One-Pot Synthesis of Quinazoline-2,4(1*H*,3*H*)-diones and 2-Thioxoquinazolinones with the Aid of Low-Valent Titanium Reagent

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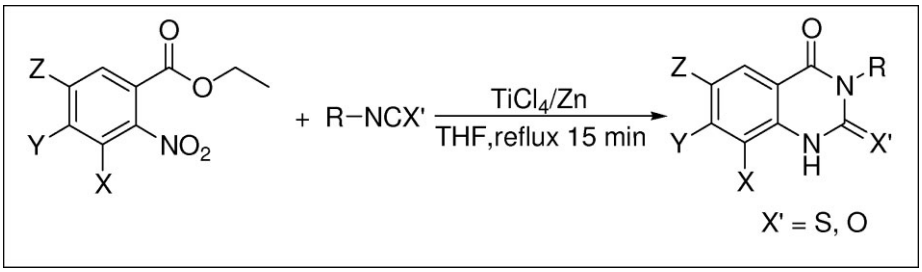

An efficient, convenient, one-pot synthesis of 2,4(1*H*,3*H*)-quinazolinediones and 2-thioxoquinazolinones was accomplished in good yields *via* the novel reductive cyclization of ethyl 2-nitrobenzoates with isocyanates or isothiocyanates mediated by $TiCl_4$/Zn system.

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INTRODUCTION

It has been reported that quinazolinones show antihypertonic, antirheumatic, antianaphylactic, antiasthmatic, tranquilizing, neuro-stimulating, and benzodiazepine binding activity [1,2]. The quinazolindione moiety, in particular, is widely found in natural purine based, alkaloids and many biologically active compounds [3]. For example, 3-substituted quinazolinones, such as SGB-1534 (**1**) and ketanserin (**2**) have been found to have antihypertensive activities mediated *via* α-adrenoceptor and serotonic receptor anatgonism [4], respectively. 6,7-Dimethoxy-1*H*-quinazoline-2,4-dione is a key intermediate for the production of the following medicines (Prazosin (Minipress) [5], Bunazosin (Detantol) [5], and Doxazosin (Cardenalin) [5]. 7-Chloro-1*H*-quinazoline-2,4-diones is also a key intermediate for the production of the medicines such as FK366 [6] and KF31327 [7].

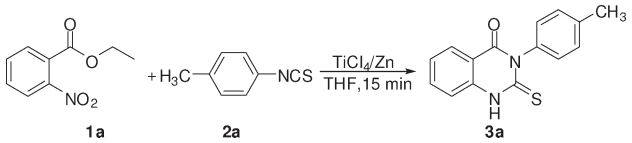
The quinazolinedione ring system can generally be prepared by the reaction of anthranilic acid with urea [8], anthranilamide with phosgene [9], and anthranilic acid with potassium cyanate [10] or chlorosulfonyl isocyanate [11]. However, these synthetic methods are considerably limited because of the usage of drastic conditions and uneasily starting materials. Different solid-phase combinatorial synthesis of quinazolinediones was reported in recent years, but these methods need long reaction times, multiple steps, or both [12]. Carbon dioxide reacted with 2-aminobenzonitriles assisted by excess amount of DBU or DBN to give corresponding 1*H*-quinazoline-2,4-diones has been reported [13]. However, the reaction time is too long (24 h). A recent report details the preparation of 2,4(1*H*,3*H*)-quinazolinediones and 2-thioxoquinazolines assisted by microwave [14], but the yields of this protocol were a little lower. It is found that all the methods mentioned earlier used amino-compounds other than nitro-compounds as starting materials. Therefore, we became interested in developing a novel and convenient synthetic method for the preparation of quinazolinedione derivatives start with nitro-compounds. Our initial studies showed that successful synthesis of various quinazolinediones from 2-nitrobenzamides and triphosgene [15]. As part of our ongoing research for novel synthesis of quinazolinediones derivatives, herein, we describe a new one-pot synthesis of quinazolinedione derivatives by treating ethyl *o*-nitrobenzoates with isothiocyanates or isocyanates under low-valent titanium reagent ($TiCl_4$/Zn).

