



Solid State Synthesis, Characterization and Anti-Microbial Studies of some Transition Metal Complexes of a Schiff Base Ligand Derived from Benzophenone and Glycine

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ABSTRACT

Schiff base was synthesized by mixing benzophenone and glycine mechanochemically. Its corresponding complexes of Cu, Co and Mn were synthesized by grinding metal (II) carbonates. The synthesized compound were characterized by elemental analysis, infrared spectroscopy, melting/decomposition temperature determination and conductivity measurements. The infrared spectroscopic analysis of the ligand shows a peak at 1624.12cm^{-1} confirm the presence of azomethane while the shift to 1600cm^{-1} , 1590cm^{-1} , 1590cm^{-1} in Mn, Cu, Co complexes respectively confirmed bond formation from azo-group to metal. The melting point temperature of the ligand at 174.20°C show that it is stable at low temperature while the decomposition temperature of Mn, Cu, Co complexes at 200°C , 230°C , 217.12°C shows that they are stable. Conductivity measurement shows that the complexes were found to be non-electrolytic as compared with the theoretical values. The ligand and its respective complexes showed antimicrobial activities against some bacteria and fungi at high concentrations ($1000\text{ }\mu\text{g}/\text{disc}$ and $500\text{ }\mu\text{g}/\text{disc}$) respectively while some showed no activity at all concentrations. However, Co complex shows significant activity against all the species at low concentration ($250\text{ }\mu/\text{disc}$).

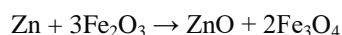
Keywords: Anti-microbial activities, Benzophenone, Glycine, Cu(II), Co(II), Mn(II), Solid State Synthesis

INTRODUCTION

Avoiding organic solvents during the reactions in organic synthesis leads to a clean, efficient and economical technology (green chemistry). Safety is largely increased, synthesis is considerably simplified as well as cost is reduced. Due to all these advantages, there is an increasing interest in the use of environmentally benign reagents and procedures. The absence of solvents coupled with the high yields and short reaction time make the procedure of this type of synthesis very attractive for the synthesis of coordination compounds (Kidwai, 2001). Mechanochemistry is a branch of chemistry which is concerned with chemical and physicochemical transformations of substances in all states of aggregation produced by the effect of mechanical energy (Kaupp, 2009).

Synthesis of control release fertilizer through physical process such as dispersion of ordinary fertilizer in to the matrix or encapsulating ordinary fertilizer in which nutrient release is slow down by diffusion. Intercalation of urea in to kaolin structure by mechanochemical process through ball milling and compared against the aqueous method. Synthesis of KMnPO_4 and NH_4MgPO_4 compounds by mechanochemical process, incorporation of nitrate ion in to Mg-Al- NO_3 type layered hydroxide structure using mechanochemical process (Ehab *et al.*, 2018).

The structural and magnetic properties of ZnO- Fe_3O_4 nanocomposites produced by the solid-state reaction (Scheme 1):



Scheme 1: Synthesis of ZnO

Upon annealing of Zn/ $\alpha\text{-Fe}_2\text{O}_3$ films under vacuum at a temperature of 450°C have been studied. Ferrimagnetic Fe_3O_4 clusters with an average grain size of 40 nm and a magnetization of $\sim 430\text{ emu}/\text{cm}^3$ at room temperature, which are surrounded by a ZnO layer with a large contact surface, have been synthesized (Byko *et al.*, 2015). Organic synthesis: the solid–solid synthesis of the uniform crystalline monohydrochloride of *o*-phenylenediamine. It is obtained by stoichiometric milling of *o*-phenylenediamine with its dihydrochloride. The latter is obtained from *o*-phenylenediamine and gaseous HCl. The charge transfer (ct) complex of tetracyanoquinodimethane (TCNQ) and the tetracene with the disulfide bridges is obtained by stoichiometric cogrinding. Solid phthalic anhydride or the naphthalene dianhydride and solid *m*-aminobenzoic acid easily form colored cocrystals by cogrinding at room temperature. Carboxylic salt hydrates can be obtained in the solid state by stoichiometric

comilling of carboxylic acids and metal carbonates (Gerd, 2016).

