Studies on ionic chelates of hafnocene with kojic acid and maltol

Ekta Malhotra, N K Kaushik* & G S Sodhi†
Department of Chemistry, University of Delhi, Delhi 110 007, (India)
Received 11 April 2001; revised 30 July 2001

Ionic chelates of hafnocene with kojic acid (I) and maltol (II) of the type \([\{\eta^5-C_5H_5\}HfL^1]X^- (Ia)\) and \([\{\eta^5-C_5H_5\}HfL^2]X^- (IIa)\) \([X = CuCl_2, ZnCl_2, CdCl_2, HgCl_2, C_6H_5NHNC\]S_2; HL^1 = kojic acid, HL^2 = maltol\] have been synthesized and characterised by IR, UV, \(^1\)H NMR and \(^{13}\)C NMR spectral studies. Conductance measurements reveal that the compounds are 1:1 electrolytes. Fluorescence studies have been carried out for the complexes containing mercury in the anionic moiety and relevant photochemical parameters have been elucidated. Thermodynamic parameters have been calculated using thermogravimetric and differential thermal analytical curves and their variations have been correlated with some structural parameters of the complexes. Activity of representative complexes vs. E.coli, S.typhi, P.aeruginosa, Z.mobilis bacterial strains and activity of all the complexes vs. A. awamori and A. niger fungal strains have been studied and the general order of activity has been deduced.

Kojic acid (I) and maltol (II), both are antibiotic substances and are known to inhibit the growth of E.coli and S.aureus\(^1\)\(^2\). Since the antibiotic activity of the ligand is altered in the presence of metal ions and the metal complexes of these ligands are of relatively high stability, owing to the formation of five-membered chelate ring, it was thought worthwhile to synthesise and characterise some hafnocene complexes of kojic acid (Ia) and maltol (IIa).

The present work is a sequel to our investigation of metal ion-biomolecule interaction\(^3\)\(^8\).

Materials and Methods

Kojic acid, maltol (Aldrich) and hafnocene dichloride (Alfa Products) were used without further purification. Chlorine and sulphur were determined gravimetrically as silver chloride and barium sulphate, respectively. Hafnium was estimated gravimetrically as HfO\(_2\). The bactericidal activities were evaluated by cup-agar diffusion method\(^9\), while the fungi were cultured on Czapek Dox Nutrient medium\(^10\).

The conductance measurements were made at 1.5x10\(^{-3}\) M solution of the complexes in nitrobenzene using Elico conductivity bridge, type CM-82. The IR and UV spectra were recorded on FTIR spectrometer Spectrum 2000 and Beckman DU-64 UV-VIS spectrophotometers, respectively. The \(^1\)H NMR and \(^{13}\)C NMR spectra were recorded on Bruker AC 300 spectrometer and fluorescence spectral studies were recorded on Hitachi 650-660 spectrofluorometer. Rigaku Thermoflex, model PTC-10A, Rigaku Corporation, Japan, was used for simultaneous recording of TG-DTA curves of complexes containing metal salts as anionic species, in air at a heating rate of 10\(^\circ\) min\(^{-1}\).

Preparation of potassium phenyldithiocarbazate (ref. 11)

Potassium phenyldithiocarbazate was prepared by placing 4.9 mL (0.050 mol) of phenylhydrazine and 2.8 g (0.050 mol) of potassium hydroxide in a minimum quantity of alcohol. To the stirred ice cold solution, 3.02 mL (0.050 mol) of carbon disulphide was added dropwise. The temperature of the reaction mixture was maintained between 0–5\(^\circ\)C. The stirring was continued for another 1h and then a mixture of ethylacetate and pet. ether (50 mL, 1:1 v/v) was added to the stirred contents and the solid product so obtained was filtered, washed repeatedly with ether and dried.

