The biphasic kinetics observed in the reaction of $Ni(tmc)^+$ with the benzyl and substituted benzyl complexes indicate that the one-electron reduction of eq 6 is followed by further reduction of the long-lived $RCo(dmgBF_2)_2A^-$ by $Ni(tmc)^+$, eq 9. Such a

$$RCo(dmgBF_2)_2A^- + Ni(tmc)^+ \rightarrow RCo(dmgBF_2)_2A^{2-} + Ni(tmc)^{2+} \quad k_2 \quad (9)$$

chemistry is reasonable on several grounds. Our results showed already that $4\text{-}BrC_6H_4CH_2Co(dmgBF_2)_2A^-$ has a relatively long lifetime; it was prepared electrolytically in solution prior to being cooled to 100 K for the ESR experiment. Also, the reduction potential of a number of $RCo(dmgBF_2)_2^{-/2-}$ couples (R = alkyl) in dmf have values around -1 V vs SCE.[16] We expect that the benzyl derivatives should be even easier to reduce, which makes reaction 9 thermodynamically favorable ($E_{1/2}(Ni(tmc)^{2+/+}) = -1.10$ V vs SCE).

The longer lifetime of $RCo(dmgBF_2)_2A^-$ for R = benzyl relative to R = alkyl can be easily rationalized. One decomposition mode, eq 3b, is eliminated by the lack of a β-hydrogen, and the hydrolysis, eq 3a, is severely inhibited by the ability of the benzyl group to delocalize electron density efficiently. The α-carbon in the reduced complex is thus less carbanionic, and solvolysis is slower than in the reduced alkyl complexes. The same reactivity pattern is observed in organometallic complexes in "normal" oxidation states. The hydrolysis of the parent organocobalt(III) complexes, $RCo(dmgBF_2)_2H_2O$, is too slow to be observed for any of the organic groups, but the more reactive organochromium(III)[38] and organonickel(II)[32b] complexes hydrolyze more readily when R is alkyl than when it is benzyl.

A different trend is observed in homolytic cleavages of metal-carbon bonds. As expected, the release of the benzyl radicals is faster than the release of primary alkyls and comparable to that of secondary alkyls.

Surprisingly, the nucleophilic attack by water on one-electron-oxidized organocobaloximes, $RCo(dmgH)_2H_2O^+$, is faster for R = benzyl than for the primary alkyls,[39,40] although one would expect the opposite on the basis of the above charge delocalization argument. In this case, it is possible that a homolytic path contributes to the decomposition of $RCo(dmgH)_2H_2O^+$, as was observed for a number of other oxidized organometallic complexes.

Acknowledgment. This research was supported by the U.S. Department of Energy, Office of Basic Energy Sciences, Chemical Sciences Division, under Contract W-7405-Eng-82.

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Hydrogen Bonding between Guanosine 5'-Monophosphate and Coordinatively Saturated Cobalt(III) and Platinum(II) Ammine and Ethylenediamine Complex Cations

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Received November 19, 1990

The compounds $[Pt(NH_3)_4][5'\text{-}GMP]\cdot 5H_2O$, $[Pt(en)_2][5'\text{-}GMP]\cdot 4H_2O$, $[Co(NH_3)_6]_2[5'\text{-}GMP]_3\cdot 13H_2O$, and $[Co(en)_3]_2[5'\text{-}GMP]_3\cdot 14H_2O$, where en = 1,2-diaminoethane and 5'-GMP = guanosine 5'-monophosphate, have been synthesized and characterized. In addition to electrostatic interactions, hydrogen-bonding interactions between the N-H sites on the ligands and the 5'-GMP have been identified in all four solids by means of FT-IR spectroscopy. In $[Co(NH_3)_6]_2[5'\text{-}GMP]_3\cdot 13H_2O$ hydrogen bonding is occurring between the NH_3 donor and the N7 site of the guanine. In the other three compounds, both the N7 and O6 sites of the guanine act as hydrogen-bond-acceptor sites. Additional hydrogen bonding between the cation and the 5'-GMP phosphate is possible in all four compounds. This could be to the same cation as the guanine is binding or to a different cation. NMR studies show that cation-anion interactions, including hydrogen bonding, persist in solution for $[Pt(en)_2][5'\text{-}GMP]$ and $[Co(en)_3]_2[5'\text{-}GMP]_3$, even in very dilute solutions of the latter. Evidence comes from the concentration dependence of the $^3J_{Pt\text{-}H}$ coupling constant in $[Pt(en)_2][5'\text{-}GMP]$ and improved resolution of the CH_2 multiplet in $[Co(en)_3]_2[5'\text{-}GMP]_3$. 5'-GMP ($\beta$-D-) selectively precipitates $[\Lambda\text{-}(+)\text{-}Co(en)_3]^{3+}$ from racemic $[Co(en)_3]^{3+}$. Models show that the $[\Lambda\text{-}(+)\text{-}Co(en)_3]^{3+}$ enantiomer can hydrogen-bond much more effectively to the 5'-GMP than the $[\Delta\text{-}(-)\text{-}Co(en)_3]^{3+}$ enantiomer.

Introduction

Compound formation between transition-metal ions and nucleotides, including mononucleotides, oligonucleotides, and nucleic acids, has been known for many years.[1,2] When the nucleotide contains guanine as the base, the transition metal typically binds covalently to the N7 atom of the guanine.[1-3] In many compounds, hydrogen bonding between a ligand on the metal and the nucleotide provides an important secondary binding site. This hydrogen bonding can occur with a site on the nucleobase, with the phosphate, or with both.[1,2,4]

In the case of Pt(II)[5-9] and Co(III)[10] ammine complexes, hydrogen bonding of the ammine ligand to the nucleotide has been found to have an important influence on the biological structure and reactivity of the nucleotide or nucleic acid. For example, the antitumor drug *cis*-diamminedichloroplatinum(II) and its analogues exhibit higher drug activity when they are able to hydrogen-bond to the nucleic acid in addition to the primary Pt-nucleobase bond.[11] With nucleic acids, the principal hydrogen-

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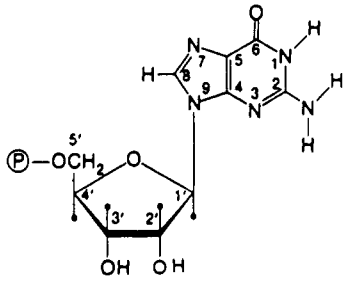
0020-1669/91/1330-3414$02.50/0

bonding interaction is between a Pt–ammine N–H and a phosphate of the nucleic acid.[8,9] With 2'-deoxyguanosine 5'-monophosphate, 5'-dGMP, evidence from UV resonance Raman studies has been found for hydrogen bonding between the Pt–ammine and the carbonyl O6 of the 5'-dGMP; a similar interaction was found in a Ni–aqua compound.[12] $[Co(NH_3)_6]^{3+}$ and $[Ru(NH_3)_6]^{3+}$, ions that stabilize the Z form of DNA,[13] bind to guanine-containing oligonucleotides via electrostatic interactions with the phosphates and hydrogen bonding to the guanine bases.[10,14] In these systems, a study of the hydrogen-bonding interactions is complicated by the metal–guanine covalent binding and by the complexity of the oligonucleotides.

