[^{1}H, ^{15}N] NMR Investigations of Pt-NH Hydrogen Bonding in d(GpG), d(pGpG), and d(TpGpG)-*N7,N7* Adducts of $[Pt(en)]^{2+}$ in Aqueous Solution

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We report studies of the pH and temperature dependences of N-H NMR resonances of [Pt(^{15}N-en){d(GpG)-*N7(1),N7(2)*}]$^{2+}$ (**1**), [Pt(^{15}N-en){d(pGpG)-*N7(1),N7(2)*}]$^{2+}$ (**2**), and [Pt(^{15}N-en){d(TpGpG)-*N7(2),N7(3)*}]$^{2+}$ (**3**) in aqueous solution using ^{15}N-edited ^{1}H and [^{1}H, ^{15}N] heteronuclear multiple quantum coherence (HMQC) 2D NMR spectroscopy. The data for **2** are consistent with strong stereospecific intramolecular H bonding involving only one of the en NH hydrogens and the deprotonated dianionic terminal 5′-phosphate group, for which the pK_a is lowered by ca. 0.5 units to 6.46. The NMR data for complex **1** are similar to those of complex **3**, suggesting either that such H bonding is very weak for a bridging monoanionic 5′-phosphate (diester) or, more likely, that these NMR methods are insensitive to its presence.

Introduction

The primary target for platinum anticancer drugs is DNA[1] and hydrogen bonds involving the NH groups of coordinated ammines and amines are thought to play an important role in formation and stabilization of Pt-DNA adducts.[2] Such H bonds have been detected, for example, in the crystal structure[3] of *cis*-[Pt(NH_3)$_2${d(pGpG)-*N7(1),N7(2)*}]$^{2+}$, crystallized at pH 4, where[4] there is weak interligand ammine-C6O H bonding and stronger intramolecular H bonding with the terminal monoanionic 5′-phosphate. Weak intramolecular ammine-C6O bonds are present in the X-ray structure of *cis*-[Pt(NH_3)$_2${d(CpGpG)-*N7(2),N7(3)*}]$^{2+}$, but phosphate-ammine contacts are absent.[5] In the crystal structure of [Pt(dien){d(ApGpA)-*N7(2)*}]$^{2+}$,[6] there are both types of weak H bonds, and these appear to determine the dihedral angle between guanine and the PtN_4 coordination plane. The existence of N-H···phosphate H bonds in polynucleotide complexes has also been inferred from analysis of CH NMR shifts, coupling constants and sugar ring puckers,[7] and theoretical calculations.[8] Two groups of workers[9-11] have suggested that the downfield shift of the GpG ^{31}P NMR resonance in Pt adducts such as [Pt(en){d(TpGpGpT)-*N7(2),N7(3)*}]$^{2+}$ may be diagnostic of NH H bonding to a 5′-phosphodiester group.

In this work we have investigated H bonding in [Pt(^{15}N-en)-{d(GpG)-*N7(1),N7(2)*}]$^{2+}$ (**1**), [Pt(^{15}N-en){d(pGpG)-*N7(1),N7(2)*}]$^{2+}$ (**2**), and [Pt(^{15}N-en){d(TpGpG)-*N7(2),N7(3)*}]$^{2+}$ (**3**) in aqueous solution, via direct observation of N-H NMR resonances using ^{15}N-edited ^{1}H and [^{1}H, ^{15}N] HMQC 2D NMR spectroscopy.[12] These polynucleotides were chosen because they allow a comparison between the H-bonding roles of terminal versus bridging 5′-phosphates to be made.

Experimental Section

Preparation of Complexes. **[Pt(^{15}N-en)(H_2O)$_2$]$^{2+}$** was prepared as described previously[13] by the addition of slightly less than 2 molar equiv of $AgNO_3$ to a solution of [Pt(^{15}N-en)Cl_2] in DMF-d_7, removal of the AgCl precipitate, and dilution with 95%H_2O/5%D_2O. For the preparation of adducts **1** and **3**, the final Pt concentration of the stock solution of [Pt(^{15}N-en)(H_2O)$_2$]$^{2+}$ was 12.5 mM (pH 3.1) and contained 3% DMF, whereas for **2** a 10.0 mM stock solution was used, containing 7% DMF, pH 3.9.

