Thermochimica Acta, 116 (1987) 357–362
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

THERMAL STUDIES ON ORGANOMERCURY(II) COMPLEXES OF ISONIAZID

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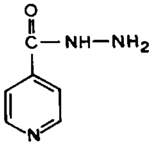
(Received 16 December 1986)

ABSTRACT

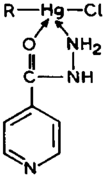
Organomercury(II) derivatives of isoniazid of the type, RHgCl(L) [R = C_6H_5, *p*-HOC_6H_4, *p*-$AcOC_6H_4$; L = isoniazid] have been synthesised. Spectral studies (IR and UV) indicate that the isoniazid moiety is bidentate. From thermogravimetric curves, the order, activation energy and apparent activation entropy of the thermal decomposition reaction have been elucidated. The heat of reaction has been calculated from differential thermal analysis curves.

INTRODUCTION

Isoniazid is an important antitubercular drug [1]. It is widely accepted together with streptomycin and *p*-aminosalicylic acid for the treatment of tuberculosis. It is thought to be of particular value against the miliary form of the disease and against tuberculosis meningitis. The interest in metal complexes of isoniazid has arisen mainly because of the disclosure that the tuberculosis activity of the drug increases very variably in the presence of metal ions [2]. To investigate this effect, we synthesised some organomercury(II) complexes (B) of isoniazid (A) and studied their thermal characteristics. This followed directly from our previous investigation on the thermal behaviour of metal ion–biomolecule systems [3].



(A)



(B)

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0040-6031/87/$03.50

Yet another reason for the growing interest in studies of metal–isoniazid complexes is to investigate the bonding mode of the ligand to the metal ion. Isoniazid may be coordinated to the metal ion through pyridine nitrogen or may act as a bidentate ligand, coordinating through carbonyl oxygen and hydrazinic nitrogen. The two bonding modes are distinguished by IR studies. Isoniazid shows characteristic amide frequencies at 1660, 1550 and 1300 cm^{-1} due to amide I (ν_{CO}), amide II and amide III stretching vibrations, respectively. The corresponding bands in the spectra of the complexes appear at ~ 1650, ~ 1530 and ~ 1325 cm^{-1}, respectively. The pyridine ring $\nu(C\stackrel{...}{-}C)$ and $\nu(C\stackrel{...}{-}N)$ vibrations in the ligand occur at 1590 and 1450 cm^{-1}, respectively. In the case of metal complexes, no significant alterations are observed in the corresponding pyridine vibrations. The shift to a lower frequency region in the case of amide I (ν_{CO}) and amide II bands and the shift to a higher frequency region in the case of amide III stretching mode indicates that the carbonyl oxygen and hydrazinic nitrogen are involved in coordination [4,5]. Since the $\nu(C\stackrel{...}{-}N)$ and $\nu(C\stackrel{...}{-}C)$ frequencies remain unaltered on complexation, the possibility of coordination through ring nitrogen is ruled out [6].

The UV spectrum of isoniazid shows two band at 216 (log ϵ 3.4) and 250 nm (log ϵ 3.5) due to absorptions of the chromophoric C=O and C=N groups, respectively. For the complexes, the former band is shifted to ca. 236 nm (log $\epsilon \sim 4.27$), while the latter remains unaltered. The shift in the absorption band due to the carbonyl chromophore is attributed to this group being involved in complexation.

It is thus evident from IR and UV studies that isoniazid acts as a bidentate ligand, coordinating through carbonyl and hydrazinic groups. In this communication we report the results of TG and DTA interpretations for some organomercury(II) isoniazid complexes.

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 in air at a heating rate of 8° min^{-1}; Stanton-Redcroft DTA-780 for recording DTA curves up to 673 K in air at a heating rate of 10° min^{-1} and chart speed of 50 cm h^{-1}.

C_6H_5HgCl [7], p-HOC_6H_4HgCl [8] and p-$AcOC_6H_4HgCl$ [9] were prepared by standard methods. A solution of isoniazid (0.05 mol) in 25 ml THF was added slowly to a solution of RHgCl (0.05 mol) in 25 ml THF. The contents were stirred for about 2 h at room temperature and filtered. The filtrate was reduced to one quarter of its original volume by evaporating the solvent under vacuum. The complexes, RHgCl(L) ($R = C_6H_5$, p-HOC_6H_4,

p-AcOC$_6$H$_4$) were precipitated on addition of petroleum ether. These were dried, washed with hot water and recrystallised from acetone.

