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Synthesis and Antifungal Activity Against of *Candida* Species for Some New Heterocyclic Compounds Containing Schiff Base, *Oxazepine* , Indoline or Imidazolo Units and Their Spectral Characterization

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Abstract

The objective of this study is to test in Vitro the twenty chemical compounds that contains Schiff base or oxazepine, indoline, imidazolo units in concentrations (50, 100, 150) mg / dl as antifungal activity, against three pathogenic *Candida* species that occur in humans. We tested one isolates of

(Candida albicans, Candida glabrata and Candida krusei). All these species affect human health. The study was carried out in the Laboratory of Public Health, directly of health for the period from May **2016 to** April 2017, Candida *spp* isolates used in this study were collected from patients admitted at some private clinical in Kirkuk city. All isolates were identified using CHROM agar and stored at -70 ^{0}C .Preparation of Schiff base (1-7) from amino pyridine derivatives with aromatic aldehyde by nucleophilic addition reactions preparation of 1,3 – oxazepine 4,7 – dione (8-13) were carried out by cyclization of appropriate Schiff bases with malic anhydride and phthalic anhydride , preparation of compounds (14 – 17) from reaction of a mixture aminopyridine derivative with potassium hydroxide then chloroacetic acid was added , preparation of compounds (18 – 20) from reaction of amino pyridine derivative and 4- phenyl phenacyl bromide , all these compounds were characterized by melting points and FT.IR spectroscopy. Some of them were characterized by H^{1}- NMR and C^{13}-NMR spectroscopy. Some compounds contain Schiff base group in compounds

(1-7) showed inhibitory effect *Candida albicans and Candida krusei*. This study demonstrates that the three *Candida* species were resistant to a range of compounds (8-13) containing oxazepine and as antifungal against , while the compound(14-17) contain Indolin show low inhabition zon for *Candida albicans* and the compound (18-20) contain imidazo group showed inhibited effect against three *Candida* species.

Keywords: antifungal activity Heterocyclic Compounds, *Candida* species.

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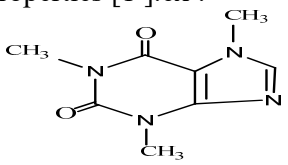
1. Introduction

Hetero cyclic compounds are widely distributed in nature essential for life in different forms, most of sugar and their derivatives including vitamins such as vitamin C present as penta compound (furan) or hexa form (pyran) which contain cyclic single atom of oxygen. Most of members of vitamin group (B_6) , pyridoxine is one of pyridine derivatives ,considered essential for dietary metabolism of amino acids in addition to alkaloids , which are nitrogen bases present in plants and many of antibiotics including penicillin containing heterocyclic system. There is a great number of heterocyclic compounds possible to obtain through laboratory preparation . They are beneficial as therapeutic and pharmaceutical chemical compounds. The heterocyclic compounds especially nitrogenous are present combined in different natural compounds in nature of plant origin called alkaloid , which are generally toxic and have medical properties [1].ex :



Caffeine

The derivative of imidazo pyridine compounds inhibit gastric internal and external secretions and possible to use for prevention or treatment the inflammatory diseases which affect the stomach and intestine [2] . The structure of 1,3-oxazepine-4,7-dione consists of a seven-membered ring along with two carbonyl groups. The cycloaddition reaction type [2+5 →7] is used in synthesis of 1,3-oxazepine[3,4] and 1,3-oxazepane[5,6] rings. Imidazole is present in anti-cancer medication like mercaptopurine that combats leukemia by interfering with DNA activities. Imidazole also exists in anti-fungal, anti-protozoal and anti-hypertensive medication. Imidazole is a part of the theophylline molecules, found in tea leaves and coffee beans, which stimulates the central nervous system [7].

Candidiasis an infection created by *Candida* is named candidiasis or candidosis. [8], *Candida* species can be co-aggregated with bacteria in biofilm and that may be an essential factor for demonstrations of candidiasis and for colonization of cavities of caries and periodontal pockets [9] . A large amount of healthy adult community holds yeast *Candida* species in the oral cavity [10] and, gastrointestinal tract and vagina [11]. Many *Candida* species are commensal and colonize the skin and mucosal surfaces of humans. Desperately ill or otherwise immunocompromised patients are wider prone to evolve both superficial and life-threatening *Candida* infections [12]. *Candida albicans* is the highest common infectious factor. This dimorphic yeast is a commensal that colonizes skin, the gastrointestinal and the reproductive tracts. Non-*C. albicans* species are emerging pathogens and can also colonize human mucocutaneous surfaces [13]. Currently, an increase in the number of yeasts that are resistant to antifungal drugs is recognized worldwide; therefore, the use of in vitro laboratory tests may aid the doctor in choosing an appropriate therapy [14]. Many effective antifungal agents were accessible for the administration of candidiasis. But isolates may exhibit intrinsic resistance to the drug all along therapy. So the use of several chemical compound as alternative agents for the control of fungal diseases is considered as an interesting alternative to synthetic fungicides [15]. Five, six and seven membered heterocyclic compounds have been of great interest due to their variety of applications particularly in the field of chemotherapeutic, anti-microbial, pesticidal, agriculture and fungicidal. Therefore, this work was directed towards the synthesis of these heterocyclic derivatives and investigation of their anti-bacterial activity.

2. Experimental

Chemicals

The chemicals used in this work are listed in table:

Supplied from	Chemicals and their manufacture chemicals
BDH	Absolute ethanol
BDH	2-aminopyridine
BDH	Malic anhydride
Merck	Phthalic anhydride
Merck	Carbon disulfide
BDH	Chloroacetic acid
Merck	Chloroacetamide
BDH	Ethyl acetoacetate
BDH	2-amino-6-methyl pyridine
Merck	4-chlorobenzaldehyde
BDH	Hydrazine hydrate
BDH	2-hydroxy benzaldehyde
Merck	Isatin
Merck	Malonic acid
Merck	2-amino - 5 -methylpyridine
BDH	*3-bromo* benzaldehyde
BDH	*p*-Phenyl phenacyl bromide
Merck	2-amino 3,5-dichloro pyridine
BDH	3-aminopyridine
BDH	*2-bromo* benzaldehyde

3. Techniques:

Melting Point:
Melting points were recorded on a hot stage Gallen Kamp melting point apparatus and were uncorrected.

Infra-Red Spectrophotometer:
FT-IR spectra were recorded using Fourier Transform infrared Shimadzu FTIR-8400 infrared spectrophotometer, Japan, KBr disc or thin film was performed by central organization of standardization and quality control center

^{1}H-NMR:

^{1}H-NMR spectra were recorded on a Fourier transform Bruker spectrometer operating at 400MHz with tetramethylsilane as internal standard in DMSO-d6. University of Vienna, Austria.

