PHYSICOCHEMICAL STUDIES OF METAL COMPLEXES OF DRUG DIAZEPAM (7-CHLORO-1-METHYL-5-PHENYL-3H-1, 4-BENZODIAZEPINE-2-ONE) IN SOLID STATE

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ABSTRACT

Thermogravimetric analyses have been used to evaluate kinetic parameters of metal complexes of diazepam. The thermal decomposition of metal complexes of diazepam drug is kinetically of zero order and the activation energy for the decomposition process lies in the range of 4-14 kcal mol$^{-1}$. I R spectra indicate that the metal complexes exist with monomeric structure through metal nitrogen bonding of 1, 4-N atom of ligand molecule.

Key words: Diazepam, Physicochemical, Mn (II), Cu (II), Zn (II), Co (II).

INTRODUCTION

The drug diazepam, a benzodiazepine drug, is among the most frequently prescribed drugs for the treatment of sleep disturbance, anxiety$^{1}$ and is used in medicines as tranquilizing and sedative hypnotic agents$^{2}$. 1, 4-Benzodiazepine can act as a monodentate, bidentate or as bridging ligand in bonding$^{3}$. The stereochemistry and chemical reactivity studies of its coordination compounds with transition metal ions help us to determine the relationship between the chemical structure and biological activity of drugs. Although a good deal of research work has been reported$^{4-6}$ for the characterization of the metal complexes of diazepam, but particularly no attention has been devoted to the study of their thermal and isothermal decomposition. The structure of ligand (diazepam) is given in Fig. 1.

EXPERIMENTAL

All the chemicals used were of AR grade and purified by standard methods. Metal complexes were prepared by the mixing of equimolar solutions of ligand (diazepam) and
metal nitrate solutions. The 1:1 stoechiometric ratio was confirmed by Fengers mass estimation method. The complexes were purified by recrystallization and TLC. The thermogravimetric analysis of metal complex was carried out at a constant heating rate \(10^0\text{C/min up to temperature 1000}^0\text{C}\) on a TGA instrument Model Perkin-Elmer (Pyris Diamond). IR spectra of metal complexes were recorded on Perkin-Elmer–842 spectrophotometer.

![Fig. 1: Diazepam (7-chloro-1-methyl-5-phenyl-3H-1,4-benzodiazepine-2-one)](image)

**RESULTS AND DISCUSSION**

The band at 1608 cm\(^{-1}\) in the free ligand is attributed to \(\nu(C = N)\), which undergoes shifting to lower region in all the complexes, indicating the participation of azomethine nitrogen N (4) in complexation. In all the complexes, the band assigned to \(\nu(N-\text{CH}_3)\) in ligand (1428 cm\(^{-1}\)) shows a lowering as compared to the ligand indicating the involvement of N (1) atom also in coordination. The band attributed to the vibrational mode \(\nu(C = O)\) appearing at (1680 cm\(^{-1}\)) in the ligand shows a small positive shift in all the complexes. The presence of new bands in the region 515 cm\(^{-1}\)-313 cm\(^{-1}\) in all the complexes is attributed to \(\nu(M-N)\) linkage.

The results of thermogravimetric analysis of metal complexes were recorded, which show that the final residue was the metal carbide as well as metal oxide and weight of residue was in good agreement with the theoretically calculated weight of metal carbide as well as metal oxide. The residue left have higher weight than metal oxide, probably it shows the presence of metal carbide formed simultaneously on heating the complexes at about 1000°C. The thermal decomposition of metal complexes can be expressed as-

It was found that the order of reaction for the decomposition of metal complexes is zero and the value of energy of activation obtained from Freeman-Carrolls, Horowitz-Metzger’s and Coats-Redfern’s equations are -
Table 1: Decomposition Scheme of M (II) Complexes

<table>
<thead>
<tr>
<th>Decomposition Scheme</th>
<th>Mn (II)</th>
<th>Cu (II)</th>
<th>Co (II)</th>
<th>Zn (II)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M (C_{16}H_{13}ClN_{2}O)(NO_{3})_{2}</td>
<td>T</td>
<td>WL</td>
<td>T</td>
<td>WL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M (C_{3}H_{5}NO)(NO_{3})_{2}</td>
<td>206-324</td>
<td>13.89</td>
<td>13.02</td>
<td>13.78</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(14.40)</td>
<td>(13.28)</td>
<td>(13.23)</td>
</tr>
<tr>
<td>MO + MC_{3} + other volatile oxides of C, H, N</td>
<td>510-660</td>
<td>26.29</td>
<td>488-586</td>
<td>397-586</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(26.74)</td>
<td>(32.47)</td>
<td>(26.01)</td>
</tr>
<tr>
<td>MO + MC_{3}</td>
<td>1003</td>
<td>53.42</td>
<td>48.31</td>
<td>9008</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(42.98)</td>
<td>(49.03)</td>
<td>(56.37)</td>
</tr>
</tbody>
</table>

