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Carbohydrate Polymers 50 (2002) 151–158

Carbohydrate
Polymers

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Metal complexes of starch dialdehyde dithiosemicarbazone

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Received 24 October 2001; revised 19 December 2001; accepted 19 December 2001

Abstract

The Ca, Cd, Co (II), Cu (II), Fe (II), Mg, Mn (II), Ni (II), Pb (II), and Zn complexes of starch dialdehyde dithiosemicarbazone (DASTSC) of 14% oxidation were prepared and characterised. Based on the measured magnetic susceptibility for the Co (II) complex the low-spin character is ascribed to these complexes. The nitrogen atoms of the C=N moiety as well as the sulphur atoms of the C=S moiety are accepted as the coordination sites for the central metal atoms. Thermal analysis pointed two thermal effects on heating DASTSC up to its decomposition. The thermograms of DASTSC complexes contained three thermal effects in the same temperature region. One mole of a metal ion could coordinate with 1.1–65.4 mole of the ligand. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: Starch dialdehyde; Starch dialdehyde dithiosemicarbazone; Metal complexes

1. Introduction

A wide range of pharmacological activity of thiosemicarbazones stimulates considerable interest with this group of compounds. They exhibited cancerostatic (Blanz & French, 1968), antiviral (Logan, Fox, Morgan, Makohon, & Pfau, 1975), bactericidal (Dobek, Klayman, Dickson, Scovill, & Tramont, 1980), and antimalarial (Klayman, Bartosevich, Griffin, Mason, & Scovill, 1979) properties. Heterocyclic thiosemicarbazones inhibit a key enzyme in synthesis of DNA precursors—ribonucleotide reductase—in cells of mammals (French, Blanz, DoAmaral, & French, 1970). Investigations of metal complexes of thiosemicarbazones revealed an increase in their pharmacological activity in respect to that of free ligand (Crim & Petering, 1967; Kumbhar et al., 1991; Padhye & Kauffman, 1985; West, Padhye, & Sonawane, 1991). Particularly iron and copper complexes efficiently destroyed tissues and blocked the DNA synthesis (Saryan, Ankel, Krishnamurti, Antholine, & Petering, 1981).

In our former studies (Barabasz, Chociej, Konitz, & Tomasik, 1986; Para, Klisiewicz-Pańszczyk, & Jurek, 2001a) results of investigation of tuberculostatic activity of starch dialdehyde thiosemicarbazones (DASTSC) (Fig. 1) were described. Depending on degree of oxidation of starch, DASTSC either promoted (Barabasz et al., 1986) or inhibited (Para et al., 2001a) growth of *Mycobacterium tuberculosis*. In this paper ligation of DASTSC oxidised to 14% with Ca, Cd, Co (II), Cu (II), Fe (II), Mg, Mn (II), Ni (II), Pb (II), and Zn ions is presented.

Their low aqueous solubility also provides other potential, non-pharmacological applications. For instance, DASTSC can be utilised for a temporary immobilisation of heavy metal ions in the soil. It might be beneficial for a crop production. In such manner beneficial soil microorganisms sensitive to heavy metal and natural pesticides, for instance, entomopathogenic nematodes (Jaworska, Sepioł, & Tomasik, 1996; Jaworska, Gorczyca, Sepioł, & Tomasik, 1997) might be inhibited from toxic action of heavy metal ions in their seasonal activity period (Para & Ropek, 2000). Complexes of DASTSC with Cu (II), Co (II), and Ni (II) exhibited interesting tuberculostatic activity in in vitro tests (Para, Klisiewicz-Pańszczyk, & Jurek, 2001b)

2. Experimental part

Starch dialdehyde of 14% oxidation was prepared according to Para, Karolczyk-Kostuch, Hajdon, and Tomasik (2000). Thiosemicarbazide (99%) was purchased from Aldrich Chemical Company, Milwaukee, WI, USA. DASTSC was prepared according to Para et al. (2000).

