Synthesis, Structure and Spectroscopic Characteristics of Some Pyridoxylidene-Trimethoprim Schiff Base Complexes of Aryltellurium(IV)

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ABSTRACT

A novel monobasic tridentate Schiff base Pyridoxylidene-trimethoprim, HPL-TMP, synthesized from Pyridoxal and Trimethoprim form stable complexes with aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides of the type PL-TMP.ArTeCl₂ and PL-TMP. Ar₂TeCl (where Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl). These have been characterized by elemental analyses, IR and ¹H NMR spectroscopy. The spectral studies predict the bonding of ligand through phenolic oxygen of Schiff base after deprotonation, nitrogen of the azomethine group and pyrimidine nitrogen to give hexa-coordinated tellurium(IV) complexes with distorted octahedral geometry.

Keywords: Pyridoxylidene-trimethoprim Schiff base, Aryltellurium, Diaryltellurium, Pyridoxal, Trimethoprim.

INTRODUCTION

Trimethoprim and its derivatives are broad spectrum antimicrobial agents with anti-parasitic activity and was first described by Roth and coworker. Schiff bases, also known as azomethine due to presence of –C=N– group have been extensively used as ligands in coordination chemistry because of their excellent donor abilities as chelating agent. Medicinal chemists have reported new derivatives of Trimethoprim(TMZ) including the Schiff base derived from Salicylaldehyde. Pyridoxal is a close analog of pyridoxine (also known as vitamins B₆). Also, aryltellurium(IV) chlorides are known to act as Lewis acids and form complexes with several N-, O- and S- donor bases. In view of this, we herein report some new
complexes derived from aryltellurium(IV) trichlorides, RTeCl$_3$ and diaryltellurium(IV) dichlorides, R$_2$TeCl$_2$ with Pyridoxylidene-trimethoprim Schiff base (HPL-TMP).

**EXPERIMENTAL**

All preparations were carried out under an atmosphere of dry N$_2$ and the solvents used were purified by standard method$^{15,16}$ before use. The purity of compounds was checked by Thin Layer Chromatography using Silica gel-G (Merck). Melting points were determined in open capillary tube and are uncorrected. Carbon, hydrogen and nitrogen analyses were obtained microanalytically from SAIF, Panjab University Chandigarh. IR(4000-400 cm$^{-1}$) and far IR(400-50 cm$^{-1}$) spectra were recorded in KBr/polyethylene pellets on a F.T. Infra-Red Spectrophotometer Model RZX (Perkin Elmer) at SAIF, Panjab University Chandigarh. Proton Magnetic Resonance Spectra were recorded in DMSO-d$_6$ using TMS as an internal reference on BRUKER AVANCE II 400 NMR spectrometer.

**Preparation of Aryltellurium(IV) Trichlorides and Diaryltellurium(IV) Dichlorides**

$p$- Methoxyphenyltellurium(IV) trichloride$^{17,18}$, bis($p$-methoxyphenyl)tellurium(IV) dichloride$^{18,19}$, $p$-ethoxyphenyltellurium(IV) trichloride$^{20}$, bis($p$-ethoxyphenyl)tellurium dichloride$^{20}$, $p$-hydroxyphenyltellurium(IV) trichloride$^{21}$, bis($p$-hydroxyphenyl) tellurium(IV) dichloride$^{21}$, 3-methyl-4-hydroxyphenyltellurium(IV) trichloride$^{22}$ and bis(3-methyl-4-hydroxyphenyl) tellurium(IV) dichloride$^{22}$ were prepared by the reactions of TeCl$_4$ with anisole, phenetole, phenol, $o$-cresol respectively, by the methods reported in the literature$^{17-22}$.

**Preparation of Pyridoxylidene-trimethoprim Schiff Base (HPL-TMP)$^{9-14}$**

Equimolar quantity of saturated methanolic solution of drug and Pyridoxal were mixed thoroughly. To this mixture 0.1% methanolic KOH was added to adjust the pH the solution between 7-8 and was refluxed for 2 hours. A clear light yellowish coloured solution was obtained. After completion of the reaction, the Schiff base ligand was isolated by crystallization after volume reduction by evaporation. The crystalline product was filtered and dried under vacuum and kept in desiccator over P$_2$O$_5$ until further use.

