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Chromium(III) Interactions with Nucleotides. II*

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Abstract

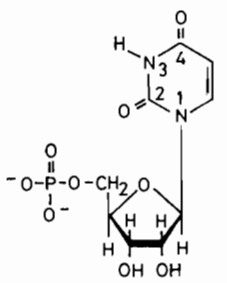
New derivatives were obtained from $Cr(urea)_6Cl_3 \cdot 3H_2O$ in an ethyl acetate medium of chromium(III) with uracil, uridine, 5′UMP, 5′CMP, 5′GMP and 5′IMP. The new derivatives were characterized by elemental analysis, electronic and infrared spectroscopy and thermal analysis. These derivatives proved to be outer sphere complexes, in which the nucleotide, the nucleoside or the base interacts with the starting complex through intramolecular hydrogen bonding.

$Cr(XMP)(OH) \cdot 3H_2O$ (XMP: 5′UMP, 5′CMP, 5′GMP and 5′IMP) complexes were obtained by hydrolysis of the above derivatives of the nucleotides. In these reactions there is a total substitution of the urea molecules. The derivatives obtained by hydrolysis were characterized in solid state by electronic and infrared spectroscopy. These results provide more insight into the biological role of chromium.

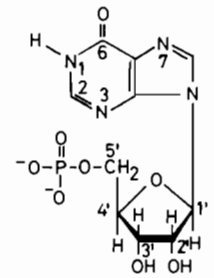
Introduction

Interest in chromium(III) complexes with nucleotides, nucleosides or bases arises from the use of these complexes as enzymatic labels [1, 2]. The biochemistry of chromium has recently become a topic of growing interest due to the presence of chromium(III) in the glucose tolerance factor (GTF) [3–13] and to its role in the enhancement of ribonucleic acid synthesis [14]. It was verified recently that some Cr(III) complexes are labile [12]; this lability occurs only with anions in chromium(III) complexes with distorted octahedral geometry. These facts seem to indicate an active role for chromium(III) in biological systems, different from the expected inert character of chromium(III) octahedral complexes.

In a previous paper [15] it was observed that $Cr(urea)_6Cl_3 \cdot 3H_2O$ reacts with 5′AMP at initial pH = 7.2 with total substitution of urea molecules. $Cr(urea)_6Cl_3 \cdot 3H_2O$ can be considered as a model of Cr(III)–aminoacid complexes. In this paper the reactions of this model complex with other nucleotides, nucleosides or bases are considered. Until now very few complexes of chromium(III) have been isolated in the solid state from Cr(III) with nucleotides, nucleosides or bases [15–21].



5′ UMP



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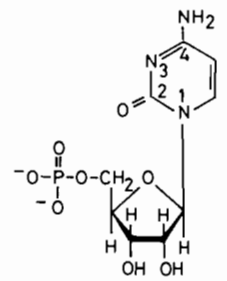
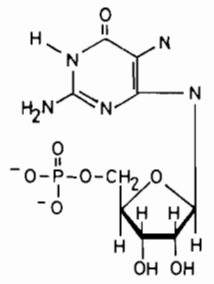


5′ CMP



5′ GMP

Experimental

The sources for nucleotides, nucleosides, bases, urea, ethyl acetate and chromium(III) chloride were

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Serva and Merck. $Cr(urea)_6Cl_3 \cdot 3H_2O$ was prepared according to literature procedures [22].

Synthesis of $Cr(urea)_6(URA)Cl_3$ and $Cr(urea)_6(URD)Cl_3$

Quantities of 1 mmol of $Cr(OCN_2H_4)_6Cl_3 \cdot 3H_2O$ (0.5278 g) and 1 mmol of uracyl (URA) or uridine (URD) were powder mixed and 25 ml of ethyl acetate were added. The mixture was heated to reflux with continuous stirring for 7 h. A green precipitate was obtained in both cases, and after cooling it was filtered, washed with 5 ml of hot ethyl acetate and dried over P_4O_{10}. *Anal.* Calc. for $Cr(urea)_6(URA)Cl_3$: C, 19.07; H, 4.45; Cl, 16.7; Cr, 7.21. Found: C, 19.05; H, 4.95; Cl, 15.13; Cr, 7.26%. The compound decomposes at 186 °C. The compound is green and very soluble in water but with decomposition. Calc. for $Cr(urea)_6(URD)Cl_3$: C, 23.6; H, 4.72; N, 25.70; Cl, 13.70; Cr, 6.83. Found: C, 24.35; H, 4.83; N, 25.64; Cl, 13.88; Cr, 6.86%. The compound is green and soluble in water with decomposition. It decomposes at 174 °C.

