# Synthesis, Characterization and biological activity study of some novel tri -metal complexes of 1,3,5 – tri [5-p- methoxy phenyl -1,3,4 – thiadiazol – 2yl] benzene.

Nada M. Abbass Alabidy/Department of Chemistry College of Science University of Baghdad

Abstract:

A new tri metal complexes of 1,3,5 – tri – [5-p-alkoxy phenyl – 1,3,4-thiadiazal- 2yl] benzene (L) formed by the condensation of three moles of metal salt with one mole of (L) which formed by condensation of 1,3,5- benzene tricarboxylic acid[3] with three equivalent of appropriate amino – thiadiazole [2] afforded the corresponding Tri- amide compounds [4], and its CO (II), Ni (II), Cu (II), Zn (II), Pd (II) and Pt (IV) complexes have been synthesized. Their structures have been elucidated on the basis of analytical, magnetic, electrical conductivity and spectral study as well as elemental analyses. The results are in agreement with the suggested structures. The results are in agreement with the suggested structure, all complexes showed octahedral geometries except pd (II) and Pt (II) complexes which were square planar. The synthesized compound and its metal complexes were tested in vitro for antimicrobial activity.

## Introduction:

The 1,3,4 – thiadiazoles are becoming of great interest, this is primarily due to the large number of uses of 1,3,4- thiadiazoles in the most diverse areas, for example in drug synthesis, scintillation material, dyestuffs industry(1, 2). It is known that many 1,3,4-thiadiazole derivatives have biological activity, with their antibacterial(3), antimycobacterial(4), antimycotic(5), antifungal(6) and inflammatory(7), Recent research has also established for these cycles metal complexe as antitumoral(8) action, antibacterial(9) and as ketol – acid reductoisomerase inhibitors(10).

The Chelating behaviour of hetrocyclic compounds with transition and other metals is reported, the range of ligands involved is large and includes pyrimidine, imidazole, triazole, quinoline and thiazole(11, 12), Although a large number of bidentate and tridentate ligands anchored to heterocyclic compound, only a few multidentate ligands like thiadiazole(1) have been anchored to metal complexes.

## Experimental/ Materials and Methods

Melting points were recorded on a heating plate microscope and are not corrected. The purity of the synthesized compounds was checked by T.L.C. techniques using a mixture of methanol and acetone (1: 1/ v) and various ratios of ethyl acetate: acetone solvent mixture as eluents and iodine chamber for spot location, and also by HPLC for (L) and some of it's metal complexes which were obtained by using HPLC (LKB), mobile phase $CH_3$ CN: $H_2O$ (80:20).

Infrared spectra were recorded on a perkin – Elmer 1310 IR spectrophotometer and Shimadzu corporation 200– 91527 IR spectrophotometer using KBr and CsI disks. Elemental (CHN) analyses were obtained by using EA elemental analyzer (Fison Ision Instrument) in Tehran Uni., faculty of sci. The metal contents were determined by atomic absorption technique using Varian AA–775 atomic absorption instrument. Electrical spectra of the ligands and its metal complexes in the region 200 – 1100nm were recorded on a shimadzu uv – visible–160 and on Cintra 5 UV – Visible spectrophotometer. Thermo gravimetric measurement of complexes was done in air at a heating rate of 10°c/min., with Perkin Elmer 3600 the mobalance. Electrical Conductivity of metal complexes was measured at room temperature in DMF ($10^{-3}$M) using Elkta Lictfahigheit conductivity meter (SIMENS). Magnetic susceptibility measurements for complexes were obtained at room temperature according to Faraday′s method by using Johnson mattey magnetic balance system division. All chemicals used were of regent grade (supplied by either Merck or Fluka) and used as supplied. Palladium (II) Chloride was converted to dichlorobis (benzonitrile) Palladium (II)(14, 15), and $H_2PtCl_6.6H_2o$ was converted to potassium hexachloroplatinate (IV) hex hydrate(16) prior to use. Complexes formation was studied in solutions to obtain the molar ratio the of the ligand and to metal ion (L:M) using DMSO as a solvents. The results of (L:M) ratio were obtained by plotting absorbance of solution mixtures at detected λmax against [L]/ [M], with constant concentration of the metal ion ($10^{4-}$M) which were treated with various amounts of the same concentration of the ligand (Table 4)(36).

