Synthesis And Characterization Of Some New Acetylenic Mannich Bases Based On Biphenyl – 4,4 - Dithiol

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Abstract

One of the most important , compound which have active hydrogen is the compound possessing (thiol group) Biphenyl-4,4-dithiol is agood example utilized in a wide field for preparation mannich bases , avariety of new acetylenic mannich bases have been Synthesized and all proposed structure were Supported by FTIR , ^{1}H – NMR, ^{13}C-NMR , Elemental analysis and microbial study .

Key words : Biphenyl ,fused ,Acetylenic, Mannich bases .

Introduction :

The development of simple synthetic routes to widely used organic compounds using readily available reagent is one of the main objective of organic Synthesis (Nitrogen and Sulfuer) atom are of a special interest because they consistute of an important class natural and non natural product[1] many of which exhibit useful biological activities [2] . One pot efficient synthesis of mannich's bases may permit the development of novel therapies for the treatment of epilepsy pain and other neurodegenerative disorder [3].

Some mannich's bases have been reported to be used as analgesic , anthelmintic , antitubercular , plant growth regulating properties [4], antiviral , antifungal and anticancer [5], moreover mannich's bases have been shown wide range pharmacological application[6] .

Materials and Methods:

Melting points were determined on (Gallen Kamp) melting point apparatus and were uncorrected , FTIR Spectra of the compounds were recorded on (SHIMADZU) FTIR - 8300 spectrometer as KBr - disc , Results were given in cm^{-1} , ^{1}H-NMR , ^{13}C - NMR , and the spectra were recorded at 200-13 and 50.32 MHz respectively in (DMSO - d_6) , the chemical shifts are reported in part per million (ppm) down field from internal tetra methyl silane (TMS) , chemical shift in (δ) value , Elemental analysis (C.H.N) analyzer , microbial study , All were performed in center of consultation University of Jordon.

Material

All the chemicals used were supplied by (Merk , Fluka , and BDH) chemical , the solvent purified by distillation and dried with calcium chloride .

Measurement and Techniques

The purity of mannich's bases productswere determind by using coloum chromatography with mixture of silica gel (mesh 60) and cyclohexane as solvent and the purity were investigated by (T.L.C) technique by using a mixture of benzen - ethanol (5 : 5 V/V) as elute and Iodine chamber for spot location .

Synthesis of phenyl(prop-2-yn-1-yl) sulfane compound with prop-2-yn-y(p-toyl)sulfane(1:1)(1)[7].

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Round bottomed flask 250 ml equipped with mechanical stirrer , then charged with (0.0075 mol ,1.575 gm) of biphenyl - 4 , $\bar{4}$ - dithiol elute in (20ml) abs . methanol and (1:1) triethyl amine (Et3N) with stirring about (15 min) in room temperature, then drop wise (0.015 mole,1.78 ml) propagyl bromide with continued stirring about (20 min), Refluxing the mixture in (55C), and for the mixture pour slowly and gradually adding to (20 ml) ice distilled water ,after that dehydrate and Recrystallization in mixture (ethanol)and water 2:1)..

Synthesis of Acetylenic Mannich Bases (2-10)[8] :

Compounds [2-10] were prepared by adding compound [1] (0.010mol , 2.86gm) and copperous chlorid ($CuCl_2$) (0.25) to (50ml) Dioxian (empty from peroxide) which heated before , then added (0.004mol , 1.2ml) formaldehyde solution (37-41)% with stirring the mixture about (10 min) with adding gradually (0.004mol) secondary amine , Refluxing the mixture (5h) in (60°C) and then to leave that mixture on ice water overnight , purified by thin layer chromotography (TLC).

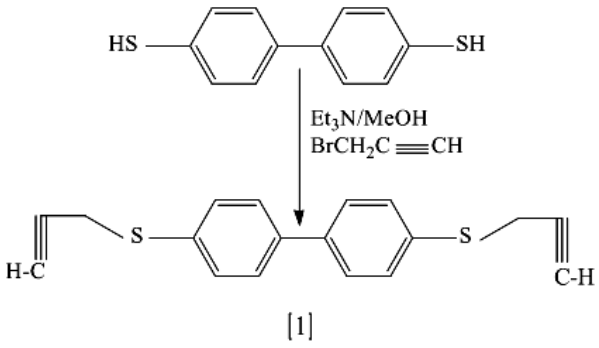
Microbial tests :

Nutrient agar was added to (1L) of distilled water in suitable conical flask with stirring and heating until completed dissolving , then the flask was stop

pered by cotton and the medium was sterilized in an autoclave for 20 minutes at (121 °C) under pressure of 15 bound / inch . The medium was placed in petridishs about (20ml) for each one and was left to cool and solidified . The studied bacteria fungi were placed on the nutrient agar surface using the loop and by streaking with processor then the discs saturated with tested compound solution. The samples were incubated for (24h) at 37°C[9-10] .

