“SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL ACTIVITIES OF BIOSENSITIVE SCHIFF BASE LIGANDS WITH Cr, Mo, W METAL CARBONYL COMPLEXES”

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Abstract

We have synthesized twelve polynuclear complexes \{M(CO)₄[SB]\} 1a-1c, 2a-2c and 3a-3c, (1a, M = Cr, SB=L¹, X = NH₂; 1b, M = Mo, SB=L¹, X = NH₂; 1c, M = W, SB=L¹, X = NH₂; 2a, M = Cr, SB=L², X = NO₂; 2b, M = Mo, SB=L², X = NO₂; 2c, M = W, SB=L², X = NO₂; 3a, M = Cr, SB=L³, X = OCH₃; 3b, M = Mo, SB=L³, X = OCH₃; 3c, M = W, SB=L³, X = OCH₃; 4a, M = Cr, SB=L⁴, X = H; 4b, M = Mo, SB=L⁴, X = H; 4c, M = W, SB=L⁴, X = H) by photochemical displacement of two CO group from M(CO)₆ by 3-aminobenzilidine-2-amino phenol [L¹], 3-nitrobenzilidine-2-amino phenol [L²], 4-methoxybenzilidine-2-amino phenol [L³] and benzilidine-2-amino phenol [L⁴]. The synthesized complexes exhibit variable degree of antibacterial activity. The complexes have been characterized by elemental analysis, IR, \[^¹^H\]-NMR spectroscopy and magnetic studies. The spectroscopic studies suggest a bidentate behavior of the ligand via phenolic-O and imine-N donor atoms with the metal (0).

Keywords- Schiff bases, coordination chemistry, N-donor Schiff bases, antibacterial activity.

Introduction
A Schiff base is a functional group that contains a carbon-nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group but not hydrogen. Schiff bases are of the general formula $R_1R_2C=N-R_3$, where $R_3$ is an aryl or alkyl group that makes the Schiff base a stable imine. Monodentate Schiff’s bases are less known to form stable complexes, probably due to the insufficient basic strength of the imino nitrogen of the C=N group.

The coordination chemistry of Schiff bases as multidentate ligands gained much importance for more than two decades because of their use as models in biological systems[1-4]. There is enormous interest presently in the field of coordination chemistry of later ‘3d’ transition metals with Schiff bases. They have also been used as biological models [5], oxygen carriers and drugs [6]. Transition metal complexes of 1, 10-phenanthroline (phen), 2,2-bipyridyl (bpy) or their modified variants are widely employed in several research areas including bioinorganic and biomedical chemistry [7-14]. Metal complexes of the Schiff bases have been widely studied due to their unusual magnetic properties, novel structural features and relevance to biological systems [15]. We have synthesized polynuclear complexes of the type 1a-1c, 2a-2c, 3a-3c, 4a-4c and 5a-5c ($1a, M = Cr, L=SB^1, R = H; 1b, M = Mo, L=SB^1, R = H; 1c, M = W, L=SB^1, R = H; 2a, M = Cr, L=SB^2, R = Me; 2b, M = Mo, L=SB^2, R = Me; 2c, M = W, L=SB^2, R = Me; 3a, M = Cr, L=SB^3, R = Eth; 3b, M = Mo, L=SB^3, R = Eth; 3c, M = W, L=SB^3, R = Eth; 4a, M = Cr, L=SB^4, R = n-pr; 4b, M = Mo, L=SB^4, R = n-pr; 4c, M = W, L=SB^4, R = n-pr; 5a, M = Cr, L=SB^5, R = Ph; 5b, M = Mo, L=SB^5, R = Ph; 5c, M = W, L=SB^5, R = Ph$) has been synthesized by photochemical displacement of two CO groups in group-6 metal carbonyls with by 3-aminobenzilidine-2-amino phenol [$L^1$], 3-nitrobenzilidine-2-amino phenol [$L^2$], 4-methoxybenzilidine-2-amino phenol [$L^3$] and benzilidine-2-amino phenol [$L^4$]. Both the ligands & their complexes were characterized on the basis of physical properties, elemental analysis data, magnetic studies, infrared and nuclear magnetic resonance spectroscopy. It was found
that the ligands have bidentate nature coordinating through phenolic-O and imine-N donor atom. Thus replacing two CO group to maintain charge density on metal centre.

