive uptake of protons from the aqueous to the membrane phase by the polyamine **1** at the membrane interface. Similar potential–pH profiles were observed for membranes 2, 4, and 5 based on lipophilic aliphatic monoamines (Fig. 2b). The increase in the potential from pH 12 to 2 for membranes 1, 2, 4 and 5 were *ca.* 300, 400, 250, and 250 mV, respectively, and a breaking point of the potential increase was observed at around pH 8, except membrane 5. For membranes 1, 2, and 4, the slope of the potential–pH curve, which was smaller than, or close to, the Nernstian slope in the alkaline region, became slightly greater than the theoretical value (super-Nernstian slope) at the pH just before the breaking point. Similar observations have been reported by Simon *et al.*[15,16] The small pH dependence at high and/or low pH regions, observed for all membranes, is likely to be due to cation and/or anion interference, respectively.[17,18]

On the other hand, the pH dependence of membrane 3 based on trihexylamine (**3**) was negligible, similarly as the blank membrane containing no particular sensory element. The absence of an appreciable pH dependence of membrane 3 can be explained by a lack of the ability of **3** to uptake protons into the membrane phase, due to insufficient lipophilicity.[19]

Membranes 6 – 9 based on heteroaromatic amines. Figure 2c shows the potential–pH profiles for membranes 6 – 9 based on lipophilic heteroaromatic amines **6** – **9**, respectively. In membrane 9, sapphyrin was incorporated as its monohydrochloride (**9**·HCl). The potential of membranes 7 and 9 increased with decreasing pH from 12 to 2 with a Nernstian slope in the range of pH 7 – 10 and 4 – 11, respectively, and plateau regions were observed at high and/or low pH regions, similarly as the membranes based on lipophilic aliphatic amines (Fig. 2a,b). The most characteristic feature of the curves for membranes 7 and 9, as compared to those of the membranes based on lipophilic aliphatic amines, is that the range of the Nernstian response is extended to a strongly acidic region. A wide Nernstian-response region ranging from pH 1 to 7 – 8 has also been observed by Simon *et al.*[17] for membranes based on aniline- and pyridine-type lipophilic amines. Membrane 8 showed very small pH dependence, which can be ascribed to a low lipophilicity of the trispyridine **8**, as in the case of membrane 3 (*vide supra*). Membrane 6 is characteristic in that the increase in EMF became negligible below pH 8, showing a significant anion interference by protonated **6**.

The pH profiles of the membranes based on lipophilic heteroaromatic amines (membranes 6, 7 and 9) indicate that protonation to these amines, although weaker as compared to the aliphatic amines in membranes 1, 2, 4 and 5, can also lead to charge separation between the protonated amine and its counteranion across the membrane interface and hence generate a membrane potential.

Potentiometric response behaviors of membranes based on aliphatic amines to phenol

Anionic potentiometric responses to undissociated, neutral phenols have previously been observed for a

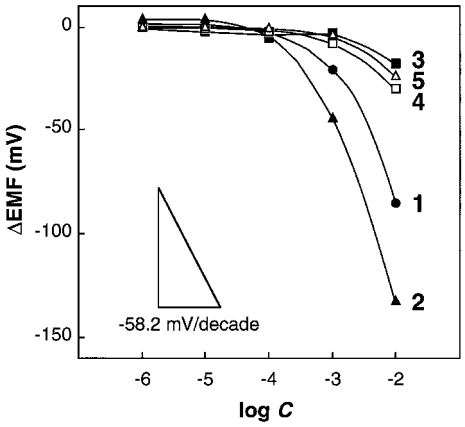

Fig. 3 Potential (ΔEMF) *vs*. concentration curves for phenol (**14**), obtained at pH 6 by PVC liquid membranes 1 – 5 based on aliphatic lipophilic amines **1** – **5**, respectively. DOP and DBP were used as the membrane solvents for membranes 1 and 2 – 5, respectively. Measured in 1.0×10^{-2} M AcONa–AcOH buffer (pH 6.2; membrane 1) or 1.0×10^{-2} M MES–NaOH buffer (pH 6.0; membranes 2 – 5) at room temperature.

