A facile one-pot *MW* approach for 3-heteroaryl-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one

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Abstract

A microwave-assisted simple, convenient, and high yielding synthetic methodology for diverse thioquinozolinones was developed by the amidine base catalyzed one-pot reaction of anthranilate ester, 1,1'-carbonothioylbis(1*H*-benzotriazole), and heterocyclic amines containing thiazole, [1,3,4]-oxadiazoles and [1,3,4]-thiadiazole heterocycles.

Keywords: Quinazolinone, DBU, benzotriazole, thiazole, oxadiazole, thiadiazole

Introduction

Synthesis of quinazolinone heterocycles is an attractive field for synthetic chemists due to their diverse range of pharmacological activities.[1,2] Methaqualone, the most popular quinazolinone drug synthesized in 1951 for its antimalarial effect,[3a] is currently being used for the assessment of the abuse liability of sedative hypnotic drugs.[3b] It has gained popularity as a euphoriant among casual recreational drug users in the Boston area. Tiodazosin, a hybrid of quinazoline and [1,3,4]-oxadiazole heterocycles has been marketed as antihypertensive agents.[3c,d] Moreover, the quinazolinone skeleton is very common in several naturally occurring alkaloids[4] displaying a wide range of biological activities useful in developing chemotherapeutic agents against many diseases and hence the exploration of this skeleton as privileged new chemical entities (NCE's) in drug discovery research is of paramount importance.

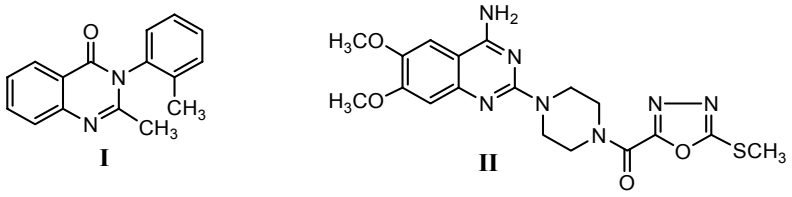


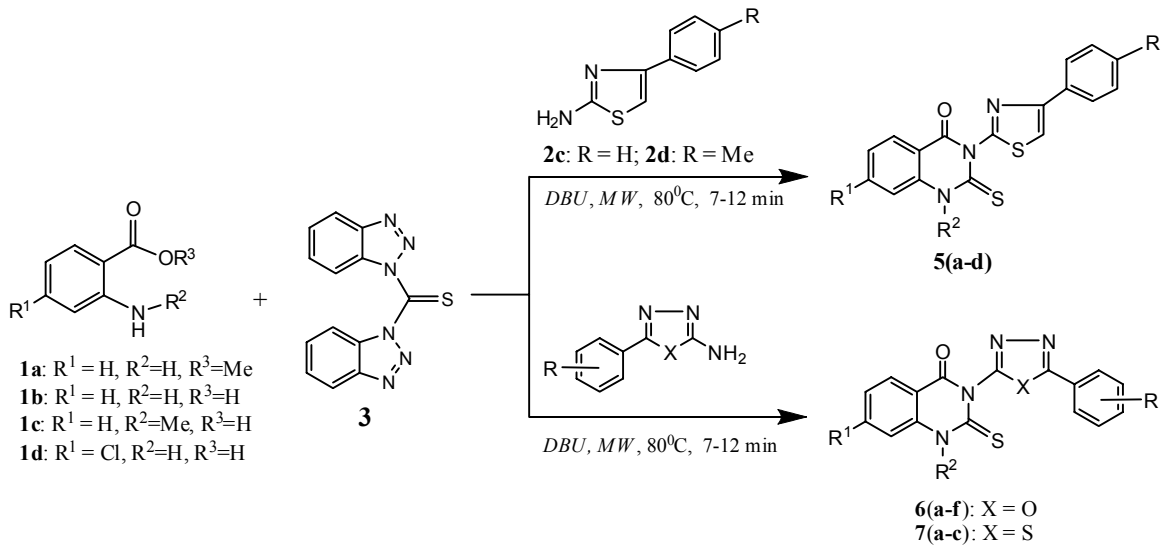
Figure 1. Structure of Methaqualone (**I**) and Tiodazosin (**II**).

