Received: 6 November 2022 | Revised: 17 February 2023 | Accepted: 22 March 2023

DOI: 10.1002/jhet.4650

ARTICLE

JOURNAL OF HETEROCYCLIC CHEMISTRY WILEY

Synthesis of new derivatives of Alkylselanyl[1,2,4]triazolo [4,3-*a*]pyrimidine as selenium-containing heterocyclic system

Zinat Darapour | **Ali Shiri**

Department of Chemistry, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran

Correspondence
Ali Shiri, Department of Chemistry, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran.
Email: alishiri@um.ac.ir

Funding information
Research Council of Ferdowsi University of Mashhad, Grant/Award Number: 3/55843

Abstract

We report a facile method to synthesize novel alkyl selanyl[1,2,4]triazolo [4,3-*a*]pyrimidine heterocyclic scaffolds. A diverse library of selenide derivatives has been prepared via the treatment of 5-bromo-2,4-dichloro-6-methylpyrimidine with potassium selenocyanate as the source of selenium. The selenocyanate anion as the nucleophile is applied to produce 5-bromo-2-chloro-4-methyl-6-selenocyanatopyrimidine (**2**). The interaction of compound (**2**) with various alkyl halides afforded alkyl selanyl pyrimidine (**3a–e**). Then, the treatment of alkyl selanyl pyrimidine (**3a–e**) with hydrazine hydrate gave the corresponding derivatives (**4a–e**) which react with various orthoesters to prepare the relative alkyl selanyl[1,2,4]triazolo[4,3-*a*]pyrimidine (**5a–o**) in good to excellent yields. The chemical structures of the whole products have been evaluated by spectroscopic analyses.

1 | INTRODUCTION

The element Selenium (Se) is an urgent trace mineral nutrient with multiple functional roles in human health [1]. The organic compounds incorporated with selenium have been widely considered because of their significant biological activities. The selenium is present in the form of selenoprotein in glutathione peroxides (GPx) and thioredoxin reductase (TrxR) which are used for cellular protection against peroxides [2, 3]. Selenium-containing heterocyclic compounds can mimic the similar function of the antioxidant activities and play an important role in regulating reactive oxygen species [4]. The selenium heterocyclic compounds have also been applied as an anti-inflammatory [5], antioxidant [6, 7], antibacterial, antiviral activities [8] as well as strengthen the security system, and treatment of diabetes (selenazine derivative ALT2017) [9]. Anti-cancer activity of organoselanyl-triazoles has also been evaluated [10]. Other biological activity assay on ebselen as an organoselenium compound is its potent M^{pro} inhibitor against SARS-CoV-2 in the covid-19 pandemic [11, 12]. The organoselenium compounds have been used as building blocks in semiconductors [13], fluorescent probes [14], and photochemical oxidations [15]. Organic selenides have also been extensively used in catalyst developments [16]. Some bioactive selenium-containing heterocyclic compounds have anti-herpetic activity (I) [17], Seleno-acyclovir (anti-HSV) (II) [18], potent anticancer properties along with *anti-Covid-19* (III) [19], antibacterial (IV) [20], antiviral (V) [21], and anticancer (VI) [22] agents. (Figure 1).

Some developing routes have been reported for synthesizing selenium heterocyclic compounds using ultrasound irradiation [23, 24], electrochemical cells [25], visible light [24], and photocatalyst [26]. The most well-known methods for C−Se bond formation are catalyzed by Cu [27] and Fe [28]. Aryl-selenides were synthesized using potassium selenocyanate, an iodonium reagent, alkyl, or glycosyl halide in the presence of sodium borohydride [29]. 1,3-Thiaselenol-2-yl-methyl selenides with bioactive properties were also reported by potassium selenocyanate via two rearrangement reactions [30, 31]. A

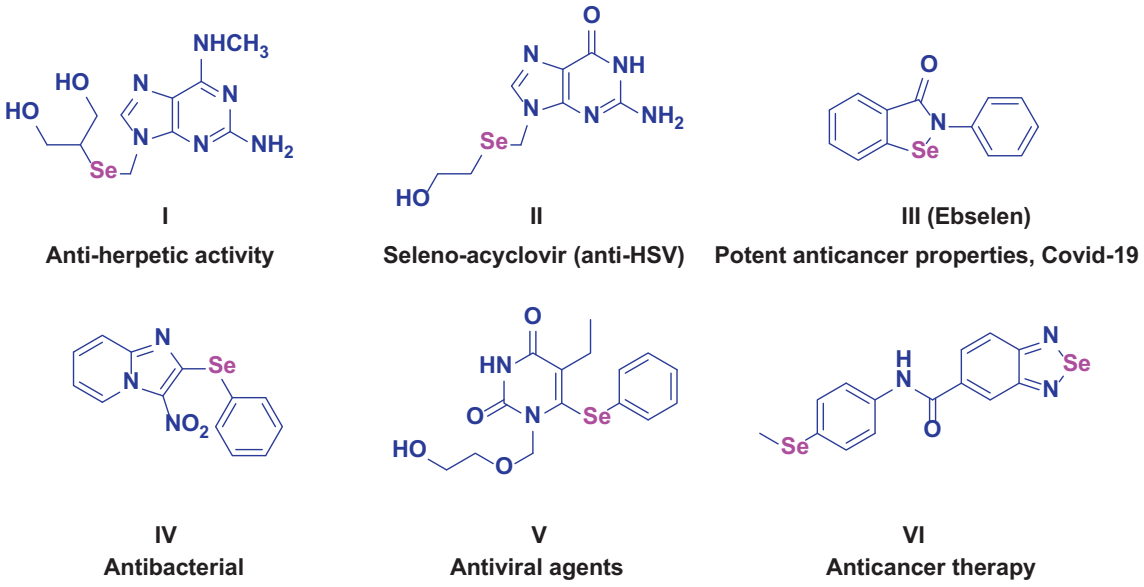


FIGURE 1 Some selenium-containing heterocyclic compounds with bioactive properties.

multicomponent reaction for synthesizing 2-amino-1,-3-selenazoles had investigated under metal-free conditions [32]. The synthesis of other organoselenium compounds including diselenides [9], heterocyclic selenides [33], selenophenes [34], and isoselenocyanates [35] have also been reported.

Pyrimidines are another important building blocks in nucleic acids and their similar analogs can be helpful for biological activity [36]. Among them, [1,2,4]triazolo [4,3-*a*]pyrimidines scaffolds are fascinating precursors for inflammatory [37], anti-proliferative activities [38], human osteosarcoma bone (MG-63) [38] and breast (MCF-7) [39] cancers.

As derivatives of [1,2,4]triazolo[4,3-*a*]pyrimidine incorporating selenium has not been synthesized and studied, it is anticipated that these compounds are good candidates for biological activities. Therefore, in continuation of our previous studies, selenopheno[2,3-e][1,2,4] triazolo[1,5-c]pyrimidine derivatives [40], [1,3]selenazolo [5,4-e][1,2,4]triazolo[1,5-c]pyrimidine [41, 42], and pyrido[1,2-e]purine [43], herein, we report the synthesis of organoselenides with metal-free procedure comprising of the alkylation of selenium anions.

2 | RESULTS AND DISCUSSION

As selenocyanates [44] are essential precursors for the synthesis of noteworthy organoselenides, diselenides and applied both as electrophilic or nucleophilic sources in organic reactions, initially, potassium selenocyanate (KSeCN) was freshly prepared through the treatment of potassium cyanide with selenium powder in ethanol under reflux conditions to afford potassium selenocyanate. Then, the precursor 5-bromo-2-chloro-4-methyl-6-selenocyanatopyrimidine (**2**) is acquired via nucleophi lic replacement of the 4-Cl atom of 5-bromo-2,4-dichloro-6-methyl-pyrimidine (**1**) with KSeCN as a nucleophilic donor in CH_3CN [30, 45, 46]. (Scheme 1) The IR spectrum of compound (**2**) illustrates a peak around $\nu = 2169\,cm^{-1}$ due to the CN group. 5-Bromo-2-chloro-4-methyl-6-selenocyanatopyrimidine (**2**) is a precursor for the preparation of Se-R derivatives (**3a**–**e**).

