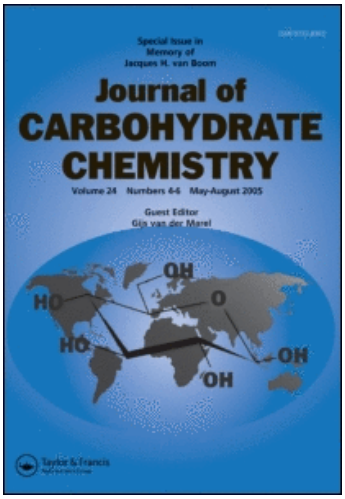

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New Synthesis of Monomeric and Polymeric Saccharide bis-Hydrazide Diamines Salts. Reaction of 2, 3, 4, 5-Tetra-*O*-acetyl Galactaric Acid bis-Hydrazides with Different Diamines

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NEW SYNTHESIS OF MONOMERIC AND POLYMERIC SACCHARIDE BIS-HYDRAZIDE DIAMINES SALTS. REACTION OF 2,3,4,5-TETRA-O-ACETYL GALACTARIC ACID BIS-HYDRAZIDES WITH DIFFERENT DIAMINES

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ABSTRACT

Reaction of 1-(2,3,4,5-tetra-*O*-acetylgalactaroyl)bis-2-[thiomethyl or thiobenzyl(thiocarbonyl)]hydrazine 1 or 2 with different bifunctional amines [piperazine (PPZ), tetraethylethylenediamine (TEED), tetramethylethylenediamine (TMED), and tetramethylpropanediamine (TMPD)] at different hydrazide/diamine ratios in methanol, gave the corresponding monomeric and polymeric bis-hydrazide salts. Elucidation of the structures of compounds prepared are discussed and mechanistic pathways for their formation are proposed.

INTRODUCTION

Schiff bases prepared by the condensation of different aldehydes and ketones with methyldithiocarbazate,[1] have been reported to react with primary and secondary amines by nucleophilic substitution reactions with the liberation of methyl mercaptan.[2] Applying this reaction to the corresponding non-saccharide carbodithioate hydrazides gave the unexpected amine salt adducts instead of nucleophilic substitution products.[3]

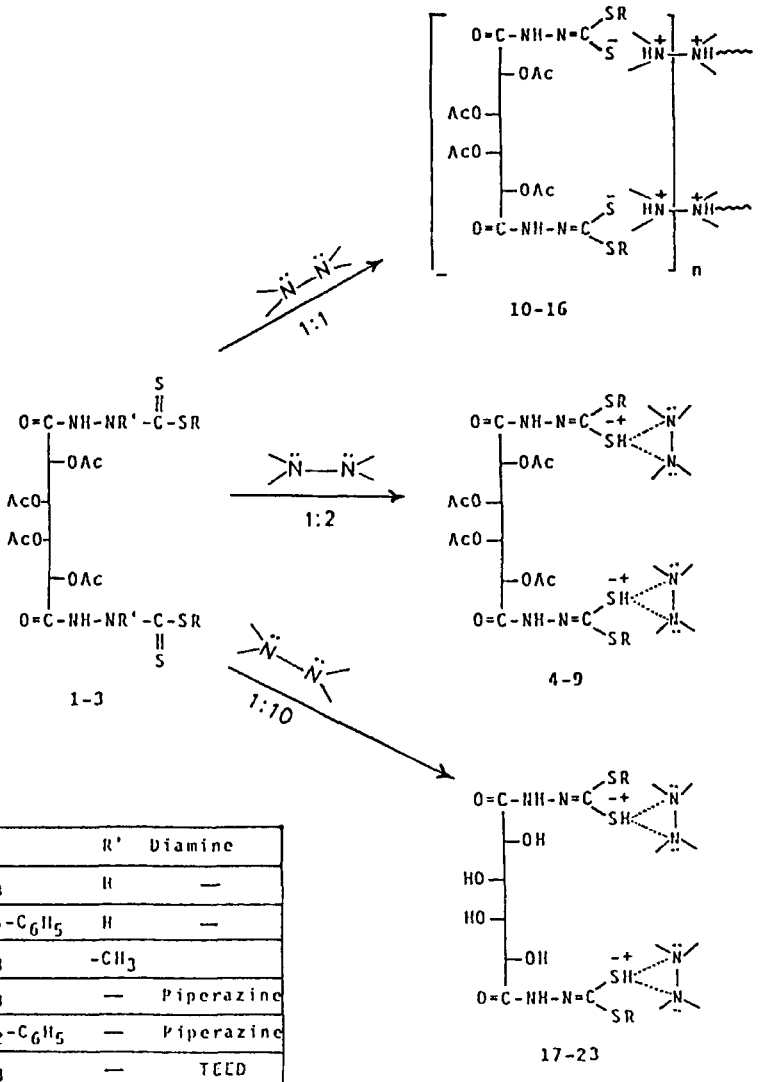
Our approach in studying this reaction was to synthesize new acetylated and deacetylated monomeric and polymeric amine salts having saccharide moieties which might facilitate the penetration of resultant products into biological systems. *S*-Methylhydrazinecarbodithioate derivatives comprise a class of compounds known to possess a wide range of chemotherapeutic activities.[4] The activities of these compounds might be modified by derivatization since small changes have been shown, in some instances to markedly alter antiviral,[5] carcinostatic, and antitumor activity.[6,7]

