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

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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 benzoazin-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 azacetalizations of aromatic aldehydes with 2-(N-substituted aminomethyl) phenols in the presence of TMSCI. Their structures were confirmed by IR, 1H-NMR, 13C-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].

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A simple strategy for 3-arylazo-4-phenyl-[1, 2, 4]triazepino[2, 3-a]quinazoline-2, 7(1H)-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 of quinazolinone 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) quinazololin-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 carbonyl group and the absence of the absorption of NH group also the \(^1\)H-NMR 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 quinazolinone derivative 2 with P\(_2\)S\(_5\) 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 schieff bases 10a,b and acetoxyhydradze derivative 11.

7, 9-dibromo-5-(3,4-Dichlorophenyl)-1,2,4-triazolo[4,3-b]quinazolin-5-one 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)quinazolin-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 \(^1\)H-NMR 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 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 QP100EX 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<sub>34</sub>H<sub>18</sub>Br<sub>2</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>4</sub> (535): C, 40.37; H, 2.24; N, 5.23
Found: C, 40.23; H, 2.22; N, 5.21; IR (cm<sup>-1</sup>): 1739 cm<sup>-1</sup> (C=O), 1616 cm<sup>-1</sup> (C=N). 1H-NMR (DMSO-d<sub>6</sub>) δ (ppm):
7.66-7.59 (m, 5H arom), 4.56 (s, 2H, CH<sub>2</sub>), 4.13 (q, 2H, CH<sub>2</sub>), 2.45 (t, 3H, CH<sub>2</sub>).

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<sub>37</sub>H<sub>20</sub>Br<sub>2</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>3</sub> (521): C, 36.85; H, 1.92; N, 10.74 Found: C, 36.87; H, 1.86; N, 10.68; IR (cm<sup>-1</sup>): 1652 cm<sup>-1</sup> (C=O), 1616 cm<sup>-1</sup> (C=N). 1H-NMR (DMSO-d<sub>6</sub>) δ (ppm): 10.02 (s, 1H, NH) disappeared by D<sub>2</sub>O. 8.06-7.80 (m, 5H arom), 6.06-5 (s, 2H, NH<sub>2</sub>) disappeared by D<sub>2</sub>O, 4.13 (s, 2HCH<sub>2</sub>).

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<sub>34</sub>H<sub>18</sub>Br<sub>2</sub>Cl<sub>2</sub>N<sub>2</sub>O (491): C, 39.10; H, 1.63; N, 5.70 Found: C, 38.90; H, 1.57; N, 5.62; IR (cm<sup>-1</sup>): 1692 and 1652 cm<sup>-1</sup>, (C=O), 1606 cm<sup>-1</sup> (C=N). 1H-NMR (DMSO-d<sub>6</sub>) δ (ppm): 7.16-7.70 (m, 5H arom), 4.13 (q, 2H, CH<sub>2</sub>), 2.45 (t, 3H, CH<sub>2</sub>).

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
(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 (30 ml), 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$_7$H$_6$Br$_2$Cl$_2$N$_2$O (463): C, 38.87; H, 1.73; N, 5.89 Found: C, 38.56; H, 1.56; N, 5.89; IR (cm$^{-1}$): 1610 cm$^{-1}$ (C=N). H-NMR (DMSO-d$_6$) $\delta$ (ppm): 7.96-7.63 (m, 5 H arom), 5.21 (s, 3H, OCH$_3$).  

**6,8-Dibromo-4-chloro-2-(3,4-Dichlorophenyl)quinazoline (6):** A mixture of 1 (5g) and phosphorus oxychloride (50 ml) and phosphorus pentachloride (10 g) was heated on water bath for 8 hours after cooling, the reaction mixture was added to crushed ice and solid separated washed with water (3x20 ml), dried and crystallized from benzene to give 6 as yellow crystals m.p over 176-178°C. Yield 74%. Anal. Calcd.: for C$_7$H$_6$Br$_2$Cl$_2$N$_2$O (467): C, 35.94; H, 1.06; N, 5.98 Found: C, 36.10; H, 1.12; N, 5.98; IR (cm$^{-1}$): 1603 cm$^{-1}$ (C=N). H-NMR (DMSO-d$_6$) $\delta$ (ppm): 8.01-7.89 (m, 5 H arom).

