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RESEARCH ARTICLE

Synthesis of New [1,3]Selenazolo[5,4-d]Pyrimidine Derivatives as Purine-Like Selenium-Containing Heterocycles

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ABSTRACT

In the research, we presented a method for synthesizing selenium-containing heterocyclic compounds. One of the key structures in this project is the derivative of 7-methyl-2-(alkylthio)-5-(amino-1-yl)-[1,3]selenazolo[5,4-*d*]pyrimidine (**3a-i**). These are synthesized in one step using the treatment of precursor 2,4-dichloro-6-methylpyrimidin-5-amine (**1**) with selenium and sodium borohydride in ethanol to obtain the compound, which subsequently reacts with carbon disulfide in pyridine to form 5-chloro-7-methyl-[1,3]selenazolo[5,4-d]pyrimidine-2(1H)-thione (**2**). This is then treated with various alkyl halides under reflux conditions in ethanol to yield various derivatives (**3a-i**). A mixture of 5-chloro-7-methyl-2-(alkylthio)-[1,3]selenazolo[5,4-*d*]pyrimidine (**3a-i**) and various primary and secondary amines is refluxed in ethanol to prepare the corresponding nucleophilic substituted products, 2-(alkylsulfanyl)-7-methyl-5-(morpholin-4-yl)-[1,3]selenazolo[5,4-*d*]pyrimidines (**4a-i**) in good yields.

1 | Introduction

Selenium is crucial in small quantities for the biological processes in humans and other living organisms, including animals. Due to its significant role, research in this area is expanding. It can be said that selenoproteins, which incorporate selenium into their structure, are vital in many aspects, such as the organism's mechanisms against stress [1], detoxification [2], antifungal [3–6], antimicrobial [7–9], and anticonvulsant activities [10]. Additionally, selenium plays an essential role in enzymes such as thioredoxin reductase [11], iodothyronine deiodinase [12], and selenophosphate synthetase [13]. Moreover, selenium-containing compounds have been found in the structure of some of the most well-known anticancer and antiviral agents [14]. For instance, selenazofurin (2-β-d-ribofuranosyl selenazole-4-carboxamide), which is 5–10 times more potent than the sulfur-containing thiazofurin congener, has been used in several in vitro and in vivo antitumor screenings [15].

Some examples of compounds containing selenium that have important medicinal properties have been shown in Figure 1. For instance, the synthesized selenazolopyridines (**I**) which are known as capable of inducing apoptosis in human breast carcinoma MCF-7 cells through scavenging of intracellular ROs. Compound (II) is a selective human carbonic anhydrase IX inhibitor with potent anti-tumor activity. The other proposed drug is Amselamine (III) which has anticancer and antioxidant properties; and finally, phenylselenazolopyrimidine (IV) has been also reported to have anti-tumor properties [16–18].

1,3-Selenazoles as a five-membered ring heterocycle are included in biologically active compounds like selenazofurin

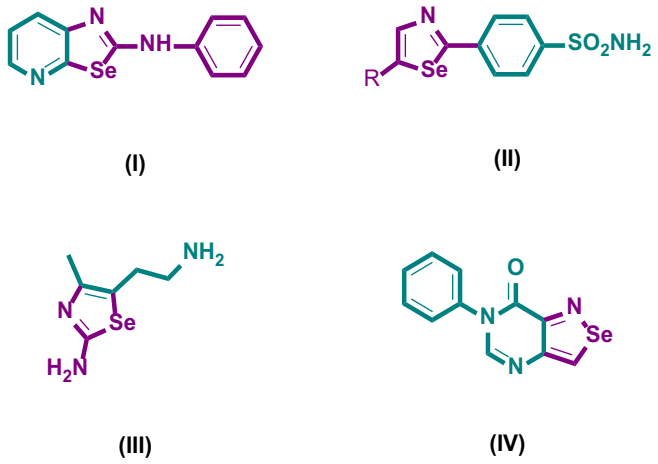


FIGURE 1 | Examples of medicinal activities of selenazoles and selenium-containing compounds.

and amselamine [19–21]. These compounds exhibit various biological properties, such as antioxidant [22–25], antimicrobial, and anticonvulsant activities [7]. The unique properties of selenazoles include their ability to deactivate free radicals [26], inhibit the proliferation of cancer cells [27, 28], and selectively inhibit human carbonic anhydrase IX [29].

The synthesis of selenium-containing compounds, particularly five-membered rings with selenium atoms linked to nitrogen-containing heterocycles, has been extensively explored [30–32]. One approach involves reacting aryliodoazides with morpholino-(phenyl)methanethione to produce diverse selenazole derivatives [33]. Another method synthesizes 1,3-selenazoles via cyclohexane carbaldehyde, potassium selenocyanate, hydrazine hydrate, and HCl under reflux, followed by reactions with 2-bromo-1-(4-alkylphenyl)ethan-1-one [4].

Shiri's group notably developed 7-imino[1,3]-selenazolo[4,5-*d*] pyrimidine-5(4H)-thione derivatives from 2,4,5-substituted-1, 3-selenazoles and phenyl isothiocyanates [34], and dihydroselenopyrimidines from 2-(bis(ethylthio)methylene)malononitrile and benzene isothiocyanate [35]. They also synthesized 5-bromo-2-chloro-4-methyl-6-selenocyanatopyrimidine via potassium isothiocyanate in acetonitrile under reflux, producing tetrazoles and 1,3-selenazole-5-carboxamides as intermediates, which were further converted to selenazolopyrimidine systems [36].