RESULTS AND DISCUSSION

In the present work new acetylated saccharide hydrazide amine salts were formed from the treatment of 1-(2,3,4,5-tetra-*O*-acetylgalactaroyl)bis-2-[thiomethyl(thiocarbonyl)]-hydrazine (1) and 1-(2,3,4,5-tetra-*O*-acetylgalactaroyl)bis-2-[thiobenzyl(thiocarbonyl)]hydrazine (2)[8] with different bifunctional amines [piperazine (PPZ), tetraethylethylenediamine (TEED), tetramethylethylenediamine (TMED), and tetramethylpropanediamine (TMPD)] in methanol at room temperature. The reaction of acetylated saccharide bis(hydrazide) 1 or 2 with the diamine in a 1:1 ratio gave the corresponding polymeric acetylated saccharide amine salts **10-16**, while in a 1:2 ratio, gave the monomeric acetylated saccharide amine salts **4-9**. Reaction of compounds **1** or **2** with the diamines in ratio of 1:10, respectively, produced the corresponding monomeric deacylated saccharide amine salts **17-23**.

Reaction of 1-(2,3,4,5-tetra-*O*-acetylgalactaroyl)bis-2-[thiomethyl(thiocarbonyl)]hydrazine (1) with one equivalent of tetramethylethylenediamine (TMED), in methanol at room

Scheme I



Cpd. No.	R	R'	Diamine
1	$-CH_3$	H	—
2	$-CH_2-C_6H_5$	H	—
3	CH_3	$-CH_3$	
4, 10, 17	$-CH_3$	—	Piperazine
5, 11, 18	$-CH_2-C_6H_5$	—	Piperazine
6, 12, 19	$-CH_3$	—	TEED
7, 13, 20	$-CH_2-C_6H_5$	—	TEED
8, 14, 21	$-CH_3$	—	TMED
9, 15, 22	$-CH_2-C_6H_5$	—	TMED
16, 23	$-CH_3$	—	TMPD

temperature, gave crystalline **14** in 73% yield. Its elemental analysis gave values corresponding to those calculated for the molecular formula $C_{24}H_{42}N_6O_{10}S_4$.

The IR spectrum of compound **14** showed absorption bands at 2450 (salt formation band), 1740 (OAc), 1660 and 1510 cm^{-1} (amide I and II), 1605 (C=N), with the disappearance of thioamide bands (I and II) of the parent acetylated saccharide bis(hydrazide) **1** at 1440 and 1480 cm^{-1}.

The ^1H NMR spectrum of compound **14** (DMSO-d_6) showed two singlets at δ 2.00 and 2.10 (12H,4 OAc), two broad singlets at 5.00 (2H, H-3, H-4) and 5.45 (2H, H-2, H-5) and a singlet at 2.30 ppm (6H, $2SCH_3$). The spectrum also contained three singlet peaks at δ 2.53 (12 H, 4 NCH_3), 2.84 (4 H,N-$(CH_2)_2$-N), and 9.70 ppm (s, 2 H, CONH).

