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THERMAL STUDIES ON ORGANOMERCURY(II) COMPLEXES OF 6-AMINO PENICILLINIC ACID

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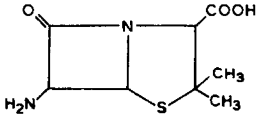
ABSTRACT

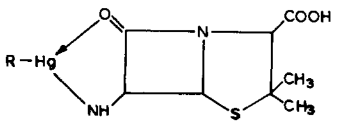
Organomercury(II) derivatives of 6-amino penicillinic acid (A) of the type RHgL (B) (R = phenyl (C_6H_5), *p*-acetoxyphenyl (*p*-$CH_3COOC_6H_4$), *p*-hydroxyphenyl (*p*-HOC_6H_4); HL = 6-amino penicillinic acid) have been synthesised. Spectral studies (IR and UV) indicate that the penicillin moiety is bidentate. From thermogravimetric curves, the order and activation energy of the thermal decomposition reaction have been elucidated. The variation of activation energy has been co-related with the nature of substituent on the phenyl ring. The thermal decomposition reaction in each case follows an F_1 type mechanism. From differential thermal analysis the activation energy and the heat of transition for thermal effects have been calculated. The fragmentation pattern has been analysed on the basis of mass spectra.

INTRODUCTION

In an earlier communication [1] we gave a brief report of our investigations on organometallic derivatives of 6-amino penicillinic acid. Our interest in the study of such complexes is mainly due to the fact that the introduction of substituents into the penicillin nucleus effects changes not only in antibiotic activity and β-lactamase susceptibility but also in physico-chemical properties.



(A)



(B)

R = C_6H_5, p-$CH_3COOC_6H_4$, p-HOC_6H_4

Such changes are effective in the present case too. For example, the

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carbonyl absorption frequency of the lactam ring of 6-amino penicillinic acid is centered at ~ 1765 cm^{-1} [2]. However, for the metal complexes it is shifted to ~ 1700 cm^{-1}, indicating that the carbonyl group is bound to the metal ion. Thus the penicillin moiety is bidentate. Similarly, whereas the UV spectra of 6-amino penicillinic acid show an intense band at 210 nm due to $\pi-\pi^*$ absorption of the lactam C=O group, the corresponding band in the case of metal complexes is shifted to 242 nm. This shift is attributed to the involvement of the lactam C=O group in complexation, thus supporting the conclusions drawn from IR studies.

In order to study the thermal behaviour of semi-synthetic antibiotics, in this communication we report the results of TG, DTA and mass spectral interpretation for organomercury(II) derivatives of 6-amino penicillinic acid.

EXPERIMENTAL

The TG curves were recorded on a Setaram G-70 thermoanalyser, in an air atmosphere at a heating rate of 8°C min^{-1}. The DTA studies up to 773 K were made on a Mettler TA-20 device in an air atmosphere, at a heating rate of 8°C min^{-1} and with a chart speed of 30 cm h^{-1}. Mass spectra were recorded at Central Drug Research Institute, Lucknow, India. C_6H_5HgCl [3], p-$CH_3COOC_6H_4HgCl$ [4] and p-HOC_6H_4HgCl [5] were prepared by standard methods.

All the complexes were prepared by a common method. A solution of RHgCl (0.50 mmol) in 25 ml THF was added slowly to a suspension of 6-amino penicillinic acid (0.50 mmol) in 25 ml THF and 10 ml triethyl amine. The contents were stirred at room temperature for about 2 h and then filtered. The filtrate was evaporated to dryness under vacuum. The solid product was suspended in about 10 ml water and 5 ml of 2 M HCl was added. The RHgL complexes precipitated. These were washed with petroleum ether and recrystallised from acetone.

