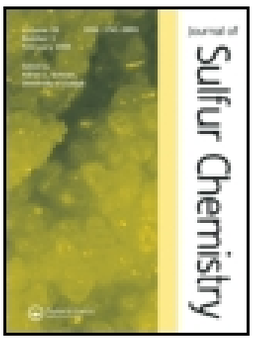

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An efficient one-pot synthesis of tetrahydrothiazolo[3,2-*a*]quinolin-6-one derivatives

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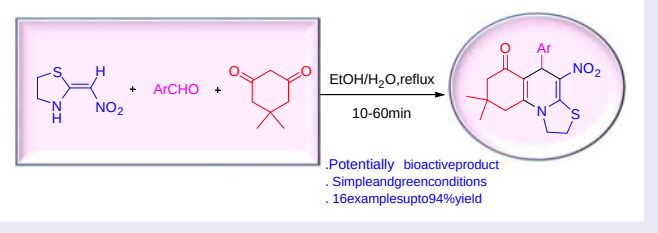
ABSTRACT

The cysteamine hydrochloride as a practical precursor of 2-(nitromethylene)thiazolidine in the one-pot synthesis of thiazoloquinoline derivatives from aromatic aldehydes and dimedone is described. This protocol involved Michael reaction, imine–enamine tautomerization, and cyclization sequence. Simple operation under mild conditions, easy accessibility of reactants, short reaction times, simple workup procedure, high atom economy, and the use of ethanol/water as a green medium make this approach attractive for the synthesis of variety of such derivatives.



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KEYWORDS
Thiazoloquinoline; 2-(nitromethylene)thiazolidine; aromatic aldehydes; dimedone; one-pot reaction

1. Introduction

Multicomponent reactions (MCRs) are excellent strategies, employed in the synthesis of several heterocycles and natural products [1]. They offer the advantage of simplicity and synthetic efficiency over conventional chemical reactions as well as selectivity, convergency, and atom economy [2].

Small-ring heterocycles including nitrogen and sulfur have been under investigation for a long time on account of their synthetic diversity and therapeutic relevance [3–5]. For example, the thiazole ring in various natural and synthetic products has generated interest of many groups on account of its useful biological properties [6]. Thiazole derivatives exhibit promising antimicrobial, anti-inflammatory, anticonvulsant, anticancer [7],

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analgesic, cardiotonic, anti-HIV, antifungal [8], antiprotozoal, antiviral [9], bactericidal [10], and antitumor [11] activities.

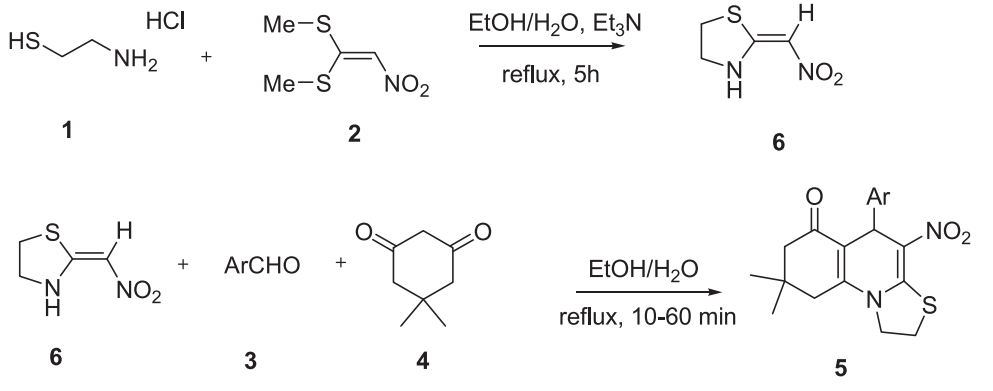
The chemistry of quinoline derivatives has received particular attention over the last few years, and a large variety of quinolines has been synthesized and assessed [12] as antibacterial, antimalarial, antiplasmodial, anticancer [13,14], anti-inflammatory, antiasthmatic, antihypertensive [15,16], antitumor [17,18], antituberculosis [19,20], tuberculostatic, and antiamoebic [21] agents. Among them, annulated thiazoloquinoline structures and those with [3,2-*a*] fusion exhibit significant biological activities [22].

Heterocyclic ketene aminals (HKAs) are becoming more and more popular among organic synthesis in the past several years [23]. The use of enamines derived from nitro ketene dithioacetal for the synthesis of a wide variety of heterocyclic systems and natural products has attracted the attention of many chemists [24–30]. Herein we synthesized a new series of thiazoloquinoline derivatives *via* a one-pot, MCR of 2-(nitromethylene)thiazolidine derived from the addition of cysteamine hydrochloride to 1,1-bis(methylthio)-2-nitroethene with aromatic aldehydes and dimedone.

