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Synthesis and Antimicrobial Study of Novel Schiff Bases and Metal Complexes

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Abstract

Novel Schiff bases (E)-6-(benzylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-aza-bicyclo heptane-2-carboxylic acid (L1) and (E)-6-(4-hydroxy benzylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-aza-bicyclo heptane-2-carboxylic acid (L2) were synthesized. Further metal complexes of these Schiff bases were synthesized using various metal nitrates. Both Schiff bases and their metal complexes were screened for antibacterial activity against different bacterial species such as Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus. Some Schiff base and metal complexes showed moderate to excellent activity.

Keywords

Schiff Bases; Metal Complexes; Biological Activity

Introduction

Coordination chemistry is the field of most active research in inorganic chemistry which leads to new products showing a wide range of applications such as fungicides, paints, pigments, polymers, pharmaceuticals, catalysis, and photoconductors (1). The coordination compounds play an important role in colorimetric, spectrophotometric and polarographic analysis (2).

Coordination chemistry deals with metals and organic ligands. There are several classes of ligands such as organo, organo-metallic, cluster and bioinorganic. In complex formation a ligand (Werner complex) binds through the lone pair of main group atom to the metal. Many metal-ligand interactions seen in nature are classical ligands (3). Schiff-bases are unique ligands which can form complexes with metal ions. In our previous work we synthesized several Schiff bases derivatives; some of them were used as precursors for the synthesis of variety of heterocyclic compounds (4-7).

Schiff bases and their complexes are of high interest among the researchers because of their biological activity including anti-tumor, antibacterial, fungicidal, antidepressants, antiphlogogistic, nematocide, anti-carcinogenic and catalytic activity (8-9).

The microorganisms absorb metal ions on their cell walls and the respiration processes of cells gets disturbed and protein synthesis is blocked thus inhibiting the further growth of organisms. Membrane of Gram-negative bacteria is surrounded by an outer membrane containing lipopolysaccharides. Schiff base metal complexes are able to combine with the lipophilic layer in order to enhance the membrane permeability of the Gram-negative bacteria. A lipid membrane surrounding to the cell favors the passage of only lipid soluble materials; thus the lipophilicity is an important factor that controls the antimicrobial activity. An increase in lipophilicity, enhances the penetration of Schiff base and its metal complexes into the lipid membranes and thus restricts the growth of organism (10).

Synthesis of new coordination compounds for cobalt (II), nikel (II) and copper (II) with Schiff base ligand derived from 4-amino antipyrine, sulphadiazine and acetoacetanilide has been studied (11). Copper (II) complexes derived from 4-nitro-2-[(2-diethylaminoethylimino)-methyl]-phenol Schiff base was reported (12). Metal complexes of Fe (II), Co (II), Ni(II), Cu(II), Zn(II) or Cd (II) with Schiff base N-(2-thienylmethylidene)-2-aminopyridine have been studied (13). Synthesis and antibacterial activity of Schiff bases and transition metal complexes derived from 2, 3-diminopyridine and o-vanillin has been study (14). Synthesis and antimicrobial activity of new metal [Mg(II), Fe(II), Co(II), Ni(II), Zn(II) and Cd(II)] complexes from 2-(1′/2′-hydroxynaphthyl) benzoxazoles was studied (15). Synthesis of Chromium (III), Iron (III) and Cobalt (III) Complexes of new Schiff bases has been studied (16). Synthesis and antimicrobial study of (E)-(4-chlorophenyl)-(4-chlorobenzylidene) acetohydrazide and (E)-(4-chlorophenyl)-(1-methoxynaphthalen-2-ylmethylene) acetohydrazide and their metal complexes has been also reported recently (17).

Thus the versatile nature of Schiff base metal complexes in biological and various applications prompted us to work in this highly desirable area. In continuation to our work; in the present studies we report the synthesis of new Schiff bases and their metal complexes. Further all the synthesized Schiff bases and complexes were screened for antibacterial activity on three bacterial species namely Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus.

