X-Ray Crystallographic and Spectroscopic Studies of the Binding of Methylmercury by the Sulphur Amino-acid DL-Penicillamine: Models for Methylmercury Poisoning of Proteins

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Methyl-DL-penicillaminatomercury(II) monohydrate, [HgMe(pen)]·H_2O (pen = DL-penicillaminate), and μ-DL-penicillaminato-bis[methylmercury(II)], [Hg_2Me_2(pen)], were prepared from appropriate amounts of methylmercury chloride (or hydroxide) and DL-penicillamine in 50% aqueous ethanol solutions. Crystals of [HgMe(pen)]·H_2O are colourless monoclinic prisms with a = 23.154, b = 9.819, c = 19.321 Å, and β = 106.4°; space group $C2/c$, Z = 16. Crystals of [Hg_2Me_2(pen)] are colourless orthorhombic needles with a = 19.695, b = 10.478, and c = 11.971; space group, $Pbcn$, Z = 8. Structures of both compounds were solved from single-crystal diffractometer data with 1 047 and 1 254 independent observed reflections for [HgMe(pen)]·H_2O and [Hg_2Me_2(pen)] respectively. Final R factors were 0.079 and 0.075 respectively. In [HgMe(pen)]·H_2O, the amino-acid, present in the zwitterionic form $^-SC(CH_3)_2CH(\overset{+}{N}H_3)COO^-$, is co-ordinated to methylmercury *via* a deprotonated sulphydryl group and in [Hg_2Me_2(pen)] the methylmercury groups are bonded to the deprotonated sulphydryl and amino-groups. The important average bond distances are: Hg–CH_3, 2.07; Hg–S, 2.36; and Hg–N, 2.13 Å. The two bonds about the mercury atoms deviate slightly but significantly from linearity because of weak interactions from neighbouring sulphur or oxygen atoms. The vibrational and n.m.r. spectra are discussed in the light of the crystal structures. Diagnostic criteria of bonding modes are assessed.

COMPLEX formation between various forms of mercury and sulphur amino-acids has wide-ranging significance for the behaviour of this element in the environment, and for the toxicology, biotransport, and metabolism of mercurials. In the specific case of methylmercury, complexes of cysteine [1] and homocysteine [2] are thought to be directly involved in processes involving methylation of mercury by micro-organisms in bottom sediments while the binding of methylmercury to cysteinyl residues of proteins may, in large part, be responsible for the specific deleterious effects of this neurotoxin.[3] Biotransport of organomercurials is governed in part by the low polarity of the complexes formed with sulphydryl-containing molecules of low molecular weight.[4] A further interesting aspect of mercury biochemistry concerns the structure and role of metallothionein,[5] a metalloprotein of molecular weight *ca.* 8 000—10 000. This fascinating molecule, which may behave as a heavy-metal detoxicant [6] but for which a precise biochemical role remains to be established, appears to be exceptionally rich in cysteine and binds zinc, cadmium, or.mercury strongly.[5] In order to gain some insight into the biochemistry of mercury, a fundamental understanding of the interaction between biologically important sites and mercury compounds is required. Such information has been sought in this laboratory *via* structural investigations of methylmercury complexes with selected amino-acids. In our initial work the molecule DL-penicillamine was chosen for study since this amino-acid was reported [7] to form exceptionally stable complexes with Hg^{2+} and is directly related to L-cysteine. The substitution of methylene protons of cysteine by *gem*-dimethyl groups not only enhances stability but also confers better solubility properties on the resulting complexes. An additional incentive for the study of penicillamine complexes is that the D-form of this amino-acid has previously been employed as an antidote for mercury poisoning.[8] In this paper we report the syntheses, vibrational spectra, and X-ray crystal-structure analyses of methyl-DL-penicillaminatomercury(II) monohydrate [HgMe(pen)]·H_2O and μ-DL-penicillaminatobis[methylmercury(II)] [Hg_2Me_2(pen)]. Although the penicillamine complexes of $[HgMe]^+$ had not previously been characterized when our work commenced, n.m.r. studies of the interaction of several amino-acids with $[HgMe]^+$ have been reported by Rabenstein and his co-workers.[9] A preliminary account of part of this work has appeared.[10]

EXPERIMENTAL

Preparation of Complexes.—Methylmercury chloride and hydroxide were purchased from Ventron (Alfa Inorganics) Corporation and DL-penicillamine was obtained from Sigma Chemical Company, St. Louis, Missouri. All other reagents and solvents were standard reagent-grade materials.

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*Methyl-*DL*-penicillaminatomercury*(II) *monohydrate*, [HgMe{(SCMe$_2$)CH($\overset{+}{N}$H$_3$)CO$_2^-$}]·H$_2$O. Methylmercury chloride (1.5 g) was dissolved in absolute ethanol (20 ml) and 3 ml of 2 mol dm^{-3} sodium hydroxide solution was added with stirring. The solution was heated to boiling, allowed to cool to room temperature, and finally cooled in an ice-bath. The cold solution was rapidly filtered through a sintered glass funnel to remove the precipitated sodium chloride. An equivalent amount of DL-penicillamine (0.89 g) in 50% aqueous ethanol (20 ml) was added to the filtered solution and the mixture stirred for 12 h at 25 °C. The volume of solution was reduced to *ca.* 15 ml by evaporation at room temperature on a rotary evaporator. Colourless crystals were obtained by evaporating the solution slowly at room temperature (Calc. for C$_6$H$_{15}$HgNO$_3$S: C, 18.87; H, 3.96. Found: C, 19.35; H, 3.85%).

μ-DL-*Penicillaminato-bis*[*methylmercury*(II)], MeHgSC(Me)$_2$CH(CO$_2^-$)$\overset{+}{N}$H$_2$HgMe. Methylmercury chloride (0.99 g) was treated with 4 ml of 2 mol dm^{-3} NaOH solution as above. DL-Penicillamine (0.30 g) was added. The volume of the solution was reduced to 10 ml. The precipitate obtained by slow evaporation of the solution was recrystallized from aqueous ethanol giving colourless needles (Found: C, 14.95; H, 2.35; N, 2.4. Calc. for C$_7$H$_{18}$Hg$_2$NO$_2$S: C, 14.48; H, 2.58; N, 2.41%).