^{13}C-NMR:

^{13}C-NMR spectra were recorded on a Fourier transform Bruker spectrometer operating at 75.47 MHz in DMSO-d6**.** University of Vienna, Austria.

Preparation of compounds (1-7)

In a 100(mL) round bottom flask , a mixture of 0.01 mol of 2- aminopyridine in 5 mL absolute ethanol and 0.01 mol of aromatic aldehyde in 5mL absolute ethanol was placed ,the reaction mixture was refluxed for 16 hrs , then it was filtered the resulting product was dried and recrystallized from ethanol yield 95% , m.p (112- 114) ^{0}C for preparation of compound (1) , the derivatives (2,3,4,5,6,7) were obtained following the
Different amino pyridine derivative with different aromatic aldehyde .

Preparation of compounds (8-10)

A mixture of equimolar amounts (0.0025 mol) of Schiff bases derivatives (8 , 9 , 10) and (0.0025 mol , 0.37 gm) of phthalic anhydride in 20 mL of dry benzene ,was refluxed with stirring for (14-16) hrs at 60 0C , the physical data are listed in Table (2).

Preparation of compounds (11-13)

A mixture of equimolar amounts (0.0025 mol) of Schiff bases derivatives (11,12,13) and (0.0025 mol , 0.24 gm) of malic anhydride in 20 mL of dry benzene ,was refluxed with stirring for (10-12) hrs at 60 0C ,the physical data are listed in table (3).

Table (1): Physical properties of compounds (1-7)

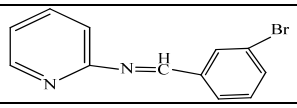
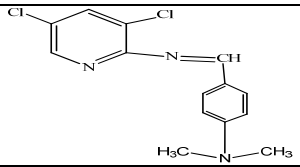
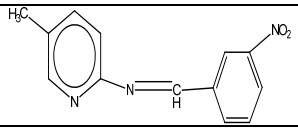
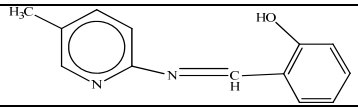
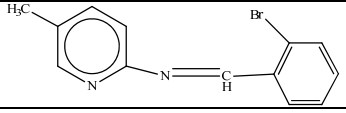
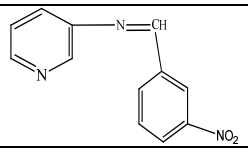
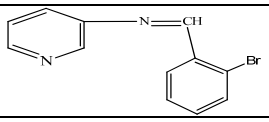
Comp .No.	Structure and name of products	M.P	Yield	Color
1		112-114	90	brown
(*E*)-*N*-(3-bromobenzylidene)pyridin-2-amine				
2		82-84	84	Green
3,5-dichloro-*N*-(4-(dimethylamino)benzylidene)pyridin-2-amine				
3		127- 130	82	yellow
5-methyl-*N*-(3-nitrobenzylidene)pyridin-2-amine				
4		105 -107	84	yellow
2-(((5-methylpyridin-2-yl)imino)methyl)phenol				
5		108- 110	87	yellow
N-(2-bromobenzylidene)-5-methylpyridin-2-amine				
6		74-76	72	Green
N-(3-nitrobenzylidene)pyridin-3-amine				
7		100- 102	85	brown
N-(2-bromobenzylidene)pyridin-3-amine				

Table (2): Physical properties of compounds (8-10)

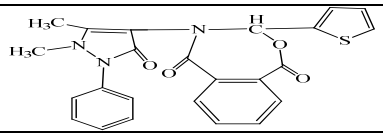
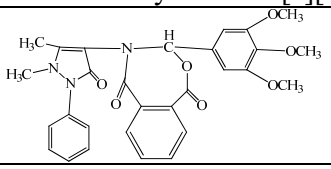
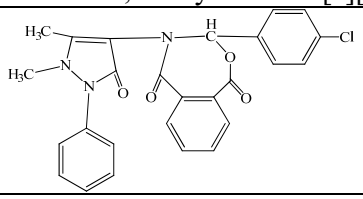
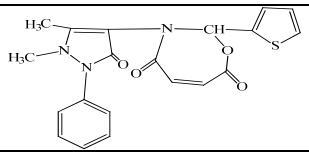
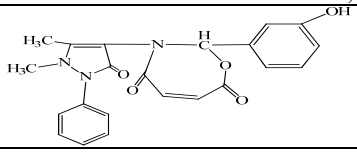
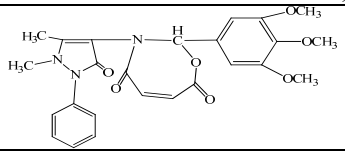
Comp .No.	Structure and Name of products	M.P	Yield	Color
8		108-182	37	brown
4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3-(thiophen-2-yl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione				
9		145-147	80	yellow
4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3-(3,4,5-trimethoxyphenyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione				
10		178- 180	45	yellow
3-(4-chlorophenyl)-4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione				

Table (3): Physical properties of compounds (11-13)

Comp .No.	Structure and name of products	M.P	Yield	Color
11		74-76	52	brown
3-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2-(thiophen-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione				
12		248-250	61	yellow
3-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2-(3-hydroxyphenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione				
13		159- 161	45	yellow
3-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione				

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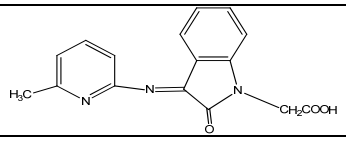
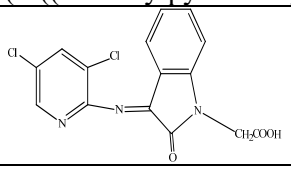
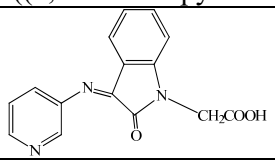
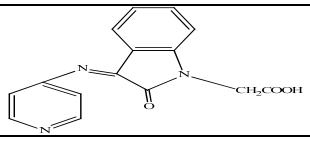
Preparation of compounds (14 -17)

A mixture of KOH (0.013 mol , 0.56 gm), 2- amino-6-methyl pyridine and (0.013 mol , 3gm) was dissolved in 25 mL absolute ethanol ,then chloroacetic acid (0.013 mol , 1.22 gm) was added and the reaction mixture was refluxed for 7hours ,yield 78% , m.p = 166- 168 ^{0}C for preparation of compound 14 . This experimental was reputed using the same amount of reactance in order to obtain other derivatives (15 – 17) the physical data are listed in Table (4).

