relaxation rate of Dy^{3+} ions in DyI_3 is not understood at present. In any event, both types of samples showed identical and correct X-ray powder diffraction patterns. The absence of detectable amounts of moisture or coordinated H_2O was established from infrared spectra. Furthermore, low-temperature ac susceptibility measurements showed that the various DyI_3 samples were paramagnetic down to 4.2 K ($\theta = -5 \pm 1$ K).

The lack of slow paramagnetic relaxation in the three compounds $DyCl_3$, $DyBr_3$, and DyI_3 at a temperature as low as 4.2 K is unusual for insulating compounds.[33] This can be tentatively explained in terms of the high point symmetry occurring at the Dy site in these crystals, which should give rise to a **g** tensor that is not largely anisotropic.[37] Hence, the relaxation rate is faster than in most compounds that present a large **g** anisotropy.[33,37]

The different relaxation behaviors observed in the two nominally identical samples of DyI_3 can conceivably be assigned to undetectable lattice defects. These may occur in a larger proportion in the dehydrated samples; the consequent lowering of local symmetry could then be responsible for an anisotropic **g** tensor and hence longer relaxation times. Alternatively, undetected paramagnetic impurities might contaminate the DyI_3 samples prepared by direct synthesis from the elements and thus be responsible for faster relaxation rate in this sample.[38]

Summary and Conclusions

The existence of the Dy^{2+} ($4f^{10}$) valence configuration of dysprosium in the solid dihalides (Dy_5Cl_{11}, $DyBr_2$, and DyI_2) is unambiguously demonstrated from the isomer shift measured ^{161}Dy Mössbauer spectroscopy. The occurrence of unresolved quadrupole interactions and the absence of paramagnetic relaxation effects confirm this assignment. Unfortunately, none of these phases could be obtained entirely pure. The mixed-valence state of Dy in Dy_5Cl_{11} and the unavoidable presence of impurities whose Debye temperatures differ widely from that of the Dy^{2+} sites complicate the interpretation of the temperature-dependent Mössbauer data. This difference of lattice vibration modes for the different sites is responsible for the unusual increase of the spectral contribution of the Dy^{3+} sites as the temperature is increased from 4.2 to 300 K.

Investigations are also reported for the dysprosium trihalides and oxyhalides. The Mössbauer study of trihalides is restricted to isomer shift measurements because of the occurrence of paramagnetic relaxation effects in the whole range of temperatures from 4.2 to 300 K.

The oxyhalides have been shown to order antiferromagnetically at temperatures below 10 K. The low-temperature (4.2 K) hyperfine parameters (hyperfine field and electric field gradient) are interpreted in terms of a crystal field Hamiltonian consistent with optical and magnetic data. Paramagnetic hyperfine structures persist at temperatures well above T_N, as is common for insulating dysprosium compounds.

Acknowledgment. The collaboration of J. Rebizant, Euratom, Karlsruhe, West Germany, in performing the X-ray diffraction measurements and analysis is gratefully acknowledged. We thank Professor Bärnighausen and W. Kuhn, University of Karlsruhe, for providing samples of DyI_2 and DyOI for comparison with our own preparations. We thank Professors Bärnighausen, Gütlich, Link, and Ensling for communicating unpublished results on $DyCl_2$ and $DyBr_2$ which are comparable to our own.

Registry No. ^{161}Dy, 13967-68-5; Dy_5Cl_{11}, 60616-39-9; $DyBr_2$, 83229-05-4; DyI_2, 36377-94-3; DyOCl, 14986-29-9; DyOBr, 15923-91-8; DyOI, 50652-54-5; $DyCl_3$, 10025-74-8; $DyBr_3$, 14456-48-5; DyI_3, 15474-63-2.

(37) See, e.g.: Altschuler, S. A.; Kozyrev, B. M. In "Electronic Paramagnetic Resonance in Compounds of Transition Elements"; Wiley: New York, 1974; pp 403-4.
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Interactions of the Carbonylbis(triphenylphosphine)rhodium(I) Cation with Purine–Pyrimidine Base Pairs As Studied by Carbon-13, Phosphorus-31, and Proton NMR

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The interactions of the electrophile $[(PPh_3)_2(CO)Rh]^+$ (denoted as Rh(I)) with purine–pyrimidine base pairs have been investigated with use of ^{13}C, ^1H, and $^{31}P\{^1H\}$ NMR analyses. Nucleoside stability orders for the electrophile have been found to be cytidine (N(3)) > guanosine (O(6)) > adenosine (N(1)) >> thymidine and uridine. Since coordination of Rh(I) to guanosine (Guo) occurs at O(6), the relative order of stability of the Guo and adenosine (Ado) interactions is somewhat surprising. The hydrogen bonding between Guo and cytidine (Cyd) has been shown to be strong enough to prevent the total breakdown of the Guo–Cyd base pair upon addition of Rh(I) to 1:1 nucleoside mixtures. In 1:1:1 Guo–Cyd–Rh(I) mixtures a complex set of equilibria exists involving Guo–Rh(I), Cyd–Rh(I), and Guo–Cyd interactions. As Cyd is added to the 1:1:1 Guo–Cyd–Rh(I) mixture, the Cyd–Rh(I) interaction increases and the Guo–Rh(I) interaction decreases, with the Guo being more extensively involved in hydrogen bonding with the excess Guo. In 1:1:2 mixtures of Guo–Cyd–Rh(I), the Guo–Rh(I) and Cyd–Rh(I) interactions are present in equal amounts. When triethylamine is added to 1:1:1 Guo–Cyd–Rh(I) mixtures, deprotonation of Guo occurs and the equilibria shift away from the Cyd–Rh(I) interaction in favor of the Rh(I)–guanosinate interaction. The effects of Rh(I) on purine–pyrimidine base pairs are discussed in terms of the possible relevance to antitumor behavior of metal complexes through hydrogen bond disruption and base mispairing in DNA.

