



Preparation new ligands containing nitrogen and spectrophotometric study with Rhenium complexes.

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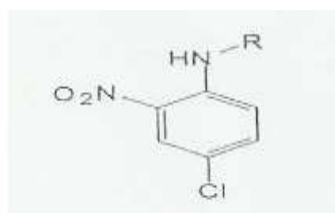
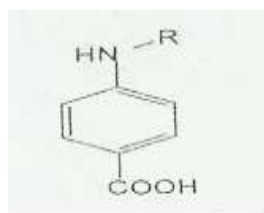
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KEY WORDS: LIGAND, RHENIUM COPLXEXE

ABSTRACT

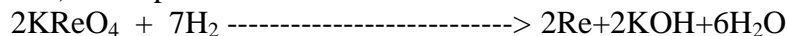
The preparation of two new ligands containing nitrogen atoms as chelates from Mannich reaction was described in this work. Using formyl aminophenols as the compound containing the active proton center, glycine as the amine, and paraformaldehyde as the aldehyde performed the reaction. The method was successful and was very promising to design ligand of various molecular structures. These ligands were capable to coordinate to rhenium metal by ligands exchange methods.

These compounds were studied spectrophotometrically, so as their complexes with rhenium by using infrared and U.V-vis absorption spectroscopy, as well as the other classical techniques such as microanalysis and molecular weight determination by depression of freezing point. The following chemical structure for preparation ligands.



INTRODUCTION

Rhenium is one of the rarest elements, occurring naturally as a mixture of two non-radioactive isotopes R^{185} (37.4%) and R^{187} (62.6%). Re is recovered from flue dusts in the roasting of MoS_2 over and from residues in the smelting of some Cu ores. It is usually left in solution as perrhenate ion (ReO_4^-). After concentration, the addition of (KCl) precipitate the sparingly soluble salt (KReO_4) compound at (20–100) atmospheres.



It has very high melting and uncreative at room temperature, but it burns in (O_2) at 400C to give the volatile oxides (Re_2O_7).

The radioactive isotopes of interest in nuclear medicine are R^{186} and R^{188}
The nuclear properties of which are summarized in Table (1)

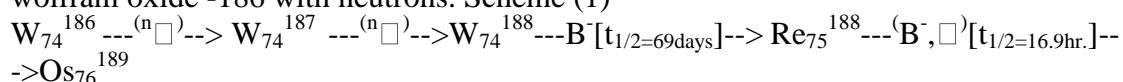
**Table: 1: Relevant nuclear properties of important Re isotopes**

Isotopes	Half-Live	Important emissions	Comments
Re ¹⁸⁶	90hr	γ, 137Kev β, 1.07, 0.93Mev	Reactor produced Contains Re ¹⁸⁵ and Re ¹⁸⁶ Usually contaminated with Re ¹⁸⁸
Re ¹⁸⁸	17hr	γ, 155Kev* β, 2.2Mev	Generator produced no (carrier added) radionuclide

* Many γ-rays of higher energies are also emitted.

1. Rhenium generator

Re¹⁸⁸ generator is used on the separation of the radionuclide Re¹⁸⁸ from irradiated wolfram oxide -186 with neutrons. Scheme (1)



(Scheme) 1: The W¹⁸⁸/Re¹⁸⁸ generator

2. The role of rhenium complexes in nuclear medicine

γ-radiation of Re¹⁸⁸ makes it possible to carry out measurement on the same apparatus for Tc^{99m} as a consequence, one can monitor the distribution and movement of a radionuclide in the body.

Re¹⁸⁸, B⁻ emitter may be used in the treatment of malignant tumors of kidneys, liver, stomach and pelvic organs with selective intra-arterial injection of radiopharmaceutical (RP).

There are prospects using (RP) for intrajoint injection in inflammatory processes as well as for treatment of pleural effusions and as cited.

For use in therapy, Re must carry to the site of action (i.e. to the tumor cells). Basically, three transportation forms are possible.

(1) As perrhenate [ReO₄]⁻ the most stable and water soluble rhenium oxide in the oxidation state (VII).

