Lipophilic Thiacrown Ether Derivatives as Neutral Silver-ion Selective Carriers

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Lipophilic mono- and di-thiacrown ethers have been synthesized and their ion selectivities evaluated as neutral carriers of polymeric membrane Ag^+-selective electrodes. High Ag^+-selectivities and excellent electrode properties were realized with the thiacrown ethers.

The multi-purpose nature of silver makes its analysis in, and recovery from, waste material of importance.[1] In this connection, crown ether derivatives have been much investigated[2–4] and although they can complex Ag^+, they possess low selectivity for the ion. Such selectivity is governed by topological considerations, cavity sizes, and the nature of the donor atoms. Enhanced selectivity for Ag^+ is achieved when one or more oxygen donor atoms are replaced by sulphur in the crown ether.[5–7] Thus, not only has 1,4,7-trioxa-10,13-dithiacyclopentadecane been employed as a neutral carrier in a Ag^+-selective electrode,[8] but we have also reported that dodecylmonothia-16-crown-5 reveals high selectivity for Ag^+.[9]

Here we describe the synthesis of a series of new lipophilic thiacrown ethers, which contain one or two sulphur atoms and three or four oxygen atoms. The properties and ion-selectivities of the thiacrown compounds as neutral carriers in a Ag^+-selective polymeric membrane electrode are also discussed.

Results and Discussion

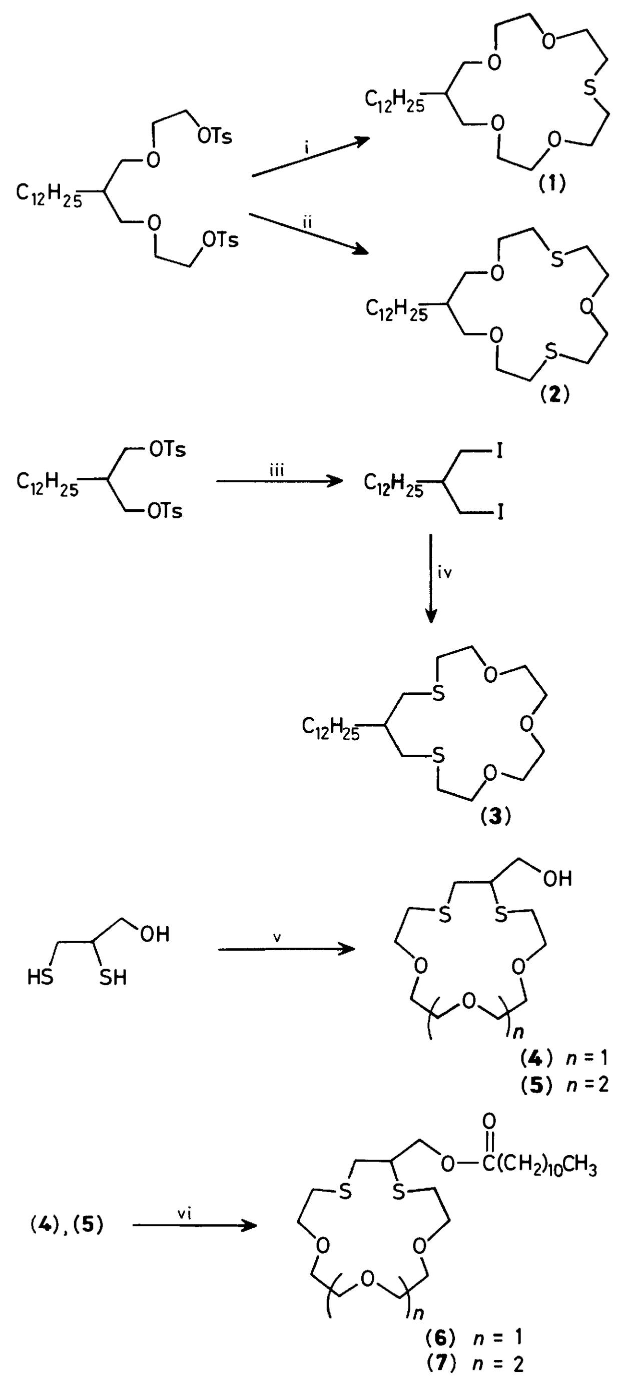
Synthesis.—Five kinds of lipophilic mono- or di- thiacrown ethers were synthesized (see Scheme). In compounds (**1**)—(**3**), a dodecyl group was introduced into a diol precursor before cyclization: 2-dodecylpropane-1,3-diol was obtained by reduction of the reaction product of diethyl malonate with dodecyl bromide. A variety of conditions were used for cyclization of the di-iodide and the dithiol but the method by Buter and Kellogg[10] using Cs_2CO_3 gave superior yields of product compared with the use of Na_2CO_3 as base[11] and the Williamson reaction. Only dithiacrown ether (**2**) was prepared from 5-dodecyl-3,7-dioxanonane-1,9-diol ditosylate and sodium 2,2′-oxydiethanethiolate because of the ease of deprotonation of the thiol with NaOH. The crude products containing many by-products were purified by silica gel chromatography to prevent decomposition of the resulting thiacrown ethers on distillation. Some of these purified products were kept under a nitrogen atmosphere, because they were unstable in air. Only Ag^+-thiacrown ether complexes (**8**)—(**10**) were isolated in crystalline form. The other Ag^+ complexes obtained by solvent extraction (see the Experimental section) failed to crystallize and were used without further purification. The Ag^+-thiacrown ethers were found to be 1:1 (Ag^+/crown) complexes by elemental analysis.