2. Results and discussion

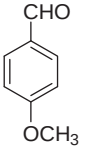
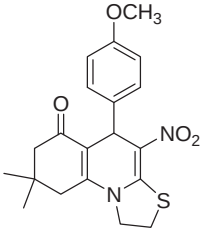
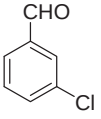
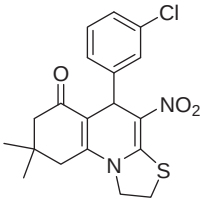
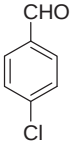
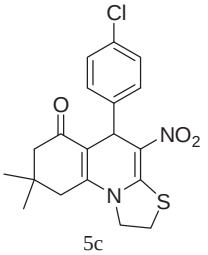
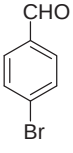
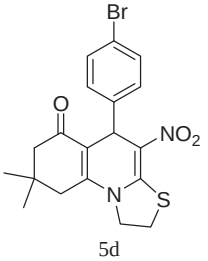
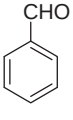
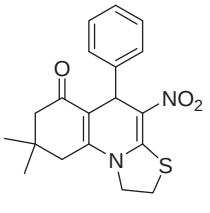
The one-pot multicomponent condensation reactions of cysteamine hydrochloride **1** with l,l-bis(methylthio)-2-nitroethene **2** in the presence of Et_3N with aromatic aldehydes **3** and dimedone **4** in EtOH/H_2O as a green solvent under reflux condition lead to corresponding thiazoloquinoline derivatives **5a–5p**, in excellent yields (Scheme 1).

The structures of compounds **5a–p** (Table 1) were characterized on the basis of their IR, ^{1}H NMR, ^{13}C NMR, and mass spectra. The mass spectrum of **5a** displayed the molecular ion peak at *m*/*z* 386, which was in agreement with the proposed structure. The IR spectrum of this compound showed absorption bands due to C=O stretching (1621 cm^{-1}) as well as 1513, 1431, and 1243 cm^{-1} due to the NO_2 and C−N groups. The ^{1}H NMR spectrum of **5a** showed two singlets for the two CH_3 groups (δ 0.84, 1.02 ppm), multiplets for the two CH_2 groups (δ 2.00–2.63 ppm), multiplets for the CH_2S group (δ 3.27–3.39 ppm), a singlet for the OCH_3 group (δ 3.65 ppm), multiplets for the CH_2N group (δ 4.11–4.47 ppm), a singlet for the CH group (δ 5.13 ppm), and the two doublets (δ 6.75, 7.09 ppm) for the aromatic region (see Figure 1). The ^{1}H-decoupled ^{13}C NMR spectrum of **5a** showed 17 distinct resonances.



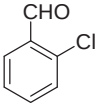
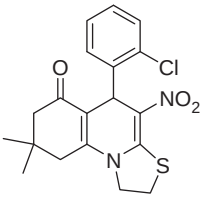
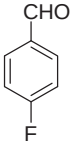
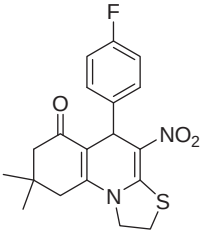
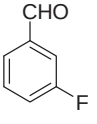
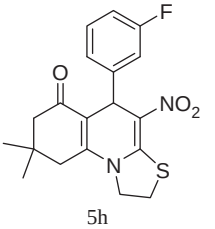
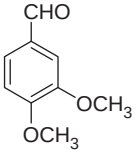
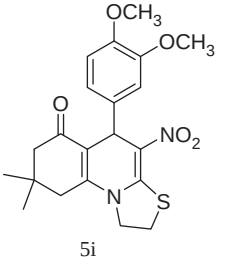
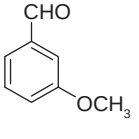
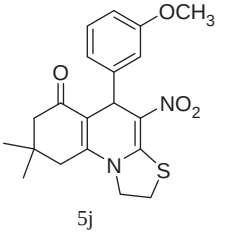
Scheme 1. Synthetic scheme for the products **5a–p**.

Table 1. Products **5a**–**p**.

Entry	ArCHO[a]	Product	Time (min)	Yield (%)
1		 5a	15	89
2		 5b	20	90
3		 5c	10	92
4		 5d	10	94
5		 5e	30	88

(*continued*).

Table 1. Continued.

Entry	ArCHO[a]	Product	Time (min)	Yield (%)
6		 5f	40	82
7		 5g	35	78
8		 5h	40	75
9		 5i	15	88
10		 5j	20	85

(*continued*).

Table 1. Continued.

