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ORIGINAL ARTICLE

Microwave promoted synthesis and antimicrobial activity of 3-thiazole substituted 2-styryl-4(3*H*)-quinazolinone derivatives

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2-Styryl-4(3*H*)-quinazolinones;
Antimicrobial activity

Abstract The present paper describes an optimized reaction condition for the microwave promoted synthesis of newer 3-thiazole substituted 2-styryl-4(3*H*)-quinazolinone derivatives, which in turn were prepared in good yield by the treatment of various 2-styryl benzoxazinone derivatives with various 2-aminothiazoles using co-solvent under microwave irradiation. All the compounds were characterized by various spectroscopic techniques and analytical methods. All newly synthesized compounds have been screened for their *in vitro* antibacterial and antifungal activities against *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus megaterium*, *Bacillus subtilis*, and *Aspergillus niger*.

1. Introduction

One of the most frequently encountered heterocycles in medicinal chemistry is 4(3*H*)-quinazolinone (**1**, Fig. 1) having broad range of biological activities (Kamal et al., 2006, 2010; Laddha et al., 2009; Malawska, 2005; Padala et al., 2003; Clercq, 2002; Nawrocka and Stasko, 2002; Sinha and Srivastava, 1994). Among the various classes of 4(3*H*)-quinazolinones, 2-styryl substituted derivatives (**2**, Fig. 1) have been gaining prominence due to the fact that its derivatives have been found to possess a wide spectrum of activities, such as tubulin polymerization inhibitor (Raffa et al., 2004), cytotoxic agent (Liu et al., 2006), Hsp90 inhibitor (Sgobba and Rastelli, 2009; Park et al., 2007), anticonvulsant (Bhandari et al., 2008; Welch

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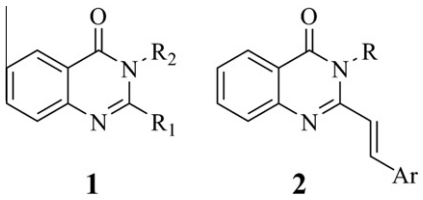


Figure 1 General structure of 4(3*H*)-quinazolinone and 2-styryl-4(3*H*)-quinazolinone.

et al., 2001), sedative-hypnotic (Jatav et al., 2008a, 2008b), Anti-proliferative (Mrozek-Wilczkiewicz et al., 2010) antibacterial, and antifungal agent (Gupta et al., 2008; Jatav et al., 2008c). Moreover, thiazoles are important pharmacodynamic heterocyclic nuclei, which when incorporated in different heterocyclic templates have been reported to possess various biological activities (Siddiqi and Ahsan, 2010 Li et al., 2009; Holla et al., 2003; Nora De Souza,2005; Hsu et al., 2003). More specifically, diverse pharmacological activities can be achieved by incorporating thiazole moiety at 3rd position of quinazolin-4(3*H*)-ones (Kumar et al., 2007; Maarouf et al., 2004; Kumar et al., 1997).

Microwave-assisted organic reactions are now well established and have gained popularity as indicated by large number of papers currently published on this topic (Caddick and Fitzmaurice, 2009; Kappe and Dallinger, 2009; Jindal and Bajaj, 2008; Katritzky and Singh, 2003; Lidström et al., 2001). Some of the interesting features of this method are milder reaction conditions, reduction of reaction times, enhanced selectivity, and associated ease of manipulation. In the light of the above observations, it was thought worthwhile to synthesize a new series of 2-styryl quinazolin-4(3*H*)-one derivatives by incorporating the thiazole moiety at 3rd position using microwave irradiation.

2. Results and discussion

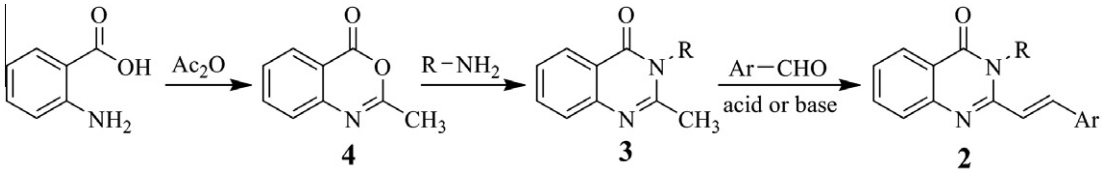
2.1. Chemistry

Although there are many reports describing the synthesis of 4(3*H*)-quinazolinones (**1**), most of these approaches are limited in that only phenyl group at R_1 is tolerated (Connolly et al., 2005). There are only a few specific reports on the preparation of the 3-substituted 2-styryl quinazolin-4(3*H*)-ones (**2**) (Raffa et al., 2004; Liu et al., 2006; Connolly et al., 2005; Wolfe et al., 1990; Philipova et al., 2006). The general method for the synthesis of these derivatives is the Knoevenagel condensation of 2-methylsubstituted quinazolinones (**3**) with aromatic aldehydes under basic (Wolfe et al., 1990; Philipova et al., 2006) or acidic (Raffa et al., 2004) conditions (Scheme 1). However, this method requires more number of steps which eventually lead to the lower yields (Raffa et al., 2004; Wolfe et al., 1990; Philipova et al., 2006). Furthermore, it proceeds via highly moisture sensitive and irritant intermediate 2-methyl-4*H*-benzo[*d*][1,3]oxazin-4-one (**4**) (Madkour, 2004), which requires a special care in its handling and storage. A new strategy was therefore planned, where 2-styryl benzoxazinones (**5**) and 2-aminothiazoles (**6**) were condensed to give the title compounds (**7**). 2-Styryl benzoxazinones were conveniently prepared by following the reported method (Fathalla et al., 2008) and were highly stable as compared to compound (**4**).

