Preparation and structural characterization of methylmercury(II) complexes of the minor tRNA-base 1-methyladenine

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Abstract

Methylmercury(II) complexes of 1-methyladenine (1made) have been isolated from aqueous solution in the pH range 2–12 and structurally characterized by ^{1}H NMR spectroscopy and X-ray analysis. The results establish N9 as the primary and N7 as the secondary binding site for CH_3Hg^+ with neutral 1-methyladenine. Crystal structure determinations for [1madeH]Cl and [1madeH_2]Cl_2 demonstrate that N9 is the first and N7 the second protonation site for 1-methyladenine. The cations $[(HgCH_3)(1made)]^+$, $[(HgCH_3)(1madeH)]^{2+}$ and $[(HgCH_3)_3(1made)]^{3+}$ display N9-, N7- and N3,N7,N9-coordination, respectively. Metallation of the amino nitrogen N6 is observed for complexes crystallized from aqueous solution at pH values above 8. The complexes $[(HgCH_3)(1madeH_{-1})]\cdot H_2O$ and $[(HgCH_3)_2(1madeH_{-1})][NO_3]\cdot 2H_2O$ exhibit N6- and N6,N9-coordination, respectively.

Introduction

Minor nucleobases have been detected in all types of polynucleotides [1]. One of the characteristic modifications of the parent purines and pyrimidines is the methylation of ring nitrogen atoms such as N1 of adenine, N7 of guanine and N3 of cytosine. The biological role of many of the minor methylated bases is still uncertain. However, it has been suggested that the presence of 7-methylguanine is necessary to optimize the activity of important functional regions of rRNA [2]. A significant increase in the percentage occurrence of methylated nucleobases in certain tumour arts is now well documented [3].

Methylation of adenine or guanine can lead to pronounced changes in the acid–base properties and coordination chemistry of the respective bioligand. For instance, the logarithmic formation constant for the binding of 3-methyladenine to the bis(acetylacetonato)nitrocobalt(III) moiety is approximately twice as large as that for the isomeric 9-methyladenine [4, 5]. Studies of metal coordination to other than 9-methylated purine bases have been very limited. On account of its ability to function as a uniligating Lewis acid with minimal steric effects, the methylmercury(II) ion has proved to be a suitable cation for the analytical characterization of binding sites in nucleobases and nucleosides [6–10]. We have recently presented systematic studies of the interaction of this cation with the methylated purines 7-methylguanine and 3-methyladenine (3made) [11, 12]. Our results establish N7 as the primary and N9 as the secondary binding site for CH_3Hg^+ with neutral 3-methyladenine (for numbering scheme in the purine ring see Figs. 2–5). The following complexes $[(HgCH_3)(3made)][NO_3]$, $[(HgCH_3)_2(3made)][NO_3]_2$ and $[(HgCH_3)_3(3madeH_{-1})][NO_3]_2\cdot H_2O$ were obtained from aqueous solutions in the pH range 2–4. N7-, N7,N9- and N6,N7,N9-coordination, respectively, were established for the complexes by X-ray structural analysis. ^{1}H NMR data indicate N6,N7- and N6,N6,N9-coordination for two complexes $[(HgCH_3)_2(3madeH_{-1})][NO_3]\cdot H_2O$ and $[(HgCH_3)_3(3madeH_{-2})][NO_3]$ isolated at a pH value of 8. No complex displaying methylmercury(II) coordination of the endocyclic pyrimidine nitrogen N1 could be obtained for 3-methyladenine. These findings are in marked contrast to the coordination properties of the isomeric 9-methyladenine, which has frequently been employed as a model compound for adenosine. Complexes $[(HgCH_3)(9madeH)][NO_3]$, $[(HgCH_3)(9madeH_{-1}]$, $[(HgCH_3)_2(9madeH_{-1})][ClO_4]$ and $[(HgCH_3)(9madeH_{-2})]$ with N1-, N6-, N1,N6- and N6,N6-coordination, respectively (X-ray structural analyses) have been prepared in aqueous solution [13–16]. These crystal structure determinations deliver, however, an exaggerated impression of the predominance of N1 coordination for neutral 9-methyladenine. Solution studies yield an intrinsic logarithmic [N1]/[N7] binding ratio of -0.1 for the interaction of CH_3Hg^+ with adenosine [17].

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We now report a systematic analysis of CH_3Hg^+ complexes of 1-methyladenine, which could be isolated from aqueous solution in the pH range 2–12. In addition we include crystal structure determinations for [3madeH]Cl and [3madeH_2]Cl_2. Our aim was to establish the primary and secondary metal binding and protonation sites for this methylated purine. We present the ^{1}H NMR spectroscopic and X-ray structural characterization of [$(HgCH_3)$(1madeH$_{-1}$)]·H_2O (**1n**·H_2O), [$(HgCH_3)$(1made)][NO_3] (**1i**), [$(HgCH_3)_2$(1madeH$_{-1}$)]-[NO_3]·$2H_2O$ (**2i**·$2H_2O$) and 2[$(HgCH_3)$(1madeH)]-[$NO_3]_2$·[$(HgCH_3)_3$(1made)][$NO_3]_3$·$4H_2O$ (2(**1ii**·**3iii**·$4H_2O$). The cations **1ii** and **3iii** are disordered in the crystal lattice of the latter compound, which is obtained at a pH value of 4–5.

