FT-IR and ^{1}H NMR Spectroscopic Studies of C2′-*endo*, C3′-*endo* Sugar Ring Conformations in 5′-GMP and 3′-GMP Nucleotides and their Platinum Complexes

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A study of the sugar conformations in *cis*-Pt-$(NH_3)_2$ (oligonucleotide) complexes in aqueous solution by high field nuclear magnetic resonance spectroscopy has been recently reported [1]. Utilizing the same technique, Polissiou *et al.* [2] demonstrated that the C2′-*endo* ⇄ C3′-*endo* and *gg* ⇄ *gt*/*tg* conformational equilibria in 5′-$GMPNa_2$ are influenced by formation of platinum complexes in aqueous solution. It was concluded that complexation at N7 of guanine increased the proportion of the C3′-*endo*, *anti*, *gg* sugar pucker. Theophanides and Tajimir-Riahi have reported FT-IR spectra in the solid state of 5′-$GMPNa_2$ and 5′-$IMPNa_2$, and of the corresponding transition metal adducts [3]. They further proposed the presence of diagnostic bands in the spectra, attributed to the various conformations of the sugar moiety.

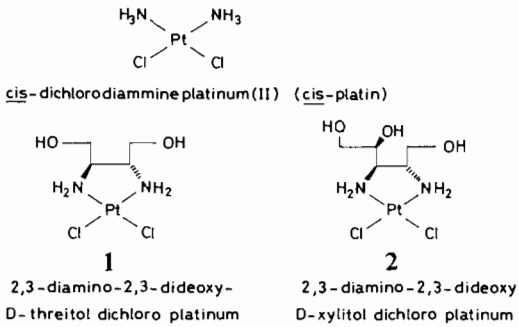

Fig. 1. Molecular structures of *cis*-platin and optically pure diamino(polyol) platinum(II) complexes.

In this study we report the conformational changes associated with the sugar portion of 5′-$GMPNa_2$ and 3′-$GMPNa_2$ upon interaction with several platinum complexes (Fig. 1) as evidenced by FT-IR spectroscopy. The results are compared with those obtained from X-ray analysis and ^{1}H NMR spectroscopic data.

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Experimental

The FT-IR spectra were recorded in the 1000–600 cm^{-1} region of the electromagnetic spectrum in search of marker bands for the different sugar puckerings. All the platinum complexes were synthesized according to the methods described in the literature [2]*.

Results and Discussion

X-ray structural analysis has shown that the sugar moiety in 5′-$GMPNa_2 \cdot 7H_2O$ [5] has the C2′-*endo*, *anti*, *gg* conformation, while the 5′-GMP free acid [6] has the C3′-*endo*, *anti*, *gg* conformation. In the crystal structure of the polymeric Cu_3(5′-GMP)$_3 \cdot 8H_2O$ [7], two of the 5′-GMP sugars have the C3′-*endo*, *anti*, *gg* conformation and the third 5′-GMP sugar has the C2′-*endo*, *anti*, *gg* conformation, the copper atom being bound to the N7 and the

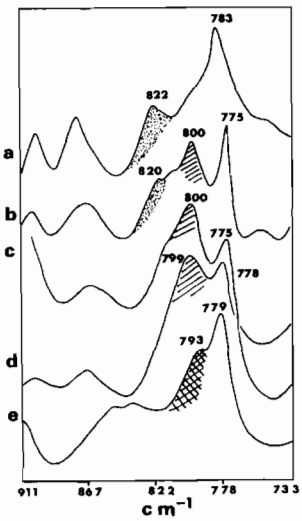

Fig. 2. FT-IR spectra of guanosine nucleotides and their platinum complexes: (a) 5′-$GMPNa_2$, (b) Cu_3(5′-GMP)$_3 \cdot 8H_2O$, (c) 5′-GMP free acid, (d) *cis*-$[Pt(NH_3)_2$(5′-GMP)$_2]^{2+}$, (e) *cis*-$[Pt(NH_3)_2$(3′-GMP)$_2]^{2+}$.

phosphate group. The FT-IR spectra of these compounds are shown in Fig. 2. It was reported [3] that the sugar ring in 5′-$GMPNa_2$ adopts a C2′-*endo*, *anti* conformation and shows a characteristic band at 822 cm^{-1} assigned to a sugar-phosphate vibrational mode. The FT-IR spectra of Cu_3(5′-GMP)$_3 \cdot 8H_2O$ also shows the marker band at 820 cm^{-1} (C2′-*endo*, *anti*). The other marker band at 800 cm^{-1} is characteristic of C3′-*endo*, *anti* conformation. The FT-IR spectra of 5′-GMP free acid and Cd(5′-GMP)$\cdot 8H_2O$

*For a synthesis and X-ray analysis of the *cis*-platinum complexes of diaminoalditols see ref. 4.