As far as the microwave assisted methods for the synthesis of quinazolinones are concerned, most of them have been reported for either 2 or 3 substituted derivatives (Bakavoli et al., 2007; Li et al., 2007; Rad-Moghadam and Mohseni, 2003; Rad-Moghadam et al., 2006). There are reports on the synthesis of 2,3-disubstituted quinazolinone using microwave irradiation but, most of them either involve the use of alkyl orthoesters (Ighilahriz et al., 2008; Dabiri et al., 2004; Lingaiah et al., 2006) or cyclic amides (Shankaraiah et al., 2009), which limit the variety of substitutions at 2nd position. Liu et al., (2007) reported one pot microwave assisted method for the generation of library of 2-styryl quinazolinones using $P(OPh)_3$ and pyridine. However, the yields were low to moderate (7.4–51%). Another drawback using $P(OPh)_3$ was its removal from the product. It could not be separated using simple purification procedures like washing or crystallization.

Recently, Zhou et al. (2004) have developed a general method for the synthesis of 3-sulfonamide-substituted quinazolinone derivatives by condensation of benzoxazinones (**5**) and substituted sulfonyl hydrazides under solvent free conditions at 130 °C. It was envisaged that this methodology could be extended to the preparation of the title compounds (**7**) under microwave irradiation. However, this protocol did not work under microwave irradiation when applied to (*E*)-2-styryl-4*H*-benzo[*d*][1,3]oxazin-4-one (**5a**) and 2-amino-5-methylthiazole (**6a**). Therefore, it was decided to use DMF as a solvent in above reaction because of its good solvating property and high loss tangent (Lidström et al., 2001). The reaction was successfully completed within 6 min of microwave irradiation at 350 W. The required compound (**7a**) was isolated in 40% yield along with 35% of diamide (**8**) after column chromatographic purification. The isolation of compound (**8**) suggests that the reaction might have proceeded with formation of this compound (Zhou et al., 2004).

Furthermore, the yield of the desired product could be improved if complete conversion of diamide to quinazolinone is possible. There are many instances which report the cyclization of diamides to quinazolinones under basic conditions (Brunton et al., 2008; Kshirsagar et al., 2007; He and Snider, 1999). In some cases, pyridine has also been used for condensation of benzoxazinones with amines (Madkour, 2004; Laddha et al., 2006; Al-Obaid et al., 2009) to corresponding quinazolinones. However, the reaction proceeded sluggishly



Scheme 1 General route for the synthesis of 2-styryl-3-substituted quinazolin-4(3*H*)-ones.

when pyridine alone was used as a solvent. This may be attributed to the less dielectric constant of pyridine. Therefore, we decided to use mixture of DMF and pyridine as solvent. In preliminary experiments with many different solvent ratios and power levels of microwave irradiation, we observed that the most favorable one was DMF:Py (2:1) at 350 W of microwave irradiation (Table 1, entry 4), which not only afforded the product in good yield, but also with better reaction rates. All the quinazolinone derivatives (**7a**–**7l**) were synthesized using these optimized reaction conditions (Scheme 2). The reaction time and yield for the different substitutions used to synthesize variety of 3-thiazole substituted 2-styrylquinazolin-4(3*H*)-ones are given in Table 2.

2.2. Antibacterial and antifungal activity

The *in vitro* antibacterial and antifungal activity of title compounds was determined using cup-plate agar diffusion method (Colins and Lyne, 1970; Dixit et al., 2010). The nearest zone of inhibition was measured in mm. The concentration (50 μg/mL) of test compounds was prepared by dissolving the compounds in dimethyl sulfoxide (DMSO). Under identical conditions, norfloxacin and clotrimazole were tested as standard drug (50 μg/mL) for bacteria and fungi, respectively. Antibacterial and antifungal activities shown by moderately active compounds toward *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853) (Gram-negative bacteria), *Bacillus megaterium* (ATCC 9885), *Bacillus subtilis* (ATCC 6633) (Gram-positive bacteria), and *Aspergillus niger* (ATCC 16404) (Fungus) are recorded in Table 3.

Table 1 Optimization of reaction conditions using co-solvent for the synthesis of (*E*)-3-(5-methylthiazol-2-yl)-2-styrylquinazolin-4(3*H*)-one (**7a**) under microwave irradiation

Entry	Solvent ratio DMF:Py	Power (W)	Reaction time (min)	Yield[a] (%)
1	1:0	350	6	40
2	1:2	350	13	71
3	1:1	350	12	75
4	2:1	350	7	78
5	2:1	280	15	77
6	2:1	420	6	72

[a] Isolated yield after recrystallization except entry 1 where column chromatography was used.