Results and Discussion :

Starting from (4 , $\bar{4}$ – (dithiol – propyne) - biphenyl): which treated with propagel bromide to give [phenyl(prop-2-yl-1-y1)sulfane compound with prop-2-yn-1-yl-(p-toyl)sulfane(1:1) compound(1).



[1]

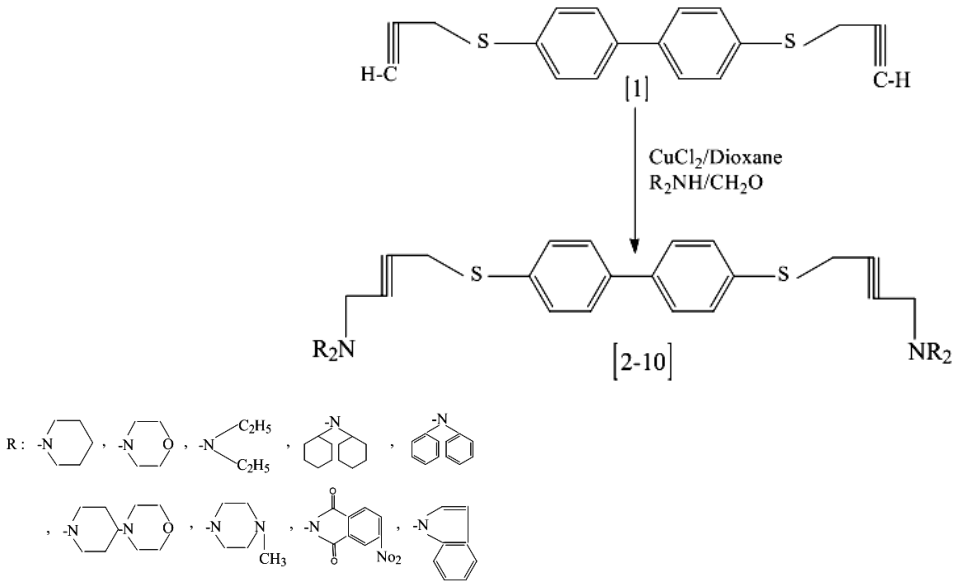
Scheme – 1 – Synthesis of path ways for Compound (1)

The FTIR spectrum showed strong stretching vibration at (1215 - 1217)cm^{-1} due to (H , ≡ CH) , (2200) cm^{-1} for (C ≡ C) , (600) cm^{-1} for (4,$\bar{4}$ - disubst) and (3080) cm^{-1} for (Ar - H); ^{1}H-NMR (DMSO- d6) δ(7.4 - 7.6)ppm due to (Ar - H) , (6.8 - 7.2)ppm due to (H, ≡CH) ; ^{13} C-NMR (DMSO -d6) S reveald : (122 - 124)ppm due to (C ≡ C) , (128 - 130)ppm for aromatic carbons .

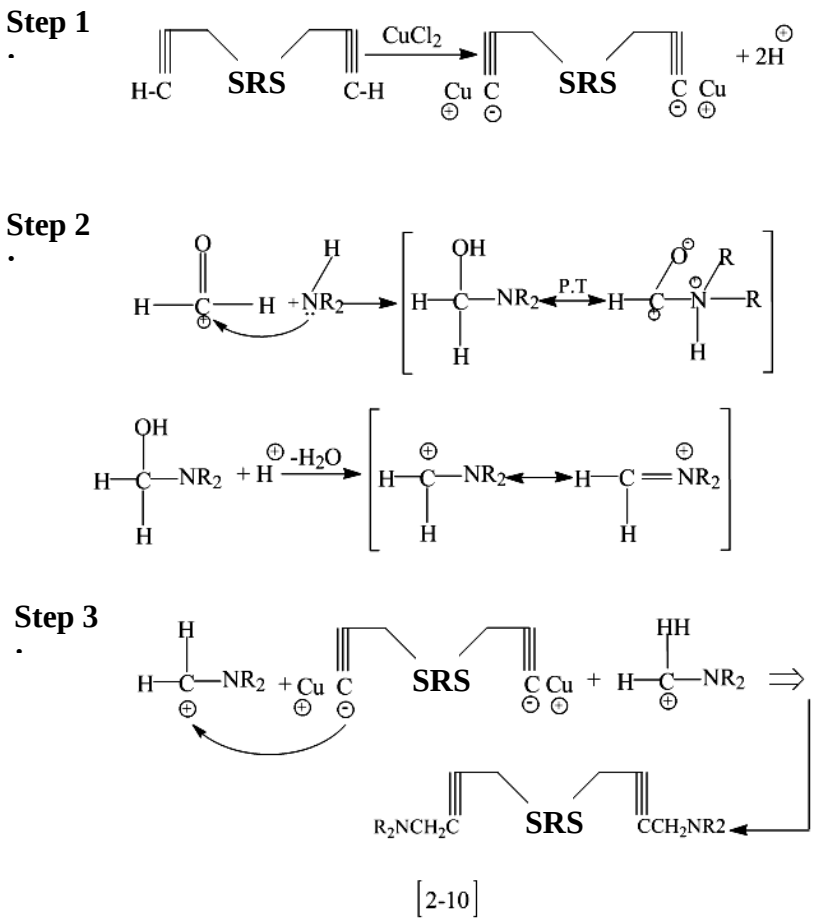
Acetylenic mannich bases(2-10) were prepared by condensation of the corresponding compound (1) with several secondary amine . refluxing Dioxane with formaldehyde solution .

