Egypt. J. Chem. **Vol. 66**, No. 6, pp. 493 – 498 (2023)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Design Synthesis and Characterization of New Quinazolin-4(3H)-ones with Anticipated Pharmacological Efficacy

M. E. Shaban and A. K. El-ziaty*

Chemistry Department, Faculty of Science Ain Shams University, Abbassia. Cairo, 11566, Egypt

Abstract

The previously mentioned 6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4(3H)-one **1** was constructed and utilized as a building block for the synthesis of quinazolinone derivatives **2–11** with significant expected medicinal efficiency . The reaction of the hydrazinyl derivative **9** with carbon disulfide led to the formation of 7,9-dibromo-5-(3,4-dichlorophenyl)-[1,2,4]triazolo[4,3-c]quinazoline-3(2H)-thione **12**. From the compound 6,8-dibromo-2-(3,4-dichlorophenyl)quinazoline-4(3H)-thione **8** came the quinazolinone derivatives **13–16.** Physical and chemical methods were used to characterize the constructed products.

Key Wards: quinazolin-4(*3H*)-one, quinazoline-4(*3H*)-thione and triazolo[4,3-c]quinazoline,

Introduction

Quinazolinones are a family of heterocyclic nitrogen compounds that have gained popularity due to the wide range of biological functions they possess.

A group of novel 4-butyl-1-substituted-4H-[1,2,4]triazolo [4,3-a] quinazolin-5-ones were synthesized by the cyclization of 3-butyl-2-hydrazino- 3H-quinazolin-4-one with various one carbon donors and showed H1-antihistaminic activity[1]. Some 2-[(E)-2 furan-2-yl-vinyl]-quinazolin- 4(3H)-ones incorporated into pyrazoline, isoxazoline, pyrimidine or pyrimidine-thione ring systems at position-3 of the quinazoline ring. The antimicrobial and antiinflammatory activities of these derivatives were investigated [2].

Thirty new 2-(substituted)-3-{[substituted]amino}quinazolin-4(3H)-one were designed and synthesized keeping in view the structural requirement of pharmacophore and evaluated for anticonvulsant activity and neurotoxicity[3]. A series of novel Schiff bases were synthesized by condensation of 3-amino-6,8-dibromo-2-phenylquinazolin- 4(3H)-ones with different aromatic aldehydes via cyclized intermediate 6,8-dibromo-2-phenyl benzoxazin-4-one. These compounds were screened for antibacterial (Staphylococcus aureus ATCC-9144, Staphylococcus epidermidis ATCC-155, Micrococcus luteus ATCC-4698, Bacillus cereus ATCC-11778, Escherichia coli ATCC-25922, Pseudomonas aeruginosa ATCC-2853, and Klebsiella pneumoniae ATCC-11298) and antifungal (Aspergillus niger ATCC-9029 and Aspergillus fumigatus ATCC-46645) activities by paper disc diffusion technique. The minimum inhibitory concentrations (MICs) of the compounds were also determined by agar streak dilution method4. The synthesis and in vitro antimicrobial activity of various 3-(1,3,4-oxadiazol-2-yl)- quinazolin-4(3H)-ones were reported, the antimicrobial activity of title compounds was examined against two gram positive bacteria (S. aureus, S. pyogenes), two gram negative bacteria (E. coli, P. aeruginosa) and three fungi (C. albicans, A. niger, A. clavatus) using the broth microdilution method. Some derivatives bearing a bromo or iodo group exhibited very good antimicrobial activity [5].

2,3-disubstituted-3,4-dihydro-2H-1,3-benzoxazines were prepared in moderate to excellent yields by aza-acetalizations of aromatic aldehydes with 2-(N-substituted aminomethyl)phenols in the presence of TMSCl. Their structures were confirmed by IR, ^{1}H-NMR, ^{13}C-NMR, MS and elemental analysis. The fungicidal activities of the target compounds were preliminarily evaluated, and some compounds exhibited good activity against *Rhizoctonia solani*[6a]. Pyrazolyl-quinazolin-4(3H)-ones have been synthesized from 2-[2-(phenylamino)phenyl] acetic acid by using efficient methods. These compounds have been screened against bacterial as

*Corresponding author e-mail: ahm512@sci.asu.edu.eg.; (A. K. El-ziaty).

