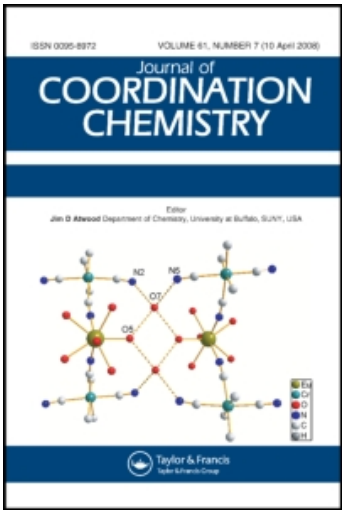

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^{13}C NMR STUDIES OF THE INTERACTION OF GOLD(I) THIOMALATE WITH 6-MERCAPTOPURINE AND ITS DERIVATIVES

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(Received 21 June 2000)

The interaction of gold(I) thiomalate, $[Autm]_n$ with thiolated nucleosides, 6-mercaptopurine (6-MP), 6-mercaptopurine-9-β-*D*-riboside (6-MPR) and 2-amino-6-mercaptopurine-9-β-*D*-riboside (2-A-6-MPR) has been studied by ^{1}H and ^{13}C NMR spectroscopy. It has been observed that these thiolated purine bases break the $[Autm]_n$ polymer and form complexes of the type []C═S-Au-tm]. The major shift in ^{13}C NMR occurs in C-6 resonances of the bases when they react with $[Autm]_n$. This is indicative of Au(I) binding with these bases through the sulfur atom only. In the case of 6-MP, it was observed that at pD 12, the N-9 proton is deprotonated causing a downfield shift in the C-8 resonance. However, coordination of Au(I) with N-9 or N-7 was not observed. Also, at its higher concentration thiomalate was ejected as a free ligand and due to its oxidation, thiomalic disulfide resonances were observed suggesting that it could behave as a thiolate ligand to gold(I). In cases of 6-MPR and 2-A-6MPR, no free thiomalate resonances in ^{13}C NMR were observed even at higher concentrations of these bases indicating that thiomalate was not released from $[Autm]_n$. At the 2 : 1 ratio of 6-MP to $[Autm]_n$, the b_1, b_2 and b_3 resonances of $[Autm]_n$ separated into two peaks indicating the existence of two geometrical isomers for the complex, 6-MP-Au-tm.

Keywords: Gold(I) thiomalate; 6-mercaptopurine; 6-mercaptopurine-9-β-*D*-riboside; 2-amino-6-mercaptopurine-9-β-*D*-riboside; ^{13}C NMR

INTRODUCTION

The thio analogues of the purine bases, 6-mercaptopurine and 2-amino-6-mercaptopurine are among the most active anti metabolites and their

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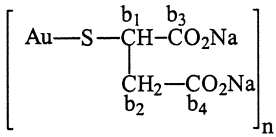
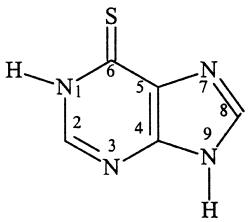
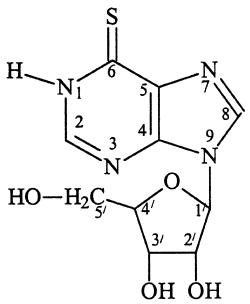
ribosides are known to exhibit antitumor activity [1, 2]. Mercaptopurine and its riboside are anticancer metabolites, clinically effective against human leukemias [3]. These thiolated compounds have seen only limited use in therapy as single agents. However, some metal complexes of purine thiones, especially those of Pt and Pd, show antitumor activity [4]. Some gold(I) purine-6-thiolate complexes are also shown to possess antiarthritic activity [5]. Cu^{+2} complexes of 6-mercaptopurine are also reported to possess



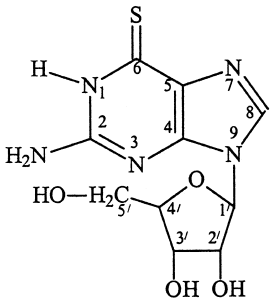
Myocrisin ([Autm]$_n$)



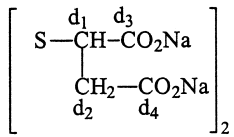
6-Mercaptopurine (6-MP)



6-Mercaptopurine riboside (6-MPR)



2-Amino-6-Mercaptopurine riboside (2-A-6-MPR)



Thiomalic disulfide ([tm]$_2$)

FIGURE 1 Structures of [Autm]$_n$, 6-mercaptopurines and [tm]$_2$ and their resonance assignments.

anti-inflammatory activity, a property that is in common with gold(I) thiolate drugs [6].

