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Synthesis, Characterization of β-amino Carbonyl Complexes via Mannich Reaction and Study of Their Antibacterial Activity

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ABSTRACT

The present report is concerned with the Synthesis of β amino carbonyl compounds via Mannich reaction. Mannich reaction of aromatic amine, aromatic aldehyde and aromatic ketone finally yield β amino carbonyl compound. The substituted group effect of aromatic amines and ketones were also discussed. Sulphamic acid used as catalyst. This β-amino ketone was react with metal acetate of Zn (II), Cu (II) form square planer complexes. Ligands and metal complexes obtained were well characterized on the basis of spectral measurement and elemental analysis. New metal complexes were tested for antibacterial activity against different bacteria.

Keywords: Mannich reaction, β-amino carbonyl compounds, Antibacterial activity, Aromatic aldehyde, Zn complex, Cu complex

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INTRODUCTION

Mannich reaction is one of the most important carban-carban bond formation reactions in organic synthesis and it is atom economy reaction. Catalytic three component Mannich reaction is important reaction to form β-amino carbonyl compounds [1,2]. β-amino carbonyl compounds are very useful compound used as building blocks in the synthesis of pharmaceuticals and natural products [3]. β-amino carbonyl derivatives are best ligand for formation of metal complexes due to present active functional group of 1.4 position, carbonyl group and NH group. Many important properties of co-ordination compounds embrace the donor ligand nature. Formation of metal complexes plays an important role in the growth of their biological activity. Polar atoms increase the water solubility of metal complexes and presence of aromatic group enhance lipid solubility due to this metal complexes easily penetrate in bacterial cell and prohibit their growth. The preferable route is the use of one pot three component strategies that allows for wide range of structural variation [4]. Many biological active compounds used as drugs possess modified pharmacological potential when administered in the form of metal based compound it is prove to be more beneficial against several diseases. At the last new metal complexes are formed. These metal complexes were tested for antibacterial activity against bacteria *Escherichia coli*, B-subtitles.

MATERIAL AND METHODS

All chemical used wear of reagent grade. Melting point was determined on Gallen kamp melting point apparatus. ^{1}H NMR Spectra were recorded with Brucker AM-300 MHZ spectrometer using tetra methyl silane as internal standard [5,6].

Magnetic susceptibility measurement for complexes was obtained at room temperature using magnetic susceptibility balance model. ^{1}H Chemical Shift Were reported in ppm level and Multiplicities are given as s (singlet), bs (broad Singlet), d (doublet), t (triplet), q (quartet) or m (multiplet) The IR Spectra of the compounds were recorded as kbr disks Mass spectra recorded on shimadzu FT-IR 408 mass spectrometer as KBr discs [7-11]. Mass spectra recorded on shimadzu MS spectrometer. Elemental micro analysis was carried using elemental analyzer. Reaction is monitored by thin layer chromatography. Compounds were purified by column chromatography using silica gel.

General procedure for the synthesis of β-amino carbonyl ligand

Benzaldehyde (0.43 mmol), Aniline (0.43 mmol), Acetophenone (0.43 mmol) are added to sulfamic acid (0.04 mmol) in alcohol (7

ml). The mixture was stirred at room Temperature for 7 h. Then add saturated aqueous $NaHCO_3$. After which it is extracted with ethyl acetate then add Na_2S0_4 for drying then solvent is removing and crystallize from ethanol. Solid obtained are dried for 8 h.

3-(4-mathoxyphenylamino)-1.3 diphenylpropan-1-one 1b

Colour-white solid, Melting point-258-261, IR-1600(C=C), 3370(N-H), ^{1}HNMR-δ ppm 3.38(d J=6 Hz 1H), 6.50(d J=7.9 Hz,2H), 6.65(m,1H), 7.06-7.4(m.1H), 7.25 (dJ=6Hz,1H), 7.2-7.4(m,2H), 6.3(d J=8 Hz, 2H), 7.04(J=8Hz,2H), 7.8 (dJ=7.8 Hz 2H), Mass Spectra M/Z=324 (M+)

Diphenyl-3-(phenylamino) propane1-one la

White solid, Melting Point 216-217, IR 1675 cm^{-1} (C=0), 1600 cm^{-1} (C=C), 3885 cm^{-1}(NH) ^{1}HNMR – δ 3-45 (dJ=6 Hz 1H), 3.51(d,J=6.2 Hz 1H), 5.02 (m,1H) 6.54 (d.J=7 Hz 2H), 6.6 (m,.H), 7.0-7.3 (m,1H), 7.24 (d.J=6.2 Hz 1H), 7.2-7.3 (m,2H), 7.3-7.5 (m,5H), 7.88 (d.J=7.7 Hz 2H), Mass spectra M/Z=301.

General procedure for the synthesis of metal complexes

Ethanolic solution of ligand amino ketone was added in the ethanolic solution of ($CuCl_2.6H_20$) (0.20 mmol) then 1 ml Triethylamine was added and resultant mixture was stirred at room temperature and then reflux for 4 h. During this period precipitation was completed and product is collected by filtration then wash with ethanol and dried under vacuum for 4 h [12,13]. Same procedure was used for synthesis of metal complexes with ($ZnCl_2.6H_2O$)

Characterization of ligand and metal complexes

A. [Cu ($C_{25}H_{24}NO_5$)] a_2

M.P. 240, exact mass-481.1, Mol. Wt.-482.01, Anal. Cal. For [Cu($C_{25}H_{24}NO_5$)] 62.30 ;H,5.02 ;Cu,13.18; N,2.91; O,16.60, 2.2.

