World Journal of Chemistry 14 (1): 07-14, 2019
ISSN 1817-3128

DOI: 10.5829/idosi.wjc.2019.07.14

Synthesis of Novel 6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4(*3H*)-one Derivatives

M.E. Shaban, A.M. Yousef, N.K. Elaaser and A.K. El-Ziaty

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

Abstract: The previously reported 6,8-Dibromo-2-(3,4-dichlorophenyl)quinazolin-4(*3H*)-one **1** was constructed and used as a building block for synthesis of the quinazolinone derivatives **2-11** with an anticipated significant pharmaceutical activities. The 7, 9-dibromo-5-(3,4-Dichlorophenyl)-[1, 2, 4]triazolo[4, 3-c]quinazoline-3(2H)-thione **12** was performed from the reaction of the hydrazinyl derivative 9 with carbon disulfide. The quinazolinone derivatives **13-16** were prepared from 6,8-Dibromo-2-(3,4-Dichlorophenyl)quinazoline-4(*3H*)-thione **8** All the newly synthesized compounds were characterized by physical and chemical tools.

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

INTRODUCTION

A series 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 method [4]. 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 were 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* [6].

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 well as fungal microorganisms. The potency of these compounds was calculated and compared with standard drugs i.e. Penicillin-G and Fluconazole. Some of the compounds showed very good antimicrobial activity [7].

Corresponding Author: A.K. El-Ziaty, Department of Chemistry, Faculty of Science, Ain Shams University, Abbassia. Cairo, 11566, Egypt.

A simple strategy for 3-arylazo-4- phenyl- [1, 2, 4] triazepino[2, 3-*a*]quinazoline-2, 7(1*H*)-diones is described. Spectral data indicated that the studied compounds exist predominantly in the hydrazone tautomeric form. The antimicrobial activity of the newly synthesized compounds was also evaluated. The results indicated that some of these compounds have moderate activity towards bacteria [8].

As a part of our research interest towards developing new routes for the synthesis of a variety ofquinazolinone derivatives with promising biological and pharmacological activities [9-24], we report in the present article 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 prepared 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 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).

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**.

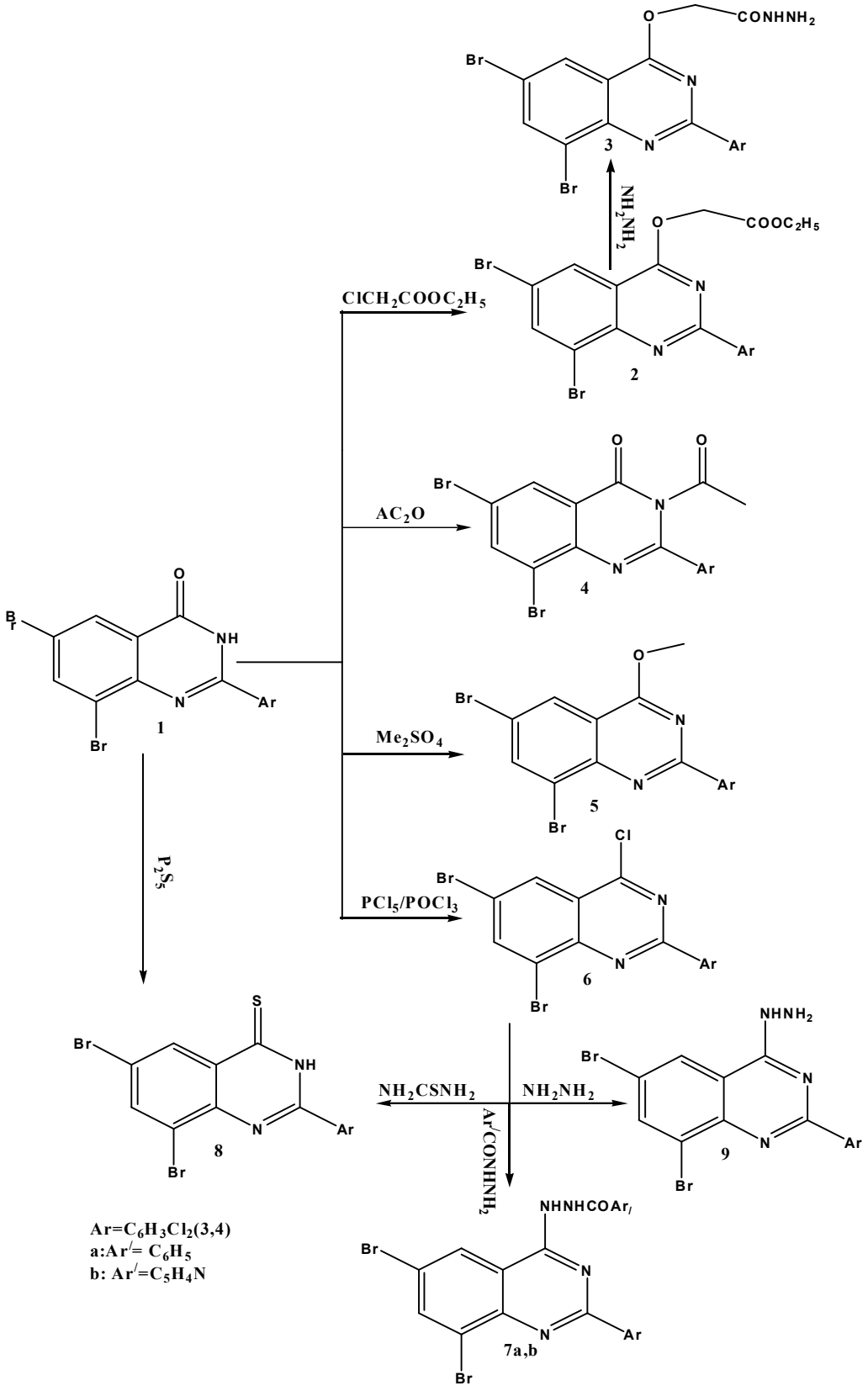
7, 9-dibromo-5-(3,4-Dichlorophenyl)-[1, 2, 4]triazolo[4, 3-c]quinazoline-3(2H)-thione **12** was constructed from the reaction of **9** with carbon disulfide, the structure of these new quinazolinone derivative were confirmed from their elemental and spectral analysis. (**c.f. Exp.**) (Scheme 2).

