Complexing Ability of Some 2-Spirothiazolid-4-one Derivatives

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2-Spirothiazolid-4-one, X-Ray, Complexing Ability

The complexes of some 2-spirothiazolid-4-one derivatives have been prepared with Cu(II), Ni(II), Co(II) and Cd(II) salts. The complexes all have a metal to ligand ratios of 1:1 or 1:2 and are all believed to have tetrahedral structures with chelating ligands. Their structures are suggested on the basis of analysis, X-ray diffraction techniques, spectral (UV-VIS, IR, 'H NMR), and thermal decomposition as well as conductivity measurements. The ligands are coordinated to the metal ions as monovalent bidentate ligands through the OCO groups. Electrical conductivity studies indicated that these complexes have activation energies in the range of semi-conducting materials. It is observed that some of the complexes are more potent as bacteriostatic agents than the free ligands.

Introduction

Thiazolidinone derivatives have considerable commercial importance as drugs [1-3] and herbicides [4]. Spiro compounds show photochromic properties, biological activity and optical activity [5-7]. Our interest in the coordination chemistry of biologically active compounds led us to study the ligating properties of some 2-spirothiazolid-4-ones whose coordination chemistry is not yet developed in the literature. We report in the present article the synthesis of Cu(II), Ni(II), Co(II) and Cd(II) chelates of some 2-spirothiazolid-4-one derivatives with the aim of investigating their biological activity. The complexes have been characterized by several tools in order to shed more light on the mode of bonding and structure of the prepared complexes.

The 2-spirothiazolid-4-ones used have the following structures:

\[ \text{I: 1-Thia-4-(2'-carboxyphenyl)azaspiro[4,5]decan-3-one (L_1); II: 1-Thia-4-(2'-carboxyphenyl)azaspiro[4,4]nonan-3-one (L_2).} \]

Experimental

All reagents used in this investigation were A.R. products (Merck or B.D.H.).

**Synthesis, 1-thia-4-(2'-carboxyphenyl)-azaspiro[4,5]decan-3-one (L_1)**

1-Oxa-4-thiaspiro[4,5]decan-2-one (1.58 g, 0.01 mol) was dissolved in 20 ml absolute ethanol. To this solution (1.3 g, 0.01 mol) anthranilic acid was added portionwise, and the mixture was refluxed for 1 h. The solvent was concentrated under reduced pressure and the reaction mixture was cooled to room temperature. L_1 was precipitated as pale yellow crystals; yield: 2.43 g (95%); m.p. 105 – 107 °C.

Calcd C 62.26 H 5.22 N 4.84 S 11.08%,

Found C 62.40 H 5.10 N 5.10 S 11.20%.

**Synthesis, 1-thia-4-(2'-carboxyphenyl)-azaspiro[4,4]nonan-3-one (L_2)**

This compound was prepared in an analogous manner from 1-oxa-4-thiaspiro[4,4]nonan-2-one; yield: 92% pale yellow crystals, m.p. 110 – 112 °C.

Calcd C 61.07 H 4.75 N 5.08 S 11.64%,

Found C 61.30 H 5.00 N 5.20 S 11.50%.

**Synthesis of the solid complexes**

The following general procedure has been adopted for the preparation of the metal chelates. The required amount of the ligand was dissolved in the least amount of ethanol and treated with the appropriate amount of a solution of CuCl_2·2H_2O, NiCl_2·6H_2O, CoCl_2·6H_2O or CdCl_2·2H_2O in the molar ratio 1:1 and 2:1 (L : M). The mixtures were...
refluxed for about 1–3 h, evaporated to a small vol-
ume, and the solid complex that separated was fil-
tered and then recrystallized from ethanol and dried
\textit{in vacuo} over preheated CaCl$_2$.

\textit{Screening for antibacterial activity}

The antibacterial activity of the metal complexes
was tested using the usual cup-plate diffusion tech-
nique [8, 9]. The culture media used are nutrient
agar (NA) media supplemented with 1 g yeast per
liter. A final concentration of 10 ppm of the test
compounds was used. The data obtained are dis-
cussed below.

