

STRUCTURE IDENTIFICATION OF 2-THIOHYDANTOIN AND ITS METAL CHELATES BY THERMAL AND SPECTRAL ANALYSIS

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(Received 6 November 1989)

ABSTRACT

The structural stabilities of 2-thiohydantoin and 5-benzal-2-thiohydantoin and their cobalt, nickel and copper chelates during thermal treatment were investigated using thermal and spectrophotometric analyses. Elemental analysis was also used to elucidate their structures. DTA and IR spectral studies support the results obtained from TG. This indicates that not only the coordinated and/or crystallisation water was lost but also that the decomposition of ligands and complexes is necessary to interpret the successive masses lost. The successive endo- and exotherms appear in narrow temperature regions for the decomposition of both ligand and complexes. They are attributed to the loss of sulphur and its oxidation to SO₂ and the consequent oxidation of C=S groups into C=O, in the case of the decomposition of the complexes, and also to the loss of nitrogen and sulphur as N₂ and SO₂ gases in the case of complete decomposition of ligand molecules. Suggested schemes for such thermal decompositions are proposed. Conditional formation constants of nickel complexes were also determined spectrophotometrically.

INTRODUCTION

The preparation, structure and behaviour of 2-thiohydantoin and its derivatives were reviewed elsewhere [1]. Although the structures of such compounds exhibit distinct differences with different cations, there has been no literature report concerning the structural relationships of 2-thiohydantoin and its derivatives and their metal chelates. Due to the reactivity of such sulphur- and nitrogen-containing compounds against viruses, protozoa, smallpox and certain types of tumours [2–4], the study of their chemistry has recently been considerably increased. It was found that some similar sulphur- and nitrogen-containing compounds and their cobalt, nickel and copper chelates have enhanced anti-microbial activities [5]. This has inspired us to study the structures of 2-thiohydantoin and 5-benzal-2-thiohydantoin and their cobalt, nickel and copper chelates by spectral and thermal analyses: this is the ultimate aim of the present investigation.

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EXPERIMENTAL

*Organic synthesis**Preparation of 2-thiohydantoin (A)*

It was reported by Johnson and Scott [6] that 2-thiohydantoin was formed by refluxing a mixture of glycine and ammonium thiocyanate in acetic anhydride to form the corresponding 1-acetyl-2-thiohydantoin; when heated with hydrochloric acid, the acyl group was cleaved and 2-thiohydantoin was obtained, m.p. 227°C. The analysis of the product is as follows: ¹H-NMR (δ ppm): 3.2 (s, 2H, CH₂); 11.5, 10.3 (2s, br, 2H, 2NH, exchangeable with D₂O).

Preparation of 5-benzal-2-thiohydantoin (B)

This was prepared according to the reported procedure [7]. A mixture of 2-thiohydantoin (A) (0.005 mol), fused sodium acetate (2.5 g) and a slight excess (0.0055 mol) of benzaldehyde in 25 ml glacial acetic acid was refluxed for 2 h. The reaction mixture was cooled, poured over cold water, and then the separated solid was filtered off, washed with water and recrystallised from acetic acid as pale yellow crystals, m.p. 260°C. The analysis of the product is as follows: ¹H-NMR (δ ppm): 6.2 (s, 1H, CH=C); 7.2–7.4 (m, 5H, aromatic protons) and 12.1, 10.8 (2s, br, 2H, 2 NH, exchangeable with D₂O).

Compounds **A** and **B** were confirmed by both elemental analyses and spectral data studies.

Preparation of the complexes

In order to prepare the M^{II}-L complexes (M \equiv Co, Ni or Cu), solutions of the ligand (L) (0.5 g per 25 ml ethanol) and of cobalt acetate, nickel chloride or copper perchlorate (0.5 g per 25 ml water) were mixed thoroughly in 1:1 ethanol:water mixture, adjusting the pH to 9 using aqueous 1:1 ammonia solution. Leaving the mixture for 48 hrs resulted in the formation of black cobalt complex **I**, dark violet nickel complex **II** and dark brown copper complexes **III** and **IV** (m.p.s > 300°C). The cobalt and copper chelates are insoluble in water whereas the nickel is partially soluble in water or in ethanol. They were recrystallised from absolute ethanol.

