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Research Article

Facile Synthesis, Characterization of New Quinazolinones with Different Azo Compounds, 1, 2, 3-Triazole Moieties and Evaluation Their Anti-bacterial Activity

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Abstract

In the present research, a series of some azo compounds (5-9) and 1,2,3-triazoles (11,12) derived from 2-methyl quinazolin-4(3*H*)-one (3) have been synthesized successfully by stepwise routes includes the following: 3-amino-2-methylquinazolin-4(3*H*)-one (3) prepared firstly by conversion of 2-aminobenzoic acid into methyl 2-aminobenzoate (1) followed by reaction with acetic anhydride to form methyl -2-acetamidobenzoate (2). The amide then allowed reacting with hydrazine hydrate to give compound (3). Diazotization reaction with sodium nitrite in the presence of hydrochloric acid yield the 3-(chlorodiazenyl)-2-methylquinazolin-4(3*H*)-one (4). Diazonium salt (4) then enter two different routes. The first route was its conversion into azo compounds (5-9) by reaction with coupling components.The second route included formation of 1,2,3triazole derivatives by interconversion of compound (4) into azido compound (10) followed by treatment with ethyl acetoacetate, acetyl acetone to give 5-methyl-1-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)-1H-1,2,3-triazole-4-carboxylic acid (11) and3-(4-acetyl-5-methyl-1*H*-1,2,3-triazol-1-yl)-2-methylquinazolin-4(3H)-one (12) in good yield. Newly synthesized derivatives were characterized spectroscopically by FTIR, ^{13}C-NMR and ^{1}H-NMR spectral technique and by determination of their physical properties. The reactions monitored by thin layer chromatography. The antibacterial potential of synthesized compounds have been tested against the growth of four gram positive and gram negative pathogenic bacterial strains using agar well diffusion method. Ampicillin trihydrate used as reference drug. The results of the antibacterial study showed that compounds (7-9)appeared good activity

Keywords: Synthesis, Characterization, Quinazolinone, Azo Compounds 1,2,3-Triazole, Anti-bacterial.

الخلاصة

في البحث الحالي سلسلة من بعض مركبات الازو (5-9) و 3,2,1-ترايازول(11،12) المشتقة من 2-مثيل كوينازولين -4(3H)ون (3) تم تحضيرها بنجاحمن خلال خطوات متعددة تضمنت مايلي: 3-امينو-2-مثيل كوينازولين 4(3H)–ون (3) حضر اولا من تحويل 2-امينو حامض بنزويك الى مثيل 2-امينوبنزوات (1) اتبع بالتفاعل مع حامض الخليك اللامائي ليكون مثيل 2-اسيتاميدو بنزوات (2). الامايد تم مفاعلته مع الهيدرازين المائي لينتج المركب (3) . تفاعل الازوتة مع نتريت الصوديوم بوجود حامض الهيدروكلوريك انتج 3-(كلوروثنائي الازينيل)-2-مثيل كوينازولين 4(3H) ون (4) . ملح الدايازونيوم (4) تم ادخاله بعد ذلك في مسارين للتفاعل . المسار الاول تضمن تحويله الى مركبات ازو (5-9) بتفاعله مع مركب ازدواج . المسار الثاني تضمن تكوين مشتقات 3,2,1-ترايازول من خلال تحويل المركب (4) الى مركب الازيدو (10) متبوعا بالمعاملة مع اثيل اسيتو اسيتايت ، اسيتايل اسيتون ليعطي 5-مثيل -1-(2-مثيل -4كوينازولين3(4H)-يل-3,2,11H-ترايازول-4-حامض كاربوكسيلي (11) و 3-(4-اسيتيل-5-مثيل-1H-3,2,1-تراياوزول-1-يل)2-مثيل كوينازولين-4(3H) ون (12) بحصيلة جيدة . المشتقات المحضرة حديثا تم تشخيصها طيفيا من خلال تقنيات طيف الاشعة تحت الحمراء ، كاربون وبروتون النووي المغناطيسي ومن خلال تحديد الخواص الفيزيائية لها. ايضا التفاعلات تمت مراقبتها من خلال كروماتوغرافيا الطبقة الرقيقة . الفعالية المضادة للبكتريا للمركبات المحضرة تم اختبارها ضد اربع سلالات من البكتريا المرضية موجبة الصبغة وسالبة الصبغة بطريقة الانتشار . استخدم الامبيسيلين كدواء قياسي . نتائج الدراسة المضادة للبكتريا اظهرت ان المركبات (7-9) ذات فعالية جيدة.

Introduction

Quinazolines and quinazolinones (Figure 1) are main classes of fused heterocycles rings for a great importance in medicinal chemistry [1]. Consisting of a pyrimidine moieties fused at 5, 6 position with benzene rings. Quinazoline is structurally related to 2and 4-quinazolinones isomers it behaves chemically like its pyrimidine counterpart with the exception that quinazoline is more basic due the electrophilic behavior at the carbon number four positions.

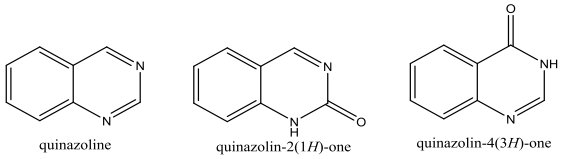


Figure 1: Chemical structure of quinazolines and quinazolinones.

