Research article Available online www.ijsrr.org ISSN: 2279–0543

International Journal of Scientific Research and Reviews

Synthesis, Characterization and Antimicrobial Activity of 2,4 Dihydroxy Acetophenone Semicarbazone and its Cu (Ii) Metal Complex

Sonawane Ratnamala P.*

* The Institute of Science, Mumbai-32. India
Email: *ratnasonawane@yahoo.in*

ABSTRACT:

The synthesis of 2,4 dihydroxyaceto phenonesemicarbazone with Cu(II) metal complex was achieved. 2,4dihydroxyacetophenone is synthesized by resorcinol with glacial acetic acid. This further treated with semicarbazide hydrochloride to form its semicarbazone. Cu(II) metal complex was prepared by dissolving equimolar quantities of metal salt and schiff base ligand in ethanol. All the target compounds were characterized by M.P, TLC, UV-visible and IR spectral data and tested for antimicrobial activity in sterile saline by Agar well diffusion method against *M. luteus, B. subtilis, S. aureus, E. coli, P. aeruginosa*bacteria . All the synthesized compounds have shown good to moderate antimicrobial activity

KEYWARDS: Semicarbazone, metal complex, antimicrobial, Schiff base, IR spectroscopy.

***Corresponding author**

Ratnamala P. Sonawane

Associate Professor,

The Institute of Science, Mumbai-32. India

Email: ratnasonawane@yahoo.in, *Mob.:* 9821846311

INTRODUCTION :

With the development of new strains of bacteria resistant to many currently available antibiotic treatments, there is increasing interest in the discovery of new antibacterial agents. Semicarbazone is a priviledged system with multiple therapeutic applications. Hydroxyacetophenones were used as starting material for the synthesis of chalcones[1] flavones[2] and Schiff bases[3,4]etc. Schiff bases of hydroxy aldehydes and ketones were widely used in co-ordination chemistry for the preparation of metal complexes[5,6]. Schiff bases and their co-ordination compounds have been gained importance now-a-days as they are useful in biochemical, anti-cancer, anti-inflammatory[7], and antipyretic[8],among others. Some of them have been used as complexing agent[9,10]and powerful corrosion inhibitors[11]. A Schiff base of hydroxyacteophenone and its complexes has a variety of applications in biological, clinical, analytical and pharmacological areas[12,13]. Earlier work has shown that some drugs showed increased activity when administered as metal chelates rather than as organic compounds[14,15,16]and that the co-ordinating possibility of hydroxyacetophenone has been improved by condensing with a variety of carbonyl compounds. The present study has been focused on the synthesis of some new hydroxyacetophenones, its derivatives, Cu metal complex and to study their antimicrobial activities Their structures were elucidated on the basis of MP, TLC, elemental analysis, UV-visible and IR spectral data. All the synthesized compounds have been screened for their biological activity by Agar well diffusion method.

MATERIAL AND METHODS:

The chemicals used in the present work were dry resorcinol, glacial acetic acid, powdered Zinc chloride, semi carbazide hydrochloride, anhydrous sodium acetate, ethanol etc. all these chemicals were purchased from Zen Scientific, Mumbai and were of AR grade. All these chemicals were used for synthesis.

Test Microorganism: The microorganism used in the present study were *M. luteus, B. subtilis, S. aureus, E. coli, P. aeruginosa.*. Microorganisms were maintained at 4^{o}C on nutrient agar slants.

The reagent 2-[1-(2,4- dihydroxyphenyl)ethylene]hydrazinecarboxamide and its Cu (II) metal complex was prepared as reported in the literature. The structure of the Schiff base is confirmed by using physical methods like melting point, TLC, elemental analysis, UV-visible and IR spectra. The newly synthesized Cucomplex was characterized on the basis of microanalysis data, elemental analysis, UV-visible and IR.