Pyridazine-linked selenium rings were synthesized using diphenylselenylidene dihydropyridazine carbonitrile with chloroacetonitrile or ethyl chloroacetate [37]. Quinoxaline-fused 1,3-selenazoles were obtained by reacting 4-hydroxyselenazolidines with methylphenylchloropyruvate and ortho-phenylenediamines [38]. Finally, 1,3-selenazolopyridines were prepared by reacting bis(3-amino-2-pyridyl) diselenides with benzaldehydes, offering a variety of functionalized selenium-containing heterocycles [2, 39–41].

As derivatives of [1,3]selenazolo[4,5-*d*]pyrimidine have not been studied and, therefore, in continuation of our previous studies, selenopheno[2,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine derivatives [42], [1,3]selenazolo[5,4-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine [43], and pyrido[1,2-*e*]purine [44], herein, we report the synthesis of various derivatives of selenium-containing heterocycles that are anticipated to be good candidates in biological assessments.

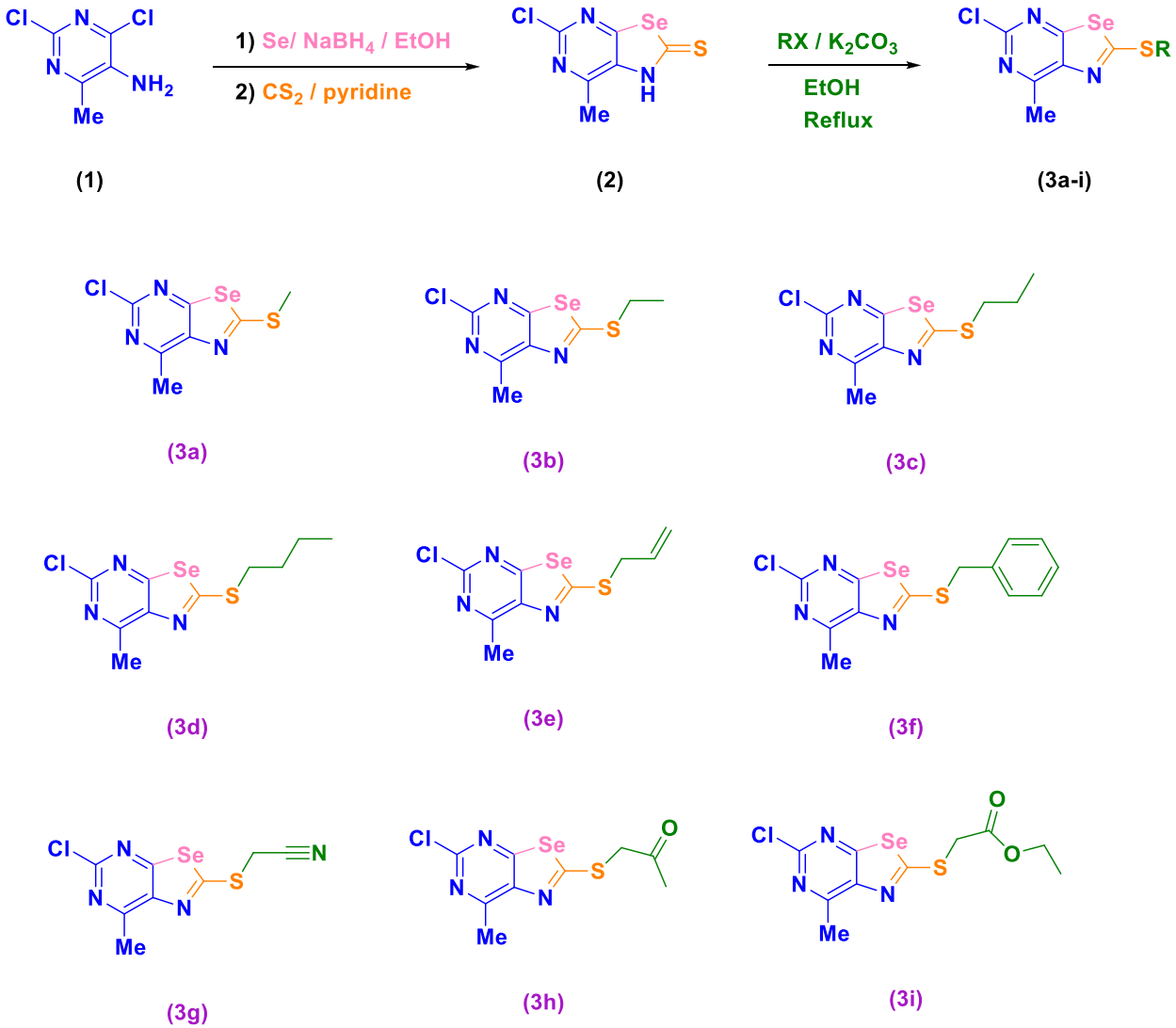
2 | Results and Discussion

In research conducted to prepare the heterocyclic system 5-chloro-7-methyl-1H,2H-[1,3]selenazolo[5,4-*d*]pyrimidin-2-thione (**2**), initially, 5-amino-2,4-dichloro-6-methylpyrimidine as the precursor (**1**) was obtained according to our previously published method [45]. Then, it is treated with selenium powder and sodium borohydride in ethanol and reacted with carbon disulfide in pyridine to obtain compound (**2**). Different derivatives of 2-(alkylthio)-5-chloro-7-methyl[1,3]selenazolo[5,4-d]pyrimidine (**3a-i**) were prepared via the reaction of it with diverse alkyl halides in K_2CO_3 as base and ethanol as solvent under reflux conditions (Scheme 1).

