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Synthesis, Identification and Evaluation Biological Activity for Some New Triazole, Triazoline and Tetrazoline Derivatives From 2-Mercapto-3-phenyl-4(3H)Quinazolinone

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Abstract

This research, involved synthesis of some new 1,2,3-triazoline and 1,2,3,4-tetrazole derivatives from anthranilic acid as starting material. The first step includes formation of 2-Mercapto-3-phenyl-4(3H)Quinazolinone (0) through reaction of anthranilic acid with phenylisothiocyanate in ethanol, then compound (0) reaction with chloro acetyl chloride in dimethyl formamide (DMF) to prepare intermediate S-(α -chloroaceto-2-yl)-3-phenylquinazolin-4(3H)-one (1); compound (1) reacted with sodium azide to yield S-(α -azidoaceto-2-yl)-3-phenylquinazolin-4(3H)-one (2), while Schiff bases (3-10) were prepared from condensation of substituted primary aromatic amines with different aromatic aldehydes in absolute ethanol as a solvent. Compound (2) reacted with Schiff bases to give 1,2,3,4-tetrazoline derivatives (11-18) which was entered in 1,3-dipolar cyclo addition reactions with some of α,β -unsaturated carbonyl compounds to give 1,2,3-triazoline (19-24) and triazole (25-27) derivatives respectively. The structure of newly synthesized compounds were identified by spectral methods their [Fourier transform infrared (FTIR) and some of them $^1\text{H-NMR}$, $^{13}\text{C-NMR}$] and measurements some of its physical properties and some specific reactions. Furthermore were studied the effects of the preparing compounds on some strains of bacteria.

Keywords: Quinazolinone, Schiff base, 1,2,3-Triazoline, 1,2,3,4-Tetrazoline, Antimicrobial

تحضير, تشخيص وتقييم الفعالية البيولوجية لبعض مشتقات التريازول, التريازولين و التترازولين

الجديدة من 2-مركبتو-3-فني-4-(3H)-كوينزولينون

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الخلاصة

تضمن البحث تحضير بعض مشتقات 1,2,3-تريازولين و 1,2,3,4-تترازولين الجديدة من حامض الانثرنيليك كمادة اساس. تتضمن الخطوة الاولى تكوين 2-مركبتو-3-فني-4-(3H)-كوينزولينون (0) من خلال تفاعل حامض الانثرنيليك مع فني-4-ايزوثايوسيانات في الايثانول. ثم يتفاعل المركب (0) مع الكلورواستاييل كلورايد ويوجد DMF كمذيب لتحضير المركب الوسيط S-(α -كلورو اسيتو-2-يل)-3-فني-4-(3H)-كوينزولينون (1); تفاعل المركب (1) مع ازيد الصوديوم ينتج S-(α -ازيد اسيتو-2-يل)-3-فني-4-(3H)-كوينزولينون (2), بينما قواعد شيف (3-10) حضرت من تكاثف الامينات الاروماتية الاولى المعوضة مع مختلف الديهايدات الاروماتية بوجود الايثانول كمذيب. تفاعل المركب (2) مع قواعد شيف ليعطي مشتقات 1,2,3,4-تترازولين (11-18) ودخلها في تفاعل الاضافة الحلقية ثنائية القطب 1,3،

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مع بعض مركبات الفا بيتا- كاربونيل غير المشبعة ليعطي مشتقات 3,2,1- ترايزولين (19-24) وترايزول (25-27) بالتعاقب. تراكيب المركبات المحضرة الجديدة شخصت من خلال الطرق الطيفية FTIR تحويلات فورير للاشعة تحت الحمراء والبعض منها $^{13}\text{C-NMR}$, $^1\text{H-NMR}$ وقياس بعض خواصها الفيزيائية بالاضافة لذلك تمت دراسة تأثير بعض المركبات المحضرة على بعض سلالات البكتيريا.

Introduction:

Quinazolinones are important heterocyclic with wider range of microbial [1] such as antimalarial [2], anticancer [3], anti-inflammatory [4], anti-hypertensive [5], anticonvulsant [6] anti-viral and cytotoxic [7]. These compounds have been synthesized from various precursors by adopting different methods [8]. The chemistry of 1,2,3-triazole acquired attention due to the diversity of their possible applications. In fact, they have been used as fungicides, herbicides, light stabilizers, fluorescent whiteners and corrosion retardants [9]. The derivatives of triazole also possess a wide variety of activities such as anti-tumor [10], antimicrobial [11], antineoplastic [12] and antiviral [13] the concept of "click" chemistry was initially introduced to promote a new approach to the development of pharmaceuticals. On the other hand 1, 2, 3, 4-tetrazole are a class of synthetic organic heterocyclic compounds consisting of five-member ring of four nitrogen and one carbon atom [14]. The most direct method to form tetrazoles is via the formal (2+3) cyclo addition of azides and nitriles [15]. Tetrazole and their derivatives possess broad spectrum of biological activities in both medicinal and pharmaceutical such as antimicrobial [16], antifungal [17], inhibitor of HCV (Hepatitis C virus) [18], potent hypoglycemic agent [19] and cholinesterase inhibitors [20]. In view of the importance of the above heterocycles we planned to synthesize new 2-Mercapto-3-phenyl-4(3H)Quinazolinone derivatives include 1,2,3-triazole and 1,2,3,4-tetrazole moieties.

Experimental

Materials and Instruments

Chemicals used in this work are supplied from Merck, BDH, Sigma Aldrich and Fluka companies and are used without further purification. Melting points were recorded using digital Stuart scientific SMP3 melting point apparatus and are uncorrected. FTIR spectra were recorded on SHIMAZU FTIR-8400 Fourier transform Infrared spectrophotometer using KBr discs in the (4000-600) cm^{-1} spectral range. $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectra were recorded on Burker 500 MHz instrument using DMSO-d_6 as solvent and TMS as internal reference. Thin layer chromatography (TLC) was carried out using Fertigfolien precoated sheets type polygramsilg and the plates were developed with iodine vapor.

