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Divalent Binuclear Copper Complexes with Macrocyclic Ligands Derived from Benzylacetone and Isatine Complexes

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ABSTRACT

The hetro precursors type (N2O2) or (N2S2) divalent copper complexes were prepared through the template reaction with the prepared precursors, which that synthesis via the reaction of benzyl acetone with o-amino phenol and reaction Isatine with o-amino thiophenal as shiff base compounds. The prepared complexes and precursors were characterised by IR, UV, Mass and 1H NMR, 13C NMR spectroscopes, the elemental micro analysis (C. H. N.S) and atomic absorption was carried out. The physical measurements were tailed m.p, solubility and magnetic susceptibility. The measurements show the suggested geometry of complexes are square planar (D4h) geometry around the metal ions.

KEYWORDS binuclear complexes, macrocyclic ligands.

Introduction:-

Organic chemists may consider any molecule containing a rins of twelve or more atoms to be a macro cycle. In general coordination chemists define a macrocycle more narrowly as a cyclic molecule with three or more potential donor atoms that can coordinate to metal center(1). A well-known example is the group of drugs known as macrolides. Hetrocyclic thiosemicarbazone and their metal complexes are among the most widely studies compounds for their potential therapeutic uses, such as antitumor, antibacterial and antifungal activity (2). The antitumor activity of thiosemicarbazones is enhanced by the presence of some metallic ions due to their ability to form chalets (3,4). The symmetrical bio sites in which an identical number of donor atoms of the same type are bound to each metal ion in similar geometries are very large in number (5). To a first approximation the nature of the donor atom may be restricted to simply (N, S, O) but a more accurate definition would specify the function grouping associated with the donor atom (6).

Expermental:-

Preparation of precursor 1(p^1) type (N_2O_2):-

In 500ml two necked flask[7-9] , equipped a condenser, and a thermometer were placed of Benzoyl acetone (1g,6.16mmol) in ETOH (15ml) was added slowly with stirring to mixture to mixture of (1.34g, 12.27mmol) of ortho amino phenol in (15ml)ETOH, the reaction mixture was refluxed for (2)hr in (80-70)C°. Which collected by filtration and dried under vacuum to give the precursor as a yellow solid, yield (1.52g, 47%), mp (142)C°.

Preparation of precursor2 (P^2)type (N_2O_2):-

In 500ml two necked flask[7-9], equipped a condenser, and a thermometer were placed of Isatin (1g, 6.79 mmol) in ETOH (15ml) was added slowly with stirring to mixture to mixture of (1.48g, 13.56mmol)of ortho amino phenol in (15ml)ETOH, the reaction mixture was refluxed for (2)hr in (80-70)C°. Which collected by filtration and dried under vacuum to give the precursor as a Brown solid, yield (3.15g, 44.64%), mp(153C°).

Preparation of precursor3 (P^3) type (N_2S_2):-

In 500ml two necked flask[7-9], equipped a condenser , and a thermometer were placed of Isatin (1g, 6.79mmol) in ETOH (15ml) was added slowly with stirring to mixture to mixture of (1.45, 13.49mmol) of ortho marcapto aniline in (15ml) ETOH, the reaction mixture was refluxed for (2)hr in (80-70) C°. Which collected by filtration and dried under vacuum to give the precursor as a Pak yellow solid, yield (1.87g,76.95%), mp(185)C°.

Preparation of precursor4 (P^4)Type(N_2S_2):-

In 500ml two necked flask[7-9], equipped a condenser, and a thermometer were placed of Benzoyl acetone (1g, 6.16mmol) in ETOH (15ml) was added slowly with stirring to mixture to mixture of (1.31g,10.47mmol)of ortho marcapto aniline in (15ml) ETOH, the reaction mixture was refluxed for (2)hr in (80-70)C°. Which collected by filtration and dried under vacuum to give the precursor as a Deep Red semisolid, yield (1.97g, 85.28%).

