International e-Conference on New Horizons And Multidisciplinary Applications In Science And Technology
In Association withInternational Journal of Scientific Research in Science and Technology
Volume 9 | Issue 6 | Print ISSN: 2395-6011 | Online ISSN: 2395-602X (www.ijsrst.com)

Synthesis and Antibacterial Screening of Metal β-diketonates

Pooja Mohobe*[1], Babita Yadao[1], Himani Pandhurnekar[1], Doyel Bhattacharya[1], Rakesh Naktode[1]
[1]Department of Chemistry, Dada Ramchand Bakhru Sindhu Mahavidyalaya, Nagpur, India

ABSTRACT

1-(2,4-dihydroxy-5-nitrophenyl)-3-(thiophen-2-yl)propane-1,3-dione (DNTPD) and its transition metal complexes were synthesized. The β-diketone ligandis synthesized by employing Baker-Venkataraman rearrangement on 4-hydroxy-5-nitro-2-(thiophen-2-yl)oxyacetophenone which was previously synthesized by p-nitroresacetophenone and thiophene-2-carboxylic acid. The synthesized compounds were characterized by physical properties, elemental analyses, ^{1}H-NMR, mass spectra,IR spectra and electronic spectra and the geometry of metal complexes have been concluded by magnetic spectra. The thermal stability ofmetal complexes has been studied by Thermogravimetric analysis. The ligand and its transition metal complexes have been studied under pathogenic bacteria like *Staphylococcus aureus, Bacillus subtilis, Proteus vulgaris, Escherichia coli* and *Proteus aeruginosa* by filter paper disc diffusion method.

Keywords: β-diketones, Metal complexes, Baker-Venkataraman rearrangement,Thermogravimetric analysis, Antibacterial activity.

I. INTRODUCTION

β-diketones are among the most widely studied compounds.They are key intermediates for the synthesis of some core heterocyclic compounds likepyrazole[1], isoxazole[2], triazole[3], flavones[4], benzodiazepine[5], pyrimidine[6], etc. Their derivatives also have wide applications in diverse areas like gas chromatography, laser technology, polymer chemistry, solvent extraction and shift reagent in NMR spectroscopy[7,8].
β-diketones are known to have keto-enol tautomerism. As β-diketones exist mainly in the enolic form and that form considered as a 1-keto 3-hydroxy variant locked in the preferred double bond geometry through hydrogen bonding, having ability to inhibit bacterias and act as an excellent antibacterial agent[9]. It exhibits several other biological activities, such as antioxidant[10], antitumor[11], antiviral[12], insecticidal[13], anti-inflammatory and anticarcinogenic activities[14], antimutagenic activity[15-17] etc. It has been used as sunscreen agent because it is a good absorber in UV region. It has been shown to protect human lymphoid cells and used as UVA-filters. β-diketone is an important pharmacophores of HIV-1 integrase inhibitors[18].
Thiophene derivatives have been very well known for their remarkable pharmacological activities and therapeutic applications. Thiophene is a bioisostere of benzene ring thus benzene ring of a biologically active compound may often be replaced by a thiophene without loss of activity[19]. Number of thiophene derivatives

have been developed and widely used as chemotherapeutic agent. It exhibits several other pharmacological activities such as anti-inflammatory, anti-atherosclerotic, antithistaminic and also used in the treatment of Alzheimer's disease[20].

In present work, we synthesized and studied the properties of 1-(2,4-dihydroxy-5-nitrophenyl)-3-(thiophen-2-yl)propane-1,3-dione and its metal complexes. The title compound was synthesized from 4-hydroxy-5-nitro-2-(thiophen-2-yl)oxyacetophenone by employing Baker-Venkataraman rearrangement[21] which was previously synthesized by Resacetophenone. The synthesized compounds were characterized by various analytical techniques and screened for antibacterial study.

