

Mixed ligand complexes of gold (III) with some amino acids and dithiocarbamates or dithiophosphates

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Abstract: Complexes of the type $[Au(L)(L^{\cdot}orL^{\cdot-})]Cl$ were prepared [L = deprotonated glycine (Gly), Alanine (Ala), Valine (Val) or Methionine (Met), L^{\cdot} = N-Methylcyclohexyldithiocarbamate(N-MeCHdtc) or Benzylidithiocarbamate(Bzdtc) anion and $L^{\cdot-}$ =0,0-Dipropyldithiophosphate (DiPrdtp) or 0,0- Dibenzyldithiophosphate (DiBzdtp) anion. The prepared complexes were characterized by elemental analysis, molar conductivity, IR and UV-Vis spectra, magnetic susceptibility and (1H -nmr) for some of the complexes. The gold(III) complexes were all square planar with the dithiocarbamates or dithiophosphates acted as bidentate ligands coordinated through the two sulfur atoms and the amino acid anions coordinated through N and O except for the methionine ligand which coordinate through S and N atoms.

Keywords: Amino Acid Complex, Dithiocarbamates, Dithiophosphates

1. Introduction

The chemistry of gold has attracted increasing attention in antitumor chemotherapy [1,2]. Complexes of gold(III) with bidentate ligands presented a number of important applications in chemotherapy, diagnostics, catalysis and surface chemistry [3,4]. Some gold complexes have been used as injections to reduce the pain and swelling of rheumatoid arthritis and tuberculosis [5]. Amino acids are well known of their biological importance as structure units that build up proteins, and their common use in nutritional supplements, fertilizers and food technology [6-8]. Dithiocarbamates, dithiophosphates and their metal complexes are important compounds in many biological, industrial and agricultural aspects [9,10]. Mixed ligand complexes plays an important role in biological activities against pathogenic microorganism [11]. This paper report the synthesis and characterization of gold(III) mixed ligand complexes with some amino acids (glycine, alanine, valine and methionine) and dithiocarbamates (N-methylcyclohexyl and benzyl) or dithiophosphates (o,o-dipropyl and o,o-dibenzyl).

2. Experimental

2.1. Materials and Methods

Sodium salt of the dithiocarbamates(N-methylcyclohexyl) and (benzyl) or dithiophosphates (o,o-Dipropyl) and (o,o-Dibenzyl) were prepared as cited in the literature [12,13], Auric acid, glycine, alanine, valine , methionine, N-methylcyclohexyl amine, benzylamine, carbon disulfide, propyl alcohol, benzyl alcohol, phosphorus pentasulfide and sodium hydroxide were either Aldrich, BDH or Fluka products. Organic solvents (dimethylformamide and diethylether) were reagent grade chemicals.

Preparation of complexes

Preparation of $[Au(N-MeCHdtc)(Gly)]Cl$

A solution of sodium aurrate $Na(AuCl_4)$ (prepared by adding aqueous solution of $NaHCO_3$ to a solution of $HAuCl_4 \cdot 4H_2O$ (0.0005mol, 0.206gm) in $(10cm^3)$ water to $PH \sim 7.0$) was added with stirring to a solution mixture of Na N-MeCHdtc(0.0005mol, 0.105gm) in $(10cm^3)$ water and aqueous solution of sodiumglycinate, NaGly, (prepared by dissolving (0.0005mol, 0.038gm) of glycine in $(5cm^3)$ water followed by the addition of aqueous solution of NaOH to $PH \sim 7.5$). The resulting precipitate was filtered, washed several times with water and dried in air.

The following complexes of Ala, Val and Met with N-MeCHdtc and complexes of the four amino acids with Bzdtc in addition to their corresponding complexes of DiPrdtp and DiBzdtp were prepared using the same method with the

same number of moles (0.0005mol) but using the appropriate weight for each:

[Au (N-MeCHdte) (Ala)] Cl(0.0445gm) of alanine [Au (NMeCHdte) (Val)] Cl (0.117gm) of valine [Au (N-MeCHdte) (Met)] Cl (0.149gm) of methionine, [Au (Bzdte) (L)] Cl (0.102gm of NaBzdte), [Au (L) (DiPrdtp)] Cl (0.118gm of NaDiPrdte and [Au(L) (DiBzdtp)] Cl(0.166gm) of NaDiBzdtp.