The reaction proceeds by the uncleophilic attack of the nucleophilic (Nitrogen atom) Secondary amine to carbonyl group in formaldehyde combined

with losses water molecule to , The suggested mechanisum for the preparation (2-10) compounds is illustrated as below :-



Scheme – 2 – Synthesis of path ways for Compound [2-10]



Scheme – 3 – Path ways mechanism preparation mannich bases Compounds

The FTIR spectra for acetylenic mannich bases showed high intensity band which was attributed to the (C-NR_2) stretching vibration between (2200-3300) cm^{-1} due to (C ≡ C) , aliphatic (- CH_2) in (2865 - 2985) cm^{-1} , (1230 - 1350) cm^{-1} for (C - N) , compound [4] showed band at (2211) cm^{-1} due to acetylenic carbons , (2955 - 2885) cm^{-1} for (CH_2) , (1310) cm^{-1} for (C - N) ; ^{1}H-NMR (DMSO -d6) δ : (7.2 - 8.1)ppm for (Ar - H) ; ^{13}C-MNR (DMSO -d6) δ : (115 - 140)ppm for aromatic carbons , (165)ppm for (C - N) . Compound [7] showed absorption at (2265) cm^{-1} for (C ≡ C) , (2910) cm^{-1} for (CH_2) , (1350) cm^{-1} for (C-N) ; ^{1}H-NMR (DMSO -d6) δ : (7.5 - 7.6)ppm due to (Ar - H) , (2.1 - 2.2)ppm for (2H , CH_2) ; ^{13}C-MNR (DMSO -d6) δ : (114 - 134)ppm due to aromatic carbons , (161 -162)ppm for (C - N) .

Compounds [8] showed absorption at (2235) cm^{-1} for (C ≡ C) , (2975 - 2987) cm^{-1} for (CH_2) and (1310) cm^{-1} for (C-N) ; ^{1}H-NMR (DMSO -d6) δ : (7.2 - 7.8)ppm due to (Ar - H) , (1.9- 2.0)ppm for (2H , CH_2) ; ^{13}C-MNR (DMSO -d6) δ : (7.2 - 7.8)ppm for (Ar-H) , (1.38 - 1.4)ppm for (3H , CH_3) , (1.9)ppm for (2H , CH_2) ; ^{13}C-MNR (DMSO -d6) δ : (26.72)ppm for (C , CH_2), (114 - 149)ppm aromatic carbons , (162 -169)ppm for (C - N) .

The characterized absorption bands of the functional groups are listed in Table (1, 2) .

Microbial study

The last part in this work involved of antimicrobial activity of the prepared acetylenic mannich bases derivatives against (staphylococcus aureus) G^+ Ve bacteria (Klebsiella Pneumania) G^- Ve bacteria and candida albicans) Fungi m inhibition zones caused by the various prepared compounds were determined and the results are listed in Table (4) .

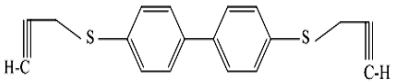
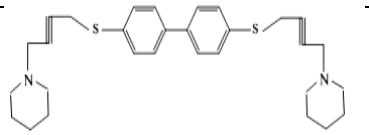
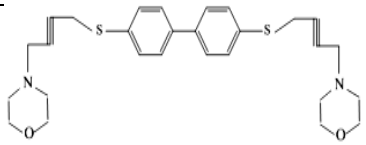
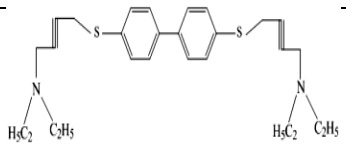
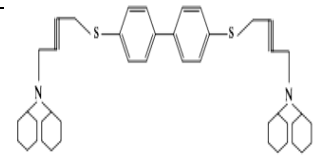
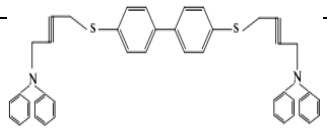
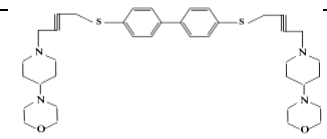
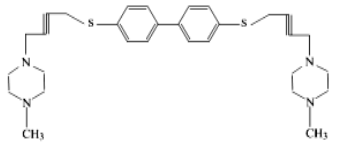
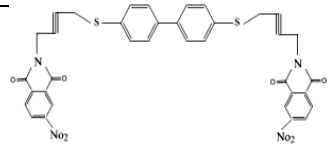
The results showed that biological activity of the studies compounds depend on nature of subtituents in their molecule , thus the compounds [6 -10] showed high biological activity due to the presence of (No_2) , electron releasing substituted hetero ring.[9]

