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THE SELENIUM-MERCURY INTERACTION: SYNTHESIS, SPECTROSCOPIC AND X-RAY STRUCTURAL STUDIES OF METHYLMERCURY-SELENOUREA COMPLEXES

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SUMMARY

The synthesis of selenium bound selenourea complexes of methylmercury, $[CH_3HgSeC(NH_2)_2]X$ (X=Cl, Br, NO_3, ClO_4) are described. A single crystal X-Ray analysis of the nitrate salt has provided for the first time bond length data pertinent to the biologically important mercury-selenium interaction. Crystals of $[CH_3HgSeC(NH_2)_2]NO_3$ belong to the space group $Pn2_1c$ with a = 7.524(1), b = 11.204(2), c = 9.738(2)Å, and Z = 4. The structure was solved and refined using 561 observed reflections measured on a Syntex $P2_1$ diffractometer to a final R value of 0.037. The mercury atom is linearly coordinated to the methyl group and the selenium atom of the selenourea with Hg-Se of 2.477(3)Å. Strong Hg-Se bonding is indicated by the X-Ray data and by the ^1H - ^{199}Hg nmr coupling constants. A comparison of spectroscopic data for analogous thio and selenourea complexes is presented.

INTRODUCTION

One of the most remarkable features of the toxicology of mercury is the ability of dietary selenium to protect against and actually reverse the toxic effects of inorganic and organomercurials [1]. There have been numerous recent reports that sodium selenite effectively counteracts mercury (Hg^{2+}) poisoning in rats or methylmercury intoxication in Japanese quail [2,3]. Trace levels of selenium in tuna fish provide protection to rats fed simultaneously with methylmercury [4] and there is evidence to indicate that selenite (SeO_3^{2-}) can release mercury from its linkage to proteins [3]. Unfortunately, although several naturally occurring selenoproteins (e.g. erythrocyte glutathione reductase) and aminoacids (e.g. selenomethionine, selenocystathionine) have now been identified [1,5] and there is general agreement that a true antagonism exists between mercury and selenium, the mechanism by which selenium decreases the toxicity of mercury is uncertain. Data on tissue levels of total mercury in animals protected by selenium supplemented diets suggest that selenium does not reduce the absorption nor increase the excretion of mercury since mercury levels are frequently as high or higher in the protected animals [1]. It seems that selenium may alter the tissue distribution of mercury or substantially modify its biological activity but until recently the pertinent chemistry of mercury-selenium compounds was virtually unexplored.

There is indirect proton-nmr evidence suggesting that selenium in selenocyanate [6] or selenoamino acids [7a,b] has a higher affinity for CH_3Hg^+ than sulfur in the corresponding thiocyanate or sulfur amino acids, but very few complexes of organomercurials with selenium ligands have been isolated and characterised. We report herein the synthesis and spectroscopic comparison of thiourea and selenourea complexes of methylmercury as well as an X-Ray analysis of $[CH_3HgSeC(NH_2)_2]NO_3$ which provides the first accurate structural data for a mercury-selenium compound.

EXPERIMENTAL

Synthesis

Hot deoxygenated aqueous solutions of CH_3HgX (X = NO_3, ClO_4, Cl, Br) (5.0 m mol) were added to a refluxing solution of a stoichiometric amount of the requisite thio or selenourea under nitrogen. After ca. 30 min., the solution was filtered and slowly evaporated to low volume under nitrogen. Failure to adequately protect the solutions from air leads to extensive decomposition. Colorless crystals of the products were filtered off, dried in a dessicator and stored in the dark (the selenourea complexes of methylmercury are light sensitive). In each case the yield based on ligand was ca. 75%.

Physical Measurements

Microanalyses (Table 1) were performed by Galbraith Microanalytical Laboratories. Infrared spectra as Nujol mulls on cesium iodide plates were run on a Perkin Elmer 180 spectrophotometer operating between 4000-200 cm^{-1}; polyethylene plates were used in the region 400-150 cm^{-1}. Spectral frequencies quoted (Table 2) are accurate to ± 2 cm^{-1}. Raman spectra as powders were run on a Jarrel Ash-400 spectrophotometer equipped with argon ion laser excitation. NMR spectra were obtained at 60 MHz on a Bruker WP-60 instrument. Chemical shifts were measured relative to the methyl resonance of sodium 2,2-dimethyl-2-silapentane-5-sulfonic acid (DSS). Chemical shift and coupling constants are listed in Table 3.

