

Synthesis and Biological evaluation of Some Nitrogen Containing Heterocycles

Nahed . F . Abdel-Ghaffar

Chemistry Department, Faculty of Science, Al-Azhar University (for girl's) Egypt
prof_nahed@yahoo.com

Abstract: A new series of quinazolin-4-one derivatives (**I-XVII**) has been synthesized and subjected to evaluate their antibacterial properties. The reactivity of these derivatives towards some nucleophilic and electrophilic reagents was investigated. Most of the synthesized compounds of the series displayed remarkable activity in comparison to standard drug. The structure – activity relationships and antimicrobial activity of the prepared compounds were also discussed.

[Nahed. F. Abdel-Ghaffar. **Synthesis and Biological evaluation of Some Nitrogen Containing Heterocycles.** Nature and Science 2011;9(7):190-201]. (ISSN: 1545-0740). <http://www.sciencepub.net>.

Keywords: Quinazolinone-4-ones, Synthesis, Antimicrobial activity

1. Introduction

Quinazolinone derivatives are known to possess a broad spectrum of biological activities and are used in pharmaceutical industry, in medicine and agriculture (Kaure, et al. 2009)⁽¹⁾

Quinazolinone derivatives have recently gained a growing interest owing to their reported biological activities. Among these activities, their uses as antioxidant agent (Al-Omar, et al. 2006)⁽²⁾, antihyperlipidemic (Fawzia, et al. 2005)⁽³⁾, antiviral (Murugesan, et al. 2003)⁽⁴⁾, antitumor (Al-Obaid, et al. 2009)⁽⁵⁾ analgesic, anti-inflammatory (Veerachamy, et al. 2002; Veerachamy, et al. 2003; Jessy, et al. 2008 ; Hamed, et al. 2010)⁽⁶⁻⁹⁾, anticonvulsant (El-Helby, et al. 2003; Shashikant, et al. 2008)^(10,11), antihypertensive, ardiotonic, antiulcerative (Kaur, et al. 2011)⁽¹²⁾ and anti-microbial (Ommeh, et al. 2004; Vivek, et al. 2008 ; Mosaad, et al. 2010; Chtrasal, et al. 2010; Reddy, et al. 2010; Adnan, et al. 2010; Patel, et al. 2010)⁽¹³⁻¹⁹⁾.

Moreover, several industrial uses were reported also for this class of compounds. Among their diverse uses, the extensive utility in the synthesis of dyes (Divyesh, et al. 2010)⁽²⁰⁾

The above mentioned biological activities together with the industrial importance of this class of compounds and our interest in this field stimulate us to synthesise several new quinazolinone derivatives and studying the antimicrobial activities of some compounds, also illustrate the mode of action of some derivatives.

2. Experimental

All melting points are not corrected. The infrared spectra were carried out on KBr disks on a pye Unicomp SP₃-200 spectrophotometer.

The ¹H NMR and ¹³C NMR spectra were measured on a Varian EM60 and JEOL-90 MHz spectrometers with TMS as internal reference, using DMSO-d₆ as solvent chemical shifts were expressed in ppm.

The mass spectra were determined on a FINNI-Gas 3300 mass spectrometer by direct Intel (Source temperature 90-300 °C, beam energy 70 eV)

Synthesis of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl) acetone (Ia), 2-amino-quinazolin-4(3H)one (Ib) and 2-amino 6-bromoquinazolin-4(3H)one (Ic): Formation of (Ia-c) .

A mixture of 5-bromo anthranilic acid or anthranilic acid (0.01 mol) and cyano acetamide and/or thiourea (0.01 mol) in 30 ml butanol and few drop of triethyl amine was refluxed for 6 hours, then allowing the mixture to cool, the solid product was collected by filtration and recrystallised from the proper solvent (c.f. table 1).

Reaction of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl) acetone (Ia) with acrylonitrile: Formation of 3-(6-bromo-2-cyanomethyl)-4-oxoquinazolin-3(4H)-yl propanenitrile (II).

A mixture of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl) acetone (Ia) (0.01 mol) and (0.01 mol) of acrylonitrile in 25 ml pyridine was heated under reflux for 2 hours, cooled then poured onto a mixture of ice and dilute hydrochloric acid. The separated solid was filtered off, washed well with water and recrystallised from the proper solvent (c.f. table 1).

Reaction of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl) acetone (Ia) with ethylchloroacetate: Formation of ethyl-2-(6-bromo-2-cyanomethyl)-4-oxoquinazolin-3(4H)-yl acetate (III).

A mixture of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl) acetone (Ia) (0.01 mol) and (0.02 mol) of ethylchloroacetate in 30 ml pyridine was heated

under reflux for 3 hours, cooled then poured onto a mixture of ice and dilute hydrochloric acid. The separated was solid filtered off, washed well with water and recrystallised from the proper solvent (c.f. table 1).

Reaction of ethyl 2-(6-bromo-2-cyanomethyl)-4-oxoquinazolin-3(4H)-yl acetate (III) with salicylaldehyde under Claisen reaction condition: Formation of ethyl-2-(6-bromo-2-cyanomethyl-4-oxoquinazolin-3(4H)-yl)-3-(2-hydroxyphenyl) acrylate (IV).

Add (0.01mol) of ethyl - 2 - (6-bromo-2-(cyanomethyl)-4-oxoquinazolin 3(4H)-yl) acetate (III) to (30ml) absolute ethyl alcohol and (0.05mol) of sodium ethoxide, then add (0.01mol) Salicylaldehyde with strong stirring by using magnetic stirrer for 2 hours. Filter the precipitate and recrystallise from the proper solvent (c.f. table 1).

Reaction of ethyl-2-(6-bromo-2-cyanomethyl)-4-oxoquinazolin-3(4H)-yl)acetate (III) with hydrazine hydrate : Formation of 2-(6-bromo-2-(cyanomethyl)-4-oxo-quinazolin-3(4H)-yl)acetohydrazide (V).

To (0.01mol) of ethyl- 2-(6-bromo-2-(cyanomethyl)-4-oxoquinazolin -3(4H)-yl) acetate (III) in 20 ml ethanol we added (0.015mol; 85%) hydrazine hydrate and the whole mixture was refluxed for 6 hours. After concentration and cooling, the obtained product was collected and recrystallised from the proper solvent (c.f. table 1).

Reaction of 2-(6-bromo-2-(cyanomethyl)-4-oxoquinazolin-3(4H)-yl) acetohydrazide (V) with salicylaldehyde: Formation of 2-(6-bromo-3-(3-hydroxy-5-(2-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-4-yl)-4-oxo-3,4-dihydroquinazolin-2-yl)acetonitrile (VI).

To (0.01mol) of 2-(6-bromo-2-(cyanomethyl)-4-oxoquinazolin-3(4H)-yl) acetohydrazide (V) in (30 ml) absolute ethyl alcohol and (0.05mol) of sodium ethoxide add salicylaldehyde with strong stirring using magnetic stirrer for 2 hours. Filter the precipitate and recrystallise from the proper solvent to give(VI) (c.f. table 1).

Reaction of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl)acetonitrile(I) with aromatic aldehydes under Claisen reaction conditions: Formation of arylidene derivatives (VIIa-d).

To (0.01mol) of

2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl) acetonitrile (I) in (30ml) absolute ethyl alcohol and (0.05mol) of sodium ethoxide add different aldehydes namely salicylaldehyde, furfuraldehyde, 2- chloro benzaldehyde and/or 3,4,5 trimethoxy benzaldehyde (0.01 mol) with strong stirring by using magnetic stirrer for 2 hours. Filter the precipitate and recrystallise from the proper solvent to give (VIIa-d) (c.f. table 1).

Reaction of (Ib,c) with carbonyl compounds: Formation of arylidene derivatives (VIIIa-e)

To (0.01mol) of (Ia,c) in (30ml) of absolute ethanol and (0.05mol) of sodium ethoxide was added different carbonyl compounds namely furfural, salicylaldehyde, acetophenone, vaniline and/or benzoyl acetone (0.01 mol) with strong stirring using magnetic stirrer for 2 hours. Filter the precipitate and recrystallise from the proper solvent to give (VIIIa-e)(c.f. table 1).

Reaction of (Ia,c) with phosphorus oxychloride: Formation of (IXa,b).

A mixture of (Ib or Ic) (0.01 mol) and Phosphorus oxychloride (5 ml) was refluxed on a water bath for 3 hours, then poured onto mixture of crushed ice and HCl. The separated solid was filtered off, washed well with water and crystallized from the proper solvent to give (IXa,b) (c.f. table 1).

Action of hydrazine hydrate and primary amine on (IXa): Formation of (X a,b).

