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# Synthesis, characterization and antimicrobial activity of palladium(II) complexes of diphenylpyraline and isothipendyl

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Two complexes of palladium with diphenylpyraline (DPH) and isothipendyl (IPH) of the formulae $[Pd(DPH)_2Cl_2]$ and $[Pd(IPH)Cl_2]$ have been synthesised and characterized by elemental analysis, IR, NMR, electronic, magnetic susceptibility, TGA and XRD data. The IR data suggests that while DPH acts as monodentate ligand, IPH acts as bidentate ligand. On the basis of spectral data, a square planar structure is proposed. These complexes are found to be more potent as antibacterial and antifungal agents than the free ligands.

Diphenylpyraline[1,2] and isothipendyl[3] drugs form stable complexes with transition metals. These drugs are found to be antiserotonin[4], antihistaminic[5,6], anticonvulsant[7] and antifungal[8] in nature and hence used in medicinal chemistry. Due to the presence of tertiary nitrogen in their molecules, these ligands are active donors especially suitable for coordination of biometals such as cobalt and copper. We have already shown that in the case of diphenylpyraline its fungal activity, at least partially, can be related to bonding of these biotics and changes in their homeostasis. Earlier we have studied the complexation of cobalt(II)[1], copper(II)[2] and iron(III)[9] with diphenylpyraline. In this note, we describe the synthesis of palladium(II) complexes with DPH and IPH and their IR, NMR, electronic, magnetic susceptibility, TGA and XRD data are reported.

## Experimental

All the chemicals used were of BDH(AR) grade. The solvents were used after distillation. The ligands used in the preparation of the complexes viz diphenylpyraline and isothipendyl were received as gift sample from Eskeyef and German Remedies and used without further purification.

The IR spectra of the ligands and their palladium(II) complexes were recorded on Hitachi Model 297 spectrophotometer in the 4000-250 $cm^{-1}$ region using nujol/KBr discs. The electronic spectra of the complexes in solution ($1.0 \times 10^{-4}$ *M*) were run on JASCO UVIDEC-610 double beam spectrophotometer using DMF as solvent. The molar conductance of the complexes in DMF ($1.0 \times 10^{-4}$ *M*) were measured at 305 K using Philips Model PR 9500 conductivity bridge. The proton NMR spectra of the ligand (IPH) and Pd-IPH complex were run on Varian EM 390 90 MHz spectrophotometer. Du Pont 9900 computer/thermal analyser with 951 TG module thermobalance was used for recording TG curves in the atmosphere of air at a heating rate of 6°C $min^{-1}$ with 5 nm $min^{-1}$ chart speed. The X-ray powder diffraction data were recorded on a DE-CER P12 X-ray machine with a diffractogram. The diffraction pattern was recorded at a chart speed of 4° (2θ) $min^{-1}$ at 5-60° (2θ) using scale 1° = 1 cm. The magnetic susceptibilities were measured at room temperature with Gouy balance using $Hg[Co(SCN)_4]$ as calibrant. The melting points of the complexes were determined using Thomas Hoover capillary melting point apparatus.

### *Preparation of the complexes*

#### $[Pd(DPH)_2Cl_2]$

Diphenylpyraline (5 mmol) in ethanol (50 ml) was slowly added to an ethanolic palladium (II) chloride solution (2.5 mmol) with continuous stirring. The solution was warmed on a water bath (70-75°C) for 1h. On cooling, a brownish solid formed was removed by filtration, washed with cold ethanol, then with ether and dried over fused $CaCl_2$ (yield: 62%; m.p. 178°C).

#### $[Pd(IPH)Cl_2]$

To a hot ethanolic solution of palladium(II) chloride (50 ml) was added a hot ethanolic solution of isothipendyl (50 ml) with vigorous stirring. On warming, the reaction mixture for ~30 min on a water bath (70°C), a brownish solid was obtained. The Pd-IPH complex formed was separated by filtration, washed with cold ethanol, then with ether and dried over fused $CaCl_2$ (Yield: 83%, m.p., 195°C).

The chloride and the metal analyses were carried out as usual by the literature methods[10,11]. The analytical data of the two complexes viz. $[Pd(DPH)_2Cl_2]$ and $[Pd(IPH)Cl_2]$ are: [Found: Pd,

14.50; N, 4.10; Cl, 10.10. Reqd for $[Pd(DPH)_2Cl_2]$: Pd, 14.39; N, 3.79; Cl, 9.60%. Found: Pd, 23.40; N, 8.90; Cl, 15.35%. Reqd. for $[Pd(IPH)Cl_2]$, Pd, 23.01; N, 9.10; Cl, 15.36%].