II. EXPERIMENTAL AND METHOD

p-Nitroresacetophenone 2

5.5g of dry resacetophenone**1** which was synthesized by Nencki reaction was dissolved in 25ml H_2SO_4 by heating it at 60-65°C for 15min. Then the reaction mixture was cooled below 10^0C and cooled nitrating mixture was added slowly maintaining the temperature of system below 10°C. It was kept 0-10°C for 15min, then poured into crushed ice with constant stirring and washed with cold water. Yield: 5.3g (74%) m.p. 142°C

4-hydroxy-5-nitro-2-(thiophen-2-yl)oxyacetophenone (HNTO) 3

0.02 mol of p-nitroresacetophenone**2** and 0.02 mol of thiophene-2-carboxylic acid were dissolved in 10ml dimethylformamide and cooled. Add 3ml $POCl_3$drop wise with constant stirring maintaining the temp below 10^0C. It was kept for 2 hours, then the reaction mixture was poured in crushed ice with stirring. Yellow solid was separated out which was washed with cold water. The product was filtered and recrystallized by alcohol. Yield: 82%; m.p.: 65°C.

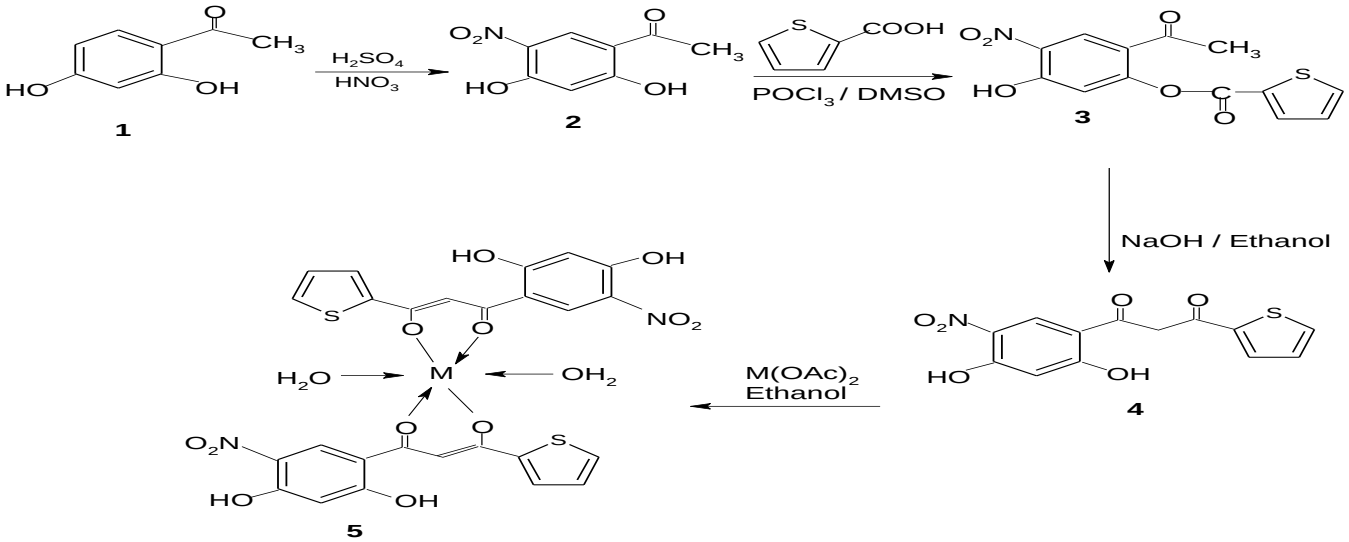
1-(2,4-dihydroxy-5-nitrophenyl)-3-(thiophen-2-yl)propane-1,3-dione(DNTPD) 4

0.02mol of 4-hydroxy-5-nitro-2-(thiophen-2-yl)oxyacetophenone**3** was dissolved in18ml dimethyl sulfoxide in a 50ml bolt-necked flask and heated to 50°C. 0.03mol of potassium hydroxide was added with mechanical stirring which was powdered rapidly in a mortar preheated in an oven at 100°C and was stirred for 15min. The reaction mixture was then cooled to room temperature and acidified by adding 25ml of 10% aqueous acetic acid with stirring. The yellow-coloured compound so obtained was filtered and recrystallized from ethanol. Yield: 64%; m.p.150°C.