A mixture of (IXa) (0.01mol) and (0.01mol) of hydrazine hydrate and/or benzyl amine (0.01mol) in 30 ml absolute ethanol was refluxed for 3 hours after concentration and cooling, the obtained product was recrystallised from the proper solvent as (Xa,b) (c.f. table 1).

Reaction of (IXa) with aromatic aldehydes: Formation arylidene derivatives (XIa,b)

To a mixture of 2-(6-bromo-4-chloroquinazolin-2-yl) acetonitrile (IXa) (0.01mol) in (50ml) of absolute ethyl alcohol and (0.5mol) of sodium metal we added different aldehydes namely 2-chloro benzaldehyde and/or anisaldehyde (0.01 mol) with strong stirring for 2 hours. The obtained precipitate was filtered off and recrystallised from the proper solvent to give(XIa,b)(c.f. table 1).

Reaction of 2-(6-bromo-4-chloro-quinazolin-2-yl) acetonitrile (IXa) and/or 2-amino-6-bromoquinazolin-4(3H) one (Ic) with 5-bromoanthranilic acid: Formation of (XIIa,b)

A solution of IXa and/or Ic (0.01 mol) and 5-bromo anthranilic acid (0.015 mol) in 30ml butanol was heated under reflux for 6 hours, the obtained product a was recrystallized after cooling from the

proper solvent to give **(XIIa,b)** (c.f. table 1).

Treatment of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl) acetonitrile (Ia) with acetylacetone: Formation of 2-(6-bromo-4-(2,4-dioxopentan-3-ylidene)-3,4-dihydroquinazolin-2-yl) acetonitrile (XIII).

A mixture of compound **(Ia)** (0.01 mol) and acetylacetone (0.01 mol) in (30 ml) absolute ethanol and (0.05 mol) of sodium ethoxide was heated under reflux for 6 hours the product obtained after cooling was crystallized from the proper solvent to give **(XIII)** (c.f. table 1).

Reaction of 2-(6-bromo-4-(2,4-dioxopentan-3-ylidene)-3,4-dihydroquinazolin-2-yl)acetonitrile (XIII) With hydrazine hydrate: Formation of 2-(6-bromo-4-(3,5-dimethyl-4H-pyrazol-4-ylidene)-3,4-dihydroquinazolin-2-yl)acetonitrile (XIV)

A mixture of compound of **(XIII)** (0.01 mol) and hydrazine hydrate (0.01 mol) in 30 ml butanol was refluxed for 6 hours after cooling the obtained solid was crystallized from the proper solvent to give **(XIV)** (c.f. table 1).

Reaction of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl)acetonitrile (Ia) with a mixture of hydrochloric acid and acetic acid 3:1 to give 8-bromo-1-methyl-4H-pyrimido [6,1-b]quinazoline-3,10-dione (XV).

Compound **(Ia)** (0.002 mol) in a mixture of hydrochloric acid and acetic acid (3:1) was heated under reflux for 3 hours. The reaction mixture was cooled, poured onto water and the formed solid was filtered off, dried and recrystallized from the proper solvent to give **(XV)** (c.f. Table 1).

Reaction of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl) acetonitrile (Ia) with 40% sulphuric acid: Formation of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl) acetamide (XVI).

The reaction of compound **(Ia)** (0.01 mol) with 40% sulphuric acid (20ml) was refluxed in water bath for 2 hours after cooling the separated solid was recrystallized from the proper solvent to give **(XVI)** (c.f. table 1).

Dye formation: Formation Of 6-bromo-2-((4-hydroxy-3-nitrophenyl)diazenyl)quinazolin-4(3H)-one (XVII)

In a 250 ml beaker dissolved 2-amino-6-bromoquinazolin-4(3H) one **(Ic)** (0.02 mol), 32 ml conc. HCL and diluted it with 40ml water. Cool in an ice bath until

the temperature falls below 5°C to form amine hydrochloride, then dissolve (0.2mol) of sodium nitrite in 75 ml of water and cool this solution also in the ice bath, then add sodium nitrite solution to the amine hydrochloride in portions while stirring the solution continuously and maintaining the temperature below 5°C cooling (diazotization).

Dissolve (0.05 mol) of 2-nitro phenol in 50 ml of 10 % sodium hydroxide and cool the solution in an ice bath and add 25gm of crushed ice to it. Then add the cold diazonium salt solution (obtained after diazotization as above) very slowly (dropwise); by stirring the solution a dye is produced as **(XVII)** and recrystallized from the proper solvent (c.f. Table 1).

3. Results and Discussion

Quinazolinone derivative **(Ia-c)** as starting material can be prepared via the interaction of 5-bromo anthranilic acid, anthranilic acid, cyanoacetamide and/or thiourea in the presence of triethylamine as base to give **(Ia-c)** (Abel-Aziz, et al. 1990.; Sarika, et al. 2007; Abbert, et al. 1962; Manson et al. 1957; Heurn et al. 1951)⁽²¹⁻²⁵⁾.

Treatment of **(Ia)** with acrylonitrile in boiling pyridine afforded the corresponding 3-(6-bromo-2-(cyanomethyl-4-oxoquinazolin-3(4H)-yl)propanenitrile **(II)**.

The reaction of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl)acetonitrile **(Ia)** with ethylchloroacetate in boiling pyridine for 48 hours gives ethyl 2-(6-bromo-2-cyanomethyl-4-oxoquinazolin-3(4H)-yl)acetate **(III)** (Brown et al. 2005; Aly, et al. 2007; Vijayakumar, et al. 2010)⁽²⁶⁻²⁸⁾.

Treatment of the ester derivative **(III)** with aromatic aldehyde namely salicylaldehyde under Claisen reaction conditions gave ethyl 2-(6-bromo-2-(cyanomethyl)-4-oxoquinazolin-3(4H)-yl)-3-(2-hydroxyphenyl) acrylate **(IV)**.

The reaction of the ester derivative **(III)** with hydrazine hydrate in boiling ethanol gives the corresponding 2-(6-bromo-2-cyanomethyl-4-oxoquinazolin-3(4H)-yl) acetohydrazide **(V)**.

Thus condensation of 2-(6-bromo-2-(cyanomethyl)-4-oxoquinazolin-3(4H)-yl) acetohydrazide **(V)** with salicylaldehyde in ethanol solution of sodium ethoxide under Claisen conditions reaction afforded the corresponding 2-(6-bromo-3-(3-hydroxy-5-(2-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-4-yl)-4-oxo-3,4-dihydroquinazolin-2-yl) acetonitrile **(VI)**.

Treatment of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl) acetonitrile **(Ia)** with aromatic aldehydes namely salicylaldehyde, furfural, 2-chloro benzaldehyde and

3, 4, 5-trimethoxy benzaldehyde under Claisen conditions reaction gives arylidene derivatives (**VII_{a-d}**).

Reaction of (**Ib,c**) with carbonyl compounds namely furfural, salicylaldehyde, acetophenone, vaniline and/or benzoyl acetone under Claisen conditions reaction gives (**VIII_{a-e}**).

As a point of interest (**Ia-c**) exists in lactam-lactim tautomeric equilibrium. Thus, in absence of solvent it reacts with electrophiles or nucleophiles in the lactim form.

So, the reaction of a nucleophilic reagent such as phosphorouschloride with (**Ia,c**) supports the presence of its lactim form. Thus, compounds (**Ia,c**) react with POCl₃ to give the corresponding 2-(6-bromo-4-chloroquinazolin-2-yl) acetonitrile (**IX**) (**Ghorab, et al. 2006**)⁽²⁹⁾.

Reaction of 2-(6-bromo-4-chloroquinazolin-2-yl) acetonitrile (**IXa**) with hydrazine hydrate and/or benzylamine gives the corresponding hydrazino and/or amino derivatives (**X_{a,b}**) respectively.

Treatment of 2-(6-bromo-4-chloroquinazolin-2-yl)acetonitrile (**IXa**) with different aldehydes namely 2-chlorobenzaldehyde and/or anisaldehyde under Claisen reaction conditions gives arylidene derivatives (**XIa,b**) respectively.

Treatment of (**IXa,c**) with 5-bromoanthranilic acid in butanol under reflux gives 6-bromo-2-methylcyanobenazopyrimidinoquinazoline (**XIIa, b**).

Treatment of 2-(6-bromo-4-oxo-3, 4-dihydroquinazolin-2-yl) acetonitrile (**Ia**) with acetylacetone in ethanol in the presence of sodium ethoxide as a catalyst under reflux gives 2-(6-bromo-4-(2,4-dioxopentan-3-ylidene)-3,4-dihydroquinazolin-2-yl) acetonitrile (**XIII**).

