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Vibrational Spectra of the Diammineplatinum(II) Disodium 5′-Uridine Monophosphate Blue Complex[†]

VICTOR BENHAM

Département de Chimie, Université de Montréal, Montreal, C.P. 6128, Succ. A, Que. H3C 3J7, Canada and Department of Chemistry, McGill University, 801 Sherbrooke St. West, Montreal, Que., H3A 2K6, Canada

IAN S. BUTLER*

Department of Chemistry, McGill University, 801 Sherbrooke St. West, Montreal, Que., H3A 2K6, Canada

KOJI OKAMOTO** and THEOPHILE THEOPHANIDES*

Département de Chimie, Université de Montréal, Montreal, C.P. 6128, Succ. A, Que., H3C 3J7, Canada

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Abstract

The blue complexes produced by reaction of *cis*-diamminediaquoplatinum(II) nitrate, [*cis*-Pt$(NH_3)_2$-$(H_2O)_2$]$(NO_3)_2$, with disodium 5′-uridine monophosphate, 5′-UMP(Na_2), in H_2O and D_2O have been investigated by FT-IR spectroscopy. On the basis of the spectral changes observed in the C=O stretching region during the reactions, chelation of the amidate N(3)··O(2) moiety to Pt(II) appears to be more likely than N(4)··O(4) chelation. The antisymmetric P–O stretching mode of the PO_3^{2-} group of 5′-UMP splits into a triplet on complex formation indicating that PO_3^{2-} plays an important role in the structure of the platinum blue complexes. In addition, the sugar moiety of 5′-UMP apparently adopts a predominantly C(3′)-endo conformation in the solid blue complex. Finally, Raman microprobe spectroscopy of the solid provides some evidence for Pt–N(3) bond formation.

Introduction

In 1975, 'platinum pyrimidine blues' [1] were shown to be antitumor agents with lower nephrotoxicities than that for the licenced anti-cancer drug cisplatin, [*cis*-diamminedichloroplatinum(II), *cis*-Pt$(NH_3)_2Cl_2$, DDP] [2, 3]. To date, apart from *cis*-diammineplatinum α-pyridone blue (PPB), which has been fully characterized [4–9], no structural evidence has been reported for these paramagnetic, amorphous blue compounds despite extensive studies of their physicochemical properties [10–13]. However, amidate-bridged, oligomeric species involving considerable Pt–Pt interaction and mixed valence states have been suggested by analogy with the known structure of PPB.

A major class of platinum pyrimidine blues is produced by the interaction of the aquated products of DDP with polyuracil, uracil, 1-methyluracil, uridine, thymine, and other related pyrimidines [2, 14–17]. In these species, the platinum atoms are either bonded to N(1) or N(3) of the pyrimidine base to form mononuclear complexes or to a combination of N(1) [or N(3)] and one of the exocyclic atoms [O(2), O(4) or N(4)] in pyrimidine-bridged binuclear complexes. Attempts to obtain structural information on these platinum blue compounds have thus far been unsuccessful [17–19] because of the wide variety of possible products due to the multiplicity of binding sites available. However, spectroscopic, magnetic and chemical evidence suggests that they contain partially-oxidized, multinuclear chains of amidate bridged *cis*-Pt$(NH_3)_2$ units [4, 5, 9].

In this paper, we present the results of a FT-IR spectroscopic investigation of the platinum blue complex produced by reaction of [*cis*-Pt$(NH_3)_2$-$(H_2O)_2$]$(NO_3)_2$ with the mononucleotide, disodium 5′-uridine monophosphate [5′-UMP$(Na)_2$] in H_2O and D_2O. Some Raman microprobe data for the solid blue complex are also reported.

Experimental

The platinum blue complex was prepared by the 1:1 reaction of [*cis*-Pt$(NH_3)_2(H_2O)_2$]$(NO_3)_2$ with 5′-UMP$(Na)_2$ (Sigma Chemical Co.) in H_2O (or D_2O).

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*Authors to whom correspondence should be addressed.

**Present address: Precious Metal Products Co. Ltd., 2015-7 Ichikawa, Chiba, 272-01, Japan.

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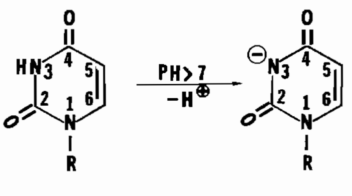
The pH (or pD) of the reaction mixture was adjusted to about 7.0, using NaOH (or NaOD). Under these conditions, the reaction proceeds slowly and a blue coloration appears after 2–3 h. The color intensified to a deep purple–blue after 24 h. The solution was then slowly evaporated to dryness to yield a solid residue.

The deuterated compound, [*cis*-Pt$(ND_3)_2(D_2O)_2$]-$(NO_3)_2$, was prepared by treating [*cis*-Pt$(NH_3)_2$-$(H_2O)_2$]Cl_2 with a solution of $AgNO_3$ (2 M) in D_2O in the dark. The solution was evaporated to near dryness and then a little D_2O was added. This evaporation–dissolution procedure was repeated several times to yield the desired product. Deuteration of 5′-UMP(Na_2) was performed in a similar manner.