The use of coordinatively saturated metal cationic complexes that are inert to substitution can lead to the formation of outer-sphere complexes with nucleotides and allows the study of only electrostatic and hydrogen-bonding effects. The observation of hydrogen bonding for such compounds in the solid state might be anticipated, but its persistence in solution in the absence of metal–nucleotide covalent bonding is likely to be highly system-specific. Cini et al.[15] have reported one such system in which NMR relaxation data and molecular mechanics calculations were used to infer cation–anion hydrogen bonding in a solution of $[Cr(H_2O)_6]^{3+}$ and $HIMP^-$ ions, the interaction sites being the phosphate and the N7 and O6 of the inosine. On the other hand, as a result of its different structure and protonation, H_2AMP only interacts via its phosphate.

We have used the coordinatively saturated, diamagnetic, inert complex cations $[Pt(NH_3)_4]^{2+}$, $[Pt(en)_2]^{2+}$, $[Co(NH_3)_6]^{3+}$, and $[Co(en)_3]^{3+}$ with the dianion of guanosine 5'-monophosphate, 5'-GMP (I). Hydrogen-bonding interactions between the aromatic portion of 5'-GMP and the amine ligands have been observed for all of the solid compounds. The interaction sites depend upon the exact nature of the metal cation. ^1H NMR spectra show that ion-pair formation occurs in solution, with indications that hydrogen bonding persists in $[Pt(en)_2][5'\text{-GMP}]$ and $[Co(en)_3]_2[5'\text{-GMP}]_3$.



5'-GMP (I)

Experimental Procedures

Materials. $Na_2(5'\text{-GMP})\cdot 3.5H_2O$ and $H_2(5'\text{-GMP})\cdot H_2O$ were purchased from Sigma Chemical Co. $Li_2(5'\text{-GMP})$ was prepared from $H_2(5'\text{-GMP})$ by published procedures.[16] $PtCl_2$, $[Pt(en)_2]Cl_2$, (2*R*,3*R*)-(+)- and (2*S*,3*S*)-(−)-tartaric acid, and D_2O (99.8 atom %) were purchased from Aldrich Chemical Co. and used as received. $[Co(NH_3)_6]Cl_3$,[17] $[Co(en)_3]Cl_3\cdot 3H_2O$,[18] [Δ-(+)-Co(en)$_3$]Cl(2*R*,3*R*-(+)-tartrate)($[\alpha]_D$: exp, +95 (*c* = 1.66); lit., +102), and [Δ-(−)-Co(en)$_3$]-Cl(2*S*,3*S*-(−)-tartrate)[19] ($[\alpha]_D$: exp, −91 (*c* = 1.01); lit., −103) were prepared by published procedures. [Λ-(+)-Co(en)$_3$]I_3 ($[\alpha]_D$ = +84 (*c* = 3.49) was a gift from Dr. Frank Walmsley. All other chemicals used were reagent grade.

Instrumental Methods. The concentrations of 5'-GMP in solutions were determined by UV spectroscopy: $\epsilon_{252} = 1.37 \times 10^4\ M^{-1}\ cm^{-1}$ at pH 7.[20] IR spectra were run on a Mattson Polaris Fourier transform infrared spectrometer as Nujol mulls (resolution of 2 cm^{-1}) and as KBr pellets. The data from the pellet spectra were not used due to suspected interaction of the KBr with the 5'-GMP.

^1H NMR spectra were run in D_2O on a General Electric QE-300 multinuclear spectrometer at 300.7 MHz. Inclusion of 0.2 mM EDTA in the samples narrowed the lines by the complexation of paramagnetic impurities but did not affect the chemical shift values. DSS or the tetramethylammonium ion (TMA^+; conversion factor to the DSS scale is 3.185 ppm) was used as an internal reference. When necessary, spectral deconvolution to determine the Pt–H coupling constant in $[Pt(en)_2]^{2+}$ complexes was done by using the GE Charm software. ^{31}P spectra were obtained on the same instrument at 121.7 MHz with concentrated phosphoric acid used as an external reference.

The optical rotations were measured with a Steeg & Reuter polarimeter using Na D radiation and either 1- or 2-dm cells. The specific rotation is reported as (actual rotation)/[(path length, dm)(concn., g/mL)]. The pH values of solutions were determined with a Fisher Accumet 825MP meter; pD values = meter reading + 0.4. For adjustment of the pD of solutions in NMR tubes, a long glass electrode (Ingold, 3-mm o.d.) was used.

Synthesis of Compounds. All syntheses were done in deionized, reverse-osmosis water. The pH of individual metal and 5'-GMP solutions was adjusted to 7–8 before reaction. The elemental analyses were performed by Midwest Microlab (Indianapolis, IN), and agreement between experimental and theoretical values is marginally satisfactory for some of the compounds. We believe this is the result of (1) the uptake of organic solvents (probably by 5'-GMP) that were impossible to remove under moderate drying conditions, (2) variation in the number of waters of hydration, which was quite sensitive to the synthetic procedure, and (3) possible difficulties in obtaining accurate experimental percentages due to the nature of the compounds. Ratilla et al. experienced similar analytical difficulties with some Pt(II) complexes.[21] Ligand dissociation, which might be suspected as a cause, has been ruled out on the basis of NMR chemical shift and integration values.

Cobalt analyses were done by an EDTA titration using pyridine for final adjustment of the pH to 5.5 and SNAZOXS as the indicator.[22] Prior to titration, $[Co(NH_3)_6]^{3+}$ complexes were decomposed by heating in a small amount of 6 M NaOH, and $[Co(en)_3]^{3+}$ complexes were heated strongly in air to convert the Co to its oxides. The decomposed samples were dissolved and neutralized with 12 M HCl.

$Pt(NH_3)_4Cl_2\cdot H_2O$. $PtCl_2$ (0.30 g) was dissolved in 20 mL of concentrated HCl with heating. The solution was diluted with 20 mL of deionized H_2O and filtered to remove a small amount of black residue. The solution was divided into two equal portions and used to prepare Magnus' salt, $[Pt(NH_3)_4][PtCl_4]$.[23] The remainder of the synthesis followed published procedures.[23]

$[Pt(NH_3)_4][5'\text{-GMP}]\cdot 5H_2O$. A 0.247-g sample of $Pt(NH_3)_4Cl_2\cdot H_2O$ dissolved in 8.0 mL of deionized H_2O was reacted with 7.5 mL of 0.093 M $Li_2(5'\text{-GMP})$. The pH of the final solution was 7.7. The solution was evaporated to 5 mL, and a white solid was precipitated by addition of 100 mL of methanol. The solid was filtered off, washed with methanol, and dried in a desiccator over P_4O_{10} (99% yield). The product gave a negative test for Cl^- with acidic $AgNO_3$ solution. Anal. Calcd (exp) for $C_{10}H_{34}N_9O_{13}PPt$: C, 16.80 (17.37); H, 4.80 (4.58); N, 17.65 (15.98). IR data (Nujol; 1800–400 cm^{-1}): 1680 (s), 1639 (s), 1605 (s), 1576 (m), 1533 (m), 1366 (s), 1346 (s, sh), 1314 (m, sh), 1208 (w), 1171 (w), 1108 (s, b), 1080 (s, b), 973 (s), 899 (w), 872 (w), 799 (m), 780 (m), 687 (w), 641 (w), 582 (vw), 538 (w), 515 (w, sh). ^1H NMR (0.089 M, D_2O, pD 8.1): δ 8.18 (s, H8), 5.90 (d, H1', $J_{1'-2'}$ = 5.7 Hz), 4.75 (m, H2'), 4.50 (m, H3'), 4.34 (m, H4'), 4.03 (m, H5', H5''). ^{31}P NMR: δ 4.42.