RESULTS AND DISCUSSION

On the basis of our previous experience, we selected ethyl 2-nitrobenzoate **1a** and the 4-methylphenyl isothiocyanate **2a** as model substrates to optimize the experimental conditions for the proposed reductive cyclization reaction (Scheme 1). The results are summarized in Table 1.

As shown in Table 1, we briefly examined the effect of different temperatures and ratio of **1a**:$TiCl_4$/Zn. The

Scheme 1



1a 2a 3a

results obtained from these experiments indicated that the reaction temperatures had a significant influence on the success of this reaction. At room temperature or 40°C, no expected compound was detected (Table 1, entries 1 and 2). To our delight at refluxed the reaction proceeded smoothly in high yield (entry 4). To further evaluate the influence of the ratio of **1a**:$TiCl_4$/Zn, this reaction was carried out with different ratio. From the results it is obvious that the best ratio is 1:3.

Having established an optimal condition for the protocol, we performed a more detailed examination of the substrates. Thus, the behavior of a variety of substrates, which include different ethyl 2-nitrobenzoates as well as different isothiocyanates or isocyanates, was examined.

First of all, we performed the reaction of a variety of ethyl 2-nitrobenzoates **1** and isothiocyanates **2** *via* $TiCl_4$/Zn system (Scheme 2, Table 2).

As shown in Table 2, it can be seen that this protocol can be applied not only to aliphatic isothiocyanates but also to aromatic isothiocyanates with either electron-withdrawing groups (such as halide groups) or electron-donating groups (such as alkyl groups) under the same conditions. Furthermore, it was particularly noteworthy that the effects of substituted ethyl 2-nitrobenzoates were also investigated. 4-Chloro and 3-methyl substitution can also give moderate to good yields. However, the reductive cyclization was hindered by severe steric hindrance. For instance, no expected product was obtained when ethyl 2-nitrobenzoate was reacted with 2,6-di-*i*-pr-substituted aryl isothiocyanate.

A second part of the research was designed to synthesize quinazoline-2,4(1*H*,3*H*)-diones *via* the novel reductive cyclization of ethyl 2-nitrobenzoates with isocyanates under the same reaction conditions (Scheme 3, Table 3).

Table 1

Optimization for the reductive cyclization reaction.

Entry	Temperature (°C)	Ratio[a]	Isolated yield (%)
1	r.t.	1:3	0
2	40	1:3	0
3	60	1:3	10
4	Reflux	1:3	93
5	Reflux	1:1	0
6	Reflux	1:2	57
7	Reflux	1:4	83
8	Reflux	1:5	80

[a] Ratio of **1** and $TiCl_4$/Zn system.

Similarly, aryl isocyanates containing electron-donating and electron-withdrawing substituents were reacted well with ethyl 2-nitrobenzoate, therefore, we can conclude that the electronic nature of the substituents has no significant effect on this reaction, but severe steric hindrance still play an important part in this reaction. Good yields were also obtained when 3-methyl or 4-Cl-substituted ethyl 2-nitrobenzoates were used. Meanwhile, it was found that isocyanates showed similar reactivity trends with isothiocyanates.

The structures of products **3** and **5** were confirmed by IR, ^{1}H NMR, ^{13}C NMR, and HRMS.

