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Green approach: an efficient synthesis of 2,4-disubstituted-1,3-thiazoles and selenazoles in aqueous medium under ultrasonic irradiation

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Abstract An efficient and rapid procedure for the synthesis of 2,4-disubstituted-1,3-thiazoles and selenazoles has been described by the reaction of α-bromoketones with thiourea, phenylthiourea and selenourea at ambient temperature in aqueous medium under ultrasonic irradiation. Analytically pure products were formed within 10–60 s in excellent yields. The advantageous features of this non-conventional methodology over conventional methods are the operational simplicity, easy handling, yield-enhancing, time-reducing, mild reaction conditions and no by-product production.

Keywords Cavitation effect · Green chemistry · Thiazoles · Selenazoles · Ultrasonication

Introduction

The applications of green chemistry principles have led to the development of cleaner and environmentally benign chemical processes. In recent years, ultrasound irradiation has been extensively applied in organic reactions because of its special sonochemical property such as the cavitation effect that accelerates both catalytic and non-catalytic synthetic reactions [1]. More energy consumption for heating and production of hazardous by-products are some disadvantageous factors of normal conventional techniques, which show adverse effects on the environment.

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Moreover, when compared to the classical thermal methods of chemical processes, an ultrasonic irradiation method has been attracting the modern synthetic chemists due to its advantageous features, i.e., decreasing reaction times, increasing yields [2, 3], easy workup procedures, avoiding harsh reaction conditions [4], better selectivity and high conversions [5].

The thiazole ring is a core structural backbone of various natural and synthetic pharmacologically active compounds such as vitamin B_1 (thiamine), penicillin, meloxicam, fanetizole and cefdinir. Thiazole derivatives have diverse applications in various fields of chemistry including medicinal and agricultural, such as anticancer [6], antitumor [7], antimalarial [8], anti-inflammatory [9], antimicrobial [10], antihypertensive [11], antiparasitic [12], HIV-1 reverse transcriptase inhibitors [13] and herbicidal properties [14]. They have also been reported as ligands at estrogen receptors [15] and novel class adenosine receptor antagonists [16], and used as organic functional materials such as fluorescent dyes [17] and liquid crystals [18], and also acting as good pharmacophores for the design of bioactive molecules such as the bioisoster of the imidazole ring [19]. Similarly, selenazoles have also been reported to possess antibacterial [20], antifilarial, antitumor [21], superoxide anion scavenging [22] properties and to act as Akt, mitogen protein kinase activator [23], and heavy metal detoxifying agents [24]. The structures of fanetizole, cefdinir and selenazofurin, and their pharmacological activities are given in Fig. 1.

In view of the importance of thiazole and selenazole derivatives in various fields of chemistry, the classical Hantzsch synthesis as well as several methodologies have been reported utilizing various catalytic systems such as ammonium-12-molybdophosphate [25], β-cyclodextrin [26], NaCl [27], HMCM-41 [28], iodine [29], TiO_2 [30], $CuPy_2Cl_2$ [31], graphite oxide [32] and silica chloride [33], and also reported in different solvent systems, such as ionic liquids [34], PEG-400 [35], glycerin [36], and water [37]. However, most of these reported methods have one or several drawbacks such as lower yields, longer reaction times, complicated isolation procedures and the use of hazardous and expensive catalysts making them environmentally unfriendly. To overcome the above limitations, and as a part of our endeavor towards the development of novel eco-friendly methodologies for the synthesis of biologically potent heterocyclic compounds [38], we propose here a versatile, simple, mild, environmentally benign and highly efficient protocol for the synthesis of 2,4-disubstituted-1,3-thiazoles and 1,3-selenazoles in aqueous medium under ultrasonic irradiation.

