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Der Pharma Chemica, 2011, 3 (4):486-490
(<http://derpharmachemica.com/archive.html>)



ISSN 0975-413X
CODEN (USA): PCHHAX

Pharmaceutically fine synthesis and their study of antimicrobial activity of metal complexes with some schiff's bases

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ABSTRACT

In this newly approached method a novel series of transition metal complexes were synthesized by reactions with various Schiff base compounds such as 2,2-{ethane-1,2-diylbis [nitriolo (E) methylidene]} Diphenol, 2,2-{propane-1,3-diylbis [nitriolo (E) methylidene]} Diphenol, 2,2-{1,3-phenylenebis [nitriolo(E) methylidene]} Diphenol, 6,6'-((1E,1E)-(propane-1,3-diylbis (azanylylidene)) bis(methanylylidene))bis(2,4-di-tertbutylphenol), 2-[(E)-(pyridin-2-ylimino) methyl] phenol, 2, 4-di-tert-butyl-6-[(E)-(pyridin-2-ylimino) methyl] phenol. Schiff base compounds were treated with transition metal ions of Ni^{2+} , Co^{+2} , Cr^{+2} , Fe^{+3} and Cd^{2+} . For current work different molar ratios of metals are used. These metal complexes were synthesized under maintained temperature at reflux condition within few hours. Such transition metal complexes of Schiff base compounds were characterized as IR, 1H -NMR, C, H, N and O and their antibacterial activity of metal complexes were studied. Simply these reactions shows bright path to new class of medicinally important compounds.

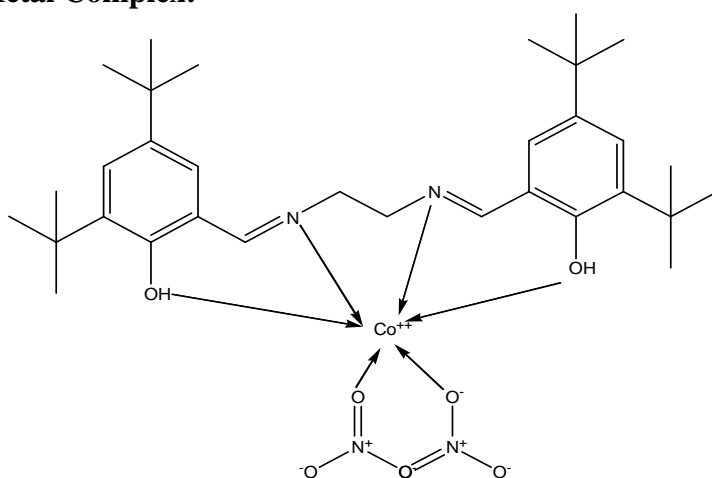
Keywords: Schiff's base compounds, Transition metal ions, Ethanol, Ammonia etc.

INTRODUCTION

According to previous literature survey there is large number of research papers appeared in last few decades regarding complexes of transition and non transition metals^{1, 2, 3, 4,5}. amino heterocycles containing two or more potential donor centers play an important role in the study of competitive reactivity of ambidentate ligands system⁶. Transition metal complexes containing pyrimidine ligands ² are commonly found in biological media and play important roles in processes such as catalysis of drug interaction with biomolecules⁷. N-Amino pyridine Schiff base chemistry is less extensive and our laboratory has been exploring this chemistry^{8, 9}. Schiff base complexes derived from 4-hydroxy salicylaldehyde have strong anticancer activity e.g., against Ehrlich as cites carcinoma (EAC) ¹⁰. The Schiff bases derived from 3-amino-5-methyl is oxazole and methoxy salicylaldehyde and naphthaldehyde were reported earlier and it was found

