Facilitated Transfer of Hydrophilic Anions across the Nitrobenzene–Water Interface by a Hydrogen-Bonding Ionophore: Applicability for Multianalyte Detection

Seiichi Nishizawa, Tomoyuki Yokobori, Takeshi Shioya, and Norio Teramae*
Department of Chemistry, Graduate School of Science, Tohoku University, Aoba-ku, Sendai 980-8578

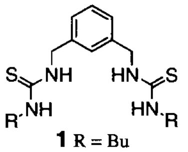
(Received July 23, 2001; CL-010682)

A hydrogen bond-forming bis-thiourea **3** can effectively facilitate the transfer of various hydrophilic anions, such as Cl^-, CH_3COO^-, $H_2PO_4^-$, HPO_4^{2-} and SO_4^{2-}, across the nitrobenzene–water interface, suggesting possible use of **3** for multianalyte detection with an amperometric sensing mode.

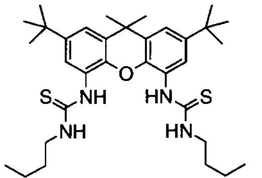
The design and synthesis of hydrogen-bonding ionophores for biologically and/or chemically important anions are of current interest in host–guest chemistry.[1] Successful applications of hydrogen-bonding ionophores in transport and potentiometric ion-selective electrodes (ISEs) have been reported.[2]

We have recently used ion transfer polarography to study anion transfer across the liquid–liquid interface facilitated by bis-thioureas, **1** or **2**,[3] as a hydrogen-bonding ionophore.[4] When **2** is present in the organic phase, a clear wave due to the facilitated transfer of a very hydrophilic anion, SO_4^{2-}, is observed whereas only positive shifts are observed for Cl^- and CH_3COO^-.[4] The analysis of ion transfer polarograms shows that the sulfate transfer process is reversible and controlled by diffusion of **2** in the organic phase.[4] This is the first observation of the *hydrogen-bonding ionophore-assisted anion transfer* across the interface between two immiscible electrolyte solutions (ITIES), suggesting possible use of hydrogen-bonding ionophores in amperometric ISEs.[5] Although there have been only a few attempts[6] to develop ionophore-based amperometric sensors for sensing of anions, recent progress[5] has suggested that a voltammetric or pulsed amperometric sensing mode may offer distinct advantages over traditional potentiometry with plasticized PVC membranes containing ionophores. Thus, studies on the electrochemistry of facilitated anion transfer by various types of hydrogen-bonding ionophores would provide further insight into their unique functions when used in an amperometric sensing mode.

In this study, facilitated transfer of hydrophilic anions across the liquid–liquid interface by bis-thiourea **3**[3a] is studied by ion transfer polarography.[7] A previous binding study[3a] in DMSO-d_6 by ^1H NMR spectroscopy shows that among bis-thioureas **1** to **3**, ionophore **3** forms the strongest complexes with anions that may act as hydrogen bond acceptors, such as $H_2PO_4^-$, CH_3COO^- or Cl^-. Umezawa and co-workers showed that a potentiometric ISE with **3** gives a high selectivity for Cl^-,[8a] while an ion channel sensor based on monolayers of the same ionophore is HPO_4^{2-} selective.[8b] In contrast to these electrochemical application studies, our attention in the present work is devoted to the possible use of **3** for multianalyte detection of hydrophilic anions if **3** is used in amperometric sensing modes. While both theoretical and experimental treatments on the multianalyte detection capability of cation-selective amperometric sensors have been described,[5] no experiments have so far been reported to address the issue of this capability of hydrogen-bonding ionophores for anion sensing.