(2) Rhenium complexes, where neutral, positive or negative complexes with oxidation state (-III to +VII) are possible, Re (V) complexes are favored.

(3) As Re moiety in any form attached or trapped to particles like dextrin and Polymer particles, colloids or liposomes.

Also Re¹⁸⁶ and Re¹⁸⁸ can be used as essential and tagged rhenium and hence, they are some other usage:

(1) As agent for the palliation of bone pain (i.e. [Re(DMPE)₃]⁺).

(2) As modularly thyroid carcinoma (i.e. [ReO(DMSA)₂]⁻).

3. Uses of rhenium metal

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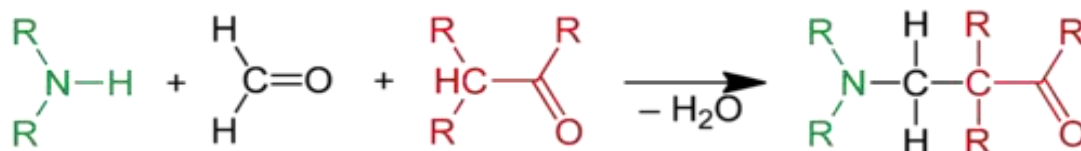


Rhenium metal or its compounds has many applications:

1. Re ribbon in mass spectrographs.
2. Thermocouples.
3. Photography.
4. Re- metal used in preparation of Re-complexes.
5. Re –compound can be used as catalysis in industry.
6. Preparation of radiopharmaceutical complexes to be used in nuclear medicine.

4. Mannich reaction

The Mannich reaction is an organic reaction which consists of an amino alkylation of an acidic proton placed next to a carbonyl functional group with formaldehyde and ammonia or any primary or secondary amine. The final product is a β - amino-carbonyl compound also known as a Mannich base. Reaction between aldimines and α -methylene carbonyl are also considered Mannich reactions because these imines form between amines aldehydes. The reaction is named after chemist car Mannich.



The Mannich reaction is an example of nucleophilic addition of an carbonyl group followed by dehydration to the Schiff base. The Schiff base is an electrophile which reacts in the second step in a electrophilic addition with a compound containing an acidic proton (which is, or had become an enol). The Mannich reaction is also considered a condensation reaction. In the Mannich reaction, ammonia or primary or secondary amines are employed for the activation of formaldehyde. Tertiary amines lack on N-H proton to form the intermediate imine α -CH-acidic compound (nucleophiles) includes carbonyl compounds, nitriles, acetylenes, aliphatic nitro compounds, α -alkyl-pyridines or imines. It is also possible to use activated phenyl group and electron-rich heterocyclic such as furan, pyrrole, and thiophene . Indole is a particularly active substrate; the reaction provides gramine derivatives.

Experimental

Materials:

- | | | |
|-----------------------------|----------------|-----|
| 1) 4-chloro,2-nitro aniline | Merch | 98% |
| 2) 2-amino pyrimidine | BDH | 99% |
| 3) Formic acid | Fluka | 99% |
| 4) Paraformalddhyde | Fluka | 99% |
| 5) Glycine | Riedel de häen | 98% |
| 6) Ethanol | Fluka | 99% |
| 7) Rhenium matel | Aldrich | 99% |
| 8) Hydrogen peroxide | Local | 35% |
| 9) Hydrochloric acid 37% | Fluka | 99% |
| 10) Acetone | Fluka | 99% |
| 11) Phenyl triphosphen | BDH | 99% |

Instrumentation:

- 1) Electrothermal melting point (BÜCHI 535)
- 2) Shimadzu Ur-visible double beam scanning spectrophotometer – 260
- 3) Pye-Unicom- sp³-100-spectrophotometer (KBr disc)



4) Elemental microanalyses were performed on a (C.H.N) analyzer; model Perkin Elmer C.H.N Elemental Analysis

Preparation formylamine:

A modified method used by mixing 0.036 moles from aromatic amine with 10 ml formic acid to round bottom flask. The mixture was refluxed for 8 hours. The formic acid non reactant was removed by distillation, then let to cool at room temperature and filtrated; the residue was washed twice by 10 ml D.W., the precipitate dried at room temperature for 36 hours. Obtained derivatives formayl amine.

