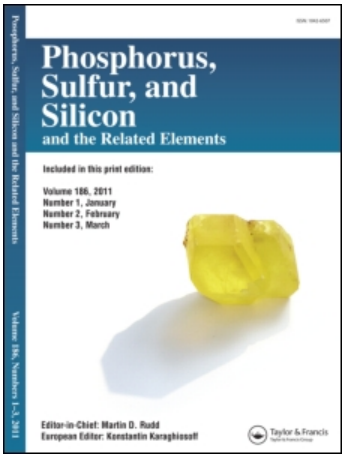


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# One-Pot, Multicomponent Condensation Reaction in Neutral Conditions: Synthesis, Characterization, and Biological Studies of Fused Thiazolo[2,3-b]quinazolinone Derivatives

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*A new series of 12-(2-chloro-6-quinoline-3-yl)-3,3,8-substituted-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-ones* ***4*** *was synthesized in one pot by condensing various 2-chloro-3-formylquinolines* ***1****, 2-amino-6-substituted-benzothiazoles* ***2****, and 1,3-cyclohexanedione* ***3*** *in ethanol. All the compounds were characterized by IR,* $^{1}H$ *NMR,* $^{13}C$ *NMR spectra and elemental analysis. All the synthesized compounds were screened for their antibacterial activity against Grampositive bacterial species* Bacillus cereus *and* Bacillus substilus*, Gram-negative bacterial species* Escherichia coli*, and their fungicidal activity against* Aspergillus niger*,* Fuserium oxisporum*,* and Rhizopus *species.*

**Keywords** 2-Aminobenzothiazole; biological activity; 2-chloro-3-formylquinoline; 1,3-cyclohexanedione; multicomponent reaction; thiazolo[2,3-b]quinazolinone



## INTRODUCTION

A multicomponent reaction (MCR) is a process in which three or more easily accessible components are combined together in a single reaction vessel to produce a final product that displays the features of all the input materials and thus offers greater possibilities for molecular diversity per step with a minimum of synthetic time and effort. A MCR is a domino process,[1–3] or, a sequence of elementary steps

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according to a program in which subsequent transformations are determined by the functionalities produced in the previous step. MCRs constitute an especially attractive synthetic strategy, since they provide easy and rapid access to large libraries of organic compounds with diverse substitution patterns. As MCRs are one-pot reactions, they are easier to carry out than multistep syntheses. Coupled with high-throughput library screening, this strategy was an important development in the drug discovery in the context of rapid identification and optimization of biologically active lead compounds. Libraries of small-molecule organic compounds are perhaps the most desired class of potential drug candidates, because standard peptides and oligonucleotides have limitations as bioavaliable therapeutics. With a small set of starting materials, very large libraries can be built up within a short time, which can then be used for research on medicinal substances.[4]



Thiazoles are a familiar group of heterocyclic compounds possessing a wide variety of biological activities, and their utility as medicaments is very established.[5–9] The thiazole nucleus is also an integral part of all the available penicillins, which have revolutionized the therapy of bacterial diseases.[10–14] A detailed literature survey[15,16] reveals that a large number of thiazole derivatives containing other heterocyclic systems have been synthesized and evaluated for their antimicrobial activity involving several strains of bacteria fungi and viruses.[17–19] Compounds having benzothiazole moiety possess diverse pharmacological activities viz. antibacterial,[20,21] anticonvulsant,[22] antitumor,[23] anti-inflammatory,[24] and antitubercular[25] properties.

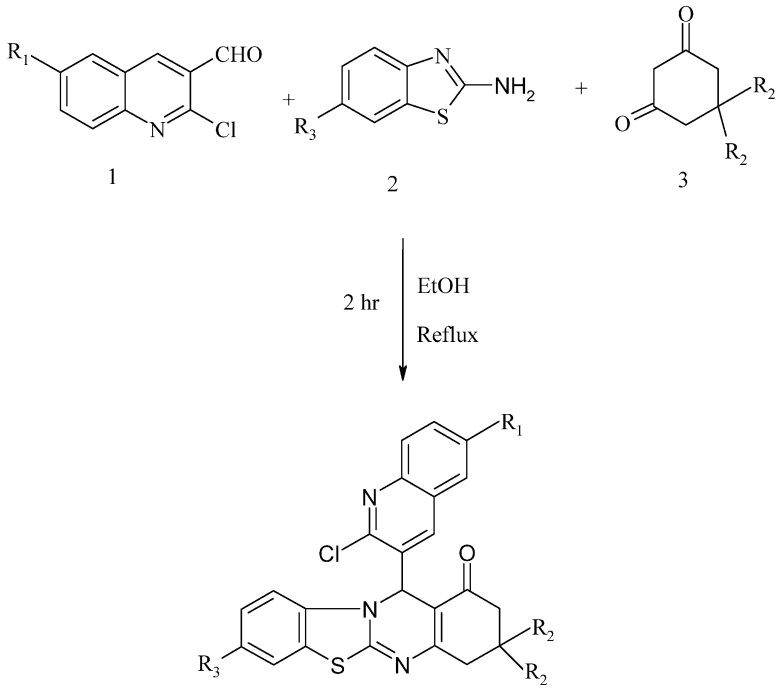
Quinazolinones are versatile nitrogen heterocyclic compounds used in many fields such as dyes, polymers, drugs, etc. The quinazolinone compounds have remarkable pharmacological activity and are widely used in the field of drugs.[26]

Quinazolinones form a large group among the pharmacologically active moieties and are generally of little toxicity without serious side effects to human body. Quinazolinones display a broad spectrum of biological and pharmacological properties such as hypertensive,[27] CNS-depressant,[28] anticonvulsant,[29] anti-Parkinsonian,[30] antibacterial,[31] anti-inflammatory,[32] and anthelmatic[33] activities. Substitution at the 2- and 3-position of quinazolinone plays a pivotal role in pharmacological activity. The above literature has motivated our research, and it was considered worthwhile to synthesize a variety of thiazoloquinazolinone derivatives by the MCR method and study their biological activity.