Many substituted quinazoline and quinazolinone derivatives possess a broad spectrum of bioactivities such as bactericidal [2], fungicidal [3], anti-tuberculosis [4], antiviral [5], muscle relaxant [6], antimalarial [7], diuretic agents [8], antiprotozoal [9], CNS depressant [10] more other biological activities. Various synthetic drugs molecules such as nolatrexate [11], albaconazole [12], afloqualone (Arofuto) [13] and proquazone (Biarison) [14] are also contain derivatives of quinazoline and quinazolinone as active functional materials.

On the other hand 1,2,3-triazole is a five-membered aromatic heterocyclic system with three nitrogen heteroatoms have been widely used in the many synthetic medicines for instance Tazobactam (Zosyn) is a 1,2,3-triazole containing compound that inhibits the action of bacterial ß-lactamases [15]. Also the literature includes numerous examples for their biological activities such as anti-microbial activity [16], anti-HIV activity [17], anti-allergic [18], anti-convulsant behaviors [19].

In addition azo dyes are compounds containing the active groups R−N=N−R' where R and R' can be either aryl (aromatic) or alkyl (aliphatic) functional groups. Several azo dyes were reported in the recent years shows variety of interesting biological activities like anti-neoplastics [20], antibacterial [21], antidiabetic [22] and antitumor [23] activities other useful chemotherapeutic agents [24].

Herein, reported the efficient synthesis of novel quinazolin-4(3*H*)-one derivatives containing moieties of substituted azo compounds (5-9), and 1,2,3-triazole (11,12).Combination of substituted diazenyl or 1,2,3-triazole moieties into quinazolinones can probably resulted new molecules were expected to possess biological activity and removal of untoward side effects.

Materials and Methodology

All chemical materials, used in this research were supplied from BDH, Fluka, Merck, Sigma-Aldrich and some other commercial suppliers were used without further purification. Melting points were designed by digital melting point device (Stuart Scientific SMP30) and are uncorrected.Thin layer chromatography (TLC) was carried out using Fertigfollen precoated sheets type Polygram Silica gel, and the plates were developed with iodine vapour.The Fourier Transform Infrared FTIR spectra were recorded on SHIMADZU (8400, Kyoto, Japan) spectrophotometer using KBr discs in the range (400-4000) cm^{-1}at ministry of industry and minerals ibn sina state company. Two types of nuclear magnetic resonance spectra ^{1}H-NMR and ^{13}C-NMR (dimethyl sulfoxide DMSO -d6 as solvent) were recorded on Bruker 300 MHZ spectrophotometer using tetra methyl saline as an internal reference standard in water, environment and arid regions research center, Al al-Bayt University (Jordon).

Synthesis of methyl-2-aminobenzoate (1)

A mixture of 2-aminobenzoic acid (2g, 0.014 mol.) and excess thionyl chloride (10 ml) was refluxed for (3 hrs.), and then the excess of thionyl chloride was evaporated. Cold absolute methanol (10 ml) was added almost readily and an instantaneous reaction occurred to give the product. After reactioncompleting the solution is cooled and methyl-2-aminobenzoate hydrochloride salt crystallizes. The mixture is diluted with 50 ml of distilled water and made basic by addition of the solution of sodium bicarbonate (10%). Oily methyl-2-aminobenzoate was extracted with petroleum

ether and then washed with sodium bicarbonate solution. The extract product is dried over sodium bisulfate and evaporated in little amount bulk with vacuum and finally collecting [25].

Synthesis of methyl -2-acetamidobenzoate (2)

Mixture of methyl 2-aminobenzoate (2.7 g, 0.017 mol.) (1)in acetic anhydride (12 ml.) was refluxed of for (1hr.). The resulted solution then cooled and poured into distilled water (100ml.). The solid product filtered, dried and recrystallized from ethanol [26].

Synthesis of 3-amino-2-methylquinazolin-4(3*H*)-one (3)

Solution of methyl -2-acetamidobenzoate (2) (2 g, 0.01 mol.) in ethanol (10 ml.) and hydrazine hydrate (10 ml.) and was heated under reflux for (4 hr.). Cooling the mixture with stirring in a distilled water (100ml.) give the crude product, was filtered washed with little amount of water and dried. Absolute ethanol was used for recrystallization [27].

Synthesis of 3-(Chlorodiazenyl)-2-methylquinazolin-4(3*H*)-one (4)

To a cooled solution of 3-amino-2-methylquinazolin-4(3*H*)-one (3) (0.01 mol, 1.65 g) in concentration hydrochloric acid (3ml.) between (0-5^{o}C) the mixture of sodium nitrite (0.01 mole, 1.5 g) in (15 ml.) of water was added gradually during (0.5hr.). The reaction mixture was stirred for further (1hr.) [28].

