Synthesis, Spectral and Biological Studies of Some Salicylidene-Trimethoprim Schiff Base Complexes of Aryltellurium(IV)

DEEPAK, K. K. VERMA and SAPANA GARG*

Department of Chemistry, Maharshi Dayanand University, Rohtak-124001, India
sapanagarg1511@gmail.com

Received 14 February 2017 / Accepted 2 March 2017

Abstract: A novel monobasic tridentate Schiff base salicylidene-trimethoprim, Sal-TMP, synthesized from trimethoprim and salicylaldehyde, form stable complexes with aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides of the type Sal-TMP.ArTeCl₂ and Sal-TMP.Ar₂TeCl₂ (where Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl). These have been characterized by elemental analyses, molar conductance, 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 hexacoordinated tellurium(IV) complexes. The complexes have also been screened for their antimicrobial activities against various bacteria and fungi organisms.

Keywords: Salicylidene-trimethoprim Schiff base, Aryltellurium(IV), Diaryltellurium(IV), Antibacterial, Antifungal activities

Introduction

Trimethoprim and its derivatives are broad spectrum antimicrobial agents with anti-parasitic activity¹-⁶ and were first described by Roth and coworker⁵. Schiff bases, also known as azomethine due to presence of –C=N– group, play important role in biological system, such as anticancer⁷-¹², antibacterial¹³-¹⁵, antiviral¹⁶-¹⁸, antifungal¹⁹-²¹ and other biological properties²²-²⁷ and also have been extensively used as ligands in coordination chemistry because of their excellent donor abilities as chelating agent²⁸-³². Medicinal chemists have reported new derivatives of trimethoprim(TMZ)³³-³⁵ including the Schiff base derived from salicylaldehyde²,³,³⁶-³⁷.

Also, aryltellurium(IV) chlorides are known³⁸-⁵⁴ 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, RTeCl₃ and diaryltellurium(IV) dichlorides, R₂TeCl₂ with salicylidene-trimethoprim Schiff base(Sal-TMP).
Experimental

All preparations were carried out under dry N₂ atmosphere and the solvents used were purified by standard methods[55,56] 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 on a ThermoFinnigan CHNS analyser. Conductivity was measured in DMSO at 25±2 °C with dip type conductivity cell on a microprocessor based conductivity bridge type MICRO SIL.

IR (4000-400 cm⁻¹) and far IR (400-50 cm⁻¹) spectra were recorded in KBr/polyethylene pellets on a FT-Infrared spectrophotometer model RZX (Perkin Elmer) at SAIF, Panjab University Chandigarh. Proton magnetic resonance spectra were recorded in DMSO-δ₆ using TMS as an internal reference on BRUKER AVANCE II 400 NMR spectrometer. The antimicrobial screening was carried out by tube dilution method at Department of Pharmaceutical Sciences, M. D. University, Rohtak, India.

Preparation of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

*p*-Methoxyphenyltellurium(IV) trichloride[57,58], bis(*p*-methoxyphenyl)tellurium(IV) dichloride[58,59], *p*-ethoxyphenyltellurium (IV) trichloride[60], bis(*p*-ethoxyphenyl)tellurium dichloride[60] *p*-hydroxyphenyltellurium(IV) trichloride[61], bis(*p*-hydroxyphenyl) tellurium(IV) dichloride[61], 3-methyl-4-hydroxyphenyltellurium(IV) trichloride[62] and bis(3-methyl-4-hydroxyphenyl)tellurium(IV) dichloride[62] were prepared by the reactions of TeCl₄ with anisole, phenetole, phenol, o-cresol respectively, by the methods reported in the literature[57-62].

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP)

Equimolar quantity of saturated methanolic solution of drug and salicylaldehyde were mixed thoroughly. To this mixture 0.1% methanolic KOH was added to adjust the pH of the solution between 7-8 and was refluxed for 2 hours. A clear yellowish-green 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 P₂O₅ until further use. Yield = 80%, M.pt.(decomp.)=188-190 °C. Analysis (Calculated) C₂₁H₂₂N₄O₄: C(63.95), H(5.62) and N(14.20); Found: C(63.50), H(5.27) and N(13.99).

Preparation of salicylidene-trimethoprim complexes of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

Aryltellurium(IV) trichlorides, ArTeCl₃ and diaryltellurium(IV) dichlorides Ar₂TeCl₂ (Ar= *p*-methoxyphenyl, *p*-ethoxyphenyl, *p*-hydroxyphenyl and 3-methyl-4-hydroxyphenyl), when reacted with sodium salt of salicylidene-trimethoprim in equimolar ratio, yield Sal-TMP.ArTeCl₂ and Sal-TMP.Ar₂TeCl₂ 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 anisole⁵⁷-⁵⁹, phenetole⁶⁰, phenol⁶¹, o-cresol⁶² (Ar-H) appears to undergo Friedel-Crafts type condensation reaction whereby TeCl₄⁺ 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.

\[
\text{Ar-H + TeCl}_4 \rightarrow \text{ArTeCl}_3 + \text{HCl} \quad (1)
\]

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

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP) by the reaction of trimethoprim drug and salicylaldehyde can be represented by following equations.

\[
\text{Sal-TMP + ArCl}_2 \xrightarrow{\text{Na/CH}_3\text{OH}} (\text{Sal-TMP}).\text{ArCl}_2
\]

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

\[
\text{Sal-TMP + ArTeCl}_3 \xrightarrow{\text{Na/CH}_3\text{OH}} (\text{Sal-TMP}).\text{ArTeCl}_2
\]

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

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.

Conductance studies

Molar conductance (\(\Lambda_M\)) data for the complexes in DMSO are compiled in Table 1. The \(\Lambda_M\) value at ca. 10⁻³ M for aryltellurium(IV) complexes in DMSO lie in the range 27.36-91.83 S cm² mol⁻¹ which predict the non electrolyte to 1:1 electrolyte⁶³,⁶⁴ type behaviour of these complexes in DMSO, probably due to ionization into ArTeCl₂Sal-TMP⁺/Ar₂TeSal-TMP⁺ and Cl⁻ in DMSO. This conductance behaviour of tellurium(IV) salicylidene-trimethoprim Schiff base complexes is different from those of transition metal complexes⁶⁵, which are reported to be non-electrolytes. The higher \(\Lambda_M\) values for some complexes may be due to steric factors and donor behaviour of DMSO to result in probable dissociation into solvated cation and L⁻ along with Cl⁻ in DMSO.

Infrared spectra

The IR data of Schiff base and its tellurium(IV) complexes are listed in Table 2. The spectra of Sal-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 ArTeCl₂/Ar₂TeCl₂.
<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Complex (Ar)</th>
<th>Empirical formula (Formula Wt.)</th>
<th>Colour (Yield, %)</th>
<th>M. Pt. °C dec.</th>
<th>Analyses % Found (Calculated)</th>
<th>( \Lambda_M ) at ca. 10^{-3} M S cm^{-2} mol^{-1} in DMSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schiff Base</td>
<td>Sal-TMP</td>
<td>C_{21}H_{22}N_{4}O_{4}</td>
<td>Yellowish-green (80)</td>
<td>188-190</td>
<td>63.50 (63.95), 5.27 (5.62), 13.99 (14.20)</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>(Sal-TMP).ArTeCl_{2} (p-methoxyphenyl)</td>
<td>C_{29}H_{28}Cl_{2}N_{4}O_{5}Te (699.05)</td>
<td>Light cream (92)</td>
<td>230-232</td>
<td>47.88 (48.11), 3.99 (4.04), 7.75 (8.01), 18.07 (18.24) (10.01)</td>
<td>53.19</td>
</tr>
<tr>
<td>II</td>
<td>(Sal-TMP).ArTeCl_{2} (p-ethoxyphenyl)</td>
<td>C_{30}H_{30}Cl_{2}N_{4}O_{5}Te (713.08)</td>
<td>Cream (85)</td>
<td>258-260</td>
<td>48.12 (48.85), 3.87 (4.24), 7.52 (7.86), 17.38 (17.89) (9.81)</td>
<td>52.88</td>
</tr>
<tr>
<td>III</td>
<td>(Sal-TMP).ArTeCl_{2} (p-hydroxyphenyl)</td>
<td>C_{27}H_{26}Cl_{2}N_{4}O_{5}Te (685.03)</td>
<td>Dark cream (94)</td>
<td>208-210</td>
<td>46.78 (47.34), 3.50 (3.83), 7.88 (8.18), 18.28 (18.63) (10.21)</td>
<td>55.73</td>
</tr>
<tr>
<td>IV</td>
<td>(Sal-TMP).ArTeCl_{2} (3-methyl-4-hydroxyphenyl)</td>
<td>C_{28}H_{28}Cl_{2}N_{4}O_{5}Te (699.05)</td>
<td>Light cream (80)</td>
<td>198-200</td>
<td>47.58 (48.11), 3.84 (4.04), 7.80 (8.01), 18.15 (18.24) (10.01)</td>
<td>58.68</td>
</tr>
<tr>
<td>V</td>
<td>(Sal-TMP).Ar_{2}TeCl (p-methoxyphenyl)</td>
<td>C_{35}H_{35}Cl_{2}N_{4}O_{6}Te (770.73)</td>
<td>Pale yellow (84)</td>
<td>130-132</td>
<td>53.84 (54.54), 4.31 (4.58), 7.11 (7.27), 16.43 (16.56) (4.60)</td>
<td>91.83</td>
</tr>
<tr>
<td>VI</td>
<td>(Sal-TMP).Ar_{2}TeCl (p-ethoxyphenyl)</td>
<td>C_{37}H_{39}Cl_{2}N_{4}O_{6}Te (798.78)</td>
<td>Light yellow (86)</td>
<td>150-152</td>
<td>54.84 (55.63), 4.53 (4.92), 6.84 (7.01), 15.50 (15.97) (4.44)</td>
<td>35.90</td>
</tr>
<tr>
<td>VII</td>
<td>(Sal-TMP).Ar_{2}TeCl (p-hydroxyphenyl)</td>
<td>C_{33}H_{31}Cl_{2}N_{4}O_{6}Te (742.68)</td>
<td>Red (89)</td>
<td>146-148</td>
<td>52.84 (53.37), 4.01 (4.21), 7.27 (7.54), 16.89 (17.18) (4.77)</td>
<td>36.00</td>
</tr>
<tr>
<td>VIII</td>
<td>(Sal-TMP).Ar_{2}TeCl (3-methyl-4-hydroxyphenyl)</td>
<td>C_{35}H_{35}Cl_{2}N_{4}O_{6}Te (770.73)</td>
<td>Brown (78)</td>
<td>140-142</td>
<td>53.80 (54.54), 4.34 (4.58), 7.09 (7.27), 16.45 (16.56) (4.60)</td>
<td>27.36</td>
</tr>
</tbody>
</table>

Values of \( \Lambda_M \) reported\textsuperscript{63,64} for 1:1 electrolytes in DMSO=50-70 S cm\(^2\) mol\(^{-1}\)
Table 2. Important infrared absorption bands (cm\(^{-1}\)) of Schiff base (Sal-TMP) and complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>(v(\text{O-H}))</th>
<th>(v(\text{N-H}))</th>
<th>(v(\text{C=N}))</th>
<th>(v(\text{C=N})_{\text{pyrimidine}})</th>
<th>(v(\text{C=O}))</th>
<th>(v(\text{Te-N}))</th>
<th>(v(\text{Te-O}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2836 w</td>
<td>3317 m 3119 m</td>
<td>1636 sh</td>
<td>1633 w 1593 s 1263 s</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>-</td>
<td>3323 m 3184 m</td>
<td>1674 mb</td>
<td>1644 mb 1587 s 1341 s 415 m 288 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>3323 m 3170 m</td>
<td>1647 sh</td>
<td>**1586 s 1304 s 420 m 295 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>3405 m*</td>
<td>3323 m 3150 m</td>
<td>1674 mb</td>
<td>1641 mb 1586 s 1341 s 419 s 270 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>3398 m*</td>
<td>3319 m 3172 m</td>
<td>1652 mb</td>
<td>1649 mb 1587 s 1333 s 450 s 277 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>3325 m 3178 m</td>
<td>1645 sh</td>
<td>**1587 s 1333 s 416 s 290 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>-</td>
<td>3320 m 3158 m</td>
<td>1640 sh</td>
<td>**1590 s 1331 s 410 m 273 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VII</td>
<td>3401 w*</td>
<td>3324 m 3168 m</td>
<td>1674 mb</td>
<td>1643 mb 1584 s 1340 s 418 s 285 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VIII</td>
<td>3463 w*</td>
<td>3304 m 3106 m</td>
<td>1634 sh</td>
<td>1643 mb 1584 s 1340 s 422 m 287 w</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

s=sharp, m=medium, mb=medium broad, sh=shoulder, w=weak. *Due to phenolic OH of Rte and R\(_2\)Te moieties; **band not resolved due to overlapping of band \(v(\text{C=N})\)

Examination of the Schiff base (Sal-TMP) spectrum shows the presence of the hydrogen bonded conjugated- chelate ring system\(^{66-68}\) with its centre at \(\sim 2832 \text{ cm}^{-1}\). Thus intramolecular H- bonding is occurring by means of the formation of a quasi six- membered ring involving the OH ----N=C bond.

![Figure 1](image-url) Hydrogen bonding

Thus band disappear on chelation with aryltellurium(IV) chlorides\(^{69}\). Hydrogen bond contributes to planarity of the molecule which helps in chelation\(^{70}\). Also an intense ligand band at 1263 cm\(^{-1}\) (phenolic –C-O) in free ligand has shifted to higher frequency side in complexes. All these indicate that the hydroxyl group of salicylaldehyde of Schiff base is involved in coordination with tellurium\(^{71-73}\).

In addition, the spectra of the Schiff base shown shoulder at 1636 cm\(^{-1}\) with slightly resolved weak band at 1633 cm\(^{-1}\) and sharp band at 1593 cm\(^{-1}\) assigned to \(v(\text{C=N})\) mode for vibration of azomethine group\(^{7,4,65,74-76}\) and \(v(\text{C=N})_{\text{pyrim}}\) for pyrimidine ring\(^{4,77}\). These shift in aryltellurium Schiff base complexes towards higher and lower value\(^{74-79}\) reflecting that ligand coordinate through nitrogen atom of azomethine and pyrimidine ring.

The medium intensity band at 3317 cm\(^{-1}\) and 3119 cm\(^{-1}\) due to \(v(\text{N-H})\) 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 270-295 cm\(^{-1}\) due to \(v(\text{Te-O})\)\(^{80,83}\) mode and medium to strong band in the range of 410-422 cm\(^{-1}\) due to \(v(\text{Te-N})\) mode\(^{84}\) 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 Sal-TMP involving azomethine nitrogen atom, phenolic oxygen after deprotonation and pyrimidine ring nitrogen giving rise to two- six and four membered chelate rings with the tellurium centre.
\(^\text{1}^\text{H} \text{NMR spectra}\)

In order to identify the solution structure of Schiff base (Sal-TMP) and its complexes, \(^\text{1}^\text{H} \text{NMR spectra were recorded in DMSO-d}_6\) and given in Table 3. The proton resonance of the \(\text{OH} \) group at 10.92 \(\delta \) ppm\(^\text{76,85}\) in Schiff base due to presence of intramolecular hydrogen bonding\(^\text{74}\) disappear on complexation indicating the involvement of phenolic oxygen in the coordination \(\text{via} \) deprotonation\(^\text{76}\). The azomethine protons which resonate as a singlet at 10.02 \(\delta \) ppm, the coordination of azomethine nitrogen to tellurium in the complexes are clearly demonstrated by a downfield shift of the peak\(^\text{86}\).

Table 3. \(^\text{1}^\text{H} \text{NMR spectral data of Schiff base (Sal-TMP) and complexes in DMSO-d}_6\)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical Shift, (\delta ) ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2.525(s, 2H, methylene), 3.551-3.745(s, 9H, -OCH(_3)), 5.672(s,1H, pyrimidine), 6.508(s, 2H, -NH(_2)), 7.526-8.169(m, 6H, aromatic proton), 10.021(s, 1H, azomethine), 10.921(s, 1H, Schiff base OH)</td>
</tr>
<tr>
<td>I</td>
<td>2.539(s, 2H, methylene), 3.598-3.840(s, 12H, -OCH(_3)), 6.574(s, 1H, pyrimidine), 6.926(s, 2H, -NH(_2)), 7.383-7.522(m, 10H, aromatic proton), 10.209(s, 1H, azomethine)</td>
</tr>
<tr>
<td>II</td>
<td>1.335(t, 3H, -OCH(_2)CH(_3)), 2.546(s, 2H, methylene), 3.963(q, 2H, -OCH(_2)CH(_3)), 3.515-3.875(s, 9H, -OCH(_3)), 6.540(s, 1H, pyrimidine), 6.950(s, 2H, -NH(_2)), 6.993-7.809(m, 10H, aromatic proton), 10.193(s, 1H, azomethine)</td>
</tr>
<tr>
<td>III</td>
<td>2.548(s, 2H, methylene), 3.601-3.783(s, 9H, -OCH(_3)), 6.569(s,1H, pyrimidine), 6.914(s, 2H, -NH(_2)), 7.370-7.787(m, 10H, aromatic proton), 8.155(s, 1H, phenolic OH of RTe), 10.201(s, 1H, azomethine)</td>
</tr>
<tr>
<td>IV</td>
<td>2.536(s, 2H, methylene), 2.527(s, 3H, -CH(_3)), 3.587-3.770(s, 9H, -OCH(_3)), 6.605(s, 1H, pyrimidine), 6.918(s, 2H, -NH(_2)), 7.051-7.671(m, 9H, aromatic proton), 8.251(s, 1H, phenolic OH of RTe), 10.239(s, 1H, azomethine)</td>
</tr>
<tr>
<td>V</td>
<td>2.528(s, 2H, methylene), 3.673-3.877(s, 15H, -OCH(_3)), 6.516(s,1H, pyrimidine), 6.882(s, 2H, -NH(_2)), 6.910-7.804(m, 14H, aromatic proton), 10.186(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VI</td>
<td>1.363(t, 6H, -OCH(_2)CH(_3)), 2.531(s, 2H, methylene), 4.019(q, 4H, -OCH(_2)CH(_3)), 3.555-3.765(s, 9H, -OCH(_3)), 6.510(s, 1H, pyrimidine), 6.924(s, 2H, -NH(_2)), 7.524-7.805(m, 14H, aromatic proton), 10.216(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VII</td>
<td>2.545(s, 2H, methylene), 3.568-3.926(s, 9H, -OCH(_3)), 6.554(s, 1H, pyrimidine), 6.884(s, 2H, -NH(_2)), 7.488-7.678(m, 14H, aromatic proton), 8.249(s, 2H, phenolic OH of R(_2)Te), 10.238(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VIII</td>
<td>2.538(s, 2H, methylene), 2.529(s, 6H, -CH(_3)), 3.555-3.750(s, 9H, -OCH(_3)), 6.502(s, 1H, pyrimidine), 6.926(s, 2H, -NH(_2)), 7.126-7.868(m, 12H, aromatic proton), 8.149(s, 2H, phenolic OH of R(_2)Te), 10.239(s, 1H, azomethine)</td>
</tr>
</tbody>
</table>

\(s=\text{singlet}, q=\text{quartet}, t=\text{triplet}, m=\text{multiplet}\)

The characteristic downfield shifting of proton signal in all complexes observed in region 5.67 \(\delta \) ppm is due to pyrimidine proton in Schiff base clearly indicate the coordination through pyrimidine nitrogen atom\(^\text{87}\). The signal due to –NH proton is observed around 6.51 \(\delta \) ppm which remain intact with slight variation in complexes is due to the proton bounded to nitrogen experience quadruple effect\(^\text{87}\). Thus salicylidene-trimethoprim act as a tridentate –N, –N, –O chelating ligand in Sal-TMP,ArTeCl\(_2\) and Sal-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 given below (Figure 2).
The salicylidene-trimethoprim Schiff base (Sal-TMP) and newly synthesized aryltellurium(IV) Schiff base complexes were evaluated for their antimicrobial activity in vitro against Gram +ve bacteria (S. aureus ATCC 11632 and B. cereus MTCC 7350), Gram -ve bacteria (E. coli ATCC 35218, P. aeruginosa ATCC 23564, S. typhi ATCC 15499 and P. rettgeri DRDE) and fungal strains (A. niger, A. fumigates and A. flavus) by tube dilution method\textsuperscript{88}. Dilution of test and standard compounds were prepared double strength nutrient broth - I.P (Antibacterial) and Sabouraud Dextrose Broth – I.P (Antifungal)\textsuperscript{89}. The samples were incubated at 37±1 °C for 24 h (bacteria), 25±1 °C for 7 days (A. niger), 30 ±1 °C for 15 days (A. flavus), 35±1 °C for 72 h (A. fumigates) respectively and results were recorded in terms of MIC (The lowest concentration of test substances which inhibited values are presented in the Table 4.

The data show that the Sal-TMP complexes of aryltellurium(IV) exhibit more antimicrobial activity towards bacteria as compared to fungii. The antibacterial activity shows following trend.

**Biological Activity**

\textbf{Figure 2.} Proposed structures of complexes

\[
\text{Sal-TMP.} \text{Ar}_2 \text{TeCl} \\
\text{Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl}
\]
Sal-TMP. Ar₂TeCl > Sal-TMP. ArTeCl₂ ≈ Sal-TMP Schiff base

Sal-TMP. Ar₂TeCl and Sal-TMP. ArTeCl₂ complexes have activity towards S. typhi and more effectively against B. cereus but Schiff base does not show activity against these bacterial strains. Schiff base and its complexes show almost similar activity against fungal strains.

**Table 4. Minimum Inhibitory Concentration, MIC, µg/mL; (-) Resistant**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Bacteria strains</th>
<th>Fungal strains</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S. aureus (ATCC 11632)</td>
<td>S. typhi (ATCC 15499)</td>
</tr>
<tr>
<td>Sal-TMP</td>
<td>2.5 - 1.25</td>
<td>5.0 -</td>
</tr>
<tr>
<td>I</td>
<td>5.0 -</td>
<td>1.25</td>
</tr>
<tr>
<td>II</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>III</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>IV</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>V</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>VI</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>VII</td>
<td>2.5</td>
<td>5.0</td>
</tr>
<tr>
<td>VIII</td>
<td>2.5</td>
<td>1.25</td>
</tr>
</tbody>
</table>

**Conclusion**

 Aryltellurium(IV) and diaryltellurium(IV) dichlorides upon reaction with Schiff base(Sal-TMP) derived from salicylaldehyde and trimethoprim yield new complexes of tellurium(IV). The synthesized complexes were characterized by elemental analyses, conductance measurement, IR and ¹H NMR spectral studies. The analytical data suggest that the Sal-TMP Schiff base complexes have 1:1 stoichiometry. The Schiff bases (Sal-TMP) in these complexes functions as a uninegative tridentate ligand through azomethine nitrogen, phenolic oxygen after deprotonation and pyrimidine ring nitrogen atoms. Based on these studies, distorted octahedral geometry with two chelating rings has been assigned to these complexes. The complexes have been observed to possess substantial antimicrobial activity especially against bacteria.

**Acknowledgement**

The authors are grateful to M. D. University, Rohtak for providing the necessary facilities. One of the authors (Deepak) is also thankful to UGC New Delhi for providing fellowship. We also thank SAIF, Panjab University Chandigarh for providing the CHN analyses and spectral data.

**References**

5. Dr. Karl Thomae Gmb H (Biberach an der Riss. DE), United States Patent. 4829058.
42. Berg M C, Diss Abstr Int., 1972, 33, 2982.
46. Garad M V, Polyhedron, 1985, 4(8), 1353-1355; DOI:10.1016/S0277-5387(00)86963-6
71. Mishra A P and Soni M, Metal Based Drugs, 2008, 71, 243; DOI:10.1155/2008/875410
89. Pharmacopoeia of India, Volume 1, Controller of Publications, Ministry of Health Department, Government of India, New Delhi, 2007, 37.
Synthesis, Spectral and Biological Studies of Some Salicylidene-Trimethoprim Schiff Base Complexes of Aryltellurium(IV)

DEEPAK, K. K. VERMA and SAPANA GARG

Department of Chemistry, Maharshi Dayanand University, Rohtak-124001, India
sapanagarg1511@gmail.com

Received 14 February 2017 / Accepted 2 March 2017

Abstract: A novel monobasic tridentate Schiff base salicylidene-trimethoprim, Sal-TMP, synthesized from trimethoprim and salicylaldehyde, form stable complexes with aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides of the type Sal-TMP.ArTeCl₂ and Sal-TMP.Ar₂TeCl (where Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl). These have been characterized by elemental analyses, molar conductance, 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 hexacoordinated tellurium(IV) complexes. The complexes have also been screened for their antimicrobial activities against various bacteria and fungi organisms.

Keywords: Salicylidene-trimethoprim Schiff base, Aryltellurium(IV), Diaryltellurium(IV), Antibacterial, Antifungal activities

Introduction

Trimethoprim and its derivatives are broad spectrum antimicrobial agents with anti-parasitic activity and were first described by Roth and coworker. Schiff bases, also known as azomethine due to presence of -C=N- group, play important role in biological system, such as anticancer, antibacterial, antiviral, antifungal and other biological properties and also 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.

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, RTeCl₃ and diaryltellurium(IV) dichlorides, R₂TeCl₂ with salicylidene-trimethoprim Schiff base(Sal-TMP).
Experimental
All preparations were carried out under dry N\textsubscript{2} atmosphere and the solvents used were purified by standard method\textsuperscript{55,56} 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 on a ThermoFinnigan CHNS analyser. Conductivity was measured in DMSO at 25±2 °C with dip type conductivity cell on a microprocessor based conductivity bridge type MICROSL.

IR (4000-400 cm\textsuperscript{-1}) and far IR (400-50 cm\textsuperscript{-1}) spectra were recorded in KBr/polyethylene pellets on a FT-Infrared spectrophotometer model RZX (Perkin Elmer) at SAIF, Panjab University Chandigarh. Proton magnetic resonance spectra were recorded in DMSO-d\textsubscript{6} using TMS as an internal reference on BRUKER AVANCE II 400 NMR spectrometer. The antimicrobial screening was carried out by tube dilution method at Department of Pharmaceutical Sciences, M. D. University, Rohtak, India.

Preparation of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

\textit{p-Methoxyphenyltellurium(IV) trichloride}\textsuperscript{57,58}, \textit{bis(p-methoxyphenyl)tellurium(IV) dichloride}\textsuperscript{58,59}, \textit{p-ethoxyphenyltellurium (IV) trichloride}\textsuperscript{60}, \textit{bis(p-ethoxyphenyl)tellurium dichloride}\textsuperscript{60}, \textit{p-hydroxyphenyltellurium(IV) trichloride}\textsuperscript{61}, \textit{bis(p-hydroxyphenyl) tellurium(IV) dichloride}\textsuperscript{61}, \textit{3-methyl-4-hydroxyphenyltellurium(IV) trichloride}\textsuperscript{62} and \textit{bis(3-methyl-4-hydroxyphenyl)tellurium(IV) dichloride}\textsuperscript{62} were prepared by the reactions of TeCl\textsubscript{4} with anisole, phenetole, phenol, \textit{o}-cresol respectively, by the methods reported in the literature\textsuperscript{57-62}.

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP)
Equimolar quantity of saturated methanolic solution of drug and salicylaldehyde were mixed thoroughly. To this mixture 0.1% methanolic KOH was added to adjust the pH of the solution between 7-8 and was refluxed for 2 hours. A clear yellowish-green 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 \textit{vacuum} and kept in desiccator over P\textsubscript{2}O\textsubscript{10} until further use. Yield = 80%, M.pt.(decomp.)=188-190 °C. Analysis (Calculated) C\textsubscript{21}H\textsubscript{22}N\textsubscript{4}O\textsubscript{4}:C(63.95), H(5.62) and N(14.20); Found: C(63.50), H(5.27) and N(13.99).

Preparation of salicylidene-trimethoprim complexes of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides
Aryltellurium(IV) trichlorides, ArTeCl\textsubscript{3} and diaryltellurium(IV) dichlorides Ar\textsubscript{2}TeCl\textsubscript{2} (Ar= \textit{p}-methoxyphenyl, \textit{p}-ethoxyphenyl, \textit{p}-hydroxyphenyl and 3-methyl-4-hydroxyphenyl), when reacted with sodium salt of salicylidene-trimethoprim in equimolar ratio, yield Sal-TMP.ArTeCl\textsubscript{2} and Sal-TMP.Ar\textsubscript{2}TeCl 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 \textit{in vacuum} desiccator over P\textsubscript{2}O\textsubscript{10}.

Results and Discussion

TeCl₄ when heated with anisole, phennetole, phenol, o-cresol (Ar-H) appears to undergo Friedel-Crafts type condensation reaction whereby TeCl₄ 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.

\[
\text{Ar-H + TeCl}_4 \rightarrow \text{ArTeCl}_3 + \text{HCl} \quad (1) \\
2 \text{Ar-H + TeCl}_4 \rightarrow \text{Ar}_2\text{TeCl}_2 + 2 \text{HCl} \quad (2)
\]

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP) by the reaction of trimethoprim drug and salicylaldehyde can be represented by following equations.

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

\[
\text{Sal-TMP} + \text{ArTeCl}_3 \xrightarrow{\text{Na/CH}_3\text{OH}} \text{(Sal-TMP).ArTeCl}_2 \quad (3) \\
\text{Sal-TMP} + \text{Ar}_2\text{TeCl}_2 \xrightarrow{\text{Na/CH}_3\text{OH}} \text{(Sal-TMP).Ar}_2\text{TeCl}_2 \quad (4)
\]

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.

Conductance studies

Molar conductance (ΛM) data for the complexes in DMSO are complied in Table 1. The ΛM value at ca. 10⁻³ M for aryltellurium(IV) complexes in DMSO lie in the range 27.36-91.83 S cm² mol⁻¹ which predict the non electrolyte to 1:1 electrolyte type behaviour of these complexes in DMSO, probably due to ionization into ArTeCl₂·Sal-TMP⁺/Ar₂Te·Sal-TMP⁺ and Cl⁻ in DMSO. This conductance behaviour of tellurium(IV) salicylidene-trimethoprim Schiff base complexes is different from those of transition metal complexes, which are reported to be non-electrolytes. The higher ΛM values for some complexes may be due to steric factors and donor behaviour of DMSO to result in probable dissociation into solvated cation and L⁻ along with Cl⁻ in DMSO.