Preparation the ligands through Mannich reaction:

Mix amount from the following to round bottom flask:

- 1) Formyl amine 0.006 mole
- 2) Paraformaldehyde 0.006 mole, 0.18 gm
- 3) Glycine 0.006 mole, 0.46 gm
- 4) Ethanol 25 ml
- 5) D.W 10 ml

Refluxed the mixture for 10 hours, then let to cool at room temperature and filtered, the residue was washed by(20 ml D.W),then the precipitate dried at room temperature for 24 hours. Obtained compound .

Synthesis of [ReOCl₃ (PPh₃)₂]

This complex was prepared using the published procedure by adding (9ml) (H₂O₂) 30% slowly to around bottom flask placed in an (ice-bath) containing (0.5gm, 2.7*10⁻³ mole) rhenium metal. The reaction mixture was allowed to concentration in (water-bath) to about (1-2 ml) then, returned to the (ice-bath).

A mixture of (5ml), 37% HCL and (5gm), 1.0*10⁻³ mole (PPh₃) dissolved in (25) acetone was added slowly with stirring and, a green yellowish precipitate formed. The reaction was allowed to reflux for 90 min, then let to cool at room temperature. A green-yellowish precipitate was collected by filtration washed with ethanol 10 ml and dried under vacuum to give 2.2 gm (98%), (m.p.= 213°C), (I.R=968 cm⁻¹) for V(Re=0).

Synthesis of oxotrichloro(N-Glycyl acetylp-amino benzoic acid) rhenium (V):

[ReOCl₃ (PPh₃)₂] (0.2gm) (0.2*10⁻³mole) was added as a solid to mixture N-Glycyl acetyl-amino benzoic acid (0.120 gm) (0.21*10⁻³ moles) in 2 ml Ethanol to round bottom flask. The mixture was reflected for 90 minutes. It was noticed that mixture colure exchanged from green yellow to dark grey, then let (37°C) and filtrated. The precipitate dried at room temperature for 24 hours. The precipitated yield obtained was 53% (0.2264 gm) with dark grey color.

Synthesis of oxotrichloro(N-Glycyl acetylp,4-chloro,2-nitro aniline) rhenium (V):

[ReOCl₃ (PPh₃)₂] (0.2gm) (0.2*10⁻³mole) was added as a solid to mixture N-Glycyl acetyl,4-chloro 2-nitro aniline) (0.120 gm) (0.2*10⁻³ moles) in 2ml ethanol to round bottom flask.

The mixture was refluxed for 90 minutes it was noticed that mixture colure exchanged from green yellow to dark orange, than let it to cool at room temperature (37°C) and filtrated. The precipitate dried at room temperature for 24 hours. The precipitate yield obtain was 55% (0.2181 gm) with

Measuring of molecular weight by depression of freezing point

The measuring of molecular weight for preparation compounds by depression of freezing point. Put 10,0ml of nitrobenzene solvent in test tub clean and dried with thermometer can be read the temperature counting 0.01C. And placed in the tube of



which the largest immersed in (ice bath) and recorded temperature with time certified the temperature, then taken out tube from (ice bath), until the return of the material condition of liquid. As augmented by article 0.5gm of unknown molecular weight with stirring until melted material . Tube will be returned to the (ice bath) with stirring and follow up of temperature change, which then proves the solution it is the degree of congelation solution , Then calculated by ΔT_f of the relationship between temperature charts and time and then extracted the molecular weight of the following equation

$$\Delta T_f = \frac{M_{\text{.wt. Solute}}}{M_{\text{.wt. Solute}}} = \frac{1000}{\text{wt. Solvent}}$$
$$\Delta T_f = T_2 - T_1$$

Results and Discussion

Identification of derivatives formyl

1. Was obtained N-formyl p-aminobenzoic acid from the introduction of a set group formyl to the initial amine group and purity competently product (4.2g,70%), was measured physical their own specification, as shown in table (2) and (4) from these table show that the chemical formula of this compound corresponds to the position of the proposed formula and that of (C.H.N.) analyzer and molecular weight in a Depression of freezing point .Have shown the Infrared spectra of this product in general the following observations which confirm the proposed formula of the compound above.

