Inorganica Chimica Acta, 108 (1985) 237–239

FT-IR and ^{1}H NMR Spectroscopic Evidence of Sugar Ring Conformational Change in NH_4GpG on Complexation to form *cis*-$[Pt(NH_3)_2(GpG)]^+$

KOJI OKAMOTO, VICTOR BEHNAM and THEOPHILE THEOPHANIDES*

Department of Chemistry, Université de Montréal, Montreal, Que., H3C 3V1, Canada

Received July 26, 1985

Abstract

The conformational change of the ribose ring in NH_4GpG and *cis*-$[Pt(NH_3)_2(GpG)]^+$ was confirmed by FT-IR spectroscopic evidence as being C2′-*endo*, C3′-*endo*, *anti*, *gg* sugar ring pucker in the solid state. These results were compared with ^{1}H NMR spectral data in aqueous solution. The FT-IR spectrum of NH_4GpG shows marker bands at 802 cm^{-1} and 797 cm^{-1} which are assigned to the C3′-*endo*, *anti*, *gg* sugar-phosphate vibrations of ribose (–pG) and ribose (Gp–), respectively. The FT-IR spectrum of *cis*-$[Pt(NH_3)_2(GpG)]^+$ (with N7–N7 chelation in the GpG sequence) shows a marker band at 800 cm^{-1} which is assigned to the C3′-*endo*, and a new shoulder band at 820 cm^{-1} related to a C2′-*endo* ring pucker. The ribose conformation of (–pG) moiety in NH_4-GpG, C3′-*endo*, *anti*, *gg* changes into C2′-*endo*, *anti*, *gg* when a platinum atom is chelated to N7–N7 in the GpG sequence.

Introduction

Until now, only three oligonucleotide–platinum complexes containing the complex d(–GpG–)·*cis*-Pt have been the subject of conformational analysis in aqueous solution [1]. In all adducts the d(–GpG–)·*cis*-Pt fragments appear to adopt a geometry in which the bases are *anti*, *gg* with respect to the sugar rings. The 5′-terminal (Gp–) ring adopts a 100% C3′-*endo* conformation, whereas the 3′-terminal (–pG) ring adopts about 70–90% C2′-*endo* conformation. In the solid state, FT-IR spectroscopy has also been useful to identify the sugar conformational change as previously reported [2].

In the present work, the conformational change of the ribose ring in NH_4GpG and *cis*-$[Pt(NH_3)_2$-$(GpG)]^+$ was confirmed by FT-IR spectroscopic evidence being C2′-*endo*, C3′-*endo*, *anti*, *gg* sugar ring pucker in the solid state. These results were compared with ^{1}H NMR (400 MHz) data in aqueous solution. The FT-IR spectra were compared to those previously reported [2], and all the platinum complexes were prepared according to the methods described in the literature [3] except that the isolation of the complex, *cis*-$[Pt(NH_3)_2(GpG)]^+$ was obtained from the crude reaction mixture which was evaporated at 40 °C to reduce the volume and then precipitated with acetone.

Results and Discussion

The ribose ring pucker in RNA double helix is normally C3′-*endo*, *anti*, *gg* [4] as is found by X-ray analyses in NaGpC and CaGpC [5]. These results strongly suggest that the two ribose rings in NH_4GpG adopt a C3′-*endo* conformation, as is also found by FT-IR spectroscopy which also supports the C3′-*endo* conformation in both (Gp–) and (–pG) ribose rings as is shown in Fig. 1.

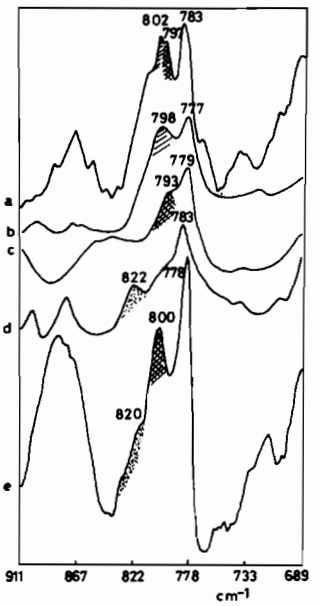

Fig. 1. FT-IR spectra of guanosine nucleotides and their platinum complexes: (a) NH_4GpG, (b) *cis*-$[Pt(NH_3)_2(5'$-$GMP)_2]^{2+}$, (c) *cis*-$[Pt(NH_3)_2(3'$-$GMP)_2]^{2+}$, (d) 5′-$GMPNa_2$, (e) *cis*-$[Pt(NH_3)_2(GpG)]^+$.