Experimental

Methylmercury(II) hydroxide (Alfa) and 1-methyladenine (Sigma) were used as received. IR spectra were recorded as 1% KBr discs on a Perkin-Elmer 297 spectrometer. ^{1}H NMR spectra were measured on a Bruker WP 200 for 5% solutions in d_6-DMSO with the DMSO signal as reference; δ values are in ppm. [1madeH]Cl and [1madeH_2]Cl_2 were prepared by neutralization of 1made by one or two equivalents of HCl, respectively, followed by slow evaporation of the solutions at r.t.

Preparation of methylmercury(II) complexes

All preparations were carried out in a well ventilated fume hood. In a typical preparation 77 mg (0.33 mmol) methylmercury hydroxide was added to an appropriate suspension of 1-methyladenine in 8 ml H_2O to yield the required metal-to-ligand ratio. The pH was adjusted to a predetermined value in the range 2–12 by addition of 1 M HNO_3 or NaOH. Clear solutions were obtained upon heating to 50 °C for 1 h. Products were obtained by slow evaporation of the solvent and after filtration were washed with ethanol and ether.

[$(HgCH_3)$(1madeH$_{-1}$]]·H_2O (**1n**·H_2O), 1:1 ratio, pH = 12. $C_7H_{11}N_5OHg$ (*M* 381.8): *Anal.* Found: C, 21.0; H, 2.70; N, 18.5. Calc.: C, 22.0; H, 2.90; N, 18.3%. ^{1}H NMR: 0.78 (s, 3H, $^2J(^{199}Hg-^1H) = 202$ Hz, $HgCH_3$), 3.60 (s, 3H, CH_3), 7.16 (s, 2H, NH_2), 7.64 (s, 1H, H8), 8.01 (s, 1H, H2) ppm.

[$(HgCH_3)$(1made)][NO_3] (**1i**), 1:1 ratio, pH 2–8; 2:1 ratio, pH 2–5. $C_7H_{10}N_6O_3Hg$ (*M* 426.8): *Anal.* Found: C, 19.5; H, 2.23; N, 20.8. Calc.: C, 19.7; H, 2.36; N, 19.7%. ^{1}H NMR: 0.85 (s, 3H, $^2J(^{199}Hg-^1H) = 203$ Hz, $HgCH_3$), 3.77 (s, 3H, CH_3), 9.20 (s, 2H, NH_2), 8.20 (s, 1H, H8), 8.51 (s, 1H, H2) ppm.

[$(HgCH_3)_2$(1madeH$_{-1}$)][NO_3]·$2H_2O$ (**2i**·$2H_2O$), 1:1 ratio, pH 9–11; 2:1 ratio, pH 8–11. $C_8H_{16}N_6O_5Hg_2$ (*M* 677.4): *Anal.* Found: C, 14.7; H, 1.86; N, 13.1. Calc.: C, 14.2; H, 2.38; N, 12.4%. ^{1}H NMR: 0.83 (s, 6H, $^2J(^{199}Hg-^1H) = 211$ Hz, $HgCH_3$), 3.78 (s, 3H, CH_3), 7.82 (s, 2H, NH_2), 7.97 (s, 1H, H8), 8.37 (s, 1H, H2) ppm.

2[$(HgCH_3)$(1madeH)][$NO_3]_2$·[$(HgCH_3)_3$(1made)]-[$NO_3]_3$·$4H_2O$ (2(**1ii**)·**3iii**·$4H_2O$), 3:1 ratio, pH 4–5. $C_{23}H_{46}N_{22}O_{25}Hg_5$ (*M* 2033.7): *Anal.* Found: C, 13.9; H, 2.05; N, 14.5. Calc.: C, 13.6; H, 2.28; N, 15.1%. ^{1}H NMR: 0.85 (s, 15H, $^2J(^{199}Hg-^1H) = 220$ Hz, $HgCH_3$), 3.78 (s, 9H, CH_3), 9.06 (s, 2H, NH_2 **3iii**), 8.43, 9.62 (s, 1H, H8 **3iii**), 9.84 (s, 4H, NH_2 **1ii**), 8.13, 8.54 (s, 2H; H2, H8 **1ii**).

X-ray structural analyses

Crystal and refinement data are summarized in Table 1. Unit cell constants were obtained from a least-squares fit to the settings of 25 reflections recorded on an Enraf-Nonius CAD4 diffractometer. Reflection data were collected on the diffractometer at variable scan rates in the θ–2θ (for [1madeH]Cl) or ω modes (for the other compounds) with Mo Kα radiation ($\lambda = 0.71073$ Å). Three monitor reflections were recorded at regular intervals. The structures were solved by Patterson or direct methods and refined by full-matrix least-squares. Anisotropic temperature factors were introduced for all non-hydrogen atoms in [1madeH]Cl, [1madeH_2]Cl_2 and **1i** and for the mercury atoms in the remaining complexes. The cations **1ii** and **3ii** are disordered in the crystal lattice of 2(**1ii**)·**3ii**·$4H_2O$, which crystallizes in the triclinic space group $P\bar{1}$. For the N7-coordinated dication **1ii**, which is present in one half of all unit cells, both of the independent 1-methyladenine sites a and b (listed in Table 2) can be occupied simultaneously. In the remaining unit cells either the a or the b position may be adopted by the purine atoms of the more voluminous N3,N7,N9-coordinated trication **3iii**. The atom pairs Hg3a/Hg9b and Hg3b/Hg9a occupy identical sites for the a and b positions of the 1-methyladenine moiety. As a result Hg7 and the purine atoms (cations a and b) display site occupation factors of 0.75, Hg3a/Hg9b and Hg3b/Hg9a in contrast 0.50. In total one formula unit of 2(**1ii**)·**3ii**·$4H_2O$ is present in the unit cell ($Z = 1$). The positions of the disordered methyl mercury carbon atoms C31a/C91a and C31b/C91b must lie within 0.40 Å of the respective sites of the purine nitrogen atom pairs N9b/N3b and N9a/N3a. They were not included in the least-squares refinement. The observed composition is in accordance with the analytical and ^{1}H NMR spectroscopic data. 1-Methyladenine hydrogen atoms were included in the final refinement cycles for [1madeH]Cl and [1madeH_2]Cl_2. Both cations are present in the amino form with N9-protonation in the former and N7,N9-protonation in the latter salt. Final difference

