Gold(III) Complexes of 2-Amino-4,6-dimethylpyrimidine

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Synopsis. The reactions of Au(III) with 2-amino-4,6-dimethyl pyrimidine (ADMPY) are reported. Complexes of Au(III) with ADMPY have been isolated from reactions in aqueous and in methanolic solutions, and characterized by elemental analysis, IR spectra ^{1}H NMR spectra, electronic absorption spectra, conductivity in DMF solutions, and thermal gravimetric analysis.

The pyrimidine ring system present in nucleic acids, several vitamins, coenzymes, and antibiotics etc., provides potential binding sites for metal ions and any information on their coordinating properties is important as a means of understanding the role of metal ions in biological systems. The interaction of metal ions with nucleic acids constituents has been the subject of extensive investigations in recent years.[1,2]

The gold complexes are interesting in biological chemistry.[3] Many gold compounds were recently found to be strong antitumor agents,[4] more promising were found the binuclear gold complexes.[4] Gold complexes with nitrogen donor ligands[3,5] have been considered suitable for modern chrysotherapy associated with the treatment of rheumatoid arthritis. The gold antiarhritic compounds include important examples of inorganic-based pharmaceuticals.[6,7]

Experimental

Preparation of the Complexes. Au(ADMPY)Cl$_3$. (1) and Au(ADMPY)Br$_3$, (2). The complexes were prepared by mixing aqueous solutions of the ligand and $HAuCl_4$. aq or $AuBr_3$ [1 : 1 ligand to metal molar ratio]. The reaction mixture was stirred for 2h at room temperature. The precipitate was filtered off, washed with small amounts of ice-cold water and dried in vacuum over silica gel. Compound **1**; yellow powder, Found: C, 16.48; H, 2.04; N, 9.80; Au, 45.80; Cl, 24.80%. Calcd for C, 16.89; H, 2.12; N, 9.85; Au, 46.18; Cl, 24.93%. Compound **2**. red-brown powder, Found: C, 12.30; H, 1.15; N, 7.20; Au, 35.32; Br, 42.02%. Calcd for C, 12.87; H, 1.62; N, 7.50; Au, 35.17; Br, 42.82%.

[Au(ADMPY)$_2$Br]$_2$Br$_4$ (3). The complex was prepared by mixing methanolic solutions of the ligand and $AuBr_3$ [3 : 1 or 2 : 1 ligand to metal molar ratio]. After stirring for 24h at room temperature no precipitate was separated. The yellow solution was evaporated to dryness under reduced pressure. When the residual was dissolved in a small volume of CH_2Cl_2 and an excess of C_6H_6 was added, a red powder was precipitated. After filtration the powder was again dissolved in CH_2Cl_2 and precipitated by C_6H_6. The complex was washed with petroleum ether and dried as before. Compound **3**. Found: C, 21.20; H, 2.77; N, 12.64; Au, 28.64; Br, 34.65%. Calcd for C, 21.10; H, 2.63; N, 12.30; Au, 28.84; Br, 35.09%.

[Au(ADMPY)$_2$Cl$_2$](ADMPY)Cl · 2H$_2$O (4). The complex was prepared by mixing methanolic solutions of the ligand and $HAuCl_4$. aq [3 : 1 or 2 : 1 ligand to metal molar ratio]. When the reaction mixture was stirred for 24 h at room temperature, no precipitate was separated. The clear solution was evaporated to a small volume (2—3 ml CH_3OH) under reduced pressure. With addition of an excess of ether, a yellow powder was precipitated. After filtration the powder was redissolved in methanol and precipitated with ether. Compound **4**. Found: C, 30,08; H, 4.02; N, 17.67; Au, 27.50; Cl, 14.80%. Calcd for C, 30.54; H, 4.37; N, 17.81; Au, 27.82; Cl, 15.02%.

Physical Measurements. Infrared spectra were recorded on a Perkin-Elmer 580 spectrophotometer on KBr pellets in the 4000—400 cm^{-1} region and on Nujol mulls supported by polyethylene windows in the 500—200 cm^{-1} region. The electronic absorption spectra of the solution in dimethylformamide were recorded on Hitachi 100-70 and Cary 17D spectrophotometers. Solid state electronic reflectance spectra were run on Varian 634 and Cary 14 spectrophotometers. Analyses and other experimental techniques were as described previously.[8,9]

Results and Discussion

The complexes **1** and **2** were non conductors in dimethylformamide solutions in agreement with their four coordination and square planar geometry. The complex **3** was 1 : 2 electrolyte while the complex **4** was 1 : 1 electrolyte in DMF solution.[10] Λ_m **1**=9; Λ_m **2**=21; Λ_m **3**=108; Λ_m **4**=46 S cm^2 mol^{-1}.