Synthesis of 2-methyl-3-(substituted diazenyl) quinazolin-4(3*H*)-one (5-9)

Appropriate coupling components (ortho-salicyladehyde, phenol, 1-napthol, aniline, chloroaniline) (0.01 mol) was dissolved in (1 ml) glacial acetic acid. After complete the desolation, the clear solution of 3-(Chlorodiazenyl)-2-methylquinazolin-4(3H) one diazonium salt (4) was added to these solutions. Mixture of reaction was stirred about (1-2 hrs.) at below 5^{o}C. Sodium acetate solution was adding drop by drop to make the pH of the solution weak acidic between the range four to five. The mixture stirred continuously for (5hrs.) on the temperature less than 5^{o}C. The products were filtered off, washed with little hot water and dried. The crude azo compound was recrystallized from suitable solvents [28].

Synthesis of 3-azido-2-methylquinazolin-4(3*H*)-one (10)

To an aqueous solution of 3-(chlorodiazenyl)-2-methylquinazolin-4(3*H*)-one (4) (2.6 g, 0.012mol.) of an aqueous solution of sodium azide (0.012 mol, 0.78 g) was added dropwise. The reaction mixture stirred about 40 min. to afford the desired product as a solid compound filtered and then dried and recrystallized from ethanol. [29]

Synthesis of 5-methyl-1-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)-1H-1,2,3-triazole-4-carboxylic acid (11)

A mixture of 3-azido-2-methylquinazolin-4(3H)-one (10) (0.01 mol, 2.83g) and ethyl acetoacetate (0.01 mole, 1.03 ml.) in methanol (30 ml) was cooled to 0^{o} C. Sodium ethoxide (25 ml) was added gradually to the mixture and heated under reflux on a water bath for (7hrs.). The crude product was washed with distilled water, filtered, dried and then recrystallized from ethanol [30].

Synthesis of 3-(4-acetyl-5-methyl-1*H*-1,2,3-triazol-1-yl)-2-methylquinazolin-4(3H)-one (12)

3-azido-2-methylquinazolin-4(3H)-one(10) (0.01 mole, 2.83g) was added portion wise into mixture of acetyl acetone (0.01 mole, 1.92 ml) and cold solution of sodium ethoxide (7ml.). Refluxing reaction mixture for (5hrs.) give solid product, it was separated and recrystallized from ethanol [31].

Anti-bacterial activity

Seven newly prepared compounds are 2-methyl-3-(substituted diazenyl) quinazolin-4(3*H*)-one (5-9), 5-methyl-1-(2-methyl-4-

oxoquinazolin-3(4*H*)-yl)-1H-1,2,3-triazole-4-carboxylic acid (11) and 3-(4-acetyl-5-methyl-1*H*-1,2,3-triazol-1-yl)-2-methylquinazolin-4(3*H*)-one (12) were screened for their*in vitro*elementary antibacterial activity against two types of Gram positive bacteria including (*Staphylococcus aureus,Bacillus subtilis*)and two types of Gram negative bacteria including (*Escherichia coli , Pseudomonas aeruginosa*) by well agar diffusion method using nutrient agar as medium [32].

Tested compounds were prepared with different concentration using 100mg/ml in dimethyl sulfoxide (DMSO) as solvent. Each solution of the prepared concentration was added to test tubs contains 5ml of the nutrient broth. Two test tubs were left one without addition to the other tube, DMSO was added only as control, the bacterial suspension was diluted and 1ml of the diluted suspension to the tubes including the control. Disks of each concentration were placed in triplicate in nutrient agar medium seeded with fresh bacteria separately. The incubation left at 37^{o}C for one day. The evaluation was carried out by measuring the diameter of inhibition zones in mm. Ampicillin trihydrate was used as reference standard for all the tested compounds.

Results and Discussion

The synthesis of the desired compounds of quinazolin-4-one derivatives containing moieties of azo (5-9) and 1,2,3-triazoles (11,12) was accomplished according to the representation (scheme 1). 3-amino-2-methylquinazolin-4(3*H*)-one (3), obtained by conversation of 2-aminobenzoic acid into 2-aminobenzoyl chloride followed by condensation of acid chloride with methanol, to give methyl 2-aminobenzoate compound (1).

Treatment of this ester with acetic anhydride produced methyl -2-acetamidobenzoate compound (2). On hydrazinolysis by refluxing with hydrazine hydrate furnished the compound (3) 3-amino-2-methylquinazolin-4(3*H*)-one. The structures of all the synthesized compounds (1-12) were established on the basis of FT-IR and some of them by ^{1}H-NMR and ^{13}C-NMR. The physical properties of all the newly synthesized compounds (1-12), shown in Table 1.

The FT-IR spectra of compounds (1-3) shown some characteristic bands proved that the preparation steps carried out successfully, for example, in spectra of compound (1) the disappearing band of OH carboxylic acid of starting material and disappearing bands of symmetrical and unsymmetrical of NH_2 group in spectra of compound (2) and appearing instead specific band at 3227 cm^{-1} belong to NH in compound (2).

