Synthesis and Characterization of New-2,3-Disubstituted Quinazolinone Derivatives as Antibacterial Agents

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Abstract

In this work, some new 2,3-disubsituted quinazolinone derivatives were synthesized. The reaction of substituted anthranilic acid with 3-chlorophenylisothiocyanate gave the compounds [3-(3-chlorophenyl)-2-mercaptoquinazoline-4(3H)-one] (1a,b). compounds (1a,b) where treated with chloroethylacetate in presence of potassium carbonate gave the compounds [-4-oxo-3, 4-dihydroquinazoline-2-yl)thio)acetate] (2a,b). Reaction with hydrazine hydrate afforded the acetohydrazides [-4-oxo-3,4-dihydroquinazoline-2-yl) thio) acetohydrazide](3a,b). The acetoohydrazides (3a,b) were treated with aromatic aldehydes to give the Schiff's bases [-N¯-(3-nitrobenzylidene)acetohydrazide] (5a,b). Treatment of derivatives (1a,b) with hydrazine hydrate afforded the hydrazine derivatives [-2-hydrazinylquinazoilne-4(3H)-one] (4a,b) which also used in synthesizing Schiff's bases [(E)(2-(3-nitrobenzyllidene)hydrazinyl)] (6a,b). Alkyl halide was treated with compounds (1a,b) in presence acetone to give of [-2-(methylthio)quinazoline-4(3H)-one] (7a,b), and with arylhalide in DMF gave the compounds [-2-((4-nitrophenyl)thio)quinazoline-4(3H)-one)] (8a,b). The structures of all prepared compounds have been elucidated using FTIR,[1] HNMR, and MASS spectroscopy. The antibacterial activity was evaluated for (1,5,6,7)a-b derivatives.

Keywords**:**2-mercaptoquinazoline-4(3H)-one, acetohydrazide, hydrazinyl, thioquinazolin, antibacterial activity.

Introduction

Quinazolinone is one of the leading and flourishing structures in medicinal chemistry [1]. Quinazolinone derivatives display a wide range of biological and pharmacological activities such as anticonvulsant, anti-inflammatory, antitumor, analgesic, anticancer, cytotoxic, anticoccidial, antibacterial and antifungal [2-5]. Quinazolinone is a frequently encountered unit in natural products such as L-vasicinone [6], chrysogine [7,8] and drugs as methaqualone [9]. A new series of 2-substitutedmercapto-quinazolin-4-one analogs was synthesized and screened. In the present study, the quinazolinone analogs were designed to contain a 2-substituted-thio functional group, this thioether moiety believed to bound to an electron-deficient carbon atom which identified as a possible pharmacophore of the antimicrobial activity [10]. On the other hand, hydrazides, hydrazones, or azomethines are of wide interest because of their diverse synthetic, biological, and clinical applications [11-12]. herein, We reported the synthesis of new hydrazone derivatives of S-linked substituted quinazolines with a number of substituted benzaldehyde in an attempt to obtain compounds with enhanced bioactivities [13].The new synthesized compounds were screened against gram-positive bacteria (*E.coli* and S.aureus) and gram-negative bacteria (K. pneumoniae, P.eruginose).

1. Experimental:

2. Materials and Methods

1. Melting point were recorded with Stuart melting point (Smp30) apparatus and were uncorrected.
2. Spectra date of (FT-IR) was recorded on Shimadzu FT-IR8400S spectrophotometer without KBr in chemistry department, college of Science, Mustansiriya University.
3. Mass spectra were recorded on a Shimadzu GC-MS Qp-2010 Ultra using (NCI-MS) mode negative chemical ionization in Chemistry Department, College of Science, Mustansiriya University.
4. [1]H-NMR spectra were recorded on a BRUKER (300.13) MHZ spectrometer in

DMSO-d6 as a solvent with TMS as an internal standard in Al-Albait university Jordan.

5. Thin layer Chromatography (TLC) was carried out by using alumina plates percoated with silica-gel, supplied by Merk. The compounds were detected with a 254-366nm UV Lamp.
6. The bacteria used were Escherichia coli, *Klebsiella pneumoniae, pseudomonas eruginosa* and *Staphylococcus aureus* in Chemistry department, college of Science, Mustansiriya University.

2.1-Synthesis of substituted 3-(3-chlorophenyl) -2-mercapto quinazolin-4(3H)-one (1a,b) [14]

A mixture of substituted anthranilic acid (0.04 mole) and 3-chlorophenylisothiocyanate (8.12 g, 0.04 mole) in ethanol (50 ml) was heated under reflux for 6 hr. The reaction mixture was cooled and solvent was evaporated under reduced pressure. The obtained residue was washed with petroleum ether, filtered, dried to give (1a, b).

2.2-Synthesis of compounds ethyl 2-((3-(3-chlorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl) thio) acetate and-6-hydroxy-4-oxo-3,4dihydroquinazolin-2-yl) thio) acetate (2a,b)[15].

To a solution of compounds (1a,b)(0.02 mole) and ethylchloroacetate (2.45 g, 0.02 mole) in (50 ml) absolute ethanol, fused K_2CO_3 (2.76 g, 0.02 mole) was added. The whole mixture was refluxed for 10 hr. The reaction mixture was filtered while hot and the filtrate was poured into ice cold water. The precipitated solid was filtered off, washed with water, dried and recrystallized from ethanol to give compounds (2a, b).

2.3-Synthesis of compounds 2-((3-(3-chlorophenyl)-4-oxo-3,4- dihydroquinazolin-2-yl) thio) acetohydrazide and 2 –hydrazinyl quinazolin -4(3H)-one (3-4) a,b [15].

A mixture of compounds (1-2) a,b (8 mmole) and hydrazin hydrate (80%) (0.6g, 1.2mmole) in (50ml) absolute ethanol was heated under reflux for 8 hr. The reaction mixture was cooled and solvent was evaporated under reduced pressure. The obtained residue was filtered, dried and recrystallized from ethyl acetate to give compounds (3-4) a,b.

2.4-Synthesis of compounds 2-((3-(3-chlorophenyl)-4-oxo-3,4-di hydro quinzolin-2-yl) thio)-N¯-(3-nitro benzylidene) aceto hydrazide (5a,b), (E) -3- (3-chlorophenyl) -2- (2- (3- nitro benzylidene) hydrazinyl) (6 a,b) [16].

A solution of hydrazide derivatives (3-4)a,b (2 mmole) in absolute ethanol (30 ml) and 3-nitrobenzaldehyde (0.3 g, 2 mmole) with (3 drops) of glacial acetic acid was refluxed for 8 hr. The reaction mixture was then cooled and solvent was evaporated under reduced pressure. The precipitate formed was poured into ice water, dried and recrystallized from ethanol to give compounds (5-6 a,b).

2.5-Synthesis of compounds 3-(3-(3-chlorophenyl)-2-(methyl thio) quinazoline (7a, b)[14].