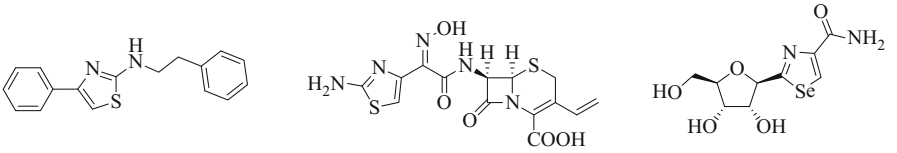


Fig. 1 Biologically active thiazole and selenazole derivatives

Experimental

Materials and methods

All the reagents and solvents were purchased from Aldrich/Merck and used without further purifications. Melting points were determined in open capillaries with Stuart SMP30 melting point apparatus and are uncorrected. The progress of the reactions as well as the purity of the compounds was checked using F_{254} silica-gel precoated TLC sheets (Merck, Mumbai, India) using hexane/ethyl acetate (8:2) as eluent, and the developed chromatogram was visualized under UV light and iodine vapors. IR spectra were recorded on a Perkin–Elmer 100S spectrophotometer (Perkin-Elmer, UK). ^{1}H NMR spectra were obtained on Bruker (400 MHz) spectrometer (Bruker, Germany) using TMS as internal standard. Elemental analyses were performed on a Carlo-Erba model EA1108 analytical unit (Triad, New Jersey, USA) and the values are ±0.4 % of theoretical values. Mass spectra were recorded on a Jeol JMSD-300 spectrometer (Jeol, Tokyo, Japan). Sonication was performed on PCi-Analytics-6.5L200H1DTC ultrasonic cleaner (PCi-Analytics, 25 and 50 kHz, input voltage range of 170–270 V AC, 50 Hz) (Mumbai, India).

General procedure for the synthesis of 2,4-disubstituted-1,3-thiazoles and selenazoles (3–16)

A 100-mL borosil test-tube was charged with phenacyl bromide (**1a**–**h**)/3(2-bromoacetyl)coumarin (**1i**–**n**) (1 mmol), thiourea (**2a**)/phenylthiourea (**2b**)/selenourea (**2c**) (1 mmol) and water (1 mL). The tube was kept in such a way that the surface of the reactants is just lower than the water level of the ultrasonic bath in which they were sonicated with a frequency of 50 kHz at 25 °C for about 10–60 s. The progress of the reaction was monitored by TLC. After completion of the reaction, the solid separated out was filtered and washed with water. Analytically pure products were obtained without further recrystallization.

Spectral data of newly synthesized compounds

4-(4-Fluorophenyl)-1,3-selenazol-2-amine (4c)

White solid; IR (KBr, ν_{max}, cm^{-1}): 3,392, 3,261 (NH_2), 1,628 (C=N), 1,098 (C–F); ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.19 (s, 1H), 7.28 (s, 1H), 7.32 (d, $J = 8.0$ Hz, 1H), 7.77–7.81 (m, 3H), 8.44 (s, 1H); MS (ESI) *m/z*: 242 $[M + H]^+$; Anal. calcd. for $C_9H_7FN_2Se$: C, 44.83; H, 2.93; N, 11.62. Found: C, 44.61; H, 3.17; N, 11.83.

4-([1,1′-Biphenyl]-4-yl)thiazol-2-amine (10a)

White solid; IR (KBr, ν_{max}, cm^{-1}): 3,370, 3,258 (NH_2), 1,625 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.27 (s, 1H), 7.39 (t, $J = 7.6$ Hz, 1H), 7.49 (t, $J = 7.2$ Hz, 2H), 7.73 (d, $J = 7.2$ Hz, 2H), 7.79 (d, $J = 8.4$ Hz, 2H), 7.84 (d,

$J = 8.4$ Hz, 2H), 8.48 (s, 2H); MS (ESI) *m/z*: 253 $[M + H]^+$; Anal. calcd. for $C_{15}H_{12}N_2S$: C, 71.40; H, 4.79; N, 11.10. Found: C, 71.16; H, 4.54; N, 11.25.

4-([1,1′-Biphenyl]-4-yl)-N-phenylthiazol-2-amine (10b)

White solid; IR (KBr, ν_{max}, cm^{-1}): 3,332 (NH), 1,698 (C=N); ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 6.99 (t, $J = 7.2$ Hz, 1H), 7.31–7.43 (m, 6H), 7.61–7.69 (m, 6H), 7.93 (d, $J = 8.4$ Hz, 2H), 10.47 (s, 1H); MS (ESI) *m/z*: 329 $[M + H]^+$; Anal. calcd. for $C_{21}H_{16}N_2S$: C, 76.80; H, 4.91; N, 8.53. Found: C, 76.57; H, 4.70; N, 8.27.

