THERMAL STUDIES ON ORGANOMERCURY(II) COMPLEXES OF 6-THIOGUANINE

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ABSTRACT

Organomercury(II) complexes involving 6-thioguanine of the type p-XC_6H_4HgL (I) (LH = 6-thioguanine; X = Me, MeO, NO_2) have been synthesized. Spectral studies (IR and UV) indicate that the 6-thioguanine moiety acts as a bidentate group. From thermogravimetric (TG) curves, the order, activation energy and apparent activation entropy of the thermal decomposition reaction have been elucidated. The variation of the activation energy has been correlated with the nature of the substituent on the phenyl ring. The heat of reaction has been obtained from differential scanning calorimetric (DSC) studies.

INTRODUCTION

6-Thioguanine belongs to a class of purine bases and is known to act as an antimetabolite drug [1]. Interest in its metal complexes has arisen for the following reasons. Firstly, as a result of antitumour activity of some metal complexes, considerable interest has been shown in the design of model complexes involving purines which could mimic the interaction of metal ions with DNA [2,3]. Secondly, the investigation of mercury–purine complexes is of particular value, since the known toxic effects of the organomercury compounds, which are attributed to the formation of mercury–sulphur bonds with sulphydryl functions in amino acids and proteins, may also be

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due, in part, to their interaction with nucleic acid constituents [4]. Therefore we have carried out the synthesis of a few organomercury(II) complexes of 6-thioguanine and have investigated their thermal behaviour.

Yet another reason for the growing interest in studies of metal–purine complexes is to investigate the bonding mode of the ligand to the metal ion. The 6-thioguanine moiety has divergent bonding sites. The evidence for the involvement of exocyclic sulphur at C6 in complexation is provided by the IR spectra. Whereas in the free ligand the ν(C=S) stretching frequency absorbs at 1220 cm^{-1}, it is shifted to ~ 1180 cm^{-1} on complexation. The bands at 1660 and 1530 cm^{-1} which are assigned respectively to the ν(C=C) and ν(C=N) stretching modes in 6-thioguanine are shifted to ~ 1570 and ~ 1490 cm^{-1} in the complexes. These results indicate that the 6-thioguanine ligand acts as a bidentate group, being coordinated to the mercury(II) ion through exocyclic sulphur at C6 and deprotonation of N7.

The UV spectrum of 6-thioguanine shows a broad band at 310 nm (log ϵ 2.0) due to the π–π* transitions of the 6-thione group. On complexation, this band is shifted to 320 nm (log ϵ ~ 3.2). The shift is attributed to the involvement of the C=S group in complexation, thus supporting the conclusions drawn from IR studies.

EXPERIMENTAL

The following instruments were used: Shimadzu infrared spectrophotometer, IR-435 for IR spectra; Perkin–Elmer UV–VIS spectrophotometer, model 554 for UV spectra; G-70 thermoanalyser, Setaram (Lyon, France) for TG studies up to 1273 K in air at a heating rate of 15°C min^{-1} and a sample size of ca. 15 mg; Du Pont device, model 1090, for recording DSC curves up to 773 K at a heating rate of 15°C min^{-1} and a sample size of ca. 5 mg. A platinum crucible was used, with alumina as the reference material.

6-Thioguanine was purchased from Sigma Chemical Co., U.S.A. and used without further purification. The aryl-mercury(II) chlorides, p-XC$_6$H$_4$HgCl (X = Me, MeO, NO$_2$) were synthesized by the method of Nesmeyanov et al. [5].
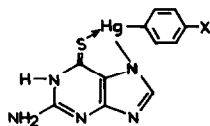
(I)

X = Me, MeO, NO$_2$

A solution of p-XC$_6$H$_4$HgCl (0.01 mol) in 25 ml DMF was slowly added to a solution of 6-thioguanine (0.01 mol) in 25 ml DMF at a pH of 8–9. The contents were stirred for 6 h at 50°C and filtered. The filtrate was slowly

added to crushed ice with vigorous stirring. The precipitate so obtained was washed successively with hot water and benzene. The resulting product was recrystallized from THF.

RESULTS

The TG curves are shown in Fig. 1.

p-MeC$_6$H$_4$HgL

From the TG curve it is observed that the mass change begins at 541 K and continues up to 793 K. The observed weight loss (45.5%) during this step corresponds to the formation of HgO. The calculated weight loss for this step is 47.3%. Above 823 K HgO slowly volatilizes. At 1173 K, the volatilization is complete and the crucible of the thermobalance is empty.

The DSC curve shows an endothermic peak with $T_{max} = 727$ K, corresponding to the decomposition of the complex to HgO.

p-MeOC$_6$H$_4$HgL

The TG of this complex reveals a weight loss in the temperature range 468–803 K. The observed weight loss of 43.3% corresponds to the formation of HgO. The theoretical weight loss for this step is 45.7%. Above 833 K HgO slowly volatilizes. The volatilization is complete at 1080 K, at which temperature the crucible of the thermobalance is rendered vacant.