All the structures are novel, and we will examine the spectral data for one of the synthesized derivatives, 5-chloro-7-methyl-2-(prop-2-en-1-sulfanyl)-[1,3]selenazolo[5,4-*d*]pyrimidine (**3e**). In the IR spectrum of this derivative, C-H stretching vibrations of both the double bond and aliphatic groups appear in the range of $\nu = 2749–3082\,cm^{-1}$ indicating the presence of an allylic group in the compound. Additionally, in the ^1H NMR spectrum, there is a single signal at δ 2.90 ppm corresponding to three hydrogens of the methyl of the pyrimidine ring. There is also a doublet signal at δ 4.05 ppm (CH_2), and peaks corresponding to C=C bond hydrogens appear as doublet of doublet at δ 5.30 (CH) and δ 5.48 (CH) ppm. A peak as a multiplet signal integrating for one hydrogen is associated with the (C<u>H</u>=CH_2) confirming the synthesis of this derivative. In the ^{13}C NMR spectrum, two groups of peaks are observed: two peaks in the aliphatic region (corresponding to CH_3 and CH_2 that are seen at δ 20.3 and 36.2 ppm, respectively), two peaks at 119.9 and 131.5 ppm correspond to the double bond carbons, and the remaining four peaks in the aromatic region (135.1–154.3) validate the synthesis of this compound. Finally, the mass spectrum of this sample shows the molecular ion peak at $m/z = 305$ and a peak at $m/z = 269$ which is related to the separation of the chlorine atom from the main structure and confirms the synthesis of the desired compound.

In the final stage, products (**4a-i**) were synthesized by reacting compounds (**3a-i**) with morpholine as a cyclic secondary amine in a triethylamine/ethanol mixture under reflux conditions. The nucleophilicity of the morpholine facilitates its reaction with the carbon-bearing chlorine atom at the 2-position of the pyrimidine moiety (Scheme 2).

All the synthesized derivatives are confirmed by the spectral and microanalytical analyses. For instance, We will focus on 4-[2-(ethylsulfanyl)-7-methyl-5-(morpholin-4-yl)-[1,3]selenazolo [5,4-d]pyrimidine] as compound (**4b**). The aliphatic C-H stretching vibration bands are observed at ν 2930–3082 cm^{-1} in the IR spectrum of this compound. In the ^1H NMR spectrum, a triplet peak corresponding to three hydrogens at δ 1.50 ppm (CH_3) indicates the presence of a methyl group. Another singlet peak with three hydrogens at δ 2.71 ppm (CH_3) corresponds to the methyl group on the pyrimidine moiety. Additionally, a multiplet peak integrating for eight hydrogens confirms the presence



SCHEME 1 | The schematic preparation of derivatives (3a-i).

of the morpholine ring. In the ^{13}C NMR spectrum, five signals in the aliphatic region correspond to $-\underline{C}H_2\underline{C}H_3$, $\underline{C}H_3$-pyrimidine, and morpholine ring carbons. The appearance of five signals in the aromatic region confirms the true structure of this compound. Also, the mass spectrum shows the molecular ion peak at $m/z = 343$ confirming the synthesis of this compound.