The polymeric structure of the acetylated saccharide amine salt **14** was proved by comparing the relative intensities of the protons in its ^1H NMR spectrum. Thus the integration values of (SCH_3): $N(CH_3)_2$: (N-CH_2-CH_2-N) were found to be 6:12:4, indicating a polymeric structure. If the structure was monomeric, the integration ratio would have been 6:24:8. All the above data confirm the polymeric structure of acetylated saccharide hydrazide amine salt **14**.

In the present work, 1-(2,3,4,5-tetra-*O*-acetylgalactaroyl)bis-2-[methyl, methylthio(thiocarbonyl)]hydrazine 3 was synthesized to prove that the amine salt formation necessitates the existence of a hydrogen atom on the nitrogen atom attached to the carbodithioate group. When 3 was treated with the diamine (TMED), in a 1:1 or 1:2 ratio at room temperature, neither nucleophilic substitution nor amine salt formation occurred, and the starting acetylated saccharide hydrazide 3 was recovered.

The same addition reaction was applied to 1-(2,3,4,5-tetra-*O*-acetylgalactaroyl)bis-2-[benzylthio(thiocarbonyl)-hydrazine] **2**, which gave the corresponding polymeric acetylated galactaric acid hydrazide amine salt **15**. The reaction of acetylated saccharide bis(hydrazides) (**1** and **2**) with different diamines (PPZ, TEED, TMED, and TMPD), were carried out to give the corresponding polymeric acetylated saccharide hydrazide amine salts (**10-16**).

On the other hand, treatment of 1-(2,3,4,5-tetra-*O*-acetylgalactaroyl)bis[methylthio(thiocarbonyl)]hydrazine (**1**) with tetramethylethylenediamine in a 1:2 ratio gave the corresponding monomeric acetylated sugar hydrazide amine salt **8**. Its elemental analysis agreed with the values calculated for the molecular formula $C_{30}H_{58}N_8O_{10}S_4$. The infrared and ^1H NMR spectra of **8** are identical to the spectra of compound **14** (Table 1-3), except that the proton integration ratios of (SCH_3): $N(CH_3)_2$: ($N-CH_2-CH_2-N$), were found to be 6:24:8. This finding is in accordance with the monomeric acetylted saccharide amine salt **8**, namely, 1-(2,3,4,5-tetra-*O*-acetylgalactaroyl)bis-2-[(tetramethylethylenediammonium)thiomethylcarbothiolate]hydrazine.

It should be mentioned that the methylene protons ($-N-CH_2CH_2-N-$), in the ^1H NMR spectrum of compound **8** appeared as a singlet peak, indicating their equivalency. This might be due to equivalent hydrogen bonding between hydrogens of the two nitrogen atoms of the diamine with the enolised thiol hydrogen atom.[9]

To study the effect of excess diamine on this type of reaction, we repeated the reaction of 1-(2,3,4,5-tetra-*O*-acetylgalactaroyl)bis-2-[methylthio(thiocarbonyl)]hydrazine (**1**) with tetraethylethylenediamine in a ratio 1:10. The

TABLE 1. Melting Points, Isolated Yields and Elemental Analysis of Compounds 4-23.