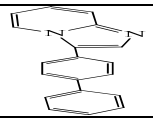
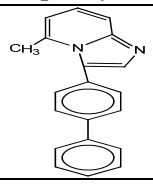
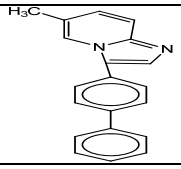
Table (4):Physical properties of compounds (14-17)

Comp .No.	Structure and Name of products	M.P	Yield	Color
14		166-168	78	orange
(E)-2-(3-((6-methylpyridin-2-yl)imino)-2-oxoindolin-1-yl)acetic acid				
15		176-178	71	red
(E)-2-(3-((3,5-dichloropyridin-2-yl)imino)-2-oxoindolin-1-yl)acetic acid				
16		186-189	51	orange
(Z)-2-(2-oxo-3-(pyridin-3-ylimino)indolin-1-yl)acetic acid				
17		165-167	52	red
(Z)-2-(2-oxo-3-(pyridin-4-ylimino)indolin-1-yl)acetic acid				

Preparation of compounds (18- 20) [16]

A mixture of 2- amino pyridine (0.02 mol , 2 gm) and compound 4-phenyl phenacyl bromide (0.02 mol , 5.5gm) was dissolved in 25 mL absolute ethanol, the reaction mixture was refluxed for 25hours , the mixture was allowed to cool at room temperature and recrystallized from ethanol to give the final product yield 78% , m.p = 218- 220 ^{0}C for Preparation of compound 18 . This experimental was reputed using the same amount of reactance in order to obtain other derivatives (19 – 20) the physical data are listed in table (5).

Table (5): Physical properties of compounds (18-20)

Comp .No.	Structure and Name of products	M.P	Yield	Color
18		218-220	75	brown
"3-biphenyl -4-ylimidazol[1,2-a] pyridine				
19		176-178	43	brown
3-([1,1'-biphenyl]-4-yl)-5-methylimidazo[1,2-a]pyridine				
20		275 (dec.)	56	Burly wood
3-([1,1'-biphenyl]-4-yl)-6-methylimidazo[1,2-a]pyridine				

Candida spp isolates investigated

Candida spp isolates used in this study were collected from patients admitted at the some privet clinical in Kirkuk city and were analysed for microscopy and culture ,from May 2016 to April 2017. All isolates were identified using CHROMagar and stored at −70 °C. clinical isolates of *Candida albicans* ,*Candida glabrata* and *Candida krusei* were used.

Antifungal susceptibility tests:

In vitro antifungal-susceptibility tests were conducted on some the ***Candida* species** (***Candida albicans* ,*Candida glabrata and Candida krusei***) using a test medium prepared with Sabouraud dextrose agar (SDA) . Twenty mL of media were poured into 9 cm diameter Petri dishes. For each treatment, 3 plates (replicates) were used . Yeast suspensions were prepared in 0.85 % NaCl. The turbidity of each suspension was adjusted to a 0.5 McFarland standard (1 x 10^5 x 10^6 cells per ml.). Using cotton-tipped swabs, each yeast suspension was inoculated onto agar plates. and added 0.5mL. of the chemical compounds the concentration of (50mg. ,100mg. and 150mg) in pour on teste media. After inoculation, plates were incubated at 35 ^{0}C incubator and observed for the presence or
absence of growth after 48 hrs . The susceptibility end point was defined as the lowest concentration of antifungal which resulted in 80% inhibition of growth compared with that of the drug-free control.

4. Results and discussion

Identification of compounds (1-7)

The FT-IR spectra of compounds (1-7) showed disappearance of the sharp bands were at (3164-3469) cm^{-1} were due to asymmetric and symmetric stretching vibrations of amino

groups(-NH_2) in 2-amino pyridine derivatives , and appearing (1591- 1660) cm^{-1}were due to the stretching vibration of (N= CH) group were listed in Table (6), Figures (1),(2), (3)and (4) show the FT-IR spectra for compounds 2,3 .

Table (6): IR-data of the synthesized derivatives of (1-7) compounds in cm^{-1}

Comp. No.	FT.IR (bands) , cm^{-1}
1.	3089.8 υ C-H(aromatic) , 1594.9 υ (N=CH) , 601 υ (C-Br)
2.	3051.3 υ C-H(aromatic), 1660.7 υ (N=CH) , 815.8 υ (C-C l)
3.	3093.8 , 2950 υ C-H(aromatic& alphatic) , 1622υ (N=CH) , 1523 (υ_{as} C-NO_2) 1352 (υ_s C-NO_2)
4	3450.9 υ (OH) , 3001.2 C-H(aromatic& alphatic) , 1610 υ (N=CH) 2917.9
5	3022.4 υ C-H(aromatic& alphatic) , 1608υ (N=CH) , 575 υ (C-Br) 2920.2
6	υ 1615. 7 (N=CH) , 1525.7 υ(C=C) , 1525 (υ_{as} C-NO_2) 1350(υ_s C-NO_2)
7	1591.2υ (N=CH) , 1588 υ (C=C) , 584υ (C-Br)

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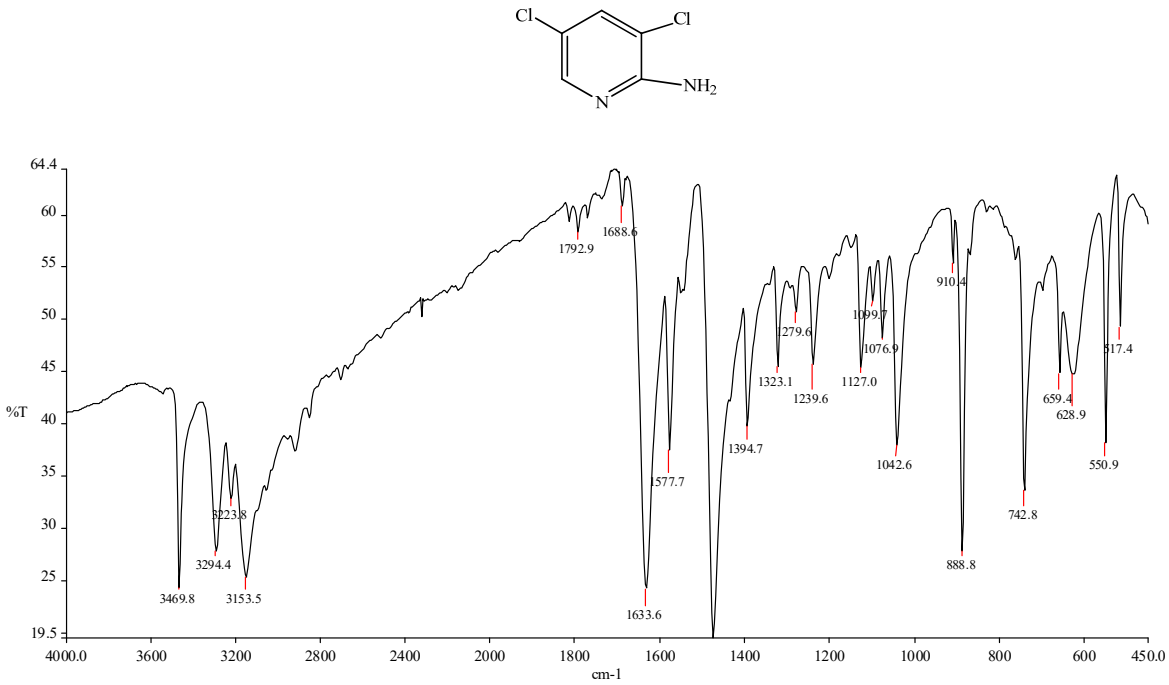
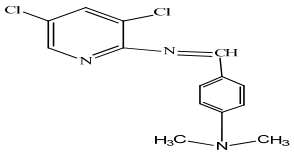