Introduction

We have recently shown that the electrophile $[(PPh_3)_2(CO)Rh]^+$ will interact with purine nucleoside derivatives in $(CD_3)_2SO$ to form complexes of the type $[Rh(PPh_3)_2(CO)(L)]PF_6$ (L = purine nucleoside).[1] One observation of this previous study that is of particular interest is the binding of the Rh(I) cation to O(6) of guanosine (Guo) in neutral $(CD_3)_2SO$ solution. We have also shown that coordination

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of the Rh(I) cation to Guo at O(6) increases the acidity of N(1)–H.[2] This observation is consistent with those made when other metal ions interact with 6-oxopurines in basic $(CD_3)_2SO$ solution.[3]

It has been postulated that the antitumor behavior of some substances might be related to their ability to interact at O(6) of the Guo constituent of DNA.[4-8] Changes in the nature of the hydrogen bonding between guanosine and cytidine (Cyd) in DNA as a result of interactions at O(6) of Guo could lead to base mispairing. Therefore, interactions that might alter hydrogen bonding between base pairs in DNA are of particular interest.

In view of the changes in acidity of N(1)–H observed when some 6-oxopurine derivatives are complexed by $[(PPh_3)_2(CO)Rh]^+$, and the possible role of hydrogen bond disruption in base mispairing, we have undertaken this study to investigate the interaction of $[(PPh_3)_2(CO)Rh]^+$ with pyrimidine nucleosides and purine–pyrimidine base pairs found in DNA and RNA.

Experimental Section

Materials. Guanosine, adenosine, cytidine, uridine, and thymidine were obtained from Sigma Chemical Corp. and were used without further purification. The cation $[(PPh_3)_2(CO)Rh]^+$ 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 placed in solution with the bases. $[Rh(PPh_3)_2(CO)_3]PF_6$ was prepared according to the method of Schrock and Osborn.[9]

Methods. The ^{13}C, ^1H, and $^{31}P\{^1H\}$ NMR spectra were obtained on a JEOL FX90Q Fourier transform spectrometer. The ^{13}C NMR spectra were measured at 22.51 MHz, with $(CH_3)_4Si$ as the internal standard. The ^1H NMR spectra were obtained at 89.55 MHz with $(CH_3)_4Si$ as the internal standard, and the $^{31}P\{^1H\}$ NMR spectra were measured at 36.19 MHz with 85% H_3PO_4 as the external standard. All spectra were obtained at ambient temperatures. Elemental microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

Sample Preparation. The $[Rh(PPh_3)_2(CO)(Cyd)]PF_6$ complex was prepared by the addition of an aquimolar amount of cytidine suspended in 25 mL of ethanol to 0.500 g of $[Rh(PPh_3)_2(CO)_3]PF_6$ in 5 mL of dichloromethane. The mixture was stirred for 7 h. After the ligand had completely dissolved and no further evolution of CO was observed, the solution was taken to dryness on a rotary evaporator, yielding a yellow solid. After the yellow solid was dissolved in dichloromethane, the volume of the solution was reduced. The product that precipitated upon addition of ether was recrystallized from dichloromethane in a yield of 82%. Anal. Calcd for $C_{46}H_{44}F_6N_3O_6P_2Rh$: C, 52.94: H, 4.25; N, 4.03. Found: C, 52.80; H, 4.43; N, 3.88.

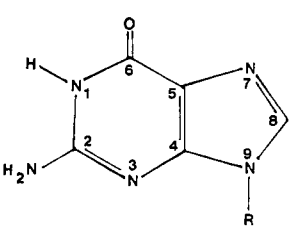
NMR solutions for the mixture studies were prepared by dissolving the appropriate quantities of $[Rh(PPh_3)_2(CO)_3]PF_6$ and nucleoside in 2.5 mL of $(CD_3)_2SO$ to give the desired rhodium-to-nucleoside ratios. The nucleoside concentration in each solution was approximately 0.15 M. For basic solutions, approximately 125 μL of triethylamine was added to the solution.

The ^{13}C NMR peak assignments were made according to the literature.[10]

Results and Discussion

Carbon and proton NMR chemical shift studies can be very useful in elucidating the nature and sites of interaction of metal species with nucleosides. Several reports[1-3,11-13] have shown that, in neutral $(CD_3)_2SO$ solutions of nucleosides, the resonances of carbon atoms adjacent to metal binding sites exhibit much greater changes in chemical shift than more remote carbon atoms, though some care must be taken when the results are interpreted.[14,15] Similar effects are observed for proton chemical shifts, but these effects are smaller and less definitive.[16]

Complexes of the cation $[(PPh_3)_2(CO)Rh]^+$ with Guo (**1**, R = ribose) and Ado (**2**, R = ribose) have been isolated and characterized with use of NMR chemical shift analyses.