Although there are several reports on the synthesis of quinazolinone heterocycles, yet the search for a convenient synthesis is on due to different drawbacks in the existing methods. Quinazolinone derivatives have generally been prepared by the reaction of anthranilic acids or its other functional derivatives with isothiocyanates,[5a] thioureas,[5b] excess of refluxing formamide,[5c] imidates,[5d] methyl-*N*-aryl/ammonium aryl dithiocarbamates,[5e,f] $CSCl_2$ either in presence of NEt_3[6a] or hydrazine,[6b] RNHCOOEt and imidazole,[6c] anhydride followed by reaction with amines,[6d] amine and CS_2 in basic medium,[6e] carbonyl compounds,[7a, b] amines,[7c] or urethanes,[7d] and more recently using ortho esters, amines, and polymer supported $FeCl_3$.[7e] Oxidation of either 3-arylimino-2-indolinones (with peracid),[8a] or 2-aminobenzonitrile followed by base catalyzed treatments with acid halides[8b] also provides this skeleton. Isotoic anhydride was used to construct the quinazolinone ring by reaction either with isothiocyanate,[8c] or both amine and isothiocyanates under *MW* condition.[8d] Cyclization of substituted 2-(carboxymethyl)benzeneisothiocyanates either with amines, amino acids, hydrazines, hydrazides, sulfohydrazides, thiosemicarbazides were utilized for the synthesis of quinazoline heterocycles.[8e,f] Recently $Ba(OH)_2$ was effectively used to catalyze the reaction between *o*-arylisothiocyanate esters and *o*-phenylenediamines under *MW* irradiation for the fused quinazoline system.[9a] 1,1'-Carbonyldiimidazole on reaction with amines may also provide these heterocycles.[9b] $PPh_3/I_2/EtN(i\text{-}Pr)_2$ catalyzed dehydration of diamides,[9c,d] and recently through its intramolecular dehydrative cyclization using $HMDS/I_2$ were utilized to construct the quinazolinone moiety.[9e] Several quinazolinone based libraries through solid phase combinatorial synthesis have also been well documented.[10a-f] Very recently we have also reported a simple and one-pot synthesis of quinazolinones *via* benzotriazole methodology.[11b] Although some of these synthetic methods are useful, but involvement of two or more steps, use of hazardous chemicals, long reaction times, low yields and limited availability of starting materials are their serious drawbacks. Therefore the synthesis of quinazolinones with diverse substitution patterns by a simple, short, and high yielding methodology has become a growing field of organic chemistry. In recent years microwave assisted chemistry has become an emerging tool for the synthesis of diverse range of molecules for medicinal interest over the conventional method. Keeping in view the above, we wish to report a microwave assisted one-pot, convenient and high yield synthesis of quinazolinones using 1,1'-carbonothioylbis(1*H*-benzotriazole).

Results and Discussion

On one hand, it is well documented that benzotriazole can not only easily enter into molecules by a variety of reactions, but after the completion of the reaction can easily be cleaved too.[11,13] On the other hand, an organic soluble amidine base DBU has been found to be an efficient and mild catalyst with an excellent reactivity in several synthesis. [14] Based on these observations and in continuation of our work to search new synthetic methodology, we

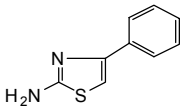
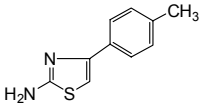
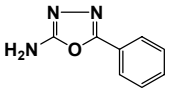
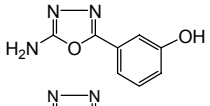
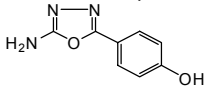
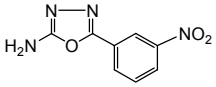
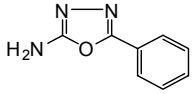
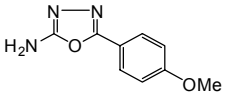
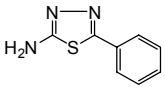
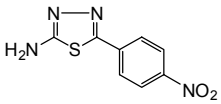
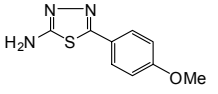
report herein a microwave assisted synthesis of novel N^3- thiazole, [1,3,4]-oxadiazoles and thiadiazole substituted 2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one by reacting heterocyclic amines, 1,1'-carbonothioylbis(1*H*-benzotriazole), and anthranilic acid or its ester derivative using DBU as catalyst.