Spectroscopic Measurements.—Solid-state i.r. spectra of Nujol mulls on caesium iodide windows were recorded on a Perkin-Elmer 180 spectrometer operating between 4 000 and 180 cm^{-1}. Raman spectra were obtained for powders by use of a modified rotating cell [11] on a Jarrell–Ash 25-100 spectrometer equipped with argon-ion (5 145 Å) excitation. The rotating-cell technique was essential to minimize sample burn-up in the laser beam. Nevertheless, some decomposition was still noticeable in all the methylmercury compounds examined. Care was taken to avoid introducing spurious bands into the Raman spectra by over-exposure of the specimens. Solution spectra in H$_2$O were run in a standard glass Raman cell. ^{1}H Nuclear magnetic resonance spectra at 60 MHz in D$_2$O were obtained on Varian T-60 or Perkin-Elmer R12B spectrometers. Chemical shifts were measured relative to the methyl resonance of the sodium salt of 2,2-dimethyl-2-silapentane-5-sulphonic acid (dss). Positive shifts correspond to resonances of protons less shielded than those of dss. Carbon-13 magnetic resonance spectra at 22.63 MHz in D$_2$O were obtained on a Bruker HFX-90 spectrometer.

X-*Ray Crystallographic Measurements.*—Crystals of [HgMe(pen)]·H$_2$O and [Hg$_2$Me$_2$(pen)], obtained from aqueous ethanol solutions, are colourless prisms and needles respectively. Weissenberg and precession photographs were used to determine the unit-cell constants and space groups. Accurate unit-cell parameters were obtained by least-squares refinement of 2θ values for 7 and 14 reflections respectively measured on a G.E. XRD-6 automatic diffractometer.

Crystal data. [HgMe(pen)]·H$_2$O, C$_6$H$_{15}$HgNO$_3$S, M = 381.8, Monoclinic, a = 23.154(33), b = 9.819(14), c = 19.321(27) Å, β = 106.4(1)°, U = 4 213.9 Å^3, D_m = 2.40 g cm^{-3} (by flotation), Z = 16, D_c = 2.14 g cm^{-3}, F(000) = 2 848. Space group $C2/c$ (C_{2h}^6, no. 15) from systematic absences. A centric space group was assumed because the ligand used was in the DL form. This choice proved to be correct by the successful refinement of the structure. Mo-K_α radiation, λ = 0.7107 Å was used; μ(Mo-K_α) = 150.8 cm^{-1}.

[Hg$_2$Me$_2$(pen)], C$_7$H$_{18}$Hg$_2$NO$_2$S, M = 578.5, Orthorhombic, a = 19.695(23), b = 10.478(13), c = 11.971 (26) Å, U = 2 470.4 Å^3, D_m = 3.06 g cm^{-3}, Z = 8, D_c = 3.11 g cm^{-3}, F(000) = 2 048. Space group $Pbcn$ from systematic absences. μ(Mo-K_α) = 254.9 cm^{-1}.

Collection and reduction of intensity data. Intensity data were measured on a Datex automated G.E. XRD-6 diffractometer which is equipped with scintillation counter, pulse-height analyser, and Hewlett–Packard Scaler timer (5201 L). The crystals of both complexes decompose when exposed to X-rays; therefore a device was incorporated to shut off the X-ray beam except during the counting process. The stability was monitored with three standard reflections which were measured after each 100 reflections. The average decrease in intensity of the standard reflections (<7%) was used as a guide for scaling all reflections to a level corresponding to a fresh crystal. Stationary-counter–stationary-crystal background counts of 10 s were made before and after each scan. The scan width in each case was determined by the equation Δθ = (1.90 + 0.60 tanθ). The scan rate was 4° min^{-1}.

For [HgMe(pen)]·H$_2$O the crystal used had dimensions of 0.15 × 0.10 × 0.08 mm and was mounted with a^* parallel to the φ axis of the diffractometer. No absorption correction was made; μR = 0.91. Of the 3 765 (2θ < 50°) independent reflections measured, 3 049 had intensities $I \geqslant 0.1\sigma(I)$ and 1 504 had intensities $I \geqslant 3\sigma(I)$. The 1 504 stronger reflections were considered as observed and used throughout the structural analysis. The small fraction of data observed resulted mainly from the scarcity of significant reflections at high 2θ angles. Thus for 2θ values between 40 and 50°, 1 587 reflections were flagged as unobserved and only 271 had intensities $I \geqslant 3\sigma(I)$; this is the price paid for using so small a crystal to avoid absorption corrections. Collection of this high-angle data was felt to be justified by the need for greater precision in light-atom positions. Standard deviations were estimated from counting statistics. For [Hg$_2$Me$_2$(pen)] the crystal measured 0.15 × 0.08 × 0.06 mm and was mounted with c^* along the φ axis of the goniostat. There were 1 047 (2θ < 40°) independent reflections measured using the stationary-crystal–stationary-counter method. A background curve was derived by measurements at intervals of 2.5° in 2θ with values of χ and φ chosen so as to be non-coincident with values for measured reflections. A second crystal was used to collect the high-angle data (40 < 2θ < 56°). The two sets of data were combined with proper scaling to give 1 254 independent observed reflections. No absorption correction was made, μR = 0.89. Lorentz and polarization factors were applied to derive the structure amplitudes in both cases.

Solution and refinement of the structures. The structures of both compounds were solved by heavy-atom methods and refined by full-matrix least-squares techniques. The atomic scattering factors were taken from ref. 12. The effects of anomalous dispersion were included for Hg. The initial R values for [HgMe(pen)]·H$_2$O and [Hg$_2$Me$_2$(pen)] were respectively 0.18 and 0.15 for all non-hydrogen atoms. With isotropic thermal parameters included for all atoms the R factors were 0.120 and 0.095. Introduction of anisotropic

[11] W. Kiefer and H. J. Bernstein, *Appl. Spectroscopy*, 1971, **25**, 609.