**Preparation of Pyridoxylidene-trimethoprim Complexes of Aryltellurium(IV) Trichlorides and Diaryltellurium(IV) Dichlorides**

Aryltellurium(IV) trichlorides, ArTeCl$_3$ and diaryltellurium(IV) dichlorides Ar$_2$TeCl$_2$ (Ar = $p$-methoxyphenyl, $p$-ethoxyphenyl, $p$-hydroxyphenyl and 3-methyl-4-hydroxyphenyl), when reacted with sodium salt of pyridoxylidene-trimethoprim in equimolar ratio, yield PL-TMP.ArTeCl$_3$ and PL-TMP.Ar$_2$TeCl$_2$ type complexes. Sodium salt of the ligand was prepared
by reacting equimolar (1:1) quantity of sodium metal and Schiff base in methanol. The solvent was distilled off to obtain sodium salt of Schiff base. Then a methanolic saturated solution of 2 mmol of aryltellurium(IV) trichloride or diaryltellurium(IV) dichloride was added dropwise to suspension of 2 mmol of sodium salt of Schiff base in about 50 mL benzene under reflux. The reaction mixture was further refluxed for 3-4 hours, cooled and precipitated sodium chloride was filtered off. The filtrate was then concentrated to about one third of original volume under reduced pressure and cooled in an ice bath to obtain coloured product. This was filtered, washed with benzene + methanol (1:1) and dried in vacuum desiccator over P₂O₅.

RESULTS AND DISCUSSION

TeCl₄ when heated with anisole, phenetole, phenol, o-cresol (Ar-H) appears to undergo Friedel-Crafts type condensation reaction whereby TeCl₃⁺ unit attacks a position para to the methoxy/ethoxy/hydroxy groups in the aromatic rings, thus resulting in the formation of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides.

\[
\text{Ar-H} + \text{TeCl}_4 \rightarrow \text{ArTeCl}_3 + \text{HCl}
\]

\[
2 \text{Ar-H} + \text{TeCl}_4 \rightarrow \text{Ar}_2 \text{TeCl}_2 + 2 \text{HCl}
\]

Preparation of Pyridoxylidene-trimethoprim Schiff base (HPL-TMP) by the reaction of trimethoprim drug and Pyridoxal can be represented by following equations.

Sodium salt of Pyridoxylidene-trimethoprim Schiff base (NaPL-TMP) reacts with aryltellurium (IV) trichlorides and diaryltellurium(IV) dichlorides in 1:1 molar ratio to yield the corresponding aryltellurium(IV) complexes.

\[
\text{HPL-TMP} + \text{ArTeCl}_3 \xrightarrow{\text{Na/CH}_3\text{OH}} \xrightarrow{-\text{NaCl}} (\text{PL-TMP}).\text{ArTeCl}
\]

\[
\text{HPL-TMP} + \text{Ar}_2\text{TeCl}_2 \xrightarrow{\text{Na/CH}_3\text{OH}} \xrightarrow{-\text{NaCl}} (\text{PL-TMP}).\text{Ar}_2\text{TeCl}
\]

All the tellurium(IV) complexes are coloured, crystalline solids, stable at room temperature and non-hygroscopic in nature. The complexes have been analysed for their tellurium, chlorine, carbon, hydrogen and nitrogen contents and the data along with their physical properties and yields are presented in Table 1.
Table 1. Analytical Data and Physical Properties of Pyridoxylidene-trimethoprim Schiff base (PL-TMP) Complexes of Tellurium(IV).