Table 2 Microwave assisted synthesis of 3-thiazole-substituted 2-styrylquinazolin-4(3*H*)-ones at 350 W

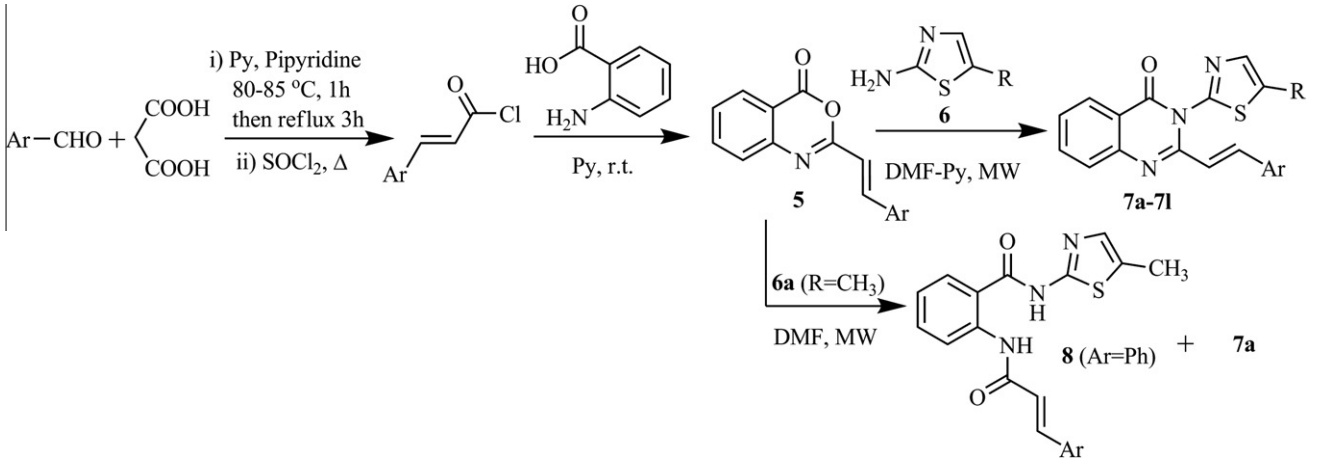
Compd No.	R	Ar	Reaction time (min)	Yield[a] (%)
7a	Me	Ph	7	78
7b	Br	Ph	7	70
7c	Br	4-OMe-Ph	8	68
7d	Br	2-NO_2-Ph	6	75
7e	Br	3-NO_2-Ph	7	69
7f	Br	4-NO_2-Ph	6	72
7g	Br	4-Cl-Ph	8	67
7h	Br	4-Me-Ph	8	69
7i	Br	2,3,4-Tri-OMe-Ph	9	54
7j	H	4-Me-Ph	7	80
7k	Me	2-NO_2-Ph	5	84
7l	Me	3-NO_2-Ph	6	81

[a] Isolated yields after recrystallization.

Table 3 Zone of growth inhibition in mm

Compd No.	Gram negative		Gram positive		Fungus
	E. coli	*P. aeruginosa*	*B. megaterium*	*B. subtilis*	*A. niger*
7a	12	10	9	12	4
7b	18	12	11	17	12
7c	–	4	–	–	–
7d	16	–	7	15	10
7e	14	14	10	–	–
7f	13	9	6	8	5
7g	10	–	13	10	14
7h	–	6	4	7	13
7i	8	4	–	–	–
7j	5	–	–	6	–
7k	12	10	9	13	9
7l	10	9	8	–	–
NF[a]	20	18	17	22	–
CT[b]	–	–	–	–	24

[a] Norfloxacin.
[b] Clotrimazole.



Scheme 2 Proposed route for the synthesis of 2-styryl-3-thiazole substituted quinazolin-4(3*H*)-one derivatives.

The results of the antimicrobial activity show that all the compounds have lesser activity than corresponding standard used. However, against *E. coli* compounds (**7b**) and (**7d**); against *P. aeruginosa* compound (**7e**); against *B. megaterium* compound (**7g**); against *B. subtilis* compound (**7b**) have comparable activity with standard. Antifungal study revealed that most of the compounds were not found sufficiently active to inhibit *A. niger* as compared to standard. Though, compound (**7g**) was found to have higher activity among all tested compounds.

3. Experimental

The MW experiments were carried out at atmospheric pressure in a glass vessel prolonged by a condenser and were performed using Scientific Microwave Synthesis System, (Catalyst™ Systems, Model: CATA-R). Melting points were determined by open capillary method and are uncorrected. The elemental analyses (C, H and N) were performed on an Elemental Vario EL analyzer and the results are within ±0.4% of the calculated values. Infrared spectra were recorded in the range of 4000–400 cm^{-1} using KBr with a Perkin–Elmer spectrum GX spectrophotometer (FT-IR) instrument. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker (400 MHz) instrument using DMSO-d_6 as a solvent as well as an internal reference standard; the chemical shifts are given in ppm (δ). The mass spectra (EI-MS) were recorded on a Shimadzu LC–MS 2010 eV mass spectrophotometer in acetonitrile. The progress of reactions and purifications was monitored by TLC plates (UV detection) on aluminium sheets coated with Silica Gel 60 F_{254} (Merck). All common reagents and solvents were purchased from commercial sources and were used without further purification, while the starting materials cinnamic acid derivatives (Koo et al., 1963) and cinnamoyl chloride derivatives (Womack and McWhirter, 1955) were synthesized by reported method. 2-Aminothiazole and 2-amino-5-methylthiazole were purchased from Sigma–Aldrich Inc., Mumbai.

*3.1. General procedure for the synthesis of (E)-2-styryl-substituted 4H-benzo[d][1,3]oxazin-4-one derivatives (**5**)*

The benzoxazinone derivatives were prepared by following the reported method (Fathalla et al., 2008). Accordingly, anthranilic acid (1.37 g, 0.01 mol) contained in a round bottomed flask was dissolved in freshly dried pyridine (5 mL). To the above solution, appropriate cinnamoyl chloride derivative (0.02 mol) was added drop wise under stirring, over a period of 15 min. The reaction mass was then allowed to stand for additional 2 h, with occasional shaking. It was then poured into 100 mL ice cold water. The solid thus obtained was filtered, washed with cold water, and recrystallized from ethanol. The yields were in the range of 66–92%.