5-Bromo-2-chloro-6-methylpyrimidine-4-selenolate is produced through the reduction reaction of selenocyanatopyrimidine (**2**) with sodium borohydride at the temperature of 0–5°C in methanol, followed by the nucleophilic substitution reaction with various alkyl halides for 30 min [47–49]. The corresponding heterocyclic alkyl selenides (**3a**–**e**) were prepared in 86%–90% yields. The ^{1}H NMR spectrum of compound (**3a**) appeared the presence of new methyl protons resonated at 2.57 ppm along with the δ 2.48 ppm which is attributed to the methyl protons of the pyrimidine ring and Se-Me, respectively. The ^{13}C NMR spectrum of compound (**3a**) showed the new signal of the methyl group (Se-CH_3) at δ 24.2 ppm while another methyl group (CH_3-pyrimidine) was revealed at δ 8.4 ppm. The unsaturated carbons with four resolved signals were observed at δ 120.8, 158.0, 165.5, and 172.4 ppm. The molecular ion peak of compound (**3a**) emerged at $m/z = 300$. The infrared spectra of alkyl selenides (**3a**–**e**) illustrate a peak around $\nu = 2922$–$3086\,cm^{-1}$, corresponding to the C-H stretching bands of the alkyl group.

SCHEME 1 The schematic preparation of derivatives (**3a–e**).

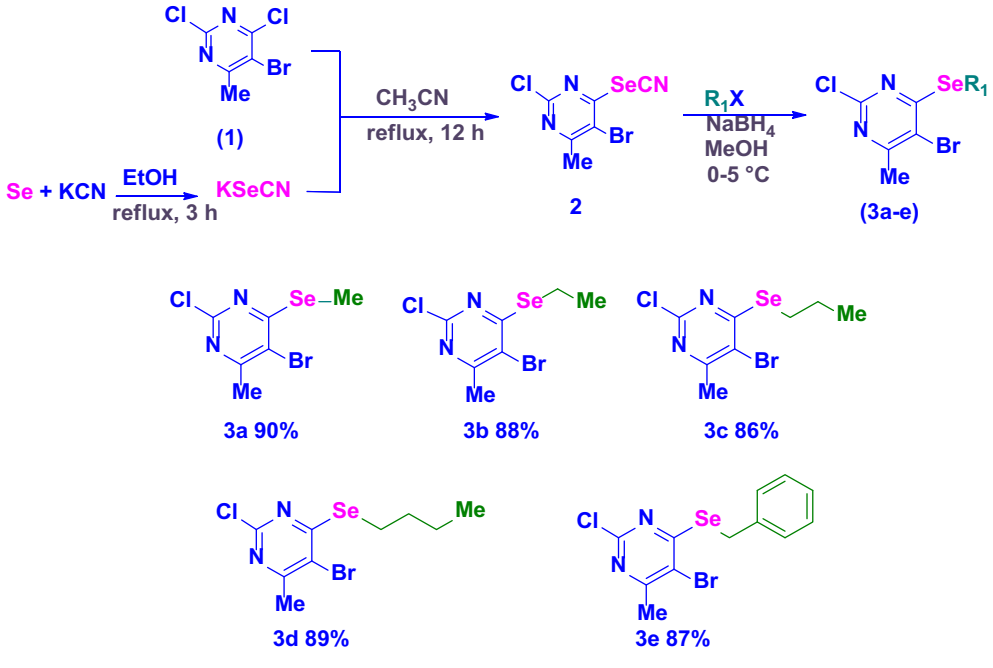
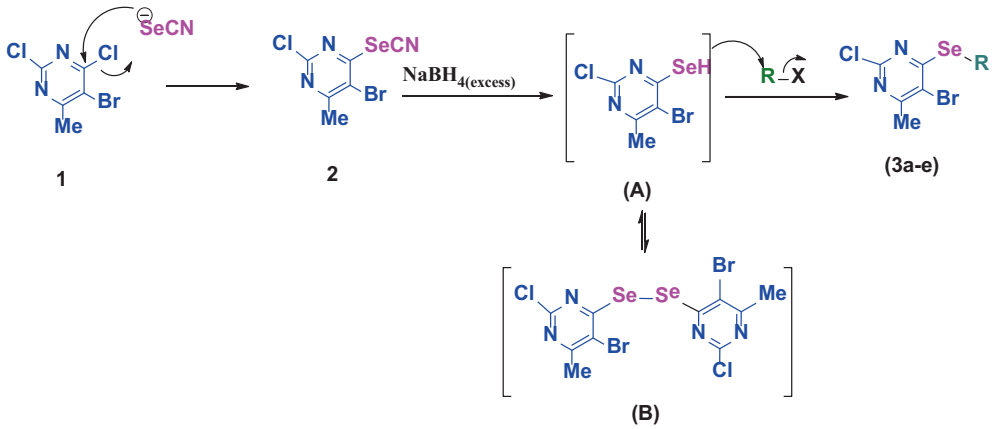
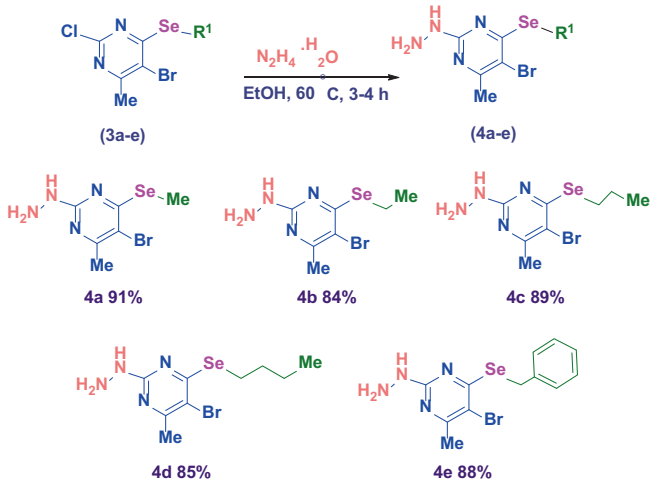


FIGURE 2 The proposed mechanism of compounds (**3a–e**).



Based on the previous studies [50–52], a plausible mechanism can be proposed. (Figure 2) The construction of a $C_{(sp2)}$—Se bond via the substitution nucleophilic intramolecular aromatic reaction (S_NAr) of 5-bromo-2,4-dichloro-6-methyl-pyrimidine (**1**) with KSeCN. KSeCN is used as both selenium and a nucleophile source. In the nucleophilic substitution reaction, the 4-Cl of compound (**1**) is substituted by a selenocyanate anion as nucleophile to acquire 5-bromo-2-chloro-4-methyl-6-selenocyanatopyrimidine product. In the next step, compound (**2**) is reduced with sodium borohydride (1 eq) to furnish the intermediate 5-bromo-2-chloro-6-methyl-pyrimidine-4-selenolate (**A**). This intermediate can be converted to 1,2-bis(5-bromo-2-chloro-6-methylpyrimidin-4-yl)diselane (**B**). Because the selenolate (**A**) is almost certainly the active nucleophile [53], the resulting 5-bromo-2-chloro-6-methylpyrimidine-4-selenolate anion as the nucleophile is subsequently treated with alkyl halides to afford the corresponding selenides (**3a–e**).

Subsequently, various derivatives of alkyl selanyl hydrazinylpyrimidine (**4a-e**) were obtained by reacting compounds (**3a-e**) with hydrazine hydrate under reflux conditions in EtOH. (Scheme 2). The ^{1}H NMR spectrum of compound (**4b**) as an example showed the presence of ethyl protons of the $SeCH_2CH_3$ group, triplet signal at δ 1.55 ppm ($J = 7.4$ Hz) for methyl and CH_2 protons resonated at δ 3.25 ppm ($J = 7.4$ Hz) as a quartet signal. A singlet signal at δ 2.48 ppm was attributed to the CH_3 on the heterocyclic pyrimidine ring. New signals at δ 9.66 and 3.36 ppm (D_2O exchangeable) also revealed the presence of new NH and NH_2 groups, respectively. The ^{13}C NMR of (**4b**) showed ethyl and methyl carbons at δ 15.7, 17.8, and 21.2 ppm in addition to other four aromatic carbons at δ 109.9, 158.3, 163.8, and 168.0 ppm. The IR also



SCHEME 2 The schematic preparation of derivatives (**4a**–**e**).

illustrated the presence of N-H stretch bonds at $\nu = 3297$ and 3257 cm^{-1}. In the mass spectrum, the molecular ion peak at *m/z* 310 has also emerged for compound (**4b**).