Synthesis of 2-mercapto-3-phenyl-4(3H)quinazolinone (0) [21]

This compound as starting material was prepared according to literature procedure. Table-1 lists their physical properties and FTIR spectral data.

Synthesis of S-(α -Chloroaceto-2-yl)-3-phenyl-4(3H)quinazolinone (1) [22]

To a mixture of compound (0) (2.5g, 0.01mol) in (16mL) dimethylformamide (DMF). anhydrous potassium hydroxide (0.56g, 0.01mol) dissolve in (10mL) of methanol was added slowly the chloroacetyl chloride (1mL, 0.01mol) and the mixture was refluxed for (4 hrs.). After time refluxed expiration the mixture was stirred overnight, then the reaction mixture was poured into ice water, the separated precipitate was filtered and recrystallized from ethanol to give a dusty crystal, physical properties and FTIR spectral data are listed in Table-1.

Preparation of S-(α -azidaceto-2-yl)-3-phenylquinazolin-4(3H)-one (2) [23]

Sodium azide (0.325g, 0.005mol,) was added to a solution of S-(α -chloroaceto-2-yl)-3-phenylquinazolin-4(3H)-one (1) (1.653g, 0.005 mol) in (10 mL) of DMF. The reaction mixture was refluxed at (90°C) for (6 hrs.) with continuous stirring. The solvent was evaporated; then off-white product was precipitated and filtered, washed well with diethyl ether and recrystallized from ethanol, physical properties and FTIR spectral data are listed in Table -1.

Table 1 - Physical properties and FTIR spectral data cm^{-1} of the prepared compounds (0-2)

Com. No.	Physical Properties				Major FTIR Absorption cm^{-1}				
	Structures	M.P. $^{\circ}\text{C}$	Yield %	Color	$\nu\text{C-H}$ arom.	$\nu\text{C-H}$ aliph..	$\nu\text{C=O}$	$\nu\text{C=C}$ arom.	Other bands
0		297-299	80	off-white	3028	-	1691	1600 1533 1487	$\nu\text{N-H}$ 3244 $\nu\text{C=N}$ 1622
1		158-160	87	white	3064	2910 2954	1735 Ketone 1683 amide	1575 1550 1490	$\nu\text{C-Cl}$ 644 $\nu\text{C=N}$ 1662
2		166-168	88	off-white	3070	2954 2898	1733 Ketone 1664 amide	1600 1531 1488	$\nu\text{C=N}$ 1620 $\nu\text{N=N-N}$ νN_3 2324 989

Preparation of *N*-(substitutedbenzylidene)-4-substitutedaniline (3-10)[24]

The Schiff bases have been synthesized by reaction of some substituted primary aromatic amines (0.01 mol) with different substituted aromatic aldehydes (0.01 mol) in absolute ethanol for (4-6) hrs. in presence of (2-3 drops) of glacial acetic acid. The precipitate formed was filtered and recrystallized from ethanol. Physical properties of dry product and FTIR spectral data are listed in Table -2.

Table 2 - Physical properties and FTIR spectral data cm^{-1} of the prepared compounds (3-10)

Com. No.	Physical Properties				Major FTIR Absorption cm^{-1}				
	Structures	M.P. $^{\circ}\text{C}$	Yield %	Color	$\nu\text{C-H arom.}$	$\nu\text{C-H aliph.}$	$\nu\text{C=N}$	$\nu\text{C=C arom.}$	Other bands
3		127-129	90	Gray	3090	2893	1622	1600 1579	νNO_2 asym 1508 sym 1340 $\nu\text{C-O-C}$ 1035
4		180-182	76	Dark-yellow	3065	2927	1620	1595 1573	$\nu\text{O-H}$ 3382
5		170-172	83	white	3095	2962	1620	1593 1572	$\nu\text{C-Cl}$ 1091 vp-position 838
6		139-141	77	Light Gray	3031	2920	1627	1589 1544	$\nu\text{C-Br}$ 997 $\nu\text{C-O-C}$ 1116 vp-position 813
7		129-131	80	yellow	3029	2916	1622	1591 1562	νNO_2 asym 1504 sym 1357 vp-position 833
8		137-139	70	Dark-yellow	3053	2898	1623	1585 1537	$\nu\text{O-H}$ 3384
9		116-118	82	Gray	3045	2848	1623	1604 1537	$\nu\text{C-Cl}$ 1107 vp-position 817
10		149-151	75	pale Gray	3085	2912	1631	1581 1560	$\nu\text{C-Br}$ 970 vp-position 827

Preparation of S-[(1-aceto-4-(substitutedphenylene)-5-(substitutedphenyl-1,4,5-trihydro-1,2,3,4-tetrazol-ine-1-yl)]-3-phenylquinazolin-4(3H)-one (11-18)[25]

(0.01mole) of appropriate Schiff base was dissolved in (25 mL) of DMF and to that (0.01mole) of S-(α -azidoaceto-2-yl)-3-phenylquinazolin-4(3H)-one (2) was added and the resultant reaction mixture was heated to (120-130) $^{\circ}\text{C}$ for overnight. The solvent was partially evaporated. Finally, the contents were filtered, dried and recrystallized from ethanol. Physical properties of dry products and FTIR spectral data are listed in Table-3.