[Pt(^{15}N-en){d(GpG)-*N7(1),N7(2)*}]$^{2+}$ (1) was prepared directly in a 5 mm NMR tube by addition of d(GpG) (1.15 mg, 1.86 μmol; obtained from Sigma) to 135 μL of a 12.5 mM stock solution of [Pt(^{15}N-en)(H_2O)$_2$]$^{2+}$ diluted with 365 μL of 5% D_2O/95% H_2O. NMR spectra were recorded after overnight incubation at 37 °C, final pH 7.30, adjusted with 0.1 M KOH.

[Pt(^{15}N-en){d(pGpG)-*N7(1),N7(2)*}]$^{2+}$ (2) was prepared directly in an NMR tube by the reaction of d(pGpG) (1.0 mg, 1.62 μmol; obtained from Oswel) to 147 μL of the 12.5 mM stock solution of [Pt(^{15}N-en)-(H_2O)$_2$]$^{2+}$ diluted with 453 μL of 95%H_2O/5% D_2O. NMR spectra were recorded after overnight incubation at 37 °C. The final Pt concentration was 2.45 mM, and the solution had a pH of 4.24 and contained 1.8% DMF. The pH was adjusted as required with 0.1 M HNO_3 and 0.1 M KOH.

[Pt(^{15}N-en){d(TpGpG)-*N7(2),N7(3)*}]$^{2+}$ (3) was prepared by reacting d(TpGpG) (1.8 μmol; obtained from Genosys) in 5 mL of H_2O with 150 μL of a 12.5 mM stock solution of [Pt(^{15}N-en)(H_2O)$_2$]$^{2+}$ for 45 min at ambient temperature, freeze-drying, and redissolving in 0.5 mL of 5% D_2O/95% H_2O. The pH (4.04) was increased with KOH solution.

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(12) Abbreviations: dGp deoxyguanosine-5′-monophosphate; DMF dimethylformamide; en 1,2-diaminoethane; HMQC heteronuclear multiple quantum coherence spectroscopy; TSP sodium (trimethylsilyl)propionate-*2,2,3,3-d*$_4$.
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Table 1. ^{1}H and ^{15}N NMR Chemical Shifts of **1** and **3** at Various pH Values and Temperatures and Comparative Data for Mononucleotide Complexes (ref 13)

complex	pH	T/K	δH8 5′-G	δH8 3′-G	δ other	δN^{1}H (δ^{15}NH)
[Pt(^{15}N-en){d(GpG)-*N7(1),N7(2)*}]$^{2+}$ (**1**)[a]	7.3	300	8.09	8.46		5.60, 5.66 (−31.1)
						5.76, 5.81 (−30.8)
	7.3	275	8.14	8.54		5.69, 5.73
						5.84, 5.88
	3.4	300	8.17	8.48		5.59, 5.61
						5.66, 5.70
[Pt(^{15}N-en){d(TpGpG)-*N7(2),N7(3)*}]$^{2+}$ (**3**)[c]	7.2	310	8.15	8.90	7.58[b]	5.53, 5.72
						5.65, 5.80
	7.2	333	8.20	8.79	7.57[b]	5.47, 5.63
						5.57, 5.76
	4.4	333	8.23	8.79	7.56[b]	5.43, 5.57 (−31.4)
						5.52, 5.76 (−31.0)
[Pt(^{15}N-en)(5′-GMP-*N7*)$_2$]$^{2+}$	4.3	310	8.50			5.75
	6.7	300	8.70			5.86, 6.11 (−30.2)
[Pt(^{15}N-en)(3′-GMP-*N7*)$_2$]$^{2+}$	4.3	300		8.42		5.69
	7.7	300		8.43		5.74
[Pt(^{15}N-en)(5′-AMP-*N7*)$_2$]$^{2+}$	7.75	300	9.58		8.18[d]	5.78, 7.21 (−26.55)
			9.67		8.16[d]	5.85, 7.32 (−26.47)