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).

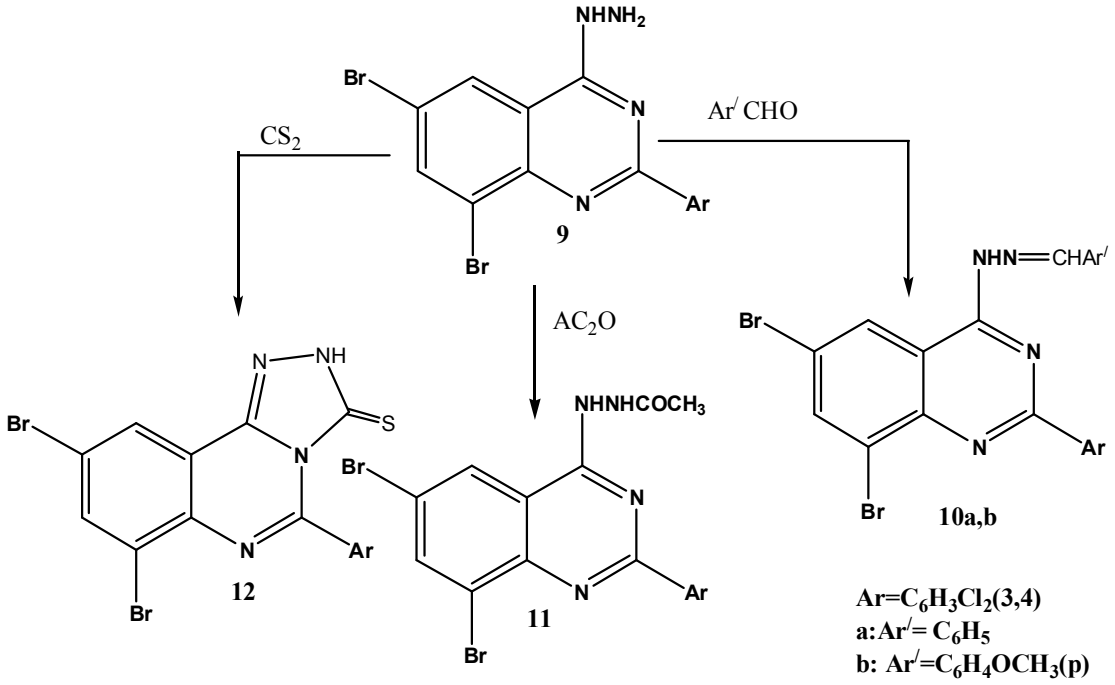
2-(6,8-Dibromo-2-(3,4-Dichlorophenyl)quinazolin-4-ylthio)acetohydrazide **16** was constructed by hydrazinolysis of **15** (Scheme 3).

