# Synthesis, Characterization and Evaluation of Antimicrobial Activity for New Heterocyclic Derivatives Containing Pentagonal, HexagonalRings.

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**Abstract:**

This research, involved a series of some new compounds containing different hetero cyclic new pentagonal and hexagonal rings, through the reaction of 2-mercapto-3-phenyl-4(3H)quinazolinone (1) with chloroacetylchloride in the presence of potassium hydroxide, and dry dimethylformamide (DMF) as a solvent to obtain the intermediate compound (2). This compound is reacted with different reagents to give four routes, the first route include direct reaction with substituted-2-aminobenzothiazole under certain conditions to give new compounds (3-9). The second route involved condensation compound (2) with 5-substituted-2-amino-1,3,4-oxadiazole in the presence of potassium carbonate anhydrous to give new compounds (10-13).while the third route involved condensation compound (2) with para-phenylenediamine in ethanol as a solvent to give the corresponding compound (14) which the conversion new substitutes 1,2,3-triazole compounds (17-18) were prepared through the reaction of compound (14) with different reagent to give compounds (15-16). And subsequent reactions to obtain compounds (17-18) respectively. The fourth route include reaction compound (2) with para-chlorosulphonylaniline to give compound (19) which the conversion new sulphanilamide compounds (20-22) were prepared through the reaction compound (19) with different primary aromatic amine. The structure of newly synthesized compounds were identified by spectral methods their [FTIR,$^{1}$HNMR, $^{13}$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 and fungicidal.

**Keywords**:quinazolinone,2-aminobenzothiazoles,substituted oxadiazoles, 1,2,3-triazole, sulphanilamide, antimicrobial.

# تحضير وتشخيص وتقييم الفعالية المضادة للمايكروبات لمشتقات المركبات غير المتجانسه الحاويه على حلقات خماسيه وسداسيه

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**الخلاصة:**

تضمن البحث سلسلة من بعض المركبات الحلقيه غير المتجانسه الجديدة الخماسية والسداسية الحلقة ، من خلال تفاعل 2-مركبتو-3-فنيل-4(H3)-كوينوزولينون (1) مع الكلوروأسيتايل كلورايد وبوجود هيدروكسيد البوتاسيوم و DMF كمذيب للحصول على المركب الوسطي (2).بعدها تفاعل المركب الوسطي باربعة مسارات

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،تضمن المسار الاول بالتفاعل المباشر مع معوضات 2-امينو بنزوثايازول تحت ظروف معينه لتعطي المركبات الجديده (3-9).وتضمن المسار الثاني تكاثف المركب (2) مع 5-معوض-2-امينو-1,2,3-، اوكسادايازول بوجود كاربونات البوتاسيوم اللامائيه، لتعطي المركبات الجديدة (10-13).بينما تضمنت الطريقه الثالثه تكاثف المركب (2) مع بارا-فنيلين داي امين في الايثانول كمذيب وحصلنا تبعا لذلك على المركب (14)، الذي تم تحويله الى معوضات 1,2,3-ترايازول المركبات (17-18) وذلك من خلال تفاعل المركب (14) مع مختلف الكواشف ليعطي المركبات (15-16) ونواصل التفاعل للحصول على المركبات (17-18) على التوالي.تضمن المسار الرابع تفاعل المركب (2) مع البارا-كلورو سلفونيل انيلين ليعطي المركب (19) الذي تم تحويله الى مركبات السلفانيل امايد(20-22) والتي تم تحضيرها من خلال تفاعل المركب (19) مع مختلف الامينات الاولية الاروماتية.تراكيب المركبات المحضرة الجديدة شخصت من خلال الطرق الطيفية [FTIR, $^{1}$H-NMR, $^{13}$C-NMR]وقياس بعض خواصها الفيزياوية بالاضافة لذلك تمت دراسة تأثير بعض المركبات المحضرة على بعض سلالات البكتيريا وفطر واحد.

## Introduction:

Quinazolinone and it's derivatives are building block for approximately 150 naturally occurring alkaloids isolated from a number of families of the plant kingdom, from microorganisms and animals [1]. In light of the growing number of applications in recent years, there has been an enormous increase in the interest among biologists and chemists in their synthesis and bioactivity of quinazolinone derivatives [2]. Quinazolinones (benzopyrimidine derivatives), are compounds with wide spectrum of biological activities, including: [3] anti cancer [4], anti convulsant [5], anti inflammatory [6,7], anti tubercular [8] and anti bacterial effects [9].For the 2-aminobenzothiazole substituted, 1,3,4-oxadiazole, constitute a potential class of compounds which possess field of biological interaction [10,11].many of them exhibit antibacterial [12], anticonvulsant [13], anticancer activitie [14].They are also applied in agriculture as herbicides, fungicides or insecticides [15].keeping these above facts in view it was through worthwhile to synthesis new compounds by incorporating quinazolinone and 2-aminobenzothiazoles derivatives or 1,3,4-oxadiazole ring in a single molecular framework. The resulted new molecules were expected to possess biological activity since they were built from two biological active compounds. For the 1,2,3-Triazoles, which can be readily prepared from click chemistry, are important building components that could be exploited in many applications in organic , organometallic, and medicinal chemistry, as well as in materials chemistry. Click chemistry is increasingly being used in medicinal chemistry research. Because it enables a modular approach to pharmacophores, it is finding applications ranging from lead discovery and optimization to the tagging of biological systems such as proteins, nucleotides and whole organisms.[16]. For the Sulfonamides are of considerable medical importance as the sulfa drugs Although they have been supplanted to a wide extent by the antibiotics such as penicillin, terramycin and chloromycetin the sulfa drugs still have their medical uses and make up a considerable portion of the output of the pharmaceutical industry[17].

## 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. $^{1}$HNMR and $^{13}$CNMR spectra were recorded on Burker 500MHzistrument using DMSO-$d_6$ as solvent and TMS as internal reference. Thin layer chromatography (TLC) was carried out using Fertigfollenprecoated sheets type polygramsilg and the plates were developed with iodine vapor.

### *Synthesis of 2-mercpto-3-phenyl-4(3H)quinazolinone* (1) [18]

A mixture of anthranilic acid (4.114g, 0.03mol), phenylisothiocyanate (3.61ml, 0.03mol) and triethylamine (3ml) in (60ml) absolute ethanol was refluxed for (3 hrs.). The reaction mixture was cooled at room temperature, then, poured on ice-cold water, stirred and filtered. The precipitate was recrystallized from methanol to give crystals. Physical properties of compound (1) are listed in table-1.

***Synthesis of S-(α-Chloroaceto-2-yl)-3-phenyl-4(3H)quinazolinone* (2) [19]**

To a mixture of compound(1) (3g , 0.01mol) in (16ml) dimethylformamide (DMF). was added slowly anhydrous potassium hydroxide (0.662g , 0.01mol) dissolve in (9ml) of methanol and was added slowly to the mixture chloro acetyl chloride (1ml, 0.01mol) and leaves the mixture refluxed for (4 hrs.).After time refluxed expiration leaves the mixture stirring overnight,then the reaction mixture was poured in to ice water, the separated precipitate was filtered and recrystallized from ethanol to give a dusty crystals, physical properties and FTIR spectral data are listed in table-1.