TABLE 1. Crystal and refinement data

Compound	[1madeH]Cl	[1madeH$_2$]Cl$_2$	**1n**·H$_2$O	**1i**	**2i**·2H$_2$O	2(**1ii**)·**3iii**·4H$_2$O
Space group	$P2_1/c$	$P2_1/n$	$P2_1/c$	$C2/c$	$P2_1/n$	$P\bar{1}$
a (Å)	4.899(1)	4.623(1)	8.404(1)	23.929(5)	20.183(5)	11.634(2)
b (Å)	18.273(5)	18.783(5)	14.364(5)	6.239(2)	6.925(2)	13.247(3)
c (Å)	8.668(1)	10.985(3)	8.281(2)	16.941(5)	10.955(3)	10.479(2)
α (°)	90	90	90	90	90	105.55(2)
β (°)	91.09(3)	102.08(4)	104.71(2)	119.30(3)	91.00(2)	108.32(1)
γ (°)	90	90	90	90	90	76.52(2)
V (Å^3)	775.8(5)	932.7(9)	966.9(5)	2206(2)	1531(1)	1457(1)
Z	4	4	4	8	4	1
D_c (g cm^{-3})	1.59	1.58	2.62	2.57	2.94	2.32
Radiation	Mo Kα	Mo Kα	Mo Kα	Mo Kα	Mo Kα	Mo Kα
μ (cm^{-1})	4.4	6.6	158.9	139.6	200.6	132.1
Scan method	θ–2θ	ω	ω	ω	ω	ω
$2\theta_{max}$ (°)	50	50	45	45	45	45
Reflections measured	1449	1660	1293	1388	1993	3796
Reflections observed	1009	1107	1062	1166	1427	3043
Rejection criterion	2σ	2σ	2σ	2σ	2σ	2σ
R	0.068	0.045	0.060	0.053	0.047	0.053
R_w	0.068	0.045	0.061	0.056	0.047	0.053
p	0.014	0.022	0.007	0.005	0.010	0.005

Fourier syntheses did not allow an unequivocal location of all hydrogen atoms in the methylmercury(II) complexes and these were, therefore, not included in the refinements. The terminal reliability indices are listed in Table 1, where $R_w = [\Sigma w(F_o - F_c)^2 / \Sigma w F_o^2]^{1/2}$. The weighting schemes used were given by $w = (\sigma^2(F_o) + p^2 F_o^2)^{-1}$ with values of p given in Table 1. Calculations were performed with SHELX-76 and with local programs. Atom positional parameters with isotropic temperature factors are listed in Table 2. Bond lengths (Å) and angles to the mercury atoms are contained in Table 3.

Discussion

The reaction of the methylmercury(II) cation with 1-methyladenine is summarized in the interaction scheme depicted in Fig. 1. It has been demonstrated by ^{13}C NMR spectroscopy that the amino form of 1-methyladenine predominates in aqeuous solution and that the major protonation site of the free base is N9 of the imidazole ring [18]. These findings are confirmed by the crystal structure determination of [1madeH]Cl reported in this work. Both the protonated imidazole nitrogen N9 and the amino nitrogen N6 participate in N–H...Cl hydrogen bonds. Respective N...Cl distances are 3.07 and 3.12 Å. The second amino hydrogen is employed for an N6–H...N7 ($2-x$, $1-y$, $2-z$) interaction of length 2.89 Å. Both imidazole nitrogens N7 and N9 are protonated in the dication of [1madeH$_2$]Cl$_2$. As for the monochloride, the crystal lattice of [1madeH$_2$]Cl$_2$ is stabilized by N9–H...Cl and N6–H...Cl hydrogen bonds to one chloride ion (Cl1). In addition N6–H...Cl and N7–H...Cl interactions occur to the second chloride ion Cl2.