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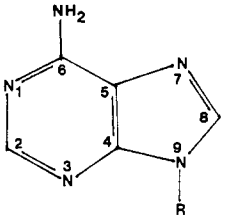

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Variations in proton chemical shifts have been shown to be quite useful in monitoring the extent of hydrogen bonding between various purine–pyrimidine base pairs.[17-20] We have found that the changes in proton chemical shifts due to variations in the extent of hydrogen bonding are not accompanied by significant changes in carbon chemical shifts. Therefore, ^{13}C chemical shift studies are not useful for monitoring hydrogen bonding in base pairs.

The ^{13}C NMR chemical shift data on 1:1 mixtures of Guo and Ado with the cation $[(PPh_3)_2(CO)Rh]^+$ (later referred to as Rh(I)) show that the spectra of the 1:1 mixtures are essentially the same as those observed for $(CD_3)_2SO$ solutions of the isolated complexes.[1] These results indicate that the interactions occurring in the 1:1 mixtures are similar to those observed for solutions of the isolated complexes.

The ^{13}C NMR spectrum of a 2:1 Guo–Rh(I) mixture in $(CD_3)_2SO$ contains a set of resonances characteristic of the complex $[Rh(PPh_3)_2(CO)(Guo)]PF_6$ and a set of resonances identical with those of the free nucleoside. These results suggest that rapid ligand exchange involving Guo is not occurring; however, the excess ligand apparently does cause slight changes in the metal–nucleoside interactions since the $^{31}P\{^1H\}$ NMR spectra exhibit small differences in the rhodium–phosphorus coupling constant for the 2:1 and 1:1 Guo–Rh(I) mixtures. These perturbations are apparently too weak to manifest themselves in the ^{13}C NMR spectra. While the exact nature of the solution phenomena caused by excess nucleoside cannot be deduced from the available data, the $^{31}P\{^1H\}$ NMR chemical shift data are reproducible and can be used as a diagnostic tool.

Pyrimidine Complexes. We have investigated the interactions of the cation Rh(I) with the following pyrimidine derivatives: cytidine (**3**; R = ribose), thymidine (**4**: X = CH_3,

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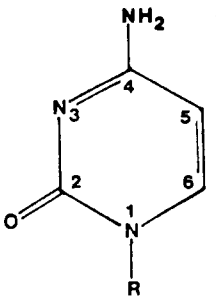

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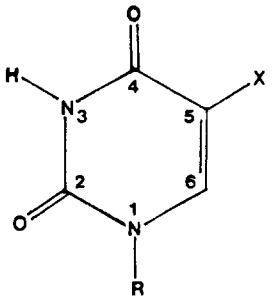


4

R = ribose) and uridine (**4**; X = H, R = ribose). The results of the present study are in agreement with previous studies[14,21-23] which show that cytidine (Cyd) is generally more reactive toward transition-metal complexation in neutral solution than thymidine (Thd) or uridine (Urd). The complex $[Rh(PPh_3)_2(CO)(Cyd)]PF_6$ can be isolated and characterized, but analogous complexes of Thd and Urd cannot be isolated. Furthermore, the ^{13}C and ^1H NMR spectra of $(CD_3)_2SO$ solutions of $[(PPh_3)_2(CO)Rh]^+$ and Thd or Urd do not show any significant perturbations of the nucleoside resonances. The $^{31}P\{^1H\}$ NMR spectra of the Thd and Urd solutions containing Rh(I) show a doublet with a chemical shift characteristic of the $[Rh(PPh_3)_2(CO)((CD_3)_2SO)]^+$ species.[1] The Urd solution, however, does show a second very weak doublet which may be indicative of the presence of a very small amount of a Urd–Rh(I) complex.

Equimolar mixtures of Cyd and Rh(I) in $(CD_3)_2SO$ do exhibit the same ^{13}C and ^1H NMR spectra as solutions of $[Rh(PPh_3)_2(CO)(Cyd)]PF_6$. Slight differences, which remain unexplained, do however occur in the J_{Rh-P} values taken from the $^{31}P\{^1H\}$ NMR spectra of the two solutions. The ^{13}C and $^{31}P\{^1H\}$ data on solutions of Rh(I) and the pyrimidine nucleosides are summarized in Tables I and II. Comparison of the chemical shifts of the carbon resonances of free Cyd and complexed Cyd suggests that Rh(I) coordinates to Cyd at N(3). Significant upfield shifts in the C(2) and C(4) resonances (4.3 and 2.1 ppm, respectively) and negligible shifts (<1 ppm) in the other carbon resonances have led to this conclusion. These results are in agreement with previous ^{13}C NMR studies involving the coordination of transition metals to N(3) of cytidine.[12-14] The ^1H NMR spectra yield little information since H(6) and NH_2 resonances are obscured by the intense proton resonances of the triphenylphosphine group.

A mixture containing a 2:1 ratio of Cyd to Rh(I) yields a ^{13}C NMR spectrum containing two sets of nucleoside resonances. One set belongs to free Cyd and the other to complexed Cyd. This result demonstrates the lack of rapid exchange of the nucleoside. The excess Cyd apparently does have a slight effect on the Cyd–Rh(I) interaction since J_{Rh-P} is slightly different from the value obtained for 1:1 Cyd–Rh(I) mixtures (Table II).