[12] 'International Tables for X-Ray Crystallography,' vol. III, Kynoch Press, Birmingham, 1968, pp. 202—216.

thermal parameters for Hg, S, N, and O in [HgMe(pen)]·H_2O and for all atoms in [Hg_2Me_2(pen)] gave final R factors of 0.079 and 0.075 respectively. The weighting schemes used for the two compounds were $w = (8.771 - 0.0977|F_o| + 0.0004|F_o|^2)^{-1}$ and $w = (3.053 - 0.0298|F_o| + 0.0001|F_o|^2)^{-1}$ giving weighted residuals R' of 0.092 and 0.098. In each case parameter shifts during the last cycle of refinement were $<0.25\sigma$.

For [HgMe(pen)]·H_2O, final difference-Fourier maps were calculated using both the 1 504 [$I \geqslant 3\sigma(I)$] observed data and the larger data set [$I \geqslant 0.1\sigma(I)$] to confirm the validity of the structural interpretation. Both difference maps were essentially the same, revealing no further significant features.

TABLE 1

Atomic co-ordinates (fractional, $\times 10^3$) and isotropic thermal parameters for [HgMe(pen)]·H_2O

Atom	x	y	z	B_{iso}/Å^2
Hg(1a)	79.98(9)	421.8(2)	234.4(1)	
Hg(1b)	46.77(9)	133.7(2)	400.3(1)	
S(a)	84.5(6)	181(13)	246.3(7)	
S(b)	48.2(5)	374(1)	397.5(6)	
O(1a)	209(1)	393(2)	283(2)	
O(2a)	233(1)	356(3)	180(2)	
O(1b)	176(1)	161(3)	451(1)	
O(2b)	204(1)	215(3)	567(2)	
O(1s)	288(2)	192(3)	104(2)	
O(2s)	303(2)	395(3)	19(2)	
N(a)	219(2)	119(3)	317(2)	
N(b)	185(1)	424(4)	411(2)	
C(1a)	215(2)	314(4)	235(2)	1.9(7)
C(2a)	206(2)	164(4)	239(2)	2.0(7)
C(3a)	140(2)	120(4)	200(2)	2.0(7)
C(4a)	137(2)	−31(4)	197(2)	2.9(8)
C(5a)	123(2)	178(5)	124(3)	4.3(11)
C(6a)	77(3)	632(6)	233(3)	5.7(14)
C(1b)	185(2)	247(4)	500(2)	2.5(8)
C(2b)	173(2)	390(4)	484(2)	2.6(8)
C(3b)	106(2)	441(4)	476(2)	2.5(8)
C(4b)	101(2)	596(5)	469(3)	4.2(10)
C(5b)	96(2)	392(4)	552(2)	3.1(8)
C(6b)	42(2)	−77(5)	410(3)	4.0(10)

Anisotropic thermal parameters ($\times 10^4$) for [HgMe(pen)]·H_2O [a]

Atom	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Hg(1a)	16.2(4)	90(2)	18.8(6)	7.1(9)	4.0(4)	2(1)
Hg(1b)	15.3(5)	91(3)	32.1(8)	−3.9(9)	1.8(4)	6(1)
S(a)	17(3)	107(16)	26.5(4)	−6(6)	15(3)	−7(7)
S(b)	8(2)	97(15)	23(4)	8(5)	−2(2)	5(6)
O(1a)	23(8)	25(34)	31(11)	−19(12)	6(8)	−21(15)
O(2a)	26(9)	86(36)	19(10)	−6(15)	10(8)	0(16)
O(1b)	11(6)	117(43)	17(10)	0(13)	2(6)	−11(16)
O(2b)	7(6)	144(45)	19(10)	−2(13)	2(6)	6(17)
O(1s)	41(6)	107(25)	20(6)	4(10)	28(5)	−8(10)
O(2s)	33(10)	99(48)	33(12)	18(17)	11(9)	31(19)
N(a)	13(7)	32(4)	16(1)	−2(13)	−8(7)	−3(16)
N(b)	19(6)	13(3)	11(7)	−19(12)	9(5)	5(14)

[a] In the form $\exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$.

A final difference map for [Hg_2Me_2(pen)] was also featureless. Final atomic co-ordinates and thermal parameters are listed in Tables 1 and 2. All computations were carried out on an IBM 360-75 system in the University of Waterloo Computing Centre, using computer programs described previously.[13] Structure-factor tables are listed in Supplementary Publication No. SUP 22067 (24 pp.).*

* For details see Notice to Authors No. 7, *J.C.S. Dalton*, 1976, Index issue.

RESULTS AND DISCUSSION

Two colourless crystalline complexes formed in the reaction of [HgMe][OH] or [HgMe]Cl with DL-penicillamine were identified by microanalysis, i.r. and n.m.r spectroscopy, and single-crystal X-ray diffraction as

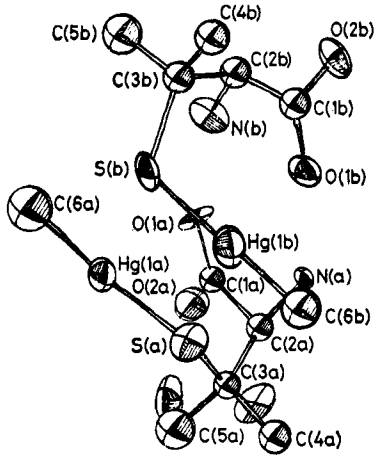

FIGURE 1 ORTEP plot and atomic numbering of methyl-DL-penicillaminatomercury(II) monohydrate. The two unlabelled atoms are oxygen atoms of water of crystallization

methyl-DL-penicillaminatomercury(II) monohydrate and μ-DL-penicillaminato-bis[methylmercury(II)].