Synthesis of hafnocene complexes

\([\{\eta^5-C_5H_5\}HfL^1]X^- (I)\) : \(X = CuCl_2\), \(X = ZnCl_2\), \(X = CdCl_2\), \(X = HgCl_2\)

The metal complexes (Ia) were prepared by adding slowly, the solution of the metal salt [CuCl\(_2\)2H\(_2\)O (0.043 g, 0.25 mmol); ZnCl\(_2\) (0.034 g, 0.25 mmol); CdCl\(_2\) (0.046 g, 0.25 mmol) or HgCl\(_2\) (0.068 g, 0.25 mmol)] in acetone (10 mL) to a stirred solution of
0.095 g (0.25 mmol) of bis(η⁵-cyclopentadienyl) hafnium(IV) dichloride and 0.035 g (0.25 mmol) of kojic acid (HL¹) (I) in acetone (20 mL). The contents were stirred for 8h and filtered. The volume of the filtrate was reduced to about one-fourth of the original and pet. ether was added. The precipitated complexes were filtered, dried and crystallized from acetone by the addition of a few drops of pet. ether.

Maltol (HL²) complexes [(η⁵-C₅H₅)₂HfL²]X⁻ (IIa) (6): X = CuCl₂; (7): X = ZnCl₂; (8): X = CdCl₂; (9): X = HgCl₂) were prepared by following a similar set of operations as above by taking 0.031 g (0.25 mmol) of maltol (II).

\[(\eta^5-C_5H_5)HfL^1]^+ [C_6H_5NHNHCS_2]^- (5)\]

A mixture of 0.095 g (0.25 mmol) of bis(η⁵-cyclopentadienyl) hafnium(IV) dichloride and 0.035 g (0.25 mmol) of kojic acid (HL¹)(I) in water (10 mL) was stirred for 8h. This was followed by the addition of 0.055 g (0.25 mmol) of potassium phenylidithiocarbazate in a minimum quantity of water. Stirring was then continued till precipitation was complete. The product was filtered, dried and recrystallized from acetone-pet. ether.

Maltol (HL²) complexes [(η⁵-C₅H₅)₂HfL²]⁺ [C₆H₅NHNHCS₂]⁻(10) were prepared by following a similar set of operations as above by taking 0.031 g (0.25 mmol) of maltol (II).

**Results and Discussion**

The complexes isolated are pure, yellow to brown in colour and are soluble in THF, DMSO, DMF and partially soluble in water. The molar conductance measurements in nitrobenzene at 1.5×10⁻³ M for these complexes fall in the range 26.5-30.2 ohm⁻¹ cm² mol⁻¹, indicating that the complexes are 1:1 electrolytes. The analytical data of the complexes along with the decomposition temperature are given in Tables 1.

The absorption bands at 1660 cm⁻¹ and 1600 cm⁻¹ are assigned to ν(C =O)¹² and ν(C=C)¹³ stretching frequencies, respectively, in the free ligands. Both the bands undergo bathochromic shifts of ca. 20 - 70 cm⁻¹ on complexation, indicating the involvement of the carbonyl group in complexation. The ν(O-H) phenolic stretching frequency¹⁴, which appears at 3200 cm⁻¹ in kojic acid (I) and at 3180 cm⁻¹ in maltol (II) disappears on complexation. Kojic acid shows an additional peak at 3500 cm⁻¹, which is due to (O-H) alcholic stretching mode. This peak remains almost unaltered on complexation. In the far IR region, the bands at 490 cm⁻¹ and 370 cm⁻¹ correspond to ν(M-O)¹⁵ and ν(M-Cl) stretching vibrations, respectively.

All the facts indicate that kojic acid and maltol, both are coordinated to the metal ion through the oxygen atom of the -OH (phenolic) group, forming five-membered chelate structures.

In the electronic spectrum the band corresponding to π-π* transition of chromophoric C = O group appear at 255 nm (log ε = 4.8) and 284 nm (log ε = 7.4) in kojic acid (I) and maltol (II) (Ref.16), respectively. The observed shift in the ligand band to ca.270 nm (log ε = ca. 3.8) and ca.294 nm (log ε = ca. 4.2), respectively, shows the involvement of the carbonyl group in complexation in both the ligands.
The $^1$H NMR spectra of kojic acid (I) (Ref. 17) gives the following signals: δ 2.65 (s, 2H, CH$_2$ at C(2)); δ 6.45 (s, 1H, H(3)) and δ 7.92 (s, 1H, H(6)). On complexation (Ia), signals due to H(3) and H(6) shifted to δ 6.83 and δ 8.15, respectively. The downfield shift of the signals for H(3) and H(6) are attributed to the involvement of carbonyl at C(4) and phenolic group at C(5) in complexation. The $^1$H NMR spectra of maltol (II) (Ref. 17) give the following signals: δ 2.25 (s, 3H, CH$_3$ at C(2)), 139.8 ppm (C(6)). In the complexes (Ia), the signal due to H(5) on complexation indicates the involvement of phenolic group at C(5) in complexation. The $^1$C NMR spectrum of kojic acid (I) (Ref. 18) showed resonance signals at 168.6 ppm (C(2)), 174.6 ppm (C(4)), 145.8 ppm (C(5)) and 139.8 ppm (C(6)). In the complexes (Ia), the signal due to H(5) on complexation indicates the involvement of carbonyl group at C(4) in complexation.