(a) Preparation of ligand:

Preparation of 1,3,5-benzene tricarboxylic acid (trimesic acid)[17] (0.05mole, 6.5g) of mesitylene [1] is added to a solution of (0.32mole, 51. 2g) of potassium permanganate and (0.16mole, 15g) of sodium carbonate in (250ml)of water and the mixture is heated under reflex (24) hours until the color of the permanganate has disappeared. The reaction mixture was filtered while still hot to get rid of $MnO_2$ precipitate. The cooled filtrate is acidified with sulphuric acid (20%), the precipitated carboxylic acid is filtered off, washed with a little cold water and used without further purification. Yield (40%), M.P ⇒330°c.

(b) Preparation of 4-n- methoxy benzoic acid (2)(17)

4-Hydroxybenzoic acid (0.08mole, 11.25g) was dissolved in (75ml) of methanol at 25°c with stirring, after the acid was dissolved, (0.2 mal, 13.12g.) of potassium hydroxide in (10ml) of distilled water was added drop wise, the reaction mixture was heated to reflux and (0.1mol) of appropriate alkyl halide was then added over (2) hours. The reaction mixture was refluxed over night, and then (50ml) of methanol was removed by evaporation. The remained of reaction mixture was cooled at 25°c and the added to (250ml) of distilled water. Hexan (25ml) was added to extract organic impurities. After discarding organic phase, the aqueous phase was heated to 40°c and neutralized with (20%) HCl. The product precipitated during the neutralization was collected by filtration and purified by recrystallization from ethanol. Yield (75%), mp (184°c).

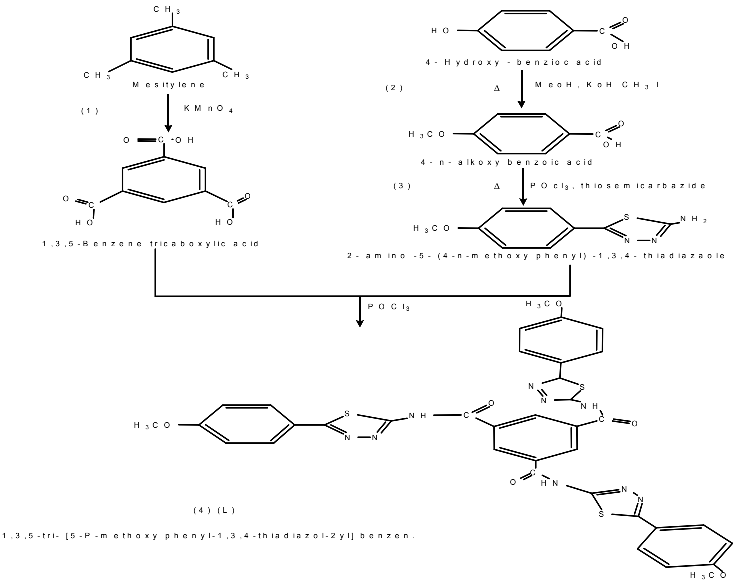
(c) Preparation of 2-amino-5-(4-n-alkoxyphenyl) -1,3,4-thiadizale (3)(17).

A mixture of appropriate 4- n- alkoxybenzoic acid (2) (0.01mole) and (0.01mole, 0.91g) of thiosemicarbazids with (5ml) of Phosphorus oxychloride was refluxed gently for (5) hours. After cooling (50ml) of eater added, the mixture was then refluxed for (7) hours and filtrated, neutralized with potassium hydroxide. The precipitate was washed with water and recrystallized from (ethanol – water) to give the titled compounds (3). Yield (65%), m.p.(188°c).