Figure(1): IR spectrum of 2-amino 3,5- dichloropyridine



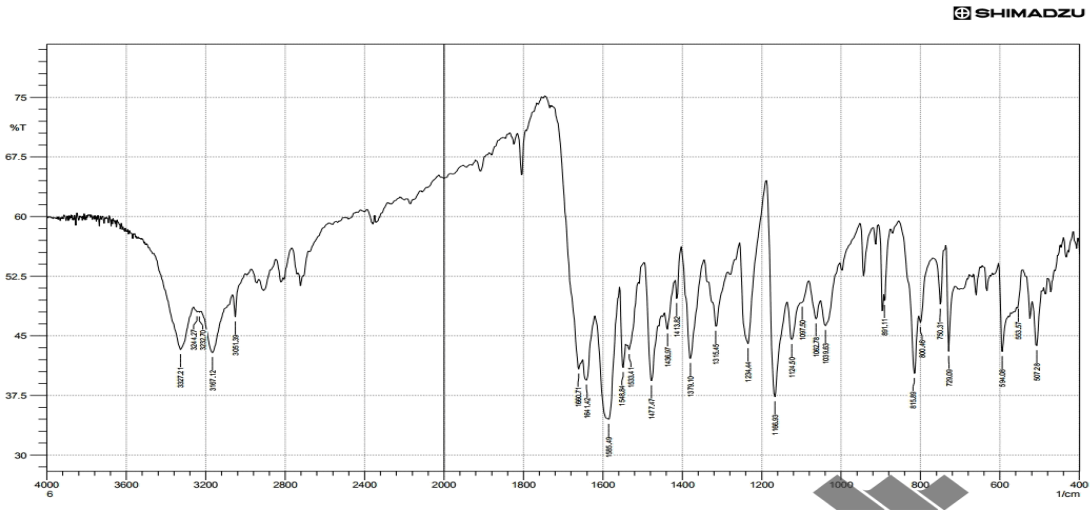


Figure (2): IR spectrum of compound (2)

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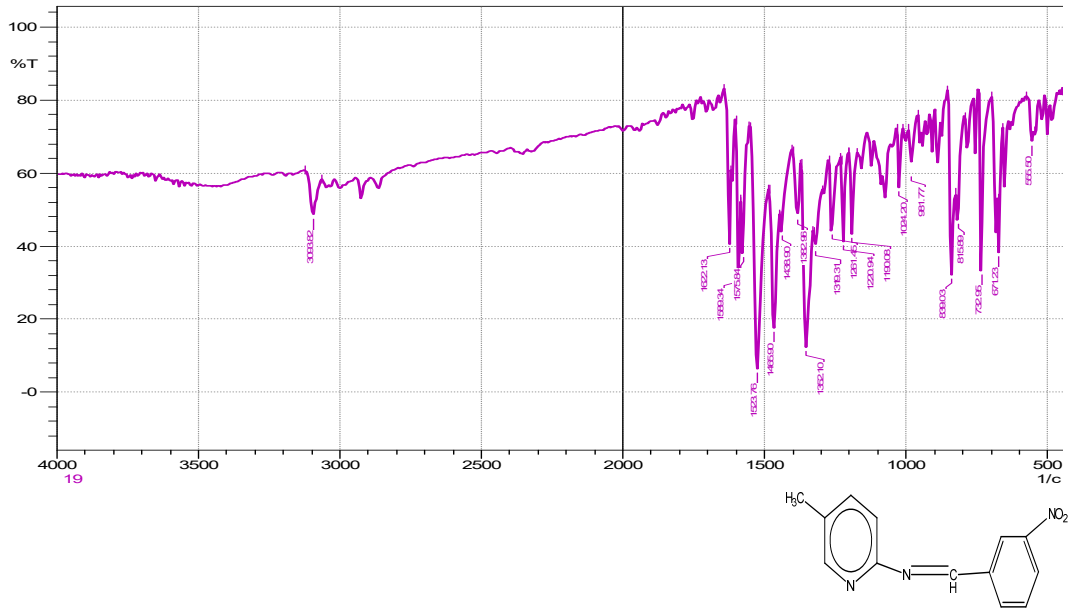


Figure (3):IR spectrum of compound (3)

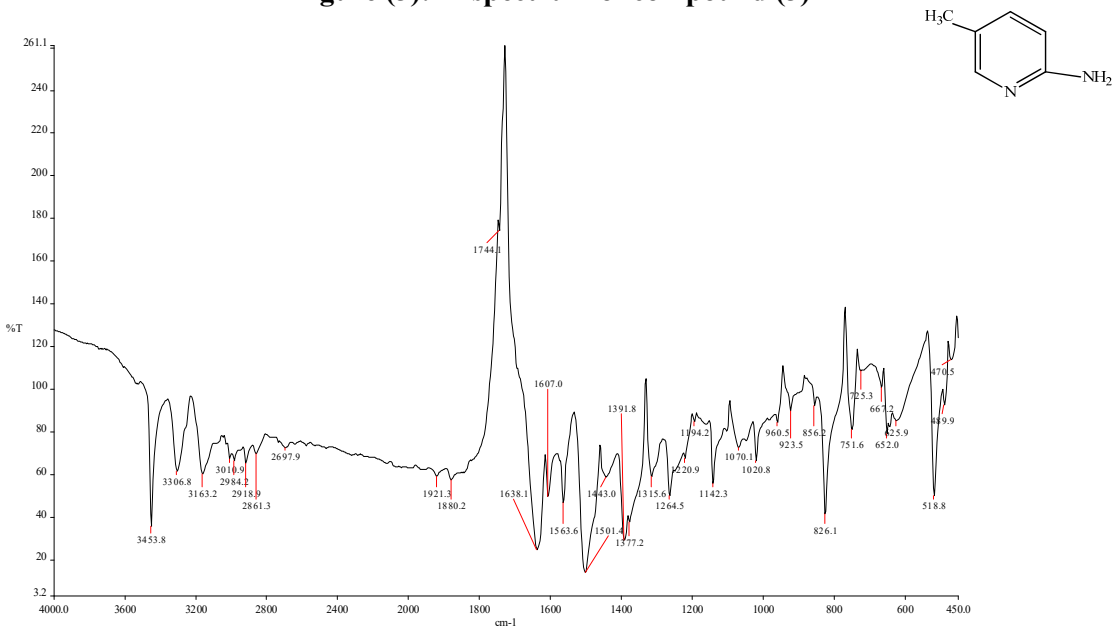


Figure (4):IR spectrum of compound 2-amino-5-methyl pyridine

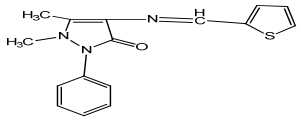
Identification of compounds (8-10)