3. Physical Measurements

Elemental analysis of carbon, hydrogen, nitrogen, and sulfur were done using Euro Vactor Model EA 3000 A (Italy) (Al al bait University, Jordan), IR spectra were recorded on Fourier-Transform (FT.IR) Spectrophotometer, Tensor27Co.Brucker 2003 at a range (400-4000 cm^{-1}) using KBr discs, Electronic spectra were recorded on a U.V-Vis. Spectrophotometer (Shimadzu, UV-1650PC-Spectrophotomete using DMF as a solvent at room temperature for the dithiocarbamate complexes (no.1-8) and at $\sim 40^\circ\text{C}$ for the dithiophosphate complexes (no.9-16) with partial dissolution. Magnetic susceptibility have been measured by Bruker B.M.6. using the Faraday method, Conductivity measurements for the dithiocarbamate complexes have been carried out using DMF as a solvent (10^{-3}M) at room temperature with conductivity Meter Model PCM3Jenway, conductivity of the dithiophosphate complexes were measured in the solid state using 3 Pope Cell. Proton nuclear magnetic resonance ($^1\text{H-nmr}$) for some of the dithiocarbamate complexes were measured using DMSO $-d_6$ as a solvent at (25°c) with BRUKER 300 MHZ (Al al bait University, Jordan), Melting and Decomposition points were done using Electrothermal 9300 Engineering LTD.

4. Result and Discussion

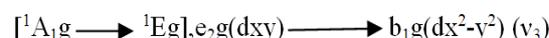
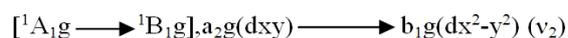
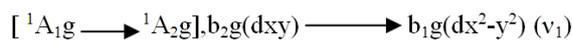
The reaction of sodium aurrate, sodium salt of amino acid and sodium salt of dithiocarbamate or dithiophosphate ligands may be reported by the following equation



Elemental analyses (Table1) revealed that the complexes have the compositions [Au (L) (L-orL'')] Cl. Molar conductivity of the dithiocarbamate complexes were measured in dimetylformamide (10-3M) solvent indicate that theses complexes are 1:1 electrolyte [14]. The corresponding dithiophosphate complexes [Au (L) (DiPrdtp)] Cl and [Au (L) (DiBzdtp)] Cl, are partially soluble in warm DMF($\sim 40^\circ\text{c}$) but insoluble in THF, cyanomethane, benzene, dichloromethane, chloroform, DMSO, DMF+DMSO mixture and ethanol. Accordingly, the conductivity of the dithiophosphate, were measured in the solid state and the results obtain, indicate their 1:1 electrolytic nature Table(2) give some physical properties in addition to elemental analysis for the prepared

complexes. The Magnetic moments of the complexes (Table 2) calculated from the corrected magnetic susceptibilities determined at room temperature indicate the diamagnetic nature, as expected for low spin d8 complexes, suggesting square planar geometries for the gold(III) complexes[15].

The electronic spectra for diamagnetic gold(III) complexes are similar to their iso electronic counter part platinum(II) complexes expected to possess three spin allowed transitions in the field of square planar geometry represented by



The electronic spectra of the prepared gold(III) complexes gave three absorption bands at the range (21230-21800 cm^{-1}), (24700-26246 cm^{-1}) and (28248-30120 cm^{-1}). These bands Can be assigned to ${}^1\text{A}_1\text{g} \rightarrow {}^1\text{A}_2\text{g} (\nu_1)$, ${}^1\text{A}_1 \rightarrow {}^1\text{B}_1\text{g} (\nu_2)$ and ${}^1\text{A}_1\text{g} \rightarrow {}^1\text{Eg} (\nu_3)$ transition respectively, (Table2), the position of these bands are in agreement with low-spin square planar geometry for gold(III) complexes [16]. Bands at values higher than 30000 cm^{-1} were assigned to charge transfer.