3 | Conclusion

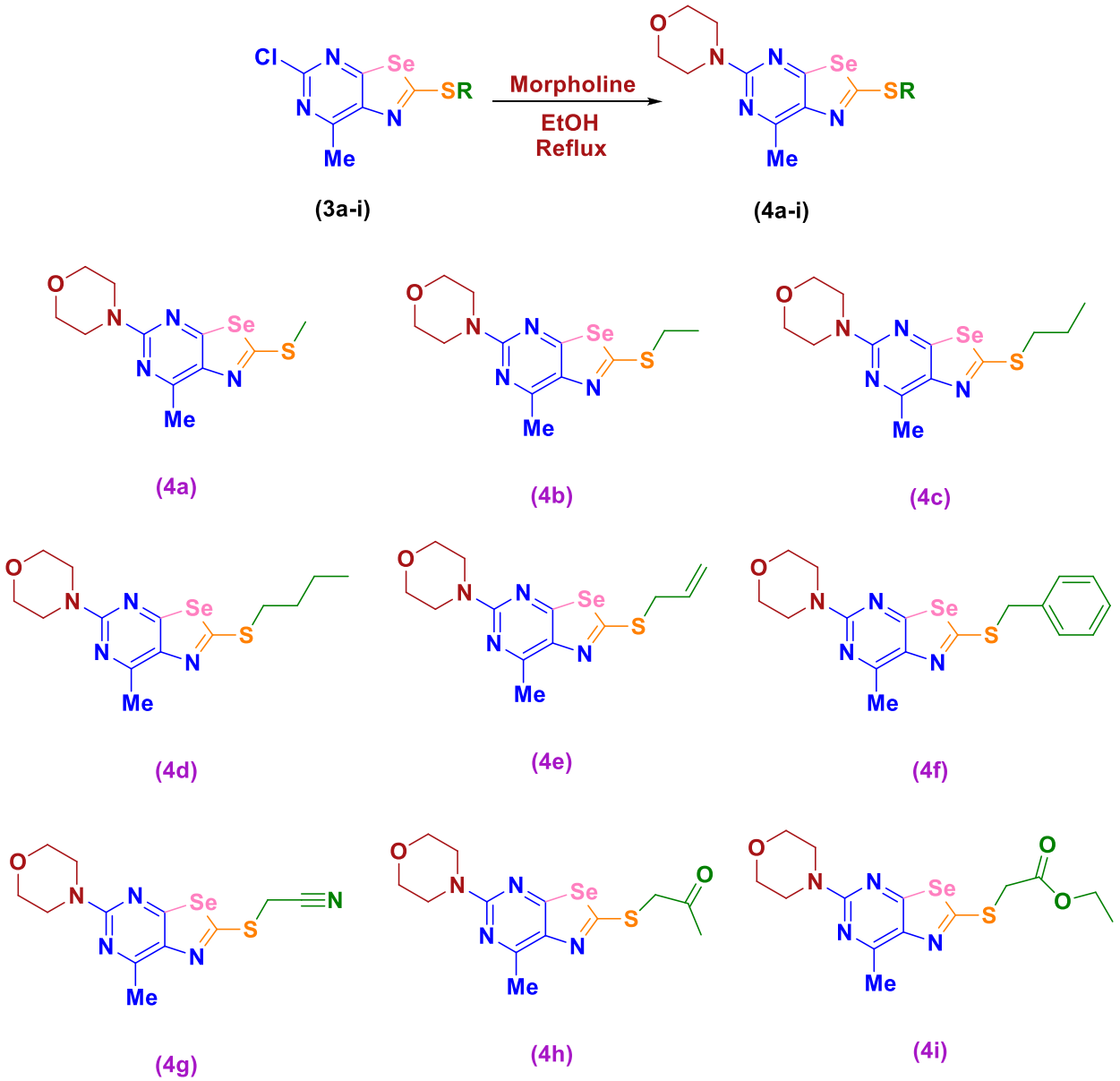
In summary, we developed a robust synthetic pathway to produce novel [1,3]selenazolo[5,4-d]pyrimidine derivatives. These selenium-containing heterocycles were synthesized using sequential reactions involving precursor 2,4-dichloro-6-methyl pyrimidin-5-amine with selenium, sodium borohydride, and subsequent nucleophilic substitutions. The characterization of these compounds through spectral and microanalytical techniques confirmed their novel structures and purity. Given the structural similarity of the synthesized compounds to biologically active purine-like frameworks, we anticipate that these derivatives exhibit significant pharmacological potential. Their properties, particularly in antioxidant, antimicrobial, and anticancer activities, suggest promising applications in medicinal chemistry. Future studies will be directed toward in vitro and in vivo evaluations to validate these bioactivities and elucidate potential mechanisms of action. This research contributes to expanding the library of selenium-based heterocyclic systems and offers insights into their role in drug development.

4 | Experimental

Melting points were measured by an Electrothermal type 9200 melting point apparatus. The ^1H NMR (300 MHz) and the ^{13}C NMR (75 MHz) spectra were obtained on a Bruker Avance DRX-300 Fourier transformer spectrometer using tetramethylsilane as an internal standard. An Avatar 370 FT-IR Thermo Nicolet spectrometer was employed to record the IR spectra and a Varian Mat CH-7 instrument for scanning mass spectra at 70 eV. Micro analytical data were obtained on a Thermo Finnigan Flash EA 1112 microanalyzer.

***The procedure for synthesizing compound (2)*:**

In order to synthesize compound (**1**) according to the previously published literature [45], the process begins with



SCHEME 2 | The schematic preparation of derivatives (4a-i).

6-methyluracil, which is substituted at the 5-position with a nitro group. Following this, the carbonyl moieties and nitro group of the resulting uracil are chlorinated and reduced, respectively, to form the primary compound needed to start the synthesis of compound (**2**). Compound (**1**) (10 mmol, 1.78 g) is treated with selenium powder (10 mmol, 0.59 g), $NaBH_4$ (10 mmol, 0.4 g) in ethanol (15 mL), and CS_2 (10 mmol, 0.49 mL) in pyridine (0.45 mL), respectively. Reaction progress was monitored by thin-layer chromatography (TLC) using chloroform and methanol (30:2) as the eluent. After the completion of the reaction, filtration and solvent removal yield a yellow solid, which is further purified by recrystallization with ethanol.

Yield = 74%; yellow powder; M.p. = 189°C–191°C, IR (KBr disc): $\underline{\nu}$ 3210, 2856, 2723, 2712, 1584, 1521, 1412, 1351, 1318, 1231 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 2.51 (s, 3H, CH_3-pyrimidine), 14.32 (s, 1H, NH), ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.6(CH_3-pyrimidine), 132.1, 145.6, 149.5, 151.3, 193.7, MS (*m/z*) = 264 (M^+), Anal. Calcd. for $C_6H_4ClN_3SSe$: C, 27.24; H, 1.52; N, 15.88; S, 12.12; Found: C, 27.65; H, 1.87; N, 15.32; S, 12.51%.

***General procedure for the synthesis of compounds (3a-i)*:**

To prepare 5-chloro-7-methyl-2-(alkylthio)-[1,3]selenazolo[5,4-*d*] pyrimidines (**3a-i**), compound (**2**) (15 mmol, 3.8 g) was treated with corresponding different alkyl halides (15 mmol) in ethanol (10 mL) as the solvent and in the presence of K_2CO_3 (1 g) under reflux conditions for 5 h. After the reaction was completed, the solid was filtered and washed with hexane (3 × 20 mL) and dried.