**N'-(6,8-Dibromo-2-(3,4-Dichlorophenyl)quinazolin-4-yl)benzohydrazide (7a):** A mixture of 6 (0.01 mol) and benzaldehyde and/or anisaldehyde (0.01 mol) 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). N, 12.33; IR (cm$^{-1}$): 1668 cm$^{-1}$ (C=O), 1605 cm$^{-1}$ (C=N). H-NMR (DMSO-d$_6$) $\delta$ (ppm): 10.92 (s, 1H, NH) and 2.12 (s, 2H, NH) disappered by D$_2$O, 7.64-7.50 (m, 5 H arom).

**7b:** Yellow crystals m.p over 300°C. Yield 44%. Anal. Calcd.: for C$_7$H$_6$Br$_2$Cl$_2$N$_2$O$_2$ (567): C, 44.48; H, 2.12; N, 9.87 Found: C, 44.38; H, 2.09; N, 9.78; IR (cm$^{-1}$): 3245 cm$^{-1}$ (NH), 1662 cm$^{-1}$ (C=O), 1606 cm$^{-1}$ (C=N). H-NMR (DMSO-d$_6$) $\delta$ (ppm): 11.02 (s, 1H, NH) and 8.03 (s, 1H, NH) disappered by D$_2$O, 7.56-7.73 (m, 5 H arom).  

**7a:** Yellow crystals m.p over 288-290°C. Yield 62%. Anal. Calcd.: for C$_7$H$_6$Br$_2$Cl$_2$N$_2$O (568): C, 44.25; H, 1.93; N, 12.32 Found: C, 44.15; H, 1.84; N, 12.32; IR (cm$^{-1}$): 3265, (NH), 1668, (C=O), 1605 (C=N). H-NMR (DMSO-d$_6$) $\delta$ (ppm): 10.92 (s, 1H, NH) and 8.12 (s, 1H, NH) disappered by D$_2$O, 7.92-7.83 (m, 5 H arom), 7.64-7.50 m, 4H arom).

**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 (0.01 mol) and phosphorous pentasulfide (0.015 mol) in dry DMF (50 ml) was refluxed for 24 hours. The unreacted P$_2$S$_5$ 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 as yellow crystals m.p over 275-277°C. Anal. Calcd.: for C$_7$H$_6$Br$_2$Cl$_2$N$_2$S (465): C, 36.13; H, 1.29; N, 6.02 Found: C, 35.93; H, 1.28; N, 5.74; IR (cm$^{-1}$): 3265, (NH), 1605 (C=N) and 1268, (C=S). H-NMR (DMSO-d$_6$) $\delta$ (ppm): 10.92 (s, 1H, NH) and 2.12 (s, 2H, NH) disappered by D$_2$O, 7.54-7.25 (m, 5 H arom).

**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 as orange crystals m.p over 300°C. Yield 37%. Anal. Calcd.: for C$_7$H$_6$Br$_2$Cl$_2$N$_2$O (467): C, 36.28; H, 1.72; N, 12.09 Found: C, 36.78; H, 1.66; N, 12.33; IR (cm$^{-1}$): 3365, 3289-3124 (NH and NH$_2$) and 1605 (C=N). H-NMR (DMSO-d$_6$) $\delta$ (ppm): 6.22 (s, 1H, NH) and 2.12 (s, 2H, NH$_2$) disappered by D$_2$O, 7.64-7.50 (m, 5 H arom).

**6,8-Dibromo-2-(3,4-Dichlorophenyl)4-(1-benzylidenehydrazine)quinazoline (10a):** A mixture of 9 (0.01 mol) and benzaldehyde and/or p-anisaldehyde (0.01 mol) was refluxed for 3 hours. The solvent was evaporated and the solid was recrystallized from the proper solvent.

**10a:** Recrystallized from benzene, yellow crystals m.p over 221-223°C. Yield 56%. Anal. Calcd.: for C$_7$H$_6$Br$_2$Cl$_2$N$_2$O (551): C, 45.73; H, 2.17; N, 10.16 Found: C, 45.62; H, 1.88; N, 10.09; IR (cm$^{-1}$): 3184, (NH) and 1605 (C=N). H-NMR (DMSO-d$_6$) $\delta$ (ppm): 7.64-7.50 m, 5 H arom) 6.01 (s, 1H, NH) disappered by D$_2$O, 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_{13}H_{13}BrCl_{2}N_{2}O (581): C, 45.43; H, 2.40; N, 9.63 Found: C, 45.79; H, 2.26; N, 8.78; IR (μm<sup>-1</sup>): 3164, (NH) and 1611 (C=N). 1H-NMR (DMSO-d<sub>6</sub>) δ (ppm): (7.54-7.40 m, 5Harom) 5.91 (s, 1H, NH) disappared by D<sub>2</sub>O, 5.26 (s, 1H =CH).

