Interactions of Bis-[μ-chloro-chlorotricarbonylruthenium(II)] and Poly-[μ-dichloro-dicarbonylruthenium(II)] with Nucleosides

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Abstract

The interactions of dimeric complex bis-[μ-chloro-chlorotricarbonylruthenium(II)], $[Ru(CO)_3Cl_2]_2$, and the polymeric complex poly-[μ-dichlorodicarbonylruthenium(II)], $[Ru(CO)_2Cl_2]_x$, with nucleosides (Nucl) in a 1:1 Ru:Nucl molar ratio for the dimer and 1:2 Ru:Nucl for the polymer, resulted in formation of the monomeric mononucleoside $[Ru(CO)_3(Nucl)Cl_2]$ and bis-nucleoside $[Ru(CO)_2(Nucl)_2Cl_2]$ complexes, respectively. The dimer $[Ru(CO)_3Cl_2]_2$ also gave the ionic bis-nucleoside complexes $[Ru(CO)_3(Nucl)_2Cl]Cl$ in the molar ratio 1:2 Ru:Nucl. The mononucleoside complexes are stable in solution while the bis-nucleoside complexes tend to lose one nucleoside in strong complexing solvents, probably by solvent substitution. The complexes $[Ru(CO)_3(Nucl)Cl_2]$ and $[Ru(CO)_2(Nucl)_2Cl_2]$ with one N(1)H ionizable imino proton undergo ionization in alkaline solution and the complexes $[Ru(CO)_3(Nucl-H^+)Cl]$ and $[Ru(CO)_2(Nucl-H^+)_2]$, respectively, were isolated. In these deprotonated complexes the nucleosides behave as bidentate ligands, while in the protonated ones they act as monodentate. All complexes were characterized by elemental analyses and various spectroscopic methods.

Introduction

The interaction of metal ions with nucleic acids, nucleosides and nucleotides has been an active area of inorganic and structural chemistry over the past years and a number of reviews exist on the subject [1–4]. In part, this interest and activity arise from the success of certain platinum compounds, particularly *cis*-diamminedichloroplatinum(II) (DDP), in the inhibition and remission of neoplastic growth [5]. It is generally conceded that platinum compounds function as chemotherapeutic agents by binding to guanine-rich portions of DNA and thereby inhibiting transcription, translation and replication [6].

It is widely accepted that N7 is the preferred coordination site in guanosine, inosine and other 6-oxopurines [7]. This site in guanosine is believed to be the primary target for platinum antitumour complexes in cellular DNA [7, 8]. To explain this specificity, several models have been proposed, one of which assumes that initial metal binding to N7 is followed by deprotonation of the N(1)H imino proton and coordination of O6 with a second coordination site on the metal, leading to an N7/O6 chelate. Although studies on model compounds have conclusively shown that such chelates can be formed with 6-thiopurines [9], evidence for chelation in 6-oxo ligands is much less convincing. This problem was examined by Kistenmacher and coworkers by means of a series of copper complexes of theophylline [10, 11]. They confirmed N7 as the primary binding site and noticed that O6 is generally hydrogen bonded with other ligands in the metal coordination sphere. The same behaviour has also been observed with other metal ions [12–15]. When hydrogen bonding ligands were not available, O6 was found to occupy an apical coordination site around copper, but the Cu–O6 distance (292 pm) was much longer than the Cu–N7 distance (~195 pm) [11]. Thus, even though this molecule can be described as a chelate in the sense that a ring exists, the two bonding interactions are hardly comparable. However, a genuine N7/O6 chelate complex was found in the crystal structure of bis(η^5-cyclopentadienyl)-theophyllinato)titanium(III), in which the Ti–N7 and Ti–O6 distances (*ca.* 221 and 228 pm, respectively) are comparable and the O6–Ti–N7 angle is 79.6° [16].

In this paper we report the results of the interactions of the dimeric $[Ru(CO)_3Cl_2]_2$ and the polymeric $[Ru(CO)_2Cl_2]_x$ complexes with purine and pyrimidine nucleosides.