Scheme 1. MW *assisted* synthesis of 2-thioxo-2,3-dihydroquinazolin-*4*(1*H*)-ones.

Thus the reaction of methyl anthranilate (**1a**) with 1,1'-carbonothioylbis(1*H*-benzotriazole) (**3**) seperatly with the benzyl amine (**2a**) and *n*-octyl amine (**2b**) using DBU as catalyst under microwave irradiation led to the formation of respective quinazolinones **4a** and **4b** in excellent yield. The products were identified by comparison of the spectral data reported earlier.[11b] Similar reaction of methyl anthranilate (**1a**) with different pharmacologically important heterocyclic amines (**2c-l**) using **3** and catalytic amount of DBU in CH_2Cl_2 under *MW* irradiation for 5-7 min resulted in the desired 3-heteroaryl-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one in good yields (Scheme 1). The results are depicted in Table 1. The products were isolated by column chromatography (230-400 mesh) using a gradient of ethyl acetate/*n*-hexane and characterized on the basis of spectroscopic data and microanalysis.

Table 1. 2-Thioxo-2,3-dihydroquinazolin-*4*(1*H*)-ones (**4-7**) synthesized *via* Scheme 1[a]

No.	4-7	Amine (**2**)	Acid/ester (**1a-d**)	Base	Time (min)	Yield [b] (%)	m.p. (^{0}C)
1	**4a**	Benzyl amine (**2a**)	**1a**	DBU	5	92	247-248[c]
2	**4b**	*n*-Octyl amine (**2b**)	**1a**	DBU	5	90	138-139[d]
3	**5a**	 **2c**	**1a**	DBU	7	86	220-222
4	**5a**	**2c**	**1a**	*DABCO*	7	88	-
5	**5a**	**2c**	**1b**	DBU	12	51	-
6	**5b**	 **2d**	**1a**	DBU	7	81	224-226
7	**5c**	**2c**	**1d**	DBU	12	55	217-219
8	**5c**	**2c**	**1d**	DABCO	12	51	-
9	**5d**	**2c**	**1c**	*DBU*	12	45	-
10	**6a**		**1a**	DBU	7	85	240-242
11	**6b**		**1a**	DBU	7	84	225-227
12	**6c**		**1a**	DBU	7	87	217-219
13	**6d**		**1a**	DBU	7	82	235-237
14	**6e**		**1d**	DBU	12	45	240-242
15	**6f**		**1a**	DBU	7	90	222-224
16	**7a**		**1a**	DBU	7	84	228-230
17	**7b**		**1a**	DBU	7	84	244-245
18	**7c**		**1a**	DBU	7	80	183-184

[a]Reaction under *MW*. [b]Isolated yield. [c](Lit.[11b] 248 ^{0}C). [d](Lit.[11b] 138 ^{0}C).