Results in Table (4) indicated that (1, 3, 4) compounds posses slightly activity against (G^+ Ve) bacteria and this was due to the hydrophilic properties of these compounds and cell wall of (G^+ Ve) bacteria On the other hands the molecule of the prepared (2,5) have hydrophilic properties and this in turn made these (G^- Ve) bacteria which posses complex (Lipo poly succharides) in their cell - wall.

finally both (1-10) compounds showed differents biological activity against (candida albicans).

Thus mostly compounds showed highly biological activity while other slightly or weakly activity .

Table (1) Depacited physical properties and Major FTIR spectra for compounds (1-10)

Comp. No.	Chemical structure	M-P °C	Coloure	%yield	Major FTIR absorption			
					$V_{C \equiv C}$	V_{CH2}	V_{C-N}	Other
1		>300	Pale yellow	82	2200	-	-	(H, ≡ CH) (1215 - 1217) (Ar - H) (3060)
2		Oily	Orange	80	2210	2870	1280	(Ar - H) (3080) (C -S) (1230)
3		Oily	Orange	75	2300	2910	1300	(C-O-C) (1106) (Ar-H) (3101)
4		218-220	Red	70	2211	2885 2945 2955	1310	(Ar-H) (3065)
5		213-215	Yellow	60	2200	2945 2985	1340	(Ar-H) (3104)
6		227-229	Brown	60	2240	2860	1309	(Ar-H) (3100)
7		Oily	Brown	60	2265	2910	1350	(C-O-C) (1165) (Ar-H) (3085)
8		Oily	Orange	65	2235	2975 2987	1310	(Ar-H) (3111)
9		232-234	Orange	60	2300	2865	1230	(C = O) (1650) (Ar-H) (1309)

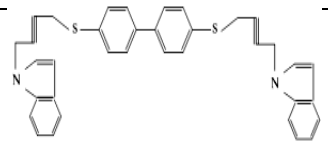
Comp. No.	Chemical structure	M-P °C	Coloure	%yield	Major FTIR absorption			
					$V_{C \equiv C}$	V_{CH2}	V_{C-N}	Other
10		238-240	Yellow	60	2260	2870	1245	(Ar-H) (31 09)

Table (2) ^{1}H – NMR and ^{13}C-NMR spectra data for some compounds

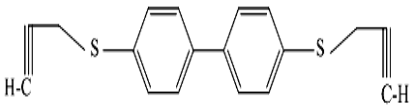
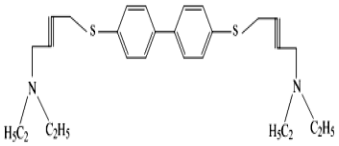
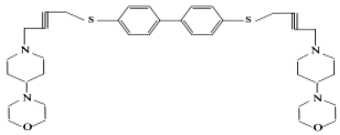
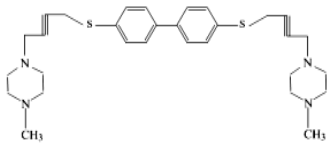
Comp. No.	Chemical structure	^{1}H – NMR	^{13}C-NMR
1		δ : 7.4 – 7.6 (Ar-H) δ : 6.8 – 7.2 (H, ≡≡ CH)	δ : 122 – 124 (C≡C) δ : 128 – 130 (aromat – carbo)
4		δ : 7.2 – 8.1 (Ar – H)	δ : (115 – 140) (aromatic – carbons) δ : (165) (C-N)
7		δ : (7.5 – 7.6((Ar-H) δ: (2.1 – 2.2) (2H, CH_2)	δ: (114 – 134) (aromatic – carbon) δ: (161 – 162) (C- N)
8		δ: (7.2 – 7.8) (Ar- H) δ: (1.9 – 2.0)) (2H, CH_2)	δ : 26 – 72 (C , CH3) δ: (114 – 149) (aromatic carbon) δ: (162 – 169) (C-N)

Table (3) Depacited Elemental analysis (C-H-N)

Comp. No.	(C-H-N) analysis calculated (found)		
	%C	%H	%N
1	87.29 (88.27)	5.34 (6.32)	-
4	77.78 (78.78)	8.33 (9.33)	6.50 (7.50)
7	80.57 (81.55)	8.83 (9.82)	4.95 (5.94)
8	74.07 (75.05)	7.82 (8.81)	11.52 (12.48)

Table (4) Microbial activity for compounds (1-10)

Comp. No.	Staphyl coccuse aureous	Klebsiella pneum onia	Candida albicans (Fungi)	Zone of inhibitionIon in (mm)	Comp. No.	Staphyl coccuse aureous	Klebsiella pneum onia	Candida albicans (Fungi)	Zone of inhibitionIon in (mm)
1	8	R	R	6	6	15	17	23	13
2	10	R	R	5	7	18	21	16	14
3	11	R	R	6	8	20	21	22	21
4	7	R	R	6	9	18	20	25	23
5	9	R	R	5	10	19	21	25	14

Key of symbol : R: Resistant , inhibition Zone < 6mm = an active , inhibition Zone (6-9) mm = slightly active , Inhibition Zone (9-12) = moderately active , Inhibition Zone > 12mm = highly active .