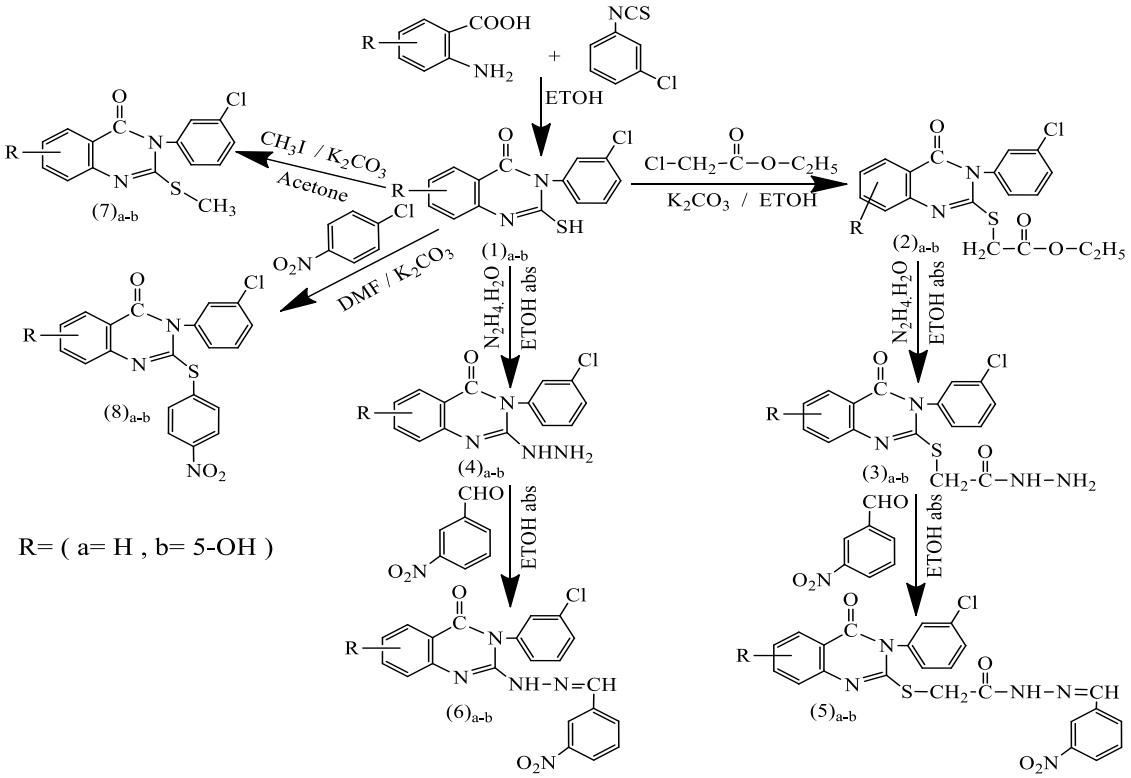
To a mixture of compounds (1a,b) (0.01mole) and anhydrous potassium carbonate (1.38 g, 0.01 mole) in dry acetone (50 ml), methyl iodide (1.42 g,0.01 mole) was added dropwise. The reaction mixture was stirred and heated under reflux for 10 hr, the reaction mixture was filtered while hot and filtrate was concentrated under reduced pressure. The obtained crude product was recrystallized from petroleum ether to give compounds (7a, b).

2.6-Synthesis of compounds 3-(3-chlorophenyl)-2-((4-nitrophenyl) thio) quinazoline (8a, b) [14].

A mixture of compound (1a-b) (0.01 mole), 1-chloro- 4- nitro benzene (1.58 g, 0.01 mole) and anhydrous potassium carbonate (1.38 g, 0.01 mole) in DMF (30 ml), was heated under reflux for 10 hr. The reaction mixture was filtered while hot and the filtrate was concentrated under reduced pressure. The obtained crude product was washed with cold water and recrystallized from ethanol to give compounds (8a, b).

Table (1)
The physical properties of compounds (1-8) a,b.

Comp. No.	*-R*	*M.F*	*M.wt*	*M.P/°C*	*Yield %*	*Colour*
1a	-H	$C_{14}H_9N_2OSCl$	288.5	302-304	83	White
1b	5-OH	$C_{14}H_9N_2O_2SCl$	304.5	290	73	White
2a	-H	$C_{18}H_{15}N_2O_3SCl$	374.5	136-139	67	White
2b	5-OH	$C_{18}H_{15}N_2O_4SCl$	390.5	161-163	64	White
3a	-H	$C_{16}H_{13}N_4O_2SCl$	360.5	228-230	60	Green
3b	5-OH	$C_{16}H_{13}N_4O_3SCl$	376.5	237	58	Green
4a	-H	$C_{14}H_{11}N_4OCl$	286.5	190-192	71	White
4b	5-OH	$C_{14}H_{11}N_4O_2Cl$	302.5	215-217	68	White
5a	-H	$C_{23}H_{16}N_5O_4SCl$	493.5	282	56	Yellow
5b	5-OH	$C_{23}H_{16}N_5O_5SCl$	509.5	295-297	52	Yellow
6a	-H	$C_{21}H_{14}N_5O_3Cl$	419.5	253-255	57	Green
6b	5-OH	$C_{21}H_{14}N_5O_4Cl$	435.5	273-276	54	Green
7a	-H	$C_{15}H_{11}N_2OSCl$	302.5	180-182	73	White
7b	5-OH	$C_{15}H_{11}N_2O_2SCl$	318.5	195-197	69	Yellow
8a	-H	$C_{20}H_{12}N_3O_3SCl$	409.5	158-161	72	Yellow
8b	5-OH	$C_{20}H_{12}N_3O_4SCl$	425.5	142	70	Yellow



Scheme (1)

Results and Discussion

In the reaction of substituted anthranilic acid with 3-chloro phenyl isothiocyanate in ethanol [14]. The structural assignment of the product was based on its melting points and spectral data (FT-IR, ^{1}H-NMR and MASS) [17,18]. The FT-IR spectrum of compounds (1a), Fig.(1) and (2a), Fig.(2) showed at (3271cm^{-1}) for(N-H) group band, at (2250-2450cm^{-1}) for (S-H) group band, at (1656-1681cm^{-1}) for(C=O) group band and at (1643-1649cm^{-1}) due to cyclic (C=N) stretching is also observed. ^{1}H-NMR spectrum of compound (1a), Fig.(3) shows the following characteristic chemical shifts in (DMSO-d$_6$) at 13.1ppm (s,1H, NH-SH), at 7.34-7.99 ppm (m,8H, Ar-H). Compound (1b), Fig.(4) shows at 12.92 ppm (s, 1H, NH-SH), at 9.95 ppm (s, 1H, OH), at 7.29-7.95 ppm (m, 7H, Ar-H). The MS spectrum of compound (1a), Fig.(5)