Synthesis of [Cu (P^1) (P^3)] complex:-

In (500)ml two necked flask[7-9] , equipped with condenser and thermometer and by using template method placed a solution of precursor 1 (0.44g,1.27mmol)in (10ml) EtOH and added of precursor 3 (0.48g,1.27mmol)in (10ml) EtOH after this was added slowly with stirring of (0.5g,1.28mmol)of pentaerthretol tetra bromide , waiting (10)mints after this added (2mol)of mixture [$CuCl_2.2H_2O$] (0.43g,2.52mmol).

Dissolved in EtOH , the reaction mixture was heated under reflux (2hr)in (80-70)C°.The collected this complex in some previous methods by filtration and washed with in excess of EtOH and dried under vacuum.

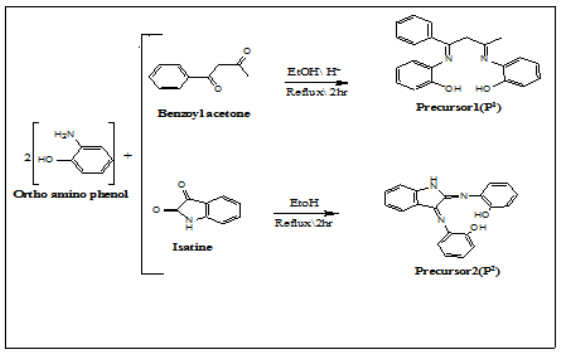
Synthesis of [Cu (P^2)(P^4)] complex:-

A similar method to that mentioned in preparation of [Cu(P^1)(P^3)] complex was used to prepared the complex of [Cu(P^2)(P^4)] (0.42g, 1.27mmol)of P2 and (0.46g ,1.27mmol)of P^4 .

Results and discussion:-

Synthesis and characterization of precursors(1, 2)type(N_2O_2):-

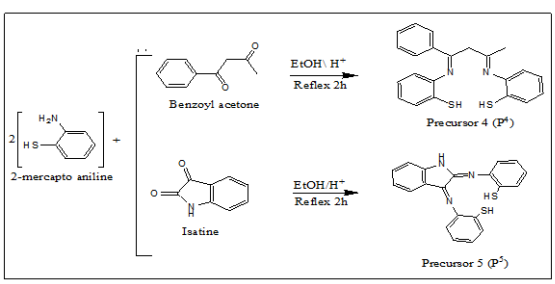
The synthesis[7-9] of precursors type (N_2O_2) carried out by condensation reaction between primary amine (ortho amino phenol) with carbonyl compounds (Benzoyl acetone, Isatine) as Schiff base reaction Scheme (1) summarized the formation of precursors(P1-2). Table (1) summarized some of physical properties of prepared compounds.



Scheme (1) synthesis route of precursors (1, 2) type N_2O_2.

Synthesis and characterization of precursors(3, 4)type(N_2S_2):

The precursor (P^3, P^4) type (N_2S_2) was prepared via condensation[7-9] reaction between raw material (2-mercapto aniline) and diketons material (Benzoyl acetone, Isatine) as Schiff base reaction, Scheme (2). Table(1) Shown some physical properties of these compounds.



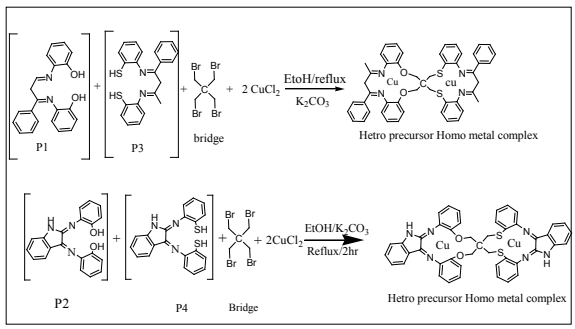
Scheme(2)The synthesis route of precursors type (N_2S_2).

T able(1) Some physical properties of precursors(1-4) type (N_2O_2) and (N_2S_2).