*3.2. General procedure for the synthesis of 2-amino-5-bromothiazole (**6c**)*

In a round bottomed flask, 2-aminothiazole (**6b**) (10.01 g, 0.1 mol) was dissolved in 75 mL of glacial acetic acid. To the above stirred solution, bromine (5.1 mL, 0.1 mol) in 15 mL of glacial acetic acid was added drop wise. The reaction mass was additionally stirred for 30 min at room temperature and was poured in 500 mL ice-cold water. The product was extracted with ethyl acetate (3 × 100 mL) and was washed successively with 10% HCl solution (2 × 70 mL) and distilled water (2 × 70 mL). The solvent was then evaporated and the product thus obtained was recrystallized from ethanol. The yield of the product was 79% and it decomposed in the range of 115–117 °C.

*3.3. General microwave assisted procedure for the synthesis of 3-thiazole-substituted 2-styrylquinazolin-4(3H)-ones (**7a–7l**)*

Appropriate benzoxazinone (**5**) (0.02 mol) and 2-aminothiazole derivative (**6**) (0.02 mol) were taken in a solution of DMF (1 mL) and pyridine (0.5 mL) contained in a two-neck round bottomed flask fitted with a device condenser. The mixture was then heated under microwave irradiation at 350 W for an appropriate time (Table 2). After cooling, the reaction mass was dissolved in ethyl acetate (40 mL) and washed with distilled water (20 mL), dil. HCl (2 × 20 mL), aq. $NaHCO_3$ (2 × 20 mL) and distilled water (20 mL) sequentially by liquid–liquid extraction. The organic layer was dried and the resulting product was further purified by recrystallization from THF. Yields are given in Table 2.

*3.4. (E)-3-(5-Methylthiazol-2-yl)-2-styrylquinazolin-4(3H)-one (**7a**)*

Mp 172–175 °C. IR (KBr) ν max/cm^{-1}: 1695 (C═O str.), 1585 (C═N str.), 1632 (C═C str.), 675 (C–S str.), 1385 (C–H bend). ^{1}H NMR (DMSO-d_6): δ 2.36 (s, 3H, CH_3), 6.93 (d, J = 15.6 Hz, 1H, CH styryl), 7.20–7.24 (m, 2H, ArH and CH thiazole), 7.42–7.44 (m, 3H, ArH), 7.55 (t, J = 7.6 Hz, 1H, ArH), 7.62 (d, J = 15.6 Hz, 1H, CH styryl), 7.7 (d, J = 6.8 Hz, 2H, ArH), 7.94 (d, J = 7.2 Hz, 1H, ArH), 8.3 (d, J = 7.6 Hz, 1H, ArH). ^{13}C NMR (DMSO-d_6): δ 11.82, 122.31, 122.84, 123.74, 123.80, 126.15, 128.54, 129.4, 130.15, 130.40, 132.58, 135.01, 138.72, 141.39, 147.32, 160.34, 164.06. MS-EI (70 eV): m/z 345.4 (M+). Anal. Calcd. for $C_{20}H_{15}N_3OS$: C, 69.54; H, 4.38; N, 12.17%. Found: C, 69.55; H, 4.29; N, 12.29%.

*3.5. (E)-3-(5-Bromothiazol-2-yl)-2-styrylquinazolin-4(3H)-one (**7b**)*

Mp 195–197 °C. IR (KBr) ν max/cm^{-1}: 1684 (C═O str.), 1593 (C═N str.), 1634 (C═C str.), 678 (C–S str.), 564 (C–Br str.). ^{1}H NMR (DMSO-d_6): δ 6.91–6.94 (m, 2H, CH thiazol and CH styryl), 7.20–7.24 (m, 2H, ArH), 7.43–7.55 (m, 3H, ArH), 7.68–7.73 (m, 2H, CH styryl and ArH), 8.3 (d, J = 7.6 Hz, 1H, ArH). ^{13}C NMR (DMSO-d_6): δ 119.86, 120.27, 122.13, 126.62, 127.53, 127.92, 128.01, 128.11, 128.43, 132.73, 136.32, 137.04, 138.78, 146.03, 147.15, 160.23, 167.43. MS-EI (70 eV): m/z 408.3 (M+), 410.3 (M+2). Anal. Calcd. for $C_{19}H_{12}BrN_3OS$: C, 55.62; H, 2.95; N, 10.24%. Found: C, 55.69; H, 2.99; N, 10.29%.

*3.6. (E)-3-(5-Bromothiazol-2-yl)-2-(4-methoxystyryl)quinazolin- 4(3H)-one (**7c**)*

Mp 212–215 °C. IR (KBr) ν max/cm^{-1}: 1686 (C═O str.), 1595 (C═N str.), 1635 (C═C str.), 672 (C–S str.), 569 (C–Br str.), 2813 (Ar–O–CH_3), 1384 (C–H bend.). ^{1}H NMR (DMSO-d_6):

δ 3.87 (s, 3H, OCH_3), 6.8–6.93 (m, 4H, CH thiazole, CH styryl, ArH), 7.32–7.54 (m, 4H, ArH), 7.69–7.74 (m, 2H, CH styryl and ArH), 8.29 (d, J = 7.6 Hz, 1H, ArH). ^{13}C NMR (DMSO-d_6): δ 57.01, 114.01, 120.27, 120.74, 122.13, 126.42, 127.53, 128.01, 128.43, 128.71, 136.32, 137.04, 137.63, 146.03, 147.23, 160.14, 160.23, 167.43. MS-EI (70 eV): m/z 439.2 (M+), 441.2 (M+2). Anal. Calcd. for $C_{20}H_{14}BrN_3O_2S$: C, 54.56; H, 3.20; N, 9.54%. Found: C, 54.43; H, 3.12; N, 9.51%.