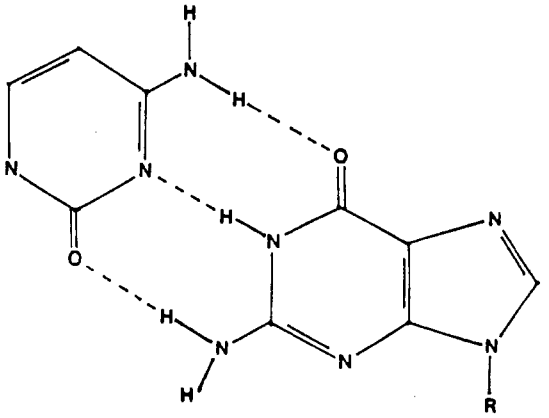
Adenosine–Thymidine Mixtures. The hydrogen bonding of the Ado–Thd base pair is minimized in $(CD_3)_2SO$. Proton NMR resonances (Table III) of Thd are not significantly shifted by the addition of Ado; however, in the presence of Thd, the NH_2 resonance of Ado is shifted downfield by 0.46 ppm for 1:1 mixtures. The carbon NMR resonances of Ado and Thd are relatively unchanged by the addition of Ado to Thd.

The ^{13}C NMR spectrum of the 1:1:1 mixture of Ado–Thd–Rh(I) contains two sets of resonances. One set corresponds to those resonances observed for Ado–Rh(I) mixtures, while the other set corresponds to resonances of uncomplexed Thd. Unfortunately, the intense triphenylphosphine resonance in the ^1H NMR spectrum masks the NH_2 resonance of Ado, precluding any assessment of changes in hydrogen bonding involving Ado and Thd. The $^{31}P\{^1H\}$ NMR spectrum of a 1:1:1 mixture of Ado–Thd–Rh(I) contains one doublet, which exhibits a chemical shift and coupling constant characteristic of the Ado–Rh(I) interaction observed in 1:1 Ado–Rh(I) mixtures.

Adenosine–Uridine Mixtures. The hydrogen bonding between Ado and Urd is also minimized in $(CD_3)_2SO$.[17,20] The NH_2 ^1H NMR resonance of Ado is shifted 0.47 ppm downfield for the 1:1 Ado–Urd mixture, while the N(3)–H resonance of Urd is shifted 0.11 ppm downfield (Table III). As expected, the carbon NMR resonances of Ado and Urd are relatively unchanged by forming 1:1 mixtures.

Two sets of resonances are observed in the ^{13}C NMR spectrum of the 1:1:1 mixture of Ado–Urd–Rh(I). One set indicates the presence of the Ado–Rh(I) interaction and the other set indicates the presence of free Urd. The ^1H NMR spectrum of the 1:1:1 mixture shows the N(3)–H resonance of Urd at 11.36 ppm, intermediate between that of free Urd and that of Urd hydrogen bonded to Ado in 1:1 Ado–Urd mixtures (Table III). These results suggest that some hydrogen-bonding interaction exists even in the presence of the rhodium interaction. The $^{31}P\{^1H\}$ NMR spectrum contains one doublet (Table II) with a chemical shift and coupling constant characteristic of the Ado–Rh(I) interaction.[1]

Guanosine–Cytidine Mixtures. The hydrogen-bonding interactions between Guo and Cyd



are much more pronounced in $(CD_3)_2SO$ than those of the Ado–Thd or the Ado–Urd system.[17,19,20] The proton resonances of N(1)–H and NH_2 of Guo shift downfield by 0.86 and 0.40 ppm, respectively, while the NH_2 resonance of Cyd shifts downfield by 0.23 ppm when a 1:1 mixture is formed with nucleoside concentrations of 0.15 M. Even for the strongly hydrogen-bonded Guo–Cyd pair, the positions of the carbon resonances of Guo and Cyd are virtually unchanged from those of the individual nucleosides in $(CD_3)_2SO$.

A 1:1:1 mixture of Guo–Cyd–Rh(I) could lead to several interactions since it has been demonstrated that the electrophile $[(PPh_3)_2(CO)Rh]^+$ has the ability to coordinate to both Guo and Cyd. The ^{13}C NMR spectrum of the 1:1:1 Guo–Cyd–Rh(I) mixture consists of three sets of resonances. One set corresponds to the resonances of free Guo, one to free Cyd, and one to complexed Cyd. Even though the ^{13}C NMR spectrum does not show it, some Guo–Rh(I) interaction is suggested by the $^{31}P\{^1H\}$ NMR spectrum, which contains two doublets (Figure 1a). The more intense doublet is characteristic of the Cyd–Rh(I) interaction, and the less intense doublet is characteristic of the Guo–Rh(I) interaction. It is possible that the amount of Guo complexed to Rh(I) is too small to give rise to a detectable set of carbon resonances for the complexed Guo. The Guo–Rh(I) interaction apparently

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Table I. ^{13}C NMR Chemical Shifts for Mixtures of Pyrimidine Nucleosides and the Carbonylbis(triphenylphosphine)rhodium(I) Cation[a]

	δ[b]								
	base				ribose				
soln composition	C(4)	C(2)	C(6)	C(5)	C(1')	C(4')	C(3')	C(2')	C(5')
Cyd	165.5	155.4	141.5	93.8	89.2	84.0	73.9	69.4	60.6
$[Rh(PPh_3)_2(CO)(Cyd)]PF_6$	163.4	151.2	141.0	93.0	89.8	83.0	73.6	67.4	58.9
1:1 Cyd-Rh(I)	163.4	151.2	141.0	92.8	89.7	82.9	73.6	67.4	58.9
Thd	163.6	150.3	136.0	109.3	83.6	87.1	70.3	*c*	61.2
1:1 Thd-Rh(I)	163.7	150.4	136.0	109.3	83.8	87.3	70.4	*c*	61.3
Urd	163.1	150.7	140.7	101.8	87.7	84.8	73.5	69.8	60.9
1:1 Urd-Rh(I)	163.1	150.7	140.6	101.7	87.7	84.8	73.5	69.8	60.8