Table 3 - Physical properties and FTIR spectral data (cm⁻¹) of the prepared compounds (11-18)

Com. No.	Physical Properties				Major FTIR Absorption cm ⁻¹				
	Structures	M.P. C°	Yield %	Color	ν C-H arom.	ν C-H aliph..	ν C=O	ν C=N	Other bands
11		118-120	66	Pale-yellow	3099	2970 2835	1735 Ketone 1681 amide	1622	ν NO ₂ asym 1514 sym 1340 ν C-O-C 1105 ν N=N 966
12		162-163	60	Dark-yellow	3031	2912	1735 Ketone 1664 amide	1620	ν O-H 3247 ν C-O-C 1143 ν N=N 966
13		116-118	70	Gray	3032	2960 2839	1735 Ketone 1681 amide	1620	ν C-Cl 1095 ν C-O-C 1143 ν N=N 964
14		240-241	72	white	3029	2914 2854	1735 Ketone 1681 amide	1622	ν C-O-C 1143 ν N=N 991 ν C=C 1615 vp-position 829
15		117-119	77	Light Gray	3045	2910	1735 Ketone 1681 amide	1623	ν NO ₂ asym 1504 sym 1336 ν N=N 964 vp-position 833
16		138-140	67	Dark-yellow	3021	2916 2854	1735 Ketone 1681 amide	1622	ν O-H 3317 ν N=N 993
17		144-147	75	Off-white	3042	2914 2854	1735 Ketone 1682 amide	1624	ν C-Cl 1081 ν N=N 991 vp-position 833
18		127-129	70	Light yellow	3026	2910 2856	1735 Ketone 1681 amide	1623	ν N=N 966 ν C-Br 881 vp-position 827

Preparation of S-(1-aceto-4,5-disubstituted-4,5-dihydro-1H-triazoline)-1-yl]-3-phenylquinazolin-4(3H)-one(19-24) and S-(1-aceto-4,5-disubstituted)-1H-triazole-3-phenylquinazolin-4(3H)-one(25-27) [26]

S-(α -azidaceto-2-yl)-3-phenylquinazolin-4(3H)-one (2) (0.01mol) was dissolved in DMF (50mL). The α,β -unsaturated compounds (0.01 mol) were added to the solution. The mixture was heated under reflux at 110°C for 24 hrs. After removing the solvent, the residue was washed with diethyl ether and recrystallized from ethanol. Physical properties of dry product and FTIR spectral data are listed in Table-4.

Table 4 - Physical properties and FTIR spectral data (cm⁻¹) of the prepared compounds (19-27)

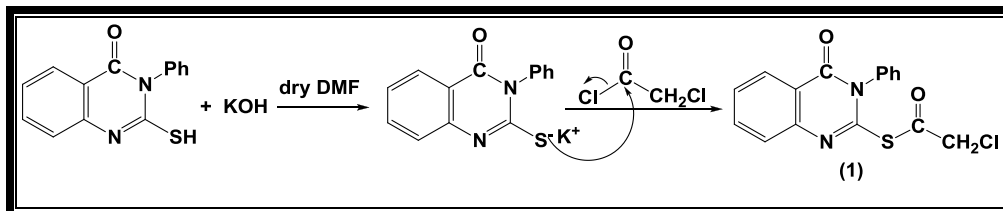
Com .No.	Physical Properties				Major FTIR Absorption cm ⁻¹				
	Structures	M.P. C°	Yield %	Color	vC-H arom.	vC-H aliph..	vC=O	vC=N	Other bands
19		152-154	80	Deep Brown	3042	2952 2914	1737 anhydride 1683 Amide and ketone	1608	vC-O-C 1295 vN=N 967
20		118-119	82	Brown	3028	2846	1737 Ketone 1660 amide	1618	vN=N 966
21		123-125	76	Deep Brown	3038	2942	1735 anhydride 1681 Amide and ketone	1610	vC-O-C 1282 vN=N 982
22		161-163	88	white	3032	2931	1738 ester 1662 ketone 1623 amide	1617	vN=N 991
23		145-147	70	Brown	3030	2971	1735 Ketone 1681 amide	1612	vC=C 1615 vN=N 985
24		129-131	74	white	3024	2966 2829	1730 Ketone 1681 Amide 1635 COOH	1627	 3435-2710 broad vN=N 933
25		158-160	80	white	3032	2966	1722 Ketone 1662 amide 1627 COCH ₃	1620	vN=N 979
26		155-156	70	white	3002	2954	1735 Ketone 1681 amide 1632 COOH	1618	 3406-2750 broad vN=N 966
27		164-166	70	Gray	3062	2954	1735 Ketone 1681 amide 1630 COCH ₃	1610	vN=N 966

Anti-microbial activity test [27]

This test was performed according to the disk diffusion method. Some of prepared compounds were tested against two strain gram +ve (*Staphylococcus aureus* and *Bacillus Subtilis*) and two strain gram -ve bacteria (*pseudomonas aeuroginosa* and *Escherichia coli*). Whattmann no.1 filter paper disk of 5mm diameter were sterilized by autoclaving for 15 min. at 121° C. The sterile disks were impregnated with different compounds (800µg/disk). Agar plates were surface inoculated uniformly with 100° µL from both culture of tested microorganism. The impregnated disk were placed on the medium suitably spaced a part and the plates incubated at 5 °C for 1 hr. to permit good diffusion and then transferred to an incubator at 37°C for 24 hrs. The inhibition zones caused by various compounds on the microorganisms were examined.