The FT-IR spectra (approximately 5000 scans) were recorded at 2–4 cm^{-1} resolution on a nitrogen-purged, Digilab IFS 15/C spectrometer equipped with a deuterated triglycine sulfate (TGS) detector and a KBr beamsplitter. Solution spectra were obtained using a home-made liquid cell fitted with a pair of matched KRS-5 windows and a 5–7 μ spacer. The inner surfaces of the windows were flat to within five fringes of the Na D-line. The Raman microprobe spectrum (2–3 cm^{-1} resolution) of the solid blue compound was obtained on an Instruments S.A. U-1000 Ramanor spectrometer using the 519.62-nm line from a rhodamine-6G dye laser (Spectra Physics) for excitation. The laser was operated at low power (10 mW at the sample) with the beam slightly defocussed in order to minimize the risk of sample decomposition during data collection.

Results and Discussion

Uracil and its N(1)-substituted derivatives, including 5′-UMP(Na_2), adopt structure I in neutral and acidic solutions [20, 21]. Moreover, deprotonation of these derivatives in alkaline solutions results in an ionic residue with a considerable degree of π-electron delocalization throughout the O(2)···C(2)···N(3)···C(4)···O(4) network [20].



I II

The effect of a variety of electrophilic groups, such as $MeHg^+$ and $[Pt(NH_3)_2]^{2+}$, on pyrimidine nucleosides has been examined by IR, Raman, and NMR spectroscopy [22–24]. In the case of uracil derivatives, these electrophilic groups apparently induce extensive π-electron delocalization throughout the pyrimidine ring when they bind to the N(3) site. Similar conjugation effects have been proposed on the basis of LCAO–SCF calculations [25]. Accordingly, in the present work, we anticipated that interaction of [*cis*-$(NH_3)_2Pt(H_2O)_2]^{2+}$ with 5′-UMP(Na_2) via N(3) would induce a resonance effect in the uracil moiety. This situation is largely attributable to the polarizing power of Pt(II) and its strong electrophilic attraction to N(3).

In an effort to obtain more information on the nature of the platinum blue interaction, the FT-IR spectra in the C=O stretching region (1800–1600 cm^{-1}) of 5′-UMP(Na_2) and the products formed during reaction with [*cis*-Pt$(NH_3)_2(H_2O)_2](NO_3)_2$ in H_2O solution were monitored as a function of time (Fig. 1). Similar data for the D_2O solution are given in Fig. 2.

There has been a longstanding debate about the assignment of the two 5′-UMP(Na_2) peaks at 1690 and 1684 cm^{-1}. Several publications have

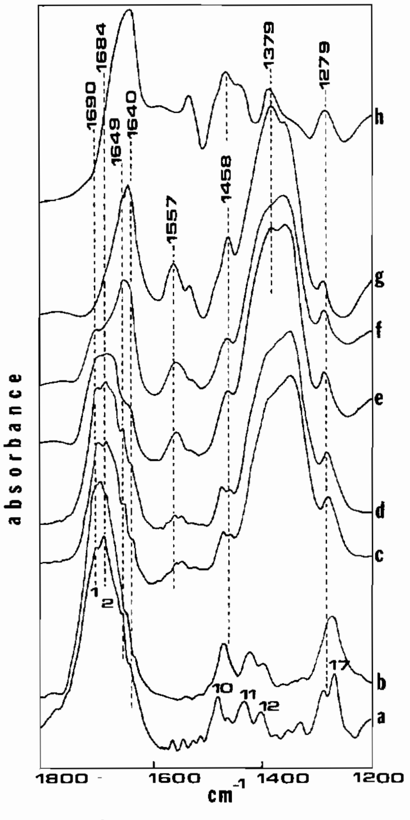


Fig. 1. Infrared spectra in the 1800–1200 cm^{-1} region of (a) solid 5′-UMP(Na_2) in H_2O, pH 6.5 and (b–g) [$(NH_3)_2$Pt-$(H_2O)_2](NO_3)_2$ + 5′-UMP(Na_2) in H_2O at 25 °C and total concentration of ~0.2 M [(c) after 30 min, pH 6.5; (d) after 1 h, pH 6.5; (e) after 4 h, pH 5.0; (f) after 8 h, pH 5.0; (g) after 24 h, pH 5.0]; (h) solid platinum blue complex.

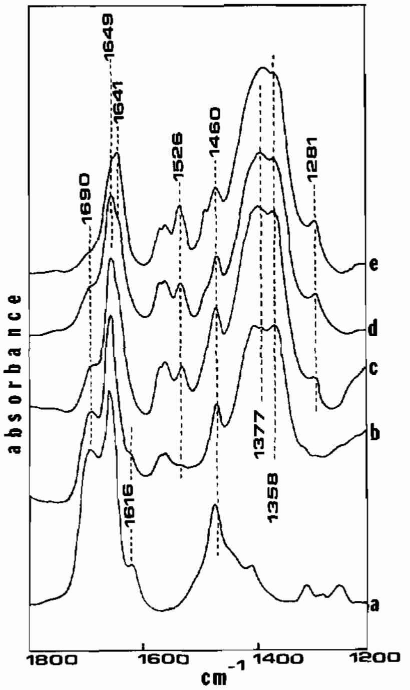


Fig. 2. Infrared spectra in the 1800–1200 cm^{-1} region of (a) 0.1 M 5'-UMP(Na$_2$) in D_2O, pH 6.5 and (b–e) [$(ND_3)_2$-$Pt(D_2O)_2$]$(NO_3)_2$ + 5'-UMP(Na$_2$) in D_2O at 25 °C and total concentration of ~0.2 M: (b) after 1 h, pD 6.0; (c) after 4 h, pD 6.0; (d) after 8 h, pD 5.4; (e) after 24 h, pD 5.4.