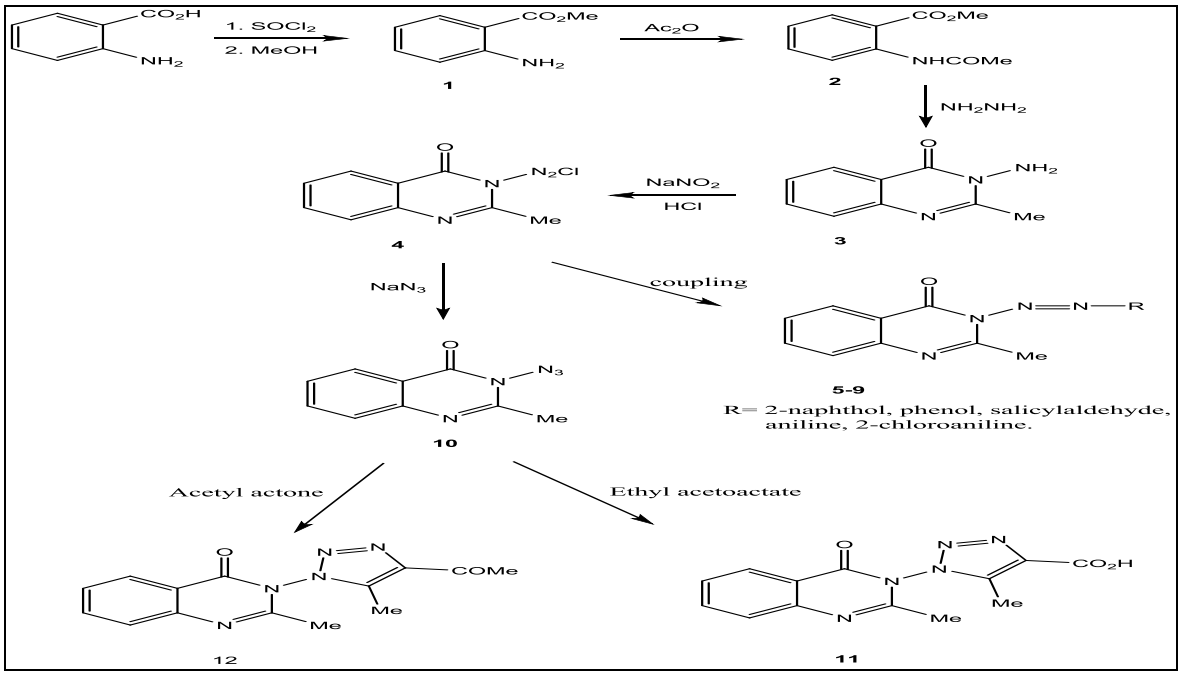
Finally, appearing of new absorption bands in spectra of compound (3) attributed to (NH_2) between 3422-3268 cm^{-1} , (C=N) at 1626 cm^{-1} and other absorption bands as shown in Table 2.

Diazonium chloride derivative of 2-methylquinazolin-4(3*H*)-one (4) obtained from diazotation of 3-amino-2-methylquinazolin-4(3*H*)-one (3). The characteristic indication in FTIR spectra that disappearance of v (NH_2) in region (3324, 3268 cm^{-1}) in addition to appearances of other absorption bands due to v(C-H) aromatic (3037 cm^{-1}) v(C-H) aliphatic (2974 cm^{-1}), v(C=O) 1709cm^{-1}and v(C=N) 1634 cm^{-1}respectively.

The first route for synthesis of azo compounds (5-9) derived from 2-methylquinazolin-4(3*H*)-one includes reaction of compound (4) with coupling components such as [2-naphthol (5), phenol (6), o-salicyladehyde (7), aniline (8) and 2-chloroaniline (9)] respectively. Physical properties of 2-methyl-3-(substituted diazenyl) quinazolin-4(3H)-one (5-9) are listed in table (1).

FTIR Spectra show the absorption bands v(N=N) (In the range1560-1531 cm^{-1}) for azo groups in addition to other bands of substituted groups v(OH) (3290-3279 cm^{-1}) and v(NH_2)(3410 -3286 cm^{-1}). All details of FTIR Spectra are listed in Table (2).

^{1}H-NMR spectroscopy was also utilized to achieve important information of some synthesized compounds structure such as (6,8,11and 12).



Scheme 1: Synthetic routes for compounds (1-12).

Table 1: Physical Properties Data of Compounds (1-12).

Comp.No.	Substituents (R)	Molecular formula	Yield (%)	Color	Melting Point (^oC)	Recryst. solvent	Rf Value (ethyl acetate eluent)
1	-	$C_8H_9NO_2$	68	colorless	259-262 b.p.	-	0.63
2	-	$C_{10}H_{11}NO_3$	66	off white	101-103	ethanol	0.55
3	-	$C_9H_9N_3O$	71	brown	153-156	ethanol	0.71
4	-	$C_9H_7N_4OCl$	78	yellow	oily	-	0.66
5	2-naphthol	$C_{19}H_{14}N_4O_2$	75	brown	179-181	ethanol	0.58
6	phenol	$C_{15}H_{12}N_4O_2$	72	yellow-green	221-223	ethanol	0.53
7	o-salicyladehyde	$C_{16}H_{12}N_4O_3$	59	light orange	255-257	ethanol -water1:1	0.71
8	aniline	$C_{15}H_{13}N_5O$	81	deep brown	192-195	water	0.62
9	2-chloroaniline	$C_{15}H_{12}N_5OCl$	79	green	201-204	ethanol -water1:1	0.56
10	-	$C_9H_7N_5O$	67	orange	165-167	ethanol	0.57
11	-	$C_{13}H_{11}N_5O_3$	78	deep yellow	186-188	ethanol	0.59
12	-	$C_{14}H_{13}N_5O_2$	76	Pale yellow	243-245	ethanol	0.52

Table 2: FTIR Spectral data cm^{-1} of compounds (1-12).

