CHAPTER - II
SYNTHESIS AND CHARACTERIZATION OF 4-ACYLOXIME-3-METHYL-1-(4’-NITROPHENYL-2-PYROZOLIN-5-ONE AND SYNTHESIS OF THEIR METAL CHELATES
2.A. PRESENT WORK:

This chapter describes the experimental methods used for the synthesis and characterization of some 4-Acyloxime-3-methyl-1-(4'-nitrophenyl)-2-pyrazolin-5-one studied in the present work.

The following ligands are used in the present study:

(I) 4-Acetyloxime-3-methyl-1-(4'-nitrophenyl)-2-pyrazolin-5-one.
[AONMPO]

Molecular formula: C_{12}H_{12}N_{4}O_{4}
Molecular weight: 276.25

Structural formula:
(II) 4-Propionyloxime-3-methyl-1-(4'-p-nitrophenyl)-2-pyrazolin-5-one. [PONMPO].

Molecular formula: $C_{13}H_{14}N_4O_4$.
Molecular weight: 290.27
Structural formula:

(III) 4-Benzoyloxime-3-methyl-1-(4'-nitrophenyl)-2-pyrazolin-5-one. [BONMPO]

Molecular formula: $C_{17}H_{14}N_4O_4$.
Molecular weight: 338.32
Structural formula:
(IV) 4-(p-Toluyloxime)-3-methyl-1(4'-nitrophenyl)-2-pyrazolin-5-one. [TONMPO].

Molecular formula: C_{18}H_{16}N_{4}O_{4}.
Molecular weight: 352.34
Structural formula:

2.B. MATERIALS

All chemicals used in the present study were of the A.R. grade quality. Ethyl acetoacetate (SD’s Fine Chemicals Ltd., Mumbai), 4-nitrophenyl hydrazine (Sigma-Aldrich, Bangalore), acetyl chloride, benzoyl chloride, propionyl chloride, p-toluly chloride, hydrochloric acid, glacial aceticacid, 1,4-dioxane, calcium hydroxide, methanol,ethanol (Qualigens-Glaxo, SD’s Fine Chemicals Ltd., Mumbai) were used without further purification.
2.C. EXPERIMENTAL

All ligands prepared in the present study are characterized by colour, m.p., elemental analyses, FT-IR, $^1$H NMR, $^{13}$C NMR and mass spectral studies. Melting points were taken in one side open capillaries. Carbon, hydrogen and nitrogen were estimated on a Perkin Elmer, Series II, 2400 C, H, N, analyzer (Central Salt and Marine Chemical Research Institute, Bhavnager, India). The infrared spectra of the ligands studied in the present work were recorded on a Shimadzu 8201 PC FT-IR model in KBr (Gujarat Laboratory, Ahmedabad, India).

The $^1$H NMR, $^{13}$C NMR spectra in DMSO of all ligands were recorded on a Bruker DRX-400 FT-NMR spectrophotometer using TMS $[(CH_3)_4Si]$ as internal standard (Zydus Research Centre, Ahmedabad, India). The mass spectra in a matrix of neat glycerol of all ligands studied in the present work were recorded on a Jeol SX-102 FAB mass spectrometer (Zydus Research Centre, Ahmedabad, India).

2.D. SYNTHESIS AND CHARACTERIZATION OF LIGANDS

The ligands AONMPO, PONMPO, BONMPO, and TONMPO used in the present study were prepared in three steps using literature[1-5] method.

(a) Preparation of 3 -methyl -1 – [4'- nitrophenyl] - 2 - pyrazolin -5-one.
(b) Preparation of 4-Acyl-3-methyl - 1-[4’-nitrophenyl]-2-pyrazolin-5-one.

(c) Preparation of 4-Acyloxime-3-methyl - 1-[4’-nitrophenyl] - 2-pyrazolin-5-one [1-5].

2.D.1. Preparation of 3-methyl - 1-[4’-nitrophenyl] - 2-pyrazolin-5-one:

It was obtained by condensing the equimolar quantities of ethyl acetoacetate with 4-Nitro phenyl hydrazine in aceticacid, containing few drops of concentrated sulphuric acid.