6-Mercaptopurine and 2-amino-6-mercaptopurine, and their ribosides are known to form complexes in solution with several metals, for example Pt(II) [1], Co(III) [7], Hg(II) [8], Cu(II) [6], Au(I) [5, 9], Mo(II) [10], Rh(III), Ru(III) and Ir(I) [3] *etc.* The antiarthritic drug disodium aurothiomalate (Myocrisin), $[Autm]_n$, exists as a polymer in the solid state as well as in solution [11, 12]. However, in the presence of other thiols, RSH, it undergoes exchange reactions forming $[Au(SR)_2]^-$ type complexes [13, 14] while with thiones it was observed to form [)C═S-Au-tm] type complexes [15, 16]. In the present study the interactions of $[Autm]_n$ with 6-mercaptopurine (6-MP), 6-mercaptopurine-9-β-*D*-riboside (6-MPR) and 2-amino-6-mercaptopurine-9-β-*D*-riboside (2-A-6-MPR) were investigated by ^1H and ^{13}C NMR spectroscopy. The structures of these ligands, $[Autm]_n$ and $[tm]_2$ are shown in Figure 1. The mercaptopurines and their ribosides are known to exist as thiones in the solid state as well as in aqueous solution at room temperature, while heating favours the thiol form [3]. It would be of interest to investigate whether these mercaptopurines act as anions, thiolates or as thiones. We show for the first time that two geometrical isomers are possible for the complex 6-MP-Au-tm, formed by 6-MP after interacting with $[Autm]_n$.

EXPERIMENTAL SECTION

Chemicals

Gold(I) thiomalate was obtained from ICN K & K Labs. 6-MP, 6-MPR 2-A-6-MPR, NaOD and DCl were obtained from Fluka Chemical Co. All chemicals were used without further purification.

pH Measurements

All pH measurements were made at 23°C with a Fischer Accumet pH meter, model 630. The pD indicates the actual meter reading for D_2O solutions with no correction for deuterium isotope effects. A pD higher than physiological pH was selected, because in each case precipitation occurs as a result of addition of thionucleosides to $[Autm]_n$ solution, and they dissolve only at higher pH. The pD was adjusted using DCl and NaOD. The pDs of all the solutions are given in Tables I and II.

^{1}H NMR Spectroscopy

^{1}H NMR spectra were obtained on a Jeol JNM-LA500 NMR spectrometer operating at the frequency of 500 MHz. The conditions were 32 k data points, 1.50 s pulse delay, and 6.20 μs pulse width. Observed proton chemical shifts for thiolated bases with and without addition of $[Autm]_n$ are given in Table I. ^{1}H NMR spectra were assigned according to the references given in the literature [13, 17].

^{13}C NMR Spectroscopy

^{13}C NMR spectra were obtained on the same spectrometer operating at the frequency of 125 MHz with ^{1}H broadband decoupling at 297 K. The conditions were 32 k data points, 1.00 s pulse delay, 4.50 μs pulse width and

TABLE I ^{1}H Chemical shifts of thiolated purine bases with and without addition of $[Autm]_n$ in D_2O

RS : $[Autm]_n$	*pD*	*H*-8	*H*-2	*H*-1′
RS = 6-MP				
1 : 0	9.96	8.07	8.17	
1 : 0	12.00	7.84	8.04	
1 : 2	9.95	8.11	8.30	
1 : 1	11.45	7.59	8.32	
1.5 : 1	11.15	7.94	8.12	
2 : 1	10.96	7.92	8.11	
RS = 6-MPR				
1 : 0	10.12	8.18	8.15	5.92 5.90
1 : 2	7.40	8.29	8.19	5.95 5.94
1 : 1	8.67	8.26	8.18	5.13 5.91
1.5 : 1	10.75	8.21	8.15	5.90 5.89
2 : 1	10.35	8.20	8.14	5.89 5.88
RS = 2-A-6-MPR				
1 : 0	11.30	7.80		5.69 5.71
1 : 2	8.20	7.88		5.71 5.72
1 : 1	9.50	7.89		5.69 5.71
1.5 : 1	10.55	7.85		5.73 5.72
2 : 1	10.87	7.84		5.71 5.72

TABLE II ^{13}C Chemical shifts of thiolated purine bases with and without addition of $[Autm]_n$ in D_2O