The significant ir spectra data of the ligands and their gold(III) complexes with assignments are listed in (Table3). The $\nu(\text{C-S})$ band in the ir spectra of the two dithiocarbamate ligands shown at 957 and 990 cm^{-1} shifted to lower region (cm^{-1}) in the ir spectra of their complexes (complex no.1-8). The shift together with the presence of one $\nu(\text{C-S})$ band only suggest the bidentate coordination of the dithiocarbamate in their complexes. The $\nu(\text{C-N})$ band position which is usually taken as a measure of the thioureide form to the structure of dithiocarbamate compounds[17], appeared in the ir spectra of the two dithiocarbamate ligands (N-MeCHdte and Bzdte) at 1454 and 1469 cm^{-1} , respectively. These positions were shifted to higher frequency values (1487-1508 cm^{-1}) on complex formation. It has been proved that this band undergoes blue shift, when the dithiocarbamate act as bidentate chelating ligand [18,19]. These observation tend to further support the bidentate nature of the dithiocarbamates in their gold(III) complexes.

The free dithiophosphate ligands exhibit $\nu_s(\text{P-S})$ band appeared at 538 and 563 cm^{-1} (Table3). These bands were shifted to lower frequencies upon complex formation (517-558 cm^{-1}). On the other hand the $\nu_{\text{as}}(\text{P-S})$ ir bands for the two dithiophosphate ligands located at 617 and 619 cm^{-1} were shifted to higher frequencies in the ange 622-644 cm^{-1} upon the formation of gold (III) complexes. These observation indicate the bidentate coordination of the dithiophosphate ligands in their complexes [20,21]

The $\nu(\text{P-O})$ band appear at 985,993 cm^{-1} in the free dithiophosphate ligands, were shifted to lower frequencies (958-977 cm^{-1}) upon complex formation.

The observed shift of $\nu(\text{P-O})$ support the bonding of the two sulfur atoms to gold(III) because the observed shift is an indication of electron drainage from the P-O towards P-S [22]

Table 1. Some physical properties and elemental analysis of the prepared complexes

Complex No.	Complex formula	Colour	M.P(C ⁰) Dec.p	Yield (%)	Elemental analysis, found/(calc.)			
					C%	H%	N%	S%
1	[Au (N-MeCHdte)(Gly)]Cl	Yellow	120*	81	24.68 (24.27)	4.02 (3.66)	6.01 (5.66)	13.60 (12.95)
2	[Au (N-MeCHdte)(Ala)]Cl	Brown	142*	79	27.05 (25.96)	4.15 (3.96)	5.86 (5.50)	13.22 (12.60)
3	[Au (N-MeCHdte)(Val)]Cl	Brown	104*	88	28.69 (29.08)	3.91 (4.50)	5.42 (5.21)	12.32 (11.94)
4	[Au (N-MeCHdte)(Met)]Cl	Deep-brown	132*	83	27.96 (27.44)	4.63 (4.25)	5.12 (4.92)	17.36 (16.90)
5	[Au (Bzdte)(Gly)]Cl	Reddish- brown	167*	79	24.78 (24.57)	2.61 (2.47)	6.47 (5.73)	13.30 (13.11)
6	[Au (Bzdte)(Ala)]Cl	Brown	185*	77	26.48 (26.27)	3.12 (2.80)	5.98 (5.57)	12.97 (12.75)
7	[Au (Bzdte)(Val)]Cl	Brown	166*	68	30.12 (29.41)	3.15 (3.41)	5.68 (5.27)	12.32 (12.07)
8	[Au (Bzdte)(Met)]Cl	Light- brown	154*	72	28.12 (27.73)	3.68 (3.22)	5.36 (4.97)	17.36 (17.08)
9	[Au (DiPrdtp)(Gly)]Cl	Brownish black	>300	63	17.24 (18.48)	3.15 (3.49)	2.78 (2.69)	12.35 (12.33)
10	[Au (DiPrdtp)(Ala)]Cl	Brownish black	>300	75	20.68 (20.25)	3.48 (3.77)	3.12 (2.62)	12.36 (12.01)
11	[Au (DiPrdtp)(Val)]Cl	Deep-brown	>300	69	23.75 (23.51)	4.01 (4.30)	2.98 (2.49)	11.36 (11.41)
12	[Au (DiPrdtp)(Met)]Cl	Brownish black	>300	82	22.45 (22.24)	4.13 (4.07)	3.12 (2.35)	17.05 (16.19)
13	[Au (DiBzdt)(Gly)]Cl	Brown	>300	63	31.12 (31.20)	3.15 (2.94)	2.12 (2.27)	10.35 (10.41)
14	[Au (DiBzdt)(Ala)]Cl	Brownish black	>300	65	32.75 (32.41)	3.53 (3.20)	2.682 (2.22)	10.36 (10.17)
15	[Au (DiBzdt)(Val)]Cl	Brownish black	>300	77	33.79 (34.68)	3.78 (3.67)	2.87 (2.12)	10.24 (9.74)
16	[Au (DiBzdt)(Met)]Cl	Brownish black	>300	82	33.42 (33.07)	3.62 (3.50)	2.31 (2.63)	14.36 (13.93)

