SYNTESIS AND SPECTRAL STUDIES OF MIXED LIGAND COMPLEXES OF CHLOROPROPAMIDE/GLICLAZIDE WITH IRON AND COBALT

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ABSTRACT

Co-ordination compounds of chloropropamide (CPM) N-Propyl-N-(P-chlorobenzene sulphonyl) urea (trade name, diabinese) and gliclazide (GCZ) 1 - (3 - azabicyclo [3,3,0] oct - 3yl) - 3 - (P- totyl sulphonyl) urea. (trade name, diamicron) are oral hypoglycemic were synthesize with iron(II) and cobalt(II), isolated in pure powderd form, yields are substantial. Stoichiometry suggest 1:1:1 ratio between drugs and metal ion. Analytical data of the complexes agrees with the compositions are C_{10}H_{12}ClN_{2}O_{3}S-Fe-C_{15}H_{20}N_{3}O_{3}S 2H_{2}O and C_{10}H_{12}ClN_{2}O_{3}S-Co - C_{15}H_{20}N_{3}O_{3}S.2H_{2}O The general structure assigned to these complexes is supported by infra-red and electronic spectral studies.

Key Words:- Complexation chloropropamide, gliclazide, iron and cobalt.

INTRODUCTION

Sulphonyl urea represented by general structure ‘I’ have long been in use as hypoglycemic agents in the treatment of Diabetes mellitus. In continuation of our previous work, on the synthesis and characterization of metal complexes of various drugs with transition metals, it has been desired necessary to synthesise and study the new type of complexes of mixed drugs in order to see as to whether it increases the potencies of the complexes or not.

Therefore in the present communication we are describing the synthesis of mixed CPM/GCZ complexes with iron and cobalt. A survey of literature indicates that Yoshinaga and Yamamotto have synthesized and studied Zn (II), Cd (II) and Hg (II) complexes with sulphonyl ureas and have recommended their use in mercury poisoning.

MATERIALS AND METHODS

Pure sample of CPM, Mf C_{10}H_{13}ClN_{2}O_{3}S m.p. 127° (lit., 127°-129°C) and GCZ, Mf C_{15}H_{13}N_{3}O_{3}S m.p. 180° (lit., 180°-182°C), CPM and TBM are soluble in absolute alcohol. Salts like ferrous sulphate and cobalt chloride were of AnalaR grade.
1 \( X = \text{Cl} \) Chloropropamide (L₁)
\( R = \text{C₃H₇} \)

2 \( X = \text{CH₃} \) Gliclazide (L₂)

SYNTHESIS:

The ligand CMP (L₁) trade name, *Diabinese* 0.691g and GCZ (L₂) *Dimicron* 0.808g while metal salts Viz., iron 0.695g and cobalt 0.594g are in 1:1:1 molar ratio L₁L₂M were dissolved separately in minimum quantity of absolute alcohol. Ligand solution was added gradually with constant stirring to metal salt solution, a thick dark brown precipitate (CPM-Fe-GCZ.2H₂O) and light pink precipitate of (CPM-Co-GCZ.2H₂O) complexes were obtained on adjusting the pH upto 6.0 by adding very dilute NaOH solution and refluxing for four hours. Dark brown crystals of Fe complex, and light pink crystals of cobalt complex were obtained. The complexes were washed with absolute alcohol, dried and weighed. Yields were 50.20% and 55.63% respectively. The decomposition temperatures are given in table 1.

Iron was estimated in complex by Cupfuron method as oxide, cobalt was estimated as, tetrapyridine dithionate\(^\text{12}\), nitrogen by Kjeldahls method using modified digestion mixture\(^\text{13}\), sulphur was estimated by Messenger’s method.

<table>
<thead>
<tr>
<th>S N</th>
<th>Composition of complexes</th>
<th>Colour (yield)</th>
<th>DC. °C</th>
<th>Metal % of Analysis(Calcd)</th>
<th>Metal</th>
<th>C</th>
<th>H</th>
<th>N</th>
<th>S</th>
<th>H₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C₁₀H₁₂ClN₂O₃S-Fe. C₁₅H₂₀N₃O₃S.2H₂O</td>
<td>Dark brown (50.20)</td>
<td>220</td>
<td>8.43</td>
<td>43.20</td>
<td>4.94</td>
<td>9.80</td>
<td>8.80</td>
<td>5.10</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>C₁₀H₁₂ClN₂O₃S-Co-C₁₅H₂₀N₃O₃S.2H₂O</td>
<td>Light pink (55.63)</td>
<td>210</td>
<td>8.80</td>
<td>43.19</td>
<td>4.24</td>
<td>10.01</td>
<td>9.50</td>
<td>5.19</td>
<td></td>
</tr>
</tbody>
</table>