4-Nitrophenyl hydrazine (25 g, 0.16 mole) was stirred in glacial acetic acid (50 mL) and warmed 40°C until complete solution resulted. The stirred mixture was cooled to room temperature and ethyl acetoacetate (21.25 g, 0.16 mole) was added rapidly. After 10 minutes at room temperature the flask was placed in an oil bath and heating is commenced to 85°C over 30 minutes. At this temperature a dense yellow precipitate formed. The reaction was left at 80 to 85 °C. for 4 hours and then the reaction mass was cooled to room temperature. The crystals were collected by filtration, washed with several small portions of acetic acid until the filtrate was colorless, then washed with water and air dried to give 21.5 g, 60% yield, m.p. 219°C-220°C.

The following general procedure was used to prepare the 4 - acyl - 3 - methyl - 1 – [4’ - nitrophenyl] - 2 - pyrazolin - 5 – one [1 – 4].

The 3 - methyl - 1 – [4’ - nitrophenyl] - 2 - pyrazolin - 5 - one (20g, 0.091mol) was placed in a three neck flask equipped with stirrer, separating funnel and reflux condensor. It was then dissolved in dioxane (120 mL) by application of heat. To the reaction mixture, calcium hydroxide (13.68g, 0.18 mol) was added, followed by the drop wise addition of the acetyl chloride (7.20g,0.091mol) or propionyl chloride(8.40g,0.091mol) or benzoyl chloride (12.80g, 0.091 mol) or p - toluyl chloride (14.16g, 0.091 mol). At this stage, the mixture became a thick paste and its temperature also increased as this being a exothermic reaction. The reaction mixture was then refluxed on oil bath for an hour. The resulting calcium chelates was then decomposed by pouring it into dilute hydrochloride acid (180 mL, 2 M). The resulting coloured compounds were collected by filtration, washed several times with water then ethanol and finally dried in the air. The product was recrystallized in hot ethanol.
(a) 4 - Acetyl - 3 - methyl - 1 - [4’ - nitrophenyl] - 2 - pyrazolin - 5 -
one:

light yellow; m. p.found: 197-198 °C; Yeild 77 %,

Analyses calculated for C_{12}H_{14}N_{3}O_{4} (261.24) :  C,55.17;  H,4.24;  N,16.09 ; %. Found :C,55.21 ; H,4.28; N,16.18 %.

FT-IR (KBr pellet, cm^{-1}) \nu_{max}: 3400-3100 br (\nu_{OH}, 5-OH group of pyrazole ring), 1650 s (\nu_{C=O}, acetyl group), 1605 s (\nu_{C=N},pyrazole ring), 1325 s (\nu_{NO2},4-nitrophenyl ring), 1416 (\nu_{C=O} pyrazole ring)

(b) 4 - Propionyl - 3 - methyl - 1 - [4’ - nitrophenyl] - 2 - pyrazolin - 5 -
one:

pale yellow; m. p.found: 160-162 °C; Yeild 86 %,

Analyses calculated for C_{13}H_{15}N_{3}O_{4} (275.27):  C,56.72;  H,4.76;  N,15.27 %. Found :C,56.60 ; H,4.59; N,15.08 %.

FT-IR (KBr pellet, cm^{-1}) \nu_{max}: 3405-3120 br (\nu_{OH}, 5-OH group of pyrazole ring), 1645 s (\nu_{C=O}, propionyl group), 1620 s (\nu_{C=N},pyrazole ring), 1325 s (\nu_{NO2},4-nitrophenyl ring), 1418 (\nu_{C=O} pyrazole ring)
(c) 4 - Benzoyl - 3 - methyl - 1 - [4’ - nitrophenyl] - 2 - pyrazolin - 5 - one :

light yellow ; m. p.found: 222 °C; Yeild: 86 %,

Analyses calculated for C_{17}H_{13}N_{3}O_{4} (323.31): C,63.16 ;H,4.05; N,13.00 %. Found: C,62.99 ;H,3.98 ;N,13.15 %.

