Gold(III) and Rhodium(III) Chloride Adducts with Adenine*

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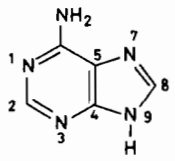
Earlier work in these laboratories has resulted in the development of a general method of preparation of metal complexes of adenine (adH; **I**) and other purines (purine, guanine, xanthine, hypoxanthine,



I

theophylline, threobromine, caffeine) from non-aqueous media [2–9]. The method consists of refluxing mixtures of the ligand and a metal salt (halide, perchlorate, nitrate, tetrafluoroborate, thiocyanate, sulfide, acetate, *etc.*; metal ions studied: Al^{3+}, V^{3+}, Cr^{3+}, Mn^{2+}, Fe^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Dy^{3+}, Th^{4+}, U^{4+}) in a mixture of absolute ethanol and triethyl orthoformate (teof; $HC(OC_2H_5)_3$) for several days (until a quantity of solid metal complex, sufficient for characterization work, is obtained) [2–9]. Most recently, we extended our synthetic work to include the complexes formed by interacting adH with various precious metal chlorides, under our preparative conditions [1], and have already reported on the preparation and characterization of $Pd(adH)Cl_2$ and $Pt(adH)_2Cl_4$ polymeric adducts [10]. Subjects of the present communication are the adducts of adH with $AuCl_3$ and $RhCl_3$, prepared by the same synthetic method. It should be mentioned here that, in view of their potential antitumor activity and other medicinal applications, there has been significant interest in complexes of gold and rhodium with nucleobases, nucleosides and nucleotides [11–29]. Interactions of nucleosides with $HAuCl_4$ in non-aqueous media leads to the formation of AuL_2Cl_3 complexes (L = nucleoside), while the corresponding interactions in aqueous solutions result in the isolation of $AuLCl_3$ complexes, which can also be obtained by suspending the AuL_2Cl_3 species in water [11, 12]. Au(III) is reduced to Au(I) in aqueous solutions of $HAuCl_4$ and nucleoside, containing HCl and l-ascorbic acid; during these reactions, white precipitates of AuL_2Cl are formed [11]. $HAuBr_4$ reactions with uridine and cytosine reportedly lead to bromination of the pyrimidine at C(5) with concomitant reduction of Au(III) to Au(I) [13, 14]. Several studies dealing with the interactions of Au(III) [15–18], Au(I) [19] and Rh(III) [20] with DNA were reported. Both Au^{3+} and Rh^{3+} appear to bind to the nucleobase and phosphate fragments of DNA [16, 20]. Raman studies of the reaction products of mixtures of adenosine, guanosine, uridine and cytidine 5′-monophosphates with $(CH_3)_2AuClO_4$ and $Rh_2(OOCCH_3)_4$ indicated that Au^{3+} reacts directly with the purine and pyrimidine ring nitrogens, while the dimeric cluster of the Rh^{2+} compound remains intact and causes almost not measurable perturbation of the electron-density of the nucleotides, although the presence of axial (probably nitrogen) ligands is suggested by color changes [21]. Adducts of the $Rh_2(OOCCH_3)_4L_2$ type (L = adenine, adenosine [22], theophylline, caffeine [23]) have been prepared [22, 23], and the crystal structure determinations of the theophylline and caffeine adducts established that these axial ligands are N(9)-bonded to the Rh^{2+} ions [23]. On the other hand, coordination of adenine to Rh^{2+} may be occurring through N(7), owing to H-bonding interactions between the exocyclic NH_2 group of this ligand and carboxylate oxygens [22, 23]. Several solid adducts of $RhCl_3$, including $Rh(adH)_2Cl_3 \cdot MeOH$ [24], $Rh(ado)Cl_3 \cdot 2MeOH$, $[Rh(ado)(NH_3)_4Cl]Cl_2 \cdot H_2O$, $[Rh(xno)(OH_2)_3Cl_2]Cl$, $[Rh(xno)_2(NH_3)_2Cl_2]Cl \cdot 2H_2O$ (ado = adenosine; xno = xanthosine) [25], two complexes with adenosine triphosphate [26] and RhL_3Cl_3 (L = 6-methyl-2-thiouracil) [27], have been prepared and characterized. Finally, a number of adducts and complexes of Rh(I) carbonyls with nucleobases and nucleosides were also reported [28, 29].