(d) Preparation of 1,3,5- tri–[5-p-methoxy phenyl-1,3,4-thiadiazol-2-yl]- benzene (4)(17).

A mixture of appropriate 2-mino-5-(4-n-methoxyphenyl- 1,3,4-thidizole (3) (0.03mole), 1,3,5- benzene tricarboxylic acid (1) (0.01mole, 2.1g.), and phosphorus oxychloride (25ml) was refluxed for (7) hours. The cold reaction mixture was poured on crushed ice and made basic by adding sodium bicarbonate solution. The separated product was filtered off and recrystallized from (Chloroform –Petroleum ether) to give title compounds (4). Yield (60%), m.p (260°c).

### *Scheme (1): Synthesis of 1,3,5-[5-P-methoxyphenyl -1,3,4-thia- diazol -2yl] benze*



## *Synthesis of Metal Complexes:*

A solution of Co(II), Ni(II), Cu(II), Zn(II) (15mg) in 4ml $CH_3OH$ was carefully layered into a solution of (L) (5mg) in $CHCl_3$ (10ml). The system was left for about two weeks at room temperature, and different colored crystals were obtained. The same synthetic procedure as for above complexes was used to synthesis the (Pd & Pt) complexes except that the mixture was heated under reflux with continuous stirring for 10h. The products were filtered and purified from reactants by washing many time with $CH_3OH$ and ether for [$Co^{+2}$($C_1$), $Ni^{+2}$ ($C_2$), $Cu^{+2}$($C_3$), $Zn^{+2}$ ($C_4$) or with DMSO, methanol and ether for [($Pd^{+2}$ ($C_5$), $Pt^{4+}$ ($C_6$)], and vacuum dried. Purity of the products was detected by TLC, using silica gel as a stationary phase and a mixture of chloroform and acetone (2:2v/v) or various ratios of methyl acetate: acetone solvent mixture as eluents.

Biological Activity study

Antibacterial activities of the prepared ligand and its metal complexes were tested in vitro for antimicrobial activity against two pathogenic microorganism viz., staphylococcus aureus (Gram +ve) and EscherichiaColi (Gram –ve). Bacterial cultures were prepared by streaking (0.1) ml of $10^6$CFU/mt both of indication strain on the whole surface of neutral agar plate. In each plate three wells (pores) were created on the nutrient agar layer using sterile cork porer. In each hole was injected 50μL of $10^{-3}$M of the studied compounds in DMSO by micropipette. The resulting cultures were incubated at 37c° for 24h. The inhibition zones caused by each compound were measured and the results were interpreted according to diameter measurements (18)

Result and Discussions:

The elemental analyses show 1:3 (ligand: metal) stoichiometry for all the complexes. The analytical data of ligand and the complexes are given in table (1). They correspond well with the general formula $LM_3X_n$ y($H_2O$) where M=Co(II) $C_1$, Ni(II)$C_2$, Cu(II)$C_3$, Zn(II)$C_4$, Pd(II)$C_5$, and Pt(IV)$C_6$, L=$C_{36}H_{27}$ $NaS_3O_6$, X=Cl in case of $C_1$,$C_3$,$C_5$ and $C_6$ while X=$NO_3$ in case of $C_2$ and $C_4$, n=2 in $C_1$, $C_2$, $C_3$, $C_4$ and $C_5$, n=4 in $C_6$. The high conductance of the chelates supports the electrolytic nature of the metal complexes.