***5-Chloro-7-methyl-2-(methylsulfanyl)-[1,3] selenazolo[5,4-d]pyrimidine (3a)*:**

Yield = 83%; yellow powder; M.p. = 125°C–127°C, IR (KBr disc): $\underline{\nu}$ 2874, 2856, 2723, 2712, 2687, 1534, 1512, 1453, 1442, 1313, 1219 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 2.49 (s, 3H, CH_3-pyrimidine), 3.19 (s, 3H, CH_3-S), ^{13}C NMR (75 MHz, $CDCl_3$): δ

14.6(CH_3-pyrimidine), 21.6(CH_3-S), 137.1, 157.6, 158.1, 159.3, 159.7, MS (*m/z*) = 278 (M^+), 244 (M^+-Cl), Anal. Calcd. for $C_8H_8ClN_3SSe$: C, 30.83; H, 2.36; N, 15.26; S, 11.96; Found: C, 30.18; H, 2.17; N, 15.08; S, 11.51%.

***5-Chloro-2-(ethylsulfanyl)-7-methyl-[1,3]selenazolo[5,4-d] pyrimidine (3b)*:**

Yield = 83%; yellow powder; M.p. = 145°C–147°C, IR (KBr disc): ν 2924, 2876, 2823, 2812, 2872, 1597, 1578, 1553, 1442, 1374, 1313, 1250, 1219 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.44 (t, *J* = 6.8 Hz, 3H, CH_3), 2.78 (s, 3H, CH_3-pyrimidine), 3.33 (q, *J* = 5.7 Hz, 2H, CH_2), ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.6 (CH_3), 21.1 (CH_3-pyrimidine), 27.7 (CH_2-S), 140.3, 151.2, 155.5, 159.3, 163.2, MS (*m/z*) = 292 (M^+), 257 (M^+-Cl), Anal. Calcd. for $C_8H_8ClN_3SSe$: C, 32.83; H, 2.76; N, 14.36; S, 10.96; Found: C, 32.44; H, 2.55; N, 14.11; S, 10.23%.

***5-Chloro-7-methyl-2-(propylsulfanyl)-[1,3] selenazolo[5,4-d]pyrimidine (3c)*:**

Yield = 79%; White powder; M.p. = 132°C–135°C, IR (KBr disc): ν 2912, 2854, 2823, 2809, 2733, 1577, 1565, 1553, 1442, 1374, 1313, 1250, 1206 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.12 (t, *J* = 6.7 Hz, 3H, CH_3-propyl), 1.84–1.94 (m, 2H, CH_2-propyl), 2.47 (s, 3H, CH_3-pyrimidine), 3.38 (t, *J* = 4.8 Hz, 2H, CH_2-S), ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.4 ($\underline{C}H_3$), 20.3 ($\underline{C}H_2$), 22.4 ($\underline{C}H_3$), 35.1 (CH_2-S), 135.1, 144.8, 146.8, 154.3, 169.1, MS (*m/z*) = 306 (M^+), 263 (M^+-propyl), 216 (M^+-S-propyl, Me) Anal. Calcd. For $C_9H_{10}ClN_3SSe$: C, 35.25; H, 3.29; N, 13.70; S, 10.45; Found: C, 35.11; H, 3.30; N, 13.56; S, 10.22%.

***2-(Butylsulfanyl)-5-chloro-7-methyl-[1,3]selenazolo[5,4-d] pyrimidine (3d)*:**

Yield = 78%; brown oil; M.p. = 156°C–158°C, IR (KBr disc): ν 2910, 2877, 2834, 2798, 2778, 1597, 1578, 1555, 1432, 1374, 1313, 1250, 1219 cm^{-1} ^1H NMR (300 MHz, $CDCl_3$): δ 0.99 (t, *J* = 6.4 Hz, 3H, CH_3-butyl), 1.49–1.58 (m, 2H, CH_2-CH_3), 1.79–1.89 (m, 2H, CH_2-CH_2), 2.86 (s, 3H, CH_3-pyrimidine), 3.39 (t, *J* = 5.2 Hz, 2H, CH_2-S), 3.85, ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.4 ($\underline{C}H_3$-butyl), 20.3 (CH_2-CH_3), 22.4 (CH_2-CH_2), 23.4 (CH_3-pyrimidine), 36.2 ($\underline{C}H_2$-S), 135.1, 144.7, 146.7, 154.3, MS (*m/z*) = 320 (M^+), 263 (M^+-butyl). Anal. Calcd. for $C_{10}H_{12}ClN_3SSe$: C, 35.45; H, 3.77; N, 13.10; S, 10.00; Found: C, 35.12; H, 3.55; N, 13.34; S, 10.23%.

***5-Chloro-7-methyl-2-(prop-2-en-1-yl-sulfanyl)-[1,3] selenazolo[5,4-d]pyrimidine (3e)*:**

Yield = 71%; White powder; M.p. = 126°C–128°C, IR (KBr disc): ν 2998, 2952, 2919, 2867, 2844, 1597, 1578, 1553, 1442, 1374, 1313, 1250, 1219, 1121, 1079, 1023 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 2.90 (s, 3H, CH_3-pyrimidine),4.04–4.07 (dd, 2H, CH_2-S), 5.28–5.32 (m, 2H, CH=C$\underline{H}_2$), 5.43–5.50 (m, 1H, CH-CH_2 prop-2-en), ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3 ($\underline{C}H_3$), 36.2 ($\underline{C}H_3$-pyrimidine), 119.9, 131.5, 135.1, 144.8, 146.8, 154.3 MS (*m/z*) = 305 (M^+), 269 (M^+-Cl). Anal. Calcd. for $C_9H_8ClN_3SSe$: C, 59.38; H, 6.98; N, 23.08; S, 10.57; Found: C, 59.22; H, 6.44; N, 23.0.1; S, 10.23%.