In the $^1$H NMR spectra of the metal complexes, the cyclopentadienyl group appeared as a multiplet in the region δ 6.9-7.0 (m, 10H). In the complexes containing phenyldithiocarbazate moiety, the multiplet in the region δ 7.7-8.1 (m, 5H) was observed due to five protons in the C$_6$H$_5$ moiety. The $^1$H NMR spectra of the metal complexes, the cyclopentadienyl group appeared as a multiplet in the region δ 6.9-7.0 (m, 10H). In the complexes containing phenyldithiocarbazate moiety, the multiplet in the region δ 7.7-8.1 (m, 5H) was observed due to five protons in the C$_6$H$_5$ moiety.

The $^1$H NMR spectra of maltol (II) (Ref. 17) give the following signals: δ 2.25 (s, 3H, CH$_3$ at C(2)); δ 6.45 (s, 1H, H(3)) and δ 8.15, respectively. The results indicate that complexation involves deprotonation of C(3) hydroxyl and chelation through C(4) carbonyl. The $^1$H NMR spectra of maltol (II) show signals at 149.2 ppm (C(2)), 143.2 ppm (C(3)), 173.2 ppm (C(4)), 113.9 ppm (C(5)) and 155.2 ppm (C(6)). In the complexes (Ia) the C(4) absorbs at ca.177.5 ppm, while the C(3) absorbs at ca.146.2 ppm. The downfield shifts indicate that the complexes are formed by deprotonation of C(3) hydroxyl and chelation through C(4) carbonyl. The methyl group at C(2) shows a resonance signal at ca. 27.1 ppm.

In the metal complexes, a resonance signal appeared at ca. 122.2 ppm due to carbons of the cyclopentadienyl rings. In case of the complexes containing anionic phenyldithiocarbazate moiety, the resonance signals observed were: ca. 153.0 ppm (C(1)); ca. 112.1 ppm (C(2,6)); ca. 130.1 ppm (C(3,5)) and ca. 119.2 ppm (C(4)), while the signal due to –CS$_2$ carbon appeared at ca. 169.0 ppm.

**Fluorescence studies**

The compounds [($\eta^5$-C$_5$H$_5$)$_2$HfL]$_n$[HgCl$_3$]$_m$ (4) and [($\eta^5$-C$_5$H$_5$)$_2$HfL]$_n$[HgCl$_3$]$_m$ (9) are fluorescent in nature. Hence fluorescence studies have been carried out.