The FT.IR spectra of compounds (8-10) showed disappearance of absorption bands at (1585- 1620) cm $^{-1}$ was due to the (C= N) of imine group and appearance of strong absorption band at (1720 -1725) cm $^{-1}$ was due to the stretching vibration of the (C= O) lactone group [17] , the appearance of the strong absorption band at (1650- 1692) cm $^{-1}$ was due to the stretching vibration of the (C= O) lactam group [18] , the other data of functional

groups were shown in the following Table (7) . Figures (5),(6), (7) and(8) show the FT-IR spectra for compounds 8,9.

Table (7): IR-data of the synthesized derivatives of (8-10) compounds in cm^{-1}

Comp. No.	I R υ (cm^{-1}) , KBr				
	υ(C- H) Aromatic Aliphatic	C=C-C=O Cyclic	υ(C= O) Lactone Lactam	υ (C=C) aromatic.	Other
8	3060 2925	1626	1725 1692	1585	
9	3062 2935	1627	1724 1689	1583	υ(O-CH_3)1232.5
10	3060 2924	1626	1720 1650	1585	υ(C-Cl) 885.2



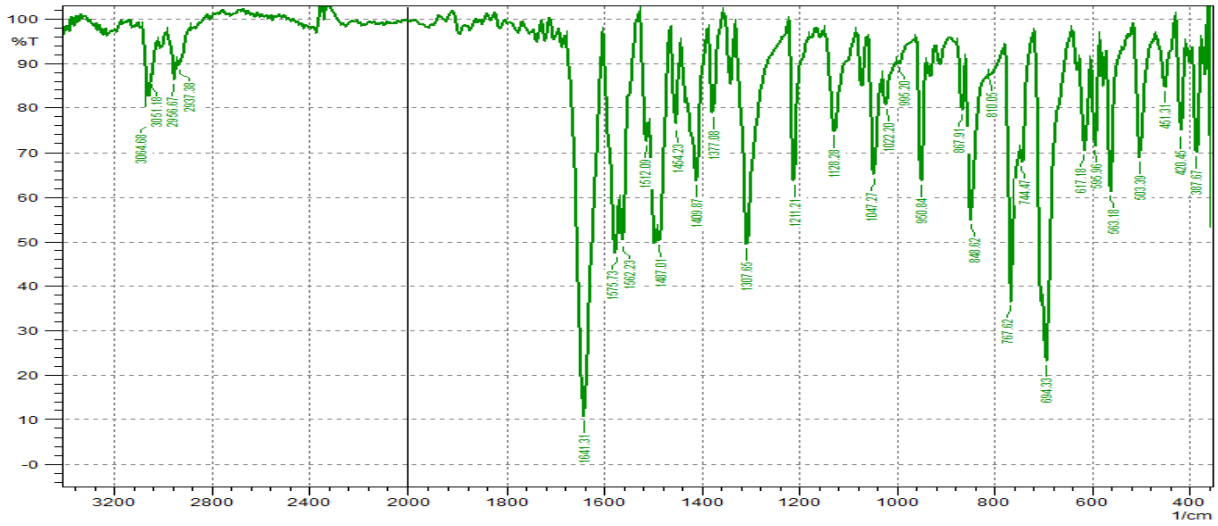
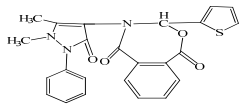


Figure (5): IR spectrum of Schiff base compound (8).



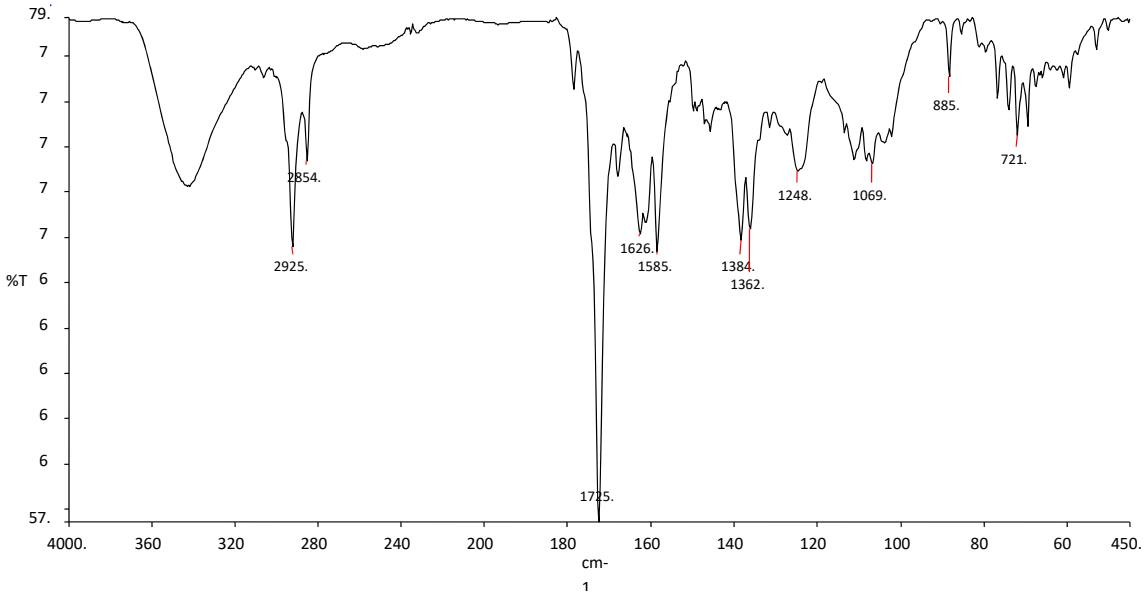
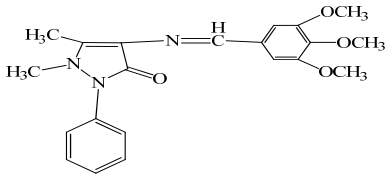


Figure (6): IR spectrum of (8).