Receive Date: 26 April 2023, Revise Date: 25 May 2023, Accept Date: 26 May 2023

DOI: 10.21608/EJCHEM.2023.207385.7905

©2023 National Information and Documentation Center (NIDOC)

well as fungal microorganisms. Quinazolinones and quinazolines were considered a nucleus of numerous pharmacological heterocycles[6b] as shown in figures 1 and 2

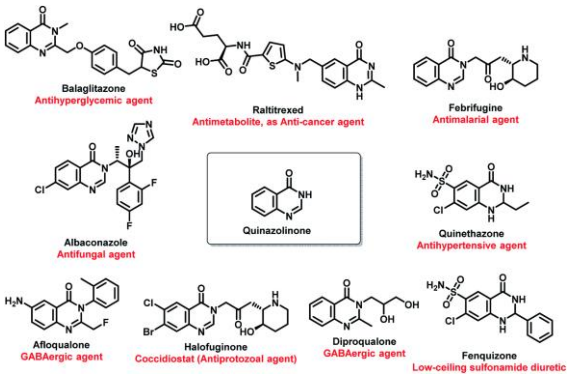


Fig.1: Pharmacological importance of quinazolinone-based drugs.

These compounds' potency was estimated and contrasted with that of conventional medicines. i.e. Penicillin-G and Fluconazole. Some of the compounds showed very good antimicrobial activity[7]. Spectral data indicated that the studied compounds exist predominantly in the hydrazone tautomeric form. The recently synthesized compounds' antibacterial efficacy was also assessed. The results indicated that some of these compounds have moderate activity towards bacteria [8].

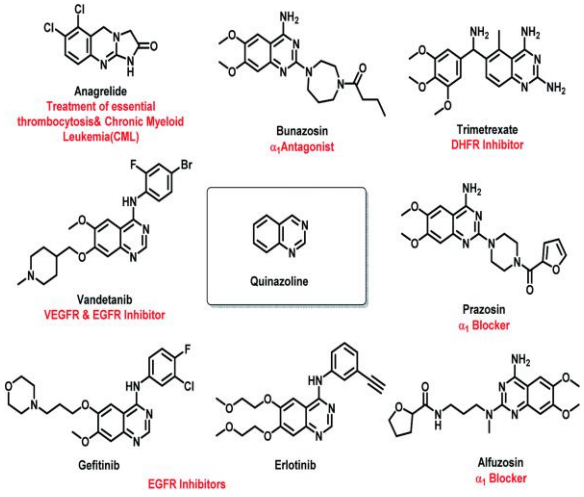


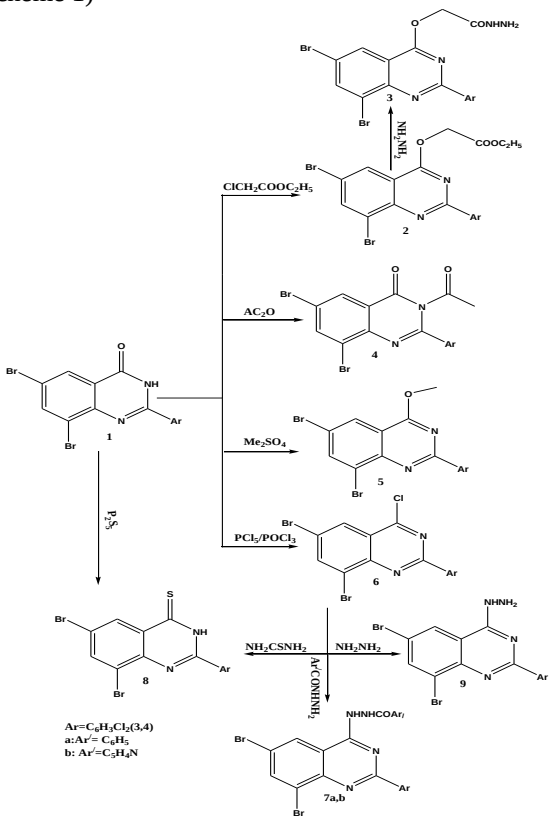
Fig.2: Pharmacological importance of quinazoline-based drugs.

As part of our research, we are interested in construction of new synthetic pathways for a range of quinazolinone substrates that have interesting biological and pharmacological properties [9-27], In this article, we provide a report. the synthesis of a new series of 6,8-dibromo-2-(3,4-dichlorophenyl) quiinazollin-4-one with anticipated pharmaceutical activities.