[a] δ H8 d(GpG) (free ligand, 300 K) 5′-G, 3′-G: 7.78, 8.03 (pH 7.3), 7.78, 8.03 (pH 6.3), 7.87, 8.08 (pH 3.4), 7.76, 8.05 (pH 7.3, 275 K). [b] 5′-T H6. [c] Shifts for d(TpGpG) (free ligand, pH 6.88, 300 K) 5′-G (H8), 3′-G (H8), 5′-T (H6): 7.82, 7.94, 7.36. [d] H2.

pH Measurements. These were made directly in NMR tubes before and after recording spectra using a Corning 240 meter equipped with an Aldrich microcombination electrode, calibrated with Aldrich buffer solutions at pH 4, 7, and 10.

NMR Spectroscopy. 500.13 MHz ^{15}N-edited ^{1}H{^{15}N} NMR and 2D [^{1}H, ^{15}N] HMQC NMR spectra were recorded on a Bruker AM-500 as previously described.[13,14]

400.03 MHz ^{1}H{^{15}N} NMR spectra were recorded on a Varian UNITY-400 spectrometer fitted with a 5 mm inverse probehead. Sample spinning was not used. Both one-dimensional ^{15}N-edited ^{1}H spectra and 2D [^{1}H, ^{15}N] spectra were recorded using an HMQC sequence, optimized for ^1J(N,H) = 71 Hz. Water suppression was achieved by presaturation of the H_2O signal for 1.5 s. Typically 128 transients were acquired. Two-dimensional spectra were acquired using the Haberkorn−Ruben (hypercomplex) method for quadrature detection in F_1. The ^{15}N spins were decoupled by irradiating with the GARP sequence at a field strength of 1.0 KHz. 2D spectra were processed using sine-bell weightings in both dimensions.

^{1}H NMR spectra were referenced to internal TSP (500 MHz spectra) or TSP in an external capillary (400 MHz spectra). ^{15}N spectra were referenced to external 1.5 M NH_4Cl in 1 M HCl (90% H_2O/10% D_2O). 161.9 MHz ^{31}P{^{1}H} NMR spectra were obtained at 295 K on a Varian UNITY-400 and were referenced to 85% H_3PO_4 (external).

pK_a Calculations. pH titration curves were fitted to the Henderson−Hasselbalch equation using the program KaleidaGraph.[15]

Results and Discussion

Reaction of [Pt(^{15}N-en)(H_2O)$_2$]$^{2+}$ with d(GpG) in a 1:1 mole ratio produced **1** as the only significant product. The H8 shifts (Table 1) are close to those previously assigned to the 5′-G and 3′-G ligands of this complex.[16] The ^{15}N-edited ^{1}H{^{15}N} NMR spectrum consisted of four resonances of equal intensity within the narrow shift range 5.6−5.8 ppm which were separated into two pairs (NH_a/NH_b and NH_c/NH_d) associated with distinct ^{15}N shifts in the 2D HMQC spectrum, Figure 1. The downfield shifts (0.33 and 0.54 ppm) of the NH peaks of **1** relative to [Pt(^{15}N-en)Cl_2] are similar to those we have observed previously[13,14] in [Pt(en)X_2]$^{2+}$ mononucleobase complexes which lack a 5′-phosphate, e.g., X = 3′-GMP and G.[13] The ^{1}H NH shifts of **1** are relatively insensitive to pH in the range 3.4−6.3, but those of the two low-field peaks N_a and N_b (assigned to a single NH_2 group) increase slightly on increasing the pH, Table 1 (Figure D1, supplementary material). All four peaks shift slightly to low field on decreasing the temperature (Table 2). The temperature coefficients are close to those observed for [Pt(^{15}N-en)Cl_2] (-3.3×10^{-3} ppm K^{-1}, present as an impurity in the stock solution of [Pt(^{15}N-en)(H_2O)$_2$]$^{2+}$) and therefore probably reflect intermolecular interactions with the solvent with little influence from intramolecular effects.