Subsequently, the reaction of compound (**4a**–**e**) with different orthoesters in refluxing acetonitrile as the solvent afforded the corresponding different derivatives of alkyl selanyl-[1,2,4]triazolo[4,3-*a*]pyrimidine (**5a**–**o**) in 76%–90% yields (Scheme 3).

The ^{1}H NMR spectrum of compound (**5b**) showed the absence of NH and NH_2 groups and the new singlet signal at δ 9.30 ppm which was identified for the hydrogen of the five-membered heterocyclic triazole ring. The signals of protons of the methyl and the methylene of the $SeCH_2CH_3$ group of compound (**5b**) on the heterocyclic pyrimidine ring were shown at δ 1.52 and 3.22 ppm, respectively. A singlet signal at δ 2.79 ppm was observed corresponding to the directly bonded methyl of the pyrimidine ring. The evidence in the ^{13}C NMR spectrum reveals three signals at δ 15.1, 18.8, and 22.7 ppm for methyl of the pyrimidine ring and ethyl of $SeCH_2CH_3$, respectively. It also confirmed the presence of a new signal at 135.0 ppm along with the presence of other unsaturated carbons at δ 108.9, 141.5, 152.3, and 165.6 ppm. The Infrared spectra also illustrated the omitting of the stretching vibration bands of NH and NH_2 in the products (**5a**–**o**).

Moreover, the regiochemistry of the cyclization reaction with triethylorthoesters has been investigated by 2D nuclear Overhauser effect spectroscopy (NOESY) on compound (**5g**). The obtained results in the NOESY spectrum of (**5g**) indicated an interaction between the protons of the CH_3 group on the pyrimidine ring ($\delta = 2.84$ ppm) and the protons of the CH_3 group of the triazole ring at ($\delta = 2.95$ ppm) and confirmed that the depicted regioisomers for (**5a-o**) are correct. (Figure 3).

3 | CONCLUSION

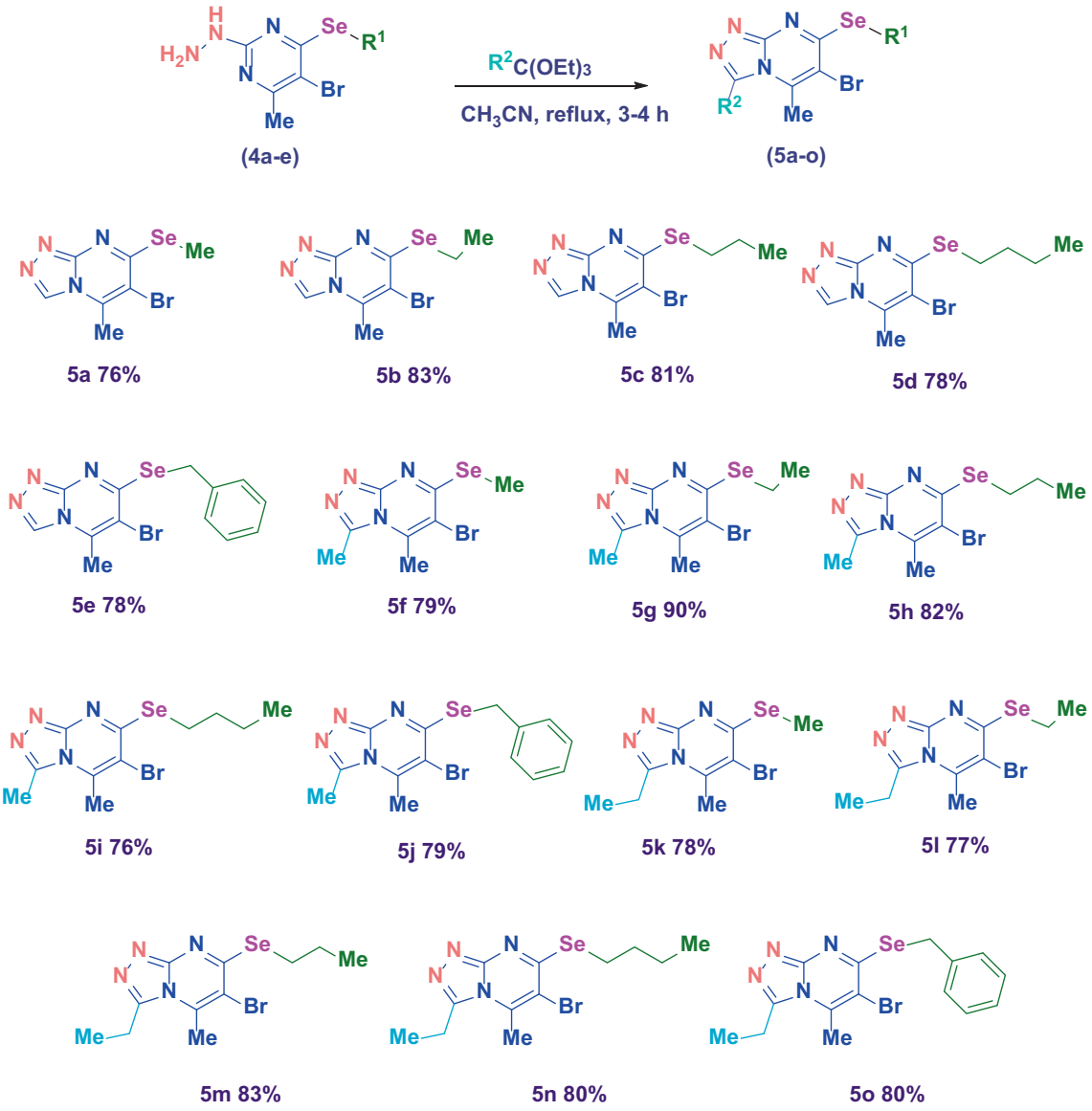
In summary, the reaction between 5-bromo-2, 4-dichloro-6-methyl-pyrimidine and potassium selenocyanate was carried out. Alkylation with different alkyl halides, followed by treatment with hydrazine hydrate and triortoesters, afforded the desired products in good yields. The advantages of alkylselenyl [1,2,4]triazolo[4,3-a]pyrimidine derivatives are metal-free conditions, free of any ligands system, air atmosphere, and easy preparation. The new derivatives of a novel selenium-containing fused heterocyclic system are expected to exhibit biological activities. Organoselenides act as nucleophiles and are used as catalysts. Other future scope of organoselenides can be used in cross-coupling reactions and Se nanoparticles. There is no limit to the preparation of these compounds; the only limitation of this study is the toxicity of selenocyanate and its decomposition with prolonged exposure to air.

4 | EXPERIMENTAL

The melting points were registered using an electrothermal-type 9200 melting point instrument. The IR spectra were registered using an Avatar 370 FT-IR Thermo Nicolet device and only the outstanding absorptions were listed. The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were registered with a Bruker Avance DRX-300 Fourier transform spectrometer. Chemical shifts were reported in parts per million downfield using tetramethylsilane (TMS) as an internal standard. The mass spectra ran using a Varian Mat CH-7 device at 70 eV. TLC using pre-coated aluminum sheets (silica gel 60 F_{254} 0.2 mm thickness), visualized by UV fluorescence light at 254 nm with an appropriate mixture of hexane and ethyl acetate.

4.1 | 5-Bromo-2-chloro-4-methyl-6-selenocyanatopyrimidine (2)

5-Bromo-2,4-dichloro-6-methylpyrimidine (2.42 g, 10 mmol), and a freshly prepared KSeCN (1.78 g, 10 mmol) in dry acetonitrile (10 mL) were allowed to stir at room temperature for 10 min, then and the mixture was heated under reflux for 24 h. The reaction was monitored using TLC n-hexane: ethyl acetate (10:3) as eluent. On completion of the reaction, the mixture was diluted with ethyl acetate. The filtrate was extracted with ethyl acetate (10 mL) and then washed with brine (10 mL). The combined organic extracts were separated and dried over anhydrous sodium sulfate, and the crude product was purified by recrystallization in n-hexane: ethyl acetate. Pale red solid, 2.48 mg, 79% yield; mp 192–194°C; ^{1}H



SCHEME 3 The schematic preparation of derivatives (**5a–o**).