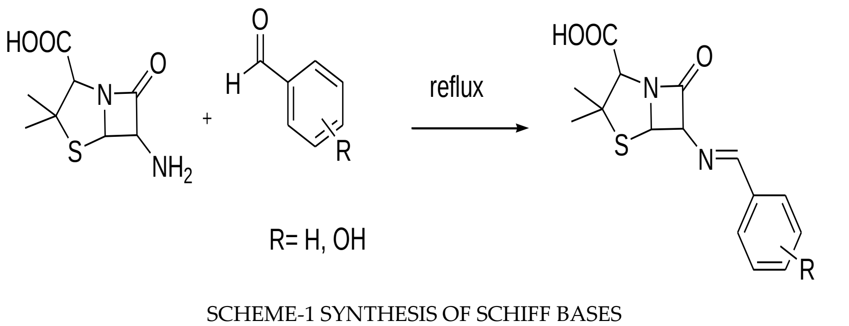
Experimental

Materials and Methods

All the materials were of commercial grade reagents. Chemicals were purchased from Spectrochem and Sigma Aldrich chemical companies in high purity which was used without further purification. Melting points were determined in open capillaries using an Electrothermal Mk3 apparatus. Infrared (IR) spectra in KBr were recorded using a Perkin-Elmer FT-IR spectrometer 65. 1H NMR spectra were recorded on 400 MHz FT-NMR spectrometer in CDCl3 as a solvent and chemical shift values were recorded in δ (ppm) related to tetramethylsilane (Me4Si) as an internal standard. The progress of the reactions was monitored on TLC (Thin Layer Chromatography). Elemental analyses were done on Elemental Varian Instrument. Mass spectra were scanned on Water-TQ Detector.

General Procedures for the Synthesis of Schiff Bases:

To an equimolar mixture of aldehyde (1 mmol) and 6-amino-3, 3-dimethyl-7-oxo-4-thia-1-aza-bicyclo [3.2.0] heptane-2-carboxylic acid (1.1 mmol) in ethanol (5 mL), 2-3 drops of glacial acetic acid was added. The contents were refluxed for appropriate time for completion of reaction. After completion of the reaction as monitored on TLC (3:7 ethyl acetate:n-hexane), excess of ethanol was evaporated. The solid obtained was filtered, washed with cold water, dried and recrystallized from ethanol.



SCHEME-1 SYNTHESIS OF SCHIFF BASES

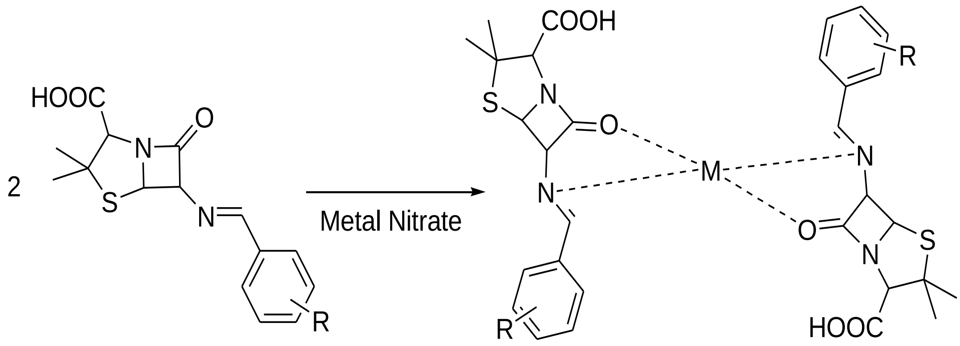
Spectral data of the representative Compound (E)-7-(4-hydroxy benzylidene amino)-3,3-dimethyl-6-oxo-2-thia-bicyclo[3.2.0] heptane-4-carboxylic acid is mentioned below:

Molecular Formula: C16H17NO4S

Elemental Analysis: C= 60.17; H= 5.37; N= 4.39; O= 20.04; S= 10.04; LRMS (m/z): 321(M+1) base peak; 1H-NMR (DMSO-d6); 1.5-1.6 (s, 6H) (2 –CH3), 3.4 (d, 1H), 3.4-3.6 (m, 2H), 4.20 (s, 1H) broad D2O exchangeable, 4.40 (d, 1H), 7.20-7.60 (m,4H), 7.90-8.00 (s, 1H), 10.00 (s, 1H. IR: 3342 (OH), 2967 (C-H), 1659 (C=N), 1515 (C=C), 1456 (C-O/C-N).