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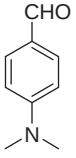
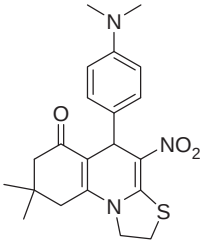
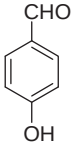
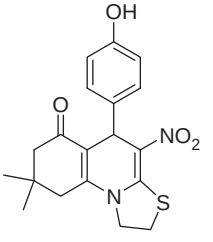
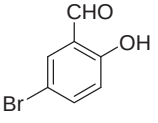
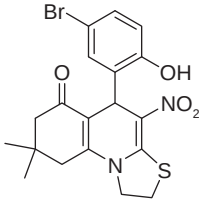
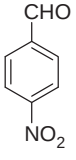
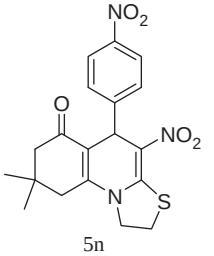
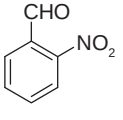
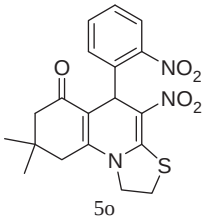
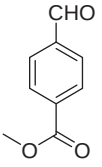
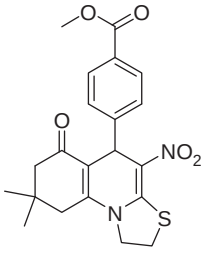
11		 5k	25	88
12		 5l	60	79
13		 5m	40	86
14		 5n	20	87
15		 5o	45	78

(*continued*).

Table 1. Continued.

Entry	ArCHO[a]	Product	Time (min)	Yield (%)
16		 5p	15	89

[a]Cysteamine hydrochloride (1 mmol), 1,1-bis(methylthio)-2-nitroethene (1 mmol), triethylamine (1 mmol), aromatic aldehyde (1 mmol), and dimedone (1 mmol) in H_2O/EtOH at reflux.

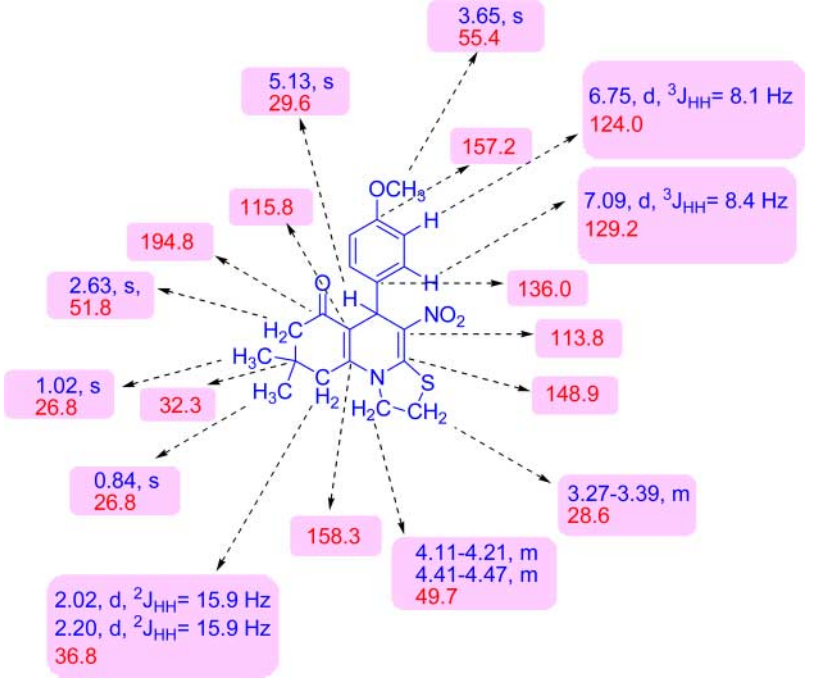
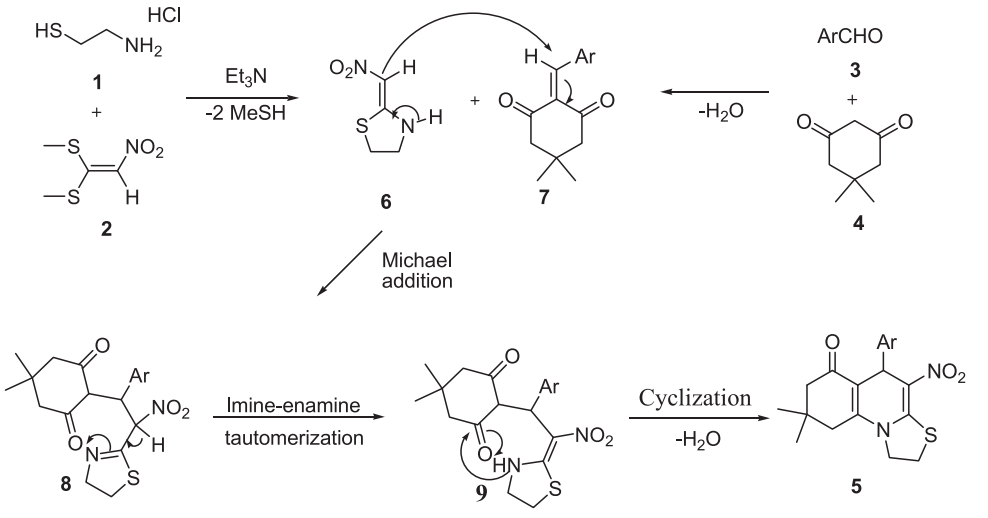


Figure 1. The ^{1}H and ^{13}C chemical shifts of **5a**.

