A Summary of the Thesis entitled

Synthesis, Characterization and Studies on d^{10} Metal Complexes Derived from Acyl Pyrazolones

To be Submitted

As a partial fulfilment for the award of the degree of

DOCTOR OF PHILOSOPHY

In

Chemistry

By

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Summary of the Thesis work

To be submitted to The Maharaja Sayajirao University of Baroda for the award of the degree of DOCTOR OF PHILOSOPHY in Chemistry.

Name of Student: Shaikh Irfan Usmanbhai

Title of the Thesis: ***"Synthesis, Characterization and Studies on d^{10} Metal Complexes Derived from Acyl Pyrazolones"***

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Date of Registration: 04th August, 2017

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The Thesis work is presented in form of the following chapters:

Chapter 1
Introduction

Chapter 2
4- Acyl Pyrazolones and their Zinc (II) Metal Complexes: Synthesis, Characterization and Structural Features

Part a: Binary Mononuclear Zinc(II) Complexes of 4-acyl Pyrazolones: Synthesis, Characterization and Structural Features

Part b: Ternary Mixed Ligand Zinc(II) Complexes of 4-Acyl Pyrazolone with 2,2'-Bipyridine and 1,10'-Phenanthroline: Synthesis, Characterization and Structural Features

Chapter 3
4-Acylhydrazone-5-Pyrazolones and their Zinc(II) Metal Complexes: Synthesis, Characterization and Crystal Study

Part a: Synthesis, Characterization and Crystal Study of Zinc(II) Complexes of 4-Acylhydrazone-5-Pyrazolones

Part b: Synthesis, Characterization and Crystal Study of Mixed Ligand Zinc(II) Complexes of 4-Acylhydrazone-5-Pyrazolone with 2,2'-Bipyridine and 1,10-Phenanthroline

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Chapter 1: Introduction

Derivatives of pyrazolone, such as aminopyrine, isopropyl antipyrine, sulpyrine and antipyrine are widely used as non-steroidal anti-inflammatory drugs that exhibit potent antipyretic and analgesic activities.[1–3]

Jensen *et al.*, (1959) reported that a direct one-step synthesis was effected by treating a solution of 1-phenyl-3-methyl-pyrazol-5-one in dioxane containing suspended calcium hydroxide as a catalyst with an acid chloride or anhydride.[4] The acylpyrazolones ligands have shown to possess structural and electronic features for versatile coordination chemistry, which has rapidly grown in the last decade and expanded to metallic elements previously underestimated. The versatility of these molecules as ligands derives mainly from the easy functionalization on the C4 carbon of pyrazolone ring with different acyl moieties that can vary in complexity.[5]

4-acylhydrazones are prepared by reaction of 4- acyl-5-pyrazolones and acylhydrazides.[6] 4-acylhydrazone-5-pyrazolones have been much less investigated than 4-acylpyrazolone, till 2019 only three papers dealing on the molecular structure of such ligands being found in the free neutral keto form.[6]

Recent studies on pyrazolone derivatives especially those which bearing semicarbazone and thiosemicarbazone moieties show compounds have potential biological activities.[6]

The ruthenium metal complexes of acyl pyrazolone derivatives were tested against ovarian carcinoma, breast carcinoma, cervical carcinoma and hepatocarcinoma, some showing interesting selectivity and efficiency.[7–9] Many of copper complexes of pyrazolone synthon were investigated for their anticancer potentials against lung carcinoma[10], ovarian carcinoma[11], epidermoid carcinoma[12], esophageal carcinoma[13], cervical carcinoma[13], liver carcinoma[14], promyelocytic leukemia[15] and acute lymphocytic leukemia[15], some complexes being very promising and efficient.[6] 1-phenyl-3-methyl-5-hydroxypyrazole-4-methylene-8′-quinolineimine, and its Cu^{II}, Zn^{II}, and Ni^{II} complexes were subjected to cytotoxic tests, and experimental results indicated that the metal complexes show significant cytotoxic activity against lung cancer A 549 cells.[16]

Based on the fact, we have synthesized zinc (II) complexes of 4-acylpyrazolone and its derivatives. All ligands and their complexes have been screened for the *in vitro* and *in silico*

anti-malarial activity. Semicarbazone and thiosemicarbazone of pyrazolone based ligands and their four zinc(II) complexes have been screened for anticancer activity.[17–19]

CHAPTER 2: 4-Acyl Pyrazolones and their Zinc (II) Metal Complexes: Synthesis, Characterization and Structural Features

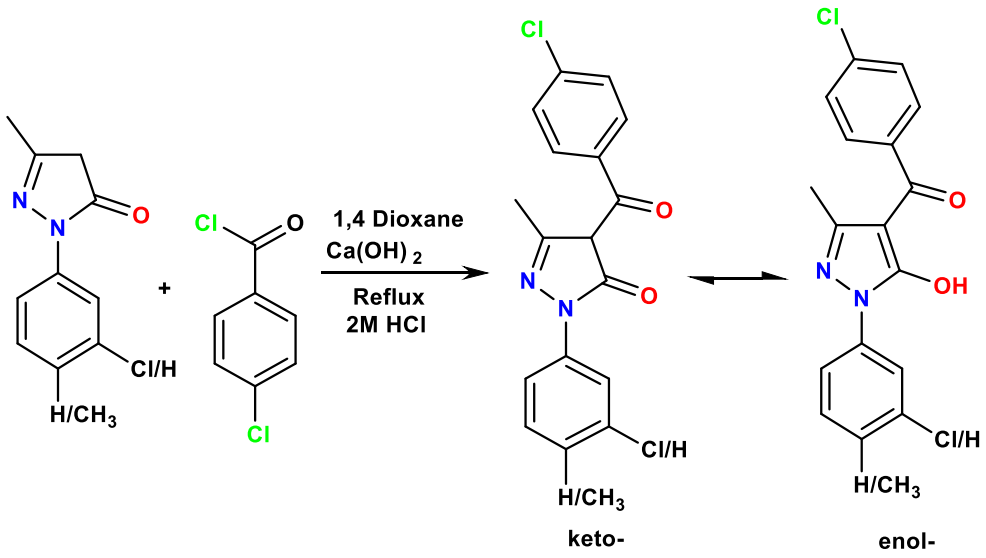
Chapter 2(a): Binary Mononuclear Zinc (II) Complexes of 4-acyl Pyrazolones: Synthesis, Characterization and Structural Features

Experimental

Syntheses of ligands

4-(4-chlorobenzoyl)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (L1)

M.P.: 105ºC, Yield: 70.85 %, M.F.: $C_{17}H_{13}ClN_2O_2$ (F.w. 312.75). IR (KBr, cm^{-1}): 1558 (C=N, cyclic), 1589 (C=O, *p*-chloro benzoyl group); 1619(C=O, Pyrazolone ring); ^{1}H NMR ($CDCl_3$, 400MHz): δ *ppm* 2.1 (s) (3H, Pyrazolone C-CH_3), 7.5-7.6 (dd, 4H Ar C-H), 7.4-7.8 (m, 5H Phenyl of pyrazolone); ^{13}C NMR ($CDCl_3$, 100MHz) δ*ppm* 191, 161, 148, 138, 137, 136, 129.3, 129.1, 128.8, 127, 121, 103, 16.[19]



Scheme 1. Synthesis of ligands L1-L3.

Synthesis of 4-(4-chlorobenzoyl)-2-(3-chlorophenyl)-5-methyl-2,4-dihydro-3H-pyrazol-3-ne (L2)

The synthesized ligand were reported in Shaikh *et. al.*, 2019, [18]. Yield: 58%. M.F.: $C_{17}H_{12}Cl_2N_2O_2$, F.w.: 347.20. M.P.: 105 °C.Λ_m (S cm^2 mol^{-1}): 8.8.FTIR (KBr) υ (cm^{-1}): 1625(s) (C=O, amide of pyrazolone), 1590(m) (C=O, *p*-chloro benzoyl), 966(s) (N-N of pyrazolone), 1486(m) (aromatic –C-C). ^{1}H NMR ($CDCl_3$) δ ppm: 2.14 (s, 3H, pyrazolone C–CH_3), 7.28-7.30 (m, 1H, m-chloro ph), 7.39-7.43 (m, 1H, *m*-chlorophenyl), 7.51-7.63 (m, 4H, *p*-chloro benzoyl), 7.83-7.85 (m, 1H, *m*-chloro ph), 7.963-7.968 (m, 1H, m-chloro ph). ^{13}C NMR ($CDCl_3$, 100MHz) δ ppm: 16 (-CH_3- pyrazolone), 103, 118, 120, 126, 128, 129, 130, 134, 135, 138, 138, 147 , 162 (C=O, amide of pyrazolone), 190 (C=O, *p*-chloro benzoyl).[19]