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TABLE I. Chemical Shifts, Coupling Constants, and Conformational Population of Guanosine Mononucleotides and their Platinum Complexes

Compound	(ppm) H8	*J* (Hz)					C(4′)–C(5′)	Ribose ^{3}E(%)
		1′2′	2′3′	3′4′	4′5′	4′5″	*gg* ⇄ *g/t*	
5′-GMPNa$_2$ [a]	8.20	6.1	5.2	3.4	3.7	3.7	65 35	36
cis-[Pt(NH$_3$)$_2$(5′-GMP)$_2$]$^{2+}$ [a]	8.63	4.4	4.6	4.7	3.4	3.6	69 31	50
[Pt(diaminodiol)$_2$(5′-GMP)$_2$]$^{2+}$ from **1**	8.83	4.4	5.2	3.8	b	b	b	40
[Pt(diaminotriol)$_2$(5′-GMP)$_2$]$^{2+}$ from **2**	8.50	4.8	4.9	4.3	b	b	b	45
	8.35	4.8	5.0	4.3				45
3′-GMPNa$_2$	8.00	5.8	5.4	3.7	3.6	3.7	66 34	39
cis-[Pt(NH$_3$)$_2$(3′-GMP)$_2$]$^{2+}$	8.46	3.2	4.9	6.3	2.8	4.3	68 32	66

[a]Ref. 2. [b]The peaks are masked by the ligands diaminodiol and diaminitriol. 400 MHz ^{1}H NMR were taken in D_2O, and DSS was used as external reference.

[3] also show the band at 800 cm^{-1}. This indicates that in Cu$_3$(5′-GMP)$_3$·8H$_2$O and 5′-GMP free acid the band at 800 cm^{-1} can be assigned to the C3′-*endo*, *anti* sugar phosphate vibrations and this is consistent with the results of X-ray analyses [5, 6, 7].

The conformation of the sugar ring in *cis*-[Pt(NH$_3$)$_2$(5′-GMP)$_2$]$^{2+}$ has been studied by ^{1}H NMR spectroscopy [2]. In aqueous solution this complex has mixed equal proportions of C2′-*endo*, *anti* and C3′-*endo*, *anti* conformations. On the other hand, in the solid state, the FT-IR spectrum of *cis*-[Pt(NH$_3$)$_2$(5′-GMP)$_2$]$^{2+}$ shows the marker band at 799 cm^{-1}, which correlates well with the bands observed in the metal complexes, Cd(5′-GMP)·8H$_2$O and Cu$_3$(5′-GMP)$_3$·8H$_2$O, corresponding to the C3′-*endo*, *anti* conformation [3]. In addition, the FT-IR spectrum of *cis*-[Pt(NH$_3$)$_2$(5′-GMP)$_2$]$^{2+}$ does not show the band at around 820 cm^{-1}, characteristic of the C2′-*endo*, *anti* conformation. Hence, the ribose ring of *cis*-[Pt(NH$_3$)$_2$(5′-GMP)$_2$]$^{2+}$ adopts a predominantly C3′-*endo*, *anti* conformation in the solid state. Similarly, in aqueous solution the conformational population of C3′-*endo* form for the diamino(polyol) bis-5′-GMP platinum(II) complexes, [Pt(diaminodiol)(5′-GMP)$_2$]$^{2+}$ and [Pt(diaminotriol)(5′-GMP)$_2$]$^{2+}$ prepared from the optically pure complexes shown in Fig. 1, were calculated to be 40 and 45%, respectively (Table I). The FT-IR spectra of these complexes in the solid state show the marker bands at 800 and 799 cm^{-1}, respectively with the absence of the band at around 820 cm^{-1}, indicating that the ribose moiety in these complexes adopts predominantly a C3′-*endo*, *anti* conformation. In Table I the conformational populations of C3′-*endo*, *anti* for 3′-GMPNa$_2$ and *cis*-[Pt(NH$_3$)$_2$(3′-GMP)$_2$]$^{2+}$ have also been calculated. In aqueous solution the C3′-*endo* conformational population of 3′-GMPNa$_2$ is 39%, and the ribose ring of 3′-GMPNa$_2$ has a larger proportion of C3′-*endo* conformation than that of 5′-GMPNa$_2$. The ribose ring of the complex, *cis*-[Pt(NH$_3$)$_2$(3′-GMP)$_2$]$^{2+}$ adopts predominantly a C3′-*endo* conformation (~66%). In the solid state, such a tendency seems to be stronger than in aqueous solution. As is shown in Fig. 2, the FT-IR spectra of 3′-GMPNa$_2$ and *cis*-[Pt(NH$_3$)$_2$(3′-GMP)$_2$]$^{2+}$ give the marker bands at 791 and 793 cm^{-1}, respectively. This indicates that both sugar rings in 3′-GMPNa$_2$ and its platinum complex adopt a predominantly C3′-*endo* conformation.

From these FT-IR and ^{1}H NMR spectroscopic studies it can be concluded that in aqueous solution, the conformational population of C3′-*endo* form of the sugar moiety in bis-5′-GMP platinum(II) complexes and 3′-GMPNa$_2$ is 40–50%, whereas in 5′-GMPNa$_2$ it is 36% and in the *cis*-[Pt(NH$_3$)$_2$(3′-GMP)$_2$]$^{2+}$ complex it is 66%. It is suggested from these results that platination or protonation at N7 of guanine causes a change in the ribose ring conformation from C2′-*endo* (822 cm^{-1}) to C3′-*endo* (~800 cm^{-1}) in 5′-GMPNa$_2$, whereas in 3′-GMPNa$_2$ and its complex, *cis*-[Pt(NH$_3$)$_2$(3′-GMP)$_2$]$^{2+}$ such a sugar conformational change is much less prevalent. This is most probably due to the phosphodiester linkage at the 3′-OH position of the sugar which is not easily perturbed by platination at the N7 site of guanine. The sugar moiety seems to be much less flexible when the phosphate group is at the 3′-OH site of the GMP molecule.

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