TABLE 1

ANALYTICAL DATA FOR METHYLMERCURY COMPLEXES

	Analysis (Found (Calcd.) (%))			
	C	H	N	X
$[CH_3HgSC(NH_2)_2]Br$	6.46	1.90	7.54	21.50
	(6.33)	(1.98)	(7.75)	(21.30)
$[CH_3HgSC(NH_2)_2]NO_3$	6.79	2.00	11.88	-
	(7.65)	(2.11)	(11.86)	-
$[CH_3HgSeC(NH_2)_2]Br$	5.74	1.69	6.69	19.09
	(5.79)	(1.81)	(6.87)	(19.19)
$[CH_3HgSeC(NH_2)_2]Cl$	6.42	1.89	7.49	
	(6.37)	(2.04)	(7.52)	
$[CH_3HgSeC(NH_2)_2]ClO_4$	5.48	1.61	6.40	-
	(5.27)	(1.73)	(7.06)	-
$[CH_3HgSeC(NH_2)_2]NO_3$	5.99	1.77	10.49	-
	(5.95)	(2.00)	(10.68)	-
$[CH_3HgSeC(NH_2)(NMe_2)]Br$	10.76	2.49	6.27	
	(10.77)	(2.62)	(6.29)	

X-RAY ANALYSIS OF $[CH_3HgSe\ C(NH_2)_2]\ NO_3$

Collection and reduction of intensity data

Unit cell and space group information were obtained from Weissenberg and precession photographs. The lattice parameters were refined by least-squares treatment of the diffractometer coordinates of 15 reflections with θ (Mo - K_α) between 10 and 15°.

Crystal data: $C_2H_7HgN_3O_3Se$, M = 400.65, Orthorhombic, a = 7.524(1), b = 11.204(2), c = 9.738(2)Å, U = 820.9Å^3, Z = 4, D_c = 3.241, D_m = 3.22 g. cm^{-3}, F(000) = 712. Space group $Pn2_1c$ (C_{2v}^9, No. 33) or Pnma (D_{2h}^{16}, No. 62) from systematic absences (hko when h = 2n + 1, okl when k + l = 2n + 1). Mo - K_α radiation, λ 0.71069Å, μ 238.8 cm^{-1}. A suitable crystal was fashioned into a sphere of diameter 0.185 mm. Three-dimensional intensity data for all unique reflections with $\theta \leqslant 28°$ were collected

TABLE 2

SELECTED INFRARED AND RAMAN DATA FOR THIOUREA, SELENOUREA AND METHYL MERCURY COMPLEXES

Ligand/Complex	Infrared (cm^{-1})		Raman (cm^{-1})	
	ν(CY)	ν(HgY)	ν(CY)	ν(HgY)
$SC(NH_2)_2$	730 vs	---	732 vs	---
$[CH_3HgSC(NH_2)_2]Br$	712 vs	260 vs	712 s	258 s
$[CH_3HgSC(NH_2)_2]NO_3$	710 vs	261 vs	712 m	260 s
$SeC(NH_2)_2$	640 m	---	640 w	
	390 vs		390 m	---
$[CH_3HgSeC(NH_2)_2]Br$	630 m		638 vs	
	385 vs	200 s	384 m	198 vs
$[CH_3HgSeC(NH_2)_2]ClO_4$	620 m		640 s	
	385 vs	196 s	386 m	196 vs
$[CH_3HgSeC(NH_2)_2]NO_3$	625 m		640 m	
	390 vs	180 s	396 w	202 vs
$[CH_3HgSeC(NH_2)_2]Cl$	625		640 m	
	387 vs	202 s	384 s	202 vs
$SeC(NH_2)(NMe_2)$	645 s			
	364 s	---	---	---
$[CH_3HgSeC(NH_2)(NMe_2)]Br$	625 s			
	351 m	194 s	352 m	192 vs

on a computer-controlled, four-circle Syntex $P2_1$ diffractometer using graphite monochromated Mo - K_α radiation. Data were collected using a coupled θ(crystal)-2θ(counter) scan from 0.8° below K_{α_1} to 0.8° above K_{α_2} with scan rates varying between 2.0 and 29.3° min^{-1}. Background counts were measured at the start and end of each scan, the total background count-time being equal to half the scan time.