Cpd.	m.p. °C	Yield	M.F.	Analysis (Theor/exp) %C	%H	%N
4	227	70	$C_{26}H_{46}N_8O_{10}S_4$	41.16 41.31	6.07 5.97	14.77 14.62
5	197	65	$C_{38}H_{54}N_8O_{10}S_4$	50.11 50.40	5.93 5.70	12.31 12.16
6	195	83	$C_{38}H_{74}N_8O_{10}S_4$	49.03 48.82	7.96 7.78	12.04 12.31
7	191	80	$C_{50}H_{82}N_8O_{10}S_4$	55.45 55.26	7.58 7.39	10.35 10.08
8	206	70	$C_{30}H_{58}N_8O_{10}S_4$	44.01 44.35	7.09 6.84	13.69 13.41
9	157	58	$C_{42}H_{66}N_8O_{10}S_4$	57.96 57.72	6.80 6.71	11.55 11.33
10	213	80	$C_{22}H_{36}N_6O_{10}S_4$	39.29 39.16	5.36 5.13	12.50 12.10
11	231	62	$C_{34}H_{44}N_6O_{10}S_4$	49.52 49.55	5.33 5.20	10.19 9.96
12	185	72	$C_{28}H_{50}N_6O_{10}S_4$	44.33 44.50	6.59 6.50	11.08 11.20
13	178	65	$C_{40}H_{58}N_6O_{10}S_4$	52.75 52.48	6.37 6.09	9.23 -
14	216	73	$C_{24}H_{42}N_6O_{10}S_4$	41.03 41.09	5.98 5.78	11.97 12.23
15	134	70	$C_{36}H_{50}N_6O_{10}S_4$	50.58 50.29	5.85 5.46	9.84 -
16	191	75	$C_{25}H_{44}N_6O_{10}S_4$	41.89 41.71	6.15 6.04	11.73 11.60
17	181	83	$C_{18}H_{38}N_8O_6S_4$	38.61 36.38	6.44 6.07	16.27 16.11
18	207	75	$C_{30}H_{46}N_8O_6S_4$	48.52 48.47	6.20 6.04	15.09 14.82
19	201	65	$C_{30}H_{66}N_8O_6S_4$	47.24 47.08	8.66 8.52	14.70 14.92
20	212	77	$C_{42}H_{74}N_8O_6S_4$	55.14 54.82	8.09 8.01	12.25 12.43
21	227	50	$C_{22}H_{50}N_8O_6S_4$	40.62 40.97	7.69 7.86	17.23 -
22	148	52	$C_{34}H_{58}N_8O_6S_4$	50.87 50.80	7.23 7.41	13.97 13.83
23	203	80	$C_{24}H_{54}N_8O_6S_4$	42.48 42.80	7.96 7.59	16.52 -

TABLE 2. Characteristic IR Spectral Data (cm^{-1}) for Compounds 4-23.

Cpds No.	C-O-CH_3 O	OH	(CONH)-I	(CONH)-II	C=N	NH	Salt	-C-N-	Ph
4	1770		1660	1500	1600	3200	2700	1435	-
5	1765		1660	1500	1590	3210	2680	1430	695
6	1765		1650	1510	1600	3100	2600	1440	-
7	1750		1640	1500	1600	3200	2650	1410	690
8	1740		1655	1570	1600	3230	2460	1430	-
9	1750		1640	1500	1595	3400	2650	1425	690
10	1770		1660	1500	1600	3200	2700	1440	-
11	1740		1650	1500	1600	3200	2500	1430	690
12	1765		1650	1510	1600	3100	2600	1425	-
13	1725		1640	1500	1605	3400	2700	1415	695
14	1740		1660	1510	1605	3225	2450	1435	-
15	1745		1635	1500	1595	3400	2600	1415	695
16	1750		1676	1510	1615	3180	2600	1430	-
17		3300	1645	1500	1600	3200	2650	1440	-
18		3320	1640	1500	1600	-	2645	1435	690
19		3350	1660	1500	1610	3200	2650	1430	-
20		3300	1650	1505	1600	3100	2640	1445	690
21		3320	1645	1500	1600	3280	2650	1440	-
22		3340	1650	1500	1600	3300	2650	1430	690
23		3250	1650	1515	1600	3000	2700	1440	-

TABLE 3. ^1H NMR Chemical Shifts of the Saccharide Amine Salts (4-19) in DMSO-d_6.