## RESULTS AND DISCUSSION

The reaction between 2-chloro 3-formyl 6-substituted quinoline[34] **1**, 2-amino-6-substituted benzothiazole[35] **2**, and substituted 1,3 cyclohexadione **3** gave thiazolo[3,2-b]quinazolinone derivatives **4** (Scheme 1). All the synthesized compounds were well characterized by their elemental analysis, IR, $^1$H NMR, and $^{13}$C NMR spectral studies.

The IR spectra of compounds **4a–x** showed an absorption band in the region of 1700–1730 cm$^{-1}$ (>C=O str.), 700–810 cm$^{-1}$(>C-Cl str.). The $^1$H NMR (DMSO-$d_6$) spectra of compounds **4a–x** exhibited the sharp singlet signal at $\delta$5.55–5.89 (s, 1H, -CH-) and the absence of a signal at $\delta$ 9.82–9.92 (s, 1H, -CHO-) for the starting material 2-chloro 3-formyl 6-substituted quinoline. Furthermore the $^{13}$C NMR ($\delta$ ppm) spectrum




$R_1$ = H, $CH_3$, $OCH_3$, Cl

$R_2$ = H, $CH_3$

$R_3$ = Cl, $CH_3$, $OCH_3$

**SCHEME 1**

showed a sharp signal at $\delta = 51.25$(C-H) (aliphatic region) ppm, which confirms the synthesis of fused thiazolo[2,3-b]quinazolinone derivatives by cyclization.

## Antibacterial Activity

The antibacterial activities of the synthesized compounds were examined in vitro by the agar diffusion cup method.[36–39] All the compounds were tested for activity against the Gram-positive bacteria *Bacillus cereus* and *Bacillus substilus* and Gram-negative bacteria *Escherichia coli*. The agar media were inoculated with different microorganisms and culture tested. The compounds were tested at 1000 ppm in DMF solution. DMF is used as control. The inhibition zones of microbial growth surrounding the disc were measured in millimeters at the end of a 24 h incubation period at 30°C for bacteria. All the compounds were screened with reference to standard drugs Ciprofloxacin and Ampicillin. The results are summarized in Table I. The antibacterial evaluation of the synthesized compounds revealed that compounds having a chloro and methoxy group **4b**, **4j**, **4m**, **4p**, **4q**, **4u**, and **4v** showed good activity against Gram-positive bacteria *B. substilus* and *B. cereus* as well as Gram-negative bacteria *E. coli* compared to the standard drug Ampicillin while moderately active compared to Ciprofloxacin.



## Antifungal Activity

The antifungal activity of the synthesized compounds were examined in vitro by the disc diffusion method.[40,41] All the compounds were tested for activity against the fungi *Aspergillus niger*, *Fuserium oxisporum*, and *Rhizopus*. The culture medium was potato dextrose agar. The agar media were inoculated with different microorganisms and culture tested. The compounds were tested at 1000 ppm in DMF solution. DMF is used as control. The inhibition zones of microbial growth surrounding the disc were measured in millimeter at the end of 48 h of incubation period at 35°C for fungi. All the compounds were screened with reference to the standard drug Griseofulvin. The results are summarized in Table II. The investigation of fungicidal screening data revealed that the compounds **4j**, **4o**, **4q**, **4q**, **4s**, **4w**, and **4x** showed good activity against *Aspergillus niger*; compounds **4g**, **4h**, **4i**, **4j**, **4p**, **4s**, and **4x** show good activity against *Fuserium oxisporum*; and compounds **4d**, **4e**, **4n**, **4o**, **4p**, and **4u** show good activity against *Rhizopus* compared to the standard drug Griseofulvin.

**TABLE I Antibacterial Activity**

| Compd. | Inhibition Zone (in mm) against | | |
|---|---|---|---|
| | *E. coli* | *B. substilis* | *B. cereus* |
| **4a** | 21 | 17 | 15 |
| **4b** | 22 | 16 | 14 |
| **4c** | 20 | 18 | 16 |
| **4d** | 20 | 18 | 16 |
| **4e** | 20 | 17 | 18 |
| **4f** | 17 | 14 | 15 |
| **4g** | 19 | – | 17 |
| **4h** | – | 17 | 15 |
| **4i** | 25 | 16 | 14 |
| **4j** | 19 | 15 | 08 |
| **4k** | 20 | 19 | 08 |
| **4l** | 16 | 15 | 19 |
| **4m** | 24 | 17 | 15 |
| **4n** | 15 | 18 | 18 |
| **4o** | 16 | 18 | 15 |
| **4p** | 25 | 18 | 19 |
| **4q** | 25 | 17 | 22 |
| **4r** | 19 | 15 | – |
| **4s** | 15 | 15 | 17 |
| **4t** | 18 | 16 | 17 |
| **4u** | 17 | 15 | 20 |
| **4v** | 27 | 18 | 24 |
| **4w** | 15 | 18 | 13 |
| **4x** | 15 | 15 | 18 |
| Ciprofloxacin | 36 | 32 | 35 |
| Ampicillin | 34 | 20 | 28 |



## CONCLUSION

Some new 2-(2-chloro-6-quinoline-3-yl)-3,3,8-substituted-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-ones **(4a–x)** were synthesized and screened for their antibacterial activity. The antimicrobial study revealed that compounds **4b**, **4j**, **4m**, **4p**, **4q**, **4u**, and **4v** show excellent activity against Gram-positive bacteria *B. substilus* and *B. cereus* as well as Gram-negative bacteria *E. coli* compared to the standard drug Ampicillin, while are moderately active compared with Ciprofloxacin. And all other synthesized compounds show significant activity against the tested Gram-positive and Gram-negative bacteria compared to the standard drug Ampicillin, while are moderately active compared with Ciprofloxacin. The antifungal study revealed that the compounds **4j**, **4o**, **4p**, **4q**, **4s**, **4x**, and **4w** show good activity against

