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Preparation and Structural Characterization of Methylmercury(II) Complexes of 3-Methyladenine

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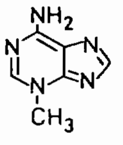
Abstract

Methylmercury(II) complexes of 3-methyladenine (3made) have been isolated from aqueous solution in the pH range 2–8 and structurally characterized. The results establish N7 as the primary and N9 as the secondary binding site for CH_3Hg^+ with neutral 3-methyladenine. The following complexes, $[(3made)HgCH_3][NO_3]$, $[(3made)(HgCH_3)_2][NO_3]_2$ and $[(3madeH_{-1})(HgCH_3)_3][NO_3]_2 \cdot H_2O$ 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. Two complexes $[(3madeH_{-1})(HgCH_3)_2][NO_3] \cdot H_2O$ and $[(3madeH_{-2})(HgCH_3)_3][NO_3]$ were prepared at a pH value of 8. ^1H NMR data suggest N6,N7- and N6,N6,N9-coordination.

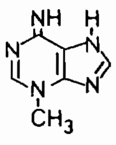
Introduction

Alkylation of endo- or exocyclic heteroatoms of purine bases can lead to pronounced changes in metal binding properties. For instance, the logarithmic formation constant for the binding of 3-methyladenine (3made) to the bis(acetylacetonato)nitrocobalt(III) moiety is approximately twice as large as that for the isomeric 9-methyladenine (9made) [1, 2].

Semi-empirical calculations [3] and NMR spectroscopic studies [4] have indicated that the amino form of 3-methyladenine **A** is thermodynamically more stable than the alternative imino forms **B** and **C**. INDO molecular orbital calculations suggest a clear preference for N7 over N1 as the primary metal binding site [5]. Coordination of the second imidazole nitrogen N9, which carries essentially the same charge as N7, will be restricted by the presence of the methyl substituent on N3 to metal cations with low coordination numbers. A crystal structure analysis of *cis*-$[(NH_3)_2Pt(3made)_2][NO_3]_2 \cdot 3H_2O$ has confirmed N7 as the platinum coordination site [5].



A



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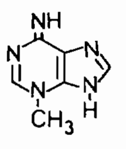

C

On account of its ability to function as a uniligating Lewis acid with minimal steric effects, the CH_3Hg^+ ion has proved to be a suitable cation for the analytic characterization of binding sites in nucleobases [6, 7]. A systematic study of the interaction of 9-methyladenine with CH_3Hg^+ led to the isolation of the following complexes [8–11], $[(9made)HgCH_3][NO_3]$, $[(9madeH_{-1})(HgCH_3)_2][ClO_4]$, $(9madeH_{-1})HgCH_3]$ and $[(9madeH_{-2})(HgCH_3)_2]$ with respectively N1-, N1,N6-, N6- and N6,N6-coordination. These results establish N1 as the primary binding site for CH_3Hg^+ with neutral 9-methyladenine and contrast with findings for other metals which, in general, display a preference for N7 [12]. An exception is found for the complex $[(9madeH)ZnCl_3]$, in which N1-coordination allows the formation of intramolecular N–H···Cl hydrogen bonds [13]. We now report a systematic analysis of the interaction of CH_3Hg^+ with 3-methyladenine in the pH range 2–8. Our aim was to establish the primary and secondary binding sites for the neutral base. We present the preparation and ^1H NMR characterization of the complexes $[(3made)HgCH_3][NO_3]$ (**1i**), $[(3madeH_{-1})(HgCH_3)_2][NO_3] \cdot H_2O$ (**2i·H$_2$O**), $[(3made)(HgCH_3)_2][NO_3]_2$ (**2ii**), $[(3madeH_{-2})(HgCH_3)_3][NO_3]$ (**3i**) and $[(3madeH_{-1})(HgCH_3)_3][NO_3]_2 \cdot H_2O$ (**3ii·H$_2$O**). In addition X-ray structural analyses were carried out on complexes **1i** and **2ii**. A partial X-ray study of **3ii·H$_2$O**, which is disordered in the crystal lattice, allowed the location of the mercury positions and, thereby, the establishment of the base coordination pattern*.

