The reverse reaction is observed when a methylene chloride solution of $[Au_8L_8]^{2+}$ is reacted with the phosphine acceptor $AuL(NO_3)$. Since $[Au_8L_8]^{2+}$ is also spherically screened by phosphine ligands again, a dissociative mechanism imposes itself:

$$[Au_8L_8]^{2+} \rightleftarrows [Au_8L_7]^{2+} + L \quad (3)$$

When 2 equiv of $AuL(NO_3)$ is added to a solution of $[Au_8L_8]^{2+}$, the final products are $[Au_9L_8]^{3+}$ and $[AuL_2]^+$.

These interconversion reactions proceed according to Scheme: As can be seen, $[Au_8L_7]^{2+}$ resides at a central place. We therefore designed a route to synthesize and isolate this species. We succeeded in the preparation of $[Au_8L_7]^{2+}$ by reacting $[Au_8L_8]^{2+}$ with $[RhCl(C_8H_{14})_2]_2$, a well -known phosphine scavenger, in a mole ratio 4:1 in CH_2Cl_2, according to

$$[Au_8L_8]^{2+} + {}^1/_4[RhCl(C_8H_{14})_2]_2 \rightarrow [Au_8L_7]^{2+} + {}^1/_4[RhClL_2]_2 + C_8H_{14} \quad (4)$$

$[Au_8L_7]^{2+}$ could be isolated in a reasonable yield (74%). From its X-ray structure analysis it has clearly been shown that this compound possesses a rather exposed central gold atom and should therefore be reactive toward Lewis bases. In order to synthesize mixed-metal clusters, we reacted $[Au_8L_7]^{2+}$ with $[Co(CO)_4]^-$ (mole ratio 1:2). From a number of as yet uncharacterized products, which were present in the reaction mixture, we succeeded in isolating a small amount of crystals of $Au_6L_4[Co(CO)_4]_2$.

Although a large number of mixed gold-transition metal compounds has been reported,[27] only a few mixed-metal clusters of gold and a transition metal are known at this moment: $Os_3(CO)_{10}(AuPPh_3)X$ (X = H[28] and halide[29]), $Os_3(CO)_{10}S_2(AuPPh_3)_2$,[29] and $V(CO)_5(AuPPh_3)_3$.[30] A promising and interesting area, which is currently under investigation, concerns the reations of the coordinatively unsaturated $[Au_8L_7]^{2+}$ with small molecules such as isocyanides and CO.

Acknowledgment. We thank Professor J. J. Steggerda for his continuous interest and useful discussions. The investigations were supported in part by the Netherlands Foundation for Chemical Research (SON) with financial aid from The Netherlands Organization for the Advancement of Pure Research.

Registry No. $[Au_9(PPh_3)_8](NO_3)_3$, 37336-35-9; $[Au_8(PPh_3)_8](NO_3)_2$, 81283-09-2; $[Au_8(PPh_3)_8](PF_6)_2$, 72271-20-6; $[Au_8(PPh_3)_7](NO_3)_2 \cdot 2CH_2Cl_2$, 81283-11-6; $Au_6(PPh_3)_4[Co(CO)_4]_2$, 79008-51-8; $Au(PPh_3)NO_3$, 14897-32-6; cobalt, 7440-48-4; gold, 7440-57-5.

Supplementary Material Available: Listings for both $[Au_8(PPh_3)_7](NO_3)_2 \cdot 2CH_2Cl_2$ and $Au_6(PPh_3)_4[Co(CO)_4]_2$ of structure factor tables and fractional coordinates of the carbon, nitrogen, oxygen, and chlorine atoms and a listing of fractional coordinates of the hydrogen atoms attached to the phenyl carbon atoms calculated for $[Au_8(PPh_3)_7](NO_3)_2 \cdot 2CH_2Cl_2$ (37 pages). Ordering information is given on any current masthead page.

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Carbon-13 and Phosphorus-31 NMR Studies of Interactions of Organorhodium Complexes with Guanosine, Inosine, 6-Mercaptoguanosine, and 8-Mercaptoguanosine in Neutral and Basic Dimethyl-d_6 Sulfoxide Solutions

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The interactions of the carbonylbis(triphenylphosphine)rhodium(I) electrophile with inosine, guanosine, 6-mercaptoguanosine, and 8-mercaptoguanosine have been investigated in neutral and basic dimethyl-d_6 sulfoxide solutions with the use of ^{13}C and $^{31}P\{^1H\}$ NMR spectroscopy. The binding of $[(PPh_3)_2(CO)Rh]^+$ to O(6) of guanosine and inosine has been found to increase the acidity of N(1)-H. Complexation of the Rh(I) cation at S(6) of 6-mercaptoguanosine has also been found to promote deprotonation at N(1), while binding at S(8) of 8-mercaptoguanosine promotes deprotonation at N(7). Data are presented that indicate that the complexation of $[(PPh_3)_2(CO)Rh]^+$ with 8-mercaptoguanosine changes the preferred site of deprotonation for the thionucleoside, providing more evidence that interactions of transition metals with nucleic base derivatives can significantly alter the chemical behavior of those derivatives. It has been shown that carbon atoms near a site of deprotonation and a site of metal complexation can experience opposing effects under basic conditions, leading to an overall negligible shift in the resonances of those carbon atoms. Problems that can arise under these conditions are discussed.