Infrared spectra

The IR data of Schiff base and its tellurium(IV) complexes are listed in Table 2. The spectra of Sal-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 ArTeCl₃/Ar₂TeCl₂.
### Table 1. Analytical data, molar conductance and physical properties of salicylidene-trimethoprim Schiff base (Sal-TMP) complexes of tellurium(IV)

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Complex (Ar)</th>
<th>Empirical formula (Formula Wt.)</th>
<th>Colour (Yield, %)</th>
<th>M. Pt. °C dec.</th>
<th>Analyses % Found (Calculated)</th>
<th>$\Lambda_M$ at ca. $10^{-3}$ M S cm$^2$ mol$^{-1}$ in DMSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schiff Base</td>
<td>Sal-TMP</td>
<td>C$<em>{21}$H$</em>{22}$N$_{4}$O$_4$</td>
<td>Yellowish –green  (80)</td>
<td>188-190</td>
<td>63.50 (63.95)</td>
<td>5.27 (5.62)</td>
</tr>
<tr>
<td>I</td>
<td>(Sal-TMP).ArTeCl$_2$ (p-methoxyphenyl)</td>
<td>C$<em>{29}$H$</em>{28}$Cl$_2$N$_4$O$_5$Te (699.05)</td>
<td>Light cream (92)</td>
<td>230-232</td>
<td>47.88 (48.11)</td>
<td>3.99 (4.04)</td>
</tr>
<tr>
<td>II</td>
<td>(Sal-TMP).ArTeCl$_2$ (p-ethoxyphenyl)</td>
<td>C$<em>{29}$H$</em>{28}$Cl$_2$N$_4$O$_5$Te (713.08)</td>
<td>Cream (85)</td>
<td>258-260</td>
<td>48.12 (48.85)</td>
<td>3.87 (4.24)</td>
</tr>
<tr>
<td>III</td>
<td>(Sal-TMP).ArTeCl$_2$ (p-hydroxyphenyl)</td>
<td>C$<em>{27}$H$</em>{26}$Cl$_2$N$_4$O$_5$Te (685.03)</td>
<td>Dark cream (94)</td>
<td>208-210</td>
<td>46.78 (47.34)</td>
<td>3.50 (3.83)</td>
</tr>
<tr>
<td>IV</td>
<td>(Sal-TMP).ArTeCl$_2$ (3-methyl-4-hydroxyphenyl)</td>
<td>C$<em>{29}$H$</em>{28}$Cl$_2$N$_4$O$_5$Te (699.05)</td>
<td>Light cream (80)</td>
<td>198-200</td>
<td>47.58 (48.11)</td>
<td>3.84 (4.04)</td>
</tr>
<tr>
<td>V</td>
<td>(Sal-TMP).Ar$_2$TeCl$_4$ (p-methoxyphenyl)</td>
<td>C$<em>{35}$H$</em>{35}$Cl$_4$N$_4$O$_6$Te (770.73)</td>
<td>Pale yellow (84)</td>
<td>130-132</td>
<td>53.84 (54.54)</td>
<td>4.31 (4.58)</td>
</tr>
<tr>
<td>VI</td>
<td>(Sal-TMP).Ar$_2$TeCl$_4$ (p-ethoxyphenyl)</td>
<td>C$<em>{35}$H$</em>{35}$Cl$_4$N$_4$O$_6$Te (798.78)</td>
<td>Light yellow (86)</td>
<td>150-152</td>
<td>54.84 (55.63)</td>
<td>4.53 (4.92)</td>
</tr>
<tr>
<td>VII</td>
<td>(Sal-TMP).Ar$_2$TeCl$_4$ (p-hydroxyphenyl)</td>
<td>C$<em>{33}$H$</em>{31}$Cl$_4$N$_4$O$_6$Te (742.68)</td>
<td>Red (89)</td>
<td>146-148</td>
<td>52.84 (53.37)</td>
<td>4.01 (4.21)</td>
</tr>
<tr>
<td>VIII</td>
<td>(Sal-TMP).Ar$_2$TeCl$_4$ (3-methyl-4-hydroxyphenyl)</td>
<td>C$<em>{35}$H$</em>{35}$Cl$_4$N$_4$O$_6$Te (770.73)</td>
<td>Brown (78)</td>
<td>140-142</td>
<td>53.80 (54.54)</td>
<td>4.34 (4.58)</td>
</tr>
</tbody>
</table>

Values of $\Lambda_M$ reported$^{61,64}$ for 1:1 electrolytes in DMSO=50-70 S cm$^2$ mol$^{-1}$
Table 2. Important infrared absorption bands (cm$^{-1}$) of Schiff base (Sal-TMP) and complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>$\nu(O-H)$</th>
<th>$\nu(N-H)$</th>
<th>$\nu(C=N)_1$</th>
<th>$\nu(C=N)_{pyrimidine}$</th>
<th>$\nu(C-O)$</th>
<th>$\nu(Te-N)$</th>
<th>$\nu(Te-O)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2836 w</td>
<td>3317 m</td>
<td>1636 sh</td>
<td>1633 w 1593 s</td>
<td>1263 s</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>-</td>
<td>3323 m</td>
<td>1674 mb</td>
<td>1644 mb 1587 s</td>
<td>1341 s</td>
<td>415 m</td>
<td>288 w</td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>3323 m</td>
<td>1647 sh</td>
<td><strong>1586 s</strong></td>
<td>1304 s</td>
<td>420 m</td>
<td>295 w</td>
</tr>
<tr>
<td>III</td>
<td>3405 m*</td>
<td>3323 m</td>
<td>1674 mb</td>
<td>1641 mb 1586 s</td>
<td>1341 s</td>
<td>419 s</td>
<td>270 w</td>
</tr>
<tr>
<td>IV</td>
<td>3389 m*</td>
<td>3319 m</td>
<td>1652 mb</td>
<td>1649 mb 1587 s</td>
<td>1333 s</td>
<td>450 s</td>
<td>277 w</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>3325 m</td>
<td>1645 sh</td>
<td><strong>1587 s</strong></td>
<td>1333 s</td>
<td>416 s</td>
<td>290 w</td>
</tr>
<tr>
<td>VI</td>
<td>-</td>
<td>3220 m</td>
<td>1640 sh</td>
<td><strong>1590 s</strong></td>
<td>1334 s</td>
<td>410 m</td>
<td>273 w</td>
</tr>
<tr>
<td>VII</td>
<td>3401 w*</td>
<td>3324 m</td>
<td>1674 mb</td>
<td>1643 mb 1584 s</td>
<td>1340 s</td>
<td>418 s</td>
<td>285 w</td>
</tr>
<tr>
<td>VIII</td>
<td>3463 w*</td>
<td>3304 m</td>
<td>1634 sh</td>
<td>1643 mb 1584 s</td>
<td>1340 s</td>
<td>422 m</td>
<td>287 w</td>
</tr>
</tbody>
</table>

$s=$sharp, $m=$medium, $mb=$medium broad, $sh=$shoulder, $w=$weak; *Due to phenolic OH of R$_2$Te moieties; **band not resolved due to overlapping of band $\nu(C=N)$

Examination of the Schiff base (Sal-TMP) spectrum shows the presence of the hydrogen bonded conjugated- chelate ring system with its centre at ~2832 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.

Figure 1. Hydrogen bonding

Thus band disappear on chelation with aryltellurium(IV) chlorides. Hydrogen bond contributes to planarity of the molecule which helps in chelation with its centre at ~2832 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.

In addition, the spectra of the Schiff base shown shoulder at 1636 cm$^{-1}$ with slightly resolved weak band at 1633 cm$^{-1}$ and sharp band at 1593 cm$^{-1}$ assigned to $\nu(C=N)_1$ mode for vibration of azomethine group and $\nu(C=O)_{pyrim.}$ For pyrimidine ring these shift 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 3317 cm$^{-1}$ and 3119 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 270-295 cm$^{-1}$ due to $\nu(Te=O)$ mode and medium to strong band in the range of 410-422 cm$^{-1}$ due to $\nu(Te-N)$ mode 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 Sal-TMP involving azomethine nitrogen atom, phenolic oxygen after deprotonation and pyrimidine ring nitrogen giving rise to two-six and four membered chelate rings with the tellurium centre.
In order to identify the solution structure of Schiff base (Sal-TMP) and its complexes, ¹H NMR spectra were recorded in DMSO-­d₆ and given in Table 3. The proton resonance of the OH group at 10.92 δ ppm disappears in Schiff base due to presence of intramolecular hydrogen bonding, indicating the involvement of phenolic oxygen in the coordination via deprotonation. The azomethine protons which resonate as a singlet at 10.02 δ ppm, the coordination of azomethine nitrogen to tellurium in the complexes are clearly demonstrated by a downfield shift of the peak.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical Shift, δ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2.525(s, 2H, methylene), 3.551-3.745(s, 9H, -OCH₃), 5.672(s,1H, pyrimidine), 6.508(s, 2H, –NH₂), 7.526-8.169(m, 6H, aromatic proton), 10.021(s, 1H, azomethine), 10.921(s, 1H, Schiff base OH)</td>
</tr>
<tr>
<td>I</td>
<td>2.539(s, 2H, methylene), 3.598-3.840(s, 12H, -OCH₃), 6.574(s, 1H, pyrimidine), 6.926(s, 2H, –NH₂), 7.383-7.522(m, 10H, aromatic proton), 10.209(s, 1H, azomethine)</td>
</tr>
<tr>
<td>II</td>
<td>1.335(t, 3H, -OCH₂CH₃), 2.546(s, 2H, methylene), 3.963(q, 2H, –OCH₂CH₃), 3.515-3.875(s, 9H, -OCH₃), 6.540(s, 1H, pyrimidine), 6.950(s, 2H, –NH₂), 6.993-7.809(m, 10H, aromatic proton), 10.193(s, 1H, azomethine)</td>
</tr>
<tr>
<td>III</td>
<td>2.548(s, 2H, methylene), 3.601-3.783(s, 9H, -OCH₃), 6.569(s,1H, pyrimidine), 6.914(s, 2H, –NH₂), 7.370-7.787(m, 10H, aromatic proton), 8.155(s, 1H, phenolic OH of RTe), 10.201(s, 1H, azomethine)</td>
</tr>
<tr>
<td>IV</td>
<td>2.536(s, 2H, methylene), 2.527(s, 3H, -CH₃), 3.587-3.770(s, 9H, –OCH₃), 6.605(s, 1H, pyrimidine), 6.918(s, 2H, –NH₂), 7.051-7.671(m, 9H, aromatic proton), 8.251(s, 1H, phenolic OH of RTe), 10.239(s, 1H, azomethine)</td>
</tr>
<tr>
<td>V</td>
<td>2.528(s, 2H, methylene), 3.673-3.877(s, 15H, -OCH₃), 6.516(s,1H, pyrimidine), 6.882(s, 2H, –NH₂), 6.910-7.804(m, 14H, aromatic proton), 10.186(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VI</td>
<td>1.363(t, 6H, –OCH₂CH₃), 2.531(s, 2H, methylene), 4.019(q, 4H, –OCH₂CH₃), 3.555-3.765(s, 9H, –OCH₃), 6.510(s, 1H, pyrimidine), 6.924(s, 2H, –NH₂), 7.524-7.805(m, 14H, aromatic proton), 10.216(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VII</td>
<td>2.545(s, 2H, methylene), 3.568-3.926(s, 9H, –OCH₃), 6.554(s, 1H, pyrimidine), 6.884(s, 2H, –NH₂), 7.488-7.678(m, 14H, aromatic proton), 8.249(s, 2H, phenolic OH of R₂Te), 10.238(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VIII</td>
<td>2.538(s, 2H, methylene), 2.529(s, 6H, -CH₃), 3.555-3.750(s, 9H, –OCH₃), 6.502(s, 1H, pyrimidine), 6.926(s, 2H, –NH₂), 7.126-7.868(m, 12H, aromatic proton), 8.149(s, 2H, phenolic OH of R₂Te), 10.239(s, 1H, azomethine)</td>
</tr>
</tbody>
</table>

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

The characteristic downfield shifting of proton signal in all complexes observed in region 5.67 δ ppm is due to pyrimidine proton in Schiff base clearly indicate the coordination through pyrimidine nitrogen atom. The signal due to –NH proton is observed around 6.51 δ ppm which remain intact with slight variation in complexes is due to the proton bounded to nitrogen experience quadruple effect. Thus salicylidene-trimethoprim act as a tridentate –N, –N, –O chelating ligand in Sal-TMP,ArTeCl₂ and Sal-TMP,Ar₂TeCl complexes giving six coordinate tellurium having distorted octahedral geometry in these complexes as predicated from IR studies as well. The proposed structures are as given below (Figure 2).
Biological Activity

The salicylidene-trimethoprim Schiff base (Sal-TMP) and newly synthesized aryltellurium(IV) Schiff base complexes were evaluated for their antimicrobial activity in vitro against Gram +ve bacteria (S. aureus ATCC 11632 and B. cereus MTCC 7350), Gram –ve bacteria (E. coli ATCC 35218, P. aeruginosa ATCC 23564, S. typhi ATCC 15499 and P. rettgeri DRDE) and fungal strains (A. niger, A. fumigates and A. flavus) by tube dilution method\(^8\). Dilution of test and standard compounds were prepared double strength nutrient broth – I.P (Antibacterial) and Sabouraud Dextrose Broth – I.P (Antifungal)\(^9\). The samples were incubated at 37±1 °C for 24 h (bacteria), 25±1 °C for 7 days (A. niger), 30±1 °C for 15 days (A. flavus), 35±1 °C for 72 h (A. fumigates) respectively and results were recorded in terms of MIC (The lowest concentration of test substances which inhibited values are presented in the Table 4.

The data show that the Sal-TMP complexes of aryltellurium(IV) exhibit more antimicrobial activity towards bacteria as compared to fungii. The antibacterial activity shows following trend.

Figure 2. Proposed structures of complexes
Sal-TMP.\(\text{Ar}_2\text{TeCl}\) > Sal-TMP.\(\text{ArTeCl}_2\) \(\approx\) Sal-TMP Schiff base

Sal-TMP.\(\text{Ar}_2\text{TeCl}\) and Sal-TMP.\(\text{ArTeCl}_2\) complexes have activity towards \(S. \text{typhi}\) and more effectively against \(B. \text{cereus}\) but Schiff base does not show activity against these bacterial strains. Schiff base and its complexes show almost similar activity against fungal strains.

**Table 4.** Minimum Inhibitory Concentration, MIC, \(\mu\)g/mL; (-) Resistant

<table>
<thead>
<tr>
<th>Compound</th>
<th>(S. \text{aureus}) (ATCC 11632)</th>
<th>(S. \text{typhi}) (ATCC 15499)</th>
<th>(P. \text{aeruginosa}) (ATCC 23564)</th>
<th>(E. \text{coli}) (ATCC 35218)</th>
<th>(B. \text{cereus}) (MTCC 7350)</th>
<th>(P. \text{rettgeri}) (DRDE strain)</th>
<th>(A. \text{niger})</th>
<th>(A. \text{fumigates}) flavus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2.5 -</td>
<td>1.25 -</td>
<td>5.0 -</td>
<td>-</td>
<td>5.0 -</td>
<td>20 -</td>
<td>5.0 -</td>
<td>1.25 -</td>
</tr>
<tr>
<td>I</td>
<td>2.5 -</td>
<td>1.25 -</td>
<td>5.0 -</td>
<td>-</td>
<td>5.0 -</td>
<td>20 -</td>
<td>5.0 -</td>
<td>1.25 -</td>
</tr>
<tr>
<td>II</td>
<td>5.0 -</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>5.0 -</td>
<td>5.0 -</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>III</td>
<td>-</td>
<td>20 - 10</td>
<td>5.0 -</td>
<td>1.25 -</td>
<td>2.5 -</td>
<td>20 -</td>
<td>5.0 -</td>
<td>5.0 -</td>
</tr>
<tr>
<td>IV</td>
<td>1.25 2.5</td>
<td>1.25 10</td>
<td>5.0 -</td>
<td>-</td>
<td>5.0 -</td>
<td>5.0 -</td>
<td>10 -</td>
<td>5.0 -</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>20 - 10</td>
<td>5.0 -</td>
<td>1.25 -</td>
<td>- 20 -</td>
<td>-</td>
<td>10 -</td>
<td>-</td>
</tr>
<tr>
<td>VI</td>
<td>1.25 2.5</td>
<td>1.25 10</td>
<td>5.0 -</td>
<td>-</td>
<td>- 5.0 -</td>
<td>-</td>
<td>-</td>
<td>5.0 -</td>
</tr>
<tr>
<td>VII</td>
<td>1.25 -</td>
<td>5.0 1.25</td>
<td>1.25 0.625</td>
<td>5.0 -</td>
<td>5.0 -</td>
<td>10 -</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>VIII</td>
<td>2.5 -</td>
<td>1.25 -</td>
<td>5.0 -</td>
<td>-</td>
<td>20 -</td>
<td>5.0 -</td>
<td>1.25 -</td>
<td>-</td>
</tr>
</tbody>
</table>

**Conclusion**

Aryltellurium(IV) and diaryltellurium(IV) dichlorides upon reaction with Schiff base(Sal-TMP) derived from salicylaldehyde and trimethoprim yield new complexes of tellurium(IV). The synthesized complexes were characterized by elemental analyses, conductance measurement, IR and \(^1\)H NMR spectral studies. The analytical data suggest that the Sal-TMP Schiff base complexes have 1:1 stoichiometry. The Schiff bases (Sal-TMP) in these complexes functions as a uninegative tridentate ligand through azomethine nitrogen, phenolic oxygen after deprotonation and pyrimidine ring nitrogen atoms. Based on these studies, distorted octahedral geometry with two chelating rings has been assigned to these complexes. The complexes have been observed to possess substantial antimicrobial activity especially against bacteria.

**Acknowledgement**

The authors are grateful to M. D. University, Rohtak for providing the necessary facilities. One of the authors (Deepak) is also thankful to UGC New Delhi for providing fellowship. We also thank SAIF, Panjab University Chandigarh for providing the CHN analyses and spectral data.

**References**

5. Dr. Karl Thomae GmbH (Biberach an der Riss. DE), United States Patent. 4829058.
42. Berg M C, Diss Abstr Int., 1972, 33, 2982.
46. Garad M V, Polyhedron, 1985, 4(8), 1353-1355; DOI:10.1016/S0277-5387(00)86963-6
89. Pharmacopoeia of India, Volume 1, Controller of Publications, Ministry of Health Department, Government of India, New Delhi, 2007, 37.
Synthesis, Spectral and Biological Studies of Some Salicylidene-Trimethoprim Schiff Base Complexes of Aryltellurium(IV)

DEEPAK, K. K. VERMA and SAPANA GARG

Department of Chemistry, Maharshi Dayanand University, Rohtak-124001, India
sapanagarg1511@gmail.com

Received 14 February 2017 / Accepted 2 March 2017

Abstract: A novel monobasic tridentate Schiff base salicylidene-trimethoprim, Sal-TMP, synthesized from trimethoprim and salicylaldehyde, form stable complexes with aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides of the type Sal-TMP.ArTeCl₂ and Sal-TMP.Ar₂TeCl₂ (where Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl). These have been characterized by elemental analyses, molar conductance, 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 hexacoordinated tellurium(IV) complexes. The complexes have also been screened for their antimicrobial activities against various bacteria and fungi organisms.

Keywords: Salicylidene-trimethoprim Schiff base, Aryltellurium(IV), Diaryltellurium(IV), Antibacterial, Antifungal activities

Introduction

Trimethoprim and its derivatives are broad spectrum antimicrobial agents with anti-parasitic activity and were first described by Roth and coworker. Schiff bases, also known as azomethine due to presence of –C=N– group, play important role in biological system, such as anticancer, antibacterial, antiviral, antifungal and other biological properties and also 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.

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, RTeCl₃ and diaryltellurium(IV) dichlorides, R₂TeCl₂ with salicylidene-trimethoprim Schiff base(Sal-TMP).
Experimental

All preparations were carried out under dry N\textsubscript{2} atmosphere and the solvents used were purified by standard method\textsuperscript{55,56} 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 on a ThermoFinnigan CHNS analyser. Conductivity was measured in DMSO at 25±2 °C with dip type conductivity cell on a microprocessor based conductivity bridge type MICROSL.

IR (4000-400 cm\textsuperscript{-1}) and far IR (400-50 cm\textsuperscript{-1}) spectra were recorded in KBr/polyethylene pellets on a FT-Infrared spectrophotometer model RZX (Perkin Elmer) at SAIF, Panjab University Chandigarh. Proton magnetic resonance spectra were recorded in DMSO-d\textsubscript{6} using TMS as an internal reference on BRUKER AVANCE II 400 NMR spectrometer. The antimicrobial screening was carried out by tube dilution method at Department of Pharmaceutical Sciences, M. D. University, Rohtak, India.

Preparation of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

\textit{p-Methoxyphenyltellurium(IV)} trichloride\textsuperscript{57,58}, bis(\textit{p-methoxyphenyl})tellurium(IV) dichloride\textsuperscript{58,59}, \textit{p-ethoxyphenyltellurium (IV)} trichloride\textsuperscript{60}, bis(\textit{p-ethoxyphenyl})tellurium dichloride\textsuperscript{60}, \textit{p-hydroxyphenyltellurium(IV)} trichloride\textsuperscript{61}, bis(\textit{p-hydroxyphenyl}) tellurium(IV) dichloride\textsuperscript{61}, 3-methyl-4-hydroxyphenyltellurium(IV) trichloride\textsuperscript{62} and bis(3-methyl-4-hydroxyphenyl)tellurium(IV) dichloride\textsuperscript{62} were prepared by the reactions of TeCl\textsubscript{4} with anisole, phenetole, phenol, \textit{o}-cresol respectively, by the methods reported in the literature\textsuperscript{57-62}.

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP)
Equimolar quantity of saturated methanolic solution of drug and salicylaldehyde were mixed thoroughly. To this mixture 0.1% methanolic KOH was added to adjust the pH of the solution between 7-8 and was refluxed for 2 hours. A clear yellowish-green 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 \textit{vacuum} and kept in desiccator over P\textsubscript{2}O\textsubscript{10} until further use. Yield = 80\%, M.pt.(decomp.)=188-190 °C. Analysis (Calculated) C\textsubscript{21}H\textsubscript{22}N\textsubscript{4}O\textsubscript{4}: C(63.95), H(5.62) and N(14.20); Found: C(63.50), H(5.27) and N(13.99).

Preparation of salicylidene-trimethoprim complexes of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

Aryltellurium(IV) trichlorides, ArTeCl\textsubscript{3} and diaryltellurium(IV) dichlorides Ar\textsubscript{2}TeCl\textsubscript{2} (Ar= \textit{p-methoxyphenyl}, \textit{p-ethoxyphenyl}, \textit{p-hydroxyphenyl} and 3-methyl-4-hydroxyphenyl), when reacted with sodium salt of salicylidene-trimethoprim in equimolar ratio, yield Sal-TMP.ArTeCl\textsubscript{3} and Sal-TMP.Ar\textsubscript{2}TeCl 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 aryldiaryl tellurium(IV) trichloride or diaryldiaryl tellurium(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 \textit{in vacuum} desiccator over P\textsubscript{2}O\textsubscript{10}.
Results and Discussion

TeCl₄ when heated with anisole⁵⁷-⁵⁹, phenetole⁶⁰, phenol⁶¹, o-cresol⁶² (Ar-H) appears to undergo Friedel-Crafts type condensation reaction whereby TeCl₅⁺ 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.

\[
\begin{align*}
\text{Ar-H} + \text{TeCl}_4 & \rightarrow \text{ArTeCl}_3 + \text{HCl} \\
2 \text{Ar-H} + \text{TeCl}_4 & \rightarrow \text{Ar}_2\text{TeCl}_2 + 2 \text{HCl}
\end{align*}
\]

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP) by the reaction of trimethoprim drug and salicylaldehyde can be represented by following equations.

\[
\begin{align*}
\text{Sal-TMP} + \text{ArTeCl}_3 & \xrightarrow{\text{Na/CH}_3\text{OH}} \text{(Sal-TMP).ArTeCl}_2 \\
\text{Sal-TMP} + \text{Ar}_2\text{TeCl}_2 & \xrightarrow{\text{Na/CH}_3\text{OH}} \text{(Sal-TMP).Ar}_2\text{TeCl}_2
\end{align*}
\]

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

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.

Conductance studies

Molar conductance \( (\Lambda_M) \) data for the complexes in DMSO are complied in Table 1. The \( \Lambda_M \) value at ca. 10⁻³ M for aryltellurium(IV) complexes in DMSO lie in the range 27.36-91.83 S cm² mol⁻¹ which predict the non electrolyte to 1:1 electrolyte type behaviour of these complexes in DMSO, probably due to ionization into ArTeCl₂Sal-TMP⁺/Ar₂TeSal-TMP⁺ and Cl⁻ in DMSO. This conductance behaviour of tellurium(IV) salicylidene-trimethoprim Schiff base complexes is different from those of transition metal complexes⁶⁵, which are reported to be non-electrolytes. The higher \( \Lambda_M \) values for some complexes may be due to steric factors and donor behaviour of DMSO to result in probable dissociation into solvated cation and \( \text{L}^- \) along with Cl⁻ in DMSO.

Infrared spectra

The IR data of Schiff base and its tellurium(IV) complexes are listed in Table 2. The spectra of Sal-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 ArTeCl₃/Ar₂TeCl₂.
<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Complex (Ar)</th>
<th>Empirical formula (Formula Wt.)</th>
<th>Colour (Yield, %)</th>
<th>M. Pt. °C dec.</th>
<th>Analyses % Found (Calculated)</th>
<th>( \Lambda_M ) at ca. 10(^{-3}) M S cm(^{-2}) mol(^{-1}) in DMSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schiff Base</td>
<td>Sal-TMP</td>
<td>C(<em>{21})H(</em>{22})N(_4)O(_4)</td>
<td>Yellowish – green (80)</td>
<td>188-190</td>
<td>63.50 (63.95)</td>
<td>5.27 (5.62)</td>
</tr>
<tr>
<td>I</td>
<td>(Sal-TMP).ArTeCl(_2) (p-methoxyphenyl)</td>
<td>C(<em>{29})H(</em>{30})Cl(_2)N(_4)O(_5)Te</td>
<td>Light cream (92)</td>
<td>230-232</td>
<td>47.88 (48.11)</td>
<td>3.99 (4.04)</td>
</tr>
<tr>
<td>II</td>
<td>(Sal-TMP).ArTeCl(_2) (p-ethoxyphenyl)</td>
<td>C(<em>{29})H(</em>{30})Cl(_2)N(_4)O(_5)Te</td>
<td>Cream (85)</td>
<td>258-260</td>
<td>48.12 (48.85)</td>
<td>3.87 (4.24)</td>
</tr>
<tr>
<td>III</td>
<td>(Sal-TMP).ArTeCl(_2) (p-hydroxyphenyl)</td>
<td>C(<em>{27})H(</em>{26})Cl(_2)N(_4)O(_5)Te</td>
<td>Dark cream (94)</td>
<td>208-210</td>
<td>46.78 (47.34)</td>
<td>3.50 (3.83)</td>
</tr>
<tr>
<td>IV</td>
<td>(Sal-TMP).ArTeCl(_2) (3-methyl-4-hydroxyphenyl)</td>
<td>C(<em>{29})H(</em>{28})Cl(_2)N(_4)O(_5)Te</td>
<td>Light cream (80)</td>
<td>198-200</td>
<td>47.58 (48.11)</td>
<td>3.84 (4.04)</td>
</tr>
<tr>
<td>V</td>
<td>(Sal-TMP).Ar(_2)TeCl (p-methoxyphenyl)</td>
<td>C(<em>{35})H(</em>{35})Cl(_4)N(_4)O(_6)Te</td>
<td>Pale yellow (84)</td>
<td>130-132</td>
<td>53.84 (54.54)</td>
<td>4.31 (4.58)</td>
</tr>
<tr>
<td>VI</td>
<td>(Sal-TMP).Ar(_2)TeCl (p-ethoxyphenyl)</td>
<td>C(<em>{35})H(</em>{35})Cl(_4)N(_4)O(_6)Te</td>
<td>Light yellow (86)</td>
<td>150-152</td>
<td>54.84 (55.63)</td>
<td>4.53 (4.92)</td>
</tr>
<tr>
<td>VII</td>
<td>(Sal-TMP).Ar(_2)TeCl (p-hydroxyphenyl)</td>
<td>C(<em>{33})H(</em>{31})Cl(_4)N(_4)O(_5)Te</td>
<td>Red (89)</td>
<td>146-148</td>
<td>52.84 (53.37)</td>
<td>4.01 (4.21)</td>
</tr>
<tr>
<td>VIII</td>
<td>(Sal-TMP).Ar(_2)TeCl (3-methyl-4-hydroxyphenyl)</td>
<td>C(<em>{35})H(</em>{35})Cl(_4)N(_4)O(_6)Te</td>
<td>Brown (78)</td>
<td>140-142</td>
<td>53.80 (54.54)</td>
<td>4.34 (4.58)</td>
</tr>
</tbody>
</table>

Values of \( \Lambda_M \) reported\(^{63,64}\) for 1:1 electrolytes in DMSO=50-70 S cm\(^{-2}\) mol\(^{-1}\)
Table 2. Important infrared absorption bands (cm\(^{-1}\)) of Schiff base (Sal-TMP) and complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>(v(O-H))</th>
<th>(v(N-H))</th>
<th>(v(C=N))</th>
<th>(v(C-N)) pyrimidine</th>
<th>(v(C=O))</th>
<th>(v(\text{Te-N}))</th>
<th>(v(\text{Te-O}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2836 w</td>
<td>3317 m</td>
<td>3119 m</td>
<td>1636 s 1593 w 1263 s</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>-</td>
<td>3323 m</td>
<td>3184 m</td>
<td>1674 mb 1644 mb 1587 s</td>
<td>1341 s</td>
<td>415 m</td>
<td>288 w</td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>3323 m</td>
<td>3170 m</td>
<td>1647 sh **1586 s</td>
<td>1304 s</td>
<td>420 m</td>
<td>295 w</td>
</tr>
<tr>
<td>III</td>
<td>3405 m*</td>
<td>3323 m</td>
<td>3150 m</td>
<td>1674 mb 1641 mb 1586 s</td>
<td>1341 s</td>
<td>419 s</td>
<td>270 w</td>
</tr>
<tr>
<td>IV</td>
<td>3398 m*</td>
<td>3319 m</td>
<td>3172 m</td>
<td>1652 mb 1649 mb 1587 s</td>
<td>1333 s</td>
<td>450 s</td>
<td>277 w</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>3325 m</td>
<td>3178 m</td>
<td>1645 sh **1587 s</td>
<td>1333 s</td>
<td>416 s</td>
<td>290 w</td>
</tr>
<tr>
<td>VI</td>
<td>-</td>
<td>3320 m</td>
<td>3158 m</td>
<td>1640 sh **1590 s</td>
<td>1331 s</td>
<td>410 s</td>
<td>273 w</td>
</tr>
<tr>
<td>VII</td>
<td>3401 w*</td>
<td>3324 m</td>
<td>3168 m</td>
<td>1674 mb 1643 mb 1584 s</td>
<td>1340 s</td>
<td>418 s</td>
<td>285 w</td>
</tr>
<tr>
<td>VIII</td>
<td>3463 w*</td>
<td>3304 m</td>
<td>3106 m</td>
<td>1634 sh 1643 mb 1584 s</td>
<td>1340 s</td>
<td>422 s</td>
<td>287 w</td>
</tr>
</tbody>
</table>

\(s=\text{sharp}, \ m=\text{medium}, \ mb=\text{medium broad}, \ sh=\text{shoulder}, \ w=\text{weak}\); **Due to phenolic OH of Rte and R\(_2\)Te moieties; \*band not resolved due to overlapping of band \(v(\text{C=N})\)

Examination of the Schiff base (Sal-TMP) spectrum shows the presence of the hydrogen bonded conjugated- chelate ring system with its centre at ~2832 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.