Elemental analysis

Elemental analyses for C, H, N and S were performed by microanalysis at Cairo University (Table 1). The metal content was analysed using a Varian Techtron (model 1100) atomic absorption spectrophotometer, as usual [8].

The absorption spectra of the ligands (10^{-5} M) and their metal complexes (10^{-5} M) were measured in a 1:1 dimethylformamide (DMF)-water mixture using a Pye Unicam SP 1750 recording spectrophotometer, with the solvent as a blank.

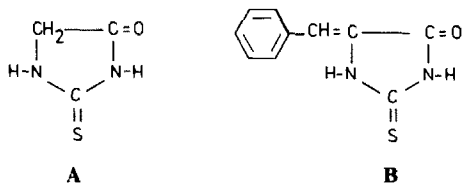
Thermogravimetric (TG) and differential thermal analyses (DTA) were done on a Shimadzu TG system (Shimadzu 30 series) thermal analyser. The weight loss and DTA of 10 mg samples were measured in the temperature range 50–400°C, using a heating rate of 10°C min⁻¹.

The IR spectra were recorded as KBr discs on a Pye Unicam SP 3-300 IR spectrophotometer over a wavenumber range of 300–4000 cm⁻¹.

¹H-NMR spectra were measured in DMSO-d₆ on a Varian EM-360 90 MHz spectrometer, using TMS as internal standard and the chemical shifts are expressed as (δ ppm) units.

RESULTS AND DISCUSSION

The aim of the present work is to study the thermal stability of 2-thiohydantoin and 5-benzal-2-thiohydantoin, two very efficient anti-microbial materials, and the effect of complex formation on this stability. Therefore the first stage of this investigation involved the structure identification of 2-thiohydantoin and 5-benzal-2-thiohydantoin and their Co, Ni and Cu chelates. 2-Thiohydantoin (**A**) and 5-benzal-2-thiohydantoin (**B**) were prepared as previously described and were characterised in our laboratory as having the structural formulae shown below.



Spectrophotometric studies on 2-thiohydantoin and 5-benzal-2-thiohydantoin and their metal chelates

Electronic spectra in solution

2-Thiohydantoin and 5-benzal-2-thiohydantoin generally have characteristic bands in the UV and near visible regions; one, at approximately 210 nm, with ϵ in the order of 10^5 , is attributed to π - π^* transitions in the heterocyclic ring and unsaturated groups of these ligands. The other band occurs at around 440 nm with $\epsilon \approx 250$ and may be attributed to n - π^* transitions due to the lone pair of electrons on donor groups such as NH, C=O and C=S. The positions of these bands depend mainly upon the electron-withdrawing or -repelling ability of the substituents.

TABLE 1
Elemental analysis of metal(II)-2-thiohydantoin and -5-benzal-2-thiohydantoin complexes, I-IV

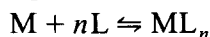
Complex ^a	Found (%)						Calculated (%)					
	C	H	N	S	M	M.W.	C	H	N	S	M	M.W.
I	22.6	3.2	17.6	19.0	17.5	310	22.02	3.67	17.13	19.58	18.02	326.93
II	21.9	4.2	16.8	19.3	17.3	315	22.03	3.67	17.14	19.59	17.97	326.71
III	21.3	2.0	16.0	19.1	19.0	328	21.7	2.4	16.89	19.30	19.16	331.55
IV	47.6	3.9	11.0	12.8	12.0	500	47.29	3.94	11.03	12.61	12.52	507.55

^a The suggested formulae of M(II)-2-thiohydantoin complexes, I-III, are $ML_2 \cdot 2H_2O$ [M \equiv Co, Ni or Cu, L \equiv $C_3H_4N_2OS$ (2-thiohydantoin)]; for complex IV, it is $CuC_{10}H_8N_2OS$ [L \equiv $C_{10}H_8N_2OS$ (5-benzal-2-thiohydantoin)].