[a] Abbreviations: Cyd = cytidine, Thd = thymidine, Urd = uridine, Rh(I) = $[(PPh_3)_2(CO)Rh]^+$. Concentration ratios are based on 0.15 M solutions in $(CD_3)_2SO$. [b] Chemical shifts are measured from $(CH_3)_4Si$ internal standard at 22.51 MHz. [c] The C(2') resonance of thymidine expected around 40.0 ppm is obscured by the intense $(CD_3)_2SO$ multiplet, which extends from 42.3 to 39.4 ppm.

Table II. ^{31}P NMR Chemical Shifts for Mixtures of Pyrimidine Nucleosides and the Carbonylbis(triphenylphosphine)rhodium(I) Cation[a]

soln composition[a]	δ[b]	J_{Rh-P}, Hz	soln composition[a]	δ[b]	J_{Rh-P}, Hz
$[Rh(PPh_3)_2(CO)(Cyd)]PF_6$	32.35	131.84	1:1 Thd-Rh(I)	29.79	112.26
1:1 Cyd-Rh(I)	32.28	126.95	1:1 Urd-Rh(I)	28.92	136.72
2:1 Cyd-Rh(I)	32.48	131.84		33.23[c]	126.95
1:2 Cyd-Rh(I)	32.55	126.95			

[a] Abbreviations: Cyd = cytidine, Thd = thymidine, Urd = uridine, Rh(I) = $[(PPh_3)_2(CO)Rh]^+$. Concentration ratios are based on 0.15 M solutions in $(CD_3)_2SO$. [b] Chemical shifts are measured from 85% H_3PO_4 external standard at 36.19 MHz. [c] Very low intensity.

Table III. ^1H NMR Chemical Shifts for Mixtures of Adenosine, Thymidine, Uridine, and the Carbonylbis(triphenylphosphine)rhodium(I) Cation[a]

	δ[b]								
	adenosine			thymidine			uridine		
soln composition	H(8)	H(2)	NH_2	N(3)-H	H(6)	CH_3	N(3)-H	H(6)	H(5)
nucleoside	7.91	7.71	6.90	11.27	7.69	1.77	11.31	7.90	5.79
1:1 Ado-Thd	8.36	8.15	7.36	11.32	7.71	1.78			
1:1:1 Ado-Thd-Rh(I)	8.37	*c*	*c*	11.33	*c*	1.81			
1:1 Ado-Urd	8.36	8.16	7.37				11.42	7.89	5.84
1:1:1 Ado-Urd-Rh(I)	8.36	7.80	*c*				11.36	7.90	5.75

[a] Abbreviations: Ado = adenosine, Urd = uridine, Thd = thymidine, Rh(I) = $[(PPh_3)_2(CO)Rh]^+$. Concentration ratios are based on 0.15 M solutions in $(CD_3)_2SO$. [b] Chemical shifts are measured from $(CH_3)_4Si$ internal standard at 89.55 MHz. [c] Masked by triphenylphosphine resonances.

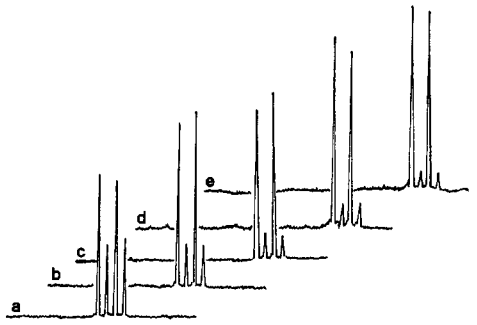

Figure 1. Traces of $^{31}P\{^1H\}$ NMR spectra of various mixtures of guanosine–cytidine–$[(PPh_3)_2(CO)Rh]^+$ in the following concentration ratios: (a) 1:1:1; (b) 1:1.5:1; (c) 1:2:1; (d) 1:2.5:1; (e) 1:2.75:1.

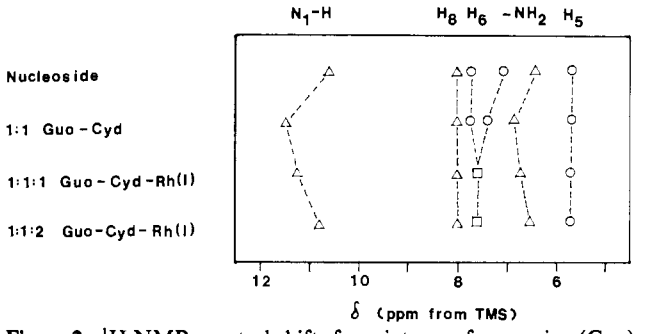

Figure 2. ^1H NMR spectral shifts for mixtures of guanosine (Guo), cytidine (Cyd), and $[(PPh_3)_2(CO)Rh]^+$: (△) Guo; (○) Cyd; (□) resonances masked by triphenylphosphine resonances.

is detectable in the $^{31}P\{^1H\}$ NMR spectrum as a result of the greater sensitivity of the phosphorus nucleus.

