^{199}Hg NMR Correlations in Methylmercury(II) Complexes of Nucleic Acid Constituents and Their Analogs

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The known toxic effects of organomercury compounds are often attributed to the formation of mercury–sulfur bonds with sulfhydryl functions in aminoacids and proteins but may also be due, in part, to their interactions with nucleic acid constituents [1]. ^{199}Hg NMR (^{199}Hg has I = ½, a natural abundance of 16.9%, and a sensitivity of 1.4%) has been used as a probe for various interactions of protein constituents with organomercury compounds in solution [2]. ^{199}Hg NMR has also been used to study the interactions of $CH_3Hg(II)$ with substituted pyridines, bipyridyls, pyrazoles and related organic compounds [3]. To our knowledge, no report on the use of ^{199}Hg NMR as a probe for $CH_3Hg(II)$–nucleic acid interactions has yet appeared in the literature. As an extension of our ^{1}H and ^{13}C NMR studies [4] of the complexes formed by the interactions of CH_3-Hg(II) and nucleic acid constituents, the ^{199}Hg NMR spectra of these complexes have been determined in $(CD_3)_2SO$. Our results (Fig. 1) indicate that the ^{199}Hg chemical shifts are characteristic of both the nature of ligand centres (L) bonded to methylmercury(II) (L–$HgCH_3$) and the ligand structural type. For ease of discussion one can divide the complexes in Fig. 1 into the categories I–VII as described below. Some of the general relationships which become apparent between ^{199}Hg chemical shifts and structure are pointed out.

*I. $CH_3Hg(II)$ Bound to Sulfur of a Pyrimidine Moiety of a Purine Molecule (**1a, 1b, 2a, 2b**)*

The ^{199}Hg shifts of the protonated cationic complexes **2a** and **2b** are found upfield compared to the ^{199}Hg chemical shifts for the corresponding neutral complexes **1a** and **1b**, and downfield from the values in the protonated cationic complexes **5** and **6** in which $CH_3Hg(II)$ is bound to an **S**-centre of imidazole or an imidazole moiety of purine (Group II).

*II. $CH_3Hg(II)$ Bound to S of Imidazole or an Imidazole Moiety of a Purine (**3, 4, 5, 6**)*

Complexes **3** and **4** have similar chemical shifts, the small difference ($\Delta\delta$ = –6.7 ppm) being presumably due to the presence of the pyrimidine moiety in **4**. The ^{199}Hg chemical shifts of the 1:1 $CH_3Hg(II)$ cationic complexes **5** and **6** are found upfield from the ^{199}Hg chemical shifts for the corresponding neutral complexes **3** and **4**.

*III. $CH_3Hg(II)$ Bound to S of Either the Pyrimidine or the Imidazole Ring of Purine with Simultaneous Binding of $CH_3Hg(II)$ to N-centres of Pyrimidine or Imidazole Moieties of Purine (**7a, 7b, 8, 9**)*

In the 2:1 cationic $CH_3Hg(II)$ complexes **7a** and **7b**, where two $CH_3Hg(II)$ groups are bound simultaneously at **S** and **N**, the ^{199}Hg chemical shifts occur upfield from the values in the corresponding 1:1 cationic $CH_3Hg(II)$ complexes **2a** and **2b**, and even further upfield from the corresponding neutral complexes **1a** and **1b**. The ^{199}Hg resonance in **8**, in which $CH_3Hg(II)$ groups are bound to **N** and **S** of the imidazole moiety of purine, occurs slightly upfield from that in **7b** and slightly downfield from **7a** in which $CH_3Hg(II)$ groups are bound to both pyrimidine and imidazole moieties of purine.

*IV. $CH_3Hg(II)$ Bound to N of Imidazole or the Imidazole Moiety of Purine (**10a, 10b, 11a, 11b, 12a, 12b**)*

In related imidazole-based complexes, **10a/10b**, in which H in the first complex is replaced by the NO_2 group in the second, the ^{199}Hg resonance of the NO_2-containing species is upfield from that associated with the corresponding H-containing species. This is probably the result of decreased electron density in the ring due to the electron withdrawing effect of the NO_2 group. As previously (*e.g.* Groups I and III), the ^{199}Hg chemical shifts in this series of complexes become more negative on going from a neutral $CH_3Hg(II)$–N complex to the corresponding cationic $CH_3Hg(II)$–N^+ complex.