attributed them to C(4)=O and [C(4)=O + C(5)=C(6)] stretching, respectively [20, 21, 26]. Ultraviolet resonance Raman data have been reported for deoxyribonucleotides, including that of uracil in H_2O and D_2O [27]. From these results and those from a normal coordinate calculation [28], it was concluded that the three peaks at 1686, 1674 and 1628 cm^{-1} are mainly due to C(2)=O(47), C(4)=O(34) and C–N stretching, respectively. In D_2O, however, the corresponding modes lose their intensity in favour of new bands at 1700 [C(2)=O(63) str.], 1654 [C(4)=O(37) str.] and 1617 cm^{-1}. In another IR study, three bands were observed for uridine in D_2O at 1691, 1657 and 1618 cm^{-1}; the two higher-energy bands were assigned to C(2)=O and C(4)=O stretching, respectively [29].

In our work, the FT-IR spectrum of solid 5'-UMP-(Na$_2$) exhibits two very strong bands at 1690 and 1684 cm^{-1} which, in solution, appear to combine and shift to higher wavenumber giving rise to a very intense band at ~1705 cm^{-1}. This shift may be related to removal of carbonyl intermolecular coupling on going from the solid to solution. In D_2O, the pattern is identical to that in the IR spectrum of uridine. Deuteration at N(3) induces approximately a 15 cm^{-1} decrease for C(2)=O stretching (~1705 → 1690 cm^{-1}) and a ~48 cm^{-1} decrease for C(4)=O stretching (~1705 → 1657 cm^{-1}), indicating that N(3)–H probably plays a significant role in the potential energy distribution of the C(4)=O stretching mode.

From the data shown in Tables I and II, it is clear that interaction of DDP with 5'-UMP(Na$_2$) leads to some marked spectral changes in both H_2O and D_2O solution, especially in the C=O stretching region. The blue formation appears to be complete after about 24 h, judging by the complete disappearance of the initial carbonyl bands and the emergence of at least two new strong peaks at 1649 and 1640 cm^{-1} in H_2O solution. While there is no information at present about the interaction of Pt(II) with the carbonyl groups, the platinum is almost certainly coordinated to the N(3) site of uracil. In addition, for uridine or any other N(1)-substituted uracil derivative, if N(3) is blocked (e.g., by methylation), there is no reaction with DDP [16].

Figure 3 illustrates the Raman microprobe spectrum of the blue solid obtained by evaporation of a H_2O solution of the platinum blue. The broad band centered at ~334 cm^{-1} is assigned to Pt–N(3) binding by analogy with the Pt–N(7) mode observed at 369 cm^{-1} in the Raman spectrum of the Zwitterion [$PtCl_3$(9-methyladeninium)]$^-$ [35]. The weak, broad feature in the 600–500 cm^{-1} region, together with the associated IR band at 507 cm^{-1} (see dotted line in Fig. 3), are attributed to Pt–NH_3 on the basis of earlier work [35, 36].

When DDP is reacted with 5'-UMP(Na$_2$) in D_2O over a 24-h period, the C(4)=O + C(5)=C(6) mode at 1657 cm^{-1} shifts to lower energy by approximately 12 cm^{-1}. This may be attributed to a decrease in bond order of the corresponding carbonyl group due to deprotonation followed by platination of N(3). In a LCAO–SCF calculation for thymidine, it was estimated that proton transfer from N(3) to give a free anion is accompanied by transfer of about 0.75 e$^-$ over the molecule via σ and π systems. The changes with 5'-UMP(Na$_2$) should be very similar. About 0.25 e$^-$ moves on to each carbonyl group and 0.1 e$^-$ moves on to the C(5)=C(6) double bond, resulting in a decrease in both the bond order and wavenumber of the normal modes that involve carbonyl and C(5)=C(6) stretching. Therefore, substitution of H(3) by [$(NH_3)_2Pt$]$^{2+}$ in 5'-UMP(Na$_2$) will result in a decrease in wavenumber and an increase in intensity for a mode involving C(4)=O + C(5)=C(6) stretching. Accordingly, the more intense IR band at 1641.0 cm^{-1}, observed 24 h after the two reactants have been mixed, is assigned to C(4)=O + C(5)=C(6). Furthermore, the C(2)=O mode at 1690 cm^{-1} has shifted considerably ($\Delta = 41$ cm^{-1}) to a lesser intense band at 1649 cm^{-1}, suggesting that C(2)=O has strong interaction with Pt(II).