Bis(β-diketonato) Cu(II) complex 5a

Complexes of β-diketone compound **4** have been synthesized by dissolving ligand and copper acetate in 2:1 mole in ethanol. The olive coloured solid **5a** precipitated was filtered and washed with hot ethanol.

Similarly, the complexes of Cobalt, Nickel, Manganese and Zinc were prepared. The yield and colour of synthesized complexes have been given in **Table 1**.



M = Cobalt, Nickle and Manganesecontains water of coordination however water of coordination is absent in copper and Zinc.

Scheme: Synthesis of reported compounds

III. RESULTS AND DISCUSSION

The synthesized compounds were characterized by its physical properties, elemental analyses, IR Spectra, 1HNMR, mass spectra, electronic and magnetic studies.

Elemental analyses

The elemental analyses of the ligand and its metal complexes were done using the Perkin Elmer 2400 CHN analyzer. It has been given in Table 1. The elemental analyses of the synthesized compounds were found in good agreement with the calculated data.

Table 1: Elemental Analyses of all the synthesized compounds:

Name of complex	Color	Yield (%)	Elemental Analyses							
			Found (%)				Calculated (%)			
			C	H	N	M	C	H	N	M
HNTO	White	82	51.58	2.81	4.02	--	50.81	2.93	4.56	--
DNTPD	Yellow	64	50.47	2.84	3.98	--	50.81	2.93	4.56	--
Mn(DNTPD)	Orange	64	44.28	3.54	3.87	7.04	44.25	3.12	3.97	7.79
Co(DNTPD)	Rust	63	45.11	3.51	3.60	8.73	44.00	3.10	3.95	8.31
Ni(DNTPD)	Chocolate yellow	85	43.97	3.15	3.97	8.97	44.00	3.10	3.95	8.28
Cu(DNTPD)	Olive	89	46.57	2.91	3.72	9.48	46.02	2.65	4.12	9.37
Zn(DNTPD)	Golden	78	45.34	2.54	4.72	9.78	45.90	2.65	4.12	9.61

Infra-red spectra

FT-IR spectra was recorded with disc on Perkin-Elmer spectrum Rx-I spectrometer. The IR spectrum of ligand and its metal complexes are summarized in Table 2 given below.

Table 2: Infrared data of 1-(2,4-dihydroxy-5-nitrophenyl)-3-(thiophen-2-yl) propane-1,3- dione and its metal complexes (cm^{-1})

	C=O	C=C	-C-O Phenolic	-C-H Aromatic	>CH Alip	-OH Phenolic	-C-O Enolic	-C=S	M-O	M-H_2O Coordinated water	C-NO_2	-CH_3
1b	1708	1600	1527	3039	2918	3435	1269	689	--	--	1483	2973
Lig	1689	1602	1527	3029	2918	3435	1230	689	--	--	1483	--
Mn (DNTPD)	1667	1659	1538	3023	2932	3423	--	710	418	793	1489	--
Co (DNTPD)	1647	1614	1544	3031	2922	3460	--	708	416	785	1503	--
Ni (DNTPD)	1654	1618	1521	3022	2932	3460	--	710	416	785	1489	--
Cu (DNTPD)	1649	1597	1527	3034	2922	3430	--	700	443	--	1503	--
Zn (DNTPD)	1657	1596	1520	3021	2917	3418	--	689	462	--	1489	--

The band appearing at 1689 cm^{-1} in case of ligand may be assigned due to the carbonyl group, which exhibited a lower shift in metal complexes. This shift indicates that the beta-diketo group of ligand may be coordinated with the transition metal ion through oxygen atom. These evidences were supported by emergence of new bands at 416 - 462 cm^{-1} in the spectra of metal complexes which may be due to the metal–oxygen vibration.