RS : $[Autm]_n$	*pD*	*C*-2	*C*-4	*C*-5	*C*-6	*C*-8	*C*-1′	*C*-2′	*C*-3′	*C*-4′	*C*-5′
RS = 6-MP											
1 : 0	9.96	149.98	153.31	131.61	171.88	147.37					
1 : 0	12.00	149.42	156.45	137.86	172.02	153.95					
1 : 2	9.95	150.95	154.77			147.08					
1 : 1	11.45	149.49	157.49	135.50	168.62	154.89					
1.5 : 1	11.15	149.54		135.34	168.78	154.79					
2 : 1	10.96	149.52	151.73	135.68	168.98	155.22					
RS = 6-MPR											
1 : 0	10.12	151.53	146.21	136.85	178.94	141.64	89.16	74.33	71.50	86.57	62.37
1 : 2	7.40				171.80	142.77	89.47	74.85	71.04	85.97	62.08
1 : 1	8.67	151.38	147.22	134.85	161.28	142.56	89.33	74.581	71.28	86.29	62.23
1.5 : 1	10.75	147.05	151.56	135.74	166.21	142.29	89.92	74.48	71.38	86.41	62.29
2 : 1	10.35	146.76	151.52	135.92	163.46	142.15	89.27	74.45	71.41	86.45	62.32
RS = 2-A-6-MPR											
1 : 0	11.30	159.35	148.12	130.86	179.66	139.20	88.86	71.71	73.96	86.56	62.51
1 : 2	8.20		149.59	128.45		140.34	88.94	71.31	74.28	86.01	62.26
1 : 1	9.50	159.08	149.25	129.03	162.12	140.07	88.95	71.50	74.08	86.29	62.37
1.5 : 1	10.55	159.30	149.14	129.42	166.90	139.88	88.94	71.57	74.02	86.38	62.44
2 : 1	10.87	159.31	148.78	130.05	168.16	139.64	88.94	71.61	74.01	86.43	62.43

TABLE III ^{13}C Chemical shifts of $[Autm]_n$ with and without addition of bases in D_2O

$[Autm]_n : RS$	PD[a]	b_1	b_2	b_3	b_4
1 : 0	6.93	47.66	48.01	181.70	179.24
RS = 6-MP					
2 : 1	9.95	43.73	48.02	184.88	181.34
1 : 1	11.45	43.74	48.14	185.05	181.22
1 : 1.5	11.15	43.91	48.14	185.28	181.26
		43.73	48.03	185.14	
1 : 2	10.96	43.89(41.14)	48.04(54.14)	185.31(180.26)	181.28
		43.74(41.23)	48.14(54.49)	185.18	(179.50)*
RS = 6-MPR					
2 : 1	7.40	–	47.82	–	179.85
1 : 1	8.67	43.77	48.08	185.17	180.95
1 : 1.5	10.75	43.76	48.08	185.08	181.09
1 : 2	10.35	43.78	48.10	184.99	181.19
		44.17			
RS = 2-A-6-MPR					
2 : 1	8.20	43.46	47.86	185.15	180.53
1 : 1	9.50	43.69	48.03	185.10	181.19
1 : 1.5	10.55	43.72	48.10	185.15	181.10
1 : 2	10.87	44.09	48.11	185.15	181.16
		43.74			

[a] From pH 6 to 12 there is no change in chemical shift of $[Autm]_n$ [19].
* Values in parentheses are for $(tm)_2$.

with an average of 20000 accumulations. The chemical shifts were measured relative to internal reference dioxane, which is at 67.40 ppm from TMS. ^{13}C chemical shifts were assigned according to the references reported earlier in the literature [7, 8, 18]. ^{13}C NMR were recorded after successive addition of ligands to $[Autm]_n$. The observed chemical shifts of various resonances for the ligands and their complexes with Au(I) are summarized in Table II. Changes in $[Autm]_n$ resonances on addition of purine ligands are given in Table III. It should be noted that $[Autm]_n$ resonances are not affected by changing pH from 6 to 12 [19].

RESULTS

Interaction of $[Autm]_n$ with 6-MP

The ^{13}C NMR spectrum of an 0.05 M solution of $[Autm]_n$ in D_2O at pD 6.93 is shown in Figure 2 (g_1 and g_2 are the CH and CH_2 resonances of glycerol respectively [15, 16]). Figures 3a and b shows the ^{13}C NMR spectrum of an 0.05 M solution of 6-MP in D_2O at two different pDs. When 0.50 equivalents of 6-MP were added as solid to an 0.05 M $[Autm]_n$ solution at

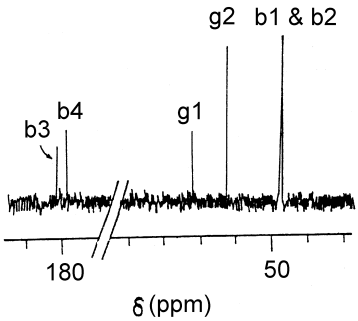


FIGURE 2 The 125 MHz ^{13}C $\{^1H\}$ NMR spectrum of 0.05 M $[Autm]_n$ in D_2O at pD 6.93.