We explored the scope of this reaction by varying the structure of the aromatic aldehydes. The reaction proceeds very cleanly under the same reaction conditions to afford a series of thiazoloquinoline derivatives **5** in 75–94% yields. The results are shown in Table 1.

Based on these results, a plausible mechanism is shown in Scheme 2. Initially, the reaction between cysteamine hydrochloride **1** and 1,1-bis(methylthio)-2-nitroethene **2** in the presence of Et_3N affords 2-(nitromethylene)thiazolidine **6** [28–30]. While the condensation of dimedone **4** with aromatic aldehyde **3** furnishes adduct **7**. Then, the



Scheme 2. Plausible mechanism for the formation of product **5**.

2-(nitromethylene)thiazolidine **6** and adduct **7** undergo a Michael addition to give intermediate **8**, which undergoes successive imine–enamine tautomerization, followed by nucleophilic addition of the secondary amino group to the carbonyl group and then cyclization, leading to the formation of **5**.

3. Conclusion

In summary, we have described a rapid and efficient one-pot protocol for the preparation of thiazoloquinolines in good yields through the reactions of 2-(nitromethylene)thiazolidine with aromatic aldehydes and dimedone under mild conditions. This protocol is an example of green chemistry since water/ethanol is used as the solvent. The other advantages of the present procedure are simplicity of the reaction and workup, mild conditions, easy accessibility of reactants, and high atom economy.

4. Experimental

4.1. General

The cysteamine hydrochloride, 1,1-bis(methylthio)-2-nitroethene, dimedone, aromatic aldehydes, and triethylamine were obtained from Merck and Aldrich and were used without further purification. NMR spectra were recorded with a Bruker DRX-300 Avance instrument (300 MHz for ^{1}H and 75.4 MHz for ^{13}C) with DMSO as solvent. Chemical shifts are given in ppm (δ) relative to internal TMS, and coupling constant (J) are reported in hertz (Hz). Melting points were measured with an electrotherma1 9100 apparatus. Mass spectra were recorded with an Agilent 5975C VL MSD with Triple-Axis Detector operating at an ionization potential of 70 eV. IR spectra were measured with Bruker Tensor 27 spectrometer.

4.2. General procedure for the synthesis of product 5

A mixture of cysteamine hydrochloride (0.113 g, 1 mmol), 1,1-bis(methylthio)-2-nitro ethylene (0.165 g, 1 mmol), 10 mL H_2O/EtOH (1:1), and triethylamine (140 µL, 1 mmol) in a 50-mL flask was refluxed for 5 h. After completion of the reaction (monitored by TLC, ethyl acetate/*n*-hexane, 1:1), aromatic aldehyde (1 mmol), dimedone (0.140 g, 1 mmol) were added to the reaction mixture, and it was stirred under reflux for the time given in Table 1. Then, the reaction mixture was cooled to room temperature and filtered to give the crude product. The solid was washed with water/ethanol (1:1) to give product **5** in good yield.

4.2.1. 1,2,8,9-Tetrahydro-5-(4-methoxyphenyl)-8,8-dimethyl-4-nitro-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5a)

Yellow powder; yield: 0.343 g (86%); m.p. 304–306°C. ^{1}H NMR (300 MHz, DMSO): 0.84 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 2.02 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.20 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.45–2.63 (*m*, 2H, CH_2), 3.27–3.39 (*m*, 2H, CH_2S), 3.65 (*s*, 3H, OCH_3), 4.11–4.21 (*m*, 1H, CH_2N), 4.41–4.47 (*m*, 1H, CH_2N), 5.13 (*s*, 1H, CH), 6.75 (*d*, $^3J_{HH}$ = 8.1 Hz, 2H, Ar), 7.09 (*d*, $^3J_{HH}$ = 8.4 Hz, 2H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.8, 28.6, 29.6, 32.3, 36.8, 49.7, 51.8, 55.4, 113.8, 115.8, 124.0, 129.2, 136.0, 148.9, 157.2, 158.3, 194.8. IR (KBr) (ν_{max}/cm^{-1}): 1621 (C=O), 1513 and 1431 (NO_2), 1243 (C−N). *m*/*z* (%) = 386 (M^+, 49), 340 (46), 311 (27), 279 (100), 233 (21), 149 (14). Anal. Calcd. for $C_{20}H_{22}N_2O_4S$ (366.46): C, 62.16; H, 5.74, N, 7.25. Found: C, 62.6; H, 5.1, N, 7.1.