FT-IR (KBr pellet, cm^{-1}) \nu_{\text{max}}: 3455-3200 br (\nu_{\text{OH}}, 5-OH group of pyrazole ring), 1645 s (\nu_{C=O}, 4-benzoyl group), 1615 s (\nu_{C=N},pyrazole ring), 1323 s (\nu_{NO_{2}}, 4-nitrophenyl ring), 1421 (\nu_{C=O} pyrazole ring)

(d) 4 - [p - Toluyl] - 3 - methyl - 1 - [4’ - nitrophenyl] - 2 - pyrazolin - 5 - one :

light yellow ; m. p.found: 183 °C; Yeild 83 %,

Analyses calculated for C_{18}H_{15}N_{3}O_{4} (337.33): C,64.09; H, 4.48 ; N , 12.46 %. Found : C,63.95; H,4.31;N,12.29 %.

FT-IR (KBr pellet, cm^{-1}) \nu_{\text{max}}: 3460-3210 br (\nu_{\text{OH}}, 5-OH group of pyrazole ring), 1650 s (\nu_{C=O}, 4-(p-toluoly group), 1618 s (\nu_{C=N},pyrazole ring), 1328 s (\nu_{NO_{2}} 4-nitrophenyl ring), 1424 (\nu_{C=O} pyrazole ring)
2.D.3. **Preparation of the 4-Acyloxime-3-methyl-1-(4'-nitrophenyl)-2-pyrazolin-5-one.**

The 4-Acyloxime-3-methyl-1(4'-nitrophenyl)-2-pyrazolin-5-one were prepared by literature method [6-7] as described below.

The Acyloximes were prepared by refluxing 1:1 mole of 4-Acyl-3-methyl-1-[4'-nitrophenyl]-2-pyrazolin-5-one and hydroxylamine hydrochloride in ethanol for two hours on water bath. The resulting mixture was allowed to stand overnight. The solid product thus obtained was collected by filtration, washed with water and air dried. The acyloximes were then recrystallized in ethanol.

2.E. **CHARACTERIZATION OF 4-ACYLOXIME-3-METHYL-1-(4'-NITROPHENYL)-2-PYRAZOLIN-5-ONES.**

An attempt has been made to characterize all the ligands (I-IV) by m.p., colour, elemental analyses, IR, $^{13}$C NMR and mass spectral studies. The $^{13}$C NMR and mass spectra of all ligands (I-IV) are shown in Figs. 2.1-2.12.

The detailed assignments of infrared bands of all ligands used in the present study is given in chapter III. The present chapter describes only important infrared bands[10-13] of all ligands used. The $^1$H and $^{13}$C chemical shifts have been assigned using reported values for the 2-pyrazolin-5-one derivatives.[14-18]

The following ligands [I-IV] were used in the present investigation to prepare the metal chelates.
(1) 4-Acetyloxime-3-methyl-1-(4'-nitrophenyl)-2-pyrazolin-5-one. (AONMPO)

Light brown; m.p. found: 195-197 °C; yield: ~79%.

Analyses calculated for C_{12}H_{12}N_{4}O_{4}: C, 52.17; H, 4.38; N, 20.28%. Found: C, 52.32; H, 4.30; N, 20.61%.

FT-IR (KBr pellet, cm^{-1}) \( \nu_{\text{max}} \):
- 3362-3117 br (\( \nu_{\text{OH}}, \text{5-OH group of pyrazole ring} \), 1675 s (\( \nu_{\text{C-O, oxime}} \), 1600 s(\( \nu_{\text{C-N, pyrazole ring}} \)) 1415 s (\( \nu_{\text{C-O(enoil), pyrazole ring}} \), 1033 s (\( \nu_{\text{N-O, oxime}} \), 1327 s (\( \nu_{\text{NO2, 4-nitrophenyl ring}} \).

\(^{1}\) H Chemical Shift (Fig. 1.1, DMSO, \( \delta \) ppm): 8.05-8.25 [-C\(_6\)H\(_4\)-NO\(_2\) (4H)], 2.42[Pyrazole –CH\(_3\), (3H)], 2.24[=NOH, (1H)], 2.13[-C-CH\(_3\), (3H)], 12.5[-C-OH,(1H)].