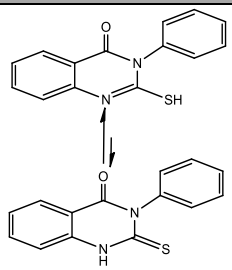
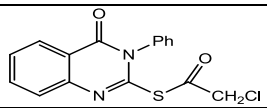
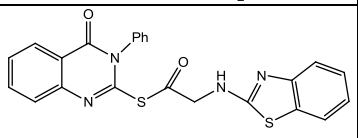
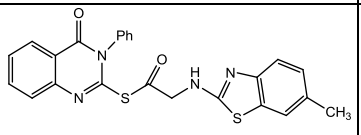
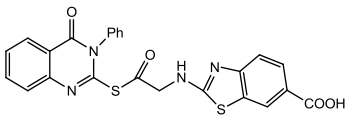
***Synthesis of S-(2-aminoacetyl substituted benzothiazole-2-yl)-3-phenyl-4(3H)quinazolinone* (3-9) [19]**

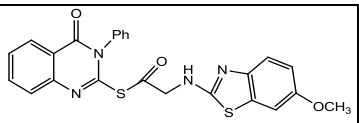
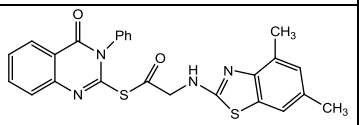
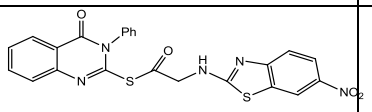
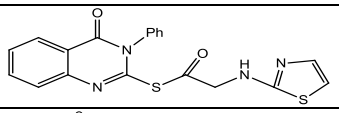
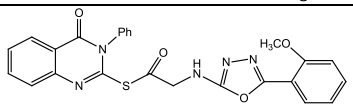
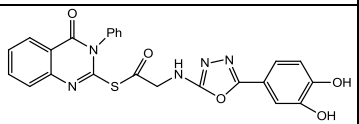
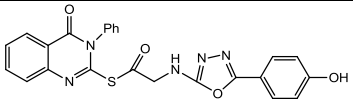
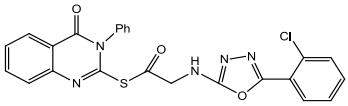
A mixture of compound (2) (1g, 0.003mol) in absolute ethanol (20 ml) and potassium carbonate anhydrous (0.41 g, 0.003mol) was refluxed and added dropwise to a solution of (0.003mol) of substited-2-aminobenzothiazole dissolved in (20 ml) of absolute ethanol, the reaction mixture was refluxed for (9-10) hrs. after cooling the separated precipitate was filtered and recrystalization from a suitable solvent. physical properties and FTIR spectral data are listed in table-1.

***Synthesisof.S-(2-aminoacetyl-5-substituted-1,3,4-oxadiazoles-2-yl)-3-phenyl-4(3H)quinazolinone* (10-13) [19]**

A mixture of compound (2) (1g, 0.003mol) in absolute ethanol (20 ml.) and potassium carbonate anhydrous (0.41g, 0.003mol) was refluxed and added dropwise to a solution of (0.003mol) of 2-amino-5-substituted-1,3,4-oxadiazole (the prepared of 2-amino-5-substituted-1,3,4-oxadiazole have synthesized as that reported in reference [15] dissolved in (20 ml.) abs.ethanol, the mixture was refluxed for (5-7)hrs. The resulted mixture was cooled to room temperature before pouring into crushed ice. The obtained precipitate was filterd, washed through by with water and dried then was purified by recrystallization from a suitable solvent. 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 (1-13)

| Com.No. | Physical Properties | | | | Major FTIR Absorption $cm^{-1}$ | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Structures | M. P. C° | Yield % | Color | ν(N-H) | ν(C-H) aliph. | ν(C=O) | ν(C=C) arom. | ν(C=N) | Others |
| 1 |  | 297-299 | 89 | Off white | 3245 | - | 1662 | 1600 1533 1487 | 1622 | ν(C-H)arom. 3028 3064 |
| 2 |  | 158-160 | 96 | White | - | 2910 | 1735 keton 1681 Amid | 1575 1550 1490 | 1662 | ν (C-Cl) 644 |
| 3 |  | 188-190 | 83 | Off White | 3394 | 2918 | 1730 keton 1662 Amid | 1560 1535 1488 | 1622 | δ (N-H) 1601 |
| 4 |  | 167-170 | 85 | Off White | 3394 | 2920 | 1731 Keton 1662 Amid | 1550 1533 1487 | 1622 | |
| 5 |  | 269-270 | 75 | Dark Grey | 3308 | 2914 | 1730 Keton 1662 Amid | 1591 1527 1488 | 1622 | ν  1719 ν  3406-3298 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **6** |  | 260-262 | 72 | Pale grey | 3410 | 2925 2993 | 1729 Keton 1662 Amid | 1550 1533 1487 | 1622 | νC-O-C.1226 |
| **7** |  | 150-152 | 65 | Pale pink | 3418 | 2920 | 1735 Keton 1683 Amid | 1550 1531 1488 | 1622 | |
| **8** |  | 235-237 | 71 | Pale yellow | 3369 | 2979 | 1735 Keton 1681 Amid | 1550 1529 1490 | 1623 | $\nu NO_2$ Asym.1525 Sym.1330 |
| **9** |  | 238-240 | 70 | Off White | 3244 | 2920 | 1735 keton 1683 Amid | 1606 1577 1548 | 1620 | ν(C-S).618 |
| **10** |  | 179-180 | 75 | Off White | 3245 | 2925 | 1739 Keton 1679 Amid | 1552 1531 1488 | 1662 | νC-O-C.1197 o-Position.759 |
| **11** |  | 239-240 | 84 | Deep brown | 3372 | 2923 | 1728 Keton 1691 Amid | 1591 1554 1535 | 1612 | νC-O-C.1155 νO-H.3430 |
| **12** |  | 109-110 | 80 | brown | 3357 | 2923 | 1720 Keton 1685 Amid | 1591 1569 | 1612 | νC-O-C1147 νO-H3418 p-Position842 |
| **13** |  | 241-242 | 81 | Off White | 3298 | 2923 | 1719 Keton 1683 Amid | 1558 1573 | 1656 | νC-O-C1263 o-Position740 ν(C-Cl)1043 |

**Synthesis of S-(P-amino acetyl-phenylene amine-2-yl)-3-phenyl-4(3H)quinazolinone (14) [19]**

A mixture of compound (2) (1g, 0.003mol) in absolute ethanol (15 ml.) and potassium carbonate anhydrous (0.41g, 0.003mol) was refluxed and added dropwise to a solution of (0.3g, 0.003mol) of p-phynelendiamine dissolved in (10 ml.) abs.ethanol, the mixture was refluxed for (6-8)hrs. The resulted mixture was cooled to room temperature before pouring into crushed ice. The obtained precipitate was filterd, washed through by with water and dried then was purified by recrystallization from a suitable solvent. Physical properties and FTIR spectral data are listed in table-2.