Results and Discussion

The interaction of nucleosides (Nucl), adenosine (Ado), cytidine (Cyd), guanosine (Guo), and inosine (Ino) with the dimeric complex $[Ru(CO)_3Cl_2]_2$ in

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methanolic solution, in a molar ratio of 2:1, resulted in the formation of the mononucleoside complexes $[Ru(CO)_3(Nucl)Cl_2]$:

$$[Ru(CO)_3Cl_2]_2 + 2Nucl \longrightarrow 2[Ru(CO)_3(Nucl)Cl_2] \quad (1)$$

Under the molar ratio 4:1, the ionic bis-nucleoside complexes $[Ru(CO)_3(Nucl)_2Cl]Cl$ were formed:

$$[Ru(CO)_3Cl_2]_2 + 4Nucl \longrightarrow 2[Ru(CO)_3(Nucl)_2Cl]Cl \quad (2)$$

On the other hand, the polymeric complex $[Ru(CO)_2Cl_2]_x$ gave the bis-nucleoside complexes $[Ru(CO)_2(Nucl)_2Cl_2]$ only:

$$[Ru(CO)_2Cl_2]_x + 2xNucl \longrightarrow x[Ru(CO)_2(Nucl)_2Cl_2] \quad (3)$$

The complexes of the series $[Ru(CO)_3(Nucl)Cl_2]$ and $[Ru(CO)_2(Nucl)_2Cl_2]$ with one ionizable imino proton N(1)H undergo ionization in alkaline solution and the new series of complexes $[Ru(CO)_3(Nucl) - H^+)Cl]$ and $[Ru(CO)_2(Nucl - H^+)_2]$ are formed:

$$[Ru(CO)_3(Nucl)Cl_2] \longrightarrow [Ru(CO)_3(Nucl - H^+)Cl] + HCl \quad (4)$$

$$[Ru(CO)_2(Nucl)_2Cl_2] \longrightarrow [Ru(CO)_2(Nucl - H^+)_2] + 2HCl \quad (5)$$

Under the same conditions the $[Ru(CO)_3(Nucl)_2Cl]Cl$ complexes gave mixtures of decomposition products with partial decarbonylation.

The analytical and conductivity data of the complexes are given in Table I and fit well with the proposed formulation.

In reaction (1) the double chloride bridge is broken and monomeric, non-ionic, mononucleoside complexes are formed. In reaction (2) the ionic bis-nucleoside complexes are formed after breakage of the double chloride bridge and subsequent substitution of one chloride in the inner coordination sphere of Ru(II). Finally, in reaction (3) all four chloride bridges are broken and the monomeric, non-ionic, bis-nucleoside complexes are formed.

The $[Ru(CO)_3Cl_2]_2$ complex shows two bands in the metal–halogen stretching region. The band at 325 cm^{-1} (higher energy) is assigned to the Ru–Cl

TABLE I. Analytical[a] and Conductivity Data of the Complexes

Compound	Ru (%)[a]	Cl (%)[a]	Λ_M (in MeOH) (ohm^{-1} cm^2 mol^{-1})
$[Ru(CO)_3(Ado)Cl_2]$	19.40(19.17)	13.75(13.47)	6
$[Ru(CO)_3(Ado)_2Cl]Cl$	13.02(12.79)	9.20(8.98)	76
$[Ru(CO)_3(AdoAc_3)_2Cl]Cl$	9.95(9.70)	7.10(6.81)	62
$[Ru(CO)_2(Ado)_2Cl_2]$	13.50(13.26)	9.60(9.31)	5
$[Ru(CO)_2(AdoAc_3)_2Cl_2]$	10.12(9.96)	6.50(6.70)	5
$[Ru(CO)_3(Cyd)Cl_2]$	20.25(20.25)	14.50(14.22)	6
$[Ru(CO)_3(Cyd)_2Cl]Cl$	13.40(13.61)	9.85(9.56)	80
$[Ru(CO)_3(CydAc_3)_2Cl]Cl$	10.35(10.16)	7.40(7.14)	65
$[Ru(CO)_2(Cyd)_2Cl_2]$	14.38(14.15)	10.30(9.94)	7
$[Ru(CO)_2(CydAc_3)_2Cl_2]$	10.70(10.46)	7.65(7.35)	6
$[Ru(CO)_3(Guo)Cl_2]$	18.95(18.75)	13.40(13.17)	8
$[Ru(CO)_3(Guo)_2Cl]Cl$	12.55(12.29)	8.90(8.63)	72
$[Ru(CO)_3(GuoAc_3)_2Cl]Cl$	9.72(9.41)	6.30(6.61)	62
$[Ru(CO)_2(Guo)_2Cl_2]$	12.48(12.72)	9.20(8.94)	6
$[Ru(CO)_2(GuoAc_3)_2Cl_2]$	9.95(9.66)	7.10(6.78)	5
$[Ru(CO)_3(Guo - H^+)Cl]$	20.38(20.10)	7.35(7.06)	
$[Ru(CO)_2(Guo - H^+)_2]$	14.25(14.01)		
$[Ru(CO)_3(Ino)Cl_2]$	19.50(19.28)	13.85(13.54)	6
$[Ru(CO)_3(Ino)_2Cl]Cl$	12.48(12.75)	8.55(8.96)	75
$[Ru(CO)_3(InoAc_3)_2Cl]Cl$	9.85(9.68)	6.50(6.80)	64
$[Ru(CO)_2(Ino)_2Cl_2]$	13.50(13.22)	9.55(9.29)	6
$[Ru(CO)_2(InoAc_3)_2Cl_2]$	9.60(9.94)	6.65(6.99)	5
$[Ru(CO)_3(Ino - H^+)Cl]$	20.45(20.72)	7.55(7.28)	
$[Ru(CO)_2(Ino - H^+)_2]$	14.90(14.62)		