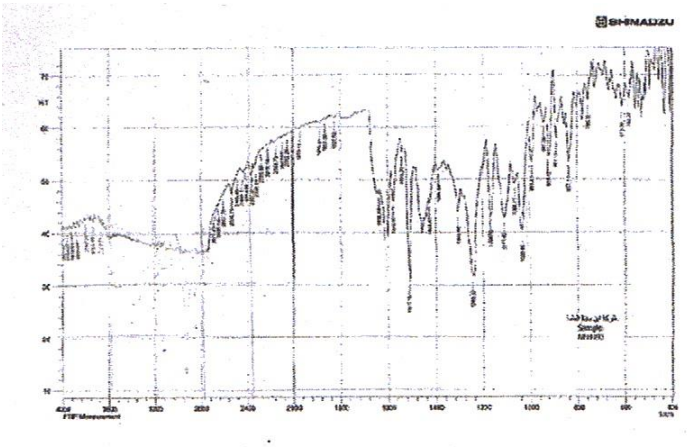


Fig (1) FTIR Spectrum of Compound (1)

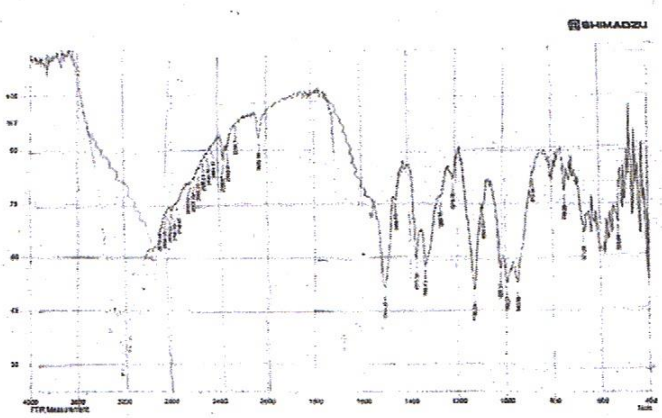


Fig (2) FTIR Spectrum of Compound (4)

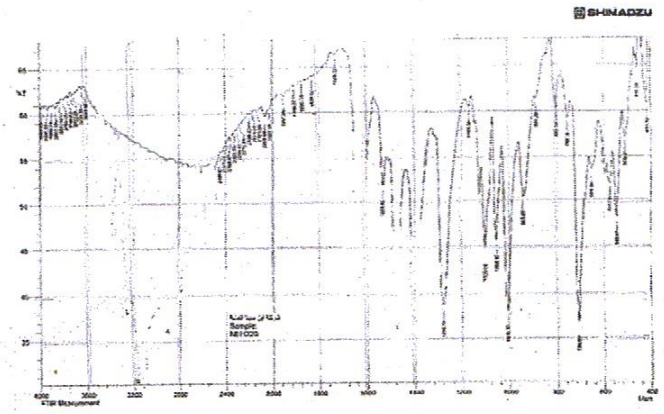


Fig (3) FTIR Spectrum of Compound (7)

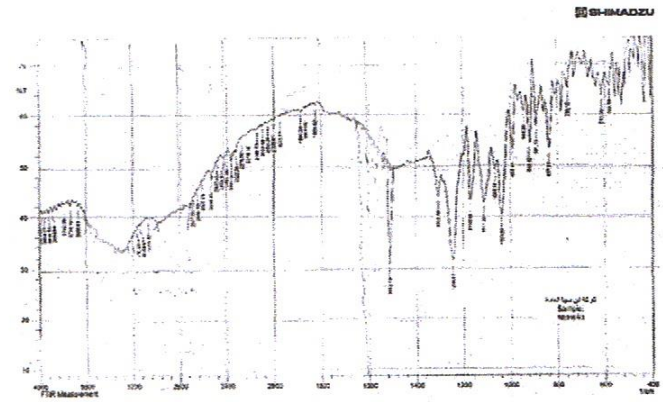


Fig (4) FTIR Spectrum of Compound (8)