***2-(Benzylsulfanyl)-5-chloro-7-methyl-[1,3] selenazolo[5,4-d]pyrimidine(3f)*:**

Yield = 70%; White powder; M.p. = 142°C–144°C, IR (KBr disc): ν 2998, 2952, 2919, 2867, 2844, 1597, 1578, 1553, 1442, 1374, 1313, 1250, 1219, 1121, 1079, 1023 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 2.80 (s, 3H, CH_3-pyrimidine), 4.54 (s, 2H, CH_2), 7.22–7.27 (m, 3H, hydrogens of benzyl ring), 7.37–7.40 (m, 2H, hydrogens of benzyl ring), ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.9 ($\underline{C}H_3$), 37.2 ($\underline{C}H_2$), 128.0, 128.1, 128.8, 129.2, 135.5, 142.8, 154.1, 161.1, 167.5, 168.1, MS (*m/z*) = 354 (M^+), 304 (M^+-Cl, Me). Anal. Calcd. for $C_{13}H_{10}ClN_3SSe$: C, 44.02; H, 2.84; N, 11.85; S, 9.04; Found: C, 43.76; H, 2.66; N, 11.21; S, 8.98%.

***5-Chloro-7-methyl-2-acetonitril-sulfanyl-[1,3] selenazolo[5,4-d]pyrimidine (3g)*:**

Yield = 77%; yellow powder; M.p. = 190°C–192°C, IR (KBr disc): ν 2963, 2852, 2819, 2767, 2744, 1697, 1678, 1593, 1442, 1374, 1313, 1250, 1219, 1121, 1079, 1023 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 2.85 (s, 3H, CH_3-pyrimidine), 4.50 (s, 2H, CH_2), ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.2 ($\underline{C}H_3$), 23.4($\underline{C}H_2$), 118.3, 140.5, 153.3, 167.3, MS (*m/z*) = 303 (M^+), 196 (M^+-Cl, S-acetonitrile). Anal. Calcd. for $C_8H_5ClN_4SSe$: C, 31.65; H, 1.66; N, 18.45; S, 10.56; Found: C, 31.33; H, 1.44; N, 18.22; S, 10.22%.

***1-((5-Chloro-7-methyl-[1,3]selenazolo[5,4-d]pyrimidin-2-yl)thio)propan-2-one (3h)*:**

Yield = 81%; brown powder; M.p. = 148°C–150°C, IR (KBr disc): ν 2998, 2952, 2919, 2867, 2844, 1597, 1578, 1553, 1442, 1374, 1313, 1250, 1219, 1121, 1079, 1023 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 2.84 (s, 3H, CH_3-pyrimidine), 3.70 (s, 3H, CH_3), 4.11 (s, 2H, CH_2), ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.5 ($\underline{C}H_3$), 20.9 ($\underline{C}H_3$), 21.5 ($\underline{C}H_2$), 114.7, 117.5, 142.2, 155.0, 162.3, 172.9, MS (*m/z*) = 320 (M^+). Anal. Calcd. for $C_9H_8OClN_3SSe$: C, 33.71; H, 2.51; N, 13.10; S, 10.00; Found: C, 33.23; H, 2.41; N, 13.01; S, 9.97%.

***Ethyl 2-((5-chloro-7-methyl-[1,3]selenazolo[5,4-d] pyrimidin-2-yl)thio)acetate (3i)*:**

Yield = 81%; brown powder; M.p. = 161°C–163°C, IR (KBr disc): ν 2967, 2943, 2923, 2873, 2811, 1597, 1547, 1553, 1432, 1374, 1313, 1250, 1219, 1121, 1079, 1023^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.39 (t, *J* = 5.2 Hz, CH_3), 2.85 (s, 3H, CH_3-pyrimidine), 4.14 (s, 2H, CH_2), 4.44 (CH_2-O), ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.3 ($\underline{C}H_3$), 19.4 ($\underline{C}H_3$-pyrimidine), 35.2 ($\underline{C}H_2$), 44.8 ($\underline{C}H_2$-O), 137.1, 151.5, 156.5, 159.2, 169.1, MS (*m/z*) = 320 (M^+). Anal. Calcd. for $C_{10}H_{10}O_2ClN_3SSe$: C, 33.71; H, 2.51; N, 13.10; S, 10.00; Found: C, 33.12; H, 2.31; N, 12.98; S, 9.97%.

***General procedure for the synthesis of compounds (4a-i)*:**

A mixture of the appropriate 5-chloro-7-methyl-2-(alkylthio)-[1 ,3]selenazolo[5,4-*d*]pyrimidine (**3a-i**) (10 mmol) and morpholine (10 mmol, 0.87 mL) was subjected to reflux in ethanol for 5 h. After the completion of the reaction, which was monitored by TLC using hexane and ethyl acetate (6:4), the mixture was cooled, and the solvent was evaporated under reduced pressure. The resulting solid was further recrystallized from ethanol and water.

***2-(Methylsulfanyl)-7-methyl-5-(morpholin-4-yl)-[1,3] selenazolo[5,4-d]pyrimidine (4a)*:**

Yield = 78%; white powder; M.p. = 117°C–119°C, IR (KBr disc): ν 2832, 2767, 2763, 2710, 1690, 1639, 1610, 1560, 1505, 1442, 1394, 1343, 1250, 1219, 1203, 1176, 1012 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ, 2.71 (s, 3H, CH_3-pyrimidine), 2.89 (s, 3H, CH_3), 3.77–3.87 (m, 8H, morpholine), ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.3 ($\underline{C}H_3$), 22.7 ($\underline{C}H_3$), 47.7 ($\underline{C}H_2$-N), 66.6 ($\underline{C}H_2$-O), 128.1, 137.5, 148.2, 151.5, 158.0, MS (*m/z*) = 343 (M^+). Anal. Calcd. for $C_{12}H_{16}ON_4SSe$: C, 41.98; H, 4.70; N, 16.32; S, 9.34; Found: C, 41.11; H, 4.21; N, 15.98; S, 9.10%.