Solid-state anaerobic digestion (SS-AD): is commonly used to treat feed stocks with high solid content such as municipal solid waste and lignocellulosic biomass. Compared to liquid state anaerobic digestion (LS-AD), SS-AD has multiple advantages including high organic loading, minimal digestate generated, and low energy requirement for heating. However, the main disadvantages limiting the efficiency of SS-AD are long solid retention time, incomplete mixing, and an accumulation of inhibitors. For a successful and efficient SS-AD, it is important to control operation parameters such as nutrient levels, C/N ratio, feedstock-to-inoculum ratio, pH, temperature, and mixing. Biogas production in SS-AD performance can be enhanced by feedstock pre-treatment, co-digestion, and supplement of additives such as biochar (Haoqin and Zhiyou 2019).

Pharmaceuticals: mechanochemical reaction in synthesis of pharmaceuticals cocrystals are define as chemical reaction induced by the direct absorption of mechanical energy, such as synthesis of metal organic frame work (MOF), organic light emitting diode (OLED). Mechanochemical process have significant over solvent base method as it takes couple of hours or even minute. Neat grinding is the easiest method in mechanochemistry which involve grinding crystal of the component in a mortar or ball mill or vibrating mill. Example includes formation of two polymorphs of ethenzamide-saccharin cocrystals via ball milling which cannot be obtained via traditional method, formation caffeine: glutaric acid cocrystals polymorph using liquid assisted grinding (LAG) (Macie *et al.*, 2019).

Intermetallic compounds: Two different mechanical alloying procedures for producing mechanically alloyed Fe-Sn powders were explored. In the first, mixtures of as-received Fe and Sn powders were mechanically alloyed. In the second, the as-received Fe powder was pre-milled first and the as-received Sn powder was then added and mechanically alloyed. Under the same liquid phase sintering conditions, the sintered materials produced via the first mechanical alloying procedure showed that the FeSn₂ content increased with increasing sintering time and left small traces

of unreacted Fe and Sn materials. In the sintered materials produced via the second mechanical alloying procedure, only the FeSn₂ phase was observed for all sintering times. The two-step process using the second mechanical alloying procedure performed better; it synthesized more of the FeSO₂ intermetallic compound (Nattaya *et al.*, 2017).

Schiff bases and their first-row transition metal complexes such as Co (II), Ni (II), Cu (II), etc., were reported to exhibit fungicidal, bactericidal, antiviral and anti-tuberculosis activity (Ortiz *et al.*, 2000). For many years it has been believed a trace of Cu (II) destroys the microbe, however, recent mechanisms become activated oxygen in the surface of metal Cu kills the microbe because Cu(II) activity is weak.

Drugs based on metal complexes are of increasing interest to medicinal chemists. The anti-tumour activity of platinum-based drugs is well known, but other metals such as gold, ruthenium, titanium and vanadium also show promise in this area. Among several modes of action, binding of metals to DNA is one of the most important. Metal complexes interact with many different sites of nucleic acids, and can bind the canonical DNA structure or lead to non-canonical forms, such as triplexes, quadruplexes, junctions, etc. In general, the favoured sites are the negatively charged phosphate groups and electron-rich N and O atoms. Perhaps the most studied transition metal drug is cisplatin, a widely used antitumor drug, which attacks the DNA as its main target, attacking both guanine and adenine. Platination leads to large structural rearrangements in DNA, ultimately resulting in cell death through apoptosis, necrosis or both. Among other transition metals V, Ti, Ru, Au, Rh, Ir, Cu and Co are considered potentially active against tumours, though DNA may not be the critical target for all such metals. Thus, transition metals represent a source of possible new drugs for treating cancer or other diseases. Several studies of metals other than platinum have also been reported (Arturo *et al.*, 2005).

This study was aimed at synthesizing Schiff base derived from benzophenone and glycine and their corresponding first row transition metal complexes (Co (II), Mn (II), Cu (II)).

