Novel Hg^{2+}-Ionophores Based on *N*-Hydroxylamide Derivatives as a Sensory Molecule for an Ion-Selective Electrode

Dwi Siswanta, Masanori Kin, Hideaki Hisamoto, and Koji Suzuki*
Department of Applied Chemistry, Keio University, 3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223

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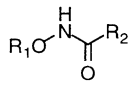
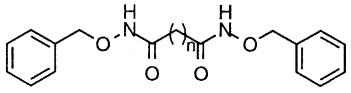
Several N-hydroxylamide derivatives were developed, exhibiting high selectivity for Hg^{2+}, which are useful as sensory molecules for a potentiometric ion sensor.

In the last decades, many intensive studies on the design and synthesis of highly selective ionophores as a sensory molecule for an ion-selective electrode (ISE) have been reported. In spite of successful progress in the designing of highly selective ionophores for alkali and alkaline earth metal ions, there is only a limited number of reports on the development of highly selective ionophores for transition and heavy metal ions.[1-2] Thus, the development of ISEs for these ions has seen little progress. For transition metal ions, nitrogen based ligands are of interest. Earlier, hydroxylamine derivatives had been employed as effective ligands mainly for Fe^{3+}, Cu^{2+}, V^{5+}, Al^{3+}, and Zn^{2+}.[3-4] Here we report the synthesis of novel nitrogen containing ionophores of the N-hydroxylamide type that showed very high selectivity for Hg^{2+}, which is a novel development in ionophore molecule design for a heavy metal ion.

Six ionophores based on N-hydroxylamide [R_1-ONH-COR_2] derivatives had been synthesized and their ion selectivity was investigated by potentiometric and ^{1}H-NMR measurements. Ionophore syntheses are as follows: O-methyl and O-benzyl hydroxylamine hydrochlorides were reacted with n-dodecanoyl chloride in pyridine to yield **1** (80%) and **2** (82%), respectively. O-Benzylhydroxylamine hydrochloride was reacted with adipoyl chloride or sebacoyl chloride in pyridine to yield **3** (82%) and **4** (86%), respectively. Ionophore **5** was prepared by reacting O-benzylhydroxylamine hydrochloride and pentadecanedioic acid using BOP (bis(2-oxo-3-oxazolidinyl)phosphinic chloride) in pyridine (yield 55%). Elemental analysis, IR and NMR data were in satisfactory agreement with the structures.[5] Ionophores **1** - **2** have one hydroxylamide unit with different units attached to the R_1 side, and **3** - **5** have two hydroxylamide units connected by alkylene chains of different length.





1: R_1= CH_3; R_2 = $C_{11}H_{23}$
2: R_1= $C_6H_5CH_2$; R_2 = $C_{11}H_{23}$

3 : n = 4
4 : n = 8
5 : n = 13

For the potentiometric selectivity measurement, the ionophores were incorporated in poly(vinyl chloride) (PVC) matrix membranes. The membrane composition was 2 wt% ionophore, 5 mol% (relative to the ionophore) KTpClPB (potassium tetrakis(4-chlorophenyl)borate), 32 wt% PVC and 66 wt% membrane solvent (o-nitrophenyl octyl ether, NPOE). The emf measurements were performed using a cell of the type:

Ag|AgCl|KCl (satd.)|| 0.3 M NH_4NO_3|| 10^{-3} M sample solution |membrane |10^{-3} M $AgNO_3$|AgCl|Ag.

All test solutions were made from nitrate salt and adjusted to pH 4.5 using 0.01 M (1M = 1 mol dm^{-3}) $Mg(CH_3COO)_2$-CH_3COOH buffer reagent. The selectivity coefficients (log k_{ij}^{pot}, i = Hg^{2+}, i = j = 10^{-3} M) were calculated from the response potentials using the separate solution method (SSM) based on the IUPAC recommendation.[6]

Table 1. Selectivity coefficient (log k_{ij}^{pot}, i = Hg^{2+}) of the electrodes based on ionophores **1** - **5**

	Ionophores					
Ion	**1**	**2**	**3**	**4**	**4**[a]	**5**
Cr^{3+}	-7.0	-10.1	-8.0	-13.1	(-8.1)	-9.5
Mn^{2+}	-6.0	-9.1	-7.6	-12.0	(-7.5)	-8.3
Fe^{3+}	-7.1	-10.3	-8.3	-12.8	(-7.9)	-9.1
Co^{2+}	-6.0	-8.8	-7.2	-11.8	(-7.4)	-7.7
Ni^{2+}	-6.2	-8.7	-8.0	-12.0	(-7.5)	-8.5
Cu^{2+}	-6.1	-8.2	-8.2	-12.1	(-7.6)	-8.7
Zn^{2+}	-6.2	-9.2	-7.9	-12.1	(-7.6)	-8.3
Cd^{2+}	-6.1	-8.9	-7.9	-11.8	(-7.4)	-8.2
Pb^{2+}	-5.7	-7.9	-2.3	-6.5	(-4.8)	-5.0
Li^{+}	-3.0	-5.8	-3.7	-9.0	(-6.0)	-4.9
Na^{+}	-2.9	-5.8	-4.1	-9.1	(-6.1)	-5.0
K^{+}	-2.8	-5.6	-3.3	-8.1	(-5.5)	-3.3
NH_4^{+}	-2.8	-5.6	-3.7	-8.6	(-5.8)	-4.0
Mg^{2+}	-6.0	-8.7	-6.8	-12.2	(-7.6)	-8.0
Ca^{2+}	-5.9	-8.5	-6.6	-12.0	(-7.5)	-8.6
Ag^{+}	-0.7	-2.2	0.6	-4.7	(-3.9)	-1.6