Results and Discussion:

The previously reported [9], 6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4(*3H*)-one **1** was synthesized, and allowed to react with different electrophilic reagents such as ethyl chloroacetat and acetic anhydride to afford ethyl 2-(6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-yloxy)acetate **2** and 3-acetyl-6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4(3H)-one **4** respectively the structure of **2** was confirmed from its I.R spectrum showed a strong absorption band at 1739 cm^{-1} for the carbony ester functional group, and the absence of the absorption of NH group also the ^{1}HNMR showed the (t,3H) and (q,2H) at 2.45 and 4.13ppm respectively. ^{1}H-NMR spectrum of **4** (DMSO-d_6) revealed the following signals at δ (ppm) 7.16-7.70 (m,5Harom.), 4.13 (s,3H,CH_3).

Hydrazinolysis of **2** afforded hydrazinoyl quinazolinone derivative **3** which structure was elucidated from its elemental and spectral analysis. Methylation and chlorination of **2** afforded 4-methoxy and 4- chloro quinazolinones **5,6** respectively, their structure were confirmed from the elemental and spectral analysis, the I.R displayed no absorption band characteristic for the carbonyl group. (Scheme 1)



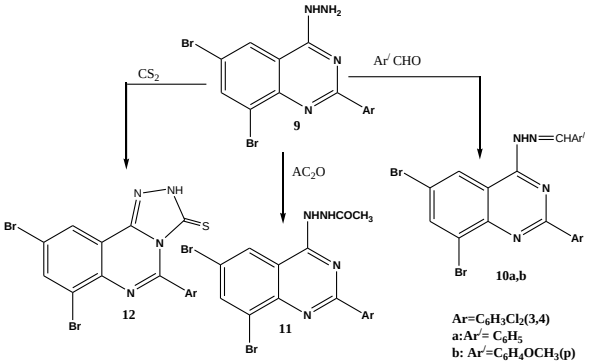
Scheme 1: Reaction on quinazolin-4(*3H*)-one building block

Nucleophilic substitution of 4-chloro quinazoline derivative **6** with benzoyl hydrazine ,nicotinoyl hydrazine and hydrazine yielded the quinazolinone derivatives **7a,b** and **9**.

Thiourea reacted with 4- chloroquinazoline derivative **6** to give 6,8-dibromo-2-(3,4-dichlorophenyl) quinazoline-4(3H)-thione **8**, the structure of **8** was elucidated chemically by synthesis, from the reaction of quinqzolinone derivative **2** with P_2S_5. and with Lawesson's reagent (Scheme 1).

4-hydrazinyl quinazoline derivative **9** was allowed to react with nucleophilic reagents such as benzaldehyde, 4- methoxy benzaldehyde and acetic anhydride gave the scheiff bases **10a,b** and acetohydrazide derivative **11**.

7,9-dibromo-5-(3,4-dichlorophenyl)-[1,2,4]triazolo[4,3-c]quinazoline-3(2H)-thione **12** was constructed from the reaction of **9** with carbon disulfide, the structure of these new quinazolinone derivative were confirmed from their elemental and spectral analysis. **(c.f. Exp.)**. (Scheme 2)



Scheme 2: Reaction on 4- Hydrazinyl-6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4(*3H*)-one

The formation of the thione derivative **8** was discussed in the following mechanism.

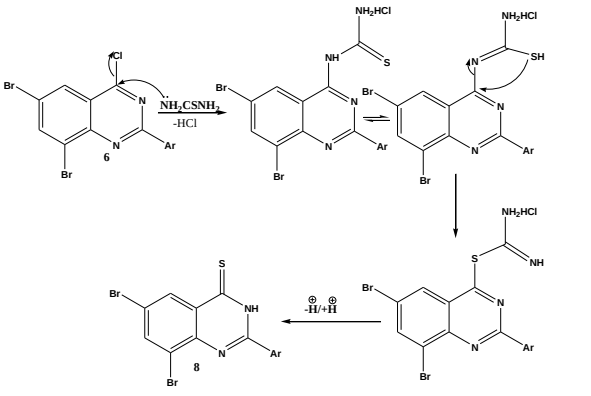
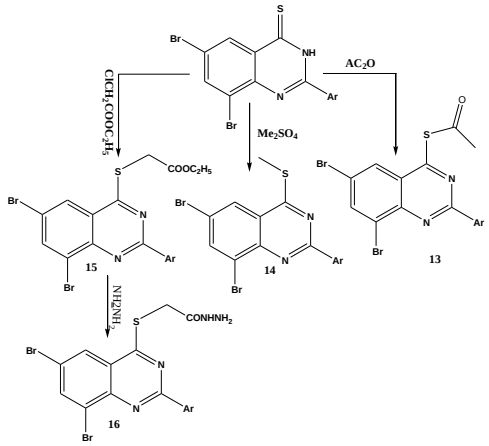


Figure 3: the mechanistic process via which compound 8 is created.