Introduction

The report of the antitumor behavior of platinum(II) compounds[1] has led to a flurry of activity over the past decade in the area of metal interactions with nucleic acids.[2-4] The interaction of metal species at O(6) of guanosine (Guo) and its derivatives has taken on added significance since it was postulated that the antitumor behavior of some substances might be linked to their ability to interact at O(6) of the

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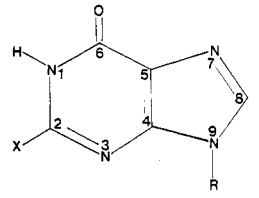
Table I. ^{13}C NMR Chemical Shifts for Various Mixtures of Inosine, Triethylamine, Ethanolamine, and the Carbonylbis(triphenylphosphine)rhodium(I) Cation[a]

	δ[b]									
	base C atoms					ribose C atoms				
inosine solns	C(6)	C(2)	C(4)	C(8)	C(5)	C(1′)	C(4′)	C(2′)	C(3′)	C(5′)
Ino	156.6	145.8	148.2	138.7	124.5	87.6	85.6	74.1	70.3	61.3
Ino-TEA	156.9	146.0	148.3	138.6	124.5	87.5	85.6	74.1	70.3	61.3
Ino-EOA	163.6	150.5	148.4	137.7	124.5	88.2	86.0	73.6	70.8	61.7
Ino-TEA-Rh(I)	162.7	151.8	146.9	136.9	124.5	88.2	85.6	73.7	70.4	61.6
Ino-EOA-Rh(I)	163.2	151.8	147.0	136.8	124.7	88.3	85.7	73.7	70.5	61.6
Ino-Rh(I)	154.6	146.8	146.4	139.0	121.5	88.2	85.3	73.7	69.4	60.7

[a] Abbreviations: Ino = inosine; TEA = triethylamine; EOA = ethanolamine; Rh(I) = $[(PPh_3)_2(CO)Rh]^+$. Concentrations (in $(CD_3)_2SO$): Ino, 0.15 M; TEA, 0.40 M; EOA, 0.80 M; Rh(I), 0.15 M. [b] Chemical shifts are measured from $(CH_3)_4Si$ internal standard at 22.51 MHz.

guanine component in DNA.[5] Recent NMR studies[6] in our laboratory have provided evidence of O(6) binding to Guo (**1**,



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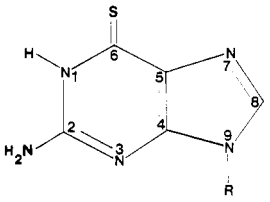
X = NH_2, R = ribose) and inosine (Ino) (**1**, X = H, R = ribose) by the electrophile $[(PPh_3)_2(CO)Rh]^+$ in neutral $(CD_3)_2SO$ solution. Marzilli and co-workers[7] have found that in basic $(CD_3)_2SO$ solutions other metal ions can also interact with Guo and Ino at O(6). Prior to these solution studies, the interactions of metal ions at O(6) of 6-oxopurine derivatives had been virtually limited to the weak interactions observed in solid-state studies.[8-11]

The work of Marzilli and our previous observations in $(CD_3)_2SO$ solutions have prompted us to further investigate rhodium(I)–nucleoside interactions in $(CD_3)_2SO$ under basic conditions. In view of the observation of Rh(I) binding at O(6) of Guo, we have also investigated the interaction of $[(PPh_3)_2(CO)Rh]^+$ with the thiolated nucleosides 6-mercaptoguanosine (s^6Guo, **2**) and 8-mercaptoguanosine



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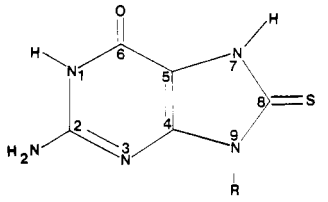

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(s^8Guo, **3**). These investigations were conducted to see whether Rh(I) binding to s^6Guo parallels the binding to Guo and to determine the nature of the binding of the Rh(I) species to s^8Guo. Like Guo, s^8Guo contains the C(6)=O functional group, but s^8Guo also contains the thiocarbonyl functional group, C(8)=S, to which Rh(I) might be expected to preferentially bind. The binding of metals to s^6Guo and s^8Guo is of interest since some thiopurine derivatives have been shown to be antitumor agents[12,13] whose antitumor activity has been shown to be enhanced when complexed to certain metal ions.[14]

Experimental Section

Materials. Guanosine, inosine, 6-mercaptoguanosine, and 8-mercaptoguanosine were obtained from Sigma Chemical Co. and were used without further purification. The $[(PPh_3)_2(CO)Rh]^+$ cation was added to $(CD_3)_2SO$ solutions of the nucleosides in the form of $[Rh(PPh_3)_2(CO)_3]PF_6$, which loses two carbon monoxide molecules when added to the nucleoside solutions. $[Rh(PPh_3)_2(CO)_3]PF_6$ was prepared according to the method of Schrock and Osborn.[15]

Methods. The ^{13}C NMR and $^{31}P\{^1H\}$ NMR spectra were obtained on a JEOL FX90Q Fourier transform (FT) spectrometer. The ^{13}C NMR spectra were measured at 22.51 MHz, with $(CH_3)_4Si$ as an internal standard. The $^{31}P\{^1H\}$ NMR spectra were measured at 36.19 MHz with 85% H_3PO_4 as an external standard. All spectra were obtained at room temperature unless otherwise specified. Recorded temperatures are accurate to ±1.0 °C.

NMR solutions were prepared by dissolving the appropriate quantities of $[Rh(PPh_3)_2(CO)_3]PF_6$ and nucleoside in 2.5 mL of $(CD_3)_2SO$ to give the desired rhodium-to-nucleoside ratio with a nucleoside concentration of approximately 0.15 M. For basic solutions, approximately 125 μL of triethylamine (TEA) or ethanolamine (EOA) was added to the solutions. The ^{13}C NMR peak assignments were made according to those in the literature.[7,16]

Results and Discussion

The carbon-13 chemical shift data from NMR studies of an equimolar mixture of the electrophile $[(PPh_3)_2(CO)Rh]^+$ with guanosine or inosine in $(CD_3)_2SO$ indicate that the Rh(I)–nucleoside interactions are the same for the 1:1 mixtures as were observed in earlier studies for the isolated complexes.[6] Binding at O(6) of Guo and Ino is supported by significant upfield shifts in the C(6) and C(5) resonances coupled with negligible shifts in the C(2) and C(8) resonances (Tables I and II).