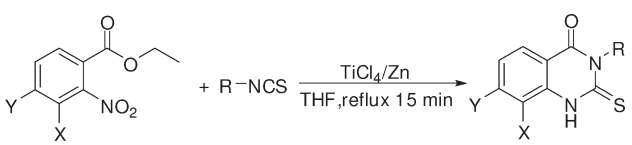
In conclusion, a series of quinazoline-2,4(1*H*,3*H*)-diones and 2-thioxoquinazolinones were synthesized induced by low-valent titanium reagent ($TiCl_4$/Zn). The protocol has been used for nitro-compounds other than amino-compounds as starting materials, which is very economic. Meanwhile, a variety of substrates can participate in the procedure with good yields. Furthermore, this method still has the advantages of short reaction time and convenient manipulation.

EXPERIMENTAL

THF was distilled from sodium-benzophenone immediately before use. All reactions were conducted under N_2 atmosphere. Melting points are uncorrected. IR spectra were recorded on Varian F-1000 spectrometer in KBr with absorptions in cm^{-1}. ^{1}H and ^{13}C NMR were determined on Varian-400 MHz spectrometer in DMSO-d_6 solution. *J* values are in Hz. Chemical shifts are expressed in ppm downfield from internal standard TMS.

General procedure for synthesis of thioxoquinazolineones 3. $TiCl_4$ (0.3 mL, 3 mmol) was added dropwise using a syringe to a stirred suspension of zinc powder (0.384 g, 6 mmol) in freshly distilled anhydrous THF (10 mL) at RT under a dry N_2 atmosphere. After completion of the addition, the mixture was refluxed for 2 h. The suspension of the low-valent titanium reagent formed was cooled to RT and a solution of ethyl 2-nitrobenzoates (1 mmol) and isothiocycanates (1 mmol) in THF (5 mL) was added dropwise. The reaction mixture was then refluxed for 15 min under N_2. After this period, the TLC analysis of the mixture showed the reaction to be completed. The reaction mixture was quenched with 5% HCl (15 mL) and extracted with $ClCH_2CH_2Cl$ (3 × 20 mL). The combined extracts were washed with water (3 × 20 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent under reduced pressure, the crude product was purified by recrystallization from 95% ethanol.

Scheme 2



1 2 3

Table 2

Synthesis of 2-thioxoquinazolinones.

Entry	X	Y	R	Products	Yields (%)[a]
1	H	H	4-$CH_3C_6H_4$	**3a**	93
2	H	H	C_6H_5	**3b**	90
3	H	H	3-$CH_3C_6H_4$	**3c**	78
4	H	H	$C_6H_5CH_2$	**3d**	86
5	H	Cl	C_6H_5	**3e**	71
6	H	Cl	4-ClC_6H_4	**3f**	72
7	H	Cl	3-$CH_3C_6H_4$	**3g**	86
8	H	Cl	$C_6H_5CH_2$	**3h**	83
9	CH_3	H	C_6H_5	**3i**	86
10	CH_3	H	4-ClC_6H_4	**3j**	89
11	CH_3	H	3-ClC_6H_4	**3k**	82
12	H	H	2,6-di-*i*-PrC_6H_4	**3l**	0

[a] Isolated yield.

2-Thioxo-3-*p*-tolyl-2,3-dihydroquinazolin-4(1*H*)-one (3a). This compound was obtained as solid with mp >300°C (ref. 16; 304°C); IR (KBr) ν: 3244, 1661, 1621, 1532, 1488, 1408, 1269, 1232, 1200, 1023, 990, 807, 759, 709, 692 cm^{-1}. ^1H NMR (DMSO-d_6): 2.37 (s, 3H, CH_3), 7.13–7.15 (m, 2H, ArH), 7.26–7.28 (m, 2H, ArH), 7.35 (t, $J = 7.6$ Hz, 1H, ArH), 7.43–7.45 (m, 1H, ArH), 7.76–7.80 (m, 1H, ArH), 7.94–7.96 (m, 1H, ArH), 13.03 (s, 1H, NH).

