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Research Article

NEW QUINAZOLIN-2,4-DIONES FROM (2,4-DIOXO-1,4-DIHYDRO-2H- QUINAZOLIN -3-YLAMINO) ACETIC ACID HYDRAZIDE

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ABSTRACT

Pyrimidines and quinazolindiones have been found as key components of some biologically and pharmaceutically relevant compounds.

Objective: Basically, we used the starting material (2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl-amino)acetic acid hydrazide 3 in the synthesis of some interesting derivatives of quinazolindione which attached to some interesting heterocyclic moieties such as triazin-6-one, phthalazine, indol-2-one, pyrazole, triazole, and oxadiazole in position 3.

Methods: Compound 3 was prepared by the reaction of 3-amino-1*H*-quinazolin-2,4-dione 1 with ethylchloroacetate to form 2 followed by treatment with hydrazine to yield hydrazide 3 which used as starting material for synthesis of pharmaceutically active quinazolin-2,4-diones.

Results: Novel derivatives of quinazolin-2,4-dione attached to some interesting heterocycles in position 3 have been synthesized as potential pharmaceuticals.

Conclusion: An efficient synthesis of biologically and pharmaceutically activequinazolin-2,4-dione derivatives has been developed. The structures of the newly synthesized compounds were characterized by IR, 1H NMR, MS, and elemental analysis technique.

Keywords: (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-yl-amino)acetic acid hydrazide, Pharmaceutical, Benzylidine malononitrile, Condensation, Carbon disulfide.

INTRODUCTION

In recent years, there has been an increasing interest in the chemistry of quinazolindiones [1-8] and pyrimidines [9,10] because of their biological and chemotherapeutical significance. In addition, quinazolines and pyrimidines are most important class of heterocyclic compounds which display antimicrobial and therapeutic actives.

Many of them show antifungal, antibacterial, anticancer, anti-malarial, anticonvulsant against electroshock, vasodilation, antitumor and anti-proliferative activities [11-24]. Derivatives of pyrimidine and quinazolindione have played a crucial role in the history of heterocyclic chemistry and been used extensively important pharmacophores and synthons in the field of organic chemistry.

Also, they have received much attention from synthetic as well as medicinal chemists because of the diverse range of their pharmacological properties including use as hypotensive, anti-inflammatory [25]. Inspired from these facts, the authors have attempted to gather these moieties hoping to produce valuable new compounds of expected antibacterial, pharmaceutical and antifungal activity.

MATERIALS AND METHODS

Materials

Melting points were uncorrected determined on an electric melting point apparatus (Kofler). IR spectra (KBr) were recorded on a Shimadzu 408 spectrometer. The ^{1}HNMR spectra were recorded by 200 and 300 MHz Varian EM 390 spectrometer; chemical shifts are reported in ppm with TMS as an internal standard and are given in δ units.

Electron impact mass spectra were obtained at 70 eV using a GC-MS sp. 1000 Shimadzu. Elemental analyses were carried out at Microanalysis Unit at Cairo University; purity of the compounds during reaction was detected by TLC.

Methods

(2,4-Dioxo-1,4-dihydro-2H-quinazolin-3-yl-amino)acetic acid ethyl ester (2)

3-Amino-1*H*-quinazolin-2,4-dione **1** (1.7 gm., 10 mmol) was added to a solution of ethylchloroacetate (15 mmol) in acetone (30 ml) in presence of finely graded K_2CO_3 (2.76 gm., 20 mmol). The reaction mixture was heated under reflux for 5 hrs. After cooling; the solid formed was filtered off and crystallized from benzene to give (2,4-Dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)-acetic acid ethyl ester **2** as white needles (Scheme 1).

Yield: 2.3 gm., 90 %. M.P.: 164 ^{o}C. FT-IR (KBr, cm^{-1}): 3354, 3267 (NH), 1741, 1650 (C=O). ^{1}H NMR (200 MHz, DMSO-d_6): 1.28 (t, 3H, CH_3); 4.24 (q, 2H, CH_2); 4.95 (s, 2H, CH_2); 6.98-7.25 (m, 4H, Ar-H); 8.29 (d, 1H, NH) and also showed the disappearance of NH signal of quinazoline moiety in DMSO-d_6. MS (m/z, %): 263 (24.68 %) correspond to the molecular formula ($C_{12}H_{13}N_3O_4$). Anal. Calcd. for $C_{12}H_{13}N_3O_4$: C, 54.75; H, 4.98; N, 15.96. Found: C, 54.79; H, 4.97; N, 15.95 %.