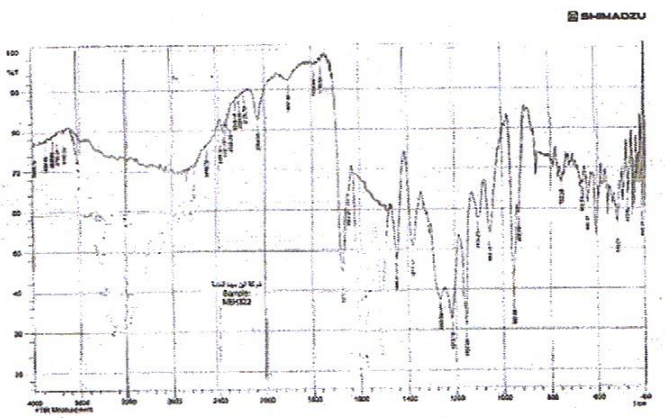


Fig (5) FTIR Spectrum of Compound (9)

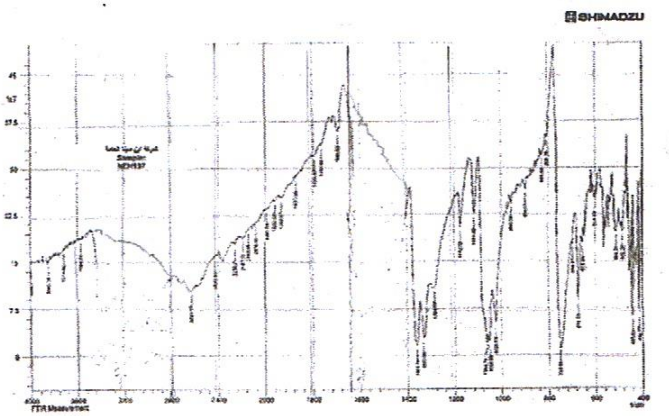


Fig (6) FTIR Spectrum of Compound (10)

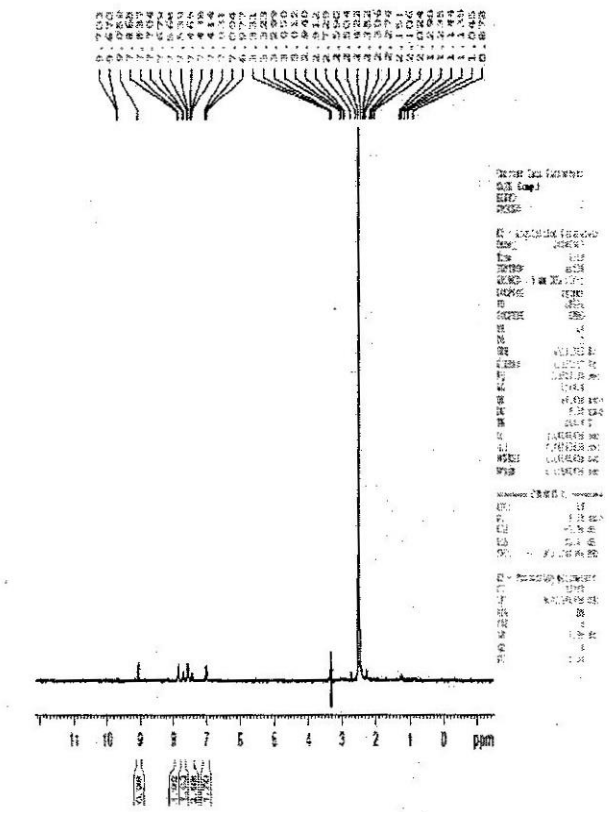


Fig (7) HNMR Spectrum of Compound (1)

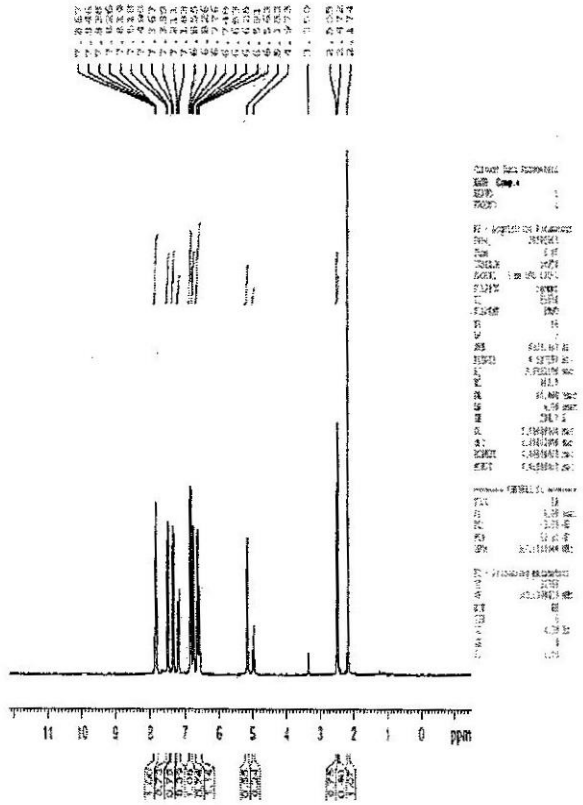


Fig (8) HNMR Spectrum of Compound (4)