Synthesis of 2,4- dihydroxyacetophenone

Briefly, the synthesis was carried out by dissolving freshly fused and powdered zinc chloride (0.24 mole) in 32 ml of glacial acetic acid by heating on sand bath. Dry resorcinol (0.2 mole) was added with stirring at 140^{o}C. The solution was heated until it just begins to boil and kept for 20 minutes at 150^{0}C. Dilute HCl (1:1) was added to the mixture and the solution was cooled to 5^{0}C. The separated product was filtered and washed with dilute HCl. The product was recrystallized from hot water. The reaction Scheme is given in Fig.1

Reaction Scheme:

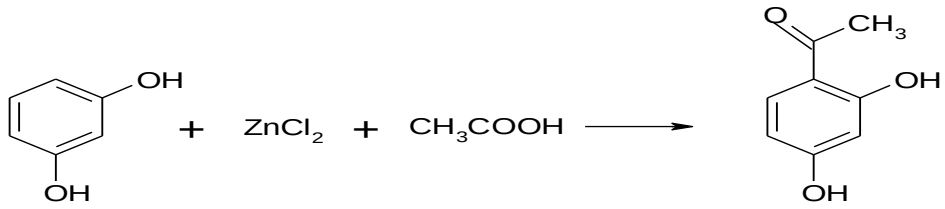

FIG.1 : REACTION SCHEME FOR THE SYNTHESIS OF 2,4- DIHYDROXYACETOPHENONE

Synthesis of Semicarbazone Derivative:

1 gram of powdered semicarbazide hydrochloride was added 0.9 gram of anhydrous sodium acetate to 5ml of water and was warmed gently until a clear solution is appeared. A solution of 1gm of 2, 4 dihydroxyacetophenone in 5ml of ethanol was added. The mixture was warmed gently in a water bath for 15 mins. The Semicarbazone rapidly crystallizes. Finally, cool filter off the 2,4dihydroxyacetophenoneSemicarbazone, washed thoroughly with water and was drained. Recry stallised from ethanol. Melting point is 201^{o}C. . The reaction Scheme is given in Fig.2

Reaction Scheme:

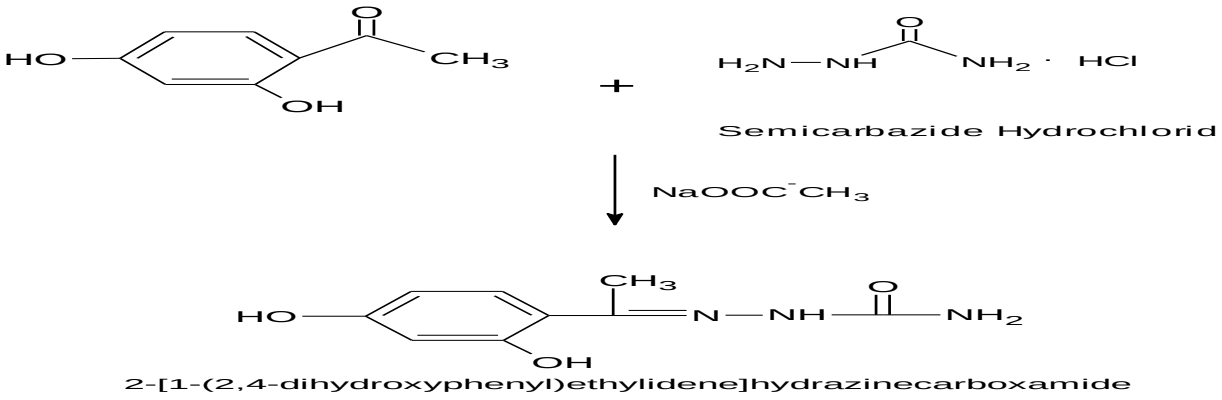

FIG.2 : Reaction Scheme For The Synthesis Of 2-[1-(2,4-Dihydroxyphenyl)Ethylene] Hydrazinecarboxamide I.E. 2,4 Dihydroxyacetophenonesemicarbazone,