Syntheses of $Cr(urea)_6Na_2(5'XMP)Cl_3 \cdot nH_2O$; (XMP: GMP, IMP, UMP and CMP)

$Cr(urea)_6Cl_3 \cdot 3H_2O$ (1 mmol) and disodium salt of nucleotide Na_2XMP (1 mmol) were powder mixed. A suspension of the mixture in ethyl acetate (25 ml) was obtained and heated with reflux at 50 °C in a temperature controlled bath for 9 h. A green precipitate was obtained in every case, washed with hot ethyl acetate and dried over P_4O_{10}.

All the complexes are green, soluble in water with decomposition, and insoluble in organic solvents. *Anal.* Calc. for $Cr(urea)_6Na_2(5'UMP)Cl_3 \cdot 2H_2O$: C, 19.53; H, 4.23; N, 21.27; P, 3.36; Na, 4.69; Cr, 5.64. Found: C, 19.56; H, 4.44; N, 20.99; P, 3.35; Na, 4.69; Cr, 5.52%. The compound decomposes at 129 °C. Calc. for $Cr(urea)_6Na_2(5'CMP)Cl_3 \cdot 2H_2O$: C, 19.56; H, 4.34; N, 22.80; P, 3.36; Cl, 11.45; Na, 5.00; Cr, 5.65. Found: C, 19.50; H, 4.44; N, 23.08; P, 4.07; Cl, 11.28; Na, 4.58; Cr, 4.76%. The compound decomposes at 147 °C. Calc. for $Cr(urea)_6Na_2(5'IMP)Cl_3 \cdot 6H_2O$: C, 18.87; H, 4.62; N, 22.02; P, 3.05; Cl, 10.32; Na, 4.50; Cr, 5.11. Found: C, 18.87; H, 4.62; N, 21.80; P, 3.93; Cl, 10.53; Na, 5.11; Cr, 4.76%. The compound decomposes at 115 °C. Calc. for $Cr(urea)_6Na_2(5'GMP)Cl_3 \cdot 3H_2O$: C, 19.63; H, 4.29; N, 24.33; P, 3.27; Cl, 10.73; Na, 4.70; Cr, 5.30. Found: C, 18.89; H, 3.69; N, 23.85; P, 4.25; Cl, 11.51; Na, 4.92; Cr, 5.07%. The compound decomposes at 156 °C.

Syntheses of $Cr(5'XMP)(OH) \cdot 3H_2O$; (XMP: GMP, IMP, UMP and CMP)

In each case $Cr(urea)_6Na_2(5'XMP)Cl_3 \cdot nH_2O$ formula complex (1 mmol) was dissolved in 12 ml of distilled water. The pH of this solution was adjusted to 6.7–7.0. This solution was heated in a thermostatic bath to 50 °C for 1 h. Almost immediately a green precipitate appeared in the heated solution; in the case of the 5'GMP derivative the precipitate appeared even with no heating. The solution was then cooled with ice, and the precipitate filtered, washed with water and vacuum dried over P_4O_{10}.

For the uracyl and uridine derivatives, no precipitate was obtained under the same conditions; in the case of the uracyl derivative, free uracyl precipitated in part but no new complex was obtained.

All the nucleotide derivatives were green and slightly soluble in water, and insoluble in the currently used organic solvents. They are stable in the desiccator at room temperature. *Anal.* Calc. for $Cr(5'UMP)(OH) \cdot 3H_2O$: C, 24.29; H, 4.04; N, 6.29; P, 6.86; Cr, 11.60. Found: C, 23.98; H, 4.38; N, 6.54; P, 7.54; Cr, 12.47%. The complex decomposes at 265 °C. Calc. for $Cr(5'CMP)(OH) \cdot 3H_2O$: C, 24.31; H, 4.27; N, 9.45; P, 6.95; Cr, 11.70. Found: C, 24.13; H, 4.34; N, 10.27; P, 6.71; Cr, 10.84%. The complex decomposes at 242 °C. Calc. for $Cr(5'IMP)(OH) \cdot 3H_2O$: C, 25.56; H, 3.80; N, 11.92; Cr, 11.08. Found: C, 25.55; H, 3.84; N, 13.46; Cr, 10.41%. The compound decomposes at 251 °C. Calc. for $Cr(5'GMP)(OH) \cdot 3H_2O$: C, 24.78; H, 3.93; N, 14.46; P, 6.40; Cr, 10.74. Found: C, 24.90; H, 4.05; N, 14.85; P, 6.34; Cr, 10.29%. The compound decomposes at 252 °C.