shows the molecular ion peak at M/Z = 288 and (1b), Fig.(6), the molecular ion peak at M/Z=304. The quinazolinones (1a-b) were converted to corresponding esters (2a- b) by treating with ethyl chloroacetate in ethanol using acatalytic amount of anhydrous potassium carbonate [15]. The FT-IR spectrum of compounds (2a,b), shows the disappearance of (NH-SH) absorption and appearance of ester carbonyl stretching band at(1735cm^{-1}), (C-H) aliphatic stretching band at (2929-2989cm^{-1}),(C-H)aliphatic bending band at (1363-1484cm^{-1}) and at (1232-1301cm^{-1}) belongs to asymmetric and symmetric (C-O-C) group. ^{1}H-NMR spectrum of compound (2a), Fig.(7) shows the appearance (t,3H,CH_2CH3) at 1.24 ppm, at 4 ppm(s,2H,S-CH_2), at 4.18 ppm (q,2H,OCH_2CH_3) and at 7.3-8ppm (s,8H,Ar-H). The FT-IR spectrum of compounds (3a,b) shows the appearance of primary (NH_2), along with a shoulder band at (3184-3321 cm^{-1}), secondary (N-H) band at (3105-3217 cm^{-1}), besides the disappearance of band at (1735cm^1) due to carbonyl group of ester and appearance of band at (1643-1651cm^{-1}) attributed for carbonyl group of hydrazide. ^{1}H-NMR spectrum of compound (3a), Fig.(8) shows the appearance of (s,1H, N-H) peak at 9.5 ppm , at 5.69 ppm (s,2H,NH_2), at 4.36 ppm(s,2H,S-CH_2) and at 7-8 ppm (m,8H,Ar-H). The FT-IR spectral of compounds (4a-b), show the appearance of primary (NH_2), along with a shoulder band at (3291-3342cm^{-1}), secondary (N-H) band at (3186-3219 cm^{-1}), besides the disappearance of band at (2250-2450 cm^{-1}) attributed to (S-H) group. ^{1}H-NMR spectrum of compound (4a) Fig.(9) shows the appearance of (s,2H,NH_2) at 5.71ppm, at 9.54ppm (s,1H,NH) and at 7.25-8 ppm (m,8H,Ar-H), compound (4b) Fig.(10) shows the appearance of (s,1H,NH) peak at 9.65ppm, at 9.35ppm (s,1H,OH), at 5.67 ppm (s,2H,NH_2) and at 7.14-8ppm (s,7H,Ar-H). The prepared compounds (5-6) a,b were synthesized by the reaction of compound (3-4) a,b and 3-nitrobenzaldehyde in ethanol in presence of acataylic amount of glacial acetic acid [16]. The FT-IR spectrum of compounds (5-6)a,b, shows the disappearance of (NH_2) stretching of hydrazine group and appearance of band for azomethine (C=N) group at (1608-1620 cm^{-1}). ^{1}H-NMR (DMSO-d6) spectrum of compound (6a), Fig.(11) shows the appearance of (s,1H,NH) peak at 10.85 ppm, at 8.75ppm (s,1H,N=CH) and at7.18-8.38 ppm (m,12H,Ar-H). The MS spectrum of compound (6b), Fig.(12) shows the molecular ion peak at M/z=433. The FT-IR spectrum of compounds (7-8) a,b, shows the appearance band at (1014-1066 cm^{-1}) for (C-S), (C-H) aliphatic band at (2972- 2985 cm^{-1}), besides the disappearance of band at (2250- 2450cm^{-1}) due to (S-H) group. ^{1}H-NMR (DMSO - d6) spectrum of compound (7a), Fig.(13) shows the appearance of (s,1H,S-CH_3) at 3.35 ppm, at 6.75-8 ppm (s,8H,Ar-H), compound (7b) Fig.(14) shows the appearance of (s,12H,Ar-H) at 7.45-8 ppm, compound (8b) Fig.(15) Shows the appearance of (s,1H,OH) at 10 ppm, at 7.26-8 ppm (s,12H,Ar-H). The MS spectrum of compound (7a) Fig.(16) illustrates M/Z=302, $[M+1]^+$ = 303 and $[M+ 29]^+$=333 due to using another ionization mode chemical ionization(CI). All the spectral data for other compounds are listed in Table (2).

Table (2)
FT-IR spectral data of compounds (1-8) a,b.

Comp No.	*υ(C-H) aromatic cm^{-1}*	*υ(C=C) aromatic cm^{-1}*	*υ(C=O) quinazoline cm^{-1}*	*υ(C=N) endo cm^{-1}*	*υ(C-N) cm^{-1}*	*Other bands cm^{-1}*
1a	3095	1616	1681	1643	1087	υ (N-H) 3271 υ(C-S)1016 υ(C-Cl)758 υ (C-SH) 2250
1b	3047	1602	1656	1649	1082	υ(C-OH) 3244 υ(C-O) 1234 υ (C-S) 1018 υ (C-S) 1018 υ(C-Cl) 732 υ (C-SH) 2450
2a	3095	1606	1695	1653	1091	υ(C-S)1016 υ (C=O) ester 1735 υ (C-O) 1301 υ (C-H) Aliphatic 2929 -2987 υ(C-Cl)797 υ (C-H) Bending 1375-1467
2b	3084	1616	1672	1654	1089	υ (C-OH)3419 υ (C=O) ester 1735υ (C-O) 1232 υ (C-Cl)736 υ (C-H) Bending 1363-1484 υ (C-H) Aliphatic 2929 -2987 υ (C-S)1020
3a	3093	1610	1678	1639	1093	υ(S-CH_2) 1475 υ(C-S) 1006 υ (C-Cl) 761 υ (C-H) Aliphatic 2955 υ (C=O) amide 1651 υ (NH_2) 3321-3296 υ (N-H) 3217
3b	3016	1587	1662	1608	1089	υ(C-OH) 3410 υ(S-CH_2) 1485 υ(C-O) 1217 υ(C-S) 1010 υ(C-Cl) 750 υ (C=O) amide 1643 υ (C-H) Aliphatic 2937 υ (NH_2) 3302 υ (N-H) 3105
4a	3093	1606	1678	1643	1093	υ(C-Cl)761 υ (N-H) 1573 bending υ (NH_2) 3291-3342 υ (N-H) 3219
4b	3051	1604	1664	1635	1085	υ(C-OH)3435 υ(C-O)1236 υ(C-Cl)748 υ (N-H) 1585 bending υ (NH_2) 3273-3302 υ (N-H) 3186
Comp No.	*υ(N-H) cm^{-1}*	*υ(C=O) quinazolin cm^{-1}*	*υ(C=O) amide cm^{-1}*	*υ(C=N) exo cm^{-1}*	*υ(C=N) endo cm^{-1}*	*Other bonds cm^{-1}*
5a	3120	1675	1666	1620	1591	υ (C=C) 1563 υ(C-N)1097 υ(C-NO_2)1346-1543 υ(C-Cl) 748 υ(C-H)aromatic 3058 υ(C-H)aliphatic 2933
5b	3152	1670	1650	1617	1585	υ(C=C)1560 υ(C-N)1091 υ(C-Cl)756 υ(C-NO_2)1335-1548 υ(C-H)aromatic 3050 υ(C-H)aliphatic 2982 υ(C-OH)3417
6a	3129	1673	-	1610	1580	υ(C=C)1568 υ(C-N)1085 υ(C-NO_2)1340-1548 υ(C-Cl)765 υ(C-H)aromatic 3070 υ(C-H)aliphatic 2923
6b	3172	1680	-	1608	1587	υ(C=C)1561 υ(C-N)1120 υ(C-NO_2)1356-1534 υ(C-Cl) 771 υ(C-H)aromatic3030 υ(C-H)aliphatic 2912 υ(C-OH)3395
Comp No.	*υ(C-H) aromatic cm^{-1}*	*υ(C=O) quinazolin cm^{-1}*	*υ(C=N) endo cm^{-1}*	*υ(C-S) cm^{-1}*	*υ(C-N) cm^{-1}*	*Other bands cm^{-1}*
7a	3088	1680	1643	1014	1089	υ(C-H)aliphatic 2985 υ(C=C)aromatic 1604 υ(S-CH_3)bending 1429 , υ(C-Cl)767
7b	3078	1681	1664	1018	1095	υ(C-OH)3217 υ(C-O)1243 υ(C-H)aliphatic 2972 υ(C=C)aromatic 1637 υ(S-CH_3)bending 1454 υ(C-Cl)760
8a	3076	1685	1640	1066	1112	υ(C=C)aromatic1579 υ(C-NO_2)1381-1525 υ(C-Cl)748
8b	3092	1687	1651	1027	1098	υ(C-OH)3224 υ(C-O)1248 υ(C-Cl) 757 υ(C=C)aromatic 1618 υ(C-NO_2)1383-1527