***2-(Ethylsulfanyl)-7-methyl-5-(morpholin-4-yl)-[1,3] selenazolo[5,4-d]pyrimidine (4b)*:**

Yield = 86%; yellow powder; M.p. = 127°C–129°C, IR (KBr disc): ν 2852, 2747, 2713, 2701, 1690, 1659, 1630, 1520, 1515, 1482, 1354, 1323, 1267, 1276, 1112 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.50 (t, *J* = 6.5 Hz, 3H, CH_3), 2.71 (s, 3H, CH_3-pyrimidine), 3.29–3.38 (m, 2H, CH_2), 3.75–3.91 (m, 8H, morpholine), ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.6 ($\underline{C}H_3$), 21.0 ($\underline{C}H_3$), 27.7 ($\underline{C}H_3$), 47.7 ($\underline{C}H_2$-N), 66.7 ($\underline{C}H_2$-O), 137.1, 157.3, 158.1, 159.3, 159.7; MS (*m/z*) = 343 (M^+). Anal. Calcd. for $C_{12}H_{16}ON_4SSe$: C, 41.98; H, 4.70; N, 16.32; S, 9.34; found: C, 41.11; H, 4.21; N, 15.98; S, 9.10%.

***2-(Propylsulfanyl)-7-methyl-5-(morpholin-4-yl)-[1,3] selenazolo[5,4-d]pyrimidine (4c)*:**

Yield = 89%; yellow powder; M.p. = 122°C–124°C, IR (KBr disc): ν 2878, 2761, 2733, 2712, 1696, 1659, 1620, 1556, 1532, 1477, 1389, 1323, 1233, 1212, 1140, 1116, 1012 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 0.96 (t, *J* = 6.7 Hz, 3H, CH_3), 1.67–1.79 (m, 2H, CH_2), 2.27 (s, 3H, CH_3-pyrimidine), 3.16–3.25 (m, 2H, CH_2-S), 3.66–3.78 (m, 8H, morpholine), ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.3 ($\underline{C}H_3$), 19.4 ($\underline{C}H_2$), 22.7 ($\underline{C}H_3$-pyrimidine), 35.2 ($\underline{C}H_2$-S), 47.7 ($\underline{C}H_2$-N-morpholine), 66.6 ($\underline{C}H_2$-O-morpholine), 128.1, 137.0, 148.2, 151.5, 156.5, MS (*m/z*) = 358 (M^+). Anal. Calcd. for $C_{13}H_{18}ON_4SSe$: C, 43.70; H, 5.08; N, 15.68; S, 8.97; Found: C, 43.17; H, 5.01; N, 15.10; S, 8.43%.

***2-(Butylsulfanyl)-7-methyl-5-(morpholin-4-yl)-[1,3] selenazolo[5,4-d]pyrimidine (4d)*:**

Yield = 77%; yellow powder; M.p. = 132°C–134°C, IR (KBr disc): ν 2889, 2797, 2764, 2734, 1687, 1679, 1640, 1532, 1534, 1426, 1376, 1334, 1246, 1231, 1203, 1196, 1045 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 0.82 (t, *J* = 6.4 Hz, 3H, CH_3), 1.47–1.67 (m, 2H, CH_2-CH_3), 1.78–1.88 (m, 2H, CH_2-CH_2), 2.72 (S, 3H, CH_3-pyrimidine), 3.32 (t, *J* = 5.7 Hz, 2H, CH_2-S), 3.78–3.88 (m, 8H, morpholine), ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.6 ($\underline{C}H_3$), 21.1 ($\underline{C}H_2$), 21.7 ($\underline{C}H_2$), 27.7 (CH_3-pyrimidine), 28.1 (CH_2-S), 44.8 ($\underline{C}H_2$-N-morpholine), 66.8 ($\underline{C}H_2$-O-morpholine) 137.7, 158.1, 159.3, 159.7, 167.7, MS (*m/z*) = 371 (M^+). Anal. Calcd. for $C_{14}H_{20}ON_4SSe$: C, 45.28; H, 5.43; N, 15.09; S, 8.63; Found: C, 45.12; H, 5.18; N, 15.00; S, 8.11%.

***2-Allylthio-7-methyl-5-(morpholin-4-yl)-[1,3] selenazolo[5,4-d]pyrimidine (4e)*:**

Yield = 82%; yellow powder; M.p. = 118°C–120°C, IR (KBr disc): ν 3143, 1303, 2889, 2797, 2764, 2734, 1687, 1679, 1640, 1532, 1534, 1426, 1376, 1334, 1246, 1231, 1203, 1196, 1045 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 2.20 (s, 3H, $C\underline{H}_3$-pyrimidine), 2.70–2.77 (m, 2H, $C\underline{H}_2$-S), 3.80–3.97 (m, 8H, morpholine), 5.28–5.44 (CH_2), 5.98–6.09 (m, 1H, $C\underline{H}$-CH_2 prop-2-en), ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.1 ($\underline{C}H_3$-pyrimidine), 31.3 ($\underline{C}H_2$-S), 44.8 ($\underline{C}H_2$-N-morpholine), 66.8 ($\underline{C}H_2$-O-morpholine), 118.1, 131.1, 132.1, 148, 156, 160, 165, MS (*m/z*) = 371 (M^+). Anal. Calcd. For $C_{13}H_{16}ON_4SSe$: C, 43.94; H, 4.54; N, 15.77; S, 9.02; Found: C, 43.71; H, 4.23; N, 15.34; S, 8.97%.