T = Temperature range (°C); WL = Weight loss (%) Found/(Cal.); M = Mn (II), Cu (II), Co (II) and Zn (II)
Table 2: Energy of activation of Mn (II), Zn (II), Cu (II) & Co (II) complexes in Kcal mol⁻¹ from different equations

<table>
<thead>
<tr>
<th>Metal complexes</th>
<th>Freeman-Carolls</th>
<th>Coat-Redfers</th>
<th>Horowitz-Metzgers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mn- DZ complex</td>
<td>10.97</td>
<td>11.26</td>
<td>11.39</td>
</tr>
<tr>
<td>Zn- DZ complex</td>
<td>10.26</td>
<td>12.83</td>
<td>12.19</td>
</tr>
<tr>
<td>Cu- DZ complex</td>
<td>9.09</td>
<td>11.78</td>
<td>10.28</td>
</tr>
<tr>
<td>Co- DZ complex</td>
<td>9.46</td>
<td>13.04</td>
<td>11.95</td>
</tr>
</tbody>
</table>

Table 3

<table>
<thead>
<tr>
<th>Metal complexes</th>
<th>Activation energy (E) (K cal mol⁻¹)</th>
<th>Activation entropy ∆S (e.u.)</th>
<th>Free energy of activation, ∆G (K cal mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mn- DZ complex</td>
<td>9.08</td>
<td>56.79</td>
<td>43.17</td>
</tr>
<tr>
<td>Zn- DZ complex</td>
<td>8.29</td>
<td>56.83</td>
<td>40.71</td>
</tr>
<tr>
<td>Cu- DZ complex</td>
<td>8.27</td>
<td>56.98</td>
<td>41.97</td>
</tr>
<tr>
<td>Co- DZ complex</td>
<td>9.08</td>
<td>57.16</td>
<td>45.31</td>
</tr>
</tbody>
</table>

The values of energy of activation obtained from these equations are in complete agreement. The usual zero order rate law expression is -

\[
\frac{dw}{dt} = K
\]  

...(1)

On comparing with the Arrhenious equation:

\[
k = Z \exp\left(\frac{-E}{RT}\right)
\]  

...(2)

or

\[
\log \frac{dw}{dt} = - \frac{E}{2.303 RT} + \log Z
\]

The values of energy of activation E were obtained from the slope (-E/2.303R) of the plots of log (dw/dt) vs (T⁻¹) and the values of entropy of activation ∆S for metal complexes are obtained from the relation -

\[
\Delta S = 2.303 R \log (Zh/KT_s)
\]  

...(3)

Where K is the Boltzman constant, h is Planck’s constant and T_s is the temperature for peak decomposition. The free energy of activation ∆G is calculated using the equation -
\[ \Delta G = E - T_s (\Delta S) \] ...

Fig. 2(a): Thermolysis curve of 1 : 1 Mn\(^{2+}\)-DZ complex

Fig. 2(b): D. T. G. record for 1 : 1 Mn\(^{2+}\)-DZ complex

Fig. 3(a): Thermolysis curve of 1 : 1 Cu\(^{2+}\)-DZ complex

Fig. 3(b): D. T. G. record for 1 : 1 Cu\(^{2+}\)-DZ complex

Fig. 4(a): Thermolysis curve of 1 : 1 Co\(^{2+}\)-DZ complex

Fig. 4(b): D. T. G. record for 1 : 1 Co\(^{2+}\)-DZ complex
Fig. 5(a): Thermolysis curve of 1 : 1 \( \text{Zn}^{2+}-\text{DZ} \) complex

Fig. 5(b): D. T. G. record for 1 : 1 \( -\text{Zn}^{2+}-\text{DZ} \) complex

Fig. 6: Freeman-Carroll’s plot

Fig. 7: Horowitz-Metzger’s plot

Fig. 8: Coats-Redfern’s plot
REFERENCE


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