that antimicrobial activity of metal complexes show increased activity compared to corresponding Schiff bases¹¹. Highly potential synthesis and characterization of new Schiff's bases derived from different Diamine and aromatic aldehyde compounds by using dichloromethane as a solvent at reflux condition¹⁵. Catalytic study of P₂O₅/SiO₂ with Schiff base compounds [21]. Co, Ni and Cu complexes have been prepared by reacting metalchloride with 4-chlorobenzaldehyde oxime, 4-methylbenzaldehyde oxime, 4-nitrobenzaldehyde oxime, 4-chlorobenzaldehyde semicarbazone, 4 methylbenzaldehydesemicarbazone, 4-nitrobenzaldehyde semicarbazone, 4-chlorobenzaldehyde phenylhydrazone, 4-methylbenzaldehyde phenyl hydrazone and 4-nitrobenzaldehyde phenylhydrazone and their antibacterial activity have been studied and compared with their ligands against *E. coli* which gave significant results of activity [22]. Synthesis of various oximes, semicarbazones, phenyl hydrazones and their complexes with different transition metals are reported in the literature [23] and found to be active as antibacterial [23], antitubercular [24],

Possible Structure of Metal Complex:



RESULTS AND DISCUSSION

In case of Schiff base compounds i.e. ligands are soluble in very common organic solvents; but its rare earth or transition metal complexes are generally soluble in DMF, DMSO and water etc. after keen observation the elemental analytical data of the complexes reveals that the compounds have a metal ligands anion stiochiometry of 1:1 ratio. The yields, melting points, time of reaction, C, H, N, O presented in Table: 1. the ligand L₅ was obtained from 2:1 molar ratio with substituted aldehyde as shown in Table: 1, but other all ligands such as L₁, L₂, L₃, L₄, L₅, and L₆ were obtained by using 1:1 molar ratio with substituted amines and aldehyde respectively. For the first time here we are kindly interested to report a new series of rare earth and transition metal complexes. The metal complexes of Schiff base compound [M₁], [M₂], [M₃], [M₄], [M₅], [M₆] were obtained by using 1:1 molar ratio with metal ions respectively at reflux condition by using absolute 99% pure ethanol within few hours as shown in table :1.

Excellent yield of all metal complex products were obtained due to addition of (10%) methanolic ammonia solution at different pH values which are not mentioned in this article because these pH values found in common range compared to other complexes. All structures of ligands and their metal complexes were predicted on Chemdraw 12.0 software. Such type of metal complexes have found their antimicrobial activity in a reference range of streptomycin as shown in Table: 2 in a excellent result.

Table -1: Physical and Analytical data of all Schiff base and its complex compounds

Compounds	Yield %	M.P.(^o C)	Time in min	Elemental Analysis (found) %			
				C	H	N	O
[M ₁]	80	148-151	2 hrs	37.81	2.96	10.86	25.03
[M ₂]	86	118-121	2.5 hrs	43.08	3.11	11.82	26.94
[M ₃]	89	240-244	2 hrs	47.82	2.99	10.81	25.02
[M ₄]	83	238-241	2.06 hrs	52.01	6.06	9.03	23.81
[M ₅]	81	166-171	2.30 hrs	32.09	2.29	15.08	35.02
[M ₆]	88	186-188	1.18 hrs	48.07	5.03	11.01	22.17

Table-2: Antimicrobial studies of some metal complexes

Name of the culture	Zone of inhibition (cm)				
	Streptomycin (control)	M ₁	M ₂	M ₃	M ₄
<i>S. aureus</i>	3.0	2.0	-	1.6	1.2
<i>B. subtilis</i>	2.0	2.5 Static	1.7 Cidal	-	1.4 static
<i>E. coli</i>	2.2	3.0 oligodynamic	1.5 oligodynamic	1.7 Oligodynamic	1.6 oligodynamic
<i>S. typhi</i>	2.8	2.1 oligodynamic	2.0 oliegodynamic	1.7 Oligodynamic	1.8 oligodynamic

As Microbial studies of the four of the drugs carried out using streptomycin as control for inhibition. The results are shown in the table with their activities. M1 compound is exhibiting the good activity against B subtilis and E coli as compare to streptomycin. While the other are compounds are having slightly less microbial activity with compared to streptomycin.