liquid membrane based on macrocyclic pentaamine **1**.[3,4] Such unexpected anionic responses to phenols (**10** – **20**) were also observed for membranes based on simpler lipophilic aliphatic amines. Figure 3 shows the anionic responses to phenol (**14**) at pH 6, observed for liquid membranes 1 – 5 based on lipophilic macrocyclic polyamine **1** and simple aliphatic monoamines **2** – **5**, respectively, despite that **14** (pK_a 9.99)[20] exists almost exclusively in its undissociated, neutral form in the aqueous solution bulk at the experimental pH. The strongest response was observed for membrane 2 based on tri(decyl)amine (**2**). The slopes of the potentiometric response curves in the concentration range of 10^{-3} – 10^{-2} M **14** were *ca*. –65 and –90 mV decade^{-1} for membranes 1 and 2, respectively. These slopes are greater than the Nernstian slope for a monovalent anion (–58.2 mV decade^{-1} at 20°C). Such strong responses to **14** were also observed for membranes based on lipophilic quaternary ammonium and phosphonium salts.[1]

On the other hand, the response to **14** by membrane 3 based on a tertiary amine with short alkyl chains was negligible compared to the blank membrane. This is similar to the result for the membrane based on a quaternary ammonium salt with short alkyl chains (tetrabutylammonium chloride).[1] The lack of response to phenol as well as to proton (Fig. 2a) can be reasonably explained on the basis of insufficient lipophilicity of **3** (or **3**·H$^+$) to be retained in the membrane phase. The responses to **14** by membranes 4 and 5 were also very weak if not negligible. These results are parallel to the solvent extraction study[21] showing a greater extractability of phenol by a protonated tertiary amine compared to a protonated secondary or primary amine.

Selectivity of membrane based on lipophilic aliphatic amines to phenol derivatives

Figure 4 shows potentiometric responses of membrane 1 to (a) phenol (**14**) and cyclohexanol (**21**), (b) catechol (**12**) and its mono- and di-*O*-methyl derivatives (**18** and **22**, respectively), and (c) benzoic acid (**23**) at pH 6 (Fig. 4a,b) or pH 5 (Fig. 4c). Whereas strong anionic responses with slopes greater than –70 mV decade^{-1} were observed at pH 6 for phenolic compounds **12**, **14** and **18**, the responses to **21** and **22** lacking a phenolic OH were negligible. A similar response behavior was observed for membrane 2. In addition, such a strong anionic response was also observed for benzoic acid (**23**; pK_a 4.204[20]) by membrane 1 at pH 5.1, at which *ca*.11% exists in its undissociated form (Fig. 4c). These results clearly demonstrate that a phenolic or more acidic OH seems to play an essential role for the strong anionic potentiometric responses by membranes based on lipophilic aliphatic amines. However, the response was negligible when the phenolic compound had a positive charge that interacts un-

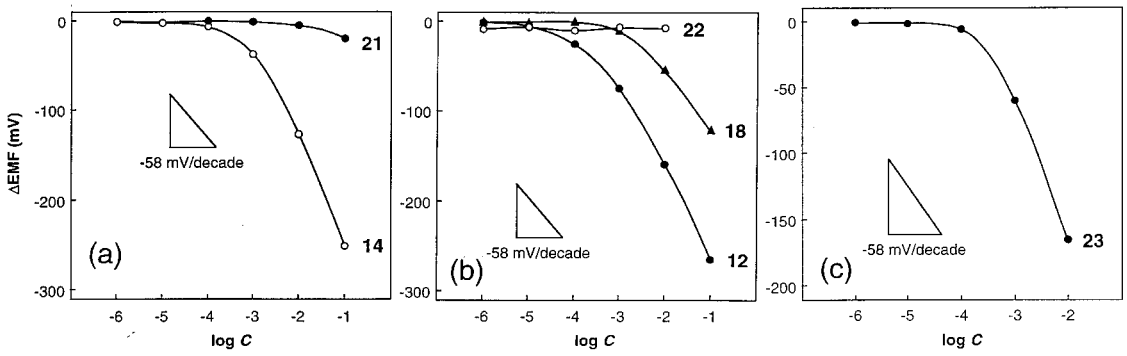

Fig. 4 Potential (ΔEMF) *vs*. concentration curves obtained by membrane 1 based on macrocyclic pentaamine **1**. (a) Analyte: phenol (**14**; pH 6.4) and cyclohexanol (**21**; pH 6.2); membrane solvent: *o*-NPOE. (b) Analyte: catechol (**12**) and its mono- and di-*O*-methyl derivatives (**18** and **22**, respectively); pH 6.1; membrane solvent: *o*-NPOE. (c) Analyte: benzoic acid (**23**); pH 5.1; membrane solvent: DOP. Measured in 1.0×10^{-2} M AcONa–AcOH buffer of respective pH at room temperature.