<table>
<thead>
<tr>
<th>Complex</th>
<th>Empirical Formula</th>
<th>Dec. (°C)</th>
<th>$\lambda^a$</th>
<th>Found (Calcd) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>[($\eta^5$-C$_5$H$_5$)$_2$HfL]$_3$[CuCl$_3$]</td>
<td>C$<em>{15}$H$</em>{23}$O$<em>2$HfC$</em>{9}$Cu</td>
<td>125</td>
<td>29.7</td>
<td>31.20, 31.23, 17.21, 17.16, 17.11, 17.11</td>
</tr>
<tr>
<td>[($\eta^5$-C$_5$H$_5$)$_2$HfL]$_3$[ZnCl$_3$]</td>
<td>C$<em>{15}$H$</em>{23}$O$<em>2$HfC$</em>{9}$Zn</td>
<td>112</td>
<td>28.8</td>
<td>31.03, 31.03, 17.00, 17.00, 17.01, 17.01</td>
</tr>
<tr>
<td>[($\eta^5$-C$_5$H$_5$)$_2$HfL]$_3$[CdCl$_3$]</td>
<td>C$<em>{15}$H$</em>{23}$O$_2$HfC$_9$Cd</td>
<td>127</td>
<td>29.2</td>
<td>28.62, 28.62, 15.80, 15.80, 15.80, 15.80</td>
</tr>
<tr>
<td>[($\eta^5$-C$_5$H$_5$)$_2$HfL]$_3$[HgCl$_3$]</td>
<td>C$<em>{15}$H$</em>{23}$O$_2$HfC$_9$Hg</td>
<td>165</td>
<td>26.6</td>
<td>25.42, 25.42, 14.20, 14.20, 14.20, 14.20</td>
</tr>
<tr>
<td>[($\eta^5$-C$_5$H$_5$)$_2$HfL]$_3$[C$_6$H$_5$NHNSCS$_2$]</td>
<td>C$<em>{15}$H$</em>{23}$O$_2$HfN$_2$S$_2$</td>
<td>148</td>
<td>26.2</td>
<td>43.58, 43.58, 28.05, 28.05, 28.05, 28.05</td>
</tr>
<tr>
<td>[($\eta^5$-C$_5$H$_5$)$_2$HfL]$_3$[CuCl$_3$]</td>
<td>C$<em>{15}$H$</em>{23}$O$_2$HfC$_9$Cu</td>
<td>140</td>
<td>29.9</td>
<td>31.75, 31.75, 2.62, 2.62, 2.62, 2.62</td>
</tr>
<tr>
<td>[($\eta^5$-C$_5$H$_5$)$_2$HfL]$_3$[ZnCl$_3$]</td>
<td>C$<em>{15}$H$</em>{23}$O$_2$HfC$_9$Zn</td>
<td>153</td>
<td>28.5</td>
<td>31.86, 31.86, 2.33, 2.33, 2.33, 2.33</td>
</tr>
<tr>
<td>[($\eta^5$-C$_5$H$_5$)$_2$HfL]$_3$[CdCl$_3$]</td>
<td>C$<em>{15}$H$</em>{23}$O$_2$HfC$_9$Cd</td>
<td>137</td>
<td>28.9</td>
<td>29.28, 29.28, 2.41, 2.41, 2.41, 2.41</td>
</tr>
<tr>
<td>[($\eta^5$-C$_5$H$_5$)$_2$HfL]$_3$[HgCl$_3$]</td>
<td>C$<em>{15}$H$</em>{23}$O$_2$HfC$_9$Hg</td>
<td>146</td>
<td>27.2</td>
<td>25.72, 25.72, 2.22, 2.22, 2.22, 2.22</td>
</tr>
<tr>
<td>[($\eta^5$-C$_5$H$_5$)$_2$HfL]$_3$[C$_6$H$_5$NHNSCS$_2$]</td>
<td>C$<em>{15}$H$</em>{23}$O$_2$HfN$_2$S$_2$</td>
<td>150</td>
<td>26.3</td>
<td>44.95, 44.95, 3.68, 3.68, 3.68, 3.68</td>
</tr>
</tbody>
</table>

Table 1—Physical and analytical data of kojic acid and maltol complexes

*in ohm$^{-1}$cm$^2$mol$^{-1}$
out for them. In accordance with the Franck-Condon principle and thermal relaxation of vibrational modes, the fluorescence spectrum is observed on the red side of the absorption spectrum in approximately mirror-image relationship. The spectrum is free from anti-Stokes effect. The pattern of the spectrum follows Levshin's rule, indicating that the geometry of the excited state is not very different from that of the ground state.

The actual radiative lifetime of the excited state, $\tau_0$, is smaller than the intrinsic radiative lifetime, $\tau_e$, indicating the possibility of non-radiating energy dissipation processes depopulating the excited state. Thus, fluorescence remains the dominant but certainly not the exclusive mode of emission. The nonradiative processes, i.e. inter-system crossing and internal conversion, compete with fluorescence. Therefore, Einstein's probability of spontaneous absorption, $B_{\text{nm}}$, exceeds the corresponding probability of spontaneous emission, $A_{\text{nm}}$. The quantum yield of fluorescence, $\phi_f$, is replaced by $\phi_{\text{isc}} > \phi_{\text{ic}}$. These priorities are also established by their respective rate constants.