RESULTS

6-[p-Acetoxyphenylmercury(II) amido] penicillinic acid, p-$CH_3COOC_6H_4HgL$

The TG curve indicates that the decomposition slowly begins at 423 K. Although at this temperature an onset of mass change is observed, the major weight loss occurs in the range 523–723 K. The observed weight loss (60%) corresponds to the formation of HgO, for which the theoretically calculated weight loss is 60.5%. Above 793 K, the HgO slowly volatilizes. At about 1223 K, the volatilization is complete and the crucible is left empty.

In the DTA curve a thermal effect begins at 423 K and an endothermic peak with T_{max} 631 K is observed. This peak corresponds to the decomposition of the complex to HgO.

6-[Phenylmercury(II) amido] penicillinic acid, C_6H_5HgL

The TG of this complex reveals a sudden weight loss in the range 473–553 K. The theoretical, as well as the observed weight loss of 56.25% correspond to the formation of HgO. Above 793 K HgO slowly volatilizes and at about 1223 K the volatilization is complete.

The DTA profile shows two endothermic peaks. The first, with T_{max} 365 K, corresponds to the melting of the complex, while the second, with T_{max} 513 K, corresponds to the decomposition of the complex to HgO.

6-[p-Hydroxyphenylmercury(II)amido] penicillinic acid, p-HOC_6H_4HgL

From the TG curve it is observed that the mass change begins at 363 K. There is, however, a major weight loss in the range 463–613 K. The observed weight loss (58.33%) corresponds to the formation of HgO. The theoretical weight loss for this step is 57.5%. Above 793 K HgO slowly volatilizes. At 1223 K the volatilization is complete and the crucible of the thermobalance is empty.

The DTA curve shows two endothermic peaks. The first thermal effect, with T_{max} 363 K, is due to the melting of the complex, while the second, with $T_{max} = 533$ K, corresponds to the decomposition of the complex.

DISCUSSION

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. 1 and the data are presented in Table 1.

The order of reaction in each case is one. A comparison of the activation energy data reveals that the p-$CH_3COOC_6H_4HgL$ complex has the lowest value of E_a. This may be explained on the basis of the electron withdrawing effect of the acetoxy group, which leads to a weakening of the Ar–Hg bond, thus making thermal degradation relatively easy. In the case of the p-HOC_6H_4HgL complex, the phenolic group is electron donating and the Ar–Hg bond is strengthened. Therefore, the value of activation energy in this case is higher than in the unsubstituted C_6H_5HgL complex.

That the Ar–Hg bond cleavage is involved in the pyrolysis of complexes is also evidenced from the mass spectra. The cleavage results in Ar^+ and HgL^+ fragments. Thus, the peaks with m/z 135, 77 and 93 correspond to the formation of $CH_3COOC_6H_4^+$, $C_6H_5^+$ and $HOC_6H_4^+$ fragments, respectively.

