Synthesis, characteristic, catalytic and antimicrobial activities of imidazolo substituted benzyldiene imines with ruthenium(II) complexes

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Abstract: The synthesis and characterization of several hexa-coordinated Ru\textsuperscript{II} complexes of the type \([\text{RuCl(CO)(EPh}_3]_2(L)]\) (\(E = \text{P or As}; L = \) monobasic bidentate anion) are reported. IR, electronic, \(^1\)H NMR, \(^{31}\)P NMR and catalytic activity of the complexes are discussed. An octahedral geometry has been tentatively proposed for all these complexes. The new complexes exhibit catalytic activity for the addition of benzyl alcohol and cyclohexanol in the presence of \(N\)-methylmorpholine-\(N\)-oxide as co-oxidant. The new complexes were also exhibited antimicrobial investigations.

Keywords: Ruthenium(II) complex, benzyldiene imine, synthesis, imidazolo.

Introduction

Benzyldiene imines have vast medicinal importance showing a number of activities such as tuberculostatic, bactericidal, fungicidal, anti-inflammatory etc.\textsuperscript{1-3}. The pharmacological importance of imidazolones and imines are also reported\textsuperscript{4-7}. Bidentate complexes have been employed as catalyst for many reactions\textsuperscript{8,9}. They are also important for designing metal complexes related to synthetic and natural oxygen carriers\textsuperscript{10}. The real impious towards developing their coordination chemistry was their physicochemical properties and significant biological activities\textsuperscript{11,12}. The chemistry of ruthenium is currently receiving a lot of attention, primarily because of the fascinating electron transfer properties displayed by the complexes of this metal\textsuperscript{13}. Ruthenium offers a wide range of oxidation states and the reactivity of the ruthenium complexes depends on the stability and interconvertibility of these oxidation states, which in turn depend on the nature of the ligand bound to the metal\textsuperscript{14,15}. In this present work, we reported the preparation, spectral, catalytic activity and antimicrobial activities of some Ru\textsuperscript{II} complexes containing bidentate ligands. The general structure of the ligands are given in Fig. 1.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{ligands.png}
\caption{Structure of the ligands.}
\end{figure}

Results and discussion

Light and air stable ruthenium(II) complexes of the general formula \([\text{RuHCl(CO)(EPh}_3]_2(L)]\) (\(E = \text{P or As}; L = \) monobasic bidentate anion) have been prepared by reacting \([\text{RuHCl(CO)(PPh}_3]_3\) and \([\text{RuHCl(CO)(AsPh}_3]_3\) with the respective ligands (Fig. 1) in a 1 : 1 molar ratio in benzene.

\begin{align*}
[\text{RuHCl(CO)(EPh}_3]_2(L)] + \text{HL} & \xrightarrow{\text{Benzene, reflux, 6 h}} [\text{RuCl(CO)(EPh}_3]_2(L)] + \text{H}_2 + \text{EPh}_3
\end{align*}

The analytical data obtained for the new complexes (Table 1) agree very well with the proposed molecular formulae. In all of the above reactions, the ligand behaves as mononegative bidentate ligands.
Table 1. Analytical data of new Ru complex

| Complex | M.p. (°C) | Yield (%) | Analysis (%): Found (Calcd) |
|---------|-----------|-----------|----------------------------|
| [RuCl(CO)(PPh₃)₂(L₁)] | 102 | 75 | C: 68.08 (68.16) 4.48 (4.59) 5.07 (5.04) |
| [RuCl(CO)(AsPh₃)₂(L₁)] | 168 | 80 | C: 63.16 (63.26) 4.21 (4.26) 4.67 (4.68) |
| [RuCl(CO)(PPh₃)₂(L₂)] | 171 | 85 | C: 66.76 (66.66) 4.71 (4.78) 4.92 (4.78) |
| [RuCl(CO)(AsPh₃)₂(L₂)] | 175 | 75 | C: 62.07 (62.10) 4.46 (4.45) 4.51 (4.45) |
| [RuCl(CO)(PPh₃)₂(L₃)] | 165 | 70 | C: 66.20 (66.19) 4.53 (4.55) 4.51 (4.45) |
| [RuCl(CO)(AsPh₃)₂(L₃)] | 170 | 70 | C: 61.52 (61.56) 4.21 (4.23) 4.58 (4.56) |
| [RuCl(CO)(PPh₃)₂(L₄)] | 170 | 75 | C: 67.10 (67.14) 4.59 (4.61) 4.90 (4.97) |
| [RuCl(CO)(AsPh₃)₂(L₄)] | 160 | 80 | C: 62.38 (62.37) 4.26 (4.29) 4.59 (4.62) |