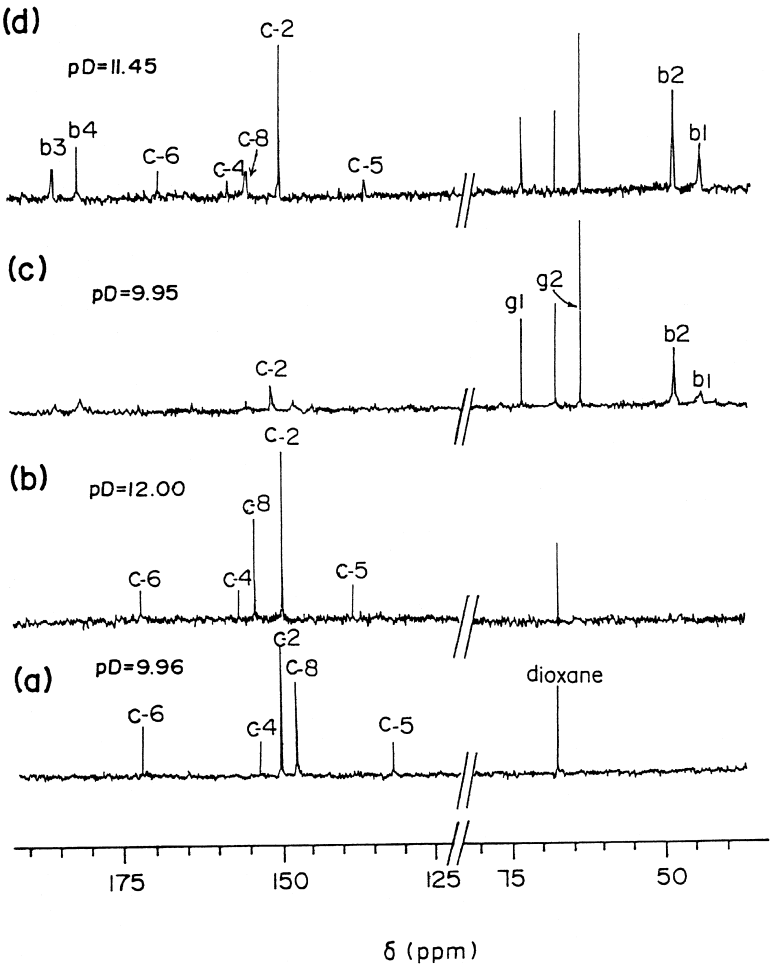


FIGURE 3 The 125 MHz ^{13}C $\{^1H\}$ NMR spectrum of 6-MP : $[Autm]_n$ at various mol ratios in D_2O: (a) and (b) 0.05 : 0, (c) 0.025 : 0.05, (d) 0.05 : 0.05.

pD 10, only the C-2 resonance was observed. C-4 and C-8 resonances were less intense compared to C-2; C-5 and C-6 resonances did not appear. The b_1 resonance of Autm shifted from 47.66 ppm to 43.73 ppm, while b_3 and b_4 were broadened as shown in Figure 3c. The chemical shifts of 6-MP were observed to be pD dependent (Tab. II). It was observed that at pD 12, C-8, C-4 and C-5 were shifted downfield because of the removal of the proton from N-9 (Fig. 3b). The chemical shift changes on further additions of 6-MP to $[Autm]_n$ solutions are compared with the chemical shifts of the base at pD 12.

On addition of 1.0 equivalent of 6-MP to the above solution at pD 11.50, the C-6 resonance shifted upfield by 3.40 ppm. C-2 remained unshifted and increased in intensity. C-4 and C-8 shifted downfield but they were less intense. The C-5 resonance shifted upfield by about 2.36 ppm. The thiomalate resonances became more distinct (Fig. 3d). At a ratio of 1 : 1.5 of base to $[Autm]_n$ the C-2, C-6, b_1, b_3 and b_4 resonances became more intense. The C-4 resonance was suppressed due to the broadening of the C-8 resonance. C-5 became more intense. At a 2 : 1 ratio of base to $[Autm]_n$, the C-6 resonance became more intense. C-4 and C-8 were broadened due to exchange between free and bound ligand. Resonances due to thiomalic disulfide, $(tm)_2$ also appeared at 41, 54, 179 and 180 ppm (d_2, d_1, d_4 and d_3

