Studies on Organomercury(II) Complexes of Isoniacinamide

Sangeeta Bhatia, N. K. Kaushik*
Department of Chemistry, University of Delhi, Delhi 110007, India
G. S. Sodhi
Department of Chemistry, SGTB Khalsa College, University of Delhi, Delhi 110007, India

Z. Naturforsch. 43b, 318–322 (1988); received December 1, 1987

Isoniacinamide, Organomercurals, Bonding Mode, Thermal Studies, Antibacterial Activity

Organomercury(II) complexes involving isoniacinamide(I) of the type, RHgCl(L)(II) [R = phenyl, o-, p-hydroxyphenyl (o-, p-HOC₆H₄), p-acetoxyphenyl (p-AcOC₆H₄), 2-furyl (2-C₆H₄O₂)]; L = isoniacinamide] have been synthesized and characterized. Conductance measurements indicate that the complexes are non-electrolytes. From IR and UV spectral studies it is concluded that isoniacinamide is coordinated to the mercury(II) ion through the ring nitrogen atom. ¹H and ¹³C NMR support the stoichiometry of the complexes. Fluorescence studies have been made for o-, p-HOC₆H₄HgCl(L) complexes. For C₆H₄HgCl(L), p-HOC₆H₄HgCl(L) and p-AcOC₆H₄HgCl(L) complexes, thermal studies (TG and DSC) have been carried out and relevant kinetic and thermodynamic parameters for thermal degradation have been enumerated. The fragmentation pattern of the complexes has been analysed on the basis of mass spectra. The C₆H₄HgCl(L) and p-AcOC₆H₄HgCl(L) complexes have been screened for antibacterial activity.

Introduction

Isoniacinamide functions are a constituent of the pyridine nucleotides, which occupy a central role as hydrogen transferring coenzymes. The pyridine ring in the coenzymes is attached in a N-glycosidic linkage to ribose [1]. The interest in the metal complexes of isoniacinamide has arisen because of the fact that although it is a polyfunctional ligand, its bonding mode to the metal ions remains the same as that in the biological system. In the present complexes, too, it is coordinated to mercury(II) ion through the pyridine nitrogen.

Further, isoniacinamide is an antibiotic substance and manifests significant therapeutic effects [2]. It is expected that the antibiotic action of a drug is enhanced in the presence of metal ions, since the introduction of metal complexes in vivo prolongs the metabolism of the drug and leads to a more pronounced biological effect. With this aim, we undertook the synthesis and characterization of some organomercury(II) complexes of isoniacinamide and screened some representative samples for antibacterial activity. This is a sequel to our investigation of metal ion-biomolecule interactions [3–6].

Experimental

The following instruments were used: Elico conductivity bridge, model CM-82 for conductance measurements; Shimadzu infrared spectrophotometer, IR-435 for IR spectra; Perkin-Elmer UV-VIS spectrometer, model 554 for UV spectra; Jeol FX-200 FT-NMR spectrometer for ¹H and ¹³C NMR spectra; Jasco FP-500 spectrofluorometer for fluorescence studies; G-70, SETARAM (Lyon, France) for recording TG curves in air at a heating rate of 8° min⁻¹. Du Pont device for recording DSC curves up to 673 K, at a heating rate of 8° min⁻¹, Mass spectra were recorded at Central Drug Research Institute, Lucknow, India.

Nitrobenzene was purified for conductance measurements by the method of Fay et al. [7]. C₆H₄HgCl [8], o-, p-HOC₆H₄HgCl [9], p-AcOC₆H₄HgCl [10] and 2-C₆H₄OHgCl [11] were synthesized by standard methods. Isoniacinamide was purchased from Aldrich Chemical Co., Inc., USA.

Preparation of complexes

A solution of isoniacinamide (0.01 mol) in 25 ml THF was added slowly to a solution of RHgCl

---

* Reprint requests to Dr. N. K. Kaushik.