(2,4-dioxo-1,4-dihydro-2H-quinazolin-3-ylamino)acetic acid hydrazide (3)

(2,4-Dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)-acetic acid ethyl ester **2** (1.31 gm., 5 mmol) was added to excess of hydrazine hydrate (1.25 ml, 10 mmol) in absolute ethanol (30 ml). The mixture was heated under reflux for 1 hr., after cooling the precipitate formed was filtered off, crystallized from DMF to give (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)-acetic acid hydrazide **3** as white needles (Scheme 1). Yield 95%. M.P.: 262 ^{o}C. FT-IR (KBr, cm^{-1}): 3330 (NH), 3200 (NH_2), 1695, 1665 (C=O). ^{1}H NMR (200 MHz, DMSO-d_6): 4.27 (s, 1H, NH); 4.78 (s, 2H, CH_2); 5.62 (s, 2H, NH_2); 7.21-8.1 (m, 4H, Ar-H); 9.37 (s, 1H, NH) and also showed the disappearance of NH signal of quinazoline moiety in DMSO-d_6. MS (m/z, %): 249 (10 %) correspond to the molecular formula ($C_{10}H_{11}N_5O_3$). Anal. Calcd. for $C_{10}H_{11}N_5O_3$: C, 48.19; H, 4.45; N, 28.10. Found: C, 48.22; H, 4.44; N, 28.09 %.

3-(3-methyl-6-oxo-5,6-dihydro-1H-[1,2,4]triazin-4-yl)-1H-quinazolin-2,4-dione (4)

(2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)acetic acid hydrazide **3** (0.5 gm., 2 mmol) was boiled in glacial acetic acid (20 ml) under reflux for 6 hrs. After cooling, the solid formed was filtered off, then recrystallized from acetic acid, and washed with water to afford 3-(3-methyl-6-oxo-5,6-dihydro-1*H*-[1,2,4]triazin-4-yl)-1*H*-quinazolin-2,4-dione **4** as white crystals (Scheme 2). Yield 90 %. M.P.: 292 ^{o}C. FT-IR (KBr, cm^{-1}): 3280, 3190 (NH), 1740 and 1675 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6): 1.97 (s, 3H, CH_3); 4.72-4.98 (dd, 2H, CH_2); 7.27-8.09 (m, 4H, Ar-H); 10.25 (s, 1H, NH); 10.65 (s, 1H, NH). MS (m/z, %): 273 (53.55 %) correspond to the molecular formula ($C_{12}H_{11}N_5O_3$). Anal. Calcd. for $C_{12}H_{11}N_5O_3$: C, 52.75; H, 4.06; N, 25.63. Found: C, 52.70; H, 4.08; N, 25.64 %.

General procedures for synthesis of Arylidines (5a, b)

A mixture of (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)-acetic acid hydrazide **3** (0.5 gm., 2 mmol) and the appropriate amount of benzaldehyde and/or anisaldehyde (2 mmol) in absolute ethanol (30 ml) in the presence of triethylamine as a base catalyst, was heated under reflux for 10-12 hrs. After cooling, the precipitated solid was filtered off, then recrystallized from dioxane to give the major *E*-isomer of (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)acetic acid benzylidine hydrazide **5a** and **5b** respectively as white crystals (Scheme 2).

Arylidine 5a:

Yield 97 %. M.P.: 306 ^{o}C. FT-IR (KBr, cm^{-1}): 3339, 3185 (NH), 1672, 1612 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6): 5.37 (s, 1H, NH); 5.66 (s, 2H, CH_2); 7.3-8.24 (m, 10H, Ar-H, NH); 8.08 (s, 1H, CH sp^2); 11.8 (s, 1H, NH). MS (m/z, %): 337 (2.76 %) correspond to the molecular formula ($C_{17}H_{15}N_5O_3$). Anal. Calcd. for $C_{17}H_{15}N_5O_3$: C, 60.53; H, 4.48; N, 20.76. Found: C, 60.49; H, 4.49; N, 20.75 %.