The work of Marzilli and co-workers[7] shows that the presence of ethanolamine in $(CD_3)_2SO$ solutions of Guo and Ino causes significant downfield shifts of the C(6) and C(2) resonances. These results are indicative of deprotonation at N(1). The addition of triethylamine to $(CD_3)_2SO$ solutions of Guo and Ino does not perturb the nucleoside resonances. However, downfield shifts in the C(6) and C(2) resonances occur upon addition of certain metal ions to solutions of the nucleosides and triethylamine. These downfield shifts are indicative of increased acidity and deprotonation at N(1)

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Table II. ^{13}C NMR Chemical Shifts for Various Mixtures of Guanosine, Triethylamine, Ethanolamine, and the Carbonylbis(triphenylphosphine)rhodium(I) Cation[a]

	δ[b]									
	base C atoms					ribose C atoms				
guanosine solns	C(6)	C(2)	C(4)	C(8)	C(5)	C(1′)	C(4′)	C(2′)	C(3′)	C(5′)
Guo	156.9	153.7	151.4	135.6	116.8	86.6	85.3	73.9	70.5	61.5
Guo-TEA	157.1	153.9	151.3	135.5	116.7	86.5	85.2	73.7	70.4	61.4
Guo-EOA	159.3	155.2	151.3	135.3	116.9	86.8	85.3	73.6	70.5	61.5
Guo-TEA-Rh(I)	157.1	155.0	150.0	135.0	115.2	87.2	84.8	73.6	69.6	61.0
Guo-EOA-Rh(I)	162.6	156.7	150.6	133.6	117.9	87.8	85.3	73.7	70.4	61.6
Guo-Rh(I)	154.8	153.4	149.6	135.6	113.8	86.9	84.7	73.5	69.2	60.8

[a] Abbreviations: Guo = guanosine; TEA = triethylamine; EOA = ethanolamine; Rh(I) = $[(PPh_3)_2(CO)Rh]^+$. Concentrations (in $(CD_3)_2SO$): Guo, 0.15 M; TEA, 0.40 M; EOA, 0.80 M; Rh(I), 0.15 M. [b] Chemical shifts are measured from $(CH_3)_4Si$ internal standard at 22.51 MHz.

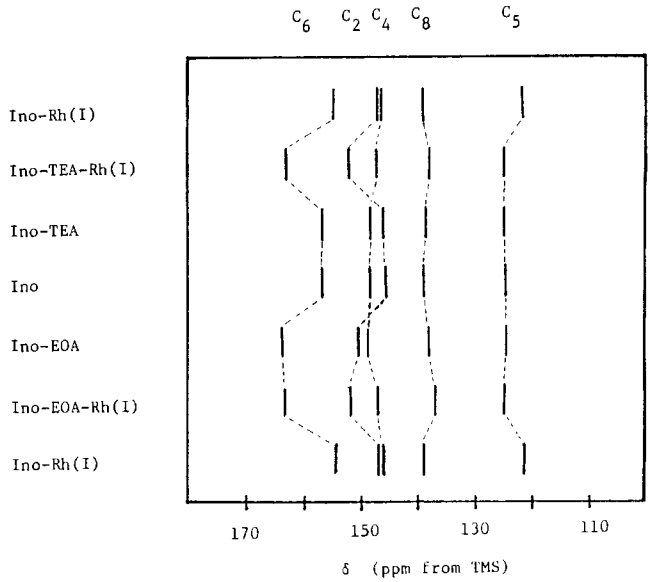

Figure 1. ^{13}C NMR spectral shifts for mixtures of inosine (Ino), triethylamine (TEA) or ethanolamine (EOA), and the carbonylbis(triphenylphosphine)rhodium(I) cation (Rh(I)).

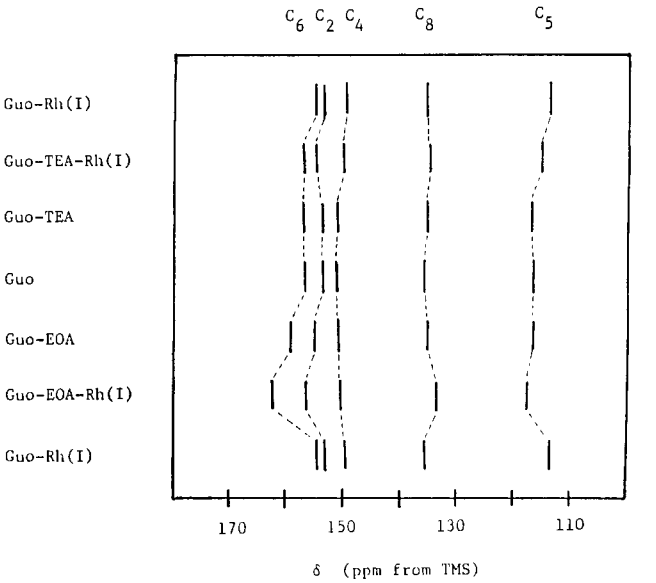

Figure 2. ^{13}C NMR spectral shifts for mixtures of guanosine (Guo), triethylamine (TEA) or ethanolamine (EOA), and the carbonylbis(triphenylphosphine)rhodium(I) cation (Rh(I)).

promoted by metal–nucleoside interactions occurring at O(6). Increased acidity of N(1)–H of 6-oxopurine derivatives through metal interaction is not restricted to interaction at O(6). Similar increases in the acidity of N(1)–H of 6-oxopurine derivatives have been observed for metal complexation at N(7).[17]

The results of our present study suggest that two opposing phenomena are occurring in basic solutions of Guo or Ino and the electrophile $[(PPh_3)_2(CO)Rh]^+$. Generally, the most pronounced perturbations in the carbon resonances result from deprotonation, which is characterized by downfield shifts in resonances of the carbon atoms adjacent to the deprotonation site. Smaller perturbations, which occur as upfield shifts, have been shown to occur in the resonances of the carbon atoms nearest the site of complexation of $[(PPh_3)_2(CO)Rh]^+$ to Guo and Ino.[6] The combination of deprotonation and complexation can result in a relatively small net shift in a carbon resonance which might obscure the importance of interactions taking place at or near the carbon atom.