Verlag der Zeitschrift für Naturforschung, D-7400 Tübingen 0932–0776/88/0300–0318/$ 01.00/0

Dieses Werk wurde im Jahr 2013 vom Verlag Zeitschrift für Naturforschung in Zusammenarbeit mit der Max-Planck-Gesellschaft zur Förderung der Wissenschaften e.V. digitalisiert und unter folgender Lizenz veröffentlicht: Creative Commons Namensnennung 4.0 Lizenz.

This work has been digitalized and published in 2013 by Verlag Zeitschrift für Naturforschung in cooperation with the Max Planck Society for the Advancement of Science under a Creative Commons Attribution 4.0 International License.
(0.01 mol) in 25 ml THF. The contents were stirred for about 2 h at room temperature and filtered. The RHgCl(L) complexes were precipitated on addition of petroleum ether to the filtrate and recrystallized from acetone.

**Results and Discussion**

Satisfactory results of elemental analysis and spectral studies reveal that the complexes are of good purity. This is also supported by TLC. The complexes are white in colour and soluble in THF, DMSO, and acetone. Conductance measurements in 10⁻³ M solution are of the order of 0.50 ohm⁻¹ cm² mol⁻¹, indicating that the complexes are non-electrolytes. Some physical characteristics and elemental analysis data are presented in Table I.

**Infrared spectra**

Isoniacinamide has three bonding sites, i.e. heterocyclic nitrogen, amido nitrogen and carbonyl oxygen. The ligand may be coordinated to the metal by one or more of these.

In complexes of carbonyl donors a significant negative shift in carbonyl frequency takes place [12]. In the present study, the carbonyl stretching frequency absorbs at ~1670 cm⁻¹, both in case of ligand and metal complexes. The same is true for ν(NH) of the amido group which absorbs at ~3325 cm⁻¹ in case of the ligand as well as the metal complexes. This rules out the possibility of bonding through the carbonyl group or the amido nitrogen.

On the other hand, IR frequencies exhibit appreciable perturbation in the fundamental vibrations of the pyridine part of the molecule. Absorption bands at 1590 cm⁻¹ due to ν(C=N) stretching frequency and at 1550 cm⁻¹ due to ν(C=N) stretching frequency of the isoniacinamide molecule are shifted to ~1620 and ~1600 cm⁻¹, respectively, on complexation [13]. Further, the pyridine ring vibrations of the ligand at 950, 605 and 405 cm⁻¹ also undergo significant positive shifts [14]. In case of metal complexes, these vibrations absorb at ca. 990, 630 and 435 cm⁻¹ indicating that coordination takes place via the pyridine nitrogen only. The ν(Hg–Cl) frequency appears at ~365 cm⁻¹.

**UV spectra**

In case of isoniacinamide, a very intense band appears at 256 nm (log ε 7.1) which is attributed to the π–π* absorptions of the carbonyl group. In the metal complexes this band is shifted to ca. 234 nm (log ε ~ 5.1). In case of metal complexes involving isoniazid [5] which is structurally quite similar to isoniacinamide, but coordinates through the carbonyl group, a positive shift is observed in the absorption band due to the C=O chromophore. In the present complexes, the negative shift in λmax value rules out the possibility of bonding through the carbonyl group.

**1H NMR spectra**

In ¹H NMR spectra, the following signals are attributed to the presence of an isoniacinamide moiety in the complexes: δ 7.70–7.92 (m, 2H, H₃₅) and δ 8.30–8.75 (m, 2H, H₂₆). The latter signal in pure isoniazid was observed at δ 8.10–8.30 (m, 2H). The downfield shift in case of metal complexes is due to the involvement of the ring nitrogen in complexation. In p-HOC₆H₄HgCl(L) and p-AcOC₆H₄HgCl(L) complexes, the resonance signals due to the C₆H₄ group and H₃₅ of isoniacinamide ligand overlap with each other and a multiplet is observed in the region δ 7.0–8.0. The furyl group in 2-C₄H₃OHgCl(L) analogue is identified by signals at δ 6.56 (d, 2H, J 9.8 Hz) and δ 7.48 (s, 1H).