The new complexes herein reported were prepared by mixing 0.8 mmol anhydrous MCl_3 (M = Au, Rh), 2.4 mmol adH, 35 ml absolute ethanol and 15 ml teof, and refluxing for five days. Following the refluxive step, the supernatant was reduced to about one-half its original volume, by heating under

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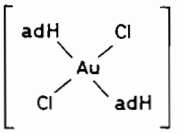
reduced pressure, and the solid complexes were separated by filtration, washed with anhydrous diethyl ether, and stored *in vacuo* over anhydrous $CaCl_2$. The complexes obtained were of the $Au(adH)_2Cl_3$ (golden brown) and $Rh(adH)Cl_3 \cdot EtOH$ (mustard yellow) types. The Au^{3+} complex dissolves in some organic solvents, including N,N-dimethylformamide (dmf), in which it shows a molar conductivity of 70 Ω^{-1} cm^2 mol^{-1} (10^{-3} M solution at 25 °C). In contrast, the Rh^{3+} complex is insoluble in organic media.

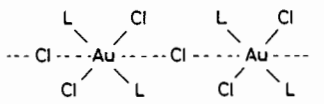
The UV–visible spectra of the free ligand and the new complexes are as follows (solid-state spectra on Nujol mulls), nm: adH: 185vvs, 208vvs, 260vvs,vb; $Au(adH)_2Cl_3$: 199vvs,sh, 237vvs,sh, 252vs,b, 285vs,sh, 299s,sh, 322s, 346s, 370ms,sh, 392m,sh, 431m,sh, 493mw,sh, 537w, vb; $Rh(adH)Cl_3 \cdot EtOH$: 191vvs,sh, 235vvs,sh, 254vvs,b, 283vs,sh, 306s,b, 328ms,b, 353ms, 396ms, 420m,sh, 496m,vb, 557w,sh. As was the case with other adH metal complexes [2, 6, 10], the $\pi \rightarrow \pi^*$ transitions of the ligand [30] undergo shifts and excessive splittings upon adduct formation with $AuCl_3$ or $RhCl_3$, while the $n \rightarrow \pi^*$ transition, which is masked in the spectrum of free adH [30], appears at 299–306 nm in the spectra of the new complexes. The strong to medium intensity maxima observed at 320–560 nm in the spectra of the complexes are mostly of the charge-transfer type, although contributions from d–d transitions ($^1A_{1g} \rightarrow {}^1T_{1g}$ and $^1T_{2g}$) are likely for the bands at 328–420 nm in the spectrum of the Rh^{3+} complex [31]. Both of the complexes are diamagnetic, as is usual for $5d^6$ or $4d^6$ compounds, which have the tendency to assume their low-spin arrangements.

The infrared spectra of both complexes at 4000–1000 cm^{-1} are characterized by strong ν_{NH} bands at 2900, 2800, 2680 and 2590 cm^{-1} (corresponding maxima in free adH: 2900, 2800, 2690, 2600 cm^{-1}), as expected for adducts of neutral adH (2.32). The ν_{NH_2}, δ_{NH_2} and ρ_{NH_2} bands of adH at 3350, 3295, 3118, at 1675 and at 1025 cm^{-1}, respectively, are only slightly shifted in the spectra of the complexes (M = Au: 3340, 3300, 3125 1672, 1022; M = Rh: 3360, 3300, 3120, 1666, 1019 cm^{-1}), so that binding of the ligand through the exocyclic NH_2 group nitrogen can be ruled out [2, 10, 24, 33, 34]. On the other hand, some of the $\nu_{C=C}$, $\nu_{C=N}$ and ring vibrations of adH at 1600–1300 cm^{-1} (occurring at 1600, 1565, 1508, 1449, 1419, 1390, 1369, 1334, 1308 cm^{-1}) undergo larger shifts and occasional splittings in the spectra of the new adducts, *viz.*, cm^{-1}: M = Au: 1640, 1597, 1559, 1525, 1509, 1470, 1438, 1423, 1389, 1327, 1302; M = Rh: 1633, 1606, 1588, 1560, 1537, 1518, 1460, 1430, 1402, 1381, 1332, 1309. These features are consistent with coordination of adH through ring nitrogens [2, 10, 32–34].