A. The emergence of a new package back to the weak group (C-H) in the region of aliphatic $(3103) \text{ cm}^{-1}$ and evidence of this link formyl group (O=C-H).

B. The emergence of a single package only for the group (N-H) in the region of $(3311) \text{ cm}^{-1}$ a result of turning the raw material of a first amine to the amine of secondary and further evidence on this link formyl group.

The spectra of U.V-vis absorption showed to peaks absorption first in 290 nm with absorbency molar $6500 \text{ molar}^{-1} \text{ cm}^{-1}$ and the second at 265nm with absorbency molar $9900 \text{ molar}^{-1} \text{ cm}^{-1}$ completely different for the boat the first p-aminobenzoic acid which has a peak absorption of one in 319 nm of absorbency molar $4400 \text{ molar}^{-1} \text{ cm}^{-1}$

2. Was obtained N-formyl 4-chloro-2-nitroaniline from the introduction of a set group formyl according to the method of work mentioned in experimental and purity competently product (4.24g,73%), was measured physical their own specification , as shown in table (2) (4), from these table show that the chemical formula of this compound corresponds to the position of proposed formula and that of (C.H.N.) analyzer and molecular weight in a Depression of freezing point. Have shown the Infrared spectra of this product in general the following observation which confirms the proposed formula of the compound above.

A. The emergence of a new package back to the carbonyl group (C=O) aliphatic , in the region of 1679 cm^{-1} and evidence of this link formyl group (CHO).

B. The emergence of a single package only for the group (N-H) in the region of 3282 cm^{-1} a result of turning the raw material of a first amine to the secondary amine and further evidence on this link formyl group.

The spectra of U.V-vis absorption showed to peaks absorption first in 247 nm with absorbency molar $2375 \text{ molar}^{-1} \text{ cm}^{-1}$ and the second at 265 nm with absorbency molar $990 \text{ molar}^{-1} \text{ cm}^{-1}$ completely different for the boat the first 4-



chloro-2-nitroaniline which has a peak absorption of one in 246 nm of absorbency molar 11650 molar cm and two in 416nm of absorbency molar 5625 molar⁻¹ cm⁻¹

Identification of ligands:

1. Was obtained N-Glycylacetyl P-amino benzoic acid according to the method of work mentioned in experimental part, and purity competently product 5.19gm, 68%, was measured physical their own specification, as shown in table3, from these table show that the chemical formula of this product corresponds to the position of the proposed formula and that of C.H.N. as shown in table 5, and molecular weight in a depression of freezing point. Have shown the infra red spectra of this product in general the following observations which confirm the proposed formula of the compound above.

A. The emergence of a new package back to the group CH₂ and displacement as a result pairing aliphatic in the region 1398 Cm-1

B. And remove package C=O to the left of 1668 to 1697 Cm as a result pairing the link.

The spectra of U.V.-vis absorption showed to peaks absorption in 296 nm with absorbency molar 2650 molar-1 Cm-1 other in 250 nm with absorbency molar 9350 molar-1 Cm-1 are completely different from the absorption peak of derivative formayl mentioned in the table 7.

2. Was obtained N-Glycylacetyly4-chloro2-nitroaniline according to the method of work mentioned in experimental part and purity competently product 4.75g, 66%, was measured physical their own specification as shown in table3, from these table show that the chemical formula of this product corresponds to the position of the proposed formula and that of C.H.N. as shown in table 5 and molecular weight in a depression of freezing point. Have shown the infra red spectra of this product in general the following observation which confirms the proposed formula of this compound above.

A. The emergence of a new package back to group O-H in the region confined 2611-3367 Cm⁻¹ evidence of the link and configuration of the boat above.

B. The emergency of a new package back to group C=O in the region 1269 Cm⁻¹ evidence of the link configuration of the boat above.

The spectra of UV-vis absorption showed to peaks absorption in 266 nm with absorbency molar 9200 molar⁻¹ cm⁻¹ other in 348 nm with absorbency molar 3400 molar⁻¹ cm⁻¹ completely different from the absorption peak of derivative formayl mentioned in the table 7.