<table>
<thead>
<tr>
<th>Complex</th>
<th>Dec. temp. [°C]</th>
<th>A⁺ [C= 1.5×10⁻³ M]</th>
<th>Found (calcd) [%]</th>
<th>Hg</th>
<th>N</th>
<th>Cl</th>
</tr>
</thead>
<tbody>
<tr>
<td>C₆H₅HgCl(L)</td>
<td>122</td>
<td>0.48</td>
<td>46.15 (46.20)</td>
<td>6.47 (6.44)</td>
<td>8.00 (8.05)</td>
<td></td>
</tr>
<tr>
<td>o-HOC₆H₄HgCl(L)</td>
<td>118</td>
<td>0.46</td>
<td>44.50 (44.57)</td>
<td>6.32 (6.21)</td>
<td>7.69 (7.76)</td>
<td></td>
</tr>
<tr>
<td>p-HOC₆H₄HgCl(L)</td>
<td>212</td>
<td>0.50</td>
<td>44.64 (44.57)</td>
<td>6.36 (6.21)</td>
<td>7.66 (7.76)</td>
<td></td>
</tr>
<tr>
<td>p-AcOC₆H₄HgCl(L)</td>
<td>185</td>
<td>0.50</td>
<td>41.04 (40.85)</td>
<td>5.50 (5.69)</td>
<td>7.10 (7.11)</td>
<td></td>
</tr>
<tr>
<td>2-C₄H₃OHgCl(L)</td>
<td>126</td>
<td>0.52</td>
<td>47.35 (47.29)</td>
<td>6.54 (6.59)</td>
<td>8.10 (8.35)</td>
<td></td>
</tr>
</tbody>
</table>

* ohm⁻¹ cm² mol⁻¹.

Table I. Physical characteristics and elemental analyses.
**13C NMR spectra**

In pure isoniacinamide the signals due to $\text{C}_2$ and $\text{C}_3$ carbons appear at 146.9 and 123.4 ppm, respectively. On complexation, the former signal is shifted to ca. 151.5 ppm, while the latter remains unaffected. The shift is attributed to the involvement of the pyridine nitrogen in complexation. In isoniacinamide, the carbonyl group shows a signal at 168.6 ppm. This value remains unaltered in complexes. The signal due to the $\text{C}_4$ carbon appears at 135.4 ppm. Table II lists the position of resonance signals observed in the $^{13}$C NMR spectra.

**Fluorescence studies**

The $\alpha$, $p$-HOC$_6$H$_4$HgCl(L) complexes are fluorescent in nature. Hence their fluorescence spectra have been recorded. The absorption band is observed at 244 nm ($\log \varepsilon$ 4), while the emission band is at 488 nm. Thus, in accordance with the Franck-Condon principle and thermal relaxation of vibrational modes, the fluorescence spectra are observed on the red side of the absorption spectra approximately in a mirror image relationship [15]. A slight distorted in the mirror image pattern arises due to the appearance of a weak band at 312 nm ($\log \varepsilon$ 1.5) because of the forbidden transitions, Hg$^6(\text{p}_1) \rightarrow$ Hg$^6(\text{s}_0)$ and $J = 0 \rightarrow J = 0$ [5].

The spectrum is free from anti-Stokes effects. The pattern of the spectrum follows Levschin’s rule, indicating that the geometry of the excited state is similar to that of the ground state [16]. The quantum yields of fluorescence, $\theta$, calculated by the relative method [17], using anthracene as the reference, are as follows: $\alpha$-HOC$_6$H$_4$HgCl(L), 0.65; $p$-HOC$_6$H$_4$HgCl(L), 0.62. Since the $\theta$ values show deviation from unity, it is inferred that fluorescence remains the dominant, but not the exclusive mode of emission. The non-radiative modes like inter-system crossing and internal conversion are likely to be contributing to the emission process.