Protonation constants pK of 11.0 (for the protonation of the amino N6 in 1madeH$_{-1}$ at 20 °C and ionic strength 0.05) and 7.11 (for the protonation of the imidazole N9 in 1made at 25 °C and zero ionic strength) have been measured spectrophotometrically for 1-methyladenine [18]. These findings indicate that the neutral base 1made will be the predominant 1-methyladenine species in moderately alkaline solutions. In neutral and alkaline solutions of methylmercury(II), CH_3HgOH is the major component. In addition to CH_3HgOH, a significant concentration of $[(CH_3Hg)_2OH]^+$ will be present in the pH range 4–7, CH_3Hg^+ only being of importance in more acid solutions [19].

$$CH_3HgOH + HN< \rightleftharpoons CH_3HgN< + H_2O \quad (1)$$

$$CH_3HgOH + N \rightleftharpoons CH_3HgN^+ \leqslant + OH^- \quad (2)$$

$$CH_3Hg^+ + HN< \rightleftharpoons CH_3HgN< + H^+ \quad (3)$$

$$CH_3Hg^+ + N \rightleftharpoons CH_3HgN^+ \leqslant \quad (4)$$

At pH values above 11 reaction (1) prevails leading to the formation of the neutral species **1n**·H$_2$O, which displays N6-metallation (Fig. 2). In addition to the methyl carbon C61, the coordination sphere of the mercury atom is completed by a weak secondary bond of length 2.95(2) Å to N3 of a symmetry related molecule ($-x$, $0.5+y$, $1.5-z$). This leads to the formation of molecule chains parallel to the b-axis.

In the 1:1 ionic species **1i**, N9 is the binding site of the methylmercury(II) cation (Fig. 3). This coordination

TABLE 2. Atom positional parameters with equivalent isotropic temperature factors (Å²)

Atom	x/a	y/b	z/c	B
[1madeH]Cl				
Cl	0.1153(3)	0.7338(1)	0.5512(2)	3.2(1)
N1	0.4174(8)	0.4103(3)	0.7200(4)	2.1(2)
N3	0.2455(9)	0.5221(3)	0.6190(5)	2.8(3)
N6	0.7806(8)	0.4004(3)	0.8972(5)	2.5(2)
N7	0.7858(8)	0.5681(2)	0.8819(5)	2.2(2)
N9	04901(9)	0.6263(3)	0.7253(5)	2.9(3)
C1	0.3888(11)	0.3313(3)	0.7195(7)	3.2(3)
C2	0.2462(10)	0.4512(3)	0.6273(6)	2.6(3)
C4	0.4366(10)	0.5543(3)	0.7103(6)	2.2(3)
C5	0.6205(10)	0.5178(3)	0.8081(6)	2.1(3)
C6	0.6146(9)	0.4424(3)	0.8128(5)	2.0(3)
C8	0.7030(12)	0.6312(3)	0.8321(7)	2.8(3)
[1madeH$_2$]Cl$_2$				
Cl1	0.7352(3)	0.1605(1)	1.1379(1)	3.0(1)
Cl2	0.4756(3)	0.3959(1)	1.0057(1)	3.6(1)
N1	1.3790(8)	0.3291(2)	1.3484(3)	2.4(2)
N3	1.6138(8)	0.4409(2)	1.4055(3)	2.8(2)
N6	0.9471(10)	0.3147(2)	1.1978(4)	3.2(2)
N7	0.9811(9)	0.4773(2)	1.1737(3)	2.5(2)
N9	1.3445(8)	0.5372(2)	1.2836(3)	2.7(2)
C1	1.3975(14)	0.2520(3)	1.3726(5)	3.6(3)
C2	1.5931(11)	0.3724(3)	1.4160(4)	3.0(2)
C4	1.3875(10)	0.4678(2)	1.3200(4)	2.3(2)
C5	1.1611(9)	0.4299(2)	1.2500(4)	2.2(2)
C6	1.1506(9)	0.3558(2)	1.2617(4)	2.3(2)
C8	1.0995(11)	0.5408(3)	1.1967(4)	2.8(2)
1n·H$_2$O				
Hg6	0.2203(1)	0.1787(1)	0.9899(1)	2.3(1)
O1	0.4897(24)	0.0193(11)	0.7839(25)	4.1(4)
N1	−0.1476(23)	0.0327(11)	0.6293(24)	2.0(4)
N3	−0.1089(25)	−0.1336(12)	0.6338(26)	2.4(4)
N6	0.0209(26)	0.1395(12)	0.7909(27)	2.5(4)
N7	0.2119(26)	−0.0405(12)	0.9330(25)	2.8(4)
N9	0.1109(23)	−0.1829(12)	0.8426(25)	2.6(4)
C1	−0.2646(31)	0.1110(15)	0.5505(31)	2.5(5)
C2	−0.1963(34)	−0.0577(16)	0.5796(35)	3.3(6)
C4	0.0174(29)	−0.1154(14)	0.7600(31)	1.9(5)
C5	0.0668(29)	−0.0312(14)	0.8196(30)	1.8(4)
C6	−0.0125(30)	0.0513(13)	0.7493(31)	1.9(5)
C8	0.2299(34)	−0.1331(16)	0.9411(34)	3.2(6)
C61	0.4198(35)	0.2213(16)	1.1874(38)	3.5(6)
1i				
Hg9	0.4178(1)	0.1765(2)	0.2602(1)	2.4(1)
C1	0.7048(9)	0.6756(44)	0.5645(14)	3.3(6)
C2	0.6267(10)	0.4292(39)	0.4544(13)	3.0(7)
C4	0.5205(9)	0.4848(33)	0.3962(12)	1.8(5)
C5	0.5300(8)	0.6645(38)	0.4445(12)	2.1(5)
C6	0.5922(8)	0.7444(32)	0.5040(13)	2.1(6)
C8	0.4259(10)	0.6044(36)	0.3633(13)	2.7(6)
C9	0.3904(12)	−0.0868(38)	0.1791(14)	3.9(8)
N1	0.6369(7)	0.6113(27)	0.5053(10)	2.2(5)
N3	0.5675(8)	0.3599(32)	0.3975(11)	3.5(5)
N6	0.6057(7)	0.9207(27)	0.5533(11)	2.1(5)
N7	0.4684(8)	0.7536(31)	0.4228(11)	3.1(6)
N9	0.4553(8)	0.4444(30)	0.3455(10)	2.8(5)
N10	0.2650(10)	0.3362(44)	0.1730(14)	6.5(6)
O11	0.2087(9)	0.3170(40)	0.1664(12)	2.4(4)
O12	0.3103(10)	0.3055(44)	0.2553(13)	3.2(5)
O13	0.2719(10	0.3488(43)	0.1086(14)	3.4(5)
2i·2H$_2$O				
Hg6	0.9804(1)	0.1856(2)	0.2252(1)	3.2(1)
Hg9	1.1351(1)	0.4347(2)	0.8114(1)	3.0(1)