Identification of Rhenium complexes:

1. Was obtained oxotrichloro N-GlycylacetylP-aminobenzoic acid rhenium V according to the method of the work mentioned in experimental part and by ligand exchange methods, prepared complex ReOCl₃(PPh₃)₂ and purity competently product 0.2g, 68% was measured physical their own specification, for the complex record and show that the chemical formula of this product corresponds to the position of the proposed formula and that of C.H.N. as shown in table 6 and molecular weight in a depression of freezing point. The spectra of U.V-vis absorption showed to peaks absorption in 270 nm with absorbency molar 10100 molar⁻¹ cm⁻¹ completely different from the ligand of absorption peak and complex ReOCl₃(PPh₃)₂.

2. Was obtained oxotrichloro N-Glycylacetyl 4-chloro2nitroaniline rhenium V according to the method of work mentioned in experimental and by ligand exchange methods to complex record ReOCl₃(PPh₃)₂ and purity competently product 0.2g, 56% was measured physical their own specification for complex record and show that the chemical formula of this product corresponds to the position of the proposed



formula and that of C.H.N. as shown in table 6 and molecular weight in a depression of freezing point.

The spectra of UV-vis. Absorption showed to peaks absorption in 270 nm with absorbency molar $20000 \text{ molar}^{-1} \text{ cm}^{-1}$ other in 450 nm with absorbency molar $5200 \text{ molar}^{-1} \text{ cm}^{-1}$ completely different from the ligand absorption peak and complex $\text{ReOCl}_3(\text{PPh}_3)_2$

Table (2) physical and chemical properties for derivatives formyl

	chemical formula	Theoretical molecular weight	molecular weight measured *	m.p
1	$\text{C}_8\text{H}_7\text{NO}_3$	165.15	166.5	225-227 °c
2	$\text{C}_7\text{H}_5\text{N}_2\text{O}_3\text{CL}$	200.49	198.2	142-145 °c

Depression of freezing point

Table (3) physical and chemical properties for legends

	chemical formula	Theoretical molecular weight	molecular weight measured *	m.p
1	$\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_5$	252.22	250.3	171-175 °c
2	$\text{C}_{10}\text{H}_{10}\text{N}_3\text{O}_5\text{CL}$	287.66	289	136-139 °c

*Depression of freezing point

Table (4) derivatives formyl (C.H.N.)Analyzer

The chemical Formula	Molecular Weight	Carbon	Hydrogen	Nitrogen
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		Theoretic al	Practical	Theoretic al	Practical	Theoretic al	Practical
$C_8H_7NO_3$	165.15	58.18	57.4	4.27	4.10	8.48	8.20
$C_7H_5CLN_2O_3$	200.49	41.94	42.0	2.51	2.30	13.97	14.0

Table (5) Legends (C.H.N.)Analyzer

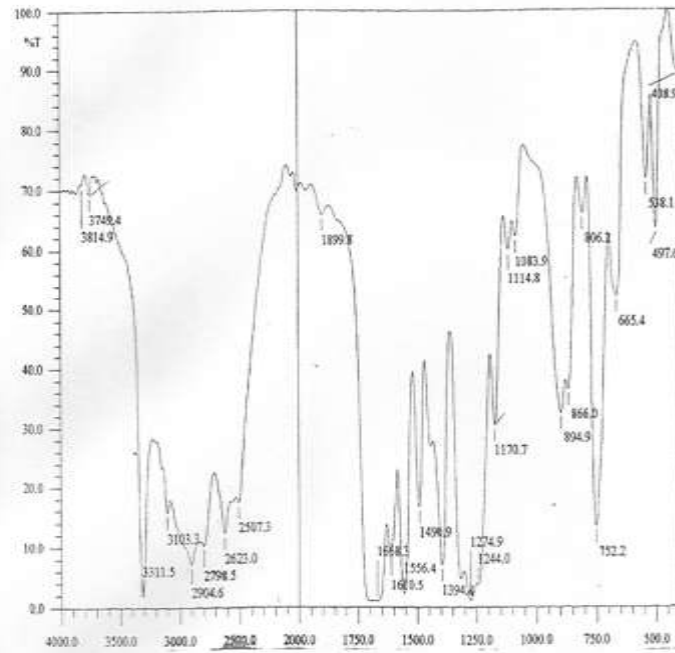
Chemical Formula	M.Wt.	Carbon		Hydrogen		Nitrogen	
		Theoretic al	Practical	Theoretic al	Practical	Theoretic al	Practical
$C_{11}H_{12}N_2O_5$	252.22	52.38	52.10	4.80	4.35	11.11	11.40
$C_{10}H_{10}CLN_3O_5$	287.66	41.75	41.35	3.50	3.15	14.61	14.90