\textbf{Measurements}

Elemental analysis for C and H was carried out
using a Perkin-Elmer 240 C instrument. The IR
spectra were scanned on a Perkin-Elmer 599 B
(4000–200 cm$^{-1}$) spectrophotometer by using the
KBr disc technique. UV-VIS spectra were recorded
on a CECIL 599 spectrophotometer using 1 cm
matched silica cells. The metal analyses
were performed by standard methods [10].
Thermogravimetric analysis was carried out in air
with Du Pont Model 951, 910 and 1090 thermal
analyzers at a heating rate of 10°C min$^{-1}$. Conduc-
tivity measurements were carried out using a pye-
bridge in DMF solution ($10^{-4}$ M), and all the meas-
urements were performed at ambient temperature
(\textasciitilde 25°C).

For electrical conductivity measurements in the
solid state, compressed pellets (1 cm$^2$ area) of
0.3–0.5 cm thickness were moulded at a pressure of
10 tons/cm$^2$. Two thin copper wires of diameter
25 mm were attached.

\textbf{Results and Discussion}

Analytical results and some physical properties
of the chelates are listed in Table I. The results of
 elemental analyses (Table I) show that one and/or
two molecules of the ligand are attached to the
M(II) ion. Therefore three types of M(II) chelates
are formed, having the formulæ [MLCl$_2$H$_2$O],
[ML$_2$H$_2$O]Cl and [M(L)$_3$], where L = L$_1$ or L$_2$,
M = Cu(II), Ni(II), Co(II) or Cd(II). It is evident
that L$_1$ and L$_2$ act as monobasic bidentate ligands
through their carboxylic group. This behaviour is
consistent with the coordination of these ligands to
M(II) in their fully ionized form, a fact which is
further supported by the IR and $^1$H NMR spectra
discussed below.

Molar conductance values of $10^{-4}$ M DMF solu-
tions of the different chelates isolated are given in
Table I. These indicate that all complexes are non-
electrolytes except for the complexes 2, 4, 6 and 14
which have the values in the range of 1:1 electro-

X-ray diffraction lines show that the positions and
line intensities for the complexes 2, 4, 6 and 14 are
similar, indicating that these complexes have the
same configuration. Also, the complexes 3, 5, 7, 9,
11, 13 and 16 have similar configuration. This be-
haviour is further support for the formation of dif-
ferent types of complexes as mentioned before.

Coordination of water is revealed also from ther-
mosgravimetric analysis of the complexes 1, 2, 4, 6,
8, 10, 12 and 14 where a definite weight loss occurs
between 160 and 190°C corresponding to the pres­
ence of one or two coordinated water molecules
except for the complexes 3, 5, 13 and 15 which do
not show any weight loss up to 190°C. Complexes
containing lattice water molecules (cf. Table I) gave
a weight loss at 100–130°C.

\textbf{IR and $^1$H NMR spectral studies}

The IR group frequencies of diagnostic impor-
tance are collected in Table II. The free ligands com-
prised a strong band at 1715 and 1675 cm$^{-1}$ of L$_1$
and L$_2$, respectively, which can be assigned to the
stretching vibration of the carbonyl group belong-
ing to the carboxyl function [12]. This band has
completely disappeared in the spectra of the metal(II)
chelates indicating coordination of the carboxylate
groups, and instead two bands appear in the regions
1555–1590 and 1445–1460 cm$^{-1}$. These two bands
are assignable to the asymmetric and symmetric
stretching of the carboxylate group, respectively
[12, 13]. The separation ($\nu_a$–$\nu_s$) of the carboxylate
stretching vibrations and their relative intensity
agree well with a carboxylate group coordinating in
its bidentate mode [14, 15]. The distinct band ap-
pearing at 1630 and 1650 cm$^{-1}$ of all complexes could
be attributed to the free $\nu$CO group belonging to
the free ligands L$_1$ and L$_2$, respectively.

The presence of coordinated and lattice water
molecules in the metal complexes has been con-
irmed by the new band appearing at
3260–3420 cm$^{-1}$ in the IR spectra of the complexes
(cf. Table II). Also, the rocking mode of coordi-
nated water molecules appeared as a weak vibra-
Table I. Analytical and physical data of the metal complexes.