(*continued*)

TABLE 2. (*continued*)

Atom	x/a	y/b	z/c	B
O1	0.2962(10)	0.4860(30)	0.3599(18)	5.0(5)
O2	0.3245(10)	0.8122(35)	0.2229(19)	5.6(5)
O21	0.6557(10)	0.4789(32)	0.3680(19)	5.5(5)
O22	0.7606(11)	0.5181(34)	0.3824(20)	5.9(5)
O23	0.7098(11)	0.5821(38)	0.2094(21)	6.6(6)
N1	0.8975(9)	0.2141(28)	0.5869(16)	2.4(4)
N3	0.9780(10)	0.3043(35)	0.7328(19)	3.7(4)
N6	0.9227(9)	0.1644(31)	0.3834(17)	2.9(4)
N7	1.0619(10)	0.2669(32)	0.4555(19)	3.5(4)
N9	1.0891(10)	0.3393(32)	0.6493(18)	3.3(4)
N20	0.7086(11)	0.5245(36)	0.3187(21)	4.4(5)
C1	0.8269(13)	0.1640(43)	0.5626(23)	3.6(5)
C2	0.9202(13)	0.2646(39)	0.7004(23)	3.5(5)
C4	1.0226(10)	0.2948(34)	0.6407(19)	2.0(4)
C5	1.0057(11)	0.2584(34)	0.5236(20)	2.5(5)
C6	0.9407(11)	0.2059(38)	0.4895(21)	2.7(5)
C8	1.1066(11)	0.3179(39)	0.5347(21)	2.7(4)
C61	1.0302(15)	0.2135(50)	0.0655(28)	5.2(7)
C91	1.1678(13)	0.5458(46)	0.9772(24)	4.1(6)
2(1ii)·**3iii**·4H$_2$O				
Hg7a	0.8013(1)	0.2630(1)	1.0058(1)	2.8(1)
Hg7b	−0.3079(1)	0.7601(1)	0.4883(1)	3.1(1)
Hg3a/9b	0.1386(1)	0.4818(1)	0.7858(1)	2.6(1)
Hg3b/9a	0.3511(1)	0.5234(1)	0.6896(1)	2.6(1)
O1	0.6979(13)	0.0687(12)	0.8668(15)	5.4(4)
O2	−0.1960(16)	0.9252(15)	0.6656(18)	7.6(5)
N10	0.8710(13)	0.0527(13)	0.2051(16)	3.8(4)
N20	0.6321(13)	0.9628(13)	0.2715(16)	3.7(4)
N30	0.5878(16)	0.5572(15)	0.6325(18)	5.1(4)
N40	−0.0889(14)	0.4464(13)	0.8532(16)	3.8(4)
O11	0.9619(13)	0.0251(12)	1.2987(15)	5.1(3)
O12	0.8292(12)	0.1508(11)	1.2179(14)	4.5(3)
O13	0.8157(14)	−0.0117(13)	1.1096(16)	6.0(4)
O21	−0.4699(14)	0.9912(14)	0.1890(17)	6.5(4)
O22	−0.3029(14)	1.0278(14)	0.3467(17)	6.5(4)
O23	−0.3345(12)	0.8646(12)	0.2668(14)	4.9(3)
O31	−0.4875(14)	0.6248(13)	0.6850(16)	6.1(4)
O32	−0.3346(13)	0.5808(12)	0.5868(15)	5.2(4)
O33	−0.4115(15)	0.4592(14)	0.6237(17)	6.9(4)
O41	0.9847(12)	0.3757(11)	0.8073(14)	4.5(3)
O42	0.9237(13)	0.5406(12)	0.8651(14)	5.1(3)
O43	0.8245(13)	0.4312(12)	0.8892(15)	5.3(4)
N1a	0.3616(11)	0.2534(11)	1.0403(13)	2.1(3)
N1b	0.1321(11)	0.7665(11)	0.4552(13)	2.3(3)
N3a	0.2880(12)	0.3774(11)	0.8925(14)	2.6(3)
N3b	0.2025(11)	0.6331(11)	0.5900(13)	2.4(3)
N6a	0.5680(13)	0.1777(12)	1.1198(15)	3.3(3)
N6b	−0.0743(12)	0.8438(12)	0.3769(14)	2.8(3)
N7a	0.6121(11)	0.3263(11)	0.9543(14)	2.5(3)
N7b	−0.1198(11)	0.6872(11)	0.5325(13)	2.3(3)
N9a	0.4496(11)	0.4242(11)	0.8335(13)	2.3(3)
N9b	0.0407(12)	0.5864(11)	0.6482(14)	2.5(3)
C1a	0.3288(16)	0.1853(15)	1.1167(19)	3.3(4)
C1b	0.1659(15)	0.8364(14)	0.3846(17)	2.8(4)
C2a	0.2711(15)	0.3180(14)	0.9658(18)	2.8(4)
C2b	0.2188(15)	0.6997(15)	0.5237(18)	3.1(4)
C4a	0.4107(14)	0.3712(14)	0.9004(17)	2.5(4)
C4b	0.0804(14)	0.6423(14)	0.5840(17)	2.3(3)
C5a	0.5074(13)	0.3106(13)	0.9770(16)	2.0(3)
C5b	−0.0148(13)	0.7063(13)	0.5146(16)	2.1(3)
C6a	0.4831(14)	0.2456(14)	1.0459(17)	2.5(4)
C6b	0.0099(15)	0.7747(14)	0.4470(18)	2.8(4)
C8a	0.5721(14)	0.3947(14)	0.8693(17)	2.8(4)
C8b	−0.0835(15)	0.6175(15)	0.6134(18)	3.0(4)
C71a	0.9888(17)	0.2065(17)	1.0441(21)	4.0(5)
C71b	−0.4927(21)	0.8200(20)	0.4545(24)	5.6(6)