$[Pt(en)_2][5'\text{-GMP}]\cdot 4H_2O$. A 0.300-g quantity of $Pt(en)_2Cl_2$ was dissolved in 8.0 mL of a 0.097 M solution of $Li_2(5'\text{-GMP})$. The solution was evaporated to dryness under reduced pressure, the resulting solid dissolved in 5 mL of deionized H_2O, and the product precipitated by addition of 100 mL of methanol. The white solid was filtered off and washed with methanol. It was dried in a desiccator over Drierite or P_4O_{10} (90% yield). The product gave a negative test for Cl^-. Anal. Calcd (exp) for $C_{14}H_{36}N_9O_{12}PPt$: C, 22.46 (23.66); H, 4.85 (4.59); N, 16.85 (16.08).

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IR data (Nujol; 1800–400 cm^{-1}): 1679 (s), 1635 (s), 1606 (s), 1576 (m), 1532 (m), 1365 (s, sh), 1306 (m), 1262 (w), 1170 (m), 1107 (s, sh), 1077 (s, b), 1058 (s, b), 972 (s), 900 (w), 863 (vw), 818 (sh), 798 (m), 781 (m), 739 (m, sh), 685 (w), 644 (vw), 583 (w), 532 (w), 517 (w). ^1H NMR (0.091 M in D_2O, 0.2 mM EDTA, pD 8.1; reference DSS): δ 8.19 (s, H8), 5.91 (d, H1′, $J_{1'-2'}$ = 5.4 Hz), 4.77 (m, H2′), 4.50 (m, H3′), 4.34 (m, H4′), 4.05 (m, H5′, H5″), 2.63 (s, en). ^{31}P: δ 4.41.

$[Co(NH_3)_6]_2[5'\text{-GMP}]_3\cdot 13H_2O$. A 2.0-mL portion of 0.20 M $[Co(NH_3)_6]Cl_3$ (pH 8) was added slowly to 6.0 mL of 0.10 M $Na_2(5'\text{-GMP})$. An orange precipitate began to form with the addition of the first drop of $[Co(NH_3)_6]Cl_3$ and continued to increase in amount with the addition of the remainder of the Co complex. The mixture was cooled in a refrigerator and suction-filtered; the orange solid was washed with small portions of cold deionized H_2O and dried in a desiccator (54% yield). Anal. Calcd (exp) for $C_{30}H_{98}N_{27}O_{37}P_3Co_2$: C, 21.97 (22.30); H, 6.02 (5.69); N, 23.06 (22.36); Co, 7.19 (7.97). IR data (Nujol; 1800–400 cm^{-1}): 1716 (s), 1688 (s), 1637 (s), 1607 (s), 1577 (m), 1531 (m), 1366 (s), 1342 (s, sh), 1311 (m, sh), 1209 (w), 1171 (m), 1136 (sh), 1066 (s, b), 970 (s), 891 (w), 872 (w), 818 (sh), 798 (m), 777 (m), 734 (m, sh), 682 (w), 637 (w), 563 (w), 528 (w), 500 (w), 445 (vw). ^1H NMR ([5′-GMP] = 0.015 M, D_2O, pD 7.9; reference DSS): δ 8.22 (s, H8), 5.94 (d, H1′, $J_{1'-2'}$ = 6.6 Hz), H2′ obscured by the HOD line, 4.49 (m, H3′), 4.32 (m, H4′), 4.00 (m, H5′, H5″).

$[Co(en)_3]_2[5'\text{-GMP}]_3\cdot 14H_2O$. A 5.0-mL portion of 0.20 M $[Co(en)_3]Cl_3$ (pH adjusted to 8.1 with NaOH) was added to 10.0 mL of 0.10 M $Na_2(5'\text{-GMP})$ (pH 7.8). The resulting orange solution was stored in the refrigerator for 2 days, during which time an orange precipitated formed. The solid was separated from the mixture by suction filtration, washed with a small amount of cold, deionized H_2O, and dried in a desiccator. Anal. Calcd (exp) for $C_{42}H_{112}N_{27}O_{38}P_3Co_2$: C, 27.80 (28.50); H, 6.22 (5.29); N, 20.85 (19.30). IR data (Nujol; 1800–400 cm^{-1}): 1691 (s), 1650 (sh), 1601 (s), 1580 (s, sh), 1531 (m), 1342 (s, sh), 1309 (m), 1260 (w), 1208 (vw), 1169 (m), 1111 (sh), 1077 (s, b), 1057 (s, sh), 1015 (s, sh), 969 (s), 861 (vw), 898 (w), 822 (sh), 797 (m), 779 (m), 690 (w), 638 (vw), 563 (w), 533 (w), 502 (w), 451 (vw). ^1H NMR ([5′-GMP] = 0.017 M, D_2O, pD 8.4, 0.2 mM EDTA; reference DSS): δ 8.21 (s, H8), 5.92 (d, H1′, $J_{1'-2'}$ = 6.0 Hz), H2′ obscured by HOD, 4.49 (m, H3′), 4.32 (m, H4′), 4.00 (m, H5′, H5″), 2.79 (m, en). ^{31}P NMR: δ 4.63.

$[Co(en)_3]_2[5'\text{-GMP}]_3\cdot 11H_2O\cdot C_3H_6O\cdot 0.5\ C_2H_5OH$. This compound was prepared as above except that, after filtration of the orange product, it was washed with ethanol and then acetone. Anal. Calcd (exp) for $C_{46}H_{115}N_{27}O_{36.5}P_3Co_2$: C, 30.00 (30.46); H, 6.29 (5.47); N, 20.54 (19.95); Co, 6.40 (6.28). Drying of this compound at 80 °C for 2 h did not remove all of the organic solvate.

Results

Only one 5′-GMP compound was formed with each of the complex cations employed, regardless of the stoichiometry of the reaction mixture. With $[Co(NH_3)_6]^{3+}$, Co:5′-GMP mole ratios of 1:6, 2:3, and 1:1 were used. Extensive Co and 5′-GMP analyses of the products confirmed the 2:3 stoichiometry (uncertainty 10%) in all cases. For the Pt compounds, starting Pt:5′-GMP mole ratios of 1:1 and 1:2 were used, with only the 1:1 compound formed. Intergration of the ^1H NMR 5′-GMP H8 and en signals of solutions agreed closely with the theoretical values. Some uncertainty in the number of waters of hydration in the compounds results from uncertainty in the elemental analyses and from the sensitivity of the compounds to isolation and drying procedures. The number of water molecules appears to be dependent on the number of 5′-GMP anions, with four to five H_2O per 5′-GMP found irrespective of the cation.

$Li_2(5'\text{-GMP})$ was used as the starting nucleotide for the Pt compounds rather than the Na salt because the Pt–5′-GMP compounds were very soluble in water as was the alkali-metal chloride byproduct. Precipitation of the Pt nucleotides with methanol allowed them to be separated from the soluble LiCl.