Results and Discussion:

The synthetic sequences for preparation of series of new 2-mercapto-3-phenyl-4(3H) quinazolinone, 1,2,3-triazoline and 1,2,3,4-tetrazoline were started from compound S-(α -chloroaceto-2-yl)-3-phenyl-4(3H) quinazolinone(1) which was prepared by reaction of 2-mercapto-3-phenyl-4(3H) quinazolinone (0) with chloro acetyl chloride in the presence of solution of potassium hydroxide in dry DMF according to the following Equation-1:



Equation 1- Preparation of compound (1)

The structure of compound(1) was confirmed by physical properties which are listed in Table-1. FTIR spectrum showing the absorption at ν cm^{-1} 2910 for C-H aliph. , 1735 for C=O (ketone); 1683 for C=O (amide) and 644 for C-Cl. $^1\text{H-NMR}$ spectrum showed singlet signal at δ = (4.00) ppm due to (-CH₂-Cl) protons. And signals at δ = (7.15-8.10) ppm due to aromatic rings protons as listed in Table-5. $^{13}\text{C-NMR}$ spectrum data of compound (1) were listed in Table-6.

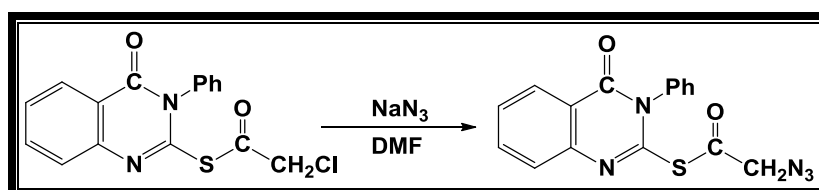
Table 5- $^1\text{H-NMR}$ spectral data (δ ppm) for selected compounds

Comp. No.	Structures	$^1\text{H-NMR}$ Spectral data(δ ppm)
1		4.00(S,2H,-CH ₂ -); 7.27-8.09(m,9H,Ar-H)
16		2.33(S,3H,-CH ₃);3.65(S,2H,-CH ₂ -);4.17(S,1H,CH-tetrazoline ring) ; 7.22-8.36 (m,16H,Ar-H) ; 10.01 (S,2H;OH)
20		3.34 (S,2H,-CH ₂ -) ; 3.69 (d,1H,CH-quinone ring); 4.00(S,2H,-CH-quinone ring);7.1-8.10(m,13H,Ar-H)
22		2.89(S,3H-OCH ₃) ; 3.35(d,2H,-CH ₂ -triazoline ring); 3.68(S,2H,-CH ₂ -) ; 4.01(t,1H,-CH-triazoline ring) ; 7.04-8.10 (m,9H,Ar-H)
24		3.41(S,2H,-CH ₂ -) ; 3.72 (S,1H,-CH-triazoline ring); 4.02(S,1H,-CH-Ph); 7.33-8.15(m,14H,Ar-H); 12.33(b,1H, —C(=O)-OH)
25		2.20(S,3H,-CH ₃) ; 3.65(S,2H,-CH ₂ -); 7.27-7.79 (m,14H,Ar-H).

Table 6- ^{13}C NMR spectral data (δ ppm) for selected compounds

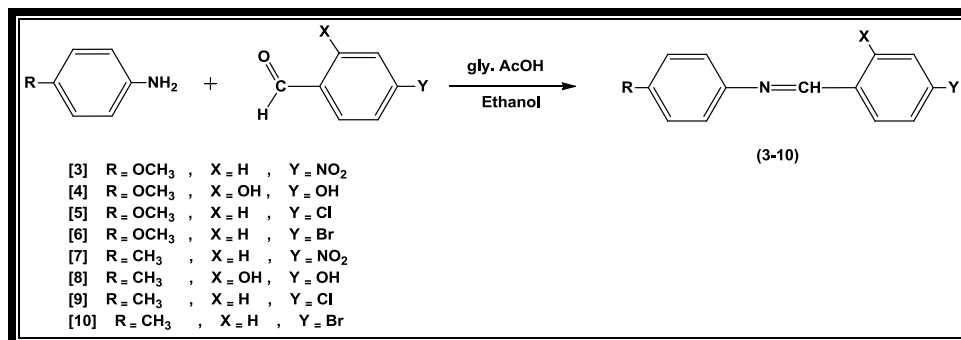
Comp. No.	Compound structure	^{13}C NMR spectral data (δ ppm)
1		52.34(C ₁); 115.58-138.62(C _{6, 7, 10, 11}); 139.42-160.54 (C _{3, 4, 5, 9}); 168.87 (C ₈); 175.91(C ₂).
16		20.54(C ₁₆) ; 52.34 (C ₁) ; 67.2 (C ₁₂) ; 102.3-126.5 (C _{6,7,11,19}) ; 127.3-130.0 (C _{4,5,10, 13,14,15,17,21});134.2-145.4(C _{3,9,18,20}); 162.9(C ₈);168.8(C ₂).
20		52.34(C ₁);68.3(C ₁₃);81.5(C ₁₂);125.80-126.5 (C _{6, 7, 10, 11, 16}) ; 129.3-131.5 (C _{9,10,16});134.2-138.7(C _{3,4,5,9,15}); 169.27(C ₈) ;176.31(C ₂); 184.8(C ₁₄).
22		34.17(C ₁₂); 52.34(C _{1,9}); 62.3(C ₉); 119.4-126.5 (C _{6,7,15}) ;128.7-135(C _{4, 5, 14}) ;146.9 (C _{3,13});160.50 (C ₈) ;168.9 (C ₂); 175.5(C ₁₁).
24		52.31(C ₁);68.3(C ₁₂);87.5(C ₁₆);110.4-125.3(C _{6, 7, 10, 11, 14, 15}) ; 128.9-135.92(C _{3,4,5,9,13}); 167.6(C ₈); 171.3 (C ₁₇); 175.9(C ₂).
25		30.65(C ₁₈); 50.8(C ₁); 115-5-124.3(C _{6,7,10,11,14,15}); 27.3-135.5(C _{3,4,5,12,13,16}); 167.6(C ₈); 174.3(C _{2,17}).

