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Spectroscopic characterization, antioxidant and antitumour studies of novel bromo substituted thiosemicarbazone and its copper(II), nickel(II) and palladium(II) complexes

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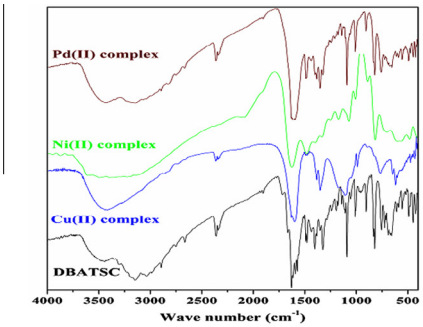
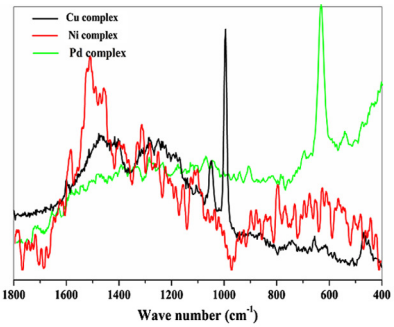
HIGHLIGHTS

- Copper(II), nickel(II) and palladium(II) complexes of DBAPTSC are synthesized.
- Tetragonally distorted octahedron copper(II) DBAPTSC is synthesized.
- Nickel(II) complex has shown good antitumour activity against HepG2 hepatoblastoma cell lines.
- The compounds are identified as semiconducting materials with the band gap data obtained from UV–visible spectra.

GRAPHICAL ABSTRACT



FT-IR spectra of DBATSC and its Cu(II), Ni(II) and Pd(II) complexes



FT-Raman spectra of DBATSC and its Cu(II), Ni(II) and Pd(II) complexes

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ABSTRACT

A new, slightly distorted octahedral complex of copper(II), square planar complexes of nickel(II) and palladium(II) with 2,4′-dibromoacetophenone thiosemicarbazone (DBAPTSC) are synthesized. The ligand and the complexes are characterized by FT-IR, FT-Raman, powder X-ray diffraction studies. The IR and Raman data are correlated for the presence of the functional groups which specifically helped in the confirmation of the compounds. In addition, the free ligand is unambiguously characterized by ^{1}H and ^{13}C NMR spectroscopy while the copper(II) complex is characterized by electron paramagnetic resonance spectroscopy (EPR). The g values for the same are found to be 2.246 (g_1), 2.012 (g_2) and 2.005 (g_3) which suggested rhombic distortions. The HOMO–LUMO band gap calculations for these compounds are found to be in between 0.5 and 4.0 eV and these compounds are identified as semiconducting materials. The synthesized ligand and its copper(II), nickel(II) and palladium(II) complexes are subjected to antitumour activity against the HepG2 human hepatoblastoma cell lines. Among all the compounds, nickel(II) complex is found to exert better antitumour activity with 57.6% of cytotoxicity.

Introduction

Thiosemicarbazones emerged as the versatile reagents that are playing prominent role in both qualitative analysis and quantitative [1,2] estimation of the trace metals and also in the bioinorganic field. Numerous thiosemicarbazone derivatives have been found to

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possess good activity against human tumours [3]. Biological activities of these thiosemicarbazone moieties are found to have enormous increase after complexation with the transition metal ions [4,5]. They have been proved as the versatile agents exhibiting antimicrobial [6,7], antitumour [8], antifungal [9], antiviral [10] and enzyme inhibitors, etc. Use of copper(II) thiosemicarbazone complexes as radiopharmaceuticals is one of the most recent advances in the sulphur chemistry [11]. Coordination of the thiosemicarbazone ligand to metal ion has greatly increased the antimicrobial activity [12,13]. Differently substituted thiosemicarbazones on coordination to copper(II) and other transition metal ions have been identified as the compounds with high cytotoxicity towards the tumour cells in vivo and in vitro [14]. In the present study, the author concentrated more in the synthesis of the bromo-substituted thiosemicarbazone ligand and its respective copper(II), nickel(II) and palladium(II) complexes. The compounds are characterized by using different spectroscopic techniques. Antitumoral activity evaluation of the free ligand and the complexes against the human hepatoblastoma cell lines is also carried out.

Materials and methods

Chemicals

All the chemicals used in the present work are of analytical grade unless reported. The organic chemicals 2-bromo-1-(4-bromophenyl)ethanone is purchased from Avara synthesis Pvt. Ltd., thiosemicarbazide is obtained from Sd-Fine chemicals, $CuCl_2$ and other organic solvents are purchased from different commercial sources and are used without further purification.