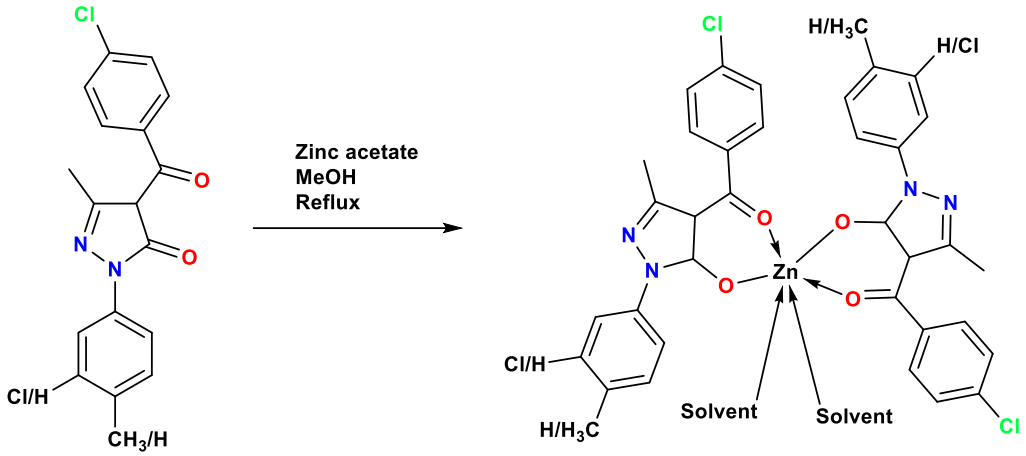
Synthesis of 4-(4-chlorobenzoyl)-5-methyl-2-(*p*-tolyl)-2,4-dihydro-3H-pyrazol-3-one (L3)

Synthesized ligand was reported in Shaikh et al., 2019.[19] Yield: 65.5 %, M.F.: $C_{18}H_{15}ClN_2O_2$, (F.w.: 326.78), M.P.: 108ºC, Λ_m (S.cm^2.mol^{-1}): 10.1, IR (KBr, cm^{-1}): 1551(C=N, cyclic), 1590 (C=O, *p*-chloro benzoyl group) 1625 (m) (C=O, Pyrazolone ring); ^{1}H NMR ($CDCl_3$, 400MHz): δ *ppm* 2.1 (s, 3H, Pyrazolone C-CH_3), 2.38-2.39(m, 1H, -CH-cyclic), 2.4 (s,3H, CH_3-Ar) , 7.28-7.30 (d, 2H, aromatic, *J*=8Hz), 7.50-7.52(m, 2H, aromatic), 7.60-7.62 (d, 2H, *p*-chloro benzoyl-, *J*=8Hz),7.72-7.74 (d, 2H, *p*-chloro benzoyl-, *J*=8Hz); ^{13}CNMR ($CDCl_3$, 100MHz) 16(-CH_3, pyrazolone), 21(-CH_3-tolyl), 30 (CH_3-pyz), 103, 121, 128.7, 129, 130, 131, 135, 136, 138, 147, 160 (C=O, amide of pyrazolone), 191 (C=O, *p*-chloro benzoyl).[19]

Synthesis of binary Zinc (II) complexes 1-3.

[$Zn(L1)_2(CH_3OH)_2$] (Complex 1)

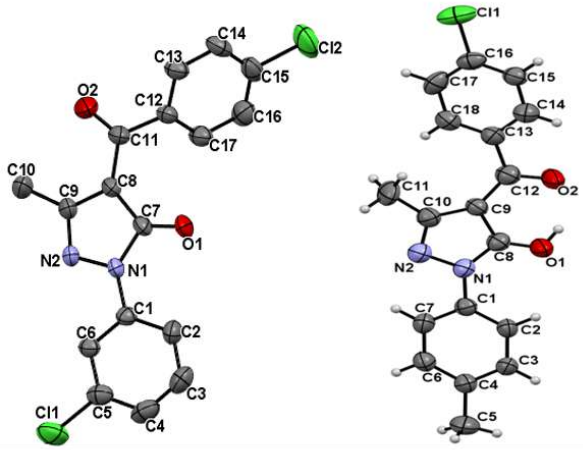
M.P. >200 ºC, Yield 78 %, M.F.: $C_{36}H_{32}Cl_2N_4O_6Zn$ (F.W.: 752.95); IR (KBr, cm^{-1}): 3109 (co-ordinated CH_3-OH), 1613 (C=O, *p*-chloro benzoyl group), 1494 (C=N cyclic), 1457 (C-O, pyrazolone ring), 505 (Zn-O); ^{1}H NMR (DMSO-d6) δ *ppm* 1.6 (s, 3H pyrazolone CH_3-), 7.53-7.42 (dd, 4H, *p*-chloro benzoyl), 7.9-7.1(Ar-H, phenyl of pyrazolone).[19]



Scheme 2. Synthesis route of binary zinc (II) complexes **1-3** of 4-acyl pyrazolone. (In the complex **1** coordinated solvent is Methanol, in complex **2** and **3** coordinated solvents are water.)

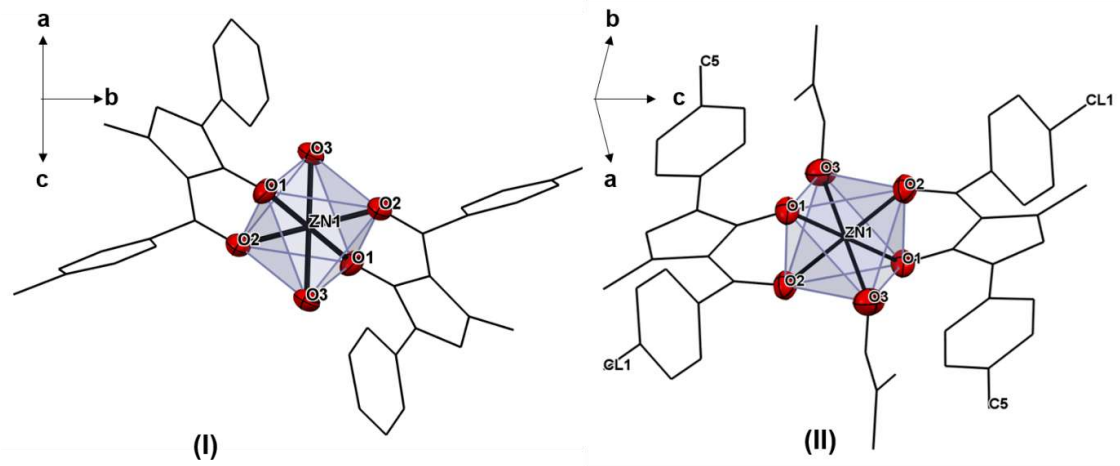
Results and Discussion

Crystal feature of ligand L2 and L3.



Crystal features of Complex 1 $[Zn(L1)_2(CH_3OH)_2]$ and Complex 3 $[Zn(L3)_2(DMF)_2]$

The axial metal-oxygen bond distances are longer than basal metal-oxygen bond distances. All atoms of the chelate and pyrazolone rings lie almost in the same plane.[19,20]



The geometry of (I) complex **1** and (II) complex **3** by polyhedral-wireframe style in mercury.

For crystallization, Complex **3** was dissolved in hot DMF and the filtrate kept for one and a half months for slow evaporation. As the water molecule has weak coordination ability than DMF, coordinated water molecules were replaced by DMF molecules during the crystallization of complex **3**.[19]

Thermogravimetric analysis

Binary complexes show the first degradation at up to 100 °C due to the coordinated solvent molecules in the complexes. Complex **2** and **3** contain water molecule in the complex and complex **1** having coordinated MeOH molecule in the complex.[19]

Electronic spectral Study

In the Uv/Vis spectra, the first intense band is attributed to a ligand-centered (LC) π–π* transition localized on the aromatic rings of the ligand and LMCT band at around 350-360 nm.[19]

Molar conductance

The 4- Acyl pyrazolones and its complexes found to be below 14 ohm^{-1} cm^2 mol^{-1}, so the conductance measurements in DMSO suggest that they are non-electrolytes.[19,21]

Conclusion

The 4-acyl pyrazolone ligands have been prepared by the acylation of pyrazolone derivatives with 4-chloro benzoyl chloride. Ligands and zinc(II) complexes have been characterized by

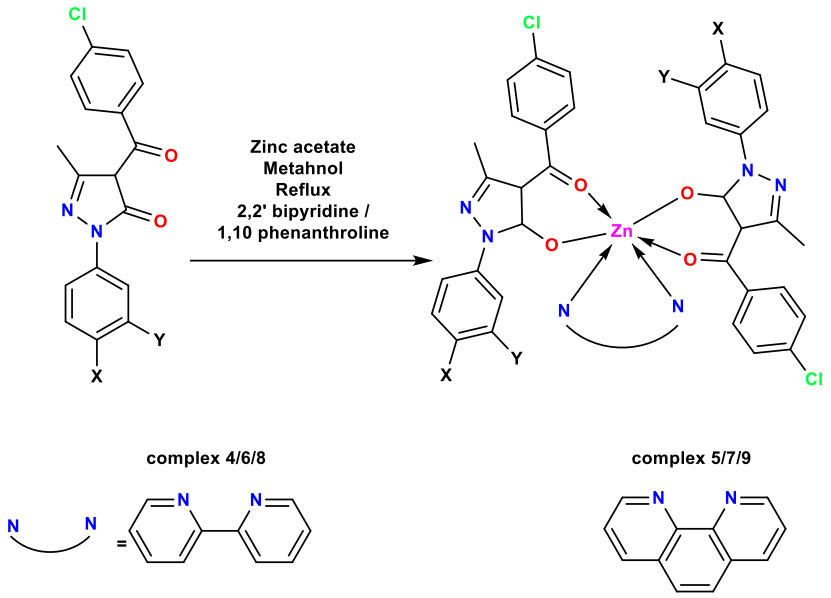
modern spectroscopic and analytical method. Single crystal of two binary zinc(II) complexes of acylpyrazolone found octahedral by SXRD study.