**TABLE II Antifungal Activity**

| Compd. | Inhibition Zone (in mm) against | | |
|---|---|---|---|
| | *A. niger* | *F. oxisporum* | *Rhizopus* |
| **4a** | 20 | 17 | 17 |
| **4b** | 17 | 19 | 20 |
| **4c** | 15 | 18 | 17 |
| **4d** | 17 | 17 | 21 |
| **4e** | 16 | 18 | 23 |
| **4f** | 17 | 17 | 17 |
| **4g** | 18 | 20 | 19 |
| **4h** | 16 | 21 | 18 |
| **4i** | 19 | 21 | 17 |
| **4j** | 23 | 20 | 19 |
| **4k** | 20 | 18 | 20 |
| **4l** | 17 | 15 | 18 |
| **4m** | 19 | 20 | 19 |
| **4n** | 18 | 20 | 22 |
| **4o** | 21 | 18 | 22 |
| **4p** | 20 | 21 | 21 |
| **4q** | 21 | 22 | 20 |
| **4r** | 20 | 19 | 20 |
| **4s** | 21 | 20 | 19 |
| **4t** | 18 | 18 | 19 |
| **4u** | 20 | 19 | 23 |
| **4v** | 20 | 19 | 21 |
| **4w** | 23 | 20 | 21 |
| **4x** | 22 | 21 | 19 |
| Griseofulvin | 27 | 25 | 25 |



*Aspergillus niger*, *Fuserium oxisporum*, and *Rhizopus* compared to the standard drug Griseofulvin. All other synthesized compounds show significant activity against *Aspergillus niger*, *Fuserium oxisporum*, and *Rhizopus* compared to the standard drug Griseofulvin.

## EXPERIMENTAL

All the melting points are uncorrected and are expressed in °C. Elemental analysis (% C, H, N) was carried out using a Perkin Elmer 2400 CHN analyzer. IR spectra of all the compounds have been recorded on a Nicolet Impact 400D FT-IR spectrophotometer using KBr disks. The $^{1}H$ NMR and $^{13}C$ NMR spectra have been recorded on a Bruker AC 400F (400MHz) instrument using TMS as internal standard in DMSO-$d_6$ as a solvent. Chemical shifts are reported in parts per million (ppm). Thin

layer chromatography (TLC) was performed on silica gel G for TLC (Merck), and spots were visualized by iodine vapors or by irradiation with ultraviolet light.

## General Procedure: 8-Substituted-12-(2-chloro-6-substituted-quinolin-3-yl)-3-3-substituted-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4a–x)

A mixture of 2-chloro-6-substituted-3-formyl quinoline (0.01 mol), 2-amino-6-substituted benzothiazole (0.01 mol), and 5,5-disubstituted-1,3-cyclohexandione (0.01 mol) in ethanol (10 mL) was refluxed with continuous stirring for 2 h and cooled. The separated solid mass was filtered, washed with a small amount of ethanol, and dried. The crude product was purified by treating it in an equimolar mixture of chloroform and methanol to obtain the pure solid sample. All the other compounds **4a–x** have been synthesized following the same method.



### *8-Chloro-12-(2-chloro-6-methyl-quinolin-3-yl)-3–3-dimethyl-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4a) [$R_1 = CH_3$, $R_2 = CH_3$, $R_3 = Cl$]*

Mp 235–236°C, Yield 83%, Anal. Calcd. For $C_{26}H_{21}Cl_2N_3OS$: C 63.35, H 4.28, N 8.50, found C 63.16, H 4.10, N 8.23. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 1.01(s, 3H, -C$\underline{H}_3$), 1.35(s, 3H, -C$\underline{H}_3$) 2.31(s, 3H, -C$\underline{H}_3$), 2.47–2.98(m, 4H, -C$\underline{H}_2$), 5.86(s, 1H, -C$\underline{H}$-), 6.29–7.50(m, 7H, Ar-$\underline{H}$). IR: $\nu_{max}$ (KBr, cm$^{-1}$): 1690(C=O str.), 1585(C=N str.), 1315(C-N str.), 790(C-S str.), 710(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.87(C$\underline{H}_3$), 25.62, 30.68(C-(C$\underline{H}_3$)$_2$), 34.54(C-(CH$_3$)$_2$), 46.31, 49.88((C$\underline{H}_2$)$_2$), 50.74(C-H), 161.02(Cl-C=N), 165.80(S-C=N), 195.38(C=O), 113.28, 115.30, 115.43, 118.76, 119.05, 124.03, 126, 127.79, 128.45, 130.28, 131.60, 132.75, 134.76, 137.06, 139.01, 148.92(C-Ar) ppm.

### *8-Methyl-12-(2-chloro-6-methyl-quinolin-3-yl)-3–3-dimethyl-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4b) [$R_1$=$CH_3$, $R_2$=$CH_3$, $R_3$=$CH_3$]*

Mp 231–232°C, Yield 85%, Anal. Calcd. For $C_{27}H_{24}ClN_3OS$: C 68.41, H 5.10, N 8.83, found C 68.34, H 5.05, N 8.67. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 0.92(s, 3H, -C$\underline{H}_3$), 1.34 (s, 3H, -C$\underline{H}_3$) 2. 31(s, 3H, -C$\underline{H}_3$), 2.38(s, 3H, -C$\underline{H}_3$), 2.27–2.98(m, 4H, -C$\underline{H}_2$), 5.85(s, 1H, -C$\underline{H}$-), 6.30–7.59(m, 7H, Ar-$\underline{H}$). IR: $\nu_{max}$ (KBr, cm$^{-1}$): 1690(C=O str.), 1585(C=N str.), 1322(C-N str.), 993(C-S str.), 715(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 21.82, 23.62(C$\underline{H}_3$), 27.20, 29.68(C-(C$\underline{H}_3$)$_2$), 34.56(C-

$(CH_3)_2$), 45.61, 49.88(($\underline{C}H_2)_2$), 50.74(C-H), 159.32(Cl-C=N), 165.88(S-C=N), 196.08(C=O), 112.48, 114.25, 115.47, 118.76, 118.05, 124.03, 125.99, 126.89, 128.45, 130.28, 131.60, 132.75, 134.76, 135.06, 13891, 148.99(C-Ar) ppm.