Crystal and Molecular Structures.—Perspective drawings of the molecular structures of [HgMe(pen)]·H_2O and [Hg_2Me_2(pen)] are shown with the atomic numbering in Figures 1 and 2. The two independent molecules of

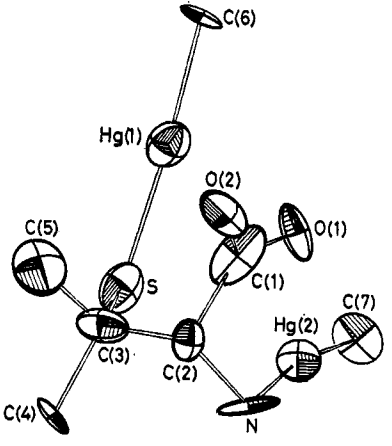

FIGURE 2 Molecular structure of μ-DL-penicillaminato-bis[methylmercury(II)]

[HgMe(pen)]·H_2O per asymmetric unit are labelled as (a) and (b) and this will be adhered to throughout the discussion. Bond distances and angles for both compounds together with data for the free-ligand hydrochloride are given in Table 3. In [HgMe(pen)]·H_2O the amino-acid, present in the zwitterionic form $^-SC(CH_3)_2$-$CH(\overset{+}{N}H_3)CO_2^-$, is co-ordinated to mercury *via* a deprotonated sulphydryl group. This interaction is thus

[13] N. J. Taylor, Y. S. Wong, P. C. Chieh, and A. J. Carty, *J.C.S. Dalton*, 1975, 438.

similar to that in methyl-L-cysteinatomercury(II) monohydrate and models the presumed methylmercury–sulphydryl interaction in poisoned cells. In $[Hg_2Me_2(pen)]$ one methylmercury moiety is co-ordinated at the deprotonated sulphydryl site while the other is attached to the amino-group. The complex is a zwitterion with the formal positive charge on mercury balanced by the ionized carboxyl group. The complexation of a second $[HgMe]^+$ moiety at the amino-site and the isolation of a stable crystalline complex of this type is significant since it demonstrates that contrary to earlier predictions, based on the apparent instability of $[HgMe(py)]^+$ (py = pyridine),[1] $[HgMe]^+$ can associate strongly with amino-groups present in biological molecules. It thus seems quite possible that even in the absence of sulphydryl sites, or their saturation, biological functions could be impaired *via* methylmercury poisoning of nitrogen sites. The formation of $[HgMe(pen)]\cdot H_2O$ can be compared with the results of n.m.r. studies of $[HgMe]^+$–L-glutathione complexation over a wide pH range.[9] Sulphydryl co-ordination is favoured independent of pH but the site of attachment of a second $[HgMe]^+$ ion is variable, with amino-group co-ordination favoured near pH 7. For *N*-acetyl-L-cysteine in acid solution, two molecules of methylmercury co-ordinate at the sulphur atom.[15] Attempts to prepare a sulphur-bridged analogue with DL-penicillamine were unsuccessful.

The Hg–S distances of 2.38(1), 2.36(1), and 2.35(1) Å

TABLE 2

Final atomic fractional co-ordinates ($\times 10^3$) and anisotropic thermal parameters ($\times 10^3$) for $[Hg_2Me_2(pen)]$

Atom	*x*	*y*	*z*	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Hg(1)	382.52(9)	314.2(2)	652.8(2)	2.25(5)	7.1(2)	7.2(1)	−0.13(7)	0.54(7)	−1.4(1)
Hg(2)	487.33(8)	235.4(1)	388.2(1)	2.33(4)	6.7(2)	5.3(1)	−0.30(7)	0.13(6)	0.6(1)
S	351.8(6)	309(1)	464(1)	2.7(3)	6(1)	9(1)	1.5(5)	0.8(5)	0.4(8)
O(1)	463(1)	104(2)	580(3)	1.2(6)	5(2)	10(3)	−1(1)	−2(1)	1(2)
O(2)	388(2)	46(4)	130(2)	2.5(9)	16(4)	6(3)	0(2)	−2(1)	0(3)
N	430(2)	66(3)	359(2)	4(1)	4(3)	1(2)	−1(1)	2(1)	0(2)
C(1)	411(2)	40(3)	560(4)	3(1)	2(3)	13(5)	−2(2)	3(2)	−2(3)
C(2)	377(2)	43(3)	447(3)	1(1)	4(3)	5(3)	0(1)	0(1)	0(3)
C(3)	320(2)	142(4)	445(3)	3(2)	9(5)	4(3)	−1(2)	−1(2)	−3(3)
C(4)	285(2)	150(6)	325(4)	2(1)	30(10)	4(3)	4(3)	−2(2)	−3(5)
C(5)	262(3)	103(5)	527(4)	3(2)	15(7)	8(4)	−1(3)	0(2)	6(4)
C(6)	403(2)	323(6)	820(3)	2(1)	24(9)	3(3)	1(3)	−2(1)	−5(4)
C(7)	552(2)	392(3)	389(4)	3(1)	3(4)	9(4)	2(2)	−1(2)	−1(3)

TABLE 3

Bond distances (Å) and angles (°) for $[HgMe(pen)]\cdot H_2O$, $[Hg_2Me_2(pen)]$, and L-pen·HCl·H_2O

Compound	$[HgMe(pen)]\cdot H_2O$		$[Hg_2Me_2(pen)]$	L-pen·HCl·H_2O *
Distances	a	b		
Hg(1)–S	2.38(1)	2.36(1)	2.35(1)	
Hg(1)–C(6)	2.07(6)	2.09(5)	2.04(4)	
Hg(2)–N			2.13(3)	
H(2)–C(7)			2.07(4)	
S–C(3)	1.86(4)	1.83(4)	1.87(4)	1.83
O(1)–C(1)	1.25(5)	1.24(5)	1.25(5)	1.18
O(2)–C(1)	1.30(5)	1.29(5)	1.30(5)	1.33
N–C(2)	1.51(5)	1.56(5)	1.51(5)	1.49
C(1)–C(2)	1.52(5)	1.45(6)	1.52(6)	1.50
C(2)–C(3)	1.55(6)	1.61(6)	1.53(6)	1.50
C(3)–C(4)	1.48(5)	1.53(6)	1.59(6)	1.59
C(4)–C(5)	1.53(6)	1.61(6)	1.56(7)	1.51
Angles				
S–Hg(1)–C(6)	175(2)	175(2)	176(1)	
N–Hg–C(7)			170(1)	
Hg(1)–S–C(3)	107(1)	111(1)	103(1)	
Hg(2)–N–C(2)			113(1)	
O(1)–C(1)–O(2)	123(2)	123(2)	123(2)	122.1
O(1)–C(1)–C(2)	122(2)	121(2)	121(2)	123.8
O(2)–C(1)–C(2)	116(2)	116(2)	116(2)	114.1
N–C(2)–C(1)	110(2)	109(2)	108(2)	105.0
N–C(2)–C(3)	108(2)	105(2)	113(2)	113.1
C(1)–C(2)–C(3)	112(2)	117(2)	111(2)	113.5
S–C(3)–C(2)	107(2)	115(2)	112(1)	108.5
S–C(3)–C(4)	108(2)	106(2)	102(2)	105.5
S–C(3)–C(5)	114(1)	113(2)	115(2)	103.9
C(2)–C(3)–C(4)	109(2)	111(2)	111(2)	114.2
C(2)–C(3)–C(5)	109(2)	101(2)	111(2)	114.5
C(4)–C(3)–C(5)	110(3)	111(2)	106(3)	

* From ref. 14.