The significant bands observed in the IR spectra of the ligand and their complexes are presented in Table 1. All the complexes showed reductions in the observed values of $\nu_{as}(NH_2)$, $\nu_s(NH_2)$ by 25—60 cm^{-1}, but they were not as large as expected if coordination of the -NH_2 nitrogen atom occurs,[9] indicating the presence of intermolecular hydrogen bonding of the -NH_2 protons.[11] No appreciable changes were observed in the 700—1000 cm^{-1} region, in which coordinated water bands appeared.[12] On the other hand, various IR absorptions of free ADMPY, corresponding to ring vibrations modes underwent more sizeable shifts and occasional splittings in the spectra of the new complexes, this is consistent with coordination of the ADMPY through ring nitrogen in the complexes.[8] The complexes **1** and **2** showed one strong band at 367 and 251 cm^{-1} respectively, which were assigned to the asymmetric stretching vibration of the X-Au-X group possibly coinciding with the ν(Au-X) of the same motion.[13] The ν(Au-Cl) stretching vibration was assigned to the very strong band at 360 cm^{-1} for the complex **4**. The appearence of one band may indicate a trans rather a cis square planar structure. The complexes exhibited an intense infrared band in the 400—430 cm^{-1} region, but no bands are observed in the spectra of the ligand in this region, this band thus must have a large ν(Au-N) character.[8]

The ^{1}H NMR spectrum of the ligand in DMSO-d_6 showed a peak at 2.15 ppm downfield from TMS, which assigned to the equivalent C_4-CH_3 and C_6-CH_3 group protons, a sharp singlet at 6.48 ppm was

Table 1. Spectra IR Data of the Ligand and Its Complexes

Compound	$\nu_s(NH_2)$ $\nu_{as}(NH_2)$		$\delta(NH_2)$	I Ring vibr. II Ring vibr. III Ring vibr.	ν(Au-N)	ν(Au-X)
ADMPY	3416vs	3390sh	1646sh	1606vs		
	3325ms	3200s	1637ms	1572m		
				1472s		
1	3422vs	3330ms	1664sh	1610vs	432msbr	367s
	3260	3170s	1655s	1560s		341w
				1490m		
2	3418vs	3320ms	1655sh	1610vs	430msbr	251s
	3240sh	3160s	1646s	1580m		246s
				1540s		
				1482w		
3	3380vs	3340sh	1680sh	1640vs	426wbr	—
	3270ms	3180s	1670s	1600ms		
				1520m		
4	3390vs	3320s	1688s	1640vs	465ms	360s
	3280sh	3210s		1602ms		
				1590ms		
				1565m		

Table 2. Electronic Spectra of Square Planar Au(III) Complexes

Compound	Absorption in solution energy (ε/cm^{-1} mol^{-1} dm^3)	Reflectance in the solid	Assignment	Reference to exp. work
$Au(py)Cl_3$		20.833sh		30
(Chloroform soln)	27.472sh	26.315sh		
	32.050(1.400)	31.250	$^1A_{1g}\rightarrow{}^1E_g$	
$Au(py)_2Cl_3$		21.740sh		30
		24.390sh		
		30.300	$^1A_{1g}\rightarrow{}^1E_g$	
ADMPY(DMF soln)	35.114(3.300)		$n\rightarrow\pi^*$	This work
1		20.830sh	$^1A_{1g}\rightarrow{}^3B_{1g}$	This work
(DMF soln)		26.370	$^1A_{1g}\rightarrow{}^1E_g$	
	34.480(5.700)		$n\rightarrow\pi^*$	
4	30.769sh(2.700)	25.860	$^1A_{1g}\rightarrow{}^1E_g$	This work
(DMF soln)	35.087(12.400)		$n\rightarrow\pi^*$	
$Au(py)Br_3$	19.320sh	19.604sh		30
(Chloroform soln)	21.980sh			
	25.125(1.500)	25.000	$^1A_{1g}\rightarrow{}^1E_g$	
	29.410	28.570sh		
$Au(py)_2Br_3$		20.000sh		30
		24.390sh		
		29.410	$^1A_{1g}\rightarrow{}^1E_g$	
2		18.180sh	$^1A_{1g}\rightarrow{}^3A_{2g}$	This work
(DMF soln)	21.050sh(150)	20.120	$^1A_{1g}\rightarrow{}^3B_{1g}$	

