Journal of Photochemistry & Photobiology, B: Biology 162 (2016) 86–92

Contents lists available at ScienceDirect

Journal of Photochemistry & Photobiology, B: Biology

journal homepage: www.elsevier.com/locate/jphotobiol

Copper complexes bearing 2-aminobenzothiazole derivatives as potential antioxidant: Synthesis, characterization

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ARTICLE INFO

Article history:
Received 14 April 2016
Accepted 17 June 2016
Available online xxxx

Keywords:
Acetoacetanilide
Knoevenagel
Antioxidant
Screening

ABSTRACT

Novel copper complexes of Schiff base ligands of 2-aminobenzothiazole derivatives were synthesized by the condensation of Knoevenagel condensate of acetoacetanilide (obtained from substituted benzaldehydes and acetoacetanilide) and 2-aminobenzothiazole. They were characterized by elemental analysis, IR, ^{1}H NMR, UV–Vis., molar conductance, magnetic susceptibility measurements and electrochemical studies. Based on the magnetic moment and electronic spectral data, square planar geometry has been suggested for all the complexes. Antibacterial and antifungal screening of the ligands and their complexes reveal that all the complexes show higher activities than the ligands. The binding behaviour of the complexes with calf thymus DNA has been investigated by electronic absorption spectra, viscosity measurements and cyclic voltammetry. The DNA binding constants reveal that all these complexes interact with DNA through intercalation binding mode. Superoxide dismutase and antioxidant activities of the copper complexes have also been studied. The antioxidant activities of the complexes showed higher activities. Thermal denaturation studies suggested the nature binding affinity of copper complexes with CT-DNA. All complexes exhibit suitable Cu(II)/Cu(I) redox potential to act as antioxidant enzymes mimic. Further, the copper complexes also showed catalase activity. It is hope that copper complexes were capable of decrease ROS levels or reduce oxidative stress in Alzheimer's patients.

1. Introduction

A natural products of β-diketones of siphonarienedione and cyclopiatalantin possessing medicinal activity as well as β-diketones are used as a powerful intermediates for the organic synthesis. 1,3-diketone system of the polyphenol diferuloylmethane (curcumin) exhibits a variety of pharmacological activities including antiinflammatory, anticarcinogenic, antibacterial and antifungal activities, hepato- and nephro-protective [1–2], thrombosis suppressing [3], myocardial infarction protective [4] most of which are accredited to its antioxidant and radical scavenging properties. Curcumin based analogs of difluro Knoevenagel condensate and their Schiff base copper complexes exhibited more effective in protease inhibition and apoptosis inducers in cancer cells [5] (Scheme 1).

Schiff bases and their complexes have been studied for their variety of biological actions by virtue of the azomethine linkage, due to its ability to reversibly bind oxygen, catalytic activity in hydrogenation of olefins, transfer of an amino group, photochromic properties and complexing ability towards some toxic metals. This high affinity for chelation of the Schiff bases towards the transition metal ions is utilized in preparing their solid complexes [6–10].

The biological activity greatly depends on the nature of the metal ion and the donor atoms of the ligands [11–12]. Metal complexes of Schiff bases derived from substituted aldehydes and heterocyclic compounds containing nitrogen, sulphur and/or oxygen as ligand atoms are of interest as simple structural models of more complicated biological systems [13–15]. Many of the aldehydes tested were found to have highly potent antimicrobial activity. These aldehydes may act as good candidates for practical applications as well as interesting lead compounds for the development of novel antimicrobial agents. Schiff bases of 2-aminobenzothiazole derivatives have been of great importance due to their synthetic flexibility and biological activity of their metal complexes [16]. Diazotized 2-aminobenzothiazole with 1,3-dicarbonyl compounds (benzoylacetone, methyl acetoacetate and acetoacetanilide) obtained a new series of tridentate compounds exist in the intramolecularly hydrogen bonded azo-enol tautomeric form in which one of the carbonyl groups of the dicarbonyl moiety had enolised and hydrogen bonded to one of the azo nitrogen atoms. The stable complexes showed a normal paramagnetic moment [17].

The interaction of transition metal complexes with nucleic acids is a major area of research due to the utility of these complexes in the design and development of synthetic restriction enzymes, spectroscopic probes, site specific cleavers and molecular photoswitches [18]. The transition metal complexes are currently used as artificial nucleases are because of their diverse structural feature, and the possibility to tune their redox potential through the choice of proper ligands [19].