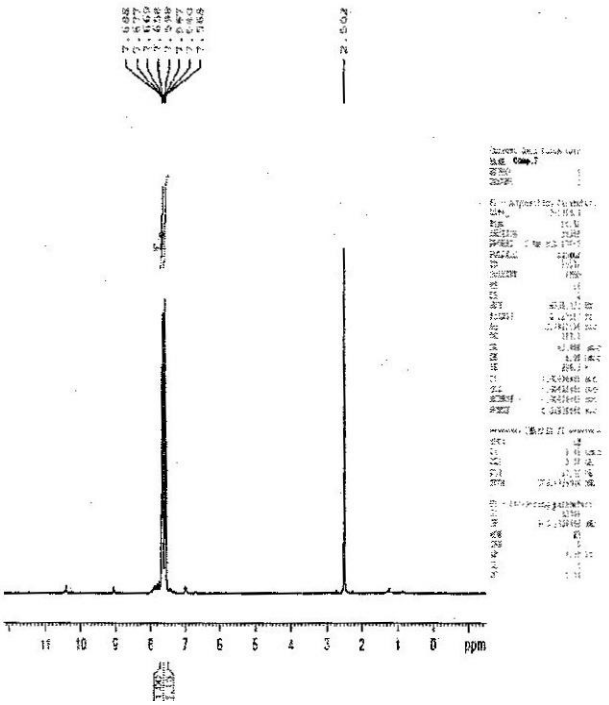


Fig (9) HNMR Spectrum of Compound (7)

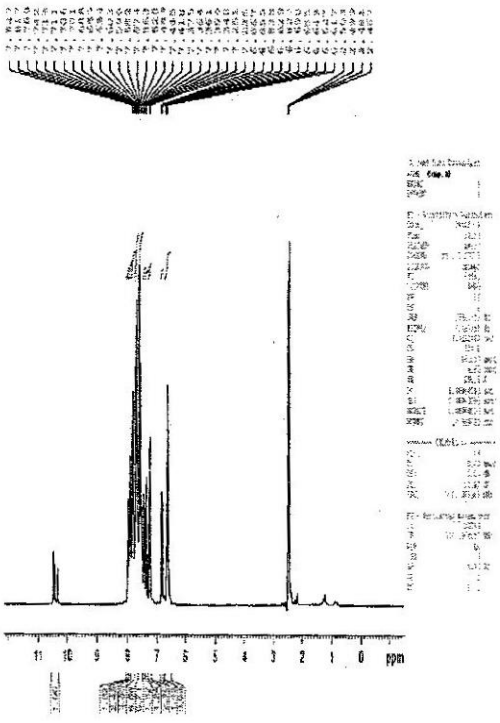


Fig (10) HNMR Spectrum of Compound (8)

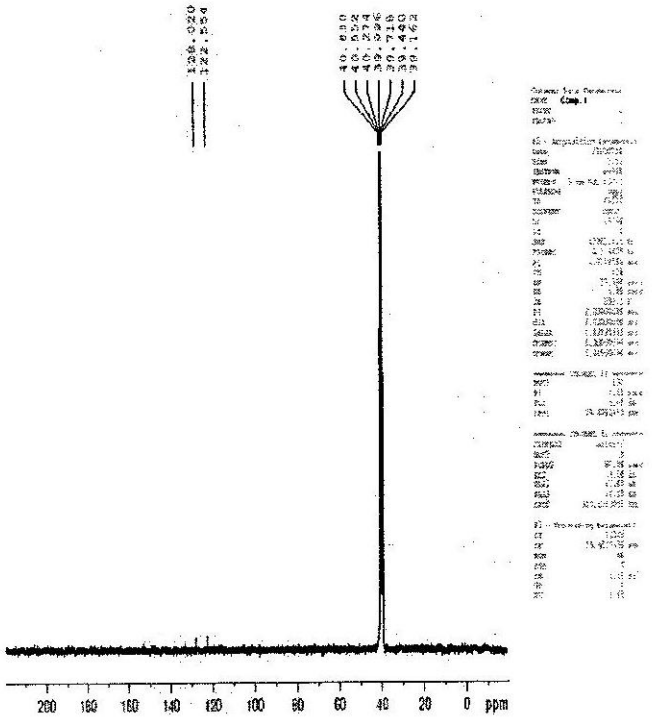


Fig (11) ^{13}CNMR Spectrum of Compound (1)