Ion-Selectivities.—Electrode responses for Ag^+-selective electrodes based on the Ag^+ complexes of thiacrown ethers (**1**)—(**7**) are shown in Figure 1. Nernstian response of Ag^+ activity change was in the range of 10^{-2}—10^{-5} mol l^{-1}. Selectivity coefficients for Ag^+ with respect to other cations of the Ag^+ electrodes are summarized in Figure 2. Both Ag^+ electrodes of the mono- and di-thiacrown ethers are highly Ag^+ selective. Hg^{2+} Interferes with the Ag^+ electrode response most seriously of all, but the selectivity coefficients (k^{Pot}_{AgM}) for Ag^+ with respect to Hg^{2+} is still in the range 6.5×10^{-3}—3.4×10^{-2} in the thiacrown ether-based electrodes. The selectivity coefficients for Ag^+ with respect to the heavy and transition metal ions are $< 10^{-3}$. Also, the selectivity coefficients for Ag^+ with respect to alkali and alkaline-earth metal ions are $< 10^{-4}$, their interference being negligible. Interestingly, the selectivities in the Ag^+ electrodes of the different thiacrown ethers are quite similar to each other in spite of a difference in the number and displacement of sulphur atoms among the thiacrown ethers. Since the selectivity of most of the thiacrown-based Ag^+-selective electrodes is superior to that of conventional Ag_2S-based Ag^+-electrodes, their future seems promising.

Experimental

General.—The membrane solvent or plasticizer, dioctyl phthalate (DOP) was distilled *in vacuo*. Poly(vinyl chloride) (PVC, average polymerization degree of 1100) was twice purified by reprecipitation from tetrahydrofuran (THF) in methanol. The metal salts were nitrates of analytical grade and purchased from Wako Pure Chemicals. Water was de-ionized and distilled.

Synthesis of 3-*Dodecyl*-1,15,11-*trioxa*-8,14-*dithiacyclohexadecane or Dodecyl-dithia*-16-*crown*-5 (**2**).—NaOH (0.2 g, 5 mmol) was added to ethanol (200 ml) and the mixture was refluxed. A solution of 5-dodecyl-3,7-dioxanonane-1,9-diyl ditosylate (1 g, 1.56 mmol) and 2,2′-oxydiethanethiol (0.216 g, 1.56 mmol) in ethanol (50 ml) was added dropwise to the refluxing solution over 4 h; the mixture was then refluxed for a further 7 h. After this, the solvent was removed under reduced pressure, and the residue diluted with water (50 ml) and extracted with $CHCl_3$ (50 ml × 3). The organic layer was separated, dried ($MgSO_4$), and evaporated under reduced pressure to give a crude, yellow viscous liquid which was purified by silica gel column chromatography [ethyl acetate–hexane (1:5), R_F 0.5] to yield thiacrown ether (**2**) as white crystals (136 mg, 20%), m.p. 38.0—38.5 °C (Found: C, 63.55; H, 10.55; S, 14.7%; M^+, 434. $C_{23}H_{46}O_3S_2$ requires C, 63.54; H, 10.67; S, 14.75%; *M*, 434); $\nu_{max.}$ 2 920 and 2 850 (CH), and 1 120 cm^{-1} (C–O–C); δ_H (100 MHz; CCl_4) 0.88 (3 H, t, *J* 6 Hz, Me), 1.20—1.84 [23 H, m, $(CH_2)_{11}CH$], 2.60—3.00 (8 H, m, CH_2SCH_2), and 3.26—4.08 (12 H, m, CH_2OCH_2).