FT-IR Spectra. The spectra of the solids run as Nujol mulls were used to detect hydrogen-bonding interactions involving the 5′-GMP ring system and structural changes in the ribose moiety. The spectra in the 1800–400-cm^{-1} range are dominated by the absorptions of the 5′-GMP moiety; the cation absorption bands are buried beneath the broad and more intense nucleotide bands. The spectra of $[Pt(NH_3)_4][5'\text{-GMP}]\cdot 5H_2O$, $[Pt(en)_2][5'\text{-GMP}]\cdot 4H_2O$, $[Co(NH_3)_6]_2[5'\text{-GMP}]_3\cdot 13H_2O$, $[Co(en)_3]_2[5'\text{-GMP}]_3\cdot 14H_2O$, and $Na_2(5'\text{-GMP})\cdot 3.5H_2O$ are shown in Figure 1. A striking feature of the spectra is the close similarity of all

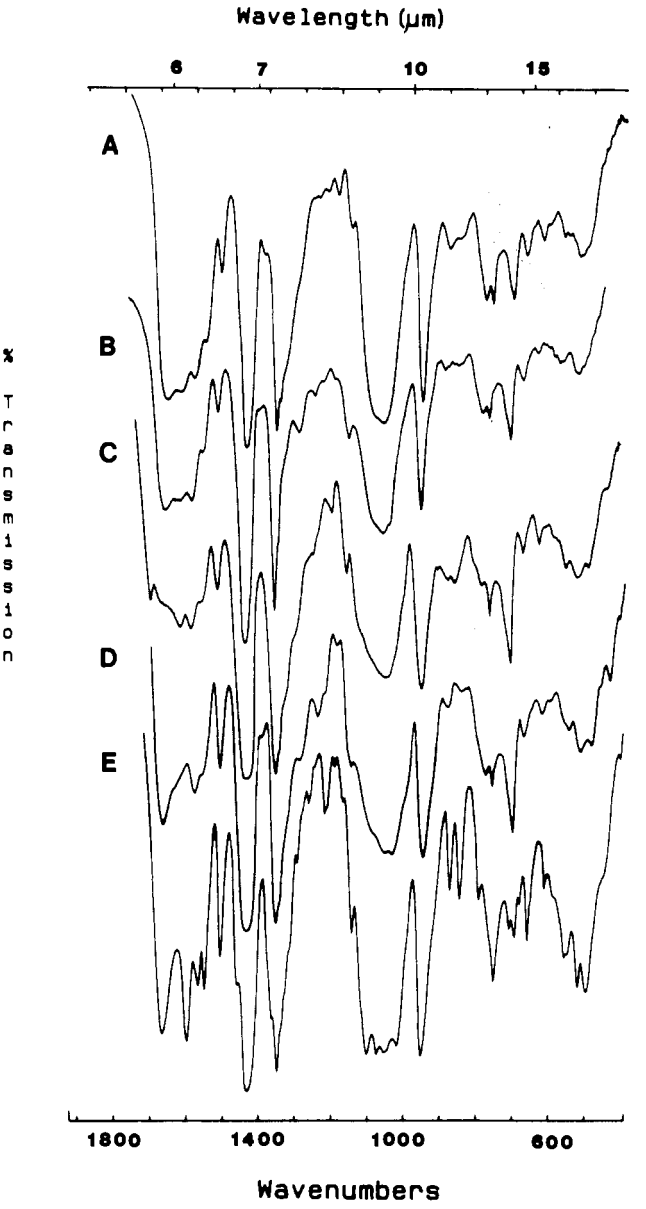

Figure 1. Solid-state FT-IR spectra as Nujol mulls: (A) $[Pt(NH_3)_4][5'\text{-GMP}]\cdot 5H_2O$; (B) $[Pt(en)_2][5'\text{-GMP}]\cdot 4H_2O$; (C) $[Co(NH_3)_6]_2[5'\text{-GMP}]_3\cdot 13H_2O$; (D) $[Co(en)_3]_2[5'\text{-GMP}]_3\cdot 14H_2O$; (E) $Na_2(5'\text{-GMP})\cdot 3.5H_2O$.

of the solid-state spectra, except that of $Na_2(5'\text{-GMP})$. The most apparent changes in the spectra, as compared to that of the starting Li or Na salt of 5′-GMP, were found in the carbonyl stretching vibration (1710–1680 cm^{-1}) and in the 850–825-cm^{-1} region; the latter contains a marker band for ribose pucker.[24] The data are summarized in Table I, and complete IR data are found under Experimental Procedures. An expansion of the 850–600-cm^{-1} region is given in Figure 2.

Compared to that of $Na_2(5'\text{-GMP})\cdot 3.5H_2O$, the ν(C=O) vibration is shifted to lower wavenumbers for all of the compounds except $[Co(NH_3)_6]_2[5'\text{-GMP}]_3\cdot 13H_2O$. A shift to higher wavenumber, as shown by $[Co(NH_3)_6]_2[5'\text{-GMP}]_3$, is known to occur upon protonation, methylation,[25] or metalation[12] at the N7 guanine-ring position. This is a result of the polarzing effect on the ring system, which strengthens the C=O bond. Hydrogen bonding to N7 is expected to have a similar effect. Hydrogen bonding

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Table I. Infrared Data (Nujol Mull)

	ν(C=O)/cm^{-1}	$\Delta\nu$(C=O)/cm^{-1} [a]	ν(ribose)/cm^{-1}
$[Pt(NH_3)_4][5'\text{-GMP}]\cdot 5H_2O$	1681	+15	803 (816 sh)
$[Pt(en)_2][5'\text{-GMP}]\cdot 4H_2O$	1680	+16	802 (817 sh)
$[Co(NH_3)_6]_2[5'\text{-GMP}]_3\cdot 13H_2O$	1717	-21	798 (818 sh)
$[Co(en)_3]_2[5'\text{-GMP}]_3\cdot 14H_2O$	1691	+5	797 (816 sh)
$Na_2(5'\text{-GMP})\cdot 3.5H_2O$	1696		822 (791 sh)
N7-H$^+$(5'-GMP) [b] in KBr	1705	-9	
cis-$[Pt(NH_3)_2(5'\text{-GMP})_2]^{2-}$ [c]	1694		799

[a] $\nu(C{=}O)_{Na_2(5'\text{-GMP})} - \nu(C{=}O)_{cpd}$. [b] Reference 27. [c] Reference 25.

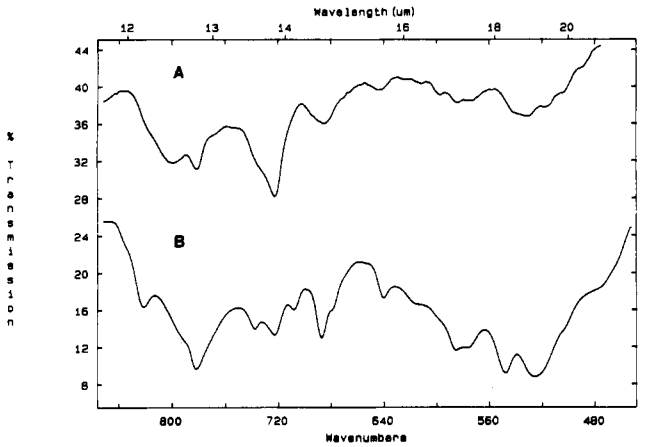

Figure 2. Solid-state FT-IR spectra as Nujol mulls (expansion of 850–400-cm^{-1} region): (A) $[Pt(en)_2][5'\text{-GMP}]\cdot 4H_2O$; (B) $Na_2(5'\text{-GMP})\cdot 3.5H_2O$.