Arylidine 5b:

Yield 88 %. M.P.: 290 ^{o}C. FT-IR (KBr, cm^{-1}): 3335, 3190 (NH), 1672, 1610 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6): 1.97- 3.81 (s, 3H, OCH_3); 4.93 (s, 1H, NH); 5.34 (s, 2H, CH_2); 7.0-8.11 (m, 9H, Ar-H); 8.0 (s, 1H, CH sp^2); 11.65 (s, 1H, NH). MS (m/z, %): 367 (21.43 %) correspond to the molecular formula ($C_{18}H_{17}N_5O_4$). Anal. Calcd. for $C_{18}H_{17}N_5O_4$: C, 58.85; H, 4.66; N, 19.06. Found: C, 58.79; H, 4.68; N, 19.07 %.

General procedures for synthesis of ethylaminoquinazolin-2,4-diones (6a, b)

A mixture of (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-yl-amino)acetic acid hydrazide **3** (2.5 gm., 10 mmol) and phthalic anhydride (10 mmol) in glacial acetic acid (50 ml), was heated under reflux for 4 hours, after which a precipitate was formed. After cooling the solid formed was filtered off, recrystallized from acetic acid to afford 3-[2-(1,4-dioxo-3,4-dihydro-1*H*-phthalazin-2-yl)-2-oxo-ethylamino]-1*H*-quinazolin-2,4-dione **6a** and afford 3-[2-oxo-2-(5,6,7,8-tetrachloro-1,4-dioxo-3,4-dihydro-1*H*-phthalazin-2-yl)-ethylamino]-1*H*-quinazolin-2,4-dione **6b** respectively as white crystals (Scheme 2).

Ethylaminoquinazolin-2,4-dione 6a:

Yield 98 %. M.P. $>$ 360 ^{o}C. FT-IR (KBr, cm^{-1}): 3180 (NH), 1740, 1700 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6): 5.2 (s, 2H, CH_2); 7.45-8.17 (m, 8H, Ar-H); 11.35 (s, 1H, NH); 12.1 (broad s, 1H, NH) and also showed the disappearance of one NH signal in DMSO-d_6. MS (m/z, %): 379 (12.61 %) correspond to the molecular formula ($C_{18}H_{13}N_5O_5$). Anal. Calcd. for $C_{18}H_{13}N_5O_5$: C, 56.99; H, 3.45; N, 18.46. Found: C, 57.03; H, 3.44; N, 18.45 %.

Ethylaminoquinazolin-2,4-dione 6b:

Yield 60 %. M.P. $>$ 360 ^{o}C. FT-IR (KBr, cm^{-1}): 3210 (NH), 1757, 1716 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6): 5.24 (s, 2H, CH_2); 7.47-8.21 (m, 4H, Ar-H); 11.59 (s, 1H, NH); 12.0 (broad s, 1H, NH) and also showed the disappearance of one NH signal in DMSO-d_6. MS (m/z, %): 517 (3.93%) correspond to the molecular formula ($C_{18}H_9N_5O_5Cl_4$) in addition to the characteristic peaks for compounds containing four chlorine atoms [1, 24] at [M+2] and [M+4]. Anal. Calcd. for $C_{18}H_9N_5O_5Cl_4$: C, 41.81; H, 1.73; N, 13.54; Cl, 27.4. Found: C, 41.84; H, 1.74; N, 13.52; Cl, 27.41 %.

(2,4-dioxo-1,4-dihydro-2H-quinazolin-3-ylamino)acetic acid [2-oxo-1,2-dihydro-indol-(3Z)-yl-idene]-hydrazide (7)

Compound **3** (0.5 gm., 2 mmol) and isatine (0.3 gm., 2 mmol) in glacial acetic acid (10 ml) were heated under reflux for 1 hr., after cooling, the resulting solid formed was filtered off and crystallized from ethanol to afford (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-yl-amino)-acetic acid [2-oxo-1,2-dihydro-indol-(3*Z*)-ylidene]-hydrazide **7** as deep yellow crystals (Scheme 2). Yield 90 %. M.P.: 340 ^{o}C. FT-IR (KBr, cm^{-1}): 3320, 3260, 3215 (NH's), 1690, 1680 (C=O). ^{1}H NMR (200 MHz, DMSO-d_6): 5.49 (s, 2H, CH_2); 5.63 (s, 1H, NH); 6.94-8.1 (m, 8H, Ar-H); 10.66 (s, 1H, NH); 11.27 (s, 1H, NH); 12.75 (s, 1H, NH). MS (m/z, %): 378 (6.11%) correspond to the molecular formula ($C_{18}H_{14}N_6O_4$). Anal. Calcd. for $C_{18}H_{14}N_6O_4$: C, 57.14; H, 3.73; N, 22.21. Found: C, 57.17; H, 3.71; N, 22.23 %.

