Synthesis, Spectral Characterization and Biological Activities of Cr(III), Co(II), Ni(II) and Zn(II) Complexes with 4-Aminoantipyrine and Azide Ion as Ligands

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Received 14 December 2012 / Accepted 13 January 2013

Abstract: The transition metal complexes of Cr(III), Co(II), Ni(II) and Zn(II) were synthesized with the ligands, 4-aminoantipyrine (4-AAP) and azide ion. The structural aspects of the metal complexes were determined from elemental analysis, molar conductance measurements, IR, \textsuperscript{1}H NMR and \textsuperscript{13}C NMR spectral studies. Thermal stability of Co(II) complex was measured and the UV-Visible spectrum of Zn(II) complex also measured. Finally the antimicrobial and antifungal activities of the complexes were carried out by disc diffusion method. From the analytical and spectral data, the formulae of the complexes are arrived. The antimicrobial screening results indicate that the metal complexes are moderately active compared with those of pure ligand, 4-AAP.

Keywords: 4-Aminoantipyrine, Azide, Complexes, Antifungal, Antimicrobial

Introduction

Heterocyclic compounds are important class of compound in organic chemistry because of their biological activities like antimicrobial, antifungal, anti-inflammatory, analgesics and anticancer drugs. 4-Aminoantipyrine is one of the heterocyclic compounds which are used in the field of medicinal chemistry\textsuperscript{1-3} because of their pharmacological, photographic, catalytic and liquid crystals applications. It is a temperature reducing pyrazole derivative\textsuperscript{4}. It is one of the synthetic drugs\textsuperscript{4} and its complexes have some applications in analytical and pharmacological areas\textsuperscript{5-9}. It is also used in the preparation of azo dyes\textsuperscript{10}. The present works aim at synthesizing Cr(III), Co(II), Ni(II) and Zn(II) complexes with 4-aminoantipyrine and azide ion as ligands and characterizing them by elemental analysis, electrical conductivity and routine spectral studies. The antimicrobial and antifungal activities of 4-AAP and its metal complexes were carried out.

Experimental

4-Aminoantipyrine was purchased from Alfa Aesar Company. The reagents, DMSO, DMF, ethanol, methanol and various metal nitrates were of analar grade.
Instruments
The elemental analysis of the metal complexes was carried out by using a CHNS (O) analyzer (Thermo Finnegan, Flash EA1112 Series) Instruments. The molar conductance value of $10^{-3}$ m complex solutions in acetonitrile was measured using a Systronic Conductivity Bridge 304 at 30 °C. The IR spectra were recorded on Shimadzu FT IR-8400S Spectrometer in 4000-400 cm$^{-1}$ range using KBr pellet. The $^1$H NMR and $^{13}$C NMR spectra of 4-AAP (Figure 1 & 2) and its complex in DMSO-d$_6$ were recorded by using 500 MHz FT NMR spectrum. The antimicrobial and antifungal studies of 4-AAP and its metal complexes were done by disc diffusion method.

Characterization of ligand 4-aminoantipyrine (1a)
The ligand 4-aminoantipyrine is used as such without further purification. IR (KBr): 3431 (NH$_2$), 2914 (Ar-H), 1650 (C=O), 1587 (C=C); $^1$H NMR (DMSO-d$_6$): 7.32-7.50 (6H, Ar-H); 3.90 (2H, s, NH$_2$); 2.80 (3H, s, N-CH$_3$); 2.10 (3H, s, CH$_3$); $^{13}$C NMR 119-130 (6C, Ar-C); 161 (C=O); 136 (C-NH$_2$); 10.40 (C-CH$_3$); 40.00 (N-CH$_3$).

![Figure 1. $^1$H NMR spectrum of 4-aminoantipyrine](image1.png)

![Figure 2. $^{13}$C spectrum of 4-aminoantipyrine](image2.png)
Synthesis of $[\text{Cr} (\text{4-AAP})_3(N_3)_3]$ (2a)

To a solution of Cr(NO$_3$)$_3$.9H$_2$O 1 g (2.5 mmol), in methanol, 4-aminoantipyrine (1a) 1.54 g (7.53 mmol), in methanol was added in drops with constant stirring. The mixture was heated in a domestic microwave oven for about 10 s. Then, sodium azide 0.49 g (7.53 mmol) in ethanol was added to the above solution and the whole mixture was heated in a microwave oven for 10 s. The precipitated dark green complex were filtered, washed with ethanol and dried. Yield 48%; (Found: C, 50.24; H, 4.94; N, 31.97. Calcd. for C$_{33}$H$_{39}$N$_{18}$CrO$_3$: C, 50.27; H, 4.95; N, 31.99%); IR (KBr): 3431 (NH$_2$), 2951 (Ar-H), 1608 (C=O), 1560 (C=C), 499 (M-O), 450 (M-N), 2067 (N$_3$).