Table 2. Electronic spectra of the ternary Ni(II) complexes (cm^{-1}), μ_{eff} (B.M.) and Molar Conductance ($\text{cm}^2\text{ohm}^{-1}\text{mol}^{-1}$)

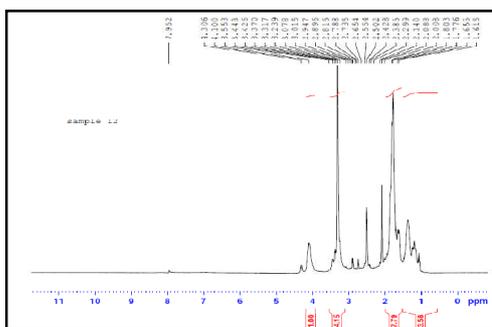
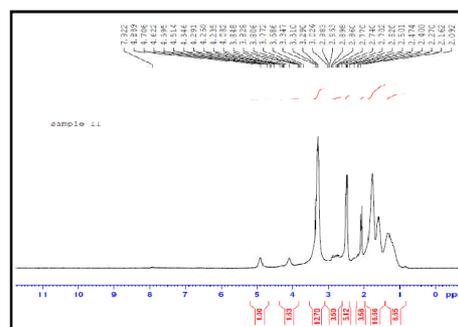
Complex no.	$^1\text{A}_{1g} \rightarrow ^1\text{A}_{2g}$	$^1\text{A}_{1g} \rightarrow ^1\text{B}_{1g}$	$^1\text{A}_{1g} \rightarrow ^1\text{E}_g$	C.T	μ_{eff} B.M.	Molar Conductance ($\text{cm}^2\text{ohm}^{-1}\text{mol}^{-1}$)
1	21505	25000	29411	31250	dia	76.9
2	21500	24700	29585	32051	dia	88.7
3	----	25641	29585	32894	dia	69.8
4	21231	25125	28248	32894	dia	85.8
5	21230	----	30120	39370	dia	80.7
6	----	26246	----	30864	dia	69.5
7	----	25840	28467	31055	dia	83.5
8	21800	25445	29411	33112	dia	87.4
9	21765	----	28769	33456	dia	3.21×10^{-6}
10	21456	25367	----	37854	dia	4.02×10^{-6}
11	----	----	29445	35099	dia	2.32×10^{-7}
12	21786	26143	28564	36543	dia	2.01×10^{-6}
13	21765	----	28760	32789	dia	2.45×10^{-6}
14	----	24896	----	34679	dia	1.42×10^{-7}
15	21657	----	28954	33476	dia	1.82×10^{-7}
16	----	24987	----	37896	dia	4.21×10^{-6}

Table 3. Selected IR bands of the ligands and complexes(cm^{-1})