Table (1) Physical Properties and analytical data of the Prepared Ligand complexes %element analysis found (calculated)

| **Molecular formula** | | **m.p.**<br>**(decomposition) temp.°c** | **% element analysis found (calculated)** | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | **Yield %** | **C** | **H** | **N** | **M** | ***Cl*** |
| **$C_1$** | **$[Co_3(L)(H_2O)_6 Cl_6]$** | **185** | **60** | **52.48**<br>**(53.59)** | **4.23**<br>**(4.84)** | **3.90**<br>**(4.47)** | **11.02**<br>**(10.05)** | **12.12**<br>**(12.65)** |
| **$C_2$** | **$[Ni_3(L)(H_2O)_6 (ONO_2)_6]$** | **210** | **45** | **40.52**<br>**(41.66)** | **4.16**<br>**(3.76)** | **10.07**<br>**(10.13)** | **9.15**<br>**(8.10)** | **-**<br>**-** |
| **$C_3$** | **$[Cu_3(L)(H_2O)_6 Cl_6]$** | **220** | **58** | **53.90**<br>**(53.20)** | **5.77**<br>**(4.80)** | **5.11**<br>**(4.43)** | **10.33**<br>**(10.71)** | **12.61**<br>**(12.56)** |
| **$C_4$** | **$Zn_3(L)(H_2O)_6(ONO)_6]$** | **240** | **70** | **40.91**<br>**(41.42)** | **3.43**<br>**(3.74)** | **10.93**<br>**(10.07)** | **7.87**<br>**(8.63)** | **-** |
| **$C_5$** | **$[Pd_3(L) Cl_6]$** | **280** | **40** | **57.10**<br>**(57.23)** | **4.12**<br>**(3.57)** | **4.42**<br>**(4.77)** | **17.89**<br>**(18.28)** | **12.75**<br>**(13.51)** |
| **$C_6$** | **$[Pt_3(L)C_{l6}]_6Cl$** | **> 300** | **39** | ***45.72***<br>***45.33*** | **3.01**<br>**(2.83)** | **3.89**<br>**(3.78)** | **24.30**<br>**(24.55)** | **21.20**<br>**(21.41)** |

## 8.1 IR spectra

In order to study the binding mode of the ligand to the metal ion in the complexes, the FTIR spectrum of the free ligand (L) was compared with the spectra of the complexes (19). The FTIR spectrum of (1) displays a broad (O-H) stretching absorption in the region of ($3260cm^{-1}$) as well as the carboxylic acid (C=O) absorption at ($1690cm^{-1}$)(20) The FI –IR spectra of 2- amino-5-(4-n-methoxy Phenyl)-1,3,4-thiadizole (3) give the evidence for the formation of the titled compounds through the disappearance of the two bands at $(3550\text{-}2750)cm^{-1}$, and ($1687cm^{-1}$) attributed to the O-H stretching frequency, and C=O of 4-n-methoxy benzoic acid together, with appearance of the band at about $(3300 – 3100)cm^{-1}$ which could be assignable to $NH_2$ group, asymmetric and symmetric stretching vibrations. A band at $(1615 – 1600)cm^{-1}$ due to the C=N group stretching frequency is also observed, the C-O-C group stretching vibration (asy & sym.) at $(1250\text{-}1020)cm^{-1}$, also νC-H bending of P-substituted appears at $(830)cm^{-1}$.(17,20,21) The FT-IR spectra, of synthesized compounds (3&4) shows the appearance of the a absorption of the carbonyl group for amide group at ($1680cm^{-1}$), as well as the appearance of the absorption of C=N for 1,3,4-thiadiazale ring at ($1600cm^{-1}$) which is a good evidence for mention of amid group. The spectroscopic data of the compounds (3&4) are shown in Table (2)

Table (2): Characteristic i.r. vibrations ($cm^{-1}$) for Comp. no. (3&4)

| Comp-no. | νasy N-H | νsy N-H | νC-H aromatic | $\nu_{as,\ sy}$ C-H aliphalic | νC=N | $\nu_{asy,\ sy}$ C-O-C | $\nu_{asy,\ sy}$ C=O |
|---|---|---|---|---|---|---|---|
| 3 | 3281 | 3105 | 3105 | 2928<br>2858 | 1611 | 1252<br>1042 | / |
| 4 | | 3301 | 3091 | 2933<br>2868 | 1604 | / | 1645 |