![Chemical Structure](image)

3/4 substituted benzylidene -2- aminophenol

**Experimental**

Reactions were carried out under dry argon or in vacuo. All solvents were dried and degassed prior to use. Infrared spectra were recorded on a Perkin-Elmer spectrophotometer (Model-577) in KBr discs and CH₂Cl₂. All the melting points were determined in an open capillary and are uncorrected. All glassware was oven dried at 120°C, molecular weight of the complexes were determined cryoscopically in benzene, cyclooctadiene (COD), n-hexane, n-pentane, benzene were purchased from E. Merck, and M(CO)₆ (M = Cr, Mo, W), dichloromethane were purchased from Aldrich and were used as supplied.

Magnetic susceptibility measurements of the complexes were carried out by Gouy method. UV irradiation were performed with a medium pressure 400W mercury lamp through a quartz bulb.

**Synthesis of the ligands:**

**Synthesis of ligand 3-aminobenzilidine-2-amino phenol [L₁]**

The ligand 3-aminobenzilidine-2-amino phenol [L₁] was prepared by literature method [16] as followed. A mixture of 3-amino benzaldehyde (1.21 g, 0.01M) with 2-aminophenol (1.09g, 0.01M) in 50 mL of ethanolic medium. The solid product formed was removed by filtration and recrystallized from ethanol. Yield 72%. 
3-aminobenzylidine -2- aminophenol

**Preparation of complexes**

**Preparation of complex \{Cr(CO)\_4[L\_1]\}**

The Cr(CO)\_6 (0.110 g, 0.5 mmol) and L\_1 (0.10 g, 0.5 mmol) were dissolved in DMF (40-50 cm\(^3\)). The solution was irradiated for 3 h. During the irradiation, the color of the reaction mixture changed from colourless to dark yellow. After the irradiation, the reaction mixture was evaporated under vacuum, yielding a dark yellow solid. After dissolving in CH\(_2\)Cl\(_2\) (10 cm\(^3\)), petroleum ether (50 cm\(^3\)) was added, resulting in the precipitation of a dark yellow solid which was washed with petroleum ether and dried under vacuum. Yield of [Cr(CO)\_4(L\_1)] : 78%.

The other bisubstituted metalcarbonyl complexes of Cr, Mo, W with L\_1, L\_2, L\_3 and L\_4 were prepared similarly.
Scheme 1 – Preparation of Ligand \([L^1]\): Reaction of 3- amino benzaldehyde with 2-aminophenol

Scheme 2 – Preparation of Complexes: Reaction of 3-aminobenzilidene-2-amino phenol \([L^1]\) with Cr(CO)₆

Table 1a – Physical and analytical data of Ligands \((L^{1-4})\)
<table>
<thead>
<tr>
<th>Ligands</th>
<th>Molecular Formula</th>
<th>Yield (%)</th>
<th>M.p. (°C)</th>
<th>Colour</th>
<th>Found (Calcd.) (%)</th>
<th>Mol. Wt.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C</td>
<td>H</td>
</tr>
<tr>
<td>a (L&lt;sup&gt;1&lt;/sup&gt;)</td>
<td>C&lt;sub&gt;13&lt;/sub&gt;H&lt;sub&gt;12&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>72.0</td>
<td>136</td>
<td>Cream</td>
<td>73.0 (73.5)</td>
<td>5.5 (5.7)</td>
</tr>
<tr>
<td>b (L&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>C&lt;sub&gt;13&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;</td>
<td>71.5</td>
<td>142</td>
<td>Light yellow</td>
<td>64.1 (64.5)</td>
<td>3.9 (4.2)</td>
</tr>
<tr>
<td>c (L&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>C&lt;sub&gt;14&lt;/sub&gt;H&lt;sub&gt;13&lt;/sub&gt;NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>74.1</td>
<td>146</td>
<td>Light yellow</td>
<td>73.4 (74.0)</td>
<td>5.5 (5.8)</td>
</tr>
<tr>
<td>d (L&lt;sup&gt;4&lt;/sup&gt;)</td>
<td>C&lt;sub&gt;13&lt;/sub&gt;H&lt;sub&gt;11&lt;/sub&gt;NO</td>
<td>78.5</td>
<td>127</td>
<td>Yellow</td>
<td>78.5 (79.1)</td>
<td>5.2 (5.6)</td>
</tr>
</tbody>
</table>