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*3ii·H_2O crystallizes monoclinic *C*2/*m* with a = 12.180(2), b = 25.522(3), c = 12.744(2) Å, β = 93.44(2)°, Z = 8. 1372 independent reflections ($2\theta \leq 45°$, Mo Kα, $F_o^2 \geq 2\sigma(F_o^2)$) were collected on an Enraf-Nonius CAD4 diffractometer; R = 0.114 for the disordered mercury atom positions. The 3 Hg···Hg distances in two disordered cations are consistent only with N6,N7,N9-coordination.

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Experimental

Methylmercury(II) hydroxide (Alfa) and 3-methyladenine (Sigma) were used as received. The analytical and ^1H NMR data for the methylmercury(II) complexes are presented in Tables 1 and 2. IR spectra were recorded as 1% KBr discs on a Perkin-Elmer 297 spectrometer.

Preparation of Methylmercury(II) Complexes

All preparations were carried out at ambient temperature in a well ventilated fune hood. In a typical experiment 0.27 mmol (0.061 g) methylmercury(II) hydroxide was added to an appropriate suspension of 3-methyladenine in 5 ml H_2O to yield the required metal-to-ligand ratio. The solution pH was adjusted to a predetermined value by addition of either 1 M HNO_3 or NaOH. Complete solution was achieved in all cases. Slow evaporation of the solutions yielded the following complexes.

[(3made)$HgCH_3$][NO_3] (**1i**), 1:1 ratio, pH = 4
[(3madeH_{-1})($HgCH_3$)$_2$][NO_3]·H_2O (**2i·H₂O**), 1:1 ratio, pH = 8
[(3made)($HgCH_3$)$_2$][NO_3]$_2$ (**2ii**), 1:1 ratio, pH = 2
[(3madeH_{-2})($HgCH_3$)$_3$][NO_3] (**3i**), 3:1 ratio, pH = 8
[(3madeH_{-1})($HgCH_3$)$_3$][NO_3]$_2$·H_2O (**3ii·H₂O**), 3:1 ratio, pH = 4

The colourless crystalline precipitates were washed with ethanol and ether. Satisfactory microanalyses (Table 1) were obtained for all complexes.

TABLE 1. Analytical Data for Methylmercury(II) Complexes of 3-methyladenine[a]

Compound	C (%)	H (%)	N (%)
1i	19.6 (19.70)	2.39 (2.36)	19.5 (19.69)
2i·H_2O	14.4 (14.57)	1.87 (2.14)	12.7 (12.75)
2ii	13.6 (13.64)	2.04 (1.86)	13.7 (13.92)
3i	12.8 (12.63)	1.67 (1.65)	10.3 (9.82)
3ii·H_2O	11.3 (11.54)	1.65 (1.83)	10.4 (10.46)

[a] Microanalyses were performed with a Perkin-Elmer 240. Calculated values are given in parentheses.

X-ray Structural Analysis

Crystal and refinement data for **1i** and **2ii** are summarized in Table 3. Unit cell constants were obtained from a least-squares fit to the settings of 25 reflections recorded on an Enraf-Nonius CAD4 diffractometer. Intensities were collected on the diffractometer at varied scan rates in the ω-mode with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). Three monitor reflections were measured at regular intervals; crystal decay was not observed. Empirical absorption corrections were applied to the reflection intensities of all data sets. The structures were solved by Patterson and difference syntheses and refined by full-matrix least-squares. Difference syntheses failed to reveal unequivocal positions for the nitrate oxygen atoms in **2ii**; these are presumably disordered and could not, therefore, be included in the final refinement cycles. Nor were hydrogen atom positions for **1i** or **2ii**. Anisotropic temperature factors were included fro the mercury atoms. The terminal reliability indices are listed in Table 3, where $R_w = [\Sigma w(F_o - F_c)^2/\Sigma wF_o^2]^{1/2}$. Weights were applied using the expression $w = (\sigma^2(F_o) + p^2F_o^2)^{-1}$, with values of p as given in Table 3.