[a]The numbers in parentheses represent the calculated figures.

terminal stretching vibration, and the band at 290 cm^{-1} (lower energy) is assigned to ν(Ru–Cl–Ru). In the IR spectrum of the polymeric complex $[Ru(CO)_2Cl_2]_x$, only the lower frequency band (295 cm^{-1}) appears, as was expected from the absence of Ru–Cl terminal groups [17]. The lower energy band [ν(Ru–Cl–Ru)] is absent from the spectra of all the complexes, and only the higher energy band [around 320 cm^{-1}, (νRu–Cl)] is present in the spectra of all the chloro complexes. This band too is absent from the spectra of the $[Ru(CO)_2(Nucl - H^+)_2]$ complexes in accordance with their formulation (see Table II).

These observations, together with the analytical results and the presence of a very strong multiple band at the terminal carbonyl stretching region, lend support to the hypothesis that the Ru–Cl–Ru and even the Ru–Cl bonds are more labile than the Ru–CO bonds, under the applied reaction conditions, as was also observed in the analogous reactions of the Rh(I) complex $[Rh(CO)_2Cl]_2$ [18, 19].

The ^1H NMR bands in the aromatic proton region are very useful in assigning the coordination sites of the nucleosides and are given in Table III.

The complexes $[Ru(CO)_3(Ado)Cl_2]$, $[Ru(CO)_3(AdoAc_3)Cl]Cl$ and $[Ru(CO)_2(AdoAc_3)_2Cl_2]$ show the bands: 7.88, 8.32, 9.10; 7.90, 8.31, 9.12; and 7.91, 8.34, 9.15 ppm assigned to NH_2, H2 and H7, respectively. Since H8 shifts downfield by 0.74, 0.76 and 0.79 ppm, while H2 is shifted by only 0.17, 0.16 and 0.19 ppm, in the respective complexes, it is concluded that N7 is the only binding site in the above complexes [20 and refs. therein].

The complexes $[Ru(CO)_3(Cyd)Cl_2]$, $[Ru(CO)_3(CydAc_3)Cl_2]$ and $[Ru(CO)_2(CydAc_3)_2Cl_2]$ show three doublets: 8.24–7.65, 6.22–6.13, 8.25–8.15; 8.45–7.68, 6.25–6.15, 8.24–8.15; and 8.43–7.66, 6.23–6.14, 8.23–8.14 ppm assigned to NH_2, H5 and H6, respectively. Both H5 and H6 are shifted downfield with the larger shift for H5. This indicates that H5 is closer to the coordination site on the ligand, probably the N3 atom [18, 19, 21 and refs. therein]. Further evidence for the participation of the N3 atom in coordination comes from the NH_2 resonance, which appears as a doublet due to hindered rotation of the C–NH_2 bond as a result of N3 coordination [19, 21 and refs. therein].

In the complexes $[Ru(CO)_3(Guo)Cl_2]$, $[Ru(CO)_3(GuoAc_3)Cl]Cl$, $[Ru(CO)_2(GuoAc_3)_2Cl_2]$, $[Ru(CO)_3(Guo - H^+)Cl]$ and $[Ru(CO)_2(Guo - H^+)_2]$, the H8 resonance is shifted by 0.85, 0.90, 0.88, 0.92 and 0.91 ppm, respectively, downfield relative to free guanosine; this is strong evidence that the N7 atom participates in coordination in all these complexes [18–23].