Acetylation of 6,8-dibromo-2 -(3,4-dichlorophenyl)quinazoline-4(*3H*)-thione **8** afforded S-6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-yl ethanethioate **13**. The structure of **13** was elucidated from its I.R spectrum showed 1695 (C=O) and 1605 (C=N). Alkylation of **8** by dimethylsulfate and ethyl chloroacetate yielded 6,8-dibromo-2-(3,4-dichlorophenyl)-4-(methylthio)quinazoline **14** and ethyl 2-(6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-ylthio)acetate **15**. The structure of **15** was confirmed from its ^{1}HNMR which reviled the following signals. 7.76-7.49 (m,5Harom.), 4.16.5 (s,2H, CH_2), 4.23 (q,2H), 2.95 (t,3H, CH_3).

2-(6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-ylthio)acetohydrazide **16** was constructed by hydrazinolysis of **15.** (Scheme 3)



Scheme 3: Reaction on 6,8-dibromo-2-(3,4-dichlorophenyl)quinazoline-4(*3H*)-thione

1. Experimental:

Electric melting point apparatus (G-K) was used to measure the melting points, which are uncorrected. Using the KBr Wafer method, the IR spectra were captured using a Pye-Unicam SP1200 spectrophotometer. On a Varian GEMINI 200 MHz NMR spectrophotometer, the 1H-NMR spectra were calculated using TMS as an internal standard and CDCl3 or DMSO-d6 as the solvent. All chemical changes are measured in ppm away from the TMS. The science faculty at Ain Shams University conducted the elemental analysis. TLC was used to keep track of the timing of each reaction and the homogeneity of the synthesized molecule.

ethyl 2-(6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-yloxy)acetate (2)

ethyl chloroacetate (0.04 mol) was added to a mixture of **1** (0.01 mol) and potassium carbonate anhydrous (0.04 mol) in dry acetone (30 ml), the reaction mixture was refluxed on water bath for 10 hours. the solvent was evaporated and the residue was collected

and triturated with water (30ml) three times, the solid produced was filtered off, dried and recrystallized from benzene to give **2** as yellow crystals. m.p: 163-164°C, yield 63%. Anal. Calcd.: for $C_{18}H_{12}Br_2Cl_2N_2O_3$ (535): C, 40.37; H, 2.24; N, 5.23 Found: C, 40.23; H, 2.22; N, 5.21; IR (υcm^{-1}): 1739 cm^{-1} (C=O$_{ester}$), 1616 cm^{-1} (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): 7.66-7.59 (m,5Harom.), 4.56 (s,2H, CH_2), 4.13 (q,2H, CH_2), 2.45 (t,3H, CH_3).

2-(6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-yloxy)acetohydrazide (3)

A mixture of **2** (0.01 mol) and hydrazine hydrate (0.01mol) was refluxed in 50 ml ethanol for 5 hours. The solvent was concentrated and the solid separated was filtered off and recrystallized from dioxane to give **3** as white crystals. m.p: 281-283°C, yield 73%. Anal. Calcd.: for $C_{16}H_{10}Br_2Cl_2N_4O_2$ (521): C, 36.85; H, 1.92; N, 10.74 Found: C, 36.67; H, 1.86; N, 10.68; IR (υcm^{-1}): 1652 cm^{-1} (C=O), 1616 cm^{-1} (C=N).3145cm^{-1} (NH) and 3345,3325NH$_2$. ^{1}H-NMR (DMSO-d_6) δ (ppm):10.02 (s,1H, NH) vanished by D_2O. 8.06-7.80 (m,5Harom.), 6.06.5 (s,2H, NH_2) vanished by D_2O, 4.13 (s, 2HCH$_2$).

3-acetyl-6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4(3H)-one (4)

A mixture of **1** (0.01mol) and acetic anhydride (20ml) was refluxed for 10 hours. The solvent was concentrated and the solid formed was filtered off and crystallized from ethanol/dioxane to give **4** as colourless crystals m.p over 300^{0}C. yield 53%. Anal. Calcd.: for $C_{16}H_8Br_2Cl_2N_4O_2$ (491): C, 39.10; H, 1.63; N, 5.70 Found: C, 38.90; H, 1.57; N, 5.62; IR (υcm^{-1}): 1692 (acetyl C=O) and 1652cm^{-1} (Cyclic C=O), 1606 cm^{-1} (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): 7.16-7.70 (m, 5Harom.), 4.13 (s,3H, CH_3).