Treatment of 2-(6-bromo-4-(2,4-dioxopentan-3-ylidene)-3,4-dihydroquinazolin-2-yl) acetonitrile (**XIII**) with hydrazine hydrate in butanol under reflux gives 2-(6-bromo-4-(3,5-dimethyl-4H-pyrazol-4-ylidene)-3,4-dihydroquinazolin-2-yl)acetonitrile (**XIV**).

Treatment of 2-(6-bromo-4-oxo-3, 4-dihydroquinazolin-2-yl) acetonitrile (**Ia**) under reflux with a mixture of hydrochloric acid and acetic acid by ratio 3:1 gives 8-bromo-1-methyl-4H-pyrimido[6,1-b]quinazoline-3,10-dione or 8-bromo-3-hydroxy-1-methyl-10H-pyrimido[6,1-b]quinazolin-10-one (**XIV**) (**Ayman, et al. 2009; Lixia et al. 2007**)^(30,31).

Treatment of 2-(6-bromo-4-oxo-3,4-dihydroquinazolin-2-yl) acetonitrile (**Ia**) with 40% sulphuric acid, the cyano group hydrolyses to give 2-(6-bromo-4-oxo-3,

4-dihydroquinazolin-2-yl) acetamide (**XVI**).

Treatment of 2-amino-6-bromoquinazolin-4(3H)-one (**Ic**) under diazotization and coupling conditions gave the diazotized 2-amino-6-bromoquinazolin-4(3H)-one which coupled with 2-nitrophenol to give 6-bromo-2-((4-hydroxy-3-nitrophenyl) diazenyl)quinazolin-4(3H)-one (**XVII**) (**Divyesh et al. 2010**)⁽²⁰⁾.

Antibacterial activities

Compounds **Ia-c**, **III, VIIIc,d**, **IXa,b, XIIb**, **XIII**, **XIV** and **XV** were tested in vitro for their antimicrobial activities by agar diffusion method (**Clin. Microbiol, 2000; Wayne, PA, 2000**)^(32,33). The tested microorganisms were obtained from the Regional Center for Mycology and Biotechnology (RCMB), Al-Azher University.

The assayed collection included Gram-Positive bacteria: *Staphylococcus aureus* (RCMB 000106) and *Bacillus subtilis* (RCMB00107) and Gram-negative bacteria: *Pseudomonas aeruginosa* (RCMB 00102) and *Escherichia coli* (RCMB00103) using *Penicillin G* and *Streptomycin* 30 ug/ml as reference drugs, in addition to four fungal strains: *Aspergillus fumigatus* (RCMB 002003), *Geotrichum candidum* (RCMB 052006), *Candida albicans* (RCMB 005002) and *Syncephalastrum racemosum* (RCMB 005003) using *Itraconazole* and *Clotrimazole* 30 ug/ml as reference drugs. The inhibition zone diameters (mm) were read for analysis. All the tested compounds were dissolved in dimethylsulfoxide (DMSO) with final concentration of 10 µg/ml of each tested compound and were tested in triplicate.

The investigation of antibacterial and antifungal screening data (table 3) revealed that some of the tested compounds have demonstrated congruent activity against all the considered microorganisms as compared with the standard drugs. Compounds **Ic, IXb**, **XIII** and **XIV** did not show any antimicrobial activity against the two Gram +ve bacteria, while all tested compounds had no effect on *Pseudomonas aeruginosa*, but for *Escherichia coli* compounds number **Ia,c**, **VIIIc**, **IXa,b**, **XIII** and **XIV** had no effect.

Compounds **III, VIIIc,d** and **XVI** showed high activity against Gram +ve bacteria while compounds **Ia, VIIIc**, **IXa, XIIb** and **XV** were moderately effective at a concentration of 10 ug/ml.

These results agree with those of (**Gupta et al., 2008**)⁽³⁴⁾ and (**Patel and Barat., 2010**)⁽³⁵⁾ who reported that quinazolinone derivatives exhibited interesting high activity against *Staphylococcus aureus* and *Bacillus subtilis*.

With regard to Gram -ve bacteria, compound **XV** was the most potent compound since it produced an inhibition zone of 19.4 mm and MIC was 78 µg/ml, while the rest compounds were moderately effective. Consequently, the tested quinazolinone derivatives were

less effective on Gram -ve bacteria as reported by others (Kluytmans et al., 1997.; Singhal et al., 2011)^(36,37).

All tested compounds had no effect on *Syncephalstrum racemosum*, while compounds VIIIc,d, IXb, XIII and XV, had no effect on the rest of the tested fungi. Compound number III was the most effective compound, while compounds Ic, XIIb and XVI were moderately effective on *Aspergillus fumigatus*. For *Geotricum candidum* and *Candida*

albicans compounds XIIa,b and XVI were moderately effective.

These results agree with those reported by many others^(31,32,37).

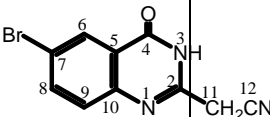
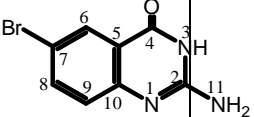
The antibacterial activity of these may be related to their ability to affect permeability of the bacterial cell wall through interacting with the peptidoglycan layer. These interactions produced a flux of protons which induces changes in cell wall and cell membrane and ultimately, cell death.

Table (1): Physical properties of synthesized compounds from (I-XVII)

Comp No.	M.P. ^o C Solvent	Yield %	Shape /Colour	Mol Formula (Mol Weight)	Elemental analysis calcd/ found				
					C	H	N	Br	Cl
Ia	250-252 EtOH	70	Yellowish brown Powder	C ₈ H ₆ N ₃ OBr (264)	45.45	2.27	15.9	30.30	
					45.50	2.30	16.00	30.28	
Ib	170 EtOH	70	Brown Powder	C ₈ H ₇ N ₃ O (161)	59.62	4.35	26.09		
					59.60	4.30	26.10		
Ic	185 EtOH	70	Yellowish brown crystals	C ₈ H ₆ N ₃ OBr (240)	40.00	2.50	17.50	33.29	
					40.03	2.52	17.53	33.32	
II	180-182 EtOH	50	White Powder	C ₁₃ H ₉ N ₄ OBr (317)	49.21	2.83	17.66	25.23	
					49.20	2.80	17.70	25.20	
III	218 Benzene	65	Chocolate Powder	C ₁₄ H ₁₂ N ₃ O ₃ Br (350)	48.00	3.42	12.00	22.85	
					48.02	3.40	12.04	22.90	
IV	205 EtOH	56	Black Powder	C ₂₁ H ₁₆ N ₃ O ₄ Br (454)	55.5	3.52	9.25	17.62	
					55.48	3.50	9.30	17.60	
V	230 Propanol	60	Dark brown Powder	C ₁₂ H ₁₀ N ₅ O ₂ Br (363)	42.85	2.97	20.83	23.80	
					42.90	3.00	20.80	23.85	
VI	280 EtOH	45	Brown Powder	C ₁₉ H ₁₄ N ₅ O ₃ Br (440)	51.81	3.18	15.90	18.18	
					51.85	3.20	15.94	18.20	
VIIa	220 EtOH	70	Brown Powder	C ₁₇ H ₁₀ N ₃ O ₃ Br (368)	55.43	2.71	11.41	21.73	
					55.40	2.72	11.43	21.70	
VIIb	195 EtOH	68	Black Powder	C ₁₅ H ₈ N ₃ O ₂ Br (342)	52.63	2.33	12.28	23.39	
					52.60	2.35	12.30	23.40	
VIIc	180 EtOH	73	White Powder	C ₁₇ H ₉ N ₃ OBrCl (386.5)	52.78	2.32	10.86	20.69	9.17
					52.80	2.35	10.90	20.70	9.15
VIIId	200 EtOH	59	White Crystal	C ₂₀ H ₁₆ N ₃ OBr (442)	54.29	3.39	9.50	18.09	
					54.30	3.41	9.52	18.12	
VIIIa	205 EtOH	48	Black Powder	C ₁₃ H ₈ N ₃ O ₂ Br (318)	49.05	2.51	13.20	25.15	
					49.10	2.53	13.22	25.17	
VIIIb	185 EtOH	50	Brown Powder	C ₁₅ H ₁₁ N ₃ O ₂ (265)	67.92	4.15	15.85		
					67.90	4.18	15.80		
VIIIc	215 EtOH	55	White Powder	C ₁₆ H ₁₃ N ₃ O (263)	72.99	4.94	15.96		
					73.00	4.90	15.98		
VIIIId	175 EtOH	60	Yellow Powder	C ₁₆ H ₁₃ N ₃ O ₃ (295)	65.08	4.41	14.23		
					65.10	4.46	14.23		
VIIIe	200 EtOH	65	White Crystals	C ₁₈ H ₁₅ N ₃ O ₂ (305)	70.81	4.92	13.76		
					70.80	4.95	13.80		
IXa	195 Benzene	70	Orange Powder	C ₁₀ H ₅ N ₃ BrCl (282.5)	42.47	1.76	14.86	28.32	12.55
					42.50	1.80	14.92	28.30	12.53
IXb	180 Benzene	70	Yellow Powder	C ₈ H ₅ N ₃ BrCl (285.5)	37.13	1.93	16.24	30.94	13.71
					37.17	1.90	16.20	30.90	13.50
Xa	230 EtOH	65	Black Powder	C ₁₀ H ₈ N ₃ Br (278)	43.16	2.87	25.17	28.77	
					43.20	2.90	25.20	28.80	
Xb	250 P.E. 40	58	Brown Powder	C ₁₇ H ₁₃ N ₄ Br (353)	57.79	3.68	15.86	22.66	
					57.82	3.71	15.90	22.70	
XIa	180 EtOH	70	Brown Powder	C ₃₁ H ₁₈ N ₃ BrCl (654)	56.88	2.75	6.42	12.23	21.71
					56.90	2.80	6.40	12.20	21.70
XIb	215 EtOH	48	Black Powder	C ₃₄ H ₂₇ N ₃ O ₃ BrCl (640.5)	63.70	4.21	6.55	12.49	5.53
					63.73	4.23	6.60	12.52	5.55
XIIa	230 EtOH	62	Dark Brown Powder	C ₁₇ H ₈ N ₄ OBr (444)	45.95	1.82	12.62	35.99	
					46.00	1.85	12.60	36.01	