Carbon, hydrogen and nitrogen contents were determined by elemental analysis at the Institute of Bio-organic Chemistry (Barcelona) using a Carlo Erba analyzer. Phosphorous was determined using the phosphomolibdovanadate method. Chromium was detected by spectrophotometric methods and sodium by flame photometry.

UV–Vis spectra were recorded in a Perkin-Elmer 552 spectrophotometer in solid state in reflectance mode, using an integrating sphere attachment.

Infrared spectra (KBr) pellets were obtained using a Perkin-Elmer 683 spectrophotometer with a Perkin-Elmer 3600 data station. A Perkin-Elmer 705 atomic absorption spectrophotometer was used in the determination of sodium. The thermogravimetric analysis was carried out between 303–703 K with static atmosphere of air at a velocity of 5 °C/min at the Institute of Applied Organic Chemistry (Barcelona).

Results and Discussion

With the derivatives of 5'UMP, URD and URA obtained in ethyl acetate (Table I) a thermogravimetric analysis was carried out. The presence of two water molecules in the derivative of the nucleotide and the absence of these in the derivatives of the

TABLE I. Thermogravimetric Data

Compound	Temperature range (°C)	% Weight loss		Tentative assignment
		Found	Calc.	
$Cr(urea)_6Na_2(5'UMP)Cl_3 \cdot 2H_2O$	0–70	3.79	3.78	$2H_2O$
	70–220	26.01	26.08	$C_5H_8O_5$ + 3Cl
	220–310	39.40	37.55	6 urea
	310–513	10.10	11.68	uracil
	residue: $Cr_2O_3 + Na_2PO_4$			
$Cr(urea)_6Cl_3(URD)$	0–183	30.52	32.02	uridine
	183–197	14.33	13.96	3 Cl
	193–330	48.51	47.20	6 urea
	residue: Cr_2O_3			
$Cr(urea)_6Cl_3(URA)$	0–184	57.10	56.68	6 urea
	184–338	32.85	33.29	uracil + 3Cl
	residue: Cr_2O_3			

TABLE II. Infrared Data for the URA and URD Derivatives (cm^{-1})[a]

Tentative assignment	URA(uracil)	$Cr(urea)_6URACl_3$	URD(uridine)	$Cr(urea)_6URDCl_3$
$\nu C_2{=}O + \nu C{=}C$	1715s,br	1716s	1694br	1689br
$\nu C_4{=}O + \nu C{=}C$	1671–33s,br	1660–43s,br	1669s	1668–45s,br
$\nu C{=}C + \delta N{-}H$			1615w	1613w
$\delta N{-}H + \nu$ ring	1508m	1499	–	–
δ ring + $\nu N{-}H$	1452s	1454m	1470s	br
δ ring + $\nu N{-}H$	1417s	1419m	1421s	1425m
δ ring + $\nu N{-}H$	1389s	1392w	1396s	1397m
δ ring + $\nu N{-}H$	1237s	1238m	1271s	1270s

[a]s, strong; m, medium; w, weak; sh, shoulder; br, broad.

base and the nucleoside was confirmed. A different thermal behavior of the base (uracil) and nucleoside (uridine) or nucleotide (5'UMP) was detected. The presence of six urea molecules was confirmed in all cases. The loss of Cl in all compounds occurs parallel to combustion of the ribose ring or the base.

In the derivative of uracil obtained in ethyl acetate (Table II), a slight shift to lower frequency as regards the free uracil occurs in the broad band assigned as $\nu C_4{=}O + \nu C{=}C$. This shifting may indicate some sort of interaction for this group. The ring bands present no noticeable modifications in frequency but do show a considerable change in relative intensity [23–26].

The frequencies of the $Cr(urea)_6Cl_3 \cdot 3H_2O$ complex appear with little change, apart from the deformation band of the N–H group at 1635 cm^{-1} which shifts to 1631 cm^{-1}, overlapping with the base bands [27].

Interpretation of the infrared results together with the analytic data seems to indicate that the chromium is coordinated to six urea molecules, and the uracil may interact with the complex through hydrogen bonding between $C_4{=}O$ and the $-NH_2$ group of a urea molecule.

The derivative of uridine (Table II) presents an infrared spectrum similar to the latter, with more overlapping between the bands, seeming to indicate interaction between the C=O groups of the base and the $-NH_2$ groups of urea molecules [23–26].