Salts: $CaCl_2 \cdot 2H_2O$, $CdCl_2 \cdot 2.5H_2O$, $CoCl_2$, $CuCl_2 \cdot 2H_2O$, $FeCl_2 \cdot 4H_2O$, $MgCl_2 \cdot 6H_2O$, $MnCl_2 \cdot 4H_2O$, $NiCl_2$, $Pb(NO_3)_2$ and $ZnCl_2$, all of analytical grade, were purchased from POCh Gliwice, Poland.

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PII: S0144-8617(02)00011-5

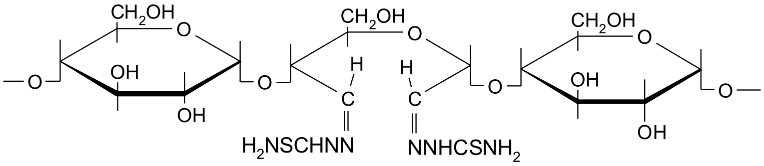

Fig. 1. Structure of DASTSC.

2.1. Preparation of complexes

DASTSC (2 g) with 0.003 moles of thiosemicarbazone residues was added to 0.25 M aq. solution (20 cm^3) of corresponding salt. Suspensions were agitated at room temperature for 3 h, then filtered on suction filter, washed with 3×20 cm^3 of distilled water and dried at 120 °C.

2.2. Solubility

Solubility at 25 °C was determined according to Richter, Augustat, and Schierbaum (1968) for 0.1 g samples suspended in 8 cm^3 of distilled water. Agitation of suspensions for 30 min was followed by 10 min centrifugation at 5000 rpm. Resulting transparent solution (5 cm^3) was transferred to the weighing dish of known weight and evaporated to dryness at 120 °C. The weight of the residue was determined.

2.3. Elemental analysis

Nitrogen content was determined by means of semi-micro-combustion analysis (Bobrański, 1956). Metal content was estimated with inductively coupled plasma-atomic emission ICP—AES, JY 238 ULTRACE JOBIN—YVON (France) spectrophotometer.

2.4. IR spectra

The spectra were recorded in thin films developed on the krs-5 crystal by evaporation of solutions. The measurement range was 650–4000 cm^{-1}. The BIO-RAD, STS— 60 V spectrophotometer (USA) was employed.

2.5. UV spectra

The spectra of 4×10^{-3} M aqueous solutions of particular salts and 5×10^{-4} M solutions of DASTSC in the above salt solutions were recorded in 10 mm quartz cells using the UV–VIS Scanning Spectrophotometer, Shimadzu UV—2101 PC (Japan). The Job method (Inczédy, 1979) provided determination of stability constant of the DASTSC–Cu (II) complex at the total Cu (II) and ligand concentration of 1.2×10^{-4} M.

2.6. Thermal analysis

Samples (0.1 g) were heated from 22 to 500 °C in corundum crucibles in the open at 10 K/min rate of temperature increase. Corundum particles having $\phi = 8$ μm were taken as the standard. Analysis was performed with computerised Paulik–Paulik–Erdey Q-1500-D (Budapest, Hungary) apparatus.

Table 1
Characteristics of starch dialdehyde dithiosemicarbazone and its metal complexes

Central metal atom	Reaction yield (%)	Water solubility (%)	Elemental analysis		
			Nitrogen (%)	Metal ions	
				$g \times 10^{-5}$/1 g DASTSC	X^a/mol M
None		4.2	5.89		
Ca	90	2.7	5.53	90	31.7
Cd	88	6.1	5.38	2750	2.9
Co (II)	92	2.1	5.25	228	18.5
Cu (II)	96	2.2	5.66	4405	1.1
Fe (II)	92	2.2	5.56	94	42.3
Mg	90	2.6	5.90	53	32.7
Mn (II)	89	3.0	5.31	62	65.4
Ni (II)	88	3.0	5.60	384	10.9
Pb (II)	87	9.9	5.74	2960	5.0
Zn	94	3.2	5.48	173	27.8

[a] The number of moles of DASTSC units.