Synthesis of Cu (II) Compex:

The Schiff base ligand (0.1mm) was taken in hot ethanol (36mL) and treated with a hot ethanolic solution of $CuCl_2.2H_2O$ (0.1mm) the light yellow transparent solution of ligand changed to green after mixing the solution. This was refluxed for 8hrs to obtain dark green colour solid. recrystallized solid was separated out on cooling and residue were left to stand overnight, filtered and dried over desiccators. Their yield ranges from 60-70% and melting points was 295^0C. The reaction Scheme is given in Fig.3

Reaction Scheme:

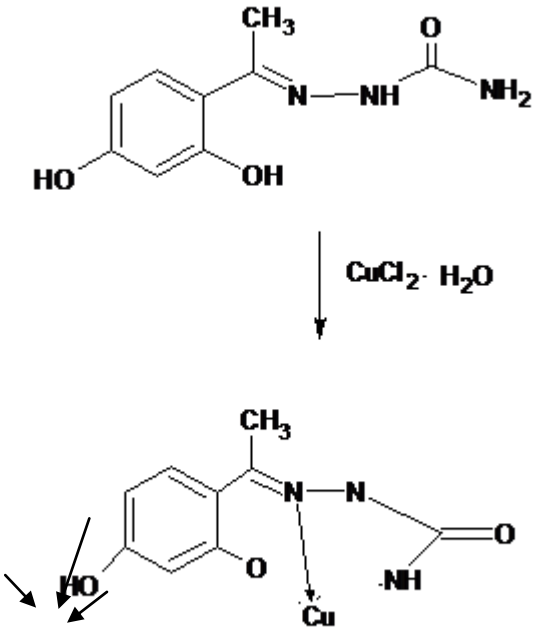

FIG.3: Reaction Scheme For The Synthesis Of Cu Complex Of 2,4 Dihydroxyacetophenone Semicarbazone

Spectral Analysis: The structure of all synthesized compounds was confirmed by Elemental analysis,Uv-visible and IR Spectroscopic technique. The absorbance measurement was carried out on ShimarzuUv-visible 2100 spectrophotometer with 1 cm quartz cell. The IR spectra were recorded on Shimadzu FT-IR-8400 instrument using KBr pellet method. (Fig. 4-6)