NMR (300 MHz, $CDCl_3$): δ = 2.69 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.3, 164.6, 159.2, 118.3, 98.4, 24.2; IR(KBr): υ 3423, 2922, 2169, 1521, 1492, 1277, 1219, 794 cm^{-1}; MS (EI,70 eV): *m/z* = 311 (M^+), 203 (M^+- SeCN). Anal. calcd. for $C_6H_3BrClN_2Se$ (%): C, 23.14; H, 0.97; N, 13.49. Found: C, 23.65; H, 0.90; N, 14.09.

4.2 | General procedure for the preparation of (3a–e)

The crude 5-bromo-2-chloro-4-methyl-6-selenocyanato-pyrimidine (**2**) (310 mg, 1 mmol) was dissolved in methanol (5 mL). The stirred solution cooled to 0°C then an excess of sodium borohydride (100 mg) was added. About 2.8 mmol alkyl halides (methyl, ethyl, propyl, butyl, benzyl) were added to the reaction mixture after stirring for 20 min. The mixture was stirred for 30 min at room temperature until the reaction was complete and a saturated sodium bicarbonate solution was added. The reaction mixture was extracted three times with ethyl acetate and water. The organic phase was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The spectral data for the prepared products are listed below.

4.2.1 | 5-Bromo-2-chloro-4-methyl-6-(methylselanyl)pyrimidine (**3a**)

Colorless oil, 27 mg, 90% yield; ^1H NMR (300 MHz, $CDCl_3$): δ = 2.57 (s, 3H, CH_3), 2.48 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.4, 165.5, 158.0, 120.8,

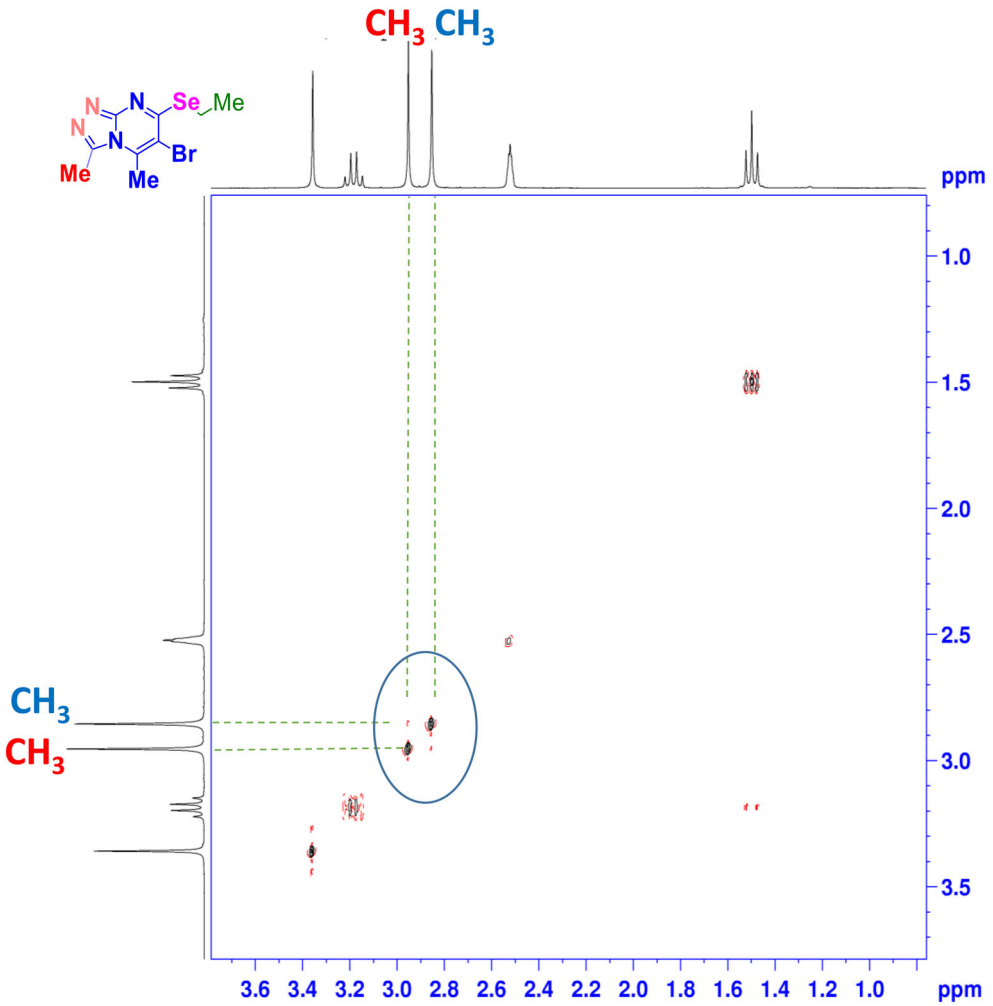


FIGURE 3 The NOESY spectrum of compound (**5g**).

24.2, 8.4; IR (KBr): υ 2937, 1529, 1489, 1270, 1218, 805, 747 cm^{-1}; MS (EI, 70 eV): $m/z = 300$ (M^+), 220 (M^+-Br); Anal. calcd. for $C_6H_6BrClN_2Se$ (%): C, 23.99; H, 2.01; N, 9.32. Found: C, 23.75; H, 1.98; N, 9.1.

4.2.2 | 5-Bromo-2-chloro-4-(ethylselanyl)-6-methylpyrimidine (**3b**)

Colorless oil, 27 mg, 88% yield; ^1H NMR (300 MHz, $CDCl_3$): δ = 3.22 (q, $J = 7.4$ Hz, 2H, CH_2), 2.59 (s, 3H, CH_3), 1.56 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.6, 165.7, 158.0, 120.8, 24.3, 22.3, 14.6; MS (EI, 70 eV): $m/z = 314$ (M^+), 284 (M^+-C_2H_5), 234 (M^+-Br), 205 (M^+-$SeCH_3$); Anal. calcd. for $C_7H_8BrClN_2Se$ (%): C 26.74, H 2.56, N, 8.91. Found: C, 26.51; H, 2.50; N, 8.67.

4.2.3 | 5-Bromo-2-chloro-4-methyl-6-(propylselanyl)pyrimidine (**3c**)

Colorless oil, 328 mg, 86% yield; ^1H NMR (300 MHz, $CDCl_3$): δ = 3.21 (t, $J = 7.2$ Hz, 2H, CH_2), 2.58 (s, 3H, CH_3), 1.91–1.79 (m, 2H, CH_2), 1.08 (t, $J = 7.3$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.6, 165.5, 157.3, 120.9, 30.5, 24.3, 22.7, 14.4; IR (KBr): υ 2868, 2962, 1622 cm^{-1}; MS (EI, 70 eV): $m/z = 328(M^+)$; Anal. calcd. for $C_8H_{10}BrClN_2Se$ (%): C, 29.25; H, 3.07; N, 8.53. Found: C, 29.01; H, 2.96; N, 8.32.

4.2.4 | 5-Bromo-4-(butylselanyl)-2-chloro-6-methylpyrimidine (**3d**)

Colorless oil, 340 mg, 89% yield; ^1H NMR (300 MHz, $CDCl_3$): δ = 3.21 (t, $J = 7.4$ Hz, 2H, CH_2), 2.55 (s, 3H, CH_3), 1.86–1.76 (m, 2H, CH_2), 1.57–145 (m, 2H, CH_2), 1.00 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5, 155.8, 142.0, 109.8, 31.6, 22.6, 22.2, 19.5, 13.4; IR (KBr): υ 2951, 2866, 1534, 1283, 706 cm^{-1}; MS (EI, 70 eV): $m/z = 342(M^+)$; Anal. calcd. for $C_9H_{12}BrClN_2Se$ (%): C, 31.56; H,3.5; N, 8.18. Found: C, 31.38; H, 2.4; N, 8.32.