Two standard reflections (240, 302) were monitored every 50 reflections and these were used to scale the data to a common level. Intensities increased by ~ 30% during the data collection with a corresponding increase in background levels. During this time, the crystal changed from colourless to dark red. After corrections for Lorentz and polarization effects, a total of 561 reflections were found to have $I \geq 3\sigma(I)$ and were utilised as observed data. An absorption correction was also applied ($\mu R = 2.2$).

(continued on p. 207)

TABLE 3

^{1}H NMR DATA FOR METHYLMERCURY COMPLEXES OF THIOUREA AND SELENOUREA

	δCH_3 (ppm)	$^2J_{^1H\,-\,^{199}Hg}$ (Hz)
$[CH_3HgSC(NH_2)_2]Br$	0.984	199.95
$[CH_3HgSC(NH_2)_2]NO_3$	0.984	199.22
$[CH_3HgSeC(NH_2)_2]Br$	1.070	191.16
$[CH_3HgSeC(NH_2)_2]NO_3$	0.988	190.92
$[CH_3HgSeC(NH_2)_2]ClO_4$	1.070	190.43
$[CH_3HgSeC(NH_2)_2]Cl$	1.005	191.41
$[CH_3HgSeC(NH_2)(NMe_2)]Br$	0.984	191.17

TABLE 4

ATOMIC COORDINATES (Fractional, x 10^4)

FOR $[CH_3HgSeC(NH_2)_2]NO_3$

Hg	2500	3583.8(9)	5880(1)
Se	911(5)	2170(3)	4358(3)
O(1)	5054(36)	3125(18)	3355(22)
O(2)	4574(37)	3978(22)	1423(19)
O(3)	3938(36)	4871(16)	3278(23)
N(1)	-2093(47)	2766(18)	6079(19)
N(2)	-2279(46)	1059(16)	4762(20)
N(3)	4564(30)	4009(18)	2751(22)
C(1)	3992(44)	222(26)	2136(28)
C(2)	-1354(37)	2005(24)	5166(30)

TABLE 5

ANISOTROPIC THERMAL PARAMETERS (x 10^3)

	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Hg	20.6(2)	9.27(8)	11.7(1)	0.3(3)	1.3(3)	-0.7(1)
Se	23.0(6)	12.8(3)	12.8(3)	-1.6(4)	3.9(4)	-3.1(3)
0(1)	43(7)	11(2)	19(3)	-1(3)	-1(4)	8(2)
0(2)	36(7)	21(3)	12(2)	-3(4)	-0(4)	2(2)
0(3)	57(9)	8(2)	23(3)	3(4)	12(5)	-4(2)
N(1)	27(7)	12(2)	12(2)	4(3)	4(3)	-4(2)
N(2)	25(5)	9(2)	15(2)	-0(4)	0(6)	1(2)
N(3)	22(5)	10(2)	13(3)	-6(3)	0(3)	-3(2)
C(1)	24(7)	12(3)	15(3)	6(4)	5(4)	2(3)
C(2)	20(6)	9(2)	16(4)	-3(3)	-5(4)	3(3)

TABLE 6

BOND LENGTHS(Å) and ANGLES (°) for $[CH_3HgSeC(NH_2)_2]NO_3$

Hg-Se	2.477(3)	C(1)-Hg-Se	177.0(8)
Hg-C(1)	2.13(3)	Hg-Se-C(2)	104.4(8)
Se-C(2)	1.89(3)	Se-C(2)-N(1)	126(1)
C(2)-N(1)	1.35(4)	Se-C(2)-N(2)	115(1)
C(2)-N(2)	1.33(4)	N(1)-C(2)-N(2)	119(1)
N(3)-O(1)	1.21(3)	O(1)-N(3)-O(2)	118(1)
N(3)-O(2)	1.29(3)	O(1)-N(3)-O(3)	125(1)
N(3)-O(3)	1.19(3)	O(2)-N(3)-O(2)	117(1)

INTERMOLECULAR CONTACTS(Å)

Hg-Se[a]	3.689(3)
Hg-O(1)	3.16(2)
Hg-O(3)	3.11(2)
O(2)-N(2)[b]	2.95(3)
O(2)-N(2)[a]	2.87(4)
O(3)-N(1)[c]	2.83(3)

a $x, \frac{1}{2}-y, \frac{1}{2}+z$; b $\frac{1}{2}+x, \frac{1}{2}+y, \frac{1}{2}-z$; c $\frac{1}{2}+x, \bar{y}, \bar{z}$.

