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Synthesis, Anti Bacteral Activity of Macrocyclic Pd (II) Metal Complexes

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ABSTRACT

A new series of macro cyclic Schiff's bases are obtained from condensation of o-phthalaldehyde and 2-amino benzyl alcohol, 2-aminobenzo hydrazine, 1, 3-diamino propane and 2-amino benzyl amine respectively. These ligands were reacted with dibromo ethane cyclization takes place to produced corresponding macro cyclic compounds which were reacted with PdCl2 salt to produced corresponding Pd (II) complexes. The newly synthesized ligands and macro cyclic Pd (II) complexes are characterized by elemental analysis, IR, 1H-NMR, Mass spectra. All these complexes and ligands are examined for their anti-bacterial activities, compared with standard drugs like Streptomycin, Ampicillin and Rifampicin.

KEYWORDS Schiff's bases, Macromolecules, Anti-bacterial activity, Pd (II) salt

INTRODUCTION:

Schiff bases are an important class of ligands in coordination chemistry and find extensive applications in different fields. Schiff bases are derived from aromatic carbonyl compounds and have been widely studied in connection with metalloprotein models and asymmetric catalysis, due to versatility of their steric and electronic properties[1]. Schiff bases and their biologically active complexes have been often used as chelating ligands in the coordination chemistry of transition metals, radiopharmaceuticals for cancer targeting[2], agrochemicals[3] model systems for biological macromolecules[4], catalysts[5] and as dioxygen carriers[6]. Tetra dentate Schiff base ligands have been used as chelating agents, these are playing vital role in coordination chemistry and its metal complexes are great attention for several years[7-10]. These complexes are also used as catalysts for wide range of organic transformations such as C-H bond activation and oxidation reactions[11-15].

In continuation of our ongoing research interest is first we intended to synthesize and examine the spectral characterization of novel Schiff base which are chelating with N, and O atoms and then to treat with Pd (II) salts to generated the corresponding Schiff base metal complexes. Finally, Schiff bases and their complexes were screened for their antibacterial activity.

EXPERIMENTAL

Materials

All the chemicals like, o-phthalaldehyde, 2-amino benzyl alcohol, 1, 3-diamino propane, 2-amino benzohydrazides were purchased from Aldrich, USA. The solvents like ethanol, methanol, DMSO were distilled out and dried up by the standard procedures. The percentage of carbon, hydrogen, nitrogen and Pd metal complexes are determined using a Perkin–Elmer CHN analyzer. Conductance of the Pd (II) complexes was measured on Digisun digital conductivity meter (model DI-909). Infrared spectra in KBr pellets were recorded with a Perkin-Elmer 283 spectrophotometer. ^{1}H NMR spectra were recorded on a Jeol 300 MHz spectrometer in DMSO-d_6. Mass spectra were recorded on CEC-21-110B and Finnegan MAT-1210 mass spectrometers.

Methods

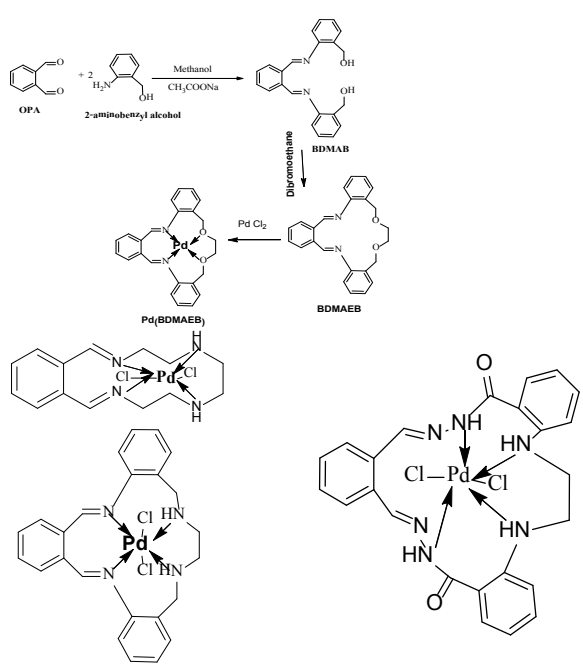
Synthesis of tetra dentate ligands (L1-L4):

A stirred solution of orthophthalaldehyde (0.02 mol) in methanol (25 mL) was added to a solution of amines like 2-amino benzyl alcohol**,** 2-amino benzohydrazide, 1,3-diamino propane and 2-amino benzyl amine (0.04 mol) in methanol (25 mL). Then added an equimolar amount of sodium acetate (0. 04 mol) and refluxed for 3-4 h. The reaction mixture was monitored by TLC, and after the completion of reaction, cooled to room temperature, precipitate formed was filtered, washed with cold methanol, diethyl ether, re-crystallized from ethanol and dried in vacuum to get corresponding Schiff base ligands. These ligands are treated with dibromo ethane (1.2mol) in the presence of anhydrous K2CO3 (3.0 mol) in DMF solvent for 4-5 h. The reaction was monitored by TLC, cooled to room temperature than poured into ice cold water, extracted with chloroform, dried and the solvent was removed under ***vacuo*** to produce the corresponding macro cyclic molecules.

Synthesis of Pd (L1-L4) Cl_2] complexes:

Macro cyclic Schiff base ligands **(L1-L4) (**1.0 mmol) was taken in methanol (20 ml) and the solution was purged with a stream of nitrogen for 10 min. Then a solution of $PdCl_2$ (0.5 mmol) in methanol was added slowly. After being stirred for 4 h at room temperature, the solvent was evaporated under ***vacuo***. Then 10 ml of diethyl ether was added to the residue, after which the crystalline solid was collected by filtration using a fine sintered-glass filter washed with ether, dried and re-crystallized from mixture of chloroform and diethylether.

Sch5eme 1: Synthesis of ligands from OPA:



RESULTS AND DISCUSSION

The present work is synthesized a novel macrocyclics containing Schiff bases derived from condensation of o-phthaladehyde with different compounds such as 2-amino benzyl alcohol, 1,3-diamino propane, 2-aminobenzohydrazide and 2-amino benzyl amine in basic medium to get corresponding ligands like **BDMAEB**, **BDMAEZ**, **BDMAED** and **BDMAEE.** The elemental analysis of these ligands are presented in **Table-1.** The synthesis of Ligands and their metal complexes has shown in **Scheme 1** and **Scheme 2** respectively.

INFRA-RED SPECTRAL STUDIES:

In IR spectra, strong intensity band is appeared in the range of 1665-1639cm^{-1} which is attributed to $\upsilon_{C=N}$ provides a strong evidence for the condensation of OPA with the $-NH_2$ group of amines and amino benzohydrazide. The IR spectra of Schiff base ligands **BDMAEB (L1)** a broad band is not appeared at 3412cm^{-1} because of absence of -OH group. The IR spectra of **BDMAEZ (L2)** and **BDMAEE (L4)** Schiff bases show a broad band in the range of 3448-3259 cm^{-1} corresponding to υ_{NH} stretching vibrations and a band is observed at around 1684 cm^{-1} due to $\upsilon_{C=O}$ stretching vibrations in ligand **BDMAEZ**. Aromatic stretching frequencies are observed for all the ligands in the range of 1442-1405 cm^{-1} and wagging frequencies are observed in the range of 3043-3014 cm^{-1} in IR spectrum. The infrared spectral data of all the ligands are presented in **Table 2**.

^{1}H NMR SPECTRAL DATA:

The newly synthesized Schiff bases were characterized by ^{1}H NMR spectra. In the ^{1}H NMR spectra of all the Schiff bases a singlet is appeared for –CH=N protons in the range of 8.12-8.42δ, suggesting the condensation of OPA with different amines. The spectra of Schiff base ligand **BDMAEZ (L2)** exhibits a broad signal in the range at 7.8-7.9 δ was appeared indicating the presence of -NH-CO proton. In all Schiff base ligands triplets were appeared due to the presence of $-CH_2-CH_2$ protons in the range of 3.42-3.46 δ and multiplets observed in the range of 6.62-7.98 δ have been assigned to the aromatic protons. The individual ^{1}H NMR data of all the Schiff base ligands were mentioned in **Table 3**.

Table 1: Analytical data of Schiff base ligands (L1-L4):

S. No.	Schiff base (L1-L4)	Molecular Formula	Analyses (%)Found (Calculated)		
			C	H	N
1.	BDMAEB	$C_{24}H_{22}N_2O_2$	77.78 (77.81)	5.89 (5.99)	7.49 (7.56)
2.	BDMAEZ	$C_{24}H_{22}N_6O_2$	67.51 (67.59)	5.16 (5.20)	19.67 (19.71)
3.	BDMAED	$C_{14}H_{20}N_4$	68.78 (68.82)	8.19 (8.25)	22.89 (22.93)
4.	BDMAEE	$C_{24}H_{24}N_4$	78.19 (78.23)	6.51 (6.57)	15.18 (15.21)

Table-2: Infrared spectral data of Schiff bases (L1-L4):

S. No.	Schiff base (L1-L4)	Selected IR bands (cm^{-1})		
	$\upsilon_{NH}/\upsilon_{SH^*}$	$\upsilon_{C=N}/\upsilon_{C=O^*}$	Aromatic	
1.	BDMAEB	-	1639	3065 w, 1416
2.	BDMAEZ	3444(NH_2),3259	1642/1687*	3041 w, 1455
3.	BDMAED	3448	1646	3003w, 1422,
4.	BDMAEE	3445	1658	3056w, 1440

Table-3: ^{1}H NMR spectral data of Schiff base ligands (L1-L4):

S. No.	Schiff base (L1-L4)	^{1}H NMR peak position (δ ppm)
1.	BDMAEB	8.30(2H, s, -CH=N), 6.86-7.42 (12H, m, Ar-H), 4.64 (4H, s, $-CH_2$-O-), 3.42 (2H, t, $-CH_2$).3.46 (2H, t, $-CH_2$)
2.	BDMAEZ	8.12 (2H,s, -CH=N), 8.2(2H, s, -NH-CO), 6.64-7.16(12H, m, Ar-H), 3.42 (2H, t, $-CH_2$), 3.44 (2H, t, $-CH_2$)
3.	BDMAED	8.26 (2H,s, -CH=N), 7.26-7.93,(4H,m, Ar-H), 3.58 (4H, t, $-CH_2$-N=), 2.72 (4H,t, $-CH_2$-NH_2), 2.78-2.80 (4H, t, $-CH_2$)
4.	BDMAEE	8.28(2H,s, -CH=N),7.16-7.48 (12H, m, Ar-H), 4.46(4H, s, $-CH_2$), 2.72(4H, t, $-CH_2$)

ANTIBACTERIAL ACTIVITY

In the current examinations, Schiff bases and the corresponding metal complexes were screened for their antibacterial activity against four different bacteria. The active Schiff bases and Schiff base metal complexes were further verified by their MIC by liquid dilution method and compared with existing antibiotics like Streptomycin and Ampicillin but less than the Rifampicin. The anti bacterial activity of Schiff's bases (L1-L4) and their Pd metal complexes were shown in **Table-4 & 5.**

Antibacterial activity of Schiff bases (L1-L4)

Table 4: Zones of inhibition of Schiff-bases (L1-L4) against four different bacteria:

S. No.	Schiff-base (L1-L4)	Conc. (µg/ml)	Zone of inhibition (mm)			
			Bacillus subtilis	Staphylococcus aureus	Escherichia coli	Klebsiella pneumonia
1.	BDMAEB	1000	13	12	-	-
2.	BDMAEZ	1000	41	43	41	36
3.	BDMAED	1000	28	34	36	41
4.	BDMAEE	1000	35	38	40	37

Based on the results, all the examined compounds were classified into four types according to their activity against bacteria (zone of inhibition) and the number of bacteria.

Class-I: Active on all four strains,
Class-II: Active on three strains,
Class-III: Active on two strains and
Class-IV: Active for one strain.

According to initial investigation of Schiff base ligands **(L1-L4)**, it is found that three ligands viz. **BDMAEZ (L2)**, **BDMAED (L3)** and **BDMAEE(L4)** were shown activity against all four dissimilar bacteria and are selected as class-I. Another ligand namely **BDMAEB (L1)** has been exhibit activity against two strains of bacteria and selected as class-III. In conclusion, it is found that only three ligands belong to class-I namely **BDMAEZ (L2)**, **BDMAED (L3)** and **BDMAEE (L4)** were shown good activity according to the extent of zone of inhibition.

Antibacterial activity of Schiff-base Pd(II) metal complexes:

Table 5: Zones of inhibition of Schiff-base Pd(II) metal complexes

Comp. No.	Schiff-base Pd(II) complexes (1000 µg/ml)	Zone of inhibition (mm)			
		B. subtilis	S. aureus	E. coli	K. pneumonia
1	[Pd(BDMAEB)]Cl_2	17	13	11	10
2.	[Pd(BDMAEZ)]Cl_2	47	46	45	39
3.	[Pd(BDMAED)]Cl_2	32	36	41	41
4	[Pd(BDMAEE)]Cl_2	38	40	42	40
Drug-1	Streptomycin	11	11	8	5
Drug-2	Ampicillin	12	12	9	6
Drug-3	Rifampicin	52	48	49	44

According to initial investigation, it is found that these Schiff base Pd (II) metal complexes shown activity against four different strains of bacteria in the order of: 2>4>3>1 for ***Bacillus subtilis***, 2>4>3>1 for ***Staphylococcus aureus***, 2>4>3>1 for ***Escherichia coli*** and 3>4>2>1 for ***Klebsiella pneumonia***.

CONCLUSION:

In the present study the coordination chemistry of macrocyclic binuclear Schiff base complexes, derived from the reaction of O-Phthalaldehyde with 2-aminobenzyl alcohol, 2-aminobenzo hydrazine, 1,3-diamino propane and 2-amino benzyl amine respectively is discussed. The macrocyclic binuclear Schiff base complexes of Pd(II)chloride metal salt have been synthesized and characterized by spectral and analytical data. The metal complexes enhanced a significant antibacterial activity compared with standard antibacterial agents. Keeping in view the rising problems of antibacterial resistance, these chemical compounds may be used for formulating novel chemotherapeutic agents and further investigation will be necessary to identify the active principle.

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