*V. $CH_3Hg(II)$ Bound to N of Pyrimidine or the Pyrimidine Moiety of Purine (**13a, 13b, 14a, 14b**)*

Complexes **13a** and **13b**, which differ only by a methyl group at C_5, have similar chemical shifts ($\Delta\delta$ = 10.9 ppm). Also, complexes **14a** and **14b**, differing by an amino group at C_2, have similar ^{199}Hg shifts ($\Delta\delta$ = 12.6 ppm).

*VI. $CH_3Hg(II)$ Groups Bound Simultaneously to N of Either Imidazole, or the Imidazole/Pyrimidine Moieties of a Purine (**15a, 15b, 16a, 16b, 17**)*

In the 2:1 cationic complexes **15a** and **15b**, in which two $CH_3Hg(II)$ moieties are bound simultaneously to the pyrimidine and imidazole moieties

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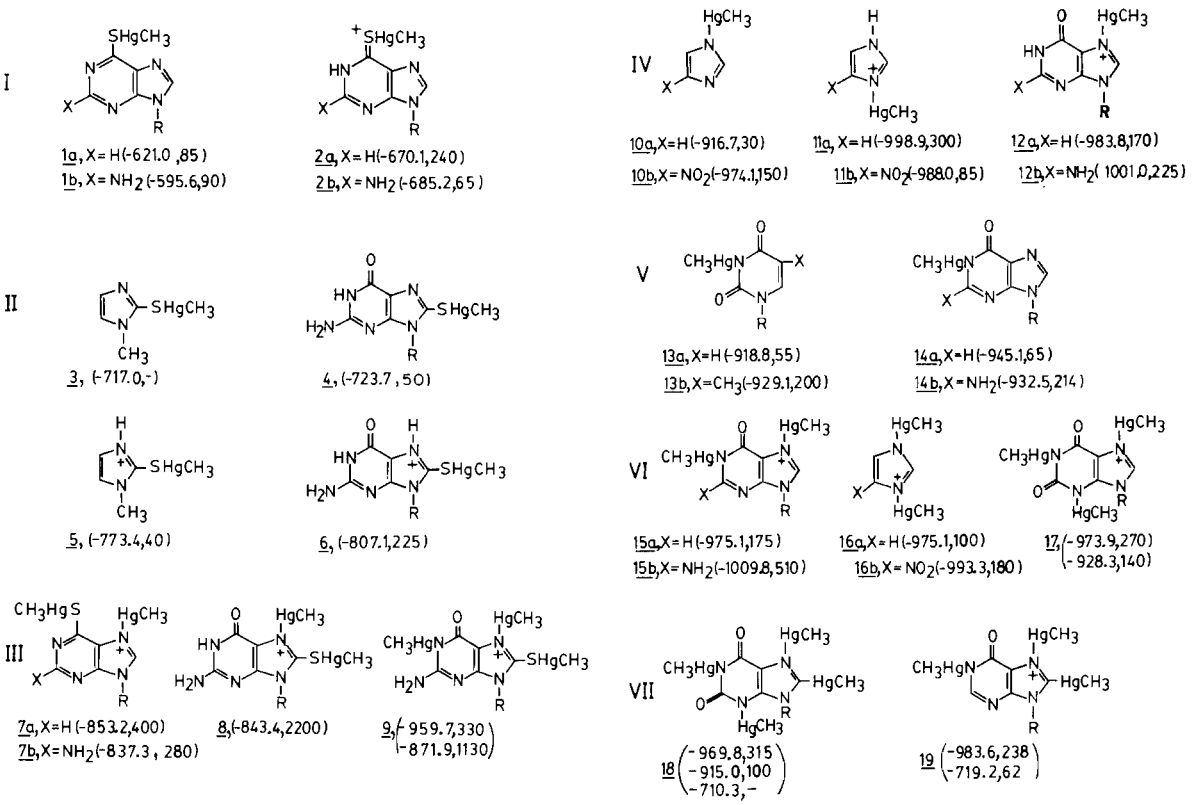

Fig. 1. Structures of the complexes listed under categories I–VII. The data in the parentheses refer to the ^{199}Hg chemical shifts (negative values, gixen in ppm relative to $(CH_3)_2Hg$) and the corresponding $\nu_{1/2}$ values in Hz (see text). Spectra were recorded on on a Bruker CXP-200 spectrometer using solutions of the complexes in DMSO-d_6 at a temperature of approximately 335 K.