[a]Calculated based on the super-Nernstian response of the ISE.

The potentiometric selectivity coefficients of the ionophores are presented in Table 1. Normally, most of the ionophores based on soft bases (nitrogen or sulfur) exhibited high potentiometric responses to silver ion relative to other cations. Therefore, this study presented very uncommon examples of ionophores that were highly selective for Hg^{2+}. In the variation of the substituted unit on the hydroxyl group (**1** - **2**), the compound having a benzyl group on the hydroxyl section (**2**) was observed to exhibit a higher Hg^{2+} selectivity than the compound having a methyl group (**1**). Based on the fact that O-benzylhydroxylamide shows an effective unit for forming a highly Hg^{2+}-selective ionophore molecule, bis-hydroxylamides **3** - **5** were then prepared with the expectation that these bis-type compounds would form more Hg^{2+}-selective ionophores. Potentiometric measurements showed that only **4** exhibited better Hg^{2+} selectivity compared to the

mono-type **2**. This shows that the octylene unit is the best fit for connecting two hydroxylamide units in order to form a selective ligand for Hg^{2+}.

The response curve of the membrane electrode based on **4** exhibited a super-Nernstian slope, c.a. 70 mV/activity decade for 10^{-5} to 10^{-2} M Hg^{2+}. The response mechanism of this electrode is unknown exactly at present, but the reproducibility of this response was good with ± 2% r.s.d. for the Hg^{2+} test samples. Selectivity factors of the ISEs based on **4** which considered the super-Nernstian slope are also indicated in Table 1. The electrode based on **4** showed fast responses (t_{95} = ~10 s) to all ions tested, but the response potential was slowly restored (~ 5 min) to the base potential after the electrode was immersed in the test solution containing Hg^{2+}.

Hg^{2+} complexation was studied by ^1H NMR measurement using **4**, which was highly selective for Hg^{2+} in the potentiometric studies. The experiment was conducted by mixing various molar ratios of the ionophore and mercuric acetate in a DMSO-d3 and $CDCl_3$ (1:9) solvent mixture. ^1H NMR-spectra of the ionophore - Hg^{2+} complex showed that, with an increase in the mixture ratio of [Hg^{2+}]/[ionophore], the peak of α-CH_2 at 2.02 ppm decreased followed by an increased new peak at 2.35 ppm. The appearance of two peaks of α-CH_2 indicates that the exchange rate of the mercuric complex and the free ligand was kinetically slow on the NMR time scale. Plotting the integration of the peak at 2.35 ppm with the molar ratio of Hg^{2+} to the ionophore indicates that **4** forms a 1:1 complex with Hg^{2+}.

Another interesting observation on the ^1H NMR-spectra was the splitting of the peak of the methylene group of the benzyl unit at 4.86 ppm, from a singlet peak to a double-singlet peak. This fact indicates that the benzene ring of the benzyl group increases the rigidity of the complex, and decreases the freedom of the methylene unit of the benzyl group. The ion-free form of **4** did not show π-π interaction between the two benzene rings in the ionophore molecule. Thus the Hg^{2+}-complex structure based on **4** is concluded to be the model shown in Figure 1.

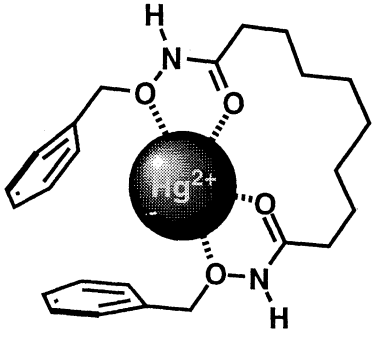


Figure 1. The proposed structure of the Hg^{2+}-**4** complex.

Similar ^1H NMR studies on **4** mixed with Ag^+ did not show any spectral shift or split as observed in the ^1H NMR spectra of the Hg^{2+}-complex. This suggests that **4** does not form stable complexes with Ag^+, which is additional evidence for the high Hg^{2+}-selectivity of **4**. Based on the selectivity factors shown in Table 1, ionophore **4** does not form a stable complex with the other tested 16 kinds of cations including Ag^+, which is the most serious interferent for the potentiometric measurement of Hg^{2+}.