N′-(6,8-Dibromo-2-(3,4-Dichlorophenyl)quinazolin-4-yl)acetohydrazide (11): The hydrazinoquinazolinoline 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_{13}H_{13}BrCl_{2}N_{2}O (505): C, 38.02; H, 1.98; N, 11.09 Found: C, 37.96; H, 1.67; N, 10.98; IR (μm<sup>-1</sup>): 3184, 3298 (NH), 1665 (C=O) and 1606 (C=N). 1H-NMR (DMSO-d<sub>6</sub>) δ (ppm): 9.21 (s, 1H, NH) disappared by D<sub>2</sub>O, 8.06-7.80 (m, 5Harom), 4.16.5 (s, 2H, CH<sub>2</sub>), 4.23 (q, 2H), 2.95 (t, 3H, J=6 Hz, CH). 13C-NMR (DMSO-d<sub>6</sub>) δ (ppm): 1662 cm (C=O), 1606 cm (C=N) ppm (m, 5Harom).

7, 9-dibromo-5-(3,4-Dichlorophenyl)-[1, 2, 4]triazolo[4, 3-c]quinazoline-3(2H)-thione (12): A mixture of 9 (0.01 mol) 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 187-189°C. Yield 63%. Anal. Calcd.: for C_{13}H_{13}BrCl_{2}N_{2}O (535): C, 39.20; H, 2.18; N, 5.08 Found: C, 39.80; H, 2.07; N, 5.50; IR (μm<sup>-1</sup>): 1722 cm (C=O<sub>anhydride</sub>), 1611 cm (C=N), 1H-NMR (DMSO-d<sub>6</sub>) δ (ppm): 7.76-7.49 (m, 5Harom), 4.16.5 (s, 2H, CH<sub>2</sub>), 4.23 (q, 2H), 2.95 (s, 3H, CH<sub>3</sub>), 3.94 (s, 3H, CH<sub>3</sub>).

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_{13}H_{13}BrCl_{2}N_{2}OS (537): C, 37.86; H, 1.57; N, 5.52 Found: C, 38.00; H, 1.34; N, 5.43; IR (μm<sup>-1</sup>): 1695 (C=O) and 1605 (C=N). 1H-NMR (DMSO-d<sub>6</sub>) δ (ppm): 7.64-7.50 m, 5Harom. and 3.94(s, 3H, CH<sub>3</sub>). 4.13 (s, 2H, CH<sub>3</sub>).

6, 8-Dibromo-2-(3,4-Dichlorophenyl)-4-(methylthio)quinazoline (14): A mixture of thion 8 (0.01mol) and potassium carbonate 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_{13}H_{13}BrCl_{2}N_{2}S (479): C, 35.75; H, 1.67; N, 5.84 Found: C, 35.67; H, 1.48; N, 5.72; IR (μm<sup>-1</sup>): 1616 cm (C=N), 1H-NMR (DMSO-d<sub>6</sub>) δ (ppm): 7.66-7.59 (m, 5Harom), 2.65 (t, 3H, CH<sub>3</sub>).

ethyl2-(6,8-Dibromo-2-(3,4-Dichlorophenyl)quinazolin-4-ylthio)acetate(15): A mixture of thion 8 and potassium carbonate 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_{13}H_{13}BrCl_{2}N_{2}O (537): C, 39.20; H, 2.18; N, 5.08 Found: C, 39.80; H, 2.07; N, 5.50; IR (μm<sup>-1</sup>): 1722 cm (C=O<sub>anhydride</sub>), 1611 cm (C=N). 1H-NMR (DMSO-d<sub>6</sub>) δ (ppm): 7.76-7.49 (m, 5Harom), 4.16.5 (s, 2H, CH<sub>2</sub>), 4.23 (q, 2H), 2.95 (s, 3H, CH<sub>3</sub>). 3.94 (s, 3H, CH<sub>3</sub>). 4.13 (s, 2H, CH<sub>3</sub>). 13C-NMR (DMSO-d<sub>6</sub>) δ (ppm):10.42 (s, 1H, NH) disappeared by D<sub>2</sub>O, 8.06-7.80 (m, 5Harom), 6.06.5 (s, 2H, NH<sub>2</sub>) disappeared by D<sub>2</sub>O, 4.13 (s, 2H, CH<sub>3</sub>). 3.94 (s, 3H, CH<sub>3</sub>).

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 quinazoline derivatives were synthesized, and their structural and spectral data were elucidated.

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