### *8-Methoxyl-12-(2-chloro-quinolin-3-yl)-3–3-dimethyl-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4c) [$R_1$ = H, $R_2$ = $CH_3$, $R_3$ = $OCH_3$]*

Mp 221–224°C, Yield 82%, Anal. Calcd. For $C_{26}H_{22}ClN_3O_2S$: C 66.18, H 4.66, N 8.83, found C 68.34, H 4.68, N 8.81. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 1.01(s, 3H, -C$\underline{H}_3$), 1.24(s, 3H, -C$\underline{H}_3$) 2.42–2.88(m, 4H, -C$\underline{H}_2$), 3.81(s, 3H, -C$\underline{H}_3$), 5.84(s, 1H, -C$\underline{H}$-), 6.32–7.76(m, 8H, Ar-H). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1710(C=O str.), 1583(C = N str.), 1326(C-N str.), 795(C-S str.), 730(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 19.82, 27.20(C-($\underline{C}H_3)_2$), 30.68($\underline{C}$-$(CH_3)_2$), 38.54, 45.66(($\underline{C}H_2)_2$), 50.08(O$\underline{C}H_3$), 52.04(C-H), 158.12(Cl-C=N), 166.88(S-C=N), 196.98(C=O), 115.48, 119.25, 119.47, 120.76, 121.05, 126.03, 127.99, 128.89, 129.45, 130.88, 131.60, 135.75, 136.76, 137.16, 138.51, 151.03, (C-Ar) ppm.

### *8-Methoxy-12-(2-chloro-6-methyl-quinolin-3-yl)-3–3-dimethyl-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4d) [$R_1$ = $CH_3$, $R_2$ = $CH_3$, $R_3$ = $OCH_3$]*

Mp 237–239°C, Yield 80%, Anal. Calcd. For $C_{27}H_{24}ClN_3OS$: C 66.18, H 4.89, N 8.58, found C 66.05, H 4.68, N 8.58. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 0.94(s, 3H, -C$\underline{H}_3$), 1.32(s, 3H, -C$\underline{H}_3$) 2,33(s, 3H, -C$\underline{H}_3$), 2.52–2.78(m, 4H, -C$\underline{H}_2$), 3.81(s, 3H, -C$\underline{H}_3$), 5.97(s, 1H, -C$\underline{H}$-), 7.10–7.89(m, 7H, Ar-H). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1670(C=O str.), 1565(C = N str.), 1327(C-N str.) 755(C-S str.),741(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.78, 25.63, 29.51(C-($\underline{C}H_3)_2$), 30.80($\underline{C}$-$(CH_3)_2$), 32.33, 34.42(($\underline{C}H_2)_2$), 50.71(O$\underline{C}H_3$), 56.43(C-H), 161.08(Cl-C=N), 165.80(S-C=N), 195.30 (C=O), 109.18, 115.45, 115.46, 118.48, 119.09, 124.58, 126.00, 126.56, 128.45, 129.32, 131.60, 132.75, 137.02, 138.50, 149.26,157.61(C-Ar) ppm.

### *8-Chloro-12-(2-chloro-quinolin-3-yl)-3–3-dimethyl-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4e) [$R_1$=H, $R_2$=$CH_3$, $R_3$=Cl]*

Mp 223–225°C, Yield78%, Anal. Calcd. For $C_{25}H_{19}Cl_2N_3OS$: C 62.72, H 3.99, N 8.93, found C 62.50, H 3.81.10, N 8.75. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 0.97(s, 3H, -C$\underline{H}_3$), 1.32(s, 3H, -C$\underline{H}_3$), 2.27–2.98(m, 4H, -C$\underline{H}_2$), 5.86(s, 1H, -C$\underline{H}$-) 6.89–7.79(m, 8H, Ar-H). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1640(C=O str.), 1565(C = N str.), 794(C-S str.), 735–39(C-

Cl str.) $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.87, 23.67(C-($\underline{C}H_3)_2$), 30.80($\underline{C}$-$(CH_3)_2$), 33.84, 48.65(($\underline{C}H_2)_2$), 56.74($\underline{C}$-H), 161.22(Cl-$\underline{C}$=N), 167.80(S-$\underline{C}$ = N), 196.10($\underline{C}$=O), 111.98, 117.20, 119.13, 120.66, 121.05, 125.23, 126.78, 128.29, 129.11, 131.88, 132.68, 133.85, 135.36, 137.06, 139.56, 149.13($\underline{C}$-Ar) ppm.

### *8-Methoxy-12-(2-chloro-6-methoxy-quinolin-3-yl)-3–3-dimethyl-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4f) [$R_1$=$OCH_3$, $R_2$=$CH_3$, $R_3$=$OCH_3$]*

Mp 240–242°C, Yield 76%, Anal. Calcd. For $C_{27}H_{24}ClN_3O_3S$: C 64.13, H 4.78, N 8.30, found C 64.09, H 4.68, N 8.02. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 0.91(s, 3H, -C$\underline{H}_3$), 1.02(s, 3H, C$\underline{H}_3$), 2.42–2.78(m, 4H, -C$\underline{H}_2$), 3.81–3.84(s, 6H, -C$\underline{H}_3$), 5.94(s, 1H, -C$\underline{H}$-), 7.13–7.91(m, 7H, Ar-$\underline{H}$) IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1690(C=O str.), 1565(C = N str.), 1343(C-N str.), 790(C-S str.), 749(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.79, 24.22(C-($\underline{C}H_3)_2$), 27.97($\underline{C}$-$(CH_3)_2$), 31.71, 32.98(($\underline{C}H_2)_2$), 43.34, 51.56(O$\underline{C}H_3$), 56.82($\underline{C}$-H), 162.58(Cl-$\underline{C}$ = N), 164.35(S-$\underline{C}$ = N), 196.30($\underline{C}$=O), 111.28, 116.31, 116.86, 118.78, 119.79, 125.38, 126.98, 127.56, 128.15, 130.22, 132.60, 133.35, 138.42, 139.10, 148.86,158.61($\underline{C}$-Ar) ppm.