Compounds	M.p C°	Colours	Wt of product (gm)	Yield %	M.Wt g/mol	Macro analysis (calc)%			
						C	H	N	S
$C_{22}H_{20}N_2O_2$ Precursor(1)	142-145	yellow	1.52	47.10	344	76.74 77.15	5.81 6.54	8.13 8.36	
$C_{20}H_{15}N_3O_2$ Precursor(2)	153-155	Brown	3.15	44.64	329.35	72.94 73.17	4.55 4.78	12.76 13.05	
$C_{22}H_{20}N_2S_2$ Precursor(3)	Sem-Solid	Deep-Red	1.97	85.28	376	70.21 70.63	5.31 5.76	7.44 7.87	17.02 17.64
$C_{20}H_{15}N_3S_2$ Precursor(4)	184-190	Pak-yellow	1.87	76.95	361	66.48 66.60	4.15 4.46	11.62 11.87	17.72 17.96

Synthesis and characterization of Hetero precursors with Homo metals complexes:-

The template method and condensation[7-9] reaction between precursor type (N_2O_2) with precursor type (N_2S_2) and bridge compound (pentaerythretol tetra bromide) with some metals ions such as (Cu^{+2}, Co^{+2}, Ni^{+2}) gave the complexes in titled, Scheme (3) illustrate this. Table(2) Shown physical properties of the complexes.



Scheme(3) Hetero precursor with Homo metals complexes.

T able(2) Some physical properties for complexes of hetero precursor with homo metal .

Compounds complexes	M.p C°	Colour	Wt of product (gm)	Yield %	M.Wt g/mol	Macro analysis (calc)%				
						M	C	H	N	S
$[Cu(I)_2P^1,P^3]$	230-234	Deep-green	1.12	95.72	911.08	13.94 14.11	64.53 64.88	4.82 5.11	6.14 6.31	7.02 7.69
$[Cu(I)_2P^2,P^4]$	205-208	Brown	0.55	63.21	881.43	14.41 14.73	61.26 61.44	3.85 4.27	9.52 9.77	7.26 7.51

FTIR Spectra for precursor 1 type (N_2O_2) :-

The FTIR spectrum(10, 11) Fig. (1) for precursor 1 showed disappearing the bands at (1600)cm-1 assigned toυ (C=O) stretching , and absence the band at (3325and 3340)cm-1 of υS (NH2) υaS (NH2) in starting material.

The new band at(1599)cm^{-1} attributed to imines group(C=N) stretching.

The bands at (3375,3304, and 3161)cm^{-1} which attributed to

υ (O-H), υ (C-H) aromatic and υ (C-H) aliphatic stretching respectively. Table (3) shown the characteristic bands.

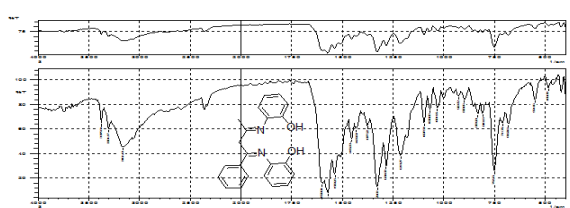


Fig.(1) FTIR spectrum of precursor 1(P^1) type(N_2O_2).

While the FTIR spectrum Fig. (2) for precursor2 showed absence the band at (1715)cm-1 assigned to υ (C=O) stretching , and absence the band at (3325 and 3340)cm-1of υ s(NH2) υas(NH2)in starting materal.

The band at (1670) cm^{-1} assigned to immine group υ (C=N) stretching.

Also appearing the exhibits bands at (3375 and 3250)cm^{-1} which assigned to

υ (O-H), υ (N-H) stretching (12) respectively. Table (3)Show the characteristic bands.

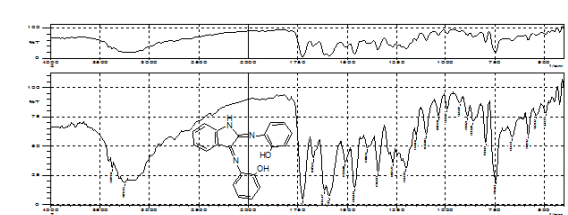


Fig.(2)FTIR spectrum of precursor 3(P^3) type(N_2O_2).

The FTIR spectrum[12] Fig. (3) for precursor 3 showed disappearing the band at (1600)cm-1assigned toυ (C=O) stretching , and absence the band at (3340 and 3345)cm-1of υ s (NH2), υas (NH2)in starting material.