Since uncomplexed Guo and uncomplexed Cyd are found in the 1:1:1 Guo–Cyd–Rh(I) mixture, it is expected that some degree of hydrogen bonding between the two nucleosides should still exist. This is supported by the ^1H NMR data (Figure 2), which show that the chemical shifts of those protons expected to be involved in hydrogen bonding are intermediate between those observed for the separate non-hydrogen-bonded nucleosides and the hydrogen-bonded nucleosides in equimolar mixtures.

The preference of $[(PPh_3)_2(CO)Rh]^+$ for Cyd is not surprising since it has been shown that Cyd often has a larger formation constant with transition metals.[14,17,22] The strength of the Guo–Cyd hydrogen bonding is such that the Rh(I) does not displace all of the Cyd from the Guo–Cyd base pair. The behavior of the 1:1:1 Guo–Cyd–Rh(I) mixture is probably best illustrated by eq 1. The Rh(I) displaces some of the Cyd from

$$\text{Guo}{\equiv}\text{Cyd} + \text{Rh(I)} \rightarrow \text{Cyd—Rh(I)} + \text{Guo—Rh(I)} + \text{Guo}{\equiv}\text{Cyd} \quad (1)$$

the Guo–Cyd base pair, leading to the predominant Cyd–Rh(I) interaction with some residual Guo–Rh(I) interaction. The remaining Cyd is still hydrogen bonded to Guo. This analysis accounts for resonances in the ^{13}C NMR spectrum attributable to complexed Cyd, free Cyd, and free Guo (^{13}C NMR does not distinguish between hydrogen-bonded and non-hydrogen-bonded Guo and Cyd).

Table IV. ^1H NMR Chemical Shifts and $^{31}P\{^1H\}$ NMR Intensity Ratios for Various Mixtures of Guanosine, Cytidine, and the Carbonylbis(triphenylphosphine)rhodium(I) Cation[a]

	^1H NMR, δ[b]						$^{31}P\{^1H\}$ NMR intensity ratios I(Cyd-Rh(I)): I(Guo-Rh(I))
	guanosine			cytidine			
soln composition	N(1)-H	H(8)	NH_2	H(6)	NH_2	H(5)	
nucleoside	10.61	7.93	6.44	7.86	7.18	5.72	
1:1 Guo-Cyd	11.47	7.96	6.84	7.87	7.41	5.78	
Guo-Cyd-Rh(I)							
1:1:2	10.81	7.96	6.56			5.78	
1:1:1	11.23	7.95	6.74			5.74	1.78
1:1.25:1	11.33	8.02	6.81			5.74	2.44
1:1.5:1	11.48	8.02	6.88			5.84	4.20
1:1.75:1	11.60	8.02	6.94			5.84	4.54
1:2:1	11.74	8.03	7.07	c	c	5.85	6.11
1:2.25:1	11.89	8.03	7.11			5.90	6.95
1:2.5:1	11.99	8.03	7.14			5.89	7.31
1:2.75:1	12.05	8.03	7.22			5.89	10.34
1:3.5:1	12.29	8.03	7.31			5.90	16.55

[a] Abbreviations: Guo = guanosine, Cyd = cytidine, Rh(I) = $[(PPh_3)_2(CO)Rh]^+$. Concentration ratios are based on 0.15 M solutions in $(CD_3)_2SO$. [b] Chemical shifts are measured from $(CH_3)_4Si$ internal standard at 89.55 MHz. [c] These resonances are masked by the triphenylphosphine resonances.

Since $(CD_3)_2SO$ is known to minimize hydrogen bonding between nucleic bases, the Guo–Cyd mixture can be interpreted as an equilibrium between the hydrogen-bonded pairs of nucleosides and the separate solvated nucleosides. As more Cyd is added to the 1:1 Guo–Cyd mixture, the lifetime of the non-hydrogen-bonded Guo is decreased, shifting the N(1)–H and NH_2 resonances of Guo farther downfield. When Guo is in excess, the Guo N(1)–H and NH_2 resonances are intermediate between their values for the free ligand and those for the 1:1 Guo–Cyd mixture. In the presence of excess Guo, the NH_2 resonance of Cyd occurs much farther downfield than the corresponding resonance of the 1:1 Guo–Cyd mixture.[19,20] Variations in the proton resonances of Guo and Cyd allow one to monitor shifts in the hydrogen-bonding equilibria between the nucleosides.

Table IV contains ^1H NMR data of Guo–Cyd–Rh(I) mixtures with various amounts of Cyd. These data reveal that as more Cyd is added, the chemical shift of N(1)–H of Cyd is increased and the lifetime of the non-hydrogen-bonded Guo is decreased. The intensity ratios of the phosphorus resonances (Table IV) indicate that there is also an increase in the amount of Cyd–Rh(I) interaction as the amount of Cyd is increased. This phenomenon can be illustrated by a shift in the equilibrium illustrated by eq 2. The increasing intensity of the

$$\text{Guo–Rh(I)} + \text{Cyd} \rightleftarrows \text{Cyd–Rh(I)} + \text{Guo} \qquad (2)$$

phosphorus doublet due to Cyd–Rh(I) interaction and the simultaneous disappearance of the Guo–Rh(I) doublet are illustrated in Figure 1. The $^{31}P\{^1H\}$ NMR data in Table IV for Guo–Cyd–Rh(I) ratios between 1:1:1 and 1:2.75:1 were used to obtain an approximate equilibrium constant of 4.0 ± 0.7 for the equilibrium illustrated in eq 2.