**Synthesis of S-(P-aminoacetyl-phenylenediazoniumsalt-2-yl)-3-phenyl-4(3H)quinazolinone (15) [20]**

A solution of compound (14) (0.82g, 0.002mol) in concentration HCL (1.5 ml) was cooled to (0-5)$c^0$. A Cooled solution of sodium nitrite (0.14g, 0.002mol) in (5ml) of water was added dropwise during 10min., and then the reaction mixture was stirred for 30min, Physical properties and FTIR spectral data are listed in table-2.

**Synthesis of S-(P-aminoacetyl-phenylene azido-2-yl)-3-phenyl-4(3H)quinazolinone(16) [20]**

(1.5 ml) of an aqueous solution of sodium azid (0.39g, 0.006mol) was added dropwise to an aqueous solution of diazonium salt (15). The mixture was stirred for 20 minutes to give an oily compound (16). Physical properties are listed in table-2.

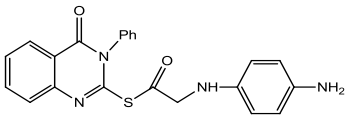
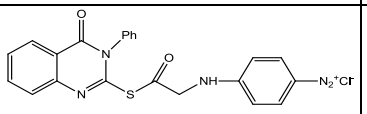
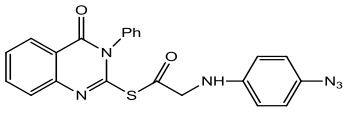
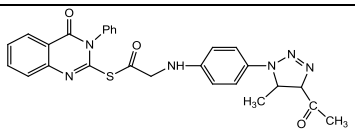
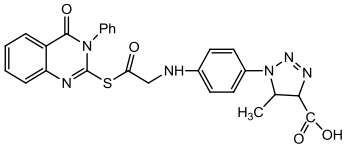
**Synthesis of S-[P-aminoacetyl-phenylene (4-acetyl-5-methyl-1H-1,2,3-triazole)-2-yl]-3-phenyl-4(3H)quinazolinone (17) [20]**

To a cold solution of sodium ethoxide (3ml.) and acetyl acetone (0.116g, 0.001mol), compound (16) (0.5g, 0.001mol) was cautiously added and the mixture was heated under reflux for (3hrs.). The resulting solid was separated and recrystallization from dry ether. Physical properties of dry product and FTIR spectral data are listed in table-2.

**Synthesis of S-[P-aminoacetyl-phenylene(4-carboxylic acid-5-methyl-1H-1,2,3-triazole)-2-yl]-3-phenyl-4(3H)quinazolinone (18) [20]**

A mixture of compound(16) (0.5g, 0.001mol) and ethyl acetoacetate (0.152g, 0,001mol) in methanol (5ml.) was cooled to 0 c. Sodium methoxide (0.001mol) in (3ml) was added gradually to the mixture and heated under reflux for (6hrs.). The crude product was recrystallization 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 (14-18)

| Com No. | Physical Properties | | | | Major FTIR Absorption $cm^{-1}$ | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Structures | M. P. C° | Yield % | Color | ν(N-H) | ν(C-H) aliph. | ν(C=O) | ν(C=C) arom. | ν(C=N) | Others |
| **14** |  | 102-105 | 75 | Deep brown | 3350 | 2929 | 1739 Keton 1691 Amid | 1575 1552 | 1666 | ν($NH_2$) 3425, 3460 δ1608 p-Position.ν 842 |
| **15** |  | oily | 70 | grey | - | - | - | - | | - |
| **16** |  | 233-235 | 82 | Deep grey | 3338 | 2972 | 1720 Keton 1664 Amid | 1575 1550 1531 | 1622 | ν(C-O).1197 νN=N-N 2123 p-Position ν840 |
| **17** |  | 142-144 | 60 | Off white | 3369 | 2850 2923 | 1735 Keton 1683 Amid | 1575 1550 | 1606 | ν(N=N).964 p-Position ν845 |
| **18** |  | 164-166 | 58 | White | 3344 | 285129 23 | 1735 Keton 1681 Amid | 1575 1544 | 1606 | ν  3462- 3330 ν(N=N).982 ν(C-O).1277 p-Position ν877 |

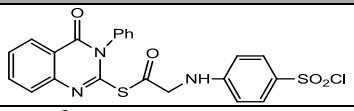
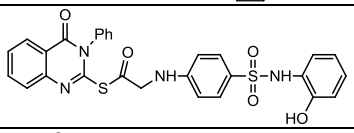
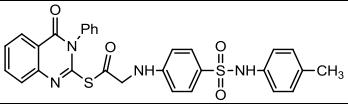
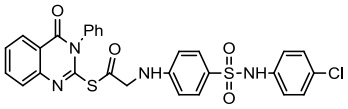
**Synthesis of S-(P-aminoacetyl-phenyleneSulfonylchloride-2-yl)-3-phenyl-4(3H)quinazolinone (19) [21]**

A mixture of compound (2) (1.5g, 0.004mol) in DMF (16 ml.) and triethylamin (0.459g, 0.004mol) was refluxed and added drop wise to a solution of (0.87g, 0.004mol) of 4-aminobenzenesulfonyl chloride dissolved in (10ml.) of DMF, the mixture was refluxed for (6-8)hrs. The resulted mixture was cooled to room temperature before pouring into crushed ice. The obtained precipitate was filterd, washed through by with water and dried then was purified by recrystallization from dry ether. Physical properties and FTIR spectral data are listed in table-3.

**Synthesis of S-(P-aminoacetyl-phenyleneSulfonyl substituted amine-2-yl)-3-phenyl-4(3H)quinazolinone (20-22) [22]**

(0.0015 mol) of substituted primary aromatic amine was dissolved in (3 ml) of dry pyridine then (0.5 g, 0.001 mol) of compound (19) was added in portions with stirring and keeping temperature below (40°C) The mixture was refluxed for three hours with continuous stirring then was cooled to room temperature. The mixture was poured into excess cold water with vigorous stirring; the obtained precipitate was filtered, washed several times with water and dried. The product was purified by recrystallization from a suitable solvent. Physical properties and FTIR spectral data are listed in table-3.