3-[2-(3,5-dimethyl-pyrazol-1-yl)-2-oxo-ethylamino]-1H-quinazolin-2,4-dione (8)

(2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-yl-amino)acetic acid hydrazide **3** (1gm., 4 mmol) was added to acetyl acetone (0.5 ml, 5 mmol) in ethanol absolute (30 ml) in presence of few drops of piperidine, the reaction mixture was heated under reflux for 6 hrs., the solvent was evaporated under vaco; the resulting formed solid was collected and crystallized from benzene to give 3-[2-(3,5-dimethyl-pyrazol-1-yl)-2-oxo-ethylamino]-1*H*-quinazolin-2,4-dione **8** as yellow crystals (Scheme 2). Yield 84 %. M.P.: 250 ^{o}C. FT-IR (KBr, cm^{-1}): 3320, 3225 (NH), 1740, 1650 (C=O). ^{1}H NMR (200 MHz, DMSO-d_6): 2.33 (s, 3H, CH_3); 2.5 (s, 3H, CH_3); 5.73 (s, 2H, CH_2); 5.76 (s, 1H, NH); 6.37 (s, 1H, CH sp^2); 7.4-8.18 (m, 4H, Ar-H) and also showed the disappearance of NH signal of quinazoline moiety in DMSO-d_6. MS (m/z, %): 313 (3.83 %) correspond to the molecular formula ($C_{15}H_{15}N_5O_3$). Anal. Calcd. for $C_{15}H_{15}N_5O_3$: C, 57.5; H, 4.83; N, 22.35. Found: C, 57.46; H, 4.81; N, 22.38 %.

5-amino-1-[2-(2,4-dioxo-1,4-dihydro-2H-quinazolin-3-ylamino)acetyl]-3-phenyl-1H-pyrazole-4-carbonitrile (9)

An equimolar amounts of (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-yl-amino)acetic acid hydrazide **3** (0.5 gm., 2 mmol) and 2-benzylidene malononitrile (0.43 gm., 3 mmol) in absolute ethanol (30 ml) in the presence of few drops of piperidine as a base catalyst, were refluxed for 6 hrs. After cooling the solid formed was filtered off, recrystallized from ethanol to afford 5-amino-1-[2-(2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)acetyl]-3-phenyl-1*H*-pyrazole-4-carbonitrile **9** as white crystals (Scheme 2). Yield 90 %. M.P.: 305 ^{o}C. FT-IR (KBr, cm^{-1}): 3330, 3270 (NH_2), 3260, 3190 (NH), 2360 (CN), 1710, 1685 (C=O). ^{1}H NMR (200 MHz, DMSO-d_6): 4.9 (s, 1H, NH); 5.38 (s, 2H, CH_2); 5.68 (s, 2H, NH_2); 7.33-8.12 (m, 9H, Ar-H); 11.83 (s, 1H, NH). Anal. Calcd. for $C_{20}H_{17}N_7O_3$: C, 59.55; H, 4.25; N, 24.30. Found: C, 59.50; H, 3.27; N, 24.31 %.

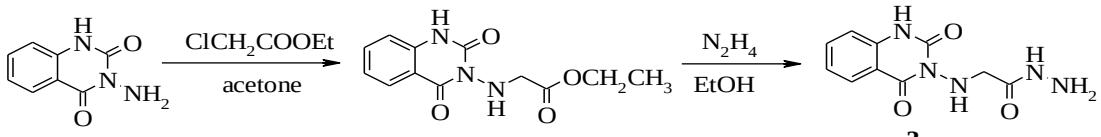
3-[(4-amino-5-mercapto-4H-[1,2,4]triazol-3-ylmethyl)-amino]-1H-quinazolin-2,4-dione (10)