between an NH_3 hydrogen atom and N7 of the guanine ring is possible and would account for the direction of the observed change in the carbonyl frequency in $[Co(NH_3)_6]_2[5'\text{-GMP}]_3$. While one might expect that N7 hydrogen bonding would have a smaller effect on ν(C=O) than protonation, the reverse is observed: $[Co(NH_3)_6]_2[5'\text{-GMP}]_3$, -21 cm^{-1}; *N7*-H$^+$ (5'-GMP), -9 cm^{-1} (see Table I). Other anomalous changes are reported in the literature, and it appears that it is not possible to predict the relative magnitude of the frequency shift. For example: for UV resonance Raman spectra in H_2O, ν(C=O) in *N7*-H$^+$ (5'-dGMP) shifts to higher frequency by 25 cm^{-1} while the Pt(II) in *cis*-$Pt(NH_3)_2$-(5'-dGMP) (1:2 complex) causes only a 9 cm^{-1} shift.[12]

Shifts of ν(C=O) to lower wavenumbers are observed for $[Co(en)_3]_2[5'\text{-GMP}]_3$, $[Pt(NH_3)_4][5'\text{-GMP}]$, and $[Pt(en)_2][5'\text{-GMP}]$. Hydrogen bonding either to the carbonyl group alone[26] or simultaneously to C=O and N7 of 5'-GMP are known to cause a decrease in the carbonyl frequency, and IR data alone cannot distinguish between the two possibilities. Examples of compounds that have both metal–N7 covalent bonds and hydrogen bonding of a metal-coordinated ligand to C=O and that exhibit a low frequency shift of the carbonyl stretching vibration are *cis*-Pt-$(NH_3)_2$-(5'-dGMP) (1:1 complex)[12] and a series of $M(H_2O)_5$-(5'-GMP)$\cdot x H_2O$ compounds, where M = Mn(II), Co(II), Ni(II), or Cd(II).[27] As discussed by Perno et al.,[12] the polarizing effect on the ring system due to N7 metalation, which strengthens the C=O bond, is opposed by hydrogen bonding to the carbonyl, which weakens the C=O bond.

A second structural diagnostic region in the IR spectra occurs at 850–800 cm^{-1}, where marker bands for sugar conformation are found. A band near 820 cm^{-1} indicates a C2'-endo ribose conformation, while a band near 800 cm^{-1} indicates a C3'-endo conformation.[24] Our Pt and Co compounds have an absorption band at ~800 cm^{-1} with a weak shoulder at ~817 cm^{-1}, and therefore, the ribose exists primarily in the C3'-endo conformation (see Figure 2 and Table I). $Na_2(5'\text{-GMP})\cdot 7H_2O$ has the C2'-endo conformation,[28,29] while the commercial $Na_2(5'\text{-GMP})\cdot 3.5\ H_2O$ has an absorption band at 822 cm^{-1} and a should at 791 cm^{-1}, indicating that the latter exists predominantly in the C2'-endo conformation, with a small percentage in the C3'-endo conformation.

The bands that result from the coupled stretching vibrations of the six-membered and five-membered guanine rings overlap considerably, and it is difficult to ascertain whether changes are occurring in this region. There is an increase in intensity of the band near 1650 cm^{-1}, but this may be a contribution from the H_2O bending mode since these compounds contain considerable water of hydration.

Table II. ^{1}H NMR Data (in D_2O; pD 7.9–8.7)

	[GMP] or [Pt]/M	δ(H8)/ppm	$^3J_{Pt-H}$/Hz
$[Co(NH_3)_6]_2[5'\text{-GMP}]_3\cdot 13H_2O$	0.015	8.211	
$[Co(en)_3]_2[5'\text{-GMP}]_3\cdot 14H_2O$	0.017	8.212	
$[Pt(NH_3)_4][5'\text{-GMP}]\cdot 5H_2O$	0.089	8.175	
$[Pt(en)_2][5'\text{-GMP}]\cdot 4H_2O$	0.091	8.190	39.6
	0.19	8.175	33.7
	0.27	8.181	32
$[Pt(en)_2]Cl_2$	0.1		41.2
$[Pt(en)_2]Cl_2 + Na_2HPO_4$	0.1 each		40.2
	0.2 each		40.0
$Na_2(5'\text{-GMP})$	0.015	8.206	
$Li_2(5'\text{-GMP})$	0.17	8.177	

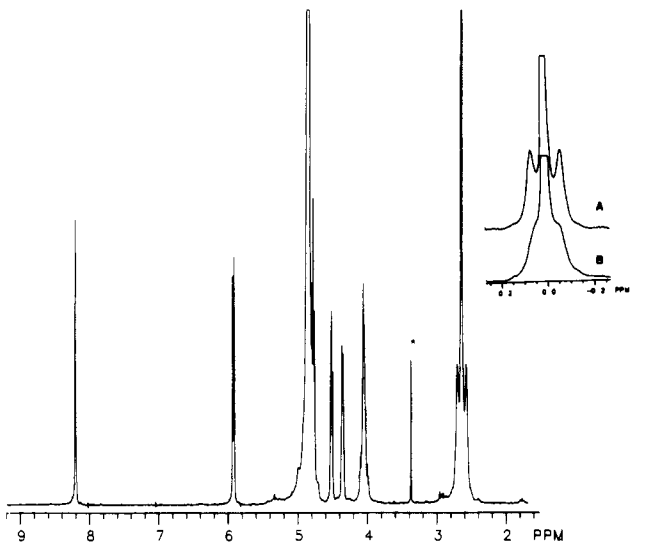

Figure 3. Proton NMR spectrum of 0.091 M $[Pt(en)_2][5'\text{-GMP}]$ in D_2O (pD 8.1; internal reference DSS). The starred line is a methanol impurity. Inset: Proton NMR spectra of the ethylenediamine resonance at 2.595 ppm in $[Pt(en)_2][5'\text{-GMP}]$ (D_2O; pD 8.0–8.2): (A) 0.091 M; (B) 0.27 M. The symmetrically placed sidebands arise from three bond Pt–H coupling.

The bands that result from the coupled stretching vibrations of the six-membered and five-membered guanine rings overlap considerably, and it is difficult to ascertain whether changes are occurring in this region. There is an increase in intensity of the band near 1650 cm^{-1}, but this may be a contribution from the H_2O bending mode since these compounds contain considerable water of hydration.

NMR Spectra. Pertinent ^{1}H NMR data are summarized in Table II, and the spectrum of 0.091 M $[Pt(en)_2][5'\text{-GMP}]$ in D_2O at pD 8.1 is shown in Figure 3. Complete NMR data are given under Experimental Procedures. Exchangeable protons (N–H

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protons of the ammonia and en, N1H, NH_2, and OH protons of the 5′-GMP) are not observable in D_2O. ^{195}Pt ($I = {}^1/_2$; 34% natural abundance) satellites arise from coupling with the CH_2 protons of en.

The chemical shifts and spin–spin couplings of the resonances of the 5′-GMP anion are very similar in all four compounds and very similar to those for 0.10 M Na_2(5′-GMP). Unlike those of Na_2(5′-GMP), they change very little with increasing concentration. The absence of an appreciable upfield shift of the H8 resonance with increasing concentration means that guanine base stacking is not occurring in solutions of the Pt(II) compounds. The solubilities of the Co(III) compounds are low, and appreciable base stacking would not be expected.