**Table 3 -** physical properties and FTIR spectral data $cm^{-1}$ of the prepared compounds (19-22)

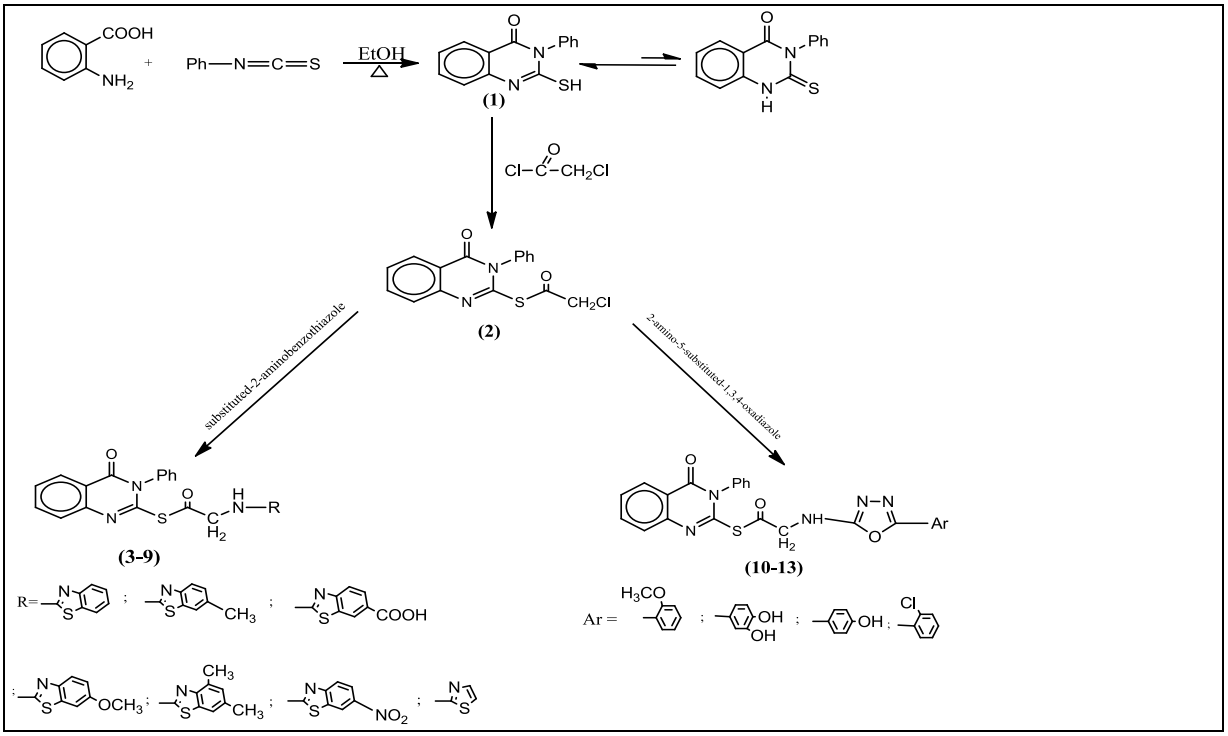
| Com. No. | Physical Properties | | | | Major FTIR Absorption $cm^{-1}$ | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Structures | M. P. C° | Yield% | Color | ν(N-H) | ν(C-H) aliph. | ν(C=O) | ν(C=C) arom. | ν(C=N) | Others |
| **19** |  | 138-140 | 87 | Deep grey | 3245 | 2920 | 1735 Keton 1683 Amid | 1577 1550 | 1610 | $\nu(SO_2)$ Sym.1143 Asym.1336 |
| **20** |  | 126-128 | 92 | Deep brown | 3245 | 2925 | 1720 Keton 1662 Amid | 1577 1535 | 1620 | $\nu(SO_2)$ Sym.1130 Asym.1330 ν (O-H) 3419 |
| **21** |  | 91-93 | 93 | Deep red | 3244 | 2852 2923 | 1718 Keton 1662 Amid | 1531 | 1608 | $\nu(SO_2)$ Sym.1157 Asym.1336 p-Position ν815 |
| **22** |  | 132-135 | 93 | brown | 3245 | 2929 | 1719 Keton 1662 Amid | 1531 | 1602 | νC-Cl 1091 $\nu(SO_2)$ Sym.1159 Asym.1338 p-Position ν825 |

**Anti-microbial activity test [23]**

The test was performed according to the disk diffusion method. Some of prepared compounds were tested against two strain gram +ve (*Staphylococcus aura* and *Bacilles*) and two strain gram –ve bacteria (*Escherichiacoli* and *pseudomanacruginosa*). Also they tested against one strain of yeast (*Candidan*). Whattman 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.

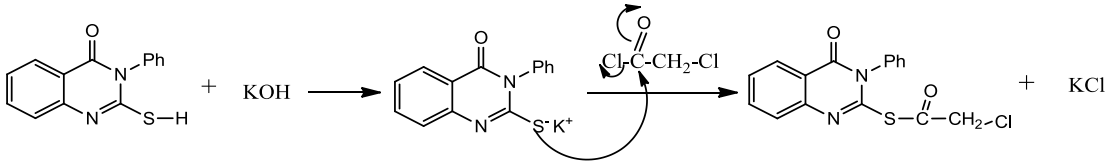
**Results and Discussion:**

The synthetic sequences for preparation of series new 2-mercapto-3-phenyl-4(3H) quinazolinone ,substituted-2-aminobenzothiazole and 5-substituted-2-amino-1,3,4-oxadiazole are out lined in the following scheme-1

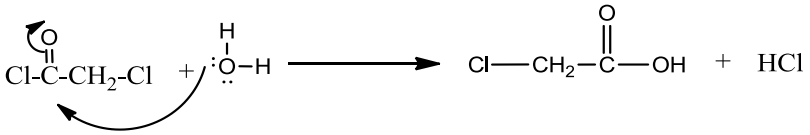



**Scheme (1):**preparation of new derivatives of 2-mercapto-3-phenyl-4(3H)-quinazolinone for compounds (1-13).

As starting material S-(α-chloroaceto -2-yl)-3-phenyl-4(3H) quinazolinone (2) was prepared by reaction compound (1) with chloro acetyl chloride in the presence solution of potassium hydroxide in dry DMF according to the following equation:

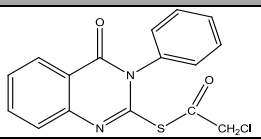
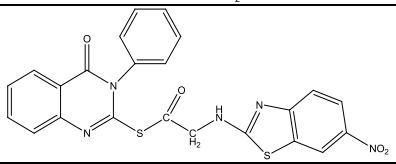
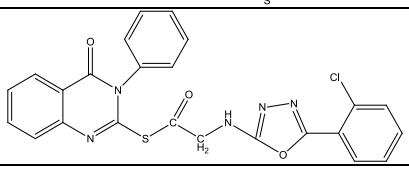



The reaction should be carried in dry condition due to that the existence of water caused to water to react with chloro acetyl chloride according to the following equation




The structure of compound (2) was confirmed by physical properties which are listed in table (1).FTIR spectra showing the absorption at ν $cm^{-1}$ 2910 for C-H aliph., 1735 for C=O (keton) ;1681 for C=O (amid) and 644 for C-Cl.$^{1}$HNMR spectrum showed singlet signal at δ= (4.49) ppm due to (-$\underline{CH_2}$-Cl) protons. and signals at δ= (7.15-8.10) ppm due to aromatic rings protons as listed in table-4 and shown in figure-1.$^{13}$CNMR spectrum data of compound (2) were listed in table-5, and shown in figure-2.