Table 2
UV and IR absorption spectra of dialdehyde starch dithiosemicarbazone and its metal complexes

Central metal atom	UV				IR	
	λ_{max} (nm)	A	λ_{max} (nm)	A	ν(CSNH$_2$ I) (cm^{-1})	ν(CSNH$_2$ II) (cm^{-1})
None	268	1.5481	339	0.4994	1604	1519
Ca	269	1.3843	339	0.4956	1625	1521
Cd	269	1.2695	340	0.4118	1614	1552
Co (II)	268	1.3731	339	0.4723	1601	1535
Cu (II)	269	0.6216	308	0.4747	1587	1535
Fe (II)	268	1.4645	339	0.4393	1623	1523
Mg	268	1.3335	339	0.4891	1637	1525
Mn (II)	268	1.4911	339	0.4550	1607	1520
Ni (II)	268	1.2921	339	0.4072	1627	1553
Pb (II)	269	1.1613	340	0.4928	1623	1537
Zn	269	1.3766	339	0.4949	1622	1547

2.7. Determination of molecular weight of DASTSC–Co (II)

Molecular weight of DASTSC–Co was determined by means of ESI (electrospray) analysis with Finning MAT 95 S (Bremen, Germany) apparatus.

2.8. Magnetic susceptibility

Magnetic susceptibility of the Co (II) complex was determined according to the Faraday method using the Cahn RG automatic electrobalance built in our laboratory. Magnetic field of $H = 3.66$ kOe at the temperature range from liquid nitrogen to 325 K was applied.

2.9. EPR spectra

Experiments were carried out on X-band Bruker ESP-500 spectrometer with the 100 KHz field modulation. The spectra were recorded at room temperature and at 77 K. EPR parameters were found by means of simulation with involvement of modified SIM 14 program (Lozos & Hoffman).

3. Results and discussion

Table 1 collects the yield of the complex formation, solubility of complexes and their elemental analysis.

The yields of the DASTSC complexes were high. Their aqueous solubility was of the same level as solubility of free ligand, but complexation with Cd and Pb (II) even slightly increased the solubility. Amount of the metal atoms involved in coordination to DASTSC varied from 1.1 to 65.4 moles of ligand per mole of metal ions. Cu (II), Cd, and Pb (II) ions coordinated DASTSC to the highest extent whereas Fe (II) and Mn (II) ions coordinated to DASTSC were at approximately 1.5 lower order of magnitude.

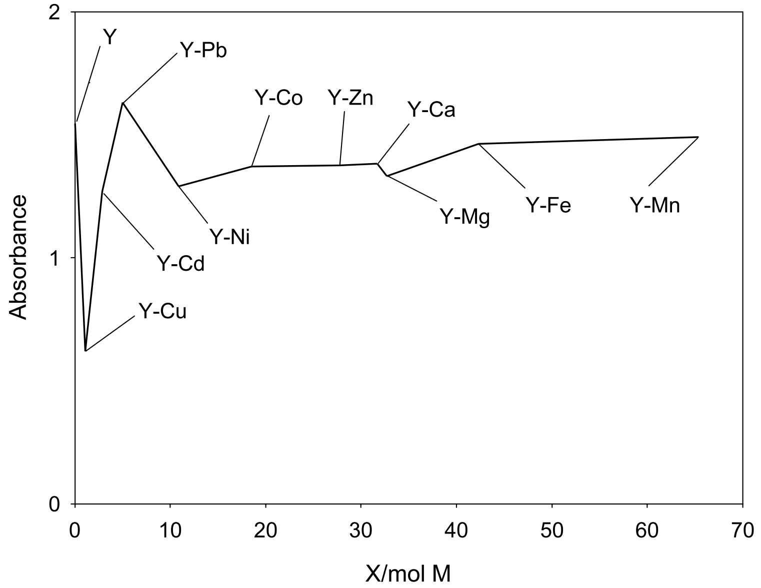

Fig. 2. Intensity changes of the UV longestwavelength band dependent on the number of metal ions in DASTSC–metal complexes (Y = DASTSC).