**Table 1** – Physical and analytical data of Complexes
<table>
<thead>
<tr>
<th>Complexes</th>
<th>Molecular Formula</th>
<th>Yield (%)</th>
<th>M.p. (°C)</th>
<th>Colour</th>
<th>Found (Calcd.) (%)</th>
<th>Mol. Wt.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C</td>
<td>H</td>
</tr>
<tr>
<td>1a</td>
<td>C$<em>{17}$H$</em>{11}$CrN$_2$O$_5$</td>
<td>78</td>
<td>146</td>
<td>Light Yellow</td>
<td>53.9 (54.4)</td>
<td>7.1 (7.5)</td>
</tr>
<tr>
<td>2a</td>
<td>C$<em>{17}$H$</em>{11}$MoN$_2$O$_5$</td>
<td>74</td>
<td>154</td>
<td>Yellow</td>
<td>48.1 (48.7)</td>
<td>6.3 (6.7)</td>
</tr>
<tr>
<td>3a</td>
<td>C$<em>{17}$H$</em>{11}$WN$_2$O$_5$</td>
<td>79</td>
<td>165</td>
<td>Yellow</td>
<td>39.5 (40.2)</td>
<td>5.1 (5.5)</td>
</tr>
<tr>
<td>1b</td>
<td>C$<em>{17}$H$</em>{9}$CrN$_2$O$_7$</td>
<td>76</td>
<td>147</td>
<td>Light Yellow</td>
<td>49.5 (50.4)</td>
<td>6.5 (6.9)</td>
</tr>
<tr>
<td>2b</td>
<td>C$<em>{17}$H$</em>{9}$MoN$_2$O$_7$</td>
<td>78</td>
<td>155</td>
<td>Yellow</td>
<td>44.8 (45.5)</td>
<td>6.0 (6.2)</td>
</tr>
<tr>
<td></td>
<td>Chemical Formula</td>
<td>IR Bands (cm⁻¹)</td>
<td>Color</td>
<td>(¹H)-NMR (ppm)</td>
<td></td>
<td></td>
</tr>
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</tr>
<tr>
<td>3b</td>
<td>C₁₇H₂WN₂O₇</td>
<td>76</td>
<td>166</td>
<td>Cream</td>
<td>37.3 (38.0)</td>
<td>1.4 (1.7)</td>
</tr>
<tr>
<td>1c</td>
<td>C₁₈H₁₂CrNO₆</td>
<td>75</td>
<td>147</td>
<td>Light Yellow</td>
<td>54.7 (55.4)</td>
<td>2.9 (3.1)</td>
</tr>
<tr>
<td>2c</td>
<td>C₁₈H₁₂MoNO₆</td>
<td>70</td>
<td>156</td>
<td>Yellow</td>
<td>49.2 (49.8)</td>
<td>2.5 (2.8)</td>
</tr>
<tr>
<td>3c</td>
<td>C₁₈H₁₂WNO₆</td>
<td>78</td>
<td>166</td>
<td>Cream</td>
<td>40.8 (41.4)</td>
<td>2.1 (2.3)</td>
</tr>
<tr>
<td>1d</td>
<td>C₁₇H₁₀CrNO₅</td>
<td>78</td>
<td>166</td>
<td>Light Yellow</td>
<td>55.9 (56.7)</td>
<td>2.4 (2.8)</td>
</tr>
<tr>
<td>2d</td>
<td>C₁₇H₁₀MoNO₅</td>
<td>74</td>
<td>164</td>
<td>Yellow</td>
<td>50.0 (50.5)</td>
<td>2.2 (2.5)</td>
</tr>
<tr>
<td>3d</td>
<td>C₁₇H₁₀WNO₅</td>
<td>79</td>
<td>175</td>
<td>Yellow</td>
<td>40.6 (41.5)</td>
<td>1.7 (2.0)</td>
</tr>
</tbody>
</table>

**Table 2a.** Selected IR bands (cm⁻¹) and (¹H)-NMR (ppm) data of L₁⁻⁴ ligands
<table>
<thead>
<tr>
<th>Ligand</th>
<th>Selected IR bands (cm⁻¹)</th>
<th>Imine ν (C=\textit{N})</th>
<th>Phenolic OH</th>
<th>(^1\text{H}-\text{NMR (in CDCl}_3\text{)} \delta \text{ ppm}</th>
</tr>
</thead>
</table>
| a      | 1594                     | 3350                   | 7.8 (s, 1H, -OH), 8.4 (s, 1H, -NH\textsubscript{2}), 7.36 (s, 4H, -C\textsubscript{6}H\textsubscript{4}) | ...
| b      | 1592                     | 3348                   | 7.9 (s, 1H, -OH), 8.4 (s, 1H, -NH\textsubscript{2}), 7.34 (s, 4H, -C\textsubscript{6}H\textsubscript{4}) | ...
| c      | 1589                     | 3343                   | 7.8 (s, 1H, -OH), 8.3 (s, 1H, -NH\textsubscript{2}), 7.32 (s, 4H, -C\textsubscript{6}H\textsubscript{4}) | ...
| d      | 1594                     | 3356                   | 7.9 (s, 1H, -OH), 8.3 (s, 1H, -NH\textsubscript{2}), 7.33 (s, 4H, -C\textsubscript{6}H\textsubscript{4}) | ...