Figure 1. Hydrogen bonding

Thus band disappear on chelation with aryltellurium(IV) chlorides. Hydrogen bond contributes to planarity of the molecule which helps in chelation with its centre at ~2832 cm\(^{-1}\). Also an intense ligand band at 1263 cm\(^{-1}\) (phenolic –C-O) in free ligand has shifted to higher frequency side in complexes. All these indicate that the hydroxyl group of salicylaldehyde of Schiff base is involved in coordination with tellurium.

In addition, the spectra of the Schiff base shown shoulder at 1636 cm\(^{-1}\) with slightly resolved weak band at 1633 cm\(^{-1}\) and sharp band at 1593 cm\(^{-1}\) assigned to \(v(\text{C=N})\) mode for vibration of azomethine group and \(v(\text{C=N})\) pyrimidine. For pyrimidine ring these shift in aryltellurium Schiff base complexes towards higher and lower values reflecting that ligand coordinate through nitrogen atom of azomethine and pyrimidine ring.

The medium intensity band at 3317 cm\(^{-1}\) and 3119 cm\(^{-1}\) due to \(v(\text{N-H})\) 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 270-295 cm\(^{-1}\) due to \(v(\text{Te-O})\) mode and medium to strong band in the range of 410-422 cm\(^{-1}\) due to \(v(\text{Te-N})\) mode 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 Sal-TMP involving azomethine nitrogen atom, phenolic oxygen after deprotonation and pyrimidine ring nitrogen giving rise to two- six and four membered chelate rings with the tellurium centre.
In order to identify the solution structure of Schiff base (Sal-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 10.92 δ ppm$^{76,85}$ in Schiff base due to presence of intramolecular hydrogen bonding$^{74}$ disappear on complexation indicating the involvement of phenolic oxygen in the coordination via deprotonation$^{76}$. The azomethine protons which resonate as a singlet at 10.02 δ ppm, the coordination of azomethine nitrogen to tellurium in the complexes are clearly demonstrated by a downfield shift of the peak$^{86}$.

| Table 3. $^1$H NMR spectral data of Schiff base (Sal-TMP) and complexes in DMSO-$d_6$ |
|---------------------------------|-----------------|
| Compound | Chemical Shift, δ ppm |
| Sal-TMP | 2.525(s, 2H, methylene), 3.551-3.745(s, 9H, –OCH$_3$), 5.672(s,1H, pyrimidine), 6.508(s, 2H, –NH$_2$), 7.526-8.169(m, 6H, aromatic proton), 10.021(s, 1H, azomethine), 10.921(s, 1H, Schiff base OH) |
| I | 2.539(s, 2H, methylene), 3.598-3.840(s, 12H, –OCH$_3$), 6.574(s, 1H, pyrimidine), 6.926(s, 2H, –NH$_2$), 7.383-7.522(m, 10H, aromatic proton), 10.209(s, 1H, azomethine) |
| II | 1.335(t, 3H, -OCH$_2$CH$_3$), 2.546(s, 2H, methylene), 3.963(q, 2H, –OCH$_2$CH$_3$), 3.515-3.875(s, 9H, –OCH$_3$), 6.540(s, 1H, pyrimidine), 6.950(s, 2H, –NH$_2$), 6.993-7.809(m, 10H, aromatic proton), 10.193(s, 1H, azomethine) |
| III | 2.548(s, 2H, methylene), 3.601-3.783(s, 9H, –OCH$_3$), 6.569(s,1H, pyrimidine), 6.914(s, 2H, –NH$_2$), 7.370-7.787(m, 10H, aromatic proton), 8.155(s, 1H, phenolic OH of RTe), 10.201(s, 1H, azomethine) |
| IV | 2.536(s, 2H, methylene), 2.527(s, 3H, -CH$_3$), 3.587-3.770(s, 9H, –OCH$_3$), 6.605(s, 1H, pyrimidine), 6.918(s, 2H, –NH$_2$), 7.051-7.671(m, 9H, aromatic proton), 8.251(s, 1H, phenolic OH of RTe), 10.239(s, 1H, azomethine) |
| V | 2.528(s, 2H, methylene), 3.673-3.877(s, 15H, –OCH$_3$), 6.516(s,1H, pyrimidine), 6.882(s, 2H, –NH$_2$), 6.910-7.804(m, 14H, aromatic proton), 10.186(s, 1H, azomethine) |
| VI | 1.363(t, 6H, –OCH$_2$CH$_3$), 2.531(s, 2H, methylene), 4.019(q, 4H, -OCH$_2$CH$_3$), 3.555-3.765(s, 9H, –OCH$_3$), 6.510(s, 1H, pyrimidine), 6.924(s, 2H, –NH$_2$), 7.524-7.805(m, 14H, aromatic proton), 10.216(s, 1H, azomethine) |
| VII | 2.545(s, 2H, methylene), 3.568-3.926(s, 9H, –OCH$_3$), 6.554(s, 1H, pyrimidine), 6.884(s, 2H, –NH$_2$), 7.488-7.678(m, 14H, aromatic proton), 8.249(s, 2H, phenolic OH of R$_2$Te), 10.238(s, 1H, azomethine) |
| VIII | 2.538(s, 2H, methylene), 2.529(s, 6H, -CH$_3$), 3.555-3.750(s, 9H, –OCH$_3$), 6.502(s, 1H, pyrimidine), 6.926(s, 2H, –NH$_2$), 7.126-7.868(m, 12H, aromatic proton), 8.149(s, 2H, phenolic OH of R$_2$Te), 10.239(s, 1H, azomethine) |

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

The characteristic downfield shifting of proton signal in all complexes observed in region 5.67 δ ppm is due to pyrimidine proton in Schiff base clearly indicate the coordination through pyrimidine nitrogen atom$^{87}$. The signal due to –NH proton is observed around 6.51 δ ppm which remain intact with slight variation in complexes is due to the proton bounded to nitrogen experience quadruple effect$^{87}$. Thus salicylidene-trimethoprim act as a tridentate –N, –N, –O chelating ligand in Sal-TMP,ArTeCl$_2$ and Sal-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 given below (Figure 2).
Biological Activity

The salicylidene-trimethoprim Schiff base (Sal-TMP) and newly synthesized aryltellurium(IV) Schiff base complexes were evaluated for their antimicrobial activity in vitro against Gram +ve bacteria (S. aureus ATCC 11632 and B. cereus MTCC 7350), Gram –ve bacteria (E. coli ATCC 35218, P. aeruginosa ATCC 23564, S. typhi ATCC 15499 and P. rettgeri DRDE) and fungal strains (A. niger, A. fumigates and A. flavus) by tube dilution method.\(^{88}\) Dilution of test and standard compounds were prepared double strength nutrient broth - I.P (Antibacterial) and Sabouraud Dextrose Broth –I.P. (Antifungal).\(^{89}\) The samples were incubated at 37±1 °C for 24 h (bacteria), 25±1 °C for 7 days (A. niger), 30 ±1 °C for 15 days (A. flavus), 35±1 °C for 72 h (A. fumigates) respectively and results were recorded in terms of MIC (The lowest concentration of test substances which inhibited values are presented in the Table 4.

The data show that the Sal-TMP complexes of aryltellurium(IV) exhibit more antimicrobial activity towards bacteria as compared to fungii. The antibacterial activity shows following trend.

Figure 2. Proposed structures of complexes

\[Ar = p\text{-methoxyphenyl, } p\text{-ethoxyphenyl, } p\text{-hydroxyphenyl and } 3\text{-methyl-4-hydroxyphenyl}\]
Sal-TMP.\textsubscript{Ar}TeCl \textgreater\ Sal-TMP.\textsubscript{Ar}TeCl\textsubscript{2} \approx\ Sal-TMP Schiff base

Sal-TMP.\textsubscript{Ar}TeCl and Sal-TMP.\textsubscript{Ar}TeCl\textsubscript{2} complexes have activity towards \textit{S. typhi} and more effectively against \textit{B. cereus} but Schiff base does not show activity against these bacterial strains. Schiff base and its complexes show almost similar activity against fungal strains.

### Table 4. Minimum Inhibitory Concentration, MIC, µg/mL; (-) Resistant

<table>
<thead>
<tr>
<th>Compound</th>
<th>Bacteria strains</th>
<th>Fungal strains</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>\textit{S. aureus} (ATCC 11632)</td>
<td>\textit{S. typhi} (ATCC 15499)</td>
</tr>
<tr>
<td>Sal-TMP</td>
<td>2.5 - 1.25 5.0 -</td>
<td>0.625 5.0 -</td>
</tr>
<tr>
<td>I</td>
<td>2.5 - 1.25 5.0 -</td>
<td>0.625 5.0 -</td>
</tr>
<tr>
<td>II</td>
<td>5.0 - 2.5 10 5.0 1.25</td>
<td>2.5 - 20 5.0 1.25</td>
</tr>
<tr>
<td>III</td>
<td>1.25 2.5 1.25 5.0 1.25</td>
<td>5.0 20 5.0 1.25</td>
</tr>
<tr>
<td>IV</td>
<td>1.25 2.5 1.25 5.0 1.25</td>
<td>5.0 20 5.0 1.25</td>
</tr>
<tr>
<td>V</td>
<td>1.25 2.5 1.25 5.0 1.25</td>
<td>5.0 20 5.0 1.25</td>
</tr>
<tr>
<td>VI</td>
<td>1.25 2.5 1.25 5.0 1.25</td>
<td>5.0 20 5.0 1.25</td>
</tr>
<tr>
<td>VII</td>
<td>1.25 2.5 1.25 5.0 1.25</td>
<td>5.0 20 5.0 1.25</td>
</tr>
<tr>
<td>VIII</td>
<td>2.5 - 1.25 5.0 -</td>
<td>0.625 5.0 -</td>
</tr>
</tbody>
</table>

### Conclusion

 Aryltellurium(IV) and diaryltellurium(IV) dichlorides upon reaction with Schiff base(Sal-TMP) derived from salicylaldehyde and trimethoprim yield new complexes of tellurium(IV). The synthesized complexes were characterized by elemental analyses, conductance measurement, IR and \textsuperscript{1}H NMR spectral studies. The analytical data suggest that the Sal-TMP Schiff base complexes have 1:1 stoichiometry. The Schiff bases (Sal-TMP) in these complexes functions as a uninegative tridentate ligand through azomethine nitrogen, phenolic oxygen after deprotonation and pyrimidine ring nitrogen atoms. Based on these studies, distorted octahedral geometry with two chelating rings has been assigned to these complexes. The complexes have been observed to possess substantial antimicrobial activity especially against bacteria.

### Acknowledgement

The authors are grateful to M. D. University, Rohtak for providing the necessary facilities. One of the authors (Deepak) is also thankful to UGC New Delhi for providing fellowship. We also thank SAIF, Panjab University Chandigarh for providing the CHN analyses and spectral data.

### References

42. Berg M C, Diss Abstr Int., 1972, 33, 2982.
46. Garad M V, Polyhedron, 1985, 4(8), 1353-1355; DOI:10.1016/S0277-5387(00)86963-6
63. Geary W J, Coord Chem Rev., 1971, 7(1), 81-122; DOI:10.1016/S0010-8554(00)80009-0
89. Pharmacopoeia of India, Volume 1, Controller of Publications, Ministry of Health Department, Government of India, New Delhi, 2007, 37.
Synthesis, Spectral and Biological Studies of Some Salicylidene-Trimethoprim Schiff Base Complexes of Aryltellurium(IV)

DEEPAK, K. K. VERMA and SAPANA GARG*

Department of Chemistry, Maharshi Dayanand University, Rohtak-124001, India
sapanagarg1511@gmail.com

Received 14 February 2017 / Accepted 2 March 2017

Abstract: A novel monobasic tridentate Schiff base salicylidene-trimethoprim, Sal-TMP, synthesized from trimethoprim and salicylaldehyde, form stable complexes with aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides of the type Sal-TMP.ArTeCl₂ and Sal-TMP.Ar₂TeCl₂ (where Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl). These have been characterized by elemental analyses, molar conductance, 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 hexacoordinated tellurium(IV) complexes. The complexes have also been screened for their antimicrobial activities against various bacteria and fungi organisms.

Keywords: Salicylidene-trimethoprim Schiff base, Aryltellurium(IV), Diaryltellurium(IV), Antibacterial, Antifungal activities

Introduction

Trimethoprim and its derivatives are broad spectrum antimicrobial agents with anti-parasitic activity¹-⁶ and were first described by Roth and coworker⁵. Schiff bases, also known as azomethine due to presence of –C=N– group, play important role in biological system, such as anticancer⁷-¹², antibacterial¹³-¹⁵, antiviral¹⁶-¹⁸, antifungal¹⁹-²¹ and other biological properties²²-²⁷ and also have been extensively used as ligands in coordination chemistry because of their excellent donor abilities as chelating agent²⁸-³². Medicinal chemists have reported new derivatives of trimethoprim(TMZ)³³-³⁵ including the Schiff base derived from salicylaldehyde²⁴,³⁶,³⁷.

Also, aryltellurium(IV) chlorides are known³⁸-⁵⁴ 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, RTeCl₃ and diaryltellurium(IV) dichlorides, R₂TeCl₂ with salicylidene-trimethoprim Schiff base(Sal-TMP).
Experimental

All preparations were carried out under dry N\textsubscript{2} atmosphere and the solvents used were purified by standard method\textsuperscript{55,56} 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 on a ThermoFinnigan CHNS analyser. Conductivity was measured in DMSO at 25±2°C with dip type conductivity cell on a microprocessor based conductivity bridge type MICROsil.

IR (4000-400 cm\textsuperscript{-1}) and far IR (400-50 cm\textsuperscript{-1}) spectra were recorded in KBr/polyethylene pellets on a FT-Infrared spectrophotometer model RZX (Perkin Elmer) at SAIF, Panjab University Chandigarh. Proton magnetic resonance spectra were recorded in DMSO-d\textsubscript{6} using TMS as an internal reference on BRUKER AVANCE II 400 NMR spectrometer. The antimicrobial screening was carried out by tube dilution method at Department of Pharmaceutical Sciences, M. D. University, Rohtak, India.

Preparation of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

\textit{p-Methoxyphenyltellurium(IV) trichloride}\textsuperscript{57,58}, \textit{bis(p-methoxyphenyl)tellurium(IV) dichloride}\textsuperscript{58,59}, \textit{p-ethoxyphenyltellurium (IV) trichloride}\textsuperscript{60}, \textit{bis(p-ethoxyphenyl)tellurium dichloride}\textsuperscript{60}, \textit{p-hydroxyphenyltellurium(IV) trichloride}\textsuperscript{61}, \textit{bis(p-hydroxyphenyl) tellurium(IV) dichloride}\textsuperscript{61}, \textit{3-methyl-4-hydroxyphenyltellurium(IV) trichloride}\textsuperscript{62} and \textit{bis(3-methyl-4-hydroxyphenyl)tellurium(IV) dichloride}\textsuperscript{62} were prepared by the reactions of TeCl\textsubscript{4} with anisole, phenetole, phenol, o-cresol respectively, by the methods reported in the literature\textsuperscript{57-62}.

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP)

Equimolar quantity of saturated methanolic solution of drug and salicylaldehyde were mixed thoroughly. To this mixture 0.1% methanolic KOH was added to adjust the pH of the solution between 7-8 and was refluxed for 2 hours. A clear yellowish-green 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\textsubscript{2}O\textsubscript{10} until further use. Yield = 80\%, M.pt.(decomp.)=188-190°C. Analysis (Calculated) C\textsubscript{21}H\textsubscript{22}N\textsubscript{4}O\textsubscript{4}: C(63.95), H(5.62) and N(14.20); Found: C(63.50), H(5.27) and N(13.99).

Preparation of salicylidene-trimethoprim complexes of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

Aryltellurium(IV) trichlorides, ArTeCl\textsubscript{3} and diaryltellurium(IV) dichlorides Ar\textsubscript{2}TeCl\textsubscript{2} (Ar= p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl), when reacted with sodium salt of salicylidene-trimethoprim in equimolar ratio, yield Sal-TMP.ArTeCl\textsubscript{3} and Sal-TMP.Ar\textsubscript{2}TeCl 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 P\textsubscript{2}O\textsubscript{10}. 

Results and Discussion

TeCl₄ when heated with anisole⁵⁷-⁵⁹, phenetole⁶⁰, phenol⁶¹, o-cresol⁶² (Ar-H) appears to undergo Friedel-Crafts type condensation reaction whereby TeCl₄⁺ 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.

\[
\text{Ar-H} + \text{TeCl}_4 \rightarrow \text{ArTeCl}_3 + \text{HCl} \quad (1)
\]

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

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP) by the reaction of trimethoprim drug and salicylaldehyde can be represented by following equations.

\[
\begin{align*}
\text{H} & \quad \text{O} \\
\text{OH} & \quad \text{H}_2\text{N} \quad \text{NH}_2 \\
\text{OCH}_3 & \quad \text{OCH}_3 \\
\text{Sal-TMP} + \text{ArTeCl}_3 & \xrightarrow{\text{Na/CH}_3\text{OH}} \text{(Sal-TMP).ArTeCl}_2 \\
& \quad \text{NaCl} \\
\text{Sal-TMP} + \text{Ar}_2\text{TeCl}_2 & \xrightarrow{\text{Na/CH}_3\text{OH}} \text{(Sal-TMP).Ar}_2\text{TeCl}_2 \\
& \quad \text{-NaCl}
\end{align*}
\]

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

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.

Conductance studies

Molar conductance (\(\Lambda_M\)) data for the complexes in DMSO are complied in Table 1. The \(\Lambda_M\) value at ca. 10⁻³ M for aryltellurium(IV) complexes in DMSO lie in the range 27.36-91.83 S cm² mol⁻¹ which predict the non electrolyte to 1:1 electrolyte⁶³,⁶⁴ type behaviour of these complexes in DMSO, probably due to ionization into ArTeCl₂.Sal-TMP⁺/Ar₂Te.Sal-TMP⁺ and Cl⁻ in DMSO. This conductance behaviour of tellurium(IV) salicylidene-trimethoprim Schiff base complexes is different from those of transition metal complexes⁶⁵, which are reported to be non-electrolytes. The higher \(\Lambda_M\) values for some complexes may be due to steric factors and donor behaviour of DMSO to result in probable dissociation into solvated cation and \(\text{L}^-\) along with \(\text{Cl}^-\) in DMSO.

Infrared spectra

The IR data of Schiff base and its tellurium(IV) complexes are listed in Table 2. The spectra of Sal-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 ArTeCl₂/Ar₂TeCl₂.
Table 1. Analytical data, molar conductance and physical properties of salicylidene-trimethoprim Schiff base (Sal-TMP) complexes of tellurium(IV)

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Complex (Ar)</th>
<th>Empirical formula (Formula Wt.)</th>
<th>Colour (Yield, %)</th>
<th>M. Pt. °C dec.</th>
<th>Analyses % Found (Calculated)</th>
<th>$\Lambda_M$ at ca. $10^{-3}$ M $S$ cm$^2$ mol$^{-1}$ in DMSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schiff Base</td>
<td>Sal-TMP</td>
<td>C$<em>{21}$H$</em>{22}$N$<em>{4}$O$</em>{4}$</td>
<td>Yellowish-green (80)</td>
<td>188-190</td>
<td>63.50 (63.95) 5.27 (5.62) 13.99 (14.20) - - -</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>(Sal-TMP).ArTeCl$_2$ (p-methoxyphenyl)</td>
<td>C$<em>{25}$H$</em>{26}$Cl$<em>2$N$</em>{4}$O$_5$Te (699.05)</td>
<td>Light cream (92)</td>
<td>230-232</td>
<td>47.88 (48.11) 3.99 (4.04) 7.75 (8.01) 18.07 (18.24) 9.89 (10.01)</td>
<td>53.19</td>
</tr>
<tr>
<td>II</td>
<td>(Sal-TMP).ArTeCl$_2$ (p-ethoxyphenyl)</td>
<td>C$<em>{25}$H$</em>{26}$Cl$<em>2$N$</em>{4}$O$_5$Te (713.08)</td>
<td>Cream (85)</td>
<td>258-260</td>
<td>48.12 (48.85) 3.87 (4.24) 7.52 (7.86) 17.38 (17.89) 9.52 (9.81)</td>
<td>52.88</td>
</tr>
<tr>
<td>III</td>
<td>(Sal-TMP).ArTeCl$_2$ (p-hydroxyphenyl)</td>
<td>C$<em>{25}$H$</em>{26}$Cl$<em>2$N$</em>{4}$O$_5$Te (685.03)</td>
<td>Dark cream (94)</td>
<td>208-210</td>
<td>46.78 (47.34) 3.50 (3.83) 7.88 (8.18) 18.28 (18.63) 9.98 (10.21)</td>
<td>55.73</td>
</tr>
<tr>
<td>IV</td>
<td>(Sal-TMP).ArTeCl$_2$ (3-methyl-4-hydroxyphenyl)</td>
<td>C$<em>{29}$H$</em>{28}$Cl$<em>2$N$</em>{4}$O$_5$Te (699.05)</td>
<td>Light cream (80)</td>
<td>198-200</td>
<td>47.84 (48.11) 3.84 (4.04) 7.80 (8.01) 18.15 (18.24) 9.85 (10.01)</td>
<td>58.68</td>
</tr>
<tr>
<td>V</td>
<td>(Sal-TMP).Ar$_2$TeCl (p-methoxyphenyl)</td>
<td>C$<em>{35}$H$</em>{35}$Cl$<em>4$N$</em>{4}$O$_6$Te (770.73)</td>
<td>Pale yellow (84)</td>
<td>130-132</td>
<td>53.84 (54.54) 4.31 (4.58) 7.11 (7.27) 16.43 (16.56) 4.42 (4.60)</td>
<td>91.83</td>
</tr>
<tr>
<td>VI</td>
<td>(Sal-TMP).Ar$_2$TeCl (p-ethoxyphenyl)</td>
<td>C$<em>{35}$H$</em>{35}$Cl$<em>4$N$</em>{4}$O$_6$Te (798.78)</td>
<td>Light yellow (86)</td>
<td>150-152</td>
<td>54.84 (55.63) 4.53 (4.92) 6.84 (7.01) 15.50 (15.97) 4.30 (4.44)</td>
<td>35.90</td>
</tr>
<tr>
<td>VII</td>
<td>(Sal-TMP).Ar$_2$TeCl (p-hydroxyphenyl)</td>
<td>C$<em>{35}$H$</em>{35}$Cl$<em>4$N$</em>{4}$O$_6$Te (742.68)</td>
<td>Red (89)</td>
<td>146-148</td>
<td>52.84 (53.37) 4.01 (4.21) 7.27 (7.54) 16.89 (17.18) 4.52 (4.77)</td>
<td>36.00</td>
</tr>
<tr>
<td>VIII</td>
<td>(Sal-TMP).Ar$_2$TeCl (3-methyl-4-hydroxyphenyl)</td>
<td>C$<em>{35}$H$</em>{35}$Cl$<em>4$N$</em>{4}$O$_6$Te (770.73)</td>
<td>Brown (78)</td>
<td>140-142</td>
<td>53.80 (54.54) 4.34 (4.58) 7.09 (7.27) 16.45 (16.56) 4.32 (4.60)</td>
<td>27.36</td>
</tr>
</tbody>
</table>

Values of $\Lambda_M$ reported$^{61,64}$ for 1:1 electrolytes in DMSO=50-70 S cm$^2$ mol$^{-1}$
**Table 2.** Important infrared absorption bands (cm\(^{-1}\)) of Schiff base (Sal-TMP) and complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>(v_{(O-H)})</th>
<th>(v_{(N-H)})</th>
<th>(v_{(C=N)})</th>
<th>(v_{(C=N)}) pyrimidine</th>
<th>(v_{(C=O)})</th>
<th>(v_{(Te-N)})</th>
<th>(v_{(Te-O)})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2836 w</td>
<td>3317 m</td>
<td>3199 m</td>
<td>1636 s</td>
<td>1633 w</td>
<td>1593 s</td>
<td>1263 s</td>
</tr>
<tr>
<td>I</td>
<td>-</td>
<td>3323 m</td>
<td>3184 m</td>
<td>1674 mb</td>
<td>1644 mb</td>
<td>1587 s</td>
<td>1341 s</td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>3323 m</td>
<td>3170 m</td>
<td>1647 mb</td>
<td><strong>1586 s</strong></td>
<td>1304 s</td>
<td>420 m</td>
</tr>
<tr>
<td>III</td>
<td>3405 m*</td>
<td>3323 m</td>
<td>3150 m</td>
<td>1674 mb</td>
<td>1641 mb</td>
<td>1587 s</td>
<td>1341 s</td>
</tr>
<tr>
<td>IV</td>
<td>3398 m*</td>
<td>3319 m</td>
<td>3172 m</td>
<td>1652 mb</td>
<td>1649 mb</td>
<td>1587 s</td>
<td>1333 s</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>3325 m</td>
<td>3178 m</td>
<td>1645 sh</td>
<td><strong>1587 s</strong></td>
<td>1333 s</td>
<td>416 s</td>
</tr>
<tr>
<td>VI</td>
<td>-</td>
<td>3320 m</td>
<td>3158 m</td>
<td>1640 sh</td>
<td><strong>1590 s</strong></td>
<td>1331 s</td>
<td>410 m</td>
</tr>
<tr>
<td>VII</td>
<td>3401 w*</td>
<td>3324 m</td>
<td>3168 m</td>
<td>1674 mb</td>
<td>1643 mb</td>
<td>1584 s</td>
<td>1340 s</td>
</tr>
<tr>
<td>VIII</td>
<td>3463 w*</td>
<td>3304 m</td>
<td>3106 m</td>
<td>1634 sh</td>
<td>1643 mb</td>
<td>1584 s</td>
<td>1340 s</td>
</tr>
</tbody>
</table>

s=sharp, m=medium, mb=medium broad, sh=shoulder, w=weak, "Due to phenolic OH of Rte and R\(_2\)Te moieties; **band not resolved due to overlapping of band \(v_{(C=N)}\)"

Examination of the Schiff base (Sal-TMP) spectrum shows the presence of the hydrogen bonded conjugated- chelate ring system\(^{66-68}\) with its centre at \(\sim 2832\) cm\(^{-1}\). Thus intramolecular H-bonding is occurring by means of the formation of a quasi six-membered ring involving OH ----N=C bond.

![Figure 1](image.png)

**Figure 1.** Hydrogen bonding

Thus band disappear on chelation with aryltellurium(IV) chlorides\(^ {69}\). Hydrogen bond contributes to planarity of the molecule which helps in chelation\(^ {70}\). Also an intense ligand band at 1263 cm\(^{-1}\) (phenolic –C=O) in free ligand has shifted to higher frequency side in complexes. All these indicate that the hydroxyl group of salicylaldehyde of Schiff base is involved in coordination with tellurium\(^ {71-73}\).

In addition, the spectra of the Schiff base shown shoulder at 1636 cm\(^{-1}\) with slightly resolved weak band at 1633 cm\(^{-1}\) and sharp band at 1593 cm\(^{-1}\) assigned to \(v_{(C=N)}\) mode for vibration of azomethine group\(^ {7,4,65,74-76}\) and \(v_{(C=N)\text{pyrim}}\). For pyrimidine ring\(^ {4,77}\) these shift in aryltellurium Schiff base complexes towards higher and lower value\(^ {74-79}\) reflecting that ligand coordinate through nitrogen atom of azomethine and pyrimidine ring.

The medium intensity band at 3317 cm\(^{-1}\) and 3119 cm\(^{-1}\) due to \(v_{(N-H)}\) 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 270-295 cm\(^{-1}\) due to \(v_{(Te-O)}\)\(^ {80-83}\) mode and medium to strong band in the range of 410-422 cm\(^{-1}\) due to \(v_{(Te-N)}\) mode\(^ {84}\) 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 Sal-TMP involving azomethine nitrogen atom, phenolic oxygen after deprotonation and pyrimidine ring nitrogen giving rise to two-six and four membered chelate rings with the tellurium centre.
In order to identify the solution structure of Schiff base (Sal-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 10.92 $\delta$ ppm$^{76,85}$ in Schiff base due to presence of intramolecular hydrogen bonding$^{74}$ disappear on complexation indicating the involvement of phenolic oxygen in the coordination via deprotonation$^{76}$. The azomethine protons which resonate as a singlet at 10.02 $\delta$ ppm, the coordination of azomethine nitrogen to tellurium in the complexes are clearly demonstrated by a downfield shift of the peak$^{86}$.