### *8-Methyl-12-(2-chloro-6-methoxy-quinolin-3-yl)-3–3-dimethyl-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4g) [$R_1$ = $OCH_3$, $R_2$ = $CH_3$, $R_3$ = $CH_3$]*

Mp 236–239°C, Yield 91%, Anal. Calcd. For $C_{27}H_{24}ClN_3O_2S$: C 66.18, H 4.94, N 8.50, found C 66.09, H 4.91, N 8.43.$^1$H-NMR (DMSO-$d_6$,400 MHz): $\delta$ = 0.90(s, 3H, -C$\underline{H}_3$), 1.02(s, 3H, -C$\underline{H}_3$) 2.29(s, 3H, -C$\underline{H}_3$), 2.42–2.68(m, 4H, -C$\underline{H}_2$), 3.81(s, 3H, -C$\underline{H}_3$), 5.98(s, 1H, -C$\underline{H}$-), 7.05–7.89(m, 7H, Ar-$\underline{H}$). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1690(C=O str.), 1585(C = N str.), 1380(C-N str.), 792(C-S str.), 790(C-Cl). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 21.79($\underline{C}H_3$), 24.28, 27.97(C-($\underline{C}H_3)_2$), 31.76($\underline{C}$-$(CH_3)_2$), 32.88, 33.94(($\underline{C}H_2)_2$), 50.55(O$\underline{C}H_3$), 56.72($\underline{C}$-H), 162.58(Cl-$\underline{C}$ = N), 164.35(S-$\underline{C}$ = N), 197.10($\underline{C}$=O), 111.28, 116.31, 116.86, 118.78, 119.79, 125.38, 126.98, 127.56, 128.15, 130.22, 132.60, 133.35, 138.42, 139.10, 148.86, 158.61($\underline{C}$-Ar) ppm.

### *8-Chloro-12-(2-chloro-6-methoxy-quinolin-3-yl)-3–3-dimethyl-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4h) [$R_1$ = $OCH_3$, $R_2$ = $CH_3$, $R_3$ = Cl]*

Mp 243–244°C, Yield 81%, Anal. Calcd. For $C_{26}H_{21}Cl_2N_3O_2S$: C 61.18, H 4.14, N 8.20, found C 61.09, H 4.05, N 8.13. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 0.93(s, 3H, -C$\underline{H}_3$), 1.02(3H, s, -C$\underline{H}_3$) 2.44–2.78(4H, m, -C$\underline{H}_2$), 3.81 (3H, s, -C$\underline{H}_3$), 5.98(1H, s, -C$\underline{H}$-), 7.15–7.84(7H, m, Ar-

H). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1690(C=O str.), 1585(C = N str.), 1379(C-N str.), 786(C-S str.), 750(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 21.79, 27.97(C-($\underline{C}H_3)_2$), 30.76($\underline{C}$-($CH_3)_2$), 32.68, 33.24(($\underline{C}H_2)_2$), 52,12(O$\underline{C}H_3$), 56.12($\underline{C}$-H), 162.23(Cl-$\underline{C}$ = N), 164.61(S-$\underline{C}$ = N), 196.08($\underline{C}$=O), 110.88, 116.33, 116.77, 118.12, 119.98, 125.91, 126.92, 127.19, 128.23, 130.34, 132.45, 133.56, 138.67 139.78, 148.89,158.02($\underline{C}$-Ar) ppm.

### *8-Methyl-12-(2-chloro-quinolin-3-yl)-3–3-dimethyl-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4i) [$R_1$ = H, $R_2$ = $CH_3$, $R_3$ = $CH_3$]*

Mp 243–245°C, Yield 78%, Anal. Calcd. For $C_{26}H_{22}Cl_2N_3OS$: C 67.84, H 4.82, N 9.23, found C 67.50, H 4.73., N 9.15. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 0.97(s, 3H, -C$\underline{H}_3$), 1.34(3H, s, -C$\underline{H}_3$), 2.34(3H, s, C$\underline{H}_3$), 2.57–2.78(4H, m, -C$\underline{H}_2$), 5.86(1H, s, -C$\underline{H}$-), 6.89–7.79(8H, m, Ar-$\underline{H}$). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1760(C=O str.), 1535(C = N str.), 1329(C-N str.), 789(C-S str.), 805(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.87($\underline{C}H_3$), 23.67, 26,73(C-($\underline{C}H_3)_2$), 31.81($\underline{C}$-$(CH_3)_2$), 33.88, 44.12(($\underline{C}H_2)_2$), 56.74($\underline{C}$-H), 161.24(Cl-$\underline{C}$ = N), 165.87(S-$\underline{C}$ = N), 196.03($\underline{C}$=O), 110.91, 117.22, 119.23, 120.60, 121.65, 125.63, 126.68, 128.89, 129.16, 131.86, 132.69, 133.89, 135.66, 137.16, 139.96, 149.03($\underline{C}$-Ar) ppm.

### *8-Chloro-12-(2-chloro-6-chloro-quinolin-3-yl)-3–3-dimethyl-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4j) [$R_1$ = Cl, $R_2$ = $CH_3$, $R_3$ = Cl]*

Mp 254–255°C, Yield 79%, Anal. Calcd. For $C_{25}H_{18}Cl_3N_3OS$: C 58.32., H 3.52, N 8.20, found C 58.24, H 3.46, N 8.13. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 0.95(s, 3H, -C$\underline{H}_3$), 1.22(3H, s, -C$\underline{H}_3$), 2.40–2.69(4H, m, -C$\underline{H}_2$), 5.98(1H, s, -C$\underline{H}$-), 7.10–7.84(7H, m, Ar-$\underline{H}$). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1690(C=O str.), 1515(C = N str.), 1319(C-N str.), 777(C-S str.), 810(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 21.00, 30.06(C-($\underline{C}H_3)_2$), 32.60($\underline{C}$-$(CH_3)_2$), 33.04, 42.67(($\underline{C}H_2)_2$), 56.12($\underline{C}$-H), 162.20(Cl-$\underline{C}$ = N), 164.60(S-$\underline{C}$ = N), 196.48($\underline{C}$=O), 110.80, 116.03, 116.70, 118.12, 119.94, 125.90, 126.02, 127.19, 128.72, 130.34, 132.05, 133.50, 138.69 139.70, 148.09,158.92($\underline{C}$-Ar) ppm.