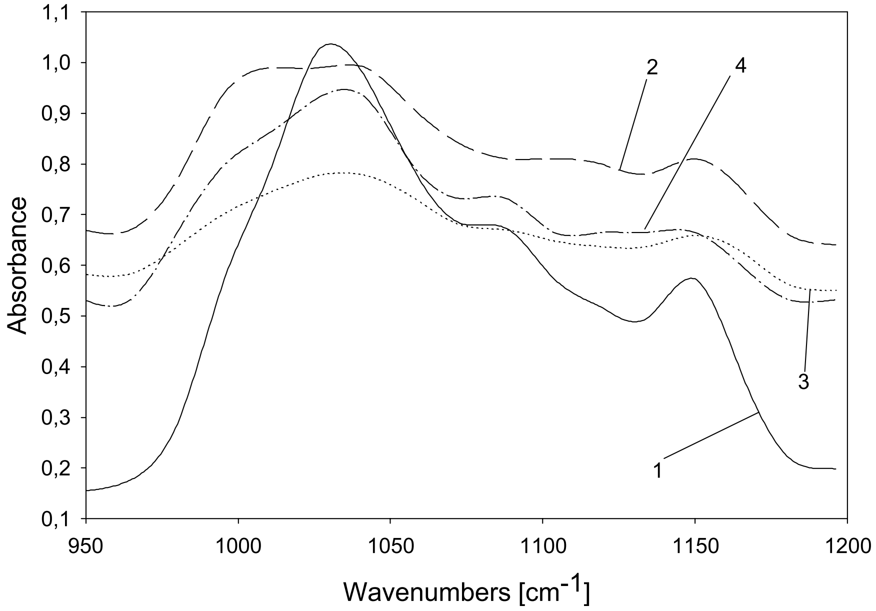

Fig. 3. IR spectra of DASTSC (1), DASTSC–Ca (2), DASTSC–Mg (3), and DASTSC–Mn (4).

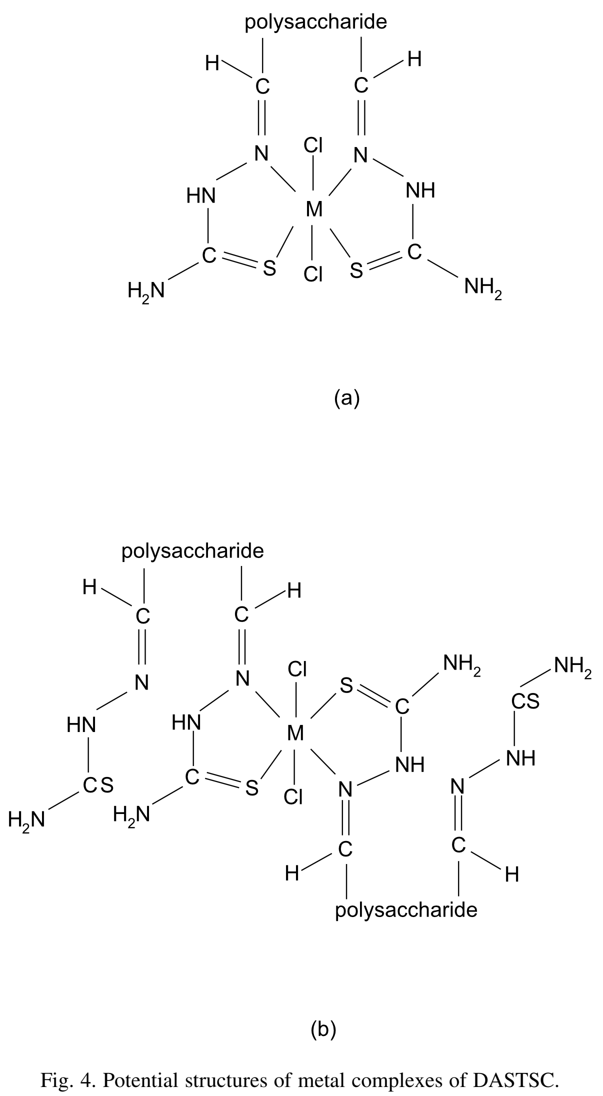

Fig. 4. Potential structures of metal complexes of DASTSC.