3-Phenyl-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (3b). This compound was obtained as solid with mp >300°C (ref. 17; 307°C); IR (KBr) ν: 3245, 1661, 1622, 1532, 1487, 1406, 1266, 1105, 988, 759, 691 cm^{-1}. ^1H NMR (DMSO-d_6): 7.26–7.28 (m, 2H, ArH), 7.33–7.37 (m, 1H, ArH), 7.38–7.42 (m, 1H, ArH), 7.45–7.50 (m, 3H, ArH), 7.76–7.80 (m, 1H, ArH), 7.96 (t, $J = 7.6$ Hz, 1H, ArH), 12.99 (s, 1H, NH).

2-Thioxo-3-*m*-tolyl-2,3-dihydroquinazolin-4(1*H*)-one (3c). This compound was obtained as solid with mp 282–284°C (ref. 18; 286–289°C); IR (KBr) ν: 3246, 1665, 1622, 1530, 1488, 1403, 1270, 1238, 1203, 913, 798, 772, 691 cm^{-1}.

3-Benzyl-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (3d). This compound was obtained as solid with mp 233–234°C (ref. 19; 230–231°C); IR (KBr) ν: 3198, 3130, 1650, 1622, 1533, 1487, 1426, 1403, 1340, 1170, 1147, 1074, 958, 754, 707, 691 cm^{-1}.

7-Chloro-3-phenyl-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (3e). This compound was obtained as solid with mp 286–288°C (ref. 20; 289 °C); IR (KBr) ν: 3185, 1661, 1616, 1528, 1479, 1385, 1337, 1276, 1260, 1217, 1191, 1123, 1075, 925, 861, 845, 751, 692 cm^{-1}. ^1H NMR (DMSO-d_6): 7.27–7.29 (m, 2H, ArH), 7.38–7.51 (m, 5H, ArH), 7.94–7.96 (m, 1H, ArH), 13.09 (s, 1H, NH).

7-Chloro-3-(4-chlorophenyl)-2-thioxo-2,3-dihydroqui-nazolin-4(1*H*)-one (3f). This compound was obtained as solid with mp 274–276°C (ref. 20; 273°C); IR (KBr) ν: 3195, 1657, 1617, 1530, 1491, 1386, 1279, 1257, 1219, 1193, 1090, 1022, 992, 924, 856, 815, 756, 680 cm^{-1}.

7-Chloro-2-thioxo-3-*m*-tolyl-2,3-dihydroquinazolin-4(1*H*)-one (3g). This compound was obtained as solid with mp 230–231°C (ref. 21; 230–232°C); IR (KBr) ν: 3193, 1659, 1617, 1525, 1479, 1385, 1258, 1192, 926, 880, 781, 757, 696 cm^{-1}. ^1H NMR (DMSO-d_6): 2.34 (s, 3H, CH_3), 7.06–7.08 (m, 2H, ArH), 7.21–7.23 (m, 1H, ArH), 7.34–7.38 (m, 2H, ArH), 7.44–7.45 (m, 1H, ArH), 7.93 (t, $J = 8.4$ Hz, 1H, ArH), 13.06 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 20.84, 114.99, 115.14, 124.39, 125.92, 128.77, 128.90, 129.16, 129.56, 133.31, 138.95, 139.92, 140.43, 159.13, 176.49.

HRMS [Found: m/z 302.0281 (M^+), calcd for $C_{15}H_{11}N_2OS^{35}Cl$: M, 302.0281].

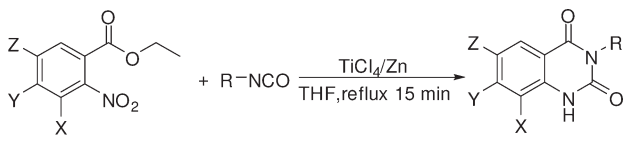
3-Benzyl-7-chloro-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (3h). This compound was obtained as solid with mp 258–260°C (ref. 21; 255–257°C); IR (KBr) ν: 3204, 1652, 1616, 1528, 1481, 1431, 1385, 1334, 1307, 1289, 1254, 1163, 1150, 1075, 948, 917, 862, 761, 726, 698 cm^{-1}. ^1H NMR (DMSO-d_6): 5.65 (s, 2H, CH_2), 7.22–7.26 (m, 1H, ArH), 7.28–7.33 (m, 4H, ArH), 7.37–7.40 (m, 1H, ArH), 7.44 (s, 1H, ArH), 7.96 (t, $J = 8.4$ Hz, 1H, ArH), 13.08 (s, 1H, NH).