And appearing the band at (1680) cm-1 attributed to imine groupυ (C=N) stretching.

Also appearing the exhibits bands at (3265,3057,and 2400) cm^{-1} which attributed to

υ (C-H)aromatic, υ (C-H)aliphatic and υ (S-H) stretching respectively.

Also the FTIR spectrum Fig. (4) for precursor 4(p^4) showed absence the band at (1715)cm^{-1} assigned toυ (C=O) stretching , also absence the band at (3340 and 3345)cm-1of υ_s (NH2), υ_{as} (NH2)in starting material. The band at (1708) cm^{-1} attributed to imines group υ (C=N) stretching.

And appearing the exhibits bands at (3354, 3292, and 2420) cm^{-1} which assigned to

υ (N-H), υ (C-H) aromatic andυ (S-H) stretching[13]respectively.

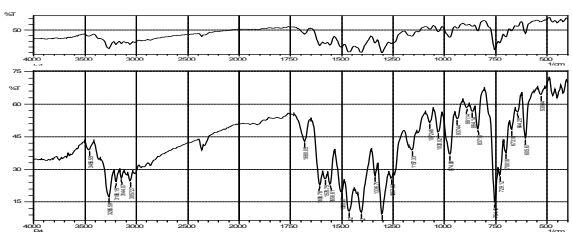


Fig.(3) FTIR spectrum of Precursor 3(p^3) type (N^2S^2).

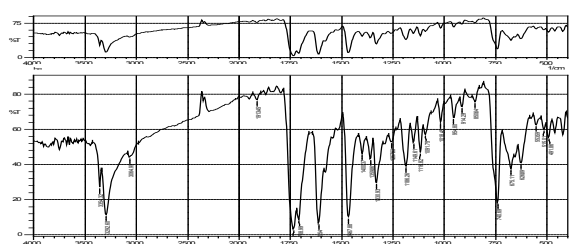


Fig.(4) FTIR spectrum of Precursor4(P^4) type (N_2S_2).

υ

Table(3) FTIR spectrum of all precursors P(1-4) type (N_2O_2) (N_2S_2).

Comp.	υ(O-H)	ar(C-H) υ	ali(C-H) υ	(C=N) υ	(N-H) υ	(S-H) υ
$C_{22}H_{20}N_2O_2$ P1	$(3375)_{br}$	$(3161)_m$	$(2988)_m$	$_s$ (1599)	----	----
$C_{30}H_{15}N_3O_2$ P2	$(3376)_{br}$	$(3132)_m$	$(2877)_w$	$_s$ (1670)	$(3250)_m$	----
$C_{22}H_{20}N_2S_2$ P3	-----	$(3057)_m$	$(2956)_w$	$(1680)_m$	-----	$(2400)_w$
$C_{20}H_{15}N_3S_2$ P4	-----	$(3292)_m$	----	$(1708)_s$	$(3354)_s$	$(2460)_w$

S= strong , W= weak , m = medium ,br=broad .

FTIR spectrum of Hetero precursors with Homo metal complexes.

The FTIR spectrum(14) for Hetro precursors [reaction between precursor type (N2O2) with precursor type (N2S2)] with copper complexes [(Cu)2 P1,P3] and [(Cu)2 P2,P4] Fig. (5), (6) respectively are displays a shifting to lower frequency for stretching bands of υ (C=N) between (1523-1583) cm-1 compared of free precursor.

The absence of observed bands for υ (OH) and υ (SH) this inductor for coordinate between metal and ligand, and appearance some exhibits bands at (607-696)cm^{-1},(483-490)cm^{-1} and(559-580)cm-1 which are attributed to υ (M-N) , υ (M-S) and υ (M-O) respectively .

This change in some [12] bands assigned to the electron delocalization towards metal centre upon coordination HOMO-LOMO) [HOMO=highest occupied molecular orbital, LOMO=lowest unoccupied molecular orbital]. The assignment of the characteristic bands is summarized in Table (4).