Also alcoholic silver nitrate test confirmed the presence of chlorine group [28]. Then, the synthesis of compound (2) is of a particular interest because this pattern is precursor for the synthesized compound (1) was converted to the *S*-(α -azido-aceto-2-yl)-3-phenylquinazolin-4(3H)-one (2) by the reaction with sodium azide in DMF, according to the following Equation-2.

**Equation 2-** preparation of compound (2)

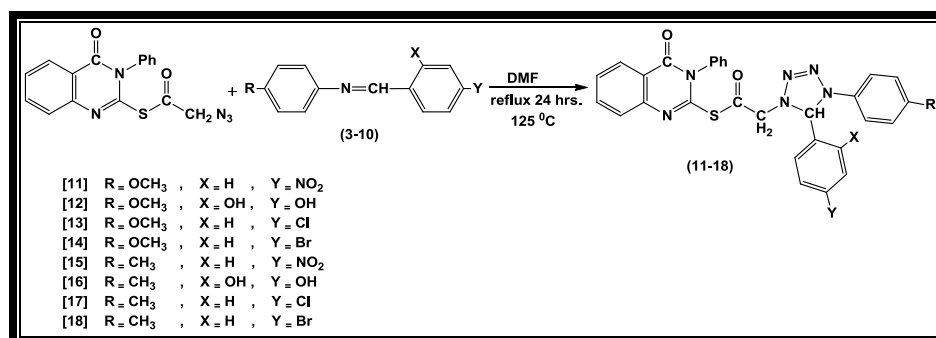
The compound (2) was characterized by FTIR spectrum showed a strong band at (2324) cm^{-1} which indicates the presence of the ($-\text{N}_3$) group and disappearance of absorption band of $\nu(\text{C}-\text{Cl})$ group at (644) cm^{-1} [29]. Also showed absorption at (1733) cm^{-1} was due to $\nu(\text{C}=\text{O})$ ketone group and at (1664) cm^{-1} was due to $\nu(\text{C}=\text{O})$ amide group. All these absorption bands are good evidence to preparation (2)

compound. Compounds (3-10) are synthesized by Schiff base reaction [30] condensation of p-substituted aniline with different aromatic aldehydes in absolute ethanol as a solvent; Equation-3. The synthesized compounds (3-10) were characterized by FTIR spectra. The FTIR spectrum showed the appearance of the stretching vibration between $(1620-1631) \text{ cm}^{-1}$ which was due to $\nu(\text{C}=\text{N})$ of imine group and the disappearance of the stretching vibration of $\nu(-\text{NH}_2)$ group and carbonyl group. Table-2 shows structural and physical properties of synthesized compounds (3-10).



Equation 3- Preparation of Schiff base compounds (3-10)

Tetrazoline derivatives compounds (11-18) were synthesized by the [2+3] cyclo addition reaction implicit a reaction between S-(α -azido-aceto-2-yl)-3-phenylquinazolin-4(3H)-one(2) with Schiff base (3-10) Equation-4.



Equation 4- Preparation of tetrazoline derivatives (11-18)

The synthesized compounds (11-18) were identified by FTIR spectra, some of them were characterized by $^1\text{H-NMR}$ spectra, the FTIR spectra of these compounds showed disappearance of absorption band at $(2324) \text{ cm}^{-1}$ due to the stretching vibrations of $(-\text{N}_3)$ group. Other characteristic bands are reported in Table-3. In the other hand $^1\text{H-NMR}$ spectral data of compounds (16) δ ppm in DMSO-d_6 solvent showed singlet signal at $\delta(2.33)$ ppm due to $(-\text{CH}_3)$ protons, singlet signal at $\delta(3.65)$ ppm due to $(-\text{CH}_2-)$ proton, singlet signal at $\delta(4.17)$ ppm due to $(-\text{CH}-)$ tetrazoline ring, signal at $\delta(7.22-8.36)$ ppm due to aromatic protons and singlet signal at $\delta(10.01)$ ppm due to (OH) proton as listed in Table-5 and shown in Figure-1, $^{13}\text{C-NMR}$ spectral data of compound (16) are listed in Table-6 and Figure-2.