The ^{13}C NMR spectrum of a 1:1:2 mixture of Guo–Cyd–Rh(I) exhibits two sets of resonances, one characteristic of the Cyd–Rh(I) interaction and one characteristic of the Guo–Rh(I) interaction. The excess Rh(I) has now displaced essentially all the Cyd from the Guo–Cyd hydrogen-bonded base pair. Once the available Cyd has been complexed by the Rh(I), the excess Rh(I) may now interact with the non-hydrogen-bonded Guo. This interpretation is supported by the ^1H NMR data (Figure 2 and Table IV), which show that the N(1)–H and NH_2 resonances of Guo have essentially returned to their free or complexed ligand positions, indicating that Guo is no longer involved in hydrogen bonding with Cyd.

The $^{31}P\{^1H\}$ NMR spectrum of the 1:1:2 Guo–Cyd–Rh(I) mixture contains two doublets with equal intensities. One doublet is characteristic of the Cyd–Rh(I) interaction and one is characteristic of the Guo–Rh(I) interaction.

The preference of $[(PPh_3)_2(CO)Rh]^+$ for Cyd over Guo is further established by the addition of Cyd to a $(CD_3)_2SO$ solution of $[Rh(PPh_3)_2(CO)(Guo)]PF_6$. After addition of an equimolar amount of Cyd, ^{13}C, ^1H and $^{31}P\{^1H\}$ NMR spectra of the solution are identical with those obtained on 1:1:1 mixtures of Guo–Cyd–Rh(I). The Guo is mostly displaced from $[Rh(PPh_3)_2(CO)(Guo)]PF_6$ by the Cyd; however, according to the ^1H NMR data, some of the Cyd becomes hydrogen bonded to the Guo, indicating the strength of the hydrogen bonding between Guo and Cyd. Previous investigations[2] have shown that the interaction of Rh(I) at O(6) of Guo leads to deprotonation at N(1) when triethylamine (TEA) is added to $(CD_3)_2SO$ solutions of Guo and Rh(I). The most acidic proton on Cyd occurs on the ribose moiety and has a pK_a much greater than that of N(1)–H of Guo;[24] therefore, the interaction of Rh(I) with 1:1 mixtures of Guo–Cyd in the presence of TEA is expected to facilitate the deprotonation of Guo and have little effect on Cyd. The ^{13}C NMR spectrum of 1:1:1:xs (xs = excess) mixtures of Guo–Cyd–Rh(I)–TEA exhibits four sets of resonances. These resonances correspond to those of the Guo–Rh(I)–TEA and Cyd–Rh(I) interactions and the uncomplexed Guo and Cyd ligands.

The $^{31}P\{^1H\}$ NMR spectrum of the 1:1:1:xs mixture of Guo–Cyd–Rh(I)–TEA exhibits three doublets. Two doublets correspond to the Guo–Rh(I)–TEA and Cyd–Rh(I) interactions indicated by the ^{13}C NMR data. The third doublet suggests the presence of the Guo–Rh(I) interaction, which was not indicated by the ^{13}C NMR data. This apparent inconsistency between the $^{31}P\{^1H\}$ and ^{13}C NMR data was encountered with Guo–Cyd–Rh(I) mixtures and is likely a result of differences in sensitivity of the two NMR techniques. Our experience has been that the nucleoside carbon resonances of the Guo–Rh(I) mixtures are much less intense than those of the free nucleoside when concentrations and instrument conditions are the same. Therefore, it is not unreasonable that secondary Guo–Rh(I) interactions occurring in the presence of other nucleosides and other interactions might not be manifested in the ^{13}C NMR spectrum, yet they may lead to observable phosphorus resonances.

The ^{13}C and $^{31}P\{^1H\}$ NMR spectra of the Guo–Cyd–Rh(I)–TEA mixtures demonstrate that the addition of TEA to Guo–Cyd–Rh(I) mixtures creates a complex set of equilibria in which there appears to be a shift away from complexation

(24) Christensen, J. J.; Rytting, J. H.; Izatt, R. M. *J. Phys. Chem.* **1967**, *71*, 2700.

of the Rh(I) to Cyd in favor of the complexation to Guo and/or the guanosinate ion. These results are not too surprising since the guanosinate ion would be expected to compete more favorably with Cyd for the electrophile than would the neutral guanosine.

Guanosine–Adenosine Mixtures. Relatively small downfield shifts of about 0.10 ppm in the ^1H resonances of N(1)–H and $-NH_2$ of Guo demonstrate that the hydrogen-bonding interactions between Guo and Ado in 1:1 mixtures in $(CD_3)_2SO$ are weak.[17,20]

The ^{13}C NMR spectrum of the 1:1:1 mixtures of Guo–Ado–Rh(I) contains two sets of resonances, one indicative of Guo–Rh(I) interactions and the other characteristic of uncomplexed Ado. The $^{31}P\{^1H\}$ NMR spectrum contains only one doublet. The chemical shift and coupling constant are consistent with the Guo–Rh(I) interaction.

The ^{13}C NMR spectrum of the 1:1:2 Guo–Ado–Rh(I) mixture contains a set of resonances consistent with the presence of Guo–Rh(I) interactions and a set consistent with the presence of Ado–Rh(I) interactions. The $^{31}P\{^1H\}$ NMR spectrum contains only one doublet; however, since the Guo–Rh(I) and Ado–Rh(I) interactions lead to approximately the same phosphorus chemical shifts and coupling constants,[1] it is probable that doublets arising from the two interactions are superimposed.