Comp.No.	v(C-H) Arom.	v(C-H) Aliph.	v(C=O) carbonyl	v(C=N)	v(C=C) Arom.	v(C-N)	Others
1	3098	2956	-	-	1598	-	v(NH_2)3422, 3342, v(C=O)1730 ester, v(C=O)1688 amide.
2	3066	2941	-	-	1579	-	v(N-H) 3227
3	3043	2933	1712	1626	1593	1344	v(NH_2) 3324, 3268.
4	3037	2974	1709	1634	1566	1338	-
5	3069	2983	1710	1645	1548	1352	v(O-H) 3290. v(N=N) 1531.
6	3071	2945	1698	1612	1583	1357	v(O-H) 3279, v(N=N) 1560.
7	3079	2928	1714	1648	1609	1318	v(O-H) 3285, v(C=O) 1690. v(N=N)1554.
8	3081	2967	1701	1628	1572	1358	v(NH_2) 3410, 3357. v(N=N) 1548.
9	3064	2969	1715	1644	1589	1341	v(NH_2) 3399, 3286, v(N=N) 1542, v(C-Cl)858.
10	3072	2949	1695	1638	1536	1345	v(N=N-N) 2122,
11	3088	2938	1718	1619	1564	1335	v(O-H) 3306, v(C=O)1736carboxyl, v(N=N) 1551.
12	3055	2977	1716	1622	1559	1330	v(C=O) 1686 carbonyl, v(N=N) 1581.

^{1}H-NMR spectrum of compound (6) displayed signals at 5.32 ppm which attributed to proton of (OH) attached to aromatic ring, and also it was showed signals between 7.04-7.75 ppm belong to aromatic protons. The protons of methyl group attached to quinazolin-4-one ring appeared as a singlet at 1.27 and 1.33 ppm, as shown in Figure 2 and listed in Table 3.

The further spectroscopic method ^{13}C-NMR is also used for characterization of newly synthesized compounds. ^{13}C-NMR spectrum of compound (6) showed signals belong to (-CH_3-) of quinazolin-4(3*H*)-one, aromatic carbons of quinazolin-4(3*H*)-one, benzene ring attached to (N=N) azo group, carbon of benzene ring bearing (OH) hydroxyl group, (N-C=N) and (C=O) carbonyl for quinazolin-4(3*H*)-one respectively as shown in Figure 3 and listed in Table 4.

On the other hand ^{1}H-NMR spectrum of compound (8) show signals due to two protons of (NH_2) amino group attached to aromatic ring, and also it was found signals belong to benzene ring protons and (-CH_3-) of quinazolin-4(3*H*)-one ring respectively. Results of ^{1}H-NMR spectrum for compound (8) were listed in Table 3. By the same way ^{13}C-NMR spectrum of compound (8) show signals due to carbons (-CH_3) of quinazolin-4(3*H*)-one, aromatic carbons of quinazolin-4(3*H*)-one, carbons of benzene ring attached to (N=N) azo group, carbon of benzene ring bearing (NH_2) amino group, (C=O) carbonyl group and (N-C=N) for quinazolin-4(3*H*)-one respectively. Results of ^{13}C-NMR spectrum for compound (8) were listed in Table 4.

The second route for synthesis of 1,2,3-triazoles (11,12) attached to 2-methylquinazolin-4(3*H*)-one includes treatment of obtained diazonium chloride (4) with calculated amount of sodium azide to yield 3-azido-2-methylquinazolin-4(3*H*)-one. (10).

The structure elucidation of compound (10) was depended on physical properties which are listed in Table 1. FTIR spectra showing the absorption band at 2122 cm^{-1} for v (N=N-N) group.

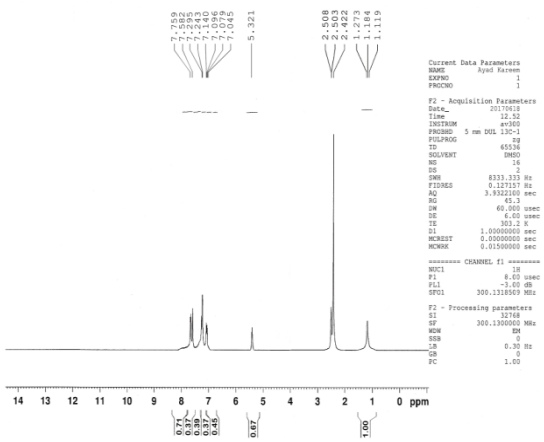


Figure 2: ^{1}H-NMR Spectrum for compound (6).

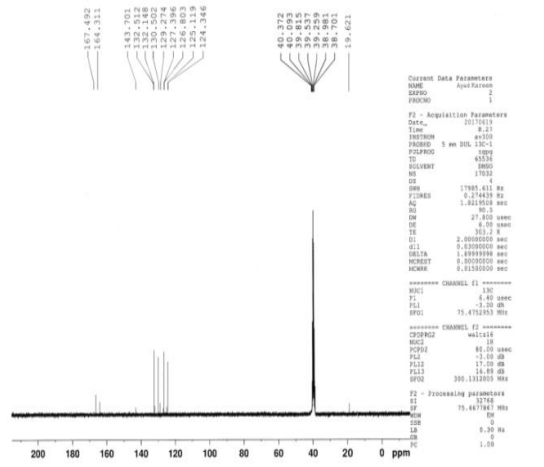


Figure 3: ^{13}C-NMR Spectrum for compound (6).