Fortunately, the individual interactions involved can be resolved by examining the appropriate mixtures. The effects of deprotonation are seen by a comparison of (a) NuH and the NuH–EOA system and (b) the NuH–Rh(I) and NuH–Rh(I)–B systems (B = EOA or TEA; NuH = nucleosides). The relative degree of deprotonation caused by coordination

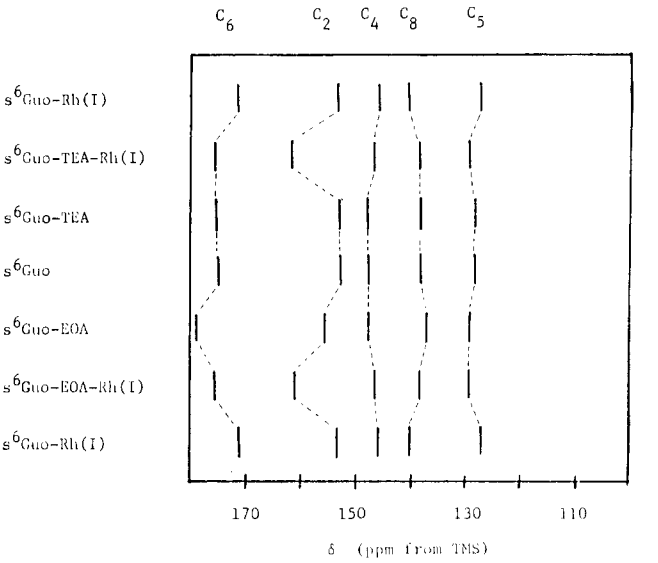

Figure 3. ^{13}C NMR spectral shifts for mixtures of 6-mercaptoguanosine (s^6Guo), triethylamine (TEA) or ethanolamine (EOA), and the carbonylbis(triphenylphosphine)rhodium(I) cation (Rh(I)).

of $[(PPh_3)_2(CO)Rh]^+$ to the nucleosides in the presence of TEA can be seen by comparing the ^{13}C NMR spectral data of the NuH–EOA–Rh(I) mixture with that of the NuH–TEA–Rh(I) mixture.

The effect of complexation is evident from a comparison of the ^{13}C NMR spectral data of the nucleosides and the

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Table III. ^{13}C NMR Chemical Shifts for Various Mixtures of 6-Mercaptoguanosine, Triethylamine, Ethanolamine, and the Carbonylbis(triphenylphosphine)rhodium(I) Cation[a]

6-mercaptoguanosine solns	δ[b] base C atoms					ribose C atoms				
	C(6)	C(2)	C(4)	C(8)	C(5)	C(1′)	C(4′)	C(3′)	C(2′)	C(5′)
s^6Guo	175.0	152.9	147.8	138.3	128.2	87.4	86.4	73.7	70.2	61.2
s^6Guo-TEA	175.1	153.0	147.8	138.3	128.3	86.3	85.2	73.7	70.2	61.1
s^6Guo-EOA	178.8	155.7	147.6	137.0	129.2	87.1	85.5	73.4	70.5	61.2
s^6Guo-TEA-Rh(I)	175.5	161.3	146.7	138.5	129.3	87.7	85.6	73.8	70.2	61.3
s^6Guo-EOA-Rh(I)	175.8	161.2	146.6	138.4	129.3	87.8	85.5	73.8	70.2	61.3
s^6Guo-Rh(I)	171.4	153.4	145.8	140.3	127.3	87.7	84.5	73.7	68.9	60.3

[a] Abbreviations: s^6Guo = 6-mercaptoguanosine; TEA = triethylamine; EOA = ethanolamine; Rh(I) = $[(PPh_3)_2(CO)Rh]^+$. Concentrations (in $(CD_3)_2SO$): s^6Guo, 0.15 M; TEA, 0.40 M; EOA, 0.80 M; Rh(I), 0.15 M. [b] Chemical shifts are measured from $(CH_3)_4Si$ internal standard at 22.51 MHz.

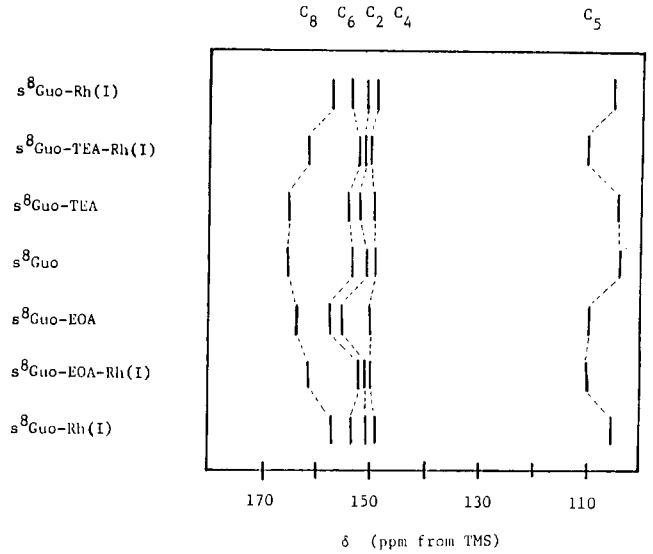

Figure 4. ^{13}C NMR spectral shifts for mixtures of 8-mercaptoguanosine (s^8Guo), triethylamine (TEA) or ethanolamine (EOA), and the carbonylbis(triphenylphosphine)rhodium(I) cation (Rh(I)).

NuH–Rh(I) mixtures. The combined effect of deprotonation and complexation is resolved by comparing the ^{13}C NMR spectral data of the individual nucleosides and their NuH–EOA–Rh(I) and NuH–TEA–Rh(I) mixtures. Figures 1–4 illustrate the ^{13}C NMR spectral data for these mixtures and show the various changes that occur in going from one system to another. The behavior of each nucleoside is analyzed separately below.

