Original Article

Synthesis, Characterization and Antibacterial Evaluation of New Schiff Base Ligand and Its Complexes of Transition Metal Ion Zn (II), based on 6-Aminopenicillanic Acid

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ABSTRACT

In the present research, 6-aminopenicillanic acid (6-APA) reaction with(n-butyl aldehyde, crotonaldehyde, terephthalaldehyde, furfuraldehyde) in ethanol to procure compounds [6-(butylidene amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid, 6-(but-2-1-ylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6,6'-((1,4-phenylenebis (methaneylylidene)) bis(azaneylylidene))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid, 6-((furan-2-ylmethylene)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid] respectively. The structure of synthesized compounds identified by spectral data (FT-IR), (^{1}H-NMR), (^{13}C-NMR) spectra and Mass Spectrometric. The Schiff base ligand and synthesis some transition metals complexes [Zn] of this ligand were described via FTIR, UV-Visible Spectroscopy and the Atomic Absorption Spectroscopy, The antibacterial activity of the ligand and complexes was tested against two different bacteria strains (Pseudomonas and Staphylococcus aureus). The ligand and its complexes were discovered to have excellent inhibitory action against bacteria (*Pseudomonas* and *Staphylococcus aureus*). As a consequence, the compounds developed might be viable alternatives for commonly used medications.

Keywords: Schiff base, 6-amino penicillanic acid, Schiff base of n-butylaldehyde,Schiff base of crotonaldehyde, Schiff base of terephthaldehyde, Schiff base of furfural

Introduction

Schiff's bases summarize yields of carbonyl compounds with primary, amines, and, they ,were ,first reported‹in‹1864 the German scientist that called Hugo Schiff.[1]. The azomethine group with the overall formula RHC=NR1, where R and R1 are aryl, cycloalkyl, alkyl, or, heterocyclic groups that may be exchanged in various ways, gives these compounds their corporate structural property Schiff bases.[2,3] The (N=CH) (imine) cluster describes these compounds,and,is,important‹in‹describing‹the‹transamination‹mechanism‹rasemination ,reaction ,in, biologic systems.[4,5] The application of these comp. as an active component is a remarkable use of these comp. corrosion inhibitor, which is based on their capacity to create a crystalline structure in a short period of time. To be secure, a monolayer must be applied to the surface. Amphetamines and other amines are two effective inhibitors. Schiff bases play an important role in aldehydes, however this is most likely due to the (C=N) bond. In many circumstances, more powerfully.[6] prepared the Schiff bases N-(4-(N,N-Diethylamino)benzylidene)naphthalen-1-amine from 1- naphthylamine with p-(N,N-diethylamino) benzaldehyde in basic medium.[7] And prepared used 4-(dimethyl amino)benzaldehyde and S-benzyl Di thiocarbamate to give the

Access this article online

Quick Response Code:

Website: www.pnrjournal.com

DOI: 10.47750/pnr.2022.13.02.015

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Received: 27 January, 2022 **Accepted:** 28 April, 2022

Published: 15 Jun, 2022

How to cite this article: Obaid MS, Karim SA, Said MH. Synthesis, Characterization and Antibacterial Evaluation of New Schiff Base Ligand and Its Complexes of Transition Metal Ion Zn (II), based on 6-Aminopenicillanic Acid. J Pharm Negative Results 2022;13(2):97-101

compound azomethine(Schiff bases).[8] Cephradine complexes with Co(II), Cu(II), Ni(II), and Zn(II) were synthesized in (1:2) (M:L) molar ratios; all complexes were octahedral with the exception of the copper complex, which was in a square planar geometry. Cephradine and its complexes were tested for antibacterial efficacy against several bacterial strains, and the antibacterial results clearly demonstrate that complexation boosted antibacterial action.[9]

Experimental

The reagents [zinc chloride, benzaldehyde, crotonaldehyde, ethanol, benzene and diethyl ether] were obtained from BDH Chemical Limited. The Sigma–Aldrich Chemical Ltd. were supplied these reagents [6-aminopenicillinic acid, pyridine, terephthalaldehyde and furfural]. Succinic anhydride and Maleic anhydride were obtained from Alpha. finally, the Mueller-Hinton Agar were obtained from Difco(U.S.A).

Instrument Analysis and Equipment

Melting Points Apparatus

Melting points were determined using SMP30 melting point apparatus and are uncorrected; College of Science for Women, University of Babylon.