Apparatus

A JASCO Corp., UV-530 spectrophotometer equipped with a 1.0 cm quartz cell is used for the absorbance studies. Infrared spectra are recorded as KBr pellets on JASCO FT-IR 4100 spectrophotometer (IIT MADRAS) in the range of 4000–400 cm^{-1}. The ^{1}H and ^{13}C NMR spectral analysis of the ligand DBAPTSC was done as DMSO-d^6 solutions by using tetramethylsilane (TMS) as the internal solvent on a Bruker-400 MHz instrument provided by the School of Chemistry, University of Hyderabad at 300 K. EPR spectra of the copper(II) complex is recorded as polycrystalline samples at 298 K on a Bruker-ER073 instrument equipped with an EMX microX source for X-band measurement using Xenon 1.1b.60 software provided by the manufacturer. Raman spectra are measured using a confocal Raman microscope (LabRam HR 800, Horiba JobinYvon SAS, France) equipped with a 432 nm He–Ne Laser (Torus Laser, Laser Quantum, France) with laser power 50 mW, 2 scans and a 50 X LWD air – dry visible objective (NA = 0.5 wd 10.6 MM LIEU Microsystems of Model BX 41) and attached with a Fieltiyar multichannel CCD detector. Each Raman spectrum is measured in the range of 400–1800 cm^{-1} with a spectral resolution of 0.35 cm^{-1}/pixel with 1800 gr/mm grating at the confocal pinhole is set to 400 nm. Lab Sepc software under windows is used to control the Raman system, form data acquisition and saving the data. X-ray powder diffraction data are collected on a Philips X'pert Pro X-ray powder diffractometer equipped with X'cellerator detector at room temperature. The scan range, step size, and time per step are 2θ = 5.00 to 40, 0.028 and 30 s, respectively.

Experimental

Synthesis of 2,4′-dibromoacetophenone thiosemicarbazone (DBAPTSC)

To a hot ethanolic solution of thiosemicarbazide (0.01 mol, 0.9102 g), solution of 2,4′-dibromoacetophenone (0.01 mol, 2.7794 g) is added slowly under constant stirring. A reddish brown coloured solution is formed after refluxion of the mixture for about 5 h. A yellowish brown coloured compound is obtained on evaporating the solvent under reduced pressure [15–17].

Synthesis of copper(II), nickel(II) and palladium(II) complexes

To 10.0 mL solution of the ligand in ethanol (0.002 mol, 0.6132 g), aqueous ethanolic solution of corresponding metal salt (0.001 mol) is added slowly under constant stirring in nitrogen atmosphere. The contents of the flask are then stirred at room temperature for 48 h to collect the dark coloured solution. The coloured solution is then allowed to evaporate at room temperature to obtain the coloured precipitate.

Antioxidant activity

To evaluate the radical scavenging activity of these compounds, a valid and standard method is employed using DPPH [18]. In DPPH method, the principle involved in evaluation of antioxidant activity is based on the conversion of DPPH into 1,1-diphenyl-2-picrylhydrazine. First preliminary analysis is carried out in order to check whether the compounds are active or not. A qualitative procedure is employed in which the sample compound (approximately 100 μg/mL) is applied as a spot on TLC plate and after the development of chromatogram using MeOH:CH_3CN (7:1) mobile phase, 0.2% DPPH (w/v) solution is sprayed on the plate. A yellow spot on the purple background indicates the antioxidant activity. For the quantitative estimation of scavenging activity, compounds are dissolved in 1% DMSO solution to give the 10.0 mL of stock solution (1.0 mg/mL). The stock is further diluted to get the sample solutions containing 25–100 μg/mL. To each sample solution containing the concentrations of 25–100 μg/mL, 3.0 mL of 0.004% methanolic DPPH (w/v) is added. After 30 min of incubation, the colour change is measured by taking the absorbance value at 517 nm using a Schimadzu UV–vis-2450 instrument. The absorbance values are compared with BHT (standard) concentrations of 25–100 μg/mL.

Antitumour activity

Cell viability is assessed by the MTT staining method [19]. Cells are harvested from 4 to 5-day-old cultures and are seeded in 96-well plates at the density of 5×10^3 cells. The HepG2 cells are treated with synthesized compounds with increasing concentrations of 20, 40, 60, 80 and 100 μM for 48 h in a final volume of 100 μL. At the end of the treatment, 20 μL of MTT (5 mg MTT/mL in PBS) is added and the cells are incubated for a further period of 4 h. In control experiments, cells are grown in the same media without the compounds. About 100 μL of DMSO is added to each culture and mixed by repeated pipetting and adding to dissolve the reduced MTT crystals. Relative cell viability is evaluated by measuring the optical density at 570 nm on microplate reader (Quant Bio-tek Instruments, Inc.). At 100 μM concentration of the synthesized compounds, three different experiments are carried out in triplicates and the mean values are reported as the cell cytotoxicity for each compound.

Result and discussion

^{1}H and ^{13}C NMR spectra of the ligand DBAPTSC

The NMR spectrum of the free ligand has provided significant evidence for the confirmation of the structure. The —NH_2 protons are observed as singlet at δ9.42 while, the —NH proton is seen as