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Complex (Ar)</th>
<th>Empirical Formula (Formula Wt.)</th>
<th>Colour</th>
<th>M. Pt. (°C) dec.</th>
<th>Analyses % Found (Calculated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schiff Base</td>
<td>HPL-TMP</td>
<td>C$<em>{2}$H$</em>{9}$N$<em>{2}$O$</em>{5}$ (439.19)</td>
<td>Yellow</td>
<td>198-200</td>
<td>C 62.99 (60.13) H 5.47 (5.73) N 15.81 (15.94) Te 16.98 (17.15) Cl -</td>
</tr>
<tr>
<td>I</td>
<td>(PL-TMP), ArTeCl$_{2}$ (p-ethoxyphenyl)</td>
<td>C$<em>{2}$H$</em>{6}$Cl$<em>{2}$N$</em>{2}$O$_{5}$Te (744.09)</td>
<td>Cream (90)</td>
<td>228-230</td>
<td>46.75 (46.81) 3.99 (4.20) 9.38 (9.41) 16.98 (17.15) 9.43 (9.53)</td>
</tr>
<tr>
<td>II</td>
<td>(PL-TMP), ArTeCl$_{2}$ (p-ethoxyphenyl)</td>
<td>C$<em>{2}$H$</em>{6}$Cl$<em>{2}$N$</em>{2}$O$_{5}$Te (758.12)</td>
<td>Light cream (85)</td>
<td>260-262</td>
<td>47.41 (47.53) 4.02 (4.39) 9.13 (9.24) 16.58 (16.83) 9.13 (9.35)</td>
</tr>
<tr>
<td>III</td>
<td>(PL-TMP), ArTeCl$_{2}$ (p-ethoxyphenyl)</td>
<td>C$<em>{2}$H$</em>{6}$Cl$<em>{2}$N$</em>{2}$O$_{5}$Te (730.07)</td>
<td>Pale yellow (90)</td>
<td>206-208</td>
<td>45.98 (46.06) 3.95 (4.00) 9.50 (9.59) 17.39 (17.48) 9.23 (9.71)</td>
</tr>
<tr>
<td>IV</td>
<td>(PL-TMP), ArTeCl$_{2}$ (3-methyl-4-hydroxyphenyl)</td>
<td>C$<em>{2}$H$</em>{6}$Cl$<em>{2}$N$</em>{2}$O$_{5}$Te (744.09)</td>
<td>Yellowish green (73)</td>
<td>192-194</td>
<td>46.73 (46.81) 3.96 (4.20) 9.27 (9.41) 16.93 (17.15) 9.40 (9.53)</td>
</tr>
<tr>
<td>V</td>
<td>(PL-TMP), ArTeCl$_{2}$ (p-ethoxyphenyl)</td>
<td>C$<em>{2}$H$</em>{6}$Cl$<em>{2}$N$</em>{2}$O$_{5}$Te (815.77)</td>
<td>Light yellow (84)</td>
<td>132-134</td>
<td>52.88 (53.00) 4.81 (4.70) 8.41 (8.58) 15.53 (15.64) 4.17 (4.35)</td>
</tr>
<tr>
<td>VI</td>
<td>(PL-TMP), ArTeCl$_{2}$ (p-ethoxyphenyl)</td>
<td>C$<em>{2}$H$</em>{6}$Cl$<em>{2}$N$</em>{2}$O$_{5}$Te (787.72)</td>
<td>Dark yellow (86)</td>
<td>148-150</td>
<td>53.91 (54.09) 5.21 (5.02) 8.21 (8.30) 15.01 (15.12) 4.07 (4.20)</td>
</tr>
<tr>
<td>VII</td>
<td>(PL-TMP), ArTeCl$_{2}$ (p-ethoxyphenyl)</td>
<td>C$<em>{2}$H$</em>{6}$Cl$<em>{2}$N$</em>{2}$O$_{5}$Te (843.82)</td>
<td>Light Red (89)</td>
<td>148-150</td>
<td>51.63 (51.84) 4.44 (4.35) 8.68 (8.89) 16.01 (16.20) 4.44 (4.50)</td>
</tr>
<tr>
<td>VIII</td>
<td>(PL-TMP), ArTeCl$_{2}$ (3-methyl-4-hydroxyphenyl)</td>
<td>C$<em>{2}$H$</em>{6}$Cl$<em>{2}$N$</em>{2}$O$_{5}$Te (815.77)</td>
<td>Light brown (78)</td>
<td>142-144</td>
<td>52.85 (53.00) 4.83 (4.70) 8.38 (8.58) 15.49 (15.64) 4.23 (4.35)</td>
</tr>
</tbody>
</table>