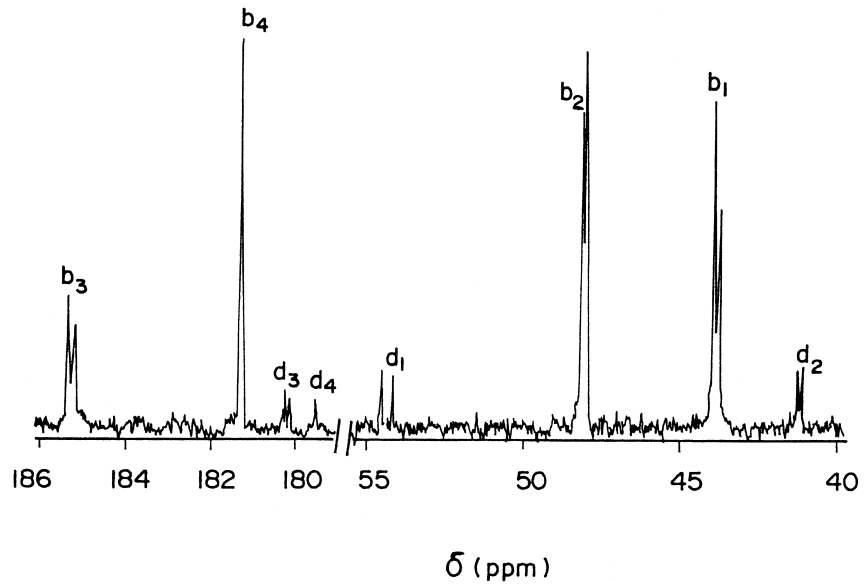


FIGURE 4 The 125 MHz $^{13}C\{^1H\}$ NMR spectrum of 6-MP : $[Autm]_n$ at 2 : 1 ratio at pD 10.96 (only $[Autm]_n$ and $(tm)_2$ resonances are shown).

respectively) [20] (Fig. 4). Splitting of b_1, b_2 and b_3 resonances of thiomalate into two peaks showed that there is a possibility that 6-MP could form two geometrical isomers on interaction with $[Autm]_n$ (Fig. 4).

Interaction of $[Autm]_n$, with 6-MPR

Figure 5a shows the ^{13}C NMR spectrum of an 0.05 M solution of 6-MPR in D_2O at pD 10.12. On addition of 0.50 equivalents of the base to an 0.05 M $[Autm]_n$ solution, only C-6 and C-8 resonances appeared. C-8 shifted upfield

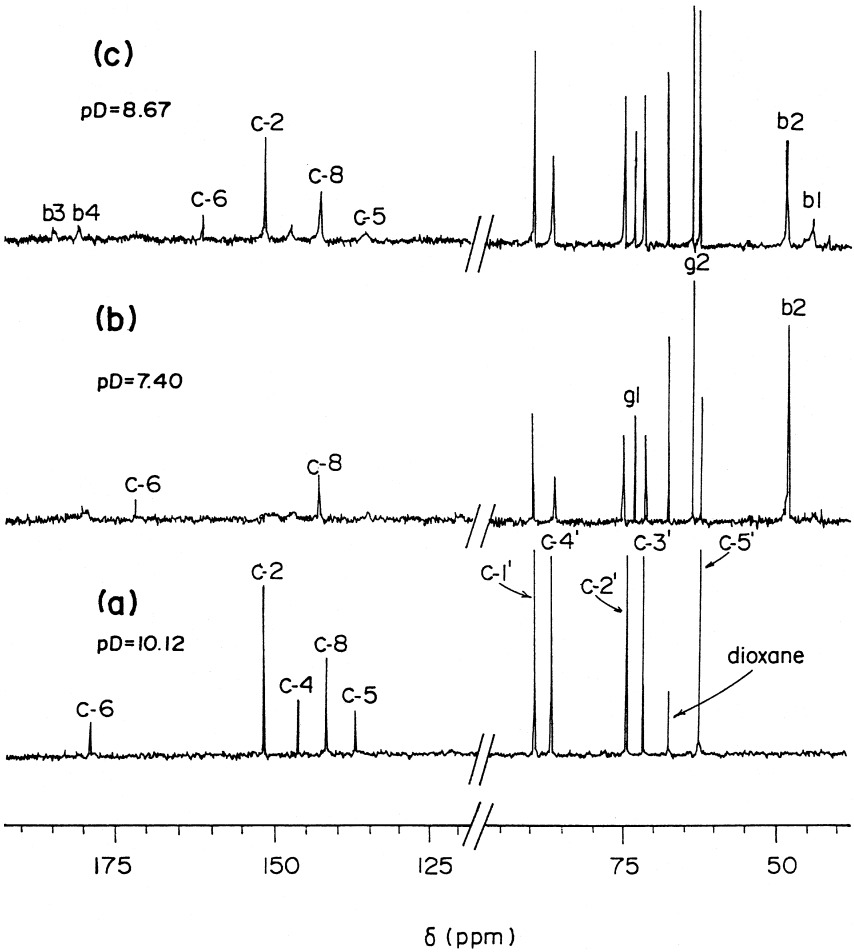


FIGURE 5 The 125 MHz ^{13}C $\{^1H\}$ NMR spectrum of 6-MPR : $[Autm]_n$ at various mol ratios in D_2O: (a) 0.05 : 0, (b) 0.025 : 0.05, (c) 0.05 : 0.05.