Microbiological Method

The synthesized compounds (1,5,6,7) a-b were screened in vitro for antimicrobial activity. The antibacterial test was performed according to the disc diffusion method [19]. The prepared agar and petridishes were sterilized by autoclaving for (15 min) at 121^{o}C, the agar plates were surface inoculated uniformly from the broth culture of the test microorganisms. In the solidified medium suitably spaced apart holes were made all (6 mm) in diameter. These holes were filled with (100 µg /ml) of the prepared compounds (1 mg of the compound dissolved in 1ml of DMSO solvent). These plates were incubated at 37 ^{o}C for (24 hr). The inhibition zone caused by the various compounds were examined [20]. The results of the preliminary screening tests are listed in Table (3).

Table (3)
Antibacterial activities of some of the synthesized compounds (1,5,6,7)a-b.

Comp. No	*E .coli*	*K .pneumoniae*	*P. eruginosa*	*S .aureus*
1a	+ +	-	-	+
1b	+ ++	-	-	+ +
5a	+ + +	-	-	+
5b	+ + +	-	-	+ +
6a	+ +	-	-	++
6b	+ + +	-	-	+ +
7a	-	-	-	-
7b	+	-	-	+

Note: (-)=NO inhibition, (+)=6-9 mm weak activity, (++)=10-14 mm moderate activity, (+++)=15-24 mm remarkable activity.

Conclusion

The screening results indicate that compounds (1b,5a,5b, and 6b) showed the remarkable activity against *E-coli*, compounds (1a,6a) showed moderate activity on this bacteria, compound (7b) weak activity and compound (7a) no inhibition against *E .coli*. Compounds (1a,5a and 7b) weak activity against *S.aureus* and compound (7a) showed no inhibition against *S. aureus*. This means that (1,5,6,7) a-b are inactive against *K. pneumoniae* and *P.aeruginosa*.

Conclusion

In conclusion, we describe procedure for the 2, 3-disusituted quinazoline derivatives were synthesized via reaction anthranilic acid derivatives and 3-chlorophenylisothiocyanate with ethanol obtained quinazoline-4(3H) one and reacted of aromatic aldehyde, aryl halide, aryl alkyl. The synthesized compounds were characterized by FT-IR, ^{1}H-NMR, MASS and antibacterial screening for the some compounds.

Acknowledgments

The authors would like to express their special thanks to the staff members of the department of chemical, collage of science, Mustansiriya University, Baghdad, Iraq, for performing the FT-IR, mass spectrophotometer and antibacterial testing of the some synthesis compounds.

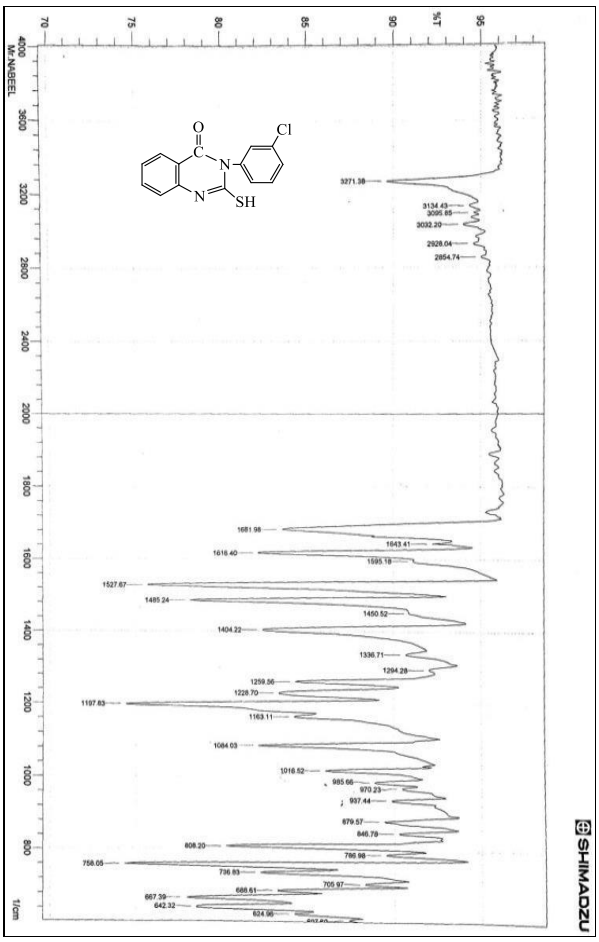


Fig.(1) FTIR spectum of compound (1a).