The 1636 cm^{-1} band of solid 5'-UMP(Na$_2$) is shifted to lower energy on complex formation: 1632.0 cm^{-1} in H_2O and 1616.0 cm^{-1} in D_2O. The

TABLE I. Observed Infrared Frequencies and Possible Assignments for the $[(NH_3)_2Pt(H_2O)_2](NO_3)_2$ + 5′-UMP(Na_2) System in H_2O and in the 1800–1200 cm^{-1} Region*

Band no.	a	b	c	d	e	f	g	h	Proposed assignments [20, 21, 26–29, 30–33]
1	1690.0(vs)	1705.0(vs)	1700.0(s)	1699.0(s)	1699.0(s)	1699.0(m)			νC(2)=O
2	1684.0(vs)		1686.0(s)	1684.0(s)	1688.0(s)				νC(4)=O + νC(5)=C(6)
3					1682.0(s)				+ δN(3)–H
4			1655.0(s)	1653.0(s)		1649.0(s)	1649.0(s)	~1645.0(s,br)	νC(2)=O
5	1636.0(m)	1632.0(m)	1638.0(m)	1638.0(s)			1640.0(s)		νC(4)=O + νC(5)=C(6)
6	1560.0(vw)		1558.0(w)	1558.0(w)	1551.0(m)	1555.0(s)	1555.0(s)	(br)	νring, νC–N (con. base)
7	1540.0(vw)		1543.0(w)	1543.0(w)					Combinations?
8	1521.0(w)		1527.0(vw)	1527.0(w)	1525.0(w)	1526.0(w)	1528.0(m)	1528.0(m)	νring, νC–N (con. base)
9	1518.0(w)		1508.0(vw)	1508.0(vw)					Combinations?
10	1476.0(ms)	1473.0(m)	1472.0(m)	1472.0(m)					νring, νC–N
			1458.0(m)	1458.0(m)	1460.0(s)	1458.0(s)	1458.0(s)	1458.0(s)	
11	1427.0(m)	1423.0(m)						~1425(s)	δC–N–H, νC–N
12	1398.0(m)	1400.0(m)	1400.0(vs)	1400.0(vs)	1380.0(vs)	1380.0(s)	1380.0(vs)	1379.0(vs)	
			1380.0(vs)	1380.0(vs)					$\nu_{asym}(NO_3)$, $\delta(NH_3)_{sym}$
13	1371.0(vw)								δCH(ribose)
14	1348.0(vw)		1348.0(vs)	1348.0(vs)	1348.0(vs)	1348.0(vs)	1348.0(vs)	(br)	
15	1328.0(w)	1327.0(vw)							νring, δC–H (base)
16	1286.0(m)	1277.0(m)	1281.0(m)	1281.0(m)	1281.0(m)	1283.0(m)	1285.0(m)	1279.0(m)	
17	1265.0(m)								νring, δN–H
		1221.0(vw)							
18	1200.0(vw)	1201.0(vw)							

*s = strong, vs = very strong, m = medium, ms = medium strong, br = broad, w = weak, vw = very weak. [a]Solid 5′-UMP(Na_2). [b]5′-UMP(Na_2) in H_2O, pH 6.5. [c–g]0.1 M $[(NH_3)_2Pt(H_2O)_2](NO_3)_2$ + 0.1 M 5′-UMP(Na_2) in H_2O, at 25 °C. [c]After 30 min, pH 6.5. [d]After 1 h, pH 5.0. [e]After 4 h, pH 5.0. [f]After 8 h, pH 5.0. [g]After 24 h, pH 5.0. [h]Solid platinum blue complex.

TABLE II. Observed Infrared Frequencies and Possible Assignments for the $[(ND_3)_2Pt(D_2O)_2](NO_3)_2$ + 5′-UMP(Na$_2$) System in D_2O and in the 1800–1200 cm^{-1} Region*

Band no.	a	b	c	d	e	f	Proposed assignments [20, 21, 26–29, 30–34, this work]
1	1690.0(vs)	1690.0(vs)	1690.0(m)	1684.0(m)	1680.0(br)		νC(2)=O
2	1684.0(vs)						νC(4)=O + νC(5)=C(6)
3							
4		1657.0(vs)	1655.0(vs)	1651.0(s)	1651.0(s)	1649.0(s)	νC(2)=O
5						1641.0(s)	νC(4)=O + νC(5)=C(6)
	1636.0(m)	1616.0(m)	1618.0(m)				νring
6	1560.0(vw)		1562.0(m)	1562.0(m)	1562.0(m)	1562.0(m)	νring, νC–N (conjugate base)
7	1540.0(vw)		1553.0(m)	1553.0(m)	1553.0(m)	1553.0(m)	
			1532.0(vw)				combinations?
8	1521.0(vw)		1520.0(vw)	1526.0(m)	1526.0(m)	1526.0(m)	νring, ν(C–N) (conjugate base)
9	1518.0(vw)						combinations?
10	1476.0(ms)				1485(n)	1485(m)	νring, νC–N
		1468.0(m)	1464.0(m)	1462.0(s)	1462.0(s)	1460(s)	
11	1427.0(m)						δC–N–H, νC–N
12	1398.0(m)	1400.0(m)	1393.0(vs)	1394.0(vs)	1394.0(vs)	1390.0(vs)	$\delta(NO_3)$, $\delta(NH_3)_S$, δCH (ribose) asym
13	1371.0(vw)			1381.0(vs)	1379.0(vs)	1377.0(vs)	
14	1348.0(vw)		1356.0(vs)	1356.0(vs)	1360.0(vs)	1360.0(vs)	
15	1328.0(w)	1300.0(w)					νring, δC–H (base)
16	1286.0(m)		1281.0(m)	1283.0(m)	1283.0(m)	1281.0(m)	
17	1265.0(m)	1271.0(vw)					νring, δN–H, νC–N
		1238.0(m)					δN–D
18	1200.0(w)						

*See footnote * of Table I. ^{a}Solid 5′-UMP(Na$_2$) in KBr. ^{b}5′-UMP(Na$_2$) in D_2O, pD 6.5. $^{c-f}$0.1 M $[(ND_3)_2Pt(D_2O)_2]$-$(NO_3)_2$ + 0.1 5′-UMP(Na$_2$) in D_2O, at 25 °C. ^{c}After 1 h, pD 6.0. ^{d}After 4 h, pD 6.0. ^{e}After 8 h, pD 5.4. ^{f}After 24 h, pD 5.4.