The nucleoside–base systems are represented by the acid–base equilibrium

$$NuH + B \rightleftarrows Nu^- + HB^+ \quad (1)$$

When the base is EOA, the equilibrium lies far to the right; however, when the base is TEA, the equilibrium lies far to the left. The addition of $[(PPh_3)_2(CO)Rh]^+$ to the nucleoside–base systems causes an increase in the acidity of N(1)–H through the interaction at O(6) of Guo and Ino. This results in a shift in the equilibrium (eq 1) to the right. These shifts are detectable by ^{13}C NMR chemical shift studies because the chemical shifts are time-averaged values of the neutral and deprotonated nucleosides.

Inosine. Basic Dimethyl Sulfoxide Solutions. The ^{13}C NMR chemical shift data for the Ino mixtures are presented in Table I. The spectral chart shown in Figure 1 outlines the changes that occur in going from one system to another. The spectral data given for the Ino–EOA and Ino–TEA systems are consistent with the results reported by Marzilli and co-workers.[7] Addition of the electropile $[(PPh_3)_2(CO)Rh]^+$ to the Ino–TEA mixture results in significant downfield shifts of C(6) and C(2) caused by deprotonation at N(1) and a smaller upfield shift at C(6) due to complexation of the rhodium to Ino.

When $[(PPh_3)_2(CO)Rh]^+$ is added to the Ino–EOA mixture, for which the equilibrium (eq 1) lies far to the right, a further downfield shift is observed for the C(2) resonance and a small upfield shift is observed for the C(6) resonance. It is interesting to note that the ^{13}C NMR spectrum of the Ino–EOA–Rh(I) mixture is essentially identical with that of the Ino–TEA–Rh(I) mixture. This implies that the extent of deprotonation is the same for both systems.

Guanosine. Basic Dimethyl Sulfoxide Solutions. The ^{13}C NMR chemical shift data for the Guo mixtures are presented in Table II, and the spectral shifts are illustrated in Figure 2.

Since the acidity of N(1)–H of Guo is less than that of Ino,[18] the acid–base equilibrium shown in eq 1 lies farther to the left for Guo than for Ino with both TEA and EOA. This is consistent with the noticeably smaller shifts observed for Guo than for Ino upon addition of EOA. The simultaneous addition of EOA and the rhodium cation to Guo causes downfield shifts in the C(2) and C(6) resonances. These shifts represent the combined effects of deprotonation and complexation. The simultaneous addition of TEA and the rhodium cation to Guo causes a downfield shift in the C(2) resonance while the C(6) resonance is essentially unaffected. At first glance this result might appear surprising; however, we have interpreted the lack of shift in the C(6) resonance as the result of deprotonation and complexation effects of about equal magnitudes but of opposite directions. This is consistent with the downfield shift of C(2) since complexation of the rhodium cation has little effect on the C(2) resonance whereas deprotonation shifts the C(2) resonance downfield.

In contrast to the case for the Ino systems, the Guo–TEA–Rh(I) and Guo–EOA–Rh(I) mixtures do not give the same ^{13}C chemical shifts for the nucleoside resonances. The spectral data suggest that different degrees of deprotonation of the nucleoside exist for the two mixtures. This would be the case if coordination of the rhodium electrophile at O(6) of Guo does not sufficiently increase the acidity of N(1)–H to allow for complete deprotonation. The relative extent of deprotonation can be readily seen by comparing the spectral data of the Guo–EOA–Rh(I) and Guo–TEA–Rh(I) mixtures with those of the Guo–Rh(I) mixture (Figure 2).

6-Mercaptoguanosine. Neutral Dimethyl Sulfoxide Solutions. The ^{13}C NMR chemical shift data for the s^6Guo mixture are presented in Table III, and the spectral changes are illustrated in Figure 3.

The addition of $[(PPh_3)_2(CO)Rh]^+$ to a neutral $(CD_3)_2SO$ solution of s^6Guo causes a large upfield shift of the C(6) resonance (3.6 ppm) and smaller upfield shifts for the C(4)

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Table IV. ^{13}C NMR Chemical Shifts for Various Mixtures of 8-Mercaptoguanosine, Triethylamine, Ethanolamine, and the Carbonylbis(triphenylphosphine)rhodium(I) Cation[a]

8-mercaptoguanosine solns	δ[b]									
	base C atoms					ribose C atoms				
	C(6)	C(2)	C(4)	C(8)	C(5)	C(1')	C(4')	C(2')	C(3')	C(5')
s^{8}Guo	153.4	150.8	149.4	165.6	104.0	88.6	85.0	70.4	70.2	62.2
s^{8}Guo-TEA	154.1	152.2	149.4	165.3	104.2	88.6	85.1	70.6	70.3	62.3
s^{8}Guo-EOA	157.6	155.6	150.2	163.7	109.4	88.6	85.3	71.1	70.7	62.2
s^{8}Guo-TEA-Rh(I)	152.2	150.7	150.2	161.7	110.1	88.6	84.3	70.9	70.4	62.9
s^{8}Guo-EOA-Rh(I)	152.5	151.0	150.2	161.5	110.2	88.6	84.2	70.9	70.4	62.2
s^{8}Guo-Rh(I) (1:1)	153.6	151.0	149.1	157.3	105.3	89.3	85.4	70.3	70.3	62.1
s^{8}Guo-Rh(I) (1:2)	153.6	150.9	149.1	157.0	105.1	89.2	85.3	70.3	70.3	62.0

[a] Abbreviations: s^{8}Guo = 8-mercaptoguanosine; TEA = triethylamine; EOA = ethanolamine; Rh(I) = $[(PPh_3)_2(CO)Rh]^+$. Concentrations (in $(CD_3)_2SO$): s^{8}Guo, 0.15 M; TEA, 0.40 M; EOA, 0.80 M; Rh(I), 0.15 M. [b] Chemical shifts are measured from $(CH_3)_4Si$ internal standard at 22.51 MHz.

and C(5) resonances (2.0 and 0.9 ppm). Downfield shifts are observed for the C(8) and C(2) resonances (2.0 and 0.5 ppm). These results are similar to those observed by Lippard and co-workers[19] during their investigations of the interactions of mercury(II) chloride with s^{6}Guo. The relatively large upfield shift of the C(6) resonance is indicative of binding of the Rh(I) electrophile at S(6). In addition, the ^1H NMR data for s^{6}Guo show the loss of the N(1)–H resonance upon addition of $[(PPh_3)_2(CO)Rh]^+$. The loss of the N(1)–H resonance is consistent with exchange broadening caused by complexation at the sulfur.[19,20]