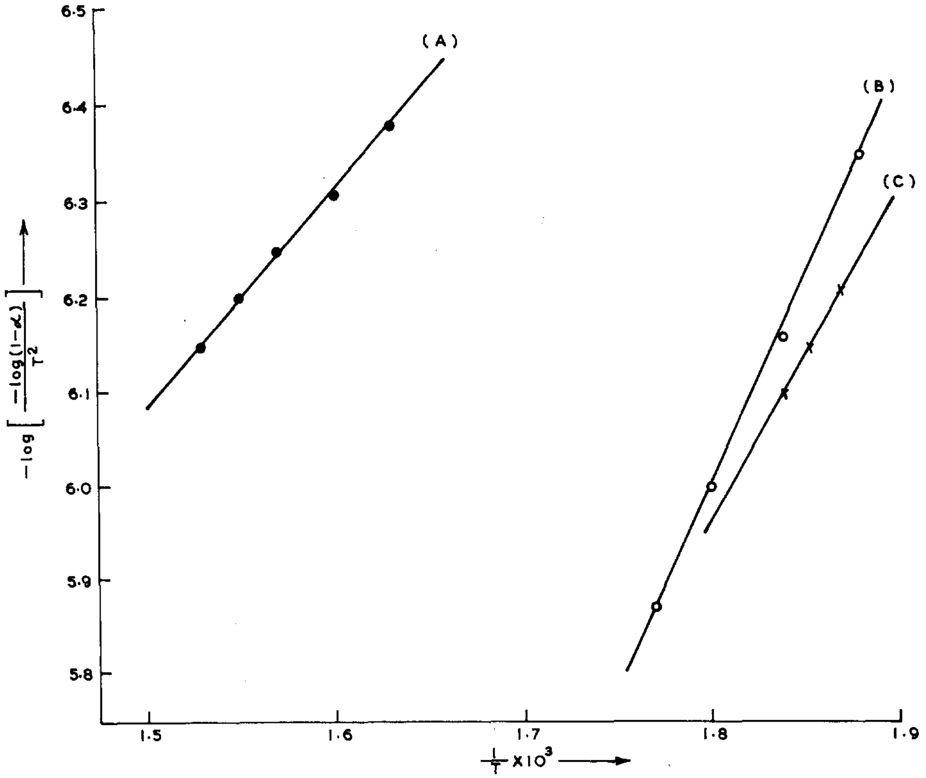

Fig. 1. Kinetic parameters from TG studies: (A) p-$CH_3COOC_6H_4HgL$; (B) C_6H_5HgL; (C) p-HOC_6H_4HgL.

The HgL^+ fragment is transformed to $(L\text{-}CH_3)^+$ with m/z 200. The latter fragment undergoes loss of second methyl group followed by the carboxylic group and the corresponding peaks are observed at m/z 185 and 140.

The mechanism of thermal reaction, in each case, has been elucidated by the method of Satava [7]. In this method, the function f(α), which depends

TABLE 1

Thermal data

Compound	TG		DTA			
	E_a (kcal mol^{-1})	n	T_{max} (K)	Thermal effect	E_a (kcal mol^{-1})	ΔH (cal g^{-1})
p-$CH_3COOC_6H_4HgL$	10.06	1	631	endothermic	41.18	56.56
C_6H_5HgL	18.30	1	365	endothermic	54.91	51.50
			513	endothermic	—	—
p-HOC_6H_4HgL	24.40	1	363	endothermic	60.99	53.78
			533	endothermic	—	—

