Interaction of Bis[μ-chlorodicarbonylrhodium(I)] with Nucleosides

G. PNEUMATIKAKIS, J. MARKOPOULOS and A. YANNOPOULOS

University of Athens, Department of Chemistry, 13A Navarinou Str., 10680-Athens, Greece

(Received November 20, 1986)

The dimeric complex bis[μ-chlorodicarbonylrhodium(I)], $[Rh(CO)_2Cl]_2$, is a versatile reagent for the preparation of Rh(I) complexes. It has been known for a long time that $[Rh(CO)_2Cl]_2$ reacts with neutral ligands, L, to give planar complexes under breakage of the double chloride bridge [1]. Recently Beck and co-workers prepared a series of analogous complexes with nucleic acid bases and nucleosides [2]. With ambivalent nucleosides (e.g. adenosine), $[Rh(CO)_2Cl]_2$ gives dinuclear complexes in which the chloride bridges are substituted with nucleoside bridges [2], as in the case of imidazolate complexes [3].

The interaction of rhodium with nucleosides has recently gained interest after the discovery that some of its compounds show anticancer activity [4, 5]. In this respect the interaction of the antitumour complex $Rh_2(CHCOO)_4$ with nucleosides and nucleotides has been studied in detail [6]. In continuation of our interest in metal ion nucleoside interactions, we further examined the reaction of the dimeric complex $[Rh(CO)_2Cl]_2$ with nucleosides and report herewith on the preparation and characterization of some new Rh(I)–nucleoside complexes, together with the investigation of some of their oxidative addition reactions and the preparation of the respective Rh(III) complexes.

*Author to whom correspondence should be addressed.

Results and Discussion

The direct interaction of $[Rh(CO)_2Cl]_2$ with nucleosides (Nucl = cytidine (Cyd), guanosine (Guo), inosine (Ino) and their tris-acetylated derivatives ($NuclAc_3$)) in a 1:4 molar ratio resulted in breakage of the double chloride bridge and the substitution of coordinated chloride:

$$[Rh(CO)_2Cl]_2 + 4Nucl \longrightarrow 2[Rh(CO)_2(Nucl)_2]Cl \quad (1)$$

The complexes behave as 1:1 electrolytes in DMF and the analytical data (Table I) fit well with the proposed formulation.

All the complexes show very strong multiple bands in the terminal carbonyl region, while both ν(Rh–Cl) and ν(Rh–Cl–Rh) bands are absent from the IR spectra of the new complexes (see Table II).

The ν(C=O) bands of the free nucleosides remain unchanged in the complexes and this excludes the participation of this group in the complexation in all cases studied.

The ^{1}H 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 complex $[Rh(CO)_2(Cyd)_2]Cl$ shows three doublets in the aromatic proton region [8.40, 7.60 ppm (NH_2); 8.20, 8.11 ppm (H(6)); 6.15, 6.08 ppm (H(5))]. Both H(5) and H(6) are shifted downfield, with the larger shift for H(5). This indicates that H(5) is closer to the coordination site on the ligand, probably the N(3) atom [2, 7 and refs. therein].

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

Compound	Rh (%)	Cl (%)	Λ_M (in DMF) (ohm^{-1} cm^2 mol^{-1})
$[Rh(CO)_2(Cyd)_2]Cl$	14.80(15.11)	4.91(5.21)	92
$[Rh(CO)_2(Cyd)_2Cl_2]Cl$	13.50(13.69)	14.36(14.17)	65
$[Rh(Cyd)_3Cl]$	11.50(11.85)	4.32(4.09)	6
$[Rh(Cyd)_3Cl_3]$	10.70(10.96)	11.56(11.34)	5
$[Rh(CO)_2(Guo)_2]Cl$	13.75(13.52)	4.83(4.66)	95
$[Rh(CO)_2(Guo)_2Cl_2]Cl$	12.55(12.37)	12.57(12.80)	60
$[Rh(Guo)_3Cl_3]$	10.21(10.41)	3.90(3.59)	7
$[Rh(Guo)_3Cl_3]$	10.10(9.71)	10.41(10.05)	6
$[Rh(CO)_2(Ino)_2]Cl$	14.35(14.08)	5.12(4.86)	94
$[Rh(CO)_2(Ino)_2Cl_2]Cl$	12.60(12.83)	12.95(13.28)	62
$[Rh(Ino)_3Cl]$	10.59(10.91)	3.95(3.76)	6
$[Rh(Ino)_3Cl_3]$	10.36(10.15)	10.28(10.50)	5