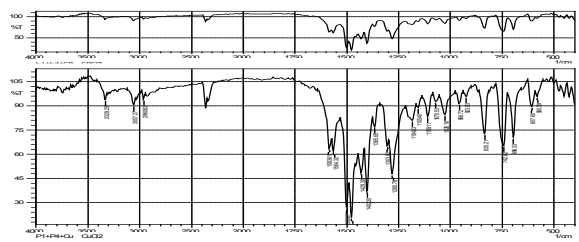


Fig.(5)FTIR spectrum of Hetro precursor [$(Cu)_2$ P^1, P^3].

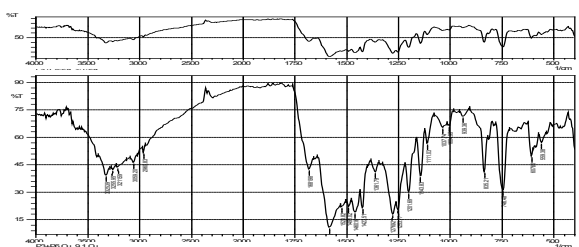


Fig.(6)FTIR spectrum of Hetero precursor [$(Cu)_2$ P^2, P^4].

Table (4) FTIR spectrum of Hetero precursors with homo metals complexes.

Compounds	ν_{ar}(C-H)	ν_{ali}(C-H)	ν(C=N)	ν(C-N)	ν(C-O)	ν(C-S)	ν(M-N)	ν(M-O)	ν(M-S)
$[(Cu)_2 P^1,P^3]$	3057s	2960m	1585s	1280s	1026m	956m	696w	580w	490w
$[(Cu)_2 P^2,P^4]$	3059s	2960w	1523m	1276m	1037w	939w	607w	559w	483m

UV-Vis spectra of Hetro precursors Homo metal complexes:-

UV-Vis spectrum of $[(Cu)_2 P^1 P^4]$complex:-

The electronic spectrum[15, 16] of complex Fig. (7) exhibits peaks at (282) nm (35460) cm^{-1} (ε_{max} =3812$molar^{-1}$. cm^{-1}) and (285) nm (35087cm^{-1}) (ε_{max} =3598 $molar^{-1}.cm^{-1}$), assigned to ligand field and charge transfer. The hetro precursors homo metal complex shows addition peaks at (422)nm (23696)cm-1 (ε_{max} =2372 $molar^{-1}.cm^{-}$) and (509) nm (19646) cm^{-1} (ε_{max} =48 $molar^{-1}$. cm^{-1}) which attributed to (d-d) transitions type ($^2A_1g \rightarrow {}^2A_2g$) and ($^2A_1g \rightarrow {}^2B_1g$) respectively this indicating of square planer structural about hetro precursors homo metal complex. Table (5) shows all these peaks.

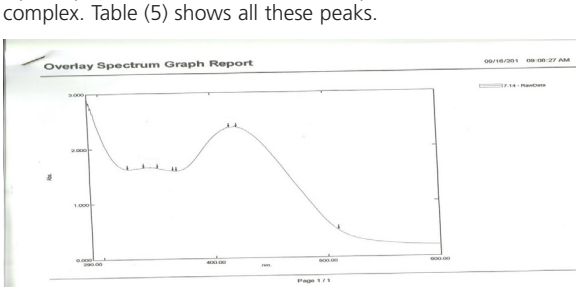


Fig.(7) Electronic spectrum of $[(Cu)_2 P^1 P^4]$ complex.

UV-Vis spectrum of $[(Cu)_2 P^3 P^5]$complex:

The electronic[15, 16] spectrum of [$(Cu)_2$ P^3 P^5] complex Fig. (8) appears peaks at (256) nm (39062) cm^{-1} (ε_{max} =3797 $molar^{-1}.cm^{-1}$) and (260) nm (38461cm^{-1}) (ε_{max} =1667 $molar^{-1}.cm^{-1}$) assigned to ligand field and charge transfer. The hetro precursor homo metal complex shows addition peaks at (468) nm (21367)cm^{-1} (ε_{max} =561 $molar^{-1}.cm^{-1}$) and (571) nm (17513) cm^{-1} (ε_{max} =237 $molar^{-1}.cm^{-1}$) which attributed to (d-d) transitions type ($^2A_1g \rightarrow {}^2A_2g$) and ($^2A_1g \rightarrow {}^2B_1g$) respectively this indicating of square planer structural about hetro precursors homo metal complex. Table (5) shows all these peaks.