IR spectra:

The IR spectra of the free ligands were compared with those of the new complexes in order to confirm the coordination of benzylidene imine to the ruthenium metal. In free Schiff base ligands, the absorption due to ν(C=N) appears in the 1600-1620 cm⁻¹ region and this band is shifted to the lower region. From the spectra of all the complexes, the coordination of azomethine nitrogen to the metal is evident. A strong band which appeared in the spectra of the ligands around 1610 cm⁻¹ due to ν(C=O) was completely disappeared and a new band was observed around 1570 cm⁻¹. This may be due to the enolisation and subsequent coordination through the deprotonated oxygen atom of the CH=CH group. In all the carbonyl complexes, the band due to terminal C=O group appeared at 1900-1944 cm⁻¹. In addition to the above, the characteristic bands due to PPh₃ or AsPh₃ were also present in the expected region.

Electronic spectra:

All the complexes are diamagnetic indicating the presence of ruthenium in +2 oxidation state in all the complexes. In the electronic spectra of all the complexes in CH₂Cl₂, three to four bands are appeared in the region 640-250 nm. The band in the region 640-750 nm is assigned to the transition 1A₁g → 3T₁g and the bands around 400-370 nm is due to 1A₁g → 3T₂g transition. The other bands in the region 320-250 nm are probably due to charge transfer transitions (t₂g → π*). The nature of the electronic spectra are similar to those observed for other octahedral ruthenium(II) complexes.

¹H NMR and ³¹P NMR spectra:

The ligand to metal bonding is further supported by ¹H NMR spectra. All the complexes showed signals in the 8.0-8.99 ppm range due to the aromatic protons of ligand and PPh₃/AsPh₃. The azomethine proton signals in the complexes lie in the 8.0-8.65 ppm range. The peak due to azomethine showed a high field shift compared to the free ligand after complexation with the metal ion indicating coordination through the azomethine nitrogen atom. Further, the signal for methyl protons appears as singlet in the region 1.6-1.9 ppm. The complexes [RuCl(CO)(PPh₃)₂(L₁)], [RuCl(CO)(AsPh₃)₂(L₁)], [RuCl(CO)(PPh₃)₂(L₂)] and [RuCl(CO)(AsPh₃)₂(L₄)] showed a singlet in the region.
Table 2. IR, electronic, $^1$H NMR and $^{31}$P NMR spectral data of new Ru$^{II}$ complexes