The band due to $\nu_{c\ =\ 0}$ and $\nu_{asy\ \&\ sy}$ (N-H) were shifted to lower frequencies in all complexes, indicating the involvement of carbonyl and (N-H) atoms in coordination with these metal ions(22, 23). Bands related to coordinated water vibrations were observed in the Spectra of $C_1$,$C_2$,$C_3$ and $C_4$ at (3480,760,630), (3500,800,640), (3470,805,715) and (3495,735, 690), respectively. The band related to nitrate ions was observed in the spectra of $C_2$ and $C_4$ at (1530,1482), (1695,1620)$cm^{-1}$ and were assigned to monodentate behaviors. Additional bands were observed at lower frequencies (610- 250$cm^{-1}$) and were attributed to M-N, M-O and M-X $\left(X = NO^{-3}, Cl^{-}\right)$ stretching modes. The important stretching vibrations of L and its metal complexes are described in Table (2).

Table (2): Important I.R. vibration ($cm^{-1}$) for the ligand and its metal complexes.

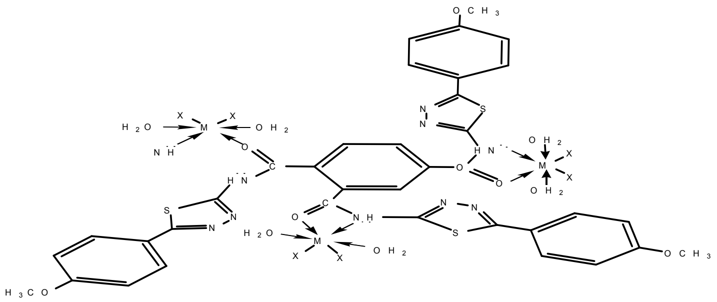
| Symbol | $\nu_{asy}$ N -H | $\nu_{(asy,sy)}$C=O | νC=N | νC-S | νNO3 | νM-O | ν M-Cl | $H_2O$ Coord. |
|---|---|---|---|---|---|---|---|---|
| L | 3301 | 1645 | 1604 | 1195 | | — | — | 750, 635 |
| C1 | 3250 | 1630 | = | = | *1385 1050 870* | 460 | 242 | 680,695 |
| C2 | 3210 | 1610 | = | = | | 456 | 253 | 750, 720 |
| C3 | 3240 | 1615 | = | = | | 457 | 263 | 749, 720 |
| C4 | 3193 | 1620 | = | = | *1368 1110 866 | | 270 | 749, 670 |
| C5 | 3072 | 1625 | = | = | | 458 | 220 | - |
| C6 | 3151 | 1617 | = | = | | 430 | 290 | - |

*monodentate

## 1.1 Electronic Spectra of the ligand and its complexes:

The electronic spectra were recorded in (DMSO) (Table 3). The most difference in an electronic spectrum of the ligand and its complexes were the shift of ligand based absorption to lower frequencies (longer wavelengths) and the appearing newer bands in the complexes in longer wavelength region. The spectral parameters 10Dg, $Dq/B', B', and\ \beta$ as well as energies of unobserved ligand fields' bands were obtained by applying observed band energies and band ratios on Tanaba- saugano diagrams of the specified metal ion (21, 26, 27). Metal complexes $C_1$,$C_2$,$C_3$ and $C_4$ exhibited spectra related to octahedral arrangement of ligand atoms around the metal ions while those of $C_5$ and $C_6$ gave squire planar geometries. Co(II), Ni(II) and Cu(II) Complexes gave high values of magnetic moments which were attributed to spin – orbital coupling(28), while Zn(II),Pd(II) and Pt(IV) complexes were diamagnetic complexes. The UV-Vis spectrum of copper complexes in DMSO solution displays a band at 11317cm$^{-1}$ and well-defined shoulder around 16598cm$^{-1}$, attributable to $^{2}B_{1}g\rightarrow$ $^{2}A_{1}g$ and $^{2}B_{1}g$ $\rightarrow$ $^{2}B_{2}g$ transition which strongly favor octahedral geometry around the central metal ion. This is further supported by the magnetic susceptibility value (2.31BM). The nickel complex is paramagnetic suggesting octahedral geometry. The electronic absorption spectrum of nickel complex shows a d-d band at 10192 cm$^{-1}$ assigned as $^{3}A_{2}g\rightarrow^{3}T_{2}g$ transition (30), which also indicates the octahedral geometry. The Cobalt complex shows a (d-d) band at 16645cm$^{-1}$ assigned to $^{4}T_{1}g(F)\rightarrow^{4}A_{2}g$ transition, which confirms octahedral and further confirmed by its magnetic susceptibility value (4.19BM)(31). The spectrum of the Zn(II) complexes ($C_4$) exhibited charge transfer bands only, which is a common phenomenon for d$^{10}$ metal complexes where d-d transition are excluded(18, 32, 33). Conductivity measurement of metal complexes in DMF solution (10$^{-3}$M) showed nonelectrolytes' nature of all complexes except those of platinum (IV). Electrolytic nature 1:3 was exhibited by all metal complexes (Ligand: metal)(34). According to the above – mentioned data in addition to those of elemental analyses and FT-IR Spectra, the structures of the metal complexes can be suggested as illustrated in Scheme (2)