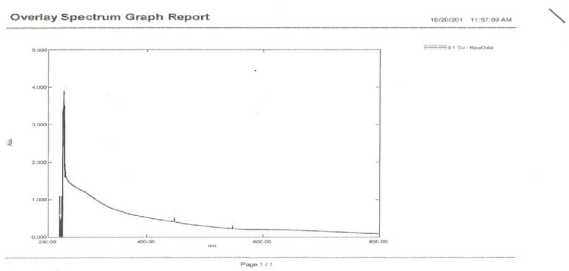


Fig.(8) Electronic spectrum of[$(Cu)_2$ P^3 P^5] complex.

Table (5): UV-Vis spectral data for Hetero precursors Homo metals complexes.

Compound	λ **nm**	ν **cm^{-1}**	Ɛmax ($molar^{-1}$cm-1) Ɛmax ($molar^{-1}$cm-1	Assignments	Expected form
[Cu_2 P^1, P^4]	282 285 422 509	35460 35087 23696 19646	3812 3598 2372 48	Ligand filed and Charge transfer $^2A_1g \rightarrow {}^2A_2g$ $^2A_1g \rightarrow {}^2B_1g$	Square planer D_4h
[Cu_2 P^3, P^5]	256 260 468 571	39062 38461 21367 17513	3797 1667 561 237	Ligand filed and Charge transfer $^2A_1g \rightarrow {}^2A_2g$ $^2A_1g \rightarrow {}^2B_1g$	Square planer D_4h

^{1}H NMR Spectra of Hetero precursors Homo metals complexes:-

^{1}H NMR Spectrum of [$(Cu)_2$ P^1 P^4] complex:-

The 1H NMR spectrum for[(Cu)2 P1 P4]complex(17) Fig.(9) in DMSO-d6 , shows disappearing of proton of hydroxyl group which that show in precursor 1(P1) at (δ = 12.8 and 10. 3) ppm and disappears the sulphide group protons in precursor4(P4) at (δ = 9.8 and 9.4ppm) this indicate to binding between the bridge and precursors. The chemical shift between (δ= 7.9– 6.5ppm) can be attributed to the six benzene ring, the signal at(δ =3.2ppm, 2H) and (δ =2.4ppm) due to the protons of methylene and methyl groups respectively. These signals are shifted compared with that in the free precursors. This shifting is caused by the lower electron density existing on these protons in the complex, the chemical shifts were summarised in Table(6).

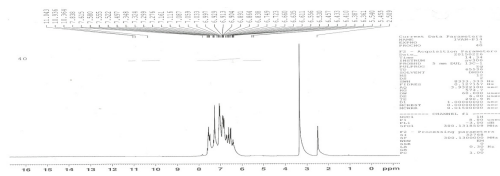


Fig.(9) ^{1}H NMR Spectrum of [$(Cu)_2$ P^1 P^4] complex

^{1}H NMR Spectrum of [$(Cu)_2$ P^3 P^5] complexes:-

The 1H NMR spectrum for[(Cu)2 P3 P5]complex(18) Fig.(10) in DMSO-d6 , shows disappearing of proton of hydroxyl group which that show in precursor 3(P3) at δ = 10.9 and 9.1) ppm and disappears the sulphide group protons in precursor5(P5) at (δ = 12.9 and 11.2ppm) this indicate to binding between the bridge and precursors. The chemical shift between (δ = 8.1– 6.3ppm) can be attributed to the six benzene ring, the signal at(δ =3.9ppm, H) and (δ =3.4ppm) due to the protons of amine and methlene groups respectively. These signals are shifted compared with that in the free precursors. This shifting is caused by the lower electron density existing on these protons in the complex, the chemical shifts were summarised in Table (6).