^{1}H NMR spectra

Itwas recorded on Brucker AC-300F (300 MHz) NMR spectrometer using $CDCl_3$and DMSO-d^6as solvent and tetramethylsilane as an internal standard.

^{1}H-NMR spectra of DNTPD show a singlet at δ= 14.90 ppm for enolic –OH group, singlet at δ=11.87 ppm for phenolic –OH group near to carbonyl group and singlet at δ=5.66 ppm for remaining –OH group near to NO_2 group. Multiplets in the region of 7.41 to 7.43 ppm correspond to the presence of aromatic hydrogen. The singlet signal at δ=8.37 ppm corresponds to –CH= group.

^{1}H NMR spectra of copper complex of DNTPD shows no peak around 14.90 ppm indicates absence of enolic –OH group which indicates deprotonation and coordination of oxygen with metal ion. The peak for –CH= protonwhich was present in the ligand exhibits a downfield shift from 8.37 ppm to 8.52 ppm which again indicates the coordination of metal with two carbonyl groups of ligand. The singlet at δ=11.72 ppm was assigned for –OH groups near to carbonyl group and singlet at δ=5.24 ppm for remaining –OH groups near to NO_2 group. Multiplets observed in the region of 7.56 to 7.77 ppm may be due to the presence of aromatic protons.

Mass spectral analysis

Mass spectras were recorded on 70-S Mass spectrometer using m-nitro benzyl alcohol matrix.Mass spectrum of DNTPD showed a molecular ion peak at 306.9 m/z and M^{+1} peak at 307.9 m/z. It showed several other peaks at

137 m/z which is a base peak, 125 m/z, 120 m/z, and 113 m/z. The expected fragmentation pattern have been shown below