**Table 3.** $^1$H NMR spectral data of Schiff base (Sal-TMP) and complexes in DMSO-d$_6$

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical Shift, $\delta$ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2.525(s, 2H, methylene), 3.551-3.745(s, 9H, -OCH$_3$), 5.672(s,1H, pyrimidine), 6.508(s, 2H, -NH$_2$), 7.526-8.169(m, 6H, aromatic proton), 10.021(s, 1H, azomethine), 10.921(s, 1H, Schiff base OH)</td>
</tr>
<tr>
<td>I</td>
<td>2.539(s, 2H, methylene), 3.598-3.840(s, 12H, -OCH$_3$), 6.574(s, 1H, pyrimidine), 6.926(s, 2H, -NH$_2$), 7.383-7.522(m, 10H, aromatic proton), 10.209(s, 1H, azomethine)</td>
</tr>
<tr>
<td>II</td>
<td>1.335(t, 3H, -OCH$_2$CH$_3$), 2.546(s, 2H, methylene), 3.963(q, 2H, -OCH$_2$CH$_3$), 3.515-3.875(s, 9H, -OCH$_3$), 6.540(s, 1H, pyrimidine), 6.950(s, 2H, -NH$_2$), 6.993-7.809(m, 10H, aromatic proton), 10.193(s, 1H, azomethine)</td>
</tr>
<tr>
<td>III</td>
<td>2.548(s, 2H, methylene), 3.601-3.783(s, 9H, -OCH$_3$), 6.569(s,1H, pyrimidine), 6.914(s, 2H, -NH$_2$), 7.370-7.787(m, 10H, aromatic proton), 8.155(s, 1H, phenolic OH of RTe), 10.201(s, 1H, azomethine)</td>
</tr>
<tr>
<td>IV</td>
<td>2.536(s, 2H, methylene), 2.527(s, 3H, -CH$_3$), 3.587-3.770(s, 9H, -OCH$_3$), 6.605(s, 1H, pyrimidine), 6.918(s, 2H, -NH$_2$), 7.051-7.671(m, 9H, aromatic proton), 8.251(s, 1H, phenolic OH of RTe), 10.239(s, 1H, azomethine)</td>
</tr>
<tr>
<td>V</td>
<td>2.528(s, 2H, methylene), 3.673-3.877(s, 15H, -OCH$_3$), 6.516(s,1H, pyrimidine), 6.882(s, 2H, -NH$_2$), 6.910-7.804(m, 14H, aromatic proton), 10.186(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VI</td>
<td>1.363(t, 6H, -OCH$_2$CH$_3$), 2.531(s, 2H, methylene), 4.019(q, 4H, -OCH$_2$CH$_3$), 3.555-3.765(s, 9H, -OCH$_3$), 6.510(s, 1H, pyrimidine), 6.924(s, 2H, -NH$_2$), 7.524-7.805(m, 14H, aromatic proton), 10.216(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VII</td>
<td>2.545(s, 2H, methylene), 3.568-3.926(s, 9H, -OCH$_3$), 6.554(s, 1H, pyrimidine), 6.884(s, 2H, -NH$_2$), 7.488-7.678(m, 14H, aromatic proton), 8.249(s, 2H, phenolic OH of R$_2$Te), 10.238(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VIII</td>
<td>2.538(s, 2H, methylene), 2.529(s, 6H, -CH$_3$), 3.555-3.750(s, 9H, -OCH$_3$), 6.502(s, 1H, pyrimidine), 6.926(s, 2H, -NH$_2$), 7.126-7.868(m, 12H, aromatic proton), 8.149(s, 2H, phenolic OH of R$_2$Te), 10.239(s, 1H, azomethine)</td>
</tr>
</tbody>
</table>

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

The characteristic downfield shifting of proton signal in all complexes observed in region 5.67 $\delta$ ppm is due to pyrimidine proton in Schiff base clearly indicate the coordination through pyrimidine nitrogen atom$^{87}$. The signal due to –NH proton is observed around 6.51 $\delta$ ppm which remain intact with slight variation in complexes is due to the proton bounded to nitrogen experience quadruple effect$^{87}$. Thus salicylidene-trimethoprim act as a tridentate –N, –N, –O chelating ligand in Sal-TMP,ArTeCl$_2$ and Sal-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 given below (Figure 2).
Biological Activity

The salicylidene-trimethoprim Schiff base (Sal-TMP) and newly synthesized aryltellurium(IV) Schiff base complexes were evaluated for their antimicrobial activity in vitro against Gram +ve bacteria (S. aureus ATCC 11632 and B. cereus MTCC 7350), Gram –ve bacteria (E. coli ATCC 35218, P. aeruginosa ATCC 23564, S. typhi ATCC 15499 and P. rettgeri DRDE) and fungal strains (A. niger, A. fumigates and A. flavus) by tube dilution method. Dilution of test and standard compounds were prepared double strength nutrient broth- I.P (Antibacterial) and Sabouraud Dextrose Broth – I.P (Antifungal). The samples were incubated at 37±1 °C for 24 h (bacteria), 25±1 °C for 7 days (A. niger), 30 ±1 °C for 15 days (A. flavus), 35±1 °C for 72 h (A. fumigates) respectively and results were recorded in terms of MIC (The lowest concentration of test substances which inhibited values are presented in the Table 4).

The data show that the Sal-TMP complexes of aryltellurium(IV) exhibit more antimicrobial activity towards bacteria as compared to fungi. The antibacterial activity shows following trend.
Sal-TMP·Ar₂TeCl > Sal-TMP·ArTeCl₂ ≈ Sal-TMP Schiff base

Sal-TMP·Ar₂TeCl and Sal-TMP·ArTeCl₂ complexes have activity towards S. typhi and more effectively against B. cereus but Schiff base does not show activity against these bacterial strains. Schiff base and its complexes show almost similar activity against fungal strains.

Table 4. Minimum Inhibitory Concentration, MIC, µg/mL; (-) Resistant

<table>
<thead>
<tr>
<th>Compound</th>
<th>Bacteria strains</th>
<th>Fungal strains</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S. aureus (ATCC 11632)</td>
<td>S. typhi (ATCC 15499)</td>
</tr>
<tr>
<td>Sal-TMP</td>
<td>2.5</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>2.5</td>
<td>-</td>
</tr>
<tr>
<td>II</td>
<td>5.0</td>
<td>-</td>
</tr>
<tr>
<td>III</td>
<td>2.5</td>
<td>1.25</td>
</tr>
<tr>
<td>IV</td>
<td>1.25</td>
<td>2.5</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>2.5</td>
</tr>
<tr>
<td>VI</td>
<td>1.25</td>
<td>2.5</td>
</tr>
<tr>
<td>VII</td>
<td>1.25</td>
<td>-</td>
</tr>
<tr>
<td>VIII</td>
<td>2.5</td>
<td>-</td>
</tr>
</tbody>
</table>

Conclusion

Aryltellurium(IV) and diaryltellurium(IV) dichlorides upon reaction with Schiff base(Sal-TMP) derived from salicylaldehyde and trimethoprim yield new complexes of tellurium(IV). The synthesized complexes were characterized by elemental analyses, conductance measurement, IR and ¹H NMR spectral studies. The analytical data suggest that the Sal-TMP Schiff base complexes have 1:1 stoichiometry. The Schiff bases (Sal-TMP) in these complexes functions as a uninegative tridentate ligand through azomethine nitrogen, phenolic oxygen after deprotonation and pyrimidine ring nitrogen atoms. Based on these studies, distorted octahedral geometry with two chelating rings has been assigned to these complexes. The complexes have been observed to possess substantial antimicrobial activity especially against bacteria.

Acknowledgement

The authors are grateful to M. D. University, Rohtak for providing the necessary facilities. One of the authors (Deepak) is also thankful to UGC New Delhi for providing fellowship. We also thank SAIF, Panjab University Chandigarh for providing the CHN analyses and spectral data.

References

42. Berg M C, Diss Abstr Int., 1972, 33, 2982.
46. Garad M V, Polyhedron, 1985, 4(8), 1353-1355; DOI:10.1016/S0277-5387(00)86963-6
71. Mishra A P and Soni M, Metal Based Drugs, 2008, 71, 243; DOI:10.1155/2008/875410
80. Verma K K, Soni D and verma, Phosphorus, Sulfur Silicon, 2000, 166(1), 231-241; DOI:10.1080/10426500008076544
89. Pharmacopoeia of India, Volume 1, Controller of Publications, Ministry of Health Department, Government of India, New Delhi, 2007, 37.
Synthesis, Spectral and Biological Studies of Some Salicylidene-Trimethoprim Schiff Base Complexes of Aryltellurium(IV)

DEEPAK, K. K. VERMA and SAPANA GARG

Department of Chemistry, Maharshi Dayanand University, Rohtak-124001, India
sapanagarg1511@gmail.com

Received 14 February 2017 / Accepted 2 March 2017

Abstract: A novel monobasic tridentate Schiff base salicylidene-trimethoprim, Sal-TMP, synthesized from trimethoprim and salicylaldehyde, form stable complexes with aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides of the type Sal-TMP.ArTeCl₂ and Sal-TMP.Ar₂TeCl₂ (where Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl). These have been characterized by elemental analyses, molar conductance, 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. The complexes have also been screened for their antimicrobial activities against various bacteria and fungi organisms.

Keywords: Salicylidene-trimethoprim Schiff base, Aryltellurium(IV), Diaryltellurium(IV), Antibacterial, Antifungal activities

Introduction

Trimethoprim and its derivatives are broad spectrum antimicrobial agents with anti-parasitic activity and were first described by Roth and coworker. Schiff bases, also known as azomethine due to presence of –C=N– group, play important role in biological system, such as anticancer, antibacterial, antiviral, antifungal and other biological properties and also 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. 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, RTeCl₃ and diaryltellurium(IV) dichlorides, R₂TeCl₂ with salicylidene-trimethoprim Schiff base(Sal-TMP).
Experimental

All preparations were carried out under dry N$_2$ atmosphere and the solvents used were purified by standard method$^{55,56}$ 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 on a ThermoFinnigan CHNS analyser. Conductivity was measured in DMSO at 25±2 °C with dip type conductivity cell on a microprocessor based conductivity bridge type MICROSL.

IR (4000-400 cm$^{-1}$) and far IR (400-50 cm$^{-1}$) spectra were recorded in KBr/polyethylene pellets on a FT-Infrared 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. The antimicrobial screening was carried out by tube dilution method at Department of Pharmaceutical Sciences, M. D. University, Rohtak, India.

Preparation of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

$p$-Methoxyphenyltellurium(IV) trichloride$^{57,58}$, bis($p$-methoxyphenyl)tellurium(IV) dichloride$^{58,59}$, $p$-ethoxyphenyltellurium(IV) trichloride$^{60}$, bis($p$-ethoxyphenyl)tellurium dichloride$^{60}$, $p$-hydroxyphenyltellurium(IV) trichloride$^{61}$, bis($p$-hydroxyphenyl) tellurium(IV) dichloride$^{61}$, 3-methyl-4-hydroxyphenyltellurium(IV) trichloride$^{62}$ and bis(3-methyl-4-hydroxyphenyl)tellurium(IV) dichloride$^{62}$ were prepared by the reactions of TeCl$_4$ with anisole, phenetole, phenol, $o$- cresol respectively, by the methods reported in the literature$^{57-62}$.

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP)

Equimolar quantity of saturated methanolic solution of drug and salicylaldehyde were mixed thoroughly. To this mixture 0.1% methanolic KOH was added to adjust the pH of the solution between 7-8 and was refluxed for 2 hours. A clear yellowish-green 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$_4$O$_{10}$ until further use. Yield = 80%, M.pt.(decomp.) = 188-190 °C. Analysis (Calculated) C$_{21}$H$_{22}$N$_4$O$_4$: C(63.95), H(5.62) and N(14.20); Found: C(63.50), H(5.27) and N(13.99).

Preparation of salicylidene-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 salicylidene-trimethoprim in equimolar ratio, yield Sal-TMP.ArTeCl$_3$ and Sal-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 P$_4$O$_{10}$. 
Results and Discussion

TeCl₄ when heated with anisole⁵⁷-⁵⁹, phenetole⁶⁰, phenol⁶¹, o-cresol⁶² (Ar-H) appears to undergo Friedel-Crafts type condensation reaction whereby TeCl₄⁺ 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.

\[
\text{Ar-H + TeCl}_4 \rightarrow \text{ArTeCl}_3 + \text{HCl} \\
2 \text{Ar-H + TeCl}_4 \rightarrow \text{Ar}_2\text{TeCl}_2 + 2 \text{HCl}
\]

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP) by the reaction of trimethoprim drug and salicylaldehyde can be represented by following equations.

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

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

All the tellurium(IV) complexes are coloured, crystalline solids, stable at room temperature and non-hygrosopic 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.

Conductance studies

Molar conductance \( (\Lambda_M) \) data for the complexes in DMSO are complied in Table 1. The \( \Lambda_M \) value at ca. 10⁻³ M for aryltellurium(IV) complexes in DMSO lie in the range 27.36-91.83 S cm² mol⁻¹ which predict the non electrolyte to 1:1 electrolyte⁶³,⁶⁴ type behaviour of these complexes in DMSO, probably due to ionization into ArTeCl₂Sal-TMP⁺/Ar₂TeSal-TMP⁺ and Cl⁻ in DMSO. This conductance behaviour of tellurium(IV) salicylidene-trimethoprim Schiff base complexes is different from those of transition metal complexes⁶⁵, which are reported to be non-electrolytes. The higher \( \Lambda_M \) values for some complexes may be due to steric factors and donor behaviour of DMSO to result in probable dissociation into solvated cation and L⁻ along with Cl⁻ in DMSO.

Infrared spectra

The IR data of Schiff base and its tellurium(IV) complexes are listed in Table 2. The spectra of Sal-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 ArTeCl₃/Ar₂TeCl₂.
Table 1. Analytical data, molar conductance and physical properties of salicylidene-trimethoprim Schiff base (Sal-TMP) complexes of tellurium(IV)

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Complex (Ar)</th>
<th>Empirical formula (Formula Wt.)</th>
<th>Colour (Yield, %)</th>
<th>M. Pt. °C dec.</th>
<th>Analyses % Found (Calculated)</th>
<th>( \Lambda_M ) at ca. 10(^{-3}) M S cm(^2) mol(^{-1}) in DMSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schiff Base</td>
<td>Sal-TMP</td>
<td>( \text{C}<em>{21}\text{H}</em>{22}\text{N}<em>{4}\text{O}</em>{4} )</td>
<td>Yellowish–green (80)</td>
<td>188-190</td>
<td>63.50 (63.95) 5.27 (5.62) 13.99 (14.20) - - -</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>(Sal-TMP).ArTeCl(_2) ( (p)-methoxyphenyl)</td>
<td>( \text{C}<em>{28}\text{H}</em>{28}\text{Cl}<em>{2}\text{N}</em>{4}\text{O}_{5}\text{Te} ) ( (699.05) )</td>
<td>Light cream (92)</td>
<td>230-232</td>
<td>47.88 (48.11) 3.99 (4.04) 7.75 (8.01) 18.07 (18.24) (10.01)</td>
<td>53.19</td>
</tr>
<tr>
<td>II</td>
<td>(Sal-TMP).ArTeCl(_2) ( (p)-ethoxyphenyl)</td>
<td>( \text{C}<em>{29}\text{H}</em>{30}\text{Cl}<em>{2}\text{N}</em>{4}\text{O}_{5}\text{Te} ) ( (713.08) )</td>
<td>Cream (85)</td>
<td>258-260</td>
<td>48.12 (48.85) 3.87 (4.24) 7.52 (7.86) 17.38 (17.89) (9.81)</td>
<td>52.88</td>
</tr>
<tr>
<td>III</td>
<td>(Sal-TMP).ArTeCl(_2) ( (p)-hydroxyphenyl)</td>
<td>( \text{C}<em>{27}\text{H}</em>{26}\text{Cl}<em>{2}\text{N}</em>{4}\text{O}_{5}\text{Te} ) ( (685.03) )</td>
<td>Dark cream (94)</td>
<td>208-210</td>
<td>46.78 (47.34) 3.50 (3.83) 7.88 (8.18) 18.28 (18.63) (10.21)</td>
<td>55.73</td>
</tr>
<tr>
<td>IV</td>
<td>(Sal-TMP).ArTeCl(_2) ( (3)-methyl-4-hydroxyphenyl)</td>
<td>( \text{C}<em>{28}\text{H}</em>{28}\text{Cl}<em>{2}\text{N}</em>{4}\text{O}_{5}\text{Te} ) ( (699.05) )</td>
<td>Light cream (80)</td>
<td>198-200</td>
<td>47.58 (48.11) 3.84 (4.04) 7.80 (8.01) 18.15 (18.24) (10.01)</td>
<td>58.68</td>
</tr>
<tr>
<td>V</td>
<td>(Sal-TMP).Ar(_2)TeCl ( (p)-methoxyphenyl)</td>
<td>( \text{C}<em>{35}\text{H}</em>{35}\text{Cl}<em>{4}\text{N}</em>{4}\text{O}_{6}\text{Te} ) ( (770.73) )</td>
<td>Pale yellow (84)</td>
<td>130-132</td>
<td>53.84 (54.54) 4.31 (4.58) 7.11 (7.27) 16.43 (16.56) (4.60)</td>
<td>91.83</td>
</tr>
<tr>
<td>VI</td>
<td>(Sal-TMP).Ar(_2)TeCl ( (p)-ethoxyphenyl)</td>
<td>( \text{C}<em>{37}\text{H}</em>{39}\text{Cl}<em>{4}\text{N}</em>{4}\text{O}_{6}\text{Te} ) ( (798.78) )</td>
<td>Light yellow (86)</td>
<td>150-152</td>
<td>54.84 (55.63) 4.53 (4.92) 6.84 (7.01) 15.50 (15.97) (4.44)</td>
<td>35.90</td>
</tr>
<tr>
<td>VII</td>
<td>(Sal-TMP).Ar(_2)TeCl ( (p)-hydroxyphenyl)</td>
<td>( \text{C}<em>{33}\text{H}</em>{31}\text{Cl}<em>{4}\text{N}</em>{4}\text{O}_{6}\text{Te} ) ( (742.68) )</td>
<td>Red (89)</td>
<td>146-148</td>
<td>52.84 (53.37) 4.01 (4.21) 7.27 (7.54) 16.89 (17.18) (4.77)</td>
<td>36.00</td>
</tr>
<tr>
<td>VIII</td>
<td>(Sal-TMP).Ar(_2)TeCl ( (3)-methyl-4-hydroxyphenyl)</td>
<td>( \text{C}<em>{35}\text{H}</em>{35}\text{Cl}<em>{4}\text{N}</em>{4}\text{O}_{6}\text{Te} ) ( (770.73) )</td>
<td>Brown (78)</td>
<td>140-142</td>
<td>53.80 (54.54) 4.34 (4.58) 7.09 (7.27) 16.45 (16.56) (4.60)</td>
<td>27.36</td>
</tr>
</tbody>
</table>

Values of \( \Lambda_M \) reported\(^{63-64}\) for 1:1 electrolytes in DMSO=50-70 S cm\(^2\) mol\(^{-1}\).
### Table 2. Important infrared absorption bands (cm\(^{-1}\)) of Schiff base (Sal-TMP) and complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>(v(O-H))</th>
<th>(v(N-H))</th>
<th>(v(C=N))</th>
<th>(v(C=N)_{pyrimidine})</th>
<th>(v(C-O))</th>
<th>(v(\text{Te-N}))</th>
<th>(v(\text{Te-O}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2836 (w)</td>
<td>3317 (m)</td>
<td>3119 (m)</td>
<td>1636 (sh)</td>
<td>1633 (w)</td>
<td>1593 (s)</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>-</td>
<td>3323 (m)</td>
<td>3184 (m)</td>
<td>1674 (mb)</td>
<td>1644 (mb)</td>
<td>1587 (s)</td>
<td>1341 (s)</td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>3323 (m)</td>
<td>3170 (m)</td>
<td>1647 (sh)</td>
<td>1641 (mb)</td>
<td>1587 (s)</td>
<td>1341 (s)</td>
</tr>
<tr>
<td>III</td>
<td>3405 (m^*)</td>
<td>3323 (m)</td>
<td>3150 (m)</td>
<td>1674 (mb)</td>
<td>1649 (mb)</td>
<td>1587 (s)</td>
<td>1341 (s)</td>
</tr>
<tr>
<td>IV</td>
<td>3398 (m^*)</td>
<td>3319 (m)</td>
<td>3172 (m)</td>
<td>1652 (mb)</td>
<td>1649 (mb)</td>
<td>1587 (s)</td>
<td>1341 (s)</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>3325 (m)</td>
<td>3178 (m)</td>
<td>1645 (sh)</td>
<td>1638 (mb)</td>
<td>1587 (s)</td>
<td>1341 (s)</td>
</tr>
<tr>
<td>VI</td>
<td>-</td>
<td>3320 (m)</td>
<td>3158 (m)</td>
<td>1646 (sh)</td>
<td>1638 (mb)</td>
<td>1587 (s)</td>
<td>1341 (s)</td>
</tr>
<tr>
<td>VII</td>
<td>3401 (w^*)</td>
<td>3324 (m)</td>
<td>3168 (m)</td>
<td>1674 (sh)</td>
<td>1643 (mb)</td>
<td>1584 (s)</td>
<td>1340 (s)</td>
</tr>
<tr>
<td>VIII</td>
<td>3463 (w^*)</td>
<td>3304 (m)</td>
<td>3106 (m)</td>
<td>1634 (sh)</td>
<td>1643 (mb)</td>
<td>1584 (s)</td>
<td>1340 (s)</td>
</tr>
</tbody>
</table>

\(s=\text{sharp, } m=\text{medium, } mb=\text{medium broad, } sh=\text{shoulder, } w=\text{weak}\); \(^*\)Due to phenolic OH of Rte and R\(_2\)Te moieties; \(^{**}\)band not resolved due to overlapping of band \(v(C=N)\)

Examination of the Schiff base (Sal-TMP) spectrum shows the presence of the hydrogen bonded conjugated- chelate ring system\(^{66-68}\) with its centre at ~2832 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.

![Figure 1. Hydrogen bonding](image)

Thus band disappear on chelation with aryltellurium(IV) chlorides\(^{69}\). Hydrogen bond contributes to planarity of the molecule which helps in chelation\(^{70}\). Also an intense ligand band at 1263 cm\(^{-1}\) (phenolic –C-O) in free ligand has shifted to higher frequency side in complexes. All these indicate that the hydroxyl group of salicylaldehyde of Schiff base is involved in coordination with tellurium\(^{71-73}\).

In addition, the spectra of the Schiff base shown shoulder at 1636 cm\(^{-1}\) with slightly resolved weak band at 1633 cm\(^{-1}\) and sharp band at 1593 cm\(^{-1}\) assigned to \(v(C=N)\) mode for vibration of azomethine group\(^{7,65,74-76}\) and \(v(C=N)_{\text{pyrim}}\). For pyrimidine ring\(^{4,77}\). These shift in aryltellurium Schiff base complexes towards higher and lower value\(^{74-79}\) reflecting that ligand coordinate through nitrogen atom of azomethine and pyrimidine ring.

The medium intensity band at 3317 cm\(^{-1}\) and 3119 cm\(^{-1}\) due to \(v(N-H)\) 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 270-295 cm\(^{-1}\) due to \(v(Te-O)\)\(^{90-83}\) mode and medium to strong band in the range of 410-422 cm\(^{-1}\) due to \(v(Te-N)\) mode\(^{84}\) 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 Sal-TMP involving azomethine nitrogen atom, phenolic oxygen after deprotonation and pyrimidine ring nitrogen giving rise to two-six and four membered chelate rings with the tellurium centre.
In order to identify the solution structure of Schiff base (Sal-TMP) and its complexes, ¹H NMR spectra were recorded in DMSO-d₆ and given in Table 3. The proton resonance of the OH group at 10.92 δ ppm disappear on complexation indicating the involvement of phenolic oxygen in the coordination via deprotonation. The azomethine protons which resonate as a singlet at 10.02 δ ppm, the coordination of azomethine nitrogen to tellurium in the complexes are clearly demonstrated by a downfield shift of the peak.

**Table 3.** ¹H NMR spectral data of Schiff base (Sal-TMP) and complexes in DMSO-d₆

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical Shift, δ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2.525(s, 2H, methylene), 3.551-3.745(s, 9H, -OCH₃), 5.672(s,1H, pyrimidine), 6.508(s, 2H, -NH₂), 7.526-8.169(m, 6H, aromatic proton), 10.021(s, 1H, azomethine), 10.921(s, 1H, Schiff base OH)</td>
</tr>
<tr>
<td>I</td>
<td>2.539(s, 2H, methylene), 3.598-3.840(s, 12H, -OCH₃), 6.574(s, 1H, pyrimidine), 6.926(s, 2H, -NH₂), 7.383-7.522(m, 10H, aromatic proton), 10.209(s, 1H, azomethine)</td>
</tr>
<tr>
<td>II</td>
<td>1.335(t, 3H, -OCH₂CH₃), 2.546(s, 2H, methylene), 3.963(q, 2H, -OCH₂CH₃), 3.515-3.875(s, 9H, -OCH₃), 6.540(s, 1H, pyrimidine), 6.950(s, 2H, -NH₂), 6.993-7.809(m, 10H, aromatic proton), 10.193(s, 1H, azomethine)</td>
</tr>
<tr>
<td>III</td>
<td>2.548(s, 2H, methylene), 3.601-3.783(s, 9H, -OCH₃), 6.569(s,1H, pyrimidine), 6.914(s, 2H, -NH₂), 7.370-7.787(m, 10H, aromatic proton), 8.155(s, 1H, phenolic OH of RTe), 10.201(s, 1H, azomethine)</td>
</tr>
<tr>
<td>IV</td>
<td>2.536(s, 2H, methylene), 2.527(s, 3H, -CH₃), 3.587-3.770(s, 9H, -OCH₃), 6.605(s, 1H, pyrimidine), 6.918(s, 2H, -NH₂), 7.051-7.671(m, 9H, aromatic proton), 8.251(s, 1H, phenolic OH of RTe), 10.239(s, 1H, azomethine)</td>
</tr>
<tr>
<td>V</td>
<td>2.528(s, 2H, methylene), 3.673-3.877(s, 15H, -OCH₃), 6.516(s,1H, pyrimidine), 6.882(s, 2H, -NH₂), 6.910-7.804(m, 14H, aromatic proton), 10.186(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VI</td>
<td>1.363(t, 6H, -OCH₂CH₃), 2.531(s, 2H, methylene), 4.019(q, 4H, -OCH₂CH₃), 3.555-3.765(s, 9H, -OCH₃), 6.510(s, 1H, pyrimidine), 6.924(s, 2H, -NH₂), 3.724-7.805(m, 14H, aromatic proton), 10.216(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VII</td>
<td>2.545(s, 2H, methylene), 3.568-3.926(s, 9H, -OCH₃), 6.554(s, 1H, pyrimidine), 6.884(s, 2H, -NH₂), 7.488-7.678(m, 14H, aromatic proton), 8.249(s, 2H, phenolic OH of R₂Te), 10.238(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VIII</td>
<td>2.538(s, 2H, methylene), 2.529(s, 6H, -CH₃), 3.555-3.750(s, 9H, -OCH₃), 6.502(s, 1H, pyrimidine), 6.926(s, 2H, -NH₂), 7.126-7.868(m, 12H, aromatic proton), 8.149(s, 2H, phenolic OH of R₂Te), 10.239(s, 1H, azomethine)</td>
</tr>
</tbody>
</table>

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

The characteristic downfield shifting of proton signal in all complexes observed in region 5.67 δ ppm is due to pyrimidine proton in Schiff base clearly indicate the coordination through pyrimidine nitrogen atom. The signal due to –NH proton is observed around 6.51 δ ppm which remain intact with slight variation in complexes is due to the proton bounded to nitrogen experience quadruple effect. Thus salicylidene-trimethoprim act as a tridentate –N, –N, –O chelating ligand in Sal-TMP,ArTeCl₂ and Sal-TMP,Ar₂TeCl complexes giving six coordinate tellurium having distorted octahedral geometry in these complexes as predicated from IR studies as well. The proposed structures are as given below (Figure 2).
Biological Activity

The salicylidene-trimethoprime Schiff base (Sal-TMP) and newly synthesized aryltellurium(IV) Schiff base complexes were evaluated for their antimicrobial activity in vitro against Gram +ve bacteria (S. aureus ATCC 11632 and B. cereus MTCC 7350), Gram –ve bacteria (E. coli ATCC 35218, P. aeruginosa ATCC 23564, S. typhi ATCC 15499 and P. rettgeri DRDE) and fungal strains (A. niger, A. fumigates and A. flavus) by tube dilution method. Dilution of test and standard compounds were prepared double strength nutrient broth– I.P (Antibacterial) and Sabouraud Dextrose Broth –I.P (Antifungal). The samples were incubated at 37±1 °C for 24 h (bacteria), 25±1 °C for 7 days (A. niger), 30 ±1 °C for 15 days (A. flavus), 35±1 °C for 72 h (A. fumigates) respectively and results were recorded in terms of MIC (The lowest concentration of test substances which inhibited values are presented in the Table 4.

The data show that the Sal-TMP complexes of aryltellurium(IV) exhibit more antimicrobial activity towards bacteria as compared to fungii. The antibacterial activity shows following trend.

![Sal-TMP.Ar₂TeCl](image)

Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl

Figure 2. Proposed structures of complexes
Sal-TMP.\textsubscript{Ar}TeCl > Sal-TMP.\textsubscript{Ar}TeCl\textsubscript{2} \approx Sal-TMP Schiff base

Sal-TMP.\textsubscript{Ar}TeCl and Sal-TMP.\textsubscript{Ar}TeCl\textsubscript{2} complexes have activity towards \textit{S. typhi} and more effectively against \textit{B. cereus} but Schiff base does not show activity against these bacterial strains. Schiff base and its complexes show almost similar activity against fungal strains.

**Table 4.** Minimum Inhibitory Concentration, MIC, µg/mL; (-) Resistant

<table>
<thead>
<tr>
<th>Compound</th>
<th>Bacteria strains</th>
<th>Fungal strains</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S. aureus (ATCC 11632)</td>
<td>S. typhi (ATCC 15499)</td>
</tr>
<tr>
<td>Sal-TMP</td>
<td>2.5</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>5.0</td>
<td>-</td>
</tr>
<tr>
<td>II</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>IV</td>
<td>1.25</td>
<td>2.5</td>
</tr>
<tr>
<td>V</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>VI</td>
<td>1.25</td>
<td>2.5</td>
</tr>
<tr>
<td>VII</td>
<td>1.25</td>
<td>-</td>
</tr>
<tr>
<td>VIII</td>
<td>2.5</td>
<td>-</td>
</tr>
</tbody>
</table>

**Conclusion**

Aryltellurium(IV) and diaryltellurium(IV) dichlorides upon reaction with Schiff base(Sal-TMP) derived from salicylaldehyde and trimethoprim yield new complexes of tellurium(IV). The synthesized complexes were characterized by elemental analyses, conductance measurement, IR and \textsuperscript{1}H NMR spectral studies. The analytical data suggest that the Sal-TMP Schiff base complexes have 1:1 stoichiometry. The Schiff bases (Sal-TMP) in these complexes functions as a uninegative tridentate ligand through azomethine nitrogen, phenolic oxygen after deprotonation and pyrimidine ring nitrogen atoms. Based on these studies, distorted octahedral geometry with two chelating rings has been assigned to these complexes. The complexes have been observed to possess substantial antimicrobial activity especially against bacteria.

**Acknowledgement**

The authors are grateful to M. D. University, Rohtak for providing the necessary facilities. One of the authors (Deepak) is also thankful to UGC New Delhi for providing fellowship. We also thank SAIF, Panjab University Chandigarh for providing the CHN analyses and spectral data.