**Table 4-** $^{1}$H-NMR spectral data (δ ppm) for selected compounds

| Comp. No. | **Structures** | **$^{1}$HNMR Spectral data($^{\delta}$ppm)** |
|---|---|---|
| **2** |  | 4.49(S,2H,O=C-C$\underline{H_2}$-Cl);7.15-8.10 (m,9H,Ar-H) |
| **8** |  | 4.17(S,2H,O=C-C$\underline{H_2}$); 4.0(S,1H,N-H);7.19-8.62 (m,12H,Ar-H) |
| **13** |  | 2.5(S,2H,O=C-$CH_2$); 3.5(S,1H,N-H);7.4-7.7(m,13H,Ar-H) |

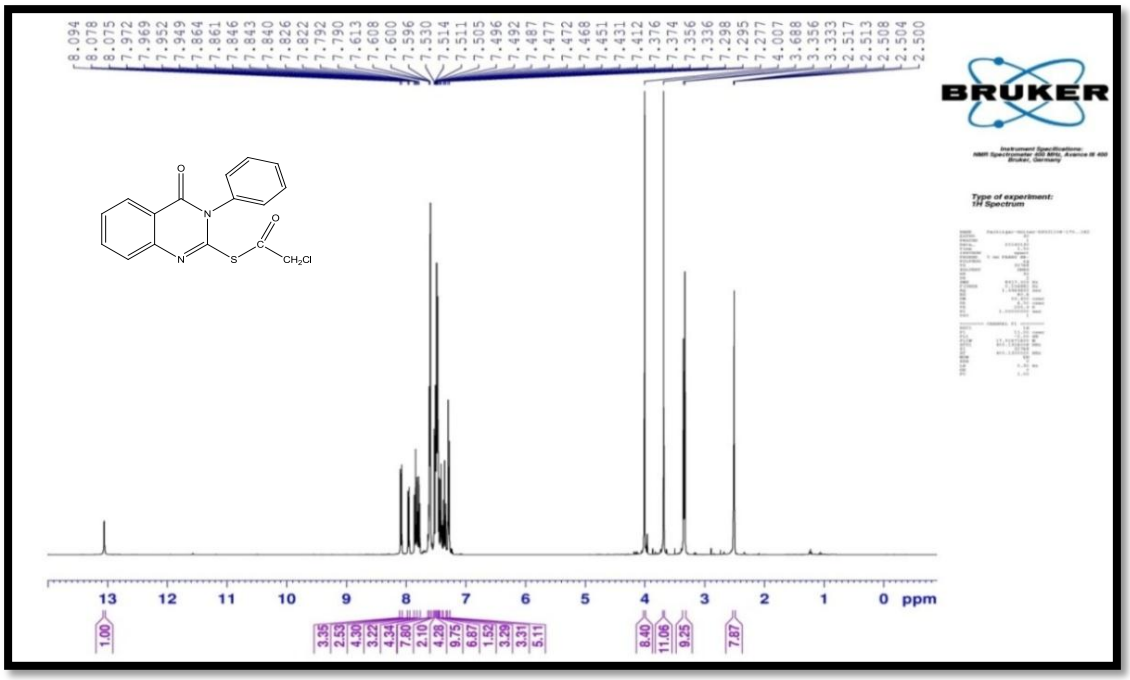
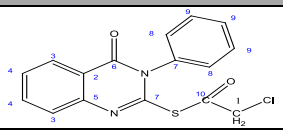
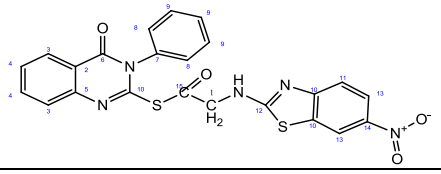
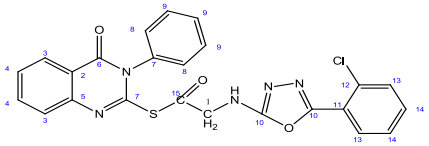



**Figure 1** -[1]HNMR spectrum of compound (2)

**Table 5**- [13]CNMR spectral data (δ ppm) for selected compounds

| Comp. No. | Compound structure | [13]CNMR spectral data (δ ppm) |
|---|---|---|
| **2** |  | 47.3(C1); 120.8-133.4 (C2,3,4,5,6,7,8,9); 188.9(C10). |
| **8** |  | 64.8(C1); 117.3-133.4 (C2,3,4,5,6,7,8,9,10,11,12); 144.3 (C13);146.9(C14); 196.5(C15). |
| **13** |  | 39.9(C1) ; 120.8-136.9 (C2,3,4,5,6,7,8,9,10,11,12); 146.9(C13) ; 159.3(C14); 196.5(C15) . |

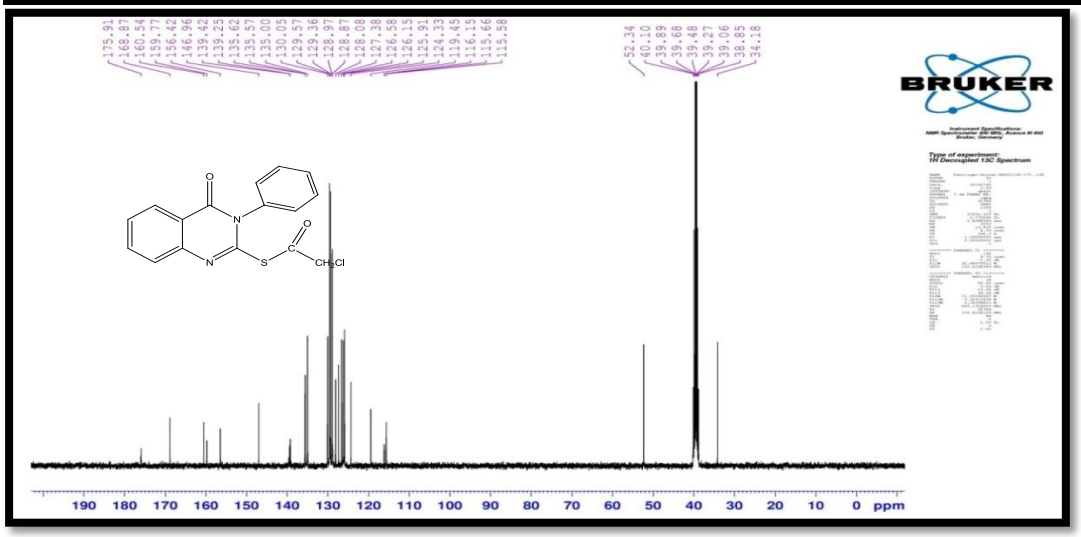



**Figure 2**-[13] CNMR spectrum of compound (2).

Also silver nitrate alcoholic test confirmed the presence of chlorine group [24].Reaction compound (2) by four different routes. The first route involved direct reaction with substituted-2-aminobenzothiazole under certain conditions to give new compounds (3-9). The second route involved reaction of 5-substituted-2-amino-1,3,4-oxadiazole in the presence of potassium carbonate anhydrous to give new compounds (10-13).These reaction are summarized in Scheme-1. The prepared compounds (3-13)were colored solids with sharp melting points and afforded in good yields. Structures of the prepared compounds (3-9) were confirmed by FTIR, $^{1}$ H NMR and $^{13}$ C-NMR spectroscopy [25]. FTIR spectra of compounds (3-9) showed clear absorption band at (3394-3244) $cm^{-1}$, (1730-1735) $cm^{-1}$, (1662-1683) $cm^{-1}$, (1622-1620) $cm^{-1}$, (1548-1606) $cm^{-1}$ due to ν –NH, ν C=O for keton, ν C=O for amid, νC=N,ν C=C arom. respectively in addition 3406-3298$cm^{-1}$ forν—C(=O)—OH group for compound (5). While disappearance the absorption of ν C-Cl group in compound (2). In the other hand$^{1}$HNMR spectra data of compound (8) δ ppm in DMSO-$d_6$ solvent showed singlet signal at δ= ( 4.17)ppm due to (-$CH_2$-C=O) protons, singlet signal at δ= (4.0)ppm due to (-NH) protons, signals at δ= (7.19-8.62) ppm due to aromatic rings protons. as listed in table-4 and shown in Figure-3. $^{13}$C-NMR spectrum data of this compound (8) were listed in table-5 and shown in figure-4.