4-([1,1′-Biphenyl]-4-yl)-1,3-selenazol-2-amine (10c)

White solid; IR (KBr, ν_{max}, cm^{-1}): 3,490, 3,240 (NH_2), 1,613 (C=N); ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.38–7.42 (m, 1H), 7.50 (t, $J = 7.2$ Hz, 2H), 7.55 (s, 1H), 7.73–7.80 (m, 6H), 9.02 (s, 2H); MS (ESI) *m/z*: 300 $[M + H]^+$; Anal. calcd. for $C_{15}H_{12}N_2Se$: C, 60.21; H, 4.04; N, 9.36. Found: C, 60.56; H, 4.34; N, 9.12.

3-(2-Aminothiazol-4-yl)-6-chloro-2H-chromen-2-one (12a)

Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,315, 3,248 (NH_2), 1,735 (C=O), 1,631 (C=N), 789 (C–Cl); ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.77 (d, $J = 7.2$ Hz, 1H), 7.93 (d, $J = 7.6$ Hz, 1H), 8.08 (s, 1H), 8.45 (s, 1H), 8.61 (s, 1H), 8.80 (s, 2H); MS (ESI) *m/z*: 279 $[M + H]^+$; Anal. calcd. for $C_{12}H_7ClN_2O_2S$: C, 51.71; H, 2.53, N, 10.05. Found: C, 51.42; H, 2.75; N, 10.37.

6-Chloro-3-(2-(phenylamino)thiazol-4-yl)-2H-chromen-2-one (12b)

Yellow solid, IR (KBr, ν_{max}, cm^{-1}): 3,359 (NH), 1,719 (C=O), 1,607 (C=N), 745 (C–Cl); ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.01 (t, $J = 7.2$ Hz, 1H), 7.38 (t, $J = 8.0$ Hz, 2H), 7.48 (d, $J = 8.8$ Hz, 1H), 7.62–7.65 (m, 1H), 7.76 (d, $J = 8.0$ Hz, 2H), 7.80 (s, 1H), 8.13 (s, 1H), 8.66 (s, 1H), 10.36 (s, 1H); MS (ESI) *m/z*: 355 $[M + H]^+$; Anal. calcd. for $C_{18}H_{11}ClN_2O_2S$: C, 60.93; H, 3.12; N, 7.90. Found: C, 60.75; H, 3.28; N, 7.72.

3-(2-Amino-1,3-selenazol-4-yl)-6-chloro-2H-chromen-2-one (12c)

Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,297, 3,441 (NH_2), 1,728 (C=O), 1,625 (C=N), 785 (C–Cl); ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.89 (d, $J = 6.8$ Hz, 1H), 7.92 (d, $J = 7.2$ Hz, 1H), 8.09 (s, 1H), 8.46 (s, 1H), 8.61 (s, 1H), 8.79 (s, 2H); MS (ESI) *m/z*: 325 $[M]^+$; Anal. calcd. for $C_{12}H_7ClN_2O_2Se$: C, 44.26; H, 2.17; N, 8.60. Found: C, 44.55; H, 2.32; N, 8.36.

3-(2-Aminothiazol-4-yl)-6-bromo-2H-chromen-2-one (13a)

Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,340, 3,186 (NH_2), 1,717 (C=O), 1,602 (C=N), 602 (C–Br); ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.19 (s, 2H), 7.40 (d,

$J = 8.8$ Hz, 1H), 7.54 (s, 1H), 7.72–7.75 (m, 1H), 8.11 (d, $J = 8.0$ Hz, 1H), 8.44 (s, 1H); MS (ESI) *m/z*: 324 $[M + H]^+$; Anal. calcd. for $C_{12}H_7BrN_2O_2S$: C, 44.60; H, 2.18; N, 8.67. Found: C, 44.45; H, 2.37; N, 8.46.

6-Bromo-3-(2-(phenylamino)thiazol-4-yl)-2H-chromen-2-one (13b)

Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,358 (NH), 1,719 (C=O), 1,605 (C=N), 558 (C–Br); ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.01 (t, $J = 7.6$ Hz, 1H), 7.37–7.44 (m, 3H), 7.75–7.81 (m, 4H), 8.28 (d, $J = 7.6$ Hz, 1H), 8.67 (s, 1H), 10.36 (s, 1H); MS (ESI) *m/z*: 400 $[M + H]^+$; Anal. calcd. for $C_{18}H_{11}BrN_2O_2S$: C, 54.15; H, 2.78; N, 7.02. Found: C, 54.36; H, 2.56; N, 7.22.