The synthesized 3-azido-2-methylquinazolin-4(3*H*)-one (10) were converted into 5-methyl-1-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)-1*H*-1,2,3-triazole-4-carboxylic acid (11) and 3-(4-acetyl-5-methyl-1*H*-1,2,3-triazol-1-yl)-2-methylquinazolin-4(3*H*)-one (12) by the cyclization reaction with ethylacetoacetate and acetyl acetone respectively.

The disappearance of absorption band of the azide group (N_3) in FTIR spectrum at (2122) cm^{-1} gets best indication for successful of condensation reaction. The spectrum also shows absorption bands v(O-H) 3306, v(C=O) 1736 carboxyl, v(N=N) 1551 of1,2,3-triazole ring for compound (11)as shown in Figure 4, While appearance of v(C=O) 1686 ketone, v(N=N) 1581of1,2,3-triazole ring compound (12) is the other evidences for complete formation of compound as shown in Figure 5.

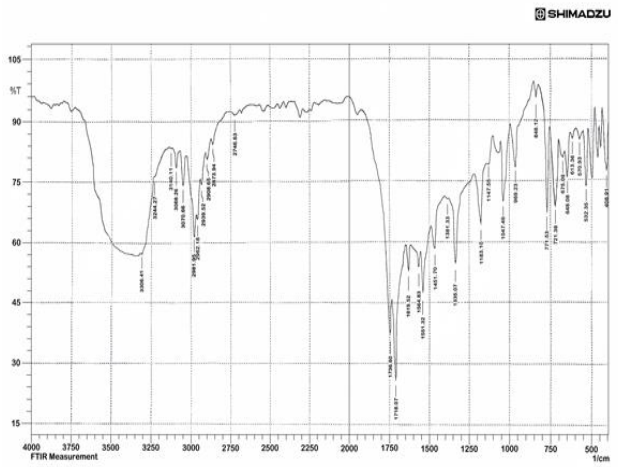


Figure 4: FTIR Spectrum for compound (11).

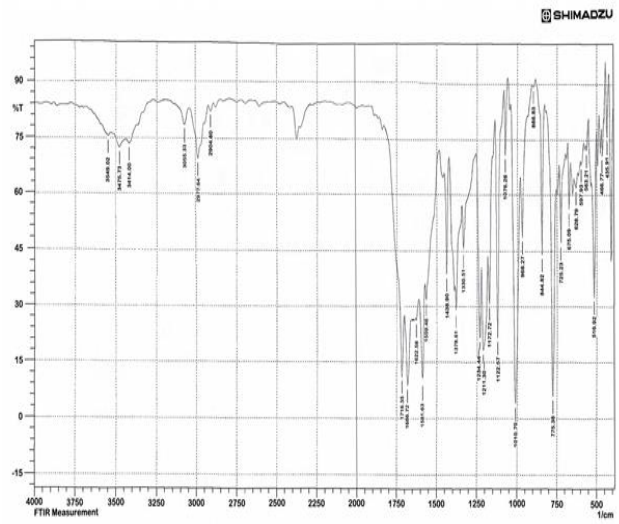


Figure 5: FTIR Spectrum for compound (12).

^{1}H-NMR spectrum of compound (11) show signals attributed to protons of (-CH_3) of quinazolin-4(3*H*)-one ring, protons of (-CH_3) attached to 1,2,3-triazole ring, aromatic ring protons and (-COOH) carboxyl proton respectively. All details for ^{1}H-NMR spectrum for compound (11) are shown in Figure 6 and listed in Table 3.

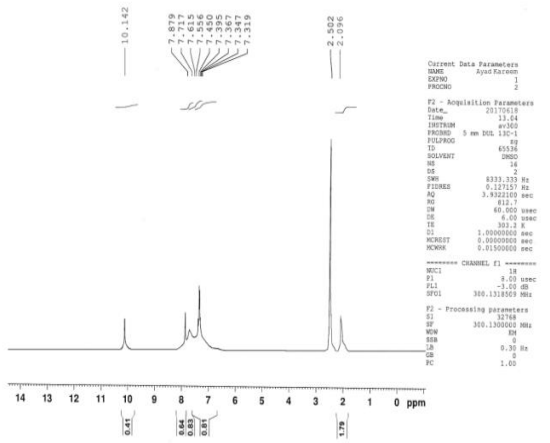


Figure 6: [1]H-NMR Spectrum for compound (11).

So [13]C-NMR spectrum of compound (11) appeared signals due to carbon (-CH_3) of quinazolin-4(3*H*)-one, carbon of (-CH_3) attached to 1,2,3-triazole ring, aromatic carbons of quinazolin-4(3*H*)-one, carbon of (N-C=N), (C=O) carbonyl group and for quinazolin-4(3*H*)-one and carbon of (COOH) carboxyl attached to 1,2,3-triazol ring respectively as shown in Figure 7 and listed in Table 4.