6,8-dibromo-2-(3,4-dichlorophenyl)-4-methoxyquinazoline (5)

To a mixture of **1** (0.01mol) and anhydrous potassium carbonate (0.04mol) in dry acetone (30ml), dimethylsulfate (0.04mol) was added, the reaction mixture was refluxed on water bath for 10 hours. The solvent was removed and the residue was triturated with water (30ml), the solid separate was filtered off, dried and recrystallized from petroleum ether(80/100)/benzene mixture to give **5** as light yellow crystals m.p over 172-174^{0}C. Yield 67%. Anal. Calcd.: for $C_{15}H_8Br_2Cl_2N_4O$ (463): C, 38.87; H, 1.73; N, 5.89 Found: C, 38.56; H, 1.56; N, 5.89; IR (υcm^{-1}): 1610 cm^{-1} (C=N).^{1}H-NMR (DMSO-d_6) δ (ppm): 7.96-7.63 (m,5Harom.), 5.21 (s,3H, OCH_3).

6,8-dibromo-4-chloro-2-(3,4-dichlorophenyl)quinazoline (6)

A mixture of **1** (5g) and phosphours oxychloride (50ml) and phosphourus pentachloride (10g) was heated on wat**er** bath for 8 hours.after cooling, the reaction mixture was added to crushed ice and solid separated washed with water(3x20ml), dried and crystallized from benzene to give **6** as yellow crystals m.p over 176-178^{0}C. Yield 74%. Anal. Calcd.: for $C_{14}H_5Br_2Cl_3N_4O$ (467.5): C, 35.94; H, 1.06; N, 5.98 Found: C, 36.10; H, 1.12; N, 5.98; IR (υcm^{-1}): 1603 cm^{-1} (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): 8.01-7.89 (m, 5H, arom.).

N'-(6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-yl)benzohydrazide (7a)

N'-(6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-yl)nicotinohydrazide (7b)

A mixture of **6** (0.01mol) and (0.01mol) of benzoyl hydrazine and /or nicotinoyl hydrazine in (15 ml) n butanol was refluxed for 48 hours. The solvent was evaporated and the solid formed was crystallized from di methylformamide to give (7a,b).

7a: yellow crystals m.p over 300^{0}C. Yield 44%. Anal. Calcd.: for $C_{21}H_{12}Br_2Cl_2N_4O$ (567):C, 44.48; H, 2.12; N, 9.87 Found: C, 44.38; H, 2,09; N, 9.78; IR (υcm^{-1}): 3245cm^{-1}(NH), 1662cm^{-1} (C=O), 1606 cm^{-1} (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): 11.02 (s,1H,NH) and 8.03 (s,1H, NH) vanished by D_2O) 7.56-7.73 (m,5H, arom.), 7.70-7.57 m,5H, arom.)

7b: yellow crystals m.p. over 288-290^{0}C. Yield 62%. Anal. Calcd.: for $C_{21}H_{11}Br_2Cl_2N_5O$ (568): C, 44.25; H, 1.93; N, 12.32 Found: C, 44.15; H, 1.84; N, 12.32; IR (υcm^{-1}): 3265,(NH), 1668, (C=O), 1605 (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): 10.92 (s,1H, NH) and 8.12 (s,1H, NH) vanished by D_2O) 7.92-7.83 (m, 5Harom.), 7.64-7.50 m, 4Harom.)

6,8-dibromo-2-(3,4-dichlorophenyl)quinazoline-4(3H)-thione (8)

Procedure A:

A mixture of **1** (0.01mol) and Lawesson's reagent (0.005mol) in dry DMF (50ml) was refluxed for 12 hours. The solid separated was filtered off and the filtrate was concentrated to the third, the solid separated was filtered off and recrystallized from dioxane .

Procedure B:

A mixture of **1** (0.01mol) and phosphotous pentasulfide(0.015mol) in dry DMF(50ml) was refluxed for 24 hours. The unreacted P_2S_5 was filtered off and the solvent was removed. The crude mass was recrystallized from dioxane.

Procedure C:

A mixture of **6** (0.01mol) and thiourea (0.01mol) in ethanol (30ml) was refluxed for 5 hours, solvent was removed and the solid was triturated with water, the crude solid was recrystallized from dioxane to give **8** as yellow crystals m.p over 275-277^{0}C. Anal. Calcd.: for $C_{14}H_6Br_2Cl_2N_2S$ (465): C, 36.13; H, 1.29; N, 6.02 Found: C, 35.93; H, 1.28; N, 5.74; IR (υcm^{-1}): 3265, (NH), 1605 (C=N) and1268, (C=S),. ^{1}H-NMR (DMSO-d_6) δ (ppm): 10.92 (s,1H, NH) vanished by D_2O) 7.54-7.25 (m, 5Harom.)