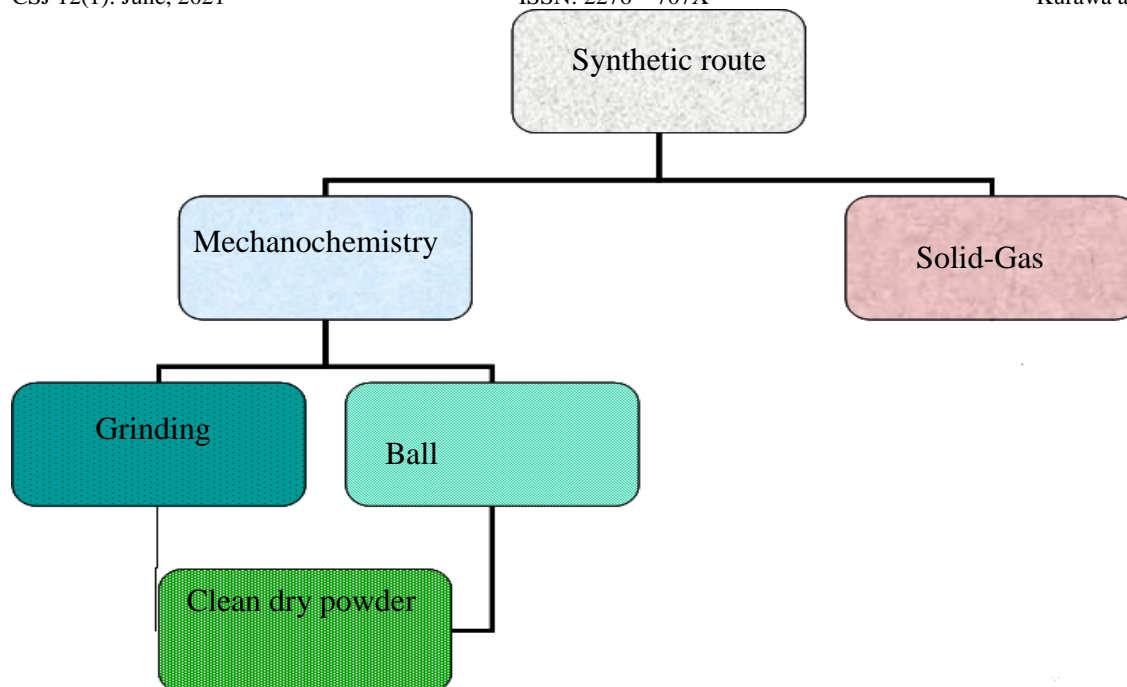


Figure 1: Solid state synthetic routes

MATERIALS AND METHODS

Materials

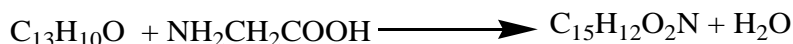
The materials used were pestle and motor, Fourier Transform Infrared Spectrophotometer (FTIR-8400S), elemental analyser (Flash 2000 organic, University of Leeds), Jenway conductivity meter (model 4000), decomposition temperature (WRS-IB microprocessor melting apparatus), UV-visible (Jenway 6305 spectrophotometer) and all the chemical used are of analytical grade, the

metals are obtained from their corresponding carbonate.

Methods

(i) Synthesis of Ligand

Benzophenone(0.02mol) and glycine (0.02mol) were ground in agate mortar for 5minutes, it becomes moist and which resulted in the formation of benzophenone-glycine oxime ligand as a white colour (Scheme 2) which was later dried in *vacuo* (Kidwai, 2001).

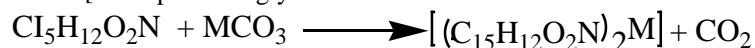


Scheme 2: Synthesis of Benzophenone-glycine oxime Ligand

Synthesis of complexes

Metal carbonates (Mn, Co and Cu) (0.01mol) were grinded with the ligand(0.02mol) which resulted in the formation of a black coloured complex (Scheme 3) of bis[benzophenone-glycine oxime]manganese(II), light purple coloured complex of bis[benzophenone-glycine

oxime]Cobalt(II), a light ash coloured complex of bis[benzophenone-glycine oxime]Copper(II). The complexes obtained were purified by recrystallization in ethanol and then dried in *vacuo* (Kidwai, 2001). The block diagram for the synthesis is shown in Figure 1.