Comp No.	M.P. ^o C Solvent	Yield %	Shape /Colour	Mol Formula (Mol Weight)	Elemental analysis calcd/found				
					C	H	N	Br	Cl
XIIb	202 EtOH	56	Dark Brown Powder	C ₁₅ H ₈ N ₄ OBr ₂ (420)	42.85	1.90	13.33	38.10	-----
					42.82	2.00	13.30	38.20	
XIII	280 EtOH	85	White crystals	C ₁₅ H ₁₂ N ₃ O ₂ Br (346)	52.02	3.46	12.13	23.12	-----
					52.00	3.50	12.10	23.10	
XIV	245 EtOH	80	Yellow crystals	C ₁₅ H ₁₂ N ₅ Br (342)	52.63	3.50	20.46	23.39	-----
					52.60	3.52	20.50	23.42	
XV	230 Butanol	55	Dark brown powder	C ₁₂ H ₈ N ₃ O ₂ Br (306)	47.05	2.61	13.72	26.10	-----
					47.12	2.60	13.70	26.14	
XVI	210 EtOH	75	Brown powder	C ₁₀ H ₈ N ₃ O ₂ Br (282)	42.55	2.83	14.89	28.36	-----
					42.60	2.80	14.92	28.40	
XVII	250 EtOH	66	Reddish brown dye	C ₁₄ H ₈ N ₅ O ₄ Br (390)	43.07	2.05	17.94	20.51	-----
					43.10	2.20	17.90	20.50	

Table (2): Spectral data of the synthesized compounds from (I-XVII).

Comp. NO.	IR Cm ⁻¹	H ¹ NMR	¹³ C NMR	Mass spectrum
Ia	3407(NH/OH); ν CH at 2936.3, 2969.3, 3081.5cm ⁻¹ ; ν C=O at 1684.4 cm ⁻¹ ; ν C \equiv N at 2219 cm ⁻¹ ; ν C=N at 1622.2 cm ⁻¹ and ν C-Br at 539.4 cm ⁻¹	2.50ppm(2H, s, CH ₂) , at 6.70-7.91ppm (3H, m, Ar-H) and at 8.0 (1H, s, NH)	167.95ppm for (C ₄) and (C ₂), at 147.19 ppm for (C ₁₀); at 138.46 ppm for (C ₈) and (C ₆); at 132.98 ppm for (C ₅); at 113.01ppm for (C ₁₂); at 110.53ppm for (C ₇); at  104.81 ppm for (C ₉); at 25.41 ppm for (CH ₁₁)	266 (M ⁻²) (2.2%), 247(9.4%), 168 (16.2%), 143 (11.9%), 117 (12.3%), 91 (17%) 171(5.1%), 131(5.8%) and m/z 63 (100%)
Ib	NH ₂ at 3359-3275 cm ⁻¹ ; NH at 3275 cm ⁻¹ ; C=O at 1710 cm ⁻¹ ; ν C=N at 1612 cm ⁻¹ and ν CH at 285,3165 cm ⁻¹	13.180 ppm (2H, s, NH ₂), 9.970 ppm (1H, s, NH) and 6.887- 8.256 ppm (3H, m, Ar-H).	167.94ppm for (C ₄), at 147.19ppm for (C ₂); at 138.49 ppm for (C ₈); at 132.97 ppm for (C ₆); at 112.91 ppm for (C ₇); at 110.53 ppm for (C ₉); at 104.81 ppm for (C ₁₀) and at 97.78ppm for (C ₅) 	161 (24.8%), 162 (34%) (M ⁺¹), 163 (17%) (M ⁻²), 147 (19%) (M ⁺¹), 105 (7.1%), 76 (100%), 75 (9.2%) (M ⁻¹) and 78 (3.7%) (M ⁻²).
Ic	NH or/OH at 3407.6cm ⁻¹ ; ν CH at 2936.3, 2969.3, 3081.5cm ⁻¹ ; ν C=O at 1684.4 cm ⁻¹ ; ν C \equiv N at 2269 cm ⁻¹ ; ν C=N at 1622.2 cm ⁻¹ and C-Br at 539.4 cm ⁻¹	13.183 ppm (2H, s, NH ₂), 9.972 ppm (1H, s, NH) and 6.887- 8.256 ppm (3H, m, Ar-H).	167.94ppm for (C ₄), at 147.19ppm for (C ₂); at 138.49 ppm for (C ₈); at 132.97 ppm for (C ₆); at 112.91 ppm for (C ₇); at 110.53 ppm for (C ₉); at 104.81 ppm for (C ₁₀) and at 97.78ppm for (C ₅)	