*Author to whom correspondence should be addressed.

0020-1693/85/$3.30

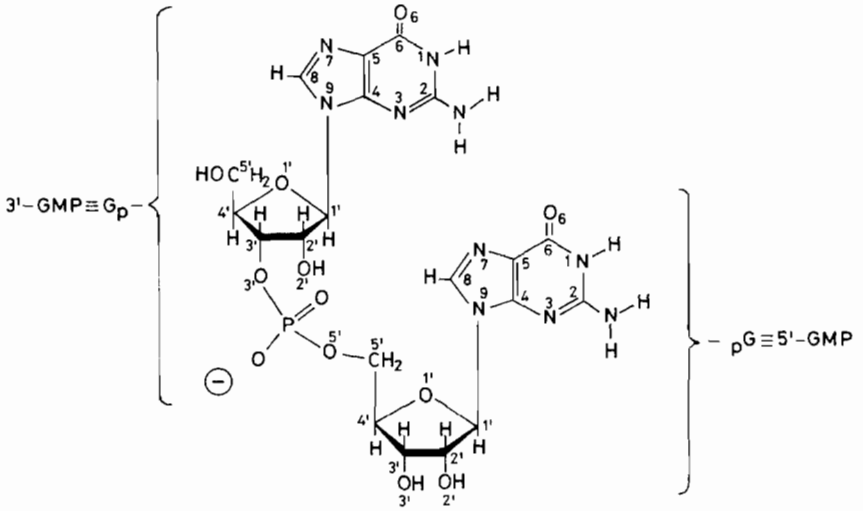

Fig. 2. Structural relationships in NH_4GpG, 3'-GMP, and 5'-GMP.

The FT-IR spectra of NH_4GpG shows marker bands at 802 and 797 cm^{-1}. The spectra of *cis*-$[Pt(NH_3)_2(5'\text{-}GMP)_2]^{2+}$ and *cis*-$[Pt(NH_3)_2(3'\text{-}GMP)_2]^{2+}$ show these bands at 798 and 793 cm^{-1}, these bands are assigned to the C3'-*endo, anti, gg* sugar–phosphate vibrations as has been reported previously [2]. However, the spectra of 5'-$GMPNa_2$, having a C2'-*endo, anti, gg* conformation, shows the marker band at 822 cm^{-1} but the characteristic band at 800 cm^{-1} is absent. As is shown in Fig. 2 the structure of NH_4GpG consists of 3'-GMP(Gp–) and 5'-GMP(–pG) fragments. The two bands of NH_4-GpG at 802 and 797 cm^{-1} are thus assigned to ribose (–pG) and ribose (Gp–), respectively. Therefore, both sugar rings adopt predominantly a C3'-*endo* conformation. In aqueous solution, an NMR conformational analysis can be obtained by calculating the percentage of C2'-*endo* conformer of the dinucleotides by taking the value of $10J_{1'2'}$ [6]. From the coupling constants (5.87 ppm, $J_{1'2'}$ = 4.8 Hz and 5.78 ppm, $J_{1'2'}$ = 4.4 Hz) in NH_4GpG the percentage of C2'-*endo* of both ribose rings were 48% and 44%, respectively, in aqueous solution. These results are different, however, from those of FT-IR spectroscopy and X-ray analysis of GpC salts in the solid state.

The FT-IR spectra of *cis*-$[Pt(NH_3)_2(GpG)]^+$ with N7–N7 chelation in the GpG sequence shows a marker band at 800 cm^{-1}, assigned to the C3'-*endo* and a new shoulder band at ~820 cm^{-1} related to a C2'-*endo* ring pucker. The former band will be related to the sugar–phosphate vibrational band of the ribose ring in (Gp–) and the latter is undoubtedly due to that of the ribose in (–pG). The band which was observed at 802 cm^{-1} in NH_4GpG corrresponding to the (–pG) ribose fragment has disappeared in *cis*-$[Pt(NH_3)_2(GpG)]^+$ and a new shoulder band has been observed at 820 cm^{-1} in the GpG–platinum complex. It seems that the C2'-*endo* sugar–phosphate vibration in the (–pG) fragment is the same as that in 5'-$GMPNa_2$.