$Au(adH)_2Cl_3$ is an analog of the AuL_2Cl_3 complexes with various nucleosides (guanosine, inosine and triacetyl derivatives) previously reported [11]. It has a similar molar conductivity (*vide supra*) to these complexes, and shows Au–ligand bands of the same type, *i.e.*, ν_{Au-Cl} at 362 and ν_{Au-N} at 285 cm^{-1} [11] (ligand bands in this region: free adH 330, 267; gold complex 330, 269 cm^{-1}). These features are consistent with a *trans*-square planar configuration for the complex (structure **II**) [11, 35, 36], with two terminal adH and two terminal



II

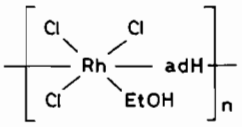


III

chloro ligands and an anionic Cl^- group. It should be noted, however, that when the AuL_2Cl_3 nucleoside complexes [11] were studied by ^{197}Au-Mössbauer spectroscopy, lower isomer shifts and quadrupole splittings than those expected for a structure similar to **II** were observed, and the possibility of a hexacoordinated polymeric structure (similar to that of $Au(phen)Cl_3$ (phen = 1,10-phenanthroline) [37]), in which each Cl^- counterion is situated between two stacked $[AuL_2Cl_2]^+$ cations, and forms a long bond to Au^{3+}, so that an octahedron elongated along the z-axis (structure *III*) is produced, was advanced [12]. Such a structure is not inconsistent with the observation of ν_{Au-Cl} at 362 cm^{-1}. In fact, $Au(phen)Cl_3$, which of necessity involves a *cis*-AuN_2Cl_4 absorbing species [37], exhibits Au–Cl IR bands at 378, 370 and 360 cm^{-1} [38]; a single ν_{Au-Cl} band would be expected in the same region for a *trans*-AuN_2Cl_4 species of type **III** [39].

$Rh(adH)Cl_3 \cdot EtOH$ differs from the previously reported $Rh(adH)_2Cl_3 \cdot MeOH$ [24] in that it is a 1:1 rather than 2:1 adduct of adH with the Rh^{3+} salt. This complex, unlike the new Au^{3+} compound, is insoluble in organic media and probably polymeric [2–10]. Three ν_{Rh-Cl} bands were detected at 357, 322 and 301 [39], along with one ν_{Rh-O}(EtOH) band at 477 [39, 40] and two ν_{Rh-N} absorptions at 260 and 240 cm^{-1} [39] (adH bands in the complex at 450, 330, 270 cm^{-1}). The complex exhibits also a band at 540 cm^{-1}, which is present in several adH metal complexes (including the new Au^{3+} complex) [2, 7, 9, 10] and probably due to a ligand mode (in the past ν_{Rh-N} was assigned at 575–490 cm^{-1} in adH, ado or xno complexes [24, 25]). The ν_{OH}(EtOH) mode appears at 3420 cm^{-1} in the spectrum of the Rh^{3+} complex [41]. In view of the presumably polymeric structure of this complex, the terminal character of the chloro ligands in this hexacoordinated species [39], and the pronounced

tendency of adH to function as a bidentate bridging ligand [42], structural type **IV** is considered as most probable.



IV

The most likely binding site for terminal adH in $Au(adH)_2Cl_3$ (structure **II** or **III** (L = adH)) is the N(9) imidazole nitrogen. In fact, N(9) is the protonation site of free adH, and, therefore, the preferred site of bonding when this ligand acts as terminal unidentate [42]; in addition, the presence of the exocyclic NH_2 substituent at C(6) of adenine blocks the N(1) site sterically, while increasing the electron-density at N(9) (relative to purine), so that binding through the latter site becomes favorable [43]. N(9) would also be one of the binding sites of bridging bidentate adH in the Rh^{3+} complex [2, 7, 9, 10, 42, 43]. As far as the second binding site of the bridging ligand is concerned, N(7) is considered as most likely, since coordination of bridging bidentate adH or purine through N(7) and N(9) has been demonstrated in metal complexes with single ligand bridges [44, 45]. The other possible combination is binding through N(3) and N(9), but this seems to be common only in magnetically subnormal Cu^{2+} complexes with multiple ligand bridges between adjacent copper(II) ions [46, 47].

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