In the $Cr(urea)_6Na_2(5'JMP)Cl_3 \cdot 2H_2O$ compound (Table III) obtained in ethyl acetate, the bands of the phosphate group undergo no noticeable modifications. It seems, therefore, that no coordination occurs through this group. The shift of the bands of the carbonyl groups may indicate, as in the previous cases, interaction of these groups with the $-NH_2$ group of the urea molecules through hydrogen bonding. The other ring bands undergo very slight variations [23–26]. The complex obtained by hydrolysis $Cr(5'UMP)(OH) \cdot 3H_2O$ (Table III) presents very different changes in the spectrum. The $C_2{=}O$ group band which had shifted to lower frequencies (1661 cm^{-1}) rises again (1683 cm^{-1}) and remains

TABLE III. Infrared Data for the Pyrimidine Nucleotides Derivatives (cm^{-1})[a]

Tentative assignment	$Na_2$5'UMP	$Cr(urea)_6Na_2$(5'UMP)$Cl_3 \cdot 2H_2O$	Cr(5'UMP)(OH)$\cdot 3H_2O$	Tentative assignment	$Na_2$5'CMP	$Cr(urea)_6Na_2$(5'CMP)$Cl_3 \cdot 2H_2O$	Cr(5'CMP)(OH)$\cdot 3H_2O$
$\nu C_2{=}O + \nu C{=}C$	1704, 1689br	1670, 1661br	1702, 1683br	$\nu C_2{=}O + \nu C{=}C + \delta NH_2$	1660s	1660s	1725s
$\nu C_4{=}O + \nu C{=}C$	1679s	1651, 1643br	overlaps	$\nu C{=}C + \nu C{=}N$	1648s	1646–26s,br	1651s
$\nu C{=}C + \delta N{-}H$	1630w	1632–15br	overlaps				
νring	1478m	overlaps	1468m	νring	1529sh	overlaps	1529sh
νring	1429m	1433w	1406w	νring	1496m	overlaps	1492s
νring + $\delta N{-}H$	1394m	1400, 1395w	1395w	νring	1405w	1411w	1406m
νring + $\delta N{-}H$	1349w	1349w	–	νring	1383w	1386w	1387w
νring	1330m	1330w	–	νring	1295m	1292m	1285s
	1284m	1285m	1273m	νring	1248m	1250sh	–
	1267sh	1266sh	overlaps				
ν(ribose) + $\nu P{-}O_3^{2-}$ (deg)	1125–81br	1126–76br,s	1119–03br,s	ν(ribose) + $\nu{-}PO_3^{2-}$ (deg)	1114–81br	1114–90br	1108–60br
$\nu{-}PO_3^{2-}$ (sym)	981s	981s	1002s	$\nu{-}PO_3^{2-}$ (sym)	976s	978s	989br

[a]s, strong; m, medium; w, weak; sh, shoulder; br, broad.

practically unchanged with respect to the starting ligand (1689 cm^{-1}). The ring frequencies vary considerably. The symmetrical tension band shifts to higher frequencies, indicating coordination with the phosphate group. This seems to indicate coordination of chromium(III) to the oxygen of the phosphate group and protonation of uracil ring or coordination to chromium(III), responsible for the change in frequency of the base bands. This all coincides with the existing literature for other derivatives of 5'UMP.

In the $Cr(urea)_6Na_2(5'CMP)Cl_3 \cdot 2H_2O$ complex obtained in ethyl acetate (Table III) there is no variation in the carbonyl group bands but there are slight changes in frequencies in the phosphate group, which may interact with the $-NH_2$ group of the urea (change from 1635 cm^{-1} in $Cr(urea)_6Cl_3 \cdot 3H_2O$ to 1626 cm^{-1}) [26–27]. In the complex obtained in water medium $Cr(5'CMP)OH \cdot 3H_2O$ (Table III) there is an increase in frequency in the carbonyl group and slight rearrangements on the ring bands. On the phosphate group bands important changes are observed, seeming to indicate coordination of this group to the metallic ion. The increase in frequency in the C=O group implies that there is probably no bonding of the carbonyl group to the metal, as reported in earlier literature. Interaction through an atom of nitrogen, possibly N(3), cannot be ruled out.