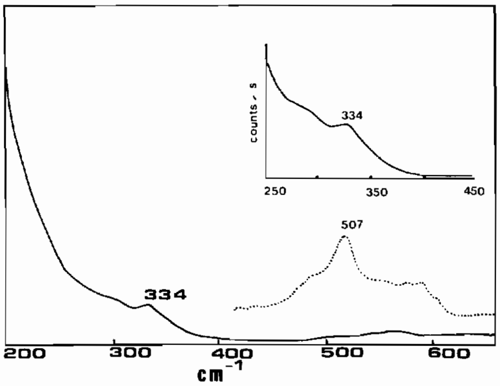


Fig. 3. Raman microprobe spectrum (solid line) of the solid platinum blue complex in the 650–200 cm^{-1} region at 25 °C. Conditions: excitation (519.62 nm), ~10 mW (at the sample); resolution, 400 μm; 95 coadded scans. The dotted line is the corresponding IR spectrum of the solid platinum blue complex.

fact that there is a difference between the spectra suggests vibrational coupling between C(4)=O and N(3)–H stretching. On the basis of normal coordinate analyses (including isotopic substitution), however, there are also major contributions to these bands from C(5)=C(6) and C(4)=O stretching [20, 21, 26, 27, 30]. In D_2O, the 1616 cm^{-1} band appears to lose its entire intensity on complexation with Pt(II).

On platination, the 1476 cm^{-1} band of solid 5′-UMP(Na$_2$) appears at 1458 cm^{-1} (in H_2O) and at 1460/1485 cm^{-1} (in D_2O). Some authors have attributed the 1476 cm^{-1} band chiefly to the π-ring [30], while others have assigned it mainly to C–N stretching [27, 28]. SCF calculations, on the other hand, have indicated that there would be an increase in overlap charge for the C(2)–N(3) and N(3)–C(4) bonds of 0.15 e$^-$ when an H(3) proton is removed. This means that all the lower-energy ring modes, particularly those associated with the above-mentioned bands, would be expected to increase. This may provide an explanation for the appearance of the IR modes observed at 1555, 1528 (H_2O) and 1562, 1553, 1526 cm^{-1} (D_2O) for the blue solutions that had reached their maximum intensities after 24 h. The fact that the spectra of platinum blue in both H_2O and D_2O are very similar suggests that the complex is essentially the same in both solvents and therefore any assignments should be independent of solvent influence. Therefore, these bands may have contributions from the ring, particularly along the C(2)–N(3)–C(4) network and may be considered as being characteristic IR marker bands for platinum blue solutions derived from N(1)-substituted uracil derivatives. An investigation of the interaction of DDP with uridine by Raman spectroscopy suggests that the only significant differences between the spectra of the colourless and blue solutions are that the latter have characteristic bands at 1526, 1485 (H_2O) and 1527, 1487 cm^{-1} (D_2O) [16]. Furthermore, it was proposed that these bands are indicative of C(2)=O and/or C(4)=O coordination by the uridine conjugate base.

In the solid state, 5′-UMP(Na_2) exhibits two medium-intense IR bands at 1286 and 1265 cm^{-1}. In H_2O, the corresponding bands seem to combine and appear at 1277 cm^{-1}, whereas in D_2O, in addition to the weak peak at ~1271 cm^{-1}, another medium intense band is observed at 1238 cm^{-1}. During the platination process, the corresponding bands in both H_2O and D_2O lose their intensity in favour of a mode at ~1280 cm^{-1}. These observations provide yet further evidence that the structure of the platinum blue in both H_2O and D_2O is very similar and therefore the 1280 cm^{-1} mode can be confidently assigned to the π-ring of the conjugate base. Further analysis of the IR spectra of 5′-UMP(Na_2) in the solid and solution media and in the absence of DDP reveals that these bands have some contributions from δ(NH) and/or ν(CN), in reasonable agreement with the literature [20, 26, 31]. By similar arguments, the 1238 cm^{-1} band of 5′-UMP(Na_2) in D_2O is ascribed to δ(ND) [20]. Support for this assignment comes from some recent FT-IR-ATR spectra of hydrated mononucleotides – for hydrated 5′-CMP(Na_2), the strong band at 1280 cm^{-1} was attributed to ring stretching band together with an external ν(CN) contribution [31].