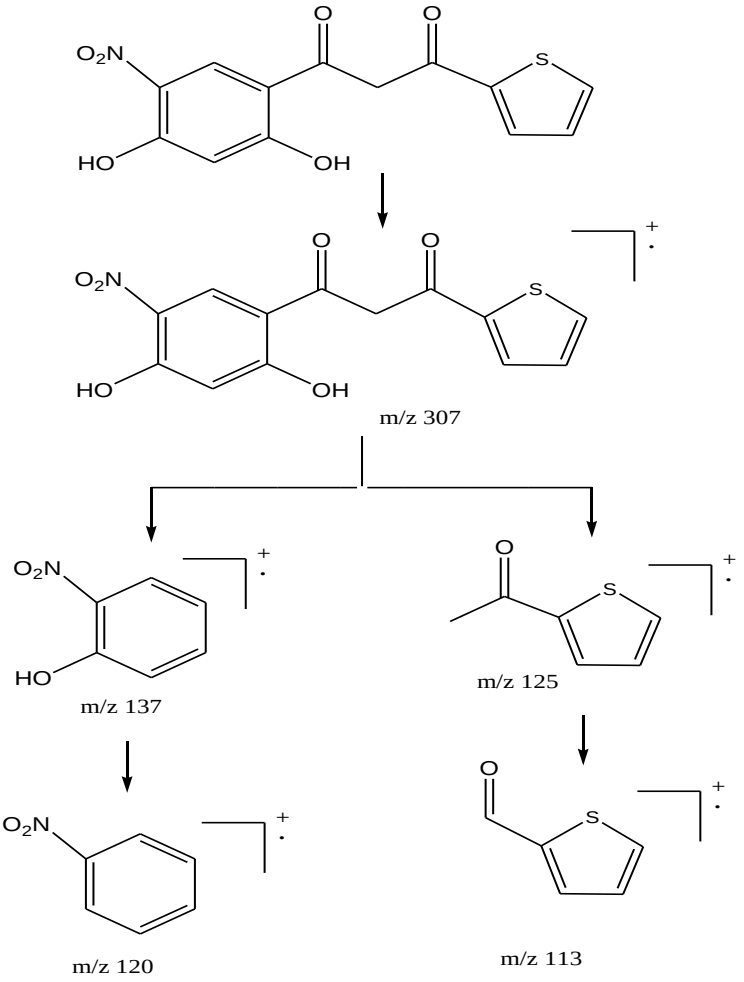


Figure 2: Expected Fragmentation Pattern of DNTPD

Magnetic and electronic spectral studies

Electronic spectra were scanned on UV-VIS-NIR Spectrophotometer Model Lambda 750 Perkin Elmer in the range of 200 – 1000 nm. Magnetic Susceptibility of the metal complexes were determined by Gouy's methodat room temperature on Sherwood Scientific Balance.

The magnetic susceptibility of the complexes were carried out at room temperature with ($Hg[Co(NCS)_4]$) as reference material. Molar susceptibilities were corrected for diamagnetism of the component atom using pascal's constant[22].

UV-Visible spectra were recorded on UV-VIS-NIR Spectrophotometer Model Lambda 750 Perkin Elmer in the range of 200 – 1000 nm. $[Mn(DNTPD)_2.2H_2O]$ complex shows 2 bands at 31.35kK which can be due to charge transfer transition for octahedral geometry[23]. The $[Co (DNTPD)_2.2H_2O]$ complex exhibited the bands at 19.76kK and 12.48kK, which may be due to $^4T_{1g}(P) \leftarrow {}^4T_{1g}$ and $^4A_{2g} \leftarrow {}^4T_{1g}$transition respectively, having octahedral geometry[24]. For $[Ni(DNTPD)_2.2H_2O]$ complex, the bands observed at 16.39 kK and 25.19 kK which may be assigned to $^3T_{1g} \leftarrow {}^3A_{2g}$ and $^3T_{1g}$ (P) $\leftarrow {}^3A_{2g}$ transition respectively indicates octahedral geometry[25], while $Cu(DNTPD)_2$ complex exhibited two bands at 14.10 kK and 28.90kK which may be due to $^2E_g \leftarrow {}^2B_{1g}$ and charge transfer respectively for square planar geometry[26]. Since $Zn(DNTPD)_2$ complex is a d^{10} system and hence is dimagnetic in nature, however, on the basis of other spectral data, its most probable

geometry is suggested to be tetrahedral[27]. The magnetic moments (μ_{eff}) and electronic data of all the complexes have been reported in **Table 3**.

Table 3: Magnetic and electronic spectral data of Ligand and its metal complexes

	Effective Magnetic Moment (μ_{eff})	Absorbance (kK)	Assignments	Stereochemistry
$Mn(DNTPD)_2.2H_2O$	5.35	31.35	Charge Transfer	Octahedral
$Co(DNTPD)_2.2H_2O$	4.87	19.76 12.48	$^4T_{1g}$ (P) ← $^4T_{1g}$ $^4A_{2g}$ ← $^4T_{1g}$	Octahedral
$Ni(DNTPD)_2.2H_2O$	3.37	16.39 25.19	$^3T_{1g}$ ← $^3A_{2g}$ $^3T_{1g}$ (P) ← $^3A_{2g}$	Octahedral
$Cu(DNTPD)_2$	1.56	14.10 28.90	^2E_g ← $^2B_{1g}$ Charge Transfer	Square Planar
$Zn(DNTPD)_2$	diamagnetic	--	--	Tetrahedral