| Complex                  | $\nu_{CN}$ ($\text{cm}^{-1}$) | $\nu_{C-O}$ ($\text{cm}^{-1}$) | $\nu_{\text{NCO}}$ ($\text{cm}^{-1}$) | $\lambda_{\text{max}}$ (nm) | $^1$H NMR (ppm)                          | $^{31}$P NMR (ppm) |
|--------------------------|-------------------------------|-------------------------------|--------------------------------------|----------------------------|------------------------------------------|-------------------|
| [RuCl(CO)(PPh$_3$)$_2$(L$_1$)] | 1585                          | 1570                          | 1520                                 | 640, 400, 325, 250         | 8.0–8.91 (m, aromatic), 8.3 (s, CH=N), 5.81 (s, CH), 1.6 (s, CH$_3$) | 28.75             |
| [RuCl(CO)(AsPh$_3$)$_2$(L$_1$)] | 1595                          | 1560                          | 1515                                 | 630, 390, 300, 250         | 8.2–8.99 (m, aromatic), 8.65 (s, CH=N), 5.82 (s, CH), 1.6 (s, CH$_3$) | a                 |
| [RuCl(CO)(PPh$_3$)$_2$(L$_2$)] | 1600                          | 1570                          | 1520                                 | 680, 380, 260              | 8.1–8.67 (m, aromatic), 8.2 (s, CH=N), 5.80 (s, CH), 1.9 (s, CH$_3$) | 28.81             |
| [RuCl(CO)(AsPh$_3$)$_2$(L$_2$)] | 1605                          | 1565                          | 1510                                 | 570, 370, 320, 250         | 8.0–8.89 (m, aromatic), 8.5 (s, CH=N), 5.81 (s, CH), 1.6 (s, CH$_3$) | a                 |
| [RuCl(CO)(PPh$_3$)$_2$(L$_3$)] | 1590                          | 1570                          | 1515                                 | 590, 400, 330, 260         | 8.3–8.99 (m, aromatic), 8.3 (s, CH=N), 5.80 (s, CH), 1.7 (s, CH$_3$), 5.6 (s, OH) | 28.80             |
| [RuCl(CO)(AsPh$_3$)$_2$(L$_3$)] | 1610                          | 1565                          | 1520                                 | 600, 390, 290, 260         | 8.2–8.92 (m, aromatic), 8.25 (s, CH=N), 5.81 (s, CH), 1.73 (s, CH$_3$), 5.7 (s, OH) | a                 |
| [RuCl(CO)(PPh$_3$)$_2$(L$_4$)] | 1600                          | 1570                          | 1520                                 | 620, 390, 270              | 8.2–8.83 (m, aromatic), 8.3 (s, CH=N), 5.80 (s, CH), 1.65 (s, CH$_3$), 5.65 (s, OH) | 28.82             |
| [RuCl(CO)(AsPh$_3$)$_2$(L$_4$)] | 1585                          | 1560                          | 1515                                 | 620, 390, 310, 270         | 8.2–8.83 (m, aromatic), 8.3 (s, CH=N), 5.82 (s, CH), 1.72 (s, CH$_3$), 5.7 (s, OH) | a                 |

* a = not recorded.
Table 3. Catalytic oxidation of alcohols by new Ru\textsuperscript{II} complexes in the presence of NMO

| Complex | Substrate   | Product | Yield\textsuperscript{a} | Turnover\textsuperscript{a} |
|---------|-------------|---------|--------------------------|----------------------------|
| [RuCl\textsubscript{2}(CO)(PPh\textsubscript{3})\textsubscript{2}(L\textsubscript{2})] | Benzylalcohol | A | 71 | 74 |
|         | Cyclohexanol | A | 67 | 71 |
| [RuCl\textsubscript{2}(CO)(AsPh\textsubscript{3})\textsubscript{2}(L\textsubscript{2})] | Benzylalcohol | A | 56 | 60 |
|         | Cyclohexanol | K | 75 | 79 |
| [RuCl\textsubscript{2}(CO)(PPh\textsubscript{3})\textsubscript{2}(L\textsubscript{2})] | Benzylalcohol | A | 75 | 76 |
|         | Cyclohexanol | K | 65 | 69 |
| [RuCl\textsubscript{2}(CO)(AsPh\textsubscript{3})\textsubscript{2}(L\textsubscript{2})] | Benzylalcohol | A | 70 | 74 |
|         | Cyclohexanol | K | 62 | 66 |
| [RuCl\textsubscript{2}(CO)(PPh\textsubscript{3})\textsubscript{2}(L\textsubscript{2})] | Benzylalcohol | A | 75 | 79 |
|         | Cyclohexanol | K | 66 | 70 |
| [RuCl\textsubscript{2}(CO)(AsPh\textsubscript{3})\textsubscript{2}(L\textsubscript{2})] | Benzylalcohol | A | 73 | 77 |
|         | Cyclohexanol | K | 59 | 63 |

\textsuperscript{a}A : Benzaldehyde; K : Cyclohexanone. \textsuperscript{a}Yield based on substrate. \textsuperscript{a}Moles of product per mole of catalyst.

5.6–5.7 ppm for OH proton. The signal for methine protons appears as singlet in the region 5.80–5.82 ppm.

The \textsuperscript{31}P NMR spectra of three complexes were recorded in order to confirm the presence of PPh\textsubscript{3} groups and to determine the geometry of the complexes. The appearance of a signal around 23.75–28.82 in the spectra of complexes confirmed the presence of magnetically equivalent phosphorous atoms and thus suggesting that the two PPh\textsubscript{3} groups are \textit{trans} to each other\textsuperscript{24}.