Phosphate Vibrational Frequencies

As the reaction of 5′-UMP(Na_2) with DDP is proceeding, the symmetric and antisymmetric phosphate stretching modes undergo significant changes in both H_2O and D_2O solution (Figs. 4 and 5). The changes are more pronounced for the antisymmetric modes and essentially independent of the solvent. The bands due to antisymmetric stretching of the terminal-PO_3^{2-} groups of 5′-UMP(Na_2) are originally at 1109 (H_2O) and 1090 cm^{-1} (D_2O). These bands are split into a triplet upon formation of the blue complex indicative of strong interaction with Pt(II) [37]. When an equimolar mixture of *cis*-$[(NH_3)_2Pt(H_2O)_2](NO_3)_2$ and KH_2PO_4 at pH 3 is kept at 30 °C in contact with air, the solution changes from pale yellow to pale green within 30 min and to deep blue within 1 h [38]. From ESR measurements on the blue solution, it has been suggested that the phosphate blues consist primarily of oligomeric chains, with strong interactions between adjacent Pt atoms, with at least some Pt–O–P–O–Pt bridging. It is therefore reasonable to assume that in our case the Pt(II) ions initially interact with the terminal-PO_3^{2-} groups to produce the blue colour and as a consequence splitting of the antisymmetric P–O stretching mode into a triplet; ~1132, 1113, ~1082 (H_2O) and ~1132, ~1113, ~1084 cm^{-1} (D_2O). Furthermore, the modes at ~1061 (H_2O) and 1049 (D_2O) are assigned to ν_{sym}(NO). The gradual intensity decrease of the 1132 cm^{-1} band in both H_2O and D_2O over a 24-h period may indicate that the $[(NH_3)_2Pt(H_2O)_2]^{2+}$ groups show a slow but growing tendency towards coordination of the uracil moiety and a decreasing interaction with the phosphate groups.

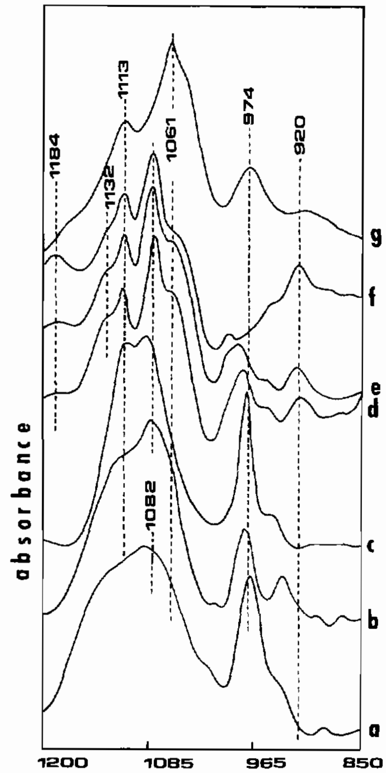


Fig. 4. Infrared spectra in the 1200–850 cm^{-1} region of (a) solid sodium D-ribose phosphate; (b) solid 5′-UMP(Na_2); (c) 0.16 M 5′-UMP(Na_2) in H_2O, pH 6.5; (d–f) $[(NH_3)_2Pt(H_2O)_2](NO_3)_2$ + 5′-UMP(Na_2) in H_2O at 25 °C and total concentration of ~0.2 M [(d) after 1 h, pH 6.5; (e) after 8 h, pH 5.0; (f) after 24 h, pH 5.0]; (g) solid platinum blue complex.

On platination, the P–O stretching modes of 5′-UMP(Na_2) at 978 (H_2O) and 974 cm^{-1} (D_2O) not only shift to higher energies, but also broaden and lose intensity appreciably. In the solid platinum blue complex (Fig. 4g), there is a corresponding broad band at 974 cm^{-1}. Clearly, the phosphate groups are active participants in the formation of the blue complex. The interaction of DDP with uracil, cytosine and thymine or any of their derivatives only produces the blue colour after several hours or, in some cases, a few days. The medium-intensity feature for solid 5′-UMP(Na_2) at ~936 cm^{-1} that seems to

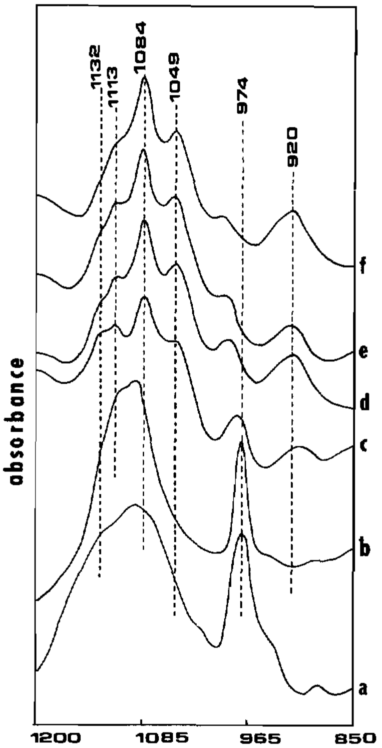


Fig. 5. Infrared spectra in the 1200–850 cm^{-1} region of (a) solid sodium D-ribose phosphate; (b) 0.1 M 5′-UMP(Na_2) in D_2O, pH 6.5; (c–f) $[(ND_3)_2Pt(D_2O)_2](NO_3)_2$ + 5′-UMP(Na_2) in D_2O at 25 °C and total concentration of ~0.2 M [(c) after 1 h, pD 6.3; (d) after 4 h, pD 6.0; (e) after 8 h, pD 6.0]; (f) after 24 h, pD 5.4].