When these ligands react with transition metal ions such as Co^{II} , Ni^{II} and Cu^{II} , the 440 nm band is shifted to 510 nm (a red shift) indicating that the groups containing N, O and S are shared in the formation of these complexes, resulting in considerable disturbance of the ligand–electron system. Also, complex formation decreases the ϵ value from 250 to 200 (hypochromic effect). By applying molar and continuous variation methods [8] at the maximum wavelength, of 510 nm, spectral studies of these complexes in DMF suggest a stoichiometry of 1 M:1 L. The conditional formation constants, K_f , of some nickel complexes were calculated spectrophotometrically by applying the relation [5]

$$K_f = [A/A_m] / [(1 - A/A_m)^{n+1} C_1^n n^n]$$

where A corresponds to the concentration of the complex molecule at equilibrium

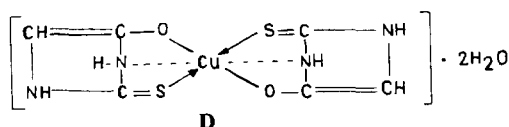
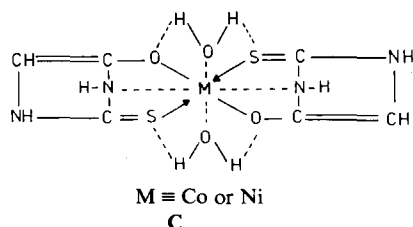


A_m is the concentration of ML at full colour development, C is the initial concentration of metal ion and n is the stoichiometric ratio which is 1 or 2 in the case of Ni complexes. These results indicate that nickel forms two chelates, 1:1 and 1:2, of $K_f = 2.3 \times 10^4$ and 0.8×10^6 , respectively. We could not apply this method to the determination of the formation constants of cobalt and copper complexes because of their lower solubility in different solvents.

IR spectra

To understand the nature of the bonding in these metal chelates, it is necessary to assign their IR bands [9]. Figure 1 shows the IR (cm^{-1}) spectra of 2-thiohydantoin (A) (3230, 3190 (2NH); 1710 (C=O); and 1230 (C=S) and of 5-benzal-2-thiohydantoin (B) (3210, 3170 (2NH), 1700 (C=O) and 1210 (C=S)).

On complex formation, the bands characteristic of amide vibrations are always shifted to higher frequencies, which confirms that the nitrogen, oxygen and sulphur are shared in the formation of the complex, as given by the structural formulae below.



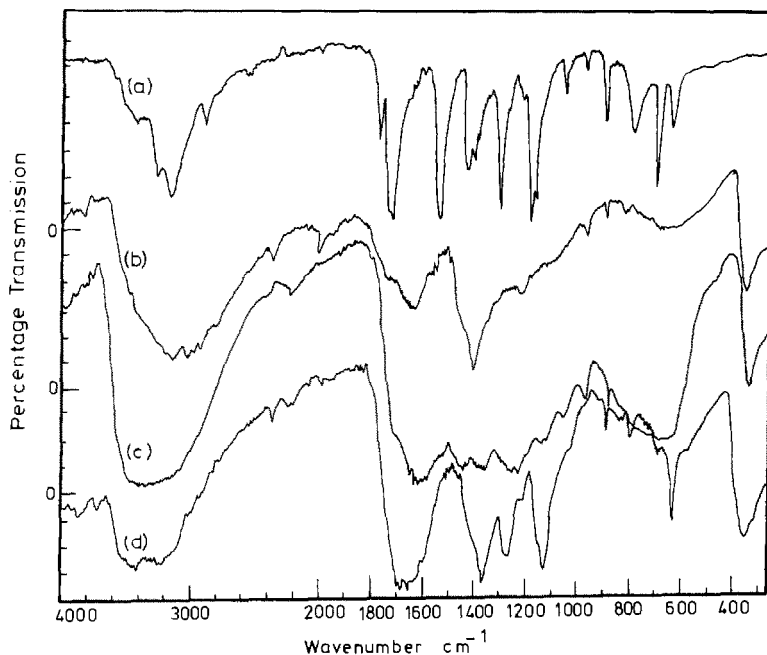


Fig. 1. IR spectra of 2-thiohydantoin (d) and its Co (a), Ni (b) and Cu (c) chelates.