**Table 2b.** Selected IR bands (cm⁻¹) and \(^1\text{H}-\text{NMR (ppm)} data of complexes**

<table>
<thead>
<tr>
<th>Complex</th>
<th>Selected IR bands (cm⁻¹)</th>
<th>Imine ν (C=\textit{N})</th>
<th>(^1\text{H}-\text{NMR (in CDCl}_3\text{)} \delta \text{ ppm}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>2067, 2015, 1957, 1932</td>
<td>1570</td>
<td>8.4 (s, 1H, -NH\textsubscript{2}), 7.36 (s, 4H, -C\textsubscript{6}H\textsubscript{4}), 3.49 (s, 2H, NH\textsubscript{2})</td>
</tr>
<tr>
<td>2a</td>
<td>2071, 2015, 1952, 1934</td>
<td>1572</td>
<td>8.4 (s, 1H, -NH\textsubscript{2}), 7.36 (s, 4H, -C\textsubscript{6}H\textsubscript{4}), 3.47 (s, 2H, NH\textsubscript{2})</td>
</tr>
<tr>
<td>3a</td>
<td>2069, 2013, 1949, 1930</td>
<td>1574</td>
<td>8.4 (s, 1H, -NH\textsubscript{2}), 7.36 (s, 4H, -C\textsubscript{6}H\textsubscript{4}), 3.52 (s, 2H, NH\textsubscript{2})</td>
</tr>
<tr>
<td>1b</td>
<td>2072, 2018, 1959, 1935</td>
<td>1577</td>
<td>8.4 (s, 1H, -NH\textsubscript{2}), 7.34 (s, 4H, -C\textsubscript{6}H\textsubscript{4})</td>
</tr>
<tr>
<td>2b</td>
<td>2072, 2018, 1958, 1935</td>
<td>1570</td>
<td>8.4 (s, 1H, -NH\textsubscript{2}), 7.34 (s, 4H, -C\textsubscript{6}H\textsubscript{4})</td>
</tr>
<tr>
<td>3b</td>
<td>2069, 2019, 1957, 1933</td>
<td>1572</td>
<td>8.4 (s, 1H, -NH\textsubscript{2}), 7.34 (s, 4H, -C\textsubscript{6}H\textsubscript{4})</td>
</tr>
</tbody>
</table>
Results and Discussion

The ligands were prepared by condensation reaction of substituted benzaldehyde and 2-aminophenol according to Scheme-1. Complexes (1a-3d) were prepared by photochemical reaction as shown in Scheme-2. Analytical data for \{M(CO)₄[L]\} (1a-3a); \{M(CO)₄[L²]\} (1b-3b); \{M(CO)₄[L³]\} (1c-3c) and \{M(CO)₄[L⁴]\} (1d-3d) where (M= Cr, Mo & W); complexes are given in Table-1.

In this study, photochemical reactions of \(\text{M(CO)}_₆\) (M=Cr, Mo & W) with 3-aminobenzilidine-2-amino phenol [\(\text{L₁}\)], 3-nitrobenzilidine-2-amino phenol [\(\text{L²}\)], 4-methoxybenzilidine-2-amino phenol [\(\text{L³}\)] and benzilidine-2-amino phenol [\(\text{L⁴}\)] ligands occurs in expected manner, and gave hither to a series of complexes (1a)-(1d); (2a)-(2d) and (3a)-(3d) occur via the displacement of two CO from \(\text{M(CO)}_₆\) (M=Cr, Mo & W) and co-ordination of metal atom via imine-N and phenolic-O donor atoms yielding \(\text{M(CO)}_₄\text{L}\) complexes.
The i.r. spectra of ligands and the corresponding complexes provide information about the metal-ligand bonding. Important IR spectral bands M(CO)₄SB (SB = 3-aminobenzilidine-2-amino phenol [L¹], 3-nitrobenzilidine-2-amino phenol [L²], 4-methoxybenzilidine-2-amino phenol [L³] and benzilidine-2-amino phenol [L⁴] and M=Cr, Mo & W) are presented in Table-2b. The evidence about metal-imine nitrogen (M–N) bond formation is the shifting of C=N vibration found at 1620-1590 cm⁻¹ in free ligand, shifts to lower wavelength 1580-1550 cm⁻¹ in complexes 1a-3d, showing that the ligand coordinate to metal via the imine donor atom [17]. Appearance of a new band around 1580 cm⁻¹ in all complexes due to ν(C-O-M) revels the participation of phenoxy oxygen in coordination [18, 19] The IR spectra of the ligands shows a broad band in the region 3250-3450 cm⁻¹ assigned to –OH group. The absence of this band, noted in the spectra of the complexes, indicates the deprotonation of the –OH group. The IR spectra of the metal chelates also shows some new bands in region 305-450 cm⁻¹ which are due to the formation of M-N bond.