TABLE 3. Bond lengths (Å) and angles (°) to the mercury atoms

1n·H_2O			
Hg6–N6	2.11(2)	Hg6–C61	2.11(3)
Hg6–N3[a]	2.95(2)		
N6–Hg6–C61	178.7(8)	N6–Hg6–N3	81.6(6)
C61–Hg6–N3	97.1(7)		
1i			
Hg9–N9	2.10(1)	Hg9–C9	2.03(1)
Hg9–O12	2.66(1)		
N9–Hg9–C9	174.3(5)	N9–Hg9–O12	82.0(4)
C9–Hg9–O12	103.7(5)		
2i			
Hg6–N6	2.11(2)	Hg6–C61	2.04(3)
Hg6–N7	3.04(2)	Hg9–N9	2.10(2)
Hg9–C91	2.07(3)	Hg9–O21[b]	2.96(2)
Hg9–O22[c]	3.03(2)		
N6–Hg6–C61	176(1)	N6–Hg6–N7	68(1)
C61–Hg6–N7	115(1)	N9–Hg9–C91	172(1)
N9–Hg9–O21[b]	86(1)	N9–Hg9–O22[c]	75(1)
C91–Hg9–O21[b]	98(1)	C91–Hg9–O22[c]	111(1)
O21[b]–Hg9–O22[c]	99(1)		
3iii			
Hg7a–N7a	2.116(8)	Hg7b–N7b	2.134(7)
Hg7a–C71a	2.08(1)	Hg7b–C71b	2.06(1)
Hg7a–O1	2.92(1)	Hg7b–O2	2.75(1)
Hg7a–O12	2.89(1)	Hg7b–O32	2.94(1)
Hg7a–O43	2.91(1)	Hg7b–O23	2.91(1)
Hg3a–N3a	2.161(8)	Hg7b–N3b	2.167(7)
Hg9a–N9a	2.145(8)	Hg9b–N9b	2.141(8)
N7a–Hg7a–C71a	175.2(4)	N7b–Hg7b–C71b	174.4(4)
N7a–Hg7a–O1	79.7(4)	N7b–Hg7b–O2	78.6(4)
N7a–Hg7a–O12	103.8(4)	N7b–Hg7b–O23	103.5(4)
N7a–Hg7a–O43	84.0(4)	N7b–Hg7b–O32	82.2(5)
C71a–Hg7a–O1	101.8(5)	C71b–Hg7b–O2	103.9(5)
C71a–Hg7a–O12	81.0(5)	C71b–Hg7b–O23	81.8(5)
C71a–Hg7a–O43	91.6(5)	C71b–Hg7b–O32	92.2(5)
O1–Hg7a–O12	73.8(4)	O2–Hb7b–O23	87.3(4)
O1–Hg7a–O43	129.2(4)	O2–Hg7b–O32	121.5(4)
O12–Hg7a–O43	157.0(4)	O23–Hg7b–O32	151.2(4)

[a] $-x, 0.5+y, 1.5-z$. [b] $0.5+x, 0.5-y, 0.5+z$. [c] $2-x, 1-y, 1-z$.

behaviour of 1-methyladenine is in contrast to that of the isomeric 3-methyladenine for which N7 is both the first protonation [20] and metal binding site (for CH_3Hg^+) [12]. **1i** can be crystallized from aqeuous solutions containing CH_3HgOH and 1-methyladenine in a 1:1 stoichiometric ratio over a wide pH range (2–8). Secondary Hg9...O12 bonds of length 2.66(1) Å to a nitrate oxygen atom are observed in the crystal lattice of **1i**. As a result of the introduction of a positive charge into the purine moiety, marked downfield shifts are observed for the H2, H8 and particularly the H6 signals in the ^1H NMR spectrum of **1i** in comparison to **1n**·H_2O. The strength of metal binding in methylmercury(II) complexes is reflected in the magnitude of the $^2J(^{199}Hg–^1H)$ coupling constants. Lower values are associated with an increased Hg–N bond strength [19]. In view of the difference in the basicities of N6 and N9, a marked increase in the value of this coupling constant might be expected on going from **1n**·H_2O to **1i**. In fact, the observed increase in $^2J(^{199}Hg–^1H)$ is marginal (202 and 203 Hz, respectively).