Scheme 3: General Procedure of Complexes Synthesis

Antimicrobial Activities

The complexes were dissolved separately in DMSO to have three different concentrations (50 µg, 500µg and 1000µg) per disc. They were placed on the surface of the culture and incubated at 37°C for 24hours. Then, *in vitro* antibacterial activity of these complexes was carried out by bio assay filter

paper disc diffusion method. The diameter of zone of inhibition produced by the complexes was compared with the standard (Cheesbrough, 2000 and Mukhtar., 2009). The bacteria used were *Escherichia Coli* and *Staphylococcus aureus*

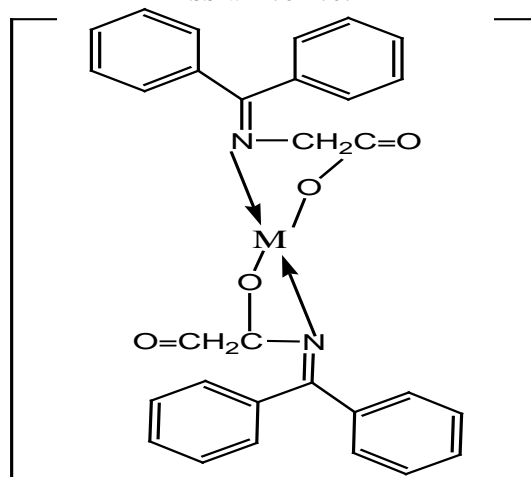


Figure 2: Propose structure of benzophenone complexes

RESULTS AND DISCUSSION

The interaction of glycine with benzophenone formed Schiff base. The complexes were found to be coloured due to charge transfer.

The infra-red spectral result of the ligand benzophenone-glycine-oxime (Table 1) shows a band at 1624.12cm^{-1} which is associated to $\nu(\text{C}=\text{N})$ stretching. The complexes of benzophenone-glycine-oxime with Manganese, Cobalt and Copper shows a band at 45.31cm^{-1} , 435.93cm^{-1} and 486.08cm^{-1} which associated with $\nu(\text{M}-\text{O})$

respectively, 512.12cm^{-1} , 521.76cm^{-1} and 525.76cm^{-1} which associated with $\nu(\text{M}-\text{N})$ respectively.

Comparing the bands in the ligand to that of the metal complexes shows that there is a shift in complexes to lower or higher frequencies which is an indication of complexation between the ligand and the metal ions, also in the complexes new band appear due to $\nu(\text{M}-\text{O})$ and $\nu(\text{M}-\text{N})$ Which confirm complexation which are absent in ligand. The wavelengths are compared with Reusch (1999).

TABLE 1: IR Spectral Data of the Metal (II) Complexes

FITR Value/ Samples	$\nu(\text{M}-\text{N})\text{ cm}^{-1}$	$\nu(\text{M}-\text{O})\text{ cm}^{-1}$	$\nu(\text{C}=\text{N})\text{ cm}^{-1}$
$[(\text{C}_{15}\text{H}_{12}\text{O}_2\text{N})_2\text{Mn}]$	512.12	450.31	1600
$[(\text{C}_{15}\text{H}_{12}\text{O}_2\text{N})_2\text{Cu}]$	521.76	435.93	1590
$[(\text{C}_{15}\text{H}_{12}\text{O}_2\text{N})_2\text{Co}]$	525.76	486.08	1590
Ligand			1624.12

Keys: M = Metal ν = Wave number;

The interaction of glycine and benzophenone resulted in the formation of benzophenone-glycine-oxime ligand which is white in colour. the ligand benzophenone-glycine-oxime melted with a melting point temperature of 174.2°C .

The interaction of benzophenone-glycine-oxime with respective divalent metal salts yield coloured complexes, the colour of the complexes is due to electronic transition from lower to higher energy level. Manganese, Cobalt and Copper complexes are black, light purple and

light ash with decomposition temperature of 200°C , 217.1°C and 230°C respectively, the high decomposition temperature of the complexes as compared to the ligand may be due the coordination between the central metal ion and the ligand. Molar conductance measurement of the complexes in DMSO (10^{-1}M) solution were also determined which lies in the range of $29.0 - 60.6\ \Omega^{-1}\text{cm}^2\ \text{mol}^{-1}$. The lower values indicate that they are non-electrolyte according to Sekhon *et al.*, 2010 (Table 2).