4.2.5 | 4-(Benzylselanyl)-5-bromo-2-chloro-6-methylpyrimidine (**3e**)

Colorless oil, 327 mg, 87% yield; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.13 (m, $5H_{aromatic}$, H_{phenyl}), 4.36 (s,

2H, CH_2), 2.47 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.4, 165.9, 157.9, 137.4, 129.4, 128.6, 127.3, 120.3, 31.9, 24.3; IR (KBr): υ 3027, 2847, 1524, 1231, 696 cm^{-1}; MS (EI, 70 eV): $m/z = 376$ (M^+), 294 (M^+-Br); Anal. calcd. for $C_{12}H_{10}BrClN_2Se$ (%): C, 38.28; H, 2.68; N, 7.44. Found: C, 38.1; H, 2.56; N, 7.28.

4.3 | General procedure for the preparation of (4a–e)

To a solution of (**3a**–**e**) (1 mmol) in ethanol (5 mL), hydrazine hydrate (3 mmol) was added. Then the mixture was heated under reflux conditions for 3 h. The advancement of the reaction was monitored by TLC using methanol: chloroform (28:1) as eluent. On completing the reaction, the solvent was evaporated. Consequently, the precipitated pale yellow solid was filtered, washed with water (2 × 10 mL) and cold ethanol (2 × 5 mL). The residue was recrystallized in ethanol to obtain the desired products.

4.3.1 | 5-Bromo-2-hydrazinyl-4-methyl-6-(methylselanyl)pyrimidine (**4a**)

Pale yellow solid, 269 mg, 91% yield; mp 169–170°C; ^1H NMR (300 MHz, DMSO-d_6): δ = 8.35 (s, 1H, NH), 4.27 (s, 2H, NH_2), 2.39 (s, 3H, CH_3), 2.34 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 167.6, 163.4, 162.0, 107.6, 24.4, 7.7; IR (KBr): υ 3279, 3248, 3040, 2558, 1530 cm^{-1}; MS (EI, 70 eV): $m/z = 296$ (M^+), 264 ($M^+-H_3N_2$), 217 (M^+-Br); Anal. calcd. for $C_6H_9BrN_4Se$ (%): C, 24.34; H, 3.06; N, 18.93. Found: C, 24.13; H, 3.01; N, 18.77.

4.3.2 | 5-Bromo-4-(ethylselanyl)-2-hydrazinyl-6-methylpyrimidine (**4b**)

Pale yellow solid, 260 mg, 84% yield; mp 138–140°C; ^1H NMR (300 MHz, DMSO-d_6): δ = 9.66, (s, 1H, NH), 3.36 (s, 2H, NH_2), 3.16 (q, $J = 7.4$ Hz, 2H, CH_2), 2.39 (s, 3H, CH_3), 1.46 (t, $J = 7.4$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 168.0, 163.8, 158.3, 109.9, 24.4, 21.2, 15.7; MS (EI, 70 eV): $m/z = 310$ (M^+), 278 (M^+-H_3N_2); Anal. calcd. for $C_7H_{11}BrN_4Se$ (%): C, 27.12; H, 3.58; N, 18.07. Found: C, 26.83; H 3.37; N, 17.89.

4.3.3 | 5-Bromo-2-hydrazinyl-4-methyl-6-(propylselanyl)pyrimidine (**4c**)

Pale yellow solid, 285 mg, 88% yield; mp 168–170°C; ^1H NMR (300 MHz, DMSO-d_6): δ = 8.35 (s, 1H, NH), 4.25 (s, 2H, NH_2), 3.14 (t, $J = 7.2$ Hz, 2H, CH_2), 2.34 (s, 3H, CH_3), 1.79–172 (m, 2H, CH_2), 0.99 (t, $J = 7.3$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 167.5, 163.5, 161.9, 107.7, 29.3, 24.6, 23.4, 14.8; IR (KBr disc): 3313, 3255, 3211, 3047, 2958, 2925, 1529, 1420, 1281 cm^{-1}; MS (EI, 70 eV): $m/z = 324$ (M^+), 280 ($M^+-C_3H_7$), 245 (M^+−Br); Anal. calcd. for $C_8H_{13}BrN_4Se$ (%): C, 29.65; H, 4.04; N, 17.29. Found: C, 29.36; H, 3.92; N, 17.17.

4.3.4 | 5-Bromo-4-(butylselanyl)-2-hydrazinyl-6-methylpyrimidine (**4d**)

Pale yellow solid, 300 mg, 89% yield; mp 105–107°C; ^1H NMR (300 MHz, DMSO-d_6): δ = 9.69 (s, 1H, NH), 3.18 (t, $J = 7.4$ Hz, 2H, CH_2), 2.38 (s, 3H, CH_3), 1.78–168 (m, 2H, CH_2), 1.48–1.36 (m, 2H, CH_2), 0.92 (t, $J = 7.4$ Hz, 3H, CH_3), NH_2 missing; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 168.0, 163.8, 158.2, 109.9, 32.3, 25.5, 23.0, 17.7, 13.9; IR (KBr): υ 3311, 3265, 2954, 2922, 1534, 1424, 1283 cm^{-1}; MS (EI, 70 eV): $m/z = 338$ (M^+), 308 ($M^+-H_3N_2$), 281 ($M^+-C_4N_9$), 258 (M^+−Br); Anal. calcd. for $C_9H_{15}BrN_4Se$ (%): C, 31.97; H, 4.47; N, 16.57. Found: C, 31.77; H, 4.4; N, 16.33.

4.3.5 | 4-(Benzylselanyl)-5-bromo-2-hydrazinyl-6-methylpyrimidine (**4e**)

Pale yellow solid; 316 mg, 85% yield; mp 105–107°C; ^1H NMR (300 MHz, $CDCl_3$): δ = 9.88 (s, 1H, NH), 7.66–7.16 (m, $5H_{aromatic}$, H_{phenyl}), 4.47 (s, 2H, CH_2), 2.38 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.8, 142.5, 136.2, 129.3, 129.0, 128.8, 128.7, 127.9, 127.5109.5, 34.1, 19.4; MS (EI, 70 eV): $m/z = 372$ (M^+), 290 (M^+−Br); Anal. calcd. For $C_{12}H_{13}BrN_4Se$ (%): C, 38.73; H, 3.52; N, 15.06. Found: C, 38.92; H, 3.47; N 14.91.

4.4 | The general method for preparation of (5a–e)

The appropriate (**4a**–**e**) (1 mmol) was added to the corresponding triethylorthoesters (1 mmol) in acetonitrile (5 mL) as solvent at 70°C for 4 h. Then the reaction mixture monitoring by TLC using methanol: chloroform (28:1) as eluent. After the completion of the reaction, the solvent was evaporated and the residue was recrystallized by ethanol to obtain the desired products.

4.4.1 | 6-Bromo-5-methyl-7-(methylselanyl)-[1,2,4]triazolo[4,3-a]pyrimidine (**5a**)

White solid; 232 mg, 76% yield; mp 208–210°C; ^1H NMR (300 MHz, DMSO-d_6): δ = 9.30 (s, 1H, CH), 2.80 (s, 3H,

CH_3), 2.49 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 165.5, 152.2, 141.4, 135.0, 108.9, 18.8, 9.4; IR (KBr): υ 3079,3020, 2926, 1598,1512, 1180, 1180, 747 cm^{-1}; MS (EI, 70 eV): m/z = 306 (M^+); Anal. calcd. for $C_7H_7BrN_4Se$ (%): C, 27.21; H, 2.31; N, 18.31. Found: C, 27.27; H, 2.22; N, 18.16.