Experimental: Melting points are uncorrected and were measured by an electric melting point apparatus (G-K). The IR spectra were recorded on a Pye-Unicam SP1200 spectrophotometer using KBr Wafer technique. The ^{1}H-NMR spectra were determined on a Varian GEMINI 200 MHz NMR spectrophotometer using $CDCl_3$ or DMSO-d_6 as solvent and TMS as an internal standard. All chemical shifts are in ppm downfield from TMS. The elemental analysis were carried out in faculty of Science, Ain Shams University. MS were recorded on Shimadzu GC-MS QP1000EX instrument in micro analytical lab, Cairo University. The monitoring of the progress of all reactions and homogeneity of the synthesized compound was carried out by TLC.

Ethyl2-(6,8-Dibromo-2-(3,4-Dichlorophenyl)quinazolin-4-yloxy) acetate (2): To a mixture of **1** (0.01 mol) 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 (30 ml), the solid produced was filtered off, dried and recrystallized from benzene to give

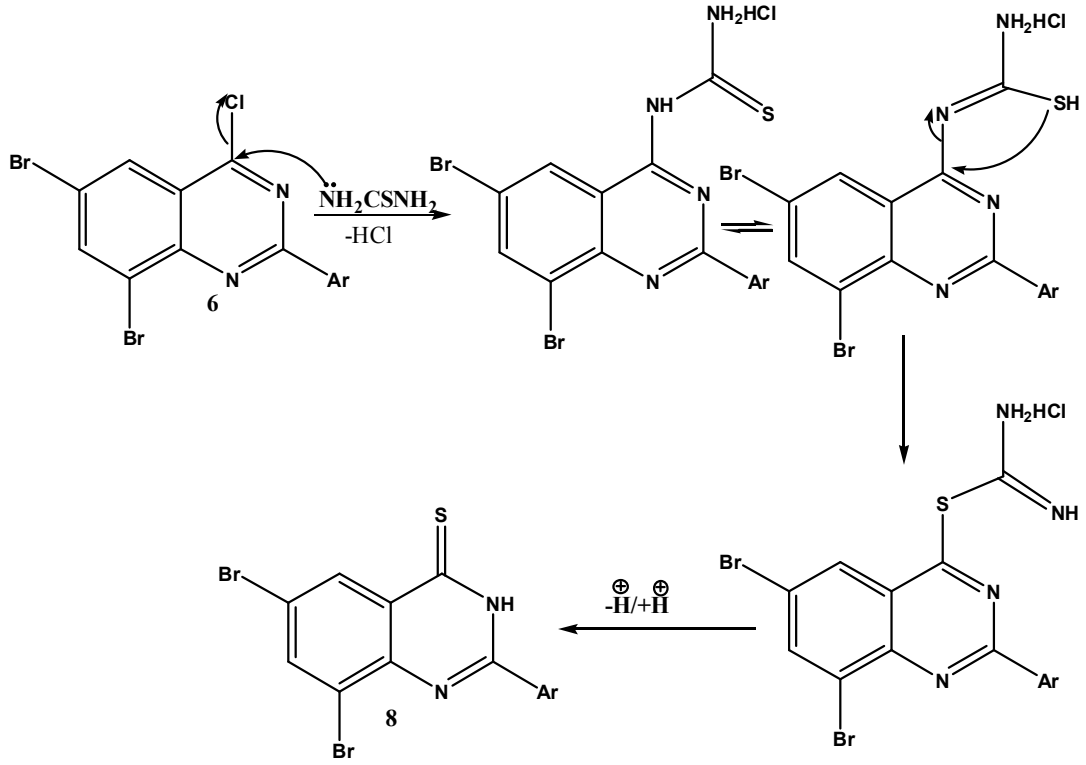


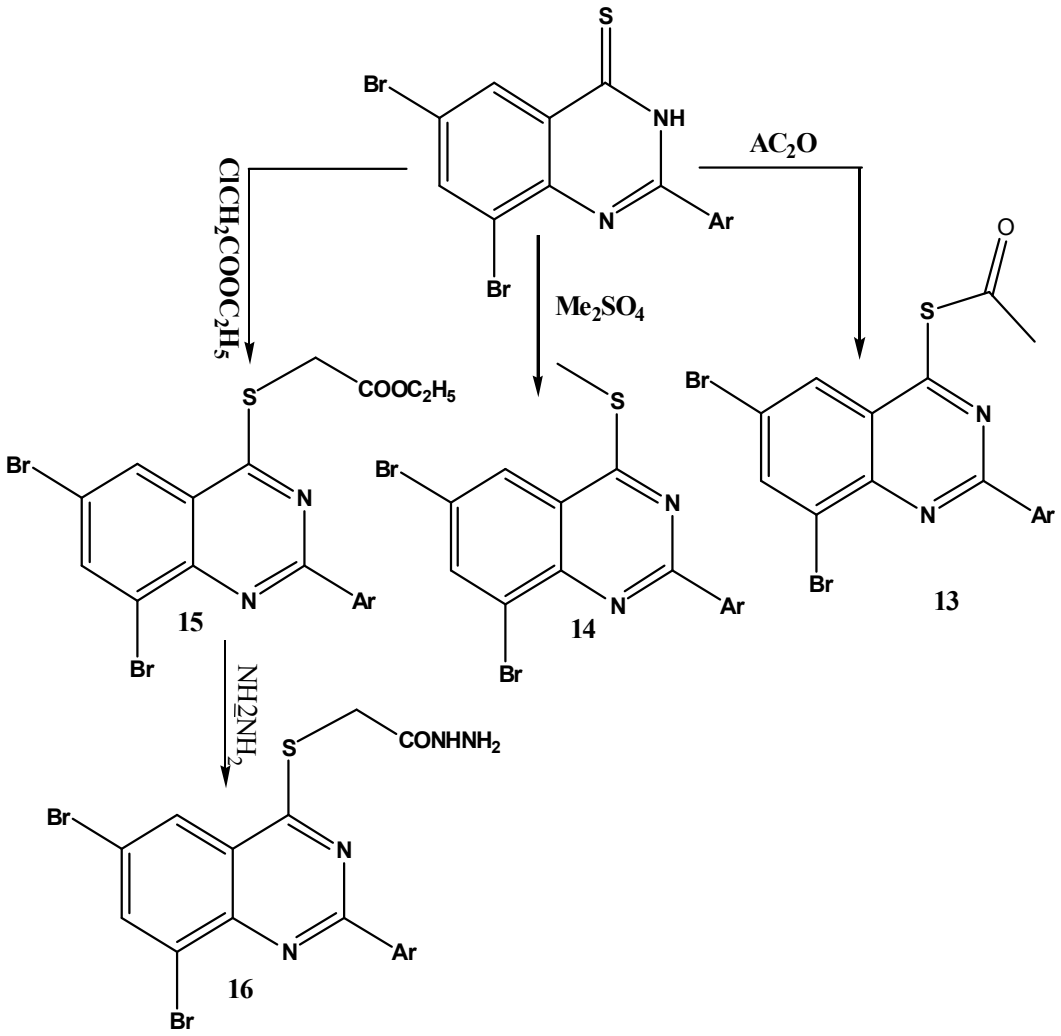
Scheme 1: Reaction on 6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4(*3H*)-one.



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





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

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) disappeared by D_2O. 8.06-7.80 (m, 5Harom), 6.06.5 (s, 2H, NH_2) disappeared 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°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 and 1652cm^{-1}, (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°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 water 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°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, 5Harom).

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°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) disappedred by D_2O) 7.56-7.73 (m, 5Harom), 7.70-7.57 m, 5Harom).