Infrared Spectra

The IR data of Schiff base and its tellurium (IV) complexes are listed in Table 2. The spectra of PL-TMP Schiff base complexes are quite complex and an attempt has therefore been made to identify the donor sites by comparing the spectra of complexes with parent ligand and ArTeCl$_{3}$/Ar$_{2}$TeCl$_{2}$. Examination of the Schiff Base (HPL-TMP) spectrum shows the presence of the hydrogen bonded conjugated-chelate ring system$^{23}$ with its centre at ~ 2800 cm$^{-1}$. Thus intramolecular H-bonding is occurring by means of the formation of a quasi six-membered ring involving the OH---N=C bond. Thus band disappear on chelation with aryltellurium(IV) chlorides$^{24}$. Hydrogen bond contributes to planarity of the molecule which help in chelation. Also an intense ligand band at 1280 cm$^{-1}$ (phenolic --C-O) in free ligand has shifted to higher frequency side in complexes. All these indicate that the hydroxyl group of Pyridoxal of Schiff base is involved in coordination with tellurium$^{25}$. In addition, the spectra of the Schiff base shown shoulder at 1630 cm$^{-1}$ with slightly resolved weak band at 1605 cm$^{-1}$ and sharp band at 1590 cm$^{-1}$ assigned to $v$(C=N) mode for vibration of azomethine group$^{26-28}$ and $v$(C=N)pyrim for

pyrimidine ring. These shifts in aryltellurium Schiff base complexes towards higher and lower value reflecting that ligand coordinate through nitrogen atom of azomethine and pyrimidine ring. The medium intensity band at 3210 cm$^{-1}$ and 3190 cm$^{-1}$ due to $\nu$(N-H) asymmetric and symmetric vibrations respectively indicate the non involvement of the nitrogen atom of NH$_2$ group attached to pyrimidine in coordination. The appearance of new weak bands around 272-297 cm$^{-1}$ due to $\nu$(Te-O)$^5$8 mode and medium to strong band in the range of 408-420 cm$^{-1}$ due to $\nu$(Te-N) mode$^9$14 further supports the involvement of phenolic oxygen (after deprotonation), azomethine and pyrimidine nitrogen atoms of Schiff base in the coordination. Thus, IR data predict the tridentate nature of HPL-TMP involving azomethine nitrogen atom, phenolic oxygen after deprotonation and pyrimidine ring nitrogen giving rise to six and four membered chelate rings with the tellurium centre.

$^1$H NMR Spectra

In order to identify the solution structure of Schiff base(HPL-TMP) and its complexes, $^1$H NMR spectra were recorded in DMSO-d$_6$ and given in Table 3. The proton resonance of the OH group at 10.124 $\delta$ ppm in Schiff base due to presence of intramolecular hydrogen bonding disappear on complexation indicating the involvement of phenolic oxygen in the coordination via deprotonation. The signal due to the methanolic proton is observed at around 5.291 $\delta$ ppm which remain intact in the complexes, this confirm that the methanolic group attached to pyridoxal ring does not participate in bonding. The azomethine protons which resonate as a singlet at 8.101 $\delta$ ppm, the coordination of azomethine nitrogen to tellurium in the complexes is clearly demonstrated by a downfield shift of the peak.

The characteristic downfield shifting of proton signal in all complexes observed in region 5.48 $\delta$ ppm is due to pyrimidine proton in Schiff base clearly indicate the coordination through pyrimidine nitrogen atom$^{30}$. The signal due to –NH proton is observed around 6.121 $\delta$ ppm which remain intact with slight variation in complexes is due to the proton bounded to nitrogen experience quadruple effect$^{30}$. Thus Pyridoxyldiene -trimethoprim act as a tridentate –N, –N, –O chelating ligand in PL-TMP.ArTeCl$_2$ and PL-TMP.Ar$_2$TeCl complexes giving six coordinate tellurium having distorted octahedral geometry in these complexes as predicated from IR studies as well. The proposed structures are as in Figure 1.

Table 2. Important Infrared Absorption Bands (cm⁻¹) of Schiff Base (HPL-TMP) and Complexes.

