Multinuclear NMR Study of the Disproportionation and Syn/Anti Isomerism in Solutions of Amino-Substituted Methylmercury Derivatives of Adenine and 9-Methyladenine

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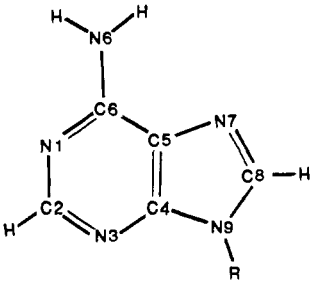
Abstract: The amino-substituted mono- and bis(methylmercury) derivatives of 9-methyladenine and 9-(methylmercuri)adenine have been investigated in Me_2SO-d_6, acetone-d_6 and $CDCl_3$ by high-field ^1H (400-MHz), ^{13}C (100.6-MHz), and ^{199}Hg (71.6-MHz) NMR. The spectra show that the $NH(HgCH_3)$ groups disproportionate to some extent into the disubstituted ($N(HgCH_3)_2$) and the unsubstituted (NH_2) groups. The equilibrium constants indicate 38% of disproportionation in Me_2SO, 27% in acetone, and only 5% in chloroform. The $N(HgCH_3)_2$ groups are partly hydrolyzed by the water present in Me_2SO, and the corresponding equilibrium constants were determined. In addition, it was found that the amino monosubstituted derivatives exist as two rotamers in solution due to slow rotation of the $NH(HgCH_3)$ group about the C6–N6 bond (rotation barrier = 66 kJ/mol in Me_2SO). Both rotamers are present in roughly equal amounts in Me_2SO and $CDCl_3$, but there is a 2:1 predominance of the anti isomer (CH_3Hg above N7) in acetone. A barrier of 69.5 kJ/mol was deduced from the ^{199}Hg spectra for rotation of the $N(HgCH_3)_2$ group about the C6–N6 bond of $(CH_3Hg)_2$(MAd-2H) in Me_2SO. By means of two-dimensional NMR spectra of (CH_3Hg)(MAd-H) in Me_2SO and dynamic NMR spectroscopy, it was shown that rotation about the C6–N6 bond is a faster process than ligand exchange between the various types of molecules in the disproportionation mixture. Although the CH_3Hg–N bonds in these compounds are labile from the standpoint of preparative chemistry, the CH_3Hg^+ groups attached to the very basic nitrogen sites do not exchange rapidly on the ^{199}Hg time scale.

Over the years, the binding of Ag^+ and Hg^{2+} ions with DNA has attracted attention, at first, because these metal ions could be used for the separation of DNA mixtures, and subsequently, because such studies provided information pertaining to the general problem of metal ion–nucleic acids interactions.[1] Relying mainly on potentiometric and UV spectral data, Simpson,[2] Davidson,[3] Eichhorn,[4] and their co-workers were able to identify for each nucleoside primary coordination sites which more recent studies generally confirmed.[5,6] In the case of adenosine, pH influence and proton liberation in the reactions were interpreted in terms of metal binding to the amino group leading to proton substitution.

More recently, research on CH_3Hg^+/DNA interactions has been stimulated by the toxicity of this cation and its possible use as a reagent in DNA denaturation and selective labeling for electron microscopy and X-ray diffraction experiments. Simpson[2] examined the equilibria taking place in aqueous solutions of CH_3Hg^+ with adenosine and concluded that one of the species formed in basic media contained the $NH(HgCH_3)$ unit. This suggestion was subsequently confirmed by Tobias and co-workers[7] by Raman spectroscopy.

Our previous work on the utilization of the uniligating CH_3Hg^+ ion as a probe to classify the affinities of donor sites in DNA constituents such as adenine[8,9] (Scheme I) revealed that methylmercuration of the amino group occurs under mild conditions.[10] Recently, we have found that CH_3Hg^+ can displace both amino protons, forming a stable compound, again under relatively mild conditions.[11] The structural characterization of these amino-substituted compounds in the solid state is reported elsewhere.[12] The present paper deals with the behavior of these molecules in solution.

Scheme I



I

The fact that most of these compounds have been structurally characterized in the solid state[12,13] made it possible to unravel the NMR results and cast some light on three major dynamic processes taking place in solution. First, we will show that the amino-substituted complexes are involved in equilibrium reactions: the amino monomercurated compounds disproportionate to some extent, whereas the dimercurated species tend to react with water, if present. Second, amino monomercuration produces two isomeric forms when rotation about the C6–N6 bond is slow, and we will show that these two rotamers both exist in equilibrium in solution. Third, this work will show that under suitable conditions the CH_3Hg^+ groups, which are labile from the standpoint of preparative chemistry, exchange slowly compared with the ^{199}Hg chemical shift difference, when they are bound to the highly basic nitrogen of the deprotonated amino group.

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Table I. ^{1}H NMR Data for MAd, HAd, and Their Derivatives

	N9–CH_3	H2	H8	NH_2	N(Hg)H	$HgCH_3$	$^2J(^{199}Hg-^1H)$
			Me_2SO-d_6[a]				
MAd (A)	3.707	8.136	8.079	7.186			
(CH_3Hg)(MAd-H) (Ba) (55%)	3.679	7.999	7.973		6.439	[0.682[b]	[183[b]
(CH_3Hg)(MAd-H) (Bs) (45%)	3.666	8.010	7.946		6.286	0.641[b]]	185[b]]
$(CH_3Hg)_2$(MAd-2H) (C)	3.633	7.886	7.828			0.584[b]	169
HAd[26,34,c]		8.15	8.13	7.15			
CH_3HgAd (D)		8.013	7.809	6.76		0.789	200
$(CH_3Hg)_2$(Ad-H)·EtOH[d] (Ea) (55%)		7.885[e]	7.687[e]		6.202	0.702[b,e]	190
$(CH_3Hg)_2$(Ad-H)·EtOH[d] (Es) (45%)		7.885[e]	7.687[e]		6.04		
$(CH_3Hg)_3$(Ad-2H)·$^1/_2H_2O$ (F)		7.779	7.562			0.653[b]	180
			$CDCl_3$[f]				
MAd (A)[33]		8.42	7.93				
(CH_3Hg)(MAd-H) (Ba) (45%)	3.817	8.223	7.749		6.105[g]	0.969	179
(CH_3Hg)(MAd-H) (Bs) (55%)	3.829	8.253	7.637		5.871[h]	0.979	184
$(CH_3Hg)_2$(MAd-2H) (C)	3.785	8.146	7.552			0.848	~160
$(CH_3Hg)_2$(Ad-H)·EtOH (Ea) (42%)		8.107	7.677		6.149	*i*	
$(CH_3Hg)_2$(Ad-H)·EtOH (Es) (58%)		8.132	7.589		5.820		
$(CH_3Hg)_3$(Ad-2H)·$^1/_2H_2O$ (F)		8.032	7.499				
			Acetone-d_6[a]				
MAd (A)	3.792	8.191	7.963	6.495			
(CH_3Hg)(MAd-H) (Ba) (65%)	3.764	8.058	7.865		6.22 (sh)	0.798	183
(CH_3Hg)(MAd-H) (Bs) (35%)	3.740	8.039	7.826		6.18 (br)	0.780	183
$(CH_3Hg)_2$(MAd-2H) (C)	3.722	7.943	7.742			*j*	*j*

[a] Chemical shifts (ppm) from Me_4Si, 298 K, 400 MHz, ^2J in Hz. [b] Value obtained on signals still in exchange. [c] A broad resonance is also found at 10.77 ppm for the imidazole proton. [d] EtOH resonances (298 K): CH_3, 1.06 (t); CH_2, 3.44 (q); OH, 4.28 (s, br). [e] Signals not split by syn/anti isomerism. [f] Chemical shifts (ppm) from Me_4Si, 233 K, 400 MHz, except for MAd, 80 MHz, 223 K. [g] $^2J(^{199}Hg-^1H)$ = 76 Hz. [h] $^2J(^{199}Hg-^1H)$ = 70 Hz. [i] Broad overlap signals; at room temperature two broad signals at 1.20 and 1.01 ppm. [j] Signal hidden underneath those of B.

Experimental Section

Reactants. CH_3HgOH (1 M aqueous solution, Alfa), $[(CH_3Hg)_3O]OH$ (Alfa), and CH_3CN (American Chem.) were used without further purification. Adenine-*6,6,8,9-d*$_4$ and 9-methyladenine-*6,6,8-d*$_3$ were obtained from undeuterated adenine (Aldrich) and 9-methyladenine (Vega) as described previously.[12,13] They were fully deuterated at C8, but deuteration was only partial at N9 (adenine) and N6 (adenine and 9-methyladenine).

Preparations. The CH_3Hg^+ complexes of adenine (HAd) and 9-methyladenine (MAd)[14] were prepared as described elsewhere.[12] They are pure crystalline solids and single-crystal X-ray diffraction work has been done for CH_3HgAd,[13] $(CH_3Hg)_3$(Ad-2H)·$^1/_2H_2O$, and $(CH_3Hg)_2$(MAd-2H).[11,12] The solid referred to as (CH_3Hg)(MAd-H) has been shown by IR spectroscopy to consist of an equimolar mixture of MAd and $(CH_3Hg)_2$(MAd-2H).[12] However, inasmuch as the solutions of this mixture contain mainly (CH_3Hg)(MAd-H) molecules, the mixture will be loosely designated by this formula.