No.	$\nu(\text{NH}_2)$	$\nu(\text{COO}^-)$		$\Delta \nu(\text{COO}^-)$	$\nu(\text{C-N})$	$\nu(\text{C-S})$	$\nu(\text{C-SMe})$	$\nu(\text{P-S})$		$\nu(\text{P-O})$	$\nu(\text{M-O})$	$\nu(\text{M-N})$
		$\nu_{\text{as}}(\text{COO}^-)$	$\nu_{\text{s}}(\text{COO}^-)$					$\nu_{\text{as}}(\text{P-S})$	$\nu_{\text{s}}(\text{P-S})$			
NaN-MeCHdtc	----	----	----	----	1469	990	----	----	----	----	----	----
NaBzdtc	----	----	----	----	1454	957	----	----	----	----	----	----
NaDiPrdp	----	----	----	----	----	----	----	619	538	993	----	----
NadiBzdp	----	----	----	----	----	----	----	617	563	985	----	----
Gly	3164	1615	1457	----	----	----	----	----	----	----	----	----
L-Ala	3082	1597	1413	----	----	----	----	----	----	----	----	----
L-Val	3080	1590	1410	----	----	----	----	----	----	----	----	----
L-Met	2956	1616	1408	----	----	----	1316	----	----	----	----	----
1	3232	1633	1396	237	1483	978	----	----	----	----	569	466
2	3115	1636	1388	248	1498	964	----	----	----	----	576	490
3	3120	1642	1370	272	1488	973	----	----	----	----	573	478
4	3112	1614	1410	204	1492	966	1338	----	----	----	----	484
5	3225	1628	1398	230	1476	947	----	----	----	----	570	488
6	3090	1637	1385	252	1485	938	----	----	----	----	569	467
7	3100	1625	1371	254	1488	944	----	----	----	----	577	498
8	2998	1608	1406	202	1479	938	1335	----	----	----	----	492
9	3232	1633	1397	236	----	----	----	624	527	977	576	478
10	3100	1639	1387	252	----	----	----	640	525	972	574	466
11	3115	1644	1380	264	----	----	----	637	523	978	565	487
12	3108	1614	1412	202	----	----	1332	632	533	975	----	490
13	3234	1628	1395	233	----	----	----	628	549	973	563	492
14	3111	1636	1382	254	----	----	----	637	557	965	572	476
15	3090	1645	1378	267	----	----	----	639	543	969	572	496
16	2996	1615	1412	203	----	----	1337	632	548	967	----	488

Table 4. $^1\text{H-NMR}$ spectral data for some complexes

Complex no.	NMR
1	$^1\text{H-nmr}$ (DMSO- d_6): δ 4.10(2H,br,NH(Gly)), δ 3.55(2H, S, $\text{CH}_2(\text{Gly})$), δ 2.01-1.61(9H,m, Chexy and Me), δ 1.51-1.03(5H,m,Chexy)ppm
2	$^1\text{H-nmr}$ (DMSO- d_6): δ 4.08(2H,br,NH(Ala)), δ 3.68 (3H, S, Me-Ala), δ 2.62(3H,S,Me.dtc) δ 2.27 and 2.12-1.52 (8H,d,Chexy) + 1H CH-Ala), δ 1.51-1.11(3H,m,Chexy)ppm
3	$^1\text{H-nmr}$ (DMSO- d_6): δ 4.91(2H,br,NHVal), δ 4.08 and 3.79(2H,S,2CHVal), δ 3.41(3H,S,Medtc), δ 2.57(1H,S,CHVal), δ 2.07-1.76(10H,m,5Chexy+5Val),1.48-0.88(6H,m,C-H Chexy)ppm
5	$^1\text{H-nmr}$ (DMSO- d_6): δ 7.99-7.34(5H,m,C-H Bzdtc), δ 5.50-4.50(3H,br,2H NHGly+1H Bzdtc), δ 2.45(2H,S,CH Gly) δ 2.20-1.90(2H,d,N- CH_2 Bzdtc)ppm
6	$^1\text{H-nmr}$ (DMSO- d_6): δ 7.40-7.08(5H,m,C ₆ H ₅ inBzdtc), δ 5.20-4.90(3H,br,NH-NH ₂ -Ala+NH Bzdtc), δ 4.30-4.21(1H,m,CH-Ala), δ 2.04(2H,S ,CH-N- CH_2 in Bzdtc), δ 1.22 (3H,S,Me-Ala)ppm.