4.2.2. 5-(3-Chlorophenyl)-1,2,8,9-tetrahydro-8,8-dimethyl-4-nitro-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5b)

Yellow powder; yield: 0.351 g (90%); m.p. 299–301°C. ^{1}H NMR (300 MHz, DMSO): 0.83 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 2.04 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.20 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.37–2.66 (*m*, 2H, CH_2), 3.36–3.41 (*m*, 2H, CH_2S), 4.12–4.21 (*m*, 1H, CH_2N), 4.44–4.52 (*m*, 1H, CH_2N), 5.17 (*s*, 1H, CH), 7.14–7.28 (*m*, 4H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.7, 28.6, 29.5, 32.3, 37.9, 49.6, 51.9, 115.0, 123.2, 126.9, 127.1, 128.3, 130.4, 133.0, 146.1, 149.5, 157.9, 194.8. *m*/*z* (%) = 390 (M^+, 10), 344 (12), 315 (6), 279 (100), 233 (13), 149 (11). Anal. Calcd. for $C_{19}H_{19}ClN_2O_3S$ (390.88): C, 58.38; H, 4.90, N, 7.17. Found: C, 58.9; H, 5.3, N, 7.0.

4.2.3. 5-(4-Chlorophenyl)-1,2,8,9-tetrahydro-8,8-dimethyl-4-nitro-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5c)

Yellow powder; yield: 0.359 g (92%); m.p. 323–325°C. ^{1}H NMR (300 MHz, DMSO): 0.82 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 2.03 (*d*, $^2J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.20 (*d*, $^2J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.38–2.64 (*m*, 2H, CH_2), 3.26–3.40 (*m*, 2H, CH_2S), 4.12–4.22 (*m*, 1H, CH_2N), 4.41–4.49 (*m*, 1H, CH_2N), 5.17 (*s*, 1H, CH), 7.21 (*d*, $^3J_{HH}$ = 8.4 Hz, 2H, Ar), 7.27 (*d*, $^3J_{HH}$ = 8.1 Hz, 2H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.8, 28.6, 29.5, 32.3, 37.5, 49.6, 51.9, 115.2, 123.4, 128.4, 130.2, 131.6, 142.8, 149.3, 157.8, 194.8. IR (KBr) (ν_{max}/cm^{-1}): 1621 (C=O), 1531 and 1431 (NO_2), 1240 (C−N). *m*/*z* (%) = 390 (M^+, 19), 344 (20), 315 (10), 279 (100), 233 (15), 149 (12). Anal. Calcd. for $C_{19}H_{19}ClN_2O_3S$ (390.88): C, 58.38; H, 4.90, N, 7.17. Found: C, 58.7; H, 5.1, N, 7.1.

4.2.4. 5-(4-Bromophenyl)-1,2,8,9-tetrahydro-8,8-dimethyl-4-nitro-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5d)

Yellow powder; yield: 0.409 g (94%); m.p. 322–324°C. ^{1}H NMR (300 MHz, DMSO): 0.82 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 2.03 (*d*, $^2J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.20 (*d*, $^2J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.39–2.63 (*m*, 2H, CH_2), 3.35–3.40 (*m*, 2H, CH_2S), 4.12–4.22 (*m*, 1H, CH_2N), 4.41–4.49 (*m*, 1H, CH_2N), 5.15 (*s*, 1H, CH), 7.16 (*d*, $^3J_{HH}$ = 7.8 Hz, 2H, Ar), 7.40 (*d*, $^3J_{HH}$ = 7.8 Hz, 2H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.8, 28.6, 29.5, 32.3, 37.6, 49.6, 51.9, 115.1, 120.1, 123.3, 130.6, 131.3, 143.2, 149.3, 157.8, 194.7. IR (KBr) (ν_{max}/cm^{-1}): 1619 (C=O), 1529 and 1431 (NO_2), 1240 (C–N). *m*/*z* (%) = 435 (M^+, 21), 419 (17), 388 (18), 279 (100), 233 (23). Anal. Calcd. for $C_{19}H_{19}BrN_2O_3S$ (435.33): C, 52.42; H, 4.40, N, 6.43. Found: C, 52.0; H, 4.6, N, 6.7.

4.2.5. 1,2,8,9-Tetrahydro-8,8-dimethyl-4-nitro-5-phenyl-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5e)

Yellow powder; yield: 0.313 g (88%); m.p. 323–325°C. ^{1}H NMR (300 MHz, DMSO): 0.82 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 2.03 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.20 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.42–2.64 (*m*, 2H, CH_2), 3.33–3.40 (*m*, 2H, CH_2S), 4.12–4.22 (*m*, 1H, CH_2N), 4.43–4.50 (*m*, 1H, CH_2N), 5.19 (*s*, 1H, CH), 7.10–7.24 (*m*, 5H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.7, 28.6, 29.6, 32.3, 37.7, 49.7, 51.9, 115.6, 123.8, 127.1, 128.2, 128.4, 143.8, 149.2, 157.6, 194.7. *m*/*z* (%) = 456 (M^+, 5), 356 (19), 310 (16), 279 (100), 233 (17), 149 (12). Anal. Calcd. for $C_{19}H_{20}N_2O_3S$ (356.43): C, 64.02; H, 5.65, N, 7.85. Found: C, 64.5; H, 5.1, N, 7.5.