Carbon disulfide (3 ml) was added drop wisely to a stirred suspension of (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)acetic acid hydrazide **3** (1 gm., 4 mmol) and potassium hydroxide (0.45 gm., 8 mmol) in ethanol absolute (50 ml) at 0-4 ^{o}C; after completion of adding carbon disulfide the reaction mixture was further stirred for 8 hrs., at room temperature. The solvent was removed under reduced pressure to give the yellow residue salt potassium *N*`-[2-(2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)acetyl]hydrazine-carbodithioate which is used directly without further purification. Hydrazine hydrate in excess (0.5 ml) in water (20 ml) was added to the salt solution, the reaction mixture was heated under reflux for 8 hrs. during the reaction it was noticed that the reaction mixture turns green colour because of the evolution of hydrogen sulfide gas, then the solution turns colorless. After indicating the completion of the reaction using TLC technique, the reaction mixture was left to cool, then neutralized with acetic acid, the resulting solid was filtered off; dried and crystallized from ethanol to afford 3-[(4-amino-5-mercapto-4*H*-[1,2,4]triazol-3-

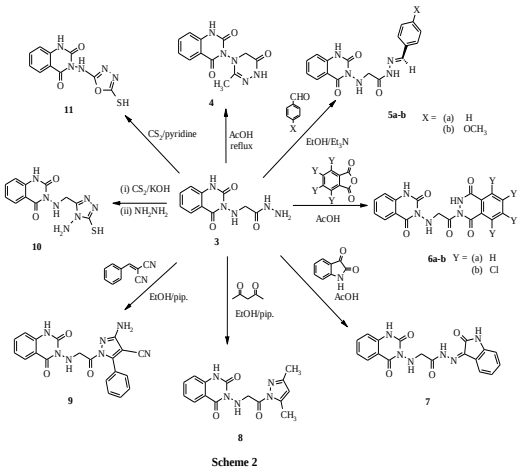
ylmethyl)-amino]-1*H*-quinazolin-2,4-dione **10** as greenish white crystals (Scheme 2). Yield 50 %. M.P.: 240 ^{o}C. FT-IR (KBr, cm^{-1}): 3360 (SH), 3300, 3260 (NH_2), 3165 (NH), 1630 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6): 4.42 (s, 2H, CH_2); 4.44 (s, 1H, NH); 5.59 (s, 2H, NH_2); 6.57-7.5 (m, 4H, Ar-H); 8.07 (s, 1H, SH); 9.59 (s, 1H, NH). MS (m/z, %): 305 (8.62 %) correspond to the molecular formula ($C_{11}H_{11}N_7O_2S$). Anal. Calcd. for $C_{11}H_{11}N_7O_2S$: C, 43.27; H, 3.63; N, 32.11; S, 10.5. Found: C, 43.30; H, 3.62; N, 32.10; S, 10.48 %.

3-[(5-mercapto-[1,3,4]oxadiazol-2-ylmethyl)-amino]-1H-quinazolin-2,4-dione (11)

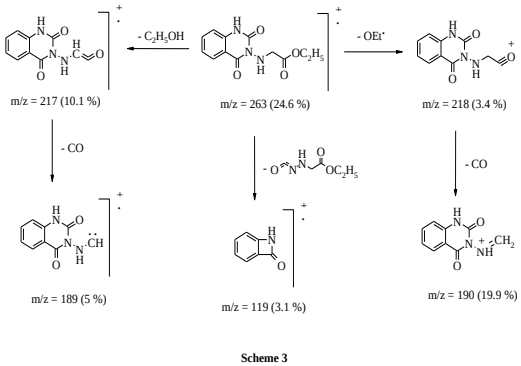
(2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)acetic acid hydrazide **3** (1.25 gm., 5 mmol) was added to a solution of carbon disulfide (0.46 ml, 6 mmol) in dry pyridine (20 ml); the reaction mixture was heated under reflux for 10 hrs., after cooling the reaction mixture was poured onto ice cold diluted (1:1) HCl, the resulting solid formed was filtered off, dried and crystallized from acetic acid to give 3-[(5-mercapto-[1,3,4]oxadiazol-2-ylmethyl)amino]-1*H*-quinazolin-2,4-dione **11** as pale yellow crystals (Scheme 2). Yield 60 %. M.P.: 242 ^{o}C. FT-IR (KBr, cm^{-1}): 3335, 3300 (NH), 1705, 1675 (C=O). ^{1}H NMR (200 MHz, DMSO-d_6): 4.94 (s, 1H, NH); 5.53 (s, 2H, CH_2); 7.34-8.13 (m, 4H, Ar-H); 8.65 (s, 1H, SH); 10.67 (s, 1H, NH). MS (m/z, %): 291 (24.64 %) correspond to the molecular formula ($C_{11}H_9N_5O_3S$). Anal. Calcd. for $C_{11}H_9N_5O_3S$: C, 45.36; H, 3.11; N, 24.04; S, 11.01. Found: C, 45.40; H, 3.1; N, 24.05; S, 10.98 %.