In an another experiment microwave irradiation of methyl anthranilate (**1a**), 4-phenyl-1,3-thiazol-2-amine (**2c**), and 1,1'-carbonothioylbis(1*H*-benzotriazole (**3)** in presence of catalytic amount of DBU in anhydrous CH_2Cl_2 for 7 min yielded the desired 3-(4-phenyl-1,3-thiazol-2-)-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (**5a**) *via* the *Bt*-equivalent isothiocyanate intermediate in good yield. The product was isolated by column chromatography (230-400 mesh) using a gradient of EtOAc-*n*-hexane (20:80) and the structure has been confirmed as cyclic (**5a**), not an open chain thiourea. *DABCO* catalysed reaction afforded the compound **5a** in good yield, but it was found to be contaminated with catalyst after elution with EtOAc-*n*-hexane (20:80) through silica gel column. The similar DBU catalysed reactions with other amines *e.g.* oxadiazoles (**2e-i**) and 2-thiadiazoles (**2j-l**) also afforded quinazolinone heterocycles **6(a-f)** and **7(a-c)** respectively in good yield (80-90%). The thermal reaction with heterocyclic amines afforded quinazolinones comparatively in very low yield and takes long reaction time than previously used aliphatic and aromatic amines.[11b] In case of anthranilic acid (**1b**) or having methyl substitution (**1d**), the reaction proceeds sluggishly and the product was obtained in a comparatively low yield even under microwave irradiation. The above described cyclative amidation reaction with some other solvents such as anhydrous $CHCl_3$, toluene, and DMF also resulted in good yields. To the best of our knowledge this is the first report of microwave assisted and DBU catalyzed one-pot synthesis of 2-thioxo-2,3-dihydroquinazolin-4(1*H*)-ones using benzotriazole methodology.

Conclusions

In conclusion, a facile and rapid method for the synthesis of diverse 2-thioxo-2,3-dihydroquinazolin-4(1*H*)-ones containing thiazoles, [1,3,4]oxadiazoles and thiadiazoles pharmacophores has been developed by amidine base catalyzed one-pot reaction of anthranilic ester, heterocyclic amines, and 1,1'-carbonothioylbis(1*H*-benzotriazole) under microwave condition.

Experimental Section

General Proceedures. Thin layer chromatography (TLC) was performed using silica gel 60 F-254 plates with I_2 vapors as detecting agents followed by spraying with *Draggendorff* reagent. Silica gel (230-400 mesh) was used for column chromatography. *TMS* (0.0 ppm) was used as an internal reference in ^{1}H NMR. Infrared spectra were recorded as KBr pellets by a Perkin Elmer RX-1 spectrometer. Melting points were determined on a Büchi 535 melting point apparatus. Elemental analyses were performed on a Perkin-Elmer 2400 C, H, N analyzer and values were found to be within ±0.5% of the calculated values. Whirlpool (Model: MP-225) microwave oven having controls as rotary knob with power 8 and MWO Power 1000 W was used for reaction.

Experiments (entry **2, 3** and **10**) were done in Biotage Initiator 60 Microwave oven at 80 ^{0}C, 80W for 5 min, where improvement in reaction yield was observed.

4-Aryl-1,3-thiazol-2-amine (**2a,b**) were prepared from different acetophenones reacting with thiourea.[12a,b] Aromatic aldehydes reacting with semicarbazide hydrochloride, and corresponding semicarbazone thus obtained on subsequent cyclization yielded 5-aryl-1,3,4-oxadiazol-2-amine (**2c-g**) in 85-92%.[12c] Similarly thiosemicarbazide afforded 5-aryl-1,3,4-thiadiazol-2-amine (**2h-j**) in good yield.[12d,e] 1,1'-Carbonothioylbis(1*H*-benzotriazole) was obtained from benzotriazole in 85%.[15]

Typical procedure for the preparation of 3-heteroaryl-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-ones

A mixture of 1,1'-carbonothioylbis(1*H*-benzotriazole (0.092 g, 0.331 mmol), 5-phenyl-1,3,4-thiadiazol-2-amine (0.062g, 0.331mmol), methyl anthranilate (0.05 g, 0.331 mmol), anhydrous CH_2Cl_2 (10 ml) in a conical flask (25ml) was irradiated under microwave for 7 min in presence of catalytic amount of DBU (0.0076g, 0.05 mmol). Progress of reaction was checked by TLC using *n*-hexane: EtOAc (4:1). The reaction mixture was dissolved in CH_2Cl_2 (75 ml), washed with 5% Na_2CO_3 solution to remove liberated benzotriazole from reaction mixture. The organic phase was separated, dried over anhydrous Na_2SO_4 and solvent evaporated under reduced pressure. The crude mass thus obtained was subjected to flash chromatography on silica gel (230-400 mesh) using EtOAc-*n*-hexane (20:80) to yield compound **5a**.