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in the two compounds (Table 3) do not differ significantly and are essentially the same as values of 2.35(1) Å in [HgMe(cyst)] (cyst = L-cysteine),[13] 2.330 Å (av) in [Hg{PhN=C(OMe)S}$_2$],[16] 2.34(1) Å in [HgPh(cyst)],[17] or 2.368 Å (av) in hexagonal HgS,[18] in all of which mercury is two-co-ordinate. Indeed it appears from recent tabulations [19,20] that all reliable Hg–S distances in truly two-co-ordinate mercury compounds lie within the very narrow range 2.32—2.42 Å. There is no discernible correlation of bond lengths with the nature of the *trans* ligand although this may be an artifact of the low accuracy of many of the determinations.

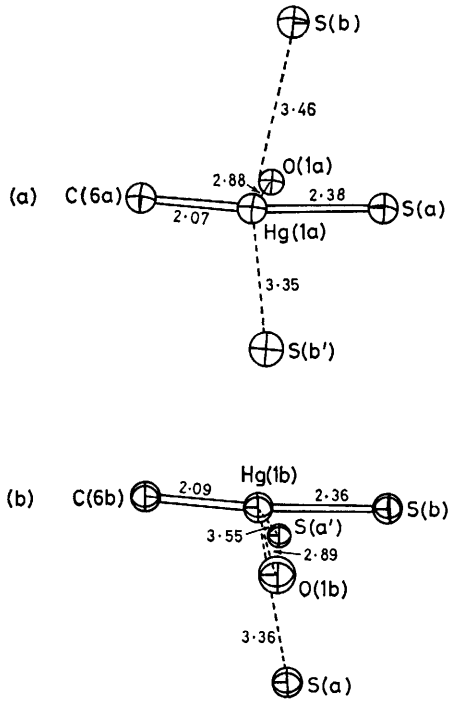

FIGURE 3 Possible weak interactions around Hg atoms in the two crystallographically independent molecules of [HgMe(pen)]·H_2O. The three atoms, C(6), Hg, and S are placed in the plane of the paper to show the direction of bending of the C(6)–Hg–S moiety. Standard deviations are σ(Hg · · · S) 0.01 and σ(Hg · · · C,O) 0.02 Å. Primed atoms represent atoms from a molecule in the equivalent position $\bar{x}$, y, $\frac{1}{2} - z$

The Hg–C distances of 2.07(6) Å in [HgMe(pen)]·H_2O and 2.09(5), 2.04(4) Å in [Hg_2Me_2(pen)] appear normal. The most accurate recent values in the literature are 2.061(2) Å in HgMeCl,[21] 2.083(5) Å in $HgMe_2$,[22] 2.029(2) Å in [$Zn(H_2O)_4${$Hg(CN)_2$}][NO_3]$_2$·$3H_2O$,[23] 2.003(5) Å in HgMeX (X = Cl, Br, or I),[24] and 1.94(1) Å in the ion $[HgMe]^+$.[25] The last two values were determined by n.m.r. spectroscopy of the oriented molecules. Although a large number of Hg–C bond lengths have been determined for two-co-ordinate HgR_2 and HgRX (X = anion) molecules [20] the high estimated standard deviations on these bond lengths preclude any assessment of structural *trans* influences.

A scan of intra- and inter-molecular distances in both molecules revealed additional interactions with each mercury atom, responsible for the slight but significant deviations of the C–Hg–S or C–Hg–N moieties from linearity. The possible interactions for the two crystallographically independent mercury atoms Hg(1a) and Hg(1b) in [HgMe(pen)]·H_2O are shown in Figure 3. In both [HgMe(pen)]·H_2O molecules there are two sulphur atoms and an oxygen atom near the mercury atom. One of the sulphur atoms has a closer contact [Hg(1a) · · · S(b') 3.35(1), Hg(1b) · · · S(a) 3.36(1) Å] than the other [Hg(1a) · · · S(b) 3.46(1), Hg(1b) · · · S(a') 3.55(1) Å]. The two covalent bonds to mercury thus bend away from the proximate sulphur atoms. The oxygen atoms in both cases are found at the same distance from the mercury atoms [2.88(3) and 2.89(3) Å]. Comparison of the above distances with sums of van der Waals radii (3.35 Å for Hg · · · S, 3.0 Å for Hg · · · O) [26] indicates the weakness of these secondary interactions. This structural feature, which illustrates the very weak residual Lewis acidity of two-co-ordinate alkylmercurials, is highly characteristic. Even attempts to force organomercury salts to adopt a co-ordination number greater than two by utilising strongly chelating ligands {*e.g.* 2,2'-bipyridyl in [HgMe(bipy)][NO_3]} result in only two strong metal–ligand bonds.[27]

In [Hg_2Me_2(pen)] the environment around mercury is simple and the small deviation of the C(6)–Hg(1)–S angle [176(1)°] from linearity is due to the close approach of O(1) to the mercury atom [Hg · · · O(1) is 2.85(2) Å]. On the other hand, the Hg(2) · · · S [2.92(1) Å] and Hg(2) · · · O(1) [2.72(3) Å] contacts represent significant interactions in the light of the van der Waals radii (see above) and are presumably responsible for the 10° deviation of the C(7)–Hg(2)–N angle from linearity.