Table (6) complex record

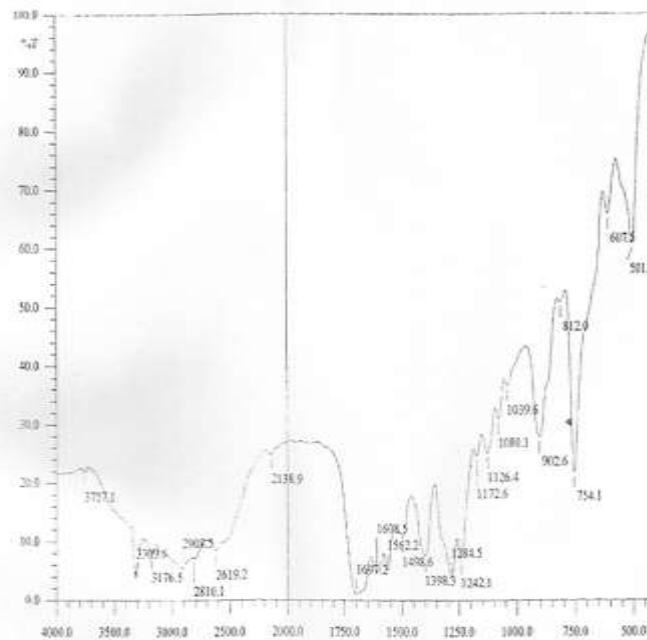
Chemical Formula	M. Wt	Theoretical M.Wt	Carbon		Hydrogen		Nitrogen	
			Theoretic al	Practical	Theoretic al	Practical	Theoretic al	Practical
$C_{11}H_{12}N_2O_6CL_3Re$	559.9	562.5	23.56	23.40	2.16	2.05	5.00	4.85
$C_{10}H_{10}N_3O_6CL_4Re$	594.9	590.3	20.14	21.88	1.69	1.65	7.05	6.98

Table (7) The region package for derivatives formyl and ligands

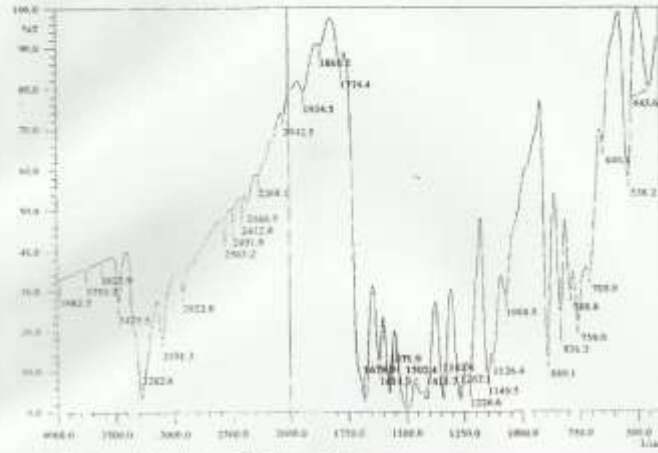
Derivatives Formyl	O-H Stretch	N-H Stretch	C=O Stretch	C=C Stretch	C-O Stretch	C-N Stretch	C-H Stretch	C-C Aromatic o.o.p	N-H Bend	N-H o.o.p	Other N=o
1	2507 3400	3311	1668	1556 1610	1244	1170	2798	665	1490	806	-
2		3282	1679	1571 1614	-	1149	2922	646	1502	788	1342 1502
Ligands 1	2500 3400	3309	1697	1562 1608	1242	1172	-	607	1448	812	-
2	2611 3867	3182	1679	1573 1614	1269	1151	-	648	1500	796	1340 1500