3-(4-Phenyl-1,3-thiazol-2-yl)-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (5a). Yield: 86%; Colorless solid, mp. = 220-224 ^{0}C; IR (KBr): ν_{max} cm^{-1} 1718.6, 1275.9, 2924.1; MS: *m/z* = 338 $[M+H]^+$; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 12.95 (bs, 1H, NH), 8.75 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 8.35 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 8.16 (m, 2H, Ar-*H*), 7.67 (m, 2H, Ar-*H*), 7.50 (t, *J* = 7.8 Hz, 1H, Ar-*H*), 7.26-7.20 (m, 3H, Ar-*H* and thiozole ring-H) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.46, 164.55, 138.87, 135.65, 133.84, 131.98, 130.38, 129.38, 129.29, 128.76, 127.28, 126.29, 124.98, 116.40, and 114.91 ppm; Anal.calcd. for $C_{17}H_{11}N_3S_2O$: C, 60.51; H, 3.29; N, 12.45; Found: C, 60.80; H, 3.53; N, 12.29 %.

The same compound **5a** was obtained starting from anthranilic acid in place of methyl anthranilate and afforded the product in 51% yield. *MW* irradiation of methyl anthranilate, 1,1'-carbonothioylbis(1*H*-benzotriazole (**3**), and 5-phenyl-1,3,4-thiadiazol-2-amine (**2c**) in presence of catalytic amount of *DABCO* afforded the compound **5a** in good yield, but compound **5a** was contaminated with catalyst and could not be isolated free from the catalyst after elution with EtOAc-*n*-hexane (20:80) through a silica gel column.

3-[4-(4-Methylphenyl)-1,3-thiazol-2-yl]-2-thioxo-2,3-dihydroquinazolin-4(1H)-one (5b). According to the procedure described for **5a**: Colorless solid. Yield 81%; mp = 224-226 ^{0}C; IR (KBr): ν_{max} cm^{-1} 1717.6, 1269.5, 2923.9; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.16 (t, *J* = 7.5 Hz, 1H, Ar-*H*), 7.99 (d, *J* = 7.5 Hz, 2H, Ar-*H*), 7.66 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 7.51 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 7.35-7.25 (m, 3H, Ar-*H*), 6.67 (s, 1H, thiozole ring-H), 4.93 (bs, 1H, NH), 2.36 (s, 3H, Ar-CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.46 164.56, 138.87, 135.65, 133.84, 131.98, 130.38,

129.38, 129.29, 128.76, 127.28, 126.29, 124.98, 116.40, 114.91, and 29.68 ppm; Anal.calcd. for $C_{18}H_{13}N_3S_2O$: C, 61.52; H, 3.72; N, 11.96; Found: C, 61.04; H, 3.98; N, 12.10 %.

3-(5-Phenyl-1,3,4-oxadiazol-2-yl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one (6a). According to the procedure described for **5a**: Colorless solid, Yield 85%; mp. = 240-242 ^{0}C; IR (KBr): ν_{max} cm^{-1} 1714.1, 1273.3, 2923.9; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.91 (bs, 1H, NH), 8.22 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 8.14 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.73 (t, *J* = 7.5 Hz, 1H, Ar-*H*), 7.71-7.54 (m, 3H, Ar-*H*), 7.35-7.18 (m, 3H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.49, 164.62, 139.34, 139.10, 135.57, 133.79, 131.95, 130.41, 129.21, 128.65, 127.58, 124.82, 116.41, and 115.12 ppm; Anal.calcd. for $C_{16}H_{10}N_4SO_2$: C, 61.52; H, 3.72; N, 11.96; Found: C, 60.76; H, 3.95; N, 13.02 %.

