Substitution of both Amino Protons by CH_3Hg^+ Ions in Adenine and Cytosine

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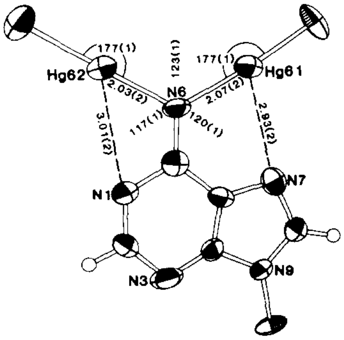
The amino lone pairs in the DNA bases adenine and cytosine are not normally available for metal complexation, since they are delocalized into the ring π system [1]. However, substitution of one of the amino protons by metal ions can take place. Examples have been reported for Pt [2], Ru [3], Ag [4] and Hg [5–8], in the solid state as well as in solution. In earlier reports from this laboratory, it was noted that the CH_3Hg^+ ion smoothly displaces an amino hydrogen of 1-methylcytosine (MCy) [7] and 9-methyladenine (MAd) [6] in water, even under slightly acidic conditions. Consequently, metal reaction at these sites in DNA should be feasible. This prompted us to examine the possibility of displacing the second amino hydrogen. This reaction was also found to take place under relatively mild conditions.

Addition of 2 equiv. of CH_3HgOH (1 *M* aq. soln.) to 1 equiv. of MAd dissolved in warm CH_3CN or DMF produced, upon cooling, a neutral compound of the formula $[(CH_3Hg)_2(MAd\text{-}2H)]$, which was shown by X-ray diffraction to contain molecule *I*. The compound is triclinic, $a = 8.701(6)$, $b = 9.127(2)$, $c = 15.043(2)$ Å, $\alpha = 82.08(2)$, $\beta = 88.86(4)$, $\gamma = 78.15(4)°$. The structure was refined on 2553 nonzero reflections to $R = 0.044$. A similar reaction occurs with the amino group of adenine (HAd), provided that a 3:1 CH_3HgOH:HAd ratio is used, in order to simultaneously substitute the imidazolic H(9) proton, which is first replaced in unblocked adenine [9]. The crystals of $[(CH_3Hg)_3(Ad\text{-}2H)]\cdot 1/2H_2O$ belong to the monoclinic C2/c space group: $a = 20.809(7)$, $b = 7.263(1)$, $c = 18.788(1)$ Å, $\beta = 104.91(4)°$, $R = 0.052$, 1108 nonzero reflections.



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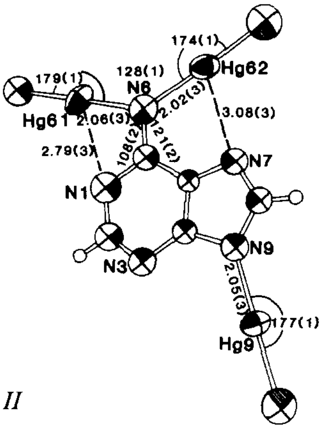
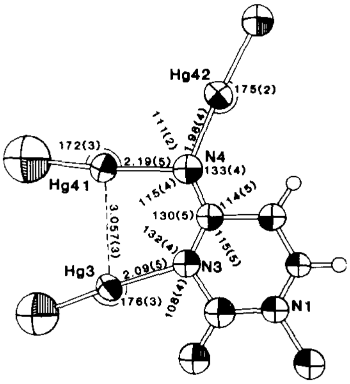


II

In complexes *I* and *II*, both NH_2 protons have been substituted by linearly coordinated CH_3Hg^+ groups. The N atom retains its sp^2 hybridization, the CH_3Hg^+ groups lying roughly in the plane of the adenine moiety. In addition to the normal Hg–N(6) bonds, there might exist weak bonding interactions between N(7) and the nearest Hg atom. A similar arrangement was found in $[(CH_3Hg)_2(MAd\text{-}H)]NO_3$, where the amino group is singly substituted [6].

With 1-methylcytosine, the $[(CH_3Hg)_3(MCy\text{-}2H)]$-$NO_3$ compound was obtained by evaporating to dryness a mixture of CH_3HgOH, CH_3HgNO_3 (~0.5 *M* aq. soln.) and MCy (ethanol) in a 2:1:1 ratio. The crystals are orthorhombic, space group Pbca: $a = 7.175(5)$, $b = 17.98(1)$, $c = 23.434(9)$ Å, $R = 0.064$, 812 nonzero reflections. In addition to the doubly substituted NH_2 group, this compound contains an extra CH_3Hg^+ ion bonded to N(3) (*III*), which is the usual target for metal ion in N(1)-blocked cytosine [10]. The resulting crowding does



III

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not introduce bond lengthening or significant deviations from linearity at the metal centers, but unequal angles at N(3), C(4) and N(4) indicate that both groups have to depart from the expected positions in order to reduce the Hg–Hg interactions. This situation is not unlike the one observed in a complex containing a singly substituted amino group [7].

In the three compounds, complete substitution on the NH_2 groups is detected by the disappearance of the IR N–H stretching and NH_2 scissoring bands observed at ~3200 and ~1675 cm^{-1}, respectively, in the free ligands [7, 11]. The broad resonances of the ligand NH_2 protons (6.9–7.2 ppm) are absent from the ^1H NMR spectra of the complexes in DMSO-d_6. A single resonance at 0.6–0.7 ppm is found for the methyl protons of all the CH_3Hg^+ groups, indicating fast exchange and/or rotation about the $C-N(HgCH_3)_2$ bonds. The $^{2}J_{^{1}H-^{199}Hg}$ coupling constants (177 Hz for *I*, 183 Hz for *II*) are the lowest observed so far for N-bonded CH_3Hg^+ complexes. From the J-pK_a relationship deduced by Rabenstein [12], the J value of 177 Hz would correspond to an average pK_a of ~13 for the two available sites on the $C-N^{2-}$ groups of MAd. Inasmuch as the J constant of 200 Hz was observed for the N(9)-bonded 1:1 CH_3Hg:HAd complex, the contribution of the two amino-bonded CH_3Hg^+ groups in *II* (175 Hz) would correspond to a similar average basicity. The MCy complex is difficult to obtain free from a small amount of a 2:1 complex. This system has to be further investigated before definite conclusions can be drawn concerning individual species in DMSO.

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