As a result of the C3-methyl substitution, the adenine base moiety will display almost C_{2v} symmetry if hydrogens are ignored and nitrogen and carbon atoms are not distinguished. The assignment of N7 (and not N9 as would be conceivable) as the mercury coordination site in **1i** is unequivocal on the basis of the following evidence: (i) the N3–C3 and N6–C6 distances of 1.50(1) and 1.32(1) Å respectively; (ii) the isotropic temperature factors of 3.6(3) Å^2 for C3 and 3.5(3) Å^2 for N6; (iii) the observation of intermolecular N6···N1 and N6···O12 (nitrate

TABLE 2. ^1H NMR Data for Methylmercury(II) Complexes of 3-Methyladenine[a]

Compound	δ(H2)	δ(H6)	δ(H8)	δ(CH_3)	δ(Hg–CH_3)	$^2J(^{199}Hg–^1H)$ (Hz)
3-Methyladenine	8.29	7.76(×2)	7.76	3.89		
1i	8.61	8.61(×2)	8.26	3.99	0.87	224.5
2i·H_2O[b]	8.45	7.43(×1)	8.07	3.89	0.82	190.0
2ii	8.64	8.66(×2)	8.34	4.02	0.86	239.5
3i	8.21		7.83	4.00	0.78	180.0
3ii·H_2O	8.51	7.64(×1)	8.34	4.03	0.83	202.5

[a] Spectra were recorded on a Bruker WP 200 spectrometer at 20 °C in saturated solutions of DMSO-d_6 using internal TMS references. All shifts are in ppm downfield from TMS. Satisfactory integration of all spectra was obtained. [b] **2i** displays a dismutation to **1i** and **3i** in DMSO-d_6 solution.

TABLE 3. Crystal and Refinement Data for Methylmercury-(II) Complexes of 3-Methyladenine

Compound	**1i**	**2ii**
Space group	$C2/c$	$P2_1/c$
a (Å)	14.218(4)	11.829(3)
b (Å)	23.475(1)	11.846(4)
c (Å)	6.951(2)	12.116(4)
β (°)	105.13(4)	99.96(4)
Volume (Å^3)	2240(2)	1672(2)
Z	8	4
D_c (g cm^{-3})	2.53	2.80
Radiation	Mo Kα	Mo Kα
μ (cm^{-1})	137.5	183.8
Scan method	ω	ω
$2\theta_{max}$ (°)	45°	45°
Reflections measured	1477	2197
Reflections observed	1164	1524
Rejection criterion	$F_o^2 < 2\sigma(F_o^2)$	$F_o^2 < 2\sigma(F_o^2)$
R	0.038	0.083
R_w	0.035	0.102
p	0.003	0.002

hydrogen bonds of respective lengths 2.97(1) and 2.75(1) Å.

Calculations were performed with the SDP suite (Enraf-Nonius) and with local programs; diagrams were drawn with RSPLOT [14]. Atom positional parameters with isotropic temperature factors are listed in Table 4, the coordination geometry of the mercury atom in **1i** in Table 5. As a result of the non-refinement of the nitrate oxygen atoms in **2ii**, the residuals and positional e.s.d.s are relatively large for this complex. A listing of bond distances and angles to Hg7 and Hg9 in **2ii** was felt, therefore, to be unjustified.

Discussion

The X-ray analysis of **1i** establishes N7 as the primary binding site for CH_3Hg^+ with 3-methyladenine. This coordination behaviour is in contrast to 9-methyladenine for which N1 is chosen by CH_3Hg^+. In addition to the methyl carbon C71, the coordina-

TABLE 4. Atom Positional Parameters with Equivalent Isotropic Temperature Factors (Å^2)