\(^{13}\) C Chemical Shift (Fig. 1.2, DMSO, \( \delta \) ppm):
- 17.4(C-1), 149.8(C-2), 117(C-3), 142.2 (C-4), 118.1(C-5 & C-9), 124.8(C-6 & C-8), 144.2(C-7), 143.8(C-10), 153.8(C-11), 16.4(C-12).

Fig: 2.1: $^1$H NMR of AONMPO
Fig 2.2: $^{13}$C NMR spectra of AONMPO
Fig: 2.3: Mass spectra of AONMPO

140309-199 3 (0.161 J Cen.2, 80.00, Hit); Cm (3:4) 277.16

H₃C
\[ \text{H}_2\text{N} \]
\[ \text{NOH} \]
\[ \text{OH} \]
\[ \text{NO}_2 \]
(II) 4-Propionyloxime-3-methyl-1-(4'-nitrophenyl)-2-pyrazolin-5-one.

Brown; m.p. found: 182-184°C; yield: ~ 69%.

Analyses calculated for C$_{13}$H$_{14}$N$_4$O$_4$: C, 53.79; H, 4.82; N, 19.31%. Found: C, 53.56; H, 4.71; N, 19.12%.

FT-IR (KBr pellet, cm$^{-1}$) $\nu_{\text{max}}$: 3343-3113 vb ($\nu_{\text{OH}}$, 5-OH group of pyrazole ring), 1670 sh ($\nu_{\text{C=N}}$, oxime), 1605 s ($\nu_{\text{C=N}}$, pyrazole ring), 1418 s ($\nu_{\text{C-O}}$, pyrazole ring), 1135 s ($\nu_{\text{N=O}}$, oxime), 1325 s ($\nu_{\text{NO2}}$, 4-nitrophenyl ring).

$^1$H Chemical Shift (Fig. 1.1, DMSO, $\delta$ ppm): 8.05-8.27[-ArNO$_2$ (4H)] 2.70(Pyrazole,-CH$_3$(3H), 2.24[-CH$_2$-CH$_2$(3H)], 2.13[=NOH$_2$(1H), 1.17[-CH$_2$(2H)], 12.6[-OH(1H)].

$^{13}$C Chemical Shift (Fig. 1.2, DMSO, $\delta$ ppm):
15.9(C-1), 117.1(C-3), 136.8(C-4), 118.1(C-5 & C-9), 124.9(C-6 & C-8), 142.3(C-7), 143.8(C-10), 148.8(C-11), 19.8(C-12), 13.2(C-13).

Mass spectral data, m/z: 290 [M$^+$], 290.9, 274, 273, 247, 246, 242, 227, 221, 220.
Fig: 2.4: \(^1\)H NMR Spectra of PONMPO
Fig. 2.5: $^{13}$C NMR Spectra of PONMPO
(III) 4-Benzoyloxime-3-methyl-1-(p-nitrophenyl)-2-pyrazolin-5-one.

Yellow; m.p. found: 156-158°C; yield: ~ 84%.

Analyses calculated for C_{17}H_{14}N_{4}O_{4}: C, 60.35; H, 4.14; N, 16.56%. Found: , 60.35; H, 4.14; N, 16.56%.

FT-IR (KBr pellet, cm\(^{-1}\)) \(\nu_{\max}\): 3100-2854 vb \(\nu_{OH}, 5-OH\) group of pyrazole ring), 1670 sh (\(\nu_{C=N}, oxime\)), 1455 s \(\nu_{C-O(eno)}, pyrazole\) ring) 1228 s \(\nu_{C-O(eno)}, pyrazole\) ring), 1141 s \(\nu_{N-O, oxime}\), 1323 s \(\nu_{NO_2, 4-nitrophenyl\ ring}\).

\(^1\)H Chemical Shift (Fig. 1.1, DMSO, \(\delta\) ppm): 7.9-8.3 \([-C_6H_4NO_2, (4H)\], 7.3-7.8 \([-C_6H_5, (5H)\], 2.49 \([-CH_3 Pz Ring, (3H)\)], 2.1 \([-NO_2, (1H)\]).

