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Methylmercury(II) complexes with 2-mercaptopyridinecarboxylic acids

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The stability constants of the complexes $[MeHgL]^-$ (H_2L = 2-mercaptopyridine-3-carboxylic acid, 2-mercaptopyridine-4-carboxylic acid, 2-mercaptopyridine-5-carboxylic acid and 2-mercaptopyridine-6-carboxylic acid) have been obtained by differential pulse polarography. The values of log β_1 are in the range 14.14–14.96 at 20 °C and ionic strength 0.1 mol dm^{-3}. The complexes MeHgHL have been isolated and characterized by chemical analysis and mass and IR spectrometry.

Keywords: Methylmercury, complexes, pyridinecarboxylic acids, stability constants, mass spectra, IR spectra

INTRODUCTION

Interest in understanding the toxic behaviour of the methylmercury(II) cation and in finding new, effective antidotes against poisoning by this agent has increased research on its solution and solid-state chemistry, especially as regards its complexes with ligands which possess the thiol group, a known receptor for the cation in biological media. Within a wider study of the coordination chemistry of the $MeHg^+$ cation with sulphydrylated ligands,[1-3] the stability constant of its complex with 2-mercaptopyridine (HMPy) has been determined[4] and the structure of MeHgMPy studied by X-ray diffraction.[5] The large value of log β (15.85) indicates a high thermodynamic stability in water, a desirable quality for therapeutic use (though not the only requisite).

The carboxylated derivatives of HMPy (Scheme 1), 2-mercaptopyridine-3-carboxylic acid [$H_2L(1)$]; 2-mercaptopyridine-4-carboxylic acid [$H_2L(2)$]; 2-mercaptopyridine-5-carboxylic acid [$H_2L(3)$] and 2-mercaptopyridine-6-carboxylic acid [$H_2L(4)$], have been extensively studied as regards their physicochemical (Ref. 6 and refs therein) and pharmacological[7] properties. We have now studied their coordination behaviour with $MeHg^+$, looking for possible influences of the carboxylate group on the stability and/or spectroscopic and structural properties of the complexes.

EXPERIMENTAL

Chemicals

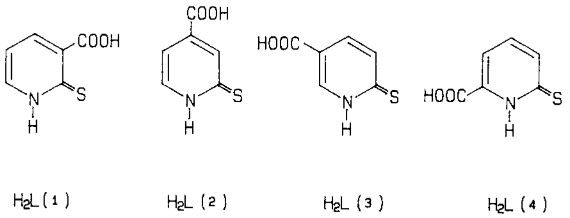
Methylmercury(II) hydroxide was prepared by stirring a methylmercury(II) chloride (ROC/RIC) suspension with excess silver(I) oxide in water.[5] The ligands were prepared by the procedure described previously.[8]

Determination of stability constants

The stability of the complexes of methylmercury(II) with the totally deprotonated ligands were obtained using differential pulse polarography (DPP) and the simplified DeFord–Hume equation for Fo (Eqn [1]).[4,9]

$$\exp[-\Delta E_p F/RT - \Delta\ln(i_p^c/i_p^s)] = \beta_1[L^{2-}] = F_0 \qquad [1]$$

where ΔE_p represents the difference between the peak potentials of methylmercury in the presence (E_p^c) and in the absence (E_p^s) of ligand, i_p^c and i_p^s



Scheme 1

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the respective *maximum* currents and β_1 the stability constant for the 1 : 1 complex of $MeHg^+$ with the ligand. Although the reduction of the cations at the mercury electrodes is complicated for the $MeHg^+$ complexes,[10, 11] the DeFord–Hume method is valid for determining their stability constants.[4, 10]

All measurements were carried out at 20 ± 0.5 °C in $NaNO_3/NaOH$ solutions with $\mu = 0.1$ and pH 12.7 (to ensure that the ligand is fully deprotonated). In this medium Eqn [1] can be used because of the relative magnitudes of the stability constants of the complexes of methylmercury(II) with OH^- and with the ligands studied here (Ref. 10 and results below).