3-(2-Amino-1,3-selenazol-4-yl)-6-bromo-2H-chromen-2-one (13c)

Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,483, 3,372 (NH_2), 1,735 (C=O), 1,620 (C=N), 587 (C–Br); ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.94 (d, $J = 8.0$ Hz, 1H), 8.03 (d, $J = 7.2$ Hz, 1H), 8.26 (s, 1H), 8.44 (s, 1H), 8.52 (s, 2H), 8.95 (s, 1H); MS (ESI) *m/z*: 371 $[M + H]^+$; Anal. calcd. for $C_{12}H_7BrN_2O_2Se$: C, 38.95; H, 1.91; N, 7.57. Found: C, 38.65; H, 1.67; N, 7.84.

3-(2-Aminothiazol-4-yl)-6,8-dibromo-2H-chromen-2-one (14a)

Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,492, 3,389 (NH_2), 1,740 (C=O), 1,692 (C=N), 593, 608 (C–Br); ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.23 (s, 2H), 7.56 (s, 1H), 8.09–8.14 (m, 2H), 8.41 (s, 1H); MS (ESI) *m/z*: 403 $[M + H]^+$; Anal. calcd. for $C_{12}H_6Br_2N_2O_2S$: C, 35.85; H, 1.50; N, 6.97. Found: C, 35.97; H, 1.39; N, 7.21.

6,8-Dibromo-3-(2-(phenylamino)thiazol-4-yl)-2H-chromen-2-one (14b)

Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,362 (NH), 1,728 (C=O), 1,603 (C=N), 501, 562 (C–Br); ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.01 (t, $J = 7.2$ Hz, 1H), 7.38 (t, $J = 8.0$ Hz, 2H), 7.77 (d, $J = 8.0$ Hz, 2H), 7.82 (s, 1H), 8.12 (s, 1H), 8.32 (s, 1H), 8.64 (s, 1H), 10.37 (s, 1H); MS (ESI) *m/z*: 479 $[M + H]^+$; Anal. calcd. for $C_{18}H_{10}Br_2N_2O_2S$: C, 45.21; H, 2.11; N, 5.86. Found: C, 45.43; H, 2.02; N, 5.67.

3-(2-Amino-1,3-selenazol-4-yl)-6,8-dibromo-2H-chromen-2-one (14c)

Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,450, 3,310 (NH_2), 1,723 (C=O), 1,600 (C=N), 539, 558 (C–Br); ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.01 (s, 1H), 8.08 (s, 1H), 8.15 (s, 1H), 8.42 (s, 1H), 8.75 (s, 2H); MS (ESI) *m/z*: 449 $[M + H]^+$; Anal. calcd. for $C_{12}H_6Br_2N_2O_2Se$: C, 32.10; H, 1.35; N, 6.24. Found: C, 32.32; H, 1.16; N, 6.42.

3-(2-Aminothiazol-4-yl)-6-methoxy-2H-chromen-2-one (15a)

Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,463, 3,352 (NH_2), 1,712 (C=O), 1,616 (C=N), 1,270 (C–O–C); ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 3.90 (s, 3H), 7.27–7.35 (m, 5H), 7.49 (s, 1H), 8.45 (s, 1H); MS (ESI) *m/z*: 275 $[M + H]^+$; Anal. calcd. for $C_{13}H_{10}N_2O_3S$: C, 56.92; H, 3.67; N, 10.21. Found: C, 57.14; H, 3.45; N, 10.39.

6-Methoxy-3-(2-(phenylamino)thiazol-4-yl)-2H-chromen-2-one (15b)

Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,313 (NH), 1,708 (C=O), 1,606 (C=N), 1,276 (C–O–C); ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 3.94 (s, 3H), 7.00 (t, $J = 7.2$ Hz, 1H), 7.32–7.40 (m, 4H), 7.49–7.51 (m, 1H), 7.75 (d, $J = 7.6$ Hz, 2H), 7.79 (s, 1H), 8.66 (s, 1H), 10.35 (s, 1H); MS (ESI) *m/z*: 351 $[M + H]^+$; Anal. calcd. for $C_{19}H_{14}N_2O_3S$: C, 65.13; H, 4.03; N, 7.99. Found: C, 65.01; H, 4.19; N, 7.83.