of purine, the ^{199}Hg resonances occur upfield by 30.0 and 77.2 ppm, respectively, from the vaues in the corresponding 1:1 neutral complexes **14a** and **14b**. For complexes **16a** and **16b**, the ^{199}Hg resonances are also upfield from those of the corresponding neutral complexes **10a** and **10b**. The differences in ^{199}Hg chemical shift between the pairs **10a/11a**, **10b/11b**, **10a/16a** and **10b/16b**, show that, in this series of complexes, H^+ addition is more effective than CH_3Hg^+ addition in bringing about the upfield shift.

A noteworthy point with respect to those complexes in groups III–VI, in which there are two CH_3-Hg(II) moieties involved in binding (**7a**, **7b**, **15a**, **15b**, **16a** and **16b**), is that a single averaged ^{199}Hg resonance is observed as a result of fast exchange, on the NMR time scale, of $CH_3Hg(II)$ between different sites [5]. This exchange is reflected in a linewidth at half-height ($\nu_{1/2}$) in the ^{199}Hg resonance larger than that observed in the corresponding complex containing only one $CH_3Hg(II)$ group (*e.g.* compare $\nu_{1/2}$ values for pairs **1a/7a**, **1b/7b**, **4/8**, *etc.*, in Fig. 1).

In a number of complexes in which three CH_3-Hg(II) groups are involved in binding to S and N or N sites only, different results are obtained. Thus, in complex **9**, where two nitrogens and one sulfur are involved in binding to $CH_3Hg(II)$ groups, two separate ^{199}Hg resonances are observed; one occurring at –959.7 ppm ($\nu_{1/2}$ = 230 Hz) and assigned to CH_3-Hg(II) bound to N_1, and a second resonance at –871.9 ppm ($\nu_{1/2}$ = 1130 Hz) assigned to the CH_3-Hg(II) groups bound to N_7 and S_8. The second ^{199}Hg resonance in **9** has a value comparable to that associated with $CH_3Hg(II)$ groups bound simultaneously to N_7 and S_8 in **8**. In complex **17**, two resonances are observed; one at –973.9 ppm ($\nu_{1/2}$ = 270 Hz) due to the two $CH_3Hg(II)$ groups rapidly exchanging between N_3 and N_7 sites, and the other at –928.3 ppm ($\nu_{1/2}$ = 140 Hz) assignable to N_1-bound CH_3-Hg(II).

VII. $CH_3Hg(II)$ Groups Bound Simultaneously to N and C of Imidazole and N of Pyrimidine Moieties of Purine (18, 19)

In complex **18**, three separate ^{199}Hg resonances, at –969.8, –915.0 and –710.3 ppm, are observed. The resonances at –969.8 ($\nu_{1/2}$ = 315 Hz) and –915.0 ppm ($\nu_{1/2}$ = 100 Hz) are comparable to the values observed in **17**. The resonance at –710.3 ppm is therefore assigned to **C**-bound $CH_3Hg(II)$. In complex **19**, two ^{199}Hg resonances have been observed,

one at −719.2 ppm ($\nu_{1/2}$ = 62 Hz) assignable to C–$HgCH_3$, and the other at −983.6 ppm ($\nu_{1/2}$ = 238 Hz) assignable to N_1- and N_7-bound $CH_3Hg(II)$. The latter resonance is comparable in frequency and width at half-height to the N_1, N_7-bound $CH_3Hg(II)$ resonance in **15a**.

It is seen that the least negative values of ^{199}Hg chemical shifts are found for complexes containing S-bonded $CH_3Hg(II)$, while the most negative values of ^{199}Hg chemical shifts are found for complexes containing N-bonded $CH_3Hg(II)$. Thus, in this series of complexes, the ^{199}Hg chemical shift of CH_3-Hg(II) bound to a ligand is a useful indicator of the nature of the ligand bound *trans* to the Hg–C bond. Comparison with ^{13}C chemical shift data [4] shows that donor atoms wich give rise to substantial ^{199}Hg shifts also give rise to substantial ^{13}C chemical shifts; thus there is a linear relationship between these quantities for the complexes described herein. This relationship presumably holds because a strongly bound ligand weakens the Hg–C bond *trans* to it and thus decreases the 'S' character in the Hg–C bond [6].

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