*3.7. (E)-3-(5-Bromothiazol-2-yl)-2-(2-nitrostyryl)quinazolin-4(3H)-one (**7d**)*

Mp 277–240 °C. IR (KBr) ν max/cm^{-1}: 1681 (C=O str.), 1594 (C=N str.), 1630 (C=C str.), 678 (C–S str.), 562 (C–Br str.), 1543 and 1393 (N=O str.). ^{1}H NMR (DMSO-d_6): δ 6.92 (s, 1H, CH thiazole), 7.15 (d, J = 15.6, 1H, CH styryl), 7.31 (t, J = 8 Hz, 1H, ArH), 7.5–7.56 (m, 3H, ArH), 7.67 (d, J = 15.6, 1H, CH styryl), 7.88 (t, J = 7.6, 1H, ArH), 8.02–8.14 (m, 3H, ArH). ^{13}C NMR (DMSO-d_6): δ 120.27, 122.13, 122.62, 127.14, 127.22, 127.53, 128.01, 128.43, 129.07, 130.11, 130.14, 131.59, 136.32, 137.04, 145.27, 146.03, 148.02, 160.23, 167.43. MS-EI (70 eV): m/z 454.1 (M+), 456.1 (M+2). Anal. Calcd. for $C_{19}H_{11}BrN_4O_3S$: C, 50.12; H, 2.44; N, 12.31%. Found: C, 50.24; H, 2.39; N, 12.39%.

*3.8. (E)-3-(5-Bromothiazol-2-yl)-2-(3-nitrostyryl)quinazolin-4(3H)-one (**7e**)*

Mp 247–250 °C. IR (KBr) ν max/cm^{-1}: 1680 (C=O str.), 1593 (C=N str.), 1631 (C=C str.), 679 (C–S str.), 563 (C–Br str.), 1545 and 1389 (N=O str.). ^{1}H NMR (DMSO-d_6): δ 6.92 (s, 1H, CH thiazole), 7.12 (d, J = 15.6, 1H, CH styryl), 7.51–7.54 (m, 2H, ArH), 7.65 (d, J = 15.6, 1H, CH styryl), 7.72–7.84 (m, 2H, ArH), 8.1–8.32 (m, 3H, ArH), 8.46 (s, 1H, ArH). ^{13}C NMR (DMSO-d_6): δ 119.53, 120.27, 121.84, 122.13, 124.32, 125.28, 127.53, 128.01, 128.43, 133.78, 136.07, 136.32, 137.04, 139.41, 146.03, 146.91, 147.22, 160.23, 167.43. MS-EI (70 eV): m/z 454.2 (M+), 456.2 (M+2). Anal. Calcd. for $C_{19}H_{11}BrN_4O_3S$: C, 50.12; H, 2.44; N, 12.31%. Found: C, 50.02; H, 2.36; N, 12.37%.

*3.9. (E)-3-(5-Bromothiazol-2-yl)-2-(4-nitrostyryl)quinazolin-4(3H)-one (**7f**)*

Mp 264–267 °C. IR (KBr) ν max/cm^{-1}: 1681 (C=O str.), 1594 (C=N str.), 1630 (C=C str.), 678 (C–S str.), 562 (C–Br str.), 1542 and 1394 (N=O str.). ^{1}H NMR (DMSO-d_6): δ 6.92 (s, 1H, CH thiazole), 7.14 (d, J = 15.6, 1H, CH styryl), 7.54–7.69 (m, 3H, CH styryl and ArH), 7.88 (d, J = 8.8 Hz, 2H, ArH), 7.99–8.13 (m, 2H, ArH), 8.24 (d, J = 8.8 Hz, 2H, ArH). ^{13}C NMR (DMSO-d_6): δ 120.27, 121.23, 122.13, 123.67, 127.53, 128.01, 12819, 128.43, 136.32, 137.04, 137.78, 139.91, 146.03, 146.57, 148.32, 160.23, 167.43. MS-EI (70 eV): m/z 454.1 (M+), 456.1 (M+2). Anal. Calcd. for $C_{19}H_{11}BrN_4O_3S$: C, 50.12; H, 2.44; N, 12.31%. Found: C, 49.99; H, 2.46; N, 12.40%.

*3.10. (E)-3-(5-Bromothiazol-2-yl)-2-(4-chlorostyryl)quinazolin-4(3H)-one (**7g**)*

Mp 270–274 °C. IR (KBr) ν max/cm^{-1}: 1688 (C=O str.), 1595 (C=N str.), 1633 (C=C str.), 671 (C–S str.), 566 (C–Br str.), 1382 (C–H bend.). ^{1}H NMR (DMSO-d_6): δ 6.9–6.93 (m, 2H, CH thiazole and CH styryl), 7.18 (dt, J = 7.6, 1.3 Hz, 1H, ArH), 7.51–7.59 (m, 4H, CH styryl and ArH), 7.75–7.78 (m, 2H, ArH), 8.31 (dd, J = 7.6, 1.3 Hz, 2H, ArH). ^{13}C NMR (DMSO-d_6): δ 120.27, 121.42, 122.13, 127.29, 127.53, 128.01, 128.43, 129.62, 132.66, 134.43, 136.32, 137.61, 137.04, 146.03, 146.61, 160.23, 167.43. MS-EI (70 eV): m/z 443.1 (M+), 445.1 (M+2), 447.1 (M+4). Anal. Calcd. for $C_{19}H_{11}BrN_3OS$: C, 51.31; H, 2.49; N, 9.45%. Found: C, 51.25; H, 2.47; N, 9.41%.