1 R = Bu
2 R = Ph



3

The ion transfer polarograms were recorded by potential-scan polarography[7a,7d,7e] with an electrolyte solution dropping electrode.[7a,7b,7d,7e] The following electrochemical cell was used to study the transfer of anions across the nitrobenzene (NB)–water interface:

Ag/AgCl/0.5 M LiCl/0.05 M NaTPB + 0.5 M LiCl/(org.) *x* mM **3** + 0.05 M $N(C_7H_{15})_4TPB$/(aq) 0.5 M electrolytes/0.5 M LiCl/AgCl/Ag

where x was 0.5 or 1.0. Potential difference between the aqueous and organic phases, $\Delta\phi$ ($= \phi_w - \phi_o$), was controlled at a scan rate of 2.5 mV s^{-1} by a conventional four-electrode potentiostat, and the values of the potentials ($\Delta\phi$) were standardized by measuring the half-wave potential $\Delta\phi_{1/2}$ of ClO_4^- (used as Na^+ salt, $\Delta\phi_{ClO_4}{}^\circ$: –0.091 V)[9] as a reference ion with the same reference electrode system. Negative current flows when anions are transferred from the aqueous phase to the organic phase. All experiments were carried out at 298 ± 0.5 K.

Ion transfer polarograms for Cl^- are shown in Figure 1. While only a background wave due to the direct Cl^- transfer is observed in the absence of **3** (Figure 1a), a well-defined wave appears in its presence (Figure 1b). Obviously, the Cl^- transfer across the interface is facilitated by **3** via formation of hydrogen bonds.

Facilitated Cl^- transfer across the NB–water interface was analyzed according to theory.[7] There is a linear relationship between $\Delta\phi$ and $\log\{i/(i_l - i)\}$ with a slope of –60 mV (inset in Figure 1), revealing the transfer of monovalent anionic species through 1:1 complexation between **3** and Cl^-.[7c,7d] The limiting current i_l is proportional to the square root of the flow rate of the aqueous solution, and also to the concentration of **3** in the NB phase (not shown). These results indicate that the transfer process of Cl^- across the interface is reversible and diffusion-controlled by **3** from the bulk NB phase to the interface.[7c,7d] The half-wave potential $\Delta\phi_{1/2}$ for the Cl^- transfer facilitated by **3** is evaluated as –0.140 V from the intercept of the linear regression curve in the inset of Figure 1. The reversible half-wave potential for the transfer reaction is given by[7c,7d]

$$\Delta\phi_{1/2} = \Delta\phi_{Cl}{}^{\circ\prime} - (RT/2F)\ln(D_I/D_{IA}) + (RT/F)\ln(K_{11}[Cl^-]_w)$$

where $\Delta\phi_{Cl}{}^{\circ\prime}$ is the ion transfer formal potential for Cl^-, and K_{11} is the association constant in the NB phase. D_I and D_{IA} are the diffusion coefficients of the ionophore and the chloride com-

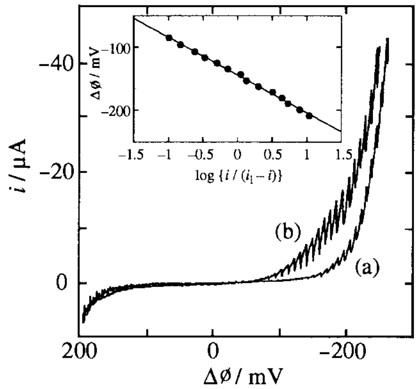


Figure 1. Ion transfer polarograms of Cl^- across the NB–water interface. Aqueous phase: 0.5 M LiCl. Organic phase: 0.05 M $N(C_7H_{15})_4TPB$ and (a) 0 mM or (b) 0.5 mM **3**. Flow rate: 25 mL h^{-1}. Inset: Relationship between Δϕ and log {$i/(i_l - i)$}. Aqueous phase: 0.5 M LiCl. NB phase: 0.05 M $N(C_7H_{15})_4TPB$ and 0.5 mM **3**. Flow rate: 25 mL h^{-1}.