Scheme. *Reagents and conditions:* i, $(HOCH_2CH_2)_2S$, NaH, dioxane; ii, $(HSCH_2CH_2)_2O$, NaOH, EtOH; iii, NaI, Me_2CO; iv, $HSCH_2(CH_2OCH_2)_3CH_2SH$, $CsCO_3$, DMF; v, $I(CH_2)_2OCH_2(CH_2OCH_2)_n CH_2O(CH_2)_2I$, $CsCO_3$, DMF; vi, $Me(CH_2)_{10}COCl$, Et_3N, benzene

Synthesis of 12-*Dodecyl*-1,4,9-*trioxa*-10,14-*dithiacyclohexadecane or Dodecyl-dithia*-16-*crown*-5 (**3**).—A mixture of 2-dodecylpropane-1,3-diyl ditosylate (2.09 g, 3.78 mmol) and NaI (1.5 g, 10 mmol) in acetone (50 ml) was refluxed for 3 h. The resulting insoluble salt was filtered off and the filtrate was evaporated under reduced pressure. To the residue was added water (30 ml) and benzene (50 ml). The organic layer was separated, washed successively with water, aqueous $Na_2S_2O_3$ and saturated brine, dried (Na_2SO_4), and evaporated to yield 2-dodecyl-1,3-di-iodopropane (1.7 g).

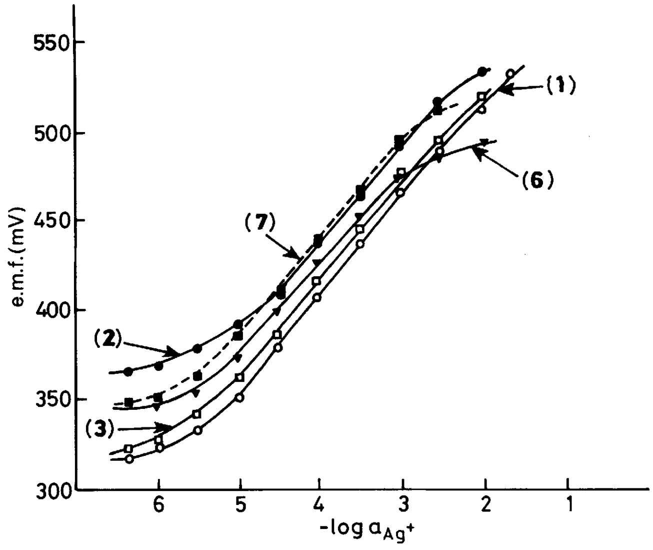


Figure 1. Electrode response of Ag^+-selective electrodes based on Ag^+ complexes of thiacrown ethers (**1**)—(**7**)

Cesium carbonate (2.0 g, 6.1 mmol) in dry dimethylformamide (DMF) (500 ml) was heated at 50 °C under a nitrogen atmosphere. To this solution the di-iodide (1.7 g) dissolved in dry DMF (100 ml) solution and 2,2′-[oxybis(ethyleneoxy)]diethanethiol (0.898 g, 3.97 mmol) was added dropwise over 5 h and the reaction was continued for over 8 h. The solvent was then removed under vacuum, water (50 ml) was added to the residue and the mixture was extracted with $CHCl_3$ (50 ml × 3). The organic layer was dried ($MgSO_4$) and evaporated to give a viscous liquid which was purified by silica gel column chromatography [ethyl acetate–hexane (1:3), R_F 0.3] to yield pure product (**3**) as aligned (373 mg, 22.0%) (Found: C, 63.55; H, 10.65; S, 14.55%; M^+, 434. $C_{23}H_{46}O_3S_2$ requires C, 63.54; H, 10.67; S, 14.75%; *M*, 434); $\nu_{max.}$ 2 900 and 2 825 (CH), and 1 115 cm^{-1} (C–O–C); δ_H(100 MHz; $CDCl_3$) 0.88 (3 H, t, *J* 6 Hz, CH_3), 1.12—1.60 (22 H, m, CH_2), 1.60—1.92 (1 H, br, CH), 2.64—2.88 (8 H, m, CH_2SCH_2), and 3.60—3.88 (12 H, m, CH_2OCH_2).