**References**

42. Berg M C, Diss Abstr Int., 1972, 33, 2982.
46. Garad M V, Polyhedron, 1985, 4(8), 1353-1355; DOI:10.1016/S0277-5387(00)86963-6
89. Pharmacopoeia of India, Volume 1, Controller of Publications, Ministry of Health Department, Government of India, New Delhi, 2007, 37.
Synthesis, Spectral and Biological Studies of Some Salicylidene-Trimethoprim Schiff Base Complexes of Aryltellurium(IV)

DEEPAK, K. K. VERMA and SAPANA GARG*

Department of Chemistry, Maharshi Dayanand University, Rohtak-124001, India
sapanagarg1511@gmail.com

Received 14 February 2017 / Accepted 2 March 2017

Abstract: A novel monobasic tridentate Schiff base salicylidene-trimethoprim, Sal-TMP, synthesized from trimethoprim and salicylaldehyde, form stable complexes with aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides of the type Sal-TMP.ArTeCl₂ and Sal-TMP.Ar₂TeCl₂ (where Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl). These have been characterized by elemental analyses, molar conductance, 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 hexacoordinated tellurium(IV) complexes. The complexes have also been screened for their antimicrobial activities against various bacteria and fungi organisms.

Keywords: Salicylidene-trimethoprim Schiff base, Aryltellurium(IV), Diaryltellurium(IV), Antibacterial, Antifungal activities

Introduction

Trimethoprim and its derivatives are broad spectrum antimicrobial agents with anti-parasitic activity and were first described by Roth and coworker. Schiff bases, also known as azomethine due to presence of –C=N– group, play important role in biological system, such as anticancer, antibacterial, antiviral, antifungal and other biological properties and also 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.

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, R₃TeCl₃ and diaryltellurium(IV) dichlorides, R₂TeCl₂ with salicylidene-trimethoprim Schiff base(Sal-TMP).
Experimental

All preparations were carried out under dry N₂ atmosphere and the solvents used were purified by standard method⁵⁵,⁵⁶ 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 on a ThermoFinnigan CHNS analyser. Conductivity was measured in DMSO at 25±2 °C with dip type conductivity cell on a microprocessor based conductivity bridge type MICROSIL.

IR (4000-400 cm⁻¹) and far IR (400-50 cm⁻¹) spectra were recorded in KBr/polyethylene pellets on a FT-Infrared spectrophotometer model RZX (Perkin Elmer) at SAIF, Panjab University Chandigarh. Proton magnetic resonance spectra were recorded in DMSO-d₆ using TMS as an internal reference on BRUKER AVANCE II 400 NMR spectrometer. The antimicrobial screening was carried out by tube dilution method at Department of Pharmaceutical Sciences, M. D. University, Rohtak, India.

Preparation of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

p-Methoxyphenyltellurium(IV) trichloride⁵⁷,⁵⁸, bis(p-methoxyphenyl)tellurium(IV) dichloride⁵⁸,⁵⁹, p-ethoxyphenyltellurium (IV) trichloride⁶⁰, bis(p-ethoxyphenyl)tellurium dichloride⁶⁰, p-hydroxyphenyltellurium(IV) trichloride⁶¹, bis(p-hydroxyphenyl) tellurium(IV) dichloride⁶¹, 3-methyl-4-hydroxyphenyltellurium(IV) trichloride⁶２ and bis(3-methyl-4-hydroxyphenyl)tellurium(IV) dichloride⁶２ were prepared by the reactions of TeCl₄ with anisole, phenetole, phenol, o-cresol respectively, by the methods reported in the literature⁵⁷-⁶２.

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP)

Equimolar quantity of saturated methanolic solution of drug and salicylaldehyde were mixed thoroughly. To this mixture 0.1% methanolic KOH was added to adjust the pH of the solution between 7-8 and was refluxed for 2 hours. A clear yellowish-green 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 P₂O₅ until further use. Yield = 80%, M.pt.(decomp.)=188-190 °C. Analysis (Calculated) C₂₁H₂₂N₄O₄: C(63.95), H(5.62) and N(14.20); Found: C(63.50), H(5.27) and N(13.99).

Preparation of salicylidene-trimethoprim complexes of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

Aryltellurium(IV) trichlorides, ArTeCl₃ and diaryltellurium(IV) dichlorides Ar₂TeCl₂ (Ar= p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl), when reacted with sodium salt of salicylidene-trimethoprim in equimolar ratio, yield Sal-TMP.ArTeCl₂ and Sal-TMP.Ar₂TeCl₂ 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 anisole⁵⁷⁻⁵⁹, phenetole⁶⁰, phenol⁶¹, o-cresol (Ar-H) appears to undergo Friedel-Crafts type condensation reaction whereby TeCl₄⁺ 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.

\[
\text{Ar-H + TeCl}_4 \rightarrow \text{ArTeCl}_3 + \text{HCl} \\
2 \text{Ar-H + TeCl}_4 \rightarrow \text{Ar}_2\text{TeCl}_2 + 2 \text{HCl}
\]

(1) (2)

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP) by the reaction of trimethoprim drug and salicylaldehyde can be represented by following equations.

![Diagram of reaction](image)

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

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

(3) (4)

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.

Conductance studies

Molar conductance (\(\Lambda_M\)) data for the complexes in DMSO are complied in Table 1. The \(\Lambda_M\) value at ca. 10⁻³ M for aryltellurium(IV) complexes in DMSO lie in the range 27.36-91.83 S cm² mol⁻¹ which predict the non electrolyte to 1:1 electrolyte type behaviour of these complexes in DMSO, probably due to ionization into \(\text{ArTeCl}_2\text{Sal-TMP}^+\text{Ar}_2\text{Te.Sal-TMP}^-\) and \(\text{Cl}^-\) in DMSO. This conductance behaviour of tellurium(IV) salicylidene-trimethoprim Schiff base complexes is different from those of transition metal complexes⁶⁵, which are reported to be non-electrolytes. The higher \(\Lambda_M\) values for some complexes may be due to steric factors and donor behaviour of DMSO to result in probable dissociation into solvated cation and \(\text{L}^-\) along with \(\text{Cl}^-\) in DMSO.

Infrared spectra

The IR data of Schiff base and its tellurium(IV) complexes are listed in Table 2. The spectra of Sal-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 \(\text{ArTeCl}_3/\text{Ar}_2\text{TeCl}_2\).
<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Complex (Ar)</th>
<th>Empirical formula (Formula Wt.)</th>
<th>Colour (Yield, %)</th>
<th>M. Pt. °C dec.</th>
<th>Analyses % Found (Calculated)</th>
<th>ΛM at ca. 10⁻³ M S cm² mol⁻¹ in DMSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schiff Base</td>
<td>Sal-TMP</td>
<td>C_{23}H_{22}N_{4}O_{4}</td>
<td>Yellowish -green (80)</td>
<td>188-190</td>
<td>63.50 (63.95) 5.27 (5.62) 13.99 (14.20)</td>
<td>- - -</td>
</tr>
<tr>
<td>I</td>
<td>(Sal-TMP).ArTeCl₂ (p-methoxyphenyl)</td>
<td>C_{25}H_{25}Cl₂N₂O₅Te (699.05)</td>
<td>Light cream (92)</td>
<td>230-232</td>
<td>47.88 (48.11) 3.99 (4.04) 7.75 (8.01) 18.07 (18.24) 9.89 (10.01)</td>
<td>53.19</td>
</tr>
<tr>
<td>II</td>
<td>(Sal-TMP).ArTeCl₂ (p-ethoxyphenyl)</td>
<td>C_{25}H_{28}Cl₂N₂O₅Te (713.08)</td>
<td>Cream (85)</td>
<td>258-260</td>
<td>48.12 (48.85) 3.87 (4.24) 7.52 (7.86) 17.38 (17.89) 9.52 (9.81)</td>
<td>52.88</td>
</tr>
<tr>
<td>III</td>
<td>(Sal-TMP).ArTeCl₂ (p-hydroxyphenyl)</td>
<td>C_{25}H_{26}Cl₂N₂O₅Te (685.03)</td>
<td>Dark cream (94)</td>
<td>208-210</td>
<td>46.78 (47.34) 3.50 (3.83) 7.88 (8.18) 18.28 (18.63) 9.98 (10.21)</td>
<td>55.73</td>
</tr>
<tr>
<td>IV</td>
<td>(Sal-TMP).ArTeCl₂ (3-methyl-4-hydroxyphenyl)</td>
<td>C_{25}H_{28}Cl₂N₂O₅Te (699.05)</td>
<td>Light cream (80)</td>
<td>198-200</td>
<td>47.58 (48.11) 3.84 (4.04) 7.80 (8.01) 18.15 (18.24) 9.85 (10.01)</td>
<td>58.68</td>
</tr>
<tr>
<td>V</td>
<td>(Sal-TMP).Ar₂TeCl₂ (p-methoxyphenyl)</td>
<td>C_{35}H_{35}Cl₂N₄O₆Te (770.73)</td>
<td>Pale yellow (84)</td>
<td>130-132</td>
<td>53.84 (54.54) 4.31 (4.58) 7.11 (7.27) 16.43 (16.56) 4.42 (4.60)</td>
<td>91.83</td>
</tr>
<tr>
<td>VI</td>
<td>(Sal-TMP).Ar₂TeCl₂ (p-ethoxyphenyl)</td>
<td>C_{35}H_{39}Cl₂N₄O₆Te (798.78)</td>
<td>Light yellow (86)</td>
<td>150-152</td>
<td>54.84 (55.63) 4.53 (4.92) 6.84 (7.01) 15.50 (15.97) 4.30 (4.44)</td>
<td>35.90</td>
</tr>
<tr>
<td>VII</td>
<td>(Sal-TMP).Ar₂TeCl₂ (p-hydroxyphenyl)</td>
<td>C_{35}H_{31}Cl₂N₄O₆Te (742.68)</td>
<td>Red (89)</td>
<td>146-148</td>
<td>52.84 (53.37) 4.01 (4.21) 7.27 (7.54) 16.89 (17.18) 4.52 (4.77)</td>
<td>36.00</td>
</tr>
<tr>
<td>VIII</td>
<td>(Sal-TMP).Ar₂TeCl₂ (3-methyl-4-hydroxyphenyl)</td>
<td>C_{35}H_{35}Cl₂N₄O₆Te (770.73)</td>
<td>Brown (78)</td>
<td>140-142</td>
<td>53.80 (54.54) 4.34 (4.58) 7.09 (7.27) 16.45 (16.56) 4.32 (4.60)</td>
<td>27.36</td>
</tr>
</tbody>
</table>

Values of ΛM reported⁶³-⁶⁴ for 1:1 electrolytes in DMSO=50-70 S cm² mol⁻¹
Table 2. Important infrared absorption bands (cm\(^{-1}\)) of Schiff base (Sal-TMP) and complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>(v_{(O-H)} )</th>
<th>(v_{(N-H)} )</th>
<th>(v_{(C=N)} )</th>
<th>(v_{(C=O)} )</th>
<th>(v_{(Te-N)} )</th>
<th>(v_{(Te-O)} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2836 w</td>
<td>3317 m 3119 m</td>
<td>1636 sh</td>
<td>1633 w 1593 s</td>
<td>1263 s</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>-</td>
<td>3323 m 3184 m</td>
<td>1674 mb</td>
<td>1644 mb 1587 s</td>
<td>1341 s</td>
<td>415 m</td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>3323 m 3170 m</td>
<td>1647 sh</td>
<td>**1586 s</td>
<td>1304 s</td>
<td>420 m</td>
</tr>
<tr>
<td>III</td>
<td>3405 m*</td>
<td>3323 m 3150 m</td>
<td>1674 mb</td>
<td>1641 mb 1586 s</td>
<td>1341 s</td>
<td>419 s</td>
</tr>
<tr>
<td>IV</td>
<td>3398 m*</td>
<td>3319 m 3172 m</td>
<td>1652 mb</td>
<td>1649 mb 1587 s</td>
<td>1333 s</td>
<td>450 s</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>3325 m 3178 m</td>
<td>1645 sh</td>
<td>**1587 s</td>
<td>1333 s</td>
<td>416 s</td>
</tr>
<tr>
<td>VI</td>
<td>-</td>
<td>3320 m 3158 m</td>
<td>1640 sh</td>
<td>**1590 s</td>
<td>1331 s</td>
<td>410 m</td>
</tr>
<tr>
<td>VII</td>
<td>3401 w*</td>
<td>3324 m 3168 m</td>
<td>1674 mb</td>
<td>1643 mb 1584 s</td>
<td>1340 s</td>
<td>418 s</td>
</tr>
<tr>
<td>VIII</td>
<td>3463 w*</td>
<td>3304 m 3106 m</td>
<td>1634 sh</td>
<td>1643 mb 1584 s</td>
<td>1340 s</td>
<td>422 m</td>
</tr>
</tbody>
</table>

*sharp, m=medium, mb=medium broad, sh=shoulder, w=weak; **Due to phenolic OH of RTe and R\(_2\)Te moieties; *band not resolved due to overlapping of band \(v_{(C=N)}\)

Examination of the Schiff base (Sal-TMP) spectrum shows the presence of the hydrogen bonded conjugated-chelate ring system\(^{66-68}\) with its centre at ~2832 cm\(^{-1}\). Thus intramolecular H-bonding is occurring by means of the formation of a quasi six-membered ring involving the OH ---\(\text{N}=\text{C}\) bond.

![Figure 1. Hydrogen bonding](image)

Thus band disappear on chelation with aryltellurium(IV) chlorides\(^{69}\). Hydrogen bond contributes to planarity of the molecule which helps in chelation\(^{70}\). Also an intense ligand band at 1263 cm\(^{-1}\) (phenolic –C-O) in free ligand has shifted to higher frequency side in complexes. All these indicate that the hydroxyl group of salicylaldehyde of Schiff base is involved in coordination with tellurium\(^{71-73}\).

In addition, the spectra of the Schiff base shown shoulder at 1636 cm\(^{-1}\) with slightly resolved weak band at 1633 cm\(^{-1}\) and sharp band at 1593 cm\(^{-1}\) assigned to \(v_{(C=N)}\) mode for vibration of azomethine group\(^{7,4,65-76}\) and \(v_{(C=O)}\)pyrim. For pyrimidine ring\(^{64,77}\). These shift in aryltellurium Schiff base complexes towards higher and lower value\(^{74-79}\) reflecting that ligand coordinate through nitrogen atom of azomethine and pyrimidine ring.

The medium intensity band at 3317 cm\(^{-1}\) and 3119 cm\(^{-1}\) due to \(v_{(N-H)}\) 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 270-295 cm\(^{-1}\) due to \(v_{(Te-O)}\)\(^{80-83}\) mode and medium to strong band in the range of 410-422 cm\(^{-1}\) due to \(v_{(Te-N)}\) mode\(^{84}\) 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 Sal-TMP involving azomethine nitrogen atom, phenolic oxygen after deprotonation and pyrimidine ring nitrogen giving rise to two-six and four membered chelate rings with the tellurium centre.
In order to identify the solution structure of Schiff base (Sal-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 $10.92 \delta$ ppm$^{76,85}$ in Schiff base due to presence of intramolecular hydrogen bonding$^{74}$ disappear on complexation indicating the involvement of phenolic oxygen in the coordination via deprotonation.$^{76}$ The azomethine protons which resonate as a singlet at $10.02 \delta$ ppm, the coordination of azomethine nitrogen to tellurium in the complexes are clearly demonstrated by a downfield shift of the peak$^{86}$.

Table 3. $^1$H NMR spectral data of Schiff base (Sal-TMP) and complexes in DMSO-d$_6$

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical Shift, $\delta$ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2.525(s, 2H, methylene), 3.551-3.745(s, 9H, -OCH$_3$), 5.672(s, 1H, pyrimidine), 6.508(s, 2H, -NH$_2$), 7.526-8.169(m, 6H, aromatic proton), 10.021(s, 1H, azomethine), 10.921(s, 1H, Schiff base OH)</td>
</tr>
<tr>
<td>I</td>
<td>2.539(s, 2H, methylene), 3.598-3.840(s, 12H, -OCH$_3$), 6.574(s, 1H, pyrimidine), 6.926(s, 2H, -NH$_2$), 7.383-7.522(m, 10H, aromatic proton), 10.209(s, 1H, azomethine)</td>
</tr>
<tr>
<td>II</td>
<td>1.335(t, 3H, -OCH$_2$CH$_3$), 2.546(s, 2H, methylene), 3.963(q, 2H, -OCH$_2$CH$_3$), 3.515-3.875(s, 9H, -OCH$_3$), 6.540(s, 1H, pyrimidine), 6.950(s, 2H, -NH$_2$), 6.993-7.809(m, 10H, aromatic proton), 10.193(s, 1H, azomethine)</td>
</tr>
<tr>
<td>III</td>
<td>2.548(s, 2H, methylene), 3.601-3.783(s, 9H, -OCH$_3$), 6.569(s, 1H, pyrimidine), 6.914(s, 2H, -NH$_2$), 7.370-7.787(m, 10H, aromatic proton), 8.155(s, 1H, phenolic OH of RTe), 10.201(s, 1H, azomethine)</td>
</tr>
<tr>
<td>IV</td>
<td>2.536(s, 2H, methylene), 2.527(s, 3H, -CH$_3$), 3.587-3.770(s, 9H, -OCH$_3$), 6.605(s, 1H, pyrimidine), 6.918(s, 2H, -NH$_2$), 7.051-7.671(m, 9H, aromatic proton), 8.251(s, 1H, phenolic OH of RTe), 10.239(s, 1H, azomethine)</td>
</tr>
<tr>
<td>V</td>
<td>2.528(s, 2H, methylene), 3.673-3.877(s, 15H, -OCH$_3$), 6.516(s, 1H, pyrimidine), 6.882(s, 2H, -NH$_2$), 6.910-7.804(m, 14H, aromatic proton), 10.186(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VI</td>
<td>1.363(t, 6H, -OCH$_2$CH$_3$), 2.531(s, 2H, methylene), 4.019(q, 4H, -OCH$_2$CH$_3$), 3.555-3.765(s, 9H, -OCH$_3$), 6.510(s, 1H, pyrimidine), 6.924(s, 2H, -NH$_2$), 7.524-7.805(m, 14H, aromatic proton), 10.216(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VII</td>
<td>2.545(s, 2H, methylene), 3.568-3.926(s, 9H, -OCH$_3$), 6.554(s, 1H, pyrimidine), 6.884(s, 2H, -NH$_2$), 7.488-7.678(m, 14H, aromatic proton), 8.249(s, 2H, phenolic OH of R$_2$Te), 10.238(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VIII</td>
<td>2.538(s, 2H, methylene), 2.529(s, 6H, -CH$_3$), 3.555-3.750(s, 9H, -OCH$_3$), 6.502(s, 1H, pyrimidine), 6.926(s, 2H, -NH$_2$), 7.126-7.868(m, 12H, aromatic proton), 8.149(s, 2H, phenolic OH of R$_2$Te), 10.239(s, 1H, azomethine)</td>
</tr>
</tbody>
</table>

The characteristic downfield shifting of proton signal in all complexes observed in region $5.67 \delta$ ppm is due to pyrimidine proton in Schiff base clearly indicate the coordination through pyrimidine nitrogen atom$^{87}$. The signal due to –NH proton is observed around $6.51 \delta$ ppm which remain intact with slight variation in complexes is due to the proton bounded to nitrogen experience quadruple effect$^{87}$. Thus salicylidene-trimethoprim act as a tridentate –N, –N, –O chelating ligand in Sal-TMP.ArTeCl$_2$ and Sal-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 given below (Figure 2).
The salicylidene-trimethoprim Schiff base (Sal-TMP) and newly synthesized aryltellurium(IV) Schiff base complexes were evaluated for their antimicrobial activity \textit{in vitro} against Gram +ve bacteria (\textit{S. aureus} ATCC 11632 and \textit{B. cereus} MTCC 7350), Gram –ve bacteria (\textit{E. coli} ATCC 35218, \textit{P. aeruginosa} ATCC 23564, \textit{S. typhi} ATCC 15499 and \textit{P. rettgeri} DRDE) and fungal strains (\textit{A. niger}, \textit{A. fumigates} and \textit{A. flavus}) by tube dilution method\textsuperscript{88}. Dilution of test and standard compounds were prepared double strength nutrient broth – I.P (Antibacterial) and Sabouraud Dextrose Broth – I.P (Antifungal)\textsuperscript{89}. The samples were incubated at 37±1 °C for 24 h (bacteria), 25±1 °C for 7 days (\textit{A. niger}), 30 ±1 °C for 15 days (\textit{A. flavus}), 35±1 °C for 72 h (\textit{A. fumigates}) respectively and results were recorded in terms of MIC (The lowest concentration of test substances which inhibited values are presented in the Table 4.

The data show that the Sal-TMP complexes of aryltellurium(IV) exhibit more antimicrobial activity towards bacteria as compared to fungii. The antibacterial activity shows following trend.

\textbf{Biological Activity}

\textit{Sal-TMP.Ar}_2\text{TeCl}

\textit{Ar} = p\text{-methoxyphenyl, p\text{-ethoxyphenyl, p\text{-hydroxyphenyl and 3-methyl-4-hydroxyphenyl}}

\textbf{Figure 2. Proposed structures of complexes}
Sal-TMP.Ar₂TeCl ≈ Sal-TMP.ArTeCl₂ ≈ Sal-TMP Schiff base

Sal-TMP.Ar₂TeCl and Sal-TMP.ArTeCl₂ complexes have activity towards S. typhi and more effectively against B. cereus but Schiff base does not show activity against these bacterial strains. Schiff base and its complexes show almost similar activity against fungal strains.

Table 4. Minimum Inhibitory Concentration, MIC, µg/mL; (-) Resistant

<table>
<thead>
<tr>
<th>Compound</th>
<th>Bacteria strains</th>
<th>Fungal strains</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S. aureus (ATCC 11632)</td>
<td>S. typhi (ATCC 15499)</td>
</tr>
<tr>
<td>Sal-TMP</td>
<td>2.5 - 1.25</td>
<td>5.0</td>
</tr>
<tr>
<td>I</td>
<td>2.5 - 1.25</td>
<td>5.0</td>
</tr>
<tr>
<td>II</td>
<td>5.0 - -</td>
<td>0.625</td>
</tr>
<tr>
<td>III</td>
<td>- 20 10</td>
<td>5.0</td>
</tr>
<tr>
<td>IV</td>
<td>1.25 2.5 1.25</td>
<td>5.0</td>
</tr>
<tr>
<td>V</td>
<td>- 20 10</td>
<td>5.0</td>
</tr>
<tr>
<td>VI</td>
<td>1.25 2.5 1.25</td>
<td>5.0</td>
</tr>
<tr>
<td>VII</td>
<td>1.25 2.5 1.25</td>
<td>5.0</td>
</tr>
<tr>
<td>VIII</td>
<td>2.5 1.25</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Conclusion

Aryltellurium(IV) and diaryltellurium(IV) dichlorides upon reaction with Schiff base(Sal-TMP) derived from salicylaldehyde and trimethoprim yield new complexes of tellurium(IV). The synthesized complexes were characterized by elemental analyses, conductance measurement, IR and ¹H NMR spectral studies. The analytical data suggest that the Sal-TMP Schiff base complexes have 1:1 stoichiometry. The Schiff bases (Sal-TMP) in these complexes functions as a uninegative tridentate ligand through azomethine nitrogen, phenolic oxygen after deprotonation and pyrimidine ring nitrogen atoms. Based on these studies, distorted octahedral geometry with two chelating rings has been assigned to these complexes. The complexes have been observed to possess substantial antimicrobial activity especially against bacteria.

Acknowledgement

The authors are grateful to M. D. University, Rohtak for providing the necessary facilities. One of the authors (Deepak) is also thankful to UGC New Delhi for providing fellowship. We also thank SAIF, Panjab University Chandigarh for providing the CHN analyses and spectral data.

References

42. Berg M C, Diss Abstr Int., 1972, 33, 2982.
46. Garad M V, Polyhedron, 1985, 4(8), 1353-1355; DOI:10.1016/S0277-5387(00)86963-6
71. Mishra A P and Soni M, Metal Based Drugs, 2008, 71, 243; DOI:10.1155/2008/875410
89. Pharmacopoeia of India, Volume 1, Controller of Publications, Ministry of Health Department, Government of India, New Delhi, 2007, 37.
Synthesis, Spectral and Biological Studies of Some Salicylidene-Trimethoprim Schiff Base Complexes of Aryltellurium(IV)

DEEPAK, K. K. VERMA and SAPANA GARG*

Department of Chemistry, Maharshi Dayanand University, Rohtak-124001, India
sapanagarg1511@gmail.com

Received 14 February 2017 / Accepted 2 March 2017

Abstract: A novel monobasic tridentate Schiff base salicylidene-trimethoprim, Sal-TMP, synthesized from trimethoprim and salicylaldehyde, form stable complexes with aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides of the type Sal-TMP.ArTeCl$_2$ and Sal-TMP.Ar$_2$TeCl (where Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl). These have been characterized by elemental analyses, molar conductance, IR and $^1$H 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 hexacoordinated tellurium(IV) complexes. The complexes have also been screened for their antimicrobial activities against various bacteria and fungi organisms.

Keywords: Salicylidene-trimethoprim Schiff base, Aryltellurium(IV), Diaryltellurium(IV), Antibacterial, Antifungal activities

Introduction

Trimethoprim and its derivatives are broad spectrum antimicrobial agents with anti-parasitic activity$^{1-6}$ and were first described by Roth and coworker$^5$. Schiff bases, also known as azomethine due to presence of $\text{–C=\text{N–}}$ group, play important role in biological system, such as anticancer$^{7-12}$, antibacterial$^{13-15}$, antiviral$^{16-18}$, antifungal$^{19-21}$ and other biological properties$^{22-27}$ and also have been extensively used as ligands in coordination chemistry because of their excellent donor abilities as chelating agent$^{28-32}$. Medicinal chemists have reported new derivatives of trimethoprim(TMZ)$^{33-35}$ including the Schiff base derived from salicylaldehyde$^{2-4,36,37}$.

Also, aryltellurium(IV) chlorides are known$^{38-54}$ 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 salicylidene-trimethoprim Schiff base(Sal-TMP).
**Experimental**

All preparations were carried out under dry N₂ atmosphere and the solvents used were purified by standard method 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 on a ThermoFinnigan CHNS analyser. Conductivity was measured in DMSO at 25±2 °C with dip type conductivity cell on a microprocessor based conductivity bridge type MICROSL.

IR (4000-400 cm⁻¹) and far IR (400-50 cm⁻¹) spectra were recorded in KBr/polyethylene pellets on a FT-Infrared spectrophotometer model RZX (Perkin Elmer) at SAIF, Panjab University Chandigarh. Proton magnetic resonance spectra were recorded in DMSO-d₆ using TMS as an internal reference on BRUKER AVANCE II 400 NMR spectrometer. The antimicrobial screening was carried out by tube dilution method at Department of Pharmaceutical Sciences, M. D. University, Rohtak, India.

**Preparation of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides**

 Preparation of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

*p*-Methoxyphenyltellurium(IV) trichloride, bis(*p*-methoxyphenyl)tellurium(IV) dichloride, *p*-ethoxyphenyltellurium (IV) trichloride, bis(*p*-ethoxyphenyl)tellurium dichloride, *p*-hydroxyphenyltellurium(IV) trichloride, bis(*p*-hydroxyphenyl) tellurium(IV) dichloride, 3-methyl-4-hydroxyphenyltellurium(IV) trichloride and bis(3-methyl-4-hydroxyphenyl)tellurium(IV) dichloride were prepared by the reactions of TeCl₄ with anisole, phenetole, phenol, *o*-cresol respectively, by the methods reported in the literature.

**Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP)**

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP)

Equimolar quantity of saturated methanolic solution of drug and salicylaldehyde were mixed thoroughly. To this mixture 0.1% methanolic KOH was added to adjust the pH of the solution between 7-8 and was refluxed for 2 hours. A clear yellowish-green 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 P₄O₁₀ until further use. Yield = 80%, M.pt.(decomp.)=188-190 °C. Analysis (Calculated) C₂₁H₂₁N₄O₄: C(63.95), H(5.62) and N(14.20); Found: C(63.50), H(5.27) and N(13.99).

**Preparation of salicylidene-trimethoprim complexes of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides**

Preparation of salicylidene-trimethoprim complexes of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

Aryltellurium(IV) trichlorides, ArTeCl₃ and diaryltellurium(IV) dichlorides Ar₂TeCl₂ (Ar= *p*-methoxyphenyl, *p*-ethoxyphenyl, *p*-hydroxyphenyl and 3-methyl-4-hydroxyphenyl), when reacted with sodium salt of salicylidene-trimethoprim in equimolar ratio, yield Sal-TMP.ArTeCl₂ and Sal-TMP.Ar₂TeCl₂ 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 P₄O₁₀.
Results and Discussion

TeCl₄ when heated with anisole⁵⁷-⁵⁹, phenetole⁶⁰, phenol⁶¹, o-cresol⁶² (Ar-H) appears to undergo Friedel-Crafts type condensation reaction whereby TeCl₄⁺ 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.

\[
\begin{align*}
\text{Ar-H} + \text{TeCl}_4 & \rightarrow \text{ArTeCl}_3 + \text{HCl} \\
2 \text{Ar-H} + \text{TeCl}_4 & \rightarrow \text{Ar}_2\text{TeCl}_2 + 2 \text{HCl}
\end{align*}
\]

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP) by the reaction of trimethoprim drug and salicylaldehyde can be represented by following equations.

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

\[
\begin{align*}
\text{Sal-TMP} + \text{ArTeCl}_3 & \rightarrow \text{Na/CH}_3\text{OH} \rightarrow (\text{Sal-TMP})\cdot\text{ArTeCl}_3 \\
\text{Sal-TMP} + \text{Ar}_2\text{TeCl}_2 & \rightarrow \text{Na/CH}_3\text{OH} \rightarrow (\text{Sal-TMP})\cdot\text{Ar}_2\text{TeCl}_2
\end{align*}
\]

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.

Conductance studies

Molar conductance (\(\Lambda_M\)) data for the complexes in DMSO are complied in Table 1. The \(\Lambda_M\) value at ca. 10⁻³ M for aryltellurium(IV) complexes in DMSO lie in the range 27.36-91.83 S cm² mol⁻¹ which predict the non electrolyte to 1:1 electrolyte²⁹,⁶⁴ type behaviour of these complexes in DMSO, probably due to ionization into ArTeCl₃·Sal-TMP⁺/Ar₂Te·Sal-TMP⁺ and Cl⁻ in DMSO. This conductance behaviour of tellurium(IV) salicylidene-trimethoprim Schiff base complexes is different from those of transition metal complexes⁶⁵, which are reported to be non-electrolytes. The higher \(\Lambda_M\) values for some complexes may be due to steric factors and donor behaviour of DMSO to result in probable dissociation into solvated cation and L⁻ along with Cl⁻ in DMSO.