1-(6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-yl)hydrazine (9)

A mixture of **6** (0.01mol) and hydrazine hydrate (0.02mol) was refluxed in (30ml) ethanol for 5 hours. The solvent was concentrated and the solid formed was filtered off and recrystallized from mixture of benzene/ethanol to give **9** as orange crystals m.p over over 300^0C. Yield 37%. Anal. Calcd.: for $C_{14}H_8Br_2Cl_2N_4$ (463): C, 36.28; H, 1.72; N, 12.09 Found: C, 36.78; H, 1.66; N, 12.33; IR (υcm^{-1}): 3365, 3289-3212(NH and NH_2) and 1605 (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): 6.22 (s,1H, NH) and 2.12 (s,2H, NH_2) vanished by D_2O), 7.64-7.50 (m, 5Harom.)

6,8-dibromo-2-(3,4-dichlorophenyl)-4-(1-benzylidenehydrazine)quinazoline (10a)
6,8-dibromo-2-(3,4-dichlorophenyl)-4-(1-methoxybenzylidenehydrazine)quinazoline (10)b

A mixture of **9** (0.01mol) and benzaldehyde and/or *p*-anisaldehyde (0.01mol) was refluxed for 3 hours. The solvent was evaporated and the solid was recrystallized fron the proper solvent.

10a: recrystallized from benzene, yellow crystals m.p over 221-223^0C. Yield 56%. Anal. Calcd.: for $C_{21}H_{12}Br_2Cl_2N_4$ (551): C, 45.73; H, 2.17; N, 10.16 Found: C, 45.62; H, 1.88; N, 10.09; IR (υcm^{-1}): 3184, (NH) and 1605 (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): (7.64-7.50 m,5Harom.) 6.01 (s,1H, NH) disappedred by D_2O), 5.87 (s,1H =CH)

10b: recrystallized from ethano/dioxane, yellow crystals m.p over over 231-233^0C. Yield 49%. Anal. Calcd.: for $C_{22}H_{14}Br_2Cl_2N_4O$ (581): C, 45.43; H, 2.40; N, 9.63 Found: C, 45.79; H, 2.26; N, 8.78; IR (υcm^{-1}): 3164, (NH) and 1611 (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): (7.54-7.40 m,5Harom.) 5.91 (s,1H, NH) disappedred by D_2O), 5.26 (s,1H =CH)

N'-(6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-yl)acetohydrazide (11)

The hydrazinoquinazolinone 9 (0.01mol) was refluxed in acetic anhydride (15ml) for 12 hours. The solvent was evaporated and the residue was recrystallized from benzene to give **11** as yellow crystals. m.p 281-283^0C. Yield 55%. Anal. Calcd.: for $C_{16}H_5Br_2Cl_2N_4O$ (505): C, 38.02; H, 1.98; N, 11.09 Found: C, 37.96; H, 1.67; N, 10.98; IR (υcm^{-1}): 3184,3298 (NH), 1665 (C=O) and 1605 (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): 10.01 (s,1H, NH) disappedred by D_2O) (7.64-7.50 m,5Harom.) 4.87 (s,3H, CH_3) and 2.11 (s,1H, NH) disappedred by D_2O),

7,9-dibromo-5-(3,4-dichlorophenyl)-[1,2,4]triazolo[4,3-c]quinazoline-3(2H)-thione (12)

A mixture of **9** (0.01mol) in alcoholic potassium hydroxide and carbon disulfide (10ml) was refluxed on water bath for four hours. The solvent was evaporated and the residue was triturated with cold hydrochloric acid, the crude solid was filtered off, washed with water, dried and recrystallized from dioxane to give **12** as brown crystals. m.p 281-283^0C. Yield 65%. Anal. Calcd.: for $C_{15}H_6Br_2Cl_2N_4S$ (505): C, 35.64; H, 1.18; N, 11.09 Found: C, 35.53; H, 1.14; N, 10.97; IR (υcm^{-1}): 3184,3298 (NH), 1665 (C=O) and 1605 (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): 9.21 (s,1H, NH) disappedred by D_2O) (7.64-7.50 m,5Harom.).