The band at $870\text{--}890\text{ cm}^{-1}$ is present at the same frequency in both ligand and complexes, but it becomes weak due to perturbation of the electron system of the ligand during complex formation. A broad band at $2800\text{--}3600\text{ cm}^{-1}$ appears only in the complexes and is mainly due to the vibration of hydrogen-bond-coordinated water molecules or molecules of water of crystallisation as in forms C and D.

Thermal analysis

Thermogravimetry is very useful for studying the thermal decomposition of solid substances involving both simple compounds [10] and complexes [11,12]. In the present investigation, 2-thiohydantoin, 5-benzal-2-thiohydantoin and their copper, nickel and cobalt complexes (I–IV) were subjected to thermal analyses (Fig. 2).

For the TG, the decomposition stages, temperature ranges, thermal products and the calculated and estimated mass losses are listed in Table 2. Estimated mass losses were based on thermogravimetric analysis (found) and the calculated mass losses were obtained using the microanalysis results for these solid compounds (Table 1).

For the ligand, L, there are two successive decomposition stages in the temperature range $150\text{--}360^\circ\text{C}$, due to the loss of sulphur atoms (estim.

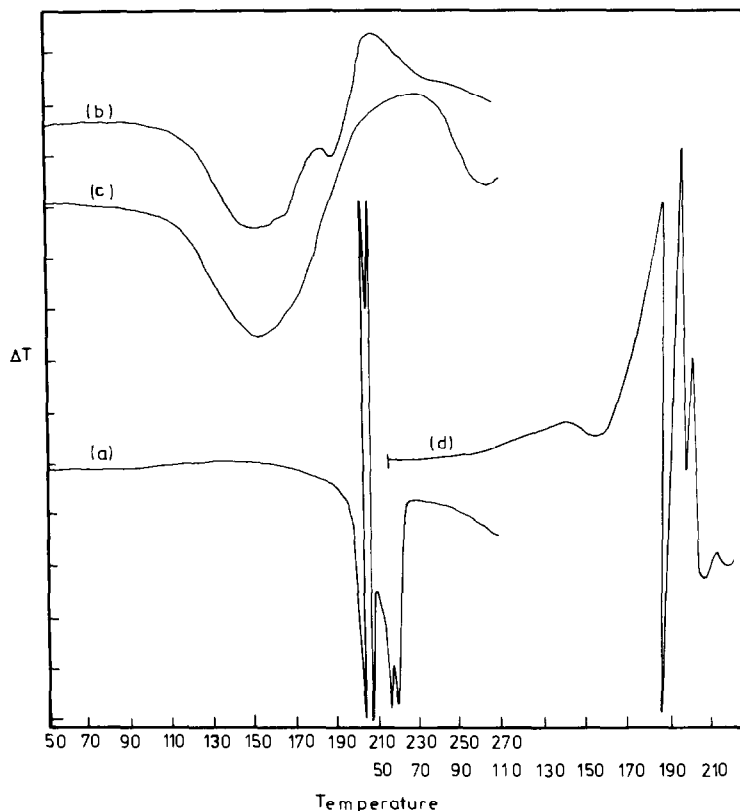


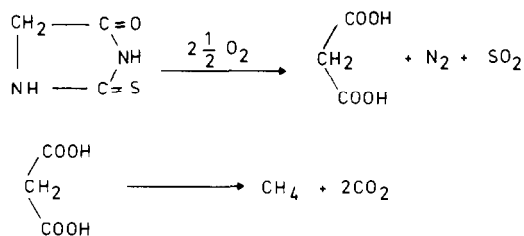
Fig. 2. DTA of 2-thiohydantoin (d) and its Co (a), Ni (b) and Cu (c) chelates.

27.7%, calcd. 27.6%) followed by the loss of two nitrogen atoms as nitrogen gas (estim. 24.5%, calcd. 24.14%). This may be explained by a change in the structural formula of 2-thiohydantoin as shown in Scheme 1.