Ligand exchange in the s^{6}Guo–Rh(I) mixture is implied from comparing the $^{31}P\{^1H\}$ NMR spectrum of the Guo–Rh(I) mixture to that of the s^{6}Guo–Rh(I) mixture and by noting the temperature dependence of the phosphorus resonance of the triphenylphosphine ligand for the s^{6}Guo mixture. The Guo–Rh(I) $^{31}P\{^1H\}$ NMR spectrum shows the triphenylphosphine resonance as a well-resolved doublet centered at 30.53 ppm (J_{Rh-P} = 125.95 Hz). The $^{31}P\{^1H\}$ NMR spectrum of the s^{6}Guo–Rh(I) mixture contains a broad singlet at 35.37 ppm, suggesting that fast ligand exchange is occurring. This is supported by variable-temperature spectra (Figure 5), which show a narrowing of the triphenylphosphine peak with increasing temperature.

Basic Dimethyl Sulfoxide Solutions. The acidity of N(1)–H of s^{6}Guo is noticeably greater than that of Guo.[21] Therefore, the acid–base equilibrium (eq 1) lies farther to the right for the s^{6}Guo systems than for the Guo systems. The ^{13}C NMR resonances of s^{6}Guo (Table III) are essentially unperturbed by the addition of TEA. However, the addition of EOA results in large downfield shifts in the C(6) and C(2) resonances of S^{6}Guo, indicating that deprotonation occurs at N(1).

The addition of $[(PPh_3)_2(CO)Rh]^+$ to the s^{6}Guo–TEA mixture causes a small downfield shift in the C(6) resonance and a large downfield shift in the C(2) resonance. The small net shift of the C(6) resonance may be attributed to the opposing effects of coordination of the rhodium cation at S(6) and deprotonation at N(1). The addition of the rhodium electrophile to the s^{6}Guo–EOA mixture causes a downfield shift of 5.5 ppm of the C(2) resonance, suggesting that further deprotonation occurs at N(1) since C(2) is insensitive to complexation at S(6). An upfield shift of 3.0 ppm is observed for the C(6) resonance when the rhodium electrophile is added to the s^{6}Guo–EOA system. This upfield shift is evidence for coordination at S(6). The net shift of the C(6) resonance from s^{6}Guo to the s^{6}Guo–EOA–Rh(I) mixture is only 0.8 ppm downfield, clearly illustrating the cancellation of the effects of deprotonation by coordination of the rhodium electrophile at S(6).

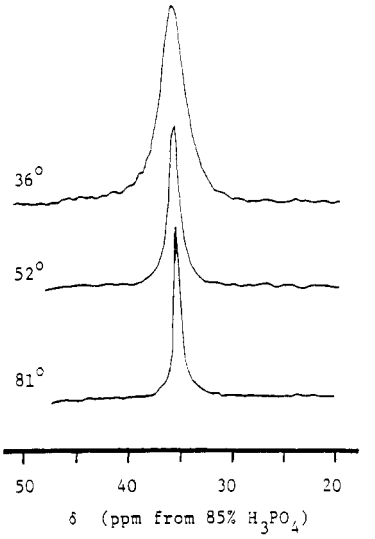

Figure 5. Temperature dependence of the $^{31}P\{^1H\}$ NMR triphenylphosphine resonance in a 1:1 mixture of $[(PPh_3)_2(CO)Rh]^+$ and 6-mercaptoguanosine in $(CD_3)_2SO$.

Deprotonation at N(1) is also evident from the comparison of spectral data (Figure 3) of the s^{6}Guo–Rh(I) mixture and of the s^{6}Guo–base–Rh(I) mixtures. These mixtures differ only by the presence of the base; therefore, the large downfield shifts in C(6) and C(2) resonances upon addition of the base illustrate the effects of deprotonation of N(1). Since the ^{13}C NMR spectra of the s^{6}Guo–TEA–Rh(I) and the s^{6}Guo–EOA–Rh(I) systems are almost identical, the extent of deprotonation is apparently the same for both systems. The $^{31}P\{^1H\}$ NMR spectra of the s^{6}Guo–TEA–Rh(I) and s^{6}Guo–EOA–Rh(I) mixtures show broad singlets for the triphenylphosphine resonances at 22.72 and 22.19 ppm, respectively. These spectra suggest that the rapid ligand exchange observed for the s^{6}Guo–Rh(I) system also occurs in the presence of base.

8-Mercaptoguanosine. Neutral Dimethyl Sulfoxide Solutions. The ^{13}C NMR chemical shift data for the s^{8}Guo mixtures are given in Table IV, and the spectral changes are illustrated in Figure 4. The addition of $[(PPh_3)_2(CO)Rh]^+$ to a neutral $(CD_3)_2SO$ solution of s^{8}Guo results in a large upfield shift (8.3 ppm) in the C(8) resonance. The other resonances undergo no significant shifts, implying that S(8) is the site of coordination of the rhodium electrophile. The ^1H NMR data reveal the loss of the N(7)–H resonance but the retention of the N(1)–H resonance. These observations are consistent with exchange broadening at N(7) due to coordination at S(8).[19,20]

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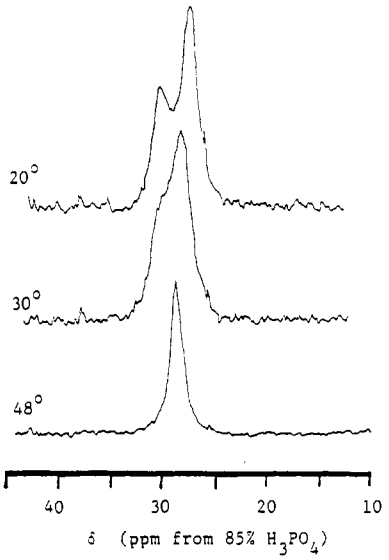

Figure 6. Temperature dependence of the $^{31}P\{^1H\}$ NMR triphenylphosphine resonances in a 1:1 mixture of $[(PPh_3)_2(CO)Rh]^+$ and 8-mercaptoguanosine in $(CD_3)_2SO$.