4.2.6. 5-(2-Chlorophenyl)-1,2,8,9-tetrahydro-8,8-dimethyl-4-nitro-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5f)

Yellow powder; yield: 0.320 g (82%); m.p. 253–255°C. ^{1}H NMR (300 MHz, DMSO): 0.83 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 1.97 (*d*, $^2J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.18 (*d*, $^2J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.39–2.63 (*m*, 2H, CH_2), 3.32–3.38 (*m*, 2H, CH_2S), 4.21–4.30 (*m*, 1H, CH_2N), 4.39–4.47 (*m*, 1H, CH_2N), 5.47 (*s*, 1H, CH), 7.10–7.35 (*m*, 4H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.7, 28.4, 29.6, 32.1, 37.3, 49.7, 51.8, 114.7, 123.2, 127.1, 128.6, 129.8, 132.5, 133.3, 140.7, 149.4, 157.9, 194.6. IR (KBr) (ν_{max}/cm^{-1}): 1627 (C=O), 1540 and 1447 (NO_2), 1225 (C−N). Anal. Calcd. for $C_{19}H_{19}ClN_2O_3S$ (390.88): C, 58.38; H, 4.90, N, 7.17. Found: C, 58.9; H, 4.5, N, 7.4.

4.2.7. 5-(4-Fluorophenyl)-1,2,8,9-tetrahydro-8,8-dimethyl-4-nitro-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5g)

Yellow powder; yield: 0.292 g (78%); m.p. 326–328°C. ^{1}H NMR (300 MHz, DMSO): 0.83 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 2.03 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.20 (*d*, $^2J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.41–2.64 (*m*, 2H, CH_2), 3.35–3.40 (*m*, 2H, CH_2S), 4.12–4.22 (*m*, 1H, CH_2N), 4.35–4.50 (*m*, 1H, CH_2N), 5.18 (*s*, 1H, CH), 6.97–7.25 (*m*, 4H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.7, 28.6, 29.6, 32.3, 37.2, 49.6, 51.9, 115.1 (*d*, $^2J_{CF}$ = 21 Hz), 123.6, 130.1, 130.2, 140.0, 149.2, 157.6, 161.1 (*d*, $^1J_{CF}$ = 243 Hz), 194.8. IR (KBr) (ν_{max}/cm^{-1}): 1626 (C=O), 1526 and 1434 (NO_2), 1199 (C−N). Anal. Calcd. for $C_{19}H_{19}FN_2O_3S$ (374.42): C, 60.94; H, 5.11, N, 7.48. Found: C, 60.6; H, 5.5, N, 7.3.

4.2.8. 5-(3-Fluorophenyl)-1,2,8,9-tetrahydro-8,8-dimethyl-4-nitro-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5h)

Yellow powder; yield: 0.280 g (75%); m.p. 273–275°C. ^{1}H NMR (300 MHz, DMSO): 0.83 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 2.04 (*d*, $^{2}J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.21 (*d*, $^{2}J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.39–2.65 (*m*, 2H, CH_2), 3.36–3.41 (*m*, 2H, CH_2S), 4.12–4.21 (*m*, 1H, CH_2N), 4.43–4.51 (*m*, 1H, CH_2N), 5.21 (*s*, 1H, CH), 6.94–7.29 (*m*, 4H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.7, 28.6, 29.5, 32.3, 37.8, 49.6, 51.9, 113.9 (*d*, $^{2}J_{CF}$ = 21 Hz), 115.0 (*d*, $^{2}J_{CF}$ = 21 Hz), 123.2, 124.4, 130.2, 130.3, 146.5, 149.5, 157.9, 162.4 (*d*, $^{1}J_{CF}$ = 243 Hz), 194.8. IR (KBr) (ν_{max}/cm^{-1}): 1632 (C=O), 1546 and 1440 (NO_2), 1223 (C−N). Anal. Calcd. for $C_{19}H_{19}FN_2O_3S$ (374.42): C, 60.94; H, 5.11, N, 7.48. Found: C, 60.4; H, 4.7; N, 7.0.

4.2.9. 1,2,8,9-Tetrahydro-5-(3,4-dimethoxyphenyl)-8,8-dimethyl-4-nitro-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5i)

Yellow powder; yield: 0.366 g (88%); m.p. 246–248°C. ^{1}H NMR (300 MHz, DMSO): 0.86 (*s*, 3H, CH_3), 1.03 (*s*, 3H, CH_3), 2.05 (*d*, $^{2}J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.21 (*d*, $^{2}J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.37–2.66 (*m*, 2H, CH_2), 3.30–3.39 (*m*, 2H, CH_2S), 3.65 (*s*, 6H, $2OCH_3$), 4.11–4.21 (*m*, 1H, CH_2N), 4.41–4.49 (*m*, 1H, CH_2N), 5.16 (*s*, 1H, CH), 6.63–6.79 (*m*, 3H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.6, 28.6, 29.7, 32.3, 36.9, 49.7, 51.8, 55.9, 55.9, 111.9, 112.4, 115.6, 120.0, 123.9, 136.3, 148.0, 148.6, 149.1, 157.2, 194.9. Anal. Calcd. for $C_{21}H_{24}N_2O_5S$ (416.48): C, 60.56; H, 5.80, N, 6.72. Found: C, 60.1; H, 5.3; N, 6.5.