<table>
<thead>
<tr>
<th>Comp.</th>
<th>ν(O-H) Phenolic</th>
<th>ν(N-H) amino group</th>
<th>ν(C=N) azomethine group</th>
<th>ν(C=N) pyrimidine</th>
<th>ν(Te-O)</th>
<th>ν(Te-N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPL-TMP</td>
<td>2800 w</td>
<td>3210 m</td>
<td>3190 m</td>
<td>1630 sh</td>
<td>1605 w</td>
<td>1590 s</td>
</tr>
<tr>
<td>I</td>
<td>-</td>
<td>3318 m</td>
<td>3148 m</td>
<td>1650 mb</td>
<td>1615 mb</td>
<td>1585 s</td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>3314 m</td>
<td>3145 m</td>
<td>1645 sh</td>
<td>1610 mb</td>
<td>1588 s</td>
</tr>
<tr>
<td>III</td>
<td>3460 m*</td>
<td>3305 m</td>
<td>3140 m</td>
<td>1677 mb</td>
<td>1619 mb</td>
<td>1575 s</td>
</tr>
<tr>
<td>IV</td>
<td>3410 m*</td>
<td>3315 m</td>
<td>3127 m</td>
<td>1650 mb</td>
<td>1609 mb</td>
<td>1579 s</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>3317 m</td>
<td>3190 m</td>
<td>1649 sh</td>
<td>1623 mb</td>
<td>1585 s</td>
</tr>
<tr>
<td>VI</td>
<td>-</td>
<td>3319 m</td>
<td>3185 m</td>
<td>1643 sh</td>
<td>1612 mb</td>
<td>1580 s</td>
</tr>
<tr>
<td>VII</td>
<td>3445 w*</td>
<td>3323 m</td>
<td>3160 m</td>
<td>1679 mb</td>
<td>1627 mb</td>
<td>1574 s</td>
</tr>
<tr>
<td>VIII</td>
<td>3470 w*</td>
<td>3303 m</td>
<td>3173 m</td>
<td>1655 sh</td>
<td>1608 mb</td>
<td>1578 s</td>
</tr>
</tbody>
</table>

s = sharp, m = medium, mb = medium broad, sh = shoulder, w = weak

*Due to phenolic OH of RTe and R₂Te moieties;

Table 3. ¹H NMR Spectral Data of Schiff Base(HPL-TMP) and Complexes in DMSO-d₆.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Phenolic-OH</th>
<th>Methanolic-OH</th>
<th>Azomethine-H</th>
<th>amino proton-H</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPL-TMP</td>
<td>10.124 s</td>
<td>5.291 s</td>
<td>8.101 s</td>
<td>6.121 s</td>
</tr>
<tr>
<td>1</td>
<td>-</td>
<td>5.332 s</td>
<td>8.156 s</td>
<td>6.124 s</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>5.278 s</td>
<td>8.149 s</td>
<td>6.127 s</td>
</tr>
<tr>
<td>3</td>
<td>9.69 s*</td>
<td>5.261 s</td>
<td>8.123 s</td>
<td>6.121 s</td>
</tr>
<tr>
<td>4</td>
<td>9.120 s*</td>
<td>5.343 s</td>
<td>8.136 s</td>
<td>6.125 s</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>5.462 s</td>
<td>8.159 s</td>
<td>6.128 s</td>
</tr>
<tr>
<td>6</td>
<td>-</td>
<td>5.473 s</td>
<td>8.183 s</td>
<td>6.123 s</td>
</tr>
<tr>
<td>7</td>
<td>9.417 s*</td>
<td>5.541 s</td>
<td>8.174 s</td>
<td>6.121 s</td>
</tr>
<tr>
<td>8</td>
<td>9.198 s*</td>
<td>5.462 s</td>
<td>8.143 s</td>
<td>6.126 s</td>
</tr>
</tbody>
</table>

s = singlet, q = quartet, t = triplet, m = multiplet

CONCLUSION

Aryltellurium (IV) and diaryltellurium(IV) dichlorides upon reaction with Schiff base (HPL-TMP) derived from Pyridoxal and trimethoprim yield new complexes of tellurium(IV). The synthesized complexes were characterized by elemental analyses, IR and ¹H NMR spectral studies. The analytical data suggest that the PL-TMP Schiff base complexes have 1:1 stoichiometry. The Schiff bases (HPL-TMP) in these complexes functions as a monobasic tridentate ligand through azomethine nitrogen, phenolic oxygen after deprotonation and pyrimidine ring nitrogen atoms. Based on these studies, ψ-octahedral geometry with two chelating rings has been assigned to these complexes.
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