### *8-Methoxy-12-(2-chloro-6-chloro-quinolin-3-yl)-3–3-dimethyl-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4k) [$R_1$=Cl, $R_2$=$CH_3$, $R_3$=$OCH_3$]*

Mp 240–242°C, Yield 76%, Anal. Calcd. For $C_{26}H_{21}Cl_2N_3O_2S$: C 58.67, H 3.52, N 8.30, found C 58.32, H 3.43, N 8.22. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 0.98(s, 3H, -C$\underline{H}_3$), 1.12(s, 3H, -C$\underline{H}_3$), 2.42–2.68(m,

4H, -C$\underline{H}_2$), 3.81 (s, 3H, -C$\underline{H}_3$), 5.94(s, 1H, -C$\underline{H}$-), 7.13–7.91(m, 7H, Ar-$\underline{H}$). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1690(C=O str.), 1585(C = N str.), 1299(C-N str.), 769(C-S str.) 824(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.79, 27.97(C-($\underline{C}H_3)_2$), 32.72($\underline{C}$-$(CH_3)_2$), 32.92, 33.32(($\underline{C}H_2)_2$), 49.78(O$\underline{C}H_3$), 56.22($\underline{C}$-H), 162.58(Cl-$\underline{C}$ = N), 164.35(S-$\underline{C}$ = N), 196.00($\underline{C}$=O), 112.28, 116.32, 116.82, 118.76, 119.72, 125.34, 126.91, 127.46, 128.45, 131.22, 132.62, 133.85, 139.42, 140.10, 147.86,159.61($\underline{C}$-Ar) ppm.

### *8-Chloro-12-(2-chloro-6-chloro-quinolin-3-yl)-3–3-dimethyl-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4l) [$R_1$ = Cl, $R_2$ = $CH_3$, $R_3$ = $CH_3$]*

Mp 242–244°C, Yield 75%, Anal. Calcd. For $C_{26}H_{21}Cl_2N_3OS$: C 63.72., H 4.43, N 8.50, found C 63.54, H 4.36, N 8.43. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 0.92(s, 3H, -C$\underline{H}_3$), 1.42(s, 3H, -C$\underline{H}_3$), 2.24(s, 3H, C$\underline{H}_3$), 2.52–2.74(m, 4H, -C$\underline{H}_2$), 5.98(s, 1H, -C$\underline{H}$-), 7.10–7.84(m, 7H, Ar-$\underline{H}$). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1690(C=O str.), 1515(C = N str.), 1369(C-N str.), 754(C-S str.), 835(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 21.00($\underline{C}H_3$), 24.89, 30.26(C-($\underline{C}H_3)_2$), 32.46($\underline{C}$-$(CH_3)_2$), 33.66, 41.45(($\underline{C}H_2)_2$), 56.88($\underline{C}$-H), 162.54(Cl-$\underline{C}$ = N), 164.17(S-$\underline{C}$ = N), 196.17($\underline{C}$=O), 111.11, 116.23, 116.76, 118.32, 119.91, 125.56, 126.12, 127.45, 128.79, 130.22, 132.35, 133.25, 138.61 139.91, 148.19,158.92($\underline{C}$-Ar) ppm.

### *8-Chloro-12-(2-chloro-6-methyl-quinolin-3-yl)-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4m) [$R_1$ = $CH_3$, $R_2$ = H, $R_3$ = Cl]*

Mp 238°C, Yield 82%, Anal. Calcd. For $C_{24}H_{17}Cl_2N_3OS$: C 61.82., H 3.79, N 9.23, found C 61.64, H 3.69, N 9.01. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 2.32(s, 3H, C$\underline{H}_3$), 2.50–2.70(m, 6H, -C$\underline{H}_2$), 5.48(s, 1H, -C$\underline{H}$-), 6.79–7.44(m, 7H, Ar-$\underline{H}$). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1690(C=O str.), 1595(C = N str.), 1379(C-N str.), 774(C-S str.), 855(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 21.00($\underline{C}H_3$), 23.89, 34.26, 36.66(($\underline{C}H_2)_3$) 56.88($\underline{C}$-H), 154.54(Cl-$\underline{C}$ = N), 164.17(S-$\underline{C}$ = N), 196.97($\underline{C}$=O), 115.11, 121.23, 123.56, 125.86. 126.04 126.12, 127.55, 130.59, 130.88, 131.55, 131.79, 135.35, 136.25, 137,67 143.61, 150.92($\underline{C}$-Ar) ppm.

### *8-Methyl-12-(2-chloro-6-methyl-quinolin-3-yl)-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4n) [$R_1$ = $CH_3$, $R_2$ = H, $R_3$ = $CH_3$]*

Mp 228°C, Yield 80%, Anal. Calcd. For $C_{25}H_{20}ClN_3OS$: C 67.33, H 4.52, N 9.42, found C 62.64, H 4.23, N 9.28. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 2.29(s, 3H, C$\underline{H}_3$), 2.31(s, 3H, C$\underline{H}_3$), 2.52–2.69(m,

6H, -C$\underline{H}_2$), 5.48(s, 1H, -C$\underline{H}$-), 6.49–7.76(m, 7H, Ar-$\underline{H}$). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1790(C=O str.), 1605(C = N str.), 1299(C-N str.), 794(C-S str.), 830(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 21.09, 22.56($\underline{C}H_3$), 23.69, 33.26, 37.66(($\underline{C}H_2)_3$), 56.88($\underline{C}$-H), 153.54(Cl-$\underline{C}$ = N), 163.17(S-$\underline{C}$ = N), 196.27($\underline{C}$=O), 112.11, 122.23, 123.86, 125.26. 126.00 126.46, 128.55, 130.19, 130.80, 132.00, 132.79, 135.55, 136.65, 138,67 144.61, 151.92($\underline{C}$-Ar) ppm.