To assign some of the ^{1}H NMR signals in the H2/H8 region, complexes were prepared with deuterated adenine and 9-methyladenine as starting materials. For the preparations described below, the filtered solids were dried in vacuo at room temperature. ^{1}H NMR showed that the samples remained fully deuterated at C8, but the amino group had partly reprotonated.

CH_3HgAd-*6,6,8-d*$_3$ was prepared as previously described.[13]

$[(CH_3Hg)_2$(Ad-D)-*6,8-d*$_2]$·CH_3CH_2OD. Deuterated adenine (70 mg, 0.5 mmol) was mixed with 1 mL of aqueous 1 M CH_3HgOH (1 mmol) in 9 mL of hot deuterated 95% ethanol (in D_2O, Merck, Sharp & Dohme Canada) under N_2. Yellowish crystals precipitated upon cooling.

$[(CH_3Hg)_3$(Ad-2*D*)-*8-d*$]$·$^1/_2D_2O$. Deuterated adenine (69 mg, 0.5 mmol) was mixed with 1.5 mL of aqueous 1 M CH_3HgOH (1.5 mmol) in 9 mL of hot deuterated ethanol (in D_2O) under N_2. The white powder precipitated after a few days.

$[(CH_3Hg)$(MAd-D)-*8-d*$]$. Deuterated 9-methyladenine (75 mg, 0.5 mmol) was mixed with 0.5 mL of aqueous 1 M CH_3HgOH (0.5 mmol) in 9.5 mL of hot CH_3CN under N_2. A white powder precipitated upon cooling. See remark above concerning the undeuterated material.

$[(CH_3Hg)_2$(MAd-2D)-*8-d*$]$. Deuterated 9-methyladenine (74 mg, 0.5 mmol) was mixed with 1 mL of aqueous 1 M CH_3HgOH (1 mmol) in 9 mL of hot CH_3CN under N_2. The colorless crystals precipitated overnight upon cooling.

NMR Measurements. Samples for ^{1}H NMR were made by dissolving 5–20 mg of material in 0.5 or 1.0 mL of either Me_2SO-d_6, acetone-d_6, or $CDCl_3$ (Merck, Sharp & Dohme Canada or Cambridge Isotope Lab). Saturated solutions were used for ^{13}C and ^{199}Hg spectra. For ^{1}H and ^{13}C spectra, Me_4Si or occasionally the residual solvent signal was used as internal reference, whereby for Me_2SO-d_6 and $CDCl_3$ solutions, the conversion constants are, respectively, 2.500 and 7.270 ppm for ^{1}H and 39.40 and 76.90 for ^{13}C spectra. The ^{199}Hg chemical shifts were referenced to an external 1.0 M CH_3HgCl solution in Me_2SO (δ = −848 ppm).[15]

Most ^{1}H, ^{13}C, and ^{199}Hg spectra were recorded on a Bruker WH-400 (^{1}H, 400.13 MHz; ^{13}C, 100.62 MHz; ^{199}Hg, 72.57 MHz) spectrometer at the Laboratoire Régional de Résonance Magnétique Nucléaire, located at the Université de Montréal, while some spectra were recorded on the Bruker WP-80 spectrometer. Temperature was controlled by a Bruker B-VT-1000 variable-temperature unit.

The integration of partially overlapping signals was carried out by using the deconvolution program LINFIT.[16]

The 2D "accordion" spectra were obtained with the pulse sequence with a 16-phase cycle published recently by Bodenhausen and Ernst.[17] The 2D exchange spectra was obtained with the NOESY pulse sequence[18] supplied in the instrument manufacturer's software package. A sweep width of several hundred hertz was used to cover a portion of the spectra; the offset was carefully adjusted to avoid fold-over problems. Typically, for the H2 and H8 portion of the spectrum, a sweep width of 600 Hz, 1024 points, 5.9 μs (90°) ^{1}H pulse width, 0.853 s acquisition time, 7 s (~H2 and H8 T_1) repetition rate, a scaling parameter $k \sim 20$ (accordion) or a mixing of 0.1–2.0 s (exchange) were used. A total of 256 spectra (consisting of 32 transients each) were collected; the array was zero-filled to provide 1.172 Hz/point resolution in both dimensions. A sine-bell function was applied to both dimensions, and the absolute value display was used.

Results and Discussion

Spectral Assignment for 9-Methyladenine and Its Derivatives in Me_2SO. Figure 1 shows the 400-MHz ^{1}H NMR spectra of 9-methyladenine (MAd)[14] and of its amino-substituted mono- and

(14) Abbreviations used for 9-methyladenine: MAd = neutral molecule, $(MAd-H)^-$ = monoanion having lost one amino proton, and $(MAd-2H)^{2-}$ = dianion having lost both amino protons. For adenine: HAd = neutral molecule, Ad^- = monoanion without imidazole proton, $(Ad-H)^{-2}$ = dianion having lost the imidazole and one amino protons, and $(Ad-2H)^{-3}$ = trianion having lost the imidazole and two amino protons.

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Table II. ^{13}C NMR Data for MAd, HAd, and Their Derivatives[a]

	N9-CH_3	C2	C4	C5	C6	C8	Hg-CH_3
			Me_2SO-d_6				
MAd (A)	29.17	152.23	149.77	118.57	155.74	141.22	
(CH_3Hg)(MAd-H) (Ba)	29.29	153.06	149.07	119.54	162.55	139.98	0.53
(CH_3Hg)(MAd-H) (Bs)	29.18	152.21	149.07	120.46	161.08	139.98	1.76
(CH_3Hg)$_2$(MAd-2H) (C)	29.20	152.37	149.05	122.38	166.94	138.68	3.1 (br)
HAd[b]		152.3	151.2	117.4	155.2	139.2	
(CH_3Hg)Ad (D)		150.78	156.17	119.16	155.34	146.46	0.84 (1575)[g]
(CH_3Hg)$_2$(Ad-H)·EtOH[c] (Ea)		151.70	155.28	120.35	162.43	145.23[d]	[0.60[e] (1560)[g]
(CH_3Hg)$_2$(Ad-H)·EtOH[c] (Es)		150.70	155.21	120.81	160.92	145.23	1.20[e]]
(CH_3Hg)$_3$(Ad-2H)·$^1/_2H_2O$ (F)		151.06	154.98	123.06	167.27	144.18	2.39 (br)
			$CDCl_3$[f]				
(CH_3Hg)(MAd-H) (Ba) (45%)	29.90[d]	153.70	149.04	120.16	162.87	138.89	1.42[e]
(CH_3Hg)(MAd-H) (Bs) (55%)		152.49		120.87	161.49	139.39	

[a] Chemical shifts (ppm) from Me_4Si, 298 K. [b] Reference 23. [c] Ethanol resonances: CH_2, 55.90; CH_3, 18.46. [d] Signals not split by syn/anti isomerism. [e] Value obtained on signals still in exchange. [f] 233 K. [g] $^1J(^{199}Hg-^{13}C)$ coupling constant in Hz given within parentheses.

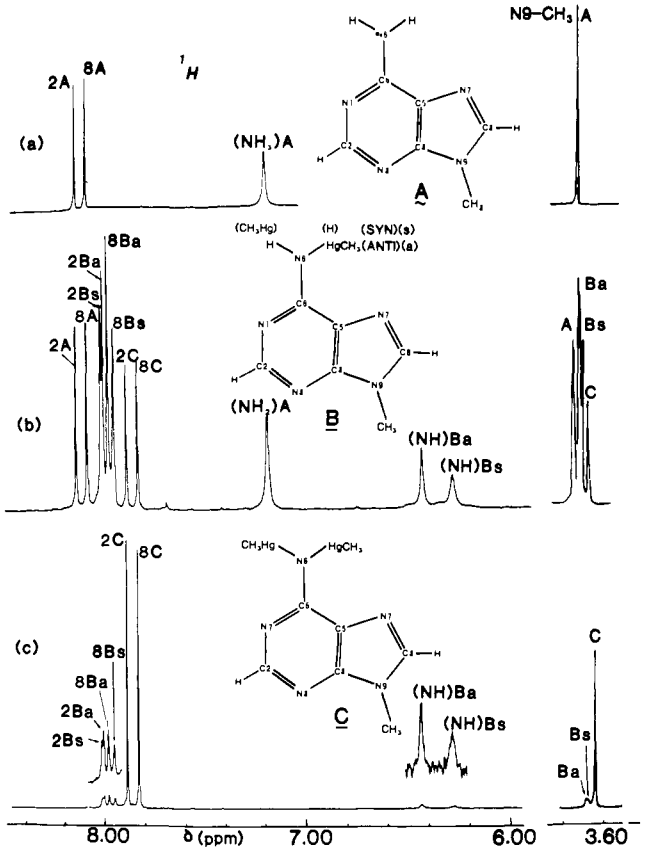


Figure 1. ^1H NMR spectra of Me_2SO-d_6 solutions of MAd (a), (CH_3Hg)(MAd-H) (b), and (CH_3Hg)$_2$(MAd-2H) (c) at 400 MHz and room temperature. Numbers in the symbols for each resonance correspond to ring position (H2 or H8), and the final letters identify the species. The high-field portion at ~3.6 ppm contains the resonances from the N9-bound methyl protons.