Table 1 Potentiometric selectivity coefficients (log $K^{pot}_{A,B}$) for membranes based on various lipophilic amines, together with acid dissociation constants (pK_a) and partition coefficients (log P_{oct}) for phenols (Y_n-C_6H_{5-n}-OH)

Analyte (Y)	Selectivity coefficient (log $K^{pot}_{14,B}$ or log $K^{pot}_{12,B}$)[a] membranes Q^+X^-[b]	1[c]	2[b]	6[b]	7[b]	9[d]	pK_a[e]	log P_{oct}[f]
10	+1.85	(+2.59)	+1.33	+1.86			7.15	1.91
(*p*-NO_2)		+2.12						
11	+1.07	(+1.12)	+0.86	+1.00			9.43	2.43
(*p*-Cl)		+0.65						
12	+0.65	(+0.47)	+0.49	+0.60	+0.54		9.36	0.95
(*o*-OH)	(0)	0	(0)	(0)	(0)	0		
13	+0.30	(+0.35)	+0.15	+0.32			10.26	1.93
(*p*-CH_3)		–0.12						
14	0	(0)	0	0	0		9.99	1.47
(H)	(–0.65)	–0.47	(–0.49)	(–0.60)	(–0.54)			
15	–0.13	(–0.13)	–0.21	–0.09			10.20	1.34
(*p*-OCH_3)		–0.60						
16	–0.27	(–0.68)	–0.35	–0.12	–0.13		9.44	0.79
(*m*-OH)	(–0.92)	–1.15	(–0.84)	(–0.72)	(–0.67)	–2.49		
17	< –1.1	(–1.64)	–1.14	–1.06	–0.60		9.91	0.55
(*p*-OH)	(< –1.7)	–2.11	(–1.63)	(–1.64)	(–1.14)	–2.78		
19		(+0.77)						
(*o*-OH, *p*-CH_3)		+0.30						
20		(+1.73)						
[*o*-OH, *p*-$C(CH_3)_3$]		+1.26						

a. The potentiometric selectivity coefficients, determined with phenol (**14**) or catechol (**12**) as a standard (log $K^{pot}_{14,B}$ and log $K^{pot}_{12,B}$, respectively), are listed in the upper and lower rows, respectively, for each phenolic analyte. The values for the alternative standard, indicated in parentheses, were estimated from the authentic values by simple subtraction. b. The potentiometric selectivity coefficients (log $K^{pot}_{14,B}$) were determined 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 (**14**) as a background. Q^+X^-: methyltrioctylammonium chloride. c. The potentiometric selectivity coefficients (log $K^{pot}_{12,B}$) were determined in 1.0×10^{-2} M AcONa–AcOH buffer (pH 6.2) at room temperature (*ca*. 20˚C) by the matched potential method in mixed solutions with 1.00×10^{-3} M catechol (**12**) as a background. d. The potentiometric selectivity coefficients (log $K^{pot}_{12,B}$) were determined for membrane 9, based on sapphyrin monohydrochloride (**9**·HCl), in 5.0×10^{-2} M trisodium citrate–citric acid buffer (pH 6.0) at room temperature (*ca*. 20˚C) by the matched potential method in mixed solutions with 1.00×10^{-5} M catechol (**12**) as a background. e. Acid dissociation constants (pK_a) at 25˚C, taken from reference.[20] f. Partition coefficients (1-octanol/water system; log P_{oct}) at room temperature, taken from reference.[24]

favorably with protonated **1**; for example, the response to dopamine (**24**; pK_a = 9.05, 10.52, and 11.98[22]) by membrane 1 was negligible at pH 6.2.[23]