TABLE 2

Mass losses of 2-thiohydantoin and 5-benzal-2-thiohydantoin, L, and their complexes (I-IV)

Compound	Temperature range (°C)	Decomposition product lost	Mass loss (%)	
			Found	Calcd.
L	150-360	S + N ₂	52.2	51.7
I	90-120	Coord. H ₂ O	5.4	5.5
	120-280	L	35.0	35.48
II	90-130	Two coord. H ₂ O	11.0	11.0
	140-360	L	35.0	35.50
III	110-140	H ₂ O cryst.	4.8	5.4
	155-210	Two S	18.8	19.3
IV	85-130	Two H ₂ O of cryst.	6.8	7.10
	140-210	Two S	13.0	12.6

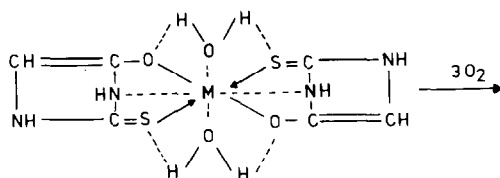


Scheme 1.

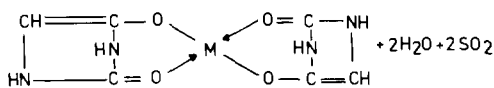
The thermal decomposition of these ligands was confirmed by DTA (Fig. 2a). In the DTA of L, there is an endothermic shift of the base line starting at 150°C, followed by a series of exo- and endotherms in the temperature range 200–230°C. There is also a broad endotherm centred at 270°C. The first endothermic base-line shift may be attributed to a decrease in the heat capacity of L. The series of exo- and endotherms confirms the mass losses of sulphur and nitrogen atoms from the moiety of the ligand, their oxidation as SO₂ and formation of N₂ gases, as shown by TG. The final exotherm represents the decomposition of the malonic acid into CO₂ and CH₄ gases, as shown in Scheme 1.

The TG of the Co, Ni and Cu complexes of 2-thiohydantoin and 5-benzal-2-thiohydantoin, I–IV, (Table 2) usually involves two stages. The first indicates the loss of either coordinated water molecules or water of crystallisation (see the structures C and D). This water loss occurs in the temperature range 90–130°C for Co and Ni complexes (est. 5.0%, calcd. 5.5%), and in the range 110–149°C for the copper chelates (est. 4.8 and 6.8%, calcd. 5.4 and 7.10%). The second mass loss, occurring in the temperature range 140–155°C for the Co and Ni chelates (est. 35.0%, calcd. 35.5%) and in the range 155–210°C for the Cu complexes (III and IV) (est. 18.8 and 13.0%, calcd. 19.3 and 12.6%), is mainly due to the loss of the ligand molecule. In general, sulphur atoms are lost from the ligand entity at a higher temperature (140–360°C) than the same loss from the chelate moieties (190–230°C). This may be explained by the sharing of the sulphur in the complex by the formation of M–S bonds and the consequent weakening of the C–S bonds in the ligand moiety. Therefore, on heating in air, sulphur is lost more easily from the complex than from ligand itself.

The DTA of the Co, Ni and Cu complexes are shown in Fig. 2b–d. For the Co and Ni complexes (Fig. 2b, c), the curve begins with an endothermic base-line shift starting at 90°C, due to the decrease of the heat capacity, followed by a broad endotherm centred at 175°C. Finally, there is a small exotherm centred at 180°C, followed by a broad exotherm at 180–235°C, for the Co complex, and at 170–270°C for the Ni complex. The first broad endotherm may be explained by the loss of water molecules and sulphur atoms. The final exotherms may be explained by chemical reactions following the mass losses as given by Schemes 1 and 2.



C or D



E

Scheme 2.

The loss of sulphur may be due to oxidation of C=S groups to C=O groups, and the oxidation of S to SO₂.

The DTA of copper complex III (Fig. 2d) indicates that the thermal behaviour of this complex is different from the Co and Ni complexes: there is an exothermic base-line shift starting at 70 °C which may be explained by an increase in heat capacity. There is also a small endotherm at 140–160 °C due to the loss of water molecules and sulphur atoms, as was indicated by TG (Table 1) in the same temperature range. Finally, there is a series of sharp endo- and exotherms in the 180–200 °C range, similar to those seen in the DTA of the ligand. This can only be explained by early loss of one ligand molecule as given by



This is then followed by decomposition of the ligand, as in Scheme 1.

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