General Procedure for Preparation of Schiff's Base Compounds:

In a typical reaction, add a mixture of aldehyde (2 mol), Diamine (1 mol) was taken in 100 ml, round bottom flask containing 10-15 ml, of Dichloromethane. Dissolve complete reaction mixture by continuous stirring then add 2-4 porcelain pieces in round flask to avoid bumping. Reflux the reaction mixture for appropriate time. The progress of reaction was monitored on TLC (PE-EtOAc 7:3) portion; after completion of reaction, filtered off the solid product and washes it with cold dichloromethane. The crude was further purified by recrystallisation in ethanol and the desired pure Schiff's base compounds were obtained in 83-93 % yield. Schiff's base compounds were identified and confirmed on the basis of spectroscopic data¹⁵.

Preparation of Metal Complexes:

0.01moles of ligands in slight excess was taken in round bottomed flask containing 15 ml anhydrous methanol and refluxed for few minutes so as to dissolve ligands completely. A solution of 0.01 mole of metal ion in 15 ml of anhydrous methanol was then added drop wise to the solution of ligands. The contents were refluxed for two hours and then cooled to observe the occurrence of precipitation which rarely found in the cold reaction mixture, a (10 %) metabolic solution of ammonia was added drop wise to increase the pH till the metal complex precipitates out completely. The complexes of different metals were precipitated at different pH range. This pH range was definite for a given complex and found to be characteristic of that complex. The precipitate was digested for one hour. Any subsequent change in the pH if observed was readjusted and contents digested again for one hour. The solid metal complex separated out was then filtered in hot condition. It was washed with portions of hot methanol, followed by

petroleum ether (40-60 °C) and dried in vacuum desiccators over anhydrous granular calcium chloride¹⁴.

General Experimental:

All chemical and solvents used for synthesis were purchased from 'A' grade Reagents (make Merck German, Aldrich) made. The metal salts Cd (NO₃)₂.4H₂O, Ni (NO₃)₂.6H₂O, Co (NO₃)₂.6H₂O, Cr (NO₃)₃.9H₂O and Fe (NO₃)₃.6H₂O were obtained from E-Merck. All solvents were dried and purified before use. Elemental analyses were performed on SHIMADZU elemental analyzer. The IR spectra were recorded by using KBr pellets on JASCO FT/IR Spectrophotometer.

Spectroscopic Data for Transition Metal Complexes:

[M₁]:Cd(II)-2, 2'-{ethane-1, 2-diylbis [nitrilo (*E*) methylylidene]} diphenol Colour-Dark Yellow, M.P.148-150 °C, FTIR (KBr pellets): 569, 652, 711, 841, 985, 1066, 1131, 1204, 1288, 1533, 1761, 1912, 2034, 2303, 2414, 2537, 2886, 2977, 3026, 3659, and 3669. ¹H NMR (200.13 MHz CDCl₃):4.12(s, 4H), 7.06 (m,4H), 7.31 (m,4H), 8.40 (s, 2H), 13.34 (bs, 2H) Anal. Calcd. For C₁₆H₁₆N₄O₈: C, 38.07; H, 3.20; N, 11.10; Found C, 37.81; H, 2.96; N,10.86;

[M₂]:Co(II)-2, 2'-{propane-1, 3-diylbis [nitrilo (*E*) methylylidene]} diphenol Colour-Brown Colour, FTIR (KBr pellets): 545, 636, 688, 746, 833, 916, 1053, 1122, 1174, 1219, 1274, 1348, 1581, 1637, 1973, 2011, 3066, and 3282. ¹H NMR (200.13 MHz CDCl₃):d 2.24(dd, 2H), 3.92(t, 4H), 7.06(m,4H), 7.41(m,4H), 8.47(s, 2H), 13.53(bs,2H). Anal. Calcd. For C₁₇H₁₈N₄O₈: C, 43.91; H, 3.90; N, 12.05;. Found C, 38.14; H, 5.35; N, 19.55.