The potentiometric selectivity coefficients ($K^{pot}_{A,B}$) for a series of phenols (**10** – **17**, **19**, **20**; Y_n-C_6H_{5-n}-OH), determined at pH 6 with membranes 1 and 2 as well as with the membrane based on methyltrioctylammonium chloride (Fig. 1) [membrane $(C_8)_3C_1N^+Cl^-$][1] are listed in Table 1, together with the pK_a values[20] and partition coefficients (1-octanol/water system; log P_{oct})[24] of each phenolic compound. The $K^{pot}_{A,B}$ values were determined by the matched potential method in mixed solutions according to Gadzekpo and Christian.[12,13] Membranes 1 and 2 showed the same response order: **10** (Y = *p*-NO_2) > **11** (Y = *p*-Cl) > **12** (Y = *o*-OH) ≥ **13** (Y = *p*-CH_3) ≥ **14** (Y = H) ≥ **15** (Y = *p*-OCH_3) > **16** (Y = *m*-OH) > **17** (Y = *p*-OH). This selectivity indicates that a phenol with a stronger acidity (smaller pK_a) and higher lipophilicity (larger log P_{oct}) induces a stronger anionic response. The effect of acidity was clearly indicated by the response orders of **10** ≫ **13** and **14** ≥ **15**, and the effect of lipophilicity by the response orders of **11** ≫ **12** > **16** and **13** > **15**. The effect of lipophilicity was also observed for membrane 1 with catechol derivatives [response order: **20** [R = $-C(CH_3)_3$] > **19** (R = $-CH_3$) > **12** (R = –H)].

A potentiometric selectivity reflecting both acidity and lipophilicity of phenols has also been observed for membrane $(C_8)_3C_1N^+Cl^-$.[1] The fact that similar selectivities for phenols were observed by membranes based on different types of sensory elements (macrocyclic pentaamine **1**, tertiary amine **2**, and a quaternary ammonium salt) indicates that, also for these membranes, the acidity and lipophilicity are the major controlling factors for potentiometric discrimination of phenols. The experimental results, showing the significance of the acidity and lipophilicity of the phenols on the potentiometric selectivities, contradict our initial view[4] that the potentiometric discrimination of the positional isomers of catechol (**12**, **16**, **17**) by the membrane based on macrocyclic pentaamine **1** is due to geometrical discrimination by two-site interactions