4.4.2 | 6-Bromo-7-(ethylselanyl)-5-methyl-[1,2,4]triazolo[4,3-a]pyrimidine (**5b**)

White solid, 265 mg, 83% yield; mp 198–206°C; ^1H NMR (300 MHz, DMSO-d_6): δ = 9.30 (s, 1H, CH), 3.22 (q, J = 7.4 Hz, 2H, CH_2), 2.79(s, 3H, CH_3), 1.52 (t, J = 7.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 165.6, 152.3, 141.5, 135.0, 108.9, 22.7, 18.8, 15.1; IR (KBr): υ 3086, 3074, 2867, 2922. 1602, 1510, 1182, 729 cm^{-1}; MS (EI, 70 eV): m/z = 320 (M^+), 290 ($M^+-C_2H_5$), 240 (M^+−Br), 211 ($M^+-C_2H_5Se$); Anal. calcd. for $C_8H_9BrN_4Se$ (%): C, 30.02; H, 2.83, N, 17.51. Found: C, 29.76; H, 2.77; N, 17.29.

4.4.3 | 6-Bromo-5-methyl-7-(propylselanyl)-[1,2,4]triazolo[4,3-a]pyrimidine (**5c**)

White solid, 269 mg, 81% yield; mp 194–195°C; ^1H NMR (300 MHz, DMSO-d_6): δ = 9.30 (s, 1H, CH), 3.23 (t, J = 7.2 Hz, 2H, CH_2), 2.79 (s, 3H, CH_3), 1.88–1.76 (m, 2H, CH_3), 1.04 (t, J = 7.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 165.5, 152.2, 141.5, 135.0, 108.9, 30.8, 22.6, 18.8, 14.8; IR (KBr): υ 3092, 2960, 2931, 1599, 1510, 1180, 951, 749 cm^{-1}; MS (EI, 70 eV): m/z 334 (M^+), 290 ($M^+-C_3H_7$), 211 ($M^+-C_3H_7Se$), 255(M^+-Br); Anal. calcd. for $C_9H_{11}BrN_4Se$ (%): C, 32.36; H, 3.32; N, 16.77. Found: C, 32.21; H, 3.23; N, 16.54.

4.4.4 | 6-Bromo-7-(butylselanyl)-5-methyl-[1,2,4]triazolo[4,3-a]pyrimidine (**5d**)

White solid, 271 mg, 78% yield; mp 168–170°C; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.65 (s, 1H, CH), 3.36 (t, J = 7.3 Hz, 2H, CH_2), 2.84 (s, 3H, CH_3), 1.91–1.81 (m, 2H, CH_2), 1.59–1.47 (m, 2H, CH_2), 0.99 (t, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO): δ = 165.6, 152.2, 141.5, 135.1, 108.9, 31.3, 28.5, 23.0, 18.8, 13.9; IR (KBr): υ 3088, 2929, 2870, 1603, 1510, 1181, 750 cm^{-1}; MS (EI, 70 eV): m/z = 348 (M^+), 306 ($M^+-C_3H_7$), 290 ($M^+-C_4H_9$), 211 ($M^+-C_3H_7Se$); Anal. calcd. for $C_{10}H_{13}BrN_4Se$ (%): C, 34.50; H, 3.76; N, 16.09. Found C, 34.69; H, 3.63; N, 16.32.

4.4.5 | 7-(Benzylselanyl)-6-bromo-5-methyl-[1,2,4]triazolo[4,3-a]pyrimidine (**5e**)

White solid, 297 mg, 78% yield; mp 158–162°C; ^1H NMR (300 MHz, DMSO-d_6): δ = 9.33 (s, 1H, CH), 7.50–7.23 (m, $5H_{aromatic}$, H_{phenyl}), 4.53 (s, 2H, CH_2), 2.79 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 165.40, 152.2, 141.9, 138.6, 135.2, 129.6, 128.9, 127.5, 108.3, 31.9, 18.8; IR (KBr): υ 3082, 2926, 1670, 1599, 1511, 1169, 749 cm^{-1}; MS (EI, 70 eV): m/z = 382 (M^+); Anal. calcd. for $C_{13}H_{11}BrN_4Se$ (%): C, 40.86; H, 2.90; N, 14.66. Found C, 41.7; H, 2.95; N, 14.8.

4.4.6 | 6-Bromo-3,5-dimethyl-7-(methylselanyl)-[1,2,4]triazolo[4,3-a]pyrimidine (**5f**)

White solid, 252 mg, 79% yield; mp 155–153°C; ^1H NMR (300 MHz, DMSO-d_6): δ = 2.95 (s, 3H, CH_3), 2.86 (s, 3H, CH_3), 2.46 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.6, 153.4, 143.0, 139.4, 110.6, 18.9, 15.62, 9.6; IR (KBr): υ 3008, 2984, 2927, 1595, 1513, 1201, 731 cm^{-1}; MS (EI, 70 eV): m/z = 320 (M^+), 239 (M^+−Br); Anal. calcd. for $C_8H_9BrN_4Se$ (%): C 30.02, H 2.83, N, 17.51. Found: C, 30.21; H, 2.76; N, 17.41.

4.4.7 | 6-Bromo-7-(ethylselanyl)-3,5-dimethyl-[1,2,4]triazolo[4,3-a]pyrimidine (**5g**)

Pale yellow solid, 300 mg, 90% yield; mp 146–149°C; ^1H NMR (300 MHz, DMSO-d_6): δ = 3.17 (q, 2H, CH_2), 2.95 (s, 3H, CH_3), 2.85 (s, 3H, CH_3), 1.48 (t, J = 7.5 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 165.2, 153.4, 144.3, 142.8, 109.3, 22.8, 19.4, 15.4, 15.1 ppm; IR (KBr): υ 3010, 2973, 2922, 1597, 1514, 1194, 885 cm^{-1}; MS (EI, 70 eV): m/z = 334 (M^+), 303 ($M^+-C_2H_5$), 224 ($M^+-C_2H_5Se$); Anal. calcd. for $C_9H_{11}BrN_4Se$ (%): C, 32.36; H, 3.32; N, 16.77. Found: C, 32.53; H, 3.26; N, 16.62.

4.4.8 | 6-Bromo-3,5-dimethyl-7-(propylselanyl)-[1,2,4]triazolo[4,3-a]pyrimidine (**5h**)

White solid, 285 mg, 82% yield; mp 127–131°C; ^1H NMR (300 MHz, DMSO-d_6): δ = 3.09 (t, J = 7.2 Hz, 2H, CH_2), 2.86 (s, 3H, CH_3), 2.76 (s, 3H, CH_3), 1.75–165 (m, 2H, CH_2), 0.94 (t, J = 7.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz,

DMSO-d_6): δ = 165.1, 153.3, 144.3, 142.8, 109.3, 30.9, 22.7, 19.4, 15.4, 14.9; IR (KBr): υ 3014, 2956, 2924, 2868, 1598, 1480, 1193, 886 cm^{-1}; MS (EI, 70 eV): m/z = 348 (M^+), 304 ($M^+-C_3H_7$), 265 (M^+−Br), 224 ($M^+-C_3H_7Se$); Anal. calcd. for $C_{10}H_{13}BrN_4Se$ (%): C, 34.50; H, 3.76; N, 16.09. Found: C, 34.29; H, 3.71; N, 15.93.

4.4.9 | 6-Bromo-7-(butylselanyl)-3,5-dimethyl-[1,2,4]triazolo[4,3-a]pyrimidine (**5i**)

White solid, 275 mg, 76% yield; mp 116–119°C; ^{1}H NMR (300 MHz, DMSO-d_6): δ =3.20 (t, J = 7.2 Hz, 2H, CH_2), 2.95 (s, 3H, CH_3), 2.85 (s, 3H, CH_3), 1.81–171 (m, 2H, CH_2), 1.51–1.38 (m, 2H, CH_2), 0.96 (t, J = 7.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 165.0, 153.3, 144.2, 142.7, 109.3, 31.3, 28.5, 23.0, 19.3, 15.3, 14.0; IR (KBr): υ 3007, 2956, 2928, 2870, 1599, 1515, 1195, 886 cm^{-1}; MS (EI, 70 eV): m/z = 362 (M^+), 302 ($M^+-C_3H_7$), 280 (M^+−Br), 224 ($M^+-C_4H_9Se$); Anal. calcd. for $C_{11}H_{15}BrN_4Se$ (%): C, 36.48; H, 4.18; N, 15.47. Found: C, 36.19; H, 4.1; N, 15.37.