<table>
<thead>
<tr>
<th>No.</th>
<th>Compound</th>
<th>Color</th>
<th>$E_a$ (eV)</th>
<th>$A_{\alpha \cdot} \text{cm}^2 \text{mol}^{-1}$</th>
<th>Calcd (Found) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Cu(C$<em>{14}$H$</em>{12}$NSO$_3$)ClH$_2$O]H$_2$O</td>
<td>green</td>
<td>0.49</td>
<td>42.55 4.28 3.30 7.57 8.37 14.98</td>
<td>(42.60 4.40 3.10 7.70 8.30 15.20)</td>
</tr>
<tr>
<td>2</td>
<td>[Ni(C$<em>{14}$H$</em>{12}$NSO$_3$)$_2$H$_2$O]Cl</td>
<td>blue</td>
<td>0.37</td>
<td>43.40 4.33 3.34 7.66 8.47 14.02</td>
<td>(43.50 4.10 3.60 7.80 8.30 13.80)</td>
</tr>
<tr>
<td>3</td>
<td>[Ni(C$<em>{14}$H$</em>{12}$NSO$_3$)$_2$]</td>
<td>yellow</td>
<td>0.30</td>
<td>56.71 4.40 4.40 10.09 9.23 14.02</td>
<td>(56.50 4.20 4.60 9.80 8.30 14.07)</td>
</tr>
<tr>
<td>4</td>
<td>[Co(C$<em>{14}$H$</em>{12}$NSO$_3$)$_2$H$_2$O]</td>
<td>dark key</td>
<td>0.30</td>
<td>43.02 4.33 3.34 7.65 8.46 14.07</td>
<td>(42.70 4.30 3.50 7.80 8.50 13.80)</td>
</tr>
<tr>
<td>5</td>
<td>[Co(C$<em>{14}$H$</em>{12}$NSO$_3$)$_2$]</td>
<td>green</td>
<td>0.29</td>
<td>56.86 4.40 4.40 10.08 9.27 14.09</td>
<td>(56.80 4.20 4.40 9.80 8.30 13.80)</td>
</tr>
<tr>
<td>6</td>
<td>[Cd(C$<em>{14}$H$</em>{12}$NSO$_3$)$_2$H$_2$O]</td>
<td>yellowish</td>
<td>0.26</td>
<td>38.15 3.84 2.96 7.68 7.50 23.80</td>
<td>(37.70 3.60 3.10 7.60 7.30 23.60)</td>
</tr>
<tr>
<td>7</td>
<td>[Cd(C$<em>{14}$H$</em>{12}$NSO$_3$)$_2$]H$_2$O</td>
<td>yellow</td>
<td>0.25</td>
<td>50.95 4.27 3.96 9.06 15.89 23.80</td>
<td>(51.20 4.40 4.20 8.80 15.80)</td>
</tr>
<tr>
<td>8</td>
<td>[Cu(C$<em>{14}$H$</em>{12}$NSO$_3$)ClH$_2$O]</td>
<td>dark-brown</td>
<td>0.46</td>
<td>42.97 3.60 3.57 8.19 9.05 16.23</td>
<td>(43.10 3.60 3.70 7.80 8.70 16.20)</td>
</tr>
<tr>
<td>9</td>
<td>[Cu(C$<em>{14}$H$</em>{12}$NSO$_3$)$_2$H$_2$O]</td>
<td>brown</td>
<td>0.42</td>
<td>51.88 4.35 4.32 9.89 9.80 16.23</td>
<td>(51.80 4.50 4.30 10.10 10.00 16.20)</td>
</tr>
<tr>
<td>10</td>
<td>[Ni(C$<em>{14}$H$</em>{12}$NSO$_3$)ClH$_2$O]H$_2$O</td>
<td>blue</td>
<td>0.39</td>
<td>41.57 3.98 3.46 7.92 8.76 14.50</td>
<td>(41.70 4.20 3.60 8.00 8.50 14.30)</td>
</tr>
<tr>
<td>11</td>
<td>[Ni(C$<em>{14}$H$</em>{12}$NSO$_3$)$_2$H$_2$O]</td>
<td>blue</td>
<td>0.35</td>
<td>57.52 4.82 4.79 10.96 10.03 16.23</td>
<td>(57.50 5.10 4.70 11.10 10.20 16.20)</td>
</tr>
<tr>
<td>12</td>
<td>[Co(C$<em>{14}$H$</em>{12}$NSO$_3$)ClH$_2$O]</td>
<td>brown</td>
<td>0.33</td>
<td>43.48 3.64 3.62 8.29 9.16 15.23</td>
<td>(43.50 3.70 3.60 7.90 9.20 15.50)</td>
</tr>
<tr>
<td>13</td>
<td>[Co(C$<em>{14}$H$</em>{12}$NSO$_3$)$_2$]</td>
<td>brown</td>
<td>0.32</td>
<td>55.35 3.98 4.61 10.55 9.69 16.23</td>
<td>(55.50 4.20 4.60 10.40 9.50 16.20)</td>
</tr>
<tr>
<td>14</td>
<td>[Cd(C$<em>{14}$H$</em>{12}$NSO$_3$)$_2$H$_2$O]</td>
<td>yellow</td>
<td>0.21</td>
<td>36.69 3.51 3.05 6.99 7.37 24.53</td>
<td>(36.70 3.70 3.00 7.20 7.80 24.50)</td>
</tr>
<tr>
<td>15</td>
<td>[Cd(C$<em>{14}$H$</em>{12}$NSO$_3$)$_2$]</td>
<td>yellow</td>
<td>0.18</td>
<td>50.87 3.65 4.23 9.70 17.00 24.53</td>
<td>(51.00 3.60 3.90 9.50 17.30 24.50)</td>
</tr>
</tbody>
</table>