*3.11. (E)-3-(5-Bromothiazol-2-yl)-2-(4-methylstyryl)quinazolin-4(3H)-one (**7h**)*

Mp 212–215 °C. IR (KBr) ν max/cm^{-1}: 1688 (C=O str.), 1595 (C=N str.), 1633 (C=C str.), 671 (C–S str.), 566 (C–Br str.), 1382 (C–H bend.). ^{1}H NMR (DMSO-d_6): δ 2.35 (s, 3H, CH_3), 6.67 (d, J = 16 Hz, 1H, CH styryl), 6.92 (s, 1H, CH thiazole), 7.18 (t, J = 7.6 Hz, 1H, ArH), 7.33 (d, J = 8 Hz, 2H, ArH), 7.62 (dd, J = 7.6, 1.3 Hz, 1H, ArH), 7.71–7.80 (m, 4H, CH styryl and ArH), 8.02 (d, J = 7.6 Hz, 1H, ArH). ^{13}C NMR (DMSO-d_6): δ 20.44, 120.27, 120.59, 122.13, 127.53, 127.68, 127.84, 128.01, 128.43, 132.37, 136.32, 136.81, 137.04, 141.51, 146.03, 147.05, 160.23, 167.43. MS-EI (70 eV): m/z 423.0 (M+), 425.0 (M+2). Anal. Calcd. for $C_{20}H_{14}BrN_3OS$: C, 56.61; H, 3.33; N, 9.90%. Found: C, 56.68; H, 3.28; N, 9.87%.

*3.12. (E)-3-(5-Bromothiazol-2-yl)-2-(3,4,5-trimethoxystyryl)-quinazolin-4(3H)-one (**7i**)*

Mp 240–242 °C (d). IR (KBr) ν max/cm^{-1}: 1689 (C=O str.), 1598 (C=N str.), 1634 (C=C str.), 674 (C–S str.), 569 (C–Br str.), 2810 (Ar–O–CH_3), 1382 (C–H bend.). ^{1}H NMR (DMSO-d_6): δ 3.87 (s, 3H, OCH_3), 3.90 (s, 6H, $(OCH_3)_2$), 6.54 (d, J = 16 Hz, 1H, CH styryl), 6.91 (s, 1H, CH thiazole), 6.93 (s, 2H, ArH), 7.02 (t, J = 7.6 Hz, 1H, ArH), 7.48 (d, J = 7.6 Hz, 1H, ArH), 7.59 (t, J = 7.6 Hz, 1H, ArH), 7.8 (d, J = 16 Hz, 1H, CH styryl), 8.16 (d, J = 7.6 Hz, 1H, ArH). ^{13}C NMR (DMSO-d_6): δ 61.03, 66.24, 103.65, 119.46, 120.27, 122.13, 127.53, 128.01, 128.43, 130.17, 136.32, 137.04, 141.44, 141.53, 146.03, 147.15, 152.55, 160.23, 167.43. MS-EI (70 eV): m/z 499.1 (M+), 501.1 (M+2). Anal. Calcd. for $C_{22}H_{18}BrN_3O_4S$: C, 52.81; H, 3.63; N, 8.40%. Found: C, 52.87; H, 3.66; N, 8.38%.

*3.13. (E)-2-(4-Methylstyryl)-3-(thiazol-2-yl)quinazolin-4(3H)-one (**7j**)*

Mp 176–178 °C. IR (KBr) ν max/cm^{-1}: 1686 (C=O str.), 1595 (C=N str.), 1634 (C=C str.), 675 (C–S str.), 565 (C–Br str.), 1382 (C–H bend.). ^{1}H NMR (DMSO-d_6): δ 2.34 (s, 3H, CH_3), 6.67 (d, J = 16 Hz, 1H, CH styryl), 6.62 (d, J = 3.2 Hz, 1H, CH thiazole), 7.08 (d, J = 3.2 Hz, 1H, CH thiazole), 7.18 (t, J = 7.6 Hz, 1H, ArH), 7.33 (d, J = 8 Hz, 2H, ArH), 7.62 (dd, J = 7.6, 1.3 Hz, 1H, ArH), 7.71–7.80 (m, 4H, CH styryl and ArH), 8.02 (d, J = 7.6 Hz, 1H, ArH). ^{13}C NMR (DMSO-d_6): δ 20.44, 112.23, 120.56, 122.13, 127.53, 127.67, 127.85, 128.01, 128.43, 132.35, 136.32, 136.83, 137.48, 141.52, 146.03, 147.08, 160.23, 164.92. MS-EI (70 eV): m/z 345.3 (M+). Anal. Calcd. for $C_{20}H_{15}N_3OS$: C, 69.54; H, 4.38; N, 12.17%. Found: C, 67.87; H, 4.66; N, 12.38%.