Synthesis of 12-*Hydroxymethyl*-1,4,7-*trioxa*-10,13-*dithiacyclopentadecane or Hydroxymethyl-dithia*-15-*crown*-5 (**4**).—Dry DMF (1.5 l) containing Cs_2CO_3 (3.58 g, 11 mmol) was heated and stirred at 50 °C under a nitrogen atmosphere. To this solution, a solution of 2,3-dimercaptopropan-1-ol (1.24 g, 10 mmol) and 1,11-di-iodo-3,6,9-trioxaundecane (4.14 g, 10 mmol) in dry DMF (200 ml) was gradually added over 5 h; this step was repeated. After the reaction, the solvent was removed, water (100 ml) was added to the residue, and the aqueous layer was extracted with $CHCl_3$ (100 ml each) several times. The combined organic layers were dried ($MgSO_4$) and evaporated. The crude liquid was purified by silica gel chromatography [ethyl acetate–benzene (3:2), R_F 0.3] to yield pure product (**4**) as a liquid (6.20 g, 73%) (Found: C, 46.25; H, 7.75; S, 22.1%; M^+, 282. $C_{11}H_{22}O_4S_2$ requires C, 46.78; H, 7.85; S, 22.70%; *M*, 282); $\nu_{max.}$ 3 400 (OH), 2 910 and 2 860 (CH), and 1 120 cm^{-1} (C–O–C); δ_H(100 MHz; $CDCl_3$) 2.60—3.00 (6 H, m, SCH_2), 3.20—3.48 (1 H, m, CH), and 3.60—3.88 (15 H, m, OCH_2, OH).

Synthesis of 15-*Hydroxymethyl*-1,4,7,10-*tetraoxa*-13,16-*dithiacyclo-octadecane or Hydroxymethyl-dithia*-18-*crown*-6 (**5**).—The synthetic procedure was similar to that for (**4**). In this case, 1,14-di-iodo-3,6,9,12-tetraoxatetradecane (4.58 g, 10 mmol) was used instead of 1,11-di-iodo-3,6,9-trioxaundecane The resulting crude product was purified by silica gel chromatography [ethylacetate–benzene (1:1); R_F 0.2] to yield (5) as a liquid 5.86 g, 60%) (Found: C, 47.9; H, 7.95; S, 19.25%; M^+, 326. $C_{13}H_{26}O_5S_2$ requires C, 47.83; H, 8.03; S, 19.64%; M, 326); $\nu_{max.}$ 3 400 (OH), 2 900 and 2 830 (CH), and 1 100 cm^{-1} (C–O–C); δ_H(100 MHz; $CDCl_3$) 2.66—3.00 (6 H, m, SCH_2), 3.12—3.36 (1 H, m, CH), and 3.60—3.88 (19 H, m, OCH_2, OH).

Synthesis of 12-*Dodecanoyloxymethyl*-1,4,7-*trioxa*-10,13- *dithiacyclopentadecane* (**6**).—A stirred mixture of (**4**) (0.572 g, 2.03 mmol), dry benzene (40 ml), and triethylamine (0.85 ml) was cooled to 0 °C and a solution of dodecanoyl chloride (1.4 ml) in dry benzene (20 ml) was gradually added to it; this solution was then stirred at room temperature for a further 6 h. After this the resulting insoluble salt was filtered off and the filtrate was washed successively with saturated aqueous $NaHCO_3$ and saturated brine. The organic layer was separated, dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by silica gel chromatography [ethyl acetate–hexane (1:3), R_F 0.3] to yield the pure product (**6**) as a liquid (541 mg, 57%) (Found: C, 59.35; H, 9.55; S, 13.85%; M^+, 464. $C_{23}H_{44}O_5S_2$ requires C, 59.45; H, 9.54; S, 13.80%; M, 464); $\nu_{max.}$ 2 900 and 2 825 (CH_2), 1 720 (CO), and 1 100 cm^{-1} (C–O–C); δ_H(100 MHz, $CDCl_3$) 0.88 (3 H, t, J 6 Hz, Me), 1.20—1.80 [18 H, m, $Me(CH_2)_9CH_2$], 2.32 [2 H, t, J 7 Hz, $O_2CCH_2(CH_2)_9Me$], 2.68—3.00 (6 H, m, SCH_2), 3.24—3.52 (1 H, m, CH), 3.60—3.86 (12 H, m, OCH_2), and 4.38 [2 H, d, J 5 Hz, $CH_2O_2C(CH_2)_{10}Me$].