4.2.10. 1,2,8,9-Tetrahydro-5-(3-methoxyphenyl)-8,8-dimethyl-4-nitro-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5j)

Yellow powder; yield: 0.328 g (85%); m.p. 215–217°C. ^{1}H NMR (300 MHz, DMSO): 0.84 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 2.04 (*d*, $^{2}J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.21 (*d*, $^{2}J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.41–2.65 (*m*, 2H, CH_2), 3.34–3.40 (*m*, 2H, CH_2S), 3.66 (*s*, 3H, OCH_3), 4.11–4.20 (*m*, 1H, CH_2N), 4.42–4.50 (*m*, 1H, CH_2N), 5.18 (*s*, 1H, CH), 6.63–6.76 (*m*, 3H, Ar), 7.10–7.16 (*m*, 1H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.7, 28.6, 29.6, 32.3, 37.5, 49.7, 51.9, 55.3, 111.7, 114.7, 115.4, 120.3, 123.6, 129.5, 145.2, 149.3, 157.6, 159.4, 194.8. Anal. Calcd. for $C_{20}H_{22}N_2O_4S$ (366.46): C, 62.16; H, 5.74, N, 7.25. Found: C, 62.4; H, 5.5; N, 7.4.

4.2.11. 5-(4-(Dimethylamino)phenyl)-1,2,8,9-tetrahydro-8,8-dimethyl-4-nitro-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5k)

Yellow powder; yield: 0.351 g (88%); m.p. 285–287°C. ^{1}H NMR (300 MHz, DMSO): 0.85 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 2.02 (*d*, $^{2}J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.19 (*d*, $^{2}J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.41–2.63 (*m*, 2H, CH_2), 2.78 (*s*, 6H, $2NCH_3$), 3.33–3.40 (*m*, 2H, CH_2S), 4.11–4.25 (*m*, 1H, CH_2N), 4.40–4.47 (*m*, 1H, CH_2N), 5.08 (*s*, 1H, CH), 6.54 (*d*, $^{3}J_{HH}$ = 8.4 Hz, 2H, Ar), 6.97 (*d*, $^{3}J_{HH}$ = 8.4 Hz, 2H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.8, 28.5, 29.6, 32.3, 36.5, 49.8, 51.8, 112.4, 116.0, 124.4, 128.7, 131.8, 148.6, 149.6, 156.8, 194.8. Anal. Calcd. for $C_{21}H_{25}N_3O_3S$ (399.50): C, 63.13; H, 6.30, N, 10.51. Found: C, 63.6; H, 5.9; N, 10.3.

4.2.12. 1,2,8,9-Tetrahydro-5-(4-hydroxyphenyl)-8,8-dimethyl-4-nitro-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5l)

Yellow powder; yield: 0.294 g (79%); m.p. 312–314°C. ^{1}H NMR (300 MHz, DMSO): 0.84 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 2.02 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.19 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.36–2.62 (*m*, 2H, CH_2), 3.23–3.38 (*m*, 2H, CH_2S), 4.10–4.19 (*m*, 1H, CH_2N), 4.40–4.48 (*m*, 1H, CH_2N), 5.09 (*s*, 1H, CH), 6.57 (*d*, $^3J_{HH}$ = 8.1 Hz, 2H, Ar), 6.97 (*d*, $^3J_{HH}$ = 8.4 Hz, 2H, Ar), 9.22 (*s*, 1H, OH). ^{13}C NMR (75.4 MHz, DMSO): 26.7, 28.5, 29.6, 32.3, 36.7, 49.7, 51.8, 115.1, 115.9, 124.2, 129.2, 134.4, 148.7, 156.4, 157.1, 194.8. Anal. Calcd. for $C_{19}H_{20}N_2O_4S$ (372.43): C, 61.27; H, 5.41, N, 7.52. Found: C, 60.8; H, 5.1; N, 7.3.

4.2.13. 5-(5-Bromo-2-hydroxyphenyl)-1,2,8,9-tetrahydro-8,8-dimethyl-4-nitro-5H-thiazolo[3,2-a]quinolin-6(7H)-one (5m)

Yellow powder; yield: 0.388 g (86%); m.p. 360–362°C. ^{1}H NMR (300 MHz, DMSO): 0.84 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 1.99 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.19 (*d*, $^2J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.35–2.58 (*m*, 2H, CH_2), 3.20–3.40 (*m*, 2H, CH_2S), 4.18–4.37 (*m*, 2H, CH_2N), 5.13 (*s*, 1H, CH), 6.62 (*d*, $^3J_{HH}$ = 8.7 Hz, 1H, Ar), 7.09 (*d*, $^3J_{HH}$ = 8.7 Hz, 1H, Ar), 7.23 (*s*, 1H, Ar), 9.68 (*s*, 1H, OH). ^{13}C NMR (75.4 MHz, DMSO): 26.5, 28.4, 29.6, 32.2, 36.6, 49.7, 51.7, 109.9, 113.2, 118.5, 122.0, 130.4, 130.6, 134.5, 149.6, 155.8, 158.1, 195.0. Anal. Calcd. for $C_{19}H_{19}BrN_2O_4S$ (451.33): C, 50.56; H, 4.24, N, 6.20. Found: C, 50.9; H, 4.6; N, 6.3.