Chapter 2(b): *Ternary Mixed Ligand Zinc (II) Complexes of 4-Acyl Pyrazolone with 2,2'-Bipyridine and 1,10-Phenanthroline: Synthesis, Characterization and Structural Features*

Experimental

Synthesis of complex 4 $[Zn(L1)_2(bpy)]$

M.P. >200ºC, Yield 82.42%, M.F.: $C_{42}H_{30}Cl_2N_6O_4Zn$ (M.W. 819.02); Metal estimation by gravimetrically and volumetrically Zn=7.12%. **FTIR (KBr, cm^{-1}):** 1622 (m) (C=O *p*-chloro benzoyl group), 1527 (s) (C=N cyclic), 1469 (C-O, pyz ring), 480 (Zn-O), 422 (Zn-N); **^{1}H NMR ($CDCl_3$, 400MHz)** (δ *ppm):* 1.62 (s, 3H, CH_3-Pyz), 7.08-7.90 (m, 2H, phenyl of pyz), 8.01-9.06 (m, 4H, 2,2′-bipyridine).[19] **^{13}C NMR ($CDCl_3$, 100MHz):** δ 16.65, 105, 120, 121, 124, 126, 128, 128.5, 129, 136, 139, 140, 148, 149, 150, 167 and 190.



Scheme 3. Synthesis route for mixed ligand complexes **4-9.** For complex **4** & **5**: X=Y=-H, complex **6 & 7**: X=-H, Y=-Cl, and complex **8** & **9**: X=-CH_3, Y=-H.

Synthesis of complex 5 $[Zn(L1)_2(phen)]$

Yield: 86.7%. M.P.: >200°C.Anal. Calcd for $C_{48}H_{40}Cl_2N_6O_4Zn$: C, 63.98; H, 4.47; N, 9.33%, Found: C, 64.01, H, 4.55; N, 9.65%. M.w.: 901.17. Λ_m ($S.cm^2.mol^{-1}$): 9.7. Metal estimation by gravimetrically and volumetrically Zn=7.26%. **FTIR (KBr, cm^{-1}):** 1562(C=N, cyclic), 1622

(C=O, 4-chloro benzoyl group), 943(s) (N-N), 1436 (s) (Ar-C-C-). **^{1}H NMR ($CDCl_3$, 400MHz) δ ppm:**1.6 (s,3H, CH_3-tolyl), 2.2 (s, 3H, Pyz-C-CH_3) , 6.99-7.02 (d, 2H, aromatic-H, *J*=8Hz), 7.24-7.31(m, 2H, ar-H), 7.60-7.62 (d, 2H, aromatic-H, *J*=8Hz),7.72-7.74(d, 2H, 4-chloro benzoyl-, *J*=8Hz).9.30-9.31 (m, 1H, aromatic), 8.49-8.51(m, 1H, phen).

Complex 6 $[Zn(L2)_2(bpy)]$

M.P. >200ºC, Yield 88.42%, Molecular formula: $C_{44}H_{34}Cl_4N_6O_4Zn$, F.W. 917.97 g/mol, Zinc estimation: 7.12%. **FTIR (KBr, cm^{-1}):** 1621 (m) (C=O p-chloro benzoyl group), 1597 (s) (C=N cyclic), 1470 (C-O, pyz ring), 481 (Zn-O), 439 (Zn-N); **^{1}H NMR ($CDCl_3$, 400MHz) δ ppm:** 1.62 (s, 3H, CH_3-Pyz), 7.08-7.90 (H- Ar protons of pyz), 8.01-9.06 (m, 4H, 2,2′-bipyridine). **^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm**: 16.5 (CH_3-pyz), 104, 117, 119, 121, 124, 126, 128, 129, 130, 134, 136, 139, 140, 141, 148, 149, 150, 166 and 190.

Complex 7 $[Zn(L2)_2(phen)]$

M.P. > 200ºC, Yield: 81.5%. Anal. Calcd for $C_{46}H_{34}Cl_4N_6O_4Zn$: C, 58.64; H, 3.47; N, 8.33%, Found: C, 58.65, H, 3.64; N, 8.92%. F.w.: 942.00 g/mol. Λ_m (S cm^2 mol^{-1}): 9.5. Metal estimation by gravimetrically and volumetrically Zn=6.94%. **FTIR (KBr, cm^{-1}):** 1622 (C=O, 4-chloro benzoyl group), 1565(C=N, cyclic), 1433 (s) (Ar-C-C-), 956(s) (N-N), 583 (M-O), 491 (M-N). **^{1}H NMR ($CDCl_3$, 400MHz) δ ppm** 2.2 (s, 3H, Pyz-C-CH_3) , 7.01-7.02 (d, 2H, ar-H, *J*=8Hz), 7.26-7.33(m, 2H, ar-H), 7.70-7.82 (d, 2H, ar-H, *J*=8Hz),7.93-8.00 (d, 2H, 4-chloro benzoyl-, *J*=8Hz).9.33-9.35 (m, 1H, aromatic), 8.53-8.55 (m, 1H, phen). **^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm** 16.58, 104, 117, 119, 124, 125, 126, 128, 129, 129.5, 130, 133, 136, 138, 139, 140, 141, 149, 149.5, 167 and 190.

Complex 8 $[Zn(L3)_2(bpy)]$

Yield 88.25%, Molecular formula: $C_{46}H_{40}Cl_2N_6O_4Zn$ (F.w. 877.14 g/mol), M.P. >200ºC; FTIR (KBr, cm^{-1}): 1626 (m) (C=O p-chloro benzoyl group), 1513 (s) (C=N cyclic), 1476 (C-O, pyz ring), 511 (Zn-O), 476 (Zn-N); **^{1}H NMR ($CDCl_3$, 400MHz) δ ppm** :1.62 (s, 3H, CH_3-pyz), 2.19(s, 3H, CH_3-toluyl), 6.99-7.68 (H-Ar, phenyl of pyz), 8.04-9.01 (m, 4H, 2,2′-bipyridine).[19] **^{13}C NMR ($CDCl_3$, 100MHz) δ ppm:** 16.67, 21, 120, 121, 126, 128, 129, 130, 140 and 150.

Complex 9 $[Zn(L3)_2(phen)]$

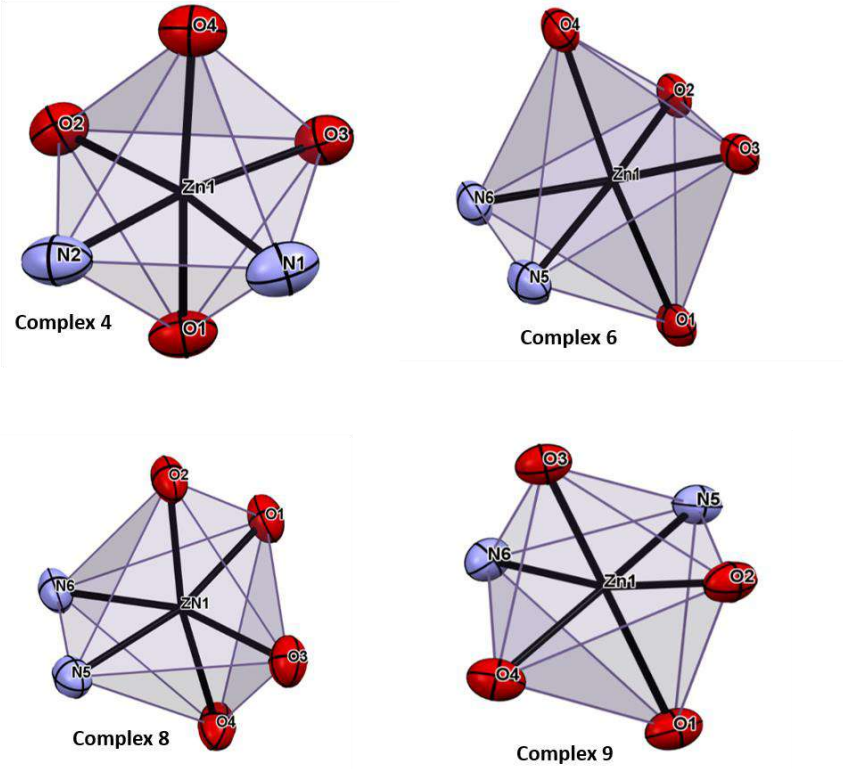
Yield: 82.60%. M.w.: 901.17. M.P.: >200°C. Molar conductance: Λ_m (S.cm^2.mol^{-1}): 9.5. Metal estimation by gravimetrically and volumetrically Zn=7.26%; Anal. Calcd for $C_{48}H_{40}Cl_2N_6O_4Zn$: C, 63.98; H, 4.47; N, 9.33%, Found: C, 64.01, H, 4.55; N, 9.65%. **FTIR (KBr, cm^{-1}):** 1622 (C=O, 4-chloro benzoyl group), 1562(C=N, cyclic), 943(s) (N-N), 1436 (s)

(Ar-C-C-). **^{1}H NMR ($CDCl_3$, 400MHz) δ *ppm*:**1.6 (s,3H, CH_3-tolyl), 2.2 (s, 3H, Pyz-C-CH_3) , 6.99-7.02 (d, 2H, aromatic-H, *J*=8Hz), 7.24-7.31(m, 2H, ar-H), 7.60-7.62 (d, 2H, aromatic-H, *J*=8Hz),7.72-7.74(d, 2H, 4-chloro benzoyl-, *J*=8Hz), 9.30-9.31 (m, 1H, aromatic), 8.49-8.51(m, 1H, phen). **^{13}C NMR ($CDCl_3$, 100MHz) δ *ppm:*** 16.7, 21, 104.3, 120, 126.6, 128, 129, 129.1.