The metal-ligand vibrations are expected below 600 cm$^{-1}$, and they offer means for correlating the stability order of the metal complexes and the strength of the M–O bond. The presence of bands between 405 and 440 cm$^{-1}$ has been suggested by some workers [17] to be due to bonding to metal through the oxygen atom of the ligand.

The electronic absorption spectra of DMF solutions of the free ligands and their complexes have been recorded in the wavelength range 300–800 nm. Some general features can be recognized:

- All the complexes comprise a broad composite band in the visible region. This band exhibits mainly two maxima, the first in the wavelength range 360–390 nm being due to intraligand transitions.
**Table II.** IR and electronic spectra of the free ligands and solid complexes.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Assignment [cm$^{-1}$]</th>
<th>$\nu$OH$^+$</th>
<th>$\nu$C=O</th>
<th>$\nu_{as}$OCO</th>
<th>$\nu_{s}$OCO</th>
<th>$\nu$M–O</th>
<th>$\lambda_{max}$ [nm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free $L_1$</td>
<td>–</td>
<td>1715</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>360, 395, 450</td>
</tr>
<tr>
<td>Cu–$L_1$</td>
<td>3300</td>
<td>–</td>
<td>1555</td>
<td>1455</td>
<td>415</td>
<td>–</td>
<td>360, 390, 480, 560</td>
</tr>
<tr>
<td>Ni–$L_1$</td>
<td>3260</td>
<td>–</td>
<td>1590</td>
<td>1460</td>
<td>440</td>
<td>–</td>
<td>365, 399, 470, 715</td>
</tr>
<tr>
<td>Ni–$2L_1$</td>
<td>3420</td>
<td>–</td>
<td>1585</td>
<td>1450</td>
<td>415</td>
<td>–</td>
<td>360, 390, 475, 660</td>
</tr>
<tr>
<td>Co–$L_1$</td>
<td>3420</td>
<td>–</td>
<td>1590</td>
<td>1460</td>
<td>415</td>
<td>–</td>
<td>360, 390, 460, 530</td>
</tr>
<tr>
<td>Co–$2L_1$</td>
<td>3400</td>
<td>–</td>
<td>1595</td>
<td>1460</td>
<td>415</td>
<td>–</td>
<td>365, 380, 465, 530</td>
</tr>
<tr>
<td>Cd–$L_1$</td>
<td>3420</td>
<td>–</td>
<td>1585</td>
<td>1450</td>
<td>415</td>
<td>–</td>
<td>360, 395, 480</td>
</tr>
<tr>
<td>Cd–$2L_1$</td>
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<td>–</td>
<td>1595</td>
<td>1455</td>
<td>430</td>
<td>–</td>
<td>370, 390, 480</td>
</tr>
<tr>
<td>Free $L_2$</td>
<td>–</td>
<td>1675</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>370, 380, 470</td>
</tr>
<tr>
<td>Cu–$L_2$</td>
<td>3460</td>
<td>–</td>
<td>1580</td>
<td>1455</td>
<td>405</td>
<td>–</td>
<td>370, 390, 475, 560</td>
</tr>
<tr>
<td>Cu–$2L_2$</td>
<td>3420</td>
<td>–</td>
<td>1585</td>
<td>1450</td>
<td>415</td>
<td>–</td>
<td>380, 390, 480, 560</td>
</tr>
<tr>
<td>Ni–$L_2$</td>
<td>3370</td>
<td>–</td>
<td>1595</td>
<td>1460</td>
<td>410</td>
<td>–</td>
<td>375, 385, 460, 625</td>
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<tr>
<td>Ni–$2L_2$</td>
<td>3360</td>
<td>–</td>
<td>1590</td>
<td>1460</td>
<td>410</td>
<td>–</td>
<td>370, 390, 460, 630</td>
</tr>
<tr>
<td>Co–$L_2$</td>
<td>3360</td>
<td>–</td>
<td>1590</td>
<td>1455</td>
<td>410</td>
<td>–</td>
<td>370, 380, 490, 530</td>
</tr>
<tr>
<td>Co–$2L_2$</td>
<td>3400</td>
<td>–</td>
<td>1595</td>
<td>1460</td>
<td>420</td>
<td>–</td>
<td>360, 390, 485, 530</td>
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<tr>
<td>Cd–$L_2$</td>
<td>3400</td>
<td>–</td>
<td>1570</td>
<td>1445</td>
<td>420</td>
<td>–</td>
<td>370, 380, 480</td>
</tr>
<tr>
<td>Cd–$2L_2$</td>
<td>3420</td>
<td>–</td>
<td>1580</td>
<td>1450</td>
<td>420</td>
<td>–</td>
<td>365, 375, 470</td>
</tr>
</tbody>
</table>