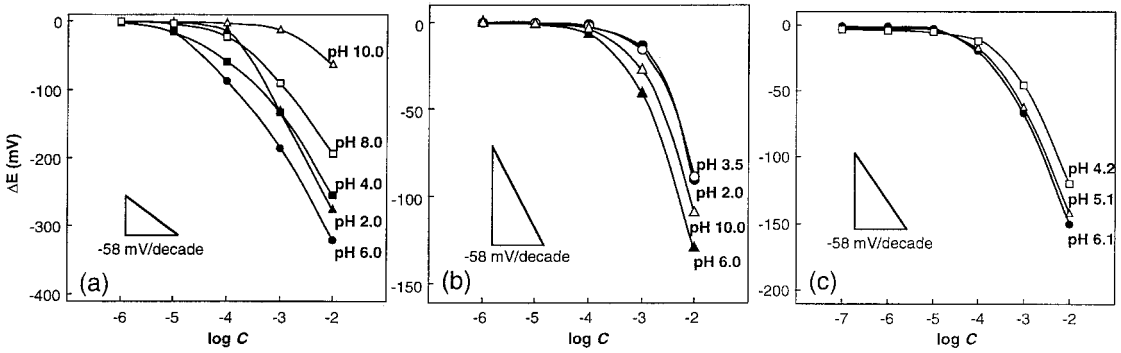

Fig. 5 Potential (ΔEMF) *vs*. concentration curves for phenols at varying pH's. (a) Responses of membrane 2 based on tri(decyl)amine (**2**) (membrane solvent: DBP) to *p*-nitrophenol (**10**) at pH 2.0, 4.0, 6.0, 8.0 and 10.0. Measured in 1.0×10^{-2} M Na_2SO_4–H_2SO_4 (pH 2.0), 1.0×10^{-2} M AcONa–AcOH buffer (pH 4.0), 1.0×10^{-2} M MES–NaOH buffer (pH 6.0), or 1.0×10^{-2} M boric acid–NaOH buffer (pH 8.0, 10.0). (b) Responses of membrane 2 to phenol (**14**) at pH 2.0, 3.5, 6.0 and 10.0. Measured in 1.0×10^{-2} M Na_2SO_4–H_2SO_4 (pH 2.0 and 3.5), 1.0×10^{-2} M MES–NaOH buffer (pH 6.0), or 1.0×10^{-2} M boric acid–NaOH buffer (pH 10.0). (c) Responses of membrane 1 based on macrocyclic pentaamine **1** (membrane solvent: *o*-NPOE) to catechol (**12**) at pH 4.2, 5.1 and 6.1. Measured in 1.0×10^{-2} M AcONa–AcOH buffer for all pH's. All measurements were carried out at room temperature.

between the polyamine and the aromatic diols.

Effect of pH on the potentiometric responses to phenols by the membranes based on lipophilic aliphatic amines

Figure 5a shows the potentiometric responses of membrane 2 to *p*-nitrophenol (**10**; $pK_a = 7.15$[20]) at five different pH's ranging from 2.0 to 10.0. It can be evidently seen that the response is very weak at pH 10.0 in contrast to strong responses at the lower pH's. This result contrasts the response behavior of the membranes based on quaternary ammonium salts, which exhibited a Nernstian response to the monoanionic form of **10** existing as the predominant species at pH 10.0.[1] Furthermore, the response to phenol (**14**; $pK_a = 9.99$[20]) at pH 10.0, at which **14** exists as both monoanionic and neutral forms, was weaker than that at pH 6.0 (Fig. 5b). These results contrast, again, the response to **14** by the membranes based on lipophilic ammonium salts, which was stronger at the pH near the pK_a of **14** than at the lower pH's.[1] The weaker anionic responses by membrane 2 at the alkaline region (pH 10.0) can be understood by considering an essential role of protonated (charged) amine at the membrane interface to exhibit a potentiometric response to either dissociated (anionic) or undissociated (neutral) phenol.

With respect to the responses to undissociated, neutral phenols in the *nonalkaline* region, a characteristic pH dependence, which is similar to that of the membranes based on lipophilic quaternary ammonium salts[1], was observed. 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. The responses of membrane 2 to **10** (Fig. 5a; pH 6.0 *vs*. 4.0, 2.0), **14** (Fig. 5b; pH 6.0 *vs*. 3.5) and other phenols (**11** – **13**, **15**; figure not shown), and of membrane 1 to **12** (Fig. 5c; pH 6.1 → 5.1 → 4.2) became weaker with decreasing pH. On the other hand, no pH dependence was observed in the pH region *far* from the pK_a, as indicated by the responses of membrane 2 to **14** at pH 3.5 and 2.0 (Fig. 5b). For the membranes based on lipophilic quaternary ammonium salts, such a pH dependence was explained by considering a process involving proton dissociation of the complexed phenol with a concomitant ejection of the acid produced to the aqueous phase (this process is facilitated with increasing pH).[1] A related process may be involved in the responses of the membranes based on lipophilic amines at the pH conditions in which the amines exist as its protonated form at the membrane interface (*vide infra*).

Potentiometric responses to phenol derivatives with membranes based on lipophilic heteroaromatic amines

Anionic potentiometric responses to neutral phenols were also observed for the membranes based on lipophilic heteroaromatic amines. Figure 6 shows the responses to phenol (**14**), observed at pH 6.0 by membranes 6 – 9. Appreciable responses were observed for membranes 6 and 7 with slopes of *ca*. –70 and –50 mV decade^{-1}, respectively, in the concentration range of 10^{-3} – 10^{-2} M. On the other hand, the response of membrane 9 to **14** was weak and that of membrane 8 was negligible. In addition, neither membrane 6 nor 7 showed an appreciable response to **21** or **22** having no phenolic OH, similarly as the membranes based on lipophilic quaternary ammonium salts[1] or lipophilic amines (Fig. 4a,b).