Since the O(6) site of s^{8}Guo is available for complexation and has been shown to be a binding site for $[(PPh_3)_2(CO)Rh]^+$ in Guo,[6] it was thought that a 2:1 mixture of $[(PPh_3)_2(CO)Rh]^+$ to s^{8}Guo might result in interaction of the rhodium electrophile at both O(6) and S(8). However, the ^{13}C NMR spectrum of the 2:1 mixture is the same as that of the 1:1 mixture with the exception of an additional small upfield shift (0.3 ppm) of the C(8) resonance. The occurrence of rapid ligand exchange for both mixtures is evident from the two broad peaks that occur in the $^{31}P\{^1H\}$ NMR spectrum taken at room temperature for each mixture. The broad peaks collapse into a single peak with decreasing line width as the temperature is increased above room temperature, as illustrated in Figure 6 for the 1:1 mixture.

Basic Dimethyl Sulfoxide Solutions. The ^{13}C NMR spectrum of the s^{8}Guo–TEA mixture shows that the addition of TEA to s^{8}Guo in $(CD_3)_2SO$ results in virtually no perturbation of the s^{8}Guo carbon resonances. However, the addition of EOA to the s^{8}Guo solution causes large downfield shifts in the C(6), C(2), and C(5) resonances (4.2, 4.8, and 5.4 ppm, respectively), indicating that deprotonation occurs at N(1).

The addition of $[(PPh_3)_2(CO)Rh]^+$ to the s^{8}Guo–TEA mixture results in a large downfield shift (5.9 ppm) in the C(5) resonance and a smaller upfield shift (3.6 ppm) in the C(8) resonance with the other carbon resonances relatively unaffected. These results indicate that the addition of $[(PPh_3)_2(CO)Rh]^+$ to the s^{8}Guo–TEA mixture promotes deprotonation at N(7). The net upfield shift of 3.6 ppm for the C(8) resonances is the result of the superimposition of the unusually large upfield shift (ca. 8 ppm) due to complexation of the rhodium cation at S(8) and the smaller downfield shift (ca. 4 ppm) due to deprotonation at N(7).

The addition of $[(PPh_3)_2(CO)Rh]^+$ to the s^{8}Guo–EOA mixture, for which deprotonation occurs at N(1), leads to the same ^{13}C and $^{31}P\{^1H\}$ NMR spectra as the s^{8}Guo–TEA–Rh(I) mixture, for which deprotonation occurs at N(7). Reasoning similar to that used to analyze the s^{8}Guo–TEA–Rh(I) mixture suggests that deprotonation occurs at N(7) and coordination at S(8) for the s^{8}Guo–EOA–Rh(I) mixture. However, coordination of the rhodium cation at N(1) or O(6) after removal of N(1)–H is a possibility that must be considered. After addition of the rhodium cation to the s^{8}Guo–EOA mixture, the C(6) and C(2) resonances are close to their positions in s^{8}Guo. Since the C(2) resonance of guanosine characteristically exhibits a large downfield shift upon deprotonation at N(1), even when complexation occurs at N(1) or O(6),[7] deprotonation at N(1) is unlikely. In addition, the significant upfield shift of the C(8) resonance is not consistent with binding at N(1).

Although the spectral data for the s^{8}Guo–EOA mixture indicates deprotonation at N(1), the complexation of $[(PPh_3)_2(CO)Rh]^+$ at S(8) apparently increases the acidity of N(7)–H such that deprotonation at N(7) instead of N(1) is now favored. Spectral data illustrated in Figure 4 for the s^{8}Guo–Rh(I) mixture and s^{8}Guo–base–Rh(I) mixtures support the conclusion that deprotonation occurs at N(7) since large downfield shifts in the C(8) and C(5) resonances occur upon addition of base.

Interestingly, the $^{31}P\{^1H\}$ NMR spectra show the triphenylphosphine resonances for the basic solutions of s^{8}Guo and $[(PPh_3)_2(CO)Rh]^+$ as well-defined doublets centered at 29.05 ppm (J_{Rh-P} = 136.72 Hz) for both bases. This indicates that the type of exchange processes discussed previously for other thioguanosine systems are not occurring for the s^{8}Guo–base–Rh(I) systems where complexation occurs at S(8) and deprotonation occurs at N(7).

Concluding Remarks. The interaction of $[(PPh_3)_2(CO)Rh]^+$ at O(6) of Guo and Ino has been shown to increase the acidity of N(1)–H. These results are consistent with earlier studies[7] involving other metals that interact at O(6) under basic conditions. In the case of Ino, TEA and EOA produce similar degrees of deprotonation at N(1) in the presence of the rhodium cation. In contrast to their behaviors with Ino, TEA and EOA do not produce similar degrees of deprotonation of N(1)–H for Guo in the presence of the rhodium cation. This is not surprising in view of the fact that N(1)–H of Guo is less acidic than N(1)–H of Ino; thus, the interaction of the rhodium cation at O(6) of Guo is apparently not sufficient to cause complete deprotonation of N(1)–H in the presence of TEA. It has been assumed that, when the rhodium cation coordinates to O(6) of Guo and Ino in neutral $(CD_3)_2SO$ solution, it remains coordinated at O(6) upon deprotonation at N(1). Although this may be a reasonable conclusion from steric considerations, the data do not rule out the possibility that the electrophile will shift from O(6) to N(1) upon deprotonation.

Evidence has been presented that indicates that coordination of the rhodium cation to the thiolated nucleosides, s^{6}Guo and s^{8}Guo, increases the acidity of N(1)–H of s^{6}Guo and N(7)–H of s^{8}Guo. The changes in acidity result from coordination of the rhodium to the sulfur in each case. In the case of s^{8}Guo, N(1)–H is the favored site of deprotonation in the absence of the rhodium cation; however, upon coordination of the cation to S(8), N(7)–H becomes the favored site of deprotonation. For the thiolated nucleosides similar degrees of deprotonation occur with TEA and EOA in the presence of the rhodium cation.