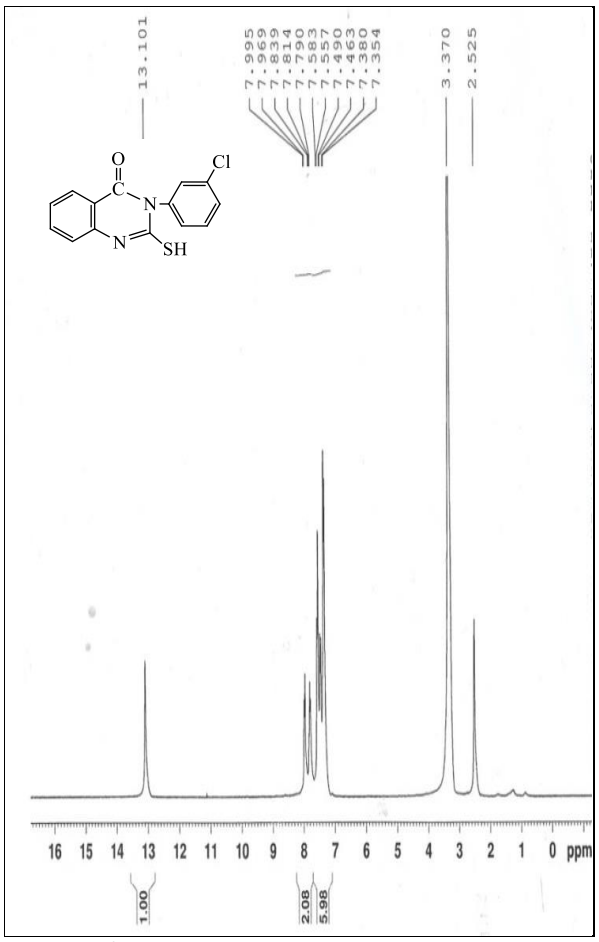


Fig.(3) ^{1}H-NMR spectum of compound (1a).

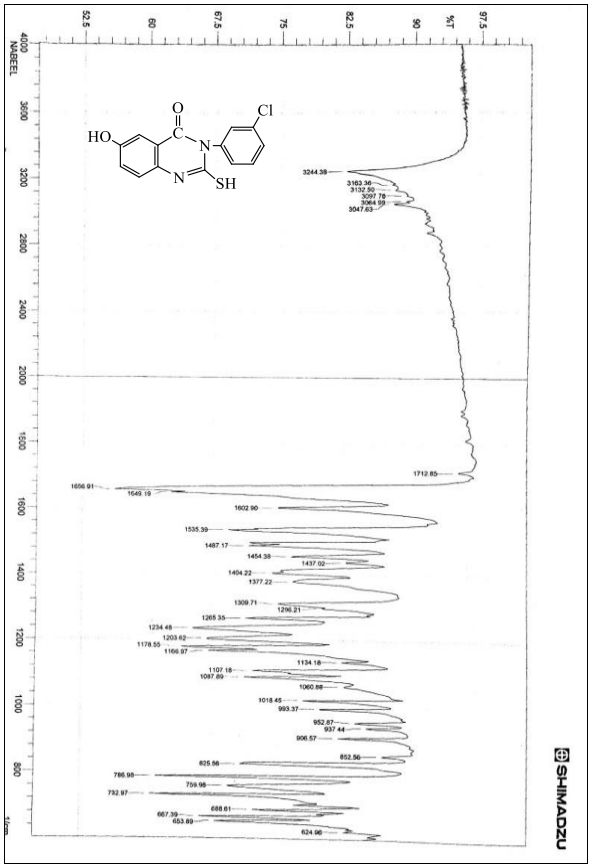


Fig.(2) FTIR spectrum of compound (1b).

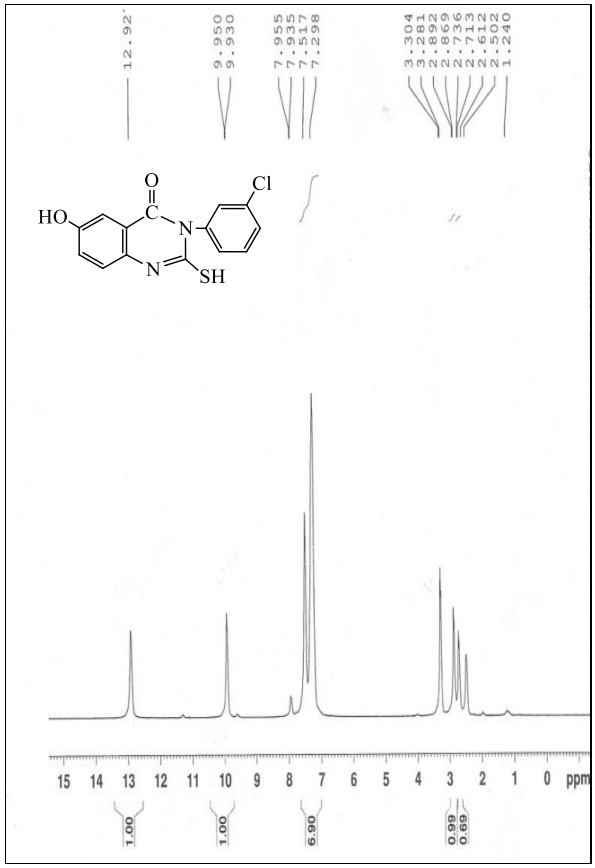


Fig.(4) ^{1}H-NMR spectrum of compound (1b).

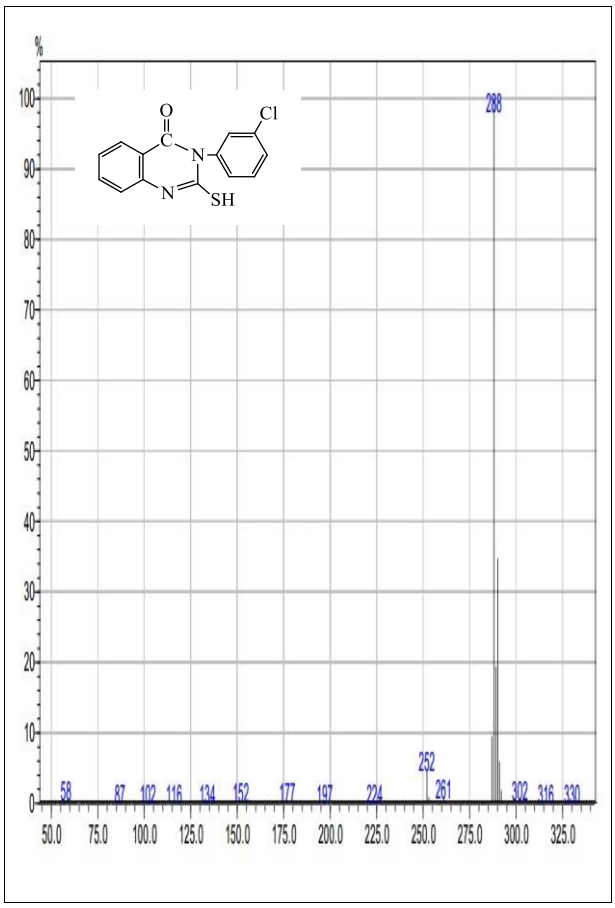


Fig.(5) MASS spectrum of compound (1a).