7b: Yellow crystals m.p over 288-290°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) disappedred 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** (0.01 mol) and Lawesson's reagent (0.005 mol) in dry DMF (50 ml) 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 (0.015 mol) in dry DMF (50 ml) 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** (0.01 mol) and thiourea (0.01 mol) in ethanol (30 ml) 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°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) disappedred 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** (0.01 mol) and hydrazine hydrate (0.02 mol) was refluxed in (30 ml) 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°C. 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) disappedred 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 over 221-223°C. 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°C. 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 (0.01 mol) was refluxed in acetic anhydride (15 ml) for 12 hours. The solvent was evaporated and the residue was recrystallized from benzene to give **11** as yellow crystals. m.p 281-283°C. 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°C. 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°C.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^{-1} (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) disappeared by D_2O. 8.06-7.80 (m, 5Harom), 6.06.5 (s, 2H, NH_2) disappeared by D_2O, 4.13 (s, 2H, CH_2).

CONCLUSION

During the current investigation, we synthesized a new building block; namely 6,8-dibromo-2-(3,4-dichlorophenyl)quinazolin-4(*3H*)-one. From that compound, a series of different quinqzoline derivatives were synthesized, and their structural and spectral data were elucidated.

ACKNOWLEDGMENTS

The authors are appreciative to Chemistry Department, Faculty of Science, Ain Shams University where the experimental part carried out in its laboratories.

Conflicts of Interest: The authors declare no conflict of interest.

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