The average values of bond lengths in the penicillamine residues in the two complexes are 1.25(5), 1.30(5), 1.53(5), and 1.53(6) Å for the C(1)–O(1), C(1)–O(2), C(1)–N, and C–C bonds respectively. These agree, within experimental error, with the values given by Marsh and Donohue,[28] from a weighted average of amino-acid data.

The equations for the least-squares planes through the atoms C(1), C(2), O(1), and O(2) are given by $0.8474X - 0.1215Y + 0.1570Z = 5.0305$ for molecule (a) and $0.9924X + 0.1194Y - 0.0313Z = 1.5368$ for molecule

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(b) in $[HgMe(pen)]\cdot H_2O$ and $-0.6047X + 0.7094Y + 0.3621Z = -2.2157$ in $[Hg_2Me_2(pen)]$, where X, Y, Z are

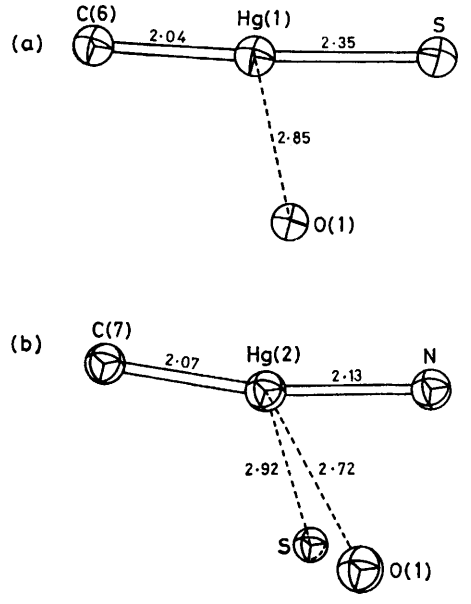

FIGURE 4 The close contacts of the two Hg atoms in μ-DL-penicillaminato-bis[methylmercury(II)]. Standard deviations are the same as in Figure 3

Cartesian co-ordinates in Å referring to a, b, and c^*. The maximum deviations of the mentioned atoms from Å for $[Hg_2Me_2(pen)]$. The large deviation in $[Hg_2Me_2(pen)]$ may relate to the short Hg–O(1) distance of 2.72(3) Å.

The conformations of the ligands are the same as those found for most sulphur-containing amino-acids;[29] *i.e.* looking along the bond C(2)–C(3), the sulphur is located between the bulky carboxyl and amino-groups. This preferred conformation can be rationalized in terms of the intramolecular attractions which exist between the mercury atoms and the carboxyl-oxygen atoms. If this weak interaction is counted, a distorted six-membered ring, Hg–S–C–C–C–O, in a chair form exists. The second methylmercury group which is bonded *via* the amino-nitrogen atom in $[Hg_2Me_2(pen)]$ is also situated in a sterically unfavourable position. The formation of a five-membered ring, Hg–N–C–C–O, from the weak intramolecular interaction between mercury and the carboxyl oxygen can also explain this preferred location.

Hydrogen bonding and packing. Both complexes are extensively hydrogen-bonded. The hydrophilic ends of the molecules are involved in these interactions. The water molecules of crystallization in $[HgMe(pen)]\cdot H_2O$ are hydrogen-bonded to each other and to amino- and carboxyl groups. Another type of intermolecular attraction occurs between the mercury and sulphur atoms. These two types of attraction form alternate layers in both compounds and sections of the layers are

TABLE 4

Some characterisitic Raman and i.r. bands for methylmercury-penicillamine complexes

DL-penicillamine (pen) Raman	DL-penicillamine (pen) I.r.	$[D_3]$pen [a] I.r.	$[HgMe(pen)]\cdot H_2O$ Raman	$[HgMe(pen)]\cdot H_2O$ I.r.	$[HgMe(D_2\text{-pen})]\cdot D_2O$ [a] I.r.	$[Hg_2Me_2(pen)]$ Raman	$[Hg_2Me_2(pen)]$ I.r.	$[Hg_2Me_2(D_2\text{-pen})]$ [a] I.r.	Assignment [b]
				3 480mw,br	2 580m,br				ν(OH), [ν(OD)]
	ca. 3 150w (sh)	2 350w (sh)		3 200m, br	2 380ms, br		3 120m, br	2 310m	$\nu(\overset{+}{N}H_3)$, $[\nu(\overset{+}{N}D_3)]$
	ca. 3 060m (sh)	2 250ms, br		3 130m, br	2 200m, br		3 050m, br	2 230ms	
2 569vs	2 570w								ν(S–H)
1 659w, br	1 654vs			1 656ms					$\delta_{asym}(\overset{+}{N}H_3)$
1 510w, br	1 508vs			1 485s					$\delta_{sym}(\overset{+}{N}H_3)$
		1 183s			1 185ms				$\delta(\overset{+}{N}D_3)$
					1 176ms				
		1 160ms			1 152ms				
		1 143ms			1 132ms				
							1 586vs	1 052m	$\delta(\overset{+}{N}H_2)$ $[\delta(\overset{+}{N}D_2)]$
						1 240w	1 230w, (sh)	1 022ms	
1 597w, br	1 600s	1 608vs, br	1 610vw, br	1 595s	1 600vs		1 586vs	1 590vs	$\nu_{asym}(COO^-)$
1 399mw	1 398s	1 389s	1 394w	1 399s	1 395s	1 390w, br	1 390m	1 370s	$\nu_{sym}(COO^-)$
576s	578ms	530s	576mw	557s	546s, br				$\rho_t(\overset{+}{N}H_3)$
552s	552m	550ms	555mw	555ms	557ms	546vs	547s	543s	$\rho_r(COO^-)$
			539vs	539m	540s	546vs	547s	540s	ν(Hg–C)
						432m	441ms, br	420ms	ν(Hg–N)
			322m	322vw, sh	312vw, sh	334m	339m	328s	ν(Hg–S)

[a] Crystals obtained from recrystallization in D_2O. [b] ν (stretching), δ_{asym} (asymmetric bending), δ_{sym} (symmetric bending), ρ_t (torsional), ρ_r (rocking).

the plane are 0.01 Å for $[HgMe(pen)]\cdot H_2O$ and 0.03 Å for $[Hg_2Me_2(pen)]$; *i.e.* the carboxyl groups are coplanar with C(2). The nitrogen atoms deviate 0.70 and 0.76 Å for molecules (a) and (b) of $[HgMe(pen)]\cdot H_2O$ and −0.86 shown in Figures 5 and 6. The almost linear C–Hg–S branch in $[HgMe(pen)]\cdot H_2O$ is perpendicular to the *ac* plane. In contrast the C–Hg–S branches are almost in the *ac* plane in the $[Hg_2Me_2(pen)]$ crystal.