***2-Benzylsulfanyl-7-methyl-5-(morpholin-4-yl)-[1,3] selenazolo[5,4-d]pyrimidine (4f)*:**

Yield = 86%; M.p. = 150°C–152°C, IR (KBr disc): ν 3098, 3021, 2899, 2779, 2734, 2721, 1689, 1646, 1622, 1542, 1534, 1456, 1366, 1344, 1286, 1245, 1233, 1176, 1095 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 3.02 (s, 3H, $C\underline{H}_3$-pyrimidine), 3.16 (s, 8H, morpholine), 4.54 (s, 2H, $C\underline{H}_2$-S), 7.18–8.00 (m, 5H, hydrogens of benzyl ring), ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.9 ($\underline{C}H_3$),37.3($\underline{C}H_2$-S), 44.8 ($\underline{C}H_2$-N-morpholine), 66.8 ($\underline{C}H_2$-O-morpholine), 128.0, 128.1, 128.8, 129.2, 135.5, 142.8, 154.1, 161.1, 167.5, 168.1, MS (*m/z*) = 322 (M^+). Anal. Calcd. for $C_{17}H_{18}ON_4SSe$: C, 43.94; H, 4.54; N, 15.77; S, 9.02; Found: C, 43.78; H, 4.22; N, 15.57; S, 9.08%.

***2-((7-Methyl-5-morpholino-[1,3]selenazolo[5,4-d] pyrimidin-2-yl)thio)acetonitrile (4g)*:**

Yield = 89%; yellow powder; M.p. = 187°C–189°C, IR (KBr disc): ν 2879, 2789, 2764, 2741, 2250, 1689, 1646, 1632, 1576, 1554, 1476, 1346, 1344, 1286, 1176, 1095 cm–1, ^1H NMR (300 MHz, $CDCl_3$): δ 2.82 (CH_3-pyrimidine), 3.53 (s, 8H, morpholine), 4.50 ($\underline{C}H_2$-S), ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.3 ($\underline{C}H_3$), 23.3($\underline{C}H_2$-S), 47.7 ($\underline{C}H_2$-N-morpholine), 66.6 ($\underline{C}H_2$-O-morpholine), 111.2, 128.1, 137.1, 151.5, 158.0, 159.2, 159.1, MS (*m/z*) = 354 (M^+). Anal. Calcd. for $C_{12}H_{13}ON_5SSe$: C, 40.68; H, 3.70; N, 19.77; S, 9.05; Found: C, 40.31; H, 3.8; N, 19.45; S, 8.98.

***1-((7-Methyl-5-morpholino-[1,3]selenazolo[5,4-d] pyrimidin-2-yl)thio)propan-2-one (4h)*:**

Yield = 79%; yellow powder; M.p. = 137°C–139°C, IR (KBr disc): ν, 2879, 2756, 2732, 2712, 1789, 1600, 1622, 1542, 1554, 1435, 1388, 1374, 1236, 1225, 1213, 1176, 1095 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 2.85 (s, 3H, CH_3-pyrimidine), 3.70 (s, 3H, CH_3), 3.80–3.99 (m, 8H, morpholine), 4.11 (s, 2H, CH_2-S), ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.6 ($\underline{C}H_3$), 34.7 ($\underline{C}H_3$), 45.0 ($\underline{C}H_2$), 47.7 ($\underline{C}H_2$-N-morpholine), 66.8 ($\underline{C}H_2$-O-morpholine), 127.7, 136.5, 147.9, 159.1, 168.1, 200.1, MS (*m/z*) = 371 (M^+). Anal. Calcd. for $C_{13}H_{16}ON_4SSe$: C, 42.05; H, 4.34; N, 15.09; S, 8.63; Found: C, 42.65; H, 4.21; N, 15.37; S, 8.55%.

***Ethyl 2-((7-methyl-5-morpholino-[1,3]selenazolo[5,4-d] pyrimidin-2-yl)thio)acetate (4i)*:**

Yield = 83%; yellow powder; M.p. = 168°C–170°C, IR (KBr disc): ν 2865, 2827, 2762, 2732, 1739, 1690, 1632, 1522, 1514, 1485, 1398, 1354, 1236, 1265, 1233, 1196, 1095 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.38–1.41 (m, CH_3), 2.85 (s, 3H, CH_3-pyrimidine), 3.79–3.85 (m, 8H, morpholine), 4.14 (s, 2H, CH_2-S), 4.41–4.48 (m, 2H, CH_2-O), ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1 ($\underline{C}H_3$), 20.5

(CH_3-pyrimidine), 34.7 ($\underline{C}H_2$-S), 45.0 ($\underline{C}H_2$-N-morpholine), 62.0 ($\underline{C}H_2$-O), 66.8 ($\underline{C}H_2$-O-morpholine), 127.7, 136.5, 156.5, 159.1, 168.1, 200.1, MS (m/z) = 401 (M^+). Anal. Calcd. For $C_{13}H_{16}ON_4SSe$: C, 40.31; H, 4.16; N, 14.47; S, 8.28; Found: C, 40.20; H, 4.30; N, 14.09; S, 8.10%.

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Data Availability Statement

The data that supports the findings of this study are available in the Supporting Information of this article.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Data S1.** Supporting Information.