The DSC profile shows an endothermic peak with $T_{max} = 772$ K, corresponding to the decomposition of the complex to HgO.
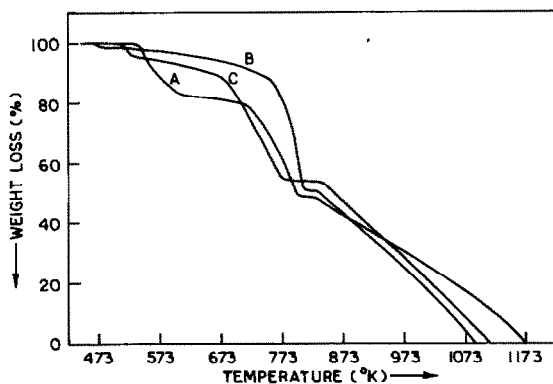

Fig. 1. TG curves: A, p-MeC$_6$H$_4$HgL; B, p-MeOC$_6$H$_4$HgL; C, p-NO$_2$C$_6$H$_4$HgL.

p-$NO_2C_6H_4HgL$

The TG curve indicates that the decomposition begins at 519 K. The observed weight loss of 40.8% in the temperature range 519–773 K corresponds to the formation of HgO. The calculated weight loss for this step is 44.3%. Above 843 K, the volatilization of HgO begins and at 1080 K, the crucible of the thermobalance is rendered vacant.

The thermal effect on the DSC curve is of endothermic nature, with $T_{max} = 690$ K. It corresponds to the decomposition of the complex to HgO.

DISCUSSION

The results of TG and DSC evaluations are presented in Table 1. From the TG curves, the order (n) and activation energy (E_a) of the thermal decomposition reaction have been elucidated by the method of Coats and Redfern [6]. The linearization curves are shown in Fig. 2.

The order of reaction in each case is unity. A comparison of the activation energy data reveals that the p-$NO_2C_6H_4HgL$ complex has the lowest value of E_a. This may be explained on the basis of electron-withdrawing effect of the nitro group, which leads to a weakening of the φ-Hg bond, thus making thermal degradation relatively easy. In the case of the p-MeC_6H_4HgL analogue, the methyl group is of electron-donating type and the φ-Hg bond is strengthened, leading to a higher value of E_a. Since the methoxy group has a greater electron donating character than the methyl group, the p-$MeOC_6H_4HgL$ complex has the highest value of E_a in the series.

The apparent activation entropy ($\Delta S^{\ddagger}$) has been calculated by the method of Zsakó [7]. The apparent activation entropy has a positive value for all the complexes. Hence, thermal degradation of these complexes is a spontaneous process. The p-$MeOC_6H_4HgL$ complex has the highest $\Delta S^{\ddagger}$ value while the p-$NO_2C_6H_4HgL$ analogue has the lowest. Hence, the former decomposes with the greatest degree of randomness and the latter with the least.

TABLE 1

Thermal data

Compound	TG						DSC		
	Temp. range (K)	Weight loss (%)		n	E_a (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J deg^{-1} mol^{-1})	Thermal effect	T_{max} (K)	ΔH (kJ mol^{-1})
		Obs.	(Calc.)						
p-MeC_6H_4HgL	541–793	45.5	(47.3)	1	17.4	2.5	Endothermic	727	293
p-$MeOC_6H_4HgL$	468–803	43.3	(45.7)	1	19.1	3.9	Endothermic	772	848
p-$NO_2C_6H_4HgL$	519–773	40.8	(44.3)	1	15.3	1.8	Endothermic	690	740
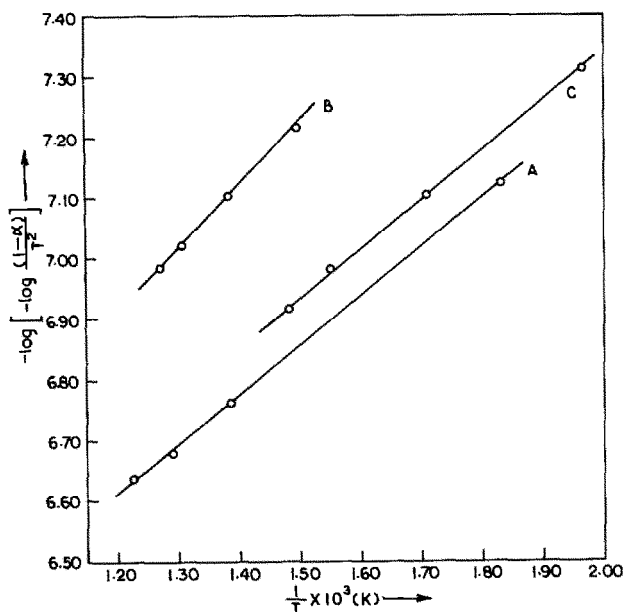
Fig. 2. Linearization curves: A, p-MeC$_6$H$_4$HgL; B, p-MeOC$_6$H$_4$HgL; C, p-NO$_2$C$_6$H$_4$HgL.

The TG data are supplemented by DSC studies. The thermal effects in each case are of endothermic nature. The heat of reaction (ΔH) has been measured from the DSC curves.

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