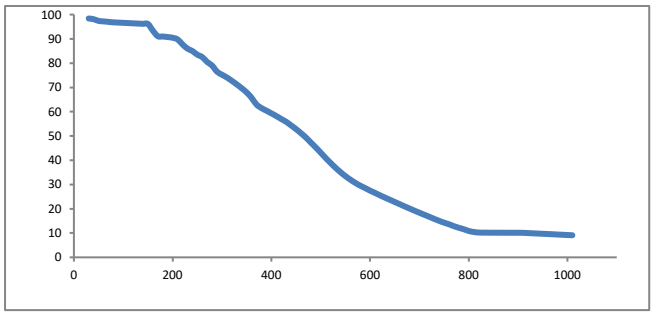
Thermogravimetric Analysis

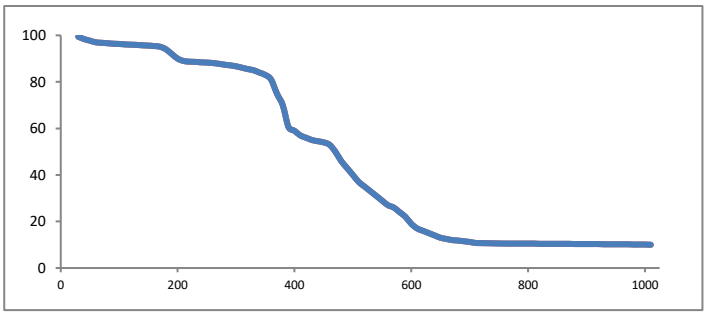
Thermogravimetric analysis was performed on Perkin Elmer SII, Diamond TG/DTA Thermogravimetric analyzer, with a temperature range of 30-1100°Cat heating rate of 10^0C at atmospheric condition. Thermal data of complexes were shown in Table 4 and Thermograms are shown in Figure 3.1.

The TGA curves of all the complexes were almost similar and indicate a continuous weight loss till a stable metal oxide was formed. Weight loss of 5.03% - 5.13% between 150^0C - 180^0C has been observed for cobalt, Nickel and Manganese complex which indicate loss of two molecules of water of coordination.

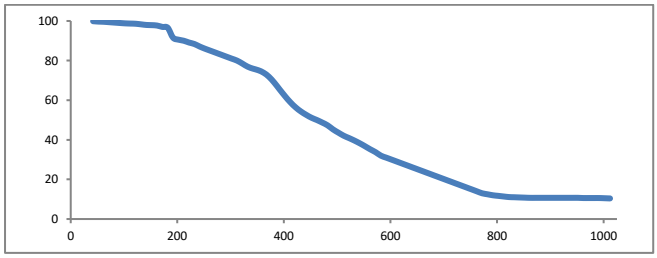
Table 4: Thermal data of the complexes

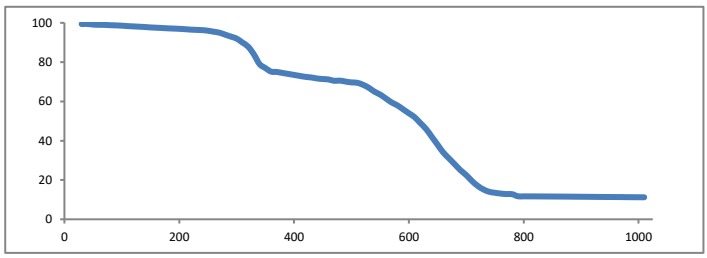
Sr. No	Complex	Coordination water Obs(calc) (%)	Decomposition Temperature (^{0}C)	% Weight loss Obs(calc)
1.	$Mn(DNTPD)_2.2H_2O$	5.06 (5.10)	515	89.55 (89.95)
2.	$Co(DNTPD)_2.2H_2O$	5.13(5.07)	480	89.48(89.48)
3.	$Ni(DNTPD)_2.2H_2O$	5.03(5.07)	532	89.29(89.47)
4.	$Cu(DNTPD)_2$	--	540	88.31(88.27)
5.	$Zn(DNTPD)_2$	--	435	87.86(88.03)