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

0020-1693/87/$3.50

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

Compound	ν(C≡O)	ν(C=O)$_{Nucl}$	ν(Rh–Cl)
Cytidine			
$[Rh(CO)_2(Cyd)_2]Cl$	1995, 1998, 2008, 2042	1660	
$[Rh(CO)_2(Cyd)_2Cl_2]Cl$	1998, 2010, 2025, 2047	1665	318
$[Rh(Cyd)_3Cl]$		1658	312
$[Rh(Cyd)_3Cl_3]$		1666	320
Guanosine		1695	
$[Rh(CO)_2(Guo)_2]Cl$	1997, 2005, 2015, 2045	1695	
$[Rh(CO)_2(Guo)_2Cl_2]Cl$	1998, 2009, 2020, 2052	1698	319
$[Rh(Guo)_3Cl]$		1693	312
$[Rh(Guo)_3Cl_3]$		1700	322
Inosine		1703	
$[Rh(CO)_2(Ino)_2]Cl$	1995, 2003, 2016, 2040	1706	
$[Rh(CO)_2(Ino)_2Cl_2]Cl$	1995, 2000, 2040, 2050	1712	320
$[Rh(Ino)_3Cl]$		1708	315
$[Rh(Ino)_3Cl_3]$		1714	325

[a]As nujol mulls.

TABLE III. ^1H NMR Chemical Shifts of the Complexes in DMSO-d_6 (ppm)

Compound	NH_2	NH	H(2)	H(5)	H(6)	H(7)
Cytidine	7.15			5.75, 5.65	7.85, 7.80	
$[Rh(CO)_2(Cyd)_2]Cl$	8.40, 7.60			6.15, 6.08	8.20, 8.11	
$[Rh(CO)_2(Cyd)_2Cl_2]Cl$	8.50, 7.58			6.22, 6.08	8.21, 8.12	
$[Rh(Cyd)_3Cl]$	8.65, 7.62			6.20, 6.10	8.18, 8.08	
$[Rh(Cyd)_3Cl_3]$	8.62, 7.70			6.23, 6.14	8.20, 8.14	
Guanosine	6.40	10.60				7.85
$[Rh(CO)_2(Guo)_2]Cl$	6.70	11.00				8.39
$[Rh(CO)_2(Guo)_2Cl_2]Cl$	6.73	11.20				8.49
$[Rh(Guo)_3Cl]$	6.72	11.10				8.37
$[Rh(Guo)_3Cl_3]$	6.75	11.30				8.48
Inosine		12.80	8.15			8.25
$[Rh(CO)_2(Ino)_2]Cl$		12.35	8.20			8.82
$[Rh(CO)_2(Ino)_2Cl_2]Cl$		12.40	8.25			8.85
$[Rh(Ino)_3Cl]$		12.37	8.22			8.80
$[Rh(Ino)_3Cl_3]$		12.45	8.28			8.84

Further evidence for the participation of the N(3) atom in the coordination comes from the NH_2 resonance, which appears as a doublet due to the hindered rotation of the C–NH_2 bond as a result of the N(3) coordination [2, 8].

In the complex $[Rh(CO)_2(Guo)_2]Cl$ the H(8) resonance is shifted by 0.54 ppm downfield relative to free guanosine and this is good evidence that the N(7) atom participates in the coordination. The complex $[Rh(CO)_2(Ino)_2]Cl$ shows two resonances at 8.20 and 8.72 ppm assigned to H(2) and H(8), respectively. The downfield shift of the H(8) resonance by 0.57 ppm is comparable to the one found in other similar cases [2, 7, 9] and may be taken as an indication of the N(7) coordination of inosine to Rh(I).

The interaction of the dimeric complex $[Rh(CO)_2Cl]_2$ with excess of nucleosides (1:6 molar ratio) at elevated temperatures (boiling methanol) resulted in breakage of the double chloride bridge as well as in the substitution of the carbonyl groups giving the square planar Rh(I) complexes $Rh(Nucl)_3Cl$, according to eqn. (2):

$$[Rh(CO)_2Cl]_2 + 6Nucl \longrightarrow 2[Rh(Nucl)_3Cl] + 4CO \quad (2)$$

Experimental

The experimental techniques have been published elsewhere [10]. The dimeric complex $[Rh(CO)_2Cl]_2$ was prepared according to the literature method [11].