While most studies on the development of nitrogen- or sulfur-containing ionophores for transition and heavy metal ions finally yielded silver ion selective ionophores, this study presents an example of a novel highly selective ionophore molecular design for Hg^{2+}.

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References and Notes

1 a) M. Oue, K. Akama, K. Kimura, M. Tanaka, and T. Shono, *J. Chem. Soc., Perkin Trans.1*, **1989**, 1675. b) S. Kamata and K. Onoyama, *Anal. Chem.*, **63**, 1295 (1991). c) J. K. Schneider, P. Hofstetter, and E. Pretsch, *Helv. Chim. Acta*, **63**, 217 (1980). d) E. Linder, K. Toth, E. Pungor, F. Behm, P. Oggenfuss, D. H. Welti, D. Ammann, W. E. Morf, E. Pretsch, and W.Simon, *Anal. Chem.*, **56**, 1127 (1984).

2 a) E. Malinowska, *Analyst*, **115**, 1085 (1990). b) V. Fiedler-Linnersund, *Anal. Chim. Acta*, **111**, 57 (1979). c) J. Casabo,L. Mestres, L. Escriche, F. Teixidor, and C. Perez-Jimenez, *J. Chem. Soc., Dalton Trans.*, **1991**, 1969. d) M. M. Bates, T. J. Cardwell, R. W. Cattrall, L. W. Deady, and K. Murphy, *Aust. J. Chem.*, **44**, 1603 (1991).

3 a) S. C. Shome, *Analyst*, **75**, 27 (1950). b) W.Szczepaniak, M.Ren, and K. Ren, *Chem. Anal.*, **24**, 51 (1979). c) K. Ren, *Chem. Anal.*, **37**, 193 (1992). d) N.V.Shvedene, N. M. Sheina, and G.V. Silasie, *Zh. Anal. Khim.*, **46**, 339 (1991). e) F. Vernon and H. Eccles, *Anal. Chim. Acta*, **77**, 145 (1975). f) J.Das and M.Pobi, *Fresenius J. Anal. Chem.*, **336**, 578 (1990). g) C. P. Brink and A. L. Crumbliss, *Inorg. Chem.*, **23**, 4708 (1984).

4 a) S. Hutchinson, G. A. Kearney, E. Horne, B. Lynch, J. D. Glennon, M. A. McKervey, and S. J. Harris, *Anal. Chim. Acta.*, **291**, 269 (1994).

5 Analytical data for **1**: ^1H-NMR (270 MHz, $CDCl_3$) δ (ppm) = 0.88 (t, 3H);1.26 (m, 16H); 1.58 (m, 2H); 2.02 (br, 2H); 3.76 (s, 3H); 8.22 (br, 1H). Found C, 68.43; H 12.16; N, 6.65%. Calcd for $C_{13}H_{27}NO_2$ (MW = 229.36): C, 68.08; H, 11.87; N, 6.11%. **2**: ^1H-NMR (270 MHz, $CDCl_3$) δ (ppm) = 0.88 (t, 3H);1.26 (m, 16H); 1.58 (m, 2H); 2.02 (t, 2H); 4.86 (s, 2H); 7.39 (m, 5H); 8.38 (br, 1H). Found C, 74.23; H 10.88; N, 4.48%. Calcd for $C_{19}H_{31}NO_2$ (MW = 305.46): C, 74.71; H, 10.23; N, 4.59%. **3**: ^1H-NMR (270 MHz, $CDCl_3$) δ (ppm) = 1.61 (s, 4H); 2.04 (br, 4H); 4.89 (s, 4H); 7.37 (s, 10H); 8.38 (br, 2H). Found C, 67.34; H 6.83; N, 7.81%. Calcd for $C_{20}H_{24}N_2O_4$ (MW= 356.42): C, 67.40; H, 6.79; N, 7.86%. **4**: ^1H-NMR (270 MHz, $CDCl_3$) δ (ppm) = 1.20 (s, 8H); 1.47 (t, 4H); 1.93 (br, 4H); 4.77 (s, 4H); 7.37 (s, 10H); 8.18 (br, 2H). Found C, 69.03; H 8.13; N, 6.79%. Calcd for $C_{24}H_{32}N_2O_4$ (MW = 412.53): C, 69.88; H, 7.82; N, 6.71%. **5**: ^1H-NMR (270 MHz, $CDCl_3$) δ (ppm) = 1.25 (s, 18H); 1.60 (t, 4H); 2.04 (br, 4H); 4.90 (s, 4H); 7.38 (s, 10H); 8.18 (br, 2H). Found C, 70.49; H 9.09; N, 5.29%. Calcd for $C_{29}H_{42}N_2O_4$ (MW = 482.66): C, 72.17; H, 8.77; N, 5.80%.

6 IUPAC Recomendation for Nomenclature of Ion-Selective Electrodes. *Pure and Appl. Chem.*, **48**, 129 (1976).