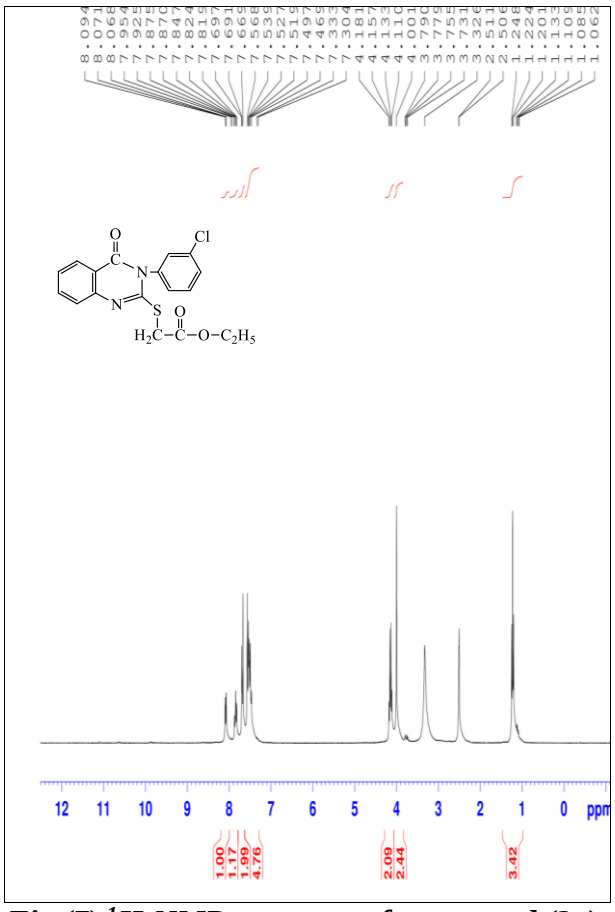


Fig.(7) ^{1}H-NMR spectrum of compound (2a).

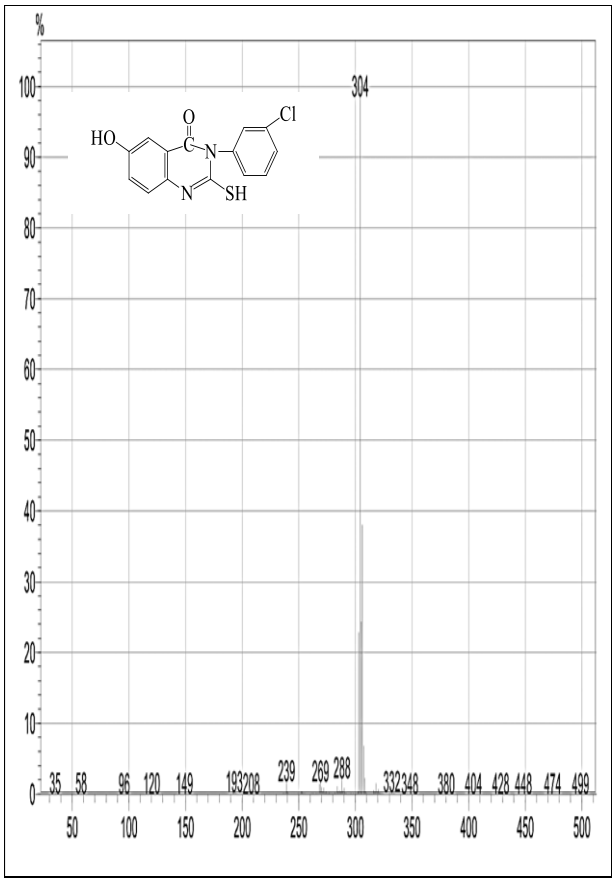


Fig.(6) MASS spectrum of compound (1b).

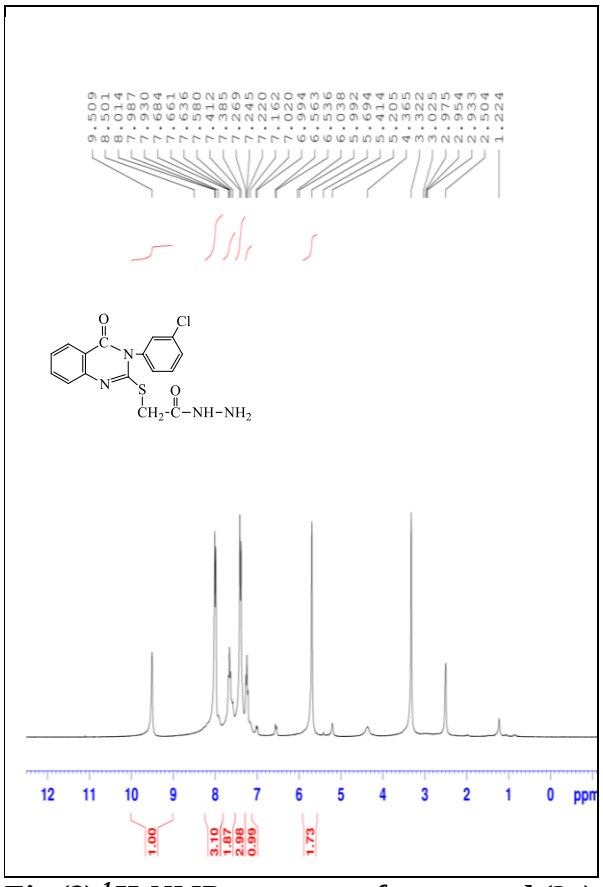


Fig.(8) ^{1}H-NMR spectrum of compound (3a).

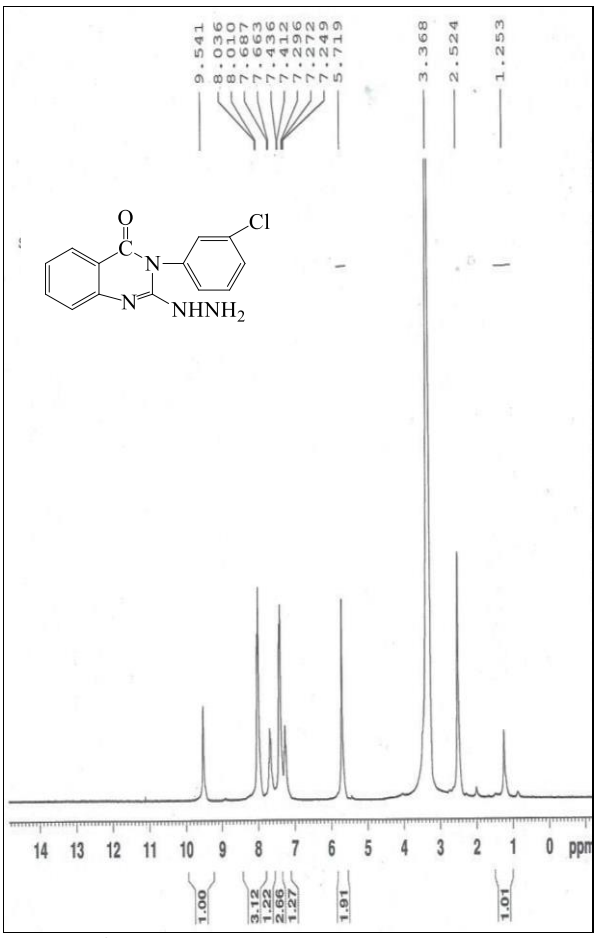


Fig.(9) ^{1}H-NMR spectrum of compound (4a).