Table 2 reports the UV and IR spectral characteristics of the complexes.

In the UV region of the spectrum of DASTSC exhibited two absorption bands at 268 nm ($A = 1.5481$) and 339 nm ($A = 0.4994$), respectively. Only coordination to Cu (II) ion changed the spectral pattern of non-coordinated DASTSC. In the Cu (II) complex the longwavelength absorption maximum moved hypsochromically to 308 nm. As a rule, coordination to the metal ions resulted in a decrease of intensity of that band. Because the longwavelength band corresponded to local excitations it was not surprising that variation in its intensity was non-linear for a number of the metal ions coordinated to DASTSC. The position of the shortwavelength band at 269 nm was completely insensitive to coordination but its intensity was roughly reduced linearly by the number of coordinated metal ions. In the spectrum of Cu (II) complex the intensity of that band decreased by half. Changes in the intensity of the longwavelength band were only roughly dependent on the number of metal ions in the complexes (Fig. 2).

None of the metal salts deviated from the general trend of UV absorbance presented in Fig. 2 indicated coordination of all metal ions to DASTSC.

Spectral changes upon coordination of DASTSC to Cu (II) provided conditions for estimation of the stability constant for the complex. The value of $K = 5 \times 10^{-5}$ was estimated in aqueous solution at the complex concentration of 1.2×10^{-4} M. Simultaneously, the ligand-to-central ion ratio of 1.3:1 was found.

The peak localised at 1519 cm^{-1} in the IR spectrum of DASTSC was the most characteristic peak in the spectrum. It was assigned to $\nu(\mathrm{CSNH_2}\ \mathrm{I})$ vibrations following suggestions of Martins Alho, Mogliani, Brousse, Moltrasio, and D'Accorso (2000). In the spectra of DASTSC complexes

Table 3
EPR spectra of the Cu (II)–DASTSC complex

G-Factor	Measurement temperature			
	Room temperature centre		Liquid nitrogen centre	
	1	2	1	2
Parallel	2.24	2.28	2.23	2.28
Perpendicular	2.10	2.00	2.07	2.01

with all metal ions other than Ca, Fe (II), and Mn (II) ions, this peak moved up by 6–33 cm^{-1}. The band at 1604 cm^{-1} assigned to $\nu(CSNH_2\ II)$ vibrations (Martins Alho et al., 2000) was taken as additional criterion for the complexation of the metal ions to DASTSC. One might see that this band also moved significantly in the spectra of all metal complexes also including complexes of Ca and Fe (II). Practically both the bands did not change their positions only in the spectrum of the presumed Mn (II) complex. Thus, one might assume that this metal ion did not coordinate to DASTSC but was solely weakly sorbed on it. Peaks of the vibrations of the thiocarbonyl (C=S) group appearing in the spectra of thiosemicarbazones below 1000 cm^{-1} (Kumar & Chandra, 1993a; West, Ingram, Kozub, Bain, & Liberta, 1996) could not be recognised in the spectrum of DASTSC and its complexes. The spectrum of DASTSC in this region was rich in bands specific for starch, moreover, overall the concentration of $CSNH_2$ groups in the macromolecule was low. Thus, the band of the vibrations of the C=S group was hidden. In the spectrum of the Ca complex two bands in the same region appeared (Fig. 3).