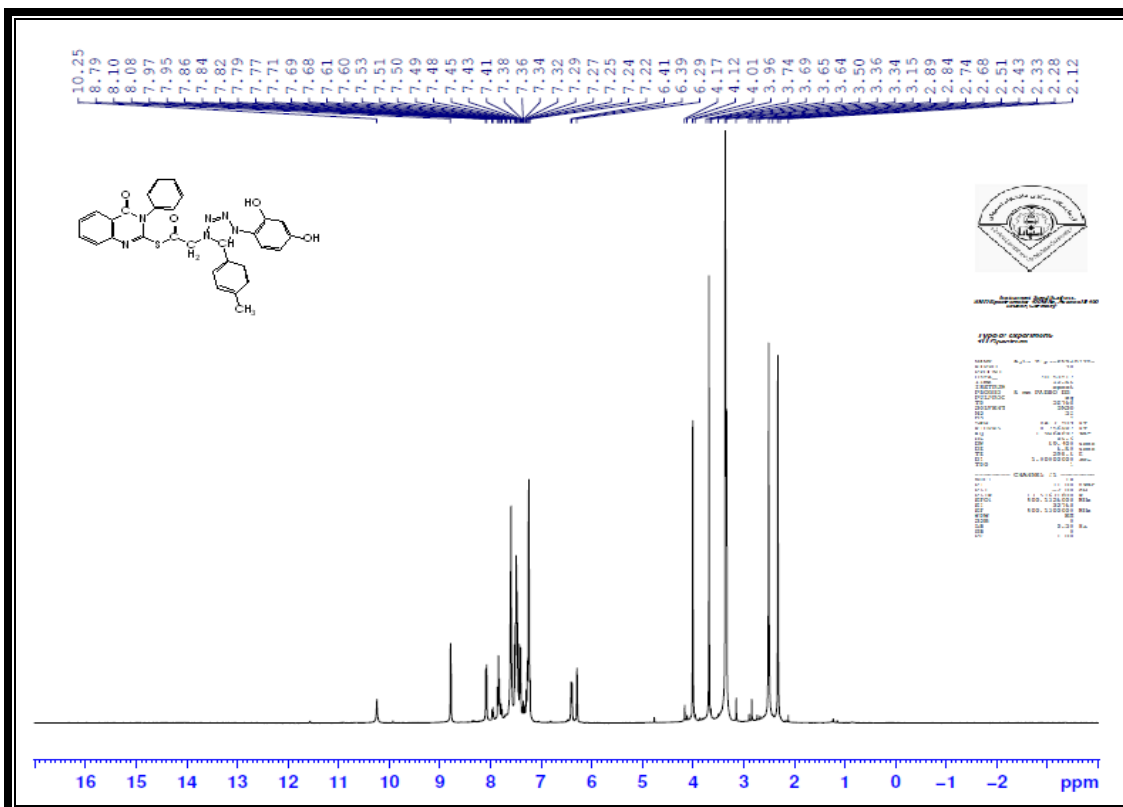


Figure 1- ¹H-NMR spectrum for compound [16]

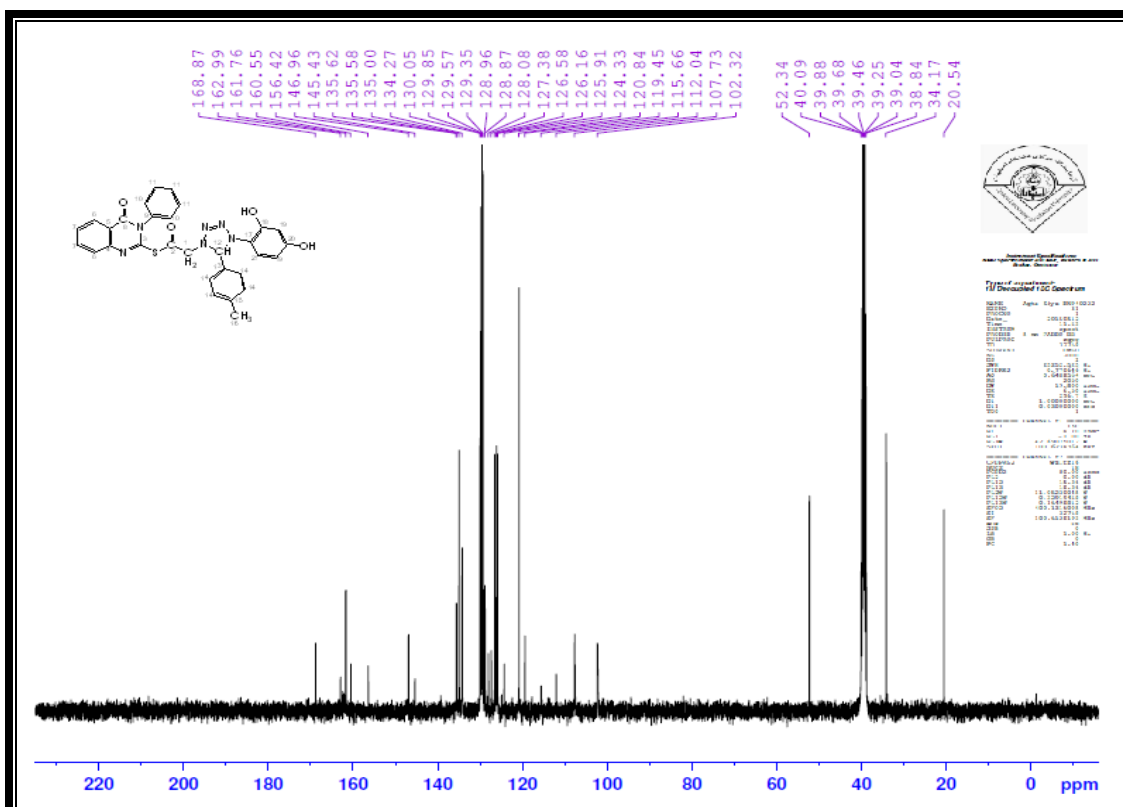
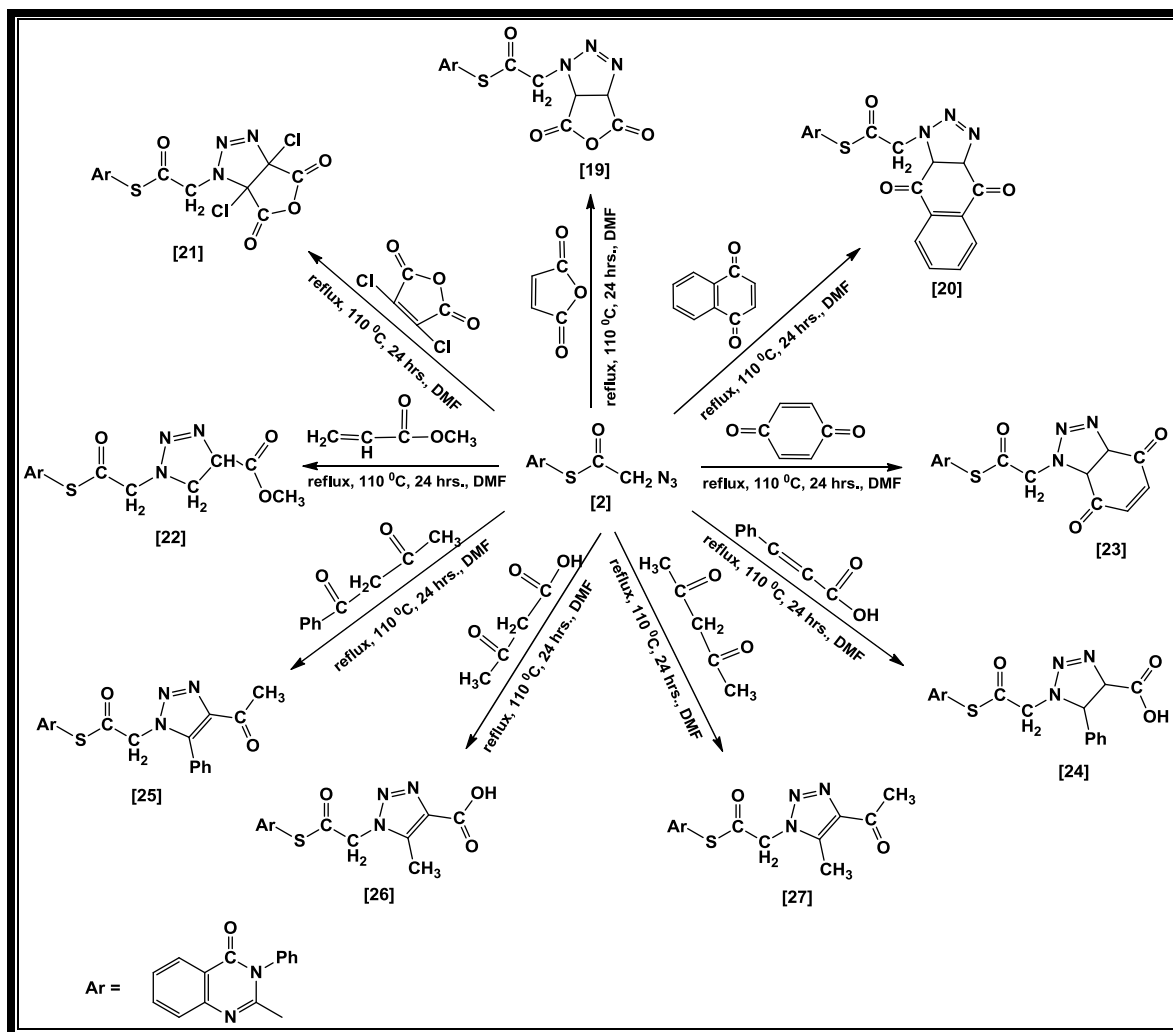