**Results and discussion**

The data reveals 1:2 (metal: ligand) stoichiometry for Pd-DPH complex and 1:1 for Pd-IPH complex.

These complexes have been found to be diamagnetic in confirmation with the square planar geometry[12]. The low molar conductance values (27.6 and 16.2 mohs $mol^{-1}$ $cm^{-2}$) indicate the non-electrolytic nature of these complexes in DMF solution.

The square planar geometry is generally found for metals of $d^8$ system. The ground state for the low spin $d^8$ system is $^1A_{1g}(=a_{1g}{}^2e_g^4\, b_{2g}{}^2)$. The ligand field excited states are $^3A_{2g}$, $^1A_{2g}$ $(b_{2g}\rightarrow b_{1g}$, $^3E_g$, $^1E_g$ $(e_g\rightarrow b_{1g})$ and $^3B_{1g}$ $(a_{1g}\rightarrow b_{1g})$. Therefore, one can expect three spin-allowed and three spin-forbidden transitions in these cases. The intensity bands arising out of transition $a_{1g}\rightarrow b_{1g}$ could not be assigned since the charge transfer intense bands (ligand → metal) mask the forbidden $d-d$ transition bands. A broad band in the region 22222-23600 $cm^{-1}$ is attributable to $^1A_{1g}\rightarrow {}^1B_{1g}$ transition[13].

The IR spectra of the complexes and the ligands were recorded in the range 4000-250 $cm^{-1}$. An absorption band appearing in the range 2250-2700 $cm^{-1}$ can be assigned[14] to tertiary nitrogen atom attached to alkyl group combined with halogen. the bands at 1600 and 1080 $cm^{-1}$ respectively in DPH ligand can be attributed to $\nu C-H$ and $\nu C-O-C$ bands. The band ~2850 $cm^{-1}$ in the IR spectra of IPH is assigned to heterocyclic nitrogen atom. The peak occurring at 1620 and 755 $cm^{-1}$ respectively in IPH are due to $\nu C=N$ and $\nu C=S$ vibrations. The $\nu C-O-C$ band in DPH and $\nu C=N$ band in IPH present at 1080 and 1620 $cm^{-1}$ respectively in the ligands remain at the same positions in the spectra of the respective complexes suggesting the non-involvement of oxygen of DPH and pyridine ring nitrogen of IPH in bonding with palladium ion. The $\nu C-S$ symmetric vibration of IPH appeared almost in the same region in its palladium complex confirming the non-bonding of sulphur atom to palladium ion. In the IR spectra of the palladium (II) complexes, the band at 2250-2700 $cm^{-1}$ totally disappeared indicating the coordination through tertiary nitrogen atom in both the ligands. In the Pd-IPH complex, the band at 2850 $cm^{-1}$ also disappears suggesting the involvement of heterocyclic nitrogen also in bonding. The Pd-Cl stretching band is observed around 295-310 $cm^{-1}$ in the IR spectra of both the palladium (II) complexes and the band around 410-435 $cm^{-1}$ is assigned to νPd-N. The non-conducting behaviour of the complex further suggests that the $Cl^-$ ion is present within the coordination sphere.

During the thermogravimetric analysis, the coordination compounds show no weight loss upto 240°C indicating that they are not hydrated. The palladium (II) complexes show only one step transformation 275-295°C corresponding to the gradual loss of ligand moiety. The coordination compounds undergo complete decomposition in the region 810-865°C and the TG curve becomes a level line. The final greenish black product obtained in each case is the metal oxide.

The proton NMR of $[Pd(IPH)Cl_2]$ complex exhibits $-CH-CH_3$ resonance at δ 1.3 ppm (doublet) and the multiplet bands ~δ 6.7 ppm are in the same position as in the free ligand. The multiplet bands at δ 7.0 ppm, δ 7.2 ppm and δ 7.8 ppm are also observed at the same positions as in the free ligand confirming the non-involvement of pyridine nitrogen in the bonding with Pd(II) ion. The signals ~δ 2.8 ppm, and δ 3.6 ppm indicate the shift of alkyl protons attached to tertiary nitrogen thereby suggesting the involvement of tertiary nitrogen atoms in coordination with Pd(II) ion. Thus $^1H$ NMR support the conclusion drawn on the basis of IR data regarding the involvement of tertiary nitrogen atoms in bonding with Pd(II) ion.