3-(2-Amino-1,3-selenazol-4-yl)-6-methoxy-2H-chromen-2-one (15c)

Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,453, 3,344 (NH_2), 1,710 (C=O), 1,617 (C=N), 1,271 (C–O–C); ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 3.93 (s, 3H), 7.18 (d, $J = 7.2$ Hz, 1H), 7.70 (d, $J = 7.2$ Hz, 1H), 7.94 (s, 1H), 8.20 (s, 1H), 8.49 (s, 1H), 8.63 (s, 2H); MS (ESI) *m/z*: 321 $[M]^+$; Anal. calcd. for $C_{13}H_{10}N_2O_3Se$: C, 48.61; H, 3.14; N, 8.72. Found: C, 48.38; H, 3.29; N, 8.91.

2-(2-Aminothiazol-4-yl)-3H-benzo[f]chromen-3-one (16a)

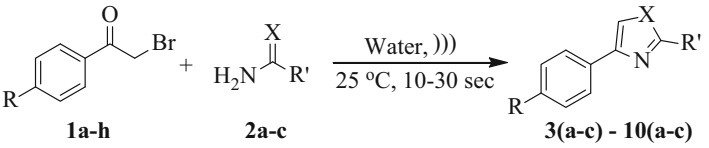
Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,358, 3,292 (NH_2), 1,702 (C=O), 1,632 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.60–7.67 (m, 4H), 7.81 (t, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.0$ Hz, 1H), 8.19–8.22 (m, 2H), 8.44 (d, $J = 8.4$ Hz, 1H), 9.24 (s, 1H); MS (ESI) *m/z*: 295 $[M + H]^+$; Anal. calcd. for $C_{16}H_{10}N_2O_2S$: C, 65.29; H, 3.42; N, 9.52. Found: C, 65.42; H, 3.25; N, 9.79.

2-(2-(Phenylamino)thiazol-4-yl)-3H-benzo[f]chromen-3-one (16b)

Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,303 (NH), 1,726 (C=O), 1,698 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.04 (t, $J = 7.2$ Hz, 1H), 7.44 (t, $J = 8.0$ Hz, 2H), 7.62–7.69 (m, 2H), 7.78–7.87 (m, 4H), 8.10 (d, $J = 8.0$ Hz, 1H), 8.21 (d, $J = 9.2$ Hz, 1H), 8.42 (d, $J = 8.4$ Hz, 1H), 9.35 (s, 1H), 10.43 (s, 1H); MS (ESI) *m/z*: 371 $[M + H]^+$; Anal. calcd. for $C_{22}H_{14}N_2O_2S$: C, 71.33; H, 3.81; N, 7.56. Found: C, 71.50; H, 3.92; N, 7.34.

2-(2-Amino-1,3-selenazol-4-yl)-3H-benzo[f]chromen-3-one (16c)

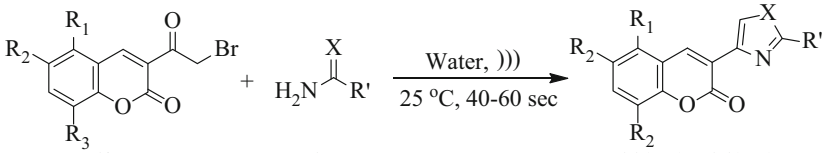
Yellow solid; IR (KBr, ν_{max}, cm^{-1}): 3,230, 3,170 (NH_2), 1,709 (C=O), 1,620 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.68 (s, 1H), 7.81 (t, $J = 8$ Hz, 2H), 8.09 (d, $J = 8.8$ Hz, 2H), 8.25 (d, $J = 9.2$ Hz, 1H), 8.66 (d, $J = 8.4$ Hz, 1H), 9.08 (s, 2H), 9.28 (s, 1H); MS (ESI) *m/z*: 341 $[M]^+$; Anal. calcd. for $C_{16}H_{10}N_2O_2Se$: C, 56.32; H, 2.95; N, 8.21. Found: C, 56.53; H, 2.65; N, 8.36.