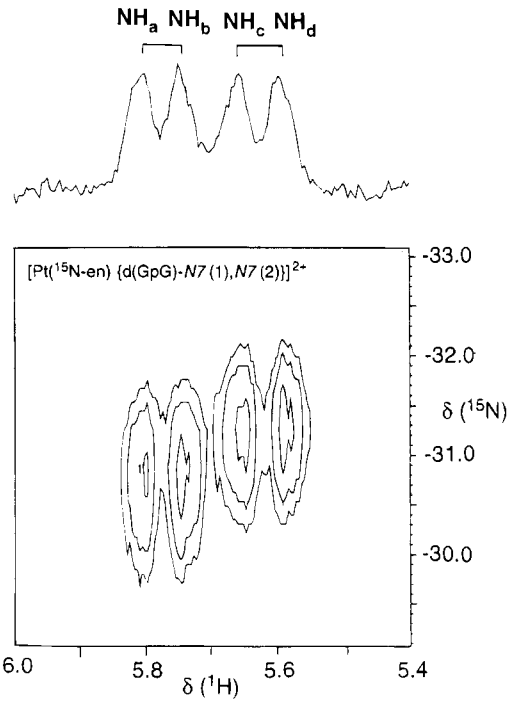

Figure 1. 500 MHz 2D [^{1}H, ^{15}N] HMQC NMR spectrum of [Pt(^{15}N-en){d(GpG)-*N7(1),N7(2)*}]$^{2+}$ **1**, pH 7.3, with an ^{15}N-edited ^{1}H{^{15}N} NMR spectrum shown as a projection. Protons on the same ^{15}N (H_a and H_b, H_c and H_d) correlate with the same ^{15}N shift.

Complex **2**, produced by reaction of d(pGpG) with [Pt(^{15}N-en)(H_2O)$_2$]$^{2+}$, gave rise to ^{1}H NMR peaks for the H8 protons with shifts similar to those reported for the diammine analogue [$Pt(NH_3)_2${d(pGpG)-*N7(1)-N7(2)*}]$^{2+}$ by Girault et al.[17] and with a similar pH dependence attributable to titration of the 5′-

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Table 2. Temperature Dependences of the en NH ^{1}H NMR Chemical Shifts of Complexes **1**, **2**, and **3** and Mononucleotide Complexes for Comparison (ref 13)[a]

complex	pH	$-10^3\,\Delta\delta/T$ (ppm K^{-1})			
		NH_a	NH_b	NH_c	NH_d
[Pt(^{15}N-en){d(GpG)-*N7(1),N7(2)*}]$^{2+}$ (**1**)	7.3	2.7	3.4	2.8	3.6
[Pt(^{15}N-en){d(pGpG)-*N7(1),N7(2)*}]$^{2+}$ (**2**)	7.3	10.1	2.4	5.9	2.4
[Pt(^{15}N-en){d(TpGpG)-*N7(2),N7(3)*}]$^{2+}$ (**3**)	7.2	1.6	4.1	3.5	2.7
[Pt(^{15}N-en)(5′-GMP-*N7*)$_2$]$^{2+}$	6.2	5.5	3.6		
[Pt(^{15}N-en)(5′-AMP-*N7*)$_2$]$^{2+}$	7.8	4.3, 1.1	4.1, 4.1		

[a] NH_a corresponds to the most deshielded NH proton, and NH_a and NH_b are assigned to one NH_2 group and H_c and H_d to the other. For complex **2**, NH_a and NH_b are assigned to the NH_2 group *cis* to the 5′-phosphate. For the mononucleotide complexes, the two en-NH_2 groups are magnetically equivalent (NH_a=NH_c, NH_b=NH_d), and the pairs of NH_a and NH_b signals for the 5′-AMP complex correspond to NH_2 groups in the two head-to-tail diastereomers.