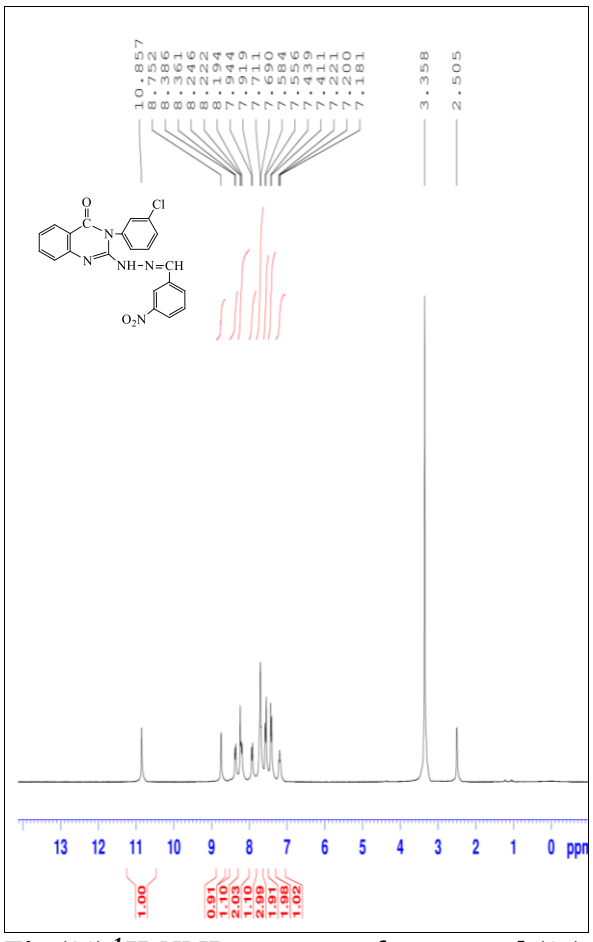


Fig.(11) ^{1}H-NMR spectrum of compound (6a).

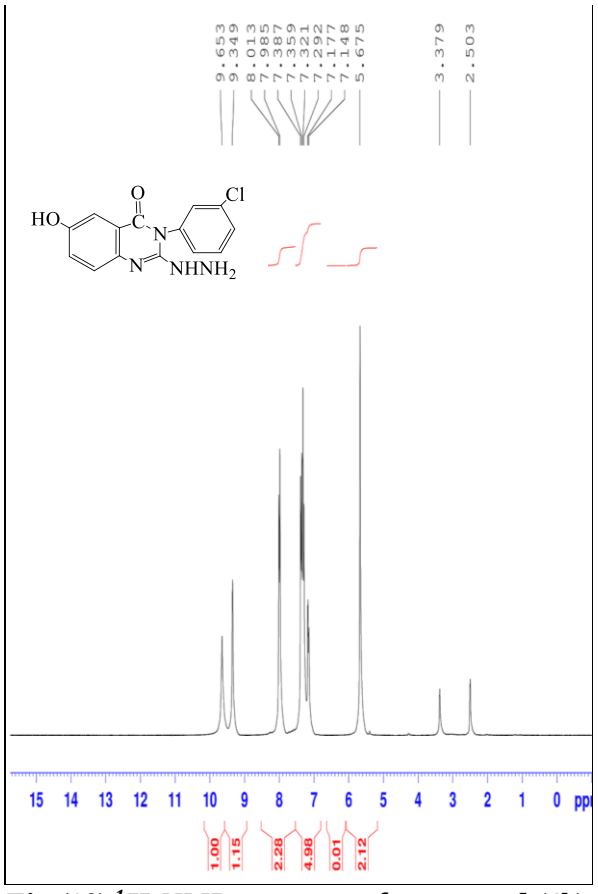


Fig.(10) ^{1}H-NMR spectrum of compound (4b).

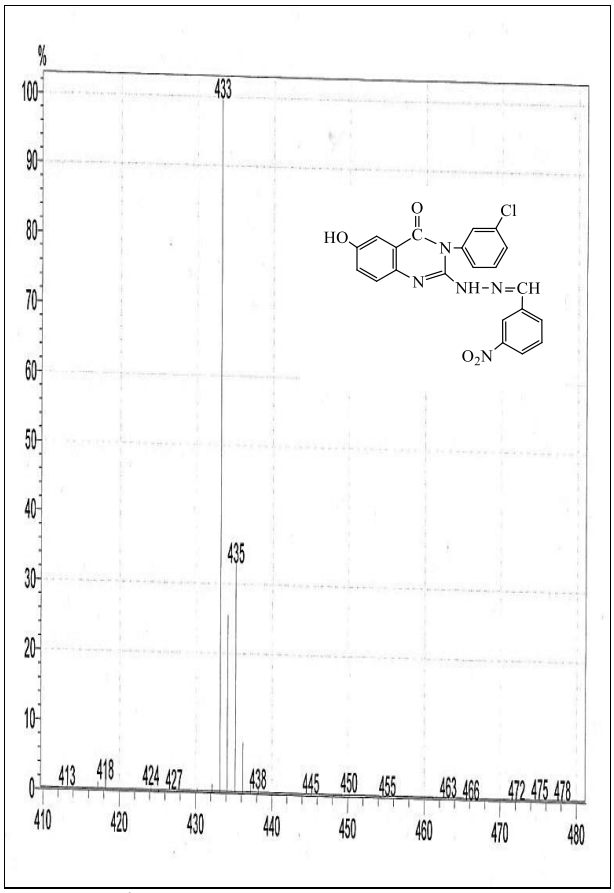


Fig.(12) ^{1}H-NMR spectrum of compound (6b).

Fig. (13) ^{1}H-NMR spectrum of compound (7a).