The summation of the rate constants for all the photochemical and photophysical processes competing with fluorescence, $\Sigma K_i$, equals the sum of $K_{\text{isc}}$ and $K_{\text{ic}}$. Thus apart from fluorescence, intersystem crossing and internal conversion, there seems to be no other mode of emission, radiative or nonradiative, in the present case. The oscillator strength, $f$, has been calculated from the relation $f = 4.31 \times 10^{-9} \Delta \tilde{V}$, which is valid if we assume a Lorentzian shape for the absorption band. The factor $\Delta \tilde{V}$ is replaced by $\Delta \tilde{V}$, where $\Delta \tilde{V}$ is the half band width of the absorption band. The relevant data are presented in Table 2.

### Table 2—Fluorescence spectral parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>$[\eta^5-C_5H_5HfL]^+[HgCl_4]^-$ (4)</th>
<th>$[\eta^5-C_5H_5HfL]^+[HgCl_4]^-$ (9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantum yield of fluorescence: $\phi_f$</td>
<td>0.53</td>
<td>0.73</td>
</tr>
<tr>
<td>Quantum yield for inter-system crossing: $\phi_{\text{isc}}$</td>
<td>0.37</td>
<td>0.33</td>
</tr>
<tr>
<td>Quantum yield for internal conversion: $\phi_{\text{ic}}$</td>
<td>0.009</td>
<td>0.007</td>
</tr>
<tr>
<td>Oscillator strength: $f$</td>
<td>0.013</td>
<td>0.012</td>
</tr>
<tr>
<td>Actual radiative lifetime: $\tau_0$ (s)</td>
<td>$5.8 \times 10^{-8}$</td>
<td>$4.5 \times 10^{-8}$</td>
</tr>
<tr>
<td>Intrinsic radiative lifetime: $\tau_e$ (s)</td>
<td>$9.3 \times 10^{-8}$</td>
<td>$6.8 \times 10^{-8}$</td>
</tr>
<tr>
<td>Rate const of fluorescence emission: $K_{\text{f}}$ (s$^{-1}$)</td>
<td>$1.0 \times 10^{8}$</td>
<td>$1.4 \times 10^{8}$</td>
</tr>
<tr>
<td>Rate const for inter-system crossing, $S_1 \rightarrow T_1$: $K_{\text{isc}}$ (s$^{-1}$)</td>
<td>$0.061 \times 10^{8}$</td>
<td>$0.072 \times 10^{8}$</td>
</tr>
<tr>
<td>Rate const for internal conversion: $K_{\text{ic}}$ (s$^{-1}$)</td>
<td>$0.0016 \times 10^{8}$</td>
<td>$0.0015 \times 10^{8}$</td>
</tr>
<tr>
<td>Einstein's absorption probability: $B_{\text{nm}}$</td>
<td>$0.41 \times 10^{8}$</td>
<td>$0.39 \times 10^{8}$</td>
</tr>
<tr>
<td>Einstein's emission probability: $A_{\text{nm}}$</td>
<td>$0.15 \times 10^{8}$</td>
<td>$0.15 \times 10^{8}$</td>
</tr>
</tbody>
</table>

### Thermal studies

Thermal studies have been carried out for complexes containing metal salts in the anionic species. The thermogravimetric studies show that the complexes finally decompose to the oxides of hafnium and the metal in the anionic moiety. In case of the complex containing mercury in the anionic moiety, the observed weight loss corresponds to the formation of HfO$_2$ only, since HgO volatilizes at such high temperatures. The mass loss data of the complexes is recorded. Mass loss, found (calc): (1) 398-673, 6.73, -1.016; (2) 385-695, 11.50, 1.077; (3) 395-669, 31.89, 10.071; (4) 438-623, 36.66, 12.171; (5) 413-710, 5.02, -1.817; (6) 426-835, 6.42, 0.571; (7) 410-773, 18.35, 4.004; (8) 420-793, 21.69, 5.450.