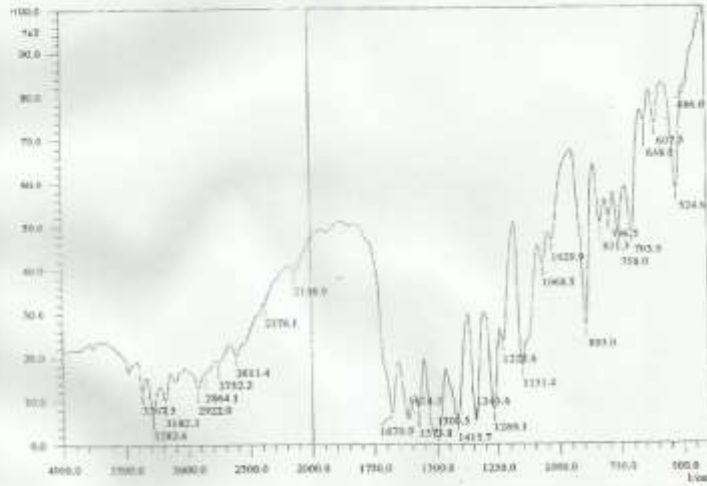
N-Formyl P-amino benzoic acid



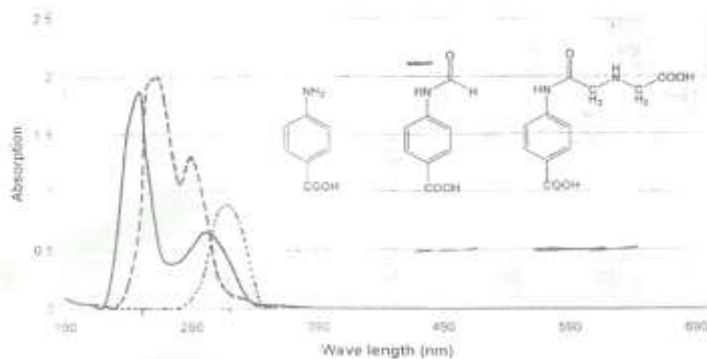
N-Glycylacetyl P-amino benzoic acid



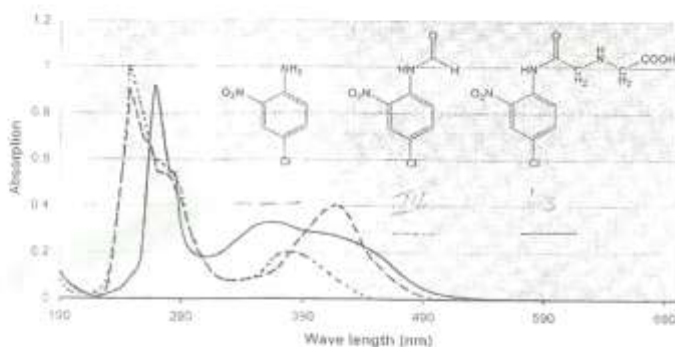
N-Formyl 4-chloro 2-nitroaniline



N-Glycylacetyl 4-chloro 2-nitroaniline



P-amino benzoic acid
N-Formyl P- amino benzoic acid
N-Glycylacetyl P- amino benzoic acid



4-chloro,2-nitro anilin
N-Formyl 4-chloro,2-nitro anilin
N-Glycylacetyl 4-chloro,2-nitro anilin

Conclusion

The results showed that obtained UV-vis spectrum of a reaction and formation of derivative formyl , ligands , and complexes of the spectrum compare the raw material , derivative formyl , ligand, and complexe. The emergence of a new absorption peak leight and the removal of other.And I.R spectrum through the appearance and disappearance of absorption peaks and the removal of.The results showed that (C.H.N) analyzer of conformity with those calculated theoretically and even Depression of freezing point .

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