Vibrational spectra. Four areas of the spectra were of particular interest, namely, the ν(N–H) and ν(O–H)

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regions, the ν(S–H) region, the ν(C=O), δ($\overset{+}{N}H_2$), and δ($\overset{+}{N}H_3$) regions, and the far-i.r. region (below 600 cm^{-1}) where metal–ligand modes are expected.

water) at 3 480 cm^{-1} in [HgMe(pen)]·H_2O all the i.r. spectra in the high-frequency region are typical of a strongly hydrogen-bonded zwitterionic amino-acid and

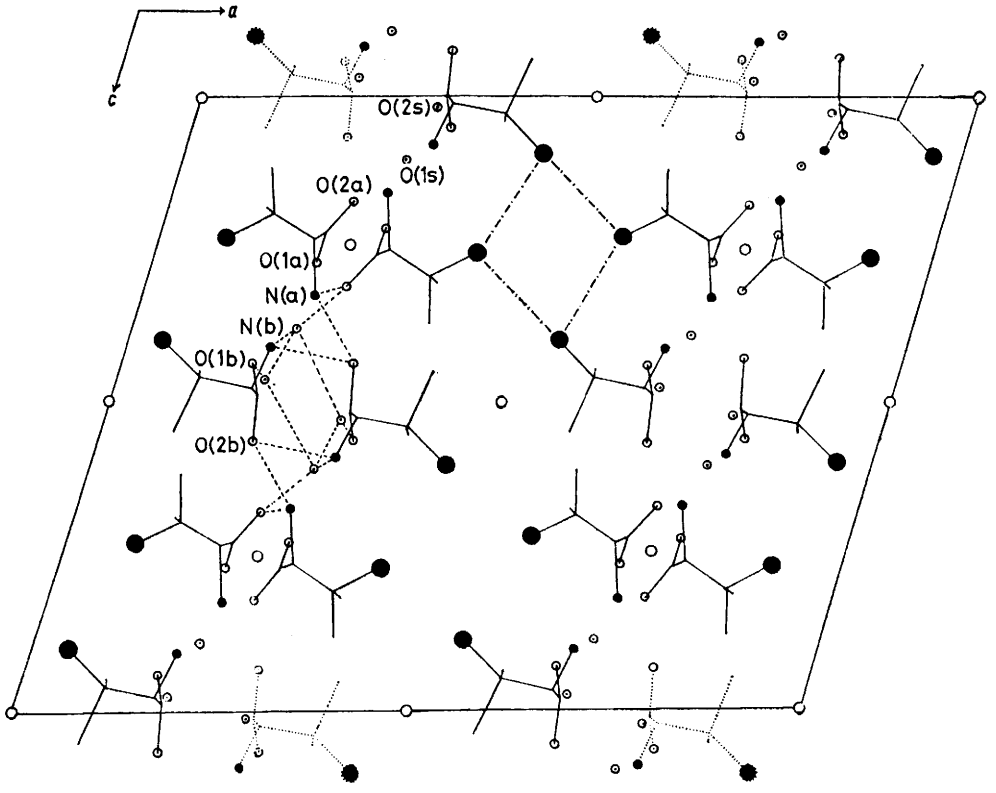

FIGURE 5 Hydrogen bonding and Hg · · · S attractions between layers in [HgMe(pen)]·H_2O. The solid circles (●) are S–Hg–C groups which are perpendicular to the *ac* plane. (○) centres of symmetry; (o) CO_2 groups; (– – – –) hydrogen bonds; (— · — · —) weak interactions

Table 4 summarizes the characteristic spectral bands and possible assignments for DL-penicillamine and the complexes. Apart from the ν(O–H) band (solvent

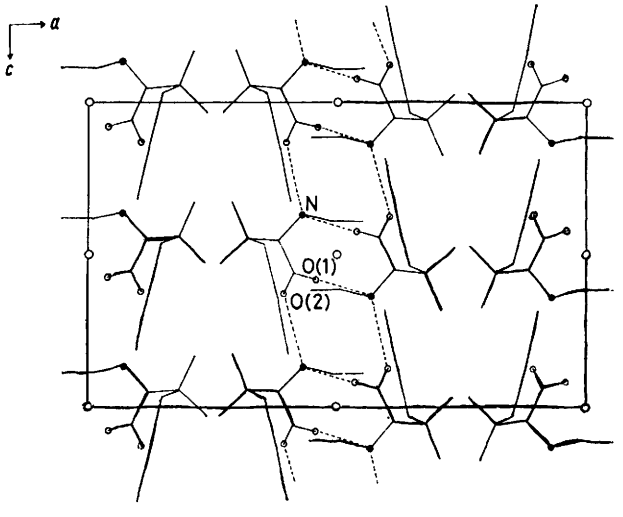

FIGURE 6 Hydrogen bonding and weak attraction between double layers in [Hg_2Me_2-μ-(pen)]. Long solid lines (——) are S–Hg–C groups which are in the *ac* plane. (○), centres of symmetry; (o), CO_2^- groups; (— — —), hydrogen bonds

not of compounds with ' free ' amino- (NH_2) and carboxyl (CO_2H) groups.[30] The band due to ν(S–H), which is weak and difficult to identify in the i.r., is the strongest band in the Raman spectra of S–H-containing amino-acids. Hence the disappearance of this band in the Raman spectrum is an excellent diagnostic test of co-ordination to a deprotonated sulphydryl ligand.