Results and discussion

Crystal structures complexes

The single crystals of complexes **4, 6, 8** and **9** are solved and studied well. SCXRD revealed that all complexes have octahedral geometry around zinc (II) ion.



Electronic spectral studies

Electronic spectra of ligands (**L1, L2** and **L3**) and their zinc complexes **4-9** were recorded in DMSO. First intense band is attributed to a ligand-centered (LC) π–π* transition localized on the aromatic rings of the ligand, while the shoulder due to its metal coordination and and LMCT band at around 350-360 nm.

Thermogravimetric analysis.

In the TGA graph of complexes **4-9**, the complexes were observed air stable. The thermal study was carried out using the thermogravimetric technique with a heating rate of 10 ^{o}C min^{-1}. In

the TGA plot of complex **4-9,** there were no degradation up to 200 ºC, therefore, the good agreement of lattice water or methanol molecule absent in the complex structure.

Molar conductance study

The conductance measurements suggest that they are non-electrolytes.[21]

Chapter 3: 4-Acylhydrazone-5-Pyrazolones and their Zinc(II) Metal Complexes: Synthesis, Characterization and Crystal Study

Chapter 3(a): Synthesis, Characterization and Crystal Study of Zinc(II) Complexes of 4-Acylhydrazone-5-Pyrazolones

Synthesis of Ligands

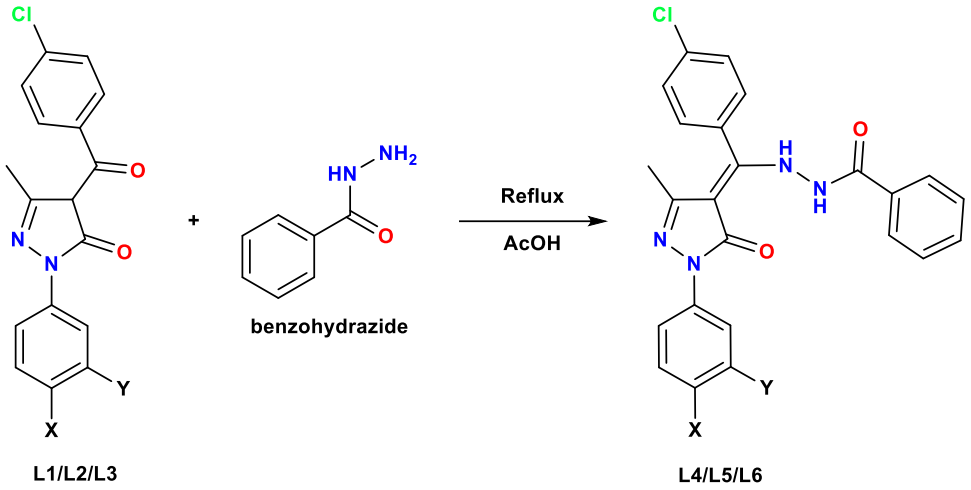
Synthesis of Ligand L4 ((Z)-N'-((4-chlorophenyl)(3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)methylene)benzohydrazide)

Yield: 65%, M.P.: 190 °C, M.F.: $C_{24}H_{19}ClN_4O_2$, F.w.: 430.89, Ele. Ana. Calcd. (Found): C, 66.90 (66.88); H, 4.44(4.56); N, 13.00(13.45) %. **FTIR selected bands (KBr) cm^{-1}:** 1640 (C=O, pyz), 1593 (C=O, bhz), 1569 (C=N, imine), 1455(C=C, pyz), 1349 (C-N, pyz), 903(C-Cl, *p*-chloro benzoyl pyz). **^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm:** 1.8 (s, 3H, Me-pyz), 7.25 (t, 1H, ph-pyz), 7.45-7.54 (m, ar-H), 7.60 (t, 1H, bhz), 7.96 (s, 1H, -NH, bhz), 8.01(d, *J*=8 Hz, ar-H**). ^{13}C NMR ($CDCl_3$, 100MHz)δ:** 16.4 (CH_3-pyz), 99.1, 100.7, 119.6, 120.2, 125.3, 127.2, 127.4, 128.0, 128.7, 128.9, 129.6, 130.5, 131.4, 132.5, 132.8, 137.1, 138.0, 138.7, 139.0, 147.9, 148.8, 153.6 (C-O), 163.3 (C=N), 163.7 (C=O). Synthesis route of ligands (L4-L6) displays in Scheme 4.

Synthesis of Ligand L5 ((Z)-N'-((4-chlorophenyl) (1-(3-chlorophenyl)-3-methyl-5-oxo-4, 5-dihydro-1H-pyrazol-4-yl) methylene) benzohydrazide)

M.P.: 195 °C, M.F.: $C_{24}H_{18}Cl_2N_4O_2$, F.w.: 465.33, EA Calcd (Found): C, 61.95(61.88); H, 3.90(3.99); N, 12.04(12.55) %. **FTIR (KBr plates) cm^{-1}:** 1641 (C=O, pyz), 1592 (C=O, bhz), 1571 (C=N, imine), 1455(C=C, pyz), 1351 (C-N, pyz), 900(C-Cl, *p*-chloro benzoyl pyz). **^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm:** 1.8 (s, 3H, CH_3-pyz), 7.21(d, 1H, m-Cl-ph, *J*=8Hz), 7.38(t, 1H, bhz), 7.51-7.64(m, 6H), 7.98(s, 1H,-NH), 8.11(d, 1H, *J*=8Hz), 15.4 (s, 1H, OH-pyz). **^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm:** 16.4 (CH_3-pyz), 98.9, 103.7, 117.8, 119.9, 120.6, 125.0,

126.6, 129.1, 130.2, 131.3, 133.0, 135.5, 138.1, 139.4, 148.0, 149.2, 153.3, 161.9 (C=N), 163.7(C=O, bhz), 190.2 (C=O, pyz).



Scheme 4. Synthesis route of ligands **L4-L6**, where **(i) L1** and **L4: X=Y=-H, (ii) L2** and **L5: X=-H; Y=-Cl**, and **(iii) L3** and **L6: X=-CH_3; Y=-H.**

Synthesis of L6 ((Z)-N'-((4-chlorophenyl) (3-methyl-5-oxo-1-(*p*-tolyl)-4,5-dihydro-1H-pyrazol-4-yl)methylene)benzohydrazide)

Yield: 72%, M.P.: 195 °C, M.F.: $C_{25}H_{21}ClN_4O_2$, F.w.: 444.92, Ele. Ana. Calcd (Found): C, 67.49(67.55); H, 4.76(4.88); N, 12.59 (12.67) %, **FTIR (KBr plates) cm^{-1}:** 1641 (C=O, pyz), 1595 (C=O, bhz), 1571 (C=N, imine), 1487(C=C, pyz), 1348 (C-N, pyz), 897 (C-Cl, *p*-chloro benzoyl pyz). **^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm:** 1.6 (s, 3H, Me-pyz), 2.40 (s, 3H, *p*-tolyl), 7.25 (d, 2H, *p*-tolyl pyz, *J*=8Hz), 7.50 (t, 2H, phenyl bhz), 7.60 (t, 2H, bhz), 7.77 (d, 2H, *p*-tolyl bhz, *J*=8Hz), 7.99 (d, 2H, phenyl, *J*=8Hz), 15.8 (s, 1H, pyz-OH) . **^{13}C NMR (DMSO-d6, 100 MHz) δ ppm:** 16.0(CH3-pyz), 21.0(p-tolyl-pyz), 118.9, 120.5, 121.1, 121.7, 128.3, 128.8, 129.0, 129.2, 129.5, 129.7, 129.9, 130.3, 131.2, 135.8, 136.7, 137.0(C-O), 147.5(C=N), 165.1(C=O, pyz).

Synthesis of complex 10-12

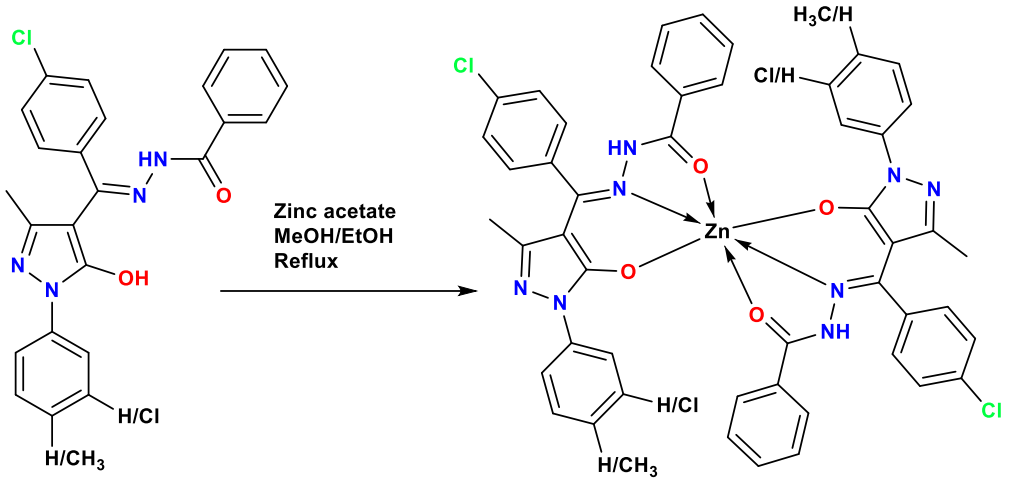
Synthesis of complex 10 [Zn $(L4)_2$]

Yield: 75%, M.P. >200 C, Molecular formula: 925.15, $C_{48}H_{36}Cl_2N_8O_4Zn$, Ele. Ana. Calcd (found): C, 62.32 (62.33); H, 3.92 (3.88); N, 12.11 (12.22) %, Metal est. Calcd (found): Zn, 7.07(7.11) %. **FTIR (KBr Plates, cm^{-1}):** 3378 (N-H, bhz), 1601(C=O, bhz), 1583 (C=N, pyz), 1565 (C=N, imine of bhz), 1286 (C-O, pyz), 917 (C=C, pyz), 440(M-O, pyz-Zn). **^{1}H NMR**

($CDCl_3$, 400MHz) δ ppm: 1.64 (s, 3H, Me-pyz), 7.01-7.90 (m, 8H, bhz-pyz), 8.09-8.11 (d, 2H, bhz-pyz), 8.95(s, 1H, N-H).