[1]H-NMR spectral data for 3-(4-acetyl-5-methyl-1*H*-1,2,3-triazol-1-yl)-2-methylquinazolin-4(3*H*)-one (12) show the following signals due to (CO-CH_3) protons attached to 1,2,3-triazole ring, (-CH_3) of quinazolin-4(3*H*)-one ring, protons of (-CH_3) attached to 1,2,3-triazole ring, aromatic ring protons respectively as listed in table (3).

Also [13]C-NMRspectral data for 3-(4-acetyl-5-methyl-1*H*-1,2,3-triazol-1-yl)-2-methylquinazolin-4(3*H*)-one (12) appears signals due to carbon of (COCH_3) methyl group attached to 1,2,3-triazol ring, (-CH_3) of quinazolin-4(3*H*)-one,carbon of (-CH_3)attached to1,2,3-triazole ring, aromatic carbons of quinazolin-4(3*H*)-one, carbon of (N-C=N), (C=O) carbonyl group and for quinazolin-4(3*H*)-one and carbon of (COCH_3) ketone group attached to 1,2,3-triazol ring respectively as listed in Table 4.

The Antibacterial Activity

The antibacterial activity of 2-methylquinazolin-4(3*H*)-one derivatives{(2-methyl-3-(substituted diazenyl) quinazolin-4(3*H*)-one (5-9), 5-methyl-1-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)-1H-1,2,3-triazole-4-carboxylic acid (11) and 3-(4-acetyl-5-methyl-1*H*-1,2,3-triazol-1-yl)-2-methylquinazolin-4(3H)-one (12)} are summarized in Table 5. The listed values for *in vitro* growth inhibitory activity of the synthesized compounds were investigated in comparison with the well-known antibacterial standard drug ampicillin trihydrate.

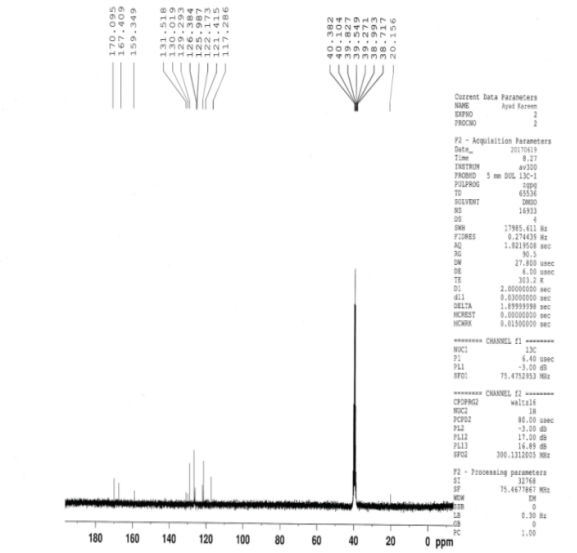


Figure 7: [13]C-NMR Spectrum for compound (11).

From the data given in Table 5 that show most of the tested compounds displayed variable degrees of antibacterial activity against Gram-positive bacteria, Gram-negative bacteria strains, in comparison to the standard in each case which revealed that these compounds are biologically active.

Blank solution of dimethyl sulfoxide gives no inhibition zone in each case against bacterial isolates. Compound 7, 8 exhibited high degree of antibacterial activity against Gram-positive bacteria (*SA*) and against Gram-negative bacteria *(EC).* On the other hand compound 9 show high activity against Gram-positive bacteria (*SA*) and against Gram-negative bacteria *(PA).*

Table 3: [1]H-NMR spectral data (δppm) for some of the synthesized compounds.

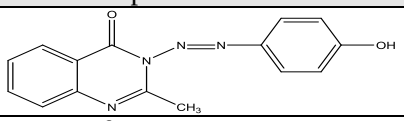
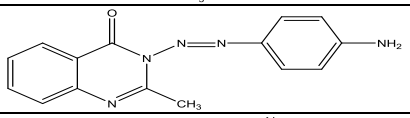
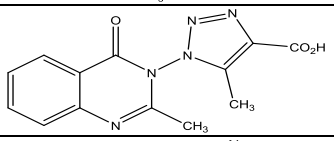
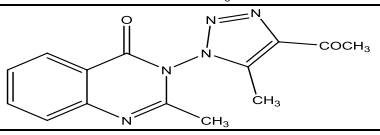
Comp.No.	Compound structure	^{1}H-NMR parameters (δppm)
6		1.27 (s, 3H, -CH_3), 5.32(s, 1H, -OH), 7.04-7.75 (m, 8H,Ar-H).
8		1.33 (s, 3H, -CH_3), 3.26 (s, 2H, -NH_2), 7.18-7.64 (m, 8H,Ar-H).
11		2.09 (s, 6H, -CH_3), 7.31-7.87 (m, 4H,Ar-H), 10.14 (s, 1H, -COOH),
12		1.74 (s, 3H, -$COCH_3$), 2.11 (s, 6H, -CH_3), 7.29-7.63 (m, 4H,Ar-H).

Table 4: ^{13}C-NMR spectral data (δppm) for some of the synthesized compounds.