Fourier Transform Infrared Spectra (FT-IR)

The FT-IR spectra were obtained as KBr discs using a Biotic 600 FT-IR spectrophotometer in the range 4000-400 cm^{-1}. Which, were recorded at the College of Science for Women University of Babylon.

Conductivity Measurements

Electrical conductivity measurements of the complexes were made with absolute

(DMSO) at 25 ºC using WTW Cond 7300 digital conductivity meter at College of,

Science for Women, Department of Chemistry, University of Babylon.

UV-Visible Spectra Measurements

UV-visible spectra of prepared ligand solutions and their complexes were recorded in ethanol absolute and DMSO. At College of Science for Women, University of Babylon.

(^{13}C, ^{1}H) NMR Spectra Measurements

The nuclear magnetic resonance spectra were measured at Isfahan University of

Technology (IUT) Iran using an instrument Bruker at (400mHz) Switzerland with (DMSO).

Flame Atomic Absorption Spectroscopy

The atomic absorption analysis was used to determine the metal contents by PERKIN ELMER,1100B,Atomic Absorption Spectrophotometer at BPC Analysis Center in Baghdad.

Mass Spectrometric

The spectra measured by Agilent Technology (HP), Model: 5973 Network Mass Selective Detector,at Isfahan University of Technology (IUT) with (DMSO).

Rotary evaporator

Laborota 4000 efficient Heidolph (Germany)at Chemistry Department /College of Science for Women, University of Babylon.

Differential Thermal Gravimeter (DTG)-60 Shimadzu (Japan)

At Chemistry Department /College of Science for Women, University of Babylon.

Materials and Methods

The Procedure of Schiffs Ligand Base

6-(butylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid(L1)

The ligand was prepared by dissolving 6-Aminopenicillanic acid (0.0231 mol,5 gm) in 35ml absolute ethanol (basic medium pyridine) and then add (0.0231 mol, 2.102ml) of (n-butyl aldehyde)the resulting mixture was refluxed for 5hrs, dried and recrystallized from absolute ethanol.

6-(but-2-1-ylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid(L2)

The ligand was prepared by dissolving 6-Aminopenicillanic acid (0.0231 mol,5 gm) in 35ml absolute ethanol (basic medium pyridine) and then add (0.0231 mol, 1.913ml) of (crotonaldehyde)the resulting mixture was refluxed for 5hrs, dried and recrystallized from absolute ethanol.

6,6'-((1,4-phenylenebis(methaneylylidene)) bis(azaneylylidene))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid)(L3)

The ligand was prepared by dissolving 6-Aminopenicillanic acid (0.0231 mol,10 gm) in 35ml absolute ethanol (basic medium pyridine) and then add (0.0231 mol, 3.098gm) of (terephthalaldehyde)the resulting mixture was refluxed for 5hrs, dried and recrystallized from absolute ethanol.

6-((furan-2-ylmethylene)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid(L4)

The ligand was prepared by dissolving 6-Aminopenicillanic acid (0.0231 mol,10 gm) in 35ml absolute ethanol (basic medium pyridine) and then add (0.0231 mol, 1.915ml) of (furfuraldehyde)the resulting mixture was refluxed for 5hrs, dried and recrystallized from absolute ethanol.

Preparation of Complex

For the preparation of complexes, a ligand (0.5gm)(L1 , L2 , L3 , L4) in (15ml) ethanol was mixed with a mole of (0.126g , 0.127g , 0.128g , 0.115g) respectively of (Zn)

The mixture was refluxed For 2h, then cooling to room temperature, the Colored complexes got precipitated slowly.

Microbiological Investigations

The culture medium was made by dissolving twenty grams of Muller-Hinton agar in 500 milliliters of distilled water. with steady stirring, following which the medium was put in an autoclave for 1 hour and then allowed to cool to 40°C until hardened. The bacteria were cultivated for 30 minutes using sterile swabs before drilling a hole in the culture medium with a sterile cork drill. The laboratory-prepared solution was put within the pits, and the dishes were placed in the incubator for 24 hours, following which the diameter of the inhibition region was measured.

Results and Discussion

FT-IR Spectral Data

The spectra of the chemical depicted characteristic bands at (3367) cm^{-1} assigned to (OH) and The band at 1732 cm^{-1} is due to β-Lactam carbonyl C=O group for both ligands.[10] At (1627) cm^{-1} assigned to (C=N), Other bands assigned for (C-H) aromatic, (C=C) aromatic (C-O) respectively.[11,12] Table (3) shows the change in (C=N), and carbonyl group (C=O). The bands within 450-482 cm^{-1} are assigned to υ(M—N) stretching vibrations, respectively.[13] These bands confirmed the coordination of the Schiff base to the metal ions.