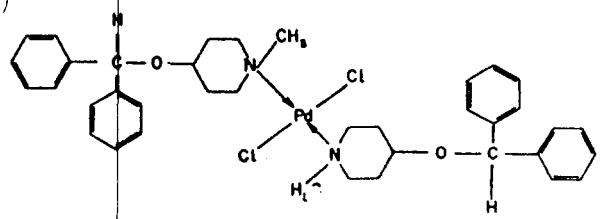
The molecular structure of $[Pd(C_{19}H_{23}ON)_2Cl_2]$ was investigated by X-ray diffraction. The diffractogram of the complex records 30 reflections between 5° and 60° (2θ) with maxima at 2θ = 8.25° and 16.7° which correspond to $d = 10.72$ and 5.306, respectively. All the main peaks have been indexed[15,16] and their $\sin^2\theta$ compared with the calculated ones. A comparison of the values reveal that there is a good agreement between the observed and calculated values of $\sin^2\theta$. The unit cell has been determined by the trial and error method[17-20]. The observed values fit well into triclinic system to give a unit cell lattice parameters a = 9.822 Å, b = 9.679 Å and c = 8.434Å, V = 803.2873 $Å^3$ and α = 96.655°, β = 89.055° and γ = 87.997°. Substitution of this cell volume primitive lattice (n = 8) for the complex $[Pd(C_{19}H_{23}ON)_2Cl_2]$ gives the theoretical value of density equal to 1.222 g $cm^{-3}$. The experimental value of density has been found to be 1.215 g $cm^{-3}$ which is in good agreement within the limits of experimental error.

Table 1—Percentage inhibition of fungicidal and bacterial growth

| Compound | *A. alternata* | | *A. flavus* | | *A. niger* | | *A. tenuis* | | *E. coli** | | *S. aureus** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0.1 | 0.25 | 0.1 | 0.25 | 0.1 | 0.25 | 0.1 | 0.25 | 0.1 | 0.25 | 0.1 | 0.25 |
| $C_{19}H_{23}ON$ | 8.3 | 14.5 | 9.5 | 19.3 | 7.4 | 16.2 | 9.2 | 17.3 | 9.4 | 16.2 | 7.6 | 14.5 |
| $C_{16}H_{19}N_3S$ | 11.3 | 19.4 | 13.0 | 22.5 | 13.4 | 24.5 | 15.0 | 24.5 | 17.1 | 29.5 | 22.3 | 40.2 |
| $[Pd(C_{19}H_{23}ON)_2Cl_2]$ | 42.6 | 80.3 | 45.5 | 87.1 | 36.5 | 75.8 | 40.2 | 76.7 | 48.3 | 76.4 | 39.5 | 65.4 |
| $[Pd(C_{16}H_{19}N_3S)Cl_2]$ | 46.9 | 87.5 | 53.8 | 94.5 | 49.7 | 87.3 | 46.5 | 89.4 | 56.5 | 87.8 | 54.3 | 91.2 |

*bacterial growth

On the basis of the above data, a four coordinate square planar geometry is proposed for the palladium(II) diphenylpyraline complex (structure I)



(I)

*Antibacterial and antifungal activity*

The antimicrobial activity of free ligands and their palladium(II) complexes clearly indicate that the compounds have both antibacterial and antifungal potency against all tested organisms.

The *in vitro* biocidal activities of the investigated compounds (0.1 and 0.25% per test) were screened against *Alternaria alternata, Aspergillus flavus, Aspergillus niger* and *Alternaria tenius* fungi. These compounds were also screened against *Staphylococcus aureus* and *Escherichia coli* bacteria following cup-diffusion technique. All plates were run in triplicate, the inhibition zones were measured and mean in millimeters was recorded. The data in Table 1 indicates that the antimicrobial activity of the complexes is more than that of the free ligands. The complexation reduces the polarity of the metal ion mainly because of partial sharing of its positive charge with donor group and possible π-electron delocalization over the whole complex molecule. This is due to the enhanced lipophilic character of the metal complex which favours its permeation through lipoid layers of fungus membrane thus improving the antimicrobial activity of the complex over the free ligand.

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