Synthesis of complex 11 [Zn $(L5)_2$].

Yield: 72%, M.P.: >200 C, Molecular formula: $C_{48}H_{34}Cl_4N_8O_4Zn$, Elem. anal. Calcd (found): C, 58.00(57.88); H, 3.45(3.77); N, 11.27(11.45), Formula weight: 994.03, Metal estimation theoretical (found): Zn, 6.58(6.75) %. **FTIR selected bands (KBr Plates, cm^{-1}):** 3378 (N-H, bhz), 1601(C=O, bhz), 1583 (C=N, pyz), 1541 (C=N, imine of bhz), 1286 (C-O, pyz), 917 (C=C, pyz), 440(M-O, pyz-Zn). **^{1}H NMR ($CDCl_3$, 400MHz) δ ppm:** 1.62 (s, 3H, Me-pyz), 7.00-8.09(m, 8H, ligand L5), 8.95 (rs, 1H, N-H, bhz). **^{13}C NMR ($CDCl_3$, 100 MHz)δ:** (16.2, 117.9, 119.8, 123.6, 126.8, 139.1, 139.6, 130.0, 130.3, 130.5, 133.0, 133.6, 137.0, 140.5, 157.9, 162.3 (C-O), 163.1 (C=N), 164.0 (C=O).



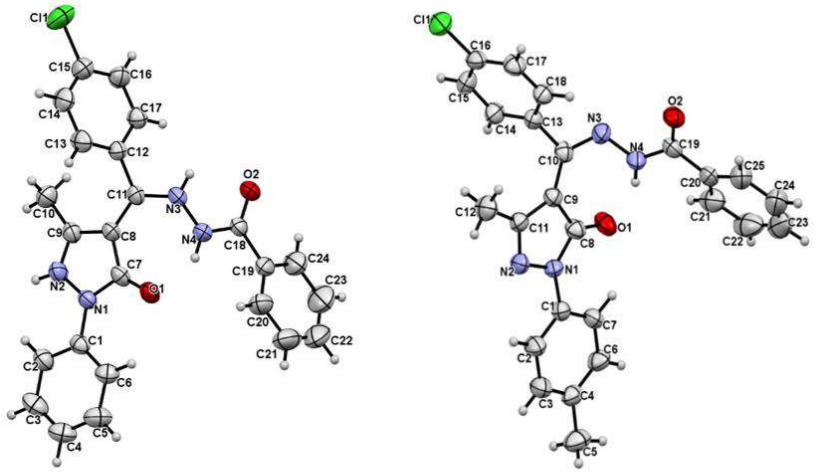
Scheme 5. Synthesis route of complex **10-12**.

Synthesis of complex 12 [Zn $(L6)_2$]

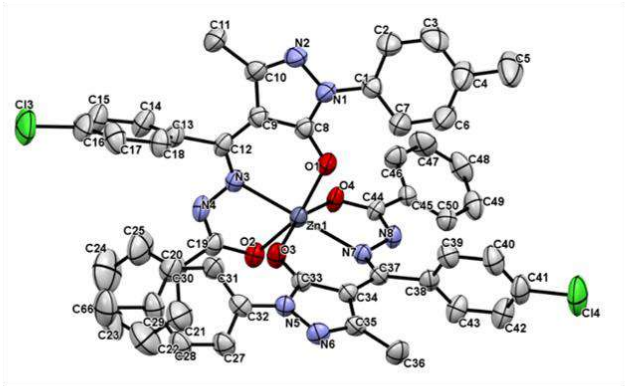
Yield: 70%, M.P.: >200 C, M.F.: $C_{50}H_{40}Cl_2N_8O_4Zn$, Elem. anal. Calcd. (Found): C, 63.00(63.34); H, 4.23(4.48); N, 11.76(12.00), F.w.: 953.20 Metal estimation theoretical (found): Zn, 6.86(7.01) %. **FTIR selected bands (KBr, cm^{-1}):** 3378 (N-H, bhz), 1616(C=O, bhz), 1567 (C=N, pyz), 1539 (C=N, imine of bhz), 1283 (C-O, pyz), 944 (C=C, pyz), 439(M-O, pyz-Zn). **^{1}H NMR ($CDCl_3$, 400MHz) ppm:** 1.62 (s, 3H, Me-pyz), 2.29(s, 3H, *p*-tolyl,-pyz), 7.01 (d, 2H, *p*-tolyl), 7.36-7.52 (m, 4H, bhz-pyz), 8.88(rs, 1H, N-H, bhz). **^{13}C NMR ($CDCl_3$, 100 MHz) *δ*:** 15.8 (CH_3-pyz), 21.0 (CH_3, *p*-tolyl), 97.1, 121.0, 126.7, 128.9, 129.0, 129.4, 129.6, 130.3, 130.4, 130.5, 132.7, 134.0, 136.8, 147.6, 157.9 (C-O), 162.7 (C=N), 163.6 (C=O).

Results and discussion

Crystal features of ligand L4, L6 and Complex 12



L4 **L6**



Complex 12

ORTEP diagram with ellipsoid 50% probability.

The single crystal was obtained and the study was carried out which is a perfect agreement of ligand formation of structure.

Thermogravimetric analysis

Thermogravimetric analysis observed of complexes **10-12**. TGA plots of all complexes showed the same degradation after 320 °C due to pyrolysis of 4-acylhydrazone-5-pyrazolones (**L4-L6**) of all three complexes. There was no degradation observe up to 300 °C. Hence, there were coordinated or lattice molecules solvent not present in complexes **10-12**. All complexes showed

air and heat stable up to 320 °C temperature. TGA graph reviled that all complexes showed the same configuration ML_2 (L=**L4/L5/L6**) in their structure geometry.

Electronic spectra of ligands (L4-L6) and complexes 10-12.

The first intense band at 270-280 nm attributed to a ligand-centered (LC) π–π* transition localized on the aromatic rings of the ligand, while the shoulder is due to its metal coordination LMCT bands observed at around 340-350 nm.

Molar conductance of ligands and complexes.

The conductance measurements suggest that they are non-electrolytes.[19,21]

Conclusion

In summary, three new 4-acylpyrazolone derivatives (**L4-L6**) were synthesized and **characterized by various spectroscopic techniques.** Study on **SXRD** has been suggested a distorted octahedral environment around the zinc through coordination of many of **trident O, *N,* O-chelating 4-acylhydrazone-5-pyrazolone ligands.**

Chapter 3(b): Synthesis, Characterization and Crystal Study of Mixed Ligand Zinc(II) Complexes of 4-Acylhydrazone-5-Pyrazolone with 2,2′-Bipyridine and 1,10-Phenanthroline

Experimental

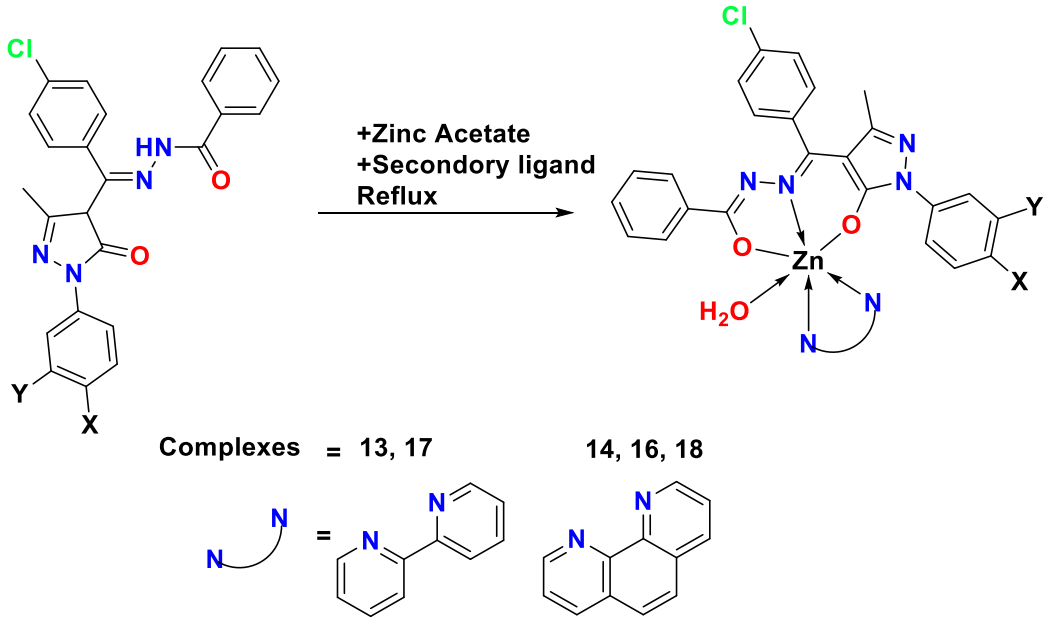
Synthesis of complexes 13-18

Synthesis of complex 13 [Zn (L4) (bpy) (H_2O)]