The isolation of the complex **2i**·$2H_2O$ for less than stoichiometric ratios of CH_3HgOH and 1-methyladenine in the pH range 9–11 emphasises that reactions (1) and (2) must be competitive in weakly alkaline solution. As expected N6 and N9 are coordinated in this complex (Fig. 4) Secondary Hg...O bonds are observed between Hg9 and the nitrate oxygen atoms O21 and O22 (Table 3). Proton resonances for H2, H6 and H8 in **2i**·$2H_2O$ occur at values intermediate to those in **1n**·H_2O and **1i**. The coupling constant $^2J(^{199}Hg–^1H)$ is significantly larger in **2i**·$2H_2O$ (211 Hz) than in **1n**·H_2O or **1i**, indicating that the average strength of the Hg–N bonds in the 2:1 ionic species is considerably weaker than in either of the 1:1 species. An analogous observation was made for CH_3Hg^+ complexes of 7-methylguanine [11]. Rapid exchange of CH_3Hg cations on the NMR time scale is typical for such complexes despite the high thermodynamic stability of the Hg–N bond, and has been studied mechanistically by Rabenstein [19].

In contrast to 3-methyladenine N6,N6-coordinated complexes could not be isolated from mildly alkaline aqueous solutions of CH_3HgOH and 1-methyladenine even in the presence of a large excess of the former component. For 3-methyladenine the complexes $[(HgCH_3)_3(3madeH_{-2})][NO_3]$ and $[(HgCH_3)_3(3madeH_{-1})][NO_3]_2 \cdot H_2O$ may be crystallized from aqueous solutions containing a 3:1 ratio of the components at respective pH values of 8 and 4. Under similar conditions only **2i**·H_2O may be isolated for 1-methyladenine from alkaline solutions in the pH range 8–11. As mentioned in the 'Introduction' methylmercury(II) coordination of the available endocyclic pyrimidine nitrogen N1 was not observed for 3-methyladenine [12]. In contrast, as depicted in Fig. 5, the pyrimidine nitrogen N3 is coordinated by CH_3Hg^+ in the complex **3iii**, which is present in the disordered crystal lattice of 2(**1ii**·**3iii**·$4H_2O$, isolated from an aqueous solution in the pH range 4–5. Under these conditions the cation $[1madeH]^+$ with N9 protonation will be the predominant 1-methyladenine species present in solution. It may, therefore, reasonably be assumed that N9 is protonated in the N7-coordinated cations **1ii**, which occupy one half of the cation sites a and b, respectively, in the disordered structure. In the dication **2ii**, which will be present in solution in this pH range, both imidazole nitrogen N7 and N9 will be coordinated by CH_3Hg^+. The coordination spheres of the Hg7 atoms in **1ii** and **3iii** are completed by secondary Hg...O bond in the range 2.75–2.94 Å to one water and two nitrate oxygen atoms, respectively. Similar interactions to nitrate ox-

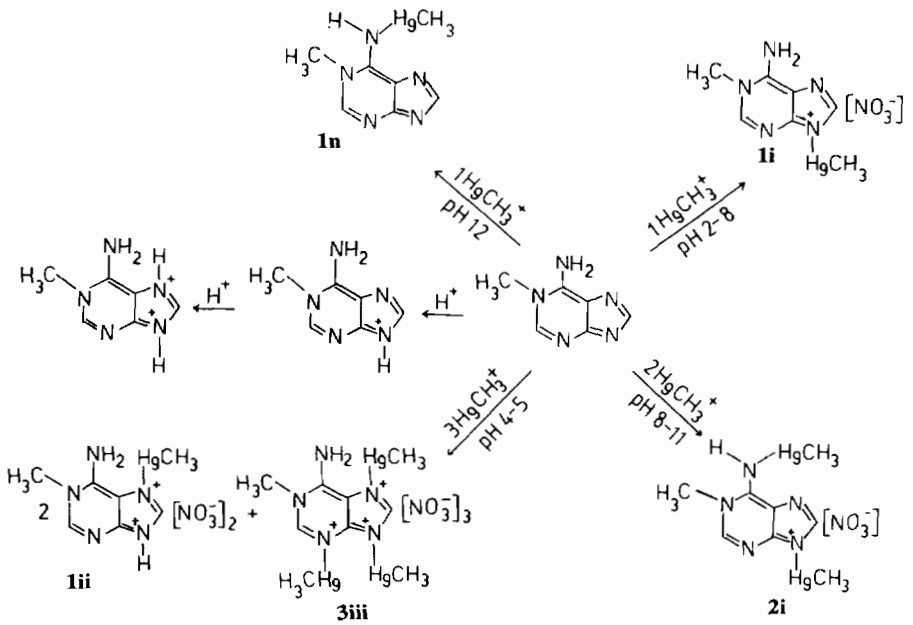

Fig. 1. Reaction of 1-methyladenine with the CH_3Hg^+ cation.