Synthesis of 15-*Dodecanoyloxymethyl*-1,4,7,10-*tetraoxa*-13,16-*dithiacyclo-octadecane* (**7**).—Compound (**7**) was synthesized in a similar way to compound (**6**). The product was purified by silica gel chromatography [ethyl acetate–hexane (1:1), R_F 0.3] to yield (**7**) as a liquid (310 mg, 80%) (Found: C, 59.05; H, 9.55; S, 12.55%; M^+, 508. $C_{25}H_{48}O_6S_2$ requires C, 59.02; H, 9.51; S, 12.60%; M, 508); $\nu_{max.}$ 2 900 and 2 840 (CH), 1 720 (CO), and 1 115 cm^{-1} (C–O–C); δ_H(100 MHz, $CDCl_3$) 0.88 (3 H, t, J 6 Hz, Me), 1.20—1.80 [18 H, m, $Me(CH_2)_9CH_2$], 2.32 [2 H, t, J 7 Hz, $OOCCH_2(CH_2)_9Me$], 2.68—3.00 (6 H, m, SCH_2), 3.16—3.44 (1 H, m, CH), 3.60—3.84 (16 H, m, OCH_2), and 4.34 [2 H, d, J 5 Hz, $CH_2OOC(CH_2)_{10}Me$].

Synthesis of Ag^+-*Thiacrown Ether Complexes.*—The Ag^+-thiacrown ether (1:1) complexes were prepared as follows. Equal volumes (4 ml) of a solution of thiacrown ether (0.05 mmol) in chloroform and 1M aqueous $AgNO_3$ were mixed and stirred in a stoppered test tube in the dark for 3 h. The organic layer was then separated and evaporated and the residue was recrystallized from benzene to yield white crystals.

Ag^+-(**1**) complex (**8**) (50 mg, 44%), m.p. 104—105 °C (Found: C, 46.7; H, 7.9; N, 2.4%. $C_{23}H_{46}O_4S{\cdot}AgNO_3$ requires C, 46.94; H, 7.88; N, 2.38%); $\nu_{max.}$ 2 920 and 2 845 (CH), 1 120 and 1 100 cm^{-1} (C–O–C).

Ag^+-(**2**) complex (**9**), was also recrystallized from benzene to yield white crystals (35 mg, 78%), m.p. 88—89 °C (Found: C, 45.4; H, 7.6; N, 2.3%. $C_{23}H_{46}O_3S_2{\cdot}AgNO_3$ requires C, 45.69; H, 7.67; N, 2.32%); $\nu_{max.}$ 2 910 and 2 840 (CH), and 1 120 cm^{-1} (C–O–C).

Ag^+-(**3**) complex (**10**), was formed in quantitative yield as white crystals, m.p. 37.5—38.5 °C (Found: C, 45.3; H, 7.8; N, 2.2. $C_{23}H_{46}O_3S_2{\cdot}AgNO_3$ requires C, 45.69; H, 7.67; N, 2.32%); $\nu_{max.}$ 2 900 and 2 840 (CH), and 1 120 cm^{-1} (C–O–C).