*3.14. (E)-3-(5-Methylthiazol-2-yl)-2-(2-nitrostyryl)quinazolin-4(3H)-one (**7k**)*

Mp 221–224 °C. IR (KBr) ν max/cm^{-1}: 1685 (C═O str.), 1596 (C═N str.), 1632 (C═C str.), 673 (C–S str.), 566 (C–Br str.), 1382 (C–H bend.). ^{1}H NMR (DMSO-d_6): δ 2.36 (s, 3H, CH_3), 7.14 (d, J = 15.6, 1H, CH styryl), 7.24 (s, 1H, CH thiazole), 7.33 (t, J = 8 Hz, 1H, ArH), 7.5–7.56 (m, 3H, ArH), 7.66 (d, J = 15.6, 1H, CH styryl), 7.87 (t, J = 7.6, 1H, ArH), 8.02–8.14 (m, 3H, ArH). ^{13}C NMR (DMSO-d_6): δ 11.82, 122.13, 122.61, 122.84, 127.15, 127.23, 127.53, 128.01, 128.43, 129.09, 130.11, 130.16, 131.59, 135.01, 136.32, 145.28, 146.03, 148.04, 160.23, 164.06. MS-EI (70 eV): m/z 390.2 (M+). Anal. Calcd. for $C_{20}H_{14}N_4O_3S$: C, 61.53; H, 3.61; N, 14.35%. Found: C, 60.24; H, 3.39; N, 14.78%.

*3.15. (E)-3-(5-Methylthiazol-2-yl)-2-(3-nitrostyryl)quinazolin-4(3H)-one (**7l**)*

Mp 229–231 °C. IR (KBr) ν max/cm^{-1}: 1689 (C═O str.), 1598 (C═N str.), 1630 (C═C str.), 678 (C–S str.), 1384 (C–H bend.), 1542 and 1398 (N═O str.). ^{1}H NMR (DMSO-d_6): δ 2.36 (s, 3H, CH_3), 7.12 (d, J = 15.6, 1H, CH styryl), 7.23 (s, 1H, CH thiazole), 7.51–7.54 (m, 2H, ArH), 7.65 (d, J = 15.6, 1H, CH styryl), 7.72–7.84 (m, 2H, ArH), 8.1–8.32 (m, 3H, ArH), 8.46 (s, 1H, ArH). ^{13}C NMR (DMSO-d_6): δ 11.82, 119.53, 121.84, 122.13, 122.84, 124.32, 125.28, 127.53, 128.01, 128.43, 133.78, 135.01, 136.07, 136.32, 139.41, 146.03, 146.92, 147.24, 160.23, 164.06. MS-EI (70 eV): m/z 390.1 (M+). Anal. Calcd. for $C_{20}H_{14}N_4O_3S$: C, 61.53; H, 3.61; N, 14.35%. Found: C, 61.02; H, 3.36; N, 14.77%.

4. Conclusions

In summary, in the present study we have successfully synthesized a series of novel 3-thiazole substituted 2-styryl-4(3*H*)-quinazolinone derivatives (**7a–7l**) in good yield using pyridine-DMF as co-solvent under microwave irradiation. The use of combination of solvent under optimized microwave conditions leads to the formation of products (**7a–7l**) with improved yields, shorter reaction time, and drastic reduction of formation of diamide (**8**). The antimicrobial activities of the synthesized compounds showed that compounds (**7b**), (**7d**), and (**7g**) have comparable inhibitory effects with the standards used.

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References

Al-Obaid, A.M., Abdel-Hamide, S.G., El-Kashef, H.A., Abdel-Aziz, A.A.-M., El-Azab, A.S., Al-Khamees, H.A., El-Subbagh, H.I., 2009. Eur. J. Med. Chem. 44, 2379.

Bakavoli, M., Sabzevari, O., Rahimizadeh, M., 2007. Chin. Chem. Lett. 18, 1466.

Bhandari, S.V., Deshmane, B.J., Dangare, S.C., Gore, S.T., Raparti, V.T., Khachane, C.V., Sarkate, A.P., 2008. Pharmacology Online 2, 604.

Brunton, S.A., Stibbard, J.H.A., Rubin, L.L., Kruse, L.I., Guicherit, O.M., Boyd, E.A., Price, S., 2008. J. Med. Chem. 51, 1108.

Caddick, S., Fitzmaurice, R., 2009. Tetrahedron 65, 3325.

Clercq, E.R.D., 2002. Biomed. Health Res. 55, 272.

Colins, C.H., Lyne, P.M., 1970. Microbial Methods. University Park Press, Baltimore.

Connolly, D.J., Cusack, D., O'Sullivan, T.P., Guiry, P.J., 2005. Tetrahedron 61, 10153.

Dabiri, M., Salehi, P., Khajavi, M.S., Mohammadi, A.A., 2004. Heterocycles 63, 1417.

Dixit, R.B., Vanparia, S.F., Patel, T.S., Jagani, C.L., Doshi, H.V., Dixit, B.C., 2010. Appl. Organomet. Chem. 24, 408.

Fathalla, O.A.E.-F.M., Kassem, E.M.M., Ibrahem, N.M., Kamel, M.M., 2008. Acta Pol. Pharm. Drug Res. 65, 11.

Gupta, V., Kashaw, S.K., Jatav, V., Mishra, P., 2008. Med. Chem. Res. 17, 205.

He, F., Snider, B.B., 1999. J. Org. Chem. 64, 1397.

Holla, B.S., Malini, K.V., Rao, B.S., Sarojini, B.K., Kumari, N.S., 2003. Eur. J. Med. Chem. 38, 313.

Hsu, L.-Y., Hu, M.-K., Liu, K.-C., 2003. Chin. Pharm. J. 55, 153.

Ighilahriz, K., Boutemeur, B., Chami, F., Rabia, C., Hamdi, M., Hamdi, S.M., 2008. Molecules 13, 779.

Jatav, V., Kashaw, S., Mishra, P., 2008a. Med. Chem. Res. 17, 169.

Jatav, V., Mishra, P., Kashaw, S., Stables, J.P., 2008b. Eur. J. Med. Chem. 43, 135.