RESULTS

The TG and DTA curves are shown in Figs. 1 and 2, respectively.

$C_6H_5HgCl(L)$

The TG curve indicates that the mass change begins at 483 K, although major weight loss occurs in the range 548–623 K. The observed weight loss (52.7%) corresponds to the formation of HgO, for which the theoretically calculated weight loss is 51.8%. The HgO slowly volatilises above 753 K. At about 1223 K the volatilisation is complete and the thermobalance crucible is rendered vacant.

In the DTA profile, an endothermic peak at T_{max} 425 K corresponds to the melting of the complex. This is followed by another endothermic peak with T_{max} 518 K, due to the decomposition of the complex to HgO.

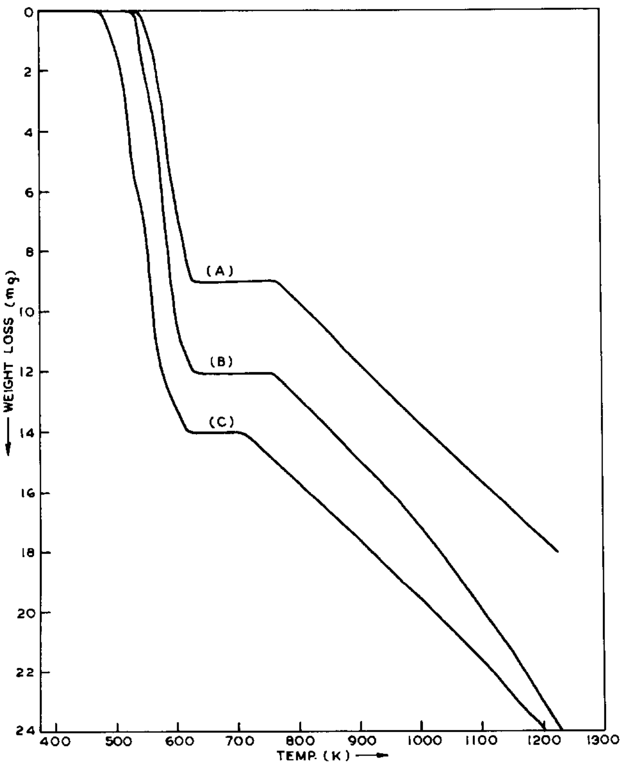

Fig. 1. TG curves: (A) $C_6H_5HgCl(L)$; (B) p-$HOC_6H_4HgCl(L)$; (C) p-$AcOC_6H_4HgCl(L)$.

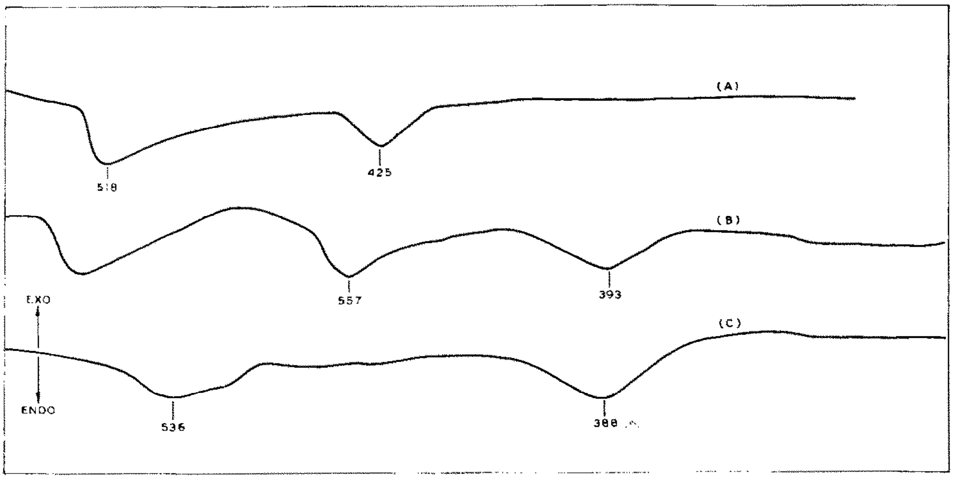

Fig. 2. DTA curves: (A) $C_6H_5HgCl(L)$; (B) p-$HOC_6H_4HgCl(L)$; (C) p-$AcOC_6H_4HgCl(L)$.

p-*HOC₆H₄HgCl(L)*

From the TG curve, it is observed that the mass change begins at 463 K. There is, however, a major weight loss in the range 533–633 K. The observed weight loss (56.0%) corresponds to the formation of HgO. The theoretical weight loss for this step is 57.3%. Above 753 K, HgO slowly volatilises. At 1223 K, the volatilisation is complete and the thermobalance crucible is left empty.