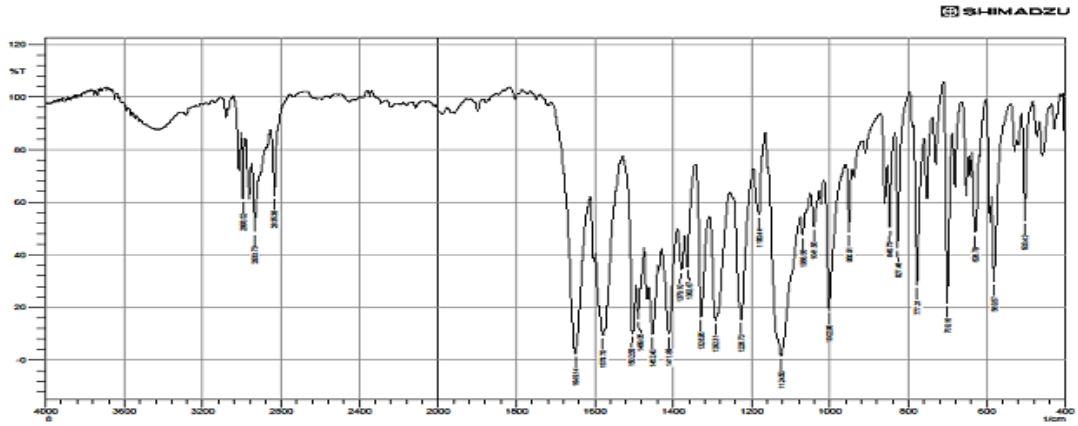


Figure (7): IR spectrum of Schiff base compound (9)

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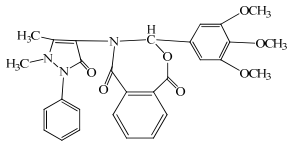

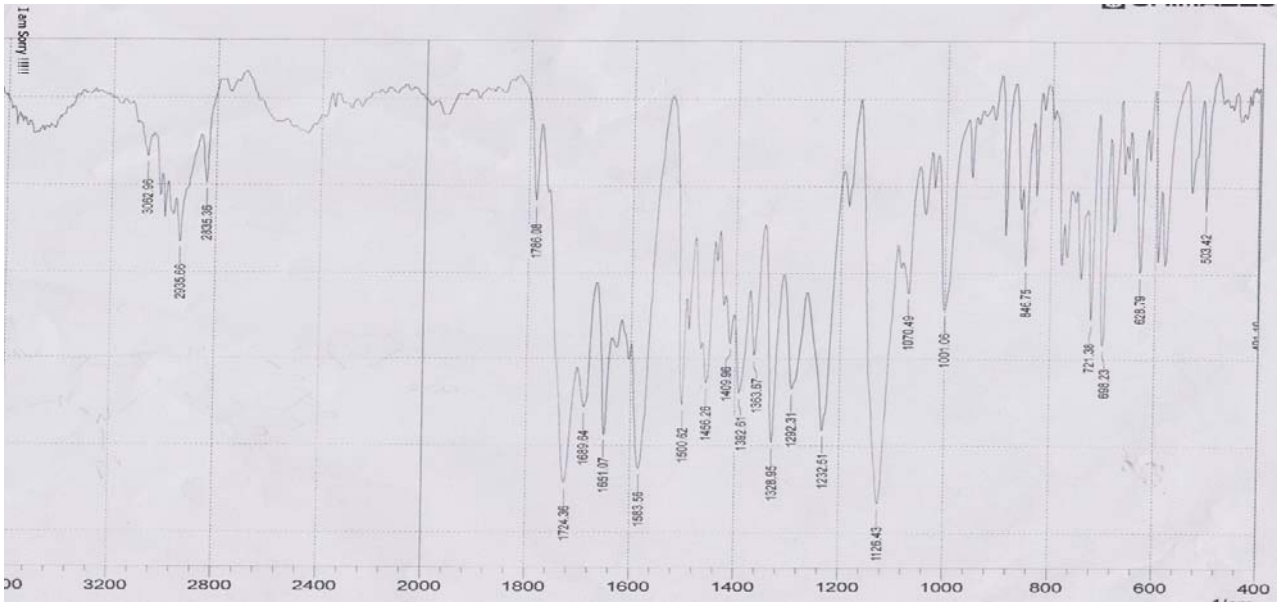

Figure (8): IR spectrum of Schiff base compound (9)

Identification of compounds (11-13)

The FT.IR spectra of compounds (11-13) showed disappearance of absorption bands at (1585- 1620) cm $^{-1}$ was due to the (C= N) of imine group and appearance of strong absorption band at (1710 -1723) cm $^{-1}$ was due to the stretching vibration of the (C= O) lactone group, the appearance of the strong absorption band at (1640- 1655) cm $^{-1}$ was due to the stretching vibration of the (C= O) lactam group, the other data of functional groups were shown in the following table (8) .

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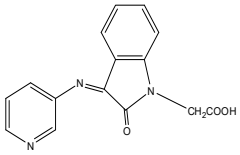
Table (8):IR-data of the synthesized derivatives of (11-13) compounds in cm^{-1}

Comp. No.	I R υ (cm^{-1}) , KBr				
	υ(C- H) Aromatic Aliphatic	O ‖ C═C—C Cyclic	υ(C= O) Lactone Lactam	υ (C=C) Aromatic.	Others
11	3042 2995	1634	1717 1655	1588	
12	3139 2926	1557	1723 1640	1488	υ(OH) 3290.9
13	3090 2933	1618	1710 1649	1502	(O-CH_3) 1292.3υ

Identification of compounds (14-17)

The FT.IR spectra of compounds (14-17) showed appearance of absorption bands at (3440 – 3650) cm^{-1} and (1730 – 1739) cm^{-1} which attributed to υ(OH) and υ (C= O) Of carboxylic acid is good evidence for this reaction , showed appearance of the sharp bands at (2968)) cm^{-1} attributed to asymmetric stretching vibrations of (- CH_2 -) , showed bands at (3070 – 3085) cm^{-1} which were assignable to (C-H) aromatic ,H^1-NMR spectrum of compound (14) , Figure (10) shows the signal at δ = 2.5 ppm was due to the methyl group (C- CH_3) ,the signal at δ =3.3 ppm was due to the methyl group (CH_2—C(=O)) , (C-H) aromatic appear at δ = 7.3- 8.3 ppm peaks as multiplate peaks ,the signal at δ = 12.09 was due to the proton of (C(=O)—OH) group , Figures (9) and (10) shows the FT-IR spectra for compounds 16 , 14 & H^1-NMR .