Fig 1. ($^1\text{H-NMR}$) spectrum of complex $[\text{Au}(\text{N-MeCHdtc})(\text{Gly})]^+ \text{Cl}^-$ Fig 2. ($^1\text{H-NMR}$) spectrum of complex $[\text{Au}(\text{N-MeCHdtc})(\text{Ala})]^+ \text{Cl}^-$

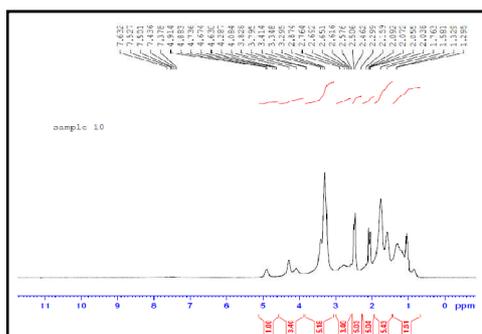


Fig 3. (¹H-NMR) spectrum of complex [Au(N-MeCHdtc)(Val)]⁺ Cl⁻

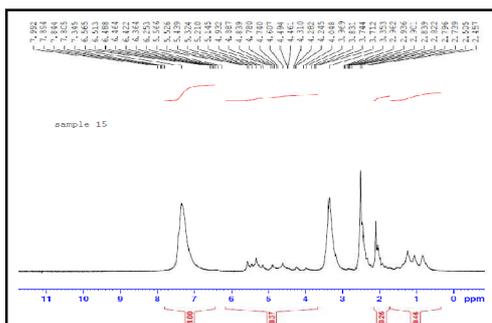


Fig 4. (¹H-NMR) spectrum of complex [Au(Bzdtc)(Gly)]⁺ Cl⁻

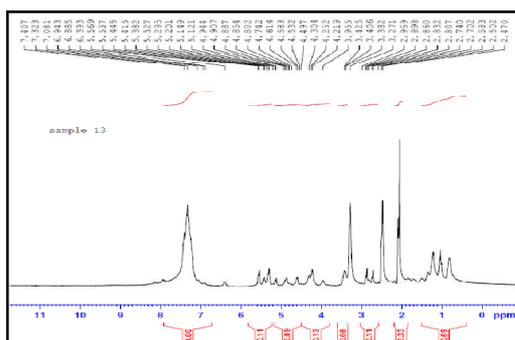
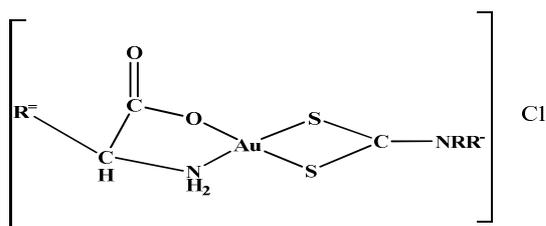
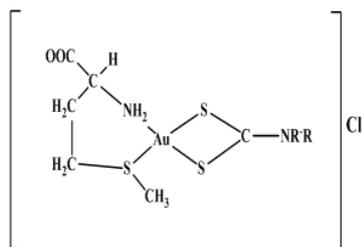


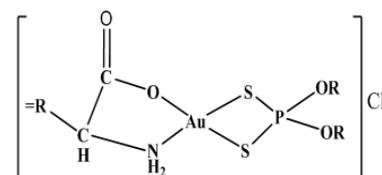
Fig 5. (¹H-NMR) spectrum of complex [Au(Bzdtc)(Ala)]⁺ Cl⁻