In the $Cr(urea)_6Na_2(5'IMP)Cl_3 \cdot 6H_2O$ complex obtained in ethyl acetate (Table IV) there seems to be interaction of the carbonyl group with the urea molecules. The 980 cm^{-1} band of the phosphate group remains unchanged [23–26]. In the derivative obtained in water medium $Cr(5'IMP)(OH) \cdot 3H_2O$, there are important changes in the spectrum, such as an increase in the carbonyl group bands and noticeable changes on the ring bands. There is bonding of the metallic ion to the phosphate group; interaction with a nitrogen of the ring cannot be ruled out.

In the $Cr(urea)_6Na_2(5'GMP)Cl_3 \cdot 3H_2O$ complex obtained in ethyl acetate (Table IV) there is a slight shift to higher frequency of the carbonyl group band; the ring bands overlap, except for the 1361 cm^{-1} band which shifts to 1385 cm^{-1}, and there are shiftings in both directions of the phosphate group and ribose phosphate bands. As in the above cases, there seems to be no direct chromium(III)–nucleotide bond, but there is hydrogen bonding between the carbonyl or nucleotide phosphate groups and the urea molecules [23–27]. The product of hydrolysis $Cr(5'GMP)(OH) \cdot 3H_2O$ presents an important decrease in frequency in the carbonyl group, seeming to indicate coordination for this group. There also seems to exist bonding with the phosphate group as suggested by shifting of the bands.

The UV–Vis bands of the starting complex

TABLE IV. Infrared Data for the Purine Nucleotide Derivatives (cm^{-1})[a]

Tentative assignment	$Na_2$5'IMP	$Cr(urea)_6Na_2$(5'IMP)$Cl_3 \cdot 6H_2O$	Cr(5'IMP)(OH)$\cdot 3H_2O$	Tentative assignment	$Na_2$5'GMP	$Cr(urea)_6Na_2$(5'GMP)$Cl_3 \cdot 3H_2O$	Cr(5'GMP)(OH)$\cdot 3H_2O$
νC=O	1679s	1631br	1690br	νC=O	1692s	1690w	1644br
νring	1593m	1580sh	1589m	νC=C + νC=N + δ−NH_2	1602m	overlaps	overlaps
νring	1551m	1551s	1553m	νring	1535s	overlaps	1536w
νring	1520m	overlaps	1514w	νring	1483s	overlaps	1486m
νring	1483m	1498sh	1465w	νring	1412m	overlaps	1415w
νring	1428m	1428w	1421w	νring	1361s	1385w	1360m
νring	1375w	1383w	1375w	νring	1325w	overlaps	1315sh
νring	1330m	1330w	1322w	νring	1236m	1235w	–
νring	1254w	1250w	–				
νring	1217s	1216m	1213m				
ν(ribose) + $\nu-PO_3^{2-}$ (deg)	1122–94br,s	1123–92br,s	1126–68br,s	ν(ribose) + $\nu-PO_3^{2-}$ (deg)	1134–70br,s	1164–84br,s	1111–84br,s
$\nu-PO_3^{2-}$ (sym)	980s	980s	990s	$\nu-PO_3^{2-}$ (sym)	976s	978m	996s

[a]s, strong; m, medium; w, weak; sh, shoulder; br, broad.

(Table V) undergo no noticeable change in the complexes obtained in ethyl acetate, confirming the hypothesis of coordination of the chromium to the urea in these complexes. In the derivatives obtained by hydrolysis the variations are somewhat greater.

The bands appearing at 388, 434 nm and 568, 694 nm on the diffuse reflectancy spectrum may be interpreted as splittings, through loss of symmetry, probably due to distortion of the octahedral environment of the metallic ion [28].

We may conclude that these results indicate that in all cases coordination occurs between the chromium and donor oxygen ligands: the urea carbonyl group in those obtained in ethyl acetate, the phosphate group and ring carbonyl groups in the derivatives by hydrolysis.

In conclusion, this study confirms labilization of the $Cr(urea)_6Cl_3 \cdot 3H_2O$ in water medium in the presence of the nucleotides 5'CMP, 5'UMP, 5'GMP and 5'IMP, causing total substitution of the urea molecules and coordination to chromium(III). This is similar to the reaction between $Cr(urea)_6Cl_3 \cdot 3H_2O$ and 5'AMP in water medium at initial pH 7.2 [15]. However, in that case the reaction occurred spontaneously in water medium. The nucleotides studied in this paper (5'CMP, 5'UMP, 5'GMP and 5'IMP) show no noticeable reaction, or at least no reaction product has been isolated in the same conditions. On the other hand, in the derivatives obtained in ethyl acetate, which have been confirmed to be compounds with intramolecular hydrogen bonding, a reaction is observed allowing for isolation of the final product in which all the urea molecules have been substituted. This process is much quicker for 5'GMP (a purine base nucleotide like 5'AMP) and occurs only with the nucleotide but with none of the bases or nucleosides studied. Once again, the lability of Cr(III) complexes occurs when they come into contact with anionic ligands, nucleotides in this case [11, 15].