Table 3. ^{1}H, ^{15}N, and ^{31}P NMR Chemical Shifts for Complex **2** and the Ligand d(pGpG) at Various pH Values and Temperatures

pH, *T*/K	δ(H8) (pG-)	δ(H8) (-Gp-)	en-CH_2	δNH ^{1}H(^{15}N)	δ^{31}P[a]	
					(pG-)	(-Gp-)
			[Pt(^{15}N-en){d(pGpG)-*N7(1),N7(2)*}]$^{2+}$ (**2**)			
4.2, 298	8.425	8.699	2.828	5.94, 5.53 (−31.2)		
				5.73, 5.49 (−31.5)	3.43	2.86
7.3, 298	8.829	8.638	2.864	6.52, 5.40 (−30.5)		
				5.70, 5.35 (−31.1)	6.45	3.23
7.3, 328	8.762	8.611	2.867	6.28, 5.38		
				5.59, 5.38		
7.3, 283	8.801	8.679	2.867	6.74, 5.50		
				5.86, 5.50		
			d(pGpG)			
3.3, 295	8.5 (br)	8.5 (br)			—[b]	2.31

[a] 295 K. [b] Not resolved.

phosphate group with a pK_a of 6.37 ± 0.09. For [Pt(NH_3)$_2$-{d(pGpG)-*N7(1)-N7(2)*}]$^{2+}$, a pK_a value of ca. 7.1 has been reported (in D_2O using pD values, i.e., 6.7 using pH* values). In the ^{31}P NMR spectrum of **2**, only the pG signal showed large pH-dependent shifts, with an associated pK_a of 6.55 ± 0.01. Both the H8 ^{1}H NMR and the pG ^{31}P NMR peaks of the free ligand d(pGpG) were very broad. These effects have been noted previously for d(pGpG)[18] and also for d(pGpGpTpT),[10] and may be due to intermolecular interactions or traces of paramagnetic metal ions. It was possible to observe a sharper pG ^{31}P NMR peak in the presence of 0.9 molar equiv (0.8 mM) of EDTA at 323 K, and a pK_a of 7.00 ± 0.03 was determined for d(pGpG) under these conditions.

The 2D [^{1}H, ^{15}N] NMR spectrum of **2** showed four non-equivalent en-NH protons (Figure D2, supplementary material), assignable to two sets of NH_2 groups with ^{15}N shifts differing by 0.6 ppm. The ^{15}N peak at −30.5 ppm can be assigned to the N *cis* to the 5′-phosphate group on account of the large low-field shift of one of its hydrogens (NH_a). The latter shows a strong pH dependence, Figure 2, and the associated pK_a (6.47 ± 0.04) shows that it is interacting directly with the 5′-phosphate. This provides strong evidence for stereospecific H bonding between one en NH and the 5′-(dianionic)phosphate group in this complex which lowers the 5′-phosphate pK_a by ca. 0.5 units (stabilization of the deprotonated form). The pH-induced shift of 0.7 ppm is larger than that observed for the low-field-shifted NH of [Pt(^{15}N-en)(5′-GMP-*N7*)$_2$]$^{2+}$ (0.4 ppm), but comparable with those of the two low-field-shifted NH protons of [Pt(^{15}N-en)(5′-AMP-*N7*)$_2$]$^{2+}$ (0.7 and 1 ppm). The latter complex adopts a head-to-tail configuration unlike that of complex **2** which is head-to-head, but the rotations of the bases in both of these complexes are slow on the NMR time scale, whereas rotation is fast for the 5′-GMP complex. It can be inferred that slow rotation allows stronger H bonding.