HRMS [Found: m/z 302.0293 (M^+), calcd for $C_{15}H_{11}N_2OS^{35}Cl$: M, 302.0281].

8-Methyl-3-phenyl-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (3i). This compound was obtained as solid with mp 152–153°C; IR (KBr) ν: 3263, 1692, 1617, 1524, 1492, 1469, 1409, 1240, 1213, 1090, 1016, 987, 795, 757, 735, 691 cm^{-1}. ^1H NMR (DMSO-d_6): 2.12 (s, 3H, CH_3), 6.15 (s, 2H, ArH), 6.57 (t, $J = 7.6$ Hz, 1H, ArH), 7.15 (d, $J = 7.2$ Hz, 1H, ArH), 7.38 (t, $J = 8.8$ Hz, 1H, ArH), 7.51 (d, $J = 7.6$ Hz, 1H, ArH), 7.65–7.69 (m, 1H, ArH), 8.04 (dd, $J_1 = 2.4$ Hz, $J_2 = 6.8$ Hz, 1H, ArH), 10.19 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 17.67, 114.57, 116.52, 116.74, 120.67, 120.73, 121.82, 123.18, 126.55, 133.19, 136.57, 147.77, 168.38.

HRMS [Found: m/z 268.0670 (M^+), calcd for $C_{15}H_{12}N_2OS$: M, 268.0670].

Scheme 3



1 **4** **5**

Table 3

Synthesis of quinazoline-2,4(1*H*,3*H*)-diones.

Entry	X	Y	Z	R	Products	Yield (%)[a]
1	H	H	H	4-ClC_6H_4	**5a**	81
2	H	H	H	3-ClC_6H_4	**5b**	89
3	H	H	H	4-$CH_3C_6H_4$	**5c**	84
4	H	H	H	3-$CH_3C_6H_4$	**5d**	92
5	H	Cl	H	3-ClC_6H_4	**5e**	75
6	H	Cl	H	3-$CH_3C_6H_4$	**5f**	90
7	CH_3	H	H	4-ClC_6H_4	**5g**	66
8	CH_3	H	H	3-ClC_6H_4	**5h**	77
9	CH_3	H	H	4-$CH_3C_6H_4$	**5i**	94
10	CH_3	H	H	3-$CH_3C_6H_4$	**5j**	90
11	CH_3	H	H	cyclohexy	**5k**	93
12	H	H	Cl	4-$CH_3C_6H_4$	**5l**	91
13	H	H	H	2,6-di-*i*-PrC_6H_4	**5m**	0

[a] Isolated yield.

3-(4-Chlorophenyl)-8-methyl-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (3j). This compound was obtained as solid with mp 182–184°C; IR (KBr) ν: 3060, 1705, 1617, 1514, 1404, 1247, 1213, 1165, 1075, 808, 762, 701 cm^{-1}. ^1H NMR (DMSO-d_6): 2.57 (s, 3H, CH_3), 7.24–7.28 (m, 1H, ArH), 7.33–7.35 (m, 2H, ArH), 7.54–7.56 (m, 2H, ArH), 7.62 (d, J = 8.0 Hz, 1H, ArH), 7.83 (d, J = 7.6 Hz, 1H, ArH), 11.90 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 17.44, 116.56, 124.26, 124.58, 125.32, 129.04, 131.01, 132.69, 136.88, 138.03, 138.45, 159.79, 176.29.