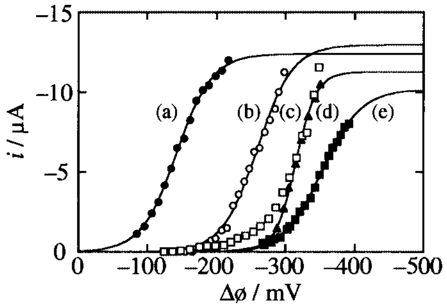


Figure 2. Plot of i, corrected for the base current, against Δϕ for the transfer of (a) Cl^- (●), (b) CH_3COO^- (○), (c) HPO_4^{2-} (□), (d) SO_4^{2-} (▲), and (e) $H_2PO_4^-$ (■). Aqueous phase: 0.5 M electrolytes as Na^+ salt except for Cl^-. NB phase: 0.05 M $N(C_7H_{15})_4TPB$ and 0.5 mM **3**. Flow rate: 25 mL h^{-1}. (–): Non-linear fitting based on the equation[7] for the reversible polarographic wave.

plex, respectively. On the assumption that D_I is nearly equal to D_{IA}, the association constant K_{11} of the 1:1 complex between **3** and Cl^- can be calculated as $(4.1 \pm 0.2) \times 10^4$ M^{-1} from the above equation. Comparison with the case in the absence of ionophores (cf. $\Delta\phi_{Cl}°$: –0.395 V; $\Delta G_{tr}°$: 38 ± 2 kJ mol^{-1})[6a,9] shows the Cl^- transfer across the NB–water interface is indeed stabilized by 26 kJ mol^{-1} through the binding with **3** in the NB phase.

Other hydrophilic anions, CH_3COO^-, $H_2PO_4^-$, HPO_4^{2-} and SO_4^{2-}, were also examined. Well-defined waves due to the ion transfer facilitated by **3** are clearly observed for all cases despite the high free energy of hydration of these anions (cf. Figure 2). This result shows a high stability of the complex between **3** and these anions in the NB phase.[10] Except for HPO_4^{2-},[11] the transfer of these anions is assisted by the formation of 1:1 complex. Significantly, as shown in Figure 2, the half-wave potentials for the facilitated transfer depend on anions, and some of them are reasonably separated ($\Delta\phi_{1/2}$ (V): Cl^-: –0.140; CH_3COO^-: –0.248; SO_4^{2-}: –0.319; $H_2PO_4^-$: –0.345). Thus, the possibility exists, that analogous to crown ether-based amperometric ISE for simultaneous determination of Na^+ and K^+,[5a,5b] the difference in half-wave potentials can be used for the identification of the analyte anions,[12] making it possible to detect various anions by the *same* ionophore. Although such a difference should be observed without ionophores, use of well-designed ionophores is essential to facilitate transfer of very hydrophilic anions from the aqueous phase to the organic phase.

In summary, we have shown the multianalyte detection capability of hydrogen-bonding ionophore **3** when used in amperometric sensing modes. This distinct feature of hydrogen-bonding ionophores is made possible by their use in amperometric sensing modes rather than potentiometric sensing modes, especially by observing the current response due to facilitated anion transfer across the interface between two immiscible electrolyte solutions. Further examination of various types of thiourea derivatives[3,13] as a hydrogen bond-forming ionophore may lead to a new design of novel amperometric anion sensors; this work is now in progress in our laboratory.

This work was supported by a Grant-in-Aid for Scientific Research (A), No. 11304054, from the Ministry of Education, Science, Sports and Culture, Japan, and RFTF of the Japan Society for the Promotion of Science.

References and Notes

1 a) F. P. Schmidtchen and M. Berger, *Chem. Rev.*, **97**, 1609 (1997). b) P. D. Beer, *Acc. Chem. Res.*, **31**, 71 (1998). c) T. S. Snowden and E. V. Anslyn, *Curr. Opin. Chem. Biol.*, **3**, 740 (1999). d) P. D. Beer and P. A. Gale, *Angew. Chem. Int. Ed.*, **40**, 486 (2001).

2 a) M. M. G. Antonisse and D. N. Reinhoudt, *Chem. Commun.*, **1998**, 443. b) P. Bühlmann, E. Pretsch, and E. Bakker, *Chem. Rev.*, **98**, 1593 (1998). c) M. M. G. Antonisse and D. N. Reinhoudt, *Electroanalysis*, **11**, 1035 (1999).