Synthesis of $[\text{Co} (\text{4-AAP})_2(N_3)_2]$ (2b)

To a solution of Co(NO$_3$)$_2$.6H$_2$O 1 g (3.4 mmol), in methanol, 4-aminoantipyrine (1a) 2.83 g (13.80 mmol), in methanol was added in drops with constant stirring. The mixture was heated in a domestic microwave oven for about 10 s. Then, sodium azide 0.45 g (6.90 mmol) in ethanol was added to the above solution and the whole mixture was heated in a microwave oven for 10 s. The precipitated dark red complex were filtered, washed with ethanol and dried. Yield 47%; (Found: C, 55.20; H, 5.62; N, 26.33. Calcd. for C$_{44}$H$_{52}$N$_{18}$CoO$_4$: C, 55.23; H, 5.64; N, 26.36%); IR (KBr): 3425 (NH$_2$), 2920 (Ar-H), 1620 (C=O), 1569 (C=C), 536 (M-O), 478 (M-N), 2098 (N$_3$).

Synthesis of $[\text{Ni} (\text{4-AAP})_2(N_3)_2]$ (2c)

To a solution of Ni(NO$_3$)$_2$.6H$_2$O 1 g (3.4 mmol), in methanol, 4-aminoantipyrine (1a) 2.83 g (13.82 mmol), in methanol was added in drops with constant stirring. The mixture was heated in a domestic microwave oven for about 10 s. Then, sodium azide 0.45 g (6.90 mmol) in ethanol was added to the above solution and the whole mixture was heated in a microwave oven for 10 s. The precipitated bluish green complex were filtered, washed with ethanol and dried. Yield 47%; (Found: C, 55.23; H, 5.43; N, 26.31. Calcd. for C$_{44}$H$_{52}$N$_{18}$NiO$_4$: C, 55.25; H, 5.44; N, 26.36%); IR (KBr): 3431 (NH$_2$), 2926 (Ar-H), 1628 (C=O), 1560 (C=C), 501 (M-O), 441 (M-N), 2098 (N$_3$).

Synthesis of $[\text{Zn} (\text{4-AAP})_2(N_3)_2]$ (2d)$^{10-13}$

To a solution of Zn(NO$_3$)$_2$.6H$_2$O 1 g (4.2 mmol), in methanol, 4-aminoantipyrine (1a) 1.37 g (6.64 mmol), in methanol was added in drops with constant stirring. The mixture was heated in a domestic microwave oven for about 10 s. Then, sodium azide 0.43 g (6.62 mmol) in ethanol was added to the above solution and the whole mixture was heated in a microwave oven for 10 s. The precipitated yellow complex were filtered, washed with ethanol and dried. Yield 71%; (Found: C, 47.47; H, 4.74; N, 30.45. Calcd. for C$_{22}$H$_{26}$N$_{12}$ZnO$_2$: C, 47.66; H, 4.69; N, 30.33%); IR (KBr): 3408 (NH$_2$), 2943 (Ar-H), 1638 (C=O), 1560 (C=C), 501 (M-O), 441 (M-N), 2091 (N$_3$); $^1$H NMR (DMSO-d$_6$): 7.32-7.50 (6H, Ar-H); 4.00 (2H, s, N-H$_2$); 2.80 (3H, s, N-CH$_3$); 2.10 (3H, s, CH$_3$); $^{13}$C NMR 119-130 (6C, Ar-C); 162 (C=O); 136 (C-NH$_2$); 10.0 (C-CH$_3$); 40.0 (N-CH$_3$).

Results and Discussion

Characterization of metal complexes

All the synthesized complexes are characterized by the following data (Figure 3 & 4). Based on elemental analysis the composition of metal complexes and percentage of various elements helps to formulate the complexes. Molar conductance values were found in the range of 40-60 ohm$^{-1}$cm$^2$mol$^{-1}$, which indicates that the complexes are non electrolyte (1:0 type)$^{14}$. 


The electronic spectrum of the zinc complex was recorded on Varian, Cary 5000 model UV-Visible-NIR Spectrophotometer. In the spectrum there is no d-d transition observed because the Zn(II) ion have d^{10} electronic configuration and the metal to ligand charge transfer spectrum value^{11-18} is observed at 274 nm.

**Thermal analysis of [Co (4-AAP)_{2}(N_3)_{2}] (2b)**

In the present investigation heating rates were suitably controlled at 20 °C/min under nitrogen atmosphere and the weight loss was measured from 50 °C to 900 °C. A weight loss of 47.56% at 450 °C corresponds to decomposition of two azide groups coordinated to metal ion and a weight loss of 11.63% at 700 °C corresponds to the decomposition of one more azide from the coordination sphere (Figure 5). The temperature at above 700 °C indicates the non-volatile metal component present in the complex.
Antimicrobial and antifungal activities

The antimicrobial and antifungal activity of 4-aminooantipyrine and its complexes were tested against the bacteria *E.coli*, *P.aurginosa*, *S.aureus* and *C. albicance* (*fungi*). The minimum inhibitory concentration values of the compounds are summarized in Table 1. These values indicate that cobalt and zinc complexes shows the higher antimicrobial activities compared with those of the free ligand.

Table 1. Antimicrobial and antifungal activities of 4-AAP and its metal complexes zone of inhibition (mm)

<table>
<thead>
<tr>
<th>Complex number</th>
<th><em>E.coli</em></th>
<th><em>P.aurginosa</em></th>
<th><em>S.aureus</em></th>
<th><em>C.albicance</em></th>
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<td>16</td>
<td>05</td>
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<td>04</td>
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References