Infrared spectra

The IR data of Schiff base and its tellurium(IV) complexes are listed in Table 2. The spectra of Sal-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 ArTeCl₃/Ar₂TeCl₂.
Table 1. Analytical data, molar conductance and physical properties of salicylidene-trimethoprim Schiff base (Sal-TMP) complexes of tellurium(IV)

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Complex (Ar)</th>
<th>Empirical formula (Formula Wt.)</th>
<th>Colour (Yield, %)</th>
<th>M. Pt. °C dec.</th>
<th>Analyses % Found (Calculated)</th>
<th>$\Lambda_M$ at ca. $10^{-3}$ M S cm$^2$ mol$^{-1}$ in DMSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schiff Base</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>(Sal-TMP).ArTeCl$_2$ (p-methoxyphenyl)</td>
<td>C$<em>{29}$H$</em>{28}$Cl$_2$N$_4$O$_5$Te$_2$ (713.08)</td>
<td>Light cream (92)</td>
<td>230-232</td>
<td>48.12 (4.24) (7.86) (17.89) (9.81)</td>
<td>52.88</td>
</tr>
<tr>
<td>II</td>
<td>(Sal-TMP).ArTeCl$_2$ (p-ethoxyphenyl)</td>
<td>C$<em>{27}$H$</em>{26}$Cl$_2$N$_4$O$_5$Te$_2$ (685.03)</td>
<td>Dark cream (94)</td>
<td>208-210</td>
<td>46.78 (3.83) (8.18) (18.63) (10.21)</td>
<td>55.73</td>
</tr>
<tr>
<td>III</td>
<td>(Sal-TMP).ArTeCl$_2$ (p-hydroxyphenyl)</td>
<td>C$<em>{29}$H$</em>{28}$Cl$_2$N$_4$O$_5$Te$_2$ (699.05)</td>
<td>Light cream (80)</td>
<td>198-200</td>
<td>47.58 (4.04) (8.01) (18.24) (10.01)</td>
<td>58.68</td>
</tr>
<tr>
<td>IV</td>
<td>(Sal-TMP).ArTeCl$_2$ (3-methyl-4-hydroxyphenyl)</td>
<td>C$<em>{33}$H$</em>{31}$Cl$_4$N$_4$O$_6$Te (742.68)</td>
<td>Pale yellow (84)</td>
<td>146-148</td>
<td>52.84 (4.01) (7.27) (16.89) (4.52)</td>
<td>36.00</td>
</tr>
<tr>
<td>V</td>
<td>(Sal-TMP).Ar$_2$TeCl (p-methoxyphenyl)</td>
<td>C$<em>{35}$H$</em>{35}$Cl$_4$N$_4$O$_6$Te (770.73)</td>
<td>Red (89)</td>
<td>140-142</td>
<td>53.80 (4.34) (7.09) (16.45) (4.32)</td>
<td>27.36</td>
</tr>
<tr>
<td>VI</td>
<td>(Sal-TMP).Ar$_2$TeCl (p-ethoxyphenyl)</td>
<td>C$<em>{35}$H$</em>{35}$Cl$_4$N$_4$O$_6$Te (770.73)</td>
<td>Brown (78)</td>
<td>140-142</td>
<td>53.80 (4.54) (7.27) (16.56) (4.60)</td>
<td></td>
</tr>
<tr>
<td>VII</td>
<td>(Sal-TMP).Ar$_2$TeCl (3-methyl-4-hydroxyphenyl)</td>
<td>C$<em>{35}$H$</em>{35}$Cl$_4$N$_4$O$_6$Te (770.73)</td>
<td>Pale yellow (84)</td>
<td>130-132</td>
<td>53.84 (4.31) (7.11) (16.43) (4.42)</td>
<td>91.83</td>
</tr>
<tr>
<td>VIII</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values of $\Lambda_M$ reported$^{61,64}$ for 1:1 electrolytes in DMSO=50-70 S cm$^2$ mol$^{-1}$
Table 2. Important infrared absorption bands (cm\(^{-1}\)) of Schiff base (Sal-TMP) and complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>(v(O-H))</th>
<th>(v(N-H))</th>
<th>(v(C=N))</th>
<th>(v(C=N)) pyrimidine</th>
<th>(v(C=O))</th>
<th>(v(Te-N))</th>
<th>(v(Te-O))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2836 w</td>
<td>3317 m</td>
<td>3119 m</td>
<td>1636 sh</td>
<td>1633 w</td>
<td>1593 s</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>-</td>
<td>3323 m</td>
<td>3184 m</td>
<td>1674 mb</td>
<td>1644 mb</td>
<td>1587 s</td>
<td>1341 s</td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>3323 m</td>
<td>3170 m</td>
<td>1647 sh</td>
<td><strong>1586 s</strong></td>
<td>1304 s</td>
<td>420 m</td>
</tr>
<tr>
<td>III</td>
<td>3405 m*</td>
<td>3323 m</td>
<td>3150 m</td>
<td>1674 mb</td>
<td>1641 mb</td>
<td>1586 s</td>
<td>1304 s</td>
</tr>
<tr>
<td>IV</td>
<td>3398 m*</td>
<td>3319 m</td>
<td>3172 m</td>
<td>1652 mb</td>
<td>1649 mb</td>
<td>1587 s</td>
<td>1341 s</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>3325 m</td>
<td>3178 m</td>
<td>1645 sh</td>
<td><strong>1587 s</strong></td>
<td>1333 s</td>
<td>416 s</td>
</tr>
<tr>
<td>VI</td>
<td>-</td>
<td>3320 m</td>
<td>3158 m</td>
<td>1640 sh</td>
<td><strong>1590 s</strong></td>
<td>1331 s</td>
<td>410 m</td>
</tr>
<tr>
<td>VII</td>
<td>3401 w*</td>
<td>3324 m</td>
<td>3168 m</td>
<td>1674 mb</td>
<td>1643 mb</td>
<td>1584 s</td>
<td>1340 s</td>
</tr>
<tr>
<td>VIII</td>
<td>3463 w*</td>
<td>3304 m</td>
<td>3106 m</td>
<td>1634 sh</td>
<td>1643 mb</td>
<td>1584 s</td>
<td>1340 s</td>
</tr>
</tbody>
</table>

\(s=\text{sharp}, \, m=\text{medium}, \, mb=\text{medium broad}, \, sh=\text{shoulder}, \, w=\text{weak}\); *Due to phenolic OH of Rte and R\(_2\)Te moieties; **band not resolved due to overlapping of band \(v(C=N)\).

Examination of the Schiff base (Sal-TMP) spectrum shows the presence of the hydrogen bonded conjugated-chelate ring system\(^{66-68}\) with its centre at \(\sim 2832 \text{ cm}^{-1}\). 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\(^{69}\). Hydrogen bond contributes to planarity of the molecule which helps in chelation\(^{70}\). Also an intense ligand band at 1263 cm\(^{-1}\) (phenolic –C-O) in free ligand has shifted to higher frequency side in complexes. All these indicate that the hydroxyl group of salicylaldehyde of Schiff base is involved in coordination with tellurium\(^{71-73}\).

In addition, the spectra of the Schiff base shown shoulder at 1636 cm\(^{-1}\) with slightly resolved weak band at 1633 cm\(^{-1}\) and sharp band at 1593 cm\(^{-1}\) assigned to \(v(C=N)\) mode for vibration of azomethine group\(^{7,8,65-76}\) and \(v(C=N)_{\text{pyrim}}\). For pyrimidine ring\(^{4,77}\). These shift in aryltellurium Schiff base complexes towards higher and lower value\(^{74-79}\) reflecting that ligand coordinate through nitrogen atom of azomethine and pyrimidine ring.

The medium intensity band at 3317 cm\(^{-1}\) and 3119 cm\(^{-1}\) due to \(v(N-H)\) 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 270-295 cm\(^{-1}\) due to \(v(Te-O)\)\(^{80-83}\) mode and medium to strong band in the range of 410-422 cm\(^{-1}\) due to \(v(Te-N)\) mode\(^{84}\) 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 Sal-TMP involving azomethine nitrogen atom, phenolic oxygen after deprotonation and pyrimidine ring nitrogen giving rise to two-six and four membered chelate rings with the tellurium centre.
In order to identify the solution structure of Schiff base (Sal-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 10.92 $\delta$ ppm$^{76,85}$ in Schiff base due to presence of intramolecular hydrogen bonding$^{74}$ disappear on complexation indicating the involvement of phenolic oxygen in the coordination via deprotonation$^{76}$. The azomethine protons which resonate as a singlet at 10.02 $\delta$ ppm, the coordination of azomethine nitrogen to tellurium in the complexes are clearly demonstrated by a downfield shift of the peak$^{86}$.

**Table 3. $^1$H NMR spectral data of Schiff base (Sal-TMP) and complexes in DMSO-$d_6$**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical Shift, $\delta$ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2.525 (s, 2H, methylene), 3.551-3.745 (s, 9H, $-\text{OCH}_3$), 5.672 (s, 1H, pyrimidine), 6.508 (s, 2H, $-\text{NH}_2$), 7.526-8.169 (m, 6H, aromatic proton), 10.021 (s, 1H, azomethine), 10.921 (s, 1H, Schiff base OH)</td>
</tr>
<tr>
<td>I</td>
<td>2.539 (s, 2H, methylene), 3.598-3.840 (s, 12H, $-\text{OCH}_3$), 6.574 (s, 1H, pyrimidine), 6.926 (s, 2H, $-\text{NH}_2$), 7.383-7.522 (m, 10H, aromatic proton), 10.209 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>II</td>
<td>1.335 (t, 3H, $-\text{OCH}_2\text{CH}_3$), 2.546 (s, 2H, methylene), 3.963 (q, 2H, $-\text{OCH}_2\text{CH}_3$), 3.515-3.875 (s, 9H, $-\text{OCH}_3$), 6.540 (s, 1H, pyrimidine), 6.950 (s, 2H, $-\text{NH}_2$), 6.993-7.809 (m, 10H, aromatic proton), 10.193 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>III</td>
<td>2.548 (s, 2H, methylene), 3.601-3.783 (s, 9H, $-\text{OCH}_3$), 6.569 (s, 1H, pyrimidine), 6.914 (s, 2H, $-\text{NH}_2$), 7.370-7.787 (m, 10H, aromatic proton), 8.155 (s, 1H, phenolic OH of RTe), 10.201 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>IV</td>
<td>2.536 (s, 2H, methylene), 2.527 (s, 3H, $-\text{CH}_3$), 3.587-3.770 (s, 9H, $-\text{OCH}_3$), 6.605 (s, 1H, pyrimidine), 6.918 (s, 2H, $-\text{NH}_2$), 7.051-7.671 (m, 9H, aromatic proton), 8.251 (s, 1H, phenolic OH of RTe), 10.239 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>V</td>
<td>2.528 (s, 2H, methylene), 3.673-3.877 (s, 1H, $-\text{OCH}_3$), 6.516 (s, 1H, pyrimidine), 6.882 (s, 2H, $-\text{NH}_2$), 6.910-7.804 (m, 14H, aromatic proton), 10.186 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>VI</td>
<td>1.363 (t, 6H, $-\text{OCH}_2\text{CH}_3$), 2.531 (s, 2H, methylene), 4.019 (q, 4H, $-\text{OCH}_2\text{CH}_3$), 3.555-3.765 (s, 9H, $-\text{OCH}_3$), 6.510 (s, 1H, pyrimidine), 6.924 (s, 2H, $-\text{NH}_2$), 7.524-7.805 (m, 14H, aromatic proton), 10.216 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>VII</td>
<td>2.545 (s, 2H, methylene), 3.568-3.926 (s, 9H, $-\text{OCH}_3$), 6.554 (s, 1H, pyrimidine), 6.884 (s, 2H, $-\text{NH}_2$), 7.488-7.678 (m, 14H, aromatic proton), 8.249 (s, 2H, phenolic OH of R$_2$Te), 10.238 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>VIII</td>
<td>2.538 (s, 2H, methylene), 2.529 (s, 6H, $-\text{CH}_3$), 3.555-3.750 (s, 9H, $-\text{OCH}_3$), 6.502 (s, 1H, pyrimidine), 6.926 (s, 2H, $-\text{NH}_2$), 7.126-7.868 (m, 12H, aromatic proton), 8.149 (s, 2H, phenolic OH of R$_2$Te), 10.239 (s, 1H, azomethine)</td>
</tr>
</tbody>
</table>

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

The characteristic downfield shifting of proton signal in all complexes observed in region 5.67 $\delta$ ppm is due to pyrimidine proton in Schiff base clearly indicate the coordination through pyrimidine nitrogen atom$^{87}$. The signal due to $-\text{NH}$ proton is observed around 6.51 $\delta$ ppm which remain intact with slight variation in complexes is due to the proton bounded to nitrogen experience quadruple effect$^{87}$. Thus salicylidene-trimethoprim act as a tridentate $-\text{N, -N, -O}$ chelating ligand in Sal-TMP,ArTeCl$_2$ and Sal-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 given below (Figure 2).
The salicylidene-trimethoprim Schiff base (Sal-TMP) and newly synthesized aryltellurium(IV) Schiff base complexes were evaluated for their antimicrobial activity in vitro against Gram +ve bacteria (S. aureus ATCC 11632 and B. cereus MTCC 7350), Gram –ve bacteria (E. coli ATCC 35218, P. aeruginosa ATCC 23564, S. typhi ATCC 15499 and P. rettgeri DRDE) and fungal strains (A. niger, A. fumigates and A. flavus) by tube dilution method. Dilution of test and standard compounds were prepared double strength nutrient broth–I.P (Antibacterial) and Sabouraud Dextrose Broth –I.P (Antifungal). The samples were incubated at 37±1 °C for 24 h (bacteria), 25±1 °C for 7 days (A. niger), 30±1 °C for 15 days (A. flavus), 35±1 °C for 72 h (A. fumigates) respectively and results were recorded in terms of MIC (The lowest concentration of test substances which inhibited values are presented in the Table 4.

The data show that the Sal-TMP complexes of aryltellurium(IV) exhibit more antimicrobial activity towards bacteria as compared to fungii. The antibacterial activity shows following trend.

**Biological Activity**

Figure 2. Proposed structures of complexes

Sal-TMP Ar₂TeCl

Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl
Sal-TMP.$\text{Ar}_2\text{TeCl} > \text{Sal-TMP.}\text{ArTeCl}_2 \approx \text{Sal-TMP Schiff base}

Sal-TMP.$\text{Ar}_2\text{TeCl}$ and Sal-TMP.$\text{ArTeCl}_2$ complexes have activity towards $S.\text{ typhi}$ and more effectively against $B.\text{ cereus}$ but Schiff base does not show activity against these bacterial strains. Schiff base and its complexes show almost similar activity against fungal strains.

Table 4. Minimum Inhibitory Concentration, MIC, µg/mL; (-) Resistant

<table>
<thead>
<tr>
<th>Compound</th>
<th>S. aureus (ATCC 11632)</th>
<th>S. typhi (ATCC 15499)</th>
<th>P. aeruginosa (ATCC 23564)</th>
<th>E. coli (ATCC 35218)</th>
<th>B. cereus (MTCC 7350)</th>
<th>P. rettgeri (DRDE strain)</th>
<th>A. niger</th>
<th>A. fumigates flavus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2.5</td>
<td>-</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>20</td>
<td>5.0</td>
<td>1.25</td>
</tr>
<tr>
<td>I</td>
<td>2.5</td>
<td>-</td>
<td>1.25</td>
<td>-</td>
<td>0.625</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>II</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.25</td>
<td>2.5</td>
<td>20</td>
<td>5.0</td>
</tr>
<tr>
<td>III</td>
<td>-</td>
<td>20</td>
<td>10</td>
<td>5.0</td>
<td>1.25</td>
<td>-</td>
<td>5.0</td>
<td>-</td>
</tr>
<tr>
<td>IV</td>
<td>1.25</td>
<td>2.5</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
<td>5.0</td>
<td>10</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>20</td>
<td>10</td>
<td>5.0</td>
<td>1.25</td>
<td>-</td>
<td>20</td>
<td>-</td>
</tr>
<tr>
<td>VI</td>
<td>1.25</td>
<td>2.5</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>5.0</td>
</tr>
<tr>
<td>VII</td>
<td>1.25</td>
<td>-</td>
<td>5.0</td>
<td>1.25</td>
<td>0.625</td>
<td>-</td>
<td>5.0</td>
<td>-</td>
</tr>
<tr>
<td>VIII</td>
<td>2.5</td>
<td>-</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
<td>20</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Conclusion

Aryltellurium(IV) and diaryltellurium(IV) dichlorides upon reaction with Schiff base(Sal-TMP) derived from salicylaldehyde and trimethoprim yield new complexes of tellurium(IV). The synthesized complexes were characterized by elemental analyses, conductance measurement, IR and $^1\text{H}$ NMR spectral studies. The analytical data suggest that the Sal-TMP Schiff base complexes have 1:1 stoichiometry. The Schiff bases (Sal-TMP) in these complexes functions as a uninegative tridentate ligand through azomethine nitrogen, phenolic oxygen after deprotonation and pyrimidine ring nitrogen atoms. Based on these studies, distorted octahedral geometry with two chelating rings has been assigned to these complexes. The complexes have been observed to possess substantial antimicrobial activity especially against bacteria.

Acknowledgement

The authors are grateful to M. D. University, Rohtak for providing the necessary facilities. One of the authors (Deepak) is also thankful to UGC New Delhi for providing fellowship. We also thank SAIF, Panjab University Chandigarh for providing the CHN analyses and spectral data.

References

42. Berg M C, Diss Abstr Int., 1972, 33, 2982.
46. Garad M V, Polyhedron, 1985, 4(8), 1353-1355; DOI:10.1016/S0277-5387(00)86963-6
89. Pharmacopoeia of India, Volume 1, Controller of Publications, Ministry of Health Department, Government of India, New Delhi, 2007, 37.
Synthesis, Spectral and Biological Studies of Some Salicylidene-Trimethoprim Schiff Base Complexes of Aryltellurium(IV)

DEEPAK, K. K. VERMA and SAPANA GARG*

Department of Chemistry, Maharshi Dayanand University, Rohtak-124001, India
sapanagarg1511@gmail.com

Received 14 February 2017 / Accepted 2 March 2017

Abstract: A novel monobasic tridentate Schiff base salicylidene-trimethoprim, Sal-TMP, synthesized from trimethoprim and salicylaldehyde, form stable complexes with aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides of the type Sal-TMP.ArTeCl$_2$ and Sal-TMP.Ar$_2$TeCl$_2$ (where Ar = $p$-methoxyphenyl, $p$-ethoxyphenyl, $p$-hydroxyphenyl and 3-methyl-4-hydroxyphenyl). These have been characterized by elemental analyses, molar conductance, IR and $^1$H 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. The complexes have also been screened for their antimicrobial activities against various bacteria and fungi organisms.

Keywords: Salicylidene-trimethoprim Schiff base, Aryltellurium(IV), Diaryltellurium(IV), Antibacterial, Antifungal activities

Introduction

Trimethoprim and its derivatives are broad spectrum antimicrobial agents with anti-parasitic activity$^{1-6}$ and were first described by Roth and coworker$^5$. Schiff bases, also known as azomethine due to presence of –C=N– group, play important role in biological system, such as anticancer$^{7-12}$, antibacterial$^{13-15}$, antiviral$^{16-18}$, antifungal$^{19-21}$ and other biological properties$^{22-27}$ and also have been extensively used as ligands in coordination chemistry because of their excellent donor abilities as chelating agent$^{28-32}$. Medicinal chemists have reported new derivatives of trimethoprim(TMZ)$^{33-35}$ including the Schiff base derived from salicylaldehyde$^{2-4,36,37}$.

Also, aryltellurium(IV) chlorides are known$^{36-54}$ 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 diaryl tellurium(IV) dichlorides, R$_2$TeCl$_2$ with salicylidene-trimethoprim Schiff base(Sal-TMP).
Experimental

All preparations were carried out under dry \( \text{N}_2 \) atmosphere and the solvents used were purified by standard method\(^{55,56} \) 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 on a ThermoFinnigan CHNS analyser. Conductivity was measured in DMSO at 25\( \pm 2 \) \( ^\circ \text{C} \) with dip type conductivity cell on a microprocessor based conductivity bridge type MICROSL.

IR (4000-400 cm\(^{-1} \)) and far IR (400-50 cm\(^{-1} \)) spectra were recorded in KBr/polyethylene pellets on a FT-Infrared spectrophotometer model RZX (Perkin Elmer) at SAIF, Panjab University Chandigarh. Proton magnetic resonance spectra were recorded in DMSO-\( \text{d}_6 \) using TMS as an internal reference on BRUKER AVANCE II 400 NMR spectrometer. The antimicrobial screening was carried out by tube dilution method at Department of Pharmaceutical Sciences, M. D. University, Rohtak, India.

Preparation of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

\( \text{p-Methoxyphenyltellurium(IV) trichloride}^{57,58} \), \( \text{bis(p-methoxyphenyl)tellurium(IV) dichloride}^{58,59} \), \( \text{p-ethoxyphenyltellurium(IV) trichloride}^{60} \), \( \text{bis(p-ethoxyphenyl)tellurium dichloride}^{60} \), \( \text{p-hydroxyphenyltellurium(IV) trichloride}^{61} \), \( \text{bis(p-hydroxyphenyl) tellurium(IV) dichloride}^{61} \), \( \text{3-methyl-4-hydroxyphenyltellurium(IV) trichloride}^{62} \) and \( \text{bis(3-methyl-4-hydroxyphenyl)tellurium(IV) dichloride}^{62} \) were prepared by the reactions of \( \text{TeCl}_4 \) with anisole, phenetole, phenol, \( \text{o-cresol} \) respectively, by the methods reported in the literature\(^{57-62} \).

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP)

Equimolar quantity of saturated methanolic solution of drug and salicylaldehyde were mixed thoroughly. To this mixture 0.1% methanolic KOH was added to adjust the pH of the solution between 7-8 and was refluxed for 2 hours. A clear yellowish-green 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 \( \text{P}_2\text{O}_{10} \) until further use. Yield = 80\%, M.pt.(decomp.)=188-190 \( ^\circ \text{C} \). Analysis (Calculated) C\(_{21}\)H\(_{22}\)N\(_4\)O\(_4\): C(63.95), H(5.62) and N(14.20); Found: C(63.50), H(5.27) and N(13.99).

Preparation of salicylidene-trimethoprim complexes of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

Aryltellurium(IV) trichlorides, \( \text{ArTeCl}_3 \) and diaryltellurium(IV) dichlorides \( \text{Ar}_2\text{TeCl}_2 \) (\( \text{Ar}=\text{p-methoxyphenyl}, \text{p-ethoxyphenyl}, \text{p-hydroxyphenyl} \) and 3-methyl-4-hydroxyphenyl), when reacted with sodium salt of salicylidene-trimethoprim in equimolar ratio, yield Sal-TMP.\( \text{ArTeCl}_2 \) and Sal-TMP.\( \text{Ar}_2\text{TeCl} \) 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 \( \text{P}_2\text{O}_{10} \).
Results and Discussion

TeCl$_4$ when heated with anisole$^{57-59}$, phenetole$^{60}$, phenol$^{61}$, o-cresol$^{62}$ (Ar-H) appears to undergo Friedel-Crafts type condensation reaction whereby TeCl$_4^+$ 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.

\[
\text{Ar-H} + \text{TeCl}_4 \rightarrow \text{ArTeCl}_3 + \text{HCl} \tag{1}
\]

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

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP) by the reaction of trimethoprim drug and salicylaldehyde can be represented by following equations.

\[
\begin{align*}
\text{Na}^+ & + \text{Cl}^- & \text{NaCl} \\
\text{H} & + \text{OH}^- & \text{H}_2\text{O} \\
\text{pH} 7-8 & & (1\% \text{KOH in methanol})
\end{align*}
\]

\[
\begin{align*}
\text{Sal-TMP} + \text{ArTeCl}_3 & \xrightarrow{\text{Na/CH}_3\text{OH}} \text{(Sal-TMP).ArTeCl}_2 \tag{3} \\
\text{Sal-TMP} + \text{Ar}_2\text{TeCl}_2 & \xrightarrow{\text{Na/CH}_3\text{OH}} \text{(Sal-TMP).Ar}_2\text{TeCl}_2 \tag{4}
\end{align*}
\]

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.

Conductance studies

Molar conductance ($\Lambda_M$) data for the complexes in DMSO are complied in Table 1. The $\Lambda_M$ value at ca. 10$^{-3}$ M for aryltellurium(IV) complexes in DMSO lie in the range 27.36-91.83 S cm$^2$ mol$^{-1}$ which predict the non electrolyte to 1:1 electrolyte$^{63,64}$ type behaviour of these complexes in DMSO, probably due to ionization into ArTeCl.$\text{Sal-TMP}^+$/Ar.$\text{Te-Sal-TMP}^+$ and Cl$^-$ in DMSO. This conductance behaviour of tellurium(IV) salicylidene-trimethoprim Schiff base complexes is different from those of transition metal complexes$^{65}$, which are reported to be non-electrolytes. The higher $\Lambda_M$ values for some complexes may be due to steric factors and donor behaviour of DMSO to result in probable dissociation into solvated cation and L$^-$ along with Cl$^-$ in DMSO.

Infrared spectra

The IR data of Schiff base and its tellurium(IV) complexes are listed in Table 2. The spectra of Sal-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$_2$. 
Table 1. Analytical data, molar conductance and physical properties of salicylidene-trimethoprim Schiff base (Sal-TMP) complexes of tellurium(IV)

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Complex (Ar)</th>
<th>Empirical formula (Formula Wt.)</th>
<th>Colour (Yield, %)</th>
<th>M. Pt. °C dec.</th>
<th>Analyses % Found (Calculated)</th>
<th>(\Lambda_M) at ca. 10(^{-3}) M S (\text{cm}^2\text{mol}^{-1}) in DMSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schiff Base</td>
<td>Sal-TMP</td>
<td>C(<em>{21})H(</em>{22})N(_4)O(_4)</td>
<td>Yellowish–green (80)</td>
<td>188-190</td>
<td>63.50 (63.95) 5.27 (5.62) 13.99 (14.20) - - -</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>(Sal-TMP).ArTeCl(_2) (p-methoxyphenyl)</td>
<td>C(<em>{29})H(</em>{30})Cl(_2)N(_4)O(_5)Te (685.03)</td>
<td>Light cream (94)</td>
<td>208-210</td>
<td>48.12 (48.85) 3.87 (4.24) 7.52 (7.86) 17.38 (18.63) 9.81 (10.21)</td>
<td>52.88</td>
</tr>
<tr>
<td>II</td>
<td>(Sal-TMP).ArTeCl(_2) (p-ethoxyphenyl)</td>
<td>C(<em>{29})H(</em>{30})Cl(_2)N(_4)O(_5)Te (713.08)</td>
<td>Cream (85)</td>
<td>258-260</td>
<td>48.11 (48.85) 3.99 (4.24) 7.52 (7.86) 17.38 (18.63) 9.81 (10.21)</td>
<td>52.88</td>
</tr>
<tr>
<td>III</td>
<td>(Sal-TMP).ArTeCl(_2) (p-hydroxyphenyl)</td>
<td>C(<em>{29})H(</em>{30})Cl(_2)N(_4)O(_5)Te (699.05)</td>
<td>Dark cream (94)</td>
<td>198-200</td>
<td>48.91 (49.14) 3.84 (3.93) 7.80 (8.01) 18.15 (18.24) 9.85 (10.01)</td>
<td>58.68</td>
</tr>
<tr>
<td>IV</td>
<td>(Sal-TMP).ArTeCl(_2) (3-methyl-4-hydroxyphenyl)</td>
<td>C(<em>{29})H(</em>{30})Cl(_2)N(_4)O(_5)Te (699.05)</td>
<td>Light cream (80)</td>
<td>198-200</td>
<td>48.91 (49.14) 3.84 (3.93) 7.80 (8.01) 18.15 (18.24) 9.85 (10.01)</td>
<td>58.68</td>
</tr>
<tr>
<td>V</td>
<td>(Sal-TMP).Ar(_2)TeCl (p-methoxyphenyl)</td>
<td>C(<em>{35})H(</em>{35})Cl(_4)N(_4)O(_6)Te (770.73)</td>
<td>Pale yellow (84)</td>
<td>130-132</td>
<td>53.84 (54.54) 4.31 (4.58) 7.11 (7.27) 16.43 (16.56) 4.42 (4.60)</td>
<td>91.83</td>
</tr>
<tr>
<td>VI</td>
<td>(Sal-TMP).Ar(_2)TeCl (p-ethoxyphenyl)</td>
<td>C(<em>{35})H(</em>{35})Cl(_4)N(_4)O(_6)Te (798.78)</td>
<td>Light yellow (86)</td>
<td>150-152</td>
<td>54.84 (55.63) 4.53 (4.92) 6.84 (7.01) 15.50 (15.97) 4.30 (4.44)</td>
<td>35.90</td>
</tr>
<tr>
<td>VII</td>
<td>(Sal-TMP).Ar(_2)TeCl (p-hydroxyphenyl)</td>
<td>C(<em>{35})H(</em>{35})Cl(_4)N(_4)O(_6)Te (742.68)</td>
<td>Red (89)</td>
<td>146-148</td>
<td>52.84 (53.37) 4.01 (4.21) 7.27 (7.54) 16.89 (17.18) 4.52 (4.77)</td>
<td>36.00</td>
</tr>
<tr>
<td>VIII</td>
<td>(Sal-TMP).Ar(_2)TeCl (3-methyl-4-hydroxyphenyl)</td>
<td>C(<em>{35})H(</em>{35})Cl(_4)N(_4)O(_6)Te (770.73)</td>
<td>Brown (78)</td>
<td>140-142</td>
<td>53.80 (54.54) 4.34 (4.58) 7.09 (7.27) 16.45 (16.56) 4.32 (4.60)</td>
<td>27.36</td>
</tr>
</tbody>
</table>

Values of \(\Lambda_M\) reported\(^{63,64}\) for 1:1 electrolytes in DMSO=50-70 S cm\(^2\)mol\(^{-1}\)
Table 2. Important infrared absorption bands (cm\(^{-1}\)) of Schiff base (Sal-TMP) and complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>(v_{(O-H)})</th>
<th>(v_{(N-H)})</th>
<th>(v_{(C=N)})</th>
<th>(v_{(C=N)}) pyrimidine</th>
<th>(v_{(C=O)})</th>
<th>(v_{(Te-N)})</th>
<th>(v_{(Te-O)})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2836 w</td>
<td>3317 m</td>
<td>3119 m</td>
<td>1636 sh</td>
<td>1633 w</td>
<td>1593 s</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>-</td>
<td>3323 m</td>
<td>3184 m</td>
<td>1674 mb</td>
<td>1644 mb</td>
<td>1587 s</td>
<td>415 m</td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>3323 m</td>
<td>3170 m</td>
<td>1647 mb</td>
<td>1649 mb</td>
<td>1587 s</td>
<td>420 m</td>
</tr>
<tr>
<td>III</td>
<td>3405 m(^*)</td>
<td>3323 m</td>
<td>3150 m</td>
<td>1647 mb</td>
<td>1649 mb</td>
<td>1587 s</td>
<td>420 m</td>
</tr>
<tr>
<td>IV</td>
<td>3398 m(^*)</td>
<td>3319 m</td>
<td>3172 m</td>
<td>1647 mb</td>
<td>1649 mb</td>
<td>1587 s</td>
<td>420 m</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>3317 m</td>
<td>3178 m</td>
<td>1645 sh</td>
<td>1643 mb</td>
<td>1584 s</td>
<td>418 m</td>
</tr>
<tr>
<td>VI</td>
<td>-</td>
<td>3320 m</td>
<td>3158 m</td>
<td>1640 sh</td>
<td>1643 mb</td>
<td>1584 s</td>
<td>418 m</td>
</tr>
<tr>
<td>VII</td>
<td>3401 w(^*)</td>
<td>3324 m</td>
<td>3168 m</td>
<td>1674 mb</td>
<td>1643 mb</td>
<td>1584 s</td>
<td>422 m</td>
</tr>
<tr>
<td>VIII</td>
<td>3463 w(^*)</td>
<td>3304 m</td>
<td>3106 m</td>
<td>1634 sh</td>
<td>1643 mb</td>
<td>1584 s</td>
<td>422 m</td>
</tr>
</tbody>
</table>

s=sharp, \(m=\)medium, \(mb=\)medium broad, \(sh=\)shoulder, \(w=\)weak; \(^*\)Due to phenolic OH of Rte and R\(_2\)Te moieties; \(^\ast\)band not resolved due to overlapping of band \(v_{(C=N)}\)

Examination of the Schiff base (Sal-TMP) spectrum shows the presence of the hydrogen bonded conjugated-chelate ring system\(^{66-68}\) with its centre at ~2832 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.