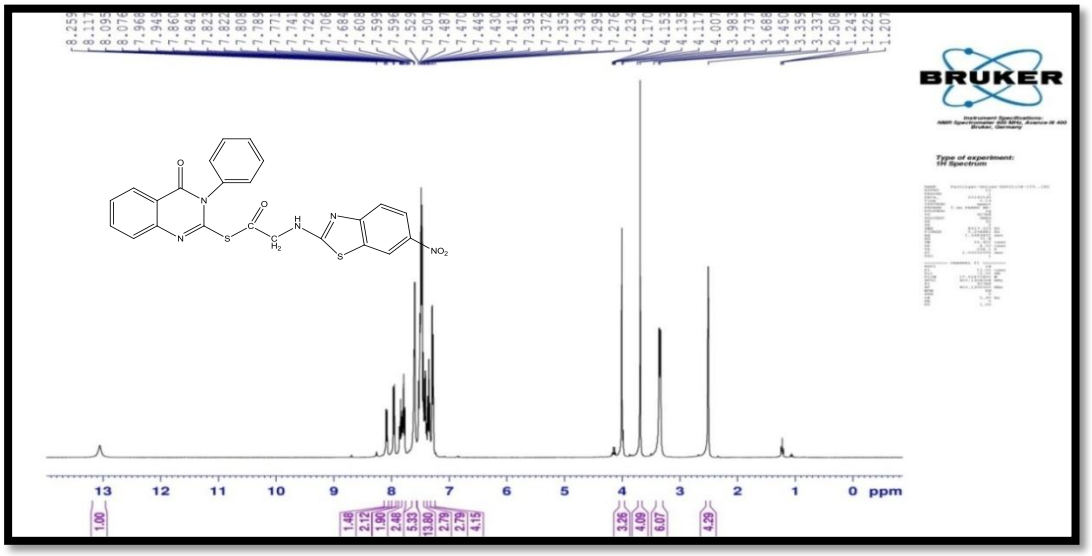



**Figure 3 -** $^{1}$HNMR spectrum of compound (8).

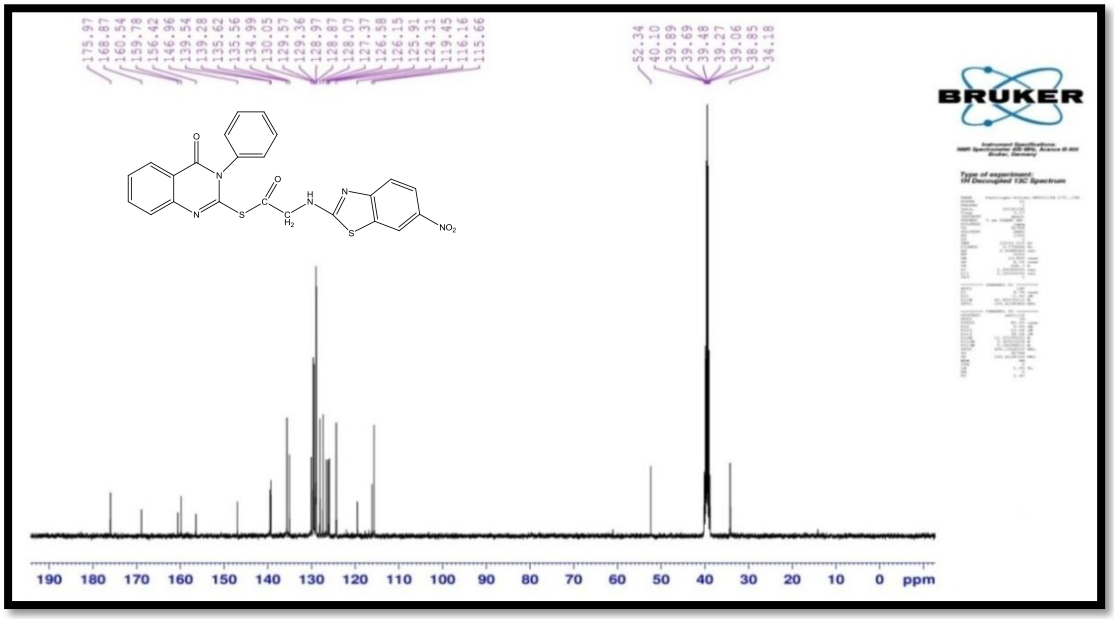



**Figure 4**-$^{13}$ CNMR spectrum of compound (8).

While FTIR spectra of compounds (10-13) show results listed in table-1. ν $cm^{-1}$ (3245-3438) for (N-H), (1739-1719) $cm^{-1}$ for (C=O) keton, (1679-1683) $cm^{-1}$ for (C=O) amid, (1662-1656) $cm^{-1}$ for (C=N), (1197-1263) $cm^{-1}$ for (C-O-C) ether in addition 3430 and 3418 $cm^{-1}$ for νO-H group for compounds (11) and (12) respectively ; 1043 $cm^{-1}$ for ν(C-Cl) group for compound (13). In the other hand $^1$HNMR spectra data of compound (13) δ ppm in DMSO-$d_6$ solvent showed singlet signal at δ= ( 2.5)ppm due to (-$CH_2$-C=O) protons, singlet signal at δ= (3.5)ppm due to (-NH) protons, signals at δ= (7.4-7.7) ppm due to aromatic rings protons. as listed in table-4 and shown in figure-5.$^{13}$C-NMR Spectral data of compound (13) are listed in table-5 and figure-6.