Solution and Refinement

The structure was solved by Patterson and Fourier methods. It was immediately obvious from the Patterson synthesis that the correct choice of space group was $Pn2_1c$. With all non-hydrogen atoms located and assigned isotropic thermal parameters, the structure was refined by least-squares methods to an R value ($R = \Sigma[|F_o|-|F_c|]/\Sigma|F_o|$) of 0.077. Atomic scattering factors were taken from reference 8 with corrections included for both the real and imaginary parts of the anomalous dispersion of mercury and selenium. Conversion to anisotropic temperature coefficients and refinement to convergence gave R = 0.037 with the weighted residual R_w ($R_w = \{\Sigma_w[|F_o|-|F_c|]^2/\Sigma_w|F_o|^2\}^{1/2}$) of 0.042 ($w^{-1} = 2.6 - 0.05|F| + 0.0004|F|^2$).

Atomic coordinates and anisotropic thermal parameters are given in Tables 4 and 5 respectively. Bond lengths and angles are listed in Table

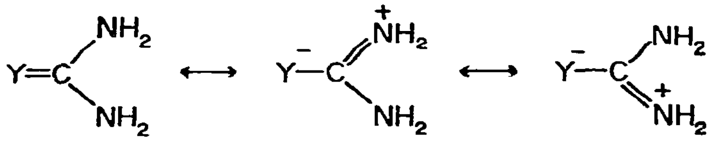
6. A list of observed and calculated structure factors has been deposited.*

X-RAY ANALYSIS OF [$CH_3HgSe\,C(NH_2)(NMe_2)$]Br

Preliminary photographic data showed crystals to be triclinic, space group P$\bar{1}$. Unit cell data were refined on the diffractometer as for the nitrate above. Crystal data: a = 6.251(1), b = 8.348(1), c = 9.570(2)Å; α = 104.39(1), β = 78.29(1), γ = 97.06(1)°; Z = 2, D_c = 3.140, D_m = 3.14 g. cm^{-3}. Intensity data were collected on the $P2_1$ diffractometer and the structure solved and refined to an R value of 0.09 using 1190 observed ($I \geq 3\sigma(I)$) reflections. Extensive decomposition during data collection limited the accuracy of the data. However, the structure is essentially the same as that of the nitrate (vide infra), except for weak inter and intramolecular interactions involving the anions. Thus we make no further comments on the structure

RESULTS AND DISCUSSION

Thio and selenourea are interesting ligands for mercury since, in principle, coordination could occur predominantly via the canonical forms 1 or 2 and 3 (Y=S or Se). The known affinity of CH_3Hg^+ for anionic sulfur sites might suggest a major contribution from 2 or 3. Addition of hot deoxygenated aqueous solutions of CH_3HgX (X=NO_3, ClO_4, Cl, Br) to a refluxing aqueous solution of thio or selenourea under nitrogen, followed by filtration and evaporation to low volume under nitrogen, gave colourless crystals analysing as [$CH_3Hg\ Y = C(NH_2)_2$]X (Y = S,Se, X = Br, NO_3; Y = Se,



1 2 3

Y = S,Se

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* A list of calculated and observed structure factors may be obtained from the author on request.

$X = Cl, ClO_4$). A substituted selenourea complex $[CH_3HgSe\,C(NH_2)(NMe_2)]Br$ was also synthesised. Infrared and Raman spectra (Table 2) are characterised by the appearance of very intense bands due to ν(Hg-Y), absent in the free ligands. Small shifts of ν(C-Y) modes to lower frequency, characteristic of coordination via sulfur or selenium are also evident. Proton nmr spectra in D_2O (Table 3) consist of a single CH_3-Hg resonance flanked by two ^{199}Hg (I = 1/2) satellites. The values of the two bond coupling constants $^2J_{^1H-^{199}Hg}$ are of interest because it has been well established by several groups of workers that an inverse relationship exists between binding constants for ligands L in linear CH_3HgL (as measured by log k) and nmr coupling constants $^2J_{^1H-^{199}Hg}$ [9]. This relationship holds presumably because a strongly bound ligand L weakens the Hg-C bond *trans* to it (the *trans* influence) and decreases the 's' character in the Hg-C bond. Since the Fermi contact term dominates the two bond mercury-proton coupling, a decrease in 's' character in the Hg-C bond results in a smaller J value. In the present context $^2J_{^1H-^{199}Hg}$ is lower by ca 10 Hz in the selenourea complexes implying stronger mercury-ligand binding in the selenourea compounds. The magnitude of $^2J_{^1H-^{199}Hg}$ in the thiourea complexes (199.6 ± 0.4 Hz) can be compared with $^2J_{^1H-^{199}Hg}$ of 223 Hz in the thioether bound CH_3Hg^+ - methionine complex [10] and a value of 174.0 Hz in the L-cysteine compound $CH_3HgSCH_2CH(NH_3)COO$ [11]. The