\(^13\)C Chemical Shift (Fig. 1.2, DMSO, \(\delta\) ppm): 14.8(C-1), 104.0(C-3), 136.9(C-4), 118.3(C-5 & C-9), 124.9(C-6 & C-8), 143.1(C-7), 143.7(C-10), 152.8(C-11), 143.0(C-12), 138.8(C-15), 131.4(C-13 & C-17) 129.2 (C-14 & C-16).

Fig. 2.7: \( ^1H \) NMR Spectra of BONMPO
Fig 2.9: Mass spectra of BONMPO

140368-201 3 (0.161) Cn (Cen.2, 80.00, Ht); Cm (3:4)

100-

360.99
393.01
414.07
472.94, 491.71
500.25, 507.08
530.23, 567.83
611.35, 654.87

100-

362.02
392.23
414.07
472.84, 491.71
500.25, 507.08
530.23, 567.83
611.35, 654.87

140368-201 3 (0.161) Cn (Cen.2, 80.00, Ht); Cm (3:4)
(IV) 4-(p-Toluyl)oxime-3-methyl 1-(4'-nitropheny)-2-pyrazolin-5-one.

Yellow; m.p. found: 157-160°C; yield: ~ 78%.

Analyses calculated for C_{18}H_{16}N_{4}O_{4}: C, 61.36; H, 4.54; N, 18.18%. Found: C, 61.36; H, 4.54; N, 18.18%

FT-IR (KBr pellet, cm^{-1}) \( \nu_{\text{max}} \): 3500-3115 \( \text{vO-H, 5-OH group of pyrazole ring} \), 1676 \( \text{sh (C=N, oxime)} \), 1458 \( \text{s (C=C, pyrazole ring)} \), 1420 \( \text{s (C=C, pyrazole ring)} \), 1145 \( \text{s (O=O, oxime)} \), 1328 \( \text{s (N=O, 4-nitrophenyl ring)} \).

\(^1\)H Chemical Shift (Fig. 1.1, DMSO, \( \delta \) ppm): 8.0-8.2 (-ArNO\(_2\), 4H), 7.2-7.6 (ArCH\(_3\)ring, 4H), 2.53 (-CH\(_3\) Pz ring, 3H), 2.38 (Ar-CH\(_3\), 3H), 2.1 (=NOH, 1H).

\(^13\)C Chemical Shift (Fig. 1.2, DMSO, \( \delta \) ppm): 14.5(C-1), 104.5(C-3), 135.5(C-4), 118.1(C-5 & C-9)124.8(C-6 & C-8), 143.4(C-7), 143.7(C-10), 152.4(C-11), 143.0(C-12), 142.0(C-15), 129.4(C-13 & C-17) 129.1 (C-14 & C-16).

Mass spectral data, m/z: 352 [M\(^+\)], 353, 334, 297, 243.
Fig: 2.10: $^1$H NMR Spectra of TONMPO
Fig 2.11: $^{13}$C NMR Spectra of TONMPO
Fig 2.12: Mass spectra of TONMPO

140309-202 3 (0.161) Cn (Cen, 2, 80.00, Ht); Crn (3:4) 353.04

2: Scan ES+ 4.53e7
2.F. SYNTHESIS OF THE CHELATES:

The following general procedure was used in the synthesis of all the metal chelates.

Metal salt was dissolved in a minimum amount of hot ethanol. The hot ethanolic ligand solution in slight excess over the metal: ligand ratio 1 : 2 for all metal chelates [except that of Cr(III) and Fe(III) chelate for which it is 1 : 3] were added dropwise with constant stirring. To the resulting mixture 2 gm. of sodiumacetate was added and then the mixture was refluxed for 3 hours. The resulting mixture thus obtained was then concentrated to half of its original volume. The product was filtered and washed several times with hot water and finally with hot ethanol. The product was dried at 45 °C. The yields of the chelates were almost quantitative.
REFERENCES