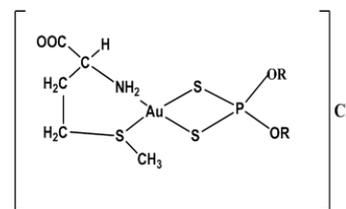
a. (R =H when R' =benzyl, R =CH₃ when R' =cyclohexyl) R''=H (Gly), -CH₃(Ala), -(CH(CH₃)₂)(Val). Complex no. 1-3, 5-7



b. R, R', as defined in Fig (6a.) Complex no.4,8



c. R = propyl or benzyl R' = as defined in Fig (6 a.) Complexes no.9-11,13-15



d. R = propyl or benzyl Complex no.12,16

Fig 6. Proposed structures for the complexes [Au(L)(L' or L'')]Cl

The values of $\nu_{as}(\text{COO}^-)$ and $\nu_s(\text{COO}^-)$ for the aminoacid ligands are given in (Table3). The corresponding values for the gold(III) complexes indicate that the $\nu_s(\text{COO}^-)$ values were shifted to lower wave numbers while the $\nu_{as}(\text{COO}^-)$ frequencies were shifted to higher wave numbers [expect for the methionine complexes (no.4,8,12 and 16)]. The values of $\Delta[\nu_{as}(\text{COO}^-) - \nu_s(\text{COO}^-)]$ for the complexes are (230-272cm⁻¹) indicate the involvement of the carboxylate anion in bonding as monodentate ligand. The values of $\Delta[\nu_{as}(\text{COO}^-) - \nu_s(\text{COO}^-)]$ for the methionine complexes were (202-204cm⁻¹) suggesting that the carboxylate is not involved in bonding[23].

The N-H vibration observed at (2956-3164cm⁻¹) in the free aminoacids were shifted to higher wave numbers (2996-3234cm⁻¹) in the ir spectra of the complexes suggesting coordination of the amino group [24]. The $\nu(\text{C-S})$ in the methionine ligand appears at 1316cm⁻¹ were shifted to higher number (1335-1338cm⁻¹) on complex formation (complex no.4,8,12 and 16), indicating the participation of methionine sulfur in bonding[25].

The ir spectra of the complexes showed the appearance of non ligand bands observed at (466-498cm⁻¹) which were assigned to $\nu(\text{Au-N})$. The appearance of bands at (565-576cm⁻¹) in the ir spectra of the complexes, with the exception of (complexes no. 4,8,12 and 16), were assigned to $\nu(\text{Au-O})$.

Proton nmr (¹H-nmr) were recorded for five of the dithiocarbamate complexes using DMSO-d₆ as solvent. The insolubility of the prepared dithiophosphate complexes in DMSO and other solvents limited the choice to samples of the dithiocarbamate complexes only. The results obtained from ¹H-nmr spectra are given in (Table4).

5. Conclusion

Mixed ligand complexes of gold(III) with four aminoacids (Gly, Ala, Val and Methionine) and two dithiocarbamates (N-MeCHdtc and Bzdtc) or two

dithiophosphates (DiPrdtp and DiBzdtp) were successfully prepared by simple mixing of a aqueous solution of the three components. The results were square planar complexes of Au(III) with the dithiocarbamate and dithiophosphate ligands behaved as bidentate coordinated through the two sulfur atoms. The aminoacid anions coordinated through the nitrogen atom of the amino group in all complexes and through the oxygen of the carboxylate group with the exception of the methionine complexes (no.4, 8, 12 and 16) where the sulfur atom replaces the carboxylate oxygen. Similar results were reported for the isostructural platinum(II) complexes with sulfur containing aminoacids [26]. Apparently the square planar preference for gold(III) might be the motive in which case the choice of using N and S binding sites are preferred regardless of the negative charge an oxygen.

The dithiophosphate complexes are insoluble in common polar and non polar solvents such as THF, dichloromethane, ethanol, DMSO, cyanomethane, chloroform, benzene and diethylether and partially soluble in warm DMF (~40°C). The insolubility is difficult to explain especially when it covers such large number of complexes. This fact inforce some limitation such as conductivity measurements in solution and ¹H-nmr measurements, yet it was possible to deduce the proposed structure in a similar way to the dithiocarbamate complexes.

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