Recently [29] a Co(II) complex with linkage isomerism has been obtained with dimethyl urea; in this complex Co(II) joins the N of the dimethyl urea ligand. This linkage isomerism seems to indicate that the $-NH_2$ groups of the urea may play a role in the Cr(III)–urea bonding, which might indicate that the environment of the Cr(III) in $(Cr(urea)_6)^{3+}$ complex is not absolutely symmetrical and would favour total substitution of the urea molecules in the presence of nucleotides. This loss of symmetry may also be due to an intermediate in the reaction when one or two of the urea molecules have been substituted by the nucleotide.

The fact that the derivatives obtained in ethyl acetate react spontaneously at an unexpected rate may indicate that the formation of the outer sphere complex $Cr(urea)_6$–nucleotide would be the slow

TABLE V. Diffuse Reflectance Data for the Complexes (nm)

Compound	Charge transfer	$\pi \rightarrow \pi^*$	$^4T_{1g} \leftarrow {}^4A_{2g}$	$^4T_{2g} \leftarrow {}^4A_{2g}$	Spin forbidden band
$Cr(urea)_6Cl_3 \cdot 3H_2O$	240s		388, 434s	568, 611s	694m
Uracil (URA)		244, 292s			
Uridine (URD)		247s			
$Na_2$5'UMP		249, 294s			
$Na_2$5'CMP		248, 308s			
$Na_2$5'IMP		240s			
$Na_2$5'GMP		242, 309s			
$Cr(urea)_6(URA)Cl_3$		244s	389, 431s	566, 609s	700m
$Cr(urea)_6(URD)Cl_3$		245s	387, 432s	566, 608s	697m
$Cr(urea)_6Na_2(5'UMP)Cl_3 \cdot 2H_2O$		244s	388, 432s	564, 608s	698s
$Cr(urea)_6Na_2(5'CMP)Cl_3 \cdot 2H_2O$	362s	250, 290s	385, 430s	564, 608s	
$Cr(urea)_6Na_2(5'IMP)Cl_3 \cdot 6H_2O$	362s	239s	388, 432s	567, 608s	
$Cr(urea)_6Na_2(5'GMP)Cl_3 \cdot 3H_2O$		243, 304s	386, 432s	566, 610s	
$Cr(5'UMP)(OH) \cdot 3H_2O$	356s	250, 284s	385, 432s	560, 609s	
$Cr(5'CMP)(OH) \cdot 3H_2O$	358s	252, 310s	385, 430s	562, 609s	
$Cr(5'IMP)(OH) \cdot 3H_2O$	364s	244s	386, 432s	562, 610s	
$Cr(5'GMP)(OH) \cdot 3H_2O$	360s	245, 311s	380, 432s	560, 609s	

step of the reaction. Eigen [30] has pointed out this phenomenon in the substitution of octahedral complexes. The synthesis carried out in ethyl acetate, a solvent with a dielectric constant lower than water, has revealed these to be outer sphere complexes, from which the substitution reaction is much faster.

Reactions of this type might occur in the glucose tolerance factor (GTF). The cystoplasmatic medium with hydrophobic components, might favour the formation of these outer sphere complexes and their subsequent reaction. So far, however, the presence of phosphates or nucleotides in GTF has not been observed. In a recent paper, Blackwell *et al.* [31] claim that GTF lacks chromium. Later studies by the same authors [9, 10], however, have indicated the activity of complexes of chromium(III) with aminoacids and nicotinic acid as analogues of GTF. In the first article [31] there is a surprising mention of an active fraction P-3: 'Unfortunately it was not possible to separate the active material from P-3 from the phosphate used in the elution of the Dowex 50 W-X2 cation exchange columns by the use of Sephadex G-15 and thus structural elucidation was not possible' ([31], p 112). The work carried out in this paper using $Cr(urea)_6Cl_3 \cdot 3H_2O$ as a model for Cr(III) complexes with aminoacids or peptidic chains and their reaction in the presence of nucleotides will perhaps provide more insight into these phenomena. Similar reactions [32] do in fact occur between Cr(III)–glutamic acid complexes and nucleotides [32].

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