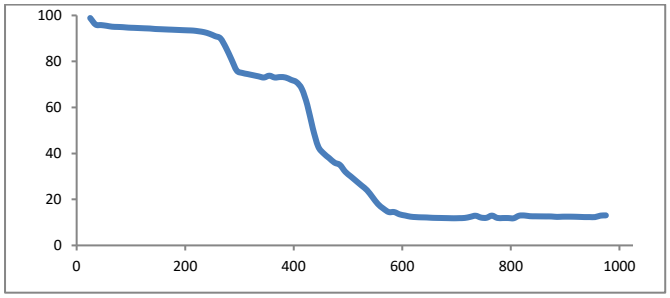


Thermogram for $Mn(DNTPD)_2.2H_2O$ Thermogram for $Co(DNTPD)_2.2H_2O$





Thermogram for $Ni(DNTPD)_2.2H_2O$ Thermogram for $Cu(DNTPD)_2$



Thermogram for $Zn(DNTPD)_2$

Figure 3: Thermograms of the Metal complexes

Antibacterial screening

The antimicrobial activities of all the compounds have been carried by filter paper disc diffusion method. The synthesized compounds were screened against pathogenic bacteria such as *Staphylococcus aureus, Bacillus subtilis, Proteus vulgaris* (Gram-positive), *Escherichia coli* and *Proteus aeruginosa* (Gram-negative)using filter paper disc diffusion method (Peach and Traey, 1950). Antibiotic drugs Ampicillin, Gentamicin and Erythromycin were used as reference. Selected pathogenic bacteria were maintained on nutrient agar medium for 36 hrs. Bacterial culture were inoculated into nutrient broth and incubated at 37 ± 2°C on a rotary shaker at 100 rpm. After 36 hrs incubation, the bacterial suspensions were used for further tests.

Antibacterial activity was then carried out using 100µg/mL of synthesized compounds. Filter paper disc soaked in solvent (chloroform) was used as negative controls while the discs soaked in standard broad-spectrum antibiotic solution (Ampicillin, Gentamicin and Erythromycin) were used as positive control. The results of tested compounds against these bacteria have been shown in **Table 5** given below. The Screening result indicates that the compounds showed moderate to excellent antibacterial activities.

Table 5: Antibacterial activity of compounds

Source	Minimum Inhibitory Concentration (MIC) µgmL-1 Diameter of Inhibition Zone (in mm)				
	Gram-negative			Gram-positive	
	E. coli	*P. aeruginosa*	*P. vulgaris*	*B. subtilis*	*S. aureus*
DNTPD	16	11	06	21	09
$Mn(II)(DNTPD)_2.2H_2O$	09	06	--	--	17
$Co(II)(DNTPD)_2.2H_2O$	29	--	07	--	14
$Ni(II)(DNTPD)_2.2H_2O$	--	14	--	--	20
$Cu(II)(DNTPD)_2$	34	09	23	15	14
$Zn(II)(DNTPD)_2$	19	--	--	06	--
Ampicillin	8	--	--	11	25
Gentamicin	28	22	10	16	10
Erythromycin	31	19	08	21	07

IV. CONCLUSION

In the present work 1-(2,4-dihydroxy-5-nitrophenyl)-3-(thiophen-2-yl)propane-1,3-dioneand its transition metal complexes have been synthesized and characterized on the basis of various instrumental techniques such as IR, NMR and mass spectra.β-diketone compound acts as bidentate ligand and co-ordinate with the transition metal atom through β-diketo group. Co(II), Ni(II) and Mn(II) contains two coordinated water however in Cu(II) and Zn(II), water of coordination is absent.

On the basis of electronic and magnetic moment it is concluded that Manganese(II), Cobalt(II) and Nickel(II) complexes possess Octahedral, Copper(II) possess Square Planar as well as Zinc(II) possess Tetrahedral geometry.The Cobalt(II), Nickel(II), Manganese(II) and Copper(II) complexes were paramagnetic while Zinc(II) was diamagnetic in nature.