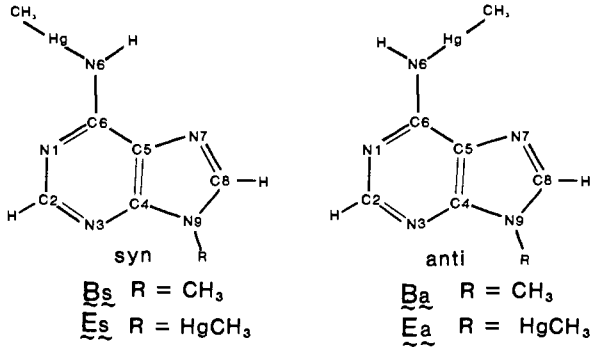
bis(methylmercury) derivatives. The MAd spectrum (Figure 1a) is in good agreement with previous reports.[19,20] Assignment of the H2 and H8 resonances at 8.14 and 8.08 ppm, labeled 2A and 8A, respectively, is based on C8-deuteration. The sharp resonance at 3.71 ppm is due to the N9-CH_3 protons, while the two amino hydrogens give rise to a single resonance at 7.19 ppm, owing to fast rotation about the C6–N6 bond. Table I contains a summary of ^1H NMR data for all compounds studied.

It has been shown by X-ray diffraction that both amino protons are replaced by CH_3Hg^+ ions in (CH_3Hg)$_2$(MAd-2H).[11,12] Accordingly, no ^1H signals were found in the NH_2 region for this derivative (Figure 1c). Displacement of hydrogen by less electron-attracting mercury produces upfield shifts of about 0.25 ppm for the H2 and H8 signals, labeled 2C and 8C, respectively, whereas the N-methyl signal is displaced by only 0.07 ppm. The Hg-CH_3 signal at 0.58 ppm is accompanied by a pair of satellites resulting from coupling with ^{199}Hg (17% natural abundance). The spectrum also reveals the presence of several weaker signals (Bs and Ba) whose chemical shifts are given in Table I and whose assignment is proved later in the text.

(CH_3Hg)(MAd-H) dissolved in Me_2SO gives a complex spectrum (Figure 1b) consisting of eight signals for ring protons (7.8–8.2 ppm), four N-CH_3 signals (3.6–3.7 ppm), and three broad resonances typical of amino protons (6.2–7.2 ppm). In fact, this solution contains, in addition to the two isomers of the monosubstituted complex (CH_3Hg)(MAd-H) (B), the uncomplexed MAd (A) and the disubstituted complex (CH_3Hg)$_2$(MAd-2H) (C). Indeed, when A or C is added to this solution, a corresponding increase of the intensity of the signals assigned to these species is observed.

As expected, the H2 and H8 signals, labeled 2B and 8B, respectively, of the monosubstituted complex B are shifted upfield from those of A. Analogously, larger induced shifts are observed for the corresponding signals of the disubstituted complex C. The replacement of one of the two amino protons of MAd by CH_3Hg^+ should release electron density into the remaining N–H bond, thereby shifting the N–H signal upfield.

The signals for the two isomers of the monosubstituted complex B corresponding to the syn and anti rotamers are labeled by s and a in Figure 1 (parts b and c). It is noteworthy to point out that similar observations have also been reported for 6-methylaminopurine.[21] The integration of the signals H2, H8, NH, and N9-CH_3 corresponding to these rotamers gives a 55:45 ratio. It will be shown later that the anti rotamer is predominant.



In an earlier report on methylmercuration of amino groups in nucleobases,[20] splitting in the H2 and H8 region of the 60-MHz

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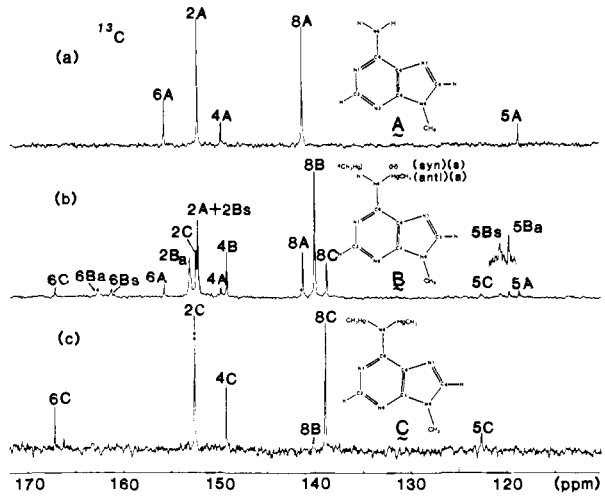

Figure 2. ^{13}C NMR spectra of Me_2SO-d_6 solutions of MAd (a), (CH_3Hg)(MAd-H) (b), and $(CH_3Hg)_2$(MAd-2H) (c) at 100 MHz and room temperature. Numbers in symbols correspond to ring position, and letters identify the species.

Table III. ^{199}Hg NMR Chemical Shifts for MAd and HAd Derivatives[a]

	N9–Hg	N6–Hg
(CH_3Hg)(MAd-H) (Ba)		−817
(CH_3Hg)(MAd-H) (Bs)		−810
$(CH_3Hg)_2$(MAd-2H) (C)		−788 (anti)
		−759 (syn)
(CH_3Hg)Ad (D)	−916	
$(CH_3Hg)_2$(Ad-H) (E)	−913[b]	−799[b]
$(CH_3Hg)_3$(Ad-2H) (F)	−914	−770 (anti)
		−742 (syn)

[a] 298 K, 72.56 MHz. [b] Signals not split by syn–anti isomerism.

spectrum of (CH_3Hg)(MAd-H) was assumed to arise from the presence of syn and anti rotamers. From the above results (Table I), it is clear that the H2 and H8 resonances reported by these authors at 7.90 and 7.83 ppm, respectively, originate from $(CH_3Hg)_2$(MAd-2H), whereas the small splittings (0.01 and 0.03 ppm, respectively) observed here for syn and anti isomers most probably were not detected at 60 MHz.

The above interpretation of the ^1H NMR spectra is supported by the corresponding ^{13}C data (Figure 2 and Table II). The signals of the MAd spectrum (Figure 2a) are labeled according to the assignment made by Chenon and co-workers.[22] Figure 2c and Table II show that replacement of both amino protons by CH_3Hg^+ ions results in a large downfield shift for C6 (11.2 ppm), a smaller downfield shift for C5 (3.8 ppm), but a small upfield shift for C8 (−2.5 ppm), while the C2 and C4 lines are not appreciably affected, being meta to the amino group. Figure 2c shows the presence of a minor signal 8B to be discussed later.

The ^{13}C spectrum of (CH_3Hg)(MAd-H) (Figure 2b) also provides evidence for disproportionation into MAd and $(CH_3Hg)_2$(MAd-2H) as it reveals the existence of signals corresponding to these species. The presence of syn and anti isomers is confirmed by the splitting of carbon signals into two components (Figure 2 and Table II). The small chemical shift differences (few Hz) between 2A–2Bs, 4Ba–4Bs, and 8Ba–8Bs are observed on the coupled ^{13}C spectrum.

The ^{199}Hg data (Figure 3 and Table III) support the ^1H and ^{13}C results. The spectrum of the Me_2SO solution of (CH_3Hg)(MAd-H) (B) shows two major signals at −810 and −817 ppm, which are assigned to species Bs and Ba, respectively, on the basis of their relative intensities. The disproportionation process revealed by the ^1H and ^{13}C spectra is evidenced here by the presence of two weaker ^{199}Hg signals at −759 and −788 ppm

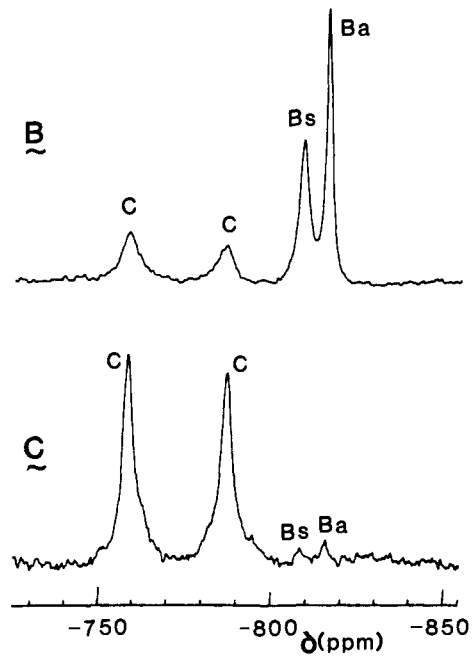

Figure 3. ^{199}Hg NMR spectra of Me_2SO-d_6 solutions of (CH_3Hg)(MAd-H) (B) and $(CH_3Hg)_2$(MAd-2H) (C) at 72.57 MHz and room temperature.

for $(CH_3Hg)_2$(MAd-2H) (C) (obviously the other disproportionation product MAd (A) does not produce ^{199}Hg signals). This same pair of signals occurs, but as the strongest features, in the spectrum of $(CH_3Hg)_2$(MAd-2H) (C). The presence of two signals for the $(CH_3Hg)_2N$ unit indicates that the exchange rate between the two CH_3Hg^+ groups is slow. The downfield signal (−759 ppm) is assigned to the syn CH_3Hg^+ group (above N1), since the CH_3Hg^+ signal for Bs was found at lower field than for Ba.