^{13}C-NMR Spectra of the Schiff base Ligand

The ^{13}CNMR the ligand's spectrum was recorded DMSO-d6 solvent was showed a signal at (40 ppm).The ^{13}CNMR spectrum of ligand (L1,L2,L3,L4) showed the azomethine carbon peak at (161,160,167,163) ppm respectively.[7] The (C=O) carboxylic group peak showed at (170,169,171,171) ppm respectively .The carbonyl group peak showed at (173,178,173,175) ppm.[14]

^{1}H-NMR Spectra of the Schiff Base Ligand

The 1H-NMR spectrum of the ligand ,DMSO-d6 solvent was showed a signal at (1.5ppm) and the first signal at δ=(1.5ppm) due (CH3) groups and signals in the range (4.7 ppm) to the proton of the carbon atom bearing the carboxylic group,The other signals at δ=(7.5ppm), due to the (N=CH) group,and the signals at δ=(11.0ppm) due (OH) groups.[15]

Mass Spectra of Ligand

In the most popular electron-impact (EI) mode, a mass spectrometer bombards molecules in the vapor phase with a high-energy electron beam and records the outcome as a

Table 1: Physical properties of the synthesized compounds

				Solubility				
Compd.	*M.P (° C)*	*Color*	*Yield (%)*	*H_2O*	*C_2H_6O*	*DMSO*	*CH_3OH*	*C_6H_6*
L_1	206-209	Yellow	78%	_	δ	+	δ	δ
L_2	215-220	Brown	90%	_	δ	+	δ	δ
L_3	260-264	Orange	85%	_	δ	+	δ	δ
L_4	212-215	Glossy black	90%	_	δ	+	δ	δ
$[Zn(L_1)_2Cl2]$	215-218	Pale yellow	70%	_	δ	+	δ	δ
$[Zn(L_2)_2Cl_2]$	257-260	Light brown	78%	_	δ	+	δ	δ
$[Zn(L_3)_2Cl_2]$	273-277	Light orange	82%	_	δ	+	δ	δ
$[Zn(L_4)_2Cl_2]$	218-221	Black	88%	_	δ	+	δ	δ

δ partial soluble

Table 2: FT-IR spectra of ligands and complexes

Compound	*C=Ocar*	*C=Olact*	*C=N*	*C=C*
L1	1772	1747	1626	_
L2	1772	1734	1674	1627
L3	1734	1783	1662	1608
L4	1772	1728	1722	1626
$[Zn(L_1)_2C_{12}]B_1$	1772	1753	1647	_
$[Zn(L_2)2C_{12}]B_2$	1772	1716	1683	1635
$[ZnL_3C_{12}]B_3$	1734	1716	1695	1608
$[Zn(L_4)2C_{12}]B_4$	1772		1697	1624

Car=carboxyl , Lact= lactam

spectrum of positive ions segregated by mass/charge (m/z) (12). A peak on the spectrum represents the parent ion centered at (270,268,530,294) fragmentation for ligand (L1,L2,L3,L4) respectively Table (4).

U.V-visible Absorption the Prepared Ligands and their Complexes

The electronic spectra of the prepared ligands (L1,L2,L3,L4) were measured in the range(200-400) nm at room temperature using ethanol and DMSO as a solvent. The spectrum of the first the value (L1,L2,L3,L4) two absorption bands. The first bands belong to the transitions (π→π*),[16] while the second bands refers to the n→π*. The spectrum of the complexes of ligands three absorption bands in the range (200-400) nm. The first and the second bands refers to the π→π* transition, while the third one is related to the transition n→π*, which appears due to the presence of a double bond in addition to the presence of heterogeneous atoms in the compound where they shitted and that confirm the coordination between the metal and the ligand.[17]

Table 3: Show to fragmentation for ligand

L1		*L2*		*L3*		*L4*	
m/z	*Abundance*	*m/z*	*Abundance*	*m/z*	*Abundance*	*m/z*	*Abundance*
41.2	28432	41.2	254592	44.2	264192	44.1	231744
75.1	3260	75.1	971840	75.2	37288	75.1	233216
114.1	1854	114.1	685120	100.1	45456	114.1	155520
137.3	3000	137.3	72824	160.2	32088	160.1	305664
160.1	1625	160.1	140032	201.2	14672	183.2	32008
183.2	618	183.2	131712	236.2	5086	207.1	20456
216.1	617	216.1	94088	313.3	3623	216.1	16728
239.2	280	239.2	13605	423.2	463	243.2	1403
263.1	248	261.2	13697	495.5	371	281.1	4252
270.2	228	268.1	5584	530.9	180	294.9	703