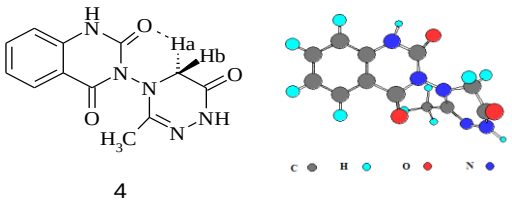
Scheme 1



Scheme 2



Scheme 3



Scheme 4

RESULTS AND DISCUSSION

In the present study, novel derivatives of quinazolin-2,4-dione attached to some interesting heterocycles such as triazin-6-one, phthalazine, indol-2-one, pyrazole, triazole, and oxadiazole in position 3 have been synthesized as potential pharmaceuticals.

Synthetic scheme **1** illustrates the synthetic pathway used to obtain (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino) acetic acid hydrazide **3** which was used as starting material in our work. Treatment of 3-amino-1*H*-quinazolin-2,4-dione **1** with ethylchloroacetate yielded (2,4-Dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)-acetic acid ethyl ester **2**. The reaction of compound **2** with hydrazine in ethanol gave (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)acetic acid hydrazide **3** in a good yield (Scheme 1). Scheme 3 outlines the main fragmentation routes for compound **2**. Scheme 2 outlines our strategies for the synthesis of some heterocyclic moieties attached to quinazoline nuclei. When compound **3** is heated under reflux in glacial acetic acid, acetylation takes place followed by ring closure through elimination of two molecules of water to afford 3-(3-methyl-6-oxo-5,6-dihydro-1*H*-[1,2,4]triazin-4-yl)-1*H*-quinazolin-2,4-dione **4** (Scheme 2). ^{1}H-NMR spectrum of **4** shows doublet-doublet peaks at δ 4.77-4.91 corresponding to methylene group CH_2 in which the two hydrogen atoms undergo geminal coupling (J= 17.1 Hz) where one of the two protons forms six membered ring hydrogen bonding as shown in scheme 4. Treatment of **3** with aromatic aldehydes namely benzaldehyde and/or anisaldehyde afforded the *E* form of (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)acetic acid benzylidine hydrazide **5a** and/or (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)acetic acid (4-methoxybenzylidene) hydrazide **5b** respectively (Scheme 2). The reaction of starting material **3** with aromatic anhydrides was intensively investigated. Ethyl amino quinazolindione derivatives **6a** and **6b** respectively are resulted by the reaction of **3** with different anhydrides namely phthalic anhydride and/or tetrachlorophthalic anhydride (Scheme 2). Condensation of **3** with isatine afforded (2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)acetic acid [2-oxo-1,2-dihydro-indol-(3*Z*)-ylidene]-hydrazide **7** (Scheme 2). Reaction of hydrazide **3** with acetyl acetone gave 3-[2-(3,5-dimethyl-pyrazol-1-yl)-2-oxo-ethylamino]-1*H*-quinazolin-2,4-dione **8** (Scheme 2). Also, we investigated the reaction of the compound **3** with 2-benzylidene malononitrile to afford 5-amino-1-[2-(2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-ylamino)-acetyl]-3-phenyl-1*H*-pyrazole-4-carbonitrile **9** (Scheme 2). Stirring of **3** with carbon disulfide and potassium hydroxide in ethanol at 0-4 ^{0}C as a first step formed an intermediate potassium salt, this intermediate followed by directly reacting with hydrazine yielded 3-[(4-amino-5-mercapto-4*H*-[1,2,4]triazol-3-ylmethyl)-amino]-1*H*-quinazolin-2,4-dione **10** (Scheme 2). Finally, reaction of compound **3** with carbon disulfide gave 3-[(5-mercapto-[1,3,4]oxadiazol-2-ylmethyl)-amino]-1*H*-quinazolin-2,4-dione **11** (Scheme 2).

CONCLUSION

An efficient synthesis of biologically and pharmaceutically active quinazolin-2,4-dione derivatives has been developed. The structures of the newly synthesized compounds were characterized by IR, ^{1}H NMR, MS, and elemental analysis technique.

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