Cytidine–Adenosine Mixtures. The NMR results for 1:1 Cyd–Ado mixtures show little evidence for the existence of hydrogen-bonded pairs in $(CD_3)_2SO$.[17,20] The ^1H NMR resonance of NH_2 of Cyd does not shift upon mixing the two nucleosides, although our results do show a small downfield shift for NH_2 of Ado. The carbon NMR resonances of the mixture have essentially the same values as those of the separate nucleosides.

The ^{13}C NMR spectrum of the 1:1:1 Cyd-Ado-Rh(I) mixture is indicative of Cyd–Rh(I) interactions and uncomplexed Ado. The $^{31}P\{^1H\}$ NMR spectrum contains a well-defined doublet with parameters characteristic of the Cyd–Rh(I) interaction. The 1:1:2 Cyd–Ado–Rh(I) mixture gives rise to a ^{13}C NMR spectrum that is consistent with the occurrence of both the Cyd–Rh(I) and the Ado–Rh(I) interactions. This interpretation is supported by the appearance in the $^{31}P\{^1H\}$ NMR spectrum of two doublets that are characteristic of the two interactions.

Concluding Remarks. Nucleoside stability orders have been determined for $[(PPh_3)_2(CO)Rh]^+$. The electrophile prefers Cyd over the other nucleosides, as evidenced by the gradual displacement of Guo by the addition of Cyd to solutions of $[Rh(PPh_3)_2(CO)(Guo)]PF_6$. It appears, however, that the hydrogen bonding between Guo and Cyd is strong enough to prevent the breakdown of all of the Guo–Cyd base pairs when Rh(I) is added in equimolar quantities to Cyd–Guo mixtures. Once enough Rh(I) has been added to completely destroy the Guo–Cyd hydrogen bonding by tying up the Cyd, further addition of the Rh(I) leads to the formation of the Guo complex.

One surprising result from this study is the order of stability of Rh(I) with Guo and Ado. Since Rh(I) interacts with Guo at O(6), undoubtedly a weakly basic site, the interaction at N(1) of adenosine would seem to be favored on the basis of the relative basicities of the two sites. However, Ado does not displace Guo from $[Rh(PPh_3)_2(CO)(Guo)]^+$; furthermore, the Guo–Rh(I) interaction occurs exclusively when Rh(I) is added to a Guo–Ado mixture. The Ado–Rh(I) interaction occurs only after enough Rh(I) is added to consume all of the Guo. This order of preference is usually observed for most metals;[22] however, in those cases the binding to Guo occurs at the more basic N(7) site. Unfortunately, it cannot be deduced from the available data whether the interaction of Rh(I) with N(1) of Ado is weaker than expected or whether the interaction at O(6) of Guo is stronger than expected.

The nucleoside stability order for Rh(I) may be summarized as Cyd (N(3)) > Guo (O(6)) > Ado (N(1)) >> Thd, Urd. This is typical of interactions in neutral solution between transition metals and nucleosides, except for the rather surprising position of the Guo O(6) interaction. However, in basic $(CD_3)_2SO$ solution where deprotonation reactions analogous to those occurring in aqueous solution may take place, the ^{13}C NMR results indicate an increase in the interaction with the guanosinate ion. The coordination of Rh(I) at O(6) of Guo promotes the loss of N(1)–H and consequently shifts the Guo–Cyd–Rh(I) equilibria in favor of the interaction of Rh(I) with the quanosinate anion. These results confirm the fact that the interaction of a transition metal at O(6) of Guo and the subsequent deprotonation at N(1) can significantly change the preference of the metal for nucleic acid constituents. In addition, ^1H NMR studies indicate that the coordination of the metal to a member of a nucleic base pair can result in significant disruptions in the hydrogen bonding between the bases. These phenomena are pertinent to understanding the interactions of transition metals with the guanine component of DNA and the manner in which these interactions might alter biological functions.

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Registry No. $[Rh(PPh_3)_2(CO)(Cyd)]PF_6$, 86610-15-3; $[Rh(PPh_3)_2(CO)(Guo)]PF_6$, 84049-95-6; $[Rh(PPh_3)_2(CO)(Ado)]PF_6$, 84049-99-0; $[Rh(PPh_3)_2(CO)((CH_3)_2SO)]^+$, 84190-74-9; $[Rh(PPh_3)_2(CO)]^+$, 72186-51-7; $[Rh(PPh_3)_2(CO)_3]PF_6$, 53433-43-5; Ado, 58-61-7; Thd, 50-89-5; Urd, 58-96-8; Guo, 118-00-3; Cyd, 65-46-3; Et_3N, 121-44-8.

Supplementary Material Available: ^{13}C shifts of Guo, Cyd, and Rh(I) mixtures (Table V), ^{13}C shifts for Ado, Thd, and Rh(I) mixtures (Table VI), ^{13}C shifts for Ado, Urd, and Rh(I) mixtures (Table VII), ^{13}C shifts for Guo, Ado, and Rh(I) mixtures (Table VIII), ^{13}C shifts for Ado, Cyd, and Rh(I) mixtures (Table IX), ^{31}P shifts and coupling constants for Guo, Cyd, Ado, and Rh(I) mixtures (Table X), and ^{31}P shifts and coupling constants for purine and pyrimidine nucleosides with Rh(I) (Table XI) (8 pages). Ordering information is given on any current masthead page.