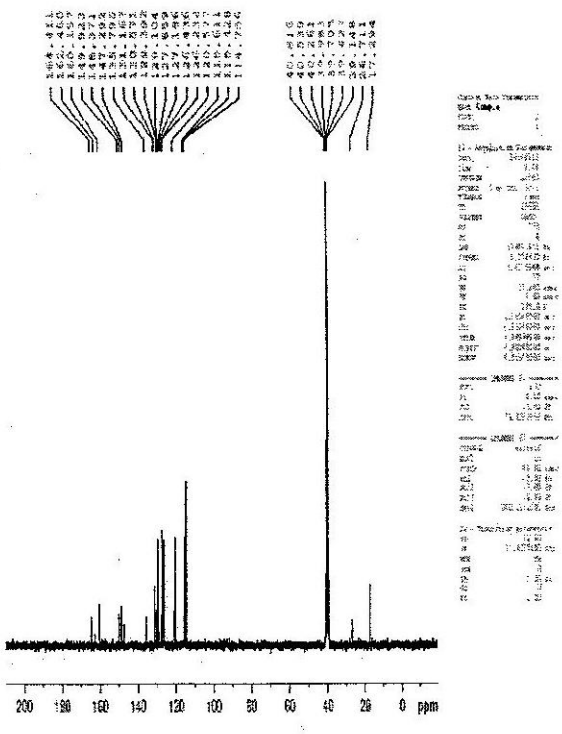


Fig (12) ^{13}CNMR Spectrum of Compound (4)

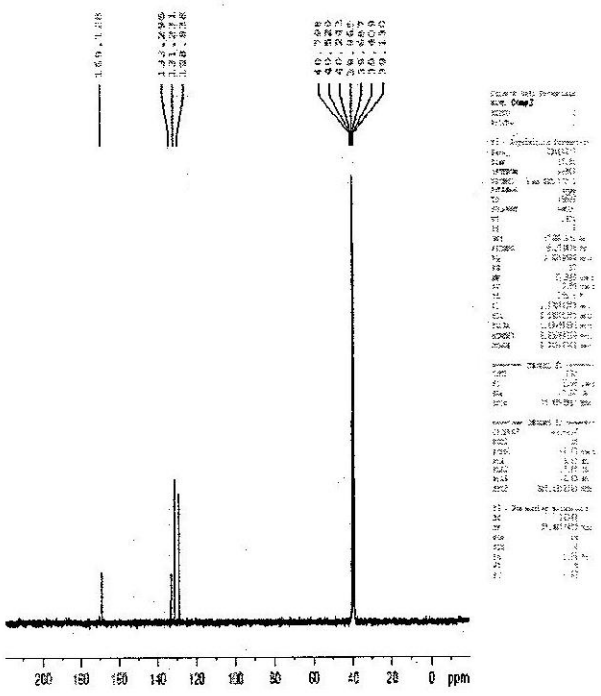


Fig (13) ^{13}CNMR Spectrum of Compound (7)

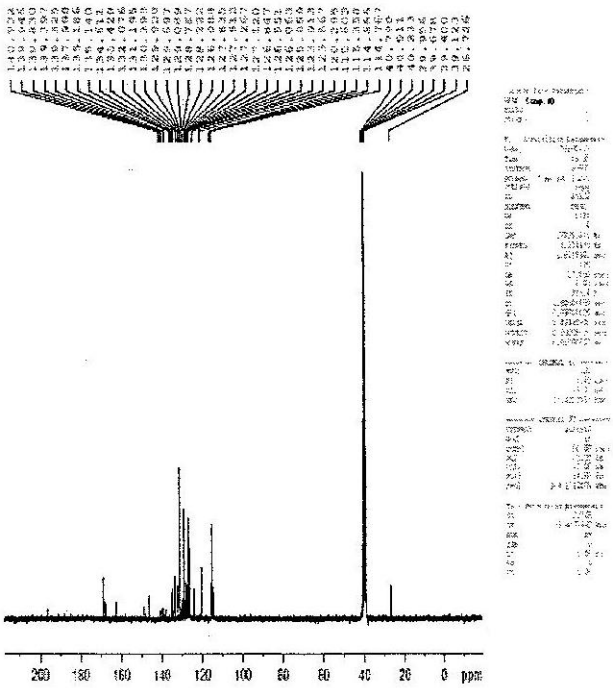


Fig (14) ^{13}CNMR Spectrum of Compound (8)

References :

.1. Monika W. ; Monika P. Ageta S. 2006; "The new derivate of 3 – [(2-morpholine – 4 – yl) ethyl] – 4 – substituted – 1,2,4 – triazoline – 5 – thiole " ; J. ANALES , (XIX), N2,: 11-14.

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تحضير وتشخيص بعض مركبات الاستيلينية لقواعد مانخ ابتداءا من ثنائي فينل - 4-4-ثنائي الثايول

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الخلاصة :

يمثل الثايول احدى المجاميع التي تحتوي على هيدروجين فعال حيث ان مركباتها تعتبر من المواد الاساسية التي تستخدم في تحضير قواعد مانخ في ضوء ذلك استخدم المركب الأساس (ثنائي المثيل – 4 ، $\bar{4}$ – ثنائي الثايول) في تحضير مجموعة من قواعد مانخ الاستيلينة والتي شخصت بواسطة استخدام تقانة (^{13}C-NMR , ^{1}H – NMR , FTIR ، والتحليل الدقيق للعناصر (C.H.N) إضافة إلى دراسة الفعالية البايولوجية لجميع المركبات المحضرة).