Atom	x/a	y/b	z/c	B_{eq}
1i				
Hg7	0.1681(1)	0.2118(1)	0.1723(1)	3.2(1)
N1	0.1282(8)	−0.0068(4)	0.1349(16)	3.0(2)
N3	0.2932(9)	−0.0121(4)	0.3221(17)	3.3(3)
N6	0.0465(9)	0.0776(4)	0.0409(17)	3.5(3)
N7	0.2461(9)	0.1355(4)	0.2724(17)	3.6(3)
N9	0.3755(9)	0.0786(4)	0.4241(17)	3.5(3)
C2	0.2091(11)	−0.0356(5)	0.2272(22)	3.5(3)
C3	0.3816(12)	−0.0474(5)	0.4136(22)	3.6(3)
C4	0.2970(10)	0.0470(5)	0.3308(20)	2.7(3)
C5	0.2157(11)	0.0782(5)	0.2316(21)	2.8(3)
C6	0.1284(11)	0.0520(5)	0.1361(21)	3.2(3)
C8	0.3396(12)	0.1323(6)	0.3803(22)	4.0(3)
C71	0.0886(13)	0.2836(7)	0.0659(24)	5.4(4)
N10	0.3692(11)	0.3122(5)	0.3634(21)	5.8(4)
O11	0.3408(9)	0.2623(4)	0.3894(17)	6.2(3)
O12	0.4198(11)	0.3328(5)	0.5202(20)	8.6(4)
O13	0.3336(11)	0.3359(5)	0.2054(21)	8.6(4)
2ii				
Hg7	0.2525(2)	0.5761(2)	0.1232(2)	3.6(1)
Hg9	0.1559(2)	1.0585(2)	−0.0160(2)	3.4(1)
N1	0.4145(43)	0.8939(40)	0.4018(41)	4.8(13)
N3	0.3366(42)	1.0178(39)	0.2685(40)	4.5(13)
N6	0.4091(40)	0.6884(38)	0.3944(38)	3.9(12)
N7	0.2262(37)	0.7536(33)	0.1491(34)	2.4(9)
N9	0.2286(37)	0.9334(39)	0.0965(35)	3.5(10)
C2	0.4046(53)	1.0158(53)	0.3644(52)	4.0(13)
C3	0.3147(52)	1.1422(47)	0.2144(49)	3.9(15)
C4	0.3027(48)	0.9244(50)	0.2082(45)	3.7(13)
C5	0.3205(43)	0.8297(40)	0.2423(40)	1.8(11)

(continued)

TABLE 4. *(continued)*

Atom	x/a	y/b	z/c	B_{eq}
2ii				
C6	0.3887(52)	0.8141(49)	0.3452(49)	4.2(15)
C8	0.2178(54)	0.8204(52)	0.0706(50)	4.3(15)
C71	0.2801(66)	0.3982(68)	0.0784(61)	7.3(23)
C91	0.0608(71)	1.2063(70)	−0.1259(67)	9.2(25)
N10	0.4148(41)	0.4047(40)	0.3896(39)	4.5(12)
N20	0.9986(46)	0.4052(48)	0.7052(44)	6.6(16)

TABLE 5. Bond Lengths (Å) and Angles (°) to the Mercury Atom in **1i**

Hg7–N7	2.125(7)	Hg7–C71	2.057(10)
Hg7–O11	2.788(8)	Hg7–O11^a	3.142(8)
Hg7–O12^a	2.936(9)	Hg7–O13^b	2.848(9)
N7–Hg7–C71	177.5(3)	N7–Hg7–O11	82.5(3)
N7–Hg7–O11^a	89.7(2)	N7–Hg7–O12^a	75.3(3)
N7–Hg7–O13^b	81.3(3)	C71–Hg7–O11	99.8(3)
C71–Hg7–O11^a	91.8(3)	C71–Hg7–O12^a	104.8(3)
C71–Hg7–O13^b	96.8(3)	O11–Hg7–O11^a	69.2(3)
O11–Hg7–O12^a	103.9(3)	O11–Hg7–O13^b	117.4(3)
O11^a–Hg7–O12^a	39.7(2)	O11^a–Hg7–O13^b	167.7(2)
O12^a–Hg7–O13^b	128.9(2)		

^{a}Denotes $\frac{1}{2} - x, \frac{1}{2} - y, 1 - z$. $^b\frac{1}{2} - x, \frac{1}{2} - y, \bar{z}$.