Spectral Assignment for N9-Methylmercurated Adenine and Its Derivatives in Me_2SO. We next turn our attention to a similar series of adenine derivatives in which the 9-methyl substituent is replaced by a 9-CH_3Hg group. Several workers have examined the tautomeric equilibrium involving the imidazolic proton of adenine.[23–25] They have concluded that the N9–H tautomer is predominant in Me_2SO and D_2O, the proportion of the N7–H tautomer being lower than 20%. Substitution of the imidazolic proton by a CH_3Hg^+ ion leads to the neutral CH_3HgAd compound, and crystallographic work[9,13] on its anhydrous and monohydrate forms has shown metal binding to N9. The ^1H, ^{13}C, and ^{199}Hg spectra of CH_3HgAd show resonances corresponding to only one species. Furthermore, when the N6–H anti proton is substituted by CH_3Hg^+, because of steric hindrance between the N6–$HgCH_3$ and N7–$HgCH_3$ groups, N7–N9 CH_3Hg^+ tautomerization is unlikely. Although tautomerism may occur to a small extent, this CH_3HgAd molecule will be regarded as an N9-substituted adenine derivative similar to MAd, but with a major difference, however, because the CH_3Hg^+ group is more electron-donating than a methyl group or a proton. Therefore, substitution of the imidazolic proton by CH_3Hg^+ results in a general release of electron density into the ring. Figure 4a and the data in table I show that this effect is particularly felt by the adjacent H8 proton, which is shielded by 0.33 ppm, and to a lesser extent by the H2 proton ($\Delta\delta$ = −0.14 ppm). The NH_2 protons also undergo an upfield shift of 0.39 ppm. Similar displacements have been observed for a N9-coordinated Pd compound.[26]

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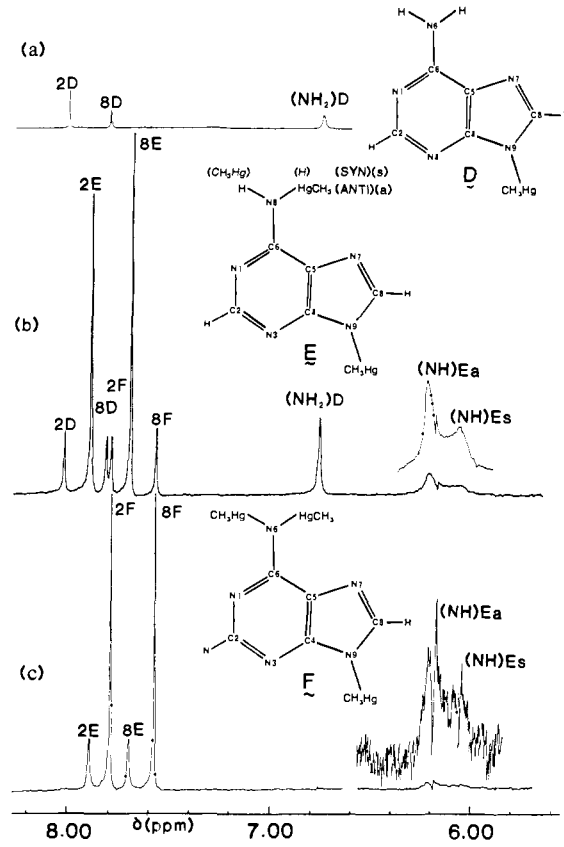

Figure 4. ^1H NMR spectra of Me_2SO-d_6 solutions of CH_3HgAd (a), $(CH_3Hg)_2$(Ad-H) (b), and $(CH_3Hg)_3$(Ad-2H) (c) at 400 MHz and room temperature. Symbols as in Figure 1.

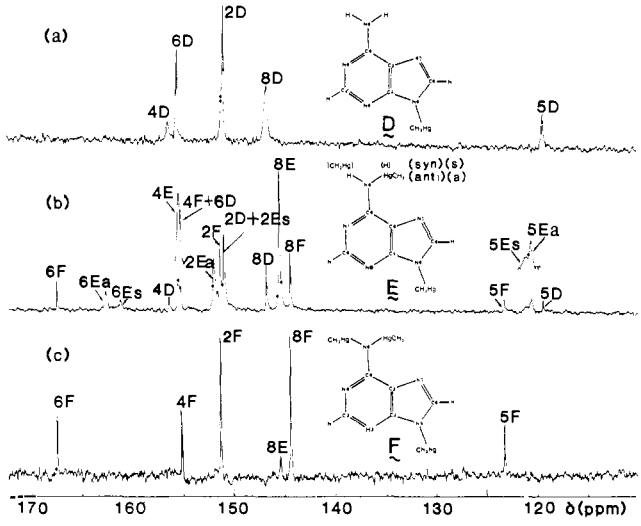

Figure 5. ^{13}C NMR spectra of Me_2SO-d_6 solutions of CH_3HgAd (a), $(CH_3Hg)_2$(Ad-H) (b), and $(CH_3Hg)_3$(Ad-2H) (c) at 100 MHz and room temperature. Symbols as in Figure 2.

Substitution of the N9–H proton by CH_3Hg^+ in CH_3HgAd (D) induces a downfield shift of all ^{13}C signals except C2 (Figure 5a and Table II). This effect is maximum for C4 and C8, the atoms closest to the site formerly occupied by the acidic proton and undoubtedly also occupied by the CH_3Hg^+ group. The N9-bound CH_3Hg^+ group of D produces a ^{199}Hg signal at −916 ppm (Figure 6 and Table III).

The $(CH_3Hg)_3$(Ad-2H) (F) compound has been shown by X-ray diffraction [12] to possess two CH_3Hg^+ groups attached to the doubly deprotonated amino nitrogen and one more CH_3Hg^+

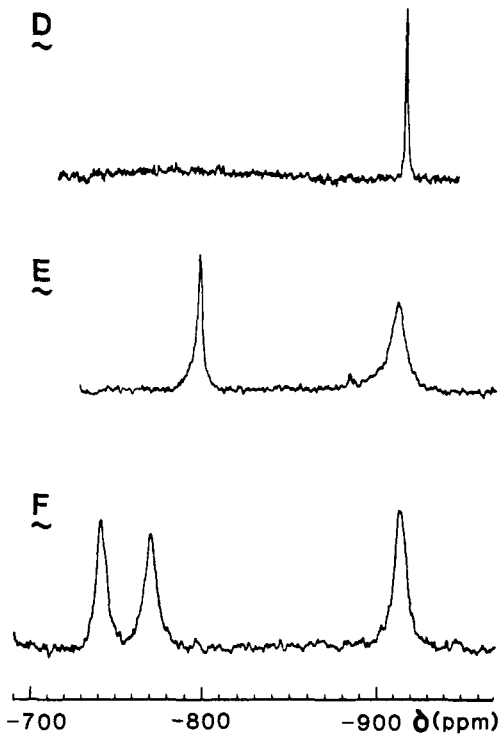

Figure 6. ^{199}Hg NMR spectra of Me_2SO-d_6 solutions of CH_3HgAd (D), $(CH_3Hg)_2$(Ad-H) (E), and $(CH_3Hg)_3$(Ad-2H) (F) at 72.57 MHz and room temperature.

group bonded to N9. The ^1H and ^{13}C signals of this species (Figures 4c and 5c, signals labeled F) are modified with respect to those of CH_3HgAd in the same direction and with the same magnitude as found for the MAd/$(CH_3Hg)_2$(MAd-2H) pair (Tables I and II). The ^{199}Hg spectrum of $(CH_3Hg)_3$(Ad-2H) shows three equally intense signals (Figure 6 and Table III). The upfield one (−914 ppm) corresponds to the CH_3Hg^+ group bound to N9, while the two CH_3Hg^+ groups of the $(CH_3Hg)_2N$ unit give rise to the signals at −770 and −742 ppm.

As to the $(CH_3Hg)_2$(Ad-H) compound, its ^1H and ^{13}C spectra (Figures 4b and 5b) are consistent with the presence of three molecular species (D, E, and F), one of which contains two rotamers (Ea and Es), as a result of partial disproportionation of E into D and F. The syn and anti isomers produce two N–H signals in Figure 4b with intensity ratio of 45:55, whereas the splitting of the H2 and H8 resonances (labeled $2E$ and $8E$, respectively) is too small to be detected. Splitting of the ^{13}C signals (Figure 5b and Table II) provides further support for the existence of syn/anti isomers in this system as well.