\textbf{Catalytic activity}:

The oxidation of alcohols was carried out with the ruthenium complexes as catalyst in the presence of N-methylmorpholine-N-oxide (NMO) as co-oxidant in chloroform (Table 3). Benzaldehyde was formed from benzylalcohol and cyclohexanol was converted into cyclohexanone after stirring for 3 h at room temperature. The products formed were quantified as their 2,4-dinitrophenyl hydrazone derivatives. In no case, there was any detectable oxidation of alcohols in the presence of NMO alone without ruthenium complexes. All of the synthesized ruthenium complexes were found to catalyze the oxidation of alcohols to carbonyl compound but the yield and turnover were found to vary with different catalysts. The yield and turnover number are comparable with those reported for the oxidation of alcohols by similar ruthenium(n) complexes\textsuperscript{24}. It has also been found that PPh\textsubscript{3} complexes possess higher catalytic activity than the AsPh\textsubscript{3} complexes\textsuperscript{25}. This may be due to the higher donor ability of the arsine ligand compared to the phosphine ligand. The relative higher product yield obtained for the oxidation of benzyl alcohol than for cyclohexanol is due to the fact that the \(\alpha\)-CH moiety of benzyl alcohol is more acidic compared to that of cyclohexanol\textsuperscript{24,26}.

The catalytic oxidation is expected to proceed via Ru\textsuperscript{IV}=O intermediate as reported by us earlier\textsuperscript{16}.

\textbf{Antimicrobial study}:

The \textit{in vitro} antimicrobial screening of the ligands and their ruthenium complexes have been carried out against \textit{Escherichia coli}, \textit{Aeromonas hydrophila} and \textit{Salmonella typhi} using a nutrient agar medium by disc diffusion method\textsuperscript{27}. The results (Table 4) show that the complexes exhibit moderate activity against \textit{Escherichia coli}, \textit{Aeromonas hydrophila} and \textit{Salmonella typhi}. The toxicity of ruthenium chelates increases on increasing the concentration\textsuperscript{28}. The increase in the antimicrobial activity of the metal chelates may be due...
Table 4. Antimicrobial activity of ligands and Ru\textsuperscript{II} new complexes

| Ligand/Complex     | Escherichia coli | Aeromonas hydrophila | Salmonella typhi |
|--------------------|------------------|----------------------|------------------|
|                    | Diameter of inhibition zones (mm) | Diameter of inhibition zones (mm) | Diameter of inhibition zones (mm) |
|                    | 0.25% 0.5% 1% | 0.25% 0.5% 1% | 0.25% 0.5% 1% |
| HL                 | 10 12 13 | 9 10 12 | 8 10 11 |
| [RuCl(CO)(PPh\textsubscript{3})\textsubscript{2}(L\textsubscript{1})] | 12 14 16 | 11 14 17 | 10 12 15 |
| [RuCl(CO)(AsPh\textsubscript{3})\textsubscript{2}(L\textsubscript{1})] | 11 13 15 | 10 11 13 | 10 12 14 |
| HL\textsubscript{2} | 10 11 13 | 10 12 13 | 10 12 13 |
| [RuCl(CO)(PPh\textsubscript{3})\textsubscript{2}(L\textsubscript{2})] | 12 14 17 | 12 14 19 | 12 14 15 |
| [RuCl(CO)(AsPh\textsubscript{3})\textsubscript{2}(L\textsubscript{2})] | 11 13 16 | 11 13 15 | 11 13 14 |
| HL\textsubscript{3} | 10 11 12 | 9 10 11 | 9 11 12 |
| [RuCl(CO)(PPh\textsubscript{3})\textsubscript{2}(L\textsubscript{3})] | 13 14 16 | 10 12 14 | 10 12 15 |
| [RuCl(CO)(AsPh\textsubscript{3})\textsubscript{2}(L\textsubscript{3})] | 12 15 16 | 10 11 13 | 10 12 14 |
| HL\textsubscript{4} | 9 10 12 | 8 10 11 | 8 11 12 |
| [RuCl(CO)(PPh\textsubscript{3})\textsubscript{2}(L\textsubscript{4})] | 11 13 14 | 10 12 13 | 11 12 13 |
| [RuCl(CO)(AsPh\textsubscript{3})\textsubscript{2}(L\textsubscript{4})] | 10 11 13 | 10 11 12 | 11 12 13 |
| Streptomycin       | 22 23 28 | 21 27 29 | 29 21 25 |