### *8-Methoxyl-12-(2-chloro-quinolin-3-yl)-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4o) [$R_1$ = H, $R_2$ = H, $R_3$ = $OCH_3$]*

Mp 218°C, Yield 81%, Anal. Calcd. For $C_{24}H_{18}ClN_3OS$: C 64.33, H 4.05, N 9.38, found C 64.21, H3.89, N 9.08. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 2.52–2.69(m, 6H, -C$\underline{H}_2$), 3.83(s, 3H, -C$\underline{H}_3$), 5.48(s, 1H, -C$\underline{H}$-), 6.41–7.86(m, 8H, Ar-$\underline{H}$). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1649(C=O str.), 1585(C = N str.), 1370(C-N str.), 810(C-S str.), 785(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.50, 23.69 33.26(($\underline{C}H_2)_3$), 47.66(O$\underline{C}H_3$), 56.88($\underline{C}$-H), 153.54(Cl-$\underline{C}$ = N), 163.17(S-$\underline{C}$ = N), 196.27($\underline{C}$=O), 112.11, 122.23, 123.86, 125.26. 126.00 126.46, 128.55, 130.19, 130.80, 132.00, 132.79, 135.55, 136.65, 138,67 144.61, 151.92($\underline{C}$-Ar) ppm.

### *8-Methoxy-12-(2-chloro-6-methyl-quinolin-3-yl)-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3- b]quinazolin-1-one (4p) [$R_1$ = $CH_3$, $R_2$ = H, $R_3$ = $OCH_3$]*

Mp 232°C, Yield 81%, Anal. Calcd. For $C_{25}H_{19}ClN_3O_2S$: C 65.00, H 4.35, N 9.18, found C 64.68, H 4.29, N 8.90. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 2.32(s, 3H, -C$\underline{H}_3$), 2.52–2.69(m, 6H, -C$\underline{H}_2$), 3.83(s, 3H, -C$\underline{H}_3$), 5.48(s, 1H, -C$\underline{H}$-), 6.43–7.26(m, 7H, Ar-$\underline{H}$). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1700(C=O str.), 1616(C = N str.), 1309(C-N str.), 784(C-S str.), 756(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.50($\underline{C}H_3$), 23.69, 25.56, 33.26(($\underline{C}H_2)_3$), 49.66(O$\underline{C}H_3$), 56.88($\underline{C}$-H), 153.51(Cl-$\underline{C}$ = N), 163.12(S-$\underline{C}$ = N), 196.37($\underline{C}$=O), 113.11, 122.43, 123.88, 125.56. 126.09 126.49, 128.58, 130.39, 130.84, 132.08, 132.70, 135.51, 136.75, 138,62 144.51, 151.82($\underline{C}$-Ar) ppm.

### *8-Chloro-12-(2-chloro-quinolin-3-yl)-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4q) [$R_1$ = H, $R_2$ = H, $R_3$ = Cl]*

Mp 225–227°C, Yield 80%, Anal. Calcd. For $C_{23}H_{15}Cl_2N_3OS$: C 61.22, H 3.34, N 9.33, found C 61.07, H 3.16, N 9.23. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 2.52–2.69(m, 6H, -C$\underline{H}_2$), 5.45(s, 1H, -C$\underline{H}$-), 6.33–7.61(m, 8H, Ar-$\underline{H}$). IR: $\nu_{max}$ (KBr, $cm^{-1}$): 1790(C=O str.), 1685(C = N str.),

1329(C-N str.), 772(C = -S str.) 721(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.50, 33.16, 36.66((C$H_2$)$_3$), 56.88(C-H), 153.55(Cl-C = N), 163.32(S-C = N), 197.02(C=O), 111.10, 121.43, 123.88, 125.56. 126.19 126.41, 128.68, 130.31, 130.71, 132.14, 132.79, 135.53, 136.85, 139,62 146.50, 151.22(C-Ar) ppm.

### *8-Methoxy-12-(2-chloro-6-methoxy-quinolin-3-yl)-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4r) [$R_1$ = $OCH_3$, $R_2$ = H, $R_3$ = $OCH_3$]*

Mp 234–236°C, Yield 80%, Anal. Calcd. For $C_{25}H_{20}ClN_3OS$: C 62.82, H 4.44, N 8.29, found C 62.66, H 3.89, N 8.64. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 2.52–2.69(m, 6H, -C$H_2$), 3.81–3.84(s, 6H, -C$H_3$), 5.45(s, 1H, -CH-), 6.38–7.63(m, 7H, Ar-H). IR: $\nu_{max}$ (KBr, cm$^{-1}$): 1770(C=O str.), 1555(C = N str.), 1339(C-N str.), 764(C-S str.), 720(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.50, 23.38, 25.89((C$H_2$)$_3$), 42.36, 44.66(OC$H_3$), 57.12(C-H), 153.65(Cl-C = N), 165.32(S-C = N), 197.31(C=O), 109.91, 120.89, 123.88, 125.86. 126.49 126.71, 128.77, 130.11, 130.51, 132.64, 132.99, 135.63, 137.15, 140,26, 145.12, 152.00(C-Ar) ppm.

### *8-Methyl-12-(2-chloro-6-methoxy-quinolin-3-yl)-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4s) [$R_1$ = $OCH_3$, $R_2$ = H, $R_3$ = $CH_3$]*

Mp 240°C, Yield 78%, Anal. Calcd. For $C_{25}H_{20}ClN_3O_2S$: C 67.58, H 5.26, N 9.56 found C 67.33, H 4.52, N 9.42. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 2.35(s, 3H, -C$H_3$), 2.52–2.69(m, 6H, -C$H_2$), 3.81(s, 3H, -C$H_3$), 5.48(s, 1H, -CH-), 6.40–7.59(m, 7H, Ar-H). IR: $\nu_{max}$ (KBr, cm$^{-1}$): 1640(C=O str.), 1515(C = N str.), 1369(C-N str.), 764(C-S str.), 712(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.52(C$H_3$), 23.79, 25.59, 33.36((C$H_2$)$_3$), 41.61(OC$H_3$), 56.88(C-H), 155.51(Cl-C = N), 162.12(S-C = N), 196.12(C=O), 112.12, 122.46, 123.89, 125.16. 126.69 127.79, 128.66, 130.71, 130.91, 132.28, 132.80, 135.53, 136.71, 139,62 142.51, 153.82(C-Ar) ppm.