3-[5-(3-Hydroxyphenyl)-1,3,4-oxadiazol-2-yl]-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (6b). According to the procedure described for **5a**: Colorless solid, Yield 84%; mp. = 225-227 ^{0}C; IR (KBr): ν_{max} cm^{-1} 1716.4, 1269.8, 2925.6; MS: *m/z* = 339 $[M+H]^+$; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.01 (bs, 1H, exchangeable NH), 8.68 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 8.17 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 8.05 (d, *J* = 8.1 Hz, 1H, Ar-*H*), 7.92 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.73 (t, *J* = 7.2 Hz, 1H, Ar-*H*), 7.57-7.52 (m, 2H, Ar-*H*), 7.45 (t, *J* = 7.5 Hz, 1H, Ar-*H*), 7.25 (bs, 1H, D_2O exchangeable OH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 175.68, 164.17, 159.85, 156.17, 148.26, 143.44, 139.63, 135.79, 133.76, 130.94, 128.89, 127.43, 125.69, 123.39, 115.77, and 114.53 ppm; Anal.calcd. for $C_{16}H_{10}N_4SO_3$: C, 56.80; H, 2.98; N, 16.56; Found: C, 58.01; H, 3.20; N, 16.98 %.

3-[5-(4-Hydroxyphenyl)-1,3,4-oxadiazol-2-yl]-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (6c). According to the procedure described for **5a**: Colorless solid, Yield 87 %; mp. = 217-219^{0}C; IR (KBr): ν_{max} cm^{-1} 1713.5, 1273.7, 2925.6; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.91 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.70 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 7.34-30 (m, two d merged, *J* = 7.8 Hz and *J* = 8.1 Hz, 3H, Ar-*H*), 7.27-7.22 (m, two t merged, *J* = 7.2 Hz, 2H, Ar-*H*), 4.0-5.0 (bs, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 175.23, 164.45, 158.78, 147.56, 146.89, 142.66, 139.00, 134.46, 132.94, 128.17, 125.67, 124.22, 116.89, and 115.58 ppm; Anal.calcd. for $C_{16}H_{10}N_4SO_3$: C, 56.80; H, 2.98; N, 16.56; Found: C, 56.42; H, 3.42; N, 17.18 %.

3-[5-(3-Nitrophenyl)-1,3,4-oxadiazol-2-yl]-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (6d). According to the procedure described for **5a**: Colorless solid, Yield 82%; mp. = 235-237 ^{0}C; IR (KBr): ν_{max} cm^{-1} 1716.9, 1274.6, 2924.6; MS: *m/z* = 368 $[M+H]^+$; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.03 (bs, 1H, NH), 8.67 (d, *J* = 8.1 Hz, 1H, Ar-*H*), 8.16 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 8.05 (d, *J* = 8.1 Hz, 1H, Ar-*H*), 7.92 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.73 (t, *J* = 7.5 Hz, 1H, Ar-*H*), 7.57-7.52 (m, 2H, Ar-*H*), 7.44 (t, *J* = 7.5 Hz, 1H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 175.68, 164.20, 159.88, 156.19, 148.27, 143.48, 139.65, 135.83, 133.83, 130.79, 128.89, 128.61, 127.46, 124.42, 119.45, and 115.97 ppm; Anal.calcd. for $C_{16}H_9N_5SO_4$: C, 52.31; H, 2.47; N, 19.07; Found: C, 53.20; H, 3.35; N, 20.01 %.

7-Chloro-3-(5-phenyl-1,3,4-oxadiazol-2-yl)-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (6e). According to the procedure described for **5a**: Colorless solid, Yield 45%; mp. = 240-242 ^{0}C; IR (KBr): ν_{max} cm^{-1} 1715.1, 1272.4, 2924.9; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.43 (bs, 1H, NH), 8.09 (dd, *J* = 7.8 Hz, 2H, Ar-*H*), 7.52 (d, *J* = 8.1 Hz, 2H, Ar-*H*), 7.02-7.20 (m, 4H); ^{13}C NMR ($CDCl_3$,

75 MHz): δ 174.99, 164.78, 145.56, 140.11, 133.16, 133.65, 131.95, 130.00, 129.12, 128.55, 127.45, 125.74, 115.82, and 115.13 ppm.