Two signals at −799 and −913 ppm are observed on the ^{199}Hg spectrum of the solution of compound E (Figure 6). The N9–$HgCH_3$ resonance (−913 ppm) is not significantly affected by the nature of the substituent at N6 (Table III): the corresponding signals for D and F occur roughly at the same position, as also does the resonance for the CH_3Hg–imidazole complex (−917 ppm).[27] As noted previously, the replacement of the N9-bonded CH_3 group (of C) by a CH_3Hg group (in F) causes both ^{199}Hg signals from the N6–$HgCH_3$ groups to be shifted downfield by ~18 ppm. The N6–$HgCH_3$ signal for compound E (−799 ppm) shows a similar shift with respect to that of Ba (Table III) and 11 ppm relative to Bs. However, in contrast with the latter species, the absence of observable splitting from syn–anti isomerism may be due to the broadness of the signals for E and/or to smaller chemical shift difference between the signals of the two rotamers.

Characterization of the Equilibrium Reactions in Me_2SO. This section deals specifically with the transformation of species in solution. The isomerism about the C6–N6 bond will be discussed later. As mentioned above, the amino monosubstituted compounds

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Table IV. Determination of the Disproportionation Constant K_1 in Me_2SO

9-Methyladenine

initial proportions			equilibrium proportions					
$[(CH_3Hg)_2$-(MAd-2H)]	$[(CH_3Hg)$-(MAd-H)]	[MAd]	$[(CH_3Hg)_2$-(MAd-2H)]	$[(CH_3Hg)$-(MAd-H)]	[MAd]	K_1[c]	$[H_2O]$	$[CH_3HgOH]$[a]
0	0.33	0.67	0.01	0.28	0.71	0.09	8.1	0.0004
0	0.50	0.50	0.03	0.45	0.52	0.08	6.6	0.0007
0	0.67	0.33	0.06	0.52	0.42	0.09	6.8	0.0012
0	0.91	0.09	0.13	0.60	0.27	0.10	9.2	0.003
0	1.00	0	0.15	0.64	0.21	0.08	11.6	0.004
0.09	0.91	0	0.20	0.62	0.18	0.09	13.3	0.006
0.33	0.67	0	0.36	0.56	0.08	0.09	14.9	0.014
0.50	0.50	0	0.48	0.47	0.05	0.11	15.7	0.024
0.67	0.33	0	0.61	0.37	0.02	0.09	17.9	0.044

Adenine

initial proportions			equilibrium proportions					
$[(CH_3Hg)_3$-(Ad-2H)]	$[(CH_3Hg)_2$-(Ad-H)]	$[CH_3HgAd]$	$[(CH_3Hg)_3$-(Ad-2H)]	$[(CH_3Hg)_2$-(Ad-H)]	$[CH_3HgAd]$	K_1[d]	$[H_2O]$	$[CH_3HgOH]$[b]
0	0.33	0.67	0.01	0.34	0.65	0.06	7.0	0.0003
0	0.50	0.50	0.05	0.47	0.48	0.11	7.5	0.0011
0	0.67	0.33	0.07	0.55	0.38	0.09	17.3	0.003
0	0.91	0.09	0.18	0.63	0.19	0.09	21.5	0.009
0	1.00	0	0.19	0.63	0.18	0.09	12.7	0.005
0.09	0.91	0	0.25	0.62	0.13	0.08	6.0	0.003
0.33	0.67	0	0.37	0.55	0.08	0.10	5.8	0.005
0.50	0.50	0	0.49	0.46	0.05	0.12	9.0	0.013
0.67	0.33	0	0.58	0.40	0.02	0.07	12.7	0.026

[a] Calculated from the K_2 constant for $(CH_3Hg)_2$(MAd-2H) (Table V). [b] Calculated from the K_2 constant for $(CH_3Hg)_3$(Ad-2H) (Table V). [c] Average $K_1 = 0.09$ (1). [d] Average $K_1 = 0.09$ (2).

were found to disproportionate into the disubstituted and the unsubstituted molecules in Me_2SO. For 9-methyladenine, this equilibrium reaction is as follows:

$$2(CH_3Hg)(MAd\text{-}H) \rightleftharpoons (CH_3Hg)_2(MAd\text{-}2H) + MAd \quad (1)$$

$$K_1 = \frac{[(CH_3Hg)_2(MAd\text{-}2H)][MAd]}{[(CH_3Hg)(MAd\text{-}H)]^2}$$

Tests were run to determine the time required to reach equilibrium and the reversibility of this system. Spectra recorded after 24 h did not differ from those taken immediately after dissolution. Solutions were also heated to 373 K, at which point averaged signals were obtained for each type of proton. After the solutions were cooled to room temperature, the original ^1H spectra were obtained with the same intensity ratios for the various components. This indicates that the system is reversible and that equilibrium is reached in the time needed to prepare the solution.

To determine K_1, various mixtures of the amino monosubstituted compound with either the unsubstituted or the disubstituted material were prepared, and their ^1H NMR spectra were obtained. (See Figures 9 and 10 in supplementary material). Relative equilibrium concentrations were determined from the signal intensities for each species. As K_1 is unitless, only relative concentrations are required. The results are summarized in Table IV. Results were obtained similarly for the adenine system (Reaction 1a). K_1 is found to lie around 0.10 for both systems.

$$2(CH_3Hg)_2(Ad\text{-}H) \rightleftharpoons (CH_3Hg)_3(Ad\text{-}2H) + CH_3HgAd \quad (1a)$$

Another reaction, not discussed above, was found to take place with the amino disubstituted compounds dissolved in Me_2SO. In addition to the major resonances originating from these molecules, weaker signals were detected (Figures 1 and 4c) which corresponded to the two rotamers of the monosubstituted molecules. It would appear that the amino monosubstituted species found in Me_2SO are produced in situ by reaction of the disubstituted molecule with H_2O.

$$(CH_3Hg)_2(MAd\text{-}2H) + H_2O \rightleftharpoons (CH_3Hg)(MAd\text{-}H) + CH_3HgOH \quad (2)$$

$$K_2 = \frac{[(CH_3Hg)(MAd\text{-}H)][CH_3HgOH]}{[(CH_3Hg)_2(MAd\text{-}2H)][H_2O]}$$

Table V. Determination of the Equilibrium Constant K_2 in Me_2SO

9-Methyladenine

$[(CH_3Hg)_2$-(MAd-2H)]	$[(CH_3Hg)$-(MAd-H)]	$[H_2O]$	K_2[a]
0.966	0.034	0.390	0.0031
0.981	0.019	0.394	0.0009
0.983	0.017	0.403	0.0008
0.970	0.030	0.558	0.0017
0.913	0.087	3.97	0.0021
0.940	0.060	17.37	0.0002
0.850	0.150	26.13	0.0010

Adenine

$[(CH_3Hg)_3$-(Ad-2H)]	$[(CH_3Hg)_2$-(Ad-H)]	$[H_2O]$	K_2
0.155	0.041	7.71	0.0014

[a] Average $K_2 = 0.0015$ (9).

To check the validity of this assumption, a series of spectra were recorded for solutions containing various amounts of water. As expected, the proportion of the monosubstituted species increased as the relative concentration of water in solution was raised (Table V). Inasmuch as CH_3HgOH and (CH_3Hg)(MAd-H) are produced in equal quantities by reaction 2, K_2 can be computed from the relative intensities of the ^1H resonances for H_2O and the two complexes.

$$K_2 = \frac{[(CH_3Hg)(MAd\text{-}H)]^2}{[(CH_3Hg)_2(MAd\text{-}2H)][H_2O]} \quad (3)$$

The values of K_2 are listed in Table V. It was subsequently checked that reaction 2 is unimportant under the conditions used to determine K_1. To do so, the equilibrium concentration of CH_3HgOH based on K_2 was determined for each solution (Table IV) from the equation

$$[CH_3HgOH] = K_2[(CH_3Hg)_2(MAd\text{-}2H)][H_2O]/[(CH_3Hg)(MAd\text{-}H)] \quad (4)$$

The values so obtained are listed in Table IV, where it can be seen that CH_3HgOH remains a marginal product in all cases.

The hydrolytic process observed here for $(CH_3Hg)_2$(MAd-2H) indicates that H_2O and (CH_3Hg)(MAd-H) should have acidities

of comparable strength in Me_2SO. Water has a pk_a of 28.2 in this solvent.[28] The acidity constant of (CH_3Hg)(MAd-H) is not known but it should not be too different from that of the free monoanion $(MAd\text{-}H)^-$, which can be indirectly estimated. This estimate is made by an extension of a relationship observed by Rabenstein[29] between the nucleophilic character of the ligand coordination site and the $^2J(^{199}Hg\text{–}^1H)$ coupling constant of the methyl protons in the CH_3Hg^+ group coordinated to the same site. The equation proposed by Rabenstein ($^2J = 249 - 5.09 \log K$) involved the complex formation constant $K = [CH_3HgL]/[CH_3Hg][L]$. Other workers[30] have defined equations of the type $^2J = a + b(pk_a)$, relating the ^2J constant with, this time, the pk_a of the ligand conjugated acid HL ($k_a = [H][L]/[HL]$). In order to determine the best values of a and b for our systems, we used the two acid dissociations for which pk_a values were available.

$$HAd \rightleftharpoons H^+ + Ad^- \qquad pk_{a1} = 9.9^{31} \qquad (5)$$

$$MAd \rightleftharpoons H^+ + (MAd\text{–}H)^- \qquad pk_{a1} = 16.7^{32} \qquad (6)$$

These pk_a values were used in conjunction with the ^2J coupling constants of CH_3HgAd and (CH_3Hg)(MAd-H) given in Table I, to obtain the linear equation $^2J = 223 - 2.35\ (pk_a)$, which is assumed to be obeyed by the present systems.