In the proton NMR spectra of 1a-3c, the phenolic OH signal disappeared which is in agreement with the formation of metal oxygen bond [20-21]. In addition, the shift of the C-O stretching vibrations in the IR spectrum shows that both imine N and phenolic O donor atoms coordinate to M atom. According to the these data, L¹, L², L³ & L⁴ ligands behave as bidentate in 1a-3d. The L¹, L², L³ & L⁴ ligands must act as a 4-electron donor in order to satisfy the 18-electron rule.

Four bands in the range (2068-2072 cm⁻¹), (2013-2018 cm⁻¹), (1949-1958 cm⁻¹) and (1932-1936 cm⁻¹) arising from ν (CO) vibrations are seen which presumably have local c₂v symmetry of M(CO)₄ unit in {M(CO)₄L¹} (1a-3a); {M(CO)₄L²}(1b-3b) and {M(CO)₄L³} (1c-3c) and {M(CO)₄L⁴} (1d-3d); where (M= Cr, Mo & W); complexes (Scheme-2). These values are in close resemblance to the values of ν (CO) vibration for other nitrogen containing disubstituted group-6 metal carbonyls [22-25]. The presence of normal ligand bands indicated that these bands were intact.
in the complexes. The nature and number of CO bands resemble closely to the bands of other known disubstituted metal carbonyls [26-28].

In addition, magnetic susceptibility measurement shows that (1a-3e) complexes were diamagnetic. Since these complexes have M(0) [M=Cr, Mo, W] with a low spin d^6 configuration. Such diamagnetism might arise from further splitting of the d-orbital in the low symmetry complexes i.e. d_{xy}^2, d_{xz}^2, d_{yz}^2, d_{x^2-y^2}, d_{z^2} [29, 30].

**Antibacterial Activity**

All the synthesized complexes were screened for their antibacterial activity by using agar diffusion method [31] against *S. aureus*, *B. subtilis* gram positive and *E. coli*, *S. paratyphi* gram negative bacteria in nutrient agar medium. Ciprofloxacin was used as standard drug for comparison.

These schiff’s Bases and their metal carbonyl complexes show antibacterial activity against *E. coli*, *S. aureus*, *B. subtilis* and *S. paratyphi*. It is found that benzilidine-2-amino phenol [L^4] studied here follow such a decomposition scheme in the cell, and diazoalkane intermediates further could alkylate the nucleophilic centres of biologically important macromolecules and in particular DNA. 3-aminobenzilidine-2-amino phenol [L^1], 3-nitrobenzilidine-2-amino phenol [L^2] and 4-methoxybenzilidine-2-amino phenol [L^3] shows moderate activity. With the help of activity data it could be observed that complexes M(CO)_3L^4(1d-3d) showed good activity against *E.coli* and *S. paratyphi*. Complexes M(CO)_3L^1 (1a-3a), M(CO)_3L^2 (1b-3b), and M(CO)_3L^3 (1c-3c) exhibited good activity against *S. paratyphi*. A comparative study of Schiff base ligands and its complexes indicate that the metal complexes exhibit higher antibacterial activity than that of free ligand.
Conclusion

The IR spectroscopic data are in well accord with a cis-chelating bidentate coordination of the ligand [32] L₁, L², L³ & L⁴ ligands behave as a bidentate ligand via imine N and phenolic O donor atom in 1a-3d. In view of above, we have now investigated the twelve new complexes 1a-3d, which have been prepared for the first time, by the photochemical reaction of metal carbonyls M(CO)₆ (M=Cr, Mo & W), with 3/4 substituted benzylidine -2- aminophenol (L¹,L²,L³ & L⁴).

The results show that benzilidine-2-amino phenol [L⁴] and its metalcarbonyl derivatives exert a good inhibitory effect on different bacterial activity, thus confirming our previous data about the cytotoxic activity of these compounds.

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References: