INTERNATIONAL JOURNAL OF PHARMACEUTICAL, CHEMICAL AND BIOLOGICAL SCIENCES

Available online at www.ijpcbs.com

Research Article

AN INNOVATIVE SYNTHESIS OF NEW MANNICH BASE, ITS METAL COMPLEXES AND THEIR ANTIBACTERIAL STUDIES

Babu. K and Pitchai. P*

Department of Chemistry, Rajah Serfoji Govt Arts College (Auto), Thanjavur, Tamil Nadu, India.

Department of Chemistry, Government Arts College (Auto), Kumbakonam, Tamil Nadu, India.

ABSTRACT

We reported synthesis of new mannich base and its transition metal complexes in green manner. The structure of synthesized compounds confirmed with help of UV, IR, ^{1}HNMR, ^{13}CNMR spectroscopic techniques and their analytical data. The antibacterial activity of ligand and complexes examined against selective gram positive and gram negative bacteria where metal complexes showed good activity than the free ligand was observed.

Keywords: Mannich base, disc diffusion method, antibacterial activity, green manner.

1. INTRODUTION

Mannich base is a three-component condensation product of active hydrogen containing compound, aldehyde and secondary amine. The formation of mannich base product depends on the nucleophilicity of substrate and pH of the reaction medium.[1] The electrochemical behavior and catalytic activity of various mannich bases were reported in literature.[2-4] The metal complexes of mannich bases have been studied extensively in recent years due to the selectivity and sensitivity of the ligands towards various metal ions.[5-9] The organic chelating agents containing amide moiety as a functional group have strong ability to form metal complexes and exhibit a variety of biological activities such as antibacterial, antifungal, anti T.B activity, anti HIV activity, antiviral, antiulcer and anti- hypertensive[10-16]. The number of studies have been done in the various mannich base complexes formed by the condensation reaction of secondary amines with different aldehyde and amides[17-20]. In the present work, we reported synthesis, characterization, antibacterial studies of new mannich base and its transition metal complexes.

2. MATERIAL AND METHODS

2.1 General

All the chemicals used were reagent grade and used without further purification. The molar conductance was measured in DMSO solvents at room temperature and magnetic moment was measured on a Gouy balance by using $CuSO_4$ as standard. The UV-Vis spectra were recorded in DMSO solvent on Shmazdu UV mini-1240 spectrophotometer and IR spectra were recorded on Perkin-Elmer FT-IR spectrophotometer using KBR pellet. The antibacterial activity of synthesized ligand and its metal complexes were studied by disc diffusion method.

2.2 Synthesis of ligand

The aqueous mixture of salicylaldehyde (2 equivalent) and thioacetamide (2 equivalent) at room temperature was neutralized with liquid ammonia. To the above mixture, piperazine (1 equivalent) was added slowly with constant stirring at room temperature. This reaction mixture was stirred 15 minutes, the yellow color solid product formed was filtered and washed with water. The progress of the reaction was monitored by TLC using hexane and ethyl acetate 7:3 solvents. Yield: 70%, Mp: 100-105^oC.

2.3 Synthesis of complexes

Hot ethanolic solution of ligand (1 equivalent) was slowly mixed with hot ethanolic solution of the metal chloride (2 equivalent) under reflux condition with constant stirring. The mixture was refluxed for 1-2 hours and after that it was cooled under ice cold condition, the colored solid complex separated out in each case. It was filtered, washed with 50% ethanol and finally dried.

3. RESULTS AND DISCUSSION

3.1 Molar conductance and Magnetic moment

The complexes prepared are various colored, powder like, air stable, soluble in dimethylformamide (DMF) and dimethylsulfoxide (DMSO). The analytical data and some physical properties of the metal complexes were listed in table 1 and synthetic scheme of complex is given in scheme 1. The molar conductivities values showed that all the complexes are non-electrolytes nature with Λm = 30-45 $\Omega^{-1}cm^2mol^{-1}$in 10^{-3} in DMSO solutions at room temperature. The μeff (1.6) value of the Cu(II) complex represented octahedral geometry with one unpaired electron. The observed μeff (2.57) value of the Ni (II) complex confirmed octahedral geometry with two unpaired electron and Zn (II) complex is diamagnetic as expected with zero unpaired electron.

3.2 UV-Visible and IR-Spectroscopy

The Cu (II) complex under the present study exhibit a broad band in the region 27200 cm^{-1}.due to transition between $^2Eg \rightarrow {}^2Tg$ which indicated octahedral geometry. The Ni (II) complex showed broad signals at 26334 and 28420 cm^{-1} which is assigned to $^3A_{2g} \rightarrow {}^3T_{1g}$ and $^3A_{2g} \rightarrow {}^3T_{2g}$ transition respectively which further confirmed the octahedral geometry of the complex. The spectra of Zn (II) complex exhibited band at 25100cm^{-1} assigned to L → M charge transfer and not for d-d transition.

The infrared bands of ligand observed at 3202, 1145 and 757cm^{-1} have been assigned to **ν**N-H, C-N-C of piperazine group and C=S group respectively. In IR spectra of all the complexes, the **ν**N-H band appeared its specific region indicated that the secondary nitrogen was not involved in coordination. A band due to $\nu C{-}N{-}C$ and C=S in all the complexes shifted towards lower frequency clearly indicated that nitrogen, sulphur involved coordination with metal ion. The above said coordination site was further confirmed by appearance of band in between 1649-1633cm^{-1} in all the complexes due to existence of C=N group during complexation (see table-2). The new bands at 530-526 cm^{-1} and 435-427 cm^{-1}in the spectra of the metal complexes were assigned to νM−N and νM−S stretching vibrations. The presence of coordinated water molecule in Cu (II) and NI(II) complex is determined by appearance of bands in between 3514-3405 cm^{-1} and 857-898 cm^{-1}assignable to the OH stretching and bending mode of vibration. The presence of phenolic OH group in all the complexes in between 3432-3340cm^{-1} indicated that which was not involved in coordination.

3.3 ^{1}H-NMR and ^{13}C-NMR spectra

The ^{1}H-NMR spectrum of the ligand showed the following resonance signals: Signals due to aromatic protons appear in between 6.77-7.65 δppm as many multipletes. The N-H proton chemical shift occurred at 8.74-8.73 δppm as weak doublet and CH methine proton appeared as doublet at 5.17-5.5.24 δppm. The piperazine protons signal occur at 2.76 δppm as singlet and methyl protons appeared as singlet at 2.50 δppm. The signal at 10.25 δppm was due to to the phenolic –OH group present in molecule. The ^{13}C-NMR spectrum of the ligand showed the following signal at 170.13(C=S), 157.16(C-OH), 129.80, 126.96, 122.13, 119.85, 117.61, 116.89 (6Ar-Carbons), 70.31(CH), 48.95($N-CH_2$), 24.04(CH_3) well supported for our expected structure.

4 Antimicrobial activity

The antibacterial activities of ligand (L) and its metal complexes were studied by usual agar disc diffusion method. The bacterial species used in the screening were staphylococcus aureus, staphylococcus epidermidis (gram positive) Escherichia coli and Pseudomonas aeruginosa (gram negative). The presence of clear zones around the wells indicated that the compound is active and diameter of the zone inhibition was deducted in millimeters by using zone diameter. The results of bactericidal screening showed that the chelating tends to make the ligand act as more powerful and potent bactericidal agents, thus killing more of the bacteria than the free ligand. The detailed data of all the synthesized compounds against gram positive and gram negative bacteria given in **table- 3.**

Scheme - 1: Synthesis of the ligand and its complexes

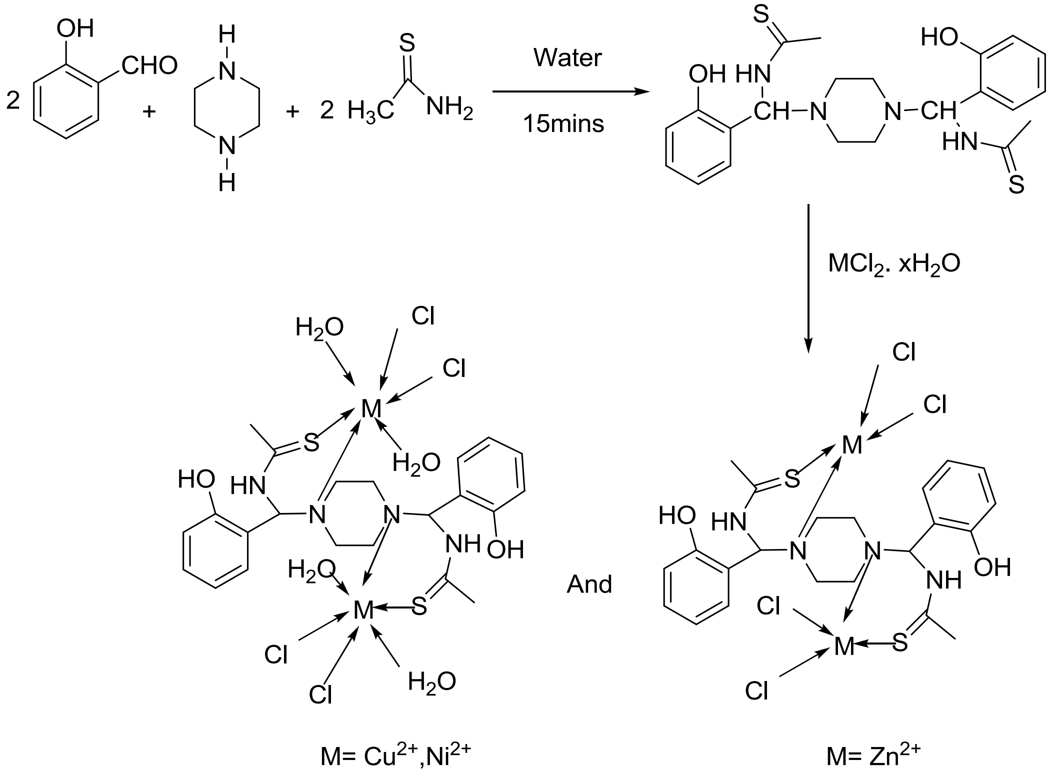

Table 1: Physical data of ligand and its complexes

Compounds	Yield(%)	Mp(°C)	Colour	*μeff* (BM)	M. conductance ($\Omega^{-1}cm^2mol^{-1}$in 10^{-3})
BMB-L	70	170-172	Light yellow	----	-----
BMB-Cu	50	240-242	Brown	1.6	45
BMB-Ni	56	198-200	green	2.5	32
BMB-Zn	40	260-262	white	Diamagnetic	30

Table 2: IR-Spectral data of ligand and its complexes

Compounds	Vibration frequency of various functional groups (in cm^{-1})					
	-OH	-NH	C=S	CNC	M-N	M-S
BMB-L	3402	3200	757	1145	-------	------
BMB-Cu	3432	3345	701	1121	526	427
BMB-Ni	3450	3340	726	1222	530	435
BMB-Zn	3447	3310	714	1119	560	452

Table 3: Antibacterial activity

S. No.	Bacteria	Standard Antibiotic Disk(streptomycin)	Zone of inhibition mm in diameter (10μg/disc)			
			BMB - L	BMB - Cu	BMB - Ni	BMB - Zn
1	Staphylococcus aureus	18	08	18	11	14
2	*Staphylococcus epidermidis*	17	10	16	12	24
3	*Escherichia coli*	24	08	18	16	15
4	*Pseudomonas aeruginosa*	25	08	15	15	11

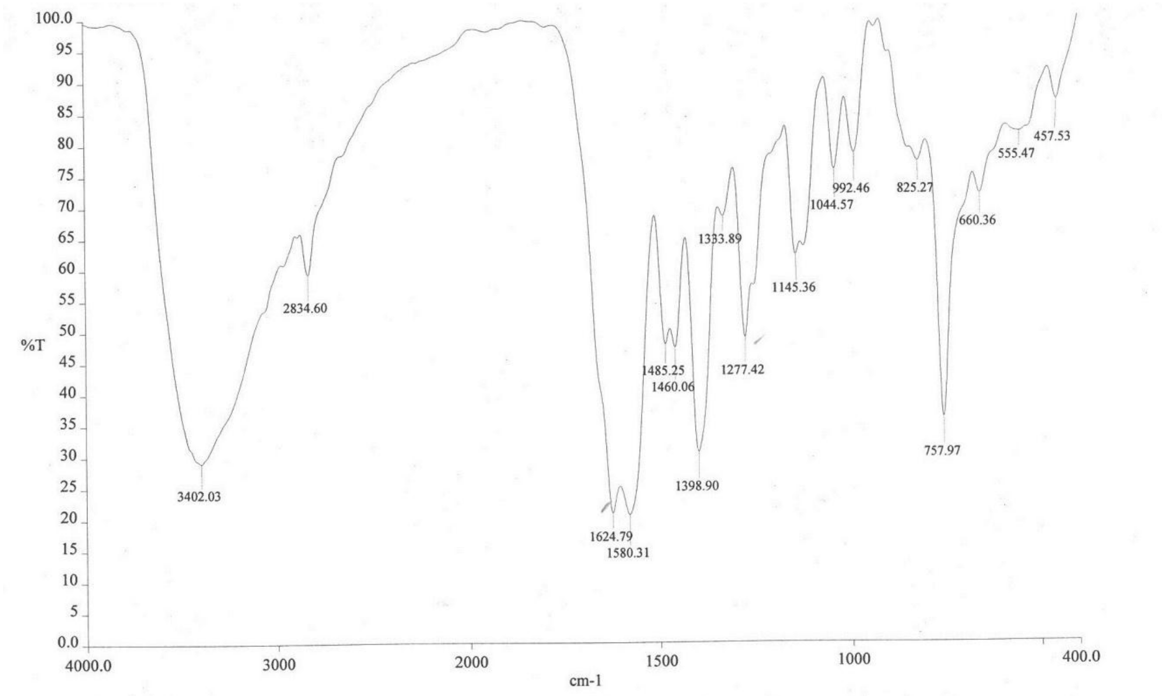

Fig. 1: FT- IR Spectra of ligand using KBr pellets

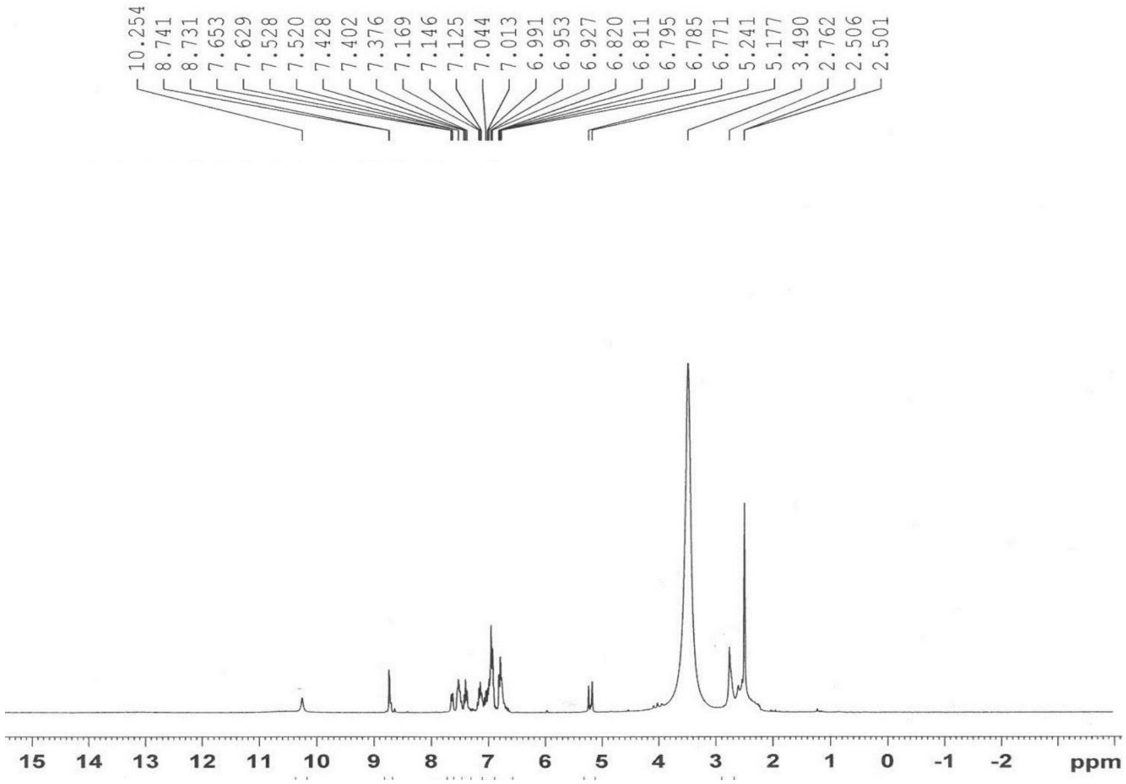

Fig. 2: 1H-NMR Spectra of ligand in DMSO-D6 solvent

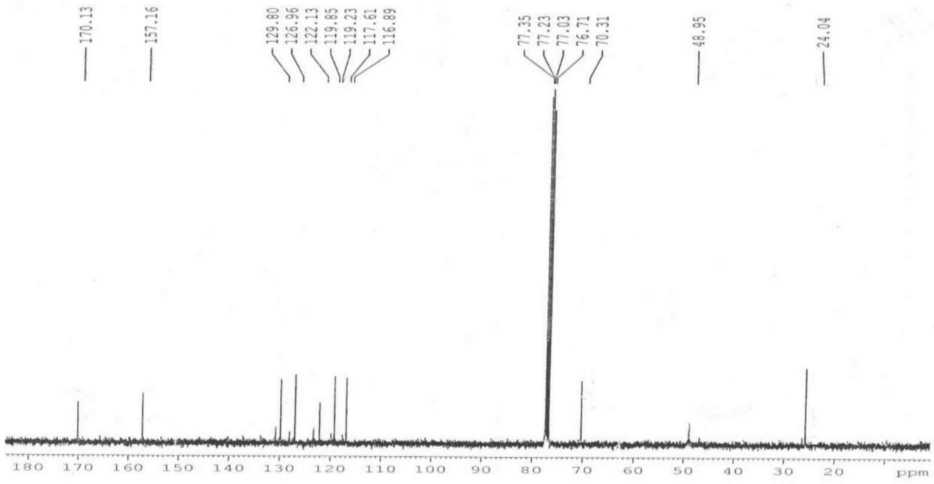

Fig. 3: 13C-NMR spectra of ligand in DMSO-D6 solvent

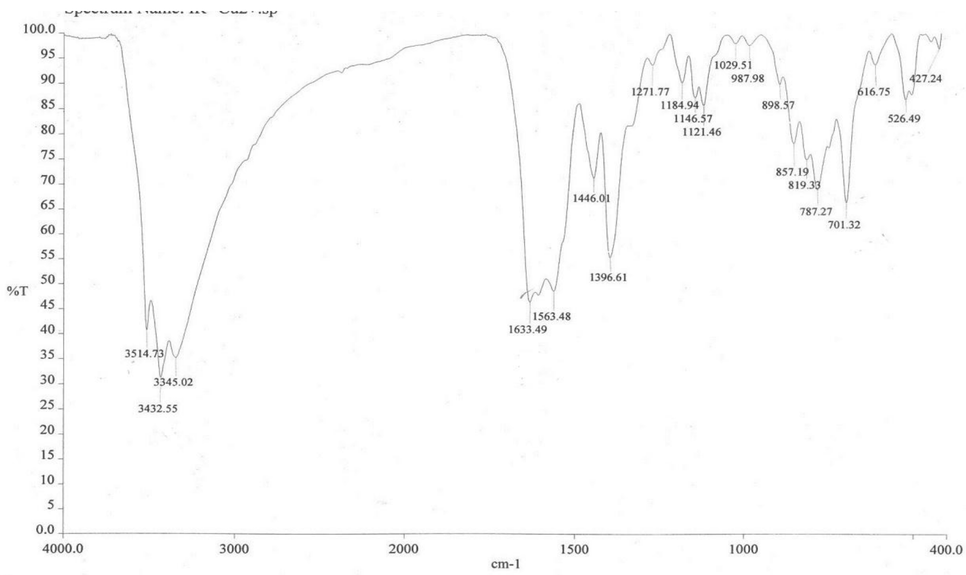

Fig. 4: FT-IR Spectra of Cu(II) complex using KBr pellets

5. CONCLUSION

It may be concluded that the ligand behaves as bidentate chelating agent and the spectroscopic techniques were well supported to our proposed structure. The metal complexes showed good microbial activity than the ligand was observed

6. ACKNOWLEDGEMENTS

We sincerely thank to Department of chemistry, Rajah Serfoji Government College for providing lab facilities.

REFERENCES

1. Cummings TF and Shelton JR. Mannich reaction mechanism. J Org Chem. 1960;25:419.
2. Subrahmanian Supriya and Aravamudhan Raghavan. Syntheses, characterization and catalytic activity of Mannich aminomethylation products of bis(glycinato)metal(II) complexes. Polyhedron. 2007;26(13):3388.
3. Michael K. Ainooson, Ilia A. Guzei and Lara C. Spencer. Pyrazolylimine iron and

cobalt, and pyrazolylamine nickel complexes: Synthesis and evaluation of nickel complexes as ethylene oligomerization catalysts. Polyhedron. 2013;53:295.

4. Amanda P. Neves, Kelly CB. Maia, Maria D. Vargas and Lorenzo C. Dinuclear copper(II) complexes of a novel 3-(aminomethyl) naphthoquinone Mannich base: Synthesis, structural, magnetic and electrochemical studies. Polyhedron. 2010;29(15):2884.
5. Mery Napitupulu, Monica Rossignoli and Geoffrey A. Lawrance. Cyclic polyamines *via* a molybdenum(0) templated Mannich-type reaction. Transition Metal Chemistry. 2007;32(6):816-821.
6. Cleare MJ. Transition metal complexes in cancer chemotherapy. Coord Chem. 1974;12:349.
7. Singh B, Singh RN and Aggarwal RC. Magnetic and spectral studies on N-(thiophene-2-carboxamido) salicyl aldimine complexes of some bivalent 3d metal ion. Polyhedron. 1985;4:401.
8. Sarika Anand. Mixed ligand complexes of Fe^{III} containing pseudohalides, nitrosyl and some mannich bases. Transition Metal Chemistry. 2007;32(6):816-821.
9. Rajesh H and Bahekar. Synthesis and Biological Evaluation of Indomethacine Conjugates with Salicylamide and It's Mannich Bases. Indian Drugs. 1998;35(10):648–651.
10. Yogeshwary SD. Synthesized Pyrazinamide Mannich Bases and its Anti T.B.Properties. Pharm Med Chem Res. Lab, BITS Pilani. 2006.
11. Pandeya SN and Shriram D. Synthesis, Antibacterial, Antifungal and Anti-HIV Activity of Schiff and Mannich Bases derived from Isatin Derivatives. Eur J Pharm Sci. 1999;9:25–31.
12. Joshi S and Khosla D. In vitro Study of Some Medicinally Important Mannich Bases derived from Anti-Tubercular Agent. Bio-Org and Med Chem. 2004;12:571 – 576.
13. Chodosh LA, Fire A, Samuels M and Sharp PA. 5, 6-Dichloro-1-beta-Dribofuranosyl benzimidazole Inhibits transcription elongation by RNA polymerase II in-vitro. J Biol Chem. 1989;264(4):2250- 2257.
14. Welage L and Berardi R. Evaluation of omeprazole, lansoprazole, pantoprazole, and rabeprazole in the treatment of acidrelated diseases. J Am Pharm Assoc. 2000;40(1):52-62.
15. Billups SJ and Carter BL. Mibefradil. A new class of calcium-channel antagonists. The Annals of Pharmacotherapy. 1998;32(6):659-671.
16. Mohamad Jaber Al-Jeboori, Ahlam Jamil Abdul-Ghani and Ahmed Jasim Al-Karawi. Synthesis and structural studies of new Mannich base ligands and their metal complexes. Transition metal chemistry, 2008;33(7):925-930.
17. Ram C. Maurya, Deen D. Mishra, Surendra K. Jaiswal and Sudipta Mukherjee. Synthesis and characterization of some novel cyanonitrosyl complexes of chromium(I) with Mannich bases, aromatic aldehyde oximes and syn-phenyl-2-pyridylketoxime. Transition metal chemistry. 1992;17(5):381-383.
18. Sathya D, Senthil Kumaran J and Jayachandramani N. Transition Metal Complexes of N-(1-Piperidinosalicylyl) acetamide and their Biological Activity. Research journal of pharmaceutical, biological and chemical sciences. 2012;3(2):905.
19. Sabastiyan A and Yosuva Suvaikin M. Synthesis, characterization and antimicrobial activity of 2-(dimethylaminomethyl) isoindoline-1,3-dione and its cobalt(II) and nickel(II) complexes. Advances in Applied Science Research. 2012;3(1):45-50.
20. Mohamad Jaber Al-Jeboori and Ahlam Jamil Abdul-Ghani. Synthesis and structural studies of new Mannich base ligands and their metal complexes. Transition Metal Chemistry. 2008;33(7):25-930.