From this equation and the ^2J value of 169 Hz for the averaged signal of the two CH_3Hg^+ groups of $(CH_3Hg)_2$(MAd-2H), the average pk_{av} for dissociations 6 and 7 is calculated to be 23. As

$$(MAd\text{-}H)^- \rightleftharpoons H^+ + (MAd\text{-}2H)^{-2} \qquad pk_{a2} \qquad (7)$$

pk_{a1} is known (16.7),[32] pk_{a2} can be calculated from $pk_{a2} = 2(pk_{av}) - pk_{a1} = \sim 29$. This places the acidity constant of (CH_3Hg)(MAd-H) close to that of water.

By a similar approach, the ^2J constant of the adenine $(CH_3Hg)_2$(Ad-H) complex (190 Hz) provides a pk_{av} value of 14 for dissociations 5 and 8.

$$Ad^- \rightleftharpoons H^+ + (Ad\text{–}H)^{-2} \qquad pk_{a2} \qquad (8)$$

$$(Ad\text{-}H)^{-2} \rightleftharpoons H^+ + (Ad\text{-}2H)^{-3} \qquad pk_{a3} \qquad (9)$$

Therefore, $pk_{a2} = 2(pk_{av}) - pk_{a1} = 18$. This value is reasonably close to the pk_{a1} of MAd (16.7)[32] for the same type of NH_2 acid group. Finally, the $(CH_3Hg)_3$(Ad-2H) complex has a ^2J constant of 180 Hz. From the pk_{av} of 18.3, the value of pk_{a3} can be estimated to be $= 3(pk_{av}) - pk_{a1} - pk_{a2} = \sim 27$, a value close to the value of ~ 29 found for the corresponding reaction 7.

Although the above discussion is expected to provide only rough estimates, it allows us to rationalize the hydrolysis of the amino-dimercurated complex in terms of the comparable acidities of H_2O and $NH(HgCH_3)$ groups. On the other hand, in agreement with our observations, the amino-monosubstituted compounds are not expected to be hydrolyzed in Me_2SO, because the NH_2 groups are much stronger acids ($pk_a \sim 16\text{–}18$) that water ($pk_a = 28$).

Solvent Effects for the 9-Methyladenine Derivatives. The amino monomercurated compounds have been found to disproportionate in $CDCl_3$ and $(CD_3)_2CO$. However, the very low solubility of the complexes in these solvents does not provide conditions as favorable for a complete investigation of the disproportion reactions. Although autoassociation in these solvents is known to occur to a greater extent than in Me_2SO,[33] this effect can be neglected because of the very dilute conditions in this study.

For the MAd system in acetone-d_6, the 400-MHz ^1H spectrum of (CH_3Hg)(MAd-H) at room temperature shows signals for the four expected species A, Ba, Bs, and C in slow exchange, whose chemical shifts are listed in Table I. The displacement of the MAd signals upon complexation are similar to those observed in the other solvents. From analysis of the signal intensities, the K_1 constant is found to be 0.035 at 298 K in acetone-d_6, again neglecting any effect of autoassociation.

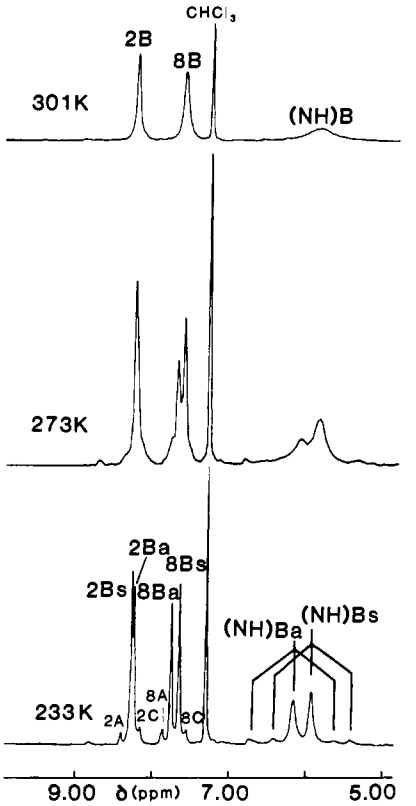

Figure 7. Low-field portion of the ^1H NMR spectra (80 MHz) of $CDCl_3$ solutions of (CH_3Hg)(MAd-H) (B) at various temperatures.

At 301 K, the ^1H spectrum of (CH_3Hg)(MAd-H) in $CDCl_3$ shows evidence of the disproportionation phenomenon: broad average lines at 80 MHz (Figure 7), while at 400 MHz broad individual lines are observed. At 233 K, sharp resonances corresponding to the four expected species A, Bs, Ba, and C are observed. The concentrations of the disproportionation products A and C are much smaller; the K_1 constant in $CDCl_3$ at 233 K is calculated to be 0.0008. The signals originating from A were identified by comparison with literature values;[33] the NH_2 group signal observed at ~ 6.5 ppm in $CDCl_3$ solution of 9-ethyladenine[33] is probably hidden under the NH satellites of B (vide infra). The signals of C were identified by comparison with the spectrum of a solution containing added C complex.

In $CDCl_3$, the disproportionation reaction is faster than in Me_2SO, and the CH_3Hg^+ group is much less labile. In fact, at 233 K where the disproportionation rate is slow compared to the chemical shift difference, the ^1H signals of the ligands and the CH_3Hg^+ groups become well-resolved. Furthermore, the N–H resonances of Ba and Bs both possess a pair of satellites observed at 80 (Figure 7) and 400 MHz due to coupling with ^{199}Hg through the amino nitrogen. These $^2J_{Hg\text{–}H}$ couplings (~ 75 Hz) through nitrogen are apparently observed for the first time.

These observations indicate that the solvent plays an important role in the disproportionation process. From the standpoint of thermodynamics, the disproportionation equilibrium is found to be progressively shifted to the right in the series $CDCl_3 <$ acetone $< Me_2SO$. The distribution of species results from the difference in solvating energy of each solvent.

Solvation also seems to be closely connected with the transfer rate of CH_3Hg^+ and H^+ ions leading to the disproportionation products. In $CDCl_3$, the disproportionation rate is faster than in Me_2SO. Furthermore, in Me_2SO, when the rates for disproportionation and for syn–anti isomerization are slow as evidenced from sharp and well-resolved ^1H and ^{13}C ligand signals for the various species, the signals of the different CH_3Hg^+ groups remain broad and unresolved. This spectral characteristic is not due to

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smaller chemical shift differences between the signals of the various CH_3Hg^+ groups; in fact these differences are larger or comparable to those of the ligands. It must be concluded that the CH_3Hg^+ group is labile in Me_2SO. This additional dynamic process has a faster rate than disproportionation or syn/anti isomerization. However, the overall exchange rate of the CH_3Hg^+ groups in Me_2SO remains slow at room temperature compared with the ^{199}Hg chemical shift differences.

Solvent Effect for the N9-Methylmercurated Adenine Derivatives. The low solubility of the three N9-methylmercurated adenine derivatives, especially of CH_3HgAd (D), precludes a detailed analysis of this system in $CDCl_3$. The ^1H spectra of $(CH_3Hg)_2(Ad-H)$ (E) show the evidence of the dynamic processes: broad H2 and H8 signals and a pair of N–H signals corresponding to Ea and Es are observed at room temperature at 400 MHz or at 273 K at 80 MHz. However, a precipitate appeared as the temperature was further decreased. At 233 K, the 400-MHz ^1H spectrum of the solution indicates the presence of Ea, Es, and F, but the signals corresponding to D are not observed, probably because of its very low solubility. Since one species is removed from the solution, the equilibrium constant K_1 cannot be calculated. The splitting of the H2 and H8 signals of E due to syn/anti isomerism not detected in Me_2SO is observed in $CDCl_3$; the signals of the ligands are very sharp and well-resolved, and their chemical shifts are given in Table I. However, the signals of the CH_3Hg^+ groups remain broad, even at 233 K. The CH_3Hg^+ groups are more labile in the N9-methylmercurated adenine derivatives than in the N9-methyladenine derivatives. This greater lability is undoubtedly due to the N9 CH_3Hg^+ group which is bound more loosely to the ring nitrogen. However, the overall exchange rate of the CH_3Hg^+ groups of the N9-methylmercurated adenine derivatives is slow even in Me_2SO at room temperature compared with the very large ^{199}Hg chemical shift differences, but the signals of E and F are significantly broader than those of B and C.