General Procedure for Preparation of Schiff Bases Metals-Complex:

A mixture of Schiff bases (2 mmol) and nitrates of metal (1 mmol,) in ethanol (5 ml) was refluxed for 3-4 hours. The pH of solution was adjusted to 7-8 by using alcoholic ammonia solution. The progress of reaction is monitored on thin layer chromatography (TLC) using petroleum ether: ethyl acetate (7:3 ml) as the mobile phase. After completion of the reaction; the reaction mass was concentrated on rotary evaporator; poured onto ice-cold water and finally recrysatllized with ethanol.



SCHEME-2 SYNTHSESIS OF SCHIFF BASE METAL COMPLEXES

Spectral Data of (E)-7-(4-hydroxy benzylidene amino)-3,3-dimethyl-6-oxo-2-thia-bicyclo[3.2.0] heptane-4-carboxylic acid Iron Complexes:

IR: 3342 (OH), 2967 (C-H), 1659 (C=N), 1515 (C=C), 1456 (C-O/C-N), 530 (M-O) and 470 (M-N).

Metal Fe %: 8.11 %.

Biological Activity of Schiff Bases and Metal Complexes:

Antibacterial activity of the synthesized Schiff bases and their complexes has been screened against bacteria Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus. Selective media (HiMedia) were used for each type of bacteria. The antibacterial activity was evaluated using agar plate method. Agar plate's surface was inoculated by spreading standardized inoculums of the test microorganism over entire surface. A hole with a diameter of 6 mm was punched aseptically with a sterile cork borer or a tip, and a volume (20 μL) of the test compound solution is introduced into the well. The Petri dishes are incubated under suitable conditions. The test compound diffuses into the agar and inhibits germination and growth of the test microorganism and then the diameters of inhibition growth zones are measured as a zone of inhibition. Results of the ligands and complexes prepared were showed moderate to excellent activity as compared to standard Penicillin Table-2.

TABLE: 2. ANTI-BACTERIAL ACTIVITY OF LIGAND AND COMPLEXES

Sr. No.	Compound	Zone of inhibition (mm)		
		Escherichia coli	Pseudomonas aeruginosa	Staphylococcus aureus
1	L_1	17 mm	09 mm	05 mm
2	L_2	10 mm	21 mm	18 mm
3	L_1(Fe)	10 mm	08 mm	07 mm
4	L_1(Co)	07 mm	05mm	05 mm
5	L_1(Ni)	10 mm	10 mm	11 mm
6	L_1(Cu)	09 mm	12 mm	09 mm
7	L_1(Zn)	10 mm	10 mm	05mm
8	L_2(Fe)	15 mm	08 mm	24 mm
9	L_2(Co)	11mm	11 mm	10 mm
10	L_2(Ni)	08 mm	05 mm	07mm
11	L_2(Cu)	09 mm	22mm	17mm
12	L_2(Zn)	07 mm	10 mm	28 mm
13	Penicillin	18 mm	20 mm	24 mm

Result and Discussions:

Novel Schiff bases (E)-6-(benzylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-aza-bicyclo heptane-2-carboxylic acid (L1) and (E)-6-(4-hydroxy benzylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-aza-bicyclo heptane-2-carboxylic acid (L2) were synthesized. The synthesis process required longer reaction time (about 45-50 hrs). The longer time of reaction may be due to the presence of lactum ring in amino compound. As compared to ligand synthesis; the time required for metal complex synthesis is less. The ligands and complexes were screened for antibacterial activity.

It is observed that ligand L2 and metal complexes 8, 11, 12 showed excellent antibacterial activities as compared to standard penicillin. Aromatic ring in a compound enhances the activity as compared to open chain compounds. Oxygen and nitrogen present increases the activity of ligands and complexes.

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