Comp. NO.	IR cm^{-1}	^1H NMR	^{13}C NMR	Mass spectrum
II	2972,2876(CH),2219(C-nitrile),1678(C=O),1614(C=N),564(C-Br)	2.52 ppm (2H, t, CH_2), 6.73- 7.92 ppm (3H, m, ArH) and 8.00ppm (1H, s,NH).		316(0.11%) (M^+), 262.45 (0.11%), 236 (0.51%), 223 (0.15%), 142.9 (0.65%), 125.75 (1.09%) and m/z 86(12.4%)
III	at 2942 cm^{-1} due to νCH ,2200 cm^{-1} due to $\nu(\text{C}\equiv\text{N})$,1676 cm^{-1} due to $\nu\text{C}=\text{O}$,1590 cm^{-1} due to $\nu\text{C}=\text{N}$ and 590 cm^{-1} due to C-Br	at 1.01ppm (3H, t, CH_3) , at 2.51ppm (2H, d, CH_2 CN), 3.38-3.49 ppm (2H, q, CH_2 CH_3), 4.34ppm (2H, S, $\text{CH}_2\text{C}=\text{O}$) and 7.817-7.842ppm (3H, m, Ar-H)		
IV	3342 cm^{-1} due to OH, 2290 cm^{-1} due to $\nu\text{C}\equiv\text{N}$,1701 cm^{-1} due to $\nu\text{C}=\text{O}$, 1606 cm^{-1} due to $\nu\text{C}=\text{N}$ and at 512 cm^{-1} due to C-Br	1.01 ppm (3H, t, CH_3), 2.50 ppm (2H,d, CH_2 CN), 3.38 – 3.49ppm (2H, q, CH_2 - CH_3) and 7.81-7.84 ppm (7H, m, Ar-H).		
V	at 3360,3468 cm^{-1} due to NH_2 , 2764-2918 cm^{-1} due to ν CH, 2250 cm^{-1} due to $\nu\text{C}\equiv\text{N}$,1680 cm^{-1} due to $\nu\text{C}=\text{O}$, 1606 cm^{-1} due to $\nu\text{C}=\text{N}$ and at 544 cm^{-1} due to C-Br	2.50 ppm (2H,d, CH_2 CN), 13.18 ppm (2H, s, NH_2), 9.97ppm (1H, s, NH), 6.70-7.90ppm (3H, m, Ar-H).		
VI	at 3418 cm^{-1} due to $\nu\text{OH}/\text{NH}$, at 2762-2820 cm^{-1} due to νCH , at 2270 cm^{-1} due to $\nu\text{C}\equiv\text{N}$, at 1700 cm^{-1} due to C=O, at 1596 cm^{-1} due to $\nu\text{C}=\text{N}$ and at 516 cm^{-1} due to $\nu\text{C}-\text{Br}$	2.32 ppm (2H,d, CH_2 CN), 9.97(1H, s, NH), 7.85-7.84 ppm (7H, m, Ar-H).		
VIIa	at 3456 cm^{-1} (νCH), 3354(νNH), at 2918-2820(νCH), at 2200($\nu\text{C}\equiv\text{N}$), at 1678($\nu\text{C}=\text{O}$), at 1600($\nu\text{C}=\text{N}$)and at 590 cm^{-1} due to C-Br.	8.13 ppm (1H,s, NH), 7.73-7.84 ppm (7H, m, Ar-H) , 7.30ppm (1H, s, $\text{CH}=\text{C}-\text{CN}$).		at 364 (6.1%) (M^+), 197 (20.4%) 199 (14.3%) (M^{+2}), 95 (14.3%), 80 (22.4%), 73 (20.4%) (M^+), 79 (22.4%), 52 (6.1%),62 (22.4%), 61 (4.1%) (M^+) and 63 (16.4%) (M^+).
VIIb	at 3412.4 (νCH), at 2499-2820 (νCH), at 2218.7($\nu\text{C}\equiv\text{N}$), at 1700 ($\nu\text{C}=\text{O}$), at 1604 ($\nu\text{C}=\text{N}$)and at 591 ($\nu\text{C}-\text{Br}$).	7.72-7.43 ppm (6H, m, Ar-H), 8.12 ppm (1H,s, NH) 7.20ppm (1H, s, $\text{CH}=\text{C}-\text{CN}$).		
VIIc	at 3467(νNH), at 3000(νCH), at 2210 ($\nu\text{C}\equiv\text{N}$), at 1705($\nu\text{C}=\text{O}$), at 1601($\nu\text{C}=\text{N}$), at 580 ($\nu\text{C}-\text{Br}$) and at 700 ($\nu\text{C}-\text{Cl}$).			
VIIId	at 3402(NH), at 2999.7, 2836 (νCH), at 2218 ($\nu\text{C}\equiv\text{N}$), at 1694 ($\nu\text{C}=\text{O}$), at 1587($\nu\text{C}=\text{N}$) and at 592 ($\nu\text{C}-\text{Br}$).	at 8.13ppm (1H, s, NH), at 7.73 - 7.84 ppm (5H, m, Ar-H) at 7.35 ppm (1H,s, $\text{CH}=\text{C}-\text{CN}$) , at 3.34 (3H, s, OCH_3), at 3.37(3H, s, OCH_3) and 3.40ppm (3H, s, OCH_3).		
VIIIa	at 3290 (νNH), at 2924- 2858 (νCH), at 1696 ($\nu\text{C}=\text{O}$), at 1608 (C=N) and at 550(νCBr)	at 2.52ppm (1H, s, $\text{CH}=\text{N}$), 6.230-7.190 ppm (6H, m, Ar-H) at 8.231 ppm (1H,s,NH)		
VIIIb	at 3352($\nu\text{NH}/\text{OH}$),at 3058-2856 (νCH) at 1679 ($\nu\text{C}=\text{O}$), at 1601($\nu\text{C}=\text{N}$).	at 9.230ppm (1H, s, OH), 2.502 ppm (1H, s, $\text{CH}=\text{N}$), 6.140-7.090 ppm (7H, m, Ar-H) at 8.230ppm (1H, s, NH)		
VIIIc	at 3383(νNH), at 2800-3040 (νCH),1650 ($\nu\text{C}=\text{O}$), at 1617(C=N).	at 3.594ppm (3H, s, CH_3), 6.148 -7.971 ppm (6H, m, Ar-H) at 8.220 ppm (1H,s,NH)		
VIIIId	at 3242 (NH), 3432(OH), at 2836-3166 (νCH), 1658 ($\nu\text{C}=\text{O}$), at 1582($\nu\text{C}=\text{N}$).	at 9.234 ppm (1H, s, OH), 2.500 ppm (1H, s, $\text{CH}=\text{N}$), 6.148-7.097 ppm (7H, m, Ar-H) at 8.231ppm (1H, s,		

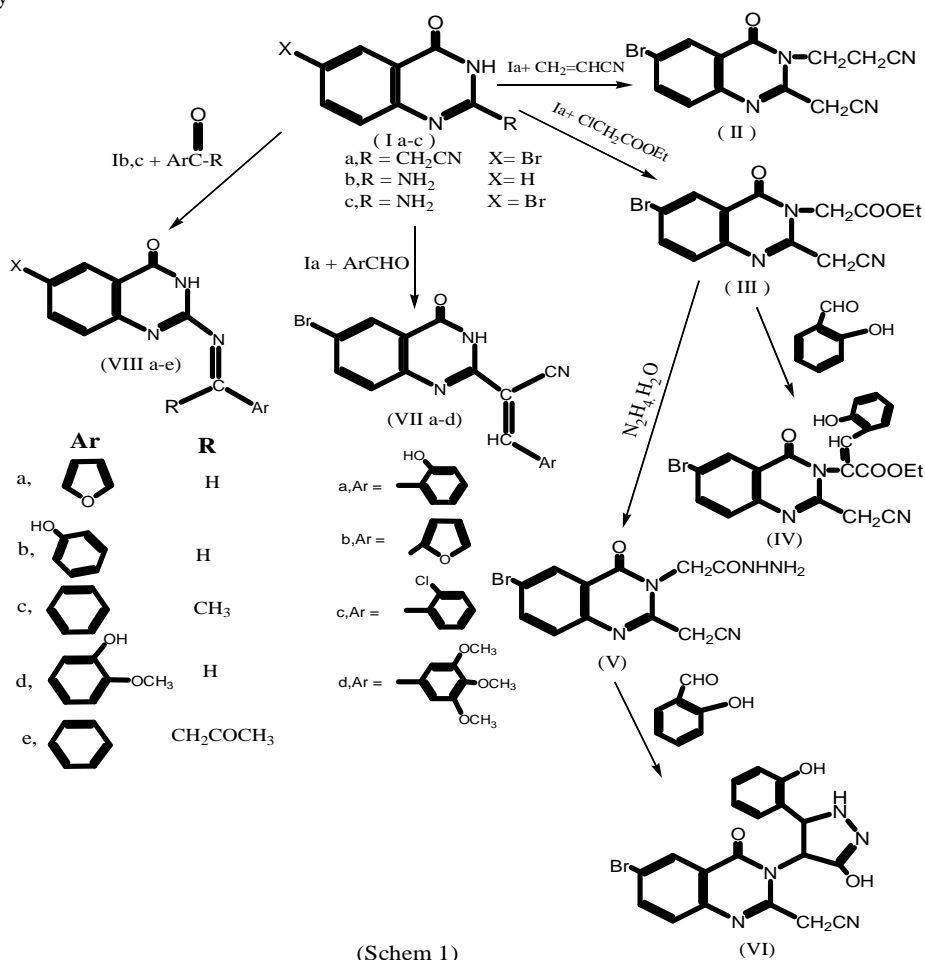
Comp. NO.	IR cm^{-1}	^1H NMR	^{13}C NMR	Mass spectrum
		NH) 3.695ppm (3H, s, CH_3)		
VIIIe	at 3380(νNH), at 2850- 3100 (νCH), 1650 ($\text{C}=\text{O}$), at 1597 ($\nu\text{C}=\text{N}$)	8.25(1H,s,NH),6.244-7.903(9 H,m,Ar-H),2.104(3H,s, CH_3), 2.492(1H,s, $\text{CH}=\text{N}$),2.50(1H,s, CH_2)		
IXa	at 2828,2858,2952, 3004, 3056 cm^{-1} due to νCH , at 2230 cm^{-1} due to $\nu\text{C}\equiv\text{N}$, at 1606 cm^{-1} due to $\nu\text{C}=\text{N}$, at 874 cm^{-1} due to $\nu\text{C}-\text{Cl}$ and at 582 cm^{-1} due to $\nu\text{C}-\text{Br}$	7.85-7.89ppm (3H, m, Ar-H) and at 3.31ppm (2H, s, CH_2CN)		at 282.65(12.62%), 281.45 (55.85%), 283.7 (8.4%), 130.75 (5.22%), 112.85 (12.17%), 98.25 (9.13%), 99.2 4.88%), 96.05 (69.89%), 88.5 (17.71%), 72.75 (100%), 207(93.17%), 195.35, 3.18%),194.35 (1.38%),196.35(1.38%), 182.55) 1.52%), 183.35 (2.22%), 181.7 (1.54%), 69.85 (11.83%) 167.95 (10.35%),155.3 (4.11%), 74.5 (21.68%), 72.75 (100%), 61 (6.24%), 63 (18.99%), 52.65 (14.09%), 142.45 (6.44%), 130.75 (5.22%),118.95(7.8%) and 79.85 (68.22%)
IXb	at 3234 - 3444 cm^{-1} due to νNH_2 , at 3078 cm^{-1} due to νCH , , at 1630 cm^{-1} due to $\nu\text{C}=\text{N}$, at 876 cm^{-1} due to $\nu\text{C}-\text{Cl}$, and at 540 cm^{-1} due to C-Br	7.83-7.87(3H,m,Ar-H),3.31(2 H,s, CH_2CN)		
Xa	at 3334-3300(NH_2), at 3300 (νNH) at 2908 (νCH), at 2250 ($\nu\text{C}\equiv\text{N}$), at 1616 ($\text{C}=\text{N}$) and at 548($\nu\text{C}-\text{Br}$).	9.7(2H,s, NH_2),3.30(2H,s, CH_2-CN),7.83-7.82(3H,m,Ar-H)		241 (4.3%) (M^{+2}), 242 (4.3%), 243 (5.4%) (M^{+1}), 244 (14.3%) (M^{+2}), 80 (60.2%), 185 (9.7%), 63 (9.7%), 62 (44.1%) (M^{+1}), 64 (2.2%) (M^{+1}), 52 (18.3%), 51 (23.7%) (M^{+1}), 53 (32.3%) (M^{+1}), 97 (58.1%), 96 (9.7%) (M^{+1}), 98 (65.6%) (M^{+1}) and 81 (100%).
Xb	at 3336 (νNH), at 2800-3100 (νCH), at 2260 ($\nu\text{C}\equiv\text{N}$), at 1600 ($\text{C}=\text{N}$) and at 520(νCBr).	7.097-7.232(8H,m,Ar-H),3.28 (2H,s, CH_2CN)		at 238 (5.2%) (M^{+2}), 131(4.5%),193 (3.9%),179(2.6%)158(3.2%),131(4.5%),132 (3.9%) (M^{+1}), 106 (26%), 91 (100%),90 (20.8%) (M^{+1}), 77 (22.7%) and 64 (13.6%)
XIa	at 2916-2846 due to C-H, at 1606 cm^{-1} due to $\nu\text{C}=\text{N}$, at 722 cm^{-1} due to $\nu\text{C}-\text{Cl}$ and at 550 cm^{-1} due to $\nu\text{C}-\text{Br}$	6.40-8.21(15H,m,Ar-H),2.48(1H,s, $\text{N}=\text{CH}$),2.51(1H,s, $\text{N}=\text{C}-\text{H}$)		
XIb	at 1610 cm^{-1} due to $\nu\text{C}=\text{N}$, at 778 cm^{-1} due to $\nu\text{C}-\text{Cl}$, at 540 cm^{-1} due to $\nu\text{C}-\text{Br}$	at 3.32(3H, s, OCH_3), 3.45 (3H, s, OCH_3), 3.77(3H s, OCH_3), at 6.42-8.2ppm (15H, m, Ar-H), at 2.49 (1H, s, $\text{N}=\text{CH}$), at 2.50 (1H, s, $\text{N}=\text{CH}$) and at 2.51 (1H, s, $\text{N}=\text{CH}$)		m/z 639 (1.51%) (M^{+1}), m/z 475.65 (1.3%), m/z 462.95 (1.87%), m/z 462.05 (1.49%), m/z 461.35 (1.43%), m/z 430.05 (6.22%),429.15 (1.34%), m/z 431.2 (1.81%), m/z 432.05 (1.23%), m/z 401.5 (3.83%), 402.55 (1.56%), m/z 341.25(6.27%), m/z342.05 (3.14%) (M^{+1}), 343.65 (1.04%) (M^{+2}), m/z328.75 (1.1%), m/z 329.5(1.17%) (M^{+1}), m/z 327.9 (2.4%) (M^{+1}), m/z 327(4.22%) (M^{+1}), m/z 295.2 (2.77%), m/z 296.8 (1.17%) (M^{+1}), m/z 281.45 (71.25%), 282.75 (12.19%) (M^{+1}), m/z 283.7(9.61%) (M^{+2}), 267.4 (19.24%), 269.15 (2.45%) (M^{+2}), 270.85 (1.14%) (M^{+3}),155 (1.7), 142.45 (1.89%),130.85 (4.15%),118.95 (9.94%), 80.9 (40.67%),76.51 (18.63%), 88.5 (10.73%), 86.75 (7.15%),73 (99.1%), 74.5 (21.68%), 72.75