In aqueous solution, the ^1H NMR spectra of the GpG–platinum complex exhibited one singlet at 6.04 ppm and one doublet at 5.87 ppm ($J_{1'2'}$ = 6.9 Hz) in agreement with results previously reported [3]. The absence of the $J_{1'2'}$ value shows that the ribose ring adopts a 100% C3'-*endo* conformation, whereas the other $J_{1'2'}$ value shows that the second ribose ring has a predominantly (~70%) C2'-*endo* conformation. These ^1H NMR results are in agreement with the FT-IR spectroscopic data. It is found that the ribose conformation in both (Gp–) 797 cm^{-1} and (–pG) 802 cm^{-1} is C3'-*endo, anti, gg* in NH_4GpG and changes into (Gp–) 800 cm^{-1} C3'-*endo, anti, gg* and (–pG) 820 cm^{-1} C2'-*endo, anti, gg,* respectively, when a platinum atom is chelated to N7–N7 in the GpG sequence. This finding may be significant to the antitumor activity of *cis*-platinum and its interaction with DNA.

In conclusion, the conformational study of NH_4-GpG and its adduct with *cis*-platinum reveals the following interesting sugar–phosphate change on complexation of the dinucleotide. In the natural free dinucleotide the sugar ring pucker in (Gp–) and (–pG) fragments is C3'-*endo, anti, gg,* however on complexation with the drug *cis*-platinum the (Gp–) sugar ring does not change, whereas the (–pG) sugar ring pucker changes predominantly into C2'-*endo, anti, gg.*

References

1 (a) J. H. J. Hartog, C. Altona, J. C. Chottard, J. P. Girault, J. Y. Lallemand, F. A. A. M. Leeuw, A. T. M. Marcelis and J. Reedijk, *Nucleic Acids Res., 10,* 4715 (1982) (b)

J. M. Neumann, S. Tran-Dinh, J. P. Girault, J. C. Chottard, T. Huynh-Dinh and J. Igolen, *Eur. J. Biochem., 141,* 465 (1984); (c) J. H. J. Hartog, C. Altona, G. A. V. Marel and J. Reedijk, *Eur. J. Biochem., 147,* 371 (1985).

2 (a) T. Theophanides and H. A. Tajmir-Riahi, *J. Biomol. Struct. Dyn., 2,* 995 (1985); (b) T. Theophanides and H. A. Tajmir-Riahi, in E. Clementi, C. Corongin, M. H. Sarma and R. H. Sarma (eds.), 'Structure & Motion: Membranes, Nucleic Acids & Proteins', Adenine, New York, 1985, p. 521.

3 (a) P. C. Kong and T. Theophanides, *Inorg. Chem., 13,* 1167 (1974); (b) J. C. Chottard, J. P. Girault, G. Chottard, J. Y. Lallemand and D. Mansuy, *J. Am. Chem. Soc., 102,* 5565 (1980); (c) J. P. Girault, G. Chottard, J. Y. Lallemand and J. C. Chottard, *Biochemistry, 21,* 1352 (1982).

4 S. Arnott and D. W. L. Hukins, *J. Mol. Biol., 81,* 93 (1973).

5 (a) J. M. Rosenberg, N. C. Seeman, R. O. Day and A. Rich, *J. Mol. Biol., 104,* 145 (1976); (b) B. Hingerty, E. Subramanian, S. D. Stellman, T. Sato, S. B. Broyde and R. Langridge, *Acta Crystallogr., Sect. B:, 32,* 2998 (1976).

6 (a) C. Altona and M. Sundaralingam, *J. Am. Chem. Soc., 95,* 2333 (1973); (b) C. Altona, *Recl. Trav. Chim. Pays-Bas, 101,* 413 (1982).