HRMS [Found: m/z 302.0281 (M^+), calcd for $C_{15}H_{11}N_2OS^{35}Cl$: M, 302.0281].

General procedure for synthesis of quinazolinedione 5. $TiCl_4$ (0.3 mL, 3 mmol) was added dropwise using a syringe to a stirred suspension of zinc powder (0.384 g, 6 mmol) in freshly distilled anhydrous THF (10 mL) at RT under a dry N_2 atmosphere. After completion of the addition, the mixture was refluxed for 2 h. The suspension of the low-valent titanium reagent formed was cooled to RT and a solution of ethyl 2-nitrobenzoates (1 mmol) and isocyanates (1 mmol) in THF (5 mL) was added dropwise. The reaction mixture was then refluxed for 15 min under N_2. After this period, the TLC analysis of the mixture showed the reaction to be completed. The reaction mixture was quenched with 5% HCl (15 mL) and extracted with $ClCH_2CH_2Cl$ (3 × 20 mL). The combined extracts were washed with water (3 × 20 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent under reduced pressure, the crude product was purified by recrystallization from 95% ethanol.

3-(4-Chlorophenyl)quinazoline-2,4(1*H*,3*H*)-dione (5a). This compound was obtained as solid with mp 298–299°C (ref. 22; 301–302°C); IR (KBr) ν: 3201, 3070, 2938, 1732, 1674, 1493, 1448, 1406, 1282, 1156, 1090, 1016, 872, 825, 757, 741, 688 cm^{-1}. ^1H NMR (DMSO-d_6): 7.23 (d, J = 7.2 Hz, 2H, ArH), 7.38–7.39 (m, 2H, ArH), 7.54–7.55 (m, 2H, ArH), 7.71 (t, J = 8.0 Hz, 1H, ArH), 7.95 (d, J = 8.0 Hz, 1H, ArH), 11.59 (s, 1H, NH).

3-(3-Chlorophenyl)quinazoline-2,4(1*H*,3*H*)-dione (5b). This compound was obtained as solid with mp 265–266°C (ref. 23; 260.5–261.5°C); IR (KBr) ν: 3248, 3204, 3065, 2938, 1734, 1652, 1594, 1493, 1437, 1400, 1340, 1275, 1168, 731, 688 cm^{-1}. ^1H NMR (DMSO-d_6): 7.22–7.25 (m, 2H, ArH), 7.33–7.35 (m, 1H, ArH), 7.51–7.52 (m, 3H, ArH), 7.71 (t, J = 8.0 Hz, 1H, ArH), 7.94 (d, J = 8.0 Hz, 1H, ArH), 11.61 (s, 1H, NH).

3-*p*-Tolylquinazoline-2,4(1*H*,3*H*)-dione (5c). This compound was obtained as solid with mp 260–262°C (ref. 24; 265–266°C); IR (KBr) ν: 3199, 3129, 3069, 3005, 1721, 1665, 1608, 1512, 1490, 1448, 1288, 1153, 1023, 869, 815, 791, 754 cm^{-1}. ^1H NMR (DMSO-d_6): 2.37 (s, 3H, CH_3), 7.10–7.19 (m, 2H, ArH), 7.21–7.24 (m, 2H, ArH), 7.27–7.29 (m, 2H, ArH), 7.68–7.72 (m, 1H, ArH), 7.93 (d, J = 7.2 Hz, 1H, ArH), 11.54 (s, 1H, NH).

3-*m*-Tolylquinazoline-2,4(1*H*,3*H*)-dione (5d). This compound was obtained as solid with mp 256–258°C (ref. 23; 252–252.6°C); IR (KBr) ν: 3255, 1721, 1668, 1620, 1607, 1490, 1433, 1398, 1272, 1157, 922, 812, 785, 758, 697 cm^{-1}. ^1H NMR (DMSO-d_6): 2.36 (s, 3H, CH_3), 7.10–7.13 (m, 2H, ArH), 7.22–7.25 (m, 3H, ArH), 7.37 (t, J = 7.6 Hz, 1H, ArH), 7.71 (t, J = 8.0 Hz, 1H, ArH), 7.94 (d, J = 8.0 Hz, 1H, ArH), 11.56 (s, 1H, NH).