We have not observed the formation of any material containing metal–N7 bonds, which would form if metal–amine dissociation occurred. In such a case, the H8 signal would be located several tenths of 1 ppm farther downfield than the 8.2 ppm observed for our compounds. For example, in adducts of $Pt(NH_3)_2Cl_2$ with 5′-GMP,[30,31] δ is found at 8.4–8.7 ppm, depending on the pH and on the number of 5′-GMP molecules (1 or 2) N7-bonded to Pt.

The distribution of the ribose conformations in solution can be calculated from $J_{H1'-H2'}$.[32] Values of 5.4–6.6 Hz are measured for solutions of the Pt(II) and Co(III) compounds, where 6.0 Hz corresponds to a 62:38 mol % mixture of C2′-endo to C3′-endo conformers. The larger the coupling constant, the greater the percentage of C2′-endo species. The values for 0.015 M Na_2(5′-GMP) and 0.17 M Li_2(5′-GMP) are 6.3 and 6.0 Hz, respectively. Therefore, in solution, the ribose conformation in Pt(II) and Co(III) compounds is largely unperturbed, in contrast with that observed in the solid state.

Coupling between either ^{195}Pt or ^{59}Co and the CH_2 protons of en groups has an appreciable effect on the spectra. As shown in Table II and Figure 3 (inset), a concentration-dependent decrease in $^3J_{Pt-H}$ of the $[Pt(en)_2]^{2+}$ ion occurs upon reaction with 5′-GMP^{2-}. Spectral deconvolution was used to determine the coupling constant in the most concentrated solution, 0.27 M, in order to distinguish between a change in the coupling constant and an observed concentration-dependent line broadening. The line broadening could be due to an increased relaxation rate resulting from ion pairing of the cation to the large 5′-GMP^{2-} ion. To further determine if the change in $^3J_{Pt-H}$ was the result of ion pairing, the NMR spectra of equimolar mixtures of $[Pt(en)_2]Cl_2$ and Na_2HPO_4 were obtained. At pD 8.1, these solutions consist of 78 mol % HPO_4^{2-} and 22 mol % $H_2PO_4^-$. The coupling constant was nearly the same as that for $[Pt(en)_2]Cl_2$ of the same concentration and was *not* concentration dependent, indicating that cation–phosphate interactions alone cannot account for the reduced $^3J_{Pt-H}$ observed for $[Pt(en)_2]$[5′-GMP].

In the $[Co(en)_3]^{3+}$ cation, the en chelate rings are less conformationally flexible than they are in $[Pt(en)_2]^{2+}$, and the CH_2 protons constitute an AA′BB′ spin system that is broadened by coupling to ^{59}Co ($I = {}^7/_2$; 100% natural abundance). Figure 4 shows the en CH_2 multiplet for $[Co(en)_3]Cl_3$, a 2:3 mixture of $[Co(en)_3]Cl_3$ and Na_2HPO_4, and $[Co(en)_3]_2$[5′-GMP]$_3$, all at pD 7.5. Ion pairing is known to occur in solutions containing $[Co(en)_3]^{3+}$ and HPO_4^{2-} ions.[33] In spectra A and B of Figure 4, especially the former, the downfield half of the multiplet is broadened, and we infer that these protons (equatorial) are coupled more strongly to Co. Decoupling of ^{59}Co resolves the multiplet into a typical, nearly symmetrical AA′BB′ pattern.[33] Similar results were observed for [Co(sepulchrate)]$^{3+}$;[34] sepulchrate is a cryptand that contains en units. In the $[Co(en)_3]_2$[5′-GMP]$_3$ ^1H NMR spectrum, a similar, but not quite so dramatic, improvement

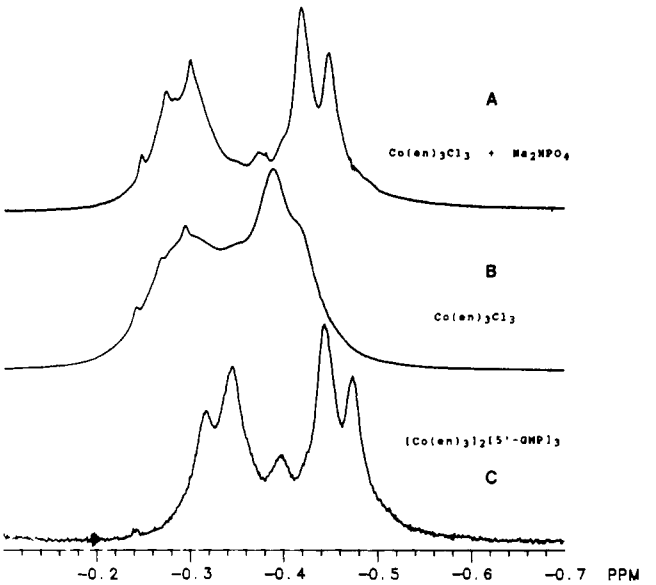

Figure 4. Ethylenediamine region of the ^1H NMR spectra of $[Co(en)_3]^{3+}$ in D_2O in the presence of various anions: (A) 0.052 M in $[Co(en)_3]^{3+}$, 0.074 M in HPO_4^{2-}, pD 8.6; (B) 0.10 M $[Co(en)_3]Cl_3$, pD 7.9; (C) 6 mM $[Co(en)_3]_2$[5′-GMP]$_3$, pD 8.4, referenced to TMA^+ at 0.00 ppm.

in resolution and near symmetrization of the en multiplet is found, but *without* using ^{59}Co decoupling.[35] The effect on the en protons in $[Co(en)_3]_2$[5′-GMP]$_3$ is much greater than in the $[Co(en)_3]^{3+}$–HPO_4^{2-} mixture, suggesting stronger phosphate interactions with the cation and/or additional $[Co(en)_3]^{3+}$–guanine base interactions. Small chemical shift changes are also observed and are most likely a result of 5′-GMP binding.

^{31}P NMR solution spectra of the Pt(II) and Co(III) complexes have single ^{31}P resonances in the 4.4–4.6 ppm range, downfield from external 18 M H_3PO_4. Spectra of 0.17 M Li_2(5′-GMP) and 1.5×10^{-2} M Na_2(5′-GMP) show resonances at 4.44 and 4.47 ppm, respectively. These values are typical of phosphate monoester dianions.[36] Changes in the O–P–O bond angle can cause large changes in the ^{31}P chemical shift,[36] but this is not observed for these compounds. Hydrogen bonding of the phosphate has only small effects on the chemical shift,[37] unless O–P–O bond angle changes accompany it.

Optical Rotation. In order to determine if 5′-GMP^{2-} (β-D; $[\alpha]_D$ = −26 for Na_2(5′-GMP) at 20 °C) might be reacting with racemic $[Co(en)_3]^{3+}$ in a stereoselective manner, the specific rotation of a $[Co(en)_3]_2$[5′-GMP]$_3$ sample was measured immediately after solution preparation from the isolated solid; $[\alpha]_D$ = +90 (c = 0.145). To test if it was [Λ-(+)-Co(en)$_3$]$_2$[β-D-(−)-5′-GMP]$_3$ that was forming in our reaction mixtures, pure samples of the two possible diastereomers were prepared from the corresponding Λ-(+)- or Δ-(−)-Co(en)$_3^{3+}$ tartrates, and their [α]'s were measured: [Λ-(+)-Co(en)$_3$]$_2$[β-D-(−)-5′-GMP]$_3$, $[\alpha]_D$ = +111 (c = 0.0996); [Δ-(−)-Co(en)$_3$]$_2$[β-D-(−)-5′-GMP]$_3$, $[\alpha]_D$ = −90 (c = 0.100). Therefore, the compound prepared from racemic $Co(en)_3Cl_3$ is nearly pure [Λ-(+)-Co(en)$_3$]$_2$[β-D-(−)-5′-GMP]$_3$. The ^1H NMR spectra of the two diastereomers were virtually identical and identical with that of the compound prepared from racemic $[Co(en)_3]Cl_3$.