Cpd. No.	$OCCH_3$	CH	SCH_3	$-SCH_2-$	$N-CH_3$	$-(CH_2)_n-$	$-CH_2-CH_3$	$-CH_2-CH_3$	NH	Aromatic protons
4	2.00(s,6H) 2.12(s,6H)	5.03(s,2H,H-3,H-4) 5.43(s,2H,H-2,H-5)	2.30(s,6H)			3.03(s,16H)			9.70(s,2H)	
5	2.00(s,6H) 2.10(s,6H)	5.10(s,2H,H-3,H-4) 5.53(s,2H,H-2,H-5)		4.20(s,4H)		3.08(s,16H)			9.80(s,2H)	7.06-7.43 (m,10H)
6	2.00(s,6H) 2.12(s,6H)	5.07(s,2H,H-3,H-4) 5.44(s,2H,H-2,H-5)	2.30(s,6H)			2.95(s,8H)	2.86(q,16H)	1.10(t,24H)	9.70(s,2H)	
8	2.00(s,6H) 2.12(s,6H)	5.06(s,2H,H-3,H-4) 5.40(s,2H,H-2,H-5)	2.33(s,6H)		2.51(s,24H)	2.85(s,8H)			9.72(s,2H)	
9	2.00(s,6H) 2.06(s,6H)	5.03(s,2H,H-3,H-4) 5.50(s,2H,H-2,H-5)		4.14(s,4H)	2.46(s,24H)	2.85(s,8H)			9.70(s,2H)	7.07-7.43 (m,10H)
10	2.00(s,6H) 2.13(s,6H)	5.03(s,2H,H-3,H-4) 5.44(s,2H,H-2,H-5)	2.26(s,6H)			3.03(s,8H)				
11	1.93(s,3H) 1.98(s,3H) 2.03(s,3H) 2.13(s,3H)	5.05(s,2H,H-3,H-4) 5.50(s,2H,H-2,H-5)		4.20(s,4H)		3.06(s,16H)			9.77(s,2H)	7.06-7.33 (m,10H)
12	2.00(s,6H) 2.10(s,6H)	5.05(s,2H,H-3,H-4) 5.38(s,2H,H-2,H-5)	2.30(s,6H)			2.91(s,4H)	2.84(q,8H)	1.08(t,12H)	9.68(s,2H)	

Cpd. No.	$OCCH_3$	CH	SCH_3	$-SCH_2-$	$N-CH_3$	$-(CH_2)_n-$	$-CH_2-CH_3$	$-CH_2-CH_3$	NH	Aromatic protons
13	2.00(s,6H) 2.20(s,6H)	5.21(s,2H,H-3,H-4) 5.63(s,2H,H-2,H-5)		4.40(s,4H)		2.98(s, 4H)	2.86(q,8H)	1.13(t,12H)		7.30-7.60 (m,10H)
14	2.00(s,6H) 2.10(s,6H)	5.00(s,2H,H-3,H-4) 5.40(s,2H,H-2,H-5)	2.30(s,6H)		2.53(s,12H)	2.84(s, 4H)			9.70(s,2H)	
15	2.00(s,6H) 2.13(s,6H)	5.20(s,2H,H-3,H-4) 5.60(s,2H,H-2,H-5)		4.30(s,4H)	2.53(s,12H)	2.90(s, 4H)				7.20-7.50 (m,10H)
16	2.06(s,6H) 2.10(s,6H)	5.20(s,2H,H-3,H-4) 5.40(s,2H,H-2,H-5)	2.43(s,6H)		2.63(s,12H)	2.02(m,2H) 2.96(t,4H)				
	OH									
17	3.70(s,6H- 4 OH,2NH)	3.10(s,2H,H-3,H-4) 4.16(s,2H,H-2,H-5)	2.36(s,6H)			4.76(s,16H)				
18	3.73(s,6H- 4 OH,2NH)	3.20(s,2H,H-3,H-4) 4.72(s,2H,H-2,H-5)		4.18(s,4H)		2.88(s,16H)				7.06-7.36 (m,10H)
19	3.63(s,6H- 4 OH,2NH)	3.80(s,2H,H-3,H-4) 4.30(s,2H,H-2,H-5)	2.30(s,6H)			2.84(s,8H)	2.90(q,16H)	1.06(t,24H)		

reaction gave compound **19**, whose elemental analysis agreed with molecular formula $C_{30}H_{66}N_8O_6S_4$ corresponding to a de-acetylated monomeric hydrazide salt. The IR spectrum of the product **19** showed absorption bands at 3350 (OH), 2650 (salt formation), 1660 and 1500 cm^{-1} (amide I and II), but lacked the stretching vibration band at 1750 cm^{-1} (ester carbonyl group). The ^1H NMR spectral data in DMSO-d_6 for the product **19** included broad singlet at δ 3.63 (6H, 4 OH, 2 NH), that disappeared upon addition of D_2O and two singlets at 3.38 (2 H, H-3, H-4), and 4.30 (2H, H-2, H-5), in addition to the peaks at 2.30 (6H, $2SCH_3$), 1.06 (t, 24 H, $CH_2\underline{CH_3}$), 2.90 (q, 6 H, $\underline{CH_2}CH_3$), and 2.84 ppm (s, 8 H, 2-N-CH_2-CH_2-N-).