3 a) P. Bühlmann, S. Nishizawa, K. P. Xiao, and Y. Umezawa, *Tetrahedron*, **53**, 1647 (1997). b) S. Nishizawa, P. Bühlmann, K. P. Xiao, and Y. Umezawa, *Anal. Chim. Acta*, **358**, 35 (1998).

4 T. Shioya, S. Nishizawa, and N. Teramae, *J. Am. Chem. Soc.*, **120**, 11534 (1998).

5 a) Y. Yamamoto, T. Osakai, and M. Senda, *Bunseki Kagaku*, **39**, 655 (1990). b) M. Senda and Y. Yamamoto, in"Liquid–Liquid Interfaces, Theory and Methods," ed. by A. G. Volkov and D. W. Deamer, CRC Press, Inc., Boca Raton, FL, 1996; pp 277–293. c) S. Sawada, H. Torii, T. Osakai, and T. Kimoto, *Anal. Chem.*, **70**, 4286 (1998). d) S. Jadhav and E. Bakker, *Anal. Chem.*, **73**, 80 (2001).

6 a) Y. Shao and S. G. Weber, *J. Phys. Chem.*, **100**, 14714 (1996). b) Y. Shao, B. Linton, A. D. Hamilton, and S. G. Weber, *J. Electroanal. Chem.*, **441**, 33 (1998). c) H. J. Lee, C. M. Pereira, A. F. Silva, and H. H. Girault, *Anal. Chem.*, **72**, 5562 (2000). d) Q. Qian, G. S. Wilson, K. Bowman-James, and H. H. Girault, *Anal. Chem.*, **73**, 497 (2001). e) H. Ohnuki, N. Ito, K. Ichikawa, and M. Kataoka, *Electrochemistry*, **69**, 187 (2001).

7 a) J. Koryta, *Electrochim. Acta*, **24**, 293 (1979). b) S. Kihara, M. Suzuki, K. Maeda, K. Ogura, S. Umetani, M. Matsui, and Z. Yoshida, *Anal. Chem.*, **58**, 2954 (1986). c) T. Kakutani, Y. Nishiwaki, T. Osakai, and M. Senda, *Bull. Chem. Soc. Jpn.*, **59**, 781 (1986). d) Z. Samec and P. Papoff, *Anal. Chem.*, **62**, 1010 (1990). e) H. Matsuda, Y. Yamada, K. Kanamori, Y. Kudo, and Y. Takeda, *Bull. Chem. Soc. Jpn.*, **64**, 1497 (1991). f) F. Reymond, P.-A. Carrupt, and H. H. Girault, *J. Electroanal. Chem.*, **449**, 49 (1998).

8 a) K. P. Xiao, P. Bühlmann, S. Nishizawa, S. Amemiya, and Y. Umezawa, *Anal. Chem.*, **69**, 1038 (1997). b) K. P. Xiao, P. Bühlmann, and Y. Umezawa, *Anal. Chem.*, **71**, 1183 (1999).

9 T. Kakiuchi, in"Liquid–Liquid Interfaces, Theory and Methods," ed. by A. G. Volkov and D. W. Deamer, CRC Press, Inc., Boca Raton, FL, 1996; pp 1–18.

10 Because precise $\Delta\phi°$ values for CH_3COO^-, $H_2PO_4^-$, and SO_4^{2-} across the NB–water interface are not available, the association constants of the 1:1 complex between **3** and these anions were not determined.

11 Polarogram of **3**–HPO_4^{2-} transfer consists of several components, indicating that several binding stoichiometries, other than a 1:1 complex, exist in the NB phase.

12 The shift in $\Delta\phi_{1/2}$ with anion concentrations[7] should also be taken into account for this purpose.

13 a) S. Nishizawa, K. Shigemori, and N. Teramae, *Chem. Lett.*, **1999**, 1185. b) T. Hayashita, T. Onodera, R. Kato, S. Nishizawa, and N. Teramae, *Chem. Commun.*, **2000**, 755. c) R. Kato, S. Nishizawa, T. Hayashita, N. Teramae, *Tetrahedron Lett.*, **42**, 5053 (2001).