Figure 2- ¹³C-NMR spectrum for compound (16)

Finally, Triazoline and Triazole derivatives (19-27) were synthesized by the(2+3) cyclo addition reaction implicit a reaction between 1,3-dipole compounds(2) and an unsaturated compound called dipolarophile [α - β -unsaturated compounds][1,4-quinone,anhydride, α - β -ester and acid ,acetyl acetone

and acetyl acetic acid]inDMF. The product of the reaction is a five membered heterocycle[triazoline and tetrazole] derivatives Scheme-1:



Scheme 1- Preparation of triazoline and triazole derivatives (19-27)

The synthesized compounds (19-27) were characterized by FTIR spectra and some of them were characterized by $^1\text{H-NMR}$ spectra. The FTIR spectra of the compounds showed disappearance of the absorption band at $(2324)\text{ cm}^{-1}$ was due to the stretching vibrations of $(-\text{N}_3)$ group. Other data of functional groups were showed in Table-4. $^1\text{H-NMR}$ spectra of compounds (20, 22, 24 and 25) showed the characteristic signals which were listed in Table-5 and showed the spectrum of compound (22) in Figure-3. $^{13}\text{C-NMR}$ spectral data of compounds (20, 22, 24 and 25) were listed in Table-6 and showed the spectrum of compound (22) in Figure-4.