The other Ag^+-thiacrown ether complexes could not be crystallized. Elemental analysis and i.r. absorptions for Ag^+-thiacrown ether complexes (**6**) and (**7**) are as follows: Ag^+-(**6**) complex (**11**), was formed in quantitative yield as a liquid, (Found: C, 44.3; H, 7.25; N, 1.95. $C_{23}H_{44}O_5S_2{\cdot}AgNO_3$ requires C, 43.53; H, 6.69; N, 2.21%); $\nu_{max.}$ 2 900 and 2 850 (CH), 1 730 (CO), and 1 100 cm^{-1} (C–O–C). Ag^+-(**7**) complex (**12**), was also formed in quantitative yield as a liquid (Found: C, 44.4; H, 7.25; N, 2.1%. $C_{25}H_{48}O_6S_2{\cdot}AgNO_3$ requires C, 44.25; H, 7.13; N, 2.06%); $\nu_{max.}$ 2 920 and 2 850 (CH), 1 740 (CO), and 1 120 cm^{-1} (C–O–C).

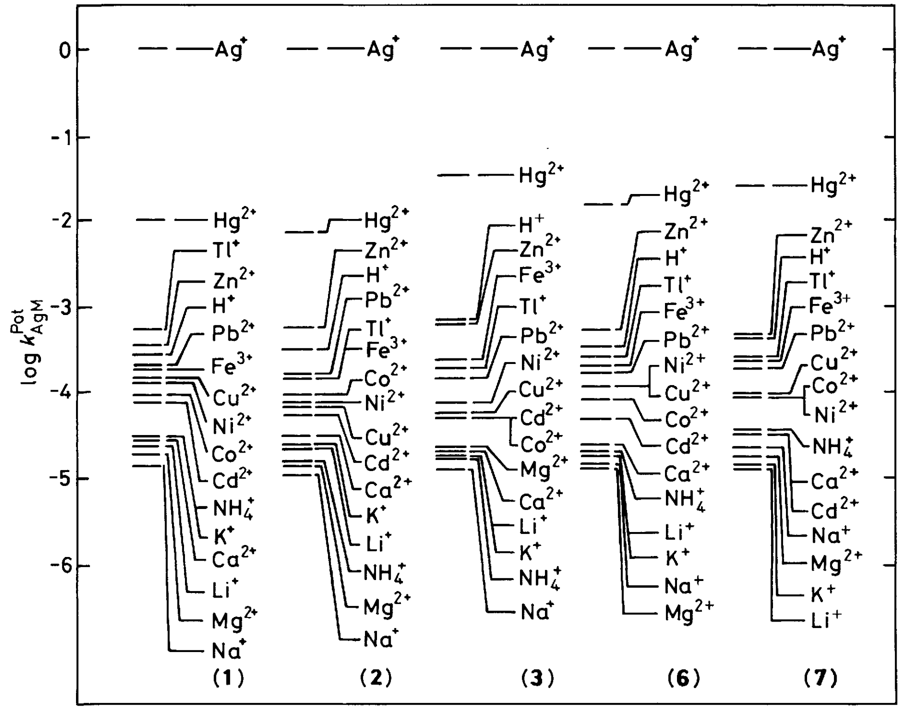


Figure 2. Selectivity coefficients for Ag^+ with respect to other cations in thiacrown-based electrodes

Fabrication of Electrodes.—The procedure for the electrode was similar to that described previously.[12] The PVC membranes containing the Ag^+-neutral carrier complex were cast from THF. A typical membrane consisted of 27.5 wt% PVC, 3.3 wt% Ag^+-thiacrown ether complex, 68.9 wt% dioctyl phthalate (DOP) as membrane solvent (plasticizer), and 0.3 wt% dipicrylamine sodium salt (NaDPA) as lipophilic salt (0.1 mol% to the Ag^+-thiacrown ether complex). A Philips IS-561 electrode body was equipped with a 7 mm diameter disc of the PVC membrane. The internal filling solution was 1×10^{-1}M aqueous $AgNO_3$. The electrodes were conditioned by soaking in 1×10^{-3}M $AgNO_3$ solution overnight.

Measurements of E.m.f.—The measurements were carried out with a pH/mV meter (Corning Model M-130) at 25 °C. The electrochemical cell was Ag–AgCl/10^{-3}M $AgNO_3$/membrane/measured solution/0.1M NH_4NO_3/4M KCl/AgCl–Ag. The potentiometric selectivity coefficients k^{Pot}_{AgM}, were determined by a mixed solution method (fixed interference method).[13] The constant background concentrations were 5×10^{-1}M for alkali and alkaline-earth metal ions and NH_4^+, 5×10^{-2}M for H^+ and heavy metal ions, and 5×10^{-5}M for Hg^{2+}.

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