Table 4: Electronic spectra

Compound	*Absorption Band ,λ nm*	*Transfers*
L1	257-349	π-π*, n-π*
L2	273-315	π-π*, n-π*
L3	268-321	π-π*, n-π*
L4	265-311	π-π*, n-π*
$[Zn(L_1)_2Cl_2]$	225-264-312	π-π*, π-π*, n-π*
$[Zn(L_2)_2Cl_2]$	215-268-306	π-π*, π-π*, n-π*
$[Zn(L_3)_2Cl_2]$	217-252-308	π-π*, π-π*, n-π*
$[Zn(L_4)_2Cl_2]$	226-269-309	π-π*, π-π*, n-π*

Table 5: Biological activity for the ligand and complexes

Compound	*Staphylococcus aureus*	*Pseudomonas*
L1	2.8 mm	1.9 mm
L2	2.9 mm	1.8 mm
L3	2.5 mm	2 mm
L4	3.1 mm	1.5 mm
$[Zn(L_1)_2Cl_2]$	2.3 mm	2.1 mm
$[Zn(L_2)_2Cl_2]$	2.1 mm	1.6 mm
$[Zn(L_3)_2Cl_2]$	2.4 mm	1.5 mm
$[Zn(L_4)_2Cl_2]$	2.8 mm	2.6 mm

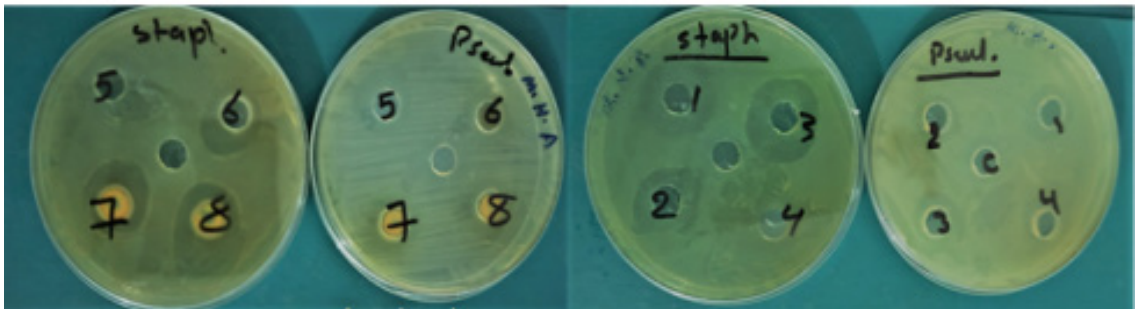

Fig. 1: Biological Activity for The Ligand and Complexes

Biological Activity for The Ligand and Complexes

The inhibitory approach was used to investigate the biological activity of the ligands and their complexes.[18] The biological activity of the ligands and their complexes was investigated using the inhibition technique for different species of bacteria. (Pseudomonas and Staphylococcus aureus) are two kinds of bacteria, When comparing the two types, we note that bacteria ligands and complexes have greater effectiveness against bacteria of the type(Staphylococcus) aureus . Results sgown in table 3 and figure 1; the compounds exhibit inhibition diameter to the types of complexes that exhibit inhibition diameter against bacteria, and the results show that the complexes exhibit greater activity than the ligand under similar conditions. This may be due to the fact that chelation significantly reduces the polarity of the ion, primarily due to partial sharing of its positive charge with the donor groups and possible electron delocalization across the entire chelate ring. Several heterocyclic systems have been investigated for the introduction of pharmaceutically significant compounds. As a result, many drugs contain heterocyclic compounds containing nitrogen.[19]

Conclusions

1. In this study, four types of ligands (L1, L2, L3, and L4) and four complexes of Transition Metal Ion Zn (II) were synthesized in the easy and traditional way with in high yield.
2. These ligands were confirmed by the following assays (FT-IR,^{13}C-NMR,^{1}H-NMR, and Mass Spectra).
3. The mole ratios [M: L] were [1:2], except (L3) the mole ratio [M: L] were [1:1].
4. According to the conductivity values, all complexes are non-electrolytes.
5. The structure of the prepared complexes was supposed to be octahedral.
6. The biological activity of ligands and complexes was studied; ligands and the complexes demonstrated the potential to inhibit against two types of bacteria (Pseudomonas and Staphylococcus aureus), the biological activity of the prepared ligands and complexes against bacteria (Staphylococcus aureus) is more effective than that of bacteria (Pseudomonas).
7. The beta-lactam ring remains unbroken.