B. [Zn ($C_{25}H_{24}NO_5$)] a_1

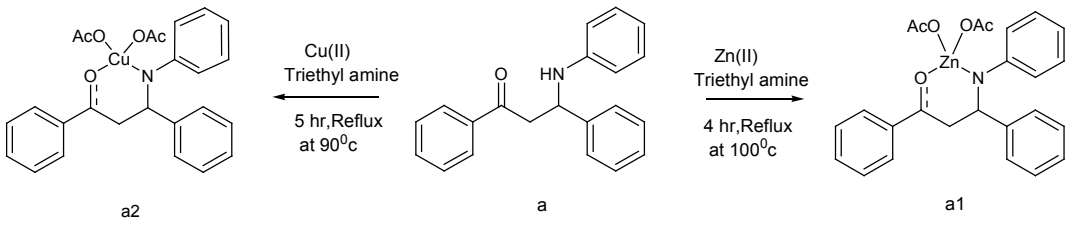
M.P. 235, exact mass-482.09, Mol. Wt.-483.85, C,62.06; Anal. Cal. For [Zn ($C_{25}H_{24}NO_5$)] H, 5.00; N, 2.89; O, 16.53; Zn, 13.51 (Scheme 1).

C. [Cu ($C_{26}H_{26}NO_6$)] b_1

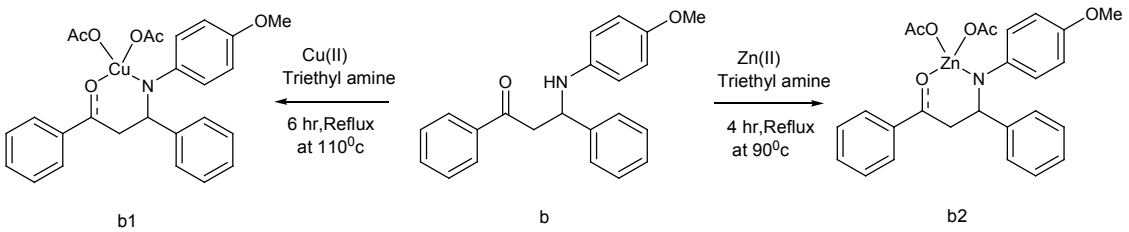
M.P. 252, exact mass-511.11, Mol. Wt.-512.03, C, 60.99; Anal. Cal. For [Cu ($C_{26}H_{26}NO_6$)] H, 5.12; Cu, 12.41; N, 2.74; O, 18.75.

D. [Zn ($C_{26}H_{26}NO_6$)] b_2

M.P. 247, exact mass-512.11, Mol. Wt; 513.88, Anal. Cal. For [Zn ($C_{26}H_{26}NO_6$)] C, 60.77; H, 5.10; N, 2.73; O, 18.68; Zn, 12.72 (Scheme 2).



Scheme 1: [Zn (C25 H24 NO5)] a1; [Cu (C25 H24 NO5)] a2



Scheme 2: [Cu (C26 H26 NO6)] b1; [Zn (C26 H26 NO6)] b2

ANTIMICROBIAL ACTIVITY

New metal complex are tested for antibacterial activity against three pathogenic bacteria E coil and B. cereus show good activity. Antimicrobial activity is evaluated by using agar disc diffusion method. The mean diameter of inhibition zone developed was calculated for each concentration. Complexes dissolved in DMSO then 20 ml agar media was poured in each petriplates. After solidification 0.1 ml of test bacteria spread over medium. Whatmann no.1 filter paper disc treated with DMSO served as Standard drug.

RESULT AND DISCUSSIONS

One pot three component condensation reaction of aromatic aldehyde, aromatic ketone with aromatic amine to provide β-amino carbonyl compound would be an ideal mannich type reaction and can be considered as one of the convenient carbon-carbon bond formation reaction. Melting point of ligand and elemental analysis confirms the stoichiometries. Ligand 1 show broad band at 3350cm^{-1} corresponding to frequency of amine group. Ligand spectra shows (C=O) group frequency 1670 cm^{-1} which is shift to lower values in all complexes. Band at 580 cm^{-1} attributed to M-N and 430 cm^{-1} attributed to M-O bonds respectively in Table 1.

Table 1: Optimization of time and yield of products

Comp. No.	Time(h)	Yield (%)
1a	7	72
1b	6	73
2	5	68
3	5	71
4	5	67
5	6	70

Biological activity

Ligands are biological active. The values indicate that metal complexes had a higher antibacterial activity than the free ligand. Such increased of the metal complexes can be explained on the basis of chelation theory [14,15]. The lipid membrane that surround the cell favors the passage of only lipid soluble material due to which liposolubility is an important factor controlling the antimicrobial activity. On chelation the polarity of metal ion is reduced to a great extent due to overlap of the ligand orbital and partial sharing of the positive charge of metal ion with donor groups. It increases the delocalization of electron over cheated ring and enhances the lipophilicity of the complex. This increased lipophilicity enhances the penetration of the complex in to lipid membranes and block the metal binding site on the enzymes of the microorganism in Table 2.

Table 2: Antibacterial and antifungal activity

Entry	*Bacillus substils*	*Escherichia coli*	*Bacillus cerus*
	[a]**ZI**	[a]**ZI**	[a]**ZI**
1a	11	n.t	12
1b	12	14	14
2	**20**	**17**	**18**
3	16	16	18
4	**17**	**18**	**19**
5	19	20	23
Strept	16.3	16.5	[c]n.t
Amoxi.	16.9	17.2	17.3

[a]Zone of inhibition in mm, [c]n.t: Not Tested

CONCLUSION

β-amino carbonyl compound is synthesized by using mannich reaction. By using β-amino carbonyl compound and metals like Cu (II) Zn (II) there is formation of metal complexes. Bidentate ligands show higher antimicrobial efficiency towards complexes with monodentate ligands.

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