Based on abundant literature data on metal complexes of thiosemicarbazones chelation with involvement of the C=S, C=N and NH_2 moieties is accepted in this paper (Fig. 4). However, around central metal atoms in the complexes numerous polysaccharide hydroxyl groups resided such that they are potential sites of coordination. Apart from the cadmium ion central metal atoms, there were the Pearson hard acids, such as the hydroxyl groups and the nitrogen atoms of the thiosemicarbazone moiety, whereas the sulphur atom of the thiocarbonyl group was the soft base. Therefore, one might point to a coexisting coordination of the C=N and NH_2 as well as OH moieties to the central metal atoms without any involvement of the sulphur atom. The IR spectral shifts of the $CSNH_2$ band observed for DASTSC did not bring any evidence for such kind of coordination. Such shifts were observed in the spectra of complexes of low-molecular thiosemicarbazones in which the coordination of the type metal–sulphur atoms was identified (Beraldo, Boyd, & West, 1998; Casas, Garcia-Tasende, & Sordo, 2000; Diaz, Pogni, Cao, & Basosi, 1998).

Thiosemicarbazones form complexes of the ML_2 type similar to semicarbazones (Battaglia, Ferrari, & Bogia, 1994; Kumar & Chandra, 1993b; Patel & Agarwala, 1996; Soliman & Khattab, 1991; Souza et al., 1991). Thus, DASTSC might coordinate to two coordination centres within one ligand or two coordination centres within two ligands as shown in Fig. 4.

Heat of formation calculated for complexes (a) ranged from −27,338 to −30,010 kJ/mole. For complexes (b) heats of formation were between −53,438 and −55,662 kJ/mole. Energy of formation calculated per one coordination bond was from −1050 to −1155 and from −1165 to −1210 kJ, respectively. These data showed preferences for the formation of the b-complexes. However, results of elemental analysis of the Cu (II)-complex (Table 1) might suggest that both types of complexes could be formed with preference for the a-complexes. EPR studies (Table 3) confirmed existence of two hardly distinguishable coordination centres in the ligand.

Results of the thermal analysis of DASTSC and its metal complexes are presented in Table 4.

All complexes retained the same amount of water as the non-complexed DASTSC. Weight loss caused by heating from 22 to 500 °C ranged from 27.9 to 33.5% for the various complexes. This fact suggested that coordination with possible intermolecular crosslinking bonds did not form any macrostructures capable of arresting water by sorption and/or inclusion. It would mean that such intermolecular bonds are random and irregular.

After loss of moisture between 22 and 165 °C, free DASTSC showed two thermal transitions (Fig. 5a). The first, endothermic step at 218 °C was assigned to melting following earlier suggestions (Kapuśniak, Ciesielski, Kozioł, & Tomasik, 1999; Tomasik, Wiejak, & Bączkowicz, 1986) made on interpretation of the thermal behaviour of polysaccharides. The second, also endothermic step at temperature depending on the complex was associated with 14.3% weight loss. This step resembled the step normally recognisable on thermal decomposition of starch. DASTSC complexes decomposed in three steps. The first two steps were the same as for free DASTSC and the third occurred in the range 230–250 °C (Table 4). It was common for all complexes except for that with Cu (II). The latter showed no thermal effect above 250 °C. Thorough inspection of the ash after combustion of the sample in the thermogravimetric crucible showed that metal copper as well as Cu_2O were absent. Thus, the exceptional behaviour of the copper complex of DASTSC did not result from oxidation of the ligand with Cu (II).

It is not clear whether intervention from coordination to the hydroxyl groups took place either apart from the coordination to the NH_2 groups or together with such mode of coordination. The coordination evokes only small changes in the pattern of the ligand as shown in Fig. 5, which contains the thermograms of DASTSC and its Co (II)-complex, respectively.

Magnetic susceptibility could be measured for the DASTSC–Co (II) complex. Effective magnetic momentum could be calculated from the result (2.92×10^{-4} K cm^3 g^{-1})

Table 4
Thermal analysis (TG, DTG) of dialdehyde starch dithiosemicarbazone and its metal complexes