Potentiometric selectivities are listed in Table 1 for membranes 6, 7 and 9 based on lipophilic heteroaromatic amines. An interesting result that should be noted is the high catechol selectivity of membrane 9 based on sapphyrin (incorporated as **9**·HCl). As clearly shown in Fig. 7a, the responses of this membrane to phenol (**14**) and the geometrical isomers of catechol (**16**, **17**) were negligible up to a concentration of ~10^{-2}

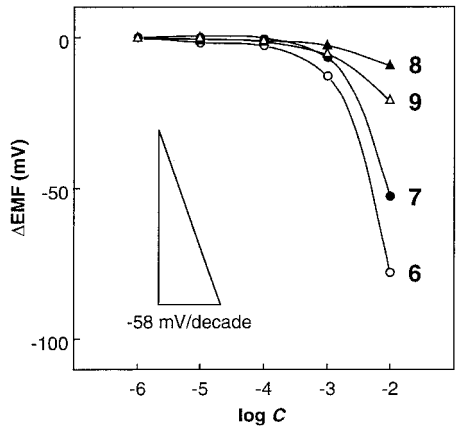

Fig. 6 Potential (ΔEMF) *vs*. concentration curves for phenol (**14**), obtained at pH 6.0 by membranes 6 – 9 based on heteroaromatic amines **6** – **9**, respectively. DBP and DOP were used as the membrane solvents for membranes 6 – 8 and 9, respectively. Measured in 1.0×10^{-2} M MES–NaOH buffer (pH 6.0; membranes 6 – 8) or 5.0×10^{-2} M trisodium citrate–citric acid buffer (pH 6.0; membrane 9) at room temperature.

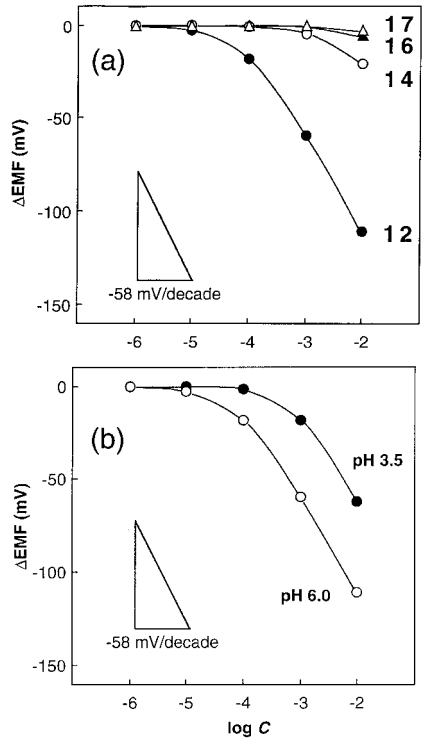

Fig. 7 Potential (ΔEMF) *vs*. concentration curves obtained by membrane 9 based on sapphyrin (**9**). (a) Curves for phenol (**14**), catechol (**12**) and its positional isomers (**16**, **17**) at pH 6.0. (b) Curves for catechol (**12**) at pH 3.5 and 6.0. DOP was used as the membrane solvent. Measured in 5.0×10^{-2} M trisodium citrate–citric acid buffer (pH 6.0 or 3.5) at room temperature.

M. The slope of the response curve for **12** was *ca*. –50 mV decade^{-1} in the concentration range of 10^{-3} – 10^{-2} M. Since this selectivity is much higher than that of any other membranes examined (Table 1), the catechol selectivity of membrane 9 may be attributed to discrete two-site interactions between the ortho dihydroxy structure of **12** and the nitrogens of sapphyrin (**9**·HCl) on a rigid macrocyclic structure. Similarly as for membranes based on lipophilic quaternary ammonium salts[1] or lipophilic aliphatic amines (Fig. 5), the response of membrane 9 to **12** became weaker with decreasing pH (Fig. 7b; pH 6.0 → 3.5), again indicating the involvement of the proton dissociation/acid ejection mechanism (*vide supra*).