The trinucleotide adduct **3** was generated as the product from reaction of [Pt(^{15}N-en)(H_2O)$_2$]$^{2+}$ with 1 molar equiv of d(TpGpG). The aromatic region of the ^{1}H NMR spectrum contained three singlets (Figure D3, supplementary material), one for each of the nonexchangeable base protons (Table 1), which were assigned on the basis of reports for Pt adducts of similar small oligodeoxyribonucleotides.[10,19,20] The ^{31}P coordination shifts[21] were also consistent with those reported for d(TpTpGpG) and d(TpGpGpT) complexes.[10] The ^{15}N-edited ^{1}H{^{15}N} NMR spectrum of **3** contained four distinct NH resonances of equal intensity in the narrow shift range 5.43−5.76 ppm (Figure 3), which were grouped into two pairs of NH_2 resonances via correlation with their slightly different ^{15}N NMR shifts in the 2D [^{1}H, ^{15}N] HMQC spectrum (Figure D4, supplementary material). The lowest field peak NH_a was unaffected by increasing the pH from 4.4 to 7.2, whereas the other three peaks shifted slightly downfield, Table 1 and Figure 3. Only the NH_a peak shows a low temperature dependence (−1.6 10^{-3} ppm K^{-1}, Table 2), the other temperature coefficients being close to that of [Pt(^{15}N-en)Cl_2]. Like those for complex **1**, the chemical shifts of these NH resonances are similar to those of Pt-en bis(guanine) derivatives which lack a 5′-phosphate.[13]

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(21) ^{31}P δΔ values (coordination shifts, pH 7); downfield shift of one ^{31}P resonance by 1.19 ppm (or 1.41 ppm depending on assignment for TpGpG itself), which compares well with 1.26 and 1.08 ppm reported for d(TpTpGpG) and d(TpGpGpT) Pt(en) adducts, respectively (ref 10). The GpG and TpG shift difference for **3** is also in good agreement with these tetranucleotide adducts (1.34 ppm, cf. 1.29 and 1.18 ppm).