by 1.1 ppm and C-6 by 7.1 ppm. The $[Autm]_n$ resonances remained broad except for b_2 (Fig. 5b). When 1.0 equivalents of 6-MPR was added to the above solution, the C-6 shifted 10 ppm further upfield. C-8 and C-4 shifted downfield by 1.2 ppm and C-5 shifted upfield by 2 ppm (Fig. 5c). There was no significant change for the C-2 resonance. As the ratio of base to $[Autm]_n$ was increased to 1.5 : 1 and 2 : 1, all resonances except that of C-2 remained broad showing exchange between free and bound ligand. C-6 shifted downfield towards the free ligand at higher concentrations of base. The b_1

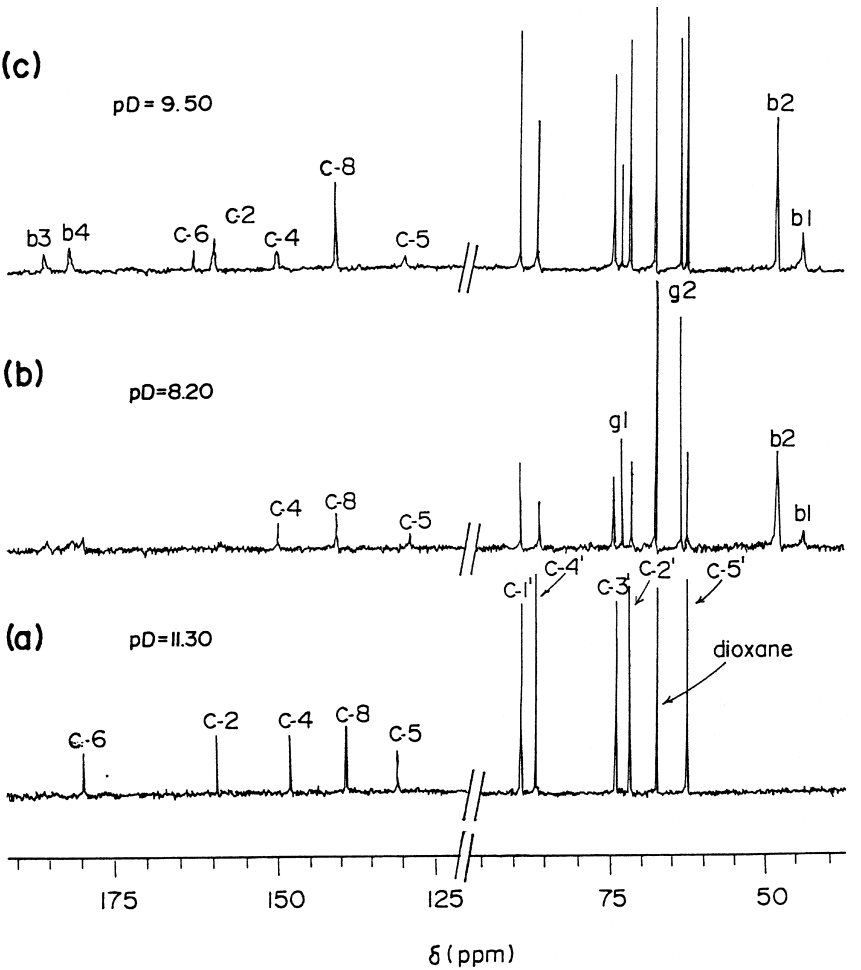


FIGURE 6 The 125 MHz ^{13}C $\{^1H\}$ NMR spectrum of 2-A-6-MPR : $[Autm]_n$ at various mol ratios in D_2O: (a) 0.05 : 0, (b) 0.025 : 0.05, (c) 0.05 : 0.05.

and b_3 resonances of thiomalate appeared more clearly. The b_1 resonance split into two peaks, attributed to the isomeric CH carbon of thiomalate.

Interaction of $[Autm]_n$ with 2-A-6-MPR

Figure 6a shows the ^{13}C NMR spectrum of an 0.05 M solution of 2-A-6-MPR in D_2O at pD 11.30. Upon addition of 0.50 equivalents of 2-A-6-MPR as solid to an 0.05 M $[Autm]_n$ solution, the C-6 and C-2 resonances were not observed. The C-5 resonance shifted upfield by 2.39 ppm and decreased in intensity. The other two resonances, C-4 and C-8 appeared as sharp peaks. The b_2 resonance of thiomalate became sharp and b_1 shifted upfield from 47.66 ppm to 43.46 ppm; the b_3 resonance shifted downfield from 181.70 ppm to 185.15 ppm (Fig. 6b).