DC = Decomposition temperature

<table>
<thead>
<tr>
<th>Ligand and Complexes</th>
<th>SO₂-NH (cm⁻¹)</th>
<th>C = O (cm⁻¹)</th>
<th>C-O (cm⁻¹)</th>
<th>M-O (cm⁻¹)</th>
<th>NH-R (cm⁻¹)</th>
<th>C=N (cm⁻¹)</th>
<th>C₆H₅-S Water of ordination (cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPM, (J.D/38)</td>
<td>1170 ± 10</td>
<td>1669</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>750</td>
</tr>
<tr>
<td></td>
<td>KN/184</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>GCZ</td>
<td>1165 ± 10</td>
<td>16640</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Complex of iron (A.W)</td>
<td>3080 ± 40</td>
<td>1650 ± 10 669</td>
<td>3070</td>
<td>2510</td>
<td>710</td>
<td>3399</td>
<td></td>
</tr>
<tr>
<td>Complex of cobalt</td>
<td>3070 ± 30</td>
<td>1649 ± 10 669</td>
<td>3080</td>
<td>2520</td>
<td>730</td>
<td>3390</td>
<td></td>
</tr>
</tbody>
</table>
RESULTS AND DISCUSSION

The infrared absorption frequencies of the various groups like SO$_2$NH, C=O, aromatic ring and alkyl group etc. found in ligand are modified on complexation in intensity as well as in the frequency. The new frequencies observed in the complexes (Fe and Co) like C-O1650±10cm$^{-1}$/1649±10cm$^{-1}$, M-O669cm$^{-1}$/669cm$^{-1}$, C=N2510cm$^{-1}$/2520cm$^{-1}$, NH-R3070cm$^{-1}$/3080cm$^{-1}$ and C$_6$H$_5$-S 710cm$^{-1}$/730cm$^{-1}$. In addition to this we have proposed structure 2 for Fe (II) and Co (II) complexes which have two molecules of water of coordination satisfying the six coordination number of Fe$^{2+}$ and Co$^{2+}$ present. In case of structure 2, is further supported by presence of very strong broad bands observe at 3399cm$^{-1}$/3390cm$^{-1}$ for water of coordination. IR results support the structure of the complex which was already suggested on the basis of stoichiometry and analytical data (table 2).

Table 3. Electronic spectra and magnetic moment values, and possible assignments of the Fe (II) and Co (II) complexes of mixed ligands

<table>
<thead>
<tr>
<th>Complexes</th>
<th>Magnetic moment</th>
<th>Electronic bands (cm$^{-1}$)</th>
<th>Possible assignment</th>
<th>Proposed geometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe(L$_1$L$_2$)(OH$_2$)</td>
<td>5.41</td>
<td>27860, 21790</td>
<td>Charge transfer</td>
<td>Octahedral</td>
</tr>
<tr>
<td>Co(L$_1$L$_2$)(OH$_2$)</td>
<td>4.10</td>
<td>21450, 14750, 12900</td>
<td>$^4$T$_1g$ $^4$A$_2g$ $^4$T$_2g$</td>
<td>Octahedral</td>
</tr>
</tbody>
</table>

The Electronic spectra of Fe (II) complex shows two bands at 27860 cm$^{-1}$ and 22790 cm$^{-1}$, the first band is assigned to charge transfer while second band would be due to $^6$Eg $^5$T$_2g$ transition suggesting an octahedral geometry around Fe (II) ion. The magnetic moment $\mu_{eff}$ is 5.41 B.M. agrees with octahedral symmetry of Fe (II) complex.

The Electronic spectra of Co (II) complex shows three bands observed at 21450 cm$^{-1}$, 14750 cm$^{-1}$ and 12900 cm$^{-1}$, assignable to $^4$T$_1g$ (P)$^4$T$_1g$ (F), $^4$A$_2g$ (F) $^4$T$_1g$ (F) and $^4$T$_2g$ (F) $^4$T$_1g$ (F) respectively, favours the octahedral environment of Co (II) complex. The $\mu_{eff}$ valuses of Co-complex has been found to be 4.10 B.M. these values of electronic absorption bands and magnetic moment indicate an octahedral geometry of Co (II) ions. Therefore a common structure 2, can be assigned to Fe (II) and Co (II) complexes.

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REFERENCES