[M₃]:Ni(II)-2,2'-{1,3-phenylenebis[nitrilo(*E*)methylylidene]}diphenol FTIR (KBr pellets): 434, 655, 711, 1138, 1349, 1526, 1620, 1776, 2314, 2890, 3046, 3308, and 3553. ¹H NMR (200.13 MHz CDCl₃): 7.04-7.48(m,12H),8.75(s,2H), 13.21(s,2H). Anal. Calcd. For C₂₀H₁₆N₄O₈: C, 48.11; H, 3.23; N, 11.22;. Found C, 57.55; H, 3.41; N, 9.95;

[M₄]:Cr(II)-6,6'-((1*E*,1'*E*)-(propane-1,3-iybis(azanylylidene))bis(methanylylidene))bis(2,4-di-tert-butylphenol) FTIR (KBr pellets): 650, 751, 829, 992, 1033, 1092, 1215, 1236, 1339, 1399, 1456, 1488, 1569, 1587, 1646, 1912, 2588, 3042, and 3326. ¹H NMR (200.13 MHz CDCl₃):1.38(s, 18H), 1.53(s,18H), 4.01(s,2H), 6.16(s,2H), 7.47(s,2H), 8.48(s,2H), 13.77(bs,2H). Anal. Calcd. For C₃₂H₄₈N₅O₁₁: C, 52.60; H, 6.62; N, 9.58; Found C, 59.70; H, 8.51; N, 7.12.

[M₅]: Fe (III) - 2-[(*E*)-(pyridin-2-ylimino) methyl] phenol FTIR (KBr pellets): 561, 615, 655, 746, 850, 893, 952, 985, 1024, 1074, 1112, 1172, 1228, 1263, 1300, 1402, 1462, 1504, 1683, 2144, 2789, 2881, 2926, 3117, and 3489. ¹H NMR (200.13 MHz CDCl₃): 7.10(m,2H), 7.30-7.62(m,4H), 7.87(dd,1H), 8.59(d,1H), 9.54(s, 1H), 13.56(s, 1H) Anal. Calcd. For C₁₂H₁₀N₅O₁₀: C, 22.75; H, 2.29; N, 15.91. Found C, 22.41; H, 2.81; N, 16.77.

[M₆]: Ni (II)- 2, 4-di-tert-butyl-6-[(*E*)-(pyridin-2-ylimino) methyl] phenol FTIR (KBr pellets): 435, 474, 576, 640, 671, 738, 815, 920, 962, 997, 1020, 1138, 1273, 1301, 1342, 1390, 1429, 1572, 1618, 1707, 1953, 2854, 2920, 2955,3134, 3298, 3338, 3450. ¹H NMR (200.13 MHz CDCl₃):4.02(s, 4H), 6.94(m,4H), 7.38(m,4H), 8.42 (s, 2H), 13.36 (bs, 2H) Anal. Calcd. For C₂₀H₂₆N₄O₇: C, 48.71; H, 5.31; N, 11.36. Found C, 48.86; H, 5.46; N, 11.76.

CONCLUSION

A novel series of transition metal complexes has been developed using Schiff's base compounds derived from different substituted Diamine and aldehyde compounds at reflux condition within few hours and found to be antimicrobially active. Such type of metal complexes possesses an inherent and novel path to a series of medicinally and scientifically importance. Simply these type of excellent compounds shows bright path towards pharmaceutical as well as chemical sciences. In short these compounds give high to excellent yields of compounds within few hours and easy work up procedure.

Acknowledgement

My sincere thanks and gratitude are due to Dr. M.A. Shukoor [Vice Principal and (Head Cenate Member Dr.babasaheb Ambedkar Marathwada University Aurangabad)] & Dr. J.D. Shaikh Lecturer Zoology Department Maulana Azad College Aurangabad for their precious support and cooperation to my research work.

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