Preparation of the Complexes

(1) Dicarbonyl-bis(nucleoside)rhodium(I) chloride, [Rh(CO)$_2$(Nucl)$_2$]Cl (Nucl = Cyd, Guo, Ino)

0.5 mmol (0.1945 g) of [Rh(CO)$_2$Cl]$_2$ and 2 mmol of the respective nucleoside (Cyd, Guo of Ino) 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 30 °C) to a small volume. The compound was then precipitated with excess ether. The yield was around 90%.

(2) Chloro-tris(nucleoside)rhodium(I), [Rh(Nucl)$_3$Cl]

0.5 mmol (0.1945 g) of [Rh(CO)$_2$Cl]$_2$ and 2 mmol of the respective nucleoside (Cyd, Guo or Ino) were suspended in 150 ml of methanol flushed with nitrogen and heated under reflux and nitrogen atmosphere for 2 h. The resulting solution was filtered and roto-evaporated to a small volume. After cooling in an ice bath for 1 h the microcrystalline material precipitated and was filtered, washed with ether and dried at 50 °C under vacuum. The yield was around 70%.

(3) Dichlorodicarbonyl-bis(nucleoside)rhodium-(III) chloride, [Rh(CO)$_2$(Nucl)$_2$Cl$_2$]Cl

0.5 mmol of the respective complex [Rh(CO)$_2$-(Nucl)$_2$]Cl was dissolved in 50 ml of methanol and to that were added 20 ml of chloroform saturated with chlorine. The solution was stirred for 1 h at room temperature. It was then roto-evaporated to a small volume and the compound was precipitated with excess ether. The yield was around 75%.

(4) Trichloro-tris(nucleoside)rhodium(III), [Rh(Nucl)$_3$Cl$_3$]

0.5 mmol of the respective complex [Rh(Nucl)$_3$-Cl] was dissolved in 50 ml of methanol and to that were added 20 ml of chloroform saturated with chlorine. The procedure (3) was then followed throughout the preparation.

The complexes are non-electrolytes and the analytical results (Table I) fit well with the proposed formulation. The carbonyl stretching of the parent dimeric complex is absent from the IR spectra of the complexes, while all spectra show a band of medium intensity in the region 310–320 cm^{-1} assigned to Rh–Cl stretching. The ν(C=O) band of the nucleosides remains essentially unchanged in the complexes and this excludes the participation of this group in coordination. The ^{1}H NMR spectra of the [Rh-(Nucl)$_3$Cl] complexes are very similar to those of the [Rh(CO)$_2$(Nucl)$_2$]Cl complexes (Table III) and it is concluded from this fact that guanosine and inosine coordinate to Rh(I) through their N(7) atom, while the N(3) atom of cytidine may be the ligation site.

The [Rh(CO)$_2$(Nucl)$_2$]Cl and [Rh(Nucl)$_3$Cl] complexes, as most other Rh(I) complexes, undergo oxidative addition reactions giving Rh(III) complexes. The reaction thoroughly studied is that with chlorine and may be represented by eqns. (3) and (4):

$$[Rh(CO)_2(Nucl)_2]Cl + Cl_2 \longrightarrow [Rh(CO)_2(Nucl)_2Cl_2]Cl \quad (3)$$

$$[Rh(Nucl)_3Cl] + Cl_2 \longrightarrow [Rh(Nucl)_3Cl_3] \quad (4)$$

The [Rh(CO)$_2$(Nucl)$_2$Cl$_2$]Cl complexes behave as 1:1 electrolytes, while the [Rh(Nucl)$_3$Cl$_3$] complexes do not conduct. The former complexes (products of reaction 3) retain the terminal carbonyl groups as is shown from their IR spectra (Table II) and are some of the very few examples of Rh(III) carbonyl complexes. Both groups of complexes exhibit strong bands around 320 cm^{-1} assigned to Rh–Cl stretchings. The ^{1}H NMR and IR spectra of both groups of complexes are very similar to those of the parent compounds, indicating that the ligation sites of the nucleosides remain unchanged (N(7) for guanosine and inosine and N(3) for cytidine) in the oxidation products.

Further oxidative addition reactions are now under investigation and the results will be published elsewhere.

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