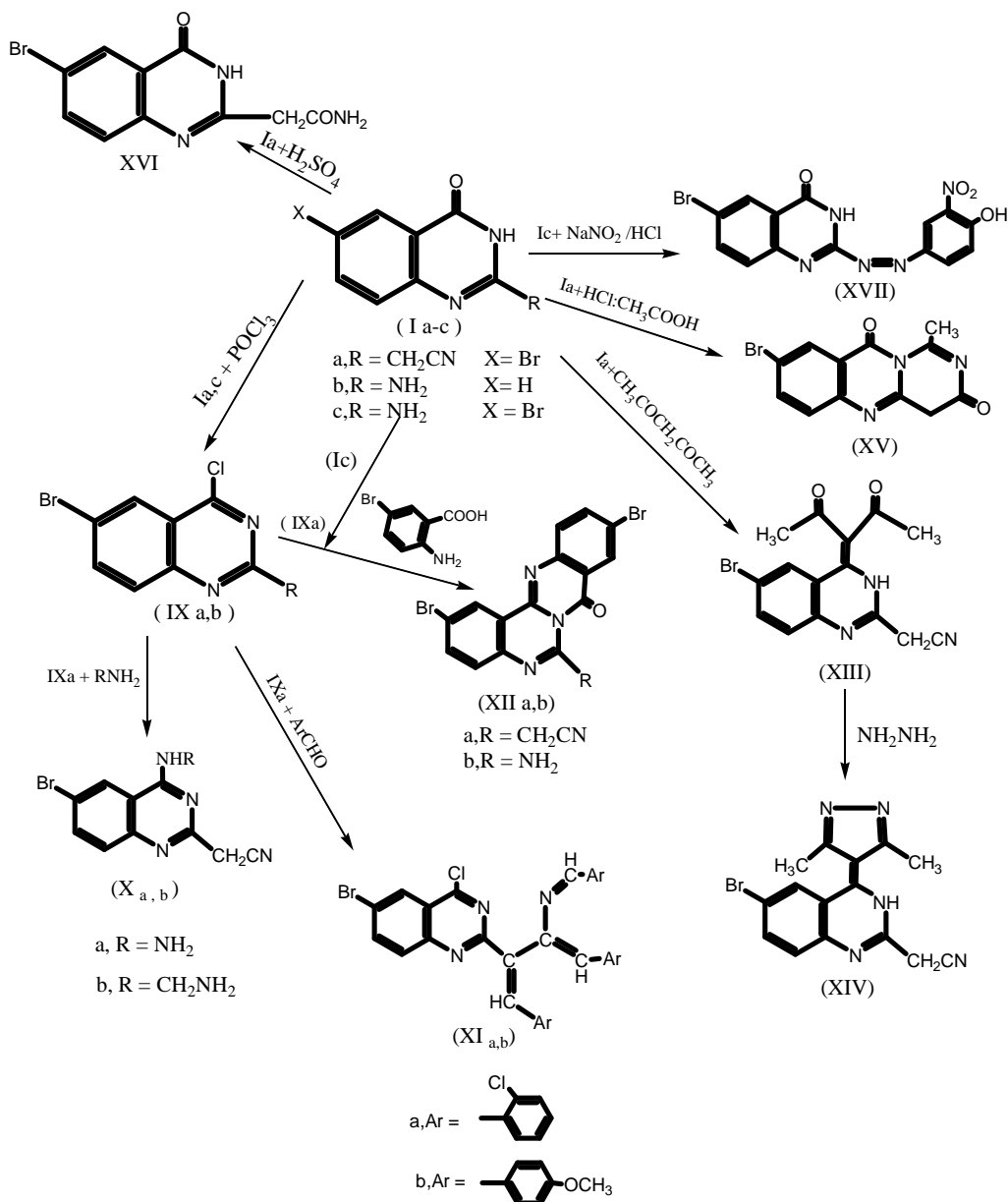
Comp. NO.	IR cm^{-1}	$^1\text{H-NMR}$	$^{13}\text{C NMR}$	Mass spectrum
				(99.1%), 61 (6.24%), 63 (18.99%) and 52.65 (14.09%)
XIIa	at 3442 cm^{-1} due to OH and/or NH, at 2852-3072 cm^{-1} due to CH, at 2206 cm^{-1} due to C=N, at 1700 cm^{-1} due to $\nu\text{C}=\text{O}$, at 1608 cm^{-1} due to $\nu\text{C}=\text{N}$ and at 518 cm^{-1} due to $\nu\text{C-Br}$			At 438 (17.1%), 405 as M^{+1} (11.4%), 406 as M^{+2} (2.9%), 296 (20.0%), 295 as M^{-1} (40.0%), 297 as M^{+1} (34.3%), 99 (22.9%) and 73 (31.4%)
XIIb	at 3352 - 3464 cm^{-1} due to NH_2 , at 2850-3078 cm^{-1} due to νCH , at 1670 cm^{-1} due to $\nu\text{C}=\text{O}$, at 1603 cm^{-1} due to $\text{C}=\text{N}$ and at 542 cm^{-1} due to $\nu\text{C-Br}$	7.627- 7.855ppm (6H, m, Ar-H) and 6.742ppm (2H, s, NH_2)		
XIII	at 3142 cm^{-1} due to NH, at 3022-2850 cm^{-1} due to νCH , at 2214 cm^{-1} due to $\nu\text{C}=\text{N}$, at 1660 cm^{-1} due to $\nu\text{C}=\text{O}$, at 1628 cm^{-1} due to $\nu\text{C}=\text{N}$ and at 520 cm^{-1} due to C-Br			at m/z 277 as M^{+1} (56.3%), m/z 148 (68.1%), m/z 147 as M^{+1} (44.9%), m/z 149 as M^{+2} (5.1%), m/z 120 (39.9%), m/z 121 as M^{+1} (18.8%), m/z 122 as M^{+2} (1.4%), m/z 119 (100%), m/z 118 as M^{+1} (20.3%), m/z 80 (56.3%), m/z 81 as M^{+1} (81.3%), m/z 83 as M^{+3} (37.3%), m/z 79 as M^{+1} (12.5%), m/z 104 (10.1%), m/z 105 as M^{+1} (22.5%), m/z 93 (8.7%), m/z 92 as M^{+1} (10.9%), m/z 80 (56.3%), m/z 67 (8.7%) and m/z 68 as M^{+1} (50.0%)
XIV	at 3294 cm^{-1} due to NH, at 2726-3138 cm^{-1} due to νCH , at 2216 cm^{-1} due to $\nu\text{C}=\text{N}$, at 1652 cm^{-1} due to $\text{C}=\text{N}$ and at 522 cm^{-1} due to C-Br	at 12.311 ppm (1H, s, NH), at 6.1, 6.15, 6.2 ppm (3H, m, Ar-H), at 2.490ppm (s, 2H, CH_2CN), and at 2.21 ppm (3H, s, CH_3) and 2.29 ppm (3H, s, CH_3)		
XV	at 3478.4 cm^{-1} due to OH, 3080.9-2857.8 cm^{-1} due to νCH , at 1676.6 cm^{-1} due to $\text{C}=\text{O}$, at 1609.6 cm^{-1} due to $\text{C}=\text{N}$ and at 586.2 cm^{-1} due to C-Br	7.85-7.1ppm (4H, m, Ar-H), 6.8ppm (1H, s, OH) and 2.4 (s, 3H, CH_3)		At m/z 306 (0.64%), m/z 305 as M^{+1} (0.09%), m/z 275.2 (16.32%), m/z 277.2 (33.27%), m/z 279 as M^{+2} (19.88%), m/z 259.15 (0.09%), m/z 210 as M^{+2} (0.11%), m/z 232.05 (0.12%), m/z 233.1 as M^{+1} (0.24%), m/z 234 as M^{+2} (0.14%), m/z 249.05 (7.41%) and m/z 250 (4.4%)
XVI	at 3468-3358 cm^{-1} due to NH_2 , at 2906 cm^{-1} due to νCH , at 1676 cm^{-1} due to $\text{C}=\text{O}$, at 1590 cm^{-1} due to $\text{C}=\text{N}$ and at 588 cm^{-1} due to C-Br			At m/z 282 (3.74%), m/z 263.4 as M^{+3} (2.55%), m/z 250 (7.41%), m/z 252.75 as M^{+1} (2.74%), m/z 252.4 as M^{+2} (4.14%), m/z 234.1 (5.87%), m/z 222.75 (3.94%), at m/z 223.65 as M^{+1} (2.67%), m/z 210.15 (4.37%), m/z 210.95 as M^{+1} (4.76%), m/z 196.2 (9.17%), m/z 172.3 (7.39%), m/z 169.45 (12.53%), at m/z 168.35 as M^{+1} (17.37%), m/z 155.8 (10.56%), m/z 143.35 (12.99%), m/z 142.35 as M^{+1} (14.98%), m/z 144.15 as M^{+1} (28.64%), m/z 80.85 (91.58%), m/z 63.4 (79.66%), m/z 50.4 (69.9%) and m/z 52.3 (62.18%)
XVII	at 3508 cm^{-1} due to OH, at 3352 cm^{-1} due to NH, at 3080-2900 cm^{-1} due to νCH , at 1674 cm^{-1} due to $\text{C}=\text{O}$, 1650 cm^{-1} due to $\text{C}=\text{N}$, at 1510 cm^{-1} due to asymmetric NO_2 , at 1312 cm^{-1} due to symmetric NO_2 and at 590 cm^{-1} due to C-Br			At m/z 428 (12%), m/z 93 (2%), m/z 298 (14%), m/z 297 (20%), m/z 295 (7.1%), m/z 277 (100%), m/z 276 (52%), m/z 275 (60%) and m/z 274 (46%)