4.4.10 | 7-(Benzylselanyl)-6-bromo-3,5-dimethyl-[1,2,4]triazolo[4,3-a]pyrimidine (**5j**)

White solid, 312 mg, 79% yield; mp 108–110°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.22 (m, 5$H_{aromatic}$, H_{phenyl}), 4.54 (s, 2H, CH_2), 2.96 (s, 6H, 2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.3, 139.8, 137.1, 129.4, 128.7, 127.3, 110.4, 33.1, 19.1, 15.7; IR (KBr): υ 3318, 3023, 2921, 2246, 2128, 1595, 1481, 1003, 700 cm^{-1}; MS (EI, 70 eV): m/z = 396 (M^+), 314 (M^+−Br); Anal. calcd. for $C_{14}H_{13}BrN_4Se$ (%): C, 42.45; H, 3.31; N, 14.14. Found: C, 42.62; H, 3.25; N, 13.99.

4.4.11 | 6-Bromo-3-ethyl-5-methyl-7-(methylselanyl)-[1,2,4]triazolo[4,3-a]pyrimidine (**5k**)

White solid, 260 mg, 78% yield; mp 106–110°C; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.25 (q, 2H, CH_2), 2.93 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 1.38 (t, J = 7.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 167.8, 163.7, 158.2, 152.3, 109.9, 25.6, 24.3, 17.9, 7.6; IR (KBr): υ 3008, 2984, 2927, 1595, 1513, 1201, 731 cm^{-1}; MS (EI, 70 eV): m/z = 334 (M^+), 318 (M^+-CH_3), 303 ($M^+-C_2H_5$), 238 (M^+-CH_3Se); Anal. calcd. for $C_9H_{11}BrN_4Se$ (%): C, 32.36; H, 3.32; N, 16.77. Found: C, 32.22; H, 3.29; N, 16.55.

4.4.12 | 6-Bromo-3-ethyl-7-(ethylselanyl)-5-methyl-[1,2,4]triazolo[4,3-a]pyrimidine (**5L**)

White solid, 267 mg, 77% yield; mp 169–171°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.28–2.90 (m, 6H, CH_3), 2.99 (s, 3H, CH_3), 1.59–1.40 (m, 4H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.6, 153.4, 147.5, 139.4, 111.1, 23.3, 22.7, 19.1, 14.6, 12.5; IR (KBr): υ 2998, 2976, 2926, 1589, 1589, 1511, 1195, 889. cm^{-1}; MS (EI,70 eV): m/z = 348 (M^+), 318 ($M^+-C_2H_5$), 269 (M^+−Br), 238 ($M^+-C_2H_5Se$); Anal. calcd. for $C_{10}H_{13}BrN_4Se$ (%): C, 34.50; H, 3.76, N, 16.09. Found: C, 34.73; H, 3.7; N, 15.85.

4.4.13 | 6-Bromo-3-ethyl-5-methyl-7-(propylselanyl)-[1,2,4]triazolo[4,3-a]pyrimidine (**5m**)

White crystals, 301 mg, 83% yield; mp 129–131°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.24–3.16 (m, 4H, CH_2), 2.89 (s, 3H, CH_3), 1.82–1.75 (m, 2H, CH_2), 1.45 (t, J = 7.4 Hz, 3H, CH_3), 1.00 (t, J = 7.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 172.9, 164.9, 148.4, 142.8, 109.4, 30.8, 22.6, 22.1, 19.5, 14.8, 12.0; IR (KBr): υ 2977, 2863, 1589, 1196, 734 cm^{-1}; MS (EI, 70 eV): m/z = 362 (M^+), 318 ($M^+-C_3H_7$); Anal. calcd. for $C_{11}H_{15}BrN_4Se$ (%): C, 36.48; H, 4.18; N, 15.47. Found: C, 36.3; H, 4.07; N, 15.61.

4.4.14 | 6-Bromo-7-(butylselanyl)-3-ethyl-5-methyl-[1,2,4]triazolo[4,3-a]pyrimidine (**5n**)

White solid, 300 mg, 80% yield; mp 230–234°C; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.22 (m, 4H, CH_2), 2.93 (s, 3H, CH_3), 1.79–1.70 (m, 2H, CH_2), 1.49–1.40 (m, 2H, CH_2), 1.37 (t, 3H, CH_3), 0.92 (t, J = 7.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 164.9, 153.4, 148.4, 142.7, 109.4, 31.3, 28.5, 23.0, 22.1, 19.5, 14.0, 12.0; IR (KBr): υ 2978, 2945, 2927, 2867, 1591, 1510, 1195, 1510, 1195, 890. cm^{-1}; MS (EI, 70 eV): m/z = 376 (M^+), 318 ($M^+-C_4H_9$); Anal. calcd. for $C_{11}H_{15}BrN_4Se$ (%): C, 38.32; H, 4.56; N, 14.89. Found: C, 38.11; H, 4.51; N, 14.73.

4.4.15 | 7-(Benzylselanyl)-6-bromo-3-ethyl-5-methyl-[1,2,4]triazolo[4,3-a]pyrimidine (**5o**)

White solid, 328 mg, 80% yield; mp 238–240°C; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.48–7.22 (m, 5$H_{aromatic}$, H_{phenyl}), 4.50 (s, 2H, CH_2), 3.27 (q, J = 7.4 Hz, 2H, CH_2), 2.52 (s, 3H, CH_3), 1.40 (t, J = 7.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.8, 148.6, 143.2, 138.7,

129.7, 128.9, 127.5, 108.9, 31.0, 22.1, 19.5, 12.1; MS (EI, 70 eV): $m/z = 410$ (M^+), 318 ($M^+-C_7H_7$); Anal. calcd. for $C_{11}H_{15}BrN_4Se$ (%): C, 43.92; H, 3.69; N, 13.66. Found: C, 43.68; H, 3.59; N, 13.51.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the Research Council of Ferdowsi University of Mashhad for financial support of this project (3/55843).

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

ORCID

Ali Shiri https://orcid.org/0000-0002-5736-6287

REFERENCES

[1] B. Hosnedlova, M. Kepinska, S. Skalickova, C. Fernandez, B. Ruttkay-nedecky, T. D. Malevu, J. Sochor, M. Baron, M. Melcova, J. Zidkova, R. Kizek, *Int. J. Mol. Sci.* **2017**, *18*, 2209.

[2] C. Jacob, G. I. Giles, N. M. Giles, H. Sies, *Angew. Chem. Int. Ed.* **2003**, *42*, 4742.

[3] H. Ungati, V. Govindaraj, M. Narayanan, G. Mugesh, *Angew. Chem. Int. Ed.* **2019**, *58*, 8156.

[4] T. Wirth, *Angew. Chem. Int. Ed.* **2015**, *54*, 10074.

[5] X. He, Y. Nie, M. Zhong, S. Li, X. Li, Y. Guo, Z. Liu, Y. Gao, F. Ding, D. Wen, Y. Zhang, *Eur. J. Med. Chem.* **2021**, *218*, 113384.

[6] M. V. Musalov, V. A. Yakimov, V. A. Potapov, S. V. Amosova, T. N. Borodina, S. V. Zinchenko, *New J. Chem.* **2019**, *43*, 18476.

[7] B. G. Singh, A. Kunwar, *Free Radical Res.* **2021**, *55*, 641.

[8] H. Lee, D. B. Jarhad, J. Yu, C. Lee, L. S. Jeong, *J. Org. Chem.* **2019**, *84*, 14414.

[9] D. Krasowska, N. Iraci, C. Santi, J. Drabowicz, M. Palomba, M. Cieslak, K. Ka, M. Julia, K. Palomba, *Molecules* **2019**, *24*, 2914.

[10] F. H. Cui, J. Chen, Z. Y. Mo, S. X. Su, Y. Y. Chen, X. L. Ma, H. T. Tang, H. S. Wang, Y. M. Pan, Y. L. Xu, *Org. Lett.* **2018**, *20*, 925.

[11] H. Sies, M. J. Parnham, *Free Rad. Biol. Med.* **2020**, *156*, 107.