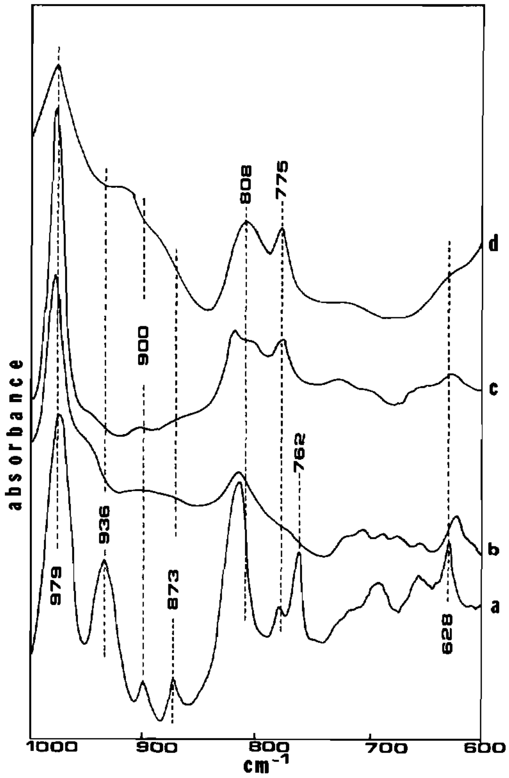


Fig. 6. Infrared spectra in the 1000–600 cm^{-1} region of (a) solid 5′-UMP(Na_2); (b) 5′-UMP(Na_2) in H_2O, pH 6.5; (c) 5′-UMP(Na_2) in D_2O, pD 6.5; (d) solid platinum blue complex.

lose most of its intensity in D_2O and shift to ~951 cm^{-1} in H_2O is attributed to a sugar vibration that is coupled to the phosphate group. On complexation, the corresponding band in both H_2O and D_2O loses intensity, most probably in favour of the medium, broad peak at ~920 cm^{-1}. Changes in the conformation of sugar may play an important role in this case. The IR spectra of the disodium guanosine 5′-monophosphate and disodium inosine 5′-monophosphate and some of their metal complexes have been recorded in the 1000–600 cm^{-1} region [39]. The spectra of the metal complexes show changes in the sugar–phosphate bands at 935 and 820 cm^{-1}. The intensities of these bands decrease in favour of a new band at ~805 cm^{-1} and the C2′-endo conformation changes to C3′-endo. Figure 6 shows that solid 5′-UMP(Na_2) displays a strong band at 816 cm^{-1} which seems to broaden and lose some of its intensity in H_2O and shifts to 800 cm^{-1} in D_2O [in this case, the 816 cm^{-1} band is probably associated with the undeuterated portion of 5′-UMP(Na_2)]. This solvent sensitive band is therefore attributed to a phosphate–sugar vibration, implying that probably the sugar conformation changes from C2′-endo (in solid and H_2O) to C3′-endo (in D_2O). From the IR spectrum of the solid platinum blue, the sugar moiety probably adopts a predominantly C3′-endo conformation due to the appearance of a band at ~808 cm^{-1}. This assignment should be treated with some caution, however, since ammine groups absorb in the same region [34, 40]. The proposed assignments for the bands observed in the 1200–850 and 850–600 cm^{-1} regions are listed in Tables III and IV, respectively.

Ammine and Nitrate Frequencies

Ammine groups exhibit two fairly strong IR bands in the 1400–1200 cm^{-1} region that have been attributed to $\delta(NH_3)_{sym}$ modes [34, 40]. Consequently, the strong absorptions observed in our work in the 1400–1300 cm^{-1} region in Figs. 1 and 2 are attributed to the ammine moiety and antisymmetric stretch of the free nitrate ion. Further features associated with the ammine moiety are the weak, broad bands located in the 1600–1500 cm^{-1} region which are gradually buried beneath the stronger π-ring modes of the conjugate base as the reaction proceeds. For platinum blues, the nitrate ions are reported to be weakly bound to the axial sites of the Pt(II) ions and essentially remain ionic [17]. Further support for this situation is obtained by comparing

TABLE III. Observed Infrared Frequencies and Possible Assignments for the $[(NH_3)_2Pt(H_2O)_2](NO_3)_2$ + 5′-UMP(Na_2) System in H_2O and D_2O in the 1200–850 cm^{-1} Region*