S-6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-yl ethanethioate (13)

A mixture of **8** (0.01mol) and acetic anhydride (20ml) was refluxed for 10 hours. The solvent was concentrated and the solid formed was filtered off and recrystallized from dioxane to give **13** as yellow crystals. m.p 289-291^0C.Yield 45%. Anal. Calcd.: for $C_{16}H_8Br_2Cl_2N_2OS$ (507): C, 37.86; H, 1.57; N, 5.52 Found: C, 38.00; H, 1.34; N, 5.43; IR (υcm^{-1}): 1695 (C=O) and 1605 (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): (7.64-7.50 m,5Harom.). and 3.94(s,3H, CH_3).

6,8-dibromo-2-(3,4-dichlorophenyl)-4-(methylthio)quinazoline (14)

A mixture of thion **8** (0.01mol) and potassium carbonat anhydrous (0.04 mol) in dry acetone (30 ml) dimethylsulfate(0.04 mol) was added, the reaction mixture was refluxed on water bath for 10 hours. the solvent was removed and the residue was triturated with water (30ml), the solid produced was filtered off, dried and recrystallized from benzene to give **14** as yellow crystals. m.p: 199-201°C. Yield 63%. Anal. Calcd.: for $C_{15}H_8Br_2Cl_2N_2S$ (479): C, 35.75; H, 1.67; N, 5.84 Found: C, 35.67; H, 1.48; N, 5.72; IR (υcm^{-1}): 1616 cm^{-1} (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): 7.66-7.59 (m,5Harom.), 2.65 (t, 3H, CH_3).

ethyl 2-(6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-ylthio)acetate(15)

A mixture of thion **8** and potassium carbonat anhydrous (0.04 mol) in dry acetone (30 ml) ethyl chloroacetate (0.04 mol) was added, the reaction mixture was refluxed on water bath for 10 hours.the solvent was removed and the residue was triturated with water (30ml), the solid produced was filtered off, dried and recrystallized from ethanol to give **15** as pale yellow crystals. m.p: 187-189°C. Yield 63%. Anal. Calcd.: for $C_{18}H_{12}Br_2Cl_2N_2O_2S$ (535): C, 39.20; H, 2.18; N, 5.08 Found: C, 39.80; H, 2.07; N, 5.00; IR (υcm^{-1}): 1722 cm^{-1}, (C=$O_{thioester}$), 1611 cm^{-1} (C=N). ^{1}H-NMR (DMSO-d_6) δ (ppm): 7.76-7.49 (m,5Harom.), 4.16.5 (s,2H, CH_2), 4.23 (q,2H), 2.95 (t,3H, CH_3).

2-(6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4-ylthio)acetohydrazide (16)

A mixture of **15** (0.01 mol) and hydrazine hydrate (0.01mol) was refluxed in 30 ml ethanol for 5 hours. The solvent was concentrated and the solid separated was filtered off and recrystallized from dioxane to give **3** as white crystals. m.p: 281-283°C, yield 73%. Anal. Calcd.: for $C_{16}H_{10}Br_2Cl_2N_4O_2S$ (537): C, 35.75; H, 1.86; N, 10.42 Found: C, 35.08; H, 1.32; N,

10.41; IR (υcm^{-1}): 1662 cm^{-} (C=O), 1606 cm^{-1} (C=N).3165cm^{-1} (NH) and 3355,3385NH_2. ^{1}H-NMR (DMSO-d_6) δ (ppm):10.42 (s,1H, NH) vanished by D_2O. 8.06-7.80 (m,5Harom.), 6.06.5 (s,2H, NH_2) vanished by D_2O, 4.13 (s,2H, CH_2).

Acknowledgment:
The authors wish to express their deep thanks and gratitude Professors A. M. Yousef and N. K. Elaaser for their valuable advice, during the preparation of this article. We wish to express our thanks and appreciation to all members of the chemistry department, Faculty of Science, ASU.

Conclusion:
In this work, we were able to synthesize and characterize several heterocyclic compounds that we hope will have medicinal effective activity.