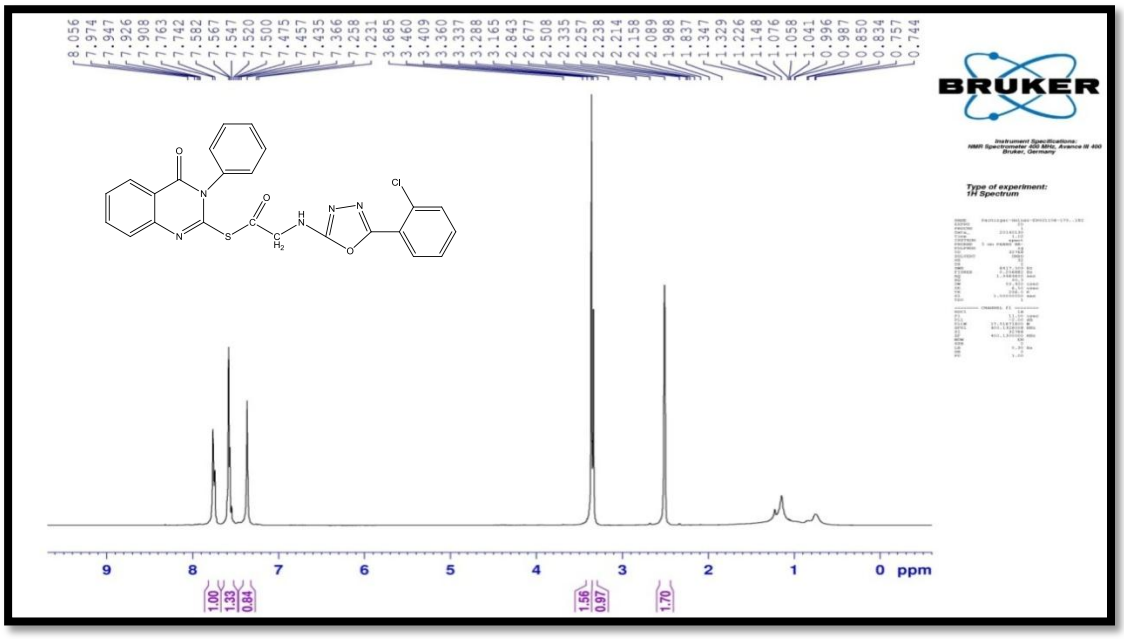



**Figure 5**- $^1$HNMR spectrum of compound (13).

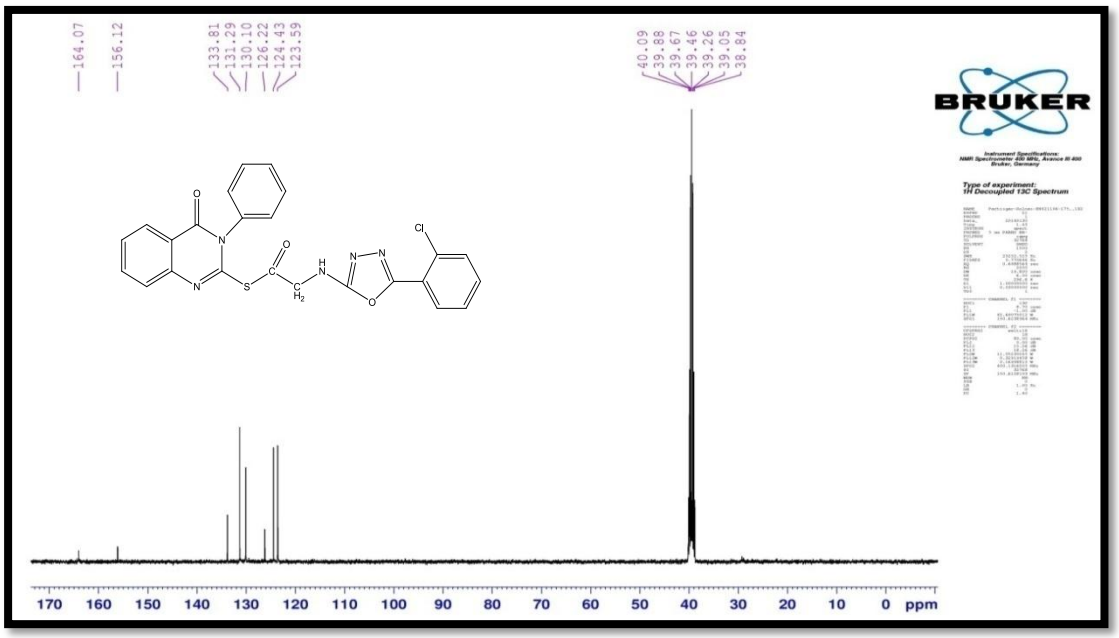
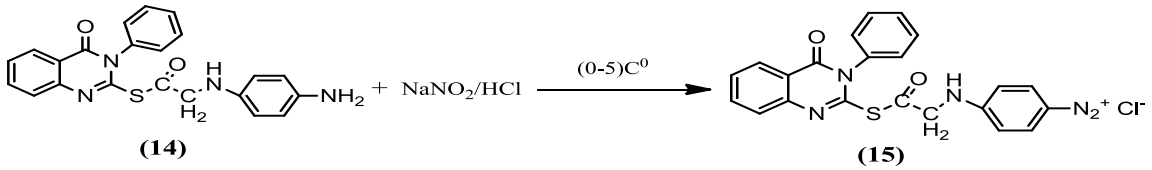
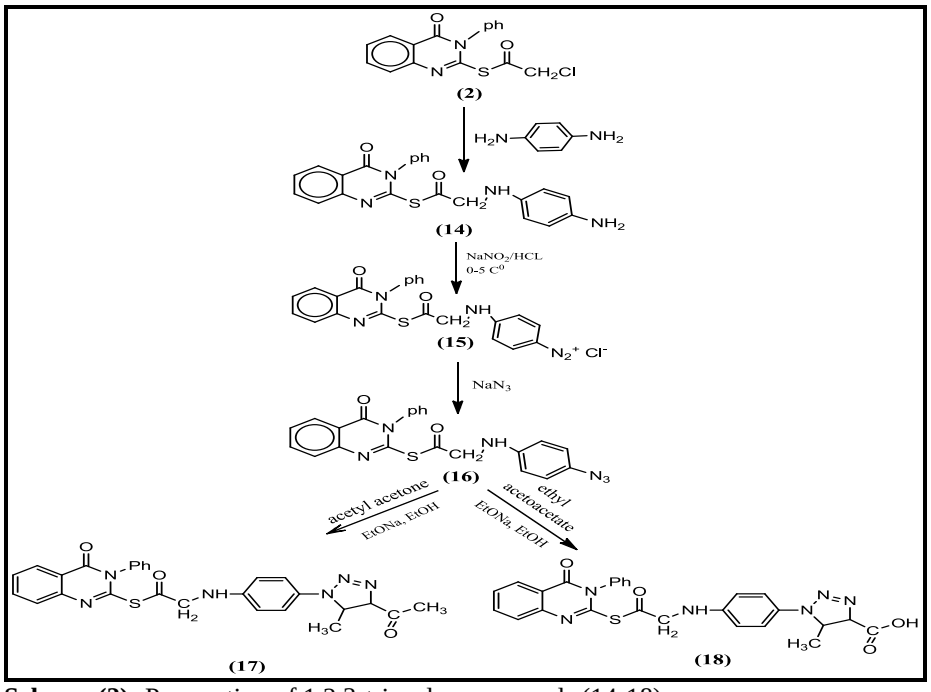



**Figure 6**- $^{13}$ CNMR spectrum of compound (13).

The third route involved synthesis of 1,2,3-triazoles compounds (17,18) by condensation compound (2) with para-phenylenediamine in ethanol as a solvent to give the corresponding compound (14). Which the diazotation of compound (14) to obtained diazonium chloride (15) according to the following equation [26].