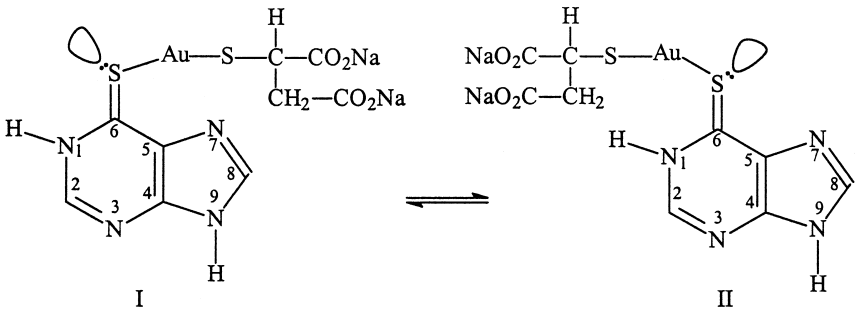
At a 1 : 1 ratio of base to $[Autm]_n$ (Fig. 6c) the C-2 resonance remained unchanged. C-4 resonance shifted downfield by 1.1 ppm and C-5 resonance shifted upfield by 1.8 ppm; C-6 resonance shifted upfield by 17.5 ppm and the C-8 resonance shifted downfield by 1.0 ppm. All the $[Autm]_n$ resonances appeared clearly and became more intense. At higher concentrations of the base (1.5 and 2.0 equivalents) all peaks except for C-2 were broadened indicating exchange between free and bound nucleoside. All the thiomalate resonances became sharp, indicating that the thiomalate was replaced by the nucleoside. At a ratio of 1.5 : 1 of base to $[Autm]_n$ the C-6 resonance shifted a little downfield due to the equilibrium between free and bound ligand. C-2 and C-8 resonances were almost unaffected. Other resonances were very much broadened. At a ratio of 2 : 1 of base to $[Autm]_n$ the C-6 resonance shifted further downfield by 2 ppm, indicating exchange between free and bound base. The b_1 resonance split into two resonances due to two isomeric forms of the complex 2-A-6-MPR-Au-tm.

DISCUSSION

Gold(I) is found in AuS_2 coordination environments for the various types of gold(I) thiolate complexes [21–23]. When excess thiol such as cysteine and glutathione are added to $[Au(SR)]_n$ polymers, they usually eject thiomalate by forming $[Au(thiolate)_2]^-$ species [14, 22, 24]. However, when thiones such as ergothionine [25], Imt (imidazolidine-2-thione) and Diaz (1,3-diazinane-2-thione) [15, 16] are added to $[Autm]_n$ solution, usually a ternary complex of the type [>C=S-Au-tm] is formed without ejecting thiomalate. In the present study, when mercaptopurines (which are soluble only at high pD)

were added to the $[Autm]_n$ solution, no free thiomalate was released from $[Autm]_n$ at a ratio of 1 : 1 suggesting that they do not bind as strongly as thiolates and they coordinate in the form of thiones. However, in the case of 6-MP, at ratios 1.5 : 1 and 2 : 1 of 6-MP to $[Autm]_n$, less intense thiomalic disulfide, $(tm)_2$ resonances are observed (Fig. 4) indicating that thiomalate is released from $[Autm]_n$ as a free ligand and is consequently oxidised to thiomalic disulfide, $(tm)_2$ [20]. Since free thiomalate [26] or $(tm)_2$ resonances are observed [13, 14] on interaction of $[Autm]_n$ with thiols, there is a possibility that 6-MP could bind to Au(I) as a thiolate ligand in addition to the thione form. Cookson *et al.* [5] reported several gold(I) complexes showing that 6-MP coordinates as a thiolate ligand. For 6-MPR and 2-A-6-MPR it is suggested that they bind to Autm only in the thione form, since no $(tm)_2$ resonances are observed on their addition to $[Autm]_n$.

For 6-MP at a 2 : 1 ratio of 6-MP : $[Autm]_n$, the $[Autm]_n$ resonances, b_1, b_2 and b_3 split into two resonances showing that 6-MP forms two geometrical isomers when bound to $[Autm]_n$. The structures of these two isomers are shown below;



In the isomer in which the Autm moiety is oriented towards imidazole ring, I, b_2 should appear downfield because the b_2 carbon atom of thiomalate is nearer to the more electronegative nitrogen atom of the aromatic ring. The peak intensities in ^{13}C NMR show that form I is less populated than II (Fig. 4). For 6-MPR and 2-A-6-MPR only b_2 is separated into two resonances while for b_2 and b_3 this splitting is not observed. This is the first example in which two isomers are observed in the ^{13}C spectrum of $[Autm]_n$ on its interaction with thiones. However, such isomers have been reported for several platinum complexes [27, 28].