Table 2: Decomposition Temperature/Melting Point Temperature and Molar Conductivity

Complexes	Decomposition/Melting point Temp. (°C)	Molar Conductivity ($\Omega^{-1} \text{cm}^2 \text{mol}^{-1}$)
$[(\text{C}_{15}\text{H}_{12}\text{O}_2\text{N})_2\text{Mn}]$	200	30.0
$[(\text{C}_{15}\text{H}_{12}\text{O}_2\text{N})_2\text{Cu}]$	230	29.0
$[(\text{C}_{15}\text{H}_{12}\text{O}_2\text{N})_2\text{Co}]$	217.12	30.7
Ligand	174.2	

The elemental analysis result revealed that the percentage of nitrogen, carbon and hydrogen in benzophenone-glycine-oxime are found to be 6.5 2%, 76.00%, 6.5 2%, 5.00% respectively while the calculated percentage was found to be 5.90%, 75.30%, 5.48% respectively.

The elemental analysis result revealed that the percentage of nitrogen, carbon and hydrogen in benzophenone-glycine-oxime complex of manganese are found to be 5.13%, 60.32% and 4.60% respectively, while the calculated percentage are found to be 4.78%, 61.45% and 4.13% in respect of nitrogen, carbon and hydrogen, Cobalt complex 4.00%, 59.87% and 3.99% respectively, while the calculated percentage are found to be 4.71%, 60.62% and 4.07% in respect of nitrogen, carbon and hydrogen, Copper complex are found to 4.98%, 59.00% and 4.65% respectively, while the calculated are found to be 4.64%, 59.69% and

4.01% in respect of nitrogen, carbon and hydrogen. elemental analysis conducted on both the ligand and its complexes confirmed the metal to ligand ratio in the complexes to be 1:2

The solubility of benzophenone-glycine-oxime (ligand) and its corresponding metal complexes was also determined in different solvents, the ligand is slightly soluble in ethanol, methanol, acetone, diethyl ether, n-hexane, chloroform, DMSO but insoluble in water. The complexes are slightly soluble in ethanol, methanol, acetone, diethyl ether, n-hexane, chloroform, DMSO but insoluble in water with the exception of Manganese complex which is soluble in DMSO and Copper complex which is insoluble in diethyl ether. The relevance of solubility is to determine the suitable solvent that would be used to carry out other analysis such anti-microbial, conductivity measurement, UV-visible.

TABLE 1: Anti-Bacterial Activity, Anti-fungal Inhibition Zones

Complexes	Concentrations ($\mu\text{g}/\text{disk}$)	<i>E. coli</i> (mm)	<i>S. aureus</i> (mm)	<i>C. albicans</i> (mm)	<i>A. flavus</i> (mm)
$[(\text{C}_{15}\text{H}_{12}\text{O}_2\text{N})_2\text{Mn}]$	250	0	0	12	0
	500	0	0	16	0
	1000	0	7	18	0
$[(\text{C}_{15}\text{H}_{12}\text{O}_2\text{N})_2\text{Cu}]$	250	0	7	10	0
	500	0	7	10	0
	1000	0	7	14	0
$[(\text{C}_{15}\text{H}_{12}\text{O}_2\text{N})_2\text{Co}]$	250	0	0	11	8
	500	0	0	12	8
	1000	0	0	12	10
Ligand	250	0	0	8	0
	500	0	0	10	0
	1000	0	0	11	0
CONTROL (Gentemecyn 18 $\mu\text{g}/\text{disk}$)		40	35		
CONTROL (Apron plus $\mu\text{g}/\text{disk}$)				38	20

Key: *E. coli* = Escherichia Coli, *S. aureus* = *Staphylococcus aureus*, *A. flavus* = *Aspergillus flavus*
C. albicans = *Candida Albicans*

The antibacterial and antifungal screening test for the ligands and their metal (II) complexes were also determined. The inhibition zone (mm) was measured for all sample treated, some shows

little or no activity as compare with Zahid *et al.*, 2000. Results are shown in table 3 above.

CONCLUSION

Schiff base was successfully synthesized via mechanochemical process using benzophenone and glycine and their respective complexes were also synthesized. The Schiff base was found to coordinate to the central metal atom through the nitrogen of the azomethane and the deprotonated oxygen of the amino acid. The elemental analysis result suggests the metal to ligand ratio to be (M: L) 1:2. The antimicrobial result showed that all the complexes are active against *C. albicans* that all the complexes are inactive against *E. coli*. Manganese and copper, complexes show significant activity against *S. Aureus*, while cobalt complex showed activity against *A. flavus*.

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