Yield: 78%, M.P. >200 C, M.F.: $C_{34}H_{27}ClN_6O_3Zn$, F.w.: 668.46 g mol^{-1}, EA Calcd. (Found): C, 61.09(61.33); H, 4.07(4.18); N, 12.57(12.25) %, Metal est. Calcd. (Found): Zn, 9.78 (9.11) %. **FTIR (KBr, cm^{-1}):** 3375 (N-H, bhz), 1601(C=O, bhz), 1567 (C=N, pyz), 1540 (C=N, imine of bhz), 1052 (C-O, pyz), 913 (C=C, pyz), 440(M-N, bhz-Zn). **^{1}H NMR ($CDCl_3$, 400MHz) *δ* ppm:** 1.53 (s, 3H, Me-pyz), 7.07 (t, 1H, *J*=7.2; 14.8 Hz, ar-H), 7.24 (t, 2H, *J*=8; 15.6 Hz,),7.38 (t, 2H, *J*=8; 15.2 Hz, bhz) 7.48-7.60 (m, 5H, bhz-pyz), 7.71(d, 2H, *J*=8Hz, ar-H), 7.79 (d, 2H, *J*=8Hz, ar-H), 8.71(N-H, bhz). **^{13}C NMR ($CDCl_3$, 100MHz) *δ*:** 16.2(CH_3-pyz), 97.3, 120.1, 124.4, 127.6, 128.2, 128.7, 128.9, 129.0, 129.6, 130.8, 131.4, 132.2, 135.2, 139.7, 160.9 (C-O), 163.2 (C=N), 166.7 (C=O).

Synthesis of complex 14 [Zn(L4)(phen)(H_2O)].

Yield: 76 %, M.P.: >200 °C, M.F.: $C_{36}H_{27}Cl_1N_6O_3Zn$, F.w.:692.48 g mol^{-1}, EA Calcd (found): C, 62.44(62.88); H, 3.93(3.78); N, 12.14(12.45), Metal estimation Calcd (found): Zn, 9.44(9.75) %. **FTIR (KBr Plates, cm^{-1}):** 3376 (N-H, bhz), 1600(C=O, bhz), 1566 (C=N, pyz), 1493 (C=N, bhz), 917 (C=C, pyz), 510(M-O, AHP-Zn), 440(M-O, pyz-Zn). **^{1}H NMR ($CDCl_3$, 400MHz) δ ppm:** 1.35 (s, 3H, Me-pyz), 7.04 (t, 1H, *J*=8; 14.4 Hz, Ar-H), 7.18 (t, 2H, *J*=5.2; 14.8 Hz), 7.38-7.74 (m, 10H, ar-H), 8.87 (N-H, bhz). **^{13}C NMR ($CDCl_3$, 100MHz) δ:** 16.2(CH_3-pyz), 97.3, 120.1, 124.4, 127.7, 128.2, 128.4, 128.7, 128.9, 129.6, 130.9, 131.5, 132.3, 135.2, 139.7, 147.4, 160.9 (C-O), 163.2 (C=N), 166.7 (C=O).

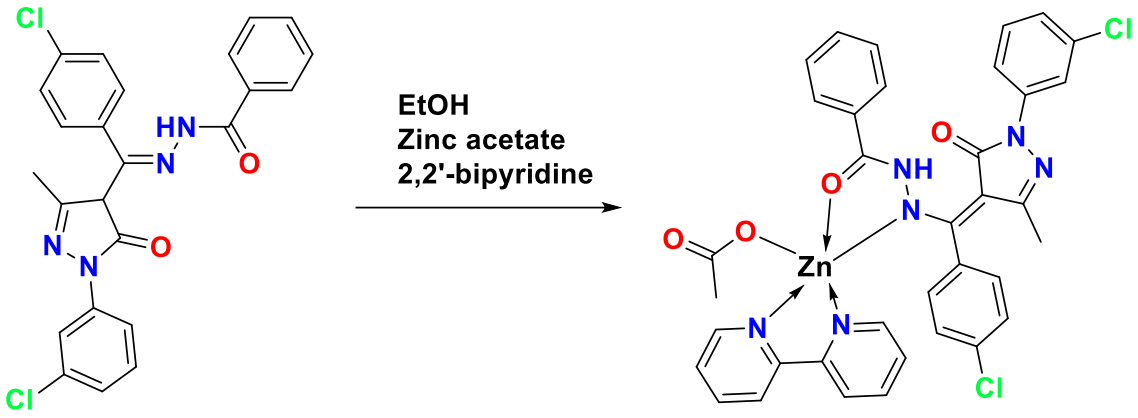


Scheme 6. Synthesis route of complexes **13, 14, 16-18.** Where for complexes **13** & **14: X=Y=** -H, **16: X=-H, Y= -Cl, 17&18: X=** -CH_3**, Y=** -H**.**

Synthesis of complex 15 [Zn(L5)(bpy)(AcO)]

Yield: 72%, M.P.: >200 °C, M.F.: $C_{38}H_{36}Cl2N_6O_5Zn$, F.w.: 793.02 g mol^{-1}, EA Calcd (found): C, 57.55(57.34); H, 4.58(4.57); N, 10.60(10.66) %, Metal estimation Calcd (found): Zn, 8.24 (8.21) %. **FTIR (KBr Plates, cm^{-1}):** 3377 (N-H, bhz), 1603(C=O, bhz), 1540 (C=N, bhz), 1285 (C-O, pyz), 954 (C=C, pyz), 513(M-O, pyz-Zn), 440(M-N, bpy). **^{1}H NMR ($CDCl_3$, 400MHz) δ ppm:** 1.51 (s, 3H, Me-pyz), 7.02(d, 2H, J=7.6 Hz, ar-H), 7.18 (t, 1H, J=5.6; 16 Hz), 7.40(t, J= 7.6; 15.2 Hz), 7.64 (m, 8H), 8.09 (t, J=2; 4 Hz), 8.88(s, 1H, N-H, bhz). **^{13}C NMR ($CDCl_3$, 100 MHz) δ:** 15.8 (CH3-pyz), 97.0, 117.9, 119.8, 123.8, 126.8, 129.0, 129.2,

129.4, 129.6, 130.0, 130.3, 130.3, 130.5, 132.9, 133.6, 137.0, 140.5, 148.5 (C-O), 157.9 (C=N), 164.02 (C=O, bhz). Synthesis route is displayed in scheme 7.



Scheme 7. Synthesis route of complex **15**.

Synthesis of complex 16 [Zn(L5)(phen)(H_2O)].

Yield: 72%, M.P.: >200 °C, M.F.: $C_{36}H_{26}Cl_2N_6O_3Zn$, F.w.:726.92 g mol^{-1}, Ele. Ana. Cald (found): C, 59.48 (59.88); H, 3.61 (3.73); N, 11.56 (12.00) %, Metal estimation Cald (found): Zn, 9.00(9.35) %. **FTIR (KBr, cm^{-1}):** 3378 (N-H, bhz), 1601(C=O, bhz), 1583 (C=N, pyz), 1541 (C=N, imine of bhz), 1285 (C-O, pyz), 918 (C=C, pyz), 513(M-O, pyz-Zn), 440(M-N). **^{1}H NMR ($CDCl_3$, 400MHz) δ ppm:** 1.51 (s, 3H, Me-pyz), 7.02 (d, 1H, J=7.6 Hz), 7.18 (t, 1H, 8; 16 Hz), 7.62 (m, 8H), 8.09(s, 1H), 8.95 (s, 1H, N-H-bhz). **^{13}C NMR ($CDCl_3$, 100 MHz) δ:** 15.8(CH_3-pyz), 97.0, 117.9, 119.8, 123.8, 126.8, 129.0, 129.2, 129.4, 130.0, 130.3, 130.3, 130.5, 132.9, 133.6, 137.0, 140.5, 148.5(C-O), 157.6(C=N), 164.0(C=O).

Synthesis of complex 17 [Zn (L6) (bpy) (H_2O)]

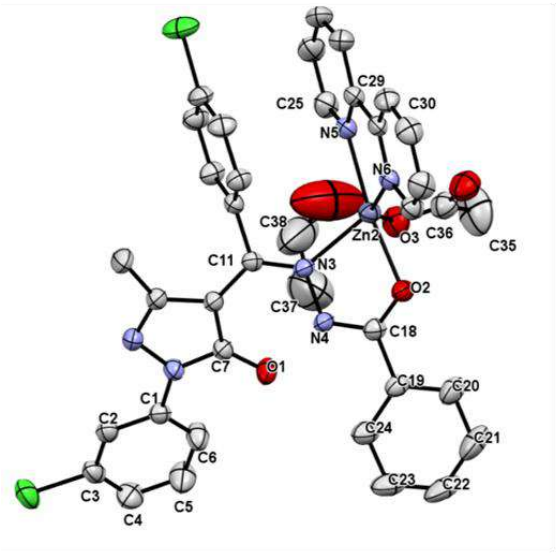
Yield: 82%, M.P.: >200 C, M.F.: $C_{35}H_{29}ClN_6O_3Zn$, F.w.:682.49 g mol^{-1}, EA Calcd (found): C, 61.60(59.88); H, 4.28(4.27); N, 12.31(12.45), Metal estimation Calcd (found): Zn, 9.58(9.75) %. **FTIR (KBr, cm^{-1}):** 3378 (N-H, bhz), 1616(C=O, bhz), 1567 (C=N, pyz), 1539 (C=N, imine of bhz), 1284 (C-O, pyz), 944 (C=C, pyz), 511(M-O, pyz-Zn), 440(M-N). **^{1}H NMR ($CDCl_3$, 400MHz) δ:** 1.53 (s, 3H , Me-pyz), 2.29(s, 3H, *p*-tolyl-pyz), 7.03(d, 2H, *J*=8.4), 7.37 (t, 2H, *J*=7.6; 15.6), 7.51 (m, 5H, bhz-pyz), 7.63 (d, 2H, *J*=8) 7.70 (d, 2H, *J*=8Hz), 8.85(N-H, bhz).