### *8-Chloro-12-(2-chloro-6-methoxy-quinolin-3-yl)-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4t) [$R_1$ = $OCH_3$, $R_2$ = H, $R_3$ = Cl]*

Mp 239°C, Yield 79%, Anal. Calcd. For $C_{24}H_{17}Cl_2N_3O_2S$: C 61.97, H 3.67, N 9.17 found C 61.81, H 3.56, N 9.01.. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 2.52–2.69(m, 6H, -C$H_2$), 3.81(s, 3H, -C$H_3$), 5.48(s, 1H, -CH-), 6.39–7.62(m, 7H, Ar-H). IR: $\nu_{max}$ (KBr, cm$^{-1}$): 1690(C=O str.), 1599(C = N str.), 1364(C-N str.), 788(C-S str.), 800(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.32, 24.39, 33.36((C$H_2$)$_3$), 47.33(OC$H_3$), 56.81(C-H), 156.01(Cl-

C = N), 163.82(S-C = N), 196.51(C=O), 111.19, 122.11, 122.89, 124.06. 126.69 127.29, 128.46, 130.51, 131.00, 132.08, 132.32, 133.53, 135.71, 138,92 143.91, 154.02(C-Ar) ppm.

### *8-Methyl-12-(2-chloro-quinolin-3-yl)-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4u) [$R_1$ = H, $R_2$ = H, $R_3$ = $CH_3$]*

Mp 228°C, Yield 80%, Anal. Calcd. For $C_{24}H_{18}ClN_3OS$: C 66.74, H 4.31, N 9.73, found C 66.50, H 4.20, N 9.61. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 2.31(s, 3H, -C$H_3$), 2.52–2.69(m, 6H, -C$H_2$), 5.44(s, 1H, -CH-), 6.44–7.70(m, 8H, Ar-H). IR: $\nu_{max}$ (KBr, cm$^{-1}$): 1690(C=O str.), 1585(C = N str.), 1379(C-N str.), 759(C-S str.), 805(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 22.01(C$H_3$), 23.29 34.16, 38.06((C$H_2$)$_3$)56.82(CH), 152.14(Cl-C = N), 163.77(S-C = N), 197.37(C=O), 112.88, 121.93, 124.96, 125.86. 126.09 126.76, 128.50, 130.09, 131.00, 132.20, 132.99, 136.55, 137.65, 138,87 145.11, 150.62(C-Ar) ppm.

### *8-Chloro-12-(2-chloro-6-chloro-quinolin-3-yl)-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4v) [$R_1$ = Cl, $R_2$ = H, $R_3$ = Cl]*

Mp 250°C, Yield 80%, Anal. Calcd. For $C_{23}H_{14}Cl_3N_3OS$: C 56.88, H 2.90, N 8.78, found C 56.75, H 2.77, N 8.63. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 2.52–2.69(m, 6H, -C$H_2$), 5.67(s, 1H, -CH-), 6.33–8.10(m, 7H, Ar-H). IR: $\nu_{max}$ (KBr, cm$^{-1}$): 1730(C=O str.), 1595(C = N str.), 1319(C-N str.), 804(C-S str.), 786(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 22.09, 34.66, 38.46((C$H_2$)$_3$), 56.82(C-H), 197.31(C=O), 152.84(Cl-C = N), 163.97(S-C = N), 110.88, 120.99, 123.66, 125.96. 126.99 127.76, 129.50, 130.59, 131.22, 132.27, 132.93, 136.65, 137.23, 138,77 144.19, 150.72 (C-Ar) ppm.

### *8-Methoxy-12-(2-chloro-6-chloro-quinolin-3-yl)-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4w) [$R_1$ = Cl, $R_2$ = H, $R_3$ = $OCH_3$]*

Mp 234–236°C, Yield 82%, Anal. Calcd. For $C_{24}H_{17}Cl2N_3O_2S$: C 59.82, H 3.55, N 8.71, found C 59.36, H 3.40, N 8.62. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 2.54–2.71(m, 6H, -C$H_2$), 3.83(s, 3H, -C$H_3$), 5.45(s, 1H, -CH-), 6.32–7.56(m, 7H, Ar-H), IR: $\nu_{max}$ (KBr, cm$^{-1}$): 1650(C=O str.), 1562(C = N str.), 1299(C-N str.), 803(C-S str.), 746(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.50, 23.69 33.26((C$H_2$)$_3$), 49.61(OC$H_3$), 56.88(C-H), 153.54(Cl-C = N), 163.17(S-C = N), 196.27(C=O), 112.11, 122.23, 123.86, 125.26. 126.00 126.46, 128.55, 130.19, 130.80, 132.00, 132.79, 135.55, 136.65, 138,67 144.61, 151.92, (C-Ar) ppm.

### *8-Methyl-12-(2-chloro-6-chloro-quinolin-3-yl)-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4x) [$R_1$ = Cl, $R_2$ = H, $R_3$ = $CH_3$]*

Mp 240°C, Yield 81%, Anal. Calcd. For $C_{24}H_{17}Cl_2N_3OS$: C 61.81, H 3.61, N 9.01, found C 60.32, H 3.31, N 8.78. $^1$H-NMR (DMSO-$d_6$, 400 MHz): $\delta$ = 2.23(s, 3H, -C<u>H</u>$_3$), 2.52–2.69(m, 6H, -C<u>H</u>$_2$), 5.62(s, 1H, -C<u>H</u>-), 6.36–7.98(m, 7H, Ar-<u>H</u>). IR: $\nu_{max}$ (KBr, cm$^{-1}$): 1740(C=O str.), 1615(C = N str.), 1339(C-N str.), 814(C-S str.), 805(C-Cl str.). $^{13}$C-NMR (DMSO-$d_6$) $\delta$ = 20.90(<u>C</u>H$_3$), 23.78, 34.29, 38.29((<u>C</u>H$_2$)$_3$), 56.41(<u>C</u>-H), 154.04(Cl-<u>C</u> = N), 162.79(S-<u>C</u> = N), 197.19(<u>C</u>=O), 110.42, 121.99, 123.00, 126.76. 127.02 127.89, 128.30, 130.89, 131.88, 132.47, 132.83, 137.65, 137.93, 139.77 143.99, 152.82(<u>C</u>-Ar) ppm.

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