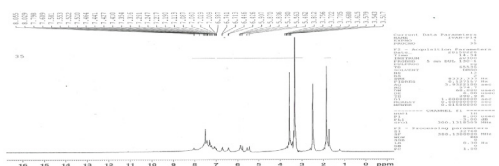


Fig.(10) ^{1}H NMR Spectrum of [$(Cu)_2$ P^3 P^5] complex.

Table (6) ^{1}H NMR data for Hetro and Homo metal complexes.

Compounds	Functional groups	Chemicals shift $_\delta$ ppm
[$(Cu)_2$ P^1 P^4]	6(benzene-ring) (CH2, CH3) groups	(8.3 - 6.4)ppm (3.4 and 2.8)ppm
[$(Cu)_2$ P^3 P^5]	6(benzene-ring) (NH) (CH2) groups	(8.7 – 7.3)ppm (3.7) ppm (3.2) ppm

REFERENCES

1- J. Reedjik, G. Wilkinson, R. D. Gillard, and J. A. Mccleverty, Eds., Vol. 2, pergamon press, oxfored, UK, (1987). | 2- S. A. F. Rostom, M. A. Shalaby, and M. A. El-Demellawy, '' polysubstituted pyrazoles- part 5. Synthesis of new 1-(4-chlorophenyl)-4-hyroxy- 1H-pyrazole-3-carboxylic acid hydrazide analogs and some derived ring systems. A novel class of potential antitumor and anti- HCV agents, ''European Journal of medicinal Chemistry, vol. 38, pp. 959, (2003). | 3- A. K. Tewari and A. Mishra, ''Synthesis and anti-inflammatory activities of N4, N5- disubstituted-3-methyl- 1H-pyrazolo[3,4-c]pyridazines" , Bioorganic& Medicinal Chemistry, vol. 9, pp, 715-718, (2001). | 4-R. H. Wiley and P. Wiley, pyrazolones, pyrazolidones and derivatives, John Wiley and sons, New York, NY, USA, (1964). | 5-A. L. Gavrilova and B. Bosnich, ''Principles of mononucleating and bionucleating ligand design, ''Chemical reviews, vol. 104, no. 2, pp. 349-383, (2004). | 6- R. Mukherjee,"Coordination chemistry with pyrazole-based chelating ligands molecular structural aspects" Coordination Chemistry Reviews, vol. 203,pp.151-218,(2000). | 7-T. E. Kokina, R. F. Klevtsova, L. A. Glinskaya, E. G. Boguslavskii, and S. V. Larionov, Russian Journal of Coordination chemistry., 1.36(1), 53-50, (2010). | 8-S. K. Mittal, S. K. Ashok Kumar, Indian Journal of Chemistry., 47A, 1676 – 1680, (2008). | 9-K. W. Y. Chan, W.T. Wong, Coord. Chem. Rev., 251, 2428, (2007). | 10- D.L.Pavia, G.R.Lampman, G.S.Kriz,"Introduction to spectroscopy 4th adition", USA.Washington., 2009. | 11- W. A. Al-Zeadan, J.Edu. Sci., 51, 45-55 (2001). | 12- Z. M. Zaki, " Spectrochim Acta "., Part A, 56, 1917 (2000). | 13- M.A.Iman, M.Manatsh, Chem., 126, 173, (1995). | 14- I. J. Sallomi and R. A. Hadad, J. Edu. Sci., 16, 2,110-124 (2004). | 15- V.Ramesh and P.Umasundari, Spectrochim.Acta, part, A,54,285, (1998). | 16- M. N. Ali, Msc. Thesis, University of Karbala, (2000). | | 17-T. Kano, S. Song, Y. Kubota, and K. Maruka, ''Highly diastereo – and enantioselective mannich reaction of synthetically flexible ketimines with secondary amine organocatalysts., Ang. Chem. Int. Ed. 51(5), p. 1191-1194, (2012). | 18- T. Kano, S. Song, and K. Maruoka, ''Molecular recognition ketomalonates by asymmetric aldol reaction of aldehydes with secondary amine organocatalysts., Chem. Commun, 48(56), P. 7073-7039, (2012).