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http://dx.doi.org/10.1016/j.jphotobiol.2016.06.030
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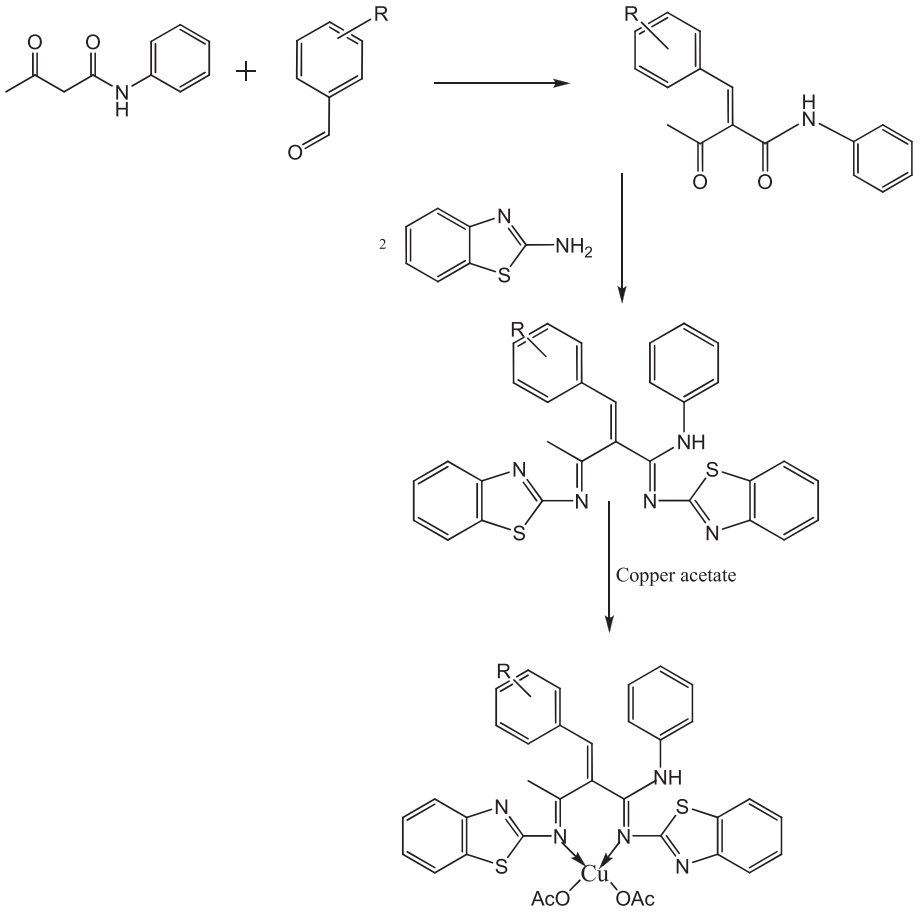

Scheme 1. Schematic outline of synthesis of ligands and their complexes.

Copper(II) complex is probably the most extensively studied among the transition metal ions This is due to their lability, their high affinity with different ligands and the wide variety of ligands geometries that can accommodate significant role either in naturally occurring biological systems or as pharmacological agents like (CuZn–SOD) superoxide dismutase and it's disproportionate the toxic $O_2^{\bullet-}$ radical into molecular oxygen and hydrogen peroxide [20–22]. In the present study we describe the synthesis and characterization of new series of curcumin analog copper complexes of Knoevenagel condensate of Schiff base of 2-aminobenzothiazole.

2. Experimental

2.1. Material

All chemicals and solvents were analaR grade and were purchased from Merck. All supporting electrolyte solutions were prepared using analytical grade reagents. Calf thymus DNA purchased from Genie Biolab, Bangalore, India.

2.2. Instrumentation

The amount of copper present in the copper complexes was estimated using ammonium oxalate method. Elemental analysis of ligands and their copper complexes were carried out using Elementar Vario EL III. Molar conductance of the complexes was measured using a coronation digital conductivity meter. The ^{1}H NMR spectra of the ligands were recorded using TMS as internal standard. Chemical shifts are expressed in units of parts per million relative to TMS. The IR spectra of the ligands and their copper complexes were recorded on a Perkin-Elmer 783 spectrophotometer in 4000–200 cm^{-1} range using KBr disc. Electronic spectra were recorded in a Systronics 2201 Double beam UV–Vis., spectrophotometer within the range of 200–800 nm regions. Magnetic moments were measured by Guoy method and corrected for diamagnetism of the component using Pascal's constants. Cyclic voltammetry was performed on a CHI 604D electrochemical analyzer with three electrode system of glassy carbon as the working electrode, a platinum wire as auxiliary electrode and Ag/AgCl as the reference electrode. Tetrabutylammoniumperchlorate (TBAP) was used as the supporting electrolyte. Solutions were deoxygenated by eradication with N_2 previous to measurements. The interactions between metal complexes and DNA were studied using electrochemical and electronic absorption techniques.

2.3. Preparation

2.3.1. Synthesis of β-Ketoanilides

An ethanolic solution of acetoacetanilide (1 M), was added drop wise in the ethanolic solution of substituted benzaldehydes (L^1-anisaldehyde, L^2-salicylaldehyde, L^3-2-bromo benzaldehyde, L^4-3,4-dimethoxy benzaldehyde) (1 M) in the presence of anhydrous potassium carbonate (1 M) in the mixture with stirring. The resulting mixture was refluxed for about 8 h. The solid thus obtained was filtered, dried and recrystallized from ethanol to obtain yellow colored β-ketoanilide(s).

2.3.2. Synthesis of Schiff Bases

Yellow colored β-ketoanilide(s) (1 M) was dissolved in ethanol added drop wise to 2-aminobenzothiazole (2 M) and stirring at room temperature. The resulting solution was refluxed about 8 h and the