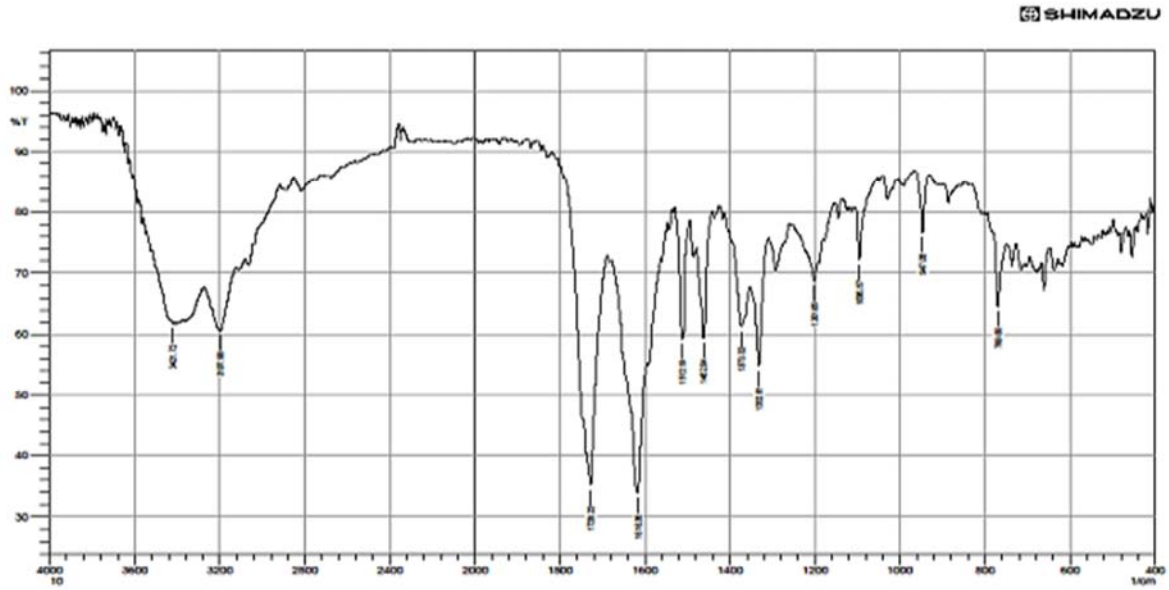
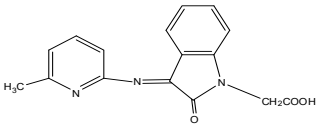


Figure (9): IR spectrum of (16)



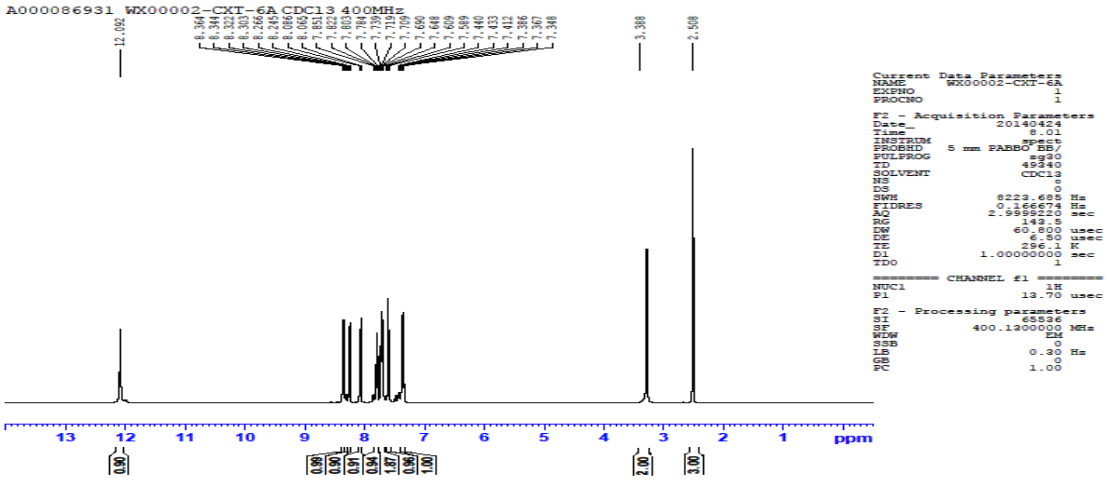


Figure (10):H[1]-NMR spectrum of (14)

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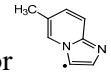
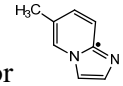
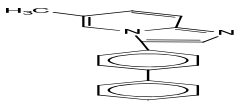
Identification of compounds (18-20)

The disappearance of bands at the general range (3313 –3453) cm^{-1},(3306 – 3164) attributed to (NH_2) amino pyridine derivatives stretching frequency together with appearances of band at general range (3053 – 3084) cm^{-1}assignable to (C-H) aromatic stretching ,the bands at range (1664 – 1682) cm^{-1} attributable to the υ(C=N) [19] of imidazole ring **,** provide disappearing at 1700 cm^{-1} which assigned to υ (C= O) Of 4-phenylphenacyl bromide, C^{13}-NMR spectrum of compound (20). A signal at δ = 18.39 is for carbon of methyl group () A signal at δ = 118.2 is for of () A signal a 119,91 is for ()A signal at δ=122.3 is for()A signal at δ=124.7 is for  A signal at δ=127.2 is for  A signal at δ=127,6s for  A signal at δ= 127.9 is for  A signal at δ=128.4 is for  A signal at δ=129,2 is for  A signal at δ=131,3 is for  A signal at δ=131,9 is for  A signal at δ=137.1 is for  A signal at δ=140.3 is for  A signal at δ=145.1 is for  . Figures (**11**) **and** (**12**) show the FT-IR spectra & C^{13}-NMR spectrum forcompounds 20.



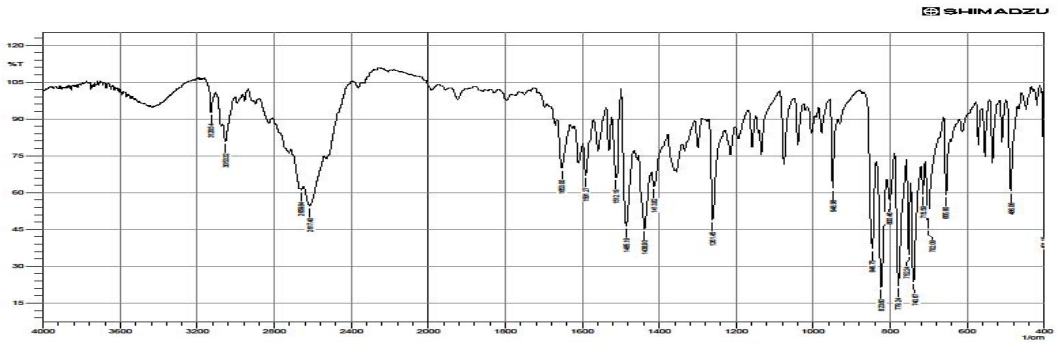


Figure (11): IR spectrum of (20)