a	b	c		d		e		f		g		h	Proposed assignments [20, 37, 39, 41, 42, this work]
		H_2O	D_2O	H_2O	D_2O	H_2O	D_2O	H_2O	D_2O	H_2O	D_2O		
								1184(w,br)		1184(w,br)		(w,br)	
				1132(s,sh)	1132(s,sh)	1132(s,sh)	(sh)	1132(s,sh)		1132(s,sh)			
(s,vbr)	(s,vbr)	1109(s)	~1105(s)	1113(s)	1115(s)	1113(s)	1113(s)	1113(s)	1113(s)	1113(s)	~1113(s)	1113(s)	$\nu_{asym}(PO_4)$
1092(s,br)		1090(s)	1092(s)										
	1084(s)			1082(s)		1082(s)		1082(s)	1084(s)	1082(s)	1084(s)		
				~1061(s)	~1049(s)	~1061(s)	1047(s)	~1061(s)	1049(s)	~1061(s)	1047(s)	~1061(s)	$\nu_{sym}(NO_3)$
~1020(w,br)	~1111.0(vw)												ν(phosphate-ribose)
								~996(m,br)	993(m)	999(w)	997(br)		
974(s)	979(s)	978(s)	974(s)	982(m)	982(m)	982(m)	990(br)	986(m)				974(m,br)	$\nu_{sym}(PO_4)$
~946(m,br)	936(m)	951(m)	~945(w,br)	956(m,br)				957(m)		~952(m,br)			ν(phosphate-ribose)
				920(m)	914(v,br)	920(m,br)	920(v,br)	922(m)	920(m,br)	920(s)	920(m,br)	916(v,br)	
893(w,br)	900(w,br)	(w,br)	899(w,br)					883(vw)		885(vw)			(sugar-stretching)
	872(w,br)	(w,br)		876(vw)		880(vw)		~876(vw)					νC–C, νC–O
				862(vw)		853(vw)				862(vw)			

*br = broad, sh = shoulder, vbr = very broad, vw = very weak. [a]Solid sodium D-ribose phosphate. [b]Solid 5′-UMP(Na_2). [c]5′-UMP(Na_2) pH, pD 6.5. [d–g]$[(NH_3)_2Pt(H_2O)_2](NO_3)_2$ + 5′-UMP(Na_2) at 25 °C in H_2O and D_2O. [d]After 1 h pH 6.5, pD 6.0. [e]After 4 h, pH 5.0, pD 6.0. [f]After 8 h, pH 5.0, pD 5.4. [g]After 24 h, pH 5.0, pD 5.4. [h]Solid platinum blue complex.

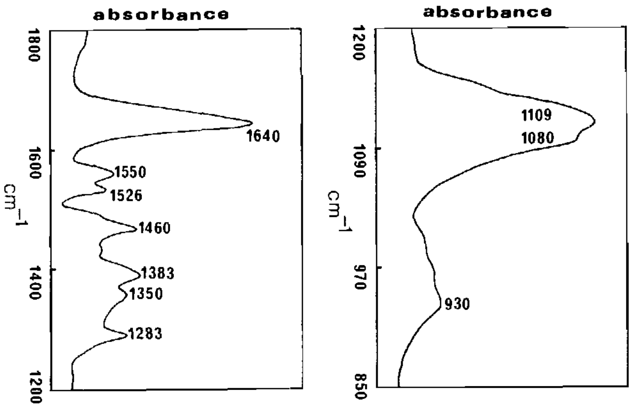


Fig. 7. Infrared spectra in the 1800–1200 and 1200–850 cm^{-1} regions of $[(NH_3)_2Pt(H_2O)_2]ClO_4$ + 5′-UMP(Na_2) in H_2O at 25 °C after 24 h.

the spectra of the platinum blue in H_2O, 24 h after the two reactants have been mixed, using ClO_4^- and NO_3^- ions as the counterions (see Figs. 1 and 7). The band at 1049 cm^{-1} (Fig. 5) and the highly intense absorption in the 1400–1300 cm^{-1} region (Fig. 2) clearly indicate that the nitrate is in its ionic form (*i.e.* planar D_{3h} symmetry). Chloride ions apparently interact strongly with the axial sites of the Pt(II) ions since addition of a small amount of NaCl to the initial reaction mixture stops formation of the blue complex completely.

Conclusions

On the basis of our vibrational investigation of the reaction of 5′-UMP(Na_2) with DDP, the following conclusions can be made:

(a) As the reaction is proceeding in H_2O (and D_2O), the IR spectra slowly transform to identical patterns in both solvents implying that most of the normal modes are solvent independent.

(b) Pt(II) is strongly coordinated to the N(3) site on the uracil moiety and possibly the C(2)=O group as well.

(c) Initially, Pt(II) is coordinated to the phosphate groups. However, as the reaction proceeds there is an increasing tendency for coordination to the N(3) site of the uracil moiety.

(d) Pt–N(3) coordination leads to a resonance structure in the ring and concomitantly to some

TABLE IV. Observed Infrared Frequencies and Possible Assignments for 5'-UMP(Na_2) and Pt-blue Complex in the 850–600 cm^{-1} Region

a	b	c	d	Proposed assignments [20, 28, 39, this work]
816.0(s)	814.0(s)	816.0(s)		ν(phosphate-ribose), C2'-endo
			808.0(s,br)	ν(phosphate-ribose), C3'-endo
		800.0(m)		
779.0(m)		774.0(s)	775.0(s)	pyrimidine
762.0(s)	769.0(w,br)			
(727–712)	719.0(m)	~723.0(w,br)	~710(v,br)	δ(NO_3)
	704.0	~695.0(w,br)		
~654.0(m)	654.0(w)	(671 – 640) (vw)		δN–H (out-of-plane)
628.0(m)	621.0(m)	625.0(m)	~620(v,br)	pyrimidine

[a]Solid 5'-UMP(Na_2). [b]5'-UMP(Na_2) in H_2O, pH 6.5. [c]5'-UMP(Na_2) in D_2O, pD 6.5. [e]Solid platinum blue complex.

characteristic bands in the 1600–1500 cm^{-1} region that can be used as marker bands for platinum blue formation.

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