Synthesis of complex 18 [Zn (L6) (phen) (H_2O)].

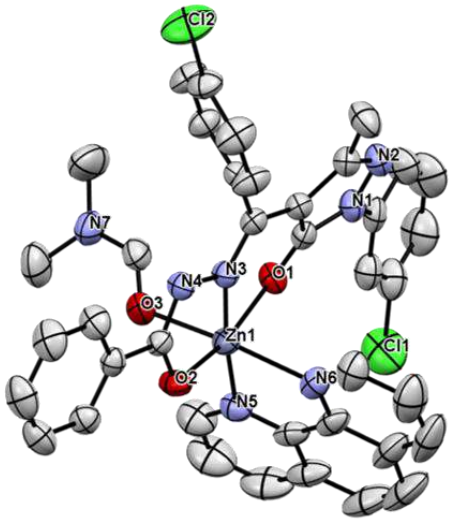
Yield: 75%, M.P.: >200 C, Molecular formula: $C_{37}H_{29}ClN_6O_3Zn$, F.w.:706.51g mol^{-1}, EA Calcd (found): C, 62.90(62.78); H, 4.14(4.27); N, 11.90(11.45), Metal estimation Calcd (found): Zn, 9.25 (9.75) %. **FTIR (KBr, cm^{-1}):** 3378 (N-H, bhz), 1616 (C=O, bhz), 1589 (C=N, pyz), 1539 (C=N, imine of bhz), 1284 (C-O, pyz), 915 (C=C, pyz), 511(M-O), 440(M-N, pyz-Zn). **^{1}H NMR ($CDCl_3$, 400MHz) δ ppm:** 1.53 (s, 3H, Me-pyz), 2.29 (s, 3H, tolyl), 7.03 (d, 2H, J=8Hz), 7.38 (t, 2H, J=8; 15.6 Hz), 7.53 (m, 7H, ar-H, AHP), 7.70 (d, 2H, J=8.4 Hz), 8.85 (N-H, bhz).

Results and Characterization

Structure features of Complex 15 [Zn(L5)(bpy)(AcO)]EtOH and Complex 16 [Zn(L5)(phen)(DMF)]



Complex 15



Complex 16

ORTEP ellipsoid with 50% probability diagrams of complex **15** and **16**. H-atoms are omitted for clarity.

Electronic spectra of 4-acylhydrazone-5-pyrazolones and its zinc(II) complexes

There is no d-d transition in all complexes due to d^{10} metal. Compounds bearing the coordinated N, N-aromatic ligands, showed an intense band at 260 nm, and a moderately intense band at 300 nm, all due to the 2,2′-bipyridine and 1,10-phenanthroline ligand. In the spectra, complexes observed LMCT band at around 380 nm.[17]

Molar conductivity of complexes

Compounds are soluble in DMSO. Complexes **13-18** molar conductance observed to be below 14 ohm^{-1} cm^2 mol^{-1}. So the conductance measurements suggest that they are non-electrolytes.[17,21,22]

Conclusion

The evidence from single crystal X-ray diffraction spectroscopy has been suggested a distorted octahedral environment around the zinc through coordination of many of O, *N*, O-chelating 4-acylhydrazone-5-pyrazolone ligand for complex **16.** The single crystal X-ray analysis of complex **15** showed distorted square pyramidal geometry. In complex **16**, DMF replacing coordinated water molecule during crystallization.

Chapter 4: Synthesis and Characterization and Biological Evolution of Zinc(II) Metal Complexes of 4-Semicarbazone-5-Pyrazolone and 4-Thiosemicarbazone-5-Pyrazolone

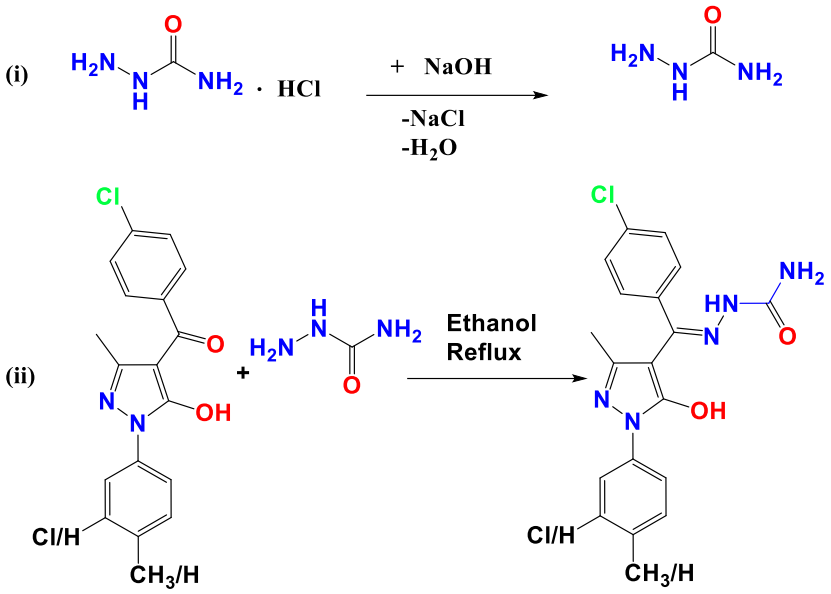
Synthesis of ligands

Synthesis of ligand L7 [(E)-2-((4-chlorophenyl)(1-(3-chlorophenyl)-5-hydroxy-3-methyl-1H-pyrazol-4-yl)methylene)hydrazine-1-carboxamide].

Yield: 75 %, M.P.:185 °C, Mol. Formula: $C_{18}H_{15}Cl_2N_5O_2$, F.w.: 404.25, Elem. Ana., Theoretical (found) %: C, 53.48 (53.40); H, 3.74 (3.88); N, 17.32 (17.87). **FTIR (KBr, cm^{-1})**: 3412, 3207 (N-H, scz), 1670 (C=O, pyz), 1629 (C=O, scz), 1590 (C=N, pyz). **^{1}H NMR (400 MHz, $CDCl_3$, δ ppm):** 2.13 (s, CH_3-pyz), 3.15 (s, 1H, NH), 7.19-7.96 (m, 6H, semi-pyz).

Synthesis of ligand L8 ((E)-2-((4-chlorophenyl)(5-hydroxy-3-methyl-1-(p-tolyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carboxamide)

Yield: 74 %, M.P.:188°C, Mol. Formula: $C_{19}H_{18}ClN_5O_2$, F.w.: 383.84, Elem. Ana. Theoretical (found): C, 59.45(58.99); H, 4.73(4.74); N, 18.25(18.55). **FTIR (KBr, cm^{-1})**: 3470 (N-H, scz), 1679 (C=O, pyz), 1600 (C=O, scz), 1565 (C=N, pyz). **^{1}H NMR (400 MHz, $CDCl_3$, δ ppm):** 1.26(s, 3H, CH_3-tolyl), 2.13 (s,3H, CH_3-pyz), 7.28-7.30(d, 2H, *p*-tolyl), 7.51-7.62(dd, 4H, *p*-chloro benzoyl), 7.71-7.73(d, 2H, *p*-tolyl). Synthesis route of ligands **L7** and **L8** displayed in scheme 8.



Scheme 8. Synthesis route of ligands **L7** and **L8**.

Scheme 9. Synthesis route of ligand **L9** and **L10**.

Synthesis of ligand L9 ((E)-2-((4-chlorophenyl)(1-(3-chlorophenyl)-5-hydroxy-3-methyl-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide)

Yield 67%, M.P.:174°C, Mol. Formula: $C_{18}H_{15}Cl_2N_5OS$, F.w.: 420.31, Elem. Ana. Theoretical (found): C, 51.44(51.45); H, 3.60(3.77); N, 16.66(16.77); S, 7.63(7.68). **FTIR (KBr, cm^{-1})**: 3331(N-H, tcz), 1662 (C=O, pyz), 1602 (C=N, tcz), 831 (C=S, tcz). **^{1}H NMR (400 MHz, $CDCl_3$, δ ppm):** 2.2 (s, 3H, CH_3-pyz), 7.30-7.31(d, 1H, m-ch-p), 7.39-7.43(t, 1H, m-ch-p), 7.51-7.63(dd, 4H, *p*-chloro-benz), 7.9(s, 1H, m-ch-p).[18]

Synthesis of ligand L10 ((E)-2-((4-chlorophenyl)(5-hydroxy-3-methyl-1-(p-tolyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide)

Yield 77%, M.P.:185°C, Mol. Formula: $C_{19}H_{18}ClN_5OS$, F.w.: 399.90. Elem. Ana. Theoretical (found): C, 57.07(57.14); H, 4.54(4.64); N, 17.51(17.55); S, 8.02 (8.88). **FTIR (KBr, cm^{-1})**:

3388 (N-H, scz), 1670 (C=O, pyz), 1547 (C=N, pyz), 859 (C=S, tcz). **^{1}H NMR (400 MHz, $CDCl_3$, ppm):** 2.1 (s, 3H, CH_3-*p*-tolyl), 2.4 (s, 3H, CH_3-pyz), 7.28-7.30(d, 2H, tolyl), 7.49-7.62 (dd, 4H, p-chloro benzoyl), 7.71-7.73(d, 2H, pyz).