The methylmercury(II) cation was added as hydroxide at a concentration of 1×10^{-5} mol dm^{-3}, and the ligand concentration was varied in 1×10^{-4} steps between 5×10^{-4} and 5×10^{-3} mol dm^{-3}. These limits ensure a practically constant concentration of ligand around the electrode during the reduction of the complex.[12] Equation [1] was fitted to the experimental data with a highly interactive program implemented on a Texas Instruments DS990 microcomputer with the operating system SBC-990-BASIC.

DP-polarograms were recorded with a PAR model 174 polarographic analyser in conjunction with a PAR 174/70 drop timer. A thermostated three-electrode cell was used throughout. The indicator electrode was a mercury dropping electrode with a mechanically controlled droptime of 2 s, the auxiliary electrode a platinum wire, and the reference a saturated calomel electrode connected to the cell via a salt bridge (1 mol dm^{-3} aqueous $NaNO_3$ solution) with Corning Vycor disc interfaces. The pulse amplitude was −50 mV and the potential scan rate was 0.5 mV s^{-1} to increase the precision of the peak potential measurements. Oxygen was removed from the polarographic solutions by bubbling oxygen-free nitrogen for 15 min before the measurements started.

Preparation of compounds

Complexes MeHgHL were prepared by adding the appropriate ligand solutions in methanol to an aqueous MeHgOH solution until a molar ratio of 1 : 1 was reached; MeHgHL(2) was obtained using a slight excess of ligand. In general there immediately formed a white solid [beige in the case of MeHgHL(1)], which was filtered off and vacuum-dried.

Chemical analyses

MeHgHL(1). Found (%): C, 23.5; H, 1.9. Calcd (%): C, 22.7; H, 1.9. M.p.: 200 °C (decomposition).
MeHgHL(2). Found (%): C, 24.1; H, 1.9. Calcd (%): C, 22.7; H, 1.9. M.P.: 250 °C (decomposition).
MeHgHL(3). Found (%): C, 24.1; H, 2.0. Calcd (%): C, 22.7; H, 1.9. M.p.: 285 °C.
MeHgHL(4). Found (%): C, 22.4; H, 1.9. Calcd (%): C, 22.7; H, 1.9. M.p.: 241 °C.

Recrystallization of MeHgHL(2) and MeHgHL(3) to improve the analytical data was not possible. Nevertheless, the mass spectra of all the compounds showed the molecular ion (*vide infra*). Although polarography showed that these complexes could be deprotonated (*vide infra*), this reaction was not explored.

Physical measurements

Analytical data were obtained from Galbraith Lab. Inc., Knoxville, Tennessee, USA. Melting points were determined in an Electrothermal apparatus. Mass spectra were recorded on a Kratos MS 50 apparatus connected to a DS90 data system and operating under EI conditions (direct insertion probe, 70 ev, 250 °C). All the ions were identified using DS90 software. The IR spectra were recorded in Nujol mulls and KBr discs on a Perkin–Elmer 180 apparatus.

RESULTS AND DISCUSSION

Stability constants

Table 1 shows the peak potential values for the various ligand concentrations used, together with the values of

$$F_0 = \exp[-\Delta E_p F/RT - \Delta\ln(i_p^c/i_p^s)]$$

calculated from them. Figure 1 shows F_0 plotted against the ligand concentration for the system $H_2L(1)$–$MeHg^+$ (very similar results were obtained for the other systems); the linearity of the plot confirms that only 1 : 1 complexes were present. At the foot of Table 1 are the parameters of the regression lines fitted to the F_0–concentration data for each system. The slopes are the stability constants of the complexes. The logarithms of the constants, also shown in Table 1, lie in the range 14.0–15.0.