The DTA curve shows two thermal effects both in the form of endothermic peaks with T_{max} values of 393 and 557 K. The former corresponds to the melting of the complex while the latter is due to its decomposition to HgO.

p-*AcOC₆H₄HgCl(L)*

The TG curve of this complex reveals a sudden weight loss in the range 473–713 K. The observed weight loss (52.1%) corresponds to the formation of HgO. The theoretically calculated weight loss is 48.8%. Above 713 K, HgO slowly volatilises and at about 1223 K, the volatilisation is complete.

Two endothermic peaks are observed in the DTA of the complex. The first with T_{max} 388 K is due to the melting of the complex and the second with T_{max} 536 K corresponds to its decomposition to HgO.

DISCUSSION

The results of the TG and DTA evaluations are presented in Table 1. From the TG curves, the order(n) and activation energy (E_a) of the thermal

TABLE 1

Thermal data

Complex	TG				DTA		
	Temp. range (K)	n	E_a (kcal mol^{-1})	$S^{\neq}$ (e.u.)	Thermal effect	T_{max} (K)	ΔH (cal g^{-1})
$C_6H_5HgCl(L)$	548–623	1	27.45	20.77	Endothermic [a]	425	–
					Endothermic	518	41.18
p-$HOC_6H_4HgCl(L)$	533–633	1	32.68	26.44	Endothermic [a]	393	–
					Endothermic	557	20.83
p-$AcOC_6H_4HgCl(L)$	473–613	1	13.72	10.30	Endothermic [a]	388	–
					Endothermic	536	39.60

[a] Due to melting.

decomposition reaction have been elucidated by the method of Coats and Redfern [10]. The linearalisation curves are shown in Fig. 3.

The order of reaction in each case is one. A comparison of the activation energy data reveals that the p-$AcOC_6H_4HgCl(L)$ complex has the lowest E_a value. This may be explained on the basis of the electron withdrawing effect of the acetoxy group, which leads to a weakening of the R–Hg bond, thus making thermal degradation relatively easy. In the case of the p-$HOC_6H_4HgCl(L)$ complex, the phenolic group is electron donating and the R–Hg bond is strengthened. Therefore, the value of activation energy in this case is higher than that in the unsubstituted $C_6H_5HgCl(L)$ complex.

The apparent activation entropy ($S^{\neq}$) has been calculated by the method of Zsakó [11]. The apparent activation entropy has a positive value for all the complexes. Hence, thermal degradation of these complexes is a spontaneous process. The p-$HOC_6H_4HgCl(L)$ complex has the highest $S^{\neq}$ value while the p-$AcOC_6H_4HgCl(L)$ analogue has the lowest. Hence, the former decomposes with the greatest degree of randomness and the latter with the least.

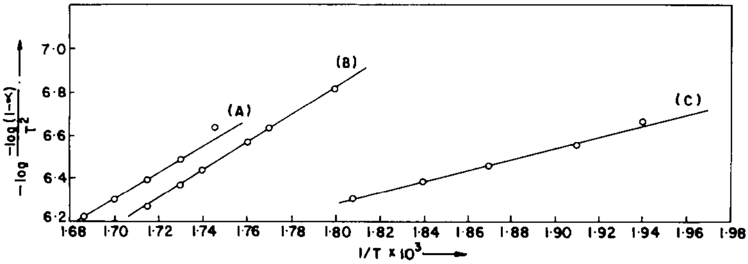

Fig. 3. Kinetic parameters from TG: (A) $C_6H_5HgCl(L)$; (B) p-$HOC_6H_4HgCl(L)$; (C) p-$AcOC_6H_4HgCl(L)$.

The TG data are supplemented by DTA studies. Each complex shows two thermal effects in the DTA curves in the form of endothermic peaks. The one at lower temperature is due to the melting of the complex and the one at higher temperature corresponds to decomposition of the complex to HgO. The heat of reaction (ΔH) has been calculated for the latter thermal effect [12]. The temperature dependent calibration coefficient was obtained from the Currell equation [13].

ACKNOWLEDGEMENTS

We take this opportunity to thank the University Grants Commission, New Delhi for the award of a Research Fellowship to one of us (S.B.). Thanks are also due to the Solid State Physics Laboratory, New Delhi for recording the DTA curves.

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