1a-h **2a-c** **3(a-c) - 10(a-c)**

R = H / F / Cl / Br / CH_3 / OCH_3 /NO_2 / C_6H_5; R' = NH_2 / NHPh; X = S / Se

Scheme 1 Synthesis of 2,4-disubstituted-1,3-thiazoles and selenazoles with phenacyl bromides (1a–h)



1i-n **2a-c** **11(a-c) - 16(a-c)**

R_1 = H; R_2 = H / Cl / Br / OCH_3; R_1 - R_2 = Benzo; R_3 = H / Br
R' = NH_2 / NHPh; X = S / Se

Scheme 2 Synthesis of 2,4-disubstituted-1,3-thiazoles and selenazoles with 3-(2-bromoacetyl)coumarins (1i–n)

Table 1 Optimizing the reaction conditions

Entry	Solvent	Ultrasound frequency (kHz)	Bath temperature (°C)	Time (s)	Yield[a] (%)
1	Water	30	25	10	96
2	Methanol	30	25	60	93
3	Acetic acid	30	25	120	86
4	Acetonitrile	30	25	120	88
5	Dimethylformamide	30	25	160	86
6	Water	30	40	10	95
7	Water	30	60	10	93
8	Water	50	25	10	98
9	Water	50	40	10	96
10	Water	50	60	10	93
11	Water:methanol (1:1 v/v)	50	25	40	91

Reaction conditions: Phenacyl bromide (1a, 1 mmol), thiourea (2a, 1 mmol), solvent (1 mL), ultrasonic irradiation

[a] Isolated yields

Results and discussion

The schematic representation for the formation of 2,4-disubstituted-1,3-thiazoles and selenazoles (**3**–**16**) is shown in Schemes 1 and 2. Various phenacyl bromides (**1a**–**h**) and 3-(2-bromoacetyl)coumarins (**1i**–**n**) on condensation with thiourea (**2a**), phenylthiourea (**2b**) and selenourea (**2c**) in aqueous medium under ultrasonic

irradiation at ambient temperature afforded the corresponding thiazoles and selenazoles (**3–16**) with excellent yields (90–99 %) in short reaction times (10–60 s). 3-(2-Bromoacetyl)coumarins (**1i–n**) were synthesized according to the literature procedure [39].

In order to find the optimal conditions, a model reaction between equimolar quantities of phenacyl bromide (**1a**) and thiourea (**2a**) was performed in different solvents like water, methanol, acetic acid, acetonitrile and dimethylformamide at 25 °C bath temperature and 30 kHz ultrasonic frequency. We observed maximum yield (96 %) of the product (**3a**) in aqueous medium within 10 s. To improve the yield of the product in aqueous medium, the reaction was carried at 40 and 60 °C bath temperatures, but we observed slight decreases in the yield of the product, which may due to the formation of unidentified impurities. The same reaction was

Table 2 Synthesis of 2,4-disubstituted-1,3-thiazoles and selenazoles (**3–10**) with phenacyl bromides

Product	R	R'	X	Time (sec)	Yield[a] (%)	Melting point (°C)	
						Observed	Literature value [Ref]
3a	H	NH_2	S	10	98	152–153	150–152 [40]
3b	H	NHPh	S	10	96	133–135	134–136 [40]
3c	H	NH_2	Se	10	97	132–133	132 [31]
4a	F	NH_2	S	25	95	117–118	119–120 [34]
4b	F	NHPh	S	25	92	111–112	110–111 [37]
4c	F	NH_2	Se	15	95	119–120	–
5a	Cl	NH_2	S	20	99	166–168	166–168 [40]
5b	Cl	NHPh	S	25	96	144–146	145–146 [40]
5c	Cl	NH_2	Se	20	97	156–157	155 [31]
6a	Br	NH_2	S	25	95	182–183	182–184 [40]
6b	Br	NHPh	S	30	93	230–232	230–232 [40]
6c	Br	NH_2	Se	25	97	176	177–178 [40]
7a	CH_3	NH_2	S	15	96	136–137	135–136 [40]
7b	CH_3	NHPh	S	20	91	102–104	102–103 [40]
7c	CH_3	NH_2	Se	15	92	167–168	166 [31]
8a	OCH_3	NH_2	S	10	98	202–204	204–206 [40]
8b	OCH_3	NHPh	S	15	94	136–138	137–138 [40]
8c	OCH_3	NH_2	Se	10	97	194–196	173 [31]
9a	NO_2	NH_2	S	30	91	284–285	284–286 [40]
9b	NO_2	NHPh	S	30	91	204–206	206–207 [40]
9c	NO_2	NH_2	Se	25	91	269–270	250 [31]
10a	C_6H_5	NH_2	S	20	94	234–236	–
10b	C_6H_5	NHPh	S	25	90	222–224	–
10c	C_6H_5	NH_2	Se	20	94	135–136	–