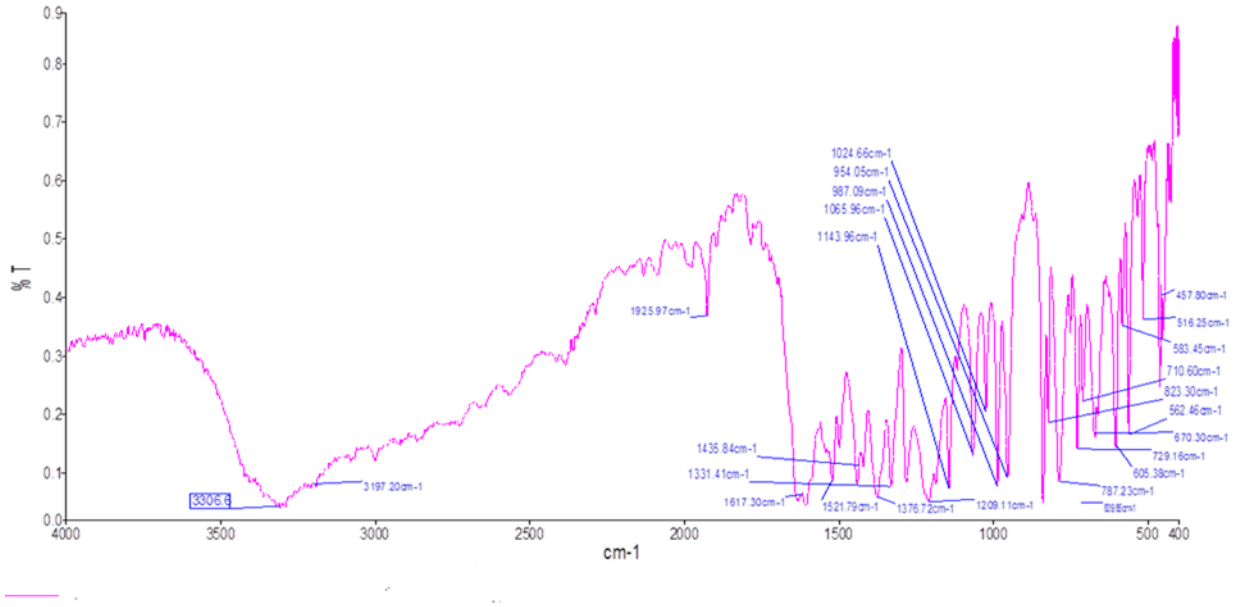

FIG 4: Ir For 2,4- Dihydroxyacetophenone

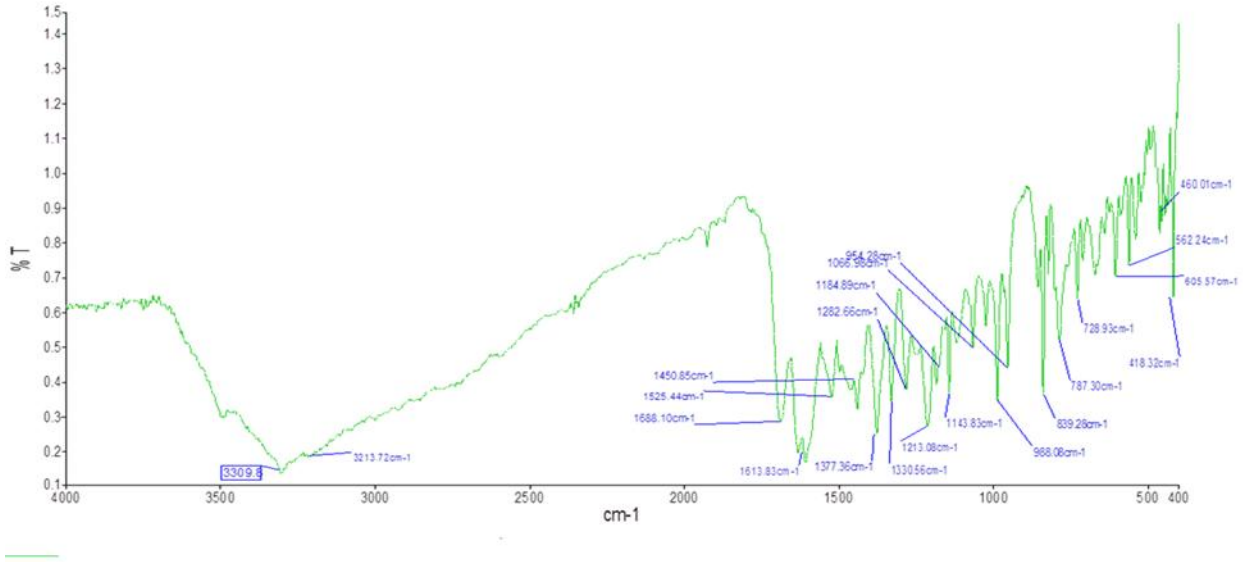

FIG 5: Ir For 2,4- Dihydroxyacetophenone Semicarbazone

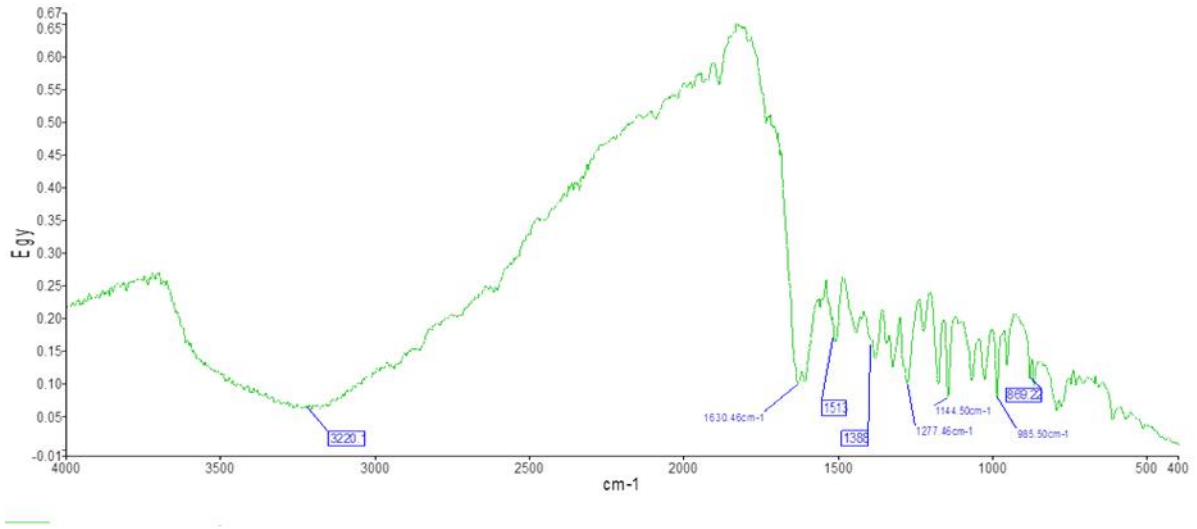

FIG 6: Ir For Cu Complex Of 2,4- Dihydroxyacetophenone Semicarbazone

Antimicrobial studies:

For antimicrobial activity the suspension of synthesized compounds and Cu (II) metal complex was made with sterile saline. In the present work the antimicrobial activities of the synthesized compounds have been screened against *M. luteus, B. subtilis, S. aureus, E. coli, P. aeruginosa*.

Preparation of test compounds: The solutions were prepared at a concentration of 1mg/µl for all the compounds.

Preparation of Plates and Microbiological assay: The antimicrobial evaluation was done by Agar well diffusion method[15,16] using Mueller Hinton Agar no.2 as the nutrient medium. The bacterial strains were activated by inoculating loop full of strain in 20 cm3 of nutrient agar and the same was incubated for 36 hrs. in an incubator at 37^{o}C. 0.1 cm3 of the activated strain was inoculated in Mueller Hinton agar. Mueller Hinton agar was kept at 45^{o}C and then poured in the petri dishes and allowed to solidify. After solidification of the media, 0.85 cm ditch was made in the plates using a sterile cork borer and these were completely filled with the test solution. The plates were incubated for 36 hrs. at 37^{o}C. The mean value obtained for the three wells was used to calculate the zone of growth inhibition of each sample. The inhibition zone formed by these compounds against the particular test bacterial strain determined the antibacterial activities of these synthesized compounds.

RESULTS AND DISCUSSION:

2,4- dihydroxyacetophenone, its semicarbazone derivative and its Cu (II) metal complex are synthesized. The synthesized compounds were purified by recrystallization method. The purity of the compounds was checked by TLC using appropriate solvent systems. The physical and analytical

parameters were checked. (Table1) The structure of all the synthesized compounds was confirmed by UV-visible and IR spectroscopic technique.