The H8 resonance of inosine in the complexes $[Ru(CO)_3(Ino)Cl_2]$, $[Ru(CO)_3(InoAc_3)_2Cl]Cl$, $[Ru(CO)_2(InoAc_3)_2Cl_2]$, $[Ru(CO)_3(Ino - H^+)Cl]$ and $[Ru(CO)_2(Ino - H^+)_2]$ is shifted downfield by

TABLE II. Some Characteristic IR Bands[a] of the Complexes (cm^{-1})

Compound	ν(C≡O)	$\nu(C{=}O)_{Nucl}$	ν(Ru–Cl)
Adenosine (Ado)			
$[Ru(CO)_3(Ado)Cl_2]$	1965, 2010, 2028, 2088, 2145		325
$[Ru(CO)_3(Ado)_2Cl]Cl$	1968, 2012, 2030, 2090, 2150		327
$[Ru(CO)_2(Ado)_2Cl_2]$	1980, 2015, 2040, 2076		326
Cytidine (Cyd)		1660	
$[Ru(CO)_3(Cyd)Cl_2]$	1965, 2010, 2028, 2085, 2142	1665	330
$[Ru(CO)_3(Cyd)_2Cl]Cl$	1670, 2015, 2035, 2093, 2148	1658	327
$[Ru(CO)_2(Cyd)_2Cl_2]$	1985, 2013, 2040, 2078	1662	328
Guanosine (Guo)		1695	
$[Ru(CO)_3(Guo)Cl_2]$	1965, 2012, 2030, 2085, 2145	1698	328
$[Ru(CO)_3(Guo)_2Cl]Cl$	1970, 2015, 2032, 2088, 2150	1700	330
$[Ru(CO)_2(Guo)_2Cl_2]$	1982, 2012, 2040, 2080	1705	328
$[Ru(CO)_3(Guo - H^+)Cl]$	1968, 2015, 2032, 2087, 2150	1620	325
$[Ru(CO)_2(Guo - H^+)_2]$	1980, 2015, 2038, 2078	1625	
Inosine (Ino)		1703	
$[Ru(CO)_3(Ino)Cl_2]$	1965, 2010, 2030, 2085, 2148	1705	327
$[Ru(CO)_3(Ino)_2Cl]Cl$	1970, 2015, 2032, 2088, 2150	1708	330
$[Ru(CO)_2(Ino)_2Cl_2]$	1985, 2015, 2040, 2080	1710	328
$[Ru(CO)_3(Ino - H^+)Cl]$	1968, 2008, 2028, 2080, 2145	1630	328
$[Ru(CO)_2(Ino - H^+)_2]$	1980, 2015, 2040, 2080	1628	

[a]In KBr pellets.

TABLE III. ^{1}H NMR Chemical Shifts of the Complexes (ppm)