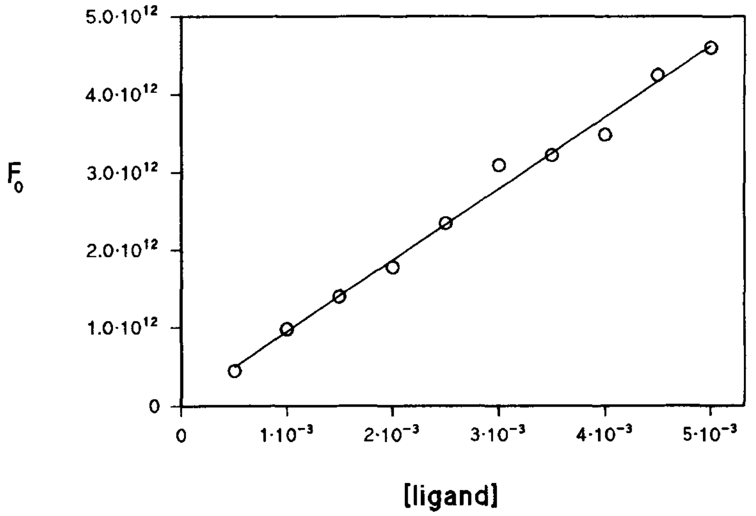

Figure 1 The DeFord–Hume function F_0 against the concentration (mol dm^{-3}) of 2-mercaptopyridine-3-carboxylic acid in $NaNO_3$/NaOH media of pH 12.7 and ionic strength 0.1 mol dm^{-3} containing 1×10^{-5} mol dm^{-3} methylmercury.

In previous work,[4] the value of $\log\beta_1$ for the complex of methylmercury with 2-mercaptopyridine was determined as 15.81. The slightly lower values of Table 1 show that the carboxylate group weakens the donor power of the ligand. The value of $\log\beta_1$ correlates with the known macroscopic protonation constants ($1/K_{a3}$) of the ligands[13–15] even when 2-mercaptopyridine is included[4,16] though in this case the regression coefficient is poorer. If microscopic —SH group protonation constants are used (6.14,[13] 6.54,[14] and 7.14,[15] for $H_2L(2)$, $H_2L(3)$ and $H_2L(4)$, respectively), the correlation with $\log\beta_1$ improves ($\log\beta_1 = 10.42 \log 1/k_{SH} + 0.60$; $r^2 = 0.9977$). A linear correlation was observed previously in other methylmercury(II) compounds with thiols.[17] The absence of more data precludes further discussion.

The values of $\log\beta_1$ obtained in this work (Table 1) are smaller than those obtained for

Table 1 Peak potential and F_0 values for different ligand concentrations, with the parameters of the linear regression of F_0 on ligand concentration, and $\log\beta_1$.

$$F_0 = \exp[-\Delta E_p F/RT - \Delta\ln(i_p^c/i_p^s)]$$

	$H_2L(1)$		$H_2L(2)$		$H_2L(3)$		$H_2L(4)$	
$[L]/10^{-3}$	E	$F_0/10^{12}$	E	$F_0/10^{11}$	E	$F_0/10^{12}$	E	$F_0/10^{12}$
0.5	−0.808	0.44	−0.773	1.10	−0.776	0.13	−0.793	0.25
1.0	−0.828	0.98	−0.778	1.35	−0.793	0.25	−0.807	0.43
1.5	−0.837	1.41	−0.786	1.85	−0.800	0.33	−0.820	0.72
2.0	−0.843	1.79	−0.794	2.54	−0.806	0.41	−0.826	0.91
2.5	−0.850	2.36	−0.798	2.97	−0.813	0.54	−0.832	1.15
3.0	−0.857	3.11	−0.805	3.92	−0.821	0.75	−0.841	1.65
3.5	−0.858	3.24	−0.809	4.59	−0.822	0.78	−0.842	1.72
4.0	−0.860	3.50	−0.816	6.06	−0.825	0.88	−0.846	2.01
4.5	−0.865	4.27	−0.816	6.06	−0.829	1.03	−0.851	2.45
5.0	−0.867	4.62	−0.819	6.83	−0.832	1.15	−0.853	2.65
r^2	0.9966		0.9954		0.9960		0.9904	
Intercept	1.12×10^{10}		-2.40×10^{10}		-7.24×10^{9}		-1.13×10^{11}	
β_1	9.19×10^{14}		1.39×10^{14}		2.27×10^{14}		5.48×10^{14}	
$\log\beta_1$	14.96		14.14		14.35		14.74	