References:

1. V. Alagarsamy; D. Shankar and S. Murugesan *Biomedicine & Pharmacotherapy* **62**, 173 (2008)
2. O. A. M. Fathalla; E. M. M. Kassem; N. M. Ibrahem and M. M. KAMEL. *Acta Poloniae Pharmaceutica* -Drug Research, **65**(1) 11 (2008)
3. P. Kumar; B. Shrivastava; S. N. Pandeya and J. P. Stables *European Journal of Medicinal Chemistry* **46** 1006 (2011)
4. P. Panneerselvam; B. A. Rather; D. R. S. Reddy and N. R. Kumar *European Journal of Medicinal Chemistry* **34** 1 (2008)
5. N. B. Patel and J. C. Patel. *Sci Pharm* **78**. 171 (2010)
6. 6a: Zi. Tang; Z. Zhu; Z. Xia; H. Liu; J. Chen; W. Xiao and X. Ou. *Molecules*, **17,** 8174 (2012) 6b: P. S. Auti , G. George and A. T. Paul RSC Adv., **10**, 41353 (2020,)
7. N. B. Patela; J. C. Patela; S. D. Patela and G. G. Baratb *the electronic journal of chemistry* **2(3)** (2010)
8. T. A. Farghaly; M. M. Edrees and M. A. Mosselhi. *Molecules*, **17**, 8483 (2012).
9. M.E. Shaban, A.M. Youssef, N.K. Elaasar. A. K .El-Ziaty. *Pak. J. Sci. Ind. Res.* **51** (3), 119 *(2008).*
10. S. A. Shiba; A.K. El-Ziaty; N.K. El-Aasar and H.A. Al-Saman. *J. Chem. Res*., 500. (2008)
11. S. A. Shiba; A.K. El-Ziaty; N.K. El-Aasar and H.A. Al-Saman. *Journal of Chemical Research*, **9**. 500. (2008)
12. El-Ziaty, A.K., Bassioni, G., Hassan, A.M.A., Derbala, H.A., Abdel-Aziz, M.S., *Journal of Chemistry*, , 5286462 (2016)
13. M.R. Mahmoud; A.K. El-Ziaty and A.M. Hussein. *Synthetic Communications.* **43** (7), 961 (2013).
14. M.M. Elshahawi; A.K. EL-Ziaty; J.M. Morsy and A.F. Aly. *Journal of Heterocyclic Chemistry* **53** (5), 1443 (2016).
15. N. S. El-Sayed; M. Sharma; H. M. Aliabadi; M. G. El-Meligy; A. K. El-Zaity; Z. A. Nageib and R. K. Tiwari. *International Journal of Biological Macromolecules* **112**, 694*(*2018)
16. W. A. M. A. El-Enany, , , S.M Gomha., , A.K El-Ziaty., ..., H.A Sallam., R.S. Ali, S*ynthetic Communications*, 50(1), pp. 85 (2020),
17. M.M. El-Shahawi and A.K. El-Ziaty *J. Chemistry* 610707 (2017)
18. A.A. El-Sayed; A.E.-G.E. Amr, A.K. EL-Ziaty and E.A. Elsayed. *Molecules* **24** (10),1965 (2019)
19. S.A. Shiba; A.K. El-Ziaty; N.K. El-Aasar and H.A. Al-Saman *Phosphorus, Sulfur and Silicon and the Related Elements* **185**(8), 1645 (2010)
20. M.R. Mahmoud; A.K. El-Ziaty; F.S.M.A bu El-Azm; M.F. Ismail and S.A. Shibab. *Journal of Chemical Research* **37**(2), 80 *(*2013)
21. M.R. Mahmoud; A.K. El-Ziaty; F.S.M.Abu El-Azm; M.F. Ismail. and S.A. Shibab. *Synthetic Communications* 44 (8),1094 (2014)
22. A.K. El-Ziaty and S.A. Shiba *Synthetic Communications* 37 (22), 4043 (2007).
23. L. A. Alshabanah , S. M. Gomha, L. A. Al-Mutabagani, T. Z. Abolibda, N. A. Abd El-Ghany, W. A. M. A. El-Enany, A. K. El-Ziaty, R. S. Ali and N. A. Mohamed *Polymers 13* Page: 1728 *(2021)*
24. S. K .Ramadan, , A.K. El-Ziaty,., E. A. E. El-Helw, *Synthetic Communications*, , 51(8), pp. 1272 (2021).
25. E. S. Shafik, A. Ismael, A. M. A. Hassan, H. A. Derbala, A. K. El-Ziaty, G. A. Elsayed. *KGK Kautschuk Gummi Kunststoffe, , 73(9), pp. 32 (2020)*
26. A.M. A. Hassan, H. A. Derbala1, Emad S. Shafik, A. I. Hussein, A. K. Elziaty and G. A. Elsayed *Egypt. J. Chem.* **63**, No. 6. Pp. 20- (2020)
27. N.S.EL-Sayed, , A.K.El-Ziaty, , M.G El-Meligy,., Z.A. Nagieb, Egyptian Journal of Chemistry, , 60(3), pp. 465 (2017)