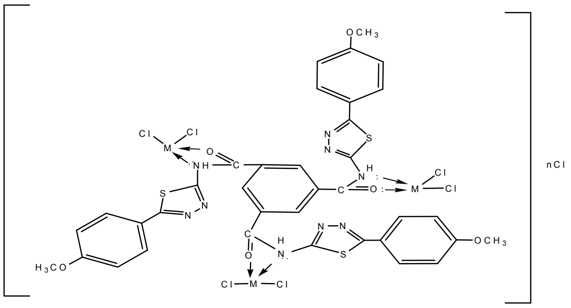
***Scheme (2) Suggested Structures of Ligand Complexes***



M=Co(II), Ni(II), Cu(II),Zn(II)

X=Cl in case of Co(II), Cu(II)

X=ONO in case of Ni(II), Zn(II)



M=Pd(II) & Pt(IV)

n = 0 in case of Pd and (6) in case of Pt(IV)

Table (3): Electronic spectra, spectral parameters, molar conductivity, and effective magnetic moments ($\mu_{eff}$) of [(5-p-methoxy phenyl – 1,3,4-thiadiazol-2yl) benzene] metal complexes.

| Comp. no | Band Position ($cm^{-1}$) | Assignment | Dq/B (B′) ($cm^{-1}$) | β | 10Dq ($cm^{-1}$) | Ω S.ml$^{-1}$. cm$^2$ | $\mu_{eff}$ (BM) |
|---|---|---|---|---|---|---|---|
| $C_1$ | $\nu_1$ 6625* | $^4T_1g \rightarrow {}^4T_2g$ | | | | | |
| Co(II) | $\nu_2$ 16645 | $^4T_1g(F) \rightarrow {}^4A_2g$ | 893 | | 6750 | Zero | 4.19 |
| | $\nu_3$ 18778 | $^4T_1g(F) \rightarrow {}^4T_1g(P)$ | (685) | 0.715 | | | |
| $C_2$ | $\nu_1$ 10192 | $^3A_2g \rightarrow {}^3T_2g$ (F) | 1.70 | | | | |
| Ni(II) | $\nu_2$ 15424 | $^3A_2g(F) \rightarrow {}^3T_1g$ (F) | 638 | 0.712 | 10210 | 7.3 | |
| | $\nu_3$ 20370 | $^3A2g(F) \rightarrow {}^3T_1g$ (P) | | | | | |
| $C_3$ | $\nu_1$ 11317 | $^2B_1g \rightarrow {}^2A_1g$ | — | — | — | 5.05 | 2.31 |
| Cu | $\nu_2$ 16598 | $^2B_1g \rightarrow {}^2B_2g$ | | | | | |
| | $\nu_3$ 32311 | $^2B_1g \rightarrow {}^2Eg$ | | | | | |
| $C_4$ | $\nu_1$ 26322 | L→M (C.T) | — | — | — | 6.0 | Diamag. |
| Zn | | | | | | | |
| $C_5$ | $\nu_1$ 16112 | $^1A_1g \rightarrow {}^1A_2g$ | — | — | — | 3.0 | Diamag. |
| Pd(II) | $\nu_2$ 20691 | $A_1g \rightarrow {}^1B_1g$ | | | | | |
| | $\nu_3$ 25211 | $^1A_1g \rightarrow {}^1Eg$ | | | | | |
| $C_6$ | $\nu_1$ 14308 | $A_1g \rightarrow {}^3T_1g$ | — | — | — | 244 | Diamag. |
| Pt(IV) | $\nu_2$ 20173 | L→M(C.T) | | | | | |