From the above data, the structure of compound **19** is 1-(2,3,4,5-tetrahydroxy-D-galacto-adipoyl)bis-2-[(tetraethyl-ethylenediammonium)methylthiocarbothiolate)]hydrazine. The excess diamine caused de-*O*-acetylation of the parent bis-(hydrazide) (**1**) and/or of the corresponding saccharide bis-(hydrazide)amine salt **19**.

The structure of de-*O*-acetylated monomeric saccharide bis(hydrazide) amine salt **19** was proved by synthesizing it in two other ways. The first way was by hydrolysis of the acetylated saccharide monomeric salt **6** with methanolic ammonia at room temperature, and the second way was by treatment of galactaric acid 1,6-bis[methylthio(thiocarbonyl)]hydrazide (**24**) with (TEED) in a molar ratio 1:2. Both methods gave authentic samples of the same monomeric de-*O*-acetylated saccharide bis-(hydrazide)amine salt **19**.

The same treatment of compound **1** and **2** with different bifunctional amines (PPZ, TMED, TEED, and TMPD), in a molar ratio 1:10, respectively, gave the monomeric de-*O*-acetylated

saccharide bis(hydrazide) salts (17-23). Their structures have been confirmed by elemental analysis and IR and ^{1}H NMR spectral (Table 1-3).

All the above prepared compounds (1-24) are optically inactive.

EXPERIMENTAL

Melting points were determined by a Kofler Block and are uncorrected. The infrared spectra were recorded on a Pye Unicam SP 1025 and/or SP 2000 spectrophotometer. ^{1}H NMR spectra were carried out at 300 MHz on Varian XL-300 and/or at 90 MHz with a Varian EM-390 spectrometer, using $(Me)_4Si$ as an internal standard and in DMSO-d_6 as a solvent. The microanalyses were performed in the Department of Chemistry, Faculty of Science, Cairo and/or Alexandria University.

Preparation of polymeric acetylated saccharide bis-(hydrazide)amine salts (10-16). The selected diamine (0.01 mol) was added to a stirred solution of the acetylated saccharide bis(hydrazide) 1 or 2 (0.01 mol) in 20 mL of methanol. After stirring for 1 h at room temperature, the precipitate was removed by filtration and washed several times with hot methanol to dissolve unreacted materials. The products are soluble in dioxane, DMF, DMA, and DMSO, but are insoluble in methanol, ethanol, benzene, and chloroform. The physical and spectral data are listed in Table (1-3).

Preparation of monomeric acylated saccharide bis-(hydrazide) amine salts (4-9). The solution of acetylated saccharide bis(hydrazide) 1 or 2 (0.01 mol), in 20 mL of methanol was added dropwise within 10 min to a solution of the selected diamine (0.02 mol) in 5 mL of methanol. After

stirring for 30 min at room temperature, the precipitate was removed by filtration, washed with hot methanol and dried. Solubility properties are the same as those of **10-16**. Melting points, isolated yield, and spectral data are listed in Table (1-3).

Preparation of monomeric saccharide bis(hydrazide)amine salts (17-23). A solution of acetylated saccharide bis-(hydrazide) 1 or 2 (0.01 mol), in 20 mL of methanol, was added to the solution of the selected diamine (0.10 mol) in 5 mL of methanol. After stirring for 4 h at room temperature, the precipitate was removed by filtration, washed several times with hot methanol and dried. Solubility properties are the same as those of **10-16**. The physical and spectral data are listed in Table (1-3).

Preparation of 2,3,4,5-tetra-*O*-acetylgalactaric acid 1,6-bis [N-methyl, methylthio(thiocarbonyl)]hydrazide (3). A solution of 2,3,4,5-tetra-*O*-acetylgalactaroyl dichloride (0.005 mol) in 10 mL of DMA was added with stirring to a solution of *N*-methyl-*S*-methylhydrazinecarbodithioate[10] (0.01 mol) in 20 mL of DMA. The reaction mixture was stirred for 1 h at room temperature, poured onto ice-water, filtered, and recrystallized from methanol: yield 80%, mp 263 °C; IR(KBr) 3125 (NH), 1755 (OAc), 1650 and 1520 (CONH-I, II), 1500 cm^{-1} (CSNH-I). ^1H NMR ($CDCl_3$) δ 2.00, 2.12 (2s, 12 H, 4 AcO), 2.48 (s, 6 H, 2 CH_3S) and 11.48 ppm (s, 2 H, 2 NH).