A possible mechanism of potentiometric responses to neutral phenols by the membranes based on lipophilic amines

The present study has disclosed that not only the membranes based on a macrocyclic polyamine[3,4] or quaternary onium salts[1] but also those based on a variety of lipophilic amines exhibit anionic potentiometric responses to neutral phenols. In our previous study[1], systematically carried out with membranes based on quaternary onium salts (Q^+X^-), we have proposed a reasonable model for anionic potentiometric responses to neutral phenols (ArOH), which is described by the following processes:

(1a) Extraction of ArOH into the membrane

$$ArOH(aq) \rightleftharpoons ArOH(mem)$$

(1b) Complexation of Q^+X^- and the extracted ArOH in the membrane

$$Q^+X^-(mem) + ArOH(mem) \rightleftharpoons Q^+X^-\cdot ArOH(mem)$$

(1c) Proton dissociation of the complexed ArOH and concomitant ejection of the acid HX into the aqueous phase

$$Q^+X^-\cdot ArOH(mem) \rightleftharpoons Q^+ArO^-(mem) + HX(mem)$$
$$HX(mem) \rightleftharpoons HX(aq)$$

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:

(1d) $Q^+X^-(interface) \rightleftharpoons Q^+X^-(mem)$

A shift of this equilibrium to the right occurs as a direct result of process (1b) as well as an indirect result of process (1c) *via* process (1b) (The involvement of the former process to anionic potentiometric responses to neutral phenols has also been mentioned by Mokrov *et al*.[25]). 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 (1b) leads to a movement of the cationic species Q^+ (membrane side) and the anionic species X^- (aqueous side) into the membrane bulk, causing a net movement of *anionic* species from the aqueous to

the membrane phase. On the other hand, the equilibrium shift by process (1c) involves a movement of the charge-separated Q^+ and X^- into the membrane bulk with subsequent ejection of H^+ (dissociated from extracted and complexed ArOH) and X^- into the aqueous solution bulk, causing in this case a net movement of *cationic* species H^+ from the membrane to the aqueous phase. A theoretical treatment based on this model reproduced the potentiometric response behaviors (slope, pH effect, detection limit) for undissociated phenols.[1]

As described earlier in relation to Fig. 2, the lipophilic amines (B) incorporated in liquid membranes in contact with aqueous solutions of acidic to neutral pH can be protonated and exist in the charge-separated state at the membrane interface (protonated amine BH^+ and its counteranion X^- on the membrane and aqueous sides, respectively). The occurrence of charge-separated species at the membrane interface as well as the similarity of the selectivities of the membranes based on lipophilic aliphatic amines (membranes 1, 2) and a quaternary ammonium salt (membrane $(C_8)_3C_1N^+Cl^-$) (Table 1) indicates that processes (2b), (2c) and (2d) are involved in the responses by the former membranes in a similar manner as processes (1b), (1c) and (1d), respectively, in the responses by the membranes based on Q^+X^-.

(2b) $BH^+X^-(mem) + ArOH(mem) \rightleftharpoons BH^+X^-\cdot ArOH(mem)$

(2c) $BH^+X^-\cdot ArOH(mem) \rightleftharpoons BH^+\cdot ArO^-(mem) + HX(mem)$

$HX(mem) \rightleftharpoons HX(aq)$

(2d) $BH^+X^-(interface) \rightleftharpoons BH^+X^-(mem)$

The shift of equilibrium (2d) by processes (2b) and (2c) leads, respectively, to a net movement of *anionic* species (X^-) from the aqueous to the membrane phase and a net movement of cationic species (H^+) from the membrane to the aqueous phase in a similar manner as the membrane based on Q^+X^- (*vide supra*).

In the case of the membranes based on lipophilic quaternary onium salts (Q^+X^-), the "acidity factor" reflects the ability of a neutral phenol to form a hydrogen bond with the anionic component X^-.[1] The similarity of the selectivities of membranes 1 and 2 to that of membrane $(C_8)_3C_1N^+Cl^-$ (Table 1) indicates that, for the membranes based on lipophilic amines (B), a similar "acidity factor", reflecting the ability of a neutral phenol to form a hydrogen bond with the counteranion X^- of the protonated amine BH^+ in process (2b), is involved in the responses to neutral phenols. In this case, however, it is also reasonable to consider that the "acidity factor" reflects the alternative mode of hydrogen bonding, which involves the phenolic oxygen and the protonated amine BH^+.