**Thermal studies**

Thermogravimetric (TG) studies have been carried out for C$_6$H$_5$HgCl(L), $\alpha$-HOC$_6$H$_4$HgCl(L) and $p$-AcOC$_6$H$_4$HgCl(L) complexes. The weight loss in each case corresponds to the formation of HgO, which slowly volatilizes beyond 763 K. The order (n) and activation energy ($E_a$) for the thermal decomposition reaction have been elucidated by the method of Coats and Redfern [18]. The linearization curve is shown in Fig. 1.

![Figure 1](image.png)

**Table II.** $^{13}$C NMR data.

<table>
<thead>
<tr>
<th>Complex</th>
<th>$R$</th>
<th>$C_1$</th>
<th>$C_2$</th>
<th>$C_3$</th>
<th>$C_4$</th>
<th>$C_5$</th>
<th>$C_6$</th>
<th>Isoniacinamide (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C$_6$H$_5$HgCl(L)</td>
<td>150</td>
<td>136</td>
<td>128</td>
<td>127.5</td>
<td>128</td>
<td>136</td>
<td></td>
<td>151.5 123.4 135.4 168.6</td>
</tr>
<tr>
<td>$\alpha$-HOC$_6$H$_4$HgCl(L)</td>
<td>138.6</td>
<td>162</td>
<td>119.5</td>
<td>132</td>
<td>112.4</td>
<td>140.4</td>
<td></td>
<td>151.4 123.4 135.3 168.6</td>
</tr>
<tr>
<td>$p$-HOC$_6$H$_4$HgCl(L)</td>
<td>147.3</td>
<td>151</td>
<td>135.3</td>
<td>156.5</td>
<td>135.3</td>
<td>151</td>
<td></td>
<td>151.4 123.4 135.3 168.5</td>
</tr>
<tr>
<td>$p$-AcOC$_6$H$_4$HgCl(L)</td>
<td>148.8</td>
<td>138</td>
<td>122</td>
<td>151</td>
<td>122</td>
<td>138</td>
<td></td>
<td>151.6 123.5 135.4 168.6</td>
</tr>
</tbody>
</table>
bond cleavage is involved in the pyrolysis of the complexes is also indicated by the mass spectra, where peaks for C$_6$H$_5^+$, HOC$_6$H$_4^+$ and AcOC$_6$H$_4^+$ fragments have been observed.

The apparent activation entropy [19], S*, has a positive value for all the complexes. The p-HOC$_6$H$_4$HgCl(L) complex has the highest value of S*, while p-AcOC$_6$H$_4$HgCl(L) has the lowest. Hence, the former decomposes with greatest degree of randomness while the latter with the least.

The TG data are supplemented by differential scanning calorimetry (DSC) studies. The thermal effects on DSC curves are endothermic in nature. The heat of reaction, $\Delta H$ has been enumerated for the thermal decomposition reaction from DSC studies. Thermal data are presented in Table III.

**Mass spectra**

The fragmentation pattern of the complexes shows that the RHg$^+$, R$^+$, HgCl$^+$ and Hg$^+$ ions dominate the mass spectra [20]. The fragmentation of the RHg$^+$ portion is similar to that reported earlier [4]. The fragmentation pattern of the ligand portion is shown in Scheme 1. The isonicinamide molecular ion 1 (m/e 122) is formed initially. It eliminates an NH$_3$ radical giving fragment 2 (m/e 106) which subsequently loses CO to give fragment 3 (m/e 78), followed by elimination of HCN, resulting in fragment 4 (m/e 51). The isonicinamide molecular ion 1 (m/e 122) constitutes the base peak.

**Antibacterial activity**

The C$_6$H$_5$HgCl(L) and p-AcOC$_6$H$_4$HgCl(L) complexes were screened against *E. coli* and *P. pyocyanaea* bacterial strains at concentrations of 25 and 50 µg ml$^{-1}$. The complexes showed greater inhibition at higher concentration. While both the samples were equally active against *E. coli*, the p-AcOC$_6$H$_4$HgCl(L) analogue showed greater inhibition against *P. pyocyanaea*. The order of activity against two microorganisms is *P. pyocyanaea* > *E. coli*.

We thank the University Grants Commission, New Delhi for the award of a research fellowship to one of us (SB).