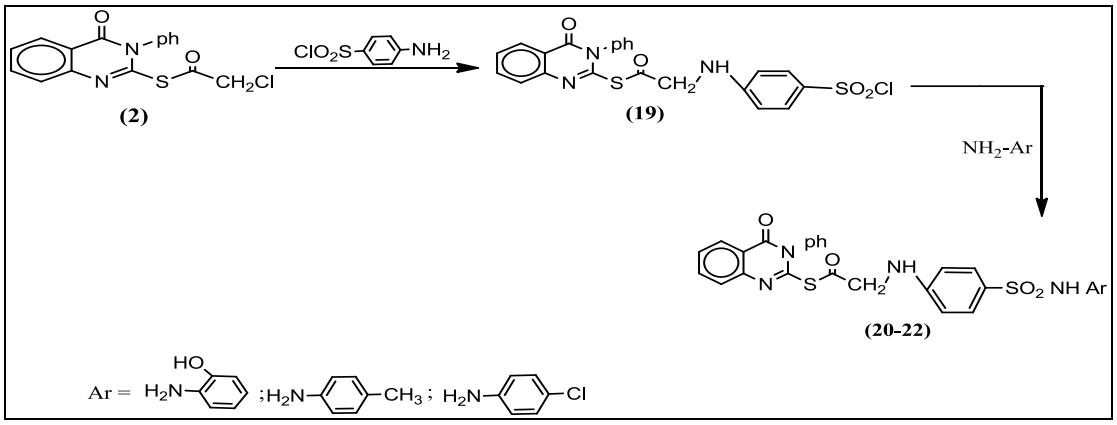



The 1,2,3-triazoles are very important organic compounds having wide spectrum of biological activities [27,28]. The reaction must be carried out in low temperature between (0-5)$C^0$ because the high temperature decomposition of diazonium salt (15), the obtained diazonium chloride (15) was treated with calculated amount of sodium azide to afford compound (16). The structure of compound (16) was confirmed by physical properties which are listed in table-2.FTIR spectra showing the absorption atν $cm^{-1}$ (2123 for N=N-N group). The azide (16) was converted to compounds (17) and (18) by the reaction with acetylacetone and ethylacetoacetate respectively. FTIR spectral showed the disappearance of the azid group ($N_3$) band in the starting material (16) at (2123 $cm^{-1}$) which is a good indication for successful condensation.The spectrum also shows absorption bands at (1735 $cm^{-1}$ for ν C=O keton; 1683 $cm^{-1}$ for ν C=O amid; 964 $cm^{-1}$ for νN=N) .for compound (17); (1735 $cm^{-1}$ for ν C=O keton; 1681 $cm^{-1}$ for ν C=O amid;982$cm^{-1}$ for νN=N in addition appearance 3462-3330 for ν —C(=O)—OH) for compound (18).Synthesis of these compound (14-18) can be summarized in Scheme (2).



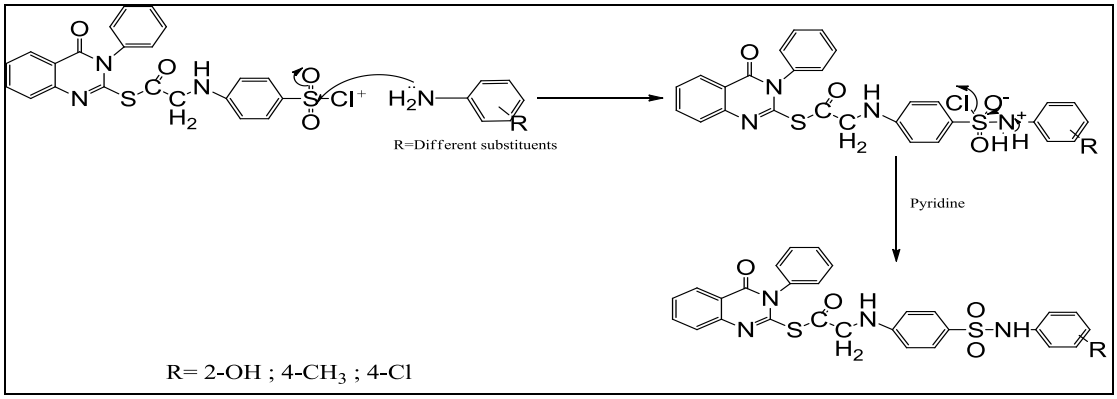

**Scheme (2):** Preparation of 1,2,3-triazole compounds (14-18).

The fourth route include reaction compound (2) with para-chlorosulphonyl aniline to give compound (19) which the conversion new sulphanilamide compounds (20-22) by the reaction of compound (19) with different substituted primary aromatic amin in dry pyridine to obtained of compounds (20,21,22).FTIR spectral showed absorption bands (1720 $cm^{-1}$ for ν C=O keton; 1662$cm^{-1}$ for ν C=O amid; 1130 $cm^{-1}$ forν $SO_2$sym; 1330 $cm^{-1}$ for ν $SO_2$asym; 757 $cm^{-1}$ for νo-Position) of compound (20). And (1718 $cm^{-1}$ for ν C=O keton, 1662 $cm^{-1}$ for ν C=O amid;1157 $cm^{-1}$ for ν $SO_2$sym, 1336 $cm^{-1}$ for ν $SO_2$asym; 815 $cm^{-1}$ for ν p-Position) of compound (21). And (1719 $cm^{-1}$ for ν C=O keton, 1662 $cm^{-1}$ for ν C=O amid, 1159 $cm^{-1}$ for ν $SO_2$sym, 1338 $cm^{-1}$ for ν $SO_2$asym; 825 $cm^{-1}$ for ν p-Position) of compound (22).Synthesis of these compound (19-22) can be summarized in Scheme-3.




**Scheme (3):** Preparation of sulphanilamid compounds (19-22).

Mechansim of the last part in this work involved nucleophilic attack of amino group in substituted primary aromatic amins on sulfur atom of compound (19) followed by elimination of HCl molecule, as indicated in Scheme-4.




**Scheme (4):**Mechanism of preparation of the compounds (20-22).

**Anti-microbial activity:**

The results of antimicrobial activity are listed in table-6. The results referred that all synthetic compounds possess moderate activity against certain types of bacteria and *Candidau*, while it did not possess any activity against others. Compound (13) possesses strong activity against *Staphylococcus aureus*, while compound (3) possess moderate activity against same bacteria. Compounds (9,18 and 22) possess moderate activity against *Bacilliessubtilus* while *Pseudomonas aeruginosa* was inhibited by compounds (2, 3,9,10,13 and17) .As far as compound (22) possesses good activity against*Candidau*.

**Table 6-** anti-microbial activity of Some the tested of prepared compounds

| Comp. No. | *Staphylococcus aureus* | *Bacilliessubtilus* | *Escherichia coli* | *Pseudomonas aeruginosa* | *Candidau* |
|---|---|---|---|---|---|
| **2** | 5 | - | - | 13 | - |
| **3** | 11 | 11 | - | 12 | - |
| **9** | - | 13 | - | 13 | 12 |
| **10** | 7 | - | - | 19 | - |
| **13** | 12 | - | - | 11 | 11 |
| **14** | - | - | - | - | 11 |
| **17** | - | - | - | 15 | 12 |
| **18** | 1 | 13 | - | - | 14 |
| **20** | - | 10 | - | - | 18 |
| **22** | - | 16 | - | - | 21 |

Solvent: DMSO; [C]: 800µg/ml

Zone of inhibition: (-) no inhibition zone, (3-6) weak, (7-10) moderate, (11-15) strong.

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