assigned to the $-NH_2$ protons and another sharp singlet at 6.38 ppm was assigned to the C_5-H proton. The ^1H NMR spectra of the complexes **1** and **2** showed a downfield shift of the signal of the C_4-CH_3 and C_6-CH_3 protons and splitting of the signal was observed it can be noted that the symmetry of the pyrimidine molecule is disturbed. The protons of the amino groups exhibit characteristic downfield shifts by ca. 1.0—2.0 ppm in all the complexes indicating the occurrence protonation and/or coordination.[9] The spectra of the complex **4** showed two broad peaks centered at 7.4 and 6.1 ppm, assigned to the protons of the amino groups coordinate and free respectively.

The electronic absorption spectral data of square planar Au(III) complexes and the assignments of the observed bands are given in Table 2. The band at ca. 25.000—26.000 cm^{-1} is assigned to the $^1A_{1g}\rightarrow{}^1E_g$ transition. Brown, McKinlay, and Smith reported[14] that the positions and intensities of the lowest energy band $^1A_{1g}\rightarrow{}^1E_g$ appear to depend on the nature of the com-

plexing species. For the complexes of Au(III) with pyrimidine derivatives it was shown that, the intensity of the lowest energy band $^1A_{1g} \rightarrow {}^1E_g$ depended on the nature of the complexing species. The intensity range was much greater for the chlorides than the bromides (Table 2).

The thermal decomposition of the complex **4** was also studied by TG/DTG technique the TG and DTG curves showed that the dehydration process took place in two steps at 100 and 110 °C, and the dehydrated compound decomposed in the temperature range of 125—500 °C. The anhydrous compound $[Au(ADMPY)_2Cl_2]Cl$ (ADMPY) dissociated in three steps, two fast decomposition between 125—225 °C and 355—500 °C and another slow one between 225—340 °C. The complex **4** underwent and the endothermic reaction at 100—110 °C with mass loss corresponding to two molecules of water and also two endothermic and one exothermic reactions at 175 and 300 and at 440 °C respectively, with mass loss corresponding to the pyrimidine ring and halogen. The residue obtained at the end of the pyrolysis at 500 °C was 27.90% of the original weight, corresponding to Au(theoretical value 27.82%).

In accordance with the trans effect, the cis Pt(II), Pd(II), and Au(III) complexes can be synthesized directly from the $[MCl_4]^{2-}$ ions by reaction with N-donor ligand in methanolic or aqueous media, indicating that Cl^- has a greater trans effect compared to the N-donor ligand (L). While the replacement of chloride ions from $[MCl_4]^{2-}$ by (L) molecules give the cis isomer for the Pt(II) complexes, when $[AuCl_4]^-$,[15] $[PdCl_4]^{2-}$ [16] ions react with N-donor ligands (L) cis-trans isomerisation took place because of the higher stability of the trans-isomer. The *trans*-$Pd(L)_2Cl_2$[16] and *trans*-$[Au(L)_2Cl_2]Cl$ [15] isomers were thermodynamically more stable, so the *trans*-$[Au(ADMPY)_2Cl_2]Cl : ADMPY : 2H_2O$ isomer was precipitated instead of cis-isomer. The uncoordinated molecule of pyrimidine probably gives more stability to the compound. The failure to isolate $[Au(ADMPY)_4]Cl_3$ complexes is attributed to steric hindrance effects.

In the solid state, the ADMPY acts as unidentate through the endocyclic nitrogen N_1 or N_3 than through the nitrogen of the amino group. ^1H NMR data obtained for the diamagnetic complexes in DMSO-d_6 solution suggests a different coordination mode in which ADMPY coordinates via amino group nitrogen atom.[17] The most plausible structures for the isolated new complexes, based on the above results, are monomeric for **1**, **2**, and **4**. The latter complex exists rather in the trans form in view of the single band observed in the far ir spectra.[15] Considering the high value of molar conductivity in DMF solution and that there are no bands in the far IR spectra assignable to ν(Au-Br), the new complex $Au(ADMPY)_2Br_3$ seems to have a dimeric square planar structure $[Au(ADMPY)_2Br]_4$.

Finally it is worth noting that the four new compounds are possible candidate for antiarthritic activity[3,6,7] while the compounds **3** and **4** are possible candidate for antitumor activity.[4,18]

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