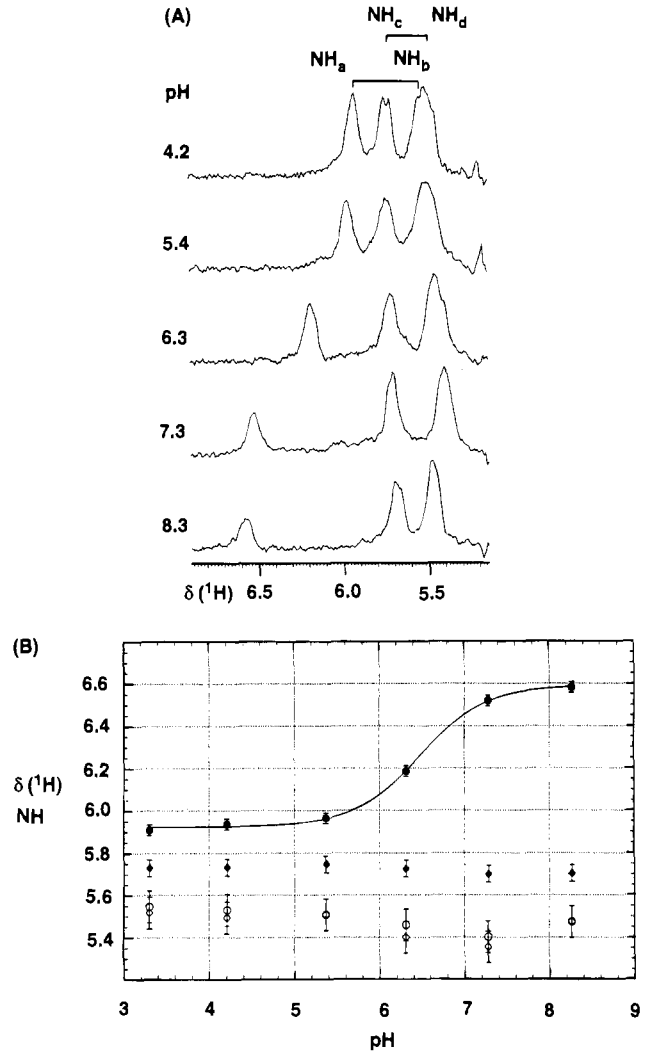

Figure 2. (A) Dependence on pH of the ^{15}N-edited ^{1}H-{^{15}N} NMR spectrum of [Pt(^{15}N-en){d(pGpG)-*N7(1),N7(2)*}]$^{2+}$ **2** at 298 K. (B) Plot of the shifts observed in A. The solid line is a computer best-fit giving a pK_a of 6.47.

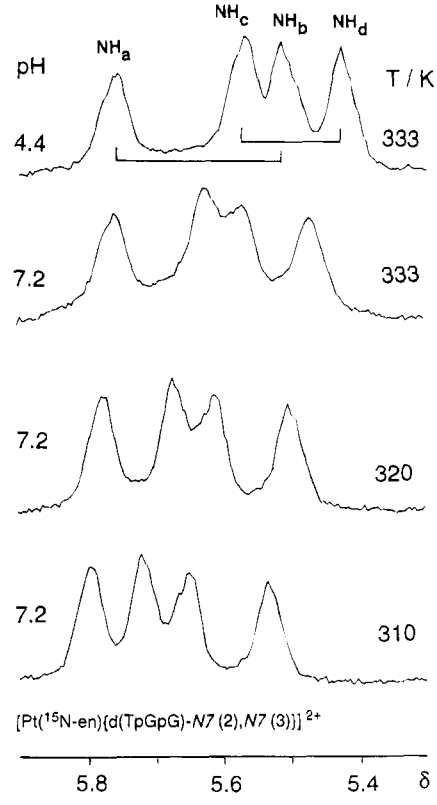

Figure 3. ^{15}N-edited ^{1}H{^{15}N} NMR spectrum of [Pt(^{15}N-en){d(TpGpG)-*N7(2),N7(3)*}]$^{2+}$ (**3**) at various temperatures and pH values. Protons on the same coordinated N atom are paired.

The *N7,N7* G-G coordinated di- and trinucleotide complexes are constrained to a head-to-head (H8's of coordinated purines on the same side of the PtN_4 plane), anti-anti, left-handed minihelical configuration in solution.[20] In head-to-tail mononucleotide complexes [Pt(en)X_2], e.g., X = 5′-GMP, 5′-dGMP, or 5′-AMP, with terminal 5′-phosphate groups, NH···5′-(dianionic)phosphate H bonding produces large low-field shifts of N-H resonances (Table 1).[13] This also appears to be the case of the dinucleotide complex **2**. Since the NH shifts of **1**, which lacks a 5′-phosphate, are similar to those of **3**, which has a 5′-phosphate, a possible conclusion is that in solution N-H···5′-phosphate H bonding in these polynucleotide complexes may be very weak. This appears to conflict with the conclusions of Kline et al.,[9] Fouts et al.,[10] and Bloemink et al.[11] who have attributed the low-field shift of GpG (3′-phosphate) ^{31}P NMR resonances in several oligonucleotide−GpG-*N7,N7* Pt(II) complexes to Pt−NH···5′-phosphate H bonding. These low-field GpG ^{31}P shifts are probably determined by distortions in the α (P−O5′) and γ (C5′−C4′) backbone torsional angles from *gauche−gauche* toward *trans−trans*. However, it is curious that if such H bonding exists that the ^{31}P shift of the 5′-phosphate is unaffected, and also that the GpG ^{31}P shift exhibits very little dependence on temperature over a wide range (5−50 °C).[10] It is possible that there are alternative explanations for the low-field ^{31}P shifts. The group in Nijmegen[22] has reported that H bonding between diester phosphates and amino groups (e.g., in poly A) leads to upfield shifts of ^{31}P resonances of up to 1.8 ppm, but note that the mechanisms underlying the shifts are not understood. The interpretation of our NH NMR data is, however, ambiguous since it cannot be assumed that a bridging 5′-phosphate (diester) in a polynucleotide will induce the same Pt−NH···phosphate H-bonding shifts as a terminal 5′-phosphate. The NH shift may simply be insensitive to such interactions.