7-Chloro-3-(3-chlorophenyl)quinazolinee-2,4(1*H*,3*H*)-dione (5e). This compound was obtained as solid with mp >300°C (ref. 23; 312°C); IR (KBr) ν: 3232, 3188, 1736, 1656, 1616, 1594, 1480, 1432, 1370, 1169, 1089, 945, 867, 837, 759, 718 cm^{-1}. ^1H NMR (DMSO-d_6): 7.25–7.35 (m, 3H, ArH), 7.52–7.53 (m, 3H, ArH), 7.95 (d, J = 8.4 Hz, 1H, ArH), 11.74 (s, 1H, NH).

7-Chloro-3-*m*-tolylquinazoline-2,4(1*H*,3*H*)-dione (5f). This compound was obtained as solid with mp >300°C (ref.17; >300°C); IR (KBr) ν: 3230, 3185, 1736, 1652, 1593, 1429, 1370, 1262, 1159, 1089, 944, 871, 815, 726, 702 cm^{-1}. ^1H NMR (DMSO-d_6): 2.35 (s, 3H, CH_3), 7.10–7.13 (m, 2H, ArH), 7.24–7.29 (m, 3H, ArH), 7.37 (d, J = 7.6 Hz, 1H, ArH), 7.93–7.95 (m, 1H, ArH), 11.68 (s, 1H, NH).

3-(4-Chlorophenyl)-8-methylquinazoline-2,4(1*H*,3*H*)-dione (5g). This compound was obtained as solid with mp 282–284°C; IR (KBr) ν: 3327, 3233, 1721, 1655, 1534, 1493, 1405, 1225, 1092, 1059, 1019, 819, 760 cm^{-1}. ^1H NMR (DMSO-d_6): 2.39 (s, 3H, CH_3), 7.14 (t, J = 7.6 Hz, 1H, ArH), 7.33 (d, J = 8.8 Hz, 1H, ArH), 7.38–7.40 (m, 2H, ArH), 7.55–7.56 (m, 3H, ArH), 10.84 (s, 1H, NH).

HRMS [Found: m/z 286.0510 (M^+), calcd for $C_{15}H_{11}N_2O_2{}^{35}Cl$: M, 286.0509].

3-(3-Chlorophenyl)-8-methylquinazoline-2,4(1*H*,3*H*)-dione (5h). This compound was obtained as solid with mp 280–282°C; IR (KBr) ν: 3233, 3089, 1726, 1665, 1605, 1506, 1476, 1405, 1330, 1266, 1147, 1088, 898, 785, 753, 691 cm^{-1}. ^1H NMR (DMSO-d_6): 2.40 (s, 3H, CH_3), 7.15 (t, J = 7.6 Hz, 1H, ArH), 7.35–7.36 (m, 1H, ArH), 7.52–7.57 (m, 4H, ArH), 7.82 (d, J = 8.0 Hz, 1H, ArH), 10.86 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 17.87, 115.18, 123.01, 124.77, 126.06, 128.80, 128.96, 129.96, 131.08, 133.56, 136.94, 137.92, 138.85, 150.94, 150.97.

HRMS [Found: m/z 286.0510 (M^+), calcd for $C_{15}H_{11}N_2O_2{}^{35}Cl$: M, 286.0509].