TABLE 1: Physical And Analytical Data

Compound	Color	M.P.(^{0}C)	λmax in nm	Elememtal analysis%		
				C	H	N
I	Off white	143	217	63.15	5.30	--
II	Pale yellow	201	342	59.01	3.90	5.45
III	Green	295	490	58.40	3.43	6.62

Spectral Data:

2,4-dihydroxyacetophenone: IR(cm^{-1}, KBr) 3307(aro, O-H str), 3197.20(aro, C-H str), 1521.79(aro, C=C str), 1925.97(OH para sub), 1800(OH ortho sub), 1617.30C=O conj), 1143.96(aro, C-O str), 823.30(para sub), 729.16(ortho sub). (Table 2)

2,4-dihydroxyacetophenone semicarbazone: : IR(cm^{-1}, KBr) 3309(aro, O-H str), 3212.72(aro, C-H str), 1525.44(aro, C=C str), 1213.08(C-N str), 1143.83(aro, C-O str), 1688.10(C=O conj), 1143.96(aro, C-O str), 839.28(para sub), 728.93(ortho sub). (Table 2)

Cu Complex of 2,4-dihydroxyacetophenone semicarbazone: IR(cm^{-1}, KBr) 3220.00(aro, O-H str), 1513.00(aro, C=C str), 1277.46(C-N str), 1144.50(aro, C-O str), 1630 (sec/tert amide), 869.22(para sub), 512.97 (M-O str) (Table 2)

TABLE 2: Spectral Data

Group & vibration	Frequency's in cm^{-1} I	Frequency's in cm^{-1} II	Frequency's in cm^{-1}III
Aro, O-H Streching vibration	3307	3309	3220.00
Aro, C-H Streching vibration	3197.20	3212.72	-----
Aro, C=C Streching vibration	1521.79	1525.44	1513.00
OH parasubsituted	1925.97	1922	-----
OH orthosubsituted	1800	1805	-----
C=O conjugation	1617.30	1688.10	
Aro, C-O Streching vibration	1143.96	1143.83	1144.50
Para substitution	823.30	839.28	869.22
Ortho substitution	729.16	728.93	727
Aro, C-N stretching	----	1213.08	1277.46
Tertiary amide	----	----	1630.00
M-O stretching	----	----	512.97

Antimicrobial Activity:

Microbial assay were carried out by agar well diffusion method. The bacterial strains were activated by inoculating loop full of strain in 20 cm3 of nutrient agar and the same was incubated for 36 hrs. in an incubator at 37^{o}C. The zone of inhibition in different bacterial strains i.e. *M. luteus, B. subtilis, S. aureus, E. coli, P. aeruginosa* against synthesized compounds shown in Table 3. Among the various bacterial strains maximum zone of inhibition was recorded in *S. aureus*and minimum zone of inhibition was observed in *M. luteus*and *P. aerug*

TABLE 3: Antibacterial Activity

Entry	Subs	Zone of Inhibition in mm				
		Gram positive Bacteria			Gram negative Bacteria	
		M. luteus	*B. subtilis*	*S. aureus*	*E. coli*	*P. aeruginosa*
1.	I	15	17	19	14	13
2.	II	15	16	20	16	14
3.	III	14	17	24	22	14
4.	Ampicillin	17	19	26	24	17

I 2,4- dihydroxyacetophenone

II 2,4- dihydroxyacetophenoneSemicarbazone

III Cu Complex of 2,4- dihydroxyacetophenone Semicarb zone

DISCUSSION:

The results indicate that inhibition depends on strain and structure. in compound I due to presence of C=O only it shows less inhibition. But in compound II due to presence of C=N imine group inhibition increases comparation to compound I. Also a broad band at 3500-3400 is attributed to intermolecular hydrogen bonded –OH group, at 1600-1700 C=O (amide) strong absorption, Medium sharp absorption band around 3200-3100 N-H stretching vibration, Strong absorption band 1600-1675 due to tertiary amide. Aromatic C-H band at 3000-2900. Physicochemical studies have been used in the elucidation of the geometry of the metal complexes with the purpose of throwing light on the structural aspects of newly synthesized Schiff base complexes. The newly synthesized ligand and its Cu (II) metal complex were characterized by elemental analysis, UV-visible, IR, TLC and repeated MPs determination studies. The susceptibility of the contain strains of bacteria towards the synthesized compounds was determined by measuring the size of inhibition diameter . Cu (II) complexes were highly effective against *M. luteus, B. subtilis, S. aureus, E. coli, P. aeruginosa* than their parent compound. It was also observed that antibacterial activity of these complexes for removing bacteria was fairly good.