The observed temperature dependences of Pt−NH ^{1}H NMR resonances do not clarify the H-bonding picture. The most strongly low-field-shifted NH resonances might be expected to have the lowest temperature dependences if they are the most strongly H-bonded and therefore shielded from solvent, but this is not the case (Table 2). In peptides the most strongly H-bonded NH protons have the lowest temperature dependences with coefficients of $<|-5 \times 10^{-3}|$ ppm K^{-1}.[23] The most low-field-shifted NH resonance of **2** (NH_a) has the highest temperature dependence ($|-10.1 \times 10^{-3}|$ ppm K^{-1}) of all those we have measured so far, and therefore new empirical rules will have to be established for Pt−amine complexes.[13] It seems likely that the temperature-induced shifts we observe are influenced by equilibria between different structural forms of the complexes.

Our data do not rule out possible contributions from N−H···C6O H bonding; this type of H bond is known to be important in stabilizing the conformation of Pt-coordinated G bases in the solid state, e.g., in *cis*-[Pt(NH_3)$_2$]{d(CpGpG)-*N7(2)-N7*(3)}]$^{2+}$,[24] and in solution has been inferred from NOE data

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to be present in the mononucleotide complexes [Pt(*N,N*-dimethyl-2,3-diaminobutane)X_2]$^{2+}$ (X = 5′-GMP or 5′-dGMP; pH 3, monoanionic phosphate groups).[25] However, we have recently observed[26] a heteronuclear NOE between the NH protons of [Pt(^{15}N-en)(5′-GMP-*N7*)$_2$]$^{2+}$ and ^{31}P at pH 7.2, which provides further confirmation that NH···5′-phosphate H bonding is involved in the stabilization of this complex. Moreover, an even stronger NOE was observed at pH 3.9 (where the phosphate group is monoanionic and most similar to a phosphodiester group), and in crystals of this complex obtained at low pH there is intramolecular NH···(monoanionic)5′-phosphate H bonding. These data suggest that NH shifts alone are indeed not simply diagnostic of H bonding with monoanionic phosphate groups.

It will be interesting to extend ^{1}H, ^{15}N NMR studies to platinated oligonucleotide duplexes to see whether possible "end-effects" in short oligonucleotides, such as those used here, influence H bonding by bridging phosphates.

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Supplementary Material Available: Dependence on pH of the ^{15}N-edited ^{1}H{^{15}N} NMR spectrum of [Pt(^{15}N-en){d(GpG)-*N7(1),N7(2)*}]$^{2+}$ **1** at 300 K (Figure D1); 400 MHz 2D [^{1}H, ^{15}N] HMQC NMR spectrum of [Pt(^{15}N-en){d(pGpG)-*N7(1),N7(2)*}]$^{2+}$ **2**, pH 7.3 with an ^{15}N-edited ^{1}H{^{15}N} NMR spectrum shown as a projection (Figure D2); 500 MHz ^{1}H NMR spectrum of [Pt(^{15}N-en){d(TpGpG)-*N7(2),N7(3)*}]$^{2+}$ **3**, pH 4.4, 333 K, showing the 4 nonequivalent NH resonances, H1′ and H8 peaks with the ^{15}N-edited ^{1}H{^{15}N} NMR spectrum shown as an insert (Figure D3); and 500 MHz 2D [^{1}H, ^{15}N] HMQC NMR spectrum of [Pt(^{15}N-en){d(TpGpG)-*N7(2),N7(3)*}]$^{2+}$ **3**, pH 4.4, 333 K with an ^{15}N-edited ^{1}H{^{15}N} NMR spectrum shown as a projection (Figure D4) (4 pages). Ordering information is given on any current masthead page.