Central metal atom	Temperature range (°C)	Corresponding weight loss (%)	Minimum of the DTG peak (°C)
None	22–165	2.6	100
	195–232	4.6	218
	232–305	14.3	280
	22–500	32.9	
Ca	22–165	2.5	100
	195–235	5.0	217
	235–259	3.5	246
	259–305	9.9	276
	22–500	31.8	
Cd	22–165	2.7	100
	190–228	5.0	212
	228–245	3.0	239
	245–284	8.0	260
	22–500	31.3	
Co (II)	22–165	3.3	100
	195–230	4.5	217
	230–250	3.2	243
	250–305	11.0	269
	22–500	33.5	
Cu (II)	22–165	2.5	100
	189–235	10.1	215
	235–245	1.5	240
	22–500	29.7	
Fe (II)	22–165	2.2	100
	193–232	4.9	218
	232–254	3.4	243
	254–306	10.5	275
	22–500	32.6	
Mg	22–165	2.8	100
	195–230	4.2	216
	230–250	2.5	242
	250–310	12.4	280
	22–500	32.6	
Mn (II)	22–165	3.0	100
	195–230	4.5	218
	230–251	2.9	241
	251–305	11.6	275
	22–500	33.2	
Ni (II)	22–165	2.3	100
	195–230	4.6	215
	230–249	3.3	243
	249–295	9.6	262
	22–500	32.3	
Pb (II)	22–165	2.0	100
	187–230	5.9	214
	230–254	3.8	243
	254–301	8.5	270
	22–500	31.9	
Zn	22–165	3.5	100
	195–231	4.5	217
	231–251	2.7	244
	251–302	11.0	276
	22–500	33.4	

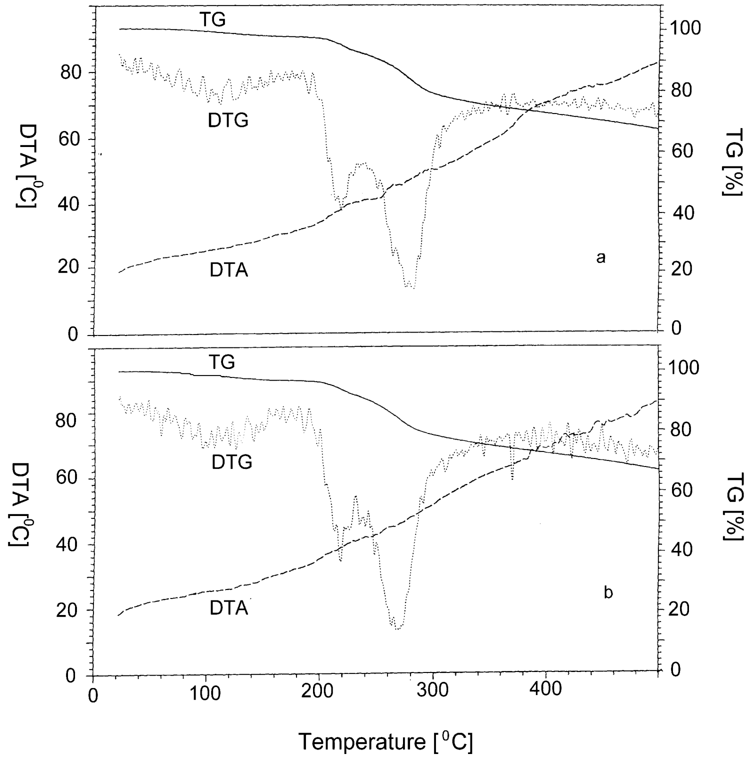

Fig. 5. Thermogram of DASTSC (a) and its Co (II)-complex (b).

of this study. Molecular weight determined for DASTSC – Co (II) was 3.97 kDa. Based on these data $m_{\mathrm{eff}} = 3.0\mu_{\mathrm{B}}$ could be calculated. Such values for low-spin complexes of Co (II) are usually between 2.2 and $2.7\mu_{\mathrm{B}}$ (Cotton & Wilkinson, 1972).

4. Conclusions

Dithiosemicarbazones of starch dialdehyde coordinate with metal ions forming complexes with structure dependent on the central metal ion. A distarch ligand of the b-type (according to Fig. 1) was proposed in the case of all atoms but Cu (II).

For steric reasons not all potential sites of coordination of the macroligand were available for coordination. Complexes are chiefly low-spin species.

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