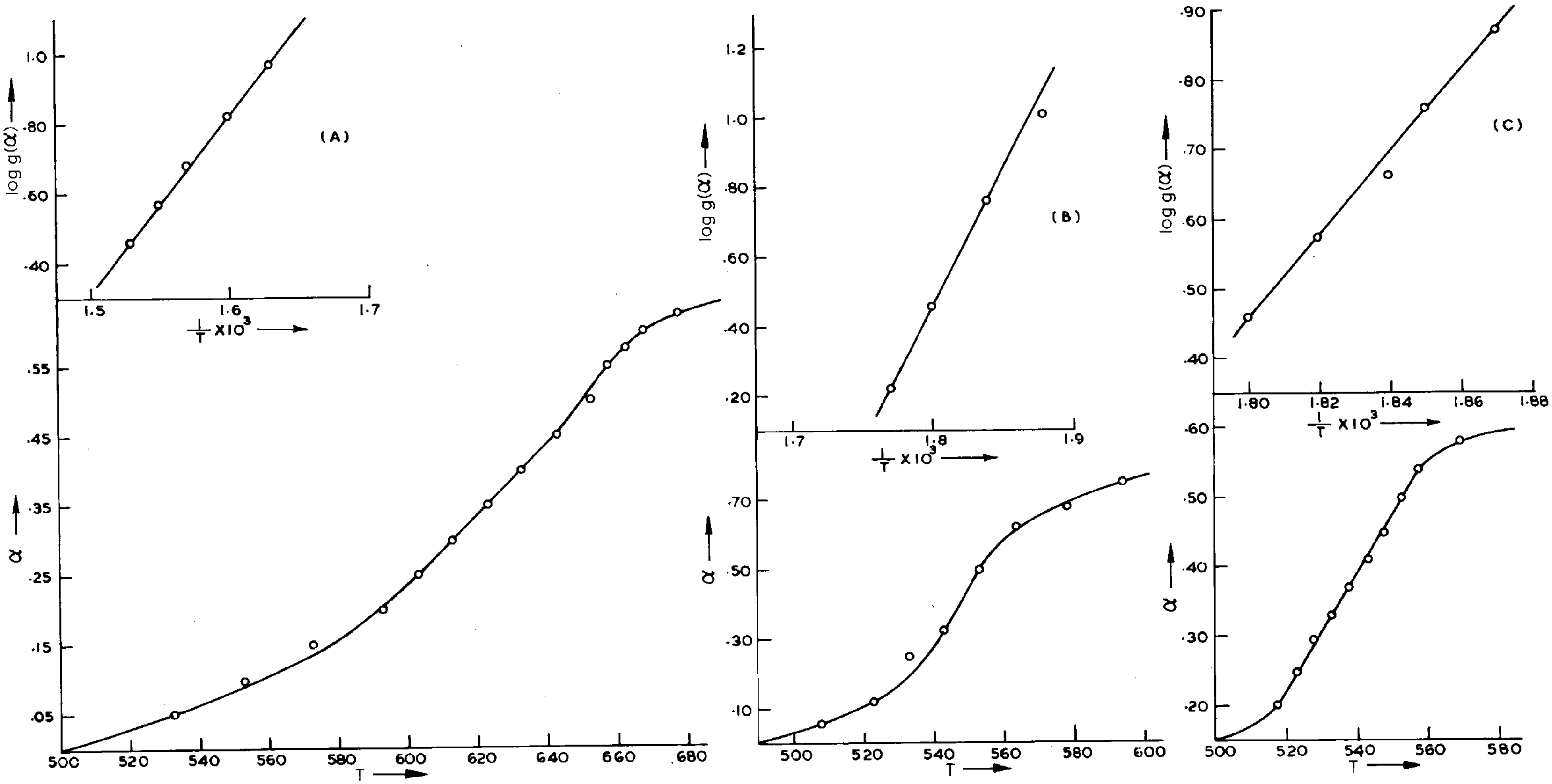

Fig. 2. Mechanism elucidation by TG: (A) p-$CH_3COOC_6H_4HgL$; (B) C_6H_5HgL; (C) p-HOC_6H_4HgL.