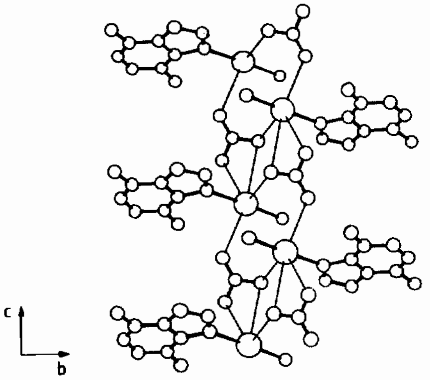

Fig. 1. Projection of the unit cell contents of **1i** perpendicular to [100].

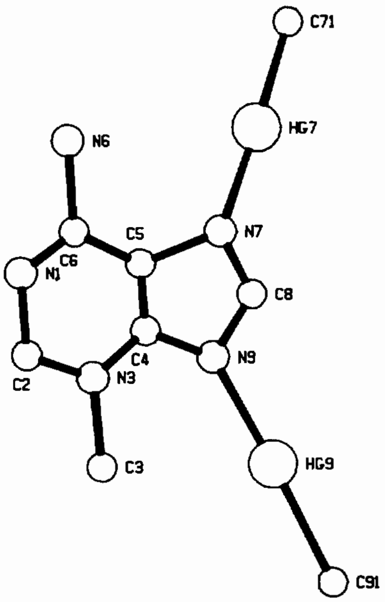

Fig. 2. N7,N9-coordination in the complex **2ii**.

tion sphere of Hg7 is completed by four weak secondary bonds to nitrate oxygen atoms as depicted in Fig. 1. Marked downfield shifts are observed for the H2, H8 and, in particular, H6 resonances in the ^{1}H NMR spectrum in comparison to the free base. Integration of this spectrum confirms the presence of two amino N6-protons.

The 2:1 complex **2ii** displays N7,N9-coordination in the solid state (Fig. 2). Small downfield shifts in the range 0.03–0.08 ppm are observed for the hetero-base protons with respect to their values in **1i**. The strength of metal binding in methylmercury(II) complexes is reflected in the magnitude of the $^2J(^{199}\text{Hg}-^1\text{H})$ coupling constants. Lower values are associated with an increased Hg–N bond strength [15]. The observed value of 239.5 in **2ii**, which represents an average value for the Hg7–N7 and Hg9–N9 bonds, is considerably larger than that of 224.5 Hz in **1i**, indicating that the metal binding propensity of the second imidazole nitrogen in the 2:1 complex must be weaker than that displayed by the primary binding site N7 in the 1:1 complex.

For the 3:1 species **3ii·H$_2$O** prepared in acidic solution (pH = 4), N6 is coordinated in addition to the two imidazole nitrogen atoms. This binding pattern is suggested for DMSO-d$_6$ solution by the ^{1}H NMR spectrum and confirmed for the solid state by consideration of the interatomic Hg···Hg distances in the partial structure established by X-ray analysis (see footnote on p. 3). As for the ionic species **1i** and **2ii**, the downfield shift for δ(H8) (0.58 ppm) is markedly larger than for δ(H2) (0.22 ppm). This is to be expected for N7,N9-binding, as this will lead to a pronounced deshielding of H8 owing to the significant reduction in electron density in the imidazole ring. The more distant H2 in the pyrimidine ring will be less influenced by this coordination pattern. An Hg–N1 interaction, on the other hand, should lead to a more significant downfield shift of the H2 resonance. Whereas δ(H8) occurs at 8.34 ppm in both **2ii** and **3ii·H$_2$O**, δ(H2) and δ(H6) are shifted upfield 0.13 and 1.02 ppm respectively upon coordination of N6. Indeed, the latter resonance experiences an upfield shift of 0.12 ppm relative to the free base. These findings suggest that the tautomeric form **A** also predominates for the 3-methyladenine ligand in complex **3ii·H$_2$O**. Steric considerations indicate that the CH$_3$Hg group must adopt a position *syn* to N1–C6.