[12] A. Rakib, Z. Nain, S. A. Sami, S. Mahmud, A. Islam, S. Ahmed, A. B. F. Siddiqui, S. M. O. F. Babu, P. Hossain, A. Shahriar, F. Nainu, T. Bin Emran, J. Simal-Gandara, *Brief. Bioinform.* **2021**, *22*, 1476.

[13] J. B. T. Rocha, C. S. Oliveira, P. A. Nogara, *Organoselenium Compounds in Biology and Medicine: Synthesis, Biological and Therapeutic Treatments*, Royal Society of Chemistry, London **2017**.

[14] S. Panda, A. Panda, S. S. Zade, *Coord. Chem. Rev.* **2015**, *300*, 86.

[15] L. M. Bouchet, J. E. Argüello, *J. Org. Chem.* **2018**, *83*, 5674.

[16] A. Arora, S. Singh, P. Oswal, D. Nautiyal, G. K. Rao, S. Kumar, A. Kumar, *Coord. Chem. Rev.* **2021**, *438*, 213885.

[17] G. Spengler, A. Kincses, T. Mosolygó, M. A. Maræ, M. Nové, M. Gajdács, C. Sanmartín, H. E. McNeil, J. M. A. Blair, E. Domínguez-Álvarez, *Molecules* **2019**, *24*, 4264.

[18] P. K. Sahu, T. Umme, J. Yu, A. Nayak, G. Kim, M. Noh, J. Y. Lee, D. D. Kim, L. S. Jeong, *J. Med. Chem.* **2015**, *58*, 8734.

[19] S. T. D. Thun-Hohenstein, T. F. Suits, T. R. Malla, A. Tumber, L. Brewitz, H. Choudhry, E. Salah, C. J. Schofield, *ChemMedChem* **2021**, *17*, e202100582.

[20] S. Kumar, N. Sharma, I. K. Maurya, A. K. Bhasin, N. Wangoo, P. Brandão, V. Félix, K. K. Bhasin, R. K. Sharma, *Eur. J. Med. Chem.* **2016**, *123*, 916.

[21] E. H. G. Da Cruz, M. A. Silvers, G. A. M. Jardim, J. M. Resende, B. C. Cavalcanti, I. S. Bomfim, C. Pessoa, C. A. De Simone, G. V. Botteselle, A. L. Braga, D. K. Nair, I. N. N. Namboothiri, D. A. Boothman, E. N. Da Silva Júnior, *Eur. J. Med. Chem.* **2016**, *122*, 1.

[22] A. C. Ruberte, D. Plano, I. Encío, C. Aydillo, A. K. Sharma, C. Sanmartín, *Eur. J. Med. Chem.* **2018**, *157*, 14.

[23] D. Armijo, L. Mendoza, K. Vizuete, A. Debut, C. Je, S. A. Dahoumane, *Molecules* **2020**, *25*, 5193.

[24] F. Penteado, T. J. Peglow, M. S. Silva, G. Perin, E. J. Lenardão, *Curr. Opin. Green Sustain. Chem.* **2020**, *26*, 100372.

[25] X. Zhang, C. Wang, H. Jiang, L. Sun, *Chem. Commun.* **2018**, *54*, 8781.

[26] S. Lapcinska, P. Dimitrijevs, L. Lapcinskis, P. Arsenyan, *Adv. Synth. Catal.* **2021**, *363*, 3318.

[27] N. Mukherjee, D. Kundu, B. C. Ranu, *Adv. Synth. Catal.* **2017**, *359*, 329.

[28] S. Guan, Y. Chen, H. Wu, R. Xu, *RSC Adv.* **2020**, *10*, 27058.

[29] Y. Guan, S. D. Townsend, *Org. Lett.* **2017**, *19*, 5252.

[30] Y. Baquedano, V. Alcolea, M. Á. Toro, K. J. Gutiérrez, P. Nguewa, M. Font, E. Moreno, S. Espuelas, A. Jiménez-Ruiz, J. A. Palop, D. Plano, C. Sanmartín, *Antimicrob. Agents Chemother.* **2016**, *60*, 3802.

[31] S. V. Amosova, A. A. Filippov, N. A. Makhaeva, A. I. Albanov, V. A. Potapov, *Beilstein J. Org. Chem.* **2020**, *16*, 515.

[32] H. W. Liu, Y. Fang, S. Y. Wang, S. J. Ji, *J. Org. Chem.* **2020**, *85*, 3508.

[33] D. Kundu, *RSC Adv.* **2021**, *11*, 6682.

[34] P. S. Hellwig, T. J. Peglow, F. Penteado, L. Bagnoli, G. Perin, E. J. Lenardão, *Molecules* **2020**, *25*, 5907.

[35] R. Neri, S. H. Bossmann, *Synthesis* **2021**, *53*, 2015.

[36] K. F. Hellendahl, F. Kaspar, X. Zhou, Z. Yang, Z. Huang, P. Neubauer, A. Kurreck, *ChemBioChem* **2021**, *22*, 2002.

[37] T. Y. Zhang, C. S. Li, P. Li, X. Q. Bai, S. Y. Guo, Y. Jin, S. J. Piao, *Mol. Diversity* **2022**, *26*, 27.

[38] R. Kamal, R. Kumar, V. Kumar, J. K. Bhardwaj, P. Saraf, A. Kumar, K. Pandit, S. Kaur, P. Chetti, S. Beura, *J. Biomol. Struct. Dyn.* **2021**, *39*, 4398.

[39] V. Pogaku, R. Krishnan, S. Basavoju, *Res. Chem. Intermed.* **2021**, *47*, 551.

[40] O. Kohandel, S. Sheikhi-Mohammareh, F. Oroojalian, T. Memariani, J. Mague, A. Shiri, *Mol. Diver.* **2021**, *26*, 1621.

[41] S. Sheikhi-Mohammareh, A. Shiri, E. H. Maleki, M. M. Matin, H. Beyzaei, P. Baranipour, F. Oroojalian, T. Memariani, *ChemistrySelect* **2020**, *5*, 10060.

[42] S. Sheikhi-Mohammareh, A. Shiri, J. Mague, *Mol. Diver.* **2022**, *26*, 923.

[43] P. Moghimi, H. Sabet-Sarvestani, O. Kohandel, A. Shiri, *J. Org. Chem.* **2022**, *87*, 3922.
[44] X. Zhang, X. B. Huang, Y. B. Zhou, M. C. Liu, H. Y. Wu, *Chem. A Eur. J.* **2021**, *27*, 944.
[45] J. Müller, A. Terfort, *Inorganica Chim. Acta* **2006**, *359*, 4821.
[46] T. E. A. Frizon, J. H. Cararo, S. Saba, G. C. Dal-Pont, M. Michels, H. C. Braga, T. Pimentel, F. Dal-Pizzol, S. S. Valvassori, J. Rafique, *Oxid. Med. Cell. Longevity* **2020**, *2020*, 1.
[47] D. Plano, Y. Baquedano, D. Moreno-Mateos, M. Font, A. Jiménez-Ruiz, J. A. Palop, C. Sanmartín, *Eur. J. Med. Chem.* **2011**, *46*, 3315.
[48] B. An, B. Wang, J. Hu, S. Xu, L. Huang, X. Li, A. S. C. Chan, *J. Med. Chem.* **2018**, *61*, 2571.
[49] P. Begines, L. Sevilla-Horrillo, A. Puerta, R. Puckett, S. Bayort, I. Lagunes, I. Maya, J. M. Padrón, Ó. López, J. G. Fernández-Bolaños, *Pharmaceuticals* **2020**, *13*, 1.
[50] Y. Cao, L. Jiang, W. Yi, *Adv. Synth. Catal.* **2019**, *361*, 4360.
[51] A. A. Heredia, A. B. Peñéñory, *RSC Adv.* **2015**, *5*, 105699.
[52] A. Ricardo, M. De Oliveira, L. Piovan, F. Simonelli, M. D. F. C. Santos, M. Belini, M. De Mello, *J. Organomet. Chem.* **2016**, *806*, 54.
[53] H. J. Reich, R. J. Hondal, *ACS Chem. Biol.* **2016**, *11*, 821.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Z. Darapour, A. Shiri, *J. Heterocycl. Chem.* **2023**, 1. https://doi.org/10.1002/jhet.4650