and the second in the range 390–480 nm attributable to an LMCT transition.

Cu(II), Ni(II) and Co(II) complexes exhibit characteristic d–d bands. Cd(II) complexes do not show any d–d bands, and their spectra are dominated only by charge transfer and ligand bands. Cu(II) complexes show a broad band at ca. 560 nm indicative of a tetrahedral structure of these complexes. The bands are assigned to d–d electronic transitions of the type $^2E_{2g} \leftarrow ^2T_{2g}$ [18]. Co(II) complexes on the other hand show a broad band at ca. 530 nm. This band is due to a d–d electronic transition and lies in the range reported for four coordinate Co(II) complexes. Thus for the present Co(II) complexes this band corresponds to the $^4A_2 \rightarrow ^4T_{1(0)}$ transition [18]. Spectral data for the Ni(II) complexes (625–715 nm) indicate a tetrahedral stereochemistry through their $^3T_1 \rightarrow ^3T_{1(0)}$ transitions [18].

**Electrical conductivities**

The electrical conductivities ($\sigma$) in ohm$^{-1}$ cm$^{-1}$ and the activation energies ($\Delta E_a$) in eV of the free ligands and of their Cu(II), Ni(II), Co(II) and Cd(II) complexes were obtained by applying: $\sigma = \sigma_0 \exp(-\Delta E_a/kT)$. The results show that the $\sigma$-values increase with increasing temperature obeying the usual behaviour of an intrinsic semiconductor. The activation energy ($E_a$) was obtained from a plot of $\ln \sigma$ against $1/T$. The values of the activation energies were calculated using the least squares method. The results are given in Table I. These data show that the activation energy values decrease slightly on going from Cd(II) to Cu(II) complexes. Furthermore, the bicomplexes have lower conductivities and activation energies than the monocomplexes.

**Antibacterial activity**

The data obtained indicate the cases where the complexes show ambient bacteriostatic activity against *C. tropicalis*, *Pseudomonas floureceus*, *Bacillus cereus*, *Serratia*. The antimicrobial activity of the complexes is higher than that of the free ligands. The antibacterial activity of the complexes against *Pseudomonas floureceus* and *Bacillus cereus* decrease in the order: Cu < Co < Cd < Ni, and the effect is similar with *Serratia* and *C. tropicalis*. 