4.2.14. 1,2,8,9-Tetrahydro-8,8-dimethyl-4-nitro-5-(4-nitrophenyl)-5h-thiazolo[3,2-a]quinolin-6(7H)-one (5n)

Yellow powder; yield: 0.262 g (87%); m.p. 315–317°C. ^{1}H NMR (300 MHz, DMSO): 0.82 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 2.03 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.21 (*d*, $^2J_{HH}$ = 16.2 Hz, 1H, CH_2), 2.42–2.66 (*m*, 2H, CH_2), 3.37–3.43 (*m*, 2H, CH_2S), 4.16–4.25 (*m*, 1H, CH_2N), 4.43–4.51 (*m*, 1H, CH_2N), 5.30 (*s*, 1H, CH), 7.50 (*d*, $^3J_{HH}$ = 8.7 Hz, 2H, Ar), 8.08 (*d*, $^3J_{HH}$ = 8.7 Hz, 2H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.8, 28.7, 29.5, 32.3, 38.4, 49.5, 51.9, 114.6, 122.9, 123.6, 129.7, 146.6, 149.8, 151.1, 158.3, 194.7. IR (KBr) (ν_{max}/cm^{-1}): 1634 (C=O), 1517 and 1438 (NO_2), 1215 (C−N). Anal. Calcd. for $C_{19}H_{19}N_3O_5S$ (401.43): C, 56.84; H, 4.77, N, 10.46. Found: C, 56.5; H, 4.9; N, 10.3.

4.2.15. 1,2,8,9-Tetrahydro-8,8-dimethyl-4-nitro-5-(2-nitrophenyl)-5h-thiazolo[3,2-a]quinolin-6(7H)-one (5o)

Yellow powder; yield: 0.235 g (78%); m.p. 276–278°C. ^{1}H NMR (300 MHz, DMSO): 0.78 (*s*, 3H, CH_3), 1.00 (*s*, 3H, CH_3), 1.95 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.16 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.41–2.62 (*m*, 2H, CH_2), 3.32–3.40 (*m*, 2H, CH_2S), 4.17–4.26 (*m*, 1H, CH_2N), 4.41–4.49 (*m*, 1H, CH_2N), 6.01 (*s*, 1H, CH), 7.33–7.80 (*m*, 4H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.9, 28.5, 29.3, 32.2, 33.8, 49.6, 52.0, 115.3, 123.3, 124.5, 128.3, 130.7, 133.5, 138.2, 148.9, 149.5, 158.5, 194.8. Anal. Calcd. for $C_{19}H_{19}N_3O_5S$ (401.43): C, 56.84; H, 4.77, N, 10.46. Found: C,56.4; H, 5.0; N, 10.1.

4.2.16. Methyl-4-(2,5,6,7,8,9-hexahydro-8,8-dimethyl-4-nitro-6-oxo-1H-thiazolo[3,2-a]quinolin-5-yl)benzoate (5p)

Yellow powder; yield: 0.368 g (89%); m.p. > 380°C. ^{1}H NMR (300 MHz, DMSO): 0.80 (*s*, 3H, CH_3), 1.02 (*s*, 3H, CH_3), 2.02 (*d*, $^2J_{HH}$ = 15.9 Hz, 1H, CH_2), 2.20 (*d*, $^2J_{HH}$ = 16.2 Hz,

1H, CH_2), 2.39–2.65 (*m*, 2H, CH_2), 3.34–3.40 (*m*, 2H, CH_2S), 3.78 (*s*, 3H, OCH_3), 4.11–4.23 (*m*, 1H, CH_2N), 4.43–4.49 (*m*, 1H, CH_2N), 5.25 (*s*, 1H, CH), 7.35 (*d*, $^3J_{HH} = 8.1$ Hz, 2H, Ar), 7.81 (*d*, $^3J_{HH} = 8.1$ Hz, 2H, Ar). ^{13}C NMR (75.4 MHz, DMSO): 26.6, 28.6, 29.6, 32.3, 38.2, 49.6, 51.9, 52.5, 115.0, 123.2, 128.4, 128.7, 129.4, 149.0, 149.5, 158.0, 166.4, 194.7. Anal. Calcd. for $C_{21}H_{22}N_2O_5S$ (414.47): C, 60.85; H, 5.35, N, 6.75. Found: C, 61.2; H, 5.0; N, 6.5.

Disclosure statement

No potential conflict of interest was reported by the authors.

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