Syn/Anti Isomerism. The amino lone pair of adenine is delocalized into the ring π system; consequently, nitrogen has a trigonal planar environment with both protons lying in the molecular plane. When rotation about the C6–N6 bond is slow, the amino protons are nonequivalent. However, a single resonance is usually observed for both protons, because of fast rotation. Such is the case for MAd and the N9-coordinated CH_3HgAd complex. Distinct signals have been detected in some cases. For example, upon addition of a uracil derivative, 9-ethyladenine forms 1:1 and 1:2 complexes by Watson–Crick or Hoogsteen pairing via hydrogen bonding. Pairing reduces the rate of rotation, and separate resonances are observed for the syn and anti protons at 220 K (100 MHz) in $CDCl_3$ solutions.[33] Solutions of adenine in CF_3CO_2H or FSO_3H contain dicationic or tricationic protonated adenine species, which show split amino signals even at room temperature (100 MHz.)[34] Coordination of Pt to N1 and N7 of adenosine has also been reported to produce resolved N–H peaks.[26]

In singly substituted amino compounds, hindered rotation about C6–N6 produces syn and anti rotamers, for which both the rotation barrier and the relative populations are informative. For 6-methylamino-9-methylpurine, the syn rotamer (CH_3 closer to N1) was found to be 24 times as abundant as the anti rotamer.[21] The influence of steric factors and hydrogen bonding with N1 and N7 in stabilizing this rotamer has been discussed.[21] In $CDCl_3$ at 303 K (80 MHz) rapid rotation takes place, whereas cooling to 243 K results in resonance splitting. Split signals have also been reported for the amino monodeprotonated dianion of adenine formed in liquid NH_3 in the presence of KNH_2 at 223 K.[35] The proportions of rotamers are 1:2 in this case, but the authors could not determine which isomer was the more abundant.

For the $NH(HgCH_3)$ derivatives B and E studied here, splitting has been observed at room temperature in Me_2SO, acetone, and $CDCl_3$. The rotamers are present in roughly equal amounts, except in acetone, where a 35:65 distribution is found.

Table VI. Free Energy of Activation ($\Delta G^\ddagger$) in Me_2SO for the syn/anti Isomerism of $[(CH_3Hg)(MAd-H)]$

^1H signal[a]	T_c (K)	$\Delta\nu$ (Hz)	K_r (s^{-1})	$\Delta G^\ddagger$ (kJ/mol)[b]
H_2	299	4.81	10.7	67.3
H8	308	13.01	28.9	66.9
$(N9)-CH_3$	301	5.90	13.1	67.3
$NH(HgCH_3)$	319	66.74	148.3	65.0

[a] 400 MHz. [b] Average: 66(1) kJ/mol.

The rotation barrier was obtained from a variable-temperature ^1H NMR experiment at 400 MHz for a Me_2SO solution of $(CH_3Hg)(MAd-H)$ (derivative B in Figure 1). The coalescence temperatures for the various signals are given in Table VI.

The $\Delta G^\ddagger$ value deduced therefrom for syn/anti isomerization is found to be 66 kJ/mol. At temperatures where the conformational exchange rate is fast, the N–H signal remains broad, suggesting that these protons are exchanging with those of residual water.

Signal assignment to the individual rotamers of $(CH_3Hg)(MAd-H)$ is based on the observation of long-range $^4J_{CH}$ coupling between C2 and the N6–H proton for one of the rotamers in the coupled ^{13}C NMR spectrum in Me_2SO. Usually not resolved except when the coupled nuclei are disposed in a "W" arrangement, $^4J_{CH}$ values are about 1–2 Hz.[36] The coupled ^{13}C spectrum of B showed a splitting of 2.1 Hz for the C2 signal of Bs, whereas the signal of the other isomer remained a singlet. Thus the syn rotamer, with a W pathway between C2 and N6–H, is identified. Furthermore, $^4J_{CH}$ is not resolved for the C2 signal of MAd because of rapid rotation.

Finally, the two ^{199}Hg signals observed for compound C in Me_2SO (Figure 3) coalesce at higher temperature ($T_c \approx 393$ K) as a result of faster rotation about the C6–N6 bond. A free energy barrier of 69.5 kJ/mol is calculated. Because of accidental coincidence of the ^1H and ^{13}C signals of C, only the ^{199}Hg spectrum provides information on bond rotation. Similarly, compound F also shows two separate ^{199}Hg signals (Figure 6) for the N6-$(HgCH_3)_2$ group.

Exchange Processes and 2-D NMR. The study of molecular exchange processes can be carried out efficiently by two-dimensional spectroscopy,[17,18,37,38] whereby the appearance of cross-peaks in the 2-D spectrum is a proof that exchange is taking place between corresponding sites. The rate constants can be determined by analysis of the cross-peak intensities obtained from several 2-D exchange spectra with different mixing times[38] or by line-shape analysis of the "accordion" spectrum.[17] A qualitative assessment of the 2-D data for the Me_2SO solution of $(CH_3Hg)(MAd-H)$ B is given here, while a quantitative analysis of this system and others will be given elsewhere.[39] The different dynamic processes occurring in this solution have been discussed earlier; four species A, Bs, Ba, and C are interchanging at different rates as represented by the following equilibria

$$Bs \rightleftharpoons Ba \qquad \text{syn} \rightleftharpoons \text{anti isomerism}$$

$$2B \rightleftharpoons A + C \qquad \text{disproportionation}$$

The H2 and H8 part of the 2-D accordion spectrum (Figure 8) identifies the entire exchange network and also confirms the proton assignments. Along the diagonal (lower left to upper right corner) appear eight peaks labeled as 2A, 8A, 2Ba, 2Bs, 8Bs, 8Ba, 2C, and 8C corresponding to the resonances of the protons H2 and H8 of the four species. Exchanging signals give rise to off-diagonal cross-peaks which are labeled by hyphened symbols identifying the exchanging sites. For example, the cross-peaks

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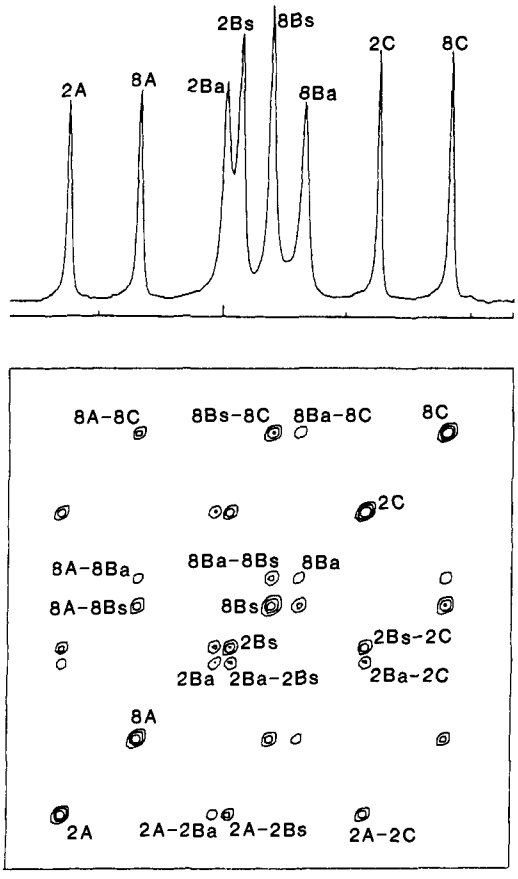


Figure 8. Contour plot of an "accordion" spectrum of the Me_2SO-d_6 solution of (CH_3Hg)(MAd-H).

2Ba–2Bs (proton H2) and 8Ba–8Bs (proton H8) result from the syn ⇌ anti equilibrium (Bs ⇌ Ba). It is useful to note that on the regular 2-D exchange spectrum with short mixing time (t_m = 0.05–0.10 s), these cross-peaks are much more intense than all other exchanging signals because the syn ⇌ anti equilibrium is a faster dynamic process. The 2A–2Ba, 2A–2Bs, 2Ba–2C, and 2Bs–2C and the analogous proton H8 exchanging signals (Figure 8) result from the direct disproportionation process 2B ⇌ A + C. The 2A–2C and 8A–8C cross-peaks indicate that A and C are also involved in an exchange process; this A ⇌ C exchange can result from the following "double disproportionation" reaction (Scheme II). Because the A ⇌ C exchange is a slower process, the A–C exchanging signals are not observed on the regular 2-D exchange spectra or are very weak when the mixing time is short (t_m = 0.1–0.3 s) but become more intense as the mixing time becomes longer (t_m = 1.0–2.0 s).