Reaction conditions: Phenacyl bromides (**1a–h**, 1 mmol), thiourea/phenylthiourea/selenourea (**2a–c**, 1 mmol), water (1 mL), ultrasonic irradiation at 50 kHz and 25 °C bath temperature

[a] Isolated pure products yield

Table 3 Synthesis of 2,4-disubstituted-1,3-thiazoles and selenazoles with 3-(2-bromoacetyl)coumarins (**11–16**)

Product	R_1	R_2	R_3	R′	X	Time (sec)	Yield[a] (%)	Melting point (°C)	
								Observed	Lit. [Ref.]
11a	H	H	H	NH_2	S	40	98	227–228	228–229 [40]
11b	H	H	H	NHPh	S	45	94	188–190	188–190 [40]
11c	H	H	H	NH_2	Se	40	96	218–220	217–218 [40]
12a	H	Cl	H	NH_2	S	55	98	206–208	–
12b	H	Cl	H	NHPh	S	60	96	215–217	–
12c	H	Cl	H	NH_2	Se	50	99	305–307	–
13a	H	Br	H	NH_2	S	55	97	210–212	–
13b	H	Br	H	NHPh	S	55	95	229–231	–
13c	H	Br	H	NH_2	Se	50	94	346–348	–
14a	H	Br	Br	NH_2	S	60	92	277–279	–
14b	H	Br	Br	NHPh	S	60	92	225–227	–
14c	H	Br	Br	NH_2	Se	60	94	326–328	–
15a	H	OCH_3	H	NH_2	S	45	99	256–258	–
15b	H	OCH_3	H	NHPh	S	45	96	222–223	–
15c	H	OCH_3	H	NH_2	Se	40	97	237–239	–
16a	Benzo		H	NH_2	S	55	93	287–289	–
16b	Benzo		H	NHPh	S	60	93	262–264	–
16c	Benzo		H	NH_2	Se	55	93	358–360	–

Reaction conditions: 3-(2-bromoacetyl)coumarin (**1i–n**, 1 mmol), thiourea/phenylthiourea/selenourea (**2a–c**, 1 mmol), water (1 mL), ultrasonic irradiation at 50 kHz and 25 °C bath temperature

[a] Isolated pure products yield

also carried out at 50 kHz ultrasonic frequency by varying the bath temperature (25, 40 and 60 °C), and observed maximum yield (98 %) of the product at 25 °C bath temperature. We also observed the decrease in the yield of the product as the temperature increased to 60 °C (Table 1). Recently, our group has reported the synthesis of 1,3-thiazoles and selenazoles in a methanol–water (1:1 v/v) solvent system [40]. Therefore, we also tested the above reaction in methanol–water (1:1 v/v) at 50 kHz ultrasonic frequency and 25 °C bath temperature, but observed only 91 % of the product yield even after 60 s. The increase in yield of the product under ultrasonic irradiation can be explained by the cavitations effect (supporting file).

Utilizing these optimal conditions (ultrasonication at 50 kHz frequency and 25 °C bath temperature in aqueous medium), a series of 1,3-thiazoles and selenazoles (**3–16**) have been synthesized by the reaction of phenacyl bromides (**1a–h**) and 3-(2-bromoacetyl)coumarins (**1i–n**) with thiourea (**2a**), phenylthiourea (**2b**) and selenourea (**2c**) in excellent yields (Tables 2 and 3). All the newly synthesized compounds were characterized by their spectral and analytical studies, and the known compounds were confirmed by comparing their melting points with the reported values.

Conclusion

In conclusion, we have efficiently synthesized a series of 2,4-disubstituted-1,3-thiazoles and selenazoles in aqueous medium under ultrasonic irradiation at ambient temperature. This non-conventional methodology has many advantages over conventional reported methods that include environmentally friendly, rapid reaction completion, easy workup procedure and analytically pure product formation in excellent yields. This method can be effectively used for large-scale production of thiazoles and selenazoles in shorter reaction times.

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