Discussion

On the basis of the IR data and CPK-model-building studies, the hydrogen-bonding interactions shown in Table III have been proposed. Structures that are consistent with all the data are given in Figure 5. In all the compounds, except $[Co(NH_3)_6]_2$[5′-GMP]$_3$, hydrogen bonding between N-bound H atoms and both the guanine N7 and C=O are believed to be occuring. For

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Table III. Hydrogen-Bonded Interactions in Solids

	sites on 5'-GMP[a]		sites on amines
$[Pt(NH_3)_4][5'\text{-GMP}]\cdot 5H_2O$	N7 and C=O	→	two NH_3 cis to each other
	phosphate, direct or via H_2O	→	one NH_3, trans to the bonded C=O
$[Pt(en)_2][5'\text{-GMP}]\cdot 4H_2O$	N7 and C=O	→	two NH_2 cis to each other, but from different en's
	phosphate, possibly via H_2O	→	one NH_2, trans to the bonded C=O
$[Co(NH_3)_6]_2[5'\text{-GMP}]_3\cdot 13H_2O$	N7 and phosphate via H_2O	→	two NH_3 cis to each other
$[Co(en)_3]_2[5'\text{-GMP}]_3\cdot 14H_2O$	N7 and C=O	→	two NH_2 cis to each other, but from different en's
	phosphate via H_2O	→	one NH_2 cis to the other two

[a] Phosphate bonding could be to a cation different from that bonding to the guanine ring system.

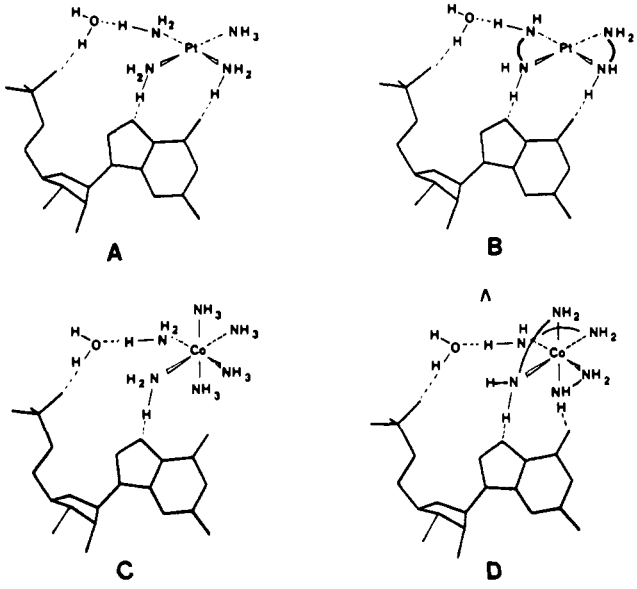

Figure 5. Proposed hydrogen-bonded structures: (A) $[Pt(NH_3)_4][5'\text{-GMP}]$; (B) $[Pt(en)_2][5'\text{-GMP}]$; (C) $[Co(NH_3)_6]_2[5'\text{-GMP}]_3$; (D) $[\Lambda\text{-}(+)\text{-}Co(en)_3]_2[5'\text{-GMP}]_3$.

$[Co(NH_3)_6]_2[5'\text{-GMP}]_3$, the shift of the carbonyl stretching vibration to higher frequencies is consistent with hydrogen bonding to only N7, although the molecular models do not show any steric reasons that would preclude additional bonding to C=O. The reason may lie in PO_4–cation interactions. Models show that if the $[Co(NH_3)_6]^{3+}$ ion hydrogen-bonds only to N7, then a direct hydrogen bond between the phosphate and an N–H is possible, but with cation hydrogen bonding to both N7 and C=O, any PO_4 interaction would have to be through a hydrogen-bonded H_2O: $O_3PO\text{–}H_2O\text{–}HN$. A strong $PO_4\text{–}H\text{–}N$ bond could favor the former cation–guanine interaction, as our data suggest.

Although the models presented in Figure 5 show bonding between one cation and one anion, it must be remembered that, as a result of the stoichiometry of the Co(III) compounds, more than one $5'\text{-}GMP^{2-}$ must be associated with each cation. It is likely that polymeric structures are formed. A variety of possibilities exist; among them are bridging phosphates or phosphate binding to one cation with the base from the same 5'-GMP binding to another cation. Such structures are consistent with the rather low solubilities of the Co(III) compounds. Polymeric structures may also occur for the Pt(II), but are not necessary to satisfy the stoichiometry.

Although hydrogen bonding between a phosphate of a nucleotide and metal-coordinated H_2O[2,38] or between a polynucleotide and metal-coordinated NH_3[8,10,11,39] has been documeted, bonding of the phosphate via a hydrogen-bonded water (bridge) molecule is also possible. Molecular mechanics calculations on the $[Pt(NH_3)_4]^{2+}\text{–}H_2O\text{–}H_2PO_4^-$ system revealed that direct and through-water bindings of the cation and anion are energetically competitive.[40] In order for en in $[Co(en)_3]_2[5'\text{-GMP}]_3$ to hydrogen-bond simultaneously to the N7, C=O, and the phosphate, a water bridge is sterically required. For $[Pt(NH_3)_4]$[5'-GMP] and $[Pt(en)_2]$[5'-GMP], models show that either direct or through-water binding to the phosphate is possible. However, if direct bonding is to occur, there must be a considerable change in the glycosidic torsion angle, χ_{CN}, although remaining in the anti range, and a considerable change in the conformation about the C4'–C5' bond (from gg to gt).[41]

The stretching vibrational absorptions of the $-PO_3^{2-}$ group, which are potentially informative, are not useful in these compounds. The strong $-PO_3^{2-}$ degenerate stretching vibration,[42] found at 1078 cm^{-1} for $Na_2(5'\text{-GMP})\cdot 3.5H_2O$, occurs at 1070–1080 cm^{-1} for the Co(III)– and Pt(II)–5'-GMP compounds (Figure 1). This region also contains a number of intense ribose vibrations that overlap the $-PO_2^-$ band and result in a very broad and poorly resolved band. The bands of the Pt compounds are somewhat narrower overall, but in general very similar to those of the Co(III) compounds. The $-PO_3^{2-}$ symmetric stretch is located at 969–973 cm^{-1} for all the comounds, a small shift from 981 cm^{-1} for $Na_2(5'\text{-GMP})\cdot 3.5H_2O$.