3-[5-(4-Methoxyphenyl)-1,3,4-oxadiazol-2-yl]-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (6f). According to the procedure described for **5a**: Colorless solid, Yield 90%; mp. = 222-224 ^{0}C; IR (KBr): ν_{max} cm^{-1} 1715.1, 1270.4, 2923.9; MS: *m/z* = 353 $[M+H]^+$; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.28 (bs, 1H, NH), 8.22 (d, *J* = 7.2 Hz, 1H, Ar-*H*), 8.14 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.80-7.56 (m, 3H, Ar-H), 7.34 (d, *J* = 7.8 Hz, 2H, Ar-*H*), 7.13 (t, *J* = 8.1 Hz, 1H, Ar-H), 3.75 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.40, 164.33, 154. 34, 140.88, 136.77, 134.79, 132.94, 131.40, 129.65, 129.50, 128.11, 125.78, 117.09, 116.66, and 52.31 ppm; Anal.calcd. for $C_{17}H_{12}N_4SO_3$: C, 57.95; H, 3.43; N, 15.90; Found: C, 58.21; H, 3.87; N, 16.52 %.

3-(5-Phenyl-1,3,4-thiadiazol-2-yl)-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (**7a**).
According to the procedure described for **5a**: Colorless solid, Yield 84%; mp. = 228-230 ^{0}C; IR (KBr): ν_{max} cm^{-1} 1715.3, 1270.9, 2924.7; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.42 (bs, 1H, NH), 8.21 (d, *J* = 7.5 Hz, 1H, Ar-*H*), 8.15 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.69 (m, 1H), 7.56 (t, *J* = 7.5 Hz, 1H, Ar-*H*), 7.35-7.16 (m, 4H), 4.9 (bs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.20, 164.10, 139.34, 139.00, 134.88, 133.65, 131.94, 129.98, 128.85, 127.50, 126.44, 123.94, 115.23, and 115.11 ppm; Anal.calcd. for $C_{16}H_{10}N_4S_2O$: C, 56.79; H, 2.98; N, 16.56; Found: C, 57.93; H, 3.50; N, 17.75 %.

3-[-4-Nitrophenyl)-1,3,4-thiadiazol-2-yl]-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (7b). According to the procedure described for **5a**: Colorless solid, Yield 84%; mp. = 244-245 ^{0}C; IR (KBr): ν_{max} cm^{-1} 1718.11, 1271.54, 2924.99; ^{1}H NMR (DMSO-D_6, 300 MHz): 9.50 (bs, 1H, NH), 8.61 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 8.20 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.78 (m, 3H, Ar-*H*), 7.38-7.33 (m, 3H, Ar-*H*); ^{13}C NMR (DMSO-D_6, 75 MHz): δ 176.46, 164.62, 147.91, 146.55, 139.33, 135.63, 133.77, 131.91, 130.40, 129.17, 128.55, 119.23, 116.44, and 115.36 ppm; Anal.calcd. for $C_{16}H_9N_5S_2O_3$: C, 50.12; H, 2.37; N, 18.27; Found: C, 51.21; H, 2.93; N, 19.33 %.

3-[-(4-Methoxyphenyl)-1,3,4-thiadiazol-2-yl]-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (7c). According to the procedure described for **5a**: Colorless solid, Yield 80%; mp. = 183-184^{0}C; IR (KBr): ν_{max} cm^{-1} 1717.5, 1270.6, 2925.3; ^{1}H NMR (DMSO-D_6, 300 MHz): δ 10.91 (bs, 1H, NH), 8.22 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 8.14 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.75-7.55 (m, 3H, Ar-H), 7.35-7.18 (m, 3H, Ar-H), 3.74 (s, 3H, OCH_3); ^{13}C NMR (DMSO-D_6, 75 MHz): δ 175.10, 164.05, 154.28, 140.07, 135.97, 134.00, 131.60, 131.40, 130.13, 129.65, 129.5, 128.11, 124.44, 116.68, and 52.33 ppm; Anal.calcd. for $C_{17}H_{12}N_4S_2O_2$: C, 55.42; H, 3.28; N, 15.21; Found: C, 56.02; H, 3.90; N, 15.84 %.

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