Table 2 Main IR data for the complexes prepared[a]

	ν(C=O)	ν(C—O)	δ(OH)	δ_{sym}Me	γ(C—H)	ν(Hg—C)
MeHgHL(0)[b]	—	—	—	1170 m	750 s, 720 s	535 m
MeHgHL (1)	1680 s, b	1390 s	1300 s	1170 m	765 s, 725 s	535 m
MeHgHL (2)	1710 s, b	1360 s	1280 s	1170 m	770 s, 735 s	540 m
MeHgHL (3)	1690 s, b	1365 m	1300 s	1165 m	770 s, 725 m	540 m
MeHgHL (4)	1700 s, b	1385 m	1310 s	1170 m	760 m, 755 m, 725 m	540 m

[a] s = strong; m = medium; b = broad. [b] HL(0), 2-mercaptopyridine.

complexes of methylmercury(II) with the amino-acids cysteine, glutathione, penicillamine and *N*-acetylpenicillamine, which are in the range 16.0–17.0.[18–20]

Mass and IR spectra

To determine the donor atoms used by the ligands we synthesized the complexes MeHgHL. The poor solubility of these complexes in common solvents prevented their study in solution, but their mass and IR spectra were studied.

Mass spectra

The ions $[M]^+$, $[MeHg]^+$, $[Hg]^+$, and $[L—H]^+$ or $[L—COOH]^+$ were the main charge carriers, together with some ligand fragments. As was observed in related compounds, e.g. methylmercury(II) thiouracillate,[2] the signal of the molecular ion $[M]^+$ was in general very intense, although the base peak corresponded to the deprotonated or decarboxylated ligand.

IR spectra

The ligand vibrations most relevant to coordination diagnosis and the organometallic fragment vibrations of all the complexes prepared are listed in Table 2 together with data for methyl(pyridine-2-thiolato)mercury(II), MeHgL(0). The structure of the latter complex, as fully determined by X-ray diffraction,[5] shows coordination through the S atom and a weak Hg–N interaction; its pyridine-ring vibration pattern is closer to that of the 2,2′-dipyridine disulphide than to that of the free ligand,[21] showing that coordination induces a thione-to-thiol transformation and restores aromaticity.[5,21,22] Since the vibration pattern of the carboxylated compounds is similar, coordination through the S atom seems likely in these too. On the other hand, the positions of ring vibrations near 1000 cm^{-1} and 650 cm^{-1}, and of the γ(C—H) vibrations, show the participation of the N atom in coordination[21] more clearly than for MeHgL(0). The ligand carboxylic acid group is protonated with the ν(C=O) band of the complexes located near 1700 cm^{-1}, and the ν(C—O) and δ(O—H) bands near 1400 and 1300 cm^{-1} respectively, being slightly shifted from their positions for the free ligands. These shifts may be due to the alteration of hydrogen bonding via the —COOH group.

With regard to the organometallic fragment, δ_{sym}Me and ν(Hg—C) are located in positions close to those found for other systems in which the Hg is bound to similar atoms.[1,5] Rigorous identification of ν(Hg—S) is difficult because the ligand spectra are complicated in the 350–200 cm^{-1} range, the bands of which probably have a contribution from ν(Hg—S).[5]

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