![Figure 1. Hydrogen bonding](image)

Thus band disappear on chelation with aryltellurium(IV) chlorides\(^{69}\). Hydrogen bond contributes to planarity of the molecule which helps in chelation\(^{70}\). Also an intense ligand band at 1263 cm\(^{-1}\) (phenolic –C-O) in free ligand has shifted to higher frequency side in complexes. All these indicate that the hydroxyl group of salicylaldehyde of Schiff base is involved in coordination with tellurium\(^{71-73}\).

In addition, the spectra of the Schiff base shown shoulder at 1636 cm\(^{-1}\) with slightly resolved weak band at 1633 cm\(^{-1}\) and sharp band at 1593 cm\(^{-1}\) assigned to \(v_{(C=N)}\) mode for vibration of azomethine group\(^{2,4,65,74-76}\) and \(v_{(C=N)_{pyrim}}\) For pyrimidine ring\(^{4,77}\). These shift in aryltellurium Schiff base complexes towards higher and lower value\(^{74-79}\) reflecting that ligand coordinate through nitrogen atom of azomethine and pyrimidine ring.

The medium intensity band at 3317 cm\(^{-1}\) and 3119 cm\(^{-1}\) due to \(v_{(N-H)}\) 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 270-295 cm\(^{-1}\) due to \(v_{(Te-O)}\) mode and medium to strong band in the range of 410-422 cm\(^{-1}\) due to \(v_{(Te-N)}\) mode\(^{84}\) 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 Sal-TMP involving azomethine nitrogen atom, phenolic oxygen after deprotonation and pyrimidine ring nitrogen giving rise to two-six and four membered chelate rings with the tellurium centre.
In order to identify the solution structure of Schiff base (Sal-TMP) and its complexes, \(^1H\) NMR spectra were recorded in DMSO-d\(_6\) and given in Table 3. The proton resonance of the OH group at 10.92 \(\delta\) ppm\(^{74,85}\) in Schiff base due to presence of intramolecular hydrogen bonding\(^{74}\) disappear on complexation indicating the involvement of phenolic oxygen in the coordination via deprotonation\(^{76}\). The azomethine protons which resonate as a singlet at 10.02 \(\delta\) ppm, the coordination of azomethine nitrogen to tellurium in the complexes are clearly demonstrated by a downfield shift of the peak\(^{86}\).

### Table 3. \(^1H\) NMR spectral data of Schiff base (Sal-TMP) and complexes in DMSO-d\(_6\)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical Shift, (\delta) ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2.525(s, 2H, methylene), 3.551-3.745(s, 9H, (-OCH_3)), 5.672(s,1H, pyrimidine), 6.508(s, 2H, (-NH_2)), 7.526-8.169(m, 6H, aromatic proton), 10.021(s, 1H, azomethine), 10.921(s, 1H, Schiff base OH)</td>
</tr>
<tr>
<td>I</td>
<td>2.539(s, 2H, methylene), 3.598-3.840(s, 12H, (-OCH_3)), 6.574(s, 1H, pyrimidine), 6.926(s, 2H, (-NH_2)), 7.383-7.522(m, 10H, aromatic proton), 10.209(s, 1H, azomethine)</td>
</tr>
<tr>
<td>II</td>
<td>1.335(t, 3H, (-OCH_2CH_3)), 2.546(s, 2H, methylene), 3.963(q, 2H, (-OCH_2CH_3)), 3.515-3.875(s, 9H, (-OCH_3)), 6.540(s, 1H, pyrimidine), 6.950(s, 2H, (-NH_2)), 6.993-7.809(m, 10H, aromatic proton), 10.193(s, 1H, azomethine)</td>
</tr>
<tr>
<td>III</td>
<td>2.548(s, 2H, methylene), 3.601-3.783(s, 9H, (-OCH_3)), 6.569(s,1H, pyrimidine), 6.914(s, 2H, (-NH_2)), 7.370-7.787(m, 10H, aromatic proton), 8.155(s, 1H, phenolic OH of RTe), 10.201(s, 1H, azomethine)</td>
</tr>
<tr>
<td>IV</td>
<td>2.536(s, 2H, methylene), 2.527(s, 3H, (-CH_3)), 3.587-3.770(s, 9H, (-OCH_3)), 6.605(s, 1H, pyrimidine), 6.918(s, 2H, (-NH_2)), 7.051-7.671(m, 9H, aromatic proton), 8.251(s, 1H, phenolic OH of RTe), 10.239(s, 1H, azomethine)</td>
</tr>
<tr>
<td>V</td>
<td>2.528(s, 2H, methylene), 3.673-3.877(s, 15H, (-OCH_3)), 6.516(s,1H, pyrimidine), 6.882(s, 2H, (-NH_2)), 6.910-7.804(m, 14H, aromatic proton), 10.186(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VI</td>
<td>1.363(t, 6H, (-OCH_2CH_3)), 2.531(s, 2H, methylene), 4.019(q, 4H, (-OCH_2CH_3)), 3.555-3.765(s, 9H, (-OCH_3)), 6.510(s, 1H, pyrimidine), 6.924(s, 2H, (-NH_2)), 7.524-7.805(m, 14H, aromatic proton), 10.216(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VII</td>
<td>2.545(s, 2H, methylene), 3.568-3.926(s, 9H, (-OCH_3)), 6.554(s, 1H, pyrimidine), 6.884(s, 2H, (-NH_2)), 7.488-7.678(m, 14H, aromatic proton), 8.249(s, 2H, phenolic OH of R(_2)Te), 10.238(s, 1H, azomethine)</td>
</tr>
<tr>
<td>VIII</td>
<td>2.538(s, 2H, methylene), 2.529(s, 6H, (-CH_3)), 3.555-3.750(s, 9H, (-OCH_3)), 6.502(s, 1H, pyrimidine), 6.926(s, 2H, (-NH_2)), 7.126-7.868(m, 12H, aromatic proton), 8.149(s, 2H, phenolic OH of R(_2)Te), 10.239(s, 1H, azomethine)</td>
</tr>
</tbody>
</table>

\(s=\)singlet, \(q=\)quartet, \(t=\)triplet, \(m=\)multiplet

The characteristic downfield shifting of proton signal in all complexes observed in region 5.67 \(\delta\) ppm is due to pyrimidine proton in Schiff base clearly indicate the coordination through pyrimidine nitrogen atom\(^{87}\). The signal due to \(-NH\) proton is observed around 6.51 \(\delta\) ppm which remain intact with slight variation in complexes is due to the proton bounded to nitrogen experience quadruple effect\(^{87}\). Thus salicylidene-trimethoprim act as a tridentate –N, –N, –O chelating ligand in Sal-TMP,ArTeCl\(_2\) and Sal-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 given below (Figure 2).
The salicylidene-trimethoprim Schiff base (Sal-TMP) and newly synthesized aryltellurium(IV) Schiff base complexes were evaluated for their antimicrobial activity in vitro against Gram +ve bacteria (S. aureus ATCC 11632 and B. cereus MTCC 7350), Gram –ve bacteria (E. coli ATCC 35218, P. aeruginosa ATCC 23564, S. typhi ATCC 15499 and P. rettgeri DRDE) and fungal strains (A. niger, A. fumigates and A. flavus) by tube dilution method. Dilution of test and standard compounds were prepared double strength nutrient broth- I.P (Antibacterial) and Sabouraud Dextrose Broth –I.P (Antifungal). The samples were incubated at 37±1 ºC for 24 h (bacteria), 25±1 ºC for 7 days (A. niger), 30 ±1 ºC for 15 days (A. flavus), 35±1 ºC for 72 h (A. fumigates) respectively and results were recorded in terms of MIC (The lowest concentration of test substances which inhibited values are shown in the Table 4.

The data show that the Sal-TMP complexes of aryltellurium(IV) exhibit more antimicrobial activity towards bacteria as compared to fungi. The antibacterial activity shows following trend.

**Figure 2.** Proposed structures of complexes

Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl

**Biological Activity**

The salicylidene-trimethoprim Schiff base (Sal-TMP) and newly synthesized aryltellurium(IV) Schiff base complexes were evaluated for their antimicrobial activity in vitro against Gram +ve bacteria (S. aureus ATCC 11632 and B. cereus MTCC 7350), Gram –ve bacteria (E. coli ATCC 35218, P. aeruginosa ATCC 23564, S. typhi ATCC 15499 and P. rettgeri DRDE) and fungal strains (A. niger, A. fumigates and A. flavus) by tube dilution method. Dilution of test and standard compounds were prepared double strength nutrient broth- I.P (Antibacterial) and Sabouraud Dextrose Broth –I.P (Antifungal). The samples were incubated at 37±1 ºC for 24 h (bacteria), 25±1 ºC for 7 days (A. niger), 30 ±1 ºC for 15 days (A. flavus), 35±1 ºC for 72 h (A. fumigates) respectively and results were recorded in terms of MIC (The lowest concentration of test substances which inhibited values are shown in the Table 4.

The data show that the Sal-TMP complexes of aryltellurium(IV) exhibit more antimicrobial activity towards bacteria as compared to fungi. The antibacterial activity shows following trend.
Sal-TMP. Ar₂TeCl > Sal-TMP. ArTeCl₂ ≈ Sal-TMP Schiff base

Sal-TMP. Ar₂TeCl and Sal-TMP. ArTeCl₂ complexes have activity towards S. typhi and more effectively against B. cereus but Schiff base does not show activity against these bacterial strains. Schiff base and its complexes show almost similar activity against fungal strains.

Table 4. Minimum Inhibitory Concentration, MIC, µg/mL; (-) Resistant

<table>
<thead>
<tr>
<th>Compound</th>
<th>S. aureus (ATCC 11632)</th>
<th>S. typhi (ATCC 15499)</th>
<th>P. aeruginosa (ATCC 23564)</th>
<th>E. coli (ATCC 35218)</th>
<th>B. cereus (MTCC 7350)</th>
<th>P. rettgeri (DRDE strain)</th>
<th>A. niger</th>
<th>A. fumigates flavus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2.5</td>
<td>-</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
<td>20</td>
<td>5.0</td>
</tr>
<tr>
<td>I</td>
<td>2.5</td>
<td>-</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>20</td>
<td>5.0</td>
<td>1.25</td>
</tr>
<tr>
<td>II</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
<td>1.25</td>
<td>2.5</td>
<td>20</td>
<td>5.0</td>
<td>-</td>
</tr>
<tr>
<td>III</td>
<td>-</td>
<td>20</td>
<td>10</td>
<td>5.0</td>
<td>-</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>IV</td>
<td>1.25</td>
<td>2.5</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>5.0</td>
<td>-</td>
<td>5.0</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>20</td>
<td>10</td>
<td>5.0</td>
<td>1.25</td>
<td>20</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>VI</td>
<td>1.25</td>
<td>2.5</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>VII</td>
<td>1.25</td>
<td>-</td>
<td>5.0</td>
<td>1.25</td>
<td>0.625</td>
<td>5.0</td>
<td>-</td>
<td>10</td>
</tr>
<tr>
<td>VIII</td>
<td>2.5</td>
<td>-</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>20</td>
<td>5.0</td>
<td>1.25</td>
</tr>
</tbody>
</table>

Conclusion

Aryltellurium(IV) and diaryltellurium(IV) dichlorides upon reaction with Schiff base (Sal-TMP) derived from salicylaldehyde and trimethoprim yield new complexes of tellurium(IV). The synthesized complexes were characterized by elemental analyses, conductance measurement, IR and ¹H NMR spectral studies. The analytical data suggest that the Sal-TMP Schiff base complexes have 1:1 stoichiometry. The Schiff bases (Sal-TMP) in these complexes functions as a uninegative tridentate ligand through azomethine nitrogen, phenolic oxygen after deprotonation and pyrimidine ring nitrogen atoms. Based on these studies, distorted octahedral geometry with two chelating rings has been assigned to these complexes. The complexes have been observed to possess substantial antimicrobial activity especially against bacteria.

Acknowledgement

The authors are grateful to M. D. University, Rohtak for providing the necessary facilities. One of the authors (Deepak) is also thankful to UGC New Delhi for providing fellowship. We also thank SAIF, Panjab University Chandigarh for providing the CHN analyses and spectral data.

References

42. Berg M C, Diss Abstr Int., 1972, 33, 2982.
46. Garad M V, Polyhedron, 1985, 4(8), 1353-1355; DOI:10.1016/S0277-5387(00)86963-6
89. Pharmacopoeia of India, Volume I, Controller of Publications, Ministry of Health Department, Government of India, New Delhi, 2007, 37.
Synthesis, Spectral and Biological Studies of Some Salicylidene-Trimethoprim Schiff Base Complexes of Aryltellurium(IV)

DEEPAK, K. K. VERMA and SAPANA GARG

Department of Chemistry, Maharshi Dayanand University, Rohtak-124001, India
sapanagarg1511@gmail.com

Received 14 February 2017 / Accepted 2 March 2017

Abstract: A novel monobasic tridentate Schiff base salicylidene-trimethoprim, Sal-TMP, synthesized from trimethoprim and salicylaldehyde, form stable complexes with aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides of the type Sal-TMP.ArTeCl$_2$ and Sal-TMP.Ar$_2$TeCl (where Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl). These have been characterized by elemental analyses, molar conductance, IR and $^1$H 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 hexacoordinated tellurium(IV) complexes. The complexes have also been screened for their antimicrobial activities against various bacteria and fungi organisms.

Keywords: Salicylidene-trimethoprim Schiff base, Aryltellurium(IV), Diaryltellurium(IV), Antibacterial, Antifungal activities

Introduction

Trimethoprim and its derivatives are broad spectrum antimicrobial agents with anti-parasitic activity$^{1-6}$ and were first described by Roth and coworker$^5$. Schiff bases, also known as azomethine due to presence of $\equiv$C=N$-$ group, play important role in biological system, such as anticancer$^{7-12}$, antibacterial$^{13-15}$, antivirals$^{16-18}$, antifungal$^{19-21}$ and other biological properties$^{22-27}$ and also have been extensively used as ligands in coordination chemistry because of their excellent donor abilities as chelating agent$^{28-32}$. Medicinal chemists have reported new derivatives of trimethoprim(TMZ)$^{33-35}$ including the Schiff base derived from salicylaldehyde$^{2-4,36,37}$.

Also, aryltellurium(IV) chlorides are known$^{38-54}$ 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 salicylidene-trimethoprim Schiff base(Sal-TMP).
Experimental

All preparations were carried out under dry N\textsubscript{2} atmosphere and the solvents used were purified by standard method\textsuperscript{55,56} 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 on a ThermoFinnigan CHNS analyser. Conductivity was measured in DMSO at 25±2 °C with dip type conductivity cell on a microprocessor based conductivity bridge type MICROSIL.

IR (4000-400 cm\textsuperscript{-1}) and far IR (400-50 cm\textsuperscript{-1}) spectra were recorded in KBr/polyethylene pellets on a FT-Infrared spectrophotometer model RZX (Perkin Elmer) at SAIF, Panjab University Chandigarh. Proton magnetic resonance spectra were recorded in DMSO-d\textsubscript{6} using TMS as an internal reference on BRUKER AVANCE II 400 NMR spectrometer. The antimicrobial screening was carried out by tube dilution method at Department of Pharmaceutical Sciences, M. D. University, Rohtak, India.

Preparation of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

\textit{p-Methoxyphenyltellurium(IV) trichloride\textsuperscript{57,58}, bis(p-methoxyphenyl)tellurium(IV) dichloride\textsuperscript{58,59}, p-ethoxyphenyltellurium (IV) trichloride\textsuperscript{60}, bis(p-ethoxyphenyl)tellurium dichloride\textsuperscript{60}, p-hydroxyphenyltellurium(IV) trichloride\textsuperscript{61}, bis(p-hydroxyphenyl) tellurium(IV) dichloride\textsuperscript{61}, 3-methyl-4-hydroxyphenyltellurium(IV) trichloride\textsuperscript{62} and bis(3-methyl-4-hydroxyphenyl)tellurium(IV) dichloride\textsuperscript{62} were prepared by the reactions of TeCl\textsubscript{4} with anisole, phenetole, phenol, o-cresol respectively, by the methods reported in the literature\textsuperscript{57-62}.}

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP)

Equimolar quantity of saturated methanolic solution of drug and salicylaldehyde were mixed thoroughly. To this mixture 0.1% methanolic KOH was added to adjust the pH of the solution between 7-8 and was refluxed for 2 hours. A clear yellowish-green 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 \textit{vacuum} and kept in desiccator over P\textsubscript{4}O\textsubscript{10} until further use. Yield = 80\%, M.pt.(decomp.)=188-190 °C. Analysis (Calculated) C\textsubscript{21}H\textsubscript{22}N\textsubscript{4}O\textsubscript{4}: C(63.95), H(5.62) and N(14.20); Found: C(63.50), H(5.27) and N(13.99).

Preparation of salicylidene-trimethoprim complexes of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

Aryltellurium(IV) trichlorides, ArTeCl\textsubscript{3} and diaryltellurium(IV) dichlorides Ar\textsubscript{2}TeCl\textsubscript{2} (Ar= p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl), when reacted with sodium salt of salicylidene-trimethoprim in equimolar ratio, yield Sal-TMP.ArTeCl\textsubscript{2} and Sal-TMP.Ar\textsubscript{2}TeCl 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 \textit{in vacuum} desiccator over P\textsubscript{4}O\textsubscript{10}.}
Results and Discussion

TeCl₄ when heated with anisole⁵⁷⁻⁵⁹, phenetole⁶⁰, phenol⁶¹, o-cresol⁶² (Ar-H) appears to undergo Friedel-Crafts type condensation reaction whereby TeCl₅⁺ 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.

\[
\begin{align*}
\text{Ar-H + TeCl}_4 & \rightarrow \text{ArTeCl}_3 + \text{HCl} \\
2 \text{Ar-H + TeCl}_4 & \rightarrow \text{Ar}_2\text{TeCl}_2 + 2 \text{HCl}
\end{align*}
\]

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP) by the reaction of trimethoprim drug and salicylaldehyde can be represented by following equations.

\[
\text{Sodium salt of salicylidene-trimethoprim Schiff base (Sal-TMP) reacts with aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides in 1:1 molar ratio to yield the corresponding aryltellurium(IV) complexes.}
\]

\[
\begin{align*}
\text{Sal-TMP} + \text{ArTeCl}_3 & \rightarrow \text{Na/CH}_3\text{OH} \rightarrow (\text{Sal-TMP}).\text{ArTeCl}_2 \\
\text{Sal-TMP} + \text{Ar}_2\text{TeCl}_2 & \rightarrow \text{Na/CH}_3\text{OH} \rightarrow (\text{Sal-TMP}).\text{Ar}_2\text{TeCl}_2
\end{align*}
\]

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.

Conductance studies

Molar conductance ($\Lambda_M$) data for the complexes in DMSO are complied in Table 1. The $\Lambda_M$ value at ca. $10^{-3}$ M for aryltellurium(IV) complexes in DMSO lie in the range $27.36$-$91.83$ S cm$^2$ mol$^{-1}$ which predict the non electrolyte to 1:1 electrolyte$^{63,64}$ type behaviour of these complexes in DMSO, probably due to ionization into $\text{ArTeCl}_3$.Sal-TMP$^+$/Ar$_2$Te.Sal-TMP$^+$ and Cl$^-\text{ in DMSO.}$ This conductance behaviour of tellurium(IV) salicylidene-trimethoprim Schiff base complexes is different from those of transition metal complexes$^{65}$, which are reported to be non-electrolytes. The higher $\Lambda_M$ values for some complexes may be due to steric factors and donor behaviour of DMSO to result in probable dissociation into solvated cation and L$^-$ along with Cl$^-$ in DMSO.

Infrared spectra

The IR data of Schiff base and its tellurium(IV) complexes are listed in Table 2. The spectra of Sal-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$_2$. 
Table 1. Analytical data, molar conductance and physical properties of salicylidene-trimethoprim Schiff base (Sal-TMP) complexes of tellurium(IV)

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Complex (Ar)</th>
<th>Empirical formula (Formula Wt.)</th>
<th>Colour (Yield, %)</th>
<th>M. Pt. °C dec.</th>
<th>Analyses % Found (Calculated)</th>
<th>$\Lambda_M$ at ca. $10^{-3}$ M S cm$^2$ mol$^{-1}$ in DMSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schiff Base</td>
<td>Sal-TMP</td>
<td>C$<em>{21}$H$</em>{22}$N$_4$O$_4$</td>
<td>Yellowish –green (80)</td>
<td>188-190</td>
<td>63.50 (63.95)</td>
<td>5.27 (5.62)</td>
</tr>
<tr>
<td>I</td>
<td>(Sal-TMP).ArTeCl$_2$ (p-methoxyphenyl)</td>
<td>C$<em>{29}$H$</em>{30}$Cl$_2$N$_4$O$_5$Te$_2$ (685.03)</td>
<td>Light cream (94)</td>
<td>208-210</td>
<td>47.78 (48.11)</td>
<td>3.50 (3.83)</td>
</tr>
<tr>
<td>II</td>
<td>(Sal-TMP).ArTeCl$_2$ (p-ethoxyphenyl)</td>
<td>C$<em>{27}$H$</em>{26}$Cl$_2$N$_4$O$_5$Te$_2$ (685.03)</td>
<td>Dark cream (94)</td>
<td>198-200</td>
<td>47.58 (48.11)</td>
<td>3.84 (4.04)</td>
</tr>
<tr>
<td>III</td>
<td>(Sal-TMP).ArTeCl$_2$ (p-hydroxyphenyl)</td>
<td>C$<em>{33}$H$</em>{31}$Cl$_4$N$_4$O$_6$Te$_2$ (742.68)</td>
<td>Red (89)</td>
<td>146-148</td>
<td>52.84 (53.37)</td>
<td>4.01 (4.21)</td>
</tr>
<tr>
<td>IV</td>
<td>(Sal-TMP).ArTeCl$_2$ (3-methyl-4-hydroxyphenyl)</td>
<td>C$<em>{37}$H$</em>{39}$Cl$_4$N$_4$O$_6$Te$_2$ (798.78)</td>
<td>Light yellow (86)</td>
<td>150-152</td>
<td>54.84 (55.63)</td>
<td>4.53 (4.92)</td>
</tr>
<tr>
<td>V</td>
<td>(Sal-TMP).Ar$_2$TeCl       (p-methoxyphenyl)</td>
<td>C$<em>{32}$H$</em>{35}$Cl$_4$N$_4$O$_6$Te$_2$ (770.73)</td>
<td>Pale yellow (84)</td>
<td>130-132</td>
<td>53.84 (54.54)</td>
<td>4.31 (4.58)</td>
</tr>
<tr>
<td>VI</td>
<td>(Sal-TMP).Ar$_2$TeCl       (p-ethoxyphenyl)</td>
<td>C$<em>{32}$H$</em>{35}$Cl$_4$N$_4$O$_6$Te$_2$ (770.73)</td>
<td>Light yellow (86)</td>
<td>130-132</td>
<td>53.84 (54.54)</td>
<td>4.31 (4.58)</td>
</tr>
<tr>
<td>VII</td>
<td>(Sal-TMP).Ar$_2$TeCl       (p-hydroxyphenyl)</td>
<td>C$<em>{32}$H$</em>{35}$Cl$_4$N$_4$O$_6$Te$_2$ (770.73)</td>
<td>Red (89)</td>
<td>146-148</td>
<td>52.84 (53.37)</td>
<td>4.01 (4.21)</td>
</tr>
<tr>
<td>VIII</td>
<td>(Sal-TMP).Ar$_2$TeCl       (3-methyl-4-hydroxyphenyl)</td>
<td>C$<em>{32}$H$</em>{35}$Cl$_4$N$_4$O$_6$Te$_2$ (770.73)</td>
<td>Brown (78)</td>
<td>140-142</td>
<td>53.80 (54.54)</td>
<td>4.34 (4.58)</td>
</tr>
</tbody>
</table>

Values of $\Lambda_M$ reported$^{61,64}$ for 1:1 electrolytes in DMSO=50-70 S cm$^2$ mol$^{-1}$
Table 2. Important infrared absorption bands (cm\(^{-1}\)) of Schiff base (Sal-TMP) and complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>(v(\text{O-H}))</th>
<th>(v(\text{N-H}))</th>
<th>(v(\text{C=N}))</th>
<th>(v(\text{C=O})_{\text{pyrim}})</th>
<th>(v(\text{C=O}))</th>
<th>(v(\text{Te-N}))</th>
<th>(v(\text{Te-O}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2836 w</td>
<td>3317 m 3119 m</td>
<td>1636 sh</td>
<td>1633 w 1593 s</td>
<td>1263 s</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>-</td>
<td>3323 m 3184 m</td>
<td>1674 mb</td>
<td>1644 mb 1587 s</td>
<td>1341 s</td>
<td>415 m</td>
<td>288 w</td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>3323 m 3170 m</td>
<td>1647 sh</td>
<td>**1586 s</td>
<td>1304 s</td>
<td>420 m</td>
<td>295 w</td>
</tr>
<tr>
<td>III</td>
<td>3405 m*</td>
<td>3323 m 3150 m</td>
<td>1674 mb</td>
<td>1641 mb 1586 s</td>
<td>1341 s</td>
<td>419 s</td>
<td>270 w</td>
</tr>
<tr>
<td>IV</td>
<td>3398 m*</td>
<td>3319 m 3172 m</td>
<td>1652 mb</td>
<td>1649 mb 1587 s</td>
<td>1333 s</td>
<td>450 s</td>
<td>-</td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>3325 m 3178 m</td>
<td>1645 sh</td>
<td>**1587 s</td>
<td>1333 s</td>
<td>416 s</td>
<td>290 w</td>
</tr>
<tr>
<td>VI</td>
<td>-</td>
<td>3320 m 3158 m</td>
<td>1640 sh</td>
<td>**1590 s</td>
<td>1331 s</td>
<td>410 s</td>
<td>273 w</td>
</tr>
<tr>
<td>VII</td>
<td>3401 w*</td>
<td>3324 m 3168 m</td>
<td>1674 mb</td>
<td>1643 mb 1584 s</td>
<td>1340 s</td>
<td>418 s</td>
<td>285 w</td>
</tr>
<tr>
<td>VIII</td>
<td>3463 w*</td>
<td>3304 m 3106 m</td>
<td>1634 sh</td>
<td>1643 mb 1584 s</td>
<td>1340 s</td>
<td>422 s</td>
<td>287 w</td>
</tr>
</tbody>
</table>

\(s=\text{sharp, } m=\text{medium, } mb=\text{medium broad, } sh=\text{shoulder, } w=\text{weak, }^*\text{Due to phenolic OH of R}_{2}\text{Te moieties; }^**\text{band not resolved due to overlapping of band }v(\text{C=N})\)

Examination of the Schiff base (Sal-TMP) spectrum shows the presence of the hydrogen bonded conjugated-chelate ring system\(^{66-68}\) with its centre at ~2832 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\(^{69}\). Hydrogen bond contributes to planarity of the molecule which helps in chelation\(^{70}\). Also an intense ligand band at 1263 cm\(^{-1}\) (phenolic –C-O) in free ligand has shifted to higher frequency side in complexes. All these indicate that the hydroxyl group of salicylaldehyde of Schiff base is involved in coordination with tellurium\(^{71-73}\).

In addition, the spectra of the Schiff base shown shoulder at 1636 cm\(^{-1}\) with slightly resolved weak band at 1633 cm\(^{-1}\) and sharp band at 1593 cm\(^{-1}\) assigned to \(v(\text{C=N})\) mode for vibration of azomethine group\(^{7,4,65-76}\) and \(v(\text{C=N})_{\text{pyrim}}\). For pyrimidine ring\(^{4,77}\). These shift in aryltellurium Schiff base complexes towards higher and lower value\(^{74-79}\) reflecting that ligand coordinate through nitrogen atom of azomethine and pyrimidine ring.

The medium intensity band at 3317 cm\(^{-1}\) and 3119 cm\(^{-1}\) due to \(v(\text{N-H})\) 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 270-295 cm\(^{-1}\) due to \(v(\text{Te-O})\)\(^{80-83}\) mode and medium to strong band in the range of 410-422 cm\(^{-1}\) due to \(v(\text{Te-N})\) mode\(^{84}\) 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 Sal-TMP involving azomethine nitrogen atom, phenolic oxygen after deprotonation and pyrimidine ring nitrogen giving rise to two-six and four membered chelate rings with the tellurium centre.
In order to identify the solution structure of Schiff base (Sal-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 10.92 δ ppm$^{76,85}$ in Schiff base due to presence of intramolecular hydrogen bonding$^{74}$ disappear on complexation indicating the involvement of phenolic oxygen in the coordination via deprotonation$^{76}$. The azomethine protons which resonate as a singlet at 10.02 δ ppm, the coordination of azomethine nitrogen to tellurium in the complexes are clearly demonstrated by a downfield shift of the peak$^{86}$.