Furthermore, the "acidity factor" may reflect the ability of a neutral phenol to form a hydrogen bond with the nonprotonated amine (B). This is also a possible process because lipophilic tertiary amines in the bulk of organic solutions have been shown to exist predominantly as their nonprotonated form, even in contact with an aqueous solution of pH 4.[17] Accordingly, process (3b) may be involved in addition to process (2b).

(3b) $B(mem) + ArOH(mem) \rightleftharpoons B\cdot ArOH(mem)$ or $BH^+\cdot ArO^-(mem)$

In this case, the following equilibrium exists between the charge-separated BH^+X^- at the membrane interface and the uncharged B in the membrane bulk.

(3d) $BH^+X^-(interface) \rightleftharpoons B(mem) + HX(aq)$

Process (3b) can also shift the equilibrium (3d) and lead to a movement of the cationic species H^+ and the anionic species X^- at the membrane and aqueous sides of the interface, respectively, to the aqueous phase bulk. This net movement of *cationic* species H^+ from the membrane to the aqueous phase leads to an anionic response to ArOH.

The pH dependence in the responses in the *nonalkaline* region (*vide supra*) is consistent with the processes described above. The decreases in the anionic response with decreasing pH in the region that is relatively near the pK_a of the phenol support the involvement of process (2c) and also (3b), and the lack of such a pH effect in the pH region *far* from the pK_a can be explained by assuming significant involvement of process (2b). The selectivities of anionic potentiometric response may be determined by the interaction of ArOH with X^-, BH^+ and/or B as well as the lipophilicity of ArOH. A theoretical treatment similar to that for the responses by the membrane based on Q^+X^- [1] will be possible, provided that the protonation state for the lipophilic amines at the membrane interface can be properly evaluated by surface sensitive techniques.

The responses to neutral phenols by the membranes based on lipophilic heteroaromatic amines would be interpreted in a similar manner but might involve different processes due to a much weaker basicity of these amines compared to aliphatic ones. With respect to membrane 9, the high selectivity for catechol (**12**) is possibly due to geometrical discrimination of the ortho dihydroxy structure of **12**, as discussed earlier. Since sapphyrin exists mainly as $\mathbf{9}\cdot H^+$ in a membrane in contact with water (see the Experimental) and $\mathbf{9}\cdot H^+$ is still capable of functioning as a hydrogen bonding *acceptor*, the characteristic geometrical discrimination (Table 1) of membrane 9 is most likely effected by the monoprotonated form of the amine ($\mathbf{9}\cdot H^+$) and not by its counteranion (X^-).

Although potentiometric responses to uncharged

species are generally regarded as being intrinsically difficult in terms of the conventional response mechanism for charged species, the present study has clearly shown that not only the membranes based on a macrocyclic polyamine[3,4] or quaternary onium salts[1] but also those based on a variety of lipophilic amines unexpectedly exhibit anionic potentiometric responses to neutral phenols. In a number of cases, the response to *neutral* phenols accompanied a greater slope compared to the theoretical slope for a monoanion. The pH-dependent potential increases and the selectivities reflecting the acidity and lipophilicity of phenols suggested a response mechanism based on a decrease in the charge separation of protonated amines (BH^+) and their counteranions (X^-) across the membrane interface. In the case of the membranes based on lipophilic aliphatic amines, possible processes leading to a decrease in this charge separation are (i) complexation between ArOH and BH^+X^-, followed by proton dissociation and ejection of HX into the aqueous phase, and (ii) complexation between ArOH and B. Whereas the complexation between ArOH and BH^+X^- in process (i) leads to a net movement of anionic species (X^-) from the aqueous to the membrane phase, the ejection of HX into the aqueous phase in processes (i) and (ii) involves a net movement of cationic species (H^+) from the membrane to the aqueous phase. The responses of the membranes based on lipophilic heteroaromatic amines may involve different processes due to a much weaker basicity of these amines compared to aliphatic amines. A high selectivity to catechol was observed for the membrane based on sapphyrin, possibly due to geometrical discrimination of the *ortho* dihydroxy structure of catechol by the nitrogen(s) on the rigid macrocyclic structure of monoprotonated sapphyrin. An understanding of the response mechanism for neutral phenols would afford a possibility for a potentiometric selectivity based on a more sophisticated structure discrimination toward uncharged molecules.

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