8-Methyl-3-*p*-tolylquinazoline-2,4(1*H*,3*H*)-dione (5i). This compound was obtained as solid with mp 284–286°C; IR (KBr) ν: 3228, 3083, 1712, 1659, 1613, 1506, 1469, 1411, 1329, 1269, 1168, 1108, 1069, 887, 814, 790, 766 cm^{-1}. ^1H NMR (DMSO-d_6): 2.38 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 7.14 (t, J = 7.6 Hz, 1H, ArH), 7.18–7.20 (m, 2H, ArH), 7.28–7.30 (m, 2H, ArH), 7.54 (d, J = 7.2 Hz, 1H, ArH), 7.82 (d, J = 8.0 Hz, 1H, ArH), 10.78 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 17.83, 21.43, 115.17, 122.91, 124.67, 126.06, 129.39, 130.01, 133.81, 136.79, 138.13, 138.81, 151.17, 163.00.

HRMS [Found: m/z 266.1056 (M^+), calcd for $C_{16}H_{14}N_2O_2$: M, 266.1055].

8-Methyl-3-*m*-tolylquinazoline-2,4(1*H*,3*H*)-dione (5j). This compound was obtained as solid with mp 240–241°C; IR (KBr) ν: 3236, 1722, 1663, 1606, 1507, 1407, 1329, 1269, 1150, 803, 780, 759, 699 cm^{-1}. ^1H NMR (DMSO-d_6): 2.36 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 7.10–7.16 (m, 3H, ArH), 7.24–7.25 (m, 1H, ArH), 7.37 (t, J = 7.6 Hz, 1H, ArH), 7.54 (d, J = 7.2 Hz, 1H, ArH), 7.81 (d, J = 8.0 Hz, 1H, ArH), 10.80 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 17.17, 20.80, 114.49, 122.28, 124.04, 125.37, 126.03, 128.67, 128.78, 129.39, 135.69, 136.16, 138.26, 138.16, 150.44, 150.47.

HRMS [Found: m/z 266.1055 (M^+), calcd for $C_{16}H_{14}N_2O_2$: M, 266.1055].

3-Cyclohexyl-8-methylquinazoline-2,4(1*H*,3*H*)-dione (5k). This compound was obtained as solid with mp 244–245°C; IR (KBr) ν: 3222, 3189, 3079, 2935, 2852, 1703, 1650, 1607, 1506, 1474, 1417, 1376, 1329, 1276, 1188, 1116, 1081, 1023, 915, 793, 754 cm^{-1}. ^1H NMR (DMSO-d_6): 1.17 (t, J = 12.8 Hz, 1H, CH_2), 1.26–1.36 (m, 2H, CH_2), 1.58–1.67 (m, 3H, CH_2), 1.78–1.82 (m, 2H, CH_2), 2.33 (s, 3H, CH_3), 2.38–2.44 (m, 2H, CH_2), 4.71–4.77 (m, 1H, CH), 7.08 (t, J = 7.2 Hz, 1H, ArH), 7.46 (d, J = 7.2 Hz, 1H, ArH), 7.78 (d, J = 7.6 Hz, 1H, ArH), 10.53 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 16.95, 25.11, 25.99, 28.33, 52.85, 114.34, 122.12, 123.62, 125.25, 135.74, 137.78, 151.07, 162.34.

HRMS [Found: m/z 258.1367 (M^+), calcd for $C_{15}H_{18}N_2O_2$: M, 258.1368].

6-Chloro-3-*p*-tolylquinazoline-2,4(1*H*,3*H*)-dione (5l). This compound was obtained as solid with mp 291–293°C (ref. 25; 291–293°C); IR (KBr) ν: 3336, 1700, 1695, 1595, 1528, 1478, 1409, 1312, 1295, 1254, 1231, 1079, 815, 773, 743 cm^{-1}. ^1H NMR (DMSO-d_6): 2.37 (s, 3H, CH_3), 7.17–7.19 (m, 2H, ArH), 7.24–7.29 (m, 3H, ArH), 7.74–7.76 (m, 1H, ArH), 7.85–7.86 (m, 1H, ArH), 11.67 (s, 1H, NH).

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