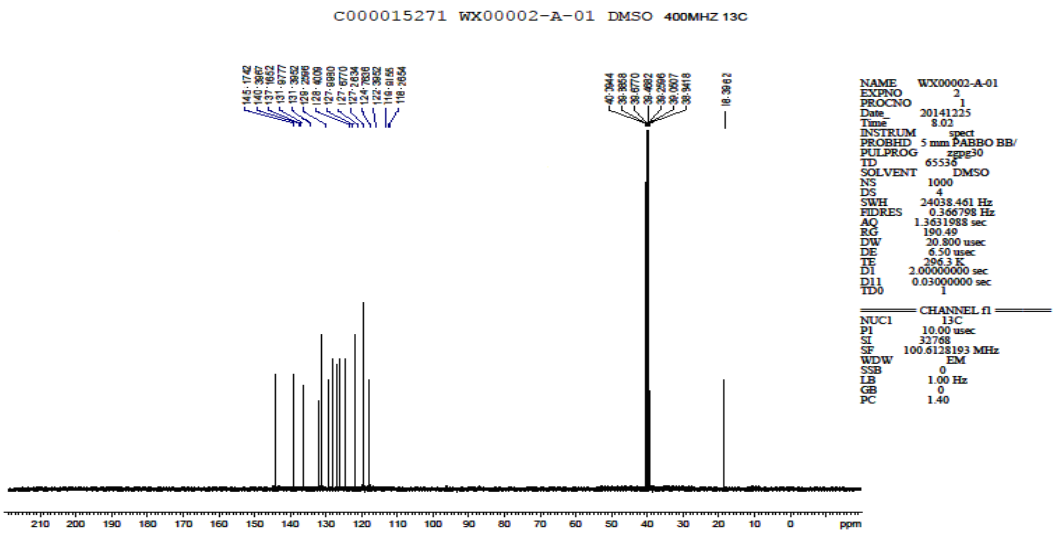


Figure (12): C^{13}-NMR spectrum of (20)

Antifungal activity against *Candida* spp

This study showed that the *Candida krusei* inhabited the compounds containing Schiff base, this compound "Schiff base" had more effect compared to the other chemical compounds, and increased the inhibition zone of *Candida krusei* by increasing the concentration, where it completely inhabited the yeast at 150 mg / dl concentration for the compounds (2,5,7), also Imidazolo compounds [19, 20] showed the inhibition of the yeast, while Indolin and Oxazepine didn't show any results of inhabiting the yeast.

On the other hand, the yeast *Candida glabrata* was inhabited by the chemical compound containing Schiff base, as for Imidazo group compounds only compound number "20" affected the inhibition of the *Candida glabrata*, but, wasn't inhabited by the chemical compounds containing Indolin and Oxapine . And *Candida albicans* was inhabited by Schiff base (1-7) and Imidazo group compounds(18-20) , as for Indolin compounds, only compound number "17" inhabited the yeast. But, Oxazepine chemical compounds didn't show any affection results against *Candida albicans.* These findings are in agreement with [20] led to a gradual increment in the anticandidal activity of MF and AF preparates. *C. albicans*, clinical resistance to antifungal as a result of reduced intracellular accumulation was reported for other pathogenic *Candida* species including *C. krusei C. glabrata, C. dubliniensis and C. tropicalis.* The azoles resistant isolates of *Candida* species mainly overexpress genes encoding multidrug efflux transporter proteins belonging to two super families, the ABC transporters and MFS[21] .The tested *Candida krusei* strain were found to be more sensitive to higher concentrations for the compounds containing Schiff base. Through the recent study, it showed that the three species of yeast (*Candida krusei, Candida glabrata* and *Candida albicans*) was most affected by the chemical compounds of Schiff base because these chemical compounds contain the active group (N= CH), as for Imidazol group compounds, they were the second most effective compounds because they contain methyl group carbon of ($\overline{\overline{CH_3}}$). While the other two compounds (Indolin(except for the compound number "20") and Oxazepine) didn't affect the inhibition of the three species (*Candida krusei, Candida glabrata* and *Candida albicans*) at all. We suspect that the three species had resistance

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against Indolin and Oxazepine compounds. These results suggested that Schiff base and Imidazo could be a therapeutic alternative with Candida species that show some degree of in vitro resistance to antifungal drugs such as ketoconazole . These results are shown in Tables(9,10,11) .

Table (9): shows the affected chemical compound as antifungal against *Candida krusei*

antifungal *candida* spp	**Comp. No.**	**50** mg / dl	**100** mg / dl	**150** mg / dl
Candida krusei	**1**	**0**	**0**	**0**
	2	**21** mm	**37** mm	**40** mm
	3	**0**	**0**	**0**
	4	**0**	**0**	**0**
	5	**18** mm	**20** mm	**25** mm
	6	**0**	**0**	**0**
	7	**22** mm	**33** mm	**41** mm
	8	**0**	**0**	**0**
	9	**0**	**0**	**0**
	10	**0**	**0**	**0**
	11	**0**	**0**	**0**
	12	**0**	**0**	**0**
	13	**0**	**0**	**0**
	14	**0**	**0**	**0**
	15	**0**	**0**	**0**
	16	**0**	**0**	**0**
	17	**0**	**0**	**0**
	18	**0**	**0**	**0**
	19	**25** mm	**27** mm	**30** mm
	20	**20** mm	**26** mm	**29** mm

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Table (10): shows the affected chemical compound as antifungal against Candida *glabrata*

antifungal *candida* spp	Comp. No.	50 mg / dl	100 mg / dl	150 mg / dl
Candida glabrata	1	0	0	0
	2	17 mm	21 mm	25 mm
	3	0	0	0
	4	0	0	0
	5	25 mm	28 mm	33 mm
	6	0	0	0
	7	21 mm	24 mm	28 mm
	8	0	0	0
	9	0	0	0
	10	0	0	0
	11	0	0	0
	12	0	0	0
	13	0	0	0
	14	0	0	0
	15	0	0	0
	16	0	0	0
	17	0	0	0
	18	0	0	0
	19	0	0	0
	20	18 mm	23 mm	25 mm

Table (11): shows the affected chemical compound as antifungal against *Candida albicans*.

antifungal *candida* spp	Comp. No.	50 mg / dl	100 mg / dl	150 mg / dl
Candida albicans	1	0	0	0
	2	0	0	0
	3	7 mm	10 mm	20 mm
	4	0	0	0
	5	28 mm	29 mm	30 mm
	6	5 mm	8 mm	15 mm
	7	25 mm	27 mm	29 mm
	8	0	0	0
	9	0	0	0
	10	0	0	0
	11	0	0	0
	12	0	0	0
	13	0	0	0
	14	0	0	0
	15	0	0	0
	16	0	0	0
	17	3 mm	5 mm	10 mm
	18	0	0	0
	19	3 mm	4 mm	15 mm
	20	27 mm	28 mm	28 mm

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