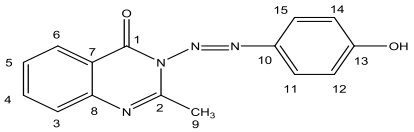
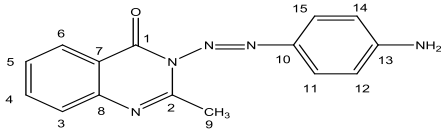
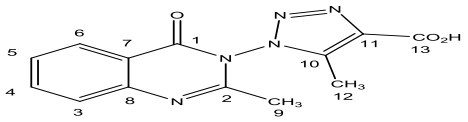
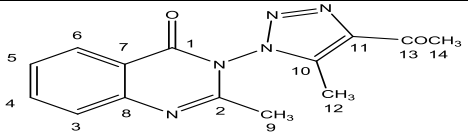
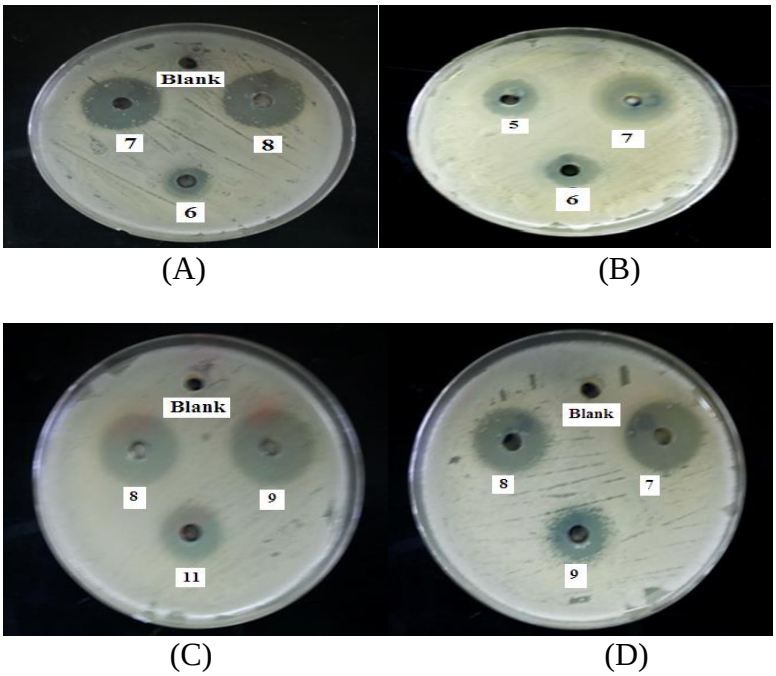
Comp.No.	Compound structure	^{13}C-NMR parameters (δppm)
6		19.62(C_9),124.34-132.51(C_3-C_8),(C_{10}-C_{12}),(C_{14}-C_{15}),143.70 (C_{13}),164.31 (C_2), 167.49 (C_1).
8		18.55 (C_9), 121.49-133.61 (C_3-C_8),(C_{10}-C_{12}),(C_{14}-C_{15}), 144.82 (C_{13}),161.02 (C_2), 166.38 (C_1).
11		20.15 (C_9,C_{12}), 117.28-131.51 (C_3-C_8),(C_{10}, C_{11}), 159.34 (C_2),167.40 (C_1), 170.09 (C_{13}).
12		21.22 (C_9,C_{12}), 48.61 (C_{14}), 118.53-135.41 (C_3-C_8),(C_{10}, C_{11}), 160.66 (C_2), 165.71 (C_1), 175.92 (C_{13}),

Table 5: Inhibition zone values (mm) for antibacterial activity of the 2-methylquinazolin-4(3*H*)-one derivatives.

Compound No.	*Staphylococcus aureus (SA)*	*Bacillus Subtilis (BS)*	*Pseudomonas aeruginosa (PA)*	*Escherichia Coli (EC)*
5	14	12	18	17
6	10	10	13	11
7	20	14	18	21
8	22	13	19	20
9	23	16	21	17
11	10	9	11	8
12	12	13	13	15
Ampicillin trihydrate (standard)	26	20	28	30
DMSO (Blank)	-	-	-	-

Figure 8 shows effect of some prepared compounds on some of these bacterial isolates. Other synthesized compounds (5, 6, 11 and 12) have acceptable degree of activity against the tested pathogenic bacteria. The structure antibacterial activity relationship (SAR) of the newly synthesized compounds revealed that the maximum activity was achieved with compounds (7, 8 and 9) having azo moieties attached with 2-methylquinazolin-4(3*H*)-one.



(A) (B)

(C) (D)

Figure 8: Inhibition zones (A) for compounds (6,7,8) and blank on *Staphylococcus aureus*(SA),(B) for compounds (5,6,7) and blank on *Bacillus Subtilis* (BS), (C) for compounds (8,9,11) and blank on *Pseudomonas aeruginosa (PA)*and (D) for compounds (7,8,9,11) and blank on *EscherichiaColi* (EC).

Conclusions

Heterocyclic compounds derived from quinazolinones were synthesized and structurally characterized by using different spectroscopic techniques. The synthetic route produced azo compounds and various 1,2,3-triazoles moieties attached with quinazolinone rings. These compounds have been successfully estimated for their anti-bacterial activity on four strains of pathogenic bactria.

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