CONCLUSION:

2,4- dihydroxyacetophenone, its semicarbazone derivative and Cu (II) metal complex were synthesized. The structures of synthesized compound were supported by IR spectroscopic technique. The antibacterial screening of these compounds shows that inhibition depends on strain and structure Presently, there is an emergence of multiple drug resistance to human pathogenic organism. So there is increasing interest and need to develop new alternative antimicrobial drugs for the treatment of infectious diseases. The clinical isolated bacteria in this study were *M. luteus, B. subtilis, S. aureus, E. coli, P. aeruginosa*.. These isolates of bacteria caused high percentage of drug resistance. The antibacterial study showed that complexes are found to be more active against *M. luteus, B. subtilis, S. aureus, E. coli, P. aeruginosa*. Compared to standard antibacterial compound the complexes show moderate activity against the selected strains of microorganisms.

REFERENCES:

1. Kuzmin V,et.al. SAR & QSAR. Environ Res 2005; 16: 219.
2. Sawodny W, Riederer M, Urban E,Preparation and thermal stability of polymeric metal chelates with schiff bases.InorgChimActa 1978; 29: 63-68.
3. OshimaS, et.al. Structural Control of Schiff Base Ligands for Selective Extraction of Copper(II). Anal Sci 2002; 18(12): 1351-1355.
4. Agarwala et al. Synthetic Lubricating oil Greases containing Metal Chelates of Schiff bases, US pat 1992; 5: 147- 567.
5. Hitoshi N, Tamao N, Hideyuki A, Manabu F, Takayuki M.Preparation and characterization of novel cyclic tetranuclear manganese (III) complexes: MnIII4(X-salmphen)6 (X-salmphenH2 = N,N′-di-substituted-salicylidene-1,3-diaminobenzene (X = H, 5-Br). Polyhedron 1997; 16: 3787-3794.
6. Punniyamurthy T,Jeet S,Kalra S, Iqbal J,Cobalt(II) catalyzed biomimetic oxidation of hydrocarbons in the presence of dioxygen and 2-methylpropanal. Tetrahedron Lett. 1995; 36(46): 8497-8500.
7. Fisher J, Rabinovitz. Nature (London) 1983; 303: 64.
8. Kleinberg J, Argersinger W, Grisworld E. Inorganic Chemistry. D. C. Health and Company. 6thCh: Boston, MA, 1960.
9. Martell E, Arthur E. Chemistry of the metal chelate compounds.Prentice-Hall inc: New York, NY, 1952.

10. Oxtoby W, David HP, Gillis CA. Principles of Modern Chemistry,6th ed. Thomson Brooks/Cole; Belmont, CA: 2008
11. Gregory JW, Josephin A. McKeon, Silvia C. Alfred Werner's Inorganic Counterparts of Racemic and Mesomeric Tartaric Acid: A Milestone Revisited. Inorg. Chem. 2004; 43(20): 6249–6254.
12. Miessler L, Gary, Donald Arthur Tarr. Inorganic Chemistry.1999; 642.
13. Patai E.S. The chemistry of carbon-nitrogen double bond. John Wiley and Sons: New York; 1970; 61-146.
14. Brand E and Sandberg M, Org. Synth. Coll. 1943; 2: 49.
15. John C. Sheehan, Victor J. Grenda, The N-(2-Hydroxyarylidene) Protecting Group in Peptide Synthesis. Amer.Chem.Soc., 1962; 84(12): 2417-2420.
16. Nogy L, Totok G, Szokoyi I and Giber J, Int. Conference of Modern Trends inactivation analysis, Maryland, U.S.A, 1928; 411