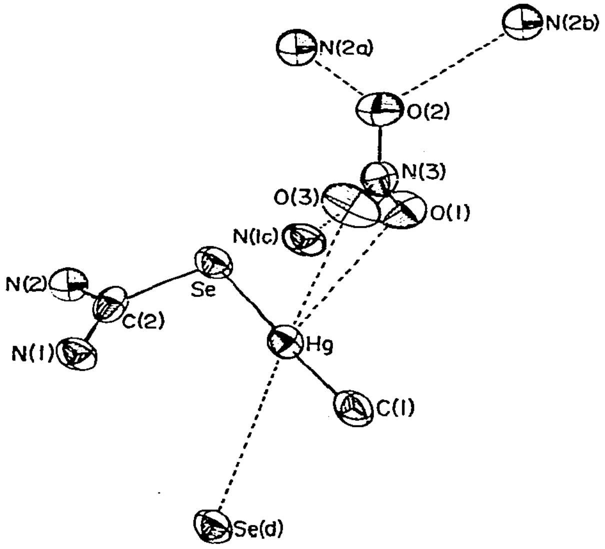

Figure 1

A perspective view of the molecular structure of $[CH_3HgSeC(NH_2)_2]NO_3$ showing the atomic numbering, inter and intramolecular contacts. Ellipsoids are drawn at the level of 50% probability.

$^{2}J_{^{1}H-^{199}Hg}$ values in the selenourea complexes are ca. 27 Hz higher than in the selenocysteine complex $CH_3HgSeCH_2CH(NH_3)(COO)$ [7b]. Thus it seems that the thio and selenoureas are intermediate between thio or selenoethers and deprotonated sulfhydryl or selenohydryl groups in their affinity for methylmercury.

An ORTEP II plot of the structure of $[CH_3HgSeC(NH_2)_2]NO_3$ is shown in Figure 1. The mercury atom is coordinated approximately linearly by a methyl group and by the selenium atom of the selenourea. In the nitrate salt there are no Hg---O contacts of importance; all Hg---O distances are > 3.10Å. The principal structural feature of interest is the Hg-Se bond length. The Hg-Se distance is 2.477(3)Å which compares with an <u>average</u> Hg-S value of 2.36 ± 0.01Å in $CH_3HgSCH_2CH(\overset{+}{N}H_3)COO^- . H_2O$ [12], and the two CH_3Hg^+ - D,L-penicillamine complexes [13]. The difference in standard covalent radii between S and Se is 0.15Å [14]. Thus, the Hg-Se bond is marginally shorter than predicted despite the fact that the selenourea is not a truly anionic ligand as are the sulfur aminoacid anions. We interpret these results as <u>direct</u> evidence for strong Hg-Se bonding.

Structural parameters within the selenourea ligands are as expected; for example, C(2) is strictly planar and the C(2)-N(1) and C(2)-N(2) distances (Av 1.340Å) are intermediate between the expected C-N single (~1.47Å) and double (1.30Å) bond lengths. Further, in the bromide complex the substituted nitrogen atom is planar, in agreement with the presence of two nonequivalent methyl resonances in the ^1H nmr spectrum. Clearly the canonical forms <u>2</u> and <u>3</u> contribute substantially to a stereochemical and electronic description of these selenoureas in their CH_3Hg^+ complexes. We are currently measuring ^{199}Hg - ^{77}Se coupling constants in mercury-selenium derivatives in an attempt to further delineate Hg-Se interactions.

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