*CalculatedMetal: ligand ratioThe metal: ligand ratios of complexes were determined by method of molar ratio at fixed wavelength of maximum absorption (35). The ligand was found to form (1:3) [ligand: metal] chelate with metal ions mentioned. The results Table (4) are in agreement with the values reported for some 1,3,4-thiadiasoles complexes(36).

Table (4) Metal: ligand ratios determination by the method of mole ratio and stability constant values

| Ligand | Metal ion | PH | $\lambda_{max}$ (nm) | Metal= ligand | β | Log β |
|---|---|---|---|---|---|---|
| [1,3,5-tri (5-p-methaxy phenyl- 1,3,4- thiadiazal 2yl benzene] | $C_1$ Co(II) | 6.3 | 530 | 3:1 | $4.836\times10^7$ | 7.6844 |
| | $C_2$ Ni(II) | 5.8 | 610 | 3:1 | $1.060\times10^6$ | 6.0253 |
| | $C_3$ Cu(II) | 6.0 | 620 | 3:1 | $4.870\times10^4$ | 4.6875 |
| | $C_4$ Zn(II) | 6.5 | 495 | 3:1 | $3.762\times10^4$ | 4.5754 |
| | $C_5$ Pd(II) | 6.3 | 420 | 3:1 | $7.515\times10^5$ | 5.8759 |
| | $C_6$ Pt(II) | 6.7 | 630 | 3:1 | $2.138\times10^7$ | 7.3300 |

$\lambda_{max}$ of L=311(nm)

## Biological Activity

The antibacterial activity of the prepared ligand and its complexes are given (Table 4). The result detected that all compounds have good biological activity and some complexes have higher activities than the free ligand. As previously reported, the metal salts do not exhibit antibacterial activity(36). Complexes of [L] with Cu(II), Pd(II) and Pt(IV) ion were as active as the original ligand the two types of pathogenic bacteria namely staphylococcus aureus and Escherichiacoli. These results indicate that the degree of growth inhibition is highly dependent on (i) the chelate effect of the ligands, (ii) The nature of donor atoms, (iii) The total charge on the complex ion, (iv) the nature of the metal ion, (v) The nature of the counter ions that the neutralize the complex, and (vi) The geometrical structure of the complex (37).

Table (4): Antibacterial activities of studied ligand and its metal complexes showing inhibition zones in diameters (mm)

| Compound | Staphylococcus aureus | Escherichia coli |
|---|---|---|
| L | + | ++ |
| $C_{1Co(II)}$ | ++ | + |
| $C_{2Ni(II)}$ | ++ | ++ |
| $C_{3\ Cu(II)}$ | ++++ | +++++ |
| $C_{4Zn(II)}$ | ++ | + |
| $C_{5\ Pd(II)}$ | ++ | ++++ |
| $C_{6\ Pt(II)}$ | +++ | +++++ |

Key to symbols

Highly active= +++ (inhibition zone>20mm)

Moderately active = ++ (inhibition zone 11-20mn)

Slightly active = + (inhibition zone 5- 10 mm)

## Conclusions:

A new tri metal complexes of [1,3,5- tri- (5-P-methoxy phenyl- 1,3,4-thiadiazol 2yl] benzene have been synthesized and characterized by elemental analyses and spectral study.