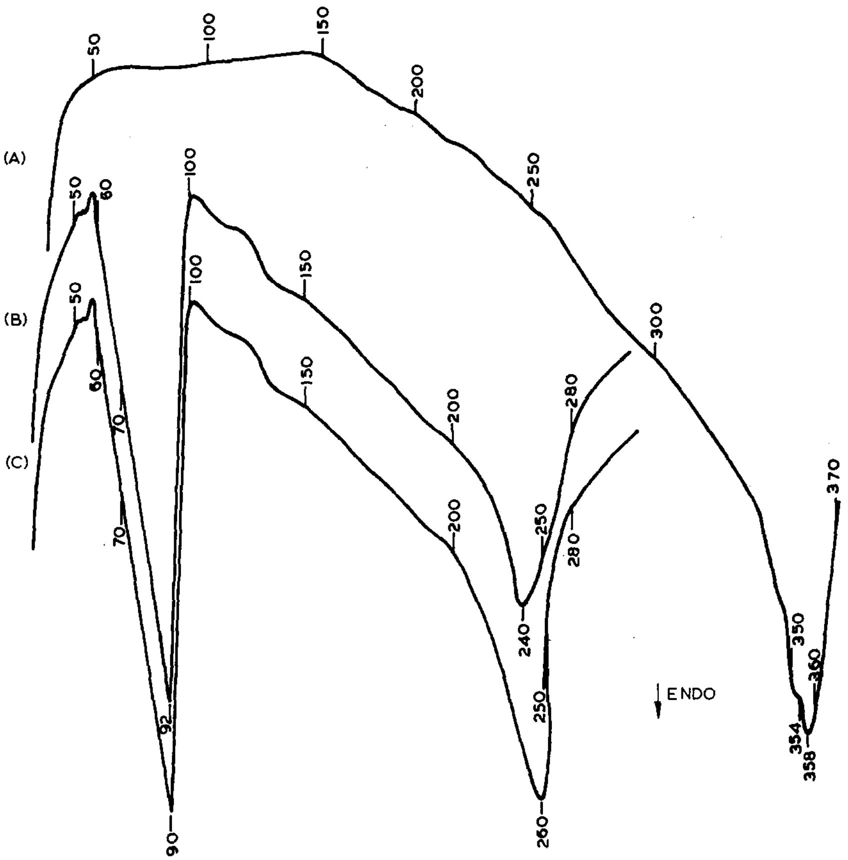

Fig. 3. DTA curves: (A) p-$CH_3COOC_6H_4HgL$; (B) C_6H_5HgL; (C) p-HOC_6H_4HgL.

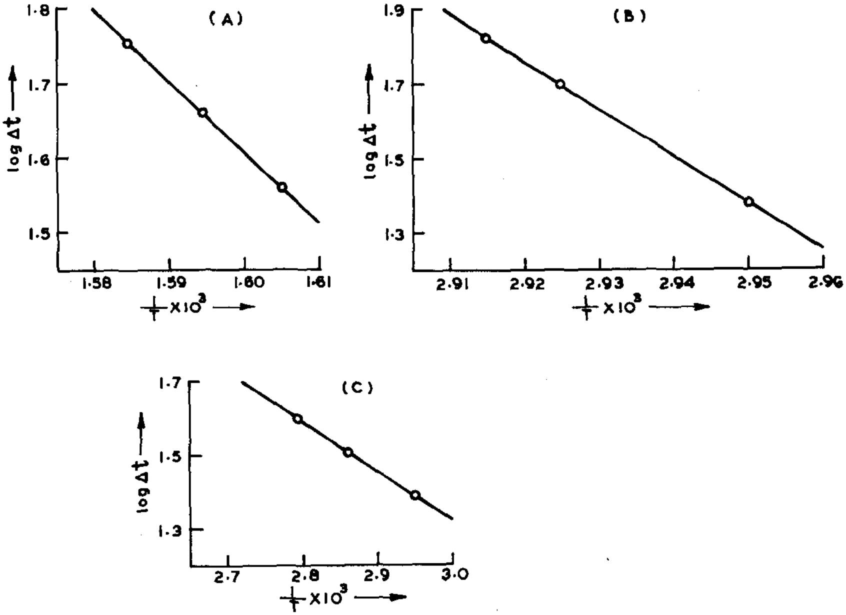

Fig. 4. Kinetic parameters from DTA: (A) p-$CH_3COOC_6H_4HgL$; (B) C_6H_5HgL; (C) p-HOC_6H_4HgL.

upon the mechanism, is given by $\int f(\alpha)^{-1}\,d\alpha = g(\alpha)$, where α is the fraction decomposed at temperature T_α. For a correct mechanism log $g(\alpha)$ must be a linear function of $1/T_\alpha$. In the present investigation it has been found that only the curve corresponding to an F_1 mechanism is a straight line. For an F_1 mechanism, the rate equation is: $-\ln(1-\alpha) = kt$ (where k is the rate constant and t is time) and the rate-controlling process is random nucleation. The curves for mechanism elucidation are presented in Fig. 2.

The TG data are supplemented by differential thermal analysis (DTA) studies. The DTA curves are shown in Fig. 3. The activation energy (E_a) for the first thermal effect has been calculated in each case [8]. The sequence of E_a values is the same as for TG. The linearization curves are depicted in Fig. 4. For the calculation of heat of transition (ΔH) [9], the temperature dependent calibration coefficient was obtained from the Currell equation [10]. The data are presented in Table 1.

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