Table (3): Anti-bacterial and anti-fungal activities by measuring zone of inhibition (mm) and MIC ($\mu\text{g/ml}$) of the tested compounds with regard to reference drugs.

Comp. No.	Gram +ve		Gram -ve		Fungi			
	S. aur. mm/MIC	B. sub. mm/MIC	P. aer. mm/MIC	E. coli mm/MIC	A. Fum. mm/MIC	G. cand. mm/MIC	C. alb. mm/MIC	S. rac. mm/MIC
Ia	13/78	14.2/78	NA	NA	11.3/13	13/156	10/156	NA
Ic	NA	NA	NA	NA	14.3/313	3.4/313	12.2/156	NA
III	24.4/19	25.4/19	NA	10.8/156	19.2/39	20.4/39	18.2/78	NA
VIIIc	13.9/313	15.2/156	NA	NA	NA	NA	NA	NA
VIII d	20.4/39	21.8/78	NA	7.4/625	NA	NA	NA	NA
IXa	15/156	13.5/313	NA	NA	10/625	12/313	11/313	NA
IXb	NA	NA	NA	NA	NA	NA	NA	NA
XIIb	18.2/78	17.3/156	NA	9.4/625	13.2/156	15.4/78	12.4/156	NA
XIII	NA	NA	NA	NA	NA	NA	NA	NA
XIV	NA	NA	NA	NA	NA	NA	NA	NA
XV	16.2/78	12.3/313	NA	19.4/78	12.2/313	16.4/78	12.4/156	NA
XVI	23.2/39	24.3/39	NA	11.2/625	15.2/156	18.4/78	15.4/87	NA
Penic. G	29.5	32.6	28.3	33.6	----	----	----	----
Strepto.	25	29	24	25	----	----	----	----
Itrac.	----	----	----	----	28	27	26	22
Clotr.	----	----	----	----	26	23	18	20

NA: No Activity



**Corresponding author**

Nahed . F. Abdel-Ghaffar

Chemistry Department, Faculty of Science, Al-Azhar
University (for girl's) Egyptprof_nahed@yahoo.com**References**

1. Abbert.A. and Barlin, G.B.; Mercapto-derivatives of diazines.; *J. Chem. Soc.* (1962) 3129
2. Abdel-Aziz, M.A.; Daboun, H.A. and Abdel-Gawad, S.M.; -yanothioacetamide and Its Derivatives in Heterocyclic Synthesis. Preparation of Several New 4-Oxoquinazolinone Derivatives.; *J. Prakt. Chem.*; (1990) 332(5) 610
3. Adnan. A. K.; Synthesis and antimicrobial activity of some new quinazolin-4(3H)-one derivatives.; *J. of Saudi Chemical Society* .; (2010) 15(2):95-100
4. Al-Obaid, M. ; Abdel-Hameid, S. G.; El-Kashef, H. A.; Abdel-Aziz, A.A.M.; El-Azab, A.S.; Al-Khamees, H.A. and El-Subbagh, H.I.; Synthesis, In-Vitro Antitumor Activity and Molecular Modeling study of Certain 2-Thieno-4(3H)-quinazolinone Analogs.; *European Journal of Medicinal Chemistry* 44(2009) 2379-2391.
5. Al-Omar, .M. A.; El-Azb, A. S.; El-Obeid, H. A. and Abdel Hameide, S.G.; Invitro Interaction of 6-Iodo-4-oxo-quinazolinone derivatives with cytosolic molybdenum hydroxylases.; *J. Saudi Chem. Soc.*, 2006-10, 113.
6. Aly. A. A.; Synthesis and antimicrobial activity of some annelated quinazolinone derivatives.; *Journal of the Chinese Chemical Society*, 2007, 54, 437-446
7. Ayman.E.R., Mohamed.I.H., Randa.E.A., Nahed.F., Farouk.M.E.