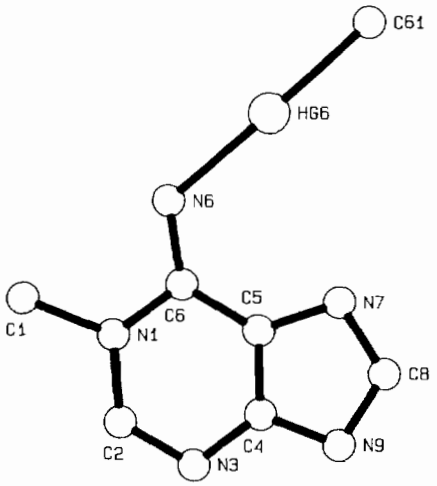

Fig. 2. Molecular structure of **1n**.

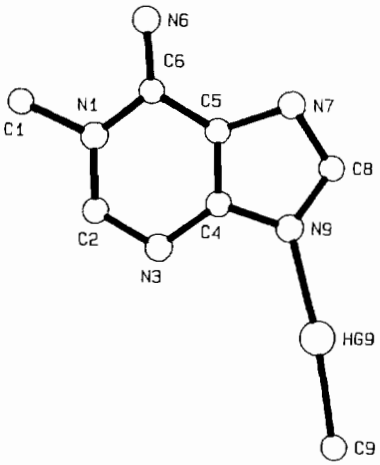

Fig. 3. Structure of the cation **1i**.

ygen atoms are also observed for Hg3 and Hg9. The integral values of the proton resonances measured for 2(**1ii**)·**3iii**·$4H_2O$ in d_6-DMSO solution are in accordance with the 2:1 ratio of the cations established for the disordered crystal structure. A marked downfield shift of 0.64 ppm is observed for the resonance of the amino protons in **1ii** (9.84 ppm) in comparison to **1i** (9.20 ppm). Observation of an average coupling constant $^2J(^{199}Hg–^1H)$ of 220 Hz in 2(**1ii**)·**3iii**·$4H_2O$ allows the conclusion that the average strength of the Hg–N bonds in **1ii** or **3iii** is markedly weaker than for monocationic or neutral 1-methyladenine complexes.

The present results confirm that the first protonation site of 1-methyladenine, the imidazole nitrogen N9, is also the primary binding site for the CH_3Hg^+ cation in a wide pH range (2–8). At pH values above 11 the anion $[1madeH_{-1}]^-$ is the predominant 1-methyladenine species present in aqueous solution and the N6-coordinated complex **1n**·H_2O may be isolated under these conditions. Presumably as a result of steric interaction between the N1-methyl group and a second N6-methylmercury(II) function a double metallation of the amino nitrogen cannot, in contrast to 3-methyladenine, be observed for 1-methyladenine. The imidazole nitrogen N7 has been demonstrated to be the chosen metal coordination site in acidic solution for both $[1madeH]^+$ and **1n**, in which N9 is either protonated or coordinated by CH_3Hg^+. In contrast to 3-methyladenine a methylmercury(II) complex **3ii** displaying coordination of the pyrimidine ring (in this case N3) could be prepared for 1-methyladenine.

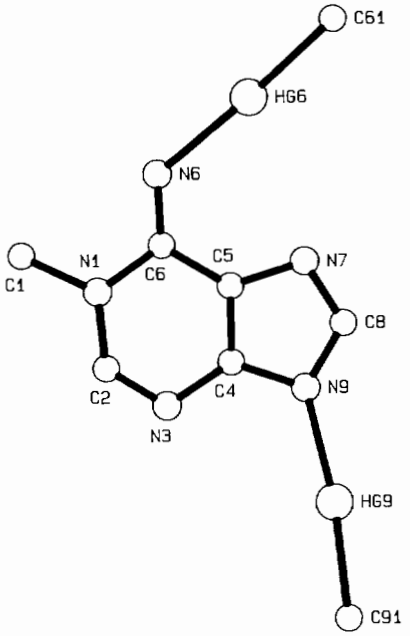

Fig. 4. Structure of the cation **2i**.

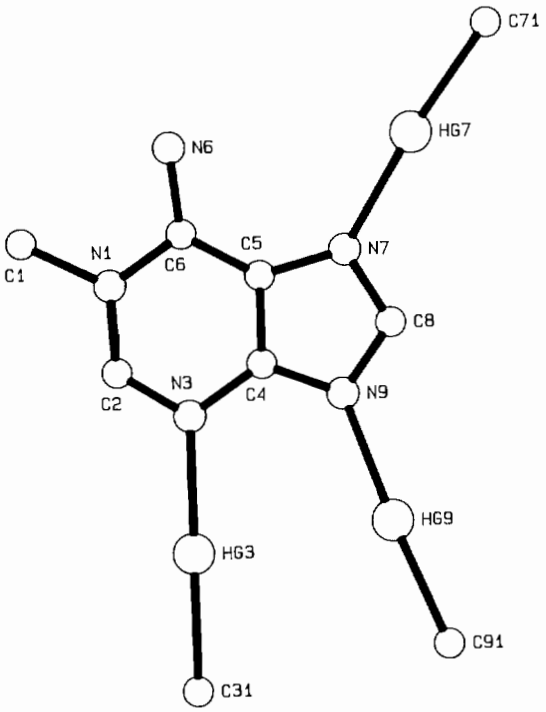

Fig. 5. Structure of the cation a of complex **3iii** (C31 and C91, whose disordered sites in the unit cell are close to those of N9b and N3b, are depicted at idealized positions).

Supplementary material

Tables of anisotropic temperature factors and observed and calculated structure factors are available from the authors on request.

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