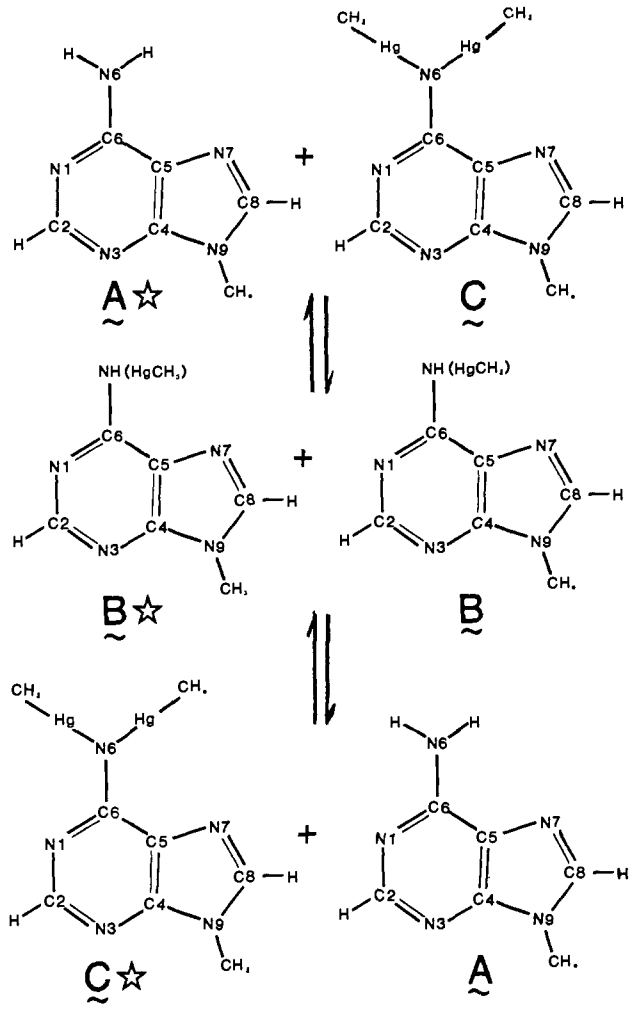
Accordion spectroscopy, therefore, appears to give a very appropriate 2-D spectrum useful to identify the entire exchange network characterized by different rate constants.

Conclusion

An obvious conclusion of the present work is that single routine NMR spectra of the compounds studied here would not provide unambiguous indications as to the purity of the samples. Indeed, $(CH_3Hg)_2$(Ad-H) was a pure, structurally characterized crystalline sample, but the NMR spectra showed substantial amounts of CH_3HgAd and $(CH_3Hg)_3$(Ad-2H) resulting from a disproportionation reaction. On the other hand, the spectra of the solid known to be a mixture of MAd and $(CH_3Hg)_2$(MAd-2H) show that these molecules are only minor species in solution, the main product being (CH_3Hg)(MAd-H). This behavior is characteristic of thermodynamically controlled systems in which equilibrium is reached rapidly on the time scale of preparative chemistry.

On the basis of the K_1 constant, corresponding to the disproportionation of the amino monosubstituted complex into the disubstituted and the unsubstituted compounds, the extent of disproportionation is calculated to be ~38% in Me_2SO for both $(CH_3Hg)_2$(Ad-H) and (CH_3Hg)(MAd-H). This reduces to ~27% in acetone and ~5% in chloroform for the MAd compound. Values for the K_1 constants in the latter two solvents were not obtained for the adenine compound due to poor solubility.

Scheme II



The amino disubstituted compounds $(CH_3Hg)_3$(Ad-2H) and $(CH_3Hg)_2$(MAd-2H) take part in a hydrolysis reaction with the water present in Me_2SO. The corresponding equilibrium constants k_2 were also determined. Partial hydrolysis of the $N(HgCH_3)_2$ group is anticipated to take place if the $NH(HgCH_3)$ group and water are acids of comparable strengths. The pk_a of water in Me_2SO is 28.2.[28] Our estimate for the pk_a of the $NH(HgCH_3)$ group is ~27, a value close enough to that of water to be consistent with the significant hydrolysis at equilibrium. However, the $NH(HgCH_3)$ group is not expected to further hydrolyze, since the pk_a of the NH_2 group of MAd (16.7)[32] and our estimate (~17) for CH_3HgAd make this proton much more acidic than that of water.

The amino monomercurated compounds (CH_3Hg)(MAd-H) and $(CH_3Hg)_2$(Ad-H) exist in solution as syn and anti rotamers, due to slow rotation of the $NH(HgCH_3)$ about the C6–N6 bond. The rotation barrier for the MAd complex in Me_2SO is 66 kJ/mol, a value similar to that reported for the $NH(CH_3)$ group in 6-methylamino-9-methylpurine (50 kJ/mol).[21] Smaller chemical shift differences and lower solubility made the energy barrier impossible to measure for the adenine compound. Both rotamers are present in roughly equal amounts in Me_2SO and $CDCl_3$, but the anti/syn ratio is close to 2:1 in acetone.

Information on the relative rates of rotation about the C6–N6 bond and ligand exchange between the various types of complexes was obtained from the 2-D accordion spectra of Me_2SO solutions of (CH_3Hg)(MAd-H) (containing 38% of disproportionation

products). Rotation of the $NH(HgCH_3)$ group about C6-N6 was found to be a much faster process than disproportionation. This rules out the possibility that the rotamers be interconverted only via scrambling of the ligand among the four species present at equilibrium.

Although the Hg-N bonds are all labile from the standpoint of preparative chemistry, the present work indicates that the CH_3Hg^+ groups bound to very basic sites tend to exchange slowly on the NMR time scale. Indeed, an individual ^{199}Hg signal of each CH_3Hg^+ group within a molecule or of different species is observed at room temperature. Furthermore, coupling between the N6-H proton and ^{199}Hg has also been detected.

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Supplementary Material Available: ^1H NMR spectra of mixtures of amino di-, mono-, and unsubstituted derivatives of 9-methyladenine (Figure 9) and 9-(methylmercuri)adenine (Figure 10) used for determining the K_1 constants (3 pages). Ordering information is given on any current masthead page.

Synthesis and Structures of Distibene (RSb=SbR) and Bridging Stibinidene (RSb) Iron Complexes

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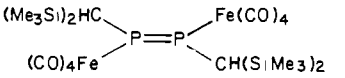
Abstract: The reaction of $(Me_3Si)_2CHSbCl_2$ (**4**) with $Na_2[Fe(CO)_4]$ affords a mixture of the distibene complex, $[Fe(\eta^2\text{-}\{(Me_3Si)_2CH\}_2Sb_2)(CO)_4]$ (**5**), and the "closed" stibinidene complex, $[Fe_2\{\mu\text{-}SbCH(SiMe_3)_2\}(CO)_8]$ (**6**). The structures of **4**, **5**, and **6** were determined by single-crystal X-ray diffraction methods. Compound **4** crystallizes in the monoclinic space group $P2_1/n$ with $a = 7.021$ (3) Å, $b = 17.129$ (10) Å, $c = 12.490$ (4) Å, and $\beta = 99.64$ (3)°. Compound **5** crystallizes in the monoclinic space group $P2_1/n$ with $a = 19.958$ (4) Å, $b = 6.635$ (1) Å, $c = 24.408$ (6) Å, and $\beta = 103.51$ (2)°. Compound **6** crystallizes in the triclinic space group $P\bar{1}$ with $a = 7.065$ (5) Å, $b = 9.179$ (2) Å, $c = 19.814$ (7) Å, $\alpha = 86.86$ (3)°, $\beta = 85.23$ (5)°, $\gamma = 70.04$ (4)°. The reaction of **5** with $Fe_2(CO)_9$ produces **6**, an unstable compound, **14**, believed to be the "open" isomer of **6**, and an iron-antimony cluster, $[\{Fe(CO)_3\}_3\{(Me_3Si)_2CHSb\}_2]$, (**15**).

The synthesis of stable compounds featuring unsupported double bonds between the heavier main-group elements has been achieved recently by use of bulky ligands.[2] With particular reference to group 5A, this strategy has proved successful for the isolation of diphosphenes (RP=PR), diarsenes (RAs=AsR), phosphaarsenes (RP=AsR), and a phosphastibene (RP=SbR). In each case the molecule contains a double bond and a lone pair of electrons on each group 5A atom. The availability of these new ligands has enabled an extensive coordination chemistry to be developed. Thus, far, a total of six different bonding modes have been recognized for RE=ER ligands.[2d,e,3] Of particular concern to the present work are the modes which feature donation by the lone pair(s) of the main-group atom, E, thus leaving an unsupported E=E bond.[3-7] The first compound of this type (**1**) was prepared by Power et al.[5] by treatment of $(Me_3Si)_2CHPCl_2$ with $Na_2[Fe(CO)_4]$. Not only does **1** possess an unsupported P=P double



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bond but it also features considerable steric loading at each phosphorus on account of the attachment of two $Fe(CO)_4$ moieties. Since all our attempts to prepare and isolate an unligated distibene (RSb=SbR) had met with failure, we turned our attention to the possibility of synthesizing an antimony-antimony double-bonded compound analogous to **1** using the methodology of Power et al.[5] While this objective was not realized, the work has resulted in a π-bonded distibene complex, a novel "closed" stibinidene (RSb) complex, and a cluster with an Fe_3Sb_2 core.

Results and Discussion

Our initial approach to the synthesis of compounds featuring antimony-antimony double bonds centered around the reaction of dichlorostibines with transition metal dianions. Experience gained with diphosphenes and their heavier congeners indicates that the nature of the products depended critically on the steric demands of the substituents. Since the three most widely used substituents are 2,4,6-$(t\text{-}Bu)_3C_6H_2$, $(Me_3Si)_3C$, and $(Me_3Si)_2CH$, our first objective was to prepare dichlorostibines bearing these

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