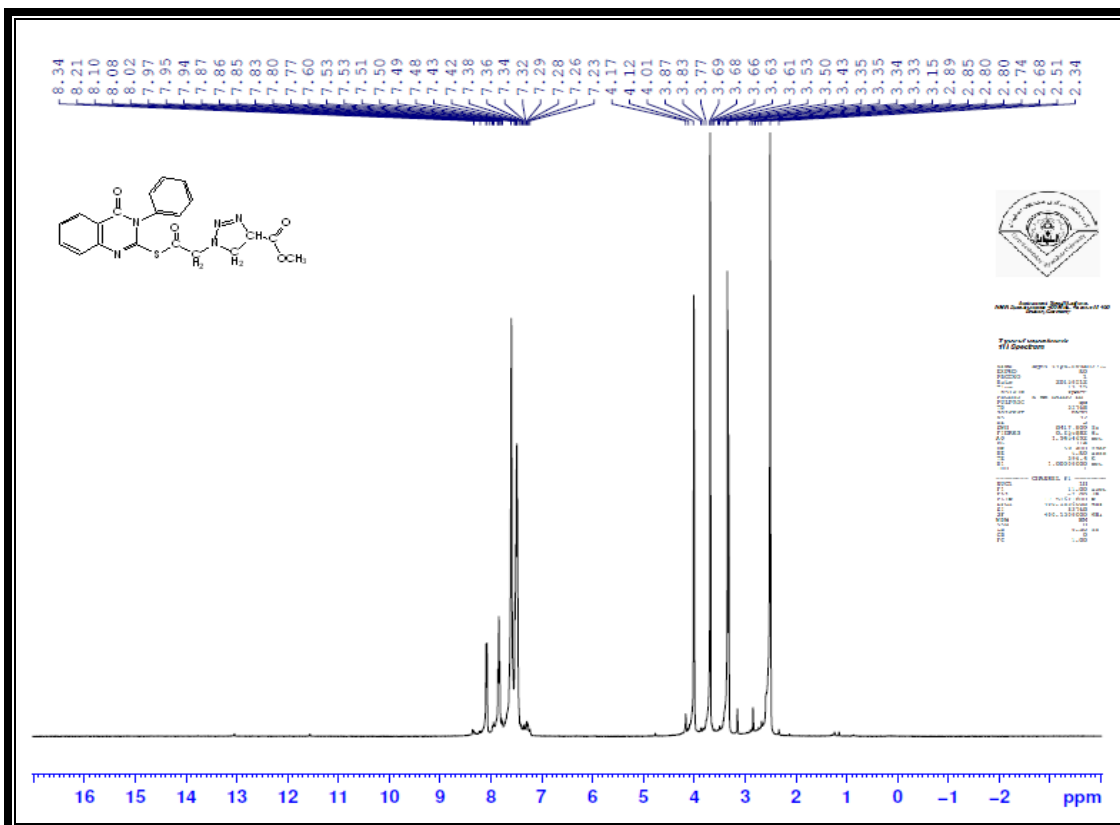


Figure 3- ¹H-NMR spectrum for compound (22)

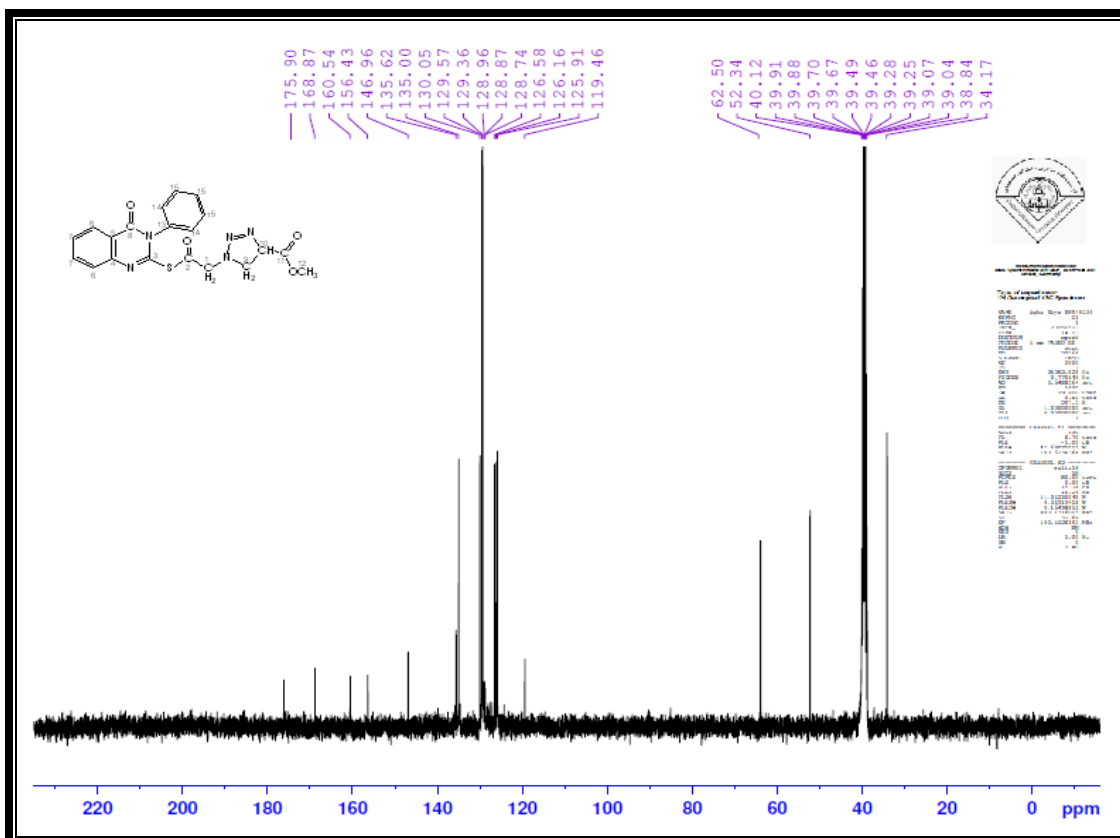


Figure 4- ¹³C-NMR spectrum for compound (22)

Anti-microbial activity:

The results of antibacterial activity are listed in Table-7. The results referred that all synthetic compounds possess moderate activity against certain types of bacteria, while they did not possess any activity against others. Compound (18) possesses strong activity against *Pseudomonas aeuroginosa*, while compounds (1, 2, 14, 18, 21 and 22) possess strong activity against *Escherichia coli*. Also compound (25) possess very strong activity against same bacteria. Compounds (2, 14, 16 and 22) was showed weak activity and (1, 5, 13, 18, 21 and 25) showed no inhibition against *Bacillus subtilis*. As far as compounds (16, 21, and 25) possess good activity against *Staphylococcus aureus* with no inhibition for compound (5, 13, 14, and 18).

Table 7- Antimicrobial activity of some of the prepared compounds

Comp. No.	<i>Staphylococcus aureus</i> +ve	<i>Bacillus subtilis</i> +ve	<i>Pseudomonas aeuroginosa</i> -ve	<i>Escherichia coli</i> -ve
1	5	-	-	13
2	4	6	7	12
5	-	-	-	-
13	-	-	11	7
14	-	3	-	11
16	11	6	-	-
18	-	-	15	11
21	13	-	-	14
22	10	7	13	11
25	16	-	-	21

- Solvent: DMSO; [C]: 800µg/ml
- Zone of inhibition: (-) no inhibition zone; (3-6) weak; (7-10) moderate; (11-21) strong.

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