Two complexes **2i·H$_2$O** and **3i** were prepared from aqueous solution at a pH value of 8. A 1:1 neutral species could not be isolated at either this or a higher pH value. Crystals of **2i·H$_2$O** or **3i** suitable for an X-ray analysis could not be grown. Inspection of the ^{1}H NMR spectra of these complexes suggests respectively N6,N7- and N6,N6,N9-coordination. In **2i·H$_2$O** only one N6-amino proton is observed, whose resonance is shifted upfield from δ(H6) in both 3-methyladenine itself (0.33 ppm) and **3ii·H$_2$O** (0.21 ppm). This suggests N6-coordination of the heterobase for which the tautomeric form A predominates. The downfield shift of the imidazole proton H8 (0.31 ppm) is significantly larger than that for the pyrimidine proton H2 (0.16 ppm), an observation which is in accordance with mercury coordination of the former ring. In general δ(CH$_3$) for the 3-methyl protons is markedly less affected by metal coordination than the endocyclic ring protons. With the exception of **2i·H$_2$O** δ(CH$_3$) lies within a narrow range 0.10–0.14 ppm downfield from its position in 3-methyladenine for the cationic species studied in this work. In **2i·H$_2$O**, however, the resonance is observed at the same value as for the free base itself. Coordination of the adjacent nitrogen N9 in the imidazole ring rather than N7 would be expected to lead to a more pronounced reduction in electron density at N3 suggesting that the latter imidazole nitrogen will be the chosen site in **2i·H$_2$O**. Dismutation of **2i** to **1i** and **3i** (approximate ratio 2:1:1) is observed in DMSO-d$_6$ solution. A similar phenomenon has been reported for an 9-methyladenine [16].

N6,N6,N9-coordination may be assumed for **3i**. No amino N6-protons are found in the ^{1}H NMR spectrum. Whereas δ(H2) is shifted 0.08 ppm upfield with respect to 3-methyladenine itself, a downfield shift of 0.07 ppm is observed for the imidazole proton H8. N7-coordination is sterically impossible for twofold in-plane coordination of N6 by CH$_3$Hg$^+$.

The present results are in agreement with theoretical calculations which predict an increase in the relative binding propensity of N7 in comparison to N1 on going from 9-methyladenine to 3-methyladenine. Indeed no example of methylmercury(II) coordination of N1 was observed. In both **2ii** and **3ii·H$_2$O** N9 of the imidazole ring is preferred as a secondary binding site.

Supplementary Material

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

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References

1 T. Sorrell, L. A. Epps, T. J. Kistenmacher and L. G. Marzilli, *J. Am. Chem. Soc., 99* (1977) 2173.

2 T. Sorrell, L. A. Epps, T. J. Kistenmacher and L. G. Marzilli, *J. Am. Chem. Soc., 100* (1978) 5756.

3 C. Bartzsch, C. Weiss and H. J. Hofmann, *J. Prakt. Chem., 326* (1984) 407.

4 M. Ishuno, T. Sakaguchi, I. Marimoto and T. Okitsu, *Chem. Pharm. Bull., 29* (1981) 2403.

5 J. D. Orbell, C. Solorzano, L. G. Marzilli and T. J. Kistenmacher, *Inorg. Chem., 21* (1982) 2630.

6 W. S. Sheldrick and P. Bell, *Inorg. Chim. Acta, 123* (1986) 181.

7 W. S. Sheldrick and P. Bell, *Inorg. Chim. Acta, 137* (1986) 181.

8 M. J. Olivier and A. L. Beauchamp, *Inorg. Chem., 19* (1980) 1064.

9 M. J. Olivier and A. L. Beauchamp, *Acta Crystallogr., Sect. B, 38* (1982) 2159.

10 S. E. Taylor, E. Buncel and A. R. Norris, *J. Inorg. Biochem., 15* (1981) 131.

11 J. P. Charland, M. Simard and A. L. Beauchamp, *Inorg. Chim. Acta, 80* (1983) L57.
12 D. J. Hodgson, *Prog. Inorg. Chem., 23* (1977) 211.
13 M. J. McCall and M. R. Taylor, *Biochem. Biophys. Acta, 390* (1975) 137.
14 W. S. Sheldrick, *RSPLOT*, a computer program for molecule and lattice plots, TU Braunschweig, 1975.
15 D. L. Rabenstein, *Acc. Chem. Res., 11* (1978) 100.
16 J.-P. Charland, M. T. P. Viet, M. St-Jacques and A. L. Beauchamp, *J. Am. Chem. Soc., 107* (1985) 8202.