Upon deuteriation, δ($\overset{+}{N}H_3$) modes shift from 1 508—1 659 cm^{-1} to 1 132—1 183 cm^{-1} for δ($\overset{+}{N}D_3$), giving additional support for the assignments in this region. These bands were not observed in [Hg_2Me_2(pen)] due to the attachment of $HgMe^+$ to the amino-group. The $\delta_{asym}(\overset{+}{N}H_2)$ modes of the Hg–N-bonded complex are obscured by the strong $\delta_{asym}(CO_2^-)$ modes, and the $\delta_{sym}(\overset{+}{N}H_2)$ bands which appear around 1 250 cm^{-1} are relatively weak. After recrystallization in D_2O, these shift to 1 050 and 1 022 cm^{-1} in [HgMe(pen)]·D_2O. However, for the carboxyl-group stretching modes, there is little change in the frequency separations [$\nu_{asym}(CO_2^-)$ — $\nu_{sym}(CO_2^-)$] upon complexation by methylmercury,

[30] See *e.g.*: (*a*) S. E. Livingstone and J. D. Nolan, *Inorg. Chem.*, 1968, **7**, 1447; (*b*) H. Shindo and T. L. Brown, *J. Amer. Chem. Soc.*, 1965, **87**, 1904.

which indicates that the interaction of the mercury atoms with these groups is relatively weak.[31] In [HgMe(pen)]·H_2O the i.r. band pattern in this region is, on the other hand, similar to that of the 'free' penicillamine in the zwitterionic form.

In the far-i.r. the Hg–C stretching modes were readily identified as a medium-intensity band in the i.r. and an intense band in the Raman spectra at *ca.* 540 cm^{-1}. This band is so close to the $\rho_r(CO_2^-)$ mode in [Hg_2Me_2(pen)] that only single bands are observed in the Raman (546 cm^{-1}) and i.r. (547 cm^{-1}) spectra. After deuterium exchange with D_2O the peaks of $\rho_r(CO_2^-)$ at 543 cm^{-1} and ν(Hg–C) at 540 cm^{-1} are identifiable.

Medium-intensity Raman bands at 322 cm^{-1} in [HgMe(pen)]·H_2O and at 334 cm^{-1} in [Hg_2Me_2(pen)] which are not observed in either the free ligand or in HgMeCl are assigned to ν(Hg–S) stretching. In [Hg_2Me_2(pen)] a similar band appeared at 339 cm^{-1} in the i.r. spectrum. However, for [HgMe(pen)]·H_2O the i.r. spectrum showed only a weak shoulder at 322 cm^{-1}. Comparative values of ν(Hg–S) are 329 cm^{-1} in HgMe(SMe),[32] 283 cm^{-1} in HgMe(SCN),[33] and 337 cm^{-1} in $Hg(SMe)_2$.[34]

The literature data for ν(Hg–N) modes are quite confusing. Assignments usually specify the region from 400 to 700 cm^{-1} for this vibration.[35,36] A medium-intensity band at 432 cm^{-1} in the Raman spectrum of [Hg_2Me_2(pen)] is tentatively assigned to ν(Hg–N). A broad medium-strong counterpart appeared at 441 cm^{-1} in the i.r. spectrum. Upon deuteriation this peak shifts 21 cm^{-1} to 420 cm^{-1} whereas all the other skeletal modes in this region shift only *ca.* 10 cm^{-1}.

Thus we can conclude that under neutral pH conditions, attachment of $HgMe^+$ to the sulphydryl group will result in the disappearance of the strong ν(S–H) band at *ca.* 2 550 cm^{-1} and the appearance of a medium-strong peak at 300 cm^{-1} due to ν(Hg–S) in the Raman spectrum. If the binding site of $HgMe^+$ is the amino-group, $\delta(\overset{+}{N}H_2)$ bands (*ca.* 1 625 and 1 520 cm^{-1}) will disappear in the i.r. spectrum and a medium-intensity peak at 400—500 cm^{-1} due to ν(Hg–N) will appear. The presence of ($HgMe^+$) in a complex is evident from the very strong ν(Hg–C) stretching mode near 500 cm^{-1} in the Raman spectrum.

TABLE 5

Hydrogen-1 and ^{13}C n.m.r. chemical shifts (δ p.p.m. relative to methyl of dds) for DL-penicillamine and its methylmercury complexes

Compound	Positions α	Δα	β	Δβ	γ	Δγ	$Hg-CH_3$	$\Delta(Hg-CH_3)$	COO^-
^1H chemical shifts									
HgMe(OH)							0.87		
DL-pen	3.73				1.53, 1.62 (av. 1.58)				
[HgMe(pen)]·H_2O	3.73	0.00			1.60, 1.60 (av. 1.60)	0.02	0.82	−0.05	
[Hg_2Me_2-μ-(pen)]	4.43	+0.70			1.47, 1.70 (av. 1.59)	0.01	0.87	0.00	
^{13}C chemical shifts									
DL-pen	66.4		45.6		29.5, 32.0 (av. 30.8)				173.0
[HgMe(pen)]·H_2O	67.8	1.4	49.7	4.1	34.4, 36.6 (av. 35.5)	4.7	12.0		
[Hg_2Me_2-μ-(pen)]	68.9	2.5	50.7	5.1	35.1, 35.6 (av. 35.4)	4.6	5.7		

Nuclear magnetic resonance spectra. Various workers have utilised n.m.r. spectroscopy to investigate mercury complexation in solution by varying pH and metal–ligand ratios. However, complementary solid-state structural data have not been available. It was of interest, therefore, to correlate our crystal structure results with ^1H and ^{13}C n.m.r. data for [HgMe(pen)]·H_2O and [Hg_2Me_2(pen)] in D_2O solution (Table 5).

A comparison of the spectra of the complexes with the 'free' amino-acid spectra allows the following conclusions to be drawn. (*i*) The chemical shift of the protons on the α-carbon atom (C_2) is virtually unaffected by complexation in [HgMe(pen)]·H_2O. However, this resonance undergoes a 0.7 p.p.m. downfield shift in [Hg_2Me_2(pen)]. This indicates that the binding site is distant from the α carbon in [HgMe(pen)]·H_2O and close to the α carbon in [Hg_2Me_2(pen)]. (*ii*) The significant ^{13}C downfield shift (4.6 and 4.7 p.p.m.) of the γ-carbon atoms in the two penicillamine complexes indicates that their sulphur atoms are bonded to methylmercury.

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[6/1675 *Received*, 1*st September*, 1976]

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