Compound	NH_2	NH	H(2)	H(5)	H(6)	H(8)	Solvent
Adenosine (Ado)	7.37		8.15			8.36	DMSO-d_6
$[Ru(CO)_3(Ado)Cl_2]$	7.88		8.32			9.10	DMSO-d_6
$[Ru(CO)_3(Ado)_2Cl]Cl$	7.90		8.31			9.12	DMSO-d_6
	(7.37)		(8.15)			(9.36)	
$[Ru(CO)_3(AdoAc_3)_2Cl]Cl$	7.92		8.32			9.15	$CDCl_3$
$[Ru(CO)_2(Ado)_2Cl_2]$	7.91		8.34			9.15	DMSO-d_6
	(7.37)		(8.16)			(8.37)	
$[Ru(CO)_2(AdoAc_3)_2Cl_2]$	7.93		8.32			9.14	$CDCl_3$
Cytidine (Cyd)	7.15			5.75 5.65	7.85 7.80		DMSO-d_6
$[Ru(CO)_3(Cyd)Cl_2]$	8.42 7.65			6.22 6.13	8.25 8.15		DMSO-d_6
$[Ru(CO)_3(Cyd)_2Cl]Cl$	8.45 7.68			6.25 6.15	8.42 8.15		DMSO-d_6
	(7.15)			(5.76 5.66)	(7.86 7.80)		
$[Ru(CO)_3(CydAc_3)_2Cl]Cl$	8.47 7.69			6.28 6.15	8.26 8.16		$CDCl_3$
$[Ru(CO)_2(Cyd)_2Cl_2]$	8.43 7.66			6.23 6.14	8.23 8.14		DMSO-d_6
	(7.15)			(5.76 5.66)	(7.86 7.80)		
$[Ru(CO)_2(CydAc_3)_2Cl_2]$	8.46 7.68			6.27 6.15	8.25 8.15		$CDCl_3$
Guanosine (Guo)	6.40	10.60				7.85	DMSO-d_6
$[Ru(CO)_3(Guo)Cl_2]$	6.70	11.02				8.70	DMSO-d_6
$[Ru(CO)_3(Guo)_2Cl]Cl$	6.58	11.05				8.72	DMSO-d_6
		(10.62)				(7.86)	
$[Ru(CO)_3(GuoAc_3)_2Cl]Cl$	6.55	11.06				8.75	$CDCl_3$
$[Ru(CO)_2(Guo)_2Cl_2]$	6.68	11.04				8.75	DMSO-d_6
		(10.61)				(7.88)	
$[Ru(CO)_2(GuoAc_3)_2Cl_2]$	6.70	11.05				8.73	$CDCl_3$
$[Ru(CO)_3(Guo - H^+)Cl]$	6.75					8.77	DMSO-d_6
$[Ru(CO)_2(Guo - H^+)_2]$	6.77					8.76	DMSO-d_6
Inosine (Ino)		12.35	8.15			8.25	DMSO-d_6
$[Ru(CO)_3(Ino)Cl_2]$		12.50	8.22			8.98	DMSO-d_6
$[Ru(CO)_3(Ino)_2Cl]Cl$		12.47	8.25			8.99	DMSO-d_6
			(8.15)			(8.25)	
$[Ru(CO)_3(InoAc_3)_2Cl]Cl$		12.53	8.25			9.08	$CDCl_3$
$[Ru(CO)_2(Ino)_2Cl_2]$		12.51	8.22			8.97	DMSO-d_6
			(8.16)			(8.26)	
$[Ru(CO)_2(InoAc_3)_2Cl_2]$		12.52	8.25			9.05	$CDCl_3$
$[Ru(CO)_3(Ino - H^+)Cl]$			8.38			9.10	DMSO-d_6
$[Ru(CO)_2(Ino - H^+)_2]$			8.35			9.12	DMSO-d_6

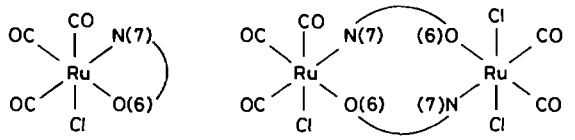
0.73, 0.83, 0.80, 0.85 and 0.87 ppm, respectively, while the H2 resonance is shifted by only 0.07, 0.10, 0.09, 0.23 and 0.20 ppm. These results are comparable to those found in other similar cases [18–23] and may be taken as an indication of the N7 coordination of inosine to ruthenium in these complexes.

The ^{1}H NMR spectra of the bis-nucleoside complexes $[Ru(CO)_3(Nucl)_2Cl]Cl$ and $[Ru(CO)_2(Nucl)_2Cl_2]$ (Nucl = Ado, Cyd, Guo and Ino) show bands assigned to both complexed and uncomplexed nucleosides (see Table III). This was attributed to substitution of one nucleoside by the strong complexing solvent (DMSO-d_6) used for recording the spectra. To support this hypothesis, the complexes $[Ru(CO)_3(NuclAc_3)_2Cl]Cl$ and $[Ru(CO)_2(NuclAc_3)_2Cl_2]$ were prepared and their ^{1}H NMR spectra were recorded in the non-complexing solvent $CDCl_3$ and, as discussed above, it was found that these complexes do not show any anomalous behaviour in this solvent.

In the non-deprotonated complexes of inosine and guanosine, the ν(C6=O) frequencies remain essentially unchanged on complexation and this excludes participation of this group in the formation of the complexes. In the deprotonated complexes $[Ru(CO)_3(Nucl - H^+)Cl]$ and $[Ru(CO)_2(Nucl - H^+)_2]$, however, these bands are shifted to lower energies by about 70–75 cm^{-1} (see Table II) and this may be taken as an indication of C(6)=O keto-oxygen involvement in coordination after N(1)H imino proton ionization [24–26]. Certainly, the double-bond character of the C(6)=O group is also lowered when the oxygen interacts covalently with a metal without loss of the N(1)H imino proton [27]. Oxygen involvement in bonding, following deprotonation of the imino proton, has also been found in the crystal structure of *cis*-diammineplatinum-a-pyridone blue, where both O^- and N atoms bridge two platinum atoms [28]. Oxygen–Ag(I) was also

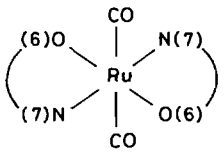
found by Kistenmacher *et al.* [29] in the crystal structure of (nitrato)(1-methylcytosine)silver(I).