Except for $Na_2(5'\text{-GMP})\cdot 7H_2O$,[28,29] $Na_2(5'\text{-GMP})\cdot 3.5H_2O$, and guanosine·$2H_2O$,[43] the ribose conformation in the solid state of many 5'-GMP salts is C3'-endo.[2,38] Our Pt(II) and Co(III) compounds also have the C3'-endo ribose pucker in the solid state. The conversion from C2'- to C3'-endo conformation has variously been ascribed to hydrogen bonding between the ligand molecule and the phosphate, electrostatic interactions between an N7-bound group and the phosphate, or polarization effects on the guanine ring system,[12] but no one explanation fits all compounds. Phosphate groups seem to be required in some cases, but not in others.[12,44] We suggest that the cause may be inter-nucleotide interactions, such as base stacking and hydrogen bonding, in the solids. As determined from the magnitude of $J_{1'\text{-}2'}$ in dilute solutions, the C2'-endo conformation is present in the greater amount (about 60%) in our compounds and many others, including guanosine and the alkali-metal[16,45] and alkaline-earth-metal[46] salts of 5'-GMP. As the concentration of the alkali-metal–5'-GMP salts is increased, strong interactions between the 5'-GMP moieties become operative.[16,45,47] At the same time, the ribose conformation shifts to increasing amounts of C3'-endo, the conformation found in A-RNA.

The presence of the en ligand in $[Pt(en)_2]$[5'-GMP] and $[Co(en)_3]_2[5'\text{-GMP}]_3$ serves as a probe for intermolecular and electrostatic interactions. Both the decrease in $^3J_{Pt\text{–}H}$ in the Pt(II) compounds and the improved resolution in the Co(III) compounds, which arises from a decrease in the $^3J_{Co\text{–}H}$ coupling constant, are interpreted as resulting from interactions between the metal complex cation and the phosphate and guanine groups of 5'-GMP.

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The strongest type of interaction should be the electrostatic attraction between the phosphate of 5'-GMP and the metal cation, and this alone might cause the observed effects. Ion pairing between $[Co(en)_3]^{3+}$ and HPO_4^{2-} in solution[48] and cation-phosphate interactions in solid $[Co(en)_3]_2[HPO_4]_3 \cdot 9H_2O$[49] occur via hydrogen bonding between the N-H protons of en and the phosphate oxygens. CPK models show that, although the 5'-GMP^{2-} ion is considerably larger than HPO_4^{2-}, if the 5'-GMP phosphate were the only site interacting with the cation, the guanine and ribose units would be sufficiently distant from the cation so as not to perturb it, and there should be no difference in the spectra of the HPO_4^{2-} and 5'-GMP^{2-} compounds. The significantly improved resolution of the en proton resonances in the NMR spectrum of $[Co(en)_3]_2[5'\text{-}GMP]_3$ suggests that additional interactions with 5'-GMP are present (Figure 4).

Changes in coupling constants occur as a result of changes in the geometry of the coupled nuclei. The most stable conformation of the ethylenediamine chelate ring is puckered, in which the CH_2 protons are gauche to each other.[50] The metal-H coupling constant is dependent on, among other factors, the metal-N-C-H dihedral angle,[51] and a flattening of the en chelate ring pucker is consistent with the experimentally observed decrease in the metal-CH_2 coupling constant. This makes the en NH_2 protons sterically more accessible to hydrogen bonding with the guanine N7. Erickson et al. have qualitatively correlated $^3J_{Pt-H}$ with the Pt-N-C-H dihedral angle for a series of Pt(II) amino acid complexes and concluded that the coupling constant decreases as the dihedral angle decreases from 180 to 0°.[52] The fact that the $^3J_{Pt-H}$ does not decrease with increasing concentration in $[Pt(en)_2]^{2+}$-HPO_4^{2-} solutions but does so in $[Pt(en)_2][5'\text{-}GMP]$ is further evidence for the persistence of cation-guanine base interactions in solution.

5'-GMP (β-D) stereoselectivity chooses the $[\Lambda\text{-}(+)\text{-}Co(en)_3]^{3+}$ enantiomer from the racemic reaction mixture on the basis of the lesser solubility of $[\Lambda\text{-}(+)\text{-}Co(en)_3]_2[5'\text{-}GMP]_3$. Each of the pure diastereomers exists, and they were readily prepared by starting with enantiomerically pure $[Co(en)_3]^{3+}$. CPK models show that the $[\Lambda\text{-}(+)\text{-}Co(en)_3]^{3+}$ ion can easily bond concurrently to the N7, C=O, and phosphate of the same 5'-GMP without any appreciable distortion of the most common 5'-GMP conformation (anti, gg). However, the $[\Delta\text{-}(-)\text{-}Co(en)_3]^{3+}$ enantiomer can only bind with difficulty to the phosphate when it is hydrogen-bonded to N7 and C=O. In this case, the orientation of the ethylene chain of en limits the accessibility of the nearest NH_2 group for hydrogen bonding with the phosphate, even with a bridging water present. The lesser solubility of $[\Lambda\text{-}(+)\text{-}Co(en)_3]_2[5'\text{-}GMP]_3$ may result in part from the three-site binding between the cation and 5'-GMP.

It has been shown that hydrogen bonds are formed between metal-coordinated amine ligands and the base of 5'-GMP in the solid compounds and that it is likely that they persist in solution, even in the competitive solvent water. Such interactions between nucleic acids and antitumor drugs or other metal complexes will increase the overall strength of the bonding and therefore lead to more effective control of certain reactions of nucleic acids.

Acknowledgments. We thank the Southwest Research Institute for a gift of platinum(IV) oxide. This research was supported by a Faculty Research Award from The University of Texas at San Antonio to J.A.W.

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Effects of Axial Ligation on the Thermolysis of Benzyl- and Neopentylcobamides: Analysis of the "Base-On" Effect

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Received June 15, 1990

The nature of the "base-on" effect, in which the base-on species of thermally labile alkylcobalamins is found to be labilized by 10^2-10^3-fold relative to the base-off species or analogous alkylcobinamide, has been studied for benzyl- and neopentylcobalamin. Appropriate correction of the observed activation parameters of the alkylcobalamins in neutral solution for the occurrence of significant amounts of the base-off species shows that the base-on effect is entirely entropic for these sterically hindered alkylcobalamins; the enthalpies of activation of the base-on and base-off species are essentially identical. Studies of the effects of exogeneous ligands on the thermolysis of the alkylcobinamides show that, within an isosteric series of 4-substituted pyridines, the carbon-cobalt bond is stabilized by increasing basicity of the trans axial ligand. In addition, for all four of the organic nitrogen donors studied, the alkyl(ligand)cobinamides are of comparable reactivity to that of the base-on alkylcobalamin. Even azide is shown to cause a significant base-on effect. Taken together with data from the literature, these results suggest that the base-on effect is primarily steric in nature, but it is the steric consequence of the *presence* of a strongly donating axial ligand that is important rather than the ligand's steric bulk. With the aid of models, a picture of the steric activation of these alkylcobalamins for Co-C bond homolysis emerges in which steric crowding of the bulky organic ligand by the upward projecting acetamide side chains is the driving force for reaction. It is believed that in the base-off cobalamins (and in the cobinamides) the ground state is entropically stabilized by a distortion of the flexible corrin ring, which provides relief of the steric congestion. Tentative support for this idea is obtained from the thermodynamics of formation of the alkyl(ligand)cobinamide complexes.

Introduction

There remains great interest in the mechanism by which 5'-deoxyadenosylcobalamin (AdoCbl)-requiring enzymes activate AdoCbl by inducing homolysis of its carbon-cobalt bond. Hay and Finke's study[1,2] of the thermolysis of AdoCbl demonstrates that such enzymes can increase the rate of thermal homolysis by a factor of at least 10^{10} at 25 °C. Most[3] of the hypotheses for this mechanism invoke steric distortion of the coenzyme as the primary driving force promoting homolysis.[2,4-10] One such hy-

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0020-1669/91/1330-3420$02.50/0