- A.; Synthesis and anti-HSV-1 evaluation of some pyrazoles and fused pyrazolopyrimidines; *Eur. J. of Med. Chem.*; (2009), 44; 3285-3292.
8. Brown. D. J. The Chemistry of heterocyclic compounds Supplement (II), Jhon Wiley, Newjersey, (2005) 64, 235 .
 9. Chatrasal.S. R.; Sanjeev. K. and Ashok .K.; Synthesis and antifungal activity of newer substituted quinazolinones.; *International J. Chem. Tech. Res.*; (2010) 2(3): 1653-1660
 10. Divyesh. R. P and Keshav. C.P.; Synthesis and characterization of reactive dyes based on 2-phenyl-3- [4-(4-aminophenylsulphonamido)]phenyl-4(3H)-quinazolinone-6-sulphonic acid .; *Arbian Jornal of Chemistry* (2010).
 11. El-Helby, A.G.A. and Abdel-Wahab, M.H.; Design and synthesis of some new derivatives of 3H-quinazolin-4-one with promising anticonvulsant activity., *Acta. Pharm.*, 53: 127-138 (2003).
 12. Fawzia. M. Refaie , Amr .Y. Esmat, Soad .M .Abdel -Gawad, Aida. M Ibrahim and Mona.A. Mohamed.; The antihyperlipidemic activities of 4(3H) quinazolinone and two halogenated derivatives in rats .; *Lipids in Health and Disease* 2005, 4, 22.
 13. Ghorab. M.M, El-Sayed. B. S, Saker .H.M, Abd Rabo. M.M.; Synthesis and antitumor activity of some novel quinazoline derivatives bearing the biologically active thione moiety.; *Arzneimittelforschung*. 2006; 56(9): 665-70
 14. Gupta.V, Kashaw.S.K, Jatav.V, Mishra.P.; *Med. Chem. Res.*, 17(2008) 205-211.
 15. Hamed, M.S.; Kamel, M.M.; Kassem, M.M.; Emad, N; Nofal, M.S. and Ahmed, F.M. ; Novel 6,8-dibromo-4(3H)-quinazolinone derivatives of promising anti-inflammatory and analgesic properties.; *Acta .Poloniae Pharmaceutica-Drug Research.*, 67(2) : 159-171 (2010)
 16. Jessy, E.M.; Vachala, D.; Navneet, K. and Srinivassan, K. K. Pharmacological potential of some novel quinazolin-4(3H)-ones.; *Pharmacology online* 2: 618-623 (2008).
 17. Kaur, R, Bansal, M, Kaur, B.; Synthesis of Some New Quinazoline Derivatives and Theoretical Studies of their Geometries.; *Chemical Sciences J.*; 2011: CSJ-18
 18. Kaure, P.; Kaur, R. and Kaur, K.; Quinazolinone peptides: New approach as potent medicinal agents.; *J. Global Pharma Technology*: 35-39 (2009).
 19. Kluytmans, J., Van. B.A, Verbrugh, H.; Nasal carriage of *Staphylococcus aureus*: epidemiology, underlying mechanisms, and associated risks.; *Clin. Microbiol. Rev.*, 10 (1997) 505-20.
 20. Lixia. Z, Lige. R, Minghui .B, Liwei .W, Jing .H, Lin. Wu, Minggang .D, Xiang .Z.; Synthesis and biological activities of quinazoline derivatives with ortho-phenol-quaternary ammonium salt groups.; *Bioorganic & Medicinal Chemistry* (2007) 15(22): 6920-6926
European Committee for Antimicrobial Susceptibility Testing (EUCAST) of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), Determination of minimum inhibitory concentrations (MICs) of antibacterial agents by agar dilution, *Clin. Microbiol. Infect. Suppl.* 6 (9) (September 2000).
 21. Manson. S. F.; The tautomerism of *N*-heteroaromatic hydroxy-compounds. Part I. Infrared spectra.; *J. Chem. Soc.*, (1957) 4874.25- Heurn. J. M, Morton. R.A. and Simpson. J. C. The addition of toluene- thiol to unsaturated compounds.; *J. Chem. Soc.*, (1951) 3318 .
 22. Mosaad. S.M.; Mohsen. M. K.; Emad. M. M. and Kassem. N. .A.; Novel 6,8-Dibromo-4(3H)quinazolinone Derivatives of Antibacterial and Antifungal Activities.; *Eur. J. Med. Chem.*, 45: 3311-3319 (2010).
 23. Murugesan. D, Periyaswamy .S, Erik. D and Seshaiha. K. S., Synthesis, Antiviral and Cytotoxic Activity of 6-Bromo-2,3-disubstituted-4(3H)-quinazolinones.; *Biol. Pharm. Bull.* 26(9): 1278-1282 (2003).
 24. National Committee for Clinical Laboratory Standards, Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically Approved Standard M7eA5, fifth ed. NCCLS, Wayne, PA, 2000.
 25. Ommeh. Sh.; Nduati. E.; Mberu. E.; Kokwaro. G.; Mash. K.; Rosowsky. A. and Nazila. A.I.; In vitro activities of 2,4-diaminoquinazoline and 2,4-diaminopteridine derivatives against *Plasmodium falciparum*.; *Antimicrobial Agents and Chemotherapy*, 48(10): 3711-3714 (2004).
 26. Patel. N.B. and Barat. G.G.; In vitro microbial studies of new pyrazolyl quinazolin-4(3H)ones.; *J. Saudi Chem. Soc.*; (2010) 14: 157-164
 27. Patel. N.B., Barat. G.G.; In Vitro Microbial Studies of New Pyrazolyl Quinazolin-4(3H) Ones. *J. Saud. Chem. Soc.*, 14(2010) 157-164.
 28. Reddy. P.S.N.; Vasantha. M. and Reddy V.D.; Antibacterial , antifungal and antifeedant activity of quinazolinonyl- lactams/quinazolinones and bis (quinazolinonyl- lactams).; *Rasayan J. Chem.*, (2010) 3(4): 635-640
 29. Sarika. M, Neelam. S, Madhuri .V, Jitendra .V, Pinki. B. P, and Suresh C. A.; Synthesis and Characterization of Some Quinazoline Derivatives as Potential Antimicrobial Agents under Microwave Irradiation.; *Bull. Korean Chem. Soc.*; (2007), 28(12): 2338
 30. Shashikant, V. B.; Bhavana, J.D.; Sudarshan, C.D.; Suraj, T. G.; Vankelesh, T.R.; Chetan, V.K. and Anik et, P.S.; Influence of Lipid-Soluble Gating Modifier Toxins on Sodium Influx in Neocortical Neurons.; *Pharmacology online*, 2 : 604-613 (2008).
 31. Singhal, N, Sharma. P.K, Dudhe, R, Kumar. N.J.; Recent advancement of triazole derivatives and their biological significance.; *Chem. Pharm. Res.*, 3(2011) 126-133.
 32. Veerachamy, A.; Velchamy, M.; Nagendran, P.; Poongavam, V. and Rajappan, R. Synthesis, Analgesic and Anti-inflammatory Activities of Some Novel 2,3-Disubstituted Quinazolin-4(3H)-ones.; *Biol. Pharm. Bull.* 26(4): 557-559 (2003).
 33. Veerachamy, A.; Viswas, R. S.; Gnanavel, V.; Veeran, P.; uniyandi, R. Ch.; Augustin, A.S.; Arunachalam, Th.; Muniyandi, R. C.; Siaaperuman, A. and Rajappan, R. Synthesis, Analgesic, Anti-inflammatory and Antibacterial Activities of Some Novel 2-Phenyl-3-substituted Quinazolin-4(3H) Ones.; *Biol. Pharm. Bull.*, 25(11): 1432-1435 (2002).
 34. Vijayakumar. K and Jafar. A.; Synthesis and biological activities of some novel substituted quinazolinone derivatives.; *Der Pharma Chemica*, 2010, 2(5): 453-457
 35. Vivek. G.; Sushil. K. K and Varsha. J.; Effect of berberine on expressions of uncoupling protein-2 mRNA and protein in hepatic tissue of non-alcoholic fatty liver disease in rats.; *J. Med Chem Res.*; (2008) 17: 205-211

6/12/2011