Synthesis of complexes 19-22

Synthesis of complex 19 [Zn(L7)$_2$]

Yield: 75 %. M.p.: >200 °C. Anal. Calcd. for $C_{36}H_{28}Cl_4N_{10}O_4Zn$: C, 49.59; H, 3.24; N, 16.07; Zn, 7.50. Found: C, 49.50; H, 3.55; N, 16.74%. F.w. 871.87. Zinc estimation: 7.55 %. FT-IR (KBr, cm^{-1}): 3358 (b) (NH-),3181 (NH_2), 2927 (b) (Ph–C–H), 1662 (C=O, scz), 1602 (C=N, cyclic), 1549 (C=N, azomethine), 1482 (m) (Ph-C-C), 867 (s) (N-N), 511 (s) (Zn–O), UV/Vis (DMSO, λmax, nm, (ε)): 275 (0.85). Λ_m ($S.cm^2.mol^{-1}$): 8.2.

Synthesis of complex 20 [Zn(L8)$_2$]

Yield: 58 %. M.p.: >200 °C. Anal. Calcd. for $C_{38}H_{34}Cl_2N_{10}O_4Zn$: C, 54.92; H, 4.12; N, 16.85. Found: C, 55.36; H, 4.05; N, 16.77%. Metal estimation 7.88%. F.w.: 831.04. FTIR (KBr, cm^{-1}): 3388 (b) (NH-),3155 (b) (NH_2), 2923 (b) (Ph–C–H), 1669(C=O. scz), 1556 (m) (C=N, cyclic), 1435 (m) (Ph-C-C), 1127 (m) (N-N), 859 (s) (N-N), 514 (s) (Zn–O). UV/Vis (DMSO, λmax, nm, (ε)): 287 (0.84). Λ_m ($S.cm^2.mol^{-1}$): 4.2.

Synthesis of complex 21 [Zn(L9)(OAc)(H_2O)](EtOH)

Yield: 66 %. M.p.: >200 °C. Anal. calcd. for $C_{22}H_{25}Cl_2N_5O_5SZn$: C, 43.47; H, 4.15; N, 11.52. Found: C, 43.36; H, 3.95; N, 11.75%. FT-IR (KBr, cm^{-1}): 3402 (b) (NH-),3159 (b) (NH_2), 2927 (b) (Ph–C–H), 1612 (C=N, pyz), 1589 (m) (C=N, cyclic), 1474 (m) (Ph-C-C), 1139 (m) (N-N), 1015 (m) (C=S), 862 (s) (N-N), 511 (s) (Zn–O), 480 (s) (Zn–N), 445 (s) (S-O). UV/Vis (DMSO, λmax, nm, (ε)): 288 (0.6). Λ_m ($S.cm^2.mol^{-1}$): 3.3.[18]

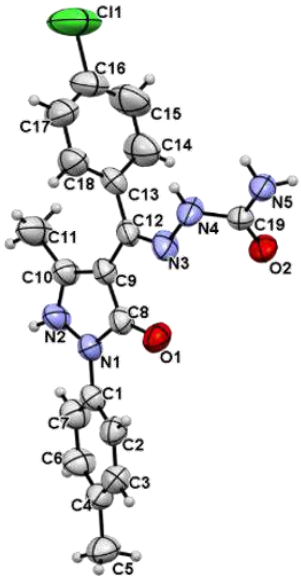
Synthesis of complex 22 [Zn(L10)$_2$]

Yield: 65 %. M.p.: >200 °C. Anal. Calcd. for $C_{38}H_{34}Cl_2N_{10}O_4Zn$: C, 54.92; H, 4.12; N, 16.85. Found: C, 54.34; H, 4.22; N, 16.88%. Metal estimation 7.88 %. FT-IR (KBr, cm^{-1}): 3423 (b) (NH-),3038 (b) (NH_2), 2977 (b) (Ph–C–H), 1597 (C=O, pyz) 1565 (m) (C=N, cyclic), 1478 (m) (Ph-C-C)), 1160 (C=N, azomethine), 855 (s) (N-N), 1016 (m) (C=S), 511 (s) (Zn–O), 480 (s) (Zn–N), 445 (s) (S-O). UV/Vis (DMSO, λmax, nm, (ε)): 287 (0.84). Λ_m ($S.cm^2.mol^{-1}$): 8.5.

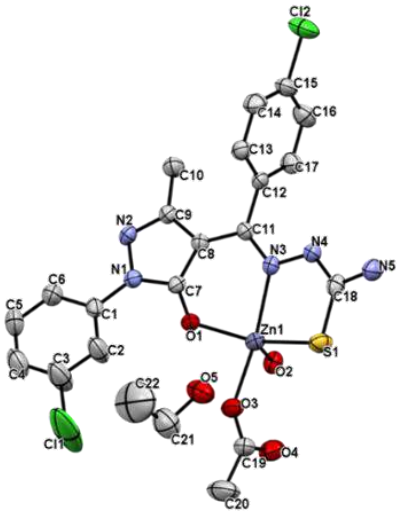
Results and discussion

Single crystal X-ray diffraction of ligand L8 and complex 21.

The molecular structure of ligand **L8** was determined by single crystal X-ray diffraction. ORTEP ellipsoid diagram of ligand **L8** and complex **21** with 50% probability. H-atoms are omitted for clarity.



S2



Complex 21

Electronic spectra of ligands and complexes

The first intense band is attributed to a ligand-centered (LC) π–π* transition localized on the aromatic rings of the ligand, while the shoulder is due to its metal coordination.

Molar conductance of ligands and complexes

The conductivities of zinc(II) metal complexes and ligands in DMSO were measured with a calibrated conductivity cell at room temperature. The low conductivity values in DMSO reveal Complexes are non-electrolytic in nature. [18,21]

Cytotoxicity of Zinc(II) complexes

All complexes have showed great results of MTT assay against A549 cell.

Conclusion

Ligands and their zinc(II) complexes have been synthesized, Characterized and screened for MTT assay against A549 cell.

Chapter 5: Molecular Docking and Antimalarial Activity of Synthesized Ligands and Zinc(II) Metal Complexes

Results and Discussions

In vitro results

Minimum Inhibitory Concentration against *P. falciparum*

All synthesized 32 compounds and 1 Control molecule were subjected to *in vitro* minimum inhibitory concentration (MIC) against Chloroquine sensitive Plasmodium falciparum using MTT assay

MIC of 4-acylpyrazolone and their zinc(II) complexes against *P. falciparum*

The lowest minimal inhibitory concentration of 0.11 µmol/L was obtained for complex **6**, followed by 0.51, 0.84, 0.9, 1.15, 1.24, 1.42, 1.56, 2.55, 2.97, 4.49, 4.54 µmol/L for complex **5, 3, 9, 2, 7, 8, 1, 4, L3, L2** and **L1** respectively. While wel-known drug Quinine shown 0.8 µmol/L.

MIC of 4-Acylhydrazone-5-pyrazolones (L4-L6) and their nine zinc(II) complexes against *P. falciparum*

The lowest minimal inhibitory concentration of 0.56 µmol/L was obtained for complex **10**, followed by 0.74, 0.77, 0.98, 1.02, 1.08, 1.42, 1.54, 2.00, 2.49, 2.83 and 5.06 µmol/L for complex **13, 14, 15, 18, 11, 17, 16, L5, L6, 12** and **L4** respectively.

MIC of 4-semicarbazone-5-pyrazolones, 4-thiosemicarbazone-5-pyrazolones and their zinc(II) complexes against *P. falciparum*

The lowest minimal inhibitory concentration of 0.65 µmol/L was obtained for S1, followed by 0.72, 1.05, 1.45, 1.90, 2.34, 2.84 and 4.35 µmol/L for **20, L8, 22, 19, L10** and **L9** respectively.

Multi target *in silico* virtual screening

Virtual screening is a computational technique used in drug discovery to search libraries of small molecules to identify those structures which are most likely to bind to a drug target, typically a protein receptor or enzyme [23,24]. This method of screening is widely used to predict the binding of a large database of ligands to a particular target, to identify the most promising compounds from the database for further study (Kitchen *et al.,* 2004; Kolb *et al.,* 2009). Millions of compounds can be tested in very less time depending upon the available

computational power for the software. In the present study, we applied a similar approach to evaluate anti-malarial potentials of compounds synthesized.

Conclusion

In the present work, we have experimented *in vitro and in silico* study for derivatives of pyrazolone compounds. The in vitro study was based on cytotoxic effects of compounds against the *P. falciparum* a deadly malarial parasite. While the molecular docking study was done against 3 different proteins downloaded from protein databank (PDB). Out of total **32**, Complex **2**, Complex **3** and Complex **17** were found to have lowest binding affinity in *in silico* virtual screening. Whereas compound 6 found to have the lowest MIC value. The results indicated the potential of these compounds to have antimalarial activity.

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