These observations, together with the ^{1}H NMR data, suggest that guanosine and inosine act as bidentate ligands in the deprotonated complexes through both their O6 and N7 atoms, either in a chelate **I**, or a dimeric **II** structure for the mononucleosidato complexes $[Ru(CO_3)(Nucl - H^+)Cl]$:

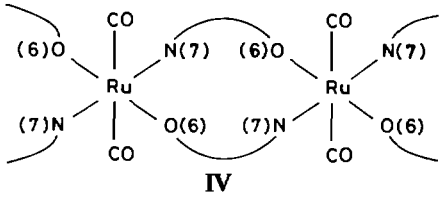


I **II**

or a bis-chelate **III** or polymeric **IV** structure for the bis-nucleosidato complexes $[Ru(CO)_2(Nucl - H^+)_2]$:



III



IV

(7)N O(6) = deprotonated nucleoside (Nucl – H^+)

In conclusion, purine and pyrimidine nucleosides in methanolic solution act as monodentate ligands towards the dimeric and polymeric Ru(II) complexes $[Ru(CO)_3Cl_2]_2$ and $[Ru(CO)_2Cl_2]_x$, causing breakage of the chloride bridges. Excess of nucleosides drives the reaction further and one chloride is substituted giving bis-nucleoside complexes. Those complexes with one N(1)H undergo deprotonation in alkaline solution giving products in which the nucleosides act as bidentate ligands.

Experimental

Materials and Methods

The nucleosides and ruthenium trichloride hydrate were purchased from Fluka A.G. and were used without further purification. The triacetyl derivatives of nucleosides and the chlorocarbonylo complexes of ruthenium(II) were prepared by the methods of Bredereck [30], and Cleare and Griffith [31], respectively.

The IR spectra were recorded on a Jasco spectrophotometer in KBr pellets. ^{1}H NMR spectra were obtained on a Varian-EM-360A high resolution spectrometer, with tetramethylsilane as internal reference. The Metrohm E 365 Conductoskop was used for the conductivity data.

Preparation of the Complexes

(1) [Ru(CO)$_3$(Nucl)Cl$_2$]

The dimeric complex $[Ru(CO)_3Cl_2]_2$ (0.258 g, 0.5 mmol) and 1 mmol of each of the nucleosides Ado, AdoAc_3, Cyd, CydAc_3, Guo, GuoAc_3, Ino and InoAc_3 were suspended in 150 ml of methanol flushed with nitrogen and stirred overnight at room temperature. The resulting solution was filtered from any undissolved material and roto evaporated (at 40 °C) to a small volume. The compound was then precipitated with excess ether. The yield was around 90%.

(2) [Ru(CO)$_3$(Nucl)$_2$Cl]Cl

Procedure (1) was followed but the ratio $[Ru(CO)_3Cl_2]_2$:Nucl was 1:4.

(3) [Ru(CO)$_2$(Nucl)$_2$Cl$_2$]

$[Ru(CO)_2Cl_2]_x$ (0.228 g) and 2 mmol of each of the nucleosides Ado, AdoAc_3, Cyd, CydAc_3, Guo, GuoAc_3, Ino and InoAc_3 were used and procedure (1) was followed.

(4) [Ru(CO)$_3$(Nucl – H$^+$)Cl]

Samples (1 mmol) of each of the complexes $[Ru(CO)_3(Nucl)Cl_2]$ (Nucl = Guo or Ino) were dissolved in 50 ml methanol, then 1 mmol KOH (in 10 ml methanol) was added and stirred for 1 h. The mixture was then filtered and roto evaporated to dryness (at 30 °C). The residue was taken up with 5 ml DMF and filtered. The compound was then precipitated from the filtrate with excess ethanol/ether (1:3). The yield was around 60%.

(5) [Ru(CO)$_2$(Nucl – H$^+$)$_2$]

Samples (1 mmol) of each of the complexes $[Ru(CO)_2(Nucl)_2Cl_2]$ (Nucl = Guo or Ino) and 2 mmol KOH were used and procedure (4) was followed. The yield was around 60%.

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