to the effect of the metal ion on the normal cell process. A possible mode of the toxicity increase may be considered in light of Tweedys chelation theory\textsuperscript{29}. Chelation considerably reduces the polarity of the metal ion because of partial sharing of its positive charge with the donor groups and possible π-electron delocalization over the whole chelate ring. Such chelation could enhance the lipophilic character of the central metal atom, which subsequently favours its permeation through the lipid layers of cell membrane. Furthermore, the mode of action of the compounds may involve the formation of hydrogen bond through the azomethine (>C=N) group with the active centers of cell constituents, resulting in interference the normal cell process\textsuperscript{30}. Though the complexes possess activity, they could not reach the effectiveness of the standard drug streptomycin. The variation in the effectiveness of the different compounds against different organisms depends either on impermeability of the cells or on the microbe of difference in ribosome of microbial cells\textsuperscript{31}.

Based on the analytical and spectral (IR, electronic, \textsuperscript{1}H NMR and \textsuperscript{31}P NMR) data, an octahedral structure (Fig. 2) has been tentatively proposed for all of the new ruthenium(II) complexes.

**Experimental**

**Material and methods:**

All the reagent used were of analar or chemically pure grade. Solvents were purified and dried according to standard procedures. RuCl\textsubscript{3}\cdot3H\textsubscript{2}O purchased from Loba Chemie was used without further purification. The carbon, hydrogen and nitrogen analyses were performed at the Central Drug Research Institute, Lucknow, India. IR spectra of the complexes were recorded as KBr pellets on a Shimadzu 8000 FT-IR spectrophotometer in the 4000-400 cm\textsuperscript{-1} range. The electronic spectra were recorded in CH\textsubscript{2}Cl\textsubscript{2} solution with a Systronics 119 spectrometer in the 800-200 nm range. \textsuperscript{1}H and \textsuperscript{31}P NMR spectra were recorded on Bruker 400 MHz or Varian FX 90Q instruments using TMS and orthophosphoric acid as references, respectively. Melting points were recorded with a Raaga heating table and are uncorrected.
Procedure:

The starting complexes [RuHCl(CO)(PPh₃)]₃², [RuHCl(CO)(AsPh₃)]₃³ and the ligands were prepared according to the literature procedures. Catalytic oxidation of alcohols and antibacterial studies were carried out according to reported procedures.

Catalytic oxidation of alcohol:

To a solution of alcohol (1 mmol) in chloroform (20 cm³), N-methylmorpholine-N-oxide (3 mmol) and the ruthenium complex (0.01 mmol) were added. The solution was stirred for 3 h at room temperature. The mixture was evaporated to dryness and extracted with diethyl ether. The ether extract was filtered and evaporated to give the corresponding aldehyde/ketone which were then quantified as their 2,4-dinitrophenylhydrazone derivatives.

Antibacterial studies:

The ligands and their complexes have been tested for in vitro growth inhibitory activity against the bacteria E. coli, Aeromonas hydrophilla and Salmonella typhi. The bacteria were cultured in nutrient agar medium in Petri plates and used as inoculum for the study. The compounds to be tested were dissolved in DMSO to a final concentration of 0.25 and 0.5% and soaked in filter paper discs of 5 mm diameter and 1 mm thickness. These discs were placed on the previously seeded plates and incubated at 35 ± 2 °C for 24 h. Streptomycin was used as standard.

Preparation of new ruthenium(II) complexes:

To a solution of [RuHCl(CO)(PPh₃)]₃, [RuHCl(CO)(AsPh₃)] (0.1 g, 0.08–0.01 mmol) in benzene (20 cm³) the respective ligands (0.03–0.08 g, 0.08–0.1 mmol) were added. The resulting solution was concentrated to ca. 3 cm³ and the product was separated by the addition of the small amount of light petroleum (60–80 °C). It was filtered and recrystallised from CH₂Cl₂/light petroleum (60–80 °C) and dried in vacuum (yield 70–85%).

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