It is interesting that the rhodium cation does not coordinate to O(6) in s^{8}Guo when the rhodium species is in excess. The preference for S(8) over O(6) is consistent with the idea that rhodium(I) is a "class b" metal and prefers the softer sulfur atom.

These investigations involving $[(PPh_3)_2(CO)Rh]^+$ suggest that unequivocal assignment of binding sites in purine nucleosides in basic solution may not be made simply on the basis of ^{13}C NMR chemical shift data since deprotonation can create an additional binding site near the original site of metal interaction. In view of the fact that deprotonation and complexation can create opposing effects on the carbon resonances of the nucleosides, a negligible net shift is sometimes observed for resonances of carbon atoms near the site of complexation. Therefore, caution should be exercised when binding sites are assigned on the basis of ^{13}C chemical shift data for nucleosides under basic conditions.

The study has provided additional evidence that metal interactions at O(6) of Guo and related nucleosides can alter the hydrogen-bonding capabilities of the nucleosides and thereby contribute to base mispairing in DNA molecules. The results that indicate enhanced deprotonation of the thionucleosides due to metal complexation are also of interest since studies have shown that selected metal complexes of thiopurines are more active against certain kinds of tumors than the thiopurines alone.[14]

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Registry No. **1** (R = ribose, X = NH_2), 118-00-3; **1** (R = ribose, X = H), 58-63-9; **2**, 85-31-4; **3**, 26001-38-7; $GuoRh^I$, 85798-23-8; $InoRh^I$, 85798-24-9; s^6GuoRh^I, 85735-72-4; s^8GuoRh^I, 85735-73-5; TEA, 121-44-8; EOA, 141-43-5.

Contribution from the Department of Chemistry, Nuclear Research Center "Demokritos", Aghia Paraskevi Attikis, Athens, Greece, and Laboratory of Inorganic Chemistry, University of Athens, Navarinou 13A, Athens, Greece

Reductive Desulfurization of Mercaptoacetic Acid

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Mercaptoacetate in large excess and in the pH range between 3 and 10 forms with V^{III} intensely yellow complexes, in two successive stages, the second of which was followed by stopped-flow methods at pH 3.6 and found to be first order in vanadium(III) and in mercaptoacetate. The activation parameters are $\Delta H^* = 57.4$ kJ mol^{-1} and $\Delta S^* = -0.8$ J mol^{-1} K^{-1}. Under similar conditions V^{II} undergoes also a two-stage complexation reaction but reacts further, giving succinic acid and hydrogen sulfide. This redox reaction is first order in vanadium(II) and in mercaptoacetate and at pH 9.6 has $\Delta H^* = 50.2$ kJ mol^{-1} and $\Delta S^* = -70$ J mol^{-1} K^{-1}. The second-order rate constant correlates with the titration curve of mercaptoacetic acid. The results are compared to analogous results for cysteine and are interpreted on the basis of a two-step chelate ring formation involving the S^- group. The activation of the V^{II} and V^{III} reactions is partly attributed to proton dissociation of the organic moiety and partly to a strain in the ring, which when combined with electron transfer leads to a break of the C–S bond. The V^{II}–mercaptoacetate system can be regarded as an electron-storing device, which can be activated by changing the proton environment.

Introduction

The reductive cleavage of the carbon–halogen bond has been investigated by many authors.[1] Most of the work was done with Cr^{2+} (aq) as the reductant. The examples of using other reductive metal ions are few.[1] Few also are the examples of breaking other carbon single bonds. Among them one could mention the presumed breaking of the carbon to nitrogen bond in the Cu^I-induced decomposition of diazonium salts[2] and the breaking of the carbon to metal bonds in transalkylation reactions.[3]

Partial reductive desulfurization of compounds associated with coal or petroleum such as dibenzothiophene can be achieved[4] with use of solvated electrons or electrolysis.

Here we report on the cleavage of the carbon to sulfur bond of mercaptoacetic acid, induced by vanadium(II), and discuss briefly some general biological implications.

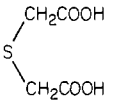
The system is studied in the pH range from ~3 to 10. In this range relatively little is known about mechanisms of redox processes.

The product of the redox process is V^{III} complexed with mercaptoacetate. The same complex is also formed when V^{III} is mixed with mercaptoacetate. The kinetics of this complexation reaction were also investigated.

Experimental Section

Mercaptoacetic acid was purchased from Riedel-de Haen A.G. The main impurities are dithiodiglycolic acid ($HOOCCH_2SSCH_2COOH$), dithioglycolide

and thiodiglycolic acid



Purification was done by fractional distillation under vacuum.[5] The solutions had to be freshly prepared and deaerated.

Determination of the concentration of mercaptoacetic acid (mac[6]) is based on the reaction[5]

$$2HSCH_2COOH + I_2 \rightarrow HOOCCH_2SSCH_2COOH + 2HI$$

Iodine is produced from IO_3^- and I^-.

Vanadium(II) was prepared electrolytically on a mercury cathode.[7] All experiments were performed under an inert atmosphere.

The kinetics were followed with a stopped-flow apparatus (Applied Photophysics), and spectra were recorded with a Cary 14.

Hydrogen sulfide was trapped in a double trap containing a saturated lead acetate solution, by purging the reaction mixture with argon. The reaction mixture was then acidified and the purging continued until all H_2S was obtained in the form of PbS.

Succinic acid was determined in the products by acidifying and passing the reaction mixture through an ion-exchange resin (Dowex 50W-X2) in order to remove vanadium. Alcohol was then added, and the precipitated sodium chloride was filtered. Then the organic acids were esterified with use of BF_3 solution in ether. The esters were separated by gas chromatography (column Apiezon L on Chromosorb G), and the ester of succinic acid was identified by mass spectroscopy.

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