The order of thermal decomposition reaction in all the complexes is found to be one. A comparison of the activation energy of complexes reveals that the $E_a$ values follow the order:

$\left[\eta^5-C_5H_5HfL\right]^+[\text{CuCl}_4]^-$ < $\left[\eta^5-C_5H_5HfL\right]^+[\text{ZnCl}_4]^-$ < $\left[\eta^5-C_5H_5HfL\right]^+[\text{CdCl}_2]^-$ < $\left[\eta^5-C_5H_5HfL\right]^+[\text{HgCl}_4]^-$.

This trend is also observed in the series of complexes of maltol ligand.

This may be explained on the basis of the fact that larger cations are stabilized by larger anions. The complex cation $\left[\eta^5-C_5H_5HfL\right]^+$ is very large in size...
and the size of the M(II) ions in the anionic moiety varies in the order Cu(II) < Zn(II) < Cd(II) < Hg(II). In case of the complex, \([\{\eta^5-C_5H_5\}_2HfLt\}^+ \cdot [HgCl_4]_2\]$, the large size of Hg(II) ion in the anionic moiety, helps in effective stabilization of the complex cation and therefore gives rise to a higher lattice energy. This makes thermal degradation of the complex relatively difficult and thus, the reaction involves a higher value of $E_a$. For the complex, \([\{\eta^5-C_5H_5\}_2HfLt\}^+ \cdot [CuCl_3]_2\]$, the small size of the Cu(II) ion in the anionic moiety leads to a relatively poor stabilization of the complex cation and to a comparatively lower lattice energy. Thus the thermal decomposition reaction involves a lower value of $E_a$.

It is, therefore, evident that the nature of metal ion in the anionic moiety contributes to the variation in the activation energy for the thermal degradation of the complexes. The energy of activation, in turn, reflects the kinetic lability of the complexes. The compounds with lower $E_a$ values are more labile as compared to those with higher $E_a$ values.

The apparent activation entropy has a positive value for most of the complexes. Hence, thermal degradation of these complexes is a spontaneous process. Within a given series, the complex containing Cu(II) ion in the anionic moiety has the lowest value of $S^\circ$, while the one containing Hg(II) ion has the highest. Hence, the former decomposes with lowest degree of randomness, while the latter with greatest.

The TG data of the complexes is supplemented by DTA studies. DTA (T$_{max}$, K): (1) 604; (2) 419, 635; (3) 625; (4) 562; (6) 620; (7) 485, 675; (8) 465, 615, 695; (9) 545, 690. The thermal effects on DTA curves are exclusively exothermic in nature. The heat of reaction (AH) for the thermal decomposition reaction has been enumerated from the DTA curves$^{24,25}$. The temperature dependent calibration coefficient has been obtained from the Currell Equation.

**Microbial assay**

The complexes containing Hg(II) and Cu(II) ions in the anionic moiety have been screened for bactericidal activity against pathogenic strains of *Escherichia coli* (E. coli), *Salmonella typhi* (S. typhi), *Pseudomonas aeruginosa* (P. aeruginosa) and *Zymomonas mobilis* (Z. mobilis) using the respective ligands as the standard for comparing the activities. The samples have been screened at two concentrations (25 µg mL$^{-1}$ and 50 µg mL$^{-1}$) in DMF. The inhibitory power of the complexes was greater than the control. The complexes, in general, inhibited the growth of bacteria to a greater extent as the concentration increased. However, the complex containing Hg(II) ion in the anionic moiety was equally active against the microorganisms at both concentrations. The order of activity with respect to the microorganisms was: $P. aeruginosa > Z. mobilis > S. typhi > E. coli$

All the complexes were tested for fungicidal activity at two concentrations (25 µg mL$^{-1}$ and 50 µg mL$^{-1}$) against *Aspergillus niger* (A. niger) and *Aspergillus awamori* (A. awamori). All the complexes were found to be highly active, however, appreciably very high activity was observed for the complexes containing zinc in the anionic moiety against the test microorganisms at the two concentrations. The complexes containing phenylthiocarbazole group as the anionic moiety showed a higher percentage of inhibition at lower concentration (25 µg mL$^{-1}$) than at higher concentration (50 µg mL$^{-1}$), unlike the other ionic chelate complexes. The order of fungicidal activity with respect to the fungus species of the metal-kojate complexes is, *A. niger > A. awamori*. However, for the maltol complexes the order of fungicidal activity with respect to the fungus species was reversed, *A. awamori > A. niger*.

**References**