These synthesized compounds were screened for antibacterial activity and found to be good antibacterial agents.

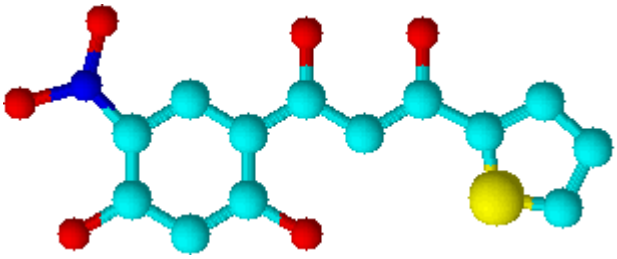


Figure 4: 3 Dimensional Structure of 1-(2,4-dihydroxy-5-nitrophenyl)-3-(thiophen-2-yl)propane-1,3-dione

V. REFERENCES

[1] . Mariano Grünebaum, Annika Buchheit, Tetrahedron. Lett., 2016, 57(14), 1555.
[2] . Su, Biyun; Hou, Yifan; Wang, Current Organic Synthesis, 2019, 16(8), 1174-1184
[3] . Wanli Cheng, Yanhua Tang,Org. Lett. 2016, 18, 23, 6168–6171.
[4] . Dong-WeiSun,Yong-Yan Zhou, 2021, 132226.
[5] . Kentaro Okuma, YukikoTanabe, Bulletin of the Chemical Society of Japan, 2015, 88, 8, 1064-1073.

[6] . NargesSeyyedi, FarhadShirini, J. Iranian Chem. Soc., 2017, 14, 1859–1867
[7] . Sonica, Kumar S., Narula A., J. Indian Chem. Society, 2004, 81, 639-643
[8] . Wenzel T.J., Morrill T.C., Lanthanide Shift Reagents in Stereochemical Analysis, VCH Publishers, Weinheim, 1986, 5, 151–173.
[9] . Verma P.N., Sheikh J.I., World Applied Science Journal, 2011, 14(8), 1154-1157.
[10] . Pravin Mahajan, MukeshNikam, J. Heterocyclic chem. 2017, 54(2), 1415.
[11] . Riccardo Pettinari, Fabio Marchetti, Europian J. Inorganic Chem.,2018, 31, 3521.
[12] . JavedSheikh, HarjeetJuneja, Journal of Saudi Chemical Society, 2013, 17(3), 269
[13] . Crouse G.D., McGowan M.J., J. Medicinal Chemistry, 1989, 32, 2148-2151.
[14] . Sheikh J., Juneja H. D., e-J. Chemistry, 2010, 7(1), 21-24.
[15] . Lin C. C., Lu Y. P., Cancer Lett., 2001, 168, 125–32.
[16] . Shen G., Khor T. O., J. Cancer Research, 2007, 67, 9937.
[17] . Angela Corona, Sebastian Seibt, Arch Pharm, 2021, e2100123.
[18] . Lednicer D., Interscience, 1999, 187.
[19] . McPherson S. D., Arch Ophthalmol., 1950, 44(3), 405-410.
[20] . Pravin S. Bodkhe, J. Engg. Sci., 2020, 11(4), 1055.
[21] . Dutta R.L and Syamal A., Elements of Magnetochemistry, 2nd ed., East West Press Pvt. Ltd., New. Delhi, 1993, 130-135
[22] . Raghu N., Gupta N., J. Serb. Chem. Soc., 2003, 68(6), 455–461
[23] . Raman N., Ravichandran S., J. Chem. Sci., 2004, 116, 215–219
[24] . Arockiadoss P.V.,Amaladasan M., International Journal of ChemTech Research, 2012, 4, 324-327
[25] . Kuppusamy K., Govindarajan S., J. Thermochimica Acta, 2004, 274, 125–138
[26] . PaliwalL.J.,Kharat R.B., Die AngewandteMakromolekulareChem, 1988, 160, 67-81