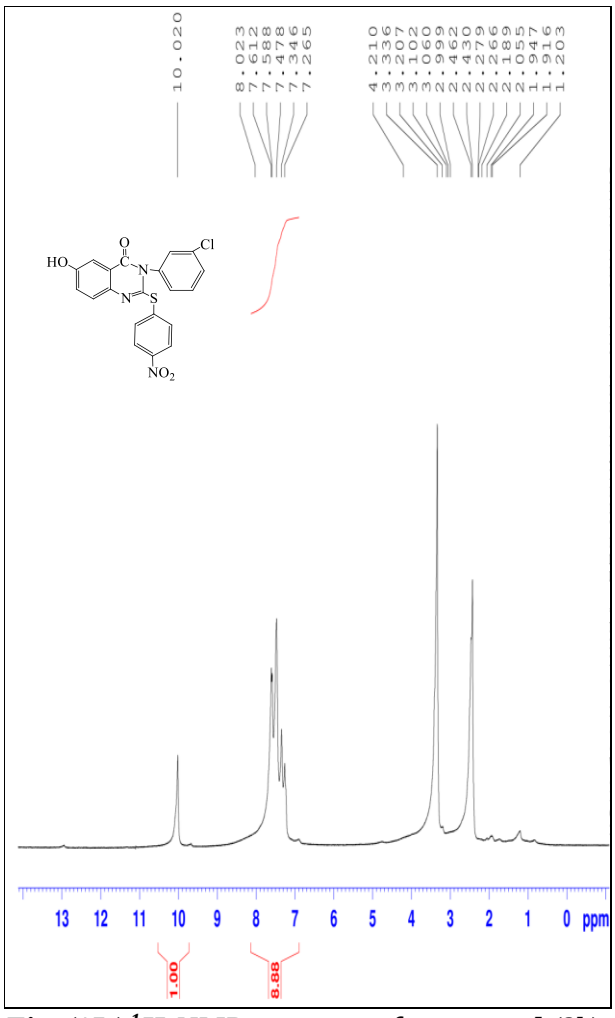


Fig. (15:) ^{1}H-NMR spectrum of compound (8b).

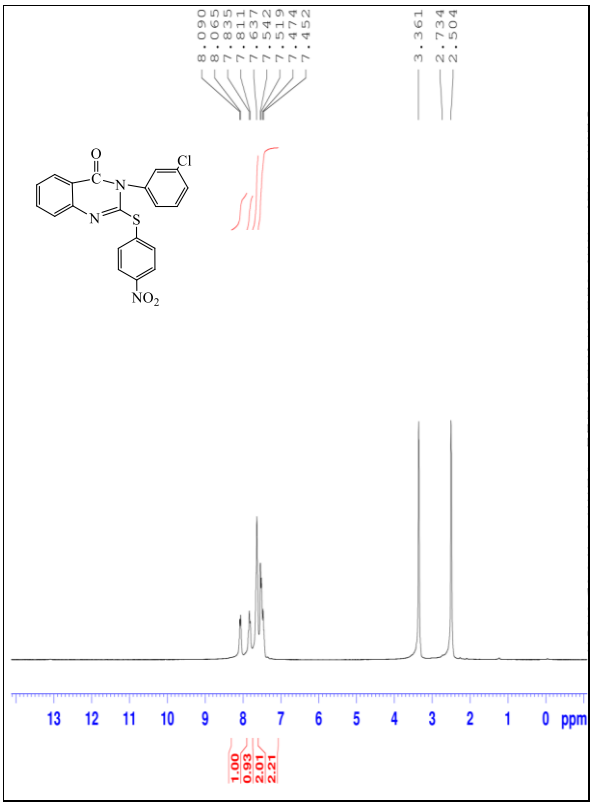


Fig.(14) ^{1}H-NMR spectrum of compound (7b).

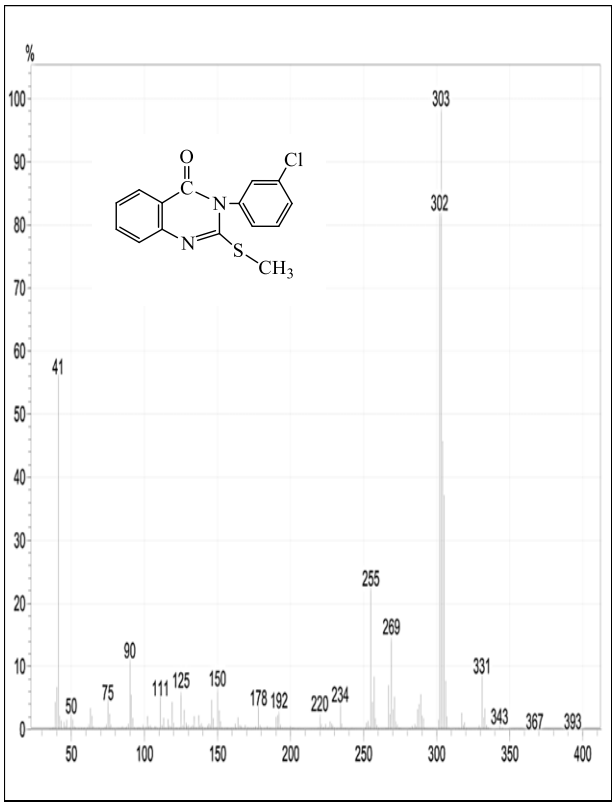


Fig. (16) MASS spectrum of compound (7a).

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الخلاصة

في هذا البحث تم تحضير بعض من مشتقات الكوينازولين ثنائية التعويض في -3,2- من تفاعل حامض الانثرانيليك مع ٣-كلوروفنيل ايزو ثايوسيانيت ليعطي المشتقات [٣-(٣-كلوروفنيل) -٢-مركبتوكوينازولين-٤-one (3H)] (1a,b). وعند تفاعل هذه المشتقات (1a,b) مع كلورو اثيل اسيتات بوجود كاربونات البوتاسيوم اعطت المركبات[٤-اوكسو-٤،٣-داي هيدروكسي كوينازولين -٢-يل) ثايو اسيتات (2a,b). أن تفاعل المشتقات (2a,b) مع الهيدرازين المائي اعطت مشتقات الاسيتوهيدرازايد (3a,b). عند تفاعل مشتقات الاسيتوهيدرازايد (3a,b) مع الالديهايدات الاروماتية اعطت قواعد شيف (5a,b). ان تفاعل المشتقان (1a,b) مع الهيدرازين المائي اعطيا مشتقات الهيدرازايد (4a,b) التي اعطى تفاعلها مع الالديهايدات الاروماتية مشتقات قواعد شيف (6a,b). عند تفاعل المشتقان (1a,b) مع هاليدات الالكيل في الاسيتون تكونت المشتقات (7a,b), اما عند تفاعلها مع الهاليدات الاروماتية في ثنائي مثيل الاميد فقد تكونت المشتقات (8a,b). لقد شخصت تراكيب المشتقات المحضرة من دراسة اطياف الاشعة تحت الحمراء و أطياف الرنين النووي المغناطيسي و أطياف الكتلة .وقد تم تقييم الفعالية ضد البكتريا للمركبات a-b (1,5,6,7).