### Table 3. $^1$H NMR spectral data of Schiff base (Sal-TMP) and complexes in DMSO-d$_6$

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical Shift, δ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2.525 (s, 2H, methylene), 3.551-3.745 (s, 9H, -OCH$_3$), 5.672 (s, 1H, pyrimidine), 6.508 (s, 2H, -NH$_2$), 7.526-8.169 (m, 6H, aromatic proton), 10.021 (s, 1H, azomethine), 10.921 (s, 1H, Schiff base OH)</td>
</tr>
<tr>
<td>I</td>
<td>2.539 (s, 2H, methylene), 3.598-3.840 (s, 12H, -OCH$_3$), 6.574 (s, 1H, pyrimidine), 6.926 (s, 2H, -NH$_2$), 7.383-7.522 (m, 10H, aromatic proton), 10.209 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>II</td>
<td>1.335 (t, 3H, -OCH$_2$CH$_3$), 2.546 (s, 2H, methylene), 3.963 (q, 2H, -OCH$_2$CH$_3$), 3.515-3.875 (s, 9H, -OCH$_3$), 6.540 (s, 1H, pyrimidine), 6.950 (s, 2H, -NH$_2$), 6.993-7.809 (m, 10H, aromatic proton), 10.193 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>III</td>
<td>2.548 (s, 2H, methylene), 3.601-3.783 (s, 9H, -OCH$_3$), 6.569 (s, 1H, pyrimidine), 6.914 (s, 2H, -NH$_2$), 7.370-7.787 (m, 10H, aromatic proton), 8.155 (s, 1H, phenolic OH of RTe), 10.201 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>IV</td>
<td>2.536 (s, 2H, methylene), 2.527 (s, 3H, -CH$_3$), 3.587-3.770 (s, 9H, -OCH$_3$), 6.605 (s, 1H, pyrimidine), 6.918 (s, 2H, -NH$_2$), 7.051-7.671 (m, 9H, aromatic proton), 8.251 (s, 1H, phenolic OH of RTe), 10.239 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>V</td>
<td>2.528 (s, 2H, methylene), 3.673-3.877 (s, 15H, -OCH$_3$), 6.516 (s, 1H, pyrimidine), 6.882 (s, 2H, -NH$_2$), 6.910-7.804 (m, 14H, aromatic proton), 10.186 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>VI</td>
<td>1.363 (t, 3H, -OCH$_2$CH$_3$), 2.531 (s, 2H, methylene), 4.019 (q, 4H, -OCH$_2$CH$_3$), 3.555-3.765 (s, 9H, -OCH$_3$), 6.510 (s, 1H, pyrimidine), 6.924 (s, 2H, -NH$_2$), 7.524-7.805 (m, 14H, aromatic proton), 10.216 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>VII</td>
<td>2.545 (s, 2H, methylene), 3.568-3.926 (s, 9H, -OCH$_3$), 6.554 (s, 1H, pyrimidine), 6.884 (s, 2H, -NH$_2$), 7.488-7.678 (m, 14H, aromatic proton), 8.249 (s, 2H, phenolic OH of R$_2$Te), 10.238 (s, 1H, azomethine)</td>
</tr>
<tr>
<td>VIII</td>
<td>2.538 (s, 2H, methylene), 2.529 (s, 6H, -CH$_3$), 3.555-3.750 (s, 9H, -OCH$_3$), 6.502 (s, 1H, pyrimidine), 6.926 (s, 2H, -NH$_2$), 7.126-7.868 (m, 12H, aromatic proton), 8.149 (s, 2H, phenolic OH of R$_2$Te), 10.239 (s, 1H, azomethine)</td>
</tr>
</tbody>
</table>

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

The characteristic downfield shifting of proton signal in all complexes observed in region 5.67 δ ppm is due to pyrimidine proton in Schiff base clearly indicate the coordination through pyrimidine nitrogen atom$^{87}$. The signal due to –NH proton is observed around 6.51 δ ppm which remain intact with slight variation in complexes is due to the proton bounded to nitrogen experience quadruple effect$^{87}$. Thus salicylidene-trimethoprim act as a tridentate –N, –N, –O chelating ligand in Sal-TMP,ArTeCl$_2$ and Sal-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 given below (Figure 2).
Biological Activity

The salicylidene-trimetoprim Schiff base (Sal-TMP) and newly synthesized aryltellurium(IV) Schiff base complexes were evaluated for their antimicrobial activity in vitro against Gram +ve bacteria (S. aureus ATCC 11632 and B. cereus MTCC 7350), Gram –ve bacteria (E. coli ATCC 35218, P. aeruginosa ATCC 23564, S. typhi ATCC 15499 and P. rettgeri DRDE) and fungal strains (A. niger, A. fumigates and A. flavus) by tube dilution method. Dilution of test and standard compounds were prepared double strength nutrient broth - I.P (Antibacterial) and Sabouraud Dextrose Broth –I.P (Antifungal). The samples were incubated at 37±1 °C for 24 h (bacteria), 25±1 °C for 7 days (A. niger), 30 ±1 °C for 15 days (A. flavus), 35±1 °C for 72 h (A. fumigates) respectively and results were recorded in terms of MIC (The lowest concentration of test substances which inhibited values are presented in the Table 4).

The data show that the Sal-TMP complexes of aryltellurium(IV) exhibit more antimicrobial activity towards bacteria as compared to fungii. The antibacterial activity shows following trend.

\[ \text{Sal-TMP.Ar}_2\text{TeCl} \]

\( \text{Ar} = p\text{-methoxyphenyl, } p\text{-ethoxyphenyl, } p\text{-hydroxyphenyl and 3-methyl-4-hydroxyphenyl} \)

**Figure 2.** Proposed structures of complexes
Sal-TMP.\textsubscript{Ar}\textsubscript{2}TeCl > Sal-TMP.\textsubscript{Ar}TeCl\textsubscript{2} \approx\text{Sal-TMP Schiff base}

Sal-TMP.\textsubscript{Ar}\textsubscript{2}TeCl and Sal-TMP.\textsubscript{Ar}TeCl\textsubscript{2} complexes have activity towards \textit{S. typhi} and more effectively against \textit{B. cereus} but Schiff base does not show activity against these bacterial strains. Schiff base and its complexes show almost similar activity against fungal strains.

**Table 4. Minimum Inhibitory Concentration, MIC, \(\mu\text{g/mL}; (-)\) Resistant**

<table>
<thead>
<tr>
<th>Compound</th>
<th>\textit{S. aureus} (ATCC 11632)</th>
<th>\textit{S. typhi} (ATCC 15499)</th>
<th>\textit{P. aeruginosa} (ATCC 23564)</th>
<th>\textit{E. coli} (ATCC 35218)</th>
<th>\textit{B. cereus} (MTCC 7350)</th>
<th>\textit{P. rettgeri} (DRDE strain)</th>
<th>\textit{A. niger}</th>
<th>\textit{A. fumigates flavus}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2.5</td>
<td>-</td>
<td>1.25</td>
<td>-</td>
<td>-</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
<td>0.625</td>
<td>5.0</td>
<td>-</td>
<td>20</td>
<td>5.0</td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>20</td>
<td>10</td>
<td>1.25</td>
<td>5.0</td>
<td>2.5</td>
<td>20</td>
<td>5.0</td>
</tr>
<tr>
<td>III</td>
<td>1.25</td>
<td>2.5</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
<td>5.0</td>
<td>10</td>
</tr>
<tr>
<td>IV</td>
<td>1.25</td>
<td>2.5</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
<td>5.0</td>
<td>-</td>
</tr>
<tr>
<td>V</td>
<td>1.25</td>
<td>2.5</td>
<td>5.0</td>
<td>1.25</td>
<td>5.0</td>
<td>2.5</td>
<td>20</td>
<td>-</td>
</tr>
<tr>
<td>VI</td>
<td>1.25</td>
<td>2.5</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>5.0</td>
</tr>
<tr>
<td>VII</td>
<td>1.25</td>
<td>-</td>
<td>5.0</td>
<td>1.25</td>
<td>0.625</td>
<td>5.0</td>
<td>-</td>
<td>10</td>
</tr>
<tr>
<td>VIII</td>
<td>2.5</td>
<td>-</td>
<td>1.25</td>
<td>5.0</td>
<td>-</td>
<td>-</td>
<td>20</td>
<td>5.0</td>
</tr>
</tbody>
</table>

**Conclusion**

 Aryltellurium(IV) and diaryltellurium(IV) dichlorides upon reaction with Schiff base(Sal-TMP) derived from salicylaldehyde and trimethoprim yield new complexes of tellurium(IV). The synthesized complexes were characterized by elemental analyses, conductance measurement, IR and \(^1\text{H} \text{NMR} \) spectral studies. The analytical data suggest that the Sal-TMP Schiff base complexes have 1:1 stoichiometry. The Schiff bases (Sal-TMP) in these complexes functions as a uninegative tridentate ligand through azomethine nitrogen, phenolic oxygen after deprotonation and pyrimidine ring nitrogen atoms. Based on these studies, distorted octahedral geometry with two chelating rings has been assigned to these complexes. The complexes have been observed to possess substantial antimicrobial activity especially against bacteria.

**Acknowledgement**

The authors are grateful to M. D. University, Rohtak for providing the necessary facilities. One of the authors (Deepak) is also thankful to UGC New Delhi for providing fellowship. We also thank SAIF, Panjab University Chandigarh for providing the CHN analyses and spectral data.

**References**

42. Berg M C, Diss Abstr Int., 1972, 33, 2982.
46. Garad M V, Polyhedron, 1985, 4(8), 1353-1355; DOI:10.1016/S0277-5387(00)86963-6
89. Pharmacopoeia of India, Volume 1, Controller of Publications, Ministry of Health Department, Government of India, New Delhi, 2007, 37.
Synthesis, Spectral and Biological Studies of Some Salicylidene-Trimethoprim Schiff Base Complexes of Aryltellurium(IV)

DEEPAK, K. K. VERMA and SAPANA GARG*

Department of Chemistry, Maharshi Dayanand University, Rohtak-124001, India
sapanagarg1511@gmail.com

Received 14 February 2017 / Accepted 2 March 2017

Abstract: A novel monobasic tridentate Schiff base salicylidene-trimethoprim, Sal-TMP, synthesized from trimethoprim and salicylaldehyde, form stable complexes with aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides of the type Sal-TMP.ArTeCl$_2$ and Sal-TMP.Ar$_2$TeCl (where Ar = p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl). These have been characterized by elemental analyses, molar conductance, IR and $^1$H 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. The complexes have also been screened for their antimicrobial activities against various bacteria and fungi organisms.

Keywords: Salicylidene-trimethoprim Schiff base, Aryltellurium(IV), Diaryltellurium(IV), Antibacterial, Antifungal activities

Introduction

Trimethoprim and its derivatives are broad spectrum antimicrobial agents with anti-parasitic activity$^{1-6}$ and were first described by Roth and coworker$^5$. Schiff bases, also known as azomethine due to presence of –C=N– group, play important role in biological system, such as anticancer$^{7-12}$, antibacterial$^{13-15}$, antiviral$^{16-18}$, antifungal$^{19-21}$ and other biological properties$^{22-27}$ and also have been extensively used as ligands in coordination chemistry because of their excellent donor abilities as chelating agent$^{28-32}$. Medicinal chemists have reported new derivatives of trimethoprim(TMZ)$^{33-35}$ including the Schiff base derived from salicylaldehyde$^{2,4,36,37}$.

Also, aryltellurium(IV) chlorides are known$^{38-54}$ 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 salicylidene-trimethoprim Schiff base(Sal-TMP).
Experimental

All preparations were carried out under dry N₂ atmosphere and the solvents used were purified by standard method 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 on a ThermoFinnigan CHNS analyser. Conductivity was measured in DMSO at 25±2 °C with dip type conductivity cell on a microprocessor based conductivity bridge type MICROSIL.

IR (4000-400 cm⁻¹) and far IR (400-50 cm⁻¹) spectra were recorded in KBr/polyethylene pellets on a FT-Infrared spectrophotometer model RZX (Perkin Elmer) at SAIF, Panjab University Chandigarh. Proton magnetic resonance spectra were recorded in DMSO-d₆ using TMS as an internal reference on BRUKER AVANCE II 400 NMR spectrometer. The antimicrobial screening was carried out by tube dilution method at Department of Pharmaceutical Sciences, M. D. University, Rohtak, India.

Preparation of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

p-Methoxyphenyltellurium(IV) trichloride⁵⁷,⁵⁸, bis(p-methoxyphenyl)tellurium(IV) dichloride⁵⁵,⁵⁶, p-ethoxyphenyltellurium (IV) trichloride⁶⁰, bis(p-ethoxyphenyl)tellurium dichloride⁶⁰, p-hydroxyphenyltellurium(IV) trichloride⁶¹, bis(p-hydroxyphenyl) tellurium(IV) dichloride⁶¹, 3-methyl-4-hydroxyphenyltellurium(IV) trichloride⁶² and bis(3-methyl-4-hydroxyphenyl)tellurium(IV) dichloride⁶² were prepared by the reactions of TeCl₄ with anisole, phenetole, phenol, o-cresol respectively, by the methods reported in the literature⁵⁷-⁶².

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP)

Equimolar quantity of saturated methanolic solution of drug and salicylaldehyde were mixed thoroughly. To this mixture 0.1% methanolic KOH was added to adjust the pH of the solution between 7-8 and was refluxed for 2 hours. A clear yellowish-green 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 P₄O₁₀ until further use. Yield = 80%, M.pt.(decomp.)=188-190 °C. Analysis (Calculated) C₂₁H₂₂N₄O₄; C(63.95), H(5.62) and N(14.20); Found: C(63.50), H(5.27) and N(13.99).

Preparation of salicylidene-trimethoprim complexes of aryltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides

Aryltellurium(IV) trichlorides, ArTeCl₃ and diaryltellurium(IV) dichlorides Ar₂TeCl₂ (Ar= p-methoxyphenyl, p-ethoxyphenyl, p-hydroxyphenyl and 3-methyl-4-hydroxyphenyl), when reacted with sodium salt of salicylidene-trimethoprim in equimolar ratio, yield Sal-TMP.ArTeCl₃ and Sal-TMP.Ar₂TeCl₂ 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 P₄O₁₀.
Results and Discussion

TeCl₄ when heated with anisole⁵⁷-⁵⁹, phenetole⁶⁰, phenol⁶¹, o-cresol⁶² (Ar-H) appears to undergo Friedel-Crafts type condensation reaction whereby TeCl₅⁺ unit attacks a position para to the methoxy/ethoxy/hydroxy groups in the aromatic rings, thus resulting in the formation of arylltellurium(IV) trichlorides and diaryltellurium(IV) dichlorides.

\[
\begin{align*}
Ar-H + \text{TeCl}_4 & \rightarrow \text{ArTeCl}_3 + \text{HCl} \quad (1) \\
2 \text{Ar-H} + \text{TeCl}_4 & \rightarrow \text{Ar}_2\text{TeCl}_2 + 2 \text{HCl} \quad (2)
\end{align*}
\]

Preparation of salicylidene-trimethoprim Schiff base (Sal-TMP) by the reaction of trimethoprim drug and salicylaldehyde can be represented by following equations.

\[
\text{Sal-TMP} + \text{ArTeCl}_3 \xrightarrow{\text{Na/CH}_3\text{OH}} (\text{Sal-TMP})\cdot\text{ArTeCl}_2 \quad (3)
\]

\[
\text{Sal-TMP} + \text{Ar}_2\text{TeCl}_2 \xrightarrow{\text{Na/CH}_3\text{OH}} (\text{Sal-TMP})\cdot\text{Ar}_2\text{TeCl}_2 \quad (4)
\]

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

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.

Conductance studies

Molar conductance (Λₘ) data for the complexes in DMSO are compiled in Table 1. The Λₘ value at ca. 10⁻³ M for arylltellurium(IV) complexes in DMSO lie in the range 27.36-91.83 S cm² mol⁻¹ which predict the non electrolyte to 1:1 electrolyte⁶³,⁶⁴ type behaviour of these complexes in DMSO, probably due to ionization into ArTeCl₃.Sal-TMP⁺/Ar₂Te.Sal-TMP⁺ and Cl⁻ in DMSO. This conductance behaviour of tellurium(IV) salicylidene-trimethoprim Schiff base complexes is different from those of transition metal complexes⁶⁵, which are reported to be non-electrolytes. The higher Λₘ values for some complexes may be due to steric factors and donor behaviour of DMSO to result in probable dissociation into solvated cation and L⁻ along with Cl⁻ in DMSO.

Infrared spectra

The IR data of Schiff base and its tellurium(IV) complexes are listed in Table 2. The spectra of Sal-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 ArTeCl₃/Ar₂TeCl₂.
### Table 1. Analytical data, molar conductance and physical properties of salicylidene-trimethoprim Schiff base (Sal-TMP) complexes of tellurium(IV)

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Complex (Ar)</th>
<th>Empirical formula (Formula Wt.)</th>
<th>Colour (Yield, %)</th>
<th>M. Pt. °C dec.</th>
<th>Analyses % Found (Calculated)</th>
<th>Λ_\text{M} at ca. 10^{-3} M S cm^2 mol^{-1} in DMSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schiff Base</td>
<td>Sal-TMP</td>
<td>C_{21}H_{22}N_{4}O_{4}</td>
<td>Yellowish -green (80)</td>
<td>188-190</td>
<td>63.50 (63.95) 5.27 (5.62) 13.99 (14.20) - - -</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>(Sal-TMP).ArTeCl_{2} (p-methoxyphenyl)</td>
<td>C_{29}H_{28}Cl_{2}N_{4}O_{5}Te_{2} (713.08)</td>
<td>Light cream (92)</td>
<td>230-232</td>
<td>47.88 (48.11) 3.99 (4.04) 7.75 (8.01) 18.07 (18.24) 9.89 (10.01)</td>
<td>53.19</td>
</tr>
<tr>
<td>II</td>
<td>(Sal-TMP).ArTeCl_{2} (p-ethoxyphenyl)</td>
<td>C_{29}H_{29}Cl_{2}N_{4}O_{5}Te_{2} (713.08)</td>
<td>Cream (85)</td>
<td>258-260</td>
<td>48.12 (48.85) 3.87 (4.24) 7.52 (7.86) 17.38 (17.89) 9.52 (9.81)</td>
<td>52.88</td>
</tr>
<tr>
<td>III</td>
<td>(Sal-TMP).ArTeCl_{2} (p-hydroxyphenyl)</td>
<td>C_{27}H_{26}Cl_{2}N_{4}O_{5}Te (685.03)</td>
<td>Dark cream (94)</td>
<td>208-210</td>
<td>46.78 (47.34) 3.50 (3.83) 7.88 (8.18) 18.28 (18.63) 9.98 (10.21)</td>
<td>55.73</td>
</tr>
<tr>
<td>IV</td>
<td>(Sal-TMP).ArTeCl_{2} (3-methyl-4-hydroxyphenyl)</td>
<td>C_{28}H_{28}Cl_{2}N_{4}O_{5}Te (699.05)</td>
<td>Light cream (80)</td>
<td>198-200</td>
<td>47.58 (48.11) 3.84 (4.04) 7.80 (8.01) 18.15 (18.24) 9.85 (10.01)</td>
<td>58.68</td>
</tr>
<tr>
<td>V</td>
<td>(Sal-TMP).Ar_{2}TeCl (p-methoxyphenyl)</td>
<td>C_{35}H_{35}Cl_{2}N_{4}O_{6}Te (770.73)</td>
<td>Pale yellow (84)</td>
<td>130-132</td>
<td>53.84 (54.54) 4.31 (4.58) 7.11 (7.27) 16.43 (16.56) 4.42 (4.54)</td>
<td>91.83</td>
</tr>
<tr>
<td>VI</td>
<td>(Sal-TMP).Ar_{2}TeCl (p-ethoxyphenyl)</td>
<td>C_{35}H_{39}Cl_{2}N_{4}O_{6}Te (798.78)</td>
<td>Light yellow (86)</td>
<td>150-152</td>
<td>54.84 (55.63) 4.53 (4.92) 6.84 (7.01) 15.50 (15.97) 4.30 (4.44)</td>
<td>35.90</td>
</tr>
<tr>
<td>VII</td>
<td>(Sal-TMP).Ar_{2}TeCl (p-hydroxyphenyl)</td>
<td>C_{33}H_{31}Cl_{2}N_{4}O_{6}Te (742.68)</td>
<td>Red (89)</td>
<td>146-148</td>
<td>52.84 (53.37) 4.01 (4.21) 7.27 (7.54) 16.89 (17.18) 4.52 (4.77)</td>
<td>36.00</td>
</tr>
<tr>
<td>VIII</td>
<td>(Sal-TMP).Ar_{2}TeCl (3-methyl-4-hydroxyphenyl)</td>
<td>C_{35}H_{35}Cl_{2}N_{4}O_{6}Te (770.73)</td>
<td>Brown (78)</td>
<td>140-142</td>
<td>53.80 (54.54) 4.34 (4.58) 7.09 (7.27) 16.45 (16.56) 4.32 (4.46)</td>
<td>27.36</td>
</tr>
</tbody>
</table>

*Values of Λ_\text{M} reported\textsuperscript{63,64} for 1:1 electrolytes in DMSO=50-70 S cm^2 mol\textsuperscript{-1}.*
Table 2. Important infrared absorption bands (cm\(^{-1}\)) of Schiff base (Sal-TMP) and complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>(v(O-H))</th>
<th>(v(N-H))</th>
<th>(v(C=N))</th>
<th>(v(C=N)) pyrimidine</th>
<th>(v(C=O))</th>
<th>(v(Te-N))</th>
<th>(v(Te-O))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sal-TMP</td>
<td>2836 w</td>
<td>3317 m</td>
<td>1636 sh</td>
<td>1633 w 1593 s 1263 s</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>-</td>
<td>3323 m 3184 m</td>
<td>1674 mb</td>
<td>1644 mb 1587 s 1341 s</td>
<td>415 m 288 w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>3323 m 3170 m</td>
<td>1647 sh</td>
<td>**1586 s 1304 s 420 m</td>
<td>295 w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>3405 m*</td>
<td>3323 m 3150 m</td>
<td>1674 mb</td>
<td>1641 mb 1586 s 1341 s</td>
<td>419 s 270 w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>3398 m*</td>
<td>3319 m 3172 m</td>
<td>1652 mb</td>
<td>1649 mb 1587 s 1333 s</td>
<td>450 s 277 w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>-</td>
<td>3325 m 3178 m</td>
<td>1645 sh</td>
<td>**1587 s 1333 s 416 s</td>
<td>290 w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>-</td>
<td>3320 m 3158 m</td>
<td>1640 sh</td>
<td>**1590 s 1331 s 410 m</td>
<td>273 w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VII</td>
<td>3401 w*</td>
<td>3324 m 3168 m</td>
<td>1674 mb</td>
<td>1643 mb 1584 s 1340 s</td>
<td>418 s 285 w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VIII</td>
<td>3463 w*</td>
<td>3304 m 3106 m</td>
<td>1634 sh</td>
<td>1643 mb 1584 s 1340 s</td>
<td>422 m 287 w</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

s=sharp, m=medium, mb=medium broad, sh=shoulder, w=weak; *Due to phenolic OH of Rte and R2Te moieties; **band not resolved due to overlapping of band \(v(C=N)\).

Examination of the Schiff base (Sal-TMP) spectrum shows the presence of the hydrogen bonded conjugated- chelate ring system\(^{66-68}\) with its centre at ~2832 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.

![Figure 1. Hydrogen bonding](image)

Thus band disappear on chelation with aryltellurium(IV) chlorides\(^{69}\). Hydrogen bond contributes to planarity of the molecule which helps in chelation\(^{70}\). Also an intense ligand band at 1263 cm\(^{-1}\) (phenolic –C-O) in free ligand has shifted to higher frequency side in complexes. All these indicate that the hydroxyl group of salicylaldehyde of Schiff base is involved in coordination with tellurium\(^{71-73}\).

In addition, the spectra of the Schiff base shown shoulder at 1636 cm\(^{-1}\) with slightly resolved weak band at 1633 cm\(^{-1}\) and sharp band at 1593 cm\(^{-1}\) assigned to \(v(C=N)\) mode for vibration of azomethine group\(^{7,6,6,74,76}\) and \(v(C=O)\)pyrim. For pyrimidine ring\(^{4,77}\). These shift in aryltellurium Schiff base complexes towards higher and lower value\(^{74,79}\) reflecting that ligand coordinate through nitrogen atom of azomethine and pyrimidine ring.

The medium intensity band at 3317 cm\(^{-1}\) and 3119 cm\(^{-1}\) due to \(v(N-H)\) asymmetric and symmetric vibrations respectively indicate the non involvement of the nitrogen atom of NH₂ group attached to pyrimidine in coordination. The appearance of new weak bands around 270-295 cm\(^{-1}\) due to \(v(Te-O)\)\(^{80-83}\) mode and medium to strong band in the range of 410-422 cm\(^{-1}\) due to \(v(Te-N)\) mode\(^{84}\) 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 Sal-TMP involving azomethine nitrogen atom, phenolic oxygen after deprotonation and pyrimidine ring nitrogen giving rise to two-six and four membered chelate rings with the tellurium centre.
\(^1\)H NMR spectra

In order to identify the solution structure of Schiff base (Sal-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 10.92 δ ppm \(^\text{76,85}\) disappear on complexation indicating the involvement of phenolic oxygen in the coordination via deprotonation \(^\text{76}\). The azomethine protons which resonate as a singlet at 10.02 δ ppm, the coordination of azomethine nitrogen to tellurium in the complexes are clearly demonstrated by a downfield shift of the peak \(^\text{86}\).

<table>
<thead>
<tr>
<th>Table 3. (^1)H NMR spectral data of Schiff base (Sal-TMP) and complexes in DMSO-d(_6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound</td>
</tr>
<tr>
<td>---------------------------</td>
</tr>
<tr>
<td>Sal-TMP</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>II</td>
</tr>
<tr>
<td>III</td>
</tr>
<tr>
<td>IV</td>
</tr>
<tr>
<td>V</td>
</tr>
<tr>
<td>VI</td>
</tr>
<tr>
<td>VII</td>
</tr>
<tr>
<td>VIII</td>
</tr>
</tbody>
</table>

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

The characteristic downfield shifting of proton signal in all complexes observed in region 5.67 δ ppm is due to pyrimidine proton in Schiff base clearly indicate the coordination through pyrimidine nitrogen atom \(^\text{87}\). The signal due to –NH proton is observed around 6.51 δ ppm which remain intact with slight variation in complexes is due to the proton bounded to nitrogen experience quadruple effect \(^\text{87}\). Thus salicylidene-trimethoprim act as a tridentate –N, –N, –O chelating ligand in Sal-TMP,ArTeCl\(_2\) and Sal-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 given below (Figure 2).
Biological Activity

The salicylidene-trimethoprim Schiff base (Sal-TMP) and newly synthesized aryltellurium(IV) Schiff base complexes were evaluated for their antimicrobial activity in vitro against Gram +ve bacteria (S. aureus ATCC 11632 and B. cereus MTCC 7350), Gram –ve bacteria (E. coli ATCC 35218, P. aeruginosa ATCC 23564, S. typhii ATCC 15499 and P. rettgeri DRDE) and fungal strains (A. niger, A. fumigates and A. flavus) by tube dilution method\(^8\). Dilution of test and standard compounds were prepared double strength nutrient broth- I.P (Antibacterial) and Sabouraud Dextrose Broth –I.P (Antifungal)\(^8\). The samples were incubated at 37±1 °C for 24 h (bacteria), 25±1 °C for 7 days (A. niger), 30 ±1 °C for 15 days (A. flavus), 35±1 °C for 72 h (A. fumigates) respectively and results were recorded in terms of MIC (The lowest concentration of test substances which inhibited values are presented in the Table 4).

The data show that the Sal-TMP complexes of aryltellurium(IV) exhibit more antimicrobial activity towards bacteria as compared to fungii. The antibacterial activity shows following trend.
Sal-TMP.Ar$_2$TeCl $> \text{Sal-TMP.ArTeCl}_2 \approx \text{Sal-TMP Schiff base}$

Sal-TMP.Ar$_2$TeCl and Sal-TMP.ArTeCl$_2$ complexes have activity towards $S$. typhi and more effectively against $B$. cereus but Schiff base does not show activity against these bacterial strains. Schiff base and its complexes show almost similar activity against fungal strains.

**Table 4. Minimum Inhibitory Concentration, MIC, $\mu$g/mL; (-) Resistant**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Bacteria strains</th>
<th>Fungal strains</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S. aureus (ATCC 11632)</td>
<td>S. typhi (ATCC 15499)</td>
</tr>
<tr>
<td>I</td>
<td>2.5 - 1.25</td>
<td>5.0 -</td>
</tr>
<tr>
<td>II</td>
<td>5.0 - -</td>
<td>1.25 -</td>
</tr>
<tr>
<td>III</td>
<td>- 20 10</td>
<td>5.0 -</td>
</tr>
<tr>
<td>IV</td>
<td>1.25 2.5 1.25</td>
<td>5.0 -</td>
</tr>
<tr>
<td>V</td>
<td>- 20 10</td>
<td>5.0 -</td>
</tr>
<tr>
<td>VI</td>
<td>1.25 2.5 1.25</td>
<td>5.0 -</td>
</tr>
<tr>
<td>VII</td>
<td>1.25 - 5.0</td>
<td>1.25 0.625</td>
</tr>
<tr>
<td>VIII</td>
<td>2.5 - 1.25</td>
<td>5.0 -</td>
</tr>
</tbody>
</table>

**Conclusion**

Aryltellurium(IV) and diaryltellurium(IV) dichlorides upon reaction with Schiff base (Sal-TMP) derived from salicylaldehyde and trimethoprim yield new complexes of tellurium(IV). The synthesized complexes were characterized by elemental analyses, conductance measurement, IR and $^1$H NMR spectral studies. The analytical data suggest that the Sal-TMP Schiff base complexes have 1:1 stoichiometry. The Schiff bases (Sal-TMP) in these complexes functions as a uninegative tridentate ligand through azomethine nitrogen, phenolic oxygen after deprotonation and pyrimidine ring nitrogen atoms. Based on these studies, distorted octahedral geometry with two chelating rings has been assigned to these complexes. The complexes have been observed to possess substantial antimicrobial activity especially against bacteria.

**Acknowledgement**

The authors are grateful to M. D. University, Rohtak for providing the necessary facilities. One of the authors (Deepak) is also thankful to UGC New Delhi for providing fellowship. We also thank SAIF, Panjab University Chandigarh for providing the CHN analyses and spectral data.

**References**

42. Berg M C, Diss Abstr Int., 1972, 33, 2982.
46. Garad M V, Polyhedron, 1985, 4(8), 1353-1355; DOI:10.1016/S0277-5387(00)86963-6
89. Pharmacopoeia of India, Volume I, Controller of Publications, Ministry of Health Department, Government of India, New Delhi, 2007, 37.