Anal. Calcd for $C_{20}H_{30}N_4O_{10}S_4$: C,39.09; H,4.89; N,9.12. Found: C,38.97; H,4.96; N,8.78.

Preparation of galactaric acid bis[methylthio(thiocarbonyl)]hydrazide (24). Ammonia solution (0.1 mol) was added with stirring to a solution of 1-(2,3,4,5-tetra-*O*-

acetylgalactaroyl)bis-2-[thiomethyl(thiocarbonyl)]hydrazine[8] 1 (0.01 mol), in 20 mL of methanol. The reaction mixture was stirred for 3 h at room temperature. The de-*O*-acetylated product that separated after the solvent was evaporated, was removed by filtration and washed with hot methanol: yield 73%, mp 210 °C, IR(KBr) 3300 (OH), 3050 (NH), 1655 and 1535 (CONH-I,II). ^{1}H NMR (DMSO-d_6) δ 2.16 (s, 6 H, $2CH_3S$), 3.52 (broad singlet, 8 H, 4 OH, 4 NH); 3.75 (s, 2 H, H-3, H-4, 2CH) and 4.22 ppm (s, 2 H, 2CH, H-2, H-5, 2CH).

Anal. Calcd for $C_{10}H_{18}N_4O_6S_4$: C,26.08 ; H,4.32 ; N,13.39. Found: C,26.28, H,4.13, N,13.92.

REFERENCES

1. L. El-Sayed, M. F. Iskander, A. El-Toukhy and S. E. Zayan, *Inorg. Chim. Acta*, **6**, 663 (1972); M. F. Iskander, M. M. Mishriky, L. El-Sayed and A. El-Toukhy, *J. Inorg. Nucl. Chem.*, **41**, 851 (1979).

2. J. P. Scovill, D. L. Klayman and C. F. Franchiro, *J. Med. Chem.*, 25, 1261 (1982); D. L. Klayman, J. P. Scovill, J. F. Bartosevich, and J. Bruce, *ibid.*, **26**, 35 (1983).

3. E. M. E. Mansour, A. A. Kassem, M. E. El-Aarabi, M. A. Nassr and A. A. El-Toukhy, *Alex. J. Pharm. Sci.*, **III(1)**, 40 (1989).

4. F. Kurzur and M. Wilkinson., *Chem. Rev.*, **70**, 111 (1970); W. E. Antholine, J. M. Knight and D. H. Pettering, *J. Med. Chem.*, **19**, 339 (1976); L. A. Saryan, E. Ankel, C. Kirshanaumurtic and D. H. Pettering, *J. Med. Chem.*, **22**, (1979) 1219; M. Mohan, M. Kumar, A. Kumar, P. H. Madhuranath and N. K. Jha, *J. Inorg. Biochem.*, **33**, 121 (1988); A. Maiti, A. K. Guha and S. Ghosh, *J. Inorg. Biochem.* **33**, 57 (1988).

5. C. J. Shipman, S. H. Smith, J. D. Drach, and D. L. Klayman, *Antimicrob. Agents Chemother.* **19** 682 (1981).

6. J. P. Scovill, D. L. Klayman, C. Lambors, G. E. Childs and J. D. Notsch, *J. Med. Chem.*, **27**, 87 (1984).

7. M. Das and S. E. Livingstone, *J. Inorg. Chim. Acta*, **19**, 5 (1976).

8. E. M. E. Mansour, A. A. Kassem, T. M. Abass, M. A. Nassr, and A. A. El-Toukhy, *J. Carbohydr. Chem.*, **10(3)**, 429 (1991).

9. K. S. Murrany in *Bilogical and Inorganic Cu Chemistry*, K. D. Karlin and J. Tubieta Eds.; Adenine Press, 1985, p 161.

10. M. Akbar Ali, S. E. Livingstone and D. J. Philips, *Inorg. Chim. Acta*, 6, 11 (1972).