References

1. Ashraf MA, Mahmood K, Wajid A, Maah MJ, Yusoff I. Synthesis, Characterization and Biological Activity of Schiff Bases.
2. Enbaraj E, Dhineshkumar E, Jeyashri KR, Logeshwari G, Ramya Devi VJ, Manikandan H, et al. Novel Synthesis of NE, N′E-4,4′-sulfonylbis(N-(substituted-dichlorobenzylidene) anilines derivative their application biological and DFT studies. In: Journal of Physics: Conference Series. IOP Publishing Ltd; 2021.
3. Spichiger-Keller, Ursula E. *Chemical sensors and biosensors for medical and biological applications*. John Wiley & Sons, 2008.
4. K.Y. Lau, A. Mayr, K.K. Cheung, Synthesis, and Biological Activity of Schiff Bases, Inorg. Chem. Acta, 1999 .pp; 285, 223.
5. Mohammed Abd Al-Khaliq Z. Synthesis , characterization and antibacterial activity of new series of sulfamethoxazole derivatives.
6. Farag AA, Migahed MA, Al-Sabagh AM. Adsorption and inhibition behavior of a novel Schiff base on carbon steel corrosion in acid media. Egyptian Journal of Petroleum. 2015 Sep 1;24(3):307–15.
7. Ibrahim MN, Sharif SAI. Synthesis, Characterization and Use of Schiff Bases as Fluorimetric Analytical Reagents (Part II) [Internet]. Vol. 8. Available from: www.e-journals.net
8. Latif MA, Tofaz T, Chaki BM, Tariqul Islam HM, Hossain MS, Kudrat-E-Zahan M. Synthesis, Characterization, and Biological Activity of the Schiff Base and Its Ni(II), Cu(II), and Zn(II) Complexes Derived from 4-(Dimethylamino)benzaldehyde and S-Benzyldithiocarbazate. Russian Journal of General Chemistry. 2019 Jun 1;89(6):1197–201.
9. Chohan Zh, Jaffery Mf. Synthesis, Characterization and Biological Evaluation of Co(Ii), Cu(Ii), Ni(Ii) And Zn(Ii) Complexes With Cephradine. Vol. 7, Metal Based Drugs. 2000.
10. Gupta Radha Raman, Mahendra Kumar, Vandana Gupta, 1998. 'Heterocyclic Chemistry Volume I Principles, Three and Four-Membered Heterocycles'', 1 st ed., Springer, Heidelberg, Berlin.
11. Mitchell Jr, J. Microscopic identification of organic compounds. Analytical Chemistry 1949; 21(4): 448-461.
12. Silverstein, R. M. & Bassler, G. C. 1962. Spectrometric identification of organic compounds. *Journal of Chemical Education,* 39, 546.
13. Charles, A. & Sivaraj, K. 2019. Synthesis, Characterization And Antimicrobial Activity Of Metal Schiff Base Complexes Derived From Pyrrole-2-Carbaldehyde
14. KAREEM, N. G. & SAID, M. H. 2021. Syntheses, and Characterization of Complexes Containing Beta-lactam Group with some Transitional Elements and Study their Biological Activity. *NeuroQuantology,* 19, 72.
15. Pavia, D. L., Lampman, G. M., Kriz, G. S. & Vyvyan, J. A. 2014. *Introduction to spectroscopy*, Cengage learning.
16. V. A. Lopyrev, N. N. Chipanina, L. G. Rozinova G. I. Sarapulova, R. G. Sultangareev, and M. G. V. (1978) 'Synthesis And Absorption Spectra Of 3,5-Diaryl-I,2,4-Triazoles', (12), Pp. 1682–1685.
17. Haddad, R., Yousif, E. and Ahmed, A. (2013) 'Synthesis and characterization of transition metal complexes of 4-Amino-5-pyridyl-4H-1, 2, 4-triazole-3-thiol', Springerplus, 2(1), pp. 1–6.
18. Alias, M, Kassum, H, Shakir, C. Synthesis, physical characterization and biological evaluation of Schiff base M (II) complexes. Journal of the Association of Arab Universities for Basic and Applied Sciences 2014; 15: 28-34.
19. Sahu, N., Sahu, J. K. and Kaushik, A. (2013) 'A Review on "Triazoles": Their Chemistry and Pharmacological Potentials', Current Research in Pharmaceutical Sciences, 03(04), pp. 108–113.