The thiolated purines are all ambidentate ligands, since they offer a multiplicity of potential binding sites, such as nitrogen and sulfur. In metal complexes they could act as monodentate ligands through sulfur or as S-6/N-7 chelating ligands [29]. In case of Au(I) and Hg(II) they coordinate

through sulfur [8, 9] while chelating mode is observed in Ru(II) [30, 31], Co(II) [7], Cd(II) [29] and Au(III) [32] complexes. In case of Hg(II) interaction with 2-A-6-MPR, it was observed that the $\rangle C{=}S$ carbon underwent a shift of 15.1 ppm indicating binding of only sulfur to Hg(II) [8]. In the present study, the largest chemical changes in ^{13}C NMR of all the bases occur at C-6 providing clear evidence for selective binding *via* the sulfur atom. This is consistent with the stronger binding expected between a class b (soft metal) such as gold(I) and a softer sulfur ligand. The carbon atom of the $\rangle C{=}S$ group undergoes a shift of up to 17 ppm upon formation of the Au-S bond in 6-MPR and 2-A-6-MPR, while in 6-MP the shift is 3.40 ppm (Tab. II). There was no significant shift for the C-8 position during the reaction, indicating that N-7 is not involved in coordination to $[Autm]_n$. Ribose hydroxyl groups do not participate in binding since their resonances remained unshifted.

In the ^1H NMR the signals near 8 ppm are due to the H-2 and H-8 protons of the free ligands and a doublet around 6 ppm is due to the anomeric proton of ribose [1, 3]. It is observed that in 6-MP, H-2 appears downfield as compared to H-8, while the opposite trend is found in 6-MPR (Tab. I). Complex formation of thiopurines with a metal should cause a downfield shift of the aromatic ring protons, nearest to the metal. This has been attributed to π electron redistribution on protonation or complex formation [33, 34]. For complexes of thiolated bases where coordination occurs through N-7, the proton at C-8 shifts more downfield than the others and becomes less intense [9]. The present study shows that in the ^1H NMR spectra of all the complexes the H-2 protons are shifted a little downfield with respect to the free ligands but shifted again upfield on addition of excess ligand. The H-2 signal also becomes less intense while the intensity of H-8 is not affected by addition to $[Autm]_n$. Since the shift in H-8 is very small, it can be concluded that N-7 is not involved in binding. For 6-MP the H-8 signal shifted upfield at pD 12, suggesting deprotonation at N-9. N_1H-H-2 coupling has not been observed in the NMR spectra, which may be due to rapid proton exchange. All exchangeable protons (NH, SH and NH_2) disappear.

In the case of 6-MP, it was observed that at more basic pD, C-8 is significantly shifted downfield indicating that deprotonation occurs at the N-9 position. Such a downfield shift upon deprotonation was also observed in 6-MP complexes of Mo(II) [10]. It has also been observed that on addition of a base to a solution of $[Ru(6\text{-}MP)_2\{P(C_6H_5)_3\}]Cl_2$ the H-8 signal in ^1H NMR is most affected, consistent with N-9 deprotonation [30]. The pK_a value for N-9 deprotonation is reported to be 9.1, while for N-1, it is 2.2

TABLE IV Difference in ^{13}C NMR chemical shifts (Δ) in ppm of the $\rangle C{=}S$ resonance of the thione at a 1 : 1 ratio of RS : $[Autm]_n$

RS	*pD*	Δ	*Reference*
6-MP	11.45	3.40	This work
6-MPR	8.67	17.66	This work
2-A-6-MPR	9.50	17.54	This work
2-Thiouracil	10.50	3.63	36
Ergothionine	7.40	2.99	25
Imt	7.40	2.55	16
Diaz	7.40	2.05	16

[35]. Since the C-8 resonance is not significantly shifted when 6-MP is added to $[Autm]_n$ at higher pD, it is suggested that N-9 is not involved in coordination and Au(I) binds only through sulfur.

In previous studies of interaction of $[Autm]_n$ with thiones by ^{13}C NMR, it has been observed that 2-thiouracil, Imt (imidazolidine-2-thione) and Diaz (1,3-diazinane-2-thione) form a ternary complex of the type [$\rangle C{=}S$-Au-tm] without ejection of tm^- as a free ligand [15, 16, 36]. In these cases the chemical shift differences between the free thione and the complex at a 1 : 1 ratio of RS : $[Autm]_n$ are 3.64, 2.55 and 2.05 ppm, respectively, whereas in the present case it is found to be around 17 ppm for 6-MPR and 2-A6-MPR, and 3.40 ppm for 6-MP. A comparison of the ^{13}C chemical shifts of the carbon atom attached to the coordinating sulfur atom of various thione ligands at the 1 : 1 ratio of thione : $[Autm]_n$ is given in Table IV. It is observed that the thiolated bases bind more strongly than simple thiones with gold(I). From this interaction it is clear that thiolated bases only form [RS-Au-tm] complexes and excess base exchanges with bound ligand.

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