Jatav, V., Mishra, P., Kashaw, S., Stables, J.P., 2008c. Eur. J. Med. Chem. 43, 1945.

Jindal, R., Bajaj, S., 2008. Curr. Org. Chem. 12, 836.

Kamal, A., Reddy, K.L., Devaiah, V., Shankaraiah, N., Rao, M.V., 2006. Mini-Rev. Med. Chem. 6, 71.

Kamal, A., Bharathi, V.E., Ramaiah, J.M., Dastagiri, D., Reddy, S.J., Viswanath, A., Sultana, F., Pushpavalli, S.N.C.V.L., Pal-Bhadra, M., Srivastava, H.K., Sastry, N.G., Juvekar, A., Sen, S., Zingde, S., 2010. Bioorg. Med. Chem. 18, 526.

Kappe, C.O., Dallinger, D., 2009. Mol. Divers. 13, 71.

Katritzky, A.R., Singh, S.K., 2003. ARKIVOC xiii, 68.

Koo, J., Fish, M.S., Walker, G.N., Blake, J., 1963. Org. Synth. Coll. Vol. 4, 327.

Kshirsagar, U.A., Mhaske, S.B., Argade, N.P., 2007. Tetrahedron Lett. 48, 3243.

Kumar, S., Shrivastava, A.K., Sarkar, P.C., 1997. Indian J. Heterocycl. Chem. 7, 109.

Kumar, A., Rajput, C.S., Bhati, S.K., 2007. Bioorg. Med. Chem. 15, 3089.

Laddha, S.S., Wadodkar, S.G., Meghal, S.K., 2006. ARKIVOC xi, 1.

Laddha, S.S., Wadodkar, S.G., Meghal, S.K., 2009. Med. Chem. Res. 18, 268.

Li, F., Feng, Y., Meng, Q., Li, W., Li, Z., Wang, Q., Tao, F., 2007. ARKIVOC i, 40.

Li, C.S., Belair, L., Guay, J., Murgasva, R., Sturkenboom, W., Ramtohul, Y.K., Zhang, L., Huang, Z., 2009. Bioorg. Med. Chem. Lett. 19, 5214.

Lidström, P., Tierney, J., Wathey, B., Westman, J., 2001. Tetrahedron 57, 9225.

Lingaiah, B.V., Ezikiel, G., Yakaiah, T., Reddy, G.V., Shanthan, R.P., 2006. Synlett, 2507.

Liu, J.-F., Kaselj, M., Isome, Y., Ye, P., Sargent, K., Sprague, K., Cherrak, D., Wilson, C.J., Si, Y., Yohannes, D., Ng, S.-C., 2006. J. Comb. Chem. 8, 7.

Maarouf, A.R., El-Bendary, E.R., Goda, F.E., 2004. Arch. Pharmacol. 337, 527.

Madkour, H.M.F., 2004. ARKIVOC i, 36.

Malawska, B., 2005. Curr. Top. Med. Chem. 5, 69.

Mrozek-Wilczkiewicz, A., Kalinowski, D.S., Musiol, R., Finster, J., Szurko, A., Serafin, K., Knas, M., Kamalapuram, S.K., Kovacevic,

Z., Jampilek, J., Ratuszna, A., Rzeszowska-Wolny, J., Richardson, D.R., Polanski, J., . Bioorg. Med. Chem. 18, 2664.
Nawrocka, W., Stasko, J.J., 2002. Boll. Chim. Farm. 141, 84.
Nora De Souza, M.V., 2005. J. Sulfur Chem. 26, 429.
Padala, S.R., Padi, P.R., Thipireddy, V., 2003. Heterocycles 60, 183.
Park, H., Kim, Y.-J., Hahn, J.-S., 2007. Bioorg. Med. Chem. Lett. 17, 6345.
Philipova, I., Dobrikov, G.K., Krumova, K., Kaneti, J., 2006. J. Heterocycl. Chem. 43, 1057.
Rad-Moghadam, K., Mohseni, M., 2003. J. Chem. Res., Synop., 487.
Rad-Moghadam, K., Mamghani, M., Samavi, L., 2006. Synth. Commun. 36, 2245.
Raffa, D., Edler, M.C., Daidone, G., Maggio, B., Merickech, M., Plescia, S., Schillaci, D., Bai, R., Hamel, E., 2004. Eur. J. Med. Chem. 39, 299.
Sgobba, M., Rastelli, G., 2009. Chem. Med. Chem. 4, 1399.
Shankaraiah, N., Markandeya, N., Espinoza-Moraga, M., Arancibia, C., Kamal, A., Santos, L.S., 2009. Synthesis, 2163.
Siddiqi, N., Ahsan, W., 2010. Eur. J. Med. Chem. 45, 1536.
Sinha, S., Srivastava, M., 1994. Prog. Drug Res. 43, 143.
Welch, W.M., Ewing, F.E., Huang, J., Menniti, F.S., Pagnozzi, M.J., Kelly, K., Seymour, P.A., Guanowsky, V., Guhan, S., Guinn, M.R., Critchett, D., Lazzaro, J., Ganong, A.H., DeVries, K.M., Staigers, T.L., Chenard, B.L., 2001. Bioorg. Med. Chem. Lett. 11, 177.
Wolfe, J.F., Rathman, T.L., Sleevi, M.C., Campbell, J.A., Greenwood, T.D., 1990. J. Med. Chem. 33, 161.
Womack, E.B., McWhirter, J., 1955. Org. Synth. Coll. Vol. 3, 714.
Zhou, Y., Murphy, D.E., Sun, Z., Gregor, V.E., 2004. Tetrahedron Lett. 45, 8049.